COMMUNICATION

ChemComm
www.rsc.org/chemcomm

A new fluoride selective electrochemical and fluorescent chemosensor based on a ferrocene–naphthalene dyad†

Francisco Otón, Alberto Tárraga,* María D. Velasco, Arturo Espinosa and Pedro Molina*
Departamento de Química Orgánica, Facultad de Química, Universidad de Murcia, Murcia, Spain. E-mail: pmolina@um.es

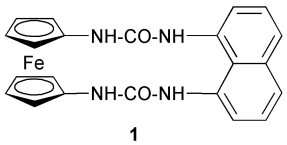
Received (in Cambridge, UK) 30th March 2004, Accepted 14th May 2004
First published as an Advance Article on the web 10th June 2004

A new difunctionalized receptor based on an aza-ferrocenophane structure shows electrochemical and fluorescent responses to fluoride anion.

The selective recognition and sensing of anions by artificial host molecules has emerged recently as a key research theme within the generalised area of supramolecular chemistry.[1] The sensing function is generally achieved by the coupling of two-well defined parts: a) selective binding sites and b) signalling subunits *e.g.* redox shifts, colour changes and fluorescence quenching or enhancement.[2] In particular, the sensing of a fluoride anion, the smallest anion, has attracted growing attention because of its important role in numerous biological processes.[3] The conventional approaches for the binding of fluoride anion have used either the specific strong affinity of a boron atom towards the fluoride anion or designed hydrogen-bonding with the fluoride anion. These binding events have been converted into an electrochemical[4] or fluorescent change[5] or more directly, a colorimetric change detectable by the naked eye.[6]

Despite the development of these classical single-signalling approximations, there is a paucity of use of multi-channel signalling receptors as potential guest reporters *via* multiple signalling patterns. This is an unfamiliar area because relatively few examples of fluoride selective fluorescent as well as chromogenic chemosensors have been reported.[7]

Owing to the relatively strong hydrogen bonding ability of the urea group, a number of molecules possessing the urea motif have been designed as neutral receptors for various anions.[2b] For strong and selective binding, this group should be preorganized to complement the target anion and minimize intramolecular hydrogen bonding. There are, however, few examples of either urea/ferrocene redox active anionophores[8] or urea/naphthalene fluorescent chemosensors of anions.[7a,9] Based on this body of work, we decided to combine in a highly preorganized system the redox activity of the ferrocene group with the photoactive behaviour of the naphthalene ring and the anion binding ability of the urea group. In this work, we report the synthesis, characterization and anion coordination properties of the new 1,3,7,9-tetraza[9]ferrocenophane **1**, in which the redox active (ferrocene) and fluorescent (naphthalene) signalling subunits are directly attached by two putative anion-binding sites. This structural motif would thus yield a combined fluorescence and redox based sensor in a single molecule.



1

1,1′-Ferrocenedicarboxylic acid was first converted to 1,1′-bis(isocyanato)ferrocene, *via* its acyl azide derivative following the published procedure.[10] Reaction of 1,8-diaminonaphthalene with 1,1′-bis(isocyanato)ferrocene in dichloromethane, under high dilution conditions, gave the ferrocenophane **1** in 68% yield. ^{1}H, ^{13}C NMR, elemental analysis and mass spectrum are consistent with the proposed structure of **1**.

The binding constants of **1** with several guest anions (as their TBA^+ salt) were determined by titration methods using ^{1}H NMR spectroscopy in DMSO-d_6 following the chemical shift change of the NH protons. The binding constant with the F^- anion was too large to be determined precisely by this method. Namely, addition of aliquots of the F^- anion to a solution of the receptor **1** caused a linear chemical shift change of the NH protons of the receptor until 2 eq of the anion was added and, after that, essentially no change of the chemical shift was observed. These results suggest that the association constant is considerably large ($> 10^4$) and, in addition, that a 1 : 2 complex is formed between the receptor and the guest. All the NH protons of the receptor **1** showed significant downfield shift ($\Delta\delta$ = +1.57 and +2.03 ppm) indicating that all four protons participate in the formation of the hydrogen-bonded complex. Addition of 1 eq of $H_2PO_4^-$ as a guest anion resulted in a lower downfield shift ($\Delta\delta$ = +1.08 and +1.42 ppm) of the NH resonances, which is also consistent with the formation of a hydrogen-bonded complex. The resulting binding curve by the mole ratio method clearly demonstrated the 1 : 1 stoichiometry of the complex. The association constant was 405 (M^{-1}) (error < 10%), which was calculated by nonlinear least-squares analysis. With Cl^-, Br^- and HSO_4^- anions, there were no chemical shift changes for the NH peaks, even when up to 10 eq of these anions were added.

The cyclic voltammetric (CV) response of **1** in DMSO—also containing 0.1 M $TBAPF_6$ as supporting electrolyte—showed a reversible one-electron oxidation process at −0.27 V *vs.* ferrocene/ferrocenium (Fe/Fe^+) couple. Electrochemical anion sensing experiments were carried out by CV. On stepwise addition of F^- (as its TBA^+ salt), a clear evolution of the wave from $E_{1/2}$ = −0.270 V *vs.* Fe/Fe^+ to $E_{1/2}$ = −0.460 V *vs.* Fe/Fe^+ ($\Delta E_{1/2}$ = −0.190 V) was observed; maximum perturbation of the CV was obtained with two equivalents of added F^- anion. This "two-wave" behaviour is diagnostic of a large value for the equilibrium constant for fluoride binding by the neutral receptor **1**. Similar "two wave" behaviour was found when two equivalents of $H_2PO_4^-$ was added $E_{1/2}$ = −0.395 V *vs.* Fe/Fe^+ ($\Delta E_{1/2}$ = −0.125 V). The binding enhancement factors (BEF) are 1628 (F^-) and 130 ($H_2PO_4^-$), respectively (Fig. 1). Remarkably, the presence of Cl^-, Br^- and

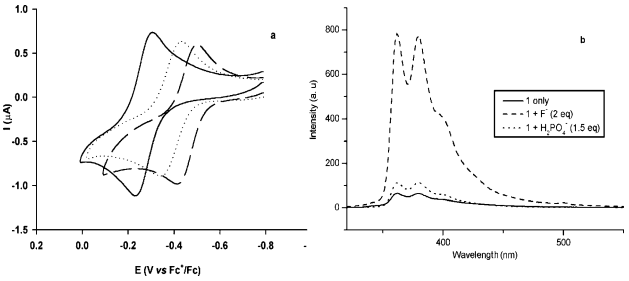


Fig. 1 (a) Cyclic voltammogram of compound **1**, before (—); after addition of 1.5 equiv of $H_2PO_4^-$ (···); after addition of 2 equiv of F^- (**---**). *Conditions*: 1 mM of 1 and 0.1 M [nBu_4NPF_6] in DMSO, using a Pt disk electrode and a scan rate = 0.1 V s^{-1}. (b) Fluorescent emission of **1** (—); upon addition of tetrabutylammonium fluoride (**---**) and dihydrogen phosphate (···) in DMF.

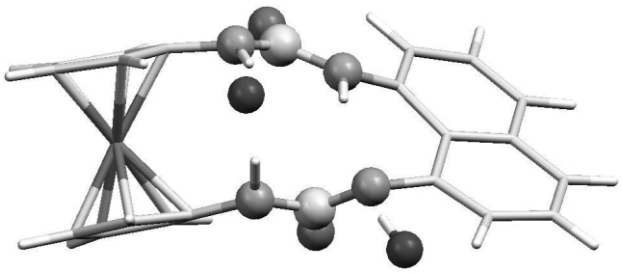
† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b4/b404601c/

DOI: 10.1039/b404601c

HSO_4^- anions had no effect on the CV, even when present in large excess. These findings underscore the selectivity of ligand **1** for F^- and $H_2PO_4^-$ anions in a relatively polar solvent (DMSO), where hydrogen bonding interactions between the urea functional groups and the anions are usually weakened by competing solvent molecules.

Assessments of the anion affinities also came from observing the extent to which the fluorescence intensity of **1** was affected in the presence of anions. Compound **1** in DMF shows a weak well-resolved naphthalene-like emission band with a maximum at 362 and 380 nm, respectively, when excited at 310 nm. The absorption spectrum between 250 and 350 nm is dominated by the broad naphthalene band with a maximum at 310 nm. Upon addition of various anions as TBA^+ salts in a 20-fold excess, no change in the emission spectra could be observed for Cl^-, Br^- and HSO_4^-. However, a strong fluorescence enhancement (1186%) was obtained in the presence of F^-. Similar emission enhancement was observed upon the addition of $H_2PO_4^-$ ion, although the magnitude of such enhancement (172%) was much smaller than for F^- ion (Fig. 1). Upon recognition, no remarkable anion binding induced changes in the absorption spectrum could be detected. Unlike many fluorescent chemosensors for F^-, the fluorescence is "switched on" rather than "switched off" upon recognition. This fact could be of interest because in sensing processes, fluorescence enhancement, rather than quenching, is usually preferred in order to observe a high signal output.

Calculations performed at the DFT[11] level of theory showed a global minimum for the **1**·2F^- complex exhibiting all four acidic urea protons involved in the binding process following an asymmetric pattern. The most acidic urea proton—at one of the naphthalene-linked NH groups (as evaluated, at the semiempirical PM3 level, by simple comparison of either Mulliken or electrostatic charges on such hydrogen atoms)—is attached to one F atom ($d_{F–H}$ = 1.101 Å), the corresponding naked N atom forming hydrogen bridge bonds with both the latter H atom ($d_{N\cdots HF}$ = 1.408 Å) and the related naphthalene-linked NH group ($d_{N\cdots HN}$ = 1.895 Å) in the other urea moiety. Both urea subunits are also connected by the other two NH groups that are hydrogen bridge bonding the second F^- anion ($d_{F\cdots HN}$ = 1.352 and 1.500 Å) in an almost linear fashion (angle F···H–N = 162.5 and 160.8°, respectively). This rigid geometry of **1**·2F^-, in which the HOMO's are involved in fluoride binding deactivates the quenching mechanism present in the uncomplexed receptor **1**, thus explaining the observed strong fluorescence enhancement.



1.2F-

In conclusion, we have designed and synthesized the new neutral receptor **1** based on an aza-ferrocenophane structure bearing two urea groups as linkers between the redox-active (ferrocene) and fluorescent (naphthalene) signalling subunits. This sensor shows both fluorescent and electrochemical anion-sensing action: it displays a selective fluorescent enhancement (12-fold) and a remarkable cathodic shift of the ferrocene oxidation wave (190 mV) with fluoride anions.

We gratefully acknowledge the grants from DGI-Spain BQU 2001-0014 and Fundación Séneca (CARM-Spain) PB/72/FS/02.

Notes and references

1 (*a*) F. P. Schmidchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609–1646; (*b*) J. W. Canary and B. C. Gibb, *Prog. Inorg. Chem.*, 1997, **45**, 1–82; (*c*) M. M. G. Antonisse and D. N. Reinhoudt, *Chem. Commun.*, 1998, 443–448; (*d*) J. L. Sessler and J. M. Davis, *Acc. Chem. Res.*, 2001, **34**, 989–997; (*e*) P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181–233; (*f*) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486–516; (*g*) P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79–128.

2 (*a*) R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419–4476; (*b*) P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 191–221; (*c*) P. D. Beer and E. J. Hayes, *Coord. Chem. Rev.*, 2003, **240**, 167–189.

3 K. L. Kirk, *Biochemistry of the Halogens and Inorganic Halides*, Plenum Press, New York, 1991, p. 58.

4 (*a*) C. Dusemund, K. R. A. S. Sandayanake and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1995, 333–334; (*b*) H. Yamamoto, A. Ori, K. Ueda, C. Dusemund and S. Shinkai, *Chem. Commun.*, 1996, 407–408; (*c*) D. Jiménez, R. Martínez-Mañez, F. Sancenón and J. Soto, *Tetrahedron Lett.*, 2002, **43**, 2823–2825.

5 (*a*) C. R. Cooper, N. Spencer and T. D. James, *Chem. Commun.*, 1998, 1365–1366; (*b*) M. Nicolas, B. Fabre and J. Simonet, *Chem. Commun*, 1999, 1881–1882; (*c*) S. Yamaguchi, S. Akiyama and K. Tamao, *J. Am. Chem. Soc.*, 2000, **122**, 6793–6794; (*d*) P. Jr. Anzenbacher, K. Jursiková and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 9350–9351; (*e*) P. Jr. Anzenbacher, A. C. Try, H. Miyaji, K. Jursiková, V. M. Lynch, M. Marquez and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 10268–10272; (*f*) S. K. Kim and J. Yoon, *Chem. Commun.*, 2002, 770–771; (*g*) T-H. Kimand and T. M. Swager, *Angew. Chem., Int. Ed.*, 2003, **42**, 4803–4806; (*h*) D. H. Lee, J. H. Im, J. H. Lee and J. I. Hong, *Tetrahedron Lett.*, 2002, **43**, 9637–9640; (*i*) C-F. Chen and Q-Y. Chen, *Tetrahedron Lett.*, 2004, **45**, 3957–3960.

6 (*a*) C. B. Black, B. Andrioletti, A. C. Try, C. Ruiperez and J. L. Sessler, *J. Am. Chem. Soc.*, 1999, **121**, 10438–10439; (*b*) P. A. Gale, L. J. Twymann, C. I. Handlin and J. L. Sessler, *Chem. Commun.*, 1999, 1851–1852; (*c*) H. Miyaji, W. Sato and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2000, **39**, 1777–1780; (*d*) H. Miyaji, W. Sato, J. L. Sessler and V. M. Lynch, *Tetrahedron Lett.*, 2000, **41**, 1369–1373; (*e*) H. Miyaji and J. L. Sessler, *Angew. Chem., Int. Ed.*, 2001, **40**, 154–157; (*f*) S. Yamaguchi, S. Akiyama and K. Tamao, *J. Am. Chem. Soc.*, 2001, **123**, 11372–11375; (*g*) M. Vázquez, L. Fabbrizzi, A. Taglietti, R. M. Pedrido, A. M. González-Noya and M. R. Bermejo, *Angew. Chem., Int. Ed.*, 2004, **43**, 1962–1965.

7 (*a*) E. J. Cho, J. W. Moon, S. W. Ko, J. Y. Lee, S. K. Kim, J. Yoon and K. C. Nam, *J. Am. Chem. Soc.*, 2002, **125**, 12376–12377; (*b*) T. Guunlaugsson, P. E. Kruger, T. C. Lee, R. Parkesh, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **44**, 6575–6578; (*c*) Y. Kubo, M. Yamamoto, M. Ikeda, M. Takeuchi, S. Shinkai, S. Yamaguchi and K. Tomao, *Angew. Chem., Int. Ed.*, 2003, **42**, 2036–2040; (*d*) H. Tong, L. Wang, X. Jing and F. Wang, *Macromolecules*, 2003, **36**, 2584–2586.

8 (*a*) M. D. Pratt and P. D. Beer, *Polyhedron*, 2003, **22**, 649–653; (*b*) B. Alonso, C. M. Casado, I. Cuadrado, M. Moran and A. E. Kaifer, *Chem. Commun.*, 2002, 1778–1779.

9 (*a*) S. Amemiya, P. Bühlmann and Y. Umezawa, *Chem. Commun*, 1997, 1027–1028; (*b*) H. Xie, S. Yi, X. Yang and S. Wu, *New J. Chem.*, 1999, **23**, 1105–1110; (*c*) M. Mei and S. Wu, *New J. Chem.*, 2001, **25**, 471–473.

10 P. M. Petrovitch, *Double Liaison*, 1996, **133**, 1093; P. M. Petrovitch, *Chem. Abstr.*, 1968, **68**, 29843s.

11 (*a*) E. J. Baerends, D. E. Ellis and P. Ros, *Chem. Phys.*, 1973, **2**, 41–51; (*b*) W. Kohn, A. D. Becke and R. G. Parr, *J. Phys. Chem.*, 1996, **100**, 12974–12980.