Redox-active Crown Ethers: Transmission of Cation Binding to a Redox Centre *via* a Conjugated Link

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The binding of Li^+ to aza-15-crown-5-linked ferrocenes results in a shift of the ferrocene oxidation wave to more positive potentials when a conjugated link exists between the azacrown nitrogen atom and the redox centre.

Interest in switchable metal ion binding and transport has resulted in a number of recent papers concerning redox-active ionophores. In general these compounds have been designed so that conformations may be adopted in which the guest metal ion is held close to the redox centre.[1–7] In this paper we seek to examine electrochemical recognition of metal ion binding *via* a conjugated link between ionophore and redox centre as an alternative to 'through-space' interactions. We report here the synthesis of the first examples, (**1**) and (**2**), of a class of compound in which ferrocene is linked through a conjugated system to the remote nitrogen atom of the aza-15-crown-5 unit,[8] and present evidence that metal-ion binding perturbs the redox potential of the ferrocene/ferricinium couple by a mechanism involving transmission of the electrostatic effect through the π-electron system.

Compound (**1**) and the acyclic analogue (**3**)† were obtained by reaction of the phosphonium salt (**4**)[9] with *N*-(4-formylphenyl)aza-15-crown-5[10] or 4-dimethylaminobenzaldehyde, followed by separation of *cis*- and *trans*-isomers (Scheme 1). Hydrogenation of (**1**) afforded compound (**5**). The methiodides (**6a** and **b**) were obtained by treatment of individual isomers (**3a** and **b**) with methyl iodide. Reaction of cyanomethylferrocene (**7**)[11] with *N*-(4-formylphenyl)aza-15-crown-5 gave the cyano derivative (**2**).

Electrochemical oxidation of compound (**5**) on a glassy carbon electrode at 25 °C in purified acetonitrile (MeCN) containing 0.1 M-$Bu_4N^+BF_4^-$ resulted in the observation of reversible redox waves at +0.64 (E_{1f}) and +1.10 V (E_{2f}) *vs.* Ag/AgCl (saturated $Me_4N^+Cl^-$), assigned to the ferrocene and dialkylaniline units, respectively, [Figure 1(a)].‡ In the case of compounds (**1a**), (**2**), and (**3**), two redox waves were again observed at potentials depending on the electronic effects of substituents. Addition of $LiBF_4$ to a solution of (**5**) in MeCN resulted in a small shift in potential of the ferrocene wave but no new redox couple was observed. The Li^+ ion is, however, clearly complexed, as shown by the disappearance of the second (dialkylaniline) oxidation wave.§ Interposition of a conjugated link between the ionophore and the ferrocene unit produced noticeably different electrochemical responses towards $LiBF_4$ titration. Addition of $LiBF_4$ to a solution of (**1a**) (E_{1f} = +0.65 V) in MeCN resulted in the clear evolution of a new ferrocene wave at +0.76 V associated with the oxidation of the complexed species (**1a**) ($FcIM^+$; Scheme 2).

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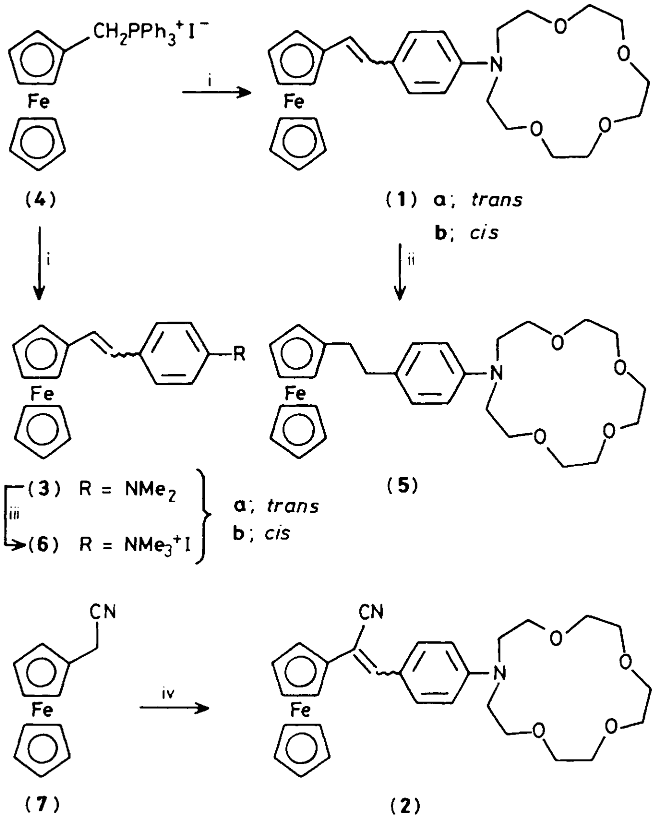
† All new compounds gave satisfactory microanalytical or high resolution mass spectral data. Spectroscopic data were consistent with the proposed structures. Selected ^1H n.m.r. data for the vinyl region $\delta(CDCl_3$; 500 MHz) are: (**1a**) 6.63(s, 2H); (**1b**) 6.14(d, 1H, *J* 12 Hz) and 6.32(d, 1H, *J* 12 Hz); (**3a**) 6.65 (s, 2H); (**3b**) 6.18(d, 1H, *J* 12 Hz) and 6.37(d, 1H, *J* 12 Hz); (**6a**) 6.66(d, 1H, *J* 16 Hz) and 7.01(d, 1H, *J* 16 Hz); (**6b**) 6.33(d, 1H, *J* 12 Hz) and 6.48(d, 1H, *J* 12 Hz).

‡ Under these conditions the half-wave potential for ferrocene was +0.75 and for *N*-phenylaza-15-crown-5 +1.12 V.

§ This conclusion was substantiated by u.v. spectroscopy.



Scheme 1. Reagents and conditions: i, *N*-(4-formylphenyl)aza-15-crown-5 or $4\text{-Me}_2NC_6H_4CHO$, Bu^nLi, tetrahydrofuran (THF), 25 °C, 12 h; ii, H_2, Pd–C, EtOH; iii, MeI, MeCN, 25°C, 40 h; iv, Bu^tOK, THF, 67 °C, 4 h.

$$\begin{array}{lcl} \mathrm{FcI} & + \mathrm{M}^+ \overset{K_1}{\rightleftarrows} & \mathrm{FcIM}^+ \\ E_{1f} \upharpoonleft\!\downharpoonright & & \upharpoonleft\!\downharpoonright E_{1c} \\ \mathrm{Fc^+I} & + \mathrm{M}^+ \overset{K_2}{\rightleftarrows} & \mathrm{Fc^+IM}^+ \\ E_{2f} \upharpoonleft\!\downharpoonright & & \upharpoonleft\!\downharpoonright E_{2c} \\ \mathrm{Fc^+I^+} & + \mathrm{M}^+ \overset{K_3}{\rightleftarrows} & \mathrm{Fc^+I^+M}^+ \end{array}$$

Scheme 2. Redox and complexation equilibria for a ferrocene-substituted ionophore, FcI; f denotes free (uncomplexed) ionophore, c denotes complexed species; $K_j = \overrightarrow{k}_j/\overleftarrow{k}_j$

On reaching a five-fold excess of $LiBF_4$ the ferrocene wave due to uncomplexed (**1a**) (FcI) had disappeared [Figure 1(b)]. Similar behaviour was observed for the first oxidation wave of (**2**), although a larger proportion of $LiBF_4$ was required to bring about the disappearance of the wave due to uncomplexed (**2**) [Figure 1(c)].

The magnitudes of the shifts in redox potential [$\Delta E = E_{1c} - E_{1f} = +0.11$ V, for both (**1a**) and (**2**)] correspond to a binding inhibition¶ on oxidation, $K_2/K_1 = 0.014$. The absence of a shift for compound (**5**) which carries a saturated link indicates that in the case of (**1a**) and (**2**) the electrostatic influence of complexed Li^+ on the nitrogen atom of the azacrown is transmitted to the ferrocene through the π-electron system, thus raising the oxidation potential. In other words, K_2 is much smaller than K_1 when the positive charge on the ferricinium ion can be relayed to the azacrown nitrogen atom, as in compounds (**1a**) and (**2**). In the case of compound (**5**) this relay effect is prevented by the saturated link, hence $K_1 \approx K_2$. In the presence of an excess of Li^+ the peak height of the second wave, corresponding to oxidation of Fc^+I, decreases in the order (**2**) > (**1a**) > (**5**). This trend can be attributed to a corresponding decrease in the rate of decomplexation $\overleftarrow{k}_2$, of the species Fc^+IM^+ with increasing electron density on the azacrown nitrogen atom. Since (**5**) (Fc^+IM^+) undergoes slow decomplexation on the voltammetric time scale, a value of $K_2 \approx 300\ dm^3\ mol^{-1}$ can be estimated from the reduction in peak height of the second wave on adding Li^+.

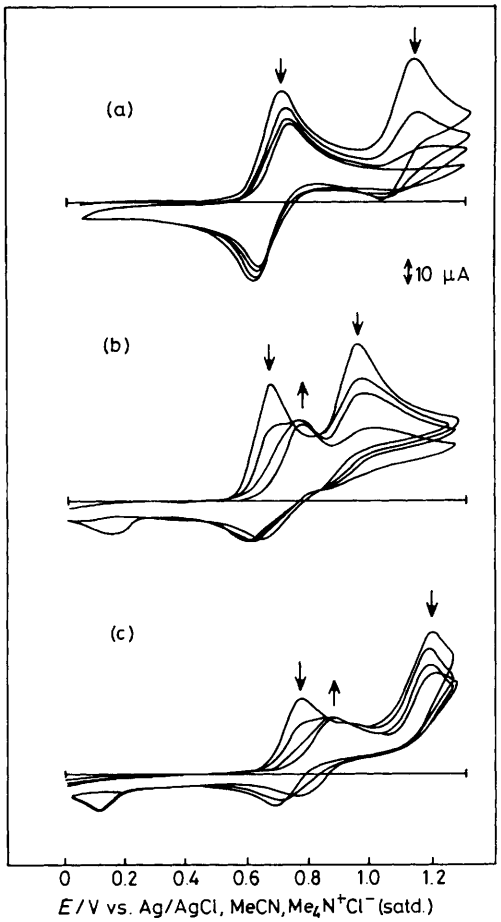


Figure 1. Cyclic voltammetry in MeCN solution of (a) compound (**5**) (3 mM), (b) compound (**1a**) (3 mM), and (c) compound (**2**) (2 mM), on addition of 0—15 mM $LiBF_4$ in MeCN. Sweep rate = 50 mV s^{-1}; scanning from 0 to + 1.35 V.

The amine (**3a**) showed electrochemical behaviour similar to that of the cyclic analogue (**1a**). Thus the ferrocene redox couple ($E_{1f} = +0.65$ V) was displaced by 0.11 V to more positive potential in the presence of $LiBF_4$. A slightly larger proportion (*ca.* 6 equiv.) of Li^+ was required before complete conversion into (**3a**) ($FcIM^+$) took place, indicating that both K_1 and K_2 are smaller for (**3a**) than for (**1a**). Some measure of the maximum shift that might be achieved upon complexation of the metal ion by nitrogen is provided by the redox potential of the methiodide (**6a**). The ferrocene oxidation wave of this

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¶ The ratio of binding constants was calculated from the expression $K_2/K_1 = \exp - (nF\Delta E/RT)$.

compound appears at +0.76 V, close to that observed for the species (**1a**) ($FcIM^+$), indicating that Li^+ induces a positive charge on nitrogen close to unity and so has little interaction with the oxygen atoms in the crown. The addition of an excess of $NaClO_4$ or KBF_4 to MeCN solutions of (**1a**), (**2**), (**3a**), or (**5**) did not give rise to new ferrocene redox couples, reflecting the lower charge densities of these cations as compared with Li^+.[1] This observation is relevant to sensor technology since an added degree of selectivity is conferred on amperometric systems as compared with the simple shape–size selectivity of conventional ligands.

Received 17th March 1987; Com. 340

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