Supplementary Information for

Selective perrhenate recognition in pure water by halogen bonding and hydrogen bonding alpha-cyclodextrin based receptors

Stuart P. Cornes, Mark R. Sambrook and Paul D. Beer*

S1. Synthesis and Characterisation

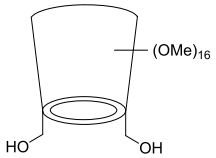
S1.1 General Remarks

All commercial solvents and reagents were used as purchased, unless otherwise stated. Anhydrous solvents were degassed with N_2 and dried by passing them through an MBraun-800 column. Water was distilled and microfiltered using a Milli-Q Millipore machine. Triethylamine was distilled and stored over KOH pellets. $Cu(MeCN)_4 \cdot PF_6$ were stored in a desiccator with P_2O_5. Chromatography was undertaken using silica gel (particle size: 40-63 μm) or preparative TLC plates (20 x 20 cm, 1 cm silica thickness). Amberlite® anion exchange columns were prepared/loaded by washing the resin with H_2O, 1M $NaOH_{(aq.)}$, H_2O, 10% wt. $NH_4NO_{3(aq.)}$, H_2O and finally the solvent system used in the exchange. TBTA was prepared following a literarture procedure.[1]

NMR spectra were recorded using Bruker AVIII400, Bruker AVII 500 (with cryoprobe), and Bruker AVIII500 spectrometers at 298 K. Mass spectra were recorded on a Waters LCT Premier instrument (low resolution) or a Bruker μTOF instrument (high resolution). Theoretical mass spectra were obtained using the Thermo Xcalibur Qual Browser software package. Isothermal titration calorimetry experiments were performed on a Microcal PEAQ-ITC automated system and an iTC MicroCalorimeter.

S 1.2 Synthetic procedures

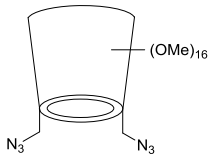
$6^{A,D}$-dihydroxy-permethylated-α-cyclodextrin 2[2,3]



To a solution of diol **1** (1.23 g, 0.51 mmol) in CH_2Cl_2 (7 mL) was added camphorsulfonic acid (2.3 mg, 0.012 mmol) and dihydropyran (129 mg, 1.53 mmol). The mixture was stirred at room temperature for 4 h, after which triethylamine (0.73 mL) and CH_2Cl_2 (40 mL) were added and the mixture was washed with H_2O (3 x 20 mL). The organics were dried over $MgSO_4$, filtered and the solvent removed under vacuum. The residue was redissolved in 7:3 THF/H_2O (50 mL), 10% Pd/C (1.00 g) was added and the mixture was placed under a $H_{2(g)}$ atmosphere (~ 5 bar). It was then stirred at room until ESI-mass spectrometry had confirmed that all of the benzyl groups had been removed (~ 4 days), before it was filtered through Celite, which was washed with 1:1 MeOH/H_2O (100 mL). The solvent was removed under vacuum and the residue was redissolved in dry, degassed DMF (50 mL). The solution was then cooled to 0°C and NaH (60% in mineral oil, 0.98 g, 24.5 mmol) and MeI (3.48 g, 24.5 mmol) were added. The mixture was warmed to room temperature and stirred for 4 h after which, H_2O (50 mL) was added to quench the remaining NaH. The mixture was then extracted with Et_2O (5 x 40 mL) and the combined organics were washed with H_2O (8 x 40 mL). The organics were dried over $MgSO_4$, filtered and the solvent removed under vacuum, with the resulting residue suspended in 80% acetic $acid_{(aq.)}$ and stirred at 40°C for 2 h. The acetic acid was removed under vacuum and co-evaporated with toluene (3 x 20 mL) and the crude material was purified by silica gel column chromatography (1:0 up to 9:1 EtOAc/MeOH) to afford the product as a white solid (261 mg, 0.22 mmol, 43%). **^{1}H NMR** (400MHz, CD_3OD) δ = 5.11 (2H, d, *J* = 3.3

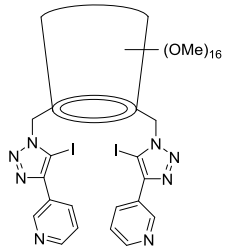
Hz, 1-H), 5.08 (2H, d, *J* = 3.3 Hz, 1-H), 5.05 (2H, d, *J* = 3.3 Hz, 1-H), 3.99 (2H, dd, *J* = 12.2 Hz, *J* = 3.7 Hz), 3.71 - 3.89 (12H, m,), 3.47 - 3.70 (52H, m,), 3.38 (6H, s, 6-OMe), 3.37 (6H, s, 6-OMe), 3.09 - 3.18 (6H, m, 2-H). **MS** (ESI-MS) *m/z*: 1214.64 $[M + NH_4]^+$ ($C_{52}H_{96}NO_{30}$ calc. 1214.60).

$6^{A,D}$-diazido-permethylated-α-cyclodextrin 3



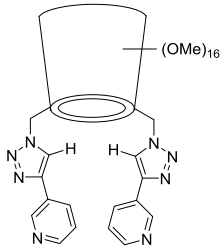
To a solution of diol **2** (200 mg, 0.17 mmol) in CH_2Cl_2 (8 mL) was added triethylamine (68 mg, 0.67 mmol) and methanesulfonyl chloride (77 mg, 0.67 mmol). The mixture was stirred at room temperature for 16 h after which it was washed with saturated $NaHCO_{3(aq.)}$ (10 mL) and H_2O (20 mL). The organics were dried over $MgSO_4$, filtered and the solvent removed under vacuum. The residue was redissolved in dry, degassed DMF (3 mL) and sodium azide (87 mg, 1.34 mmol) was added, with the mixture stirred at 80°C for 16 h. The reaction was then cooled to room temperature, H_2O (10 mL) was added and the mixture was extracted with Et_2O (5 x 20 mL). The organics were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvent removed under vacuum to afford the product as a glassy solid (200 mg, 0.16 mmol, 96 %). **^{1}H NMR** (400MHz, $CDCl_3$) δ = 5.04 - 5.08 (4H, m, 1-H), 5.02 (2H, d, *J* = 3.4 Hz, 1-H), 3.97 (2H, dd, ^2J = 10.7 Hz, *J* = 3.2 Hz, 6-H), 3.36 - 3.91 (76H, m, OCH_3, 3-H, 4-H, 5-H, 6-H), 3.13 - 3.22 (6H, m, 2-H). **MS** (ESI-MS) *m/z*: 1269.63 $[M + Na]^+$ ($C_{52}H_{90}N_6O_{28}Na$ calc. 1269.57).

Bis-iodotriazole derivative 4



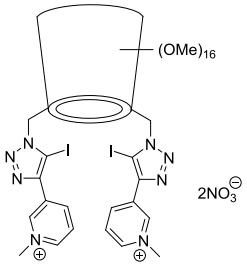
To a solution of bis-azide **3** (40 mg, 0.032 mmol), 3-iodoethynyl pyridine (15 mg, 0.064 mmol) and TBTA (3.4 mg, 0.006 mmol) in THF (2 mL) was added $Cu(MeCN)_4PF_6$ (4.8 mg, 0.013 mmol). The mixture was stirred at room temperature for 16 h after which it was diluted with CH_2Cl_2 (20 mL) and washed with 0.02 M EDTA/1M $NH_4OH_{(aq.)}$ (20 mL) and brine (2 x 20 mL). The organics were dried over $MgSO_4$, filtered and the solvent removed under vacuum. The crude material was purified by preparative thin layer chromatography (93:7 CH_2Cl_2/MeOH) to afford the product as a white solid (55 mg, > 99%). **^{1}H NMR** (400MHz, $CDCl_3$) δ = 9.27 (2H, br. s., py-H), 8.59 (2H, br. s., py-H), 8.31 (2H, d, *J* = 7.9 Hz, py-H), 7.35 (2H, br. s., py-H), 5.26 - 5.30 (2H, m, 6-H), 5.14 (2H, d, *J* = 3.3 Hz, 1-H), 5.03 (2H, d, *J* = 3.2 Hz, 1-H), 4.93 (2H, d, *J* = 3.1 Hz, 1-H), 4.48 - 4.68 (4H, m, 5-H, 6-H), 4.14 (2H, d, *J* = 9.0 Hz), 3.46 - 3.80 (52H, m, 2-OMe, 3-OMe, 3-H, 4-H, 5-H, 6-H), 3.42 (2H, t, *J* = 9.0 Hz, 4-H), 3.20 - 3.28 (4H, m, 2-H), 3.13 (6H, s, 6-OMe), 3.10 (2H, dd, *J* = 10.0 Hz, *J* = 3.2 Hz, 2-H), 3.01 (6H, s, 6-OMe), 2.78 - 2.84 (2H, m, 6-H), 2.71 - 2.77 (2H, m, 6-H). **MS** (ESI-MS) *m/z*: 1727.44807 $[M + Na]^+$ ($C_{66}H_{98}I_2N_8O_{28}Na$ calc. 1727.44721).

Bis-prototriazole derivative 5



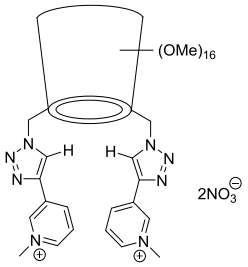
To a solution of bis-azide **3** (40 mg, 0.032 mmol), 3-ethynyl pyridine (6.6 mg, 0.064 mmol) and TBTA (3.4 mg, 0.006 mmol) in CH_2Cl_2 (2 mL) was added DIPEA (12 mg, 0.096 mmol) followed by $Cu(MeCN)_4PF_6$ (4.8 mg, 0.013 mmol). The mixture was stirred at room temperature for 16 h after which it was diluted with CH_2Cl_2 (20 mL) and washed with 0.02 M EDTA/1M $NH_4OH_{(aq.)}$ (20 mL) and brine (2 x 20 mL). The organics were dried over $MgSO_4$, filtered and the solvent removed under vacuum. The crude material was purified by preparative thin layer chromatography (93:7 CH_2Cl_2/MeOH) to afford the product as a white solid (40 mg, 86%). **^{1}H NMR** (400MHz, $CDCl_3$) δ = 8.79 (2H, s, py-H), 8.41 - 8.49 (2H, m, py-H), 8.02 - 8.11 (4H, m, py-H, triazole CH), 7.19 (2H, dd, *J* = 7.8 Hz, *J* = 4.9 Hz, py-H), 5.15 - 5.27 (4H, m, 1H, 6-H), 4.95 - 5.05 (4H, m, 1-H), 4.69 (2H, dd, ^2J = 14.4 Hz, *J* = 8.2 Hz, 6-H), 4.29 - 4.41 (2H, m, 5-H), 4.06 (2H, dd, *J* = 8.8 Hz, *J* = 2.7 Hz, 5-H), 3.42 - 3.72 (52H, m, 2-OMe, 3-OMe, 3-H, 4-H, 5-H, 6-H,), 3.29 (2H, t, *J* = 9.1 Hz, 4-H), 3.22 (2H, dd, *J* = 9.4 Hz, *J* = 3.2 Hz, 2-H), 3.09 - 3.18 (16H, m, 6-OMe, 2-H), 3.02 - 3.08 (2H, m, 6-H), 2.96 (2H, d, ^2J = 10.6 Hz, 6-H). **^{13}C NMR** (101MHz, $CDCl_3$) δ = 149.1, 146.7, 144.4, 132.7, 126.6, 123.6, 121.8, 100.4, 100.2, 99.2, 84.4, 82.4, 82.1, 81.9, 81.8, 81.5, 81.2, 81.1, 81.0, 71.3, 71.2, 71.0, 70.5, 69.9, 61.8, 61.8, 61.6, 59.1, 58.9, 58.1, 58.0, 57.9, 52.0. **MS** (ESI-MS) *m/z*: 1475.65528 $[M + Na]^+$ ($C_{66}H_{100}N_8O_{28}Na$ calc. 1475.65393).

XB receptor 6



Bis-iodotriazole derivative **4** (55 mg, 0.032 mmol) was dissolved in $CHCl_3$ (2.5 mL) and methyl iodide (0.7 mL) was added. The mixture was stirred at 40ºC for 48 h after which, it was cooled to room temperature and the solvent removed under vacuum. The residue was redissolved in 3:1 MeOH/H_2O (20 mL) and passed through a nitrate-loaded Amberlite® column five times. The solvent was removed under vacuum to afford **6** as an off-white solid (55 mg, 0.029 mmol, 92%). **^{1}H NMR** (500MHz, $CDCl_3$) δ = 9.42 (2H, br. s., py-H), 9.10 - 9.19 (2H, m, py-H), 9.01 (2H, d, *J* = 8.1 Hz, py-H), 8.14 (2H, t, *J* = 6.6 Hz, py-H), 5.15 - 5.24 (4H, m, 1-H, 6-H), 5.02 (2H, br. s., 1-H), 4.88 (2H, br. s., 1-H), 4.53 - 4.70 (10H, m, N^+-CH_3, 5-H, 6-H), 4.10 (2H, d, *J* = 7.0 Hz, 5-H), 3.82 (2H, d, *J* = 10.1 Hz,), 3.44 - 3.73 (52H, m, 2-OMe, 3-OMe, 3-H, 4-H, 5-H, 6-H), 3.24 (8H, s, 6-OMe, 2-H), 3.16 - 3.21 (2H, m, 2-H), 3.08 - 3.15 (2H, m, 2-H), 2.93 (6H, s, 6-OMe), 2.76 - 2.87 (4H, m, 6-H). **^{13}C NMR** (126MHz, $CDCl_3$) δ = 145.6, 142.5, 142.2, 141.2, 131.3, 128.6, 100.7, 100.4, 98.8, 84.9, 83.3, 82.4, 82.2, 82.1, 81.7, 81.4, 81.1, 81.0, 71.6, 71.4, 71.3, 70.1, 69.7, 61.9, 61.8, 61.7, 59.3, 59.3, 58.4, 57.9, 57.8, 52.6, 49.2. **MS** (ESI-MS) *m/z*: 867.25132 $[M - 2NO_3]^{2+}$ ($C_{68}H_{104}I_2N_8O_{28}$ calc. 867.25192).

HB receptor 7



Bis-prototriazole derivative **5** (30 mg, 0.023 mmol) was dissolved in $CHCl_3$ (2 mL) and methyl iodide (0.5 mL) was added. The mixture was stirred at 40ºC for 48 h after which, it was cooled to room temperature and the solvent removed under vacuum. The residue was redissolved in 3:1 MeOH/H_2O (20 mL) and passed through a nitrate-loaded Amberlite® column five times. The solvent was removed under vacuum to afford **7** as a pale-orange solid (35 mg, 0.022 mmol, 95%). **^{1}H NMR** (500MHz, $CDCl_3$) δ = 9.57 (2H, br. s., py-H), 8.96 (2H, d, *J* = 7.6 Hz, py-H), 8.78 (2H, s, triazole CH), 8.68 (2H, br. s., py-H), 7.97 (2H, br. s., py-H), 5.18 - 5.25 (2H, m, 1-H), 5.01 - 5.11 (4H, m, 1-H, 6-H), 4.86 (2H, br. s., 1-H), 4.71 - 4.79 (2H, m, 5-H), 4.48 - 4.61 (8H, m, N^+-CH_2, 6-H), 4.21 (2H, d, *J* = 8.1 Hz, 5-H), 3.78 - 3.92 (6H, m), 3.43 - 3.76 (46H, m), 3.38 (2H, t, *J* = 9.1 Hz, 4-H), 3.32 (6H, s, 6-OMe), 3.21 - 3.27 (2H, m, 2-H), 3.09 - 3.18 (4H, m, 2-H), 2.91 - 3.00 (8H, m, 6-OMe, 6-H), 2.79 (2H, d, ^2J = 10.7 Hz, 6-H). **^{13}C NMR** (126MHz, $CDCl_3$) δ = 143.8, 141.7, 140.1, 139.6, 132.2, 128.4, 125.7, 100.6, 100.2, 98.3, 83.9, 82.4, 82.2, 82.2, 81.6, 81.3, 81.2, 71.7, 71.4, 71.0, 70.3, 68.9, 61.9, 61.8, 61.6, 59.1, 59.0, 58.8, 57.9, 57.8, 52.4, 48.8. **MS** (ESI-MS) *m/z*: 741.35553 $[M - 2NO_3]^{2+}$ ($C_{68}H_{106}N_8O_{28}$ calc. 741.35528).

S1.3 Spectral Characterisation

Bis-iodotriazole derivative 4

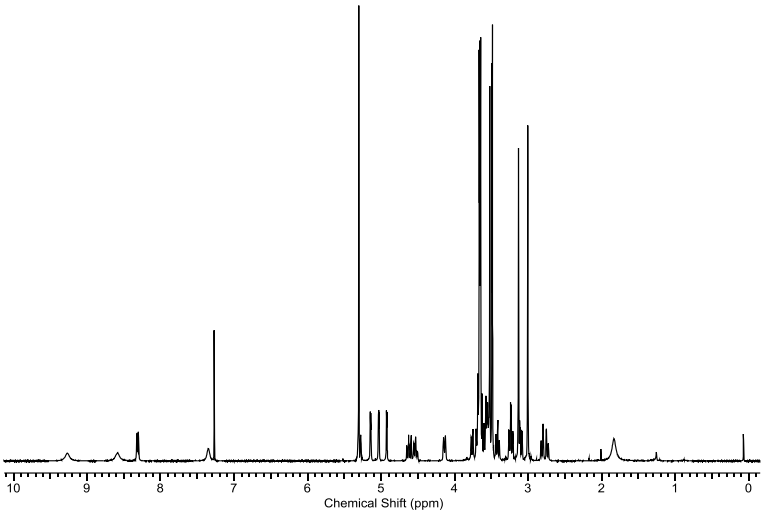


Figure S1-1: ^{1}H NMR of bis-iodotriazole derivative **4** in $CDCl_3$ at 298 K (400 MHz).

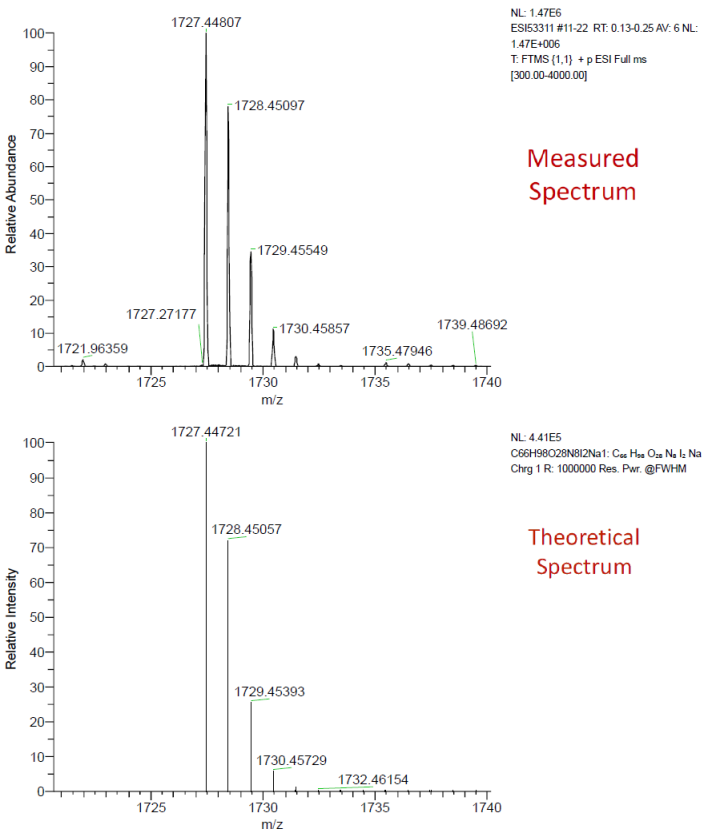


Figure S1-2: High- resolution mass spectrum of bis-iodotriazole derivative **4**.

Bis-prototriazole derivative 5

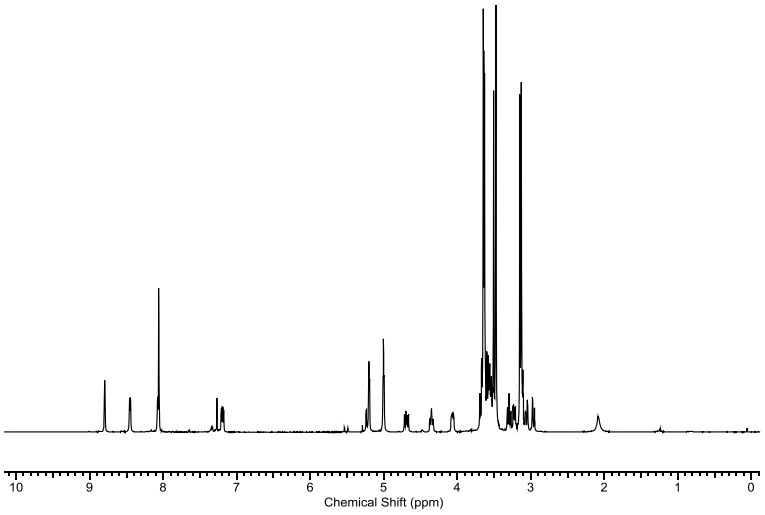


Figure S1-3: ^{1}H NMR of bis-prototriazole derivative **5** in $CDCl_3$ at 298 K (400 MHz).

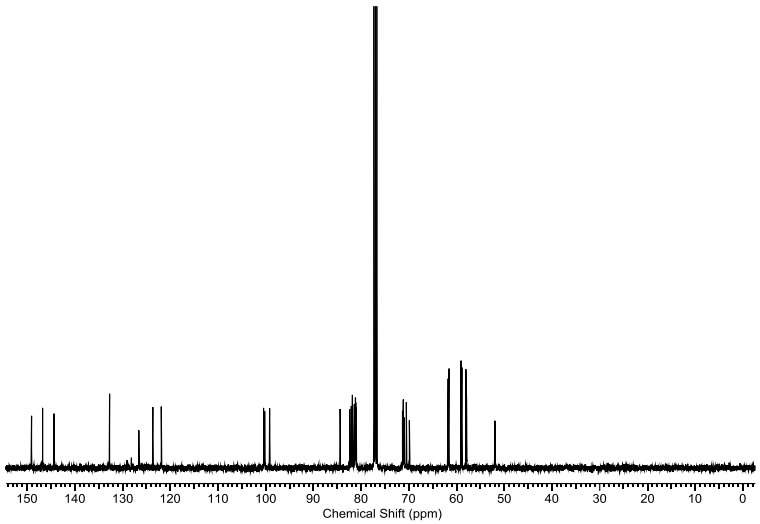


Figure S1-4: ^{13}C NMR of bis-prototriazole derivative **5** in $CDCl_3$ at 298 K (101 MHz).

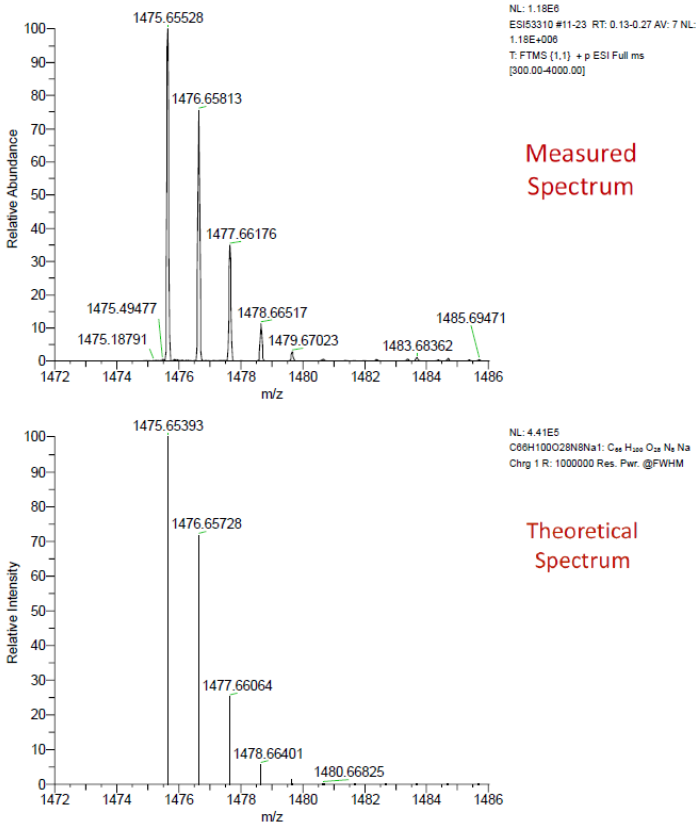


Figure S1-5: High-resolution mass spectrum of bis-prototriazole derivative **5**.

XB Receptor 6

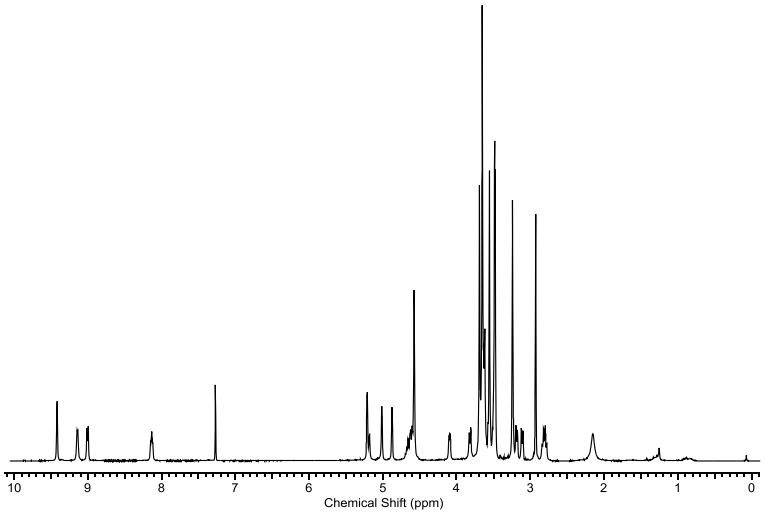


Figure S1-6: ^{1}H NMR of XB receptor **6** in $CDCl_3$ at 298 K (500 MHz).

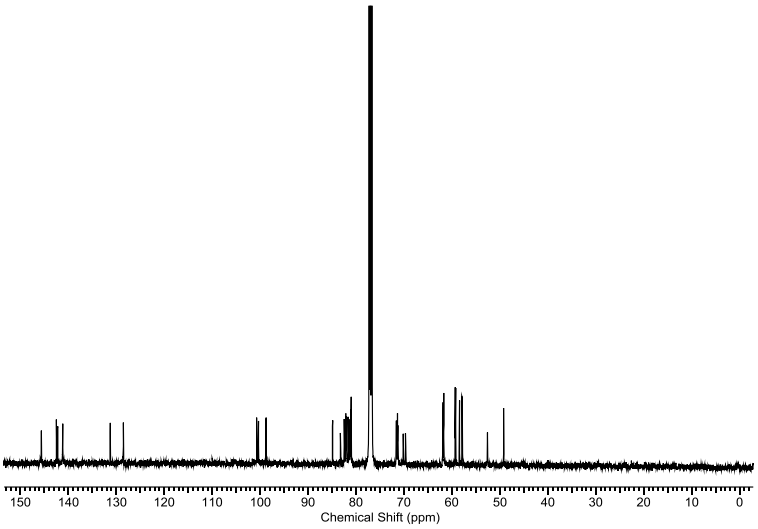


Figure S1-7: ^{13}C NMR of XB receptor **6** in $CDCl_3$ at 298 K (126 MHz).

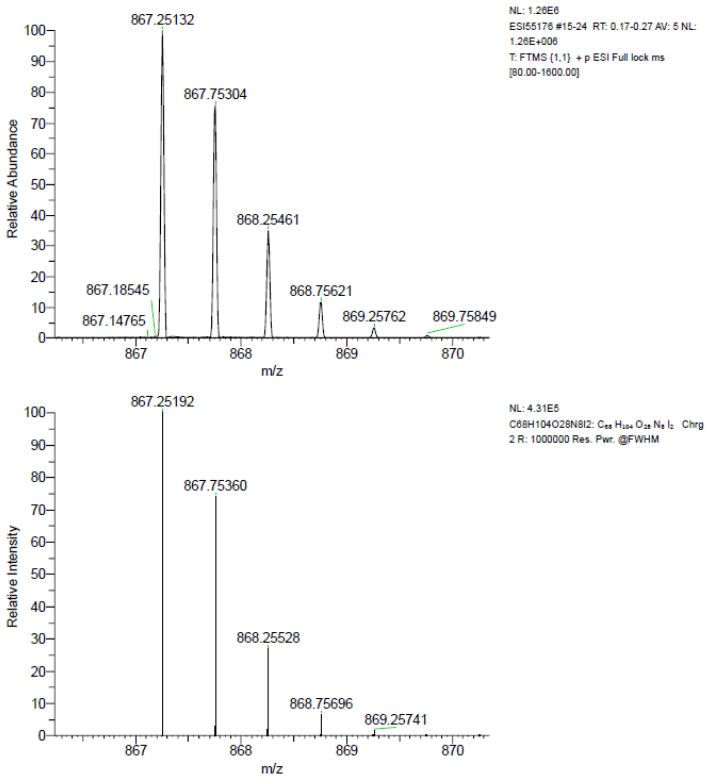


Figure S1-8: High-resolution mass spectrum of XB receptor **6**.

HB Receptor 7

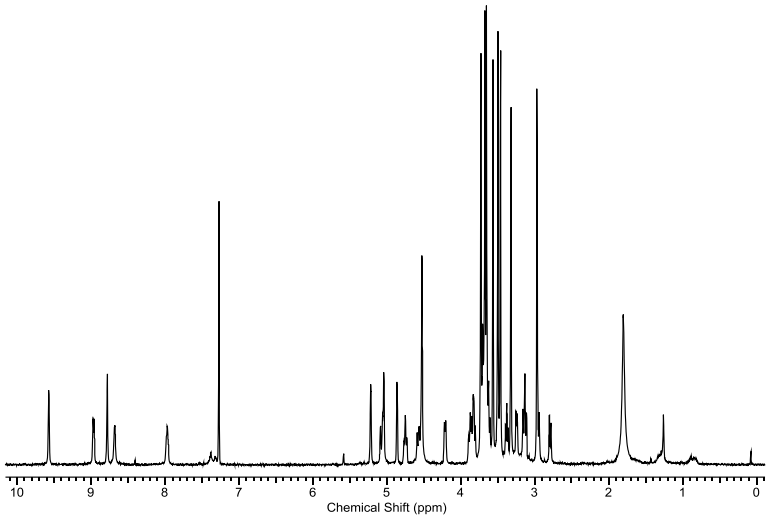


Figure S1-9: ^{1}H NMR of HB receptor **7** in $CDCl_3$ at 298 K (500 MHz).

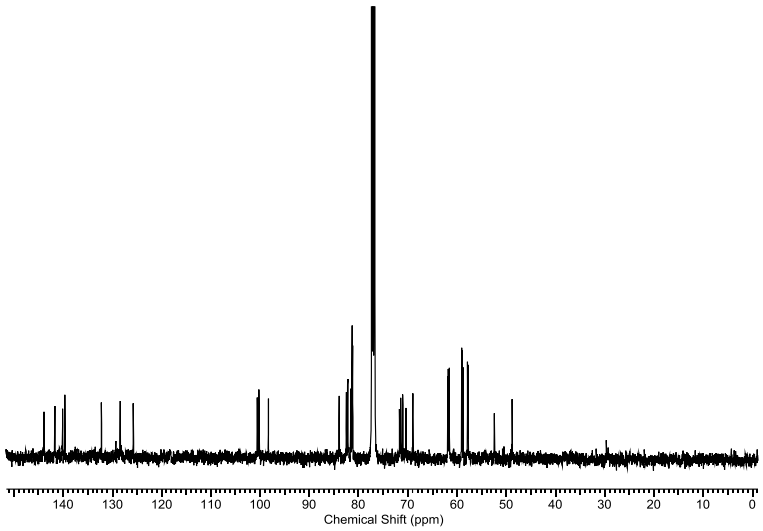


Figure S1-10: ^{13}C NMR of HB receptor **7** in $CDCl_3$ at 298 K (126 MHz).

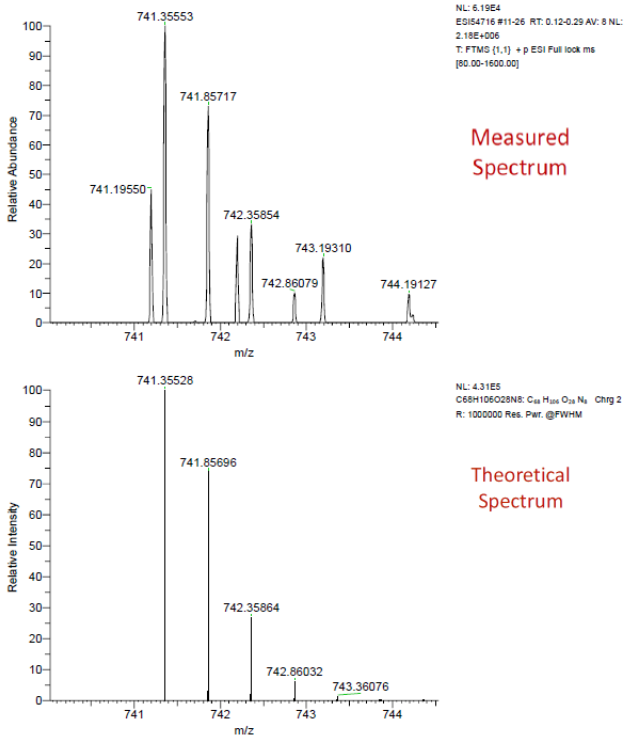


Figure S1-11: High-resolution mass spectrum of HB receptor **7**.

S2 ^{1}H NMR titration experiments

S2.1 Protocol

^{1}H NMR titration experiments were performed in unbuffered D_2O on a Bruker AVIII500 spectrometer operating at 500 MHz and at a temperature of 298 K. A 0.5 mL initial volume of the host was used at a concentration of 1.5 mM. Solutions of the respective anions, as sodium salts, were added in aliquots, with the chemical shift of the appropriate protons followed over 17 additions (up to 120 equivalents). The spectra were referenced to acetone (δ = 2.22 ppm), which was added as an internal standard (< 0.05 % of the total volume of the solution). Association constants were calculated from the data obtained using the WinEQNMR2 software package.[4] An estimate of the association constant and the limiting chemical shifts were added to the programs input file, along

with the observed chemical shift of the proton followed and the concentrations of host and guest in each spectrum recorded. Refinement of the data using a non-linear least-squares regression analysis gave an optimised fit between the observed and calculated data for a 1:1 binding stoichiometry. Estimates for the standard error of the association constant calculated were provided by the program, as a standard deviation. However, these errors are only related to the fitting process and do not account for the systematic errors associated with the experimental procedure.

S2.2 Titration Data

XB Receptor 6

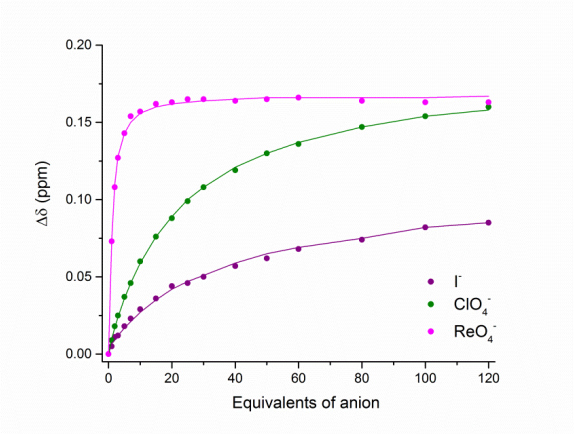


Figure S2-1: Experimental titration data (points) and calculated 1:1 binding isotherms (lines) for the addition of sodium salts of various anions to **6**, monitoring protons $5^{C,F}$-*H* (D_2O, 298 K, 500 MHz).

HB Receptor 7

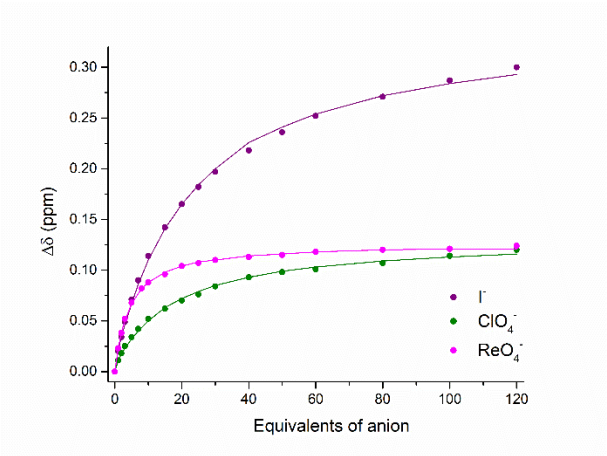


Figure S2-2: Experimental titration data (points) and calculated 1:1 binding isotherms (lines) for the addition of sodium salts of various anions to **7**, monitoring protons $5^{C,F}$-*H* (D_2O, 298 K, 500 MHz).

S3 Isothermal titration calorimetry experiments with $NaReO_4$

S3.1 Protocol

The isothermal titration calorimetry experiments were performed on a Microcal PEAQ-ITC automated system for receptor **6** and an iTC MicroCalorimeter for receptor **7** in unbuffered distilled water at 298 K. An initial concentration of the host of 0.2 mM was used, with a 20 mM solution of $NaReO_4$ added in 35 aliquots. The data from the first addition of 0.5 µL was discarded, with data collected for the subsequent 34 additions of 1 µL. Heats of dilution were measured by a preliminary titration of $NaReO_4$ into water. Values of K_a and ΔH were calculated using the MicroCal PEAQ-ITC Analysis Software, *via* a non-linear least squares regression fit of the experimental data to the one-set of sites model. These values were then used to determine the ΔG and ΔS values.

S3.2 Titration Data for receptor 7

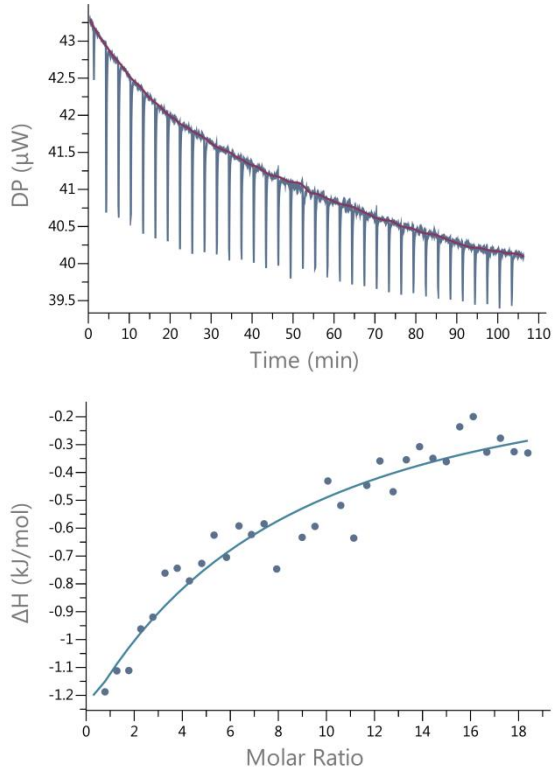


Figure S3-1: (top) Raw ITC data for the sequential addition of $NaReO_4$ to **7** (H_2O, 298 K); (bottom) integrated heat plot obtained from titration.

S4 References

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