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Synthesis and structural characterisation of the first bis(bora)calixarene: a selective, bidentate, fluorescent fluoride sensor†

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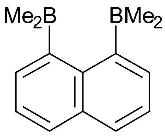
A bis(bora)calixarene, 3, the first lower-rim boron derivatised calixarene to be structurally characterised, is synthesised by the reaction of $PhBCl_2$ with 4-*tert*-butylcalix[4]arene, and is demonstrated to be a sensitive and selective fluorescent fluoride sensor.

The design of synthetic molecular sensors for anions is an area of chemistry that has received considerable attention in recent years.[1] In the case of fluoride ions this has been for a range of applications[2–4] and has utilized one of two distinct binding strategies. First, protic receptors have been designed that bind anions *via* hydrogen bonding.[1] Second, Lewis acid receptors have also been exploited that rely on either electrostatic or covalent bonding interactions with anions. In particular for the latter case, boron centres have proved to be excellent selective receptors for fluoride ions. Katz described bidentate naphthalene derivatives of organoboranes **1** and showed them to exhibit enhanced fluoride binding over related monodentate species.[5] More recently, James and co-workers[6] established the use of boronic acids (**2**, R = H) as fluoride receptors. They and others[7] have demonstrated that aryl boronic acids exhibit selective fluoride binding and that they are potentially useful sensors, with detection being monitored by fluorescence, electrochemical or colorimetric means.



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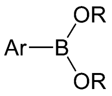

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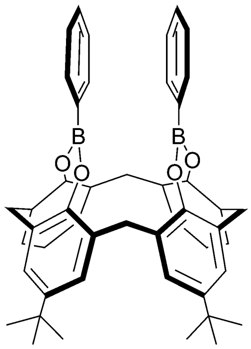

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In this context, we speculated that boron-derivatised calixarenes may offer advantages over known fluoride receptors. For example, the synthesis of **3** (for clarity, all *tert*-butyl groups are not shown) and related compounds is very straightforward (*i.e.*, two steps from commercially available starting materials), and, unlike in **1**, the fluorophore may be varied *independently* of the scaffold. We herein describe the synthesis and X-ray structure of a prototypical bis(bora)calixarene **3** together with an evaluation of its utility as a new class of fluorescent Lewis acidic fluoride sensor.

In contrast to recently reported attempts at organoboron derivatisation of the lower-rim of calixarenes,[8] we found that reaction of tetralithiated 4-*tert*-butylcalix[4]arene with an organoboron dichloride proceeded in good yield to give **3** as an analytically pure, colourless solid.† Recrystallisation of **3** from acetonitrile yielded crystals suitable for X-ray diffraction.‡

The structure of **3** (Fig. 1) confirms its identity as an acetonitrile solvate of the expected bis(bora)calixarene. Although a wide range of lower-rim main-group functionalised calixarenes has been described,[9,10] to our knowledge, **3** is the first example of a lower-rim *boron* derivatised calixarene to have been structurally characterized.

In the solid state, the calixarene retains a cone conformation,[11] the two boron atoms are approximately trigonal planar and the two phenyl groups adopt a parallel and eclipsed conformation.

As a potential selective anion receptor, **3** has some interesting structural features. First, the two adjacent Lewis acidic boron centres in **3** are held a distance of 3.429 Å apart by the calixarene scaffold, thereby defining an excellent bidentate Lewis acid cavity for one fluoride anion. Second, for steric reasons, approach of an anion is expected to be highly favoured in an *endo* fashion (*i.e.*, *between* the two Lewis acid centres) precluding complications in detection due to alternative *exo*-binding of fluoride which will be significantly weaker (Scheme 1). Third, since it is well established that binding of anions and neutral Lewis bases to boron centres can result in quenching of fluorescence of directly attached fluorophores[6] the B–Ph groups provide a simple means of monitoring anion binding to **3**.

In **3**, the phenyl groups attached to boron provide sufficient fluorescence intensity to allow binding events to be followed by fluorescence spectroscopy (λ_{ex} = 320 nm, λ_{em} = 395 nm).

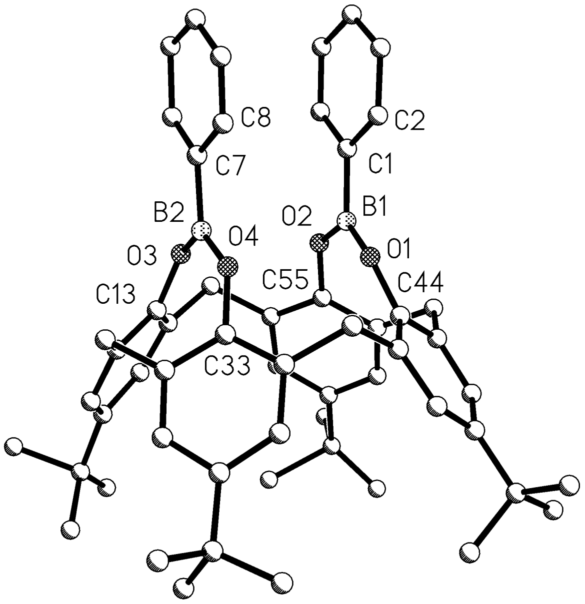

Fig. 1 Molecular structure of $3 \cdot 1.5CH_3CN$. Hydrogen atoms and acetonitrile omitted for clarity. Selected bond distances (Å) and angles (°): B1–O1, 1.382(9); B1–O2, 1.372(8); B2–O3, 1.390(10); B2–O4, 1.360(10); B1–C1, 1.536(10); B2–C7, 1.542(11); O1–B1–O2, 127.0(6); O1–B1–C1, 118.0(6); O2–B1–C1, 114.9(6); O3–B2–O4, 126.9(7); O3–B2–C7, 116.3(8); O4–B2–C7, 116.9(8).

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† Electronic supplementary information (ESI) available: synthetic and spectroscopic details for the preparation of **3**; details of the fluorescence titration of **3** with F^- including details on the procedure used for calculation of binding constants; and details of the crystal structure refinement. See http://www.rsc.org/suppdata/cc/b4/b404937c/

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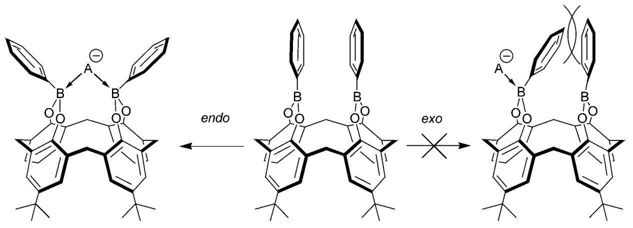

Scheme 1

Titration of a chloroform solution of **3** with Bu_4NF results in a decrease of the fluorescence of the boron-bound phenyl group of **3** (Fig. 2). Similar titrations with Bu_4NCl and Bu_4NBr have no significant effect on the fluorescence spectrum of **3**, thereby demonstrating its expected selectivity for fluoride. The high binding constant obtained for a 1 : 1 complex ($\log K_1 = 6.3 \pm 0.4$)† supports the expectation that a bidentate '*endo*', binding mode is favoured,[12] and suggests the potential for more highly fluorescent (bora)calixarenes to detect very low concentrations of fluoride. A nonlinear fluorescence response is observed that indicates that a further association between the 1 : 1 complex and the ligand may occur at the relatively high concentrations necessary for measurement of the phenylboron derivative. In the case of **3**, such a scenario is geometrically feasible *via* orthogonal approach of a second bis(bora)calixarene to the 1 : 1 complex. However, this additional binding should become insignificant for more highly fluorescent species.

In conclusion, we have described the first synthesis and structural characterization of a lower-rim boron-substituted calixarene and have shown it to be a selective and sensitive fluorescent fluoride sensor. These results provide impetus for further development of (bora)calix[*n*]arenes as anion sensors. Further investigation will include: improvements in sensitivity by incorporation of other boron-bound fluorophores; tuning of anion selectivity (and potentially simultaneous cation selectivity) by boronation of a range of calix[*n*]arenes; and immobilization of (bora)calix[*n*]arenes *via* the proven methods of upper-rim calixarene derivatisation.

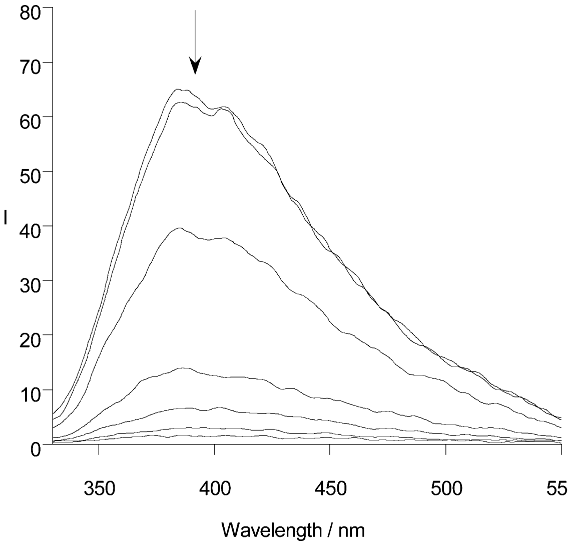

Fig. 2 Change in fluorescence spectrum of **3** (0.010 mol dm^{-3} in chloroform) with addition of $Bu_4N^+F^-$ (0, 0.001, 0.002, 0.005, 0.007, 0.008, 0.009 and 0.010 mol dm^{-3} for highest to lowest absorptions, respectively).

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Notes and references

‡ Crystal data for **3**·1.5CH$_3$CN, $C_{56}H_{62}B_2O_4\cdot(CH_3CN)_{1.5}$: $M_r = 882.26$, monoclinic, space group $P2_1/n$, $a = 11.0360(5)$, $b = 21.5750(10)$, $c = 22.0480(13)$ Å, $\beta = 100.5070(16)°$, $T = 150$ K, $U = 5161.6(5)$ Å^3, $Z = 4$, $d_{calc} = 1.135$ Mg m^{-3}, μ(Mo–Kα) = 0.069 mm^{-1}, 24829 reflections with $2\theta \leq 46°$ measured, 7101 unique ($R_{int} = 0.1449$) and 3310 observed [$I > 2\sigma(I)$]. Final residuals for 594 parameters: $R_1 = 0.1028$, $wR_2 = 0.2723$ (observed reflections) and $R_1 = 0.2036$, $wR_2 = 0.3238$ (all data). CCDC 231529. See http://www.rsc.org/suppdata/cc/b4/b404937c/ for crystallographic data in .cif format.

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11 Observation of four methylene resonances in the ^{1}H NMR spectrum suggests that this conformation is also retained in solution.† This is expected since chelation of the calixarene lower-rim to two boron atoms will impart a high degree of rigidity on the system.

12 Values reported for the binding constant of fluoride to monodentate boron centres (log*K*) include 0.6,[6b] 1.0,[7a] and 5.4.[7b] Although meaningful comparisons are difficult, our results suggest that the sterically inhibited monodentate '*exo*' binding mode is an unlikely candidate for the 1 : 1 complex.