

A Self-Assembled Receptor for the Recognition of Phosphate and Acetate Anions in Neutral Aqueous Solution

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Supporting Information

General:

Commercial reagents were purchased from Aldrich, Fluka or Sigma and were used as received unless otherwise specified. The half-sandwich complex **1** was prepared according to literature procedures.^{1,2}

The synthesis of neutral helicate **4** was carried out under an atmosphere of dry dinitrogen using standard Schlenk techniques.

¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker 400 MHz spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) and are calibrated relative to solvent residual peaks.

Synthesis of ligand 2:

Piperazine (0.50 g, 5.75 mmol), 3-hydroxy-2-pyridone (1.61 g 13.8 mmol) and formaldehyde (1.0 mL, 13.8 mmol, 37% in H₂O) were heated for 24h in EtOH (130 mL). A cream-colored precipitate formed which was isolated and dried in vacuum. The crude product was obtained in 85% purity and 90% yield (1.72 g, 5.17 mmol). The product was purified by reversed phase HPLC (H₂O/CH₃CN + 0.1% TFA; gradient: 98:2 to 96:4).

¹H-NMR (400 MHz, 0.1 DCI in D₂O): δ = 3.76 (s, br, 8H, NCH₂, piperazine), 4.47 (s, 4H, NCH₂), 6.47 (d, ³*J* = 7 Hz, 2H, pyridone), 7.13 (d, ³*J* = 7 Hz, 2H, pyridone). ¹³C-NMR (101 MHz, 0.1 DCI in D₂O): δ = 49.0 (NCH₂, piperazine), 54.3 (NCH₂), 110.6, 119.3, 125.4, 147.6, 159.2 (pyridone). Anal Calcd for C₂₀H₂₂F₆N₄O₈: C, 42.8 ; H, 3.9 ; N, 10.0. Found: C, 42.5 ; H, 3.6 ; N, 9.5.

Synthesis of complex 4:

A mixture of the half-sandwich complex **1** (15 mg, 30 μ mol) and the TFA salt of ligand **2** (16.8 mg, 30 μ mol) was stirred in water (10 mL) until a clear solution was obtained. The solution was carefully layered with NEt₃. Orange crystals were obtained in 52% yield (14.5 mg, 5.21 μ mol). Vapour diffusion of NEt₃ gave similar yields (16.0 mg, 58%).

¹H-NMR (400 MHz, CDCl₃): δ = 1.47 (m, br, 6H, NCH₂), 1.88 (m, br, 6H, NCH₂), 2.47 (m, br, 6H, NCH₂), 2.69 (m, br, 6H, NCH₂), 3.24 (d, ²*J* = 17 Hz, 6H, NCH₂), 3.40 (d, ²*J* = 17 Hz, 6H, NCH₂), 5.52 (s, 36H, C₆H₆), 5.77 (d, ³*J* = 6 Hz, 6H, pyridone), 6.65 (d, ³*J* = 6 Hz, 6H, pyridone). ¹³C-NMR (101 MHz, in CDCl₃): δ = 46.4 (NCH₂, piperazine), 56.3 (NCH₂), 81.7 (C₆H₆), 107.9, 127.0, 132.0, 153.2, 169.7 (pyridone).

Attempts to obtain satisfactory elemental analysis data of complex **4** were not successful. This is likely due to the fact that crystals of complex **4** contain a huge amount of water (39.5 molecules of H₂O !), which are partially lost upon drying and handling of the crystals.

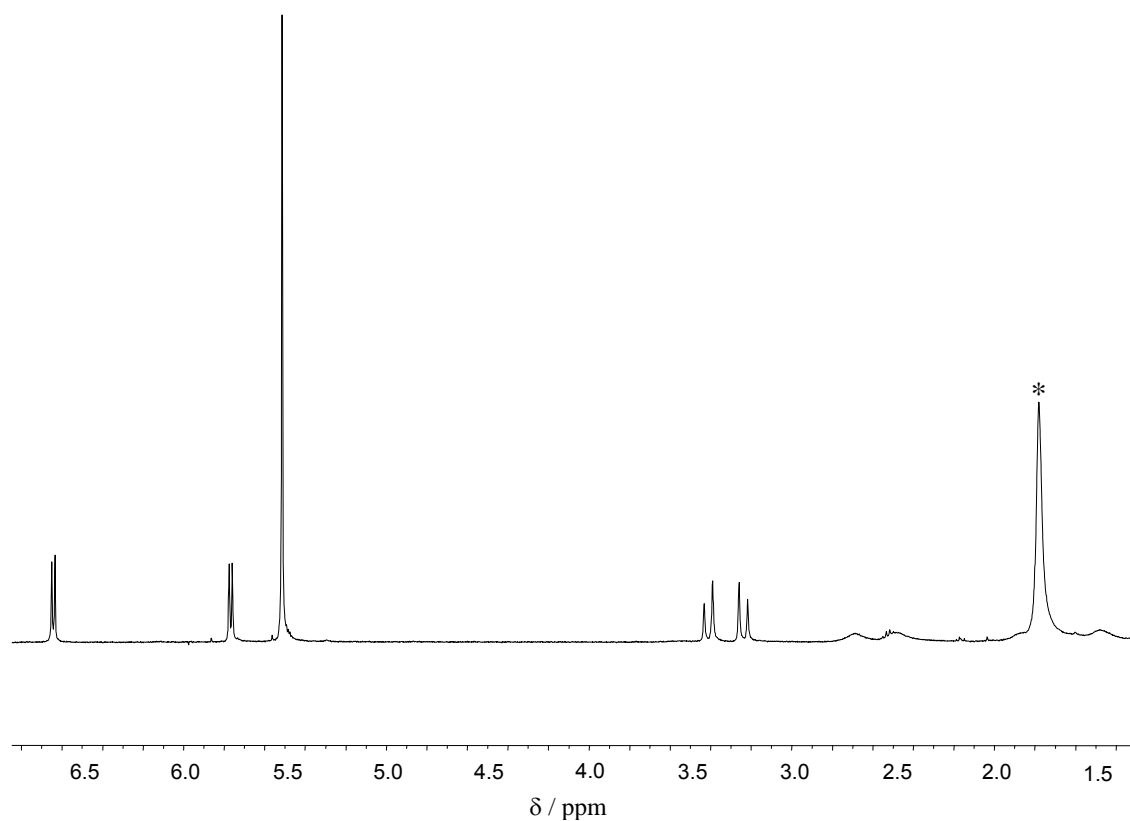


Figure S1. ¹H-NMR spectrum (CDCl₃) of complex **4**. The water peak is noted by an asterisk (*).

¹H-NMR spectroscopy for the self-assembly of complex **3:**

The self-assembly of the receptor **3** in D₂O was achieved in an NMR tube by successive additions of aliquots of LiOH in the same solvent and monitored by ¹H-NMR. Figure S2 represents the ¹H-NMR spectra of the initial mixture of the Ru complex **1** and the bis(dihydropyridine) ligand **2** (bottom); and, after addition of 5 equivalents of LiOH to the latter, of the self-assembled complex **3** (up).

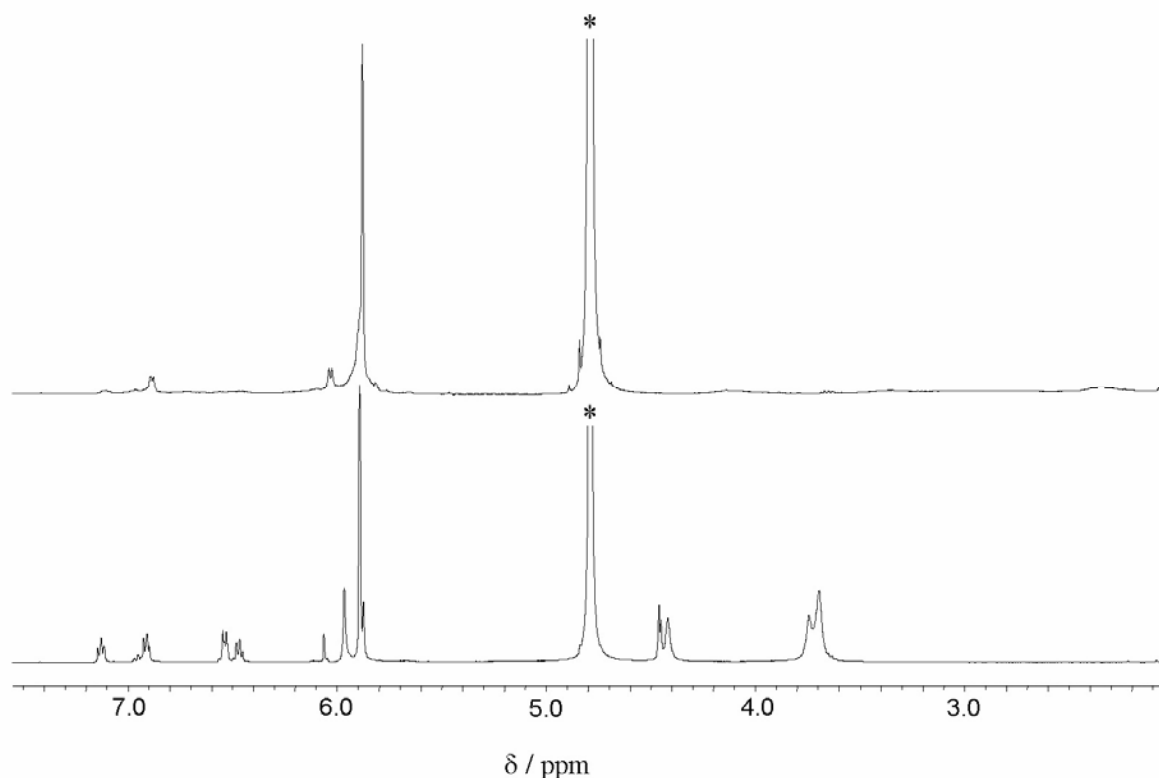


Figure S2. $^1\text{H-NMR}$ spectra recorded in D_2O for the self-assembly of receptor **3** by addition of LiOH . The water peak is noted by an asterisk (*).

Binding studies:

Solutions of substrates were made up from potassium salts of each anion in D_2O and added as aliquots to an NMR tube containing the receptor **3** in the same solvent. The sample tube was shaken carefully after each addition and $^1\text{H-NMR}$ spectra were recorded at 298 K. Parts of the spectra recorded after additions of phosphate to **3** are shown in Figure S2, and those for the additions of acetate to **3** are shown in Figure S6.

The linewidth of the peaks were analysed according to a 1:1 binding model, using the non-linear least squares curve-fitting program WinEQNMR.³ The program yields binding constants K_a and limiting linewidths as output. Another non-linear least squares curve-fitting program designed within Excel using the 1:1 binding model equation led to the same values and the resulting binding curves (experimental vs. calculated) data are shown in Figure S4 and S7.

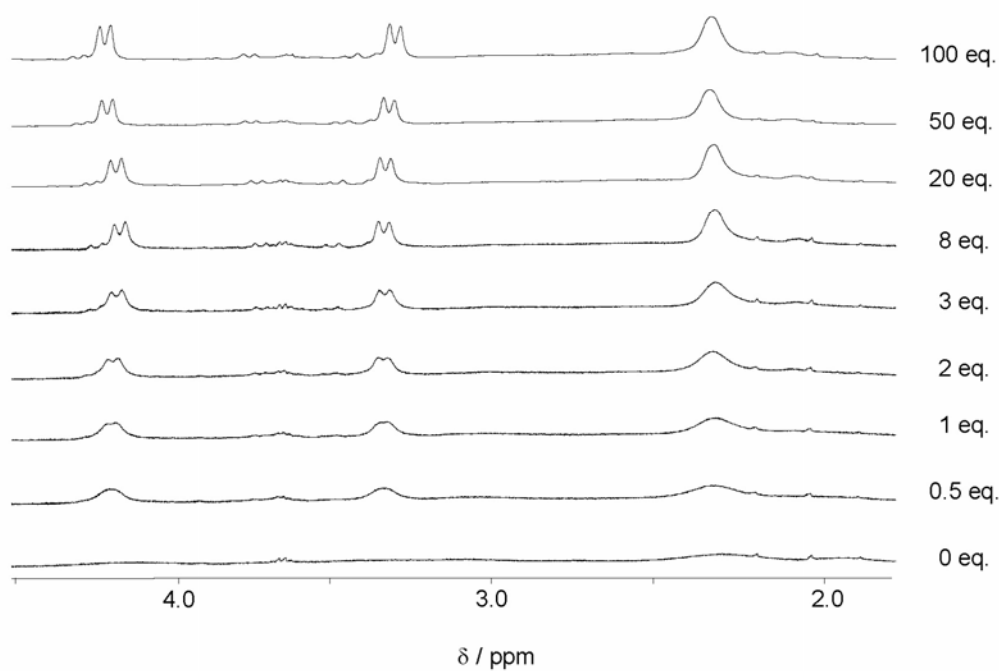


Figure S3. Part of the ^1H NMR spectra recorded for the binding study of receptor **3** vs potassium phosphate in D_2O . $[\mathbf{3}]_{\text{initial}} = 2.7 \text{ mM}$.

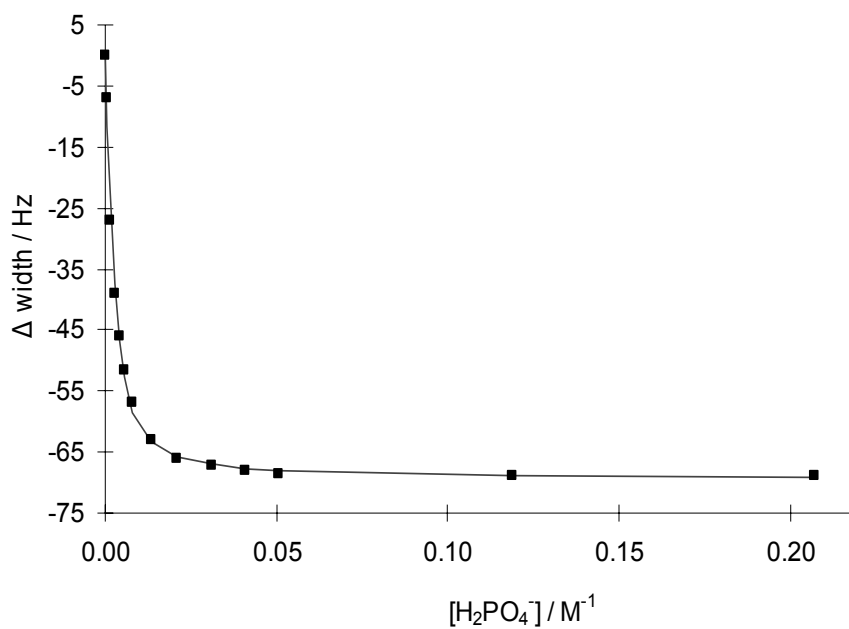


Figure S4. Analysis of data from Figure S3 (signal at 2.3 ppm) according to a 1:1 binding model. $K_a = 950 (\pm 150) \text{ M}^{-1}$.

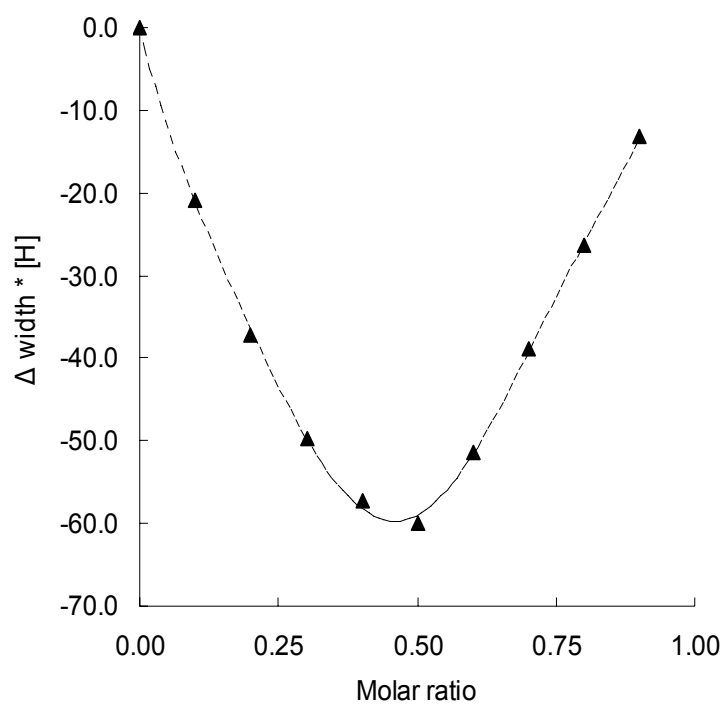


Figure S5. Job's plot for the recognition of phosphate by receptor **3** in D₂O.

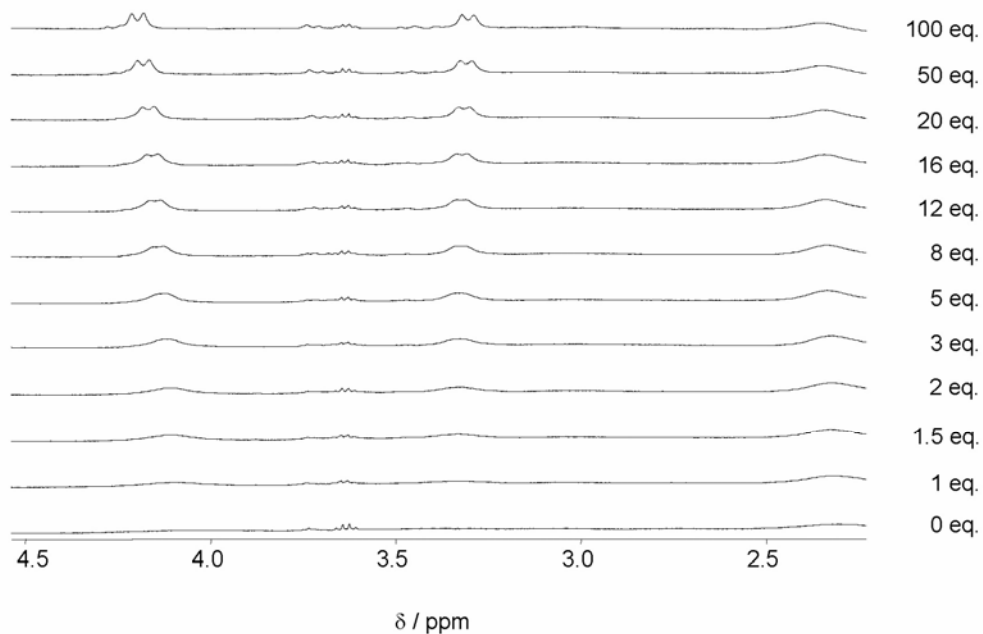


Figure S6. Part of the ¹H NMR spectra recorded for the binding study of receptor **3** vs potassium acetate in D₂O. [**3**]_{initial} = 2.7 mM.

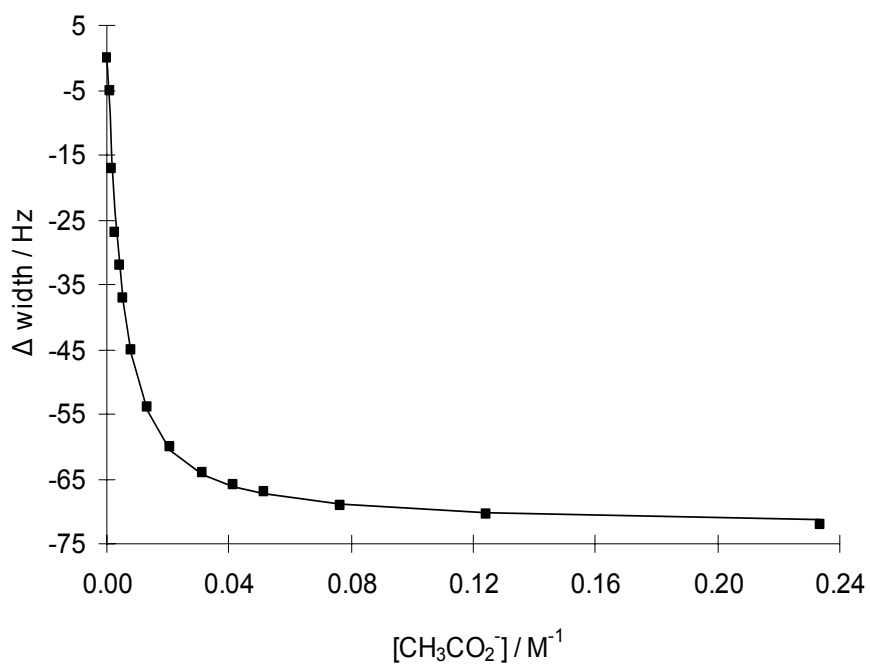


Figure S7. Analysis of the data from Figure S6 (signal at 2.3 ppm) according to a 1:1 binding model. $K_a = 270 (\pm 20) \text{ M}^{-1}$.

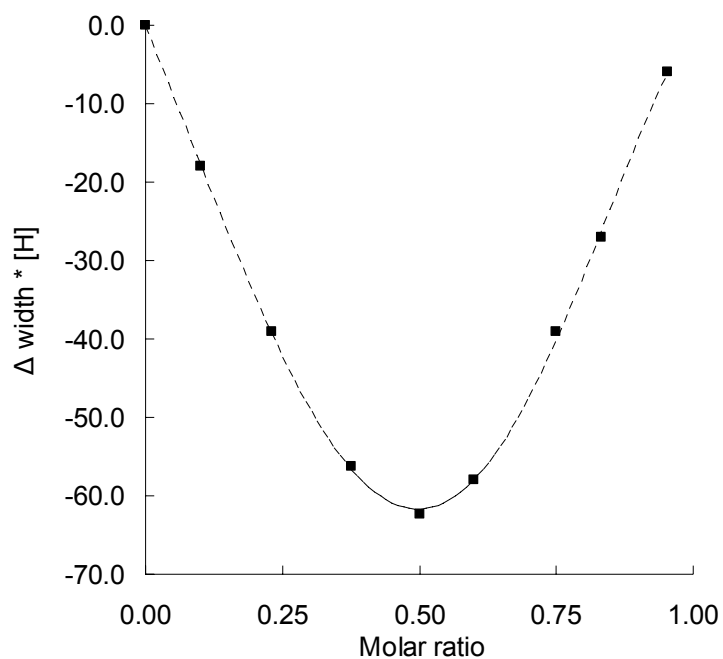


Figure S8. Job's plot for the recognition of acetate by receptor **3** in D_2O .

Calorimetric measurements:

The titration experiments were carried out using a Microcal VP-ITC microcalorimeter with a cell volume of 1.3922 mL. The formation of the Host-Guest assemblies has been studied by adding 5 μL aliquots of a solution of the appropriate anion to a solution of the receptor **3** in the calorimetric cell at 303 K, and monitoring the heat change after each addition. Additions of the anions solutions into neat solvent were also performed and the heat changes measured were subtracted from the corresponding titrations.

Following data collection, the Microcal Origin software was used to apply a 1:1 binding algorithm to the data, the fit of which yielded a binding affinity, enthalpy change and entropy change for each titration.

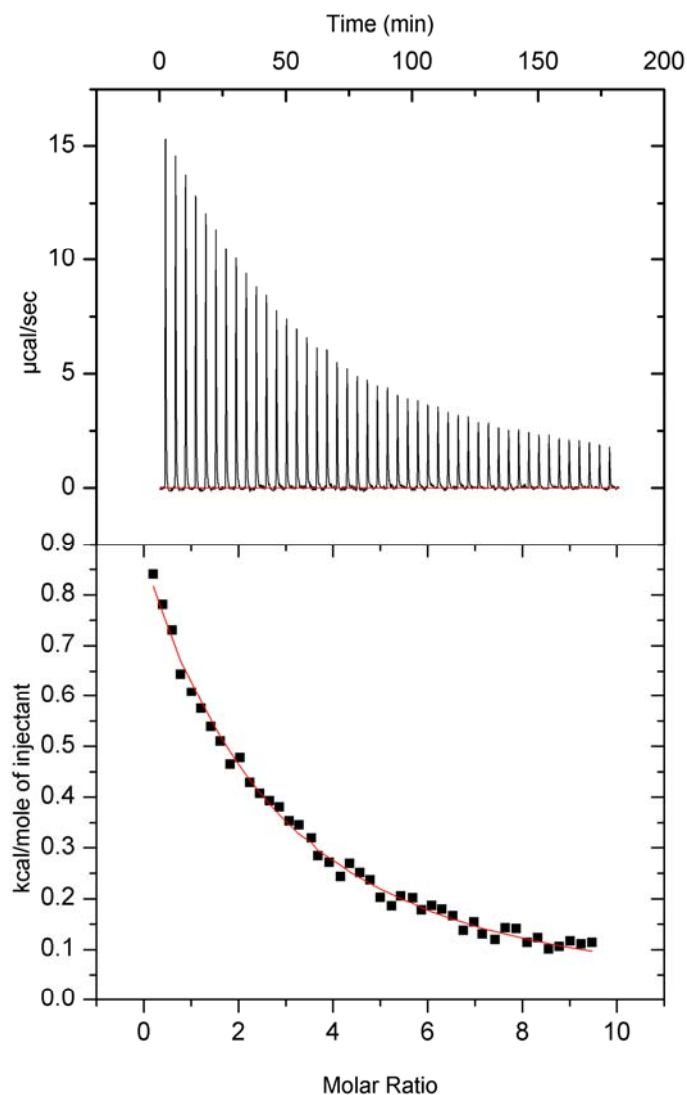


Figure S9. Calorimetric titration of receptor **3** (1.8 mM) with potassium phosphate (100 mM) in D_2O . $K_a = 130 (\pm 3) \text{ M}^{-1}$, $\Delta H^\circ = +4.4 (\pm 0.1) \text{ kcal/mol}$ and $T\Delta S^\circ = +7.3 \text{ kcal/mol}$.

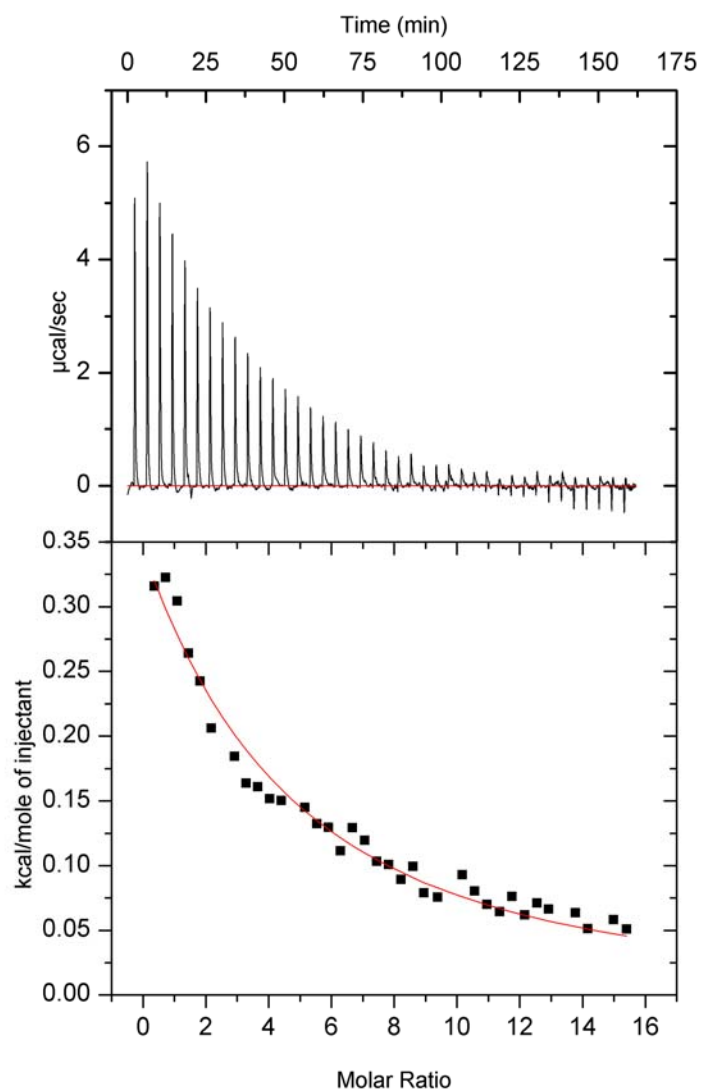


Figure S10. Calorimetric titration of receptor **3** (2.5 mM) with potassium acetate (250 mM) in D₂O. $K_a = 45 (\pm 2) M^{-1}$, $\Delta H^\circ = +3.2 (\pm 0.1) \text{ kcal/mol}$ and $T\Delta S^\circ = +5.5 \text{ kcal/mol}$

References:

- 1 M. A. Bennett and A. K. Smith, *J. Chem. Soc. Dalton Trans.*, 1974, 233.
- 2 R. M ; Bellabarba, M. Nieuwenhuyzen and G. C. Saunders, *Inorg. Chim. Acta*, 2001, **323**, 78.
- 3 M. J. Hynes, *J. Chem. Soc. Dalton Trans.*, 1993, 311.