

**Supporting Information for**  
**Small triiminopyrrolic molecular cage with high affinity and selectivity for**  
**fluoride**

Hye Jin Han,<sup>a</sup> Ju Hyun Oh,<sup>a</sup> Jonathan L. Sessler,<sup>\*,b</sup> and Sung Kuk Kim<sup>\*,a</sup>

*<sup>a</sup>Department of Chemistry and Research Institute of Natural Science, Gyeongsang National University, Jinju, 660-701, Korea, and <sup>b</sup>Department of Chemistry, The University of Texas at Austin, 105 E. 24<sup>th</sup>, Street-Stop A5300, Austin, Texas 78712-1224*

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## 1. General experimental and synthetic details

Solvents and reagents used for the synthetic work were purchased from Aldrich, TCI, or Alfa Aesar and used without further purification. Compound **5** was prepared as reported previously.<sup>1</sup> NMR spectra were recorded on a Bruker Advance-300 MHz instrument. The NMR spectra were referenced to residual solvent peaks and the spectroscopic solvents were purchased from either Cambridge Isotope Laboratories or Aldrich. Fast atom bombardment (FAB) mass spectra (MS) were recorded on a JMS-700 (JEOL) spectrometer. UV/Vis spectra were measured on a Mega-800 (SCINCO) spectrometer. TLC analyses were carried out using Sorbent Technologies silica gel (200 mm) sheets. Column chromatography was performed on Sorbent Technologies silica gel 60 (40–63 mm).

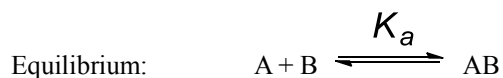
### Compound 6

To 30 ml of DMF chilled to 0 °C was added dropwise POCl<sub>3</sub> (1.40 ml, 14.9 mmol) in an ice bath. After the resulting reaction mixture was stirred for 20 min, the tripodal compound (**5**) (1.00 g, 2.48 mmol) dissolved in DMF (20 mL) was added to the reaction mixture dropwise. The resulting solution was allowed to warm to room temperature and stirred for 2 h. The mixture was quenched with aqueous Na<sub>2</sub>CO<sub>3</sub>, stirred for an additional 1 h, and then placed in the refrigerator overnight. The resulting light-yellow precipitate was collected by filtration and washed with water. Recrystallization of the resulting powder from THF/diethyl ether gave the triformylated compound (**6**) (1.04 g, 86% yield) as an off-white solid: <sup>1</sup>H NMR (300 MHz, 5% DMSO-*d*<sub>6</sub> in CDCl<sub>3</sub>) δ 10.40 (s, 3H, pyrrolic NH), 9.36 (s, 3H, COH), 6.83 (d, 3H, β-pyrrolic CH), 5.73 (d, 3H, β-pyrrolic CH), 4.09 (s, 6H, CH<sub>2</sub>-pyrrole), 2.59-2.51 (m, 12H, CH<sub>2</sub>CH<sub>3</sub>), 1.04 – 0.99 (m, 18H, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>) δ 178.6, 142.4, 140.8, 132.8, 132.4, 108.9, 40.3, 27.7, 23.5, 15.6 ppm. HRMS (ESI) *m/z* 483.2522 [M]<sup>+</sup> calcd for C<sub>30</sub>H<sub>33</sub>N<sub>3</sub>O<sub>3</sub>, found 483.2526.

#### Cage 4

A mixture of compound **6** (600 mg, 1.23 mmol) and 1,3,5-tris(aminomethyl)-2,4,6-triethylbenzene (307 mg, 1.23 mmol) in methanol was stirred overnight at room temperature. The ivory-colored precipitate that resulted was collected by filtration; this afforded cage **4** in quantitative yield. :  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 (s, 3H, imine-*CH*), 6.61 (d,  $J = 3.6$  Hz, 3H,  $\beta$ -pyrrolic *CH*), 6.11 (d,  $J = 3.6$  Hz, 3H,  $\beta$ -pyrrolic *CH*), 4.70 (s, 6H,  $\text{CHNCH}_2$ ), 4.06 (s, 6H,  $\text{CH}_2$ -pyrrole), 2.47 (q,  $J = 7.5$  Hz, 12H,  $\text{CH}_2\text{CH}_3$ ), 1.12 (dt,  $J = 15.6, 7.5$  Hz, 18H,  $\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  152.2, 143.0, 142.5, 135.9, 133.5, 131.9, 128.5, 114.3, 107.8, 77.5, 77.1, 76.7, 54.9, 49.6, 27.9, 23.6, 22.8, 16.3, 14.7; HR FAB-MS  $m/z$  679.4488  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{45}\text{H}_{55}\text{N}_6$ , found 679.4496.

**Determination of binding constants by  $^1\text{H}$  NMR spectroscopy under conditions of slow equilibrium on the  $^1\text{H}$  NMR time scale.**

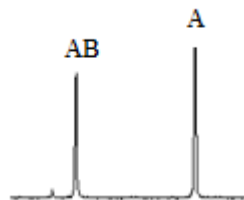


$$\text{Equilibrium constant: } K_a = \frac{[\text{AB}]}{[\text{A}][\text{B}]} = \frac{[\text{AB}]}{(c(\text{A}) - [\text{AB}])(c(\text{B}) - [\text{AB}])} \quad (1)$$

$c(\text{A})$  and  $c(\text{B})$  are the initial concentrations of A and B, and  $[\text{A}]$ ,  $[\text{B}]$  and  $[\text{AB}]$  are the equilibrium concentrations of the three species.

A and B is in slow exchange with the complex AB on the  $^1\text{H}$  NMR time scale.

Two signals for one specific proton on A can be seen in the spectrum, corresponding to complexed and uncomplexed A:



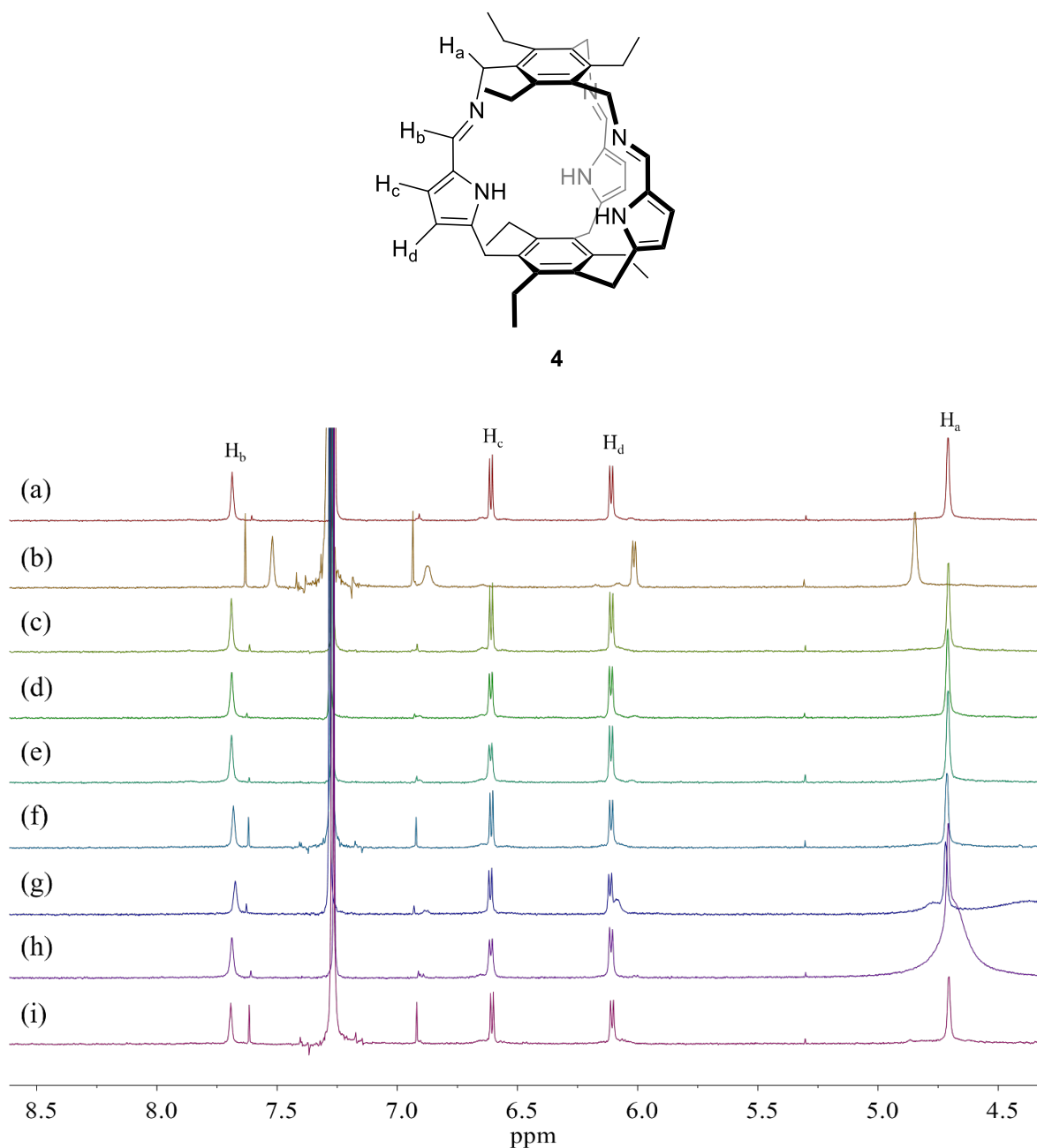
*Single-point Methods*

$K_a$  is determined from the integrals of complexed and uncomplexed A. If  $I(\text{A})$  denotes the integral of a signal for one specific proton of A and  $I(\text{AB})$  the integral for the same proton in the complex, the concentration of AB at equilibrium is Substituting in eq. (1) yields

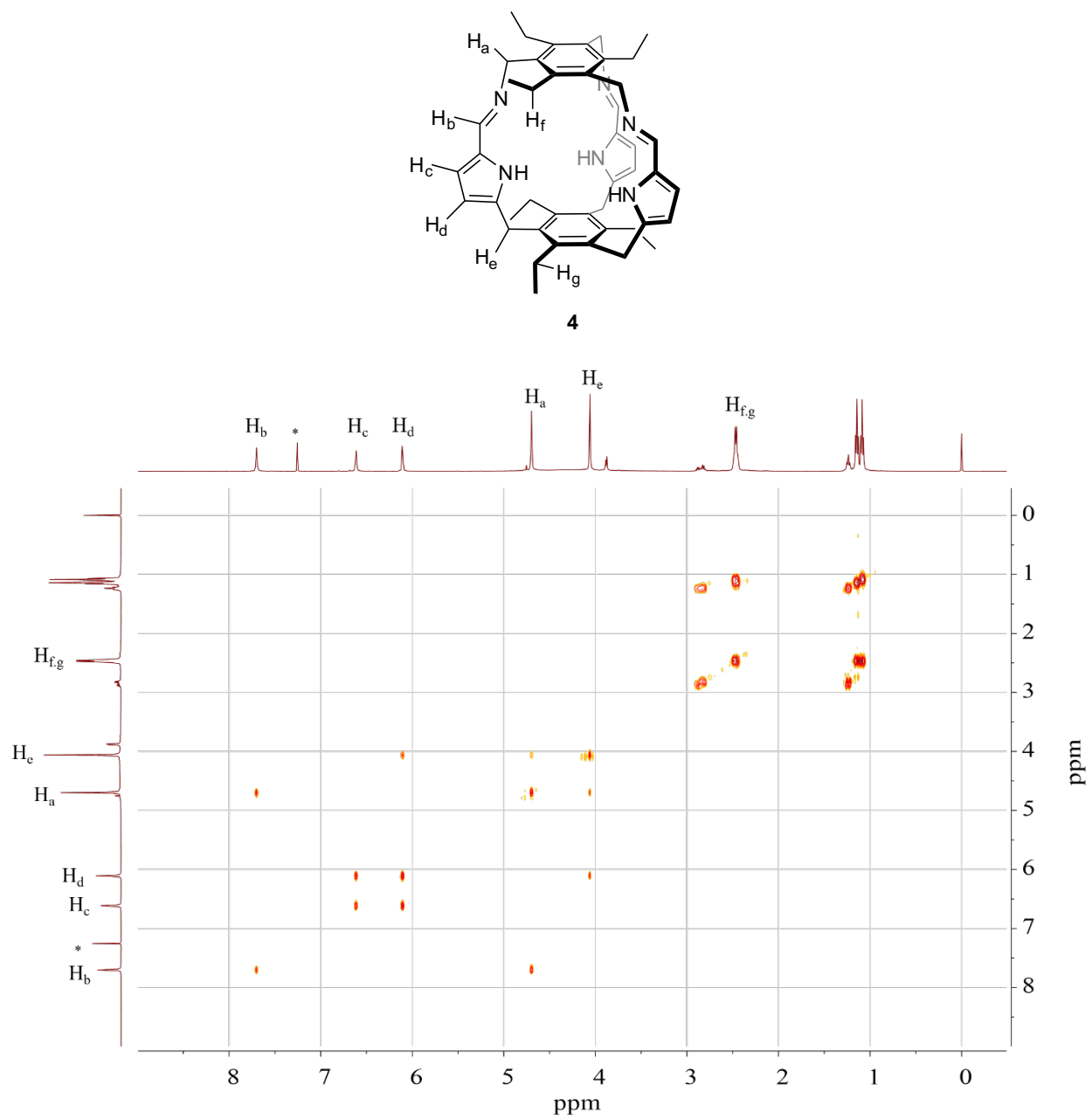
$$[\text{AB}] = \frac{I(\text{AB})}{I(\text{A}) + I(\text{AB})} c(\text{A}) \quad (2)$$

$$K_a = \frac{I(\text{AB})}{I(\text{A}) \left( c(\text{B}) - \frac{I(\text{AB})}{I(\text{A}) + I(\text{AB})} c(\text{A}) \right)} \quad (3)$$

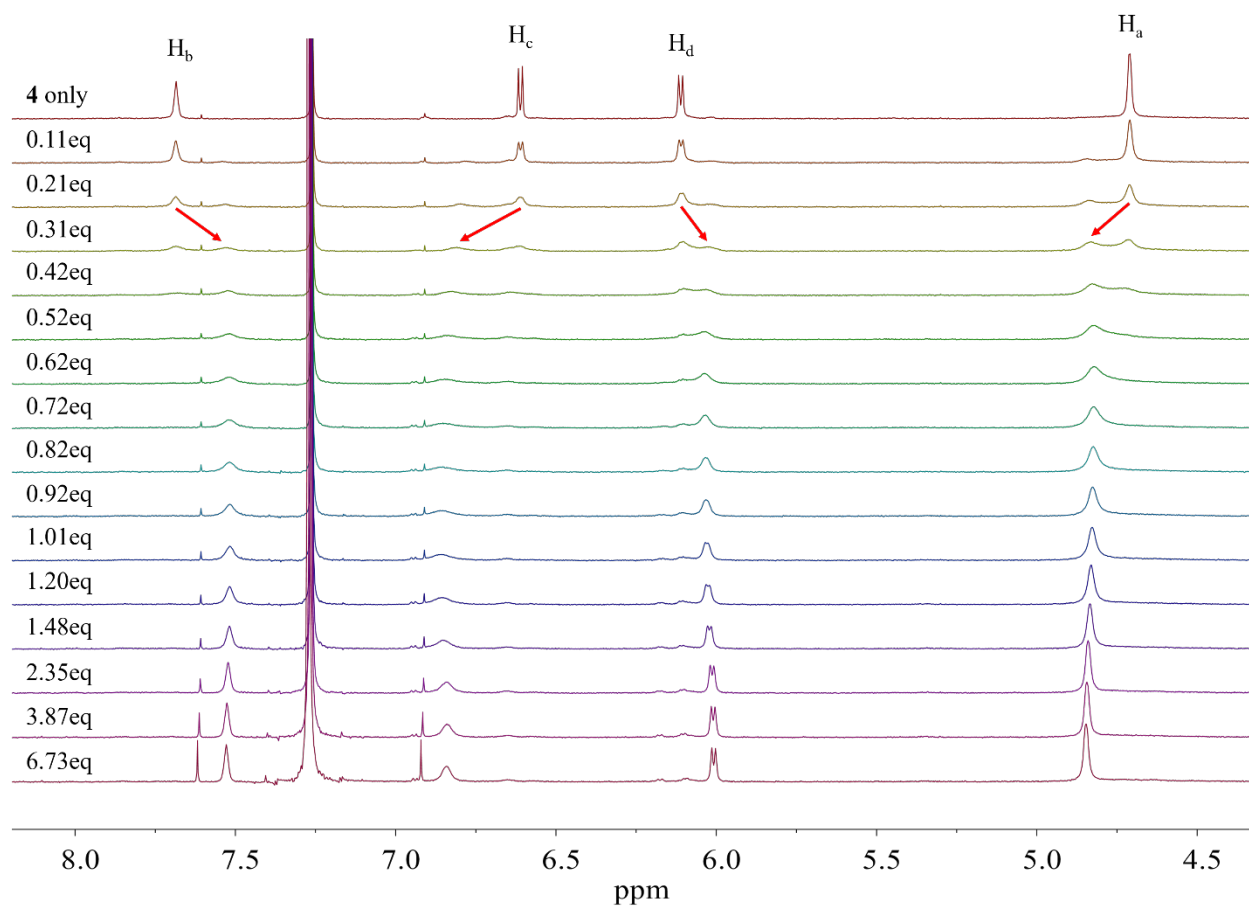
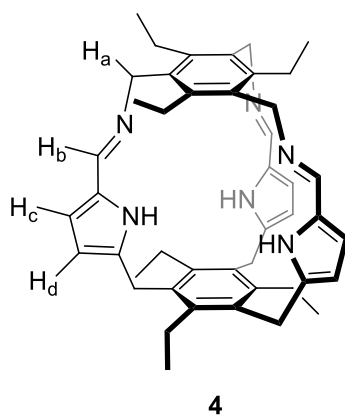
## 2. $^1\text{H}$ NMR spectral data



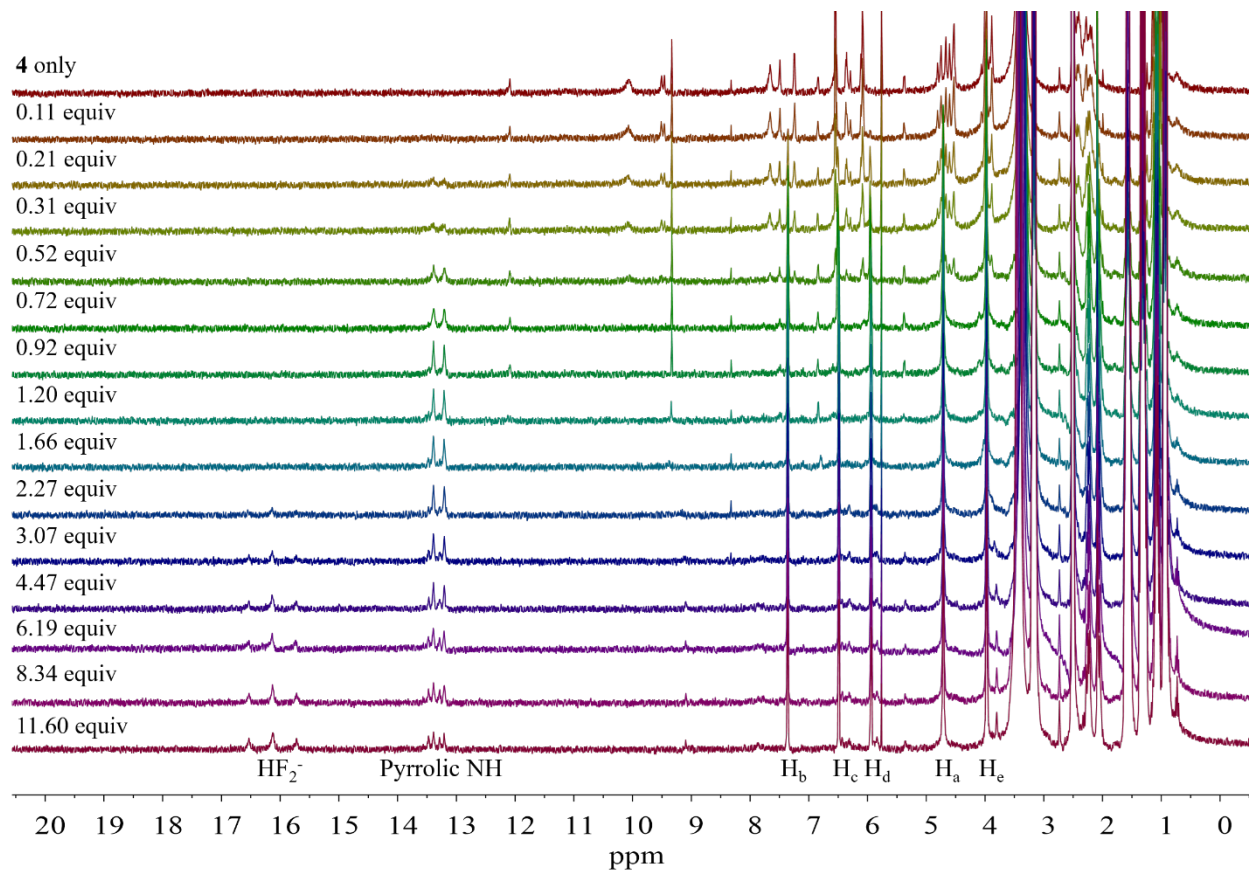
**Figure S1.** Partial  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ) of (a) **4** (3 mM) only, (b) **4** + excess TBAF (tetrabutylammonium fluoride), (c) **4** + excess TBACl (tetrabutylammonium chloride), (d) **4** + excess TBABr (tetrabutylammonium bromide), (e) **4** + excess TBAI (tetrabutylammonium iodide), (f) **4** + excess TEAHCO<sub>3</sub> (tetraethylammonium bicarbonate), (g) **4** + excess TBA<sub>2</sub>SO<sub>4</sub> (tetrabutylammonium sulfate), (h) **4** + excess TBAH<sub>2</sub>PO<sub>4</sub> (tetrabutylammonium dihydrogenphosphate), and (i) **4** + excess (TBA)<sub>3</sub>HP<sub>2</sub>O<sub>7</sub> (tris-tetrabutylammonium hydrogenpyrophosphate).



**Figure S2.** H-H COSY NMR spectrum of cage 4 in CDCl<sub>3</sub>.

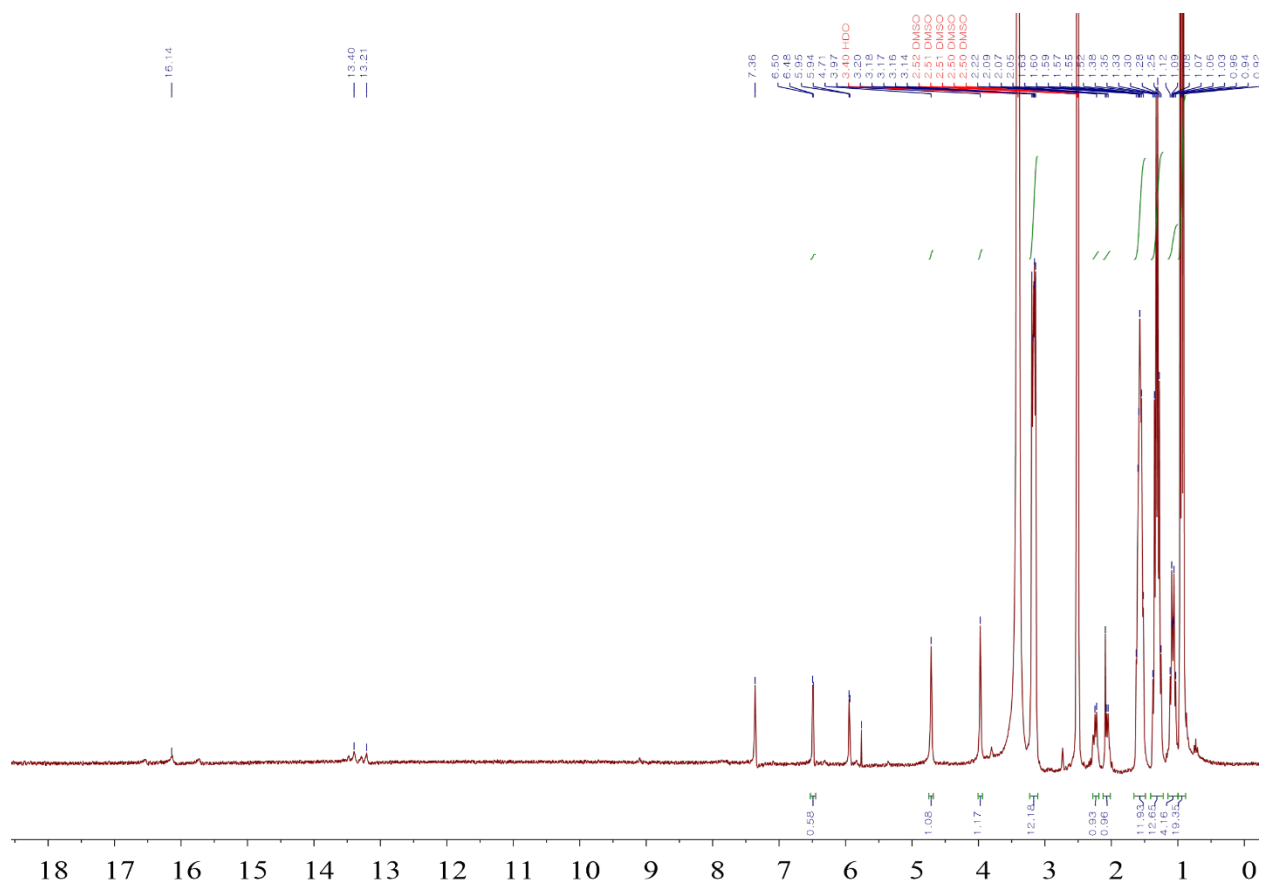


**Figure S3.**  $^1\text{H}$  NMR spectra recorded during the titration of **4** (3 mM) with tetrabutylammonium fluoride (TBAF) in  $\text{CDCl}_3$ .

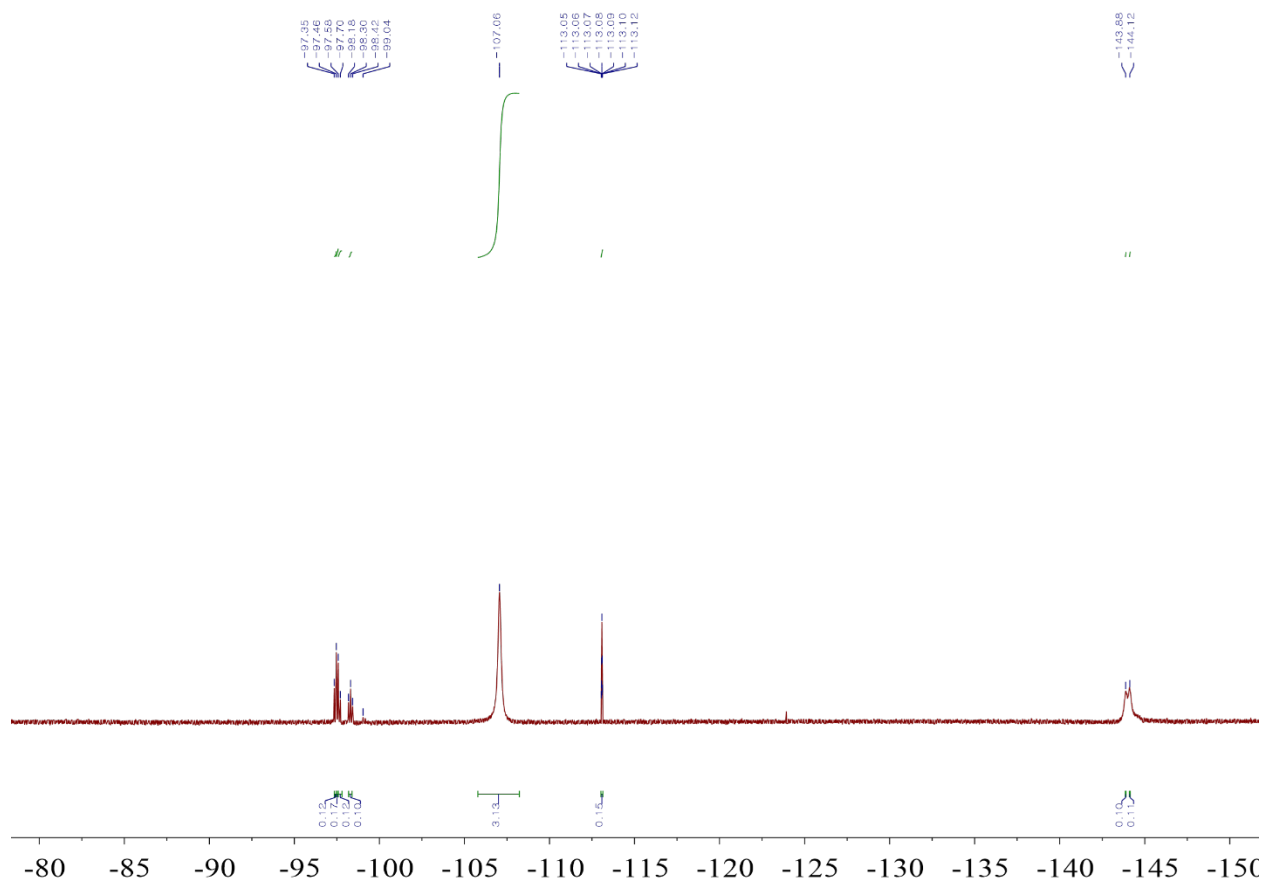


**Figure S4.** <sup>1</sup>H NMR spectra recorded during the titration of cage **4** (3 mM) with TBAF in DMSO-*d*<sub>6</sub>.

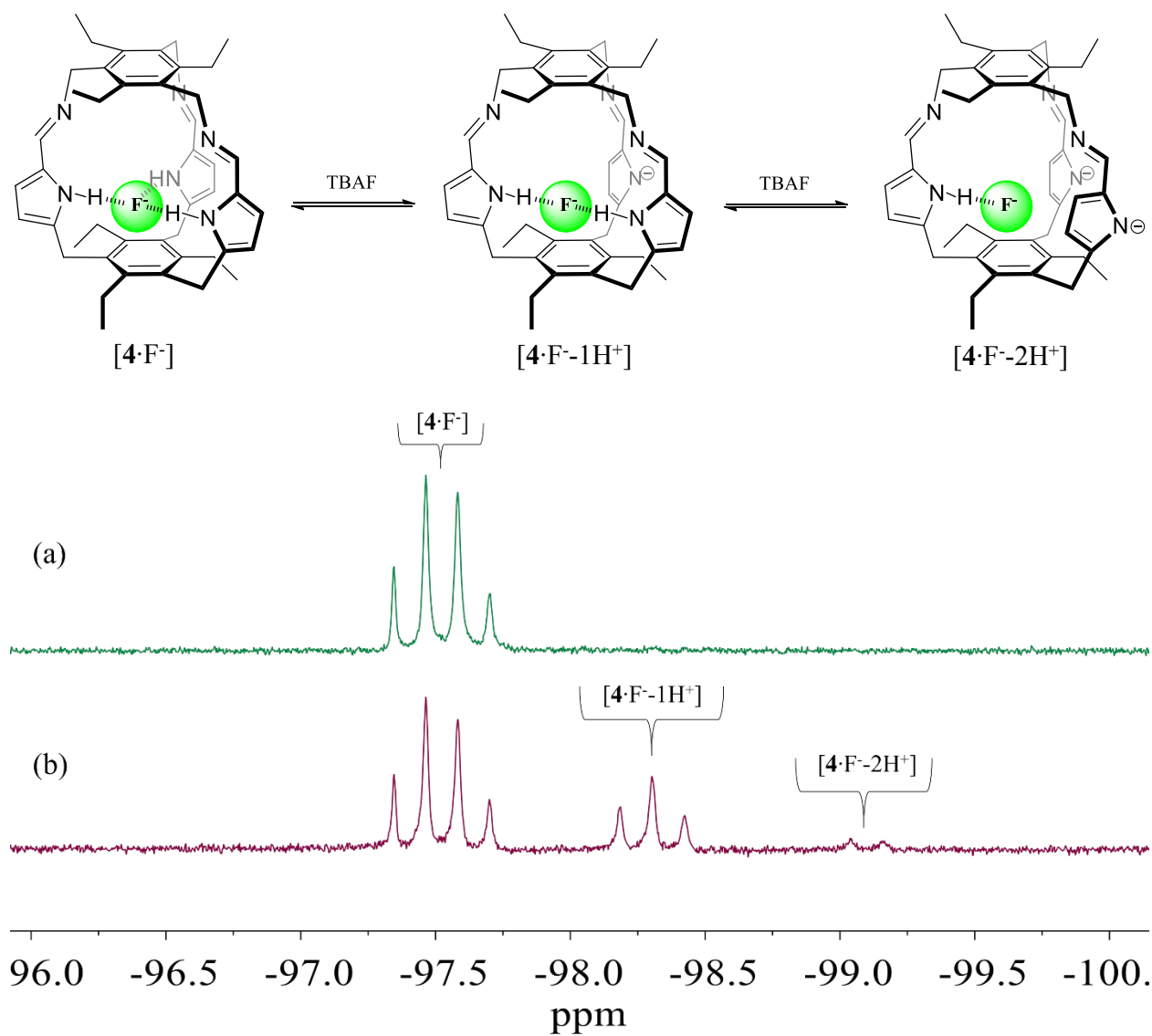




**Figure S5.**  $^1\text{H}$  NMR spectrum of cage **4** (27 mM) with 6.0 equiv. of TBAF in  $\text{DMSO-}d_6$ .



**Figure S6.**  $^{19}\text{F}$  NMR spectrum of cage **4** (27 mM) with 6.0 equiv. of TBAF in  $\text{DMSO-}d_6$ . The NMR spectrum were recorded after the samples were allowed to stand overnight at room temperature. Fluorobenzene was used as an internal reference standard.



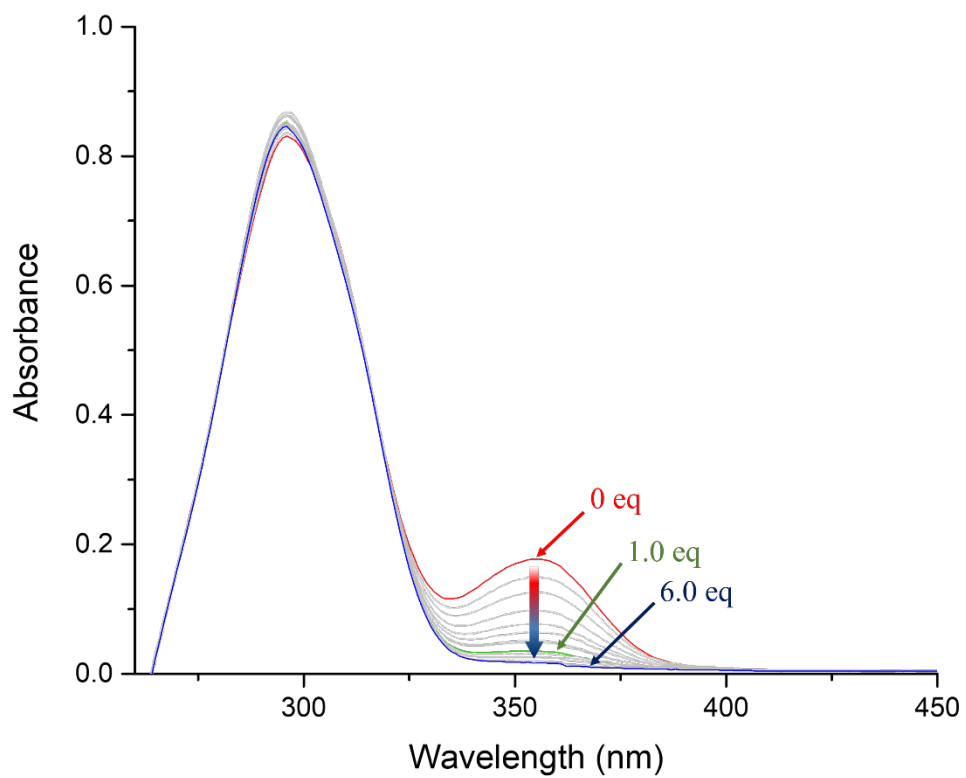
**Figure S7.** <sup>19</sup>F NMR spectra of cage **4** (27 mM) recorded in the presence of 6.0 equiv. of TBAF in DMSO-*d*<sub>6</sub> (a) right after adding TBAF to the solution of cage **4** and (b) after allowing the mixture to stand overnight at room temperature.

### **3. UV/Vis spectroscopic titrations**

Stock solutions of all the compounds studied were made up in DMSO with the final concentrations being between  $1.25 \times 10^{-5}$  M. ACS grade solvents were purchased and used without purification. The stock solutions were appropriately diluted with solvents to obtain concentrations suitable for study.

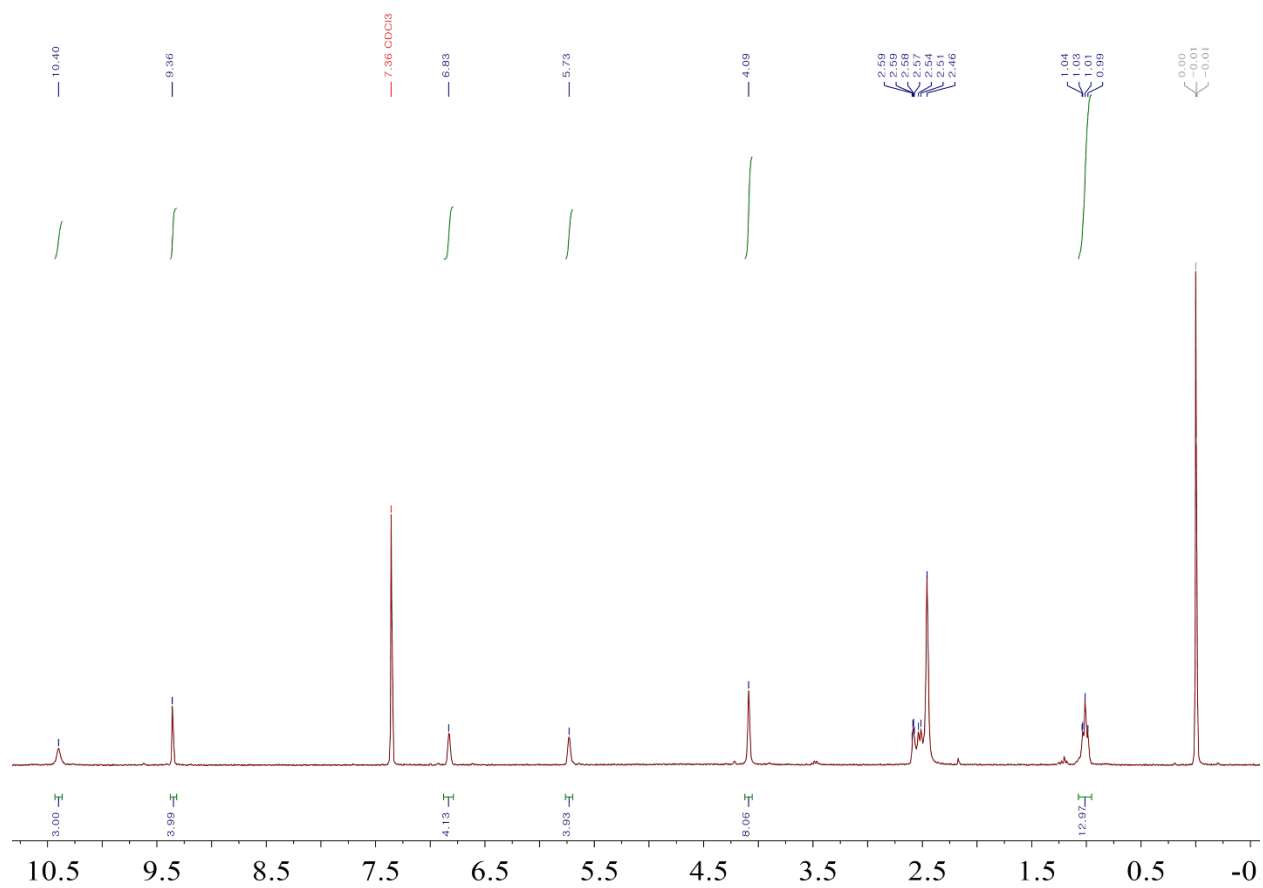
#### **Binding constants determined by UV-vis titrations**

Upon addition of incremental amounts of anions to a DMSO solution of receptor **4**, changes in the absorbance features of **4** ( $1.67 \times 10^{-5}$  M of **4** was used, unless otherwise stated) were seen. Equilibrium constants corresponding to the complex formation were calculated using BindFit v5.0 downloaded from “<http://app.supramolecular.org/bindfit/>”.

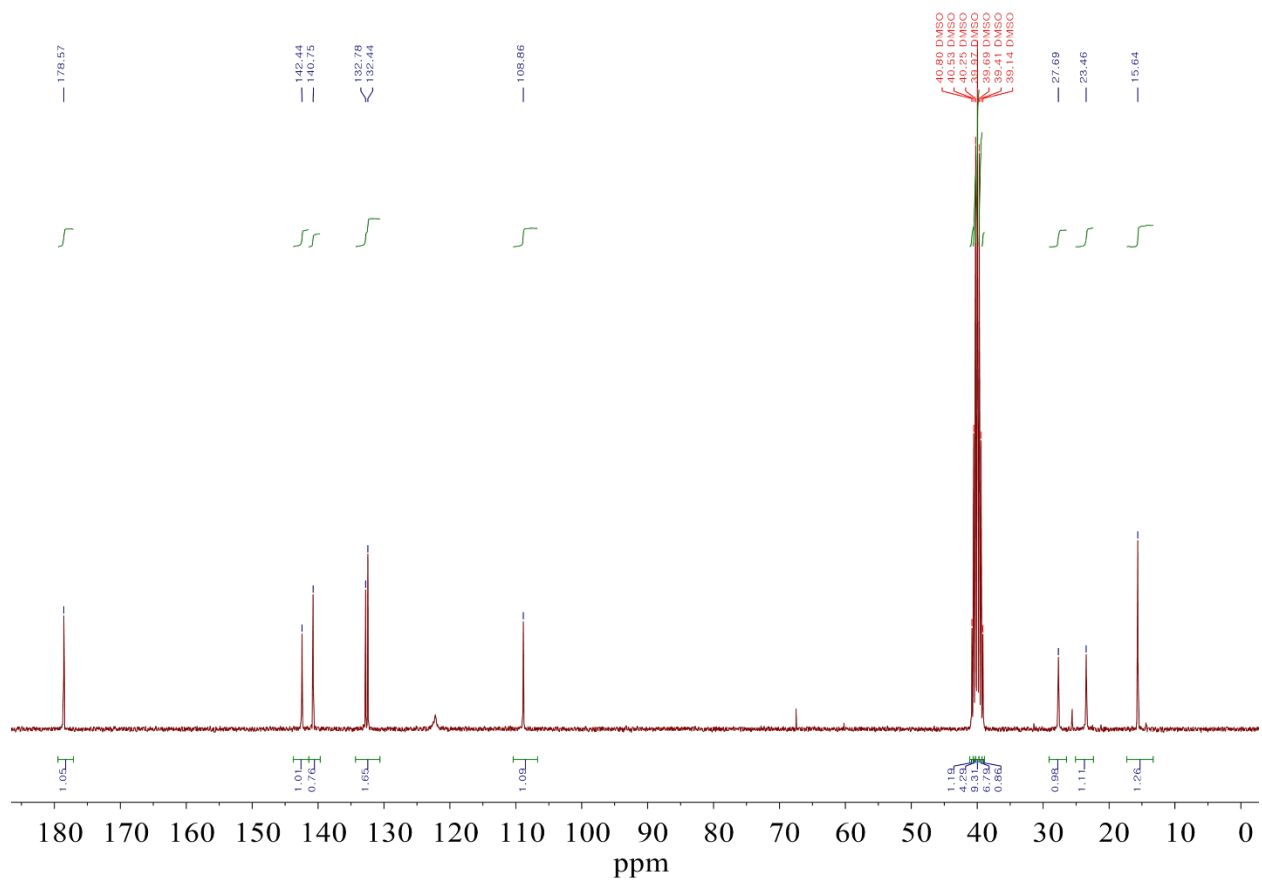


**Figure S8.** UV-vis spectra of cage **4** ( $1.67 \times 10^{-5}$  M) recorded in DMSO in the presence of increasing quantities of TBAF (tetrabutylammonium fluoride,  $0 \sim 6.0 \times 10^{-5}$  M).

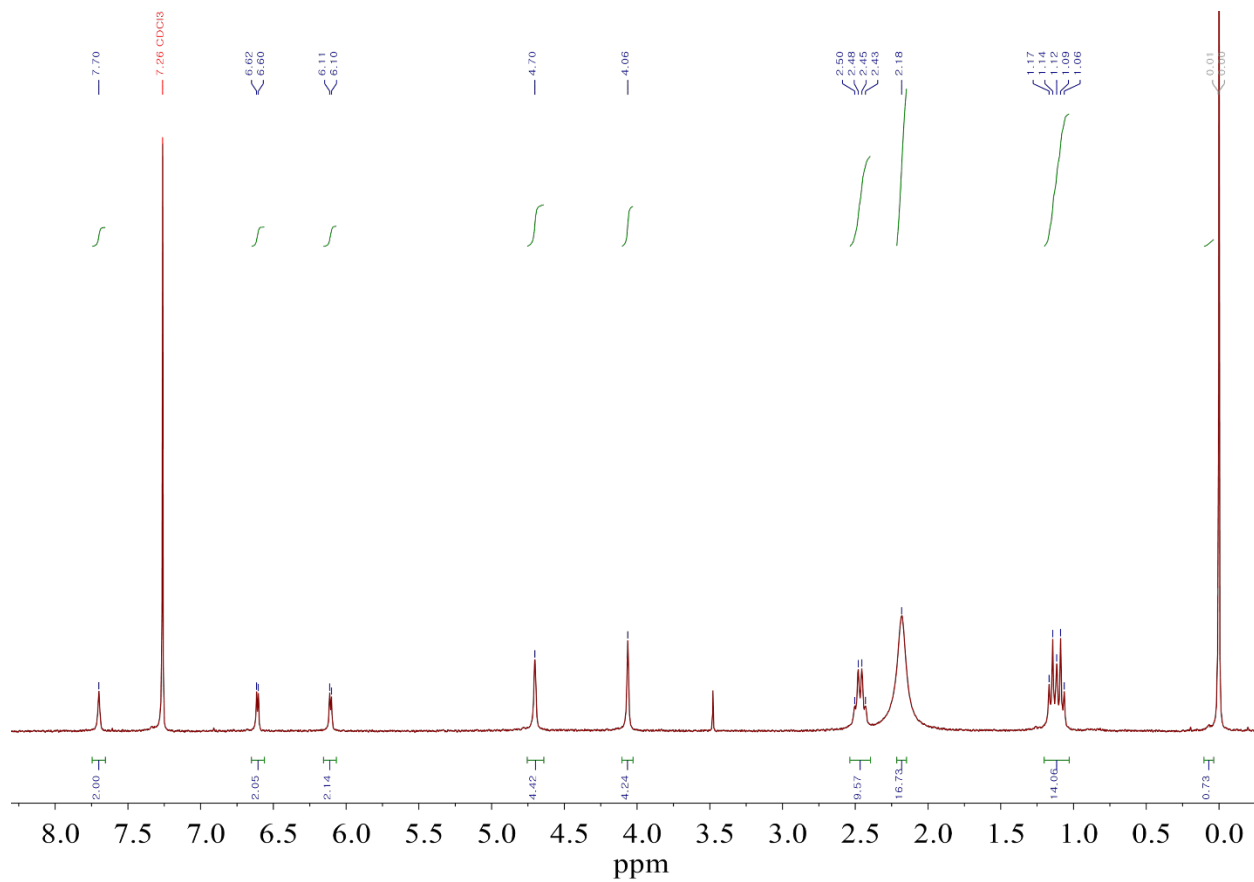
## 4. $^1\text{H}$ and $^{19}\text{F}$ NMR spectra



**Figure S9.**  $^1\text{H}$  NMR spectrum of compound **6** recorded in 5%  $\text{DMSO-}d_6$  in  $\text{CDCl}_3$ .

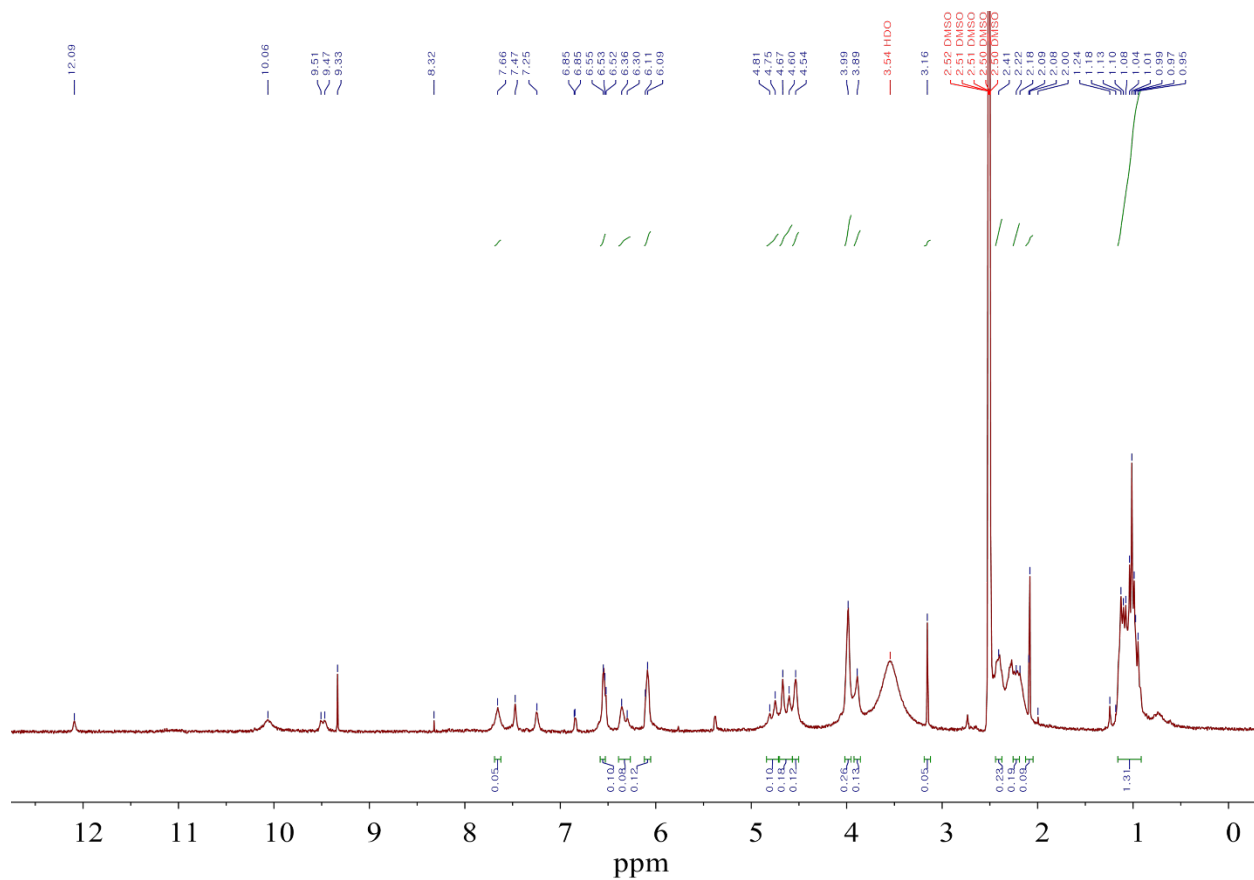


**Figure S10.**  $^{13}\text{C}$  NMR spectrum of compound **6** recorded in  $\text{DMSO-}d_6$ .

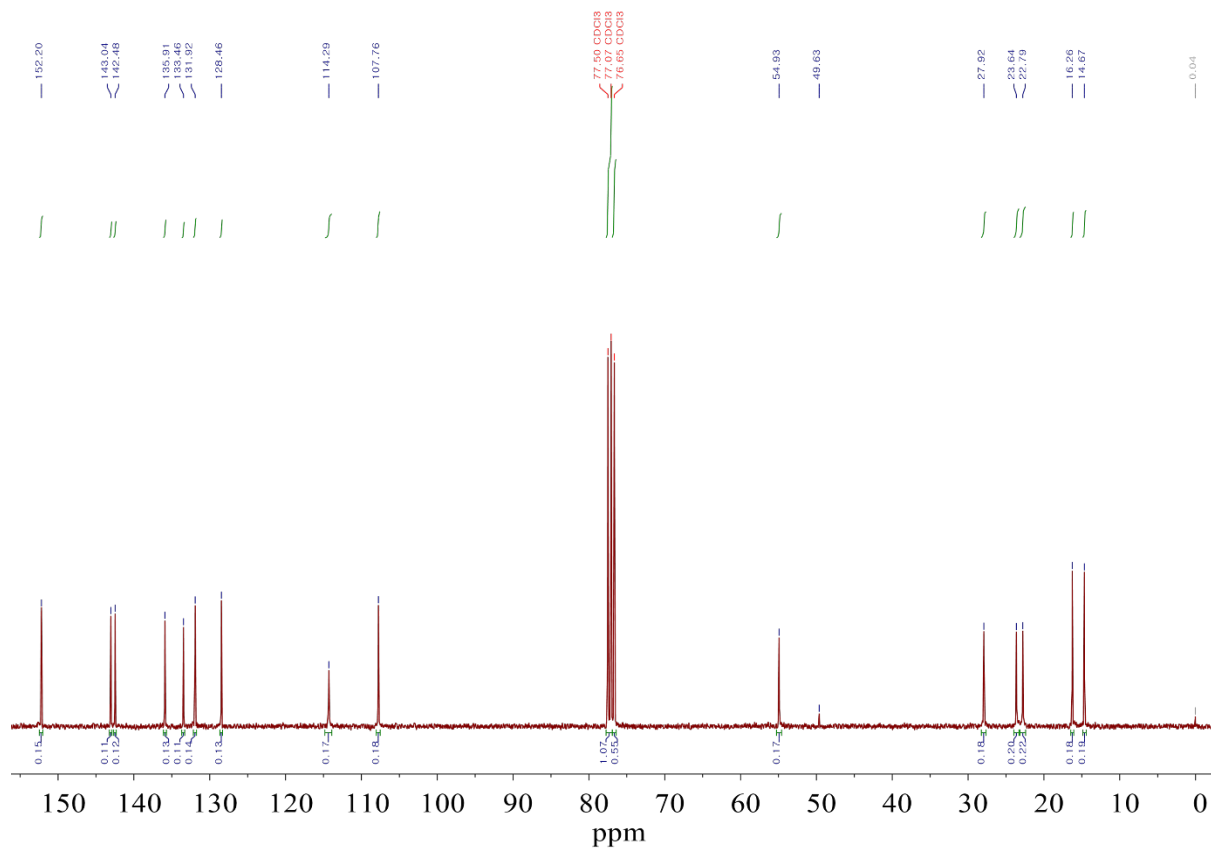


**Figure S11.**  $^1\text{H}$  NMR spectrum of **4** recorded in  $\text{CDCl}_3$ .





**Figure S12.** <sup>1</sup>H NMR spectrum of cage **4** recorded in DMSO-*d*<sub>6</sub>.



**Figure S13.**  $^{13}\text{C}$  NMR spectrum of cage 4 recorded in  $\text{CDCl}_3$ .

## References

1. Cacciarinim, M.; Nativi, C.; Norcini, M.; Staderini, S.; Francesconi, O.; Roelens, S. *Org. Biomol. Chem.* **2011**, *9*, 1085-1091.