Pergamon

Tetrahedron Letters 43 (2002) 8453–8457

TETRAHEDRON
LETTERS

Synthesis of the first homobimetallic thiazole–ferrocene ligand displaying metal–metal interaction and redox-switchable proton affinity

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Received 11 September 2002; accepted 24 September 2002

Abstract—The previously unreported 2,5-bis(ferrocenyl)thiazole **4**, prepared from α-aminoacetylferrocene and chlorocarbonylferrocene in two steps, exhibits two reversible redox processes, indicating a significant electronic interaction between the iron centres. Electrochemical investigation of the protonated ligand revealed a reversible electrochemically-driven deprotonation/reprotonation process. © 2002 Elsevier Science Ltd. All rights reserved.

Since the advent of mixed-valence chemistry in 1967,[1] the study of electronic interactions in systems containing multiple, identical metal-centered fragments that individually display fast reversible one-electron exchange, has been a topic of interest particularly reviewed.[2]

Owing to the high stability, ease functionalization and well-defined electrochemistry, many complexes bearing two ferrocenyl moieties linked together with a wide variety of structural motifs have been synthesized to investigate the effectiveness of the bridging groups for the internuclear interaction. In this kind of system, variation of the nature of the molecular framework of the bridge enable the extent of communication between the centers to be modulated, as reflected in the electrochemical response.[3]

When electron communication between two ferrocenyl moieties is not allowed, the system will exchange two electrons through two one-electron processes whose potentials are separated only by the statistical term $\Delta E = 35.6$ mV at 298° K.[4] However, intramolecular communication between the two iron centers causes the ΔE value to increase, which can be used to evaluate the magnitude of their intramolecular electron-communication.[5] Such redox coupling has been discussed to occur through two main paths: (1) through-bond interactions, such as inductive effects, electron hopping, and electron delocalization through a bridging coordinating unit, and/or (2) through-space electrostatic and magnetic interactions.

Indeed, molecular design of a framework that supports electronic interaction is an issue of recent interest as possible components of not only molecular electronic devices but also electron-storage systems.[6] Although different extents of metal–metal interactions have been revealed for homobimetallic complexes in which the two ferrocene units are coupled intimately by π-unsaturated bridges,[7] examples showing electronic coupling between the ferrocenyl units through a heterocycle[8] or metallocycle[9] are rare.

In continuation of our studies on the synthesis of ferrocenylsubstituted azaheterocycles,[10] we wish to present here the synthesis of a new type of biferrocene derivative, namely 2,5-bis(ferrocenyl)thiazole **4**, and its electrochemical behavior with regard to the electronic communication between the two redox nuclei through the heteroaromatic ring.

Compound **4** was prepared in 30% overall yield by a two-step sequence. Acylation of α-aminoacetylferrocene[11] **1** with chlorocarbonyl ferrocene **2** in the presence of Et_3N provided the β-ketoamide **3** in 49% yield, which was converted into **4** in 62% yield,[12] by the action of the Lawesson's reagent (LR). The related ferrocenylthiazoles **5** and **6**, which have only one redox site, were also prepared only for comparison

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Keywords: ferrocenes; thiazoles; electrochemistry; protonation.

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PII: S0040-4039(02)02097-X

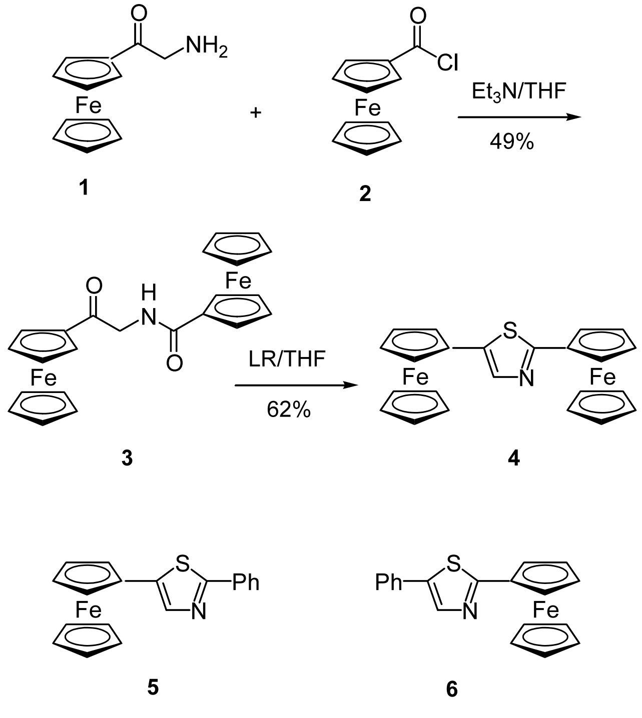
purposes following the above described sequence. Compound **5**, was obtained in a 20% overall yield from **1** and benzoyl chloride, whereas compound **6** was prepared in 56% overall yield from phenacylamine and **2** (Scheme 1).

Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were used to evaluate the strength of the interaction between the metal centers in the homobimetallic complex **4**. The cyclic voltammogram of **4** (Fig. 1a) shows two closely spaced reversible one-electron oxidations for the ferrocenyl groups, likewise the DPV voltammogram (Fig. 2a) also exhibits two well resolved oxidation waves of the same area.[13] An estimate for the extent of the ferrocenyl–ferrocenyl interaction is obtained from the wave splitting, $\Delta E_{1/2} = 140$ mV. The comproportionation constant Kc relative to the equilibrium given in Eq. (1), was calculated,[14] resulting a value of $Kc = 2.32\times10^2$. This value indicates that the partially oxidized $\mathbf{4}^+$ can be classified as Class II mixed-valence species according to the Robin-Day classification.[1,15]

$$2[\mathrm{Fe(II)–Fe(III)}] \rightleftharpoons [\mathrm{Fe(II)–Fe(II)}]+[\mathrm{Fe(III)–Fe(III)}] \tag{1}$$

The difference between the oxidation waves of the ferrocenyl groups in compound **4** (140 mV) is smaller than those for simple biferrocene[15] (420 mV), whereas the value is slightly larger than those for most bis-ferrocenyl compounds with π-conjugated bridges such as 1,4-bis(ferrocenyl)butadiene[17] (129 mV) and 1,4-bis(ferrocenyl)butadiyne[16] (120 mV).

One might speculate that the difference in the oxidation potentials of the two ferrocenyl groups in **4** could be due to the fact that they are intrinsically inequivalent.



Scheme 1.

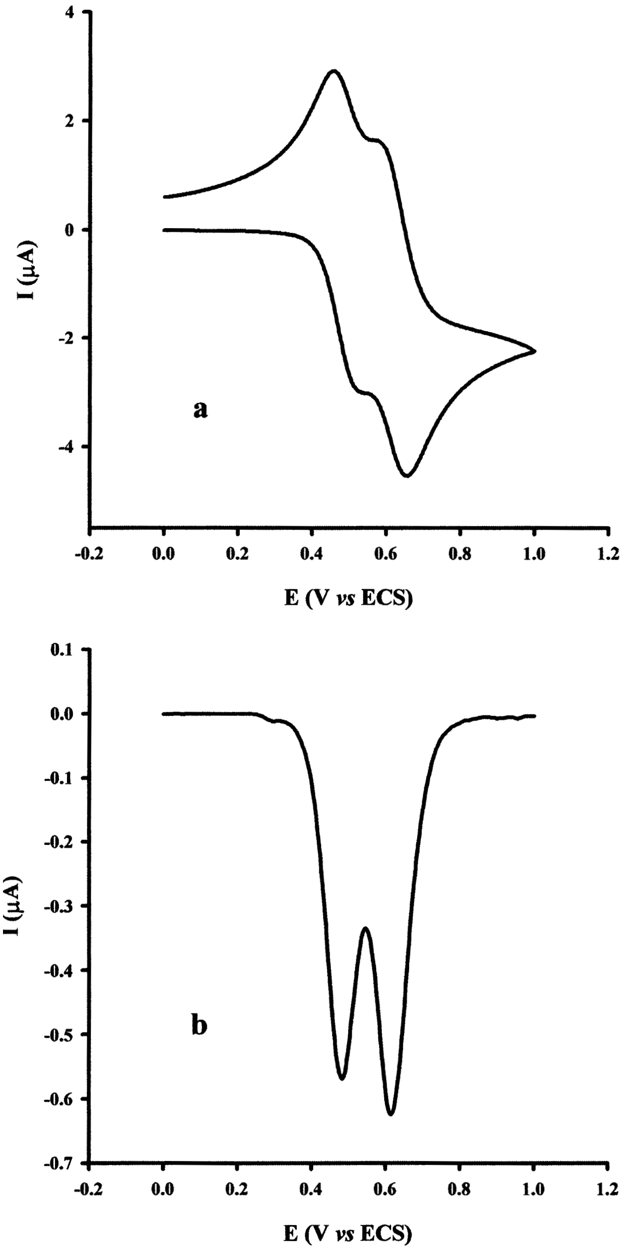


Figure 1. (a) Cyclic voltammogram of compound **4**. Conditions: 1 mM of **4** and 0.1 M of Bu_4NClO_4 in CH_3CN/CH_2Cl_2 (3:2) at a Pt-disk electrode, scan rate: 0.2 V s^{-1}. (b) Differential pulse voltammogram of compound **4**; pulse amplitude: 10 mV: pulse width: 50 ms; amplitude: 10 mV; scan rate: 0.004 V s^{-1}; other conditions as in (a).

In order to separate the combined effects of chemical inequivalence and electronic communication through the thiazole ring, the electrochemical behavior of simple ferrocenylthiazoles **5** and **6** was studied.

The CV voltammograms of compounds **5** and **6**, which display a single anodic process with features of chemical and electrochemical reversibility, showed that 5-ferrocenyl thiazole **5** is more easily oxidized than the isomeric 2-ferrocenylthiazole **6**, $E_{1/2} = 0.521$ versus 0.569 mV, which is in agreement with the results of OM calculations of varying degrees of sophistication of the thiazole ring, which mostly place a slightly higher electron density at position C(5) than C(2).[18]

These data reveal that the electrochemical response associated with the chemical inequivalence of the two ferrocenyl groups in compound **4** is estimated to be 48 mV. From these results, the thiazole ring in **4** is found to connect the two ferrocene subunits and facilitates metal–metal interaction: it displays its ability to function as electroconducting spacer for molecular wire application.

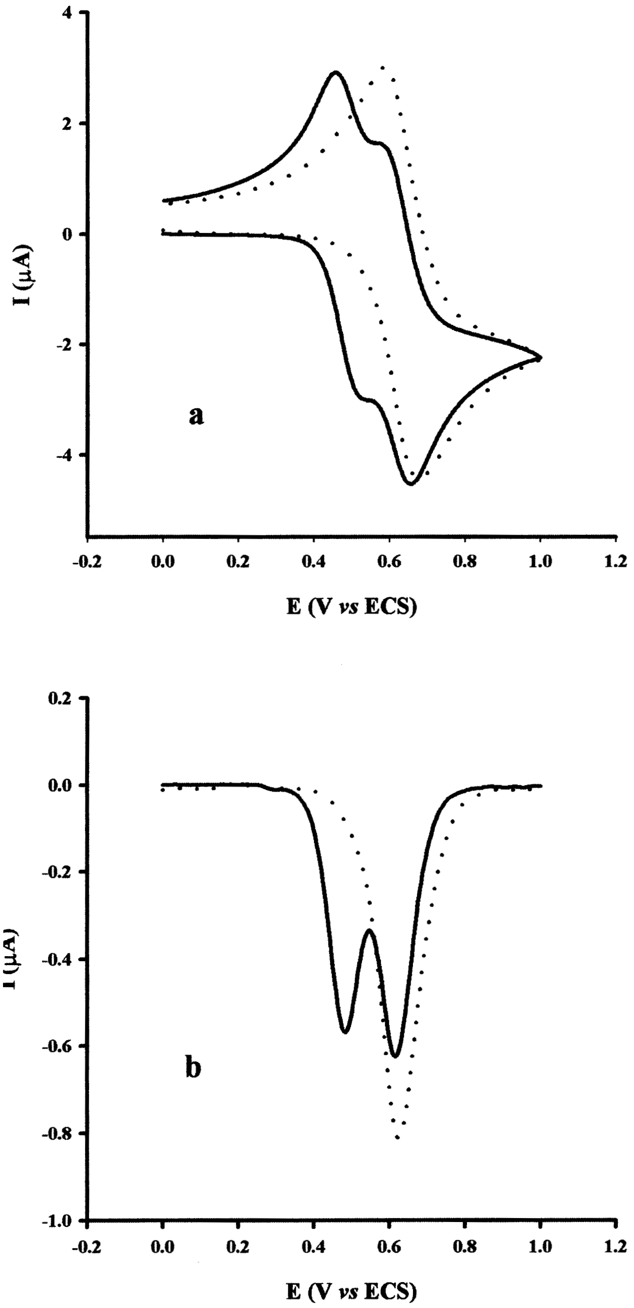


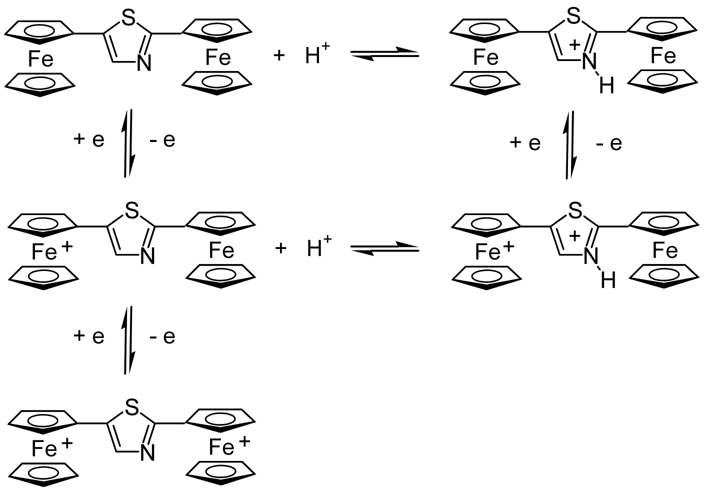
Figure 2. (a) Voltammetric response of compound **4** before (continuous line) and after protonation with 1 equiv. of HBF_4 (dotted line). (b) Differential pulse voltammogram before (continuous line) and after protonation with 1 equiv. of HBF_4 (dotted line). 1 mM in sample and other conditions as in Fig. 1.

One of the most interesting attributes of compound **4** is the presence of two ferrocene redox-active moieties in proximity of the proton-binding thiazole site. Binding and electron-transfer events can influence each other owing to the short distance between their respective sites. So, the electrochemical behavior of the ferrocenyl thiazoles **5** and **6** and bis(ferrocenyl)thiazole **4** was investigated in the presence of variable concentrations of HBF_4. Upon protonation by addition of stoichiometric quantities of HBF_4 in CH_3CN to a solution of compounds **5** and **6** in CH_3CN/CH_2Cl_2 (3:2), the redox potential of the ferrocene nucleus was shifted anodically. The protonation-induced redox shift was higher for compound **6** ($\Delta E_{1/2}=152$ mV) than for compound **5** ($\Delta E_{1/2}=72$ mV). These values are in good agreement with the linear relationship between the inverse iron–nitrogen separation and the shifts of the potentials found upon protonation of several kinds of aza-substituted ferrocenes.[19] The CV voltammogram of compound **4** upon protonation under the same conditions showed a clear evolution of the first wave from $Ep=0.488$–0.631 V, whereas there was no effect on the second. Remarkably, the current intensity of the cathodic peak of the second wave increases, while that of the first one decreases with a linear dependence on the equivalents of the added acid. In particular, the second wave reaches the maximun current intensity value at 1.0 equiv. of added acid, and at this point the first wave disappears[20] (Fig. 1b and Fig. 2b). The occurrence of this wave at the same potential for the unprotonated **4** suggests that after oxidation of the ferrocene unit linked at position **5**, the adduct is deprotonated and subsequent oxidation takes place on the partially oxidized $\mathbf{4}^{+}$. In other words, these results show that $\mathbf{4{\cdot}H}^{+}$ adduct undergoes reversible electrochemically induced deprotonation/reprotonation processes on a time scale faster than that of electrochemical experiment (Scheme 2).

In conclusion, the electrochemical study of the new bisferrocene ligand **4** reveals for the first time that the thiazole ring acts as a molecular wire connecting the two electron rich organoirons centres and a reversible switching can be induced by chemical input (protonation) and where the output is electrochemical (CV or DPV).[21] In addition, it should be noted that the two states of **4**, neutral and protonated, are characterized not only by different electrochemical properties but also by different colors. In principle, both outputs could be useful to process information at the molecular level.

Acknowledgements

We gratefully acknowledge the financial support of the DGI (Ministerio de Ciencia y Tecnologia, Spain) (Project No. BQU2001-0014).



Scheme 2. Schematic representation of the electrochemically induced deprotonation/reprotonation of **4·H**$^+$.

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12. Selected spectral data of **4**: IR (Nujol) 1594, 1546, 1496, 1456, 1412, 1261, 1107, 1065, 1031, 1002, 874, 823 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.12 (s, 5H), 4.15 (s, 5H), 4.32 (s, 2H), 4.41 (s, 2H), 456 (s, 2H), 4.86 (s, 2H), 7.51 (bs, 1H); ^{13}C NMR (CDCl$_3$) δ 67.38 (2×CH, Cp), 67.58 (2×CH, Cp), 68.99 (2×CH, Cp), 69.93 (2×CH, Cp), 70.00 (5×CH, Cp), 70.14 (5×CH, Cp), 76.64 (q, Cp), 78.58 (q, Cp), 136.61 (q, thiaz.), 137.20 (CH, thiaz.), 166.87 (q, thiaz.); EIMS *m*/*z* (rel. intensity): 453 (M$^+$, 100), 332 (14), 211 (34), 210 (34), 121 (49), 56 (35); anal. calcd for $C_{23}H_{19}Fe_2NS$: C, 60.96; H, 4.23; N, 3.09; found: C, 61.21; H, 4.39; N, 2.97%.
13. All processes observed were reversible, according to the criteria of (i) separation of 60 mV between cathodic and anodic peaks; (ii) close-to-unity ratio of the intensities of the cathodic and anodic currents, and (iii) constancy of the peak potential on changing sweep rate in the CVs. The same halfwave potential values have been obtained from the DPV peaks and from an average of the cathodic and anodic cyclic voltammetric peak.

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