Anion complexation and electrochemical behaviour of ferrocene-appended amido-pyrrole clefts†

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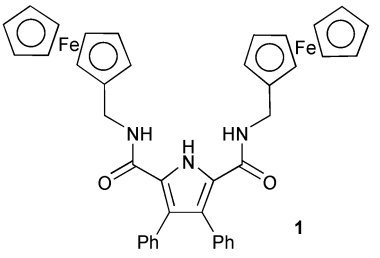
Two amido-pyrrole cleft anion receptors bearing two ferrocene reporter groups have been synthesised and crystallographically characterised; the receptors contain either a non-conjugated or conjugated link between the anion-binding amido-pyrrole unit and the ferrocene reporter groups. The anion binding affinities and electrochemical behaviour of the receptors in the absence and presence of anions have been studied by ^{1}H NMR titration techniques and cyclic voltammetry using a Pt microdisc working electrode, respectively.

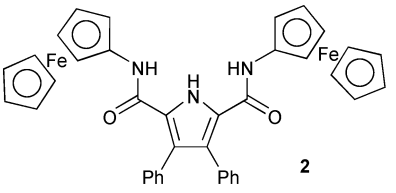
Sensors for cationic, anionic or neutral guests containing ferrocene reporter groups have been synthesised by a number of research groups world-wide.[1,2] Many of these systems that bind anions show a significant perturbation (usually a shift towards negative potentials) of the ferrocene/ferrocenium voltammetry upon anion binding. The pathway used to 'communicate' the binding event to the reporter group is of vital importance and must be considered at the design stage of a new receptor. Through-space, through-bond, direct coordination, interference and conformational change pathways have been identified as bridging the binding site/reporter group divide.[3] We have recently identified a possible direct-coordination pathway mediating binding and electrochemical sensing in a ferrocene appended calix[4]pyrrole.[4] We therefore decided to synthesise two ferrocene-appendedamido-pyrrole cleft species[5] containing a non-conjugated link (**1**) and a conjugated link (**2**) between the anion binding site (amido-pyrrole cleft) and reporter group (ferrocene) in an attempt to exploit possible CH–anion interactions which may be possible in anion complexes of **2**, but which are less likely in **1** due to the greater conformational flexibility of the receptor, and, in addition, to study the effect of the through-bond pathway[6] on anion recognition in these systems.

Receptors **1** and **2** were synthesised by reaction of either ferrocenylmethylamine[7] or ferrocenylamine[7] with 3,4-diphenyl-1*H*-pyrrole-2,5-dicarbonyl dichloride[5] in dichloromethane, in the presence of triethylamine and a catalytic quantity of DMAP, followed by purification by column chromatography. The compounds were fully characterised by ^{1}H and ^{13}C NMR and high resolution mass spectrometry.

Crystals of the receptors were grown by slow evaporation of dichloromethane and dichloromethane/diethyl ether solutions of **1** and **2**, respectively. The crystal structures of **1** (Fig. 1) and **2** (Fig. 2) reveal the formation of solid-state dimers (a motif that has been observed for other 2-substituted pyrrole species).[5,8,9]

† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra of **1** and **2**, ^{1}H NMR titrations of **1** and **2** with various putative anionic guests and with chloride following ferrocene CH resonances. See http://www.rsc.org/suppdata/nj/b2/b202989h/





Association constants for receptors **1** and **2** with a variety of anionic guests were determined by ^{1}H NMR titration techniques.[10] Previous studies of amido-pyrrole cleft-type receptors were conducted in acetonitrile-d_3 or DMSO-d_6–0.5% water and showed that the receptors were selective for oxo-anions such as benzoate and dihydrogenphosphate. Unfortunately, receptors **1** and **2** were not sufficiently soluble in acetonitrile to conduct all these studies in that solvent, hence, dichloromethane-d_2 was used for the NMR studies and regular dichloromethane used for the electrochemistry. The results are presented in Table 1 and show that, in general, receptor **2** has a higher affinity for anions than receptor **1**, with receptor

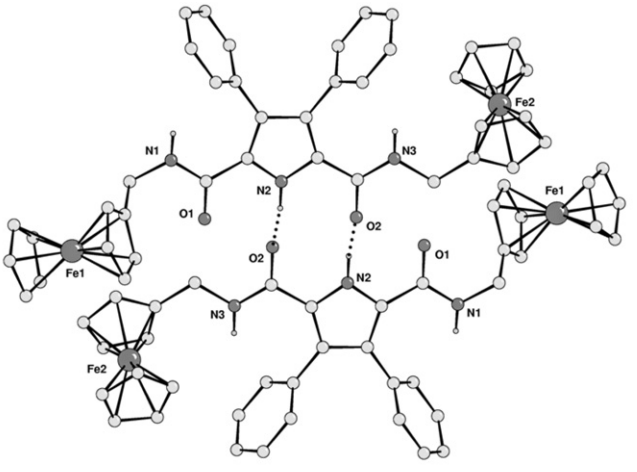


Fig. 1 The X-ray crystal structure of **1** showing dimer formation in the solid state *via* NH–O hydrogen bonds [N···O 2.961(3) Å].

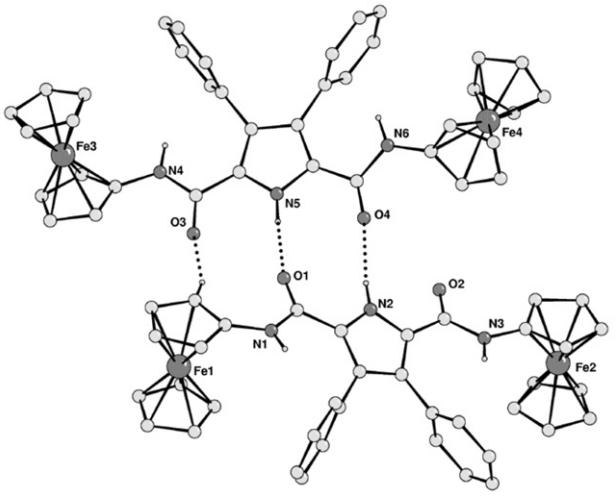


Fig. 2 The X-ray crystal structure of **2** showing dimer formation in the solid state *via* NH–O and CH–O hydrogen bonds [N···O 2.795(4) and 3.020(3) Å; C···O 3.2245(5) Å].

2 binding benzoate and fluoride most strongly. One ferrocene CH resonance in compound **2** shiftsconsiderably during the titrations (the corresponding shift not being observed in the case of compound **1**—see ESI). This may be due to the formation of a CH···anion hydrogen bond,[4] but could also be due to the presence of the conjugated bond pathway between the anion binding site and the cyclopentadienyl ring.[6] The enhanced affinity of compound **2** with respect to compound **1** may be due to the higher rigidity of the former compound with the more flexible ferrocene groups of the latter possibly blocking the anion binding site. Dilution studies were performed and showed no evidence of self-association in solution. For example, in the case of compound **2**, over the concentration range 2.6×10^{-4} to 3.5×10^{-2} M, no significant shift in the ^{1}H NMR proton resonances was observed.

The steady state voltammetric response of **1** and **2** in presence and absence of guest anions was recorded with a platinum microdisc electrode. The electrochemical oxidation of **1** ($E_{1/2} = 0.182$ V) is more difficult than that of **2** ($E_{1/2} = 0.080$ V), but both appear to be reversible, $E_{3/4} - E_{1/4} = 55$ and 48 mV, respectively. With some anions, the voltammetric wave is seriously distorted as the product of the electrochemical reaction passivates the electrode. For example with $H_2PO_4^-$ and HSO_4^-, the voltammogram of **1** does not reach the limiting current expected and the reverse scan decays rapidly. In many cases, an electrochemical pretreatment was found necessary to clean the electrode. Exceptfor Br^-, all anions where found to shift the wave negatively with respect to that without anions; see Table 1 for a summary of the difference in half-wave potentials. Taking into account an error of ±10 mV, it is clear that Br^- does not affect the electrochemistry of either receptor **1** or **2**. Fluoride produces the largest shifts, but, intriguingly, yields two waves with compound **2**. We are currently investigating the cause of this phenomenon. Interestingly, the strong affinity of receptor **2** with benzoate also corresponds to a significant shift of the voltammetric wave. It is important to point out that the association constants determined by NMR correspond to the complexation of the anion by the neutral receptor, whereas the voltammetric shifts reflect the interaction of the guest anion with the oxidised receptor. These two sets of data are related by the association constant of theanion to the oxidised receptor through the scheme of one square.[11] However, the shifts observed with F^- and benzoate are significant and clearly indicate that the electrochemical oxidation of the receptors is affected by the bound anion.

Table 1 Association constants of receptors **1** and **2** with various anions (added as their tetrabutylammonium salts) in dichloromethane-d_2 and voltammetric shifts in the ferrocene/ferrocenium redox couple of receptors in the presence of three equivalents of the anion in dichloromethane

	Compound **1**		Compound **2**	
	K_a/M^{-1}	ΔE/mV	K_a/M^{-1}	ΔE/mV
F^-	170	−130	705	−125 and −255[a]
Cl^-	< 20	−75	70	−55
Br^-	< 20	0	< 20	−10
$H_2PO_4^-$	45	—[b]	145	—[b]
HSO_4-	45	—[b]	75	−40
Benzoate	35	−60	1820	−120

[a] Two waves are observed. [b] The voltammetric wave is seriously distorted because the product of the electrochemical reaction passivates the electrode.

This communication shows that, in addition to functioning as anion receptors, amido-pyrrole clefts have potential to function as electrochemical anion sensor species. The electrochemical properties of compounds **1** and **2** (and other electrochemically active amido-pyrrole clefts) is currently the subject of further investigation, the results of which will be published in due course.

Experimental

Synthesis of 1

3,4-Diphenyl-1*H*-pyrrole-2,5-dicarbonyl dichloride (1.2 g, 0.0032 mol) was dissolved in dry dichloromethane (50 mL). The solution was stirred under a nitrogen atmosphere and triethylamine (0.711 g, 0.0070 mol), DMAP (catalytic quantity) and ferrocenemethylamine (1.51 g, 0.0070 mol) were added. The reaction mixture was stirred overnight under a nitrogen atmosphere. The dichloromethane solvent was removed *in vacuo* and the residue dissolved in acetonitrile (50 ml). The resultant precipitate was filtered, washed with acetonitrile (3 × 15 ml) and water (3 × 15 ml) and dried under high vacuum for two hours. The precipitate was purified by preparative layer chromatography on silica plates eluted with dichloromethane–2% methanol, affording the final product, **1**, in 31% yield (0.69 g) as an orange powder. ^{1}H NMR in CD_2Cl_2, δ (ppm):3.89 (m, 4H, FcH), 3.96 (m, 10H, FcH), 4.05 (m, 4H, FcH), 4.10 (m, 4H, CH_2), 5.75 (br s, 2H, amide NH), 7.23 (m, 4H, ArH), 7.30 (m, 6H, ArH), 10.21 (s, 1H, pyrrole NH). ^{13}C NMR in $CDCl_3$, δ (ppm): 39.2, 67.7, 68.3, 68.8, 84.8, 124.2, 126.1, 128.4, 129.3, 131.2, 133.6, 160.2. ES^+ mass spectrum, m/z: 701 (M^+). HRES MS: $C_{40}H_{35}N_3O_2Fe_2$ calc 701.1423, found 701.1437 Δ = 2.0 ppm.

Synthesis of 2

3,4-Diphenyl-1*H*-pyrrole-2,5-dicarbonyl dichloride (0.83 g, 0.00241 mol) was dissolved in dry dichloromethane (50 mL). The solution was stirred under a nitrogen atmosphere and triethylamine (0.487 g, 0.00481 mol), DMAP (catalytic quantity) and ferrocenylamine (0.9 g, 0.00481 mol) were added. The reaction mixture was stirred overnight under a nitrogen atmosphere. The dichloromethane solvent was removed *in vacuo* and the residue dissolved in acetonitrile (80 ml) and magnetically stirred; the solution was then filtered. Water (100 ml) was added to the solution and caused the product to separate out from solution as an oil. The oil was dissolved in acetone, dried and then purified by column chromatography on silica gel eluted with dichloromethane–2% methanol, affording the final product, **2**, in 13% yield (0.21 g) as an orange powder.^{1}H NMR in CD_2Cl_2, δ (ppm):3.95 (m, 4H,

FcH), 4.02 (m, 10H, FcH), 4.31 (m, 4H, FcH), 6.69 (br s, 2H, amide NH), 7.35 (m, 4H, ArH), 7.7.46 (m, 6H, ArH), 10.29 (s, 1H, pyrrole NH). ^{13}C NMR in $CDCl_3$, δ (ppm): 62.5, 65.3, 69.5, 93.3, 124.7, 126.4, 128.9, 129.5, 131.3, 133.6, 158.6. ES^+ mass spectrum, m/z: 673 (M^+). HRES MS: $C_{38}H_{31}N_3O_2Fe_2$ calc 673.1110, found 673.1107 $\Delta = 0.4$ ppm.

Crystal data for 1

$C_{40}H_{35}N_3O_2Fe_2$, $M_r = 701.41$, $T = 120(2)$ K, monoclinic, space group $C2/c$, $a = 16.1333(5)$, $b = 10.3709(3)$, $c = 37.6445(12)$ Å, $\beta = 97.9820(10)°$, $V = 6237.5(3)$ Å^3, $\rho_{calc} = 1.494$ g cm^{-3}, $\mu = 0.973$ mm^{-1}, $Z = 8$, reflections collected: 11 432, independent reflections: 5096 ($R_{int} = 0.0706$), final R indices [$I > 2\sigma(I)$]: $R1 = 0.0474$, $wR2 = 0.0817$, R indices (all data): $R1 = 0.0929$. $wR2 = 0.0938$.

Crystal data for 2

$C_{38}H_{31}N_3O_2Fe_2$, $M_r = 673.36$, $T = 120(2)$ K, triclinic, space group $P\bar{1}$, $a = 12.7602(3)$, $b = 14.1906(4)$, $c = 17.3431(5)$ Å, $\alpha = 87.721(1)$, $\beta = 83.137(1)$, $\gamma = 75.782(2)°$, $V = 3022.22(14)$ Å^3, $\rho_{calc} = 1.480$ g cm^{-3}, $\mu = 1.001$ mm^{-1}, $Z = 4$, reflections collected: 36 068, independent reflections: 10 432 ($R_{int} = 0.0867$), final R indices [$I > 2\sigma(I)$]: $R1 = 0.0456$, $wR2 = 0.0862$, R indices (all data): $R1 = 0.0968$. $wR2 = 0.1016$.

CCDC reference number 184544. See http://www.rsc.org/suppdata/b2/b202989h/ for crystallographic data in CIF or other electronic format.

Cyclic voltammetry

Steady state voltammograms were recorded at room temperature, at 20 mV s^{-1}, with a 25 μm diameter Pt microdisc, prepared as reported previously,[12] and a silver wire counter-reference electrode located in a separate compartment with 0.1 M $AgNO_3$. The potential was controlled with a HiTek PPR1 waveform generator and the current measured with a homemade current follower. The microdisc was cleaned with 0.3 μm alumina on a polishing microcloth. Before each voltammogram, the electrode was held at −2.5 V for 12 s, then at −0.175 V for 12 s. This pre-treatment was found necessary to obtain reproducible voltammetry. Dichloromethane solutions containing 0.5 mM ferrocene compound, 1.5 mM tetrabutylammonium salt of the anion of interest and 0.1 M tetrabutylammonium tetrafluoroborate supporting electrolyte were purged with argon between recordings and kept under an argon blanket during recordings. A series of voltammogramswas recorded for each solution.

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References

1 (*a*) T. Saji *Chem. Lett.*, 1986, 275; (*b*) T. Saji and I. Kinoshita, *J. Chem. Soc., Chem. Commun.*, 1986, 716; (*c*) J. C. Medina, T. T. Goodnow, M. T. Rojas, J. L. Atwood, B. C. Lynn, A. E. Kaifer and G. W. Gokel, *J. Am. Chem. Soc.*, 1992, **114**, 10 583; (*d*) P. D. Beer, Z. Chen, M. G. B. Drew and P. A. Gale, *J. Chem. Soc., Chem. Commun.*, 1995, 1851; (*e*) S. R. Collinson, T. Gelbrich, M. B. Hursthouse and J. H. R. Tucker, *Chem. Commun.*, 2001, 555; (*f*) H. Plenio and C. Alberle, *Angew. Chem., Int. Ed.*, 1998, **37**, 1397; (*g*) L. O. Abouderbala, W. J. Belcher, M. G. Boutelle, P. J. Cragg, J. Dhaliwal, M. Fabre, J. W. Steed, D. R. Turner and K. J. Wallace, *Chem. Commun.*, 2002, 358.

2 For examples of ferrocene-containing anion sensors involving pyrrole, see: (*a*) J. L. Sessler, A. Gebauer and P. A. Gale, *Gazz. Chim. Ital.*, 1997, **127**, 723; (*b*) M. Scherer, J. L. Sessler, A. Gebauer and V. Lynch, *Chem. Commun.*, 1998, 85; (*c*) M. Scherer, J. L. Sessler, M. Moini, A. Gebauer and V. Lynch, *Chem. Eur. J.*, 1998, **4**, 152; (*d*) J. L. Sessler, R. S. Zimmerman, G. J. Kirkovits, A. Gebauer and M. Scherer, *J. Organomet. Chem.*, 2001, **637**, 343.

3 P. D. Beer, P. A. Gale and G. Z. Chen, *J. Chem. Soc., Dalton Trans.*, 1999, 1897.

4 P. A. Gale, M. B. Hursthouse, M. E. Light, J. L. Sessler, C. N. Warriner and R. S. Zimmerman, *Tetrahedron Lett.*, 2001, **42**, 6759.

5 (*a*) P. A. Gale, S. Camiolo, C. P. Chapman, M. E. Light and M. B. Hursthouse, *Tetrahedron Lett.*, 2001, **42**, 5095; (*b*) P. A. Gale, S. Camiolo, G. J. Tizzard, C. P. Chapman, M. E. Light, S. J. Coles and M. B. Hursthouse, *J. Org. Chem.*, 2001, **66**, 7849; (*c*) S. Camiolo, P. A. Gale, M. B. Hursthouse, M. E. Light and A. J. Shi, *Chem. Commun.*, 2002, 758.

6 P. D. Beer, C. Blackburn, J. F. McAleer and H. Sikanyika, *Inorg. Chem.*, 1990, **29**, 378.

7 For the preparation of the ferrocene amines, see: (*a*) G. R. Knox, P. L. Pauson and D. Willison, *Organometallics*, 1990, **9**, 301; (*b*) K. Kavallieratos, S. Hwang and R. H. Crabtree, *Inorg. Chem.*, 1999, **38**, 5184; (*c*) P. Spencer, *Polyaza Redox-Active Acyclic and Macrocyclic Compounds Designed to Bind Cations and Anions*, D.Phil thesis, University of Oxford, 1994.

8 C. Schmuck and J. Lex, *Eur. J. Org. Chem.*, 2001, 1519.

9 A. T. Dubis and S. J. Grabowski, *New J. Chem.*, 2002, 165.

10 M. J. Hynes *J. Chem. Soc., Dalton. Trans.*, 1993, 311.

11 P. D. Beer, P. A. Gale and Z. Chen, *Adv. Phys. Org. Chem.*, 1998, **31**, 1.

12 G. Denuault *Chem. Ind.*, 1996, **18**, 678.