Synthesis of a four-armed cage molecule and its pH-controlled complexation with paraquat

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References
1. Materials and methods

All reagents were commercially available and used as supplied without further purification. BMP32C10 (1), BMP32C10 diol (5),\(^1\) 2,2′-dihydroxy-BMP32C10,\(^2\) bis(1,2,3-phenylene) cryptand \(2b^3\) and 2,6-bis(p-toluenesulfonyloxymethyl)pyridine\(^4\) were synthesized by published literature procedures. \(^1\)H NMR spectra were collected on a temperature-controlled 400 MHz or 500 MHz spectrometer. \(^13\)C NMR spectra were recorded on a Bruker AVANCE DMX-400 or DMX-500 spectrometer. Low-resolution electrospray ionization mass spectra (LRESI-MS) were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with ESI interface and ion trap analyzer. High-resolution electrospray ionization mass spectra (HRESI-MS) were obtained on a Bruker 7-Tesla FT-ICR mass spectrometer equipped with an electrospray source (Billerica, MA, USA). The melting points were collected on a SHPSIC WRS-2 automatic melting point apparatus.
2. Synthesis of compound 1

Pyridine (0.01 mL, 0.100 mmol) and dichloromethane (800 mL) were added into a 1000 mL round-bottom flask. Pyridine-2,6-dicarbonyl (91.8 mg, 0.450 mmol) in dichloromethane (50.0 mL) and bis(1,2,3-phenylene) cryptand 2b (220 mg, 0.30 mmol) in dichloromethane (50.0 mL) were added at a speed of 2.5 mL/h, separately. Then the mixture was left reacting at room temperature for 4 days. The solvent was removed and the residue was purified by flash column chromatography (SiO₂: methanol:ethyl acetate = 1:100) to give 1 as a white solid (30 mg, 12%); m.p. 135.8–136.6 °C. The product has been indentified by ¹H NMR. The ¹H NMR spectrum is shown in Fig. S1. ¹H NMR (400 MHz, CDCl₃, room temperature) δ (ppm): 8.34 (4H, m), 8.05 (1H, m), 8.00 (1H, m), 6.52 (4H, s), 5.45 (4H, s), 5.20 (4H, s), 4.01–4.14 (12H, m), 3.80–3.88 (12H, m), 3.68 (8H, m). LRESIMS is shown in Fig. S2: m/z 863.3 [M + H]⁺ (100%), 885.2 [M + Na]⁺ (52.9%), 901.2 [M + K]⁺ (11.6%). HRESIMS: m/z calcd for [M + Na]⁺ C₄₄H₅₀N₂NaO₁₆⁺, 885.3053; found 885.3029, error –2.7 ppm.

Fig.S2 ¹H NMR spectrum (400 MHz, CDCl₃, room temperature) of 1.
3. Synthesis of compound 2a

K₂CO₃ (276 mg, 2.00 mmol), KPF₆ (92.0 mg, 0.500 mmol) and CH₃CN (80.0 mL) were added into a 150 mL round-bottom flask under nitrogen atmosphere. A CH₃CN (20.0 mL) solution of 2,2'-dihydroxy BMP32C10 (114 mg, 0.200 mmol) and 2,6-bis(p-toluenesulfonyl oxy)methyl)pyridine (89.5 mg, 0.200 mmol) were added at a speed of 1.00 mL/h at reflux. The mixture was then stirred at reflux for 5 days. The solution was filtrated and concentrated to give a crude product, which was purified by flash column chromatography (ethyl acetate) to give 2a (75 mg, 56%) as a white solid; m.p. 103.3–105.4 °C. The ¹H NMR spectrum of 2a was shown in Fig. S3. ¹H NMR (500 MHz, CD₃COCD₃, room temperature) δ (ppm): 7.97 (3H, m), 6.96 (2H, J = 8.5 Hz, t), 6.66 (4H, J = 8.5 Hz, d), 5.20 (4H, s), 4.14–4.16 (8H, m), 3.80–3.82 (8H, m), 3.57–3.59 (8H, m), 3.48–3.51 (8H, m). The ¹³C NMR spectrum of 2a is shown in Fig. S4. ¹³C NMR (100 MHz, CDCl₃, room temperature) δ (ppm): 153.1, 124.0, 119.7, 107.2, 75.4, 71.0, 70.7, 70.0, 69.2. LRESIMS is shown in Figure S5: m/z 672.4 [M + H]⁺ (100%), 694.2 [M + Na]⁺ (16.7%). HRESIMS: m/z calcd for [M + H]⁺ C₃₅H₄₅NNaO₁₂⁺, 672.3015; found 672.2988, error –4.0 ppm.
Fig. S3 $^1$H NMR spectrum (500 MHz, acetone-$d_6$, room temperature) of 2a.

Fig. S4 $^{13}$C NMR spectrum (100 MHz, chloroform-$d$, room temperature) of 2a.

Fig. S5 LRESI mass spectrum of 2a.
4. Job plot of 1\rightleftharpoons 5 based on UV-Vis data in 1:1 acetonitrile/chloroform

![Job plot](image)

**Fig. S6** Job plot showing the 1:1 stoichiometry of the complex 1\rightleftharpoons 5 in 1:1 acetonitrile/chloroform. \([1]_0 + [5]_0 = 0.50\) mM. \([1]_0\) and \([5]_0\) are the initial concentrations of 1 and 5, respectively.

5. Determination of association constants of 1\rightleftharpoons 5 and 4\rightleftharpoons 5

The association constants of complexes 1\rightleftharpoons 5 and 4\rightleftharpoons 5 were determined by probing the charge-transfer band of the complexes by UV-vis spectroscopy and employing a titration method. Progressive addition of a 1:1 acetonitrile/chloroform solution with high guest 5 concentration and low host 1 or 4 concentration to a 1:1 acetonitrile/chloroform solution with the same concentration of host 1 or 4 resulted in an increase of the intensity of the charge-transfer band of the complex. Treatment of the collected absorbance data at \(\lambda = 403\) nm with a non-linear curve-fitting program afforded the corresponding association constants \((K_a)\): 2.5 \((\pm 0.5) \times 10^4\) M\(^{-1}\) for 1\rightleftharpoons 5, and 2.7 \((\pm 1.4) \times 10^6\) M\(^{-1}\) for 4\rightleftharpoons 5.

The non-linear curve-fitting was based on the equation:

\[
A = \frac{(A_\infty[H]_0)}{(0.5[G]_0 + 0.5([H]_0 + 1/K_a) - (0.5 ([G]_0^2 + 2[G]_0(1/K_a - [H]_0)) + (1/K_a + [H]_0^2)^{0.5})}}
\]

(Eq. S1)

Where \(A\) is the absorption intensity of the charge-transfer band \((\lambda = 403\) nm) at \([G]_0\), \(A_\infty\) is the absorption intensity of the charge-transfer band \((\lambda = 403\) nm) when the host is completely complexed, \([H]_0\) is the fixed initial concentration of the host, and \([G]_0\) is the initial concentration of the guest.
Fig. S7 Titration curve (top) and non-linear fitting curve (bottom) of host 1 and guest 5.
Fig. S8 Titration curve (top) and non-linear fitting curve (bottom) of host 4 and guest 5.
6. Electrospray ionization mass spectrum of an equimolar 1:1 acetonitrile/chloroform solution of \( \text{I} \) and \( \text{S} \)

![Mass Spectrum](image)

**Fig. S9** Positive electrospray ionization mass spectrum of an equimolar 1:1 acetonitrile/chloroform solution of \( \text{I} \) and \( \text{S} \) gave strong mass fragments at \( m/z \) 524.2 (81.3%), 863.2 (100%) and 885.1 (20.5%), corresponding to \([\text{I} \rightarrow \text{S} - 2\text{PF}_6]^{2+}, [\text{I} + \text{H}]^{+}\) and \([\text{I} + \text{Na}]^{+}\), respectively.

7. Partial \(^1\)H NMR spectra on the pH-controlled complexation between \( \text{I} \) and \( \text{S} \)

![NMR Spectra](image)

**Fig. S10** Partial \(^1\)H NMR spectra (400 MHz, CDCl\(_3\)/CD\(_3\)CN 1:1, 295 K) of: a) \( \text{S} \), b) 4.00 mM \( \text{I} \) and \( \text{S} \), c) a solution of 4.0 \( \mu \)L of trifluoroacetic acid-\( d \) and 0.5 mL of 4.00 mM \( \text{I} \) and \( \text{S} \), d) a solution of 4.0 \( \mu \)L of trifluoroacetic acid-\( d \), 8.0 \( \mu \)L of triethylamine, and 0.5 mL of 4.00 mM \( \text{I} \) and \( \text{S} \), and e) \( \text{I} \).
8. Crystal structure of complex $4\supset\supset 5$ 

*Fig. S11* Crystal structure of complex $4\supset\supset 5$: 4 is red, 5 is blue, and the acetone molecule is black.

**References:**


