A Redox-switchable Ligand for which the Binding Ability is enhanced by Oxidation of its Ferrocene Unit

Giancarlo De Santis, Luigi Fabbrizzi,* Maurizio Licchelli, Piersandro Pallavicini and Angelo Perotti
Dipartimento di Chimica Generale, Università di Pavia, 27100 Pavia, Italy

Electrochemical investigations on a ferrocene-modified tetraamine diketone ligand have demonstrated an unusual enhancement of the binding ability towards Ni^{2+} when the redox subunit is switched to the ferrocenium form.

Considerable attention has been paid in the last few years to conjugate systems containing a redox function and a fragment able to bind a metal cation; these systems can behave either as chemical sensors[1] or as redox-switchable ligands.[2] In particular, the redox and binding properties of quinone-modified lariat ethers and podands,[3] of ferrocene-containing polythioethers (polythia ferrocenophanes)[4] and of conjugate molecules containing one or more crown ethers or polythiapolyaza crown ethers and one or more ferrocene units[5] have been investigated. The most interesting quantity pertinent to these systems is ΔE ($\Delta E = E_{\frac{1}{2}c} - E_{\frac{1}{2}u}$), *i.e.* the difference between the potentials due to the redox functions in the complexed ($E_{\frac{1}{2}c}$) and uncomplexed ($E_{\frac{1}{2}u}$) molecules. All the reported ΔE values are positive: quite reasonably, the presence of a positive charge (the complexed metal cation) close to the redox centre makes easier the attainment of a lower oxidation state ($\Delta E > 0$ in the case of reducible redox functions) and more difficult the attainment of a higher oxidation state ($\Delta E > 0$ in the case of oxidizable redox functions).

We have now synthesised the new ferrocene-modified, water-soluble, tetradentate ligands H_2L^1 and L^2 by aminolysis of diethyl (ferrocenylmethyl)malonate[6] with ethane-1,2-diamine and through the reduction of H_2L^1 with diborane in tetrahydrofuran, respectively. The ligand H_2L^1 contains a dioxotetraamino binding framework[7] and is able to complex Ni^{2+} in water, with the simultaneous release of the two amido protons, forming the neutral, square-planar complex $[NiL^1]$ [equation (1)]. On the other hand, L^2 bears a tetraamine binding fragment[8] and binds Ni^{2+} in aqueous solution to give a square stereochemistry [equation (2)]. The complexation

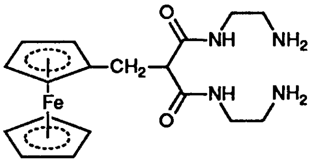
$$H_2L^1 + Ni^{2+} \rightleftharpoons [NiL^1] + 2H^+ \qquad (1)$$

$$L^2 + Ni^{2+} \rightleftharpoons [NiL^2]^{2+} \qquad (2)$$

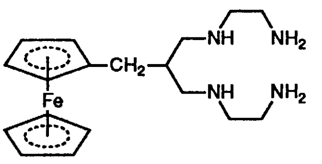
constants pertinent to equations (1) and (2) (*i.e.* K_{red}, see following discussion) have been determined by means of potentiometric titration experiments (Table 1).

Differential pulse voltammetry (DPV) and cyclic voltammetry (CV) of the uncomplexed systems H_2L^1 and L^2 in aqueous solution (0.1 mol dm^{-3} in $NaClO_4$) were carried out at pH values at which the presence of charged (protonated) species is precluded (see Table 1) and disclosed in both cases a one-electron reversible redox process, ascribed to oxidation of the ferrocene moiety to ferrocenium, $E_{\frac{1}{2}}$ 402 and 351 mV *vs.* normal hydrogen electrode (NHE), respectively. In spite of the similarity of the appended binding fragments, the ferrocene subunits display a strikingly different electrochemical behaviour upon co-ordination of the ligands to Ni^{2+}. In particular, DPV and CV experiments on aqueous solutions of $[NiL^1]$ and $[NiL^2]^{2+}$ (0.1 mol dm^{-3} in $NaClO_4$; pH adjusted to values at which 100% of the metal in solution was in the desired complexed form, see Table 1) revealed an opposite trend: in the case of $[NiL^2]^{2+}$, the ferrocene–ferrocenium redox change takes place at a more positive potential than in the free ligand ($\Delta E = +25$ mV); in the case of $[NiL^1]$ this oxidation takes place at a more negative value ($\Delta E = -42$ mV). Thus, paradoxically, the presence of a proximate positively charged centre (Ni^{2+}) makes it distinctly easier, and not more difficult, to form the positively charged ferrocenium subunit. The case of $[NiL^1]$ represents, to our knowledge, the first example of a redox-functionalized ligand that features a negative ΔE.

The apparent paradox can be explained in terms of electro-



H_2L^1

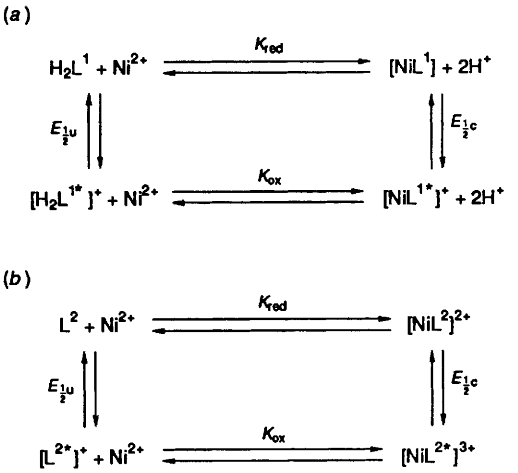


L^2

Table 1 Electrochemical and complexation equilibria data for H_2L^1 and L^2 and their nickel(II) complexes

	H_2L^1	L^2
log K_{red}	−9.73(5)	15.10(5)
log K_{ox}[a]	−9.0(1)	14.7(1)
$E_{\frac{1}{2}}$/mv (uncomplexed)[b]	402[c] (10.5)	351[c] (11.0)
$E_{\frac{1}{2}}$(nickel complex)[b]	360[c] (10.5)	376[c] (7.0) 1067[d] (7.0)

[a] Calculated on the basis of the experimentally determined ΔE (see text) and log K_{red} values. [b] *vs.* NHE, in aqueous solution, 0.1 mol dm^{-3} in $NaClO_4$, ±3 mV; the pH values at which the experiments were carried out are given in parentheses. Notice that the pK_a values for the first protonation are 8.85(1) for H_2L^1 and 9.95(1) for L^2; no variation was observed in the voltammograms on increasing the pH to the limiting value of 12. [c] Relative to ferrocene–ferrocenium. [d] Relative to the Ni^{II}–Ni^{III} couple.



Scheme 1

static effects. Placing a dipositive Ni^{2+} cation in the tetramine donor set of L^2 makes the oxidation of the proximate ferrocene subunit more difficult. On the other hand, on complexation H_2L^1 becomes deprotonated and a double negative charge forms on the ligand system. This negative charge is not completely offset by the Ni^{2+} ion and the oxidation potential of the appended ferrocene is thereby shifted cathodically.

A thorough explanation of the above effect is given, from a different point of view, by Scheme 1,[9] in which the complexation and redox equilibria pertinent to ligand H_2L^1 (*a*) or L^2 (*b*) with Ni^{2+} are summarized: K_{red} represents the complexation constant relative to the neutral, ferrocene-bearing ligands, while K_{ox} is relative to the oxidized, *ferrocenium*-bearing ligands. Equation (3)[9] holds for the situation described by Scheme 1 and

$$\Delta E = (RT/nF)\ln(K_{red}/K_{ox}) \qquad (3)$$

allows one to calculate K_{ox} from the experimentally obtained ΔE and K_{red} values. In particular (see Table 1), $K_{ox} > K_{red}$ in the case of H_2L^1 and $K_{ox} < K_{red}$ in the case L^2. Ligand L^2 displays behaviour typical of all reported ferrocene-modified ligands,[1,5,10] in which a decrease in the complexation constant is observed when a metal cation is co-ordinated by a ligand bearing a charged substituent (*e.g.* ferrocenium) instead of a neutral one (ferrocene).

The case of H_2L^1 can be explained by a closer examination of the complexation process [equation (1)]. This can be split into two steps, represented by equations (4) and (5), whose equilibrium constants are K_4 and K_5 (notice that individual values of K_4 and K_5 cannot be determined). Thus, $K_{red} = K_4K_5$. Similar equations (4*) and (5*) can be written for the oxidized,

$$H_2L^1 \rightleftharpoons [L^1]^{2-} + 2H^+ \qquad (4)$$

$$[L^1]^{2-} + Ni^{2+} \rightleftharpoons [NiL^1] \qquad (5)$$

$$[H_2L^{1*}]^+ \rightleftharpoons [L^{1*}]^- + 2H^+ \qquad (4^*)$$

$$[L^{1*}]^- + Ni^{2+} \rightleftharpoons [NiL^{1*}]^+ \qquad (5^*)$$

ferrocenium-bearing ligand **1** $[H_2L^{1*}]^+$. In this case, $K_{ox} = K_4{}^*K_5{}^*$. The electrostatic repulsive effect, exerted by the positively charged ferrocenium subunit in $[H_2L^{1*}]^+$ on the leaving amido protons, makes the value of $K_4{}^*$ higher than that of K_4. On the other hand, K_5 should be higher than $K_5{}^*$, following the general trend. Thus, it appears that $K_4{}^*$ increases with respect to K_4 more significantly than $K_5{}^*$ decreases with respect to K_5, and on balance $K_{ox} > K_{red}$.

The compound H_2L^1 represents the first example of a new class of redox-switchable ligands, capable of binding enhancement towards cations upon oxidation of the appended redox function. It should be noted that $[NiL^2]^{2+}$ undergoes a further one-electron reversible oxidation process, which is ascribed to the Ni^{II} to Ni^{III} change. Its $E_{\frac{1}{2}}$ value (1067 mV *vs.* NHE) is more positive than that observed for plain $[NiL^3]^{2+}$ (L^3 = 3,7-diazanonane-1,9-diamine) (1032 mV *vs.* NHE), as expected,[11] due to the electrostatic repulsive effects exerted by the proximate ferrocenium subunit. The complex $[NiL^1]$ displays a further irreversible wave in both CV and DPV profiles.

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