A cavity extended water-soluble resorcin[4]arene: synthesis, pH-controlled complexation with paraquat, and application in controllable self-assembly

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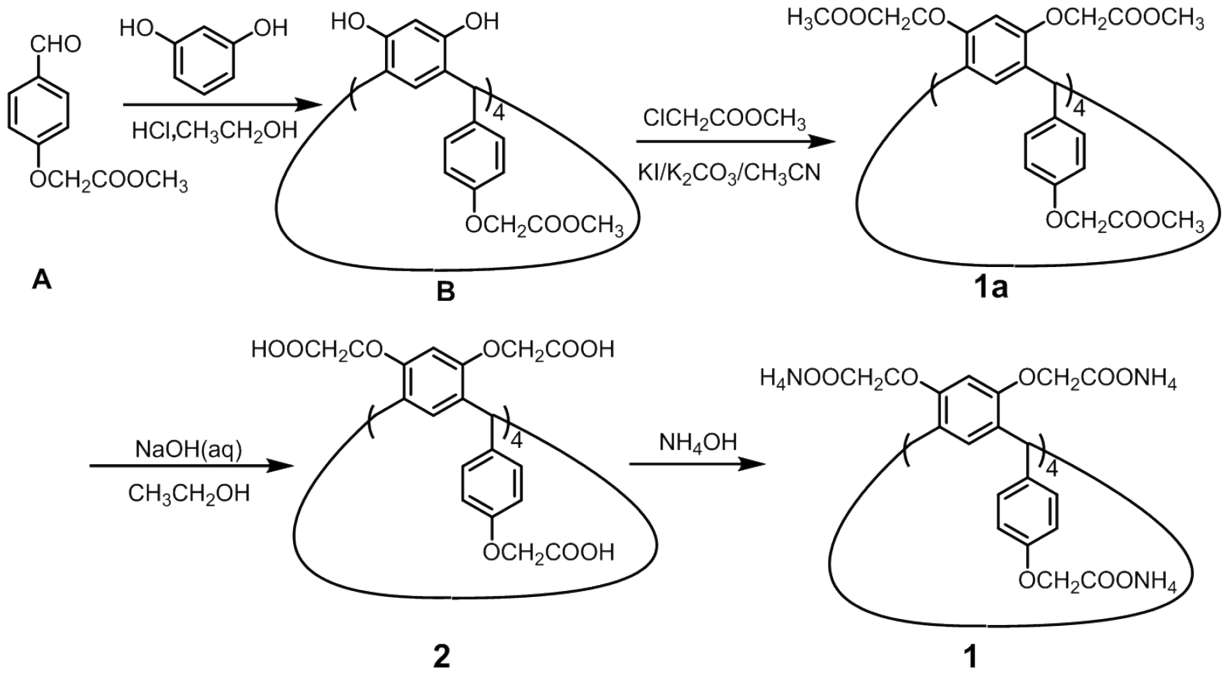
Electronic Supplementary Information (15 pages)

1. Materials and methods

All reagents were commercially available and used as supplied without further purification. Solvents were either employed as purchased or dried according to procedures described in the literature. **G2**[S1] was prepared according to a published procedure. ^{1}H NMR and ^{13}C HMR spectra were recorded with a Bruker Avance DMX 400 spectrophotometer using the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. MALDI-TOF MS was performed with a Bruker UltrafleXtreme instrument. Transmission electron microscopy investigations were carried out on a HITACHI HT-7700 instrument. Dynamic light scattering was carried out on a Malvern Nanosizer S instrument at room temperature. The ITC experiment was performed on a VP-ITC micro-calorimeter (Microcal, USA). Mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. Photographs were taken by Cannon 550D.

*2. Synthesis of compound **1***

Scheme S1. Synthetic route to **1**.



*2.1 Synthesis of compound **1a***

A (2.33 g, 12.0 mmol) and HCl (0.50 mL, 12.0 mmol) were added to a solution of 1,3-dihydroxybenzene (1.10 g, 10.0 mmol) in ethanol (200 mL) under vigorous stirring. The mixture was refluxed at 80.0 °C for 24 hours. The resulting precipitated product **B** was collected by filtration and dried completely under vacuum. To a solution of **B** (3.46 g, 3.00 mmol) in acetonitrile (100 mL) was added methyl chloroacetate (3.91g, 36.0 mmol) and K_2CO_3 (8.29 g, 60.0 mmol). The mixture was heated at 80.0 °C under gas protection for 2 days. Then the reaction mixture was cooled to room temperature and filtered. Then the filtrate was concentrated under vacuum, and then the residue was purified by recrystallized in a mixture of acetonitrile and methanol (*v* : *v*, 1 : 4) to get product **1a** as a white solid. The yield of **1a** was 75.6%. The ^{1}H NMR spectrum of **1a** is shown in Fig. S1. ^{1}H NMR (400 MHz, chloroform-*d*, 293 K) δ (ppm): 3.68 (s, 3H), 3.74 (s, 3H), 3.81 (d, J = 4 Hz, 1H), 4.24–4.28 (m, 2H), 4.35 (d, J = 5 Hz, 2H), 4.41 (d, J = 2 Hz, 2H), 4.55–4.58 (m, 2H), 5.69 (s, 0.5H), 5.87 (s, 1H), 6.17 (s, 0.5H), 6.28 (d, J = 3 Hz, 1H), 6.55 (s, 4H). The ^{13}C NMR spectrum of **1a** is shown in Fig. S2. ^{13}C NMR (100 MHz, chloroform-*d*, 293 K) δ (ppm): 169.71, 169.26, 155.83, 154.18, 129.74, 126.90, 113.98, 113.77, 67.34, 65.38, 61.11, 52.10, 51.95, 42.25, 14.19. The MALDI-TOF MS spectrum of **1a** is shown in Fig. S3: *m*/*z* calcd for [**1a** + K + H_2O]$^+$ 1778.481; found 1778.303.

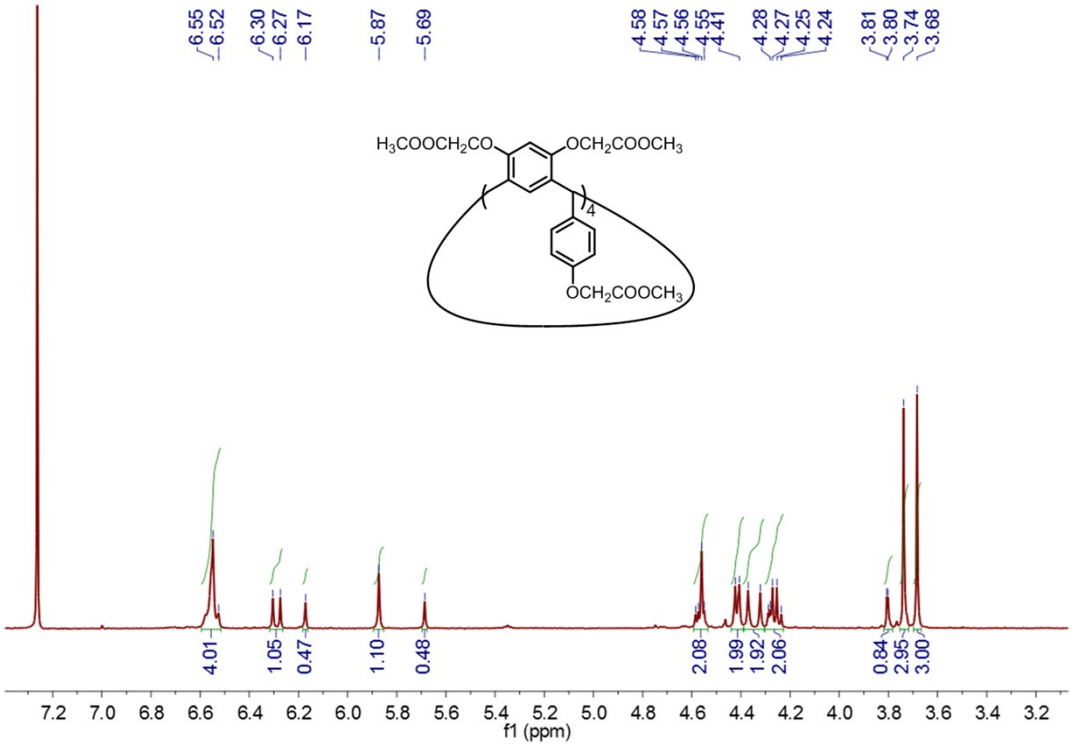


Fig. S1 ^{1}H NMR spectrum (400 MHz, chloroform-*d*, 293K) of **1a**.

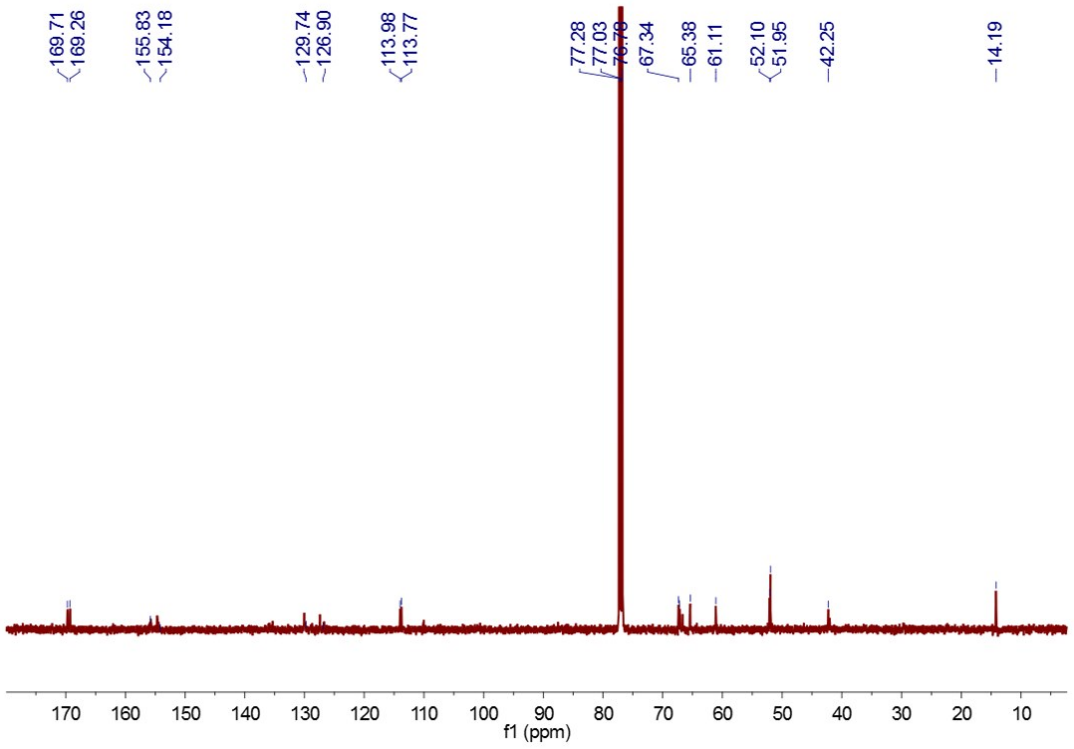


Fig. S2 ^{13}C NMR spectrum (100 MHz, chloroform-*d*, 293K) of **1a**.

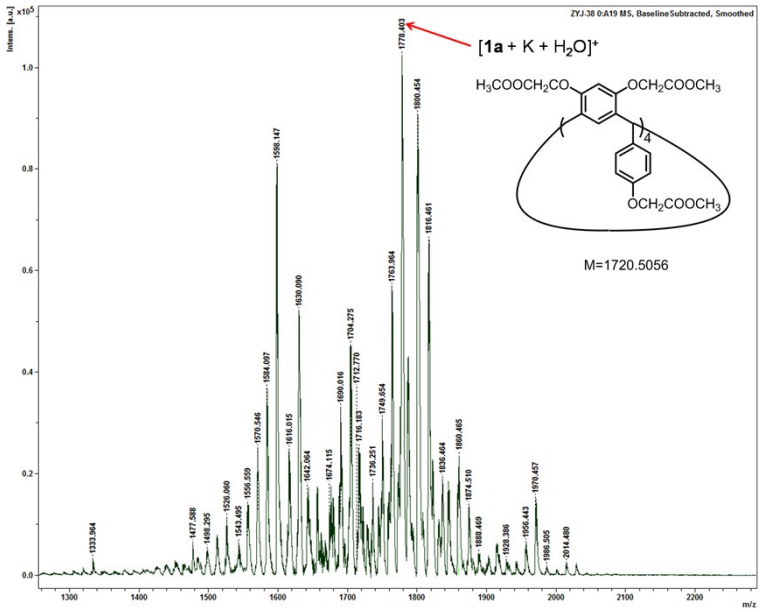


Fig. S3 MALDI-TOF MS spectrum of **1a**.

*2.2 Synthesis of compound **2***

A solution of **1a** (495 mg, 0.167 mmol) in anhydrous ethyl alcohol (40.0 mL) was treated with 40% aqueous sodium hydroxide (40.0 mL) at 70.0 ºC for 24 h. Then the reaction mixture was evaporated under vacuum, diluted with water (25.0 mL) and acidified with aqueous HCl solution. The resulting precipitate was filtered, washed with water, and dried to afford product **2** (100%) as a white powder. The ^{1}H NMR spectrum of **2** is shown in Fig. S4. ^{1}H NMR (400 MHz, DMSO-d_6, 293 K) δ (ppm): 4.20 (d, J = 3 Hz, 1H), 4.36 (d, J = 4 Hz, 1H), 4.47–4.56 (m, 4H), 5.70 (d, J = 3 Hz, 1H), 6.15 (s, 0.5H), 6.41 (s, 0.5H), 6.50–6.60 (m, 5H), 12.83 (s, 3H). The ^{13}C NMR spectrum of **2** is shown in Fig. S5. ^{13}C NMR (100 MHz, DMSO-d_6, 293 K) δ (ppm): 170.28, 170.24, 170.16, 155.41, 154.29, 153.71,134.45, 131.06, 129.79, 127.33, 126.45, 124.94, 113.45, 100.34, 99.45, 66.28, 65.93, 64.42, 41.70. The MALDI-TOF MS spectrum of **2** is shown in Fig. S6: *m*/*z* calcd for [**2** + Na]$^{+}$ 1575.307; found 1575.977.

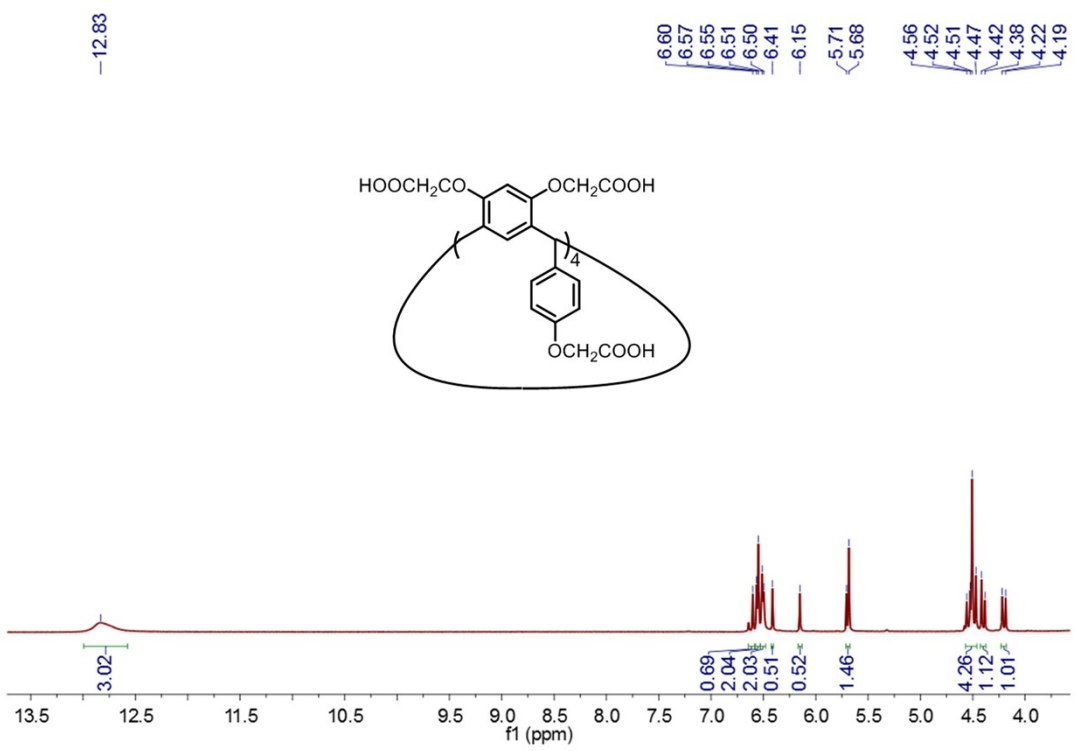


Fig. S4 ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 293K) of **2**.

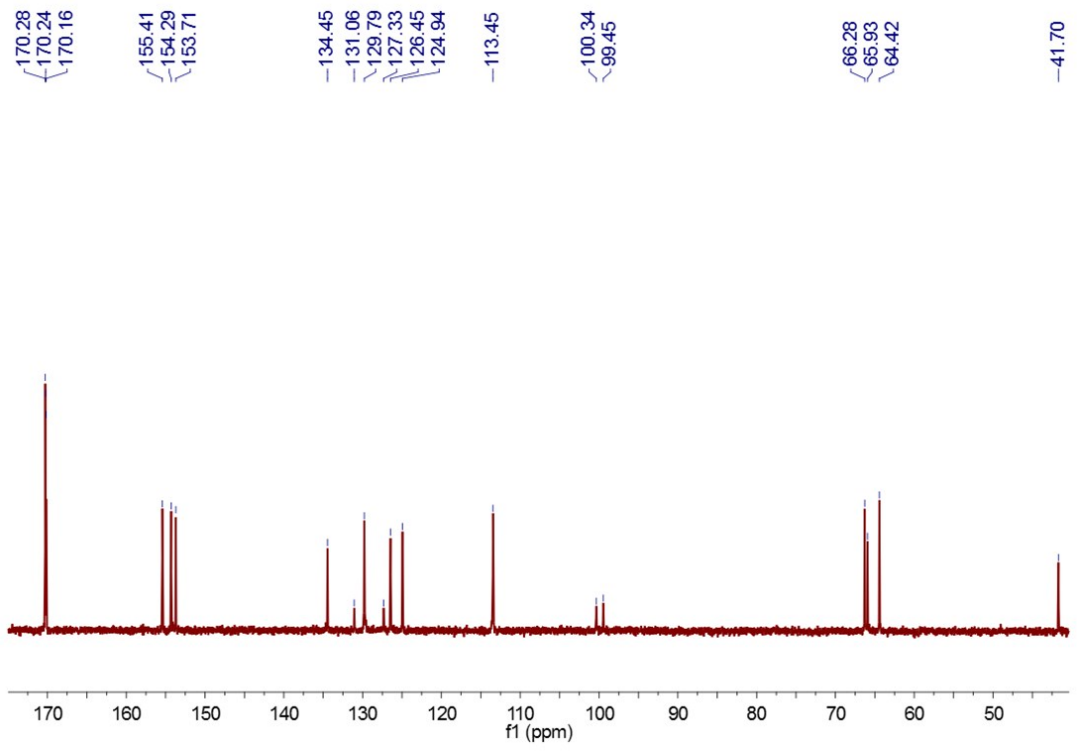


Fig. S5 ^{13}C NMR spectrum (100 MHz, DMSO-d_6, 293K) of **2**.

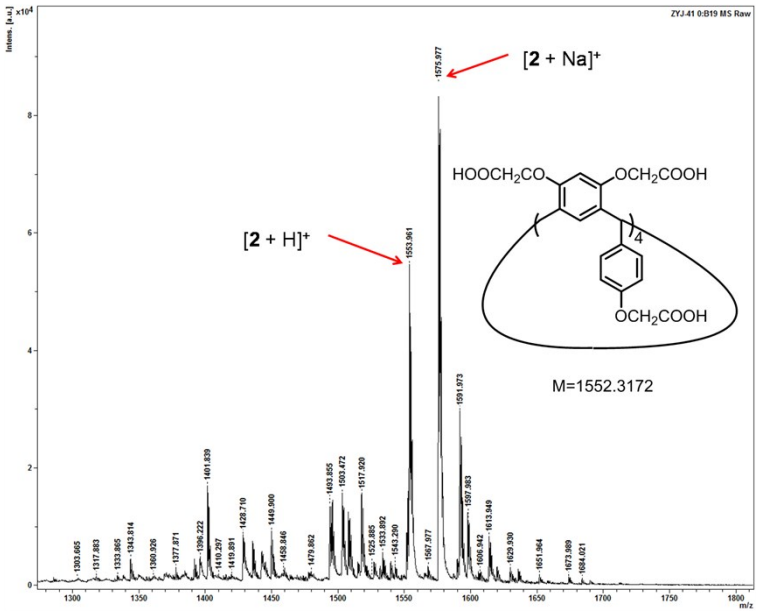


Fig. S6 MALDI-TOF MS spectrum of **2**.

*2.3 Synthesis of compound **1***

Compound **2** (260 mg, 0.167 mmol) and ammonium hydroxide solution (25−28 %, 50.0 mL) were stirred at room temperature for 0.5 h. Water was then removed by rotary evaporation to afford **1** as white powder. The yield of **1** was 100%. The ^{1}H NMR spectrum of **1** is shown in Fig. S7. ^{1}H NMR (400 MHz, D_2O, 293 K) δ (ppm): 6.63–6.75 (m, 4H), 6.43 (d, J = 6 Hz, 1H), 6.18 (s, 0.5H), 5.84 (s, 1H), 5.56 (s, 0.5H), 4.45 (s, 2H), 4.34–4.40 (m, 2H), 4.14 (d, J = 4 Hz, 2H). The ^{13}C NMR spectrum of **1** is shown in Fig. S8. ^{13}C NMR (100 MHz, D_2O, 293 K) δ (ppm): 176.92, 176.74, 176.23, 156.03, 154.97, 154.46, 134.58, 129.84, 128.36, 126.52, 125.79, 114.05, 101.19, 99.28, 68.86, 68.10, 66.54, 42.06. The MALDI-TOF MS spectrum of **1** is shown in Fig. S9: *m*/*z* calcd for [**1** – $4NH_3$ – $5H_2O$ – NH_4^-]$^+$ 1580.442; found 1579.874.

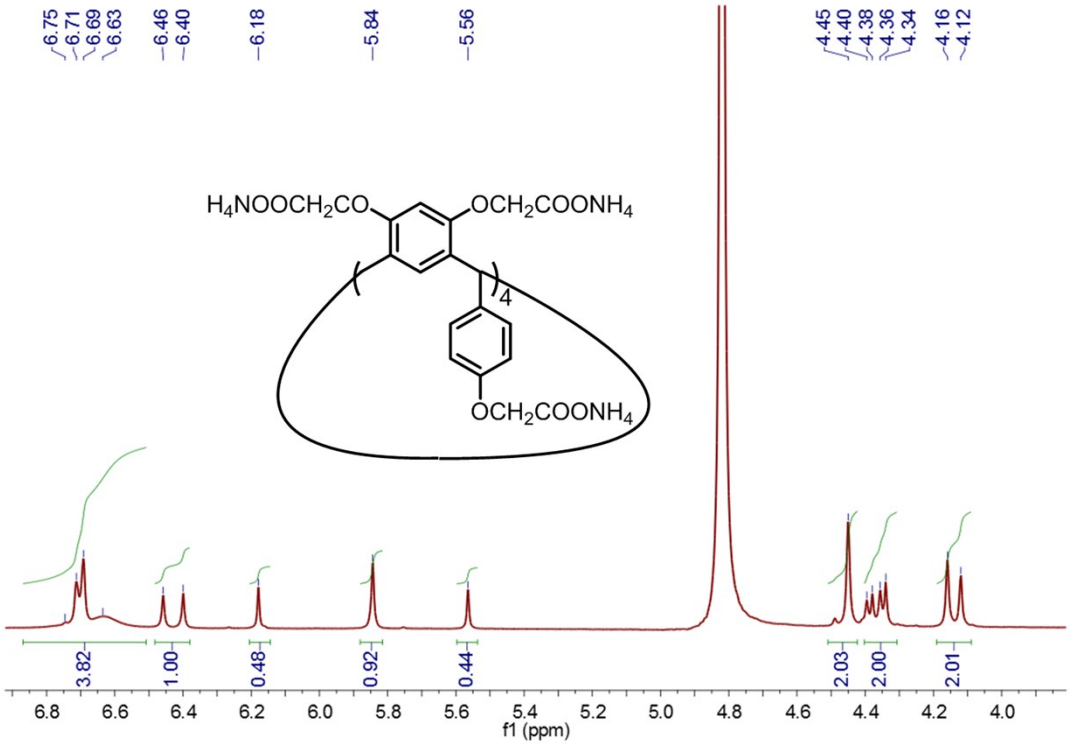


Fig. S7 ^{1}H NMR spectrum (400 MHz, D_2O, 293K) of **1**.

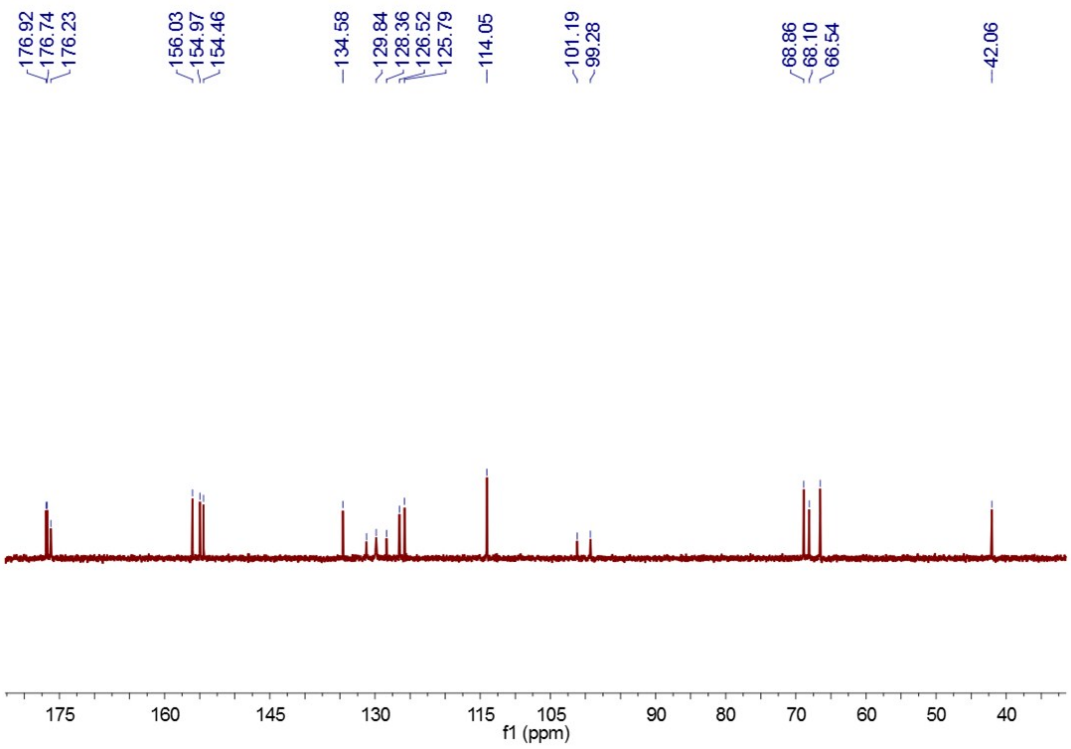


Fig. S8 ^{13}C NMR spectrum (100 MHz, D_2O, 293K) of **1**.

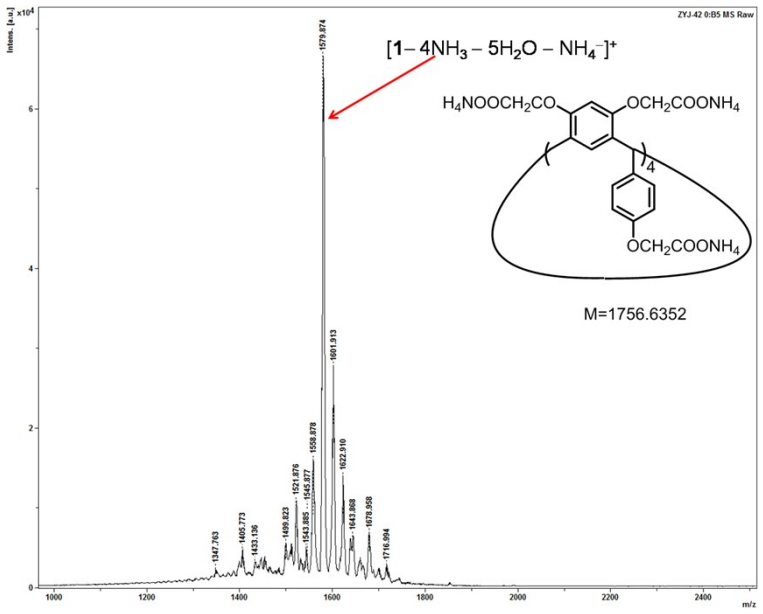


Fig. S9 MALDI-TOF MS spectrum of **1**.

3. A photo showing color changes after host–guest complexation

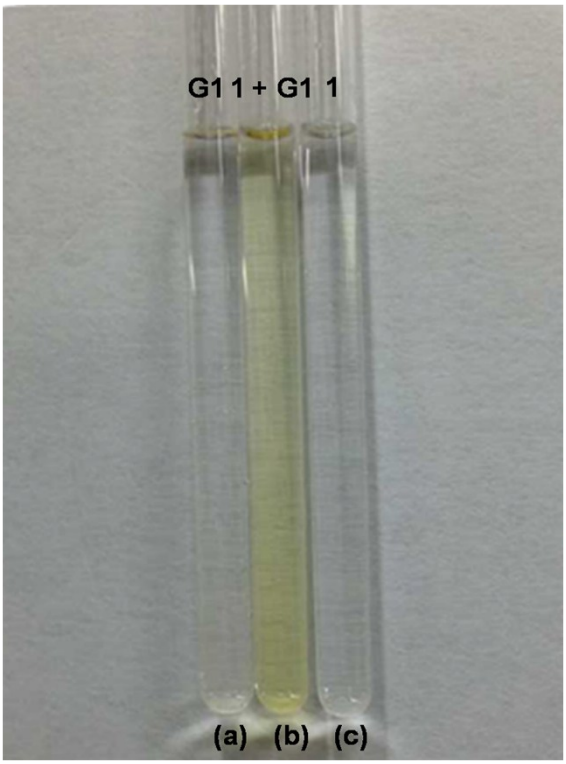


Fig. S10 A photo showing color changes after host–guest complexation in D_2O: (a) **G1** alone; (b) an equimolar solution of **1** and **G1**; (c) **1** alone;

*4. 2D NOESY NMR spectrum of the complexation between **1** and **G1***

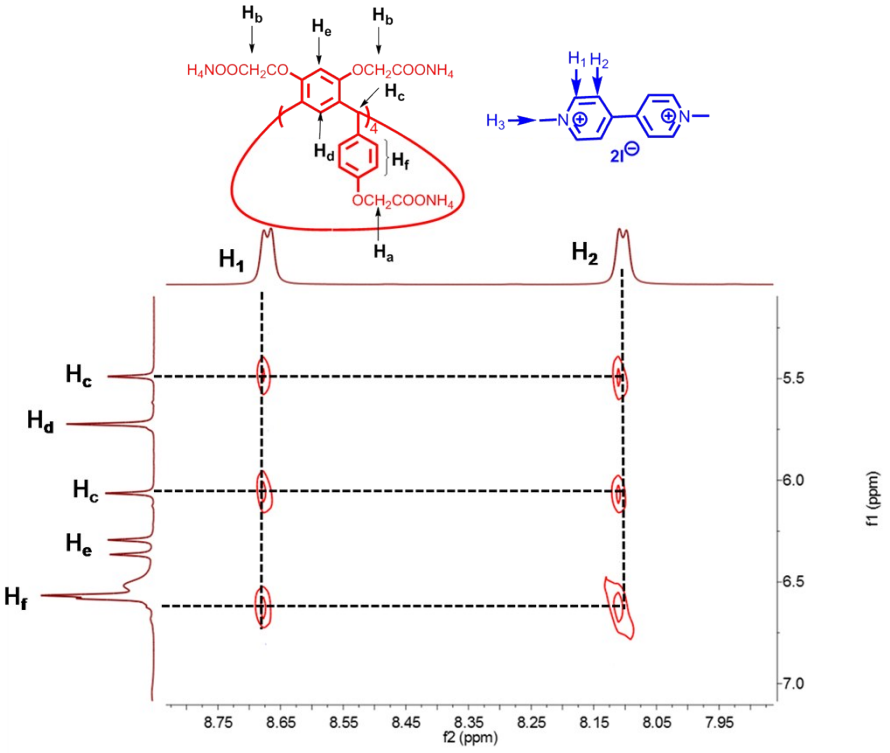


Fig. S11 2D NOESY NMR (500 MHz, D_2O, 293 K) spectrum of a solution of **1** (5.00 mM) and **G1** (5.00 mM).

*5. [1]H NMR titration of **1** with **G1***

[1]H NMR titration was done with solutions which had a constant concentration of **G1** (1.00 mM) and varying concentrations of **1**. By a non-linear curve-fitting method, the association constant between the guest **G1** and host **1** was calculated.

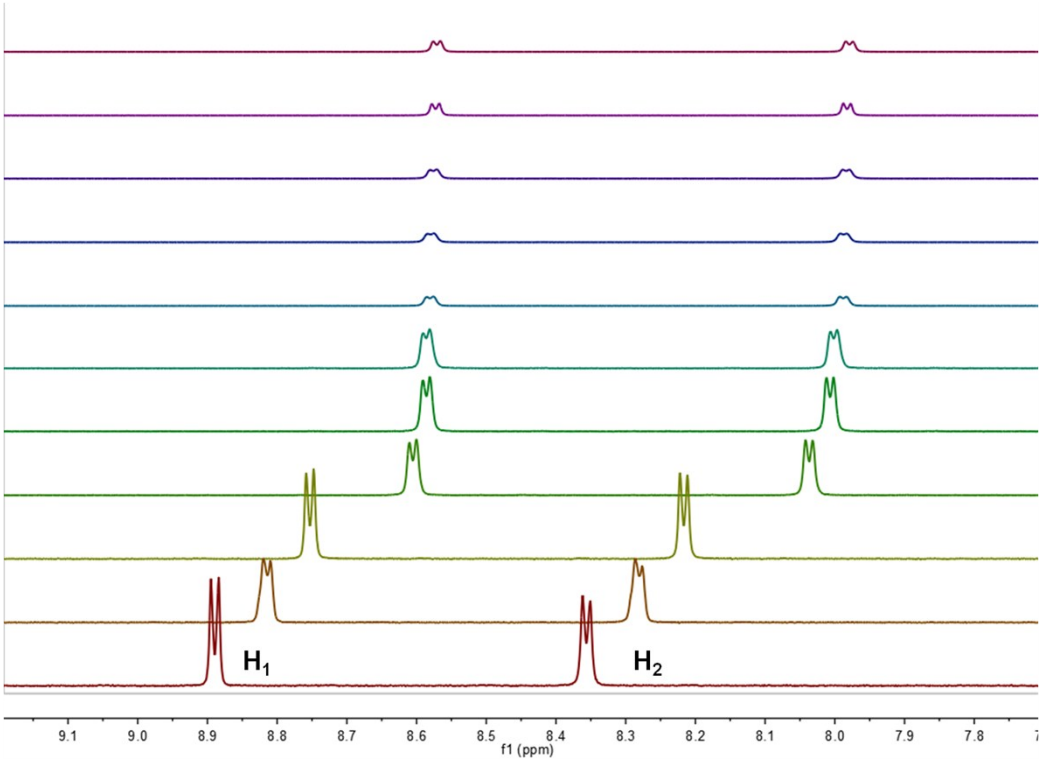


Fig. S12 [1]H NMR spectra (D_2O) of **G1** at a concentration of 1.0 mM with different concentrations of **1**.

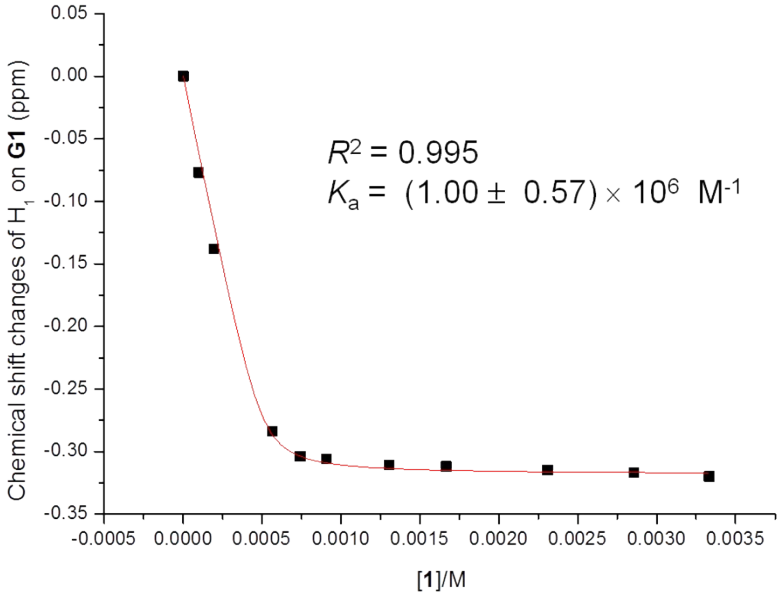


Fig. S13 The chemical shift changes of H on **G1** upon addition of **1**. The red solid line was obtained from the non-linear curve-fitting.

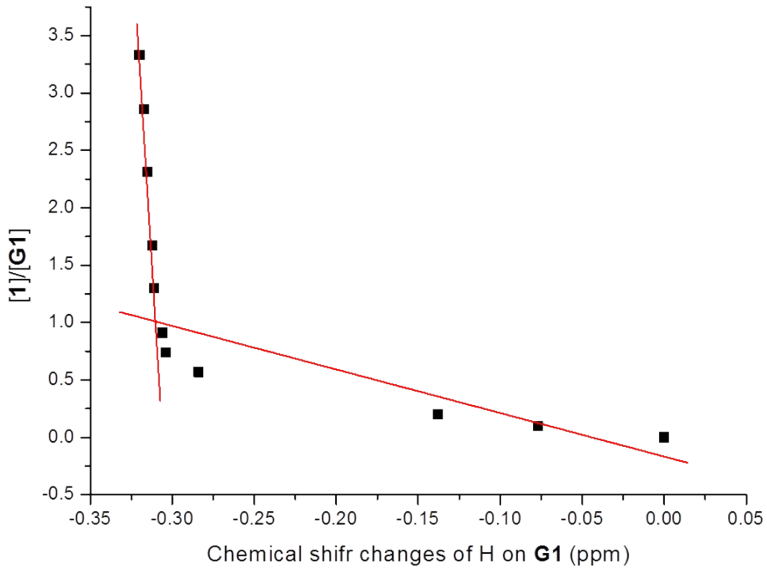


Fig. S14 Mole ratio plot for **1** and **G1**, showing a 1:1 complexation stoichiometry.

*6. Photographs showing pH-controlled host–guest complexation between **1** and **G1***

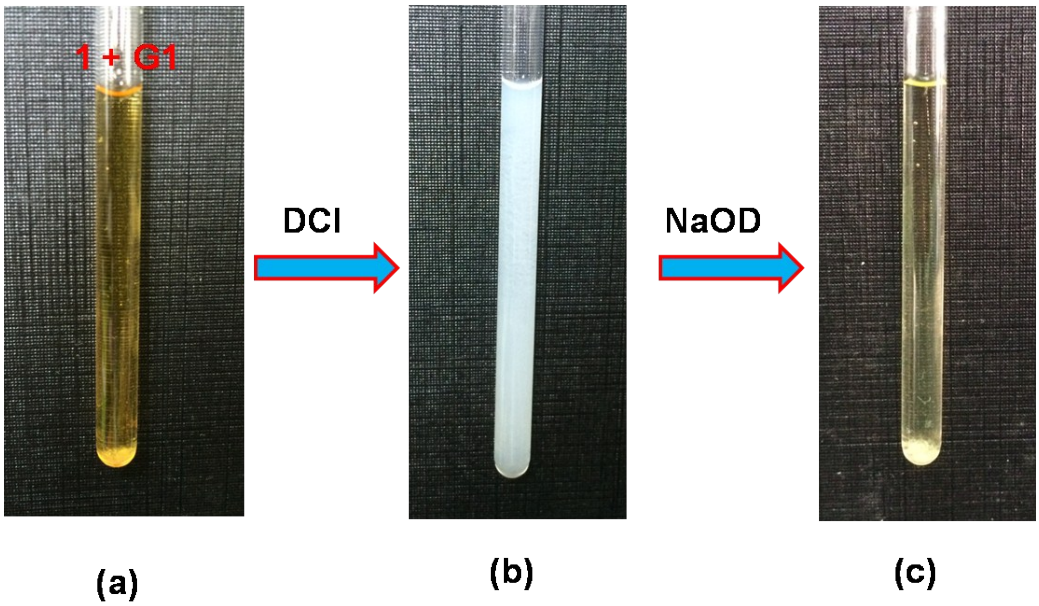


Fig. S15 Photographs of aqueous solutions: (a) 2.00 mM **1** and 10.00 mM **G1**; (b) after adding 2.0 μL of an aqueous DCl solution (20%) to a; (c) after adding 1.5 μL of an aqueous NaOD solution (30%) to b.

7. Dynamic light scattering result of ***G2***

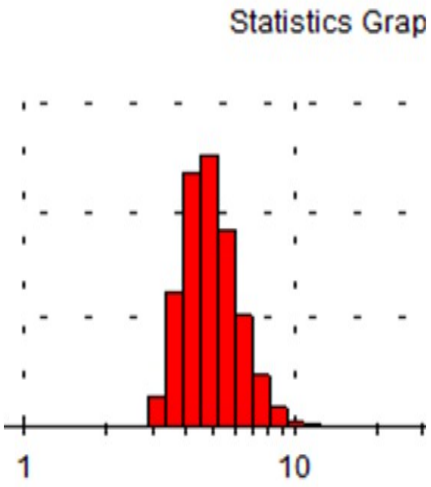


Fig. S16 Dynamic light scattering result of **G2** with an aqueous solution of 5.00×10^{-4} M.

8. Determination of critical aggregation concentration of ***1⊃G2*** *in water*

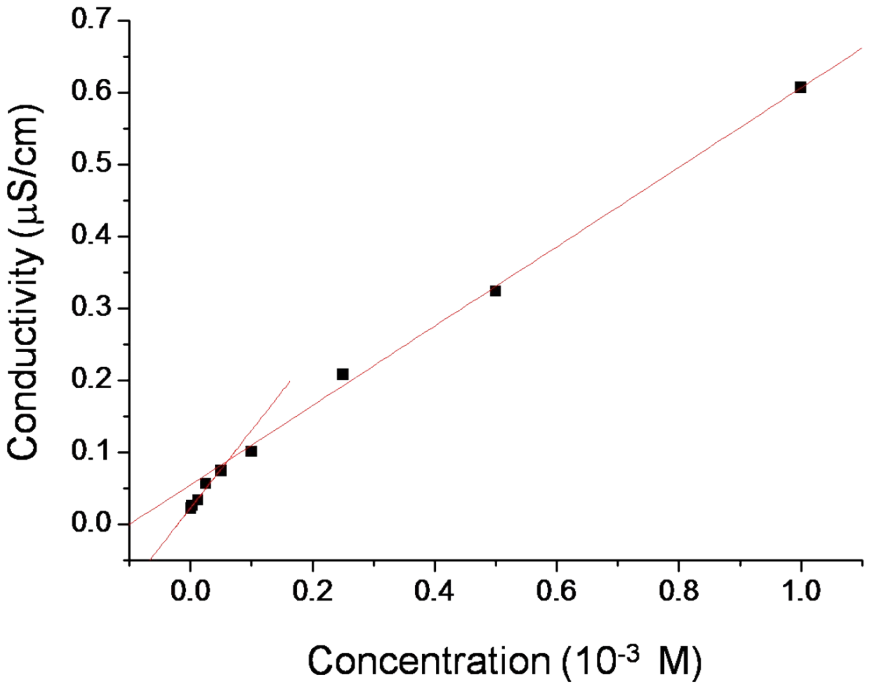


Fig. S17 Conductivity as a function of the concentration of **1⊃G2**. There are two linear segments in the curve and a sudden reduction of the slope, implying that the CAC of **1⊃G2** is approximately 6.78×10^{-5} M.

*9. Enlarged TEM image of **1⊃G2***

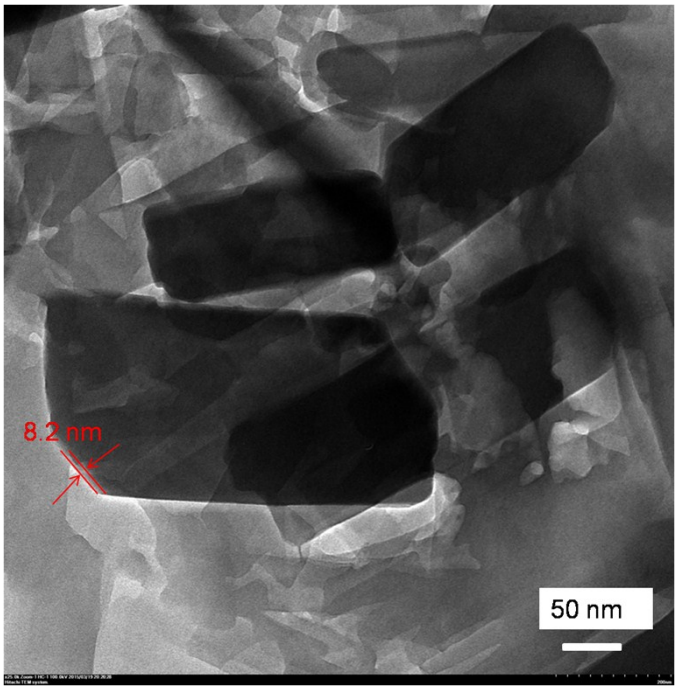


Fig. S18 Enlarge TEM of **1⊃G2**.

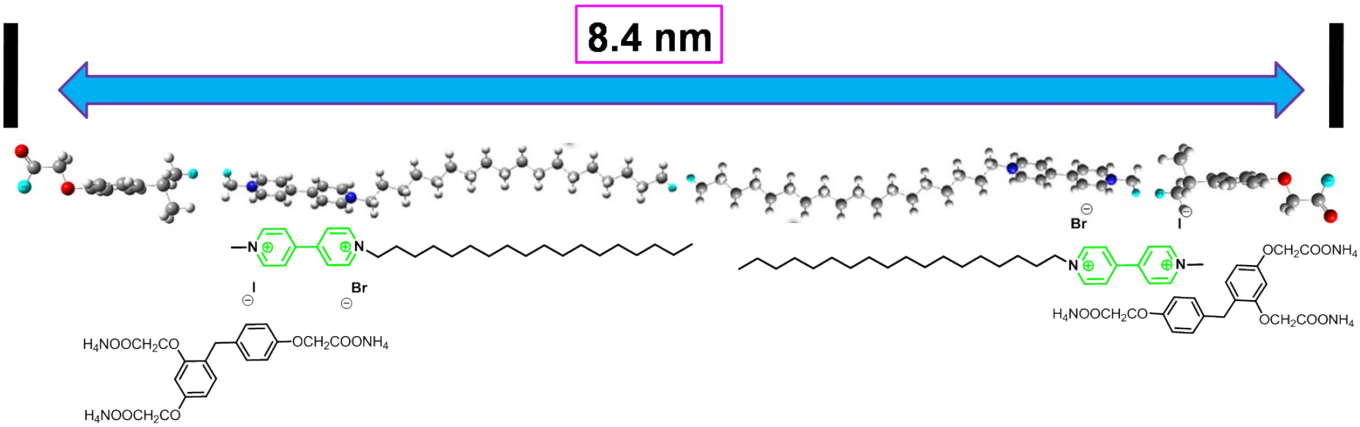


Fig. S19 Model of two extended **G2** molecules and two monomers of **1** produced using ChemBio3D Ultra 13.0.

References:

S1. (*a*) J. A. Barltrop and A. C. Jackson, *J. Chem. Soc. Perkin Trans.* 2. 1998, 367; (*b*) U. Rauwald and O. A. Scherman, *Angew. Chem., Int. Ed.,* 2008, **47**, 3950; (*c*) M. Lamberto, E. E. Rastede, J. Decker and F. M. Raymo, *Tetrahedron Lett.,* 2010, **51**, 5618.