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Multidentate Lewis acids: synthesis, structure and mode of action of a redox-based fluoride ion sensor†

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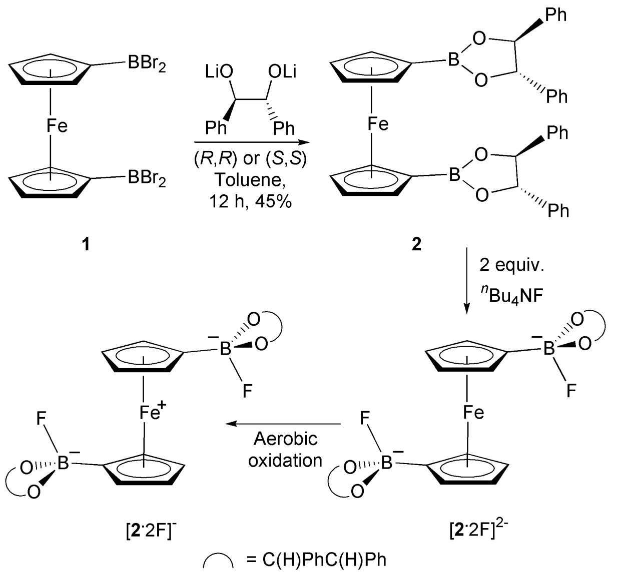
The mode of action of the bidentate bis(boronate) Lewis acid 2 as a fluoride ion sensor is shown to involve selective anion binding together with an electrochemical response.

The selective binding or recognition of specific anionic species has been the subject of considerable recent research effort,[1] in part reflecting potential applications in anion separation technologies and in sensors.[2] Fluoride ion recognition in particular has received much attention,[3] not only because of potential relevance to health and environmental issues,[4] but also because of the relatively strong bonds formed with the hydrogen bond donors which typically form the binding site.[5] In some cases binding makes use not only of an array of appropriately positioned hydrogen bond donor functions within the receptor, but also of the intrinsic electrostatic attraction inherent in a cationic host.[6] Recognition studies involving alternative methods of anion binding (*e.g.* coordination to a site of appreciable Lewis acidity) have received much less attention,[7–10] although there are reports of guest binding by multi-site receptors containing three-coordinate boron centres[8,9] and of hydroxide binding by cationic boryl derivatives of cobalticenium.[10]

Mindful of recent developments in the field of multidentate boron-containing Lewis acids,[11] we have therefore sought to investigate the potential for anion binding, recognition and sensing by bidentate boron-containing Lewis acids based around a ferrocene backbone (*e.g.* **2**). Such systems offer the advantages of synthetic ease and ready spectroscopic and electrochemical investigation, compared, for example, to analogous systems based on *ortho*-phenyl frameworks. In addition, ready modification to include chiral acceptor functions offers the potential for such systems to act as enantioselective anion binding agents and/or as chiral sources of achiral anions.

The synthesis of the air-stable 1,1′-bis(dialkoxyboryl)ferrocene **2** was readily achieved in gram quantities from 1,1′-bis(dibromoboryl)ferrocene[12] using the generic method outlined in Scheme 1. Spectroscopic and analytical data for **2** are fully in accord with the proposed structure,‡ and these inferences have been confirmed by the results of a single-crystal X-ray diffraction study (see Fig. 1).§ Interestingly, the conformation of the molecule is such that the two boryl substituents do not adopt the staggered orientation expected on steric grounds, as is found, for example, in the structure of 1,1′-bis(dibromoboryl)ferrocene.[12] The torsion angle of 54.4° [for ∠C(5)–centroid–centroid–C(24)] finds precedent among similar molecules only in 1,1′-Fc($BC_{11}H_{17}SnCH_3$)$_2$.[13] That the structure of **2** does not vary appreciably between crystals obtained from light petroleum (bp 40–60 °C) and those of the solvate **2**·2C_6H_6 rules out interaction with solvent molecules (*e.g.* π-stacking between phenyl rings and benzene solvent) as a conformationally significant factor. Additionally, the relative orientations of phenyl rings are such that π-stacking between C_6H_5 groups attached to different boryl substituents can be ruled out. Conceivably the molecular conformation is therefore determined by the energetics of packing in the crystalline state. The closest possible approach between the two boron centres in **2** is 2.87 Å (for an eclipsed conformation). Given that B–F distances for B–F–B units (*e.g.* in the anion $B_2F_7^-$[14]) are of the order 1.5 Å, we speculated that **2** might therefore act as a chelating host for F$^-$.



Scheme 1

Reaction of **2** with two or more equivalents of ^{n}BuN$_4$F (or KF/18-crown-6) in chloroform or dichloromethane solution under aerobic conditions leads to a colour change from orange to pale green. By contrast, no colour change is observed if the reaction is carried out with the exclusion of air, or if even a large excess of an alternative anion (*e.g.* Cl$^-$, Br$^-$, I$^-$, BF_4^-, PF_6^-, $H_2PO_4^-$, HSO_4^- or NO_3^- as the ^{n}Bu$_4$N$^+$ salt) is added. Evidence obtained from spectroscopic and electrochemical measurements suggests that this colour change is brought about by initial complexation of F$^-$ anions to *both* of the boron centres in **2** (giving [**2**·2F]$^{2-}$), followed by aerobic oxidation of the iron

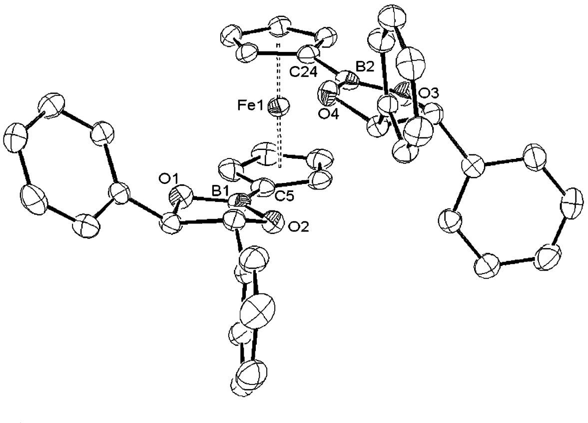


Fig. 1 Molecular structure of **2** (hydrogen atoms omitted for clarity). Relevant bond lengths (Å) and angles (°): Fe(1)–(η^5-C_5H_5) centroid 1.652(3), 1.651(3), C(24)–B(2) 1.538(4), B(2)–O(3) 1.378(3), B(1)···B(2) 3.808(4), C(5)–centroid–centroid–C(24) 54.4(2).

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† Electronic supplementary information (ESI) available: details of NMR and UV/Vis spectroscopic measurements. See http://www.rsc.org/suppdata/cc/b2/b200828a/

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centre in the adduct to yield the green ferrocenium derivative [**2**·2F]$^-$ (Scheme 1). Highly selective binding of F$^-$ by **2** therefore means that this sensor response is not observed for other anions.

The fact that **2** binds F$^-$ in chloroform solution, but interacts minimally with other anions under the same conditions can be demonstrated by ^{11}B and ^{19}F NMR spectroscopy (ESI†), changes in the spectra being wholly consistent with binding of F$^-$ to a three-coordinate boron centre. The solution binding properties of **2** in CDCl$_3$ were further investigated by ^{1}H NMR titration under anaerobic conditions. The response of the resonance due to the methine protons of the cyclic boronate to successive addition of alicquots of solid ^{n}Bu$_4$NF is shown in Fig. 2.¶ Two features of the graph obtained indicate that **2** binds two equivalents of F$^-$ (a stoichiometry confirmed by a Job plot). Firstly, little (if any) extra shift in the resonance is observed on further addition of >2 equivalents of ^{n}Bu$_4$NF. Secondly, the initial form of the dependence of δ_H on [F$^-$] (for [F$^-$] < 0.08 mol dm^{-3}) can be fitted to a quadratic expression ($R^2 = 0.9949$) (ESI†). Such a dependence not only implies the binding of two equivalents of F$^-$,[9] but also yields values of 4.1 and 9.8 mol^{-1} dm^3 for the successive complexation constants K_1 and K_2. The binding of F$^-$ by **2** is therefore clearly weak, although similar to that reported by Takaya *et al.* for the binding of benzylamine by a similar bidentate receptor ($K_1K_2 = 18.8$ mol^{-2} dm^6).[9] In our hands no changes in the ^{1}H or ^{11}B NMR spectra of **2** were observed upon addition of large excesses (>20 equivalents) of Cl$^-$, Br$^-$, I$^-$, BF$_4^-$, PF$_6^-$, H$_2$PO$_4^-$, HSO$_4^-$ or NO$_3^-$.

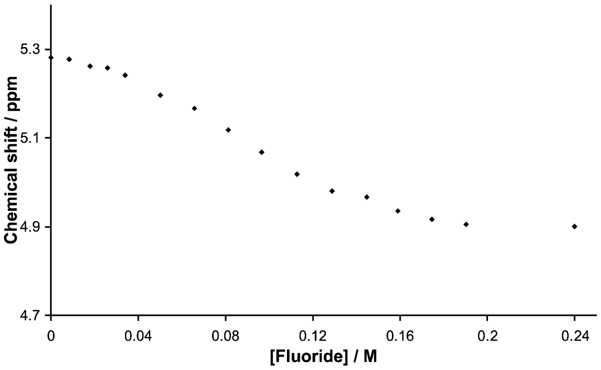

Fig. 2 Plot of chemical shift (δ_H) *vs.* fluoride ion concentration, for the methine protons of the cyclic boronate fragment of **2**.

Attempts to carry out NMR titration experiments under aerobic conditions were frustrated by significant broadening of the relevant signals. Under these conditions monitoring of the reaction of **2** with ^{n}Bu$_4$NF in chloroform by UV/Vis spectroscopy reveals that the bands at 341 and 449 nm characteristic of **2** are quantitatively replaced by features at 428 and 629 nm upon the addition of 2 equivalents of fluoride (ESI †). Ferrocene itself has no significant absorptions above 530 nm, whereas the ferrocenium cation displays a feature at 617 nm attributed to a $^2E_{2g} \rightarrow {}^2E_{1u}$ LMCT process.[15] The appearance of a band at 629 nm on addition of fluoride is therefore highly suggestive of oxidation of the iron centre to give a ferrocenium species. Confirmation that addition of excess fluoride to a solution of **2** in dichloromethane renders the iron centre easier to oxidize can be shown electrochemically. Relative to the ferrocene/ferrocenium couple, oxidation of **2** in dichloromethane solution (containing 0.1 mol dm^{-3} ^{n}Bu$_4$NPF$_6$ electrolyte) occurs at +206 mV, a value which is shifted anodically by 146 mV on addition of excess fluoride.

It can therefore be shown that the mode of action of **2** as a fluoride ion sensor involves (i) the selective binding of two equivalents of fluoride; (ii) a 146 mV anodic shift of the oxidation potential of the iron centre in the presence of fluoride; and (iii) the generation of a final product containing a ferrocenium-type chromophore. These observations together with the fact that the sensor only works under aerobic conditions, are consistent with the chemistry outlined in Scheme 1, in which fluoride complexation to **2** renders the iron centre susceptible to aerobic oxidation.

Attempts to develop the binding properties of **2** in the fields of ion selective electrodes and chiral discrimination, and to develop stronger multi-boron receptors are ongoing.

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Notes and references

‡ *Spectroscopic data* for **2**: MS(EI): M$^+$ = 630, exact mass (calc.) m/z 630.1836, (obs.) 630.1834. ^{1}H NMR ([^{2}H$_6$]benzene, 21 °C), δ 4.39 [m, 2H, C$_5$H$_4$], 4.44 [m, 2H, C$_5$H$_4$], 4.88 [m, 2H, C$_5$H$_4$], 4.99 [m, 2H, C$_5$H$_4$], 5.30 [s, 4H, CH of chelate], 7.04-7.26 [m, 20H, C$_6$H$_5$]. Accidental degeneracy of two of the four unique cyclopentadienyl hydrogens is observed in CDCl$_3$: ([^{2}H]chloroform, 21 °C), δ 4.55 [m, 2H, C$_5$H$_4$], 4.61 [m, 2H, C$_5$H$_4$], 4.71 [m, 4H, C$_5$H$_4$], 5.28 [s, 4H, CH of chelate], 7.37 [m, 20H, C$_6$H$_5$]. ^{13}C NMR ([^{2}H]chloroform, 21 °C), δ 72.9, 73.5, 75.1, 75.5 [CH of C$_5$H$_4$], 86.9 [CH of chelate], 126.2, 128.4, 128.8 [aromatic CH], 140.1 [aromatic quaternary]. ^{11}B NMR ([^{2}H]chloroform, 21 °C), δ 34.0 (br). Elemental analysis: calc. for C$_{38}$H$_{32}$B$_2$FeO$_4$, C 72.43, H 5.08; obs., C 72.61, H 5.13%.

§ *Crystallographic data* for **2**: C$_{38}$H$_{32}$B$_2$FeO$_4$; orthorhombic, space group $P2_12_12_1$, a = 10.656(2), b = 15.002(3), c = 19.920(4) Å, U = 3181.4(11) Å^3, D_c = 1.314 Mg m^{-3}, Z = 4, T = 150(2) K, orange block, 0.40 × 0.16 × 0.16 mm, 23416 reflections collected, 7212 independent [R_{int} = 0.0783] which were used in all calculations. R_1 = 0.0414, wR_2 = 0.0777 for observed unique reflections [$F^2 > 2\sigma(F^2)$] and R_1 = 0.0645, wR_2 = 0.0845 for all 7212 unique reflections. Max./min. residual electron densities: 0.300/−0.309 e Å^{-3}. CCDC reference number 178314. See http://www.rsc.org/suppdata/cc/b2/b200828a/ for crystallographic data in CIF or other electronic format.

¶ In common with earlier studies of neutral molecule binding by (R,R)-1,2-(Ph$_2$C$_2$H$_2$O$_2$B)$_2$C$_6$H$_4$,[9] the signal due to the CH protons of the OCH(Ph)CH(Ph)O chelate remains a singlet even upon binding of fluoride. This implies that the kinetics of F$^-$ association/dissociation are rapid on the NMR timescale, as was found by Takaya and coworkers for the binding of benzylamine.[9]

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