Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Chelate cooperativity effects on the formation of di- and trivalent pseudo[2]rotaxanes with diketopiperazine threads and tetralactam wheels

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1. Experimental Details

General: Reagents were purchased from Aldrich, ACROS or Fluka and used without further purification. Dry solvents were purchased from ACROS Organics and used as received. Yields refer to chromatographically and spectroscopically homogeneous materials. Thin-layer chromatography (TLC) was performed on precoated silica gel 60/F254 plates (Merck KGaA). Silica gel (0.04-0.063 mm; Merck) was used for column chromatography. TLMs were synthesized according to literature procedures.

NMR spectroscopy and NMR titrations: ^{1}H (400 MHz) and ^{13}C (101 MHz) spectra were obtained on a Bruker ECX 400 instrument at 298 K. ^{1}H (500 MHz) and ^{13}C (126 MHz) spectra were obtained on JEOL ECP 500 or Bruker AVANCE 500 instruments at 298 K. ^{1}H (700 MHz) and ^{13}C (176 MHz) spectra were obtained on a Bruker AVANCE 700 instrument at 298 K.
All chemical shifts are reported in ppm with signals of $CHCl_3$ (7.26 ppm (^{1}H) and 77.16 ppm (^{13}C)) as internal standards; coupling constants are in Hz. The following abbreviations were used to indicate NMR multiplicities: s (singlet), d (doublet), t (triplet), m (multiplet), br (broad). Titration experiments were carried out in $CDCl_3$ at 25 °C on the Bruker AVANCE 700 instrument.

Analytical mass spectrometry: Samples were measured on an Agilent 6210 ESI-TOF, Agilent Technologies, Santa Clara, CA, USA or an Ionspec QFT-7, Agilent Technologies, Santa Clara, CA, USA. In case of the Agilent 6210 ESI-TOF, the solvent flow rate was adjusted to 4-15 µL/min and the spray voltage was set to 4 kV. The drying gas flow rate was adjusted to 15 psi (1 bar). All other parameters were optimized for a maximum abundance of the respective $[M+Na]^+$. The Ionspec QFT-7 is equipped with a 7 T superconducting magnet and a Micromass Z-spray ESI source, Waters Co., Saint-Quentin, France. The solvent flow rate was adjusted to 4 µL/min and the spray voltage set to 3.8 kV. All other parameters were optimized for a maximum abundance of the respective $[M+Na]^+$ ions. Solvents (HPLC gradient grade) were purchased at LGC Promochem.

Syntheses of the macrocyclic hosts[1] and compound **1**[2] were performed according to literature-known procedures.

Synthesis and analytical data of new compounds:

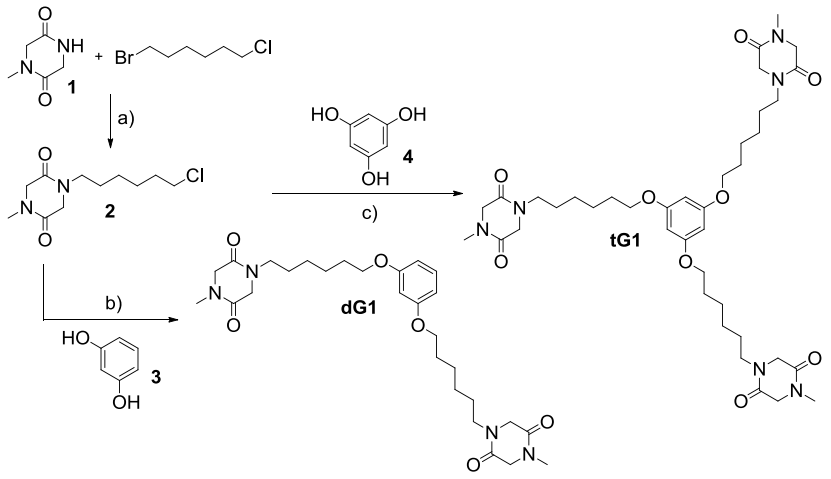

*Figure S1: Synthesis of divalent guest **dG1** as well as trivalent guest **tG1**. Reaction conditions: a) NaH, DMF, 12 h, r.t.; b) NaOH, DMSO, 5 d, 125 °C; c) NaOH, DMSO, 5 d, 125 °C.*

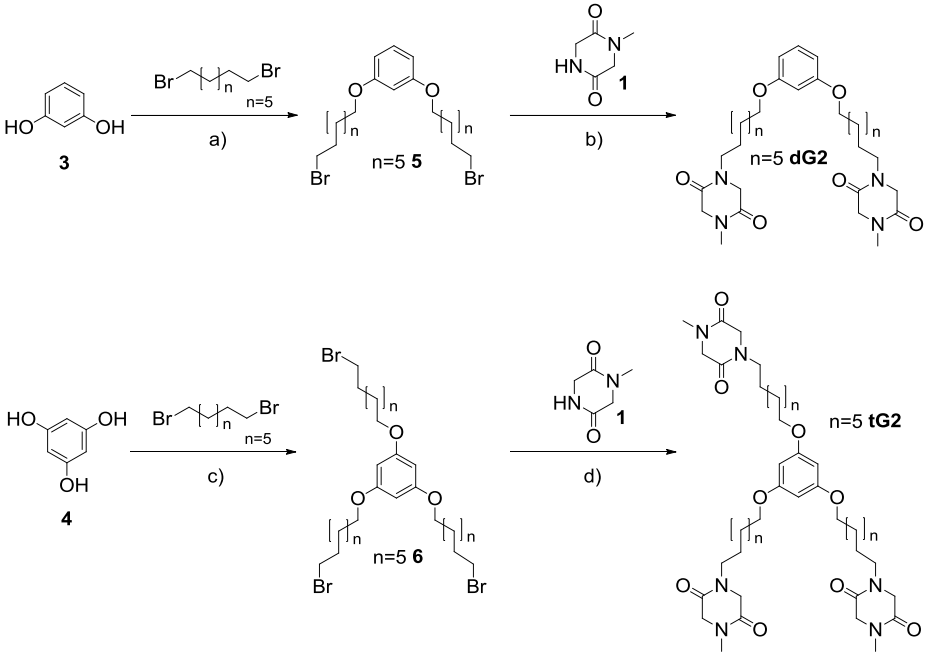

*Figure S2: Synthesis of divalent guest **dG2** (top) as well as trivalent guest **tG2** (bottom). Reaction conditions: a) 18-crown-6, acetone, 18 h, reflux; b) NaH, DMF, 12 h, r.t.; c) 18-crown-6, acetone, 18 h, reflux; d) b) NaH, DMF, 12 h, r.t.*

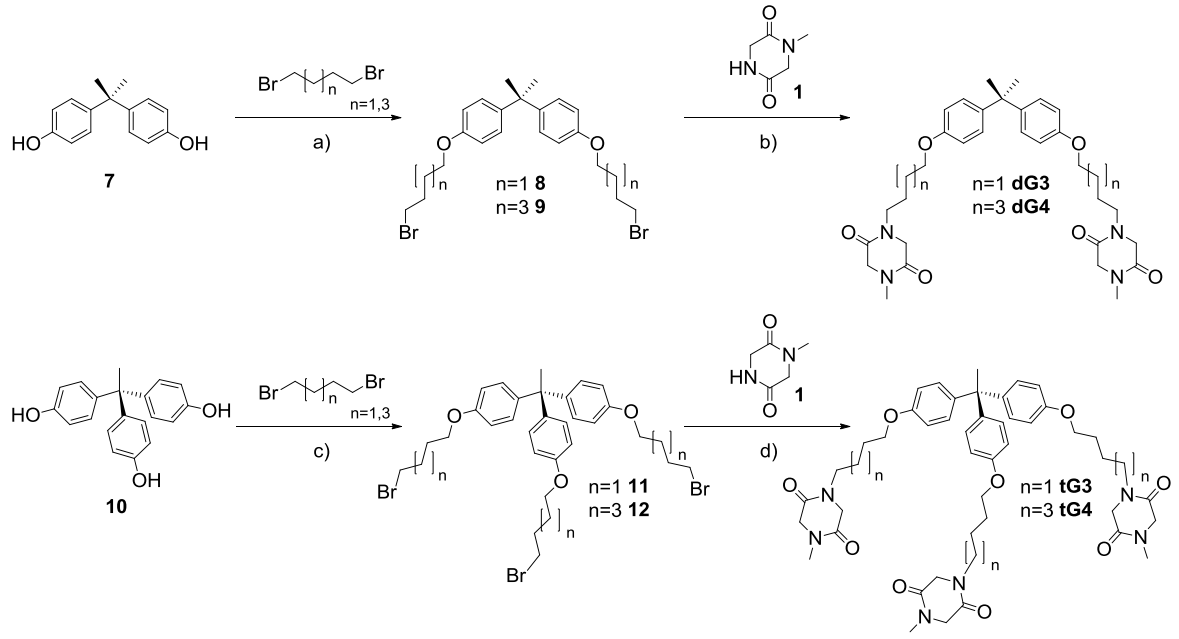

*Figure S3: Synthesis of divalent guests **dG3** and **dG4** (top) as well as trivalent guests **tG3** and **tG4** (bottom). Reaction conditions: a) 18-crown-6, acetone, 18 h, reflux; b) NaH, DMF, 12 h, r.t.; c) 18-crown-6, acetone, 18 h, reflux; d) b) NaH, DMF, 12 h, r.t..*

Synthesis of the divalent and trivalent guest molecules

4,4'-((1,3-Phenylenebis(oxy))bis(hexane-3,1-diyl))bis(1-methylpiperazine-2,5-dione) dG1

A suspension of sodium hydroxide (44 mg, 1.10 mmol) and benzene-1,3-diol **3** (60 mg, 0.54 mmol) in 2 mL DMSO was added stepwise to a solution of 1-(6-chlorohexyl)-4-methylpiperazin-2,5-dione **2** (271 mg, 1.1 mmol) in 2 mL DMSO. The solution was stirred for 5 d at 125 °C. Afterwards the reaction was quenched by the addition of 10 mL dest. water. The mixture was washed with DCM (5 x 20 mL) and the organic layer evaporated. Remaining DMSO was removed by the use of a kugelrohr destillation. The desired product **dG1** was obtained after chromatographic work-up (SiO_2, $CHCl_3$/MeOH/NEt_3 10:0.2:0.2) as colourless oil (30 mg, 0.06 mmol, 11%).

^{1}H (500 MHz, $CDCl_3$): δ = 7.13 (t, *J* = 8.2 Hz, 1H, Ar**H**), 6.46 – 6.41 (m, 3H, Ar**H**), 3.95 (s, 4H, C**H**$_2$), 3.91 (t, *J* = 6.3 Hz, 8H, C**H**$_2$), 3.40 – 3.36 (m, 4H, C**H**$_2$), 2.96 (s, 6H, C**H**$_3$), 1.78 – 1.71 (m, 4H, C**H**$_2$), 1.61 – 1.54 (m, 4H, C**H**$_2$), 1.52 – 1.44 (m, 4H, C**H**$_2$), 1.39 – 1.31 (m, 4H, C**H**$_2$) ppm. **^{13}C (126 MHz, $CDCl_3$)**: δ = 163.6, 163.0, 160.4, 129.9, 106.7, 101.4, 67.7, 51.9, 49.8, 46.0, 33.4, 29.2, 26.6, 25.9 ppm. HR-MS (ESI, positive mode, $CHCl_3$/MeOH): *m/z* calcd. for $[M+Na]^+$: 553.3000; found: 553.3079 (Δ = 14.3 ppm).

4,4',4''-((Benzene-1,3,5-triyltris(oxy))tris(propane-3,1-diyl))tris(1-methylpiperazine-2,5-dione) tG1

A suspension of sodium hydroxide (64.8 mg, 1.62 mmol) and benzene-1,3,5-triol **4** (66.8 mg, 0.53 mmol) in 2 mL DMSO was added stepwise to a solution of 1-(6-chlorohexyl)-4-methylpiperazin-2,5-dione **2** (370 mg, 1.59 mmol) in 2 ml DMSO. The solution was stirred for 3 d at 125 °C. Afterwards the reaction was quenched by the addition of 10 mL dest. water. The mixture was washed with DCM (5 x 20 mL) and the organic layer evaporated. Remaining DMSO was removed by the use of a kugelrohr destillation. The desired product **tG1** was obtained after chromatographic work-up (SiO_2, $CHCl_3$/MeOH/NEt_3 10:0.2:0.2) as colourless solid (146 mg, 0.20 mmol, 38%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.97 (d, *J* = 5.1 Hz, 6H, C**H**$_2$), 3.89 (t, *J* = 6.5, 3H, C**H**$_2$), 3.53 (t, *J* = 6.6, 3H, C**H**$_2$), 3.41 – 3.38 (m, 6H, C**H**$_2$), 2.98 (s, 9H, C**H**$_3$), 1.80 – 1.72 (m, 6H, C**H**$_2$), 1.62 – 1.56 (m, 8H, C**H**$_2$), 1.51 – 1.44 (m, 6H, C**H**$_2$), 1.39 – 1.32 (m, 6H, C**H**$_2$) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 163.5, 163.0, 160.8, 93.8, 67.7, 51.8, 49.7, 45.9, 45.8, 44.9, 33.2, 32.4, 29.0, 26.5, 26.5, 26.4, 26.0, 25.8 ppm. HR-MS (ESI, pos. mode, $CHCl_3$/MeOH): *m/z* calcd. for $[M+Na]^+$: 779.4314; found: 779.4320 (Δ = 0.8 ppm).

4,4'-((1,3-Phenylenebis(oxy))bis(octane-8,1-diyl))bis(1-methylpiperazine-2,5-dione) dG2

Under protective gas, sodium hydride (85.3 mg, 3.56 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (304 mg, 2.37 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) **5** (500 mg, 1.02 mmol) was added slowly. The reaction mixture was stirred for 12 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate, the solvent was removed under reduced pressure. The desired product **dG2** was obtained after HPLC work-up (instrument: Knauer, column: Reprosil Saphir 100 C18 10 µm 250x50 mm, UV-detector, ACN/H_2O 50:50) as a light yellow solid (150 mg, 0.16 mmol, 16%).

^{1}H **NMR (700 MHz, $CDCl_3$):** δ = 7.14 (t, *J* = 8.2 Hz, 1H), 6.47 (dd, *J* = 8.2, 2.3 Hz, 2H), 6.44 (t, *J* = 2.3 Hz, 1H), 3.97 (s, 4H), 3.96 (s, 4H), 3.93 – 3.91 (m, 4H), 3.39 – 3.37 (m, 4H), 2.98 (s, 6H), 1.77 – 1.73 (m, 4H), 1.58 – 1.54 (m, 4H), 1.44 – 1.43 (m, 4H), 1.35 – 1.32 (m, 12H) ppm. ***^{13}C*** **NMR (126 MHz, $CDCl_3$):** δ = 163.70, 163.06, 160.48, 129.89, 106.78, 101.57,

67.99, 52.00, 49.82, 46.13, 33.39, 29.35, 29.32, 26.77, 26.70, 26.10 ppm. MS (ESI-ToF, positive mode, DCM/MeOH): *m/z*: $[M+Na]^+$ calcd.: 609.3623, found: 609.3633 (Δ = 1.6 ppm).

4,4',4''-((Benzene-1,3,5-triyltris(oxy))tris(octane-8,1-diyl))tris(1-methylpiperazine-2,5-dione) tG2

Under protective gas, sodium hydride (90.0 mg, 3.75 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (321 mg, 2.50 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) **6** (500 mg, 0.72 mmol) was added slowly. The reaction mixture was stirred for 12 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate, the solvent was removed under reduced pressure. The desired product **tG2** was obtained after HPLC work-up (instrument: Knauer, column: Reprosil Saphir 100 C18 10 µm 250x50 mm, UV-detector, ACN/H_2O 60:40) as a white solid (78 mg, 0.09 mmol, 13%).

***^{1}H* NMR (700 MHz, $CDCl_3$):** δ = 6.04 (s, 3H), 3.97 (s, 6H), 3.96 (s, 6H), 3.90 – 3.88 (m, 6H), 3.39 – 3.37 (m, 6H), 2.98 (s, 9H), 1.73 – 1.72 (m, 6H), 1.56 – 1.54 (m, 6H), 1.43 – 1.41 (m, 6H), 1.34 – 1.30 (m, 18H) ppm. ***^{13}C* NMR (126 MHz, $CDCl_3$):** δ = 163.69, 163.05, 161.08, 93.92, 68.04, 52.01, 49.82, 46.12, 33.38, 29.33, 26.78, 26.71, 26.11 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+Na]^+$ calcd.: 863.5253, found: 863.5249 (Δ = 1.6 ppm).

4,4'-(4,4'-(4,4'-(Propane-2,2-diyl)bis(4,1-phenylene))bis(oxy)bis(butane-4,1-diyl))bis(1-methylpiperazine-2,5-dione) dG3

Under protective gas, sodium hydride (50.4 mg, 2.10 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (179 mg, 1.40 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) **8** (299 mg, 0.600 mmol) was added slowly. The reaction mixture was stirred for 12 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate the solvent was removed under reduced pressure. The desired product **dG3** was obtained after

preparative TLC work-up (SiO_2, $CHCl_3$/EE/MeOH 3:1:0.2) as a white solid (131 mg, 0.220 mmol, 37%).

***^{1}H* NMR (500 MHz, $CDCl_3$):** δ = 7.12 (d, *J* = 8.9 Hz, 4H), 6.77 (d, *J* = 8.8 Hz, 4H), 3.96 (m, 12H), 3.47 (t, *J* = 6.8 Hz, 4H), 2.97 (s, 6H), 1.77 (m, 8H), 1.62 (s, 6H) ppm. ***^{13}C* NMR (126 MHz, $CDCl_3$):** δ = 163.62, 163.22, 156.77, 143.36, 127.87, 113.93, 67.12, 51.99, 49.79, 45.75, 41.81, 33.39, 31.18, 26.64, 23.50, 1.15 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+H]^+$ calcd.: 593.3334, found: 593.3379 (Δ = 10.6 ppm), $[M+Na]^+$ calcd.: 615.3153, found: 615.3198 (Δ = 7.3 ppm), $[M+K]^+$ calcd.: 631.2892, found: 631.2927 (Δ = 5.5 ppm).

4,4',4''-(4,4',4''-(4,4',4''-(Ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(butane-4,1-diyl))tris(1-methylpiperazine-2,5-dione) tG3

Under protective gas, sodium hydride (88.8 mg, 24.0 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (428 mg, 3.30 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) **11** (526 mg, 0.74 mmol) was added slowly. The reaction mixture was stirred for 24 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate, the solvent was removed under reduced pressure. The desired product **tG3** was obtained after preparative TLC work-up (SiO_2, $CHCl_3$/EE/MeOH 3:1:0.2) as a light yellow oil (318 mg, 0.37 mmol, 50%).

***^{1}H* NMR (500 MHz, $CDCl_3$):** δ = 6.96 (d, *J* = 8.9 Hz, 6H), 6.75 (d, *J* = 8.9 Hz, 6H), 3.98 (s, 6H), 3.96 (s, 6H), 3.94 (m, 6H), 3.47 (t, *J* = 6.6 Hz, 6H), 2.96 (s, 9H), 2.08 (s, 3H), 1.76 (m, 12H) ppm. ***^{13}C* NMR (126 MHz, $CDCl_3$):** δ = 163.57, 163.19, 156.91, 141.97, 129.73, 113.69, 67.09, 51.96, 50.70, 49.75, 45.71, 33.36, 26.59, 23.49 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+Na]^+$ calcd.: 875.4319, found.: 875.4317 (Δ = 0.2 ppm).

4,4'-(((Propane-2,2-diylbis(4,1-phenylene))bis(oxy))bis(hexane-6,1-diyl))bis(1 methylpiperazine-2,5-dione) dG4

Under protective gas, sodium hydride (75.7 mg, 3.16 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (269.6 mg, 2.1 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4'-(propane-2,2-diyl)bis(((6-bromohexyl)oxy)benzene) **9** (500.0 mg, 0.90 mmol) was added slowly. The reaction mixture was stirred for 12 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate, the solvent was removed under reduced pressure. The desired product **dG4** was obtained after preparative TLC work-up (SiO_2, $CHCl_3$/EE/MeOH 3:1:0.2) as a white solid (131 mg, 0.220 mmol, 37%).

***^{1}H*-NMR (700 MHz, $CDCl_3$):** δ = 7.12 (d, *J* = 8.9 Hz, 4H), 6.77 (s, 2H), 6.77 (s, 2H), 3.96 (d, *J* = 5.0 Hz, 12H), 3.50 – 3.32 (m, 4H), 2.97 (s, 6H), 1.89 – 1.67 (m, 8H), 1.62 (s, 6H), 1.59 (p, *J* = 7.6 Hz, 4H), 1.51 – 1.46 (m, 4H), 1.37 (q, *J* = 7.9 Hz, 4H) ppm. ***^{13}C*-NMR (126 MHz, $CDCl_3$):** δ = 163.64, 163.06, 156.96, 143.17, 127.82, 113.90, 67.69, 51.99, 49.84, 46.06, 41.77, 33.38, 31.19, 29.32, 26.69, 26.62 , 25.97 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+Na]^+$ calcd.: 671.3779, found: 671.3805 (Δ = 3.9 ppm).

4,4',4''-(((Ethane-1,1,1-triyltris(4,1-phenylene))tris(oxy))tris(hexane-6,1-diyl))tris(1-methylpiperazine-2,5-dione) tG4

Under protective gas, sodium hydride (79.2 mg, 3.30 mmol) was washed three times with hexane. The purified sodium hydride was suspended with 60 mL dry DMF and 1-methylpiperazine-2,5-dione **1** (282 mg, 2.20 mmol) was added. The mixture was stirred for 1 h at r.t. Then 4,4',4''-(ethane-1,1,1-triyl)tris(((6-bromohexyl)oxy)benzene) **12** (500 mg, 0.63 mmol) was added slowly. The reaction mixture was stirred for 24 h. Afterwards the reaction was quenched by the addition of a saturated ammonium chloride solution. The water phase was washed once with hexane and three times with DCM. The combined DCM phases were washed with1 M HCl, dest. H_2O and brine. After drying with magnesium sulfate, the solvent was removed under reduced pressure. The desired product **tG4** was obtained after HPLC work-up (instrument: Knauer, column: Reprosil Saphir 100 C18 10 µm 250x50 mm, UV-detector, ACN/H_2O 90:10) as a light yellow high viscous oil (219 mg, 0.23 mmol, 37%).

***[1]H* NMR (700 MHz, $CDCl_3$):** δ = 6.97 (d, *J* = 8.9 Hz, 6H), 6.76 (d, *J* = 8.9 Hz, 6H), 3.97 (s, 6H), 3.96 (s, 6H), 3.92 – 3.90 (m, 6H), 3.41 – 3.39 (m, 6H), 2.97 (s, 9H), 2.08 (s, 3H), 1.77 – 1.75 (m, 6H), 1.60 – 1.58 (m, 6H), 1.50 – 1.48 (m, 6H), 1.38 – 1.37 (m, 6H) ppm. ***[13]C* NMR (126 MHz, $CDCl_3$):** δ = 163.65, 163.08, 157.13, 141.87, 129.73, 113.70, 67.70, 52.00, 50.71, 49.84, 46.07, 33.39, 29.32, 26.70, 26.63, 25.98 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+Na]^+$ calcd.: 959.5253, found: 959.5250 (Δ = 0.3 ppm).

Synthesis of the guest molecule precursors

1-(3-Chlorohexyl)-4-methylpiperazine-2,5-dione 2

Under protective gas, sodium hydride (164 mg, 4.10 mmol) was washed with hexane. Afterwards the pure sodium hydride was suspended with 35 mL DMF and 1-methylpiperazin-2,5-dione **1** (350 mg, 2.73 mmol) was added. The reaction mixture was stirred for 1 h. After the addition of 1-bromo-3-chlorohexane (0.81 mL, 5.46 mmol), the reaction mixture was stirred for additional 12 h. The reaction was quenched by the addition of a small amount of NH_4Cl solution. 30 mL DCM were added and the organic layer was washed with 30 mL HCl (1 M), dest. H_2O and brine. After drying over $MgSO_4$, the solvent was removed under reduced pressure. The desired product **2** was obtained as a yellow oil (615 mg, 2.49 mmol, 91%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.86 (d, *J* = 7.2 Hz, 4H, C**H**$_2$), 3.42 (t, *J* = 6.6 Hz, 2H, C**H**$_2$), 3.30 – 3.26 (m, 2H, C**H**$_2$), 2.87 (s, 3H, C**H**$_3$), 1.66 (dt, *J* = 14.4, 6.7 Hz, 2H, C**H**$_2$), 1.47 (p, *J* = 7.6 Hz, 2H, C**H**$_2$), 1.36 (dt, *J* = 14.9, 7.2 Hz, 2H, C**H**$_2$), 1.26 – 1.19 (m, 2H, C**H**$_2$) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 163.3, 162.8, 51.6, 49.5, 45.6, 44.7, 33.0, 32.2, 26.3, 26.2, 25.8 ppm. **HR-MS (ESI, pos. mode, $CHCl_3$/MeOH):** *m/z* calcd. for $[M+Na]^+$: 269.1027 ($[M+Na]^+$); found: 269.1019 (Δ = 3.0 ppm).

4,4'-(Propane-2,2-diyl)bis((4-bromobutoxy)benzene) 5

Under protective gas, potassium carbonate (1.66 g, 12.0 mmol), 1,8-dibromooctane (9.78 mL, 7.18 g, 26.4 mmol) and 18-crown-6 (0.174 g, 0.660 mmol) were mixed with 100 mL acetone. Afterwards 1,3-dihydroxybenzene **3** (363 mg, 3.30 mmol) was added and the mixture was heated to reflux 18 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was dissolved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was distilled to remove remaining 1,8-dibromooctane (190

°C, 5 mbar) and was afterwards purified by HPLC (SiO_2, Hex/EE 99:1). The desired product **5** was obtained as a white solid (345 mg, 0.70 mmol, 21%).

^{1}H* NMR (500 MHz, $CDCl_3$):** δ = 7.18 (d, J = 8.8 Hz, 4H), 6.83 (d, J = 8.8 Hz, 4H), 3.97 (t, J = 6.4 Hz, 4H), 3.45 (t, J = 6.8 Hz, 4H), 2.02 – 1.88 (m, 4H), 1.86 – 1.79 (m, 4H), 1.68 (s, 6H), 1.59 – 1.48 (m, 8H) ppm.^{13}C* NMR (126 MHz, $CDCl_3$):** δ = 160.36, 129.75, 106.62, 101.45, 67.85, 33.94, 32.81, 29.25, 29.20, 28.71, 28.11, 25.99 ppm. **HR-MS (ESI, pos. mode, $CHCl_3$/MeOH):** *m/z* calcd. for $[M+Na]^+$: 515.0954 ($[M+Na]^+$); found: 515.0971 (Δ = 3.3 ppm).

4,4',4''-(Ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) 6

Under protective gas, potassium carbonate (9.05 g, 65.5 mmol), 1,8-dibromooctane (27.2 mL, 40.0 g, 147 mmol) and 18-crown-6 (872 mg, 3.30 mmol) were mixed with 100 mL acetone. Afterwards 1,3,5-trihydroxybenzene **4** (2.06 g, 16.3 mmol) was added and the mixture was heated to reflux 18 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was solved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was distilled to remove remaining 1,8-dibromooctane (190 °C, 5 mbar) and was afterwards purified by column chromatography (SiO_2, Hex/EE 15:1). The desired product **6** was obtained as colourless oil (2.94 g, 4.21 mmol, 26%).

***^{1}H*-NMR (400 MHz, $CDCl_3$):** δ = 6.05 (s, 3H), 3.90 (t, *J* = 6.5 Hz, 6H), 3.40 (t, *J* = 6.8 Hz, 6H), 1.89 – 1.72 (m, 12H), 1.44 – 1.34 (m, 24H) ppm. ***^{13}C*-NMR (101 MHz, $CDCl_3$):** δ = 161.07, 158.28.00, 93.93, 91.90, 68.04, 34.10, 32.91, 29.32, 29.29, 28.81, 28.22, 26.09 ppm. **HR-MS (ESI, pos. mode, $CHCl_3$/MeOH):** *m/z* calcd. for $[M+Na]^+$: 723.1243 ($[M+Na]^+$); found: 723.1256 (Δ = 1.8 ppm).

4,4'-(Propan-2,2-diyl)bis((4-brombutoxy)benzol) 8

Under protective gas, potassium carbonate (1.70 g, 12.4 mmol), 1,4-dibromobutane (3.11 mL, 5.70 g, 26.4 mmol) and 18-crown-6 (0.170 g, 0.660 mmol) were mixed with 100 mL acetone. Afterwards bisphenol A **7** (753 mg, 3.30 mmol) was added and the mixture was heated to reflux 18 h. Die reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was solved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was purified by column chromatography (SiO_2, Hex/EE 15:1). The desired product **8** was obtained as white solid (537 mg, 1.08 mmol, 33%).

***^{1}H*-NMR (500 MHz, $CDCl_3$):** δ = 7.13 (d, *J* = 8.7 Hz, 4H), 6.79 (d, *J* = 8.7 Hz, 4H), 3.97 (t, *J* = 6.0 Hz, 4H), 3.49 (t, *J* = 6.6 Hz, 4H), 2.06 (m, 4H), 1.93 (m, 4H), 1.64 (s, 6H) ppm. ***^{13}C*-NMR (126 MHz, $CDCl_3$):** δ = 156.79, 143.33, 127.86, 113.87, 66.81, 41.80, 33.70, 31.19, 29.64, 28.09 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+Na]^+$ ber.: 519.0510, gef.: 519.0556 (Δ = 8.9 ppm), $[M+K]^+$ ber.: 535.0250, gef.: 535.0288 (Δ = 7.1 ppm).

4,4',4''-(Ethan-1,1,1-triyl)tris((4-brombutoxy)benzol) 11

Under protective gas, potassium carbonate (9.00 g, 65.3 mmol), 1,4-dibromobutane (17.6 mL, 31.7 g, 147 mmol) and 18-crown-6 (863 mg, 3.30 mmol) were mixed with 100 mL acetone. Afterwards 4,4',4''-(ethane-1,1,1-triyl)triphenole **10** (5.00 g, 16.3 mmol) was added and the mixture was heated to reflux 18 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was dissolved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was purified by column chromatography (SiO_2, Hex/EE 15:1). The desired product **11** was obtained as colourless oil (5.86 g, 8.20 mmol, 51%).

***^{1}H* NMR (400 MHz, $CDCl_3$):** δ = 6.98 (d, *J* = 8.9 Hz, 6H), 6.77 (d, *J* = 8.9 Hz, 6H), 3.97 (t, *J* = 6.0 Hz, 6H), 3.49 (t, *J* = 6.6 Hz, 6H), 2.10 (s, 3H), 2.06 (m, 6H), 1.93 (m, 6H) ppm. ***^{13}C* NMR (101 MHz, $CDCl_3$):** δ = 156.99, 142.00, 129.76, 113.71, 66.85, 50.74, 33.65, 29.66, 28.10 ppm. **MS (ESI-ToF, positive mode, DCM/MeOH):** *m/z*: $[M+K]^+$ calcd.: 747.0081, found: 747.0118 (Δ = 5.0 ppm).

4,4'-(Propane-2,2-diyl)bis(((6-bromohexyl)oxy)benzene) 9

Under protective gas, potassium carbonate (3.32 g, 24.0 mmol), 1,6-dibromohexane (8.0 mL, 12.88 g, 52.8 mmol) and 18-crown-6 (0.349 g, 1.52 mmol) were mixed with 100 mL acetone. Afterwards 4,4'-(propane-2,2-diyl)diphenol **7** (1.51 mg, 6.60 mmol) was added and the mixture was heated to reflux 18 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was dissolved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was distilled to remove remaining 1,6-dibromohexane (160 °C, 5 mbar) and was afterwards purified by HPLC (SiO_2, Hex/EE 98:2). The desired product **9** was obtained as white solid (528 mg, 0.952 mmol, 14%).

***^{1}H* NMR (500 MHz, $CDCl_3$):** δ = 7.18 (d, *J* = 8.8 Hz, 4H), 6.83 (d, *J* = 8.8 Hz, 4H), 3.97 (t, *J* = 6.4 Hz, 4H), 3.45 (t, *J* = 6.8 Hz, 4H), 2.02 – 1.88 (m, 4H), 1.86 – 1.79 (m, 4H), 1.68 (s, 6H),

1.59 – 1.48 (m, 8H) ppm.***^{13}C*** **NMR (126 MHz, $CDCl_3$):** δ = 156.88, 143.04, 127.72, 113.81, 67.61, 41.68, 33.89, 32.75, 31.15, 29.72, 27.99, 25.39 ppm. **HR-MS (ESI, pos. mode, $CHCl_3$/MeOH):** *m/z* calcd. for $[M+Na]^+$: 577.1111 ($[M+Na]^+$); found: 577.1118 (Δ = 1.2 ppm).

4,4',4''-(Ethane-1,1,1-triyl)tris(((6-bromohexyl)oxy)benzene) 12

Under protective gas, potassium carbonate (9.05 g, 65.5 mmol), 1,6-dibromohexane (22.9 mL, 35.9 g, 147 mmol) and 18-crown-6 (872 mg, 3.30 mmol) were mixed with 100 mL acetone. Afterwards 4,4',4''-(ethane-1,1,1-triyl)triphenol **10** (5.00 g, 16.3 mmol) was added and the mixture was heated to reflux 18 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was solved in DCM and washed three times with dest. water. The organic layer was dried with magnesium sulfate and the solvent was removed. The crude product was distilled to remove remaining 1,6-dibromohexane (160 °C, 5 mbar) and was afterwards purified by column chromatography (SiO_2, Hex/EE 15:1). The desired product **12** was obtained as colourless oil (4.61 g, 5.80 mmol, 30%).

^{1}H **NMR (500 MHz, $CDCl_3$):** δ = 7.16 (t, *J* = 8.1 Hz, 1H), 6.61 – 6.35 (m, 3H), 3.93 (t, *J* = 6.5 Hz, 4H), 3.41 (t, *J* = 6.8 Hz, 4H), 1.88 – 1.67 (m, 8H), 1.47 – 1.35 (m, 16H) ppm. ***^{13}C*** **NMR (126 MHz, $CDCl_3$):** δ = 160.36, 129.75, 106.62, 101.45, 67.85, 33.94, 32.81, 29.25, 29.20, 28.71, 28.11, 25.99 ppm. **HR-MS (ESI, pos. mode, $CHCl_3$/MeOH):** *m/z* calcd. for $[M+Na]^+$: 819.1281 ($[M+Na]^+$); found: 819.1256 (Δ = 3.0 ppm).

2. ITC data

ITC experiments were performed at 298 K in dry $CHCl_3$ on a TAM III (Waters GmbH, TA Instruments, Eschborn, Germany). In a typical titration experiment, a solution of host **H1-H3** (800 µL, 0.5-2 mM) was placed in the sample cell. A solution of guest **mG, dG1-4 and tG1-4** (240 µL, 5-10 mM) was placed in an injection syringe and was added stepwise. The titration schedule consisted of 30 consecutive injections of 8 µL each with a 15 min to 25 min interval in between. Heats of dilution were measured by blank titrations. The obtained data were analyzed with the instrument's internal software package and was fitted with a 1:1, 2:1 and 3:1 binding model.

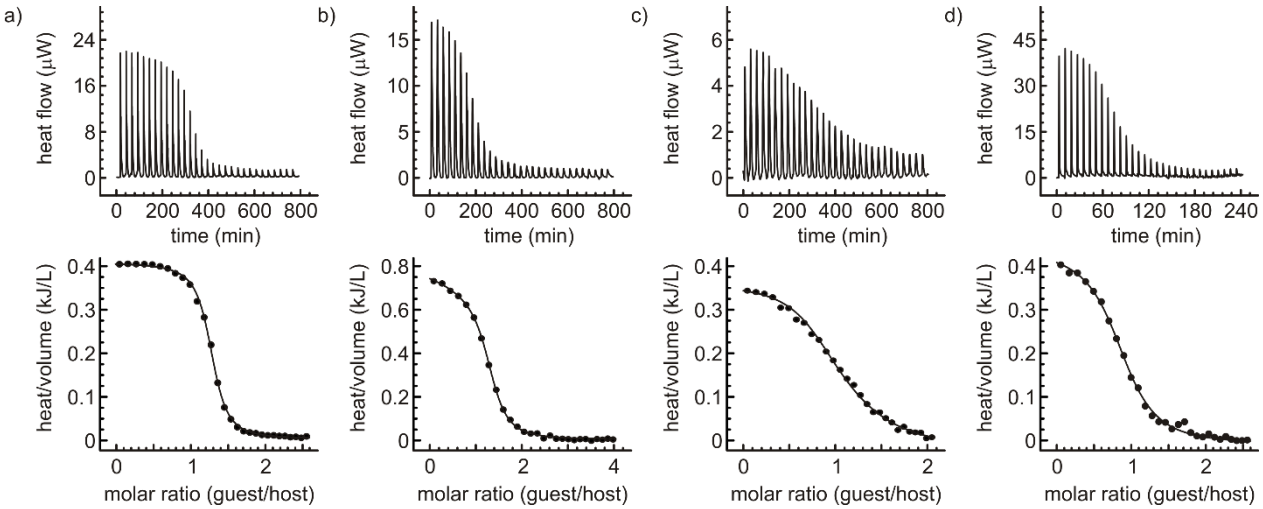

*Figure S4: ITC plots of the titration of a) divalent macrocycle **H2** (cell) and divalent thread **dG1** (syringe), b) divalent macrocycle **H2** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and divalent thread **dG1** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

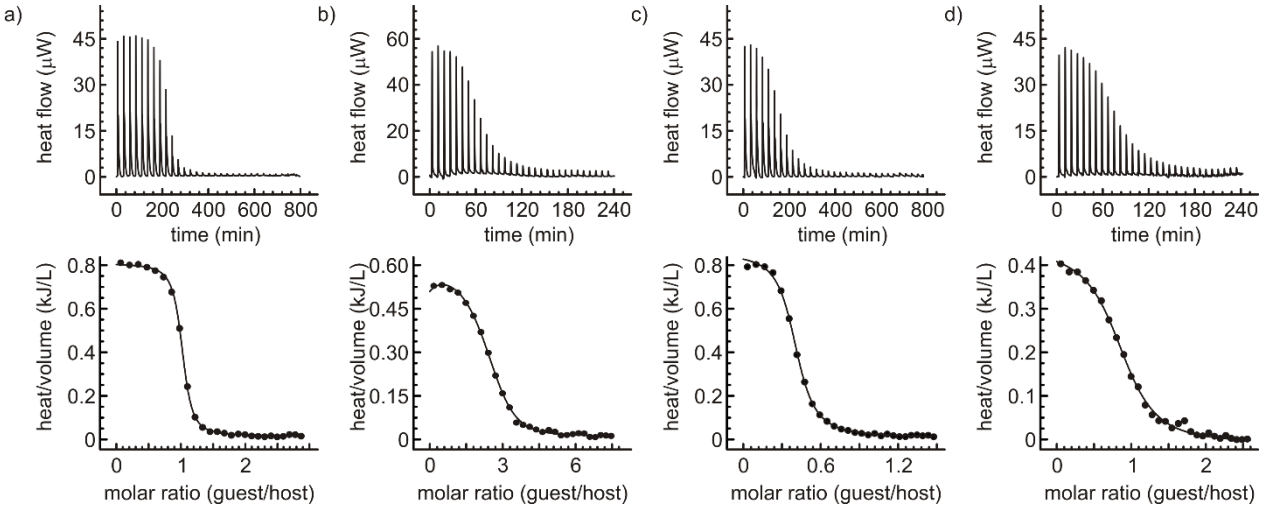

*Figure S5: ITC plots of the titration of a) trivalent macrocycle **H3** (cell) and trivalent thread **tG1** (syringe), b) trivalent macrocycle **H3** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and trivalent thread **tG1** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

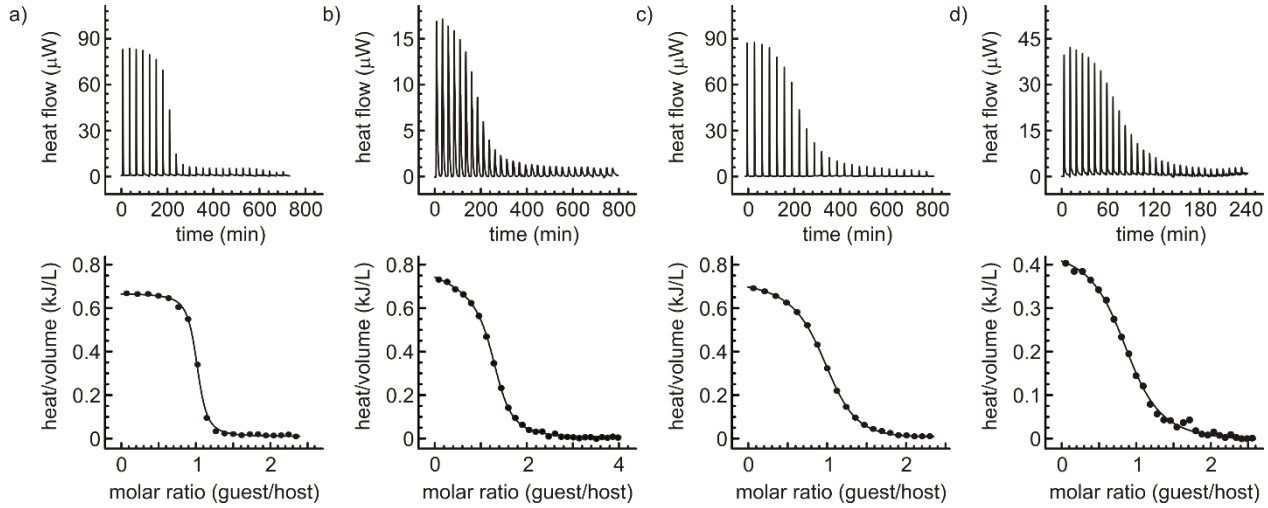

*Figure S6: ITC plots of the titration of a) divalent macrocycle **H2** (cell) and divalent thread **dG2** (syringe), b) divalent macrocycle **H2** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and divalent thread **dG2** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

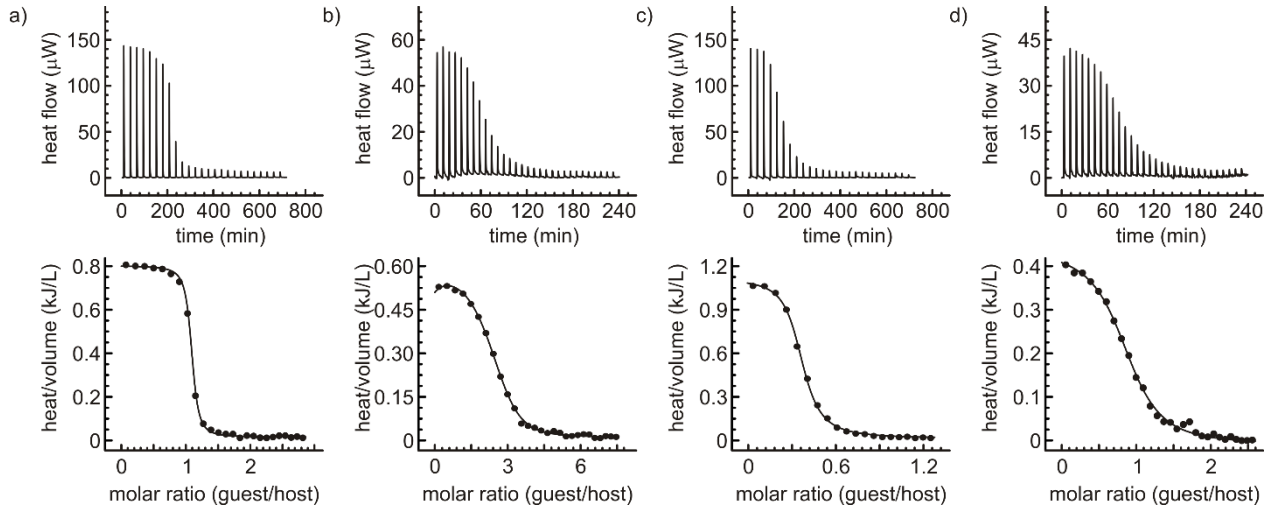

*Figure S7: ITC plots of the titration of a) trivalent macrocycle **H3** (cell) and trivalent thread **tG2** (syringe), b) trivalent macrocycle **H3** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and trivalent thread **tG2** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

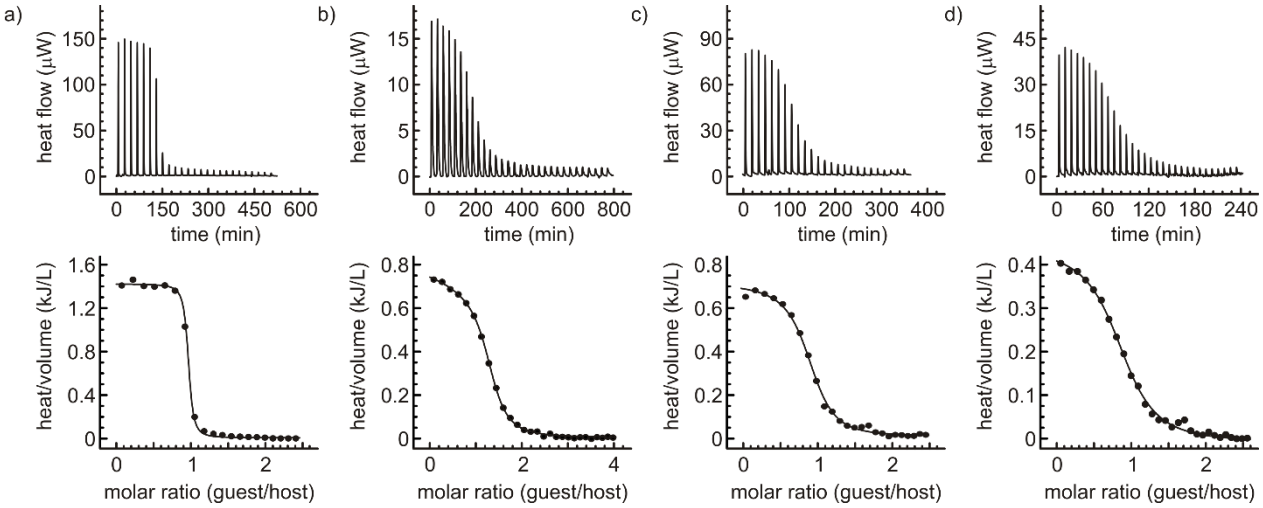

*Figure S8: ITC plots of the titration of a) divalent macrocycle **H2** (cell) and divalent thread **dG3** (syringe), b) divalent macrocycle **H2** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and divalent thread **dG3** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

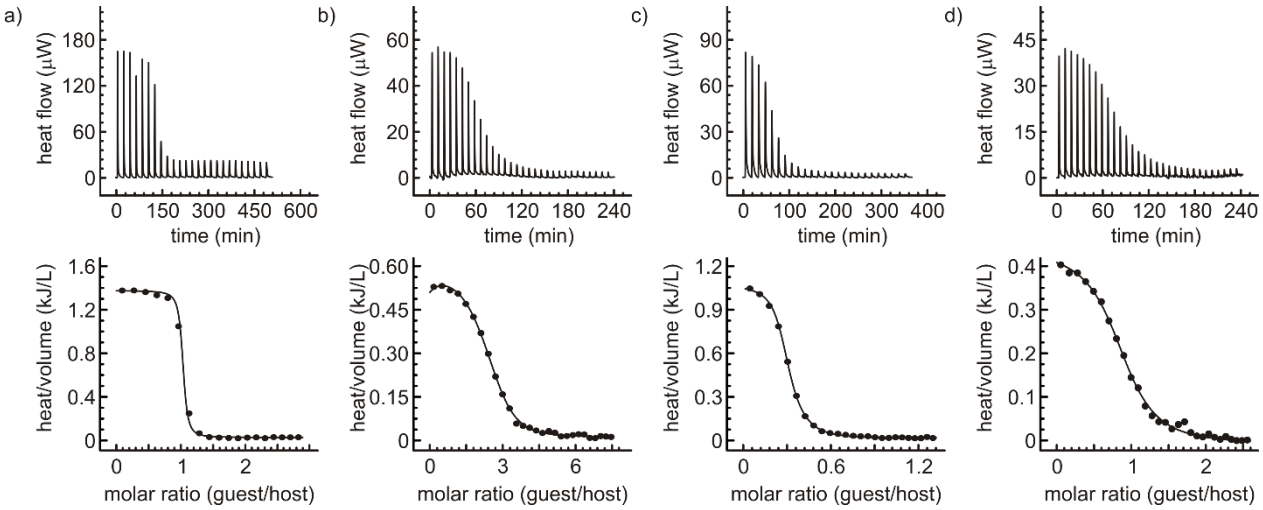

*Figure S9: ITC plots of the titration of a) trivalent macrocycle **H3** (cell) and trivalent thread **tG3** (syringe), b) trivalent macrocycle **H3** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and trivalent thread **tG3** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

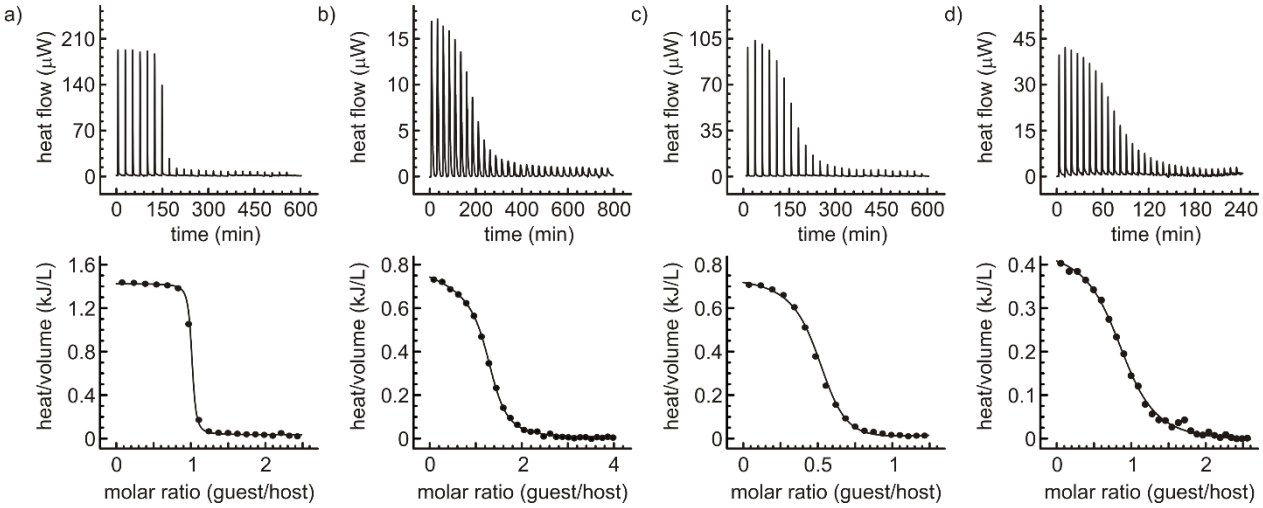

*Figure S10 ITC plots of the titration of a) divalent macrocycle **H2** (cell) and divalent thread **dG4** (syringe), b) divalent macrocycle **H2** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and divalent thread **dG4** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

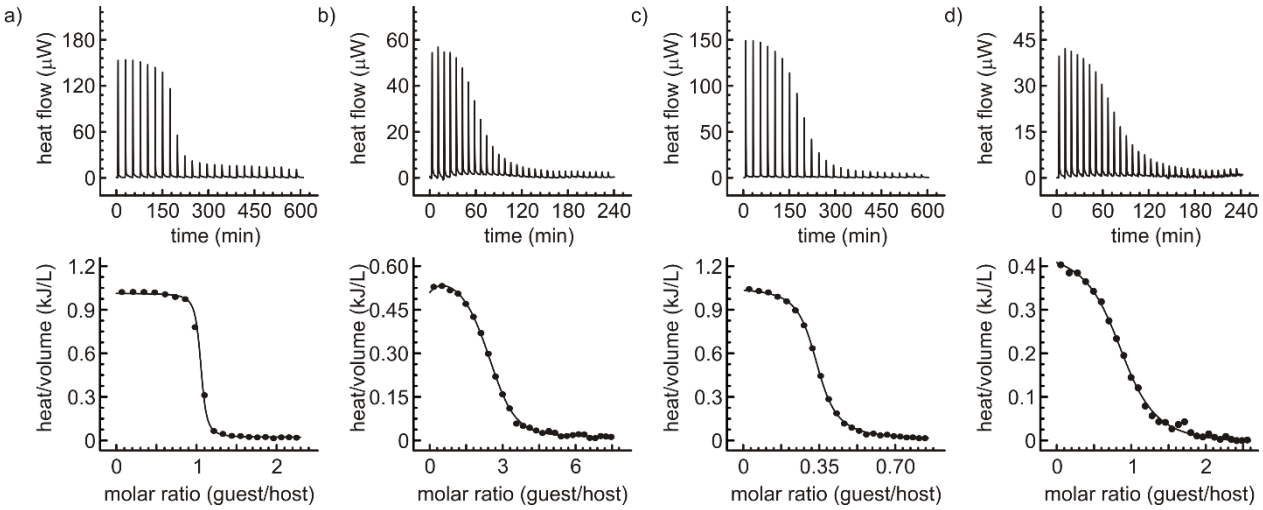

*Figure S11: ITC plots of the titration of a) trivalent macrocycle **H2** (cell) and trivalent thread **tG4** (syringe), b) trivalent macrocycle **H2** (cell) and monovalent thread **mG** (syringe), c) monovalent macrocycle **H1** (cell) and trivalent thread **tG4** (syringe) and d) monovalent macrocycle **H1** (cell) and monovalent thread **mG** (syringe) in $CHCl_3$.*

3. Statistical factors and Double Mutant Cycle Analysis

The DMC can be regarded as equilibrium between four different complexes **A**, **B**, **C** and **D** (eq. 1). In case of a multivalent pseudorotaxane (Figure S12), **A** is the multivalent complex consisting of a multivalent host and a multivalent guest molecule. Complexes **B** and **C** are combinations of one multivalent compound and the corresponding monovalent counterparts. Complex **D** corresponds to the monovalent complexes.

The equilibrium expressed in equation 1 contains the same number of hosts and guests of all types on both sides and thus corresponds to a double mutant cycle (Figure S12) takes the divalent pseudorotaxane as an example), in which the two mutations are cleavage of (a) the spacer between the guest binding sites and (b) the spacer between the host binding sites.

$$B + C \rightleftarrows A + D \qquad \text{eq. 1}$$

$$\Delta\Delta G = \Delta G^{A} + \Delta G^{D} - \Delta G^{B} - \Delta G^{C} \qquad \text{eq. 2}$$

$$K = \frac{K^{A} \cdot K^{D}}{K^{B} \cdot K^{C}} \qquad \text{eq. 3}$$

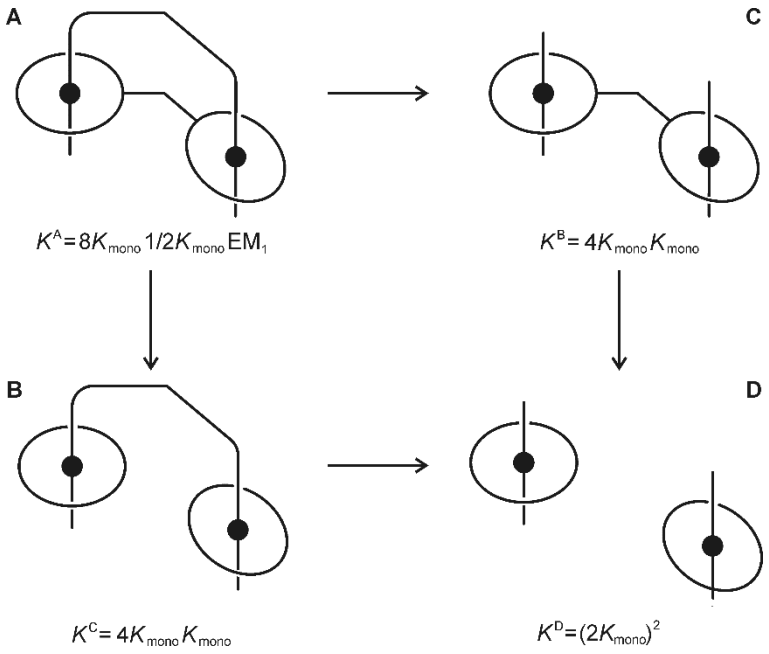

Figure S12: Double mutant cycle of the divalent pseudorotaxanes including the theoretical calculation of the association constants K^{A}-K^{D} and the statistical factors.

Equation 2 describes the free enthalpy change $\Delta\Delta G$ for the equilibrium in eq. 1. It can be expressed as the difference of the contributions of the individual complexes. The corresponding equilibrium constant K is shown in eq. 3. The association constants K^{A} – K^{D} can be experimentally determined by ITC experiments and can be expressed by the use of the monovalent association constant K_{mono}, the corresponding statistical factors and in case

of the multivalent pseudorotaxanes the effective molarities *EM*. The theoretical equilibrium constants for the studied divalent and trivalent pseudorotaxanes are shown in Figure S12 and Figure S13.

For the determination of the statistical factors, we used the direct count method[3] and double-checked the factors by those obtained with the symmetry factor method.[4, 5] The statistical factor for an equilibrium between threaded and unthreaded state is given by the ratio of the number of chemically plausible different microspecies of the products to the starting materials.

a) Divalent pseudorotaxane:

A: Divalent host with divalent guest

First threading step: Two arms of the guest, two binding sites in the host molecule, threading is possible from two different sites of the host's cavities resulting in 2 * 2 * 2 = 8 different microspecies.

Second threading step: 2 * 2 = 4 different microspecies.

$$K^A = 8K_{mono}\frac{1}{2}K_{mono}EM \qquad \text{eq. 4}$$

B: Divalent host with monovalent guest

First threading step: Two binding sites in the host molecule, one monovalent guest, threading is possible from two different sites of the host's cavities resulting in 2 * 2 = 4 different microspecies.

Second threading step: 2 * 2 = 4 different microspecies. Here, we have to include again all possible "spins" of the bound guest molecules because they can thread in independently form bottom or top (↑↑, ↑↓, ↓↑, ↓↓)

$$K^B = K_1^B K_2^B = 4K_{mono}K_{mono} \qquad \text{eq. 5}$$

C: Monovalent host with trivalent guest

Complexes **B** and **C** have the same statistical factors.

$$K^C = K_1^C K_2^C K_3^C = 4K_{mono}K_{mono} \qquad \text{eq. 6}$$

D: Monovalent host with monovalent guest

Threading can occur from both sites of the host's cavitiy. Therefore, we count two different microspecies for complex **D**.

$$K^D = (2K_{mono})^2 \qquad \text{eq. 7}$$

The overall equilibrium constant can then be written in form of equation 8. As K^A - K^D are experimental observables, the effective molarity can be determined from four titration experiments.

$$K = \frac{K^A K^D}{K^B K^C} = EM \qquad \text{eq. 8}$$

b) Trivalent pseudorotaxane:

A: Trivalent host with trivalent guest

First threading step: Three arms of the guest, three binding sites in the host molecule, threading is possible from two different sites of the host's cavitiesresulting in 3 * 3 * 2 = 18 different microspecies.

Second threading step: Based on the eighteen microspecies of complex **A** we count 18 * 2 = 36 different microspecies for the second binding step microspecies.

Third threading step: The threading of the last arm of the guest leads to 3 * 2 * 2 = 12 microspecies. Here we have to note that a singly threaded guest can rotate around itself. Therefore, there are not only 6, but 12 prossible microspecies.

$$K^A = 18K_{mono}2K_{mono}EM_1\frac{1}{3}K_{mono}EM_2 \qquad \text{eq. 9}$$

B: Trivalent host with monovalent guest

First threading step: Three binding sites in the host molecule, one monovalent guest, threading is possible from two different sites of the host's cavitiesresulting in 3 * 2 = 6 different microspecies.

Second threading step: 3 * 4 = 12 different microspecies. Here we have to include all possible "spins" of the bound guest molecules because they can thread in independently form bottom or top (↑↑, ↑↓, ↓↑, ↓↓)

Third threading step: Following the same rules as for the second threading step, we count 8 different microspecies.

$$K^B = K_1^B K_2^B K_3^B = 6K_{mono}2K_{mono}\frac{2}{3}K_{mono} \qquad \text{eq. 10}$$

C: Monovalent host with trivalent guest

Complexes **B** and **C** have the same statistical factors.

$$K^C = K_1^C K_2^C K_3^C = 6K_{mono}2K_{mono}\frac{2}{3}K_{mono} \qquad \text{eq. 11}$$

D: Monovalent host with monovalent guest

The threading can occur from both sites of the host's cavitiy. Therefore, we count two different microspecies for complex **D**.

$$K^D = (2K_{mono})^3 \qquad \text{eq. 12}$$

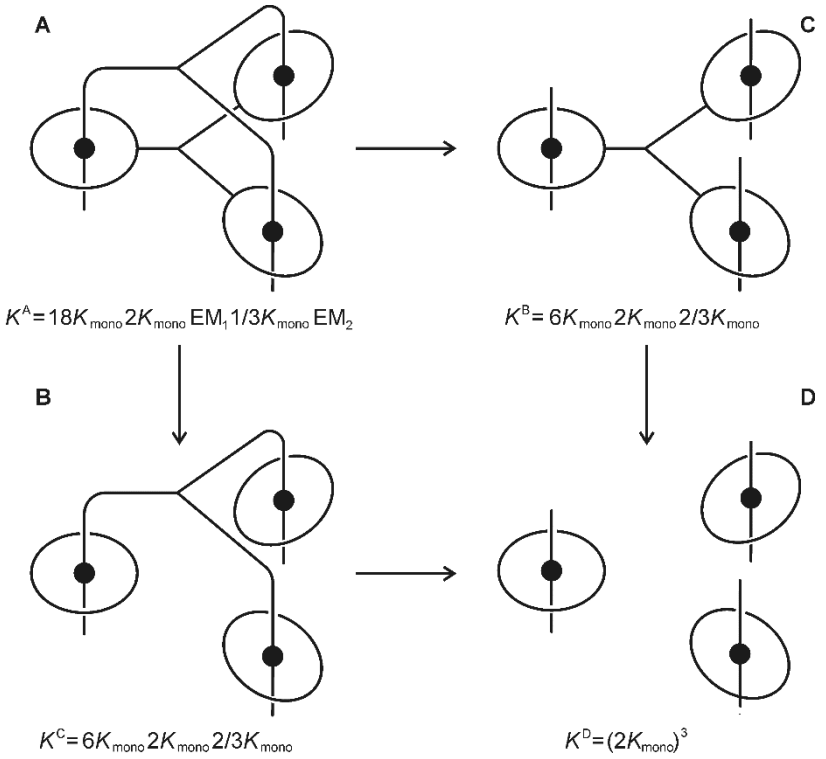

Figure S13: Double mutant cycle of the trivalent pseudorotaxanes including the theoretical calculation of the association constants K^A - K^D and the statistical factors.

Figure S13 shows the chemical double mutant cycle for the trivalent pseudorotaxanes.

The overall equilibrium constant is given by equation 13.

$$K = \frac{K^A K^D}{K^B K^C} = \frac{3}{2} EM_1 EM_2 \qquad \text{eq. 13}$$

To evaluate chelate cooperativity for the trivalent pseudorotaxanes, we use an apparent *EM* value as defined in eq. 14, because the spacer structures of the di- and trivalent pseudorotaxanes are somewhat different and thus EM_1 of the trivalent pseudorotaxane may be different from the *EM* determined for the divalent one.

$$EM = \sqrt{EM_1 EM_2} \qquad \text{eq. 14}$$

4. Cache Modeling

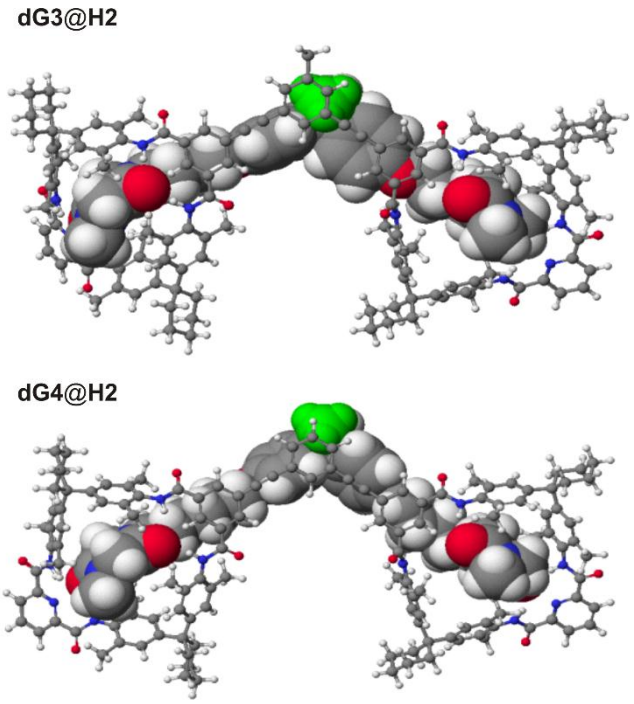

Figure S14: MM2 force-field-optimized structures of the divalent pseudorotaxanes with a preorganised spacer unit, ***dG3@H2*** *(top) and* ***dG4@H2*** *(bottom). The calculations were performed with the MM2 force field implemented in the CACHE 5.0 program package (Fujitsu, Krakow/Poland). In these two cases, both binding sites can adopt favorable geometries, but due to the different lengths of the alkyl chains, the spacer-spacer interactions differ. In the top structure, the benzene spacer connecting the two macrocycles is unfavorably located under the methyl group protruding from the spacer centerpiece connecting the two diketopiperazines. In the bottom structure, a more favorable edge-to-face interaction between that benzene ring and protons from the other spacer are possible.*

5. ^{1}H, ^{13}C NMR and MS Spectra

Multivalent threads

4,4'-((1,3-Phenylenebis(oxy))bis(hexane-3,1-diyl))bis(1-methylpiperazine-2,5-dione) dG1

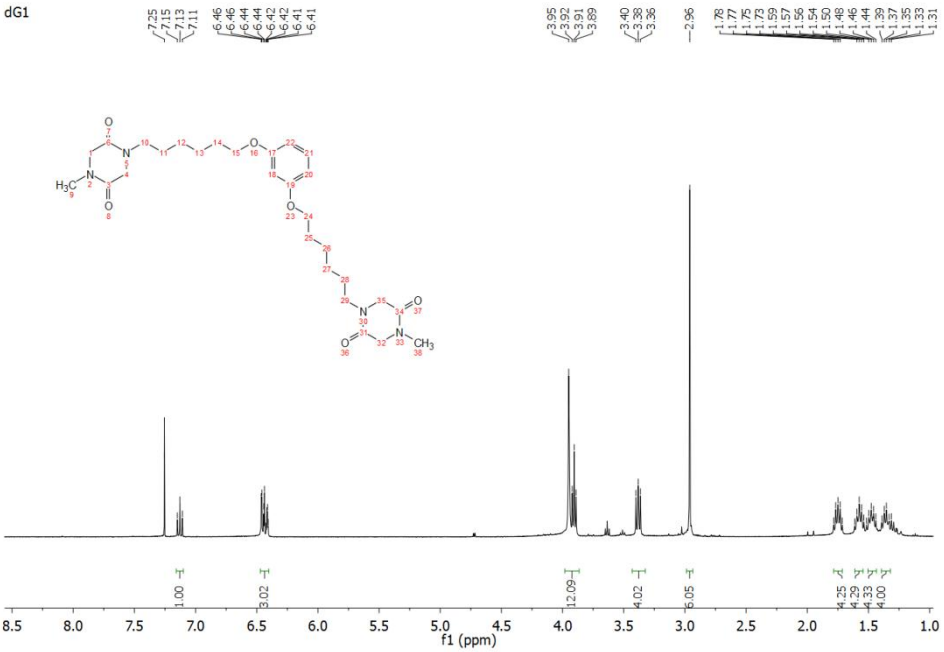

*Figure S15: ^{1}H NMR spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(hexane-3,1-diyl))bis(1-methylpiperazine-2,5-dione) **dG1** (400 MHz, $CDCl_3$, 298 K).*

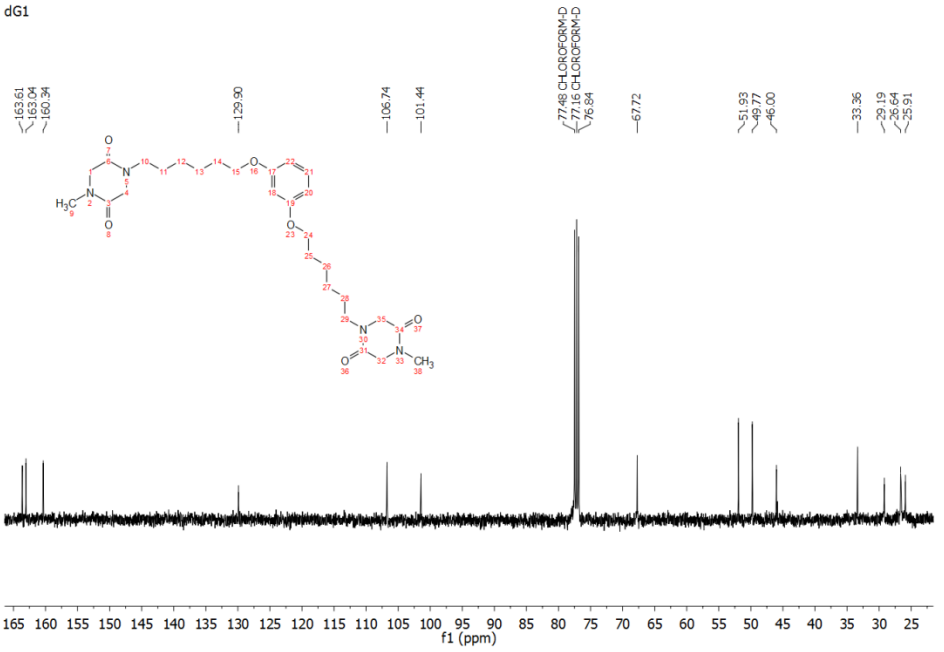

*Figure S16: ^{13}C NMR spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(hexane-3,1-diyl))bis(1-methylpiperazine-2,5-dione) **dG1** (101 MHz, $CDCl_3$, 298 K).*

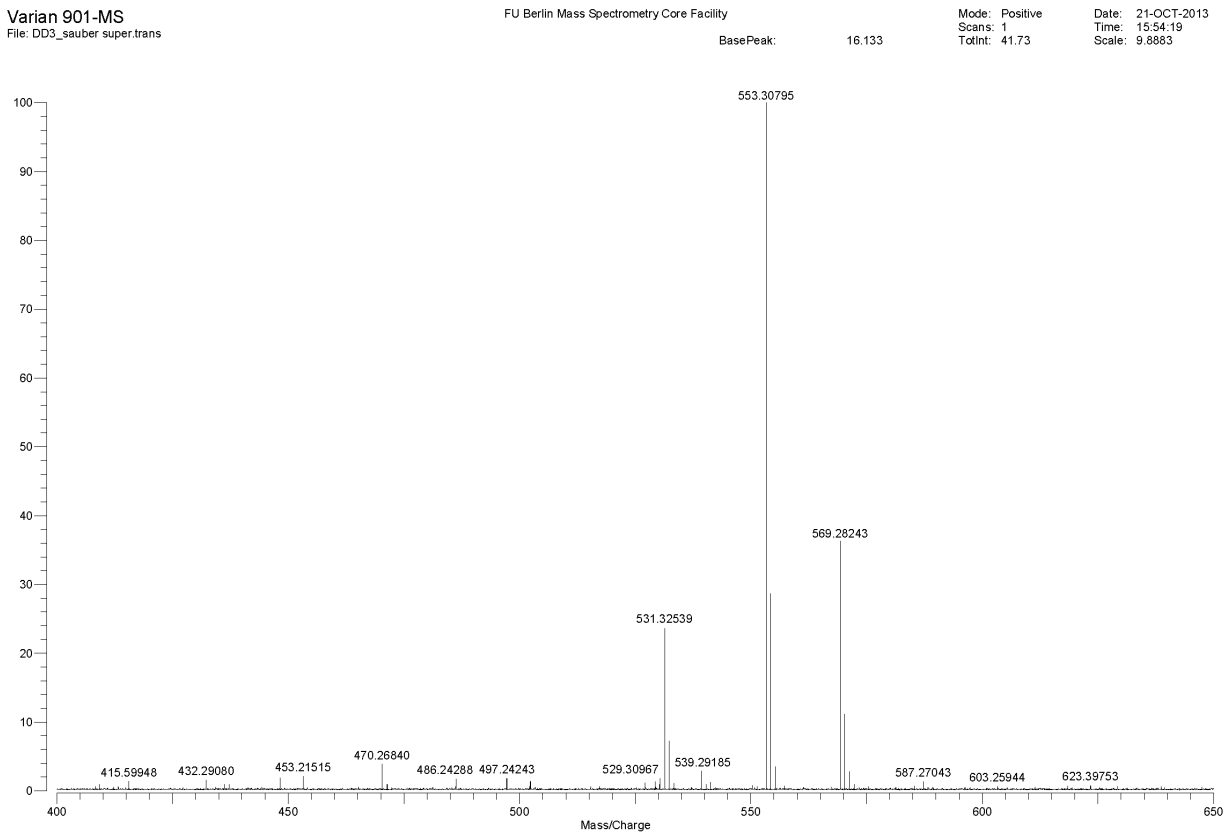

Figure S17: ESI MS spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(hexane-3,1-diyl))bis(1-methylpiperazine-2,5-dione) ***dG1*** *($CHCl_3$/CH_3OH, positive mode).*

4,4',4''-((Benzene-1,3,5-triyltris(oxy))tris(propane-3,1-diyl))tris(1-methylpiperazine-2,5-dione) tG1

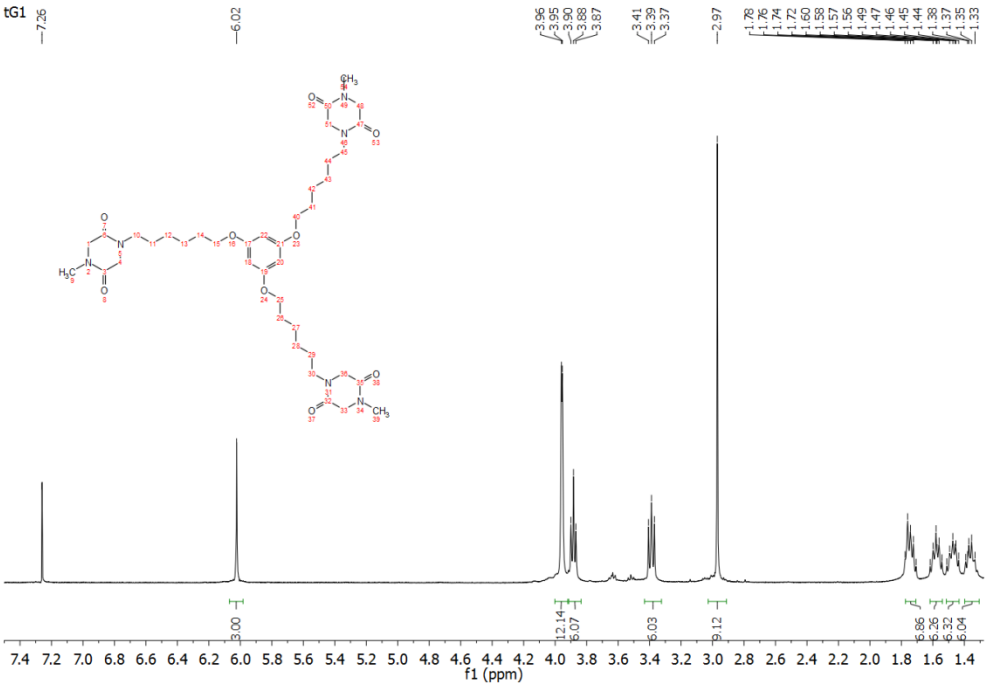

*Figure S18: ^{1}H NMR spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(propane-3,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG1** (400 MHz, $CDCl_3$, 298 K).*

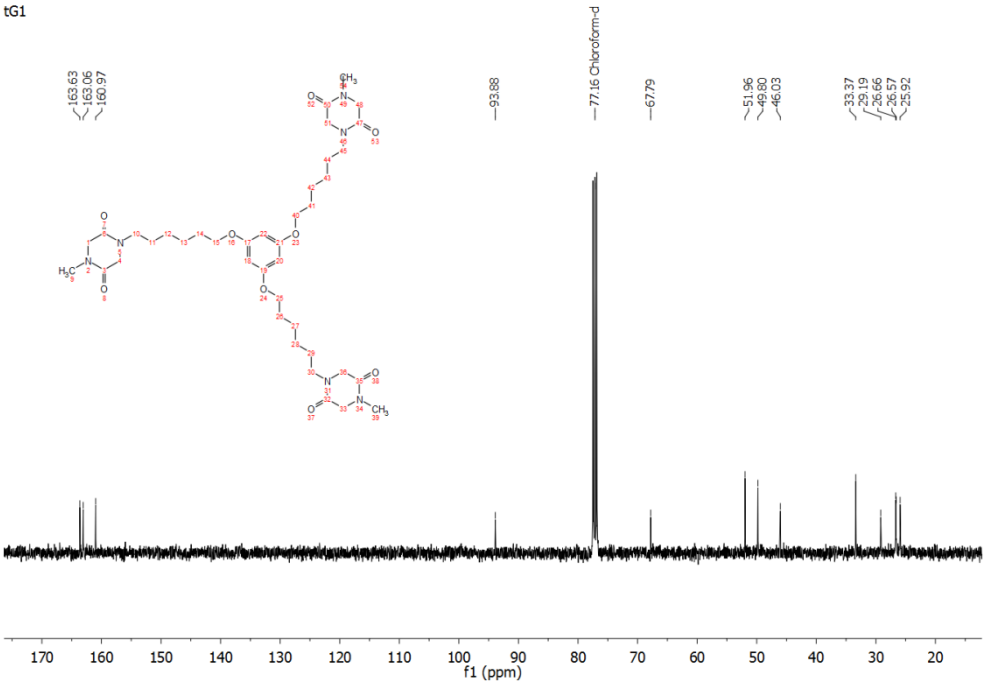

*Figure S19: ^{13}C NMR spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(propane-3,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG1** (101 MHz, $CDCl_3$, 298 K).*

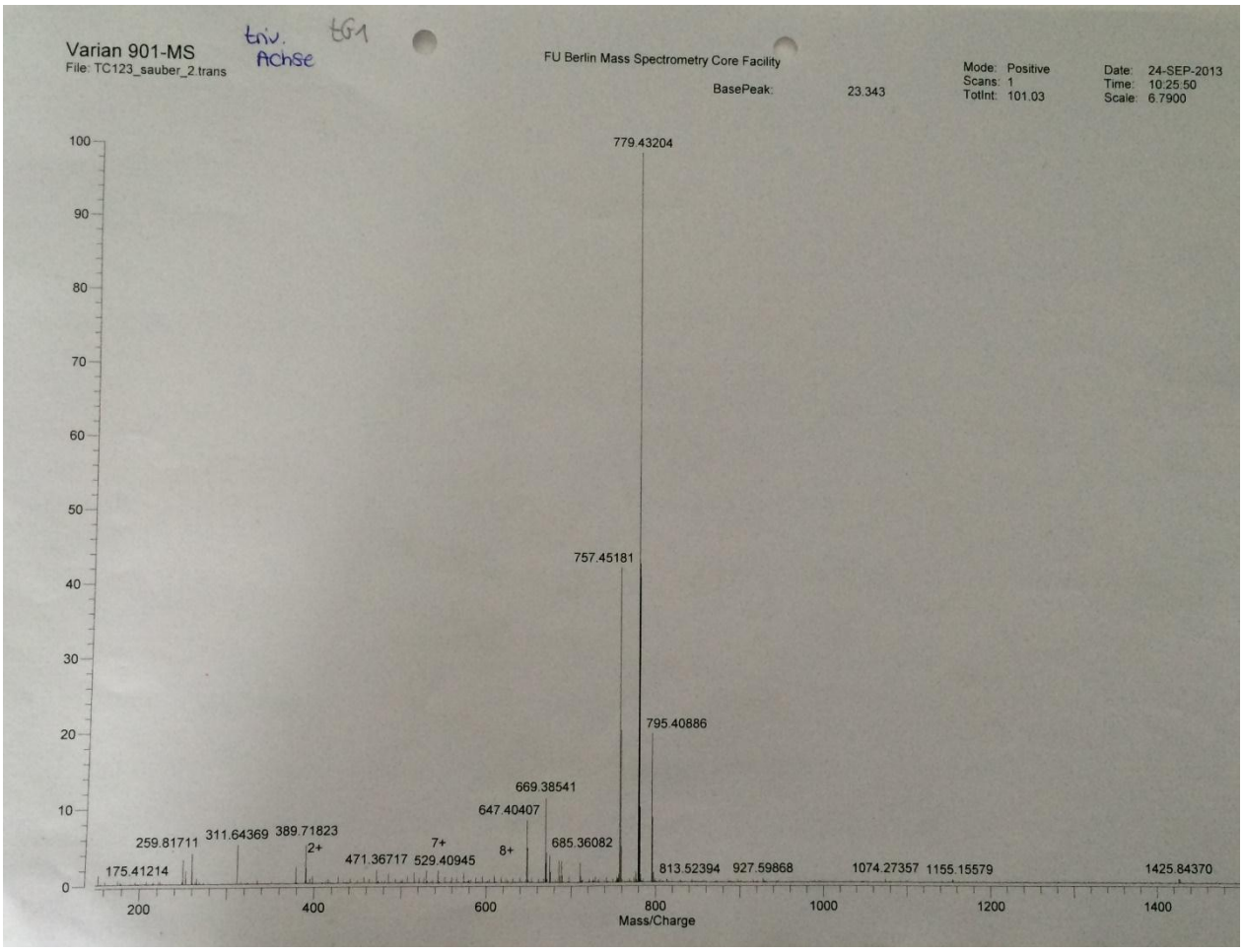

Figure S20: ESI MS spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(propane-3,1-diyl))tris(1-methylpiperazine-2,5-dione) ***tG1*** *($CHCl_3$/CH_3OH, positive mode).*

4,4'-((1,3-Phenylenebis(oxy))bis(octane-8,1-diyl))bis(1-methylpiperazine-2,5-dione) dG2

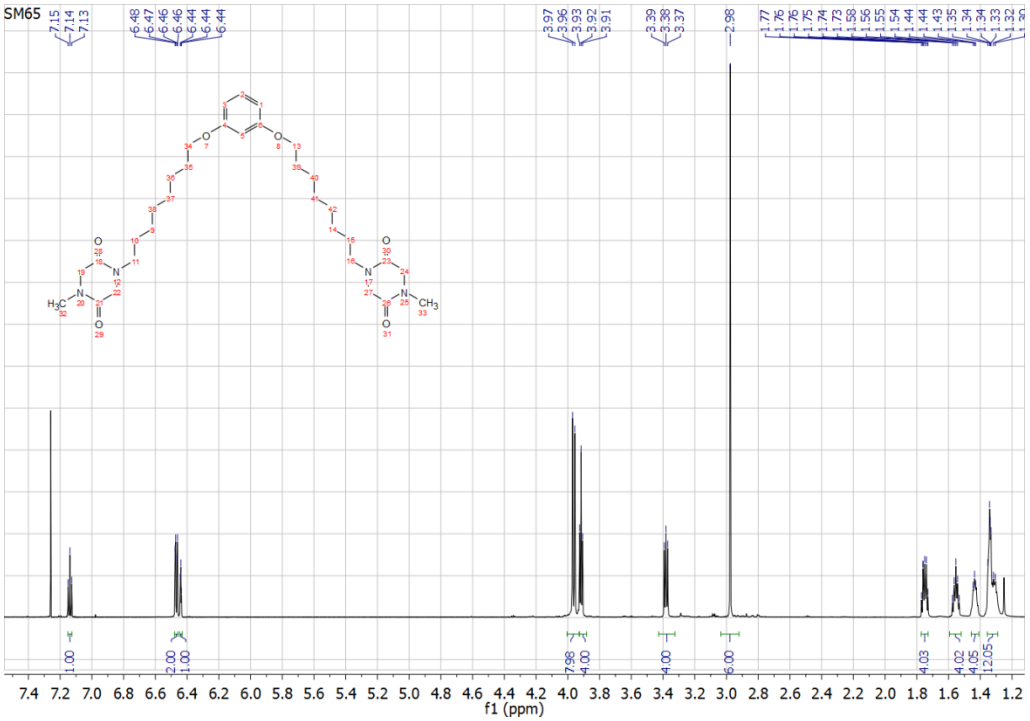

Figure S21: ^{1}H NMR spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(octane-8,1-diyl))bis(1-methylpiperazine-2,5-dione) ***dG2*** *(700 MHz, $CDCl_3$, 298 K).*

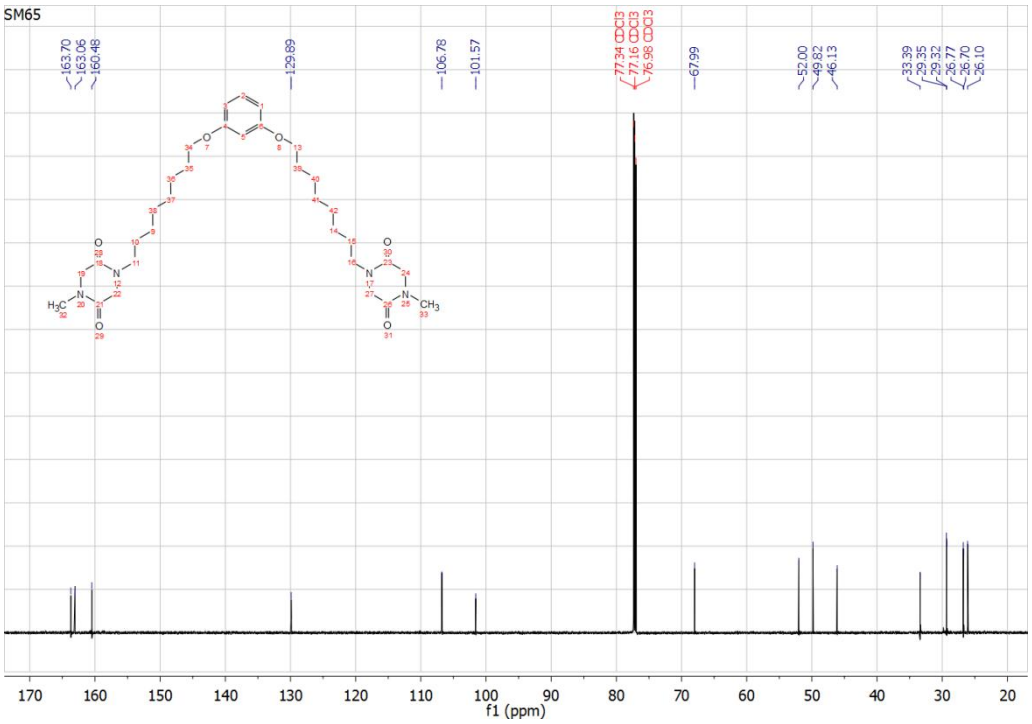

Figure S22: ^{13}C NMR spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(octane-8,1-diyl))bis(1-methylpiperazine-2,5-dione) ***dG2*** *(176 MHz, $CDCl_3$, 298 K).*

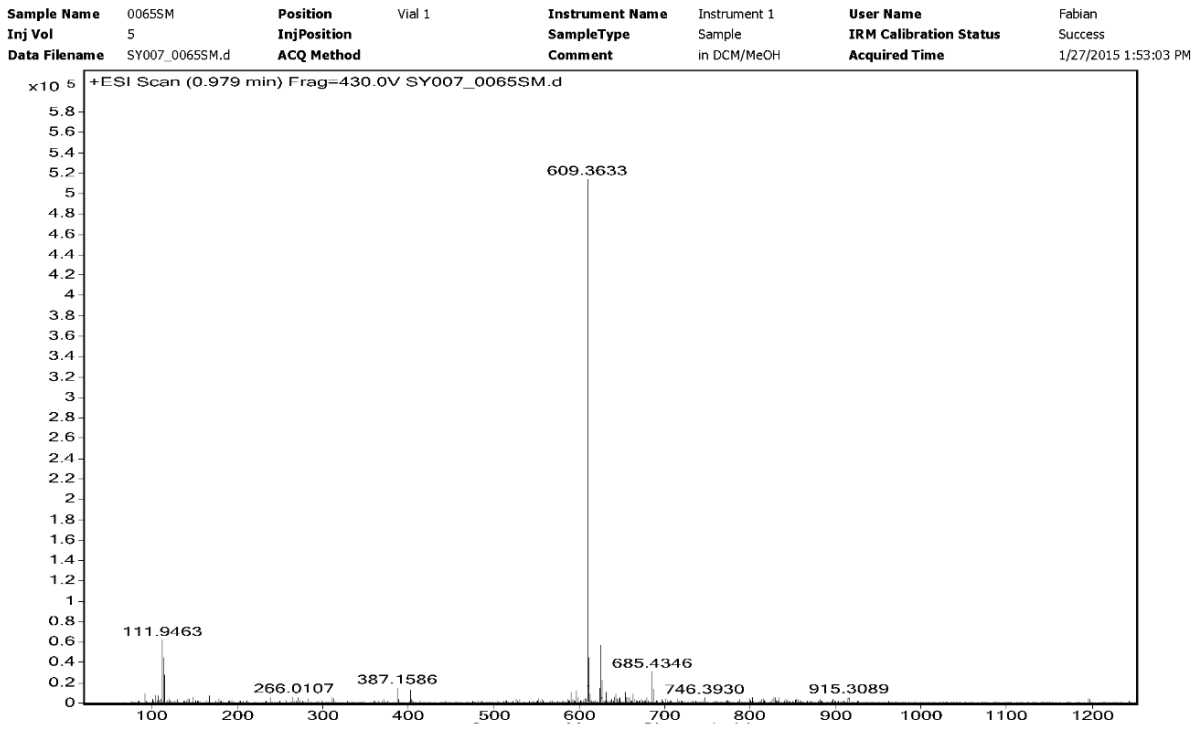

Figure S23: ESI MS spectrum of 4,4'-((1,3-phenylenebis(oxy))bis(octane-8,1-diyl))bis(1-methylpiperazine-2,5-dione) ***dG2*** *(CH_2Cl_2/CH_3OH, positive mode).*

4,4',4''-((Benzene-1,3,5-triyltris(oxy))tris(octane-8,1-diyl))tris(1-methylpiperazine-2,5-dione) tG2

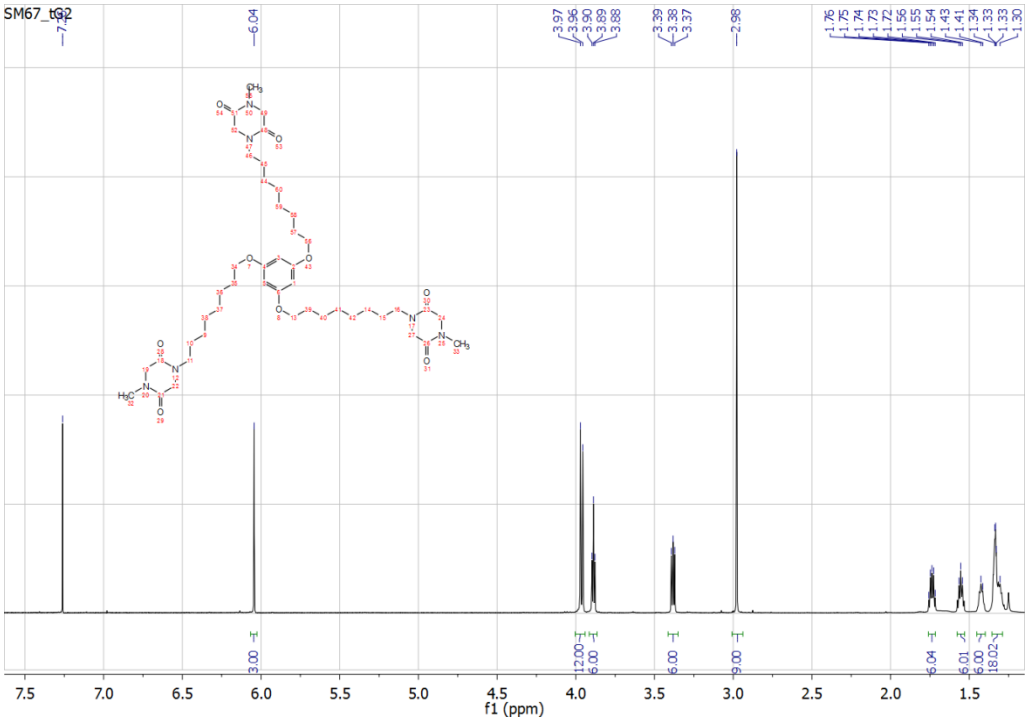

*Figure S24: ^{1}H NMR spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(octane-8,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG2** (700 MHz, $CDCl_3$, 298 K).*

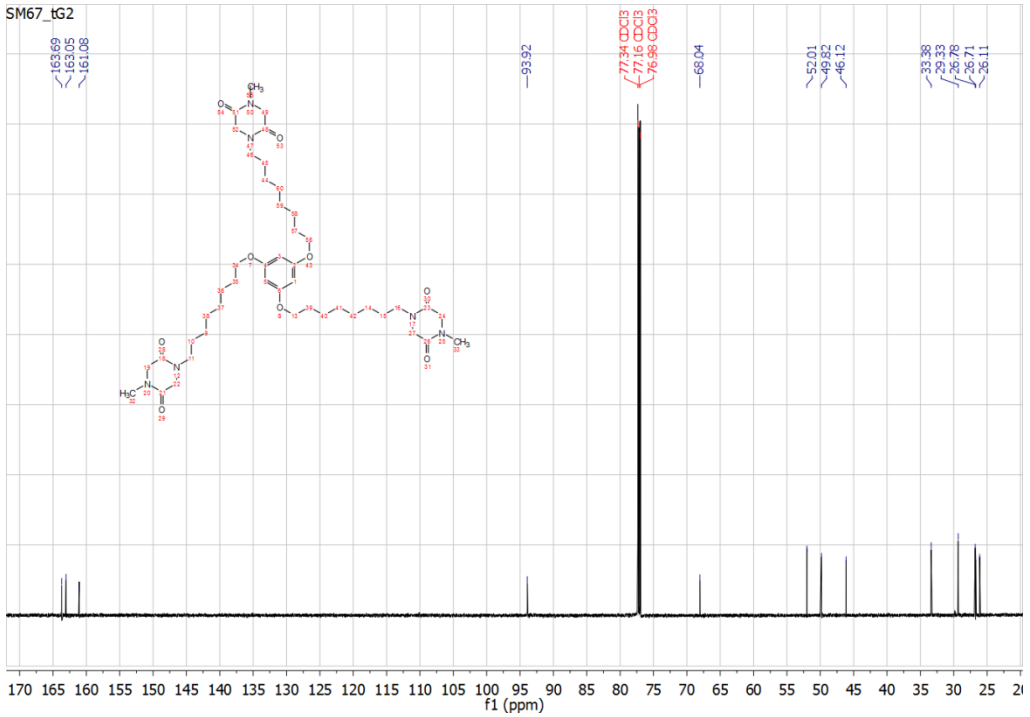

*Figure S25: ^{13}C NMR spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(octane-8,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG2** (176 MHz, $CDCl_3$, 298 K).*

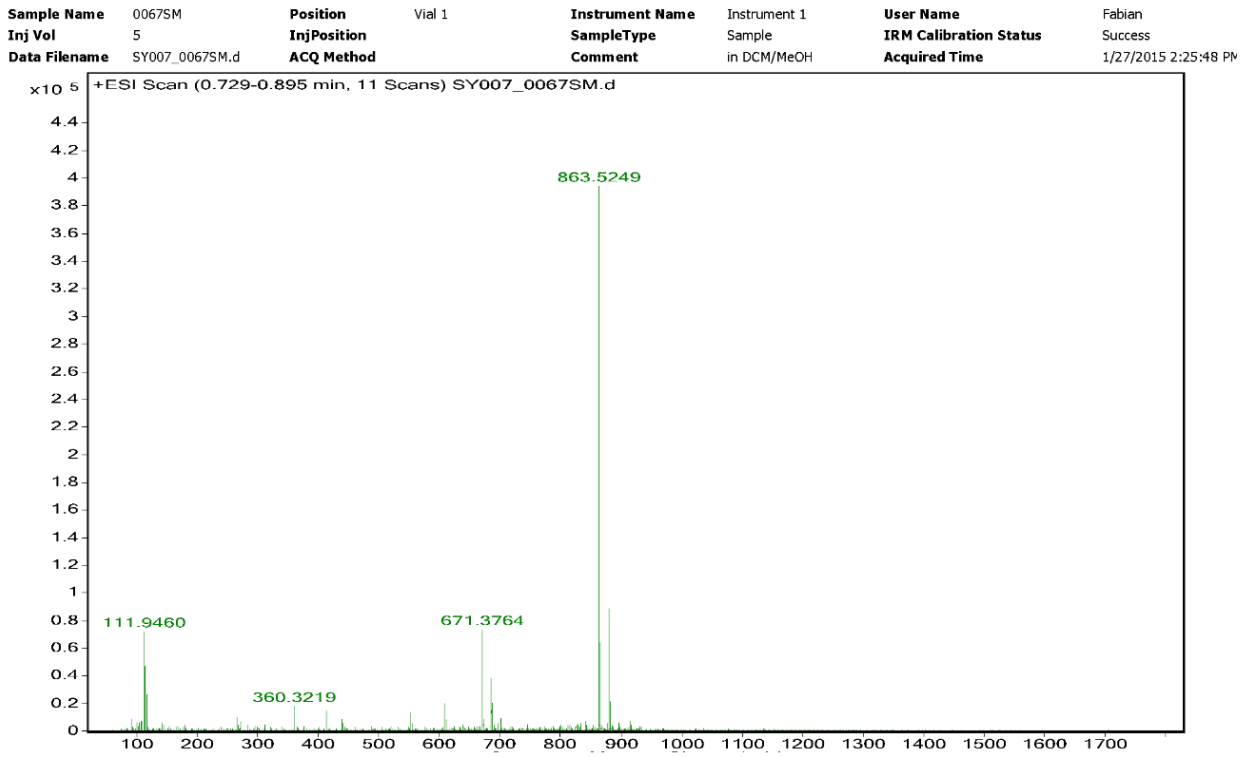

Figure S26: ESI MS spectrum of 4,4',4''-((benzene-1,3,5-triyltris(oxy))tris(octane-8,1-diyl))tris(1-methylpiperazine-2,5-dione) ***tG2*** *(CH_2Cl_2/CH_3OH, positive mode).*

4,4'-(4,4'-(4,4'-(Propane-2,2-diyl)bis(4,1-phenylene))bis(oxy)bis(butane-4,1-diyl))bis(1-methylpiperazine-2,5-dione) dG3

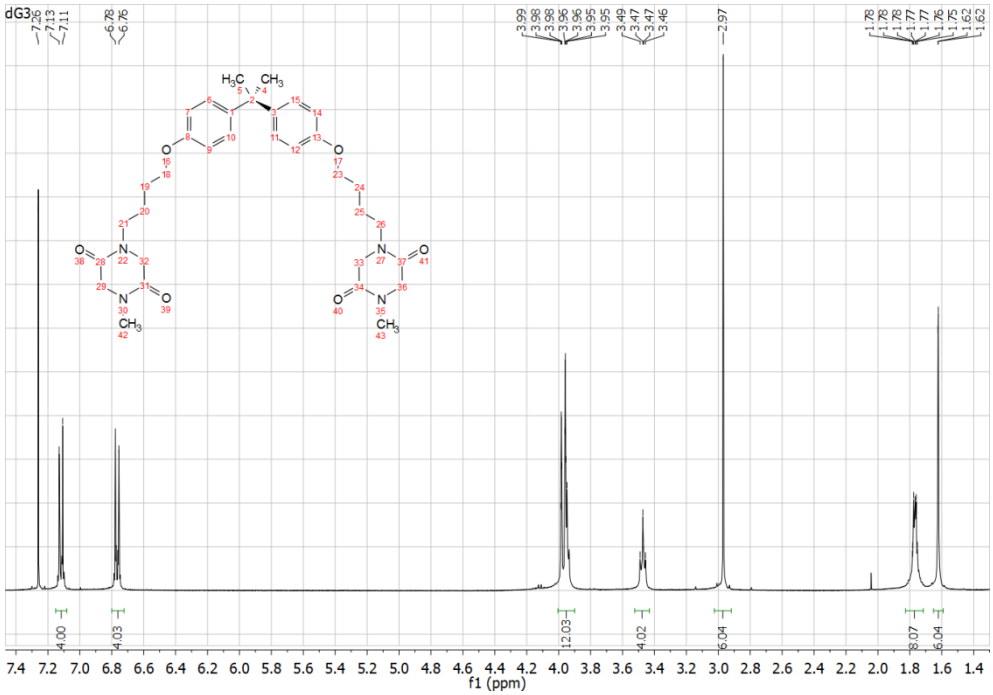

*Figure S27: ^{1}H NMR spectrum of 4,4'-(4,4'-(4,4'-(propane-2,2-diyl)bis(4,1-phenylene))bis(oxy)bis(butane-4,1-diyl))bis(1-methylpiperazine-2,5-dione) **dG3** (500 MHz, $CDCl_3$, 298 K).*

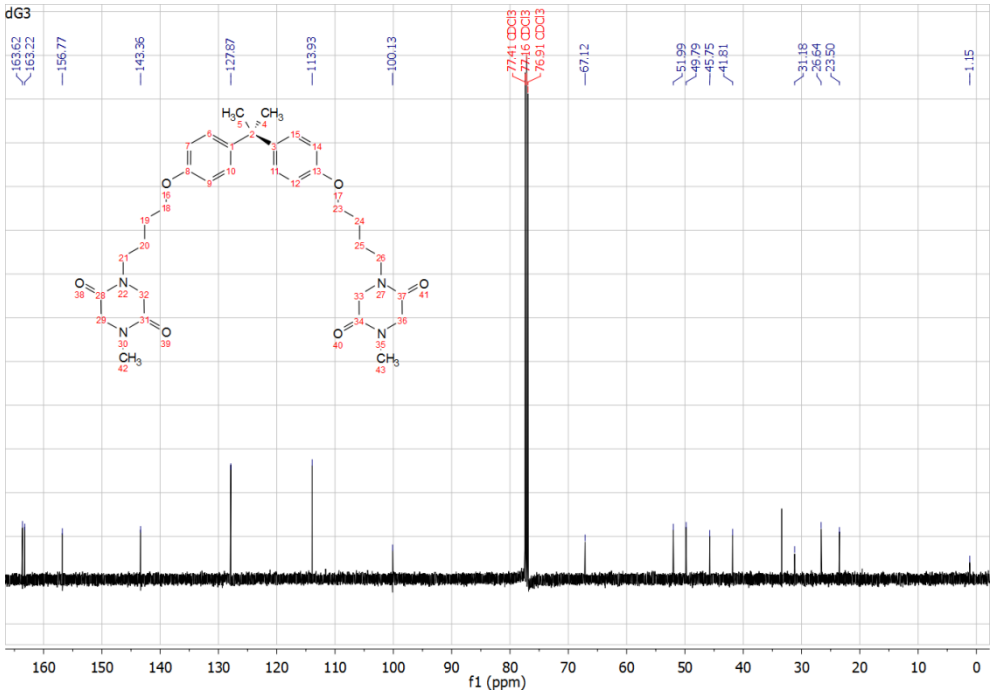

*Figure S28: ^{13}C NMR spectrum of 4,4'-(4,4'-(4,4'-(propane-2,2-diyl)bis(4,1-phenylene))bis(oxy)bis(butane-4,1-diyl))bis(1-methylpiperazine-2,5-dione) **dG3** (126 MHz, $CDCl_3$, 298 K).*

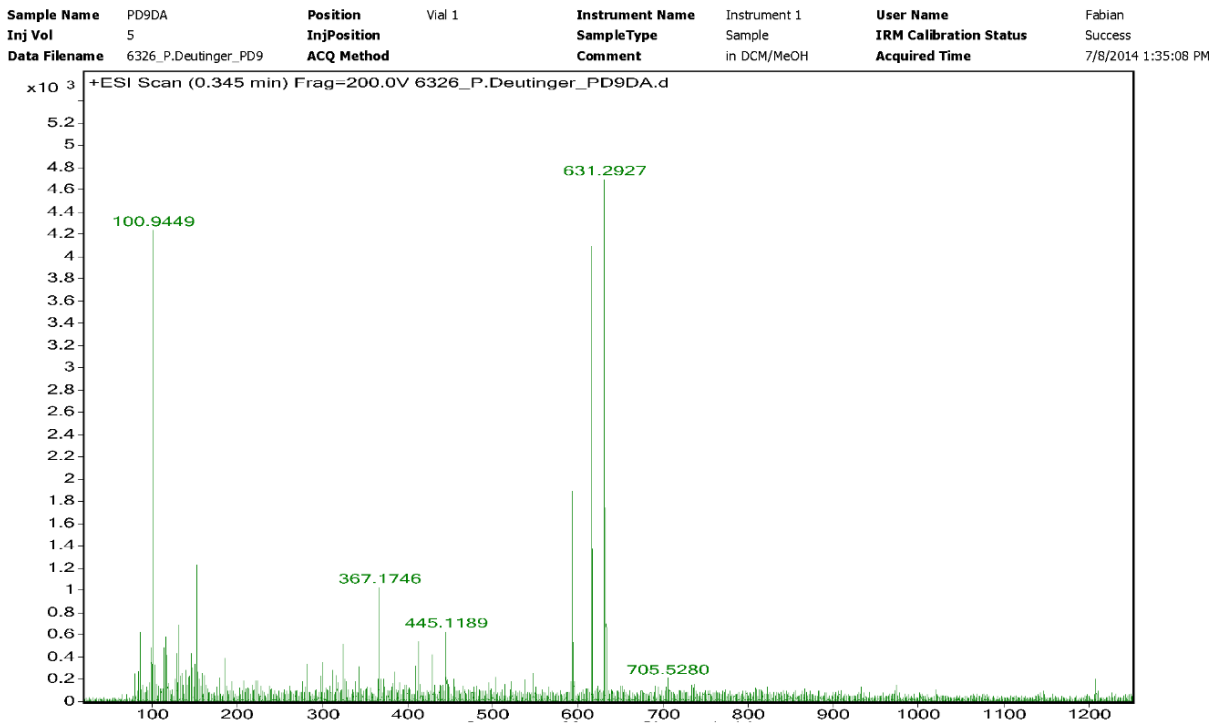

Figure S29: ESI MS spectrum of 4,4'-(4,4'-(4,4'-(propane-2,2-diyl)bis(4,1-phenylene))bis(oxy)bis(butane-4,1-diyl))bis(1-methylpiperazine-2,5-dione) ***dG3*** *(CH_2Cl_2/CH_3OH, positive mode).*

4,4',4''-(4,4',4''-(4,4',4''-(Ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(butane-4,1-diyl))tris(1-methylpiperazine-2,5-dione) tG3

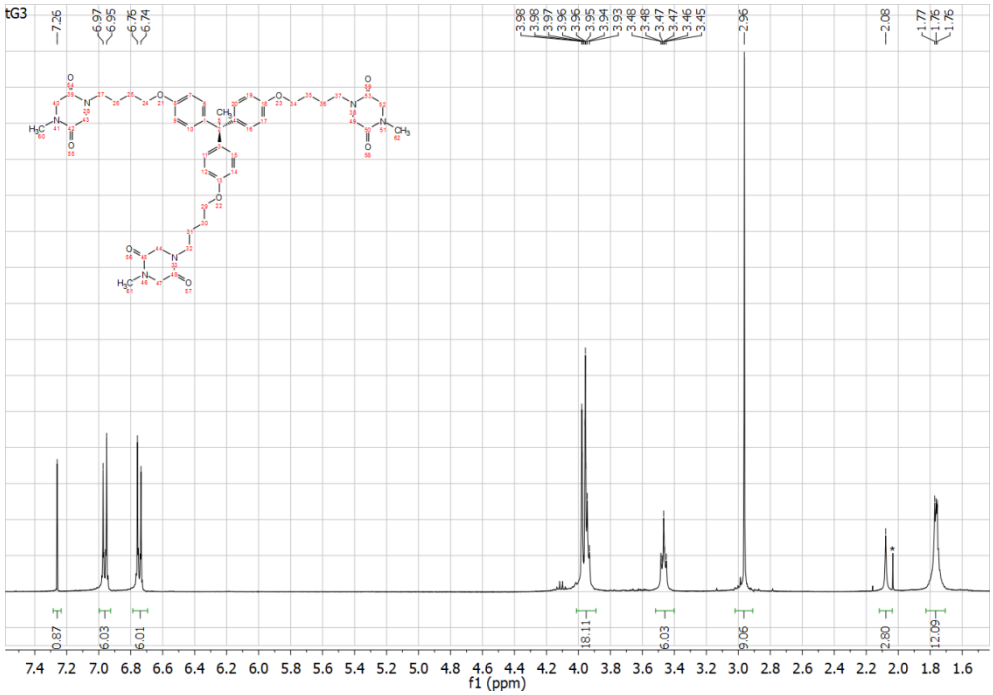

*Figure S30: ^{1}H NMR spectrum of 4,4',4''-(4,4',4''-(4,4',4''-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(butane-4,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG3** (500 MHz, $CDCl_3$, 298 K).*

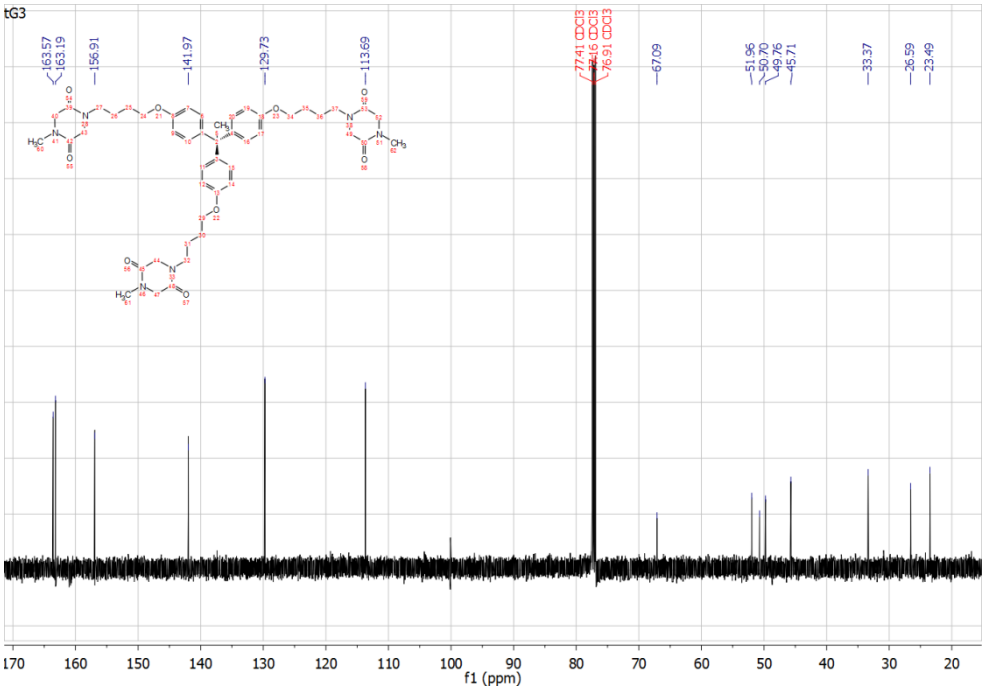

*Figure S31: ^{13}C NMR spectrum of 4,4',4''-(4,4',4''-(4,4',4''-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(butane-4,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG3** (126 MHz, $CDCl_3$, 298 K).*

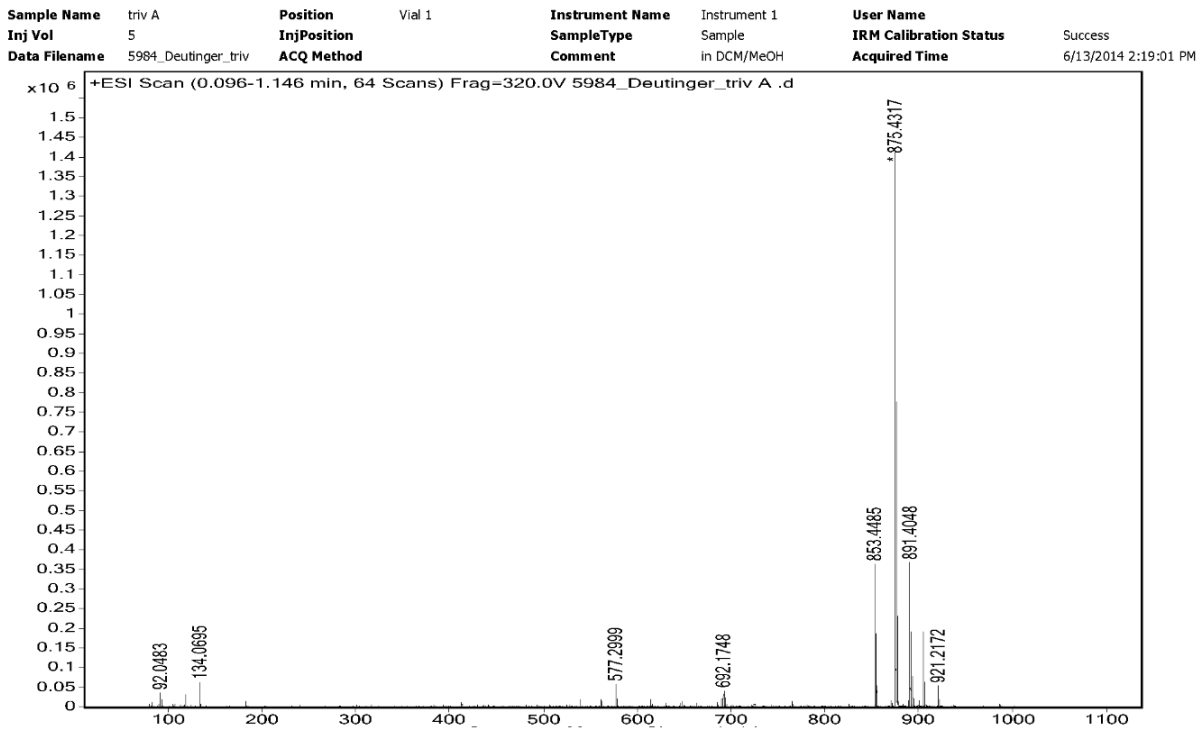

Figure S32: ESI MS spectrum of 4,4',4''-(4,4',4''-(4,4',4''-(ethane-1,1,1-triyl)tris(benzene-4,1-diyl))tris(oxy)tris(butane-4,1-diyl))tris(1-methylpiperazine-2,5-dione) ***tG3*** *(CH_2Cl_2/CH_3OH, positive mode).*

4,4'-(((Propane-2,2-diylbis(4,1-phenylene))bis(oxy))bis(hexane-6,1-diyl))bis(1 methylpiperazine-2,5-dione) dG4

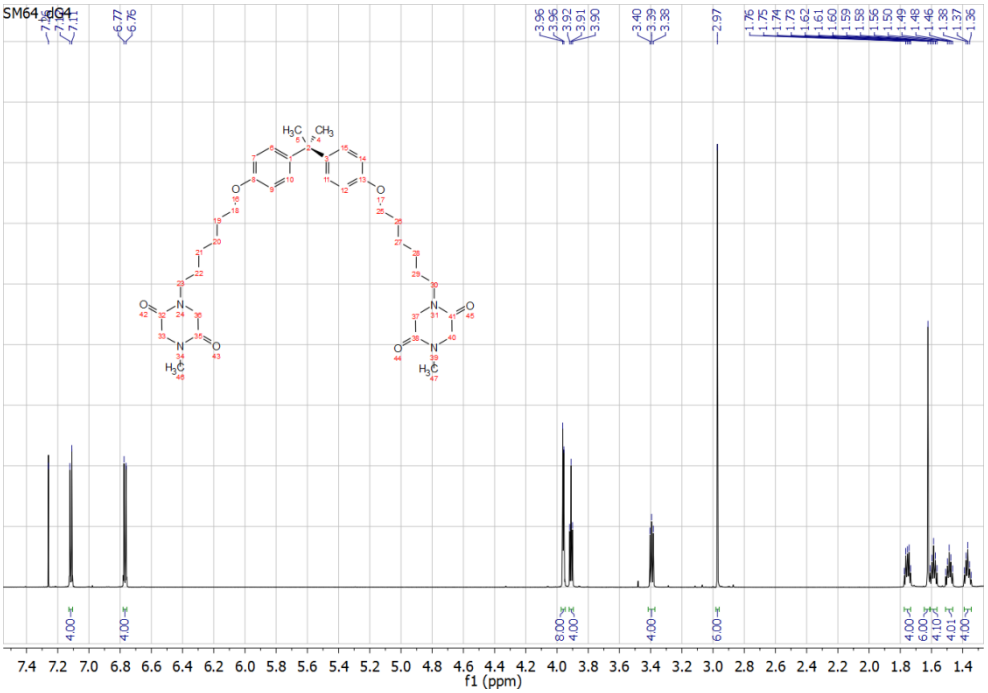

Figure S33: ^{1}H NMR spectrum of 4,4'-(((propane-2,2-diylbis(4,1-phenylene))bis(oxy))bis(hexane-6,1-diyl))bis(1 methylpiperazine-2,5-dione) ***dG4*** *(700 MHz, $CDCl_3$, 298 K).*

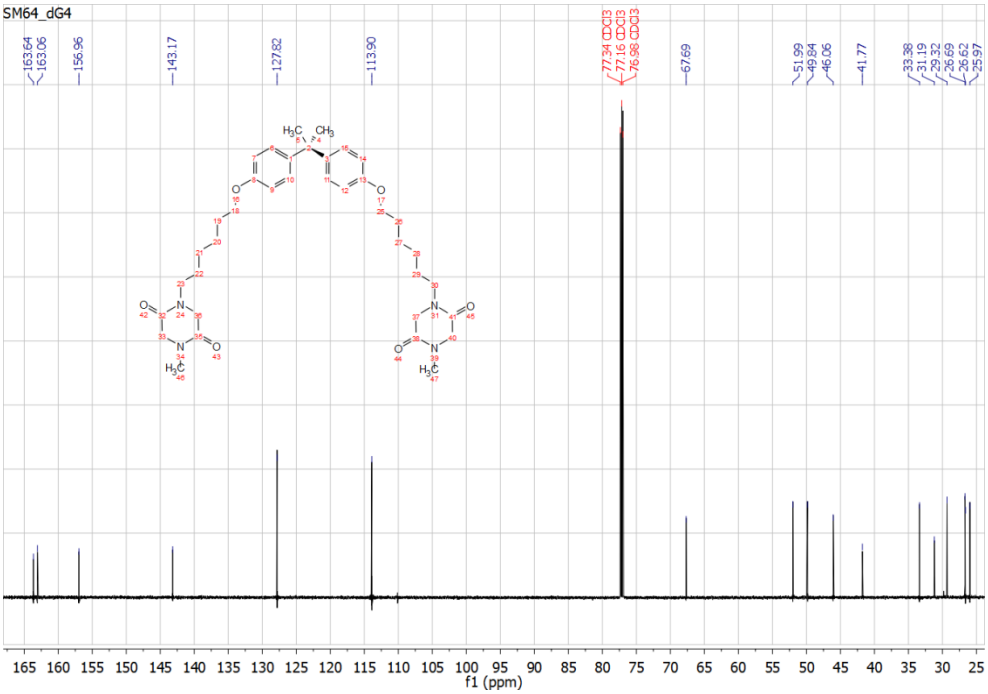

Figure S34: ^{13}C NMR spectrum of 4,4'-(((propane-2,2-diylbis(4,1-phenylene))bis(oxy))bis(hexane-6,1-diyl))bis(1 methylpiperazine-2,5-dione) ***dG4*** *(176 MHz, $CDCl_3$, 298 K).*

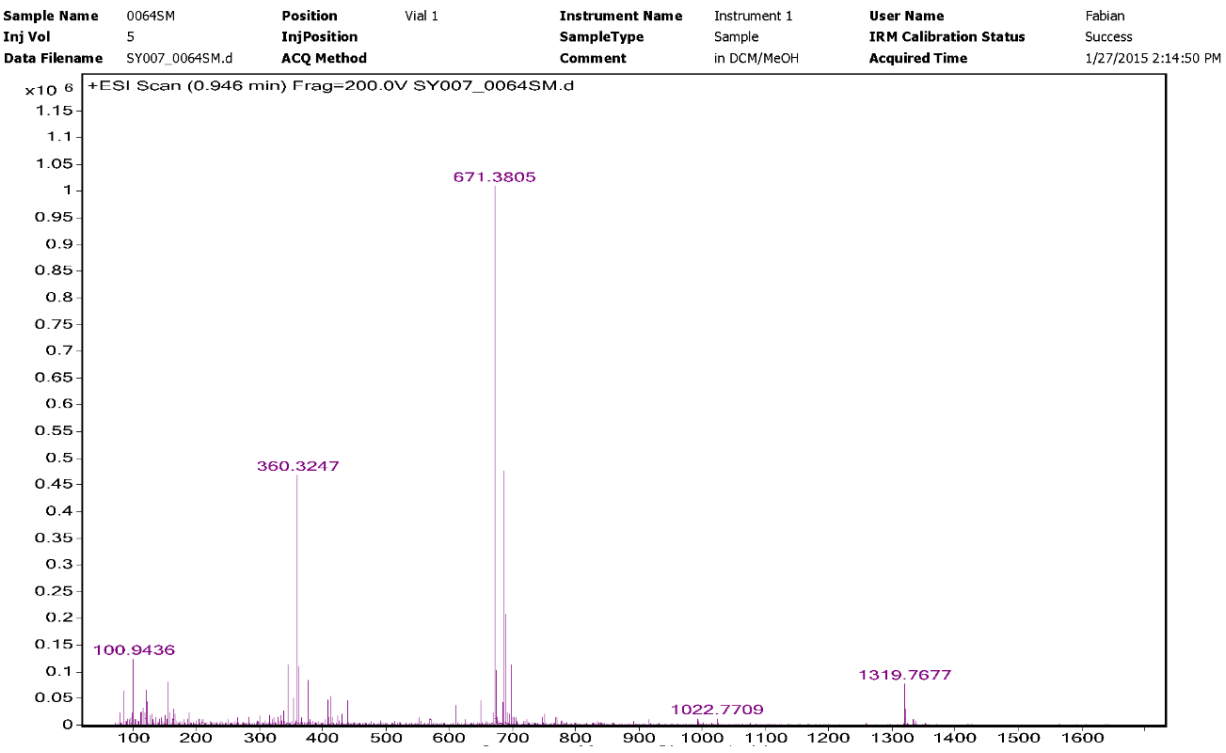

Figure S35: ESI MS spectrum of 4,4'-(((propane-2,2-diylbis(4,1-phenylene))bis(oxy))bis(hexane-6,1-diyl))bis(1 methylpiperazine-2,5-dione) ***dG4*** *(CH_2Cl_2/CH_3OH, positive mode).*

4,4',4''-(((Ethane-1,1,1-triyltris(4,1-phenylene))tris(oxy))tris(hexane-6,1-diyl))tris(1-methylpiperazine-2,5-dione) tG4

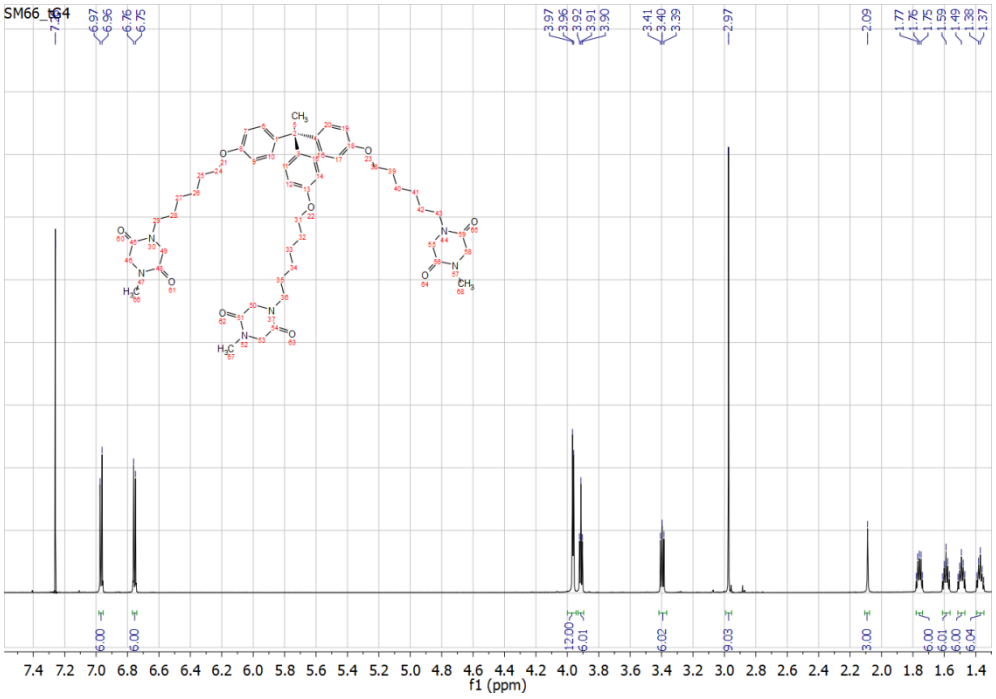

*Figure S36: ^{1}H NMR spectrum of 4,4',4''-(((ethane-1,1,1-triyltris(4,1-phenylene))tris(oxy))tris(hexane-6,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG4** (700 MHz, $CDCl_3$, 298 K).*

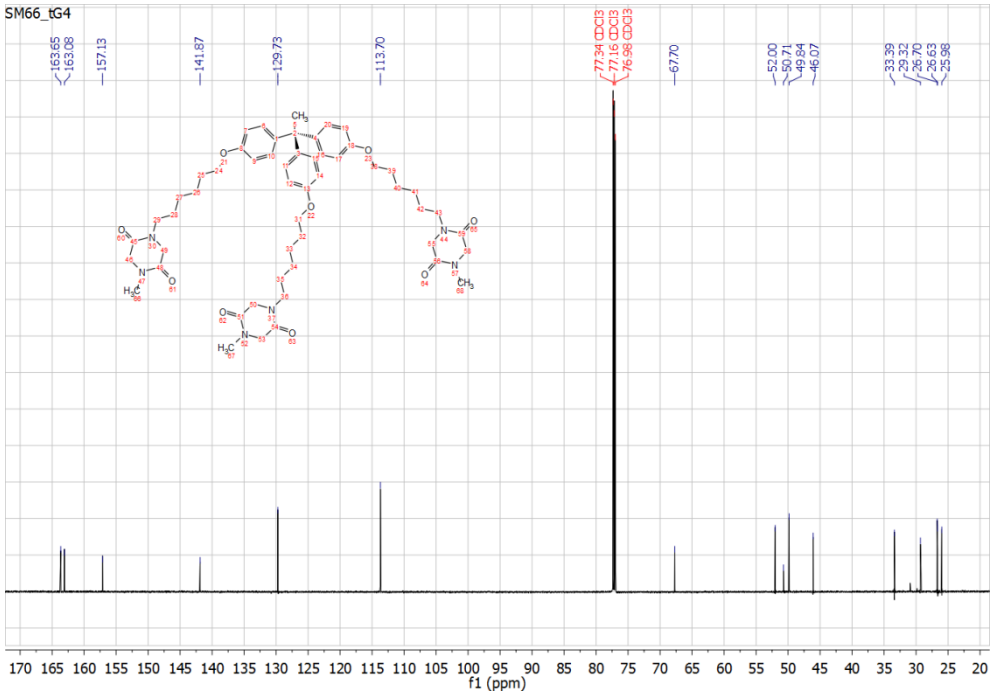

*Figure S37: ^{13}C NMR spectrum of 4,4',4''-(((ethane-1,1,1-triyltris(4,1-phenylene))tris(oxy))tris(hexane-6,1-diyl))tris(1-methylpiperazine-2,5-dione) **tG4** (176 MHz, $CDCl_3$, 298 K).*

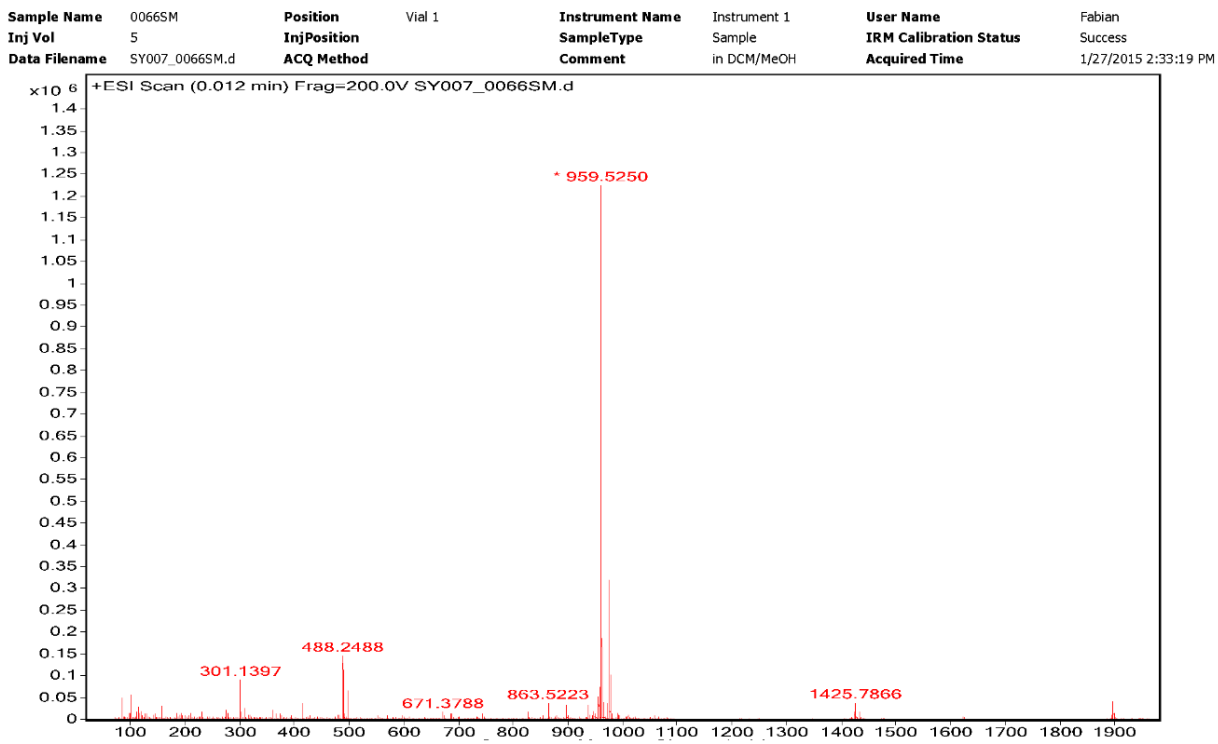

Figure S38: ESI MS spectrum of 4,4',4''-(((ethane-1,1,1-triyltris(4,1-phenylene))tris(oxy))tris(hexane-6,1-diyl))tris(1-methylpiperazine-2,5-dione) ***tG4*** *(CH_2Cl_2/CH3OH, positive mode).*

Thread precursors

1-(3-Chlorhexyl)-4-methylpiperazin-2,5-dion 2

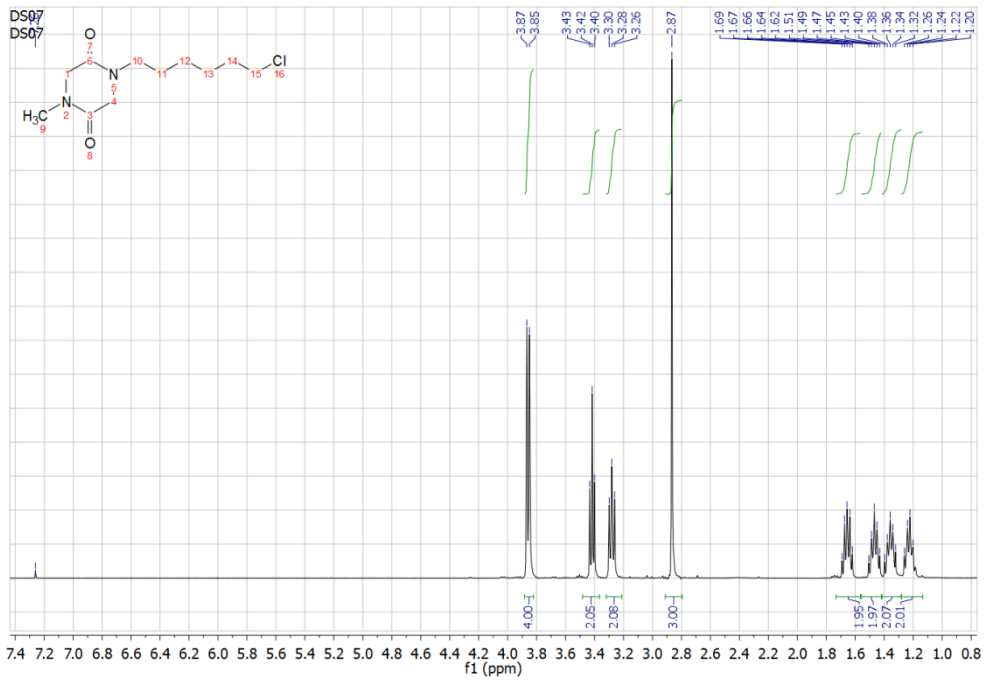

*Figure S39: ^{1}H NMR spectrum of 1-(3-chlorhexyl)-4-methylpiperazin-2,5-dion **2** (400 MHz, $CDCl_3$, 298 K).*

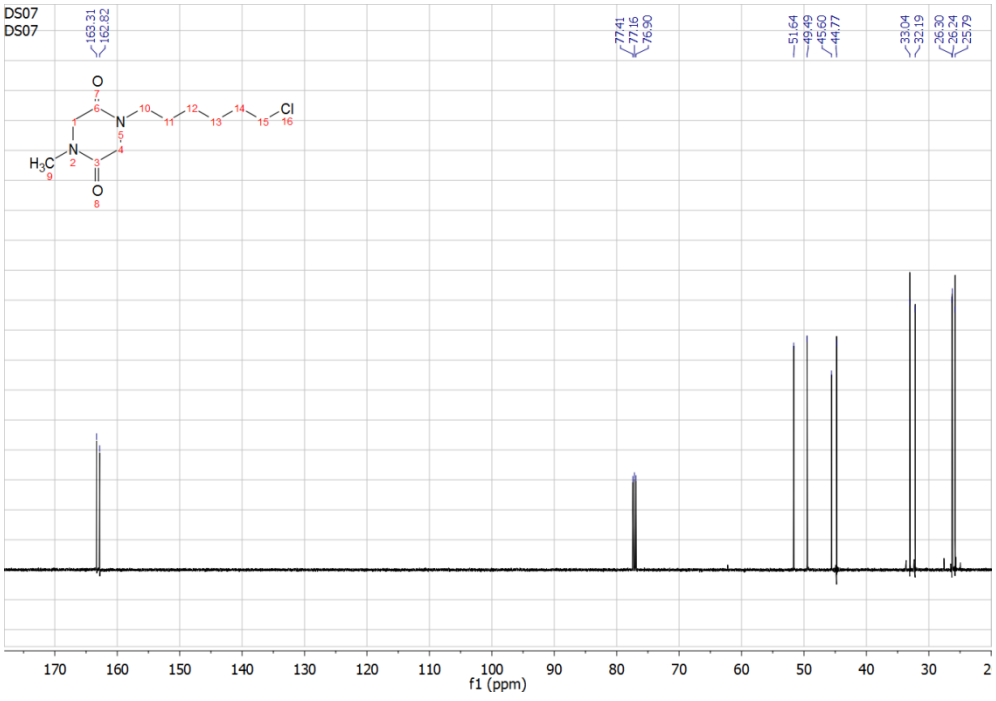

*Figure S40: ^{13}C NMR spectrum of 1-(3-chlorhexyl)-4-methylpiperazin-2,5-dion **2** (101 MHz, $CDCl_3$, 298 K).*

4,4'-(Propane-2,2-diyl)bis((4-bromobutoxy)benzene) 5

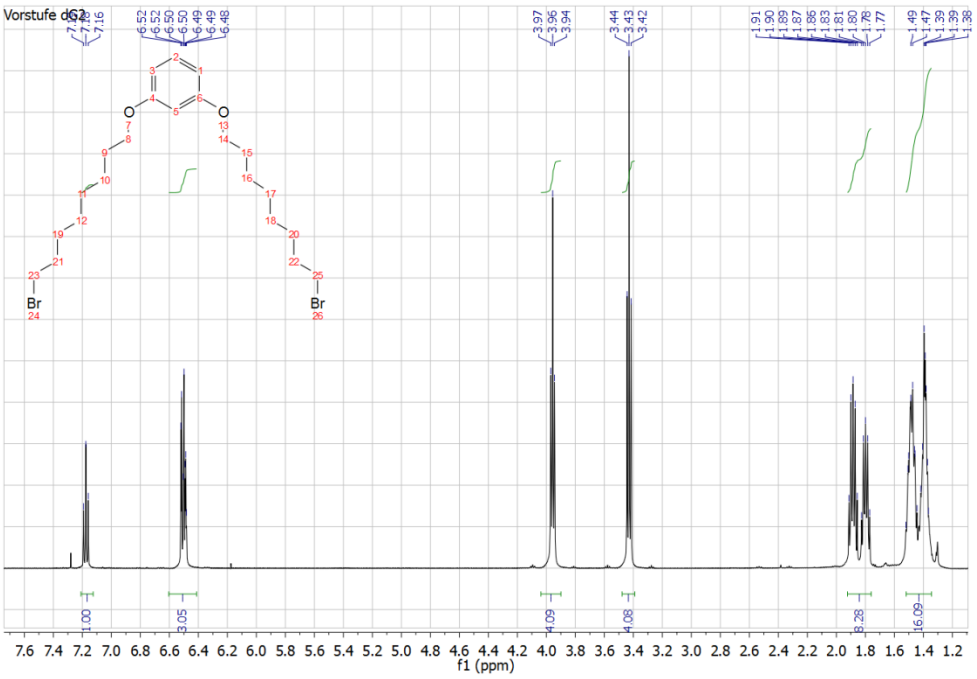

Figure S41: ^{1}H NMR spectrum of 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) ***5*** *(500 MHz, $CDCl_3$, 298 K).*

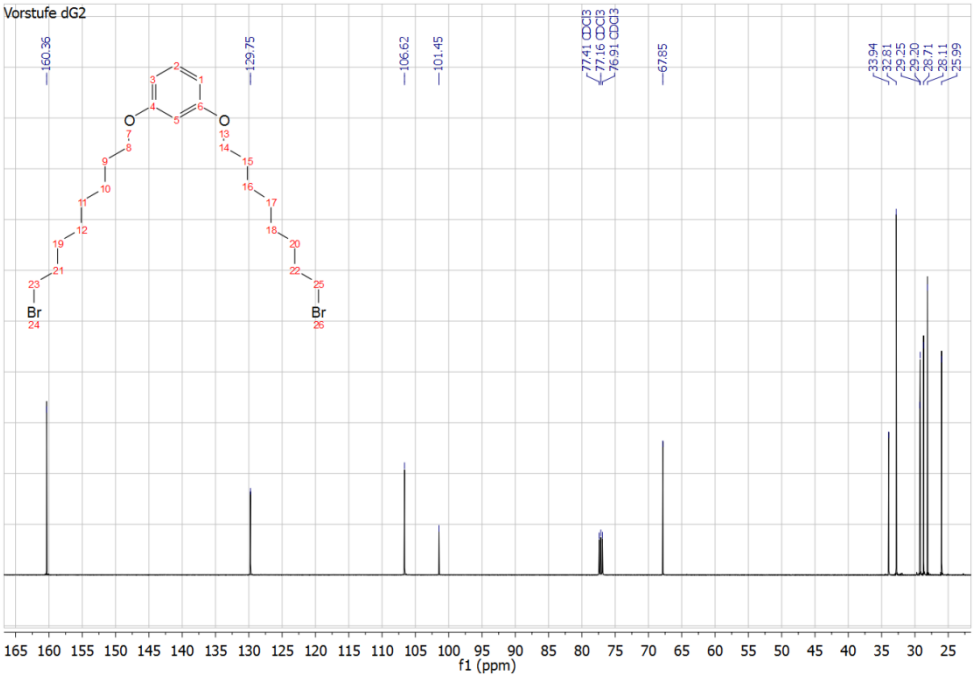

Figure S42: ^{13}C NMR spectrum of 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) ***5*** *(126 MHz, $CDCl_3$, 298 K).*

4,4',4''-(Ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) 6

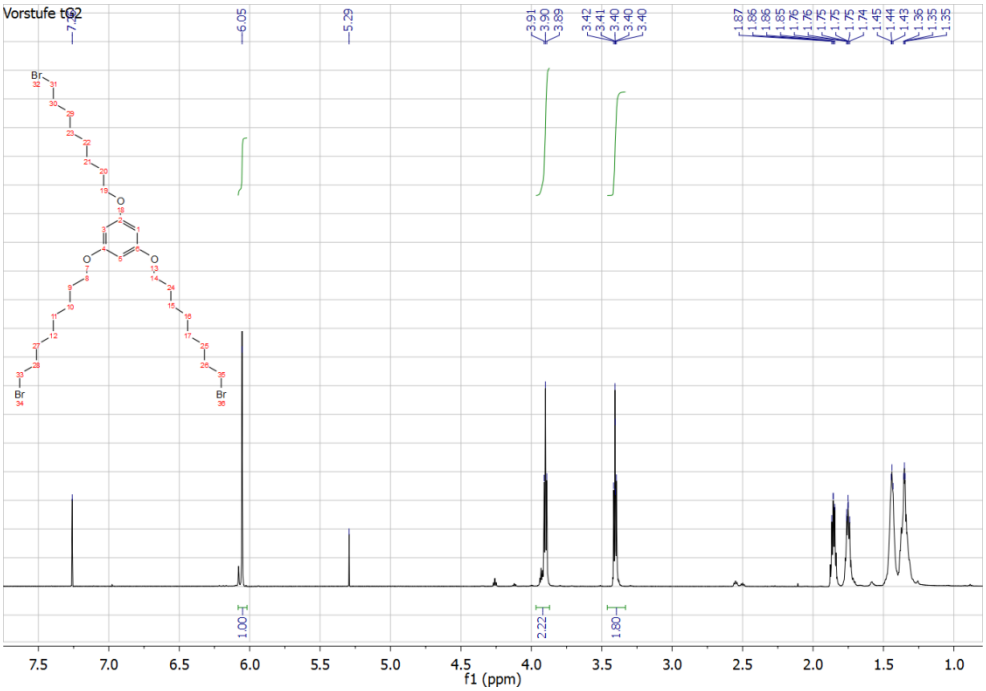

*Figure S43: ^{1}H NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene**) 6** (500 MHz, $CDCl_3$, 298 K).*

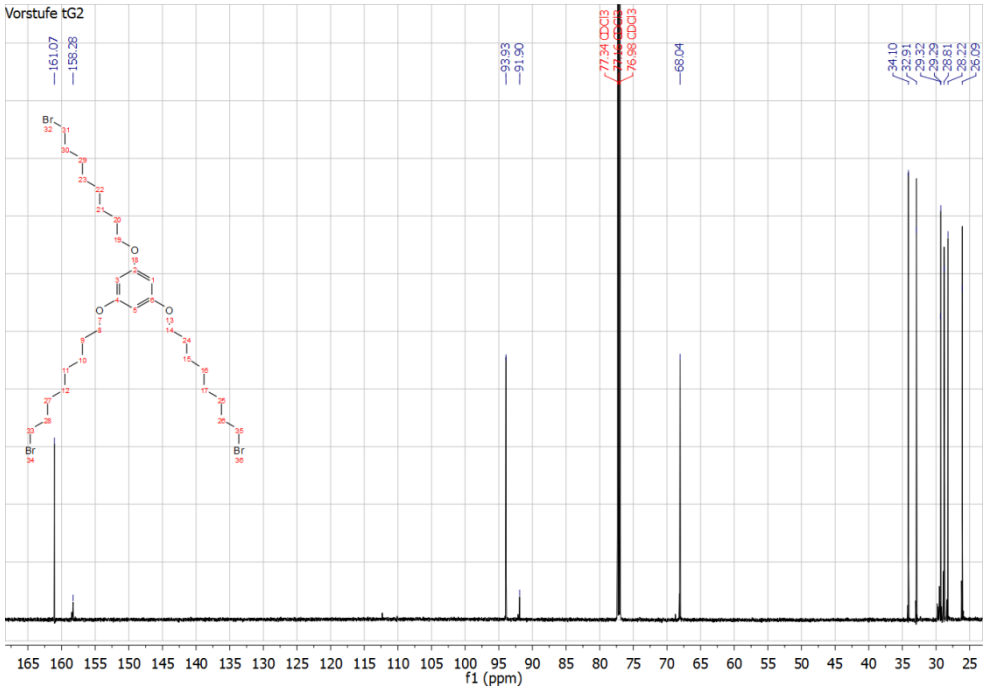

*Figure S44: ^{13}C NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene**) 6** (126 MHz, $CDCl_3$, 298 K).*

4,4'-(Propane-2,2-diyl)bis((4-bromobutoxy)benzene) 8

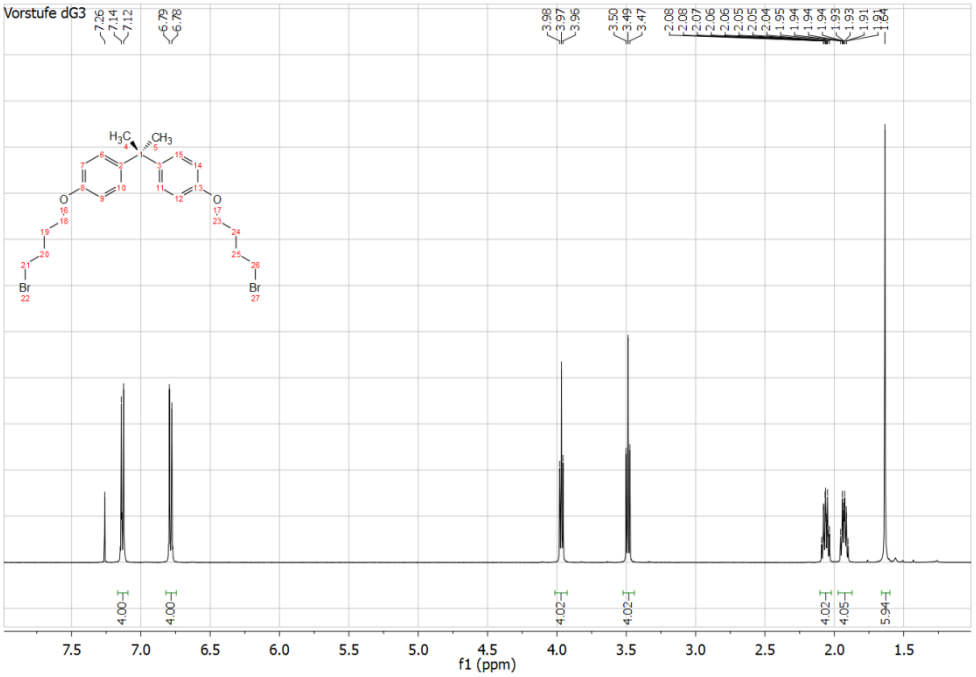

*Figure S45: ^{1}H NMR spectrum of 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) **8** (500 MHz, $CDCl_3$, 298 K).*

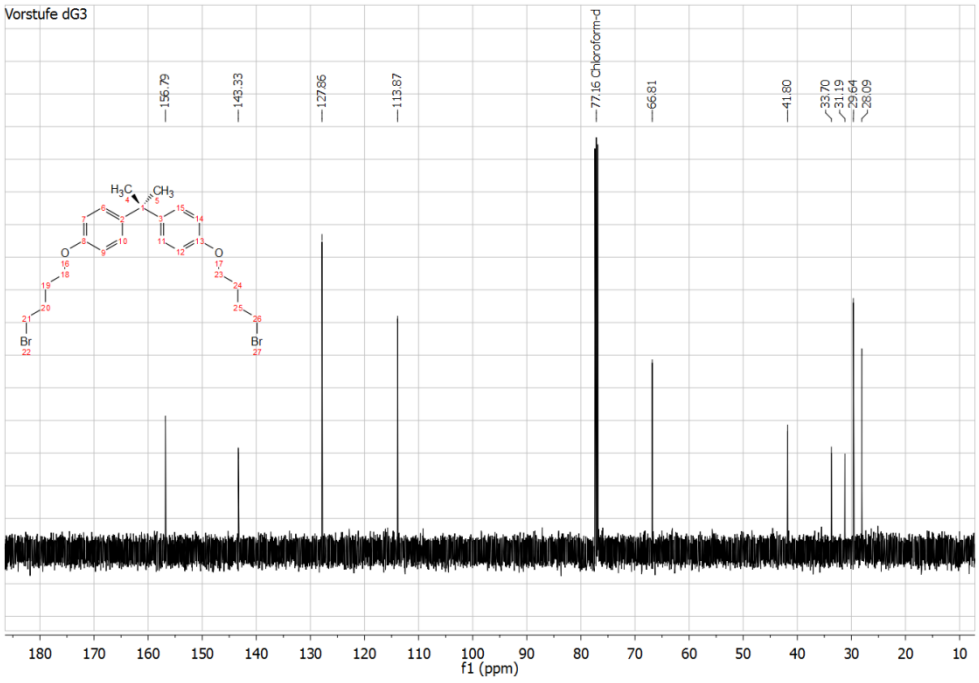

*Figure S46: ^{13}C NMR spectrum of 4,4'-(propane-2,2-diyl)bis((4-bromobutoxy)benzene) **8** (126 MHz, $CDCl_3$, 298 K).*

4,4',4''-(Ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) 11

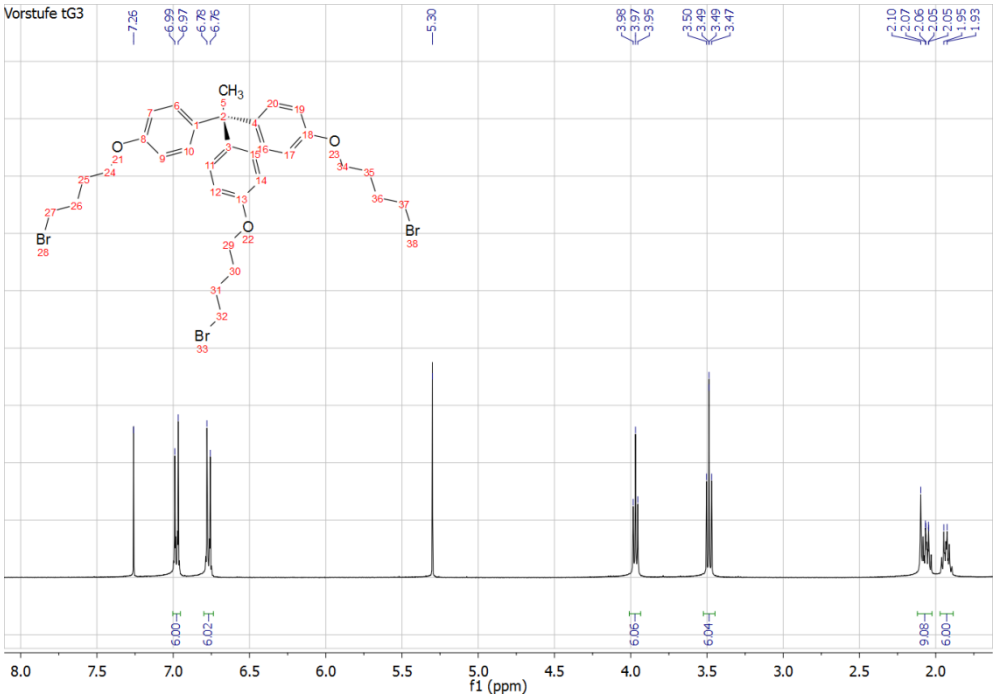

*Figure S47: ^{1}H NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) **11** (500 MHz, $CDCl_3$, 298 K).*

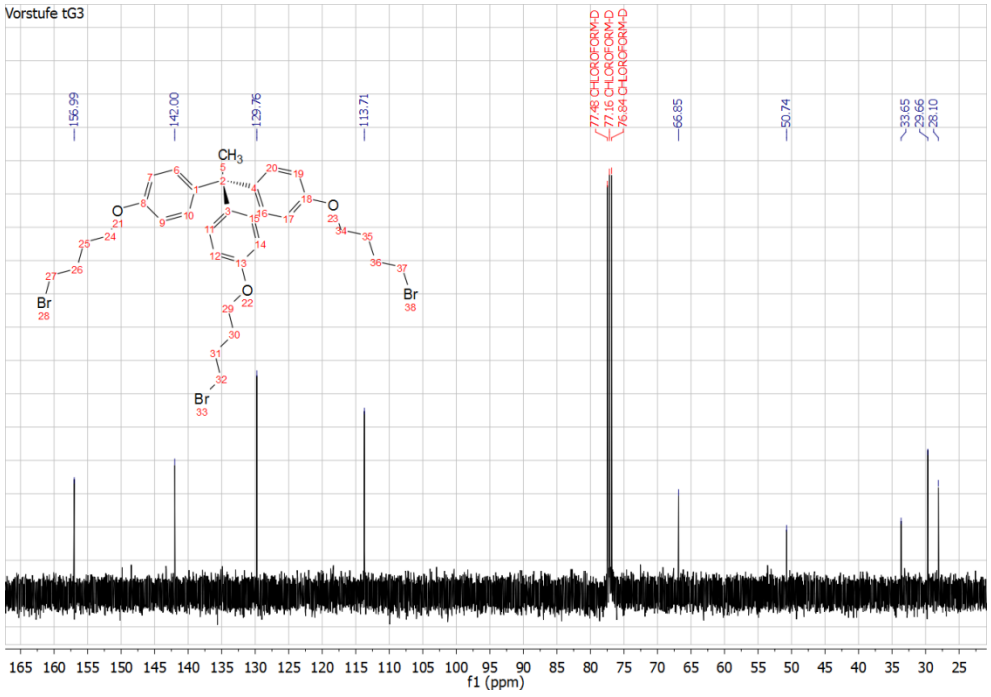

*Figure S48: ^{13}C NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris((4-bromobutoxy)benzene) **11** (126 MHz, $CDCl_3$, 298 K).*

4,4'-(Propane-2,2-diyl)bis(((6-bromohexyl)oxy)benzene) 9

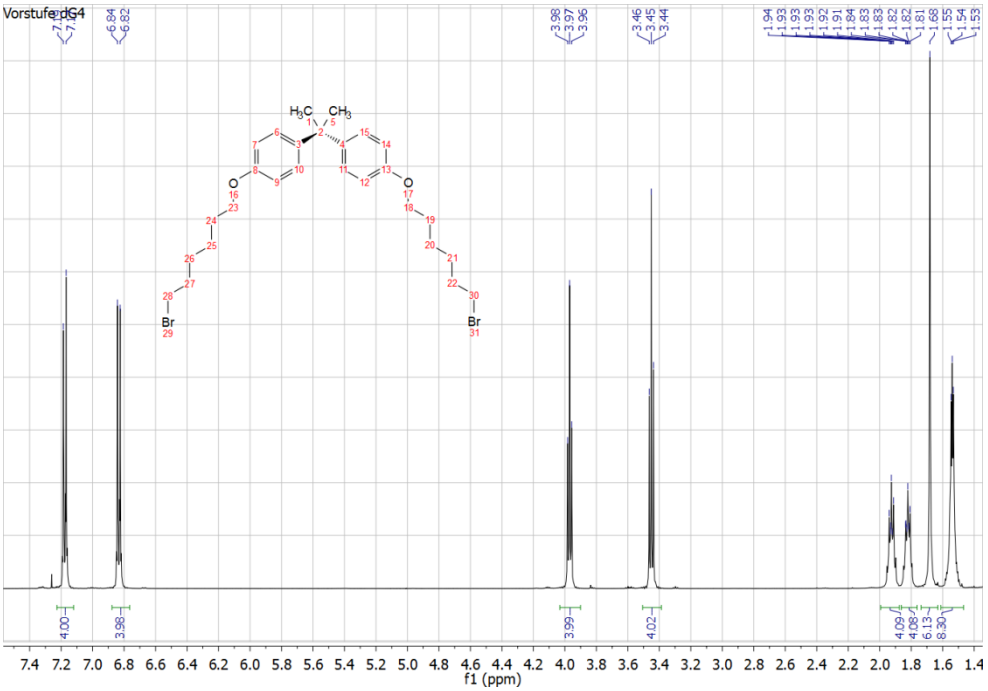

*Figure S49: ^{1}H NMR spectrum of 4,4'-(propane-2,2-diyl)bis(((6-bromohexyl)oxy)benzene) **9** (500 MHz, $CDCl_3$, 298 K).*

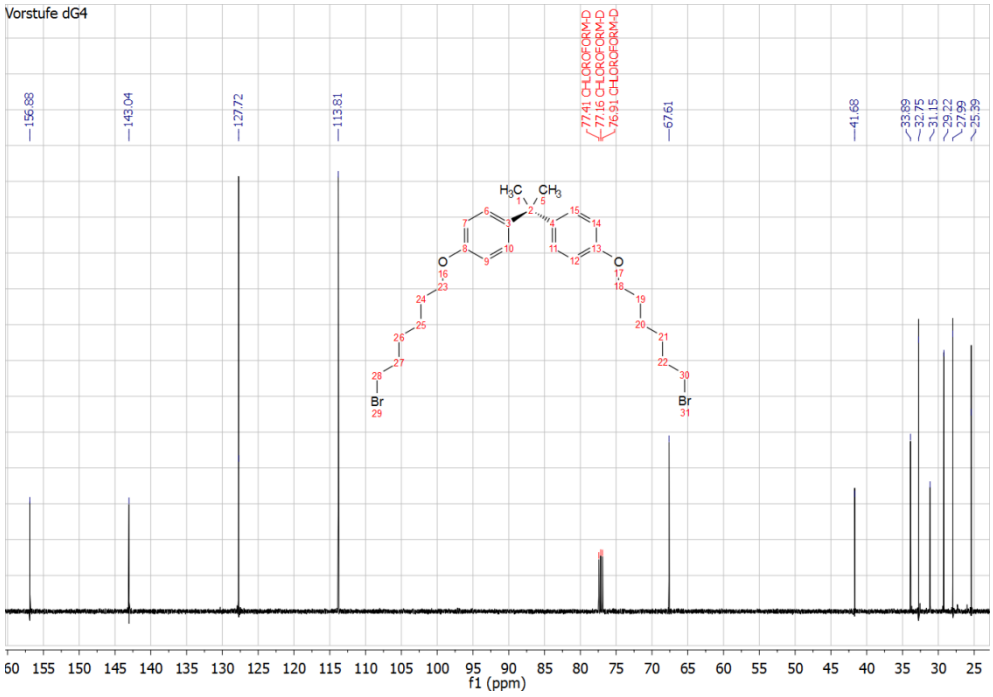

*Figure S50: ^{13}C NMR spectrum of 4,4'-(propane-2,2-diyl)bis(((6-bromohexyl)oxy)benzene) **9** (126 MHz, $CDCl_3$, 298 K).*

4,4',4''-(Ethane-1,1,1-triyl)tris(((6-bromohexyl)oxy)benzene) 12

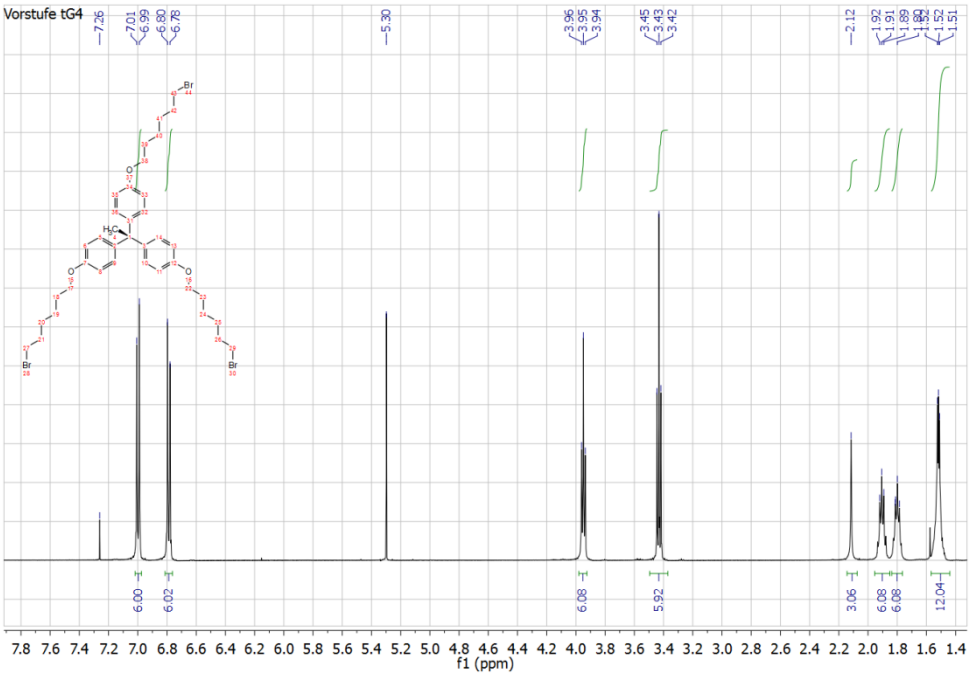

Figure S51: ^{1}H NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris(((6-bromohexyl)oxy)benzene) ***12*** *(500 MHz, $CDCl_3$, 298 K).*

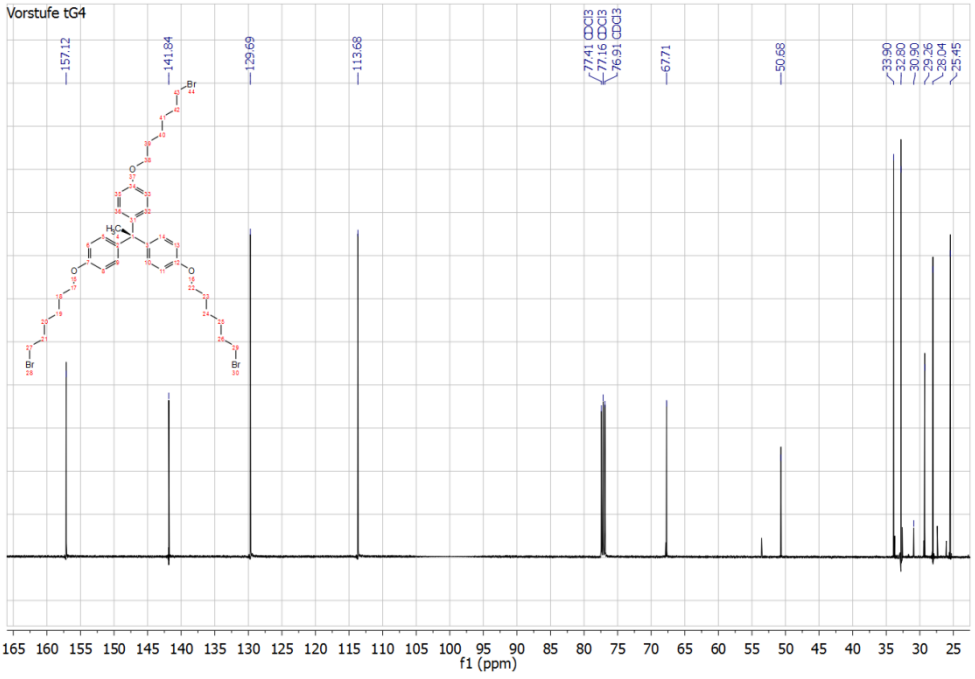

Figure S52: ^{13}C NMR spectrum of 4,4',4''-(ethane-1,1,1-triyl)tris(((6-bromohexyl)oxy)benzene) ***12*** *(126 MHz, $CDCl_3$, 298 K).*

6. References

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