Selective Electrochemical Recognition of the Dihydrogen Phosphate Anion in the Presence of Hydrogen Sulfate and Chloride Ions by New Neutral Ferrocene Anion Receptors

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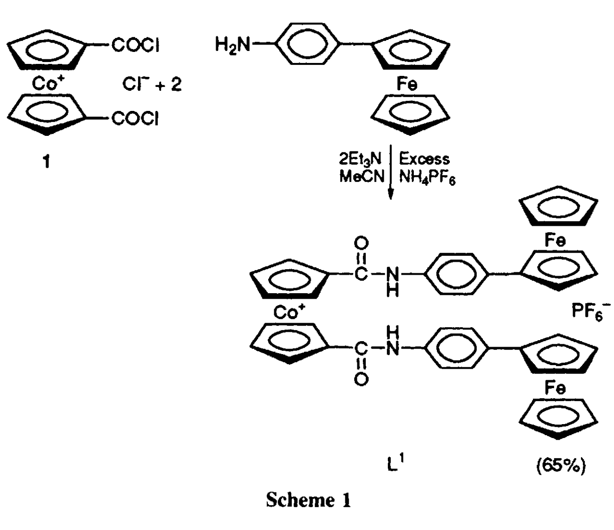
New neutral ferrocene anion receptors L^3, L^4, L^5 selectively complex, electrochemically recognise and respond to the dihydrogen phosphate guest anion in the presence of excess amounts of hydrogen sulfate and chloride anions.

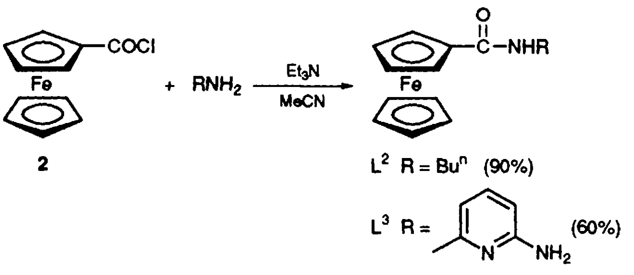
The molecular recognition of anionic guest species[1] by positively charged[2] or electron deficient neutral[3] abiotic organic receptor molecules is an area of intense current interest. Anions play ubiquitous roles in chemical and biochemical processes and some are presently of great environmental and medical concern.[4] We have recently reported the first and only redox-responsive class of anion receptor based on the redox-active, pH-independent, positively charged cobalticinium moiety and demonstrated that the simple combination of cobalticinium unit together with an amide N–H group are the essential components for anion recognition.[5] In light of this work and influenced by how nature uses *neutral* globular protein domains to bind sulfate[6] and phosphate[7] anions using solely, respectively, seven and twelve complementary anion-hydrogen bond arrangements we decided to construct new, neutral organometallic ferrocene derivatives that contain various hydrogen bond donor and acceptor sites for anion recognition. This communication illustrates that these simple amide and amine containing systems can be designed to selectively complex and, for the first time, *selectively electrochemically* recognise the dihydrogen phosphate anion in the presence of excess amounts of hydrogen sulfate and chloride anionic guest species.

The first indication that neutral amide containing ferrocene derivatives may electrochemically recognise anions in their own right came from the electrochemical anion coordination properties of the novel multimetallocene compound L^1 which was prepared according to Scheme 1. Proton NMR titration investigations with tetrabutylammonium salts ($Bu^n{}_4N^+X^-$, X = $H_2PO_4^-$, HSO_4^-, Cl^-) in acetonitrile indicated the receptor formed 1:1 solution complexes with each of the anionic guests. Cyclic voltammetric electrochemical anion recognition investigations revealed not only the cobalticinium/cobaltocene redox couple to undergo cathodic perturbations of up to 230 mV with $H_2PO_4^-$ but also the ferrocene/ferrocenium couple to shift cathodically by up to 90 mV in the presence of $H_2PO_4^-$ (Table 1). As a consequence of these electrochemical findings the new neutral ferrocene amide containing derivatives L^2–L^4 were prepared, (Schemes 2 and 3), including a novel calix[4]arene derivative L^5 (Scheme 4).

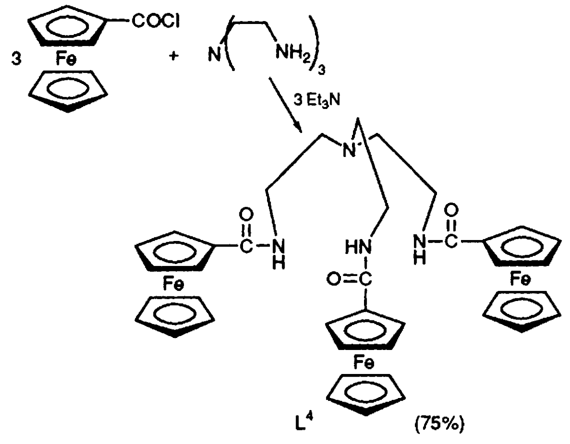
Remarkable downfield shifts of the respective amide protons, ranging from Δδ 0.9 to 2.5 ppm, were exhibited by



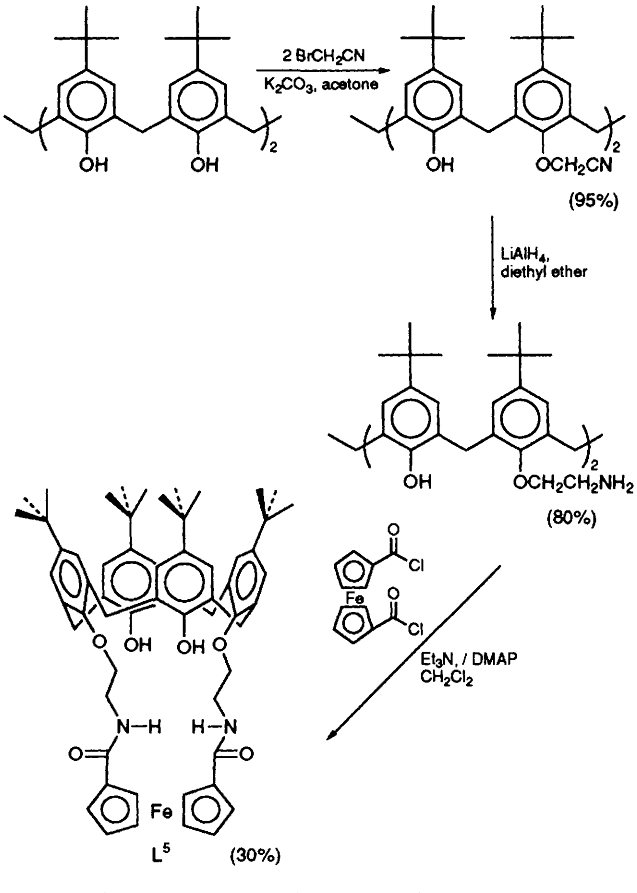
Scheme 1



Scheme 2



Scheme 3



Scheme 4 DMAP = 4-dimethylaminopyridine

Table 1 Electrochemical data for L^1[a]

	Ferrocenyl redox couple/mV	Cobalticinium redox couple/mV
E_{pa}(free)[b]	240	−810
E_{pc}(free)[b]	180	−870
$\Delta E(H_2PO_4^-)$[c,d]	90	230
$\Delta E(H_2SO_4^-)$[c,d]	60	90
$\Delta E(Cl^-)$[c,d]	40	70

[a] Obtained in MeCN solution containing 0.1 mol dm^{-3} $[NBu_4]BF_4$ as supporting electrolyte. Solutions were *ca.* 1 × 10^{-3} mol dm^{-3} in compound and potentials were determined with reference to a Ag^+/Ag electrode at 21 ± 1 °C, 50 mV s^{-1} scan rate. [b] E_{pa} and E_{pc} represent the anodic and cathodic peak potentials. [c] Cathodic shifts in the metallocene redox couples produced by presence of anion (5 equiv.) added as their tetrabutylammonium salts. [d] As the concentration of anion increased the cathodic current peak potential of the ferrocene/ferricinium redox couple began to exhibit the features of an EC mechanism.

Table 2 Electrochemical data for L^{2-5}[a]

Compound	L^2/mV	L^3/mV	L^4/mV	L^5/mV
E_{pa}(free)[b]	290	360	320	450
E_{pc}(free)[b]	265	270	220	380
$\Delta E(H_2PO_4^-)$[c,d]	60	100	180	110
$\Delta E(HSO_4^-)$[c,d]	20	40	50	<5
$\Delta E(Cl^-)$[c,d]	30	<5	20	40

[a] Refer to footnote *a*, Table 1. [b] E_{pa} and E_{pc} represent the anodic and cathodic current peak potentials of the ferrocene/ferricinium redox couple of the free ligand. [c] Cathodic shifts in the ferrocene redox couples produced by presence of anion (5 equiv.) added as their tetrabutylammonium salts. [d] As the concentration of anion increased the cathodic current peak potential of the ferrocene/ferricinium redox couple began to exhibit the features of an EC mechanism.

receptors L^3–L^5 on addition of $Bu^n{}_4N^+X^-$ ($X^- = H_2PO_4$, HSO_4^-, Cl^-) salts to deuteriated acetonitrile–Me_2SO NMR solutions. The resulting titration curves suggested L^3–L^5 to form solution complexes of 1 : 1 stoichiometry with all three anionic guests. Relatively smaller amide perturbations were observed with L^2, which only contains one amide moiety, and it was not possible to elucidate the L^2 : anion stoichiometries from the respective NMR titration results.

The reversible redox couple values and results of electrochemical anion recognition experiments are shown in Table 2. Significant anion guest induced cathodic perturbations of the respective ferrocenyl oxidation current peak potentials are observed with all receptors. Interestingly, as the concentration of the anionic guest increased, the shape of the oxidation wave changed from a reversible redox process to an EC mechanism. It is noteworthy that L^4, which contains a tetrahedral cavity exhibits the largest magnitude of cathodic shift (180 mV) with the complementary shaped $H_2PO_4^-$ anionic guest.

Of particular relevance to amperometric chemical sensor technology were the novel results of electrochemical competition experiments. When an equimolar mixture of $H_2PO_4^-$, HSO_4^- and Cl^- was added to acetonitrile electrochemical solutions of L^3, L^4 and L^5 the respective ferrocene–ferricinium redox couples shifted cathodically by an amount approximately the same as that induced by the $H_2PO_4^-$ anion alone. The same result was even obtained when HSO_4^- and Cl^- anions were in tenfold excess concentrations over $H_2PO_4^-$. Analogous competition experiments with the two anions HSO_4^- and Cl^- suggested an overall selectivity order for L_3, L_4, L_5 of $H_2PO_4^- > HSO_4^- > Cl^-$.[8] These results suggest L^3, L^4 and L^5 are first generation prototype dihydrogen phosphate-selective amperometric sensors, capable of detecting the $H_2PO_4^-$ anion in the presence of tenfold excess amounts of HSO_4^- and Cl^- ions.

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