



A novel porphyrin–homooxacalix[3]arene conjugate which creates a C_3 -symmetrical capsular space

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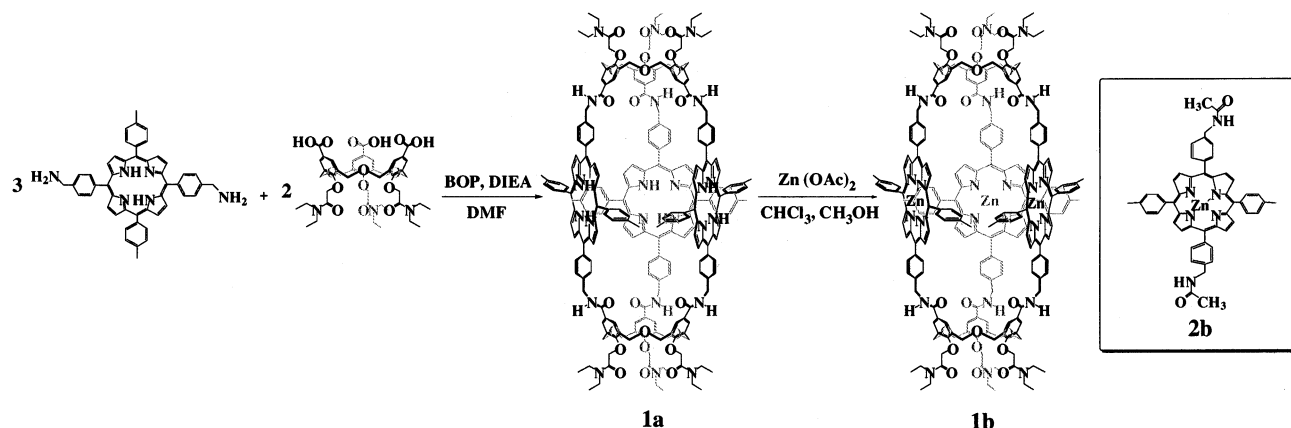
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Abstract—A novel capsular molecule in which three porphyrin-based building blocks are capped by two ionophoric calixarene molecules has been synthesized for the first time. The Zn(II) complex showed a high encapsulation ability for C_3 -symmetrical guest molecules. In addition, the binding properties were allosterically controlled by added Na^+ or CH_3OH . © 2001 Elsevier Science Ltd. All rights reserved.

A great deal of effort has been directed toward multiporphyrin arrays such as molecular wires,¹ molecular switches,² photosynthetic systems,³ artificial antenna models,⁴ photosensitizers for DNA cleavage⁵ and photocurrent generation.⁶ The combination of these excellent porphyrin functions with host–guest chemistry has large potential in the future, but is much less developed so far. A few cyclic host compounds composed of covalently-linked multiporphyrins have been synthesized, and some of them can include guest molecules such as pyridine derivatives with the aid of the axial coordination.^{7,8} The findings suggest that molecular capsules with a specific cavity size and a specific symmetry for each guest would have higher association constants and higher selectivities for specific guest molecules. In these host–guest complexa-

tion systems, if the guest binding can be changed by some stimulus from the outside, they should act as on–off-switched systems that eventually lead to molecular devices. We have noticed that a calix-[*n*]arene family would be useful as a potential scaffold to design such switch-functionalized systems because the structure of calix[*n*]aryl amide derivatives can be readily changed by alkali metal cations bound to the lower rim.⁹ In homooxacalix[3]aryl amide derivatives, for example, the calixarene phenyl rings are changed from the standing conformation to the flattening one by bound Na^+ . Here, we report a novel type of a homooxacalix[3]arene dimer triply linked by Zn–porphyrin moieties. We have found that the C_3 -symmetrical capsular cavity shows unique responsive properties for C_3 -symmetrical guests.



Scheme 1.

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Capsular molecule **1b** was designed considering that (i) a C_3 -symmetrical cavity would encapsulate C_3 -symmetrical guest molecules and (ii) two ionophoric sites at the calixarene lower rim would change the capsular shape and rigidity in response to Na^+ binding. Compound **1a** was synthesized according to Scheme 1. The product was identified by IR, NMR and mass (MALDI-TOF) spectral evidence and elemental analysis. This compound was treated with $\text{Zn}(\text{OAc})_2$ in a chloroform–methanol (1:1 v/v) mixed solvent to give **1b**. The product was isolated by column chromatography as a pure compound and identified by similar analytical methods. Compound **2b** was synthesized to use as a reference.

The ^1H NMR spectral peaks of **1b** were significantly broadened in CDCl_3 , but became sharp in $\text{CDCl}_3/\text{CD}_3\text{OD}=9:1$ (v/v) (Fig. 1A). One may thus consider that peak broadening is due to the intramolecular hydrogen-bonding interactions (e.g. interpillar $\text{CO}\cdots\text{HN}$), which operate strongly in aprotic solvents and extensively suppress the conformational freedom of **1b**. If **1b** adopts a regular C_3 -symmetrical structure, the calixarene phenyl protons should appear as a singlet.¹⁰ In fact, however, several split peaks are still observable even in $\text{CDCl}_3/\text{CD}_3\text{OD}=9:1$ (v/v) (Fig. 1B), indicating that **1b** is still distorted somewhat from the C_3 -symmetrical structure. Examination using the CPK molecular and computational models reveals that the *meso*-tolyl groups in porphyrins hit each other, making the adop-

tion of the regular C_3 -symmetrical structure sterically difficult. It can be seen from Fig. 2 that the energy-minimized structure of **1b** is very distorted, enjoying several $\text{CO}\cdots\text{HN}$ hydrogen-bonding interactions.

We measured the ^1H NMR spectra to confirm whether or not the conformational change is induced by added Na^+ . When NaClO_4 (5 equivalents to **1b**) was added in CDCl_3 , all peaks were sharpened (Fig. 1C). This sharp splitting pattern was scarcely changed by the addition of 10% CD_3OD . The minor influence of CD_3OD indicates that the hydrogen bonds are already cleaved by the complexation of Na^+ ions. It is known that phenyl rings in homooxacalix[3]aryl amide are significantly flattened by the binding of Na^+ to the lower rim.¹⁰ In the binding of Na^+ to **1b**, the phenyl rings are so flattened that the distance between the interpillar CONH group is lengthened and the intramolecular hydrogen bonds are cleaved.

Here, we evaluated whether this novel molecular capsule is capable of including some guest molecules and the inclusion properties are controlled allosterically by the Na^+ induced structural change. When tris(2-aminoethyl)amine (TREN) $[(1-100)\times 10^{-6} \text{ mol dm}^{-3}]$ was added to a CHCl_3 solution of **1b** ($1.00\times 10^{-6} \text{ mol dm}^{-3}$) at 25°C , the Soret band (λ_{max} 423 nm) shifted to 419 nm with a tight isosbestic point (420 nm) (Fig. 3). It is known that Soret band shifts to longer wavelength when amine derivatives complex as an axial ligand with Zn(II) porphyrin.¹¹ Contrary to our expectation, however, the absorption spectral change showed a blue-shift to 419 nm with increasing TREN concentration (Fig. 3). It is also known that the Soret band shifts to shorter wavelength when porphyrins are positioned face-to-face.¹² This spectral change thus supports the view, together with the above ^1H NMR spectroscopic data, that being different from conventional 1:1 Zn(II) porphyrin/amine complexes, the spectral change in **1b**/TREN complex is related to a TREN-induced conformational change to reduce the steric crowding among Zn(II) porphyrins. The continuous variation plot¹³ established that **1b** forms a 1:1 complex with

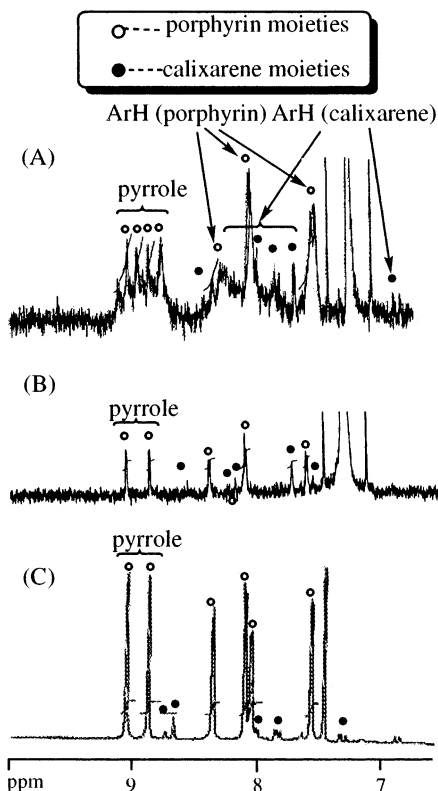


Figure 1. Partial ^1H NMR spectra of **1b** (0.1 mM) in the absence (A) and presence (B) of NaClO_4 in CDCl_3 , and (C) in the absence of NaClO_4 in $\text{CDCl}_3/\text{CD}_3\text{OD}=9:1$ (v/v); 25°C , 600 MHz.

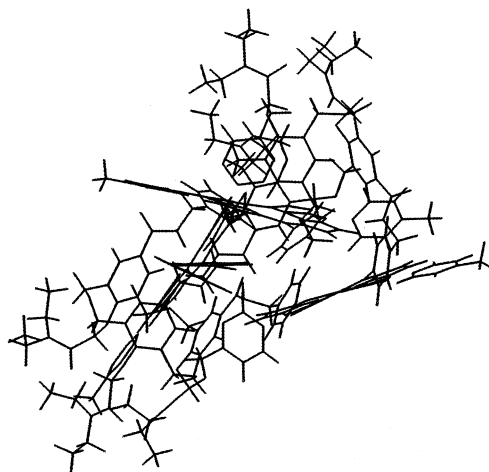


Figure 2. Energetically minimized structure by molecular modeling of **1b**.

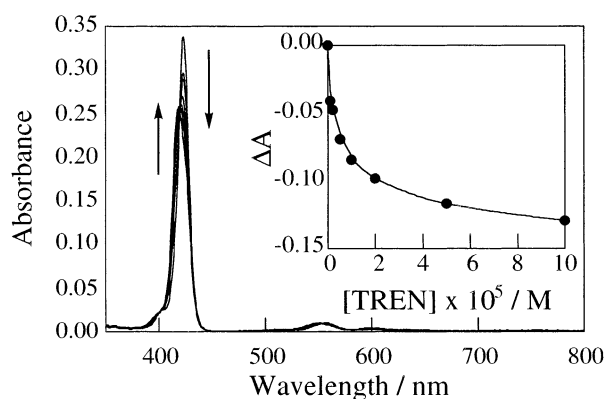


Figure 3. Absorption spectral change in **1b** (1.0×10^{-6} mol dm^{-3}); $[\text{TREN}] = 0\text{--}0.1 \times 10^{-4}$ mol dm^{-3} . Insert $[(\Delta A)$ at 423 nm] versus $[\text{TREN}]$ plot in CHCl_3 at 25°C .

TREN, and the association constant (K_{ass}) was estimated to be 1.72×10^5 dm^3 mol^{-1} for TREN from the plots in Fig. 3. This value is much larger than that for complexation of *n*-propylamine with **2b** (3.0×10^3 dm^3 mol^{-1}).

In the presence of NaClO_4 (5.00×10^{-6} mol dm^{-3}) in CHCl_3 , the same measurements were carried out. The K_{ass} values were estimated to be 2.2×10^2 dm^3 mol^{-1} for *n*-propylamine and 1.5×10^8 dm^3 mol^{-1} for TREN. The results indicate that Na^+ addition somewhat decreases the K_{ass} for *n*-propylamine, whereas it increases that for TREN by about three orders of magnitude. Conceivably, Na^+ addition disrupts the intramolecular hydrogen bonds to arrange **1b** into a more symmetrical one suitable for the TREN binding. One may thus consider that the Na^+ ion acts as a positive effector which can enhance the K_{ass} by three orders of magnitude.

The absorption spectra were measured under the same conditions both in the absence and the presence of NaClO_4 (1.00×10^{-2} mol dm^{-3}) in $\text{CHCl}_3/\text{CH}_3\text{OH} = 9:1$ (v/v). The K_{ass} values were estimated to be 2.2×10^6 dm^3 mol^{-1} and 1.1×10^7 dm^3 mol^{-1} for TREN, respectively. Ordinarily, K_{ass} values in CHCl_3 are larger than those in $\text{CHCl}_3/\text{CH}_3\text{OH}$. In fact, the K_{ass} value of *n*-propylamine and reference **2b** in CHCl_3 is 20 times larger than that in $\text{CHCl}_3/\text{CH}_3\text{OH}$ (Table 1). However, the present system shows the reversed result that the K_{ass} of amine derivatives for **1b** is increased by CH_3OH addition. The K_{ass} value of TREN to **1b** in CHCl_3 is less than one-fifteenth of that in $\text{CHCl}_3/\text{CH}_3\text{OH}$. The

results clearly indicate that in $\text{CHCl}_3/\text{CH}_3\text{OH} = 9:1$ (v/v) the K_{ass} is already large enough even in the absence of Na^+ , and Na^+ addition scarcely affects the TREN affinity of **1b**. Based on the foregoing ^1H NMR spectral data, one can consider that added CD_3OD weakened the intramolecular hydrogen-bonding interaction to facilitate the subsequent TREN binding.

In conclusion, the present paper reports the first functional capsular molecule in which three porphyrin-based building blocks are capped by two ionophoric calixarenes. We have found that this capsular molecule **1b** not only includes C_3 -symmetrical TREN with a large association constant, but also shows the positive allosteric binding properties in communication with Na^+ or CH_3OH . The further applications of these novel, functional systems to porphyrin-mediated molecular recognition, redox reactions, photochemical reactions, etc. are continuously studied in this laboratory.

Acknowledgements

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Table 1. Association constants (dm^3 mol^{-1}) of amine derivatives for **1b** and **2b**

Host	Additive	<i>n</i> -Propylamine	TREN
1b	None	1.69×10^2	1.72×10^5
1b	CH_3OH (10 vol%)	1.88×10^2	2.63×10^6
1b	NaClO_4	2.11×10^2	1.52×10^8
1b	$\text{CH}_3\text{OH}/\text{NaClO}_4$	1.97×10^2	1.11×10^7
2b	None	3.20×10^3	
2b	CH_3OH (10 vol%)	1.59×10^2	

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