Neutral Ferrocenoyl Receptors for the Selective Recognition and Sensing of Anionic Guests

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A range of neutral, hydrogen-bonding ferrocenoyl anion receptors and redox sensors operable in nonaqueous solvents are reported and a series of anion-binding and -sensing experiments presented. Thioamide-based receptor **L2** binds halide anions more effectively than its carboxamide analogue **L1**, with the thioamide (N−H) group proving to be a better NMR antenna for detecting the recognition event. The binding of this class of neutral hydrogen-bonding receptor has favorable $\Delta H°$ and unfavorable $\Delta S°$. Multidentate amide receptor **L5** binds halide guests more strongly, with the effect of solvent on this binding process being studied. The introduction of a primary amine functionality (**L4**) causes remarkably strong HSO_4^- binding, the first reasoned report of selectivity for this acidic anionic guest. Analogously to many biological anion recognition processes, different binding modes operate dependent on guest acidity. In this way, the chemical properties of the substrate are addressed, yielding novel anion selectivities. All the receptors investigated exhibit electrochemical anion recognition. Typically, an EC mechanistic response is observed as ferrocene oxidation "switches-on" electrostatic interactions with the bound guest. Remarkable cathodic shifts of the ferrocene oxidation wave are also induced (up to 220 mV with HSO_4^- and 240 mV with $H_2PO_4^-$) as the proximate bound negative charge stabilizes positively charged ferrocenium. Difunctional receptor **L8** shows a large, novel UV−visible spectroscopic enhancement with $H_2PO_4^-$.

Introduction

Effective biological function requires the selective recognition and binding of active substrates.[1] Interestingly, the majority of enzyme substrates are negatively charged,[2] and it is, therefore, perhaps surprising that the field of anion coordination chemistry only came to prominence relatively recently. From the first reports of anion receptors in the late 1960s,[3] research has progressed with gathering speed.[4] Receptors can bind anionic guests with various physical interactions. Polynuclear Lewis acidic receptors bind anions via the formation of multiple *orbital overlap interactions*,[5] as do coordination arrays of positively charged metal ions.[6] Positively charged quaternized nitrogen hosts ensnare anionic guests using *electrostatic interactions*,[7] as do multimetal-centered cages.[8] Electrostatic forces are supplemented by *hydrogen bonds* for protonated polyammonium,[9] expanded porphyrin,[10] and guanidinium[11] derivatives. Neutral *hydrogen bond donors* have also been used for anion binding, with particular interest in amide[12] and urea[13] groups.

Interestingly, reports of the design and synthesis of receptors capable of optically[14] or electrochemically[15] detecting the bound anion are rare. An efficient way of achieving *sensing* is to incorporate metal centers into the receptor.[16] We have previously reported the first classes of redox-responsive anion receptors containing H-bonding amide (CO−NH) linked cobaltocenium organometallic groups[17] or ruthenium(II) bipyridyl coordination groups.[18] They bind and electrochemically rec-

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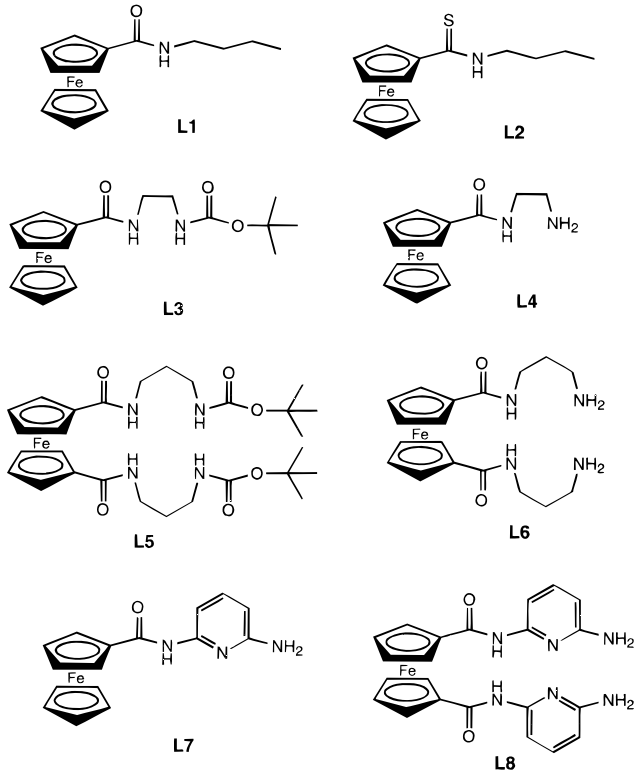
Table 1. Structures of Receptors **L1**−**L8**



ognize anionic guests in polar solvents, functioning via hydrogen bonds between amide and anion, supplemented by electrostatic interaction with the cationic metal center. Recently, however, we also reported *neutral anion receptors* appended with ferrocene functional groups.[19] *Ferrocene is a unique functional handle* because it does not directly interact with the anion until it is oxidized to the ferrocenium cation, at which stage electrostatic interactions with the guest are "switched-on". In this paper, the preparations of a series of simple amide-functionalized ferrocene derivatives are described (Table 1) and their anion recognition properties investigated. The thermodynamics of anion coordination and the effect of solvent on neutral hydrogen-bond-donating receptors are both reported.

In the past, the development of neutral receptors utilizing hydrogen-bond *donors* has been stressed as a way of introducing anion selectivity analogous to that of enzymes.[20] Most of the synthetic receptors reported so far, however, select $H_2PO_4^-$ over HSO_4^-. This would be expected because of the greater basicity of the former anion and its consequent ability to form stronger hydrogen bonds.[21a] Nature, however, uses a variety of hydrogen-bonding groups, *both donors and acceptors*, to discriminate between anionic guests,[21b,c] and we therefore report the incorporation of neutral amine groups into the receptors. These groups can act as both hydrogen-bond donors and acceptors,

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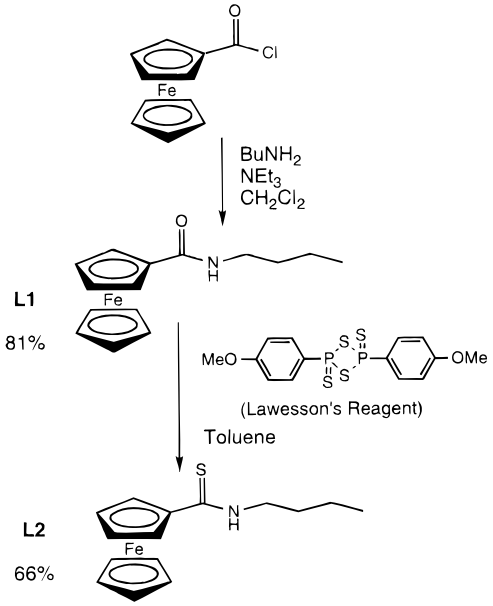
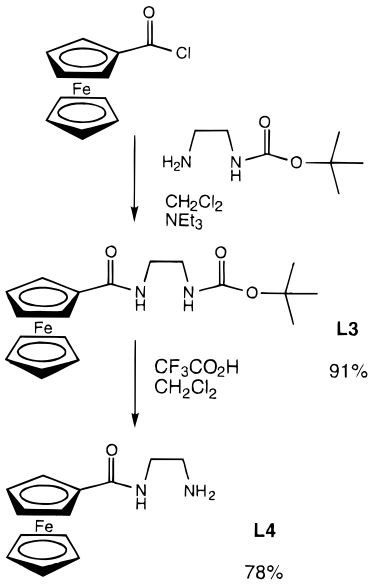
Scheme 1. Synthesis of Receptors **L1** and **L2**



Scheme 2. Synthesis of Receptors **L3** and **L4**



tuning the recognition process and leading to *novel anion selectivities*. Emphasis is placed on the potential of all these novel receptors as *anion-selective redox sensors*.

Results and Discussion

Synthesis of Anion Receptors. The novel acyclic amide-substituted ferrocenes were prepared in good yield via condensation reactions. ((Butylamino)carbonyl)ferrocene (**L1**) was synthesized by the condensation of (chlorocarbonyl)ferrocene with 1-aminobutane and 1 equiv of triethylamine in CH_2Cl_2 (Scheme 1).[19c] Compound **L1** was converted to ((butylamino)-thiocarbonyl)ferrocene (**L2**) by refluxing with Lawesson's reagent in toluene.

Receptors **L3**−**L6** were synthesized using protecting-group methodology. (Chlorocarbonyl)ferrocene was condensed with mono-BOC-protected 1,2-diaminoethane, producing **L3** in high yield. Trifluoroacetic acid was then used to remove the BOC protecting group, giving a high yield of mixed amide−amine receptor **L4** (Scheme 2). Receptor **L5** was synthesized by the condensation of 1,1′-bis(chlorocarbonyl)ferrocene with 2 equiv

Table 2. Stability Constants Derived from Proton NMR Titrations (Errors ≤10%) Measured at 25 °C

receptor	solvent	anion	K (M^{-1})
L1	$CDCl_3$	Cl^-	4.7
L1	$CDCl_3$	$H_2PO_4^-$	5.0[a]
L2	$CDCl_3$	Cl^-	21
L2	$CDCl_3$	$H_2PO_4^-$	6.0
L3	$CDCl_3$	$H_2PO_4^-$	5.0[a]
L3	$CDCl_3$	HSO_4^-	8.5[a]
L4	$CDCl_3$	NO_3^-	15
L4	$CDCl_3$	$H_2PO_4^-$	120
L4	$CDCl_3$	HSO_4^-	>10 000
L4	CD_3CN	Cl^-	17
L4	CD_3CN	$H_2PO_4^-$	130
L4	CD_3CN	HSO_4^-	7500
L5	$CDCl_3$	Cl^-	22.5
L5	$CDCl_3$	Br^-	24
L5	$CDCl_3$	I^-	23
L5	$CD_3CN/CDCl_3$ (50:50)	Cl^-	29.5
L5	DMSO	Cl^-	5.0

[a] Errors ≤33% due to very weak titration profiles.

of monoprotected 1,3-diaminopropane. Deprotection was achieved using CF_3CO_2H/CH_2Cl_2 (50/50), forming receptor **L6**, which was unstable, especially in solution.

Receptor **L7** was synthesized by reacting (chlorocarbonyl)-ferrocene with a solution of 2,6-diaminopyridine (1 equiv), triethylamine (1 equiv), and a small quantity of 2-(dimethylamino)pyridine in CH_3CN.[19c] Receptor **L8** was synthesized by condensing 1,1'-bis(chlorocarbonyl)ferrocene with an excess (10 equiv) of 2,6-diaminopyridine and triethylamine (1 equiv) in CH_2Cl_2.

Anion Coordination Investigations.[22] **(a) Proton NMR studies.** The recognition of anions in solution was initially investigated by ^{1}H NMR titrations. This approach allows an accurate characterization of the interaction between the uncharged receptors and various anionic guests. The addition of tetrabutylammonium anion salts to $CDCl_3$, CD_3CN, or DMSO-d_6 NMR solutions of the receptors led to perturbations of the receptors' proton resonances. In particular, the N−H resonance shifted downfield, indicative of the formation of a hydrogen bond between this group and the anionic substrate.

Receptors **L1** and **L2** were titrated with tetrabutylammonium chloride in $CDCl_3$. The halide guest caused a much larger perturbation of **L2** (0.6 ppm with 1 equiv) than of **L1** (0.1 ppm with 1 equiv). This was also true for the addition of $H_2PO_4^-$ to these receptors. The thioamide therefore acts as a more *sensitive NMR antenna* for detecting the presence of anionic guests. The curvature of these titration profiles was used to evaluate stability constants via the EQNMR computer program by assuming a 1:1 binding stoichiometry (Table 2).[23] The binding constants are low (the receptor is neutral and can only form a single H-bond), but it is notable that the chloride anion is more strongly bound by thioamide **L2**. This parallels recent investigations which have shown thioureas to be more effective for anion binding than their urea analogues.[13b] The observation can be theoretically justified by the greater acidity of thioamides compared to carboxamides,[24] the amide proton being more able to form hydrogen bonds.

A variable-temperature NMR investigation of a 1:1 mixture of **L2** and tetrabutylammonium chloride in $CDCl_3$ was performed. On lowering of the temperature, a large downfield shift of the NMR peaks was observed (i.e., the coordination equilibrium shifts toward the complex). Using a method recently reported by Davies and co-workers,[25b] the thermodynamic parameters for the anion coordination equilibrium were evaluated (assuming they are invariant with temperature). The derived *thermodynamic parameters* from both N−H and Fc H proton fitting show tolerable agreement (Figure 1), and consequently, although crude,[26] this method probably gives a good indication of $\Delta H°$ and $\Delta S°$ values for this class of H-bond-donating receptor. $\Delta H°$ is favorable (the formation of an H-bond releasing energy), while $\Delta S°$ is unfavorable (presumably due to the association of two mobile species and the loss of receptor conformational freedom). A balance between favorable $\Delta H°$ and unfavorable $\Delta S°$ is a common feature of the recognition event in both chemistry and biology.[27]

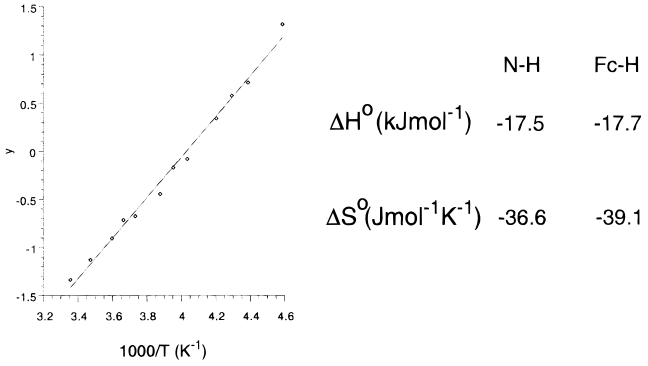


Figure 1. Fitting of VT ^{1}H NMR data to obtain thermodynamic parameters.

Multidentate anion receptor **L5** was investigated with halide anions in $CDCl_3$. The amide proximate to the ferrocene group is more perturbed than that close to the *tert*-butyl site, but as the size of the anion increases ($Cl^- < Br^- < I^-$), this effect becomes less pronounced. This is possibly because the larger ionic radius of the iodide anion allows it to bridge the two amide groups more effectively. EQNMR was once again used to calculate stability constants (Table 1). These binding constants are higher than those for **L1**, showing the benefit of a *multidentate binding site*. Such multidentate binding sites are, of course, extensively used by enzymes.[28] Perhaps surprisingly, **L5** did not bind chloride more strongly than it bound iodide in spite of its higher charge density. This may be due to the greater ability of I^- to bridge the two N−H groups, offsetting its lower charge density, but solvent effects may also be important, with tetrabutylammonium chloride showing more aggregation in nonpolar solvents such as $CDCl_3$, hindering its recognition (see below).

The effect of solvent on anion coordination was investigated. Tetrabutylammonium halides associate in nonpolar solvents.[29]

(22) Numerous attempts to isolate anion complexes in the solid state were made. These were unsuccessful, possibly due to the neutrality of the receptor systems.

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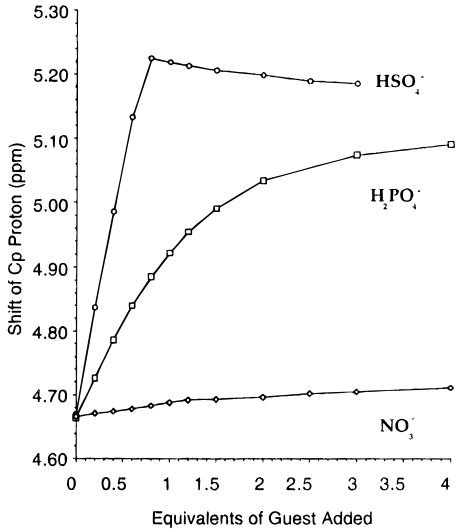

Figure 2. ^{1}H NMR titration curves for receptor **L4** with anionic guests (in $CDCl_3$).

The importance of such ion pairing was shown by following the NMR resonance of the tetrabutylammonium (chloride) cation in the presence of varying mole fractions of **L5**. In $CDCl_3$, the environment of Bu_4N^+ is dependent on the quantity of receptor present. This indicates that **L5** and Bu_4N^+ both compete for the anionic guest and highlights the importance of ion-pairing in $CDCl_3$. Obviously in more polar solvents such as DMSO these effects are reduced and the tetrabutylammonium cation is unaffected. Stability constants for **L5** with Cl^- were determined in various solvents (Table 2). In DMSO, binding was very weak, which is a consequence of the amide receptor being heavily solvated, hindering interaction with the anionic guest.[30] Even in mixed $CD_3CN/CDCl_3$, the dipolar solvent can solvate the anion, limiting the value of *K*.[29b]

Difunctional "amide−amine" receptor **L4** strongly binds some anionic guests (Figure 2, Table 2), in particular HSO_4^-. Normally, however, neutral hydrogen-bond-donating receptors select $H_2PO_4^-$ over HSO_4^-, because the former anion is more basic and better able to accept hydrogen bonds from the N−H groups.[21,31] Comparison of the stability constants with those for **L3** in $CDCl_3$ clearly shows that the presence of the amine group is essential for strong HSO_4^- binding (Table 2). Examining the relative perturbations at the different protons of **L4** on the addition of 1 equiv of guest anion also yields an interesting conclusion (Figure 3). HSO_4^- causes a larger relative perturbation at the "amine end" of the difunctional receptor, while $H_2PO_4^-$ (and also Cl^- and NO_3^-) interacts more strongly at the "amide end". HSO_4^- is considerably more acidic than $H_2PO_4^-$,[21a] and it is therefore probable that the amine group of **L4** can act as a base, accepting a proton from this guest. If guest acidity is indeed important, then carboxylic acids should also interact with **L4**. Bromoacetic acid interacts similarly to HSO_4^- with **L4** but causes a smaller perturbation of NMR peaks. Apart from illustrating the importance of guest acidity, this also proves that the process is guest sensitive; *i.e., proton transfer is accompanied by hydrogen-bond formation and anion coordination*. The formation of a charge-separated hydrogen bond would be consistent with stronger HSO_4^- binding in less polar $CDCl_3$ than in CD_3CN, as is indeed observed. The titrations of **L4** with acidic guests in $CDCl_3$ showed unusual line shapes (e.g., Figure 2) which may be explained by the

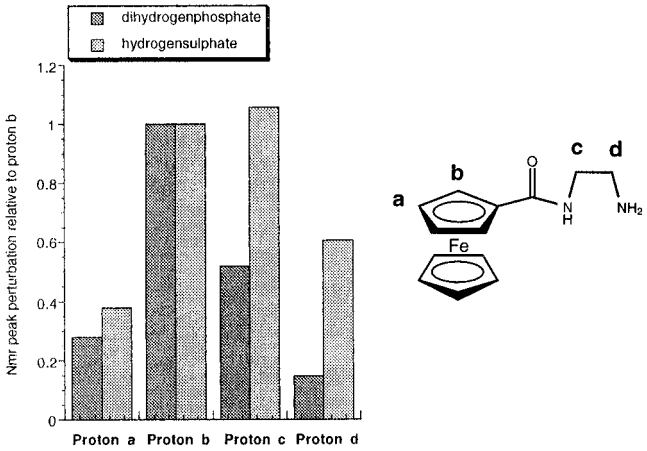

Figure 3. Relative ^{1}H NMR peak perturbations of receptor **L4** with $H_2PO_4^-$ and HSO_4^- guests in $CDCl_3$.

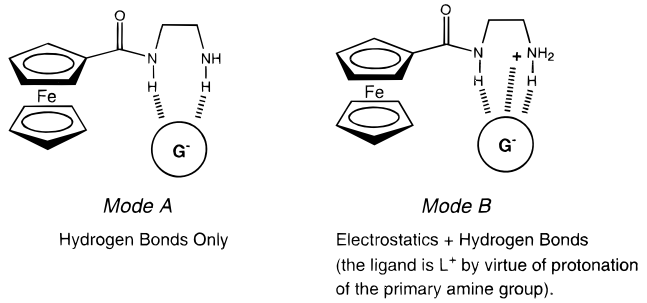

Figure 4. Two different modes of anion binding operating for difunctional receptor **L4**.

contribution of an aggregated component of higher stoichiometry (2:1 anion:**L4**).

It is therefore proposed that **L4** shows two different modes of anion binding (Figure 4). Mode A operates for nonacidic guests and relies on the receptor donating hydrogen bonds from the amide (and probably to a lesser extent amine)[17b] group to the guest. Mode B operates for acidic guests and consists of proton transfer followed by hydrogen bonding and electrostatic interaction with the resultant guest anion. It is probable that the moderately strong $H_2PO_4^-$ binding lies intermediate between these two modes for **L4**.

To the best of our knowledge, this is the first report of a receptor making use of this type of *chemical selectivity* to yield a novel order of anion coordination strength.

Mixed amide−amine receptor **L8** was also investigated using NMR titration methods. Unfortunately, partial precipitation during NMR titrations prevented EQNMR analysis, although titration curves were sharp for both $H_2PO_4^-$ and HSO_4^-. The NMR peaks shifted dramatically. Similar to the case of **L4**, the protons most affected during the titration were dependent on the guest added, with HSO_4^- causing a greater relative perturbation of Ar H (proximate to amines) and $H_2PO_4^-$ a greater relative perturbation of Fc H (proximate to amide).

(b) Electrochemical Studies. An important feature of novel receptors **L1**−**L8** is the incorporation of a redox center proximate to the anion-binding site. This gives these receptors the capability of electrochemically sensing anionic guests.

The cyclic voltammetry of **L1** with anionic guests has been reported elsewhere.[19c] In summary, no electrochemical shift of the ferrocene oxidation wave was observed on the addition of chloride anions. The reduction wave, however, flattened, the redox process becoming irreversible. This is indicative of an EC mechanism: after the ***e***lectron transfer of the oxidation, a ***c***hemical process occurs which prevents reduction from being

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Table 3. Electrochemical Data for Free Receptors Measured at 25 °C

receptor	solvent	$E_{1/2}$ (V)
L1	CH_3CN	0.18
L2	CH_3CN	0.21
L4	CH_3CN	0.27
		0.70[a] (amine)
L5	$CH_3CN/CHCl_3$ (50:50)	0.41
L7	CH_3CN	0.22
		0.95[a] (amine)
L8	CH_3CN	0.49[a]
		0.73[a] (amine)

[a] Irreversible redox wave; thereore, E_{pa} quoted.

Table 4. Electrochemical Response of Receptors to Anionic Guests Measured at 25 °C

receptor	solvent	anion	ΔE_{pa}[a] (mV)
L1	CH_3CN	Cl^-	0
L2	CH_3CN	Cl^-	0
L4	CH_3CN	Cl^-	35
L4	CH_3CN	$H_2PO_4^-$	165
L4	CH_3CN	HSO_4^-	220
L4	CH_3CN	$BrCH_2COOH$	0
L5	$CH_3CN/CHCl_3$ (50:50)	Cl^-	80
L5	$CH_3CN/CHCl_3$ (50:50)	Br^-	45
L7	CH_3CN	Cl^-	10
L7	CH_3CN	$H_2PO_4^-$	120
L7	CH_3CN	HSO_4^-	5
L8	CH_3CN	Cl^-	50
L8	CH_3CN	$H_2PO_4^-$	240
L8	CH_3CN	HSO_4^-	85

[a] Cathodic shift of oxidation peak after the addition of 5 equiv of guest.

observed (e.g., adsorption of the oxidized complex onto the working electrode surface). Receptor **L2**, like **L1**, also showed a single reversible CV wave although at a more cathodic potential, indicating a greater degree of electron withdrawal by the thioamide, hindering ferrocene oxidation (Table 3). As for receptor **L1**, however, the addition of chloride anions caused no shift of the oxidation wave. The reduction wave, however, diminished in intensity, indicating a clear *EC mechanistic response* to the addition of chloride anions. The chloride anion has no effect on the cyclic voltammogram of unfunctionalized ferrocene in acetonitrile, proving the *presence of the H-bond-donating amide unit is essential*.[19c]

Receptor **L5** was investigated in mixed CH_3CN/CH_2Cl_2 (50:50) due to lack of solubility in CH_3CN. The receptor showed a single reversible redox wave. Halide anions were added in substoichiometric quantities, and once again, an onset of EC mechanistic behavior was observed, with the reduction peak flattening. In this case, however, the potential of the *oxidation peak shifted cathodically*, the coordination of an anionic guest close to the ferrocene group facilitating its oxidation (Table 4). The redox shifts are among the largest reported for electrochemical halide recognition. Chloride invoked a larger electrochemical response than bromide probably because of its higher negative charge density. Unsubstituted ferrocene was investigated in this solvent mixture (to ensure that simple ion-pairing was not the cause of the redox response) but showed no response to halide guests.

Mixed amide−amine receptor **L4** was investigated in CH_3CN solution by cyclic voltammetry and showed *dramatic redox responses with anionic guests* (Table 4). A reversible wave attributable to the ferrocene subunit ($E = 0.27$ V) and an irreversible secondary oxidation wave ($E = 0.7$ V) probably corresponding to the amine oxidation process were observed. The addition of tetrabutylammonium chloride caused the onset of EC mechanistic behavior and a cathodic shift of the oxidation wave (as for **L5**). Notably, the amine oxidation peak disappeared, providing tentative evidence for the involvement of this group in halide coordination (through the formation of a hydrogen bond).[17b] Tetrabutylammonium *hydrogen sulfate*, however, caused a *remarkable response*. A new oxidation peak emerged at a potential cathodically shifted 220 mV from that of the free receptor (the largest redox response to this guest). Therefore, the strong coordination of HSO_4^- (in the form of doubly charged SO_4^{2-} with proton transfer) substantially affects the ease of receptor oxidation. Once again, the CV became irreversible, but in this case a reductive stripping peak was observed. This indicates that the oxidised complex is adsorbed onto the electrode surface and then at a particular reduction potential desorption occurs, a large current being observed. Tetrabutylammonium dihydrogen phosphate showed a response intermediate between the two extremes above. The oxidation peak shifted 165 mV cathodically but the reduction behavior was more complex. The CV became irreversible, and between 2 and 4 equiv of $H_2PO_4^-$ addition, a small stripping peak was observed. This stripping peak, however, disappeared on the addition of further $H_2PO_4^-$. This provides further evidence for $H_2PO_4^-$ binding intermediately between modes A and B (Figure 4). It should be noted that dihydrogen phosphate caused a similar stripping reponse of unfunctionalized ferrocene but *no cathodic shift* of the oxidation wave.[19c] Finally, the effect of $BrCH_2COOH$ on the receptor was investigated. It caused no electrochemical response, consistent with its coordination at the amine group (and little interaction with the amide) too distant from the redox center to communicate its presence. Receptor **L4**, therefore, shows an electrochemical response to anionic guests which mirrors its novel selectivity for HSO_4^-. This illustrates the ability of the *ferrocene functional antenna* to *detect and report* subtle recognition events.

The electrochemical behavior of **L7** and **L8** with anionic guests was also investigated in acetonitrile solution. Receptor **L7** showed a reversible redox wave attributable to the ferrocene group and a secondary irreversible amine oxidation wave. Receptor **L8** showed an irreversible ferrocene oxidation wave and an irreversible amine oxidation wave. On immediate repetition of the scan, no redox current was observed, indicating that oxidized **L8** adsorbs onto the working electrode. Receptor **L7** showed electrochemical behavior with anions analogous to that of **L4**, except that the cathodic shift induced by HSO_4^- was much diminished (Table 4). Receptor **L8** gave large redox responses with all the anionic guests (Table 4), $H_2PO_4^-$ causing one of the largest anion-induced electrochemical responses yet reported (240 mV). The redox wave of **L8** remained irreversible. Receptor **L8** showed larger redox responses than **L7**, presumably because of the greater ability of two amide groups to *communicate* anion recognition to the ferrocene subunit.

(c) UV−Visible Spectroscopy. In general, these receptors showed minimal UV−visible responses to the addition of anionic guest species. Receptor **L8**, however, showed a particularly interesting UV−visible reponse to the addition of $H_2PO_4^-$ (Figure 5). The d−d band at 443 nm (in CH_3CN) shifted 10 nm to shorter wavelength and showed a large (500%) increase in intensity. This change was visible to the naked eye, with the solution becoming brighter in color. The addition of tetrabutylammonium hydrogen sulfate caused no such UV response, the d−d band being perturbed by less than 10%. Interestingly, however, the presence of 5 equiv of HSO_4^- inhibited the response of the receptor to $H_2PO_4^-$. This is in

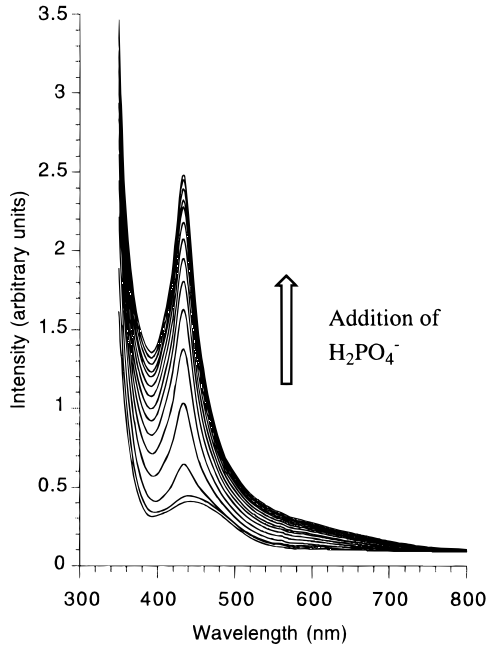

Figure 5. UV−visible spectroscopic response of receptor **L8** to $H_2PO_4^-$ in CH_3CN.

agreement with the NMR and electrochemical results for **L8** discussed above. Acidic HSO_4^- binds to the receptor primarily at the amine units, distant from the ferrocene group and leaving its UV−vis spectrum relatively unaffected. Basic $H_2PO_4^-$, however, binds primarily at the amide units (binding strength enhanced by the amine groups) proximate to the ferrocene unit, causing a large UV perturbation. The presence of bound HSO_4^-, therefore, sterically and electronically hinders $H_2PO_4^-$ binding and diminishes the UV−vis response. Interestingly, receptor **L7**, with only one amide substituent, did not show this type of UV−visible response to $H_2PO_4^-$. Receptor **L8** is therefore one of the first to incorporate hydrogen-bond-acceptor and -donor sites for anion binding and also a ferrocene group which *reports on the novel modes of anion recognition by UV−visible spectroscopy*.

Conclusions

A range of new ferrocene-based neutral anion receptors and sensors operable in nonaqueous solvents have been reported. Thioamide **L2** binds halide anions more effectively than **L1**, with the thioamide group proving a better NMR antenna for detecting the recognition event. The binding of this class of receptor has favorable $\Delta H°$ and unfavorable $\Delta S°$. Both receptors showed EC electrochemical responses to anionic guests. Multidentate **L5** binds halide guests more strongly and electrochemically senses their presence by cathodic shifts of its oxidation wave. A range of solvent effects was shown to be applicable for this type of neutral hydrogen-bond-donating receptor.

The introduction of an amine unit yielded difunctional receptor **L4**, which is capable of both donating and accepting hydrogen bonds. This receptor showed a remarkably strong NMR and electrochemical response to HSO_4^-. The amine group therefore yields novel selectivity for acidic anionic guests. This was attributed to two different binding modes for this type of receptor dependent on guest acidity (Figure 7). Receptor **L8** showed a remarkable response to $H_2PO_4^-$, with an electrochemical cathodic shift of 240 mV and a large UV−visible spectroscopic enhancement. Once again, different sites of primary interaction were proposed for this host dependent on guest acidity.

These receptors show great potential for the development of novel electrochemical sensory devices and indicate the way in which subtle binding site modifications, inspired by biology, can lead to dramatic fundamental changes in anion recognition properties. It is hoped that, in the future, the simple effects discussed will be incorporated into structurally more complex hosts to achieve selective electrochemical sensing of complex biologically functional anionic guests.

Experimental Section

Solvent and Reagent Pretreatment. Where necessary, solvents were purified prior to use and stored under nitrogen. Acetonitrile was predried over class 4 Å molecular sieves (4−8 mesh) and then distilled under nitrogen from calcium hydride. Dichloromethane was distilled from calcium hydride, toluene was dried by distillation from sodium, and triethylamine was distilled from KOH. Unless otherwise stated, commercial grade chemicals were used without any further purification. (Chlorocarbonyl)ferrocene,[32] 1,1′-bis(chlorocarbonyl)ferrocene,[33] *N*-(*tert*-butoxycarbonyl)-1,2-ethanediamine,[34] *N*-(*tert*-butoxycarbonyl)-1,3-propanediamine,[34] and receptors **L1** and **L7**[19c] were synthesized via literature procedures.

Instrumentation. NMR spectra were recorded on either a Bruker AM 300 instrument or a Varian Unity Plus 500 machine. The Bruker spectrometer operates at 300 MHz for ^{1}H NMR and 75.47 MHz for ^{13}C NMR. The Varian spectrometer functions at 500 MHz for ^{1}H NMR and 125.7 MHz for ^{13}C NMR. In both cases, the solvent deuterium signal was used as the internal reference. All elemental analyses were carried out by the Inorganic Chemistry Laboratory Microanalysis Service of this university. Fast atom bombardment (FAB) mass spectrometry was performed at the University College of Swansea by the EPSRC service. Infrared spectra were recorded on a Mattson 10410E Polaris Fourier transform spectrometer scanning from 4000 to 400 cm^{-1}, ultraviolet−visible spectrometry was carried out on a Perkin-Elmer Lambda 6 UV−vis spectrophotometer, and electrochemical measurements were obtained on a Princeton Applied Research potentiostat/galvanostat, Model 273. The working electrode was glassy carbon, the counter electrode platinum wire, and the reference electrode Ag/Ag^+ (in CH_3CN).

Syntheses of Receptors. [(Butylamino)thiocarbonyl]ferrocene (L2). Receptor **L1** (0.1 g) was dissolved in dry toluene (30 mL), and the mixture was refluxed for 4 h with Lawesson's reagent (0.085 g).[35] A color change from yellow to orange-red was observed. The reaction mixture was evaporated to dryness. Column chromatography eluting with CH_2Cl_2/MeOH (98:2), followed by recrystallization from MeOH/H_2O, gave pure product. Yield: 66% (0.07 g). ^{1}H NMR ($CDCl_3$): δ 7.23 (1H, b s, N−*H*), 4.83 (2H, dd obs t (J = 1.89 Hz), Fc *H*), 4.27 (2H, dd obs t (J = 1.88 Hz), Fc *H*), 4.19 (5H, s, Fc *H*), 3.78 (2H, q (J = 6.66 Hz), C*H*$_2$−NH), 1.72 (2H, quin (J = 7.17 Hz), C−C*H*$_2$−C), 1.47 (2H, sex. (J = 7.41 Hz), C−C*H*$_2$−C), 1.01 (3H, t (J = 7.33 Hz), C*H*$_3$). ^{13}C NMR: δ 199.3 (*C*═S), 83.87 (Fc *C*−C), 70.94 (Fc *C*−H), 70.59 (Fc *C*−H), 68.54 (Fc *C*−H), 45.38 (*C*−N), 30.43 (*C*H$_2$), 20.19 (*C*H$_2$), 13.77 (*C*H$_3$). Anal. Calcd for $FeC_{15}H_{19}NS·0.5H_2O$: C, 58.07; H, 6.50; N, 4.51. Found: C, 58.44; H, 5.95; N, 3.77. FABMS, *m*/*z*: 301 (M)$^+$, 236 (M − Cp)$^+$, 180 (M − FeCp)$^+$, 121 (M − CpCSNH-(CH$_2$)$_3$CH$_3$)$^+$. IR (KBr disk), cm^{-1}: 3316 (N−H stretch), 2957/2930 (C−H stretches), 1531 (C═S(I)), 1279 (C═S(II)).

[((*N*′-(*tert*-Butoxycarbonyl)-2-aminoethyl)amino)carbonyl]ferrocene (L3). (Chlorocarbonyl)ferrocene (0.7 g) was dissolved in dry dichloromethane (25 mL), and the solution was added dropwise under nitrogen to a stirred solution of *N*-(*tert*-butoxycarbonyl)-1,2-ethanediamine (0.45 g) and triethylamine (0.31 g), also in dry CH_2Cl_2 (25 mL). The mixture was stirred for 20 h and then washed with water (3 × 50 mL) and dried over $MgSO_4$. The solvent was removed in vacuo, revealing a crude orange product. This was purified by silica gel

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column chromatography, eluting with CH_2Cl_2/MeOH (90:10). Yield: 91% (0.96 g). ^{1}H NMR ($CDCl_3$): δ 6.67 (1H, b s, N−*H*), 5.13 (1H, b s, N−*H*), 4.71 (2H, dd obs s, Fc *H*), 4.33 (2H, dd obs s, Fc *H*), 4.20 (5H, s, Fc *H*), 3.44 (2H, d (J = 4.80 Hz), CH_2−N), 3.36 (2H, t (J = 4.81 Hz), CH_2−N), 1.44 (9H, s, CH_3). ^{13}C NMR: δ 171.1 (*C*═O), 157.2 (*C*═O), 79.74 (*C*−$(CH_3)_3$), 75.86 (Fc *C*−C), 70.37 (Fc *C*−H), 69.71 (Fc *C*−H), 68.12 (Fc *C*−C), 40.99 (*C*H_2), 40.59 (*C*H_2), 28.39 (*C*H_3). Anal. Calcd for for $FeC_{18}H_{24}N_2O_3$: C, 58.08; H, 6.50; N, 7.53. Found: C, 58.67; H, 7.07; N, 7.72. EIMS, *m*/*z*: 372 $(M)^+$, 316 $(M - C(CH_3)_3 + H)^+$, 272 $(M - COOC(CH_3)_3 + H)^+$, 243 $(FcCONHCH_2 + H)^+$, 229 $(FcCONH_2)^+$, 213 $(FcCO)^+$, 185 $(Fc)^+$, 121 $(FeCp)^+$. IR (KBr disk), cm^{-1}: 3342 (N−H stretch), 3096/2978/2934/2870 (C−H stretches), 1703 (C═O(I)), 1625 (C═O(I)), 1522 (C═O(II)), 1468 (C═O(II)).

[((2-Aminoethyl)amino)carbonyl]ferrocene (L4). Receptor **L3** was dissolved in CF_3CO_2H/ CH_2Cl_2 (50:50, 10 mL), and the mixture was stirred for 20 min. The solvent was then removed under reduced pressure. The residue was dissolved in concentrated KOH(aq) (30 mL) and the product extracted into CH_2Cl_2 (3 × 50 mL). The organic extracts were dried over Na_2CO_3 and filtered, and the filtrate was evaporated to dryness. The product did not require further purification. Yield: 78%. ^{1}H NMR ($CDCl_3$): δ 6.25 (1H, b s, CON−*H*), 4.69 (2H, dd obs t (J = 1.88 Hz), Fc *H*), 4.35 (2H, dd obs t (J = 1.86 Hz), Fc *H*), 4.21 (5H, s, Fc *H*), 3.45 (2H, q (J = 5.84 Hz), CH_2−NH), 2.92 (2H, t (J = 5.89 Hz), CH_2−NH_2), 1.52 (2H, s, NH_2). ^{13}C NMR: δ 170.51 (*C*═O), 76.28 (Fc *C*−C), 70.31 (Fc *C*−H), 69.70 (Fc *C*−H), 68.10 (Fc *C*−H), 41.94 (*C*−N), 41.58 (*C*−N). Anal. Calcd for $FeC_{13}H_{16}N_2O{\cdot}0.5H_2O$: C, 55.54; H, 6.09; N, 9.96. Found: C, 55.40; H, 6.16; N, 9.90. FABMS, *m*/*z*: 272 $(M)^+$, 295 $(M + Na)^+$, 405 $(M + Cs)^+$, 229 $(FcCONH_2)^+$, 213 $(FcCO)^+$, 185 $(Fc)^+$, 121 $(FeCp)^+$. IR (KBr disk), cm^{-1}: 3371/3324 (N−H stretch), 3300 (broad NH_2 stretch), 3074/2968/2923 /2909/2862 (C−H stretches), 1634 (C═O(I)), 1537 (C═O(II)).

1,1′-Bis[((*N*-(*tert*-butoxycarbonyl)-3-aminopropyl)amino)carbonyl]ferrocene (L5). 1,1′-Bis(chlorocarbonyl)ferrocene (0.61 g) was dissolved in dry toluene (15 mL), and the solution was added dropwise to *N*-(*tert*-butoxycarbonyl)-1,3-propanediamine (0.89 g) and triethylamine (0.52 g), also in dry toluene (25 mL). The mixture was stirred for 1 h, and a color change from red to orange was observed. The solution was then filtered and the filtrate evaporated to dryness. The product was dissolved in dichloromethane (30 mL), and the mixture was washed with water (3 × 50 mL). The organics were then dried over $MgSO_4$ and filtered, and solvent removed under reduced pressure. Further purification was achieved by alumina gel chromatography eluting with CH_2Cl_2/MeOH (99:1). Yield: 70% (0.75 g). ^{1}H NMR ($CDCl_3$): δ 7.48 (2H, b t, N−*H*), 5.24 (2H, b t, N−*H*), 4.58 (4H, dd obs s, Fc *H*), 4.39 (4H, dd obs t (J = 1.82 Hz), Fc *H*), 3.46 (4H, q (J = 6.02 Hz), NH−CH_2), 3.28 (4H, q (J = 6.15 Hz), NH−CH_2), 1.76 (4H, quin (J = 6.08 Hz), C−CH_2−C), 1.46 (18H, s, CH_3). ^{13}C NMR: δ 170.6 (*C*═O), 156.7 (*C*═O), 79.31/78.58 (Fc *C*−C/*C*$(CH_3)_3$), 70.98 (Fc *C*−H), 70.60 (Fc *C*−H), 37.42 (*C*−N), 36.19 (*C*−N), 30.10 (C−CH_2−C), 28.44 (*C*H_3). Anal. Calcd for $FeC_{28}H_{42}N_4O_6{\cdot}0.5H_2O$: C, 56.47; H, 7.28; N, 9.41. Found: C, 56.86; H, 7.46; N, 9.07. FABMS, *m*/*z*: 586 $(M)^+$, 587 $(M + H)^+$, 609 $(M + Na)^+$. IR (KBr disk), cm^{-1}: 3365/3304 (N−H stretches), 2964/2938 (C−H stretches), 1691.5 (C═O(I)), 1645 (C═O(I)), 1555.5 (C═O(II)), 1530 (C═O(II)), 1296 (C-O stretch), 1279 (C-O stretch).

1,1′-Bis-[((3-aminopropyl)amino)carbonyl]ferrocene (L6). Receptor **L5** was deprotected using standard BOC-deprotection methodology as discussed above for the synthesis of **L4**. A color change from orange to deep red was observed. The product was isolated as before but was partially unstable and only characterized by proton NMR. Yield: 47%. ^{1}H NMR ($CDCl_3$): δ 7.72 (2H, b s, CON−*H*), 4.50 (4H, dd obs t (J = 1.59 Hz), Fc *H*), 4.35 (4H, dd obs t (J = 1.39 Hz), Fc *H*), 3.50 (4H, q (J = 6.11 Hz), CON−CH_2), 2.89 (4H, t (J = 6.26 Hz), CH_2−NH_2), 1.77 (4H, quin (J = 6.36 Hz), C−CH_2−C), 1.46 (4H, b s, NH_2). Electrochemistry: single irreversible oxidation wave; E_{pa} = 0.460 V (CH_3CN).

1,1′-Bis[((6-aminopyridyl)amino)carbonyl]ferrocene (L8). 1,1-Bis(chlorocarbonyl)ferrocene (0.20 g) dissolved in dry dichloromethane (15 mL) was added dropwise to an excess of 2,6-diaminopyridine (0.42 g) and triethylamine (0.14 g), also in dry CH_2Cl_2 (15 mL). The mixture was stirred for 3 h under nitrogen. The solution was then washed with water (3 × 50 mL), dried over Na_2CO_3, and pumped to dryness. The product was isolated by column chromatography on silica eluting with CH_2Cl_2/MeOH (75:25) and recrystallized from CH_2Cl_2/hexane. Yield: 51% (0.12 g). ^{1}H NMR ($CDCl_3$): δ 8.15 (2H, s, CON−*H*), 7.56 (2H, d (J = 7.50 Hz), Py *H*), 7.41 (2H, t (J = 8.00 Hz), Py *H*), 6.22 (2H, d (J = 8.00 Hz), Py *H*), 4.83 (4H, dd obs s, Fc *H*), 4.48 (4H, dd obs s, Fc *H*), 4.36 (4H, b s, NH_2). ^{13}C NMR: δ 167.7 (*C*═O), 157.1 (Py *C*−N), 149.8 (Py *C*−N), 140.0 (Py *C*−H), 104.2 (Py *C*−H), 103.6 (Py *C*−H), 77.75 (Fc *C*−C), 72.68 (Fc *C*−H), 70.25 (Fc *C*−H). Anal. Calcd for $FeC_{18}H_{20}N_6O_2{\cdot}0.5H_2O$: C, 56.79; H, 4.55; N, 18.06. Found: C, 56.52; H, 4.59; N, 17.81. FABMS, *m*/*z*: 457 $(M + H)^+$, 479 $(M + Na)^+$ IR (KBr disk), cm^{-1}: 3450−3200 (N−H + O−H stretches, broad), 1662 (Py), 1620 (C═O(I)), 1575 (Py), 1532 (C═O-(II)), 1453 (Py), 791 (Py H bend).

Proton NMR Titration Studies. Proton NMR titrations were typically performed by dissolving 5 × 10^{-6} mol of receptor in a deuterated solvent (0.5 mL) in an NMR tube. The guest being investigated was then added as a 0.1 M solution using a microsyringe in order to add substoichiometric quantities while the NMR spectrum of the receptor was monitored. Stability constants were evaluated from titration data using the EQNMR fitting program.[23]

Electrochemical Investigations. Typically, 1 × 10^{-5} mol of receptor was dissolved in a suitable solvent (5 mL) and tetrabutylammonium tetrafluoroborate (0.16 g) was added. The guest under investigation was then added as a 0.1 M solution using a microsyringe while the cyclic and square-wave voltammetric properties of the solution were monitored.[36]

UV−Visible Spectroscopic Investigations. Typically 2.5 × 10^{-6} mol of receptor was dissolved in a suitable solvent (2.5 mL) (ionic strength 0.1 made up with tetrabutylammonium tetrafluoroborate), and the solution was placed in a quartz cuvette. Once again, the guest was added using a microsyringe (as a 0.1 M solution).

Acknowledgment. We thank the EPSRC for a studentship (A.R.G.) and use of the mass spectrometry service of University College Swansea, as well as BP for a scholarship (D.K.S.).

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