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Multi-step regulation of anion recognition by redox-active pseudocryptand

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Abstract—We synthesized an artificial redox-active Fe-pseudocryptand as an anion receptor to respond to electrochemical oxidation and reduction. Spectroscopic study and X-ray crystallography showed that the assembled urea chains and the isocyanuric platform generate an anion-binding cavity through favorable multiple hydrogen bonds and anion–π interactions. As the positive charge of the Fe center increases, the anion affinity is effectively increased due to an enhanced electrostatic interaction between the Fe atom and the anionic guest. This is the first efficient multi-step regulation of Cl^- selective anion recognition by the redox-active pseudocryptand.

Regulation of guest-binding by external stimulus leads to molecular functions with cooperative and allosteric effects.[1] In particular, multi-responses of host molecules are currently of great interest in terms of sophisticated functions such as feedback, cascade array of functions, and amplification of molecular information.[2] The stepwise control of a host's binding affinity is useful for an increased dynamic range of sensitivity in molecular sensing. Hence, one multi-responsive host may detect a guest at vastly different concentrations. This concentration flexibility avoids the laborious synthesis of hosts with different binding affinities to the guest.

Recently, anion recognition has received considerable attention due to the diverse behaviors of anions such as nucleophiles, bases, redox reagents, and environmental pollutants.[3] Electrochemical methods are useful and important for anion sensing, and for controlling the binding properties of anion receptors. Although there are many hosts with a single electrochemical response,[4] multi-step regulation of guest binding by redox processes has not been reported.[5] Pseudocryptand,[6] which bears a redox-active metal center, should be a well-organized framework for anion recognition in response to redox communication because the redox-active site, which provides an attracting electrostatic interaction with the anionic guests, can be placed near the guest-binding cavity. However, pseudocryptand for anion recognition has rarely been reported.[7] Thus, we designed an artificial redox-active pseudocryptand **1**·Fe as a multiple anion receptor to respond to oxidation and reduction. Metallohost **1**·Fe consists of an Fe^{II}-bipyridine unit as a stepwise redox-active center and three urea chains for electrostatic and hydrogen bonding sites for anions, respectively. The Fe^{II} center was expected to be oxidized to give the Fe^{III} species and reduced to form the $[\mathbf{1}\cdot Fe]^+$ and $[\mathbf{1}\cdot Fe]^0$ states because a tris(2,2′-bipyridine)-Fe^{II} complex exhibits a single one-electron reversible oxidation and several reversible one-electron reductions, which are assigned to a ligand-based reduction.[8] As the positive charge of the Fe center increases, the anion affinity should effectively increase due to an enhanced electrostatic interaction between the Fe atom and the anionic guest (Scheme 1). We also imagined that the assembled urea chains and the isocyanuric platform generate an anion-binding cavity through favorable multiple hydrogen bonds and anion–π interactions.[9,10] Herein we report the first efficient multi-step regulation of selective anion recognition by the redox-active pseudocryptand **1**·Fe.

Tribromide **2**[11] was treated with NaN_3 to quantitatively yield triazide **3** (Scheme 2). Host **1** was synthesized in

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Keywords: Anion recognition; Pseudocryptand; Receptor; Redox switch.

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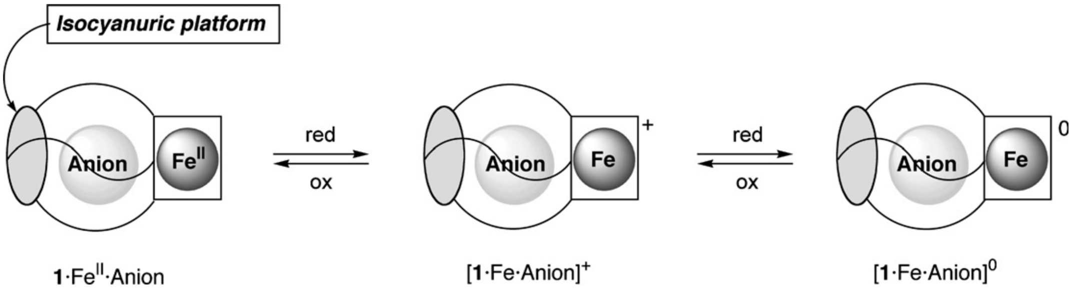
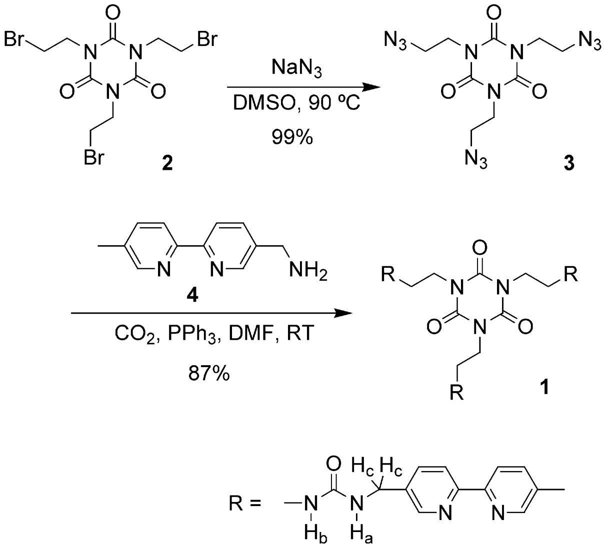


Scheme 1. Multi-step regulation of anion recognition using the electrochemical method.



Scheme 2. Synthesis of ligand **1**.

87% yield by the reaction of **3**, **4**,[12] PPh_3, and CO_2 in DMF. Treatment of **1** with $Fe(BF_4)_2$ (1 equiv) afforded pseudocryptand **1**·Fe in 89% yield. The structures of **1** and **1**·Fe were characterized by ^1H NMR, ^{13}C NMR, UV–vis spectrometry, IR, elemental analysis, and ESI MS (*m*/*z* 494.71 for $[\mathbf{1}\cdot\mathrm{Fe}]^{2+}$). Complexation of **1** with Fe^{II} proceeded smoothly in DMF–MeOH (1:1) to give a red solution. Upon the addition of Fe^{II} into the solution of **1**, the MLCT absorption characteristic of an Fe^{II}-bipyridine octahedral complex appeared at 519 nm. UV–vis titration by monitoring the MLCT absorption suggested quantitative binding of **1** to Fe^{II}. X-ray crystallographic analysis revealed the characteristic bent-helical conformation of **1**·Fe where three chains were assembled due not only to the metal complexation, but also to the linear and bent hydrogen bonds of the urea moieties (Fig. 1a).[13,14]

^1H NMR spectroscopy indicated a strong affinity of **1**·Fe to Cl^- in DMF-d_7 (Fig. 2). Compared to that of free **1**·Fe, a new resonance of urea protons (NH_b), which are close to the isocyanuric core, was observed in the lower field, indicating that complexation with Cl^- is slow on the NMR timescale. In contrast, the other urea protons (NH_a) of the Cl^- complex appeared in a higher field. Consequently, the hydrogen bonds are suggested to be strengthened and weakened in solution for NH_b and NH_a, respectively. X-ray analysis for **1**·Fe and **1**·Fe·Cl strongly supported that formation and dissociation of the hydrogen bonds of the NH protons causes these chemical shift changes. In the solid state the NH_a protons of **1**·Fe·Cl are oriented outward of the pseudocryptand cavity (Fig. 1b). Thus, upon the complexation with Cl^- all the hydrogen bonds seen in the NH_a of **1**·Fe are broken. Instead, all the NH_b protons upon Cl^- binding make a hydrogen bond with the Cl^-, because the distances between the N(H_b) and Cl are in the range of 3.20–3.26 Å, which are indicative of hydrogen bonding between the H_b and Cl. X-ray structure of **1**·Fe·Cl also showed that significant C–H ··· Cl contacts between Cl and the methylene protons (H_c) adjacent to the $Fe(bipyridine)_3$ moiety assist the Cl^- binding. The ^1H NMR spectrum of **1**·Fe·Cl clearly showed that the attractive C–H ··· Cl contacts in solution exist because a signal for one of the two picolyl protons (H_c) in the chain of the pseudocryptand shifted downfield (ca. 0.5 ppm). The isocyanuric platform should contribute to a favorable interaction with Cl^- because the distance between Cl^- and the isocyanuric ring centroid is ca. 3.2 Å in the crystal.[10] Br^- had a smaller effect on the ^1H NMR than Cl^-. However, I^- and NO_3^- did not change the ^1H NMR. This anion effect on the spectra strongly suggests a high Cl^- selectivity of **1**·Fe.

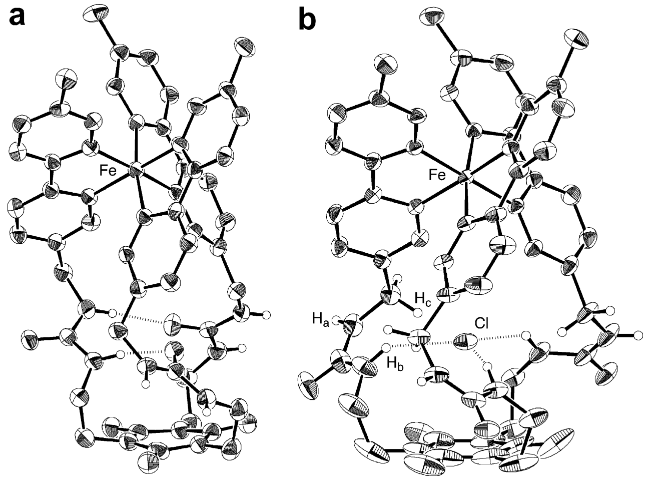


Figure 1. Crystal structures of (a) **1**·Fe and (b) **1**·Fe·Cl. Thermal ellipsoids are plotted at 30% probability level.

Cyclic voltammetry indicated that the metallohost **1**·Fe (1.0 mM in DMF) has a practically reversible redox

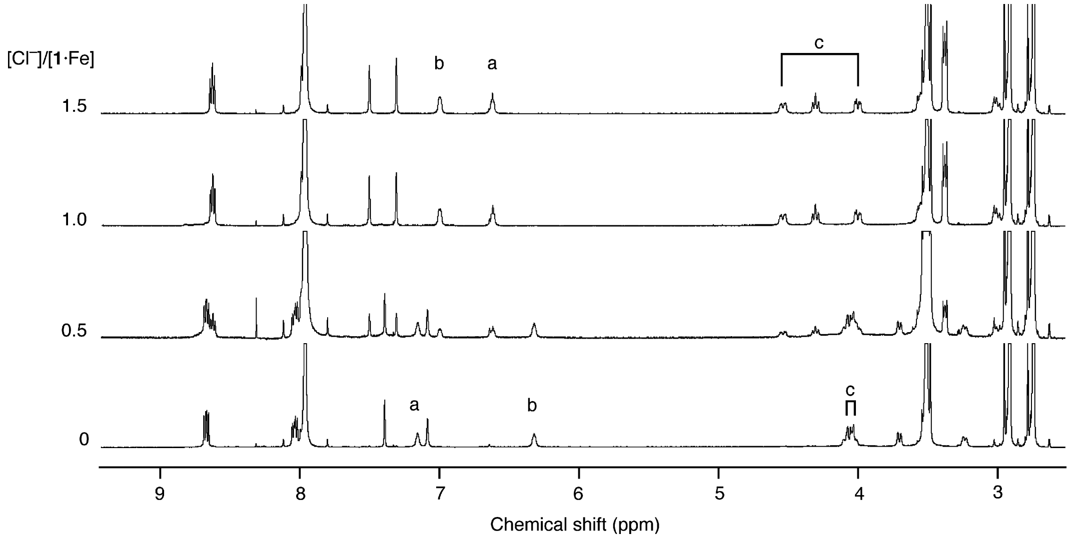
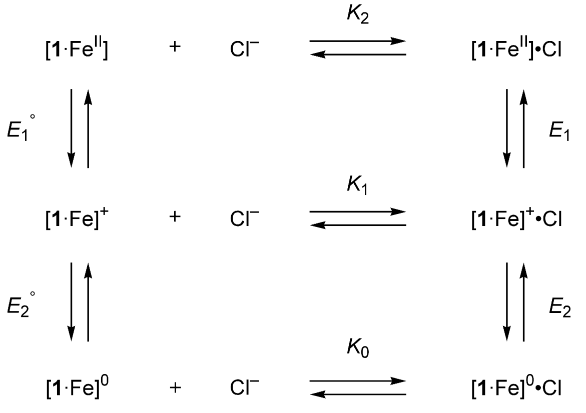


Figure 2. ^1H NMR (600 MHz, DMF-d_7) spectral changes of **1**·Fe (1.0 mM) upon adding n-Bu_4NCl.

process among **1**·Fe^{III}, **1**·Fe^{II}, [**1**·$Fe]^+$, and [**1**·$Fe]^0$. The cathodic shifts of the redox potentials for the above metal complexes are expected upon complexation of **1**·Fe with Cl^- due to the stabilization of the corresponding oxidized states. Indeed, more negative potentials were observed for **1**·Fe^{II}/[**1**·$Fe]^+$ and [**1**·$Fe]^+$/[**1**·$Fe]^0$ in the presence of Cl^- using differential pulse voltammetry in DMF. The negative shifts again confirm the stabilization of the more positive oxidation states of the complexes due to the Cl^- binding. In contrast, Br^- caused a much smaller shift, while I^- and NO_3^- did not cause a shift.[15] The binding affinities of **1**·Fe to anions were determined by analyzing the shifts in the presence of the guests (Table 1). The electrochemical measurements also confirmed a high Cl^- selectivity. The association constants, $\log K_2$, $\log K_1$, and $\log K_0$ (K_2, K_1, K_0 in M^{-1}, Scheme 3), for **1**·Fe^{II}, [**1**·$Fe]^+$, and [**1**·$Fe]^0$ to Cl^- are 3.87, 3.00, and 2.03, respectively, although that for **1**·Fe^{III} was not estimated due to the overlapping potentials of Fe^{II}/Fe^{III} and Cl^-/Cl^0. This significant enhancement by the factor of 10 and 70 is clearly reflected by the positive charge of the Fe complex unit. As suggested by the NMR titration, the binding affinity to Br^- is much weaker, but the binding affinity is also well regulated by the positive charge of the metallo moiety. This is the first example of a multi-step regulation for anion recognition by redox reactions.



Scheme 3. Recognition of Cl^- by [**1**·Fe] in varying oxidation states.

Table 1. Association constants[a]

Anion	$\log K_2$ (**1**·Fe^{II})	$\log K_1$ ([**1**·$Fe]^+$)	$\log K_0$ ([**1**·$Fe]^0$)
Cl^-	3.87 ± 0.05	3.00 ± 0.07	2.03 ± 0.04
Br^-	2.38 ± 0.09	1.82 ± 0.15	—

[a] [**1**·Fe] = 0.5 mM, in DMF, Pt electrode, [n-Bu_4NClO_4] = 0.1 M, 293 K.

We achieved the synthesis of the first switchable pseudocryptand as a Cl^- selective anion receptor and the multiple regulation of the anion recognition by an electrochemical redox process. This type of two-step controllable systems should help develop novel approaches to fine molecular devices such as a ternary logic gate. We are currently exploring multi-site recognition of more complicated guests with an anionic moiety by utilizing the NH groups located outside the cavity.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.12.143.

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