

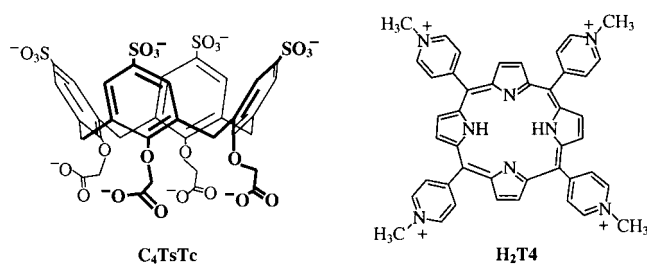
anisotropically. Some disorder in one of the cyanide groups and the (S)-pn ligands coordinated to  $\text{Mn}^{2+}$  ions was also observed. The occupancy of the disordered atoms and the  $\text{K}^+$  ion was determined by population analysis. The refinement converges with  $R_1 = 0.0615$  for 2520 data ( $I > 4\sigma(I)$ ),  $wR_2 = 0.1371$  for 5405 unique data ( $2.81 \leq \theta \leq 28.33^\circ$ ), Flack parameter = 0.06(5), max/min residual electron density 0.527/−0.298  $\text{e} \text{ \AA}^{-3}$ . Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-165941. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

## Calixarene – Porphyrin Supramolecular Complexes: pH-Tuning of the Complex Stoichiometry\*\*

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The rich chemistry of calixarenes and porphyrins as (polytopic) receptors and photoactive species, respectively, as well as the enormous possibility of functionalizing the periphery of these molecules have boosted the synthesis of their covalent conjugates for use as possible molecular devices.<sup>[1]</sup> It has recently been shown, for example, that covalent porphyrin–calixarene conjugates behave as molecular tweezers when individual specific functions are synergistically exploited.<sup>[2]</sup> Some preliminary data on the formation of noncovalent complexes have also been reported but, to date, no structural data on such supramolecular species have been presented.<sup>[3]</sup>

Here we present a spectroscopic and structural study that shows that the cationic porphyrin ( $\text{H}_2\text{T4}$ ) and the anionic sulphonated calixarene ( $\text{C}_4\text{TsTc}$ ) blocked in a *cone* conformation and bearing carboxylic functions<sup>[4]</sup> form quite stable supramolecular complexes, both in the solid state and in



aqueous solution. Furthermore, the  $\text{H}_2\text{T4}:\text{C}_4\text{TsTc}$  molar ratio is tuned by the protonation state of the  $\text{C}_4\text{TsTc}$  carboxylate groups.

The absorption and fluorescence spectra of  $\text{H}_2\text{T4}$  are characterized by an intense absorption band at 422 nm (Soret band) and an emission at 650 nm, respectively.  $\text{C}_4\text{TsTc}$  absorbs in the far UV region (about 200 nm) and, at pH 6, emits at 307 and 602 nm. However, at pH 2.2, where the four carboxylic groups of  $\text{C}_4\text{TsTc}$  are all protonated ( $\text{pK}_{\text{a}1} = 3.03$ ,  $\text{pK}_{\text{a}2} = 3.27$ ,  $\text{pK}_{\text{a}3} = 3.97$ ,  $\text{pK}_{\text{a}4} = 4.57$ ),<sup>[5]</sup> the emissions are almost completely quenched.

The interaction of  $\text{H}_2\text{T4}$  with  $\text{C}_4\text{TsTc}$  at pH 6 and  $I = 0.05 \text{ M}$  (NaCl) is accompanied by significant hypochromism and broadening of the Soret band (see inset of Figure 1) and remarkable quenching of both the porphyrin and calixarene emissions. The spectroscopic features of  $\text{H}_2\text{T4}$  at pH 2.2 following complex formation with  $\text{C}_4\text{TsTc}$  ( $I = 0.05 \text{ M}$ ) are very similar to those observed at pH 6.

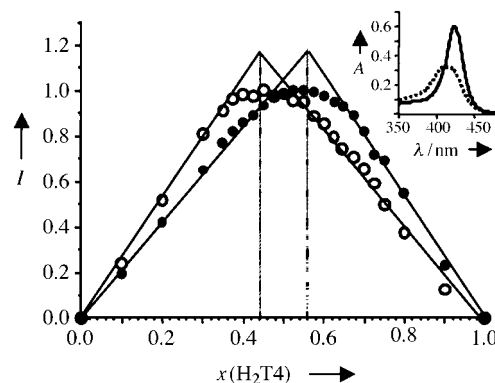


Figure 1. Normalized absorption Job plots at pH 2.2 (○) and 6 (●). The inset shows the absorption spectrum of  $\text{H}_2\text{T4}$  (2.8  $\mu\text{M}$ ) before (—) and after (---) the addition of  $\text{C}_4\text{TsTc}$  (2.2  $\mu\text{M}$ ).

However, the Job plots performed at pH 2.2 and 6 show there is a large difference in the ratio of the complex formed (Figure 1). The maximum value at a porphyrin molar fraction of 0.44 at pH 2.2 indicates the formation of species with a 4:3  $\text{C}_4\text{TsTc}:\text{H}_2\text{T4}$  ratio, whereas the maximum value at a porphyrin molar fraction of 0.56 at pH 6 indicates the formation of species with a 4:5  $\text{C}_4\text{TsTc}:\text{H}_2\text{T4}$  ratio. We were able to obtain single crystals of the porphyrin–calixarene complexes at  $\text{pH} \approx 2$  (**1**) and at pH 6 (**2**).

In agreement with the results from the solution study, the  $\text{H}_2\text{T4}:(\text{C}_4\text{TsTc}+\text{H}_2\text{T4})$  molar ratio is 0.43 (2 calixarene moieties, 1.5 porphyrin molecules, and 2 sodium ions) in the asymmetric unit of the crystals obtained at  $\text{pH} \approx 2$  (**1**).<sup>[6]</sup> Here,

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[\*\*] This work was supported by the Italian MURST (PRIN MM03185591).

the “central”  $H_2T4$  unit of a trimeric  $H_2T4$  ensemble is arranged on a crystallographic center of symmetry (1/4, 1/4, 0), and each of its methylpyridinium moieties is inserted into a tetra-anionic  $C_4TsTc$  molecule from the sulphonate side of the calixarene (Figure 2). The ditopic nature of  $C_4TsTc$  allows it

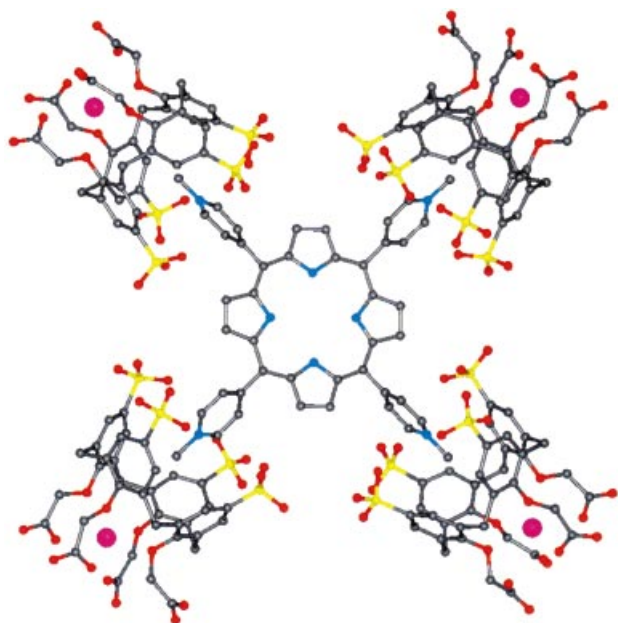


Figure 2. The host–guest interactions in the centrosymmetric unit formed by the central porphyrin cation with calixarene molecules and  $Na^+$  ions (violet circles).

to host one sodium ion on each carboxylate side of the calixarenes. In both **1** and **2** the  $Na^+$  ions are hepta-coordinated by oxygen atoms of the hydroxymethylmethoxy residues at distances in the range of 2.1–2.6 Å. The centrosymmetric unit is sandwiched by two porphyrin rings, which are rotated by 45° with respect to the central one. The resulting neutral supramolecular complex is characterized by a porphyrin mean plane separation of 4.2 Å between the nearly planar porphyrin rings (Figure 3a). The crystal is built up by these supramolecules in such a way as to form large channels (19 × 32 Å; Figure 4), in which the solvent molecules are disordered.

Unlike the crystals obtained at pH 2, the asymmetric unit of the crystals obtained at pH 6<sup>[6]</sup> contains two hepta-anionic calixarene molecules, three tetracationic porphyrin rings, and two sodium ions, with a  $H_2T4:(C_4TsTc+H_2T4)$  molar ratio of 0.6. This value corresponds to a  $C_4TsTc:H_2T4$  molar ratio of 4:6. Seemingly, this result disagrees with the 4:5 ratio obtained in solution. However, a closer look at the structure of **2** readily explains the difference. In fact, the same trimeric ensemble observed in **1**, still arranged on a crystallographic center of symmetry, is also present in **2**, but now, as a result of the deprotonation of the carboxylic groups, the trimeric “core” is stacked with two additional porphyrin rings, one above and one below. Each porphyrin ring is rotated by 45° with respect to the external  $H_2T4$  molecules of the trimeric core unit and leads to the 4:5 complex of Figure 3b. The nearly planar five porphyrin rings are separated by a mean plane distance of

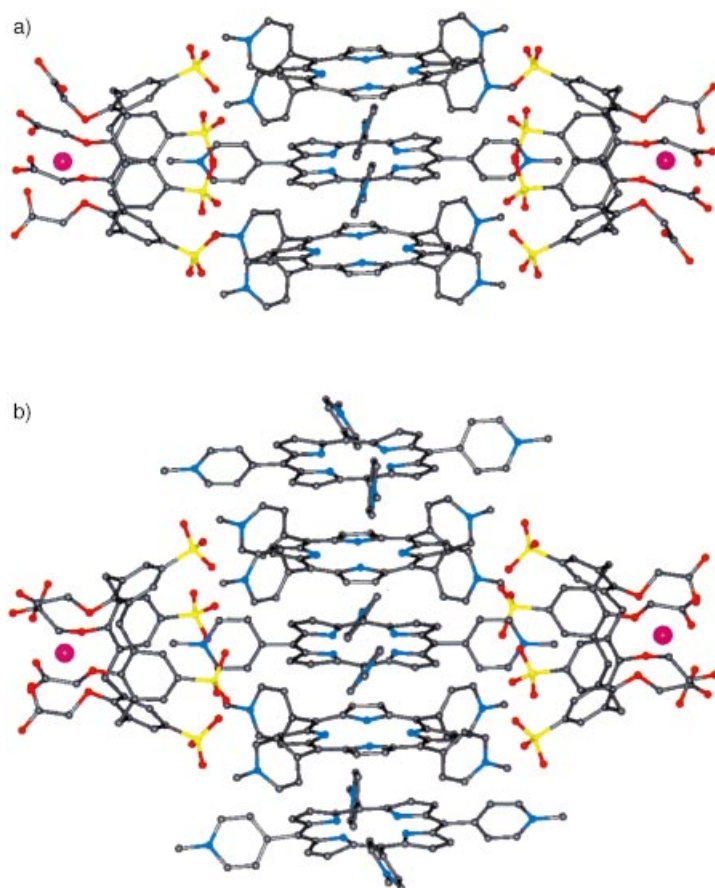


Figure 3. Side views of the neutral supramolecular complex in **1** (a) and the anionic supramolecular complex in **2** (b). In both cases the crystallographic centers of symmetry are at the center of the central porphyrin ring. The two calixarene molecules interacting with the central porphyrin ring above and below the plane have been omitted for clarity.

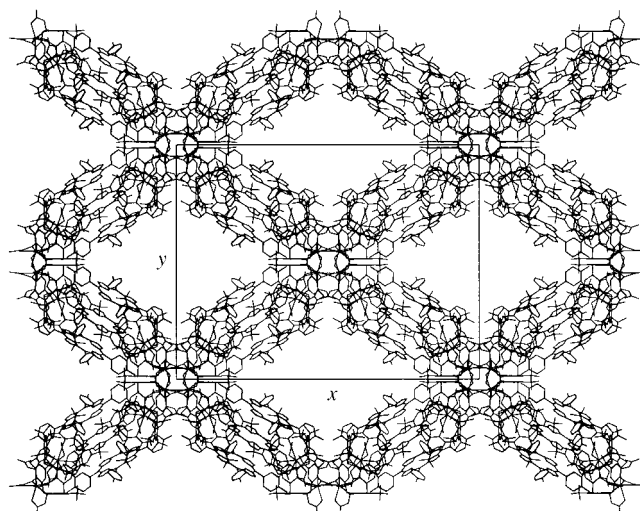


Figure 4. Crystal packing of **1** as viewed along the  $z$  axis. The channels containing the solvent molecules are shown. The trimeric units are arranged in such a way as to form the walls of the channels.

4.1 Å. The sixth tetracationic  $H_2T4$  unit—arranged on the crystallographic twofold axes—is isolated with respect to the 4:5 core, and essentially balances the charge of the tetra-anionic supramolecule. The isolated porphyrin rings and the

supramolecular anion are packed in such a way as to form two series of interconnected channels which contain the disordered solvent molecules.

Both complexes are stabilized by a synergistic network of noncovalent interactions: 1) electrostatic interactions between the positive residues on the porphyrin rings and the anionic sulphonate groups, 2) stacking interactions between the porphyrin rings, and possibly 3)  $\text{CH}\cdots\pi$  interactions between the  $\text{N}^+-\text{CH}_3$  groups and the  $\text{C}_4\text{TsTc}$  molecules. Quite intriguingly, the stoichiometry of the species in the solid state is preserved in solution.

In conclusion, the ditopic nature of  $\text{C}_4\text{TsTc}$  seems to be crucial. The presence of sulphonated and carboxylate groups on the upper and lower rim, respectively, allows for the organization of cationic porphyrins by shielding their like-charge repulsion and providing various sites (the cavity and the anionic groups) for different kinds of weak interactions, as well as the modulation of the number of assembled cationic porphyrins by changing the protonation state of the carboxylic groups.<sup>[11]</sup> The final result is the formation of stable porphyrin self-aggregates in aqueous solution having a well-defined and tunable stoichiometry. This point is relevant considering that, with few exceptions,<sup>[12]</sup> porphyrin self-aggregation in water leads to species having ill-defined stoichiometry.

### Experimental Section

The supramolecular complexes were prepared and crystallized by the vapor-diffusion method with hanging drops at 18 °C by using Linbro multi-well tissue plates as containers for the reservoir solutions. The stock solutions used were 7 mM  $\text{C}_4\text{TsTc}$  (A) and 14 mM  $\text{H}_2\text{T4Cl}_4$  (B). Crystals of **1** were obtained in drops formed by mixing solution A (4  $\mu\text{L}$ ) with solution B (2  $\mu\text{L}$ ) that were set to equilibrate against a reservoir solution of glacial acetic acid (60–70%, 1 mL). The crystals used in the diffraction experiments (typical dimensions 0.4 × 0.4 × 0.3 mm) were obtained with 65% glacial acetic acid (pH ≈ 2). Crystals of **2** were obtained in drops formed by mixing solution A (2  $\mu\text{L}$ ), solution B (2  $\mu\text{L}$ ), and reservoir solution (2  $\mu\text{L}$ ) which were set to equilibrate against a reservoir solution (1 mL) containing polyethylene glycol (PEG 300, 30–40% (v/v)) as the precipitant and 0.1 M sodium acetate buffer (pH 6.0). The crystals used in the diffraction experiments (typical dimensions 0.6 × 0.6 × 0.4 mm) were obtained with 35% PEG 300. Crystals of **1** and **2** deteriorate quickly when left in air.

wavelengths of 0.9300 Å for **1** and 0.7100 Å for **2**. The crystals were mounted in loops and frozen to 100 K. The crystal of **1** was cryoprotected by vaseline oil and the crystal of **2** was directly cryocooled. The diffraction data were indexed and integrated using MOSFLM<sup>[7]</sup> and scaled with SCALA (Collaborative Computational Project, No. 4, 1994). The structures of **1** and **2** were solved by direct methods (SHELXS-97<sup>[8]</sup>) and refined by full-matrix least-squares methods on  $F^2$  (SHELXL-97<sup>[8]</sup>). Bond lengths and angles of the porphyrins and calixarenes were restrained. **1**:  $\text{C}_{276}\text{H}_{204}\text{N}_{24}\text{O}_{96}\text{S}_{16}\text{Na}_4 \cdot 70\text{H}_2\text{O}$ ,  $M_r = 7259$ , monoclinic, space group  $\text{C}2/c$ ;  $a = 48.34$ ,  $b = 35.47$ ,  $c = 25.59$  Å,  $\beta = 109.03^\circ$ ,  $V = 44721$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calcd}} = 1.078$  g cm<sup>-3</sup>,  $F(000) = 15184.0$ ,  $\mu = 0.16$  mm<sup>-1</sup>; 1030 parameters, 501 restraints; max./min. residual electron density 0.84/−0.72 e Å<sup>-3</sup>. Total reflections collected 29111 (resolution 1.20 Å), of which 12420 were unique ( $R_{\text{merge}} = 0.0101$ ). Final  $R_1 = 0.218$  and  $wR_2 = 0.480$ ,  $S(\text{GOF}) = 2.9$  for 7379 observed reflections ( $I > 2\sigma(I)$ ). **2**:  $\text{C}_{408}\text{H}_{312}\text{N}_{48}\text{O}_{96}\text{S}_{16}\text{Na}_4 \cdot 97\text{H}_2\text{O}$ ,  $M_r = 9775$ , monoclinic, space group  $\text{C}2/c$ ,  $a = 52.05$ ,  $b = 30.32$ ,  $c = 36.10$  Å,  $\beta = 114.05^\circ$ ,  $V = 51986$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calcd}} = 1.249$  g cm<sup>-3</sup>,  $F(000) = 20536$ ,  $\mu = 0.16$  mm<sup>-1</sup>. Total reflections collected 49705 (resolution 1.00 Å), of which 26167 were unique ( $R_{\text{merge}} = 0.0642$ ). Final  $R_1 = 0.256$  and  $wR_2 = 0.555$ ,  $S(\text{GOF}) = 3.8$  for 16461 observed reflections ( $I > 2\sigma(I)$ ); 1402 parameters, 626 restraints; max./min. residual electron density 3.66/−0.78 e Å<sup>-3</sup>. The large values of  $R_1$  and  $wR_2$  are common for supramolecular complexes having very large unit cells<sup>[9]</sup> and a large number of disordered solvent molecules. Several examples of these structures with values of  $R_1$  of about 0.20 and above have been reported.<sup>[10]</sup> In addition, the poor quality of the single crystals and the loss of crystallinity during the X-ray exposure did not allow the collection of good diffraction patterns. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-167496 (**1**) and -167497 (**2**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Received: July 20, 2001 [Z17548]

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