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# Porphyrin-Containing Molecular Capsules: Metal Mediated Dimerization of a Bis-Porphyrin Cavity

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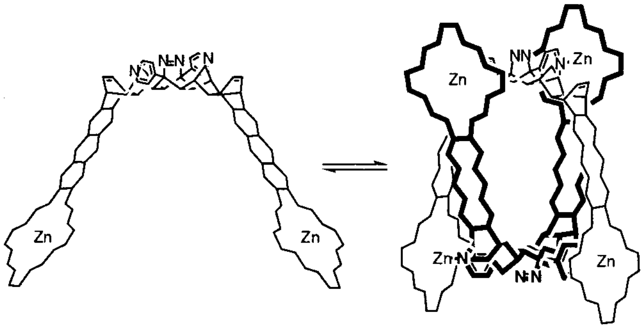
## ABSTRACT



**A self-complementary V-shaped bis-porphyrin cavity has been synthesized that is capable of dimerization to form a capsule structure. Self-assembly of the dimer occurs via metal ion coordination and produces an internal volume for guest encapsulation.**

Molecular systems that can enclose space in a controlled fashion are receiving active attention in the current literature.[2] Noncovalent interactions and self-assembly protocols are emerging as alternatives superior to assemblies largely prepared by covalent synthesis. In particular, capsule systems that reversibly form have been predominantly based on hydrogen bonds. These include Rebeks' "sportsballs", which stem from the glycoluril building block; urea-functionalized calixarene dimers reported independently by Rebek, Bohmer, Reinhoudt and de Mendoza;[2] and giant spherical arrays constructed from calixarene units.[3] Metal ion coordination has also been explored as a means of host assembly and has been reviewed.[4]

Recent developments in this field have seen the incorporation of the porphyrin or phthalocyanine moieties into capsule systems utilizing both metal ion coordination and hydrogen bonding interactions.[5] Most porphyrin-containing systems have formed around a templating guest, which not only serves to position the porphyrin units but also voids the cavity for further guest encapsulation by filling the interior portion of the resulting container system.[6] We report herein a porphyrin-containing molecular capsule **1** that assembles from two self-complementary V-shaped units (Figure 1). Simultaneous intermolecular coordination between the zinc metalloporphyrins and suitably positioned pyridyl ligands of each cavity enable capsule formation, producing a interior cavity of suitable size for the encapsulation of guests.[7]

We have reported[6c] the synthesis of the V-shaped bis-porphyrin system **5a** having a metal−metal separation of 22 Å (Figure 2). Reaction of 2-pyridyl *s*-tetrazine **3a** and **2** under

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[2] Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647 and references therein.

[3] Orr, G. W.; Barbour, L. J.; Atwood, J. L. *Science* **1999**, *285*, 1049.

[4] Fujita, M. *Chem. Soc. Rev.* **1998**, *27*, 417. Jones, C. J. *Chem. Soc. Rev.* **1998**, *27*, 289. Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.

[5] Lutzen, A.; Starnes, S. D.; Rudkevich, D. M.; Rebek, J., Jr. *Tetrahedron Lett.* **2000**, *41*, 3777. Ikeda, A.; Ayabe, M.; Shinkai, S.; Sakamoto, S.; Yamaguchi, K. *Org. Lett.* **2000**, *2*, 3707.

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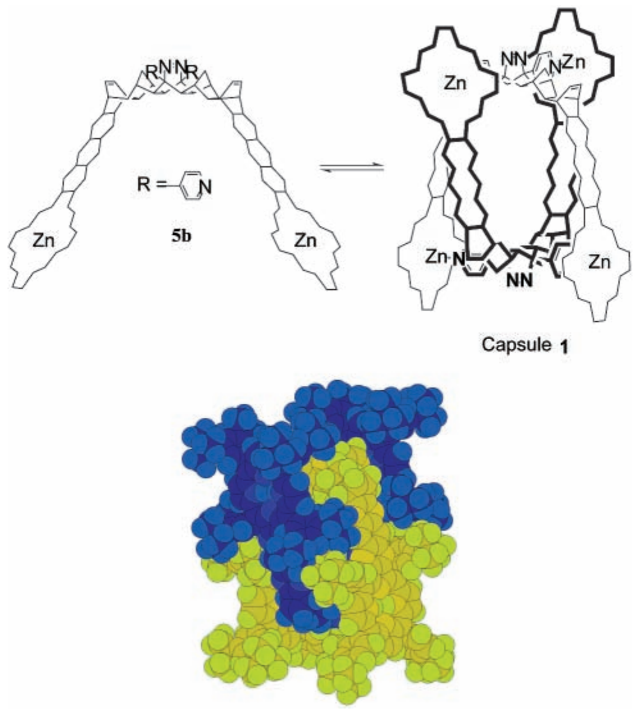

**Figure 1.** Schematic representation of the capsule dimerization of **5b**; space filling model of the capsule.

high-pressure conditions afforded cavity **4a**, followed by metalation to give **5a**. In seeking suitably sized guests with terminal groups that can coordinate to the metalloporphyrin sites of host **5a**, we were guided by best-fit dimensions determined by molecular modeling. Indeed several 5,15-dipyridylporphyrins[8] and dipyridyldiimides were successfully complexed within **5a** with association constants of $10^8$ $M^{-1}$.[9] The walls of the host collapsed approximately 2 Å when complexing such guests.

From these experiments it was established that the cavity could modify the porphyrin center-to-center separation to accommodate smaller guests. We reasoned that this could be used to create a bis-porphyrin host that could dimerize by a self-complementary process. Incorporation of the pyridyl groups onto the edge of the cavity backbone should allow the metalloporphyrin of one cavity to coordinate with the pyridyl groups of the partner cavity at the same time as the complementary set of coordination sites were undertaking a similar complexation.

In order for this dimerization to occur successfully, deformation of cavity **5a** by 7 Å was necessary to simultaneously coordinate the spacer pyridyl ligands. To examine the feasibility of such a large change in the host geometry a model guest was targeted, viz., the alicyclic norbornane **6**[10] (Figure 3). $^1$H NMR spectroscopy was used to observe the complexation of **6** within **5a**.[11] Figure 3 represents the chemical shift changes for proton resonances of **6**, which are characteristic of guests held in close proximity to porphyrin macrocycles.

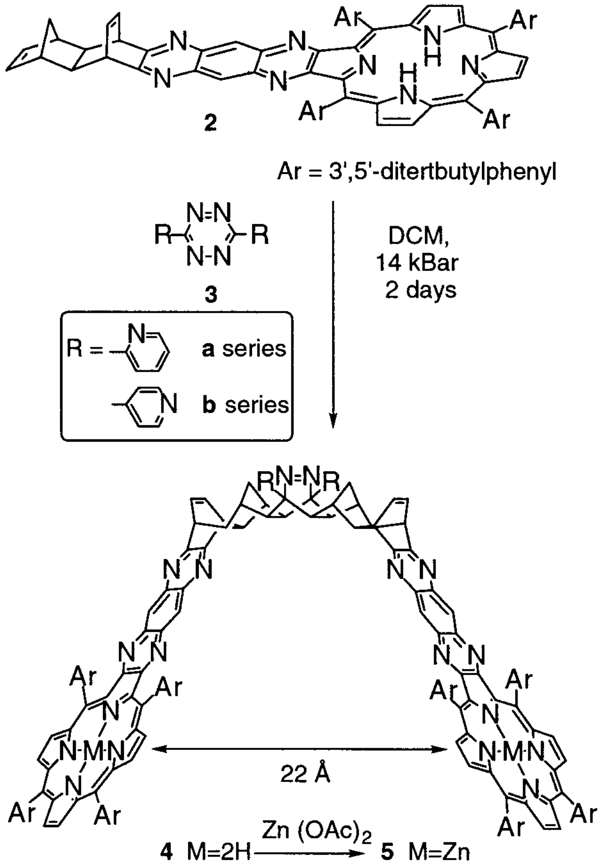

**Figure 2.** Synthesis of V-shaped bis-porphyrin cavities utilizing the *s*-tetrazine coupling protocol.

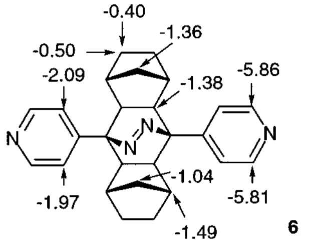

**Figure 3.** $^1$H chemical shift changes observed when **6** is complexed within **5a** in chloroform solution.

Demonstrating the successful complexation of **6** augured well for capsule formation, and attention was turned to the

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(6) (a) Felluga, F.; Tecilla, P.; Hillier, L.; Hunter, C. A.; Licini, G.; Scrimin, P. *Chem. Commun*. **2000**, 1087. (b) Reek, J. N. H.; Schenning, A. P. H. J.; Bosman, A. W.; Meijer, E. W.; Crossley, M. J. *Chem. Commun*. **1998**, 11. (c) Johnston, M. R.; Gunter, M. J.; Warrener, R. N. *Chem. Commun*. **1998**, 2739.

(7) Examination of the structure of **1** by molecular modeling, which was carried out by John Ripmeester and Konstantin Udachin, allowed the cavity volume to be estimated at 472 Å$^3$.

(8) Flamigini, L.; Talarico, A. M.; Barigelletti, F.; Johnston, M. R. *Photochem. Photobiol. Sci.* **2002**, *1*, 190.

(9) Flamigini, L.; Johnston, M. R. *New J. Chem.* **2001**, *25*, 1368.

bis-porphyrin cavity **b** series containing terminal 4-pyridyl ligands from the host backbone (Figure 2). The synthesis of bis-porphyrin cavity **4b** paralleled that of **4a** but used the tetrazine **3b** in the coupling reaction. Characterization of cavity **4b** also yielded NMR shifts similar to those of **4a** for all proton resonances, with the exception of the pyridyl protons.[12]

The self-complementary nature of **5b** implies that two possible modes of dimerization exist. The first is outlined in Figure 1 and results in capsule formation. The second is the precursor to the formation of a linear polymeric chain of **5b** (not shown).

The linear dimerization possibility was modeled using **5a** and **4b** and resulted in the observation of shifts on the alicyclic backbone of **4b** similar to those observed when **6** was complexed within **5a**. The porphyrin resonances of **4b** were largely uneffected by this complexation.

Metalation of bis-porphyrin **4b** gave the self-complementary cavity **5b** (Figure 2). The $^1$H NMR spectra of **5b** were observed to be considerably solvent-dependent. In DMF, THF, chloroform, or benzene broad indecipherable spectra were observed, whereas sharp spectra were seen in toluene, *o*-xylene, and DCM (Supporting Information). Similiar solvent-dependent behavior has been reported for self-complementary systems and have been related to the ability of the solvent to act as a guest within the capsule: a maximum occupancy of 55% of the available space is reported.[13]

In solvents where sharp spectra are observed, all resonances have undergone shifts from those expected for **5b** by analogy with **5a**, i.e., there is no evidence for free **5b** in solution, but rather for complexed species only. This situation is observed from milli- to micro-concentrations, implying dimerization is occurring at least over this concentration range, if not more. In the case of micromolar concentrations, $^1$H NMR spectra were acquired over 12 h. Shifts similar to those observed for the alicyclic backbone of guests **4a** or **6** when complexed with **5a** are also seen for the backbone resonances of **5b** in the complexed form.

In addition to the changes in chemical shifts observed with the **5a·6** complex, changes were seen in resonances of the *meso*-aromatic and *tert*-butyl moieties. In particular, half of the *meso*-aromatic proton resonances were shifted downfield (av $\Delta\delta$ 0.3 ppm) as well as half of the *tert*-butyl resonances (av $\Delta\delta$ 0.5 ppm respectively). These changes are thought to result from the close proximity of each of the upper *meso*-aromatic rings in **5b** to the upper *meso*-aromatic rings of its complementary partner when positioned within the capsule structure **1**. This interaction only occurs around the central "equatorial" section of **1** and explains why only half of the *meso*-aromatic and *tert*-butyl resonances are affected.[14] Such shifts have not been observed previously in other bis(4-pyridyl) guest complexes with **5a** and are not predicted to occur if a polymeric material had been formed.

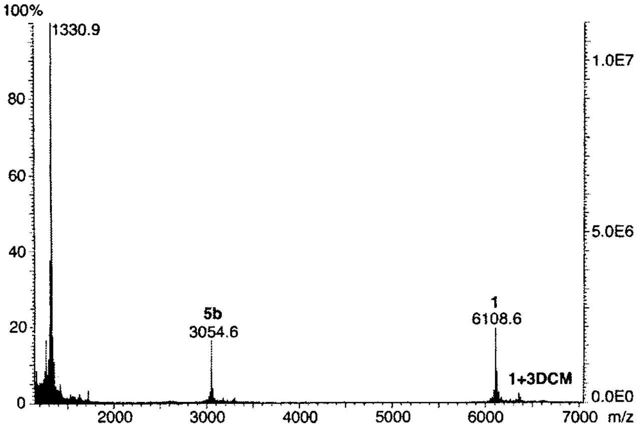

**Figure 4.** FAB MS spectra of capsule **1** recorded in DCM.

To date we have not observed the presence of resonances for encapsulated guests, although a range of guests with various shapes and sizes have been examined. Baffled by this fact we are currently undertaking modeling studies to ascertain the reason behind this phenomena as regards the various "door" mechanisms of guest exchange.[15]

Examination using FAB-MS (Figure 4) revealed the presence of a molecular ion for cavity **5b** (*m*/*z* 3054) and capsule **1** (*m*/*z* 6109), as well as capsule with included DCM (*m*/*z* 6358). Since NMR gives no indication as to the presence of free **5b** in solution, the observation of **5b** in the FAB spectrum presumably is a result of capsule dissociation within the spectrometer.

Additional evidence for capsule formation in solution was acquired by pulse field gradient-stimulated echo (PFG-STE) NMR spectroscopy. This technique has been successfully applied to systems providing information on the size of molecular aggregates in solution.[16] Examination of DCM solutions of **5a** and **5b** (containing added toluene) were conducted using a variety of gradient pulse and evolution times, yielding diffusion coefficients that were subsequently converted to an average molecular radius. In the case of cavity **5a**, an average molecular radius of 12.3 Å compares well with a theoretical value of 12.8 Å obtained from molecular modeling. For capsule **5b** a molecular radius of 13.8 Å is consistent with the theoretical value of 14 Å for **1**.

As we have the capacity to systematically extend the cavity backbone and ligands, cavity systems of larger volumes may

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(10) Margetic, D.; Warrener, R. N. Unpublished result.

(11) The NMR spectrum of uncomplexed **6** contains four pyridyl proton resonances, which coalesce at temperatures above ambient as a result of restricted rotation around the pyridyl−alicyclic backbone bond.

(12) All materials were characterized by $^1$H NMR (400 MHz) and high-resolution electrospray mass spectroscopy.

(13) Mecozzi, S.; Rebek, J., Jr. *Chem. Eur. J.* **1998**, *4*, 1016.

(14) With the capsule positioned as in Figure 1, the central section flanked by tetrazananthracene moieties has been designated "equatorial". It is within this area that interactions occur between *meso*-aromatic and *tert*-butyl groups of each bis-porphyrin half of the capsule.

(15) Wang, X.; Houk, K. N. *Org. Lett.* **1999**, *1*, 591.

(16) Timmerman, P.; Weidmann, J.-L.; Jolliffe, K. A.; Prins, L. J.; Reihoudt, D. N.; Shinkai, S.; Frish, L.; Cohen, Y. *J. Chem. Soc., Perkin Trans. 2* **2000**, *2*, 2077. Keresztes I.; Williard, P. G. *J. Am. Chem. Soc.* **2000**, *122*, 10228.

be constructed. In addition, our construction techniques allow inside functionality to be attached to the monomer bisporphyrins and that aspect, along with guest encapsulation within **1**, is currently being explored in our laboratories.

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**Supporting Information Available:** Experimental procedures and analytical data for **4b** and **5b** and $^1$H NMR spectra of **5b** in different solvents. This material is available free of charge via the Internet at http://pubs.acs.org.

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