Electronic Supplementary Material (ESI) for ChemComm.

Transforming a chemically labile [2+3] imine cage into a robust carbamate cage

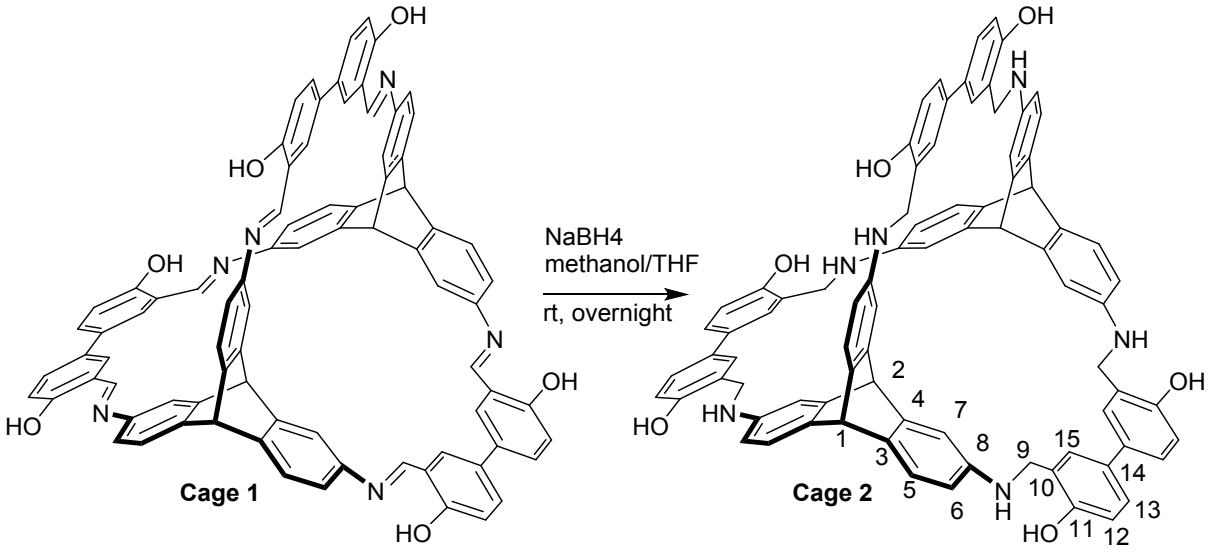
Xin-Yue Hu,[a] Wen-Shan Zhang,[b] Frank Rominger,[a] Irene Wacker,[b] Rasmus R. Schröder,[b,c] and Michael Mastalerz[a,b]*

-Supporting Information-

1. General remarks

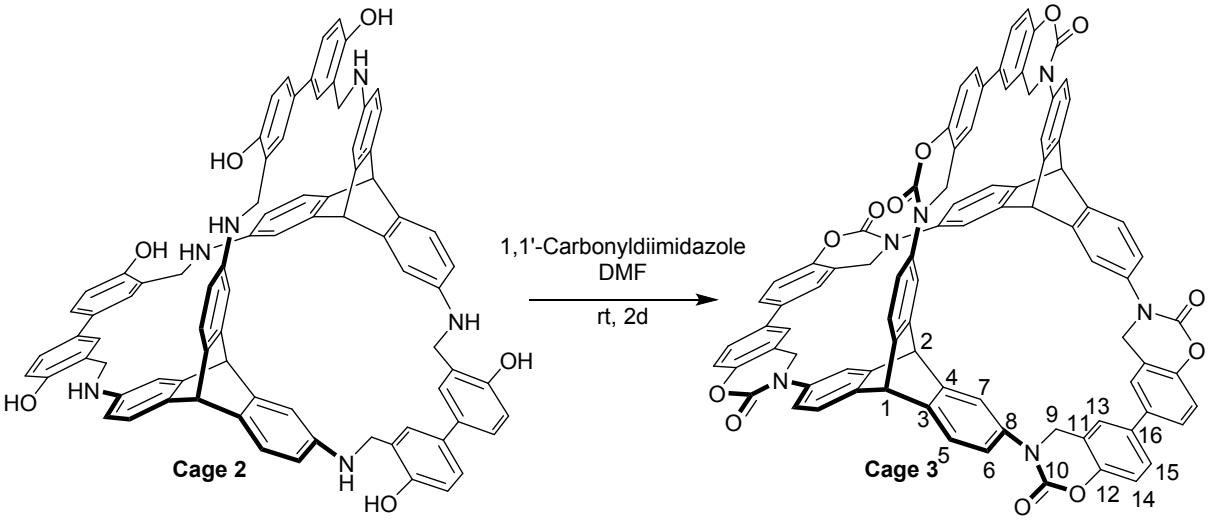
Commercially available reagents were obtained from Chempur, Alfa Aesar, Sigma-Aldrich or VWR and have been used without further purification unless otherwise mentioned. DMF was dried by BaO and activated alumina and distilled at 56 °C, 20 mmHg. Cage **1** was synthesized according to literature procedures[1]. Thin-layer chromatography was done using silica gel 60 F254 plates from Merck and were examined under UV-light irradiation (254 and 365 nm). Flash column chromatography was performed on silica gel (particle size: 0.040−0.063 mm) from Macherey-Nagel. Melting points (not corrected) were measured on a Büchi B-540. NMR spectra were recorded on a Bruker Avance III 500 (^{1}H NMR: 500 MHz; ^{13}C NMR: 125 MHz) or a Bruker Avance III 300 (^{1}H NMR: 300 MHz; ^{13}C NMR: 75 MHz) spectrometer at 298 K, unless otherwise mentioned. IR spectra were recorded on a Fourier transform spectrophotometer (Bruker Lumos) equipped with a germanium ATR crystal. HRMS (MALDI) experiments were carried out on a Bruker Autoflex Speed MALDITOF, JEOL AccuTOF GCx with an internal calibration (PEG) in positive mode on TOF mass spectrometer using DCTB (trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile) as matrix. Elemental analysis was performed by the Microanalytical Laboratory of the University of Heidelberg using an Elementar vario MICRO cube. TGA was measured on a Mettler-Toledo TGA/DSC1 instrument with a TGA/DSC-Sensor 1100 equipped with a MX1 balance (Mettler-Toledo) and a GC100 gas control box for nitrogen supply. Crystal structure analysis was accomplished on a STOE Stadivari diffractometer with a copper source (λCuKα = 1.54178 Å). The surface area and porosity was characterised by nitrogen adsorption and desorption analysis at 77.35 K with an autosorb computer-controlled surface analyser (AUTOSORB- iQ, Quantachrome). Powder X-ray diffraction was measured using a Stoe Stadi 611KLS/N 61263 diffractometer. The samples used for BET experiment were first dissolved in DMSO and precipitated in water, then stirred in acetone and petroleum ether to exchange the residual DMSO and dried in vacuum at 200 °C (16 h). The samples were degassed at 200 °C (3 h) before being analysed. The BET surface area was calculated by assuming a value of 0.162 nm^2 for the cross-sectional area of the nitrogen molecules. The NLDFT model and isotherm data were used to calculate the pore size distribution (N2 at 77K on carbon, NLDFT cylinder pores, NLDFT equilibrium model). Scanning electron micrographs of Figure 4 were acquired using a Zeiss Ultra 55 instrument with a low accelerating voltage. The powder sample was suspended in isopropanol and drop-casted on a small piece of silicon wafer, which was pretreated by plasma cleaning.

2. Synthesis of Compounds



Amine cage 2.

Cage 1 (30 mg, 0.02 mmol) was suspended in 10 mL methanol and 5 mL THF, and 40 mg (1.05 mmol) $NaBH_4$ was added to the solution. The suspension was stirred for 15h at room temperature. Methanol was removed by rotary evaporation. The white solid was suspended in 10 mL water, and then extracted with ethyl acetate (10 × 3 mL). The combined organic phase was dried with Na_2SO_4 and the solvent was removed by rotary evaporation. The solid was dried in vacuum at 90°C, giving 16 mg (54%) of **2** as light yellow solid. Mp > 410 °C. ^{1}H NMR (300 MHz, DMSO-d6): δ = 9.38 (s, 6H, -OH), 7.61 (d, J = 0.9 Hz, 6H, 15-H), 7.24 (dd, J = 6, 1.2 Hz, 6H, 13-H), 7.00 (br s, 6H, 7-H), 6.96 (d, J = 9 Hz, 6H, 5-H), 6.78 (d, J = 6 Hz, 6H, 12-H), 6.16 (d, J = 9 Hz, 6H, 6-H), 5.39 (s, 6H, -NH), 5.32 (s, 2H, bridgehead-H), 4.98 (s, 2H, bridgehead-H), 4.15 (d, J = 3 Hz, 12H, 9-H) ppm. ^{13}C NMR (DMSO-d6, 125 MHz, 373.15K): δ = 154.69 (s, C-11), 146.91 (s, C-4), 146.53 (s, C-3), 136.02 (s, C-8), 131.61 (s, C-14), 127.41 (s, C-15), 126.73 (s, C-10), 125.67 (s, C-13), 123.20 (s, C-5), 116.19 (s, C-12), 110.14 (s, C-7), 108.45 (s, C-6), 55.62 (s, bridgehead-C), 51.14 (s, bridgehead-C), 43.62 (s, C-9) ppm. IR(ATR):$\tilde{\nu}$ = 3341(w, br), 2921(w), 2868(w), 1655(m), 1608(s), 1486(s), 1442(m), 1384(m), 1345(m), 1243(s), 1183(s), 1150(m), 1116(m), 1093(m), 1058(m), 991(m) 940(w), 813(s), 775(m), 668(w) cm^{-1}. MS (MALDI-TOF, DCTB): m/z M^+ = 1229.495 Elemental analysis calculated for $C_{82}H_{64}N_6O_6 \cdot 4H_2O$: C 75.67%, H 5.58%, N 6.46%. Found: C 75.51%, H 5.52%, N 6.45%



Carbamate cage 3: 30 mg (0.024 mmol) of **2** and 70 mg (0.43 mmol) carbonyldiimidazole were dissolved in dry DMF (3 mL) and the reaction mixture stirred for two days at room temperature. DMF was removed by rotary evaporation. The crude product was suspended into 0.1 M NaOH solution and stirred for 1h. The precipitate was collected by filtration and washed with water (10 × 3 mL). The crude product was purified by column chromatography (SiO_2, DCM: methanol = 50:1) and dried in vacuum to give pure cage compound **3** (20mg, 62%) as light yellow solid. mp > 410 °C. ^{1}H NMR (300 MHz, DMSO-d6): δ = 7.56 (d, J = 12 Hz, 6H, 6-H), 7.45 (dd, J = 12,1.8 Hz, 6H, 15-H), 7.33 (d, J = 1.8 Hz, 6H, 13-H), 7.30 (dd, J = 12, 1.8 Hz, 6H, 5-H), 7.21 (m, 12H), 5.85 (s, 2H, bridge-H), 5.54 (s, 2H, bridge-H), 4.85 (s, 12H, 9-H) ppm. ^{13}C NMR (DMSO-d6, 125 MHz, 373.15K): δ = 150.61 (s, C-12), 150.32 (s, C-11), 146.83 (s, C-3), 144.12 (s, C-4), 139.07 (s, C-8), 137.72 (s, C-16), 128.07 (s, C-15), 125.88 (s, C-13), 124.54 (s, C-5), 124.27 (s, C-6), 122.39 (s, C-11), 121.04 (s, C-7), 116.54 (s, C-14), 53.43 (s, bridgehead-C), 52.07 (s, bridgehead-C), 50.73 (s, C-9) ppm. MS (MALDI-TOF, DCTB): m/z M^+ = 1385.367. IR (ATR): $\tilde{\nu}$ = 1729 (s), 1609 (w), 1478 (m), 1437 (m), 138 5(m), 1236 (s), 1216 (m), 1177 (s), 1159(s), 1106 (s), 1000 (m), 922 (m), 881(w), 830 (m), 790 (w), 773 (w), 750 (m), 679 (w), 630 (w) cm^{-1} Elemental analysis calculated for $C_{88}H_{52}N_6O_{12}\cdot 3H_2O\cdot$DMF: C: 72.26%, H: 4.33%, N: 6.48%. Found: C: 72.10%, H: 4.25%, N: 6.43%

3. NMR Spectra

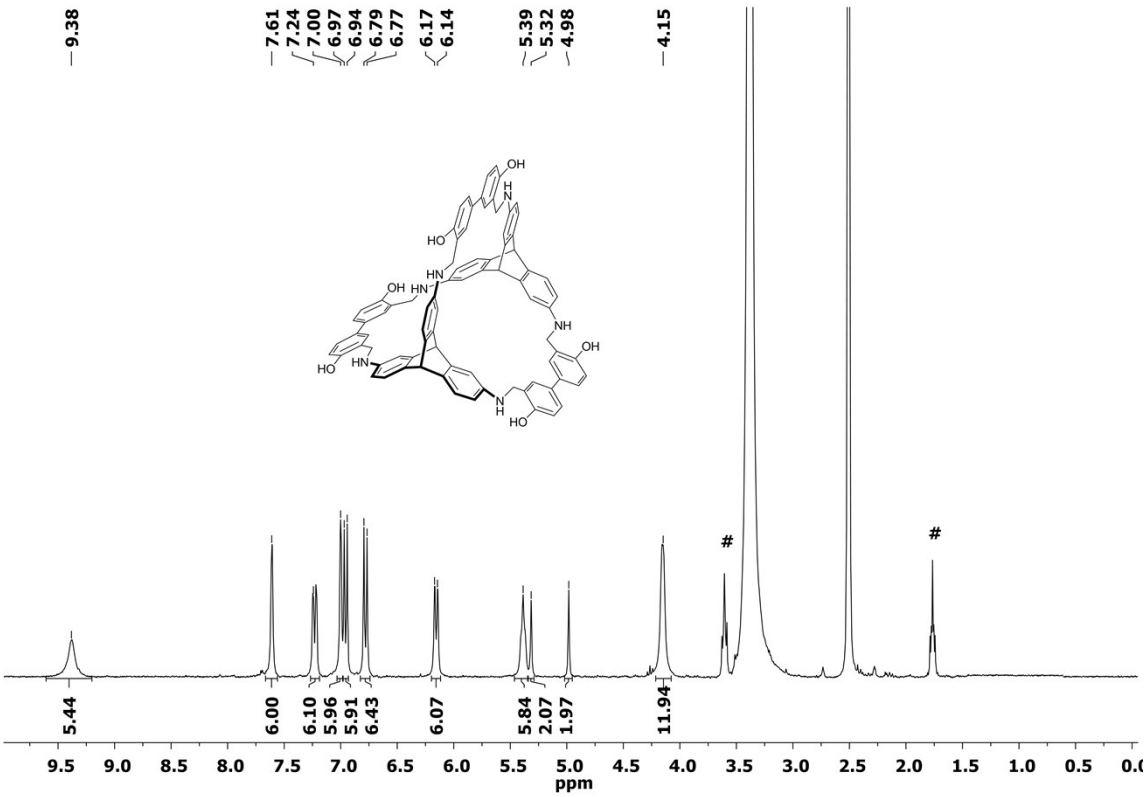


Figure S1.[1]H NMR spectrum (DMSO-d6, 300 MHz) of cage **2**, # marks residual THF.

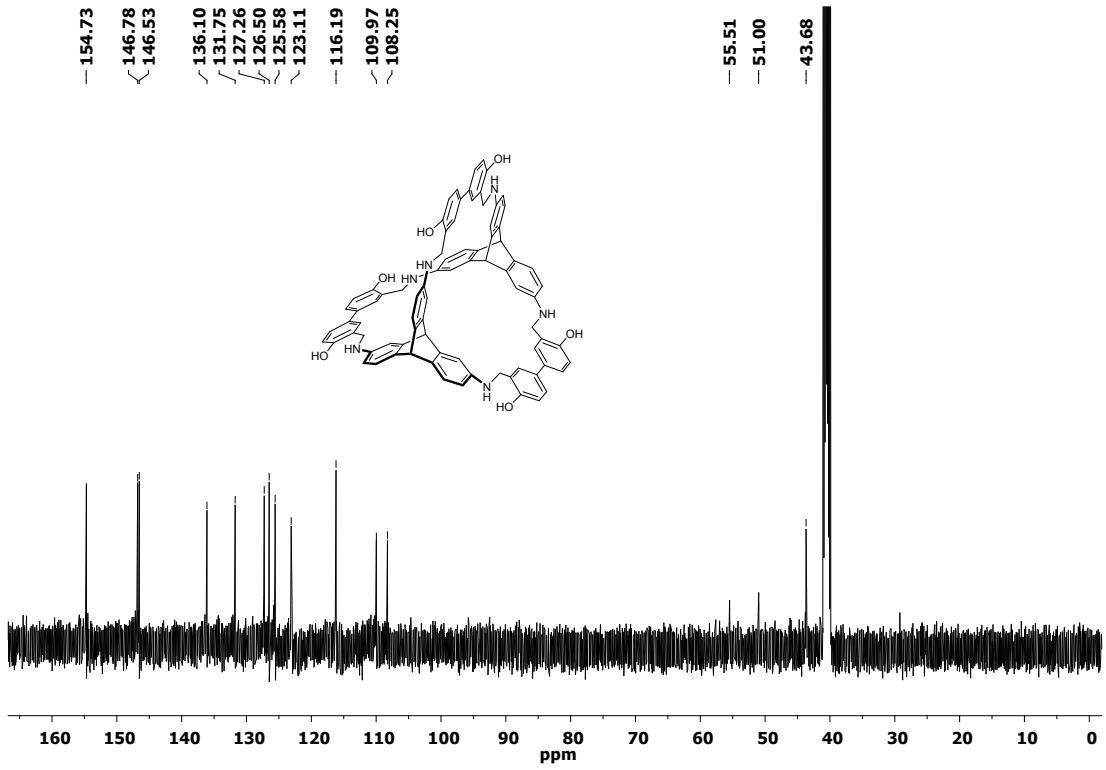


Figure S2. [13]C NMR spectrum (DMSO-d6, 125 MHz, 373.15 K) of cage **2**.

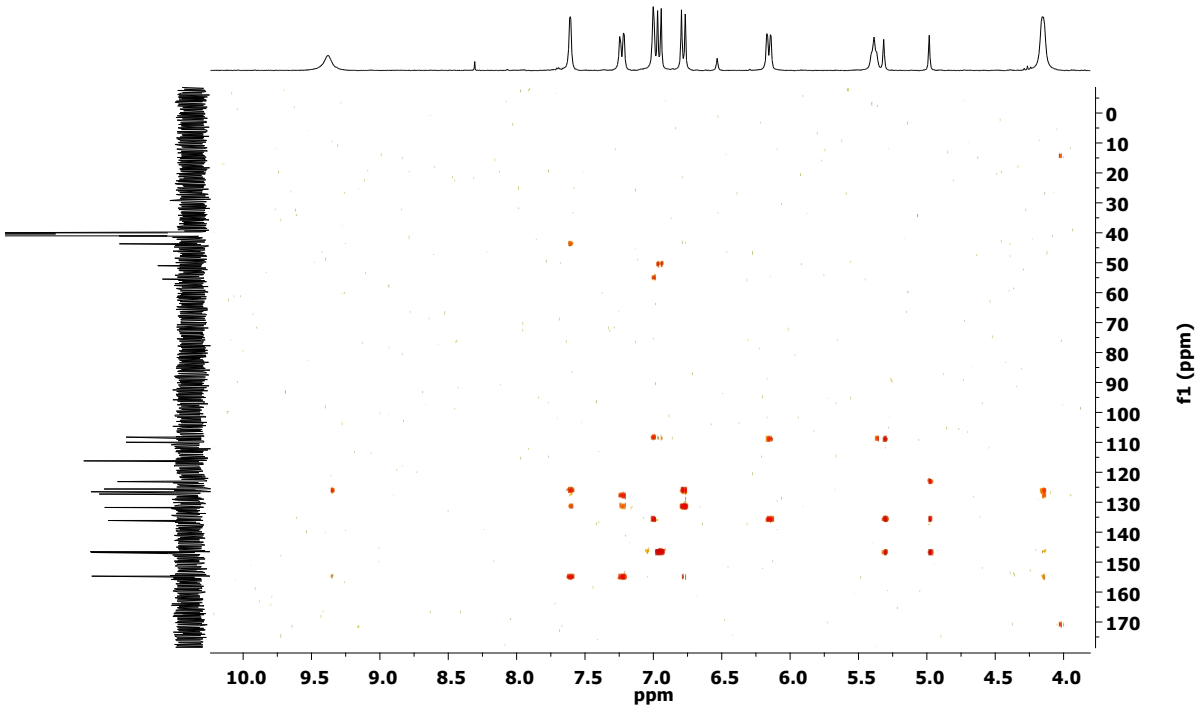


Figure S3. ^{1}H- ^{13}C HMBC NMR spectrum (DMSO-d6) of cage **2**.

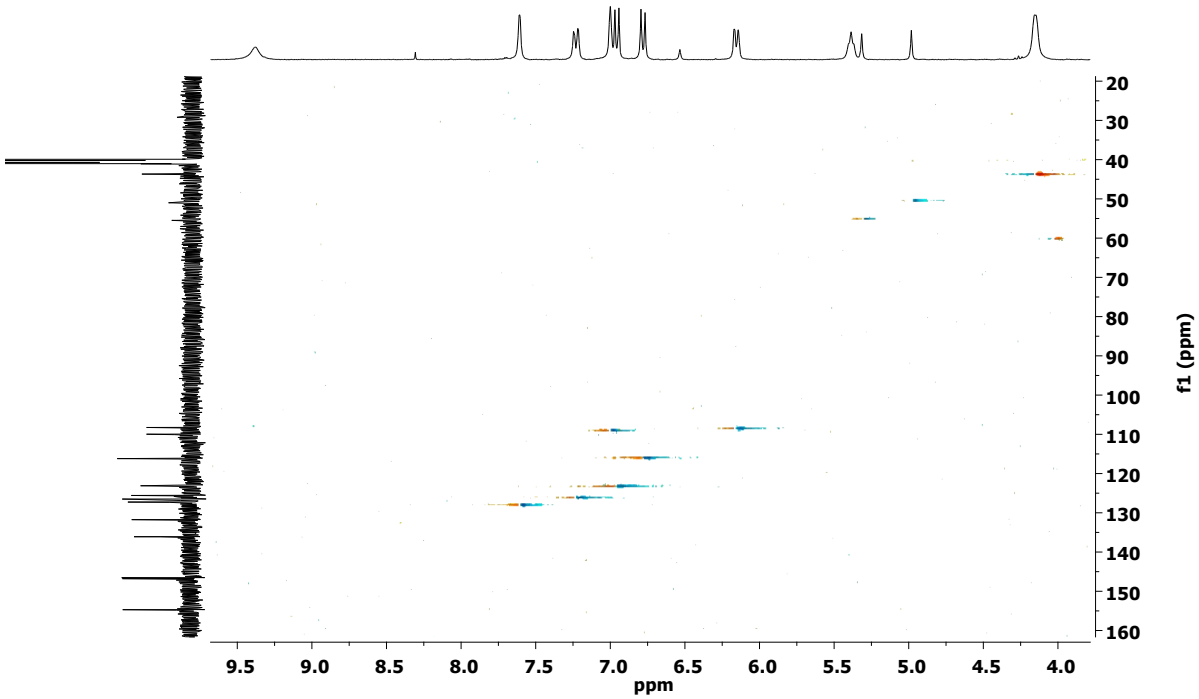


Figure S4. ^{1}H- ^{13}C HSQC NMR spectrum (DMSO-d6) of cage **2**.

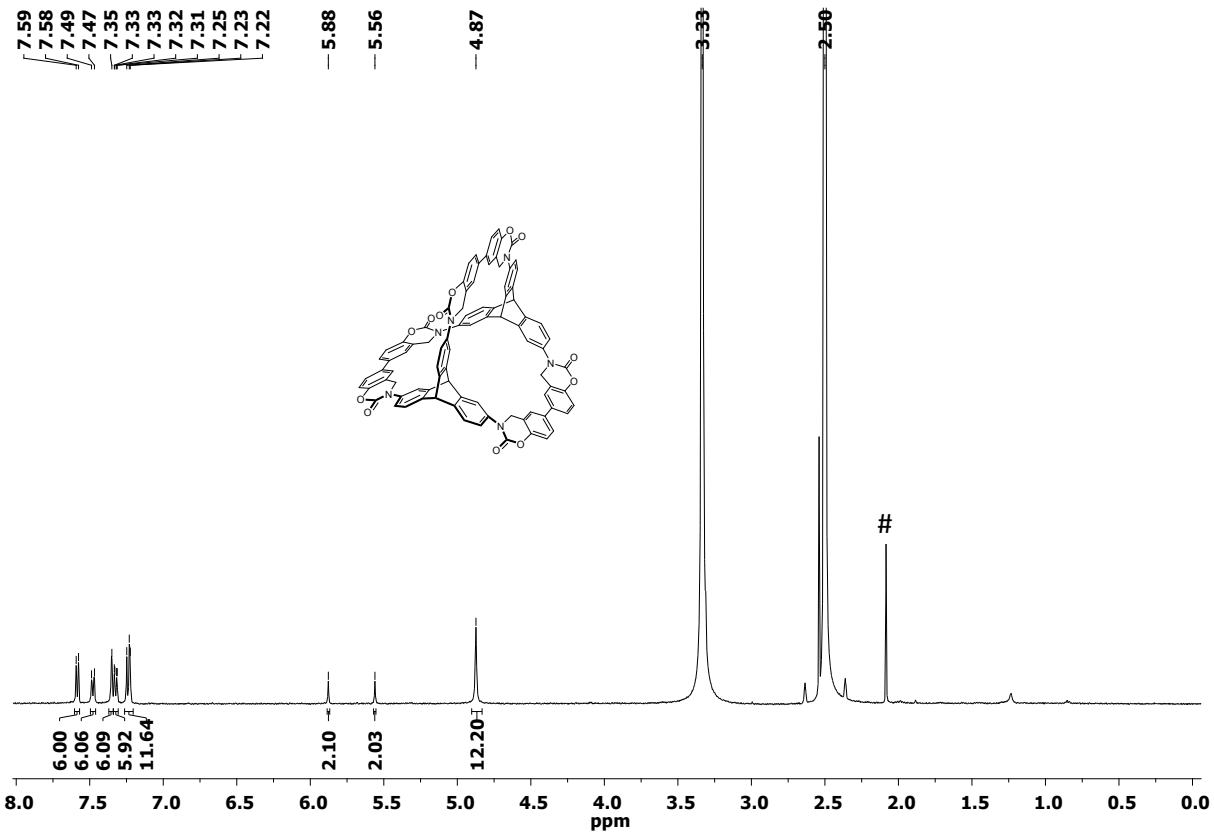


Figure S5. [1]H NMR spectrum (DMSO-d6, 300 MHz) of cage **3**, # marks residual acetone.

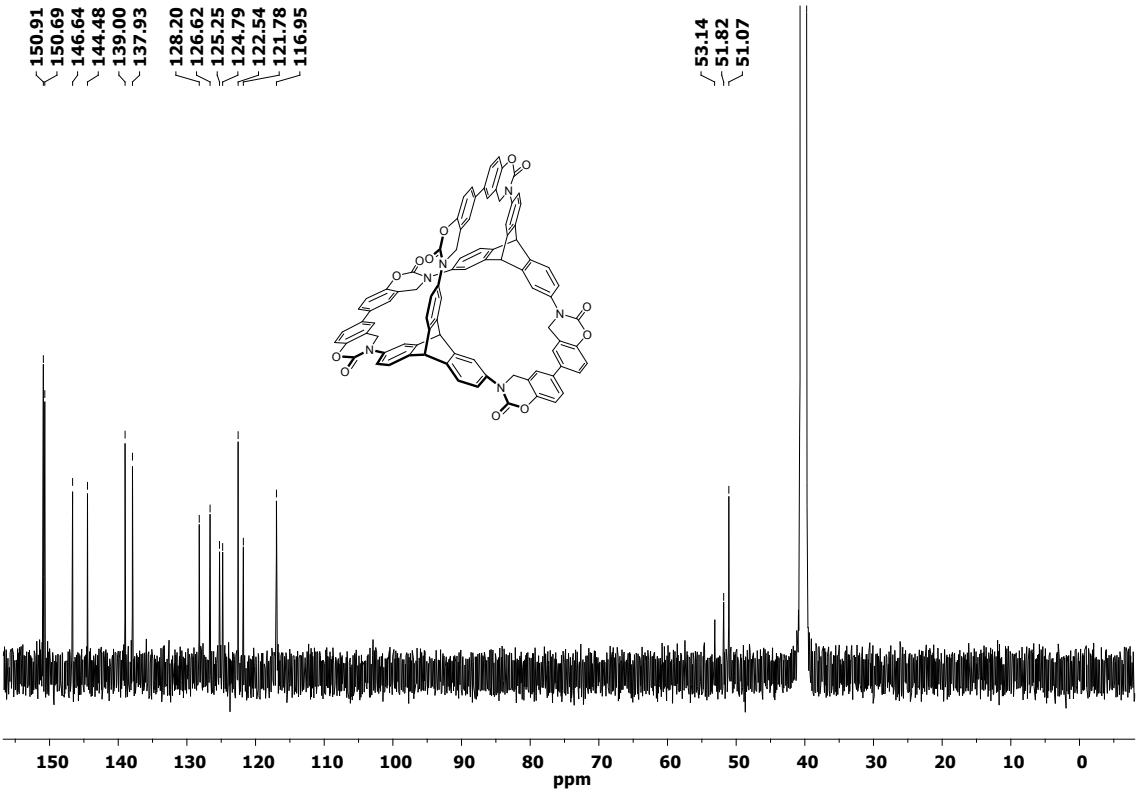


Figure S6. [13]C NMR spectrum (DMSO-d6, 300 MHz, 375.15 K) of cage **3**.

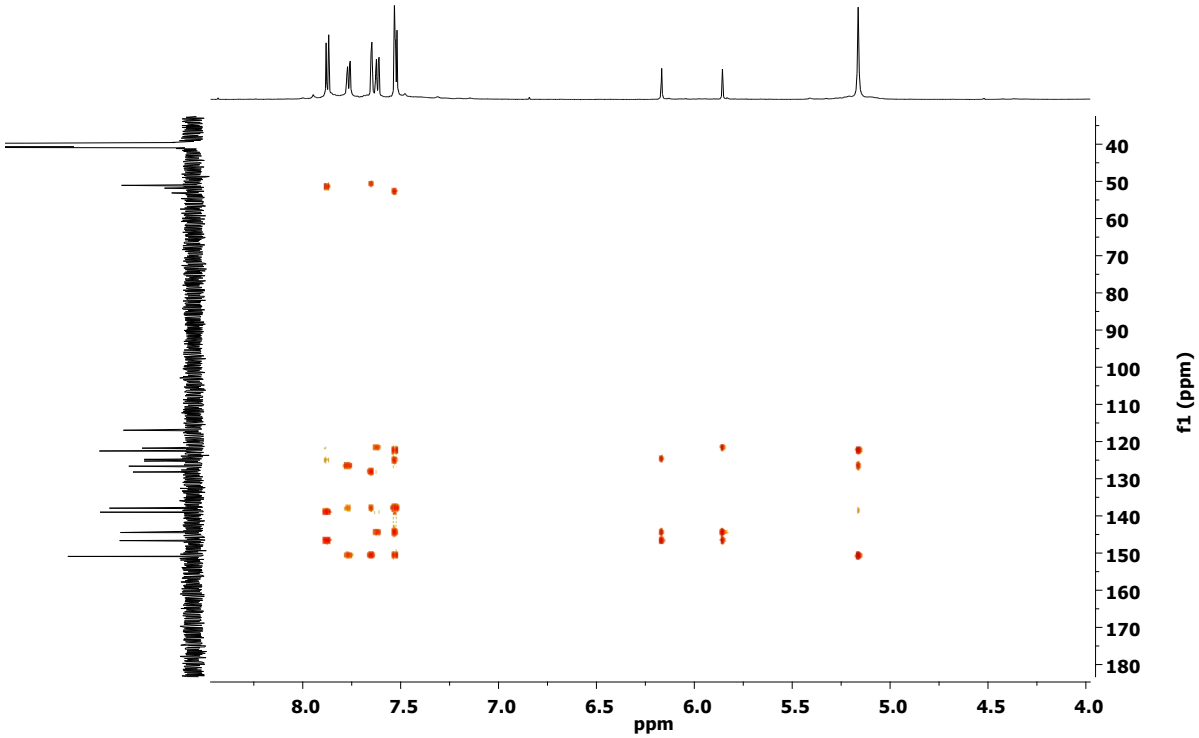


Figure S7. ^{1}H-^{13}C HMBC NMR spectrum (DMSO-d6) of cage **3.**

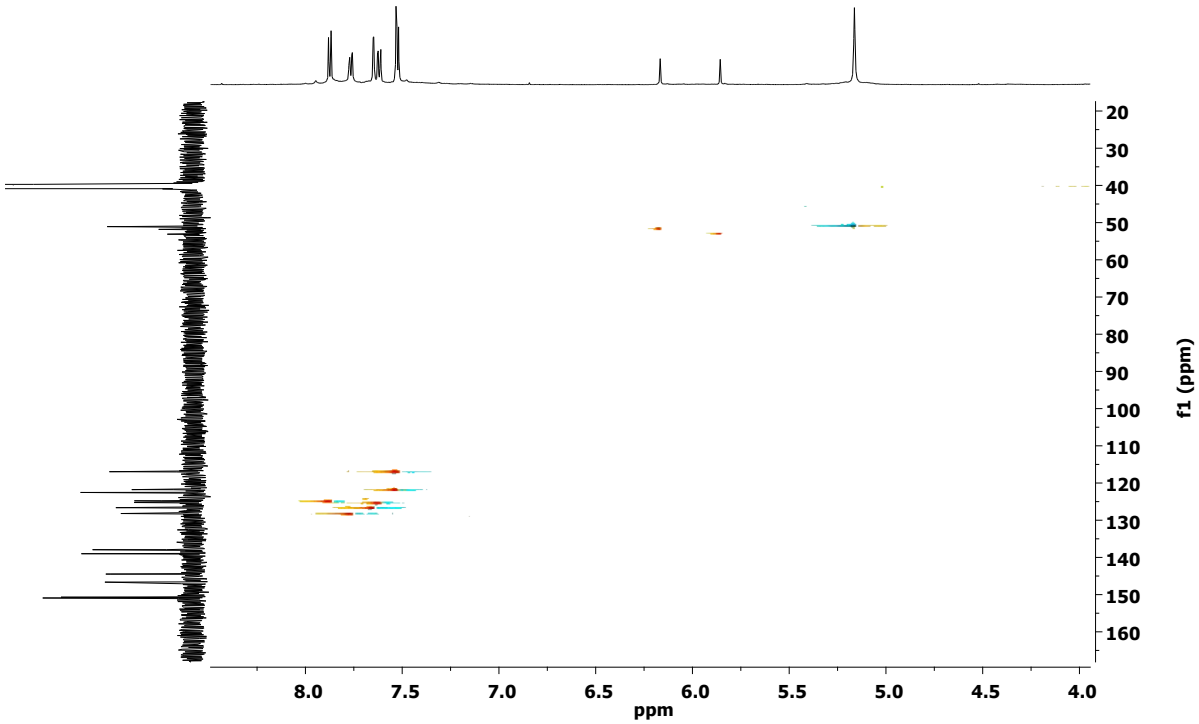


Figure S8. ^{1}H-^{13}C HSQC NMR spectrum (DMSO-d6) of cage **3**.

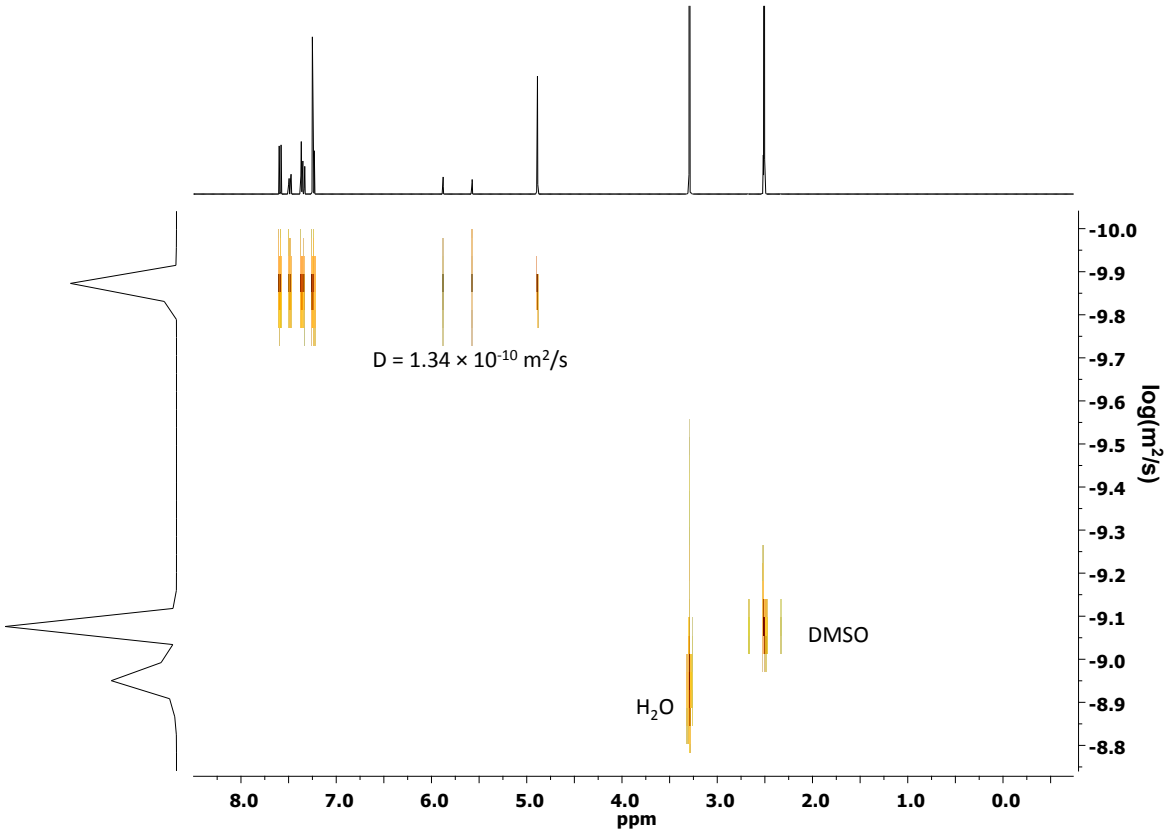


Figure S9. DOSY NMR spectrum (600 MHz, DMSO-d6) of cage **3**. Solvodynamic radius according to Stokes-Einstein equation is r = 0.82 nm.

4. Mass spectrometry

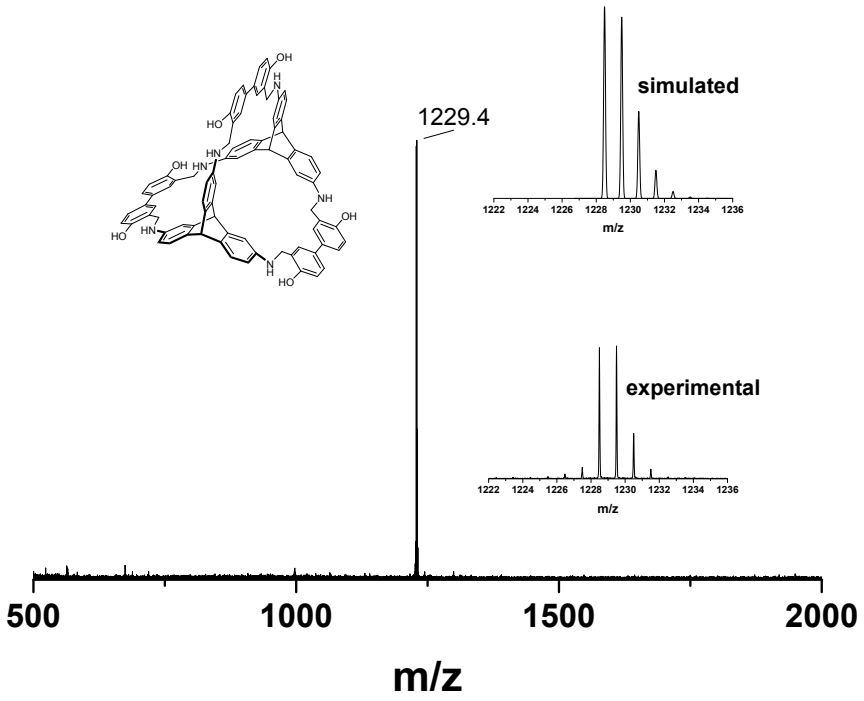


Figure S10. MALDI-TOF Mass spectrum of cage **2** (matrix DCTB).

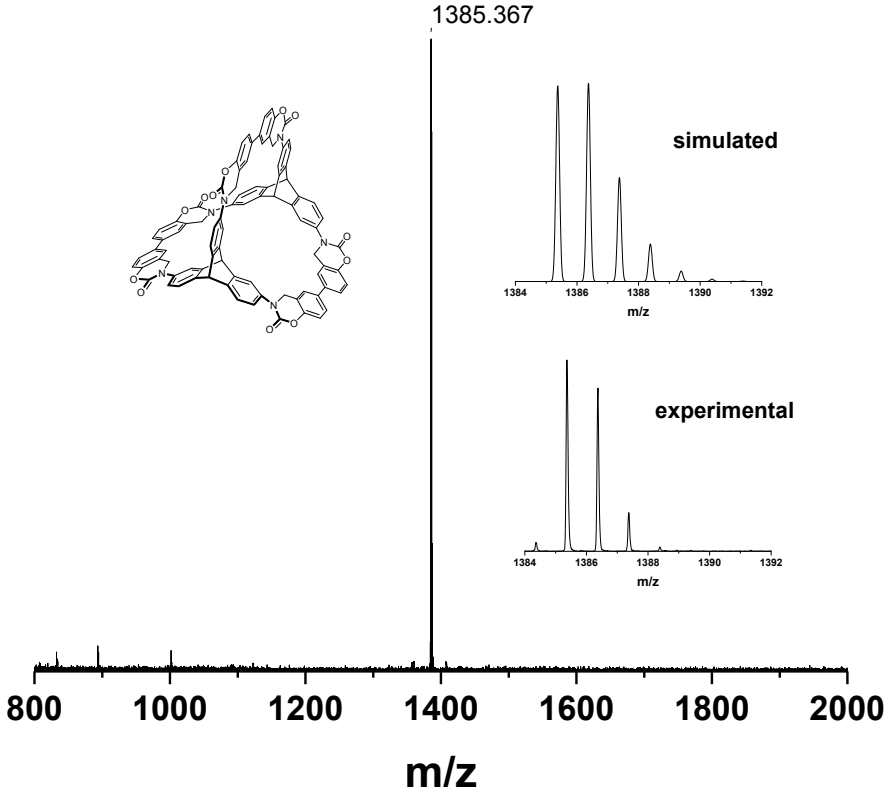


Figure S11. MALDI-TOF Mass spectrum of cage **3** (matrix DCTB).

5. IR Spectra

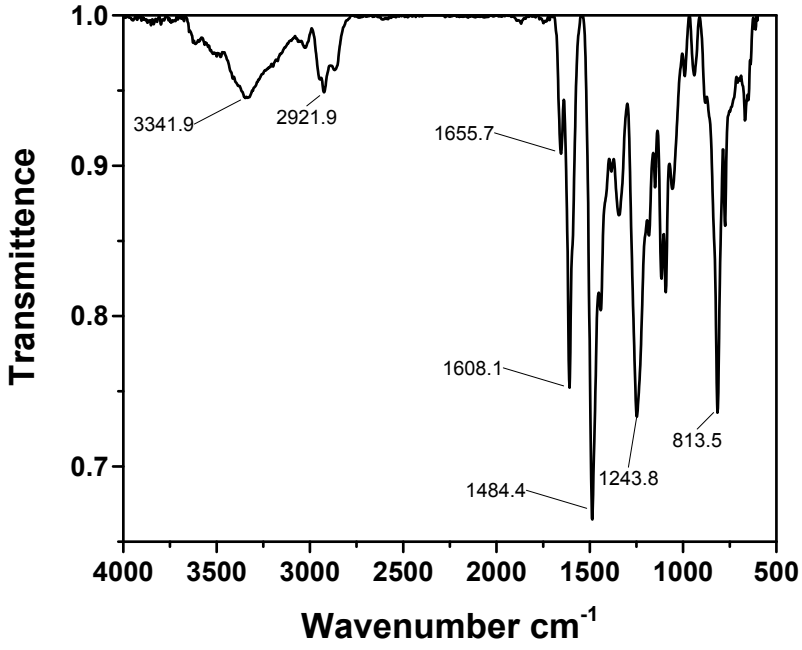


Figure S12. FTIR (ATR, neat) spectrum of cage **2**.

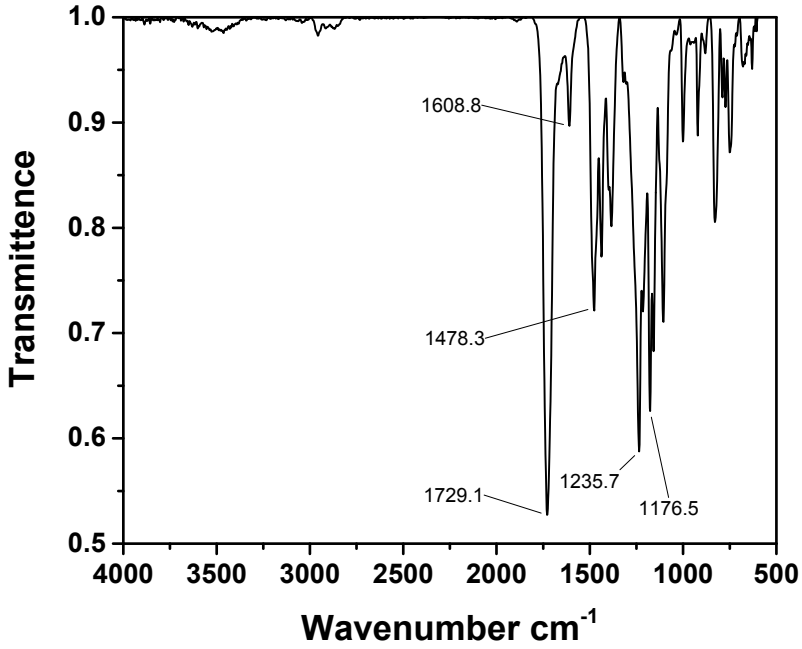


Figure S13. FTIR (ATR, neat) spectrum of cage **3**.

6. Thermogravimetric Analysis

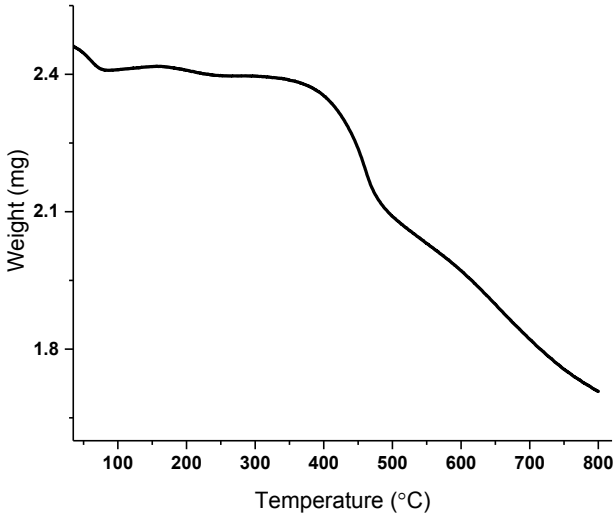


Figure S14. Thermogravimetric curve of cage **3**.

7. Gas sorption

Activation protocols:

First sample: Cage **3** was added in DMSO and heated to dissolve. Any non-dissolved solid was removed by filtration to give a clear transparent solution, which was added dropwise into water. A colorless precipitation appeared, and the mixture was stirred for 5 h and kept still for 2 d. The solid was collected by filtration and washed with water (5 x) and immersed in acetone (HPLC grade) for 4 h (repeated 7 cycles). The same was done with n-pentane. The product was dried in vacuum at 200 °C (16 h) and degassed at 200 °C (3 h) before gas sorption analysis.

Second sample: Cage **3** was dissolved in hot DMSO and dropped into hot methanol. The clear solution was slowly cooled to room temperature. After three weeks, the formed precipitate was collected and activated as described above. The final product was dried in vacuum at 150 °C. The samples were degassed at 200 °C (3 h) before being analysed.

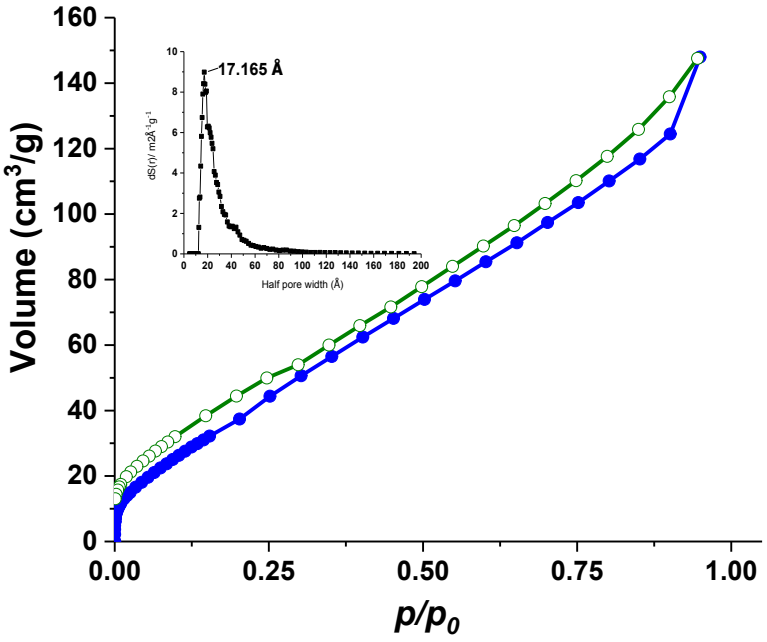


Figure S15. Nitrogen sorption isotherm of cage **3** at 77 K. Filled circles corresponds to adsorption and empty circles corresponds to desorption. The inset shows the pore-size distribution by NL-DFT (N2 at 77K on carbon, NLDFT cylinder pores, NLDFT equilibrium model, fitting error: 2.7%).

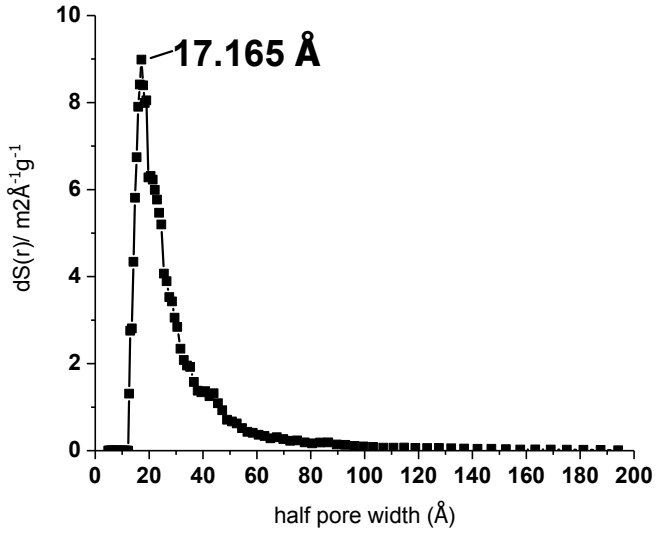


Figure S16. pore-size distribution by NL-DFT (N2 at 77K on carbon, NLDFT slit pores, NLDFT equilibrium model, fitting error: 3.359%).

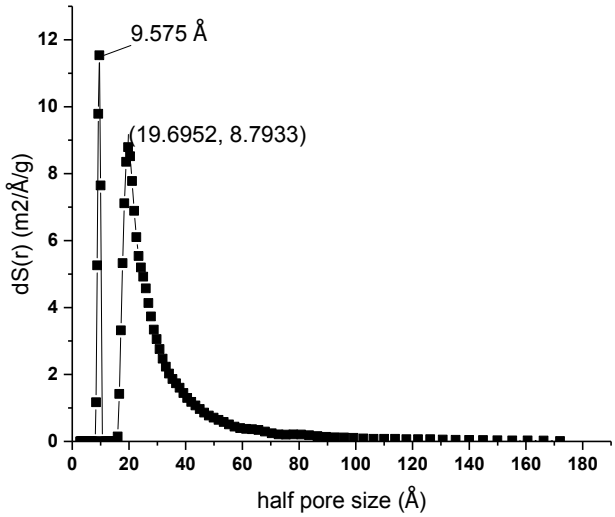


Figure S17. pore-size distribution by QS-DFT (N2 at 77K on carbon, slit/cylindr. pores, QSDFT equilibrium model, fitting error: 1.927%).

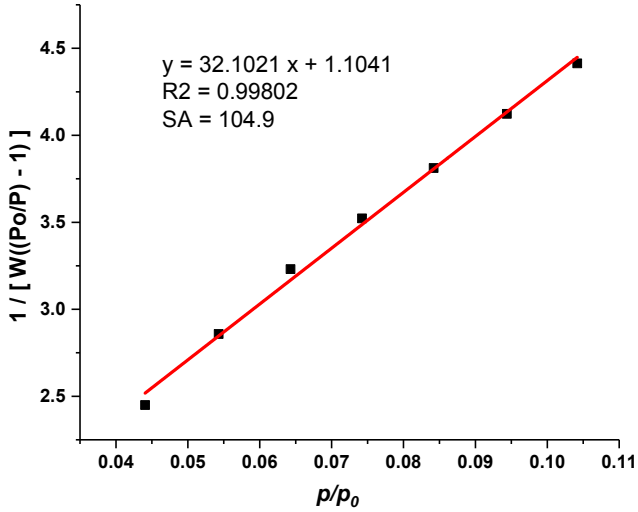


Figure S18. BET plot of cage **3** calculated from the nitrogen isotherm at 77 K. (first run)

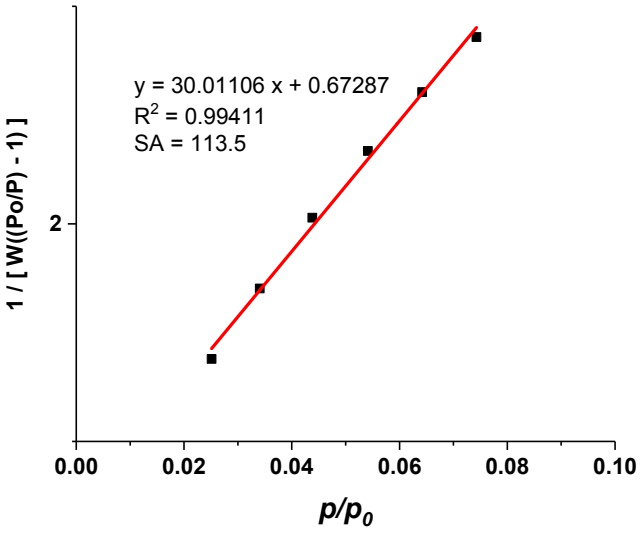


Figure S19. BET plot of cage **3** calculated from the nitrogen isotherm at 77 K (second run).

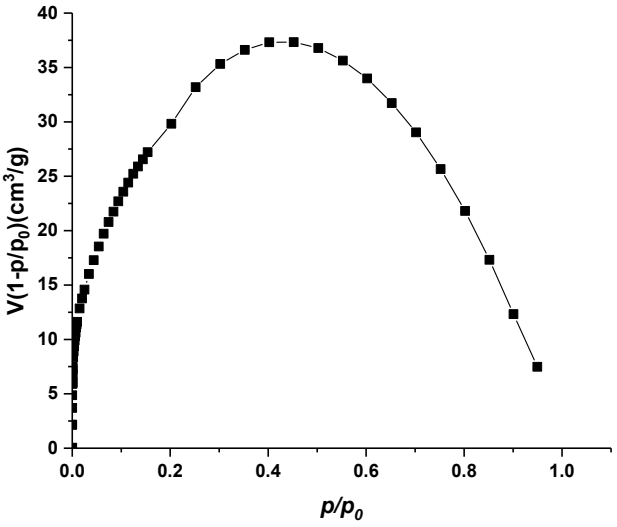


Figure S20. Rouquerol plot of cage **3** calculated from the nitrogen isotherm at 77 K.

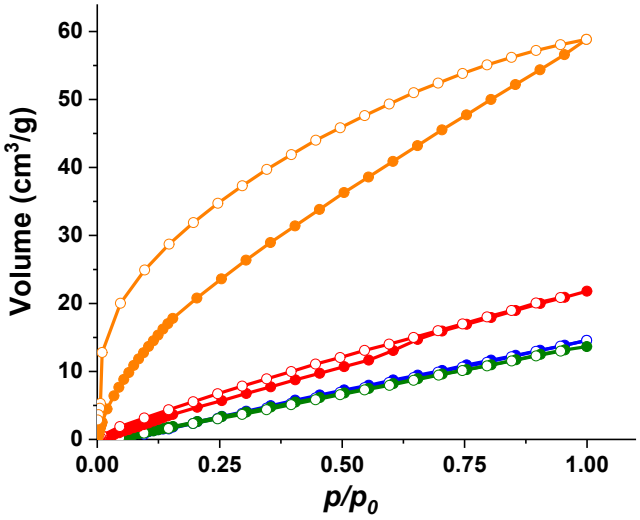


Figure S21. Gas sorption isotherms of cage **3** at 273 K. Filled circles corresponds to adsorption and empty circles corresponds to desorption. blue: nitrogen; green: hydrogen; red:CH_4; orange: CO_2

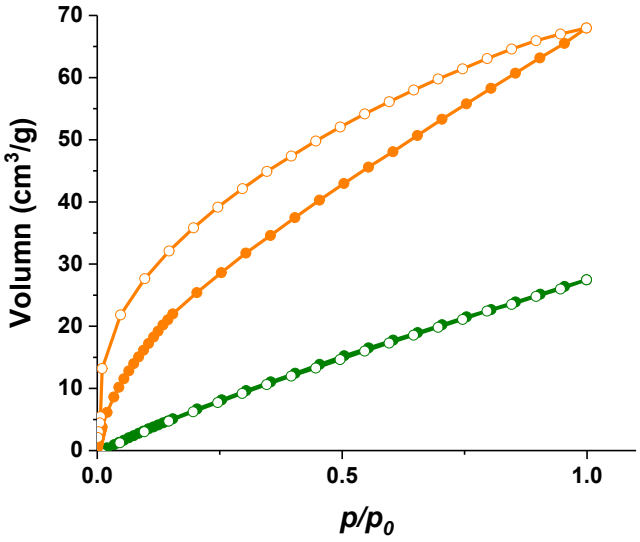


Figure S22. Gas sorption isotherms of cage **3** at 263 K. Filled circles corresponds to adsorption and empty circles corresponds to desorption. Green: CH_4; orange: CO_2.

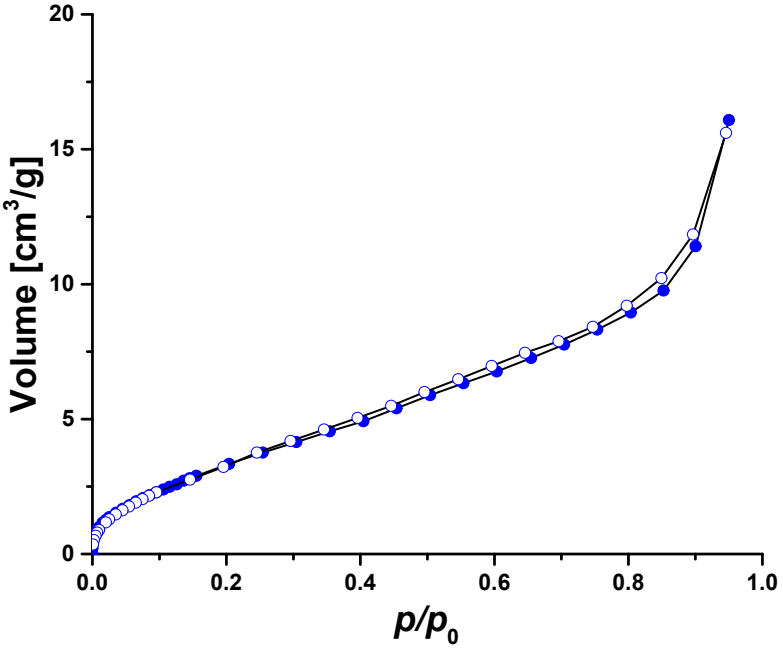


Figure S23. Nitrogen sorption isotherm of cage **2** at 77 K. Filled circles corresponds to adsorption and empty circles corresponds to desorption.

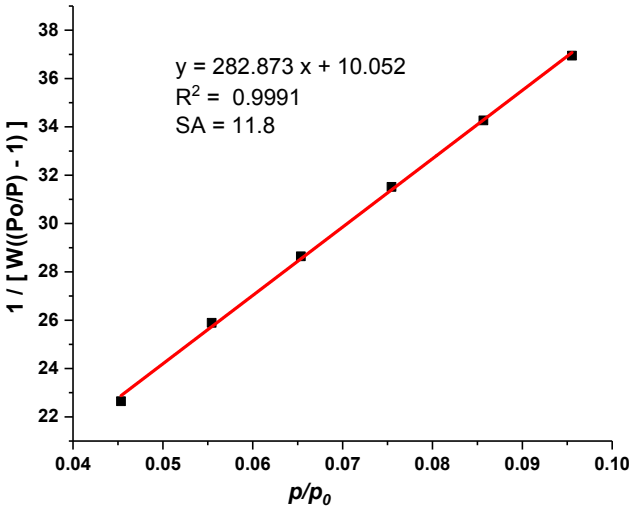


Figure S24. BET plot of cage **2** calculated from the nitrogen isotherm at 77 K.

8. Calculation of the heat of adsorption:

In this case, the calculation is based on the Clausius-Clapeyron eqution:

$$Q = -\frac{RT_1T_2}{T_2 - T_1} ln \frac{P_1}{P_2}$$

Q is the enthalpy of the adsorption ($J \cdot mol^{-1}$)

R is the universal gas constant($J \cdot K^{-1} \cdot mol^{-1}$)

T_1, T_2 is the temperature (K)

P_1, P_2 is the pressure when the uptake of the gas is the same ($\Delta < 0.005$ mmol/g) at different temperature (Pa).

Set up the gas uptake values (mmol/g) at 273 K as X column and set the Y column values as the calculation results of Q.

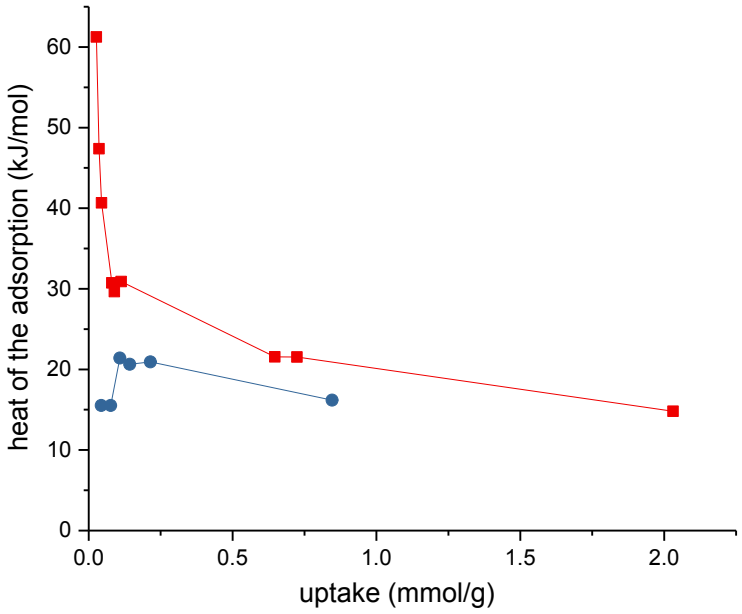


Figure S25. Calculated heat of adsorption for cage **3**, red:carbon dioxide;blue:CH_4.

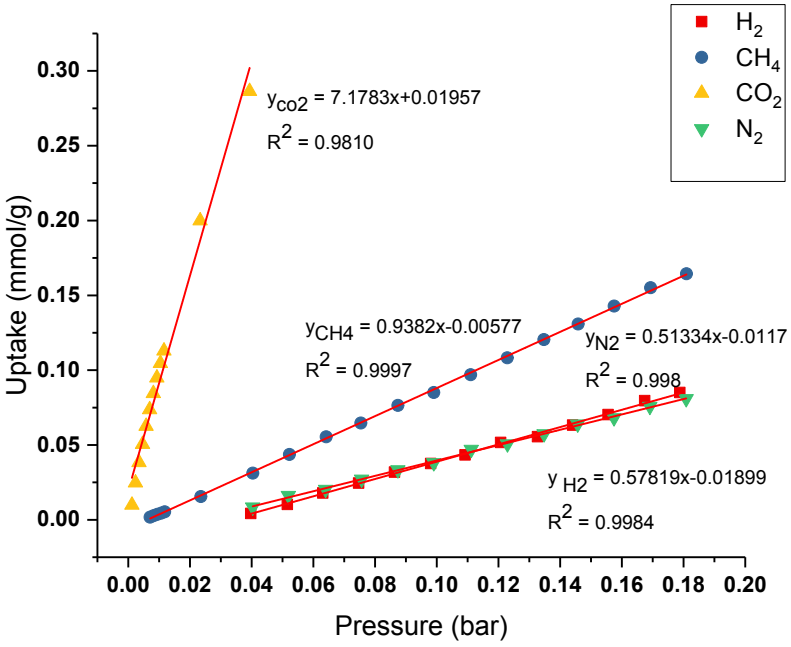


Figure S26. Initial slope calculation for CO_2, CH_4, N_2 and H_2 isotherms collected at 273 K (P<0.2 bar)

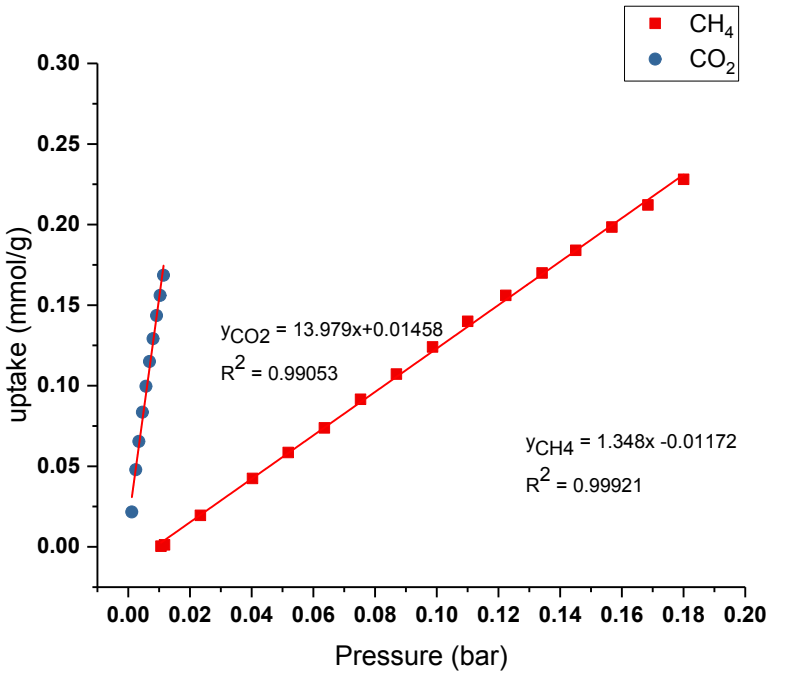


Figure S27. Initial slope calculation for CO_2, CH_4, N_2 and H_2 isotherms collected at 273 K (P<0.2 bar)

Table S1a. The selectivity of cage **3** calculated from Henry law constants from data at the low pressure regime.

CO_2/CH_4(273K)	CO_2/N_2(273K)	H_2/N_2(273K)	CO_2/CH_4(263K)
7.6	13.9	1.1	10.4

Table S1b. Summary of gas sorption data

	cc/g	mmol/g	wt%
N_2(77K)	147.9	6.6	18.5
H_2(77K)	97.3	4.3	0.88
CO_2(273 K)	58.8	2.6	11.6
CH_4(273 K)	21.8	0.97	1.6
H_2(273 K)	13.6	0.61	0.12
N_2(273 K)	14.5	0.65	1.8
CO_2(263 K)	68.0	3.0	13.3
CH_4(263 K)	27.5	1.2	1.9

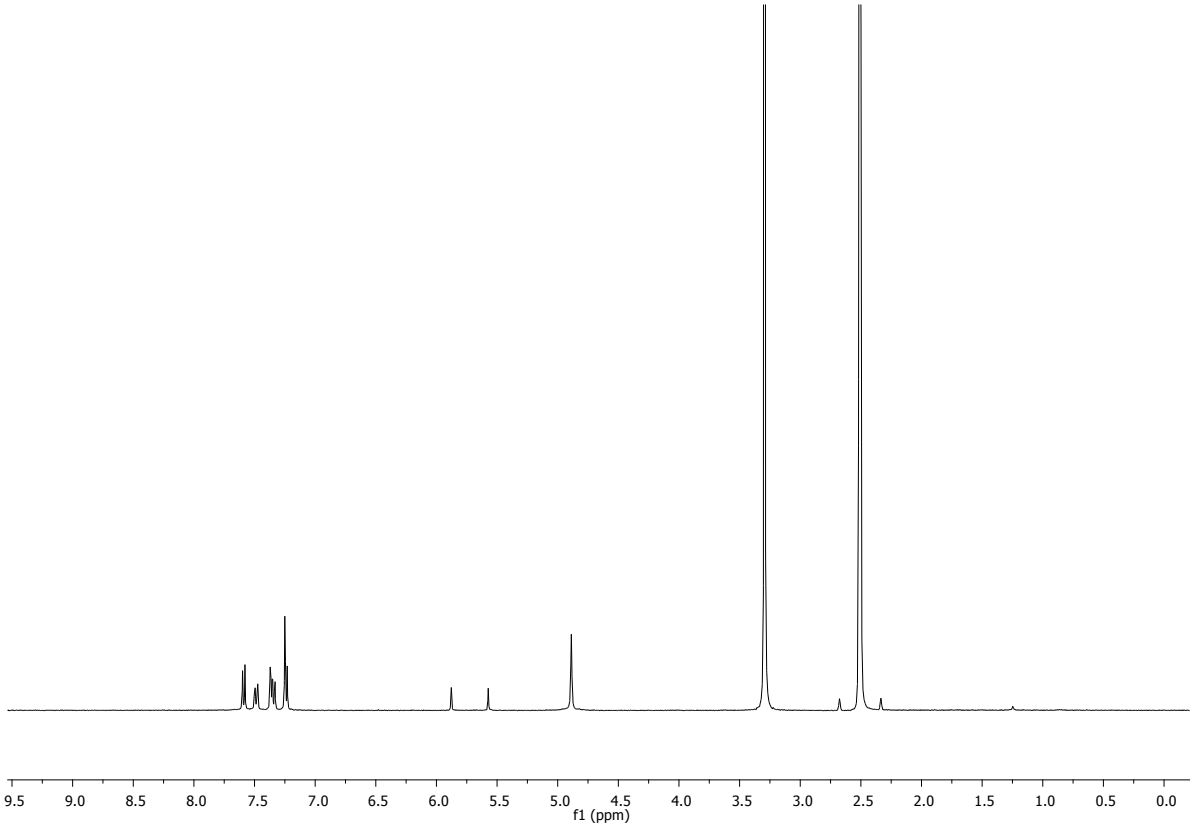


Figure S28. ^{1}H NMR spectra of cage **3** after gas sorption.(500 MHz, DMSO-d6)

9. PXRD

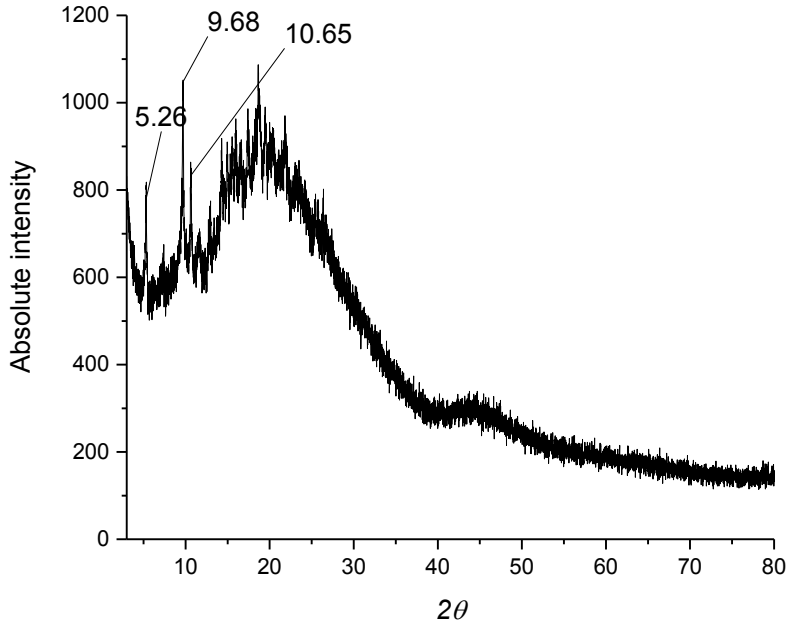


Figure S29. Powder X-ray diffractogram of cage **3**.

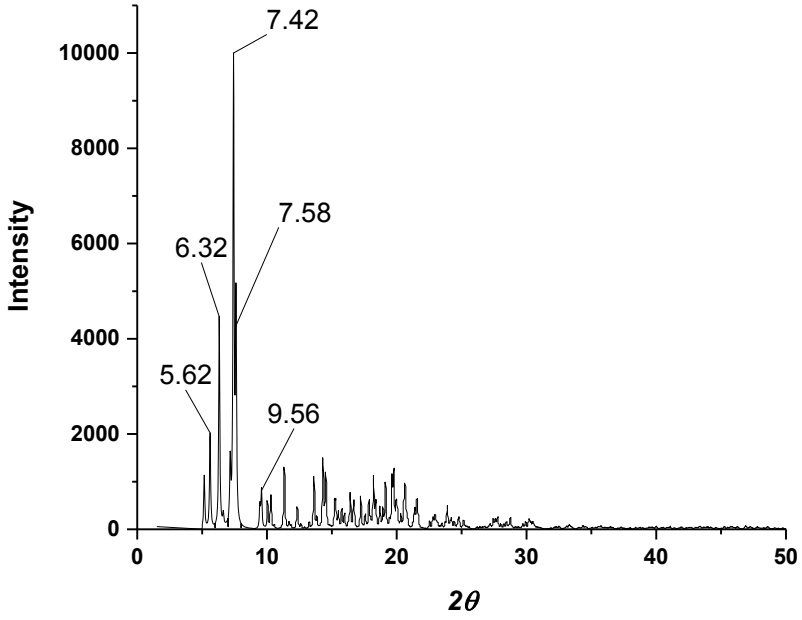


Figure S30. Simulated XRD pattern calculated from single crystal structure of cage **3** (polymorph α)

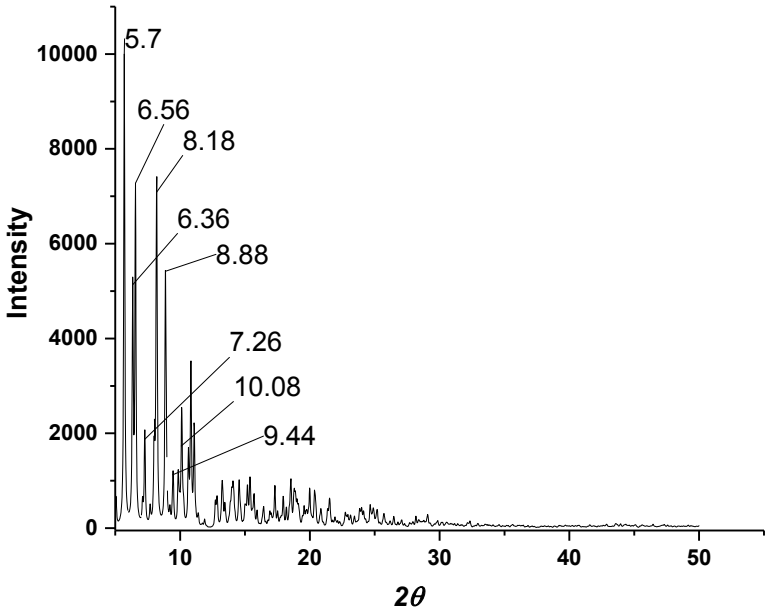


Figure S31. Simulated XRD pattern calculated from single crystal structure of cage **3** (polymorph β)

10. Stability tests

To investigate the stability of **cage 3** in different pH environment, we weighed a certain amount of **cage 3** (see in Table 1) and stirred it in 1 mL HCl or NaOH solution. After the treatment, the solid was collected by filtration, washed with water (5 × 5 mL), dried in vacuum at 90 °C for 4h and weighed again. Then ^{1}H NMR experiments were carried out and the spectra compared with the starting material.

Table S2. The weight change in pH-stability experiment of cage **3**

Entry	Treatment	Weight(before) (mg)	Weight(after) (mg)	Weight loss(%)
1	10 M HCl (16 h)	3.3	3.1	6.1
2	10 M HCl (8 h, 100 °C)	3.4	2.7	20.7
3	1 M HCl (16 h)	2.7	2.5	7.4
4	1 M HCl (16 h, 100 °C)	3.1	2.9	6.4
5	1 M HCl (5 d)	3.7	3.5	5.4
6	10 M NaOH (16 h)	4.2	0.6	85.7
7	1 M NaOH (16 h)	1.9	1.8	5.2
8	1 M NaOH (16 h, 100 °C)	2.9	2.8	3.5
9	1 M NaOH (5 d)	3.2	3.1	3.1
10	trifluoroacetic acid (conc. 16 h,)	4.5	4	11
11	16 M HNO_3 (16 h)	5.3	4.5	15

Table S3. The weight change in pH-stability experiment of cage **1**

Entry	Treatment	Weight (before) (mg)	Weight (after)(mg)	Weight loss(%)
1	1 M HCl (16 h)	5.9	2	66.1
2	0.1 M HCl(16 h)	4.4	3.5	20.4
3	0.01 M HCl (16 h)	4.2	3.8	9.5
4	0.001 M HCl (16 h)	5.2	4.9	5.7
5	0.0001 M HCl (16 h)	3.4	3.3	2.9
6	0.0001 M HCl (16 h,100 °C)	3.4	3.0	13.3
7	0.00001 M HCl (16 h)	3.8	3.6	5.2
8	0.00001 M HCl (16 h,100 °C)	3.6	3.3	8.3
9	1 M NaOH (16h)	5	0	100
10	0.1 M NaOH (16h)	3.6	2.7	25
11	0.01 M NaOH (16h)	4.6	4.1	10.8
12	0.001 M NaOH(16h)	3.4	3.2	5.8
13	0.0001 M NaOH (16 h)	3.8	3.7	2.6
14	0.0001 M NaOH (16 h,100 °C)	2.9	2.7	6.9

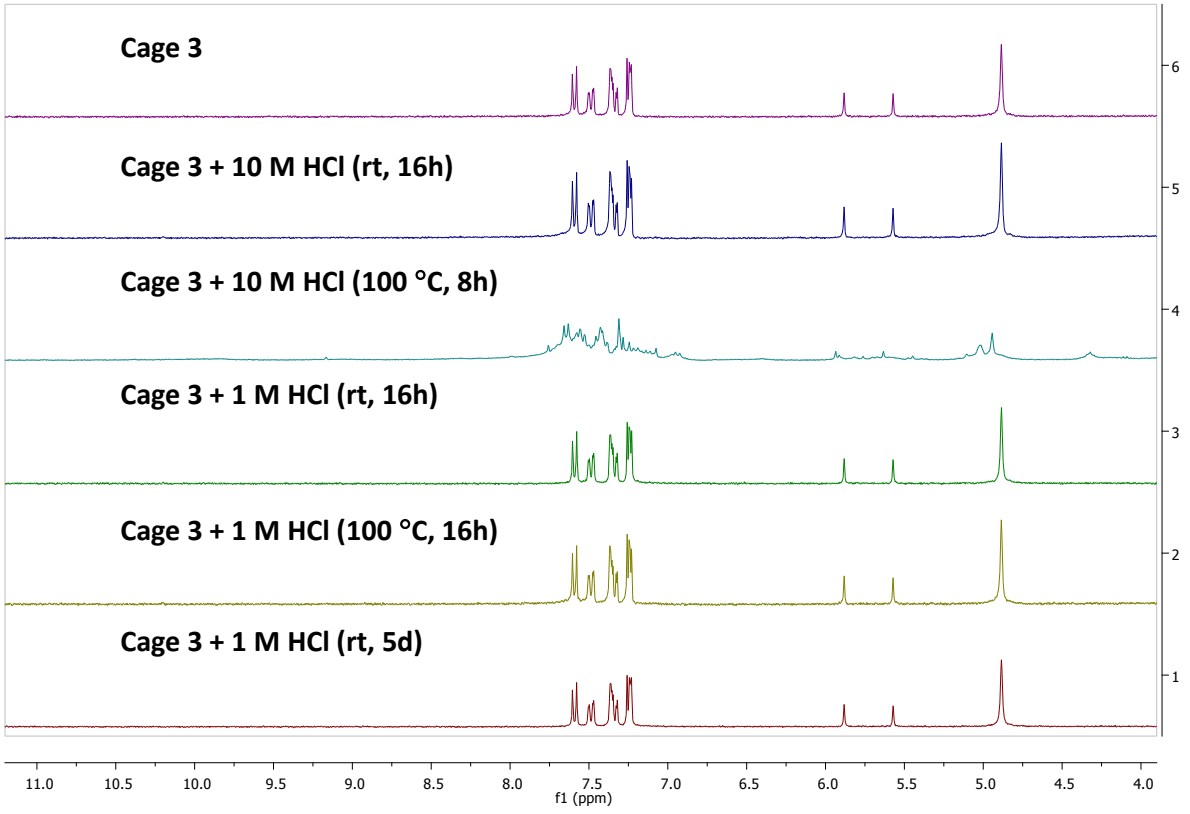


Figure S32. ^{1}H NMR spectra of cage **3** after treatment with HCl (300 MHz, DMSO-d6).

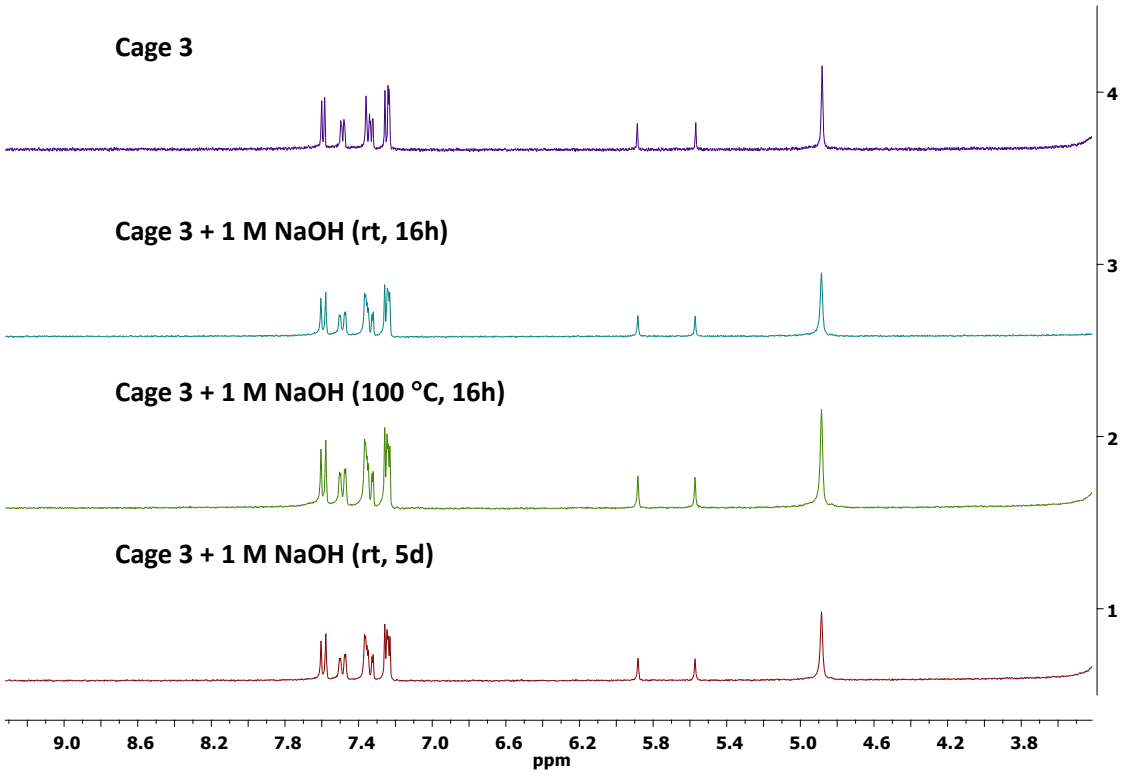


Figure S33. ^{1}H NMR spectra of cage **3** after treatment with NaOH (300 MHz, DMSO-d6).

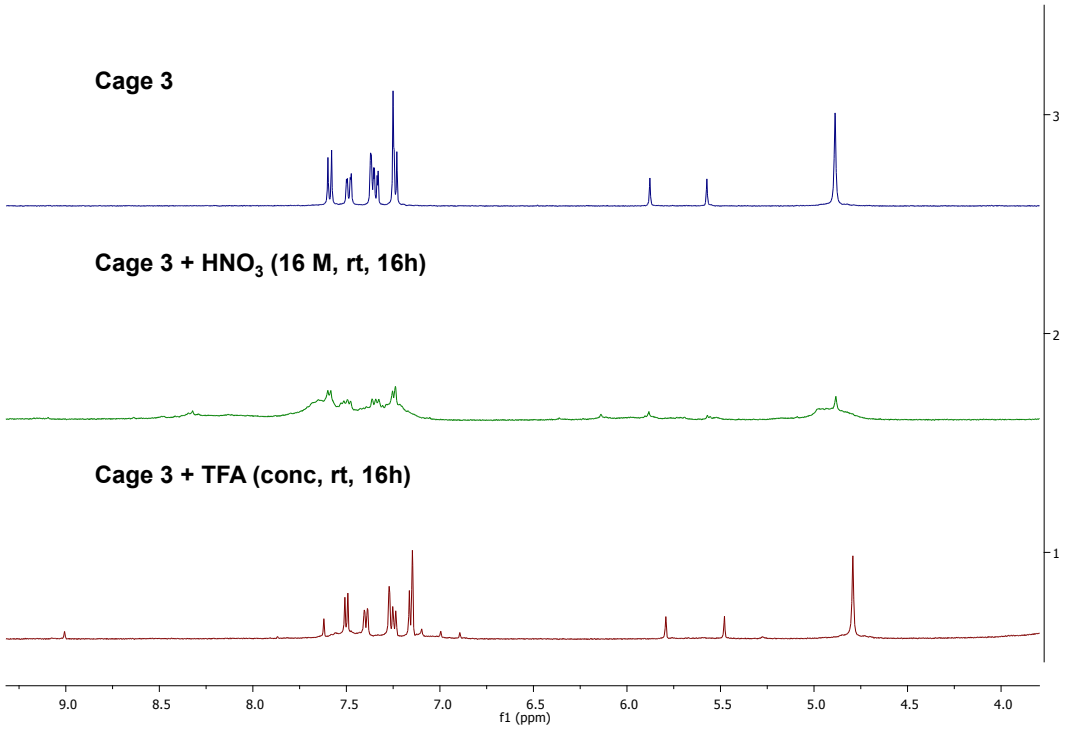


Figure S33. ^{1}H NMR spectra of cage **3** after treatment with HNO_3 and trifluoroacetic acid (300 MHz, DMSO-d6).

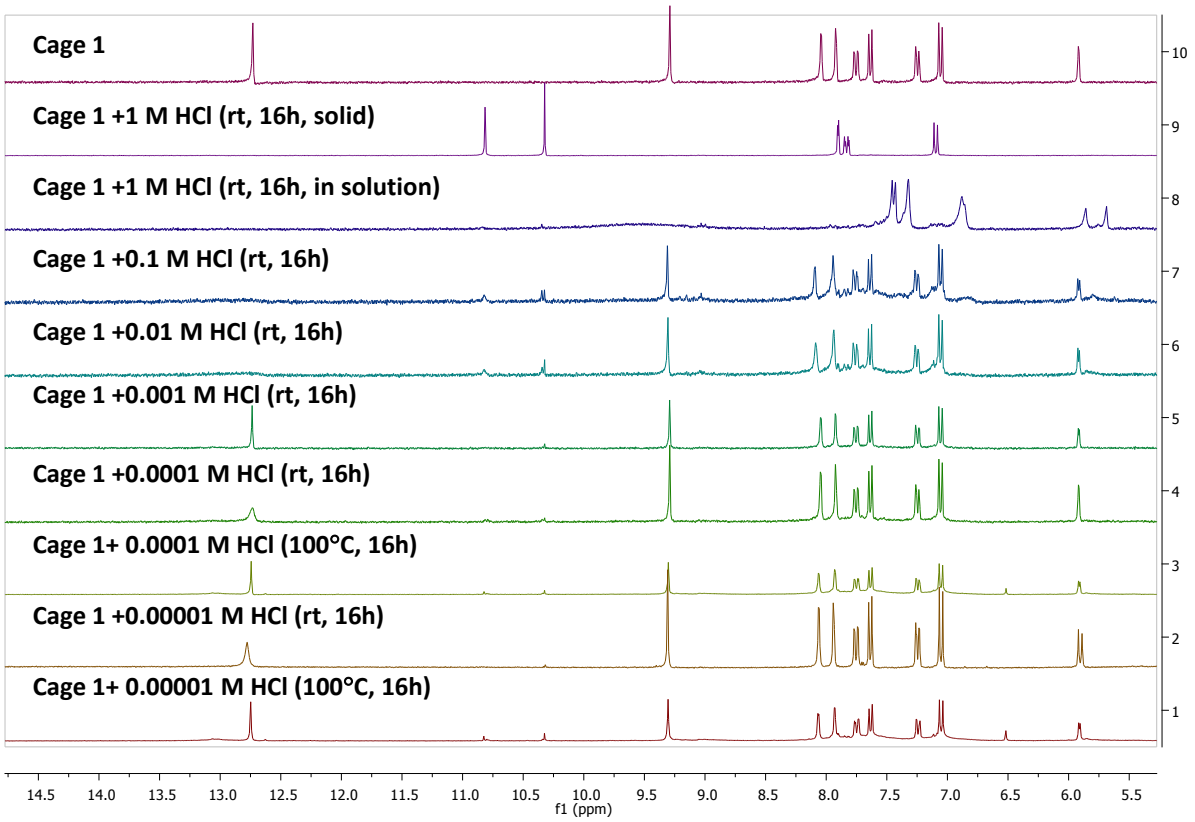


Figure S34. ^{1}H NMR spectra of cage **1** after treatment with HCl (300 MHz, DMSO-d6).

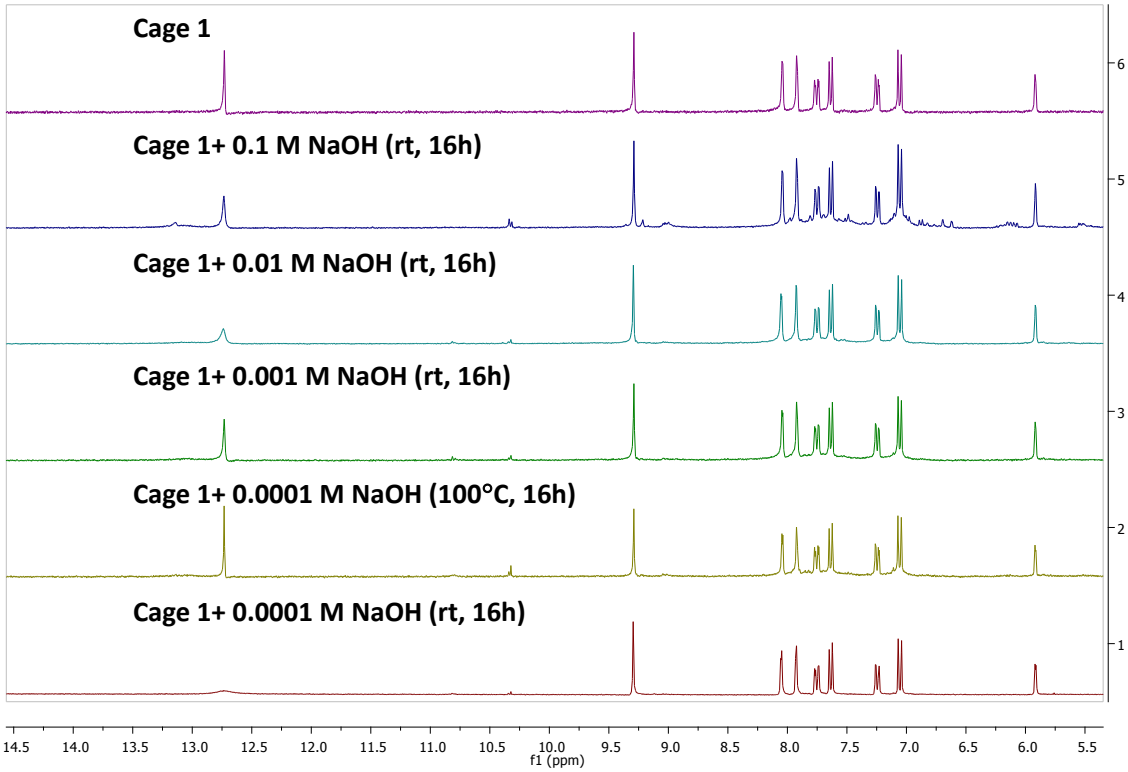


Figure S35. ^{1}H NMR spectra of cage **1** after treatment with NaOH (300 MHz, DMSO-d6).

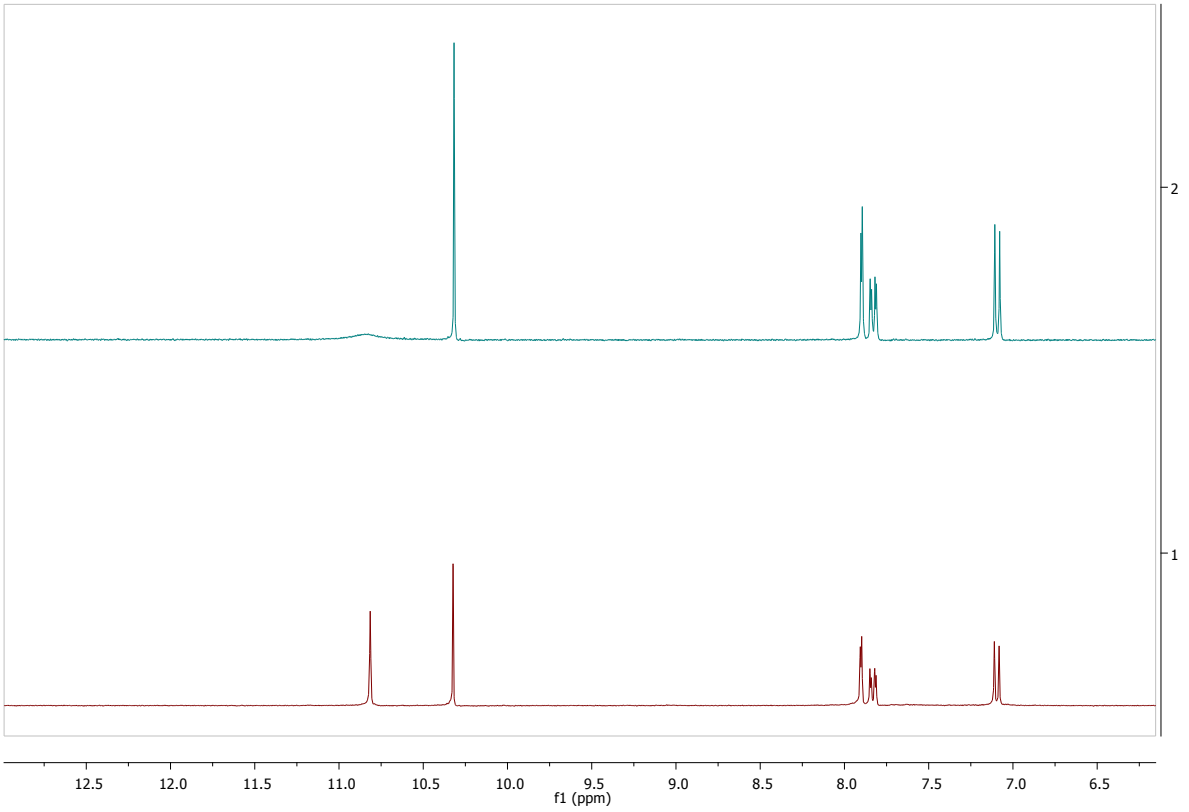


Figure S36. [1]H NMR spectrum of the collected solid after treatment of cage **1** with 1 M HCl (bottom) and the spectrum of bissalicylaldehyde (top) (300 MHz, DMSO-d6).

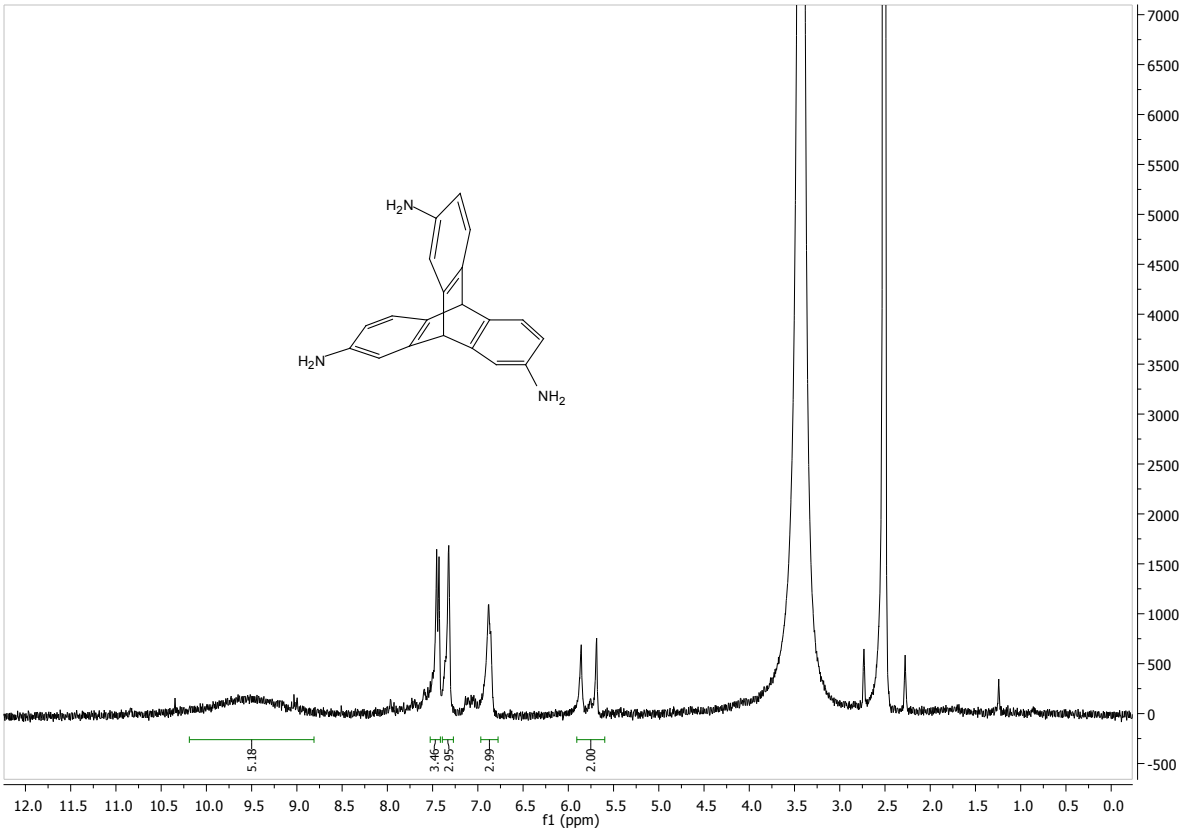


Figure S37. [1]H NMR spectra of the extracted aqueous solution after treatment of cage **1** with 1 M HCl (bottom) and the spectra of bissalicylaldehyde (top) (300 MHz, DMSO-d6).

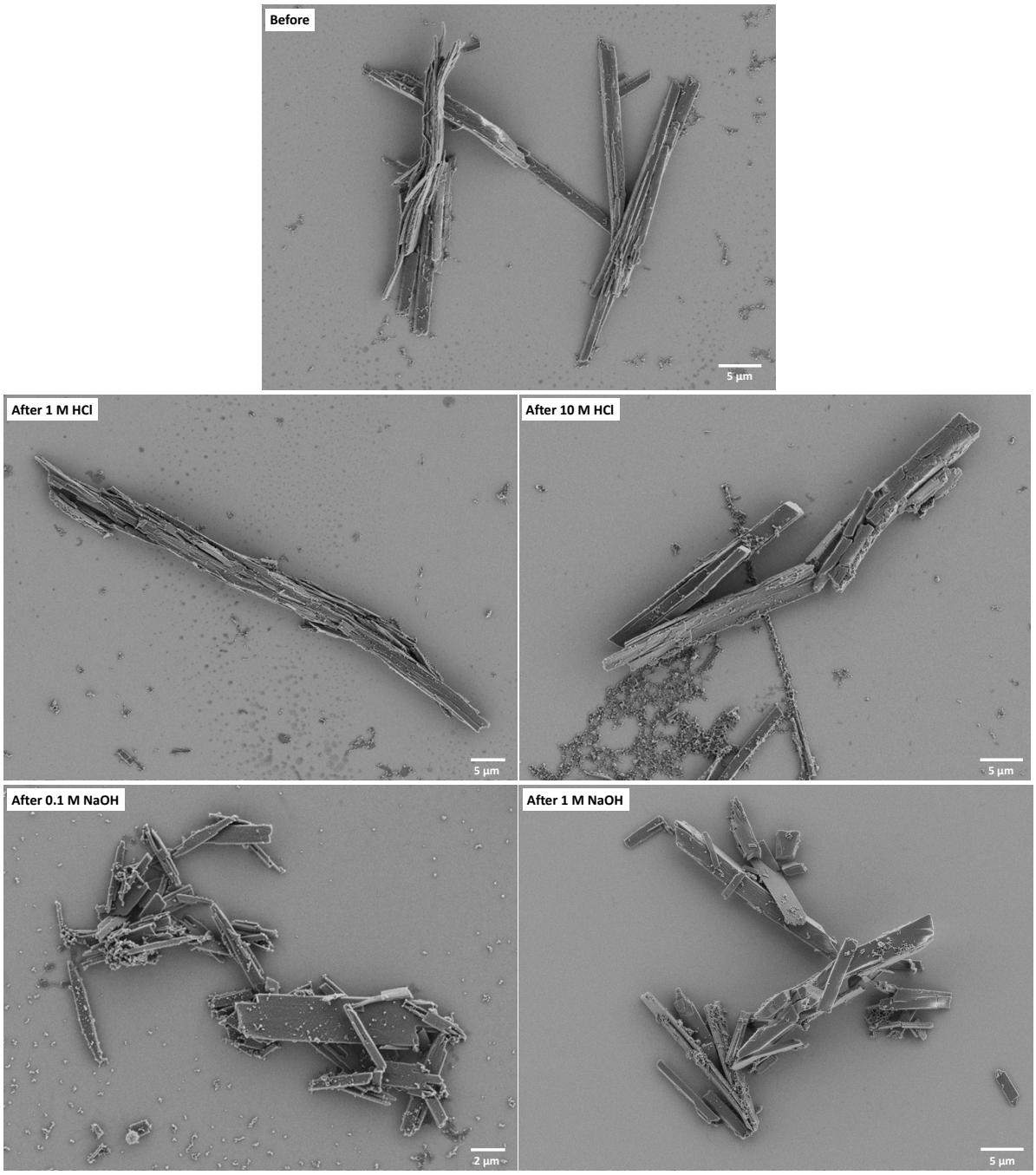


Figure S38. Comparison of crystallites of carbamate cage **3** by SEM before and after treatment with acid or base overnight.

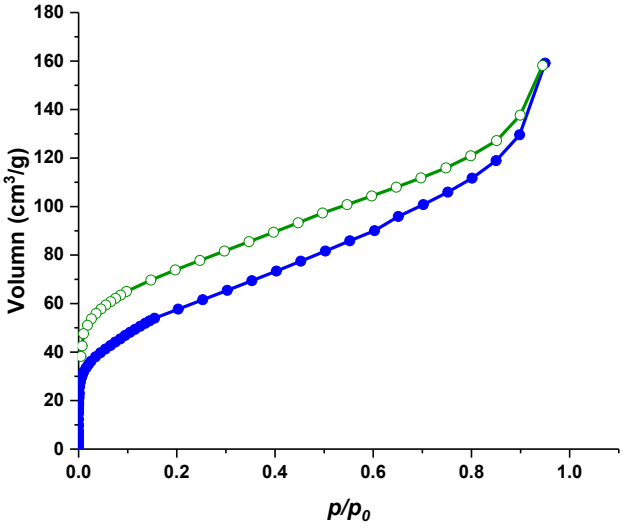


Figure S39. Nitrogen sorption isotherm of cage **3** after treatment with 10 M HCl(16 h, rt) at 77 K. Filled circles corresponds to adsorption and empty circles corresponds to desorption.

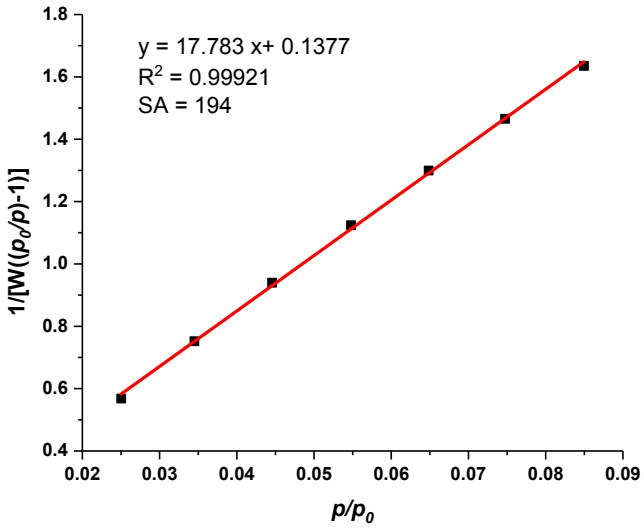


Figure S40. BET plot of cage **3** after treatment with 10 M HCl (16 h, rt) calculated from the nitrogen isotherm at 77 K.

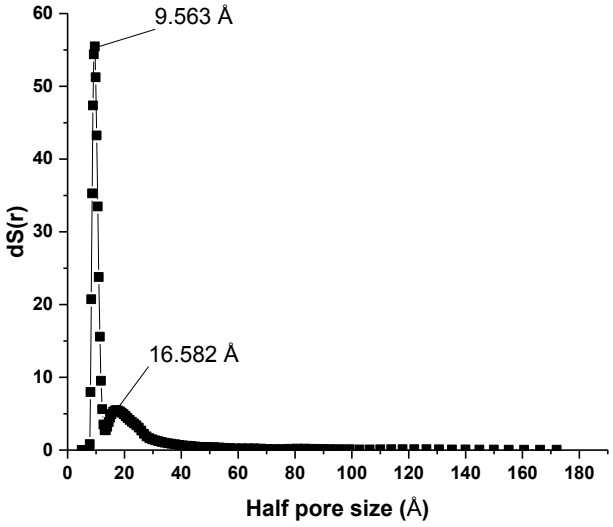


Figure S41. Pore-size distribution of cage **3** after treatment with 10 M HCl (16 h, rt) by QS-DFT (N_2 at 77K on carbon, cylindr. pore, QSDFT equilibrium model, fitting error: 1.731%).

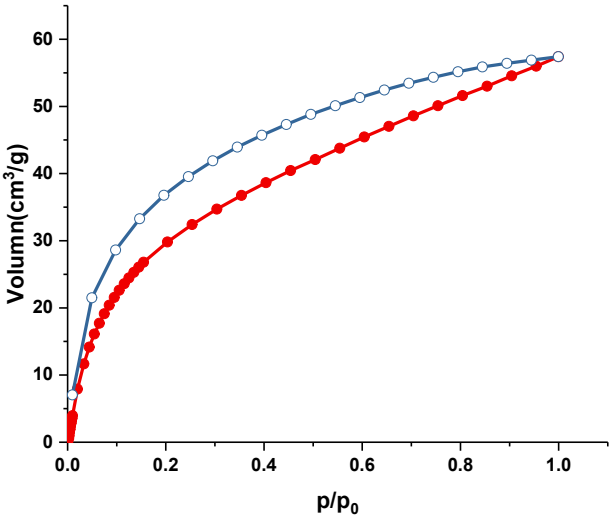


Figure S42. CO_2 sorption isotherms of cage **3** after treatment with 10 M HCl (16 h, rt) at 273 K.

[1] Schneider, M.W.; Oppel, I.M.; Mastalerz, M. *Chem. Eur. J.* **2012**, *18*, 4156-4160.