Molecular Recognition of Carbohydrates by Functionalized Zinc Porphyrins

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A trifunctional porphyrin host [*cis*-5,15-bis(8-quinolyl)porphyrinato]zinc **1** exhibits a marked affinity for octyl β-D-glucopyranoside **12** in $CHCl_3$ with an association constant of 41 400 $dm^3\ mol^{-1}$; solvent effects on the binding are compared with those for [*cis*-5,15-bis(2,7-dihydroxy-1-naphthyl)porphyrinato]zinc **3**.

The molecular zrecognition of carbohydrates[1] is one of the challenging goals of artificial receptor chemistry, owing to the structural diversity of carbohydrates and their important functions in biological processes. As demonstrated for arabinose-binding protein, complementary molecular shape and complementary arrangement of hydrogen bonding groups between host and guest are key features for a high selectivity of recognition.[2] Solvent effects on the recognition are also an important aspect, particularly for such polar guests. We describe three porphyrin hosts, **1**–**3**, having one zinc (Lewis acidic) atom and two hydrogen-bonding groups consisting of either nitrogen or hydroxy groups, and focus on their binding selectivity for carbohydrate derivatives in chloroform and chloroform–alcohol mixed solvents.

Host **1** has a zinc atom as a Lewis acidic site and two basic nitrogen atoms.[3] In the binding site of host **1**, the lone-pair electrons of the two basic nitrogen atoms of quinolyl groups turn inwards and act as hydrogen bonding acceptors. In the binding sites of hosts **2** and **3**, two phenolic hydroxy groups can form hydrogen bonds with guests, and presumably act as hydrogen bonding donors owing to their acidity. These hydroxy groups are located near the host surface and are more or less sensitive to solvation interaction. To form a hydrogen bond with a guest, unrestricted bond rotation in host **1** is required, while restriction of rotation along the C–O bond of host **2** and **3** is required, resulting in the unfavourable entropy loss for binding.

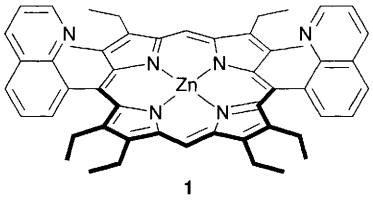
The binding constants were determined in amylene-containing chloroform at 15 °C by UV–VIS titration experiments.† All binding experiments showed 1 : 1 stoichiometry. The red shift from 412 to 424 nm is observed upon addition of the guest species, which is consistent with the coordination of a hydroxy group to zinc.[4] The binding constants are listed in Table 1.‡ Principal results are summarized as follows. (*a*) Host **1** shows marked affinity for octyl β-D-glucopyranoside **12** with a binding constant of 41400 $dm^3\ mol^{-1}$. (*b*) Diols **8**–**11** are bound more strongly than monools and ethers **4**–**7**. (*c*) Among the diols, *trans*-diols **8** and **10** are bound more tightly than the corresponding *cis*-diols **9** and **11**.[1e] (*d*) Diols with a primary hydroxy group (**10** and **11**) are more strongly bound to hosts **1** and **2** than diols with secondary hydroxy groups (**8** and **9**). (*e*) Host **2** binds **10**–**15** less tightly by 1.0–3.1 kcal mol^{-1} (1 cal = 4.184 J) than host **1**, indicating that the binding pocket of host **1** is better organized to recognize carbohydrate derivatives than that of host **2**.

The effects of the addition of methyl alcohol and *tert*-butyl alcohol to chloroform on the binding constants are shown in Figs. 1 and 2. The binding affinity of host **1** towards **12** is

Table 1 Binding constants K and $\Delta G°$ for complexation of porphyrin hosts **1** (or **2**) with guests in chloroform at 15 °C[a]

	K/$dm^3\ mol^{-1}$ ($\Delta G°$/kcal mol^{-1})	
Guest	Host **1**	Host **2**
4	3 (−0.63)	3 (−0.63)
5	3 (−0.63)	19 (−1.68)
6	5 (−0.92)	17 (−1.62)
7	7 (−1.11)	5 (−0.92)
8	210 (−3.05)	140 (−2.80)
9	60 (−2.32)	43 (−2.15)
10	2600 (−4.50)	320 (−3.29)
11	560 (−3.62)	88 (−2.56)
12	41 400 (−6.08)	180 (−2.96)
13	6800 (−5.05)	270 (−3.21)
14	7300 (−5.09)	600 (−3.66)
15	6800 (−5.05)	530 (−3.59)

[a] In amylene-containing $CHCl_3$. [**1**] = 5.4 × 10^{-6}–7.4 × 10^{-6}, [**2**] = 4.6 × 10^{-6}–5.8 × 10^{-6}, [**4**–**7**] = 0–3.4 × 10^{-1}, [**8**–**11**] = 0–9.6 × 10^{-3}, [**12**–**15**] = 0–9.6 × 10^{-3} mol dm^{-3}.



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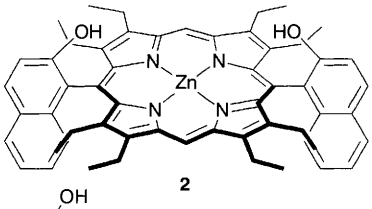

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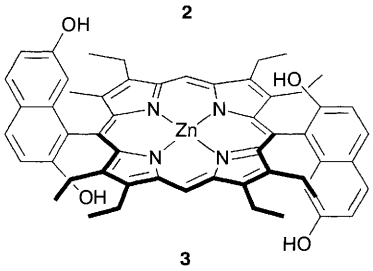

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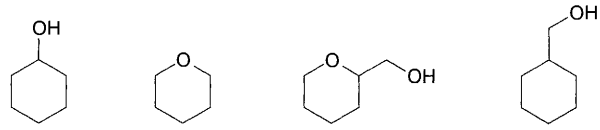
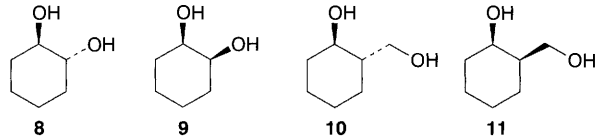
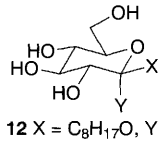


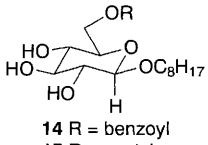
4 **5** **6** **7**



8 **9** **10** **11**



12 X = $C_8H_{17}O$, Y = H
13 X = H, Y = $C_8H_{17}O$



14 R = benzoyl
15 R = acetyl

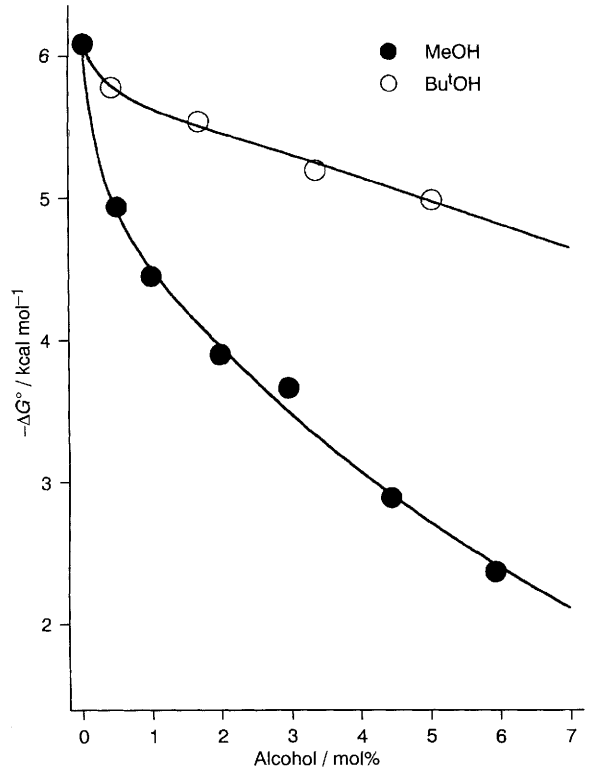


Fig. 1 Plot of the association free energy ($-\Delta G°$) between host **1** and octyl glucopyranoside **12** against alcohol concentration in $CHCl_3$ at 15 °C

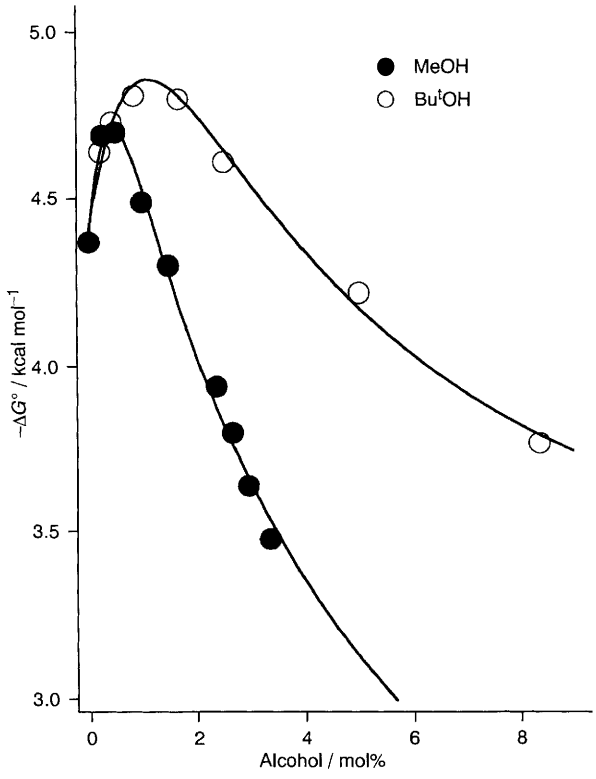


Fig. 2 Plot of the association free energy ($-\Delta G°$) between host **3** and octyl glucopyranoside **12** against alcohol concentration in $CHCl_3$ at 15 °C

reduced as the molar fraction of alcohol increases. Host **3** shows a binding constant of 2090 $dm^3\ mol^{-1}$ with **12** in chloroform in the absence of alcohol. Interestingly, the binding constants increase with the addition of methyl alcohol and *tert*-butyl alcohol, followed by a decrease upon further addition of alcohols as shown in Fig. 2. This contrasting result between host **1** and **3** may be due to differences in the binding pocket: that of host **3** is more exposed to solvent and the host–guest complex can be stabilized by additional hydrogen bonding with alcohols. A similar binding enhancement was reported recently.[1g] In the X-ray structure of arabinose-binding protein, participation of water molecules in the hydrogen-bonding network is found.[2] The present enhancement of binding by alcohols may be ascribed to a similar interaction mode.

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Footnotes

† The binding constants were determined by non-linear least-squares curve-fitting to the absorbance changes at 410–425 nm.

‡ Direct evidence for complexation is provided by induced circular dichroism (CD) observed in the Soret region of **1** and **2** upon the addition of the sugar derivatives **12**, **14** and **15**. The induced CD was varied as the temperature was varied from 15 to −90 °C, suggesting that more than one host–guest conformer is formed. Our previous study of porphyrin receptors for amino acid esters showed that only multi-point adducts exhibit induced CD.[5] Therefore the present induced CD suggests that **1** and **2** formed multi-point adduct with sugar derivatives.

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