

Highly stable cage-like complexes by self-assembly of tetracationic Zn(II) porphyrinates and tetrasulfonatocalix[4]arenes in polar solvents†

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Tetracationic Zn(II) porphyrinates and tetraanionic calix[4]arenes can be assembled in polar solvents to obtain cage-like complexes in an entropy driven process. These structures are remarkably stable even in the presence of water or competing salts.

Metalloporphyrins are well known for their ability to bind a variety of small molecules^{1–6} and for their catalytic properties.^{7,8} Moreover, they have been intensively studied with respect to their occurrence in metalloporphyrin-dependent proteins,^{9,10} in which they display largely differentiated chemical properties. The chemical behavior of a metalloporphyrin is strongly affected by the surrounding environment.¹¹ For example, the peptidic backbone in metalloporphyrin-dependent proteins is able to fine-tune the chemical properties of the metal center by means of non-covalent interactions. Most studies with synthetic porphyrins heavily rely on the covalent modification of the macrocyclic structure,^{1,12} while studies on porphyrins with a non-covalently organized periphery have hardly been reported so far. In this communication we describe the formation and characterization of cage-like complexes **1·2**, consisting of cationic porphyrins **1** and anionic calix[4]arenes **2** (see Fig. 1), that are very stable in polar solvents such as MeOH, DMSO and DMPU.^{‡§}

Zinc(II) meso-tetrakis(*N*-alkylpyridinium-3-yl)-porphyrins **1a–c** were prepared in three steps starting from pyridine-3-carboxyaldehyde and pyrrole in an overall yield of 14–18% following literature procedures.⁵ Tetrasulfonatocalix[4]arene **2** was obtained in 84% yield by sulfonation of the parent 25,26,27,28-tetrakis(2-ethoxyethoxy)calix[4]arene with concentrated sulfuric acid using a slightly modified literature procedure.¹³

The assembly process was first studied by UV spectroscopy. Addition of calix[4]arene **2** to a solution of porphyrins **1** in MeOH ($2\text{--}3 \times 10^{-6}$ M) causes a bathochromic shift (3–5 nm) of the porphyrin's Soret band with a concomitant 20–25% decrease in ϵ (molar absorptivity) at λ_{max} . This behavior is characteristic for cationic pyridiniumyl porphyrins that form ion-pair complexes in water.¹⁴ Non-linear least-squares fitting analysis of the spectral changes using a 1:1 binding model gave association constants in the order of 10^7 M⁻¹ for the complexes **1·2** (see Table 1). The presence of a well-defined isosbestic point during the titration strongly supports the proposed formation of a 1:1 complex. These high values most likely reflect the perfect complementarity in charge distribution of the two interacting molecular ions leading to the formation of strong, cooperative salt bridges. Nevertheless these ion-pair complexes remain highly dynamic structures as we were unable to observe any time dependent phenomenon either by NMR or by UV-vis experiments.

In order to determine the thermodynamic parameters associated with the assembly formation, the stability constant of complex **1a·2** was determined at different temperatures. Van't Hoff analysis of the binding data revealed that the process is

strongly entropically driven (129 ± 24 J K⁻¹ mol⁻¹) with a very small exothermic contribution (-8.0 ± 6.7 kJ mol⁻¹). Therefore, we conclude that the release of solvent molecules is the

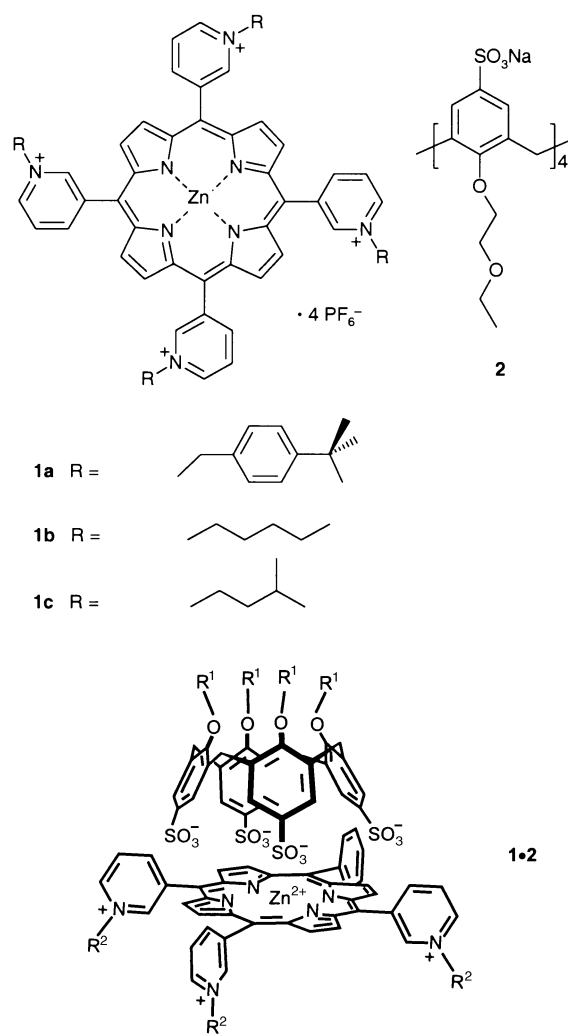


Fig. 1 Molecular structure of components **1**, **2**, and 1:1 complex **1·2**.

Table 1 Association constants for the assembly of cationic zinc porphyrinates **1** with the anionic calix[4]arene **2**

Assembly	Solvent	Log $K_{1:1}$
1a·2	CH ₃ OH	7.11 ± 0.04
1b·2	CH ₃ OH	7.04 ± 0.20
1c·2	CH ₃ OH	7.15 ± 0.09
1a·2	DMSO	6.21 ± 0.03
1a·2	DMPU	6.16 ± 0.01
1a·2	H ₂ O–DMPU $x_{\text{water}} = 0.26$	6.04 ± 0.02

† Electronic supplementary information (ESI) available: Figs. 3–6. See <http://www.rsc.org/suppdata/cc/b0/b006960o/>

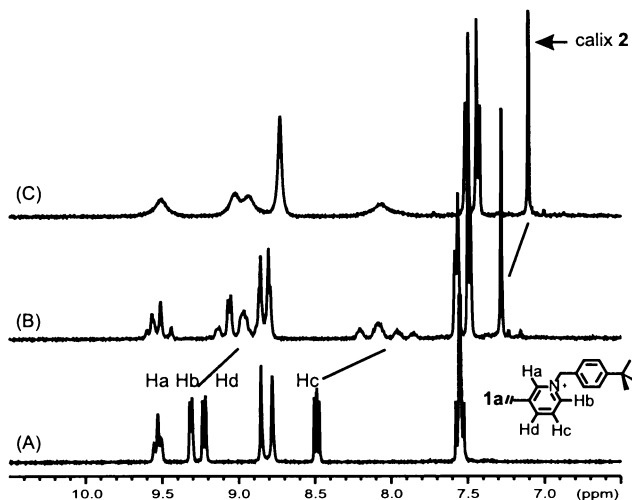


Fig. 2 ^1H NMR of (A) porphyrin **1a**, (B) 1:1 mixture of **1a** and **2** at 298 K, (C) 1:1 mixture of **1a** and **2** at 343 K.

main driving force for the formation of the highly stable ion-pair complexes **1**·**2** in MeOH.¹⁵

Structural investigation of complex **1a**·**2** by ^1H NMR spectroscopy was performed in $\text{CD}_3\text{CN}-\text{D}_2\text{O}$ (6.5:1.5). At ambient temperatures the porphyrin proton signals show a complicated set of signals that indicate the presence of a mixture of isomeric structures with reduced symmetry. The calix[4]arene strongly influences the atropisomerization equilibrium of the porphyrin,⁵ without inducing a particular conformational preference. Coalescence of the various signals occurs at higher temperatures, whereby the position of the averaged signals is significantly shifted upfield in comparison to the corresponding signals in the free porphyrin. The largest shifts are observed for protons H_b , H_c and H_d (0.3–0.7 ppm) (see Fig. 2), which suggests that these protons are located in closest proximity to the calix[4]arene unit. Molecular simulation studies (CHARMM 24.0) support this view and further show that the structure in which the alkyl chains are pointing away from the calix[4]arene minimizes the distance between opposite charges in the two building blocks.[¶]

The cage-like structure of these ion-pair complexes prompted us to study their formation in other polar solvents such as DMSO and DMPU, from which the individual molecules are more bulky than MeOH. Titration experiments with **1a** and **2** in these solvents also gave well-defined isobestic spectral variations. However, no shift in the maximum (DMSO) or a 5 nm blue shift (DMPU) was observed. This indicates a different solvation shell around the porphyrin upon formation of the complex in these solvents. Moreover, the $K_{1:1}$ values are one order of magnitude smaller than in MeOH (Table 1), which might indicate that MeOH is probably a very good guest for the cage-like complex^{||} and enhances the stability of the system. Further experiments on solvent or guest encapsulation in these cage-like structures are currently ongoing in our laboratories.

Furthermore, we examined the effect of adding salts on the stability of the ion-pair complexes: association constants were determined for assembly **1a**·**2** in DMSO at different concentrations of NaClO_4 . A logarithmic plot of $K_{1:1}$ and $[\text{NaClO}_4]$ shows a bimodal linear relationship with a slope of 1.91 ± 0.11 for $[\text{NaClO}_4] > 2 \times 10^{-3}$ M. This behavior suggests that, at high concentrations of Na^+ , calix[4]arene **2** complexes two Na^+ ions in a cooperative fashion, as indicated by the sharp curvature at the breaking point, with $\beta = 2.2 \times 10^5 \text{ M}^{-2}$. Determination of

the $K_{1:1}$ value at 10^{-2} M of Bu_4NClO_4 clearly showed a smaller effect in comparison to NaClO_4 at the same concentration ($\text{p}K_{1:1} = 5.22 \pm 0.08$ and 4.56 ± 0.03 for Bu_4NClO_4 and NaClO_4 respectively). Therefore, it can be concluded that addition of inert salts, as much as 4500 times the concentration of the building blocks, only reduces the stability of the complex by a factor of 10.

Finally, we have found that the influence of the presence of water on the stability of the assemblies is very small. The log $K_{1:1}$ value is 6.04 ± 0.02 in a $\text{H}_2\text{O}-\text{DMPU}$ mixture ($x_{\text{water}} = 0.26$), which is comparable to the value of 6.16 ± 0.01 obtained in pure DMPU (see Table 1).

In conclusion we have shown that stable cage-like complexes are obtained by self-assembly of cationic porphyrins and anionic calix[4]arenes in polar solvents. These assemblies are formed as a result of multiple electrostatic interactions between oppositely charged building blocks and are highly stable in polar solvents, like MeOH, DMSO and DMPU. Furthermore, they remain stable even in the presence of water and, to a large extent, upon the addition of electrolytes.

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Notes and references

‡ DMPU = 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1H)-one.

§ Self-assembled molecular capsules formed by means of ionic interactions have been reported using cyclotrimeric building blocks¹⁶ or cyclodextrin derivatives.¹⁷ In the first case the authors did not report the formation constant for the 1:1 complex and they observed the presence of oligomers at 7 mM in DMSO- d_6 . In the paper dealing with cyclodextrins indirect proof for the existence of the capsules was obtained from the calculation of self-diffusion coefficients via ^1H NMR techniques.

¶ The symmetrical situation as observed from a gas-phase simulation (see ESI) is likely reflecting the structure of the complex at temperatures higher than rt.

|| Coordination of MeOH to zinc(II) porphyrin hosts have been observed in several cases.¹⁸

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