Compounds based on a triethyl- or trimethoxybenzene scaffold bearing pyrazole, pyridine and pyrimidine groups: Syntheses and representative binding studies towards carbohydrates

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1. $^1$H NMR titrations of compound 2 with the tested carbohydrates (Figure S1)
2. Representative WinEQNMR plots (Figures S2 and S3)
3. Representative mole ratio plots (Figures S4-S9)
4. Crystallographic data (Tables S1-S3)
5. Molecular modeling calculations (Figure S15)
6. $^1$H and $^{13}$C NMR spectra of compounds 1-12 (Figures S12a/b-S23a/b)
1. $^1$H NMR titrations of compound 2 with the tested carbohydrates (examples).

![Figure S1](image1.png)

**Figure S1.** Partial $^1$H NMR spectra (CDCl$_3$, 400 MHz) of compound 2 after the addition of 0.00 – 5.00 equiv of (a) β-glucoside 37 and (b) β-galactoside 38; [2] = 1.01 mM. Shown are $-CH_2-NH$-pyridine signals of 2.

2. Plots of the chemical shifts of the receptor resonances as a function of added carbohydrate (WinEQNMR program).

![Figure S2](image2.png)

**Figure S2.** Plot of the observed chemical shifts of the NH resonances of 2 as a function of added β-glucoside 37 in CDCl$_3$ ("mixed" 1:1 and 2:1 receptor-sugar binding model).

![Figure S3](image3.png)

**Figure S3.** Plot of the observed chemical shifts of the NH resonances of 2 as a function of added β-galactoside 38 in CDCl$_3$ ("mixed" 1:1 and 1:2 receptor-sugar binding model).
Representative mole ratio plots.

Figure S4. Mole ratio plot: Titration of compound 2 with β-glucoside 37 in CDCl₃ (analysis of the complexation-induced shift of the NH signal of 2).

Figure S5. Mole ratio plot: Titration of compound 2 with β-glucoside 37 in CDCl₃ (analysis of the complexation-induced shift of the pyrazole-CH signal of 2).

Figure S6. Mole ratio plot: Titration of compound 2 with β-glucoside 37 in CDCl₃ (analysis of the complexation-induced shift of the second pyrazole-CH signal of 2).
**Figure S7.** Mole ratio plot: Titration of compound 2 with β-galactoside 38 in CDCl₃ (analysis of the complexation-induced shift of the NH-signal of 2).

**Figure S8.** Mole ratio plot: Titration of compound 2 with β-galactoside 38 in CDCl₃ (analysis of the complexation-induced shift of the methyl-pyrazole-signal of 2).

**Figure S9.** Mole ratio plot: Titration of compound 2 with β-galactoside 38 in CDCl₃ (analysis of the complexation-induced shift of the pyrazole-CH signal of 2).
4. Crystallographic data (Tables S1 – S3).

**Table S1.** Crystallographic and structure refinement data of compound 5.

<table>
<thead>
<tr>
<th>Compound</th>
</tr>
</thead>
</table>
| **Empirical formula** | **C$_{324}$H$_{45}$N$_{9}$ · CHCl$_{3}$**  
| **Formula weight** | 675.14  
| **Crystal system** | Triclinic  
| **Space group** | $P-1$  
| $a$ (Å) | 10.9296(8)  
| $b$ (Å) | 12.9710(9)  
| $c$ (Å) | 13.4323(8)  
| $\alpha$ (°) | 80.199(2)  
| $\beta$ (°) | 80.299(2)  
| $\gamma$ (°) | 71.803(2)  
| $V$ (Å$^3$) | 1769.0(2)  
| **Z** | 2  
| **$F$(000)** | 716  
| **$D_c$ (Mg m$^{-3}$)** | 1.267  
| **$\mu$ (mm$^{-1}$)** | 0.296  
| **Data collection** |  
| **Temperature (K)** | 100(2)  
| **No. of collected reflections** | 30661  
| **within the $\theta$-limit (°)** | 2.1 – 27.1  
| **Index ranges $\pm h, \pm k, \pm l$** | -14/14, -16/16, -16/17  
| **No. of unique reflections** | 7730  
| **$R_{int}$** | 0.0246  
| **Refinement calculations: full-matrix least-squares on all $F^2$ values** |  
| **Weighting expression $w$** | $(\sigma^2(F_o^2) + 0.0437P)^{1/2}/1.1784P$  
| **No. of refined parameters** | 430  
| **No. of $F$ values used [$F>2\sigma(F)$]** | 4444  
| **Final $R$-Indices** |  
| $R_1 = \Sigma|\Delta F|/\Sigma F_0$ | 0.0403  
| $wR^2$ on $F^2$ | 0.1049  
| $S$ (Goodness of fit on $F^2$) | 1.040  
| Final $\Delta \rho_{max}/\Delta \rho_{min}$ ($\rho$ Å$^{-3}$) | 0.41/0.54  

$P = (F_o^2 + 2F_c^2)/3$

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S5
Table S2. Selected conformational parameters of 5.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dihedral angles (°)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mpln(A)/mpln(B)</td>
</tr>
<tr>
<td></td>
<td>mpln(A)/mpln(C)</td>
</tr>
<tr>
<td></td>
<td>mpln(A)/mpln(D)</td>
</tr>
<tr>
<td></td>
<td>mpln(B)/mpln(C)</td>
</tr>
<tr>
<td></td>
<td>mpln(B)/mpln(D)</td>
</tr>
<tr>
<td></td>
<td>mpln(C)/mpln(D)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Torsion angles (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(2)-C(13)-N(1)-C(14)</td>
</tr>
<tr>
<td>C(13)-N(1)-C(14)-N(2)</td>
</tr>
<tr>
<td>C(4)-C(20)-N(4)-C(21)</td>
</tr>
<tr>
<td>C(20)-N(4)-C(21)-N(5)</td>
</tr>
<tr>
<td>C(6)-C(27)-N(7)-C(28)</td>
</tr>
<tr>
<td>C(27)-N(7)-C(28)-C(29)</td>
</tr>
<tr>
<td>N(7)-C(28)-C(29)-N(8)</td>
</tr>
</tbody>
</table>

\(^a\) mpln means mean plane through the aromatic ring.

Table S3. Geometric parameters for hydrogen bond type contacts of compound 5.

<table>
<thead>
<tr>
<th>Atoms involved</th>
<th>Symmetry</th>
<th>Distance /Å</th>
<th>Angle /°</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-H···A</td>
<td></td>
<td>D-H</td>
<td>D···A</td>
</tr>
<tr>
<td>N(1)-H(1)···N(8)</td>
<td>1-x, 1-y, -z</td>
<td>0.88(1)</td>
<td>2.985(2)</td>
</tr>
<tr>
<td>N(4)-H(4)···N(7)</td>
<td>1-x, 1-y, -z</td>
<td>0.88(1)</td>
<td>2.937(2)</td>
</tr>
<tr>
<td>N(9)-H(9)···N(2)</td>
<td>1-x, 1-y, -z</td>
<td>0.89(1)</td>
<td>2.886(2)</td>
</tr>
<tr>
<td>C(11)-H(11A)···N(8)</td>
<td>x, y, z</td>
<td>0.99</td>
<td>3.512(2)</td>
</tr>
<tr>
<td>C(1A)-H(1A)···centroid(D)(^a)</td>
<td>-1+x, y, 1+z</td>
<td>1.00</td>
<td>3.635(2)</td>
</tr>
</tbody>
</table>

\(^a\) Means centre of the aromatic ring. Ring D: N(8),N(9),C(29)…C(31).
5. Molecular modeling calculations (examples).

a) [Image description: Energy-minimized structure of the 1:1 complex formed between 7 and methyl β-D-glucopyranoside (MacroModel V.9.8, OPLS_2001 force field, MCMM, 50000 steps. Color code: receptor N, blue; receptor C, grey; receptor N, red; the sugar molecule is highlighted in orange).]

b) [Image description: Examples of hydrogen bonds in the complex (schematic illustration).]

**Figure S10.** (a) Energy-minimized structure of the 1:1 complex formed between 7 and methyl β-D-glucopyranoside (MacroModel V.9.8, OPLS_2001 force field, MCMM, 50000 steps. Color code: receptor N, blue; receptor C, grey; receptor N, red; the sugar molecule is highlighted in orange). (b) Examples of hydrogen bonds in the complex (schematic illustration).

**Figure S11.** Energy-minimized structure of 11 (MacroModel V.9.8, OPLS_2001 force field, MCMM, 50000 steps).
6. $^1$H and $^{13}$C NMR spectra of compounds 1-12 (Figures S12-S24).

Figure S12a. $^1$H NMR spectrum of 1 in CDCl$_3$ (0.05 M).

Figure S12b. $^{13}$C NMR spectrum of 1 in CDCl$_3$. 
Figure S13a. $^1$H NMR spectrum of 2 in CDCl$_3$.

Figure S13b. $^{13}$C NMR spectrum of 2 in CDCl$_3$. 
Figure S14a. $^1$H NMR spectrum of 3 in CDCl$_3$.

Figure S14b. $^{13}$C NMR spectrum of 3 in CDCl$_3$. 
Figure S15a. $^1$H NMR spectrum of 4 in CDCl$_3$ (0.06 M).

Figure S15b. $^{13}$C NMR spectrum of 4 in CDCl$_3$. 
Figure S16a. $^1$H NMR spectrum of 5 in CDCl$_3$ (0.06 M).

Figure S16b. $^{13}$C NMR spectrum of 5 in CDCl$_3$. 
Figure S17a. $^1$H NMR spectrum of 6 in methanol-d$_4$.

Figure S17b. $^{13}$C NMR spectrum of 6 in methanol-d$_4$. 
Figure S18a. $^1$H NMR spectrum of 7 in CDCl$_3$ (0.06 M).

Figure S18b. $^{13}$C NMR spectrum of 7 in CDCl$_3$. 
Figure S19a. $^1$H NMR spectrum of 8 in methanol-d$_4$.

Figure S19b. $^{13}$C NMR spectrum of 8 in methanol-d$_4$. 
Figure S20a. $^1$H NMR spectrum of 9 in CDCl$_3$.

Figure S20b. $^{13}$C NMR spectrum of 9 in CDCl$_3$. 
Figure S21a. $^1$H NMR spectrum of 10 in CDCl$_3$.

Figure S21b. $^{13}$C NMR spectrum of 10 in CDCl$_3$. 
Figure S22a. $^1$H NMR spectrum of 11 in CDCl$_3$ (0.06 M).

Figure S22b. $^{13}$C NMR spectrum of 11 in CDCl$_3$. 
Figure S23a. $^1$H NMR spectrum of 12 in DMSO-$d_6$.

Figure S23b. $^{13}$C NMR spectrum of 12 in DMSO-$d_6$. 