Synthesis, Structure, and Electrochemistry of an Electron-Rich Chiral Diaminoferrocene, (*S*,*S*)-Bis(2,5-dimethylpyrrolidinyl)ferrocene

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*Summary: The chiral diamine (S,S)-bis(2,5-dimethylpyrrolidinyl)ferrocene (**6**) was prepared from diaminoferrocene and (2R,5R)-2,5-hexanediol cyclic sulfate in the presence of a base. The short C−N bond, long Fe−C(N) bond, and planar nitrogen observed in the crystal structure of **6** are consistent with efficient N-to-Cp electron donation. The resulting electron-rich metal center (with the most negative shift in redox potential yet observed for aminoferrocenes) was characterized electrochemically.*

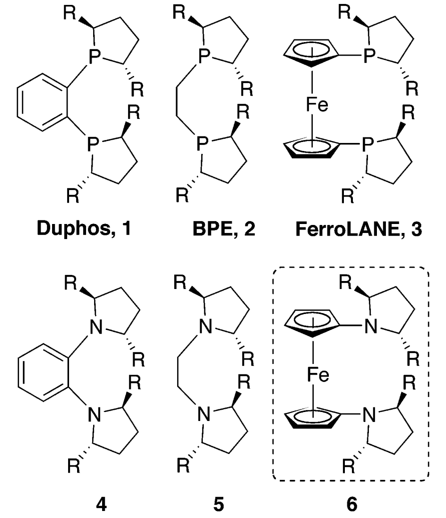
Introduction

Chiral bis(2,5-dialkylphospholanes) such as Duphos (**1**) and BPE (**2**) are very successful ligands in asymmetric catalysis.[1,2] Although several analogous bis(2,5-dialkylpyrrolidines) (**4**, **5**) and analogues with 3,4-substituents have been prepared,[3,4] a chiral diamine **6** analogous to FerroLANE (**3**)[5] has not yet been reported. To take advantage of the special features of the ferrocene backbone, including its large bite angle and its flexibility,[6] we report here the synthesis and structural and electrochemical characterization of chiral (*S*,*S*)-bis(2,5-dimethylpyrrolidinyl)ferrocene (**6**).

Results and Discussion

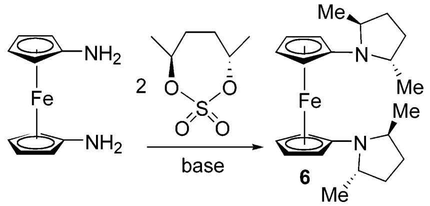
As in the synthesis of FerroLANE[5] and a related phosphinamine,[7] ligand **6** (Natamine)[8] was prepared from diaminoferrocene[9] and (2*R*,5*R*)-2,5-hexanediol cyclic sulfate[1] in the presence of a base (NaH or BuLi). These one-pot syntheses afforded **6** as red-orange crystals in modest (18−34%) yield, which is comparable to overall yields reported for the multistep preparations of the analogous ligands **4** and **5**.[3,4]

Chart 1. Chiral Bis(2,5-dialkylphospholanes) and Bis(2,5-dialkylpyrrolidines)[a]



[a] The (*S*,*S*)-enantiomers are drawn for convenience. Although both hands of **1**−**3** were prepared, only (*R*,*R*)-**4** and -**5** were reported.[1,4,5]

Scheme 1. Synthesis of Natamine (6)[a]



[a] Conditions: (a) (i) THF, reflux, 24 h; (ii) 4 NaH, 0 °C; (iii) reflux, 24 h; (b) (i) 2 n-BuLi; (ii) 2.2 equiv of cyclic sulfate; (iii) 2 n-BuLi.

Complex **6** was characterized by elemental analyses and mass spectroscopy. As expected for a chiral molecule, its ^{1}H NMR spectrum showed signals for four inequivalent types of Cp protons, and five ^{13}C NMR Cp resonances were observed.

Two views of the crystal structure of **6** are shown in Figure 1. Crystallographic data and bond lengths and angles appear in Tables 1 and 2 and the Supporting Information.

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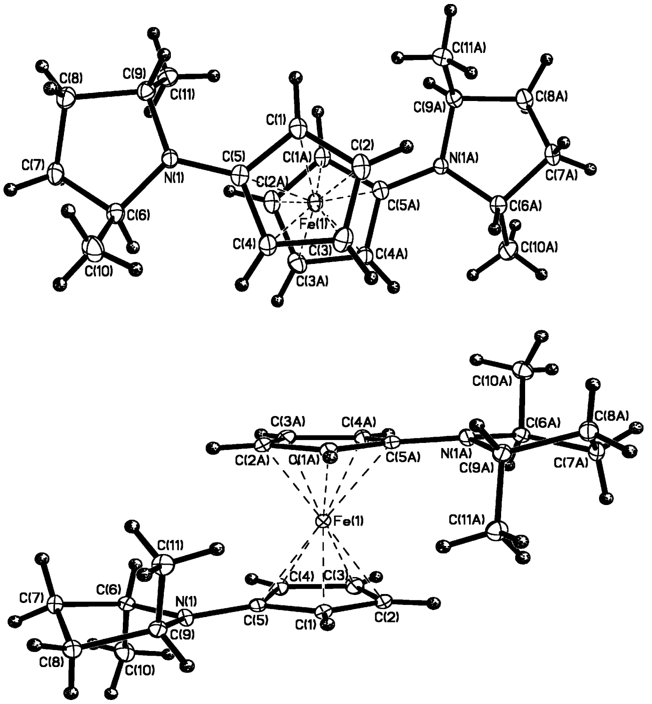


Figure 1. ORTEP diagrams of (*S*,*S*)-bis(2,5-dimethylpyrrolidinyl)ferrocene (**6**). Selected bond distances (Å): Fe(1)–C(1) 2.048(2), Fe(1)–C(2) 2.0241(18), Fe(1)–C(3) 2.024(2), Fe(1)–C(4) 2.058(2), Fe(1)–C(5) 2.134(2), C(5)–N(1) 1.377(2), N(1)–C(9) 1.462(2), N(1)–C(6) 1.472(3). Selected bond angles (deg): C(1)–Fe(1)–C(1A) 108.25(2), C(2)–Fe(1)–C(5A) 108.56(10), C(3)–Fe(1)–C(4A) 107.01(9), C(4)–Fe(1)–C(3A) 107.01(9), C(5)–Fe(1)–C(2A) 108.56(10), C(5)–N(1)–C(9) 123.32(15), C(5)–N(1)–C(6) 121.52(16), C(6)–N(1)–C(9) 113.12(15).

Table 1. Crystallographic Data for 6

empirical formula	$C_{22}H_{32}FeN_2$
fw	380.35
space group	P2(1)2(1)2
a, Å	10.3055(10)
b, Å	13.7375(14)
c, Å	6.7946(7)
α, deg	90
β, deg	90
γ, deg	90
V, Å^3	961.92(17)
Z	2
D(calc), g cm^{-3}	1.313
μ(Mo Kα), mm^{-1}	0.791
diffractometer	Bruker CCD
R(*F*), %[a]	3.29
R(*wF*^{2}), %[a]	6.61
absolute struct param	0.015(18)

[a] Quantity minimized = $R(wF^2) = \sum[w(F_o^2 - F_c^2)^2]/\sum[(wF_o^2)^2]^{1/2}$; $R = \sum\Delta/\sum(F_o)$, $\Delta = |(F_o - F_c)|$, $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, $P = [2F_c^2 + \mathrm{Max}(F_o,0)]/3$.

In comparison to related aminoferrocenes (Table 2), complex **6** contained an unusually short C–N bond, a long Fe–C(N) bond, and a planar nitrogen. These observations are consistent with efficient pyrrolidine-to-Cp electron donation[15] and an important contribution from resonance structure **6′**, as proposed for the diaminocobaltocenium cation.[12,16]

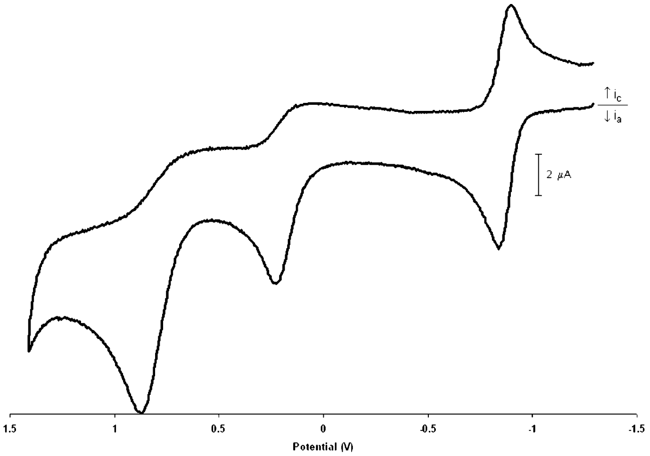
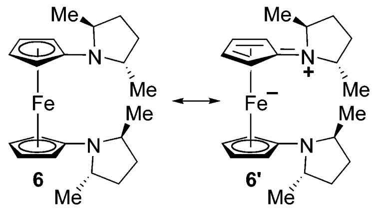


Figure 2. Cyclic voltammetry scan of the oxidation of 1.0 mM **6** in MeCN/0.1 M NBu_4PF_6 at 100 mV/s.

Chart 2. Resonance Structures for 6



This structural model, which predicts an electron-rich Fe center, is consistent with the results of electrochemical studies, which were conducted in MeCN and in CH_2Cl_2 (Figure 2 and Table 3). In MeCN, complex **6** showed a reversible oxidation wave with $E_{1/2} = -0.82$ V vs the $Fc^{0/+}$ couple and two irreversible waves at 0.31 and 1.03 V vs $Fc^{0/+}$. The electrochemistry of **6** was also examined in CH_2Cl_2 using two different supporting electrolytes in order to determine if the solvent and/or the supporting electrolyte affected the stability of the oxidation product of these more positive waves. This stabilization has been noted in the oxidation of ruthenocene in the presence of $[NBu_4]^+[B(C_6F_5)_4]^-$,[17] but there was not a significant impact in oxidative electrochemistry of **6**. In both MeCN and CH_2Cl_2 with $[NBu_4]^+[B(C_6F_5)_4]^-$ there are two waves at potentials more positive than $Fc^{0/+}$ and one wave at potentials more negative than $Fc^{0/+}$. A similar pattern was noted in the oxidative electrochemistry of 1,1′-bis(dimethylamino)ferrocene ((1,1′)-Fc$(NMe_2)_2$).[20] However, unlike the waves less positive than $Fc^{0/+}$, the irreversible oxidation waves in **6** occur at more positive potentials than the corresponding waves in (1,1′)-Fc$(NMe_2)_2$.

These data show that Natamine is the most electron-rich aminoferrocene yet reported, and even more electron-rich than decamethylferrocene (Table 3). The Hammett parameter, σ_p, can be estimated from the equation E_L

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(11) Wrackmeyer, B.; Klimkina, E. V.; Milius, W. *Inorg. Chem. Commun.* **2004**, *7*, 412–416.

(12) Inyushin, S.; Shafir, A.; Sheats, J. E.; Minihane, M.; Whitten, C. E., Jr.; Arnold, J. *Polyhedron* **2004**, *23*, 2937–2942.

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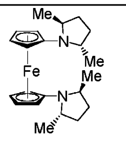
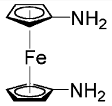
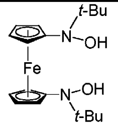
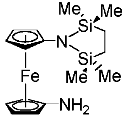
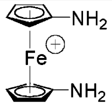
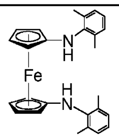
(14) (a) See ref 11. (b) Wrackmeyer, B.; Klimkina, E. V.; Milius, W. *Struct. Chem.* **2004**, *15*, 333–337. (c) Wrackmeyer, B.; Klimkina, E. V.; Milius, W. *Inorg. Chem. Commun.* **2004**, *7*, 884–888.

(15) Ohwada, T.; Hiaro, H.; Ogawa, A. *J. Org. Chem.* **2004**, *69*, 7486–7494.

(16) As noted by a reviewer, even shorter C–N and longer Fe–C(N) bonds were observed in the 1,1′-diaminoferrocenium cation (entry 5, Table 2), consistent with contribution from a resonance structure analogous to **6′**, where Cp-to-Fe donation is favored by the positive charge at the metal center.

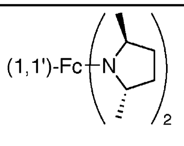
(17) Ramachandran, B. M.; Trupia, S. M.; Geiger, W. E.; Carroll, P. J.; Sneddon, L. G. *Organometallics* **2002**, *21*, 5078–5090.

Table 2. Selected Bond Distances (Å) and Angles (deg) for 1,1′-Diaminoferrocenes[a]

Entry	Structure	Fe-C(N)	Fe-C (max/min)[b]	C(Cp)-N	N bond angles	Ref.
1		2.134(2)	2.058(2), 2.024(2)	1.377(2)	123.32(15) 121.52(16) 113.12(15)	This work
2		2.074(3)[c]	2.060(3), 2.027(3)	1.411(5)[c]	d	9
3		2.038(2)	2.046(2), 2.038(2)	1.438(2)	115.5(1) 105.5(2)[e] 103.7(2)[e]	10
4		2.106(3)[f] 2.096(4)[g]	2.067(4), 2.021(4)	1.414(4)[f] 1.397(5)[g]	123.1(2)[f] 123.1(2)[f] 113.76(15)[f]	11
5		2.174(7)[c]	2.084(6), 2.032(6)	1.365(9)[c]	d	12
6		h	h	1.409(2)[i]	122.1(1)[i]	13

[a] The structures of some related aminoferrocenophanes[14] are not included here, to avoid structural effects of ring strain. [b]Maximum and minimum values for the Fe−C (Cp carbons not bonded to N) bond lengths. [c]Average values for the two independent molecules in the unit cell. [d]In several of these structures, the N−H protons were not located, so bond angles at N were not reported. [e]The OH groups were disordered, so average values for angles involving O are reported. [f]Data for the Cp-NSi$_2$ ring. [g]Data for the Cp-NH$_2$ ring. [h]The Fe−C(Cp) distances were not reported. [i]Average values.

Table 3. Oxidation Potentials of Diaminoferrocenes[a]

Entry	Compound	$E_{1/2}$, V	Solvent	Supporting electrolyte	Reference
1	(1,1')-Fc(N(t-Bu)(OH))$_2$	-0.1	CH_3CN	n-Bu$_4$NPF$_6$	10
2	(1,1')-Fc(NPh$_2$)$_2$	-0.40	CH_3CN	$NaClO_4$	18
3[b]	(1,1')-Fc(NHPh)$_2$	-0.46	CH_2Cl_2	b	19
4	(1,1')-Fc(NH$_2$)$_2$	-0.602	CH_3CN	n-Bu$_4$NPF$_6$	9
5[c]	(1,1')-Fc(NMe$_2$)$_2$	-0.63	CH_3CN	n-Bu$_4$NClO$_4$	20
6	(1,1')-Fc(NHSiMe$_3$)$_2$	-0.632	CH_3CN	n-Bu$_4$NPF$_6$	21
7		-0.82 -0.86 -0.89	CH_3CN[d] CH_2Cl_2[e] CH_2Cl_2[f]	n-Bu$_4$NPF$_6$ n-Bu$_4$NPF$_6$ (n-Bu$_4$N)(B(C$_6$F$_5$)$_4$)	this work
8	Cp$_2$*Fe	-0.51	CH_3CN	n-Bu$_4$NPF$_6$	22

[a] Measurements were done vs Fc$^{0/+}$ at room temperature unless otherwise stated. The abbreviation (1,1′)-Fc in column 2 stands for 1,1′-ferrocenediyl. [b]vs SCE (−0.06 V, corresponds to −0.46 V vs Fc$^{0/+}$); the supporting electrolyte was not reported. [c]vs SCE (−0.23 V, corresponds to −0.63 V vs Fc$^{0/+}$). [d]For the irreversible waves, E_p vs Fc$^{0/+}$ was 0.31 and 1.03 V. [e]For the irreversible wave, E_p vs Fc$^{0/+}$ was 0.39 V. A second anticipated wave was not observed; its potential may lie outside the solvent window. [f]For the irreversible waves, E_p vs Fc$^{0/+}$ was 0.59 and 0.83 V.

$= 0.45\sigma_p + 0.36$, where E_L is defined as (1/2)$E°$ vs NHE in CH_2Cl_2.[23] The estimated σ_p for the 2,5-dimethylpyrrolidinyl group is −1.03, which is one of the most negative σ_p values for a neutral substituent.[24]

Conclusion

The chiral diamine (*S*,*S*)-bis(2,5-dimethylpyrrolidinyl)ferrocene (**6**) contains a short C−N bond, a long Fe−C(N) bond, and planar nitrogen, consistent with efficient

N-to-Cp electron donation. The resulting electron-rich metal center (with the most negative shift in redox potential yet observed for aminoferrocenes) was characterized electrochemically.

Experimental Section

General Details. All reactions and manipulations were performed in dry glassware under a nitrogen atmosphere at 20 °C in a drybox or using standard Schlenk techniques. Petroleum ether (bp 38−53 °C), ether, THF, CH_2Cl_2, and toluene were dried using activated alumina columns similar to those described by Grubbs.[25] Acetone and acetonitrile were degassed by purging with N_2 and stored over molecular sieves.

All NMR spectra were recorded by using Varian 300 or 500 MHz spectrometers. ^1H or ^{13}C NMR chemical shifts are reported vs Me_4Si and were determined by reference to the residual ^1H or ^{13}C solvent peaks. Coupling constants are reported in Hz. Unless otherwise noted, peaks in NMR spectra are singlets and absolute values are reported for coupling constants. Elemental analyses were provided by Schwarzkopf Microanalytical Laboratory. Mass spectra were obtained at the University of Illinois Urbana−Champlaign. Reagents were from commercial suppliers, except for (2*R*,5*R*)-2,5-hexanediol cyclic sulfate[1] and (1,1′)-$Fc(NH_2)_2$,[9] which were prepared by literature procedures.

(*S*,*S*)-Bis(2,5-dimethylpyrrolidinyl)ferrocene (Natamine, 6). Method 1. (1,1′)-$Fc(NH_2)_2$ (250 mg, 1.16 mmol) and (2*R*,5*R*)-2,5-hexanediol cyclic sulfate (416.2 mg, 2.312 mmol, 2 equiv) were dissolved in 3 mL of THF and placed into a Schlenk tube. The reaction mixture was refluxed at 66 °C for 22 h. After 30 min of heating a black precipitate began to collect on the bottom of the flask and the solution changed color to dark orange-brown. The reaction mixture was cooled to 0 °C, and NaH (66.6 mg, 2.77 mmol, 2.2 equiv) was added via syringe as a slurry in 3 mL of THF. Gas started to evolve immediately. The reaction flask was kept at room temperature for 1 h and then refluxed for 22 h. A second portion of NaH (33 mg, 1.4 mmol, in 3 mL of THF) was added to the reaction mixture, because the precipitate did not dissolve completely. The mixture was refluxed for 24 h, quenched with 20 mL of water, and extracted with Et_2O (3 × 30 mL). The organic layers were combined and washed with brine and water, then dried over $MgSO_4$. The solvent was removed in vacuo, and the orange-brown oily residue was recrystallized from MeOH (dried over molecular sieves, degassed), yielding (*S*,*S*)-bis(2,5-dimethylpyrrolidinyl)ferrocene as a dark red-brown crystalline solid (111.1 mg, 22%). Recrystallization from hexanes resulted in analytically pure compound.

Method 2. To a stirred orange solution of (1,1′)-$Fc(NH_2)_2$ (106 mg, 0.490 mmol) in 15 mL of THF was added n-BuLi (615 μL, 0.984 mmol, 1.6 M solution in hexanes, 2 equiv) via syringe. The reaction mixture was stirred for 1.5 h. It changed color to cherry-red immediately upon addition of n-BuLi, and after 15 min an orange precipitate appeared. (2*R*,5*R*)-2,5-Hexanediol cyclic sulfate (178 mg, 0.99 mmol, 2 equiv) was added as a solution in 5 mL of THF. The mixture was stirred for 1 h, an additional 2 equiv of n-BuLi (615 μL, 0.984 mmol, 1.6 M solution in hexanes) was added via syringe, and the mixture was stirred for 2.5 h more. The reaction mixture was quenched with 5 mL of MeOH, extracted with 25 mL of hexanes, and filtered. The solvent was removed in vacuo, and the orange-brown oily residue contained a mixture of **6** and monosubstituted (2,5-dimethylpyrrolidinyl)aminoferrocene (**7**), as well as some unreacted diaminoferrocene. After recrystallization from MeOH, (*S*,*S*)-bis(2,5-dimethylpyrrolidinyl)ferrocene was obtained as a dark red-brown crystalline solid (40 mg, 18% yield). If the reaction times are extended to 2−3 h for each step, only compound **9** is formed, in 34% yield.

Anal. Calcd for $C_{22}H_{32}N_2Fe$: C, 69.47; H, 8.48; N, 7.36. Found: C, 69.39; H, 8.67; N, 7.31. MS (EI): *m*/*z* 380.2 (M^+, 100%), HRMS (EI): calcd 380.1915; found 380.1914. ^1H NMR (C_6D_6): δ 3.98−3.91 (m, 2H, Cp), 3.91−3.85 (m, 2H, Cp), 3.69−3.64 (m, 2H, Cp), 3.64−3.60 (m, 2H, Cp, overlapped with previous signal), 3.55−3.45 (m, 4H, CH), 2.00−1.85 (m, 4H, CH_2), 1.30−1.15 (m, 4H, CH_2), 1.14 (d, $J = 6.0$, 12H, Me). $^{13}C\{^1H\}$ NMR (C_6D_6): δ 110.1 (quat, Cp), 64.4 (CH, Cp), 64.3 (CH, Cp), 56.5 (CH, Cp), 55.0 (CH), 53.1 (CH, Cp), 30.8 (CH_2), 19.0 (CH_3).

(*S*,*S*)-(2,5-Dimethylpyrrolidinyl)aminoferrocene (7) was observed as a byproduct in some syntheses of Natamine and tentatively identified in the mixture by its ^1H NMR spectrum. ^1H NMR (C_6D_6): δ 3.85−3.83 (m, 1H, Cp), 3.83−3.81 (m, 1H, Cp overlapped with previous signal), 3.79 (4H, Cp), 3.57−3.55 (m, 1H, Cp), 3.55−3.53 (m, 1H, Cp, overlapped with previous signal), 3.38−3.30 (m, 2H, CH), 2.06 (br, 2H, NH_2), 1.89−1.86 (m, 2H, CH_2), 1.06 (d, $J = 6$, 6H, Me).

Electrochemistry Dichloromethane (CH_2Cl_2) was purified under argon using a Solv-tek solvent purification system similar to one previously described.[25] Acetonitrile (MeCN) was distilled from CaH_2 under argon prior to use. Tetrabutylammonium hexafluorophosphate ($[NBu_4]^+[PF_6]^-$) was purchased from Aldrich and dried in vacuo prior to use. $Li[B(C_6F_5)_4]\cdot(OEt_2)_{2.5}$ was purchased from Boulder Scientific Co. and metathesized to tetrabutylammonium tetrakis(pentafluorophenyl)borate ($[NBu_4]^+[B(C_6F_5)_4]^-$) using the literature procedure.[26] Ferrocene was purchased from Strem and sublimed prior to use.

All electrochemical experiments were conducted using a Princeton Applied Research 263-A potentiostat and analyzed by Power Suite software. The analyte solutions were prepared in a glovebox immediately prior to use. The solution was then removed from the glovebox and added to a solution of the desired supporting electrolyte in an electrochemical cell. The final concentration of analyte was 1.0 mM in all experiments, while the supporting electrolyte concentration was 0.1 M for $[NBu_4]^+[PF_6]^-$ and 0.05 M for $[NBu_4]^+[B(C_6F_5)_4]^-$. The solution was flushed with argon and stirred prior to the experiment, and a blanket of argon was kept over the solution for the duration of the experiment. Scans were made from 100 to 1000 mV/s at intervals of 100 mV/s. The 1.5 mm glassy-carbon working electrode was polished with a 1 μm diamond paste, rinsed with acetone, and then polished with a micron diamond paste. Prior to use, the working electrode was washed with acetone and then CH_2Cl_2 or MeCN. A nonaqueous Ag/AgCl electrode separated from the solution by a fine glass frit was used as the reference electrode, and a platinum wire served as the counter electrode. Data were collected at ambient temperature (22 ± 1 °C), and ferrocene was added as an internal standard at the end of all experiments.

Acknowledgment. We thank the National Science Foundation for support, and John Arnold and Alexandr Shafir (UC Berkeley) for advice on preparation of diaminoferrocene.

Supporting Information Available: Details of the crystallographic studies, including a CIF document. This information is available free of charge via the Internet at http://pubs.acs.org.

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