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LETTERS

Ferrocene-substituted calix[4]pyrrole: a new electrochemical sensor for anions involving CH···anion hydrogen bonds

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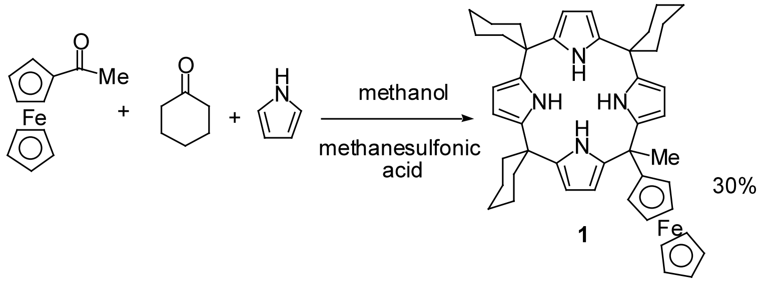
Abstract—A new calix[4]pyrrole **1** containing a ferrocene moiety attached to one of the *meso*-positions has been synthesised by co-condensation of pyrrole, cyclohexanone and acetylferrocene. The crystal structure of **1** has been elucidated whilst ^{1}H NMR titration studies in acetonitrile-d_3/DMSO-d_6 9:1 v/v have revealed that **1** binds fluoride, chloride, and dihydrogen phosphate in this solvent mixture. Electrochemical studies using cyclic voltammetric and square-wave voltammetric techniques show cathodic shifts of up to 100 mV (approx.) with dihydrogen phosphate anions. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The development of new receptors and sensors for anionic species provides a continuing challenge to the supramolecular chemistry community.[1] The use of ferrocene as an electrochemically active 'reporter group' has been explored by a number of research groups worldwide and has been used to produce redox-active sensors for cations, anions, and neutral species.[2] In the vast majority of these examples, no direct coordination of the guest to the ferrocene moiety occurs. An example of direct coordination to ferrocene in a redox-active receptor has been reported by Gokel and co-workers involving Ag···Fe interactions.[3] Our interest in anion complexation and detection has led to the development of a variety of fluorescent[4] and colorimetric[5] anion sensor systems based upon calix[4]pyrrole, an easy to make tetrapyrrolic macrocycle capable of forming hydrogen bonded complexes with a variety of halides and oxo-anions.[6] While we were initially successful in preparing anion selective electrodes containing calix[4]pyrroles,[7] our attempts to synthesise discrete molecular electrochemical sensors based on loosely linked calix[4]pyrrole and ferrocene conjugates gave unusual results with the systems displaying both cathodic and anodic shifts upon addition of anions.[8] We therefore decided to employ the ferrocene moiety in a much more intimate role in the anion complexation process and design a calixpyrrole that would allow for the possibility of direct Fc-H···anion binding interactions.[9] We achieved this by co-condensing acetylferrocene, cyclohexanone, and pyrrole and isolating a mono-ferrocene calix[4]pyrrole **1**.



Scheme 1.

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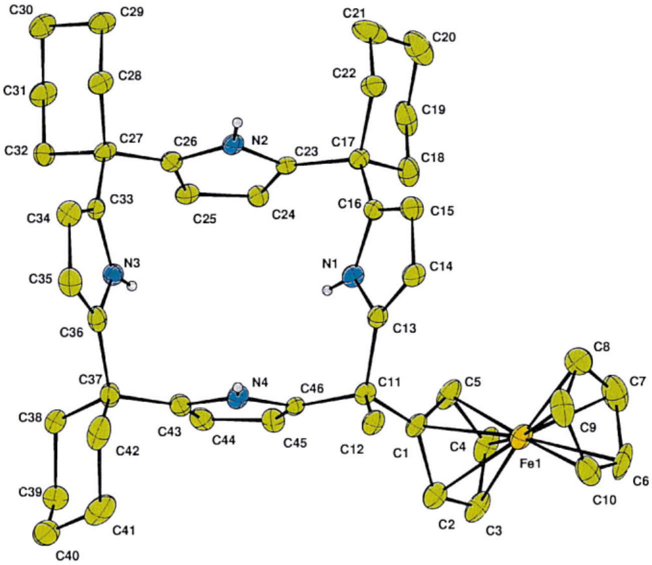

Figure 1. X-Ray crystal structure of **1**.

2. Results and discussion

Compound **1** was synthesised by co-condensation of acetylferrocene, pyrrole and cyclohexanone (Scheme 1). A mixture of pyrrole (2 g, 0.0299 mole), acetyl ferrocene (1.7 g, 0.0075 mole), cyclohexanone (2.2 g, 0.0223 mole) and a catalytic quantity of methanesulfonic acid were added to methanol (100 ml) and stirred under nitrogen overnight. The reaction mixture was neutralised with triethylamine and the solvent removed in vacuo. The residue was separated by column chromatography on silica gel eluting with dichloromethane/hexane (2:1 v/v). The mono-ferrocene calix[4]pyrrole **1** was isolated as an orange powder in 30% yield.[10]

Crystals of **1** suitable for X-ray crystallographic analysis (Fig. 1) were obtained from an acetonitrile solution of the macrocycle.[11] As in the case of most other calix[4]pyrrole macrocycles, the uncomplexed receptor adopts the 1,3-alternate conformation in the solid state.

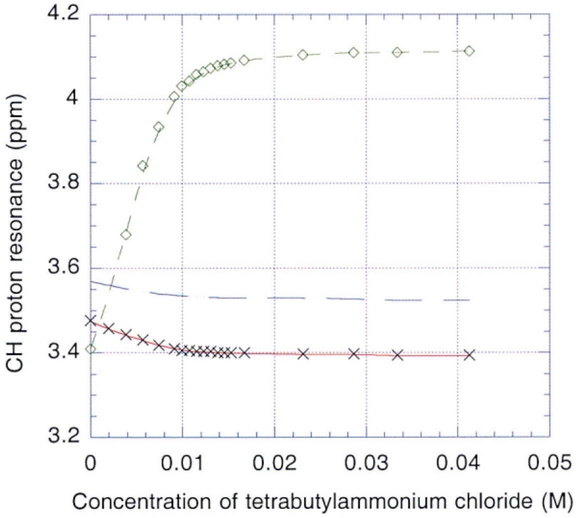

Figure 2. Ferrocene CH resonance shifts upon addition of chloride anions (α protons in green, β in blue and unsubstituted Cp in red).

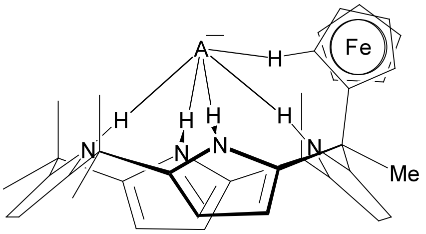

Figure 3. Schematic representation of the ferrocene CH and calixpyrrole NH hydrogen-bonding interactions that are thought to stabilise the bound anion in complexes derived from **1**.

Binding studies were conducted using ^{1}H NMR titration techniques in DMSO-d_6/acetonitrile-d_3 (1:9 v/v), with association constants being elucidated using the EQNMR computer program.[12] The results are shown in Table 1 and reveal that compound **1** coordinates fluoride, chloride and dihydrogen phosphate in this solvent mixture. The NH proton resonances broadened during the titrations making them unsuitable for the calculation of the association constants. However, one ferrocene CH resonance shifted downfield allowing for the calculation of K_a and providing evidence for the formation of CH···anion hydrogen bonds in solution (Fig. 2). This is shown schematically in Fig. 3. Unfortunately, it was not possible to elucidate an accurate association constant with dihydrogen phosphate by this method, as the ferrocene CH resonance was partially obscured during this titration.

Table 1. Association constants and Fc/Fc$^+$ redox potentials for compound **1** with various anionic guest species

Anion	K_a (M^{-1})[a]	$E_{1/2}$ (Fc/Fc$^+$) (mV) versus Ag/AgCl[b]	ΔE (mV)
No anion	n/a	+444	n/a
Fluoride	3375	+368	−76
Chloride	3190	+408	−36
Bromide	50	+432	−12
Dihydrogen phosphate[13]	304[c]	+350 (approx.)	−100 (approx.)
Hydrogen sulfate[14]	[d]	+436	<10

[a] Errors estimated<20%. Measured in acetonitrile-d_3/DMSO-d_6 9:1 (v/v)

[b] $E_{1/2}$ values obtained from SWVs.

[c] The CH proton resonance was partially obscured during this titration; therefore, this value should be treated with caution.

[d] No shifts were observed.

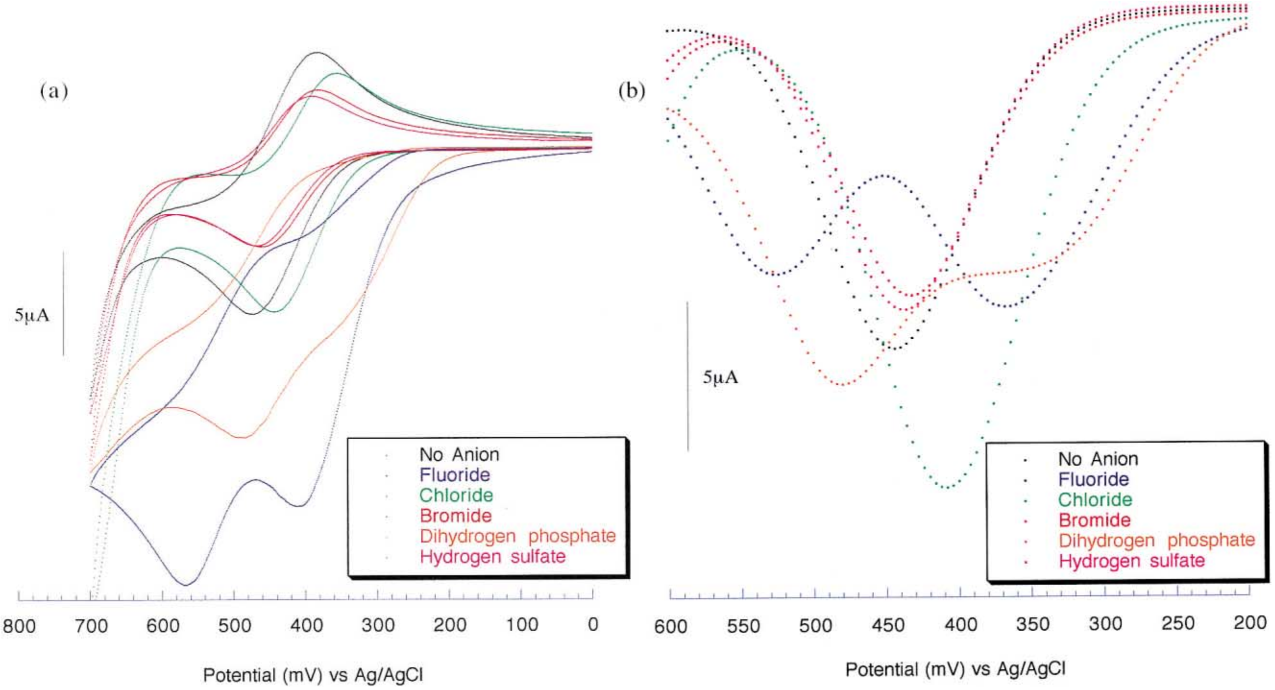

Figure 4. Cyclic (a) and square-wave (b) voltammograms of **1** (5×10^{-4} M) recorded in $CH_3CN/DMSO$ 9:1 v/v containing 0.1 M tetrabutylammonium hexafluorophosphate using a Pt disk working electrode, a Pt gauze counter electrode and a Ag/AgCl reference electrode. Voltammetry was carried out under a dry argon atmosphere.

Electrochemical studies were conducted using square-wave and cyclic voltammetric techniques. The redox potentials from square-wave voltammograms (SWVs) of the receptor in acetonitrile/DMSO (9:1 v/v) are shown in Table 1. Among the halide anions, binding of fluoride induces the largest cathodic shift in the ferrocene/ferrocenium couple (76 mV), followed by chloride (36 mV) and bromide (12 mV). Dihydrogen phosphate causes the SWV to shift cathodically by approximately 100 mV. The cyclic voltammograms (CVs) and SWVs of **1** between 0 and 800 mV versus Ag/AgCl at 25°C in the absence and presence of anions are shown in Fig. 4. Note that in the voltammograms recorded in the presence of fluoride and dihydrogenphosphate, redox processes corresponding to oxidation of the calix[4]pyrrole skeleton have shifted into this potential window.

3. Conclusions

Receptor **1** functions as an electrochemical sensor for anions. Solution state ^{1}H NMR spectroscopic studies provide support for a direct coordination mechanism involving hydrogen bond formation between the ferrocene cyclopentadienyl group and the bound anion. We are continuing to investigate the properties of this and other ferrocene modified calix[4]pyrroles. The results of these studies will be reported in due course.

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References

1. (a) Gale, P. A. *Coord. Chem. Rev.* **2001**, *213*, 79; (b) Gale, P. A. *Coord. Chem. Rev.* **2000**, *199*, 181; (c) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486.
2. (a) Beer, P. D.; Gale, P. A.; Chen, G. Z. *J. Chem. Soc., Dalton Trans.* **1999**, 1897; (b) Collinson, S. R.; Gelbrich, T.; Hursthouse, M. B.; Tucker, J. H. R. *Chem. Commun.* **2001**, 555; (c) Plenio, H.; Aberle, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 1397.
3. Medina, J. C.; Goodnow, T. T.; Rojas, M. T.; Atwood, J. L.; Lynn, B. C.; Kaifer, A. E.; Gokel, G. W. *J. Am. Chem. Soc.* **1992**, *114*, 10583.
4. Miyaji, H.; Anzenbacher, Jr., P.; Sessler, J. L.; Bleasdale, E. R.; Gale, P. A. *Chem. Commun.* **1999**, 1723.
5. Gale, P. A.; Twyman, L. J.; Handlin, C. I.; Sessler, J. L. *Chem. Commun.* **1999**, 1851.
6. (a) Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1; (b) Sessler, J. L.; Gale, P. A. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 6, p. 257.
7. Král, V.; Sessler, J. L.; Shishkanova, T. V.; Gale, P. A.; Volf, R. *J. Am. Chem. Soc.* **1999**, *121*, 8771.
8. Sessler, J. L.; Gebauer, A.; Gale, P. A. *Gazz. Chim. Ital.* **1997**, *127*, 723.
9. For a seminal review of intermolecular interactions in organometallic solids, see: Braga, D.; Grepioni, F. *Chem. Commun.* **1996**, 571.
10. Spectroscopic data for compound **1**: ^{1}H NMR (300 MHz, CD_3CN): δ 1.42 (18H, br. m, CH_2), 1.90–2.05 (15H, br. m, CH_2 and CH_3), 3.93 (2H, m, FcH), 4.02 (5H, s, FcH),

4.12 (2H, m, FcH), 5.68 (2H, m, $CH_{pyrrole}$), 5.82 (6H, m, $CH_{pyrrole}$), 7.38 (2H, s, NH), 7.43 (2H, s, NH); ^{13}C NMR (75.48 MHz, $CDCl_3$): δ 21.99, 22.23, 25.69, 26.07, 33.45, 34.09, 35.91, 38.03, 66.29, 66.83, 68.30, 99.24, 101.77, 102.18, 102.73, 103.35, 104.53, 135.32, 136.52, 137.52, 137.96; ES MS (positive mode) M^+ @ $m/z = 718$.

11. Data were collected on a Nonius Kappa CCD area detector diffractometer with a rotating anode generator following standard procedures. Full crystallographic data for the structure analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 164777. Crystal data for $C_{52}H_{63}FeN_7$: $M_r = 841.94$, $T =$ 150(2) K, monoclinic, space group $P21/c$, $a = 12.8096(6)$, $b = 15.8408(3)$, $c = 22.9401(6)$ Å, $\beta = 102.931(3)°$, $V =$ 4536.8(3) Å^3, $\rho_{calcd} = 1.233$ g cm^{-3}, $\mu = 0.376$ mm^{-1}, $Z = 4$, reflections collected: 20690, independent reflections: 6485 ($R_{int} = 0.1249$), final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0878$, $wR_2 = 0.2292$, R indices (all data): $R_1 = 0.1597$, $wR_2 =$ 0.2850.
12. Hynes, M. J. *J. Chem. Soc.*, *Dalton Trans.* **1993**, 311.
13. Light, M. E.; Camiolo, S.; Gale, P. A.; Hursthouse, M. B. *Acta Crystallogr.* **2001**, *E57*, o727–o729.
14. Light, M. E.; Gale, P. A.; Hursthouse, M. B. *Acta Crystallogr.* **2001**, *E57*, o705–o706.