Electronic Supplementary Material (ESI) for Chemical Science.

Electronic Supporting Information

Extraction and transport of sulfate using macrocyclic squaramide receptors

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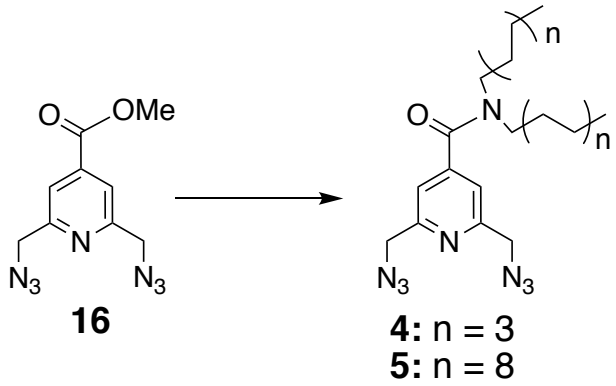
Contents

General experimental

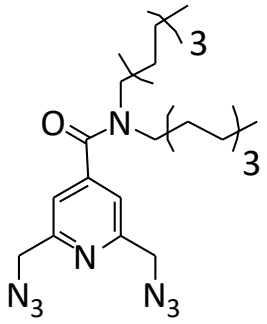
^{1}H NMR spectra were recorded using a Bruker Avance III 500 spectrometer at a frequency of 500 MHz, a Bruker Avance III 400 spectrometer at a frequency of 400 MHz or a Bruker Avance III 300 spectrometer at a frequency of 300 MHz, and are reported as parts per million (ppm) with DMSO-*d*$_6$ (δ_H 2.50 ppm) or $CDCl_3$ (δ_H 7.26 ppm) as an internal reference. The data are reported as chemical shift (δ), multiplicity (br = broad, s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant (*J* Hz) and relative integral. ^{13}C NMR spectra were recorded using a Bruker Avance III 500 spectrometer at a frequency of 125 MHz or Bruker Avance III 400 spectrometer at a frequency of 100.6 MHz and are reported as parts per million (ppm) with DMSO-*d*$_6$ (δ_C 39.5 ppm) or $CDCl_3$ (δ_C 77.0 ppm) as an internal reference. High-resolution ESI spectra were recorded on a Bruker BioApex Qe 7T Fourier Transform Ion Cyclotron Resonance mass spectrometer (FTICR) with an Apollo Dual source, via syringe infusion. Inductively coupled plasma mass spectrometry (ICP-MS) was performed on a Perkin Elmer Nexia 300X in kinetic enrgy discrimination mode with Helium collision gas used. Analytical TLC was performed using precoated silica gel plates (Merck Kieselgel 60 F254). Tetrabutylammonium salts were used as supplied and were stored in a vacuum desiccator over silica drying beads and phosphorous pentoxide. Unless otherwise stated, all other reagents were commercially available and used as supplied. Methyl 2,6-bis(azidomethyl)isonicotinate (**16**) was prepared according to literature procedures.[1-2]

Synthesis and characterization of novel compounds



Scheme S1: Synthesis of compounds **4** and **5**.

2,6-Bis(azidomethyl)-*N,N*-dioctylisonicotinamide (**4**)



A solution of NaOH (17.6 mg, 0.44 mmol) in water (0.5 mL) was added to a solution of methyl 2,6-bis(azidomethyl)isonicotinate **16** (109 mg, 0.44 mmol) in THF (6 mL). The resulting mixture was stirred for 16 hours at room temperature and then neutralized by additional of HCl (aq.) (1 M). The solvent was removed under reduced pressure to give a colorless solid. The resulting solid was dissolved in anhydrous CH_2Cl_2 (10 mL) under an atmosphere of argon. Carbonyldiimidazole (CDI) (80 mg, 0.48 mmol) was slowly added at room temperature, and the mixture was stirred until no further gas (CO_2) evolution was observed. The solvent was removed under reduced pressure to give an oily residue which was re-dissolved in $ClCH_2CH_2Cl$ (10 mL) under argon. Methyl trifluoromethanesulfonate (MeOTf) (52 µL, 0.48 mmol) was added at room temperature and stirred for 2 min before the addition of a solution of freshly distilled *N,N*-dioctylamine (116 mg, 0.48 mmol) and *N*-methylmorpholine (NMM) (78 mg, 0.48 mmol) in anhydrous $ClCH_2CH_2Cl$ (3 mL). The mixture was stirred for 2 h at room temperature and the solvent was removed under reduced pressure. The resulting oil was purified by flash silica gel chromatography (2:98 v/v methanol/ dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave the product **4** (151 mg, 75%) as a colourless solid. **M.p.** 100 – 105 °C; **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.80 – 0.95 (m, 6 H), 1.22 – 1.35 (m, 20 H), 1.47 – 1.53 (m, 2 H), 1.54 – 1.64 (m, 2 H), 3.10 (t, *J* = 7.6 Hz, 2 H), 3.46 (t, *J* = 7.6 Hz, 2 H), 4.50 (s, 4 H), 7.23 (s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): 14.02, 14.07,

22.5, 22.6, 26.5, 27.0, 27.4, 28.8, 29.0, 29.2, 29.3, 31.7, 31.8, 44.9, 48.9, 55.2, 118.2, 147.1, 156.6, 168.4, 1 signal obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{24}H_{40}N_8ONa$ $[M + Na]^+$ 479.3217, found 479.3222; **ν_{max} (film)/cm^{-1}:** 2925, 2854, 2098, 1634, 1560.

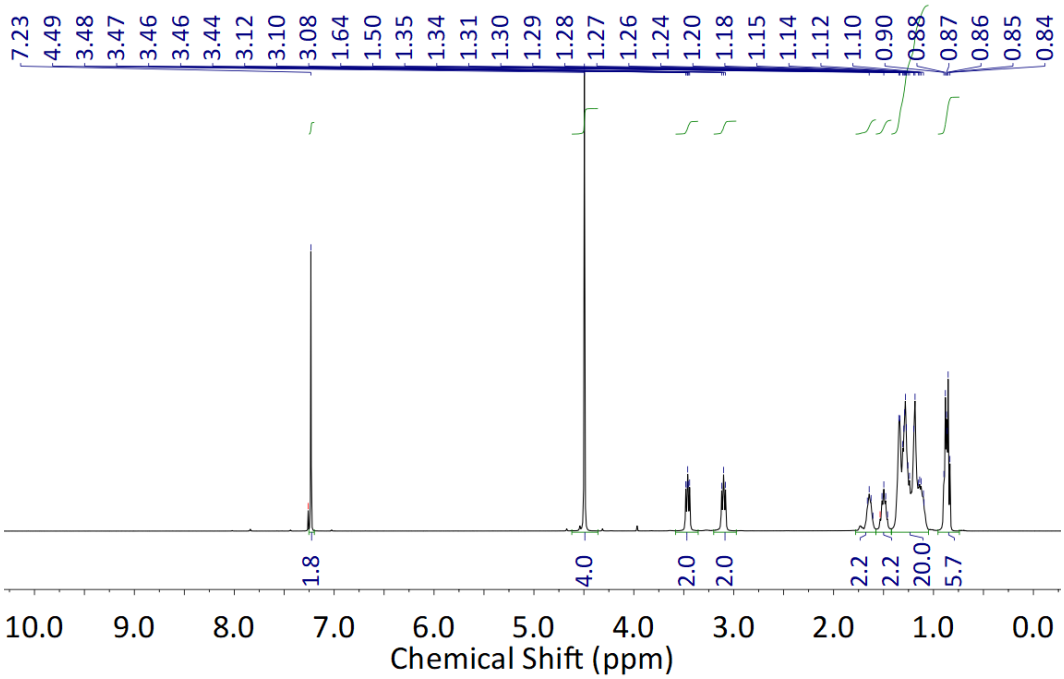


Figure S1 ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K).

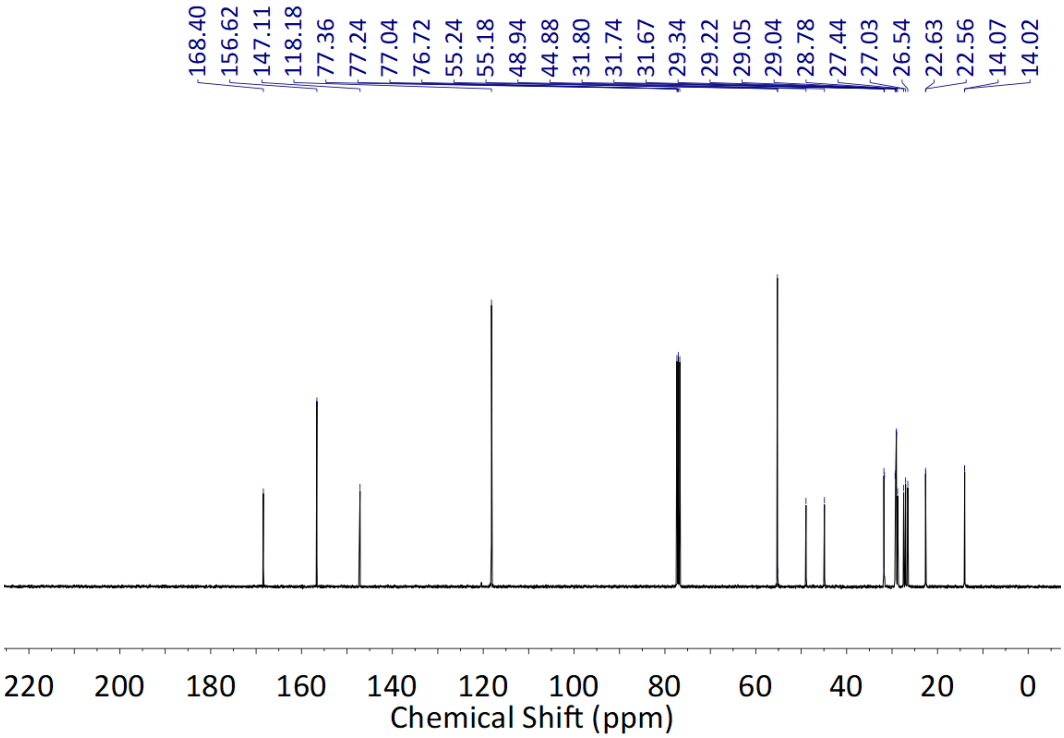
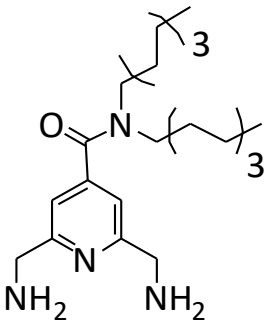


Figure S2 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 298 K).

2,6-Bis(aminomethyl)-*N,N*-dioctylisonicotinamide (**6**)



Ph_3P (126 mg, 0.48 mmol) was added to a solution of azide **4** (100 mg, 0.22 mmol) in THF (3 mL) and the resulting solution was stirred at room temperature for 2 hours, then 0.1 mL water was added to the mixture and stirring was continued at room temperature for 16 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this oil to flash silica gel chromatography (0.1/5:95 v/v ammonium/methanol/ dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **6** (70 mg, 79%) as a beige solid. **M.p.** 86 - 90 °C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.86 - 091 (m, 6 H), 1.11 – 1.34 (m, 20 H), 1.35 – 1.53 (m, 2 H), 1.56 – 1.70 (m, 2 H), 3.12 (t, *J* = 7.7 Hz, 2 H), 3.47 (t, *J* = 7.7 Hz, 2 H), 4.00 (s, 4 H), 7.10 (s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 14.0, 14.1, 22.5, 22.6, 26.5, 27.0, 27.4, 28.7, 29.0, 29.2, 29.4, 29.7, 31.7, 31.8, 44.7, 47.5, 48.8, 116.4, 146.1, 161.9, 169.4; **HRMS** (ESI, MeOH) calcd. for $C_{24}H_{44}N_4OH$ $[M + H]^+$ 405.3588, found 405.3593; **ν_{max} (film)/cm^{-1}:** 3335 (broad), 2925, 2855, 1630, 1558.

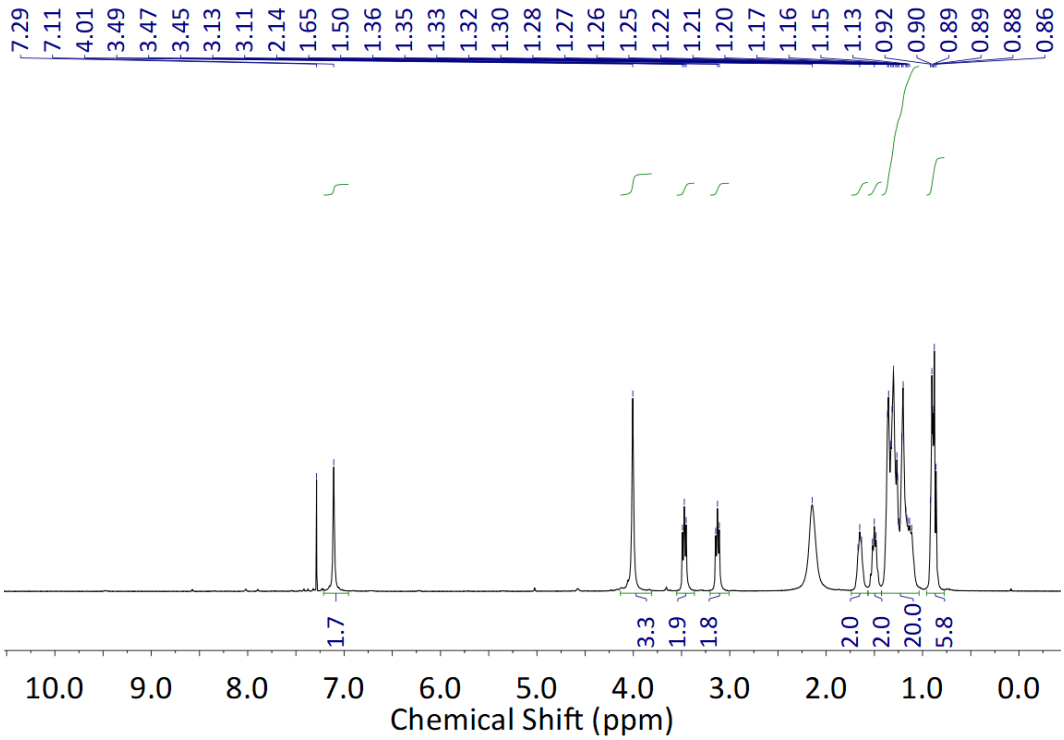


Figure S3 ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K).

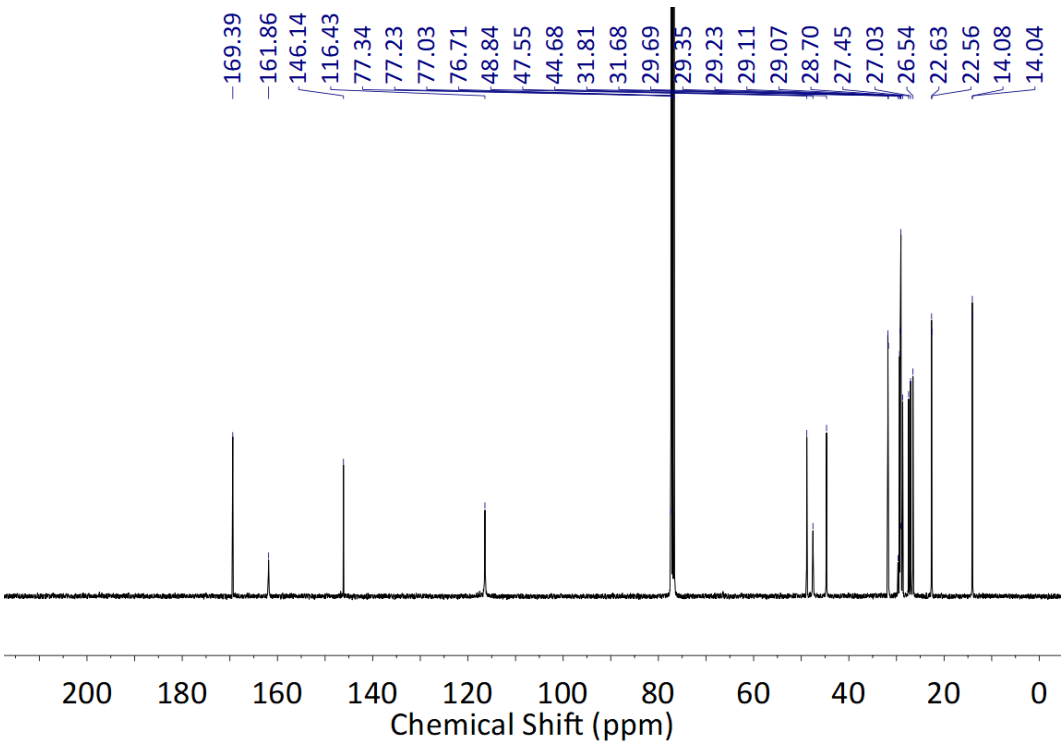
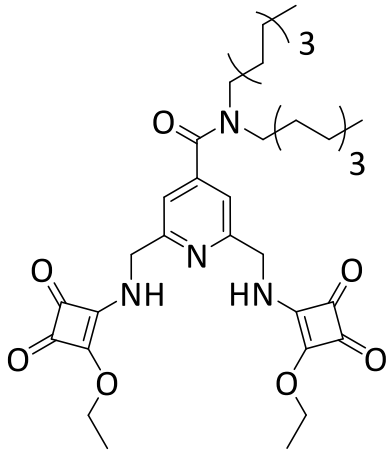


Figure S4 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 298 K).

2,6-Bis(((2-ethoxy-3,4-dioxocyclobut-1-en-1-yl)amino)methyl)-*N,N*-dioctylisonicotinamide (**8**)



Diamine **6** (56.6 mg, 0.14 mmol) was added to a solution of diethyl squarate (52 mg, 0.30 mmol) in EtOH (6 mL) at room temperature and the resulting mixture was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (5:95 v/v methanol/ dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **8** (75 mg, 82%) as a beige solid. **M.p.** 80 - 86 °C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl$_3$): 0.82 – 0.87 (m, 6 H), 1.08 – 1.34 (m, 20 H), 1.35 – 1.51 (m, 8 H), 1.61 (s, 2 H), 3.14 (t, *J* = 7.2 Hz, 2 H), 3.42 (t, *J* = 7.2 Hz, 2 H), 4.58 – 5.09 (m, 8 H), 7.12 (s, 2 H), 8.02 (br s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl$_3$): 14.02, 14.06, 1538, 22.5, 22.6, 26.5, 27.0, 27.4, 28.7, 29.0, 29.2, 29.3, 31.7, 31.8, 44.9, 48.6, 48.9, 117.9, 147.0, 155.9, 168.2, 172.6, 177.8, 183.2, 189.1, 2 signal obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for

$C_{36}H_{52}N_4O_7Na$ $[M + Na]^+$ 675.3728, found 675.3739; **ν_{max} (film)/cm^{-1}:** 3233 (broad), 2926, 2855, 1803, 1710, 1604.

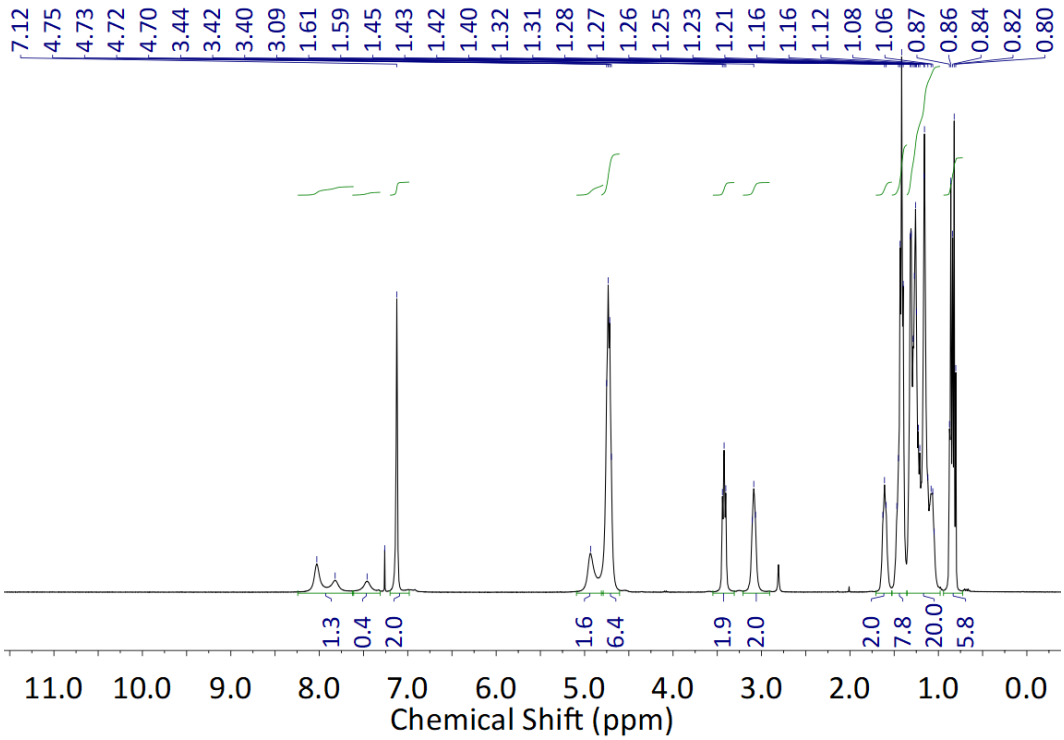


Figure S5 ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K).

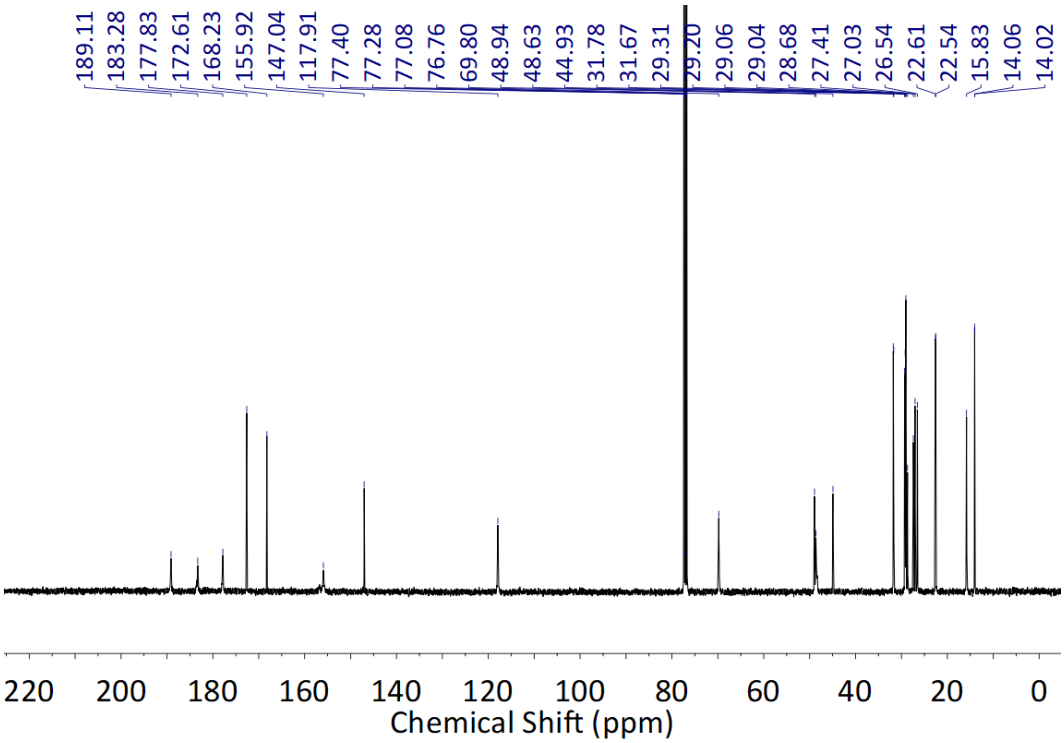
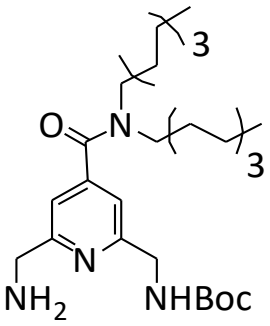


Figure S6 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 298 K).

Tert-butyl ((6-(aminomethyl)-4-(dioctylcarbamoyl)pyridin-2-yl)methyl)-carbamate (**10**)



Diamine **6** (114 mg, 0.28 mmol) was added to a solution of Boc_2O (60 mg, 0.14 mmol) in CH_2Cl_2 (20 mL) at room temperature and the resulting mixture was stirred at room temperature for 16 hours. The solvent was then removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (0.2:0.78:92 v/v ammonia solution/methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.5) gave amine **10** (71 mg, 49%) as a beige solid. **M.p.** 90 - 96 °C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.80 – 0.88 (m, 6 H), 1.01 – 1.36 (m, 20 H), 1.40 – 1.51 (m, 11 H), 1.60 – 1.68 (m, 2 H), 3.09 (t, *J* = 7.7 Hz, 2 H), 3.44 (t, *J* = 7.7 Hz, 2 H), 3.99 (s, 2 H), 4.42 (d, *J* = 5.2 Hz, 2 H), 5.57 (br s, 1 H), 7.06 (s, 1 H), 7.10 (s, 1 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 14.1, 22.5, 22.6, 26.5, 27.0, 27.4, 28.4, 28.6, 28.7, 29.0, 29.2, 29.3, 31.7, 31.8, 44.7, 45.7, 47.5, 48.8, 79.5, 116.7, 116.8, 146.2, 155.9, 157.8, 161.9, 169.1, 1 signal obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{29}H_{52}N_4O_3H$ $[M + H]^+$ 505.4112, found 505.4118; **ν_{max} (film)/cm^{-1}:** 3340 (broad), 2927, 2855, 1713, 1631.

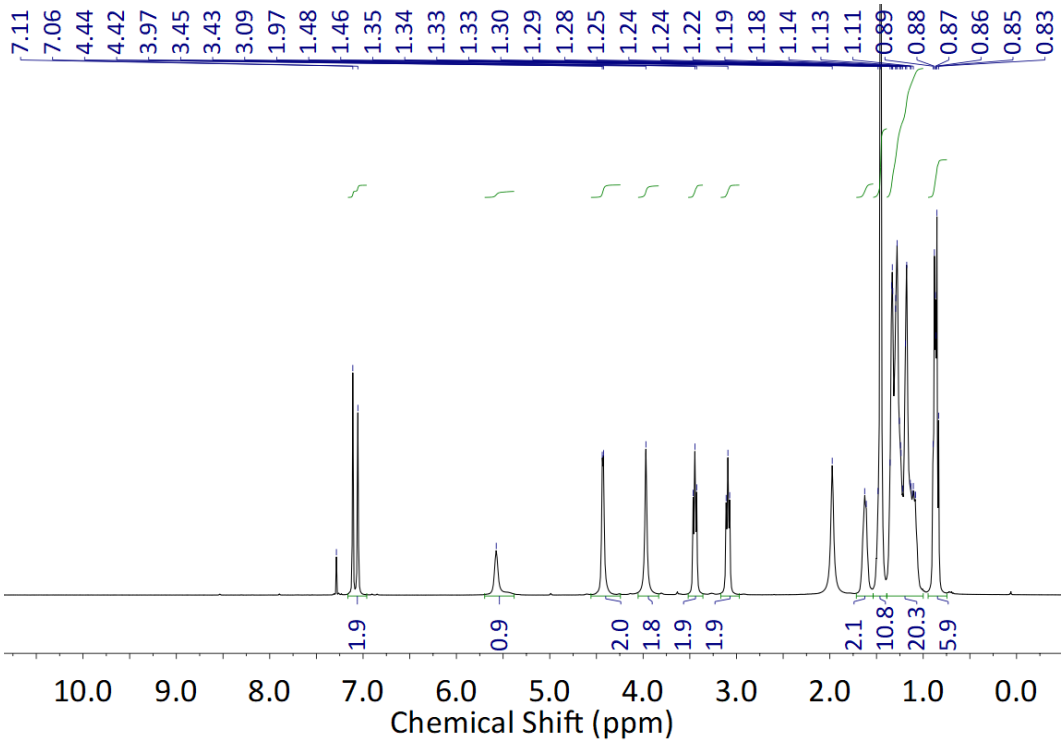


Figure S7 ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K).

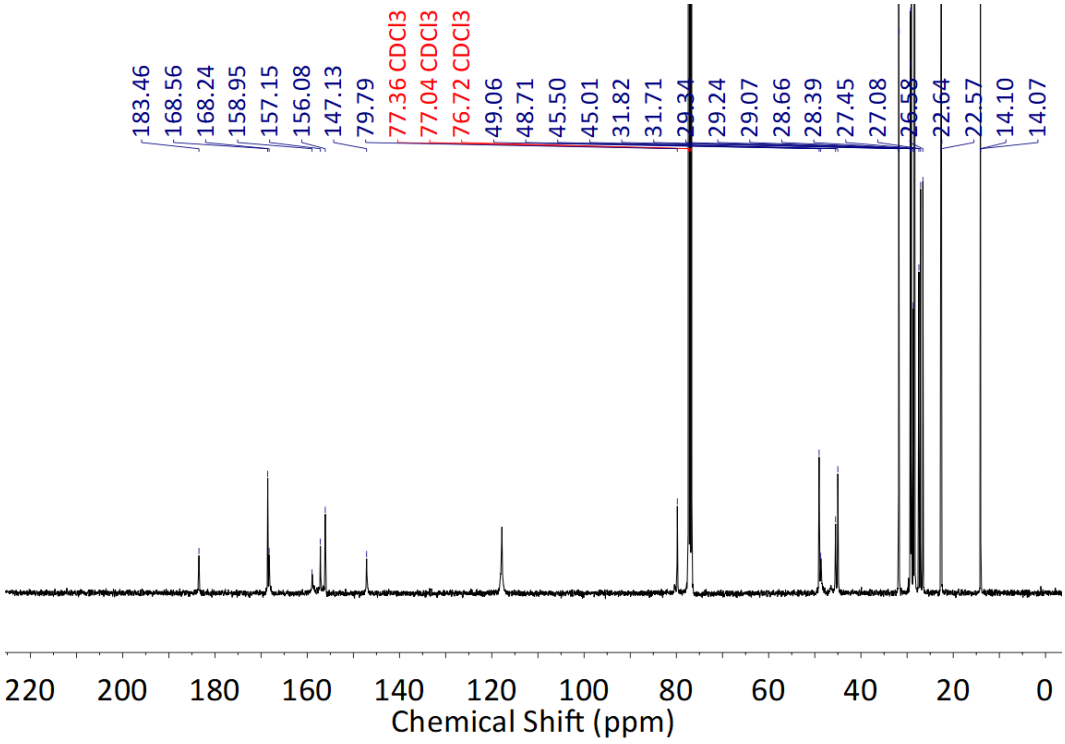
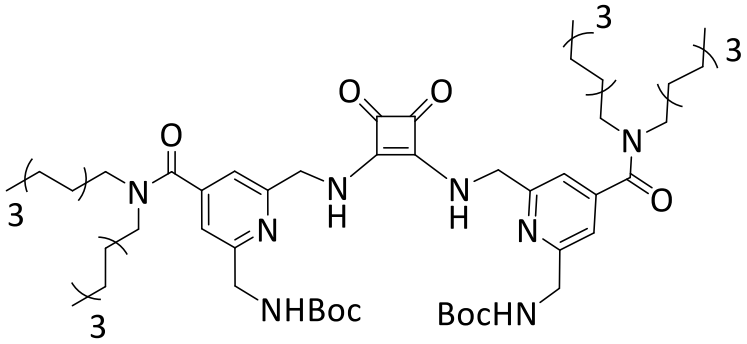


Figure S8 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 298 K).

Squaramide **12**



Compound **10** (32 mg, 0.064 mol) was added to a solution of diethyl squarate (23 mg, 0.14 mmol) and Et_3N (0.1 mL) in EtOH (5 mL) at room temperature. The resulting solution was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (5/95 v/v methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **12** (116 mg, 46%) as a beige oil. **^{1}H NMR** (400 MHz, $CDCl_3$): 0.83 – 0.91 (m, 12 H), 1.06 – 1.29 (m, 40 H), 1.45 (s, 18 H), 1.61 (s, 4 H), 1.72 (s, 4 H), 3.07 (t, J = 7.6 Hz, 4 H), 3.43 (t, J = 7.6 Hz, 4 H), 4.41 (d, J = 6 Hz, 4 H), 4.49 (s, 4 H), 5.47 (br s, 2 H), 7.13 (s, 4 H), 8.04 (br s, 2 H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): 14.2, 24.6, 27.2, 27.5, 28.4, 28.7, 29.1, 29.3, 29.4, 29.5, 29.7, 29.8, 31.7, 31.9, 44.1, 45.2, 47.2, 49.4, 79.7, 116.7, 116.8, 126.5, 137.4, 155.9, 163.2, 172.6, 177.8, 183.3, 189.1; **HRMS** (ESI, MeOH) calcd.

for $C_{62}H_{102}N_8O_8Na_2$ $[M + 2Na]^{2+}$ 566.3802, found 566.3803; **ν_{max} (film)/cm^{-1}:** 3354 (broad), 2927, 2855, 2147, 1987, 1716, 1631.

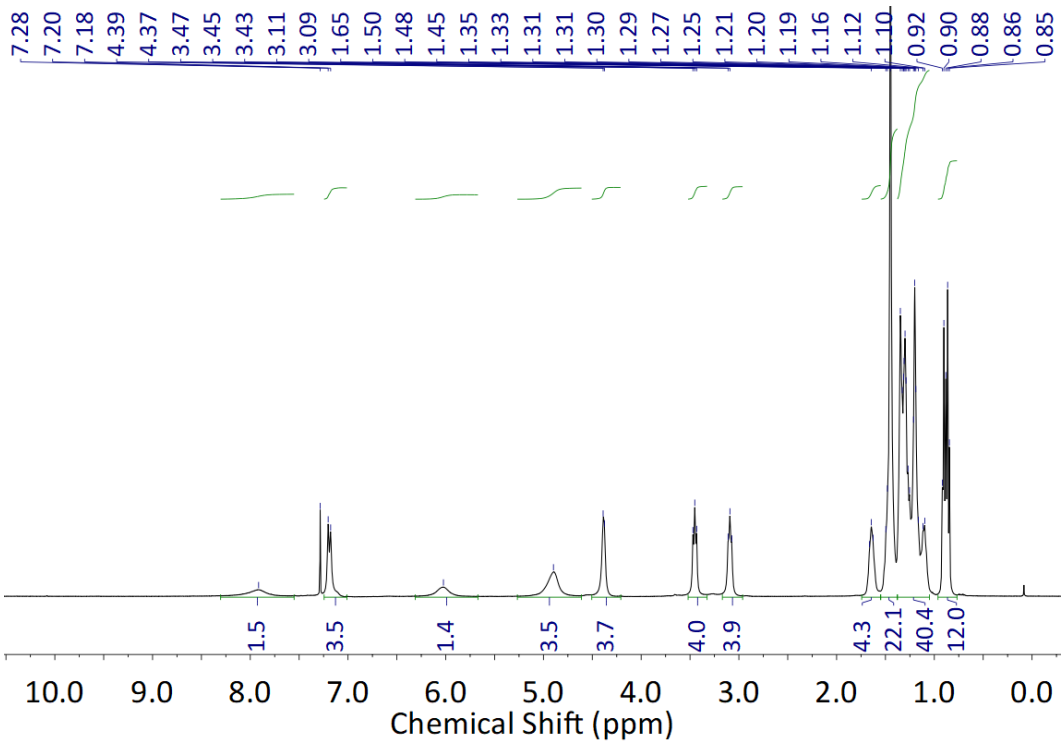


Figure S9 ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K).

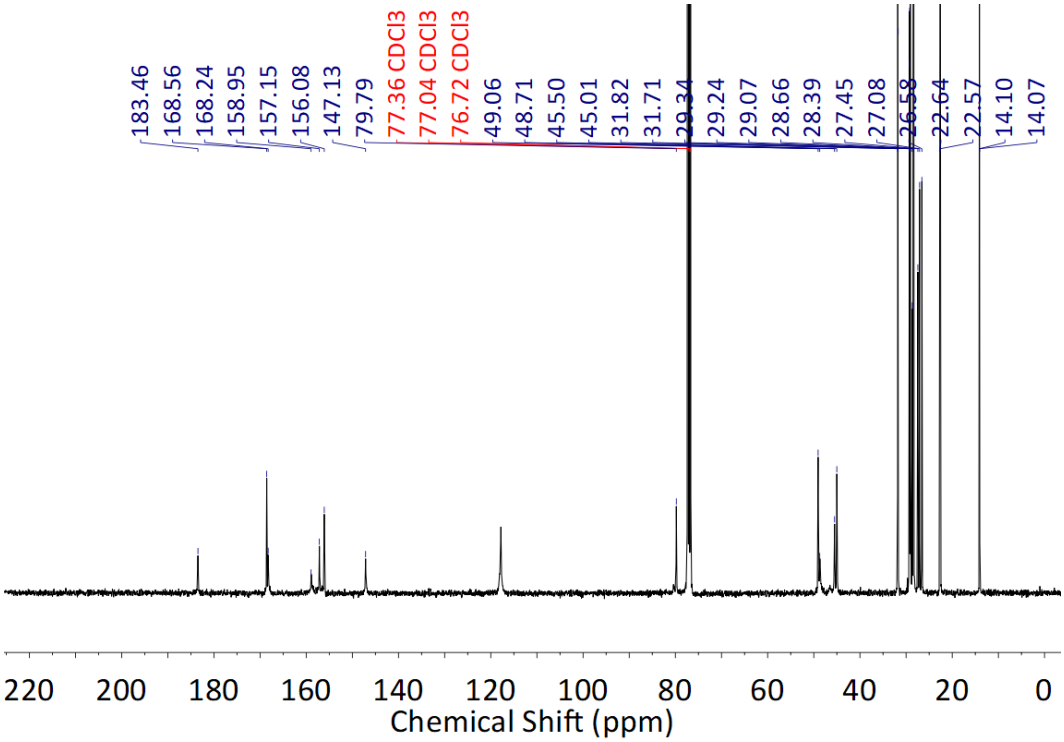
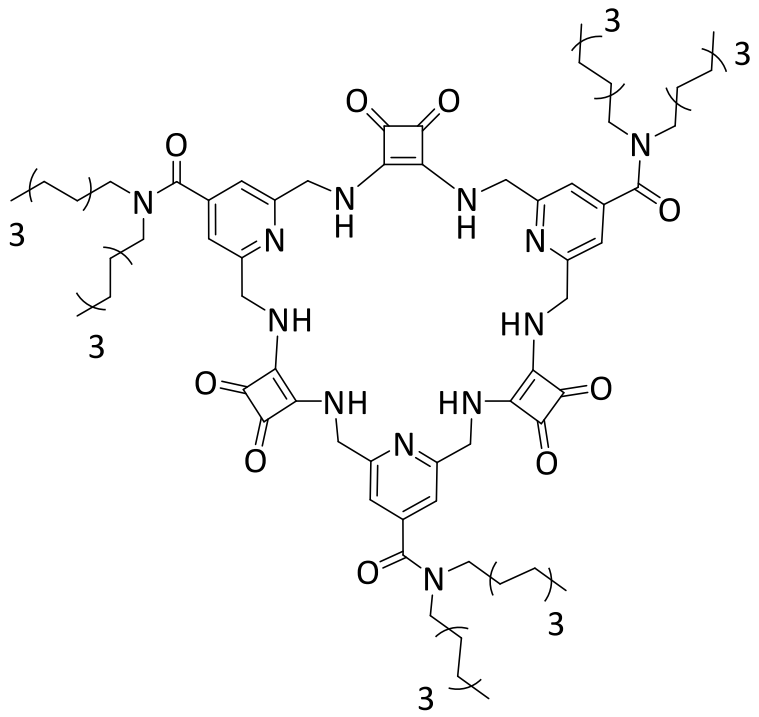


Figure S10 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 298 K).

Macrocycle **1**



Compound **12** (76 mg, 0.07 mmol) was dissolved in a solution of TFA/CH_2Cl_2 (1:1 v/v, 3 mL) before the reaction mixture was stirred at room temperature for 2 hours and then concentrated under reduced pressure. The resulting oil was dissolved in EtOH (3 mL) then added in a solution of **8** (46 mg, 0.07 mmol) and Et_3N (0.5 mL) in EtOH (50 mL) and the resulting mixture was stirred at room temperature for 48 hrs. The solvent was then removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (5/95 v/v methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.3) gave the macrocycle **1** (57 mg, 56%) as a beige solid. **M.p.** 262 – 268 °C (decomp.); **^{1}H NMR** (400 MHz, DMSO-d_6): 0.79 – 0.90 (m, 18 H), 0.98 – 1.29 (m, 60 H), 1.41 (s, 6 H), 1.56 (s, 6 H), 3.04 (s, 6 H), 3.36 (s, 6 H), 4.81 (s, 12 H), 7.23 (s, 6 H), 8.02 (br s, 6 H); **^{13}C NMR** (100.6 MHz, DMSO-d_6): 14.3, 14.4, 22.4, 22.5, 26.3, 26.8, 27.4, 28.4, 28.9, 29.1, 29.2, 29.5, 31.6, 31.7, 44.5, 48.6, 118.2, 146.8, 158.2, 168.3, 183.3, 2 signals obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{84}H_{126}N_{12}O_9Na$ $[M + Na]^+$ 1447.9845, found 1447.9829; **ν_{max} (film)/cm^{-1}:** 3237 (broad), 2925, 2851, 1801, 1714, 1609.

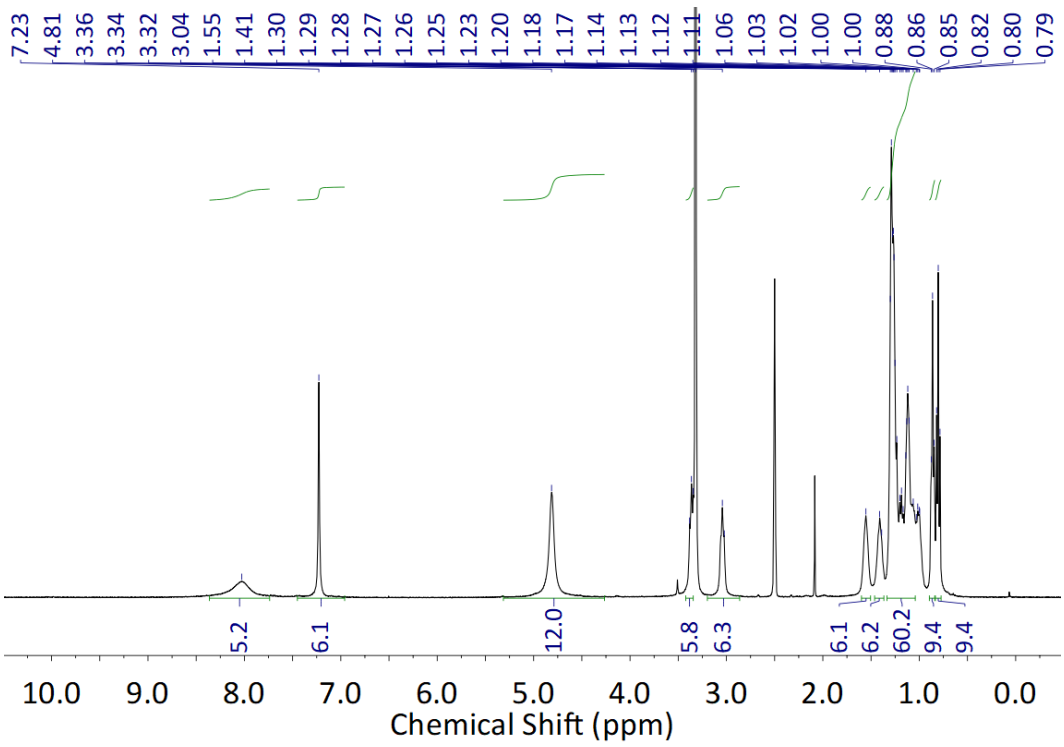


Figure S11 ^{1}H NMR (DMSO-d_6, 400 MHz, 298 K).

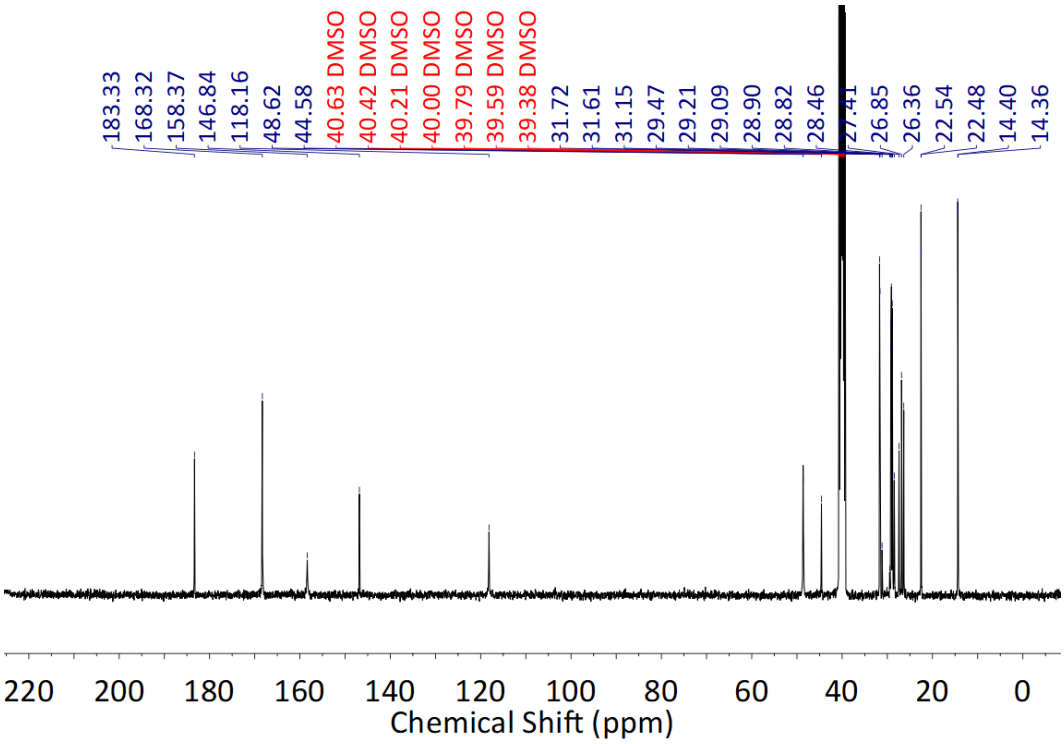
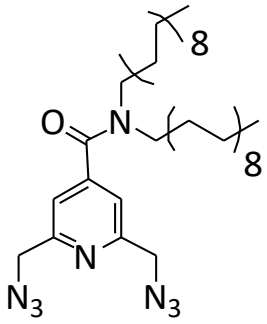


Figure S12 ^{13}C NMR (DMSO-d_6, 100.6 MHz, 298 K).

2,6-Bis(azidomethyl)-*N,N*-dioctadecylisonicotinamide (**5**)



A solution of NaOH (47.6 mg, 1.19 mmol) in water (0.5 mL) was added to a solution of methyl 2,6-bis(azidomethyl)isonicotinate **16** (294 mg, 1.19 mmol) in THF (10 mL). The resulting mixture was stirred for 16 hours at room temperature and then neutralized by additional of HCl (aq.) (1 M). The solvent was removed under reduced pressure to give a colorless solid. The resulting solid was dissolved in anhydrous CH_2Cl_2 (10 mL) under an atmosphere of argon. Carbonyldiimidazole (CDI) (232 mg, 0.25 mmol) was slowly added at room temperature, and the mixture was stirred until no further gas (CO_2) evolution was observed. The solvent was removed under reduced pressure gave an oily residue which was re-dissolved in $ClCH_2CH_2Cl$ (10 mL) under argon. Methyl trifluoromethanesulfonate (MeOTf) (160 μL, 1.43 mmol) was added at room temperature and stirred for 2 min before the addition of a solution of *N,N*- dioctadecylamine (746 mg, 1.43 mmol) and *N*-methylmorpholine (NMM) (232 mg, 1.43 mmol) in anhydrous $(CH_2)_2Cl_2$ (20 mL). The mixture was stirred for 12 hours at 60℃ and the solvent was removed under reduced pressure. The resulting oil was purified by flash silica gel chromatography (4:1 v/v hexane/ethyl acetate elution) and concentration of the appropriate fractions (R_f 0.4) gave the product **5** (750 mg, 85%) as a colorless solid. **M.p.** 120 – 125 ◦C; **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.87 (t, *J* = 6.8 Hz, 6 H), 1.11 – 1.38 (m, 60 H), 1.45 – 1.55 (m, 2 H), 1.59 – 1.70 (m, 2 H), 3.10 (t, *J* = 7.7 Hz, 2 H), 3.46 (t, *J* = 7.72 Hz, 2 H), 4.50 (s, 4 H), 7.24 (s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 168.38, 156.59, 147.18, 118.20, 55.22, 55.20, 48.96, 44.90, 31.93, 29.71, 29.66, 29.63, 29.60, 29.51, 29.42, 29.37, 29.14, 28.79, 27.46, 27.05, 26.57, 22.69, 14.11.; **HRMS** (ESI, MeOH) calcd. for $C_{44}H_{80}N_8ONa$ $[M + Na]^+$ 759.6347, found 759.6355; **ν_{max} (film)/cm^{-1}:** 2923, 2853, 2103, 1639, 1466.

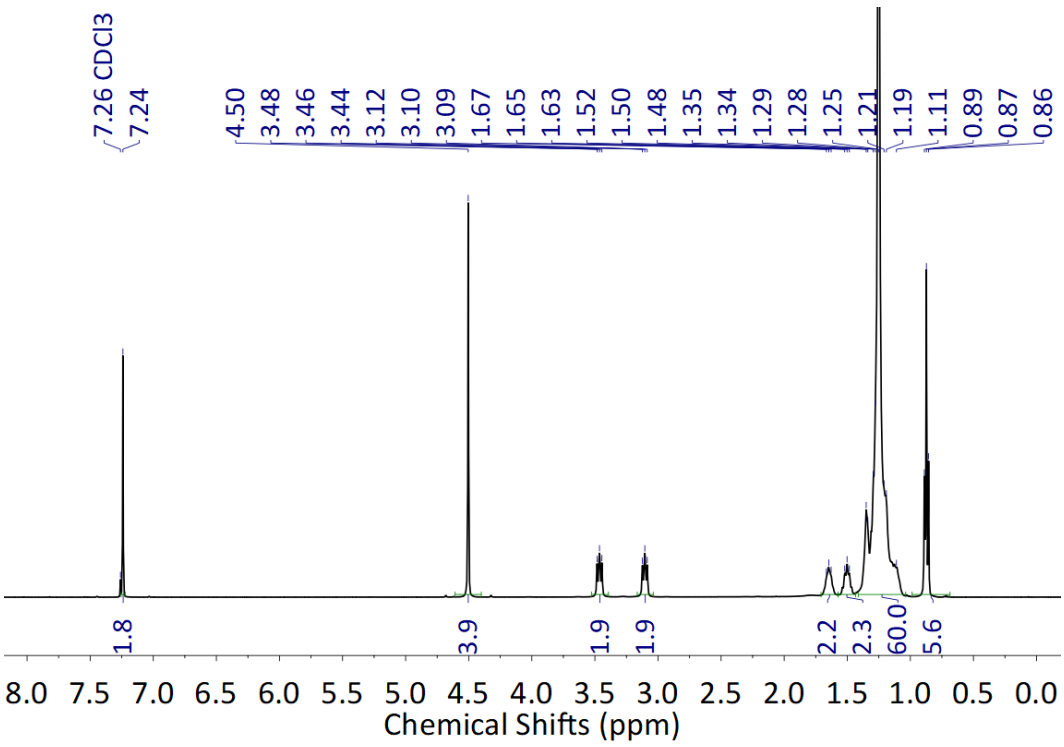


Figure S13 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K).

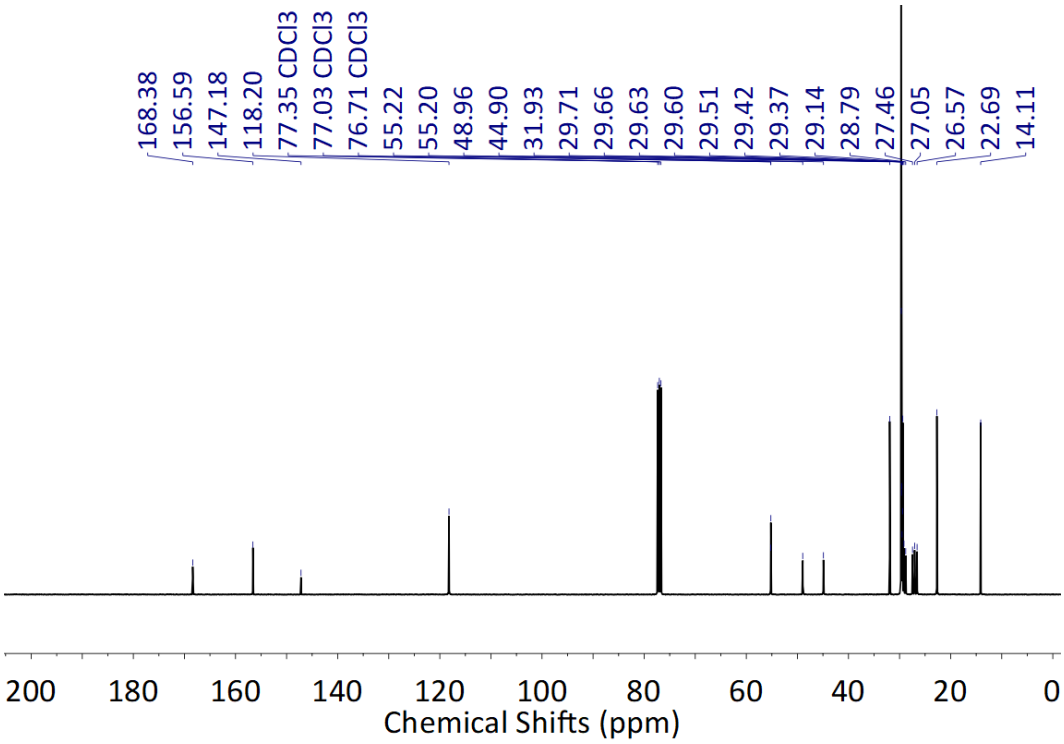
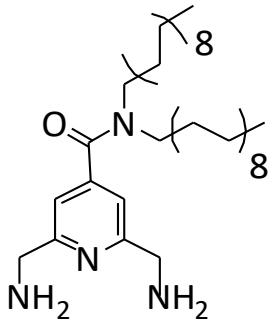


Figure S14 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K).

2,6-Bis(aminomethyl)-*N,N*-dioctadecylisonicotinamide (**7**)



Ph_3P (130 mg, 0.49 mmol) was added to a solution of azide **5** (165 mg, 0.22 mmol) in THF (3 mL) and the resulting solution was stirred at room temperature for 2 hours, then 0.1 mL water was added to the mixture and stirring was continued at 60℃ for 36 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this oil to flash silica gel chromatography (0.1:5:95 v/v ammonium/methanol/ dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **7** (130 mg, 87%) as a beige solid. **M.p.** 110 - 115 ˚C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.87 (t, *J* = 6.8 Hz, 6 H), 1.11 – 1.38 (m, 60 H), 1.45 – 1.55 (m, 2 H), 1.59 – 1.70 (m, 2 H), 3.10 (t, *J* = 7.7 Hz, 2 H), 3.45 (t, *J* = 7.7 Hz, 2 H), 3.98 (s, 4 H), 7.08 (s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 169.40, 161.98, 146.13, 116.37, 48.84, 47.65, 44.68, 31.92, 29.69, 29.65, 29.60, 29.52, 29.44, 29.42, 29.35, 29.15, 28.72, 27.46, 27.05, 26.56, 22.68, 14.10, 1 signal obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{44}H_{84}N_4OH$ $[M + H]^+$ 685.6718, found 685.6726; **ν_{max} (film)/cm^{-1}:** 3439 (broad), 2917, 2849, 1675, 1467.

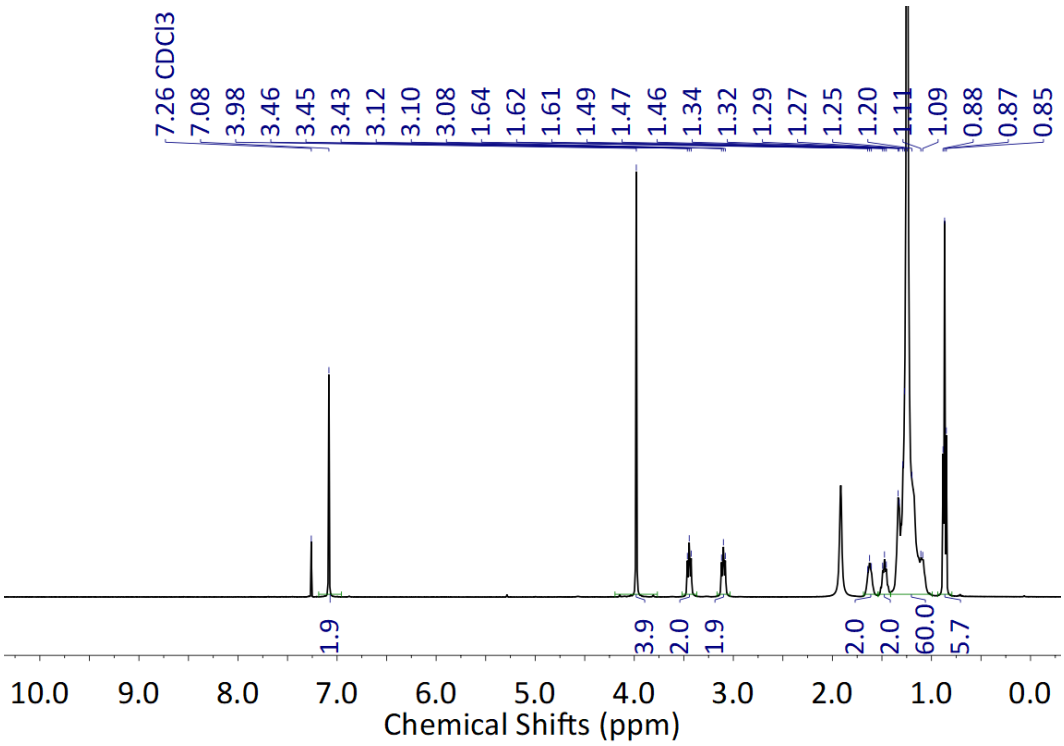


Figure S15 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K).

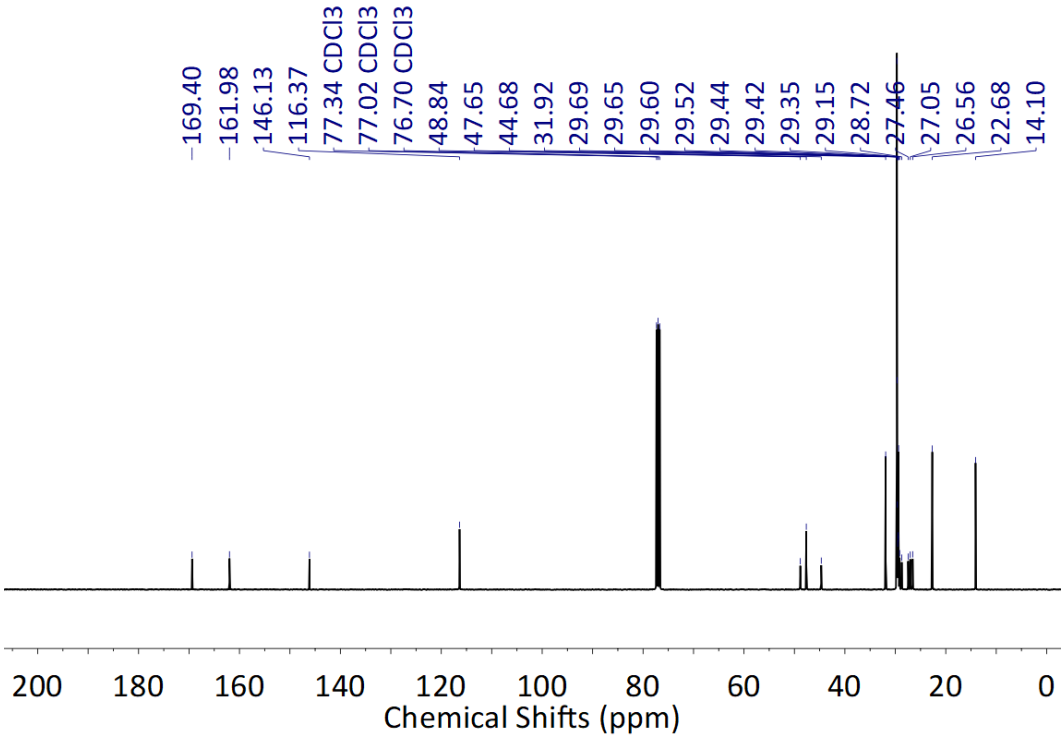
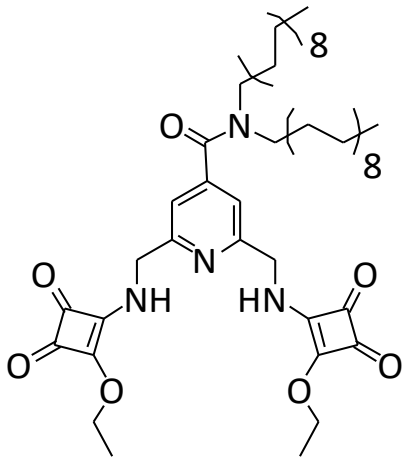


Figure S16 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K).

2,6-Bis(((2-ethoxy-3,4-dioxocyclobut-1-en-1-yl)amino)methyl)-*N,N*-dioctadecyl-isonicotinamide (**9**)



Diamine **7** (102 mg ,0.15 mmol) was added to a solution of diethyl squarate (57 mg, 0.33 mmol) in 1:1 v/v CH_2Cl_2/EtOH (15 mL) at room temperature and the resulting mixture was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (5:95 v/v methanol/ dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **9** (110 mg, 79%) as a beige solid. **M.p.** 95 - 100 °C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.88 (t, *J* = 6.8 Hz, 6 H), 0.97 – 1.39 (m, 60 H), 1.47 (t, *J* = 7.0 Hz, 8 H), 1.57 – 1.69 (m, 2 H), 3.10 (t, *J* = 7.7 Hz, 2 H), 3.45 (t, *J* = 7.7 Hz, 2 H), 4.52 – 5.20 (m, 8 H), 6.89 (br s, 1 H), 7.16 (s, 2 H), 7.81 (br s, 1 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 189.37, 183.06, 177.90, 172.40, 168.16, 155.69, 147.07, 117.85, 69.88, 48.97, 48.43, 44.95, 31.91, 29.70, 29.67, 29.65, 29.61, 29.56, 29.45, 29.40, 29.35, 29.19, 28.73, 27.44, 27.07, 26.60,

22.68, 15.86, 14.11; **HRMS** (ESI, MeOH) calcd. for $C_{56}H_{92}N_4O_7Na$ $[M + Na]^+$ 955.6968, found 955.6866; **ν_{max} (film)/cm^{-1}:** 3241 (broad), 2918, 2850, 1711, 1607, 1467.

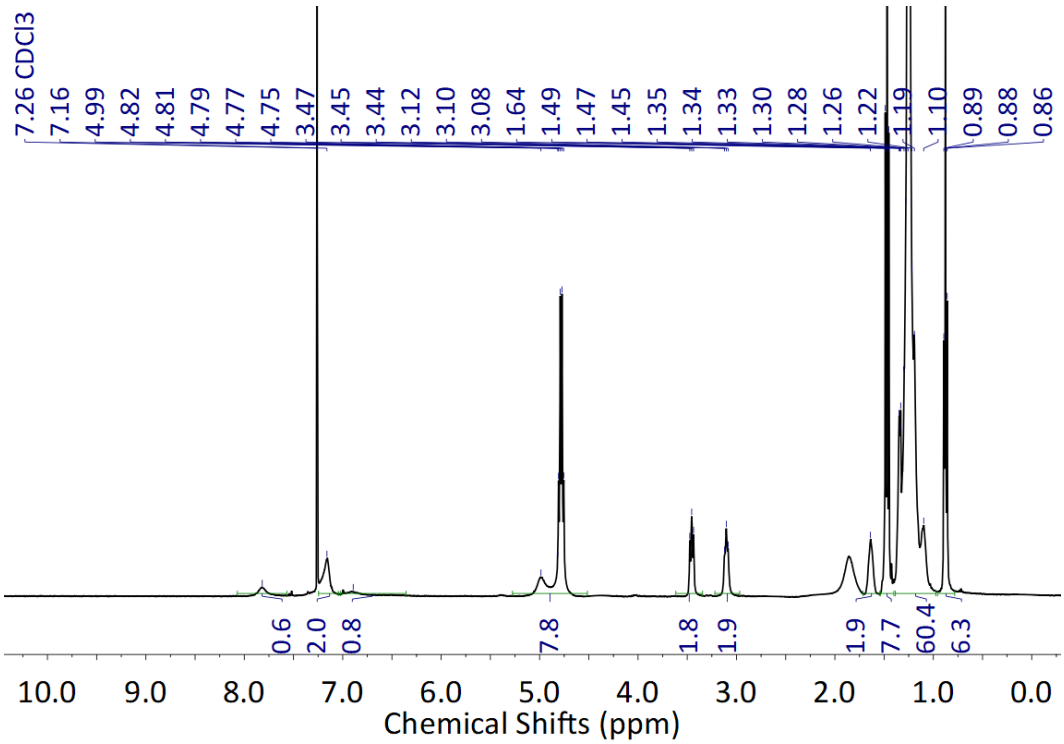


Figure S17 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K).

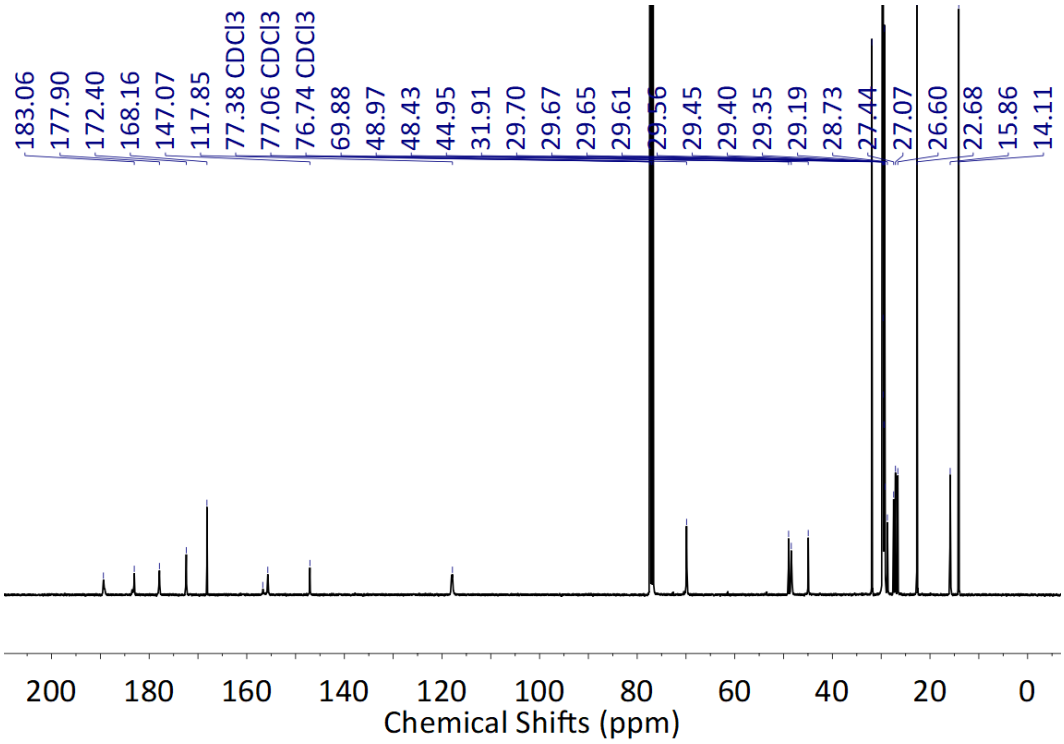
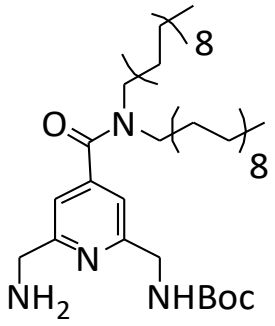


Figure S18 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K).

Tert-butyl ((6-(aminomethyl)-4-(dioctadecylcarbamoyl)pyridin-2-yl)methyl)-carbamate (**11**)



Diamine **7** (74.0 mg, 0.112 mmol) was added dropwise to a solution of Boc_2O (24 mg, 0.112 mmol) in CH_2Cl_2 (50 mL) at room temperature and the resulting mixture was stirred at room temperature for 16 hours. The solvent was then removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (0.1:5:95 v/v ammonia solution/methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.5) gave compound **11** (68 mg, 62%) as a beige solid. **M.p.** 90 - 95 °C (decomp.); **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.86 (t, *J* = 6.8 Hz, 6 H), 1.01 – 1.38 (m, 60 H), 1.38 – 1.53 (m, 11 H), 1.54 – 1.68 (m, 2 H), 2.63 (br s, 2 H), 3.09 (t, *J* = 7.7 Hz, 2 H), 3.44 (t, *J* = 7.7 Hz, 2 H), 4.0 (s, 2 H), 4.4 (d, *J* = 5.2 Hz, 2 H), 5.6 (s, 1 H), 7.06 (s, 1 H), 7.10 (s, 1 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 169.10, 157.83, 155.93, 146.28, 116.89, 116.83, 79.58, 48.88, 47.19, 45.77, 44.74, 31.92, 29.70, 29.65, 29.60, 29.54, 29.44, 29.42, 29.35, 29.16, 28.72, 28.41, 27.45, 27.05, 26.59, 22.68, 14.09, 2 signal obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{49}H_{92}N_4O_3H$ $[M + H]^+$ 785.7242, found 785.7251; **ν_{max} (film)/cm^{-1}:** 3343 (broad), 2922, 2852, 1717, 1633, 1465.

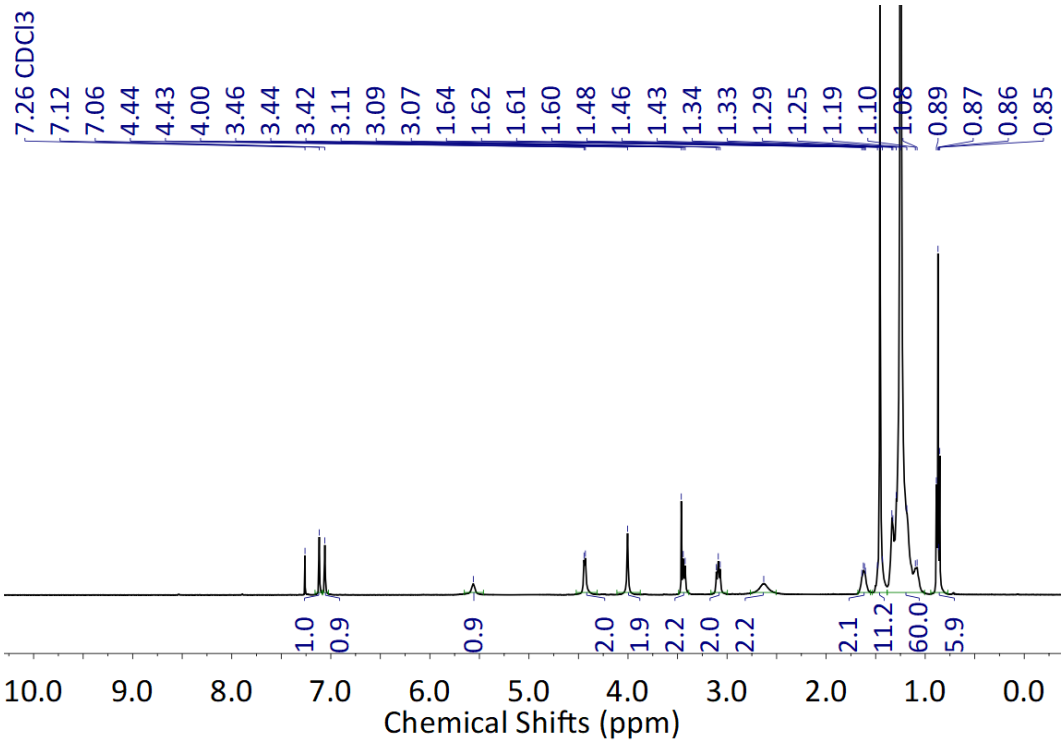


Figure S19 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K).

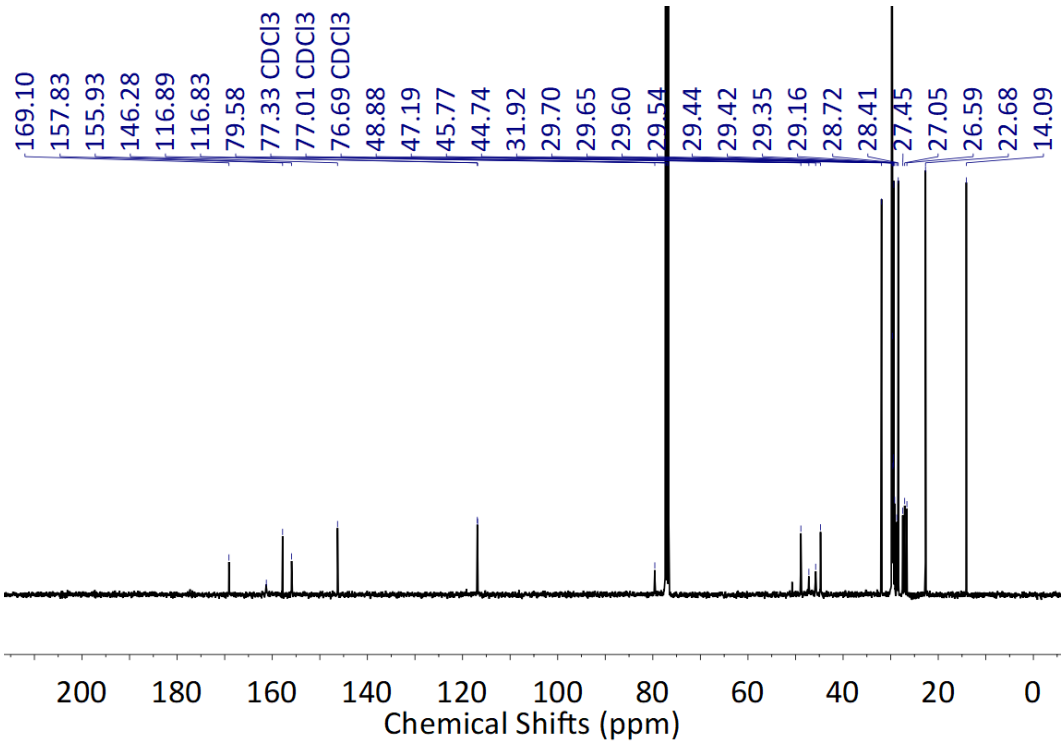
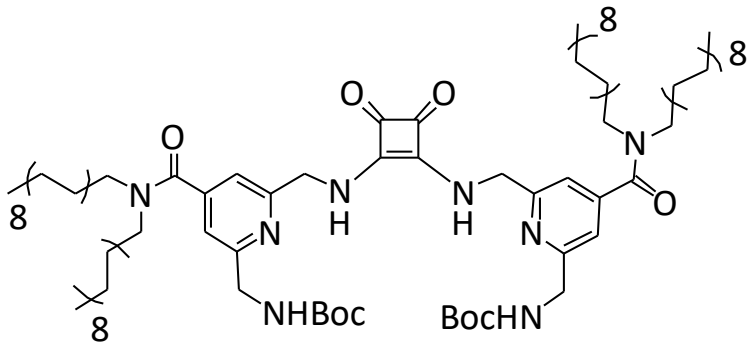


Figure S20 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K).

Squaramide **13**



Amine **11** (224 mg, 0.28 mmol) added to a solution of diethyl squarate (24 mg, 0.14 mmol) in 1:1 v/v CH_2Cl_2/EtOH (20 mL) at room temperature. The resulting solution was stirred at room temperature for 16 hours. The solvent was removed under reduced pressure to give a yellow oil. Subjection of this material to flash silica gel chromatography (5/95 v/v methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.4) gave compound **13** (140 mg, 60%) as a beige oil. **^{1}H NMR** (400 MHz, C*D*Cl_3): 0.85 (t, *J* = 6.8 Hz, 12 H), 0.93 – 1.34 (m, 120 H), 1.34 – 1.52 (m, 22 H), 1.52 – 1.74 (m, 4 H), 3.05 (t, *J* = 7.7 Hz, 4 H), 3.41 (t, *J* = 7.7 Hz, 4 H), 4.3 (s, 4 H), 4.8 (s, 4 H), 6.0 (br s, 2 H), 6.9 – 7.2 (m, 4 H), 7.85 (br s, 2 H); **^{13}C NMR** (100.6 MHz, C*D*Cl_3): δ 183.47, 168.73, 168.25, 159.02, 157.39, 156.09, 146.70, 117.49, 79.69, 49.10, 45.67, 45.04, 31.91, 29.70, 29.64, 29.56, 29.45, 29.41, 29.34, 29.16, 28.69, 28.38, 27.46, 27.10, 26.61, 22.66, 14.08, 4 signals obscured or overlapping; **HRMS** (ESI, MeOH) calcd. for $C_{102}H_{182}N_8O_8Na_2$ $[M + 2Na]^{2+}$ 846.6932, found 846.6937; **ν_{max} (film)/cm^{-1}:** 3312 (broad), 2918, 2850, 1711, 1607, 1467.

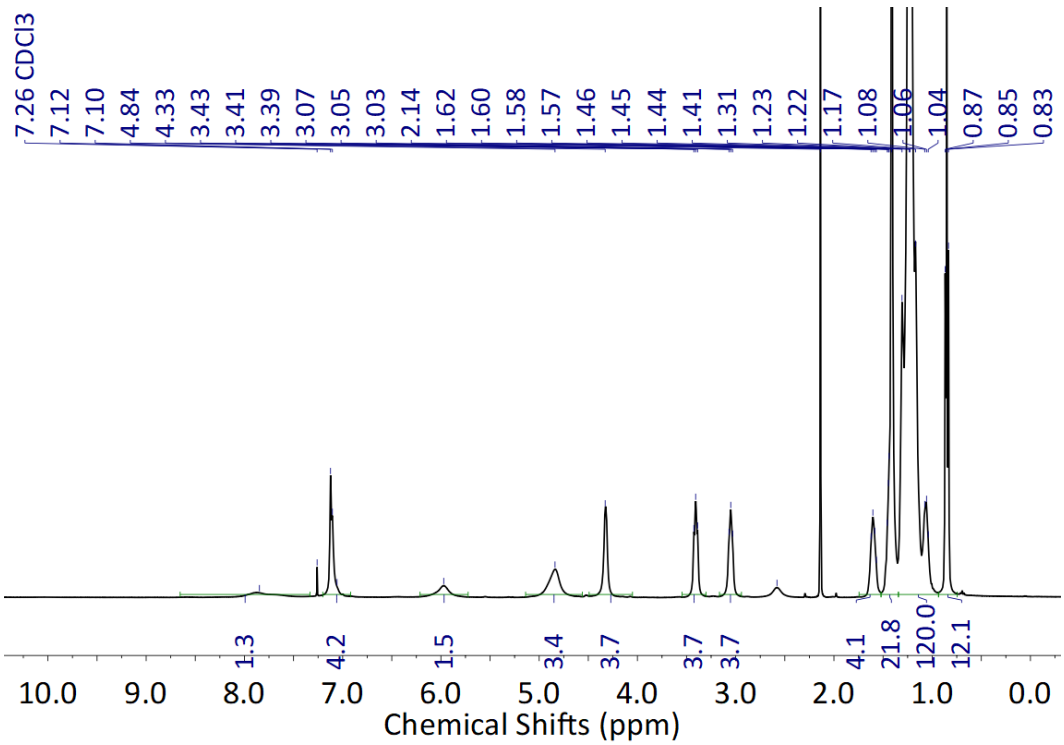


Figure S21 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K). (Acetone peak: 2.14)

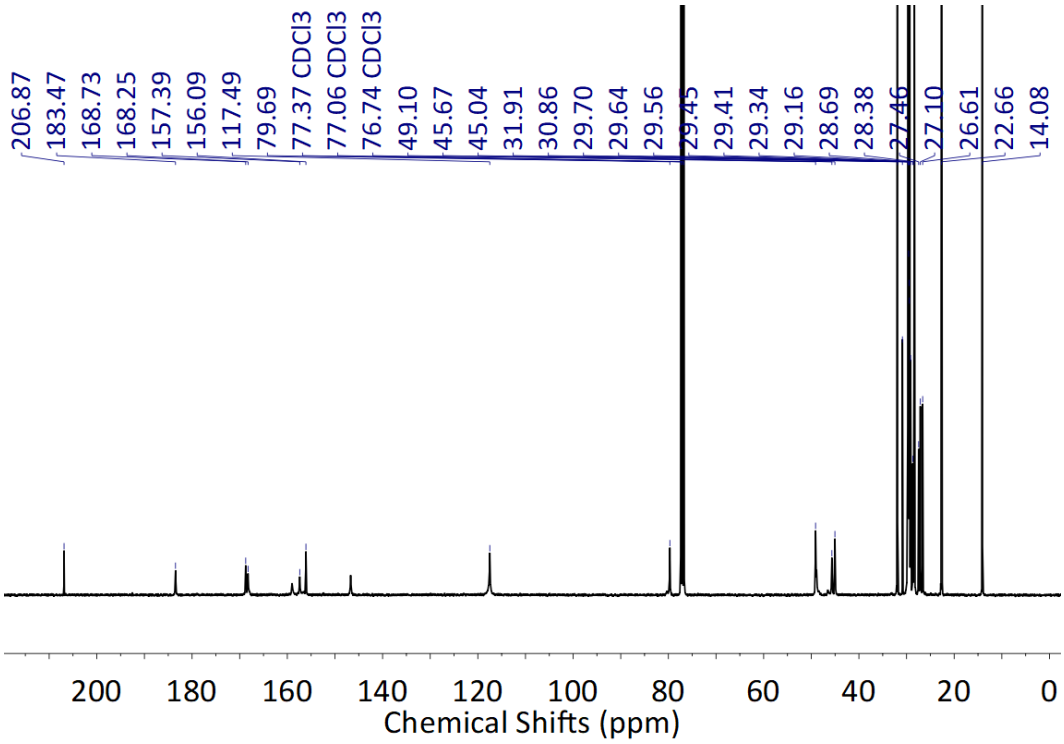
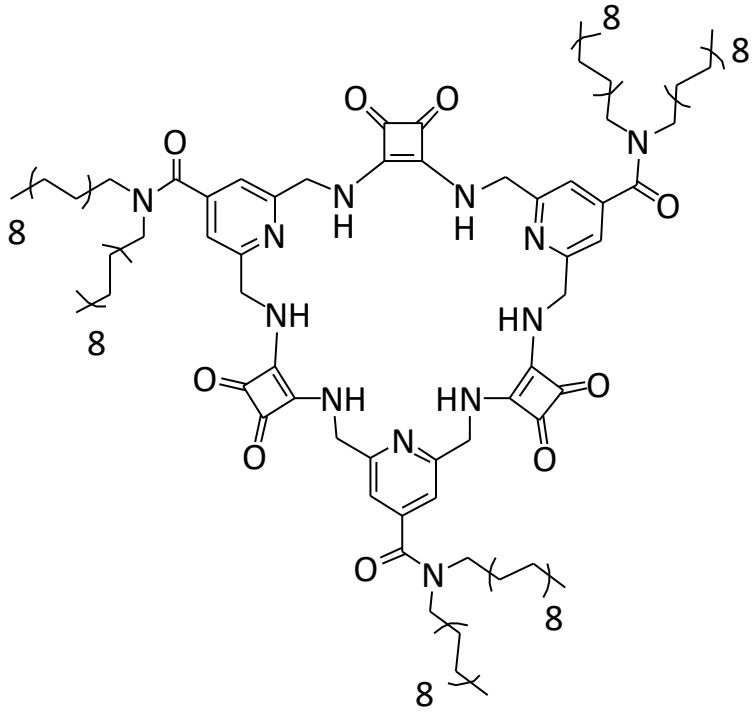


Figure S22 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K). (Acetone peaks: 206.87, 30.86)

Macrocycle **2**



Compound **13** (53 mg, 0.032 mmol) was dissolved in a solution of TFA/CH_2Cl_2 (1:1 v/v, 3 mL) and the reaction mixture was stirred at room temperature for 2 hours, then concentrated under reduced pressure. The solid was washed with 5% $NaHCO_3$ solution (5 mL) then dried under stream of N_2 (g). The resulting solid was dissolved in 20 mL toluene and then added to a solution of **9** (30 mg, 0.032 mmol) and $TBAH_2PO_4$ (10.8 mg, 0.032 mmol) in EtOH/toluene/hexane 10/45/45 v/v/v (500 mL) and stirred at 60℃ for 48 hrs. The solvent was then removed under reduced pressure to give a yellow solid. Subjection of this material to flash silica gel chromatography (1/99 to 5/95 v/v methanol/dichloromethane elution) and concentration of the appropriate fractions (R_f 0.3) gave compound **2** (42 mg, 58%) as a beige solid. **M.p.** 252 – 258 ˚C (decomp.); **^{1}H NMR** (400 MHz, $CDCl_3$): 0.86 (t, *J* = 6.8 Hz, 18 H), 0.98 – 1.41 (m, 180 H), 1.38 – 1.55 (m, 6 H), 1.55 – 1.69 (m, 6 H), 3.08 (t, *J* = 7.7 Hz, 6 H), 3.42 (t, *J* = 7.7 Hz, 4 H), 4.9 (br s, 12 H), 7.1 (s, 6 H), 7.7 (br s, 6 H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 189.29, 183.18, 177.99, 172.37, 168.08, 155.74, 147.20, 147.20, 118.25, 69.92, 48.98, 44.97, 31.92, 29.70, 29.65, 29.46, 29.41, 29.35, 29.19, 28.75, 27.46, 27.08, 26.68, 26.62, 22.68, 15.86, 14.10; **HRMS** (ESI, MeOH) calcd. for $C_{144}H_{246}N_{12}O_9H_2$ $[M + 2H]^{2+}$ 1144.9653, found 1144.9645; **ν_{max} (film)/cm^{-1}:** 3254 (broad), 2920, 2851, 1598, 1535, 1466.

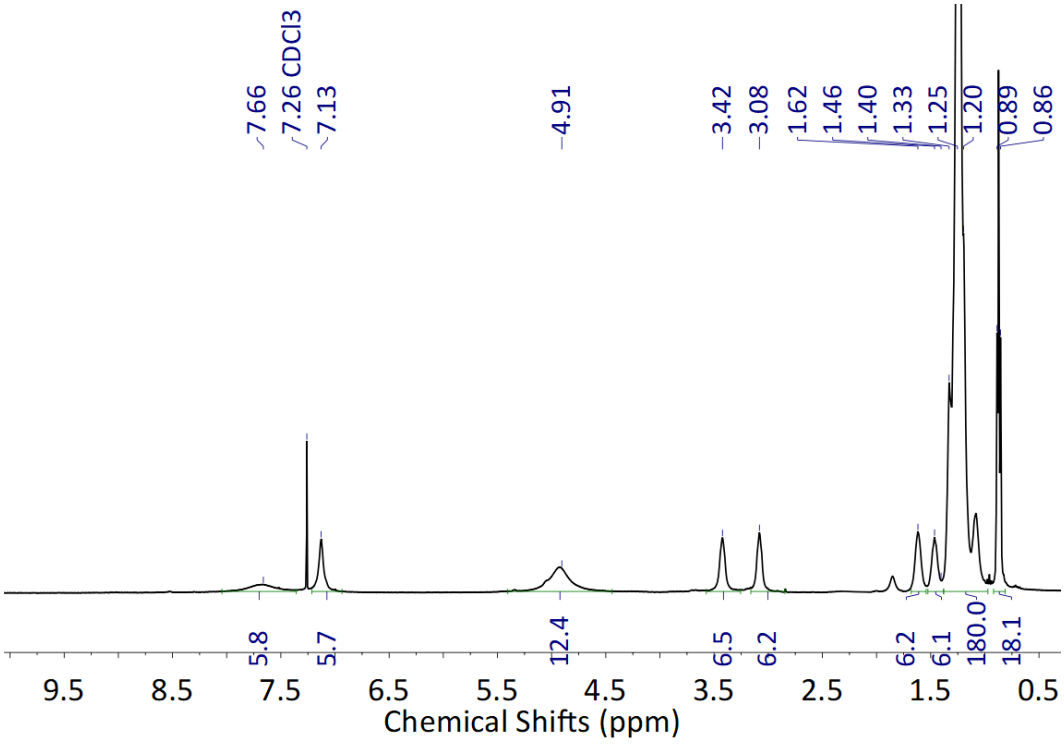


Figure S23 ^{1}H NMR ($CDCl_3$, 400 MHz, 300 K).

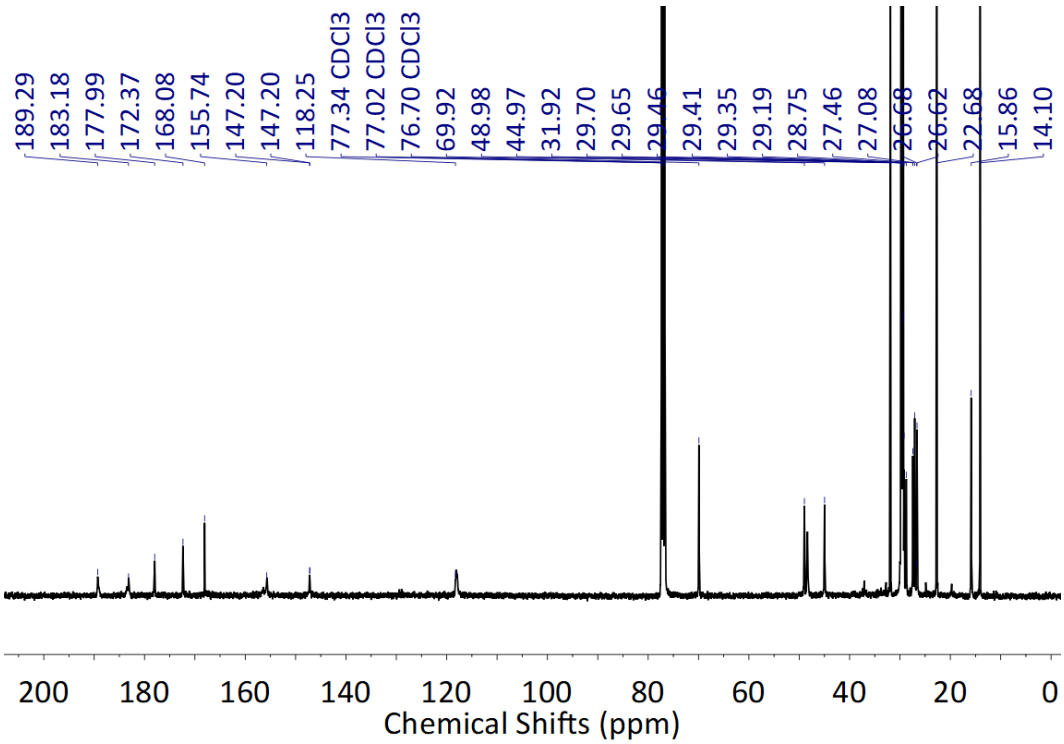


Figure S24 ^{13}C NMR ($CDCl_3$, 100.6 MHz, 300 K).

^{1}H NMR Binding studies

Both salt and receptor were dried under high vacuum for 48 hours prior to use. A 2.5 mM stock solution of the receptor was accurately prepared in the stated deuterated solvents using a volumetric flask. Tetrabutylammonium (TBA) sulfate or nitrate to be titrated were weighed into separate 2 mL vials, and 200 µL deuterated solvents (v/v) containing 2.5 mM receptors were added to anions using pipettes (Eppendorf). The concentration of anion was approximately 70 times that of the host (i.e. 160 – 180 mM). In each case, 550 µL of host solution in an NMR tube was titrated with aliquots of anion stock solution, and after each addition, the ^{1}H NMR spectrum was recorded on a Bruker Avance III 400 or Bruker Avance III 500 spectrometer after thorough mixing at 300 K. Typically, additions were performed in the following order: 10 × 1.5 µL, 2 × 7.5 µL, 4 × 14 µL (total 86 µL). Typically, a total of at least 12 equiv. of anion was added to the receptor solutions.

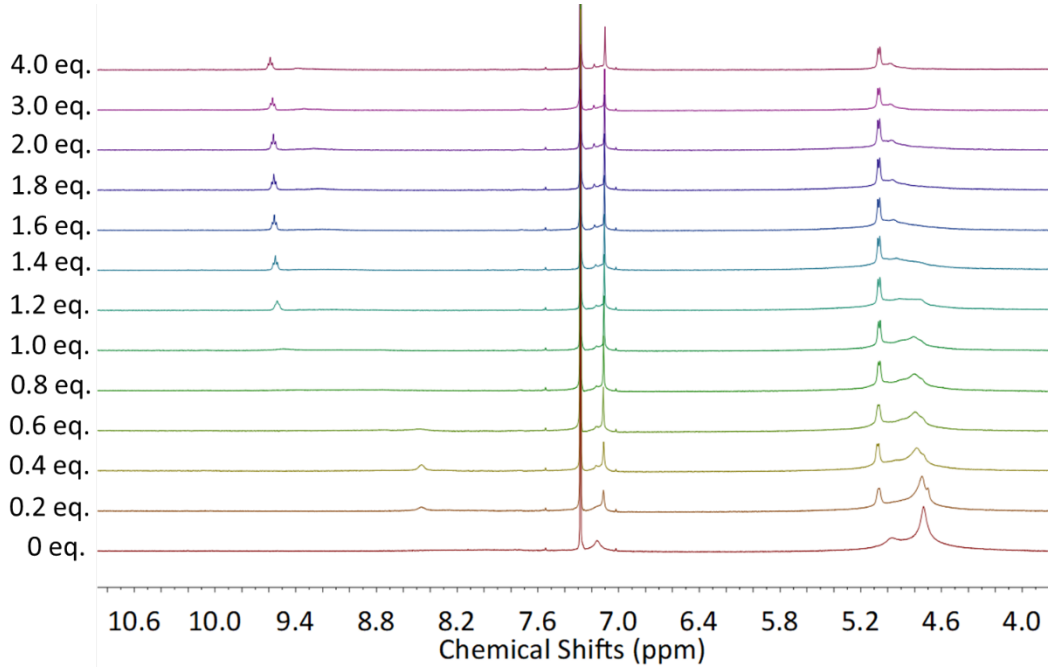


Figure S25. Titration of **2** with 0.0 – 4.0 equiv. $(TBA)_2SO_4$ in H_2O saturated $CDCl_3$.

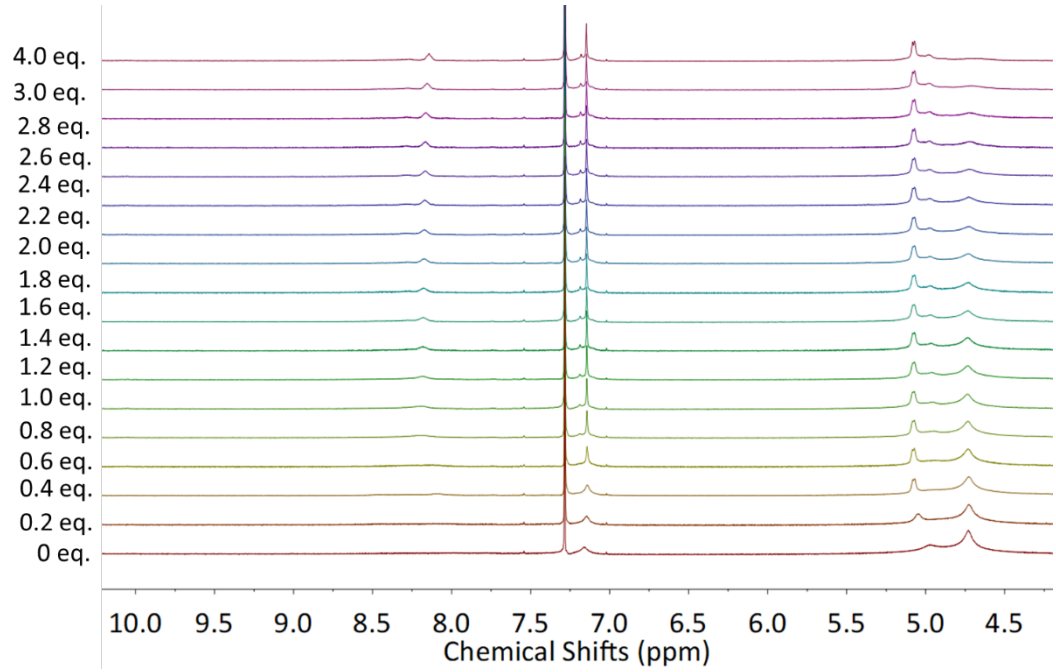


Figure S26. Titration of **2** with 0.0 – 4.0 equiv. $TBANO_3$ in H_2O saturated $CDCl_3$.

Sulfate extraction procedure

The ability of macrocycles **1** and **2** to extract sulfate ions from aqueous solution was qualitatively investigated using a liquid-liquid extraction technique monitored by ^1H NMR. Two methods were used as follows:

(i) To evaluate the direct sulfate extraction ability, an aqueous solution (Milli-Q water, type I) containing TBA_2SO_4 or Na_2SO_4 was layered on a $CDCl_3$ solution containing either **1** or **2**.

(ii) To evaluate the sulfate-nitrate ion exchange ability, an aqueous solution (Milli-Q water, type I) containing Na_2SO_4 was layered on a $CDCl_3$ solution containing either **1** or **2** and 2.0 eq. $TBANO_3$.

The mixtures were mixed at 3000 rpm for 1 min using a Vortex mixer (VELP® ZX4 Advanced IR Vortex Mixer) to ensure efficient diffusion of two layers with subsequent centrifugation (Camlab® Choice D1008 mini centrifuge) for 1 min. The organic layer was then separated and screened by ^1H NMR.

Extraction using Macrocycle 1

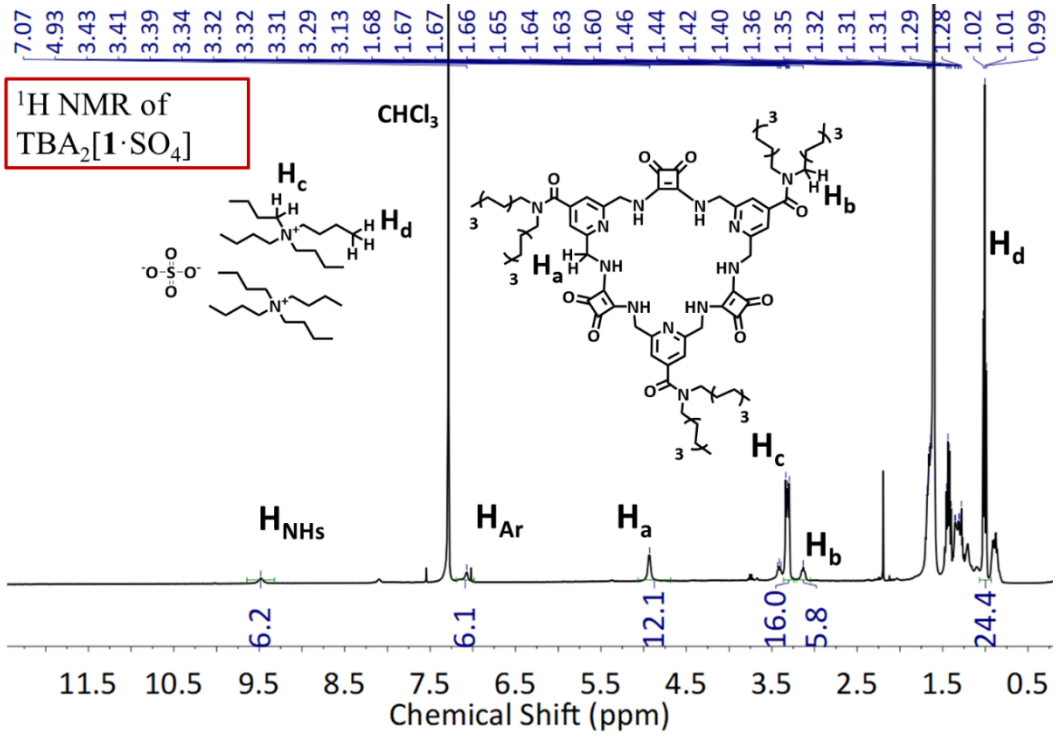


Figure S27. ^{1}H NMR of the precipitate formed upon shaking compound **1** with $(TBA)_2SO_4$. Stoichiometry of the resulting **1**·SO_4 complex was determined as 1:1 by integration of the macrocycle proton signals for H_a, H_b, H_{Ar} and H_{NH} and the tetrabutylammonium signals for H_c and H_d. The chemical shift of the macrocycle NH signal (δ 9.5 ppm) is comparable to that observed at the endpoint of the direct titration of **1** with $(TBA)_2SO_4$ in $CDCl_3$.

Extraction using Macrocycle **2**

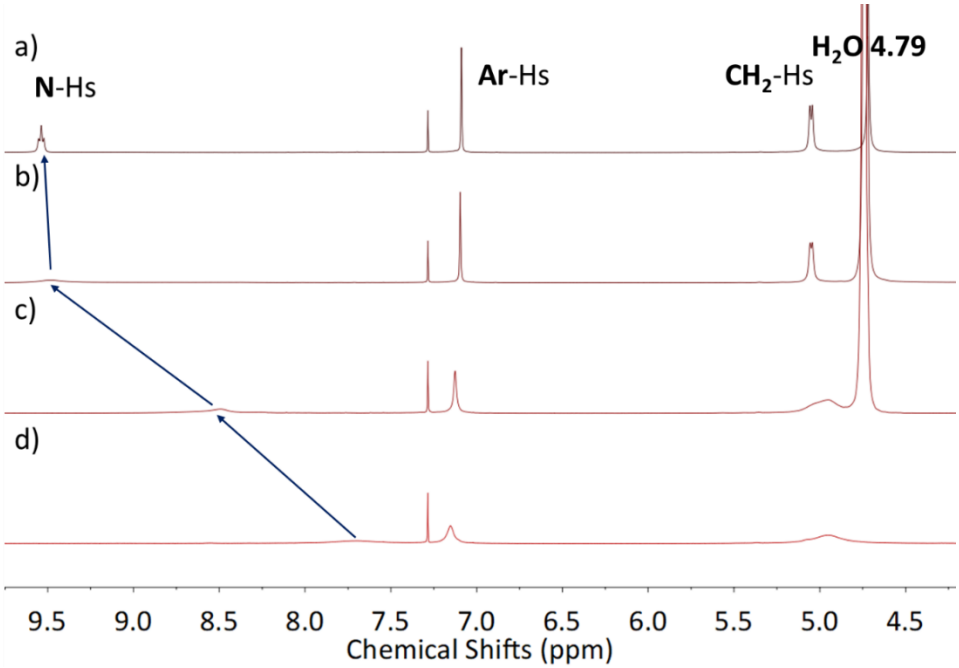


Figure S28. L-L sulfate extraction using **2** (45 mM) in $CDCl_3$ with aqueous solutions containing a) 150 mM $(TBA)_2SO_4$; b) 50 mM $(TBA)_2SO_4$; c) 25 mM $(TBA)_2SO_4$; d) H_2O.

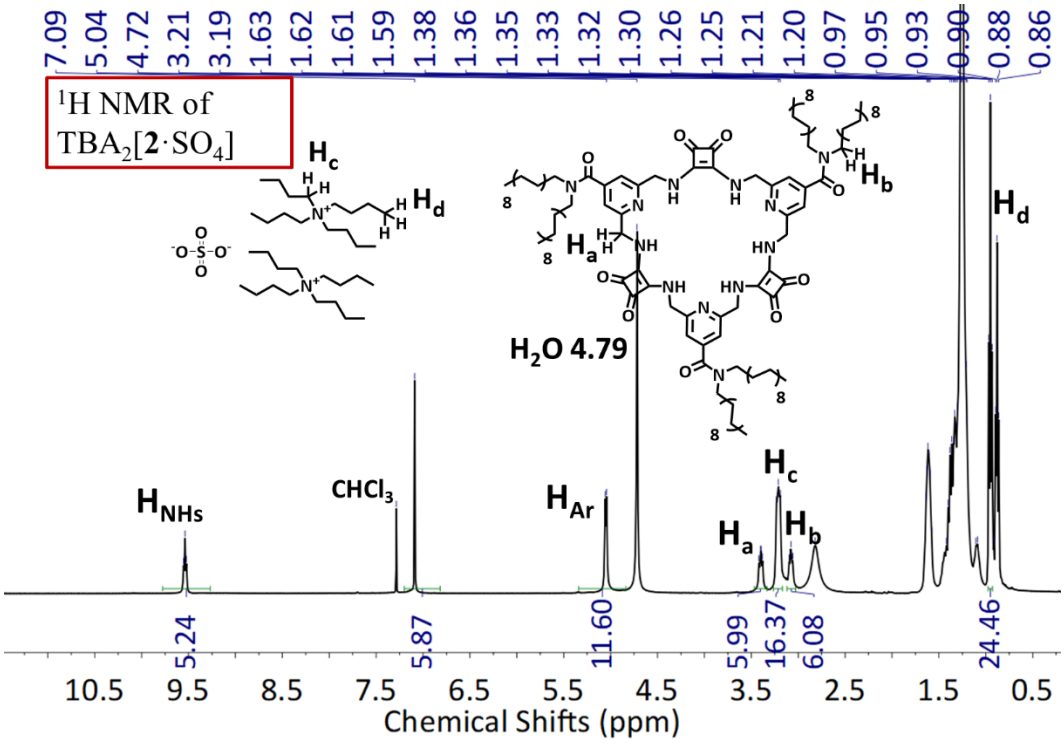


Figure S29. ^1H NMR of **2** (45 mM) in $CDCl_3$ after shaking with an aqueous solution containing 150 mM $(TBA)_2SO_4$; Stoichiometry of the resulting **2**·SO_4 complex was determined as 1:1 by integration of the macrocycle proton signals for H_a, H_b, H_{Ar} and H_{NH} and the tetrabutylammonium signals for H_c and H_d.

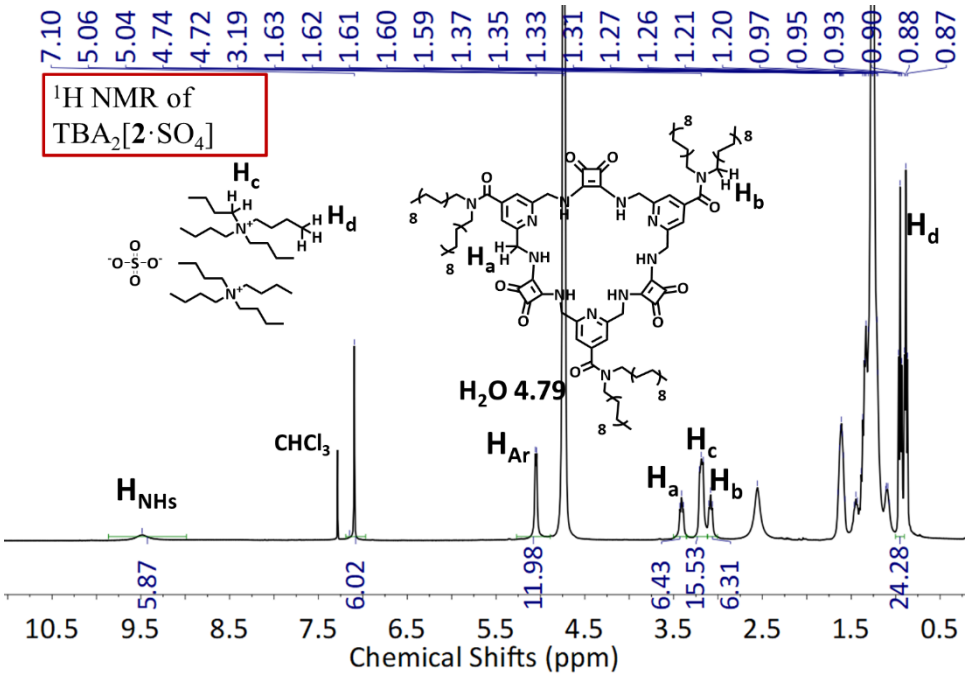


Figure S30. ^{1}H NMR of **2** (45 mM) in $CDCl_3$ after shaking with an aqueous solution containing 50 mM $(TBA)_2SO_4$; Stoichiometry of the resulting **2**·SO_4 complex was determined as 1:1 by integration of the macrocycle proton signals for H_a, H_b, H_{Ar} and H_{NH} and the tetrabutylammonium signals for H_c and H_d.

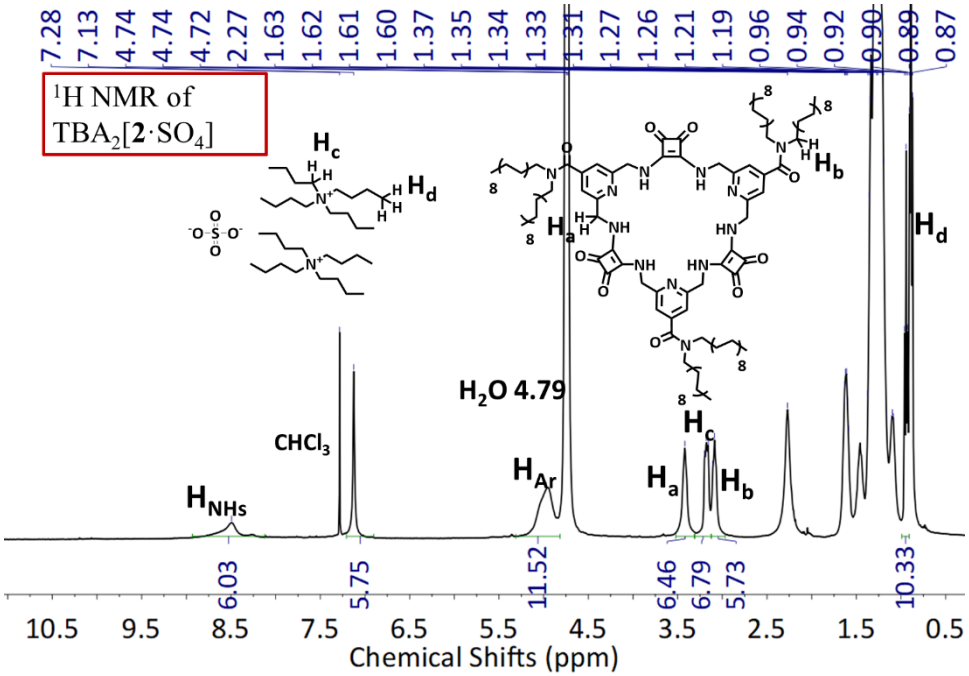


Figure S31. ^{1}H NMR of **2** (45 mM) in $CDCl_3$ after shaking with an aqueous solution containing 25 mM $(TBA)_2SO_4$. Stoichiometry of the resulting **2**·SO_4 complex was determined as 9:5 by integration of the macrocycle proton signals for H_a, H_b, H_{Ar} and H_{NH} and the tetrabutylammonium signals for H_c and H_d.

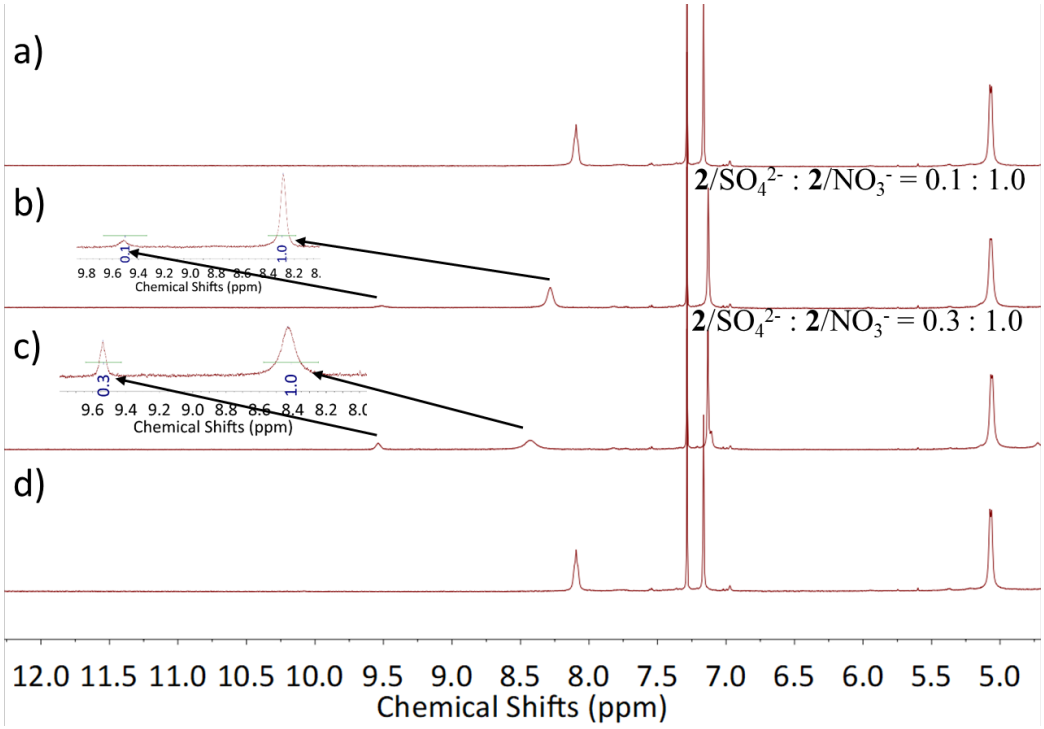


Figure S32. Sulfate-nitrate exchange experiments. Conditions: a) Aqueous: 20 mM Tris buffer (pH 7.4); $CDCl_3$: 5 mM of [3]MSQ **2** with 2.0 eq. $TBANO_3$. b) Aqueous: 500 mM Na_2SO_4 in 20 mM Tris buffer (pH 7.4); $CDCl_3$: [3]MSQ **2** with 2.0 eq. $TBANO_3$. c) Aqueous: 500 mM Na_2SO_4 in 20 mM (pH 3.2, HNO_3); $CDCl_3$: [3]MSQ **2** with 2.0 eq. $TBANO_3$. d) Wash of solution c) with 100 mM $Ba(NO_3)_2$.

U-tube transport studies

Source phase **A** (300 µL) and receiving phase **B** (300 µL) were prepared using analytical grade salts and Milli-Q water. The chloroform phase **C** (900 µL) was stirred at 300 rpm during the experiment to ensure efficient diffusion. Samples were collected every 3 days, and after 21 days, the experiment was stopped. The sulfate concentration was analyzed by following methods:

(i) Where no Ba^{2+} was present in phase **B** (Table S1, Exp 1 and 2), sulfate concentration was measured via a addition of known amount of $BaCl_2$ (excess) to form a $BaSO_4$ precipitate (K_{sp} = 1.084 × 10^{-10}, 25 °C), followed by centifuation and analysis of the non-precipitated Ba^{2+} concentration using inductively coupled plasma mass spectrometry (ICP-MS, PerkinElmer® NexION™ 300).

(ii) Where Ba^{2+} was present in receiving phase **B** resulting in precipitation of $BaSO_4$ (Table S1, Exp 3 – 5), following centrifugation of phase **B**, the concentration of the remaining non-precipitated Ba^{2+} was analysed using ICP-MS.

(iii) In all experiments, the final sulfate concentration was also measured by ICP-MS via the concentration of sulfide.[3-4]

All transport conditions are listed in Table S1 and Table S4. Working curves were prepared using comercially available PerkinElmer® multi-element mixed standard solutions with $y[Ba^{2+}] = 0.011x + 0.000$ ($R^2 = 0.9999$; DL: 0.1146 ppb) and $y[SO_4^{2-}] = 0.015x + 0.000$ ($R^2 = 0.9942$; DL: 552 ppb). Concentrations (mM) of sulfate and barium were calculated based on working curves with estimated error < 5%. All transport experiments were performed in at least duplicate giving values with estimated error < 15%.

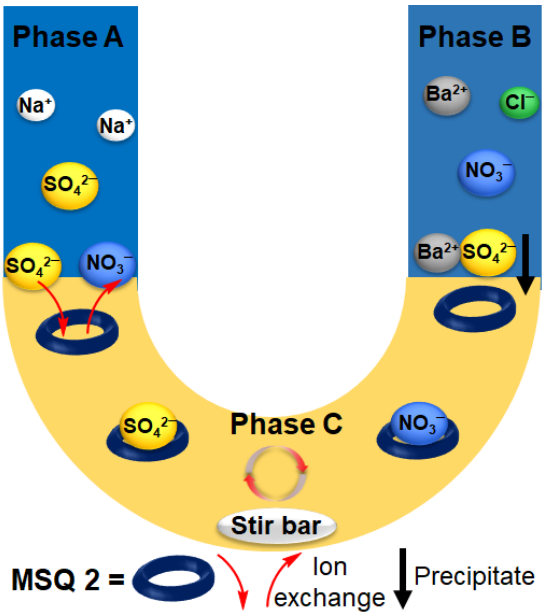


Figure S33. Illustration of U-tube transport experiment.

Table S1. Conditions for U-tube transport experiments

Exp	Source phase A (300 µL)	Receiving phase B (900 µL)	Organic phase C (300 µL)
1	500 mM Na_2SO_4 in 20 mM Tris buffer (pH 7.4)	20 mM Tris buffer (pH 7.4)	10 mM **2** in $CHCl_3$
2	500 mM Na_2SO_4 in 20 mM Tris buffer (pH 7.4)	20 mM Tris buffer (pH 7.4)	10 mM **2** and 50 mM $TBANO_3$ in $CHCl_3$
3	500 mM Na_2SO_4 in 20 mM Tris buffer (pH 7.4)	300 mM $BaCl_2$ in 20 mM Tris buffer (pH 7.4)	10 mM **2** and 50 mM $TBANO_3$ in $CHCl_3$
4	500 mM Na_2SO_4 in H_2O (pH 3.2, HNO_3)	300 mM $BaCl_2$ in H_2O (pH 3.2, HNO_3)	10 mM **2** and 50 mM $TBANO_3$ in $CHCl_3$
5	500 mM Na_2SO_4 in H_2O (pH 9.4, NaOH)	300 mM $BaCl_2$ in H_2O (pH 9.4, NaOH)	10 mM **2** and 50 mM $TBANO_3$ in $CHCl_3$
6	500 mM Na_2SO_4 in 20 mM Tris buffer (pH 7.4)	300 mM $BaCl_2$ in 20 mM Tris buffer (pH 7.4)	50 mM $TBANO_3$ in $CHCl_3$

Table S2. $[SO_4^{2-}]$/mM in the receiving phase calculated based on the concentration of Ba^{2+} detected by ICP-MS*

Days	Exp 1	Exp 2	Exp 3	Exp 4	Exp 5	Exp 6
0	$< 10^{-6}$	$< 10^{-6}$	$< 10^{-6}$	$< 10^{-6}$	$< 10^{-6}$	$< 10^{-6}$
3	$< 10^{-6}$	2.4609	5.407	5.906	4.639	$< 10^{-6}$
6	$< 10^{-6}$	4.6954	10.642	11.269	8.919	$< 10^{-6}$
9	$< 10^{-6}$	7.0609	16.008	16.946	12.789	$< 10^{-6}$
12	$< 10^{-6}$	9.2542	20.900	22.210	16.718	$< 10^{-6}$
15	$< 10^{-6}$	11.2334	25.880	26.960	20.543	$< 10^{-6}$
18	$< 10^{-6}$	13.0710	30.218	31.370	23.713	$< 10^{-6}$
21*	$< 10^{-6}$	14.8618	34.408	35.668	26.198	$< 10^{-6}$

* The final sulfate concentrations in each experiment were also measured by ICP-MS via the concentration of sulfide, which gave similar results to those measured by Ba^{2+} ions (Table S3).

Table S3. The final $[SO_4^{2-}]$/mM concentration in each experiment measured by ICP-MS.*

Days	Exp 1	Exp 2	Exp 3	Exp 4	Exp 5	Exp 6
21*	$< 10^{-6}$	15.861	32.730	34.020	26.210	$< 10^{-6}$

* Values measured via sulfide differ by less than 5% from those measured indirectly via Ba^{2+} ions.

Table S4. Conditions for competitive U-tube transport experiments

	Source phase A	Receiving phase B	Organic phase C
1	100 mM Na_2SO_4 and Na_2HPO_4, 500mM $NaNO_3$ and NaCl (pH 7.4)	300 mM $BaCl_2$ (pH 7.4)	50 mM $TBANO_3$ $CHCl_3$
2	100 mM Na_2SO_4 and Na_2HPO_4, 500mM $NaNO_3$ and NaCl (pH 7.4)	300 mM $BaCl_2$ (pH 7.4)	10 mM receptor **2** and 50 mM $TBANO_3$ in $CHCl_3$

Table S5. $[SO_4^{2-}]$/mM in the receiving phase calculated based on the concentration of Ba^{2+} detected by ICP-MS.

Days	Exp 1	Exp 2
21	$< 10^{-6}$	3.210

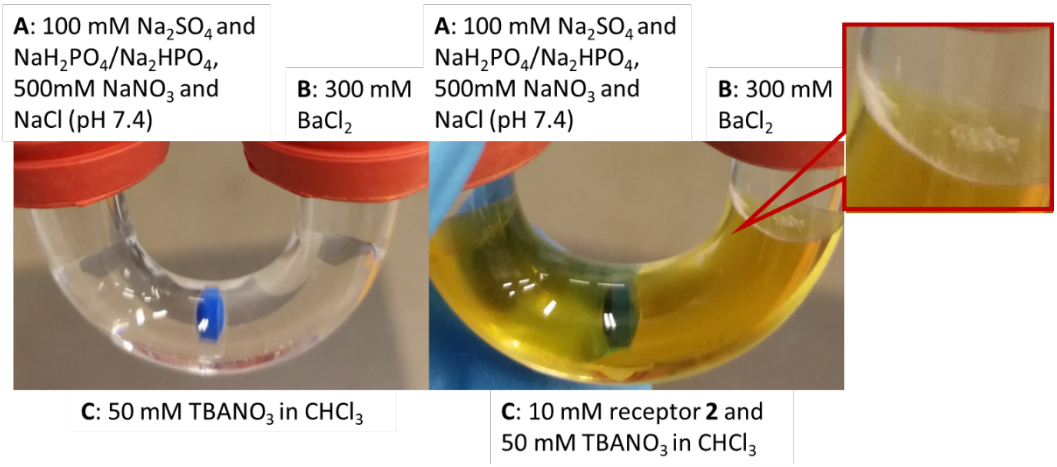


Figure S34. Selected pictures of sulfate transport: blank (left) and compound **2** (right) at 21 days.

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