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Mono- and bis-ferrocene 2,5-diamidopyrrole clefts: solid-state assembly, anion binding and electrochemical properties

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Abstract

Four amido-pyrrole cleft anion receptors bearing one or two ferrocene reporter groups have been synthesised and crystallographically characterised. The receptors contain either a non-conjugated (**1** and **3**) or conjugated (**2** and **4**) 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.

Keywords: Anion binding; Pyrrole; Ferrocene; Self-assembly; Electrochemical sensor

1. Introduction

Pyrrolic anion receptors have been shown to be both effective and selective in their complexation properties. Early systems developed by Sessler et al. were based upon expanded porphyrins (e.g.: sapphyrin) that bound small anions such as fluoride within the protonated core of the macrocycle [1]. Later systems based on non-aromatic macrocycles such as the calixpyrroles also showed selectivity for halides [2] whilst complex and elegant receptors such as the bipyrrole based catenane reported by Sessler, Vögtle and co-workers exhibits high affinity for phosphates [3]. More recently, attention has been directed to acyclic systems such as the dipyrrolylquinoxalines [4], guanidinium functionalised pyrroles [5] and amido-pyrrole clefts [6]. A number of groups have synthesised a variety of electrochemical sensors for anions [7]. Electrochemical sensors for anions based upon pyrrole are fairly rare. Sessler et al. have reported *ansa*-ferrocene type systems that show significant perturbations in their electrochemical properties in the presence of anionic guests [8], whilst Gale, Sessler and co-workers have recently reported a ferrocene funtionalised calix [4]pyrrole in which a ferrocene CH group is believed to form a hydrogen bond to a bound anion [9]. In this paper, we report the synthesis of four ferrocene appended 2,5-diamido-pyrrole clefts and their anion binding and electrochemical properties in the absence and presence of anions [10].

2. Experimental

2.1. Synthesis

2.1.1. 3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid diferrocenylmethyl-amide 1

3,4-Diphenyl-1H-pyrrole-2,5-dicarbonyl dichloride [10] (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 [11] (1.51 g, 0.0070 mol) were added. The reaction mixture was stirred overnight under a nitrogen atmosphere. The dichloromethane solvent was removed in

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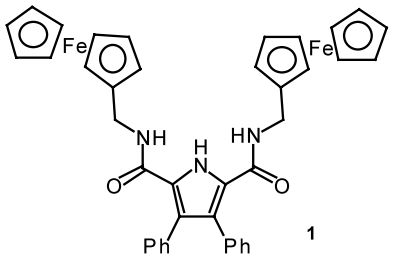
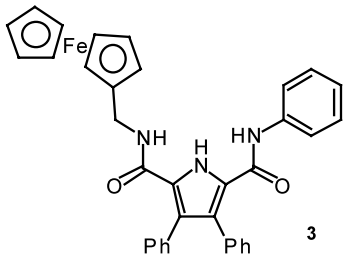
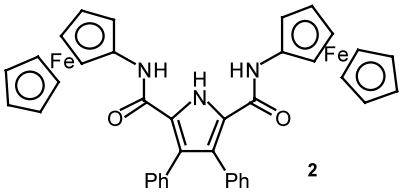
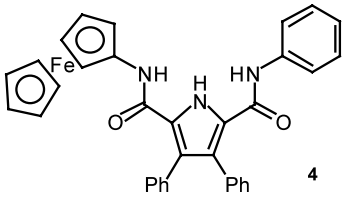








vacuo and the residue dissolved in acetonitrile (50 ml). The resultant precipitate was filtered, washed with acetonitrile (3 × 15 ml) and water (3 × 15 ml) and dried under high vacuum for 2 h. The precipitate was purified by preparative layer chromatography on silica plates eluted with dichloromethane/methanol 2% affording the final product **1** in 31% yield (0.69 g) as an orange powder. ^{1}H NMR in CD_2Cl_2 300 MHz, 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 $CDCl_3$ 400 MHz 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.

2.1.2. 3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid bis-ferrocenylamide 2

3,4-Diphenyl-1H-pyrrole-2,5-dicarbonyl dichloride [10] (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 [11] (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 purified by column chromatography on silica gel eluted with dichloromethane/methanol 2% affording the final product **2** in 13% yield (0.21 g) as an orange powder. ^{1}H NMR in CD_2Cl_2 300 MHz 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 $CDCl_3$ 300 MHz 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 Δ = 0.4 ppm.

2.1.3. 3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid monomethyl ester 6

3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid dimethyl ester **5** [12] (4 g, 0.0119 mol) was suspended in methanol (200 ml). The suspension was magnetically stirred and heated to reflux forming a solution. Potassium hydroxide (0.67 g, 0.119 mol) was added in water (50 ml). After refluxing overnight, the solution was left to cool to room temperature. The solution was acidified to pH 1 using concentrated hydrochloric acid, forming a white precipitate. This was removed by filtration and washed with water (3 × 50 ml). The white solid was dissolved in ether, and the aqueous layer that formed was removed. The organic layer was dried with magnesium sulfate, filtered and then the solvent removed in vacuo. The product **6** was obtained in a 78% yield (3 g) as a white powder. ^{1}H NMR in DMSO, 300 MHz, δ (ppm): 3.74 (s, 3H, CH_3), 7.13–7.26 (m, 10H, Ar), 12.31 (s, 1H, NH), 12.86 (s, 1H, OH). ^{13}C NMR in DMSO, 400 MHz, δ (ppm): 51.73, 51.82, 121.57, 122.15, 123.35, 126.87, 126.96, 127.06, 127.56, 127.59, 127.64, 130.31, 130.88, 131.02, 131.14, 133.76, 133.94, 134.16, 160.77, 161.81. ES$^-$ mass spectrum, *m/z*: 320 $(M–H^+)^-$, 641 $(2M–H^+)^-$.

2.1.4. 5-(Ferrocenylmethyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid methyl ester 7

3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid monomethyl ester **6** (1.49 g, 0.0047 mol), ferrocenemethylamine (1 g, 0.0047 mol) were magnetically stirred under a nitrogen atmosphere in dimethylformamide (50 ml). Benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (2.45 g, 0.0047 mol), triethylamine (0.47 g, 0.0047 mol) and a catalytic quantity of 1-hydroxybenzotriazole hydrate were added and the

solution stirred in the dark. After 72 h the dimethylformamide was removed under high vacuum. Acetonitrile (50 ml) was added and a precipitate formed. The orange solid was collected by filtration and washed with acetonitrile (3 × 15 ml). Purification was achieved by column chromatography on silica gel eluting with dichloromethane-2% methanol. Crystallisation was achieved by slow evaporation of dichloromethane:-methanol (2:1) solution of the product. After drying under high vacuum the product **7** was obtained in 69% yield (1.66 g). Elemental analysis: Found: C, 69.06; H, 4.81; N, 5.12. $C_{30}H_{26}FeN_2O_3$ requires C, 69.51; H, 5.06; N, 5.40%. ^{1}H NMR in $CDCl_3$, 300 MHz, δ (ppm): 3.77 (s, 3H, CH_3), 3.87 (s, 2H, FcH), 3.96 (s, 5H, FcH), 4.04 (s, 2H, FcH), 5.89 (s, 1H, amide NH), 7.09–7.31 (m, 10H, Ar), 10.10 (s, 1H, pyrrole NH). ^{13}C NMR in CD_2Cl_2, 400 MHz, δ (ppm): 37.92, 50.64, 66.49, 67.10, 67.70, 83.71, 119.23, 124.40, 125.04, 126.07, 126.47, 127.37, 128.16, 129.92, 130.16, 130.56, 132.50, 132.57, 158.68, 159.80. ES^+ mass spectrum, *m/z*: 518 (M^+). HRES MS: $C_{30}H_{26}FeN_2O_3$ Calc. 518.1287, Found: 518.1277 $\Delta = 2.0$ ppm.

2.1.5. 5-(Ferrocenylmethyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid 9

5-(Ferrocenylmethyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid methyl ester **7** (1.2 g, 0.0023 mol) was suspended in methanol (75 ml), and heated to reflux under a nitrogen atmosphere. Potassium hydroxide (0.13 g, 0.0023 mol) was added in water (20 ml). After refluxing overnight the solution was left to cool. Hydrochloric acid was added to the solution until it reached pH 1. The resulting solid was collected by filtration. The solid was dissolved in chloroform (100 ml) and the aqueous layer that formed residual water in the solid was separated. The organic layer was dried with magnesium sulfate and then filtered. The solvent was removed in vacuo. Thin layer chromatography on silica plates eluting with dichloromethane-2% methanol revealed that the residue contained some starting material. Trituration with acetonitrile (200 ml) gave a yellow solid which was collected by filtration. After drying this was shown to be the pure acid (0.36 g). The solution was reduced in vacuo, and the resulting solid was purified by column chromatography on silica gel eluting with dichloromethane-2% methanol. This gave a second crop of material (0.2 g) giving a total yield of 48% (0.56 g). Elemental analysis: Found: C, 64.18; H, 4.50; N, 5.12. $C_{29}H_{24}FeN_2O_3 + 0.56CH_2Cl_2$ requires C, 64.36; H, 4.59; N, 5.08%. ^{1}H NMR in $CDCl_3$, 300 MHz, δ (ppm): 3.86 (s, 2H, FcH), 3.96 (s, 5H, FcH), 4.04 (s, 2H, FcH), 4.14 (d, 2H, $J = 5.46$, CH_2), 5.91 (s, 1H, amide NH), 7.12–7.31 (m, 10H, Ar), 10.41 (s, 1H, pyrrole NH). ^{13}C NMR in CD_2Cl_2, 400 MHz, δ (ppm): 37.87, 48.57, 67.34, 67.91, 68.31, 85.35, 121.57, 124.84, 126.02, 126.23, 126.90, 127.36, 129.08, 130.64, 130.76, 134.34, 159.48, 162.28. ES^+ mass spectrum, *m/z*: 504 (M^+), 527 ($M+Na^+$). HRES MS: $C_{29}H_{24}FeN_2O_3$ Calc. 504.1130, Found: 504.1127 $\Delta = 0.9$ ppm.

2.1.6. 3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid 2-ferrocenylmethyl-amide 5-phenylamide 3

5-(Ferrocenylmethyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid **9** (0.45 g, 0.0009 mol) and aniline (0.083 g, 0.0009 mol) were magnetically stirred under nitrogen in dimethylformamide (30 ml). Benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (0.494 g, 0.00095 mol), triethylamine (0.09 g, 0.0009 mol) and a catalytic quantity of 1-hydroxybenzotriazole hydrate were added and the flask stirred in the dark. After 72 h the dimethylformamide was removed under high vacuum. Acetonitrile (50 ml) was added and a precipitate formed. The orange solid was collected by filtration and washed with acetonitrile (3 × 15 ml). The solid was purified by column chromatography on silica gel eluting with dichloromethane-2% methanol. Crystallisation was achieved by slow evaporation of an acetonitrile:dichloromethane (2:1) solution of the receptor. After drying under high vacuum the product was obtained in 14% yield (0.07 g). Elemental analysis: Found: C, 71.28; H, 4.94; N, 7.06. $C_{35}H_{29}FeN_3O_2 + 0.16CH_2Cl_2$ requires C, 71.35; H, 4.99; N, 7.10%. ^{1}H NMR in CD_2Cl_2, 300 MHz, δ (ppm): 3.88 (s, 2H, FcH), 3.95 (s, 5H, FcH), 4.04 (s, 2H, FcH), 4.13 (d, 2H, $J = 5.46$, CH_2), 5.80 (s, 1H, ferrocene amide NH), 7.00–7.43 (multiple overlapping peaks, 16H, ArH and NH), 10.31 (s, 1H, pyrrole NH). ^{13}C NMR in DMSO-d_6, 400 MHz, δ (ppm): 39.03, 68.45, 68.53, 69.38, 86.19, 120.44, 124.51, 125.25, 125.47, 127.33, 127.63, 128.09, 128.62, 128.90, 129.14, 129.76, 131.59, 131.69, 134.88, 134.98, 139.75, 159.60, 160.74. ES^+ mass spectrum, *m/z*: 579 (M^+). HRES MS: $C_{35}H_{29}FeN_3O_2$ Calc. 579.1604, Found: 579.1610 $\Delta =$ 1.1 ppm.

2.1.7. 5-(Ferrocenyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid methyl ester 8

3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid monomethyl ester **6** (1.76 g, 0.0055 mol), ferrocenylamine (1.1 g, 0.0055 mol) were magnetically stirred under nitrogen in dimethylformamide (50 ml). Benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (2.86 g, 0.0055 mol), triethylamine (0.55 g, 0.0055 mol) and a catalytic quantity of 1-hydroxybenzotriazole hydrate were added before wrapping the flask in foil. After 72 h the dimethylformamide was removed under high vacuum. Diethylether (7 × 50 ml) was added to the resultant oil, resulting in a precipitate that was collected and dried (0.19 g). The remaining solution was reduced in vacuo leaving another oil, which was purified using column chromatography on silica gel eluting with dichloromethane-2% methanol. After drying under

high vacuum the product was obtained as a foam (2.3 g) a combined yield of 79% (2.49 g). Crystallisation was achieved by slow evaporation of ether:dichloromethane (4:1) Elemental analysis: Found: C, 69.18; H, 4.64; N, 6.12. $C_{29}H_{24}FeN_2O_3$ requires C, 69.06; H, 4.80; N, 5.55%. ^{1}H NMR in $CDCl_3$, 300 MHz, δ (ppm): 3.79 (s, 3H, CH_3), 3.96 (s, 2H, FcH), 4.02 (s, 5H, FcH), 4.31 (s, 2H, FcH), 6.75 (s, 1H, amide NH), 7.21–7.46 (m, 10H, Ar), 10.08 (s, 1H, pyrrole NH). ^{13}C NMR in CD_2Cl_2, 300 MHz, δ (ppm): 29.82, 51.81, 62.24, 65.11, 69.30, 120.32, 127.19, 127.54, 127.64, 127.72, 127.93, 128.67, 128.95, 129.30, 130.68, 130.82, 131.14, 131.71, 132.88, 133.43, 158.28, 160.84. ES$^+$ mass spectrum, m/z: 504 (M^+). HRES MS: $C_{29}H_{24}FeN_2O_3$ Calc. 504.1131, Found: 504.1123 $\Delta = 1.5$ ppm.

2.1.8. 5-(Ferrocenyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid 10

5-(Ferrocenyl-carbamoyl)-3,4-diphenyl-1H-pyrrole-2-carboxylic acid methyl ester **8** (2.4 g, 0.0048 mol) was dissolved in methanol (125 ml), and heated to reflux under a nitrogen atmosphere.

Sodium hydroxide (6 g, 0.15 mol) was added in water (120 ml). The solution was kept at 95 °C for 2 h then left to cool. Hydrochloric acid was added to the solution until it reached pH 1 resulting in a precipitate. The resulting solid was collected by filtration and dissolved in dichloromethane (200 ml) and the aqueous layer separated. The organic layer was dried with magnesium sulfate and then filtered. The solvent was removed in vacuo and the product dried under high vacuum. The compound needed no further purification and was obtained in 49% yield (1.15 g). Crystallisation was achieved by slow evaporation of a chloroform:dichloromethane (1:1) solution of the receptor. Elemental analysis: Found: C, 65.36; H, 4.67; N, 5.28. $C_{28}H_{22}FeN_2O_3 + 0.33CH_2Cl_2$ requires C, 65.61; H, 4.41; N, 5.40%. ^{1}H NMR in $CDCl_3$, 300 MHz, δ (ppm): 3.96 (s, 2H, FcH), 4.01 (s, 5H, FcH), 4.29 (s, 2H, FcH), 6.81 (s, 1H, amide NH), 7.21–7.47 (m, 10H, Ar), 10.80 (s, 1H, pyrrole NH). ^{13}C NMR in CD_2Cl_2, 400 MHz, δ (ppm): 62.16, 65.05, 69.22, 120.33, 125.74, 126.77, 127.13, 127.49, 127.81, 128.23, 128.57, 129.19, 130.60, 130.94, 131.02, 132.39, 132.61, 133.19, 158.46, 164.42. ES$^+$ mass spectrum, m/z: 490 (M^+). HRES MS: $C_{28}H_{22}FeN_2O_3$ Calc. 490.0974, Found: 490.0972 $\Delta = 0.5$ ppm.

2.1.9. 3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid 2-ferrocenylamide 5-phenylamide 4

5-(Ferrocenyl-carbamoyl)-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid **10** (0.8 g, 0.0016 mol) and aniline (0.15 g, 0.0016 mol) were magnetically stirred under nitrogen in dimethylformamide (50 ml). Benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (0.85 g, 0.02 mol), triethylamine (0.17 g, 0.0016 mol) and a catalytic quantity of 1-hydroxybenzotriazole hydrate were added before wrapping the flask in foil. After 72 h the dimethylformamide was removed under high vacuum. The residue was dissolved in acetonitrile (50 ml). Water (50 ml) and dichloromethane (300 ml) were added to the solution. The organic layer was then separated and dried over magnesium sulfate and the solvent removed in vacuo. The resultant oil was purified using column chromatography on silica gel eluting with dichloromethane-2% methanol. Crystallisation was achieved from a methanol/dichloromethane solution of the receptor. After drying under high vacuum the product was obtained in 38% yield (0.35 g). Elemental analysis: Found: C, 69.36; H, 5.07; N, 7.00. $C_{34}H_{27}FeN_3O_2 + 0.33CH_2Cl_2$ requires C, 69.45; H, 4.70; N, 7.08%. ^{1}H NMR in $CDCl_3$, 300 MHz, δ (ppm): 3.95 (s, 2H, FcH), 4.03 (s, 5H, FcH), 4.32 (s, 2H, FcH), 6.71 (s, 1H, ferrocene amide NH), 7.04–7.47 (multiple overlapping peaks, 16H, ArH and NH), 10.36 (s, 1H, pyrrole NH). ^{13}C NMR in CD_2Cl_2, 400 MHz, δ (ppm): 53.42, 62.15, 64.92, 69.13, 92.88, 119.21, 124.15, 124.36, 124.69, 126.03, 126.31, 128.26, 128.59, 128.66, 129.00, 129.16, 130.86, 131.02, 132.90, 133.09, 137.49, 157.91, 158.22. ES$^+$ mass spectrum, m/z: 565 (M^+), 1153 ($2M + Na^+$). HRES MS: $C_{34}H_{27}FeN_3O_2$ Calc. 566.1525, Found: 566.1513 $\Delta = 2.2$ ppm.

2.2. Electrochemistry

Steady state voltammograms were recorded at room temperature, at 20 mV s^{-1}, with a 25 μm diameter Pt microdisc prepared as reported previously [13] 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 voltammograms. Dichloromethane solutions with 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 voltammograms was recorded for each solution.

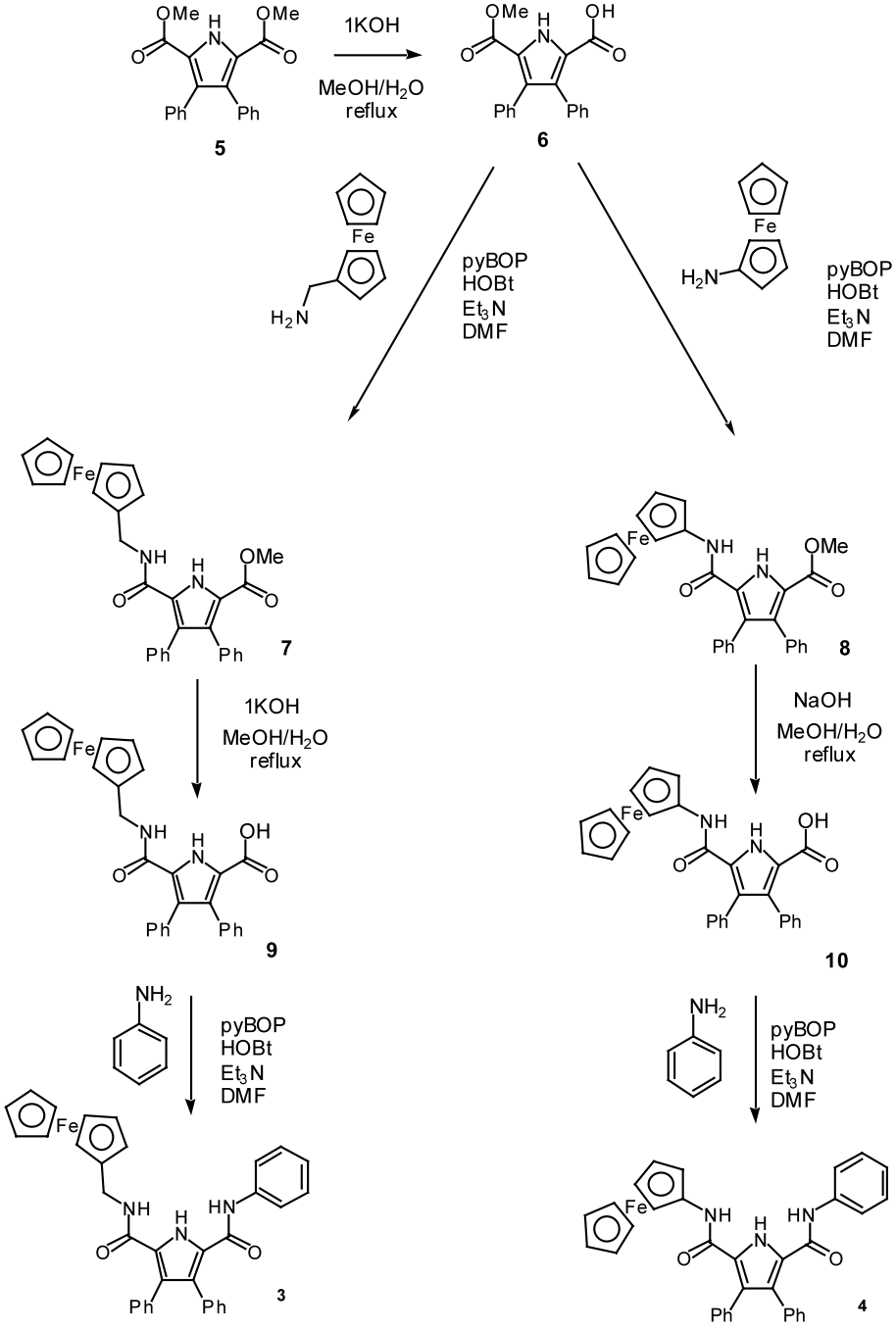
3. Synthesis

Receptors **1** and **2** were synthesised by reaction of either ferrocenylmethylamine [11] of ferrocenylamine [11] with 3,4-diphenyl-1H-pyrrole-2,5-dicarbonyl dichloride [10] in dichloromethane in the presence of

triethylamine and a catalytic quantity of DMAP followed by purification by column chromatography. Receptors **3** and **4** were synthesised by mono-de-esterifying 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid dimethyl ester **5** to produce a mono-ester mono-acid **6**. This was then coupled to either ferrocenylmethylamine or ferrocenylamine to afford the mono-esters **7** and **8**, respectively which were subsequently de-esterified affording the mono-acids **9** and **10** and then coupled to aniline affording receptors **3** and **4** (Scheme 1). The compounds were fully characterised by ^{1}H and ^{13}C NMR and high-resolution mass spectrometry (Section 2).

4. Crystal structures of 1–4 and intermediates

The crystal structures of the intermediates and final products show a number of interesting hydrogen bonding interactions [14]. Data were collected on a Bruker Nonius Kappa CCD area detector diffractometer with a



Scheme 1.

Table 1
Crystallographic data and CCDC deposition numbers

Compound number	**1**	**2**	**3**	**4**	**7**	**8**	**10**
CCDC number	See Ref. [10]	See Ref. [10]	189 976	189 980	189 978	189 977	189 979
Empirical formula	$C_{40}H_{35}N_3O_2Fe_2$	$C_{38}H_{31}N_3O_2Fe_2$	$C_{35}H_{29}N_3O_2Fe$	$C_{35}H_{31}N_3O_3Fe$	$C_{30}H_{26}N_2O_3Fe_2$	$C_{29}H_{24}N_2O_3Fe$	$C_{30}H_{27}N_2O_5Cl_3Fe$
Formula weight	701.41	673.36	579.46	597.48	518.38	504.35	657.74
Crystal system	monoclinic	triclinic	triclinic	triclinic	orthorhombic	triclinic	triclinic
Space group	$C2/c$	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$	$Pbca$	$P\bar{1}$	$P\bar{1}$
a (Å)	16.1333(5)	12.7602(3)	9.3589(7)	10.6570(5)	6.0816(4)	10.4568(4)	11.0968(4)
b (Å)	10.3709(3)	14.1906(4)	16.076(2)	10.9323(6)	24.850(2)	11.6216(5)	11.1517(4)
c (Å)	37.6445(12)	17.3431(5)	17.627(3)	13.7118(10)	31.120(3)	11.78872(6)	11.9917(5)
α (°)		87.721(1)	86.856(12)	88.074(2)		61.172(2)	102.233(2)
β (°)	97.982(1)	83.137(1)	89.616(12)	82.029(2)		70.776(2)	95.688(2)
γ (°)		75.782(2)	84.448(9)	65.031(2)		67.863(2)	92.374(3)
Z	8	4	4	2	8	2	2
μ (mm^{-1})	0.973	1.001	0.612	0.568	0.678	0.696	0.845
Crystal	Yellow plate	Red prism	Orange block	Orange blade	Orange needle	Orange plate	Orange block
Crystal size (mm)	0.15 × 0.10 × 0.03	0.15 × 0.10 × 0.03	0.25 × 0.15 × 0.10	0.25 × 0.20 × 0.03	0.20 × 0.03 × 0.03	0.14 × 0.10 × 0.02	0.16 × 0.12 × 0.06
Reflections collected	11 432	36 068	21 893	19 514	3244	16 609	21 381
Independent reflections (R_{int})	5096 (0.0706)	10 432 (0.0867)	21 862 (0.0104)	4086 (0.0787)	3244 (0.0000)	5111 (0.0439)	6433 (0.0476)
Data/restraints/parameters	5096/0/424	10 432/360/909	21 862/0/740	4086/0/382	3244/0/326	5111/0/326	6433/6/382
Goodness-of-fit on F^2	0.984	0.955	1.042	1.016	0.970	1.040	1.029
Final R indices [$F^2 > 2\sigma(F^2)$]	$R_1 = 0.0474$, $wR_2 = 0.0817$	$R_1 = 0.0456$, $wR_2 = 0.0862$	$R_1 = 0.0591$, $wR_2 = 0.1380$	$R_1 = 0.0622$, $wR_2 = 0.1560$	$R_1 = 0.0549$, $wR_2 = 0.1098$	$R_1 = 0.0435$, $wR_2 = 0.0963$	$R_1 = 0.0551$, $wR_2 = 0.1407$
R indices (all data)	$R_1 = 0.0929$, $wR_2 = 0.0938$	$R_1 = 0.0968$, $wR_2 = 0.1016$	$R_1 = 0.0833$, $wR_2 = 0.1541$	$R_1 = 0.0986$, $wR_2 = 0.1782$	$R_1 = 0.1092$, $wR_2 = 0.1289$	$R_1 = 0.0651$, $wR_2 = 0.1048$	$R_1 = 0.0746$, $wR_2 = 0.1542$
Largest difference peak and hole (e $Å^{-3}$)	0.472 and −0.434	0.325 and −0.380	0.534 and −0.375	0.514 and −0.479	0.489 and −0.455	0.461 and −0.505	1.553 and −0.584

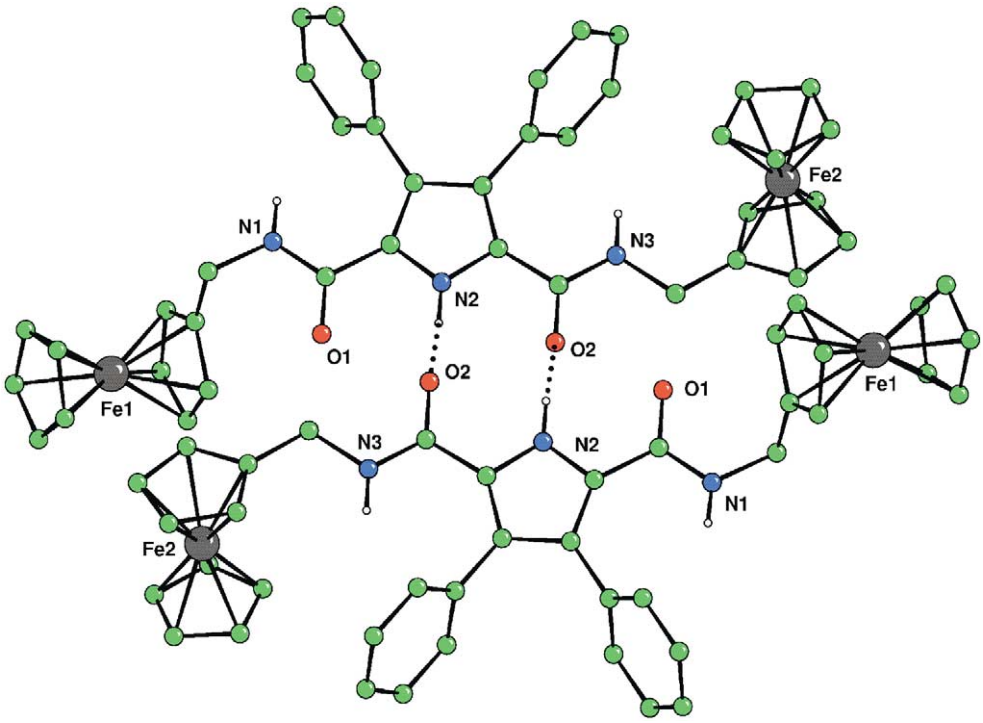


Fig. 1. The X-ray crystal structure of **1** showing dimer formation in the solid-state via NH–O hydrogen bonds (N···O 2.961(3) Å).

rotating anode generator following standard procedures. Full crystallographic data for the structure analyses have been deposited with the Cambridge Crystallographic Data Centre. Crystal data and CCDC deposition numbers or references for the seven structures are shown in Table 1.

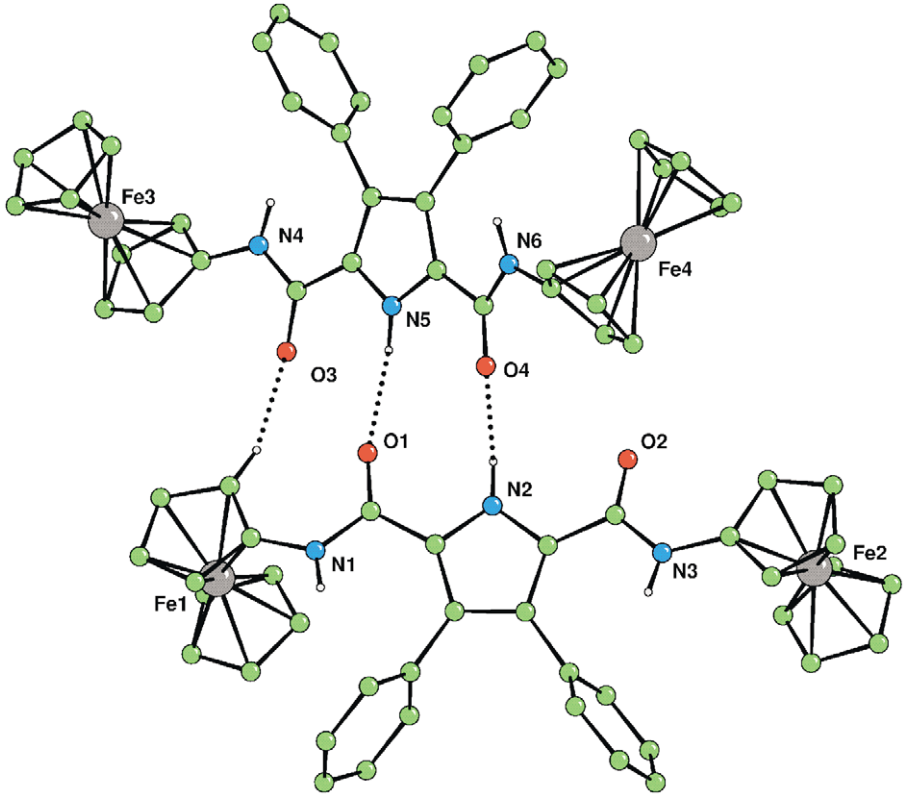


Fig. 2. X-ray crystal structure of **2** showing dimer formation in the solid-state via NH–O and CH–O hydrogen bonds (N···O 2.795(4) and 3.020(3) Å C···O 3.2245(5) Å).

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) [6].

Compound **7** forms infinite chains along the *b* glide plane via NH–O hydrogen bonds (N···O = 2.906(5) Å) shown in Fig. 3(b).

Compound **8** crystallised from chloroform/dichloromethane forms centrosymmetric dimers via CH–O hydrogen bonds (C···O = 3.432(6) Å) from the ferrocene C–H to the amide carbonyl oxygen. These dimers form a hexagonal close packed array when viewed down the *c* axis as shown in Fig. 4(b).

Compound **10** crystallised from chloroform/dichloromethane forms centrosymmetric dimers via typical OH–O carboxylic acid type hydrogen bonds (O···O = 2.648(4) Å) (Fig. 5). In addition a chloroform molecule is bound to the pyrrolic nitrogen via an NH–Cl interaction (N···Cl = 3.431(6) Å).

The crystal structure of compound **3** crystallised from acetonitrile/dichloromethane reveals two molecules in the asymmetric unit differing in the orientation of the ferrocene (Fig. 6). Centrosymmetric dimers are formed via NH–O (N···O = 2.900(4) Å) and CH–O (C···O = 3.473(5) Å) hydrogen bonds from the methylene spacer group.

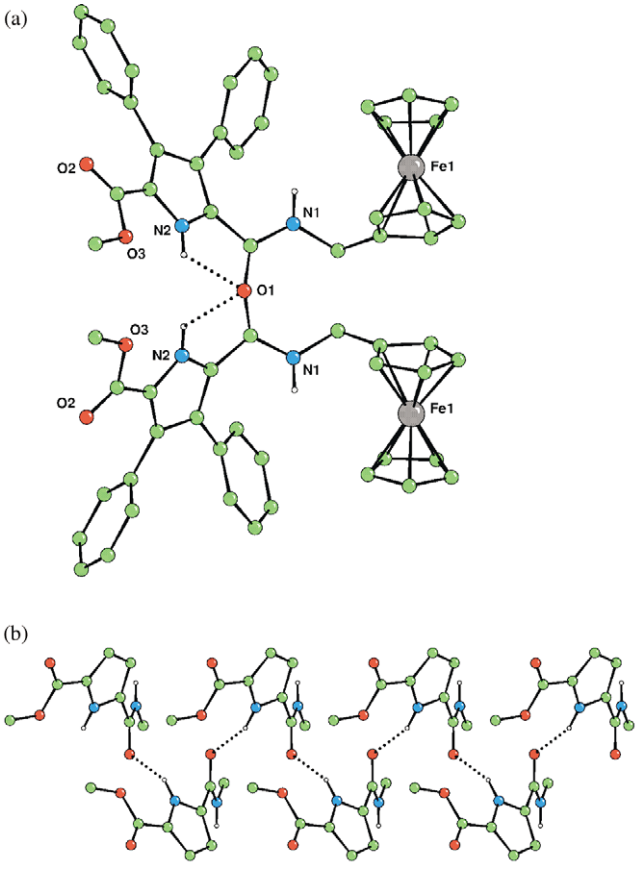


Fig. 3. Crystal structure of compound **7** (a) and packing diagram showing formation of infinite chains along the b-glide plane (b) (phenyl and ferrocenyl groups omitted for clarity).

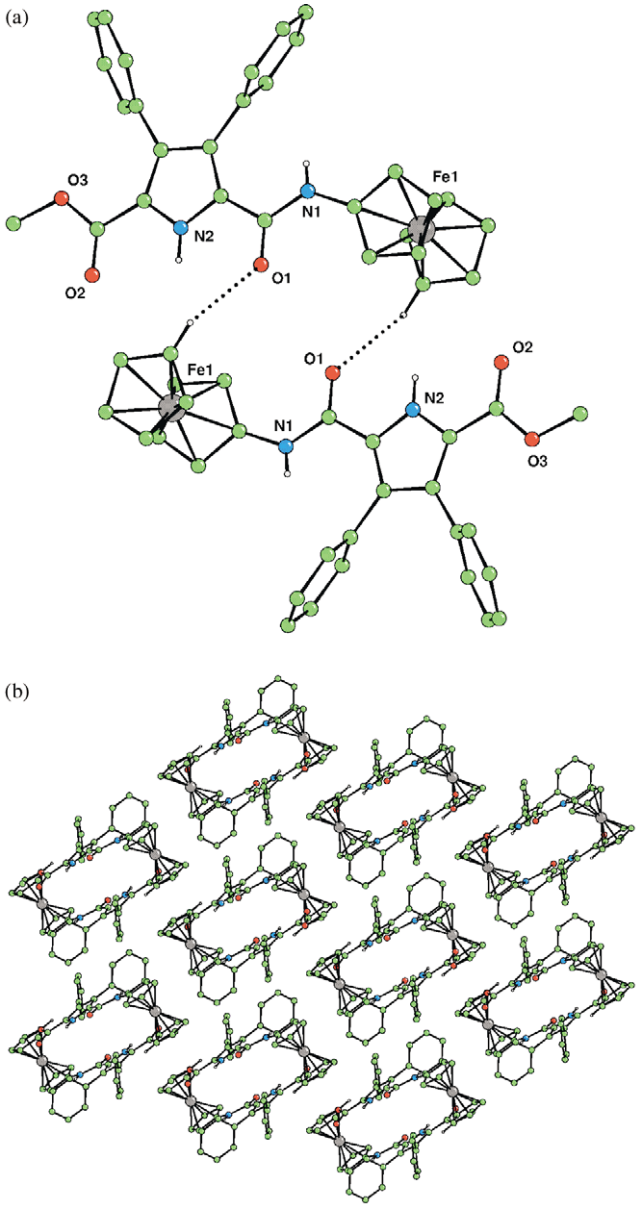


Fig. 4. Crystal structure of compound **8** (a) and packing diagram viewed down *c* axis (b).

Compound **4** crystallised from methanol/dichloromethane does not form dimers or chains but instead binds a methanol molecule via NH–O (N···O = 2.930(6) Å) and O–HO (O···O = 2.696(6) Å) hydrogen bonds (Fig. 7).

5. Anion binding studies and electrochemistry

Association constants for receptors **1**–**4** with a variety of anionic guests were determined by ^{1}H NMR titration techniques (Table 2) [15]. For solubility reasons, di-

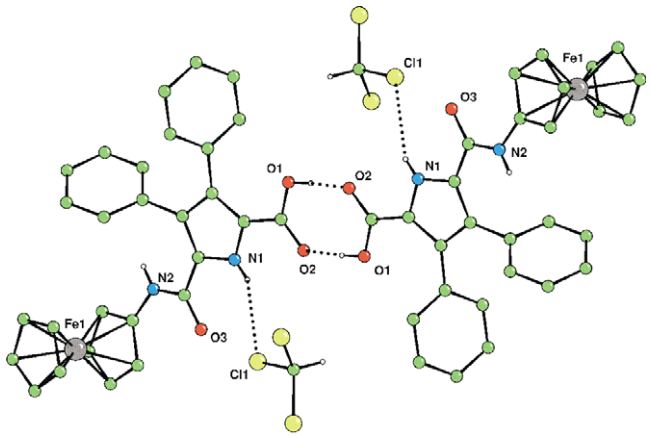


Fig. 5. Crystal structure of compound **10**.

chloromethane was used in both the ^{1}H NMR and electrochemical studies. We have recently observed unusual ^{1}H NMR titration behaviour upon addition of fluoride to other 2,5-diamidopyrrole cleft species due to fluoride acting as a base [16]. Whilst in these studies, the titration data could be adequately fitted to a 1:1 receptor:anion binding model, we believe, in-light of the electrochemical behaviour reported below, that this data should still be treated with caution. Excluding the fluoride data, it was observed that receptors **1** and **3** are poor anion receptors with receptor **1** binding all the other putative anionic guests with association constants lower than 50 M^{-1}. Compounds **2** and **4**, containing the directly conjugated ferrocene moiety, have moderate to high affinities for benzoate (as has been observed with similar receptors [6]) and also show a significant interaction with dihydrogenphosphate. The ^{1}H NMR titration profile of compound **2** and benzoate is shown in Fig. 8(a).

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}–3.5×10^{-2} M no significant shift in the ^{1}H NMR proton resonances was observed.

The steady state voltammetric response of the four receptors in presence and absence of guest anions was recorded with a platinum microdisc electrode. **1** and **3** were found to oxidise at very similar potentials ($E_{\frac{1}{2}}$ = 0.182 and 0.170 V, respectively). Although the oxidation of **2** and **4** was found to be easier than that of **1** and **2**, their half-wave potentials are significantly different ($E_{\frac{1}{2}}$ = 0.080 and 0.058 V, respectively). In all cases the oxidation wave appears to be reversible, $E_{\frac{3}{4}} - E_{\frac{1}{4}} = 55$, 48, 55 and 63 mV, respectively. Interestingly, the limiting currents (4.4, 3.7, 2.0 and 1.8 nA, respectively) reflect the number of ferrocene reporter groups. Except for the doubling of the limiting current, the voltammetric responses of **1** and **3** are almost identical. In contrast the voltammetric responses of **2** and **4** are significantly

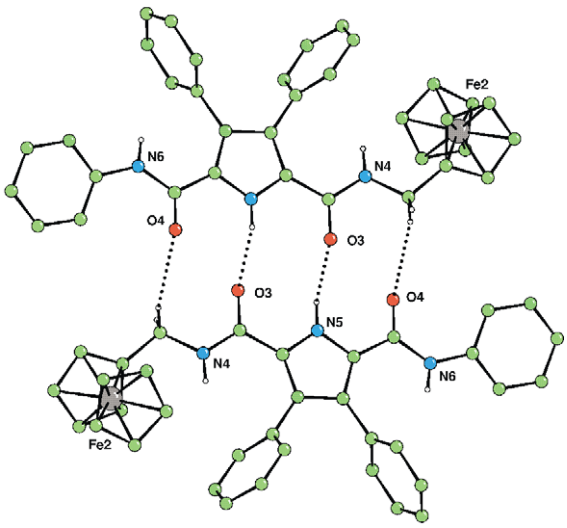


Fig. 6. Crystal structure of compound **3**.

different. With the non-conjugated link, the ferrocene reporter groups are unaffected by the rest of the molecule and yield identical voltammetric responses. With the conjugated link, the redox activity of the ferrocene groups is clearly affected by the rest of the molecule. An example CV (obtained upon addition of benzoate to receptor **2**) is shown in Fig. 8(b).

With some anions, the voltammetric wave is seriously distorted as the product of the electrochemical reaction passivates the electrode. For example $H_2PO_4^-$ affects the voltammetry of all receptors; the voltammograms do not reach the expected plateaus, a significant hysteresis appears between the forward and reverse scans and it becomes difficult to determine the half-wave potential. To obtain a clean electrode surface, the electrode was held at a large negative potential for a few seconds before the start of each scan. This pre-treatment removed the passivating material sufficiently to alleviate the need for polishing the electrode between scans.

The voltammetric wave of the host-guest complexes was found to shift negatively with all anions except with

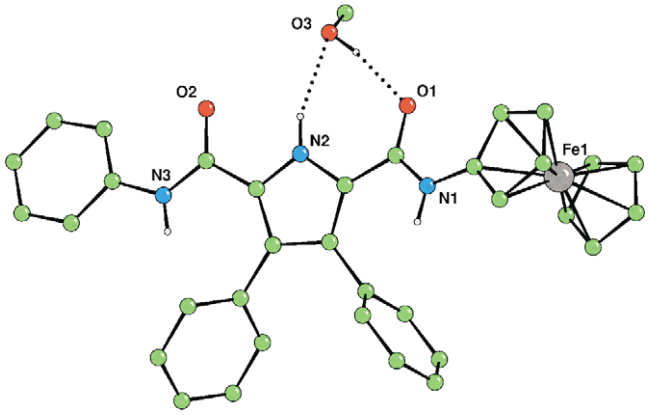


Fig. 7. Crystal structure of compound **4**.

Table 2
Association constants of receptors **1**–**4** with various anions (added as their tetrabutylammonium salts) in dichloromethane-d_2 and voltammetric shifts in ferrocene/ferrocenium redox couple of receptors in the presence of three equivalents of the anion in dichloromethane

	Compound **1**		Compound **2**		Compound **3**		Compound **4**	
	K_a (M^{-1})	ΔE (mV)	K_a (M^{-1})	ΔE (mV)	K_a (M^{-1})	ΔE (mV)	K_a (M^{-1})	ΔE (mV)
F^-	170	−131	704	−123 and −255[b]	1518	−55	1582	−28 and −232[b]
Cl^-	< 20	−76	68	−53	< 20	−30	54	−26
Br^-	< 20	0	< 20	−12	< 20	0	< 20	+7
$H_2PO_4^-$	44	[a]	143	[a]	35	−130[a]	296	−248[a]
HSO_4^-	47	[a]	76	−37	69	−3	47	−29
Benzoate	34	−60	1827	−122	213	−80	807	−150

[a] With some anions, the voltammetric wave is seriously distorted as the product of the electrochemical reaction passivates the electrode.
[b] Two waves are observed.

bromide which did not affect the electrochemistry of the hosts. In an ideal situation, these negative shifts should reflect the increasing ease of oxidation of anion complexes with respect to the free receptors. However, other effects such as the possible deprotonation of the host (e.g. upon addition of fluoride) or passivation of the electrode surface by the product of the electrochemical oxidation can complicate the results.

Compounds **2** and **4** show a moderate to strong affinity for benzoate by ^{1}H NMR titration experiments. The large shifts observed for the ferrocene/ferrocenium couple in these cases reflect the affinity for this anion and also the presence of a conjugated bond pathway between the anion binding site and the ferrocene reporter groups.

6. Concluding remarks

This paper has demonstrated that in addition to functioning as an oxo-anion selective anion binding motif, when appended with ferrocene reporter group(s), 2,5-diamidopyrrole clefts show interesting solid-state assembly properties via a variety of classical and non-classical hydrogen bonds, as well as functioning as prototypical electrochemical anion sensors. The electrochemistry of these systems is complicated by the passivation of the electrode surface in the case of dihydrogenphosphate whilst fluoride anions cause complex two-wave behaviour which we believe may be due to deprotonation of the pyrrole NH group. However, large shifts observed upon addition of benzoate to electrochemical solutions of the receptors **2** and **4** reveal significant negative shifts of the ferrocene/ferrocenium couple which are attributed to complex formation with this oxo-anion and subsequent facile oxidation of the complex.

7. Supplementary material

Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre (Table 1 for deposition numbers). Copies

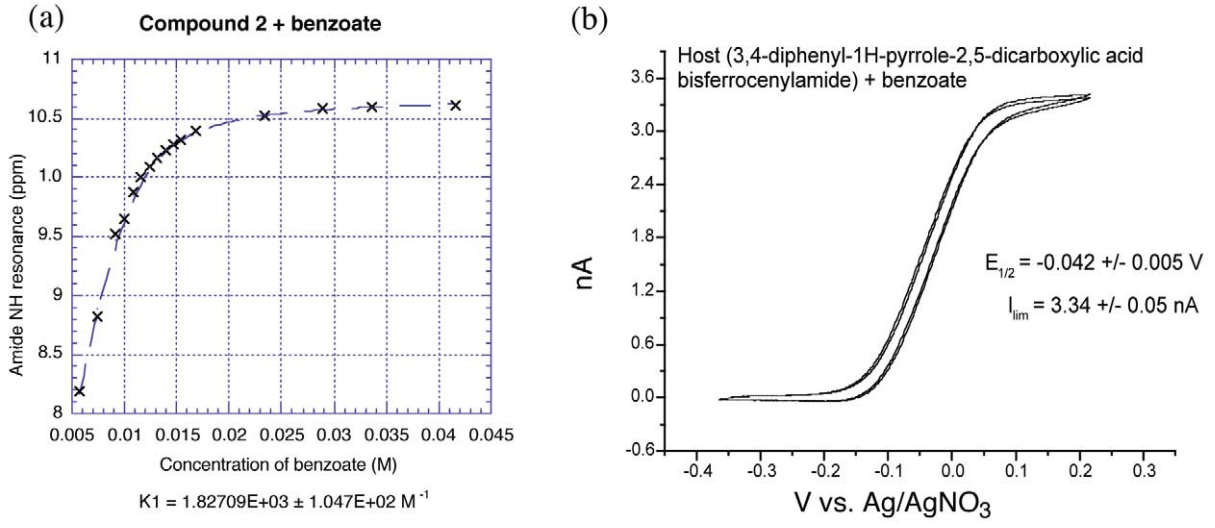


Fig. 8. (a) ^{1}H NMR titration of compound **2** with tetrabutylammonium benzoate in dichloromethane-d_2 and (b) microelectrode cyclic voltammogram of **2** in the presence of three equivalents of tetrabutylammonium benzoate.

of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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