Supporting Information

Triamide macrocyclic chloride receptors via a one-pot tandem reduction-condensation-cyclization reaction

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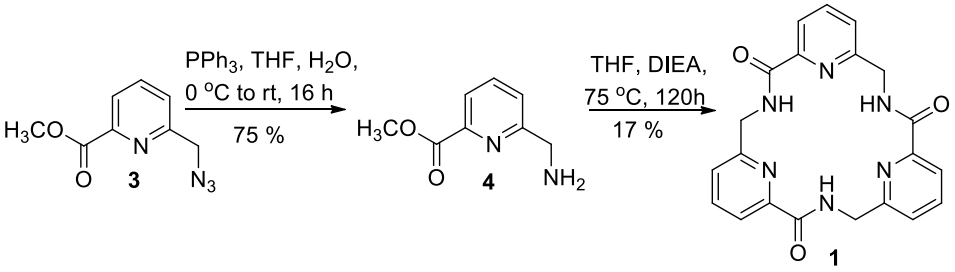
General methods

All air-sensitive experiments were carried out using oven-dried glassware under nitrogen atmosphere using standard schlenk-techniques. Oven-dried cannula or syringe was used to transfer air-sensitive solvents and solutions. All the reagents were purchased from commercial suppliers and used without further purification unless stated otherwise. Molecular sieves were activated in vacuo at 100 °C for 5 h. Ethyl acetate (EA), dichloromethane (DCM), methanol (MeOH) and hexane (Hex) for routine use such as work-up and chromatography were purified by simple distillation. Solvents for reactions were distilled from the requisite drying agent and stored over activated 4 Å molecular sieves. Tetrahydrofuran (THF) was distilled from sodium benzophenoneketyl. *N*, *N*-diisopropylethylamine (DIEA), dichloromethane and acetonitrile were distilled from calcium hydride. Methanol was distilled from magnesium methoxide. *N*, *N*-dimethylformamide (DMF) was dried over activated 4 Å molecular sieves at least 24 h prior to the experiment. For ester bond formation, 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) was used as coupling reagent. For flash column chromatography, silica gel (200-400 mesh) was purchased from Acme chemicals. Analytical Thin layer chromatography (TLC) was performed on MERCK precoated silica gel 60 F254 TLC plates.

NMR spectra were recorded with Bruker 400 or Bruker 500 spectrometers using $CDCl_3$, CD_3CN or DMSO-d_6 as solvents and referenced using residual solvent peaks as the standard. The NMR chemical shift (δ) and coupling constant (*J*) values were reported in parts per million (ppm) and Hertz (Hz), respectively. Spin multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), quintet (quint), apparent quintet (app. quint.), multiplet (m). High resolution mass spectra (HRMS) were recorded on the MICRO-Q-TOF mass spectrometer using the ESI technique. FT-IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. KBr pellets were used to record the IR spectra. IR spectra peaks are reported in wave numbers (cm^{-1}) as strong (s), medium (m), weak (w), and broad (br).

Synthesis and analytical data of compounds

Synthesis of macrocycle 1

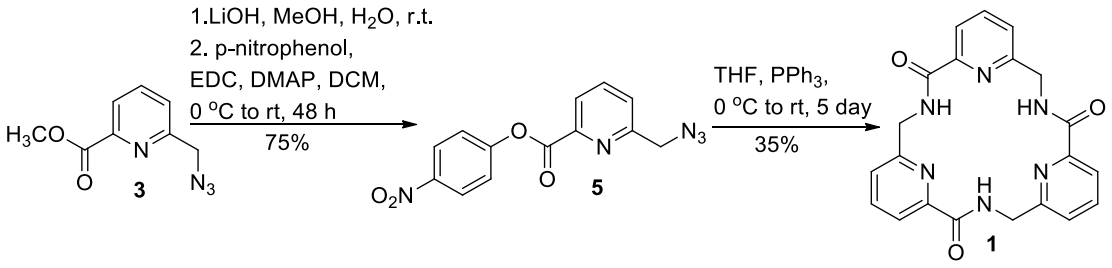


Macrocycle 1 (method 1):

A solution of azide **3** (0.98 g, 5.1 mmol, 1 equiv) in THF (10 mL) was cooled to 0 °C and PPh_3 (2.01 g, 7.6 mmol, 1.5 equiv) was added over a period of 5 min. Subsequently, the reaction mixture was allowed to warm to room temperature and stir for 16 h. Water (6 mL) was added to the reaction mixture and the resulting solution was further allowed to stir for 1 h. The solvents were concentrated in vacuo to give a yellow solid, which was purified by flash column chromatography (DCM/MeOH, 96:4) to afford 0.64 g (75 %) of the corresponding amine **4** as a yellow oil. TLC R_f = 0.3 (DCM/MeOH, 96:4).

To a solution of aromatic amino acid **4** (0.31g, 1.87 mmol, 1 equiv) in THF (40 mL), DIEA (1.13 mL, 6.54 mmol, 3.5 equiv) was added. The reaction mixture was allowed to reflux at 75 °C for 120 h. The organic solvents were removed in vacuo to give a yellow solid, which was purified by flash column chromatography (Hex/EA/MeOH, 65:30:5) to afford 0.043 g (17%) of the macrocycle **1** as a white solid. TLC R_f = 0.42 (Hex/EA/MeOH, 55:40:5).

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.87 (bs, 3H; N*H*), 8.18 (d, *J* = 7.6 Hz, 3H; H_{Ar}), 7.86 (t, *J* = 7.6 Hz, 3H; H_{Ar}), 7.49 (d, *J* = 7.6 Hz, 3H; H_{Ar}), 4.84 (d, *J* = 5.6 Hz, 6 H; CH_2); **^{13}C NMR** (125 MHz, $CDCl_3$, 25 °C): δ 164.1, 155.7, 149.9, 138.6, 125.5, 121.8, 44.3; **IR** (KBr pellet): ν 3334(br, s), 2922(s), 1674(s), 1596(s), 1444(s), 992(m), 829(m), 764(m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_{21}H_{18}N_6O_3Na$ (MNa^+), 425.1338, found 425.1350.



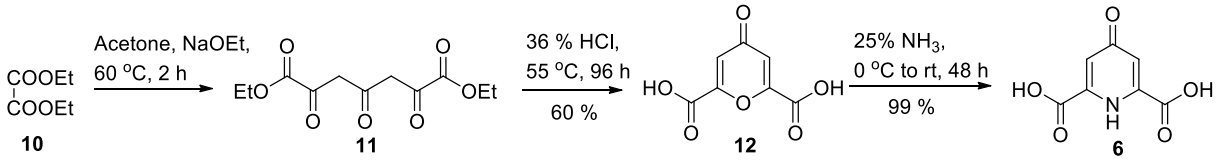
Macrocycle 1 (method 2):

To a solution of compound **3** (0.3 g, 1.56 mmol, 1 equiv) in MeOH and water (9 mL, 2:1 v/v), LiOH (0.2 g, 4.6 mmol, 3 equiv) was added. After completion of reaction, MeOH was removed in vacuo. The solution was diluted with water (30 mL) and washed using ethyl acetate (3 × 30 mL). The aqueous layer was acidified using 5% aqueous HCl and extracted using ethyl acetate (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated in vacuo to get 0.27 g of the desired acid which was used for the next step without further purification. A solution of acid (0.27 g, 1.51 mmol, 1 equiv) and *p*-nitrophenol (0.21 g, 1.51 mmol, 1 equiv) in DCM was cooled to 0 °C. EDC (0.4 g, 2.27 mmol, 1.5 equiv), followed by DMAP (0.09 g, 0.8 mmol, 0.5 equiv) were added to the solution over a period of 5 min. The reaction mixture was allowed to warm to room temperature and stir for 48 h. After completion of reaction, DCM was removed. The residue was dissolved in ethyl acetate (50 mL) and sequentially washed with water (3 × 30 mL) and saturated aqueous $NaHCO_3$ (10 × 30 mL). The organic layer was concentrated in vacuo and the residue was purified by flash column chromatography (Hex/EA, 90:10) to afford 0.34 g (75 %) of compound **5** as yellow solid. TLC R_f = 0.23 (Hex/EA, 80:20).

A solution of azide **5** (0.082 g, 0.27 mmol, 1 equiv) in THF (120 mL) was cooled to 0 °C and PPh_3 (0.108 g, 0.41 mmol, 1.5 equiv) was added over a period of 5 min. Subsequently, the reaction mixture was allowed to warm to room temperature and stir for 12 h. Water (0.015 mL, 0.82 mmol, 3 equiv) was added to the reaction mixture and the resulting solution was further allowed to stir for 120 h at 75 °C. The solvents were concentrated in vacuo to give a yellow solid, which was purified by flash column chromatography (Hex/EA/MeOH, 65:30:5) to afford 8.1 mg of the macrocycle **1** as a white solid. The overall yield for two steps was 22%. TLC R_f= 0.42 (Hex/EA/MeOH, 55:40:5).

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 8.86 (bs, 3H; N*H*), 8.19 (d, *J* = 7.65 Hz, 3H; H_{Ar}), 7.87 (t, *J* = 7.7 Hz, 3H; H_{Ar}), 7.50 (d, *J* = 7.25 Hz, 3H; H_{Ar}), 4.85 (d, *J* = 5.6 Hz, 6 H; CH_2).

Synthesis of macrocycle 2



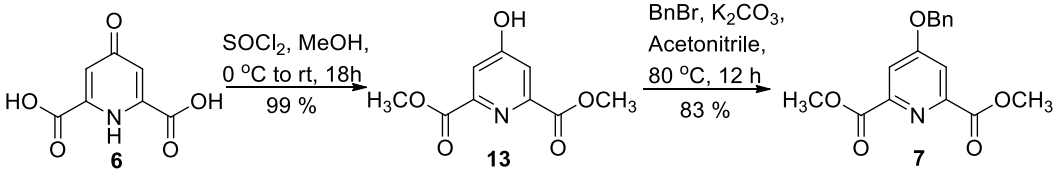
Chelidamic acid 6: [1]

To a solution of sodium ethoxide (17.02 g, 250.3 mmol, 2.0 equiv) in ethanol (60 mL), was added acetone (9.0 mL, 122.8 mmol, 1.0 equiv), diethyl oxalate **10** (38.0 g, 260.2 mmol, 2.12 equiv) and ethanol (30 mL) by using a cannula. After addition was complete, the reaction mixture was allowed to stir for 2 h at 60 °C. Subsequently, 36 % HCl (50 mL) and water (25 mL) were slowly added and the reaction mixture was further allowed to proceed for 24 h at 55 °C. Approximately 100 mL of solvent was removed in vacuo in the presence of a secondary trap. Subsequently, 36 % HCl (23 mL) and water (70 mL) were added to the residual reaction mixture and stirring was further continued for 72 h at 55 °C. The precipitated crystals were filtered and washed sequentially with water (200 mL) and acetone (100 mL). The residue was recrystallized from boiling water in the presence of charcoal (4 g) to afford 13.6 g (60 %) of compound **12** as a white solid. TLC R_f = 0.6 (10 % aqueous NaCl solution / EtOH, 30:70).

^{1}H NMR (500 MHz, DMSO-d_6, 25 °C): δ 6.86 (s, 2H; C*H*); **^{13}C NMR** (125 MHz, DMSO-d_6, 25 °C): δ 179.8, 161.0, 155.8, 117.8 ; **IR** (KBr pellet): ν 3473(br, s), 3101(w), 3072(s), 1731(s), 1648(m), 1446(m), 909(m), 871(m) cm^{-1}.

Aqueous 25 % NH_3 solution (60 mL) was added to chelidonic acid **12** (1.76 g, 9.57 mmol, 1.0 equiv) at 0 °C. The resulting suspension was allowed to warm to room temperature and stirred for 48 h. Approximately 20 mL of solvent was removed in vacuo in the presence of a secondary trap. The residue was boiled with charcoal (0.5 g) for 10 min and filtered. The filtrate was cooled to 0 °C and acidified to pH 1 with 36 % aqueous HCl solution. The white crystals obtained were isolated by filtration, washed with ice cold water and then dried in vacuo to give 1.73g (99 %) of chelidamic acid **6** as a white solid. TLC R_f = 0.33 (10 % aqueous NaCl solution / EtOH, 30:70).

^{1}H NMR (500 MHz, DMSO-d_6, 25 °C): δ 7.54 (s, 2H; H_{Ar}); **^{13}C NMR** (125 MHz, DMSO-d_6, 25 °C): δ 166.7, 165.3, 149.1, 114.8; **IR** (KBr pellet): ν 3665(br, s), 3534(br, s), 3052(w), 2952(w), 1738(m), 1671(m), 1453(m), 910(w) 875(m) cm^{-1}.



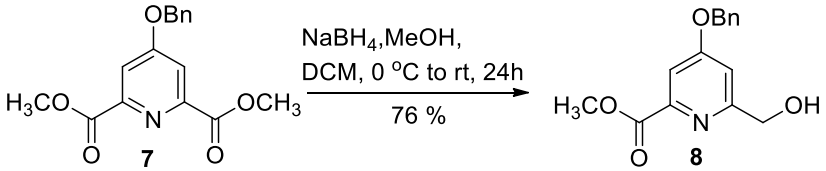
Compound 7:

To a solution of chelidamic acid **6** (0.24 g, 1.31 mmol, 1 equiv) in MeOH (8 mL) at 0 ºC, was slowly added $SOCl_2$ (0.29 mL, 3.93 mmol, 3 equiv) over a period of 5 min. Subsequently, the reaction mixture was allowed to stir for 18 h at RT. The reaction mixture was concentrated in vacuo in the presence of a secondary trap, to afford the desired product **13** (0.27 g, 99%) as a white solid, which was used for the next step without further purification. TLC R_f = 0.6 (DCM/MeOH, 95:5).

IR (KBr pellet): ν 3415(br), 3010(s), 2925(s), 1721(s), 1606(m), 1454(s), 979(s), 889(m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_9H_{10}NO_5$ (MH^+), 212.0559, found 212.0567.

To a solution of compound **13** (3.3 g, 15.6 mmol, 1 equiv) in acetonitrile (80 mL), K_2CO_3 (4.3 g, 31.3 mmol, 2 equiv) and benzyl bromide (2.17 mL, 18.8 mmol, 1.2 equiv) were added. The reaction was allowed to reflux for 12 h at 80 °C, following which it was cooled to room temperature and the inorganic salts were filtered off. The resultant filtrate was concentrated in vacuo in the presence of a secondary trap and purified by flash column chromatography (Hex/EA, 60:40) to afford 3.91 g (83 %) of compound **7** as white solid. TLC R_f = 0.23 (Hex/EA, 60:40).

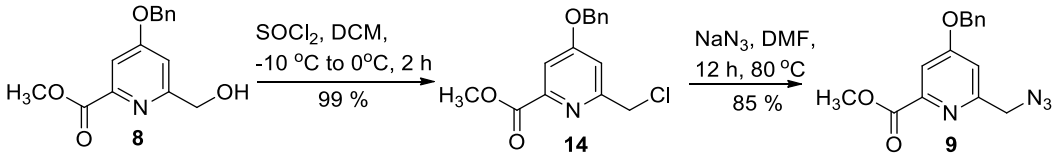
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.88 (s, 2H; H_{Ar}), 7.44-7.33 (5H; H_{Ar}), 5.21 (s, 2 H; CH_2), 3.99 (s, 6H; OCH_3); **^{13}C NMR** (100 MHz, $CDCl_3$, 25 °C): δ 166.8, 165.2, 149.9, 134.8, 129.0, 128.8, 127.8, 114.9, 70.9, 53.3; **IR** (KBr pellet): ν 3021(s), 2956(m), 1751(s), 1590(s), 1442(s), 910(w), 876(m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_{16}H_{16}NO_5$ (MH^+), 302.1028, found 302.1015.



Compound 8:

To a solution of diester **7** (1.2 g, 3.99 mmol, 1 equiv) in 2:1 DCM-MeOH (40 mL) at 0 °C, $NaBH_4$ (0.16 g, 4.15 mmol, 1.04 equiv) was added over 15 min. After the addition was complete, the reaction mixture was allowed to stir for 24 h at room temperature (first 30 min. at 0°C). Saturated aqueous NH_4Cl (50 mL) was added to the reaction mixture, following which the organic solvents were removed in vacuo. DCM (100 mL) was added and the reaction mixture was washed with water (3 × 50 mL).The organic layer was dried over Na_2SO_4 , filtered, and concentrated in vacuo. Purification by flash column chromatography (Hex/EA, 50:50) afforded 0.827 g (76 %) of compound **8** as a white solid. TLC R_f = 0.23 (Hex/EA, 50:50).

^{1}H NMR (500 MHz, DMSO-d_6, 25 °C): δ 7.51 (d, J = 2.5 Hz, 1H; H_{Ar}), 7.47 (d, J = 7.0 Hz, 2H; H_{Ar}), 7.41 (t, J = 7.0 Hz, 2H; H_{Ar}), 7.36 (tt, J = 7.5, 1.0 Hz, 1H; H_{Ar}), 7.31 (d, J = 2.5 Hz, 1H; H_{Ar}), 5.55 (t, J = 6.0 Hz, 1H; O*H*), 5.29 (s, 2H; CH_2), 4.56 (d, J = 5.5 Hz, 2H; CH_2), 3.86 (s, 3H; OCH_3); **^{13}C NMR** (125 MHz, DMSO-d_6, 25 °C): δ 165.8, 165.2 164.5, 148.4, 135.9, 128.5, 128.2, 127.8, 110.0, 109.7. 69.6, 63.8, 52.4; **IR** (KBr pellet): ν 3427(br, s), 3020(w), 2921(m), 1729(s), 1599(s), 1443(m), 910(w), 855(w), 748 (m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_{15}H_{16}NO_4$ (MH^+), 274.1079, found 274.1078.



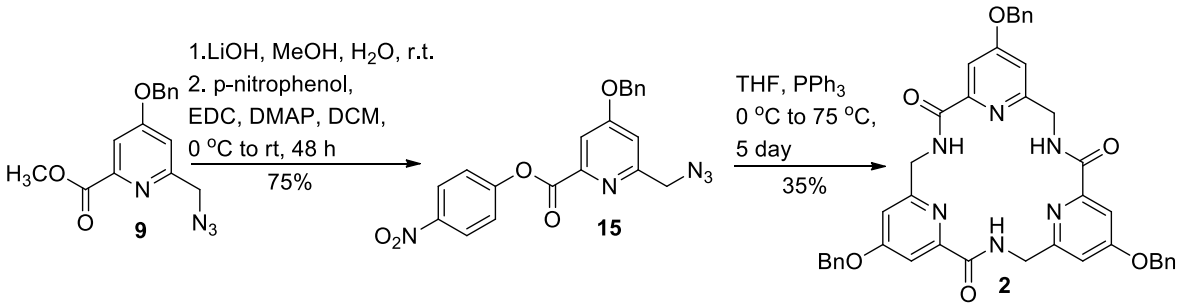
Azide 9:

To a solution of compound **8** (0.79 g, 2.89 mmol, 1 equiv) in DCM (12 mL) at -10 °C was slowly added $SOCl_2$ (0.95 mL, 13.0 mmol, 4.5 equiv). After the addition was complete, the reaction mixture was warmed to 0 °C and allowed to stir for 2 h. Solvents were removed

in vacuo in the presence of a secondary trap. The resulting suspension was dissolved in DCM (50 mL) and sequentially washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and water (2 × 50 mL). The organic layer was concentrated in vacuo to give the chloro derivative **14** (0.85 g) as a yellow oil. The product was used for the next step without further purification.

To a solution of chloro derivative **14** (0.85 g, 2.92 mmol, 1 equiv) in DMF (15 mL), NaN_3 (0.95 g, 14.6 mmol, 5 equiv) was added, following which the reaction mixture was allowed to stir at 80 °C for 12 h. DMF was removed in vacuo to give a white residue which was dissolved in DCM (150 mL) and filtered. The filtrate was concentrated in vacuo and purified by flash column chromatography (Hex/EA, 80:20) to afford 0.74 g of azo compound **9** as transparent oil. The overall yield for two steps was 84%. TLC R_f=0.27 (Hex/EA, 80:20).

^{1}H NMR (500 MHz, DMSO-d_6, 25 °C): δ 7.60 (d, J = 2.0 Hz, 1H; H_{Ar}), 7.48 (d, J = 8.0 Hz, 2H; H_{Ar}), 7.41 (t, J = 7.5 Hz, 2H; H_{Ar}), 7.36 (d, J = 7.5 Hz, 1H; H_{Ar}), 7.34 (d, J = 2.0 Hz, 1H; H_{Ar}), , 5.29 (s, 2H; CH_2), 4.55 (s, 2H; CH_2), 3.87 (s, 3H; OCH_3); **^{13}C NMR** (125 MHz, DMSO-d_6, 25 °C): δ 166.0, 164.9, 157.9, 149.1, 135.7, 128.6, 128.3, 127.9, 112.2, 110.9, 69.9, 54.2, 52.5; **IR** (KBr pellet): ν 3032(w), 2950(m), 2105(s) 1728(s), 1596(s), 1445(s), 998(w), 875(m), 743(m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_{15}H_{15}N_4O_3$ (MH^+), 299.1144, found 299.1154.



Macrocycle 2:

To a solution of compound **9** (1.1 g, 3.7 mmol, 1 equiv) in MeOH and water (40 mL, 2:1 v/v), LiOH (0.5 g, 11.1 mmol, 3 equiv) was added. After completion of reaction, MeOH was removed in vacuo. The solution was diluted with water (30 mL) and washed using ethyl acetate (3 × 30 mL). The aqueous layer was acidified using 5% aqueous HCl and extracted

using ethyl acetate (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated in vacuo to get 1.04 g of the desired acid which was used for the next step without further purification. A solution of acid (1.04 g, 3.7 mmol, 1 equiv) and *p*-nitrophenol (0.5 g, 3.7 mmol, 1 equiv) in DCM was cooled to 0°C. EDC (1.1 g, 5.49 mmol, 1.5 equiv), followed by DMAP (0.22 g, 1.8 mmol, 0.5 equiv) were added to the solution over a period of 5 min. The reaction mixture was allowed to warm to room temperature and stir for 48 h. After completion of reaction, DCM was removed in vacuo. The residue was dissolved in ethyl acetate (50 mL) and sequentially washed with water (3 × 30 mL) and saturated aqueous $NaHCO_3$ (10 × 30 mL). The organic layer was concentrated in vacuo and the residue was purified by flash column chromatography (Hex/EA, 70:30) to afford 1.13 g (76%) of compound **15** as yellow solid. The overall yield for two steps was 75 %. TLC R_f = 0.3 (Hex/EA, 70:30).

A solution of azide **15** (2.44 g, 6.0 mmol, 1 equiv) in THF (120 mL) was cooled to 0 °C and PPh_3 (2.36 g, 9.0 mmol, 1.5 equiv) was added over a period of 5 min. Subsequently, the reaction mixture was allowed to warm to room temperature and stir for 12 h. Water (0.32 mL, 18.0 mmol, 3 equiv) was added to the reaction mixture and the resulting solution was further allowed to stir for 120 h at 75 °C. The solvents were concentrated in vacuo to give a yellow solid, which was purified by flash column chromatography (DCM/Acetone, 99.5:0.5) to afford 0.505 g (35 %) of the macrocycle **2** as a pale yellow solid. TLC R_f= 0.43 (DCM/MeOH, 99:1). Trace amounts of $POPh_3$ could not be removed by column chromatography. Hence, the yield was calculated by the NMR spectroscopy.

^{1}H NMR (500 MHz, DMSO-d_6, 25 °C): δ 9.41 (t, *J* = 5.5 Hz, 3H; N*H*), 7.65-7.59($H_{Ar,}$ $POPh_3$), 7.55 (d, *J* = 2.5 Hz, 3H; H_{Ar}), 7.47 (d, *J* = 7.0 Hz, 6H; H_{Ar}), 7.41 (t, *J* = 7.0 Hz, 6H; H_{Ar}), 7.37-7.33(6H; H_{Ar}), 5.29 (s, 6H; CH_2), 4.68 (d, *J* = 5.5 Hz, 6 H; CH_2); **^{13}C NMR** (125 MHz, DMSO-d_6, 25 °C): δ 166.1, 163.3, 158.0, 151.6, 135.9, 131.53, 131.45, 128.6, 128.2, 127.9, 111.5, 107.3, 69.7, 43.6; **IR** (KBr pellet): ν 3426(br, s), 3001(m), 2920(m), 1661(m), 1598(s), 1434(m), 954(s), 842(w), 703(m) cm^{-1}; **HRMS (ESI$^+$):** calcd. for $C_{42}H_{36}N_6O_6Na$ (MNa^+), 743.2594, found 743.2586.

Crystal structure of macrocycle 1

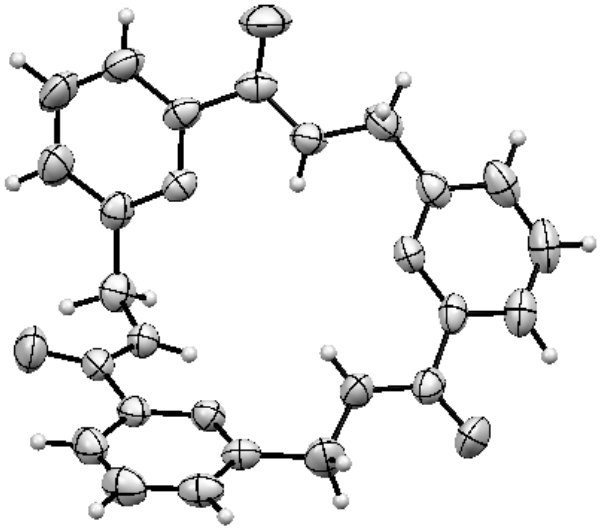


Fig. S1. ORTEP Diagram for macrocycle **1**.

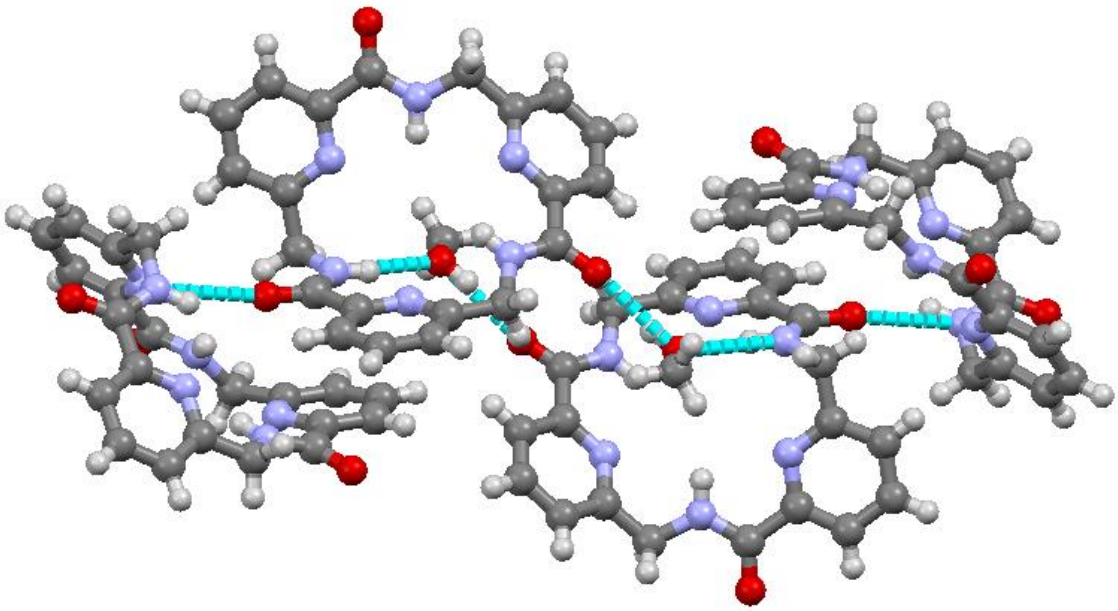


Fig. S2. Crystal structure of macrocycle **1** with MeOH entrapped.

Crystal structure of macrocycle 2

a) b)

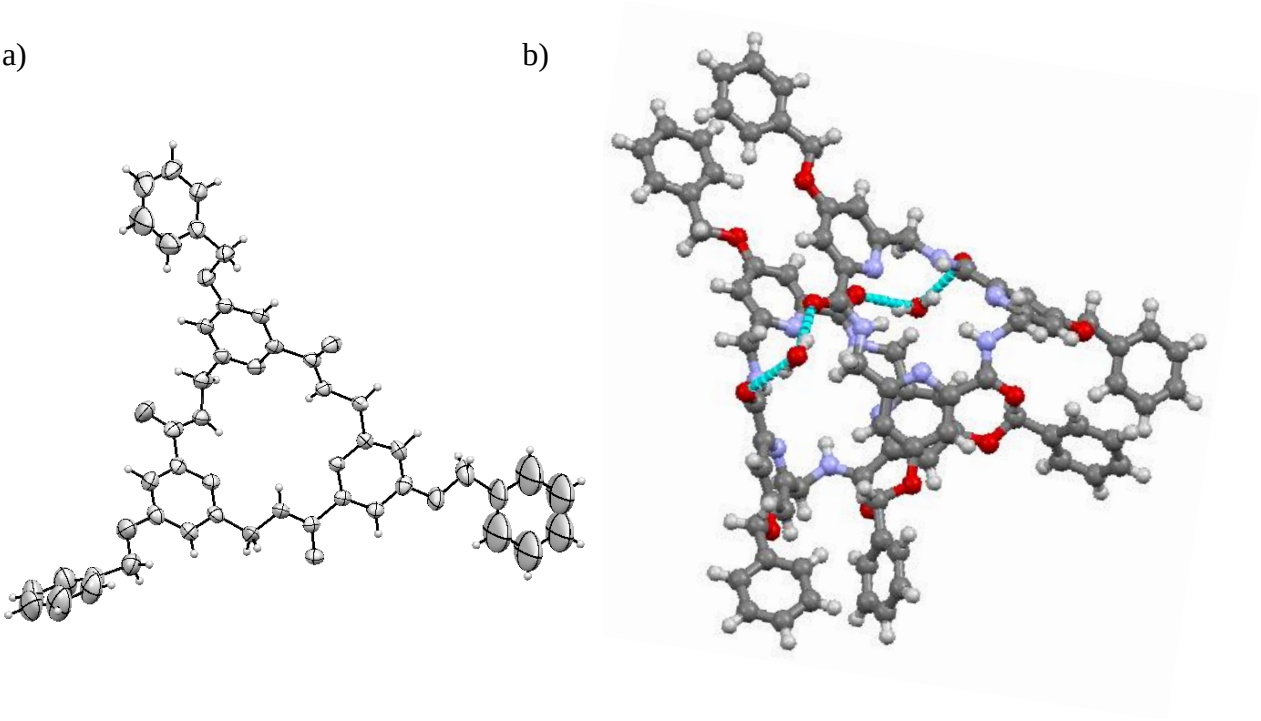


Fig. S3. a) ORTEP Diagram for macrocycle **2, b)** Solid state self-assembled crystal dimer of macrocycle **2** through H_2O molecule.

^{1}H NMR titration of macrocycle 1 (0.01 M) with Cl^- [2-5]

The hygroscopic guest $Bu_4N^+Cl^-$ and the host (macrocycle **1)** were dried under high vacuum for 12 h prior to the solution preparation. All the TBA salts were transferred and weighed in a glove box under argon atmosphere. Macrocycle **1** was dissolved in $CDCl_3$ (4 mL) to prepare the stock solution of the receptor (0.0125 M). Of this solution, 400 µL was added to each of the NMR tubes, which was then sealed in order to avoid solvent evaporation. Stock solutions of the guest (1 M) was prepared by dissolving the salt in $CDCl_3$. The requisite number of NMR samples were prepared adding increasing amounts of the guest solution (0-100 µL) to 400 µL of the host solution. All samples were made up to a final volume of 500 µL with $CDCl_3$, so that the concentration of the host (0.01 M) remained constant over the course of the experiment. The chemical shifts of amide NH protons of the macrocycle **1** were plotted against the guest concentration. The binding constants were determined using the Bindfit software.[2-5]

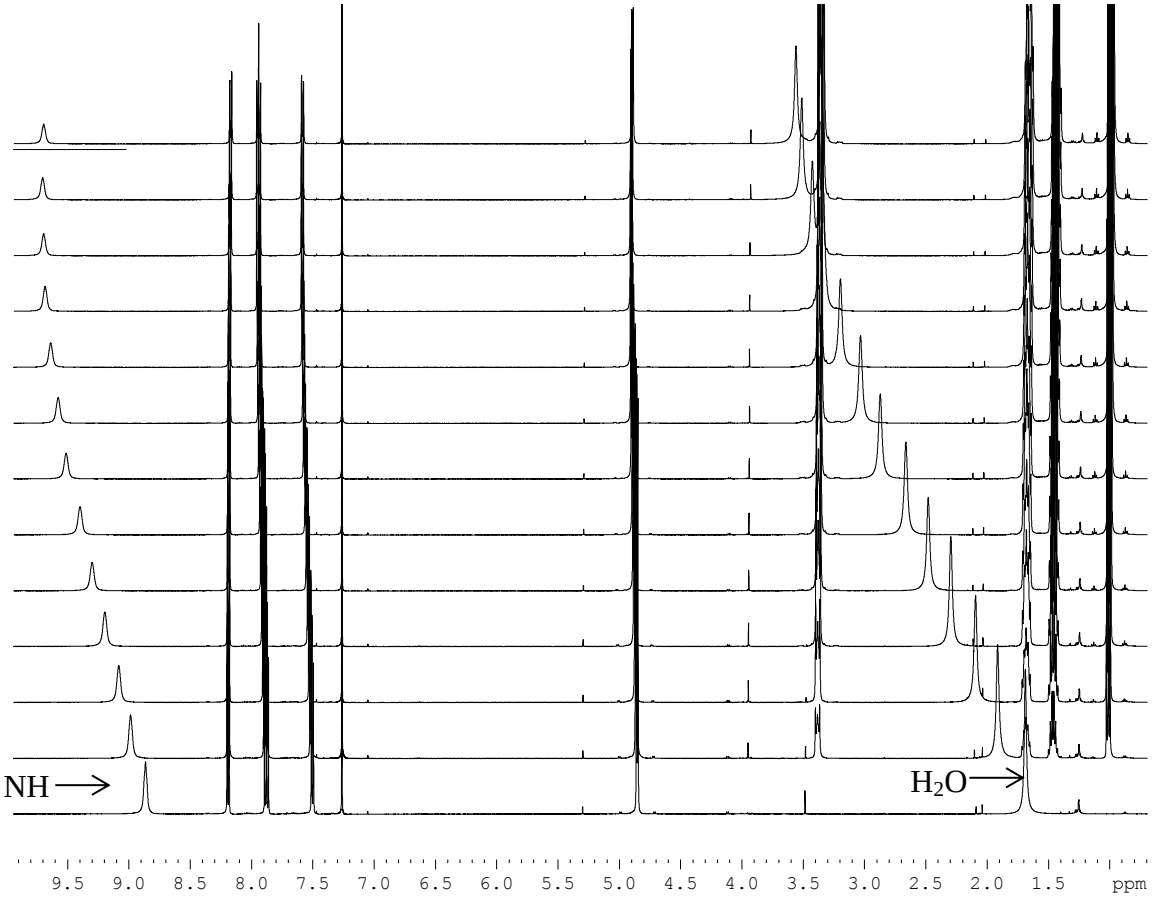


Fig. S4. Representative stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.01M) with TBACl (0- 6 equiv in increasing intervals of 0.5 equiv) in $CDCl_3$

Table S1. Representative data obtained for NMR titration of macrocycle **1** with TBACl

No.	Conc. **1** (M)	Conc. Cl^- (M)	Equiv guest	NH-δ (ppm)	H_2O-δ (ppm)
1	0.01	0	0	8.8619	1.6885
2	0.01	0.005	0.5	8.9836	1.9146
3	0.01	0.01	1	9.0802	2.0949
4	0.01	0.015	1.5	9.1937	2.2964
5	0.01	0.02	2	9.2968	2.481
6	0.01	0.025	2.5	9.3958	2.6635
7	0.01	0.03	3	9.5093	2.8722
8	0.01	0.035	3.5	9.5752	3.033
9	0.01	0.04	4	9.6353	3.1937
10	0.01	0.045	4.5	9.6806	3.35
11	0.01	0.05	5	9.6921	3.4226
12	0.01	0.055	5.5	9.7005	3.5112
13	0.01	0.06	6	9.6920	3.5597

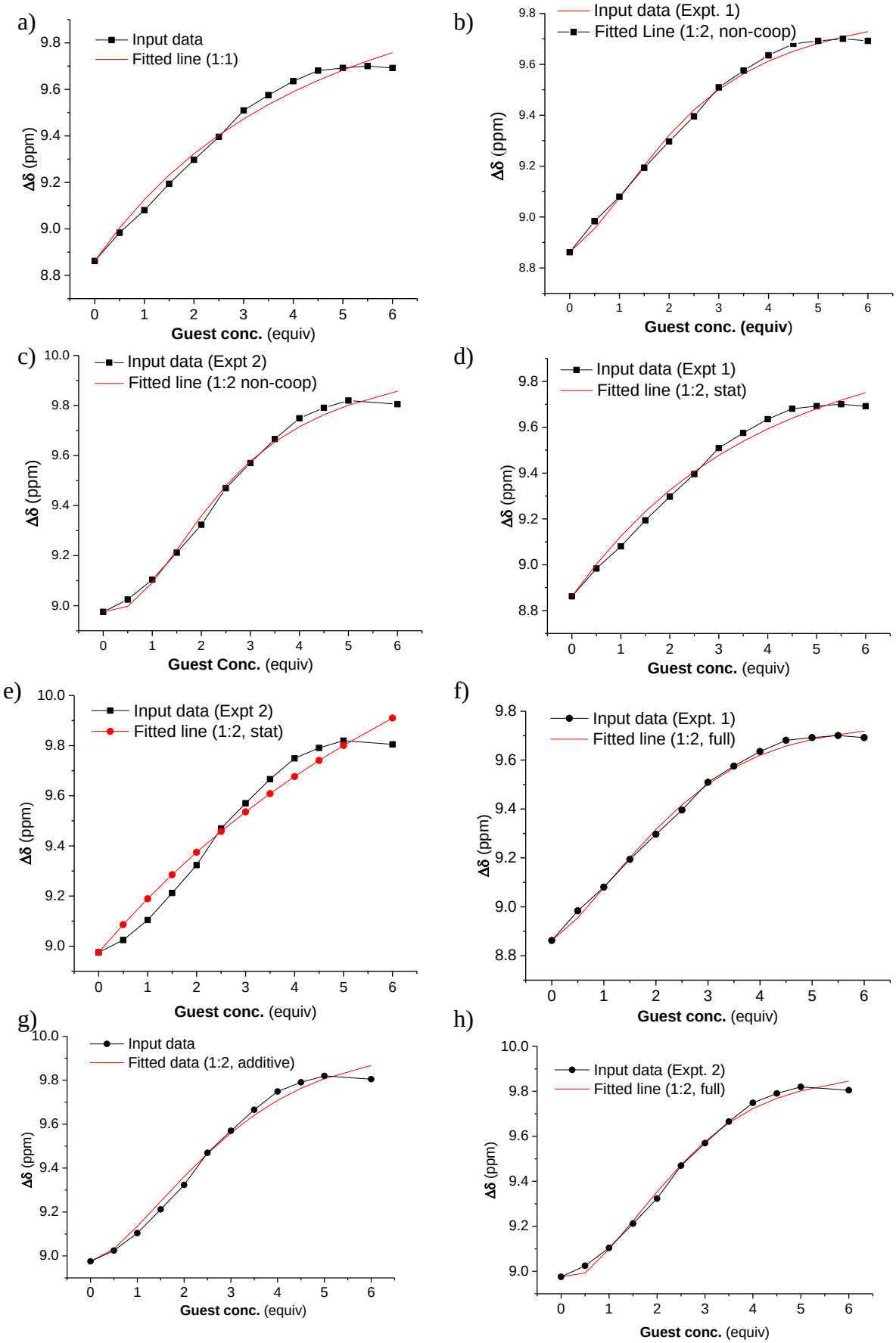


Fig. S5. Data fits a) 1:1 H-G model; 1:2 H-G models. b) Expt 1 (non-coop), c) Expt 2 (non-coop); d) Expt 1 (stat); e) Expt. 2 (stat); f) Expt. 1. (full); g) Expt. 2 (full); h) Expt. 2 (stat)

Table S2. Comparison of different models obtained using Bindfit Software.

No.	Expt	Model	K_1	K_2	δH	δHG	$δHG_2$	Cov_{fit}
1.	1	1:1[a]	24.11	n.a.	8.9	10.4	n.a.	0.015
2.	2	1:1	Fit Failed					
3.	1	1:2 (non-coop)[b]	342.99	85.75	8.9	9.0	9.9	0.005
4.	2	1:2 (non-coop)[c]	387.03	96.76	8.9	8.9	10.1	0.007
5.	1	1:2 (stat)[d]	75.2	18.8	8.9	9.6	10.3	0.014
6.	2	1:2 (stat)[e]	22.12	5.53	8.9	10.2	11.5	0.04
7.	1	1:2 (full)[f]	0.94	7589.9	8.9	16.8	9.8	0.003
8.	2	1:2 (full)[g]	1.4	8676.4	8.9	-11.7	9.95	0.005
9.	1	1:2 (add)	Fit Failed					
10.	2	1:2 (add)[h]	0.41	9674.7	8.9	9.5	10.0	0.009

[a] http://app.supramolecular.org/bindfit/view/5108ea49-5a9f-45ba-9fec-0ee28c0566b3;

[b] http://app.supramolecular.org/bindfit/view/d2da14b4-5c29-4591-a6e7-bdceaf7325a0;

[c] http://app.supramolecular.org/bindfit/view/2733446b-c882-4129-b5d5-ca42ab05fb87;

[d] http://app.supramolecular.org/bindfit/view/efb9e518-88a1-4c5a-aafa-914924eae52b;

[e] http://app.supramolecular.org/bindfit/view/c60778e3-044e-4f20-ace4-5cb702c95e2b;

[f] http://app.supramolecular.org/bindfit/view/0b52eebe-7062-4062-8dcc-717523eace2b

[g] http://app.supramolecular.org/bindfit/view/85279e4e-ec34-4c2d-b922-5505ab077706

[h] http://app.supramolecular.org/bindfit/view/9259073a-3338-42a3-9e9b-f59e80b6ba5d

Job's plot experiment

For the Job's plot experiment, equimolar solutions (0.02 M) of $Bu_4N^+Cl^-$ and macrocyclic **1** in $CDCl_3$ were prepared and mixed in various ratios. ^{1}H NMR spectra of each of these solutions were recorded and analysed.

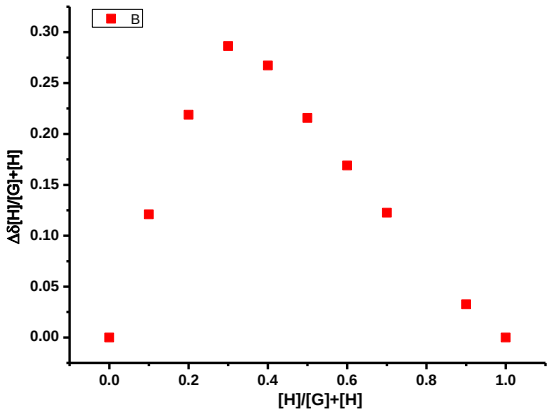


Fig. S6. Job's plot of **1** with TBACl

Dilution experiment

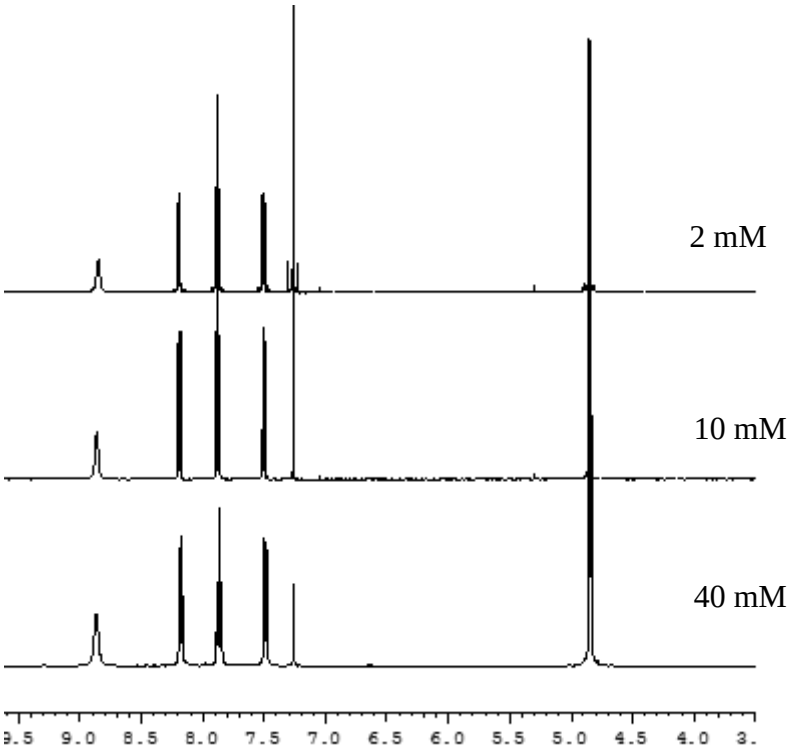
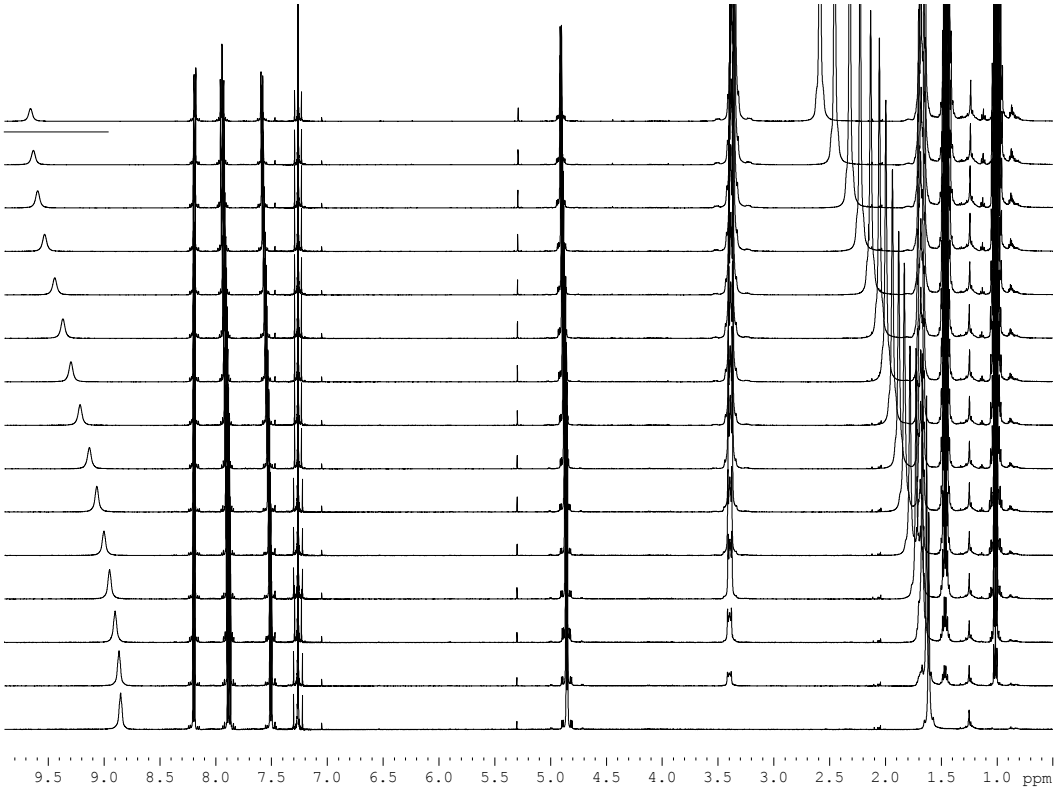


Fig. S7. Stacked NMR spectra of different concentrations of macrocycle **1** in $CDCl_3$.

^{1}H NMR titration of macrocycle 1 (0.002 M) with various TBAX salts [2-5]

The hygroscopic guest $Bu_4N^+X^-$ and the host (macrocycle **1)** were dried under high vacuum for 12 h prior to the solution preparation. All the TBA salts were transferred and weighed in a glove box under argon atmosphere. Macrocycle **1** was dissolved in $CDCl_3$ (4 mL) to prepare the stock solution of the receptor (0.0025 M). Of this solution, 400 µL was added to each of the NMR tubes, which was then sealed in order to avoid solvent evaporation. Stock solutions of the guest (0.2 M) were prepared by dissolving the salt in $CDCl_3$. The requisite number of NMR samples were prepared adding increasing amounts of the guest solution (0-100 µL) to 400 µL of the host solution. All samples were made up to a final volume of 500 µL with $CDCl_3$, so that the concentration of the host (0.002 M) remained constant over the course of the experiment. The chemical shifts of amide NH protons of the macrocycle **1** were plotted against the guest concentration. The binding constants were determined using the Bindfit software.[2-5]

a



b)

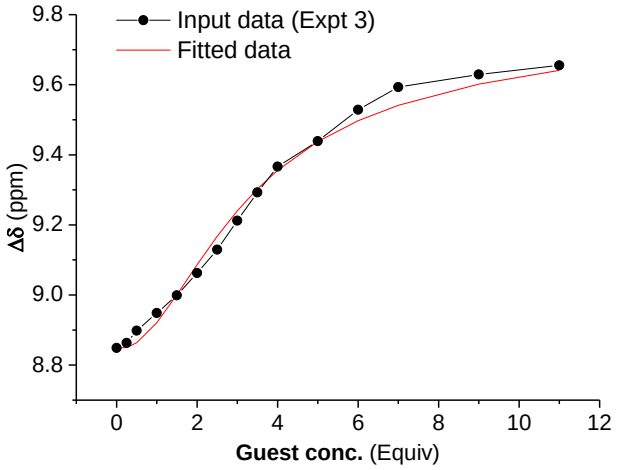


Fig. S8. a) Stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.002M) with TBACl (0-11 equiv in increasing intervals of 0.5 equiv) in $CDCl_3$. b) Data fit to 1:2 non-cooperative model.

Table S3. Representative data obtained for NMR titration of macrocycle **1** with TBACl

S. No.	Conc. **1** [M]	Conc. Cl^- [M]	Equiv. Cl^-	NH-δ (ppm)	H_2O-δ (ppm)
1	0.002	0	0	8.8492	1.6123
2	0.002	5E-4	0.25	8.8634	1.6325
3	0.002	1E-3	0.5	8.8984	1.6709
4	0.002	0.002	1	8.9488	1.726
5	0.002	0.003	1.5	8.9989	1.7778
6	0.002	0.004	2	9.0624	1.8316
7	0.002	0.005	2.5	9.1296	1.8817
8	0.002	0.006	3	9.2119	1.9379
9	0.002	0.007	3.5	9.2927	1.9971
10	0.002	0.008	4	9.3665	2.0522
11	0.002	0.01	5	9.4391	2.1332
12	0.002	0.012	6	9.5285	2.2274
13	0.002	0.014	7	9.593	2.3202
14	0.002	0.018	9	9.6291	2.4551
15	0.002	0.022	11	9.6552	2.5874
16	0.002	0.03	15	9.6122	2.7477

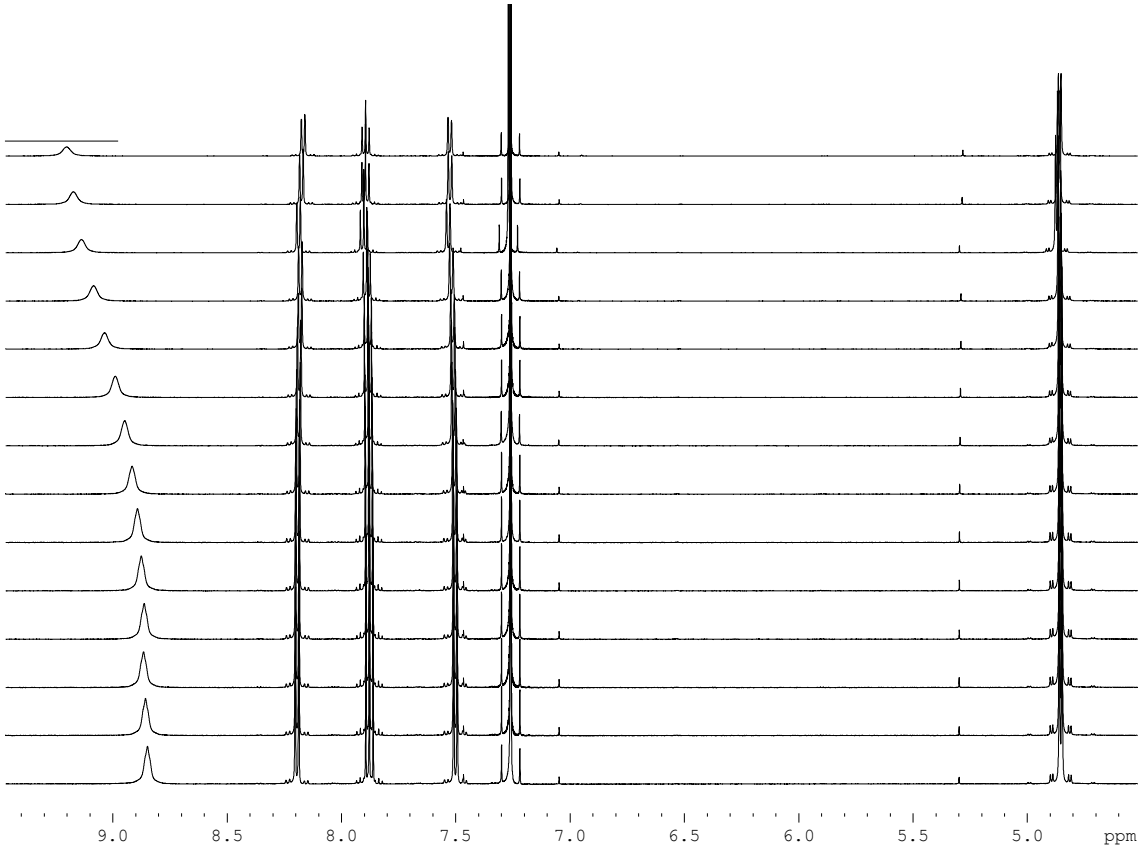


Fig. S9. Stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.002M) with TBABr (0- 20 equiv in increasing intervals of 0.05 equiv) in $CDCl_3$.

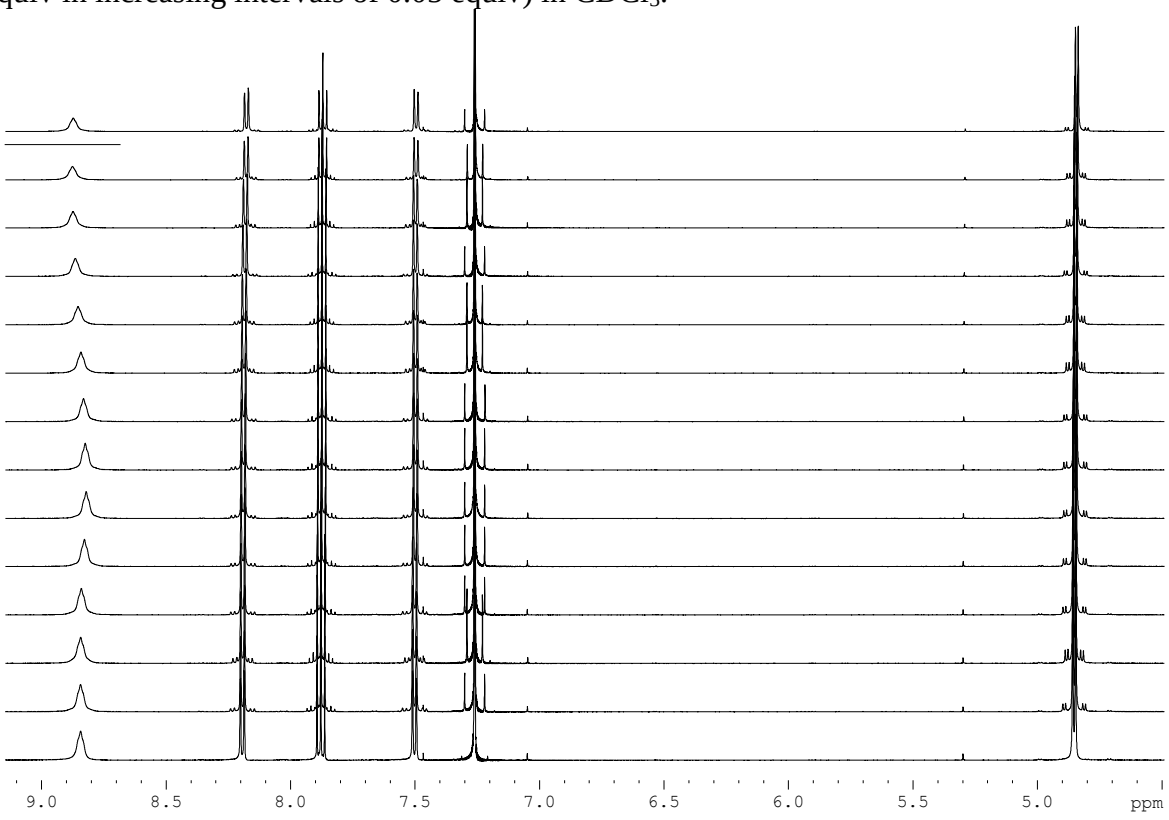


Fig. S10. Stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.002M) with TBAI (0- 15 equiv in increasing intervals of 0.05 equiv) in $CDCl_3$.

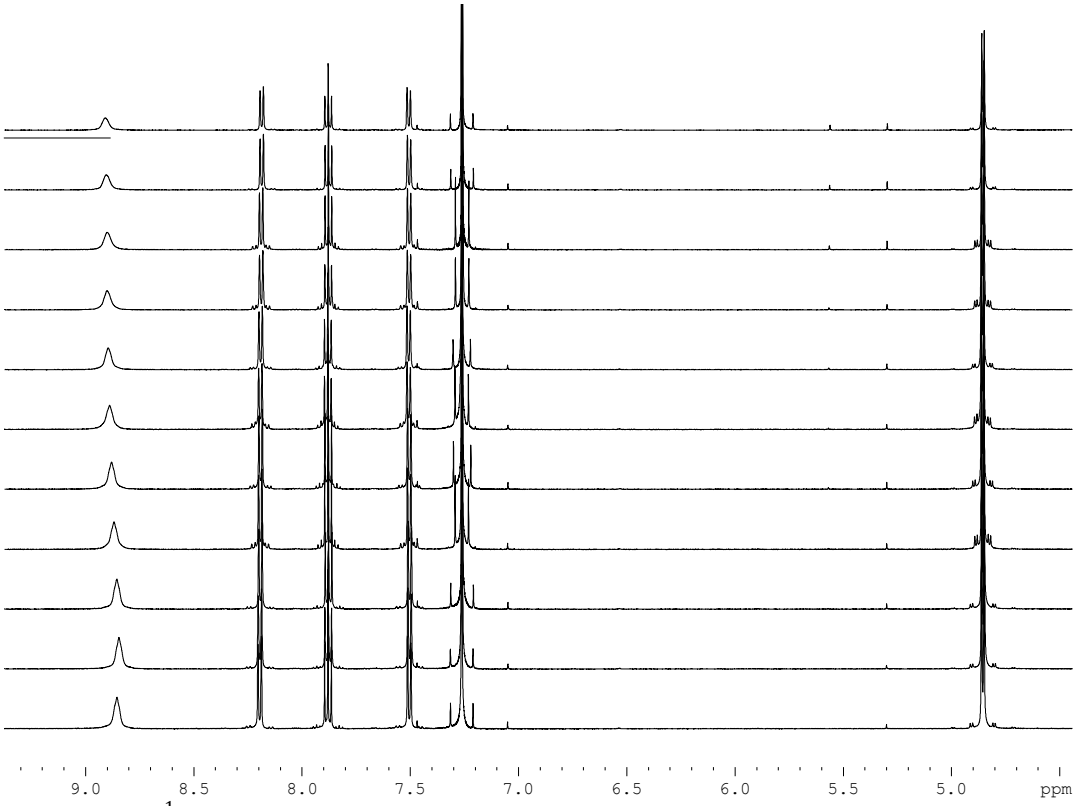


Fig S11. Stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.002M) with $TBAHSO_4$ (0-10 equiv in increasing intervals of 0.05 equiv) in $CDCl_3$.

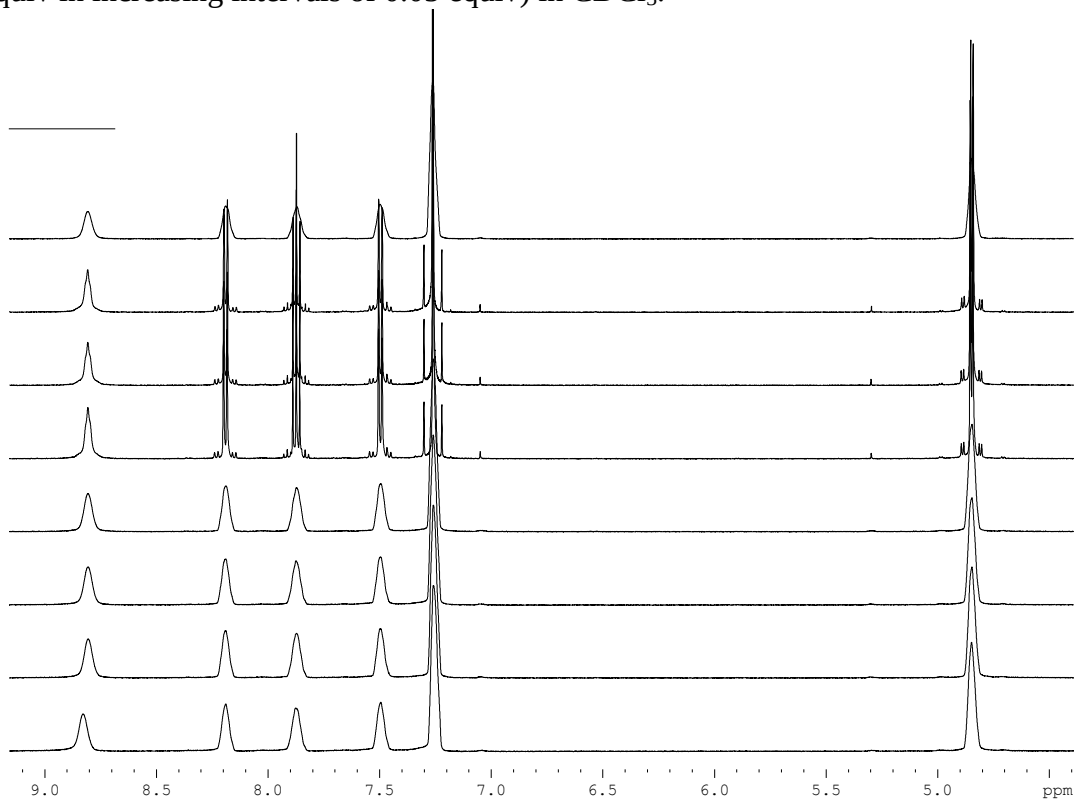
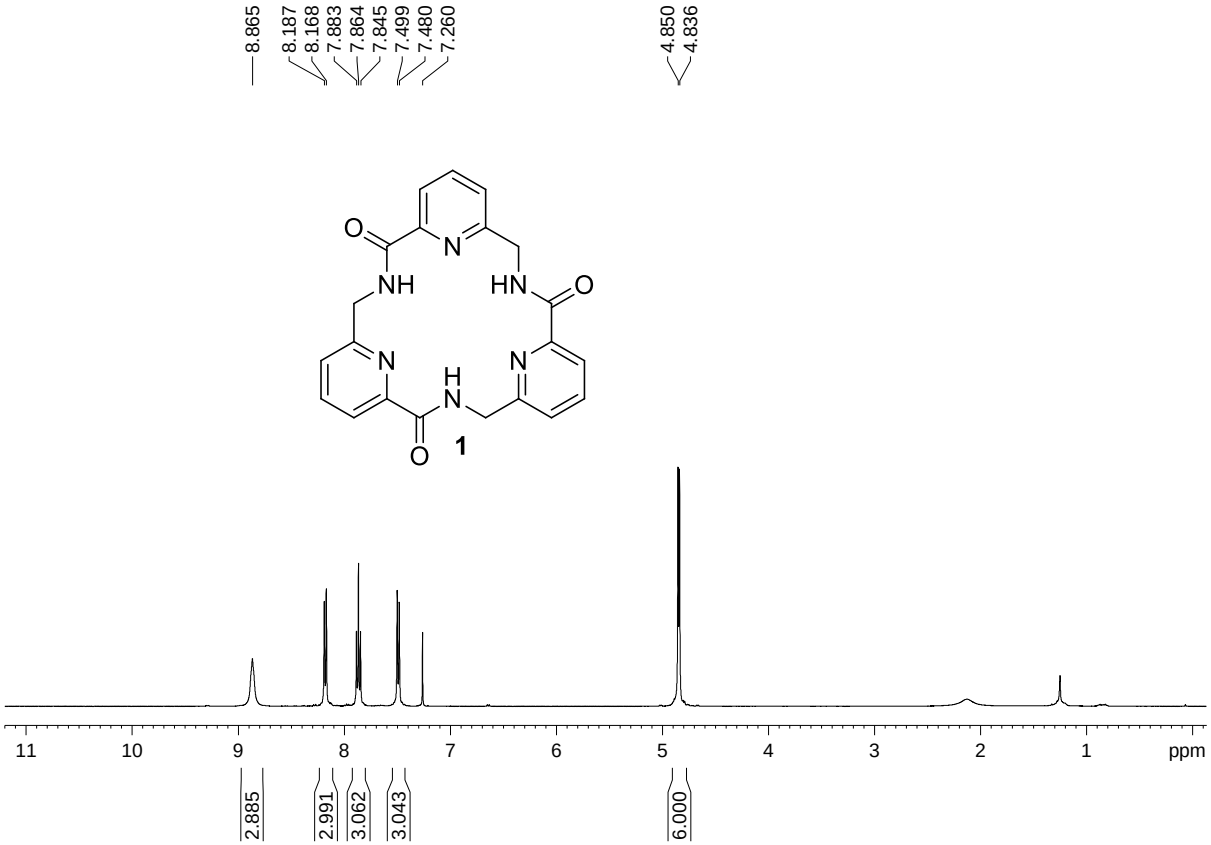


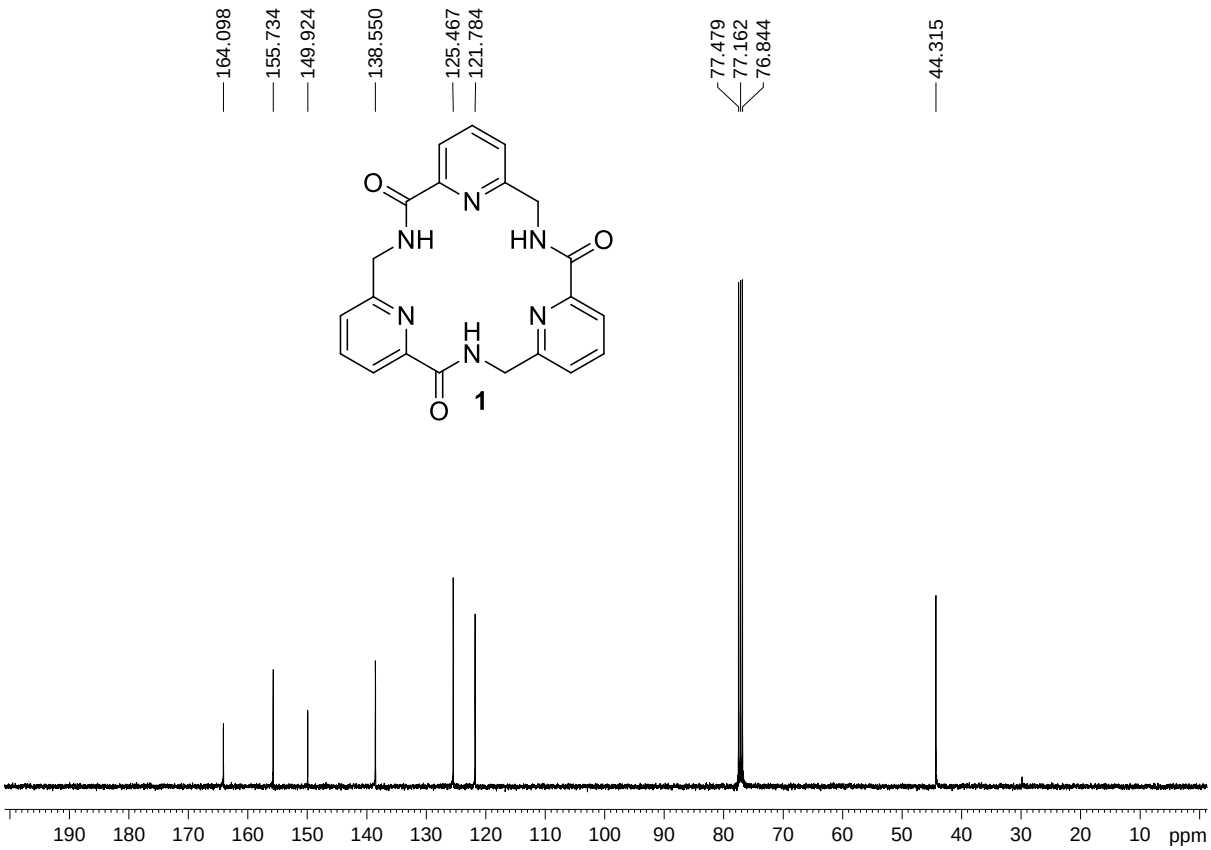
Fig. S12. Stacked ^{1}H NMR spectra for titration of macrocycle **1** (0.002M) with $TBAH_2PO_4$ (0- 15 equiv in increasing intervals of 0.05 equiv) in $CDCl_3$

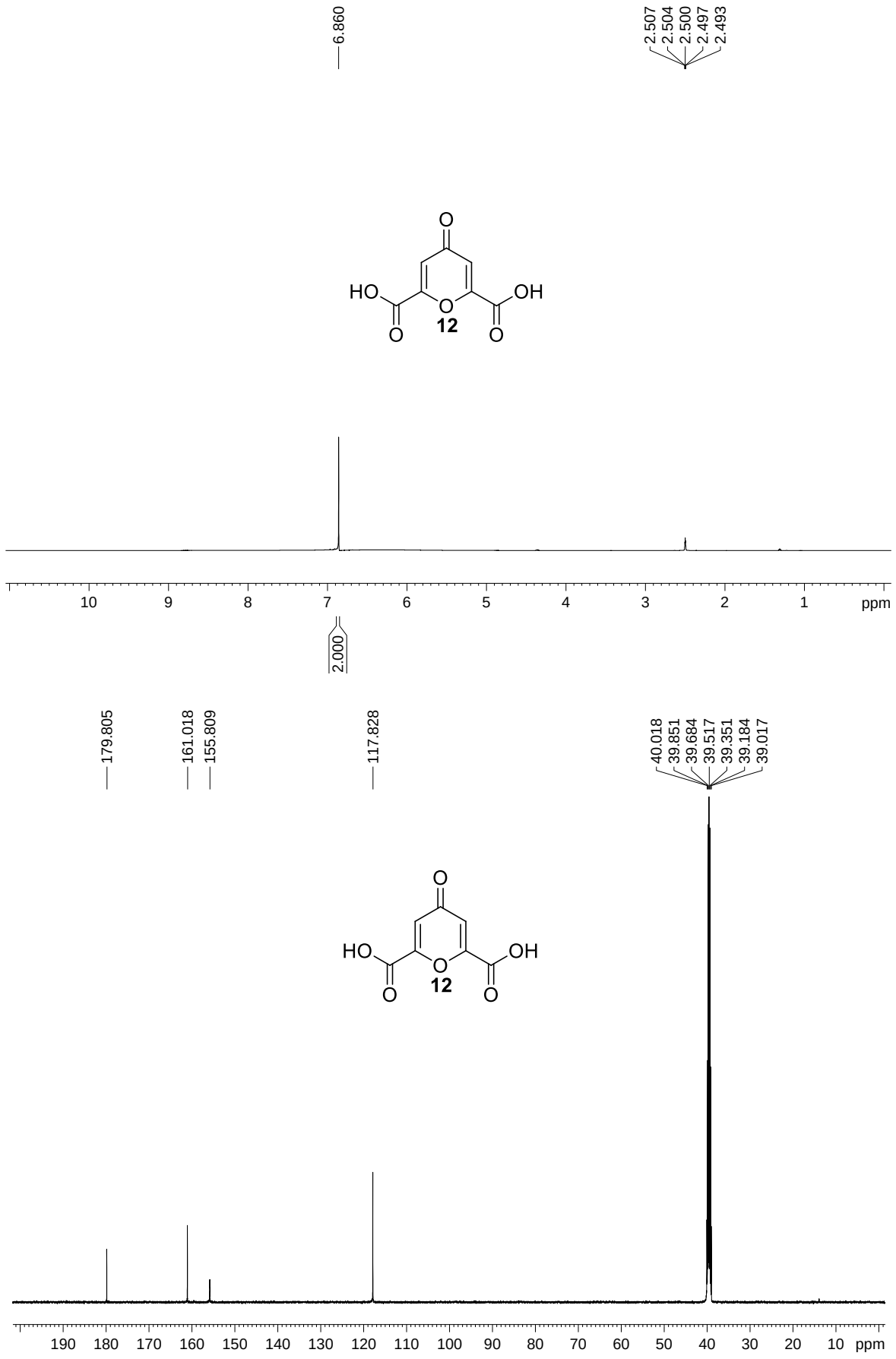
References

1. G. Howáth, C. Rusa, Z. Köntös, J. Gerencsér and P. Huszthy, *Synth. Commun.* 1999, **29**, 3719-3731.
2. P. Thordarson, *Chem. Soc. Rev.*, 2011, **40**, 1305-1323.
3. D. B. Hibbert and P. Thordarson, *Chem. Commun.*, 2016, **52**, 12792-12805.
4. E. N. W. Howe, M. Bhadbhade and P. Thordarson, *J. Am. Chem. Soc.*, 2014, **136**, 7505-7516.
5. www. supramolecular.org

NMR spectra of compounds



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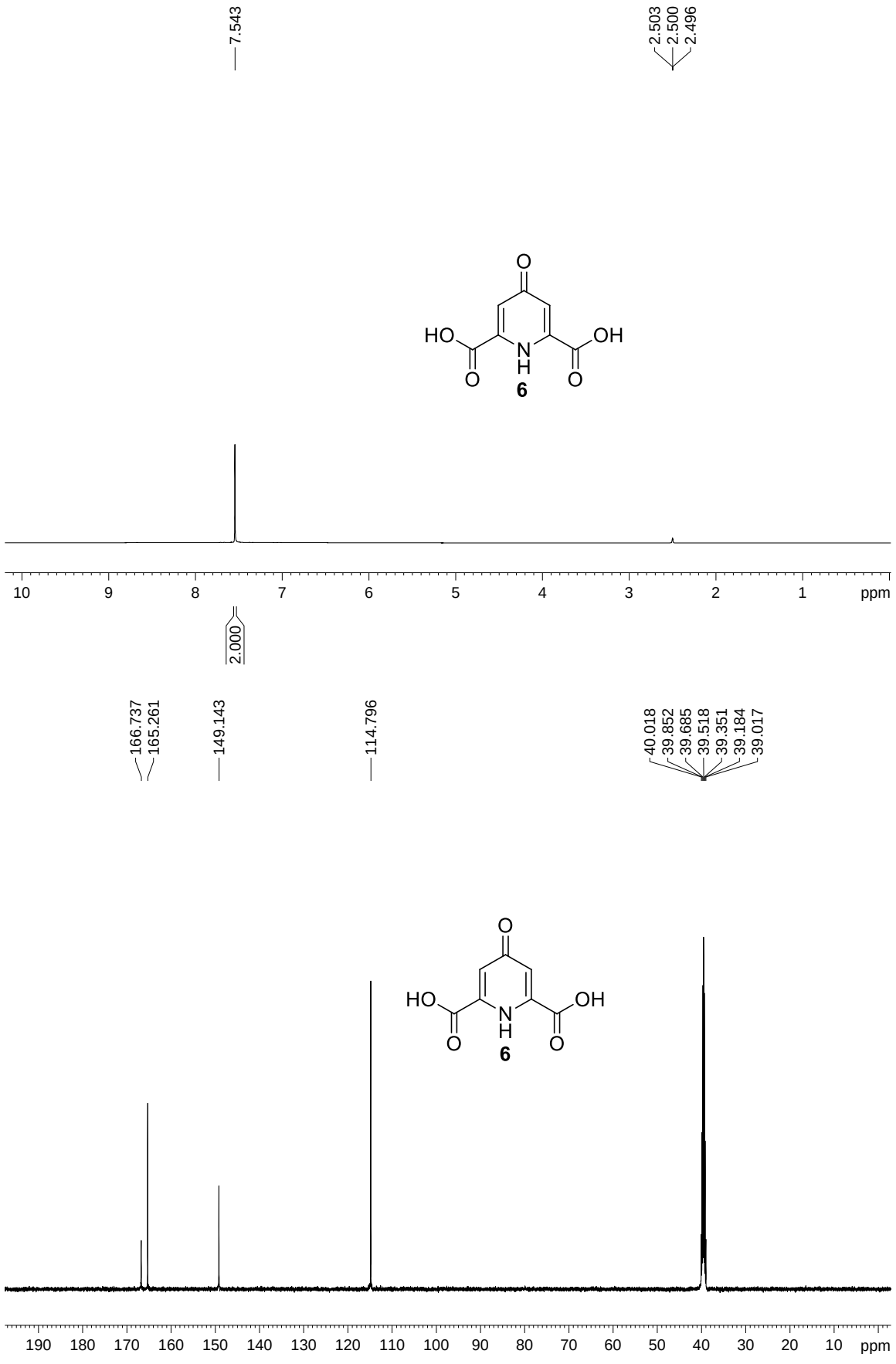
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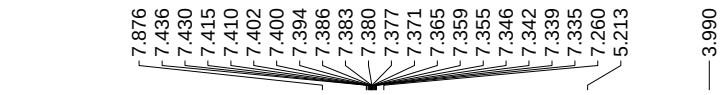
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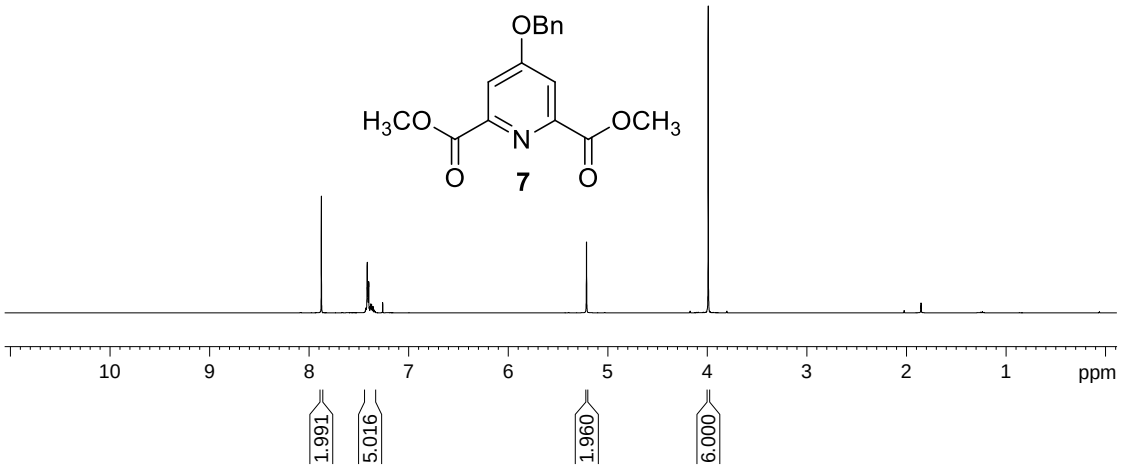
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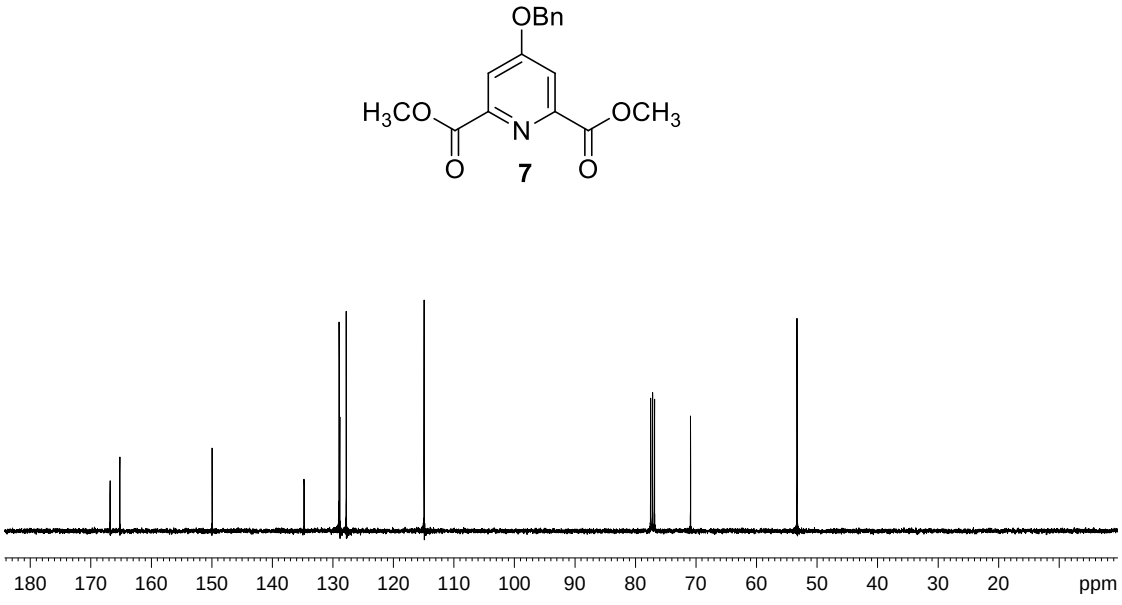
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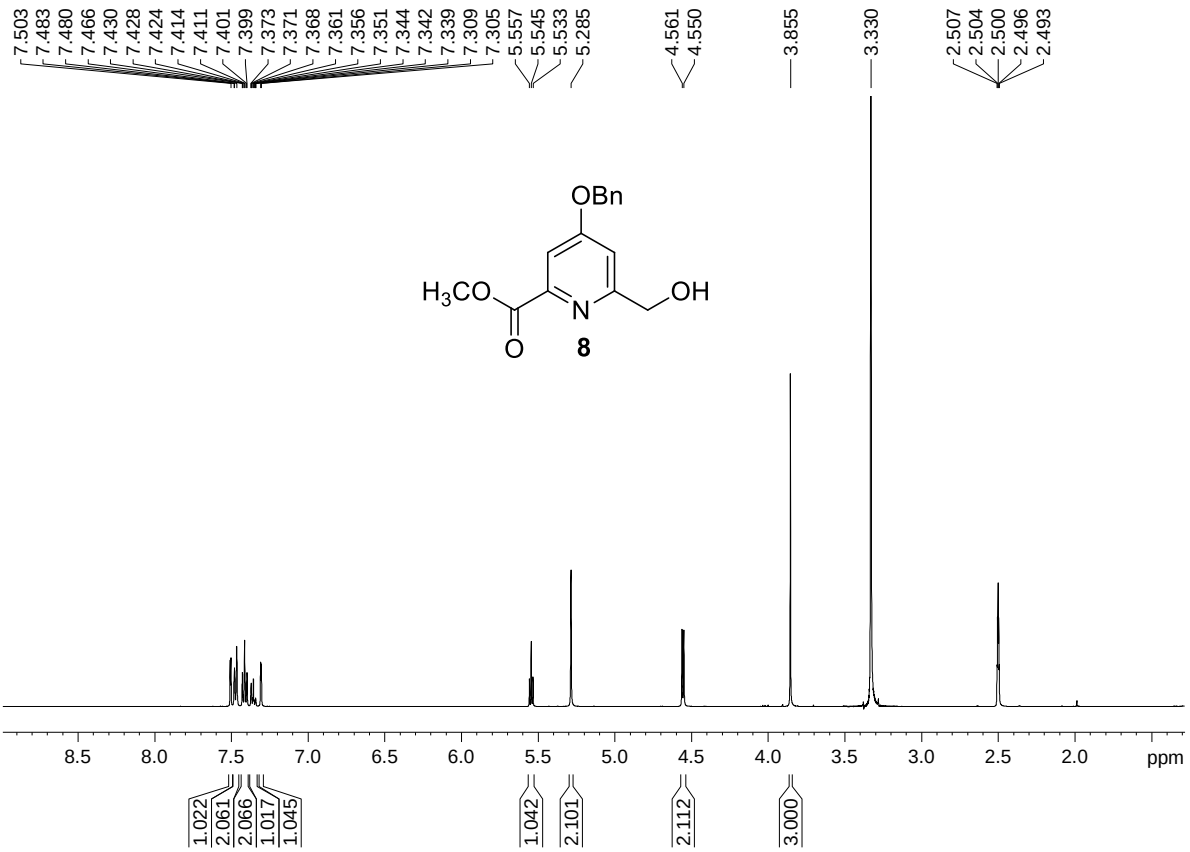
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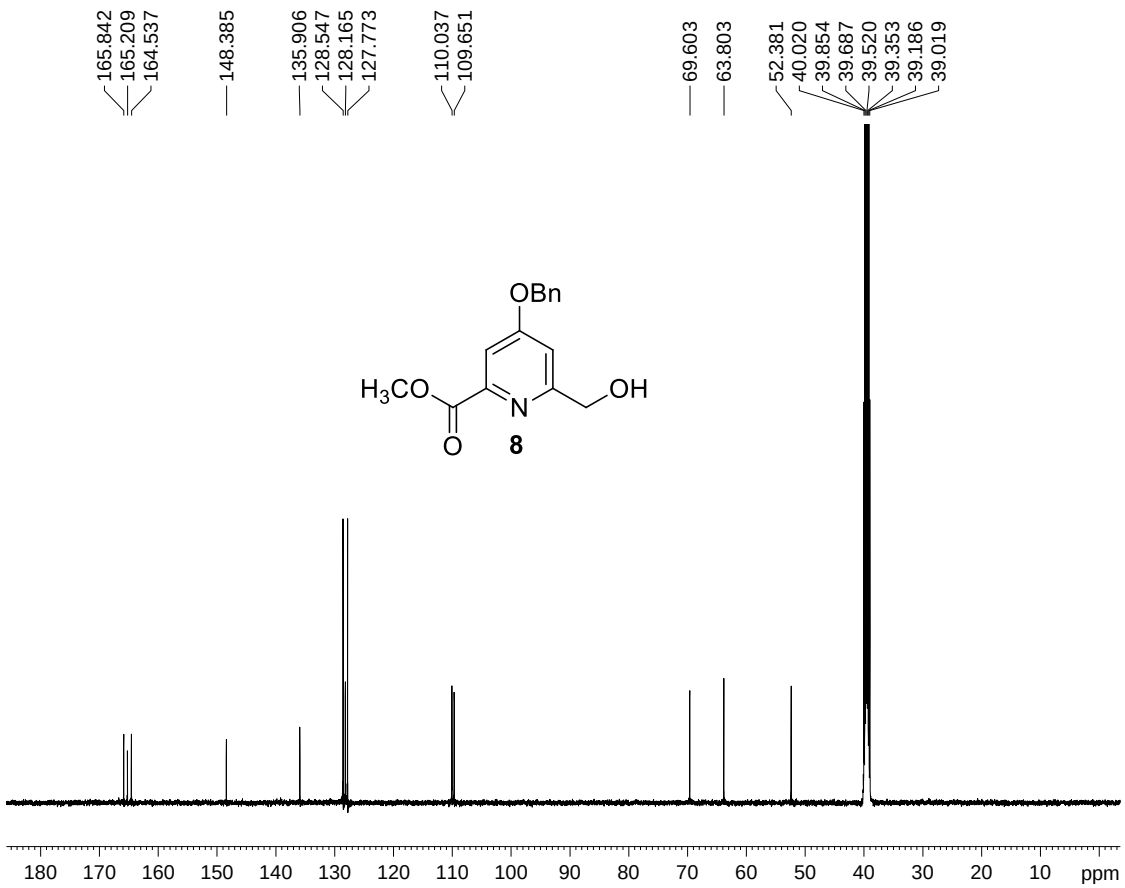
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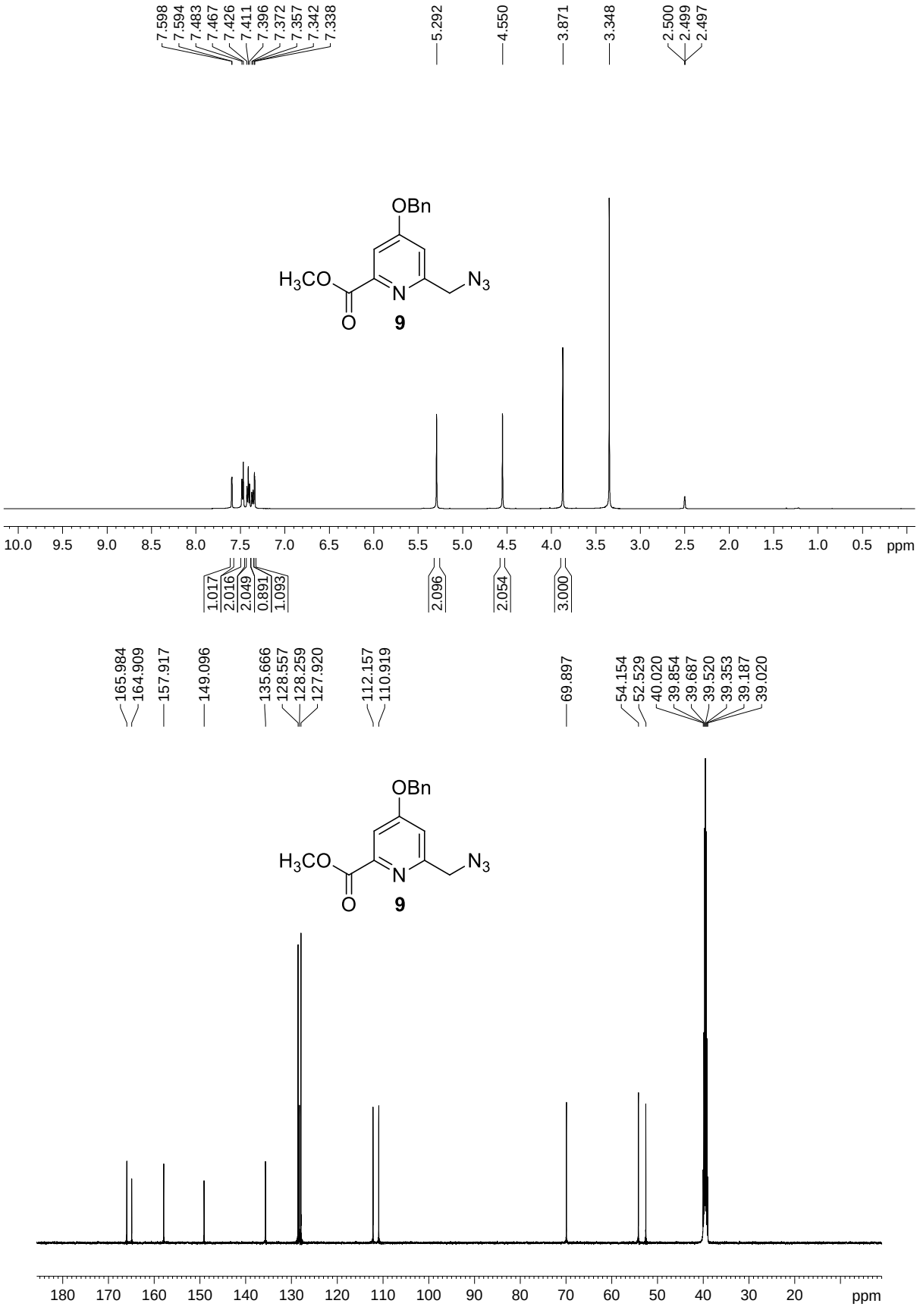
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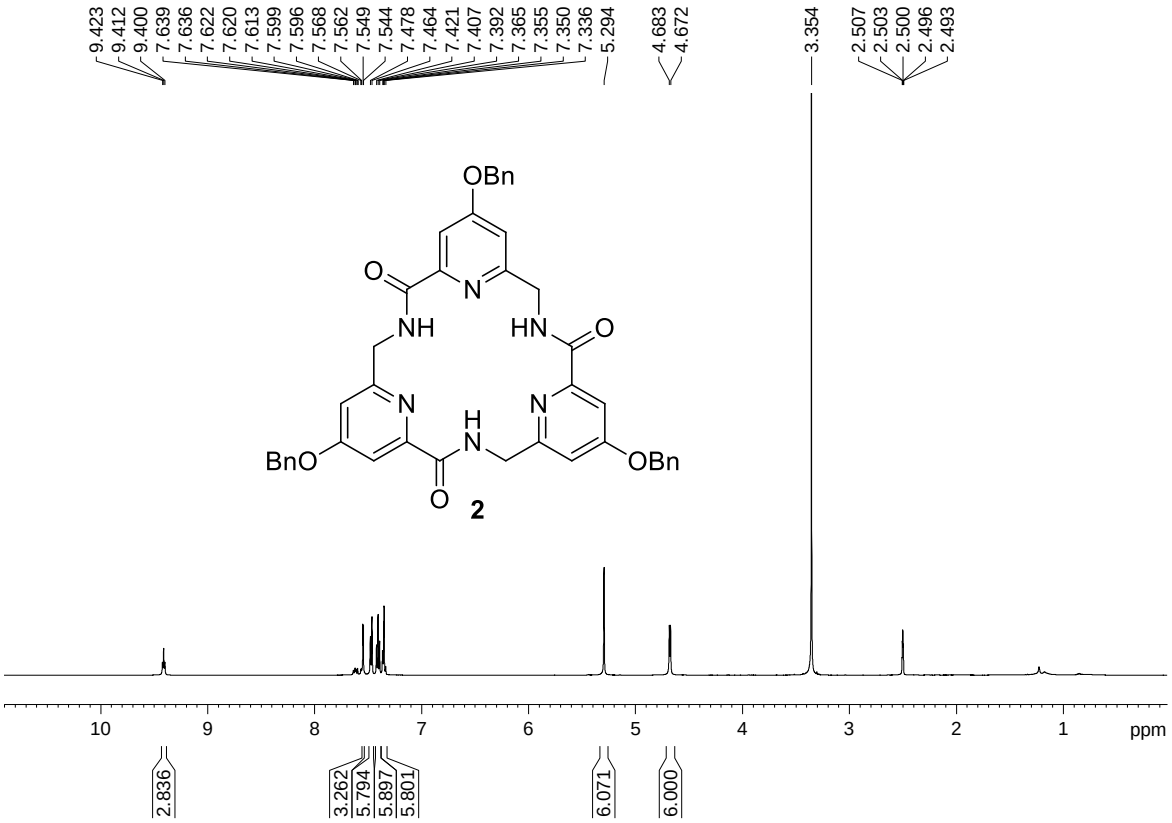
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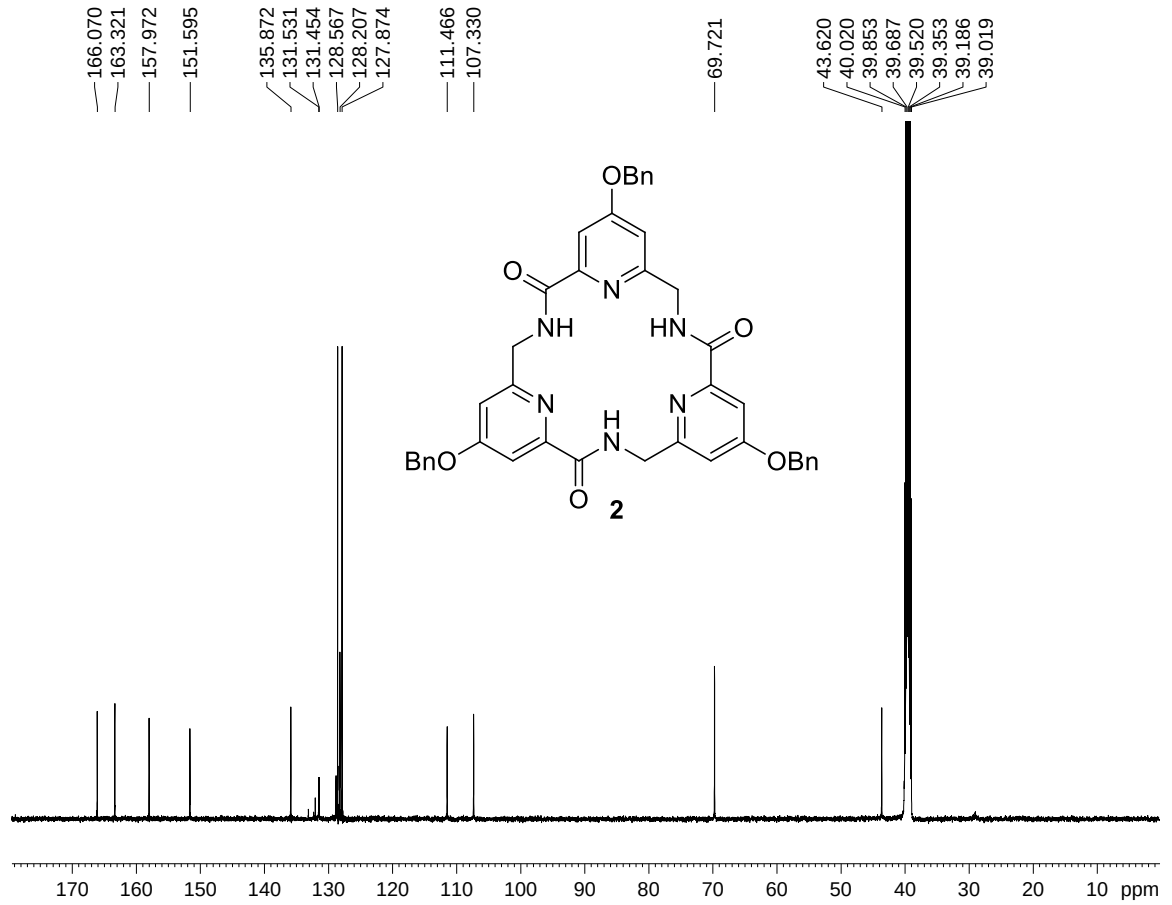
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