Binding Properties of Calixarene-based Cofacial Bisporphyrins

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Calixarene-based porphyrins in which the calixarene scaffold is connected with porphyrin units by an alkyl chain as a spacer have been prepared. Porphyrin with ethano bridge exhibits extremely high affinity ($10^9 \, \mathrm{M}^{-1}$) for diazabicyclo-[2.2.2]octane (DABCO).

Various cofacial bisporphyrins have been developed due to their highly preorganized and geometrically controlled structures.[1] These well-defined bisporphyrins exhibit unique properties, such as the direct four-electron reduction of oxygen to water,[2,3] or the specific binding of host molecules,[4,5] which can be attributed to the spatial arrangement of the porphyrin units. In order to realize the cofacial arrangement some aromatic compounds such as anthracene,[6] biphenylene,[7] or dibenzofuran[8] have been employed as the platform by which two porphyrin units are anchored. They are known as Pac-Man porphyrins. The calixarene platform can be considered as another candidate to build a face-to-face arrangement.[9,10] Thus, calixarene-based porphyrins in which the porphyrin units can be arranged in the cofacial orientation have been prepared and their binding features against the bidentate guests, such as diazabicyclo[2.2.2]octane (DABCO) and 1,4-pyrazine, have been examined recently.[11,12] It has been found that the predefined, cofacial arrangement of the porphyrin moieties shows high affinity for a bidentate ligand bearing two nitrogen atoms.[13] The spacer which connects the porphyrin to the calixarene platform might play a critical role in binding ability because the distance between two cofacial porphyrin units is adjusted by this spacer. However, systematic studies concerning the length of the spacer in relation with binding properties of cofacial porphyrin units seem very limited.

Thus, we designed calixarene-based cofacial porphyrins with various lengths of the alkyl chain as the spacer and investigated their ability to bind DABCO and other related compounds.

The calixarene scaffold **1** (Chart 1) which is fixed in a cone conformation was obtained according to a reported method.[14] The benzaldehydes **2a**–**2c** were synthesized using the coupling of 4-hydroxybenzaldehyde and the corresponding dibromoalkane, followed by the reaction of 4-hydroxynitrobenzene. The nitroporphyrins **3a**–**3c** were prepared from the acid-catalyzed condensation of **2a**–**2c** and *p-tert*-butylbenzaldehyde with 2.0 equiv of dipyrromethane[15] followed by oxidation with 3 equiv of DDQ[16,17] in the yields of 18% (**3a**), 12% (**3b**), and 16% (**3c**). Reduction of **3a**–**3c** with hydrogen gas in the presence of 10% Pd/C gave the corresponding aminoporphyrins **4a**–**4c** quantitatively. The desired Zn(II) calixarene-based cofacial porphyrins **5a**–**5c** were obtained by the simple coupling of **1** and **4a**–**4c**, followed by metalation using zinc acetate in the yields of 39% (**5a**), 62% (**5b**), and 49% (**5c**).[18]
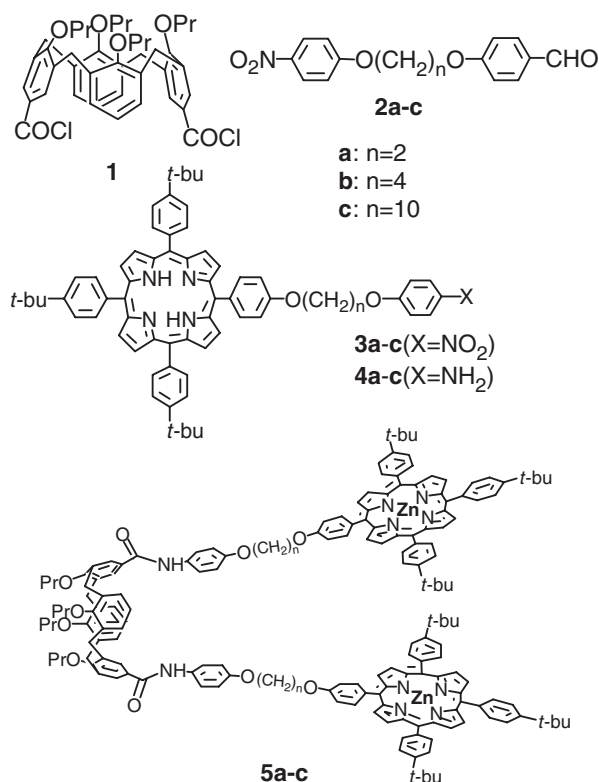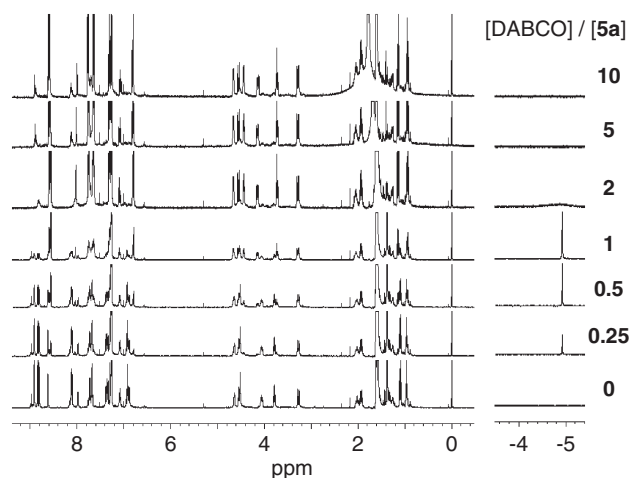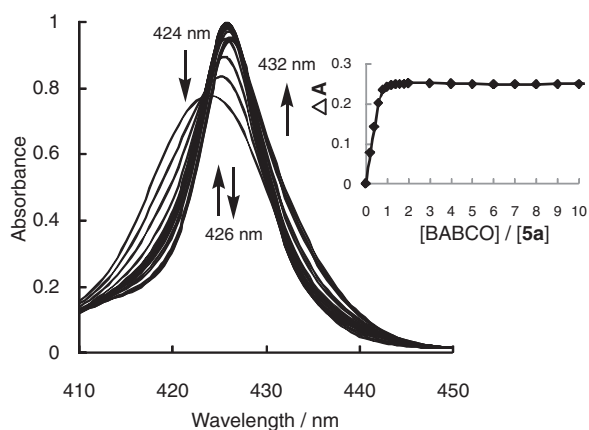

Chart 1.

^{1}H NMR spectral titration has been carried out for **5a**–**5c** with DABCO. Figure 1 shows the profile of the ^{1}H NMR spectrum of **5a** on addition of DABCO. A characteristic singlet at -4.8 ppm appears when the ratio of [DABCO]/[**5a**] is 0.25. This shielded peak strongly indicates the existence of a DABCO molecule inserted in between two porphyrin units. At the ratio of 1, all DABCO added is bound to **5a**. In the course of addition of DABCO aromatic signals of **5a** are considerably simplified. Concomitantly the signals corresponding to the porphyrin β-pyrrolic protons are shielded, which stems from shortening of the distance between two porphyrin units by binding DABCO. After 1:1 stoichiometry the DABCO signal completely disappears. Even on addition of a large excess of DABCO, the peaks of their protons are no more observed. This strongly suggests that the excess addition of DABCO induces fast exchange between the bound and free DABCO.

UV–visible titration was also carried out to study the complexation in this system. Upon addition of DABCO, the original Soret band at 424 nm corresponding to the free **5a** gradually decreased and a sharp band at 426 nm appeared as shown in Figure 2. The plot of the change of the absorbance at

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Figure 1. NMR titration of **5a** with DABCO in CDCl$_3$ at 298 K.

Figure 2. Absorption spectral change in the titration of **5a** with DABCO in CDCl$_3$ at 298 K. The plot of ΔA_{426} against [DABCO]/**5a** is inserted.

Table 1. Association constants for **5a**–**5c** with DABCO[a]

Host	K_1/M^{-1}	K_2/M^{-1}
5a	1.0×10^9	5.2×10^4
5b	8.0×10^7	2.2×10^4
5c	1.3×10^7	7.9×10^3

[a]At 298 K in CHCl$_3$.

Figure 3. DABCO binding modes in **5a**–**5c**.

Chart 2.

The association constant increases as the length of the spacer chain decreases. Although **5a**–**5c** are flexible as to the porphyrin moiety, preorganization of the two zinc porphyrin units in **5a** seems to accommodate the internal cavity to the N–N bond in DABCO. A large enhancement observed for the stability of the complex between **5a** and DABCO should be noted, because **5a** exhibits the strongest affinity for DABCO in comparison with previously reported association constants.

Sanders and Hunter[4] have shown that cyclophane-type porphyrin dimers bind DABCO with association constants in the order of $10^6\,M^{-1}$. An increase by one order of magnitude in the association constants with DABCO ($10^7\,M^{-1}$) was achieved employing the highly preorganized porphyrin–calixarene conjugates.[11] More recently the association constants with DABCO in the order of $10^8\,M^{-1}$ have been reported for the cofacial bisporphyrins bridged by the calixarene spacer[12] or the benzo orthocarbonate.[19] In such a binding feature it is suggested that a high degree of preorganization derived from the rigid connection of the porphyrins to calixarene hinge could be a dominant factor. On the other hand **5a**–**5c** show similar values as the association constant (K_2), indicating that these values are not related to the cavity.

In order to acquire deeper insight into this cofacial structure we have carried out the complexation of **5** and the pyridine derivatives **6a**–**6c** (Chart 2).

In this case it is relatively easy to alter the length of the guest molecules **6a**–**6c**. The association constants K_1 and K_2 obtained by UV titration[18] are summarized in Table 2.

The host molecule **5a** having shorter spacer chain exhibits a large association constant (K_1) for **6b** and **6c** in comparison with **6a**. The association constant (K_1) for **6a** decreases about two orders of magnitude. The space between the cofacial two porphyrin units in **5a** can accommodate **6b** extensively, meaning that it fits the molecular length (about 11.4 Å) of **6b**.
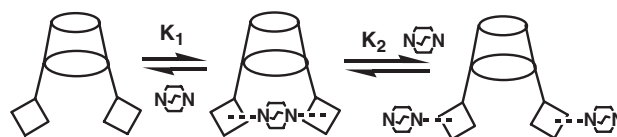
426 nm against the ratio of [DABCO]/[**5a**] is also inserted in Figure 2, showing a sharp saturation beyond the ratio of 1:1. These findings confirm the formation of a 1:1 sandwich complex. As the concentration of DABCO is increased, the peak at 426 nm decreases and the shoulder at 432 nm is clearly recognized. This new appearance may be characteristic of the 1:2 **5a**–DABCO complex, because the band at 432 nm is observed when DABCO was added to the zinc complex of **3a**. Two isosbestic points are indicative of two sequential two-state equilibriums. The relatively sharp peak also suggests that DABCO is bound strongly in the cavity as the sandwich complex, because such a peak is due to separation of two porphyrin units by the inserted DABCO molecule. In the Q band region upon the addition of DABCO decreases of the absorption intensity at 551 and 595 nm were observed accompanied by increases of the absorption intensity at 563 and 604 nm.

The association constants[18] determined from UV titrations are summarized in Table 1. The constants K_1 and K_2 refer to the 1:1 sandwich-type complex and the 1:2 complex, respectively, as illustrated in Figure 3.
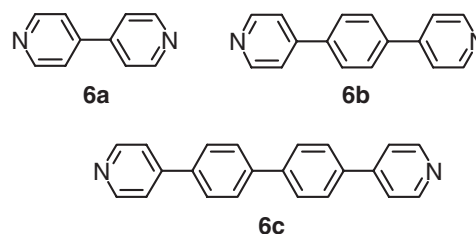
Table 2. Association constants for **5a** and **5c** with **6a**–**6c**[a]

Host	K_1/M^{-1}		
	6a	**6b**	**6c**
5a	4.0×10^4	2.6×10^6	1.8×10^6
5c	1.4×10^6	5.2×10^6	1.1×10^7
	K_2/M^{-1}		
5a	2.2×10^3	1.6×10^4	8.1×10^3
5c	1.4×10^4	2.7×10^4	3.9×10^4

[a]At 298 K in CHCl₃.

On the contrary the host molecule **5c** with longer spacer chain exhibits a larger association constant (K_1) as the length of the guest molecule becomes longer. Comparing with **5a**, **5c** is likely to have more space between two porphyrin units, resulting in the large association constants for **6c**. These results obviously reflect that the cofacial structure connected to the calixarene skeleton by the methylene spacer plays a crucial role in such binding. As expected similar association constants (K_2) were obtained for **6a**–**6c** due to the binding of the guest molecule outside the cavity.

It should be noted that the largest association constant ever reported was obtained for the binding of the cofacial porphyrins against DABCO by employing the calixarene moiety as the platform and appropriate spacer length.

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