Electronic Supplementary Information

Synthesis of a water-soluble 2,6-helic[6]arene derivative and its strong binding abilities towards quaternary phosphonium salts: an acid/base controlled switchable complexation process

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1. Materials and methods

Host **H1** was synthesized according to our previously reported method.[S1] Guest **P1** and other reagents were commercially available and used as received. Guests **P2** and **P3** were prepared according to the literature procedures.[S2, S3] ^{1}H NMR spectra and 2D Roesy spectra were recorded on the Brucker® Avance III 500 MHz NMR spectrometers at 298 K. Electrospray ionization mass spectra (ESI-MS) were recorded on the Thermo Fisher® Exactive high-resolution LC-MS spectrometer. Melting points were determined using WRR melting point apparatus, and were not corrected.

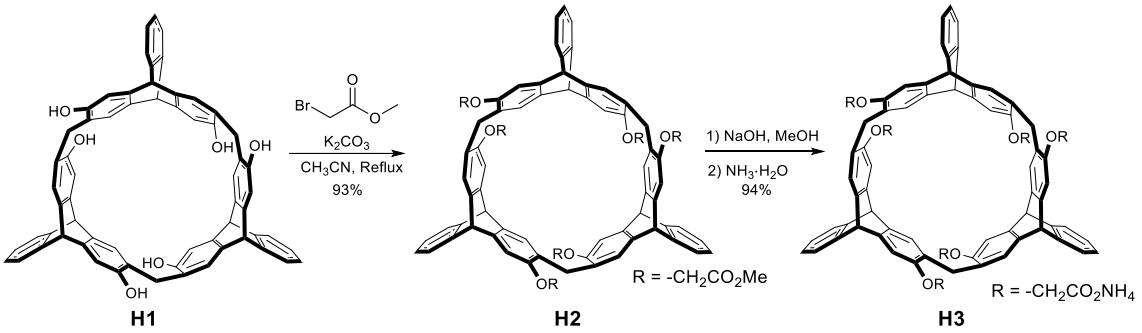
References:

S1. G.-W. Zhang, P.-F. Li, Z. Meng, H.-X. Wang, Y. Han and C.-F. Chen, *Angew Chem. Int. Ed.*, 2016, **55**, 5304–5308.

S2. H. Büttner, J. Steinbauer and T. Werner, *ChemSusChem*, 2015, **8**, 2655–2669.

S3. M. E. Krafft, K. A. Seibert, T. F. N. Haxell and C. Hirosawa, *Chem. Commun*., 2005, **46**, 5772–5774.

2. Synthesis of H2 and H3



Scheme S1. Synthesis of water-soluble 2,6-helic[6]arene **H3**.

Methoxycarbonyl-substituted 2,6-helic[6]arene H2: To a solution of 2,6-helic[6]arene (100 mg, 0.11 mmol) in CH_3CN (25 mL) was added K_2CO_3 (462 mg, 3.30 mmol). The reaction mixture was stirred for 1 h under nitrogen atmosphere, and then added methyl bromoacetate (504 mg, 3.30 mmol). The mixture was heated at 80 ^oC for another 24 hours, and then cooled to room temperature and filtered. The filtrate was concentrated under reduced pressure, and the crude product was purified by flash column chromatography (eluent: 20:1 ethyl acetate and CH_2Cl_2) to afford **H2** (136 mg, 93 %) as a white solid. M.p. 170-172 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.57 (s, 6H), 7.33–7.26 (m, 6H), 6.93–6.95 (m, 6H), 6.69 (s, 6H), 5.08 (s, 6H), 4.60–4.62 (m, 12H), 3.95 (s, 18H), 3.80 (s, 6H). ^{13}C NMR (126 MHz, D_2O): δ 169.7, 152.4, 145.9, 144.6, 138.4, 126.7, 126.5, 124.9, 123.2, 108.5, 66.3, 53.4, 28.9, 14.2. HRMS (ESI): *m/z* calcd for $[M + NH^4]^+$ $C_{81}H_{66}O_{18}NH_4^+$, 1344.4587; found *m/z* 1344.4593.

Carboxylic acid substituted 2,6-helic[6]arene H3: To a solution of **H2** (120 g, 1.5 mmol) in CH_3OH (10 mL) was added 40 % aqueous sodium hydroxide (10 mL), and the

mixture was stirred and refluxed overnight. After CH_3OH was removed by evaporation under vacuum, the residue was diluted with deionized water (10 mL) and acidified with hydrochloric acid. The precipitate was collected by filtration, washed with cold water (10 mL × 3) and dried under vacuum to give carboxylic acid substituted 2,6-helic[6]arene. To the solid was added 20 mL of ammonium hydroxide solution (25-28 %), and the mixture was then stirred at room temperature for 4 h. The solvent was removed by rotary evaporation to give water-soluble host **H3** (114 mg, 94 %) as a beige solid. M.p. >300 °C. ^{1}H NMR (500 MHz, D_2O): δ 7.48 (s, 6H), 7.33–7.31 (m, 6H), 6.93–6.90 (m, 6H), 6.82 (s, 6H), 5.28 (s, 6H), 4.34–4.36 (m, 12H), 3.74 (s, 6H). ^{13}C NMR (126 MHz, D_2O): δ 177.2, 152.7, 146.0, 144.9, 138.0, 126.9, 125.5, 125.3, 123.3, 109.3, 67.9, 52.2, 28.2. HRMS (ESI): *m/z* calcd for $[M\text{-}3NH_4\text{-}3NH_3]^{3-}$ $C_{75}H_{51}O_{18}^{3-}$, 413.1031; found *m/z* 413.1031.

3. ^{1}H NMR and ^{13}C NMR spectra of the new compounds

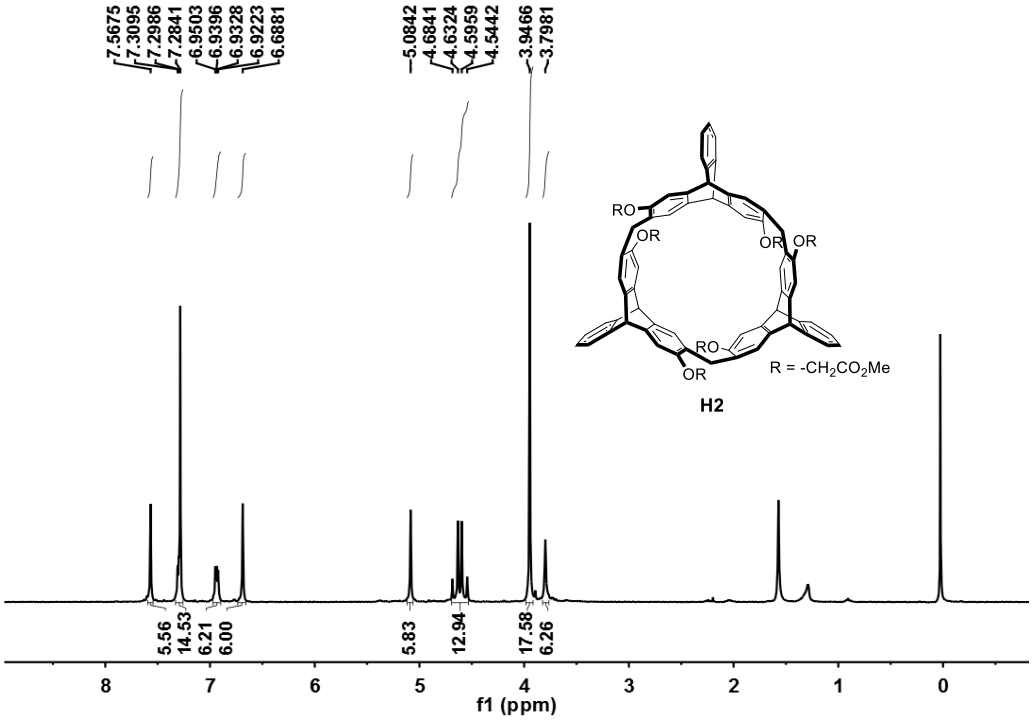


Fig. S1. ^{1}H NMR spectrum (500 MHz, 298 K, $CDCl_3$) of **H2**.

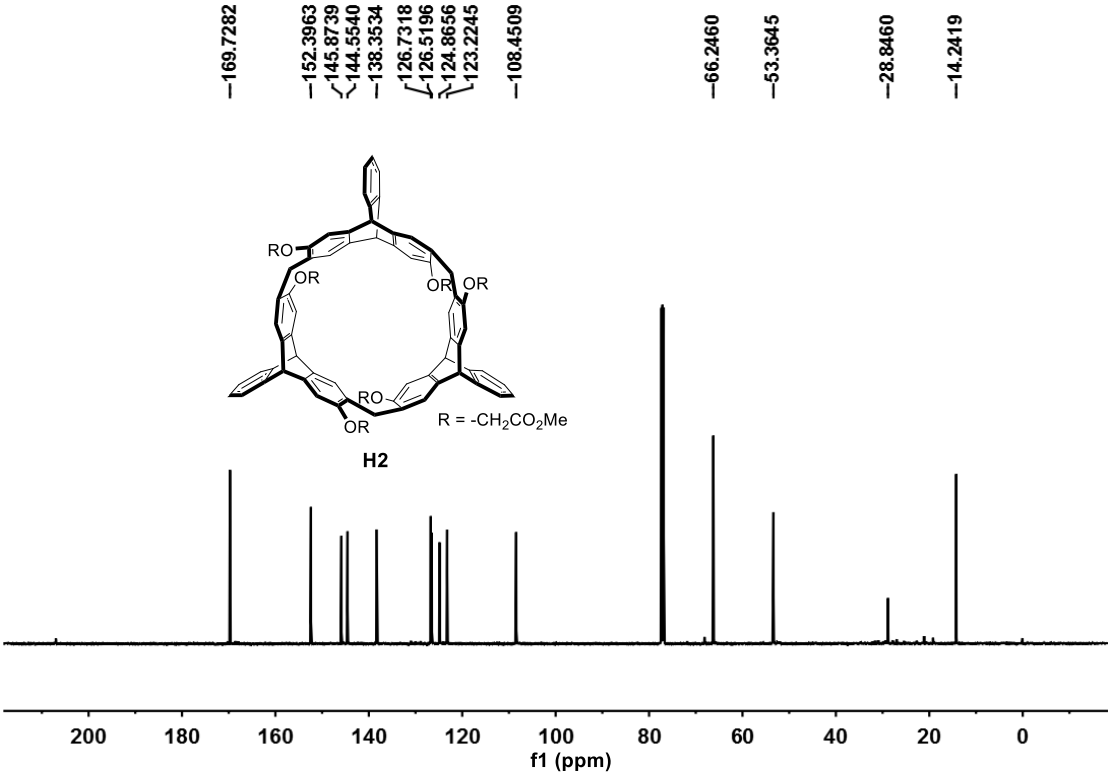


Fig. S2. ^{13}C NMR spectrum (126 MHz, 298 K, $CDCl_3$) of **H2**.

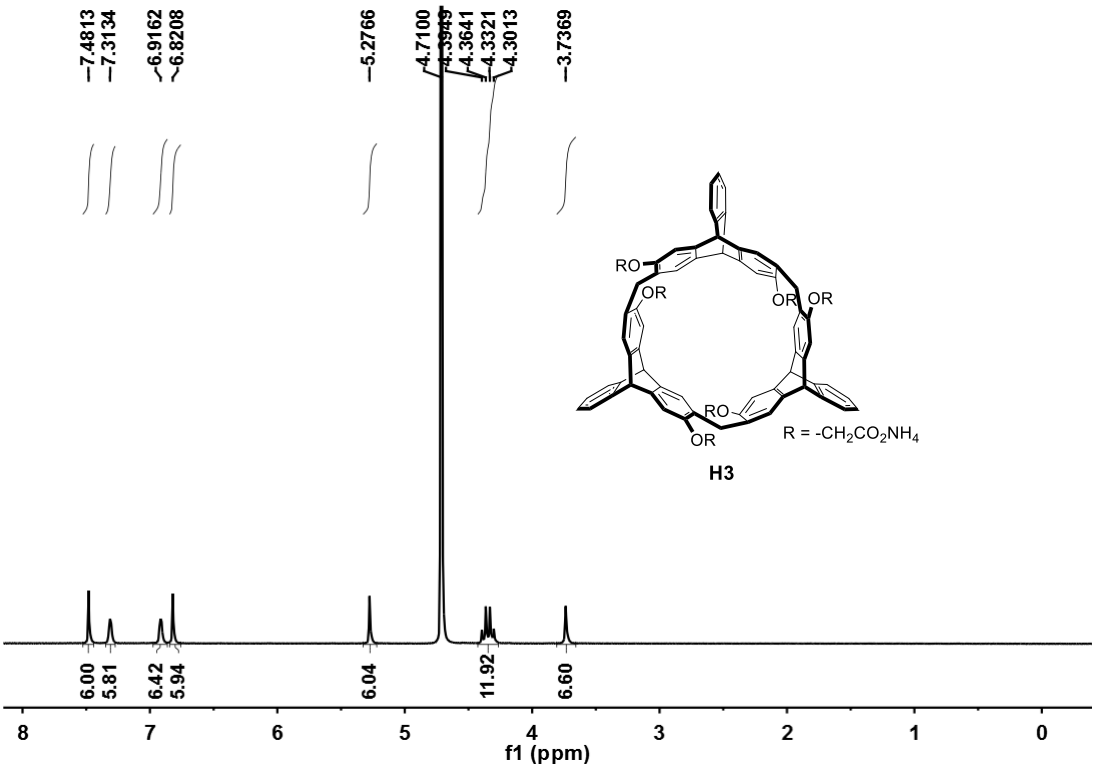


Fig. S3. ^{1}H NMR spectrum (500 MHz, 298 K, D_2O) of **H3**.

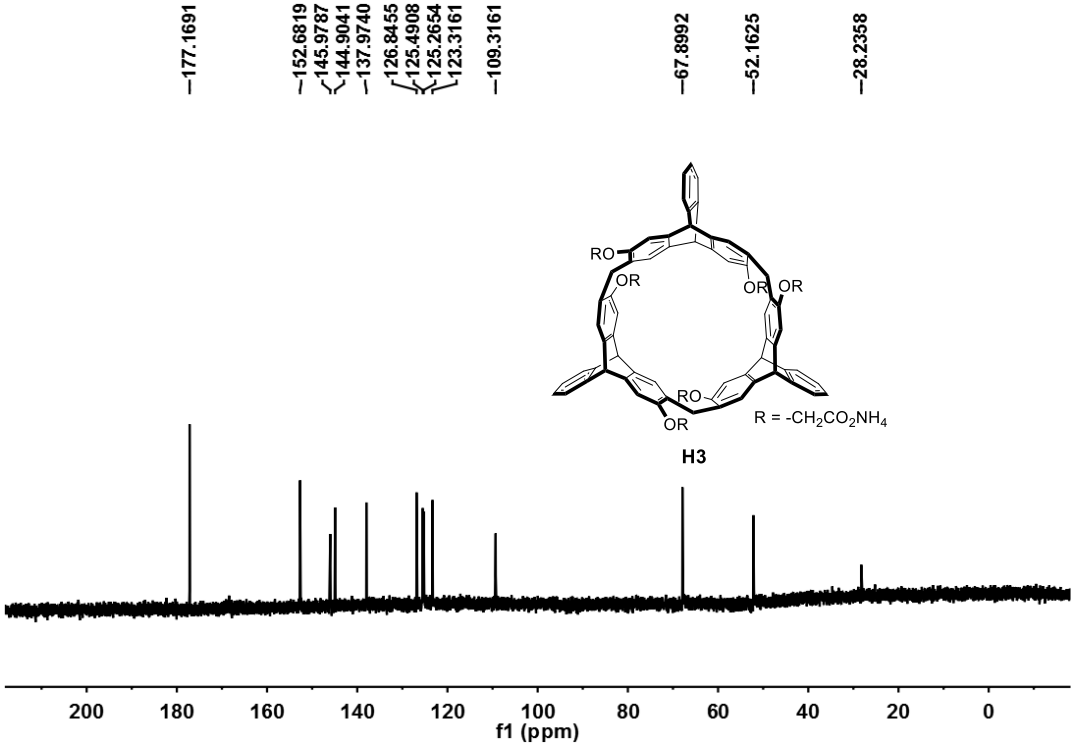


Fig. S4. ^{13}C NMR spectrum (126 MHz, 298 K, D_2O) of **H3**.

4. ^{1}H NMR studies on complexation between the host and the guests

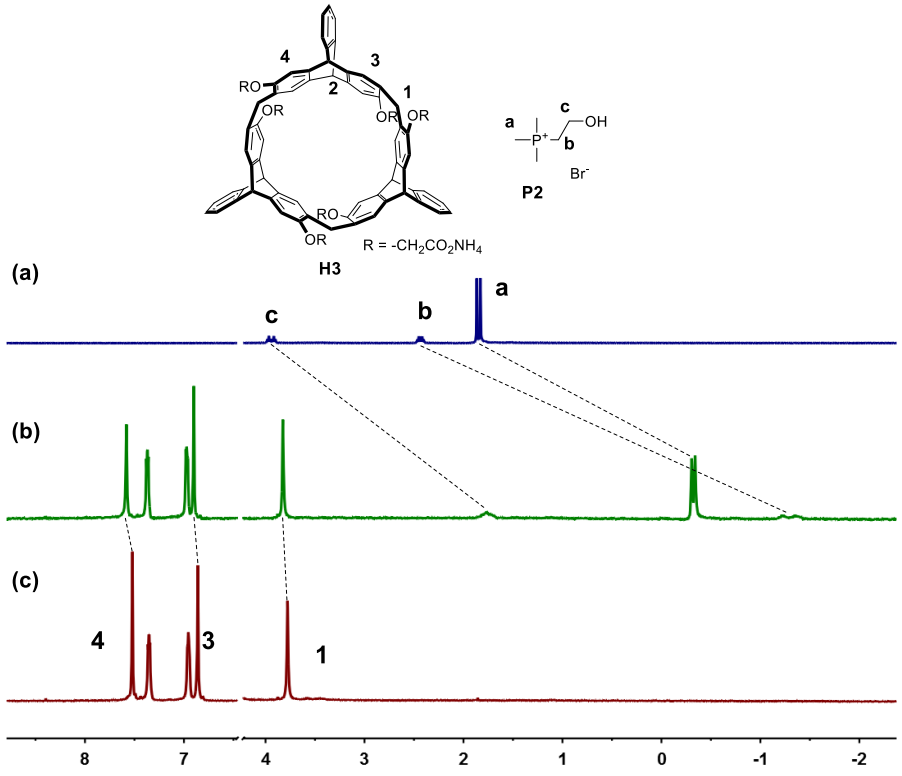


Fig. S5. ^{1}H NMR spectra (500 MHz, 298K, D_2O) of (a) guest **P2**, (b) host **H3** + 1.0 equiv. **P2**, (c) host **H3**. $[\mathbf{H3}]_0$ = 2.00 mM.

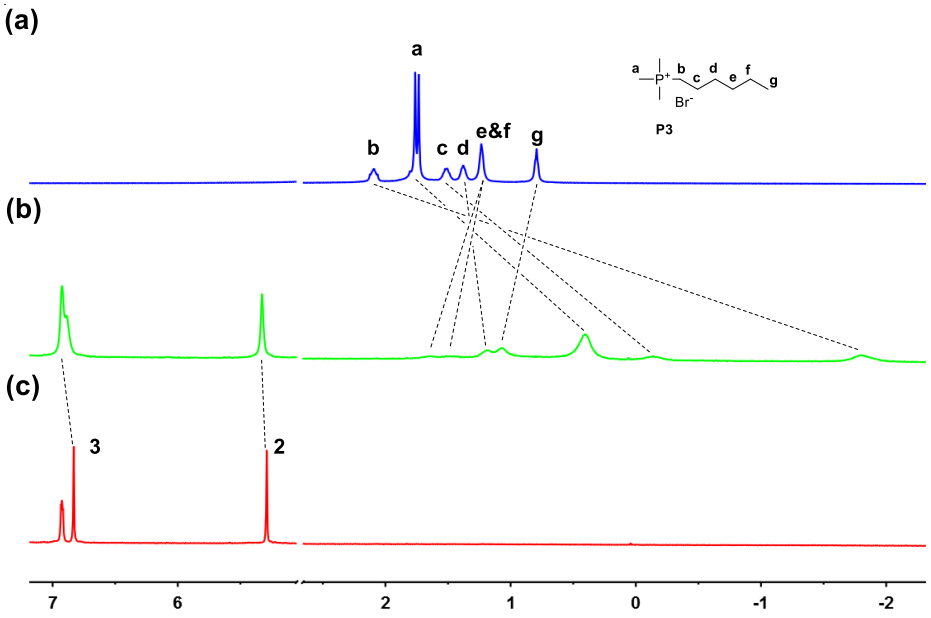


Fig. S6 ^{1}H NMR spectra (500 MHz, 298K, D_2O) of (a) guest **P3**, (b) host **H3** + 1.0 equiv. **P3**, (c) host **H3**. $[\mathbf{H3}]_0$ = 2.00 mM.

5. Job plots for the complexes

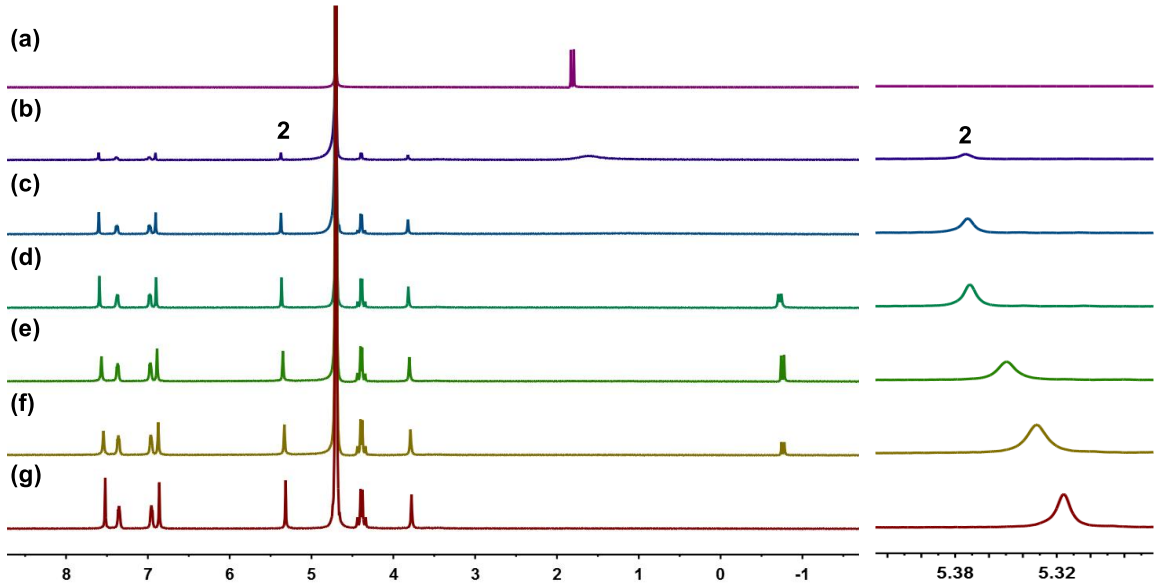


Fig. S7 ^{1}H NMR spectra (400 MHz, 298K, D_2O) of (a) 4.0 mM **P1**, (b) 0.4 mM **H3** + 3.6 mM. **P1**, (c) 1.2 mM **H3** + 2.8 mM. **P1**, (d) 2.0 mM **H3** + 2.0 mM. **P1**, (e) 2.8 mM **H3** + 1.2 Mm **P1**, (f) 3.6 mM **H3** + 0.4 mM **P1**, (g) 4.0 mM **H3**.

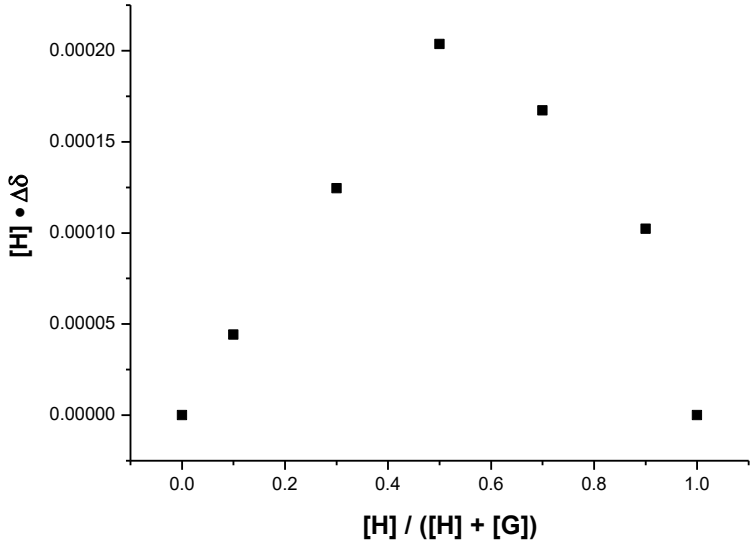


Fig. S8 Job plot for the complexation of **H3** and **P1** in D_2O at 298 K.

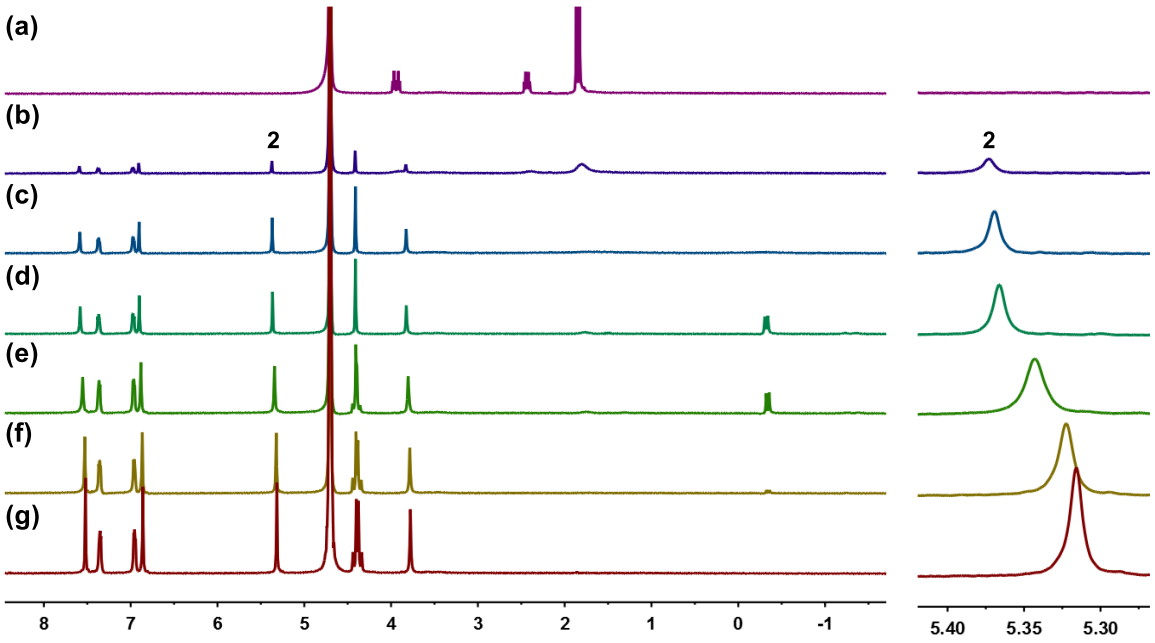


Fig. S9 ^{1}H NMR spectra (400 MHz, 298K, D_2O) of (a) 4.0 mM **P2**, (b) 0.4 mM **H3** + 3.6 mM. **P2**, (c) 1.2 mM **H3** + 2.8 mM. **P2**, (d) 2.0 mM **H3** + 2.0 mM. **P2**, (e) 2.8 mM **H3** + 1.2 Mm **P2**, (f) 3.6 mM **H3** + 0.4 mM **P2**, (g) 4.0 mM **H3**.

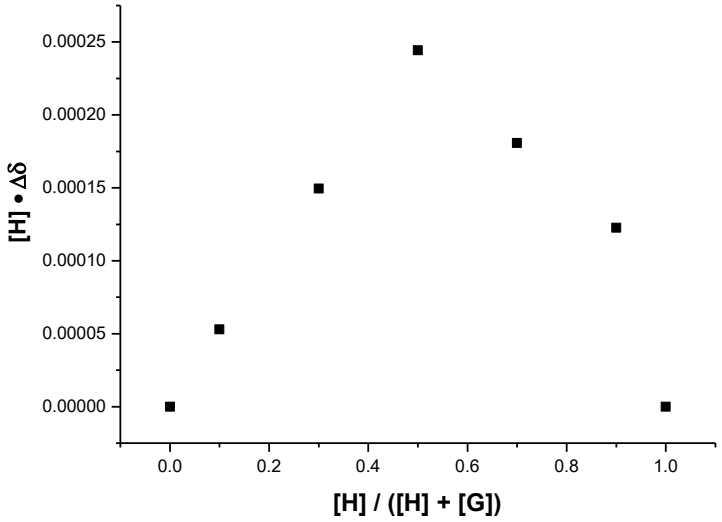


Fig. S10 Job plot for the complexation of **H3** and **P2** in D_2O at 298 K.

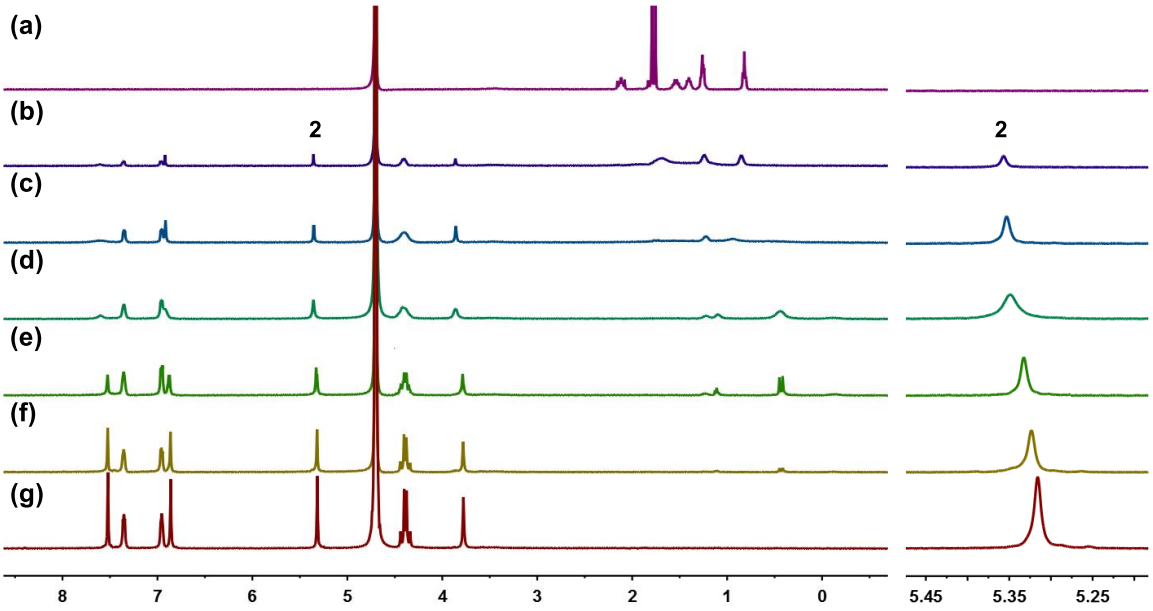


Fig. S11 ^{1}H NMR spectra (400 MHz, 298K, D_2O) of (a) 4.0 mM **P3**, (b) 0.4 mM **H3** + 3.6 mM. **P3**, (c) 1.2 mM **H3** + 2.8 mM. **P3**, (d) 2.0 mM **H3** + 2.0 mM. **P3**, (e) 2.8 mM **H3** + 1.2 Mm **P3**, (f) 3.6 mM **H3** + 0.4 mM **P3**, (g) 4.0 mM **H3**.

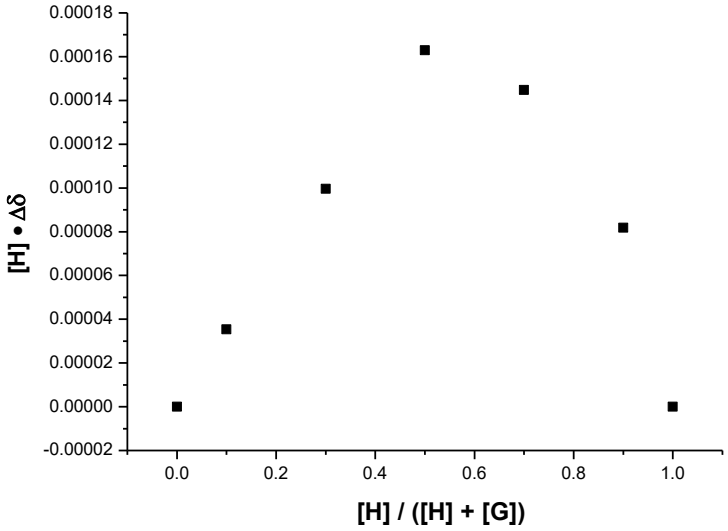


Fig. S12 Job plot for the complexation of **H3** and **P3** in D_2O at 298 K.

6. ITC experiments

All measurements were performed in the TAM III calorimeter (TA Instruments, USA) with a stainless steel sample cell of 1 mL. The sample cell was initially loaded with 0.6 mL of H_2O or **H3** solution. The guest solution was injected into the sample cell via a 500 μL Hamilton syringe controlled by a 612 Thermometric Lund pump. A series of injections were made until the desired concentration range had been covered. The system was stirred at 90 rpm with a gold propeller. The observed enthalpy (ΔH_{obs}) was obtained by integration over the peak for each injection in the plot of heat flow P against time t. By fitting the observed enthalpy curves plotted against the molar ratio of guest to host, the association constants (K_a) and the enthalpy changes (ΔH) were derived. The free energy changes (ΔG) were calculated from $\Delta G = -RT \ln K_a$, and the entropy changes were from $\Delta S = (\Delta H - \Delta G)/T$. All of the measurements were conducted at 298.15 ± 0.01 K.

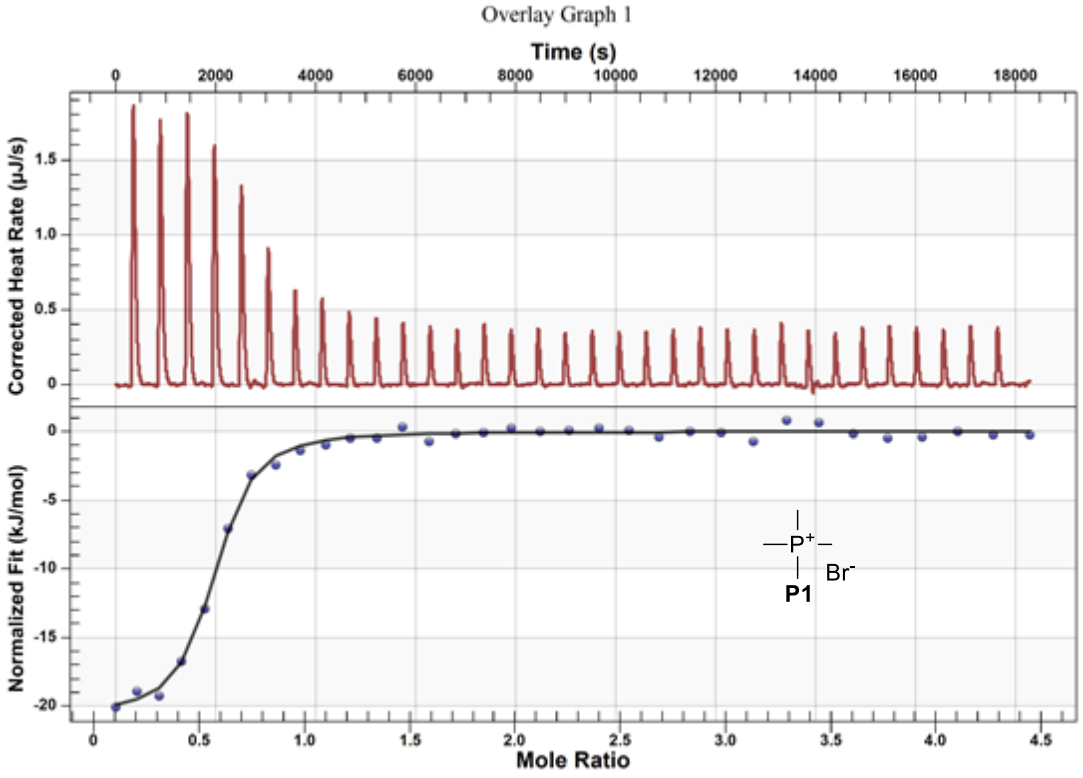


Fig. S13 ITC experiment of **H3** and **P1** in aqueous solution at 298 K.

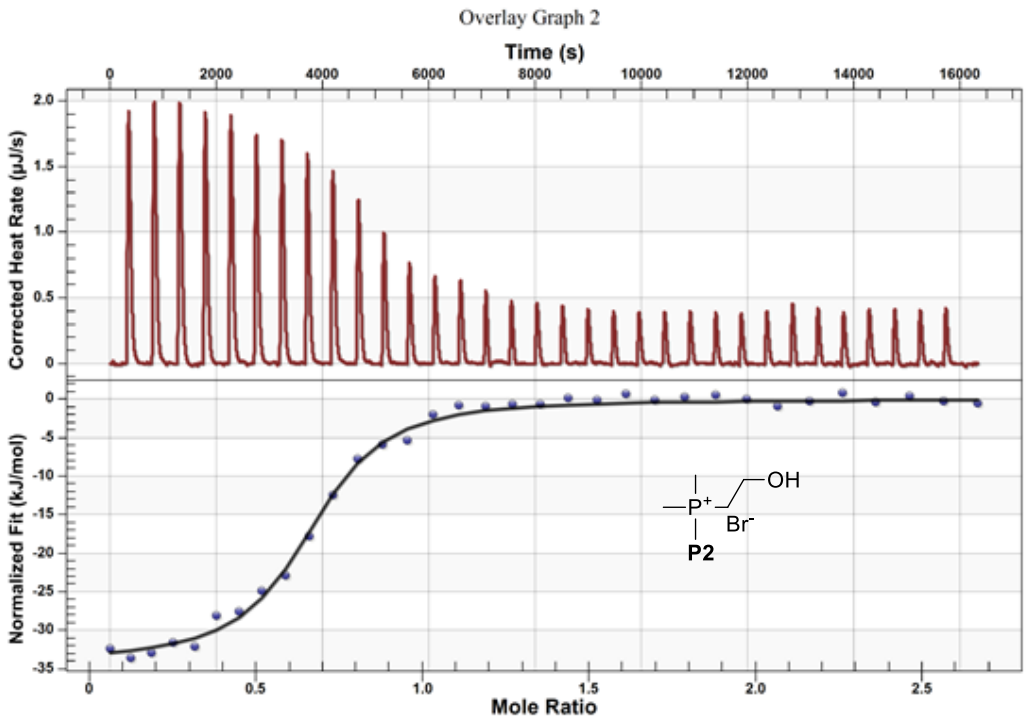


Fig. S14 ITC experiment of **H3** and **P2** in aqueous solution at 298 K.

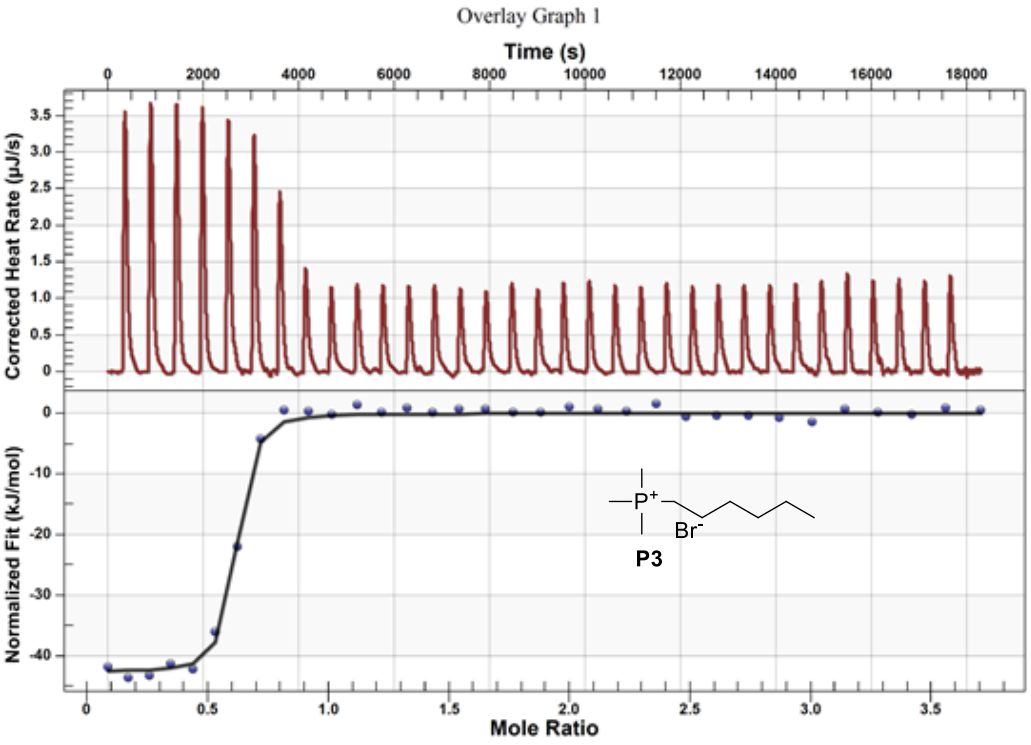


Fig. S15 ITC experiment of **H3** and **P3** in aqueous solution at 298 K.

7. 2D ROESY spectra of the complexes

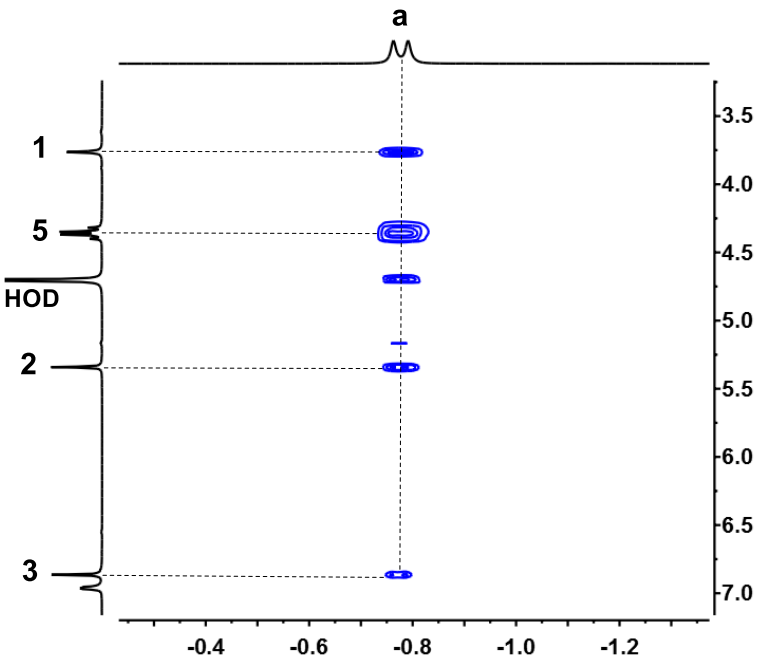


Fig. S16 2D ROESY spectrum (500 MHz, 298K, D_2O) of the complex based on **H3** and **P1** (25.00 mM for each).

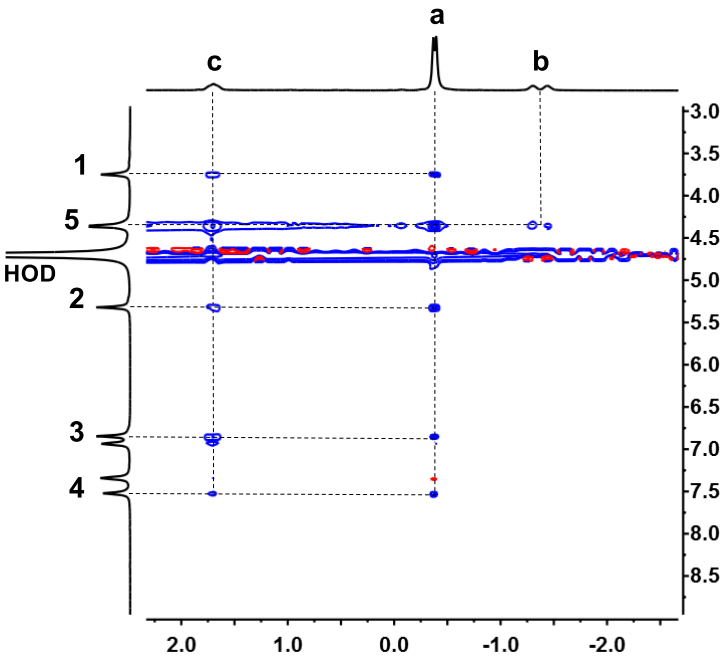


Fig. S17 2D ROESY spectrum (500 MHz, 298K, D_2O) of the complex based on **H3** and **P2** (25.00 mM for each).

8. Acid/base controlled switchable complexation process

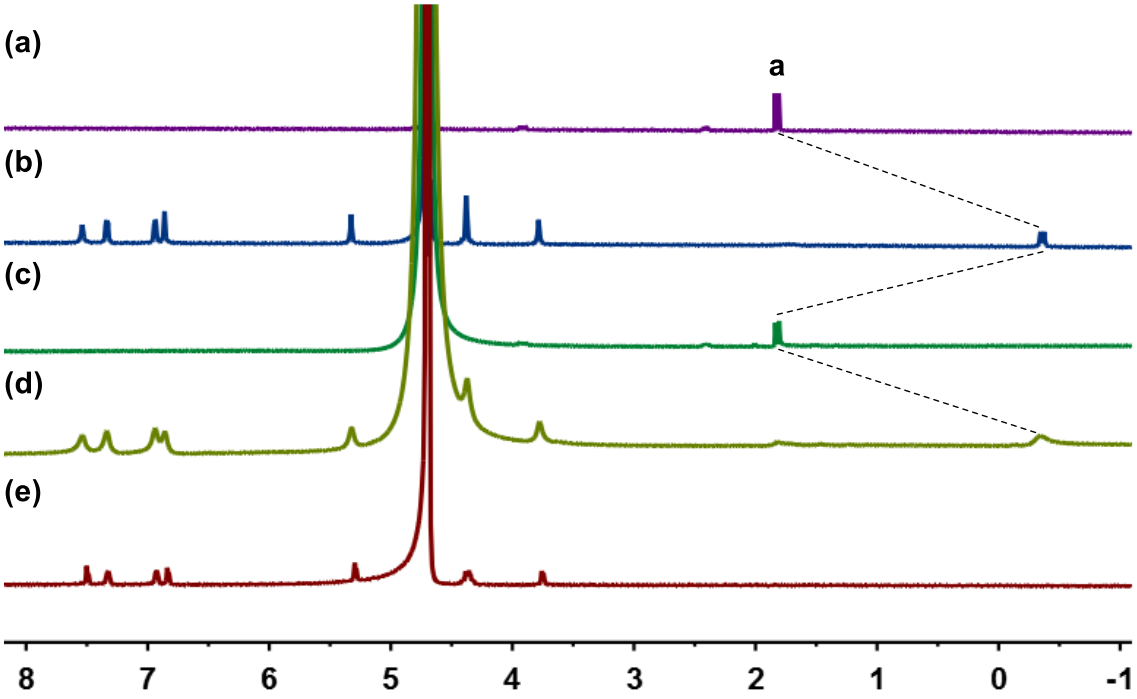


Fig. S18 Partial ^{1}H NMR spectra (500 MHz, 298 K, D_2O) of (a) 0.50 mM free guest **P2**, (b) after addition of 1.0 equiv of **H3** to (a); (c) after addition of 1.0 μL of aqueous DCl solution (35 wt %) to (b); (d) after addition of 1.5 μL of aqueous NaOD solution (30 wt %) to (c); (e) 0.50 mM free host **H3**.

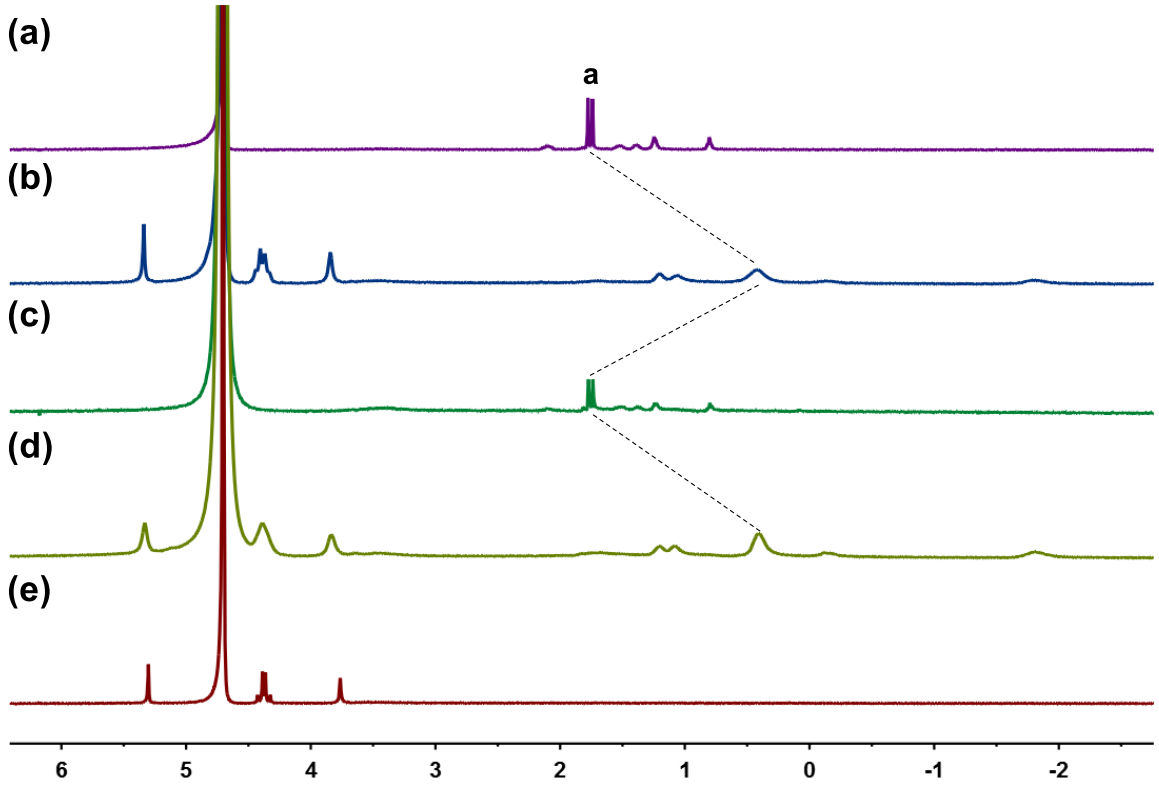


Fig. S19 Partial ^{1}H NMR spectra (500 MHz, 298 K, D_2O) of (a) 0.50 mM free guest **P3**, (b) after addition of 1.0 equiv of **H3** to (a); (c) after addition of 1.0 μL of aqueous DCl solution (35 wt %) to (b); (d) after addition of 1.5 μL of aqueous NaOD solution (30 wt %) to (c); (e) 0.50 mM free host **H3**.