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Chiral Amplification of Chiral Porphyrin Derivatives by Templated Heteroaggregation

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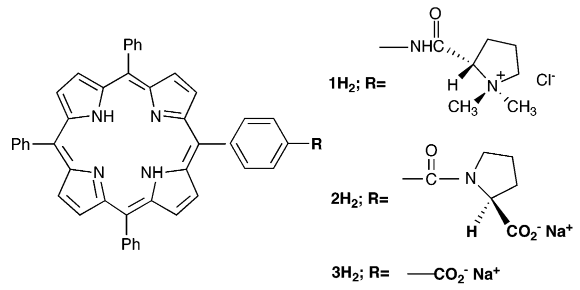
The control of molecular organization in porphyrin-based self-assembled architectures[1] constitutes a mandatory step for the construction of systems mimicking, among others, the antenna systems of photosynthetic bacteria.[2] This topic can be also of deep impact in the area of research devoted to the bottom-up approach to molecular materials[3] and for sensors application.[4] In particular, the evolution of chiral porphyrin systems, at a supramolecular level, mainly relies on (i) the aggregation of achiral porphyrin platforms on chiral templates, such as DNAs, RNA, and other natural or synthetic polymers,[5] (ii) chiral ligand coordination,[6] and (iii) spontaneous symmetry breaking upon self-association at the air/water interface, or by directional stirring.[7,1b]

During the course of our studies on porphyrin derivatives as Cytochrome P450 mimics[8] carried out in aqueous solvent mixtures, we found that the presence of a cationic chiral, functionality on the porphyrin periphery, namely a (L)-prolininium moiety **$1H_2$** (Chart 1), steers the self-aggregation process toward the formation of large porphyrin aggregates featuring high supramolecular chirality.[8b]

Prompted by these results we carried out some detailed spectroscopic studies (UV-visible, CD, and RLS) on the aggregation of amphiphilic chiral cationic porphyrin derivatives carried out in the presence of chiral aggregates of the anionic, that is, negatively charged, chiral analogue **$2H_2$**. Porphyrin derivatives were obtained by following a straightforward synthetic procedure (see ESI for details).[8b,c]

Aggregation experiments on **$1H_2$** and **$2H_2$**, at micromolar concentration were carried out in water/ethanol 75−25 (v:v) mixtures. This bulk composition promotes efficient porphyrin self-aggregation process to form J-type aggregates, as witnessed by the broadening and bathochromic shift of the relative Soret band (vide infra). Circular dichroism spectroscopy revealed that the aggregation promotes the formation of large chiral suprastructures, steered by the presence of the appended chiral functionality. The relative CD spectra are reported in Figure 1, traces a and b. It is worth noting that in nonaggregative conditions porphyrin solutions result in being CD silent in the Soret band region. Interesting features are evidenced by these systems. If the self-aggregation of **$1H_2$** (7.5 μM) is carried out in the presence of preformed chiral aggregates of **$2H_2$** (15 μM), a remarkable amplification of the CD intensity is observed.[9] This should indicate a strong template effect exerted by the presence of the anionic assemblies, onset by electrostatic forces. This effect is retained also at **$1H_2$** molar excess (Figure 1), and increases by increasing the template (**$2H_2$**) concentration.[10] Moreover, related cationic[11] or anionic (**$3H_2$**), nonchiral, amphiphilic porphyrin aggregates are CD silent, safely ruling out the effect of the scattering in the observed phenomenon. Experiments carried out at 0.25 M NaBr ionic strengths, as well as those performed in more water-rich solvent (i.e., H_2O/EtOH 90:10 v/v), showed negligible amplification effects. This corroborates the given hypothesis on the electrostatic nature of the interactions involved. The presence of the template has a profound effect also in the kinetic of aggregation that can be conveniently followed by UV−visible spectroscopy (Figure 2).[12] In the absence of anionic template the aggregation of **$1H_2$** has been shown to follow a fractal-type kinetic,[8b] whereas the templated aggregation features a coupled first-order kinetic, with distinct first-order rate constants, i.e., $k_1 = 6.9 \times 10^{-2}$ and $k_2 = 6.3 \times 10^{-3}$ min^{-1}, respectively (see Supporting Information (SI)). The faster rate constant refers to the templated aggregation step, while the slower rate would be related to a concomitant slower deposition phenomenon. This is witnessed by the slow formation of a uniform yellow porphyrin solid film on the cuvette walls.[11] Remarkably these films present interesting CD features (see SI for details). This aspect can be of great added value, for the construction of chiral porphyrin solid film for enantioselective molecular

Chart 1



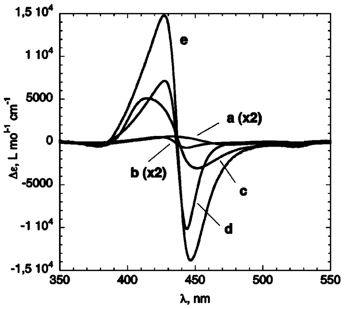


Figure 1. CD spectra of porphyrin aggregates in H_2O/EtOH (75/25 v/v): (a) **$1H_2$** (5 μM); (b) **$2H_2$** (10 μM). Templated aggregation on [**$2H_2$**] = 5 μM: (c) [**$1H_2$**] = 5 μM; (d) [**$1H_2$**] = 10 μM; (e) [**$1H_2$**] = 20 μM.

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10.1021/ja071249k CCC: $37.00 © 2007 American Chemical Society

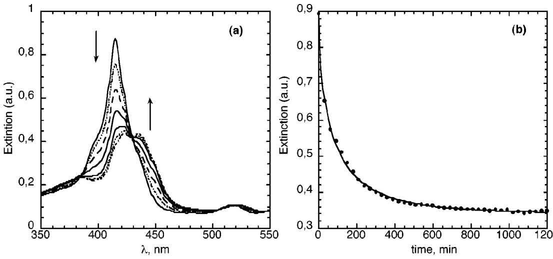

Figure 2. (a) UV−visible spectral changes of the templated aggregation of **1H$_2$** (7.5 μM) in the presence of **2H$_2$** (15 μM) in H$_2$O/EtOH (75/25 v/v) with time. (b) Fit of the experimental data points to the calculated curve (see SI).

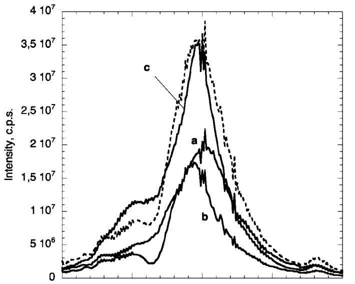

Figure 3. RLS spectra of porphyrins in H$_2$O/EtOH (75:25): (a) **1H$_2$** (7.5 μM); (b) **2H$_2$** (15 μM); (c) templated aggregation (virtual sum of traces a and b, see text).

recognition and sensing. It is worth noting that also the rate of aggregation is increased by 1 order of magnitude, the untemplated aggregation being 6.0×10^{-3} min^{-1} at the same porphyrin bulk concentration.[8b] The templated aggregation rates increase by increasing either the concentration of **1H$_2$** and **2H$_2$**. Detailed kinetic studies are under way and the results will be reported elsewhere. The aggregation kinetic can be also followed by CD spectroscopy, obtaining coherent results, in terms of kinetic behavior and rate constant values, indicating that these two techniques are detecting the same phenomenon.[13]

The templated architectures show remarkable thermal stability, showing only marginal changes on increasing the temperature from 25 to 75 °C (see SI). Noteworthy, the CD intensity of **1H$_2$** templated aggregates is satisfactorily retained in the presence of added achiral *p*-carboxylate porphyrin derivative **3H$_2$** (threefold molar excess), which should act as an electrostatic "competitor". The CD intensity in fact decreases by about only 30%, with respect to the initial value, even after prolonged standing. Conversely, the CD intensity of untemplated chiral aggregates of **1H$_2$** is virtually extinguished upon addition of aggregates of **3H$_2$**, within the time of mixing (see SI). Negligible template effect has been observed by **1H$_2$** aggregates on aggregation of **2H$_2$** counterpart. This finding can be interpreted on the basis of different structural factors, such as packing, nature and exposition of the charged groups on the surface of the aggregates, and solvation effects.[14]

Resonance light scattering (RLS) spectroscopy studies[15] give further insights on the observed phenomenon. The intensity of the RLS emissions of the **1H$_2$** templated aggregates is virtually the superposition of the "sum" of the independently aggregated structures, as reported in Figure 3. This should indicate, as already pointed out by UV-visible spectroscopy, the absence of extended electronic coupling between the cationic and the anionic suprastructures, ruling out the formation of intercalated $\pi-\pi$ stacked species, which would have featured an intensified RLS intensity, caused by the increased electronic coupling.

In summary, the results obtained show that the electrostatic-templated heteroaggregation of porphyrin derivatives induces a remarkable amplification of the chirality of the final suprasctructure. This can be of importance, inter alia, for the construction of complex porphyrin architectures in which the final supramolecular chirality can be tuned ad hoc.

Acknowledgment. The authors wish to thank Prof. Robert F. Pasternack, for helpful discussion. The involvement of Dr. Veronica Cantonetti in the early synthesis of porphyrin derivatives is gratefully acknowledged. We also thank MIUR-FIRB (Project No. RBNE01KZZM) and CNR, Dipartimento Progettazione Molecolare, for financial support.

Supporting Information Available: Experimental details on synthesis of porphyrins, kinetic studies, and CD spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) Templated aggregation experiments have been carried out by adding to 1 mL of **1H$_2$** ethanol solution, 3 mL of **2H$_2$** aqueous solution, ensuring that the final porphyrin concentrations span the range of 0.75 to 3×10^{-5} M. The relative CD or UV-visible spectra were then acquired at 25 °C. This procedure ensures a 75:25 H$_2$O/EtOH (v/v) final solvent composition.
(10) A levelling off effect occurs at ca. six-fold molar excess of **1H$_2$** (≥ 30 μM). However, this is accompanied by evident cloudiness of the solutions, with consequent precipitation of some solid material occurring with time.
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(12) The presence of clear isosbestic points indicates the formation of species featuring well-defined morphology. Moreover, the presence of two distinct absorbance maxima for **1H$_2$** (436 nm) and **2H$_2$** (425 nm) aggregates indicate negligible electronic coupling between porphyrin heteroaggregates.
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(14) These results can be of importance for the exploitation of the phenomena involved in the hierarchical heteroassembly of porphyrin derivatives. See for example De Napoli, M.; Nardis, S.; Paolesse, R.; Vicente, M. G. H.; Lauceri, R.; Purrello, R. *J. Am. Chem. Soc*. **2004**, *126*, 5934.
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JA071249K