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Non-Covalent Synthesis in Aqueous Solution of Discrete Multi-Porphyrin Aggregates with Programmable Stoichiometry and Sequence

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Multi-(metallo)porphyrin systems have been extensively investigated for their numerous applications as supramolecular devices; for example, model systems of the photosynthetic center, sensors, photoactive species, nonlinear optical devices, and other.[1] The approaches mostly used to build these supramolecular systems are the covalent or noncovalent syntheses in nonaqueous environments. Until now the noncovalent syntheses of multi-porphyrin systems in aqueous solution have, in fact, been limited to the formation of trimeric species[2] or to more complex systems which, however, have ill-defined stoichiometry.[3] An additional limitation of the latter approach is that porphyrin sequence is not under control. Here we show that a very simple approach allows for the noncovalent syntheses of supramolecular species: (i) having a predetermined porphyrin stoichiometry and sequence and (ii) containing at least four different porphyrins (or metalloporphyrins). This result has been achieved owing to the templating role of the calixarenes and to the remarkable stability of the species formed in each complexation step.

We have recently shown that it is possible to modulate the stoichiometry of the noncovalent conjugates formed by the tetracationic porphyrin H_2T_4 (Figure 1, a) and the anionic calixarene C_4TsTc (Figure 1b). Stoichiometry tuning is afforded by changing with pH the protonation state of C_4TsTc carboxylic groups: that is, charge modulation of these moieties allows for stoichiometry tuning.[4,5] Then the role of C_4TsTc is two-fold: (i) they shield the electrostatic repulsion between the like-charged porphyrins owing to the presence of the sulfonic and carboxylic groups and, (ii) they provide an environment where various types of noncovalent interactions can be arranged. Solution (Job plots) and solid-state data indicate evidence for the formation of the 3:4 (H_2T4:C_4TsTc) species at pH 2.2 and of the 5:4 complex at pH 6.0. Crystal data show that both complexes share a 1:4 core (Figure 2) in which each of the four *N*-methylpyridinium groups of the central H_2T4 interacts with the sulfonic groups of a C_4TsTc unit. The 3:4 and 5:4 complexes are built by piling, respectively, two and four additional porphyrins to the 1:4 unit.

However, the lack at pH 6.0 (in pure Millipore water) of the 3:4 species[4] is not conceivable. This species forms, in fact, in conditions in which carboxylic groups are protonated (pH 2.2)[5] and their shielding ability is poor. Consequently, the 3:4 should form even more at pH 6.0 because now carboxylic groups are deprotonated and exert a very effective attracting and shielding role.[5]

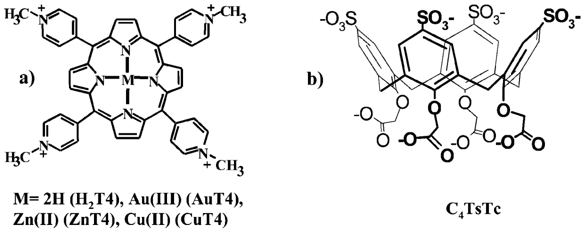

Figure 1. Schematic structure of (a) *meso*-tetrakis(*N*-methylpyridyl-4)-porphyrin (H_2T4) and its metal derivatives (MT4) and (b) of 5,11,17,23-tetrasulfonato-25,26,27,28-tetrakis(hydroxycarbonylmethoxy)-calix[4]arene (C_4TsTc, cone conformation).

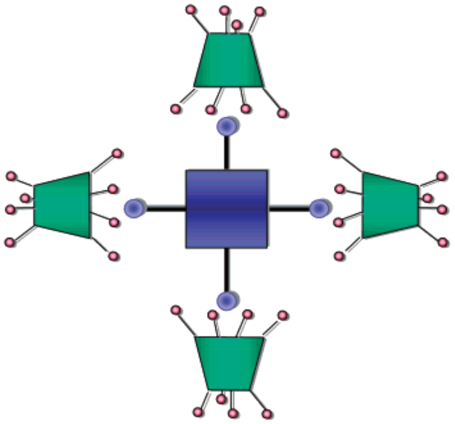

Figure 2. Sketch of the (X-ray determined)[4] 1:4 unit structure.

Then, to better characterize the system we have performed absorption and fluorescence titrations by adding porphyrins to aqueous solutions of calixarene (pH 6.0, no buffer added).[6] As already reported,[4] the main porphyrin absorption band (Soret band) experiences a quite strong hypochromicity when H_2T4 is added to an aqueous solution containing C_4TsTc (see for comparison the behavior in the absence of calixarene, line b in Figure 3). In addition, the titration curve in Figure 3 (curve a) shows the presence of five break-points, indicating the formation of various species, namely, the 1:4, 3:4, 5:4, 6:4, and 7:4 complexes.[7] The same trend is observed when monitoring the calixarene or porphyrin fluorescence (data not shown).

The presence of various, distinct break-points suggests the possibility of performing a step-wise synthesis of ***mixed***-porphyrin supramolecular complexes; that is, the stoichiometric addition of various porphyrins to the 1:4 species should lead to the gradual formation of mixed-porphyrin supramolecular complexes. This approach works very well as can be verified by plotting calixarene emissions versus the moles of porphyrin required for four calixarene moles (i.e., $[H_2T4] \times 4/[C_4TsTc]$) (Figure 4). Here, after the formation of $H_2T4-(C_4TsTc)_4$ (break-point at 1), the addition of 2

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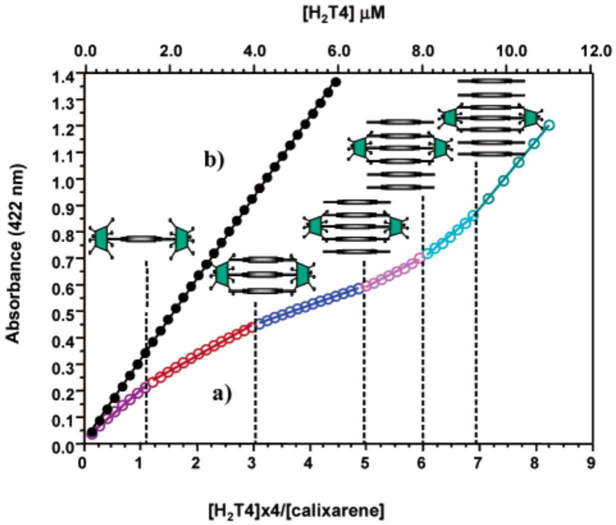

Figure 3. Soret band intensity following addition of increasing amounts of H_2T4 to a calixarene (5.7 μM) aqueous solution (curve a) and pure water (curve b). The different break-points (curve a) are evidenced by dotted lines, and the corresponding species (side view) are sketched just above them. For the sake of clarity the two calixarenes above and below the reading plane have been omitted.

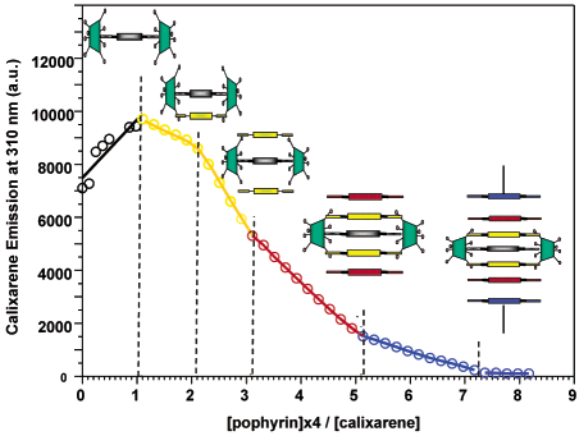

Figure 4. Calixarene emission following the addition of various porphyrins vs the moles of porphyrins required for four calixarene moles ([MT4] × 4/[C_4TsTc]). The different break points are evidenced by dotted lines, and the corresponding species (side view) are sketched just above them. For the sake of clarity the two calixarenes above and below the reading plane have been omitted. The black, yellow, red, and blue lines represent the additions (and sketched structures) of H_2T_4, AuT_4, CuT_4, and ZnT_4, respectively.

equiv of AuT4 leads to the two mixed AuT4-H_2T4-(C_4TsTc)$_4$ and (AuT4)$_2$−H_2T4−(C_4TsTc)$_4$ species (break-points at 2 and 3, respectively). The successive addition of 2 equiv of CuT4 allows for the formation of (CuT4)$_2$−(AuT4)$_2$−(C_4TsTc)$_4$ (break-point at 5), and eventually, 2 additional equiv of ZnT4 leads to a (ZnT4)$_2$−(CuT4)$_2$−(AuT4)$_2$−H_2T4−(C_4TsTc)$_4$ complex (break-point at 7). It is clearly possible to stop the synthesis at any of these steps or to change the addition order to obtain the desired complex both in terms of stoichiometry and sequence.

The structure of the 1:4 complex (Figure 2) shows that the porphyrin core is not directly involved in the interactions with calixarenes, implying that the presence of a central metal ion should not hinder the formation of this complex. Accordingly, also the gold(III) derivative behaves as the free porphyrin,[8] the only difference being that complexation stops at a 5:4 ratio.[9] The possibility of synthesizing the 1:4 species holds, very likely, for all of the metal derivatives of H_2T4, allowing for the design and syntheses of a huge number of mixed metalloporphyrin supramolecular species.[10]

The step-by-step modulation of the species stoichiometry by addition of the precise stoichiometric ratio of the components suggests that complexation is almost quantitative. Most likely, this is due to a combination of thermodynamic (high stability of the complexes) and kinetic (inertness of the species) effects. A similar behavior has been recently observed in supramolecular aggregates formed by ***multicharged*** achiral cationic and anionic porphyrins and allows these complexes to retain the memory of the chirality induced during the onset of the complex.[11,12]

This is a clear example of how the noncovalent synthesis of supramolecular complexes in aqueous solution can approach the same accuracy of the covalent (and noncovalent in nonaqueous environment) synthesis in controlling both the stoichiometry and the sequence of the various components. The easy experimental approach and the high yield of this procedure open new frontiers in the design and synthesis of specific multi-porphyrin aggregates having a wide range of possible applications: from models of heme-proteins to molecular devices. In our opinion this “mixing-and-shaking” templated synthetic procedure is a candidate as an innovative general approach to build noncovalent robust supramolecular species in aqueous solution.

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(5) The four pK_a values of C_4TsTc are: pK_{a1} = 3.03, pK_{a2} = 3.27, pk_{a3} = 3.97, pK_{a4} = 4.57 as determined by Arena, G.; Calì, R.; Lombardo, G. G.; Rizzarelli, E.; Sciotto, D.; Ungaro, R.; Casnati, A. *Supramol. Chem.* **1992**, *1*, 19−24.
(6) pH does not vary during the titration.
(7) A closer look at the titration reported in Figure 3 shows slope changes at both the 2:4 and 4:4 ratios. However, the break points are not sharp enough to clearly state the formation of these species. On the other hand, the formation of the 2:4 species is well recognized in Figure 4.
(8) Complexation has been followed by monitoring C_4TsTc emission quenching because AuT4 does not emit.
(9) Most likely this limitation is due to the presence of an extra positive charge in the porphyrin core.
(10) Preliminary observations show that penta- and hexacoordinated porphyrins can also form the 1:4 complex and successively all the other mixed species with planar (or pentacoordinated) porphyrins. In fact, the mean distance of the porphyrin-to-porphyrin planes is about 4.1 Å,[4] while the distance between an axially coordinated water molecule and the porphyrin plane is about 2.5 Å.
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