Supporting Information

Carbohydrate Receptors Combining both a Macrocyclic Building Block and Flexible Side Arms as Recognition Units: Binding Properties of Compounds with CH₂OH Groups as Side Arms

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1 Description of the binding studies

1.1 \( ^1\)H NMR titrations

\( ^1\)H NMR titrations were carried out in CDCl\(_3\) at 25°C (chloroform was stored over activated molecular sieves and deacidified). Dilution experiments show that the receptors do not self-aggregate in the used concentration range.

Stock solutions in CDCl\(_3\) were prepared for the receptor and sugar. These solutions and the corresponding solvent were combined in a manner so that the concentration of the receptor was kept constant and that of the sugar varied. For each titration 15-20 samples were prepared and the \( ^1\)H NMR spectra were recorded. For each receptor-sugar system at least two \( ^1\)H NMR titrations were carried out.

1.2 Microcalorimetric titrations.

Isothermal titration calorimetry (ITC) measurements were performed in CDCl\(_3\) and water-containing CDCl\(_3\) at 298 K using a power compensation calorimeter VP-ITC (Malvern). A solution of octyl-\( \beta\)-d-glucopyranoside was injected stepwise (8 µL × 30 times) into a dilute solution of receptor (appr. 0.3 mM) in CDCl\(_3\) or water-containing CDCl\(_3\) (0.035 mol/L and 0.07 mol/L \( \text{H}_2\text{O}\) in CDCl\(_3\)). The measured heat rate was recorded as a function of time and converted into enthalpies by integration of the appropriate reaction peaks using NanoAnalyze software provided by TA Instruments. Dilution effects were corrected by subtracting the results of a blank experiment. For each receptor-sugar system at least three titrations were carried out.

It should be noted that initial microcalorimetric studies were performed using microcalorimeter TAM (Thermal Activity Monitor, Thermometrics); however, the required long measurement time (up to 20 h compared with 2 h in the case of VP-ITC) was less favorable for the investigation of the binding processes in chloroform.

1.3 Binding studies in two-phase systems: Liquid-liquid extraction (CDCl\(_3/\text{H}_2\text{O}\))

To study the extraction of monosaccharides from water into organic phase, aqueous sugar solutions (1 M) were equilibrated with the corresponding receptor in chloroform (1 mM solution) at 25 °C. Solutions of receptor in chloroform were then shaken vigorously with aqueous carbohydrate, the phases were separated, and the organic phase was passed through hydrophobic filter paper to remove residual aqueous solution (similar to the procedure used by Davis et al., see references below). The chloroform was evaporated and the residue analysed by \( ^1\)H NMR, first in CDCl\(_3\) and afterwards in DMSO-\( \text{d}_6\) (after the evaporation of CDCl\(_3\)).
Microcalorimetric titrations in water-containing CDCl₃.

2.1 Titration of 13 with 24 in water-containing CDCl₃ (0.035 mol/L H₂O)

**Figure S1.** ITC thermogram (left) and titration curve-fitting (right) of 13 with 24 in water-containing CDCl₃ (0.035 mol/L H₂O). Titration mode: addition of 24 (cₚ₀ = 3.09 mM) into 13 (cₜₖ = 0.30 mM) at 298 K in 30 steps.

2.2 Titration of 13 with 24 in water-containing CDCl₃ (0.07 mol/L H₂O)

**Figure S2.** ITC thermogram (left) and titration curve-fitting (right) of 13 with 24 in water-containing CDCl₃ (0.07 mol/L H₂O). Titration mode: addition of 24 (cₚ₀ = 3.02 mM) into 13 (cₜₖ = 0.30 mM) at 298 K in 30 steps.
2.3 Titration of 12 with 24 in water-containing CDCl₃ (0.035 mol/L H₂O)

![Graph](image)

**Figure S3.** ITC thermogram (left) and titration curve-fitting (right) of 12 with 24 in water-containing CDCl₃ (0.035 mol/L H₂O). Titration mode: addition of 24 (cₛyringe = 3.01 mM) into 12 (c_cell = 0.30 mM) at 298 K in 30 steps.

2.4 Titration of 13 with 24 in water-containing CDCl₃ (0.035 mol/L H₂O)

![Graph](image)

**Figure S4.** ITC thermogram (left) and titration curve-fitting (right) of 12 with 24 in water-containing CDCl₃ (0.07 mol/L H₂O). Titration mode: addition of 24 (cₛyringe = 3.01 mM) into 12 (c_cell = 0.30 mM) at 298 K in 30 steps.
3 Molecular modelling calculations (examples)

Program MacroModel V.8.5, OPLS 2001 force field, MCMM, 50000 steps.

Figure S5. Energy-minimized structure of the 1:1 complex formed between 13 and octyl-β-glucoside 24. Shown are three structures with lowest energy: (a) octyl chain of 24 between the bridges, (b) octyl chain next to the bridges.

Figure S6. Examples of energy-minimized structures of compound 12 (Color code: N, blue; O, red; C, gray). The possible intramolecular OH···O, NH···O and NH···π interactions are shown as broken lines.
Figure S7. (a) Energy-minimized structure of 13 with marked intramolecular OH···O and NH···O hydrogen bonds indicated by the calculations. (b) Energy-minimized structure of the 1:1 complex formed between 13 and octyl β-glucoside 24.

4 ROESY experiments for 13•24 and 14•24
Figure S8. Partial ROESY spectrum of receptor 13 (a) and 14 (b) (1 mM) with β-glucoside 24 (1 mM) showing intermolecular connections between carbohydrate and receptor (mixing time = 165 ms)
5. $^1$H and $^{13}$C NMR spectra of compounds 12-14, 17 and 18.

5.1. $^1$H and $^{13}$C NMR spectra of compound 12.

Figure S9. $^1$H NMR spectrum of compound 12 in CDCl$_3$.

Figure S10. $^{13}$C NMR spectrum of compound 12 in CDCl$_3$. 
5.2. $^1$H and $^{13}$C NMR spectra of compound 13.

**Figure S11a.** $^1$H NMR spectrum of compound 13 in CDCl$_3$ (0.3 mM).

**Figure S11b.** $^1$H NMR spectrum of compound 13 in CDCl$_3$ (≈ 1 mM).
Figure S12. $^{13}$C NMR spectrum of compound 13 in CDCl$_3$.

5.3 $^1$H and $^{13}$C NMR spectra of compound 14.

Figure S13. $^1$H NMR spectrum of compound 14 in CDCl$_3$. 
Figure S14. $^{13}$C NMR spectrum of compound 14 in CDCl$_3$.

5.4 $^1$H and $^{13}$C NMR spectra of compound 17.

Figure S15. $^1$H NMR spectrum of 17 in CDCl$_3$. 
Figure S16. $^{13}$C NMR spectrum of 17 in CDCl$_3$. 
5.5 $^1$H and $^{13}$C NMR spectra of compound 18.

Figure S17. $^1$H NMR spectrum of 18 in CDCl$_3$.

Figure S18. $^{13}$C NMR spectrum of 18 in CDCl$_3$/CD$_3$OD 50:1 (v/v).