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

Mingming Zhang, Bo Zheng, and Feihe Huang*

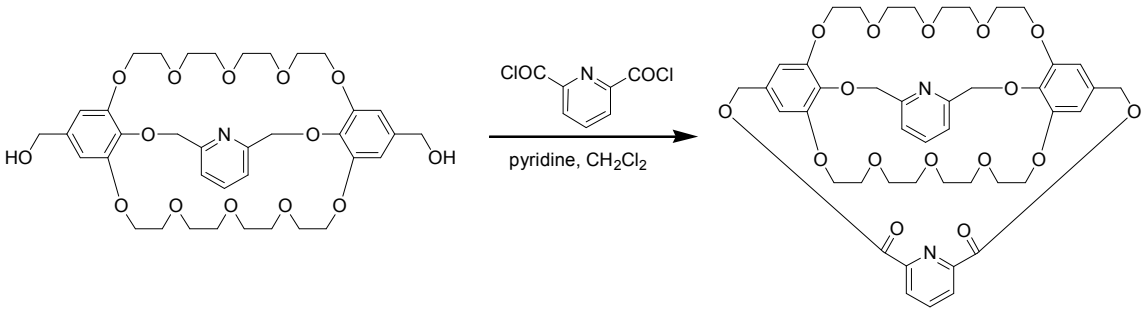
Department of Chemistry, Zhejiang University, Hangzhou, Zhejiang 310027, P. R. China,
Fax and Tel: +86-571-8795-3189; Email address: fhuang@zju.edu.cn.

Electronic Supplementary Information (10 pages)

1. Materials and methods

All reagents were commercially available and used as supplied without further purification. BMP32C10 (**1**), BMP32C10 diol (**5**),[S1] 2,2'-dihydroxy-BMP32C10,[S2] bis(1,2,3-phenylene) cryptand **2b**[S3] and 2,6-bis(*p*-toluenesulfonyloxymethyl)pyridine[S4] 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***



2b **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 (SiO_2: 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 ^{1}H NMR. The ^{1}H NMR spectrum is shown in Fig. S1. ^{1}H NMR (400 MHz, $CDCl_3$, 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 $[M + Na]^+$ $C_{44}H_{50}N_2NaO_{16}^+$, 885.3053; found 885.3029, error –2.7 ppm.

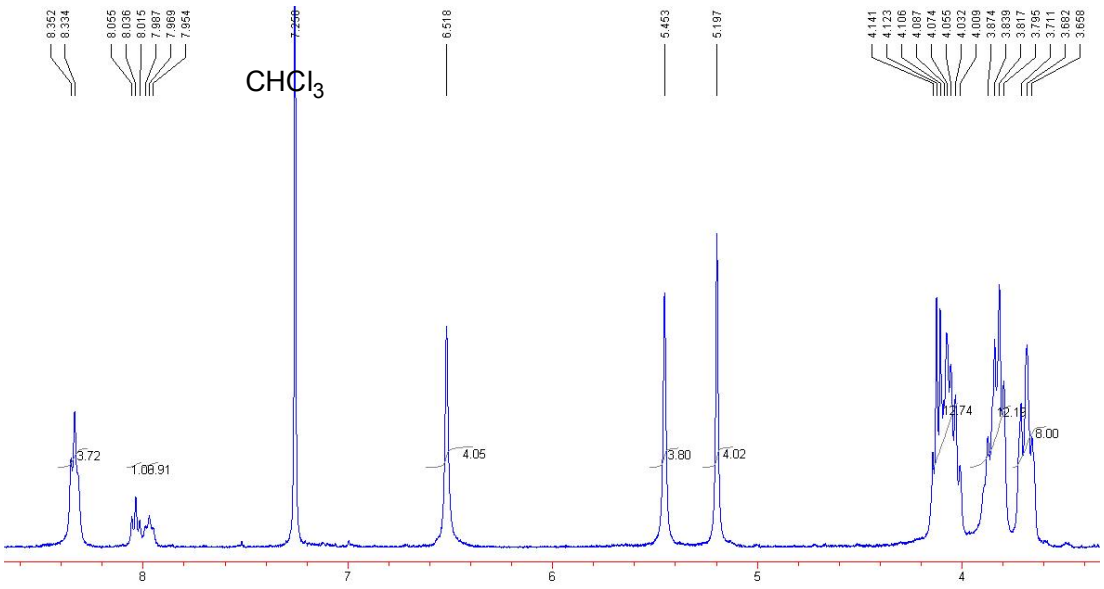


Fig.S2 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, room temperature) of **1**.

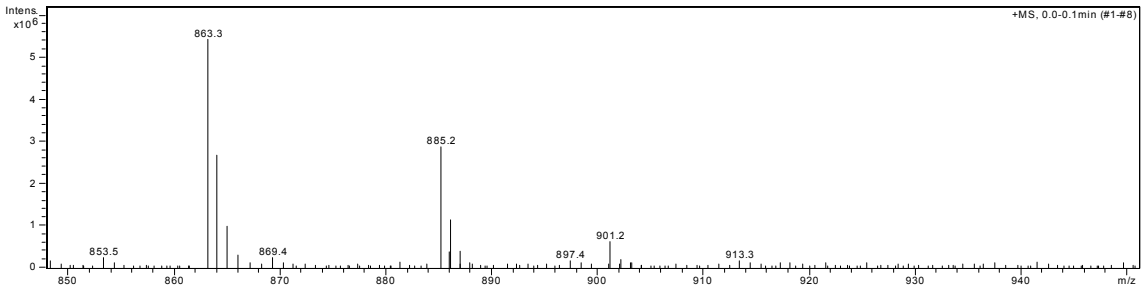
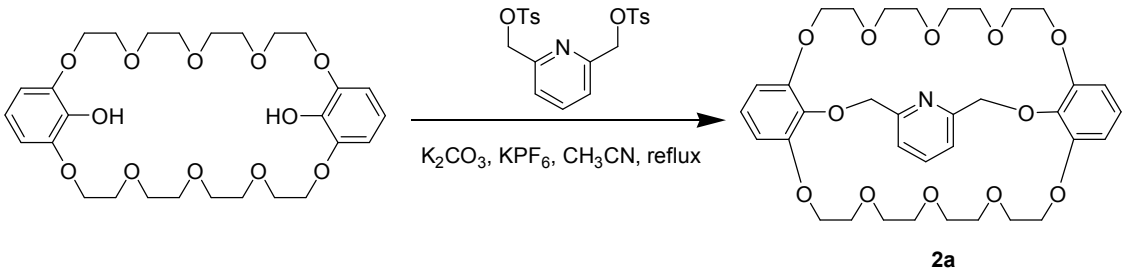


Fig. S2 LRESI mass spectrum of **1**.

3. Synthesis of compound ***2a***



2a

K_2CO_3 (276 mg, 2.00 mmol), KPF_6 (92.0 mg, 0.500 mmol) and CH_3CN (80.0 mL) were added into a 150 mL round-bottom flask under nitrogen atmosphere. A CH_3CN (20.0 mL) solution of 2,2'-dihydroxy BMP32C10 (114 mg, 0.200 mmol) and 2,6-bis(*p*-toluenesulfonyloxymethyl)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 ^{1}H NMR spectrum of **2a** was shown in Fig. S3. ^{1}H NMR (500 MHz, CD_3COCD_3, 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 ^{13}C NMR spectrum of **2a** is shown in Fig. S4. ^{13}C NMR (100 MHz, $CDCl_3$, 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 $[M + H]^+$ $C_{35}H_{45}NNaO_{12}^+$, 672.3015; found 672.2988, error –4.0 ppm.

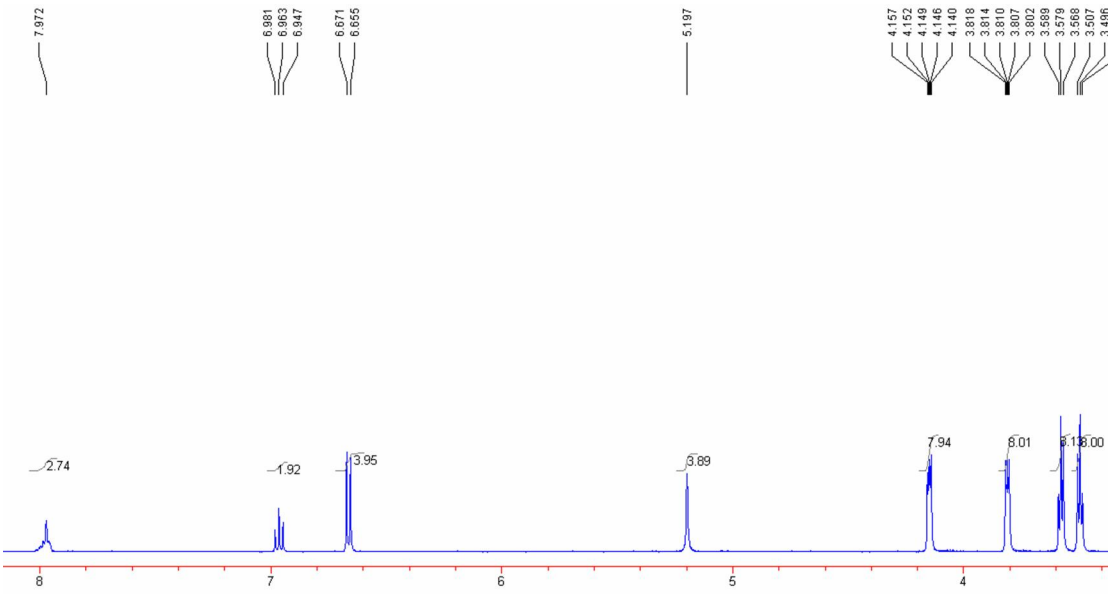


Fig. S3 ^{1}H NMR spectrum (500 MHz, acetone-d_6, room temperature) of **2a**.

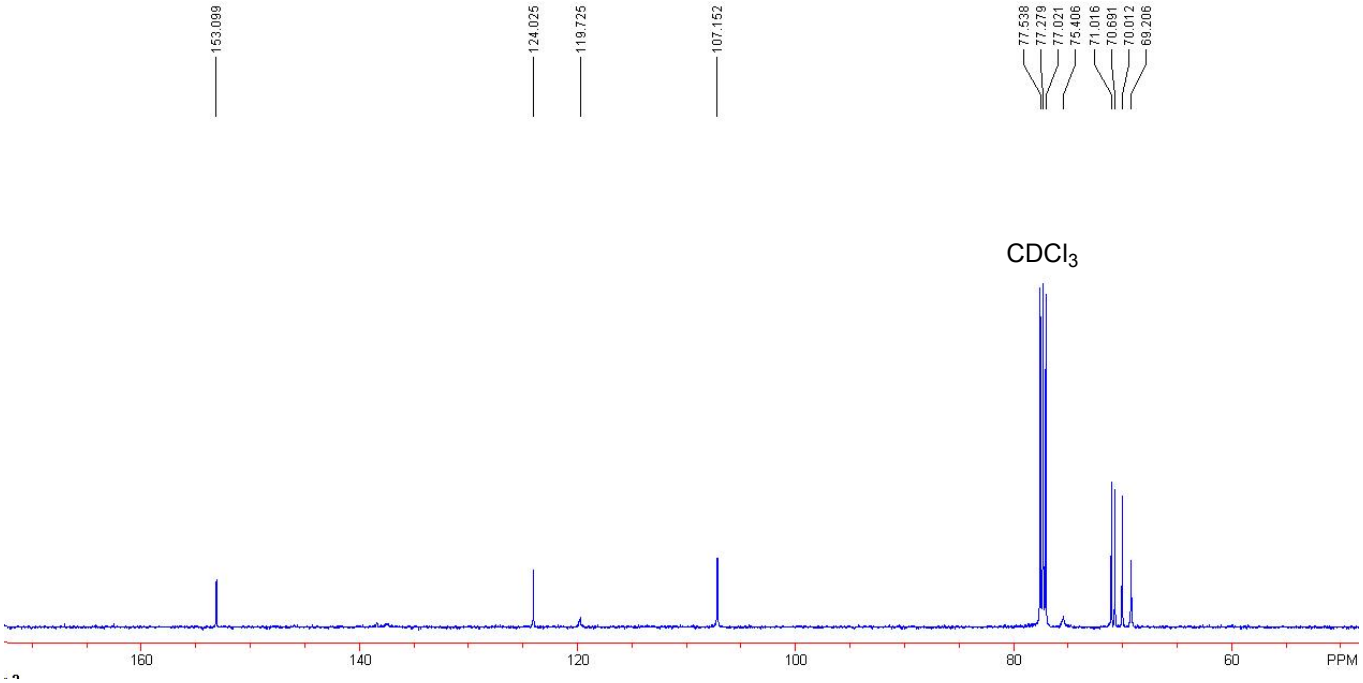


Fig. S4 ^{13}C NMR spectrum (100 MHz, chloroform-*d*, room temperature) of **2a**.

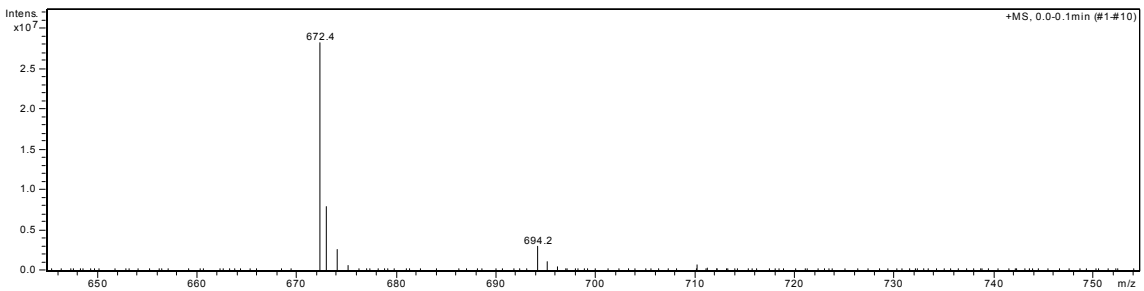


Fig. S5 LRESI mass spectrum of **2a**.

*4. Job plot of **1**⊃**5** based on UV-Vis data in 1:1 acetonitrile/chloroform*

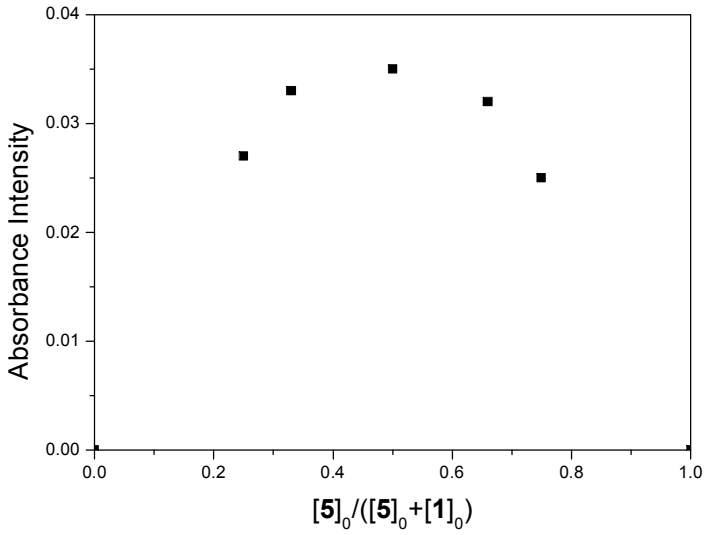


Fig. S6 Job plot showing the 1:1 stoichiometry of the complex **1**⊃**5** in 1:1 acetonitrile/chloroform. $[\mathbf{1}]_0 + [\mathbf{5}]_0 = 0.50$ mM. $[\mathbf{1}]_0$ and $[\mathbf{5}]_0$ are the initial concentrations of **1** and **5,** respectively.

*5. Determination of association constants of **1**⊃**5** and **4**⊃**5***[S5]

The association constants of complexes **1**⊃**5** and **4**⊃**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 λ = 403 nm with a non-linear curve-fitting program afforded the corresponding association constants (K_a): 2.5 (± 0.5) × 10^4 M^{-1} for **1**⊃**5**, and 2.7 (± 1.4) × 10^6 M^{-1} for **4**⊃**5**.

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

$$A = (A_\infty/[H]_0)\ (0.5[G]_0 + 0.5([H]_0+1/K_a)-(0.5\ ([G]_0^2+(2[G]_0(1/K_a - [H]_0)) + (1/K_a + [H]_0)^2)^{0.5})) \qquad \text{(Eq. S1)}$$

Where A is the absorption intensity of the charge-transfer band (λ = 403 nm) at $[G]_0$, A_∞ is the absorption intensity of the charge-transfer band (λ = 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.

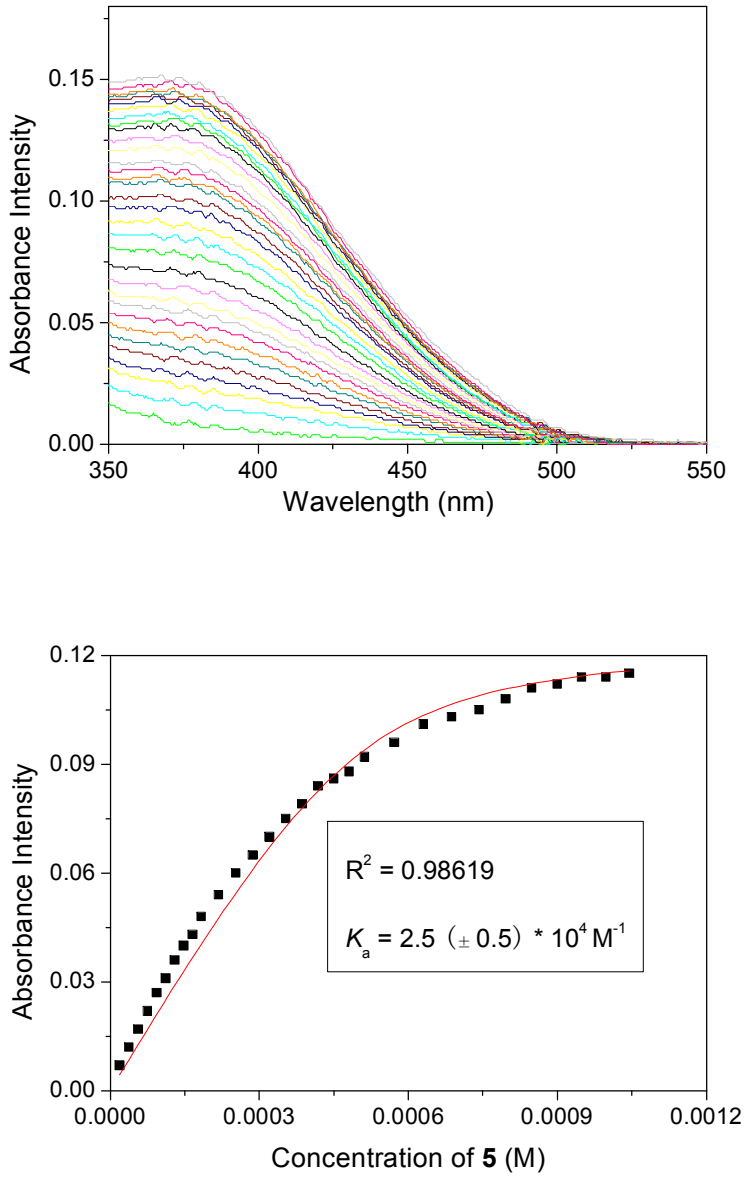


Fig. S7 Titration curve (top) and non-linear fitting curve (bottom) of host **1** and guest **5**.

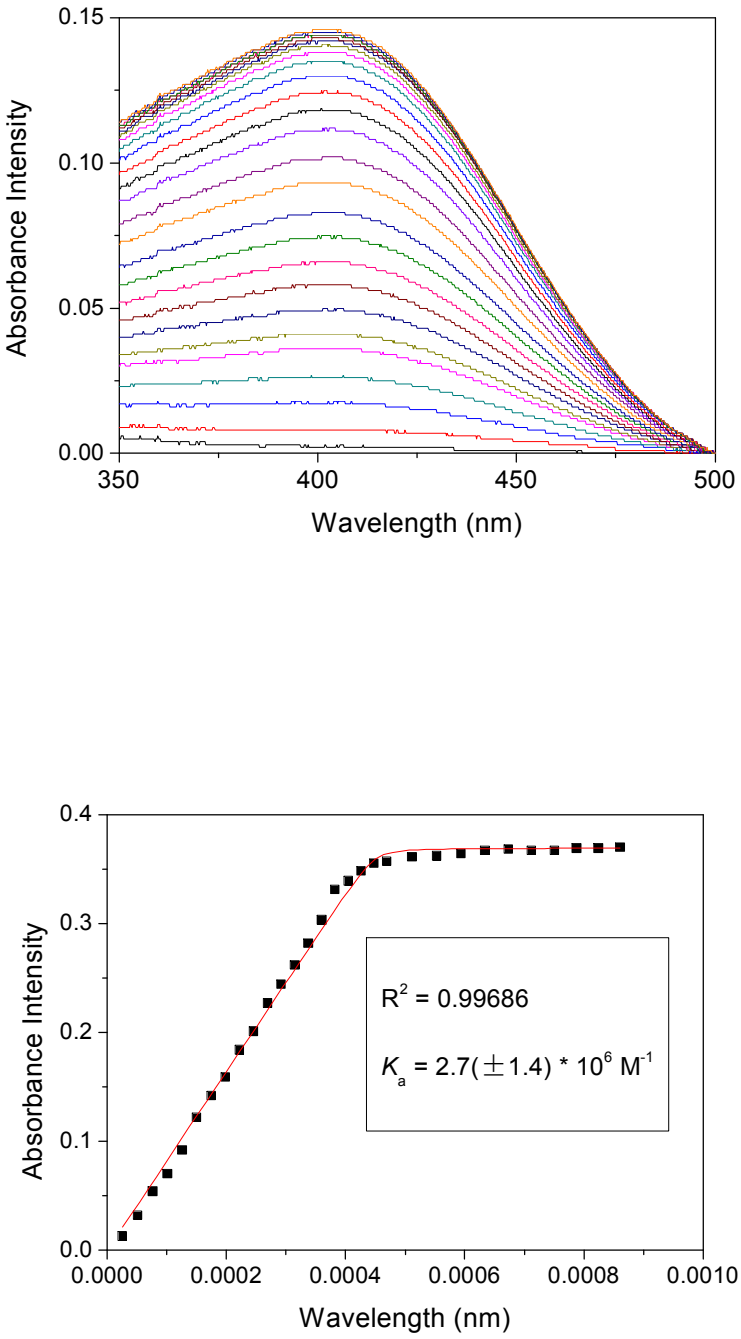


Fig. S8 Titration curve (top) and non-linear fitting curve (bottom) of host **4** and guest **5**.

*6. Electrospray ionization mass spectrum of an equimolar 1:1 acetonitrile/choloroform solution of **1** and **5***

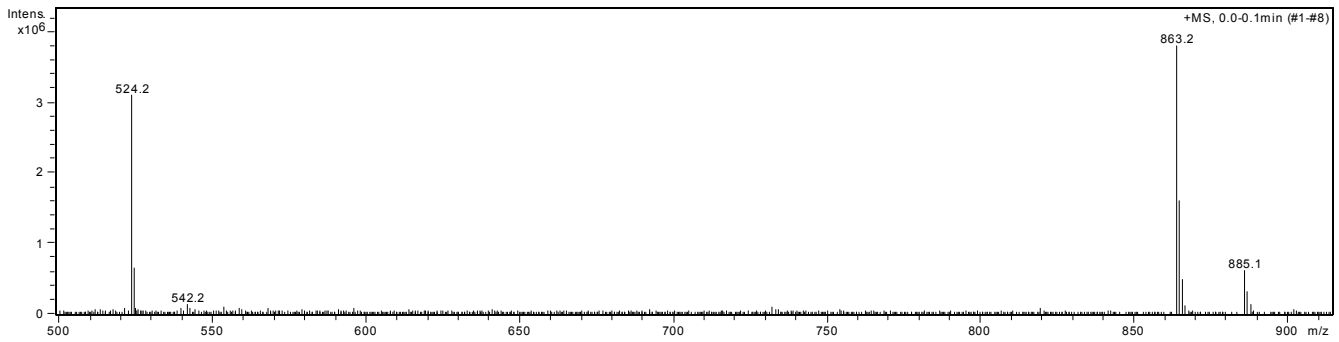


Fig. S9 Positive electrospray ionization mass spectrum of an equimolar 1:1 acetonitrile/choloroform solution of **1** and **5** gave strong mass fragments at *m/z* 524.2 (81.3%), 863.2 (100%) and 885.1 (20.5%), corresponding to $[\mathbf{1}\supset\mathbf{5} - 2PF_6]^{2+}$, $[\mathbf{1} + H]^+$ and $[\mathbf{1} + Na]^+$, respectively.

*7. Partial ^1H NMR spectra on the pH-controlled complexation between **1** and **5***

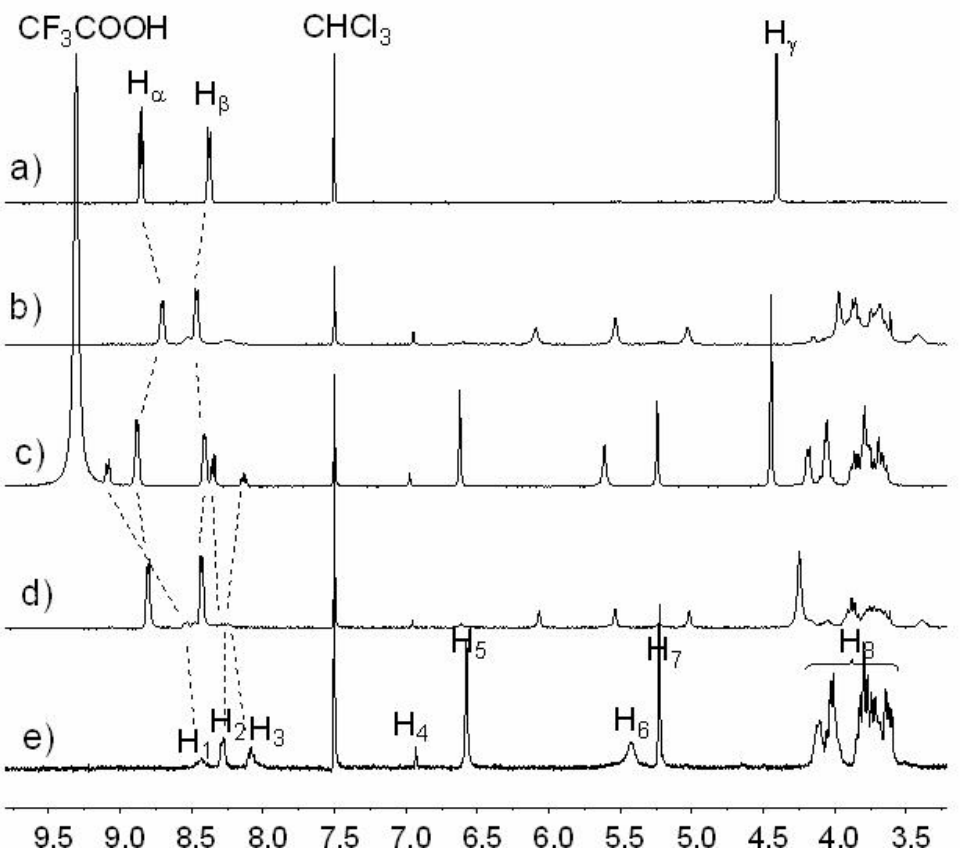


Fig. S10 Partial ^1H NMR spectra (400 MHz, $CDCl_3/CD_3CN$ 1:1, 295 K) of: a) **5**, b) 4.00 mM **1** and **5**, c) a solution of 4.0 μL of trifluoroacetic acid-*d* and 0.5 mL of 4.00 mM **1** and **5**, d) a solution of 4.0 μL of trifluoroacetic acid-*d*, 8.0 μL of triethylamine, and 0.5 mL of 4.00 mM **1** and **5**, and e) **1**.

8. Crystal structure of complex ***4⊃5***[S6]

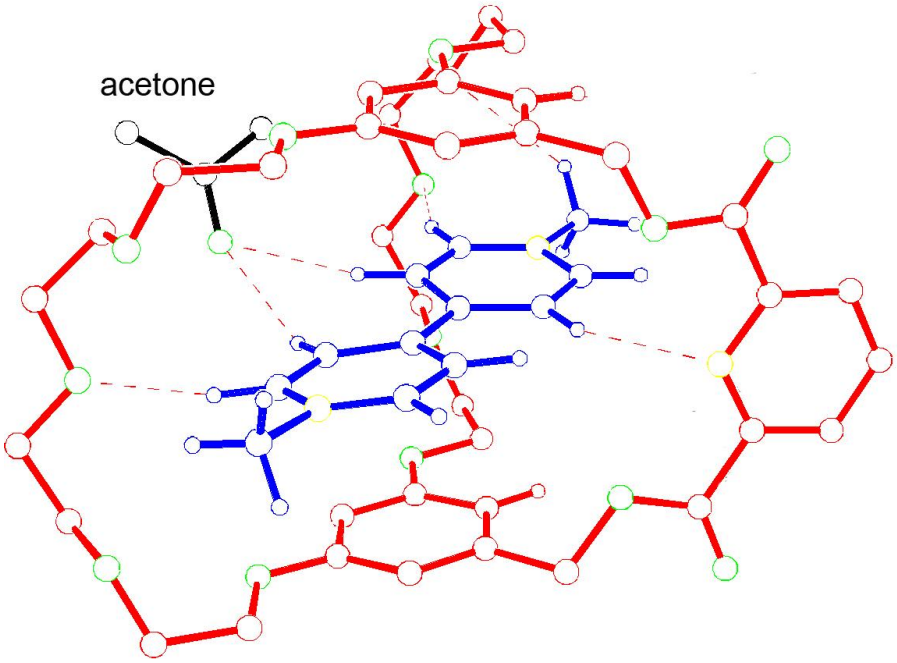


Fig. S11 Crystal structure of complex **4⊃5**: **4** is red, **5** is blue, and the acetone molecule is black.

References:

S1. H. W. Gibson and D. S. Nagvekar, *Can. J. Chem.* 1997, **75**, 1375–1384.

S2 M. Zhang, Y. Luo, B. Zheng, X. Yan, F. R. Fronczek and F. Huang, *Eur. J. Org. Chem.*, 2010, 6798–6803.

S3 M. Zhang, B. Zheng, B. Xia, K. Zhu, C. Wu and F. Huang, *Eur. J. Org. Chem.*, 2010, 6804–6807.

S4 J. S. Bradshaw, P. Huszthy, C. W. McDaniel, C. Y. Zhu, N. K. Dalley, R. M. Izatt and S. Lifson, *J. Org. Chem.* 1990, **55**, 3129–3137.

S5. (a) K. A. Connors, *Binding Constants*; Wiley: New York, 1987; (b) Corbin, P. S. Ph.D. Dissertation, University of Illinois at Urbana-Champaign, Urbana, IL, 1999; (c) P. R. Ashton, R. Ballardini, V. Balzani, M. Belohradsky, M. T. Gandolfi, D. Philp, L. Prodi, F. M. Raymo, M. V. Reddington, N. Spencer, J. F. Stoddart, M. Venturi and D. J. Williams, *J. Am. Chem. Soc.* 1996, **118**, 4931–4951.

S6. F. Huang, K. A. Switek, L. N. Zakharov, F. R. Fronczek, C. Slebodnick, M. Lam, J. A. Golen, W. S. Bryant, P. E. Mason, A. L. Rheingold, M. Ashraf-Khorassani and H. W. Gibson, *J. Org. Chem.*, 2005, **70**, 3231–3241.