Supplementary Material (ESI) for New Journal of Chemistry

Supplementary Material:

Lysine dendrimers based on thiacalix[4]arene core moieties as molecular scaffolds for supramolecular host systems

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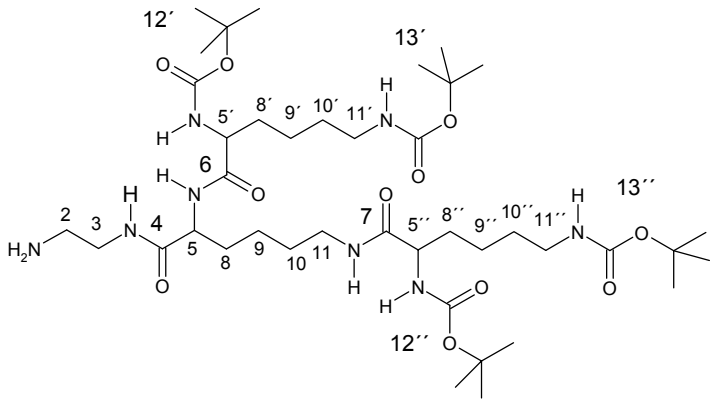
Experimental

L-lysine monodendron 2nd generation with N-(2-aminoethyl)amide group at the focal side NH_2-G2

Lysine monodendron 2nd generation[13] (CO_2Me-G2; 1.20 g, 1.5 mmol) was dissolved in MeOH (10 ml) and 1,2-diaminoethane (20 ml) was added. The resulting solution was stirred at room temperature for 4 days protected from light. The solvent and excess 1,2-diaminoethane were evaporated under reduced pressure and the residue was dissolved in ethyl acetate (70 ml). The organic solution was washed with water (2 x 50 ml) and brine solution (1 x 50 ml) and dried

over Na_2SO_4. The desired compound **NH_2-G2** was obtained as a colorless glassy solid in a yield of 89 %.

^{1}H NMR (DMSO-d_6): δ = 1.10 – 1.80 (8-8´´, 9-9´´, 10-10´´); 1.37 (12´, 12´´, 13´, 13´´); 2.54 (t, 2); 2.87 (m, 11´, 11´´); 2.99 (m, 11); 3.03 (m, 3); 3.81 (m, 5´´); 3.85 (m, 5´); 4.17 (m, 5); 6.29, 6.36, 6.42 (signals of minor NH-rotamers of 12´, 12´´, 13´, 13´´); 6.66 (d, 12´´); 6.72 (m, 13´, 13´´); 6.86 (d, 12´); 7.67 (d, 6); 7.69 (t, 7); 7.79 ppm (t, 4). ^{13}C NMR (DMSO-d_6): δ = 22.52 (9); 22.83 (9´, 9´´); 28.22, 28.32 (CH_3 of 12´, 12´´, 13´, 13´´); 28.79 (10); 29.24 (10´, 10´´); 31.44 (8´); 31.89, 31.96 (8, 8´´); 38.41 (11); 39.69 (11´, 11´´); 41.25 (2); 42.29 (3); 52.38 (5); 54.33 (5´´); 54.54 (5´); 77.34 ($C(CH_3)_3$ of 13´, 13´´); 77.93, 78.15 ($C(CH_3)_3$ of 12´, 12´´); 155.29 (C=O of 12´´); 155.46 (C=O of 12´); 155.61 (C=O of 13´, 13´´); 171.46 (4); 171.90 (7); 171.96 ppm (6). MALDI-TOF-MS: $C_{40}H_{76}N_8O_{11}$ (845.08); mass (m/z) = 868.4 ($M+Na^+$).

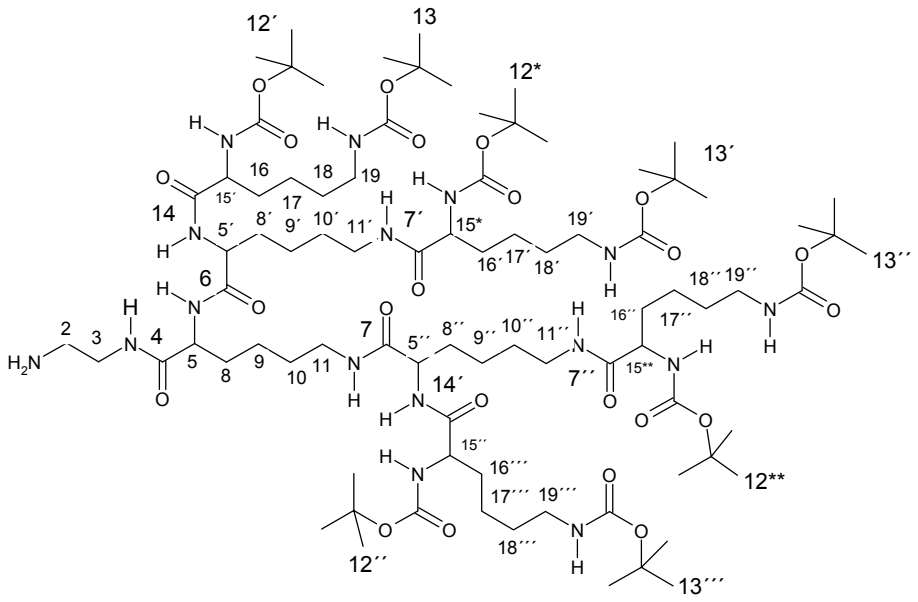


L-lysine monodendron 3rd generation with N-(2-aminoethyl)amide group at the focal side NH_2-G3

Lysine monodendron 3rd generation[13] (CO_2Me-G3; 0.64 g, 0.37 mmol) was dissolved in methanol (4 ml) and 1,2-diaminoethane (10 ml) was added. The resulting solution was stirred at room temperature for 4 days protected from light. The solvent and excess 1,2-

diaminoethane were evaporated under reduced pressure and the residue was dissolved in ethyl acetate (90 ml). The organic solution was washed with water (2 x 50 ml) and dried over Na_2SO_4. The desired compound **NH_2-G3** was obtained as a colorless glassy solid in a yield of 81 %.

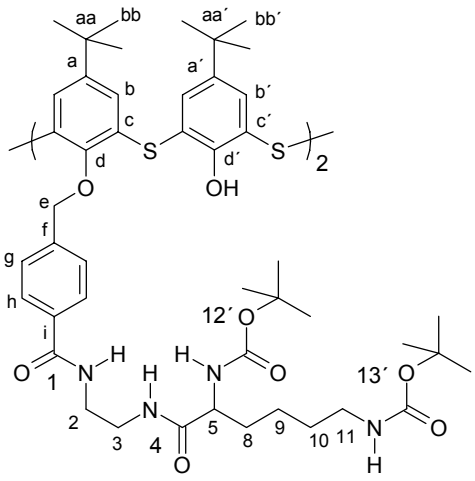
^{1}H NMR (DMSO-d_6): δ = 1.10 – 1.80 (8-8′′, 9-9′′, 10-10′′, 16-16′′′, 17-17′′′, 18-18′′′); 1.36 (CH_3 signal of 12′, 12′′, 12*, 12**, 13-13′′′); 2.55 (t, 2); 2.87 (m, 19-19′′′); 2.99 (m, 11-11′′); 3.04 (m, 3); 3.84 (m, 15′, 15′′, 15*, 15**); 4.16, 4.22 (m, 5-5′′); 6.28, 6.35, 6.43 (signals of minor NH-rotamers of 12′, 12′′, 12*, 12**, 13-13′′′); 6.65 (12*, 12**); 6.70 (13-13′′′); 6.87 (12′, 12′′); 7.63 (d, 6); 7.70 (7-7′′); 7.75, 7.82 ppm (4, 14, 14′). ^{13}C NMR (DMSO-d_6): δ = 22.52, 22.80, 22.83 (9-9′′, 17-17′′′); 28.25 (CH_3 of 12′, 12′′, 12*, 12**, 13-13′′′); 28.78 (10-10′′); 29.24 (18-18′′′); 31.40, 31.70, 31.88, 32.06 (8-8′′, 16-16′′′); 38.44 (11-11′′); 39.66 (19-19′′′); 41.19 (2); 42.16 (3); 52.20 (5); 52.35, 52.71 (5′, 5′′); 54.33, 54.55, 54,60 (15′, 15′′, 15*, 15**); 77.34 ($C(CH_3)_3$ of 13-13′′′); 77.95, 78.17 ($C(CH_3)_3$ of 12′, 12′′, 12*, 12**); 155.29, 155.49 (C=O of 12′, 12′′, 12*, 12**); 155.60 (C=O of 13-13′′′); 171.20 (6); 171.37 (14, 14′); 171.92 (7-7′′); 172.26 ppm (4).



5,11,17,23-Tetra-*tert*-butyl-25,27-di{[4-(*N*-(2-(*N*-(1-(*N*-*tert*-butoxycarbonyl)amino-5-(*N*-*tert*-butoxycarbonyl)aminopent-1-yl)carbonyl)aminoethyl)aminocarbonyl)phenyl]-methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol 2[12] (*cone* conformer*)* – ***conversion of 1 with BOP instead of CDI described in literature***[12].

Thiacalix[4]arene diacid **1** (0.33 g, 0.34 mmol) and **NH_2-G1** (0.29 g, 0.75 mmol) were suspended in anhydrous dichloromethane (15 ml). DIEA (0.56 g, 4.3 mmol, 0.76 ml) was added to the reaction solution and the mixture was stirred resulting in a clear solution. After the addition of BOP (0.30 g, 0.68 mmol) the resulting reaction solution was stirred at room temperature for 16 h. Dichloromethane (60 ml) was added to the reaction solution and the solution was washed with aqueous $KHSO_4$ solution (0.5 M, 2 x 30 ml) and aqueous $NaHCO_3$ solution (saturated, 2 x 30 ml). The organic layer was dried over Na_2SO_4. Finally, the solvent was distilled off and the residue was purified by column chromatography (using gradient CH_2Cl_2/MeOH starting from 50:1) to isolate 0.506 g of **2** (yield = 86 %).

^{1}H NMR (DMSO-d_6): δ = 0.77 (s, bb); 1.21 (m, 9); 1.30 (s, bb´); 1.33 (m overlapped by 12´, 13´, and bb´, 10); 1.34, 1.35 (2 s, 12´, 13´); 1.46, 1.57 (2 m, 8); 2.86 (m, 11); 3.26 (m, 3); 3.35 (m, 2); 3.72, 3.84 (2 m, 5); 5.48 (s, e); 6.36, 6.68 (signal of minor NH-rotamers of 12´and 13); 6.36, 6.74 (br s, 12´, 13´); 7.04 (s, b); 7.57 (d, g); 7.77 (s, b´); 7.86 (d, h); 7.94 (s, OH); 7.95 (t, 4); 8.38, 8.43 ppm (br s and t, 1). ^{13}C NMR (DMSO-d_6) δ = 22.83 (9); 28.20, 28.30 (CH_3 of 12´, 13); 29.22 (´10); 30.36 (bb); 31.14 (bb´); 31.68 (8); 33.79 (aa); 33.97 (aa´); 38.35 (3); 39.27 (2); 39.68 (11); 54.48, 55.70 (5); 75.34 (e); 77.31, 77.97 (*C*$(CH_3)_3$ of 12´, 13´); 121.52 (c´); 127.46 (h); 127.90 (g); 128.64 (c); 132.53 (b); 134.26 (i); 134.79 (b´); 139.66 (f); 142.84 (a´); 148.13 (a); 154.94 (d); 155.25 (d´); 155.38 (C=O of 12´); 155.58 (C=O of 13´); 166.09 (1); 172.61 ppm (4). MALDI-TOF-MS: $C_{92}H_{128}N_8O_{16}S_4$ (1730.35); mass (m/z) = 1752.7 ($M+Na^+$).

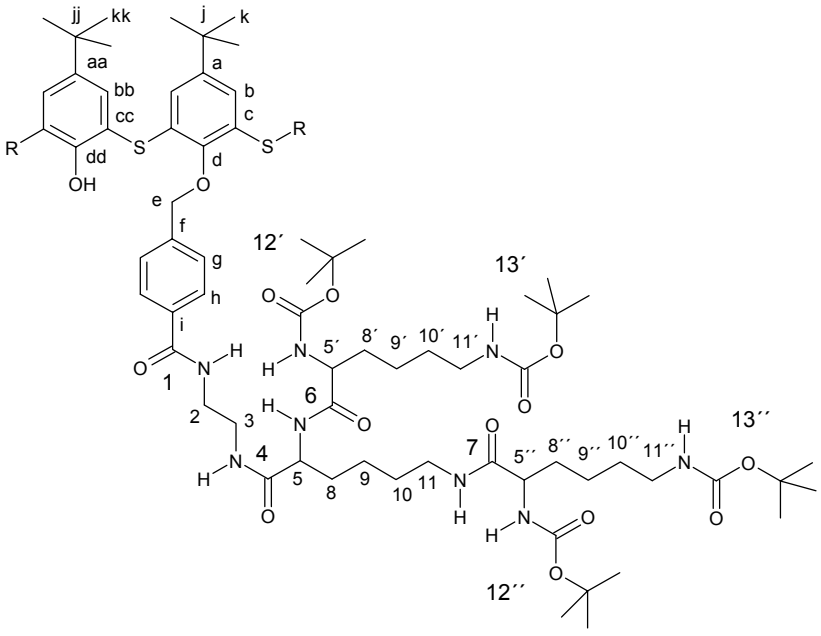


5,11,17,23-Tetra-*tert*-butyl-25,27-di{[4-(N-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol 3 (*cone* conformer).

Thiacalix[4]arene diacid **1** (0.11 g, 0.11 mmol) and **NH_2-G2** (0.21 g, 0.25 mmol) were suspended in dichloromethane (10 ml). DIEA (0.17 g, 1.32 mmol, 0.23 ml) was added and the mixture was stirred resulting in a clear solution. Then, BOP was added (0.11 g, 0.25 mmol) and the resulting solution was stirred at room temperature for 16 h. Dichloromethane (60 ml) was added and the solution was washed with aqueous $KHSO_4$ solution (0.5 M, 2 x 30 ml) and aqueous $NaHCO_3$ solution (saturated, 2 x 30 ml). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Finally, the residue was purified by column chromatography (using gradient CH_2Cl_2/MeOH starting from 50:1) to isolate 0.25 g of **3** (yield = 86 %).

^{1}H NMR (DMSO-d_6) = 0.77 (s, k); 1.29 (s, kk); 1.35 (s, 12´, 12´´, 13´, 13´); 1.10 – 1.70 (8-8´´, 9-9´´, 10-10´´); 2.87 (m, 11´, 11´´); 2.95, 3.00 (2 m, 11); 3.24 (m, 3); 3.36 (m, 2); 3.70 (5´ and 5´´ minor rotamer); 3.82 (m, 5´´); 3.87 (m, 5´); 4.20 (q, 5); 5.48 (s, e); 6.27, 6.34, and

6.41 (signals of minor NH-rotamers of 12′, 12′′, 13′, 13′); 6.61 (d, 12′′); 6.68 (t, 13′, 13′′); 6.85 (d, 12′); 7.03 (s, b); 7.57 (d, g); 7.69 (m, 7); 7.70 (m, 6); 7.76 (s, bb); 7.88 (d, h); 7.94 (s, OH); 8.06 (t, 4); 8.42 ppm (t, 1). ^{13}C NMR (DMSO-d_6) = 22.53 (9); 22.85, 22.88 (9′, 9′′); 28.23, 28.33 (CH_3 of 12′, 12′′, 13′, 13′′); 28.82 (10); 29.24 (10′, 10′′); 30.38 (k), 31.17 (kk); 31.42 (8′); 31.92 (8); 31.99 (8′′); 33.79 (j); 33.97 (jj); 38.38, 38.45 (3, 11); 39.19 (2); 39.72 (11′, 11′′); 52.40 (5); 54.35 (5′′); 54.54 (5′); 75.37 (e); 77.35 ($C(CH_3)_3$ of 13′, 13′′); 77.96, 78.18 ($C(CH_3)_3$ of 12′, 12′′); 121.56 (cc); 127.52 (h); 127.96 (g); 128.69 (c); 132.54 (b); 134.26 (i); 134.82 (bb); 139.68 (f); 142.86 (aa); 148.13 (a); 154.94 (d); 155.29 (dd, C=O of 12′′); 155.50 (C=O of 12′); 155.62 (C=O of 13′, 13′′); 166.10 (1), 171.91 (4); 171.94 (7); 172.09 ppm (6). IR (cm^{-1}) = 3303.6 (NH), 3078.7 (NH), 2976.3, 2933.1, 2866.4 (C-H), 1685.4 (C=O), 1643.3 (amide I), 1245.3 (C-O), 1164.3 (C=C-O-C), 780.4, 743.7 (arene). MALDI-TOF-MS: $C_{136}H_{208}N_{16}O_{28}S_4$ (2643.52); mass (m/z) = 2666.8 ($M+Na^+$).



5,11,17,23-Tetra-*tert*-butyl-25,27-di{[4-(N-(N_α-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol

4 (*cone* conformer).

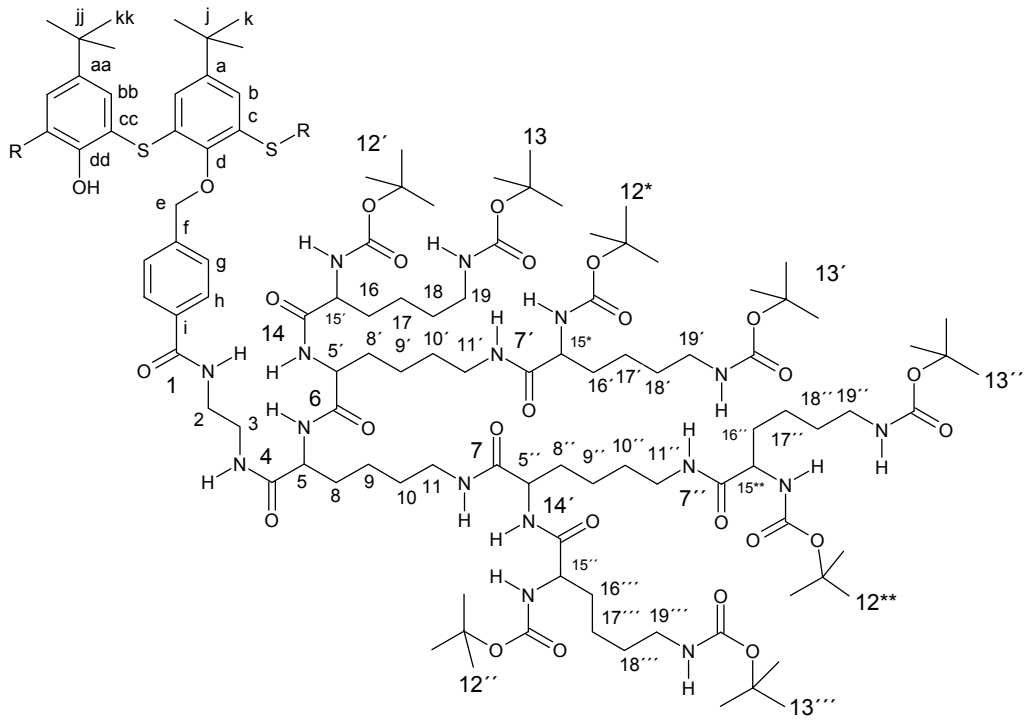
Synthetic route A: Thiacalix[4]arene diacid **1** (0.12 g, 0.12 mmol) and **NH_2-G3** (0.53 g, 0.30 mmol) were dissolved in DMF (10 ml). DIEA (0.19 g, 1.5 mmol, 0.26 ml) was added followed by the addition of BOP (0.12 g, 0.27 mmol) and the resulting solution was stirred at room temperature for 16 h. Finally, the solvent was distilled off and the residue was purified by column chromatography (using gradient CH_2Cl_2/MeOH starting from 30:1) to isolate 0.438 g of **4** (yield = 82 %).

Synthetic route B: **5** (0.15 g, 0.084 mmol), CO_2H-G2[13] (0.31 g, 0.39 mmol), and DIEA (0.13 g, 0.18 ml, 1.0 mmol) were dissolved in dichloromethane (15 ml). Then, BOP (0.17 g, 0.39 mmol) was added at room temperature and the resulting reaction solution was stirred at room temperature for 16 h. After the addition of MeOH (50 ml) the solution was transferred to a bigger flask and the organic solvents were evaporated under reduced pressure. The obtained residue was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 30:1 to 10:1) to isolate 0.258 g of **4** (yield = 69 %).

Synthetic route C: **3** (127 mg, 0.048 mmol) was dissolved in a mixture of dichloromethane and trifluoroacetic acid (3 ml, 1:1). The solution was stirred at room temperature for 1 h and evaporated under reduced pressure. Dichloromethane (5 ml) was added followed by the addition of DIEA (0.31 g, 0.42 ml, 2,4 mmol) and CO_2H-G1[13] (0.15 g, 0.42 mmol). After the addition of BOP (0.19 g, 0.42 mmol) the resulting reaction mixture was stirred at room

temperature overnight. Then, methanol (50 ml) was added to the reaction solution. Finally, the solvent was distilled off and the residue was purified by column chromatography (using gradient CH_2Cl_2/MeOH starting from 30:1) to isolate 0.128 g of **4** (yield = 60 %).

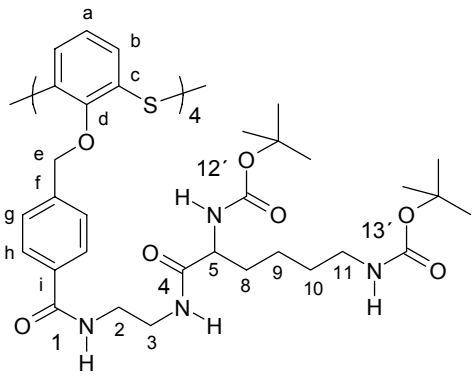
^{1}H NMR (DMSO-d_6): δ = 0.77 (s, k); 1.10 – 1.60 (8-8′′, 9-9′′, 10-10′′, 16-16′′′, 17-17′′′, 18-18′′′); 1.29 (s, kk); 1.36 (s, 12′, 12′′, 12*, 12**, 13-13′′′); 2.86 (m, 19-19′′′); 2.98 (m, 11-11′′); 3.24 (m, 3); 3.36 (m, 2); 3.82 (m, 15′, 15′′, 15*, 15**); 4.16, 4.22 (2 m, 5-5′′); 5.48 (s, e); 6.28, 6.34, 6.42 (signals of minor NH-rotamers of 12′, 12′′, 12*, 12**, 13-13′′′); 6.62 (d, 12*, 12**); 6.68 (t, 13-13′′′); 6.86 (d, 12′, 12′′); 7.02 (s, b); 7.57 (d, g); 7.61 (d, 6); 7.68 (m, 7-7′′); 7.75 (s, bb); 7.81 (m, 14, 14′); 7.87 (d, h); 7.91 (s, OH); 7.99 (m, 4); 8.41 ppm (t, 1). ^{13}C NMR (DMSO-d_6): δ = 22.55, 22.84 (9-9′′, 17-17′′′); 28.22, 28.32 (CH_3 of 12′, 12′′, 12*, 12**, 13-13′′′); 28.80 (10-10′′); 29.25 (18-18′′′); 30.38 (k); 31.16 (kk); 31.40 - 31.92 (8-8′′, 16-16′′′); 33.80 (j); 33.96 (jj); 38.48 (3, 11-11′′); 39.32 (2); 39.72 (19-19′′′); 52.22, 52.36, 52.68 (5-5′′); 54.36, 54.59, 54.68 (15′, 15′′, 15*, 15**); 75.43 (e); 77.35 ($C(CH_3)_3$ of 13-13′′′); 77.97, 78.18, 78.21 ($C(CH_3)_3$ of 12′, 12′′, 12*, 12**); 121.56 (cc); 127.50 (h); 128.00 (g); 128.66 (c); 132.53 (b); 134.26 (i); 134.80 (bb); 139.68 (f); 142.84 (aa); 148.08 (a); 154.72, 154.95, 155.30, 155.51 (d, dd, C=O of 12′, 12′′, 12*, 12**); 155.62 (13-13′′′); 166.09 (1); 171.22 (6); 171.48, 171.78, 171.95, 172.34 (7-7′′, 14, 14′); 172.58 ppm (4). IR (cm^{-1}) = 3286.0.0 (NH), 3090.0 (NH), 2975.8, 2933.4, 2865.0 (C-H), 1686.3 (C=O), 1636.8 (amide I), 1245.7 (C-O), 1164.1 (C=C-O-C), 779.1 (arene). MALDI-TOF-MS: $C_{224}H_{368}N_{32}O_{52}S_4$ (4469.87 g/mol); mass (m/z) = 4492.8 ($M+Na^+$).



25,26,27,28-Tetrakis{[4-(*N*-(2-(*N*-(1-(*N*-*tert*-butoxycarbonyl)amino-5-(*N*-*tert*-butoxy-carbonyl)aminopent-1-yl)carbonyl)aminoethyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene 8[12] (*1,3-alternate* conformer) – ***conversion of 7 with BOP instead of CDI described in literature.***[12]

Thiacalix[4]arene tetraacid **7** (0.10 g, 0.080 mmol) and **NH_2-G1** (0.15 g, 0.40 mmol) were suspended in dichloromethane (10 ml). After the addition of DIEA (0.50 g, 3.9 mmol, 0.68 ml) the mixture was stirred resulting in a clear solution. Then, BOP (0.16 g, 0.36 mmol) was added to the reaction solution and the resulting solution was stirred at room temperature for 16 h. The solution was taken up in additional dichloromethane (60 ml) and washed with aqueous $KHSO_4$ solution (0.5 M, 2 x 30 ml) and aqueous $NaHCO_3$ solution (saturated, 2 x 30 ml). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 50:1 to 10:1) to isolate 0.177 g of **8** (yield = 87 %).

^{1}H NMR (DMSO-d_6): δ = 1.22 (m, 9); 1.34 (m, 10); 1.36 (s, 12′, 13′); 1.48, 1.58 (2 m, 8); 2.86 (q, 11); 3.31, 3.37 (2 m, 3); 3.43 (m, 2); 3.75, 3.87 (2 q, 5); 5.21 (s, e); 6.45 (t, a); 6.34, 6.68 (2 t, 13′); 6.36, 6.73 (2 t, 12′); 7.01 (d, b); 7.14 (d, g); 7.90 (d, h); 8.01 (t, 4); 8.53 ppm (t, 1). ^{13}C NMR (DMSO-d_6): δ = 22.85 (9); 28.22, 28.30 (CH_3 of 12′, 13′); 29.25 (10); 31.73 (8); 38.45 (3); 39.34 (2); 39.66 (11); 54.51 (5); 70.64 (e); 77.32, 78.00 ($C(CH_3)_3$ of 12′, 13′); 123.70 (a); 126.34 (g); 126.81 (h); 128.72 (c); 133.17 (i); 134.57 (b); 140.43 (f); 155.38 (C=O of 12′); 155.58 (C=O of 13′); 159.42 (d); 166.45 (1); 172.65 ppm (4). MALDI-TOF-MS: $C_{128}H_{176}N_{16}O_{28}S_4$ (2515.18 g/mol); mass (m/z) = 2537.7 ($M+Na^+$).

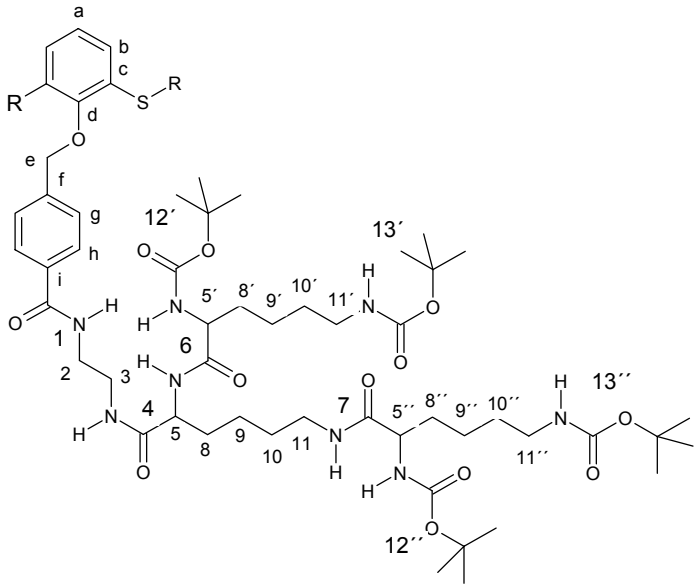


25,26,27,28-Tetrakis{[4-(N-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene 9 (*1,3-alternate* conformer).

Synthetic route A: Thiacalix[4]arene tetraacid **7** (0.10 g, 0.080 mmol) and **NH_2-G2** (0.34 g, 0.40 mmol) were suspended in dichloromethane (10 ml). DIEA (0.50 g, 3.9 mmol, 0.68 ml) was added and the mixture was stirred resulting in a clear solution. Then, BOP was added (0.16 g, 0.36 mmol) and the resulting solution was stirred at room temperature for 16 h. The solution was taken up in additional dichloromethane (60 ml) and washed with aqueous $KHSO_4$ solution (0.5 M, 2 x 30 ml) and aqueous $NaHCO_3$ solution (saturated, 2 x 30 ml). The

organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH starting from 50:1) to isolate 0.24 g of **9** (yield = 69 %).

Synthetic route B: **11** (0.06 g , 0.022 mmol) and CO_2H-G_1[13] (0.0762 g, 0.22 mmol) were dissolved in DMF (3 ml). After the addition of DIEA (0.227 g, 0.3 ml, 1.76 mmol) and BOP (0.0968g, 0.22 mmol) the resulting reaction mixture was stirred at room temperature for 16 h. Then, cold water was added until precipitation of a solid appeared. The solid was collected by filtration and washed with water. The solid was purified by additional column chromatography (SiO_2, $CHCl_3$ and $CHCl_3$/MeOH 20:1) to isolate 0.072 g of **9** (yield = 75 %). ^{1}H NMR (DMSO-d_6) = 1.10 – 1.75 (8-8′′, 9-9′′, 10-10′′); 1.36 (s, 12′, 12′′, 13′, 13′′); 2.86 (q, 11′, 11′′); 2.97 (m, 11); 3.30, 3.37 (2 m, 3); 3.42 (m, 2); 3.82 (m, 5′′); 3.88 (m, 5′); 4.22 (m, 5); 5.20 (s, e); 6.24, 6.34, 6.42 (signals of minor NH-rotamers of 12′, 12′′, 13′, 13′′); 6.46 (t, a); 6.62 (d, 12′′); 6.68 (m, 13′, 13′′); 6.86 (d, 12′); 7.01 (d, b); 7.13 (d, g); 7.69 (t, 7); 7.70 (d, 6); 7.90 (d, h); 8.09 (t, 4); 8.53 ppm (t, 1). ^{13}C NMR (DMSO-d_6) = 22.56 (9); 22.85, 22.88 (9′, 9′′); 28.23, 28.32 (CH_3 of 12′, 12′′, 13′, 13′′); 28.85 (10); 29.25 (10′, 10′′); 31.42 (8′); 31.92 (8); 32.00 (8′′); 38.46 (3, 11), 39.30 (2); 39.81 (11′, 11′′); 52.44 (5); 54.35 (5′′); 54.55 (5′); 70.70 (e); 77.36 ($C(CH_3)_3$ of 13′, 13′′); 77.97, 78.21 ($C(CH_3)_3$ of 12′, 12′′); 123.71 (a); 126.44 (g); 126.86 (h); 128.74 (c); 133.20 (i); 134.60 (b); 140.45 (f); 155.32, 155.52 (C=O of 12′, 12′′); 155.62 (C=O of 13′, 13′′); 159.44 (d); 166.51 (1), 171.91 (4); 171.95 (7); 172.10 ppm (6). IR (cm^{-1}) = 3303.2 (NH), 3078.3 (NH), 2975.7, 2933.2, 2866.7 (C-H), 1687.6 (C=O), 1642.1 (amide I), 1244.9 (C-O), 1162.4 (C=C-O-C), 779.0, 752.0 (arene). MALDI-TOF-MS: $C_{216}H_{336}N_{32}O_{52}S_4$ (4341.53); mass (m/z) = 4364.9 ($M+Na^+$).



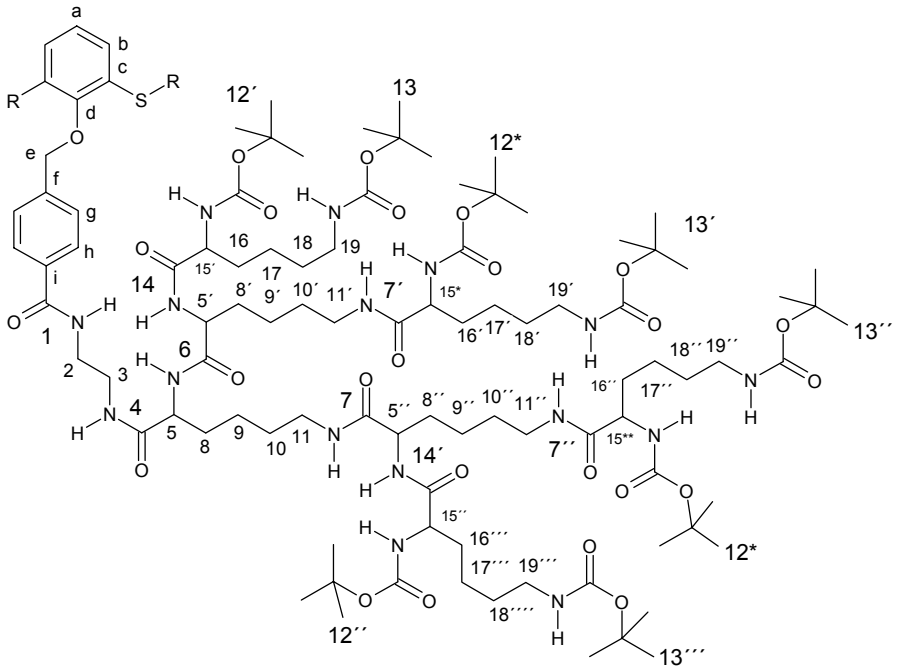
25,26,27,28-Tetrakis{[4-(N-(N_α-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-N_ε-(N_α-Boc-N_ε-Boc-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol 10 (*1,3-alternate* conformer).

Synthetic route A: Thiacalix[4]arene tetraacid **7** (0.081 g, 0.065 mmol) and **NH_2-G3** (0.50 g, 0.28 mmol) were suspended in DMF (10 ml). DIEA (0.26 g, 2.0 mmol, 0.35 ml) was added and the mixture was stirred resulting in a clear reaction solution. After the addition of BOP (0.13 g, 0.28 mmol) the resulting solution was stirred at room temperature for 16 h. The solution was taken up in ethyl acetate (100 ml) and washed with aqueous $KHSO_4$ solution (0.5 M, 2 x 30 ml) and aqueous $NaHCO_3$ solution (saturated, 2 x 30 ml). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by

column chromatography (SiO_2, CH_2Cl_2/MeOH starting from 30:1) to isolate 0.119 g of **10** **(**yield = 23 %).

Synthetic route C: **12** (0.0784 g, 0.017 mmol) and CO_2H-G_1[13] (0.118 g, 0.34 mmol) were dissolved in DMF (15 ml). After the addition of DIEA (0.70 g, 0.95 ml, 5.44 mmol) and BOP (0.15 g, 0.34 mmol) the resulting solution was stirred at room temperature for 23 h. Then, cold water was added until precipitation of a solid appeared. The solid was collected by filtration and washed with water. The solid was purified by column chromatography (SiO_2, $CHCl_3$/MeOH starting from 50:1) to isolate 0.106 g of **10** (yield = 77.9 %).

^{1}H NMR (DMSO-d_6): δ = 1.10 – 1.75 (8-8′′, 9-9′′, 10-10′′, 16-16′′′, 17-17′′′, 18-18′′′); 1.34 (s, 12′, 12′′, 12*, 12**, 13-13′′′); 2.86 (m, 19-19′′′); 3.00 (m, 11-11′′); 3.34 (m, 3); 3.43 (m, 2); 3.82 (m, 15*, 15**); 3.86 (m, 15′, 15′′); 4.18 (m, 5′, 5′′); 4.25 (m, 5); 5.20 (s, e); 6.28, 6.34, 6.42 (signals of minor NH-rotamers of 12′, 12′′, 12*, 12**, 13-13′′′); 6.47 (t, a); 6.62 (d, 12*, 12**); 6.68 (t, 13-13′′′); 6.86 (d, 12′, 12′′); 7.02 (d, b); 7.14 (d, g); 7.61 (d, 14); 7.69 (m, 7′, 7′′); 7.77 (m, 6); 7.82 (m, 7, 14′); 7.88 (d, h); 8.02 (t, 4); 8.52 ppm (t, 1). ^{13}C NMR (DMSO-d_6): δ = 22.55, 22.85 (9-9′′, 17-17′′′); 28.20, 28.30 (CH_3 of 12′, 12′′, 12*, 12**, 13-13′′′); 28.82 (10-10′′); 29.21 (18-18′′′); 31.40, 31.62, 31.87, 32.05 (8-8′′, 16-16′′′); 38.46 (3, 11-11′′); 39.13 (2); 39.71 (19-19′′′); 52.19, 52.35, 52.70 (5-5′′); 54.33, 54.55, 54.64, 55.60 (15′, 15′′, 15*, 15**); 70.46 (e); 77.32 ($C(CH_3)_3$ of 13-13′′′); 77.93, 78.17 ($C(CH_3)_3$ of 12′, 12′′, 12*, 12**); 123.59 (a); 126.54 (g); 126.81 (h); 128.68 (c); 133.23 (i); 134.58 (b); 140.36 (f); 155.28, 155.49 (C=O of 12′, 12′′, 12*, 12**); 155.58 (13-13′′′); 159.42 (d); 166.42 (1); 171.19 (6); 171.49, 171.75, 171.91 (7-7′′, 14, 14′); 172.35 ppm (4). IR (cm^{-1}) = 3288.4 (NH), 3090.2 (NH), 2975.2, 2932.7, 2864.6 (C-H), 1688.1 (C=O), 1636.4 (amide I), 1245.2 (C-O), 1163.5 (C=C-O-C), 778.9, 753.0 (arene). MALDI-TOF-MS: $C_{392}H_{656}N_{64}O_{100}S_4$ (7994.22); mass (m/z) = Degradation of **10** during investigation shown in Figure 6e-SM.

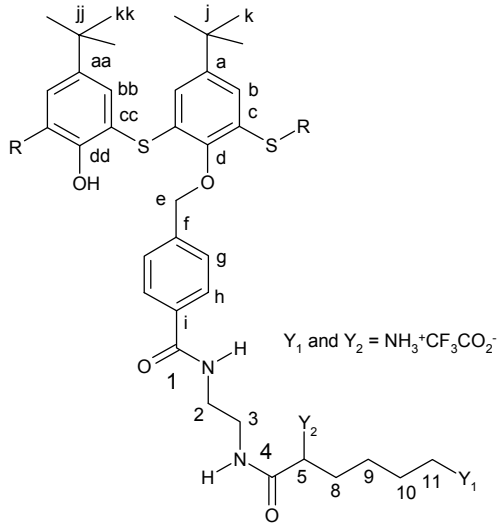


5,11,17,23-Tetra-*tert*-butyl-25,27-di{[4-(N-(1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol tetra ammonium trifluoroacetate 5 (*cone* conformer).

2 (0.18 g, 0.10 mmol) was dissolved in a mixture of dichloromethane (2 ml) and trifluoroacetic acid (2 ml). The solution was stirred at room temperature for 1 h. The solvent was evaporated and diethyl ether (10 ml) was added to the residue. The mixture was stirred for 1 h resulting in solidifying of the desired compound **5**. The solid was filtered off over a glass filter and washed with diethyl ether (2 x 10 ml). **5** was obtained as a white amorphous solid in 89 % yield.

^{1}H NMR (DMSO-d_6) = 0.77 (s, k); 1.30 (s, kk); 1.32 (m, 9); 1.52 (m, 10); 1.70 (m, 8); 2.74 (m, 11); 3.32, 3.39 (m, 3); 3.41 (q, 2); 3.71 (m, 5); 5.49 (s, e); 7.03 (s, b); 7.59 (d, g); 7.74 (t, NH_3^+ of Y_1); 7.77 (s, bb); 7.89 (d, h); 7.93 (s, OH); 8.15 (d, NH_3^+ of Y_2); 8.53 (t, 1); 8.60 ppm (t, 4). ^{13}C NMR (DMSO-d_6) = 21.26 (9); 26.60 (10); 30.36 (k); 30.43 (8); 31.16 (kk); 33.82 (j): 34.00 (jj); 38.51 (11); 38.55 (3); 38.84 (2); 52.24 (5); 75.38 (e); 116.25 (q, $CF_3CO_2^-$);

121.50 (cc); 127.51 (h); 128.01 (g); 128.62 (c); 132.54 (b); 134.16 (i); 134.90 (bb); 139.82 (f); 142.96 (aa); 148.23 (a); 154.87 (d); 155.23 (dd); 158.27 (q, $CF_3CO_2^-$); 166.20 (1); 168.72 ppm (4).

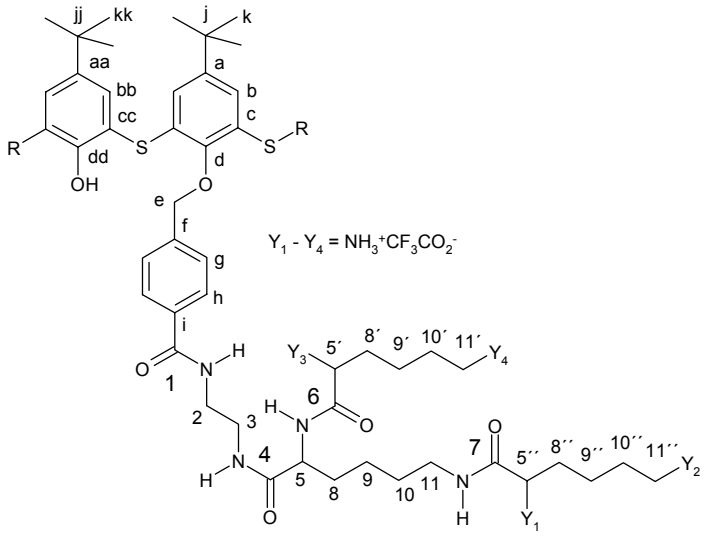


5,11,17,23-Tetra-*tert*-butyl-25,27-di{[4-(N-(N_α-(1,5-diaminopent-1-ylcarbonyl)-N_ε-(1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix[4]arene-26,28-diol 11 octaammonium trifluoroacetate 6 (*cone* conformer).

3 (**127 mg, 0.048 mmol**) was dissolved in a mixture of dichloromethane (5 ml) and trifluoroacetic acid (5 ml). The solution was stirred at room temperature for 2 h. The solvent was evaporated and diethyl ether (15 ml) was added to the residue. The mixture was stirred under ice bath cooling for 1 h resulting in solidifying of the desired compound **6**. The solid was filtered off over a glass filter and washed with diethyl ether (2 x 10 ml). **6** was obtained as a white amorphous solid in 93 % yield.

^{1}H NMR (DMSO-d_6) = 0.77 (s, k); 1.20 – 1.48 (9-9´´, 10); 1.30 (s, kk´); 1.53 (10´, 10´´); 1.55 (1H of 8); 1.69 (1H of 8; 8´, 8´´); 2.75 (m, 11´, 11´´); 3.07 (m, 11); 3.24 (1H of 3); 3.34 (1H of 3; 2); 3.69 (m, 5´´); 3.82 (m, 5´); 4.24 (m, 5); 5.49 (s, e); 7.02 (s, b); 7.59 (d, g); 7.76 (s,

bb); 7.81 (NH_3^+ of Y_2 + Y_4); 7.88 (s, OH); 7.89 (d, h); 8.15 (NH_3^+ of Y_1); 8.18 (NH_3^+ of Y_3); 8.26 (t, 4); 8.47 (t, 7); 8.52 (t, 1); 8.58 ppm (d, 6). ^{13}C NMR (DMSO-d_6) = 21.03, 21.24 (9′, 9′′); 22.80 (9); 26.39, 26.48 (10′, 10′′); 28.59 (10); 30.34 (k), 30.46, 30.50 (8′, 8′′); 31.12 (kk); 31.73 (8); 33.78 (j); 33.94 (jj); 38.34 (3); 38.46, 38.51 (11′, 11′′); 38.73 (11); 39.01 (2); 51.82 (5′); 52.09 (5′′); 53.00 (5); 75.46 (e); 117.05 (q, $CF_3CO_2^-$); 121.49 (cc); 127.48 (h); 128.03 (g); 128.58 (c); 132.51 (b); 134.19 (i); 134.85 (bb); 139.73 (f); 142.89 (aa); 148.14 (a); 154.89 (d); 155.22 (dd); 158.52 (q, $CF_3CO_2^-$); 166.16 (1), 168.19 (7); 168.41 (4); 171.43 ppm (6).

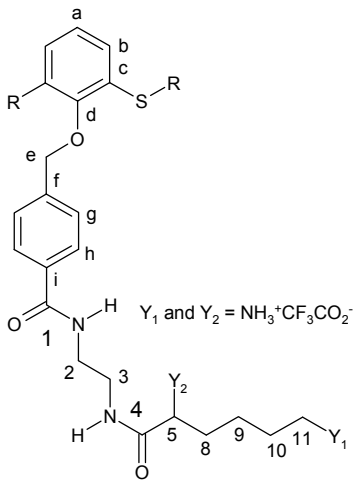


25,26,27,28-Tetrakis{[4-(N-(1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix-[4]arene octaammonium trifluoroacetate 11 (*1,3-alternate* conformer).

8 (0.14 g, 0.057 mmol) was stirred in a mixture (4 ml, 1:1) of trifluoroacetic acid and dichloromethane (1:1) at room temperature for 1 h. After the evaporation of the organic solvents under reduced pressure anhydrous diethyl ether (10 ml) was added and the resulting mixture was stirred at room temperature for 1 h. The solid was collected by filtration and

washed with anhydrous diethyl ether (3x10 ml). **11** was dried in vacuum yielding 0.118 g (80.8 %) as a white solid.

^{1}H NMR (DMSO-d_6) = 1.35 (m, 9); 1.54 (m, 10); 1.73 (m, 8); 2.76 (m, 11); 3.36, 3.41 (2 m, 3); 3.45 (m, 2); 3.73 (m, 5); 5.21 (s, e); 6.47 (t, a); 7.04 (d, b); 7.16 (d, g); 7.79 (NH_3^+ of Y_1); 7.88 (d, h); 8.16 (NH_3^+ of Y_2); 8.64 ppm (m, 1, 4). ^{13}C NMR (DMSO-d_6) = 21.32 (9); 26.61 (10); 30.53 (8); 38.53 (11); 38.67 (3); 38.99 (2); 52.23 (5); 70.83 (e); 117.24 (q, $CF_3CO_2^-$); 123.64 (a); 126.70 (g); 126.86 (h); 128.71 (c); 133.27 (i); 134.59 (b); 140.46 (f); 158.48 (q, $CF_3CO_2^-$); 159.49 (d); 166.59 (1); 168.86 ppm (4).



25,26,27,28-Tetrakis{[4-(N-(N_α-(1,5-diaminopent-1-ylcarbonyl)-N_ε-(1,5-diaminopent-1-ylcarbonyl)-1,5-diaminopent-1-ylcarbonyl)aminocarbonyl)phenyl]methoxy}-2,8,14,20-tetrathiacalix-[4]arene hexadecaammonium trifluoroacetate 12 (*1,3-alternate* conformer). **9** (0.22 g, 0.0507 mmol) was stirred in a mixture (6 ml, 1:1) of trifluoroacetic acid and dichloromethane at room temperature for 6h. After the evaporation of the organic solvents under reduced pressure anhydrous diethyl ether (20 ml) was added and the resulting mixture was stirred at room temperature for 2 h. The solid was collected by filtration and washed with

anhydrous diethyl ether (3x10 ml). **12** was dried in vacuum yielding 0.172 g (74 %) as a white solid.

^{1}H NMR (DMSO-d_6) = 1.2 – 1.5 (9-9´´, 10); 1.56 (m, 10´, 10´´); 1.71 (m, 8-8´´); 2.76 (m, 11´, 11´´); 3.09 (m, 11); 3.28 (m, 3); 3.38 (m, 2); 3.71 (m, 5´´); 3.84 (m, 5´); 4.26 (q, 5); 5.20 (s, e); 6.50 (t, a); 7.06 (m, b); 7.17 (d, g); 7.87 (h and NH_3^+ from Y_2 + Y_4); 8.20 (NH_3^+ of Y_1 + Y_3); 8.31 (t, 4); 8.51 (m, 7); 8.62 ppm (m, 1, 6). ^{13}C NMR (DMSO-d_6) = 21.11, 21.28 (9´, 9´´); 22.88 (9); 26.44, 26.51 (10´, 10´´); 28.65 (10); 30.50, 30.54 (8´, 8´´); 31.80 (8); 38.50 (11´, 11´´); 38.56 (3); 38.78 (11); 39.06 (2); 51.89 (5´); 52.12 (5´´); 53.06 (5); 70.89 (e); 117.17 (q, $CF_3CO_2^-$); 123.59 (a); 126.83, 126.88 (g, h); 128.65 (c); 133.33 (i); 134.58 (b); 140.34 (f); 158.49 (q, $CF_3CO_2^-$); 159.44 (d); 166.48 (1), 168.23 (7); 168.46 (6); 171.47 ppm (4).

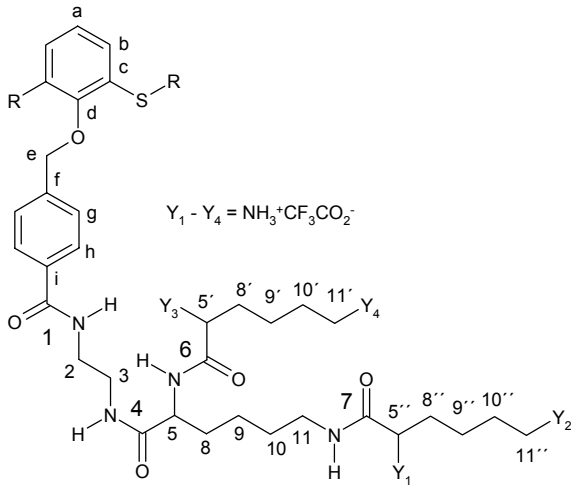


Figure Caption for Supplementary Material

Figure S1 Synthesis of N-2-aminoethyl-substituted lysine monodendron NH_2-G1,[12] NH_2-G2, and NH_2-G3

Figure S2 ^{13}C NMR spectra of **2** (a), **3** (b), and **4** (c) based on thiacalix[4]arene diacid **1** showing the C=O region of the amide and urethane groups. The aromatic amide group at about 166 ppm (carbon is described as 1 in the NMR part of the lysine dendrimers) presents the critical linkage between thiacalix[4]arene moiety and lysine monodendrons. The lysine dendrimers **8** – **10** also outline the important aromatic amide group at about 166 ppm as critical linkage between thiacalix[4]arene moiety and lysine monodendrons.

Figure S3 Comparison of the ^{13}C NMR spectra for the carbonyl carbon of the aromatic amide group at about 166 ppm for **10** realized by synthetic route A and C. Non-completely converted acid groups in **10** is given obtained from synthetic route A (conversion of **7** with H_2N-G3). Therefore, two ^{13}C signals (assigned by ⁎) for the aromatic amide group are observed.

Figure S4 Chromatograms of **8** (2515.18 g/mol), **9** (4341.53 g/mol)), and **10** (7984.0 g/mol) obtained from SEC investigations. Knowing that the use of the SEC for the determination of molecular weights from 500 g/mol to 10.000 g/mol is partly difficult caused by the solvation effects, influence of end groups or the partly missing of the statistical coil (to have the necessary hydrodynamic volume for the separation and determination of the molecular weights). Nevertheless, the separation of the molar masses of the dendrimers **8** – **10** followed the SEC separation mechanism. An unimodal weight distribution is

given for the tetrasubstituted thiacalix[4]arene core moieties. Only for **10** higher molecular weight parts are indicated. Here, the presence of possible associates of **10** is assumed. This fact is further under investigation to explain more in detail. In general, it can be assumed that the desired compounds were realized supported by the SEC, MALDI-TOF-MS and NMR investigations (see also Table 1-SM on page 29). The SEC investigations, possessing only a relative calibration (see Experimental in Letter), were carried out with a binary solvent mixture (DMAc/H_2O) containing 3 g LiCl per liter.

Figure S5 Comparison of the synthetic routes for the realization of the lysine dendrimer **10**. SEC investigations show that non-completely converted acid groups of the core moiety, using synthetic route A, exhibited. This result supports the NMR results for **10** realized by synthetic route A and C.

Figure S6 MALDI-TOF-MS spectra of **2**, **4**, **8**, **9**, and **10**. In all cases, except for **10**, the desired molar mass of the lysine dendrimers was determined. Due to the degradation of the Boc-groups during MALDI-TOF-MS investigations of the lysine dendrimers **2**, **4**, **8**, **9**, and **10** additional mass signals for lower masses were observed compared to the desired molar masses as well.

Table S1 Comparison of the theoretical molar mass of **8** – **10** with the molar masses obtained from MALDI-TOF-MS and SEC

Figure S1. Synthesis of N-2-aminoethyl-substituted lysine monodendron NH_2-G1,[12] NH_2-G2, and NH_2-G3

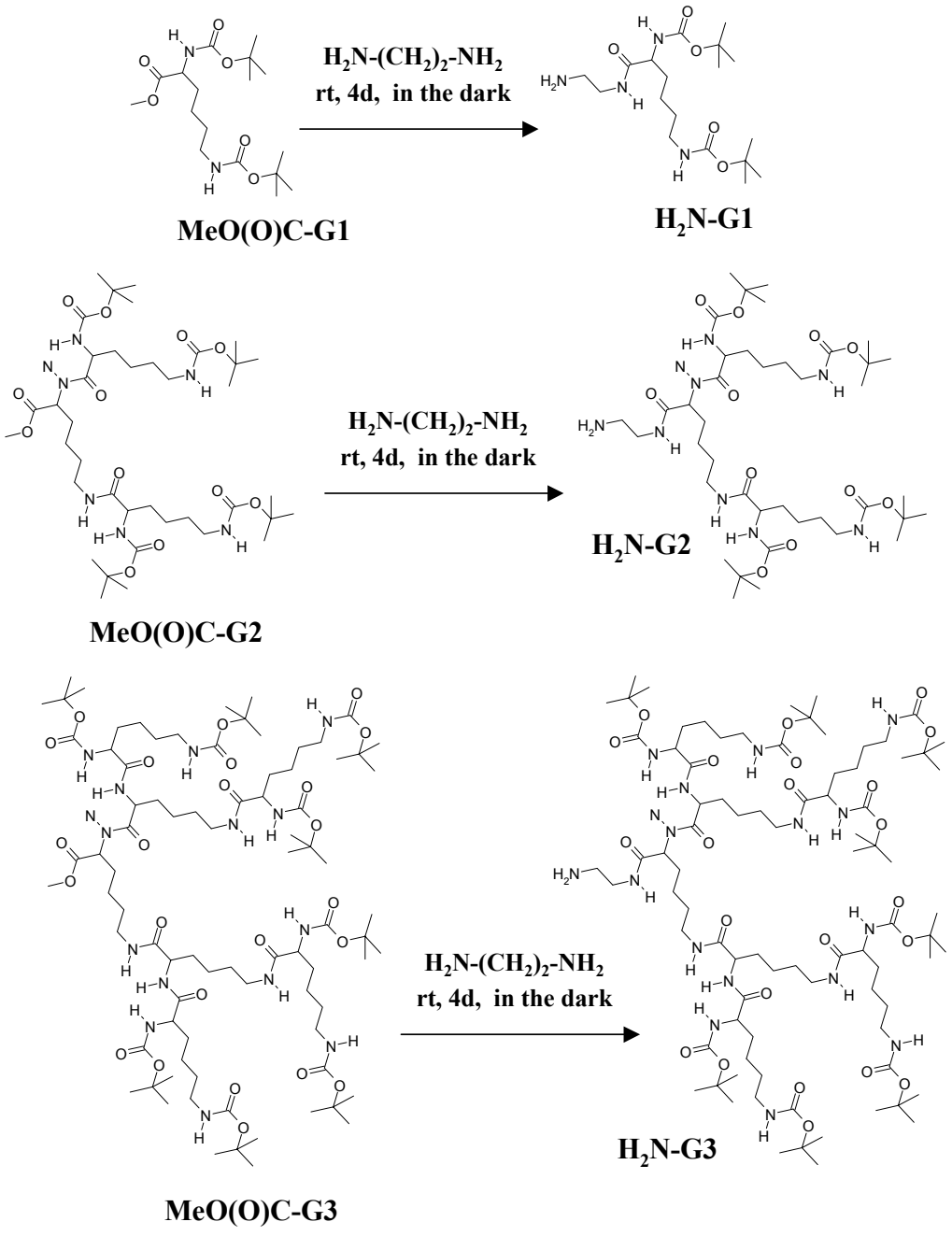


Figure S2. ^{13}C NMR spectra of **2** (a), **3** (b), and **4** (c) based on thiacalix[4]arene diacid **1** showing the C=O region of the amide and urethane groups. The aromatic amide group at about 166 ppm (carbon is described as 1 in the NMR part of the lysine dendrimers) presents the critical linkage between thiacalix[4]arene moiety and lysine monodendrons. The lysine dendrimers **8** – **10** also outline the important aromatic amide group at about 166 ppm as critical linkage between thiacalix[4]arene moiety and lysine monodendrons.

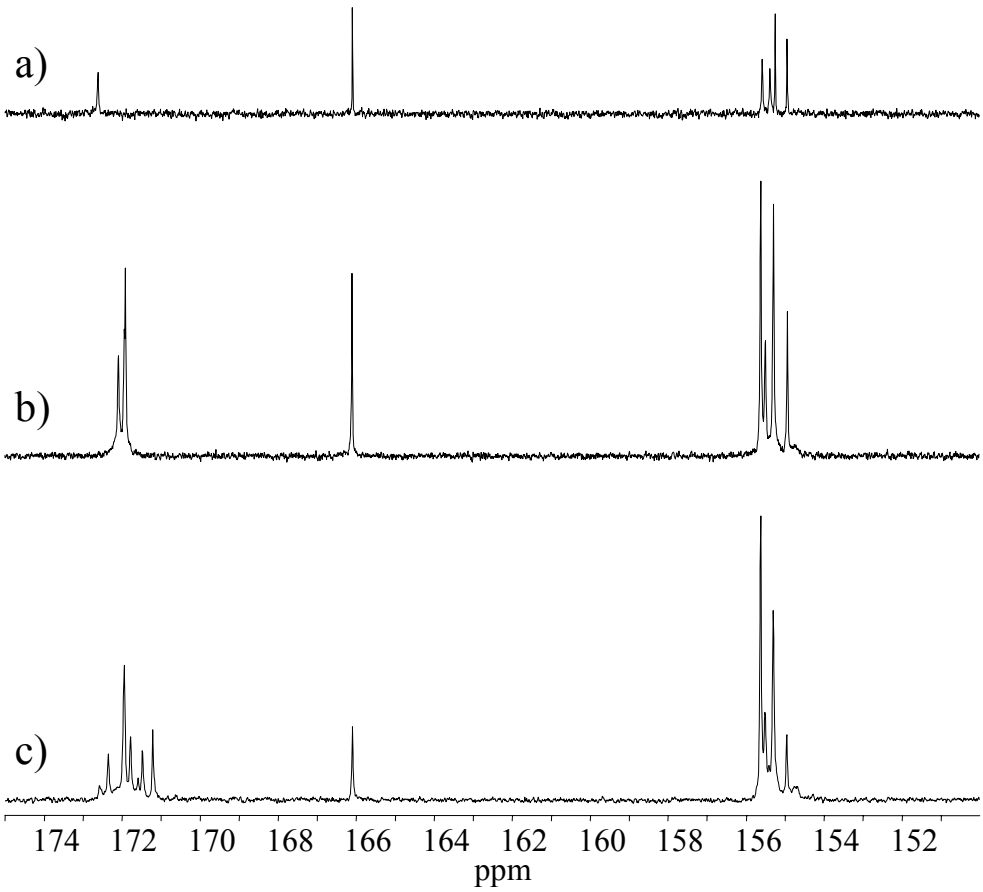


Figure S3. Comparison of the ^{13}C NMR spectra for the carbonyl carbon of the aromatic amide group at about 166 ppm for **10** realized by synthetic route A and C. Non-completely converted acid groups in **10** is given obtained from synthetic route A (conversion of **7** with H_2N-G3). Therefore, two ^{13}C signals (assigned by ⁎) for the aromatic amide group are observed.

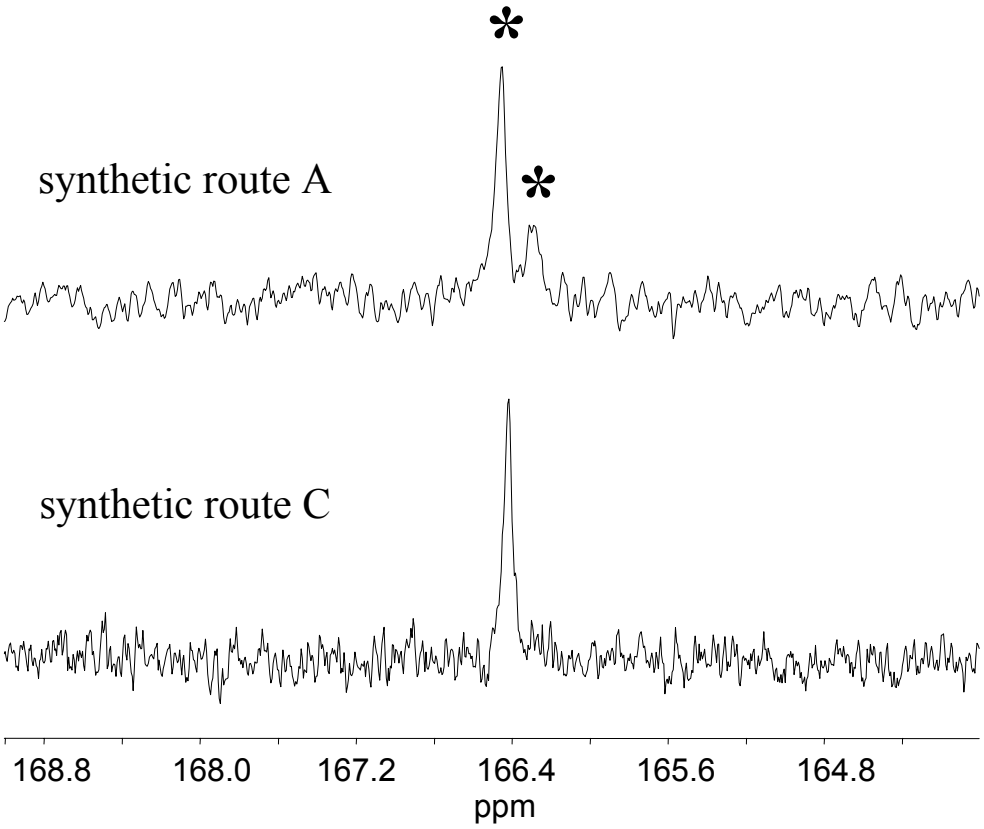


Figure S4. Chromatograms of **8** (2515.18 g/mol), **9** (4341.53 g/mol)), and **10** (7984.0 g/mol) obtained from SEC investigations. Knowing that the use of the SEC for the determination of molecular weights from 500 g/mol to 10.000 g/mol is partly difficult caused by the solvation effects, influence of end groups or the partly missing of the statistical coil (to have the necessary hydrodynamic volume for the separation and determination of the molecular weights). Nevertheless, the separation of the molar masses of the dendrimers **8** – **10** followed the SEC separation mechanism. An unimodal weight distribution is given for the tetrasubstituted thiacalix[4]arene core moieties. Only for **10** higher molecular weight parts are indicated. Here, the presence of possible associates of **10** is assumed. This fact is further under investigation to explain more in detail. In general, it can be assumed that the desired compounds were realized supported by the SEC, MALDI-TOF-MS and NMR investigations (see also Table S1 on page 29). The SEC investigations, possessing only a relative calibration (see in Letter), were carried out with a binary solvent mixture (DMAc/H_2O) containing 3 g LiCl per liter.

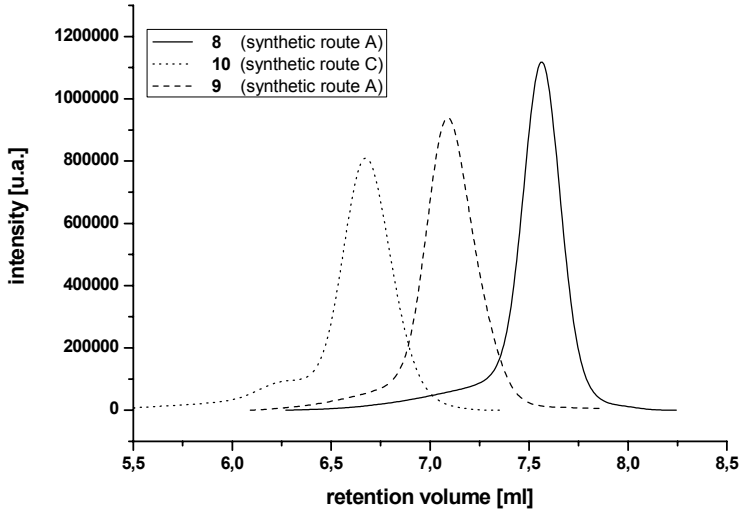


Figure S5. Comparison of the synthetic routes for the realization of the lysine dendrimer **10**. SEC investigations show that non-completely converted acid groups of the core moiety, using synthetic route A, exhibited. This result supports the NMR results for **10** realized by synthetic route A and C.

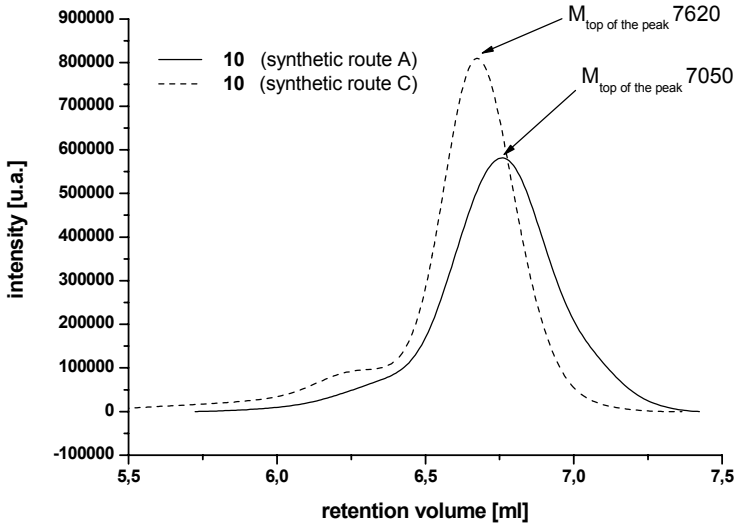
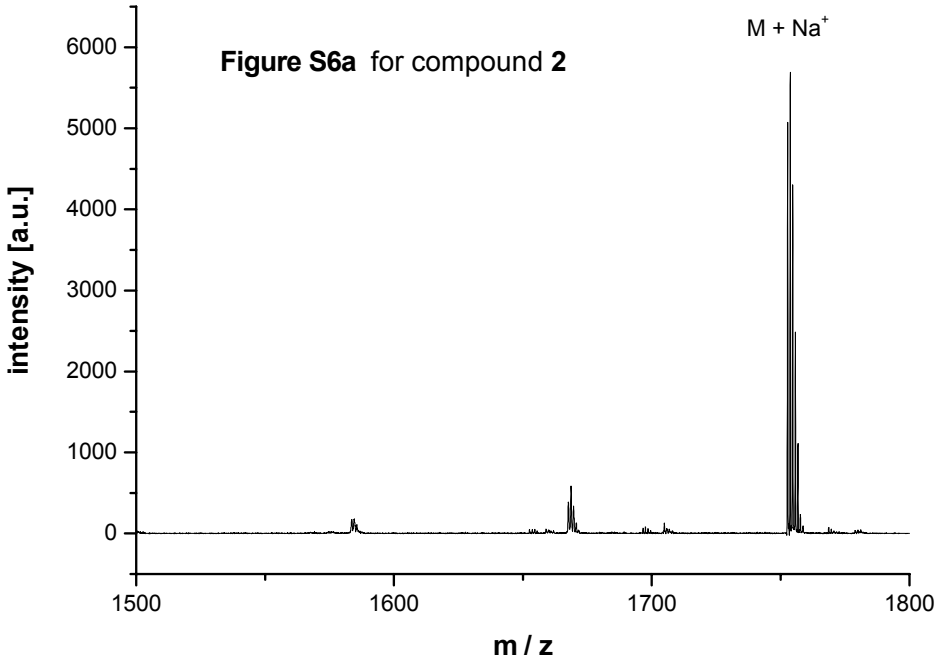
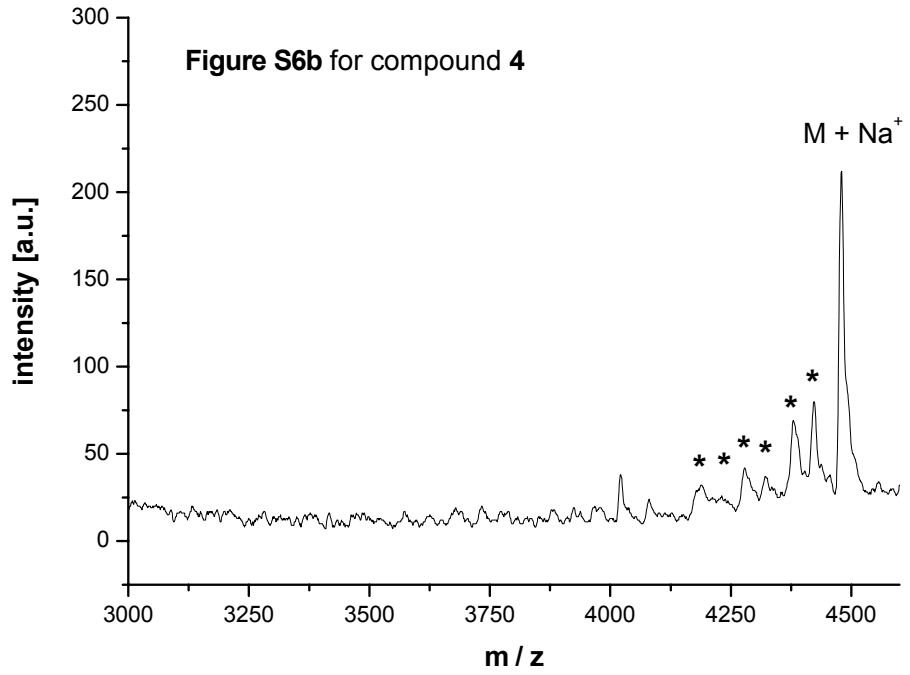
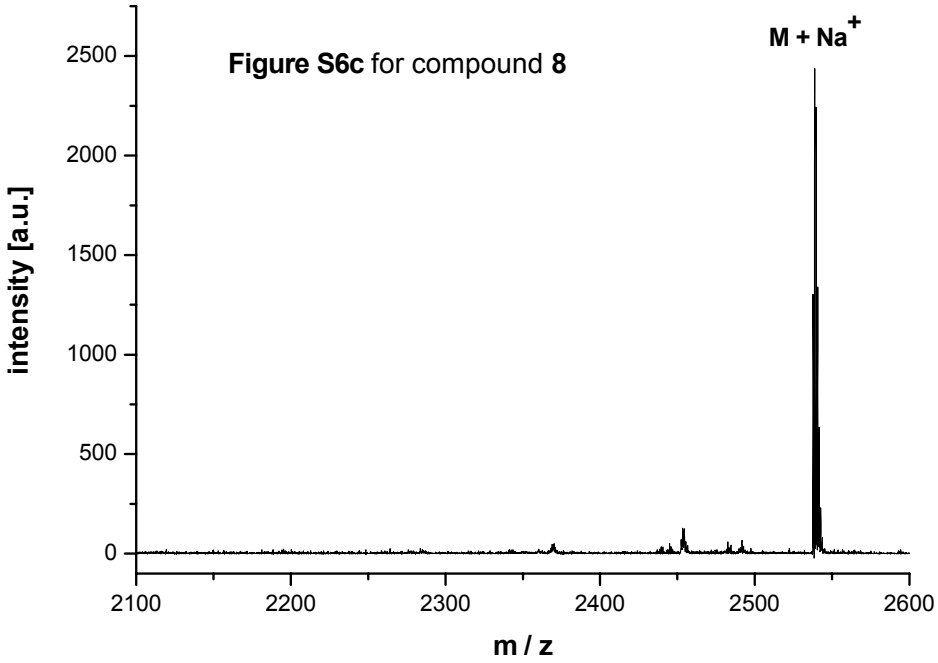
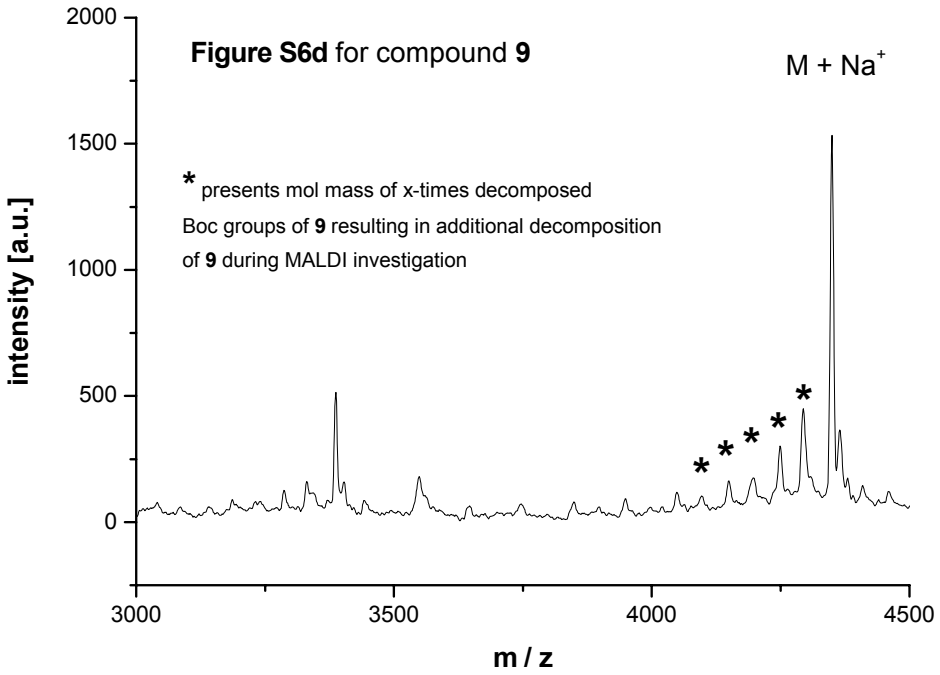


Figure S6a – S6e. MALDI-TOF-MS spectra of **2**, **4**, **8**, **9**, and **10**. In all cases, except for **10**, the desired molar mass of the lysine dendrimers was determined. Due to the degradation of the Boc-groups during MALDI-TOF-MS investigations of the lysine dendrimers **2**, **4**, **8**, **9**, and **10** additional mass signals for lower masses were observed compared to the desired molar masses as well.









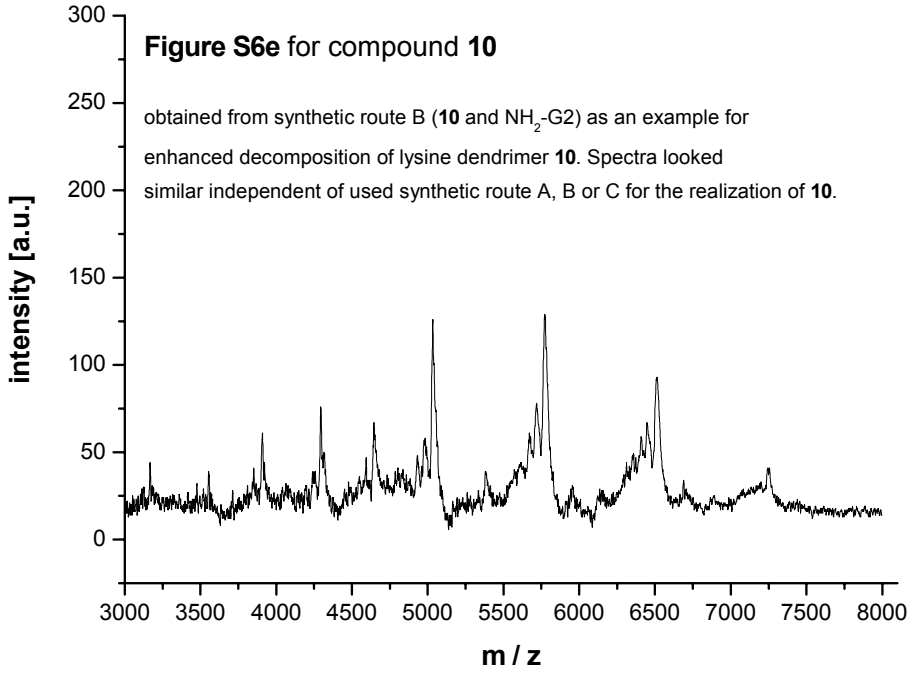


Table S1. Comparison of the theoretical molar mass of **8** – **10** with the molar mass obtained from MALDI-TOF-MS and SEC

dendrimer	molar mass$_{theoretical}$	molar mass$_{Maldi}$	molar mass$_{SEC,\ top\ of\ the\ peak}$
	g/mol	*g/mol*	*g/mol*
8	2515.18	2537.7 ($M+Na^+$)	2850
9	4341.53	4364.9 ($M+Na^+$)	4990
10	7994.22	-[1]	7620

[1] no determination of molar mass caused by decomposition during MALDI investigations