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Supporting Information

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An allosterically-regulated molecular shuttle[**]

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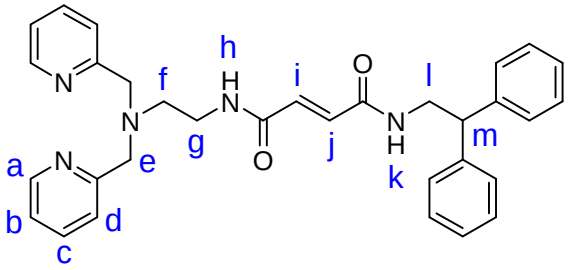
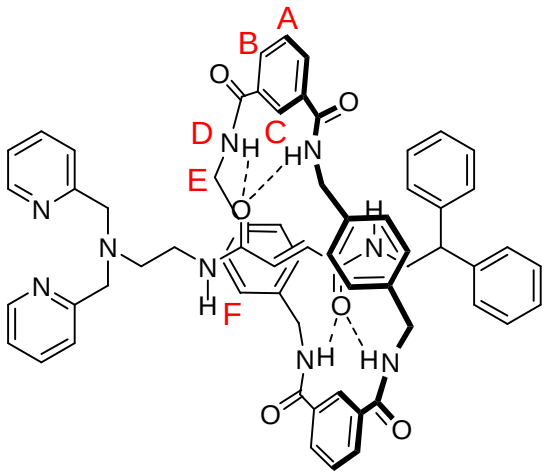
Experimental procedures

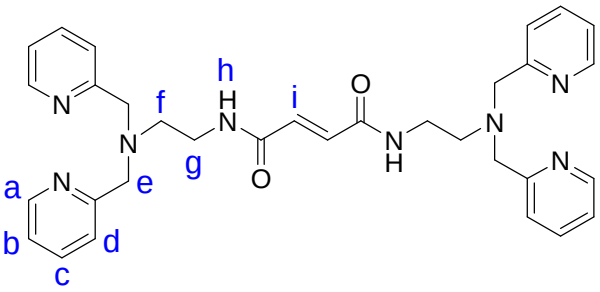
bis-(2-picolyl)amine (BPA),[1] (2-aminoethyl)bis(2-pyridylmethyl)amine,[2] N-(2,2-diphenylethyl)-fumaric acid[3] and 2,2-diphenylethyl-4-(12-aminododecylamino)-4-oxobutanoate[3] were prepared according to published procedures. All other reagents were purchased from commercial sources and used without further purification.



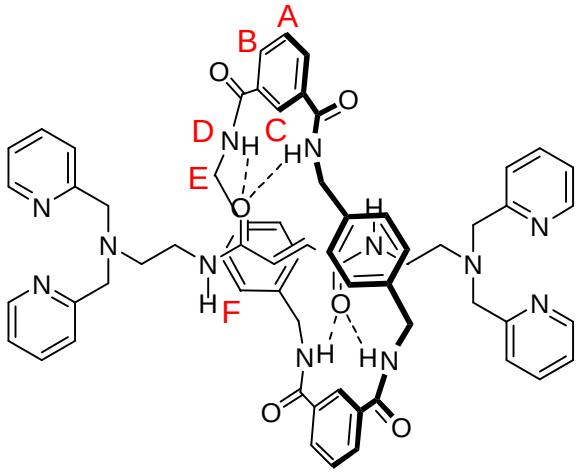
N^1-(2-(bis(pyridine-2-ylmethyl)amino)ethyl)-N^4-(2,2-diphenylethyl)fumaramide: Oxalyl chloride (8.1 mL 2M in CH_2Cl_2, 16.2 mmol) was added to N-(2,2-diphenylethyl)-fumaric acid (3.2 g, 11 mmol) in dichloromethane (20 mL) at room temperature. The reaction mixture was warmed to 40 ^oC and stirred for 3 hr at which point all the acid was dissolved in the yellow solution. All volatiles were removed under vacuum and the residue was triturated with $CHCl_3$ (3 x 5 mL). The yellow residue was taken up in $CHCl_3$ (30 mL) and added to a solution of (2-aminoethyl)bis(2-pyridylmethyl)amine (2.61 g, 11 mmol) and triethylamine (2.2 g, 22 mmol) in $CHCl_3$ (200 mL) at 0 ^oC. The reaction mixture was slowly allowed to warm to room temperature and stirred for an additional 14 h. The reaction mixture was then washed with saturated aqueous 1M NaOH (3 x 20 mL), saturated aqueous sodium chloride (2 x 20 mL) and water (2 x 30 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless solid. Yield 6.3 g (89 %); m.p. 170-172°C; ^{1}H NMR (400 MHz, CD_2Cl_2): δ (ppm) = 8.46 (d, 3H, *J* = 4.9 Hz, Py$\underline{H}_a$, N$\underline{H}_h$), 7.54 (t, 2H, *J* = 7.6 Hz, Py$\underline{H}_c$), 7.25-7.12 (m, 12H, Ar$\underline{H}$, Py$\underline{H}_d$), 7.08 (t, 2H, *J* = 4.8 Hz, Py$\underline{H}_b$), 6.91 (d, 1H, *J* = 15.2 Hz, C$\underline{H}_i$), 6.63 (d, 1H, *J* = 15.2 Hz, C$\underline{H}_j$) 6.09 (b, 1H, N$\underline{H}_k$), 4.16 (t, 1H, *J* = 8.0 Hz, C$\underline{H}_m$), 3.90 (t, 2H, C$\underline{H}_l$), 3.78 (s, 4H, C$\underline{H}_e$), 3.26 (q, 2H, *J* = 6.0 Hz, C$\underline{H}_g$), 2.69 (t, 2H, *J* = 5.8 Hz, C$\underline{H}_f$); ^{13}C NMR (100 MHz, CD_2Cl_2): δ (ppm) = 193.0 (s, NH$\underline{C}$O), 174.1, 164.1, 159.7, 157.9, 157.8, 149.5, 142.3, 136.8, 134.2, 132.0, 128.3, 127.2, 123.4, 122.5, 60.1, 50.9, 44.3, 38.3.



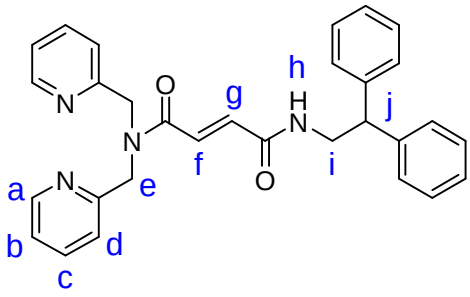
([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(*N*^{1}-(2-(bis(pyridine-2-ylmethyl)amino)ethyl)-*N*^{4}-(2,2-diphenylethyl)fumaramide) rotaxane (1): A flask containing *N*^{1}-(2-(bis(pyridine-2-ylmethyl)amino)ethyl)-*N*^{4}-(2,2-diphenylethyl)fumaramide (2 g, 3.8 mmol) in $CHCl_3$ (250 mL) was fitted with a rubber septum and large magnetic stir bar and stirred vigorously. To this were simultaneously added a mixture of *p*-xylylene diamine (4.2 g, 30.8 mmol) and triethylamine (6.2 g, 61.6 mmol) in $CHCl_3$ (50 mL) and isophthaloyl dichloride (6.2 g, 30.8 mmol) in $CHCl_3$ (50 mL) at equal rates *via* motor-driven syringe pumps over a period of 4-6 hours. The resulting suspension was filtered over celite and concentrated under reduced pressure. To the residue was added acetone (100 mL) and the resulting suspension was filtered, the filtrate collected and concentrated under reduced pressure. The remaining residue was subjected to column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.2:0.8:0.005 v/v ratio as eluent to yield, in order of elution, the unconsumed thread and [2]rotaxane. Yield = 3.7 g (91 %); m.p. >205°C (decomp); ^{1}H NMR (400 MHz, CD_2Cl_2): δ (ppm) = 9.54 (b, 1H, N$\underline{H}_a$), 8.50 (s, 2H, Ar$\underline{H}_C$), 8.32 (s, 2H, *J* = 4.6 Hz, Py$\underline{H}_a$), 8.00 (d, 4H, *J* = 6.6 Hz, Ar$\underline{H}_B$), 7.89 (b, 1H, N$\underline{H}_k$), 7.75 (t, 4H, *J* = 4.8 Hz, Ar$\underline{H}_D$), 7.50 (t, 4H, *J* = 7.6 Hz, Py$\underline{H}_c$, Ar$\underline{H}_C$), 7.19-7.06 (m, 12H, Ar$\underline{H}$, Py$\underline{H}_d$), 6.93 (t, 2H, Py$\underline{H}_b$), 6.84 (s, 8H, Ar$\underline{H}_F$), 5.79 (d, 1H, *J* = 14.6 Hz, C$\underline{H}_i$), 5.64 (d, 1H, *J* = 14.6 Hz, C$\underline{H}_j$) 4.40-4.18 (m, 8H, C$\underline{H}_m$, C$\underline{H}_E$), 3.83 (t, 2H, C$\underline{H}_l$), 3.79 (s, 4H, C$\underline{H}_e$), 3.24 (m, 2H, C$\underline{H}_g$), 2.75 (t, 2H, *J* = 5.6 Hz C$\underline{H}_f$); ^{13}C NMR (100 MHz, CD_2Cl_2): δ (ppm) = 167.0, 166.0, 165.8, 158.3, 158.1, 149.6, 142.3, 137.6, 137.2, 134.4, 131.6, 130.8, 129.7, 129.5, 129.2, 128.2, 127.4, 125.3, 124.5, 123.3, 52.1, 50.9, 44.7, 44.5, 37.9.



***N*[1],*N*[4]-bis(2-(bis(pyridin-2-ylmethyl)amino)ethyl)fumaramide:** To a mixture of (2-aminoethyl)bis(2-pyridylmethyl)amine (3.3 g, 14.0 mmol) and triethylamine (1.7 g, 17.1 mmol) in $CHCl_3$ (200 mL) at 0 ^oC was slowly added a solution of fumaryl chloride (1.0 g, 6.8 mmol) in $CHCl_3$ (50 mL). After addition this was allowed to warm to room temperature and stirred overnight. The mixture was then washed with 1M NaOH (2 x 50 mL) and water (2 x 50 mL) and the volatiles where removed under reduced pressure. The residue was recrystalized from acetone (20 mL). Yield 7.0 g (92 %); m.p. 146-148 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.65 (b, 2H, N$\underline{H}_h$), 8.54 (d, 4H, *J* = 4.8 Hz, Py$\underline{H}_a$), 7.54 (t, 4H, *J* = 7.6 Hz, Py$\underline{H}_c$), 7.24 (d, 4H, *J* = 7.8 Hz, Py$\underline{H}_d$), 7.09 (t, 4H, *J* = 7.8 Hz, Py$\underline{H}_b$), 7.04 (s, 2H, C$\underline{H}_i$), 3.84 (s, 8H, C$\underline{H}_e$), 3.42 (dd, 4H, *J* = 6.1 Hz, C$\underline{H}_f$), 2.77 (dd, 4H, *J* = 5.8 Hz, C$\underline{H}_g$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 164.5 (s, NH$\underline{C}$O), 158.9 (s, Py$\underline{C}$), 149.2 (s, Py$\underline{C}$), 136.7 (s, Py$\underline{C}$), 132.9 (s, Py$\underline{C}$), 123.1 (s, Py$\underline{C}$), 122.3 (s, $\underline{C}_i$), 59.8 (s, $\underline{C}_e$), 52.4 (s, $\underline{C}_f$), 38.0 (s, $\underline{C}_g$).

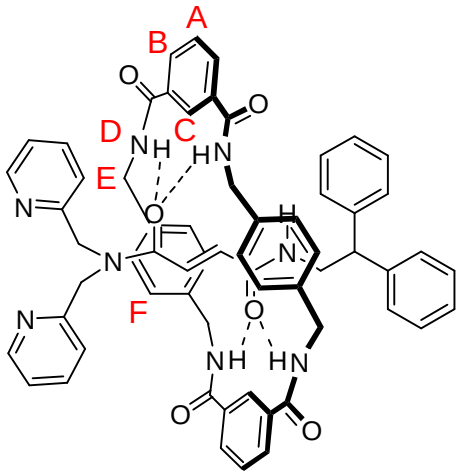


([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(N^1,N^4-bis(2-(bis(pyridin-2-ylmethyl)amino)ethyl)fumaramide) rotaxane (2): Synthesis of [2]rotaxane **2** was similar to that described for **1** except that thread N^1,N^4-bis(2-(bis(pyridin-2-ylmethyl)amino)ethyl)fumaramide (0.6 g, 1.0 mmol) was used. The quantities of the other components were: *p*-xylylene diamine (1.1 g, 8.0 mmol), isophthaloyl dichloride (1.6 g, 8.0 mmol) and triethylamine (2.0 g, 20.0 mmol). The residue was separated by column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 1 g (93 %); m.p. >200 ^oC (decomp); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 9.49 (s, 2H, N$\underline{H}_h$), 8.91 (s, 2H, Ar$\underline{H}_C$), 8.34 (d, 4H, *J* = 5.1 Hz, Py$\underline{H}_a$), 8.21 (d, 4H, *J* = 6.5 Hz, Ar$\underline{H}_B$), 8.11 (t, 4H, *J* = 4.8 Hz, Ar$\underline{H}_D$), 7.58-7.49 (m, 6H, Ar$\underline{H}_A$, Py$\underline{H}_c$), 7.15 (d, 4H, *J* = 7.6 Hz, Py$\underline{H}_d$), 6.98 (m, 4H, Py$\underline{H}_b$), 6.85 (s, 8H, Ar$\underline{H}_F$), 5.89 (s, 2H, C$\underline{H}_i$), 4.36 (b, 8H, C$\underline{H}_E$), 3.80 (s, 8H, C$\underline{H}_e$), 3.31 (m, 4H, C$\underline{H}_f$), 2.74 (t, 4H, *J* = 5.8 Hz, C$\underline{H}_g$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 191.4 (NH$\underline{C}$O), 166.5 (NH$\underline{C}$O), 158.1 (d, Py$\underline{C}$), 149.1 (Py$\underline{C}$), 137.0 (Ar$\underline{C}$), 137.0 (Py$\underline{C}$), 134.0 (Py$\underline{C}$), 131.7 (Ar$\underline{C}$), 129.7 (Ar$\underline{C}$), 129.2 (Ar$\underline{C}$), 124.5 (Ar$\underline{C}$), 123.4 (Py$\underline{C}$), 122.7 ($\underline{C}H_i$), 59.3 (s, $\underline{C}_e$), 44.1 (d, $\underline{C}_f$), 38.7 (s, $\underline{C}_g$).



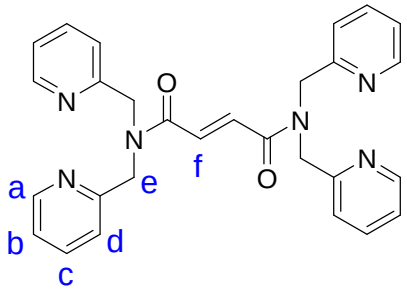
***N^1*-(2,2-diphenylethyl)-*N^4*,*N^4*-bis(pyridine-2-ylmethyl)fumaramide:** EDCI (4.1 g, 21.2 mmol) was added in small batches to a solution of *N*-(2,2-diphenylethyl)-fumaric acid (2.5g, 8.4 mmol) and DMAP (2.6 g, 21.2 mmol) in dichloromethane (200 mL) at room temperature. The reaction mixture was stirred for 10 min after which time *bis*-(2-picolyl)amine (2.0 g, 10 mmol) was added in one portion. The reaction mixture was allowed to stir at room

temperature for an additional 14 h. The reaction mixture was washed with saturated aqueous 1M NaOH (3 x 20 mL), saturated aqueous sodium chloride (2 x 20 mL) and water (2 x 30 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless solid. N^1-(2,2-diphenylethyl)-N^4,N^4-bis(pyridine-2-ylmethyl)fumaramide was recrystalized from acetone. Yield 3.5 g (87 %); m.p. 54-56 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.48 (d, 1H, J = 4.8 Hz, Py$\underline{H}_a$), 8.42 (d, 1H, J = 4.8 Hz, Py$\underline{H}_a$), 7.55 (m, 2H, Py$\underline{H}_c$), 7.35 (d, 1H, J = 14.6 Hz, C$\underline{H}_f$), 7.24-7.07 (m, 14H, Ar$\underline{H}$, Py$\underline{H}_b$, Py$\underline{H}_d$), 6.75 (d, 1H, J = 14.6 Hz, C$\underline{H}_g$), 5.85 (b, 1H, N$\underline{H}_h$), 4.73 (s, 4H, C$\underline{H}_e$), 4.13 (t, 1H, J = 7.8 Hz, C$\underline{H}_j$), 3.88 (t, 2H, J = 5.8 Hz, C$\underline{H}_i$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 166.1, 164.0, 156.7, 155.9, 149.9 (d), 142.3, 141.4, 135.0, 130.2, 128.5 (t), 128.1, 128.0 (t), 127.0 (d), 126.6, 126.5, 122.6 (t), 121.1, 77.2, 52.9, 51.6, 50.4, 44.1.

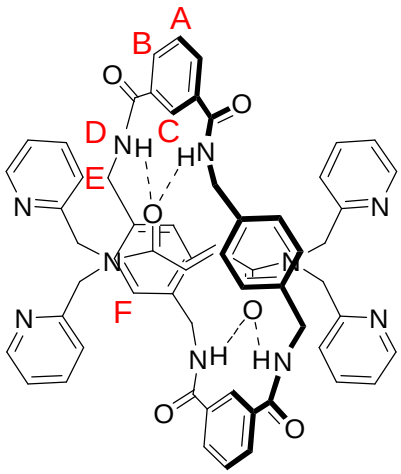


([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(N^1-(2,2-diphenylethyl)-N^4,N^4-bis(pyridine-2-ylmethyl)fumaramide) rotaxane (3): Synthesis of [2]rotaxane **3** was similar to that described for **1** except that thread N^1-(2,2-diphenylethyl)-N^4,N^4-bis(pyridine-2-ylmethyl)fumaramide (1.5 g, 3.1 mmol) was used. The quantities of the other components were: *p*-xylylene diamine (3.4 g, 25.2 mmol), isophthaloyl dichloride (5.1g, 25.2 mmol) and triethylamine (5.1 g, 50.4 mmol). The residue was separated by column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 3.0 g (96 %); m.p. >200 °C (decomp); ^{1}H NMR (400

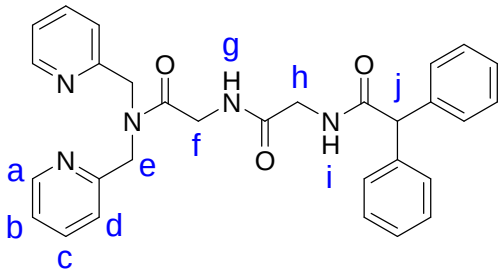
MHz, $CDCl_3$): δ (ppm) = 8.51 (d, 1H, Py$\underline{H}_a$), 8.28 (b, 3H, Py$\underline{H}_a$, Ar$\underline{H}_C$), 8.04 (d, 2H, *J* = 7.8 Hz, Ar$\underline{H}_B$), 7.88 (b, 1H, N$\underline{H}_h$), 7.48 (m, 6H, Ar$\underline{H}_A$, Ar$\underline{H}_D$), 7.40 (t, 1H, Py$\underline{H}_c$), 7.25-7.11 (m, 12H, Ar$\underline{H}$, Py$\underline{H}_c$, Py$\underline{H}_b$), 7.02 (t, 1H, Py$\underline{H}_b$), 6.78 (d, 1H, *J* = 7.6 Hz, Py$\underline{H}_d$), 6.72 (s, 8H, C$\underline{H}_F$), 6.61 (d, 1H, *J* = 7.6 Hz, Py$\underline{H}_d$), 6.04 (d, 1H, *J* = 14.7 Hz, C$\underline{H}_f$), 5.68 (d, 1H, *J* = 14.7 Hz, C$\underline{H}_g$), 4.52 (s, 2H, C$\underline{H}_e$), 4.46 (s, 2H, C$\underline{H}_e$), 4.29-4.18 (m, 9H, C$\underline{H}_E$, C$\underline{H}_j$), 3.84 (t, 2H, *J* = 5.8 Hz C$\underline{H}_i$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 166.0 (t), 157.5, 156.1, 154.6, 149.8 (d), 149.3, 141.6, 141.5, 136.8 (t), 133.5, 132.6, 131.5, 130.2, 129.0 (t), 128.8, 128.5, 127.9 (d), 127.2, 127.0, 126.5, 123.7 (d), 123.0, 121.2, 77.0, 53.3, 53.0, 52.5, 50.4, 45.8, 44.9, 43.9.



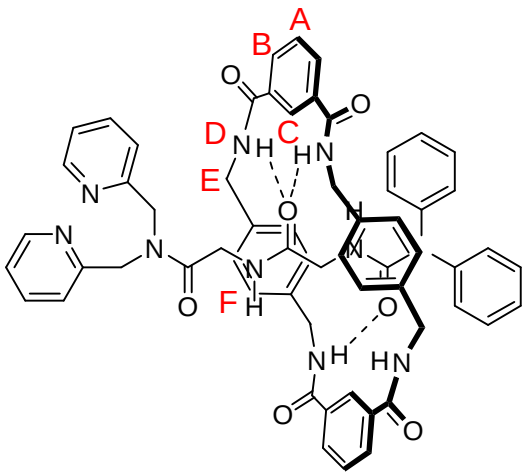
***N*^{1},*N*^{1},*N*^{4},*N*^{4}-tetrakis(pyridin-2-ylmethyl)fumaramide:** To a mixture of *bis*-(2-picolyl)amine (2.0 g, 10 mmol) and triethylamine (1.2 g, 12 mmol) in $CHCl_3$ (200 mL) at 0 ^{o}C was slowly added a solution of fumaryl chloride (0.8 g, 5 mmol) in $CHCl_3$ (50 mL). After addition this was allowed to warm to room temperature and stirred overnight. The mixture was then washed with 1M NaOH (2 x 50 mL) and water (2 x 50 mL) and the volatiles where removed under reduced pressure. The residue was purified by column chromatography 1:10 methanol/$CHCl_3$. Yield 2.2 g (92 %); m.p. 128-130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.47 (d, 2H, *J* = 2.1 Hz, Py$\underline{H}_a$), 8.43 (d, 2H, *J* = 2.1 Hz, Py$\underline{H}_a$), 7.56 (t, 4H, *J* = 7.8 Hz, Py$\underline{H}_c$), 7.50 (s, 1H, C$\underline{H}_f$), 7.25 (d, 2H, *J* = 7.9 Hz, Py$\underline{H}_d$), 7.20 (s, 1H, C$\underline{H}_f$), 7.12-7.09 (m, 6H, Py$\underline{H}_b$, Py$\underline{H}_d$), 4.78 (s, 4H, C$\underline{H}_e$), 4.74 (s, 4H, C$\underline{H}_e$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 157.9 (s, N$\underline{C}$O), 149.9 (s, Py$\underline{C}$), 137.0 (s, Py$\underline{C}$), 132.2 (s, Py$\underline{C}$), 122.6 (s, Py$\underline{C}$), 121.2 (s, Py$\underline{C}$), 53.1 (s, $\underline{C}_e$), 51.4 (s, $\underline{C}_e$), 45.8 (s, $\underline{C}_f$).



([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(N^1,N^4,N^4-tetrakis(pyridin-2-ylmethyl)fumaramide) rotaxane (4): The synthesis of [2]rotaxane **4** was similar to that described for **1** except that thread N^1,N^4,N^4-tetrakis(pyridin-2-ylmethyl)fumaramide (1 g, 2.1 mmol) was used. The quantities of the other components were: *p*-xylylene diamine (2.3 g, 16.7 mmol), isophthaloyl dichloride (3.4 g, 16.7 mmol) and triethylamine (3.4 g, 33.5 mmol). The residue was separated by column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 2 g (95 %); m.p. >200 ^oC (decomp); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.55 (d, 2H, *J* = 4.5 Hz, Py$\underline{H}_a$), 8.46 (s, 2H, Ar$\underline{H}_C$), 8.28 (d, 2H, *J* = 4.5 Hz, Py$\underline{H}_a$), 8.17 (d, 4H, J = 7.8 Hz, Ar$\underline{H}_B$), 7.51 (t, 2H, *J* = 7.8 Hz, Ar$\underline{H}_A$), 7.47 (t, 4H, N$\underline{H}_D$), 7.24-7.19 (m, 14H, Ar$\underline{H}_F$, Py$\underline{H}_c$, Py$\underline{H}_b$), 7.09 (d, 2H, *J* = 7.8 Hz, Py$\underline{H}_d$), 7.03 (t, 2H, *J* = 7.8 Hz, Py$\underline{H}_b$), 6.64 (d, 2H, Py$\underline{H}_d$), 4.85 (b, 4H, C$\underline{H}_E$), 4.64 (s, 4H, C$\underline{H}_e$), 4.54 (s, 4H, C$\underline{H}_e$), 3.45 (b, 4H, C$\underline{H}_E$); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 166.1, 165.6, 157.9, 154.7, 149.7, 137.3, 136.8, 133.5, 131.9, 129.6, 129.2, 129.0, 124.1, 123.2, 123.0, 53.4, 52.8.

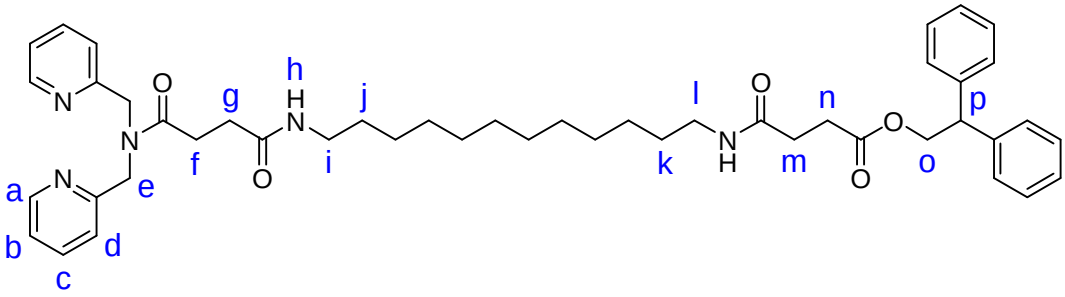


***N*-(2-(2-(bis(pyridine-2-ylmethyl)amino)-2-oxoethylamino)-2-oxoethyl)-2,2-diphenylethanamide:** EDCI (2.2 g, 11.5 mmol) was added in small batches to a solution of 2-(2-(2,2-diphenylethanamido)acetamido)acetic acid (1.5 g, 4.6 mmol) and DMAP (1.4 g, 11.5 mmol) in dichloromethane (200 mL). The reaction mixture was stirred for 10 min, after which time *bis*-(2-picolyl)amine (0.9 g, 4.6 mol) was added in one portion, and the mixture was stirred for an additional 14 h at room temperature. The reaction mixture was then washed with saturated aqueous sodium hydrogen carbonate (3 x 50 mL) and saturated aqueous sodium chloride (2 x 50 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless solid. The remaining residue was subjected to column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 2.1 g (88 %); m.p. 152-154 ^oC; ^1H NMR (400 MHz, CD_3CN): δ (ppm) = 8.47 (d, 1H, J = 4.8 Hz, Py$\underline{H}_a$), 8.44 (d, 1H, *J* = 4.8 Hz, Py$\underline{H}_a$), 7.67-7.60 (m, 2H, Py$\underline{H}_c$), 7.29-7.13 (m, 14H, Ar$\underline{H}$, Py$\underline{H}_b$, Py$\underline{H}_d$), 6.91 (b, 2H, N$\underline{H}_g$, N$\underline{H}_i$), 4.95 (s, 1H, C$\underline{H}_j$), 4.58 (s, 4H, C$\underline{H}_e$), 4.15 (d, 2H, *J* = 4.8 Hz, C$\underline{H}_h$), 3.77 (d, 2H, *J* = 5.5 Hz, C$\underline{H}_f$); ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 202.1 (N$\underline{C}$O), 157.5 (NH$\underline{C}$O), 149.3 (NH$\underline{C}$O), 148.8 (Py$\underline{C}$), 139.7 (Py$\underline{C}$), 136.6 (Py$\underline{C}$), 136.3 (Py$\underline{C}$), 128.5 (Py$\underline{C}$), 128.1 (Ar$\underline{C}$), 126.6 (Ar$\underline{C}$), 122.4 (Ar$\underline{C}$), 121.9 (Ar$\underline{C}$), 121.7, 121.4, 51.64, 51.05, 40.8.



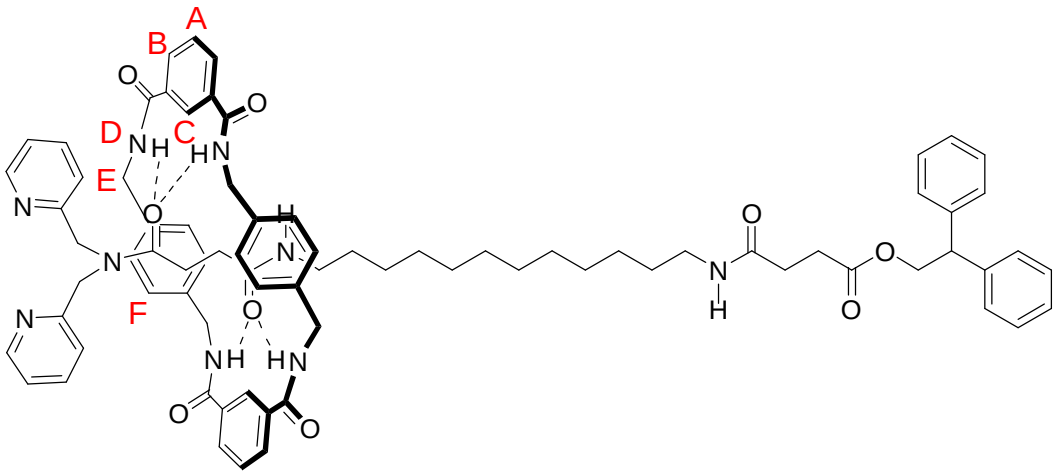
([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(*N*-(2-(2-(bis(pyridine-2-ylmethyl)amino)-2-oxoethylamino)-2-oxoethyl)-2,2-

diphenylethanamide) rotaxane (5): The synthesis of [2]rotaxane **5** was similar to that described for **1** except that thread *N*-(2-(2-(bis(pyridine-2-ylmethyl)amino)-2-oxoethylamino)-2-oxoethyl)-2,2-diphenylethanamide (1 g, 2.0 mmol) was used. The quantities of the other components were: *p*-xylylene diamine (2.1 g, 15.8 mmol), isophthaloyl dichloride (3.2 g, 15.8 mmol) and triethylamine (3.2 g, 31.6 mmol). The residue was separated by column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 1.1 g (53 %); m.p. >200 ^oC (decomp); ^1H NMR (400 MHz, CD_3CN): δ (ppm) = 8.48 (s, 2H, Ar$\underline{H}_C$), 8.35 (d, 1H, J = 5.3 Hz, Py$\underline{H}_a$), 8.24 (d, 1H, J = 5.3 Hz, Py$\underline{H}_a$), 8.02 (d, 4H, Ar$\underline{H}_B$), 7.52 (m, 6H, Ar$\underline{H}_A$, Ar$\underline{H}_D$), 7.40 (t, 2H, Py$\underline{H}_c$), 7.25-7.03 (m, 12H, Ar$\underline{H}$, Py$\underline{H}_b$), 6.80 (d, 1H, J = 8.1 Hz, N$\underline{H}_i$), 6.74 (d, 2H, J = 7.8 Hz, Py$\underline{H}_d$), 6.64 (b, 1H, N$\underline{H}_g$), 4.86 (s, 1H, C$\underline{H}_j$), 4.44 (d/d, 4H, C$\underline{H}_E$), 4.39 (s, 2H, C$\underline{H}_e$), 4.22 (s, 2H, C$\underline{H}_e$), 4.14 (d/d, 4H, C$\underline{H}_E$), 3.22 (d, 2H, J = 5.3 Hz C$\underline{H}_h$), 3.16 (d, 2H, J = 5.0 Hz C$\underline{H}_f$); ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 165.5, 157.2, 137.1, 133.9, 130.6, 128.7, 128.6, 128.3, 128.1, 126.7, 124.4, 43.2.



2,2-diphenylethyl 4-(12-(4-(bis(pyridine-2-ylmethyl)amino)-4-oxobutanamido)dodecyl amino)-4-oxobutanoate: To a solution of 2,2-diphenylethyl-4-(12-aminododecylamino)-4-oxobutanoate (1.0 g, 2.1 mmol) in THF (200 mL) was added succinic anhydride (0.21 g, 2.1 mmol) and the reaction mixture was warmed to 60 ^oC for 1 hr. The reaction mixture was then allowed to stir for an additional 4-5 hrs at room temperature, at which point all volatiles were removed under reduced pressure. The residue was taken up in dichloromethane (200 mL) and to this was added DMAP (0.6 g, 5.2 mmol) and EDCI (1 g, 5.2 mmol) in small batches at

room temperature. The reaction mixture was stirred for 10 min after which time *bis*-(2-picolyl)amine (0.5g, 2.1 mmol) was added in one portion. The reaction mixture was allowed to stir at room temperature for an additional 14 h. The reaction mixture was then washed with saturated aqueous 1M NaOH (3 x 20 mL), saturated aqueous sodium chloride (2 x 20 mL) and water (2 x 30 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless solid. Yield 1.34 g (78 %); m.p. 88-90 °C; ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.55 (d, 1H, *J* = 4.8 Hz, Py$\underline{H}_a$), 8.47 (d, 1H, *J* = 4.8 Hz, Py$\underline{H}_a$), 7.73-7.67 (m, 2H, Py$\underline{H}_c$), 7.35-7.22 (m, 14H, Ar$\underline{H}$, Py$\underline{H}_b$, Py$\underline{H}_d$), 6.49 (b, 1H, N$\underline{H}_h$), 6.30 (b, 1H, N$\underline{H}_m$), 4.73 (s, 2H, C$\underline{H}_e$), 4.65 (s, 2H, C$\underline{H}_e$) 4.61 (d, 2H, *J* = 7.6 Hz, C$\underline{H}_p$), 4.36 (t, 1H, *J* = 7.6 Hz, C$\underline{H}_q$), 3.10 (m, 4H, C$\underline{H}_i$, C$\underline{H}_l$), 2.74 (t, 2H, *J* = 6.6 Hz, C$\underline{H}_f$), 2.42 (m, 4H, C$\underline{H}_g$, C$\underline{H}_n$), 2.30 (t, 2H, *J* = 7.0 Hz, C$\underline{H}_o$), 1.41 (b, 4H, C$\underline{H}_j$, C$\underline{H}_k$), 1.27 (b, 16H, C$\underline{H}_2$); ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 157.6, 157.1, 149.2, 148.7, 136.5, 136.2, 128.2, 127.7, 126.4, 122.2, 121.7, 121.3, 121.2, 65.9, 52.5, 50.9, 49.4, 38.5, 30.5, 29.7, 29.0, 28.9, 28.8, 28.7, 28.0, 26.2.



([2](1,7,14,20-Tetraaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(2,2-diphenylethyl 4-(12-(4-(bis(pyridine-2-ylmethyl)amino)-4-oxobutanamido)dodecylamino)-4-oxobutanoate) (6): The synthesis of [2]rotaxane **6** was similar to that described for **1** except that thread 2,2-diphenylethyl 4-(12-(4-(bis(pyridine-2-ylmethyl)amino)-4-oxobutanamido)dode cylamino)-4-oxobutanoate (1.0 g, 1.2 mmol) was used in this case. The quantities of the other components were: *p*-xylylene diamine (1.7g, 12.2 mmol), isophthaloyl

dichloride (2.5 g, 12.2 mmol) and triethylamine (2.5 g, 24.4 mmol). The residue was separated by column chromatography on silica gel using dichloromethane:methanol:NH_4OH (aq) in a 9.6:0.4:0.0025 v/v ratio as eluent. Yield 0.7 g (42 %); m.p. 62-64 ^{o}C; ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.57 (s, 2H, Ar$\underline{H}_C$), 8.30 (d, 1H, *J* = 4.0 Hz, Py$\underline{H}_a$), 8.13 (d, 3H, *J* = 9.4 Hz, Ar$\underline{H}_B$, Py$\underline{H}_a$), 7.67 (b, 4H, Ar$\underline{H}_D$), 7.60 (t, 2H, *J* = 7.9 Hz, Ar$\underline{H}_A$), 7.43 (t, 2H, Py$\underline{H}_c$), 7.34-7.21 (m, 12H, Ar$\underline{H}$, Py$\underline{H}_b$, Py$\underline{H}_d$), 7.10 (b, 9H, Py$\underline{H}_b$, Ar$\underline{H}_F$), 6.81 (d, 1H, *J* = 7.8 Hz, Py$\underline{H}_d$), 6.68 (b, 1H, N$\underline{H}_m$), 6.40 (b, 1H, N$\underline{H}_h$), 4.60 (m, 4H, C$\underline{H}_p$, C$\underline{H}_e$), 4.40 (m, 10H, C$\underline{H}_F$, C$\underline{H}_e$) 4.33 (t, 1H, C$\underline{H}_a$), 3.04 (m, 4H, C$\underline{H}_i$, C$\underline{H}_l$), 2.38 (t, 2H, C$\underline{H}_o$), 2.26 (t, 2H, C$\underline{H}_n$), 1.41-1.37 (m, 4H, C$\underline{H}_j$, C$\underline{H}_k$), 1.22 (m, 18H, C$\underline{H}_2$, C$\underline{H}_f$) 1.03 (m, 2H, C$\underline{H}_g$); ^{13}C NMR (100 MHz, CD_3CN): δ (ppm) = 173.2, 165.3, 157.3, 157.2, 155.6, 149.3, 149.2, 141.6, 138.0, 136.5, 134.0, 128.9, 128.5, 127.9, 126.6, 123.6, 122.8, 122.5, 122.4, 121.0, 66.1, 53.1, 52.2, 49.6, 42.9, 39.0, 38.8, 29.9, 29.3, 29.1, 29.0, 28.8, 28.7, 27.5, 26.4, 26.3.

[1] J. W. Canary, Y. Wang, R. Roy Jr., *Inorg. Synth*. **1998**, *32*, 70-75,

[2] G. S. Matouzenko, A. Bousseksou, S. Lecocq, P. J. van Koningsbruggen, M. Perrin, O. Kahn, A. Collet, *Inorg. Chem.* **1997**, *36*, 2975-2981.

[3] A. Altieri, G. Bottari, F. Dehez, D. A. Leigh, J. K. Y. Wong, F. Zerbetto, *Angew. Chem. Int. Ed.* **2003**, *42*, 2296-2300.