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Sensors

An Electroactive Nitrogen-Rich [4.4]Ferrocenophane Displaying Redox-Switchable Behavior: Selective Sensing, Complexation, and Decomplexation of Mg^{2+} ions**

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Redox-responsive ligands that contain a ferrocene unit as the redox-active group have been one of the most extensively studied groups among the numerous examples of these ligands.[1] These ferrocene-containing ligands have been widely investigated because of their electrochemical response upon complexation of a suitable guest molecule or ion. A positive shift of the Fe^{II}/Fe^{III} redox couple is observed on coordination of a metal ion because the proximity of the metal alters the ability of the ferrocene framework to be oxidized.[1,2] A further exciting challenge that has been less explored is the design of redox-switchable ligands that are not only able to monitor binding (namely, a shift in the $E_{1/2}$ value upon metal complexation is observed) but are also able to act as an actuator through the progressive electrochemical release of the metal cation (that is, the binding constant upon electrochemical oxidation is decreased). In this context, some electroactive tetrathiafulvalene (TTF) derivatives that exist in three different redox stages (as a neutral species, radical cation, and dication) have been described as tunable materials that can bind a metal cation when neutral (TTF) and then expel it upon oxidation (TTF^{2+}).[3] This is an

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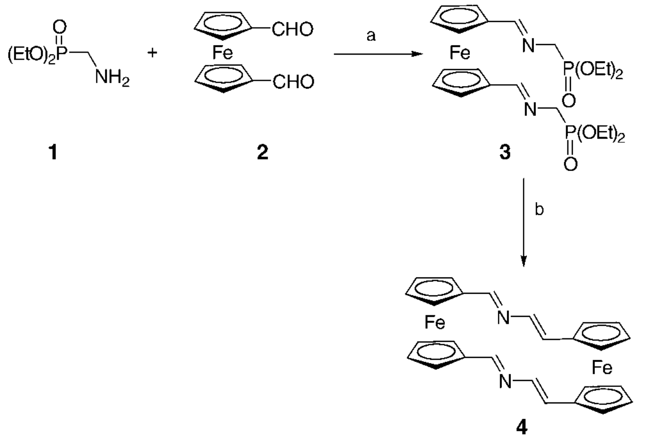
unfamiliar area in ferrocene-based ligands and it has been only described in a very few cases: first, in an early report about the abrupt decrease in the binding strength of Na$^+$ ions by electrochemical oxidation of a pentaoxa[13]ferrocenophane[4] and then, later on, in a few compounds that had only one ferrocenyl redox-active center.[5]

On the basis of this work, we designed a new highly preorganized molecular system that links two ferrocene subunits that have dissimilar electronic environments through a conjugated double bridge, which comprises a putative cation-binding site. This molecular system should show three different oxidation states with different binding abilities so that a metal cation can be bound in its neutral state and then released upon oxidation of the complexed species. Herein, we report the preparation of one such system, the redox-switchable, azaferrocenophane ligand **4**, that fulfils those electronic and structural characteristics. We also report the ability of **4** to selectively recognize Mg^{2+} ions and the unequivocal demonstration of electrochemical-mediated control of successive trapping and expulsion of Mg^{2+} ions. Furthermore, the ability of **4** to transport Mg^{2+} ions through a liquid membrane is described, in which the switchable activation/deactivation of the ligand is carried out electrochemically.

Compound **4** was prepared (Scheme 1) from the readily available diethyl aminomethylphosphonate (**1**),[6] which was condensed with 1,1′-diformylferrocene[7] (**2**) to give the corresponding *N*-substituted diethyl aminomethylphosphonate **3** in excellent yield (95%). Generation of the metalloenamine by reaction with *n*BuLi at −78 °C and subsequent reaction with one equivalent of 1,1′-diformylferrocene (**2**) provided 2,17-diaza[4,4]ferrocenophane **4** in 31% yield, which was recrystallized from THF and characterized by ^{1}H NMR and ^{13}C NMR spectroscopic, FAB mass-spectrometric, and elemental analysis.



Scheme 1. Synthesis of 2,17-diaza[4,4]ferrocenophane **4**: a) anhydrous Na_2SO_4/CH_2Cl_2, RT, 4 h; b) *n*BuLi/THF, −78 °C, and then **2**, 12 h, RT.

The X-ray crystal structure reveals that the two bridges of compound **4** are in the *E*,*E* form in the solid state (and also in solution as observed by ^{1}H NMR spectroscopy) and that they have an *s-trans* configuration (Figure 1).[8] Consequently, ferrocenophane **4** has two nitrogen atoms that are arranged in such a way that they can act as a chelating agent for a metal cation: the nitrogen atoms are eclipsed at a distance of 3.48 Å and have their nonbonding pair of electrons on the same side of the molecule.

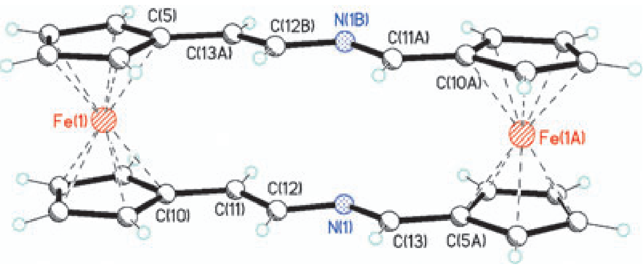


Figure 1. Crystal structure of the ferrocenophane **4**.

One of the most interesting attributes of ferrocenophane **4** is the presence of two differentiated redox-active ferrocene moieties close to the cation-binding bisaldimine site. The metal-recognition properties of **4** were evaluated by optical and electrochemical analysis. The cyclic voltammetric (CV) and Osteryoung square-wave voltammetric (OSWV) analyses of **4** (Figure 2) show two well-resolved quasi-reversible one-electron oxidations in a 1:1 ratio at formal potentials of +0.44 and +0.89 V versus decamethylferrocene (DMFc). The first reversible oxidation process arises from the oxidation of the ferrocene unit at the 4-position of the two bridges, while the second is associated with the oxidation of the ferrocene unit at

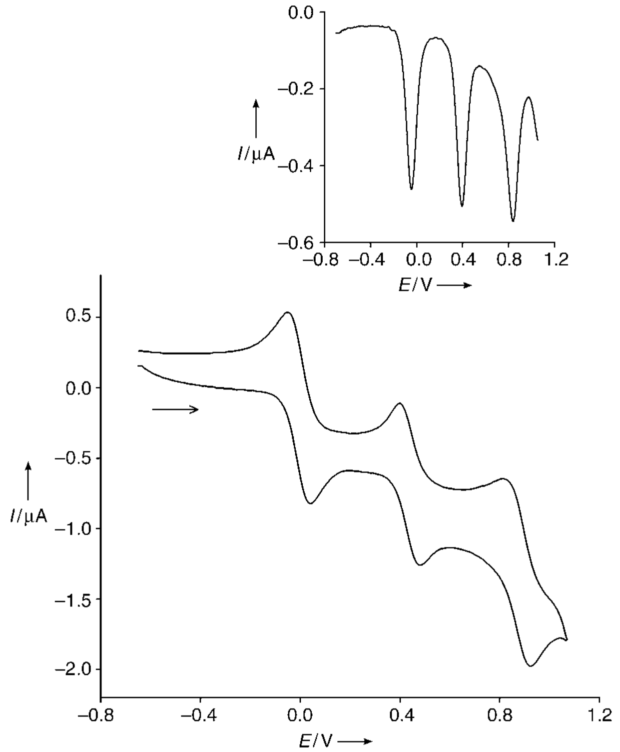


Figure 2. Cyclic voltammogram of **4** in CH_2Cl_2. Conditions: 1 mM of **4** and 0.1 M nBu_4NClO_4, a Pt-disk electrode, and a scan rate of 0.1 V s^{-1} in the presence of DMFc as the internal standard. Upper inset: square-wave voltammogram of compound **4** (1 mM) in $CH_2Cl_2/(nBu)_4N^+ClO_4^-$ recorded at 0.1 V s^{-1}.

the 1-position. Whereas, no perturbation of the voltammograms was observed upon addition of Ca^{2+}, Li^{+}, Na^{+}, and K^{+} ions, even in a large excess, a significant modification was observed for the first oxidation wave upon addition of Mg^{2+} ions (see the Supporting Information). In contrast, the second oxidation wave was apparently not perturbed on the addition of Mg^{2+} ions. This particular behavior is characteristic of a large equilibrium constant for the binding of Mg^{2+} ions by the neutral receptor.[9] The fact that the second oxidation process of complex $[Mg_2(\mathbf{4})]^{4+}$ practically occurs at the same potential as that observed for the free ligand **4** (that is, the $\mathbf{4}^{+}/\mathbf{4}^{2+}$ couple) suggests that the complex is disrupted after the first monoelectronic oxidation of complex $[Mg_2(\mathbf{4})]^{4+}$ and the second oxidation really takes place on the uncomplexed mono-oxidized species $\mathbf{4}^{+}$. Therefore, ligand **4** behaves as a switchable receptor that appears to be a very attractive carrier for the selective transport of Mg^{2+} ions.

The UV/Vis spectrum of the neutral ligand **4** is characterized by a very strong absorption band at 331 nm ($\varepsilon = 17200\,\text{M}^{-1}\,\text{cm}^{-1}$), which is assigned to a high-energy ligand-centred π–π^* electronic transition, and a lower-energy weaker band at 500 nm ($\varepsilon = 1600\,\text{M}^{-1}\,\text{cm}^{-1}$), which is attributed to a metal-to-ligand charge-transfer (CT) process (d–π^*).[10] Such spectral characteristics confer an orange color to the neutral ferrocenophane **4**. The mono-oxidized species $\mathbf{4}^{+}$ has a remarkable green–brown color and exhibits absorption bands at 355 nm ($\varepsilon = 17000\,\text{M}^{-1}\,\text{cm}^{-1}$) and 528 nm ($\varepsilon = 1900\,\text{M}^{-1}\,\text{cm}^{-1}$) along with a weak CT band at 1353 nm ($\varepsilon = 400\,\text{M}^{-1}\,\text{cm}^{-1}$). The presence of this weak CT band is a clear manifestation of the electronic coupling between the two redox-active ferrocene groups through the conjugated azadiene bridges. The dioxidized species $\mathbf{4}^{2+}$ exhibits a yellowish color and shows absorption bands at 334 nm ($\varepsilon = 17600\,\text{M}^{-1}\,\text{cm}^{-1}$) and 512 nm ($\varepsilon = 1400\,\text{M}^{-1}\,\text{cm}^{-1}$) along with one ligand-to-metal CT band at 1027 nm ($\varepsilon = 290\,\text{M}^{-1}\,\text{cm}^{-1}$).

The addition of increasing amounts of $Mg(ClO_4)_2$ to a solution of **4** in CH_2Cl_2 caused a progressive appearance of a band at 350 nm ($\varepsilon = 19900\,\text{M}^{-1}\,\text{cm}^{-1}$) and a new, more intense band located at $\lambda = 520$ nm ($\varepsilon = 3700\,\text{M}^{-1}\,\text{cm}^{-1}$) as well as the complete disappearance of the initial band at 500 nm. A well-defined isosbestic point at 339 nm indicates that a neat interconversion between the uncomplexed and complexed species occurs (Figure 3). The new band is red-shifted by 20 nm and is responsible for the change of color from orange (neutral ferrocenophane **4**) to deep purple (complexed ferrocenophane $[Mg_2(\mathbf{4})]^{4+}$). This color change can be used for a "naked-eye" detection of Mg^{2+} ions even in the presence of Ca^{2+} ions. The high-energy band of **4** is also red-shifted by 19 nm upon complexation of Mg^{2+} ions. It is important to note that the appearance of an Mg^{2+} ion induced sigmoidal curve in the titrations suggests that a 1:2 host-to-guest complex is formed via the corresponding 1:1 complex. In this case, the binding mode should be estimated on the basis of the following biphasic equilibria:

$$\mathbf{4} + Mg^{2+} \rightleftharpoons [Mg(\mathbf{4})]^{2+};\ K_{11} \qquad (1)$$

$$[Mg(\mathbf{4})]^{2+} + Mg^{2+} \rightleftharpoons [Mg_2(\mathbf{4})]^{4+};\ K_{12} \qquad (2)$$

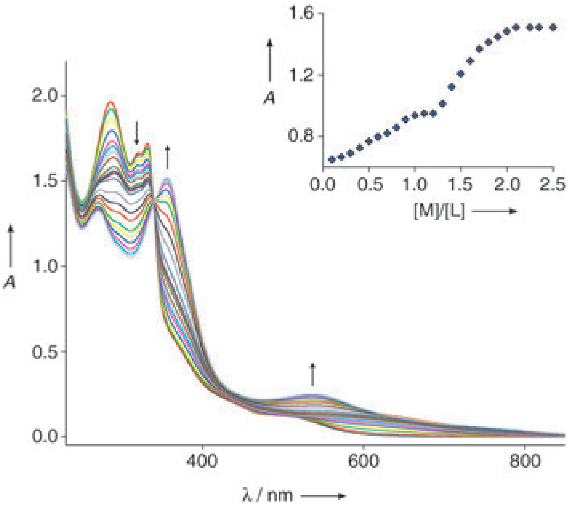


Figure 3. UV/Vis spectra obtained during the titration of **4** with $Mg(ClO_4)_2$ in CH_2Cl_2 ($c = 10^{-4}$ mol dm^{-3}). The initial spectrum is of the neutral species **4** and the final spectrum is of $[Mg_2(\mathbf{4})]^{4+}$. The arrows indicate the absorptions that increased (up) and decreased (down) during the titration experiments. Upper inset: change of absorbance at 537 nm upon addition of $Mg(ClO_4)_2$.

The two association constants, calculated by nonlinear least-squares analysis, were found to be $K_{11} = 9.8 \times 10^{5}$ and $K_{12} = 6.3 \times 10^{5}\,\text{M}^{-1}$, respectively.

A spectro–electrochemical study of the electrochemically induced, switchable chemosensor properties of complex $[Mg_2(\mathbf{4})]^{4+}$ was carried out. Thus, two equivalents of $Mg(ClO_4)_2$ were added to a solution of **4** in CH_2Cl_2 with $[n\text{Bu}_4\text{N}]PF_6$ (0.15 M) as the supporting electrolyte to obtain the complexed ferrocenophane $[Mg_2(\mathbf{4})]^{4+}$ species. The complex was oxidized at +1.0 V versus $Ag/AgNO_3$ until complete oxidation was reached and the color of the solution changed from deep purple to yellow (Figure 4). The optical spectrum of the resulting solution was the same as that obtained by the bielectronic oxidation of the free ligand **4** to $\mathbf{4}^{2+}$, thus suggesting that decomplexation of the two Mg^{2+} ions occurs during the electrochemical oxidation. The solution was completely reduced at +0.35 V versus $Ag/AgNO_3$, and the initial spectrum of the complex was fully recovered together with its purple color. Thus, the free dioxidized ligand $\mathbf{4}^{2+}$ is reduced to **4**, which has a large binding affinity for Mg^{2+} ions and nitites the formation of complex $[Mg_2(\mathbf{4})]^{4+}$. Oxidation of complex $[Mg_2(\mathbf{4})]^{4+}$ and its subsequent reduction were carried out over several cycles in a chronoamperometric experiment (Figure 4). The optical spectrum was recorded after each step and found to be fully recovered on completion of the step; thus, demonstrating the reversibility of the complexation/decomplexation process.

A preliminary study of the ability of the ferrocenophane **4** to transport Mg^{2+} ions across a CH_2Cl_2 liquid membrane was also undertaken. The CH_2Cl_2 membrane seperates two aqueous phases, the "source" and "receiving" phases, that are layered at the two branches of an H-type cell with a working electrode in one of the branches (see the Supporting Information). This study measures the time-dependence of the transportation of Mg^{2+} ions by the carrier **4** across the

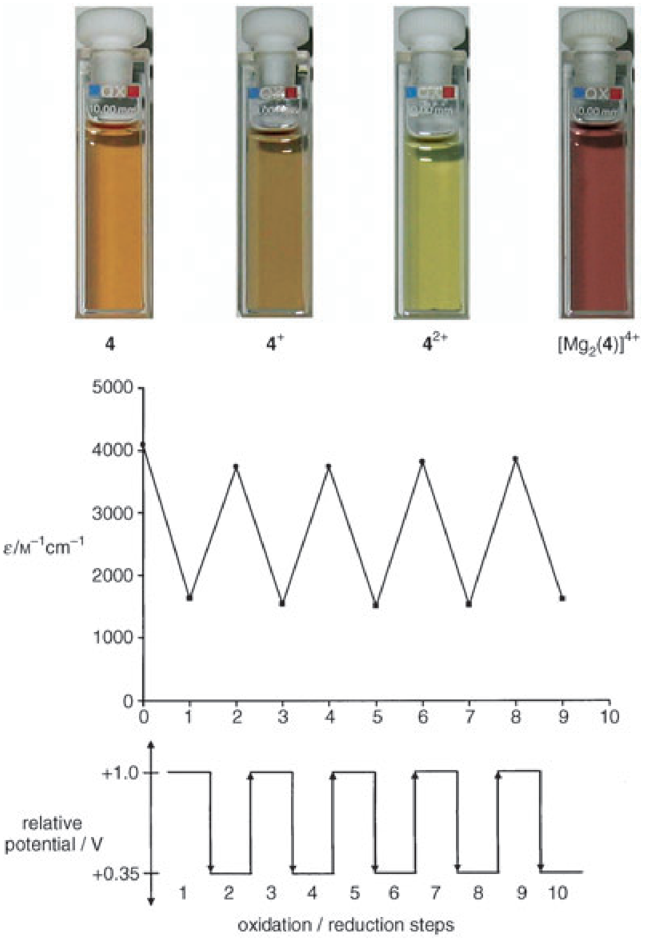


Figure 4. Top: colors shown by the studied species. Bottom: stepwise oxidation and reduction cycles carried out in CH_2Cl_2 by chronoamperometric analysis, which uses fixed potentials at +1.00 and +0.35 V and follows the changes observed by visible spectroscopy at 520 nm.

CH_2Cl_2 liquid membrane. The transport of Mg^{2+} ions was studied in the presence of **4** but in the absence of any applied potential at the working electrode of the H-type cell in a preliminary control experiment. Then, by oxidation of the carrier **4** a controlled potential electrolysis at the working electrode was performed while a constant potential of +0.95 V (versus $Ag/AgNO_3$) was maintained. The transport rate of the Mg^{2+} ions increased abruptly and the stationary state was achieved rapidly after starting the electrolysis (see the Supporting Information). These results are attributed to the decreased ion-binding ability of $\mathbf{4}^{2+}$ with respect to the neutral carrier **4**. A transport rate of Mg^{2+} ion of 3.2×10^{-6} mol h^{-1} was observed in the control experiment with no applied potential but it was increased to 2.1×10^{-5} mol h^{-1} when the controlled potential electrolysis was applied. Thus, electrochemical oxidation leads to a nearly sevenfold increase in the transport rate.

In conclusion, we have reported the first example of a redox-switchable receptor composed of two electronically coupled, electroactive ferrocene subunits that selectively recognizes Mg^{2+} ions through complexation. Transport and release of the Mg^{2+} ions by an external electrochemical stimulus is shown to be possible. The combination of two ferrocene subunits that have dissimilar electronic environments connected by two conjugated bridges with cation-binding sites is shown to be an attractive strategy for preparing new reversible redox-switchable ion carriers.

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[8] X-ray single-crystal diffraction data for **4** was collected on a Nonius KappaCCD diffractometer with an area detector and graphite-monochromized $Mo_{K\alpha}$ radiation ($\lambda = 0.71074$ Å). Crystal data: $C_{26}H_{22}Fe_2N_2$, $M_r = 474.16$, monoclinic, space group *C2/c* with $a = 20.5134(3)$, $b = 9.9522(2)$, $c = 9.9596(4)$ Å, $\alpha = 90.00$, $\beta = 106.986(2)$, $\gamma = 90.00$, $V = 1944.59(9)$ Å^3, $Z = 4$, T = 233 K, $\mu = 15.08\ \mathrm{cm}^{-}$. Least-squares refinement based on measured reflections with $I > 2\sigma(I)$ led to convergence with a final $R1 =$

0.0240, $wR2 = 0.0592$, and GOF = 1.063. CCDC-262815 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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