Easily-prepared hydroxy-containing receptors recognise anions in aqueous media

Mahbod Morshed, Stephanie A. Boer, Michael Thomas and Nicholas G. White*

Despite their readily availability, O–H groups have received relatively little attention as anion recognition motifs. Here, we report two simple hydroxy-containing anion receptors that are prepared in two facile steps followed by anion exchange, without the need for chromatographic purification at any stage. These receptors contain a pyridinium bis(amide) motif as well as hydroxyphenyl groups, and bind mono- and divalent anions in 9:1 CD3CN:D2O, showing a selectivity preference for sulfate. Notably, a “model” receptor that does not contain hydroxy groups shows only very weak sulfate binding in this competitive solvent mixture.

Introduction

While O–H···anion hydrogen bonds are known to be important in biological anion recognition processes,1 they have received little use in synthetic anion receptors. This is surprising given they can be potent hydrogen bond donors and are often easy to synthesise (in contrast to many other anion receptors, which frequently require tedious syntheses). Notable O–H containing anion receptors include Wang and Kass’ flexible aliphatic polyols,2 while unsubstituted catechol can bind halide anions in acetonitrile3 and commercially-available hydroxy-containing dyes can sense a range of anions in CH2Cl2.4 While the vast majority of systems use only hydroxy groups to bind anions,2–5 a few examples of “mixed” receptors containing both O–H and N–H donors are known.6 Compounds that function through O–H···anion interactions have also received limited use as anion transporters7 and in anion-templated assembly,8 although in these cases too they are relatively underutilised.

To investigate this class of receptors further, in this study we have incorporated hydroxy groups into positively-charged anion host systems.9 We demonstrate that simple, readily-prepared compounds can complex a range of anions in acetonitrile containing 10% water. This contrasts with hydroxy-containing anion receptors prepared to date, which have typically functioned in organic solvents or organic solvents containing a maximum of 1% water.6d,6f,10

Initially we synthesised systems where the positive charge was on the same aromatic moiety as the hydroxy group, i.e. 3-hydroxypyridinium and 8-hydroxyquinolinium derivatives,11 but found in these cases that the hydroxy group was too acidic, and prone to deprotonation upon addition of moderately basic anions.12 Instead, we used the pyridinium-3,5-bis(amide) scaffold developed by Beer,13 and prepared the new receptors 1+ and 2+ shown in Fig. 1, which contain phenolic motifs with the hydroxy groups either ortho or meta to the amide nitrogen atom. We also prepared receptor 3+ as a “model” system that does not contain any hydroxy groups.

![Fig. 1 Structures of receptors used in this work.](image-url)
Results and discussion

Receptor synthesis

Receptors 1·I and 2·I containing hydroxy groups respectively ortho and meta to the amide nitrogen atom were prepared as the iodide salts in two steps using amide coupling reactions to give 4–6, followed by alkylation with ethyl iodide (Scheme 1). Subsequent anion exchange using silver(I) tetrafluoroborate gave 1·BF₄ and 2·BF₄, suitable for anion recognition experiments. A “model” system, 3·BF₄, containing phenyl groups instead of phenol groups was prepared in an analogous manner.

Notably, all of these receptors can be readily prepared in good overall yield and do not require chromatographic purification at any stage. We had initially attempted to prepare the tetraphenylborate salts of 1·I and 2·I, these salts appeared to be unstable and decomposed during purification. Small amounts of 1·BPh₄ and 2·BPh₄ could be isolated and used for anion recognition studies and gave similar results to those obtained with 1·BF₄ and 2·BF₄ (see ESI).

Scheme 1 Synthesis of amides 4–6 and subsequent conversion to 1·BF₄, 2·BF₄ and 3·BF₄.

Anion recognition studies

Anion recognition was studied using ¹H NMR titration experiments: initially, anions as their tetrabutylammonium (TBA) salts were added to solutions of 1·BF₄ and 2·BF₄ in 95:5 CD₃CN:CD₂O. This resulted in downfield shifts of the interior pyridinium C–H proton resonances, and smaller shifts in some of the phenyl ring resonances (the O–H and N–H signals are not visible in these solvent mixtures due to H/D exchange). An example, the addition of chloride anion to 2·BF₄ in 95:5 CD₃CN:CD₂O is shown in Fig. 2.

The movements of the interior pyridinium resonances were fitted to 1:1 binding isotherms using the Bindfit programme (weblinks to full binding data and fits are provided in the ESI). As shown in Table 1, both hydroxy-containing receptors bind chloride in 95:5 CD₃CN:CD₂O, with the meta-phenol receptor 2⁺ binding more strongly than the simple phenyl-substituted receptor 3⁺, while the ortho-phenol system 1⁺ binds more weakly.

Table 1 Association constants (M⁻¹) for addition of anions to receptors 1·BF₄, 2·BF₄ and 3·BF₄ in 95:5 CD₃CN:CD₂O.

<table>
<thead>
<tr>
<th>Anion</th>
<th>1·BF₄</th>
<th>2·BF₄</th>
<th>3·BF₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl⁻</td>
<td>2.4(1) × 10⁻²</td>
<td>1.4(1) × 10⁻³</td>
<td>8.4(1) × 10⁻²</td>
</tr>
<tr>
<td>I⁻</td>
<td>1.6(1) × 10⁻²</td>
<td>1.6(1) × 10⁻²</td>
<td>1.6(1) × 10⁻²</td>
</tr>
</tbody>
</table>

Anions added as TBA salts, binding constants determined using Bindfit, the asymptotic error is provided at the 95% confidence interval in parentheses; peak movements too small to infer binding.

Both 2·BF₄ and 3·BF₄ bind iodide weakly in this solvent mixture, while peak shifts with 1·BF₄ were too small to calculate a binding constant. Addition of acetate or sulfate to either of the hydroxy-containing receptors in 95:5 CD₃CN:CD₂O resulted in precipitation (see ESI for binding of these anions to 3·BF₄). Therefore, we conducted further anion recognition experiments in more competitive 90:10 CD₃CN:CD₂O (Table 2).

In this solvent, both ortho and meta-phenol receptors bind fluoride and sulfate more strongly than phenyl-substituted 3⁺, while the ortho-substituted receptor also binds acetate more strongly than 3⁺. The increased binding of the
hydroxy-containing receptors is particularly noticeable for \( \text{SO}_2^- \), which is bound quite strongly by \( 1^+ \) and \( 2^+ \) but only weakly by \( 3^+ \) (Fig. 3).

### Table 2

<table>
<thead>
<tr>
<th>Anion</th>
<th>1·BF&lt;sub&gt;4&lt;/sub&gt;</th>
<th>2·BF&lt;sub&gt;4&lt;/sub&gt;</th>
<th>3·BF&lt;sub&gt;4&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{F}^- )</td>
<td>76(3)</td>
<td>2.0(1) \times 10^2</td>
<td>41(1)</td>
</tr>
<tr>
<td>( \text{Cl}^- )</td>
<td>61(1)</td>
<td>1.7(1) \times 10^2</td>
<td>1.3(1) \times 10^2</td>
</tr>
<tr>
<td>( \text{OAc}^- )</td>
<td>3.0(1) \times 10^2</td>
<td>ppt</td>
<td>72(1)</td>
</tr>
<tr>
<td>( \text{SO}_2^- )</td>
<td>8.3(5) \times 10^2</td>
<td>1.5(1) \times 10^3</td>
<td>1.4(1) \times 10^2</td>
</tr>
</tbody>
</table>

*aAnions added as TBA salts, TBA-F used as hydrate, binding constants determined using Bindfit<sup>4</sup> the asymptotic error<sup>5</sup> is provided at the 95% confidence interval in parentheses.; bprecipitation observed after 2.0 equivalents.

Interestingly, while \( 3^+ \) tends to bind more strongly than \( 1^+ \) in 95:5 CD<sub>3</sub>CN:CD<sub>3</sub>OD, this trend is reversed in 90:10 CD<sub>3</sub>CN:CD<sub>3</sub>OD with the hydroxy-substituted receptor generally binding more strongly, suggesting a greater tolerance to increasing water content. In both solvent systems, \( 2^+ \) binds more strongly than either \( 1^+ \) or \( 3^+ \), and possible reasons for this are discussed later.

**Fig. 3** Movement of interior pyridinium C–H resonance of 1·BF<sub>4</sub>, 2·BF<sub>4</sub> and 3·BF<sub>4</sub> upon addition of TBA<sub>2</sub>SO<sub>4</sub> in 90:10 CD<sub>3</sub>CN:CD<sub>3</sub>OD. Points represent observed data, lines represent 1:1 binding isotherms fitted using Bindfit.<sup>4</sup>

### Solid state structures

We were able to obtain single crystals of several salts of \( 1^+ \), \( 2^+ \) and \( 3^+ \) and analysed these by single crystal X-ray crystallography: the structures of 1·F, 1·BF<sub>4</sub>, 1·I, 1·TBA·SO<sub>4</sub><sup>5</sup> and 2·I are shown in Fig. 4, while structures of 3·BF<sub>4</sub>, 3·Cl and 3·I are provided in the ESI (Figs. S20–S22). Interestingly, the amide groups in the solid state structures of all four salts of \( 1^+ \) adopt a syn-anti conformation, with one amide N–H pointing inwards (syn), while the other points out towards the pyridinium nitrogen atom (anti).

While this syn-anti conformation is expected for these type of isophthalamide-like systems in the absence of a coordinating guest,<sup>16</sup> a syn-syn conformation is commonly observed upon anion binding.<sup>17</sup> However, in the solid state structures of \( 1^+ \), extended assemblies (dimers or polymers) are observed where the anion acts as a bridge between neighbouring receptors. A similar phenomenon is observed in the structure of 2·I, but not in the structures of 3·Cl and 3·I. Generally, it would appear that the additional O–H hydrogen bond donors present in \( 1^+ \) and \( 2^+ \) favour the formation of extended structures in the solid state.

O–H···anion and N–H···anion hydrogen bond lengths are shortest (both in absolute terms and as a % of the sum of the vdW radii<sup>18</sup>) for the fluoride complex, followed by sulfate with iodide having the longest hydrogen bonds (61–63, 67–70 and 81–88% of the sum of the vdW radii for \( \text{F}^- \), \( \text{SO}_2^- \) and \( \text{I}^- \), respectively). Interestingly, in complexes where both O–H···anion and N–H···anion interactions are present, the H···anion distances are always slightly shorter for the O–H···anion hydrogen bonds than for the N–H···anion hydrogen bonds (see Table S2 for a detailed analysis of hydrogen bonding interactions).

While the solid state structures show extended assemblies in the solid state, it is clear that these structures are not representative of the compounds in solution. Indeed, \(^1\)H NMR data including DOSY NMR data (Figs. S58–S61) show no evidence of aggregation or oligomeric assemblies. This suggests that the extended structures arefavoured by crystallisation. Given the low concentrations used for anion binding studies (2.0 mM) and the limited binding strengths, it is perhaps not surprising that extended structures do not form in solution.

The NMR data also suggest that anion binding predominantly occurs within the hosts’ cleft rather than outside as is sometimes observed in the solid state. For example, the interior pyridinium C–H resonance (b, see Fig. 2 for assignments) shows substantial shifts on addition of anions, while the exterior pyridinium resonance (a) shows much less movement. Both the formation of discrete 1:1 complexes and binding of anions within the hosts’ clefts is also supported by MD simulations.

### Molecular dynamics simulations

It is noticeable that in the structures of 1·BF<sub>4</sub> and 1·I (Fig. 4b) there is a short intramolecular O–H···O hydrogen bond (H···O = 1.76, 1.77 Å). If this interaction were significant in solution, it would reduce the possibility of the hydroxy groups hydrogen bonding to an anion guest, and may explain the weaker binding observed for \( 1^+ \) compared to \( 2^+ \).

To investigate this further, and to obtain more information about the mode of anion binding in solution, molecular dynamics (MD) simulations were conducted in virtual 95:5 CH<sub>3</sub>CN:H<sub>2</sub>O investigating 1·Cl, 2·Cl, 1·TBA·SO<sub>4</sub> and 2·TBA·SO<sub>4</sub>. Simulations were conducted using GROMACS 2016.1<sup>19</sup> in conjunction with the GROMOS 54a7 force field.<sup>20</sup> Water was represented explicitly as a single point charge model<sup>21</sup> and parameters for 1<sup>+, 2+</sup>, TBA<sup>+</sup> and acetonitrile were calculated using the Automated Topology Builder<sup>22</sup> (see the ESI for full details of simulations).
During the course of the simulations of 1·Cl and 1·TBA·SO₄, several different conformations are observed, two of which are particularly notable. Frequently, the O–H groups form intramolecular hydrogen bonds to the carbonyl oxygen atoms (Figs. 5a and S62), while a tetradentate mode of binding is also observed in which both amide and both hydroxy groups hydrogen bond to the anion (Figs. 5b and S63). As shown in Fig. S64, the intramolecular hydrogen bond occurs frequently meaning that the O–H donors are often not free to bind to the anion. No such intramolecular H-bond is possible in 2⁺ presumably explaining the higher anion binding affinities observed with this receptor.

Interestingly, the simulations of 2·Cl and 2·TBA·SO₄ show that the O–H groups rarely hydrogen bond directly to the anions. Instead, they bind to water molecules within the anions’ coordination sphere. While these water molecules are relatively dynamic, a common arrangement has two water molecules and the anion sandwiched between the two hydroxy groups as shown in Figs. 5c and 5d. Gibb has recently reported MD simulations that show that anions can be bound in a partially hydrated state within the hydrophobic cavity of a cavitand receptor, and it is interesting that we see a similar phenomenon in a system without an obviously hydrophobic binding site.

Generally, while 1⁺ and 2⁺ show relatively strong binding in competitive aqueous media, the MD studies suggest that their structures are far from ideal for anion binding, whether this is due to competition from intramolecular H-bonding or non-ideal H-bond donor arrangements. This suggests that future, optimised receptors containing O–H donors may be capable of significantly stronger anion recognition.

Conclusions
This work reports a new family of hydroxy-containing anion receptors that can be prepared readily from inexpensive precursors without the need for chromatographic purification. These receptors are able to bind anions in aqueous acetonitrile, showing a selectivity preference for sulfate in 90:10 CD₃CN:CD₂O. Importantly, receptor 3⁺ which does not contain hydroxy groups shows very little sulfate binding in this solvent. More generally, the hydroxy-containing systems seem to tolerate increasing amounts of water more readily than 3⁺. This suggests that future optimised receptors may be able to bind anions in media containing significantly more water, and work towards this goal is continuing in our laboratory.
Experimental

General remarks

All reagents and solvents were bought from commercial suppliers and used as received. Details of instrumentation and characterization are provided in the Supporting Information.

General procedure for the synthesis of bis(amides) 4–6

Pyridine-3,5-dicarboxylic acid (0.836 g, 5.00 mmol), EDCI·HCl (2.11 g, 11.0 mmol) and the appropriate aniline derivative (10.0 mmol) were dissolved in DMF (25 mL) and trimethylamine (1.53 mL, 1.11 g, 11.0 mmol) was added. The resulting brown solution was stirred at room temperature under a nitrogen atmosphere for 4 days. This was then added to a solution of NH₄Cl (1.1 g, 20 mmol) in water (100 mL), stirred briefly and left to stand for an hour. The resulting precipitate was isolated by filtration, washed with water (5 × 10 mL) and dried thoroughly in vacuo to give 4–6 as pale powders.

4: Isolated as a pale brown powder, yield: 0.966 g (2.77 mmol, 55%).

1H NMR (d₆-DMSO): 9.94 (br. s, 2H), 9.73 (br. s, 2H), 9.25 (s, 2H), 8.81 (s, 1H), 7.62 (d, J = 7.6 Hz, 2H), 7.08 (t, J = 7.7 Hz, 2H), 6.84 (d, J = 7.7 Hz, 2H), 6.85 (t, J = 7.6 Hz, 2H) ppm. 13C NMR (d₆-DMSO): 163.5, 151.0, 150.1, 1347, 129.8, 126.3, 125.3, 125.1, 119.0, 116.0 ppm. IR (inter alia): 1671, 1651 cm⁻¹ (C=O stretch). HR-ESI-MS (neg.): 348.0985, calc. for [M⁻H]⁻, C₁₉H₁₄N₃O₄: 348.0984 Da. mp > 250 °C.

5: Isolated as a white powder, yield: 1.02 g (3.22 mmol, 64%).

1H NMR (d₆-DMSO): 10.45 (s, 2H), 9.48 (s, 2H), 9.22 (s, 2H), 8.76 (s, 1H), 7.36 (s, 2H), 7.07–7.22 (m, 4H), 6.54 (d, J = 7.6 Hz, 2H) ppm. 13C NMR (d₆-DMSO): 163.4, 157.6, 151.0, 139.8, 134.6, 130.3, 129.4, 111.2, 111.1, 107.4 ppm. IR (inter alia): 1655 cm⁻¹ (C=O stretch). HR-ESI-MS (neg.): 348.0978, calc. for [M⁻H]⁻, C₁₉H₁₄N₃O₄: 348.0984 Da. mp > 250 °C.

6: Isolated as a pale yellow powder, yield: 0.860 g (2.71 mmol, 54%).

1H NMR (d₆-DMSO): 10.60 (br. s, 2H), 9.27 (d, J = 2.1 Hz, 2H), 8.83 (t, J = 8.1 Hz, 1H), 7.80 (t, J = 7.7 Hz, 4H), 7.40 (t, J = 7.7 Hz, 4H), 7.15 (t, J = 7.7 Hz, 2H) ppm. 13C NMR (d₆-DMSO): 163.4, 151.0, 138.7, 134.7, 130.3, 128.7, 124.1, 120.4 ppm. IR (inter alia): 1664, 1643 cm⁻¹ (C=O stretch). HR-ESI-MS (pos.): 318.1236, calc. for [6+H]⁺, C₁₉H₁₆N₂O₂, i.e. [6·H]⁺ = 318.1237 Da. mp > 250 °C.

1·I

A heavy-walled vial was charged with 4 (0.489 g, 1.40 mmol), THF (7 mL), ethanol (7 mL) and then iodoethane.
were removed days, the reaction was cooled to room temperature, and then further in a freezer. The reaction was filtered to give a pale yellow powder, which was washed with further ethanol (2 × 0.5 mL) and dried in vacuo. After 1 day, all material had dissolved to give a milky white suspension. After 7 days during which time the milky white suspension turned yellow, a heavy-walled vial was charged with 5 (0.087 g, 0.25 mmol) THF (2.25 mL) and ethanol (0.25 mL). The suspension was sonicated for 10 minutes and then ethyl iodide (0.20 mL, 0.39 g, 2.5 mmol) was added. The vial was sealed and heated to 90 °C (oil bath temperature) for 7 days during which time the milky white suspension turned yellow. After this time, the reaction was filtered and the pale yellow powder isolated by filtration and washed with ethanol (3 × 1 mL). After drying in vacuo, this gave 2·I (0.025 g, 0.049 mmol, 20%). The combined filtrates were taken to dryness under reduced pressure. Ethanol (3 mL) was added and the brown suspension boiled briefly. After cooling to room temperature this was filtered to give a pale yellow powder, which was washed with ethanol (2 × 0.5 mL) and dried in vacuo to give further 2·I (0.046 g, 0.091 mmol, 36%). Combined yield: 0.071 g (0.14 mmol, 56%).

H NMR (d6-DMSO): 10.78 (s, 2H), 9.72 (s, 2H), 9.61 (s, 2H), 9.48 (s, 1H), 7.33 (s, 2H), 7.16–7.24 (m, 4H), 6.61 (d, J = 7.9 Hz, 2H), 4.80 (q, J = 7.2 Hz, 2H), 1.66 (t, J = 7.2 Hz, 3H) ppm. 13C NMR (d6-DMSO): 159.9, 157.7, 146.4, 142.0, 139.0, 134.2, 129.7, 112.0, 111.0, 107.5, 57.4, 16.2 ppm. IR (inter alia): 1680, 1601 cm–1 (C=O stretch). HRESI-MS (pos.): 378.1457, calc. for [M]+, C21H20N3O4: 378.1454 Da. mp > 250 °C.

A heavy-walled vial was charged with 6 (0.317 g, 1.00 mmol), ethanol (10 mL) and THF (10 mL). Ethyl iodide (5 mL) was added, and the vial was sealed, and heated to 90 °C (oil bath temperature) for 6 days. During this time, all solids dissolved and a brown solution was formed. After 6 days, the reaction was cooled to room temperature, resulting in the precipitation of a yellow solid. All volatiles were removed in vacuo, and ethanol (40 mL) was added to the brown gunky solid, resulting in the brown material dissolving leaving a yellow microcrystalline solid. The suspension was heated to boiling for 5 minutes, then cooled to room temperature, and the solid isolated by filtration, washed with ethanol (3 × 5 mL) and dried in vacuo to give 3·I as a very pale yellow microcrystalline solid. Yield: 0.381 g (0.805 mmol, 80%).

H NMR (d6-DMSO): 10.92 (br. s, 2H), 9.76 (d, J = 1.6 Hz, 2H), 9.53 (t, J = 1.6 Hz, 1H), 7.78 (d, J = 7.9 Hz, 4H), 7.46 (dd, J = 7.9, 7.9 Hz, 4H), 7.22 (t, J = 7.9 Hz, 2H), 4.82 (q, J = 7.3 Hz, 2H), 1.67 (t, J = 7.3 Hz, 3H) ppm. 13C NMR (d6-DMSO): 160.0, 146.5, 142.0, 137.9, 134.1, 129.0, 124.9, 120.4, 57.5, 16.2 ppm. IR (inter alia): 1687, 1666 cm–1 (C=O stretch). HRESI-MS (pos.): 346.1548, calc. for C21H20N4O2, i.e. 3+ = 346.1550 Da. mp: 228–230 °C.

A solution of silver(I) tetrafluoroborate (0.039 g, 0.20 mmol) in acetonitrile (3 mL) was added to a suspension of the appropriate iodide salt (0.101 g, 0.20 mmol) in acetone (2 mL). This was stirred for 2 hours under a nitrogen atmosphere with the exclusion of light, and then filtered through a short plug of celite. The celite was washed with further acetone (5 mL total) and the combined filtrates added to diethyl ether (50 mL). This was swirled briefly and then left to stand resulting in the formation of a yellow precipitate. This was isolated by filtration, washed with diethyl ether and dried thoroughly in vacuo.

1·BF4: Isolated as golden-yellow crystals, yield: 0.072 g (0.15 mmol, 77%).

H NMR (d6-acetone): 9.85 (d, J = 1.3 Hz, 2H), 9.75 (br. s, 2H), 9.63 (s, 1H), 8.86 (s, 2H), 7.94 (d, J = 7.9 Hz, 2H), 7.11–7.15 (m, 2H), 7.01 (dd, J = 8.1, 1.4 Hz, 2H), 6.92–6.96 (m, 2H), 5.15 (q, J = 7.3 Hz, 2H), 1.89 (t, J = 7.3 Hz, 3H) ppm. 19F NMR (d6-acetone): –151.2 ppm. IR (inter alia): 1670, 1657 cm–1 (C=O stretch). MS (ESI-pos.): 378.1, calc. for C21H20F4N4O8, i.e. 1+ = 378.2; 843.5, calc. for C42H40F4N4O8, i.e. [(1+)2·BF4] = 843.3 Da. mp: 211–212.5 °C.

2·BF4: Isolated as a foamy golden-yellow solid, yield: 0.063 g (0.14 mmol, 68%).

H NMR (d6-acetone): 10.07 (br. s, 2H), 9.76 (d, J = 1.6 Hz, 2H), 9.52 (br. s, 1H), 8.54 (br. s, 2H), 7.45 (s, J = 2H), 7.20–7.26 (m, 4H), 6.69–6.72 (m, 2H), 5.11 (q, J = 7.3 Hz, 2H), 1.87 (t, J = 7.3 Hz, 3H) ppm. 19F NMR (d6-acetone): –150.4 ppm. IR (inter alia): 1682, 1662 cm–1 (C=O stretch). MS (ESI-pos.): 378.1, calc. for C21H20F4N4O8, i.e. 2+ = 378.2; 843.4, calc. for C42H40F4N4O8, i.e. [(2+)2·BF4] = 843.3 Da. mp: decomposition apparent at ~ 222 °C.

3·BF4: Isolated as pale yellow microcrystals, yield: 0.077 g (0.18 mmol, 88%).

H NMR (d6-acetone): 10.19 (s, 2H), 9.80 (d, J = 1.6 Hz, 2H), 9.53 (t, J = 1.6 Hz, 1H), 7.78 (d, J = 7.9 Hz, 4H), 7.46 (dd, J = 7.9, 7.9 Hz, 4H), 7.22 (t, J = 7.9 Hz, 2H), 4.82 (q, J = 7.3 Hz, 2H), 1.67 (t, J = 7.3 Hz, 3H) ppm. 13C NMR (d6-DMSO): 160.0, 146.5, 142.0, 137.9, 134.1, 129.0, 124.9, 120.4, 57.5, 16.2 ppm. IR (inter alia): 1687, 1666 cm–1 (C=O stretch). HRESI-MS (pos.): 346.1548, calc. for C21H20N4O2, i.e. 3+ = 346.1550 Da. mp: 228–230 °C.

General anion exchange procedure to give 1·BF4, 2·BF4, and 3·BF4.
Hz, 2H), 9.58 (t, J = 1.6 Hz, 1H), 7.82–7.86 (m, 4H), 7.40–7.45 (m, 4H), 7.20–7.25 (m, 2H), 5.13 (q, J = 7.3 Hz, 2H), 1.88 (t, J = 7.3 Hz, 3H) ppm. 19F NMR (d£-acetone): −150.4 ppm. IR (inter alia): 1682, 1655 cm−1 (C=O stretch). MS (ESI-pos.): 346.1, calc. for C22H23NO2F2, i.e. 3* = 346.2; 779.5, calc. for C26H34BF6N2O4, i.e. [3*]2−: BF4−] = 779.3. mp: 172.5–174 °C.

Conflicts of interest
There are no conflicts to declare.

Acknowledgements
We thank Michael McGtigue (Australian National University) for contributing to preliminary synthetic work, and the Australian Research Council for supporting this research (Discovery Early Career Research Award, DE170100200).

Notes and references
† A notable exception is Gabbi’s recently-reported borinic acid receptor, which recognises fluoride in 4:1 THF-H2O. This receptor functions through formation of a covalent B–F bond and a non-covalent B–OH−...F− hydrogen bond.10
§ This structure is of low quality and could only be refined with isotropic displacement parameters. See the ESI for further details. It was necessary to use PLATON-SQUEEZE23 during refinement.


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