

# Anion recognition and redox sensing amplification by self-assembled monolayers of 1,1'-bis(alkyl-N-amido)ferrocene†

Paul D. Beer,\* Jason J. Davis,\* Daniel A. Drillsma-Milgrom and Fridrich Szemes

*Inorganic Chemistry Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QR.*

*E-mail: paul.beer@chem.ox.ac.uk, Jason.davis@chem.ox.ac.uk; Fax: +44 (0)1865 272690; Tel: +44 (0)1865 272632*

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**Surface pre-organisation within robust amidoferrocene self-assembled monolayers can be exploited in the selective electrochemical sensing of anions in both organic and aqueous media.**

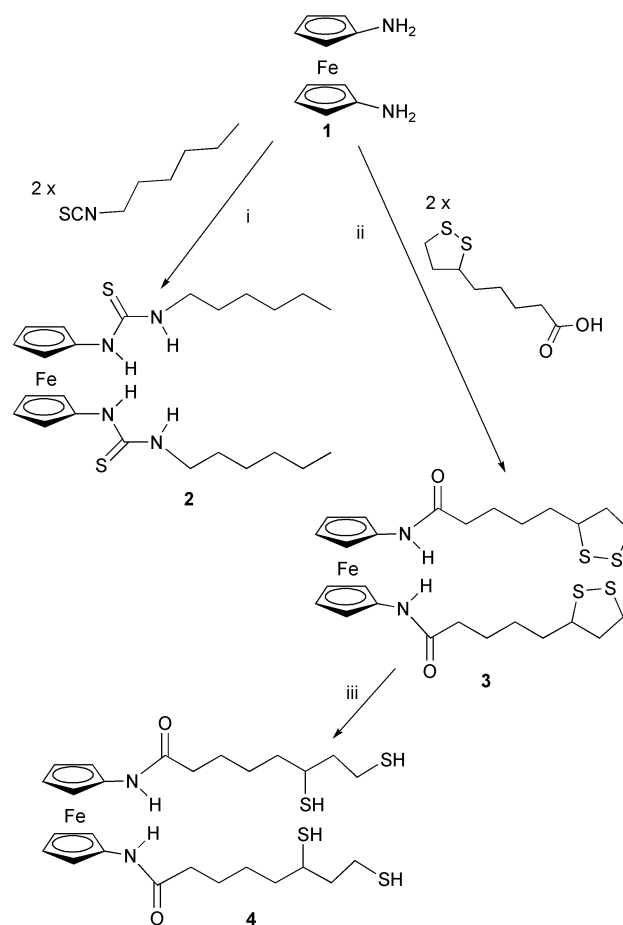
The combined processes of molecular-scale recognition and surface self-assembly offer a powerful route to the development of both refined sensing systems and, more generally, new technological devices based on controlling and analysing interactions at the nanometre scale. We,<sup>1–4</sup> and others,<sup>5–7</sup> have exploited the redox-active ferrocene moiety in the selective *electrochemical* sensing of anions in organic and aqueous media. In particular acyclic, macrocyclic and calixarene amide-functionalised ferrocene derivatives have all been shown to undergo substantial cathodic perturbations of the respective metallocene redox couple in the presence of a variety of anions of biological and environmental importance.

The methods of surface self-assembly are especially amenable to the fabrication of robust sensory devices capable of analyte detection under a variety of solution-phase conditions. Thiol-based monolayers, in particular, can be formed and characterised with comparative ease. The electrochemical properties of ferrocene-based alkanethiol self-assembled monolayers have been studied in detail by Creager *et al.*<sup>8,9</sup> By introducing hydrogen bond donor amide groups, we report here the generation of robust monolayers which have selective anion recognition properties. In particular, by directly linking amido functionalities to the ferrocene redox centre, the hydrogen-bond mediated recognition of specific anions/oxoanions is accompanied by a significant perturbation of the ferrocene redox potential. Importantly, by anchoring the sensing unit to the electrode, this response is significantly amplified by the surface pre-organisation of the host such that anion recognition in an aqueous medium is possible.

The new 1,1'-bis substituted ferrocene thiourea and amide derivatives **2** and **3** were prepared in very good yields *via* condensation reactions of 1,1-diaminoferrocene<sup>10</sup> (**1**) with hexyl thiocyanate or an activated thioctic acid derivative (Scheme 1). The addition of various tetrabutylammonium anion salts to CD<sub>3</sub>CN–CDCl<sub>3</sub> (2:1 v/v) <sup>1</sup>H NMR solutions of **2** and **3** resulted in significant perturbations of the respective amide protons. The resulting titration curves all suggested a 1:1 receptor:anion stoichiometry and the computer programme EQNMR was used<sup>11</sup> to determine stability constant values. Table 1 shows that thiourea derivative **2** forms the strongest anion complexes and exhibits the selectivity trend H<sub>2</sub>PO<sub>4</sub><sup>–</sup> > AcO<sup>–</sup> > Cl<sup>–</sup>. In contrast, the amide receptor **3** displays a selectivity preference AcO<sup>–</sup> > H<sub>2</sub>PO<sub>4</sub><sup>–</sup> > Cl<sup>–</sup>, a trend that reflects the decreasing basicity of the anion guest.

The organic-phase diffusive voltammetry of these redox-active molecules (in CH<sub>3</sub>CN–CH<sub>2</sub>Cl<sub>2</sub>) was studied† initially at polished edge-plane graphite electrodes; faradaic currents and half-wave potentials for **3** were as expected (Table 2). Disappointingly, the thiourea derivative **2** displayed irreversible

electrochemical characteristics (anodic peak potential  $E_{pa}+70$  mV) which precluded anion recognition studies. The addition of molar excesses of TBA anion salts to solutions of **3** led to significant cathodic perturbation of the ferrocene wave. It is noteworthy that, by directly linking the amido group to the ferrocene ring, hydrogen bonded anion recognition events are accompanied by substantial cathodic perturbations of the ferrocene wave; as large as 210 mV in magnitude with the dihydrogen phosphate anion (Table 2).



**Scheme 1** Reagents and conditions: i, THF, reflux, 3 h, 75%; ii, DCC, CH<sub>2</sub>Cl<sub>2</sub>, rt, 3 h, 70%; iii, NaBH<sub>4</sub> (4 equiv.), EtOH–MeOH, rt, 24 h, 80%.

**Table 1** Stability constants in a mixture of acetonitrile-d<sub>3</sub> and deuteriochloroform (2:1 v/v)

Anion	K [M <sup>–1</sup> ] <sup>a</sup>	
	<b>2</b>	<b>3</b>
Cl <sup>–</sup>	2300	100
CH <sub>3</sub> COO <sup>–</sup>	18600	570
H <sub>2</sub> PO <sub>4</sub> <sup>–</sup>	24200	360

<sup>a</sup> Errors < 10%.

† Electronic supplementary information (ESI) available: electrochemical analysis and monolayer preparation/characterisation details. See <http://www.rsc.org/suppdata/cc/b2/b205340n/>

**Table 2** Diffusive voltammetric data of **3**

	Cl <sup>-</sup>	Br <sup>-</sup>	H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>
$E_{p_a} - E_{p_c}/\text{mV}$	60	60	90
$I_{p_a}/I_{p_c}$	1	1	1.1
$\Delta E/\text{mV}^a$	40	20	210

<sup>a</sup> Error  $\pm 5$  mV.  $E_{p_a} - E_{p_c}$  is the peak separation referenced to Ag/AgNO<sub>3</sub>. The diffusive half wave potential,  $E_{1/2}$ , defined as  $(E_{p_a} - E_{p_c})/2$  is  $-20$  mV.  $\Delta E$  denotes the coordination-induced cathodic shift in half wave potential in the presence of 8–9 mM anion. Scans were carried out at 295 K in 100 mM TBA·BF<sub>4</sub> (2:1 v/v CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>CN) supporting electrolyte.

**Table 3** Voltammetric data and anion coordination-induced cathodic shifts observed with a self-assembled monolayer of compound **3**

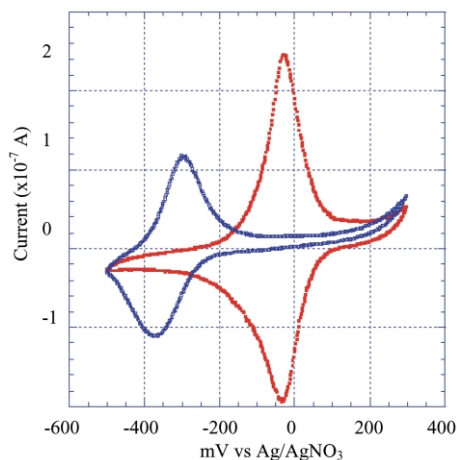
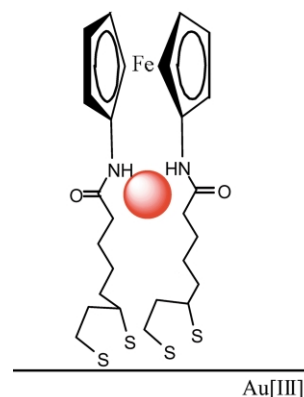
	Cl <sup>-</sup>	Br <sup>-</sup>	H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>
$E_{p_a} - E_{p_c}/\text{mV}$	60	40	60
$I_{p_a}/I_{p_c}$	1.4	1.2	1.2
$\Delta E/\text{mV}^a$	100	30	300

<sup>a</sup> Error  $\pm 10$  mV. The SAM  $E_{1/2}$  is  $-20$  mV vs. Ag/AgNO<sub>3</sub>. Monolayers of **4** had indistinguishable half wave potentials.  $\Delta E$  denotes the coordination-induced cathodic shift in half wave potential in the presence of 8–9 mM anion. Scans were carried out at 295 K in 100 mM TBA·BF<sub>4</sub> (2:1 v/v CH<sub>2</sub>Cl<sub>2</sub>:CH<sub>3</sub>CN) supporting electrolyte.

Monolayers of **3** and **4** were prepared on gold macroelectrodes in the usual way.<sup>†</sup> Both the disulfide and thiol derivatives formed adlayers on clean gold electrodes with stable, reversible, ferrocene/ferrocenium electrochemical responses in both organic and aqueous electrolyte (Table 3).<sup>†</sup>

Perhaps the most striking aspect of data obtained on confining **3** to a monolayer is the consistent observation of “surface sensing amplification”; that is, anion-induced cathodic shifts are consistently greater (Fig. 1) than observed diffusively, highlighting significant advantages associated with preorganisation of the host pseudo macrocycle on a surface (Fig. 2). Specifically, redox responses are more cathodically shifted by (approximately) 90 and 60 mV for phosphate and chloride respectively. Cathodically shifted waves were all characterised by greater peak separation (and often lower faradaic current) than observed in the precursor ferrocene couple. Such an increased peak separation is both indicative of a relatively slow rate of electron transfer to the underlying gold surface ( $k_{et}$  calculated to be  $< 100$  s<sup>-1</sup>) and possible anion coordination-induced structural changes within the film.

Competition experiments carried out on the addition of dihydrogen phosphate to electrolytic solutions of **3**, 100 fold excess in halide, confirmed the ability of H<sub>2</sub>PO<sub>4</sub><sup>-</sup> to compete effectively for the amide binding site; only the resultant H<sub>2</sub>PO<sub>4</sub><sup>-</sup>-shifted ferrocene couple is observed. This is the case both when **3** is analysed diffusively and surface-confined.

**Fig. 1** The voltammetric response of a monolayer of **3** in the absence (red) and presence (blue) of H<sub>2</sub>PO<sub>4</sub><sup>-</sup> (8 mM).**Fig. 2** Schematic of anion binding within the surface-confined host **3**.

The effects of host surface pre-organisation become apparent particularly in comparisons of solution-phase anion binding <sup>1</sup>H NMR studies with diffusive and surface-confined electrochemical analyses. Significantly, in the former, with **3** only very weak binding to the perchlorate anion, a model anion species for the environmentally important radioactive pertechnetate anionic pollutant from the nuclear industry, is detectable in CD<sub>3</sub>CN:CDCl<sub>3</sub> (2:1 v/v) solvent (no stability constant could be calculated). Interestingly, no electrochemical sensing is observed in diffusive cyclic voltammetric studies. By confining **3** within a monolayer, however, reproducible cathodic shifts of 20–25 mV are observed on perchlorate anion binding.

Coordination-mediated anion detection in an aqueous medium is challenging due to the accompanying unfavourable energetic requirements of dehydration and the low binding constants of anions, particularly to neutral anionophores.<sup>1</sup> Monolayers of **3** or **4** in water, however, give reproducible cathodic shifts (15–20 mV)<sup>†</sup> in the presence of perchlorate, a comparatively poorly hydrated anion. In competition experiments carried out with SAMs of **3** and **4** with molar equivalents of perchlorate and dihydrogen phosphate in CH<sub>3</sub>CN:CHCl<sub>3</sub>, H<sub>2</sub>PO<sub>4</sub><sup>-</sup> is selectively detected. In water, however, perchlorate is selectively sensed.

In summary, we have synthesised a novel 1,1'-bis(alkyl-*N*-amido)ferrocene with, selective, anion binding properties. By introducing disulfide or thiol anchoring moieties into the structure, well-behaved, robust, anion sensing monolayers can be prepared. Importantly, such surface pre-organisation significantly amplifies the redox responses observed with phosphate, halides and perchlorate; binding of the latter anionic guest species can be detected in an aqueous environment.

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