

# Electrochemical Reduction of Cobaltocenium in the Presence of $\beta$ -Cyclodextrin

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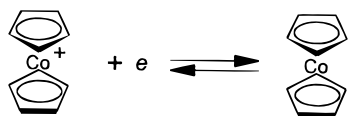
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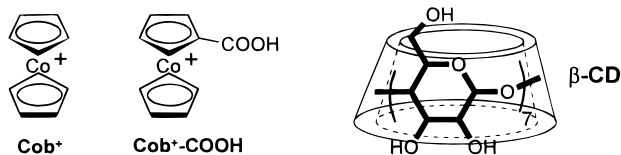
The cathodic voltammetric behavior of cobaltocenium ( $\text{Cob}^+$ ) and carboxycobaltocenium ( $\text{Cob}^+-\text{COO}^-$ ) in aqueous solution was investigated in the presence of  $\beta$ -cyclodextrin ( $\beta$ -CD). The one-electron reduction of  $\text{Cob}^+$  leads to the deposition on the electrode surface of the reduced, neutral form, cobaltocene (Cob). In contrast, the reduction of  $\text{Cob}^+-\text{COO}^-$  does not produce any deposits because  $\text{Cob}-\text{COO}^-$  is water soluble. Upon addition of the CD host, the voltammetric waves of both compounds shift to less negative values revealing the formation of inclusion complexes between the reduced forms and the  $\beta$ -CD host. In the case of  $\text{Cob}^+$ , the formation of the  $\beta$ -CD·Cob complex results in the disappearance of the distortions in the current–potential curves which were associated with the deposition of free Cob. Digital simulations of the voltammetric responses in the presence of  $\beta$ -CD led to the determination of the corresponding equilibrium association constants. The values obtained were 2000 and 1800 L/mol for the complexation of Cob and  $\text{Cob}-\text{COO}^-$ , respectively, by  $\beta$ -CD. The cobaltocenium (oxidized) forms were not appreciably bound by the  $\beta$ -CD host.

## Introduction

Bis(cyclopentadienyl)cobalt(III) or cobaltocenium is a highly stable, 18-electron complex which is isoelectronic with its iron(II) analog, ferrocene. While ferrocene is neutral and can be easily oxidized to an iron(III) cationic species, cobaltocenium is positively charged and undergoes a reversible one-electron reduction to yield the uncharged, 19-electron cobaltocene:<sup>1</sup>



Ferrocene is an excellent substrate for inclusion complexation by cyclodextrin (CD) hosts.<sup>2–9</sup> Among the three unmodified CDs,  $\beta$ -CD forms the most stable inclusion complex with



ferrocene and its derivatives, with reported binding constants in the  $(1-5) \times 10^3 \text{ M}^{-1}$  range. However, ferrocene oxidation

leads to a substantial decrease in complex stability as the positively charged ferrocenium species is not bound effectively inside the nonpolar cavity of  $\beta$ -CD.<sup>7,8</sup> In principle, cobaltocenium may afford exactly the reverse situation. Its cationic nature probably makes it a poor substrate for inclusion complexation by  $\beta$ -CD, but its electroreduced, neutral form is anticipated to bind strongly to this CD host. In this work, we report detailed electrochemical studies concerning the effects of  $\beta$ -CD on the electrochemical reduction of cobaltocenium and carboxycobaltocenium. These two compounds, along with the  $\beta$ -CD receptor, afford interesting examples of the coupling of electron transfer reactions with host–guest complexation.

## Experimental Section

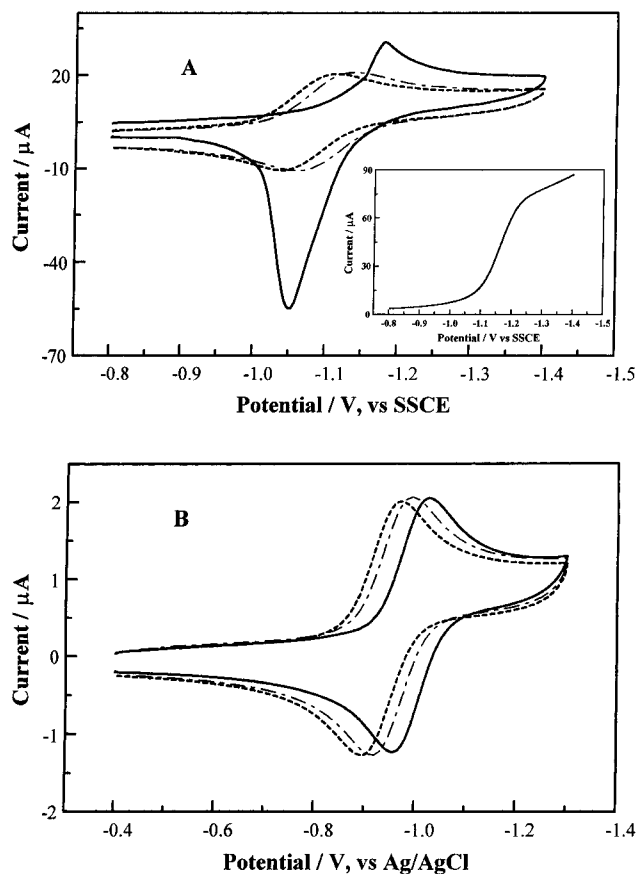
**Materials.** Cobaltocenium hexafluorophosphate ( $\text{Cob}^+\text{PF}_6^-$ ) was purchased from Aldrich and used without further purification. The hexafluorophosphate salt of carboxycobaltocenium ( $(\text{Cob}^+-\text{COOH})\text{PF}_6^-$ ) was prepared as reported by Sheats and Rausch.<sup>10</sup> The material obtained from this procedure contained about 25% 1,1'-dicarboxycobaltocenium hexafluorophosphate. Pure  $(\text{Cob}^+-\text{COOH})\text{PF}_6^-$  was isolated after repeated washings with hot acetone (the dicarboxy derivative is insoluble in acetone) and recrystallization from acetone–hexane.  $\beta$ -CD was a gift from Cerestar and used as received. The hydrated molecular weight of  $\beta$ -CD (1297.1 g/mol) was used throughout this work. All other chemicals were of the best quality commercially available. Deionized water was further purified by passage through a pressurized, four-cartridge Barnstead Nanopure system to a final resistivity of  $18 \text{ M}\Omega\cdot\text{cm}$  or higher.

**Equipment.** <sup>1</sup>H NMR spectra were recorded in a Varian VXR-400 NMR spectrometer operating at 400 MHz. All the electrochemical experiments were performed with a BAS 100 B/W workstation (Bioanalytical Systems, West Lafayette, IN). A glassy carbon disk working electrode ( $0.08 \text{ cm}^2$ ), Pt counter electrode, and sodium chloride saturated calomel (SSCE) reference electrode were fitted to a 10-mL, single-compartment electrochemical cell. A smaller glassy carbon electrode ( $0.008 \text{ cm}^2$ ) and/or Ag/AgCl reference electrode were utilized in some voltammetric experiments. Digital simulations of the experi-

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**Figure 1.** (A) Cyclic voltammograms (scan rate: 0.1 V/s) of 1.0 mM  $\text{Cob}^+$  in 0.1 M NaCl aqueous solution containing 0 mM  $\beta$ -CD (—), 4.0 mM  $\beta$ -CD (---), and 10.0 mM  $\beta$ -CD (- - -) (working electrode: 0.08  $\text{cm}^2$ ). The inset shows the NPV response in the absence of  $\beta$ -CD. (B) Cyclic voltammograms (scan rate: 0.1 V/s) of 1.0 mM  $\text{Cob}^+\text{-COO}^-$  in 0.1 M phosphate buffer (pH = 7) containing 0 mM  $\beta$ -CD (—), 4.0 mM  $\beta$ -CD (---), and 10.0 mM  $\beta$ -CD (- - -) (working electrode: 0.008  $\text{cm}^2$ ).

mental cyclic voltammograms were carried out with the Digi-Sim 2.1 software package.<sup>11</sup>

**Procedures.** The surface of the working electrode was polished with a 0.05- $\mu\text{m}$  alumina/water slurry on a felt surface and rinsed with purified water before each cyclic voltammetric run. The cell resistance was compensated by the BAS 100 B/W instrument. The solutions for the electrochemical experiments were purged with nitrogen and kept under an inert atmosphere throughout the measurements. Typically, a 1.0 mM solution of the cobaltocenium compound in 0.1 M supporting electrolyte solution (NaCl was used with cobaltocenium and pH 7 phosphate buffer with carboxycobaltocenium) was prepared for the electrochemical experiments. The concentration of  $\beta$ -CD in the solution was adjusted to the desired level (within the 0–10 mM range) by adding carefully weighted amounts of solid CD host.

## Results and Discussion

The cathodic voltammetric behavior of  $\text{Cob}^+$  is complicated by the insolubility of its reduced form (Cob, cobaltocene) in aqueous media. The one-electron reduction of  $\text{Cob}^+$  then results in the deposition of electrogenerated cobaltocene on the electrode surface. A typical example of the resulting voltammetric response is shown in Figure 1A. Note the distortions of the cathodic peak and the shape and size of the anodic peak on scan reversal, which clearly indicate the deposition of cobaltocene on the working electrode. In contrast,  $\text{Cob}^+\text{-COOH}$

exhibits reasonable aqueous solubility in its reduced state ( $\text{Cob-COOH}$ ) and, therefore, its cathodic voltammetric behavior is perfectly reversible (see Figure 1B). While we did not attempt to control the solution pH in the experiments with  $\text{Cob}^+\text{PF}_6^-$ , we used a pH 7 phosphate buffer electrolyte in the experiments with  $\text{Cob}^+\text{-COOH}$  due to its acidic character. We estimated the  $\text{p}K_a$  of this compound from pH measurements of its aqueous solutions. The resulting  $\text{p}K_a$  value was  $\sim 1.3$  so that complete ionization is expected at pH 7.<sup>7</sup> Therefore, under the conditions of our experiments, carboxycobaltocenium is better formulated as a zwitterion,  $\text{Cob}^+\text{-COO}^-$ , which yields an anionic species,  $\text{Cob-COO}^-$ , upon electrochemical reduction and maintains reasonable solubility in aqueous media.

Since the reduction of  $\text{Cob}^+$  leads to the deposition of its reduced form on the electrode surface, normal pulse voltammetry (NPV) was utilized to determine the half-wave potential ( $E_{1/2}$ ) for this reduction process. NPV is convenient for the study of electrochemical processes in which the product is insoluble because, after each pulse, the potential of the working electrode is returned to the initial value at which any electrogenerated deposits are redissolved. A typical NPV response is shown in the insert of Figure 1A. The half-wave potential for the  $\text{Cob}^+/\text{Cob}$  redox couple was found to be  $-1.15$  V vs SSCE, in close agreement with previously reported values.<sup>12</sup> The corresponding value for the  $\text{Cob}^+\text{-COO}^-/\text{Cob-COO}^-$  redox couple was determined to be  $-0.99$  V vs Ag/AgCl (or  $-1.03$  V vs SSCE) by cyclic voltammetry (CV). The electron-withdrawing effect exerted by the carboxylic acid group is clearly evident in the substantial positive shift observed in the half-wave potential value. Therefore, the reduction of  $\text{Cob}^+\text{-COO}^-$  is thermodynamically easier than that of  $\text{Cob}^+$ .

The absence of precipitation effects in the case of carboxycobaltocenium allows a better assessment of the electrochemical reversibility of this redox couple. In the time scale of our CV experiments (scan rates 0.05–1.0 V/s), we always observed reversible current–potential responses characterized by peak-to-peak potential splittings ( $\Delta E_p$ ) around 60 mV and approximately equal cathodic and anodic peak currents. Furthermore, a plot of the cathodic peak current as a function of the (scan rate)<sup>1/2</sup> is linear.<sup>13</sup> Therefore, the cobaltocenium derivative exhibits near-ideal voltammetric behavior in the absence of the CD host.

Cobaltocenium itself does not form a stable complex with  $\beta$ -CD. We verified this point by performing control  $^1\text{H}$  NMR spectroscopic experiments. For instance, addition of a 10-fold excess of  $\beta$ -CD to a  $\text{D}_2\text{O}$  solution of  $\text{Cob}^+\text{PF}_6^-$  leads only to very small changes in the chemical shift of the cobaltocenium protons ( $\Delta\delta < 0.05$  ppm). In contrast to this finding, the voltammetric behavior of both cobaltocenium compounds is strongly affected by the presence of  $\beta$ -CD in the solution. In the case of  $\text{Cob}^+$ , the addition of 2 or more equivalents of  $\beta$ -CD removes the precipitation effects due to the insolubility of cobaltocene (see Figure 1A). The presence of  $\beta$ -CD induces a shift to less negative potentials (see Table 1) in the voltammetric waves of both cobaltocenium compounds. Qualitatively, these findings are consistent with an EC electrochemical reduction mechanism<sup>14</sup> and reveal that the reduced form, cobaltocene, is bound by the  $\beta$ -CD host.

Figure 1B shows the effect of  $\beta$ -CD additions on the voltammetric behavior of  $\text{Cob}^+\text{-COO}^-$ . In this case the most

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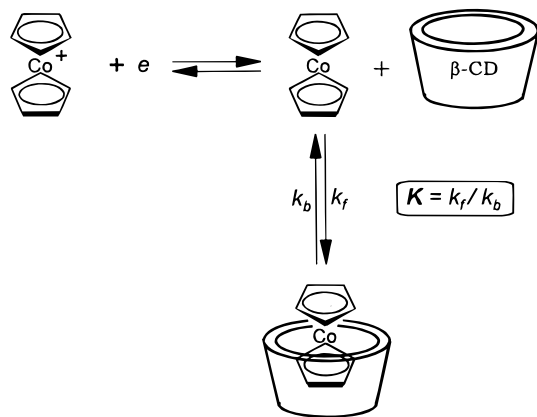
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**Table 1.** Cyclic voltammetric Potential Data (at 25 °C) for the Reduction of Cobaltocenium Compounds (1.0 mM) in the Absence and in the Presence of Variable Concentrations of  $\beta$ -CD

[ $\beta$ -CD]/ [guest]	Cob <sup>+</sup> <sup>a</sup>		Cob <sup>+</sup> -COO <sup>-</sup> <sup>b</sup>	
	$E_{1/2}$ (V vs SSCE)	$\Delta E_p^c$ (mV)	$E_{1/2}$ (V vs SSCE)	$\Delta E_p^c$ (mV)
0	-1.15 <sup>d</sup>		-1.03	64
1	-1.13	101	-1.02	70
2	-1.12	85	-1.01	71
3	-1.10	69	-1.00	72
4	-1.09	69	-0.99	72
6	-1.08	69	-0.98	72
10	-1.06	69	-0.97	72

<sup>a</sup> In 0.1 M NaCl. <sup>b</sup> In 0.1 M pH 7 phosphate buffer. <sup>c</sup> Measured at 0.1 V/s. <sup>d</sup> This value was obtained from NPV experiments.

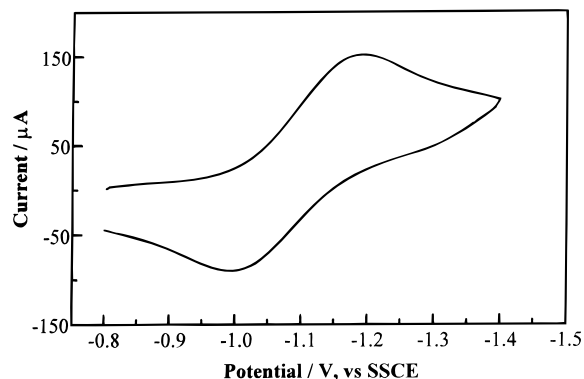
**Scheme 1.** Electrochemical Reduction of Cobaltocenium in the Presence of  $\beta$ -CD



noticeable CD-induced effect is the anodic potential shift of the voltammetric waves, which is consistent with an EC mechanism. Inspection of Table 1 also reveals that the  $\Delta E_p$  values for the Cob<sup>+</sup>-COO<sup>-</sup>/Cob-COO<sup>-</sup> redox couple increase slightly over the value observed in the absence of  $\beta$ -CD. The voltammograms in Figure 1B also show that the presence of  $\beta$ -CD does not change significantly the peak currents, particularly in the forward scan. This finding reflects the lack of association between the initial form of the redox couple (Cob<sup>+</sup>-COO<sup>-</sup>) and the CD host, since the complexation of the initial redox form with the CD should give rise to a substantial decrease in the effective diffusion coefficient, leading to smaller peak currents.<sup>7,8</sup>

Qualitatively, our voltammetric data are consistent with a reduction mechanism in which the uncomplexed cobaltocenium compound picks up one electron to yield the corresponding cobaltocenium radical cation which readily forms a stable inclusion complex with  $\beta$ -CD, as represented in Scheme 1. Note that CD complexation of the cobaltocenium species was not included in the proposed mechanism since our NMR data demonstrate that this interaction is not very significant. Furthermore, direct oxidation of the cobaltocenium-CD inclusion complex is not considered likely for reasons discussed below.

A simple way to check whether the Cob-CD complex can be oxidized directly is to perform CV experiments with shorter time scales. For instance, when the potential of the working electrode is scanned fast enough, the oxidation rate of the inclusion complex may be limited by the rate of the dissociation reaction. This situation will only be encountered if dissociation must precede oxidation, i.e., if the inclusion complex does not undergo direct electron transfer with the electrode surface. Figure 2 shows a CV obtained at 10 V/s in which the anodic



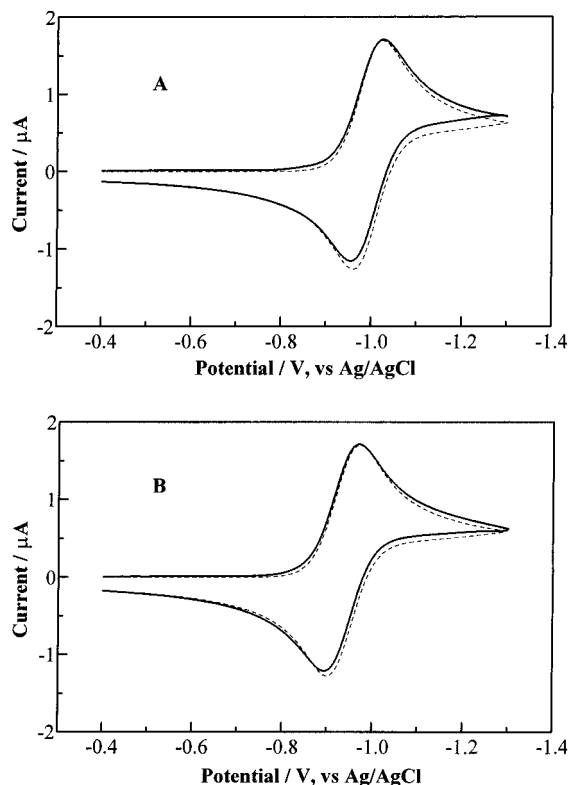
**Figure 2.** Cyclic voltammogram on glassy carbon (0.08 cm<sup>2</sup>) of 1.0 mM Cob<sup>+</sup> in 0.1 M NaCl aqueous solution also containing 10.0 mM  $\beta$ -CD. Scan rate: 10 V/s. The plotted current–potential curve was obtained after subtraction of the background response of a 0.1 M NaCl solution.

peak on scan reversal is flattened. In this voltammogram, the anodic peak current is less than half the value of the cathodic peak current. At lower scan rates (100 mV/s) both peak currents are approximately equal. Although these findings might be affected by uncompensated solution resistance, the experimental indications are consistent with the mechanistic proposal. In addition to this, this behavior agrees with previous observations recorded in the literature about the electroactivity of CD inclusion complexes of ferrocene<sup>7,8</sup> and reduced viologen<sup>15</sup> derivatives.

Once the mechanism of Scheme 1 is accepted as a sensible proposal, digital simulations can be used to obtain further support for this mechanism as well as to determine the association equilibrium constant between cobaltocenium and the CD host ( $K$ ). Figure 3A shows the simulated and experimental voltammograms for Cob<sup>+</sup>-COO<sup>-</sup> in the absence of  $\beta$ -CD. Obtaining a simulated voltammogram that fits the experimental data well is trivial in this case as the electron transfer process is reversible and free from any coupled chemical reactions. However, it must be pointed out that the fit is poor in the potential region negative from -1.0 V. This is expected as the experimental currents in this potential range contain a significant contribution from solvent reduction ( $2\text{H}^+ + 2e \rightarrow \text{H}_2$ ) which is not taken into account by the simulations. This feature is common to all our simulated voltammograms.

In the presence of  $\beta$ -CD, the simulations are more challenging because one has to optimize thermodynamic and kinetic parameters for the complexation equilibrium as well as for the electron transfer process. An example of the fit between simulated and experimental voltammograms is provided in Figure 3B. Notice that the fit is very good throughout the voltammogram and the only potential region exhibiting a poor fit reflects the already mentioned current contributions from hydrogen evolution which cannot be simulated. The optimization of the fit between simulated and experimental voltammograms affords a powerful tool to determine the relevant thermodynamic, kinetic, and electrochemical parameters. The resulting values are listed in Table 2.

The formal potential for the Cob<sup>+</sup>/Cob couple obtained from the simulations is about 20 mV more positive than the half-wave potential obtained from NPV experiments. This small difference is probably due to the precipitation on the electrode surface of the reduced Cob species. This experimental complication may be also responsible for the rather small value for



**Figure 3.** Cyclic voltammogram (at 0.1 V/s) on glassy carbon (0.008  $\text{cm}^2$ ) of 1.06 mM  $\text{Cob}^+\text{-COO}^-$  in 0.1 M phosphate buffer (pH = 7) also containing (A) 0.0 mM  $\beta\text{-CD}$  and (B) 10.0 mM  $\beta\text{-CD}$ : Experimental voltammogram (solid line) after background subtraction; digital simulation (dotted line) obtained with the parameter values shown in Table 2.

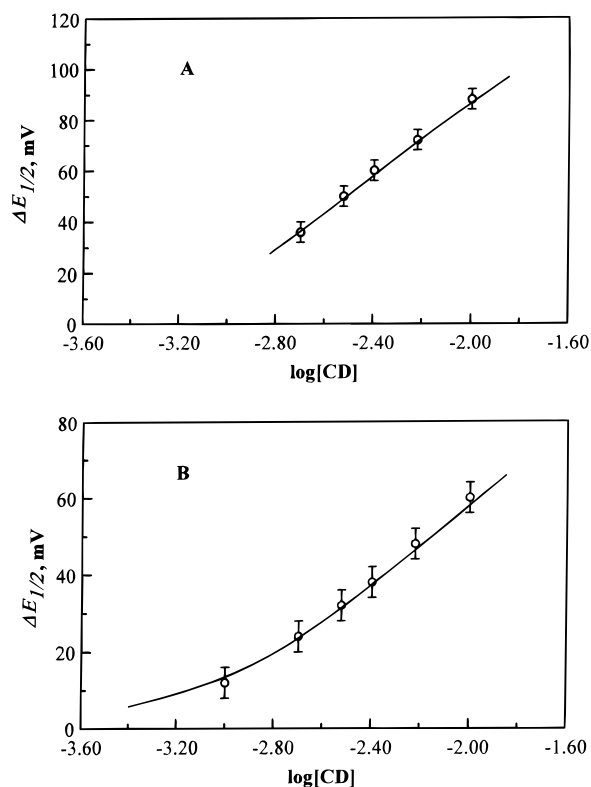
**Table 2.** Thermodynamic, Kinetic, and Electrochemical Parameters Obtained from Digital Simulations of the Cyclic Voltammetric Responses of Aqueous Solutions Containing Cobaltocenium Compounds and  $\beta\text{-CD}$  at 25  $^\circ\text{C}$

param	$\text{Cob}^+{}^a$	$\text{Cob}^+\text{-COO}^-{}^b$
$E^{0'}$ (V vs SSCE) <sup>c</sup>	-1.13	-1.03
$k^0$ (cm/s) <sup>d</sup>	>0.1	>0.1
$D_{\text{O}}$ ( $\text{cm}^2/\text{s}$ ) <sup>e</sup>	$7.2(\pm 0.2) \times 10^{-6}$	$7.0(\pm 0.2) \times 10^{-6}$
$D_{\text{R}}$ ( $\text{cm}^2/\text{s}$ ) <sup>f</sup>	$1.4(\pm 0.2) \times 10^{-6}$	$7.0(\pm 0.2) \times 10^{-6}$
$D_{\text{complex}}$ ( $\text{cm}^2/\text{s}$ ) <sup>g</sup>	$1.8(\pm 0.2) \times 10^{-6}$	$1.6(\pm 0.2) \times 10^{-6}$
$K$ (L/mol) <sup>h</sup>	$2000 \pm 200$	$1800 \pm 200$
$k_{\text{f}}$ ( $\text{M}^{-1} \text{s}^{-1}$ ) <sup>i</sup>	$4.8 \times 10^7$	$3.6 \times 10^7$

<sup>a</sup> In 0.1 M NaCl. <sup>b</sup> In 0.1 M pH 7 phosphate buffer. <sup>c</sup> Formal potential for the one-electron reduction of the cobaltocenium compound. <sup>d</sup> Standard rate constant for the corresponding heterogeneous electron transfer process. <sup>e</sup> Diffusion coefficient for the oxidized (cobaltocenium) species. <sup>f</sup> Diffusion coefficient for the reduced (cobaltocene) species. <sup>g</sup> Diffusion coefficient for the cobaltocene- $\beta\text{-CD}$  inclusion complex. <sup>h</sup> Association equilibrium constant as defined in Scheme 1. <sup>i</sup> Bimolecular association rate constant as defined in Scheme 1.

the diffusion coefficient of Cob which was estimated from the simulations. Notice that the diffusion coefficients given in Table 2 for  $\text{Cob}^+\text{-COO}^-$  and  $\text{Cob-COO}^-$  are identical, reflecting the fact that in this case both redox partners are perfectly soluble. On the other hand, the simulations yield a diffusion coefficient value for inclusion complexes which are similar to previously reported  $D$  values for CD inclusion complexes.<sup>7,8</sup>

The binding constants ( $K$ ) given in Table 2 are in the same range determined for the  $\beta\text{-CD}$  complexation of ferrocene derivatives.<sup>7-9</sup> This is not surprising due to the similarities in size and hydrophobic character between cobaltocene and ferrocene. The kinetic rate constants for the bimolecular



**Figure 4.** Plots of the CD-induced half-wave potential shifts ( $\Delta E_{1/2}$ ) for the reduction of (A)  $\text{Cob}^+$  and (B)  $\text{Cob}^+\text{-COO}^-$  as a function of the total concentration of  $\beta\text{-CD}$ . Simulated values (—); experimental data (○) with 8 mV error bars.

association between  $\beta\text{-CD}$  and cobaltocene are also similar to those previously reported for CD complexation processes.<sup>7</sup>

In order to assess the quality of the parameters given in Table 2, we investigated how well the simulations fit the experimental voltammograms throughout a range of CD concentrations. To do this, we selected the apparent half-wave potential as a value which is clearly affected by the varying concentrations of the host. The points plotted in Figure 4 are the experimentally measured shifts of the  $E_{1/2}$  value for the reduction of both cobaltocenium compounds as a function of  $\beta\text{-CD}$  concentration, and the continuous line was obtained from simulations using the fixed set of parameters given in Table 2. The fit is very good over the entire CD concentration range surveyed, which was only limited by the solubility of  $\beta\text{-CD}$ . These results lend further credibility to the values obtained from the digital simulation of the cyclic voltammetric responses.

In conclusion, we have shown in this work that while cobaltocenium and carboxycobaltocenium do not interact significantly with  $\beta\text{-CD}$ , their reduced partners do form stable inclusion complexes with this host, as summarized in Scheme 1. The thermodynamic stability of the resulting inclusion complexes is comparable to that of  $\beta\text{-CD}$  complexes of ferrocene derivatives.

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