Kinetic and spectroscopic studies on the self-aggregation of a *meso*-substituted amphiphilic corrole derivative

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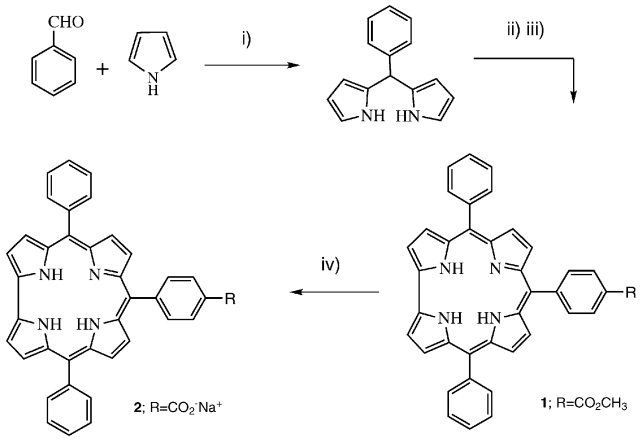
The solvent promoted aggregation behaviour of a *meso*-substituted amphiphilic corrole derivative occurs with the formation of aggregates with regular morphology, different from those obtained in the case of related porphyrin structures, opening interesting perspectives for the application of these derivatives in important fields of research.

The controlled organisation of functional heterocyclic chromophores, such as porphyrinoids and alike, into highly ordered self-assembled arrays is an appealing area of research with great potential in many different fields such as, for example, the construction of systems mimicking biological functions,[1] for sensor applications,[2] and in materials science,[3] owing to their unique and intriguing photophysical and optoelectronic properties, as a consequence of excitonic interactions between adjacent dye units, which make them useful for specific applications.[4]

While studies on the self-aggregation of tetrapyrrolic macrocycles, such as porphyrins or chlorins, have been widely reported in the literature,[5] there has been very little work on the same topic for other porphyrinoids, such as phthalocyanines[6] or corroles.[7] The paucity of such information is probably related to the elaborate and time-consuming preparation of these macrocycles. Fortunately, in the past decade, the "corrole scenario" has changed in a striking way with the development of efficient synthetic procedures,[8] allowing exploitation of the potential applications of such tetrapyrrolic derivatives in catalysis, sensors or medicine.[9] Also, an array of several highly selective methods for peripheral substitution[8b,10] at β-pyrrolic and *meso*-carbon positions has enabled researchers to decorate the aromatic platform easily, with polar groups located in specific positions, conferring upon them, for example, amphiphilic character. This finding was the fundamental key for novel investigations of such charged compounds as efficient biomimetic oxidation systems[7d,11] and highly potent inhibitors of growth factor activity *in vitro* and *in vivo*,[7a] as they are easily soluble in physiological environments.

While the practical implications of charged corroles begin to be successfully explored, to the best of our knowledge no studies have been reported on the self-aggregation properties of such corroles, although this aspect is of fundamental interest in the above-mentioned applications. Prompted by the results obtained in the case of amphiphilic porphyrin derivatives,[12] we extended the same philosophy to related corrole derivatives, with the aim of investigating the unknown aggregation properties of such an important class of molecules. The exploitation of this strategy to the case of corroles may open important perspectives for the achievement of new supramolecular materials, owing to the special properties of these macrocycles, such as, for example, their ability to coordinate transition metal cations in non-conventional, hypervalent oxidation states and their interesting photophysical and electrochemical properties.[10c,13] For this purpose we required the preparation of a triphenylcorrole bearing a carboxylic group at the *meso-para*-phenyl position of the macrocycle, which acts as a "polar head" of the whole hydrophobic structure. Exploiting a new efficient methodology recently reported by Gryko and Koszarna,[8d] we were able to prepare the mono-substituted corrole precursor **1** in satisfactory yield, whose alkaline hydrolysis afforded the target carboxylic derivative **2**, as shown in Scheme 1.

Aggregation experiments on **2** have been carried out in mixed water–ethanol solvent mixtures, typically at 5×10^{-6} M, at 298 K. In the composition range of 100% to 50% ethanol (v/v) the macrocycle is in monomeric form, as clearly evidenced by the shape of the Soret band positioned at 413 nm. Further increase of water proportion triggers the aggregation process, as witnessed by the broadening and a small hypsochromic shift of the Soret band (*ca.* 2 nm).† It is interesting to note that, in similar conditions, the corresponding anionic porphyrin results in the formation of J-type aggregates.[12b] The different behaviour featured by the



Scheme 1 Synthetic scheme of the preparation of corrole **2**. *Reagents and conditions*: (i) H_2O, HCl, rt; (ii) *p*-CHO-C_6H_4–CO_2CH_3, HCl, H_2O, MeOH; (iii) *p*-chloranil, $CHCl_3$; (iv) NaOH, EtOH, ΔT, 2 h.

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anionic corrole is certainly due to the different geometry of the tetrapyrrolic platform, inferred by the direct pyrrole–pyrrole bond. This structural constraint evidently drives the aggregation toward the formation of supramolecular species characterised by a different packing motif, in a face-to-face fashion. The involvement of hydrogen bonding, between the carboxylate group and the inner hydrogen atoms of the corrole core, would also play a role in the observed phenomenon. Concomitant kinetic studies have been performed in water–ethanol 50 : 50 (v/v) composition. In this solvent composition the aggregation rate is rather small, however, the self-aggregation process can be triggered by the addition of NaBr.‡ [14] It is well known that the increase of the ionic strength of the medium promotes the aggregation process by the hydrophobic effect, as reported in the case of templated aggregation of water-soluble porphyrin derivatives on DNA, RNA or other polymeric matrices.[5] Kinetic runs were carried out by following the decrease of the Soret band intensity (at 413 nm) with time. A typical absorbance *vs*. time profile is reported in the inset of Fig. 1. Also in this case, the aggregation occurs in a well-defined fashion, with the formation of slightly blue-shifted species. The presence of several isosbestic points indicates that the aggregation process occurs toward the formation of a narrow distribution of structurally similar species. The experimental decays can be excellently fitted by a stretched exponential kinetic, which is described by eqn (1) (see experimental section). This is reported in the inset of Fig. 1, in which the close adherence of the calculated fit to the experimental values is emphasised. The kinetic behaviour can be interpreted on the basis of the so-called diffusion limited aggregation (DLA) mechanism, in which large aggregates are formed by interaction between initial smaller cluster (seeds) and monomers.[15a] Notable examples have been reported in the aggregation of charged cyanine dyes on charged polymeric templates, such as poly(vinylsulfonate),[15b] or in our very recent work, focused on the synthesis and aggregation properties of porphyrin-*C*-glycoside conjugates.[15c] The aggregation rate has been found to be dependent on the ionic strength of the solution, spanning over one order of magnitude, from *ca*. 0.5 to 5×10^{-3} min^{-1}, on increasing salt concentration from 0.10 to 3.50 M, respectively.§ The aggregation factor, *n*, which is related to the availability of nucleation centres during the cluster growth, remains virtually unchanged. The results are summarised in Table 1. Concomitant fluorescence and resonance light scattering (RLS) studies give more insights on the aggregation phenomenon. The corrole emission (λ_{max} = 654 nm) is gradually quenched on going from ethanol to water-rich solvent composition, paralleling the behaviour observed *via* UV-visible means. Interestingly, a new, hypsochromically-shifted band appears in pure water (λ_{max} = 635 nm), which can be inferred as due to the formation of the protonated form of corrole, $\mathbf{2H^+}$, upon excited state proton-transfer equilibrium from the solvent, as evidenced by the relative excitation spectra (Fig. 2; right plot, inset).¶ Very surprisingly, RLS spectra were silent, indicating that the aggregation process occurs with the formation of species with a small number of corrole units ($n \leq 25$).[5b]

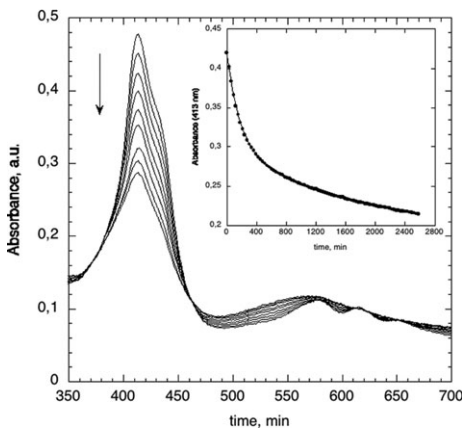

Fig. 1 UV-visible spectral changes of corrole **2** (5.0×10^{-6} M) upon aggregation (H_2O–EtOH, 50 : 50 (v/v); [NaBr] = 1.667 M; T = 298 K). Uppermost trace: t = 0, lowermost trace: t = 2600 min. Inset: corresponding kinetic profile at λ = 413 nm.

These preliminary results showed that amphiphilic corrole derivatives could be successfully prepared by a straightforward synthetic procedure, in good yields. These substrates feature interesting properties in terms of solvent promoted self-aggregation, toward the formation of specific supramolecular structures. The differences shown, with respect to the aggregation properties of similar porphyrin derivatives, point out the effect of the macrocycle structure on the self-recognition process. The extension to more elaborate substrates, *e.g*. featuring chiral, charged groups, would make possible the building of assemblies with interesting stereochemical features.

Experimental‖

Kinetic studies

Kinetic experiments were performed at 298 K, on a Perkin Elmer λ18 spectrophotometer by measuring the UV-visible spectroscopic changes of **2** with time. Corrole aqueous solutions, suited for kinetic studies, were prepared as follows. Proper aliquots of a **2** millimolar stock solution in ethanol (15 to 150 μL) were added to 2.0 mL of ethanol in an 8 mL glass vial. To this solution 2.0 mL of proper NaBr solutions were then added and the resulting solution vigorously shaken. A 3 mL portion was rapidly transferred to a quartz cuvette and the relative UV-visible spectra acquired in a time-drive scan. This procedure ensures a 50 : 50 H_2O–EtOH (v/v) final solvent composition, with a final **2** concentration spanning in the range of 0.25 to 5.0×10^{-5} M. Values of k were obtained

Table 1 Kinetic parameters for the aggregation of corrole $\mathbf{1H_2}$[a]

Entry	[NaBr]/M	k/min^{-1}	n
1	0.10	4.8×10^{-4}	0.58
2	0.385	6.5×10^{-4}	0.61
3	1.67	2.2×10^{-3}	0.65
4	2.50	4.0×10^{-3}	0.59
5	3.50	5.0×10^{-3}	0.63

[a] $[\mathbf{1H_2}] = 5.0 \times 10^{-6}$ M; T = 298 K, in EtOH–H_2O, 50 : 50 (v/v).

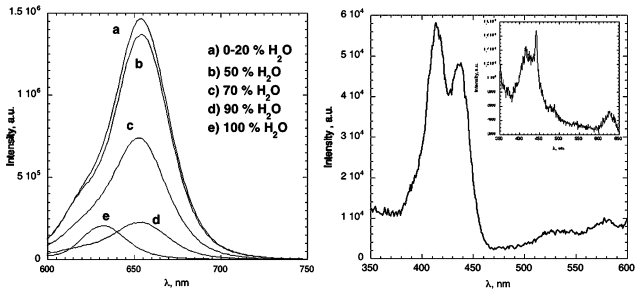

Fig. 2 Left: fluorescence spectra of **2** (5×10^{-6} M) at different EtOH–water compositions. Right: excitation spectra in water, at $\lambda = 635$ and $\lambda = 660$ nm (inset).

by analysing the absorbance *vs.* time data points, by a stretched exponential equation (eqn (1)):

$$E = E_0 + (E_{inf} - E_0)\exp[-(kt)^n] \quad (1)$$

where E, E_0, E_{inf} are the extinction values at time t, initially, and at equilibrium, respectively. The kinetic parameters, k and n, were obtained by nonlinear least-squares regression fit (Kaleidagraph® program, Synergy Software, 2003) over hundreds of experimental data points. Experiments have been run in duplicate, with reproducibility within 5% ($R^2 \geq 0.9996$).

Synthesis

10-(4-Carboxymethylphenyl)-5,15-diphenylcorrole (1). In a 250 mL round bottomed flask, 5-phenyldipyrromethane (1 mmol) and 4-acetoxybenzaldehyde (0.5 mmol) were dissolved in CH_3OH (50 mL), following Gryko and Koszarna's method reported in the literature.[8d] Subsequently, a solution of HCl_{aq} (36%, 2.5 mL) in H_2O (50 mL) was added, and the reaction was stirred at room temperature for 1 h. The mixture was extracted with $CHCl_3$, and the organic layer was washed twice with H_2O, dried on Na_2SO_4, filtered, and diluted to 250 mL with $CHCl_3$. *p*-Chloranil (1.5 mmol) was added, and the mixture was stirred overnight at room temperature. The reaction mixture was then concentrated to half the volume and passed over a silica column (SiO_2, CH_2Cl_2–hexane, 2 : 1). All the fractions containing the desired corrole were combined and evaporated to dryness. The resulting solid was suspended in boiling EtOH, cooled, and filtered to give 108 mg (0.18 mmol, 37% yield) of pure product as a violet crystalline solid.

UV-Vis: λ_{max} ($\varepsilon/10^4$, in $CHCl_3$): 417 (9.54), 577 (1.61), 612 (1.23), 643 (0.74) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.99 (d, 2H, β-pyrr), 8.91 (d, 2H, β-pyrr), 8.62 (d, 2H, β-pyrr), 8.54 (d, 2H, β-pyrr), 8.46–8.37 (m, 6H, phenyl), 8.29 (d, 2H, phenyl), 7.87–7.74 (m, 6H, phenyl), 4.12 (s, 3H, $-CO_2Me$). FAB-MS (NBA), *m*/*e*: 585 $[M + H]^+$.

Sodium 10-(4-carboxylatephenyl)-5,15-diphenylcorrole (2). In a 250 mL round bottomed flask corrole (**1**) (100 mg, 0.17 mmol) was dissolved in 100 mL of 95% EtOH and NaOH (0.2 g) was added. The mixture was stirred at reflux temperature for 2 h, then cooled to 25 °C and filtered, washing the precipitate several times with distilled H_2O. The residue was dried on air and then dissolved with a mixture of $CHCl_3$ and CH_3OH, and the solvent evaporated under reduced pressure. The green solid was dissolved in 100 mL of $CHCl_3$ and washed with a saturated solution of aqueous NH_4Cl. The organic phase was then dried on anhydrous Na_2SO_4 and the solvent was reduced to a small volume, and purified by column chromatography (SiO_2, $CHCl_3$–MeOH 5%). All the fractions containing the desired corrole were collected, reduced to a small volume and washed with NaOH 0.1 M (3 × 100 mL). The crystallisation from CH_2Cl_2–*n*-pentane afforded 83 mg of the title corrole (0.14 mmol, 84% yield) as a dark green solid.

UV-Vis. λ_{max} ($\varepsilon/10^4$, in $CHCl_3$): 417 (9.40), 577 (1.41), 612 (1.10), 643 (0.72) nm; λ_{max} ($\varepsilon/10^4$, in EtOH): 413 (8.30), 579 (1.32), 614 (1.10), 650 (0.65) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.02 (d, 2H, β-pyrr), 8.92 (d, 2H, β-pyrr), 8.63 (d, 2H, β-pyrr), 8.54 (d, 2H, β-pyrr), 8.49 (d, 2H, phenyl), 8.40–8.32 (m, 6H, phenyl), 7.84–7.75 (m, 6H, phenyl). FAB-MS (NBA), *m*/*e*: 570 [base; $M + H - Na]^+$, 526 [35%; $M - Na - CO_2]^+$.

Acknowledgements

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References

† In the case of the aggregation of porphyrin derivatives, the hypsochromic shift has been inferred to be due to the formation of H-type aggregates. See, for example ref. 4*c*.

‡ Substituted free-base corroles have been reported to be quite unstable in chlorinated solvent upon exposure to ambient light (see ref. 13*b*). In the bulk conditions of the present work, some decomposition occurs only upon prolonged standing. However, negligible degradation of **2** occurs during aggregation promoted by NaBr.

§ A value of 2×10^{-5} min^{-1} can be estimated, for the unpromoted aggregation of **2**, from a *k vs.* NaBr concentration plot.

¶ The spectral features, such as a split Soret band (λ_{max} = 414, and 437 nm) and a new Q band at λ_{max} = 626 nm, strongly corroborate the formation of the protonated corrole form. See for example ref. 13*c*.

‖ Reagents and solvents (Sigma-Aldrich, Fluka and Carlo Erba Reagenti) were of synthetic grade and used without further purification. Silica gel 60 (70–230 mesh) was used for chromatographic purification. ^{1}H NMR spectra were recorded on a Bruker AV300 (300 MHz) spectrometer. Chemical shifts are given in ppm relative to tetramethylsilane (TMS). UV-Vis spectra were measured on a Cary 1 spectrophotometer equipped with a temperature-controlled cell holder. Fluorescence and RLS spectra were run on a SPEX Fluoromax spectrofluorometer. Mass spectra (FAB) were recorded on a VG-Quattro spectrometer in the positive-ion mode using *m*-nitrobenzyl alcohol (NBA, Aldrich) as a matrix.

1 T. S. Balaban, *Acc. Chem. Res.*, 2005, **38**, 612.
2 (*a*) R. Purrello, S. Guerrieri and R. Lauceri, *Coord. Chem. Rev.*, 1999, **190–192**, 683; (*b*) R. Paolesse, D. Monti, L. La Monica, M. Venanzi, A. Froiio, S. Nardis, C. Di Natale, E. Martinelli and A. D'Amico, *Chem.–Eur. J.*, 2002, **8**, 2476; (*c*) L. S. Dolci, E. Marzocchi, M. Montalti, L. Prodi, D. Monti, C. Di Natale, A. D'Amico and R. Paolesse, *Biosens. Bioelectron.*, 2006, **22**, 399.
3 J. A. A. W. Elemans, R. Van Hameren, R. J. Nolte and A. E. Rowan, *Adv. Mater.*, 2006, **18**, 1251.
4 (*a*) M. Kasha, H. R. Rawls and M. A. El-Bayoumi, *Pure Appl. Chem.*, 1965, **11**, 371; (*b*) J. M. Ribó, J. M. Bofill and J. Crusatz, *Chem.–Eur. J.*, 2001, **7**, 2733.
5 (*a*) R. F. Pasternack, *Chirality*, 2003, **15**, 329; (*b*) R. F. Pasternack and P. Collings, *Science*, 1995, **269**, 935.

6 (*a*) N. Kobayashi, *Coord. Chem. Rev.*, 2002, **227**, 129; (*b*) M. Kimura, H. Ueki, K. Ohta, K. Hanabusa, H. Shirai and N. Kobayashi, *Langmuir*, 2002, **18**, 7613.

7 (*a*) D. Aviezer, S. Cotton, M. David, A. Segev, N. Khaselev, N. Galili, Z. Gross and A. Yayon, *Cancer Res.*, 2000, **60**, 2973; (*b*) A. Mahammed, H. B. Gray, J. J. Weaver, K. Sorasaenee and Z. Gross, *Bioconjugate Chem.*, 2004, **15**, 738; (*c*) H. Agadjanian, J. J. Weaver, A. Mahammed, A. Rentsendorj, S. Bass, J. Kim, I. J. Dmochowski, H. B. Gray, Z. Gross and L. K. Medina-Kauwe, *Pharm. Res.*, 2006, **23**, 367; (*d*) A. Mahammed and Z. Gross, *J. Am. Chem. Soc.*, 2005, **127**, 2883; (*e*) Z. Gershman, I. Goldberg and Z. Gross, *Angew. Chem., Int. Ed.*, 2007, **46**, 4320.

8 (*a*) R. Paolesse, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, New York, 2000, vol. 2, p. 201; (*b*) S. Nardis, D. Monti and R. Paolesse, *Mini-Rev. Org. Chem.*, 2005, **2**, 355; (*c*) D. T. Gryko, *Eur. J. Org. Chem.*, 2002, 1735; (*d*) B. Koszarna and D. T. Gryko, *J. Org. Chem.*, 2006, **71**, 3707.

9 I. Aviv and Z. Gross, *Chem. Commun.*, 2007, 1987.

10 (*a*) R. Paolesse, S. Nardis, M. Venanzi, M. Mastroianni, M. Russo, F. R. Fronczek and M. G. H. Vicente, *Chem.–Eur. J.*, 2003, **9**, 1192; (*b*) I. Saltsman, A. Mahammed, I. Goldberg, E. Tkachenko, M. Botoshansky and Z. Gross, *J. Am. Chem. Soc.*, 2002, **124**, 7411; (*c*) S. Nardis, F. Mandoj, R. Paolesse, F. R. Fronczek, K. M. Smith, L. Prodi, M. Montalti and G. Battistini, *Eur. J. Inorg. Chem.*, 2007, 2345.

11 A. Mahammed and Z. Gross, *Angew. Chem., Int. Ed.*, 2006 **45**, 6544.

12 (*a*) D. Monti, V. Cantonetti, M. Venanzi, F. Ceccacci, C. Bombelli and G. Mancini, *Chem. Commun.*, 2004, 972; (*b*) D. Monti, M. Venanzi, G. Mancini, C. Di Natale and R. Paolesse, *Chem. Commun.*, 2005, 2471; (*c*) D. Monti, M. Venanzi, M. Stefanelli, A. Sorrenti, G. Mancini, C. Di Natale and R. Paolesse, *J. Am. Chem. Soc.*, 2007, **129**, 6688.

13 (*a*) J. Bendix, I. J. Dmochowski, H. B. Gray, A. Mahammed, L. Simkhovich and Z. Gross, *Angew. Chem., Int. Ed.*, 2000, **39**, 4048; (*b*) T. Ding, E. A. Alemán, D. A. Modarelli and C. J. Ziegler, *J. Phys. Chem. A*, 2005, **109**, 7411; (*c*) J. Shen, J. Shao, Z. Ou, W. E. B. Koszarna, D. T. Gryko and K. M. Kadish, *Inorg. Chem.*, 2006, **45**, 2251.

14 We choose NaBr, as a salt, owing to its higher lipophilicity, compared to its more hydrophilic NaCl counterpart. It has been reported that the nature of the counterion can affect the aggregation of water-soluble porphyrin derivatives, see: G. De Luca, A. Romeo and L. Monsù Scolaro, *J. Phys. Chem. B*, 2005, **109**, 7149.

15 (*a*) N. Micali, F. Mallamace, A. Romeo and L. Monsù Scolaro, *J. Phys. Chem. B*, 2000, **104**, 5897; (*b*) M. A. Castriciano, A. Romeo and L. Monsù Scolaro, *J. Porphyrins Phthalocyanines*, 2002, **6**, 431; (*c*) P. Štepanek, M. Dukh, D. Šaman, J. Moravcova, L. Kniezo, D. Monti, M. Venanzi, G. Mancini and P. Drasar, *Org. Biomol. Chem.*, 2007, **5**, 960.