Sensors

Selective Electrochemical Detection of Hydrogen Fluoride by Ambiphilic Ferrocene Derivatives[**]

Christopher Bresner, Simon Aldridge, Ian A. Fallis,* Cameron Jones, and Li-Ling Ooi*

The selective detection of specific anions or whole acids/metal salts (HX or MX) in the presence of potentially competitive contaminants represents a fundamental chemical challenge for applications, for example, in sensor devices and in separation technologies.[1–4] In the former case, such a process typically involves recognition of both anionic and cationic components, accompanied by an appropriate reporter response.[2,3] Within this sphere, the detection of hydrogen fluoride represents a particularly timely goal, given its industrial use and its well-documented liberation in the hydrolysis of the fluorinated G-type chemical warfare agents (CWAs).[4–7] Given the low ambient levels of volatile fluorides, a potential sensor for airborne Sarin or Soman utilizes HF as the target analyte.

Selective binding of the fluoride anion by Lewis acid receptors based on boronic acid/ester has been reported by a number of groups.[4,8,9] Furthermore, significant electrochemical shifts have been shown to accompany the binding event for systems incorporating directly linked receptor and ferrocene components.[8a,b,d] Given the selective detection of fluoride demonstrated for these systems, we wondered whether incorporation of a suitable Lewis basic component within an appropriate molecular framework might facilitate selective HF recognition, either by binding of an intact HF

---

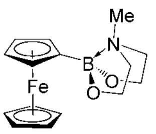
[*] C. Bresner, Dr. S. Aldridge, Dr. I. A. Fallis, Prof. C. Jones, Dr. L.-L. Ooi
Centre for Fundamental and Applied Main Group Chemistry
School of Chemistry, Cardiff University
Main Building, Park Place
Cardiff, CF10 3AT (UK)
Fax: (+44) 292-087-4030
E-mail: aldridges@cardiff.ac.uk

[**] We would like to thank the EPSRC for a studentship (C.B.), for financial aid (grant GR/S98771/01), and for access to the National Mass Spectrometry facility.

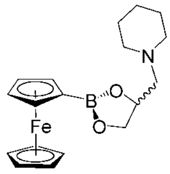
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200500527

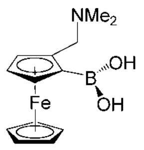
entity or distinct H^+ and F^- components. With this in mind, we set out to examine the response to hydrogen fluoride exposure of the mixed Lewis acid/Lewis base systems **1**–**3**.



1



2



3

The compounds chosen sought to probe the stability of different molecular architectures to HF and to further examine the effect (if any) of the intramolecular N→B interaction in the H–F bond breaking process.

Compounds **1** and **2** can be synthesized by a one-pot process from $FcBBr_2$ [Fc = $(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)$][10] and one equivalent of the appropriate reagent, that is, $(Me_3SiOCH_2CH_2)_2NMe$ for **1** and *rac*-$(C_5H_{10}N)CH_2CH(OLi)CH(OLi)$ for **2**. The structure of **1** was corroborated by single-crystal X-ray diffraction (Figure 1), which also confirmed the presence of an intramolecular N→B bond (1.735(3) Å).[11] Although suitable single crystals of **2** were not forthcoming, the three-coordinate nature of the boron center was implied by the ^{11}B NMR chemical shift ($\delta_B = 32.3$ ppm) and the ferrocene-based oxidation potential ($E_{1/2} = -0.5$ mV (96 mV)[12]), which are characteristic of this type of pendant boryl function [for comparison, $\delta_B = 34.1$ ppm, $E_{1/2} = +116.0$ mV (80 mV) for $FcBO_2C_2H_2Ph_2$ (three-coordinate boron)[13] and $\delta_B = 13.4$ ppm, $E_{1/2} = -190.5$ mV (85 mV) for **1** (four-coordinate boron)].

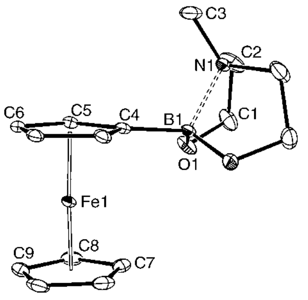


Figure 1. Molecular structure of $FcB(OCH_2CH_2)_2NMe$ (**1**) with ORTEP ellipsoids set at the 50% probability level; hydrogen atoms are omitted for clarity. Relevant bond lengths [Å] and angles [°]: $Fe1\text{-}Cp_{centroid}$ 1.649(2), $Fe1\text{-}C_5H_4BRR'_{centroid}$ 1.645(2), B1-N1 1.735(3), B1-O1 1.443(2), B1-C4 1.595(4); $B1\text{-}C4\text{-}C_5H_4BRR'_{centroid}$ 176.3(1).

The NMR spectroscopic and electrochemical (CV) monitoring of the reactions of **1** and **2** with hydrogen fluoride (as the collidine complex 2,4,6-trimethylpyridine·$(HF)_{1.5}$) showed that the reaction requires three equivalents of HF to be driven to completion, and that a common ferrocene- and boron-containing product is formed in each case [quartet $\delta_B = 3.7$ ppm, $J_{BF} = 49.8$ Hz; $E_{1/2} = -320$ mV (75 mV)]. For the reaction with **1**, crystallographic investigation of the product revealed that this is the $[FcBF_3]^-$ anion,[14] isolated in this case as the $[(HOCH_2CH_2)_2N(H)Me]^+$ salt (**4**, Figure 2).

Given that **4** is formed by rupture of the boronic ester linkages in **1**, it is clear that the design of an ambiphilic receptor system that survives exposure to HF necessitates the avoidance of structurally significant B–O bonds. Consequently, we have examined the whole acid sensing properties of 2-(*N*,*N*-dimethylaminomethyl)ferrocene boronic acid (**3**), a compound which was originally reported by Marr et al.,[15] and which has, for example, also been investigated by Shinkai and by Norrild and Søtofte as a carbohydrate sensor.[16] Tethering of the Lewis acidic and Lewis basic components to the cyclopentadienyl ring through B–C and N–C bonds allows isolation of an intact, charge-neutral HF host–guest complex.

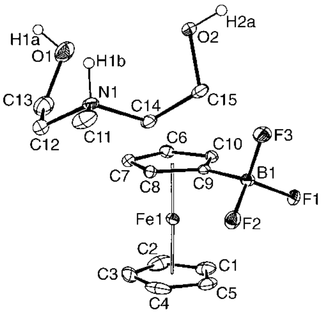


Figure 2. Molecular structure of $[(HOCH_2CH_2)_2N(H)Me][FcBF_3]$ (**4**) with ORTEP ellipsoids set at the 50% probability level; hydrogen atoms (except those attached to O1, O2, and N1) are omitted for clarity. Relevant bond lengths [Å] and angles [°]: $Fe1\text{-}Cp_{centroid}$ 1.648(3), $Fe1\text{-}C_5H_4BRR'_{centroid}$ 1.644(3), B1-F1 1.435(3), B1-F2 1.423(3), B1-F3 1.405(4), B1-C9 1.590(4); $B1\text{-}C9\text{-}C_5H_4BF_{3\,centroid}$ 179.6(2).

In practice, the reaction of **3** with three equivalents of HF in acetonitrile leads to the isolation of the zwitterionic species $[(\eta^5\text{-}C_5H_5)Fe\{\eta^5\text{-}C_5H_3(BF_3)(CH_2NMe_2H)\}]$ (**5**) in about 68% yield. The structure of **5** has been elucidated from spectroscopic and X-ray diffraction measurements and reveals—in addition to substitution of the two boronic acid OH groups by fluorine atoms[17]—the binding of a single equivalent of HF (Figure 3). The residual intramolecular H···F interaction is

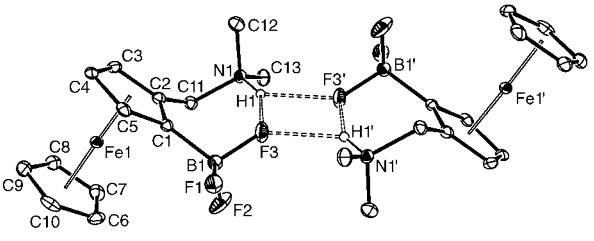


Figure 3. Hydrogen-bonded dimeric structure of $[(\eta^5\text{-}C_5H_5)Fe\{\eta^5\text{-}C_5H_3(BF_3)(CH_2NMe_2H)\}]$ (**5**) in the solid state with ORTEP ellipsoids set at the 50% probability level; hydrogen atoms (except that attached to N1 and N1') are omitted for clarity. Relevant bond lengths [Å] and angles [°]: $Fe1\text{-}Cp_{centroid}$ 1.643(5), $Fe1\text{-}C_5H_3BF_{3\,centroid}$ 1.640(5), B1-C1 1.600(6), B1-F1 1.413(5), B1-F2 1.382(5), B1-F3 1.431(5), F3-H1 2.204, F3-H1' 2.124, N1-H1 0.930, N1-F3 2.996(4), N1-F3' 2.854(3); $B1\text{-}C1\text{-}C_5H_3CBF_{3\,centroid}$ 176.6(3), N1-H1-F3 142.5, N1-H1-F3' 134.4.

relatively weak, as evidenced by a separation of 2.204 Å (0.92 Å for gaseous HF),[18] and is best viewed as an ionic hydrogen bond between the BF_3^- and NMe_2H^+ fragments.[19] In the solid state these hydrogen-bonded units are linked through additional intermolecular H···F interactions (2.124 Å) into centrosymmetric dimers.

The key feature of whole acid binding by **3** is its selectivity for HF over other acids. This can not only be demonstrated electrochemically, but also results in distinct *opposing* responses for HF and, for example, HCl. Thus, the voltammograms for **3** and **5** reveal a cathodic shift of −80 mV on HF binding [$E_{1/2} = +37.5$ mV (85 mV) for **3** and −43 mV (75 mV) for **5**; Figure 4, top]. The oxidation potential for **5** is markedly less negative than that for $[FcBF_3]^-$ [$E_{1/2} = -320$ mV (75 mV)], reflecting the overall charge neutrality of **5**. However, the net cathodic shift (with respect to **3**) is consistent with transformation of a three-coordinate electron-withdrawing boronic acid group into a net electron-donating four-coordinate boronate.[20] An entirely different electrochemical response is observed on addition of excess HCl to **3** (Figure 4, bottom). Here a significant anodic shift (+149.5 mV) is observed, and this (together with the lack of any discernable shift in the ^{11}B NMR spectrum of **3** on addition of HCl) is consistent with protonation of the amine functionality, but with no significant Lewis base coordination at the boron center. The identification of this species as cationic $[(\eta^5\text{-}C_5H_5)Fe\{\eta^5\text{-}C_5H_3[B(OH)_2](CH_2NMe_2H)\}]^+$ is given further credence by the addition of excess fluoride. This leads to an upfield shift in the ^{11}B NMR resonance (to $\delta_B = 3.0$ ppm) and to a CV trace that is essentially identical to that measured for an authentic sample of **5**. Thus it would appear that the opposing senses of the electrochemical shifts observed for **3** with HF and HCl[*] reflect the intrinsic selectivity of the boronic acid moiety for fluoride.[4,8]

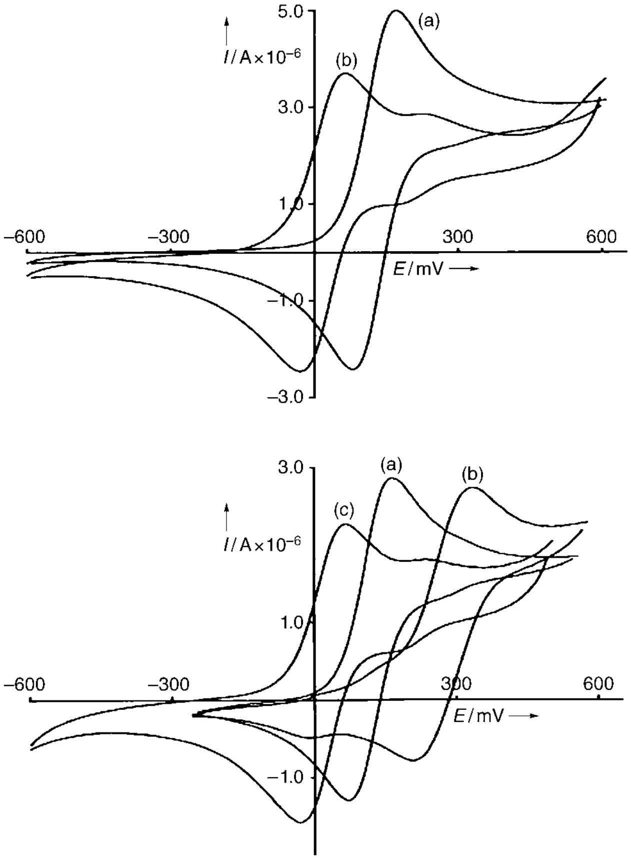


Figure 4. Top: Cyclic voltammograms of **3** (a) and of **5** (b). Bottom: Cyclic voltammograms of **3** (a), of **3** after addition of HCl (b), and of **3** after subsequent addition of nBu_4NF (c).

In conclusion, it has been demonstrated that by avoiding structurally significant B–O bonds it is possible to construct robust organometallic receptor systems capable of selectively binding hydrogen fluoride. Such a system has been shown to be capable of differentiating between exposure to HF and exposure to related acids (such as HCl) by providing opposing electrochemical responses. This in turn can be related to the much stronger affinity of fluoride for boronic acid/ester receptors compared to other conjugate bases such as chloride.

Experimental Section

Details of the preparation and characterization of **1** and **2**, details of the reaction of **1** with HF, and characterizing data for **4** are included in the Supporting Information.

5: To **3** (24.4 mg, 0.085 mmol) in acetonitrile (ca. 20 cm^3) was added 2,4,6-trimethylpyridine·$(HF)_{1.5}$, (3 equiv of HF), and the reaction mixture was stirred for 20 min. Monitoring by ^{11}B NMR spectroscopy indicated complete conversion into a single product. Cannula filtration followed by cooling to −30 °C yielded **5** as a yellow-orange solid (yield: 18.0 mg, 68.4 %). ^{1}H NMR ([D$_3$]acetonitrile, 300 MHz, 20 °C): $\delta = 2.57$ (s, 3H, NCH_3), 2.83 (s, 3H, NCH_3), 3.75 (d $J = 13$ Hz, 1H, CH_2N), 4.08 (s, 5H, C_5H_5), 4.15 (m, 3H, C_5H_3), 4.55 (d $J = 13$ Hz, 1H, CH_2N), 6.98 ppm (v br s, 1H, NH). ^{13}C NMR ([D$_3$]acetonitrile, 76 MHz, 20 °C): $\delta = 40.7$ (br, NCH_3), 43.3 (br, NCH_3), 60.0 (NCH_2), 68.7 (CH of C_5H_5), 68.4, 70.6, 73.8 (CH of C_5H_3), 77.6 ppm (C-bound quaternary of C_5H_3), B-bound quaternary of C_5H_3 not observed. ^{11}B NMR ([D$_3$]acetonitrile, 96 MHz, 21 °C): $\delta = 3.0$ ppm (q, $J_{\text{B-F}} = 49$ Hz). ^{19}F NMR ([D$_3$]acetonitrile, 283 MHz, 21 °C): $\delta = -133.9$ ppm (q, $J_{\text{F-B}} = 49$ Hz). IR (KBr disk): $\tilde{\nu} = 3174$ s (NH), 1489 w, 1473 w, 1448 w, 1388 m, 1297 w, 1248 w, 1187 m, 1165 w, 1139 m, 1102 s, 1035 s, 1009 s, 946 s, 921 s, 890 m, 853 m, 813 s, 757 w cm^{-1}. MS(EI): $[M-HF]^+ = 291$ (75 %), calcd 291.0683, found 291.0685; $[M-HF-NMe_2]^+ = 247$ (100 %), calcd 247.0185, found 247.0186.

For the crystal structure determinations of **1**, **4**, and **5** a suitable crystal was covered in predried mineral oil and mounted on an Enraf-Nonius Kappa CCD diffractometer at 150(2) K. Crystal data for **1** ($C_{15}H_{20}BFeNO_2$): orthorhombic, space group *Pnma*, $a = 12.522(3)$, $b = 10.602(2)$, $c = 10.421(2)$ Å, $V = 1383.5(5)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.503$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 1.089$ mm^{-1}; 8254 unique reflections were collected ($3.2 < \theta < 27.5°$); final *R* factor $R_1 = 0.034$. Crystal data for **4** ($C_{15}H_{23}BF_3FeNO_2$): monoclinic, space group $P2_1/n$, $a = 5.8490(1)$, $b =$

---

[*] That the response of **3** towards HCl is typical of other inorganic and organic acids (i.e., that there is little or no interaction of the conjugate anion with the boronate moiety) has been shown for related systems[8d] and can be demonstrated explicitly for **3** by cyclic voltammetry. Exposure of **3** to other sources of fluoride (e.g. KF/[18]crown-6) is accompanied by an electrochemical response (a cathodic shift of about 450 mV in MeCN) typical of fluoride coordination to the boron center[8d,13] but with no significant interaction of the tertiary amine function with the cation (K$^+$).

8.6140(2), $c = 32.1360(9)$ Å, $\beta = 92.210(1)°$, $V = 1617.9(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.531$ g cm^{-3}, $\mu(\text{Mo}_{K\alpha}) = 0.970$ mm^{-1}; 3667 unique reflections were collected ($3.0 < \theta < 27.5°$); final R factor: $R_1 = 0.047$. Crystal data for **5** ($C_{13}H_{17}BF_3FeN$): monoclinic, space group $P2_1/a$, $a = 11.6268(5)$, $b = 7.3492(4)$, $c = 15.7888(7)$ Å, $\beta = 104.684(3)°$, $V = 1305.1(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.583$ g cm^{-3}, $\mu(\text{Mo}_{K\alpha}) = 1.174$ mm^{-1}; 2982 unique reflections were collected ($3.1 < \theta < 27.5°$); final R factor: $R_1 = 0.056$. CCDC 263113 (**1**), CCDC 263114 (**4**), and CCDC 263115 (**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: February 11, 2005
Published online: May 17, 2005

Keywords:
molecular recognition · boron · electrochemistry · metallocenes · sensors

---

[1] For reviews on anion binding, see: a) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.* **1997**, *97*, 1515–1566; b) F. P. Schmidtchen, M. Berger, *Chem. Rev.* **1997**, *97*, 1609–1646; c) P. A. Gale, J. A. Sessler, V. Kral, *Chem. Commun.* **1998**, 1–8; d) P. D. Beer, P. A. Gale, *Angew. Chem.* **2001**, *113*, 502–532; *Angew. Chem. Int. Ed.* **2001**, *40*, 486–516; ; e) J. J. Lavigne, E. V. Anslyn, *Angew. Chem.* **2001**, *113*, 3212–3215; *Angew. Chem. Int. Ed.* **2001**, *40*, 3118–3130; ; f) P. A. Gale, *Coord. Chem. Rev.* **2003**, *213*, 191–221; g) R. Martínez-Mánez, F. Sancernón, *Chem. Rev.* **2003**, *103*, 4419–4476.

[2] For a recent example of whole metal salt (MX) binding, see: V. Gasperov, S. G. Galbraith, L. F. Lindoy, B. R. Rumbel, B. W. Skelton, P. A. Tasker, A. H. White, *Dalton Trans.* **2005**, 139–145.

[3] For an example of metal fluoride binding, see: M. T. Reetz, C. M. Niemeyer, K. Harms, *Angew. Chem.* **1991**, *103*, 1515–1517; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1472–1474.

[4] C. R. Cooper, N. Spencer, T. James, *Chem. Commun.* **1998**, 1365–1366.

[5] H. Sohn, S. Létant, M. J. Sailor, W. C. Trogler, *J. Am. Chem. Soc.* **2000**, *122*, 5399–5400.

[6] Y.-C. Yang, J. A. Baker, J. R. Ward, *Chem. Rev.* **1992**, *92*, 1729–1743.

[7] For a recent example of G-agent sensing, see: S.-W. Zhang, T. M. Swager, *J. Am. Chem. Soc.* **2003**, *125*, 3420–3421.

[8] a) C. Dusemund, K. R. A. S. Sandanayake, S. Shinkai, *J. Chem. Soc. Chem. Commun.* **1995**, 333–334; b) H. Yamamoto, A. Ori, K. Ueda, C. Dusemund, S. Shinkai, *Chem. Commun.* **1996**, 407; c) A. Yuchi, A. Tatebe, S. Kani, T. D. James, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 509–510; d) S. Aldridge, C. Bresner, I. A. Fallis, S. J. Coles, M. B. Hursthouse, *Chem. Commun.* **2002**, 740–741; e) S. Arimori, M. G. Davidson, T. M. Fyles, T. G. Hibbert, T. D. James, G. I. Kociok-Kohn, *Chem. Commun.* **2004**, 1640–1641.

[9] For recent examples of fluoride binding by other three-coordinate boron-containing systems, see: a) S. Yamaguchi, S. Akiyama, K. Tamao, *J. Am. Chem. Soc.* **2001**, *123*, 11372–11375; b) Y. Kubo, M. Yamamoto, M. Ikeda, M. Takeuchi, S. Shinkai, K. Tamao, *Angew. Chem.* **2003**, *115*, 2082–2086; *Angew. Chem. Int. Ed.* **2003**, *42*, 2036–2040; ; c) S. Solé, F. P. Gabbaï, *Chem. Commun.* **2004**, 1284–1285; d) G. E. Herberich, U. Englert, A. Fischer, D. Wiebelhaus, *Eur. J. Inorg. Chem.* **2004**, 4011–4020.

[10] T. Renk, W. Ruff, W. Siebert, *J. Organomet. Chem.* **1976**, *120*, 1–25.

[11] For examples of intramolecular N→B bonds in closely related systems, see: a) A. A. Korlyukov, K. A. Lyssenko, M. Y. Antipin, V. N. Kirin, E. A. Chernyshev, S. P. Knyazev, *Inorg. Chem.* **2002**, *41*, 5043–5051; b) S. Aldridge, R. J. Calder, D. L. Coombs, C. Jones, J. W. Steed, S. J. Coles, M. B. Hursthouse, *New J. Chem.* **2002**, *26*, 677–686.

[12] Electrochemical data are reported for solutions in acetonitrile, referenced with respect to the ferrocene/ferrocenium couple. Peak-to-peak separations are given in parentheses.

[13] C. Bresner, PhD Thesis, Cardiff University, 2005.

[14] T. D. Quach, R. A. Batey, A. J. Lough, *Acta Crystallogr. Sect. E* **2001**, *57*, m320–m321.

[15] G. Marr, R. E. Moore, B. W. Rockett, *J. Chem. Soc. C* **1968**, 24–27.

[16] a) A. Ori, S. Shinkai, *J. Chem. Soc. Chem. Commun.* **1995**, 1771–1772; b) J. C. Norrild, I. Søtofte, *J. Chem. Soc. Perkin Trans. 2* **2001**, 727–732.

[17] R. L. Giles, J. A. K. Howard, L. G. F. Patrick, M. R. Probert, G. E. Smith, A. Whiting, *J. Organomet. Chem.* **2003**, *680*, 257–262.