Chiral H- and J-Type Aggregates of *meso*-Tetrakis(4-sulfonatophenyl)porphine on α-Helical Polyglutamic Acid Induced by Cationic Porphyrins

Roberto Purrello,*,† Luigi Monsu' Scolaro,‡ Emanuele Bellacchio,† Sergio Gurrieri,§ and Andrea Romeo‡

Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria 6, 95125, Catania, Italy, Dipartimento di Chimica Inorganica, Chimica Analitica e Chimica Fisica, Università di Messina, ICTPN CNR Sezione di Messina, Messina, Italy, and Istituto per lo Studio delle Sostanze Naturali di Interesse Alimentare e Chimico-Farmaceutico, CNR, Catania, Italy

Introduction

Aggregation of water-soluble porphyrins on polymeric matrixes is, in principle, a simple strategy for "building" tailored supramolecular species. To date, only interactions of porphyrins with matrices carrying opposite charges have been studied because of the repulsion between components bearing charges of the same sign.[1] It has also been reported the formation of accordion *heteroaggregates* between anionic and cationic porphyrins, which leads to a partial charge neutralization.[2] We thought, therefore, it should be possible to form chiral hetero-aggregates on a polymeric charged template, although the matrix and one of the components have the same charge. We present here evidence of the formation of chiral ternary heteroaggregates in which cationic porphyrins act as "spacers" between an anionic chiral polymeric matrix and anionic porphyrins.

We used the copper(II), gold(III), manganese(III), and zinc-(II) derivatives of *meso*-tetrakis(*N*-methylpyridinium-4-yl)por-phine (MT4) as cationic porphyrins. The first two are planar, while the latter two are respectively hexa- and pentacoordinated.[3] We chose to employ these metal derivatives because of their peculiar steric and electronic properties. In particular, AuT4 presents a blue-shifted Soret band in contrast to the other metal derivatives and it is very easy to reduce, leading to the radical anion rather than the reduced metal.[4] These features might be useful to better understand the role of the cationic porphyrins in fostering the formation of these supramolecular species. We

* Corresponding author. Fax: +39 95 580 138. E-mail: rpurrello@dipchi.unict.it.
† Università di Catania.
‡ Università di Messina.
§ CNR, Catania.

(1) (a) Pasternack, R. F.; Giannetto, A.; Pagano, P.; Gibbs, E. J. *J. Am. Chem. Soc.* **1991**, *113*, 7799. (b) Mukundam, N. E.; Pethö, G.; Dixon, D. W.; Kim, M. S.; Marzilli, L. G. *Inorg. Chem.* **1994**, *33*, 4676. (c) Schneider, H.-J.; Wang, M. *J. Org. Chem.* **1994**, *59*, 7473. (d) Lauceri, R.; Campagna, T.; Contino, A.; Purrello, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 215.
(2) (a) Shimidzu, T.; Tomokazu, I. *Chem. Lett.* **1981**, 853. (b) Ojadi, E.; Selzer, R.; Linschitz, H. *J. Am. Chem. Soc* **1985**, *107*, 7783. (c) Hofstra, U.; Koehorst, R. B. M.; Schaafsma, T. J. *Chem. Phys. Lett.* **1986**, *130*, 555. (d) Endisch, E.; Fuhrhop, J.-H.; Buschmann, J.; Luger, P.; Siggel, U. *J. Am. Chem. Soc.* **1996**, *118*, 6671.
(3) Hoard, J. L. *Porphyrins and Metalloporphyrins*; Elsevier: Amsterdam, 1975.
(4) Abou-Gamra, Z.; Harriman, A.; Neta, P. *J. Chem. Soc., Faraday Trans.* **1986**, *2*, 2337.

Table 1. Visible-Absorption and RLS Features of J- and H-Aggregates of H_2TPPS

| | absorption spectra[a] | | |
	B-bands	Q-bands	RLS spectra[b]
J-aggregates	489	668, 707	490
H-aggregates	422	575, 625	not observed

[a] pH 3.5; 4×10^{-5} M ≤ [H_2TPPS] ≤ 5×10^{-4} M; ref 7a. [b] pH 1.2; $I = 0.1$ M, [H_2TPPS] = 2.5×10^{-6} M; ref 7b.

would like to recall, in fact, that among these MT4, only CuT4 forms aggregates on DNA or RNA.[5]

The anionic porphyrin selected for our study is the *meso*-tetrakis(4-sulfonatophenyl)porphine (H_2TPPS), whose proto-nated form (H_4TPPS, pK_a = 4.8)[6] forms both J-type (edge-to-edge) and H-type (face-to-face) aggregates, depending on its concentration, pH, and ionic strength.[7a] However, in the micromolar concentration range, only the formation of the J-aggregate has been observed at pH close to 1.[7b] The spectroscopic features of these two aggregates can be assigned by means of visible absorption and resonance light scattering (RLS) measurements (Table 1).[7a,b]

We have used polyglutamic acid as a matrix, which at the pH investigated in the present work (pH 2.9) is mostly protonated and therefore in a α-helix conformation.[8]

Experimental Section

Polylglutamic acid was obtained from Sigma Chemical Company. Its concentration is expressed as moles of glutamic residues per liter. *meso*-Tetrakis(4-sulfonatophenyl)porphine and *meso*-tetrakis(*N*-meth-ylpyridinium-4-yl)porphine were obtained from Mid-Century as the tetrasodium and tetrachloride salts, respectively. Porphyrin metalation was performed by literature methods.[9] RLS[10] measurements were recorded on a SPEX F111 spectrofluorimeter and were carried out using disposable methacrylate cuvettes. Absorption measurements were carried out on an HP8452 A instrument. Circular dichroism (CD) spectra were recorded on a Jasco J-600 spectrometer. Doubly distilled water was used throughout.

Results and Discussion

We started our investigation using ZnT4 as cationic porphyrin. Figure 1 shows the absorption spectrum (curve a) (recorded after 1 h of incubation) of a solution of H_2TPPS (5 μM) at *pH 2.9* in the presence of poly-L-glutamate (50 μM) and ZnT4 (5 μM). Together with the expected band at 436 nm (due to the absorption of both ZnT4 and H_4TPPS) there are two additional bands at about 490 and 700 nm. In addition, the RLS spectrum (Figure 1, curve b) shows a very intense band at about 500 nm and a smaller signal at about 720 nm (not shown). The RLS and absorption bands observed around 500 and 700 nm are diagnostic of the presence of H_2TPPS J-aggregates (Table 1).

(5) (a) Pasternack, R. F.; Brigandi, R. A.; Adams, M. J.; Williams, A. P.; Gibbs, E. J. *Inorg. Chem.* **1990**, *29*, 4483. (b) Pasternack, R. F.; Gurrieri, S.; Lauceri, R.; Purrello, R. *Inorg. Chim. Acta* **1996**, *246*, 7 and references therein.
(6) Fleischer, E. B.; Palmer, J. M.; Srivastava, T. S.; Chatterjee, A. *J. Am. Chem. Soc.* **1971**, *93*, 3162.
(7) (a) Ribo, J. M.; Crusats, J.; Farrera, J.-A.; Valero, M. L. *J. Chem. Soc.*, *Chem. Commun.* **1994**, 681. (b) Pasternack, R. F.; Schaefer, K. F.; Hambright, P. *Inorg. Chem.* **1994**, *33*, 2062.
(8) Cantor, C. R.; Schimmel, P. R. *Biophysical Chemistry*; Freeman, New York, 1980.
(9) Hermann, O.; Husain Mehdi, S.; Corsini, A *Can. J. Chem.* **1978**, *56*, 1084.
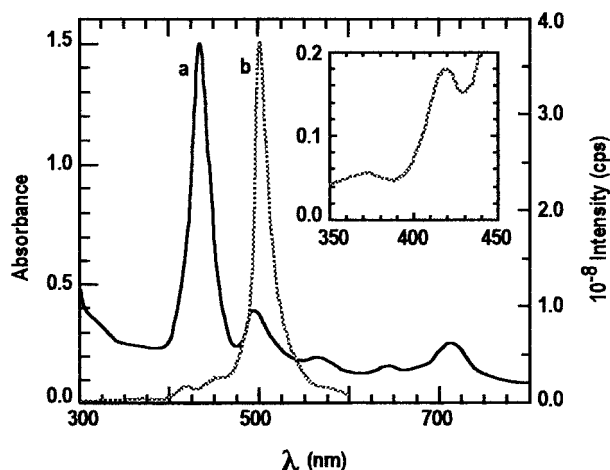(10) Pasternack, R. F.; Collings, P. J. *Science* **1995**, *269*, 935.

Figure 1. Absorption (a) and RLS (b) spectra at pH 2.9 (citrate buffer 5 mM) of H$_2$TPPS (5 μM) in the presence of ZnT4 (5 μM) and poly-L-glutamate (50 μM).
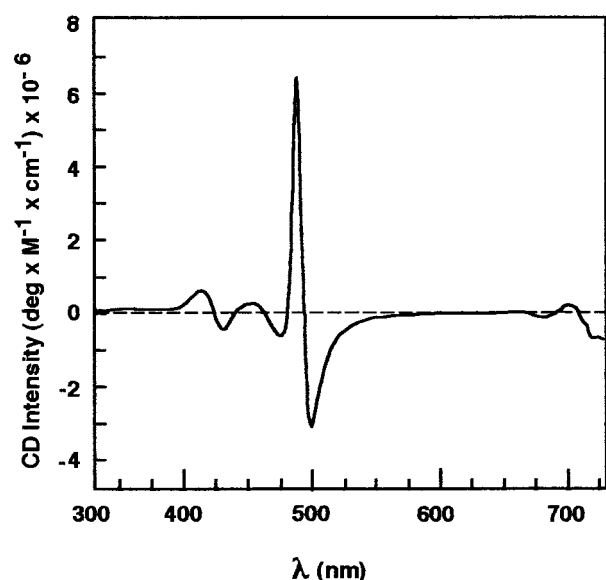

Figure 2. CD spectrum of the same solution of Figure 1.

In the RLS spectrum, we have also observed a feature at 420 nm (inset of Figure 1) which might be assigned to the formation of H-type aggregates.[7a]

It is worth mentioning at this point that the presence of the cationic porphyrin is essential, in these experimental conditions, for the formation of H$_2$TPPS aggregates. In fact, in the absence of ZnT4, none of the spectroscopic features associated with aggregation of the protonated form of H$_2$TPPS has been observed.

The CD spectrum (Figure 2) of the ternary complex shows a very intense induced bisignate signal having a maximum at 490 nm (total intensity $\Delta\epsilon \approx |2500|$ M^{-1} cm^{-1}), together with smaller conservative features centered at about 420 and 720 nm (total intensity of both bands, $\Delta\epsilon \approx |600|$ M^{-1} cm^{-1}). We assign the 490 and 720 nm bands to the first observation of a chiral J-aggregate of H$_2$TPPS at this unusual pH value. The presence of a CD band at 420 nm increases our confidence in assigning the CD and RLS features to the formation of a chiral H-type aggregate.

Surprisingly, using the same concentrations of H$_2$TPPS (5 μM) and poly-L-glutamic acid (50 μM) and one-fifth of the stoichiometric amount of ZnT4 (1 μM), the intensity of the CD bands is reduced only by 30%. The observation that the ternary complex concentration does not scale down linearly with the

concentration of ZnT4 indicates that anionic and cationic porphyrins are not forming the 1:1 heteroaggregates[2] and suggests that ZnT4 serves as a "spacer" to minimize the repulsion between the two negative components. This hypothesis is supported by (i) the observation that a pH increase of only 0.2 units (i.e. a small increase in the number of negative charges on the matrix) causes a 50% reduction of the induced CD signal, most likely because of the stronger repulsion between the anionic porphyrins and the matrix and (ii) the fact that in the absence of ZnT4 but at very high salt concentration (NaCl > 0.5 M) we observed the same spectroscopic features characteristic of the chiral H- and J-aggregates. The much lower concentration of cationic porphyrins required to induce the formation of these ternary complexes is indicative of their higher efficiency, which must be related to specific molecular recognition processes.[1d] Most likely, ZnT4 is monodispersed on the matrix, shielding the negative charges. This allows the anionic porphyrins to approach the (partially) anionic chiral polypeptide and gain chirality.

Interestingly, when poly-D-glutamic acid was used, we observed the mirror image of the CD features at 422, 490, and 700 nm. This confirms that the aggregates of the anionic porphyrin owe their chirality to the polypeptide matrix even though they interact with it only indirectly, "through" the cationic porphyrin.

However, not all the cationic porphyrins show the same behavior. In fact, using both MnT4 and AuT4 we have obtained results similar to those found for ZnT4. Instead, in the presence of CuT4 both the CD and RLS signals characteristic of H$_2$TPPS H- and J-aggregates are barely detectable. A possible explanation is that CuT4 and H$_2$TPPS form 1:1 heteroaggregates, not bound to the chiral matrix, which compete against the formation of the chiral ternary species. Accordingly, preliminary absorption data show that at pH 2.9 in the absence of polyglutamate, AuT4, MnT4 and ZnT4 still induce the formation of H$_2$TPPS J-aggregates, whereas CuT4 forms with H$_2$TPPS heteroaggregates in a 1:1 ratio. This different behavior can be readily explained considering that (i) penta- and hexacoordinated porphyrins are not allowed to form "stacked" 1:1 complexes for steric reasons and (ii) since the planar Au(III) porphyrin is in a higher oxidation state compared to the Cu(II) one, it presents a "net" positive charge in the porphyrin core. This causes an electrostatic repulsion between the Au(III)T4 and the protonated H$_2$TPPS core, thus disfavoring the "stacked" interactions and leading to the formation of H$_2$TPPS aggregates.

Conclusions

We have presented evidence that some cationic porphyrins can induce the formation of chiral ternary heteroaggregates. The role of such cationic porphyrins is 2-fold: (i) they drive the formation of H- and J-type aggregates of H$_2$TPPS under unusual experimental conditions, depending on their steric and/or electronic features, and (ii) they act as "spacers", by shielding the electrostatic repulsion between the anionic matrix and the negative sulfonic groups of H$_2$TPPS. This allows a "long-distance" interaction of the matrix with the aggregates which, as a consequence, gain chirality.

These observations may open new perspectives in the field of supramolecular chemistry toward the formation of "tailored" species.

IC971432M