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A novel self-indicative vesicle based on a iron(II) complex

Paula Garcia,[a] João Marques,[a] Eulália Pereira,*[a] Paula Gameiro,[a] Roberto Salema[b] and Baltazar de Castro[a]

[a] *CEQUP/Faculdade de Ciências do Porto, Rua do Campo Alegre, 687, 4169-007 Porto, Portugal. E-mail: efpereir@fc.up.pt*

[b] *Instituto Botânico – Faculdade de Ciências do Porto, Rua do Campo Alegre, 1191, 4160-007 Porto, Portugal*

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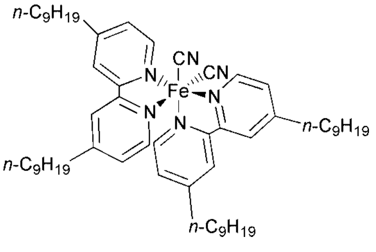
An iron(II) complex with a lipophilic derivative of 2,2′-bipyridine was synthesized and found to aggregate in aqueous solution, yielding vesicles with a mean diameter of 1000 nm; preliminary cyclic voltammetry experiments show that the complex forms redox-active films at the electrode surface.

The design of new amphiphilic molecules incorporating transition metal complexes is a recent topic of interest due to their potential use in catalysis,[1] medicine[2] and materials science.[3] Self-assembling amphiphilic systems containing metal ions are particularly promising since they combine the special solvation and interfacial behaviour of organised media with the rich chemical reactivity of transition metal complexes. Several applications may be envisaged for this type of molecules, such as the development of environmentally friendly catalysts, medical applications such as carriers of diagnostic metals and metal-complex drugs with specific targeting ability, and as models for biological membrane processes. Nevertheless, the special characteristics imparted by metal ions in organised media are much more poorly understood.[4]

In this work we have synthesised and studied the complex *cis*-bis(4,4′-dinonyl-2,2′-bipyridine)dicyanoiron(II) **1**. Complexes of the type $[FeL_2(CN)_2]$, where L is a bidentate diimmine ligand, have been extensively used as inorganic solvatochromic probes of solvent polarity. In the course of a systematic study on the solvatochromic behaviour of complexes of this type with different hydrolipophilic balance[5] we have prepared complex **1**, using a published procedure with minor modifications.[6] Synthesis of 4,4′-dinonyl-2,2′-bipyridine was performed by reaction of 4,4′-dimethyl-2,2′-bipyridine with lithium diisopropylamide, followed by condensation with 1-bromooctane.[7] The desired complex was obtained by reaction of $(NH_4)_2Fe(SO_4)_2 \cdot 5H_2O$ with three-fold the stoichiometric amount of the ligand, followed by addition of an excess of KCN; purification by chromatography afforded the pure complex.† Its solvatochromic behaviour was studied in a large range of solvents with different properties, from methanol to *n*-pentane. The results obtained are indicative that the solvatochromic sensitivity of **1** is similar to that of the related complex *cis*-$[Fe(bpy)_2(CN)_2]$, which is, however, insoluble in low-polarity solvents. Thus, the introduction of two nonyl chains in the diimmine ligand results in a complex that may act as a solvent polarity probe in lipophilic systems.



In order to evaluate possible preferential solvation effects we have studied the solvatochromic behaviour of complex **1** in water–methanol, water–acetone and water–acetonitrile. The solvatochromic behaviour in water–methanol mixtures is very different from that observed in the two other mixed solvents (Fig. 1). Addition of water to a methanol solution of **1** results in a small but regular decrease of λ_{max}, and thus indicates the absence of preferential solvation. On the contrary, the addition of small amounts of water to acetone or acetonitrile solutions results in a sharp decrease in band maxima, typical of a strong preferential solvation by water.

In the three mixed solvents studied at water content of 33, 40 and 50% (v:v) in methanol, acetone and acetonitrile, respectively, an abrupt increase in λ_{max} is observed with a perceptible colour change from red to deep blue (typical of a very lipophilic environment) accompanied by the appearance of turbidity. Light-scattering of these solutions shows that they contain aggregates with a mean hydrodynamic diameter of *ca.* 1000 nm.‡ Since light-scattering studies and the morphology of the aggregates may depend on the presence of small quantities of organic solvent, we have repeated the analysis using several reported methods for the preparation of lipid aggregates in aqueous solutions,[8]§ and the results were similar. The size of the aggregates was confirmed by electron microscopy (Fig. 2). Several grids were observed and in all of them a regular and relatively homogeneous population of round aggregates were observed with most of them with diameters varying between 870 and 1020 nm.¶

The type of aggregate formed was identified by a well established method,[8b,9] with 4(5)-carboxyfluorescein as a fluorescent probe, that is highly hydrophilic and auto-quenches at high concentrations. Aggregates were prepared in an aqueous 1 M solution of 5(6)-carboxyfluorescein, and separated from unincorporated probe by passing through a Sephadex G-50 column. Elution profiles showed clearly two fluorescent bands, one corresponding to the free aqueous probe and the other to the solution containing the aggregated complex (confirmed by UV–VIS spectroscopy). Addition of TRITON-X to the fraction

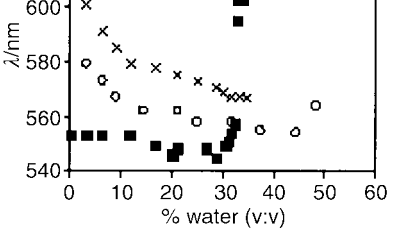


Fig. 1 Variation of λ_{max} of the LMCT band of complex **1** with water content in mixed solvents methanol–water (■), acetone–water (×) and acetonitrile–water (○).

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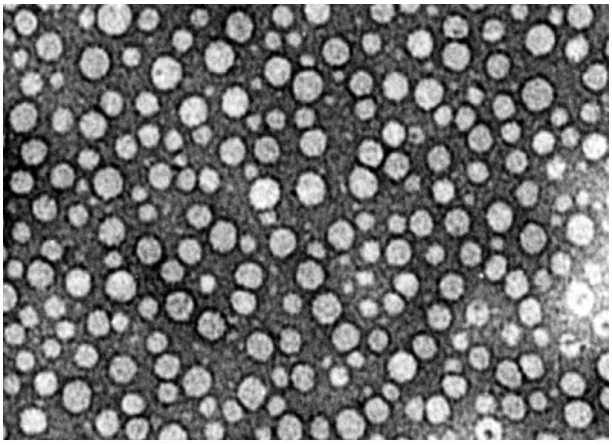

Fig. 2 Negative stain transmission electron micrograph of vesicles at magnification 3000×.

containing the aggregates causes their disruption and an 100-fold increase in fluorescence intensity is observed. This result clearly shows that complex **1** aggregates by forming vesicles—double layer spherical aggregates containing an inner aqueous core.

Preliminary studies of the redox behaviour of this complex in the monomeric and aggregated forms were performed by cyclic voltammetry. Solutions of **1** in acetonitrile show one reversible redox process ($E_{1/2}$ = 0.39 V *vs.* Ag/AgCl,1 M NaCl), a value that is significantly lower than that of $[Fe(bpy)_2(CN)_2]$ obtained in the same conditions ($E_{1/2}$ = 0.49 V *vs.* Ag/AgCl,1 M NaCl), which shows that the introduction of the alkyl chains results in a stabilization of the +3 oxidation state for Fe. Addition of water up to a concentrations of 55% (v/v) does not affect the voltammograms of $[Fe(bpy)_2(CN)_2]$, but for the more lipophilic complex the redox process gradually changes toward more positive potential ($E_{1/2}$ = 0.50 V for 55% H_2O–MeCN). In water rich solvents, where formation of vesicles in solution is observed, immersion of a platinum or vitreous carbon electrode in the solution for 5 min leads to the formation of a redox active film with $E_{1/2}$ = 0.60 V.

The results obtained in this work show that complex **1** is a new metallo-surfactant that readily forms vesicles in water-rich media and with solvatochromic properties that make aggregation self-indicated. This aggregation behaviour provides a simple way to localize metal-ion reactivity in organized media, and the preliminary studies performed by CV show that aggregation, although affecting the redox potential of the iron center, does not inhibit its redox behaviour. Complex **1** is thus a promising compound to test possible synergetic effects of conjugating redox reactivity and the special solvation effects of organized systems, *e.g.* in redox catalysis of lipophilic compounds in water-rich media.

Notes and references

† Chromatography in silica gel 60 (Merck, 230–400 mesh) using acetone and methanol as eluents. δ_H(200 MHz, $CDCl_3$): 0.83–0.90 (m, 12 H, 4 × $-CH_3$); 1.24–1.37 (m, 56 H, 4 × $-(CH_2)_7CH_3$); 2.61 (t, *J* 7.9 Hz, 4 H, 2 × Ar–CH_2); 2.77 (t, *J* 7.9 Hz, 4 H, 2 × Ar–CH_2); 6.88 (d, *J* 5.8 Hz, 2 H, 2 × 4-Ar-H); 7.12 (d, *J* 5.7 Hz, 2 H, 2 × 3-Ar-H); 7.22 (t, *J* 5.6 Hz, 2 H, 2 × 4′-Ar-H); 7.80 (s, 4 H, 2 × 6,6′-Ar-H); 9.81 (d, *J* 5.6 Hz, 2 H, 2 × 3′-Ar-H). MS (10 keV, FAB$^+$): *m*/*z*: 925 (3) (M^+); 899 (37) [$M^+ - CN$]; 873 (23) [$M^+ - (CN)_2$].

‡ Dynamic light-scattering was used to determine the diameter of the aggregates, using a Malvern Instrument ZetaSizer 5000, with a 5 mV He–Ne laser operating at 633 nm. Measurements were performed at a scattering angle of 90° at a temperature of 25 °C. All the measurements were performed 2 and 24 h after preparation of the samples. Correlation analysis was performed using CONTIN software from Malvern Instruments.

§ One of the methods more commonly used was the following: 0.1 ml of a methanol solution of the complex (2.0×10^{-4} M) was injected with a Hamilton air-tight syringe into 10 ml of an aqueous solution at 60 °C, under Ar bubbling. After injection the solution was maintained at the same temperature for 5 min with Ar bubbling for complete organic solvent elimination.

¶ A drop of the solution was placed onto 400 mesh copper grids coated with Parlodion (nitrocellulose) film stabilised with vacuum evaporated carbon. After 30 s the excess fluid was drained off with filter paper and a drop of the negative stain added. After 1 min the remainder of the 2% aqueous solution of phototungstic acid with the pH adjusted to 7.2 with 0.1 M NaOH was removed with filter paper and the grid immediately placed in the electron microscope.

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