7 EXPERIMENTAL SECTION

7.1 General

All chemicals were purchased from Acros, Aldrich, Fluka, and Lancester and used without further purification. Solvents were purified and dried, if necessary, according to standard methods.[228] The catalyst $Pd(PPh_3)_4$ was synthesized according to literature[229], stored in a glove-box (O_2: < 2.0 ppm, H_2O: < 0.3 ppm), and used without further characterization. For reactions with this catalyst, the solvents, solutions or suspensions were degassed by a repeated cycle of evacuation and flushing with nitrogen. All reactions with moisture sensitive reagents were performed in dried glassware after a repeated cycle of evacuation and heating followed by flushing with nitrogen. All experiments under a protective atmosphere were carried out with nitrogen (purity 4.0 or 5.0) purchased from Linde or Messer Griesheim. The solvents used for column chromatography were destilled prior to use. Lyophilization from water was performed by using deionized, destilled, *'MilliQ'* (Millipore) (0.45 μm) filtered water.

The compounds' names were generated with *AutoNom Vers. 2.1* (Beilstein Institute, 1998). For clarity reasons and because of the missing IUPAC directions for dendrimer nomenclature a simplified term is added in front of each dendrimer's name. For example, in ***(Boc-N)$_3$3D0*** the text in parentheses (here ***Boc-N***) defines the functional endgroup, the subscript number (here ***$_3$***) is number of those groups, the regular sized number (***3***) gives the total number of modifiable endgroups, and finally the letter ***D*** plus a number (here **0**) stands for a dendrimer of the corresponding specific generation.

7.2 Analyses

Melting points:

Melting points were recorded using a Büchi *510* (open capillaries, uncorrected values).

NMR spectroscopy:

NMR spectra were recorded with a Bruker *AB 250 MHz* or Bruker *AC 500 MHz.* The signal of the non-deuterated solvent served as internal standard. If not stated otherwise, measurements were performed at room temperature. The deuterated solvents were purchased from Merck or Deutero GmbH.

EI and FAB mass spectrometry:

Spectra were recorded with a Varian *MAT 771* and *CH6* (EI) or Type *CH5DF* (FAB) spectrometer. Given are the kind of ionization (EI, FAB), the potential of ionization (70 eV or 80 eV), and the temperature of the ion source (EI) or the matrix material (FAB). The high resolution mass spectra were obtained according to the peak match method (*MAT 771)*.

MALDI-TOF mass spectrometry:

Spectra were recorded with a Bruker *Reflex* with delayed extraction source. Given are the recording mode (linear or reflector), the matrix, and the values for the lowest mass isotope of a specific ion (not for the isotope with the highest intensity).

Elemental analysis:

Elemental analysis were performed using a Perkin-Elmer *EA 240*. In most cases a deviation of up to 0.4 % from the calculated carbon value was accepted. Because of the polarity of the prepared compounds it was generally difficult to obtain correct data from elemental analysis. This was specifically so for the deprotected and dansylated dendrimers, and for some of the free carboxylic acids, for which the carbon values obtained differed from the calculated ones by up to 1 %.

Absorption and emission spectroscopy** (in collaboration)**:

Ethanol (spectroscopic grade, Merck) was used as solvent for the spectroscopic measurements. UV-absorption and fluorescence spectra were recorded with a Hitachi *F-4500 Fluorescence Spectrometer*.

7.3 Chromatography

Analytical TLC:

Reactions were monitored by thin layer chromatography (TLC) using TLC silica coated aluminium plates $60F_{254}$ (Merck). Compounds were detected by UV light (254 nm or 366 nm) and/or by treatment with a solution of ninhydrine in ethanol (0,1 %) followed by heating.

Column Chromatography:

Column chromatography was run with Machery-Nagel *'Kieselgel 60 M'* (230-400 mesh) ASTM, grain size 40-60 pm. Usually the crude product was pre-adsorbed onto small amounts of silica gel and thereafter purified by chromatograpy.

RP-HPLC:

Analytical: *(a)* HPLC system consisting of a Knaur *Eurosphere*® column (C_{18}, 5 µm, 4 × 120 mm), a Gynkotek *Mod. 480* pump, and a Gynkotek *UVD 340 S diode array* detector (detection at λ = 220 nm and λ = 254 nm).

(b) HPLC system consisting of a *Jupiter*™ column (C_{18}, 5 µm, 4.6 × 250 mm), a Thermo Separation Products *P4000* pump, and a Thermo Separation Products *UV6000 LP* detector (detection at λ = 220 nm).

(c) HPLC system consisting of a Machery-Nagel *Nucleosil*® column (C_{18}, 5 µm, 4 × 250 mm), a Knaur *HPLC pump 64*, and a Knaur *2501 UV Detector* (detection at λ = 220 nm).

Preparative: *(a)* HPLC system consisting of a Knaur *Eurosphere*® column (C_{18}, 7 µm, 32 × 250 mm), a Gynkotek *Mod. 480* pump, and a Gynkotek *UVD 340 S diode array* detector (detection at λ = 220 nm and λ = 254 nm).

(b) HPLC system consisting of a Vydac *218TP102 'efficiency protein and peptide'* column (C_{18}, 10 µm, 22 × 250 mm), a Thermo Separation Products *P4000* pump, and a Thermo Separation Products *UV1000* detector (detection at λ = 220 nm).

(c) HPLC system consisting of a Machery-Nagel *Nucleosil*® column (C_{18}, 7 µm, 32 × 240 mm), a Knaur *K1800* pump, and a Knaur *2501 UV Detector* (detection at λ = 220 nm and λ = 254 nm).

For analysis and purification of peptide **59** HPLC systems *b* and *c* were used according to the following protocols:

analytical: *(b)* *flow rate:* 1 ml/min; *eluent:* linear gradient of 0-100 % acetonitrile in water (within 30 min);

(c) *flow rate:* 1 ml/min; *eluent:* acetonitrile/water/TFA (49.98:49.97:0.05);

preparative: *(b)* *flow rate:* 15 ml/min; *eluent:* linear gradient of 0-100 % acetonitrile in water (within 30 min);

(c) *flow rate:* 15 ml/min; *eluent:* acetonitrile/water/TFA (49.98:49.97:0.05);

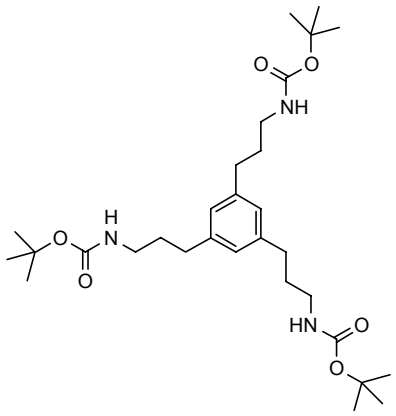
All other compounds were analysed and purified using HPLC system *a*.

7.4 Syntheses

Compounds **2**[230], **3**[231], **10**[184], **13**[232], **14**[166b], **15**[110, 166b], **16**[110], **17**[166a], **18**[166a], **19**[166a], and **37**[192] were prepared according to literature procedures, and gave satisfactory NMR, MS and elemental analysis data. Compounds **51** and **52** were already published[166a] but in the course of this work prepared by a different procedure.[201] Compounds **9a**[233] and **23**[234] are included in the experimental section because lack of experimental and/or spectroscopical data in the literature. Compounds **7**[235] and **8**[236] were prepared differently than in the referenced literature procedures and therefore described in full detail. I am grateful to Dr. M. Beinhoff for providing **10**.

7.4.1 Compounds of Chapter 4.2.1

(Boc-N)$_3$3D0: **1,3,5-Tris[(*tert*-butyloxycarbonylamino)propyl]benzene (4)**



9-BBN (15.4 g, 126 mmol) was added at 0 °C to a solution of *tert*-butyl allylcarbamate **3** (16.5 g, 105 mmol) in dry toluene. The reaction mixture was allowed to warm up to room temperature and stirred for additional 12 h. Then 1,3,5-tribromobenzene **1** (7.87 g, 25.0 mmol) and a 1 M solution of KOH in water (225 ml) were added. After degassing the reaction mixture $Pd(PPh_3)_4$ (1.16 g, 1.00 mmol) was added. The reaction mixture was degassed repeatedly thereafter and stirred at 50 °C for 24 h. After complete reaction (TLC) the layers were separated, the organic phase was washed with brine once, and the aqueous phase was extracted with diethyl ether. The combined organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo*. Column chromatography (silica gel, hexane/ethyl acetate (3:1/v:v) as eluent) and subsequent recrystallization from hexane/ethyl acetate (4:1/v:v) yielded the Boc-protected core **4** (12.9 g, 23.5 mmol, 94.0 %) as a colorless solid.

R_f = 0.30 (hexane/ethyl acetate (3:1/v:v)).

M.p. 89 °C.

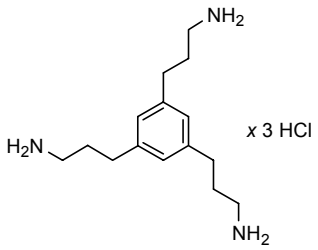
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 27 H, CH_3), 1.75 (m, 6 H, CH_2), 2.54 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 3.08 (m, 6 H, CH_2N), 4.65 (s, br, 3 H, NH), 6.78 (s, 3 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 28.38 (CCH_3), 31.58 (CH_2), 32.85 (CH_2Ar), 40.07 (CH_2N), 78.97 (CCH_3), 126.10 (Ar*C*), 141.67 (Ar*C*), 155.95 (CO).

MS (EI, 80 eV, 180 °C): *m/z* (%): 549 (3.2) $[M]^+$, 449 (49.8) $[M\text{-}C_5H_8O_2]^+$, 263 (100).

EA for **$C_{30}H_{51}N_3O_6$ (549.74):** calcd (%): C 65.54, H 9.35, N 7.64; found (%): C 65.47, H 9.06, N 7.51.

(N)$_3$3D0: 1,3,5-Tris(3-aminopropyl)benzene trishydrochloride (5)



The Boc-protected core **4** (8.80 g, 16.0 mmol) was dissolved in THF and stirred with a 25% HCl solution (28.0 ml, 192 mmol) for 12 h at room temperature. Part of the pure product already precipitated from the reaction mixture, for the other part the solvent was removed *in vacuo*, the residue dissolved in ethanol and precipitated with diethyl ether. The procedure yielded the trishydrochloride **5** (5.49 g, 15.3 mmol, 95.6 %) as a colorless solid.

M.p. > 290 °C (decomp).

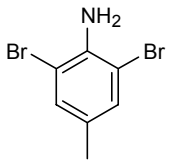
^{1}H NMR (500 MHz, CD_3OD): δ = 2.04 (m, 6 H, CH_2), 2.74 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 2.99 (t, ^3J (H,H) = 7.8 Hz, 6 H, CH_2N), 7.05 (s, 3 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 30.16 (CH_2), 33.34 (CH_2Ar), 40.35 (CH_2N), 127.55 (Ar*C*), 142.45 (Ar*C*).

MS (EI, 80 eV, 200 °C): *m/z* (%): 249 (15.0) $[M]^+$, 219 (100.0) $[M\text{-}CH_2NH_2]^+$.

HRMS: *m/z:* monoisotopic mass calcd for **$C_{15}H_{27}N_3^+$**: 249.22050, found: 249.22221.

1-Amino-2,6-dibromo-4-methylbenzene (7)



p-Toluidine (50.0 g, 467 mmol) in glacial acid (500 ml) was heated carefully until a clear solution was obtained. Then a solution of Br_2 in glacial acid was added dropwise in the dark, and the reaction mixture was stirred for 3 h at room temperature. After complete reaction (TLC) an ice/water mixture (500 - 600 ml) was added. After filtration the precipitate was washed extensively with water, and

recrystallized from methanol. The procedure yielded the desired product **7** (83.5 g, 315 mmol, 67.5 %) as colorless crystals (needles).

R_f = 0.69 (DCM/methanol (19:1/v:v)).

M.p. 73 °C. (Lit. : 73 °C[237], 79 °C[235]).

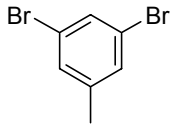
^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_3), 4.36 (s, br, 2 H, NH), 7.20 (s, 2 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.78 (CH_3), 108.69 (Ar*C*), 129.30 (Ar*C*), 132.14 (Ar*C*), 139.49 (Ar*C*).

MS (EI, 80 eV, 40 °C): *m/z* (%): 267 (49.5), 265 (100), 263 (52.4) $[M]^+$, 168 (29.2) $[M-^{79}Br]^+$, 184 (32.0) $[M-^{81}Br]^+$, 105 (12.2) $[C_7H_7N]^+$.

EA for **$C_7H_7NBr_2$ (264.95):** calcd (%): C 31.73, H 2.66, N 5.29; found (%): C 31.72, H 2.44, N 5.15.

1,3-Dibromo-5-methylbenzene (8)



To a solution of 1-amino-2,6-dibromo-4-methylbenzene **7** (50 g, 189 mmol) in ethanol (500 ml) concentrated sulfuric acid (70 ml) was added dropwise while the temperature of the reaction mixture increased. When the temperature had dropped below 50 °C, sodium nitrite (33.9 g, 491 mmol) was added under vigorous stirring, and the reaction mixture was heated carefully until the diazonium-decomposition started. After the N_2-evolution had stopped completely, the reaction mixture was stirred under reflux for 3 - 4 h. After complete reaction an ice/water mixture (500 - 600 ml) was added, the precipitating crude product washed extensively with water, and purified by column chromatography (silica gel, hexane as eluent). The procedure yielded the desaminated product **8** (41.3 g, 165 mmol, 87.3 %) as colorless crystals.

R_f = 0.50 (hexane).

M.p. 39-40 °C. (Lit. : 37-40 °C[236a], 39 °C[236b]).

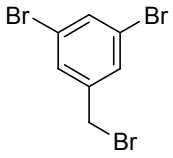
^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 7.22 (s, 2 H, Ar*H*), 7.45 (s, 1 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.87 (CH_3), 122.61 (Ar*C*), 130.88 (Ar*C*), 131.09 (Ar*C*), 141.73 (Ar*C*).

MS (EI, 80 eV, 30 °C): *m/z* (%): 252 (49.0), 250 (100), 248 (51.7) $[M]^+$, 171 (35.3) $[M-^{79}Br]^+$, 169 (36.5) $[M-^{81}Br]^+$, 90 (29.0) $[C_7H_6]^+$.

EA for **$C_7H_6Br_2$ (249.93):** calcd (%): C 33.64, H 2.42; found (%): C 33.60, H 2.47.

1,3-Dibromo-5-bromomethylbenzene (9a)



A solution of 1,3-dibromo-5-methylbenzene **8** (10.0 g, 40 mmol), NBS (7.12 g, 40 mmol), and a catalytic amount of AIBN in dry tetrachloromethane was heated to reflux for 90 min. After complete reaction (TLC), the solution was cooled in an ice bath and the succinimide removed by filtration. The solution was washed three times with brine, dried with magnesium sulfate, and the solvent removed *in vacuo*. The crude product was purified by column chromatography (silica gel, hexane as eluent) to yield the dibromobenzyl bromide **9a** (8.52 g, 25.9 mmol, 64.8 %) as a colorless solid.

$\boldsymbol{R_f}$ = 0.29 (hexane).

M.p. 86-88 °C. (Lit. : 92.2-92.4 °C[233b]).

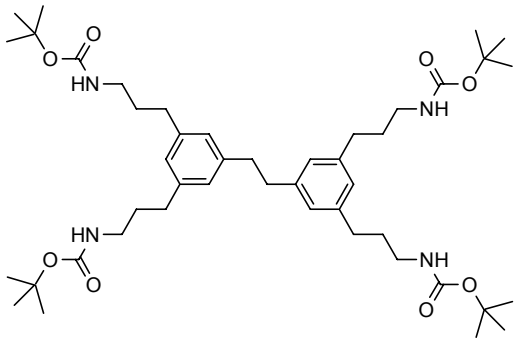
^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.34 (s, 2 H, CH_2), 7.45 (s, 2 H, Ar*H*), 7.58 (s, 1 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 30.67 (CH_2), 123.04 (Ar*C*), 130.78 (Ar*C*), 134.02 (Ar*C*), 141.28 (Ar*C*).

MS (EI, 80 eV, 30 °C): *m/z* (%): 332 (5.7), 330 (17.2), 328 (17.6), 326 (6.0) $[M]^+$, 251(48.9) $[M-^{79}Br]^+$, 249 (100) $[M-^{79}Br]^+$, 247 (52.6) $[M-^{81}Br]^+$, 168 (10.6) $[C_7H_5{}^{79}Br]^+$, 89 (27.7) $[C_7H_5]^+$.

EA for **$C_7H_5Br_3$ (328.83):** calcd (%): C 25.57, H 1.53; found (%): C 24.97, H 1.28.

1,2-Bis{3,5-bis-[(*tert*-butyloxycarbonylamino)propyl]phenyl}ethane (11)



9-BBN was added at 0 °C to a solution of *tert*-butyl allylcarbamate **3** (2.64 g, 16.8 mmol) in dry toluene. The reaction mixture was allowed to warm up to room temperature and stirred for additional 12 h. Then 1,2-Bis-(3,5-dibromophenyl)ethane **10** (1.39 g, 2.79 mmol) and a 1 M solution of KOH in water (36 ml) were added. After degassing the reaction mixture $Pd(PPh_3)_4$ (208 mg, 0.18 mmol) was added. The reaction mixture was degassed repeatedly thereafter and stirred at 50 °C for 24 h. After complete reaction (TLC) the layers were separated, the organic phase was washed with brine once, and the aqueous phase was extracted with diethyl ether. The combined organic layers were dried over magnesium sulfate and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate (4:1/v:v) as eluent) to yield the Boc-protected tetrafunctional core **11** (585 mg, 721 µmol, 25.8 %) as a colorless solid.

$\boldsymbol{R_f}$ = 0.27 (hexane/ethyl acetate (2:1/v:v)).

M.p. 138 °C.

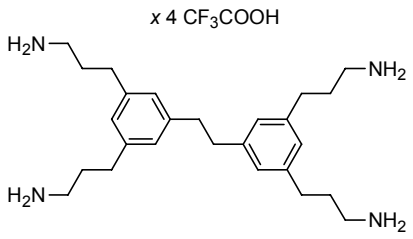
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 (s, 36 H, CH_3), 1.75 (m, 8 H, CH_2), 2.55 (t, ^3J (H,H) = 7.7 Hz, 8 H, CH_2Ar), 2.80 (s, 4 H, CH_2), 3.10 (m, 6 H, CH_2N), 4.62 (s, br, 4 H, NH), 6.79 (s, 6 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 28.46 (C*C*H_3), 31.72 (CH_2), 32.98 (CH_2Ar), 37.95 (*(C*H_2Ar*)$_2$*), 40.33 (CH_2N), 126.05 (Ar*C*), 126.24 (Ar*C*), 141.04 (Ar*C*), 142.08 (Ar*C*), 156.01 (CO).

MS (FAB+, MNBA/DCM): *m/z* (%): 811 (0.2) $[M+H]^+$, 711 (5.8) $[M-C_5H_8O_2+H]^+$, 511 (3.5) $[M-3\cdot(C_5H_8O_2)+H]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{46}H_{74}N_4O_8$ (811.10):** calcd (%): C 68.12, H 9.20, N 6.91; found (%): C 67.99, H 8.83, N 6.59.

1,2-Bis[3,5-bis-(3-aminopropyl)phenyl]ethane tetratrifluoroacetate (12)



The Boc-protected core **11** (81 mg, 0.10 mmol) was dissolved in DCM (2 ml). TFA (2 ml) was added, and the reaction mixture was stirred for 1 h at room temperature. After complete reaction (TLC) the solvent was removed *in vacuo* to give the deprotected core **12** (87 mg, 100 %) as a colorless oil which could be lyophilized from water.

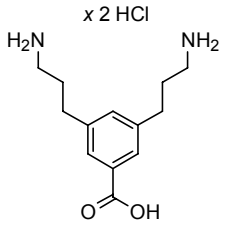
M.p. 102-104 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.99 (m, 8 H, CH_2), 2.70 (t, ^3J (H,H) = 7.6 Hz, 8 H, CH_2Ar), 2.87 (s, 4 H, CH_2), 2.97 (t, ^3J (H,H) = 7.8 Hz, 8 H, CH_2N), 6.96 (s, 6 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 30.27 (CH_2), 33.38 (CH_2Ar), 39.03 (*(C*H_2Ar*)$$_2$*), 40.30 ($CH_2N$), 127.04 (Ar*C*), 127.59 (Ar*C*), 142.10 (Ar*C*), 143.81 (Ar*C*).

MS (FAB+, MNBA/methanol): *m/z* (%): 411 (28.48) $[M+H]^+$, 410 (100) $[M]^+$;
monoisotopic mass calcd for $\mathbf{C_{26}H_{42}N_4^+}$: 410.3, found: 410.4.

3,5-Bis(3-aminopropyl)benzoic acid bishydrochloride (20)



The Boc-protected G1 acid **16** (2.18 g, 5.00 mol) was dissolved in THF (150 ml) and concentrated (37 %) hydrochloric acid (10 ml) was added. The reaction mixture was stirred for 8 h at room temperature. Part of the pure product already precipitated from the reaction mixture and was collected by filtration. The remaining solution was kept at 4 °C for additional 12 h. During that time the rest of pure **20** precipitated. The procedure yielded the desired amino acid bishydrochloride **20** (1.11 g, 3.59 mmol, 71.8 %) as a colorless solid.

M.p. >290 °C (decomp).

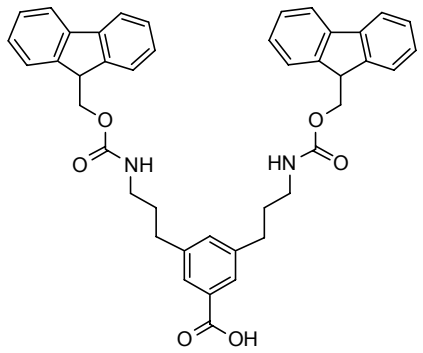
^{1}H NMR (250 MHz, $(CD_3)_2SO$): δ = 1.88 (m, 4 H, CH_2), 2.69 (m, 8 H, CH_2Ar + CH_2N), 7.34 (s, 1 H, Ar*H*), 7.63 (s, 2 H, Ar*H*), 8.31 (s, br, NH), 12.94 (s, br, OH).

^{13}C NMR (63 MHz, $(CD_3)_2SO$): δ = 28.50 (CH_2), 31.70 (CH_2Ar), 38.19 (CH_2N), 127.13 (Ar*C*), 131.17 (Ar*C*), 133.07 (Ar*C*), 141.69 (Ar*C*), 167.41 (CO).

MS (FAB+, MNBA/methanol): *m/z* (%): 237 (100) $[M+H]^+$.

EA for $C_{13}H_{22}N_2O_2Cl_2$ **(309.23):** calcd (%): C 50.49, H 7.17, N 9.06; found (%): C 50.57, H 7.09, N 8.87.

3,5-Bis[(9-fluorenylmethoxycarbonylamino)propyl]benzoic acid (21)



The deprotected G1 acid **20** (1.55 g, 5.00 mmol) was dissolved in a solution of sodium carbonate (1.59 g, 15.0 mmol) in water (125 ml). Afterwards THF (125 ml) and an aqueous solution of sodium carbonate (10 % Na_2CO_3 in water, 10.6 ml) were added. The reaction mixture was then cooled to 0 °C, and within 30 min a solution of Fmoc-Cl (2.85 g, 11.0 mmol) in THF and DIPEA (4.42 g, 1.87 ml, 11.0 mmol) were slowly added by turns. The solution was stirred thereafter for 60 min at room temperature. After complete reaction (TLC) some water (200 ml) was added, and the mixture was washed once with diethyl ether to remove small amounts of 9-fluorenylmethanol and of the dibenzofulven polymer. The solution was then acidified to a pH of 1-2 by addition of 1 M hydrochloric acid and extracted repeatedly with ethyl acetate. The combined organic layers were washed once with water and dried with magnesium sulfate. After evaporation of the solvent the crude product was purified by column chromatography (silica gel, DCM cont. 3 % methanol as eluent) to yield the Fmoc-protected G1 dendron **21** (2.49 g, 3.66 mmol, 73.3 %) as a colorless solid.

R_f = 0.16 (DCM/methanol (97:3/v:v)).

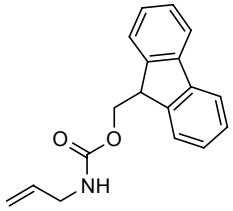
M.p. 176 °C.

^{1}H NMR (250 MHz, $(CD_3)_2SO$): δ = 1.70 (m, 4 H, CH_2), 2.59 (t, ^3J (H,H) = 7.3 Hz, 4 H, CH_2Ar), 3.00 (m, 4 H, CH_2N), 4.20 (t, ^3J (H,H) = 6.4 Hz, 2 H, CH_{Fmoc}), 4.31 (d, ^3J (H,H) = 6.4 Hz, 4 H, $CH_{2\ Fmoc}$), 7.30 (t, ^3J (H,H) = 7.3 Hz, 4 H, ArH_{Fmoc}), 7.33 (s, 1 H, Ar*H*), 7.39 (t, ^3J (H,H) = 7.3 Hz, 4 H, ArH_{Fmoc}), 7.61 (s, 2 H, Ar*H*), 7.68 (d, ^3J (H,H) = 7.3 Hz, 4 H, ArH_{Fmoc}), 7.87 (d, ^3J (H,H) = 7.3 Hz, 4 H, ArH_{Fmoc}).

^{13}C NMR (63 MHz, $(CD_3)_2SO$): δ = 31.24 (CH_2), 32.21 (CH_2Ar), 38.71-40.71 (CH_2N *hidden by the solvent signal*), 46.98 (CH_{Fmoc}), 65.30 ($CH_{2\ Fmoc}$), 120.22 (ArC_{Fmoc}), 125.25 (ArC_{Fmoc}), 126.88 (ArC_{Fmoc}), 127.15 (Ar*C*), 127.70 (ArC_{Fmoc}), 131.04 (Ar*C*), 133.13 (Ar*C*), 140.89 (ArC_{Fmoc}), 142.29 (Ar*C*), 144.10 (ArC_{Fmoc}), 156.27 (CO_{Fmoc}) 167.68 (CO_2H).

MS (FAB+, MNBA/DCM/DMSO): *m/z* (%): 681 (8.6) $[M+H]^+$, 179 (100) $[C_{14}H_{10}+H]^+$; monoisotopic mass cacd for $\mathbf{C_{43}H_{41}N_2O_6^+}$: 681.3, found: 681.4.

(9-Fluorenylmethoxycarbonyl)allylcarbamate (23)



A solution of allylamine **22** (1.14 g, 20.0 mmol) in a solvent mixture of THF (40 ml) and an aqueous solution of sodium carbonate (10 % Na_2CO_3 in water, 44.6 ml) was cooled to 0 °C. Within 30 min a solution of Fmoc-Cl (5.68 g, 22.0 mmol) in THF was added dropwise. The reaction mixture was then stirred for additional 60 min at room temperature. After complete reaction (TLC), the precipitating dibenzofulven polymer was removed by filtration and the solution was then neutralized by addition of aqueous $NaHSO_4$. After repeated extractions with diethyl ether the combined organic layers were dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product recrystallized from hexane/ethyl acetate (1:1/v:v) to yield pure **23** (5.06 g, 18.1 mmol, 90.5 %) as colorless crystals.

$\boldsymbol{R_f}$ = 0.31 (DCM/methanol (19:1/v:v)).

M.p. 124 °C.

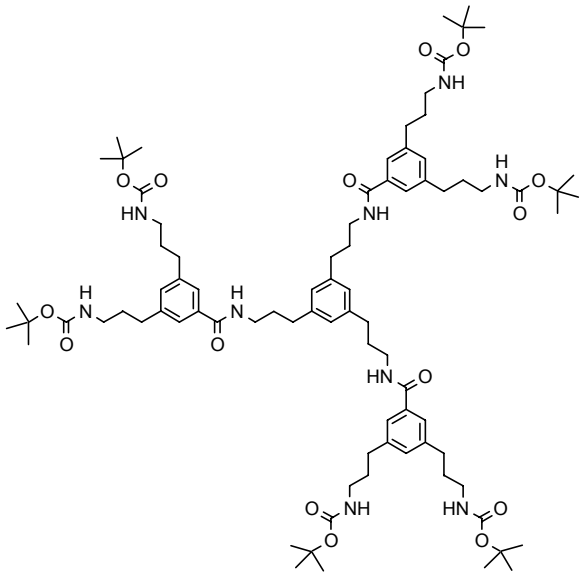
^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.81 (m, 2 H, CH_2NH), 4.21(t, ^3J (H,H) = 6.9 Hz, 1 H, CH_{Fmoc}), 4.42 (d, ^3J (H,H) = 6.9 Hz, 4 H, $CH_{2\ Fmoc}$), 4.87 (s, br, 1 H, NH), 5.13 (m, 2 H, CH_2=CH), 5.82 (m, 1 H, C*H*=CH_2), 7.30 (t, ^3J (H,H) = 7.9 Hz, 2 H, ArH_{Fmoc}), 7.39 (t, ^3J (H,H) = 7.5 Hz, 2 H, ArH_{Fmoc}), 7.59 (d, ^3J (H,H) = 7.9 Hz, 2 H, ArH_{Fmoc}), 7.76 (d, ^3J (H,H) = 7.9 Hz, 4 H, ArH_{Fmoc}).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 43.44 (*C*H_2N), 47.25 (CH_{Fmoc}), 66.66 ($CH_{2\ Fmoc}$), 116.07 (*C*H_2=CH), 119.93 (ArC_{Fmoc}), 124.98 (ArC_{Fmoc}), 127.00 (ArC_{Fmoc}), 127.64 (ArC_{Fmoc}), 134.41 (*C*H=CH_2), 141.30 (ArC_{Fmoc}), 143.92 (ArC_{Fmoc}), 156.22 (CO).

MS (FAB+, MNBA/methanol): *m/z* (%): 302 (1.52) $[M+Na]^+$, 280 (20.5) $[M+H]^+$, 179 (100) $[C_{14}H_{10}+H]^+$.

EA for $\mathbf{C_{18}H_{17}NO_2}$ **(279.33):** calcd (%): C 77.40, H 6.13, N 5.01; found (%): C 77.22, H 5.99, N 4.90.

(Boc-N)$_6$6D1: **1,3,5-Tris{3,5-bis[(*tert*-butyloxycarbonylamino)propyl]-*N*-propylbenzamide}benzene (25)**



The free acid **16** (1.83 g, 4.20 mmol) was dissolved in dry DCM, HOBt (674 mg, 4.40 mmol) was added, and the solution was stirred for 15 min. Afterwards the reaction mixture was cooled down to - 20 °C, EDC (882 mg, 4.60 mmol) was added, and the mixture was subsequently stirred for additional 2 h. During that time the reaction mixture was allowed to warm up to room temperature slowly. After complete reaction (TLC), the mixture was cooled down to - 30 °C, and DIPEA (2.01 ml, 1.53 g, 11.8 mmol) was added. The trisamine core **5** (359 mg, 1.00 mmol) was dissolved in a small amount of dry methanol and slowly added to the reaction mixture under vigorous stirring. The solution was stirred for additional 16 h, and during that time allowed to warm up to room temperature slowly. After complete reaction the solution was washed twice with sodium hydrogencarbonate solution and once with brine. The organic layer was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by column chromatography (silica gel, dichloromethane cont. 2 % methanol as eluent) to afford the G1 dendrimer **25** (1.18 g, 784 µmol, 78.4 %) as a colorless foam.

R_f = 0.37 (DCM/methanol (19:1/v:v)).

M.p. 89 °C.

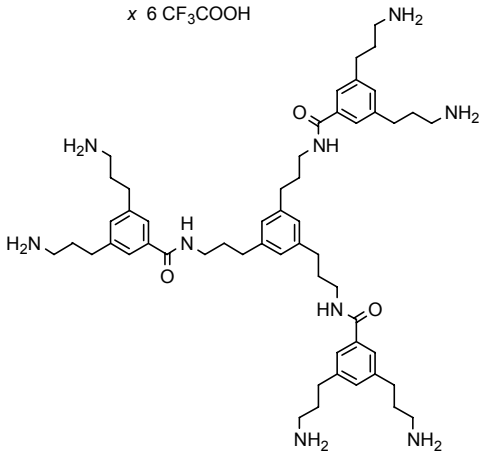
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 (s, 54 H, CH_3), 1.72 (m, 12 H, CH_2), 1.94 (m, 6 H, CH_2), 2.55 (m, 6 H + 12 H, CH_2Ar), 3.05 (m, 12 H, CH_2N), 3.41 (m, 6 H, CH_2N), 4.78 (m, br, 6 H, NH), 7.85 (s, 3 H, Ar*H*), 7.02 (s, br, 3 H, NH), 7.03 (s, 3 H, Ar*H*), 7.37 (s, 6 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 28.41 (CCH_3), 30.85 (CH_2), 31.35 (CH_2), 32.48 (CH_2), 33.16 (CH_2), 39.58 (CH_2), 48.77 (CH_2), 79.10 (CCH_3), 124.79 (Ar*C*), 126.28 (Ar*C*), 131.45 (Ar*C*), 134.91 (Ar*C*), 141.71 (Ar*C*), 141.78 (Ar*C*), 156.09 (CON_{Boc}), 167.75 (CON).

MS (FAB+, MNBA/DCM/DMSO): *m/z* (%): 1505 (17.8) $[M+H]^+$, 1504 (17.8) $[M]^+$, 1404 (57.1) $[M\text{-}C_5H_8O_2]^+$, 1304 (22.8) $[M\text{-}2\cdot(C_5H_8O_2)]^+$, 1204 (23.3) $[M\text{-}3\cdot(C_5H_8O_2)]^+$, 1104 (22.8) $[M\text{-}4\cdot(C_5H_8O_2)]^+$, 1004 (21.5) $[M\text{-}5\cdot(C_5H_8O_2)]^+$, 904 (100) $[M\text{-}6\cdot(C_5H_8O_2)]^+$.

MS (MALDI-TOF, dithranol): *m/z* = 1543 $[M+K]^+$, 1527 $[M+Na]^+$;
monoisotopic mass calcd for $\mathbf{C_{84}H_{129}N_9NaO_{15}}^+$: 1526.95, found: 1526.94.

(N)$_6$6D1: **1,3,5-Tris[3,5-bis(3-aminopropyl)-*N*-propylbenzamide]benzene hexatrifluoroacetate (26)**



The Boc-protected G1 dendrimer **25** (336 mg, 223 µmol) was dissolved in a small amount of DCM (10 ml). TFA (2 ml) was added, and the reaction mixture was stirred for 1 h at room temperature. After complete reaction (TLC) the solvent was removed *in vacuo* to give the deprotected dendrimer **26** (348 mg, 219 mmol, 98.2 %) as a colorless oil which could be lyophilized from water.

M.p. 97 °C.

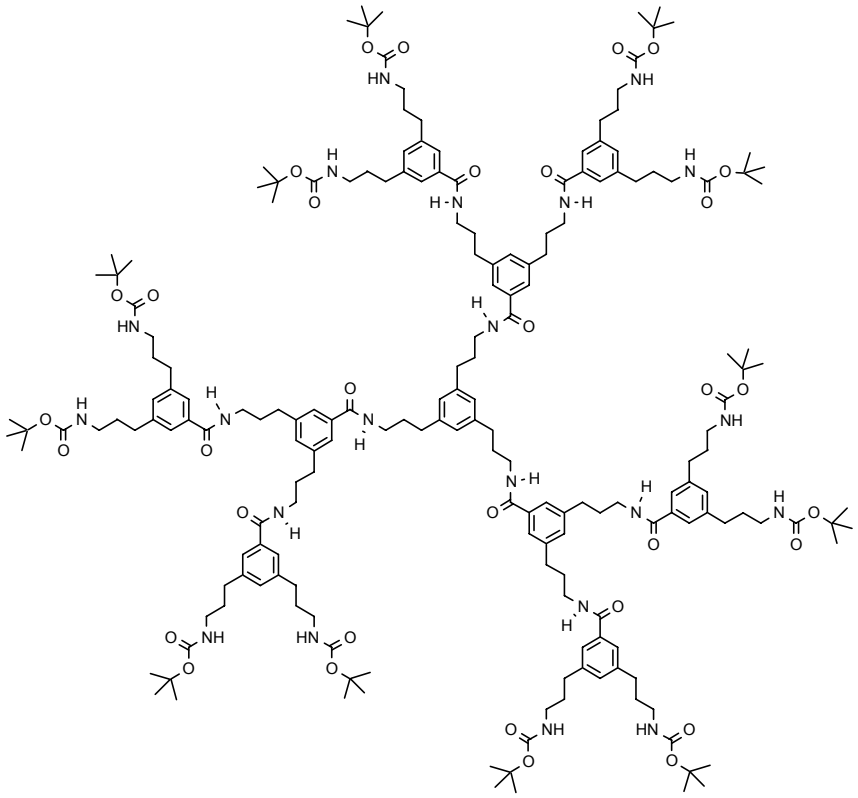
^{1}H NMR (250 MHz, CD_3OD): δ = 2.02 (m, 6 H + 12 H, CH_2), 2.69 (t, ^3J (H,H) = 7.4 Hz, 6 H, CH_2Ar), 2.79 (t, ^3J (H,H) = 7.8 Hz, 12 H, CH_2Ar), 2.99 (t, ^3J (H,H) = 7.5 Hz, 12 H, CH_2N), 3.44 (t, ^3J (H,H) = 7.1 Hz, 6 H, CH_2N), 6.97 (s, 3 H, Ar*H*), 7.33 (s, 3 H, Ar*H*), 7.57 (s, 6 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 30.12 (CH_2), 32.21 (CH_2), 33.28 (CH_2), 34.33 (CH_2), 40.26 (CH_2), 40.87 (CH_2), 126.30 (Ar*C*), 127.26 (Ar*C*), 132.66 (Ar*C*), 136.58 (Ar*C*), 142.71 (Ar*C*), 143.23 (Ar*C*), 170.24 (CON).

MS (FAB+, DNSO/2-nitrophenol): *m/z* (%): 927 (3.3) $[M+Na]^+$, 905 (15.6) $[M+H]^+$, 219 (100) $[C_{13}H_{19}N_2O]^+$.

MS (MALDI-TOF, CCA): *m/z* = monoisotopic mass calcd for $\mathbf{C_{54}H_{82}N_9O_3}^+$: 904.65, found: 904.85 $[M+H]^+$.

(Boc-N)$_{12}$12D: **1,3,5-Tris(3,5-bis-{3,5-bis[(*tert*-butyloxycarbonylamino)propyl]-*N*-propyl-benzamide}-*N*-propylbenzamide)benzene (27)**



The G2 acid **19** (830 mg, 800 µmol) was dissolved in dry DCM. HOBt (130 mg, 851 µmol) was added, and the reaction mixture was stirred for 15 min at room temperature. The mixture was cooled down to – 20 °C and EDC (171 mg, 890 µmol) was added. The solution was stirred for additional 2 h and allowed to warm up to room temperature. After complete reaction (TLC) the mixture was cooled down to - 30 °C and (381 µl, 290 mg, 2.24 mmol) DIPEA was added. The trisamine core **5** (65.0 mg, 180 µmol) was dissolved in a small amount of dry methanol and slowly added to the reaction mixture under vigorous stirring. The solution was stirred for additional 12 h and during that time allowed to warm up to room temperature. Afterwards the mixture was washed twice with sodium hydrogencarbonate solution and once with brine. The organic layer was dried over magnesium sulfate, and the solvent removed *in vacuo*. The crude product was purified by column chromatography (silica gel, DCM cont. 4 % methanol as eluent) to afford the G2 dendrimer **27** (526 mg, 154 µmol, 85.6 %) as a colorless foam.

R_f = 0.19 (DCM/methanol (19:1/v:v)).

M.p. 106 °C.

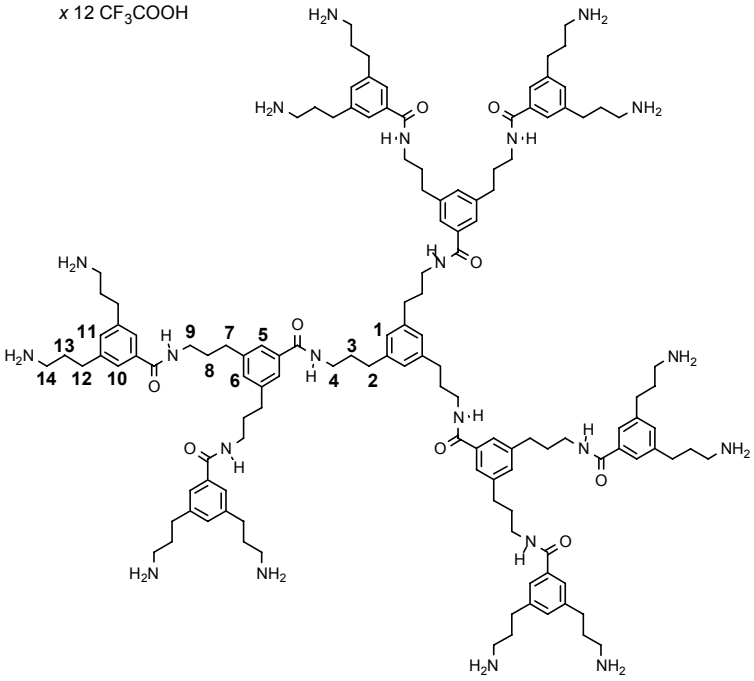
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 108 H, CH_3), 1.69 (m, 24 H, CH_2), 1.82 (m, 12 H, CH_2), 1.86 (m, 6 H, CH_2), 2.52 (m, 24 H + 12 H + 6 H, CH_2Ar), 3.29 (m, 24 H, CH_2N), 3.31 (m, 12 H, CH_2N), 3.37 (m, 6 H, CH_2N), 4.94 (s, br, 12 H, NH), 6.83 (s, 3 H, Ar*H*), 7.00 (s, 3 H, Ar*H*), 7.03 (s, 6 H, Ar*H*), 7.28 (s, br, 6 H + 3 H, NH), 7.31 (s, 6 H, Ar*H*), 7.43 (s, 12 H, Ar*H*).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.43 (C*C*H$_3$), 29.68 (CH$_2$), 30.74 (CH$_2$), 31.33 (CH$_2$), 32.51 (CH$_2$), 32.85 (CH$_2$), 33.37 (CH$_2$), 39.32 (CH$_2$), 39.66 (CH$_2$), 53.40 (CH$_2$), 79.06 (*C*CH$_3$), 124.91 (Ar*C*), 126.33 (Ar*C*), 131.38 (Ar*C*), 131.63 (Ar*C*), 134.73 (Ar*C*), 134.83 (Ar*C*), 141.75 (Ar*C*), 141.84 (Ar*C*), 141.95 (Ar*C*) 142.04 (Ar*C*), 156.16 (CON$_{Boc}$), 167.86 (CON), 167.96 (CON).

MS (MALDI-TOF, IAA): *m/z:* 3452 $[M+K]^+$, 3436 $[M+Na]^+$;
monoisotopic mass calcd for **$C_{192}H_{285}N_{21}NaO_{33}^+$**: 2436.12, found: 2436.29.

(N)$_{12}$12D2: **1,3,5-Tris{3,5-bis[3,5-bis(3-aminopropyl)-*N*-propylbenzamide]-*N*-propylbenzamide}benzene dodecatrifluoroacetate (28)**

The Boc-protected G2 dendrimer **27** (180 mg, 54.1 µmol) was dissolved in DCM (8 ml). TFA (2 ml) was added, and the reaction mixture was stirred for 2 h at room temperature. After complete reaction (TLC) the solvent was removed *in vacuo* to give the deprotected G2 dendrimer **28** (192 mg, 53.6 µmol, 99.1 %) as a colorless oil which could be lyophilized from water.



M.p. 110-112 °C.

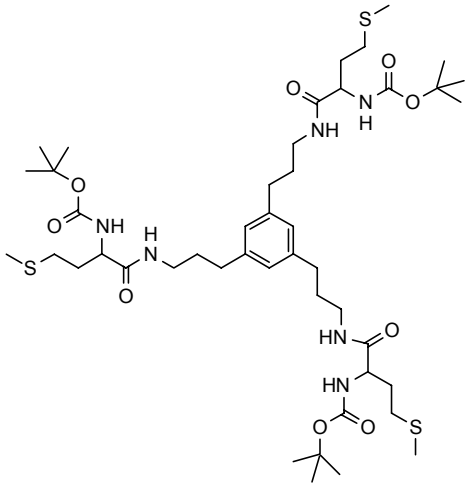
^{1}H NMR (500 MHz, CD_3OD): δ = 1.97 (m, 18 H, *H*-3 + *H*-8), 2.02 (m, 24 H, *H*-13') 2.67 (t, ^3J (H,H) = 7.4 Hz, 6 H, *H*-2), 2.73 (t, ^3J (H,H) = 7.6 Hz, 12 H, *H*-7), 2.77 (t, ^3J (H,H) = 7.8 Hz, 24 H, *H*-12), 2.98 (t, ^3J (H,H) = 7.7 Hz, 24 H, *H*-14), 3.43 (m, 18 H, *H*-9 + *H*-4), 6.96 (s, 3 H, *H*-1), 7.30 (s, 3 H, *H*-6), 7.32 (s, 6 H, *H*-11'), 7.50 (s, 6 H, *H*-5), 7.55 (s, 12 H, *H*-10').

^{13}C NMR (126 MHz, CD_3OD): δ = 30.11 (CH$_2$), 31.95 (CH$_2$), 32.04 (CH$_2$), 33.28 (CH$_2$Ar), 34.19 (CH$_2$Ar), 34.35 (CH$_2$Ar), 40.27 (CH$_2$N), 40.72 (CH$_2$N), 40.86 (CH$_2$N), 126.02 (Ar*C*), 126.30 (Ar*C*), 127.33 (Ar*C*), 132.69 (Ar*C*), 132.91 (Ar*C*), 136.01 (Ar*C*), 136.50 (Ar*C*), 142.72 (Ar*C*), 143.25 (Ar*C*), 143.70 (Ar*C*), 170.22 (CON), 170.48 (CON).

MS (MALDI-TOF, CCA): *m/z:* 2252 $[M+K]^+$, 2236 $[M+Na]^+$, 2214 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{132}H_{190}N_{21}O_9^+}$: 2213.51, found: 2213.55.

7.4.2 Compounds of Chapter 4.2.2

(Boc-Met)$_3$3D0: **1,3,5-Tris[L-(3-methylsulfanyl-1-propylcarbamoylpropyl)carbamic acid *tert*-butyl ester]benzene (30a)**



The hydroxysuccinimide ester **29a** (3.74 g, 10.8 mmol) was dissolved in dry dichloromethane under a nitrogen atmosphere, and the solution was cooled down to - 10 °C. Afterwards DIPEA (1.57 ml, 1.16 g, 9.00 mmol) and a solution of core **5** (1.08 g, 3.00 mmol) in dry methanol was added dropwise. The reaction mixture was stirred for additional 12 h, and during that time allowed to warm up to room temperature. After complete reaction the mixture was washed twice with sodium hydrogencarbonate solution and once with brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the crude product was subsequently purified by column chromatography (silica gel, DCM cont. 2 % methanol as eluent) under a nitrogen atmosphere. The procedure yielded **30a** (2.40 g, 2.54 mmol, 84.7 %) as a colorless foam.

R_f = 0.32 (DCM/methanol (19:1/v:v)).

M.p. 162 °C.

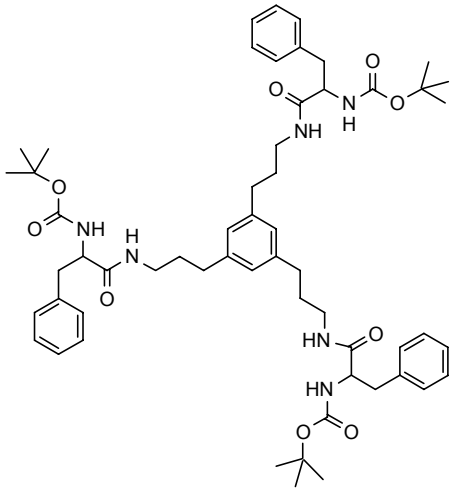
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 27 H, CCH_3), 1.80 (m, 6 H, CH_2), 1.98 (m, 3 H, CHC*H*$_2$), 2.03 (m, 3 H, CHC*H*$_2$), 2.08 (s, 9 H, SCH_3), 2.55 (m, 6 H + 6 H, CH_2Ar + CH_2S), 3.17 (m, 6 H, CH_2N), 4.34 (m, br, 3 H, CH), 5.80 (s, br, 3 H, NH), 6.77 (s, 3 H, Ar*H*), 7.17 (s, br, 3 H, NH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.31 (SCH_3), 28.36 (C*C*H$_3$), 30.26 (CH_2S), 30.51 (CH_2), 31.98 (CH*C*H$_2$), 32.28 (CH_2Ar), 38.34 (CH_2N), 53.61 (CH), 79.91 (*C*CH$_3$), 126.45 (Ar*C*), 141.24 (Ar*C*), 155.90 (CON_{Boc}), 171.98 (CON).

MS (FAB+, MNBA/ethanol): *m/z* (%): 965 (1.5) $[M+Na]^+$, 943 (2.4) $[M+H]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{45}H_{78}N_6O_9S_3$ (943.33):** calcd (%): C 57.29, H 8.33, N 8.91, S 10.20; found (%): C 57.24, H 8.29, N 8.88, S 10.26.

(Boc-Phe)$_3$3D0: **1,3,5-Tris[L-(2-phenyl-1-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]benzene (30b)**



The hydroxysuccinimide ester **29b** (3.91 g, 10.8 mmol) was dissolved in dry DCM under a nitrogen atmosphere and cooled down to 0 °C. Subsequently DIPEA (1.57 ml, 1.16 g, 9.00 mmol) and a solution of **5** (1.08 g, 3.00 mmol) in dry methanol were added dropwise. The reaction mixture was stirred for additional 12 h, and during that time allowed to warm up to room temperature. After complete reaction the mixture was washed twice with sodium hydrogencarbonate solution and once with brine, dried over magnesium sulfate, and the solvent was evaporated *in vacuo*. Column chromatography (silica gel; DCM cont. 3 % methanol as eluent) afforded **30b** (2.37 g, 2.39 mmol, 79.7 %) as a colorless solid.

R_f = 0.46 (DCM/methanol (19:1/v:v)).

M.p. 190 °C.

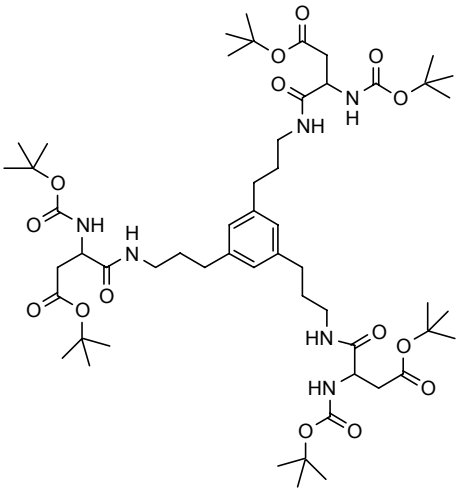
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 27 H, CH_3), 1.65 (m, 6 H, CH_2), 2.39 (t, ^3J (H,H) = 6.4 Hz, 6 H, CH_2Ar), 3.02 (m, 6 H, CH_2N), 3.02 (m, 6 H + 3 H, CH_2N + $CHCH_2$), 3.10 (m, 3 H, $CHCH_2$), 4.44 (m, br, 3 H, CH), 5.64 (s, br, 3 H, NH), 6.67 (s, 3 H, Ar*H*), 6.81 (s, br, 3 H, NH), 7.19 (m, 15 H, ArH_{phe}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.31 (CCH_3), 30.45 (CH_2), 32.25 (CH_2Ar), 38.29 ($CHCH_2$), 38.95 (CH_2N), 55.42 (CH), 79.84 (CCH_3), 126.31 (Ar*C*), 126.65 (ArC_{phe}), 128.40 (ArC_{phe}), 129.35 (ArC_{phe}), 137.05 (ArC_{phe}), 141.05 (Ar*C*), 155.52 (CON_{Boc}), 171.69 (CON).

MS (FAB+, MNBA/methanol/DMSO): *m/z* (%): 1013 (0.3) $[M+Na]^+$, 991 (0.9) $[M+H]^+$, 120 (100) $[C_8H_{10}N]^+$.

EA for **$C_{57}H_{78}N_6O_9$ (991.26):** calcd (%): C 69.06, H 7.93, N 8.48; found (%): C 69.10, H 7.83, N 8.29.

(Boc/tBu-Asp)$_3$3D0: **1,3,5-Tris(L-3-*tert*-butoxycarbonylamino-*N*-propylsuccinamic acid *tert*-butyl ester)benzene (30c)**



The hydroxysuccinimide ester **29c** (2.67 g, 6.90 mmol) was dissolved in dry DCM and cooled down to - 10 °C. DIPEA (1.02 ml, 775 mg, 6.00 mmol) and a solution of core **5** (718 mg, 2.00 mmol) in dry methanol were added dropwise. The reaction mixture was stirred for additional 12 h, and during that time allowed to warm up to room temperature. After complete reaction the mixture was washed twice with sodium hydrogen-carbonate solution and once with brine, dried over magnesium sulfate, and the solvent was evaporated *in vacuo*. Column chromatography (silica gel, DCM cont. 3 % methanol as eluent) afforded pure **30c** (1.88 g, 1.77 mmol, 88.5 %) as a colorless foam.

R_f = 0.39 (DCM/methanol (19:1/v:v)).

M.p. 80 °C.

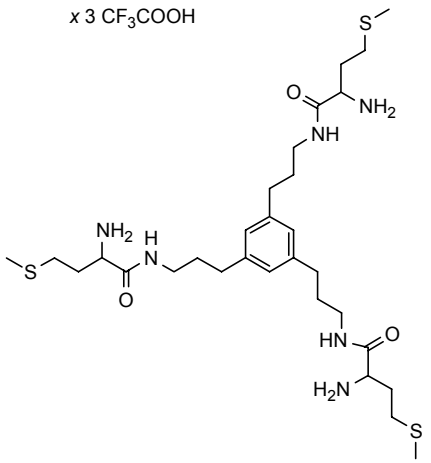
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42 (s, 27 H, CH_3), 1.43 (s, 27 H, CH_3), 1.79 (m, 6 H, CH_2), 2.55 (t, ^3J (H,H) = 7.4 Hz, 6 H, CH_2Ar), 2.62 (dd, ^2J (H,H) = 16.7 Hz, ^3J (H,H) = 6.7 Hz, 3 H, CHCH_2), 2.80 (dd, ^2J (H,H) = 16.7 Hz, ^3J (H,H) = 5.0 Hz, 3 H, CHCH_2), 3.19 (q, ^3J (H,H) = 6.6 Hz, 6 H, CH_2NH), 4.42 (m, br, 3 H, CH), 5.79 (s, br, 3 H, CHN*H*), 6.71 (s, br, 3 H, CONH), 6.78 (s, 3 H, Ar*H*).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.02 (C*C*H_3), 28.32 (C*C*H_3), 30.81 (CH_2), 32.56 (CH_2Ar), 37.49 (CH*C*H_2), 38.75 (CH_2N), 50.85 (CH), 80.26 (*C*CH_3), 81.45 (*C*CH_3), 126.31 (Ar*C*), 141.42 (Ar*C*), 155.57 (CON_{Boc}), 170.93 (CO_{tBu}), 171.09 (CON).

MS (FAB+, MNBA/DCM): *m/z* (%): 1064 (0.4) $[M+H]^+$, 964 (2.3) $[M-C_5H_8O_2]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{54}H_{90}N_6O_{15}$ (1063.32):** calcd (%): C 61.00, H 8.53, N 7.90; found (%): C 60.84, H 8.22, N 7.73.

(Met)$_3$3D0: **1,3,5-Tris(L-2-amino-4-methylsulfanyl-*N*-propylbutyramide)benzene tris-trifluoroacetate (31a)**



Under a nitrogen atmosphere dendrimer **30a** (755 mg, 800 µmol) was dissolved in a 'cleavage cocktail' mixture of DCM/TFA/EDT/thioanisole/methanol/TIPS (50:37.5:5:5:2:0.5/v:v), and stirred for 1 h at room temperature. After complete reaction (TLC) the 'cleavage cocktail' mixture was removed *in vacuo* to give the deprotected methionine G0 dendrimer **31a** (778 mg, 790 µmol, 98.8 %) as a colorless oil, which could be lyophilized from water.

M.p. 84-86 °C.

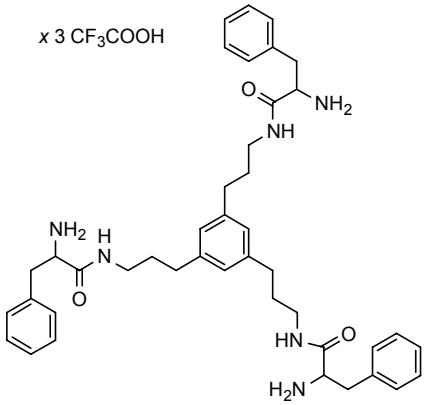
^{1}H NMR (500 MHz, CD_3OD): δ = 1.87 (m, 6 H, CH_2), 2.16 (s, 9 H, SCH_3), 2.17 (m, 6 H, CHC*H*$_2$), 2.62 (m, 6 H, SCH_2), 2.65 (m, 6 H, CH_2Ar), 3.25 (m, 3 H, C*H*$_2$N), 3.34 (m, 3 H, C*H*$_2$N), 3.99 (t, ^3J (H,H) = 6.6 Hz, 3 H, CH), 6.92 (s, 3 H, Ar*H*).

^{13}C NMR (126 MHz, CD_3OD): δ = 15.16 (SCH_3), 29.93 (SCH_2), 32.10 (CH_2), 32.19 (CH*C*H$_2$), 34.10 (CH_2Ar), 40.37 (CH_2NH), 53.87 (CH), 127.28 (ArC), 143.06 (ArC), 169.68 (CON).

MS (EI, 80 eV, 290 °C): *m/z* (%): 642 (6.5) $[M]^+$, 568 (23.12) $[M\text{-}C_3H_6S]^+$, 539 (88.2) $[M\text{-}C_4H_9NS]^+$, 350 (100) $[M\text{-}C_{12}H_{26}N_3OS_2]^+$.

HRMS: *m/z:* monoisotopic mass calcd for $\mathbf{C_{27}H_{48}N_6O_3S_2^+}$: 568.32366 $[M\text{-}C_3H_6S]^+$, found: 568.32294.

(Phe)$_3$3D0: **1,3,5-Tris(L-2-amino-3-phenyl-*N*-propylpropionamide)benzene tris-trifluoroacetate (31b)**



The L-phenylalanine G0 dendrimer **30b** (991 mg, 1.00 mmol) was dissolved in DCM/methanol (19:1/v:v) (40 ml). TFA (5 ml) was added, and the reaction mixture was stirred at room temperature for 1 h. After complete reaction (TLC) the solvent was removed *in vacuo* to afford the deprotected L-phenylalanine dendrimer **31b** (1.02 g, 987 µmol, 98.7 %) as a colorless solid.

M.p. 115-117 °C.

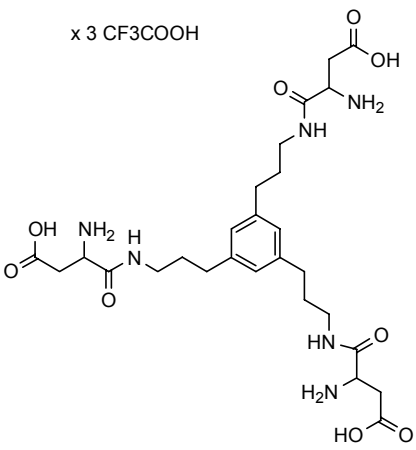
^{1}H NMR (500 MHz, CD_3OD): δ = 1.72 (m, 6 H, CH_2), 2.49 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 3.15 (m, 3 H, CH_2N), 3.16 (m, 3 H, CH_2N), 3.26 (m, 6 H, $CHCH_2$), 4.09 (t, ^3J (H,H) = 7.5 Hz, 3 H, CH), 6.81 (s, 3 H, Ar*H*), 7.32 (m, 9 H, ArH_{phe}), 7.35 (m, 6 H, ArH_{phe}).

^{13}C NMR (126 MHz, CD_3OD): δ = 32.16 (CH_2), 34.22 (CH_2Ar), 39.02 (CH_2N), 40.54 ($CHCH_2$), 56.15 (CH), 127.48 (Ar*C*), 129.08 (ArC_{phe}), 130.33 (ArC_{phe}), 130.80 (ArC_{phe}), 136.02 (ArC_{phe}), 143.21 (Ar*C*), 169.73 (CON).

MS (EI, 80 eV, 150-180 °C): *m/z* (%): 690 (2.8) $[M]^+$, 513 (59.3) $[M\text{-}C_{10}H_{13}N_2O]^+$, 44 (100) $[C_3H_8]^+$.

HRMS: *m/z:* monoisotopic mass calcd for **$C_{42}H_{54}N_6O_3$**: 690.42622, found: 690.42572.

(Asp)$_3$3D0: **1,3,5-Tris-(L-3-amino-*N*-propyl-succinamic acid)benzene tris-trifluoroacetate (31c)**



To a solution of **30c** (106 mg, 100 µmol) in DCM (10 ml), TFA (4 ml) was added, and the reaction mixture was stirred for 2 h at room temperature. After complete reaction (TLC) the solvent was removed *in vacuo* to yield the deprotected aspartic acid G0 dendrimer **31c** (92 mg, 98 µmol, 98 %) as a colorless oil, which could be lyophilized from water.

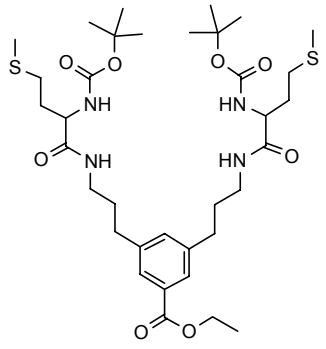
M.p. 106-109 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.86 (m, 6 H, CH_2), 2.64 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 2.87 (dd, ^2J (H,H) = 17.5 Hz, ^3J (H,H) = 7.8 Hz, 3 H, CHCH_2), 2.94 (dd, ^2J (H,H) = 17.6 Hz, ^3J (H,H) = 5.2 Hz, 3 H, CHCH_2), 3.23 (m, 3 H, CH_2N), 3.31 (m, 3 H, CH_2N), 4.19 (m, 3 H, CH), 6.92 (s, 3 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 31.92 (CH_2), 33.85 (CH_2), 36.41 (CH_2), 40.27 (CH_2), 51.22 (CH), 127.39 (Ar*C*), 143.00 (Ar*C*), 169.19 (CON), 173.12 (COO).

MS (FAB-, MNBA, methanol): *m/z* (%): 593 (2.3) $[M-H]^-$, 113 (89.9) $[C_4H_5N_2O_2]^-$;
monoisotopic mass calcd for **$C_{27}H_{41}N_6O_9^-$**: 593.3, found: 593.3 $[M-H]^-$.

Ethyl-3,5-bis[L-(3-methylsulfanyl-1-propylcarbamoylpropyl)carbamic acid *tert*-butyl ester] benzoate (32a)



The Boc-L-methionine hydroxysuccinimide ester **29a** (1.59 g, 4.60 mmol) was dissolved in dry DCM under a nitrogen atmosphere, and cooled down to - 10 °C. DIPEA (680 µl, 517 mg, 4.00 mmol) and the G1 hydrochloride **15** (675 mg, 2.00 mmol) dissolved in dry methanol were added dropwise. The reaction mixture was allowed to warm up to room temperature and was stirred for additional 12 h. After complete reaction (TLC) the organic layer was washed twice with sodium hydrogencarbonate solution and once with brine. The organic phase was subsequently dried over magnesium sulfate, and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (silica gel, DCM cont. 2-3 % methanol as eluent) to afford dendron **32a** (1.15 g, 1.58 mmol, 79.0 %) as a colorless foam.

***R*$_f$** = 0.09 (DCM/methanol (49:1/v:v)).

M.p. 75 °C.

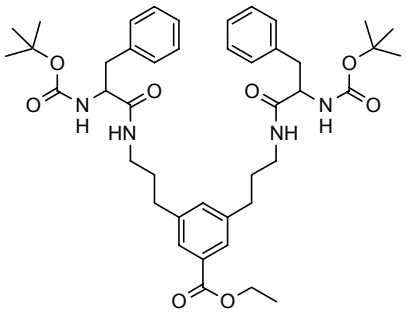
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (t, ^3J (H,H) = 7.1 Hz, 3 H, CH_2CH_3), 1.37 (s, 18 H CCH_3), 1.81 (m, 4 H, CH_2), 1.92 (m, 2 H, CHCH_2), 2.02 (m, 2 H, CHCH_2), 2.05 (s, 6 H, SCH_3), 2.51 (t, ^{3}J (H,H) = 7.3 Hz, 4 H, CH_2Ar), 2.61 (m, 4 H, SCH_2), 3.15 (m, 4 H, CH_2N), 4.29 (m, br, 2 H, CH), 4.31 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH$_3$), 5.69 (d, br, ^3J (H,H) = 6.1 Hz, 2 H, CHN*H*), 7.05 (s, br, 2 H, CONH), 7.14 (s, 1 H, Ar*H*), 7.62 (s, 1 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.26 (CH_2CH_3), 15.24 (SCH_3), 28.28 (CCH_3), 30.23 (CH_2), 30.44 (CH_2), 32.00 (CH_2), 32.11 (CH_2), 38.16 (CH_2), 53.62 (CH), 60.83 (CH_2CH_3), 79.83 (CCH_3), 127.16 (Ar*C*), 130.78 (Ar*C*), 133.60 (Ar*C*), 141.42 (Ar*C*), 155.89 (CON_{Boc}), 166.63 (CON), 172.09 (COO).

MS (FAB+, MNBA/DCM): *m/z* (%): 727 (10.3) $[M+H]^+$, 627 (22.2) $[M-C_5H_8O_2+H]^+$, 527 (62.0) $[M-2\cdot(C_5H_8O_2)+H]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{35}H_{58}N_4O_8S_2$ (726.99):** calcd (%): C 57.82, H 8.04, N 7.71; found (%): C 57.54, H 7.94, N 7.60.

Ethyl-3,5-bis[L-(2-phenyl-1-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]benzoate (32b)



A solution of the Boc-L-phenylalanine hydroxysuccinimide ester **29b** (5.22 g, 14.4 mmol) in dry DCM was cooled down to 5 °C. DIPEA (2.09 ml, 1.55 g, 12.0 mmol) and the bishydrochloride dendron **15** (2.02 g, 6.00 mmol), dissolved in dry methanol, were added slowly. The reaction mixture was allowed to warm up to room temperature slowly and was stirred for additional 12 h. After complete reaction (TLC) the organic layer was washed twice with sodium hydrogencarbonate solution and once with brine. The organic phase was subsequently dried over magnesium sulfate. The solvent was evaporated under reduced pressure, and column chromatography (silica gel, DCM cont. 2 % methanol as eluent) afforded the Boc-L-phenylalanine dendron **32b** (3.72 g, 4.90 mmol, 81.7 %) as a colorless solid.

R_f = 0.59 (DCM/methanol (19:1/v:v)).

M.p. 121 °C.

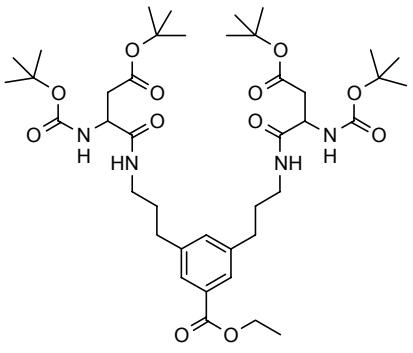
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (s, 18 H, CCH_3), 1.36 (t, ^3J (H,H) = 7.3 Hz, 3 H, CH_2CH_3), 1.69 (m, 4 H, CH_2), 2.47 (t, ^{3}J (H,H) = 7.0 Hz, 4 H, CH_2Ar), 3.03 (m, 4 H, CH_2N), 3.05 (m, 4 H, $CHCH_2$), 4.40 (m, br, 2 H, CH), 4.33 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH_3), 5.61 (d, br, ^3J (H,H) = 5.9 Hz, 2 H, CHN*H*), 6.68 (s, br, 2 H, CONH), 7.05 (s, 1 H, Ar*H*), 7.19 (m, 10 H, ArH_{Phe}), 7.60 (s, 2 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.33 (CH_2CH_3), 28.31 (CCH_3), 30.42 (CH_2), 32.11 (CH_2), 38.25 (CH_2), 38.82 (CH_2), 52.00 (CH), 60.87 (CH_2CH_3), 79.98 (CCH_3), 126.78 (Ar*C*), 127.16 (Ar*C*), 128.51 (Ar*C*), 129.34 (Ar*C*), 130.84 (Ar*C*), 133.57 (Ar*C*), 136.98 (Ar*C*), 141.47 (Ar*C*), 155.61 (CON_{Boc}), 166.69 (CON), 171.64 (COO).

MS (FAB+, MNBA/DCM): *m/z* (%): 781 (0.2) $[M+Na]^+$, 759 (5.0) $[M+H]^+$, 659 (11.2) $[M-C_5H_8O_2+H]^+$, 559 (35.8) $[M-2(C_5H_8O_2)+H]^+$, 120 (100) $[C_8H_{10}N]^+$, 57 (70.1) $[C_4H_9]^+$.

EA for **$C_{43}H_{58}N_4O_8$ (758.94):** calcd (%): C 68.05, H 7.70, N 7.38; found (%): C 67.79, H 7.66, N 7.31.

Ethyl-3,5-bis(L-3-*tert*-butoxycarbonylamino-*N*-propylsuccinamic acid *tert*-butyl ester) benzoate (32c)



A solution of the Boc/*t*Bu-protected hydroxysuccinimide ester **29c** (2.67 g, 6.90 mmol) in dry DCM was cooled down to - 10 °C. DIPEA (1.02 ml, 775 mg, 6.00 mmol) and a solution of the G1 hydrochloride **15** (1.01 g, 3.00 mmol) in dry methanol were added dropwise. The reaction mixture was then allowed to warm up to room temperature while being stirred for additional 12 h. After complete reaction (TLC) the organic layer was washed twice with sodium hydrogencarbonate solution and once with brine. The crude product was purified by column chromatography (silica gel, DCM cont. 3 % methanol as eluent) to afford dendron **32c** (2.11 g, 2.61 mmol, 87.0 %) as a colorless foam. R_f = 0.45 (DCM/methanol (19:1/v:v)).

M.p. 60 °C.

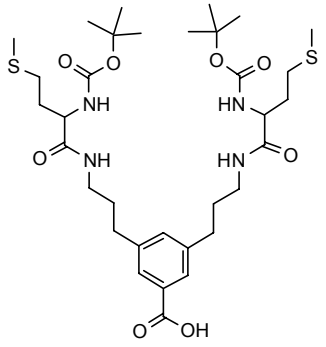
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34 (t, ^3J (H,H) = 7.4 Hz, 3 H, CH_2CH_3), 1.41 (s, 18 H, CCH_3), 1.42 (s, 18 H, CCH_3), 1.81 (m, 4 H, CH_2), 2.61 (dd, ^2J (H,H) = 16.5 Hz, ^3J (H,H) = 4.68 Hz, 2 H, $CHCH_2$), 2.62 (t, ^3J (H,H) = 7.0 Hz, 4 H, CH_2Ar), 2.83 (dd, ^2J (H,H) = 16.5 Hz, ^3J (H,H) = 4.8 Hz, 2 H, $CHCH_2$), 3.22 (q, ^3J (H,H) = 5.9 Hz, 4 H, CH_2NH), 4.34 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH_3), 4.41 (m, br, 2 H, CH), 5.75 (d, br, ^3J (H,H) = 8.1 Hz, 2 H, CHN*H*), 6.67 (t, br, ^3J (H,H) = 5.5 Hz, 2 H, CONH), 7.16 (s, 1 H, Ar*H*), 7.65 (s, 1 H, Ar*H*).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.23 (CH_2CH_3), 27.92 (CCH_3), 28.21 (CCH_3), 30.77 (CH_2), 32.44 (CH_2Ar), 37.45 ($CHCH_2$), 38.65 (CH_2N), 50.86 (CH), 60.72 (CH_2CH_3) 80.05 (CCH_3), 81.35 (CCH_3), 127.05 (Ar*C*), 130.68 (Ar*C*), 133.21 (Ar*C*), 141.61 (Ar*C*), 155.45 (CON_{Boc}), 166.57 (CO_{tBu}), 170.88 (CON).

MS (EI, 80 eV, 260 °C): *m/z* (%): 806 (13.2) $[M]^+$, 706 (50.4) $[M\text{-}C_5H_8O_2]^+$, 56 (57.9) $[C_4H_8]^+$.

EA for **$C_{41}H_{66}N_4O_{12}$ (806.98):** calcd (%): C 61.02, H 8.24, N 6.94; found (%): C 60.70, H 8.03, N 6.91.

3,5-Bis[L-(3-methylsulfanyl-1-propylcarbamoylpropyl)carbamic acid *tert*-butyl ester]benzoic acid (33a)



The L-methionine G1 dendron **32a** (2.18 g, 3.00 mmol) was dissolved in methanol/water/THF (3:1:1/v:v) under a nitrogen atmosphere, a 1 M KOH solution (24.0 ml, 24.0 mmol) was added, and the reaction mixture was subsequently heated to 40 °C for 12 h. After complete reaction (TLC), acetic acid was added to give a pH = 5, and the product subsequently extracted with DCM. The combined organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo*. Chromatographic workup (silica gel, DCM cont. 4 % methanol as eluent) gave the desired product **33a** (1.68 g, 2.40 mmol, 80.0 %) as a colorless foam.

***R*$_f$** = 0.11 (DCM/methanol (19:1/v:v)).

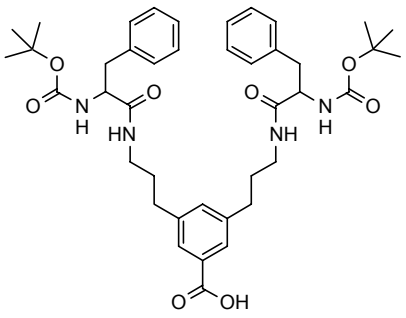
M.p. 89 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.48 (s, 18 H, CCH_3), 1.88 (m, 4 H, CH_2), 1.91 (m, 2 H, $CHCH_2$), 2.03 (m, 2 H, $CHCH_2$), 2.08 (s, 6 H, SCH_3), 2.53 (m, 4 H, SCH_2), 2.67 (t, ^3J (H,H) = 7.8 Hz, 4 H, CH_2Ar), 3.22 (m, 4 H, CH_2N), 4.14 (t, ^3J (H,H) = 6.7 Hz, 2 H, CH), 7.30 (s, 1 H, Ar*H*), 7.69 (s, 2 H, Ar*H*), 8.05 (m, br, 2 H, CONH).

^{13}C NMR (63 MHz, CD_3OD): δ = 15.39 (SCH_3), 28.71 (CCH_3), 31.15 (CH_2), 31.15 (CH_2), 31.85 (CH_2), 32.95 (CH_2), 33.59 (CH_2), 55.12 (CH), 80.68 (CCH_3), 128.31 (Ar*C*), 131.98 (Ar*C*), 134.37 (Ar*C*), 143.22 (Ar*C*), 157.51 (CON_{Boc}), 169.98 (CON), 174.43 (COO).

MS (FAB+, MNBA/DCM): *m/z* (%): 699 (4.8) $[M+H]^+$, 599 (7.9) $[M-C_5H_8O_2+H]^+$, 499 (23.5) $[M-2\cdot(C_5H_8O_2)+H]^+$, 57 (100) $[C_4H_9]^+$;
monoisotopic mass calcd for $\mathbf{C_{33}H_{55}N_4O_8S_2^+}$: 699.4, found: 699.5 $[M+H]^+$.

3,5-Bis[L-(2-phenyl-1-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]benzoic acid (33b)



To a solution of the phenylalanine G1 dendron **32b** (1.29 g, 1.70 mmol) in methanol/water/THF (3:1:1), a 1 M KOH solution (13.6 ml, 13.6 mmol) was added, and the reaction mixture was stirred at 50 °C for 12 h. After complete saponification (TLC), acetic acid was added to give pH = 5. The product was subsequently extracted with DCM, and the organic phases were dried with magnesium sulfate. Evaporation of the solvent and subsequent chromatographic purification (silica gel, DCM cont. 4% methanol) afforded the G1 acid **33b** (1.15 g, 1.57 mmol, 92.4 %) as a colorless foam.

$\boldsymbol{R_f}$ = 0.25 (DCM/methanol (19:1/v:v)).

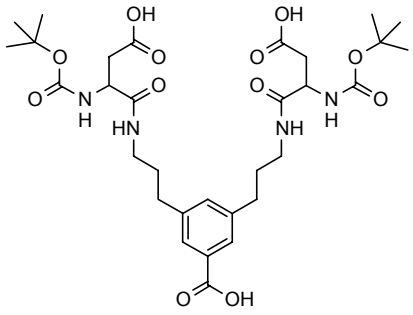
M.p. 152 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.41 (s, 18 H, CCH_3), 1.75 (m, 4 H, CH_2), 2.59 (t, ^{3}J (H,H) = 7.7 Hz, 4 H, CH_2Ar), 2.90 (m, 2 H, CHC*H*$_2$), 3.06 (m, 2 H, CHC*H*$_2$), 3.19 (m, 4 H, CH_2N), 4.32 (t, ^{3}J (H,H) = 7.3 Hz, 2 H, CH), 7.25 (s, 1 H, Ar*H*), 7.28 (m, 10 H, ArH_{phe}), 7.70 (s, 2 H, Ar*H*), 8.00 (m, br, CONH).

^{13}C NMR (63 MHz, CD_3OD): δ = 28.67 (C*C*H$_3$), 31.88 (CH_2), 33.65 (CH_2), 39.52 (CH_2), 39.84 (CH_2), 57.62 (CH), 80.66 (*C*CH$_3$), 127.75 (Ar*C*), 128.37 (Ar*C*), 129.44 (Ar*C*), 130.39 (Ar*C*), 132.11 (Ar*C*), 134.46 (Ar*C*), 138.55 (Ar*C*), 143.46 (Ar*C*), 157.46 (CON$_{Boc}$), 170.09 (CON), 174.17 (COO).

MS (FAB+, MNBA/DCM): *m/z* (%): 753 (6.9) $[M+Na]^+$, 731 (14.2) $[M+H]^+$, 631 (19.6) $[M-C_5H_8O_2+H]^+$, 531 (67.8) $[M-2\cdot(C_5H_8O_2)+H]^+$, 120 (100) $[C_8H_{10}N]^+$, 57 (38.2) $[C_4H_9]^+$;
monoisotopic mass calcd for $\mathbf{C_{41}H_{54}N_4NaO_8^+}$: 753.4, found: 753.5 $[M+Na]^+$.

3,5-Bis(L-3-*tert*-butoxycarbonylamino-*N*-propylsuccinamic acid)benzoic acid (33c)



To a solution of the protected aspartic acid dendron **32c** (1.61 g, 2.00 mmol) in methanol/water/THF (3:1:1), a 1 M KOH solution (16 ml, 16 mmol) was added, and the reaction mixture was stirred at 40 °C for 6 - 12 h. The reaction was continuously monitored by TLC. Acetic acid was added to give a pH = 5, and the product subsequently extracted with DCM. The united organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo*. Chromatographic workup (silica gel, DCM cont. 5 % methanol as eluent) gave the *t*Bu-deprotected acid **33c** (882 mg, 1.32 mmol, 66.0 %) as a colorless foam.

$\boldsymbol{R_f}$ = 0.17 (DCM/methanol (19:1/v:v)).

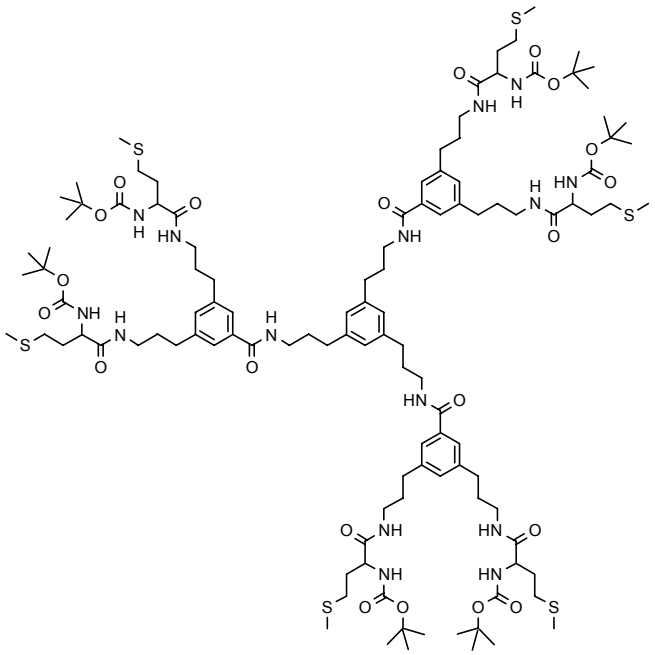
M.p. 78 °C.

^{1}H NMR (250 MHz, CD_3OD): δ = 1.40 (s, 18 H, CCH_3), 1.82 (m, 4 H, CH_2), 2.68 (m, 8 H, CH_2Ar + CH_2CH), 3.20 (q, ^3J (H,H) = 7.4 Hz, 4 H, CH_2N), 4.41 (t, br, ^3J (H,H) = 6.7 Hz, 2 H, CH), 7.29 (s, 1 H, Ar*H*), 7.71 (s, 2 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 25.84 (CCH_3), 32.03 (CH_2), 33.92 (CH_2), 36.11 (CH_2), 40.25 (CH_2), 52.27 (CH), 127.89 (Ar*C*), 132.05 (Ar*C*), 134.42 (Ar*C*), 143.29 (Ar*C*), 169.99 (CON), 174.12 (COO).

MS (FAB-, MNBA, methanol): *m/z* (%): 665 (100) $[M-H]^-$;
monoisotopic mass calcd for $\mathbf{C_{31}H_{45}N_4O_{12}^-}$: 665.3, found: 665.4 $[M-H]^-$.

(Boc-Met)$_6$6D1: **1,3,5-Tris{3,5-bis[L-(3-methylsulfanyl-1-propylcarbamoylpropyl)-carbamic acid *tert*-butyl ester]-*N*-propylbenzamide}benzene (34a)**



The G1 acid **33a** (1.10 g, 1.58 mmol) was dissolved in dry DCM under a nitrogen atmosphere. HOBt (246 mg, 1.61 mmol) was added, and the mixture was stirred at room temperature for 15 min. Afterwards the reaction mixture was cooled down to - 20 °C, EDC (323 mg, 1.68 mmol) was added, and the flask was allowed to warm up to room temperature while being stirred for additional 2 h. After the active ester had formed (TLC), the reaction was cooled down to - 30 °C, DIPEA (726 µl, 552 mg, 4.30 mmol), and the trishydrochloride core **5** (123 mg, 340 µmol), dissolved in 5 ml dry methanol, were added dropwise. The reaction mixture was stirred for additional 18 h, and during that time was allowed to warm up to room temperature slowly. After complete reaction (TLC), the mixture was washed twice with sodium hydrogencarbonate solution and once with brine. The organic layer was dried over magnesium sulfate, he solvent evaporated under reduced pressure and the crude product purified by column chromatography (silica gel, DCM cont. 2 % methanol as eluent) to afford the G1 dendrimer **34a** (421 mg, 184 µmol, 54.1 %) as a colorless foam.

R_f = 0.21 (DCM/methanol (19:1/v:v)).

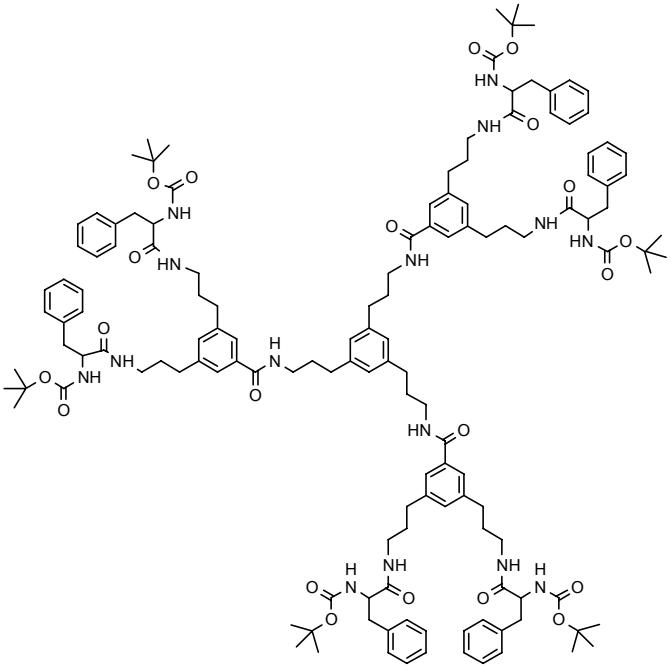
M.p. 171 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.39 (s, 54 H, CCH_3), 1.80 (m, 12 H, CH_2), 1.83 (m, 6 H, $CHCH_2$), 1.92 (m, 6 H, CH_2), 1.97 (m, 6 H, $CHCH_2$), 2.05 (s, 18 H, SCH_3), 2.49 (m, 12 H, SCH_2), 2.63 (m, 6 H + 12 H, CH_2Ar + CH_2S), 3.17 (m, 12 H, CH_2N), 3.38 (m, 6 H, CH_2N), 4.18 (m, br, 6 H, CH), 6.95 (s, 3 H, Ar*H*), 7.21 (s, 3 H, Ar*H*), 7.46 (s, 6 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 28.71 (CCH_3), 30.94 (CH_2), 31.34 (CH_2), 31.65 (CH_2), 32.84 (CH_2), 33.32 (CH_2), 33.95 (CH_2), 39.37 (CH_2), 40.48 (CH_2), 54.79 (CH), 80.66 (CCH_3), 125.75 (Ar*C*), 126.96 (Ar*C*), 132.53 (Ar*C*), 135.56 (Ar*C*), 142.67 (Ar*C*), 142.74 (Ar*C*), 157.09 (CON_{Boc}), 169.86 (CON), 173.90 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2330 $[M+K]^+$, 2313 $[M+Na]^+$;
monoisotopic mass calcd for $\mathbf{C_{114}H_{183}N_{15}NaO_{21}S_6^+}$: 2313.19, found: 2313.55.

(Boc-Phe)$_6$6D1: **1,3,5-Tris{3,5-bis[L-(2-phenyl-1-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]-*N*-propylbenzamide}benzene (34b)**



To a solution of the G1 acid **33b** (1.53 mg, 2.10 mmol) in a mixture of dry DCM/DMF (19:1/v:v) HOBt (297 mg, 2.20 mmol) was added, and the reaction mixture was stirred for 15 min at room temperature. The flask was cooled down to 0 °C, EDC (441 mg, 2.30 mmol) was added, and the solution was stirred for additional 2 h while warming up to room temperature. When the formation of the active ester was complete (TLC), the reaction mixture was cooled down to 5 °C again. Then DIPEA (1.03 ml, 763 mg, 5.90 mmol) and the trishydrochloride core **5** (179 mg, 500 µmol), dissolved in 5 ml of dry methanol, were added slowly. The reaction mixture was allowed to warm up to room temperature slowly while being stirred for additional 18 h. After complete reaction (TLC) the solution was washed twice with sodium hydrogencarbonate solution and once with brine, and the organic layer was dried over magnesium sulfate. Evaporation of the solvent under reduced pressure and purification by column chromatography (silica gel, DCM cont. 3 % methanol as eluent) gave the Boc-protected phenylalanine G1 dendrimer **34b** (575 mg, 241 µmol, 48.2 %) as a colorless foam.

$\boldsymbol{R_f}$ = 0.32 (DCM/methanol (19:1/v:v)).

M.p. 173 °C.

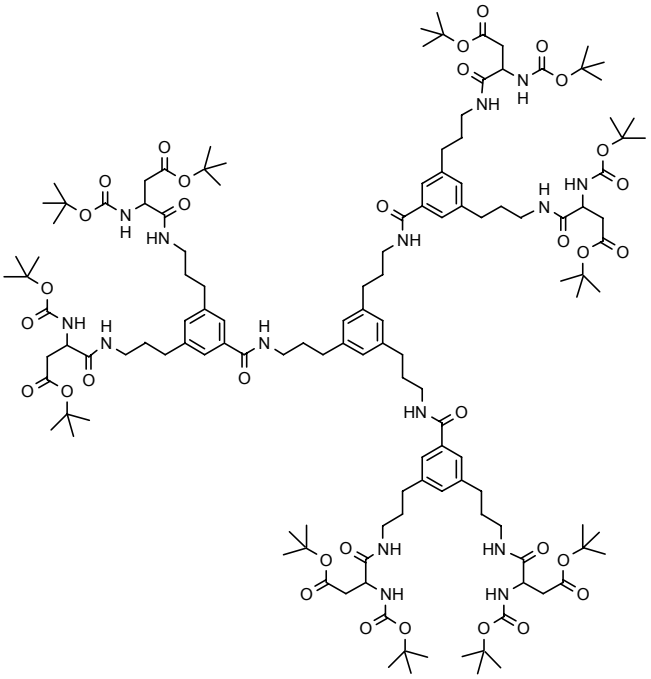
^{1}H NMR (500 MHz, $CDCl_3/CD_3OD$): δ = 1.37 (s, 54 H, CCH_3), 1.72 (m, 12 H, CH_2), 1.96 (m, 6 H, CH_2), 2.51 (t, br, 12 H, CH_2Ar), 2.66 (t, ^3J (H,H) = 7.5 Hz, 6 H, CH_2Ar), 2.96 (m, 6 H, $CHCH_2$), 3.03 (m, 6 H, $CHCH_2$), 3.11 (m, 12 H, CH_2N), 3.42 (m, 6 H, CH_2N), 4.31 (m, br, 6 H,

CH), 6.92 (s, 3 H, Ar*H*), 7.06 (s, 3 H, Ar*H*), 7.19 (m, 18 H, ArH_{phe}), 7.25 (m, 12 H, ArH_{phe}), 7.38 (s, 6 H, Ar*H*).

^{13}C NMR (126 MHz, CD_3OD): δ = 28.50 (C*C*H_3), 30.78 (CH_2), 31.30 (CH_2), 32.86 (CH_2), 33.61 (CH_2), 38.94 (CH_2), 39.21 (CH_2), 40.15 (CH_2), 56.47 (CH), 80.44 (*C*CH_3), 125.39 (Ar*C*), 126.68(Ar*C*), 127.20 (Ar*C*), 128.86 (Ar*C*), 129.43 (Ar*C*), 129.70 (Ar*C*), 132.18 (Ar*C*), 135.16 (Ar*C*), 137.32 (Ar*C*), 142.27 (Ar*C*), 156.41 (CON_{Boc}), 169.40 (CON), 172.90 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2425 $[M+K]^+$, 2409 $[M+Na]^+$;
monoisotopic mass calcd for $C_{114}H_{183}N_{15}NaO_{21}S_6^+$: 2409.36, found: 2409.36.

(Boc/tBu-Asp)$_6$6D1: **1,3,5-Tris[3,5-bis(L-3-*tert*-butoxycarbonylamino-*N*-propylsuccinamic acid *tert*-butyl ester)-*N*-propylbenzamide]benzene (34c)**



A solution of the L-aspartic acid hydroxysuccinimide ester **29c** (522 mg, 1.35 mmol) in dry DCM was cooled down to - 10 °C. The G1 dendrimer **26** (238 mg, 150 µmol), dissolved in dry methanol (3 ml), and DIPEA (153 µl, 116 mg, 900 µmol) were added dropwise. The solution was stirred at - 10 °C for 1 h, and was afterwards allowed to warm up to room temperature slowly while being stirred for additional 18 h. After complete reaction (TLC) the mixture was washed twice with sodium hydrogencarbonate solution and once with brine. The organic phase was dried over magnesium sulfate, the solvent subsequently evaporated *in vacuo*, and the crude product was purified by column chromatography (silica gel, DCM cont. 3 % methanol as eluent) to afford pure **34c** (269 mg, 106 µmol, 70.7 %) as a colorless foam.

R_f = 0.15 (DCM/methanol (19:1/v:v)).

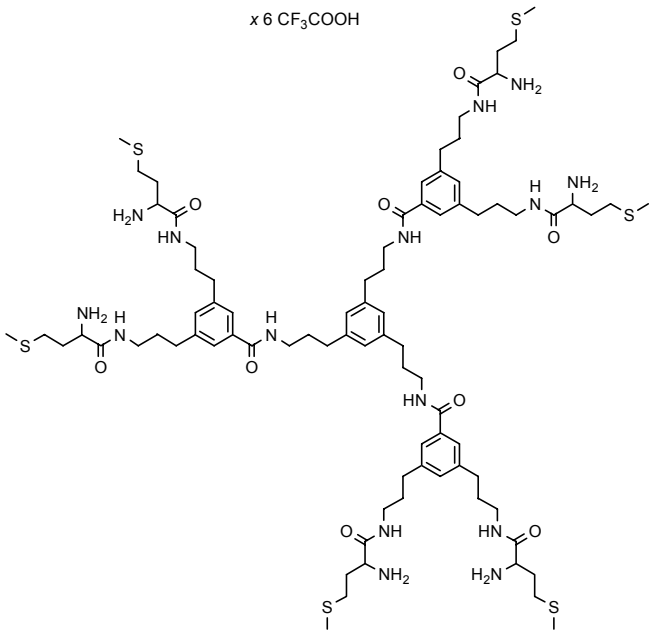
M.p. 107 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39 (s, 54 H, CC*H*$_3$), 1.41 (s, 54 H, CC*H*$_3$), 1.75 (m, 12 H, CH_2), 1.95 (m, 6 H, CH_2), 2.55 (t, ^3J (H,H) = 7.2 Hz, 12 H, CH_2Ar), 2.64 (t, ^3J (H,H) = 7.7 Hz, 6 H, CH_2Ar), 2.44 (dd, ^2J (H,H) = 16.7 Hz, ^3J (H,H) = 6.3 Hz, 6 H, CHC*H*$_2$), 2.79 (dd, ^2J (H,H) = 16.7 Hz, ^3J (H,H) = 5.2 Hz, 6 H, CHC*H*$_2$), 3.13 (m, 6 H, C*H*$_2$N), 3.19 (m, 6 H, C*H*$_2$N), 3.42 (m, 6 H, CH_2N), 4.42 (m, br, 6 H, CH), 5.80 (d, br, ^3J (H,H) = 7.7 Hz, 6 H, CHN*H*), 6.75 (t, br, ^3J (H,H) = 5.6 Hz, 6 H, CONH), 6.90 (s, 3 H, Ar*H*), 7.05 (s, 3 H, Ar*H*), 7.17 (t, br, 3 H, CONH), 7.37 (s, 6 H, Ar*H*).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.02 (C*C*H$_3$), 28.33 (C*C*H$_3$), 30.64 (CH_2), 30.78 (CH_2), 32.28 (CH_2), 33.07 (CH_2), 37.54 (CH_2), 38.43 (CH_2), 39.61 (CH_2), 51.01 (CH), 80.23 (*C*CH$_3$), 81.55 (*C*CH$_3$), 125.07 (Ar*C*), 126.34 (Ar*C*), 131.56 (Ar*C*), 134.86 (Ar*C*), 141.51 (Ar*C*), 141.69 (Ar*C*), 155.59 (CON$_{Boc}$), 167.95 (CON), 170.97 (CO$_{tBu}$), 171.06 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2570 $[M+K]^+$, 2554 $[M+Na]^+$;
monoisotopic mass calcd for **$C_{132}H_{207}N_{15}NaO_{33}^+$**: 2553.49, found: 2553.59.

(Met)$_6$6D1: **1,3,5-Tris[3,5-bis(L-2-amino-4-methylsulfanyl-*N*-propylbutyramide)-*N*-propylbenzamide]benzene hexatrifluoroacetate (35a)**



The Boc-protected G1 dendrimer **34a** (150 mg, 65.4 µmol) was dissolved in a 'cleavage cocktail' mixture (10 ml) containing DCM/TFA/EDT/thioanisole/methanol/TIPS (50:37.5:5:5:2:0.5/v:v) under a nitrogen atmosphere, and stirred for 1 h at room temperature. After complete deprotection (TLC), the 'cleavage cocktail' mixture was removed by repeated evaporation under reduced pressure by using methanol as solvent. The residue was dried under high vacuum, and lyophilization from water afforded the desired product **35a** (150 mg, 63.1 µmol, 96.5 %) as a colorless solid.

M.p. 91-92 °C.

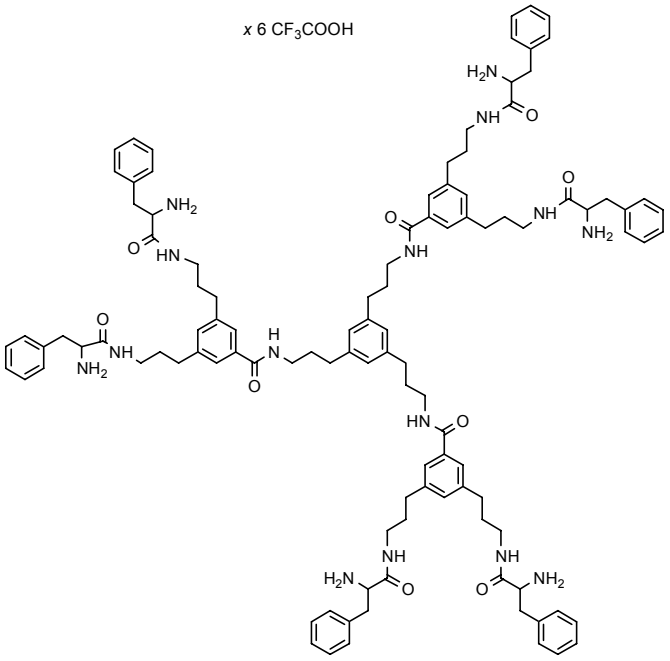
^{1}H NMR (500 MHz, CD_3OD): δ = 1.91 (m, 12 H, CH_2), 1.97 (m, 6 H, CH_2), 2.14 (s, 18 H, SCH_3), 2.13 (m, 6 H, CHC*H*$_2$), 2.17 (m, 6 H, CHC*H*$_2$), 2.61 (m, 12 H, CH_2S), 2.69 (m, 6 H, CH_2Ar), 2.72 (m, 12 H, CH_2Ar), 3.28 (m, 6 H, C*H*$_2$N), 3.33 (m, 6 H, C*H*$_2$N), 3.43 (t, ^3J = (H,H) = 7.1 Hz, 6 H, CH_2N), 4.00 (t, ^3J (H,H) = 6.6 Hz, 6 H, CH), 6.97 (s, 3 H, Ar*H*), 7.28 (s, 3 H, Ar*H*), 7.51 (s, 6 H, Ar*H*).

^{13}C NMR (126 MHz, CD_3OD): δ = 15.47 (SCH_3), 30.25 (SCH_2), 32.16 (CH_2), 32.41 (CH_2), 32.46 (CH*C*H$_2$), 34.22 (*C*H$_2$Ar), 34.61 (*C*H$_2$Ar), 40.55 (CH_2N), 41.12 (CH_2N), 54.08 (CH), 126.37 (Ar*C*), 127.61 (Ar*C*), 133.13 (Ar*C*), 136.49 (Ar*C*), 143.51 (Ar*C*), 143.75 (Ar*C*), 170.04 (CON), 170.77 (CON).

MS (MALDI-TOF, CCA): *m/z:* 1691 $[M+H]^+$;
monoisotopic mass calcd for **$C_{84}H_{136}N_{15}O_9S_6^+$**: 1690.90, found: 1690.91 $[M+H]^+$.

(Phe)$_6$6D1: **1,3,5-Tris[3,5-bis(L-2-amino-3-phenyl-*N*-propylpropionamide)-*N*-propyl-benzamide]benzene hexatrifluoroacetate (35b)**

To a solution of the Boc-protected G1 dendrimer **34b** (24 mg, 10 µmol) in DCM (4 ml), TFA (1.5 ml) was added, and the reaction mixture was stirred for 1 h at room temperature. When cleavage of the Boc protecting group was complete (TLC), the solvent was removed *in vacuo* to yield the deprotected G1 L-phenylalanine dendrimer **35b** (25 mg, 9.9 µmol, 99 %) after lyophilization from water.



M.p. 126-127 °C.

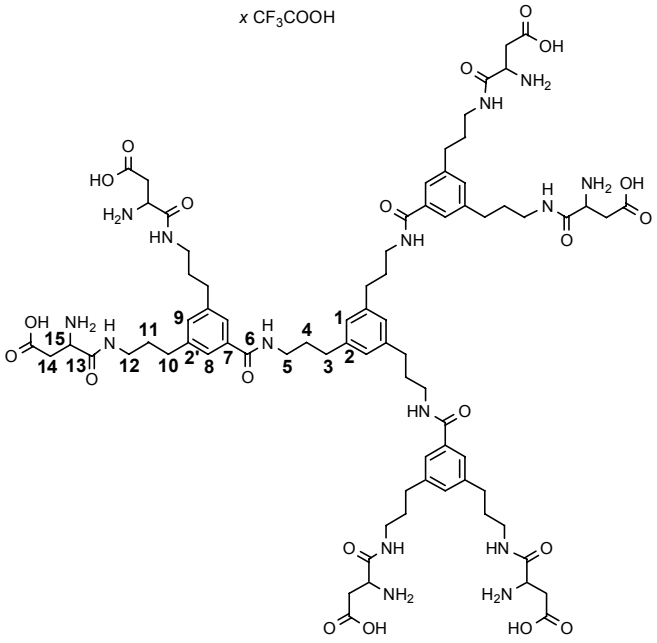
^{1}H NMR (500 MHz, CD_3OD): δ = 1.74 (m, 12 H, CH_2), 1.96 (m, 6 H, CH_2), 2.56 (t, ^3J (H,H) = 7.6 Hz, 12 H, CH_2Ar), 2.69 (t, ^3J (H,H) = 7.5 Hz, 6 H, CH_2Ar), 3.13 (m, 12 H, CHC*H*$_2$), 3.16 (m, 6 H, CH_2N), 3.27 (m, 6 H, CH_2N), 3.43 (t, ^3J (H,H) = 7.1 Hz, 6 H, CH_2N), 4.08 (t, ^3J (H,H) = 7.5 Hz, 6 H, CH), 6.97 (s, 3 H, Ar*H*), 7.16 (s, 3 H, Ar*H*), 7.29 (m, 18 H, ArH_{phe}), 7.35 (m, 12 H, ArH_{phe}), 7.45 (s, 6 H, Ar*H*).

^{13}C NMR (126 MHz, CD_3OD): δ = 31.95 (CH_2), 32.49 (CH_2), 34.08 (CH_2Ar), 34.63 (CH_2Ar), 39.05 (CH_2), 40.44 (CH_2N), 41.13 (CH_2N), 56.18 (CH), 126.32 (Ar*C*), 127.61 (Ar*C*), 129.14 (ArC_{phe}), 130.37 (ArC_{phe}), 130.80 (ArC_{phe}), 133.08 (Ar*C*), 136.01 (ArC_{phe}), 136.42 (Ar*C*), 143.54 (Ar*C*), 143.68 (Ar*C*), 169.75 (CON), 170.80 (CON).

MS (MALDI-TOF, CCA): *m/z:* 1825 $[M+K]^+$, 1809 $[M+Na]^+$, 1787 $[M+H]^+$;
monoisotopic mass calcd for **$C_{108}H_{136}N_{15}O_9^+$**: 1787.06, found: 1787.21.

(Asp)$_6$6D1: **1,3,5-Tris[3,5-bis(L-3-amino-*N*-propylsuccinamic acid)-*N*-propylbenzamide]-benzene hexatrifluoroacetate (35c)**

To a solution of dendrimer **20c** (101 mg, 40.0 µmol) in DCM (2 ml), TFA (2 ml) was added, and the solution was stirred at room temperature for 1 h. When the deprotection was complete (TLC), the solvent was repeatedly removed *in vacuo*. Lyophilization from water afforded the deprotected L-aspartic acid dendrimer **35c** (91 mg, 40 µmol, 100 %) as a colorless solid.



M.p. 155-156 °C.

^{1}H NMR (500 MHz, CD_3OD):
δ = 1.89 (m, 12 H, *H*-11), 1.97 (m, 6 H, *H*-4), 2.71 (m, 18 H, *H*-3 + *H*-10), 2.93 (dd, ^2J (H,H) = 17.8 Hz, ^3J (H,H) = 7.9 Hz, 6 H, *H*-15,15'), 3.00 (dd, ^2J (H,H) = 17.8 Hz, ^3J (H,H) = 5.0 Hz, 6 H, *H*-15',15), 3.26 (m, 6 H, *H*-12,12'), 3.32 (m, 6 H, *H*-12,12'), 3.38 (t, ^3J (H,H) = 7.1 Hz, 6 H, *H*-5), 4.17 (m, 6 H, *H*-14), 6.92 (s, 3 H, *H*-1), 7.23 (s, 3 H, *H*-9), 7.45 (s, 6 H, *H*-8).

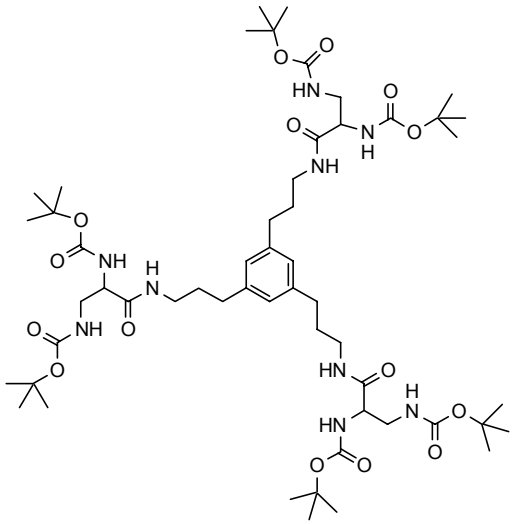
^{13}C NMR (126 MHz, CD_3OD): δ = 32.08 (*C*-11), 32.38 (*C*-4), 34.07 (C-10), 34.65 (C-3), 36.52 (*C*-15), 40.54 (*C*-12), 41.22 (*C*-5), 51.51 (*C*-14), 126.37 (*C*-8), 127.62 (*C*-1), 133.26 (*C*-9), 136.41 (*C*-7), 143.52 (*C*-2,2'), 143.77 (*C*-2',2), 169.41 (*C*-13), 170.83 (*C*-6), 173.02 (*C*-16).

MS (MALDI-TOF, CCA): *m/z:* 1595 $[M+H]^+$;

monoisotopic mass calcd for $\mathbf{C_{78}H_{112}N_{15}O_{21}}^+$: 1594.82, found: 1594.85 $[M+H]^+$.

7.4.3 Compounds of chapter 4.2.3

(Boc-Dpa)$_3$3D0: **1,3,5-Tris[(2-*tert*-butoxycarbonylamino-1-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]benzene (38)**



A solution of **37** (4.11 g, 13.5 mmol) in a mixture of dry DCM/DMF (14:1/v:v) was cooled down to - 20 °C. DIPEA (2.30 ml, 1.74 g, 13.5 mmol) and a solution of TBTU (4.43 g, 14.1 mmol) in DMF were added slowly and allowed to warm to room temperature. The reaction mixture was stirred at room temperature for additional 30 min, cooled down to - 20 °C again, followed by the dropwise addition of DIPEA (3.80 ml, 2.91 g, 22.5 mmol) and a solution of the trishydrochloride core **5** (1.08 g, 3.00 mmol) in dry methanol. The mixture was stirred for additional 12 h and during that time allowed to warm to room temperature. After complete reaction (TLC), the mixture was washed twice with sodium hydrogencarbonate solution, once with brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure and column chromatography (silica gel, DCM cont. 4 % methanol as eluent) afforded the desired product **38** (2.66 g, 2.40 mmol, 80.0 %) as a colorless foam.

R_f = 0.21 (DCM/methanol (19:1/v:v)).

M.p. 113 °C.

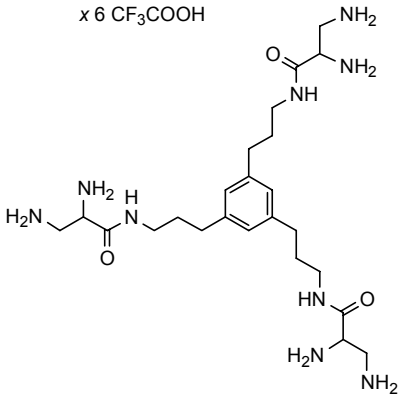
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 27 H, CH_3), 1.40 (s, 27 H, CH_3), 1.79 (m, 6 H, CH_2), 2.54 (t, ^3J (H,H) = 7.0 Hz, 6 H, CH_2Ar), 3.14 (m, 6 H, CH_2N), 3.44 (m, 6 H, $CHCH_2$), 4.26 (m, br, 3 H, CH), 5.56 (s, br, 3 H, NH_{Boc}), 6.05 (s, br, 3 H, NH_{Boc}), 6.79 (s, 3 H, Ar*H*), 7.08 (s, br, 3 H, CONH).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.30 (CCH_3), 30.39 (CH_2), 32.08 (CH_2Ar), 38.14 (CH_2N), 42.56 ($CHCH_2$), 55.60 (CH), 77.25 (CCH_3), 79.66 (CCH_3), 126.52 (Ar*C*), 141.14 (Ar*C*), 156.10 (CON_{Boc}), 157.05 (CON_{Boc}), 170.75 (CON).

MS (FAB+, MNBA/DCM/methanol): *m/z* (%): 1131 (0.9) $[M+Na]^+$, 1009 (4.8) $[M-C_5H_8O_2+H]^+$, 609 (2.2) $[M-5\cdot(C_5H_8O_2)+H]^+$, 508 (21.2) $[M-6\cdot(C_5H_8O_2)]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{54}H_{93}N_9O_{15}$ (1008.37):** calcd (%): C 58.52, H 8.46, N 11.37; found (%): C 58.31, H 8.23, N 11.33.

(Dpa)$_3$3D0: **1,3,5-Tris(2,3-diamino-*N*-propylpropionamide)benzene hexatrifluoroacetate (39)**



To a solution of the Boc-protected diaminopropionic acid G0 dendrimer **38** (554 mg, 500 µmol) in DCM (10 ml) TFA (5 ml) was added, and the mixture was stirred for 1 h at room temperature. After complete reaction (TLC) the solvent and the excess of TFA were removed *in vacuo*. Lyophilization from water yielded deprotected **39** (595 mg, 499 µmol, 99.8 %) as a colorless solid.

M.p. 101-103 °C.

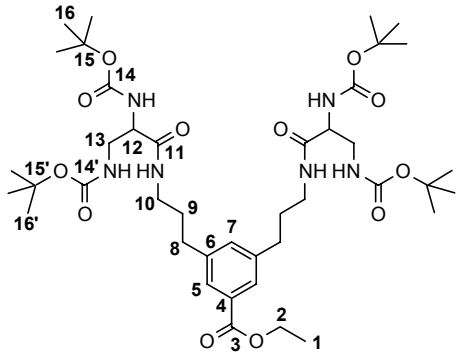
^{1}H NMR (500 MHz, CD_3OD): δ = 1.89 (m, 6 H, CH_2), 2.66 (t, ^3J (H,H) = 7.7 Hz, 6 H, CH_2Ar), 3.25 (m, 3 H, CH_2N), 3.38 (m, 3 H, CHCH_2), 3.40 (m, 3 H, CH_2N), 3.47 (dd, ^2J (H,H) = 13.7 Hz, ^3J (H,H) = 5.5 Hz, 3 H, CHCH_2), 4.19 (t, ^3J (H,H) = 6.0 Hz, 3 H, CH), 6.94 (s, 3 H, Ar*H*).

^{13}C NMR (63 MHz, CD_3OD): δ = 31.77 (s, CH_2), 33.97 (s, CH_2Ar), 40.65 (s, CH_2N), 41.13 (s, $CHCH_2$), 52.23 (s, CH), 118.03 (q, ^1J (C,F) = 294.4 Hz, *C*F_3CO_2H), 127.34 (s, Ar*C*), 142.97 (s, Ar*C*), 163.35 (q, ^2J (C,F) = 34.2 Hz, CF_3CO_2H), 166.99 (s, CON).

MS (FAB+, MNBA/DMSO): *m/z* (%): 640 (1.1) $[M+Cs]^+$, 508 (3.2) $[M+H]^+$.

EA for **$C_{36}F_{18}H_{51}N_9O_{15}$ (1191.81):** calcd (%): C 36.28, H 4.31, N 10.58; found (%): C 35.89, H 4.38, N 10.70.

Ethyl-3,5-bis[(2-*tert*-butoxycarbonylamino-2-propylcarbamoylethyl)carbamic acid *tert*-butyl ester]benzoate (40)



A solution of the Boc-protected diaminopropionic acid **37** (3.96 g, 13.0 mmol) in a solvent mixture of dry DCM/DMF (29:1/v:v) was cooled down to - 20 °C. Under vigorous stirring TBTU (4.34 g, 13.5 mmol), dissolved in DMF, and DIPEA (2.21 ml, 1.68 g, 13.0 mmol) were added slowly. The reaction mixture was stirred at - 20 °C for additional 30 min, and was then allowed to warm up to room temperature. After complete formation of the active ester (TLC), the reaction mixture was cooled down to - 20 °C again. The G1 hydrochloride **15** (1.69 g, 5.00 mmol) was dissolved in a small amount of dry methanol, and, together with DIPEA (3.91 ml, 2.97 g, 23.0 mmol), was added to the reaction mixture slowly. The solution was stirred for additional 30 min at - 20 °C, and was then allowed to warm up to room temperature slowly. After being stirred for additional 12 h the solution was washed twice with sodium hydrogencarbonate solution, and once with brine. The organic phase was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product was purified by column chromatography (silica gel, DCM cont. 3 % methanol as eluent) to give the desired product **40** (3.79 g, 4.52 mmol, 90.4 %) as a colorless solid.

R_f = 0.31 (DCM/methanol (19:1/v:v)).

M.p. 147 °C.

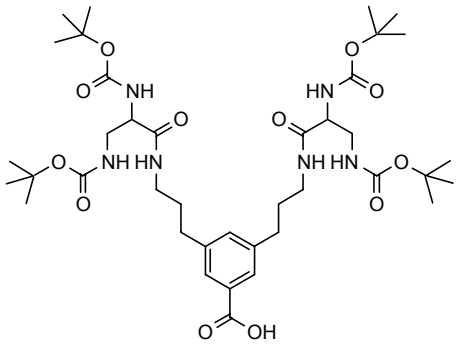
^{1}H NMR (250 MHz, [D$_7$] DMF): δ = 1.40 (t, ^3J (H,H) = 7.2 Hz, 3 H, CH_2CH_3), 1.43 (s, 18 H, CCH_3), 1.45 (s, 18 H, CCH_3), 1.86 (m, 4 H, CH_2), 2.75 (t, ^3J (H,H) = 8.2 Hz, 4 H, CH_2Ar), 3.27 (m, 4 H, CH_2N), 3.46 (m, 4 H, $CHCH_2$), 4.25 (m, 2 H, CH), 4.39 (q, ^3J (H,H) = 7.3 Hz, 2 H, CH_2CH_3), 6.73 (d, br, ^3J (H,H) = 7.3 Hz, 2 H, CHN*H*), 6.86 (t, br, 2 H, NH_{Boc}), 7.45 (s, 1 H, Ar*H*), 7.74 (s, 2 H, Ar*H*), 8.14 (t, br, 2 H, CON*H*).

^{13}C NMR (126 MHz, [D$_7$] DMF): δ = 14.52 (*C*-1), 28.44 (*C*-16,16'), 31.88 (*C*-9), 33.16 (*C*-8), 39.15 (*C*-10), 42.98 (*C*-13), 56.37 (*C*-12), 61.30 (*C*-2), 78.74 (*C*-15,15'), 78.99 (*C*-15',15), 127.39 (*C*-5), 131.19 (*C*-7), 134.25 (*C*-4), 143.47 (*C*-6), 156.28 (*C*-14,14'), 157.08 (*C*-14',14), 166.89 (*C*-11), 171.04 (*C*-3).

MS (FAB+, MNBA/DCM): *m/z* (%): 859 (1.8) $[M+Na]^+$, 837 (1.1) $[M+H]^+$, 737 (6.1) $[M-C_5H_8O_2+H]^+$, 637 (2.0) $[M-2\cdot(C_5H_8O_2)+H]^+$, 537 (3.9) $[M-3\cdot(C_5H_8O_2)+H]^+$, 57 (100) $[C_4H_9]^+$.

EA for **$C_{41}H_{68}N_6O_{12}$ (837.01):** calcd (%): C 58.83, H 8.19, N 10.04; found (%): C 58.62, H 7.96, N 10.05.

3,5-Bis[(2-*tert*-butoxycarbonylamino-2-propylcarbamoylethyl)-carbamic acid *tert*-butyl ester]benzoic acid (41)



To a solution of the G1 ester **40** (3.87 g, 4.60 mmol) in methanol/THF/water (3:1:1) KOH (2.08 g, 37.0 mmol) was added, and the reaction mixture was stirred for 12 h at 50 °C. After complete reaction (TLC) acetic acid was added to give pH = 5, and the desired product was subsequently extracted with DCM. The combined organic layers were dried over magnesium sulfate, and the solvent was evaporated *in vacuo*. Chromatographic separation (silica gel, DCM cont. 5 % methanol as eluent) gave the G1 acid **41** (3.22 g, 3.98 mmol, 86.5 %) as a colorless solid.

R_f = 0.38 (DCM/methanol (19:1/v:v)).

M.p. 118 °C.

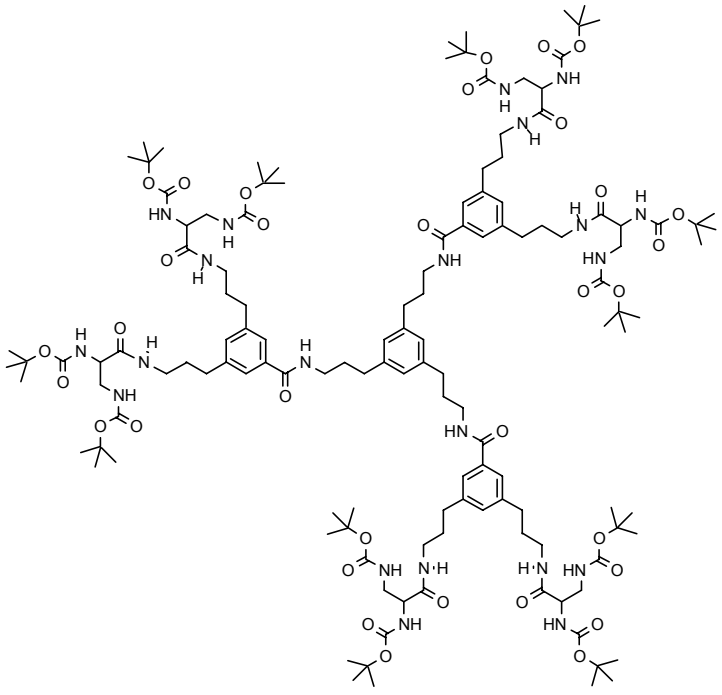
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.37 (s, 18 H, CCH_3), 1.40 (s, 18 H, CCH_3), 1.80 (m, 4 H, CH_2), 2.60 (t, br, 4 H, CH_2Ar), 3.16 (m, 4 H, CH_2N), 3.42 (m, 2 H, $CHCH_2$), 3.47 (m, 2 H, $CHCH_2$), 4.32 (m, 2 H, CH), 5.61 (s, br, 2 H, NH), 6.13 (d, br, 2 H, NH), 7.19 (s, 1 H, Ar*H*), 7.30 (s, br, 2 H, NH), 7.65 (s, 2 H, Ar*H*).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.30 (CCH_3), 30.33 (CH_2), 32.09 (CH_2), 38.14 (CH_2), 42.48 (CH_2), 55.41 (CH), 79.75 (CCH_3), 80.14 (CCH_3), 127.66 (Ar*C*), 130.14 (Ar*C*), 134.25 (Ar*C*), 141.51 (Ar*C*), 156.14 (CON_{Boc}), 157.07 (CON_{Boc}), 169.53 (COO), 170.96 (COO).

MS (FAB+, MNBA/DCM/methanol): *m/z* (%): 831 (1.3) $[M+Na]^+$, 809 (0.1) $[M+H]^+$, 709 (1.5) $[M-C_5H_8O_2+H]^+$, 609 (0.8) $[M-2\cdot(C_5H_8O_2)+H]^+$, 509 (1.7) $[M-3\cdot(C_5H_8O_2)+H]^+$, 409 (20.8) $[M-4\cdot(C_5H_8O_2)+H]^+$, 57 (100) $[C_4H_9]^+$.

EA for $C_{39}H_{64}N_6O_{12}$ **(808.96):** calcd (%): C 57.90, H 7.97, N 10.39; found (%): C 57.64, H 7.96, N 10.28.

(Boc-Dpa)$_6$6D1: **1,3,5-Tris{3,5-bis[(2-*tert*-butoxycarbonylamino-2-propylcarbamoyl-ethyl)carbamic acid *tert*-butyl ester]-*N*-propylbenzamide}benzene (42)**



The G1 acid **41** (1.46 g, 1.80 mmol) was dissolved in a solvent mixture of dry DCM/DMF (14:1/v:v), and cooled down to - 10 °C. TBTU (607 mg, 1.90 mmol), dissolved in a small amount of DMF, and DIPEA (306 µl, 233 mg, 1.80 mmol) were added slowly under vigorous stirring. The reaction mixture was allowed to warm up to room temperature, and stirred at room temperature for additional 30 min. After complete formation of the active ester (TLC) the reaction mixture was cooled down to 0 °C, and the trishydrochloride core **5** (144 mg, 400 µmol), dissolved in a small amount of dry methanol, and DIPEA (510 µl, 388 mg, 3.00 mmol) were added dropwise. The mixture was allowed to warm up to room temperature slowly, and was then stirred for additional 18 h. After the reaction was finished (TLC), the solution was washed once with sodium hydrogencarbonate solution, and once with brine. The organic phase was dried with magnesium sulfate. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography (silica gel, DCM cont. 5 % methanol as eluent) to yield the G1 dendrimer **42** (601 mg, 229 µmol, 57.3 %) as a colorless solid.

R_f = 0.23 (DCM/methanol (9:1/v:v)).

M.p. 141 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.44 (s, 54 H, CCH_3), 1.47 (s, 54 H, CCH_3), 1.86 (m, 12 H, CH_2), 1.97 (m, 6 H, CH_2), 2.68 (m, 18 H, CH_2Ar), 3.22 (m, 12 H, CH_2N), 3.32 (m, 6 H,

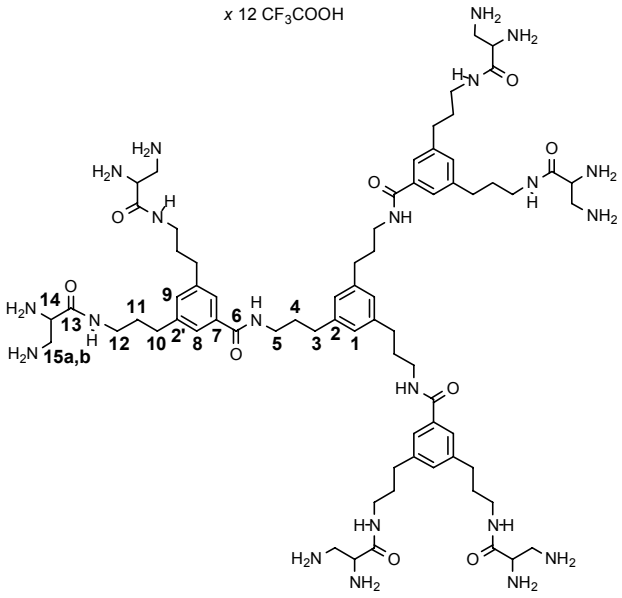
CHC*H*$_2$), 3.41 (m, 6 H, CHC*H*$_2$), 3.43 (m, 6 H, CH$_2$N), 4.20 (m, br, 6 H, CH), 6.96 (s, 3 H, Ar*H*), 7.26 (s, 3 H, Ar*H*), 7.48 (s, 3 H, Ar*H*).

^{13}C NMR (126 MHz, CD$_3$OD): δ = 29.08 (C*C*H$_3$), 32.23 (CH$_2$), 32.43 (CH$_2$), 33.98 (CH$_2$Ar), 34.61 (CH$_2$Ar), 40.04 (CH$_2$N), 41.07 (CH$_2$N), 43.52 (CH*C*H$_2$), 57.21 (CH), 80.77 (*C*CH$_3$), 81.10 (*C*CH$_3$), 126.44 (Ar*C*), 127.64 (Ar*C*), 133.36 (Ar*C*), 136.31 (Ar*C*), 143.49 (Ar*C*), 143.73 (Ar*C*), 157.98 (CON$_{Boc}$), 158.96 (CON$_{Boc}$), 170.71 (CON), 173.25 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2660 [M+K]$^+$, 2644 [M+Na]$^+$;
monoisotopic mass calcd for **$C_{132}H_{213}N_{21}NaO_{33}^+$**: 2643.55, found 2643.77 [M+Na]$^+$.

(Dpa)$_6$6D1: 1,3,5-Tris[3,5-bis(2,3-diamino-*N*-propylpropionamide)-*N*-propylbenzamide]-benzene dodecatrifluoroacetate (43)

To a vigorously stirred solution of dendrimer **42** (105 mg, 40.0 µmol) in DCM (5 ml) TFA (5 ml) was added. The reaction mixture was stirred for 1 h at room temperature. When deprotection was complete (TLC) the solvent was removed *in vacuo* and the desired product lyophilized from water. The procedure yielded the deprotected G1 dendrimer **43** (110 mg, 39.4 µmol, 98.5 %) as a colorless solid.



M.p. 119-121 °C.

^{1}H NMR (500 MHz, CD$_3$OD): δ = 1.92 (m, 18 H, *H*-11 + *H*-4), 2.68 (t, ^3J (H,H) = 7.4 Hz, 6 H, *H*-3), 2.73 (t, ^3J (H,H) = 7.6 Hz, 12 H, *H*-10), 3.25 (m, 6 H, *H*-5), 3.43 (m, 12 H, *H*-12), 3.45 (dd, ^2J (H,H) = 13.9 Hz, ^3J (H,H) = 6.3 Hz, 6 H, *H*-15a), 3.52 (dd, ^2J (H,H) = 13.9 Hz, ^3J (H,H) = 5.4 Hz, 6 H, *H*-15b), 4.29 (t, ^3J (H,H) = 5.8 Hz, 6 H, *H*-14), 6.96 (s, 3 H, *H*-1), 7.29 (s, 3 H, *H*-9), 7.51 (s, 6 H, *H*-8).

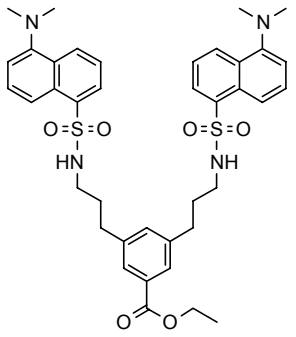
^{13}C NMR (126 MHz, CD$_3$OD): δ = 31.86 (s, *C*-11), 32.37 (s, *C*-4), 34.15 (s, *C*-10), 34.61 (s, *C*-3), 40.85 (s, *C*-5), 41.13 (s, *C*-12), 41.47 (s, *C*-15), 52.55 (s, *C*-14), 118.36 (q, ^1J (C,F) = 292.5 Hz, *C*F$_3$CO$_2$H), 126.36 (s, *C*-8), 127.61 (s, *C*-1), 133.21 (s, *C*-9), 136.43 (s,

C-7), 143.51 (s, *C*-2,2'), 143.73 (s, *C*-2',2), 163.49 (q, ^{2}J (C,F) = 35.4 Hz, CF_3CO_2H), 167.48 (s, *C*-6), 170.84 (s, *C*-13).

MS (MALDI-TOF, CCA): *m/z:* 1459 $[M+K]^+$, 1443 $[M+Na]^+$, 1421 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{72}H_{118}N_{21}O_9^+}$: 1420.94, found: 1420.93.

7.4.4 Compounds of chapter 4.2.4

Ethyl-3,5-bis[3-(5-dimethylaminonaphthalene-1-sulfonylamino)propyl]benzoate (44)



A solution of dry triethylamine (1.25 ml, 911 mg, 9.00 mmol) and the bishydrochloride dendron **15** (506 mg, 1.5 mmol) were dissolved in a small amount of dry methanol and added dropwise at room temperature to a solution of 5-dimethylamino-naphthalene-1-sulfonyl chloride (dansyl chloride) (1.21 g, 4.50 mmol) in dry DCM. The reaction was continuously monitored by TLC and stirred in the dark for 1 h. After complete reaction (TLC) the solution was washed once with brine, once with saturated sodium carbonate solution, and once again with brine. The organic phase was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by column chromatography (silica gel, hexane/ethyl acetate (2:1/v:v) as eluent). The procedure yielded the dansylated G1 dendron **44** (1.05 g, 1.44 mmol, 96.0 %) as a bright yellow oil which could be lyophilized from dioxane.

$\boldsymbol{R_f}$ = 0.27 (hexane/ethyl acetate (2:1/v:v)).

M.p. 75-76 °C.

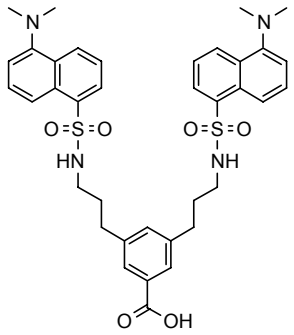
^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34 (t, ^3J (H,H) = 7.4 Hz, 3 H, CH_3), 1.66 (m, 4 H, CH_2), 2.47 (t, ^3J (H,H) = 7.4 Hz, 4 H, CH_2Ar), 2.88 (m, 4 H, CH_2N), 2.89 (s, 12 H, NCH_3), 4.31 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH_3), 5.11 (t, br, 2 H, NH), 6.84 (s, 1 H, Ar*H*), 7.19 (d, ^3J (H,H) = 7.4 Hz, 2 H, ArH_{Dns}), 7.50 (s, 2 H, Ar*H*), 7.51 (m, 4 H, ArH_{Dns}), 8.20 (d, ^3J (H,H) = 7.4 Hz, 2 H, ArH_{Dns}), 8.33 (d, ^3J (H,H) = 8.8 Hz, 2 H, ArH_{Dns}), 8.56 (d, ^3J (H,H) = 8.8 Hz, 2 H, ArH_{Dns}).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 14.33 (CH_3), 31.03 (CH_2), 32.24 (CH_2Ar), 42.61 (CH_2N), 45.56 (NCH_3), 60.91 (CH_2CH_3), 115.54 (ArC_{Dns}), 119.58 (ArC_{Dns}), 123.56 (ArC_{Dns}), 127.11 (Ar*C*), 128.30 (ArC_{Dns}), 129.60 (ArC_{Dns}, 3 signals), 130.16 (ArC_{Dns}), 130.78 (Ar*C*), 133.11 (Ar*C*), 135.05 (ArC_{Dns}), 141.36 (Ar*C*), 150.87 (ArC_{Dns}), 166.59 (CO).

MS (EI, 80 eV, 300 °C): *m/z* (%): 730 (55.2) $[M]^+$, 259 (10.6) $[C_{12}H_{14}N_2O_2S]^+$, 171 (100) $[C_{12}H_{13}N]^+$.

EA for **$C_{39}H_{46}N_4O_6S_2$ (730.94):** calcd (%): C 64.08, H 6.34, N 7.67; found (%): C 63.71, H 6.48, N 7.65.

3,5-Bis[3-(5-dimethylaminonaphthalene-1-sulfonylamino)propyl]benzoic acid (45)



A solution of the dansylated G1 dendron **44** (731 mg, 1.00 mmol) and KOH (449 mg, 8.00 mmol) in a solvent mixture of methanol/water/THF (3:1:1) was stirred at 40 °C for 18 h. After complete reaction (TLC) a 0.1 M aqueous solution of $KHSO_4$ was slowly added to give a pH = 3. As soon as the solution turned turbid, the product was repeatedly extracted with DCM. The combined organic layers were dried with magnesium sulfate, the solvent evaporated, and the crude product purified by column chromatography (silica gel, DCM cont. 5 % methanol as eluent) to yield the dansylated acid **45** (644 mg, 916 µmol, 91.6 %) as a bright yellow solid (foam).

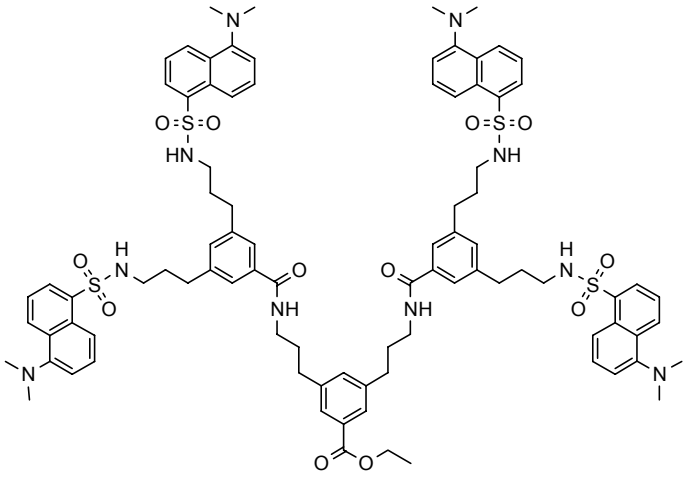
$\boldsymbol{R_f}$ = 0.44 (DCM/methanol (9:1/v:v)).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.66 (m, 4 H, CH_2), 2.48 (t, ^3J (H,H) = 7.7 Hz, 4 H, CH_2Ar), 2.86 (m, 16 H, CH_2N + NCH_3), 5.12 (t, ^3J (H,H) = 5.9 Hz, 2 H, NH), 6.89 (s, 1 H, Ar*H*), 7.16 (d, ^3J (H,H) = 7.3 Hz, 2 H, ArH_{Dns}), 7.51 (m, 4 H, ArH_{Dns}), 7.52 (s, 2 H, Ar*H*), 8.2 (d, ^3J (H,H) = 7.3 Hz, 2 H, ArH_{Dns}), 8.31 (d, ^3J (H,H) = 8.2 Hz, 2 H, ArH_{Dns}), 8.52 (d, ^3J (H,H) = 8.2 Hz, 2 H, ArH_{Dns}).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 30.95 (CH_2), 32.19 (CH_2Ar), 42.55 (CH_2N), 45.44 (NCH_3), 115.31 (ArC_{Dns}), 118.89 (ArC_{Dns}), 123.30 (ArC_{Dns}), 127.71 (Ar*C*), 128.44 (ArC_{Dns}), 129.52 (ArC_{Dns}), 129.65 (ArC_{Dns}, 2 signals), 129.81 (ArC_{Dns}), 130.41 (Ar*C*), 133.97 (Ar*C*), 134.76 (ArC_{Dns}), 141.59 (Ar*C*), 151.75 (ArC_{Dns}), 170.54 (CO).

MS (FAB+, MNBA/DCM): *m/z* (%): 703 (7.7) $[M+H]^+$, 170 (14.1) $[C_{12}H_{12}N]^+$.

Ethyl(3,5-bis{3,5-bis[3-(5-dimethylaminonaphthalene-1-sulfonylamino)propyl]benzamide}-*N*-propylbenzamide)benzoate (46)



A solution of dry triethylamine (836 µl, 607 mg, 6 mmol) and the deprotected dendron **18** (444 mg, 400 µmol) in dry methanol were added dropwise to a vigorously stirred solution of dansyl chloride (647 mg, 2.40 mmol) in dry DCM at room temperature. The reaction mixture was stirred for additional 60 min in the dark. The reaction was continuously monitored by TLC. After complete reaction, the mixture was washed once with brine, once with saturated sodium carbonate solution, and once again with brine. The sovent was evaporated under reduced pressure and the crude product purified by column chromatography (silica gel, cont. 2 % methanol as eluent) to give the dansylated G2 dendron **46** (530 mg, 324 µmol, 81.0 %) as a yellow-greenish oil that could be lyophilized from dioxane.

R_f = 0.52 (DCM/methanol (19:1/v:v)).

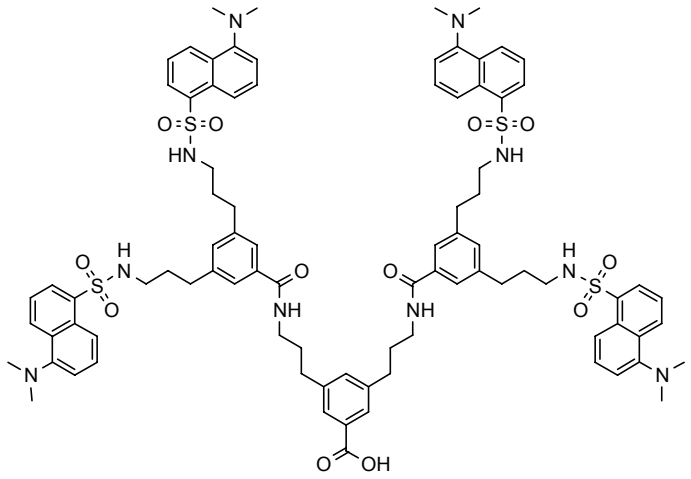
M.p. 120-121 °C

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, ^3J (H,H) = 7.4 Hz, 3 H, CH_3), 1.60 (m, 8 H, CH_2), 1.89 (m, 4 H, CH_2), 2.43 (t, ^3J (H,H) = 7.0 Hz, 8 H, CH_2Ar), 2.64 (t, ^3J (H,H) = 7.4 Hz, 4 H, CH_2Ar), 2.78 (m, 8 H, CH_2N), 2.83 (s, 24 H, NCH_3), 3.33 (m, 4 H, CH_2N), 4.28 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH_3), 5.58 (t, ^3J (H,H) = 5.5 Hz, 4 H, NH), 6.75 (s, 2 H, Ar*H*), 6.96 (t, ^3J (H,H) = 5.1 Hz, 2 H, NH), 7.12 (d, ^3J (H,H) = 8.1 Hz, 4 H, ArH_{Dns}), 7.24 (s, 1 H, Ar*H*), 7.28 (s, 4 H, Ar*H*), 7.44 (m, 8 H, ArH_{Dns}), 7.67 (s, 2 H, Ar*H*), 8.15 (d, ^3J (H,H) = 7.4 Hz, 4 H, ArH_{Dns}), 8.32 (d, ^3J (H,H) = 8.1 Hz, 4 H, ArH_{Dns}), 8.49 (d, ^3J (H,H) = 8.8 Hz, 4 H, ArH_{Dns}).

^{13}C NMR (126 MHz, $CDCl_3$/CD_3OD): δ = 14.02 (CH_3), 30.37 (CH_2), 30.52 (CH_2), 31.83 (CH_2Ar), 32.79 (CH_2Ar), 39.34 (CH_2N), 41.79 (CH_2N), 45.45 (NCH_3), 60.94 (CH_2CH_3), 115.61 (ArC_{Dns}), 120.05 (ArC_{Dns}), 123.61 (ArC_{Dns}), 124.85 (Ar*C*), 127.02 (Ar*C*), 129.22 (ArC_{Dns}), 129.42 (ArC_{Dns}, 2 signals), 129.50 (ArC_{Dns}), 130.31 (ArC_{Dns}), 130.47 (Ar*C*), 131.51 (Ar*C*), 133.25 (Ar*C*), 134.26 (Ar*C*), 135.06 (ArC_{Dns}), 141.40 (Ar*C*), 141.99 (Ar*C*), 150.81 (ArC_{Dns}), 167.08 (CO), 168.45 (CO).

MS (MALDI-TOF, dithranol): *m/z:* 1672 $[M+K]^+$, 1656 $[M+Na]^+$, 1634 $[M+H]^+$; monoisotopic mass calcd for $\mathbf{C_{98}H_{105}N_{10}O_{12}S_4^+}$: 1633.68, found: 1633.69.

3,5-Bis{[3,5-bis(5-dimethylaminonaphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide}benzoic acid (47)



The dansylated G2 dendron **46** (500 mg, 306 µmol) and KOH (206 mg, 3.67 mmol) were dissolved in a solvent mixture of methanol/water/THF (3:1:1) and stirred at 40 °C for 18 h. After complete reaction (TLC) a 0.1 M aqueous solution of $KHSO_4$ was slowly added to give a pH = 3; as soon as the solution turned turbid the product was repeatedly extracted with DCM. The combined organic layers were dried with magnesium sulfate and the solvent was evaporated *in vacuo*. Column chromatography (silica gel, DCM cont. 5 % methanol as eluent) gave the dansylated G2 acid **47** (419 mg, 261 µmol, 85.3 %) as a bright yellow oil.

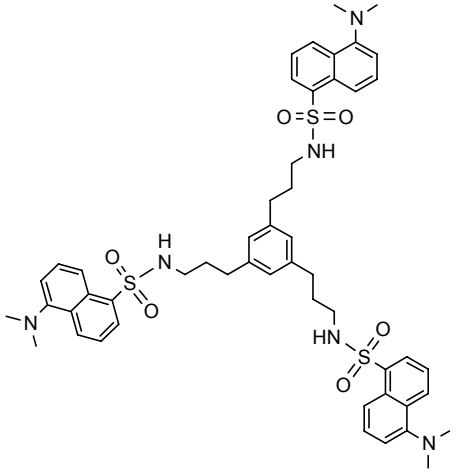
$\boldsymbol{R_f}$ = 0.17 (DCM/methanol (19:1/v:v)).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.51 (m, 8 H, CH_2), 1.91 (m, 4 H, CH_2), 2.42 (t, ^3J (H,H) = 7.0 Hz, 8 H, CH_2Ar), 2.67 (t, ^3J (H,H) = 7.2 Hz, 4 H, CH_2Ar), 2.80 (m, 8 H, CH_2N), 2.85 (s, 24 H, NCH_3), 3.33 (m, 4 H, CH_2N), 4.28 (q, ^3J (H,H) = 7.1 Hz, 2 H, CH_2CH_3), 5.41 (s, 4 H, NH), 6.67 (s, 2 H, Ar*H*), 7.22 (s, 4 H, Ar*H*), 7.24 (d, ^3J (H,H) = 8.1 Hz, 4 H, ArH_{Dns}), 7.38 (s, 1 H, Ar*H*), 7.51 (m, 8 H, ArH_{Dns}), 7.68 (s, 2 H, NH), 7.71 (s, 2 H, Ar*H*), 8.12 (d, ^3J (H,H) = 7.4 Hz, 4 H, ArH_{Dns}), 8.36 (d, ^3J (H,H) = 8.8 Hz, 4 H, ArH_{Dns}), 8.45 (d, ^3J (H,H) = 8.2 Hz, 4 H, ArH_{Dns}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.39 (CH_2), 30.82 (CH_2), 32.13 (CH_2Ar), 32.94 (CH_2Ar), 39.68(CH_2N), 42.43 (CH_2N), 45.37 (NCH_3), 115.32 (ArC_{Dns}), 119.19 (ArC_{Dns}), 123.27 (ArC_{Dns}), 125.01 (Ar*C*), 127.56 (Ar*C*), 128.30 (ArC_{Dns}), 129.24 (ArC_{Dns}), 129.62 (ArC_{Dns}, 2 signals), 129.70 (ArC_{Dns}), 130.15 (Ar*C*), 131.55 (Ar*C*), 133.76 (Ar*C*), 134.47 (ArC_{Dns}), 135.10 (Ar*C*), 141.53 (Ar*C*), 142.25 (Ar*C*), 151.53 (ArC_{Dns}), 168.10 (CO), 169.48 (CO).

MS (FAB+, MNBA, methanol, DMSO): *m/z* (%): 1607 (0.7) $[M+H]^+$, 1373 (0.2) $[M-C_{12}H_{12}NO_2S]$, 685 (0.6) $[C_{37}H_{41}N_4O_5S_2]^+$, 170 (58.1) $[C_{12}H_{12}N]^+$.

(Dns)$_3$3D0: **1,3,5-Tris[3-(5-dimethylaminonaphthalene-1-sulfonylamino)propyl]benzene (48)**



To a vigorously stirred solution of 5-dimethylaminonaphthalene-1-sulfonyl chloride (dansyl chloride) (1.46 g, 5.40 mmol) in dry DCM, dry triethylamine (2.00 ml , 1.46 g, 14.4 mmol) and the trishydrochloride core **5** (431 mg, 1.20 mmol), dissolved in a small amount of dry methanol, were added dropwise at room temperature. The reaction was stirred for 1 h in the dark and was continuously checked via TLC. After complete reaction the organic layer was washed once with brine, once with a saturated sodium carbonate solution, and once again with brine. Column chromatography (silica gel, DCM cont. 1 % methanol as eluent) gave the dansylated G0 dendrimer **48** (1.04 g, 1.10 mmol, 91.7 %) as a bright yellow-greenish solid.

R_f = 0.46 (DCM/methanol (49:1/v:v)).

M.p. 96 °C.

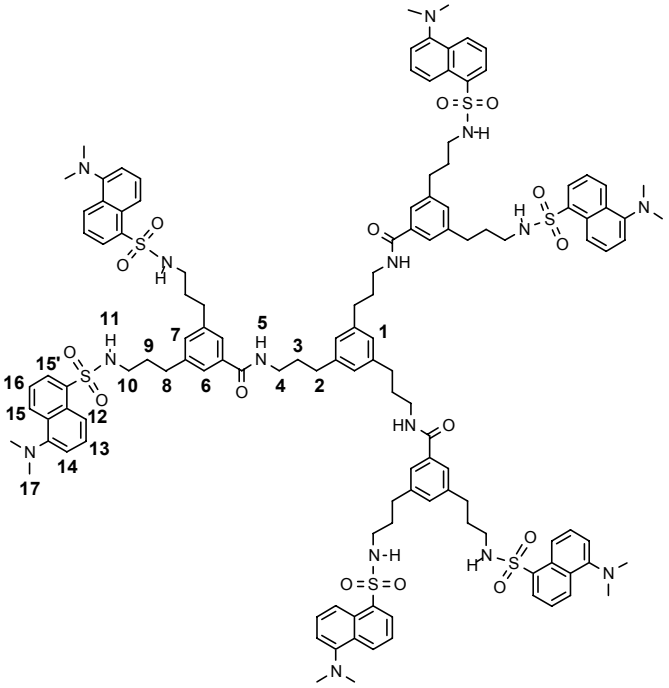
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C): δ = 1.57 (m, 6 H, CH_2), 2.31 (t, ^3J (H,H) = 7.5 Hz, 6 H, CH_2Ar), 2.84 (q, ^3J (H,H) = 6.6 Hz, 6 H, CH_2N), 2.85 (s, 18 H, NCH_3), 4.97 (t, br, ^3J (H,*N*H) = 5.4 Hz, 3 H, NH), 6.40 (s, 3 H, Ar*H*), 7.14 (d, ^3J (H,H) = 7.6 Hz, 3 H, ArH_{Dns}), 7.45 (t, ^3J (H,H) = 7.9 Hz, 3 H, ArH_{Dns}), 7.50 (t, ^3J (H,H) = 8.1 Hz, 3 H, ArH_{Dns}), 8.19 (d, ^3J (H,H) = 7.6 Hz, 3 H, ArH_{Dns}), 8.30 (d, ^3J (H,H) = 8.7 Hz, 3 H, ArH_{Dns}), 8.51 (d, ^3J (H,H) = 8.4 Hz, 3 H, ArH_{Dns}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 31.03 (CH_2), 32.34 (CH_2Ar), 42.64 (CH_2N), 45.44 (NCH_3), 115.28 (ArC_{Dns}), 119.01 (ArC_{Dns}), 123.30 (ArC_{Dns}), 126.11 (Ar*C*), 128.35 (ArC_{Dns}), 129.57 (ArC_{Dns}), 129.64 (ArC_{Dns}), 129.77 (ArC_{Dns}), 130.28 (ArC_{Dns}), 134.93 (ArC_{Dns}), 141.14 (Ar*C*), 151.70 (ArC_{Dns}).

MS (EI, 80 eV, 320 °C): *m/z* (%): 948 (2.0) $[M]^+$, 714 (1.4) $[M-C_{12}H_{12}NO_2S]^+$, 171 (100) $[C_{12}H_{13}N]^+$, 64 (38.3) $[SO_2]^+$.

HRMS: *m/z:* monoisotopic mass calcd for $\mathbf{C_{51}H_{60}N_6O_6S_3^+}$: 948.37365, found: 948.37652.

(Dns)$_6$6D1: **1,3,5-Tris{3,5-bis[3-(5-dimethylamino-naphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide}benzene (49)**



A solution of dry triethylamine (1.26 ml, 923 mg, 9.12 mmol) and the G1 dendrimer **26** (477 mg, 300 µmol) in dry methanol were added slowly to a vigorously stirred solution of dansyl chloride (1.17 g, 4.32 mmol) in dry DCM at room temperature. The reaction mixture was continuously monitored by TLC and stirred in the dark for 6 h. After complete reaction the solution was washed once with brine, once with a saturated sodium carbonate solution, and once again with brine. The organic phase was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by column chromatography (silica gel, DCM cont. 2-3 % methanol as eluent). The procedure yielded the dansylated G1 dendrimer **49** as a bright yellow-greenish oil (512 mg, 222 µmol, 74.0 %) which could be lyophilized from dioxane.

$\boldsymbol{R_f}$ = 0.50 (DCM/methanol (19:1/v:v)).

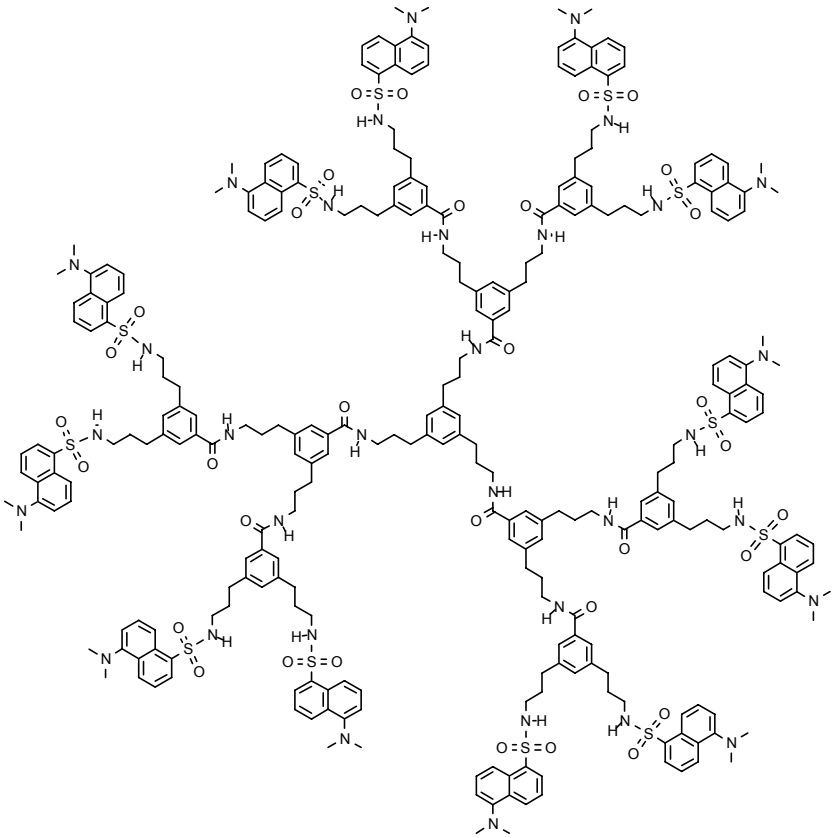
M.p. 114-117 °C.

^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ = 1.61 (m, 12 H, *H*-9), 1.83 (m, 6 H, *H*-3), 2.42 (t, ^3J (H,H) = 7.2 Hz, 12 H, *H*-8), 2.53 (t, ^3J (H,H) = 6.8 Hz, 6 H, *H*-2), 2.80 (q, ^3J (H,H) = 6.3 Hz, 12 H, *H*-10), 2.84 (s, 36 H, *H*-17), 3.32 (q, ^3J (H,H) = 6.5 Hz, 12 H, *H*-4), 5.52 (s, br, 6 H, *H*-11), 6.75 (s, 3 H, *H*-7), 6.77 (t, br, ^3J (H,*N*H) = 5.4 Hz, 3 H, *H*-5), 6.82 (s, 3 H, *H*-1), 7.12 (d, ^3J (H,H) = 7.3 Hz, 6 H, *H*-14), 7.26 (s, 6 H, *H*-6), 7.42 (m, 12 H, *H*-13 + *H*-16), 8.14 (d, ^3J (H,H) = 7.2 Hz, 6 H, *H*-15,15'), 8.33 (d, ^3J (H,H) = 8.7 Hz, 6 H, *H*-12), 8.50 (d, ^3J (H,H) = 8.5 Hz, 6 H, *H*-15',15).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.56 (CH_2), 30.77 (CH_2), 32.09 (CH_2Ar), 33.26 (CH_2Ar), 39.78 (CH_2N), 42.34 (CH_2N), 45.51 (NCH_3), 115.50 (ArC_{Dns}), 119.62 (ArC_{Dns}), 123.47 (ArC_{Dns}), 125.00 (Ar*C*), 126.15 (Ar*C*), 128.26 (ArC_{Dns}), 129.33 (ArC_{Dns}), 129.38 (ArC_{Dns}), 129.57 (ArC_{Dns}), 129.99 (ArC_{Dns}), 131.42 (Ar*C*), 134.64 (Ar*C*), 135.07 (ArC_{Dns}), 141.45 (Ar*C*), 141.93 (Ar*C*), 151.51 (ArC_{Dns}), 167.81 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2341 $[M+K]^+$, 2325 $[M+Na]^+$, 2303 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{126}H_{148}N_{15}O_{15}S_6^+}$: 2302.96, found: 2303.08.

(Dns)$_{12}$12D2: **1,3,5-Tris(3,5-bis{3,5-bis[3-(5-dimethylamino-naphthalene-1-sulfonyl-amino)propyl]-*N*-propylbenzamide}-*N*-propylbenzamide)benzene (50)**



A solution of dry triethylamine (166 µl, 121 mg, 1.20 mmol) and the deprotected G2 dendrimer **28** (72 mg, 20 µmol) in dry methanol were added dropwise to a vigorously stirred solution of dansyl chloride (194 mg, 720 µmol) in dry DCM at room temperature. While the solution was stirred in the dark for additional 12 h the reaction was continuously monitored by TLC. After complete reaction the solution was washed once with brine, once with a saturated sodium carbonate solution, and once again with brine. The organic phase was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by column chromatography (silica gel, DCM cont. 2-4 % methanol as eluent). The procedure afforded the desired G2 dendrimer **50** (65 mg, 13 µmol, 65 %) as a bright yellow-greenish oil which could be lyophilized from dioxane.

$\boldsymbol{R_f}$ = 0.44 (DCM/methanol (19:1/v:v)).

M.p. 132-134 °C.

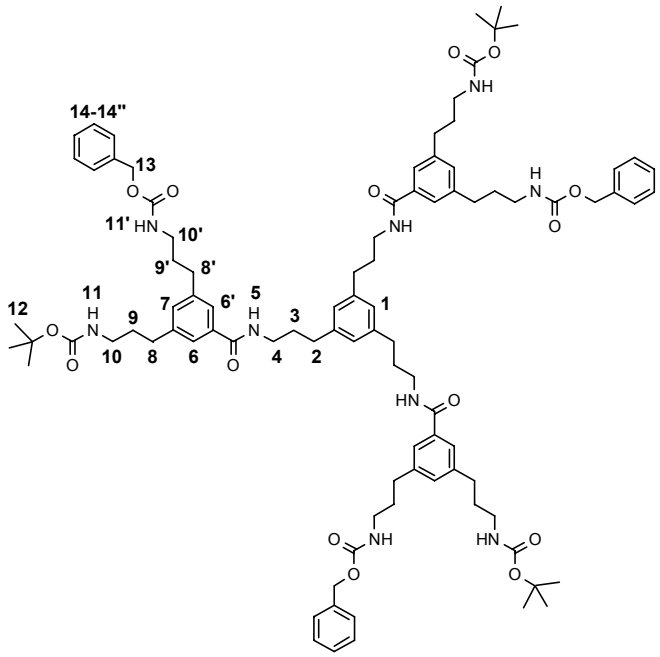
^{1}H NMR (500 MHz, CD_3OD, 30 °C): δ = 1.63 (m, 24 H, CH_2), 1.80 (m, 6 H, CH_2), 1.86 (m, 12 H, CH_2), 2.45 (m, 24 H + 6 H, CH_2Ar), 2.46 (t, ^{3}J (H,H) = 6.9 Hz, 12 H, CH_2Ar), 2.59 (m, 24 H, CH_2N), 2.92 (s, 72 H, NCH_3), 3.31 (m, 6 H, + 12 H, CH_2N), 6.75 (s, 3 H, Ar*H*), 6.78 (s, 6 H, Ar*H*), 7.12 (s, 3 H, Ar*H*), 7.26 (s, 6 H, Ar*H*), 7.29 (s, 12 H, Ar*H*), 7.38 (d, ^{3}J (H,H) = 5.5 Hz, 12 H, ArH_{Dns}), 7.49 (m, 24 H, ArH_{Dns}), 8.13 (d, ^{3}J (H,H) = 7.3 Hz, 12 H, ArH_{Dns}), 8.41 (d, ^{3}J (H,H) = 8.0 Hz, 12 H, ArH_{Dns}), 8.55 (d, ^{3}J (H,H) = 8.7 Hz, 12 H, ArH_{Dns}).

^{13}C NMR (126 MHz, CD_3OD, 30 °C): δ = 30.04 (CH_2), 30.61 (CH_2), 31.18 (CH_2), 32.51 (CH_2Ar), 33.34 (CH_2Ar), 33.62 (CH_2Ar), 39.87 (CH_2N), 40.15 (CH_2N), 42.50 (CH_2N), 46.02 (NCH_3), 116.46 (ArC_{Dns}), 123.50 (ArC_{Dns}), 124.31 (ArC_{Dns}), 125.27 (Ar*C*), 125.38 (Ar*C*), 128.49 (ArC_{Dns}), 129.55 (ArC_{Dns}), 129.70 (ArC_{Dns}), 129.98 (ArC_{Dns}), 130.03 (ArC_{Dns}), 132.08 (Ar*C*), 132.19 (Ar*C*), 134.85 (Ar*C*), 134.91 (Ar*C*), 135.88 (ArC_{Dns}), 140.23 (Ar*C*), 142.06 (Ar*C*), 142.26 (Ar*C*), 142.56 (Ar*C*), 152.53 (ArC_{Dns}), 169.06 (CON), 169.09 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 5048 $[M+K]^+$, 5032 $[M+Na]^+$, 5010 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{276}H_{322}N_{33}O_{33}S_{12}}^+$: 5010.12, found: 5010.21 $[M+H]^+$.

7.4.5 Compounds of Chapter 4.2.5

(Cbz-N)$_3$(Boc-N)$_3$6D1: **1,3,5-Tris{3-[3-(benzyloxycarbonylamino)propyl]-5-[3-(*tert*-butyl-oxycarbonylamino)propyl]-*N*-propylbenzamide}benzene (53)**



To a solution of the mixed-protected G1 acid **52** (5.41 g, 11.5 mmol) in dry DCM HOBt (1.63 g, 12.1 mmol) was added under a nitrogen atmosphere, and the suspension was stirred at room temperature for 20 min. Thereafter, the mixture was cooled down to - 20 °C, EDC (2.43 g, 12.7 mmol) was added, and the reaction was allowed to warm up to room temperature slowly while being stirred for additional 2 h. After complete formation of the active ester (TLC), the reaction mixture was cooled down to - 20 °C again. A solution of the trishydrochloride core **4** (918 mg, 2.56 mmol) and DIPEA (7.6 ml, 5.6 g, 43 mmol) in dry methanol was added dropwise while the solution was stirred at - 20 °C for 1 h. The reaction was allowed to warm up to room temperature slowly and was stirred for additional 24 h. After complete reaction (TLC) the solution was washed twice with sodium hydrogencarbonate solution, and once with brine. The organic phase was dried over magnesium sulfate, and the solvent removed *in vacuo*. Column chromatography (silica gel, DCM cont. 3 % methanol as eluent) afforded the mixed-protected G1 dendrimer **53** (2,61 g, 1.62 mmol, 63.3 %) as a colorless solid.

R_f = 0.43 (DCM/methanol (19:1/v:v)).

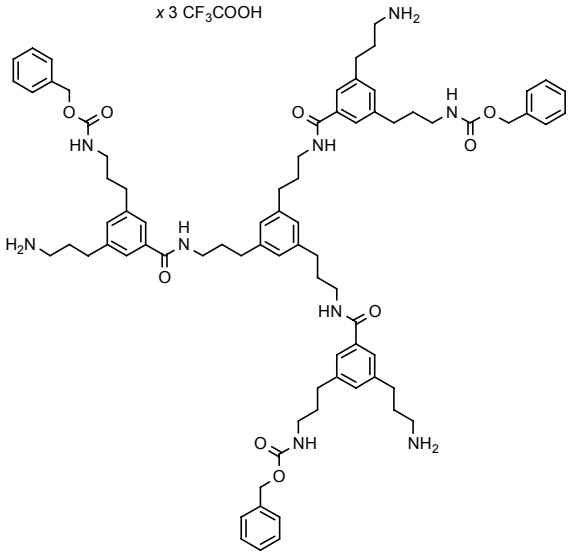
M.p. 66 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (s, 27 H, *H*-12), 1.69 (m, 6 H, *H*-9,9'), 1.74 (m, 6 H, *H*-9',9), 1.89 (m, 6 H, *H*-3), 2.54 (m, 12 H, *H*-8 + *H*-8'), 2.58 (t, ^3J (H,H) = 7.2 Hz, 6 H, *H*-2), 3.02 (m, 6 H, *H*-10), 3.10 (m, 6 H, *H*-10'), 3.37 (m, 6 H, *H*-4), 4.72 (s, br, 3 H, *H*-11), 5.03 (s, 6 H, *H*-13), 5.17 (s, br, 3 H, *H*-11'), 6.83 (s, 3 H, *H*-1), 7.02 (s, 3 H, *H*-7), 7.11 (s, br, 3 H, *H*-5), 7.29 (m, 15 H, *H*-14,14',14''), 7.36 (s, 3 H, *H*-6,6'), 7.38 (s, 3 H, *H*-6',6).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.41 (CCH_3), 30.70 (CH_2), 31.12 (CH_2), 31.31 (CH_2), 32.44 (CH_2Ar), 33.13 (CH_2Ar), 39.63 (CH_2N + CH_2N), 40.15 (CH_2N), 66.55 (CH_2Ar_{Cbz}), 79.17 (CCH_3), 124.82 (Ar*C*), 124.90 (Ar*C*), 126.27 (Ar*C*), 127.97 (ArC_{Cbz}), 128.02 (ArC_{Cbz}), 128.45 (ArC_{Cbz}), 131.56 (Ar*C*), 134.74 (Ar*C)*, 136.59 (ArC_{Cbz}*)*, 141.68 (Ar*C)*, 141.75 (Ar*C)*, 141.82 (Ar*C)*, 156.10 (CON_{Boc}), 156.55 (CON_{Cbz}), 167.86 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 1645 $[M+K]^+$, 1629 $[M+Na]^+$;
monoisotopic mass calcd for **$C_{93}H_{123}N_9NaO_{15}^+$**: 1628.90, found: 1628.99.

(Cbz-N)$_3$(N)$_3$6D1: **1,3,5-Tris{3-[3-(benzyloxycarbonylamino)propyl]-5-(aminopropyl)-*N*-propylbenzamide}benzene tristrifluoroacetate (54)**



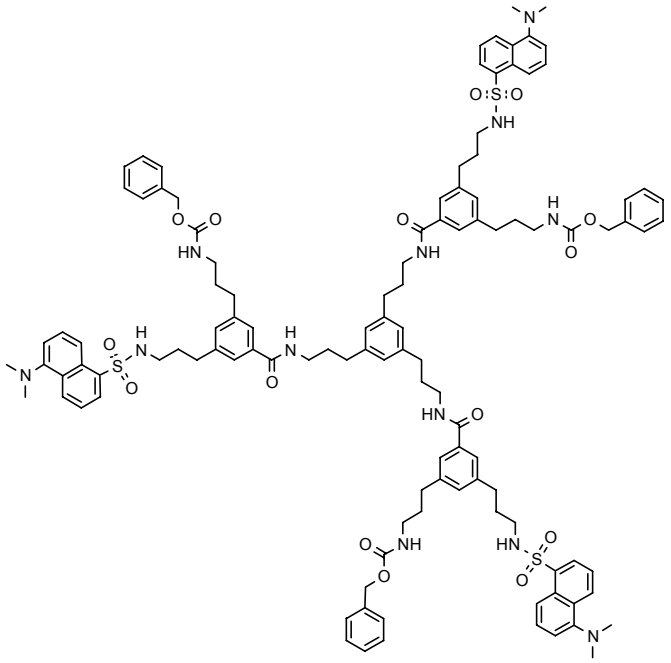
To a solution of the mixed-protected G1 dendrimer **53** (2.41 g, 1.50 mmol) in DCM (100 ml) TFA (25 ml) was added, and the reaction mixture was stirred for 1 h at room temperature. After complete reaction (TLC) the solvent was repeatedly removed *in vacuo* to afford the partially deprotected dendrimer **54** (2.09 g, 1.35 mmol, 90.0 %) as a colorless oil.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.81 (m, 6 H, CH_2), 1.91 (m, 6 H, CH_2), 1.96 (m, 6 H, CH_2), 2.64 (m, 12 H, CH_2Ar), 2.71 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 2.91 (t, ^3J (H,H) = 7.7 Hz, 6 H, CH_2N), 3.10 (t, ^3J (H,H) = 6.7 Hz, 6 H, CH_2N), 3.37 (t, ^3J (H,H) = 7.1 Hz, 6 H, CH_2N), 5.05 (s, 6 H, CH_2Ar_{Cbz}), 6.91 (s, 3 H, Ar*H*), 7.22 (s, 3 H, Ar*H*), 7.29 (m, 15 H, ArH_{Cbz}), 7.44 (s, 3 H, Ar*H*), 7.48 (s, 3 H, Ar*H*).

^{13}C NMR (126 MHz, CD_3OD): δ = 30.38 (CH_2), 32.38 (CH_2), 32.69 (CH_2), 33.55 (CH_2Ar), 33.92 (CH_2Ar), 34.61 (CH_2Ar), 40.51 (CH_2N), 41.11 (CH_2N), 41.37 (CH_2N), 67.66 (CH_2Ar_{Cbz}), 126.38 (Ar*C*), 126.56 (Ar*C*), 127.61 (Ar*C*), 128.96 (Ar*C*), 129.26 (Ar*C*), 129.77 (Ar*C*), 133.11 (Ar*C*), 136.67 (Ar*C*), 138.74 (Ar*C*), 142.64 (Ar*C*), 143.52 (Ar*C*), 144.13 (Ar*C*), 159.22 (CON_{Cbz}), 170.60 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 1307 $[M+H]^+$;
monoisotopic mass calcd for **$C_{78}H_{100}N_9O_9^+$**: 1306.76, found: 1306.76 $[M+H]^+$.

(Cbz-N)$_3$(Dns)$_3$6D1: **1,3,5-Tris{3-[3-(benzyloxycarbonylamino)propyl]-5-(5-dimethylaminonaphthalene-1-sulfonylamino)propy}-*N*-propylbenzamide}benzene (55)**



A solution of the G1 trifluoroacetate **54** (2.09 g, 1.35 mmol) and dry triethylamine (2.82 ml, 2.05 g, 20.3 mmol) in dry methanol (20 ml) was added dropwise to a vigorously stirred solution of dansyl chloride (2.18 g, 8.10 mmol) in dry DCM (250 ml). The reaction was monitored by TLC. After complete reaction, the mixture was washed once with brine, once with a saturated sodium carbonate solution, and once again with brine. The organic layer was dried over magnesium sulfate, and the solvent was removed *in vacuo*. Chromatographic purification (silica gel, DCM cont. 4 % methanol as eluent) afforded the partially dansylated G1 dendrimer **55** (2.68 g, 1.34 mmol, 99.3 %) as a bright yellow solid.

R_f = 0.38 (DCM/methanol (19:1/v:v)).

M.p. 98-101 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.61 (m, 6 H, CH_2), 1.67 (m, 6 H, CH_2), 1.82 (m, 6 H, CH_2), 2.47 (m, 12 H, CH_2Ar), 2.52 (t, ^3J (H,H) = 7.1 Hz, 6 H, CH_2Ar), 2.77 (q, ^3J (H,H) = 6.2 Hz, 6 H, CH_2N), 2.85 (s, 18 H, NCH_3), 3.06 (q, ^3J (H,H) = 6.7 Hz, 6 H, CH_2N), 3.31 (q, ^3J (H,H) = 6.0 Hz, 6 H, CH_2N), 5.02 (s, 6 H, CH_2Ar_{Cbz}), 5.15 (t, br, 3 H, NH), 5.82 (s, br, 3 H, NH), 6.80 (s, 3 H, Ar*H*), 6.86 (s, 3 H, Ar*H*), 7.00 (s, br, 3 H, NH), 7.14 (d, ^3J (H,H) = 7.3 Hz, 3 H, ArH_{Dns}), 7.26 (m, 15 H, ArH_{Cbz}), 7.28 (s, 3 H, Ar*H*), 7.36 (s, 3 H, Ar*H*), 7.42 (m, 6 H, ArH_{Dns}), 8.13 (d, ^3J (H,H) = 7.3 Hz, 3 H, ArH_{Dns}), 8.36 (d, ^3J (H,H) = 8.7 Hz, 3 H, ArH_{Dns}), 8.52 (d, ^3J (H,H) = 8.5 Hz, 3 H, ArH_{Dns}).

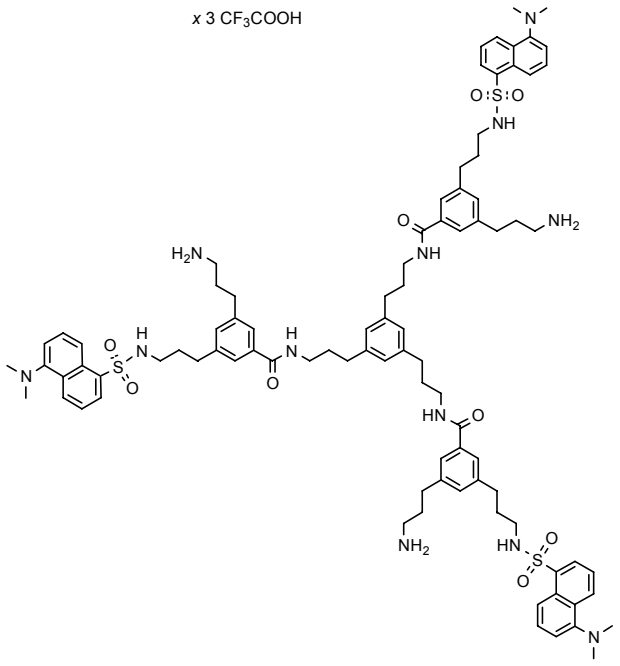
^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.72 (CH_2), 30.83 (CH_2), 31.19 (CH_2), 32.12 (CH_2Ar), 32.55 (CH_2Ar), 33.31 (CH_2Ar), 39.80 (CH_2N), 40.36 (CH_2N), 42.28 (CH_2N), 45.60 (NCH_3), 66.65 (CH_2Ar_{Cbz}), 115.59 (ArC_{Dns}), 119.40 (ArC_{Dns}), 123.50 (ArC_{Dns}), 123.58 (ArC_{Dns}), 124.93 (Ar*C*), 125.21 (Ar*C*), 126.31 (Ar*C*), 128.05 (ArC_{Cbz}), 128.11 (ArC_{Cbz}), 128.30 (ArC_{Dns}),

128.56 (ArC_{Cbz}), 129.46 (ArC_{Dns}), 130.16 (ArC_{Dns}), 131.53 (Ar*C*), 134.94 (Ar*C*), 135.23 (ArC_{Dns}), 136.70 (ArC_{Cbz}), 141.42 (Ar*C*), 141.90 (Ar*C*), 142.00 (Ar*C*), 151.65 (ArC_{Dns}), 156.69 (CON$_{Cbz}$), 167.90 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2028 $[M+Na]^+$, 2006 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{114}H_{133}N_{12}O_{15}S_3^+}$: 2005.92, found: 2005.94.

(N)$_3$(Dns)$_3$6D1: **1,3,5-Tris{3-(aminopropyl)-5-[(5-dimethylamino-naphthalene-1-sulfonyl-amino)propyl)-*N*-propylbenzamide}benzene tristrifluoroacetate (56)**

A solution of the mixed dansylated dendrimer **55** (401 mg, 200 µmol) in TFA (8 ml) was stirred for 7 days at room temperature. The reaction was continuously monitored by TLC. After complete reaction the solvent was repeatedly removed *in vacuo* to afford the deprotected dendrimer **56** as a yellow-greenish solid (379 mg, 198 µmol, 99.0 %) after lyophilization from water.



M.p. 119-120 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.68 (m, 3 H, CH_2), 1.96 (m, 12 H, CH_2), 2.56 (t, ^3J (H,H) = 7.4 Hz, 6 H, CH_2Ar), 2.66 (t, ^3J (H,H) = 7.6 Hz, 6 H, CH_2Ar), 2.71 (t, ^3J (H,H) = 7.7 Hz, 6 H, CH_2Ar), 2.84 (t, ^3J (H,H) = 6.7 Hz, 6 H, CH_2N), 2.87 (s, 18 H, NCH_3), 2.95 (t, ^3J (H,H) = 7.7 Hz, 6 H, CH_2N), 3.40 (t, ^3J (H,H) = 5.6 Hz, 6 H, CH_2N), 6.96 (s, 3 H, Ar*H*), 7.09 (s, 3 H, Ar*H*), 7.27 (d, ^3J (H,H) = 6.9 Hz, 3 H, ArH_{Dns}), 7.34 (s, 3 H, Ar*H*), 7.49 (s, 3 H, Ar*H*), 5.53 (t, ^3J (H,H) = 7.9 Hz, 3 H, ArH_{Dns}), 7.58 (t, ^3J (H,H) = 8.1 Hz, 3 H, ArH_{Dns}), 8.14 (d, ^3J (H,H) = 7.3 Hz, 3 H, ArH_{Dns}), 8.39 (d, ^3J (H,H) = 8.8 Hz, 3 H, ArH_{Dns}), 8.53 (d, ^3J (H,H) = 8.5 Hz, 3 H, ArH_{Dns}).

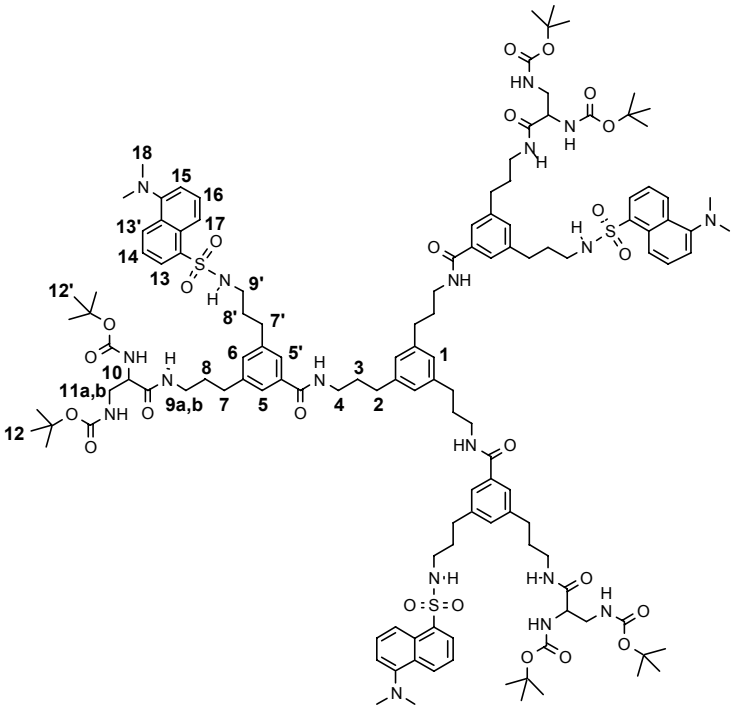
^{13}C NMR (126 MHz, CD_3OD): δ = 30.39 (CH_2), 32.39 (CH_2), 32.42 (CH_2), 33.54 (CH_2Ar), 33.55 (CH_2Ar), 34.63 (CH_2Ar), 40.53 (CH_2N), 41.12 (CH_2N), 43.37 (CH_2N), 46.13 (NCH_3), 116.81 (ArC_{Dns}), 120.90 (ArC_{Dns}), 124.66 (ArC_{Dns}), 126.37 (Ar*C*), 126.54 (Ar*C*), 127.63 (Ar*C*), 128.28 (ArC_{Dns}), 129.46 (ArC_{Dns}), 130.42 (ArC_{Dns}), 131.37 (ArC_{Dns}), 133.07 (Ar*C*),

136.50 (ArC_{Dns}), 137.32 (ArC_{Dns}), 142.61 (Ar*C*), 142.99 (Ar*C*), 143.55 (Ar*C*), 143.81 (Ar*C*), 153.25 (ArC_{Dns}), 170.57 (CON).

MS (FAB+, MNBA, methanol): *m/z* (%): 1604 (1.2) $[M+H]^+$, 170 (42.5) $[C_{12}H_{12}N]^+$.

MS (MALDI-TOF, dithranol): *m/z:* monoisotopic mass calcd for $\mathbf{C_{90}H_{115}N_{12}O_9S_3^+}$: 1603.81, found: 1603.81.

(Boc-Dpa)$_3$(Dns)$_3$6D1: **1,3,5-Tris{3-[(2-*tert*-butoxycarbonylamino-2-propylcarbamoyl-ethyl)carbamic acid *tert*-butylester]-5-[(5-dimethylamino-naphthalene-1-sulfonylamino)-propyl]-*N*-propylbenzamide}benzene (57)**



A solution of the Boc-protected diaminopropionic acid **37** (274 mg, 900 µmol) in dry DCM/DMF (18:2/v:v) was cooled down to - 20 °C. DIPEA (153 µl, 116 mg, 900 µmol), and TBTU (303 mg, 945 µmol), dissolved in dry DMF (8 ml), were added slowly under vigorous stirring. The reaction mixture was allowed to warm up to room temperature and stirred for additional 30 min. After complete formation of the active ester (TLC) the solution was cooled down to - 20 °C again. DIPEA (204 µl, 155 mg, 1.20 mmol) and the deprotected dansylated dendrimer **56** (195 mg, 100 µmol), dissolved in a small amount of methanol (2 ml), were added dropwise to the vigorously stirred solution. The reaction mixture was stirred at - 20 °C for 1 h, and was then allowed to warm up to room temperature slowly. Afterwards the solution was stirred at room temperature for additional 24 h. When the reaction was complete (TLC), the solution was washed twice with a saturated sodium carbonate solution, and once with brine. The organic phase was dried over magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by column chromatography (silica gel, DCM cont. 4 % methanol as eluent). Lyophilization from dioxane gave the mixed dansyl- and diaminopro-

pionic acid-functionalized dendrimer **57** (81 mg, 33 µmol, 33 %) as a brilliant yellow-greenish solid.

M.p. 122-123 °C.

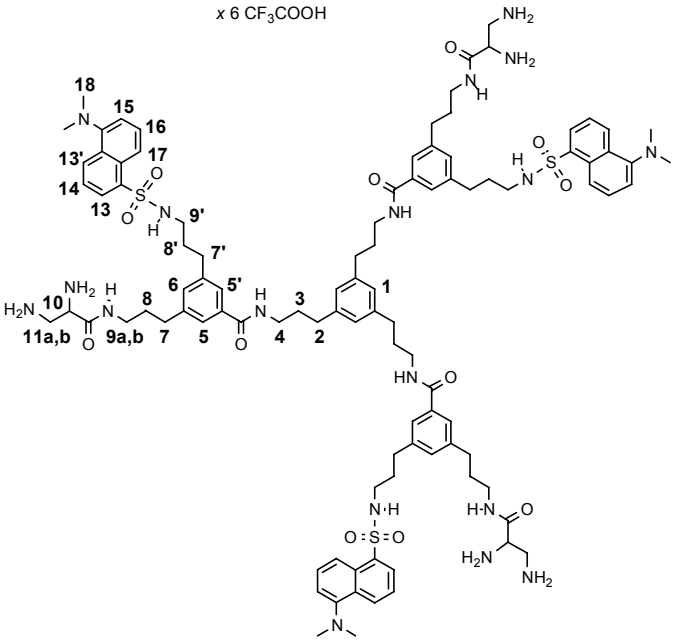
^{1}H NMR (500 MHz, CD_3OD): δ = 1.42 (s, 27 H, *H*-12,12'), 1.44 (s, 27 H, *H*-12',12), 1.61 (m, 6 H, *H*-8'), 1.78 (m, 6 H, *H*-8), 1.92 (m, 6 H, *H*-3), 2.46 (t, br, 6 H, *H*-7'), 2.58 (t, br, 6 H, *H*-7), 2.64 (t, br, 6 H, *H*-2), 2.84 (t, ^3J (H,H) = 6.5 Hz, 6 H, *H*-9'), 2.96 (s, 18 H, *H*-18), 3.19 (m, 6 H, *H*-9a), 3.30 (m, 3 H, *H*-11a), 3.38 (m, 3 H, *H*-11b), 3.40 (m, 6 H, *H*-9b), 4.17 (t, ^3J (H,H) = 5.9 Hz, 3 H, *H*-10), 6.93 (s, 3 H, *H*-1), 6.97 (s, 3 H, *H*-6), 7.26 (s, 3 H, *H*-5'), 7.40 (m, 6 H, *H*-5 + *H*-15), 7.60 (m, 6 H, *H*-14 + *H*-16), 8.18 (d, ^3J (H,H) = 7.3 Hz, 3 H, *H*-13,13'), 8.51 (m, 6 H, *H*-17 + *H*-13',13).

^{13}C NMR (126 MHz, CD_3OD): δ = 29.04 (CCH_3), 29.06 (CCH_3), 32.24 (CH_2), 32.35 (CH_2), 32.45 (CH_2), 33.65 (CH_2Ar), 33.97 (CH_2Ar), 34.62 (CH_2Ar), 40.11 (CH_2N), 41.08 (CH_2N), 43.53 (CH_2N + CH_2CH), 46.50 (NCH_3), 57.26 (CH), 80.81 (CCH_3), 81.14 (CCH_3), 117.42 (ArC_{Dns}), 120.29 (ArC_{Dns}), 125.32 (ArC_{Dns}), 126.35 (Ar*C*), 126.36 (Ar*C*), 127.66 (Ar*C*), 129.37 (ArC_{Dns}), 130.65 (ArC_{Dns}), 131.23 (ArC_{Dns}), 133.14 (Ar*C*), 136.23 (ArC_{Dns}), 137.78 (ArC_{Dns}), 137.89 (ArC_{Dns}), 143.46 (Ar*C*), 143.52 (Ar*C*), 143.70 (Ar*C*), 151.80 (ArC_{Dns}), 158.02 (CON_{Boc}), 158.98 (CON_{Boc}), 170.64 (CON), 173.25 (CON).

MS (MALDI-TOF, dithranol): *m/z:* 2500 $[M+K]^+$, 2484 $[M+Na]^+$;
monoisotopic mass calcd for $\mathbf{C_{129}H_{180}N_{18}NaO_{24}S_3^+}$: 2484.25, found: 2484.21.

(Dpa)$_3$(Dns)$_3$6D1: **1,3,5-Tris[3-(2,3-diamino-*N*-propylpropionamide)-5-[(5-dimethylamino-naphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide]benzene hexatrifluoroacetate (58)**

To a solution of dendrimer **57** (37.0 mg, 15.0 µmol) in DCM (3 ml) TFA (2 ml) was added, and the solution was stirred for 1 h at room temperature. After complete reaction (TLC) the solvent was repeatedly removed *in vacuo*. Lyophilization from water yielded the deprotected mixed dansyl- and diaminopropionic acid-modified dendrimer **58** as a brilliant yellow-greenish solid (37.0 mg, 14.5 µmol, 96.7 %).



M.p. 110-112 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.66 (m, 6 H, *H*-8'), 1.88 (m, 6 H, *H*-8), 1.94 (m, 6 H, *H*-3), 2.53 (t, ^3J (H,H) = 7.4 Hz, 6 H, *H*-7'), 2.66 (m, 12 H, *H*-7 + *H*-2), 2.84 (t, ^3J (H,H) = 6.7 Hz, 6 H, *H*-9'), 2.96 (s, 18 H, *H*-18), 3.21 (m, 3 H, *H*-9a), 3.39 (m, 6 H, *H*-4), 3.41 (m, 3 H, *H*-9b), 3.46 (dd, ^2J (H,H) = 14.0 Hz, ^3J (H,H) = 6.2 Hz, 3 H, *H*-11a), 3.53 (dd, ^2J (H,H) = 13.9 Hz, ^3J (H,H) = 5.4 Hz, 3 H, *H*-11b), 4.30 (t, ^3J (H,H) = 5.6 Hz, 3 H, *H*-10), 6.96 (s, 3 H, *H*-1), 7.07 (s, 3 H, *H*-6), 7.29 (s, 3 H, *H*-5'), 7.40 (d, ^3J (H,H) = 7.6 Hz, 3 H, *H*-15), 7.45 (s, 3 H, *H*-5), 7.58 (t, ^3J (H,H) = 7.9 Hz, 3 H, *H*-14), 7.63 (t, ^3J (H,H) = 8.2 Hz, 3 H, *H*-16), 8.18 (d, ^3J (H,H) = 7.3 Hz, 3 H, *H*-13,13'), 8.48 (d, ^3J (H,H) = 8.7 Hz, 3 H, *H*-17), 8.53 (d, ^3J (H,H) = 8.5 Hz, 3 H, *H*-13',13).

^{13}C NMR (126 MHz, CD_3OD): δ = 31.86 (CH_2), 32.31 (CH_2), 32.45 (CH_2), 33.59 (CH_2Ar), 34.11 (CH_2Ar), 34.61 (CH_2Ar), 40.87 (CH_2N), 41.10 (CH_2N), 41.28 (CH_2N), 43.42 (CH_2CH), 46.35 (NCH_3), 52.42 (CH), 117.29 (ArC_{dns}), 121.80 (ArC_{dns}), 125.09 (ArC_{dns}), 126.24 (Ar*C*), 126.41 (Ar*C*), 127.65 (Ar*C*), 129.40 (ArC_{dns}), 130.59 (Ar*C*), 130.86 (ArC_{dns}), 131.22 (ArC_{dns}), 133.14 (Ar*C*), 136.28 (ArC_{dns}), 137.03 (ArC_{dns}), 137.53 (ArC_{dns}), 143.54 (Ar*C*), 143.57 (Ar*C*), 143.58 (Ar*C*), 151.91 (ArC_{dns}), 166.95 (CON), 170.73 (CON).

MS (MALDI-TOF, CCA): *m/z:* 1900 $[M+K]^+$, 1884 $[M+Na]^+$, 1862 $[M+H]^+$;
monoisotopic mass calcd for $\mathbf{C_{99}H_{133}N_{18}O_{12}S_3^+}$: 1861.95, found: 1862.02.

7.4.6 Compounds of chapter 4.2.6

General remarks

Peptides **59** and **60** were synthesized by manual solid phase peptide synthesis techniques using standard PE syringes (10 ml or 20 ml) equipped with a PE filter as reaction vessels. The synthesis started with the commercially available *o*-chlorotrityl resin (Novabiochem) which was initially pre-loaded with Fmoc-glycine.

Pre-loading of the *o*-chlorotrityl resin

Pre-loading of the resin was performed with the Fmoc-protected amino acid glycine (1.5 eq.), which was dissolved in dry DMF (1 µg/ml) and treated in an ultrasonic bath for 1-2 min. Afterwards dry DCM (1 ml/100 mg resin) and DIPEA (6 eq.) were added. The solution was then added to the *o*-chlorotrityl resin and stirred at room temperature for 2 h. At the end or the reaction methanol was added (100 µl/100 mg resin). After 5 min the resin was sucked off, washed four times with DCM and thereafter four times with methanol. After evaporation of the solvent *in vacuo* the loading was determined by weight increase of the resin.

Coupling of amino acids by the Fmoc strategy

To a solution of the Fmoc-protected amino acid (3 eq.) in a small amount of dry DMF the coupling reagent TBTU (or HBTU) (3 eq.) and DIPEA (3 eq.) were added. The solution was stirred at room temperature for 30 sec, and then added to the resin. The mixture was stirred at room temperature for 50 min. The reaction was continuously monitored by MALDI-TOF mass spectrometry. To do so a small amount of the resin was washed with DMF and DCM and then treated with 1 % TFA in DCM to cleave the peptide from the resin. If the reaction was found to be not complete, it was allowed to proceed for a longer time. After complete reaction the resin was sucked off and washed with DMF (3*x*), DCM (3*x*), isopropanol (3*x*), and once again with DCM.

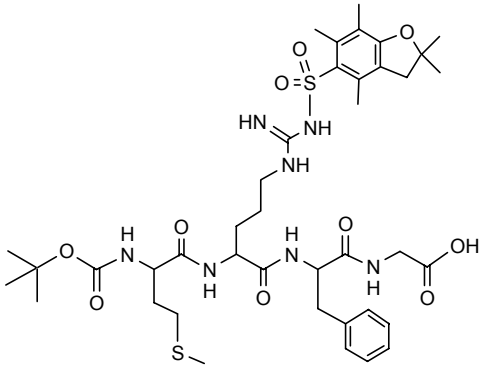
To cleave off the Fmoc protecting group the resin was added to a solution of 4 vol.% DBU and 4 vol.% piperidine in DMF (5 ml/100 mg resin). The mixture was stirred occasionally over a period of 15 min at room temperature. After complete deprotection (MALDI-TOF MS-monitored) the resin was sucked off and washed with DMF (3*x*), DCM (3*x*), isopropanol (3*x*), and once again with DCM.

Cleavage of the crude peptide from the resin

To cleave the protected peptide from the *o*-chlorotrityl resin, the resin was suspended in

DCM (2 ml/100 mg resin), and HFIP (0.5 ml/100 mg resin) was added under vigorous stirring. The reaction mixture was then stirred at room temperature for additional 60 min. After complete reaction (MALDI-TOF MS) the resin was filtered off and washed repeatedly with DCM. The filtrate was collected, the solvent removed *in vacuo*, and the crude product purified by RP-HPLC (systems *b* and *c*).

***Boc*-Met-Arg(*Pbf*)-Phe-Gly-OH (59)**



The procedure started from the Fmoc-Gly pre-loaded resin (1.00 g, *loading* 950 µmol/g, 950 µmol) (see general remarks) and was performed as described above under an argon atmosphere. TBTU was used as coupling reagent. RP-HPLC (systems *b* and *c*, *eluents:* linear gradient of 0-100 % acetonitrile in water (within 30 min) or acetonitrile/water/TFA (49.98:49.97:0.05) gave the protected tetrapeptide **59** as a colorless oil (581 mg, 674 µmol, 70.9 %) which could be lyophilized from acetonitrile/water.

$\boldsymbol{R_f}$ = 0.54 (ethyl acetate/methanol (2:1/v:v)).

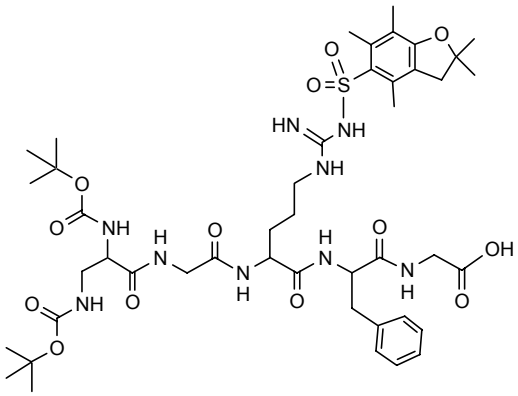
M.p. 126-128 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.46 (s, 9 H + 2 H, $C(CH_3)_{3,\,Boc}$ + CH_2), 1.49 (s, 6 H, $C(CH_3)_{2,\,Pbf}$), 1.63 (m, 1 H, $CH_{2,\,Arg}$), 1.73 (m, 1 H, CH_2), 1.87 (m, 1 H, CH_2), 1.98 (m, 1 H, CH_2), 2.10 (s, 3 H, $SCH_{3,\,Met}$), 2.13 (s, 3 H, $CH_{3,\,Pbf}$), 2.52 (m, 2 H, CH_2), 2.55 (s, 3 H, $CH_{3,\,Pbf}$), 2.62 (s, 3 H, $CH_{3,\,Pbf}$), 2.97 (m, 1 H, CH_2), 3.05 (s, 2 H, $CH_{2,\,Pbf}$), 3.16 (m, 1 H, CH_2), 3.23 (m, 2 H, CH_2), 3.93 (d, ^3J (H,H) = 1.7 Hz, 2 H, $CH_{2,\,Gly}$), 4.16 (m, 1 H, CH_{Arg}), 4.33 (m, 1 H, CH_{Met}), 4.70 (m, 1 H, CH_{Phe}), 7.21 (m, 2 H, ArH_{Phe}), 7.27 (m, 3 H, ArH_{Phe}).

^{13}C NMR (126 MHz, CD_3OD): δ = 12.80, 15.63, 18.64, 19.88, 26.47, 28.99 ($CCH_{3,\,Boc}$), 30.63, 31.49, 32.89, 38.99, 42.11, 44.22, 54.46, 55.35, 56.03 (CH), 81.07 (CH), 88.11 (CH), 118.02 (Ar*C*), 125.76 (Ar*C*), 128.09 (Ar*C*), 129.77 (Ar*C*), 130.62 (Ar*C*), 134.99 (Ar*C*), 135.67 (Ar*C*), 138.25 (Ar*C*), 138.64 (Ar*C*), 157.45 (CON_{Boc}), 159.29 (CN_{Arg}), 172.92 (CO), 173.78 (CO), 173.98 (CO), 175.08 (CO).

MS (FAB-, MNBA/DMSO): *m/z* (%): 860 (100) $[M-H]^-$, 761 (3.1) $[C_4H_7O_2]^-$;
monoisotopic mass calcd. for $\mathbf{C_{40}H_{58}N_7O_{10}S_2^-}$: 860.4, found: 860.4.

(*Boc*)$_2$-Dpa-Gly-Arg(*Pbf*)-Phe-Gly-OH (60)



The synthesis of pentapeptide **60** was performed with HBTU as coupling reagent as described above. The only exception was that coupling of the Boc-protected D/L-2,3-diaminopropionic acid **37** was performed with TATU instead of HBTU. Purification of the crude product by RP-HPLC gave the protected pentapeptide (162 mg, 166 µmol, 74.8 %) as a colorless oil which could be lyophilized from acetonitrile/water.

R_f = 0.19 (ethyl acetate/methanol (2:1/v:v)).

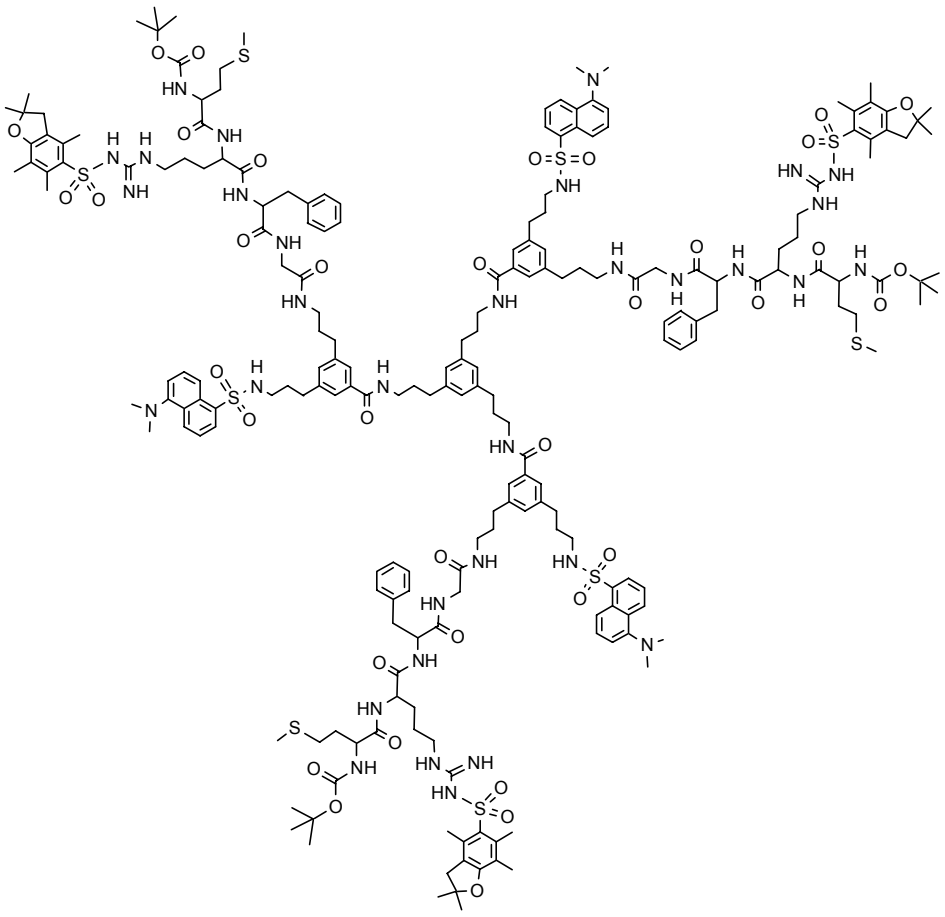
M.p. 121-123 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 1.41 (m, br, 2 H, $CH_{2,\,Arg}$), 1.47 (s, 18 H $C(CH_3)_{3,\,Boc}$), 1.49 (s, 6 H, $C(CH_3)_{2,\,Pbf}$), 1.66 (m, 2 H, $CH_{2,\,Arg}$), 2.12 (s, 3 H, $CH_{3,\,Pbf}$), 2.55 (s, 3 H, $CH_{3,\,Pbf}$), 2.61 (s, 3 H, $CH_{3,\,Pbf}$), 2.99 (m, 1 H, CH_2), 3.04 (s, 2 H, $CH_{2,\,Pbf}$), 3.08 (m, 1 H, CH_2), 3.14 (m, 2 H, CH_2), 3.30 (m, 1 H, CH_2), 3.48 (m, 1 H, CH_2), 3.88 (m, 2 H, $CH_{2,\,Gly}$), 3.97 (m, 2 H, $CH_{2,\,Gly}$), 4.16 (m, 1 H, CH_{Arg}), 4.24 (m, 1 H, CH_{Dpa}), 4.70 (m, 1 H, CH_{Phe}), 7.19 (m, 2 H, ArH_{Phe}), 7.28 (m, 3 H, ArH_{Phe}).

^{13}C NMR (126 MHz, CD_3OD): δ = 12.81, 18.70, 19.88, 26.71, 29.02 ($CCH_{3,\,Boc}$), 29.94, 38.68, 41.82, 42.22, 43.02, 44.28, 55.37, 56.25, 57.36, 80.86 (CH), 81.45 (CH), 87.96 (CH), 118.74 (Ar*C*), 126.34 (Ar*C*), 128.05 (Ar*C*), 129.77 (Ar*C*), 130.64 (Ar*C*), 133.82 (Ar*C*), 134.71 (Ar*C*), 138.96 (Ar*C*), 139.71 (Ar*C*), 158.39 (CON_{Boc}), 159.07 (CON_{Boc}), 160.19 (CN_{Arg}), 173.11 (CO), 173.51 (CO), 173.81 (CO), 174.11 (CO), 174.31 (CO).

MS (FAB+, MNBA/DMSO): *m/z* (%): 996 (12.7) $[M+Na]^+$, 975 (70.1) $[M+H]^+$;
monoisotopic mass calcd. for $\mathbf{C_{45}H_{68}N_9O_{13}S^+}$: 974.5, found: 974.6.

(Boc-Met-Arg(Pbf)-Phe-Gly)$_3$(Dns)$_3$6D1: **1,3,5-Tris{3-(*Boc*-Met-Arg(*Pbf*)-Phe-Gly-)-5-[(5-dimethylamino-naphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide}benzene (61)**



To a solution of peptide **59** (207 mg, 240 µmol) in dry DMF the coupling reagent HATU (100 mg, 264 µmol) and DIPEA (133 µl, 101 mg, 780 µmol) were added at 0 °C under a nitrogen atmosphere and stirred for additional 5 min. After complete formation of the active ester (TLC) a solution of the deprotected, partially dansylated dendrimer **56** (97 mg, 50 µmol) in a small amount of dry DMF was added dropwise at 0 °C. The solution was allowed to warm up to room temperature slowly and stirred for additional 12 hours in the dark. After complete reaction (TLC-monitored) the reaction mixture was washed once with a saturated sodium carbonate solution, and once with brine. The organic phase was dried over magnesium sulfate, the solvent removed under reduced pressure and the crude product purified by column chromatography (silica gel, DCM cont. 5 % methanol as eluent). The procedure afforded the oxidized peptide dendrimer **61** (110 mg, 26.6 µmol, 53.2 %) as a bright yellow, fluorescent oil which could be lyophylized from dioxane.

R_f = 0.46 (DCM/methanol (9:1/v:v)).

M.p. 180-181 °C.

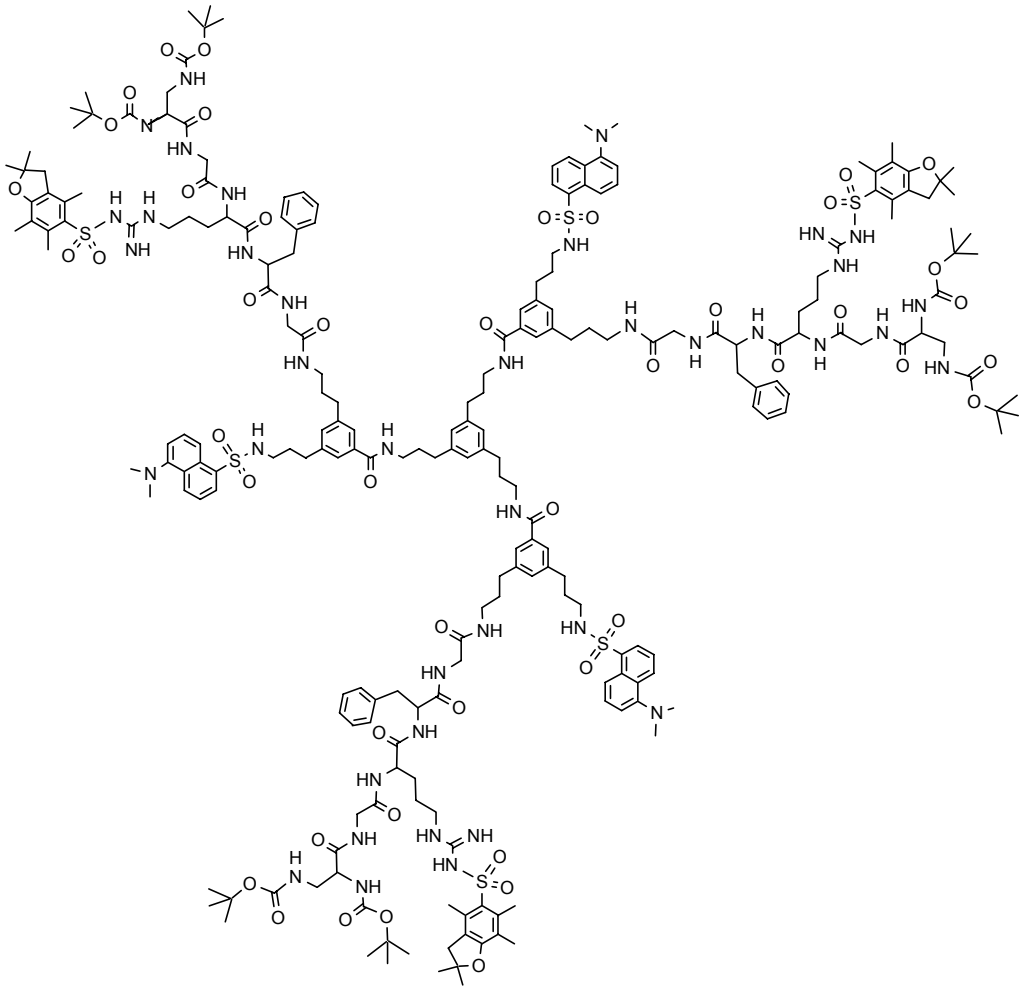
^{1}H NMR (500 MHz, [D$_7$]-DMF): δ = 1.38 (m, 9 H + 6 H, $CCH_{3,\,Boc}$ + CH_2), 1.43 (s, 18 H, $C(CH_3)_{2,\,Pbf}$), 1.49 (m, 6 H, CH_2), 1.63 (m, 6 H, CH_2), 1.72 (m, 6 H, $CH_{2,\,Dendr.}$), 1.77 (m, 6 H,

$CH_{2,\ Dendr.}$), 1.91 (m, 6 H, $CH_{2,\ Dendr.}$), 2.04 (s, 9 H, SCH_3), 2.01 (m, 6 H, CH_2), 2.06 (s, 9 H, $CH_{3,\ Pbf}$), 2.53 (s, 9 H + 6 H, $CH_{3,\ Pbf}$ + CH_2), 2.56 (m, 6 H, $CH_2Ar_{Dendr.}$), 2.60 (s, 9 H, $CH_{3,\ Pbf}$), 2.64 (m, 12 H, $CH_2Ar_{Dendr.}$), 2.86 (s, 18 H, NCH_3), 2.93 (m, 6 H, CH_2), 3.00 (m, 6 H, CH_2), 3.13 (m, 6 H, $CH_2N_{Dendr.}$), 3.19 (m, 6 H, $CH_2N_{Dendr.}$), 3.24 (m, 6 H, $CH_2N_{Dendr.}$), 3.41 (t, ^3J (H,H) = 6.7 Hz, 6 H, CH_2), 3.86 (m, 6 H, $CH_{2,\ Gly}$), 4.21 (m, br, 3 H, CH_{Arg}), 4.34 (m, 3 H, CH_{Met}), 4.57 (m, 3 H, CH_{Phe}), 6.95 (s, 3 H, Ar*H*), 7.04 (s, 3 H, Ar*H*), 7.17 (d, br, ArH_{Dns}), 7.26 (m, 15 H, ArH_{Phe}), 7.50 (s, 3 H, Ar*H*), 7.60 (m, 3 H + 3 H, Ar*H* + ArH_{Dns}), 7.65 (t, ^3J (H,H) = 6.7 Hz, 3 H, ArH_{Dns}), 8.20 (d, ^3J (H,H) = 7.3 Hz, 3 H, ArH_{Dns}), 8.45 (d, ^3J (H,H) = 8.7 Hz, 3 H, ArH_{Dns}), 8.53 (d, ^3J (H,H) = 8.5 Hz, 3 H, ArH_{Dns}).

MS (MALDI-TOF, dithranol): *m/z:* 4165 $[M+2O]^+$, 4181 $[M+3O]^+$;
monoisotopic mass calcd. for $\mathbf{C_{210}H_{285}N_{33}O_{38}S_9}^+$: 4164.89, found: 4164.69.

[(Boc)$_2$-Dpa-Gly-Arg(Pbf)-Phe-Gly]$_3$(Dns)$_3$6D1:

1,3,5-Tris{3-[(*Boc*)$_2$-Dpa-Gly-Arg(*Pbf*)-Phe-Gly-]-5-[(5-dimethylamino-naphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide}benzene (62)



To a solution of peptide **60** (124 mg, 127 µmol) in dry DMF the coupling reagent HATU (53.2 mg, 140 µmol) and DIPEA (70.3 µl, 53.4 mg, 413 µmol) were added at 0 °C and stirred for additional 5 min. After complete formation of the active ester (TLC) the reaction mixture was cooled down to – 20 °C and a solution of the deprotected, partially dansylated dendrimer **56** (42.5 mg, 26.5 µmol) in a small amount of dry DMF was added dropwise under vigorous stirring. The solution was then allowed to warm up to room temperature slowly and stirred for additional 12 hours in the dark. After complete reaction (TLC-monitored) the reaction mixture was washed once with a saturated sodium carbonate solution, and once with brine. The organic phase was dried with magnesium sulfate and the solvent removed *in vacuo*. Column chromatography (silica gel, DCM cont. 7 % methanol as eluent) gave the dansylated peptide dendrimer **62**

(82.1 mg, 18.3 µmol, 69.1 %) as a light yellow, fluorescent oil which could be lyophylized from dioxane.

R_f = 0.16 (DCM/methanol (9:1/v:v)).

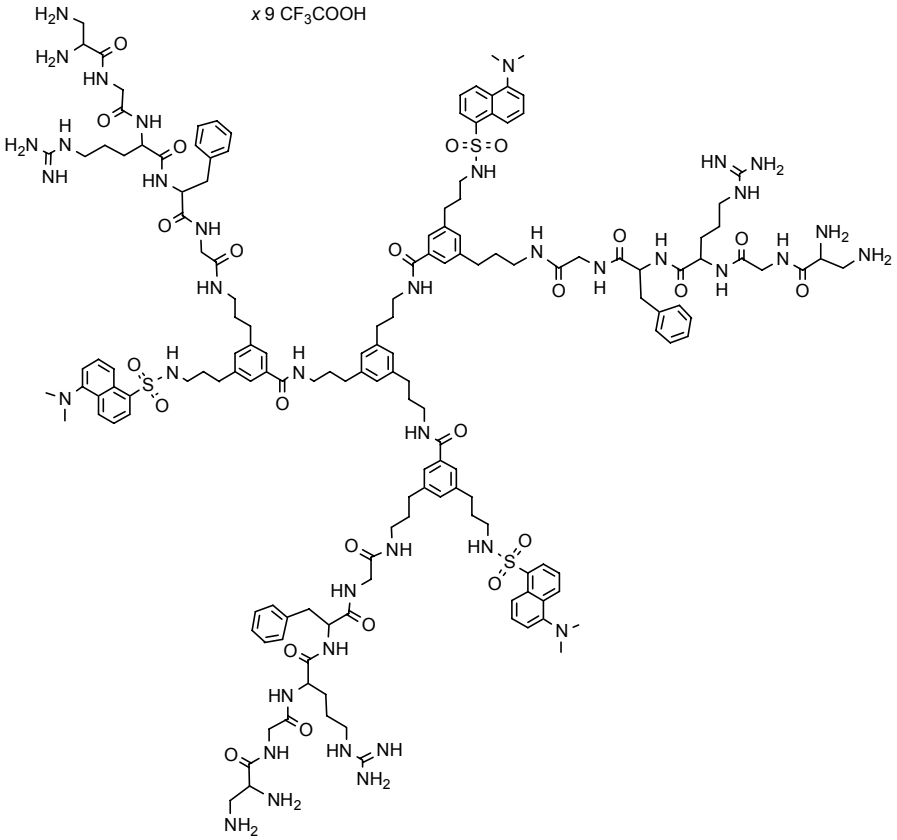
M.p. 152-153 °C.

^{1}H NMR (500 MHz, CD_2Cl_2/CD_3OD): δ = 1.35 (m, br, 6 H, $CH_{2,\,Arg}$), 1.41 (s, 27 H $C(CH_3)_{3,\,Boc}$), 1.43 (s, 27 H $C(CH_3)_{3,\,Boc}$), 1.45 (s, 18 H, $C(CH_3)_{2,\,Pbf}$), 1.63 (m, 6 H, CH_2), 1.70 (m, 6 H, $CH_{2,\,Dendr.}$), 1.80 (m, 6 H, $CH_{2,\,Dendr.}$), 1.94 (m, 6 H, $CH_{2,\,Dendr.}$), 2.09 (s, 9 H, $CH_{3,\,Pbf}$), 2.51 (s, 9 H, $CH_{3,\,Pbf}$), 2.54 (m, 6 H, $CH_2Ar_{Dendr.}$), 2.57 (s, 9 H, $CH_{3,\,Pbf}$), 2.62 (m, 6 H, $CH_2Ar_{Dendr.}$), 2.84 (m, 6 H, $CH_2Ar_{Dendr.}$), 2.87 (m, 6 H + 18 H, CH_2 + $CH_{2,Dns}$), 2.99 (s, 18 H, $NCH_{3,\,Pbf}$), 3.16 (m, 6 H, CH_2), 3.28 (m, 3 H, CH_2N) 3.38 (m, 6 H + 6 H, $CHCH_{2,\,Dpa}$ + CH_2N), 3.44 (m, 6 H, CH_2), 3.84 (m, 6 H, $CH_{2,\,Gly}$), 3.87 (m, 6 H, $CH_{2,\,Gly}$), 4.15 (m, 3 H, CH_{Arg}), 4.15 (m, 3 H, CH_{Dpa}), 4.51 (m, 3 H, CH_{Phe}), 6.92 (s, 3 H, Ar*H*), 7.04 (s, 3 H, Ar*H*), 7.11 (d, ^3J (H,H) = 5.8 Hz, 3 H, ArH_{Dns}), 7.23 (m, 15 H, ArH_{Phe}), 7.34 (s, 3 H, Ar*H*), 7.42 (s, 3 H, Ar*H*), 7.52 (t, ^3J (H,H) = 8.0 Hz, 3 H, ArH_{Dns}), 7.56 (t, ^3J (H,H) = 8.2 Hz, 3 H, ArH_{Dns}), 8.17 (d, ^3J (H,H) = 7.2 Hz, 3 H, ArH_{Dns}), 8.34 (d, ^3J (H,H) = 8.5 Hz, 3 H, ArH_{Dns}).

^{13}C NMR (126 MHz, CD_2Cl_2/CD_3OD): δ = 12.50 ($CH_{3,\,Pbf}$), 18.16 ($CH_{3,\,Pbf}$), 18.60 ($CH_{2,\,Arg}$), 19.41 ($CH_{3,\,Pbf}$), 28.43 ($CCH_{3,\,Boc}$), 28.58 ($CCH_{3,\,Boc}$), 30.15 (CH_2), 31.00 (CH_2), 31.26 (CH_2), 31.48 (CH_2), 31.64 (CH_2), 32.69 (CH_2), 32.92 (CH_2), 33.64 (CH_2), 36.94 (CH_2), 39.10 (NCH_3), 40.21 (CH_2), 42.07 (CH_2), 42.64 (CH_2), 43.19 (CH_2), 43.32 (CH_2), 43.53 (CH_2), 43.71 (CH_2), 45.57 (CH_2), 55.07 (CH), 56.13 (CH), 56.34 (CH), 115.72 (Ar*C*), 119,47 (Ar*C*), 123.72 (Ar*C*), 125.29 (Ar*C*), 125.34 (Ar*C*), 125.46 (Ar*C*), 126.70 (Ar*C*), 127.23 (Ar*C*), 128.66 (Ar*C*), 128.94 (Ar*C*), 129.55 (Ar*C*), 129.61 (Ar*C*), 129.72 (Ar*C*), 130.14 (Ar*C*), 130.37 (Ar*C*), 130.67 (Ar*C*), 132.30 (Ar*C*), 132.78 (Ar*C*), 133.51 (Ar*C*), 135.09 (Ar*C*), 135.74 (Ar*C*), 137.77 (Ar*C*), 137.91 (Ar*C*), 138.74 (Ar*C*), 142.38 (Ar*C*), 142.44 (Ar*C*), 142.71 (Ar*C*), 152.43 (Ar*C*), 157.04 (CON_{Boc}), 159.16 (CON_{Boc}), 163.78 (CN_{Arg}), 168.45 (CO), 169.41 (CO), 170.47 (CO), 171.71 (CO), 172.88 (CO), 173.64 (CO).

MS (MALDI-TOF, dithranol): *m/z:* 4165 $[M+2O]^+$, 4181 $[M+3O]^+$;
monoisotopic mass calcd. for $\mathbf{C_{225}H_{309}N_{39}O_{45}S_6^+}$: 4492.13, found: 4492.10.

(H-Dpa-Gly-Arg-Phe-Gly-)$_3$(Dns)$_3$6D1: **1,3,5-Tris{3-(*H*-Dpa-Gly-Arg-Phe-Gly]-5-[(5-dimethylamino-naphthalene-1-sulfonylamino)propyl]-*N*-propylbenzamide}benzene nonatrifluoroacetate (63)**



The protected peptide dendrimer **62** (25.0 mg, 5.57 µmol) was dissolved in aqueous TFA (95 %) and stirred at room temperature for 3 h. After complete reaction (TLC) the solvent was removed under reduced pressure and the deprotected dendrimer repeatedly re-dissolved in methanol/water (1:1/v:v). Finally the solvent was removed *in vacuo* to yield the desired deprotected peptide dendrimer **63** (17.3 mg, 5.55 µmol, 99.6 %) as a light yellow, fluorescent oil, which could be lyophylized from acetonitrile/water (3:1/v:v).

M.p. 152-154 °C.

^{1}H NMR (500 MHz, CD_3CN/D_2O): δ = 1.23 (m, br, 6 H, $CH_{2,\,Arg}$), 1.33 (m, br, 6 H, $CH_{2,\,Arg}$), 1.56 (m, 6 H, $CH_{2,\,Dend.}$), 1.60 (m, 6 H, $CH_{2,\,Dendr.}$), 1.75 (m, 6 H, $CH_{2,\,Dendr.}$), 2.40 (t, ^3J (H,H) = 7.5 Hz, 6 H, $CH_2Ar_{Dendr.}$), 2.45 (t, ^3J (H,H) = 7.7 Hz, 6 H, $CH_2Ar_{Dendr.}$), 2.50 (t, ^3J (H,H) = 7.3 Hz, 6 H, $CH_2Ar_{Dendr.}$), 2.77 (t, ^3J (H,H) = 6.9 Hz, 6 H, $CH_2N_{Dendr.}$), 2.89 (m, 3 H, $CH_{2,\,Phe}$), 2.95 (t, ^3J (H,H) = 6.9 Hz, 6 H, CH_2N_{Arg}), 3.01 (m, 6 H, $CH_2N_{Dendr.}$), 3.05 (m, 3 H, $CH_{2,\,Phe}$), 3.23 (t, ^3J (H,H) = 5.7 Hz, 6 H, $CH_2N_{Dendr.}$), 3.32 (s, 18 H, NCH_3), 3.45 (d, 6 H, $CH_{2,\,Dpa}$), 3.93 (t, ^3J (H,H) = 5.7 Hz, 6 H, $CH_{2,\,Gly}$), 4.22 (6 H, $CH_{2,\,Gly}$, hidden by the sovent signal), 4.14 (m, 3 H, CH_{Arg}), 4.33 (t, ^3J (H,H) = 5.8 Hz, 3 H, CH_{Dpa}), 4.49 (t, ^3J (H,H) = 7.5 Hz, 3 H, CH_{Phe}), 6.83 (s, 3 H, Ar*H*), 6.99 (s, 3 H, Ar*H*), 7.09 (s, 3 H, Ar*H*), 7.13 (m, 15 H, ArH_{Phe}), 7.27 (s, 3 H, Ar*H*), 7.75 (m, 6 H, ArH_{Dns}), 8.18 (d, ^3J (H,H) = 7.4 Hz, 3 H, ArH_{Dns}), 8.32 (d, ^3J (H,H) = 8.7 Hz, 3 H, ArH_{Dns}), 8.73 (d, ^3J (H,H) = 8.8 Hz, 3 H, ArH_{Dns}).

^{13}C NMR (126 MHz, CD_3CN/D_2O): δ = 25.10 (CH_2), 29.23 (CH_2), 31.19 (CH_2), 31.29 (CH_2), 31.48 (CH_2), 32.69 (CH_2), 33.03 (CH_2), 33.71 (CH_2), 37.82 (CH_2), 39.64 (CH_2), 40.34 (CH_2), 41.46 (CH_2), 42.99 (CH_2), 43.28 (CH_2), 43.45 (CH_2), 47.75 (CH_2), 45.57 (NCH_3), 51.42 (CH_{Arg}), 54.35 (CH_{Dpa}), 55.28 (CH_{Phe}), 115.94 (ArC_{Dns}), 119.52 (ArC_{Dns}), 124.58 (Ar*C*), 124.91 (Ar*C*), 125.58 (ArC_{Dns}), 126.34 (Ar*C*), 126.98 (ArC_{Dns}), 127.07 (ArC_{Phe}), 127.15 (ArC_{Dns}), 128.10 (ArC_{Dns}), 128.79 (ArC_{Phe}), 129.36 (ArC_{Phe}), 129.72 (Ar*C*), 130.11 (ArC_{Dns}), 131.99 (Ar*C*), 135.23 (Ar*C*), 137.51 (Ar*C*), 137.58 (Ar*C*), 139.71 (Ar*C*), 139.78 (Ar*C*), 142.87 (Ar*C*), 143.11 (Ar*C*), 143.44 (Ar*C*), 157.64 (CN_{Arg}), 167.40 (CO), 169.85 (CO), 171.15 (CO), 171.21 (CO), 173.55 (CO), 173.63 (CO).

MS (MALDI-TOF, CCA): *m/z:* 3114 $[M+H]^+$;
monoisotopic mass calcd. for $\mathbf{C_{156}H_{213}N_{39}O_{24}S_3^+}$: 3113.59, found: 3113.65.

7.5 Cell culture

MCF-7 cells:

The human MCF-7 breast cancer cell line was obtained from the American Culture Collection (ATCC, Rockville, MD). The MCF-7 cells were maintained in MEM Eagle´s medium containing L-glutamine, supplemented with $NaHCO_3$ (2.2 g/l), sodium pyrovate (110 mg/l), gentamycin (50 mg/l) and 10% fetal calf serum (FCS) using 75 cm^2 culture flasks in a water-saturated atmosphere (95% air/5 % CO_2) at 37°C. The cells were serially passaged weekly following trypsinization using 0,05 % trypsin / 0,02 % ethylenediaminetetraacetic acid (EDTA). Mycoplasma contamination was routinely monitored, and only mycoplasma-free cultures were used.

HeLa cells:

Human HeLa-cells were cultured at 37 °C in a humidified atmosphere with 5 % CO_2 in RPMI 1640 containing 10 % fetal bovine serum, 100 µg/ml penicillin, 100 µg/ml streptomycin and additional glutamine and non-essential amino acids with the following final concentrations: 4 mM glutamine, 1 mM alanine, 1.5 mM aspartic acid, 1.2 mM asparagine, 1.2 mM glutamic acid, 1.2 mM glycine, 1.2 mM proline, and 1.3 mM serine.

7.6 *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.[238] 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 2-3 days 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 4 °C. 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: $$T/C_{corr}\,[\%] = [(T-C_0)/(C-C_0)] \times 100 \quad (1)$$

Cytocidal effect: $$T\,[\%] = [(T-C_0)/C_0] \times 100 \quad (2)$$

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 Analytikjena *Flashscan S19* microplatereader.

7.7 Fluorescence microscopy

The day before exposition to the dendrimers, HeLa cells were seeded in 12-well plates containing a 12-mm glass cover slip in such a density that the next day about 60 % confluency was obtained. Dendrimers were added to the cells in a concentration of 5 μM. 20 hours after adding the dendrimer, cells were washed in PBS, fixed with 4 % paraformaldehyde and probed with the rabbit polyclonal antibody R1[239] raised against the membrane isoforms of LAP-2 and a Cy2-conjugated goat anti-rabbit IgG antibody as secondary antibody following standard procedures.[239]

The fluorescence images of the cells were obtained with the Zeiss laser-scanning microscope *LSM 510* and a plan-neofluar 63 × 1.25 oil-immersion objective. The dyes were excited at 364 nm (dansyl-labelled dentrimers) or 488 nm (Cy2) and fluorescent light was collected by a photomultiplier after passage through a 505-530 nm BP filter. Differential interference contrast (DIC) images were taken in parallel.