

## Notes

## A Ferrocene Derivative Redox Sensor for Mercuric Ion: Synthesis and Electrochemical Study

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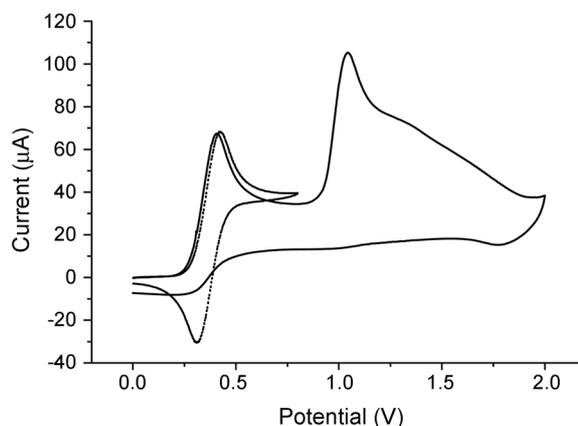
**Key Words :** Ferrocene, Mercuric ion, Electrochemistry, Redox sensor

The sensitive detection of mercuric ion is currently a task of prime importance for environmental or biological concerns. To develop sensitive mercuric ion sensors, various receptors consisting of a mercuric ion recognition unit and a probe exhibiting physical responses upon the coordination of mercuric ion have been reported.<sup>1</sup> Among them, ferrocene derivatives are often applied to redox sensors due to the unique electrochemical property.<sup>2</sup> In the presence of mercuric ions, the ion-recognition event induces the significant electrochemical changes at the redox active ferrocenyl moiety. In addition, the ease of functionalization of ferrocene leads to the synthesis of assorted ferrocene derivatives possessing the metal ion binding unit.<sup>2</sup> Recently, our research has focused on the development of new ferrocene complexes as redox sensors for the mercuric ion detection. In this account, we report the synthesis and electrochemical analysis of 2-(ethylthiomethyl)-N-ferrocenylmethyl aniline in the presence of various metal ions, illustrating this ferrocene complex as a sensitive and selective redox sensor for the detection of mercuric ion.

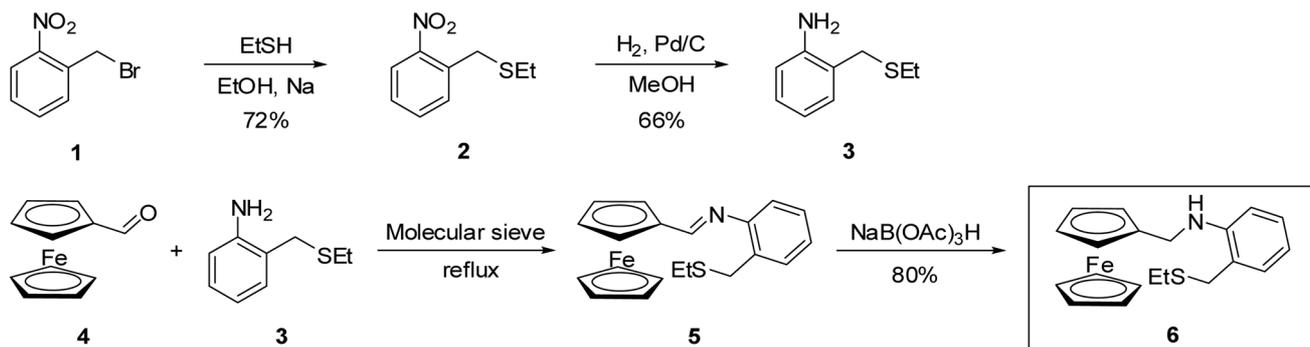
As shown in Scheme 1, 1-(bromomethyl)-2-nitrobenzene **1** was treated with ethanethiol with sodium metal to afford ethyl(2-nitrobenzyl)sulfide **2** in 72% yield. Subsequent reduction of compound **2** provided 2-(ethylthiomethyl)-aniline **3** which reacted with ferrocene carboxaldehyde **4**, forming imine **5**. Due to the instability of compound **5** on the silica gel, compound **5** was not isolated and subject to the reduction conditions using NaB(OAc)<sub>3</sub>H to give 2-(ethyl-

thiomethyl)-N-ferrocenylmethyl aniline **6** in 80% yield.

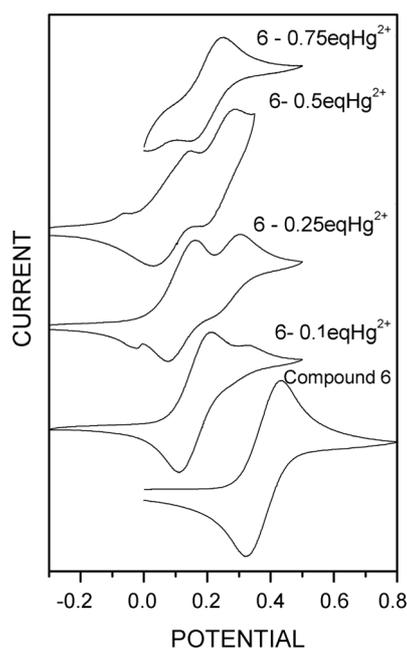
With compound **6** in hand, electrochemical properties of compound **6** were evaluated in the absence of any metal ion *via* cyclic voltammetry (CV). In the range of 0.0 to 2.0 V, two oxidation peaks appear at 0.41 V and 1.04 V during the anodic scan, and no reduction peak was observed in the reverse scan, shown in Figure 1. When the anodic scan was reversed at 0.80 V subsequent to the 1<sup>st</sup> oxidation at 0.41 V, the reversible reduction peak at 0.30 V was detected, with the peak separation of *ca.* 0.11 V. Accordingly, the first oxidation peak at 0.41 V was speculated to be the oxidation of the ferrocene entity of compound **6**. The second oxidation



**Figure 1.** Cyclic voltammograms of compound **6** obtained in 0.1 M LiClO<sub>4</sub> acetonitrile solution at a scan rate of 100 mV/s.



**Scheme 1.** Synthesis of 2-(ethylthiomethyl)-N-ferrocenylmethyl aniline **6**.

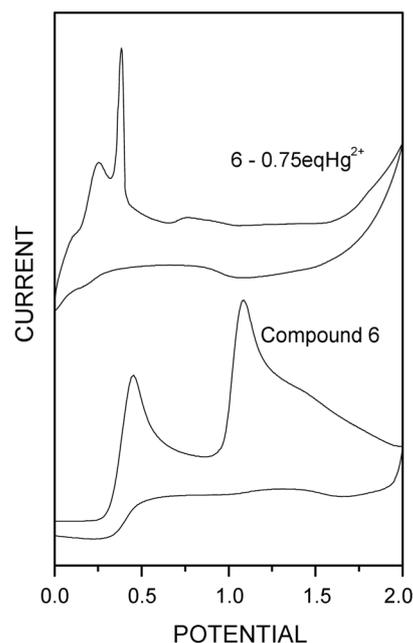


**Figure 2.** Cyclic voltammograms of the Fc/Fc<sup>+</sup> redox couple in compound **6** with 0, 0.1, 0.25, 0.5, 0.75 eq of Hg<sup>2+</sup> added in 0.1 M LiClO<sub>4</sub> acetonitrile solution at a scan rate of 100 mV/s in the potential range of 0.0 V and 0.8 V.

peak at 1.04 V was attributed to the oxidation of amine functional group. In light of previous reports regarding the electrochemical oxidation followed by irreversible chemical reaction of the amine group affording aldehydes or nitrile,<sup>3,4</sup> the irreversible second anodic wave was attributed to the electrochemical reaction and subsequent irreversible chemical reaction of amine of compound **6**.

Subsequent to the electrochemical study of metal free compound **6**, the CVs of compound **6** in the solution containing different concentrations of mercuric ion were obtained (Figure 2). Upon increasing the concentrations of mercuric ion, the anodic peak of Fc/Fc<sup>+</sup> redox couple of compound **6** at 0.41 V was severely shifted toward cathodic direction to 0.19 V (cathodic shift  $\Delta E = -0.22$  V), which was ascribed to the weak interaction of sulfur in compound **6** with mercuric ion. The cathodic shift of the redox couple of ferrocene derivatives induced by the weak interaction of metal ions was previously reported by Guo and co-workers.<sup>5</sup>

In addition to the cathodically shifted peak of the Fc/Fc<sup>+</sup> redox couple of compound **6**, a new Fc/Fc<sup>+</sup> redox couple peak at 0.33 V stemming from the binding of compound **6** and mercuric ion appeared as shown in Figure 2. Due to the cationic nature of compound **6** through the binding with mercuric ion, the oxidation potential wave of mercuric ion bound compound **6** was anodically shifted to 0.33 V from the oxidation potential of 0.19 V of the metal free compound **6**. The newly formed redox waves exhibited *ca.* 0.096 V separation between the anodic and cathodic peaks, showing quasi-reversibility. Noticeably, as the concentration of mercuric ions was increased, the current of the new potential wave was continuously growing. On the other hand, the

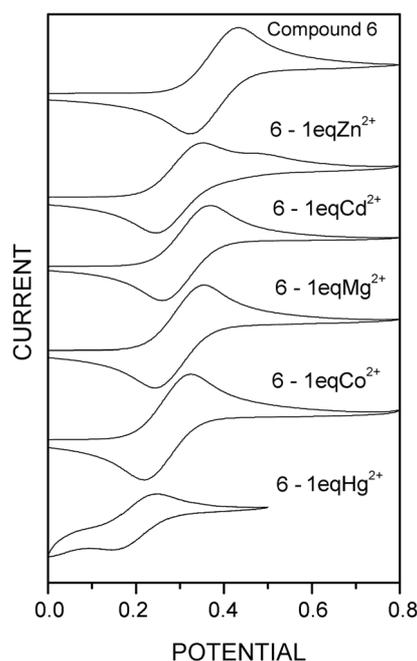


**Figure 3.** Cyclic voltammograms obtained from compound **6** with 0 and 0.75 eq of Hg<sup>2+</sup> added in 0.1 M LiClO<sub>4</sub> acetonitrile solution at a scan rate of 100 mV/s (0.0-2.0 V).

current of the potential wave of metal free compound **6** was gradually reduced. The equilibrium constant ratio indicating the binding affinity difference of compound **6** and 1 electron oxidized compound **6** toward mercuric ion was evaluated, using the well-known equation correlating the electrochemical potential with the thermodynamic value (eq. 1).<sup>6</sup> Inserting the half wave potential difference value,  $\Delta E$  (0.14 V,  $E_{1/2}^{\text{complex}} - E_{1/2}^{\text{free ionophore}}$ ) calculated from the CVs of compound **6** with/without mercuric ion, the ratio of the complex formation constants  $K_{\text{neutral}}/K_{\text{ox}}$  was calculated to be 233. Resulting equilibrium constant ratio means that the unoxidized compound **6** is 233 times stronger binding to mercuric ion than 1 electron oxidized compound **6**.

$$E_{1/2}^{\text{complex}} - E_{1/2}^{\text{free ionophore}} = (RT/nF)\ln(K_{\text{neutral}}/K_{\text{ox}}) \quad (1)$$

Subsequent to the electrochemical study in the range of 0.0 V to 0.8 V, the anodic scan was expanded to 2.0 V to investigate the changes of the second anodic peak at 1.04 V corresponding to the amine in compound **6** in the presence of high concentration of mercuric ion. As illustrated in Figure 3, the second oxidation peak of compound **6** disappeared upon the addition of mercuric ions. Accordingly, the tight binding of mercuric ion to compound **6** is speculated to occur at the amine unit. Sulfur together with nitrogen in compound **6** is also assumed to cooperatively bind mercuric ion. In addition to the significant decrease in the oxidation current of the second anodic wave of compound **6**, a sharp anodic peak was observed at 0.38 V upon the addition of 0.75 equivalents of mercuric ion as shown in Figure 3. With high concentrations of mercuric ion added, unbound mercuric ion is assumed to be reduced at the surface of electrode in the negative potential region, where the reduced mercury



**Figure 4.** Cyclic voltammograms of compound **6** with 1 eq  $\text{Hg}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Mg}^{2+}$  at a scan rate of 100 mV/s.

goes through the anodic stripping during the anodic scan. Therefore, when higher than 0.75 equivalents of mercuric ions were added, potential waves of compound **6** were scanned in the limited potential range to prevent the reduction and oxidation of mercuric ion at the electrode surface, as shown in Figure 2. Similar to the anodic stripping peak of mercury observed in the cyclic voltammograms of compound **6** and mercuric ion, the anodic stripping of metallic silver has been reported in the electrochemical studies of the solution containing  $\text{Ag}^+$ .<sup>7</sup>

To examine the selectivity of compound **6** to mercuric ion, cyclic voltammograms of compound **6** in the presence of 1 equivalent of  $\text{Hg}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Mg}^{2+}$  with respect to compound **6** were obtained in  $\text{CH}_3\text{CN}$  containing  $\text{LiClO}_4$  electrolytes. The potential range exhibiting reversible  $\text{Fc}/\text{Fc}^+$  redox potential waves was chosen to evaluate compound **6** as a redox sensor. As illustrated in Figure 4, in the presence of mercuric ion, the  $\text{Fc}/\text{Fc}^+$  redox potential wave of compound **6** was dramatically changed compared to that with  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Mg}^{2+}$ . Upon the addition of  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , or  $\text{Mg}^{2+}$  to compound **6**, the  $\text{Fc}/\text{Fc}^+$  redox couple was negatively shifted without producing any new redox potential waves, indicating weak interaction of compound **6** with these metal ions. Overall, the electrochemical studies of compound **6** with different metal ions demonstrated the excellent selectivity of compound **6** toward  $\text{Hg}^{2+}$  over  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Mg}^{2+}$ .

The combination of electrochemically active ferrocene carboxaldehyde and 2-(ethylthiomethyl)aniline as a metal ion recognition site has formed 2-(ethylthiomethyl)-*N*-ferrocenylmethyl aniline **6**, a sensitive and selective electrochemical sensor for  $\text{Hg}^{2+}$ . Both nitrogen and sulfur of compound **6** participate in the mercuric ion binding coopera-

tively. The coordination of mercuric ion affects the electronic environment of the ferrocene entity proximal to nitrogen and sulfur, forming a new anodically shifted  $\text{Fc}/\text{Fc}^+$  redox couple. The potential difference between metal free compound **6** and  $\text{Hg}^{2+}$  bound compound **6** was used to understand the quantitative binding ability of compound **6** toward  $\text{Hg}^{2+}$ . In contrast to  $\text{Hg}^{2+}$ , the  $\text{Fc}/\text{Fc}^+$  redox couple of compound **6** with  $\text{Zn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ , or  $\text{Mg}^{2+}$  did not show noticeable changes of potential waves, illustrating the selectivity of compound **6** to  $\text{Hg}^{2+}$ .

## Experimental

Anhydrous solvents were transferred by an oven dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Dichloromethane and 1,2-dichloroethane were distilled from calcium hydride. THF was distilled from benzophenone ketyl. Acetonitrile was purchased from Fluka and distilled from calcium hydride. Ethanol and methanol were distilled from sodium metal. Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) spectra were recorded with a Varian Mercury plus (400 MHz) spectrometer. Chemical shifts are reported in delta ( $\delta$ ) units, part per million (ppm) downfield from trimethylsilane. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance ( $^{13}\text{C}$  NMR) spectra were recorded with a Varian Mercury plus (100 MHz) spectrometer. Chemical shifts are reported in delta ( $\delta$ ) units, part per million (ppm) relative to the center of the triplet at 77.00 ppm for deuteriochloroform. Elemental analysis was carried out at the Inter-University Center Natural Science Facilities, Seoul National University. Electrochemical data were recorded on a potentiostat/galvanostat (PARC (Princeton Applied Research), model 263) with Electrochemistry Power Suite Module and Cyclic voltammetry software. The three-electrode cell consisting of Pt disc (the working electrode), Ag wire (the pseudo reference electrode), and Pt wire (the auxiliary electrode) was employed. Compound **6** (0.01 M) were dissolved in  $\text{CH}_3\text{CN}$  solution containing 0.1 M  $\text{LiClO}_4$ . The resulting solutions were subject to cyclic voltammetry experiments at a scan rate of 100 mV/s. Compound **2**<sup>8</sup> and **3**<sup>9</sup> exhibited spectral properties consistent with previous literature reports.

**2-(Ethylthiomethyl)-*N*-ferrocenylmethyl aniline 6:** 2-(ethylthiomethyl)aniline **3** (67 mg, 0.4 mmol) was dissolved in the dichloromethane solution (2 mL) of ferrocene carboxaldehyde **1** (95 mg, 0.48 mmol) and molecular sieve. The mixture was refluxed for 12 hrs under the nitrogen atmosphere. After being cooled to room temperature, the solution was filtered through Celite and the filtered solution was evaporated. This mixture was dissolved in 1,2-dichloroethane (5 mL), and subsequently  $\text{NaB}(\text{OAc})_3\text{H}$  (101 mg, 0.48 mmol) was added. The reaction mixture was allowed to stir overnight at room temperature. The solution was diluted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 10$  mL), extracted with saturated  $\text{NaHCO}_3$  (15 mL), and washed with water ( $2 \times 10$  mL). The organic layer dried over  $\text{MgSO}_4$  and the solvent was evaporated. The purification was conducted *via* flash column chromato-

graphy (SiO<sub>2</sub>, 20:1, hexanes:ethyl acetate) to provide **6** (116 mg, 0.32 mmol) as a yellow oil in 80% yield. TLC R<sub>f</sub> = 0.74 (3:1, hexanes:ethyl acetate). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ = 7.19 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 6.0 Hz, 1H), 6.70 (m, 2H), 4.74 (br, 1H), 4.28 (s, 2H), 4.22 (s, 5H), 4.15 (s, 2H), 4.01 (s, 2H), 3.77 (s, 2H), 2.45 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 3.2 Hz, 3H) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 Hz) δ = 146.5, 130.6, 128.7, 121.3, 116.9, 111.2, 86.5, 68.8, 67.9, 67.6, 43.2, 33.8, 25.4, 14.8. FABMS 365.0900 calcd for C<sub>20</sub>H<sub>23</sub>FeNS; Found, 365.0900. FTIR (KCl) 3350, 3091, 2964, 2853, 1604, 1509, 1461, 1261, 1311, 1105, 820, 745 cm<sup>-1</sup>.

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