Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Maltodextrin recognition by a macrocyclic synthetic lectin

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Contents

General methods

Commercially available reagents were purchased from Sigma-Aldrich, Alfa-Aesar, Fluorochem, Frontier Scientific, VMR, Acros Organics, Frontier Scientific or Carbosynth and used as purchased unless specified otherwise. Carbohydrates used in binding studies were purchased from either Sigma-Aldrich or Carbosynth. Solvents were used as supplied unless specified otherwise. Anhydrous tetrahydrofuran, dichloromethane, toluene, and acetonitrile were purified using a Grubbs apparatus[1] manufactured by Anhydrous Engineering. Air and moisture sensitive procedures were conducted using standard Schlenk techniques.

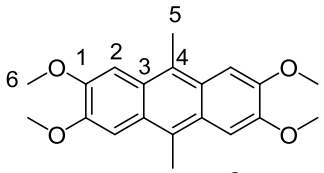
Thin-layer chromatographic (TLC) analysis was performed using aluminium plates pre-coated with silica (Merck silica gel 60 F_{254}); TLC plates were visualised using UV-light (254 or 365 nm) or developed using solutions of potassium permanganate, ninhydrin, iodine, ceric ammonium molybdate, or phosphomolybdic acid. Column chromatography employed 60 Å silica gel (Sigma Aldrich, 35-70 micron particle size). High pressure liquid chromatography (HPLC) was conducted using an apparatus consisting of a Waters 600 control unit, a Waters 2998 photodiode array detector, and a Waters Prep Degasser; for analytical experiments an XSELECT CSH C_{18} 5 µm (4.6 x 150 mm) column was employed, for preparative experiments an XSELECT CSH C_{18} 5 µm (19 x 250 mm) column was used.

^{1}H, ^{13}C, and ^{19}F NMR spectra were obtained at 298 K (unless specified otherwise) and performed either at 400 MHz on a Varian 400-MR, Bruker Nano 400, or Jeol ECS 400 spectrometer; 500 MHz on a Varian VNMRS500a, Varian VNMRS500b, or Bruker Avance III HD 500 Cryo spectrometer; or at 600 MHz using a Varian VNMRS600 Cryo spectrometer. Chemical shifts observed in NMR spectroscopic experiments were quoted in parts per million (ppm) and referenced using residual solvent peaks for ^{1}H and ^{13}C experiments, and $CFCl_3$ for ^{19}F experiments, to which the instruments were externally calibrated.

Low-resolution mass spectra were recorded on a Bruker ESQUIRE 300 apparatus for electrospray ionization (ESI) experiments, whereas high resolution mass spectra were recorded on a Bruker Apex 4e 7.0T FT-MS for ESI, a Waters Synapt G25 for nanospray, or an Applied Biosystems 4700 spectrometer for matrix-assisted laser desorption/ionization (MALDI) experiments. Infra-red (IR) spectra of compounds were recorded on a Perkin-Elmer Spectrum One FT-IR apparatus fitted with an attenuated total reflectance (ATR) accessory which facilitated the direct examination of compounds in the solid or liquid phase; frequencies were quoted in wavenumbers (cm^{-1}). Ultraviolet/visible (UV/vis) absorption experiments were conducted using an Agilent Cary 300 spectrometer. Fluorescence spectra were recorded using either PerkinElmer LS45 or Horiba FluoroMax-4 fluorimeters. Optical experiments were conducted in Hellma QS-101 or QS-111 cuvettes using water purified using a Millipore purification apparatus; in-cuvette stirring was effected using Fisherbrand PTFE-immured 5 mm x 2 mm magnetic bars.

Synthetic Procedures

2,3,6,7-Tetramethoxy-9,10-dimethylanthracene (2)



2

The procedure was adapted from that of Müller and co-workers.[2] 1,2-Dimethoxybenzene (163 ml, 1.09 mol) was added to sulphuric acid (70% v/v in H_2O), and the flask cooled to -10 °C. A mechanical stirring apparatus was introduced, and the reaction mixture was stirred vigorously. Acetaldehyde (120 ml, 2.14 mol) was added dropwise over 2 h; care was taken to ensure the reaction temperature did not exceed 5 °C. The formation of a precipitate caused the mechanical stirring apparatus to become ineffective, so it was disengaged. The reaction was left overnight, and then poured into EtOH (2.5 L); the precipitate was isolated by filtration, washed with EtOH (1 L), water (2 L), and air dried, giving **2** as a celadon solid (98 g, 300 mmol, 55%). **^{1}H NMR** (Figure S1)($CDCl_3$, 400 MHz): δ = 2.95 (s, 6H, C(5)H_3), 4.08 (s, 12H, C(6)H_3), 7.40 (s, 4H, C(2)H) ppm. *Lit*[3] **^{1}H NMR**: δ = 2.95, 4.08, 7.40 ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.7 (C2), 125.6 (C4), 123.8 (C5), 102.6 (C3), 55.6 (C1), 14.7 (C6); **ESI-MS**: *m/z* observed (calculated) for $[C_{20}H_{22}O_4 + H]^+$ = 327.16 (327.3).

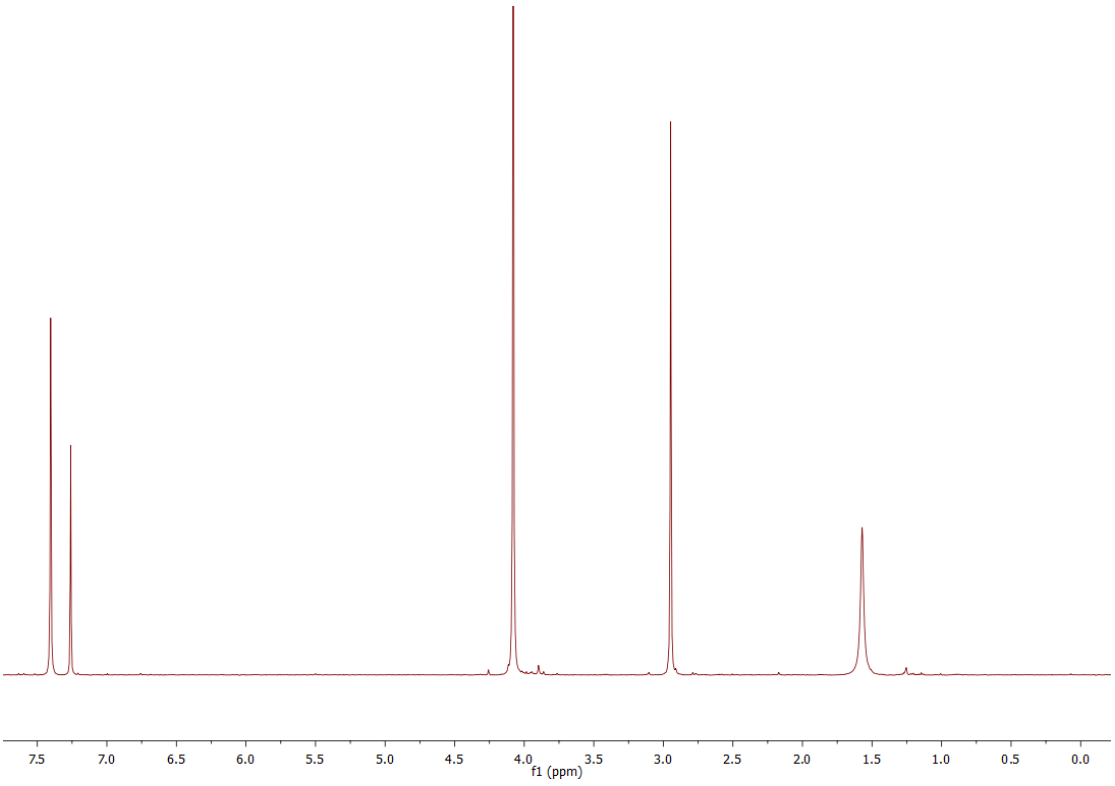
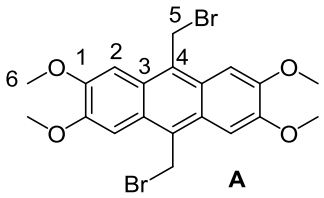


Figure S1- ^{1}H NMR spectrum of **2** in $CDCl_3$.

2,3,6,7-Tetramethoxy-9,10-bis(bromomethyl)anthracene (A)



A

In a dry, inert atmosphere, DCM (100 ml) was added to dimethyl anthracene **2** (4.68 g, 9.67 mmol), NBS (6.36 g, 35.7 mmol), and ABCN (30.0 mg, 0.12 mmol), and the reaction mixture stirred, and heated under reflux for 4 h. The reaction mixture was cooled (0 °C), and the precipitate isolated by filtration, giving pure **A** as a yellow solid (4.17 g 8.61 mmol, 89%). The residual organic fraction from the previous filtration step was washed with $NaOH_{(aq)}$ (300 ml, 0.1 M), dried ($MgSO_4$), and concentrated under reduced pressure to give a further crop of **A** (total yield 4.59 g, 9.48 mmol, 98%) **^{1}H NMR** (Figure S2) ($CDCl_3$, 400 MHz): δ = 4.12 (s, 12H, C(6)H_3), 5.36 (s, 6H, C(5)H_2), 7.42 (s, 4H, C(2)H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) 150.0 (C2), 125.9 (C4), 125.6 (C5), 101.7 (C3) 55.9 (C1), 28.7 (C6). **ESI-MS**: *m/z* observed (calculated) for $[C_{20}H_{20}Br_2O_4 + H]^+$ = 484.97 (484.98). **FTIR** ν_{max} (neat)= 2939 (m, Ar-H), 1249 (s, CO).

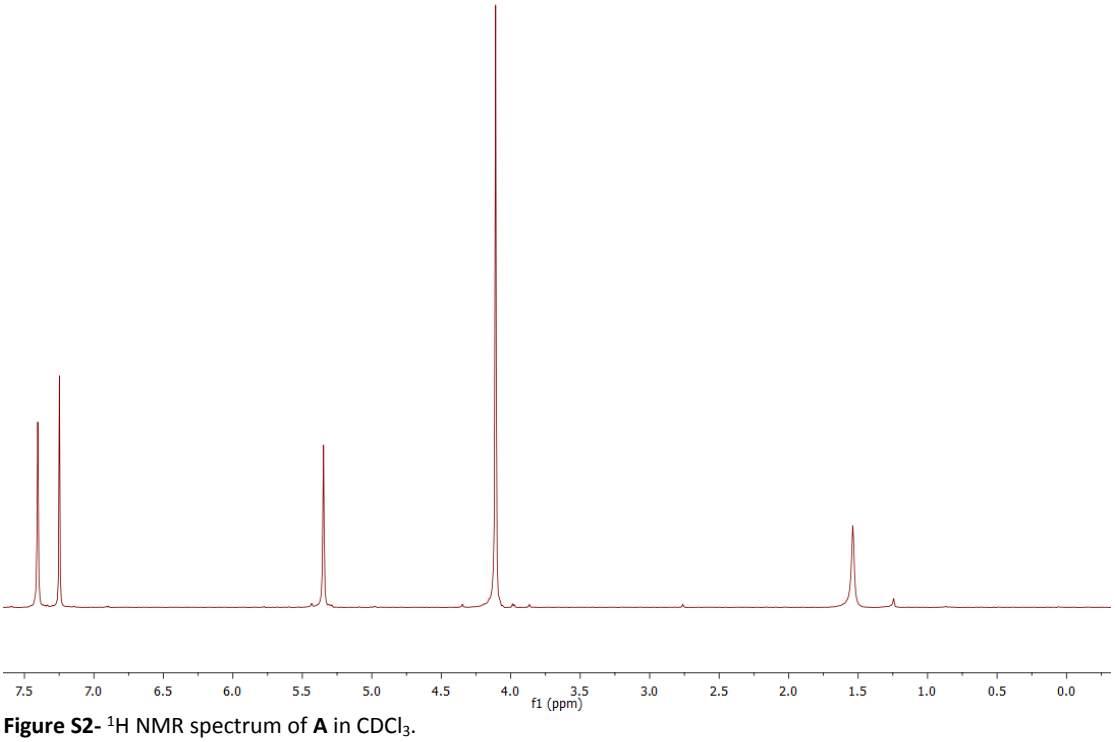
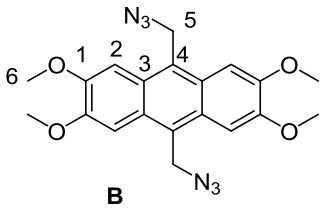


Figure S2- ^{1}H NMR spectrum of **A** in $CDCl_3$.

2,3,6,7-Tetramethoxy-9,10-bis(azidomethyl)anthracene (B)



B

In a dry, inert atmosphere, MeCN (75 ml) was added to dibromo compound **A** (2.80 g, 5.78 mmol) and NaN_3 (1.54 g, 23.7 mmol); the reaction mixture stirred, and heated to 80 °C overnight. The reaction mixture was cooled (0 °C), and the precipitate isolated by filtration, washed with water (100 ml), and air-dried, giving pure **B** as a brown solid (1.65 g, 4.05 mmol, 70%). The residual organic fraction from the previous filtration step was concentrated under reduced pressure and re-dissolved in EtOAc (400 ml). The organic phase was washed with $NaOH_{(aq)}$ (300 ml, 1 M), dried ($MgSO_4$), and concentrated under reduced pressure to give a further crop of **B** (total yield 2.24 g, 5.49 mmol, 95%). **^{1}H NMR** (Figure S3)($CDCl_3$, 400 MHz): δ = 4.08 (s, 12H, C(6)H_3), 5.17 (s, 6H, C(5)H_2), 7.40 (s, 4H, C(2)H) ppm. **^{13}C NMR** (Figure S4) ($CDCl_3$, 101 MHz): *δ* = 47.68 (C5), 56.00 (C6), 101.74 (C2), 123.71 (C3), 126.75 (C4), 150.16 (C1). **ESI-MS**: *m/z* observed (calculated) for $[C_{20}H_{20}N_6O_4 + Na]^+$ = 431.14 (431.18).

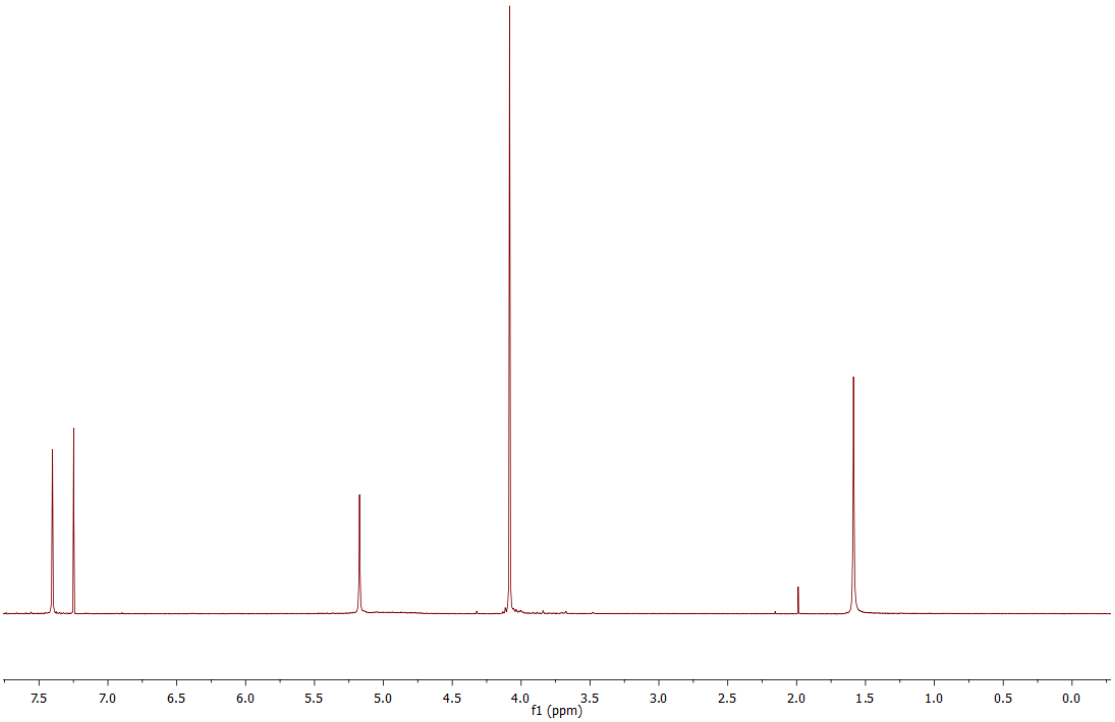


Figure S3- ^{1}H NMR spectrum of **B** in $CDCl_3$.

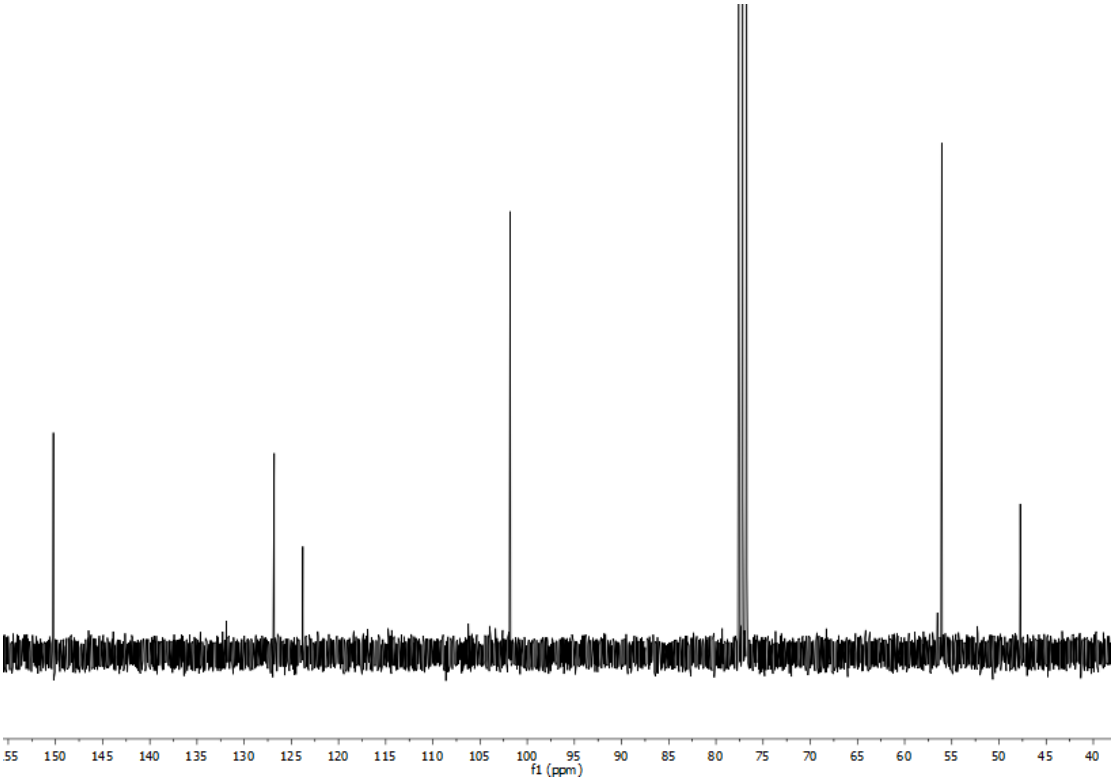
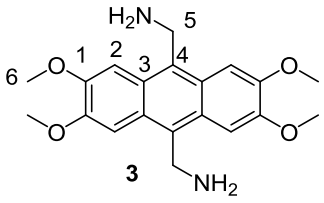


Figure S4- ^{13}C NMR spectrum of **B** in $CDCl_3$.

2,3,6,7-Tetramethoxy-9,10-bis(aminomethyl)anthracene (3)



In a dry, inert atmosphere, diazide **B** (68.6 mg, 168 µmol) was dissolved in THF (1 ml), and the reaction mixture stirred. PMe_3 (5.50 ml, 1M in THF, 5.50 mmol) was added, and the reaction mixture stirred for 3 h. Degassed water (3 ml) was added, and the reaction mixture stirred for 14 h. The reaction mixture was concentrated under reduced pressure, after which toluene (2 ml) was added and the reaction sonicated; filtration allowed for obtention of pure diamine **3** as a beige solid (52.1 mg, 146 µmol, 87%). **^{1}H NMR** (Figure S5)($CDCl_3$, 400 MHz): δ = 4.08 (s, 12H, C(6)H_3), 5.17 (s, 6H, C(5)H_2), 7.40 (s, 4H, C(2)H) ppm. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 149.7(C2), 125.5 (C4), 125.3 (C5), 101.9 (C3), 56.0 (C1), 39.5 (C6). **IR** (solid) = 3332 (w, NH), 1132 (s, CO). **HRMS** (EI) calc. for $C_{20}H_{24}N_2O_4$ $[M+Na]^+$ 379.1634, found $[M+Na]^+$ 379.1628.

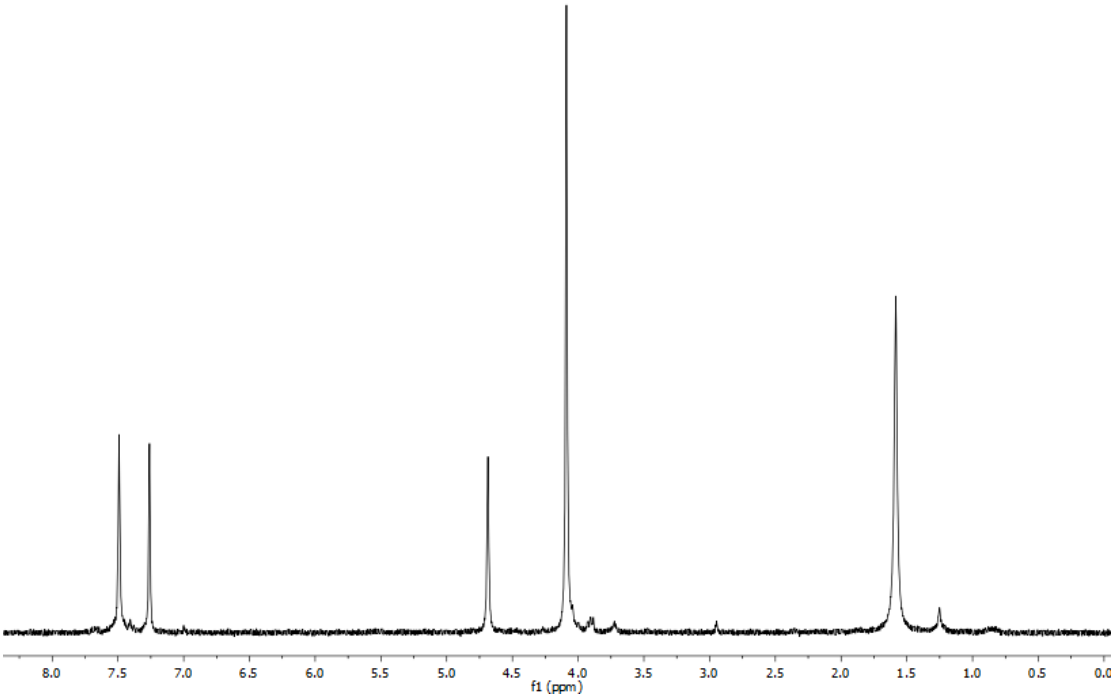
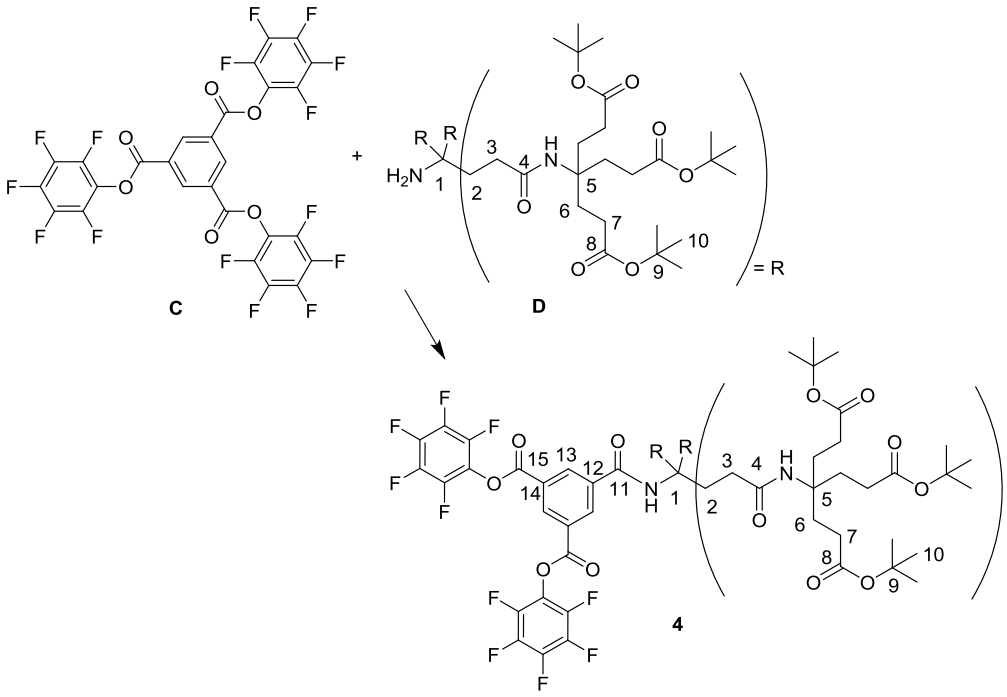


Figure S5- ^{1}H NMR spectrum of **3** in $CDCl_3$.

Linker reagent 4



The procedure was adapted from that of Destecroix et al.[4] In a dry, inert atmosphere, THF (7 ml) was added to triester **C** (1.70 g, 2.40 mmol) and amine **D** (1.15 g, 0.7 mmol). DIPEA (1 ml) was added, and the reaction stirred at room temperature for 2 days. The reaction mixture was concentrated under reduced pressure, and purified by column chromatography (80 ml SiO_2, Et_2O:hexane, 50:50 →Et_2O, Ø = 5.5 cm), giving pure **4** as a white solid (1.22 g, 0.623 mmol, 89%). **^{1}H NMR** (Figure S6)($CDCl_3$, 400 MHz): δ = 1.39 (s, 81H, C(10)H_3), 1.89 – 1.95 (m, 24H, C(2)H_2, C(6)H_2), 2.09 – 2.21 (m, obscured, C(7)H_2), 2.25 – 2.37 (m, 6H, C(2)H_2), 6.01 (s, 3H, C(4)ONH), 9.06 (s, 2H, C(13)H), 9.22 (s, 1H, C(15)H), 9.57 (s, 1H, C(12)ONH) ppm. *Lit*[4] **^{1}H NMR** δ = 1.31, 1.84, 2.08, 2.23, 8.96, 9.15, 9.47 ppm.

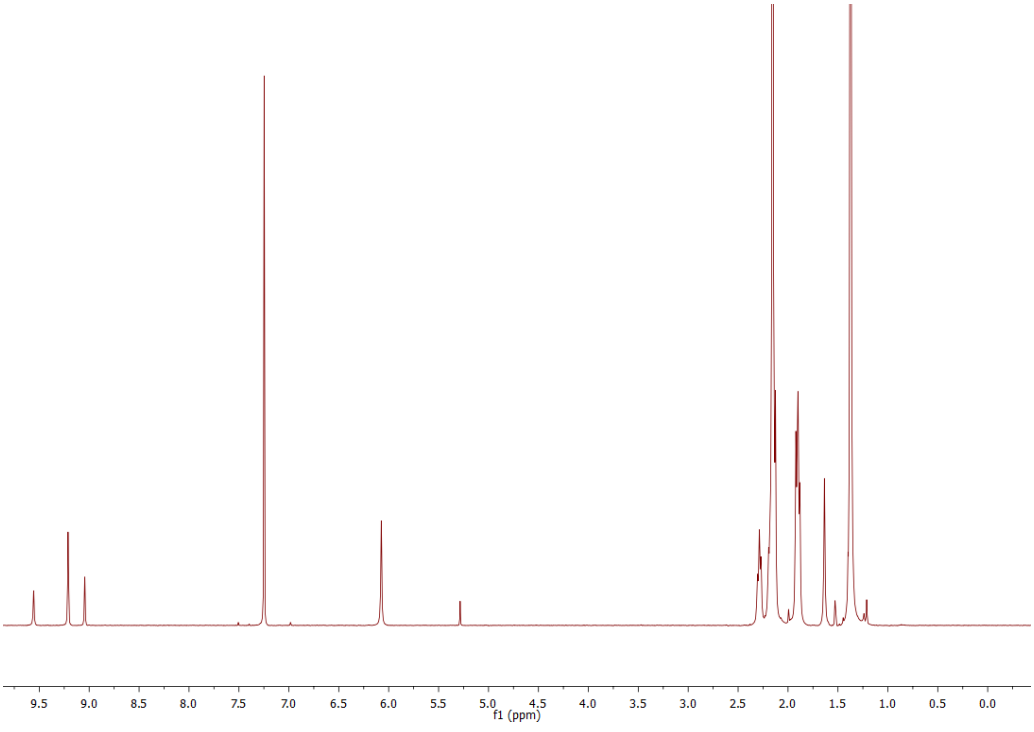
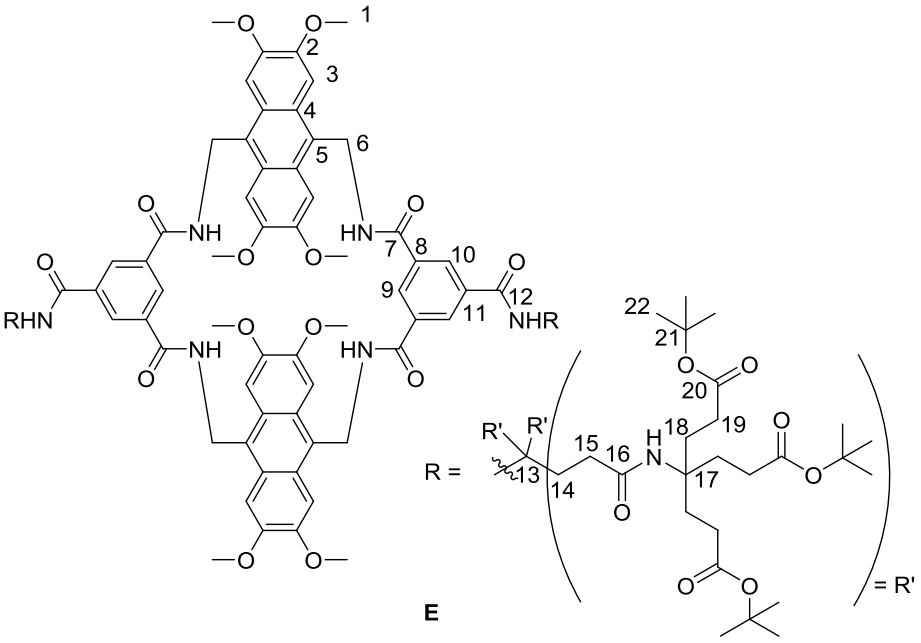


Figure S6- ^{1}H NMR spectrum of **4** in $CDCl_3$.

tBu-protectecd octamethoxy macrocycle E



E

In a dry, inert atmosphere, diamine **3** (60.0 mg, 168 µmol) was dissolved in THF (800 ml), and DIPEA (5 ml) was added; the solution was stirred and the reaction vessel protected from light using aluminium foil. Linker reagent **4** (329 mg, 168 µmol) was dissolved in THF (50 ml) and added over 33 h via syringe-pump. The reaction was stirred for 64 h, after which the solvent was removed under reduced pressure. The residue was dissolved in chloroform (200 ml) and washed with $NH_4Cl_{(aq)}$ (200 ml, saturated), brine (200 ml), and the organic phase dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was dissolved in acetone (4.2 ml), water (1.8 ml) was added, and the solution passed through a syringe filter (0.45 µm). The resulting clear solution was injected into a preparative HPLC apparatus (reverse phase column, Hichrom Kromasil, 150 x 21.2 mm, 5 µm), and eluted with water:acetone (30:70 ramped to 0:100 over 30 min; flow rate = 17 ml/min). The fraction eluting at *ca.* 25 min was isolated and lyophilized, giving pure **E** (89 mg, 45.4 µmol, 27%) **^{1}H NMR** (Figure S7)(*d*3-MeOD, 600 MHz): δ = 1.47 (s, 4.08 (s, 162H, C(22)H_3), 1.97—2.03 (m, 48H, C(18)H_2), 2.19—2.28 (m, 48H, C(19)H_2/C(14)H_2), 2.30-2.36 (m, 12H, C(15)$_2$), 3.90 (s, 24H, C(1)H_3), 5.38 (s, 8H, C(6)H_2), 7.47 (s, 8H, C(3)H), 7.73 (s, 2H, C(9)H), 8.60 (s, 4H, C(10)H) ppm*. **ESI-MS**: *m/z* observed (calculated) for $[C_{210}H_{316}N_{12}O_{56} + 2Na]^{2+}$ = 1975.10 (1975.10), $[C_{210}H_{316}N_{12}O_{56} + 3Na]^{3+}$ = 1324.3997 (1324.3950)

* Macrocycle **E** was found to degrade quite rapidly in organic solvents, probably through oxidation by singlet O_2. See: J. M. Baumes, J. J. Gassensmith, J. Giblin, J. J. Lee, A. G. White, W. J. Culligan, W. M. Leevy, M. Kuno and B. D. Smith, *Nature Chem.*, 2010, **2**, 1025-1030; H. H. Wasserman, J. R. Scheffer and J. L. Cooper, *J. Am. Chem. Soc.*, 1972, **94**, 4991-4996. For this reason we were unable to obtain a clean 13C NMR spectrum at this stage. After deprotection to 5 and dissolution in water the macrocycle was more stable, presumably due to the short lifetime of singlet oxygen in aqueous solutions.

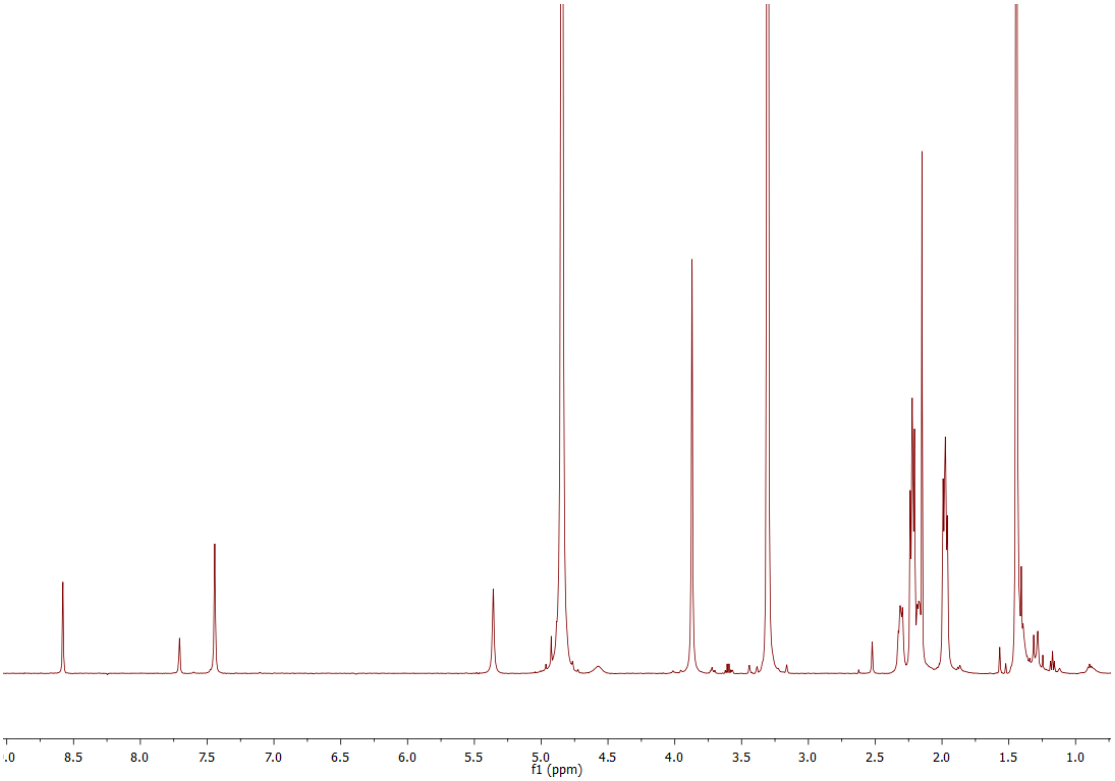
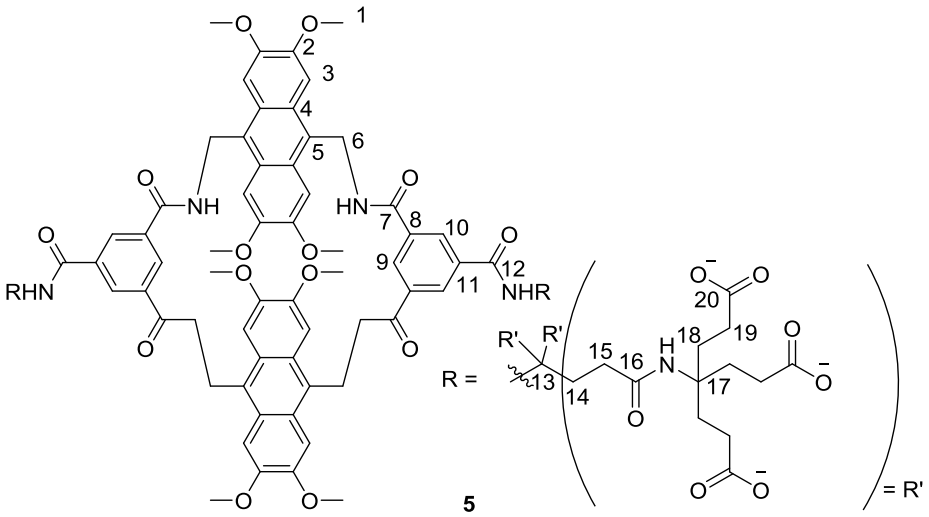


Figure S7- ^{1}H NMR spectrum of protected receptor **E** in *d*3-MeOD.

Receptor 5



In a dry, inert atmosphere, protected macrocycle **E** (10.0 mg, 2.56 µmol) was dissolved in DCM (1 ml) and trifluoroacetic acid (0.5 ml) was added. The reaction mixture was stirred for 4 h, after which it was concentrated under reduced pressure; any residual trifluoroacetic acid removed by three successive co-evaporations with toluene, and then chloroform. The residue was dissolved in a minimum amount of acetone, and water was added. The suspension was lyophilised, and water was added to the residue; the pH was adjusted to 7 ($NaOH_{(aq)}$) and the solution was lyophilised again to give pure **5** as a white powder which was stored in an inert atmosphere (8.40 mg, 2.55 µmol, 100%). **^{1}H NMR** (Figure S8)(D_2O, 600 MHz): δ = 1.77-1.86 (24H, C(19)H_2), 1.99-2.10 (m, 36H, C(18)H_2, C(15)H_2), 2.20 (d, *J*=7.7 Hz, 12H, C(14)H_2), 3.76 (s, 24H, C(1)H_3), 5.27 (s, 8H, C(6)H_2), 7.33 (app s, 10H, C(9)H, C(3)H), 8.33 (s, 4H, C(10H) ppm. **^{13}C NMR** (125 MHz, D_2O) δ 182.9 (C20), 175.1 (C7), 174.9 (C16), 173.4 (C12), 148.8 (C2), 133.9 (C10), 130.2 (C9), 130.0 (C8), 126.0 (C4), 125.8 (C5), 102.0 (C3), 59.0 (C13), 58.3 (C17), 37.5 (C6), 31.7 (C14), 31.5 (C18), 30.6 (C19), 30.2 (C15).

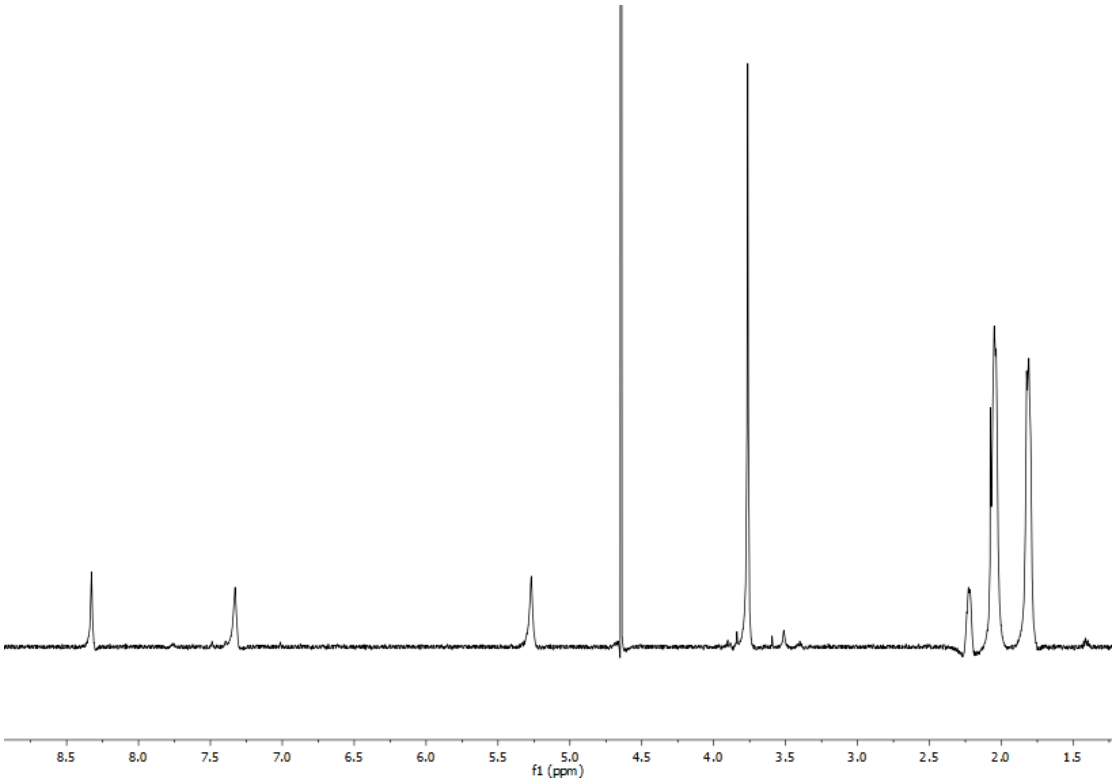


Figure S8- ^{1}H NMR spectrum of **5** in D_2O.

^{1}H NMR binding studies and associated experiments

^{1}H NMR titration methodology

All ^{1}H NMR titrations were performed using a Varian VNMRS600 Cryo spectrometer at 298 K. All receptors were purity-tested before titrations by ^{1}H NMR integrations with DMF as internal standard. As a general procedure, a stock solution of analyte (macrocycle) in D_2O was prepared and used to dissolve a sample of titrant (carbohydrate); using a stock solution of titrant ensured that its concentration remained fixed throughout the experiment. During a titration, aliquots of titrant solution were added to an NMR tube containing a predetermined volume (typically 500 μL) of analyte solution and the corresponding ^{1}H NMR spectra recorded. Where the titrant was a reducing sugar, solutions were prepared 24 hr before use to ensure adequate sugar equilibration.

In the case of fast exchange binding on the ^{1}H NMR timescale, signals associated with the analyte were observed to move over the duration of a titration; association constants were determined by monitoring the change in chemical shift (Δδ) for a selected proton resonance belonging to the analyte species. The Δδ values were analysed using a non-linear least squares fitting protocol implemented within Microsoft Excel, designed to calculate binding affinity (K_a) with the assumption of 1:1 host:guest stoichiometry. An estimated error for K_a was calculated from individual data points by assuming the determined K_a and Δδ values. In most cases the fits were good, but significant departures were observed for *N*-acetyl-D-glucosamine (**9**), methyl N-acetyl-β-D-glucosaminide (**10**) and D-galactose (**11**). For these substrates the data were also analysed using a programme which considers both 1:1 and 1:2 host:guest stoichiometries. This gave improved fits (as expected) and somwhat higher values for the 1:1 binding constants K_{11}. NMR spectra, fitting curves and association constants, including K_{11} and K_{12} where relevant, are shown in Figures S12 – S42.

Receptor 5 Dilution Study

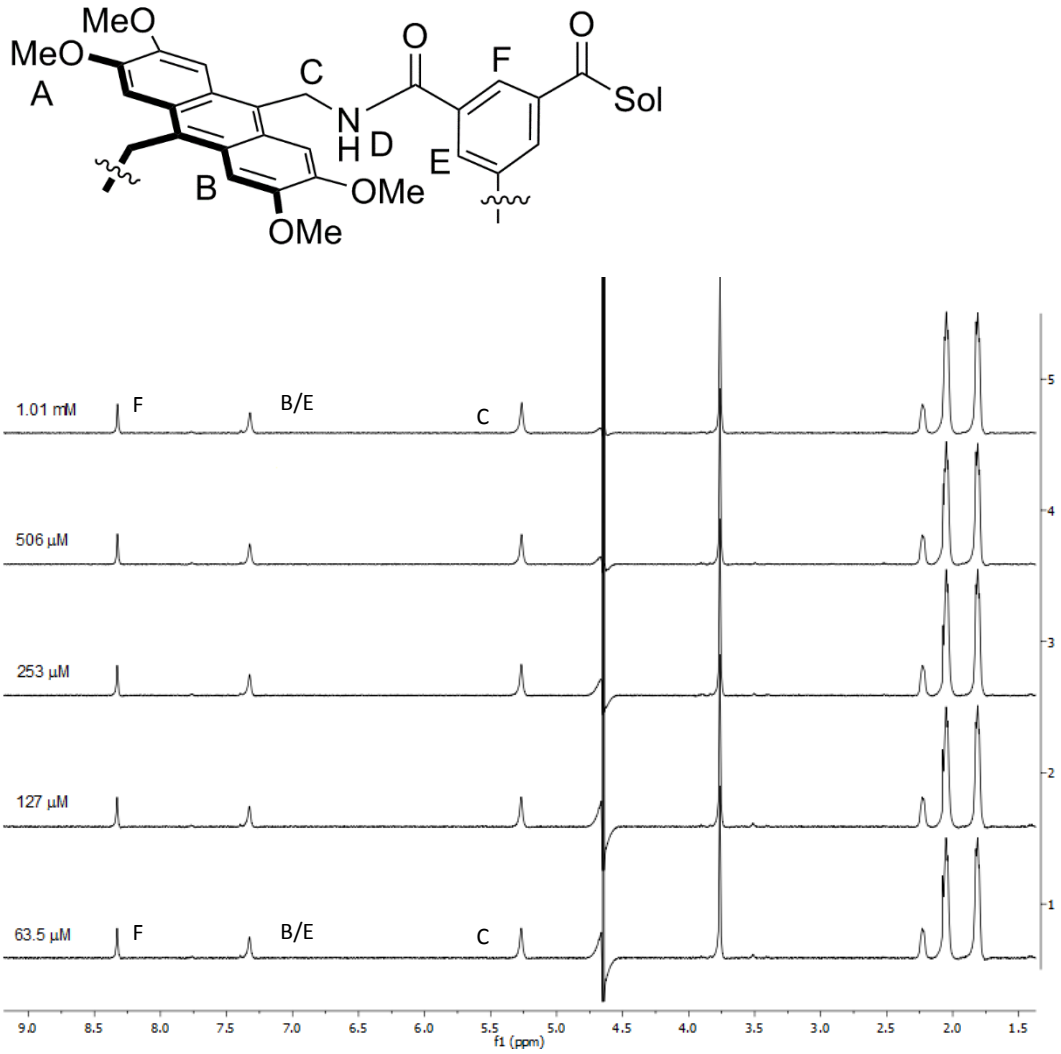


Figure S9- ^{1}H NMR dilution study of macrocycle **5** performed in D_2O at 298 K (full spectrum). Sol = solubilising group.

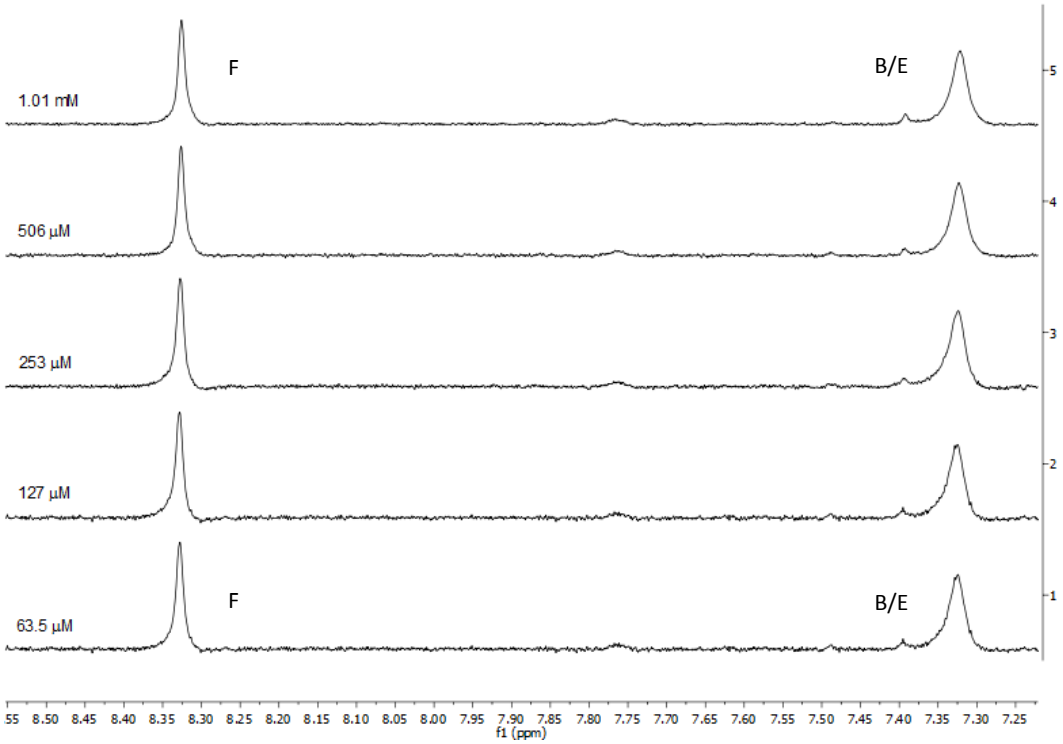


Figure S10-^{1}H NMR dilution study of receptor **5** performed in D_2O at 298 K (aromatic region).

VT Study

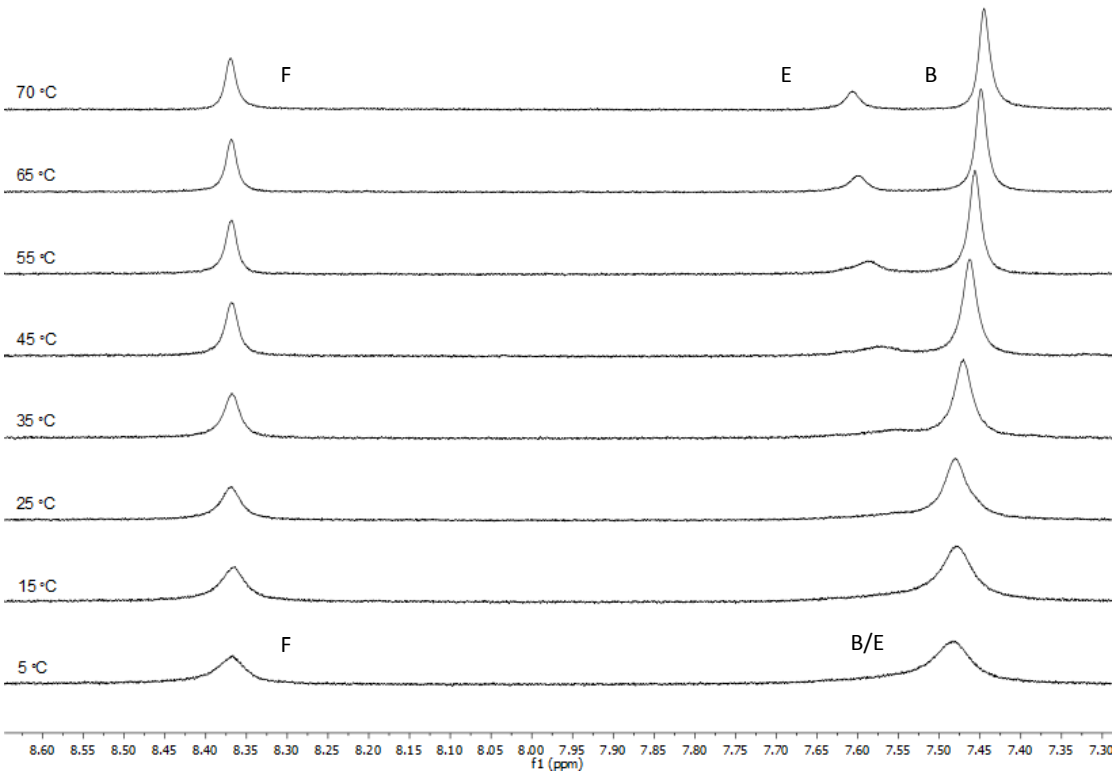


Figure S11- Variable temperature ^{1}H NMR study of receptor **5** (0.75 mM) in D_2O measured at 500 MHz.

D-Glucose (6)

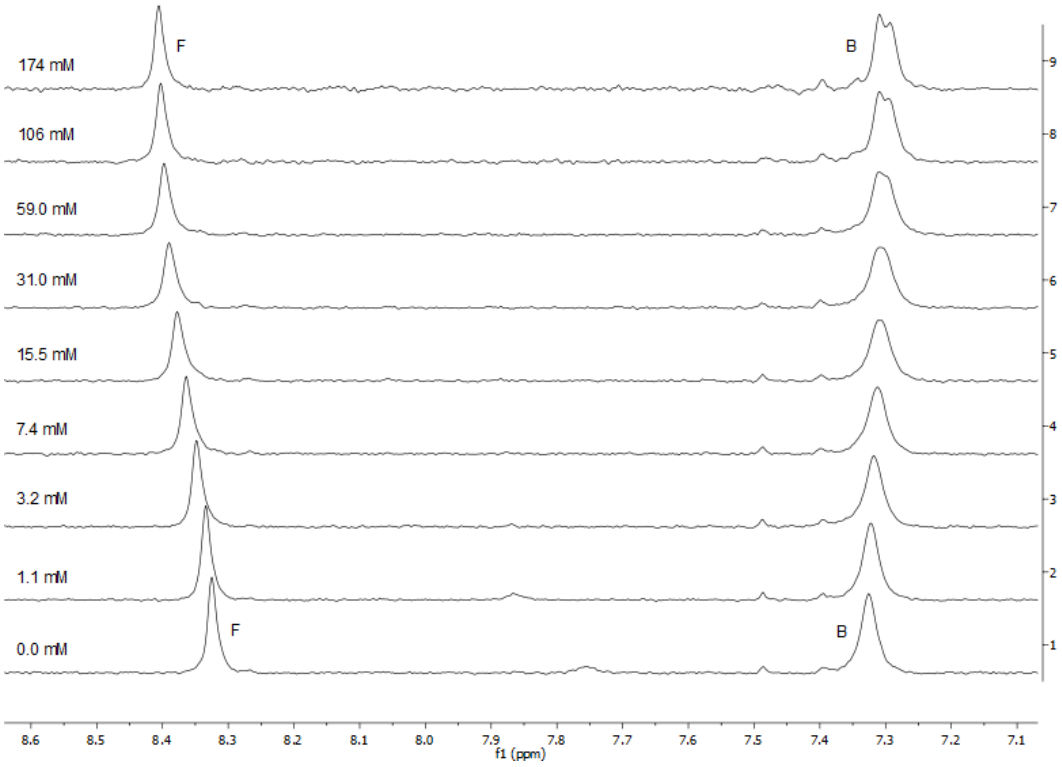


Figure S12- ^{1}H NMR titration of receptor **5** (33 μM) against D-glucose (**6**) in D_2O at 298 K.

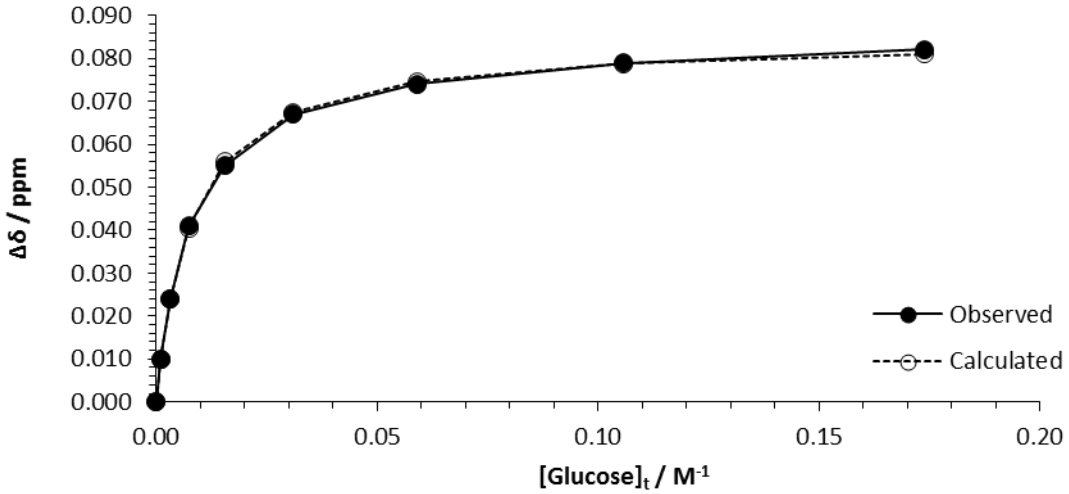


Figure S13- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-glucose (**6**) in D_2O at 298 K (K_a = 124 ± 1 M^{-1} (0.8%)).

Methyl β-D-glucoside (7)

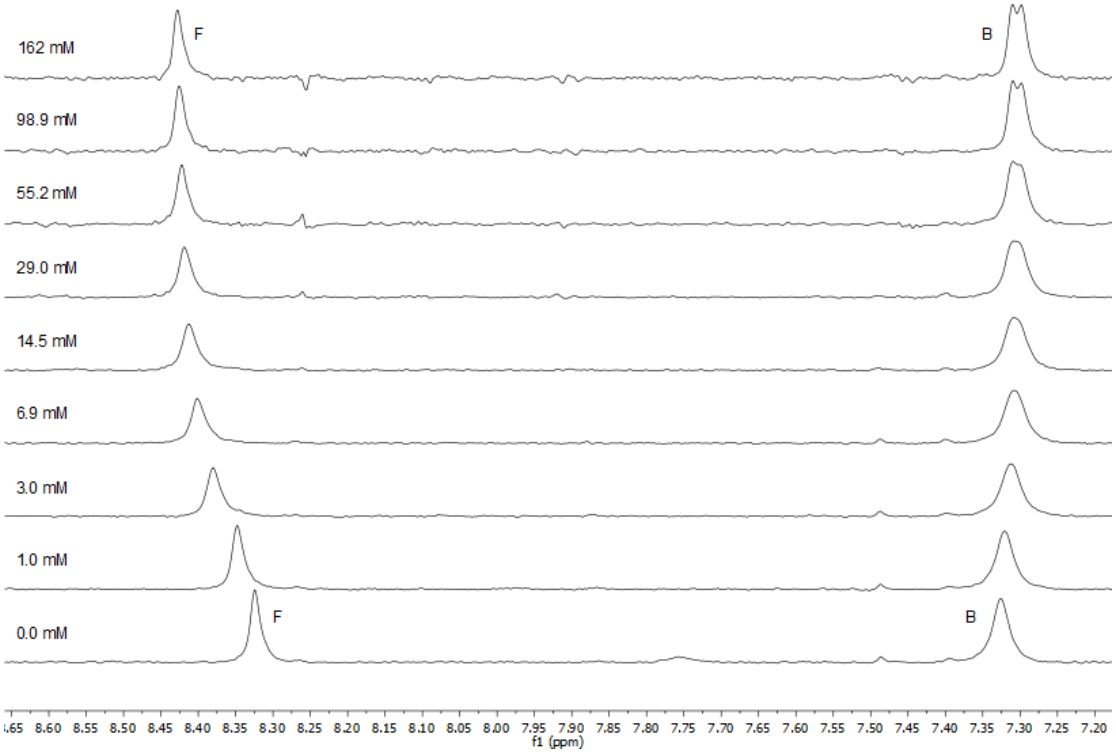


Figure S14- ^{1}H NMR titration of receptor **5** (33 μM) against methyl *β*-D-glucoside (**7**) in D_2O at 298 K.

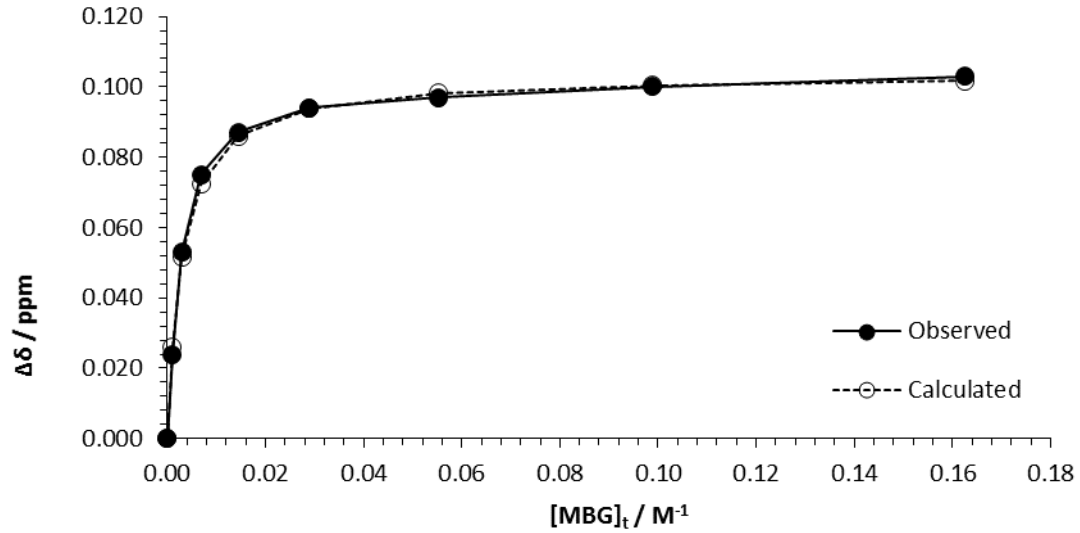


Figure S15- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against methyl *β*-D-glucoside (MBG, **7**) in D_2O at 298 K (K_a = 337 ± 11 M^{-1} (3.3%)).

Methyl *α*-D-glucoside (8)

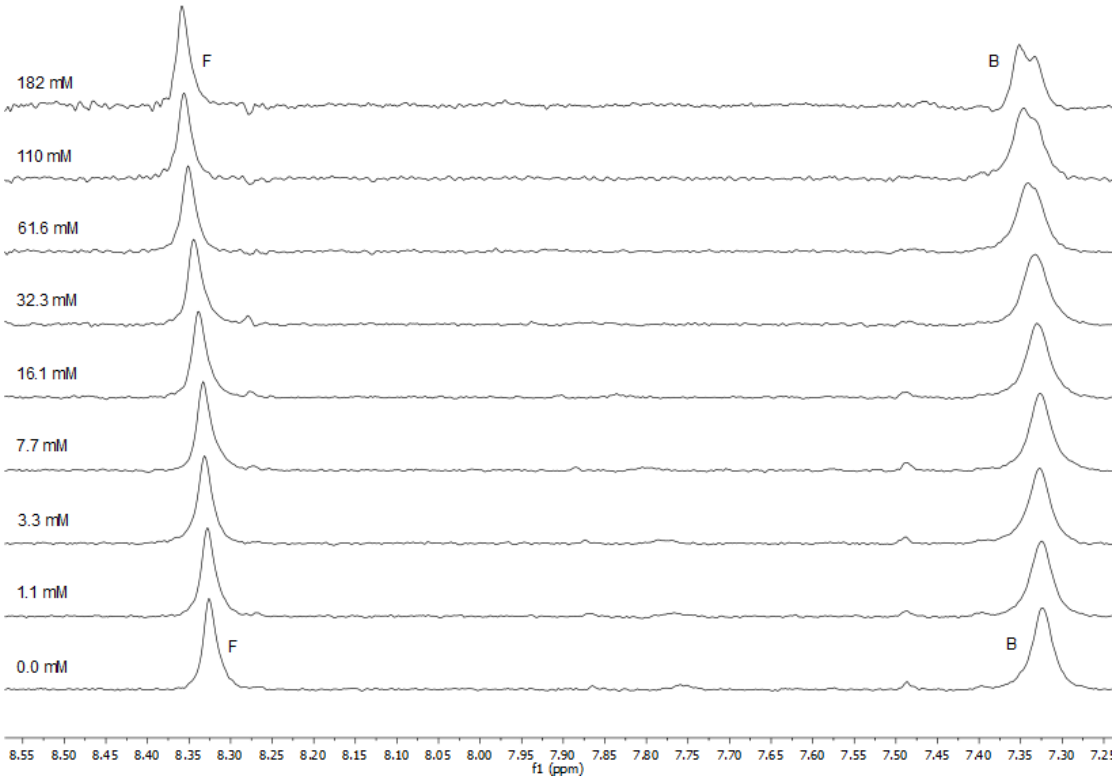


Figure S16- ^{1}H NMR titration of receptor **5** (33 μM) against methyl *α*-D-glucoside (**8**) in D_2O at 298 K.

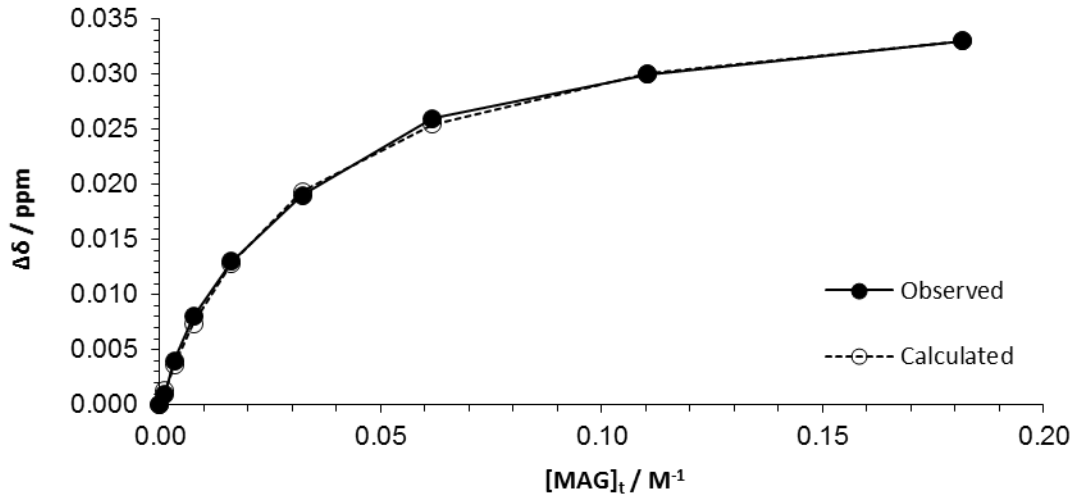


Figure S17- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against methyl *α*-D-glucoside (MAG, **8**) in D_2O at 298 K (K_a = 30 ± 3 M^{-1} (10%)).

***N*-Acetyl-D-glucosamine (GlcNAc, 9)**

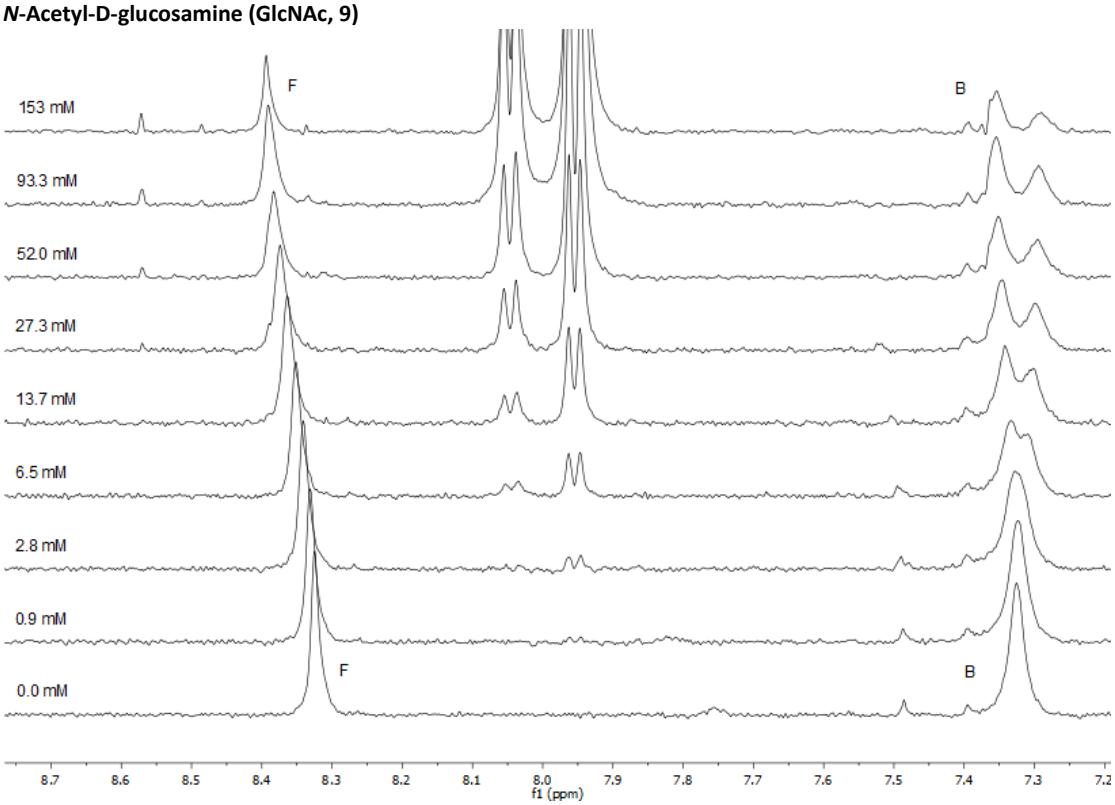


Figure S18- ^{1}H NMR titration of receptor **5** (33 μM) against *N*-acetyl-D-glucosamine (**9**) in D_2O at 298 K.

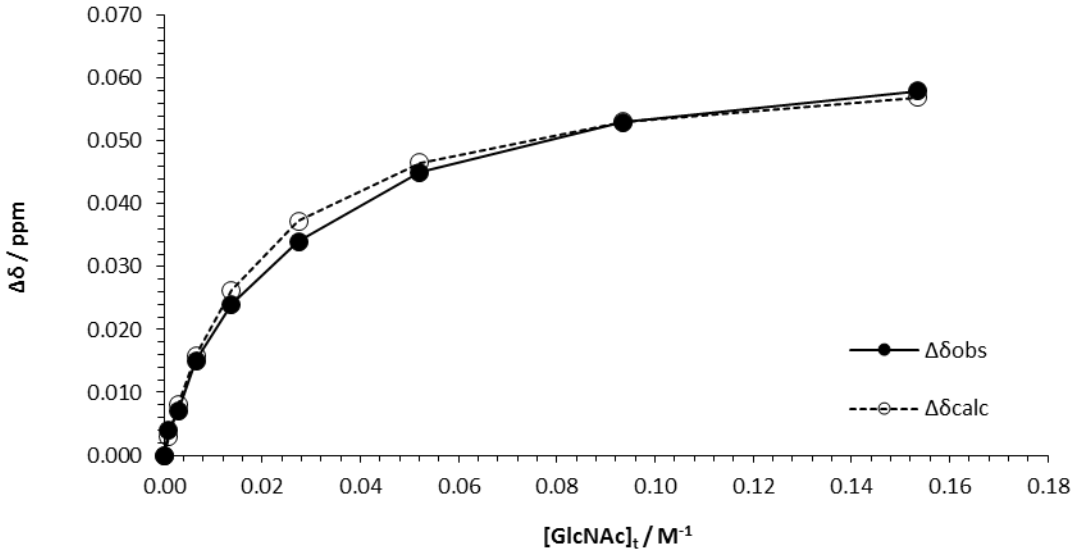


Figure S19- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against *N*-acetyl-D-glucosamine (**9**) in D_2O at 298 K (K_a = 51 ± 8 M^{-1} (16%)).

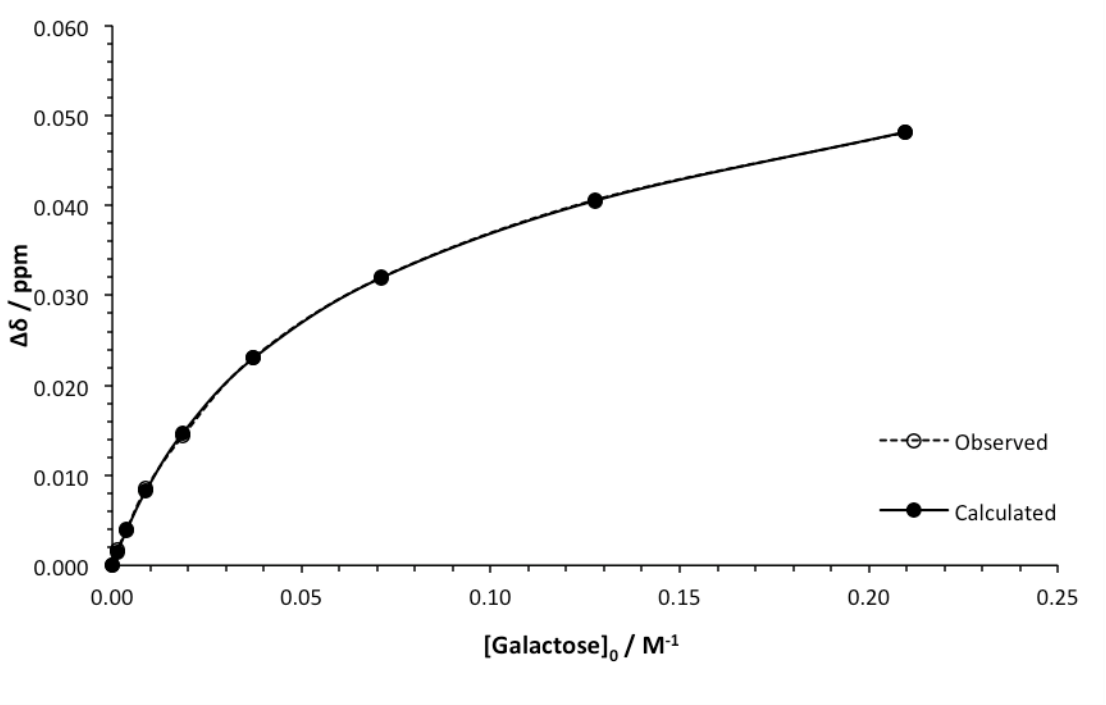


Figure S20- 2:1 Binding isotherm for the titration of receptor **5** (33 μM) against *N*-acetyl-D-glucosamine (**9**) in D_2O at 298 K (K_{11} = 111 ± 9 M^{-1} (8.1%), K_{12} = 1 ± 1 M^{-1} (100%)).

Methyl *N*-acetyl-*β*-D-glucosaminide (10)

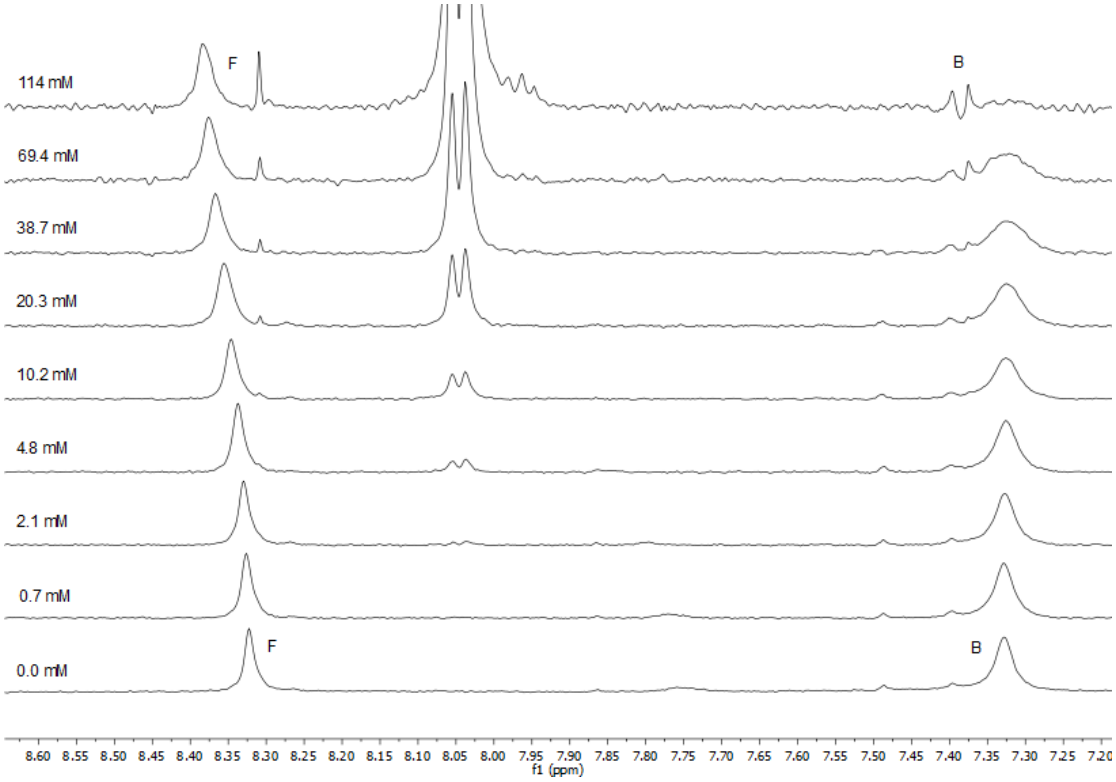


Figure S21- ^{1}H NMR titration of receptor **5** (33 μM) against methyl *N*-acetyl-*β*-D-glucosaminide (**10**) in D_2O at 298 K.

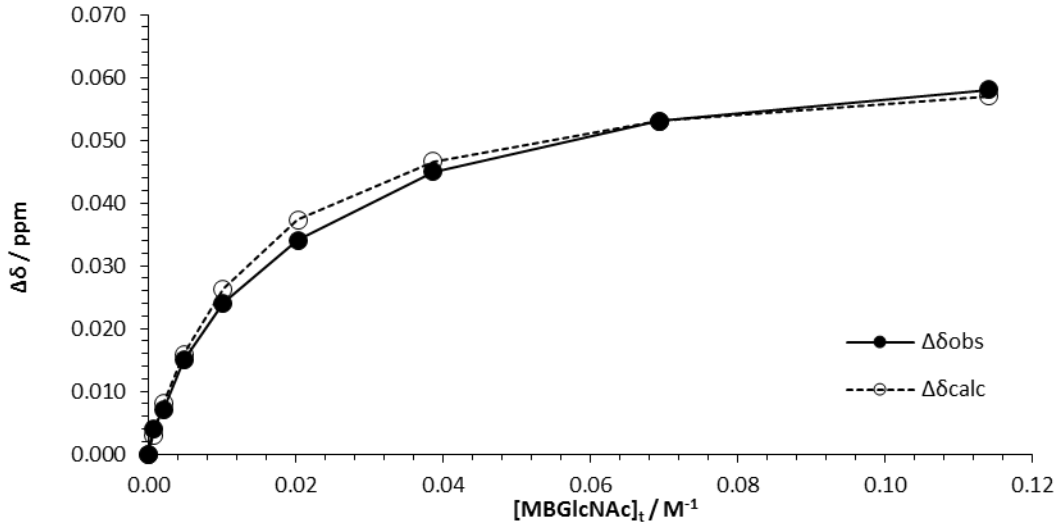


Figure S22- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against methyl N-acetyl-β-D-glucosaminide (MBGlcNAc, **10**) in D_2O at 298 K (K_a = 68 ± 11 M^{-1} (16%)).

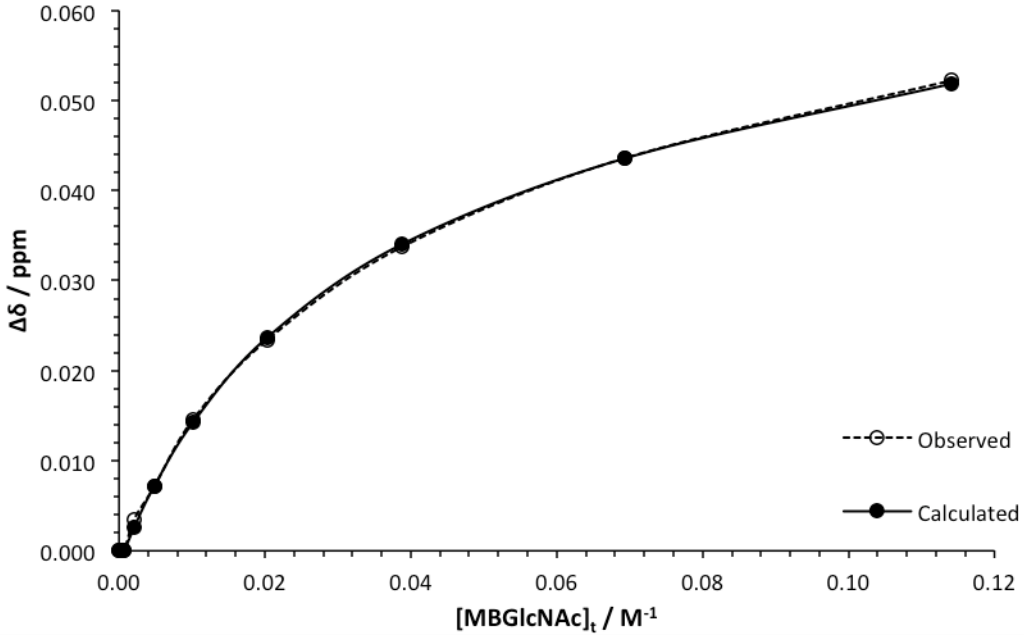


Figure S23- 2:1 Binding isotherm for the titration of receptor **5** (33 μM) against methyl *N*-acetyl-*β*-D-glucosaminide (MBGlcNAc, **10**) in D_2O at 298 K (K_{11} = 74 ± 2 M^{-1} (2.7%), K_{12} = 1 ± 0.1 M^{-1} (10%))**.**

D-Galactose (11)

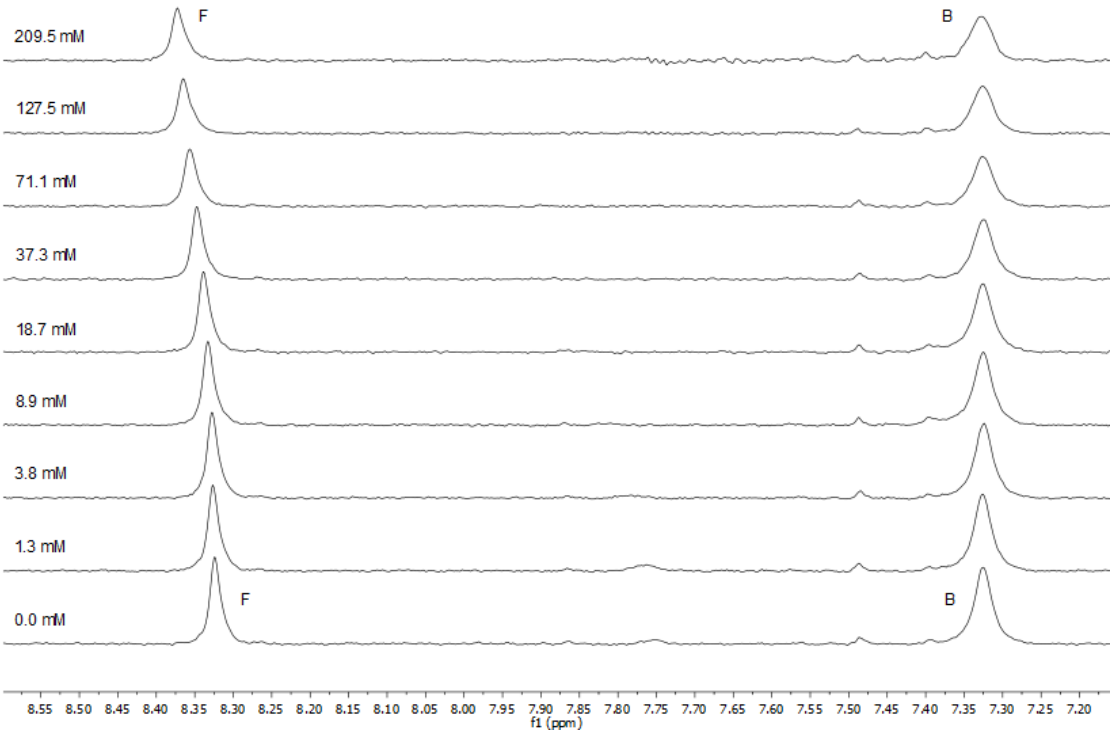


Figure S24- ^{1}H NMR titration of receptor **5** (33 μM) against D-galactose (**11**) in D_2O at 298 K.

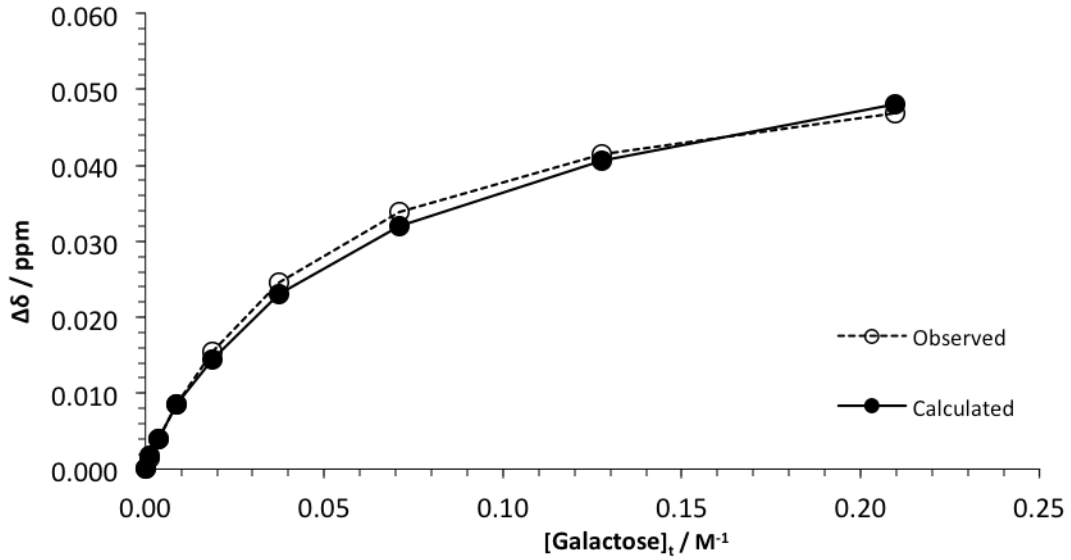


Figure S25- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-galactose (**11**) in D_2O at 298 K (K_a = 19 ± 2 M^{-1} (11%)).

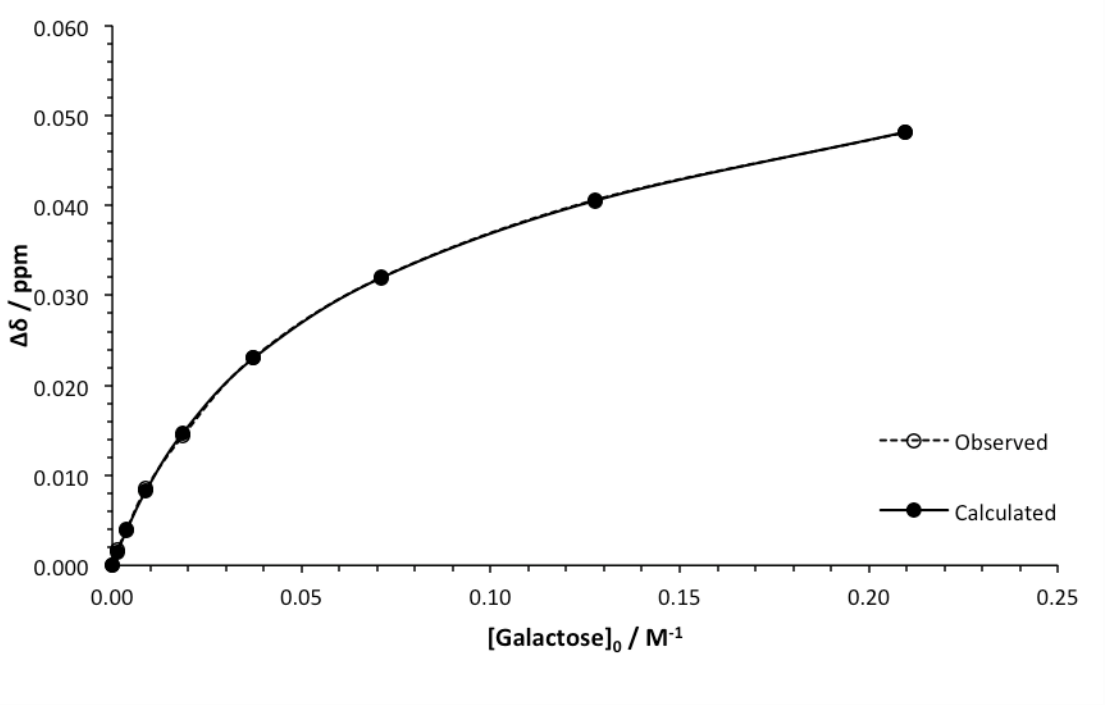


Figure S26- 2:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-galactose (**11**) in D_2O at 298 K (K_{11} = 24 ± 0.5 M^{-1} (0.02%), K_{12} = 1 ± 0.7 M^{-1} (70%)).

D-Mannose (12)

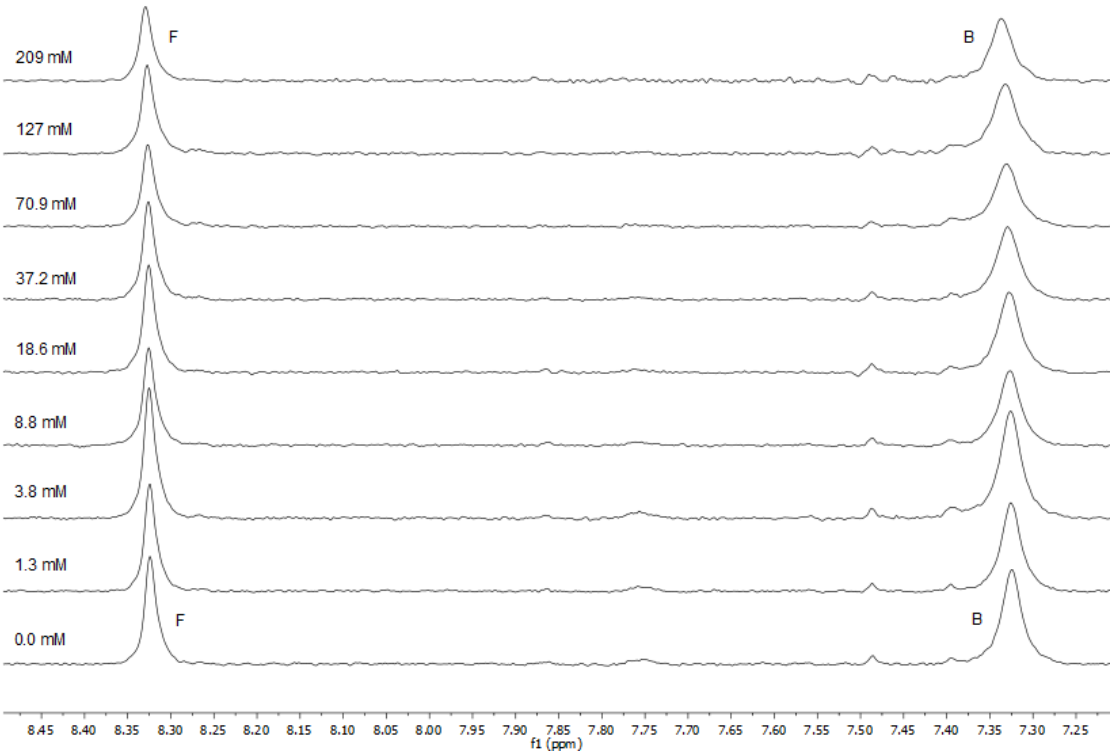


Figure S27- ^{1}H NMR titration of receptor **5** (33 μM) against D-mannose (**12**) in D_2O at 298 K.

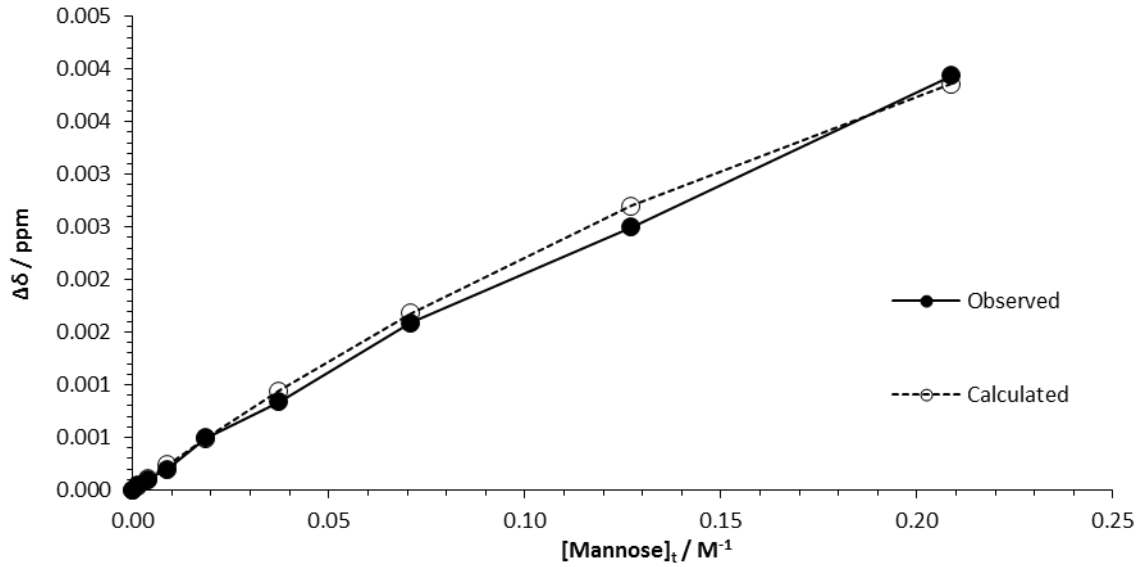


Figure S28- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-mannose (**12**) in D_2O at 298 K (K_a = 2 M^{-1} ± 0.43 M^{-1} (22%)).

D-Cellobiose (13)

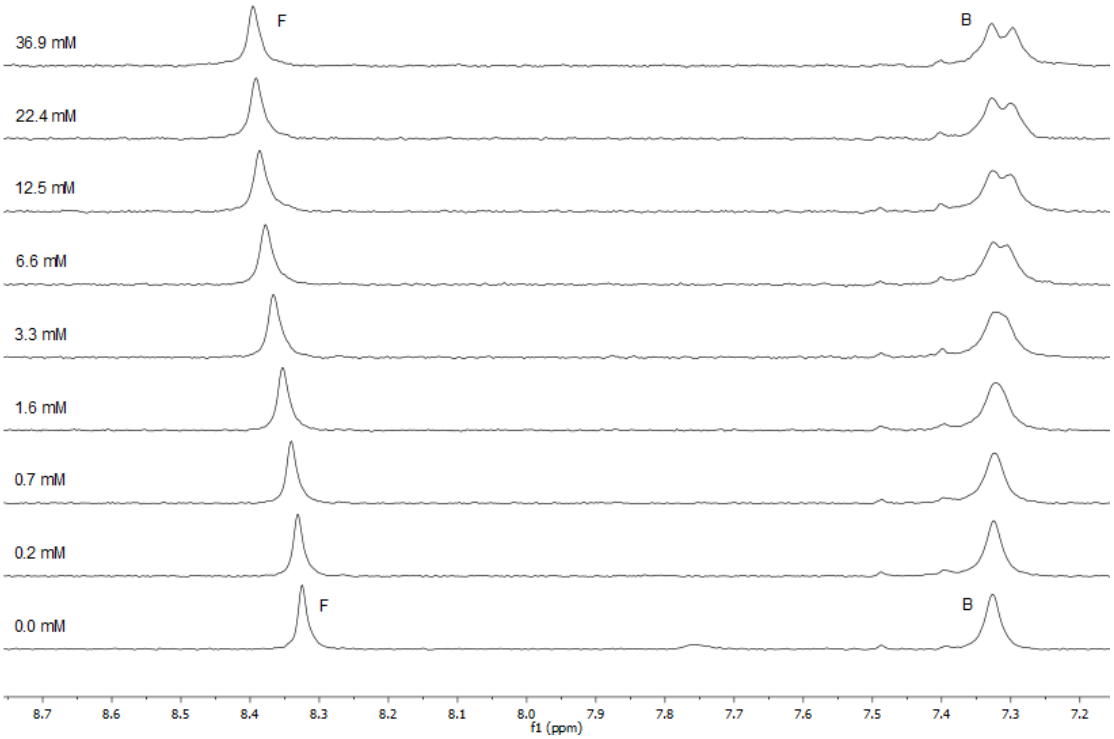


Figure S29- ^{1}H NMR titration of receptor **5** (33 μM) against D-Cellobiose (**13**) in D_2O at 298 K.

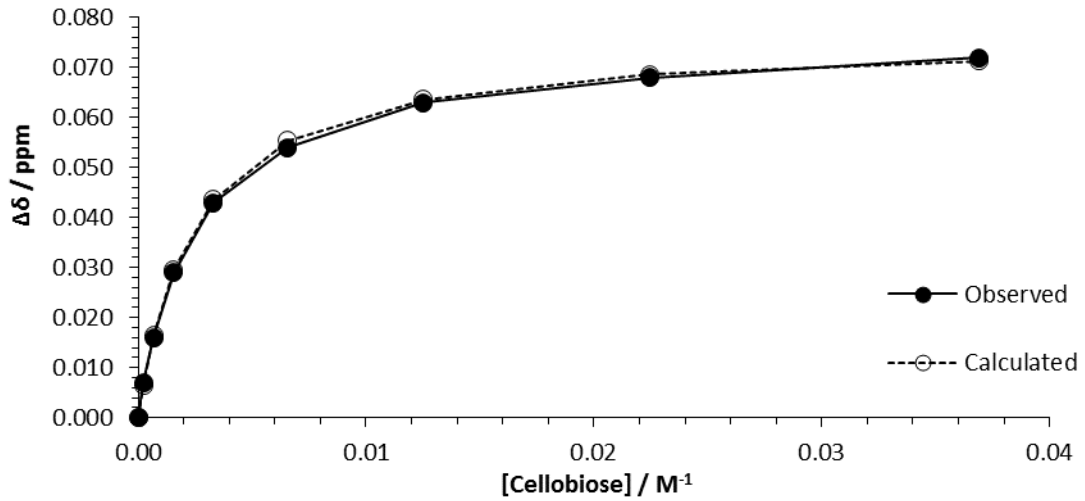


Figure S30- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-cellobiose (**13**) in D_2O at 298 K (K_a = 412 M^{-1} ± 16 M^{-1} (3.8%)).

D-Cellotriose (14)

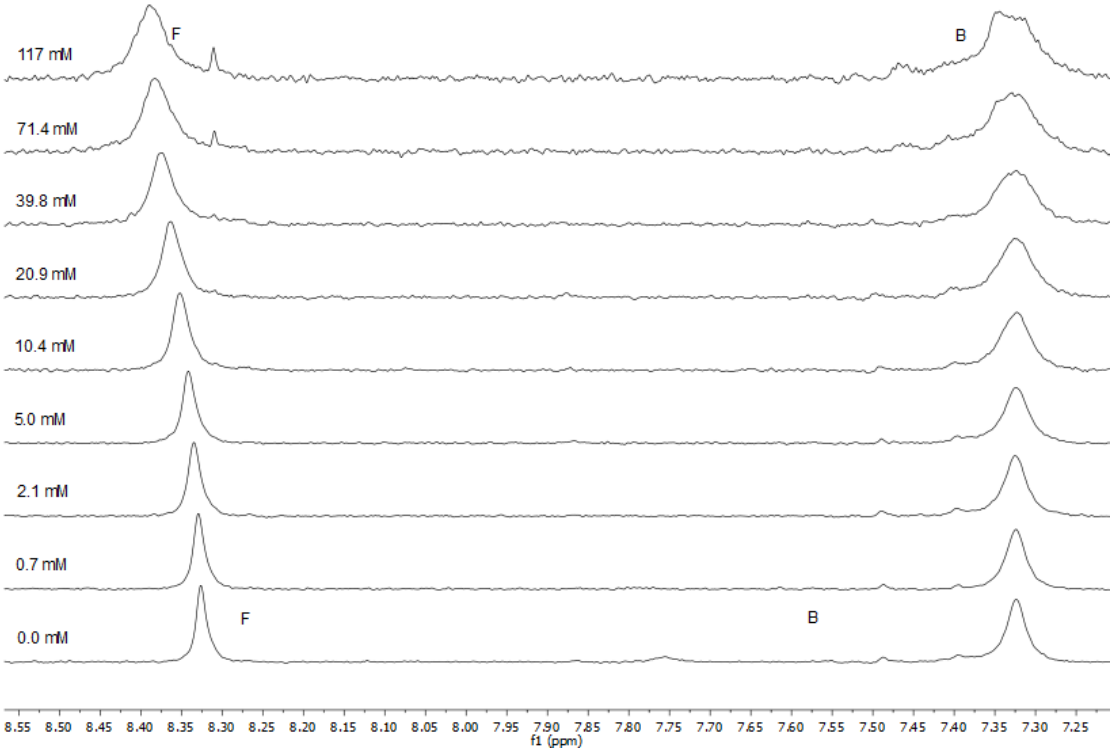


Figure S31- ^{1}H NMR titration of receptor **5** (33 μM) against D-Cellotriose (**14)** in D_2O at 298 K.

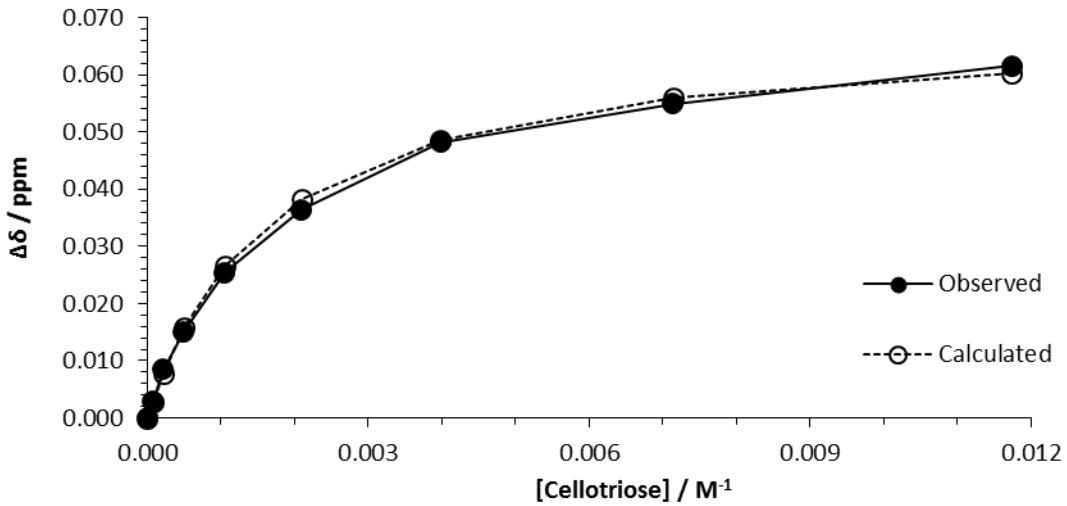


Figure S32-1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-cellotriose (**14**) in D_2O at 298 K (K_a = 608 M^{-1} ± 31 M^{-1} (5.1%)).

D-Cellotetraose (15)

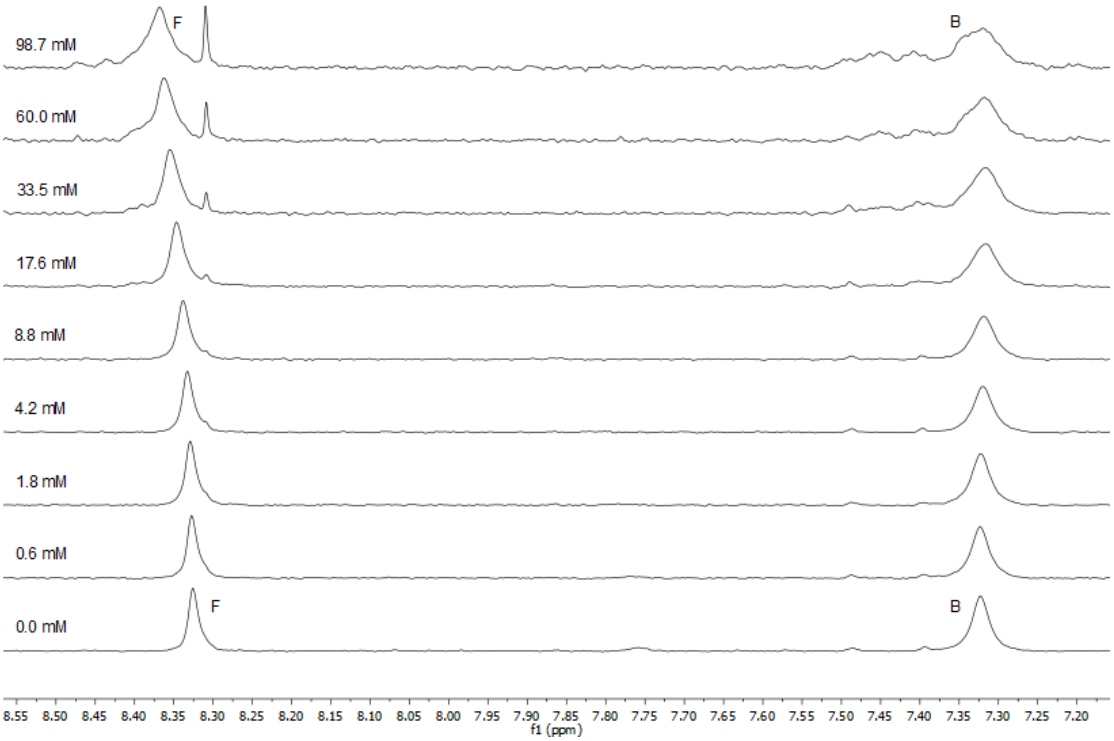


Figure S33- ^{1}H NMR titration of receptor **5** (33 μM) against D-cellotetraose (**15**) in D_2O at 298 K.

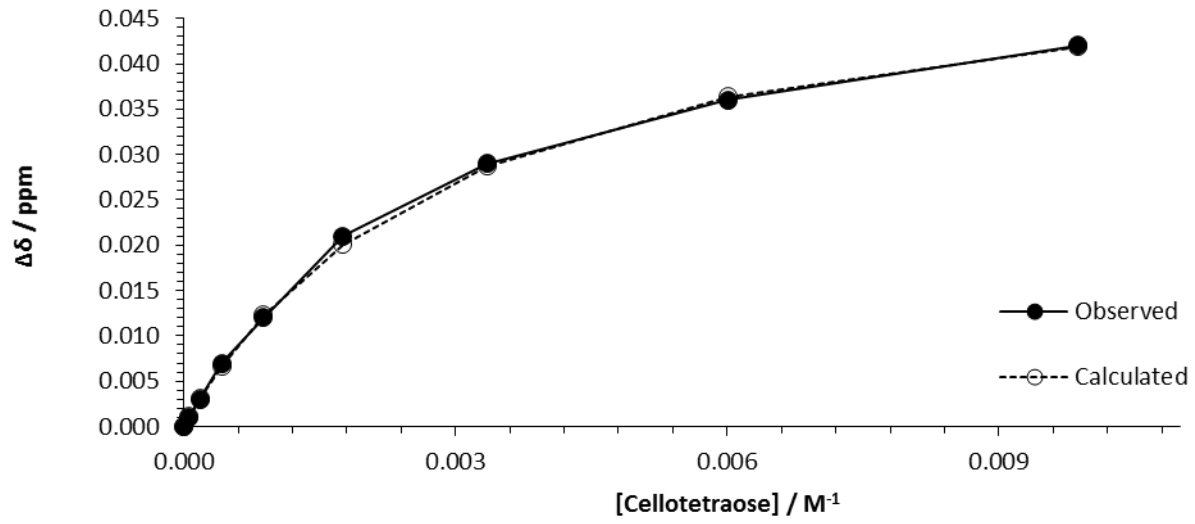


Figure S34- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-ellotetraose (**15**) in D_2O at 298 K (K_a = 333 M^{-1} ± 13 M^{-1} (3.9%)).

D-Lactose (16)

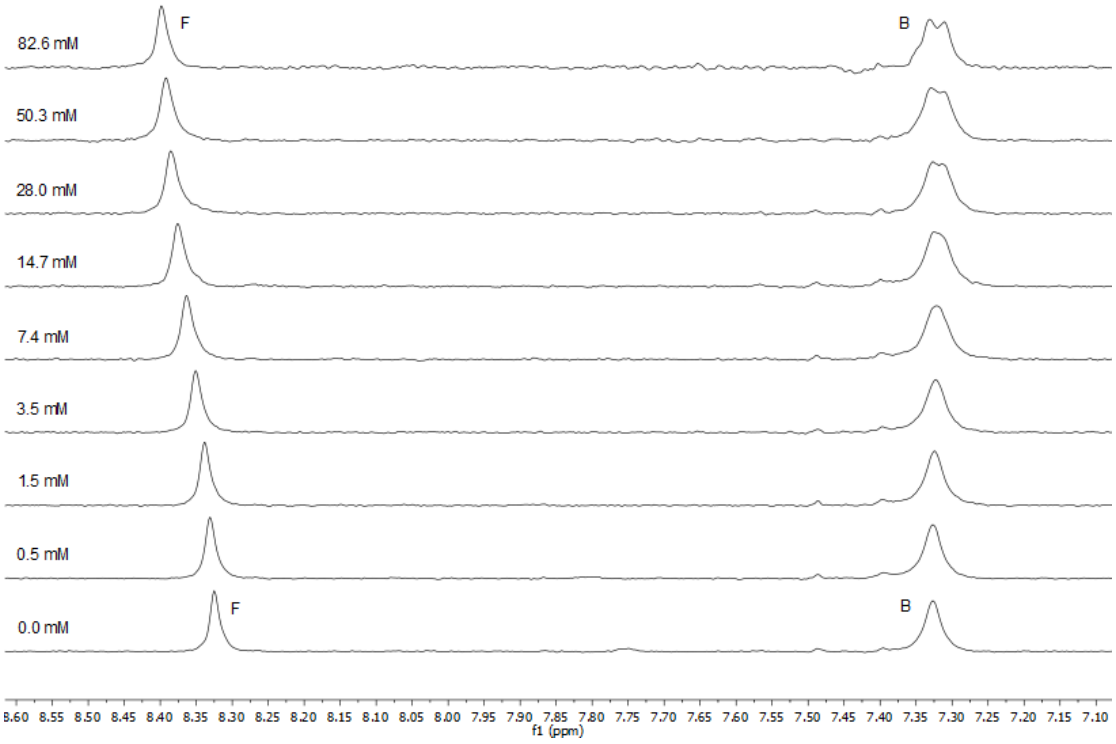


Figure S35- ^{1}H NMR titration of receptor **5** (33 μM) against D-lactose (**16**) in D_2O at 298 K.

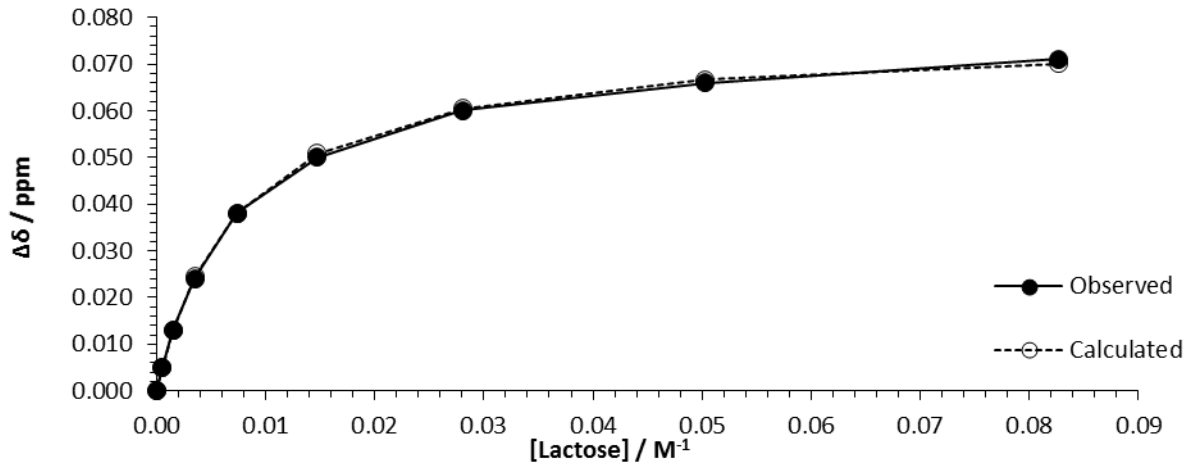


Figure S36- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-lactose (**16**) in D_2O at 298 K (K_a = 135 M^{-1} ± 2.1 M^{-1} (1.6%)).

D-Maltose (17)

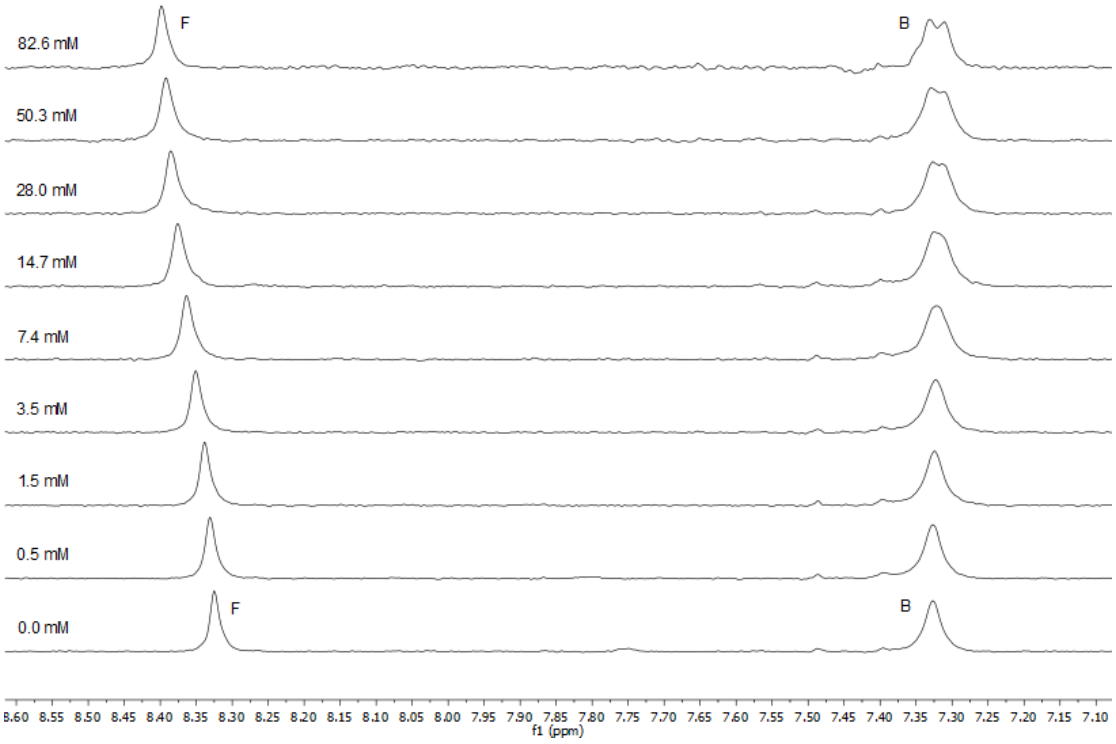


Figure S37- ^{1}H NMR titration of receptor **5** (33 μM) against D-maltose (**17**) in D_2O at 298 K.

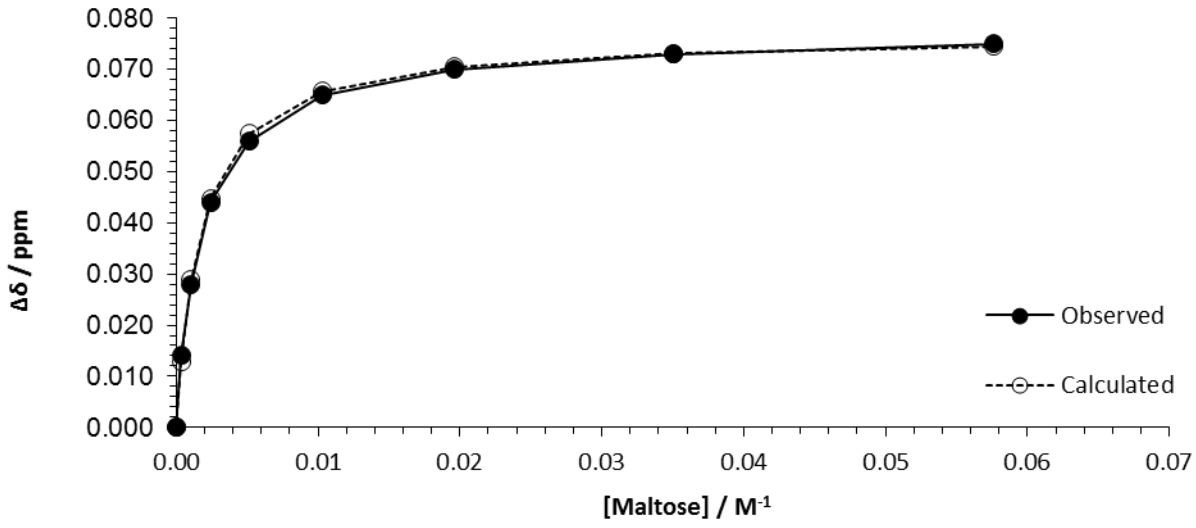


Figure S38- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-maltose (**17**) in D_2O at 298 K (K_a = 579 M^{-1} ± 22 M^{-1} (3.8%)).

D-Maltotriose (18)

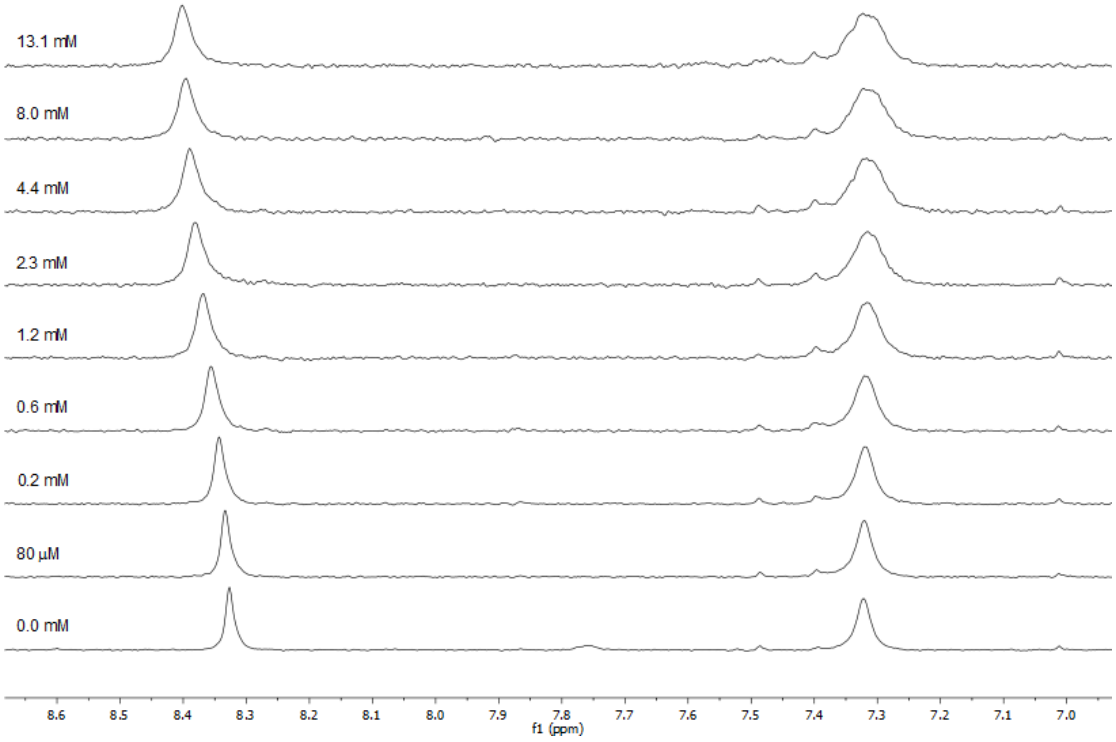


Figure 39- ^{1}H NMR titration of receptor **5** (33 μM) against D-maltotriose (**18**) in D_2O at 298 K.

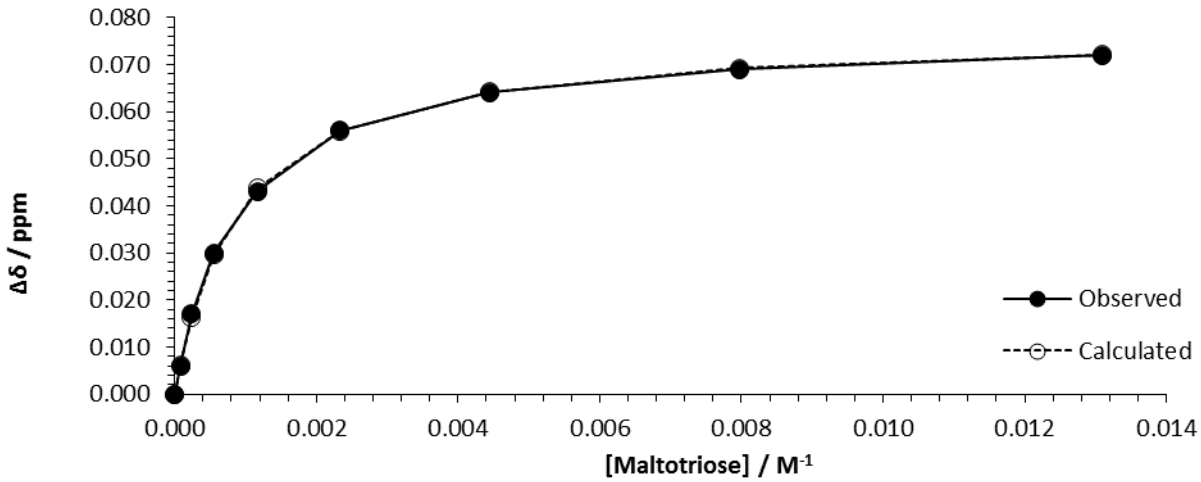


Figure S40- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-maltotriose (**18**) in D_2O at 298 K (K_a = 1149 M^{-1} ± 31 M^{-1} (2.7%)).

D-Maltotetraose (19)

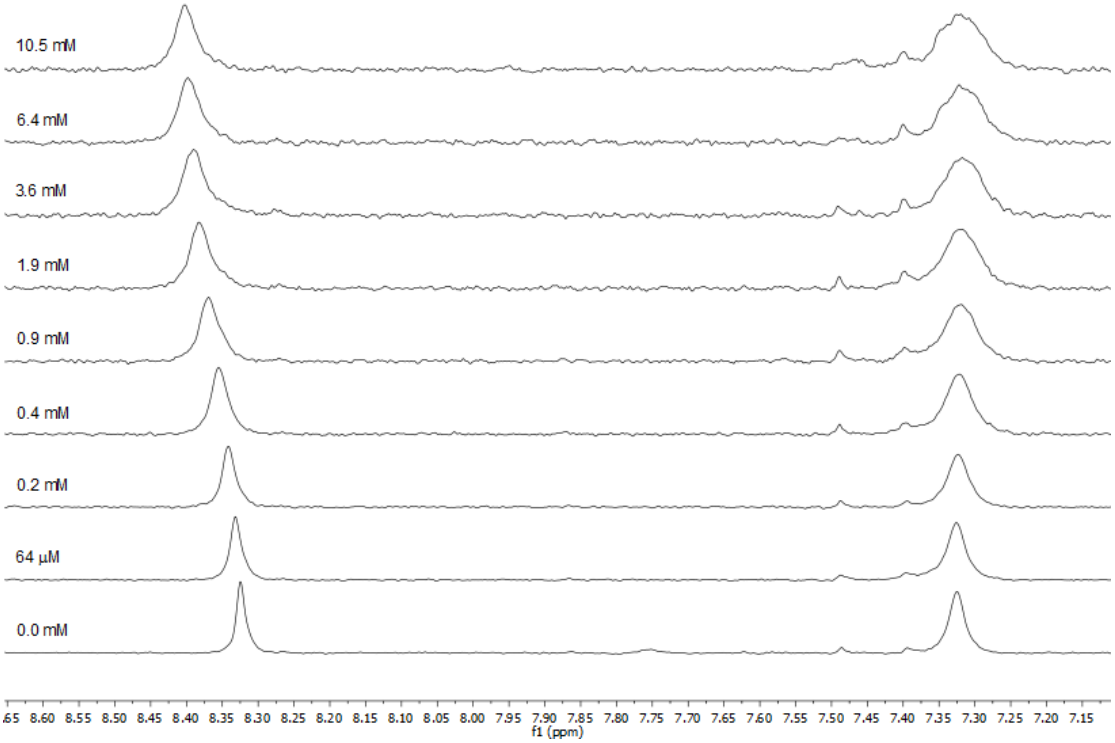


Figure S41- ^{1}H NMR titration of receptor **5** (33 μM) against D-maltotetraose (**19**) in D_2O at 298 K.

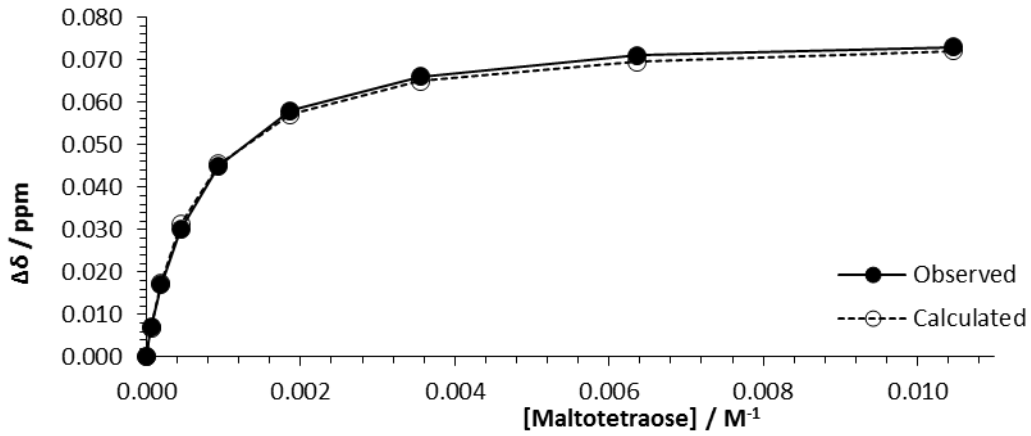


Figure S42- 1:1 Binding isotherm for the titration of receptor **5** (33 μM) against D-maltotetraose (**19**) in D_2O at 298 K (K_a = 1618 M^{-1} ± 39 M^{-1} (2.4%)).

Isothermal titration microcalorimetry (ITC) experiments

ITC methodology

ITC experiments were performed on a MicroCal iTC200 at 298 K. Stock solutions of carbohydrates were made up in pure HPLC grade water and allowed to equilibrate overnight. Receptor solutions were made up in pure HPLC grade water. The sample cell volume was 0.20 mL. Each titration experiment included 25-40 successive injections. Output traces and analyses are shown in Figs. S43-S46. Thermodynamic data in kJ mol^{-1} are summarised in Table S1 (p S35).

D-Glucose (6)

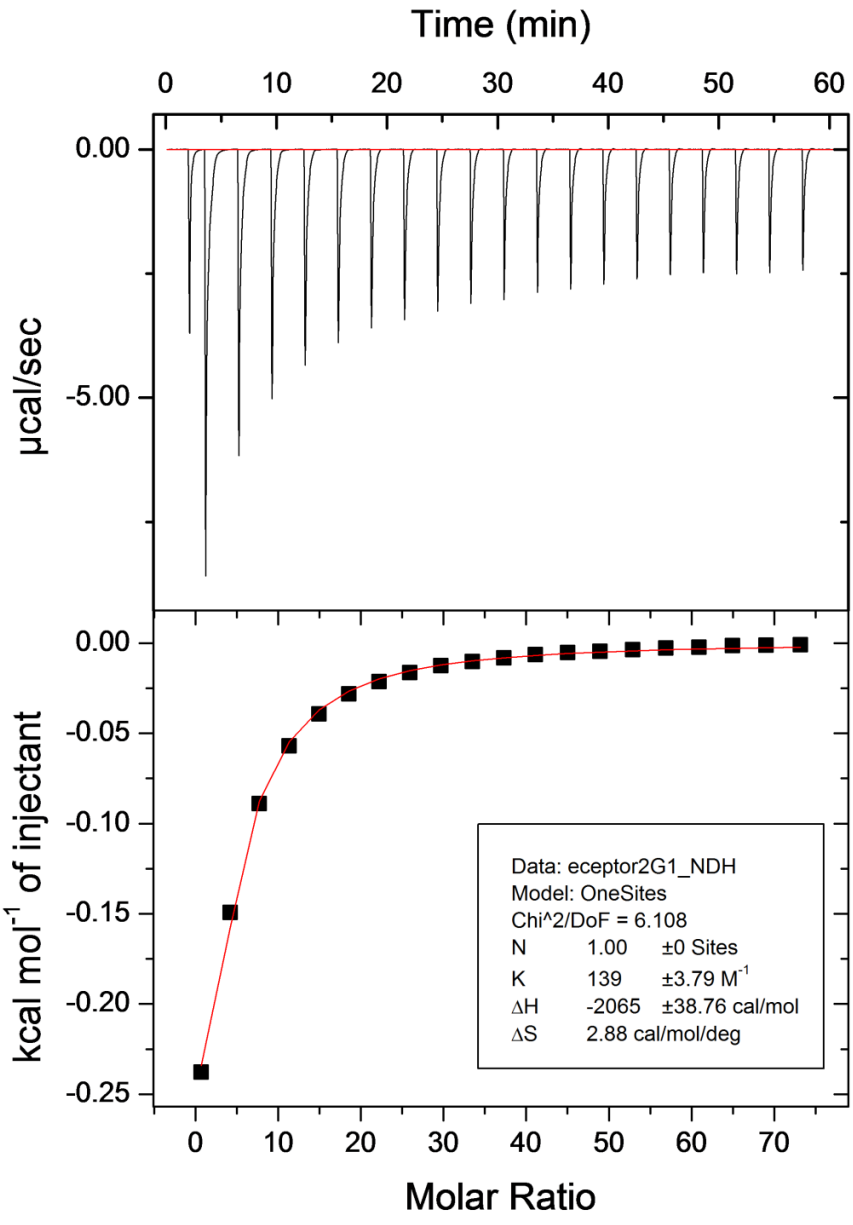


Figure S43 - Output from the ITC experiment for the titration of D-glucose (**6**) (350 mM) to receptor **5** (1.0 mM). The binding affinity is calculated as 139 M^{-1}.

D-Cellobiose (13)

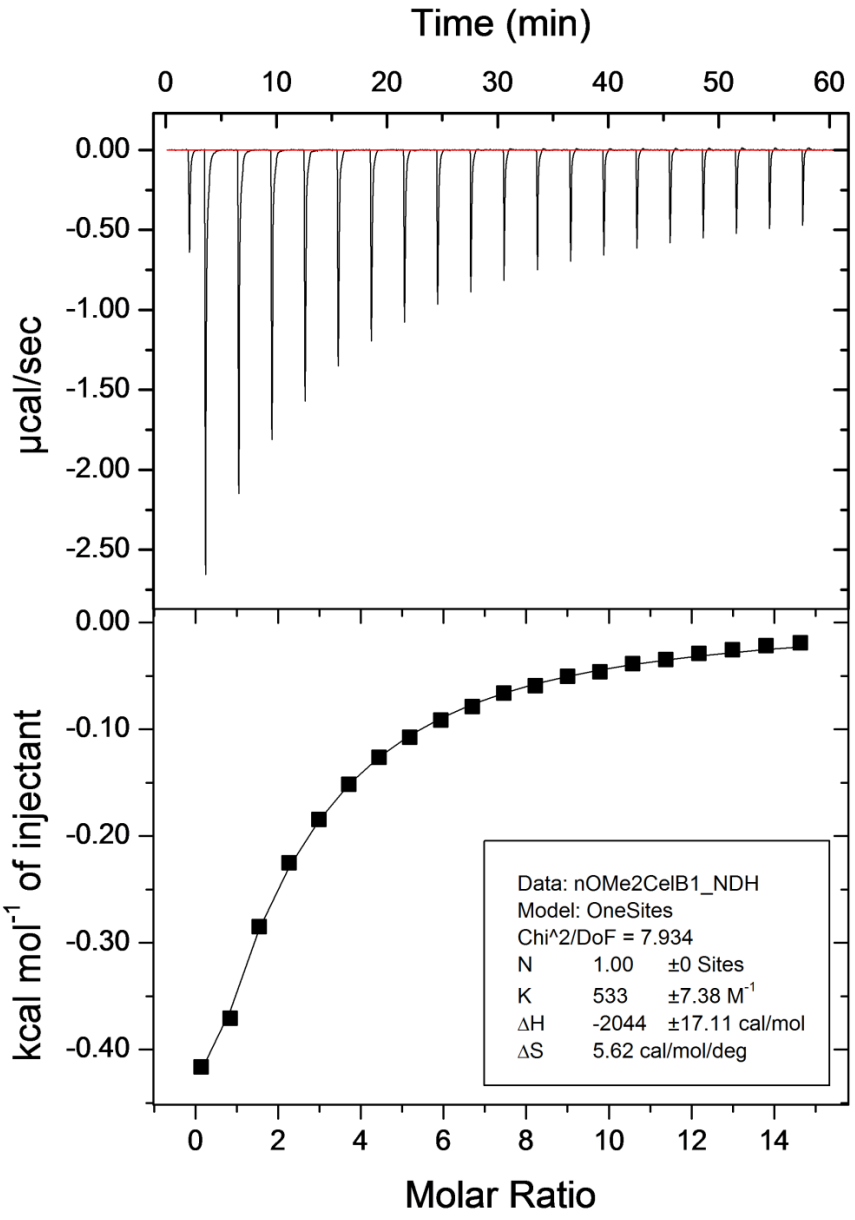


Figure S44 - Output from the ITC experiment for the titration of D-cellobiose (**13**) (50 mM) to receptor **5** (0.5 mM). The binding affinity is calculated as 533 M^{-1}.

D-Maltose (17)

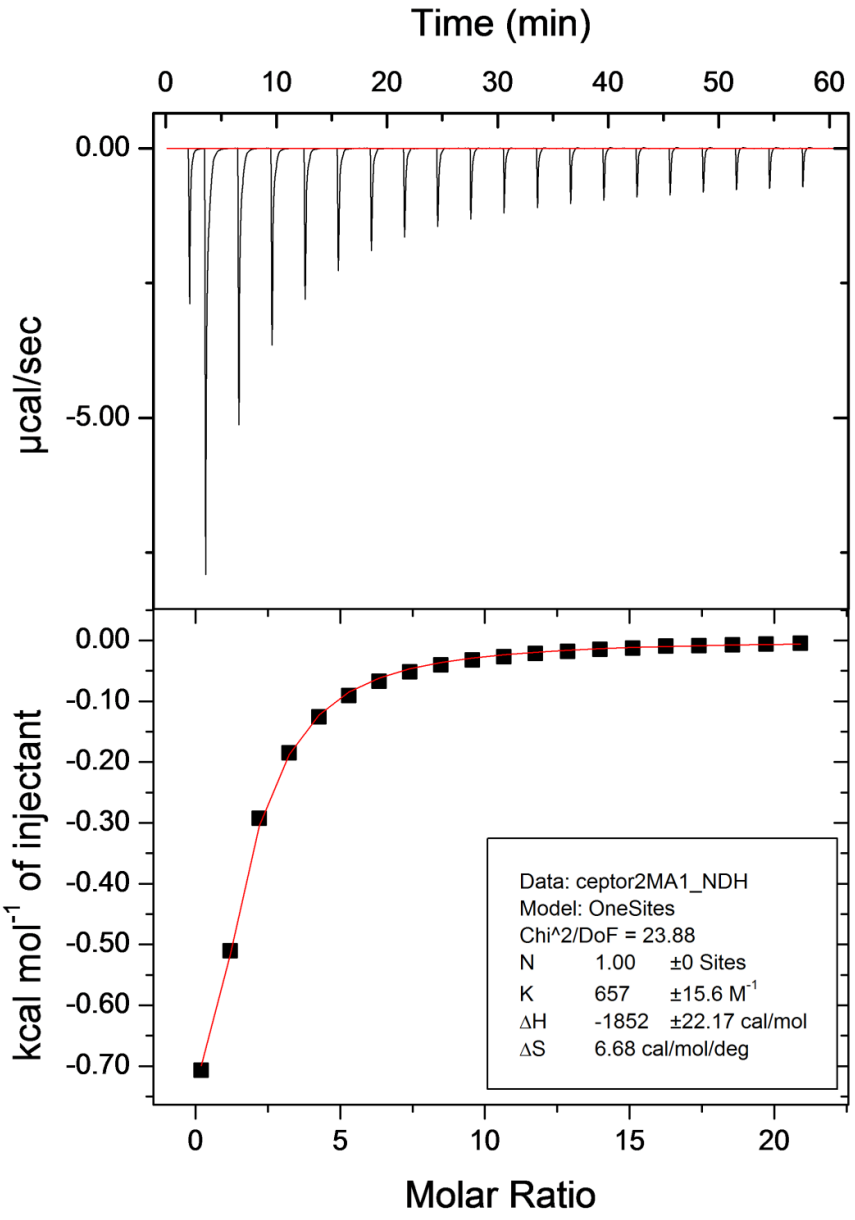


Figure S45 - Output from the ITC experiment for the titration of D-maltose (**17**) (100 mM) to receptor **5** (1.0 mM). The binding affinity is calculated as 657 M^{-1}.

Table S1. Thermodynamic data from ITC binding studies of carbohydrates + **5** in water. T = 298 K.

Substrate	K_a (M^{-1})	ΔG (kJ mol^{-1})	ΔH (kJ mol^{-1})	TΔS (kJmol^{-1})
glucose **6**	139	-12.2	-8.6	3.5
cellobiose **13**	533	-15.6	-8.6	7.0
maltose **17**	657	-16.1	-7.7	8.3

References

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2. A. Müller, M. Raltschewa and M. Papp, *Berichte Dtsch. Chem. Ges. B Ser.*, 1942, **75**, 692–703.
3. R. Wang, M. Zhang, X. Liu, L. Zhang, Z. Kang, W. Wang, X. Wang, F. Dai and D. Sun, *Inorg. Chem.*, 2015, **54**, 6084–6086.
4. H. Destecroix, C. M. Renney, T. J. Mooibroek, T. S. Carter, P. F. N. Stewart, M. P. Crump and A. P. Davis, *Angew. Chem. Int. Ed.*, 2015, **54**, 2057–2061.