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# An Exploration of Ferrocenyl Ureas as Enantioselective Electrochemical Sensors for Chiral Carboxylate Anions

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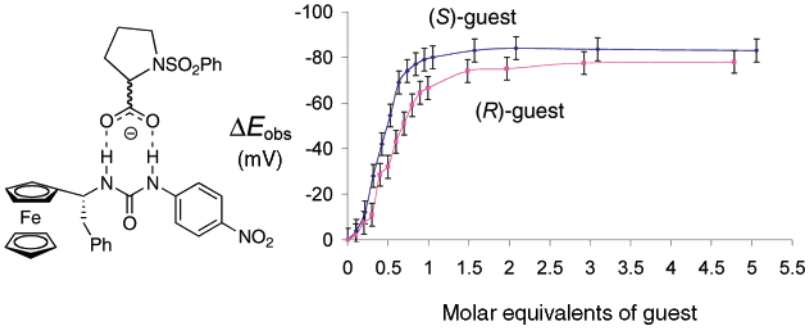


The syntheses of a series of chiral ureas containing the redox-active ferrocene group are described. Each of these bind chiral carboxylates in organic solvents through hydrogen-bonding interactions, as evidenced by spectroscopic and cyclic voltammetry measurements, the latter allowing these guests to be electrochemically sensed in solution. The enantioselectivity in the complexation of the protected amino acid *N*-benzenesulfonylproline by a ferrocenylbenzyl host is high enough to allow opposite enantiomers to be distinguished by electrochemical means.

## Introduction

As part of the ongoing interest in chiral recognition within the field of supramolecular chemistry, the development of enantioselective sensors continues apace, the incentive being to find a convenient means of identifying one enantiomer of a particular chiral target with respect to its mirror image.[1,2] Although recent progress has been made in this area using photoactive receptors that give an optical readout of chiral binding processes,[1] less attention has been paid to the development of analogous redox-active systems for an electronic (voltage or current) readout.[2] This is in spite of the myriad redox-active supramolecular receptors and sensors for various achiral species that have been developed over the past two decades.[3] The continued interest in redox sensing stems partly from the facts that not only can electrochemical sensors be highly sensitive but also suitable receptors can be readily immobilized onto electrode surfaces[4] as potentially applicable devices.

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[†] University of Birmingham.
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(1) For recent reviews and articles on photo-active enantioselective sensors, see: (a) Pu, L. *Chem. Rev.* **2004**, *104*, 1687. (b) Heo, J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 941. (c) Qing, G. Y.; He, Y. B.; Zhao, Y.; Hu, C. G.; Liu, S. Y.; Yang, X. *Eur. J. Org. Chem.* **2006**, *6*, 1574. (d) Wang, Q.; Chen, X.; Tao, L.; Wang, L.; Xiao, D.; Yu, X. Q.; Pu, L. *J. Org. Chem.* **2007**, *72*, 97. (e) Zhao, J. Z.; James, T. D. *J. Mater. Chem.* **2005**, *15*, 2896. (f) Mei, X.; Wolf, C. *J. Am. Chem. Soc.* **2006**, *128*, 13326. (g) Lee, S. J.; Lin, W. B. *J. Am. Chem. Soc.* **2002**, *124*, 4554.

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(3) For recent examples of redox-active receptors and sensors for various charged and neutral species, see: (a) Tucker, J. H. R.; Collinson, S. R. *Chem. Soc. Rev.* **2002**, *31*, 147. (b) Westwood, J.; Coles, S. J.; Collinson, S. R.; Gasser, G.; Green, S. J.; Hursthouse, M. B.; Light, M. E.; Tucker, J. H. R. *Organometallics* **2004**, *23*, 946. (c) Miyaji, H.; Gasser, G.; Green, S. J.; Molard, Y.; Strawbridge, S. M.; Tucker, J. H. R. *Chem. Commun.* **2005**, 5355. (d) Gasser, G.; Belousoff, M. J.; Bond, A. M.; Kosowski, Z.; Spiccia, L. *Inorg. Chem.* **2007**, *46*, 1665. (e) Oton, F.; Tarraga, A.; Espinosa, A.; Velasco, M. D.; Molina, P. *J. Org. Chem.* **2006**, *71*, 4590. (f) Wong, W. W. H.; Curiel, D.; Lai, S. W.; Drew, M. G. B.; Beer, P. D. *Dalton Trans.* **2005**, 774. (g) Bu, J. J.; Lilienthal, N. D.; Woods, J. E.; Nohrden, C. E.; Hoang, K. T.; Truong, D.; Smith, D. K. *J. Am. Chem., Soc.* **2005**, *127*, 6423. (h) Aranzaes, J. R.; Belin, C.; Astruc, D. *Angew. Chem., Int. Ed.* **2006**, *45*, 132. (i) Debroy, P.; Banerjee, M.; Prasad, M.; Moulik, S. P.; Roy, S. *Org. Lett.* **2005**, *7*, 403. (j) Bucher, C.; Devillers, C. H.; Moutet, J. C.; Royal, G.; Saint-Aman, E. *New J. Chem.* **2004**, *28*, 1584.

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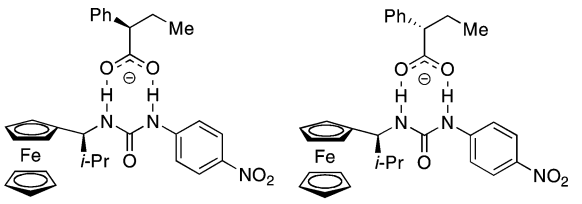



**FIGURE 1.** Diastereomeric complexes **1a** and **1b** formed with (*R*)- and (*S*)-2-phenylbutyrate.

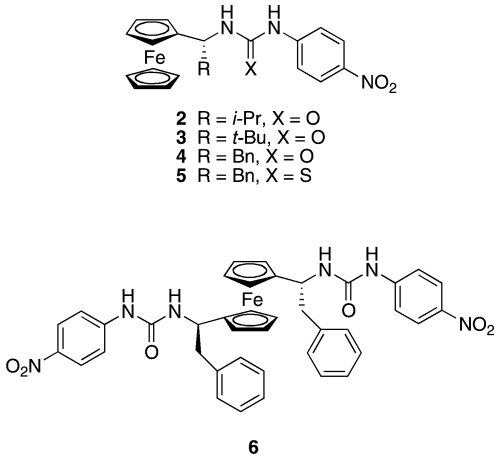



**FIGURE 2.** New redox-active receptors for the binding and sensing of chiral carboxylate anions.

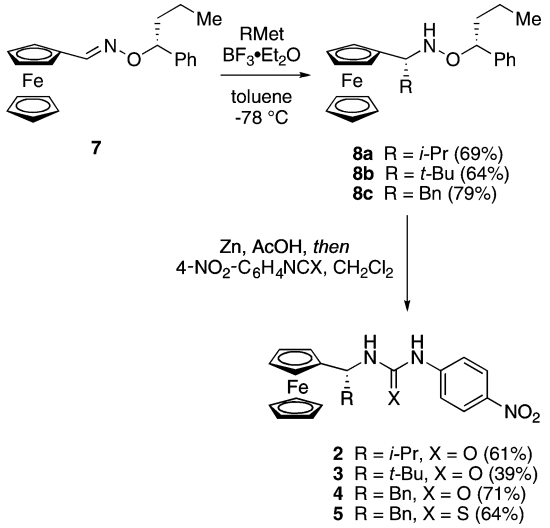
Previous studies in our group have involved the design and synthesis of a chiral α-ferrocenylalkylurea-based receptor that exhibits very modest selectivity toward carboxylate enantiomers.[5] Thus, the binding constants for complexes **1a** and **1b** between (*S*)-1-ferrocenyl-2-methylpropyl-4-nitrophenyl urea and (*R*)- and (*S*)-tetrabutylammonium 2-phenylbutyrate (Figure 1) were 2910 and 2350 $M^{-1}$, respectively, in DMSO solution, as determined by UV spectroscopy. The binding could also be monitored by cyclic voltammetry, although the cathodic shift upon binding was essentially the same for both enantiomers of the guest anion.

On the basis of our preliminary studies,[5] we now report on a range of related receptors (Figure 2), designed to probe the effect of (a) changing the α-alkyl group (compounds **2**, **3**, and **4**), (b) modifying the urea binding site (compound **5**), and (c) introducing two binding units (compound **6**) on the chiral binding and sensing properties of these systems. The results of this detailed study are reported herein.

## Results

**1. Synthesis.** The synthesis of the new ferrocene-based receptors was based on our chiral oxime ether methodology.[6] Thus, commercially available ferrocenecarboxaldehyde was converted into the (*R*)-oxime ether **7** by reaction with (*R*)-(−)-*O*-(1-phenylbutyl)hydroxylamine.[6a] Addition of organometallic reagents in the presence of boron trifluoride diethyl etherate

**SCHEME 1. Synthetic Route for the Mono-urea Receptors**




gave the hydroxylamines **8** in good yield and with excellent diastereoselectivity (>95% de). On the basis of previous work,[6b] the configuration of the new chiral center was expected to be (*R*), and the stereochemistry of the addition of the isopropyl Grignard reagent had been confirmed in the enantiomeric series in our preliminary studies.[5] Following cleavage of the N−O bond in the hydroxylamines **8**, the resulting amines were treated with 4-nitrophenyl isocyanate to give the ureas **2**−**4**. Similarly, reaction of the amine derived from **8c** with 4-nitrophenyl isothiocyanate gave the corresponding thiourea **5** (Scheme 1).

Receptor **6** was synthesized since bis-ureas have previously been shown to be effective binders of carboxylates in organic solvents, with some forming 1:1 complexes where the guest is wedged between two urea moieties.[7] Its synthesis started from ferrocene-1,1′-bis-carboxaldehyde,[8] which was readily converted into the bis-oxime ether **9**. Double addition of benzylmagnesium chloride proceeded with high diastereoselectivity to give the bis-hydroxylamine derivative **10**. Cleavage of the N−O bonds was followed by reaction with 4-nitrophenyl isocyanate to give the desired receptor (Scheme 2).

The neutral form of each enantiomer of the three chiral guests used for the studies, 2-phenylbutyric acid, **11**, mandelic acid, **12**, and the protected amino acid *N*-benzenesulfonyl proline, **13** (Figure 3), was converted into the corresponding salt by the addition of tetrabutylammonium hydroxide in methanol.

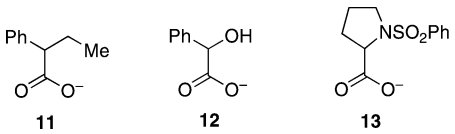



**FIGURE 3.** Structures of the chiral carboxylates used as guests in this study (used as their tetrabutylammonium salts).

**2. Binding Studies by Spectroscopy.** Mono-urea receptors **2**−**5** were found to bind carboxylate ions in $CD_3CN$ and DMSO solution, as evidenced by significant changes to the $^1H$ NMR

(4) For a recent review, see: Zhang, S.; Cardona, C. M.; Echegoyen, L. *Chem. Commun.* **2006**, 4461.

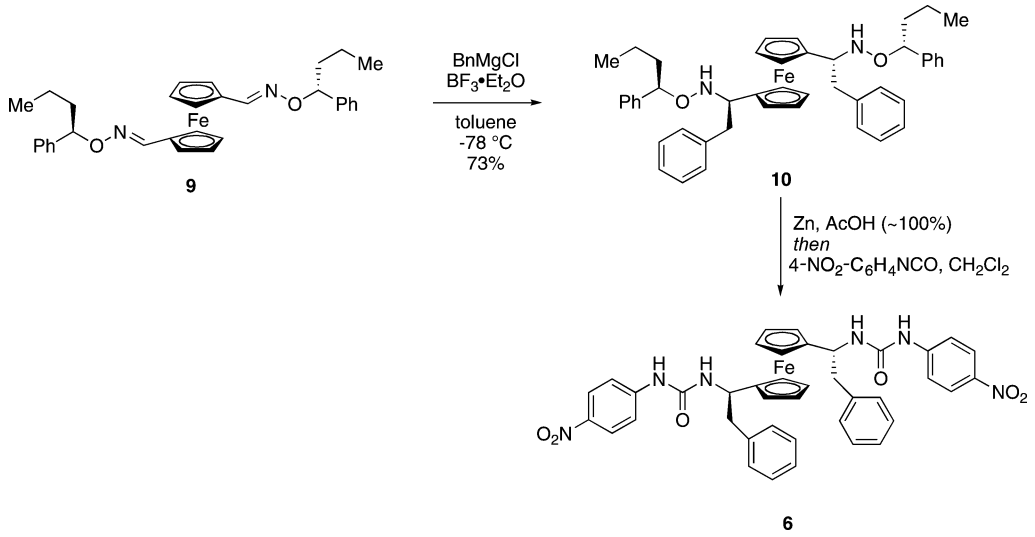
(5) Laurent, P.; Miyaji, H.; Collinson, S. R.; Prokes, I.; Moody, C. J.; Tucker, J. H. R.; Slawin, A. M. Z. *Org. Lett.* **2002**, *4*, 4037.

(6) (a) Moody, C. J.; Lightfoot, A. P.; Gallagher, P. T. *J. Org. Chem.* **1997**, *62*, 746. (b) Moody, C. J. *Chem. Commun.* **2004**, 1341.

(7) (a) For a review of various receptors that bind carboxylates, see: Fitzmaurice, R. J.; Kyne, G. M.; Douheret, D.; Kilburn, J. D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 841. (b) Nishizawa, S.; Buhlmann, P.; Iwao, M.; Umezawa, Y. *Tetrahedron Lett.* **2005**, *36*, 6483.

(8) Alavoine, G. G. A.; Doisneau, G.; Fillebeenkhan, T. *J. Organomet. Chem.* **1991**, *412*, 381.

**SCHEME 2. Synthetic Route to the Bis-urea Receptor 6**




spectrum of each host (ca. 5 mM) upon addition of guest carboxylates. As expected, large downfield shifts (ca. +4 ppm) in the resonances for the urea NH protons were observed, which confirmed the urea moiety as the binding site, with Job plots establishing the stoichiometry as 1:1 (see the Supporting Information for representative examples).

Only marginal differences were seen between NMR spectra of receptors with equivalent amounts of opposite enantiomers. In addition, the binding interaction was too strong to allow very accurate binding constant values to be determined at NMR concentrations (ca. $10^{-3}$ M). However, as found previously,[5] the nitrobenzene chromophore on each receptor allowed the binding process to be followed by UV−vis spectroscopy at lower concentrations (ca. $10^{-5}$ M) in $CH_3CN$ or DMSO. In the case of receptors **2**−**4**, a significant bathochromic and slightly hyperchromic shift in the charge-transfer band centered at ca. 340 nm was observed upon addition of **11**, as shown in Figure 4 for a titration of **3** with (*R*)-**11**. In addition, a clear isosbestic point was observed at 347 nm, which can be interpreted[9] as indicating the presence of just two absorbing species in solution.

It was found that the most reliable method for obtaining binding constants with small errors for the complexes with the mono-ureas was to use the Benesi−Hildebrand equation. To ensure that a significant amount of complexation was only achieved in the presence of a large excess of guest, as required by this method,[9,5] DMSO was used as the solvent rather than MeCN. In this solvent, similar changes were observed to the UV−vis spectra upon addition of guest species, although the changes in $\lambda_{max}$ values and intensities were smaller. The reciprocal of the increase in absorption intensity at a particular wavelength was plotted against the reciprocal of guest concentration, with the resulting data at a series of wavelengths used to obtain the binding constant (see the Supporting Information for more details). A representative example is given in Figure 5, depicting the graphs for (*R*)-**11** and (*S*)-**11** with receptor **4** from a titration in DMSO.

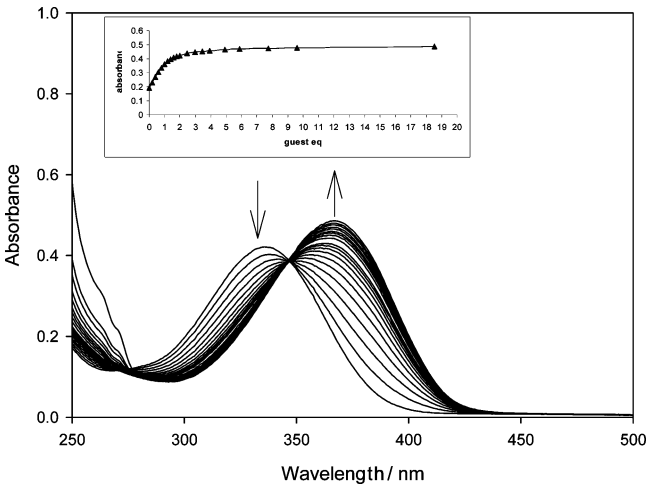



**FIGURE 4.** UV−vis titration of **3** (0.025 mM) in $CH_3CN$ against molar equivalents of (*R*)-**11**, showing the band at 347 nm decreasing and a band at 368 nm emerging as the 1:1 complex forms: **3** at 0.025 mM; + 0.2 equiv of (*R*)-**11**; + 0.4 equiv; + 0.6 equiv; + 0.8 equiv; + 1.0 equiv; + 1.2 equiv; + 1.4 equiv; + 1.6 equiv; + 1.8 equiv; + 2 equiv; + 2.5 equiv; +3 equiv; + 3.5 equiv; + 3.9 equiv; + 4.9 equiv; + 5.9 equiv; + 7.8 equiv; + 9.6 equiv; + 18.5 equiv. The inset shows the increase of absorbance at 368 nm upon the addition of (*R*)-**11**.

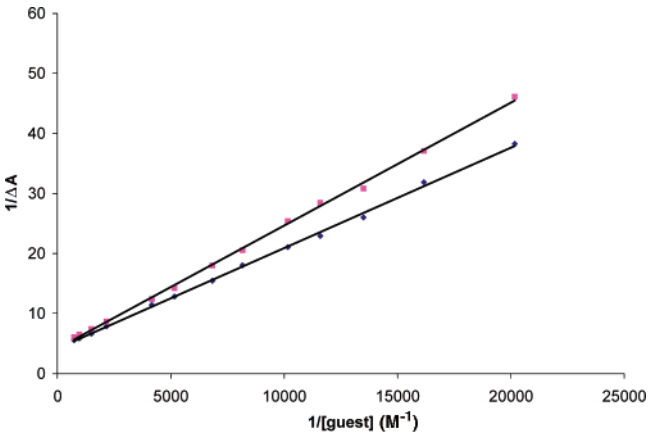



**FIGURE 5.** Benesi−Hildebrand plots for receptor **4** with (*R*)-**11** (pink squares) and (*S*)-**11** (blue diamonds) in DMSO at 380 nm.

The binding constants for receptors with each enantiomer of the three chiral guests are presented in Table 1. Moderate

(9) Connors, K. A. *Binding Constants: The Measurement of Molecular Complex Stability*; J. Wiley & Sons: New York, 1987.

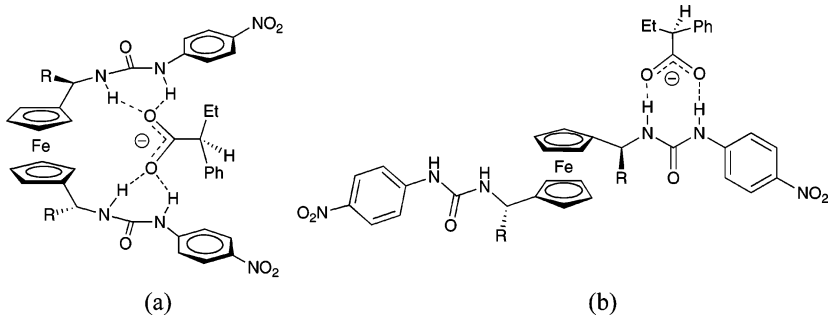



**FIGURE 6.** Two possible structures of the 1:1 complex between **6** and (*S*)-**11** (R = benzyl).

enantioselectivity at best is observed for **11** with receptors **2**−**5**. Although the differences in value for three of complexes with **11** fall within the confidence limits of the experiments, the (*S*) isomer is marginally preferred over its (*R*) counterpart for all four receptors, which is consistent with previous binding studies on the opposite enantiomer of receptor **2** (vide infra).[5] For guests **12** and **13**, the values are less uniform for each receptor and the enantioselectivity is more marked for certain complexes, most notably for those between ferrocenylbenzyl urea **4** and **13**, where the (*S*) isomer is again preferred. The overall order of binding strength for the receptors follows **11** > **12** ∼ **13**.

The bis-urea receptor, compound **6**, was also found to bind carboxylates **11**−**13** strongly in acetonitrile solution, as indicated by NMR spectroscopy. For example, upon addition of 1 equiv of guest (*S*)-**11** to a 5 mM solution of **6**, large shifts in the urea proton signals were observed, which were similar to those found for the corresponding mono-urea **4** with this guest under the same conditions. This data, along with the observation that the addition of further amounts of guest had only a small effect on these signals, indicates that just 1 equiv of guest is sufficient to render the NH protons of **6** fully complexed. This suggests the formation of a discreet 1:1 complex involving both urea arms as shown in Figure 6a,[7] rather than a complex where at any one time, only one urea group partakes in H-bonding interactions, as shown in Figure 6b.

A Job plot supported this finding, with a clear maximum being found at a molar ratio of 0.5 and no evidence for significant amounts of 2:1 complex formation under the conditions used (Figure 7a). However upon changing the solvent to DMSO, a Job plot clearly the presence of both 1:1 and 2:1 complexes (Figure 7b), with a maximum appearing between a mol fraction of 0.33 and 0.5.

The computer software program Letagrop,[10] was used to obtain a 1:1 binding constant in $CH_3CN$ between **6** and (*S*)-**11** of log $K = 5.78 \pm 0.2$, a value significantly higher than that between this guest and mono-urea **4** in the same solvent (log $K = 5.04 \pm 0.02$). No enantioselectivity was apparent using **6** although this assessment was compounded by large error values, possibly caused by the observation of a 2:1 complex in the presence of large excess of guest (see the Supporting Information for more details).

**3. Binding Studies Using Electrochemistry.** Cyclic voltammetry experiments revealed that all receptors underwent a reversible oxidation in dry $CH_3CN$ at 293 K, corresponding to the $Fc/Fc^+$ redox process. Formal electrode potentials (vs decamethylferrocene, dmfc as an internal reference) for each compound, $E^{o\prime}$, where $E^{o\prime} = (E_{pa} + E_{pc})/2$, are given in the Supporting Information, along with the conditions used for these experiments.

**TABLE 1. Binding Constant Values, log *K* (±0.04) at 293 K in DMSO, Obtained by UV−vis Spectroscopy Using the Benesi−Hildebrand Method**

| | (*S*)-**11** | (*R*)-**11** | (*S*)-**12** | (*R*)-**12** | (*S*)-**13** | (*R*)-**13** |
|---|---|---|---|---|---|---|
| **2** | 3.38 | 3.31 | 3.22 | 3.12 | 3.15 | 3.11 |
| **3** | 3.34 | 3.31 | 2.95 | 3.10 | 3.02 | 3.03 |
| **4** | 3.42 | 3.33 | 2.98 | 2.93 | 3.25 | 3.03 |
| **5** | 3.72 | 3.64 | *a* | *a* | *a* | *a* |

[a] Not determined.

For each of the mono-ureas **2**−**5**, the addition of 1 equiv of either enantiomer of the carboxylates **11**, **12**, and **13** ($CH_3CN$, receptor concentration = ca. 0.5 mM) resulted in a pronounced cathodic shift in the ferrocene-centered redox couple to indicate the sensing of these species in solution. A typical series of cyclic voltammograms is depicted in Figure 8, which shows the effect of adding 1 and then 5 equiv of guest (*S*)-**11** to receptor **2**.

Table 2 lists the shifts in millivolts, $\Delta E^{o\prime}$, observed in the ferrocene-centered redox couple of each mono-urea receptor upon complexation of various carboxylates, where $\Delta E^{o\prime}$ is defined as $E^{o\prime}_{complex} - E^{o\prime}_{host}$. Clearly the values vary with the carboxylate used, with the redox response to mandelate **12** significantly less than that for either **11** or **13**.

As found in previous studies on complexes **1a** and **1b**,[5] no differences in $\Delta E^{o\prime}$ values were observed upon the addition of an excess of either enantiomer of **11** to receptors **2**, **3**, or **4**. Although small differences were more apparent in several cases for guests **12** and **13**, these all fall within the confidence limit. However, a titration[11] plotting the observed shift in $\Delta E_{obs}$ value (where $\Delta E_{obs} = E_{obs} - E^{o\prime}_{host}$) for receptor **4** against molar equivalents of **13** (Figure 9a) indicated that, after taking confidence limits into account, there was indeed a discernible difference in the electrochemical response to the binding of opposite enantiomers in the region around equimolar amounts of host and guest. However, this was found not to be the case when similar titrations were carried out either on this guest with other receptors (for the corresponding titration with **3**, see the Supporting Information) or on this receptor with other guests, as shown in Figure 9b.

For the thiourea receptor **5**, although cathodic shifts were clearly observed upon complexation, irreversible behavior was

(10) Molard, Y.; Bassani, D. M.; Desvergne, J. P.; Moran, N.; Tucker, J. H. R. *J. Org. Chem.* **2006**, *71*, 8523 and references therein.

(11) At substoichiometric amounts of guest, one-wave voltammetric behavior was observed, with the redox wave gradually shifting to more cathodic potentials upon addition of increasing amounts of guest. For a discussion of this topic, see: Miller, S. R.; Gustowski, D. A.; Chen, Z. H.; Gokel, G. W.; Echegoyen, L.; Kaifer, A. E. *Anal. Chem.* **1988**, *60*, 2021.

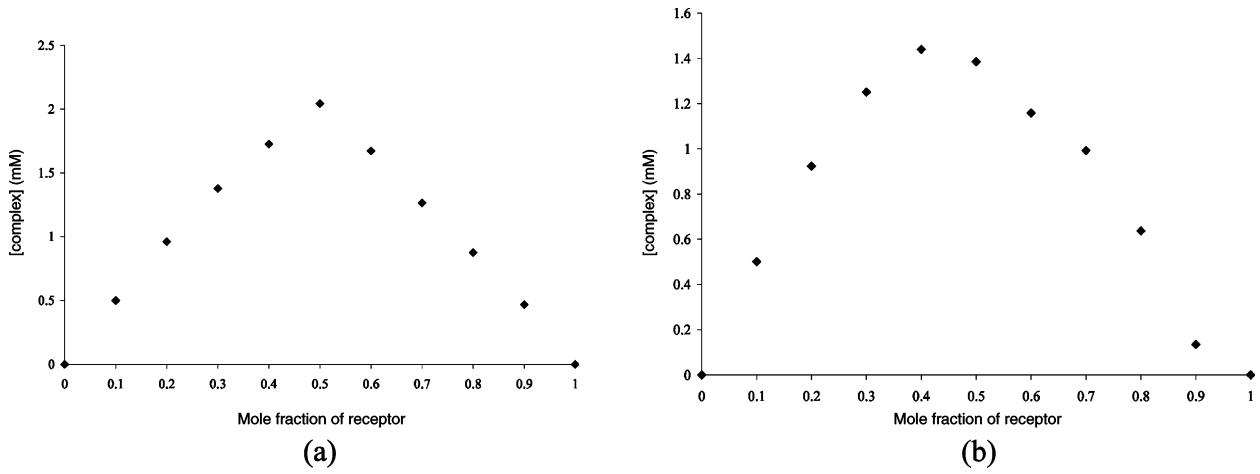



**FIGURE 7.** $^1$H Job plot of **6** with (*S*)-**11** in (a) $CH_3CN$ and (b) DMSO (5 mM total concentration).

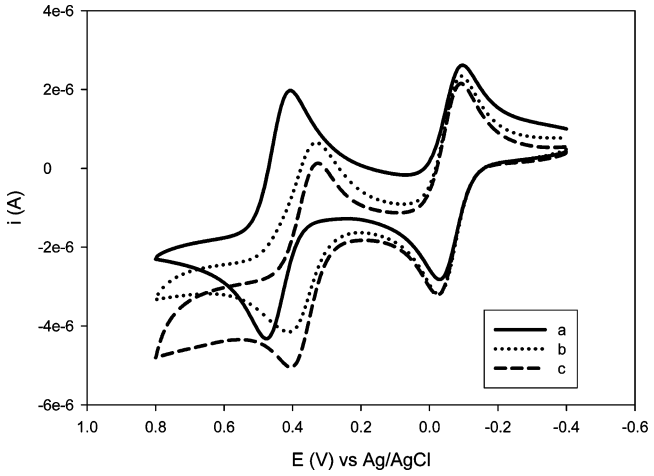



**FIGURE 8.** Cyclic voltammograms of **2** (0.55 mM) and decamethylferrocene (0.34 mM) in (a) the absence, (b) the presence of 1 equiv, and (c) the presence of 5 equiv of (*S*)-**11** in $CH_3CN$.

**TABLE 2. $\Delta E^{o\prime}$ Values (vs dmfc) Recorded upon Complexation of Various Chiral Carboxylates by Receptors 2−5 (ca. 0.5 mM) in $CH_3CN$**

| | $\Delta E^{o\prime}$ [a] (vs dmfc)/mV | | | | | |
|---|---|---|---|---|---|---|
| | **11** | | **12** | | **13** | |
| receptor | *S* | *R* | *S* | *R* | *S* | *R* |
| **2** | −84 | −83 | −57 | −57 | −84 | −81 |
| **3** | −81 | −82 | −73 | −76 | −96 | −92 |
| **4** | −81 | −82 | −59 | −63 | −83 | −78 |
| **5** | −92[b] | −93[b] | *c* | *c* | *c* | *c* |

[a] The confidence limit is ±5 mV. [b] Redox wave displayed irreversible behavior upon complexation. [c] Not determined.

apparent using either glassy carbon or platinum working electrodes (see the Supporting Information), possibly indicating the partial decomposition of the complex upon its oxidation.

The addition of equimolar amounts of enantiomers of **11**−**13** to the bis-urea **6** (ca. 0.5 mM in acetonitrile) induced, in each case, a cathodic shift in its ferrocene-centered redox wave (Figure 10, Table 3). The shifts were generally smaller than those observed for the corresponding complexes with the mono-urea **4**. However, the addition of further amounts of guest, up to a 10-fold excess, shifted the potential by approximately the same amount again, which was consistent with the eventual formation of 2:1 complexes (Table 3).

Compared to the 1:1 complexes with the mono-ureas **2**−**5**, slightly larger differences in the $\Delta E^{o\prime}$ values for each enantiomer of the three guests were recorded for the 2:1 complexes with **6**. However, although the (*R*)-enantiomers gave the slightly larger potential shifts each time and slightly different titration profiles were observed for each enantiomer beyond the addition of 1 equiv of guest (see the Supporting Information), these values also fall within the confidence limits of the experiments. In addition the redox waves became slightly irreversible as the 2:1 complex were formed, as evidenced by larger $\Delta E_p$ values (see the Supporting Information).

## Discussion

All of the mono-urea receptors **2**−**5** bind the carboxylates strongly in MeCN and DMSO. Receptor **2** is the opposite enantiomer of the urea previously reported[5] that was also found to bind enantiomers of 2-phenylbutyrate, **11**, forming complexes **1a** and **1b** (Figure 1). Therefore, as expected, the very moderate enantioselectivity previously shown by the (*S*)-receptor toward (*R*)-**11** in DMSO[5] is now shown by the (*R*)-receptor toward (*S*)-**11** (Table 1). Guest **11** gives fairly consistent binding data and enantioselectivities as the R group on the α-carbon is changed in receptors **2**−**4**. In addition, as expected from previous studies,[7a] it is bound more strongly by the thio-urea receptor **5**, although there is no improvement in enantioselectivity. The lower p$K_a$ value of mandelic acid compared to 2-phenylbutyric acid[12] accounts for the smaller binding constants with the weaker conjugate base, **12**. However, compared to **11**, it is clear that binding strengths and enantioselectivities are more varied for guests **12** and the protected amino acid **13** as the receptor is changed (Table 1). The most striking results are obtained for **13** in that for receptors **2** and **3** there is little or no enantioselectivity, whereas for receptor **4** the enantioselectivity improves to such an extent that the (*S*)-enantiomer is bound approximately 1.7 times more strongly than its mirror image. The benzyl group in **4** must play a prominent role in this difference, possibly contributing toward a combination of $\pi$-stacking and steric effects that together would be absent in receptors **2** and **3**.

(12) The p$K_a$ of **11** is not known but α-hydroxy acids are more acidic than their ethyl counterparts, for example; glycolic acid, p$K_a$ = 3.8, butanoic acid, p$K_a$ = 4.8.

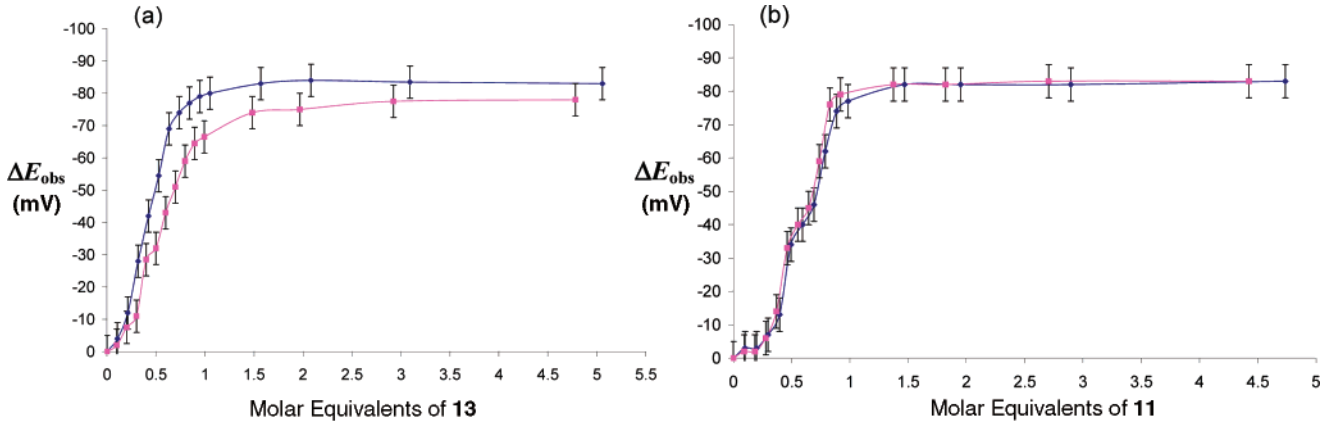



**FIGURE 9.** Titration of the $\Delta E_{obs}$ value in $CH_3CN$ of the redox wave of receptor **4** against (a) molar equivalents of (*S*)-**13** (blue diamonds) and (*R*)-**13** (pink squares) (b) molar equivalents of (*S*)-**11** (blue diamonds) and (*R*)-**11** (pink squares).

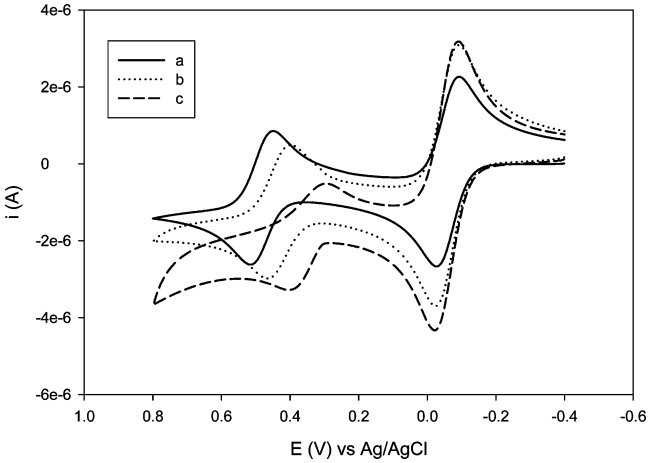



**FIGURE 10.** Cyclic voltammetry of (a) **6** (0.44 mM) and decamethylferrocene (0.77 mM), (b) **6** and 1 equiv of (*S*)-**11**, and (c) **6** in the presence of 10 equiv of (*S*)-**11** in $CH_3CN$.

**TABLE 3. $\Delta E^{o\prime}$ Values (vs dmfc) Recorded upon the Addition of 1 and 10 equiv of Various Chiral Carboxylates to Receptor 6 (5 mM) in $CH_3CN$**

| | $\Delta E^{o\prime}$ [a] (vs dmfc)/mV | | | | | |
|---|---|---|---|---|---|---|
| | **11** | | **12** | | **13** | |
| | S | R | S | R | S | R |
| 1 equiv | −67 | −74 | −55 | −58 | −55 | −52 |
| 10 equiv | −141 | −146 | −103 | −112 | −127 | −136 |

[a] The confidence limit is ±5 mV.

As expected, the bis-urea **6** can form both 1:1 and 2:1 complexes, although a 1:1 complex is clearly favored more in acetonitrile than in DMSO, as evidenced by the NMR Job plots with (*S*)-**11** (Figure 7). This suggests that in this less competitive solvent the formation of a 1:1 complex conformation as depicted in Figure 6a, in which both urea arms simultaneously bind to the guest, is predominant. The fact that the 1:1 binding constant for the complex between the **6** and (*S*)-**11** in acetonitrile is higher than that for the analogous complex with monosubstituted **4** is consistent with four simultaneous H-bonds (rather than two from one arm) creating such a ditopic complex. Although a 2:1 complex in acetonitrile could be detected by UV−vis titrations (see the Supporting Information) and electrochemical studies, presumably it was not present in sufficient quantities to be observed under the conditions used for the Job plot (5 mM total concentration).

As demonstrated by the cyclic voltammograms in Figures 8 and 10, chiral carboxylates **11**−**13** can be sensed by inducing negative shifts in the ferrocene-centered redox couples of each receptor, giving another example of the sensing of organic molecules by redox-active supramolecular receptors.[3a−c] The values listed (Table 2) are quoted relative to dmfc as an internal reference ($E^{o\prime} = -60$ mV vs Ag/AgCl), which was unaffected by the presence of guest species. The negative shifts in potential result from each anion pushing electron density on to the ferrocene center, making the complexes easier to oxidize than their free forms. Such a process would explain why the less basic guest **12**, containing its electronegative oxygen atom, imparts a smaller redox response to complexation in the case of receptors **2**−**4**. Interestingly this same guest also has a smaller effect on the nitrobenzene band in the UV−vis spectra of these receptors (see the Supporting Information), presumably for the same reason, since this would be expected to lower the stability of the charge-transfer excited-state with respect to the ground state.

The $\Delta E^{o\prime}$ values given in Table 2 can also be rationalized by relating them to the relative stabilities of the oxidized and reduced forms of each complex, $K_{ox}$ and $K_{red}$, respectively.[3a,13] The negative shifts observed here simply indicate that all of the H-bonded complexes are more stable in their oxidized (ferrocenium) forms (i.e., $K_{ox} > K_{red}$), as expected for complexes with anions. Where two anions can bind, for example, with ditopic **6**, then the shift in potential is approximately twice as large, in line with two centers of negative charge being in close proximity to the ferrocene unit.

As for the electrochemical differentiation between enantiomers, the system **4**/**13** clearly gives the best result in this respect, with enantiomers of the proline derivative giving markedly different titration profiles (Figure 9a) compared to those for the same receptor with different guest enantiomers (Figure 9b) or those for the same set of enantiomers with other receptors (see the Supporting Information). The binding data indicates that the main origin of this effect comes from the increased enantioselectivity of receptor **4** toward **13** (Table 1), rather than from any marked difference in the redox response

(13) Mabbott, G. A. *J. Chem. Educ.* **1983**, *60*, 697.

to complexation. The latter explanation would have been more relevant if larger differences in $\Delta E^{o\prime}$ value between opposite enantiomers had been observed in the case of **4** and **13** only, which is clearly not the case (Table 3). The former explanation can also account for why the optimum chiral sensing effect in system **4**/**13** occurs at around equimolar amounts of host and guest, since at this point under these concentration conditions, less of the (*R*) enantiomer is bound by **4**, so the cathodic shift in the redox wave (under one-wave voltammogram behavior) is significantly less negative than it is for the (*S*) enantiomer. Nevertheless, the fact that the (*S*) enantiomer imparts a slightly more negative cathodic shift upon complexation serves to augment the sensing effect observed at equimolar concentrations.

## Conclusion

The complexation of chiral carboxylate anions in organic solvents by a series of chiral ferrocenylalkylureas has been shown to occur through complementary H-bonding interactions. The binding of these guests in close proximity to the ferrocene unit affects the electrode potential of this redox-active center, allowing these organic guest species to be sensed electrochemically at submillimolar concentrations. Although there are no large differences between the shifts in potential upon the complexation of opposite enantiomers, this work has shown that electrochemical differentiation between enantiomers can still be achieved if guest enantioselectivity is sufficiently large. Further work will be directed toward the design of more enantioselective receptor systems, the results of which will be reported in due course.

## Experimental Section

**(*E*)-(*R*)-(+)-*O*-(1-Phenylbutyl)ferrocene-1-carboxaldoxime 7.** This was obtained from the condensation of (*R*)-(−)-*O*-(1-phenylbutyl)hydroxylamine[6a] with ferrocene-1-carboxaldehyde under the usual conditions.[6] The crude product was purified by column chromatography on silica gel, eluting with ether−light petroleum (1:25) to give the *title compound* (85%) as a red solid: mp 56−58 °C (ether/light petroleum); $[\alpha]_D^{31}$ −246 (*c* 1.00, $CHCl_3$); IR (KBr/cm$^{-1}$) 3094, 3053, 3022, 2960, 2925, 2863, 1609, 1445, 1102, 1040, 1025, 933, 820, 748, 697; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.96 (1 H, s), 7.29 (5H, m), 5.10 (1 H, t, *J* 6.8), 4.49 (1 H, m), 4.44 (1 H, m), 4.28 (2 H, m), 4.07 (5 H, m), 1.96 (1 H, m), 1.76 (1 H, m), 1.51−1.25 (2 H, m), 0.95 (3 H, t, *J* 7.3); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 148.8 (CH), 142.9 (C), 128.1 (CH), 127.2 (CH), 126.8 (CH), 84.7 (CH), 76.6 (C), 69.8 (CH), 69.7 (CH), 69.1 (CH), 68.0 (CH), 67.2 (CH), 38.2 ($CH_2$), 18.9 ($CH_2$), 14.1 (Me); MS (CI) 362 ($MH^+$, 100), 246 (75); found $MH^+$ 362.1204, $C_{21}H_{23}FeNO$ + H requires 362.1207. Anal. Calcd for $C_{21}H_{23}FeNO$: C, 69.8; H, 6.4; N, 3.9. Found: C, 69.8; H, 6.4; N, 3.8.

**General Procedure for Organometallic Additions to Oxime Ether.** The oxime ether (3.9 mmol, 1 equiv) was dissolved in toluene (10 mL) under nitrogen and cooled to −78 °C. Boron trifluoride diethyl etherate (11.8 mmol, 3 equiv) was added and the mixture stirred for 15 min. The organometallic reagent (11.8 mmol, 3 equiv) was added dropwise over 30 min at this temperature and the mixture stirred until all starting material was consumed (TLC analysis). The reaction mixture was then quenched at this temperature with aqueous saturated ammonium chloride solution (10 mL) and allowed to warm to room temperature. The product was extracted with ether (3 × 15 mL), and the extracts were combined, dried ($K_2CO_3$), filtered, and evaporated. The residue was purified by column chromatography on silica gel. The diastereoselectivity of the addition was determined by analysis of the NMR spectrum of the product focusing particularly on the signals due to the NC*H* at the new chiral center and the OC*H* of the auxiliary.

**(1*R*,1′*R*)-(+)-1-Ferrocenyl-2-methyl-*N*-(1-phenylbutoxy)-1-propylamine 8a.** Obtained from the addition of isopropylmagnesium chloride to (*E*)-(*R*)-(+)-*O*-(1-phenylbutyl)ferrocene-1-carboxaldoxime **7**. The crude product was purified by column chromatography on silica gel, eluting with ether−light petroleum (1:35) to give the *title compound* (69%, >95% de) as a yellowish powder: mp 65−66 °C (from aqueous acetone); $[\alpha]_D^{25}$ −131.8 (*c* 1.00, $CHCl_3$); IR (KBr)/cm$^{-1}$ 3083, 3027, 2945, 2919, 2904, 2863, 1455, 1404, 1107, 1025, 989, 815, 758, 692; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.35 (5 H, m), 5.91 (1 H, br s), 4.67 (1 H, br), 4.08 (2 H, m), 3.94 (2 H, m), 3.97 (5 H, s), 3.51 (1 H, d, *J* 3.6), 2.18 (1 H, m), 1.86 (1 H, m), 1.57 (2 H, m), 1.37 (1 H, m), 0.95 (3 H, t, *J* 7.2), 0.83 (3 H, d, *J* 7.0), 0.75 (3 H, d, *J* 6.8); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 143.5 (C), 128.5 (CH), 127.5 (CH), 126.6 (CH), 85.0 (CH), 69.5 (CH), 68.4 (CH), 67.4 (CH), 66.72 (CH), 66.66 (CH), 64.4 (CH), 38.8 ($CH_2$), 29.8 (CH), 19.7 (Me), 19.3 ($CH_2$), 16.7 (Me), 14.0 (Me); the C (Fc) was too weak to be visible in the $^{13}$C NMR spectrum; MS (CI) 406 ($MH^+$, 5%), 256 (25), 241 (95), 166 (20), 150 (100); found $MH^+$ 406.1824, $C_{24}H_{31}FeNO$ + H requires 406.1833. Anal. Calcd for $C_{24}H_{31}FeNO$: C, 71.1; H, 7.7; N, 3.5. Found: C, 70.9; H, 7.8; N, 3.6.

**(1*R*,1′*R*)-(−)-1-Ferrocenyl-2,2-dimethyl-*N*-(1-phenylbutoxy)-1-propylamine 8b.** Obtained from the addition of *tert*-butyllithium to (*E*)-(*R*)-(+)-*O*-(1-phenylbutyl)ferrocene-1-carboxaldoxime **7**. The crude product was purified by column chromatography on silica gel, eluting with ether−light petroleum (1: 40) to give the *title compound* (64%, >95% de) as a yellow powder: mp 90−92 °C; $[\alpha]_D^{27}$ -145.8 (*c* 1.00, $CHCl_3$); IR (neat)/cm$^{-1}$ 2954, 2932, 2915, 2870, 1454, 1428, 1362, 1106, 1060, 1028, 1002, 973, 907, 877, 824, 815, 777; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.28−7.46 (5 H, m), 5.98 (1 H, brs), 4.65 (1 H, s), 4.16 (1 H, s), 3.88−4.12 (7 H, m), 3.80 (1 H, s), 3.25 (1 H, s), 1.80−1.90 (1 H, m), 1.52−1.64 (1 H, m), 1.38−1.50 (1 H, m), 1.20−1.33 (1 H, m), 0.92 (3 H, t, *J* 4.6), 0.88 (9 H, s); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 143.1 (C), 128.5 (CH), 127.6 (CH), 127.2 (CH), 89.6 (C), 84.5 (CH), 70.3 (CH), 68.3 (CH), 68.0 (CH), 67.2 (CH), 66.0 (CH), 65.9 (CH), 38.3 ($CH_2$), 34.6 (C), 27.4 (Me), 19.3 ($CH_2$), 14.2 (Me); MS (ES) 419 ($M^+$, 5), 255 (100), 186 (4), found $M^+$ 419.1925, $C_{25}H_{33}FeNO$ requires 419.1906. Anal. Calcd for $C_{25}H_{33}FeNO$: C, 71.6; H, 7.9; N, 3.3. Found: C, 71.5; H, 8.0; N, 3.4.

**(1*R*,1′*R*)-(−)-1-Ferrocenyl-2-phenyl-*N*-(1-phenylbutoxy)-1-ethylamine 8c.** Obtained from the addition of benzylmagnesium chloride to (*E*)-(*R*)-(+)-*O*-(1-phenylbutyl)ferrocene-1-carboxaldoxime **7**. The crude product was purified by column chromatography on silica gel, eluting with ether−light petroleum (1:25) to give the title compound (79%, >95% de)) as an orange powder: mp 76 − 78 °C; $[\alpha]_D^{26}$ −17.6 (*c* 1.00, $CHCl_3$); IR ($CHCl_3$)/cm$^{-1}$ 2960, 2933, 2872, 2398, 1602, 1494, 1454, 1105, 1000, 912, 837; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.05−7.38 (10 H, m), 5.69 (1 H, s), 4.53 (1 H, t, *J* 6.5), 3.91−4.25 (8 H, m), 3.88 (1 H, s), 3.76 (1 H, s), 3.28 (1 H, dd, *J* 12.9, 5.3), 2.84 (1 H, dd, *J* 12.9, 6.7), 1.74−1.86 (1 H, m), 1.64−1.40 (2 H, m), 1.23−1.38 (1 H, m), 0.92 (3 H, t, *J* 7.2); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 143.3 (C), 139.2 (C), 129.7 (CH), 128.4 (CH), 128.0 (CH), 127.4 (CH), 126.6 (CH), 125.9 (CH), 88.6 (C), 85.1 (CH), 68.2 (CH), 67.5 (CH), 66.8 (CH), 66.3 (CH), 61.5 (CH), 40.8 ($CH_2$), 38.6 ($CH_2$), 19.3 ($CH_2$), 14.1 (Me); MS (ES) 476 ($MNa^+$, 11), 453 ($M^+$, 8), 289 (100); found $M^+$ 453.1767, $C_{28}H_{31}FeNO$ requires 453.1750.

**General Procedure for the Synthesis of Chiral Ureas and Thioureas from Hydroxylamines 8.** (a) Zinc dust (15 mmol) was added to the hydroxylamine **8** (0.38 mmol) dissolved in acetic acid−water (6 mL, 1:1). The mixture was placed in a sonic bath at 40 °C until all of the starting material was consumed (TLC, typically 1.5−6 h). The zinc was filtered and rigorously washed with water and ether. The filtrate was extracted with ether (2×), the aqueous layer was basified to pH 12 with aqueous sodium hydroxide solution (4 M), and then saturated ammonium chloride solution was added to disperse any emulsion formed. The solution was then further

extracted with dichloromethane (3×). The dichloromethane organic layers were combined, dried ($K_2CO_3$), filtered, and evaporated to yield the crude amine (45−86%), used without further purification or characterization. (b) A solution of 4-nitrophenyl isocyanate (or isothiocyanates) (7.09 mmol) in dichloromethane (5 mL) was slowly added, over 2 min, to a solution of the above amine (5.91 mmol) in dichloromethane (25 mL), at 0 °C. The resulting mixture was stirred at room temperature for 6 h. Evaporation of the solvents under reduced pressure left an orange oil, which was purified by flash column chromatography.

**(*R*)-(+)-*N*-(4-Nitrophenyl)-*N*′-[1-(1-ferrocenyl-2-methyl)propyl]urea 2.** Obtained from cleavage of hydroxylamine **8a** (0.300 g, 0.74 mmol) followed by reaction of the crude amine with 4-nitrophenyl isocyanate (0.116 g, 0.71 mmol). Workup and purification by column chromatography eluting with light petroleum−ethyl acetate (3:1) gave the *title compound* as an orange solid (0.190 g, 61% over two steps): mp 153 − 155 °C; $[\alpha]_D^{29}$+31.8 (*c* 1.00, acetone); IR (neat)/cm$^{-1}$ 2961, 2930, 1643, 1614, 1561, 1514, 1467, 1411, 1341, 1331, 1303, 1237, 1178, 1110, 1027, 1003, 853, 836, 815, 751; $^1$H NMR (400 MHz; acetone-*d*) $\delta$ 8.68 (1 H, s), 8.17 (2 H, d, *J* 9.3), 7.80 (2 H, d, *J* 9.3), 6.36 (1 H, d, *J* 9.6), 4.75 (1 H, dd, *J* 9.7, 4.9), 4.21 − 4.24 (1 H, m), 4.15 (5 H, m), 4.10 − 4.13 (3 H, m), 1.77 − 1.88 (1 H, m), 0.85 (3 H, d, *J* 6.8), 0.79 (3 H, d, *J* 6.8); $^{13}$C NMR (100 MHz; acetone-*d*) $\delta$ 155.9 (C), 149.1 (C), 143.2 (C), 126.8 (CH), 119.0 (CH), 92.3 (C), 70.4 (CH), 69.8 (CH), 69.0 (CH), 68.9 (CH), 67.1 (CH), 55.9 (CH), 36.7 (CH), 20.5 (Me), 19.0 (Me); MS (ES) 421 ($M^+$, 100); found $M^+$ 421.1090, $C_{21}H_{23}FeN_3O_3$ requires 421.1083.

**(*R*)-(+)-*N*-(4-Nitrophenyl)-*N*′-[1-(1-ferrocenyl-2,2-dimethyl)propyl]urea 3.** Obtained from cleavage of hydroxylamine **8b** (156 mg, 0.37 mmol) followed by reaction of the crude amine with 4-nitrophenyl isocyanate (33 mg, 0.20 mmol). Workup and purification by column chromatography eluting with light petroleum−ethyl acetate (4:1) gave the *title compound* as orange crystalline squares (63 mg, 39% over two steps): mp 208−210 °C; $[\alpha]_D^{31}$ +91.8 (*c* 0.98, acetone); IR (neat)/cm$^{-1}$ 3375, 2966, 1648, 1613, 1557, 1513, 1330, 1303, 1235, 1109, 1048, 822, 809; $^1$H NMR (400 MHz; acetone-*d*) $\delta$ 8.67 (1 H, s), 8.17 (2 H, d, *J* 9.2), 7.80 (2 H, d, *J* 9.2), 6.51 (1 H, d, *J* 10.0), 4.57 (1 H, d, *J* 10.0), 4.27 (1 H, s), 4.15 (5 H, s), 4.09 − 4.11 (3 H, m), 0.83 (9 H, s); $^{13}$C NMR (100 MHz; acetone-*d*) $\delta$ 154.1 (C), 147.3 (C), 141.4 (C), 124.9 (CH), 117.1 (CH), 89.4 (C), 69.9 (CH), 68.5 (CH), 67.2 (CH), 66.5 (CH), 65.6 (CH), 57.3 (CH), 35.6 (C), 26.0 (Me); MS (ES) 435 ($M^+$, 100); found $M^+$ 435.1268, $C_{22}H_{25}FeN_3O_3$ requires 435.1240.

**(*R*)-(+)-*N*-(4-Nitrophenyl)-*N*′-[1-(1-ferrocenyl-2-phenyl)ethyl]urea 4.** Obtained from the cleavage of hydroxylamine **8c** (68 mg, 0.15 mmol) followed by reaction of the crude amine with 4-nitrophenyl isocyanate (25 mg, 0.15 mmol). Workup and purification by flash column chromatography eluting with light petroleum−ethyl acetate (4:1) gave the *title compound* as an orange fluffy powder (50 mg, 71% over two steps): mp 73−75 °C; $[\alpha]_D^{31}$ +4.7 (*c* 0.98. acetone); IR (neat)/cm$^{-1}$ 3382, 2927, 2360, 1661, 1611, 1550, 1502, 1328, 1303, 1232, 1178, 1110, 849, 821, 752; $^1$H NMR (400 MHz; acetone-*d*) $\delta$ 8.60 (1 H, s), 8.13 (2 H, d, *J* 9.3), 7.70 (2 H, d, *J* 9.3), 7.12−7.28 (5 H, m), 6.16 (1 H, d, *J* 9.1), 5.06−5.14 (1 H, m), 4.19 (5 H, s), 4.15−4.18 (2 H, m), 4.10−4.14 (2 H, m), 3.18 (1 H, dd, *J* 13.8, 5.4), 2.99 (1 H, dd, *J* 13.8, 8.3); $^{13}$C NMR (100 MHz; acetone-*d*) $\delta$ 155.5 (C), 149.0 (C), 143.3 (C), 140.5 (C), 131.4 (CH), 129.9 (CH), 128.0 (CH), 126.7 (CH), 119.0 (CH), 93.3 (C), 70.4 (CH), 69.3 (CH), 69.1 (CH), 68.6 (CH), 68.0 (CH), 51.8 (CH), 44.7 ($CH_2$); MS (ES) 492 ($MNa^+$, 70), 289 (100); found M + $Na^+$ 492.0973, $C_{25}H_{23}FeN_3NaO_3$ requires 492.0981.

**(*R*)-(−)-*N*-(4-Nitrophenyl)-*N*′-[1-(1-ferrocenyl-2-phenyl)ethyl]thiourea 5.** Obtained from the cleavage of hydroxylamine **8c** (90 mg, 0.20 mmol) followed by reaction of the crude amine with 4-nitrophenyl isothiocyanate (36 mg, 0.20 mmol). Workup and purification by column chromatography light petroleum−ethyl acetate (4:1) gave urea as an orange oil (62 mg, 64% over two steps): $[\alpha]_D^{28}$ −131.2 (*c* 0.43, acetone); IR (neat)/cm$^{-1}$ 1595, 1500, 1329, 1307, 1237, 1109, 820, 750; $^1$H NMR (400 MHz; acetone-*d*) $\delta$ 9.43 (1 H, s), 8.18 (2 H, d, *J* 8.7), 7.98 (2 H, d, *J* 8.7), 7.70 (1 H, s), 7.12 − 7.31 (5 H, m), 5.84 (1 H, s), 4.27 (1 H, s), 4.18 (5 H, s), 4.14 (1 H, s), 4.11 (2 H, s), 3.21 (2 H, d, *J* 6.8); $^{13}$C NMR (100 MHz; acetone-*d*) $\delta$ 181.6 (C), 147.9 (C), 144.9 (C), 140.1 (C), 131.4 (CH), 129.9 (CH), 128.1 (CH), 126.2 (CH), 123.2 (CH), 91.6 (C), 70.4 (CH), 69.5 (CH), 69.2 (CH), 69.1 (CH), 68.0 (CH), 56.2 (CH), 43.6 ($CH_2$); MS (ES) 508 ($MNa^+$, 23), 486 ($MH^+$, 23), 289 (100); found M + $Na^+$ 508.0733, $C_{25}H_{23}FeN_3NaO_2S$ requires 508.0753.

**Bis-(*E*)-(*R*)-*O*-(1-phenylbutyl)ferrocene-1,1′-biscarboxaldoxime 9.** Obtained from the condensation of (*R*)-(−)-*O*-(1-phenylbutyl)hydroxylamine with ferrocene-1,1′-biscarboxaldehyde[8] under the usual conditions.[6] The crude product was purified by column chromatography on silica gel, eluting with ether−light petroleum (1:13) to give the *title compound* (64%) as a red solid: mp 38 − 39 °C; $[\alpha]_D^{31}$ −408.6 (*c* 1.00, $CHCl_3$); IR (film)/cm$^{-1}$ 3083, 3058, 3022, 2955, 2925, 2868, 1609, 1450, 1373, 1358, 1312, 1240, 1102, 1055, 1020, 933, 758, 692; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.79 (2 H, s), 7.32 (10 H, m), 5.11 (2 H, t, *J* 6.9), 4.37 (2 H, d, *J* 1.3), 4.31 (2 H, d, *J* 1.9), 4.16 (4 H, t, *J* 1.9), 1.96 (2 H, m), 1.78 (2 H, m), 1.43 (4 H, m), 0.97 (6 H, t, *J* 7.4); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 148.1 (CH), 143.0 (C), 128.2 (CH), 127.2 (CH), 126.8 (CH), 84.8 (CH), 77.7 (C), 70.9 (CH), 70.8 (CH), 69.0 (CH), 68.3 (CH), 38.3 ($CH_2$), 18.9 ($CH_2$), 14.0 (Me); MS (CI) 537 ($MH^+$, 100), 389 (45); found $MH^+$ 537.2195, $C_{32}H_{36}FeN_2O_2$ + H requires 537.2204. Anal. Calcd for $C_{32}H_{36}FeN_2O_2$: C, 71.6; H, 6.8; N, 5.2. Found: C, 71.6; H, 6.8; N, 5.2.

**(*R*,*R*,*R*,*R*)-(−)-1,1′-Bis[2-phenyl-1-(1-phenylbutoxyamino)ethyl]ferrocene 10.** Obtained from the addition of benzylmagnesium chloride (12.79 mmol) to the ferrocene bis-oxime ether **9** (1.83 mmol). The crude product was purified by column chromatography on silica gel, eluting with ether light petroleum (1:12) to give the *title compound* (73%, >95% de) as a orange oil: $[\alpha]_D^{27}$ −35.2 (*c* 1.00, $CHCl_3$); IR (neat)/cm$^{-1}$ 3085, 3062, 3028, 2956, 2931, 2871, 1740, 1603, 1494, 1454, 1415, 1376, 1307, 1237, 1202, 1176, 1156, 1106, 1070, 1026, 1003, 978, 901, 829; $^1$H NMR (400 MHz; $CDCl_3$) $\delta$ 7.04−7.38 (20 H, m), 5.59 (2 H, s), 4.49 (2 H, dd, *J* 7.7, 5.9), 3.83 − 3.89 (2 H, m), 3.79−3.83 (2 H, m), 3.70−3.74 (4 H, m), 3.62−3.68 (2 H, m), 3.23 (2 H, dd, *J* 13.1, 6.3), 2.78 (2 H, dd, *J* 13.1, 7.0), 1.73−1.85 (2 H, m), 1.40−1.61 (4 H, m), 1.25−1.35 (2 H, m), 0.93 (6 H, t, *J* 7.2); $^{13}$C NMR (100 MHz; $CDCl_3$) $\delta$ 143.1 (C), 139.1 (C), 129.7 (CH), 128.3 (CH), 128.0 (CH), 127.3 (CH), 126.5 (CH), 125.9 (CH), 88.8 (C), 85.1 (CH), 68.6 (CH), 67.9 (CH), 67.3 (CH), 66.7 (CH), 61.4 (CH), 40.5 ($CH_2$), 38.6 ($CH_2$), 19.2 ($CH_2$), 14.1 (Me); MS (ES) 721 ($MH^+$, 100), 556 (34) 391 (51); found $MH^+$ 721.3460, $C_{46}H_{52}FeN_2O_2$ + H requires 721.3451.

**(*R*,*R*)-(−)-1,1′-Bis[3-(4-nitrophenyl)ureido(2-phenylethyl)]ferrocene 6.** Reductive cleavage of hydroxylamine **10** (0.411 g, 0.57 mmol) and zinc dust (3.73 g, 57.0 mmol). Workup gave crude (*R*,*R*)-1,1′-bis[1-amino-2-phenylethyl]ferrocene as a light orange powder (0.242 g, ∼100%), which was used without further purification or characterization. Urea **6** was prepared from the primary amine (46 mg, 0.11 mmol) and 4-nitrophenyl isocyanate (39 mg, 0.24 mmol). After workup, purification by column chromatography on silica gel, eluting with ethyl acetate−light petroleum (3.5:6.5), gave the *title compound* (59 mg, 72%) as an orange oil: $[\alpha]_D^{23}$ −28.2 (*c* 1.1, acetone); IR (neat)/cm$^{-1}$ 1659, 1601, 1547, 1502, 1328, 1303, 1230, 1178, 1111, 1047, 856, 834, 729, 713; $^1$H NMR (400 MHz; acetone-*d*) $\delta$ 8.60 (2 H, s), 8.05−8.14 (4 H, m), 7.60−7.70 (4 H, m), 7.04−7.28 (10 H, m), 6.26 (2 H, d, *J* 9.1), 5.11−5.22 (2 H, m), 4.14−4.28 (8 H, m), 3.20 (2 H, dd, *J* 13.8, 5.3), 3.02 (2 H, dd, *J* 13.8, 8.5); $^{13}$C NMR (100 MHz; acetone-*d*) $\delta$ 155.7 (C), 148.8 (C), 143.3 (C), 140.4 (C), 131.3 (CH), 129.9 (CH), 128.0 (CH), 126.6 (CH), 119.1 (CH), 93.8 (C), 70.2 (CH), 70.0 (CH), 69.5 (CH), 68.8 (CH),

51.8 (CH), 44.6 ($CH_2$); MS (ES) 753 ($MH^+$, 30), 292 (64), 219 (100); found $MH^+$ 753.2093, $C_{40}H_{36}FeN_6O_6$ + H requires 753.2124.

**Preparation of the Tetrabutylammonium Carboxylate Salts.** The carboxylic acid (6 mmol) was dissolved in MeOH (6 mL), and tetrabutylammonium hydroxide (1 M in MeOH; 6 mmol) was added. The solution was stirred overnight at room temperature. The solvent was removed, and the residue dried under high vacuum before being recrystallized from diethyl ether (compound **13** was used as a dry oil).

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**Supporting Information Available:** NMR spectra of receptors and conditions used for binding constant determinations and electrochemistry. This material is available free of charge via the Internet at http://pubs.acs.org.

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