Diols and anions can control the formation of an exciplex between a pyridinium boronic acid with an aryl group connected *via* a propylene linker†

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The exciplex formation between a pyridinium boronic acid and phenyl group connected *via* a propylene linker can be monitored using fluorescence. Addition of pinacol affords a cyclic boronate ester with enhanced Lewis acidity that increases the strength of its cation–π stacking interaction causing a four-fold fluorescence enhancement.

Cation–π interactions have been widely exploited in supramolecular chemistry, where they play pivotal roles in the design of host–guest assemblies[1] and synthetic receptors.[2] These type of interactions have also proven useful for synthesis,[3] where their presence has been invoked to explain the selectivity of nucleophilic catalysts,[4] cyclopropanations,[5] cycloadditions,[6] and various nucleophilic additions.[7] In the biological arena cation–π interactions have been implicated in many biomolecular recognition events,[8] whilst they also play an important role in stabilising the secondary and tertiary structures of proteins.[9]

We have recently reported on the stacking behaviour of pyridinium cations[10] **2** (Fig. 1) that contain a phenyl group connected to a pyridine fragment *via* a propylene linker (Avasthi and co-workers have described this type of spacer as a Leonard linker).[11,12] The enhanced cation–π stacking interactions (Fig. 2) in these pyridinium species **2**, relative to the parent pyridine **1**, enabled us to develop a fluorescence sensor for common alkylating agents such as methyl iodide.[13] Herein we report that this methodology has been exploited for the development of a novel pyridine–boronic acid **4** that can function as a cation–π stacking fluorescence sensor for diols.

We initially targeted preparation of a new type of pyridinium salt **3a** whose nitrogen atom is attached to a phenyl group *via* a propylene linker. This was easily achieved *via* treatment of pyridine with 1-bromo-3-phenylpropane at reflux for 24 hours to give 1-(3-phenylpropyl)pyridinium bromide **3a** in quantitative yield.[14] Fluorescent analysis of this pyridinium salt **3a** revealed a characteristic exciplex consistent with the presence of a strong cation–π stacking interaction. This results in strong fluorescence occurring in non-polar solvents, with a reduced fluorescence in polar solvents (Fig. 3). It was found that the strength of the exciplex emission of this type of pyridinium species was highly dependent on the nature of its associated counter anion. Therefore, addition of excess tetrabutylammonium fluoride and tetrabutyl ammonium chloride to pyridinium bromide **3a** in CH_2Cl_2 resulted in quenching of the fluorescence.[15] While addition of tetrabutylammonium hexafluorophosphate to pyridinium bromide **3a** gave pyridinium hexafluorophosphate **3d** which exhibited a 2.6 fold enhancement in fluorescence (Fig. 4).[15]

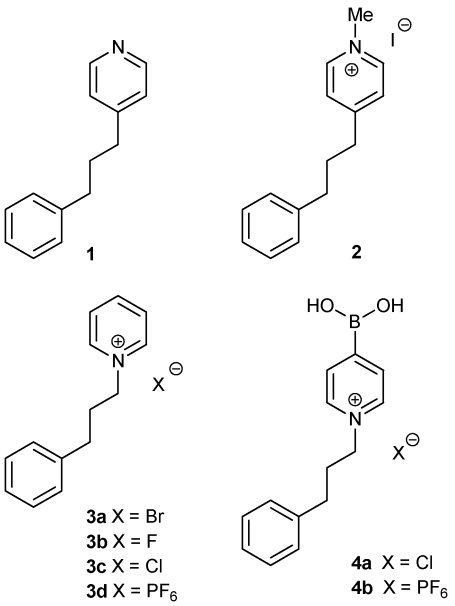

Fig. 1 Pyridine **1** and *N*-alkyl-pyridinium salts **2–4**.

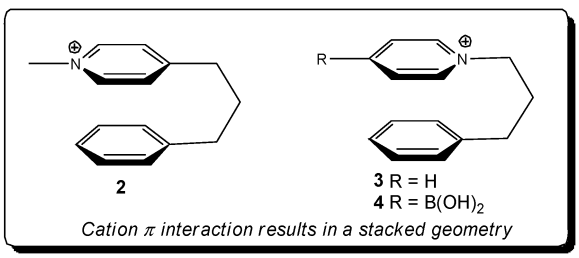

Fig. 2 The relative concentration of stacked cation–π interactions of *N*-alkyl-pyridinium species **2**/**3** can be measured using the fluorescence of their resultant exciplexes.

Boronic acids are capable of reversible formation of strong covalent bonds with the hydroxyl groups of diols to form cyclic boronate esters.[16] Formation of this type of cyclic

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† Electronic supplementary information (ESI) available: Synthetic procedures for the preparation of pyridinium salts **3a**, **4a** and **4b**, and fluorescence analysis data are provided. See DOI: 10.1039/c0cc03099f

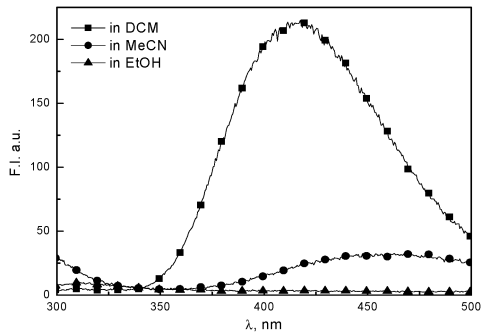

Fig. 3 Fluorescence spectra of **3a** (1.0×10^{-4} mol L^{-1}) in different solvents, 25 °C. λ_{ex} 260 nm.

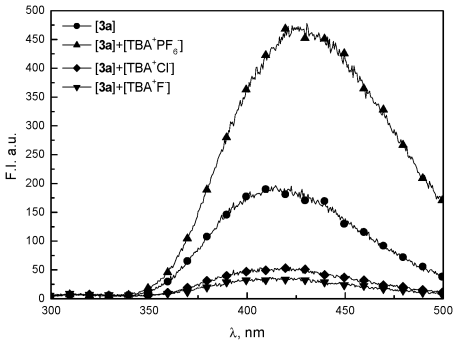

Fig. 4 Fluorescence spectra of **3a** (1.0×10^{-4} mol L^{-1}) in the presence of added anions Cl^-, F^- and PF_6^- (1.0×10^{-4} mol L^{-1}), 25 °C. λ_{ex} 260 nm.

boronate ester leads to an increase in the Lewis acidity of the boron atom, with this change in acidity having been exploited many times for sensing molecules that contain diol functionality. Consequently, we were interested in exploring the fluorescent response of pyridinium boronic acid **4a** towards the presence of diols. Pyridinium boronic acids like **4** have pK_a values between 3.6–4.4,[17] which contrasts favourably with the pK_a value of 8.70 for phenylboronic acid.[18] This lower pK_a value of pyridinium boronic acid **4** is attributed to the formation of a neutral zwitterionic pyridinium hydroxyboronate species, with diol binding resulting in the formation of anionic tetrahedral boronate species, that are potentially very useful for the design of receptors that bind diols at neutral pH.

Pyridinium boronic acid chloride **4a** was prepared by treatment of 4-(5,5-dimethyl-1,3,2-dioxanborinanyl)pyridine with 1-bromo-3-phenylpropane at reflux for 48 hours in acetonitile, followed by purification using ion exchange chromatography that results in removal of the diol protecting group and counterion exchange to afford **4a** in 60% yield. Subsequent addition of potassium hexafluorophosphate to a methanol solution of chloride **4a** gave hexafluorophosphate **4b** in 95% yield as a white solid.[19]

Addition of tetrabutylammonium fluoride, chloride and bromide salts to the hexafluorophosphate **4b** in CH_2Cl_2 resulted in quenching of the fluorescence,[20] in line with the fluorescence response previously observed for bromide **3a** in CH_2Cl_2. Addition of pinacol to **4a** in CH_2Cl_2 caused a 4-fold fluorescence enhancement (Fig. 5), whilst addition of ethanol resulted in essentially no change in fluorescence.[21] In contrast,

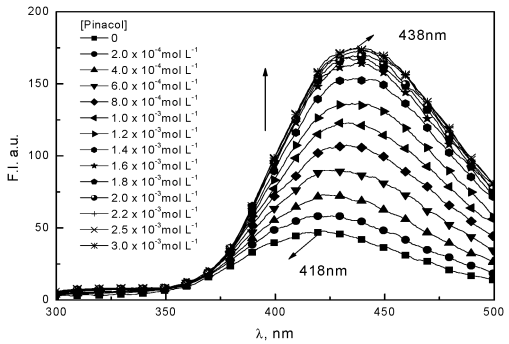

Fig. 5 Titration of pyridinium boronic acid chloride **4a** (1.0×10^{-4} mol L^{-1}) in CH_2Cl_2 with pinacol at 25 °C. λ_{ex} 260 nm.

addition of pinacol did not affect the fluorescence intensity of pyridinium bromide **3a**, or pyridinium boronic acid hexafluorophosphate **4b**.[22]

Formation of cyclic boronate esters from a boronic acid and diol is known to enhance the Lewis acidity of the boron centre.[16,23] Therefore, it is proposed that addition of pinacol to **4a** affords boronate ester **5** that exhibits enhanced cation–π interactions between its pyridinium fragment and its aryl group.[24] This enhanced cation–π interaction increases the fluorescence response of this system because more of the fluorescent exciplex is formed. The fluorescence response of bromide salt **3a** is not affected by the addition of pinacol, because this system does not contain a boronic acid fragment to act as a recognition site for pinacol. Addition of ethanol does not affect the fluorescence response of chloride salt **4a** because only cyclic boronate ester results in enhanced Lewis acidity. In the case of hexafluorophosphate salt **4b**, addition of pinacol does not cause a fluorescence enhancement indicating that the counter anion plays an important role in the diol controlled exciplex formation (Scheme 1).

In conclusion, we have shown that it is possible to modulate cation–π stacking interactions using external inputs, and that those changes can be monitored using the fluorescence of the exciplex formed between the pyridinium boronic acid and the phenyl group connected through a propylene spacer. We are currently exploring the use of this signalling motif in more demanding polar solvent systems where we believe we will be able to exploit these type of cation–π stacking interactions for the development of fluorescence sensors for saccharides.

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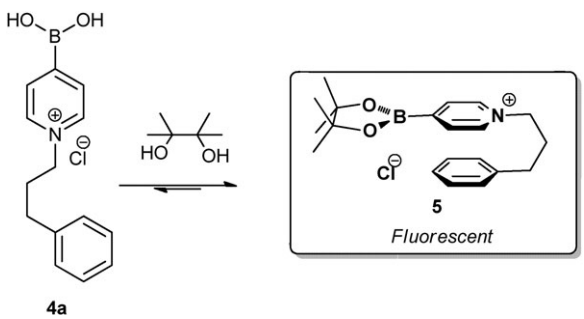

Scheme 1 Cation–π stacking geometry is favoured when pinacol is added to **4a** to afford boronate ester **5**.

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24 Boronate ester formation was verified by ^{1}H NMR spectroscopic analysis.

