COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Interaction of a chirally functionalised porphyrin derivative with chiral micellar aggregates†

Donato Monti,*[a] Veronica Cantonetti,[a] Mariano Venanzi,[a] Francesca Ceccacci,[b] Cecilia Bombelli[b] and Giovanna Mancini[b]

[a] *Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi "Tor Vergata", Via della Ricerca Scientifica 1, I-00133 Rome, Italy. E-mail: monti@stc.uniroma2.it; Fax: +39 0672594328; Tel: +39 0672594738*

[b] *CNR Istituto di Metodologie Chimiche – Sezione Meccanismi di Reazione, c/o Dipartimento di Chimica, Università "La Sapienza", P.le A. Moro 5, I-00185 Rome, Italy*

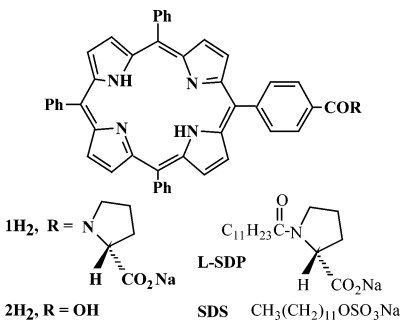
Received (in Cambridge, UK) 6th January 2003, Accepted 23rd February 2004
First published as an Advance Article on the web 16th March 2004

The functionalisation of a porphyrin derivative with a chiral functionality results in a selective interaction with chiral micellar aggregates.

The study of the interaction of porphyrin derivatives with membrane models, such as micelles or liposomes, represents an important area of research aimed at, for example, the development of Cytochrome P450 mimics,[1] or the achievement of systems for clinical uses such as the photodynamic therapy of tumors (PDT) and related diseases.[2] The activity of these systems is influenced by the interactions between the included porphyrins and the surfactants, that can be effectively modulated by structural features of the involved species.[3] Among others, chiral recognition plays a striking role in these effects. To the best of our knowledge, studies on chiral recognition of chirally functionalised porphyrin derivatives by chiral micellar aggregates have not been reported,[4] although the study of the interaction of porphyrins with DNAs, and chiral synthetic polymers constitutes an active and fascinating area of research.[5]

Here we report our results on the interaction of a proline-functionalysed porphyrin derivative (**1H$_2$**) with micellar aggregates formed by sodium dodecyl sulfate (SDS) or sodium *N*-dodecanoyl-L-prolinate (L-SDP; Scheme 1). Parallel studies, carried out on a related *p*-carboxyphenyl-porphyrin derivative (**2H$_2$**), should give important information on the nature of porphyrin–surfactant interactions modulated by chiral recognition.

Micellar solutions are constituted by 0.1 M surfactant aqueous solutions, well above their critical micelle concentration.‡[6] UV-visible spectra of **1H$_2$** in L-SDP feature the expected bands whose λ_{max} are slightly red-shifted with respect to that observed in ethanol solution (Fig. 1, and ESI Table S1). The corresponding absorbance *vs.* concentration plot has been found to be linear well above the porphyrin/surfactant concentration ratio $R = 0.005$ (ESI Fig. S1). In contrast, the inclusion of **1H$_2$** in SDS results in the formation of self aggregated species, as witnessed by the gradual broadening and hypochromicity of the Soret band, at value of R above 0.0001.[7] The red-shift up to 450 nm indicates the formation of J-type aggregates.[8] This put in evidence the role of the chiral functionality on the efficiency of the solute–micelle molecular recognition process.



Scheme 1 Porphyrins and surfactants employed in the studies.

Detailed fluorescence spectroscopy studies, such as steady state, time resolved, and fluorescence anisotropy, have been carried out in order to give further insights into the mode (*i.e.* monomer or aggregated state) and the topology of the inclusion in micellar phases. The results are summarised in Table 1. The emission spectra reveal a substantial decrease of fluorescence intensity, along with a slight red shift of the emission maxima, in SDS (λ_{em} = 647 nm with respect to λ_{em} = 645 nm in L-SDP and ethanol) ascribable to porphyrin quenching, confirming the occurrence of aggregation. In all the media investigated, the fluorescence time decays of **1H$_2$** are well described by a single exponential lifetime (τ), typical of the emission of monomer species.[3,7a]

As far as fluorescence anisotropy[9] measurements are concerned, the results obtained show an increased anisotropy coefficient (r) compared to that observed in ethanol, confirming the inclusion in the micellar aggregates.§ Fluorescence quenching experiments have been carried out on the **1H$_2$**/L-SDP system, in order to get more insight into the location within the biomembrane model. The use of "depth-dependent" lipophilic quenchers[10] such as 2-bromooctanoic acid and 16-bromohexadecanoic acid (C2-Br, and C16-Br, respectively) provided some information on the location of **1H$_2$**

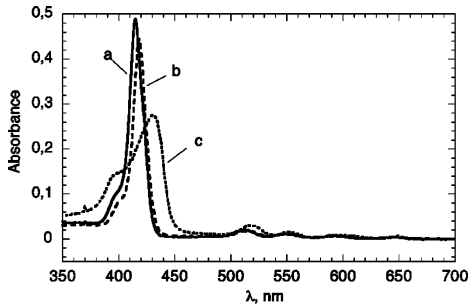


Fig. 1 UV-vis spectra of **1H$_2$** (1.7×10^{-5} M) in a) EtOH; b) L-SDP 0.1 M; c) SDS 0.1 M.

Table 1 Fluorescence time decays (τ/ns) and anisotropy coefficients (r) of **1H$_2$** (8.5×10^{-6} M) in various media[a]

Medium	Φ_{rel}	τ	r
EtOH	1	12.4 ± 0.1	0.008 ± 0.001
L-SDP	0.97	12.5 ± 0.1	0.023 ± 0.001
L-SDP[b]	0.97	12.5 ± 0.1	0.023 ± 0.002
L-SDP[c]	0.89		
L-SDP[d]	0.75		
SDS	0.32	11.4 ± 0.1	0.019 ± 0.002
SDS[b]	0.24	11.6 ± 0.1	0.025 ± 0.002

[a] [surfactants] = 0.1 M; λ_{exc} = 513 nm, λ_{em} = 645 nm; T = 25 °C. [b] [**1H$_2$**] = 1.7×10^{-5} M. [c] [**C16-Br**] = 5.0×10^{-3} M. [d] [**C16-Br**] = 2.0×10^{-2} M.

† Electronic supplementary information (ESI) available: experimental and spectroscopic details. See http://www.rsc.org/suppdata/cc/b3/b317054c/

DOI: 10.1039/b317054c

in the chiral micellar aggregates. The fluorescence is quenched by C16-Br whereas it is not affected by C2-Br (Table 1 and ESI Fig. S2, Inset) indicating location of the macrocycle in an inner region of the surfactant.

CD spectroscopy studies reveal that the inclusion of **1H$_2$** in L-SDP micelles results in an intense, bisignate, positive band centred at *ca.* 440 nm ($[\theta]_{max}$ $\pm 5 \times 10^4$ deg cm^2 dmol^{-1}; Fig. 2, trace a) as a result of excited-state interaction between chromophores held in a chiral conformation[11] upon chiral recognition by the micelle.¶ Fluorescence quenching experiments demonstrate that this chiral recognition takes place in an internal region of the aggregate, far from the polar head groups and that, consequently, it does not arise from a close interaction with the stereogenic centers of the monomers. The independence of the molar ellipticity on the porphyrin concentration (*i.e.* well above $R = 0.005$), and the sharpness of the Soret band (UV-vis), ruled out the formation of porphyrin aggregates. In contrast, a solution of **1H$_2$** in SDS features an intense, coupled CD band with opposite (*i.e.* negative) sign, centered at 450 nm, whose intensity, higher than that observed in L-SDP, is largely dependent on the porphyrin concentration (Fig. 2, trace b). This finding, along with the presence of substantial broadening of the Soret band (UV-vis), implies the formation of porphyrin chiral aggregates, with the L-proline appended residues steering the helical sense of the self-assembling process.[12] This is confirmed by the fact that CD spectra of **1H$_2$**, run in aggregative conditions (increased water proportion of solvent mixture), feature an intense, bisignated band (Fig. 3) with negative sign, analogous to that observed in the case of **1H$_2$** in SDS. Again, $[\theta]$ values increase with increasing porphyrin concentration, indicating the evolution of the chiral system upon aggregate growth. On the other hand, the achiral **2H$_2$** derivative is CD silent once included in L-SDP micelles in either monomeric form (*i.e.* at $R \leq 0.0001$) or in aggregative conditions (*i.e.* $R > 0.0001$).

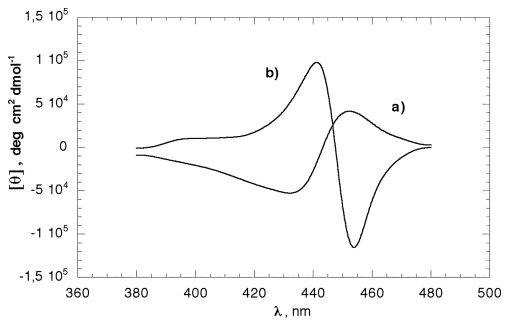


Fig. 2 CD spectra of **1H$_2$** (1.0×10^{-5} M) in a) L-SDP 0.1 M; b) SDS 0.1 M.

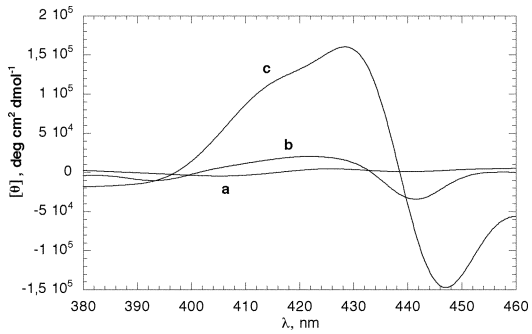


Fig. 3 CD spectra of **1H$_2$** (8.5×10^{-6} M) in ethanol/water mixtures at increasing water proportion: a) 65%; b) 85%; c) 95%.

In summary, these studies point out that chiral recognition in self-aggregate systems may be the result of a complex combination of events. Here we have the evidence of a recognition phenomenon that is induced by the chiral head groups in an internal groove of the aggregate. These results are of importance for the development of stereoselective Cytochrome P450 biomimetic systems. Studies on related redox-active metalloporphyrin derivatives are in progress and will be reported in the near future.

Notes and references

‡ The "bulk pH" of 0.1 M L-SDP solution is 8.9. Studies in water and in SDS aqueous solutions have been carried out at pH 9.0 (Buffer solution, Aldrich).

§ The increase of r for the inclusion of **1H$_2$** in SDS, at different concentrations, can be inferred as resulting from some porphyrin aggregation.

¶ Ethanol solutions of **1H$_2$** are CD silent in the 350–700 nm range (*i.e.* porphyrin B and Q bands region) even in the presence of 0.10 M L-SDP. In these non-aggregating conditions the surfactant is not micellised, this implies that the stereochemical information possessed by the surfactant aggregates must be read-out by the included macrocycles upon molecular recognition. However, the CD spectrum features the typical dichroic band of the L-proline group centred at 230 nm, with $[\theta] = 5500$ deg cm^2 dmol^{-1}, at λ 230 nm (ESI Fig. S3). Moreover, the presence of 0.10 M sodium *N*-acetyl-L-prolinate (*i.e.* non-aggregating, polar head mimic) does not affect the CD spectroscopic features of **1H$_2$** solutions.

1 A. P. H. J. Schenning, J. H. Lutje Spelberg, D. H. W. Hubert, J. H. van Esch, M. C. Feithers and R. J. M. Nolte, *Chem. Eur. J.*, 1998, **4**, 871 and references therein; D. Monti, P. Tagliatesta, G. Mancini and T. Boschi, *Angew. Chem., Int. Ed.*, 1998, **37**, 1131; S. Borocci, F. Marotti, G. Mancini, D. Monti and A. Pastorini, *Langmuir*, 2001, **17**, 7198.

2 R. K. Pandey and G. Zheng, *Porphyrins as Photosensitizers in Photodynamic Therapy*, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, New York, 2000, vol. 6, ch. 43, p 1579; M. Yokoyama, *Drug targeting with polymeric micelle drug carriers*, in *Supramolecular design for biological applications*, ed. N. Yui, CRC Press, New York, 2002, ch. 11, p. 245.

3 D. Monti, M. Venanzi, V. Cantonetti, S. Borocci and G. Mancini, *Chem. Commun.*, 2002, 774 and references therein.

4 For some recent reports on chiral recognition in micellar phases see: H. Nakagawa, Y. Kobori, M. Yoshida and K.-i. Yamada, *Chem. Commun.*, 2001, 2692; S. Borocci, F. Ceccacci, L. Galantini, G. Mancini, D. Monti, A. Scipioni and M. Venanzi, *Chirality*, 2003, **15**, 441 and references therein.

5 (*a*) R. F. Pasternak, E. J. Gibbs, D. Bruzewicz, D. Stewart and K. S. Engstrom, *J. Am. Chem. Soc.*, 2002, **124**, 3533; (*b*) E. Bellacchio, R. Lauceri, S. Guerrieri, L. Monsù Scolaro, A. Romeo and R. Purrello, *J. Am. Chem. Soc.*, 1998, **120**, 12353.

6 The cmc of SDS is 8.2 mM, see for example, J. H. Fendler and E. J. Fendler, *Catalysis in Micellar and Macromolecular Systems*, Academic Press, New York, 1975. The cmc of L-SDP has been reported to be 3.0 mM: I. Grassert, K. Schinkowski, D. Vollhardt and G. Oehme, *Chirality*, 1998, **10**, 425. We found, by means of various techniques, a value of 10.0 mM.

7 (*a*) A. P. H. J. Schenning, D. H. W. Hubert, J. M. C. Feiters and R. J. M. Nolte, *Langmuir*, 1996, **12**, 1572; (*b*) C. Schell and H. K. Hombrecher, *Chem. Eur. J.*, 1999, **5**, 587.

8 J. M. Ribó, J. M. Bofill, J. Crusats and R. Rubires, *Chem. Eur. J.*, 2001, **7**, 2733 and references therein.

9 R. F. Steiner, *Topics in Fluorescence Spectroscopy Vol. 2: Principles*, ed. J. R. Lakowicz, Plenum Press, New York, 1991.

10 M. R. Eftink, *Biophysical and Biochemical Aspects of Fluorescence Spectroscopy*, Plenum Press, New York, 1987.

11 For a recent survey on ICD in micellar systems see: S. Allenmark, *Chirality*, 2003, **15**, 409.

12 J.-H. Furhop, C. Demoulin, C. Boettcher, J. König and U. Siggel, *J. Am. Chem. Soc.*, 1992, **114**, 4159. For recent reports on symmetry-breaking in the self-association of achiral porphyrin derivatives, see: R. Rubires, J.-A. Farrera and J. M. Ribó, *Chem. Eur. J.*, 2001, **7**, 436.