Supplementary material for

"Piperazine Bridged Resorcinarene Cages"

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CONTENT:

I. General ……S1

II. Synthetic procedure, ^{1}H, ^{13}C NMR and ESI-TOF mass spectra of **2a**…….....S2

III. Synthetic procedure, ^{1}H,^{13}C, $^{1}H^{13}C$ HMQC, $^{1}H^{13}C$ HMBC, $^{1}H^{1}H$ COSY NMR and ESI-TOF mass spectra of **2b** ……S5

IV. Synthetic procedure, ^{1}H, ^{13}C NMR and ESI-TOF mass spectra of **2c** ……..S10

General

Melting points were determined with a Mettler Toledo FP62 capillary melting point apparatus and are uncorrected. Elemental analyses were carried out with a Varian ELIII elemental analyzer. ^{1}H and ^{13}C NMR, $^{1}H^{1}H$ COSY, $^{1}H^{13}C$ HMQC and $^{1}H^{13}C$ HMBC spectra were recorded on Bruker Avance DRX 500 (500 MHz for ^{1}H and 126 MHz for ^{13}C) spectrometer. ^{1}H and ^{13}C assignments were mainly based on $^{1}H^{1}H$ COSY, $^{1}H^{13}C$ HMQC and $^{1}H^{13}C$ HMBC 2D correlation spectra. All signals are expressed as δ values in ppm using residual solvent signal as internal standard. J values are given in Hz. The mass spectrometric studies was perform with a micromass LCT ESI-TOF instrument. Since the instrument does not permit MS/MS experiments, the fragmentation behavior of the samples were examined by in-source fragmentation induced collisions with the gas molecules present in the ion source. For this purpose, the ions were accelerated to different kinetic energies by tuning the sample cone voltage to different settings. At low voltage, the ions are not significantly accelerated and undergo fragmentations only to a minor extent upon collision with the surrounding gas molecules. With a high sample cone voltage, the ions approach the sample cone at a higher velocity and collisions with the surrounding gas lead to much more pronounced fragmentations.

All materials were commercial and used as such unless otherwise mentioned. Resorcinarene **1a-c** were prepared according to literature procedure.[1]

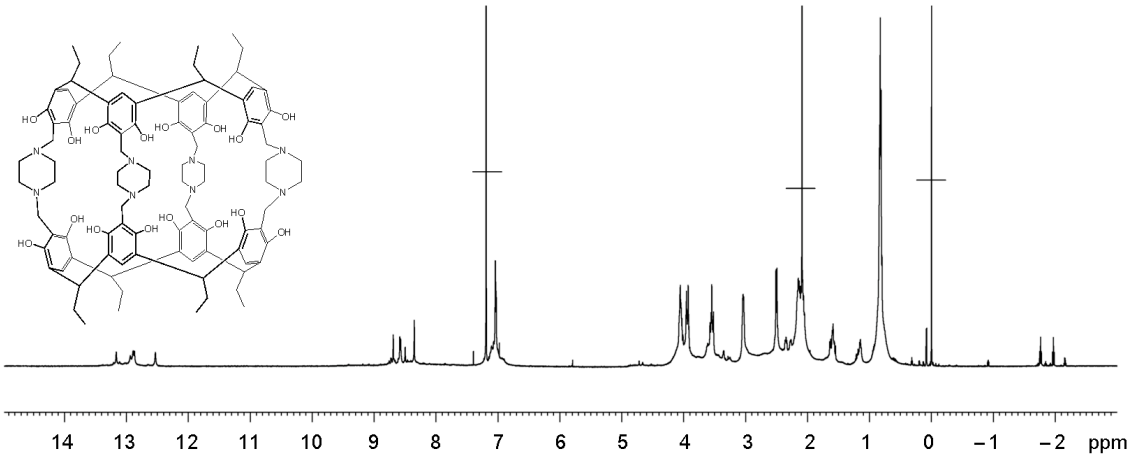
[1] (a) Timmerman, P.; Verboom, W.; Reinhoudt, D. *Tetrahedron* **1996**, *52*, 2663; (b) Jasat, A.; Sherman, J. C. *Chem. Rev.* **1999**, *99*, 931.

General procedure for the preparation of the covalent resorcinarene cages

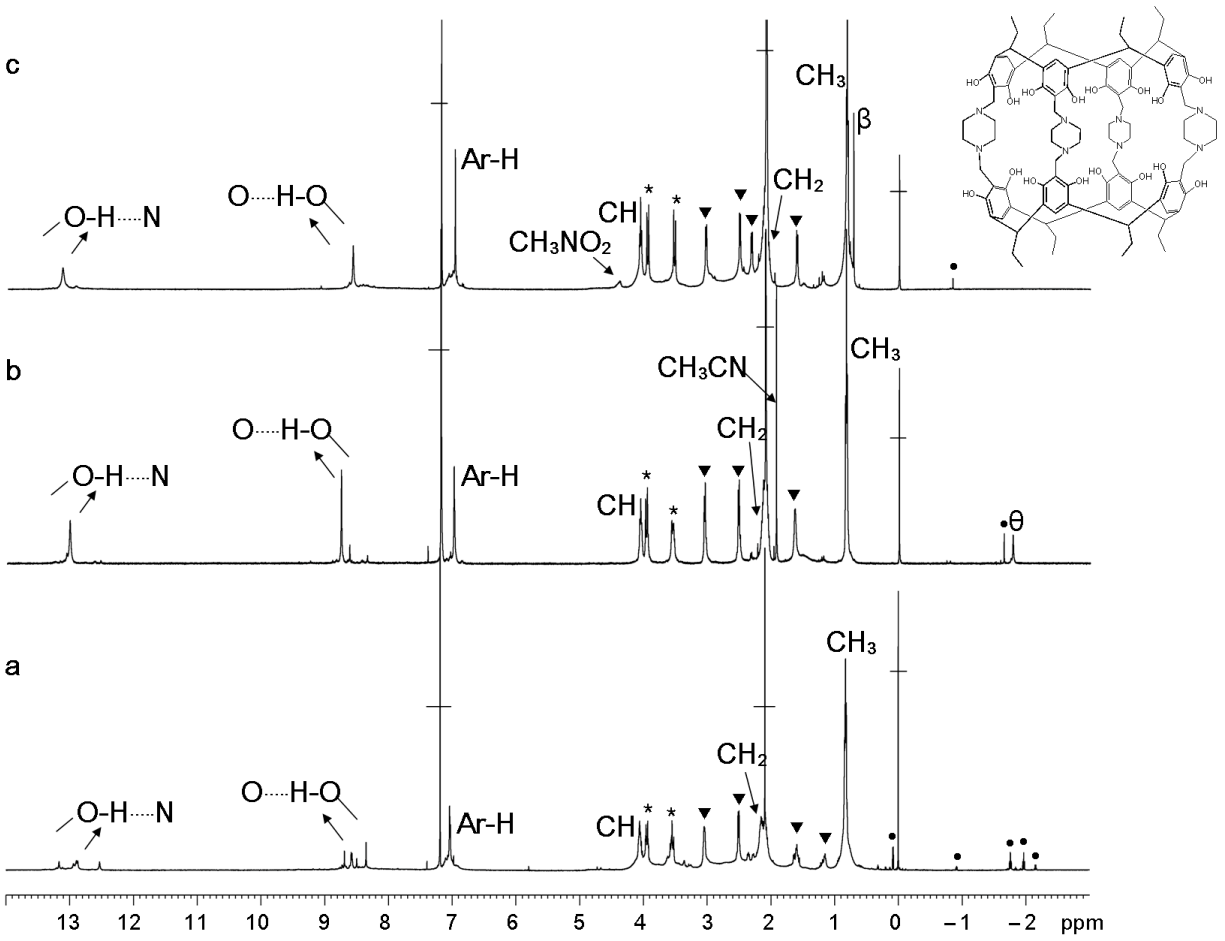
To a solution of excess formaldehyde (35 % aqueous solution) and a few drops of glacial acetic acid in ethanol (1.0 L), a solution of resorcinarene **1** (1.5 mmol) in ethanol (250 mL) and a solution of piperazine (3.0 mmol) in ethanol (250 mL) were added drop wise with flow rate of approximately 10 µL/min at 80 ^{o}C. The reaction mixture was reflux for a further 6 h and the solvent was evaporated in vacuum. The crude product was subject to chromatography and washed thoroughly with methanol to give the product.

C_2Resorcinarene cage **2a**

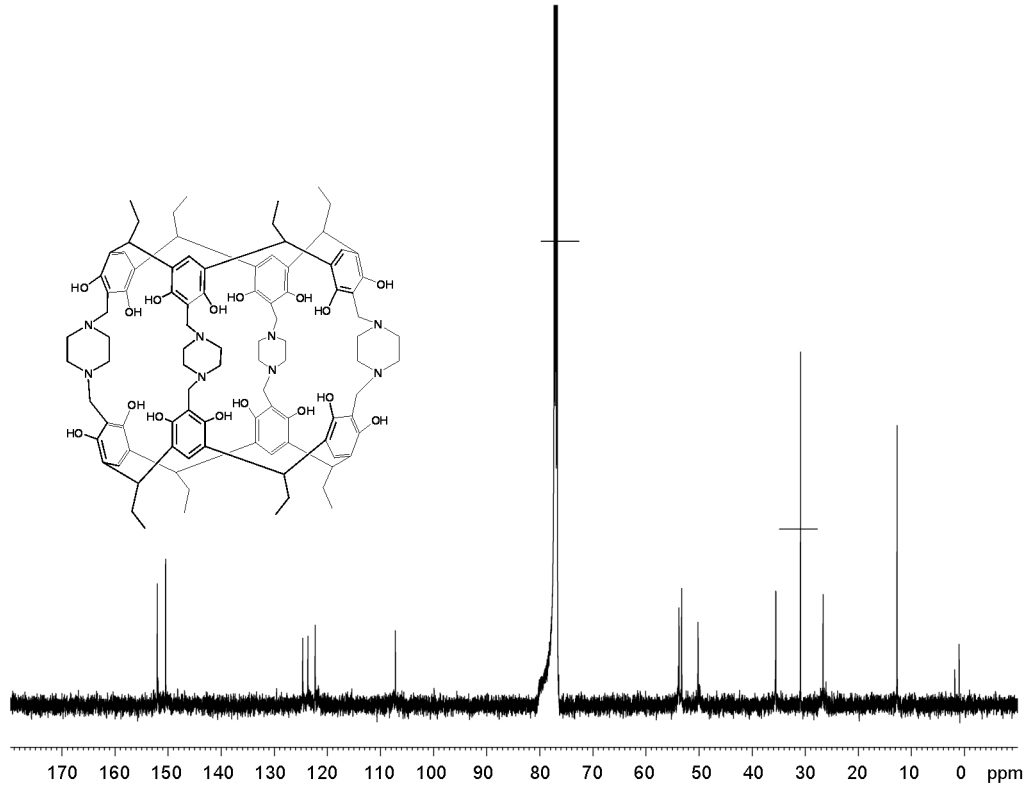
Formaldehyde (3 mL), ethanol (1.0 L), resorcinarene **1a** (1.0 g, 1.66 mmol) and piperazine (0.28 g, 3.32 mmol). Purification via flash chromatography (RediSep Flash Column (silica) 40/12g, from Teledyne Isco; eluent: CH_2Cl_2/CH_3OH 10 %) gave the product (0.43g, 32 %) as a cream white powder. Mp > 300 ^{o}C. (found C,64.31, H, 6.78, N, 6.08. $C_{96}H_{120}N_8O_{16}$·0.5CH_3OH·0.5CH_3CH_2OH 2CH_2Cl_2 requires C, 64.57, H, 7.02, N, 6.05). [$C_{96}H_{120}N_8O_{16}$ MW 1642.02; ESI-TOF MS $[M+H]^+$ 1641.93]. ^{1}H NMR (500 MHz, $CDCl_3$, 30 °C) δ: 12.96 (br, 8H, ArO*H*), 8.76 (br, 8H, ArO*H*), 7.11 (br, 8H, Ar*H*), 4.12 (m, 8H, C*H*), 4.00 (m, 8H, ArCH_2N), 3.62 (m, 8H, ArCH_2N), 3.11 (d, *J* 8.1 Hz, 8H, NCH_2R), 2.56 (d, 8H, *J* 8.1 Hz, NCH_2R), 2.22 (m, 20H, NCH_2R, CH_2), 1.66 (m, 8H, NCH_2R), 1.22 (br, 4H, NCH_2R), 0.90 (m, 24H, CH_3), 0.11 (d, *J* 5.7), -0.84 (t, *J* 5.3), -1.68 (t, *J* 7.0), -1.89 (t, *J* 7.1), -2.07 (t, *J* 5.3); ^{13}C NMR (126 MHz, $CDCl_3$, 30 °C) δ: 152.0, 150.5, 124.6, 123.6, 122.3, 107.2, 53.8, 53.2, 50.1, 35.5, 26.6, 12.6.



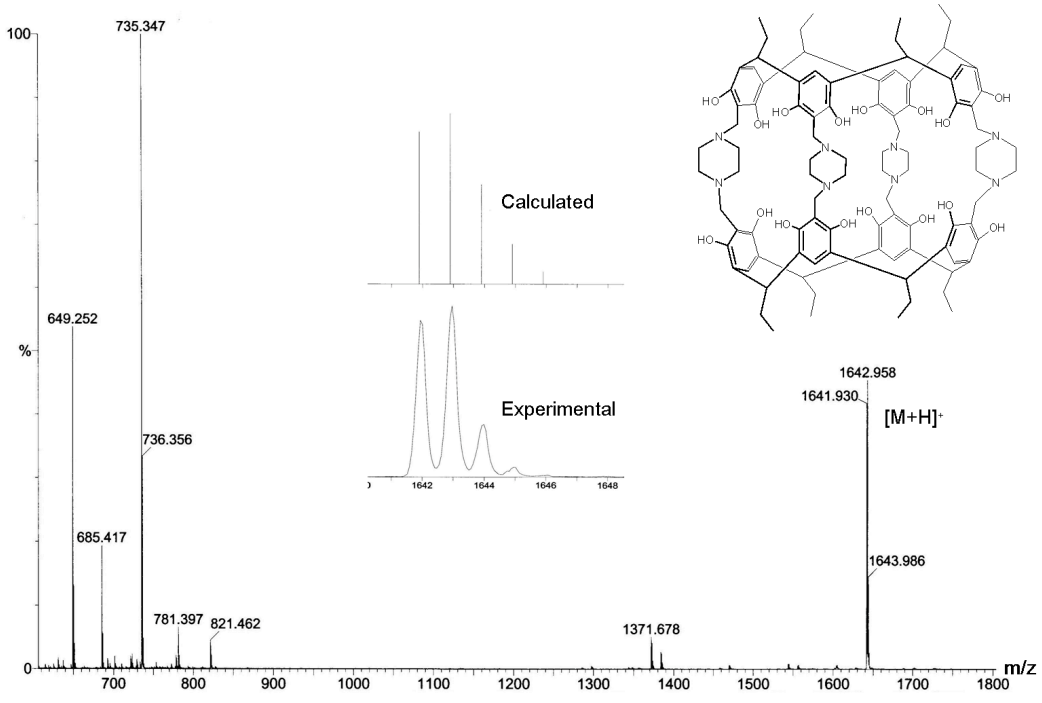
SI Fig. 1: ^{1}H NMR spectrum of **2a** in $CDCl_3$ at 303 K



SI Fig. 2: ^{1}H NMR spectra of **2a** in $CDCl_3$ at 303 K: a) after chromatography, revealing strongly overlapping doublets for the diastereotopic ArCH_2N (*), and four multiplets for the equally diastereotopic piperazine protons (▼) and encapsulated solvent molecules (•) corresponding to methanol, ethanol and dichloromethane (solvents used in synthesis and chromatography), b) after boiling for 2h in distilled MeCN showing that it is encapsulated (θ), c) after boiling for 2h in CH_3NO_2 showing that it is encapsulated (β). Some of the previously encapsulated solvent molecules (•) were not completely replaced by now encapsulated MeCN (θ) and CH_3NO_2 (β) molecules (b and c).



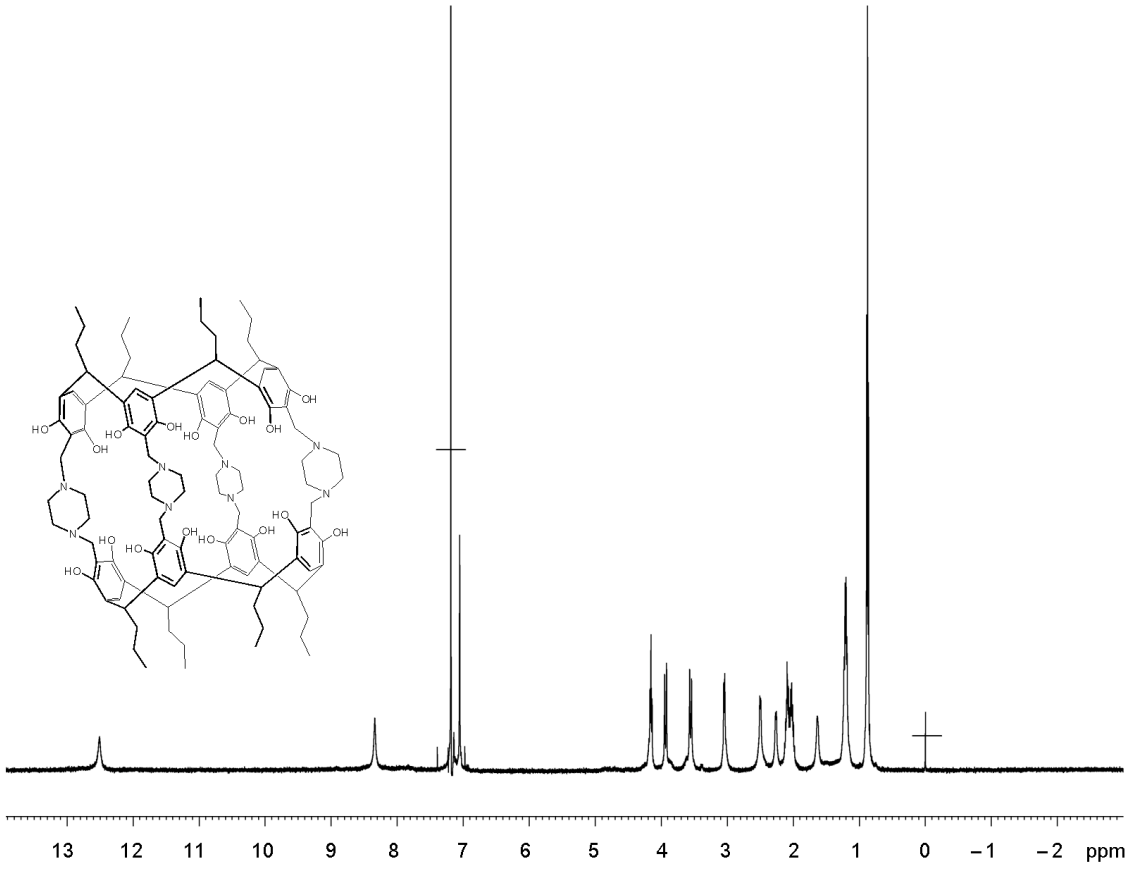
SI Fig. 3: ^{13}C NMR spectrum of **2a** in $CDCl_3$ at 303 K



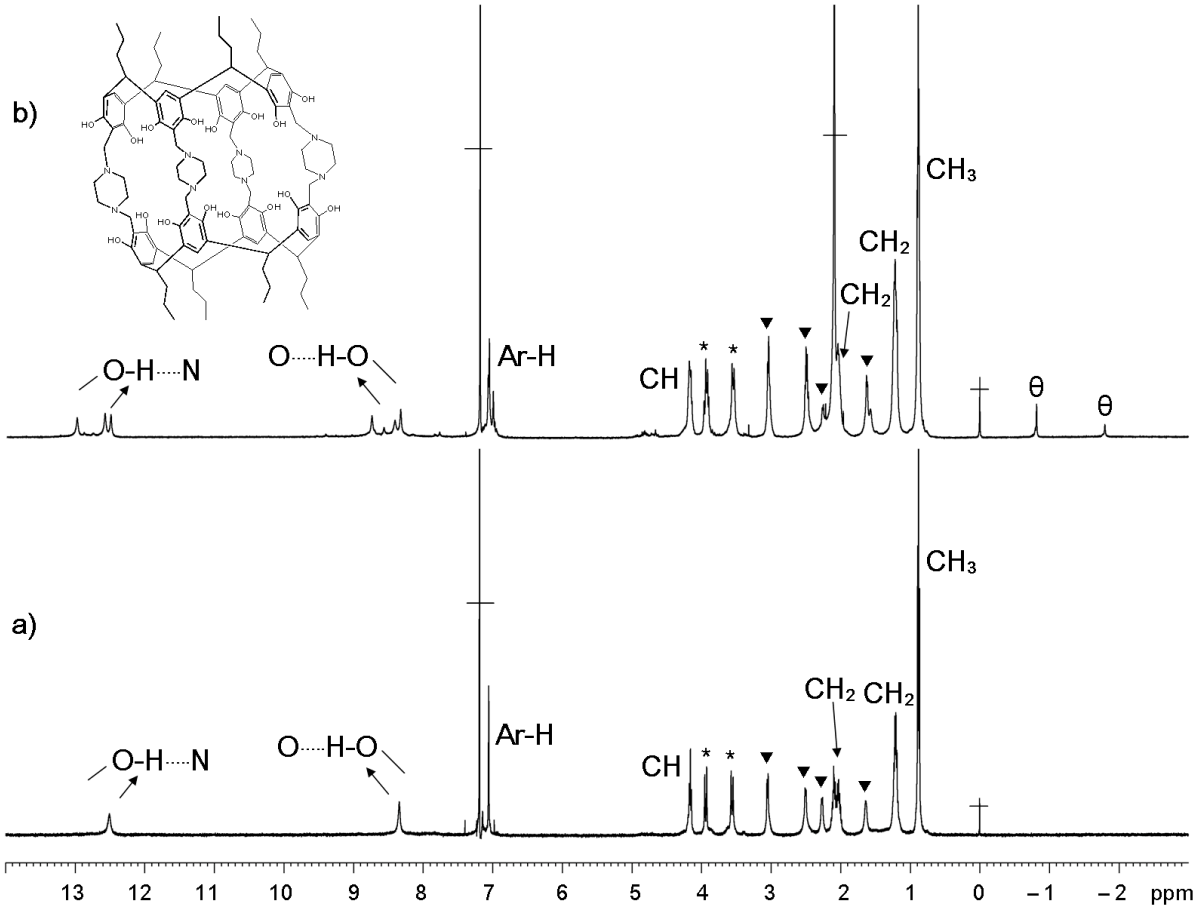
SI Fig. 4: ESI-TOF Mass Spectrum of **2a** ($MeOH/CH_2Cl_2/H^+$)

C_3Resorcinarene cage **2b**

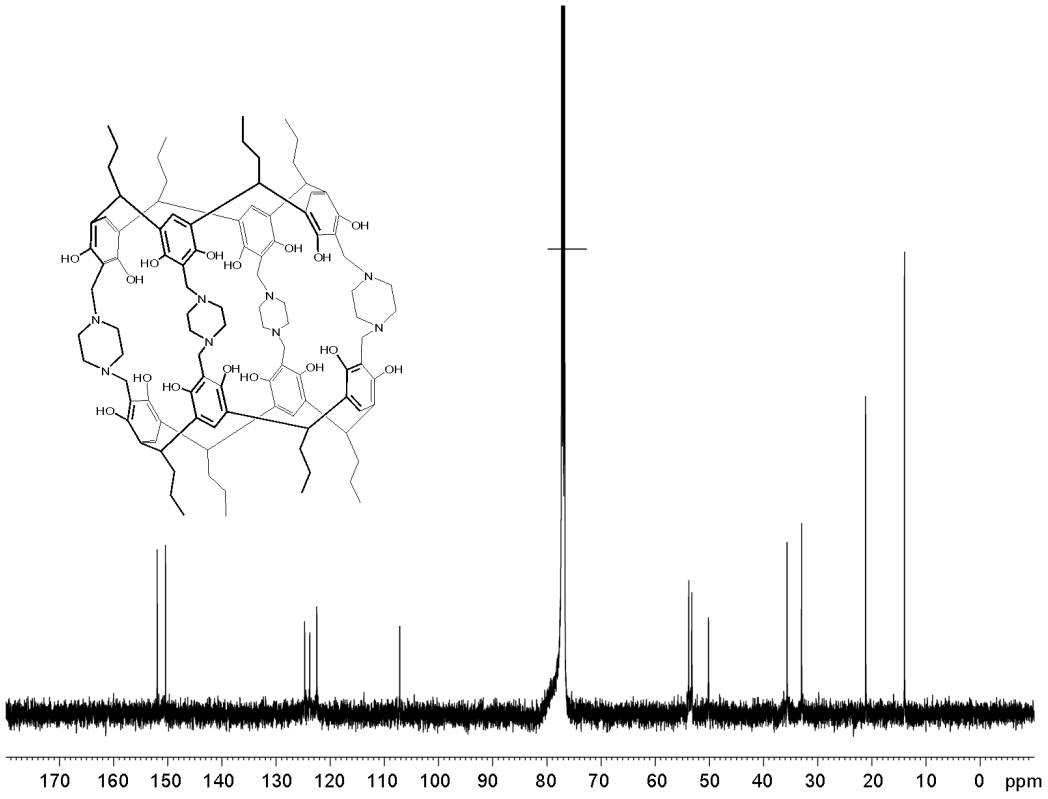
Formaldehyde (3 mL), ethanol (1.0 L), resorcinarene **1b** (1.0 g, 1.5 mmol) and piperazine (0.26 g, 3.0 mmol). Purification via flash chromatography (RediSep Flash Column (silica) 40/12g, from Teledyne Isco; eluent: CH_2Cl_2/CH_3OH 10 %) gave the product (0.48 g, 36 %) as a cream white powder. Mp > 300 ^oC. (found C, 69.07, H, 7.66, N, 5.70. $C_{104}H_{136}N_8O_{16}\cdot 1.5CH_3OH\cdot 0.5CH_2Cl_2$ requires C, 69.01, H, 7.81, N, 6.07). [$C_{104}H_{136}N_8O_{16}$ MW 1754.24; ESI-TOF MS $[M+H]^+$ 1754.35]. ^1H NMR (500 MHz, CD_2Cl_2, 30 °C) δ: 12.50 (br, 8H, ArO*H*), 8.34 (br, 8H, ArO*H*), 7.05 (s, 8H, Ar*H*), 4.15 (t, *J* 7.9 Hz, 8H, C*H*), 3.95 (d, *J* 13.7 Hz, 8H, ArCH_2N), 3.57 (d, *J* 14.0 Hz, 8H, ArCH_2N), 3.05 (d, *J* 7.9 Hz, 8H, NCH_2R), 2.50 (d, *J* 7.3, 8H, NCH_2R), 2.27 (d, *J* 6.7, 8H, NCH_2R), 2.02 (m, 16H, CH_2), 1.64 (br, 8H, NCH_2R), 1.25 (m, 16H, CH_2), 0.89 (t, *J* 7.3 Hz, 24H, CH_3); ^{13}C NMR (126 MHz, CD_2Cl_2, 30 °C) δ: 151.9, 150.4, 124.7, 123.8, 122.5, 107.1, 53.7, 53.2, 50.1, 35.6, 32.9, 21.1, 13.9.



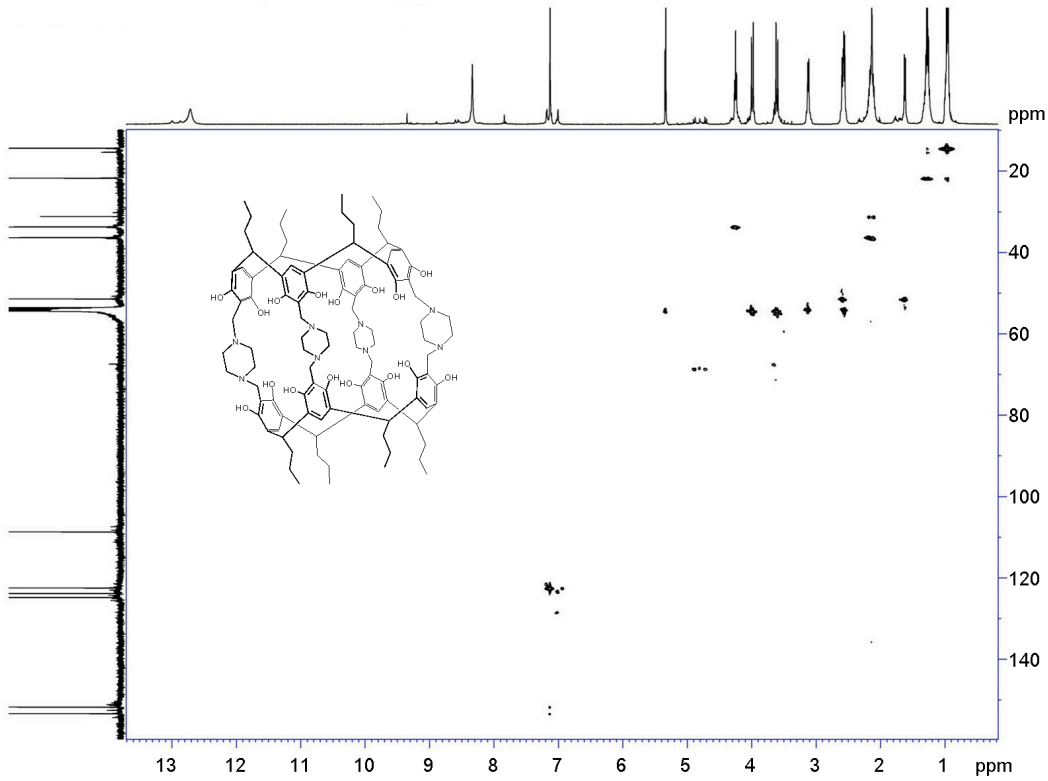
SI Fig. 5: ^1H NMR spectrum of **2b** in $CDCl_3$ at 303 K



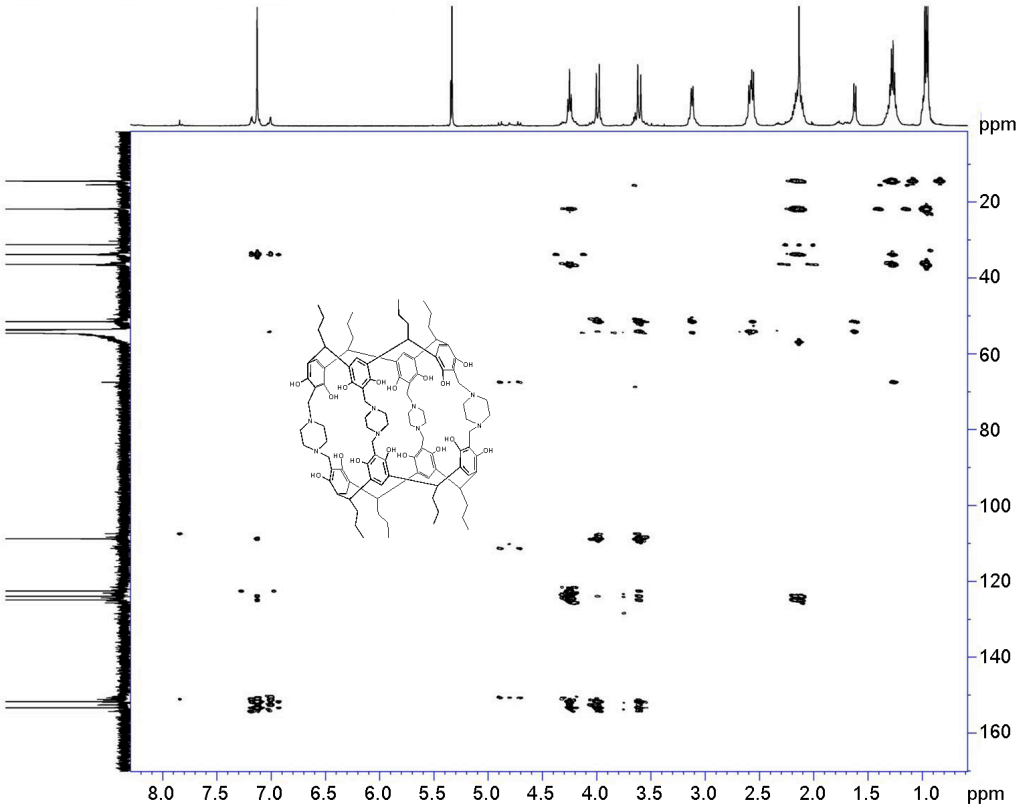
SI Fig. 6: ^{1}H NMR spectra of **2b** in $CDCl_3$ at 303 K: a) after chromatography, revealing two doublets for the diastereotopic ArCH_2N (*), and four doublets for the equally diastereotopic piperazine protons (▼), b) after boiling in distilled MeCN for 2h and dried revealing similar coupling pattern and encapsulated MeCN solvents peaks (θ) upfield.



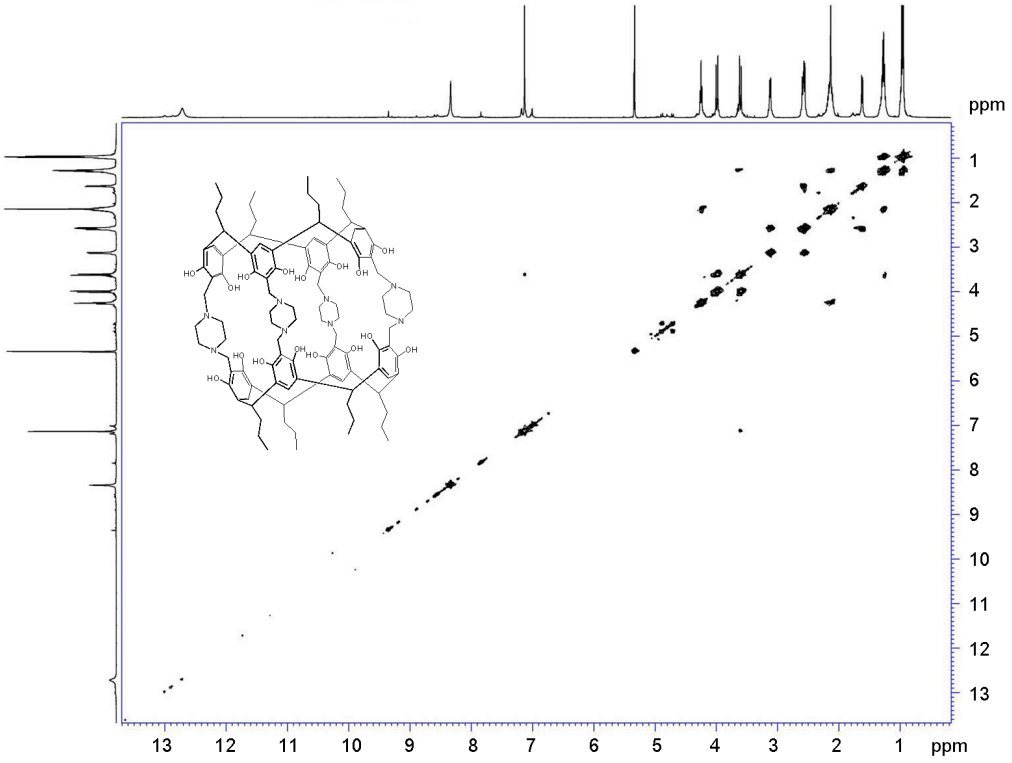
SI Fig. 7: ^{13}C NMR spectrum of **2b** in $CDCl_3$ at 303 K



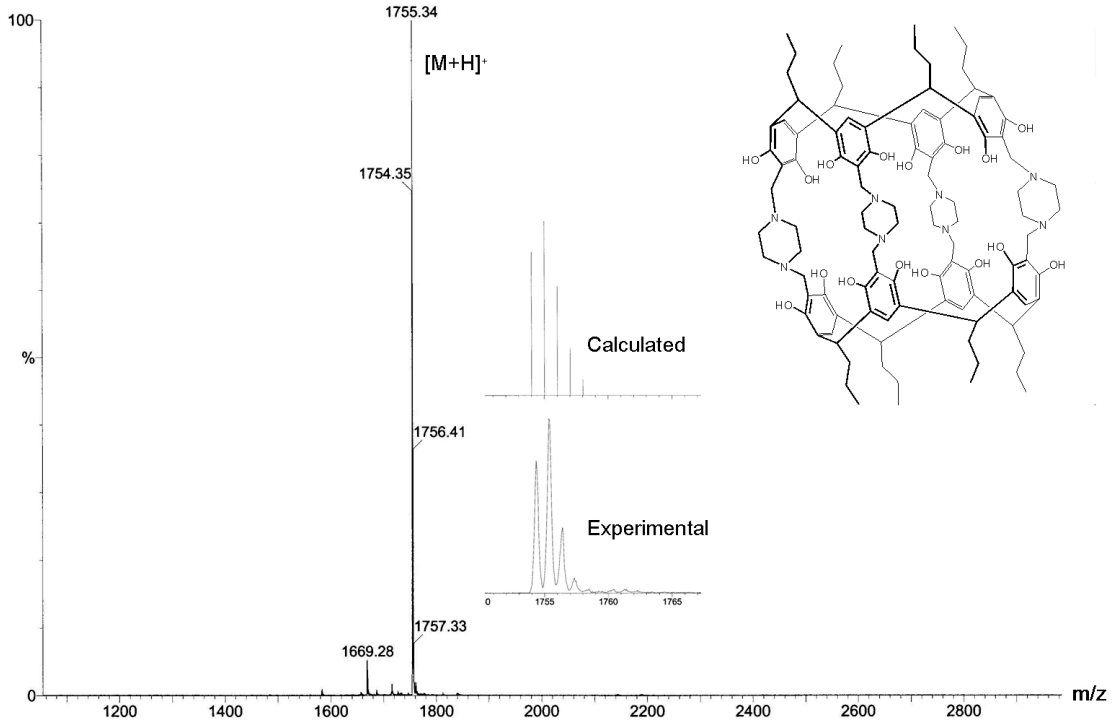
SI Fig. 8: ^{1}H ^{13}C HMQC 2D NMR spectrum of **2b** in CD_2Cl_2.



SI Fig. 9: ^{1}H ^{13}C HMBC 2D NMR spectrum of **2b** in CD_2Cl_2.



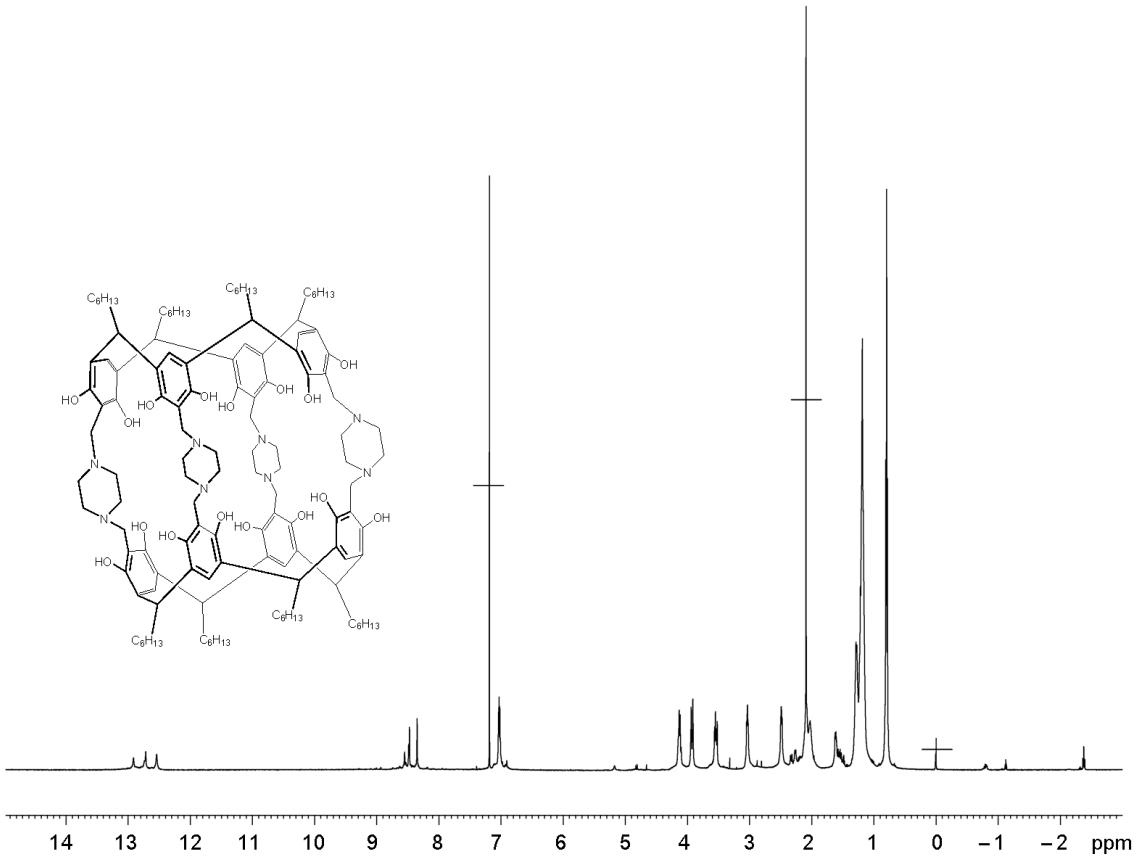
SI Fig. 10: ^{1}H ^{1}H COSY 2D NMR spectrum of **2b** in CD_2Cl_2.



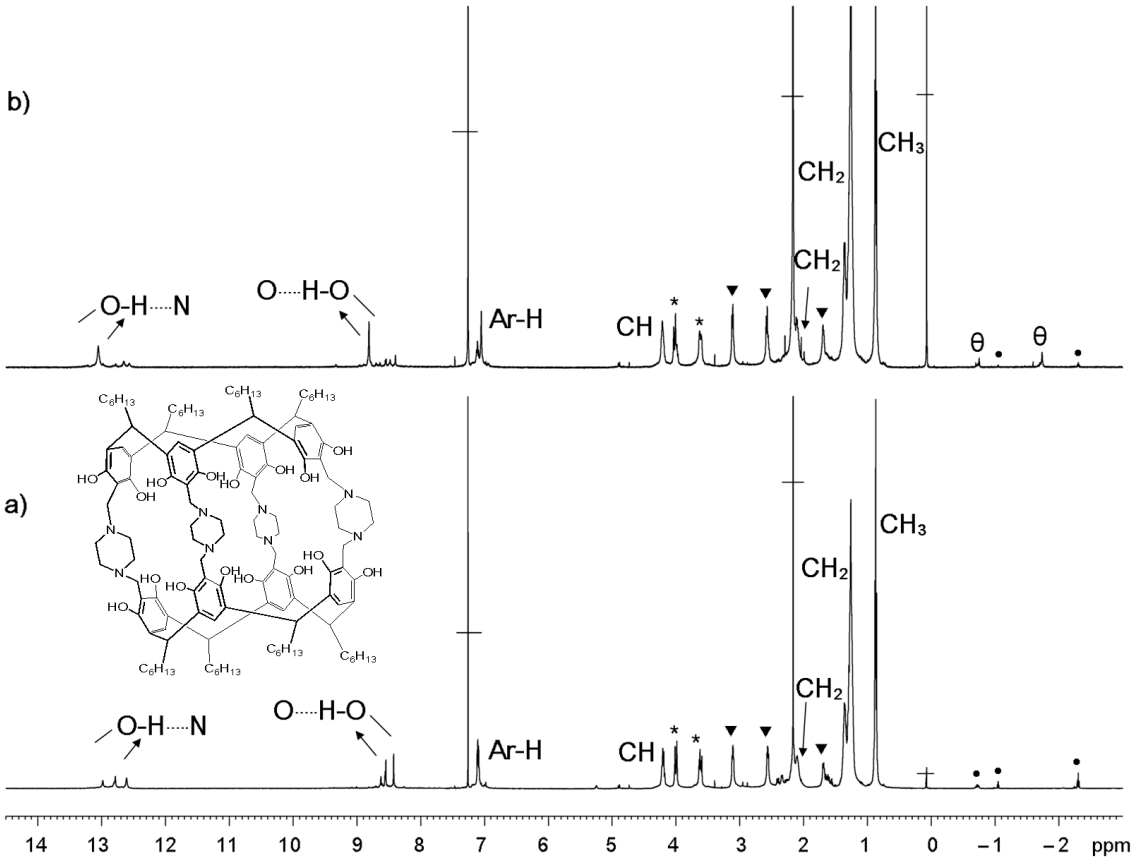
SI Fig. 11: ESI-TOF Mass Spectrum of **2b** ($MeOH/CH_2Cl_2/H^+$)

C_6Resorcinarene cage **2c**

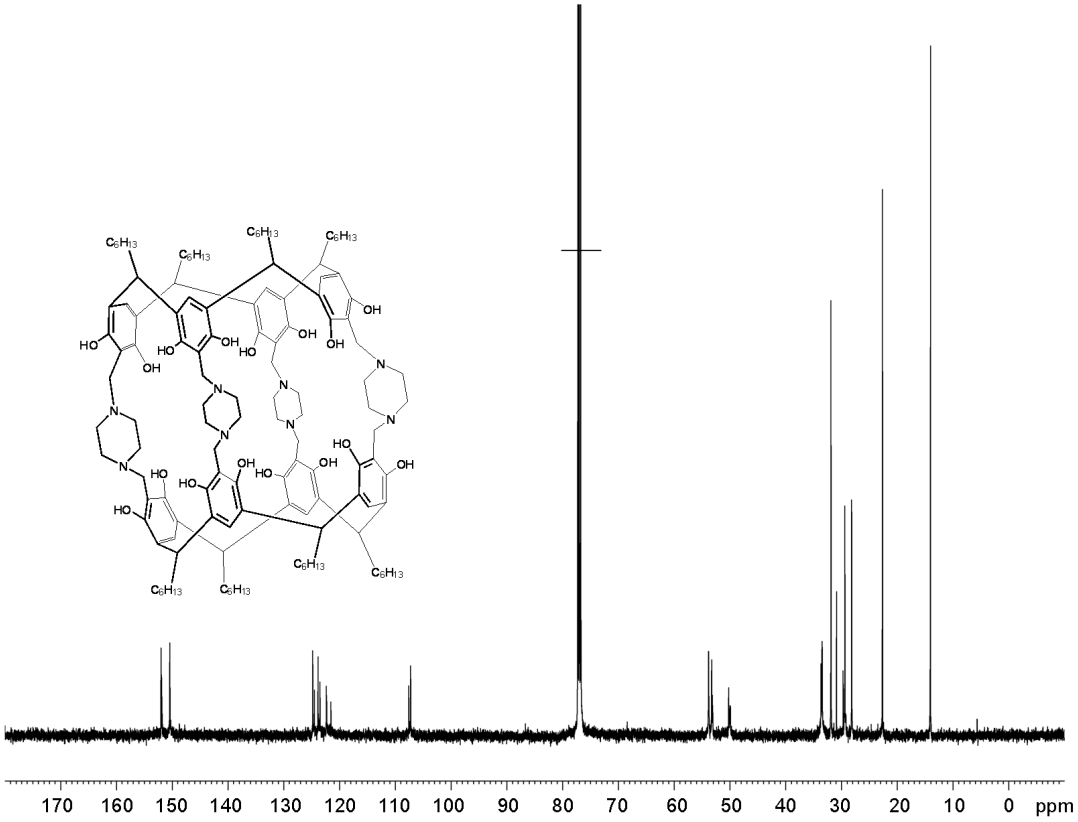
To a solution of excess formaldehyde (3 mL) and some drops of glacial acetic acid in CH_2Cl_2 (600 mL) a solution of resorcinarene **1c** (0.5 g, 0.6 mmol) in CH_2Cl_2 (100 mL) and a solution of piperazine (0.1 g, 1.2 mmol) in CH_2Cl_2 (100 mL) were added drop wise with flow rate of 10 µL/min at rt. The reaction mixture was stir at room temperature for 24 h which was then evaporated in vacuum. The crude product was subjected to column chromatography (eluent: CH_2Cl_2/CH_3OH 10 %) to give the product (0.178 g, 28 %) as a brownish power. Mp > 300 ^oC. (found C, 70.23, H, 8.69, N, 5.01. $C_{128}H_{184}N_8O_{16}\cdot1.5CH_2Cl_2\cdot0.5CH_3CH_2OH$ requires C, 69.93, H, 8.54, N, 5.00). [$C_{128}H_{184}N_8O_{16}$ MW 2090.87; ESI-TOF MS $[M+H]^+$ 2090.39]. ^1H NMR (500 MHz, $CDCl_3$, 30 ^oC) δ: 12.71 (m, 8H, ArO*H*), 8.47 (m, 8H, ArO*H*), 7.03 (m, 8H, Ar*H*), 4.13 (br, 8H, C*H*), 3.94 (d, 8H, *J* 13.9 Hz, ArCH_2N), 3.55 (dd, 8H, *J* 7.0 Hz, ArCH_2N), 3.03 (br, 8H, NCH_2R), 2.50 (br, 8H, NCH_2R), 2.03 (m, 24H, NCH_2R, CH_2), 1.62 (br, 8H, NCH_2R), 1.29 (br, 84H, CH_2), 0.79 (t, *J* 6.8 Hz, 24H, CH_3), -0.78 (m), -1.12 (t, *J* 5.6),-2.37 (t, *J* 7.5); ^{13}C NMR (126 MHz, CD_2Cl_2, 30 ^oC) δ: 151.9, 150.4, 124.7, 123.8, 122.3, 121.5, 107.2, 53.8, 53.2, 50.1, 33.4, 31.8, 29.3, 28.1, 22.6, 14.0.



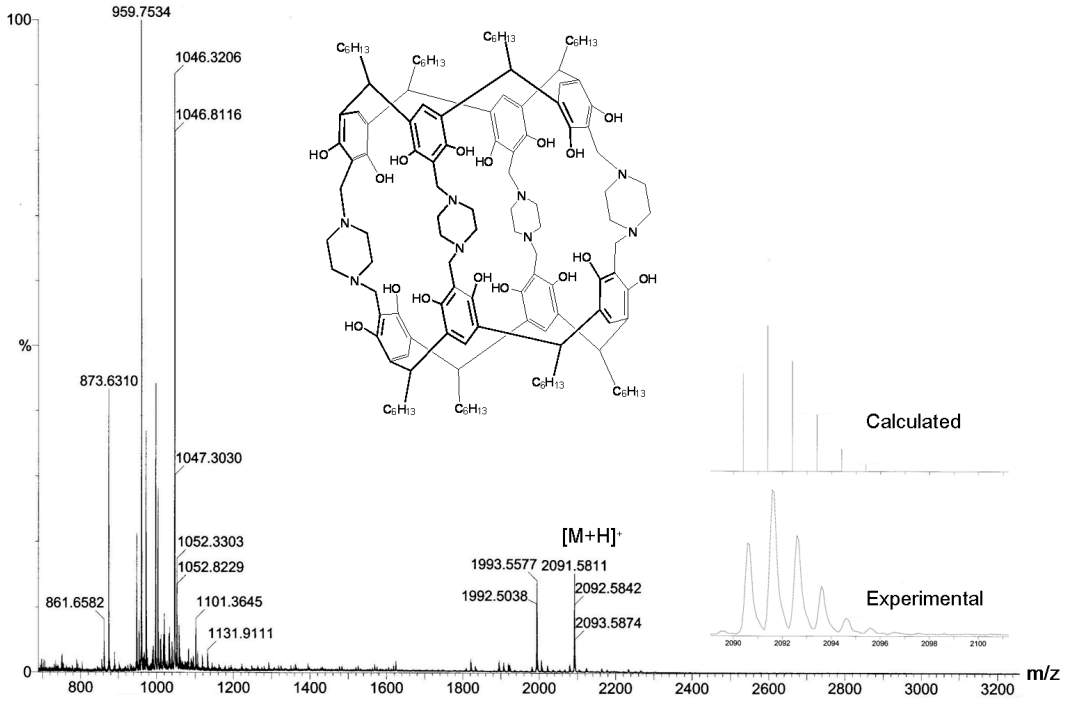
SI Fig. 12: ^1H NMR spectrum of **2c** in $CDCl_3$ at 303 K



SI Fig. 13: ^{1}H NMR spectra of **2c** in $CDCl_3$ at 303 K: a) after chromatography, revealing two doublets for the diastereotopic ArCH_2N (*), and four overlapping multiplets for the equally diastereotopic piperazine protons (▼) showing residual encapsulated solvent molecules (•) from the synthesis, b) after boiling for 2h in distilled MeCN showing similar coupling pattern. Some of the previously encapsulated solvent molecules (•) were not completely replaced by now encapsulated MeCN (θ) molecules.



SI Fig. 14: ^{13}C NMR spectrum of **2c** in $CDCl_3$ at 303 K



SI Fig. 15: ESI-TOF Mass Spectrum of **2c** ($MeOH/H^+$)