Self-assembly of a ferrocene-substituted porphyrin capable of electrochemically sensing neutral molecules *via* a "tail on–tail off" process

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The supramolecular assembly of a ferrocene–porphyrin conjugate allowed ferrocene-based electrochemical sensing of the metalloporphyrin axial coordination *via* a "tail on–tail off" binding process.

Due to its unique structural and electronic properties, combined with extensive chemical reactivity, the redox responsive unit ferrocene has been incorporated into a large variety of substrate-specific receptors.[1] Ferrocene-appended porphyrins have in particular received attention mainly because of their potential applications in molecular electronic devices or as models for multiple-electron transfer reactions.[2] While numerous examples of ferrocene-appended porphyrins exist, directly connected ferrocene–porphyrin conjugates are rare.[3] We considered that a direct linkage would promote communication between the fragments and enable their use as electrochemical sensors. Here, we report the synthesis and characterisation of such a ferrocene–porphyrin conjugate wherein the ferrocene is further substituted by a hexylamine "tail" and show that the self-assembly observed in solution allows unprecedented ferrocene-based electrochemical sensing of neutral species *via* a metalloporphyrin-centred "tail on–tail off" binding process.[4]

Scheme 1 illustrates the synthesis of the ferrocene–porphyrin conjugate **7**. The sequence starts with the mono-protection of the known diformyl ferrocene **1**[5] according to a modified literature procedure[6] to give **2** in *ca.* 70% yield. The MacDonald type condensation of the latter with tolyldipyrromethane in the presence of TFA, followed by oxydation with chloranil, afforded a mixture of ferrocene-substituted porphyrin derivatives from which **3** was isolated in 8% yield. **4** was obtained from **3** by removal of the cyclic dithioketal using a mixture of Ag⁺ ions and *N*-chlorosuccinimide (NCS). A nitrogenous "tail" was introduced onto the ferrocene moiety by reaction of *n*-hexylamine with the regenerated formyl group to produce **5**.[7] This was immediately reduced with an excess of NaBH₄ to produce **6**.

Finally, the zinc complex **7**† was prepared quantitatively in a dichloromethane–methanol mixture using the acetate salt of the metal cation.

The ¹H NMR spectrum of **7**, recorded in CDCl₃ and assigned using ¹H–¹H and ¹H–¹³C correlation spectroscopies, evidenced an interaction between the amine "tail" and the porphyrin metal center (Fig. 1). In particular, five unresolved signals were observed at high field, between 0 and −5 ppm, reflecting the effect of the porphyrin ring current on the coordinated amine fragment. Even the ferrocene protons were seen to be significantly shifted and observed as a broad signal at 2.1 ppm. The ¹H NMR spectrum of **7** was found to be essentially concentration independent over the concentration range of the ¹H NMR measurements ($\Delta\delta < 0.1$ ppm for 7×10^{-2} M $\geq C \geq 7 \times 10^{-5}$ M in CDCl₃). These interactions were further confirmed by UV-Vis spectroscopy measurements showing a Soret band located at 429 nm (CH₂Cl₂, RT), as compared to 419 nm observed for square planar ZnTPP analogues.[8] While the spectra of **7** recorded in the concentration range of 10^{-5} to 10^{-3} M showed no change in the absorption wavelengths, further dilution induced significant shifts, *e.g.* 424 nm at 5×10^{-8} M. These concentration dependent features brought us to consider inter-molecular interactions leading to a $(\mathbf{7})_n$-type supramolecular assembly.[9] Vapor pressure osmometry experiments were performed to assess the self-assembled structure evidenced in solution. Measurements in toluene between concentrations of 5×10^{-3} and 15×10^{-3} M at 60 °C yielded an effective molecular weight of 1957 ± 30, showing that **7** forms a dimeric structure under these conditions.[10] Insight into the geometry of such species, obtained through molecular modeling,[11] is depicted in Fig. 2.

Electrochemical investigations carried out in CH₂Cl₂ containing 0.1 M TBAP also evidenced an assembling phenomenon. Using cyclic or differential pulsed voltammetry, five different oxidation processes were observed (Fig. 3): a reversible ferrocene-based oxidation at $E_{1/2} = 60$ mV (*vs.* Fc⁰⁄⁺) followed by four porphyrin-based oxidations at 280, 370, 630 and 810 mV. As has already been observed for polymeric structures,[12] the shoulder at 280 mV on the first porphyrin oxidation wave arises from interactions between the porphyrin rings in the supramolecular assembly. The irreversible oxydation process at 630 mV can be attributed to the second porphyrin oxidation to give an electrophilic species known to irreversibly lead to isoporphyrins in the presence of nucleophiles.[13] The last oxidation process, at 810 mV, thus result most presumably from the oxidation of an isoporphyrin cation wherein the nitrogenous "tail" has been incorporated into the porphyrin framework.

Cleavage of the supramolecular structure was induced upon addition of nitrogenous bases to a CH₂Cl₂ solution of **7** and
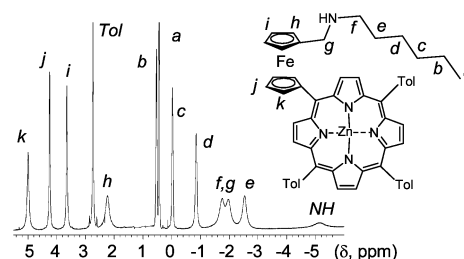
Scheme 1 *Reagents and conditions*: *i* (70%), CH₂Cl₂, Ar, SH(CH₂)₂SH (1.05 eq.), BF₃·OEt₂, col. chromat. (SiO₂, hexane–20% EtOAc); *ii* (8%), CH₂Cl₂, Ar, tolyldipyrromethane (1 eq.), TFA (cat.), 30 min; chloranil, col. chromat. (SiO₂, CH₂Cl₂–50% hexane); *iii* (70%), THF/CH₃CN/H₂O, AgNO₃ (6 eq.), NCS (6 eq.), col. chromat. (SiO₂, CH₂Cl₂–0.5% MeOH); *iv–v* (80%), THF, mol. sieves, Ar, CH₃(CH₂)₅NH₂ (1.2 eq.), 16 h; diethyl ether/EtOH, NaBH₄ (5 eq.), 3 h, col. chromat. (SiO₂, CH₂Cl₂–5% MeOH); *vi* (100%), CH₂Cl₂, ZnOAc₂.H₂O/MeOH (excess), 10 h, col. chromat. (SiO₂, CH₂Cl₂–5% MeOH).

In scheme: **1** : R¹ = CHO, R² = CHO; **2** : R¹ = CH(S(CH₂)₂S), R² = CHO; **3** : R³ = CH(S(CH₂)₂S), Z = tolyl, M = H₂; **4** : R³ = CHO, Z = tolyl, M = H₂; **5** : R³ = CH=N(CH₂)₅CH₃, Z = tolyl, M = H₂; **6** : R³ = CHNH(CH₂)₅CH₃, Z = tolyl, M = H₂; **7** : R³ = CHNH(CH₂)₅CH₃, Z = tolyl, M = Zn^II

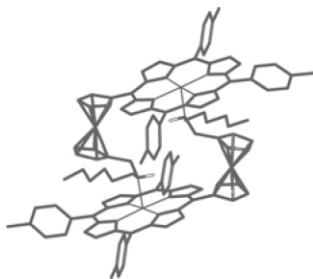**Fig. 1** Part of the ¹H NMR spectrum of **7** (RT, CDCl₃, 500 MHz).

Fig. 2 Molecular modeling of (**7**)$_2$ using InsightII-Discover 2000.
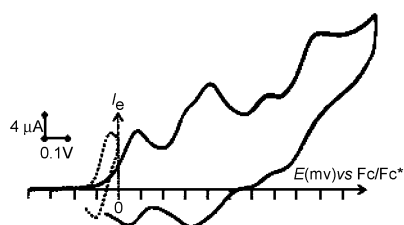

Fig. 3 (—) Cyclic voltammogram of a 5 × 10^{-4} M CH$_2$Cl$_2$ (TBAP, 0.1 M) solution of **7**; (···) cyclic voltammogram corresponding to the ferrocenyl moiety of **7** after addition of 10 equivalents of pyridine (v = 100 mV s^{-1}, 3 mm diameter carbon disk).

evidenced through the low-field shift of the ^{1}H NMR signals, a slight red shift in the absorption maximum observed in the UV-Vis spectrum and, as expected, by means of electrochemical techniques. Confirming the assumption that the shape of the first porphyrin-based oxidation is inherent to intermolecular assembling, addition of pyridine or imidazole causes the disapearance of the shoulder observed at *ca.* 280 mV, along with a marked irreversibility for all the porphyrin-based oxidation processes.

On the other hand, the oxidation of the ferrocenyl moiety remains reversible in the presence of coordinating bases and allowed us to electrochemically monitor the axial coordination of the metalloporphyrin *via* a "tail on–tail off" binding process. The Fc/Fc$^+$ half-wave potential negatively shifted by 110, 140 and 150 mV upon the addition of an excess pyridine, imidazole and 2-methylimidazole respectively (Fig. 4). Compared to the rare reported molecular receptors able to electrochemically sense neutral guests,[1,14] the ΔE values induced by the addition of nitrogenous bases to the redox active supramolecular assembly **7** are particularly high.[15] In addition, the differences between the potential decays, which reflect the individual binding strengths,[16] emphasize the efficient electronic communication between the π-aromatic systems of the porphyrin and the ferrocene moieties.

In conclusion, we synthesized a novel functionalized ferrocene-substituted porphyrin and showed that a self-assembly phenomenon, coupled with efficient electronic communication throughout the receptor, allows an unprecedented ferrocene-based electrochemical sensing of neutral species *via* a metalloporphyrin-centred "tail on–tail off" binding process.[17] While current work is focused on studying in detail this dynamic
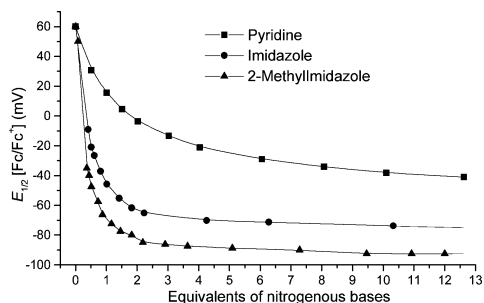

Fig. 4 Evolution of the ferrocene potential in **7** as a function of the addition of nitrogenous bases. Same conditions as in Fig. 3.

process, this result reveals the relevance of directly connected ferrocene–porphyrin conjugates as electrochemical sensors and will lead us to consider new and effective multipoint architecture for the electrochemical recognition of target molecules.

Notes and references

† *Spectroscopic data for* **7**: MS (MALDI-TOF): [M]$^+$ = 939.2; ^{1}H NMR (CDCl$_3$, 500 MHz, 293 K): δ −5.18 (bs, 1H), −2.54 (bs, 2H), −1.98 (bs, 2H), −1.76 (bs, 2H), −0.86 (bs, 2H), −0.03 (bs, 2H), 0.43 (t, ^3J = 7 Hz, 3H, –CH$_2$CH$_3$), 0.52 (m, 2H, –CH$_2$CH$_3$), 2.23 (bs, 2H, Fc), 2.72 (s, 3H, Ph–CH$_3$), 2.73 (s, 6H, Ph–CH$_3$), 3.64 (bs, 2H, Fc), 4.24 (bs, 2H, Fc), 5.0 (bs, 2H, Fc), 7.53–7.60 (m, 6H), 8.07–8.15 (m, 6H), 8.87 (m, 6H), 9.82 (bs, 2H, β-pyr). ^{13}C NMR (CDCl$_3$, 62.5 MHz, 293 K): 13.5, 21.5, 22.0, 23.9, 24.9, 30.2, 42.8, 42.9, 69.4, 69.5, 71.0, 78.2, 82.5, 90.7, 116.1, 120.2, 120.9, 127.1, 130.7, 131.4, 131.5, 134.3, 134.7, 136.7, 140.2, 140.4, 149,2, 149.8, 150.0, 150.2; λ_{max}/nm (CH$_2$Cl$_2$) (log ε) 429 (5.43), 580 (4.06), 631 (4.28); Elemental analysis: calc. for C$_{58}$H$_{53}$FeN$_5$Zn, C 74.00, H 5.67, N 7.44%; obs. C 73.15, H 5.66, N 7.30%.

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