Articles

Binding and Electrochemical Recognition of Barbiturate and Urea Derivatives by a Regioisomeric Series of Hydrogen-Bonding Ferrocene Receptors

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A series of ferrocene-containing amidopyridyl receptors, in two regioisomeric forms (1,1′ and 1,3), have been shown to bind cyclic organic molecules in chloroform through complementary hydrogen-bonding interactions. Complexation was monitored by NMR spectroscopy and by cyclic voltammetry. The magnitude of the host−guest binding strength and the redox response to complexation depend on both the type and the relative position of the amidopyridyl groups on the cyclopentadienyl rings of the ferrocene.

Introduction

Among the numerous examples of redox-active supramolecular receptors in the literature,[1] those that contain a ferrocene as the redox-active reporter group have been the most extensively studied. In the past, ferrocene derivatives that bind, and allow the electrochemical sensing of, cations[2] and anions[3] have been reported. The various bonding and non-bonding interactions that allow these charged species to be electrochemically recognized have been reviewed in detail.[1b] More recently, we and others have developed ferrocene receptors for neutral molecules.[4] These receptors operate through the formation of covalent[4b,k] or, more often, noncovalent[4a,c−j] bonds with a guest molecule. In some cases, for example in the formation of hydrogen-bonded complexes with imides[4e] or carboxylic acids,[4g] complexation leads to a change in the oxidation potential of the ferrocene, allowing switching or sensing behavior to be examined. Here we report our studies on receptors **1**−**6** (Figure 1) and show how the relative positions of the hydrogen-bonding groups on each ferrocene (1,1′ or 1,3) can have a marked effect on both the guest binding strength and the redox response to complexation. Initial results on the binding studies with the 1,3-systems were published previously.[4f]

Results and Discussion

I. Receptor Design and Synthesis. The organometallic receptors **1**−**6** are based on analogous organic

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(2) For recent examples of ferrocene compounds that bind and electrochemically respond to metal cations, see: (a) Ion, A.; Buda, M.; Moutet, J.-C.; Saint-Aman, E.; Royal, G.; Gautier-Luneau, I.; Bonin, M.; Ziessel, R. *Eur. J. Inorg. Chem*. **2002**, 1357. (b) Plenio, H.; Aberle, C.; Al Shihadeh, Y.; Lloris, J. M.; Martínez-Mánez, R.; Pardo, T.; Soto, J. *Chem. Eur. J*. **2001**, *7*, 2848. (c) Sutcliffe, O. B.; Chesney, A.; Bryce, M. R. *J. Organomet. Chem*. **2001**, *637*−*639*, 134. (d) Carr, J. D.; Coles, S. J.; Hursthouse, M. B.; Tucker, J. H. R. *J. Organomet. Chem*. **2001**, *637*−*639*, 304. (e) Brindley, G. D.; Fox, O. D.; Beer, P. D. *J. Chem. Soc., Dalton Trans*. **2000**, 4354. (f) Costa, J.; Delgado, R.; Drew, M. G. B, Félix, V.; Saint-Maurice, A. *J. Chem. Soc., Dalton Trans*. **2000**, 1907.

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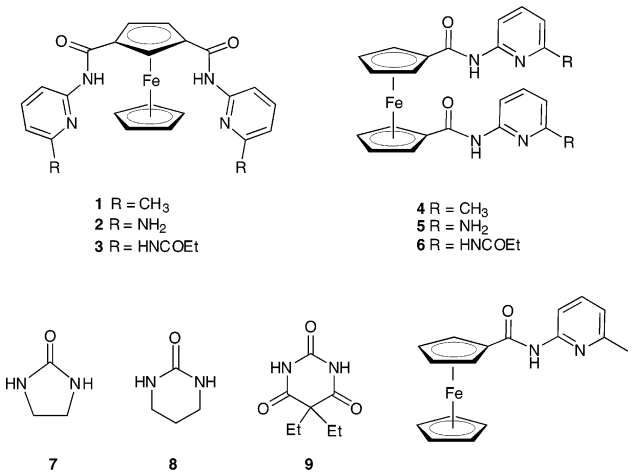

Figure 1. Receptors and substrates used in this study.

receptors originally published by Hamilton that were found to bind a series of cyclic organic molecules in nonprotic organic solvents.[5] By incorporation of a ferrocene spacer group between the hydrogen-bonding units, we reasoned that the strength of the binding interaction with such molecules could be controlled (i.e. switched "on" or "off") by oxidation of the ferrocene unit and also the binding process could be followed by electrochemistry, allowing the guest species to be sensed in solution. The receptors were designed so that the two hydrogen-bonding groups were located on either one (**1**−**3**) or both (**4**−**6**) cyclopentadienyl (Cp) rings of ferrocene. Compounds **4**[6] and **5**[3h,7] have been reported previously and were therefore synthesized according to the literature procedures from 1,1′-ferrocenedicarboxylic acid. Compound **6** was prepared from **5** by reaction with propionyl chloride in THF. Regioisomers **1**−**3** were prepared in a similar fashion from 1,3-ferrocenedicarboxylic acid.[8] All new compounds were characterized by multinuclear NMR spectroscopy, mass spectrometry, and elemental analysis.

II. X-ray Crystallography. Crystals of **1** and **6**, suitable for X-ray diffraction, were grown from solutions in diethyl ether−chloroform and hexane−chloroform, respectively. The molecular structures are shown in Figures 2 and 3, respectively. Unfortunately, the quality of the crystals of **6** was such that only bond connectivity is detectible for this receptor; thus, no bond lengths or bond angles can be presented. However, it is clear that from an inspection of both structures that a cavity for the inclusion of a guest species can be created, in the case of **1**, by 180° rotation of one amidopyridine unit about a Cp−CO bond (i.e. C10−C11 or C7−C18) or, in the case of **6**, by mutual rotation of the Cp units (which are staggered by 8 and 14° in **1** and **6**, respectively), with the Fe atom acting as an "atomic ball bearing". In each case, the hydrogen-bonding donor and acceptor groups (NH and py-N) on each amidopyridine unit are oriented in the same direction, but the two arms in each structure are oriented opposite to each other. The crystal structure of **1** is that of stacked corrugated sheets (see the Supporting Information), which are formed by two hydrogen bonds to adjacent molecules (D···A distances: N−H···O = 3.128(7) Å and N−H···N = 3.259(6) Å). In **6**, however, the crystal structure is a three-dimensional pattern (see the Supporting Information), generated by the arms from one molecule H-bonding in a perpendicular geometry to the arms from another molecule.

III. NMR Binding Studies and Electrochemistry. The interactions of receptors **1**−**6** with the neutral molecules **7**−**9** were studied by ^{1}H NMR spectroscopy in $CDCl_3$ at millimolar concentrations. These guest molecules have the appropriate hydrogen-bonding donor and acceptor groups for interaction with both amidopyridine groups on each receptor. Where complexation was observed, this was evidenced by marked downfield shifts in the signals corresponding to the amide and amine protons of the receptors and also the Cp protons adjacent to each amide group. For example, the amine proton resonance of **5** underwent a downfield shift of +0.95 ppm upon the addition of 5 molar equiv of barbital (**9**), as shown in Figure 4. For receptors **3** and **6**, the downfield shift in the signal for the two amide protons adjacent to the propionyl group upon the addition of **9** was more marked than that for the two amide protons adjacent to the ferrocenoyl group (e.g. for **6** in $CDCl_3$, +1.1 and +0.45 ppm, respectively, upon the addition of 9 molar equiv of barbital (**9**)).

Previous studies by us on receptors **1**−**3** revealed that 1:1 complexes were formed with **7**−**9**,[4f] as evidenced by NMR studies and an X-ray crystal structure of the complex between **3** and **9**, shown schematically in Figure 5. Job plots from the NMR data with receptors **4**−**6** (at a total concentration of host and guest between ca. 2 and 6 mM) revealed that where the binding interaction was significant, discreet 1:1 complexes were also formed, as shown in Figure 6 for receptors **4** and **5** with guests **8** and **9**, respectively, where the highest complex concentration is observed at a mole fraction of 0.5. Given that a 1:1 complex is predominant at millimolar concentrations and that there was no evidence for a 2:1 (guest/host) complex, the most likely structure for the 1:1 complex consists of the guest being wedged between the arms of the receptor, as shown schematically in Figure 5b for the complex between **4** and **8**.

The titration data were used to calculate the 1:1 binding constant for each complex, K, where K = [complex]/[receptor][guest], with the aid of the computer program EQNMR.[9] The data for all six receptors are presented in Table 1. As expected, a stronger host−guest interaction was observed for receptors **1**−**3**, since these can easily form the required planar cavity for binding planar guests. In contrast, for regioisomers **4**−**6**, the two amidopyridine units have to turn in toward each other to accommodate guests **7**−**9** in a 1:1 complex (Figure 5b), which, to avoid disrupting the planarity of the conjugated amidopyridine, is likely to be achieved through rotation of the hydrogen-bonding units about the two Cp−CO bonds. It is possible that other recently reported ferrocene-based receptors[7] for **9** can adopt such

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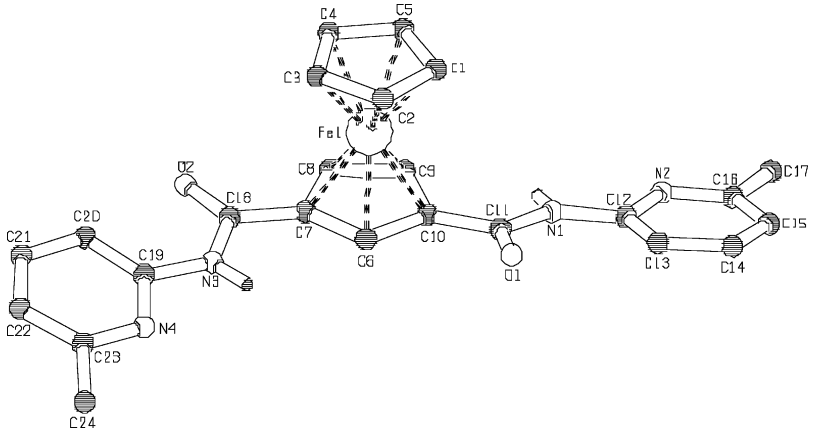

Figure 2. Molecular structure of **1** with some hydrogen atoms and a diethyl ether solvate molecule omitted for clarity.

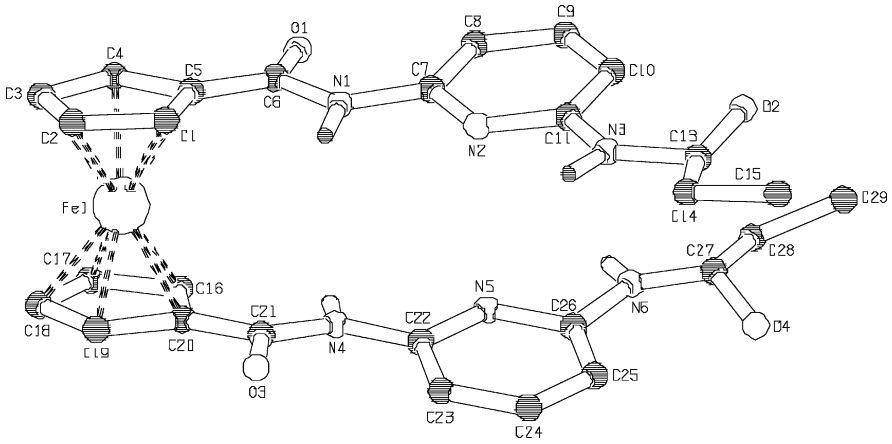

Figure 3. Molecular structure of **6** with some hydrogen atoms omitted for clarity.

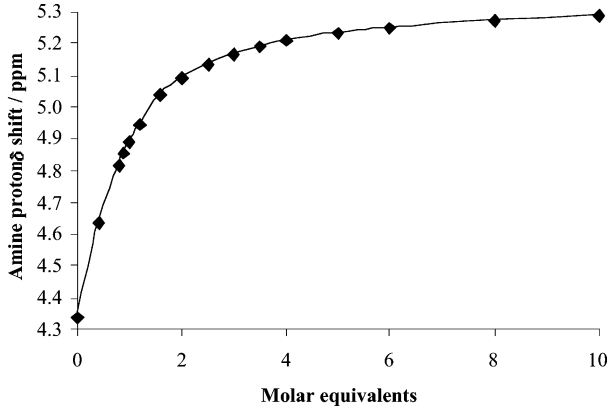

Figure 4. Titration curve showing the downfield shift of the ^{1}H NMR amine resonance of **5** (ca. 1 mM in $CDCl_3$) upon the addition of aliquots of barbital **9**.

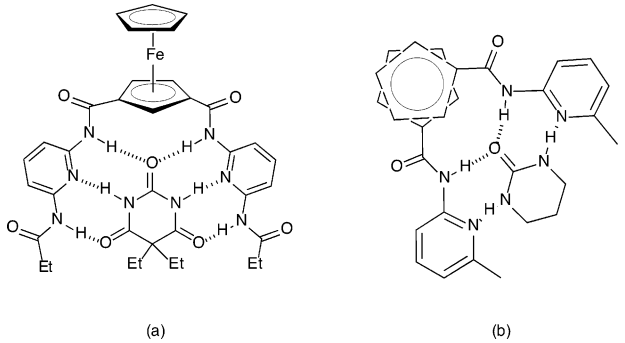

Figure 5. Schematic drawings of the complexes formed by the (a) 1,3-receptors as represented by the [**3**:**9**] complex and (b) 1,1′-receptors as represented by the [**4**:**8**] complex.

a complex conformation, since binding constants of a similar order of magnitude were observed in $CDCl_3$.

In general, the trends in binding constant for each receptor are similar, which reflect a similar binding mode for both types of hosts. For example, the smallest guest, ethyleneurea (**7**), is bound considerably more weakly by all six receptors than trimethyleneurea (**8**), which contains one additional methylene group. Likewise, barbital (**9**) forms strong complexes with receptors **2** and **3**, as well as with **5** and **6**, due to its ability to form two additional hydrogen bonds with these receptors. Similar trends in stability were seen in the receptors designed by Hamilton, containing an isophthalic spacer group.[5] It is interesting to note that conversion of two primary amines in receptors **2** and **5** to two secondary amide groups in **3** and **6** leads to a decrease in the binding constant with barbital. Such an effect has been observed previously in anion binding studies.[3h] Although sterics may play a role, it is likely that the pyridine nitrogen becomes a more effective H-bond acceptor when the pyridine is made more electron-rich by an electron-donating group at the adjacent carbon. Presumably the strength of the binding interaction between **9** and receptors **1** and **4** is lower than that between **8** and **1** and **4** due to unfavorable diagonal secondary electrostatic repulsions, as discussed in a recent review.[10] These factors can also explain why only receptors **1** and **4** form significant complexes with

(10) For a recent discussion on this topic, see: Sijbesma, R. P.; Meijer, E. W. *Chem. Commun.* **2003**, 5.

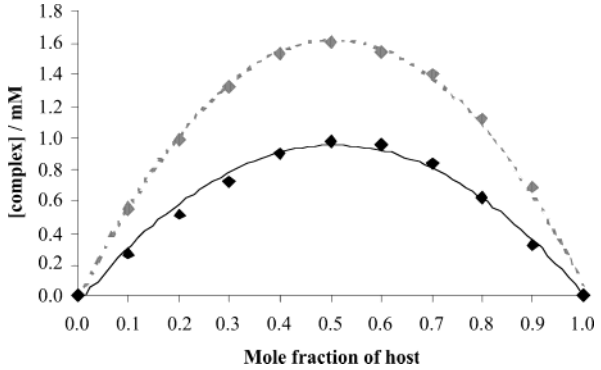

Figure 6. Job plots in $CDCl_3$ of receptor **4** with trimethyleneurea (**8**) (black diamond, total concentration 2.6 mM) and receptor **5** with barbital (**9**) (gray diamond, total concentration 5.5 mM).

Table 1. Binding Constants[a] (K/M^{-1}) for Receptors 1−6 with Substrates 7−9 in $CDCl_3$

	7	8	9
1	250	600	195
2	*b*	110	3200
3	*b*	25	2150
4	60	240	200
5	*b*	80	2125
6	*b*	*b*	575

[a] Binding constants at 293 K. The margin of error is ±5%, from repeat titrations and/or as calculated from the curve fit using the EQNMR program. Data for compounds **1**−**3** were previously presented in ref 4f. [b] Weak binding with, in some cases, several complexes formed in solution, as evidenced by Job plots.

ethyleneurea and propyleneurea. The additional hydrogen-bond donor groups in **2**, **3**, **5**, and **6** are not involved in hydrogen-bond formation but still contribute to unfavorable diagonal interactions.

Cyclic voltammetry was performed on these receptors in dry CH_2Cl_2 to determine the effect of complexation on the ferrocene-centered redox couple (see Experimental Section for further details). Possibly due to adsorption of the oxidized amine onto the electrode surface, the voltammograms for receptors **2** and **5** indicated a quasi-reversible reaction at best (e.g. for **2**, $\Delta E_p \approx 150$ mV), and no thermodynamic parameters were obtained. For the other four receptors, **1**, **3**, **4**, and **6**, their voltammograms all indicated reversible, one-electron transfers, for which the formal potentials, $E^{\circ\prime}$, were determined as $E_{\mathbf{1}}^{\circ\prime} = 0.45$ V, $E_{\mathbf{4}}^{\circ\prime} = 0.44$ V, $E_{\mathbf{3}}^{\circ\prime} = 0.41$ V, and $E_{\mathbf{6}}^{\circ\prime} = 0.40$ V vs $E^{\circ\prime}(Fc^{+/0})$. There was thus little dependence of $E^{\circ\prime}$ on whether the two amide groups were located on the same or different Cp rings. In either case the positive values of $E^{\circ\prime}$ relative to that of ferrocene reflect the electron-withdrawing nature of the amide units.

Electrochemical data for receptors **1**, **3**, **4**, and **6** in the presence of an excess of at least 20 molar equiv of guest are presented in Table 2. Upon addition of the guest species to solutions of the receptors (hosts), the voltammetry remained indicative of a reversible reaction for receptors **4** and **6** with all guests and for receptor **1** with guest **9**, hence enabling determination of $E^{\circ\prime}$ values. A degree of quasi-reversibility ($\Delta E_p = 99$ mV; cf. 67 mV for the internal ferrocene standard) resulted upon addition of guest **9** to receptor **3** but did not prevent reasonable estimation of $E^{\circ\prime}$. In all cases except those of receptor **6** with guests **7** and **8**, $E^{\circ\prime}$ shifted

Table 2. Shift in Formal Potential,[a] $\Delta E^{\circ\prime} = E^{\circ\prime}_{com} - E^{\circ\prime}_{host}$, for the Ferrocene-Centered Redox Couple of Selected Receptors upon the Addition of Substrates in CH_2Cl_2

	guest $\Delta E^{\circ\prime}$/mV		
host	**7**	**8**	**9**
1	*b*	*b*	−15
3	*c*	*b*	−20
4	−60	−50	−35
6	≤−5	≤−5	−35
10	−30	−25	*c*

[a] Formal potentials, $E^{\circ\prime}$, at ambient temperature, referenced to $E^{\circ\prime}(Fc^{+/0})$ as internal reference, were determined as the midpoint between the anodic and cathodic peaks potentials ($E_{pa} + E_{pc}$)/2; the margin of error was ±5 mV. [b] Poorly defined voltammogram; see text for details. [c] Not determined.

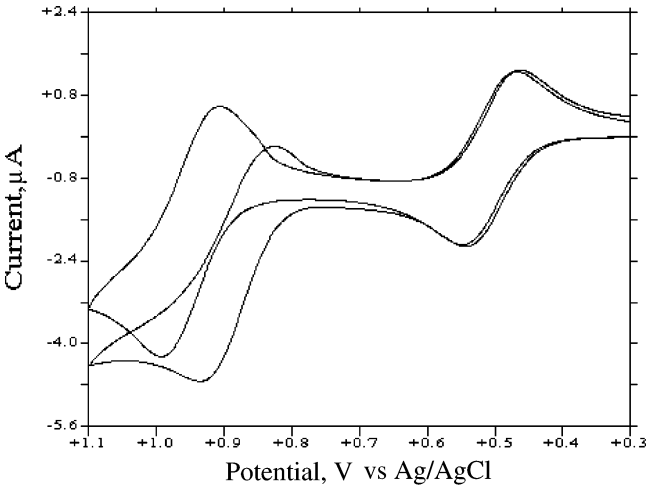

Figure 7. Cyclic voltammograms in CH_2Cl_2 of **4** ($E^{\circ\prime} = 0.95$ V vs Ag/AgCl, 1 mM) overlaid with **4** + excess ethyleneurea (**7**) ($E^{\circ\prime} = 0.89$ V vs Ag/AgCl). Fc^+/Fc was used an internal reference in each case ($E^{\circ\prime} = 0.51$ V vs Ag/AgCl).

negatively relative to that of the receptor alone. These shifts were always coincident with the observation by NMR of significant complexation, and such behavior has been observed previously in related receptor systems where either anions[3] or neutral molecules[4] were bound. In Figure 7 the voltammograms of **4** in CH_2Cl_2 are shown shifting negatively upon the addition of ethyleneurea (**7**) by the amount $\Delta E^{\circ\prime} = -60$ mV, where $\Delta E^{\circ\prime} = E^{\circ\prime}_{com} - E^{\circ\prime}_{host}$. These negative shifts are consistent with the H bond between the amide NH of the receptor and the oxygen of the guest increasing the electron density on the receptor, making the ferrocene unit easier to oxidize.

It has previously been demonstrated that changes in $E^{\circ\prime}$ upon complexation can be used to estimate the host−guest binding constant in different oxidation states of the receptor.[1] The negative shifts upon complexation indicate that the host−guest binding constant increases upon oxidation of the ferrocene unit, leading to binding enhancements of up to 1 order of magnitude (e.g. for receptor **4** and guest **7**, $K_{ox}/K_{red} = 11(\pm 2)$[11]). It is likely that the ferrocenium forms of these receptors bind these guests more strongly, owing to the positive charge withdrawing electron density away from the amide

(11) Estimated[1a−e] using the equation $K_{ox}/K_{red} = \exp[-nF(\Delta E^{\circ\prime})/RT]$; see: Mabbott, G. A. *J. Chem, Educ.* **1983**, *60*, 697.

units, thus making the amide proton a better and stronger hydrogen bond donor. The ferrocene unit is in fact more electron donating than benzene, which may partly explain why receptor **3** binds barbital more weakly than the analogous receptor designed by Hamilton containing a 1,3-isophthalic spacer group.[5a]

Possibly due to insolubility of the complex, particularly in the oxidized form, poorly defined voltammograms were obtained for receptors **1** and **3** in the presence of guests **7** and **8**, precluding determination of $\Delta E^{\circ\prime}$. However, it was possible to determine values of $\Delta E^{\circ\prime}$ for the addition of guest **9**, barbital, to all the receptors. From these, it is clear that the 1,1′-systems provide a larger response to redox to complexation, indicated by an approximate doubling of $\Delta E^{\circ\prime}$ for **4** and **6** compared to **1** and **3**. A possible explanation for this difference comes from the fact that, in the 1,1′-systems, the guest is wedged between the amidopyridine units (Figure 5b) closer to the center of the ferrocene unit, whereas for the 1,3-systems, the guest is bound further away. Consequently, binding has less of an effect on the electronic properties of the ferrocene, so that the complex with the ferrocenium form is stabilized to a lesser extent. Previous studies have shown how the binding by ferrocene receptors of guest species between the 1,1′-derivatized Cp units maximizes the redox response to complexation.[4g,h] Control studies with receptor **10**,[6] which contains only one amidopyridine arm, revealed that the addition of an excess amount (ca. 20 molar equiv) of **7** and **8** induced negative shifts of −30 and −25 mV, respectively, in the values of $\Delta E^{\circ\prime}$ in dichloromethane ($E_{\mathbf{10}}{}^{\circ\prime} = 0.24$ V vs $E^{\circ\prime}(Fc^{+/0})$ before complexation). Clearly, therefore, the magnitude of the redox response observed with receptor **4** and guests **7** and **8** can also be directly related to the participation of both amidopryidine arms in the complexation process.

Conclusion

The complexation of neutral cyclic organic molecules by a series of ferrocene-containing receptors has been achieved through the formation of complementary hydrogen bonds. The presence of the redox-active ferrocene group has allowed the complexation process to be followed and the strength of the host−guest binding interaction to be controlled using electrochemistry. Further studies will be directed toward developing similar redox-switched effects in related host−guest systems.

Experimental Section

General Comments. Reagent grade reactants and solvents were used as received from chemical suppliers. Anhydrous solvents were dried by the usual procedures and were stored over 4 Å molecular sieves. All reactions were carried out under an inert atmosphere of nitrogen. Compounds **4**,[6] **5**,[3h,7] and **10**[6] were prepared according to literature procedures. 1,3-Ferrocene dicarbonyl chloride was prepared by slight modification of literature procedures.[8] Column chromatography was performed on B.D.H. alumina (neutral, Brockman activity I). Mass spectrometry was carried out by the EPSRC National Mass Spectrometry Service at the University of Wales, Swansea, U.K.

Electrochemistry. Cyclic voltammograms were recorded at 293 K using a BAS 100b electrochemical analyzer. The experiments on each receptor (1 mM) were performed in dry, nitrogen-purged CH_2Cl_2, with tetrabutylammonium perchlorate (0.1 M) as supporting electrolyte. A standard three-electrode configuration was employed, with a Pt-disk working electrode, Pt-wire counter electrode, and an Ag/AgCl/$NaCl_{aq}$ (3 M) reference electrode (all BAS electrodes), though all $\Delta E^{\circ\prime}$ values are reported relative to $E^{\circ\prime}(Fc^{+/0})$ added as an internal standard. The potential sweep rate for the voltammograms was 50 or 100 mV s^{-1}.

1,3-Bis[((6-methylpyrid-2-yl)amino)carbonyl]ferrocene (1). Under a nitrogen atmosphere, 1,3-ferrocene dicarbonyl chloride (0.77 g, 2.5 mmol), 2-amino-6-methylpyridine (0.54 g, 5 mmol), and triethylamine (0.556 g, 5.5 mmol) were dissolved in dry dichloromethane (125 mL). The reaction mixture was then stirred for 24 h, before the solvent was removed under reduced pressure. The residue was then purified by chromatography on alumina using dichloromethane as eluant at first and then a mixture of dichloromethane and methanol (99:1). Compound **1** was recrystallized from a mixture of chloroform and diethyl ether; upon standing in a freezer red crystals were obtained (0.188 g, 17%). Anal. Calcd for $C_{24}H_{22}N_4O_2Fe$: C, 63.42; H, 4.88; N, 12.33. Found: C, 63.08; H, 4.72; N, 11.98. MS (FAB+): *m*/*z* 455 (MH^+). Mass: calcd for $C_{24}H_{23}N_4O_2Fe$, 455.170; found, 455.1168. IR (CH_2Cl_2): ν_{NH} 3415 cm^{-1}, ν_{CO} 1680 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, 303 K): δ 2.49 (s, 6H, CH_3), 4.37 (s, 5H, Cp H), 5.08 (s, 2H, Cp H), 5.51 (1H, s, Cp H), 6.94 (d, 2H, $^3J_{HH} = 7$ Hz, py H), 7.63 (dd, 2H, $^3J_{HH} = 7$ Hz, $^3J_{HH} = 8$ Hz, py H), 8.11 (m, 4H, $^3J_{HH} = 8$ Hz, py H and N−H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 303 K): 24.1, 65.8, 68.5, 71.0, 78.5, 110.8, 119.3, 138.8, 150.6, 156.9, 167.2.

1,3-Bis[((6-aminopyrid-2-yl)amino)carbonyl]ferrocene (2). Under a nitrogen atmosphere, 2,6-diaminopyridine (1.88 g, 17.2 mmol) and triethylamine (0.404 g, 4 mmol) were dissolved in dry tetrahydrofuran. Over the course of 3 h, a solution of 1,3-ferrocene dicarbonyl chloride (0.535 g, 1.72 mmol) in dry tetrahydrofuran (20 mL) was added dropwise. The reaction mixture was then stirred for 24 h, before the solvent was removed under reduced pressure. The residue was then purified by chromatography on neutral alumina using dichloromethane as eluant at first and then a mixture of dichloromethane and methanol (99:1), from which an orange band was collected. The dark solid obtained was then washed with diethyl ether, in order to remove the remaining 2,6-diaminopyridine. Compound **2** was recrystallized from a mixture of chloroform and diethyl ether; upon standing in a freezer a pale orange powder was obtained (0.27 g, 32%). Anal. Calcd for $C_{22}H_{20}N_6O_2Fe$ (+1 equiv of H_2O): C, 55.68; H, 4.68; N, 17.72. Found: C, 55.89; H, 4.15; N, 17.83. Mass: calcd for $C_{22}H_{21}N_6O_2Fe$, 457.1075; found, 457.1068. IR (CH_2Cl_2): ν_{NH} 3452 and 3359 cm^{-1}; ν_{CO} 1670 and 1650 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, 303 K): δ 4.36 (s, 5H, Cp-H), 5.04 (s, 2H, Cp H), 5.43 (1H, s, Cp H), 6.29 (d, 2H, $^3J_{HH} = 8$ Hz, py H), 7.50 (dd, 2H, $^3J_{HH} = 8$ Hz, py H), 7.63 (d, 2H, $^3J_{HH} = 8$ Hz, py H and N−H), 7,87 (s, 2H, N−H).

1,3-Bis[((6-propionylaminopyrid-2-yl)amino)carbonyl]ferrocene (3). Under a nitrogen atmosphere, 1,3-bis[((6-amino-2-pyridyl)amino)carbonyl]ferrocene (0.213 g, 0.5 mmol) and triethylamine (0.11 g, 1.1 mmol) were dissolved in dry tetrahydrofuran (15 mL). To this was added dropwise a solution of propionyl chloride (0.5 mL, 5.75 mmol) in tetrahydrofuran (10 mL). After the reaction mixture was stirred overnight, the solvent was removed under reduced pressure. The residue was dissolved in saturated sodium hydrogen carbonate solution (40 mL) and extracted with dichloromethane (3 × 30 mL), and the combined organic layers were dried over anhydrous magnesium carbonate. The solution was then filtered and the solvent removed under reduced pressure. The residue was then purified by chromatography on silica using chloroform as eluant at first and then a mixture of chloroform and methanol (99.5:0.5). Compound **3** was recrys-

tallized from a mix of dichloromethane and diethyl ether; upon standing in the freezer an orange powder was obtained (0.12 g, 42%). Anal. Calcd for $C_{28}H_{28}N_6O_4Fe$ (+0.5 equiv of H_2O): C, 58.22; H, 5.06; N, 14.56. Found: C, 58.23; H, 4.88; N, 14.74. MS (FAB+): *m*/*z* 569 (MH^+). Mass: calcd for $C_{28}H_{29}N_6O_4Fe$, 569.1599; found, 569.1589. IR (CH_2Cl_2): ν_{NH} 3415 cm^{-1}; ν_{CO} 1683. ^1H NMR ($CDCl_3$, 300 MHz, 303 K): δ 1.28 (t, 6H, $^3J_{HH}$ = 7.5 Hz, CH_3), 2.46(q, 4H, $^3J_{HH}$ = 7.5 Hz, CH_2), 4.37 (s, 5H, Cp H), 5.05 (s, 2H, Cp- H), 5.42 (1H, s, Cp H), 7.59 (s, 2H, N−H), 7.76 (dd, 2H, $^3J_{HH}$ = 8 Hz, py H), 7.84 (s, 2H, N−H), 7.97 (m, 4H, py H).

1,1′-Bis[((6-propionylaminopyrid-2-yl)amino)carbonyl]ferrocene (6). Propionyl chloride (0.4 g, 4.38 mmol) in anhydrous THF (15 cm^3) was added dropwise, at 0 °C, to a stirred solution of **5** (1.0 g, 2.19 mmol) and triethylamine (0.44 g, 4.38 mmol) in dry THF (40 cm^3). The reaction mixture was stirred for 6 days. The solution was concentrated in vacuo and the resulting solid dissolved in CH_2Cl_2 (50 cm^3) and washed with saturated sodium hydrogen carbonate solution (3 × 50 cm^3). The organic phase was dried over magnesium sulfate and filtered and the solvent removed. The crude product was purified by column chromatography on neutral alumina (CH_2Cl_2) and recrystallized from CH_2Cl_2−hexane to yield pure **6** (0.57 g, 1.0 mmol, 46%) as an orange solid. Mp: 125 °C dec. Anal. Calcd for $C_{28}H_{28}N_6O_4Fe$ (+1.0 equiv H_2O): C, 57.4; H, 5.2; N, 14.3. Found: C, 56.9; H, 5.1; N, 13.8. UV/vis (λ_{max}/nm (ϵ/mol^{-1} dm^3 cm^{-1}); CH_2Cl_2): 448 (365). IR (CH_2Cl_2): ν_{max}(C=O) 1697/1679 cm^{-1}. ^1H NMR(400 MHz, $CDCl_3$): δ 8.00 (2H, s, N*H*COFc), 7.89 (2H, d, *J* = 9.2 Hz, C*H*C(N)NHCOEt), 7.86 (2H, d, *J* = 8.1 Hz, C*H*C(N)NHCOFc), 7.63 (2H, t, *J* = 8 Hz, C*H*CHC(N)NH), 7.52 (2H, s, N*H*COEt), 4.83 (4H, t, *J* = 2 Hz, C*H*C(CONH)), 4.54 (4H, t, *J* = 1.9 Hz, C*H*CHC(CONH)), 2.42 (4H, q, *J* = 7.4 Hz, C$H_2$$CH_3$), 1.27 (6H, t, *J* = 7.6 Hz, CH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.06 (Fc*C*ONH), 167.73 (Et*C*ONH), 149.54 (N*C*(NH)CH), 149.42 (N*C*(NH)CH), 140.59 (*C*HCHC(N)NH), 109.42 (*C*HC(N)NH), 109.28 (*C*HC(N)NH), 77.60 (*C*CONH), 72.52 (*C*HCHC(CONH)), 70.49 (*C*HC(CONH)), 30.78 (*C*$H_2$$CH_3$), 9.28 ($CH_2$*C*$H_3$). MS (*m*/*z*; EI): 569 (M^+).

Collection and Refinement of X-ray Diffraction Data for 1 and 6. Data were collected by means of combined ψ and ω scans on a Nonius KappaCCD area detector situated at the window of a Nonius FR591 rotating anode (λ(Mo Kα) = 0.710 73 Å). The structures were solved by direct methods with SHELXS-97 and refined using SHELXL-97.[12] Hydrogen atoms were included in the refinement, but thermal parameters and geometry were constrained to ride on the atom to which they are bonded. The data were corrected for absorption effects using SORTAV.[13] The data for **6** were very weak, due to the crystal size, and despite several attempts to collect data it was not possible to obtain diffraction out to high angle, causing difficulties in the structure refinement. A highly disordered diethyl ether solvate is present in the structure of **1**, which was modeled over several fractionally occupied positions. Supplementary data in the form of CIF files have been deposited with the Cambridge Crystallographic Data Centre under the numbers CCDC 217298 (**1**) and CCDC 217299 (**6**). Geometrical and crystallographic data are summarized in Table 3, while the molecular structures are presented in Figures 2 and 3.

Table 3. Crystallographic Data for Compounds 1 and 6

	6	**1**
empirical formula	$C_{28}H_{28}FeN_6O_4$	$C_{24}H_{22}FeN_4O_2 \cdot C_4H_{10}O$
formula wt	568.41	528.44
cryst syst, space group	hexagonal, $P3_2$	monoclinic, *C*2/*c*
a/Å	14.0600(7)	11.862(2)
b/Å	14.0600(9)	17.910(4)
c/Å	15.9528(13)	24.123(5)
α/deg	90	90
β/deg	90	90.95(3)
γ/deg	120	90
V/$Å^3$	2731.1(3)	5124.2(18)
Z, calcd density (Mg m^{-3})	3, 1.037	8, 1.344
abs coeff (mm^{-1})	0.448	0.625
F(000)	888	2144
cryst size (mm^3)	0.30 × 0.02 × 0.02	0.3 × 0.15 × 0.15
θ range (deg)	3.05−23.25	3.24−27.50
no. of rflns collected/unique	30 746, 5221	24 406/5830
R_{int}	0.1515	0.0744
no. of data/restraints/params	5221/240/311	5830/30/363
final *R* indices ($I > 2\sigma(I)$): R1, wR2	0.1338, 0.3369	0.0623, 0.1642
R indices (all data): R1, wR2	0.1827, 0.3684	0.1144, 0.1872
ρ_{max}, ρ_{min} (e $Å^{-3}$)	0.609, −0.500	0.677, −0.630

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Supporting Information Available: Figures giving intermolecular H-bonded arrays and thermal ellipsoid plots for **1** and **6**; crystal data are given as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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