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A self-assembled phthalocyanine dimer

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Abstract

The synthesis of phthalocyanines **1a** and **1b** appended with four glycoluril modules is presented. ^{1}H NMR spectroscopy showed that **1a** and **1b** self-assemble by means of hydrogen bonding to form discrete dimers. Capsule formation is solvent dependent where the dimeric assembly is most pronounced in aromatic solvents.

Keywords: phthalocyanine; self-assembly; supramolecular chemistry; hydrogen bonds.

Reversibly formed, self-assembled capsules are recently devised systems that provide new forms of molecular recognition.[1] Increasingly, these systems are incorporating function; one particularly attractive function is as a reaction chamber.[2] It could be advantageous to incorporate metallo catalytic sites into these chambers, in a manner that has proven successful for other reversibly formed, self-assembled systems,[3] and we describe here our initial steps toward this goal.

Phthalocyanine was selected as framework for receptor scaffolding: the known catalytic properties,[4] the C_{4v} symmetry and the extended aromatic π surface that the molecule presents are all attractive features. The phthalocyanine core, in combination with the workhorse glycoluril and its self-complementary hydrogen bonding motif, leads to structure **1** (Fig. 1). Inspection of the model suggests that it is preorganized for self-assembly and it does indeed give a discrete dimeric capsule in solution.

The synthesis of **1** (Scheme 1) started with the bromination of *o*-xylene to give 4,5-dimethyl-1,2-dibromobenzene[5] followed by a Rosenmund–von Braun reaction to give 4,5-dimethyl-1,2-dicyanobenzene.[6] A second bromination afforded 4,5-di(bromomethyl)-1,2-dicyanobenzene,[7] which was coupled with the PMB-protected glycoluril **2**[8] to give **3**. Deprotection of **3** with ceric ammonium nitrate (CAN)[8] proceeded smoothly to give the phthalocyanine precursor **4**, which was cyclized to the metallated phthalocyanine product **1a** and **1b** by gentle reflux of **4** in *n*-pentanol with $Ni(OAc)_2$ or $Zn(OAc)_2$ and a catalytic amount of DBU.[9] At this stage, purification of **1a** and **1b** proved to be quite tedious and not trivial. This, in part, is due to the necessity to separate the four stereoisomers of **1** produced in the synthesis. Borrowing the terminology popular in porphyrin chemistry, we describe

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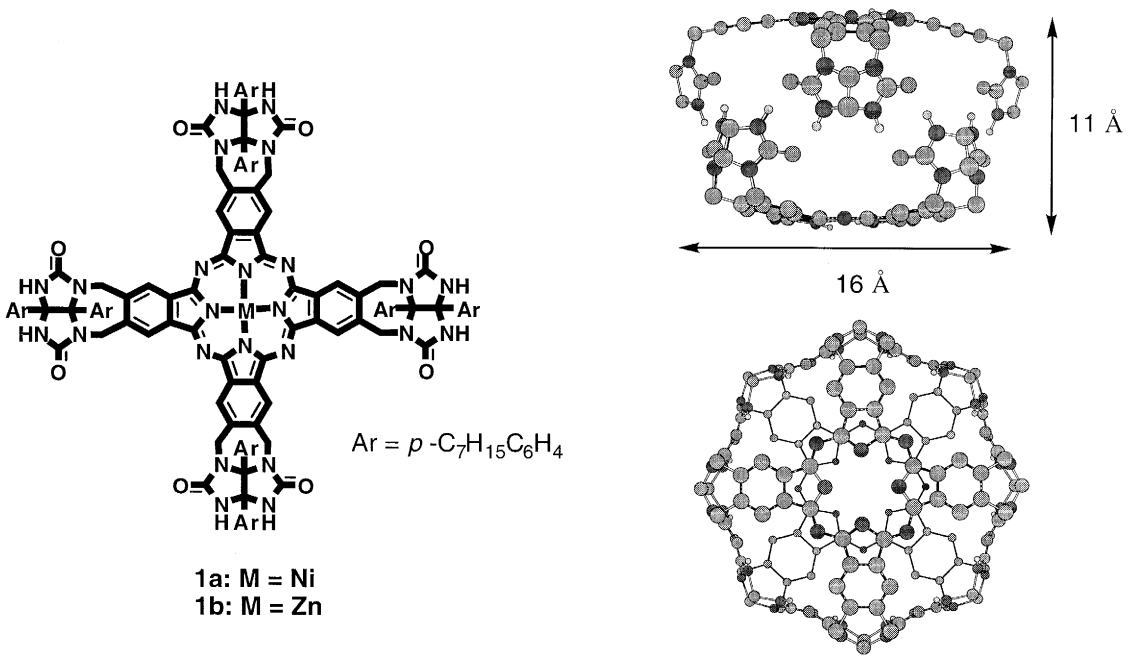
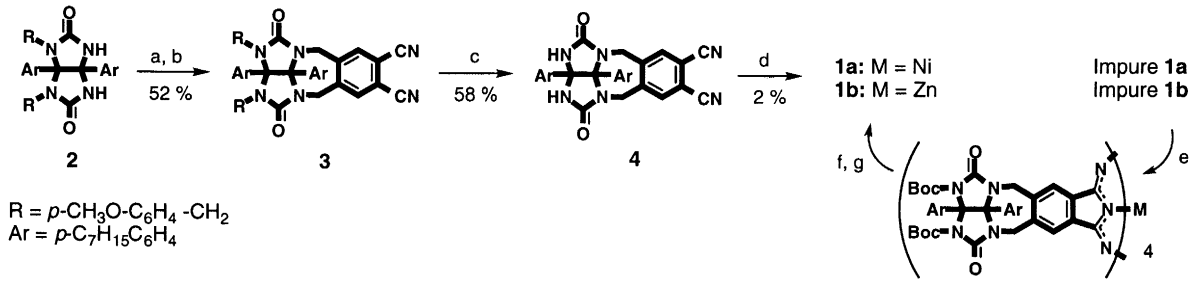


Fig. 1. Phthalocyanine **1** and the energy minimized metal free dimeric assembly — side view and top view. CH hydrogens and C_7H_{15} chains are omitted for viewing clarity

the four stereoisomers as αααα, ααβ, ααββ, and αβαβ with respect to the orientation of the four glycolurils, with the further understanding that the isomers are not interconvertible. To our delight, it was found that extraction of the crude reaction mixture with *p*-xylene enriched the sample in the desired αααα-isomer, which was then further purified by chromatography. During the course of the synthesis, it was also found that impure **1** could be derivatized to the less polar Boc-protected derivative which was purified by chromatography over silica gel; deprotection afforded **1** in return.



Scheme 1. Reagents and conditions: (a) NaH, DMF, rt; (b) 4,5-di(bromomethyl)-1,2-dicyanobenzene; (c) CAN, CH_3CN:THF:H_2O 7:3:1, rt; (d) $M(OAc)_2$, cat. DBU, *n*-pentanol, reflux; (e) Boc-anhydride, THF, DMAP; (f) purify over silica gel; (g) CH_2Cl_2, TFA

Molecular modelling of **1** dimer using Macromodel[10] and the Amber*[11] force field suggested that the assembly offers a spacious binding cavity. An internal volume of ~275 Å^3 was calculated using GRASP.[12] At least two molecules of benzene can fit comfortably inside. The overall shape can best be described as a molecular box somewhat similar to the jelly doughnut,[13] a structure that was shown to encapsulate disc-like molecules (benzene and cyclohexane, for example).

^{1}H NMR spectroscopy was used to determine if the molecule self-assembled as predicted, through the seam of 16 hydrogen bonds. The telltale sign indicating assembly is the chemical shift of the glycoluril-NH signal — in the assembled state, it is expected downfield of 8 ppm, whereas in the non-assembled state this signal is expected upfield of 6 ppm.[2,8,13,14] From Table 1, which lists the chemical shift of the glycoluril-NH of **1a** and **4** in a variety of solvents, it is apparent that **1** assembles in aromatic solvents. In *p*-xylene-d_{10}, for instance, the chemical shift of the glycoluril-NH of **1a** and **1b** is 9.05 and 8.90 ppm, respectively, indicative of the self-assembled dimer. In contrast, the glycoluril-NH resonance of **4** falls at 4.97 ppm in *p*-xylene-d_{10}. Fig. 2 provides a portion of the ^{1}H NMR spectrum of **1a** in *p*-xylene-d_{10}. In order to verify the nature of the resonance at 9.05 ppm as belonging to that of the glycoluril-NH, a drop of D_2O was added to the NMR sample, which resulted in the disappearance of the signal at 9.05 ppm (from Fig. 2a). Compounds **1a** and **1b** have also been shown to self-assemble in toluene-d_8, benzene-d_6, and cyclohexane-d_{12}. It is likely that the mere fact that **1** assembles in *p*-xylene assisted in the purification of the compound. In the assembled state, **1** exposes 16 solubilizing alkyl groups to the solvent while shielding two of its four aromatic surfaces. As a result, **1** is more soluble than the other three stereoisomers in *p*-xylene and facilitates its own purification.

Table 1
^{1}H NMR chemical shift of the glycoluril-NH of **1a** and **4** in different solvents[a]

1a	δ (N-H)	**1a**	δ (N-H)	**4**	δ (N-H)
$CDCl_3$	5.42	*p*-Xylene-d_{10}	9.05	$CDCl_3$	5.93
CD_2Cl_2	*b*	Benzene-d_6	9.11	*p*-Xylene-d_{10}	4.97
Decaline-d_{18}	*b*	Toluene-d_8	9.14		
Acetone-d_6	*b*	Cyclohexane-d_{12}	9.57		

[a] Solvent peak was utilized as internal standard.

[b] A complicated spectrum is obtained in these solvents which we attribute to non-specific aggregation.

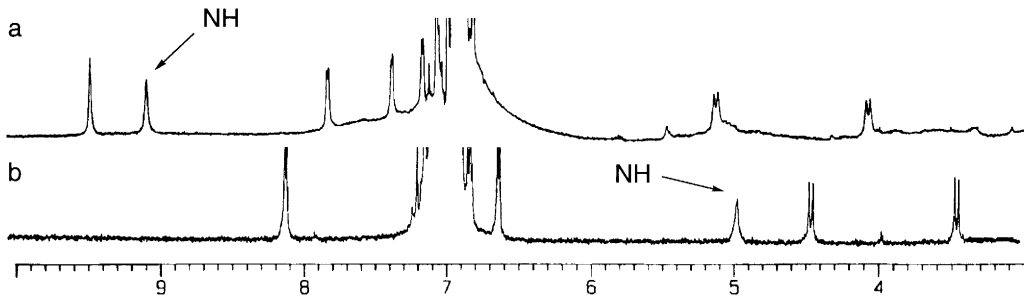


Fig. 2. Portion of the ^{1}H NMR spectra of **1a** (a) and **4** (b) in *p*-xylene-d_{10}

Compound **1** does not assemble in $CDCl_3$, CD_2Cl_2, *cis*/*trans*-decaline-d_{18}, or acetone-d_6. The lack of assembly of **1** in these solvents indicates that the dimeric assembly formed in aromatic solvents may enjoy additional stabilization from interior π-stacking interactions. With two molecules of benzene included within the cavity, the volume shrinks slightly to 270 Å^3 with a packing coefficient of 62% which is slightly higher than the ideal packing coefficient of ~55%.[15] The two benzene molecules stack with opposite phthalocyanine units at 3.4–3.5 Å and with each other at 3.8 Å.

The molecular recognition and catalytic properties of this assembly are currently being investigated and will be reported in due course.

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