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Preliminary Communication

Selective electrochemical recognition of bidentate anionic guests in competitive solvents using novel ferrocenyl thiourea and guanidinium receptors

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Abstract

Novel ferrocenyl-based redox-active bidentate receptors exhibit selective binding and redox recognition of basic bidentate anionic guests, including the binding and redox recognition of $P_2O_7^{4-}$ in highly competitive aqueous solvent mixtures. © 1997 Elsevier Science S.A.

The crucial role of anionic substrates in biological processes is largely responsible for the recent and rapidly expanding field of anion coordination chemistry [1,2]. The synthesis of receptors containing a functional unit, often a metal centre, capable of sensing anion binding has also been an important target [3–5]. The use of ferrocene as a functional antenna to detect anion binding has only recently been reported [6–8]. This paper presents novel ferrocenyl receptors incorporating bidentate hydrogen-bonding groups in various structural arrangements known to be capable of anion chelation [9–11], including the first example of a guanidinium group appended with a redox-active subunit. These hosts selectively bind and electrochemically sense basic, bidentate anions, such as $P_2O_7^{4-}$ in biologically relevant, competitive hydrogen-bonding aqueous solvents.

Condensing benzoyl chloride with ammonium thiocyanate in acetone, and subsequent condensation with ferrocenemethylamine provided L1 as a yellow solid in 67% yield (Scheme 1). Receptor L2 was synthesised in 50% yield by condensing ferrocenemethylamine with phenyl-isothio cyanate in CH_2Cl_2 solution (Scheme 2). Receptor L3 was produced using the methodology of Rasmussen et al. (Scheme 3) [12] and was isolated as an iodide salt.

Proton NMR titrations were used to study the behaviour of L1–L3 with anions. Surprisingly, L1 showed no interaction with $H_2PO_4^-$ anion in either $CDCl_3$ or DMSO-d_6 solution. X-ray diffraction quality crystals of L1 [1] were obtained from $MeOH/CH_3CN/H_2O$ and explain the lack of binding (Fig. 1). Atoms C(16), N(17), C(18), N(20), C(21) and O(28) are almost coplanar (maximum deviation, 0.06 Å) and there is a strong intramolecular hydrogen bond between N(17)–H and O(28) ($r_{N-O} = 2.655$ Å). It is proposed that this hydrogen bond prevents L1 from binding the $H_2PO_4^-$ bidentate anionic guest.

Compound L2, however, interacted strongly with $H_2PO_4^-$, the resultant titration curves being analysed using EQNMR to yield stability constants (Table 1) [13]. The strength of $H_2PO_4^-$ binding, particularly in polar DMSO-d_6 reflects the complementarity of bidentate host and guest. The binding constant was lower in non-polar $CDCl_3$, probably due to aggregation of $H_2PO_4^-$ with Bu_4N^+. Notably, L2 did not complex HSO_4^-, probably due to its lower basicity, making it less able to accept H-bonds. L2 therefore selectively recognises $H_2PO_4^-$ over HSO_4^-. Receptor L3 was investi-

[1] Crystal data for L: $C_{19}H_{18}FeN_2OS$, $M = 378.26$, monoclinic, spacegroup $P2_1/c$, $a = 12.983(12)$, $b = 6.045(6)$, $c = 22.23(2)$ Å, $\beta = 99.89(1)$ Å, $U = 1719$ Å^3, $Z = 4$, $dc = 1.462$ mg/m^3, 3805 reflections measured, 2443 unique (R(int) = 0.0363), refined on F^2 to R 0.0389.

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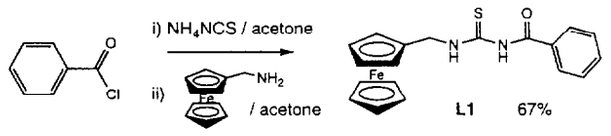
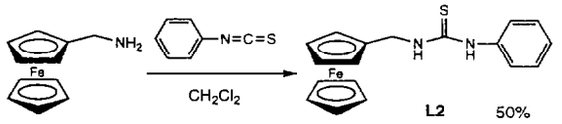
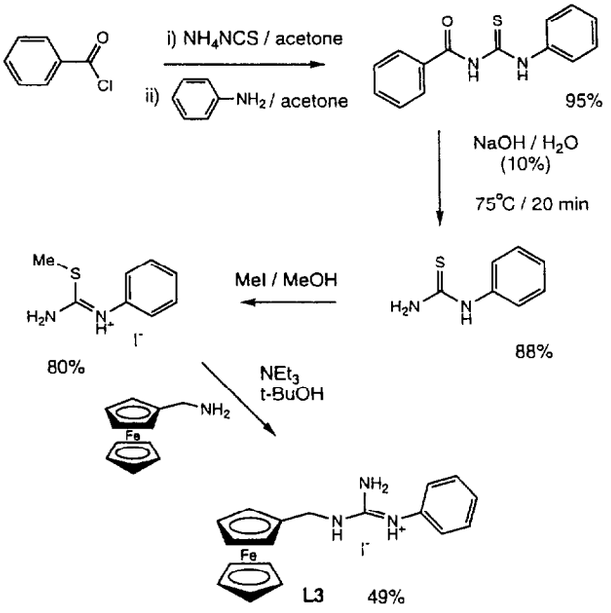


Scheme 1.



Scheme 2.



Scheme 3.

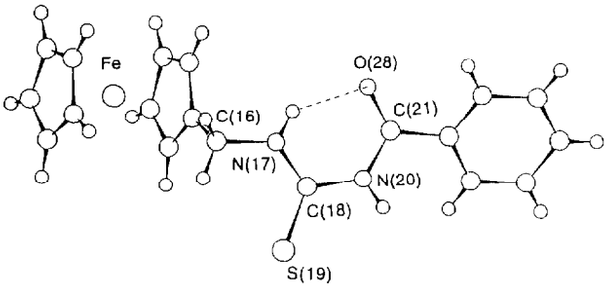


Fig. 1. Crystal structure of receptor L1 showing the intramolecular hydrogen bond.

Table 1
Stability constants calculated from ^{1}H-NMR titrations

Anion	Solvent	K (M^{-1}) L1	K (M^{-1}) L2
$H_2PO_4^-$	$CDCl_3$	0	125
$H_2PO_4^-$	DMSO	0	260
HSO_4^-	DMSO	–	< 5

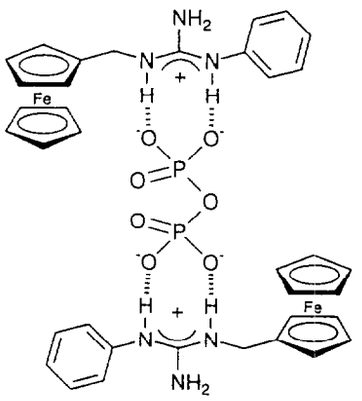


Fig. 2. Receptor L3 forms a complex of 2:1 stoichiometry with $P_2O_7^{4-}$.

gated using ^{1}H-NMR titrations in DMSO-d_6 solution with various guests ($H_2PO_4^-$, acetate, benzoate). EQNMR was used, but the data could not be adequately fitted to a 1:1 model, indicative of the possible existence of other stoichiometries, perhaps because L3 can exist in various conformations. Competition experiments showed that $H_2PO_4^-$ was still bound even in the presence of HSO_4^-. L3 is therefore selective for the basic anionic guest. Of particular relevance to biological recognition were NMR studies of L3 with $P_2O_7^{4-}$ in MeOH/H_2O (50/50), a competitive H-bonding solvent. The $P_2O_7^{4-}$ anion has considerable biological importance, being an end-product of ATP metabolism. It can also play active roles, for example stimulating chloride channel opening [14]. ^{1}H-NMR titrations indicated L3 interacted with $P_2O_7^{4-}$, but not $H_2PO_4^-$, presumably because the highly charged pyrophosphate anion interacts with positively charged guanidinium even in H-bonding solvents. The data were fitted to a 2:1 model (L3:anion) and K elucidated as 4600 M^{-2} (Fig. 2).

Cyclic voltammetry was used to investigate the ability of the receptors to sense anion binding. Receptor L2 sensed the presence of $H_2PO_4^-$ in CH_3CN solution. The ferrocene oxidation wave shifted 170 mV cathodi-

Table 2
Electrochemical response of receptor L3 to anionic guests

Anion	ΔE [a] (mV)
Chloride	35
Benzoate	65
Acetate	95
Dihydrogenphosphate	125

[a] Cathodic shift of the oxidation wave of receptor L3 with 10 equivalents of anionic guest added as tetrabutylammonium salts in DMSO solution; solutions were 2×10^{-3} mol dm^{-3} in receptor, temperature = 293 K.

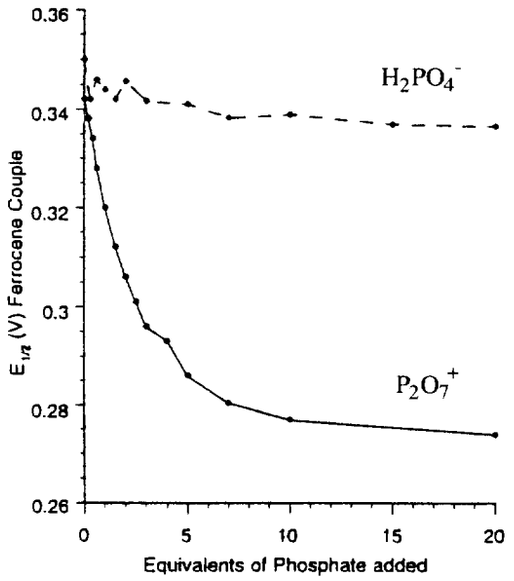


Fig. 3. The electrochemical response of receptor L3 ferrocene redox couple to anionic guests in competitive MeOH/H_2O (50/50) solvent.

cally (with 5 eq. guest), indicative of oxidation being facilitated by the proximate coordination of a negative charge. The ferrocene reduction wave flattened, indicating an EC mechanism [15]. The electrochemical response of L3 to various anions was studied in DMSO. The ferrocene oxidation wave shifted cathodically (Table 2) and the reduction peak flattened (EC mechanism). The presence of 10 equivalents of chloride anion had little effect on the redox response to $H_2PO_4^-$, indicating that L3 selects the bidentate guest. Receptor L3 also showed an electrochemical response to $P_2O_7^{4-}$ (but not $H_2PO_4^-$) in competitive MeOH/H_2O (50/50) (Fig. 3). The reversible ferrocene redox wave shifted 70 mV cathodically whilst the secondary, irreversible (guanidinium) oxidation wave shifted anodically. A control experiment with conc. KOH (in MeOH/H_2O) showed that this response was not equivalent to L3 deprotonation; the receptor therefore electrochemically recognises $P_2O_7^{4-}$ in the aqueous solvent mixture.

In conclusion, three novel bidentate receptors have been reported. Receptors L2 and L3 have non-hindered binding sites and show selective binding and redox recognition of basic bidentate anionic guests. Of particular interest is the ability of L3 to operate in competitive, hydrogen bonding aqueous solvent mixes, showing biologically relevant $P_2O_7^{4-}$ electrochemical sensing.

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