Inclusion Compounds

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Ternary Complexes Comprising Cucurbit[10]uril, Porphyrins, and Guests**

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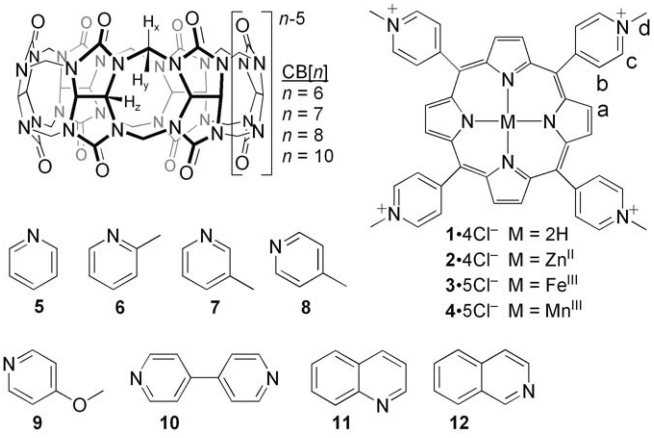
Porphyrins are prized components of functional systems and assembled structures because of their remarkable photophysical, electrochemical, and catalytic properties in both designed and natural systems.[1] Accordingly, much effort has been directed toward the covalent and noncovalent modification of porphyrins and their incorporation into larger more complex and functional systems. For example, covalently modified porphyrins have been exploited in the preparation of enzyme-mimetic catalysts for oxidation reactions,[2] as sensors for a variety of analytes,[3] and as a component of artificial photosynthetic systems.[1] The noncovalent assembly of porphyrins has been exploited in numerous ways, including as a means to control transport in molecular wires, to control energy migration, and to build catalysts.[4] Of particular relevance to our studies are reports on the encapsulation of porphyrins inside self-assembled coordination cages, calixarenes, and cyclodextrins.[5]

We, and others, have been studying the synthesis and recognition properties of the cucurbit[*n*]uril family (CB[*n*])[6,7] of molecular containers. These CB[*n*] molecular containers possess remarkable binding affinities and selectivities (K_a values up to $10^{12}\,M^{-1}$; K_{rel} values up to 10^6)[8] and high environmental responsiveness which render them useful as a component of molecular machines, sensors, and biomimetic systems.[9] We wondered whether it would be possible to combine the advantageous chemical, photochemical, and catalytic properties of the porphyrins with the binding properties of the CB[*n*] family in a noncovalent fashion.[10] For this purpose we elected to use CB[10][7e]—with its spacious 870-Å^3 cavity—as a suitable molecular container for cationic porphyrins. We report the formation and characterization of a series of CB[10]·porphyrin complexes and the ability of CB[10]·**2** to form ternary complexes with a variety of aromatic amines in water (Scheme 1).



Scheme 1. Structure of compounds used in this study.

We first sought to investigate the complexation between CB[10] and porphyrins **1** and **2**. Somewhat surprisingly—given that the van der Waals width of tetrapyridyl porphyrins **1**–**4** (ca. 15.3 Å) exceeds that of the CB[10] portal in its idealized cylindrical form (ca. 12.4 Å)—we found that mixing CB[10] with **1** or **2** in D_2O results in the formation of the CB[10]·**1** and CB[10]·**2** complexes as evident by ^{1}H NMR spectroscopy (Figure 1). Electrospray mass spectra recorded for CB[10]·**1**–CB[10]·**4** indicate the formation of 1:1 complexes (see the Supporting Information). Several features of the ^{1}H NMR spectrum of CB[10]·**2** are intriguing. First, upon complexation, the eight symmetry-equivalent β protons (H_a) of D_{4h}-**2**—which appear as a singlet in free **2**—split into two singlets (H_a and $H_{a'}$) which reflects a reduction in symmetry (C_{2v}) upon complexation. The singlet for $H_{a'}$ is shifted upfield significantly as a result of the well-known anisotropic effects of the CB[*n*] cavity.[8a,11] Second, the protons on the outside of CB[10] (H_x, H_y, H_z) undergo upfield shifts in the spectrum as a result of the substantial anisotropic effect of the porphyrin ring. In the absence of structural data from X-ray crystallography we were forced to rely on these induced shifts in the NMR spectra, molecular mechanics calculations (MMFF), and symmetry considerations to deduce the geometry of the CB[10]·**2** complex (Figure 2). Complexation of **2** by CB[10] results in a substantial flattening of the CB[10] cavity, which

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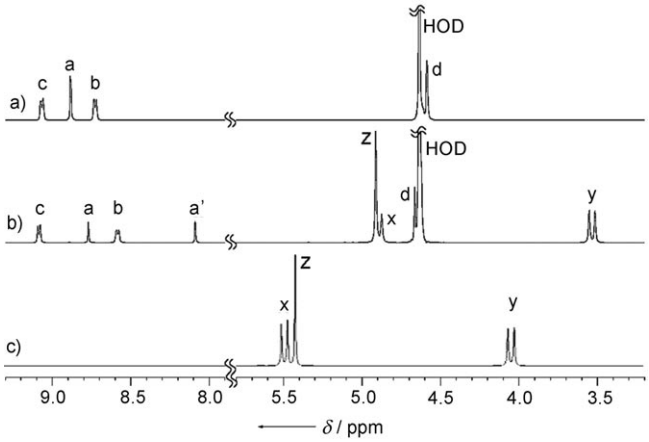

Figure 1. ^{1}H NMR spectra recorded (400 MHz, RT, D_2O) for: a) **2**, b) CB[10]·**2**, and c) CB[10] (20% DCl).

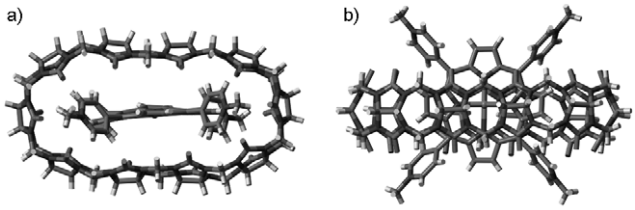

Figure 2. a) Top and b) side views of the MMFF-minimized geometry of CB[10]·**2**.

highlights the ability of CB[10] to change shape to accommodate its guest(s). Interestingly, this ellipsoidal deformation does not impose large energetic costs toward association or dissociation of the CB[10]·**2** complex.[12]

Given the known ability of CB[*n*] macrocycles to fundamentally alter the UV/Vis and fluorescence behavior of chromophoric guests,[9b,13] we wondered whether the desirable photophysical and electrochemical characteristics of a porphyrin macrocycle (for example, **2**) would be altered upon formation of a complex (CB[10]·**2**). Interestingly, the UV/Vis spectra recorded for CB[10]·**1**–CB[10]·**4** do not reveal any significant changes in the λ_{max} values of **1**–**4** upon complexation (see the Supporting Information). Similarly, the fluorescence spectrum recorded for CB[10]·**2** is quite similar to that of uncomplexed **2**, as is its fluorescence lifetime (see the Supporting Information; CB[10]·**2**: (1.40 ± 0.17) ns; **2**: (1.07 ± 0.11) ns). We also studied the electrochemistry of the corresponding Fe^{III} and Mn^{III} systems (CB[10]·**3** and CB[10]·**4**). Quite interestingly, the half-wave potentials for the Fe^{III}/Fe^{II} and Mn^{III}/Mn^{II} couples within CB[10]·**3** and CB[10]·**4** are relatively unaffected by complexation with CB[10], although we do observe a slight decrease in the current levels as a consequence of the lower diffusivity of the CB[10]·porphyrin complexes. Accordingly, we conclude that encapsulation within CB[10] preserves the interesting photophysical and electrochemical properties of the porphyrin while protecting it from the effect of external quenchers (for example, molecular oxygen) or other potential reactive species.[14]

Encouraged by the clear evidence for the preservation of the properties of the porphyrin ring, we decided to investigate whether the CB[10]·**2** binary complex would promote intimate contact between three species—namely CB[10], porphyrin **2**, and guests—which would be advantageous in a variety of advanced applications. We initially studied the interaction of CB[10]·**2** with pyridine by ^{1}H NMR (Figure 3 a–d) and UV/Vis spectroscopic titrations (see the Supporting Information) because of the well-known ability of zinc porphyrins to engage in zinc–ligand interactions. Quite interestingly, the signal for H_x of CB[10] undergoes a significant downfield shift ($\Delta\delta = 0.25$ ppm) during the titration. We believe this downfield shift is due to binding of pyridine (**5**) inside the CB[10]·**2** complex (to form CB[10]·**2**·**5**), which "inflates" the complex and increases the average distance between H_x and the porphyrin ring, thereby resulting in decreased shielding and a concomitant downfield

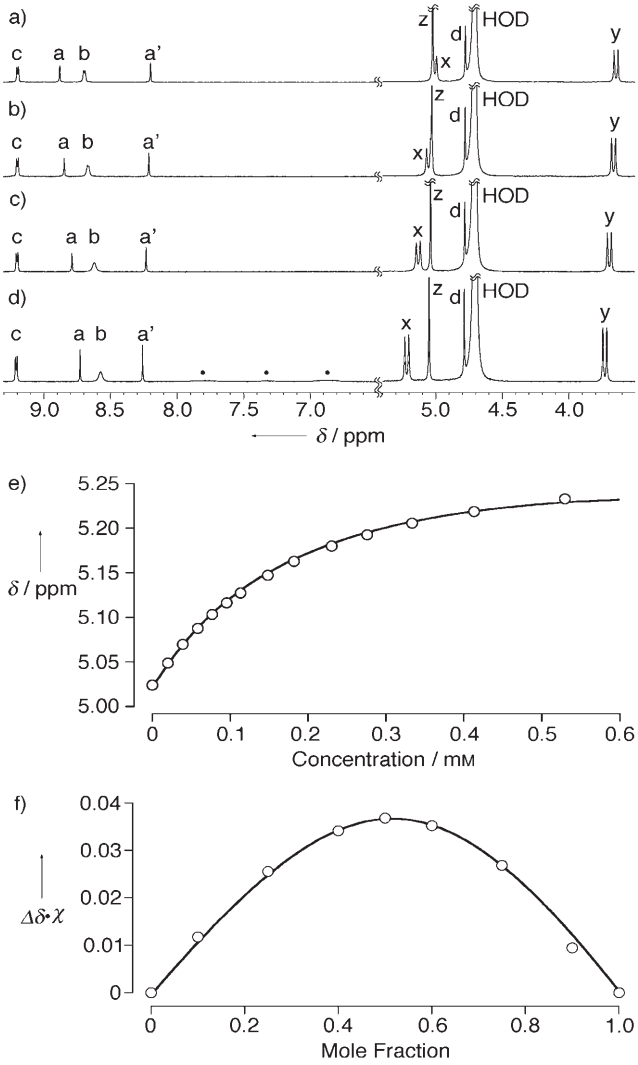

Figure 3. ^{1}H NMR spectra (400 MHz, 25 mM sodium phosphate buffered D_2O, pD 7.4) for: a) CB[10]·**2** (100 μM) alone and in the presence of pyridine (**5**), b) 39 μM, c) 148 μM, and d) 529 μM. e) Plot of chemical shift versus [**5**] used in the determination of the K_a value. f) Job plot for mixtures of CB[10]·**2** and **5** at a total concentration of 1 mM.

shift of the signal. We constructed a Job plot to verify a 1:1 binding model, which was then used to extract a binding constant for CB[10]·**2**·**5** ($K_a = (9700 \pm 300)\,M^{-1}$) from the titration data by monitoring the chemical shifts of either H_a of **2** or H_x of CB[10] (Figure 3e,f). Unfortunately, we were not able to observe any change in the chemical shifts of the protons on guest **5** because of exchange-induced broadening. Only minor changes were observed in the intensity and position of the Q band (566 to 562 nm) in the UV/Vis spectrum, which suggested that direct zinc–pyridine coordination does not occur within CB[10]·**2**·**5**. Apparently, it is energetically more favorable for pyridine (**5**) to form a ternary complex (CB[10]·**2**·**5**) that benefits from π–π stacking interactions.

To gain further support for the π–π stacking rather than metal–ligand coordination model we examined the behavior of bulkier and more hydrophobic guests **6**–**10**. Stronger binding is observed for guests **6**–**9** which fit well to a 1:1 binding model (**6**: $(112000 \pm 17000)\,M^{-1}$; **7**: $(127000 \pm 22000)\,M^{-1}$; **8**: $(48000 \pm 3400)\,M^{-1}$; **9**: $(25600 \pm 500)\,M^{-1}$). These results are consistent with a π–π-stacked geometry and the enhanced hydrophobicity of guests **6**–**9** relative to **5**. When 4,4′-bipyridine (**10**) was added to a solution of CB[10]·**2**, we observed the formation of a tight 1:1 complex whose K_a value was inaccessible by ^{1}H NMR or UV/Vis spectroscopic titration. At substoichiometric amounts of **10** (0.25 and 0.5 equiv) we observed ^{1}H NMR resonances for **10** at $\delta = 3.55$ and 6.38 ppm which are significantly upfield shifted relative to those of free **10**, which resonate at $\delta = 7.73$ and 8.59 ppm (see the Supporting Information). The magnitude of these shifts ($\Delta\delta = 2.2$–4.2 ppm) is indicative of an offset π–π-stacked rather than an orthogonal zinc–ligand-type geometry.[15] We further surveyed the scope of guests that bind within CB[10]·**2** and found that aromatic compounds (benzene, toluene, ethylbenzene) and heteroaromatic compounds (**11**, **12**, furan, pyrrole, imidazole, 2,6-picoline) exhibit the spectroscopic earmarks of binding (see the Supporting Information). Interestingly, alicyclic amines such as pyrrolidine and negatively charged guests such as *p*-toluenesulfonic acid do not bind with CB[10]·**2**. We conclude that the CB[10]·**2** complex efficiently combines the preference of CB[10] to complex cationic species with the pronounced ability of porphyrins to engage in π–π interactions.

In summary, we have shown that CB[10]—with its spacious 870-Å^3 cavity—is capable of acting as a host for free base and metalated tetra(*N*-methylpyridinium)porphyrins. Despite the large ellipsoidal deformation of CB[10] upon complexation, the complexed porphyrins retain their fundamental UV/Vis, fluorescence, and electrochemical properties. These CB[10]·porphyrin complexes thereby combine the useful recognition properties of the CB[*n*] family (for example, environmental responsiveness)[9a] with the function of the porphyrins. Besides the ability of CB[10]·**2** to promote the formation of ternary complexes with suitable guests in water, the implications of this research are broad. For example, the ability of CB[10] to protect and preserve the properties of encapsulated porphyrins suggests application in a wide variety of areas including enzyme-mimetic catalysts for oxidation chemistry, targeted phototherapeutic agents, as an insulating unit for conjugated molecular wires, and in the construction of light-harvesting materials and photovoltaic devices.[1–4]

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[11] The pyridyl protons of **1** and **2** do not split upon formation of CB[10]·**1** and CB[10]·**2** as a result of rapid rotation around the porphyrin–pyridyl bond.

[12] At 10 μM total concentration, the CB[10]·**2** complex begins to dissociate (6%) into free CB[10] and **2** as observed by ^{1}H NMR spectroscopy, which allows us to estimate the value of K_a for this complex ($K_a \approx 10^6\ M^{-1}$). We attempted to measure the dissociation rate constant for CB[10]·**2** by the addition of an excess of tighter binding CB[5]. The exchange reaction to yield CB[10]·CB[5] was complete before an NMR spectrum could be measured (ca. 60 s).

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[14] Porphyrin **2** does not exhibit solvatochromic changes in its UV/Vis or fluorescence spectra in MeOH or EtOH. The lack of change in the UV/Vis, fluorescence, and electrochemical properties of the CB[10]·porphyrin complexes was surprising given the precedents with smaller CB[*n*] derivatives (Refs. [9] and [13]) and may reflect that the larger cavity of CB[10] provides a microenvironment similar to that of these polar solvents.

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