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

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Abstract: Despite their ready 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 CD_3CN:D_2O, 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. In the solid state, X-ray crystallographic studies show that the receptors tend to form extended assemblies with anions; however ^{1}H and DOSY NMR studies as well as molecular dynamics simulations show that only 1:1 complexes are present in solution. Molecular dynamics simulations suggest that one of the receptors suffers from competing intramolecular hydrogen bonding, while another binds partially-hydrated anions, with the receptor's O–H groups forming hydrogen bonds to water molecules within the anion's coordination sphere.

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).

In the early 2000s, it was shown that unsubstituted catechol can bind halide anions in acetonitrile[2] and that commercially-available hydroxy-containing dyes can sense a range of anions in CH_2Cl_2.[3] More recently Jeong's group[4] has prepared elegant butynol-containing receptors, and Wang and Kass have demonstrated that flexible aliphatic polyols[5] can complex halide anions. While many systems use only hydroxy groups to bind anions,[2-3,5-6] a few examples of "mixed" receptors containing both O–H and N–H donors are known.[4,7] Compounds that use O–H···anion interactions have also received limited use as anion transporters[8] and in anion-templated assembly,[9] although in these cases too they are relatively underutilised.

Nearly all O–H containing anion receptors have been neutral and have functioned in organic solvents, or in rare cases organic solvents containing 1% water.[4a,4c][10] In an effort to move towards systems that can function in water, in this work we prepare the cationic hydroxy-containing[11] anion host systems **1**$^+$ and **2**$^+$ (Figure 1). We demonstrate that these simple, readily-prepared compounds can complex a range of anions in acetonitrile containing 10% water and use NMR spectroscopy, X-ray crystallography and molecular dynamics (MD) simulations to interrogate guest binding.

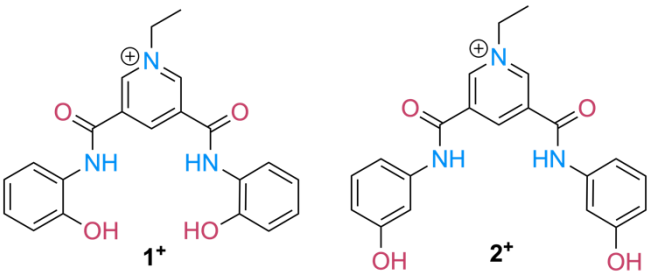

Figure 1. Structures of receptors used in this work.

Results and Discussion

Receptor design and synthesis

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 (Figure 2),[12] but found that the hydroxy groups were too acidic, and prone to deprotonation upon addition of moderately basic anions.[13]

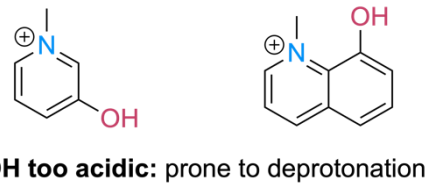

Figure 2. Hydroxypyridinium and hydroxyquinolinum compounds that were initially investigated as anion receptors, but were prone to deprotonation.

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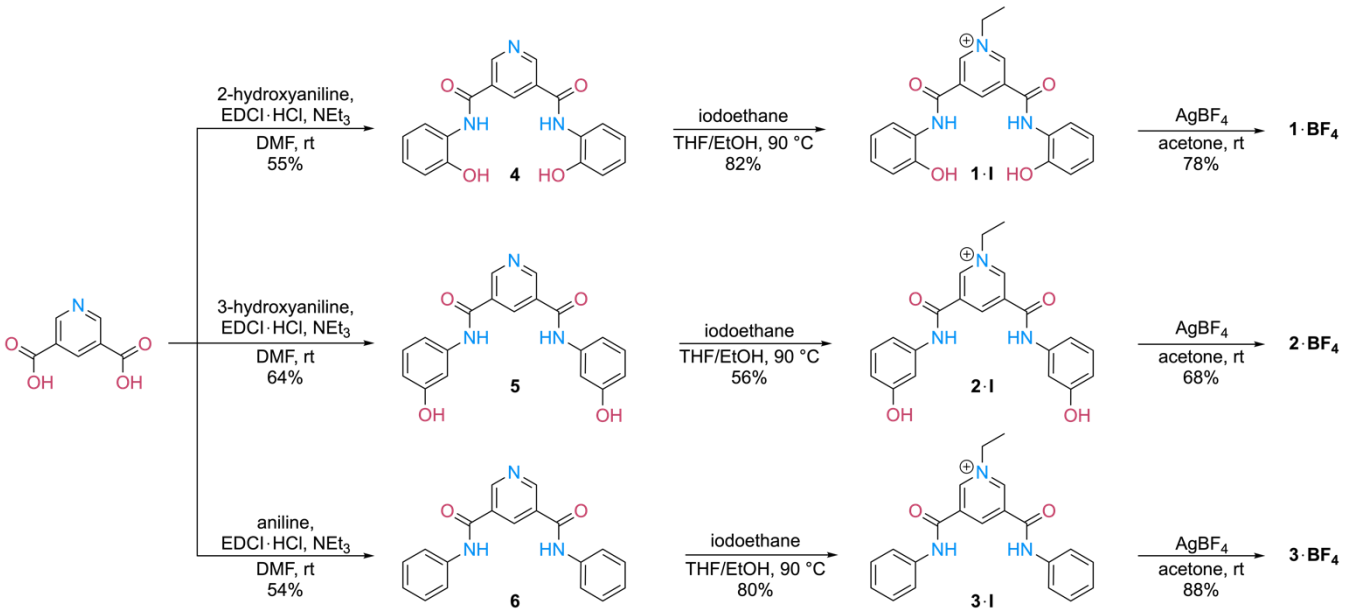

Scheme 1. Synthesis of amides **4–6** and subsequent conversion to **1·BF$_4$**, **2·BF$_4$** and **3·BF$_4$**.

Instead, we used the pyridinium-3,5-bis(amide) scaffold developed by Beer,[14] and prepared the new receptors **1**$^+$ and **2**$^+$ shown in Figure 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.

In order to prepare the cationic receptors **1**$^+$–**3**$^+$, we first prepared the neutral bis(amides) **4**–**6**. We initially attempted to react the appopriate aniline derivative with pyridine-3,5-dicarboxylic acid using dicyclohexylcarbodiimide (DCC) with or without 1-hydroxybenzotriazole (HOBT) to effect amide formation. These reactions gave good conversion to the products (as shown by ^{1}H NMR spectroscopy) but it proved difficult to remove the dicyclohexylurea byproduct of the coupling reaction. Instead we found that **4**–**6** could be prepared readily in 54–64% yields using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI) as its HCl salt, as addition of $NH_4Cl_{(aq)}$ solution to the DMF reaction mixture resulted in precipitation of clean product (Scheme 1).

Alkylation of **4**–**6** using ethyl iodide gave **1·I**, **2·I** and **3·I** in moderate to good yields. We initially attempted to prepare the tetraphenylborate salts of **1**$^+$–**3**$^+$, as the ability to "see" the BPh_4^- anion by ^{1}H NMR spectroscopy is useful in ensuring complete anion metathesis during their preparation. However, in the case of **1·BPh$_4$** and **2·BPh$_4$**, these salts appeared to be unstable and decomposed during purification. Small amounts of **1·BPh$_4$** and **2·BPh$_4$** could be isolated and used for anion recognition studies and gave similar results to those obtained with **1·BF$_4$** and **2·BF$_4$** (see Supporting Information).

Instead, we used silver(I) tetrafluoroborate in acetone to perform anion metathesis to give **1·BF$_4$**, **2·BF$_4$** and **3·BF$_4$**. Filtering the acetone reaction solutions removed silver(I) iodide, and subsequent addition of diethyl ether gave crystalline BF_4^- salts suitable for use in anion recognition experiments.[15] Notably, all of these receptors can be readily prepared in good overall yield and do not require chromatographic purification at any stage.

Anion recognition studies

The anion recognition properties of the receptors were studied using ^{1}H NMR titration experiments: initially, anions as their tetrabutylammonium (TBA) salts were added to solutions of **1·BF$_4$** and **2·BF$_4$** in 95:5 CD_3CN:D_2O. 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). As an example, the addition of chloride anion to **1·BF$_4$** and **2·BF$_4$** in 95:5 CD_3CN:D_2O is shown in Figure 3.

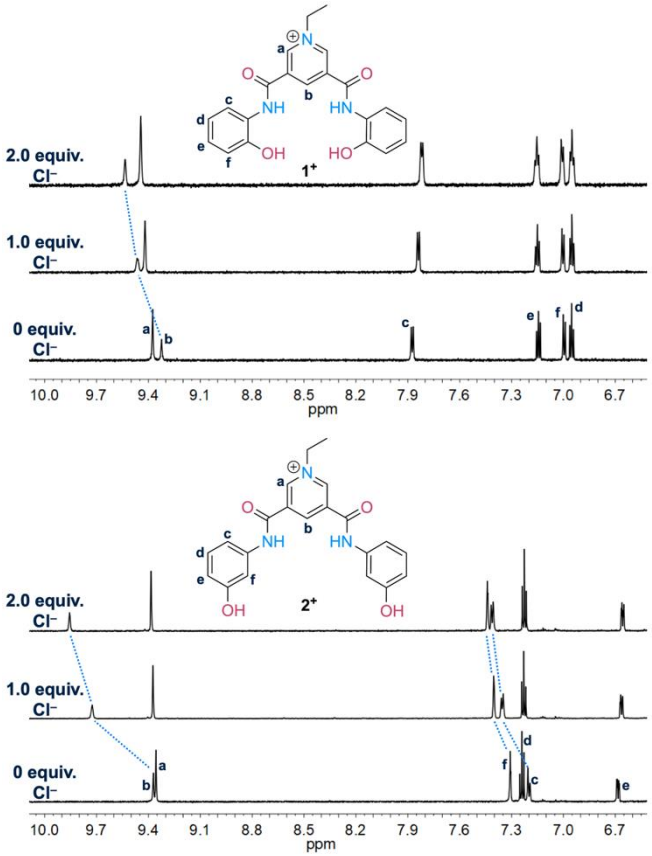

Figure 3. Truncated ^{1}H NMR spectra of **1·BF$_4$** and **2·BF$_4$** upon addition of chloride anion (anion added as TBA salt, 2.0 mM in 95:5 CD_3CN:D_2O, 700 MHz, 298 K).

The movements of the interior pyridinium resonances (b in Figure 3) were fitted to 1:1 binding isotherms using the *Bindfit* programme[16] (weblinks to full binding data and fits are provided in the Supporting Information). As shown in Table 1, both hydroxy-containing receptors bind chloride in 95:5 CD_3CN:D_2O, 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[a] to receptors **1·BF$_4$**, **2·BF$_4$** and **3·BF$_4$** in 95:5 CD_3CN:D_2O.

Anion	**1·BF$_4$**	**2·BF$_4$**	**3·BF$_4$**
Cl^-	$2.4(1) \times 10^2$	$1.4(1) \times 10^3$	$8.4(1) \times 10^2$
I^-	nb[b]	$1.6(1) \times 10^2$	$1.4(1) \times 10^2$

[a] Anions added as TBA salts, binding constants determined using Bindfit,[16] the asymptotic error[17] is provided at the 95% confidence interval in parentheses. [b] Peak movements too small to infer binding.

Both **2·BF$_4$** and **3·BF$_4$** bind iodide weakly in this solvent mixture, while peak shifts with **1·BF$_4$** were too small to calculate a binding constant. Addition of acetate or sulfate to either of the hydroxy-containing receptors in 95:5 CD_3CN:D_2O resulted in precipitation (see Supporting Information for binding of these anions to **3·BF$_4$**). Therefore, we conducted further anion recognition experiments in more competitive 90:10 CD_3CN:D_2O.

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$^+$** (Table 2). The increased binding of the hydroxy-containing receptors is particularly noticeable for SO_4^{2-}, which is bound quite strongly by **1$^+$** and **2$^+$** but only weakly by **3$^+$** (Figure 4).

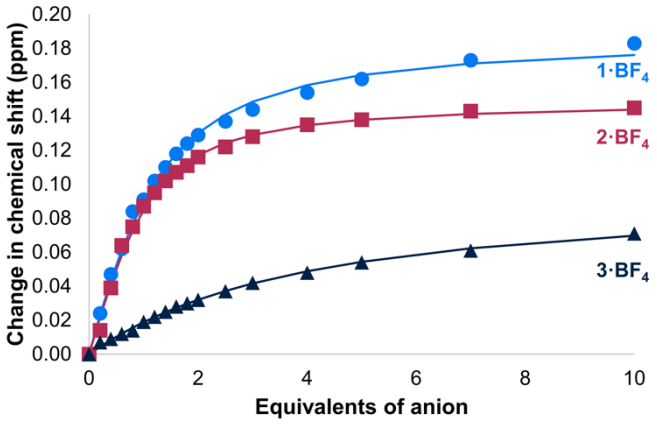

Figure 4. Movement of interior pyridinium C–H resonance of **1·BF$_4$**, **2·BF$_4$** and **3·BF$_4$** upon addition of $TBA_2 \cdot SO_4$ in 90:10 CD_3CN:D_2O. Points represent observed data, lines represent 1:1 binding isotherms fitted using *Bindfit*.[16]

Interestingly, while **3$^+$** tends to bind more strongly than **1$^+$** in 95:5 CD_3CN:D_2O, this trend is reversed in 90:10 CD_3CN:D_2O 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.

Table 2. Association constants (M^{-1}) for addition of anions[a] to receptors **1·BF$_4$**, **2·BF$_4$** and **3·BF$_4$** in 90:10 CD_3CN:D_2O.

Anion	**1·BF$_4$**	**2·BF$_4$**	**3·BF$_4$**
F^-	76(3)	$2.0(1) \times 10^2$	41(1)
Cl^-	61(1)	$1.7(1) \times 10^2$	$1.3(1) \times 10^2$
OAc^-	$3.0(1) \times 10^2$	ppt[b]	72(1)
SO_4^{2-}	$8.3(5) \times 10^2$	$1.5(1) \times 10^3$	$1.4(1) \times 10^2$

[a] Anions added as TBA salts, binding constants determined using Bindfit,[16] the asymptotic error[17] is provided at the 95% confidence interval in parentheses. [b] Precipitation observed after 2.0 equivalents of anion.

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$_4$**, **1·I**, **1·TBA·SO$_4$**,[18] and **2·I** are shown in Figure 5, while structures of **3·BF$_4$**, **3·Cl** and **3·I** are provided in the Supporting Information (Figures 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,[19] a *syn-syn* conformation is commonly observed upon anion binding.[20] 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[21]) 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 F^-, SO_4^{2-} and 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).

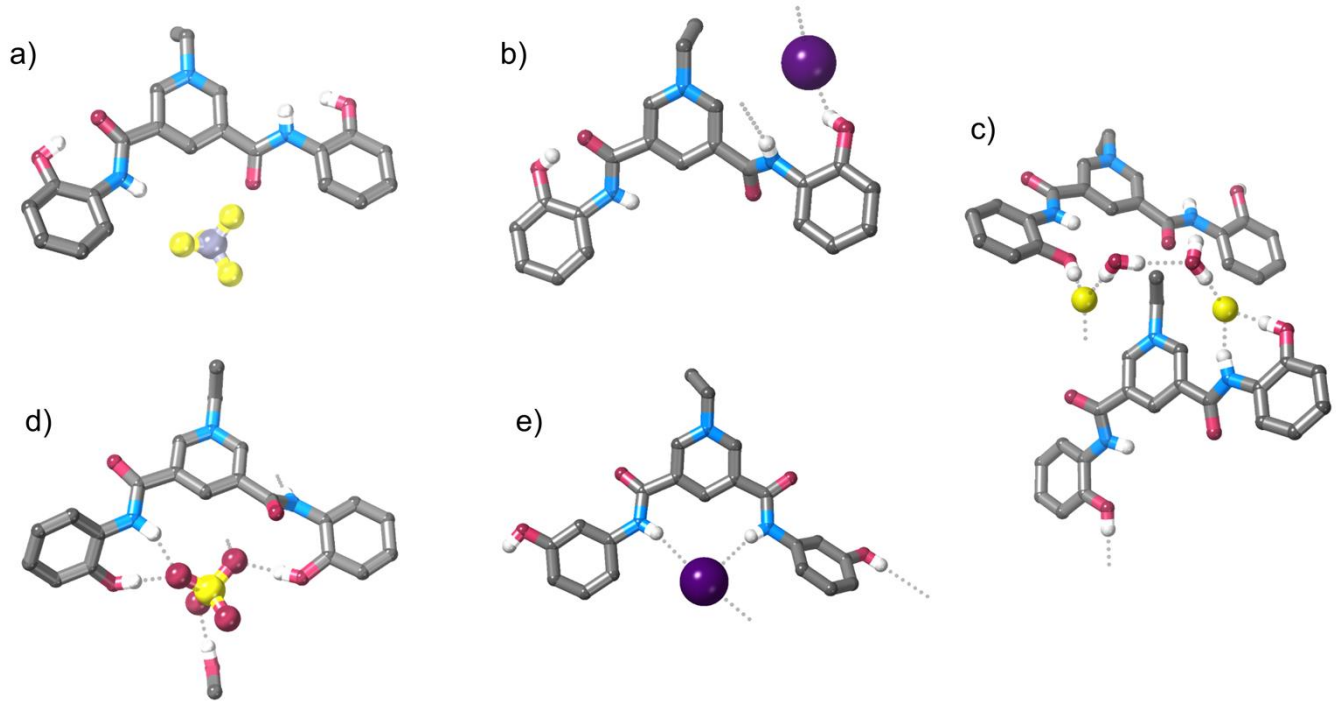

Figure 5. X-ray crystal structure of a) **1·BF$_4$**, b) **1·I**, c) **1·F**, d) **1·TBA·SO$_4$** and e) **2·I**. Intermolecular hydrogen bonds are shown as dotted lines. Most hydrogen atoms, and TBA cation in **1·TBA·SO$_4$** are omitted for clarity. NB: Crystals and structure refinement for **1·TBA·SO$_4$** are of low quality and PLATON-SQUEEZE was used.[18] Colour key: carbon = grey; hydrogen = white; nitrogen = blue; oxygen = red; boron = pale grey (Figure 5a); fluorine = yellow (Figure 5a, 5c); sulfur = yellow (Figure 5d), iodine = purple.

Structure of receptor·anion complexes in solution

While the X-ray crystal 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 (Figures S58 – 61) show no evidence of aggregation or oligomeric assemblies. This suggests that the extended structures are favoured 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 Figure 3 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.

MD simulations

It is noticeable that in the structures of **1·BF$_4$** and **1·I** (Figure 5a and 5b) 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_3CN:H_2O investigating **1·Cl**, **2·Cl**, **1·TBA·SO$_4$** and **2·TBA·SO$_4$.** Simulations were conducted using GROMACS 2016.1[22] in conjunction with the GROMOS 54a7 force field.[23] Water was represented explicitly as a single point charge model[24] and parameters for **1**$^+$, **2**$^+$ and acetonitrile were calculated using the Automated Topology Builder[25] (see Supporting Information for full details of simulations).

During the course of the simulations of **1·Cl** and **1·TBA·SO$_4$**, 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 (Figures 6a and S62), while a tetradentate mode of binding is also observed in which both N–H and both O–H groups hydrogen bond to the anion (Figures 6b and S63). As shown in Figure 6e, the intramolecular hydrogen bond occurs frequently meaning that the O–H donors are not often 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·SO$_4$** 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 Figures 6c and 6d. 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,[26] and it is interesting that we see a similar phenomenon in a system without an obviously hydrophobic binding site.

Generally, while these receptors 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.

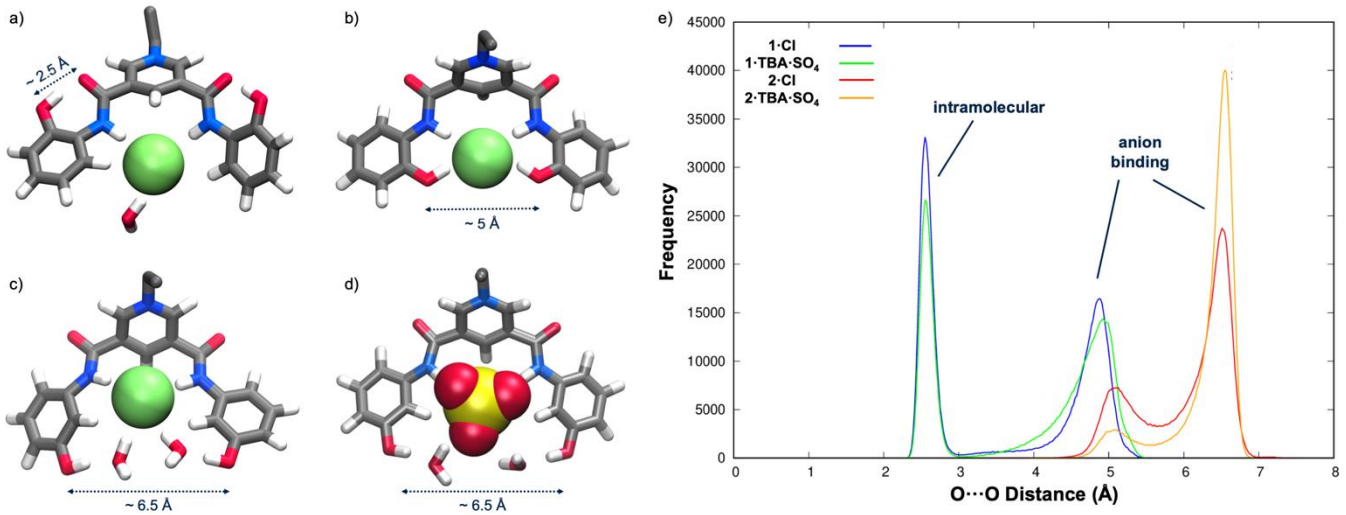

Figure 6. Overview of MD simulations of **1·Cl**, **1·TBA·SO$_4$**, **2·Cl** and **2·TBA·SO$_4$** in 95:5 CH_3CN:H_2O. a) – d): Representative snapshots and approximate O···O distances of frequently-occurring binding modes. The two common binding conformations in complexes of **1**$^+$ are shown, as is binding of hydrated anions by **2**$^+$; e) chart showing frequency of O···O distances. Colour key for Figures 6a–6d: carbon = grey; hydrogen = white; nitrogen = blue; oxygen = red; sulfur = yellow; chlorine = green.

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 CD_3CN:D_2O. 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 Section

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 NH_4Cl (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%).
^{1}H NMR (d_6-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), 6.94 (d, J = 7.7 Hz, 2H), 6.85 (t, J = 7.6 Hz, 2H) ppm. ^{13}C NMR (d_6-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). HRESI-MS (neg.): 348.0985, calc. for $[M^{-H}]^-$, $C_{19}H_{14}N_3O_4$: 348.0984 Da. mp > 250 °C.

5: Isolated as a white powder, yield: 1.02 g (3.22 mmol, 64%).
^{1}H NMR (d_6-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. ^{13}C NMR (d_6-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). HRESI-MS (neg.): 348.0978, calc. for $[M^{-H}]^-$, $C_{19}H_{14}N_3O_4$: 348.0984 Da. mp > 250 °C.

6: Isolated as a pale yellow powder, yield: 0.860 g (2.71 mmol, 54%).
^{1}H NMR (d_6-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. ^{13}C NMR (d_6-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). HRESI-MS (pos.): 318.1236, calc. for $C_{19}H_{16}N_3O_2$, 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 (1.12 mL, 2.18 g, 14.0 mmol). The vial was sealed and sonicated for 10 minutes, and the resulting mustard-yellow suspension heated to 90 °C (oil bath temperature) for 7 days. After 1 day, all material had dissolved to give a golden-brown solution, and after 3 days, a yellow precipitate had formed. After 7 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 (20 mL) and then dried *in vacuo*. Yield: 0.512 g (1.01 mmol, 72%).
^{1}H NMR (d_6-DMSO): 10.30 (br. s, 2H), 9.93 (br. s, 2H), 9.69 (s, 2H), 9.44 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.11 (dd, J = Hz, 2H), 6.98 (d, J = 8.0, 8.0 Hz, 2H), 6.88 (dd, J = 8.0, 8.0 Hz, 2H), 4.80 (q, J = 7.0 Hz, 2H), 1.65 (t, J = 7.0 Hz, 3H) ppm .^{13}C NMR (d_6-DMSO): 160.3, 149.9, 146.3, 142.3, 133.9, 126.7, 124.8, 124.5, 118.9, 115.9, 57.3, 16.1 ppm. IR (inter alia): 1660 cm^{-1} (C=O stretch). HRESI-MS (pos.): 378.1457, calc. for $[M]^+$, $C_{21}H_{20}N_3O_4$: 378.1454 Da. mp > 250 °C.

2·I
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 to a yellow suspension. 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%).
^{1}H NMR (d_6-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. ^{13}C NMR (d_6-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, 1661 cm^{-1} (C=O stretch). HRESI-MS (pos.): 378.1454, calc. for $[M]^+$, $C_{21}H_{20}N_3O_4$: 378.1454 Da. mp > 250 °C.

3·I
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%).
^{1}H NMR (d_6-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. ^{13}C NMR (d_6-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 $C_{21}H_{20}N_3O_2$, i.e. **3**$^+$ = 346.1550 Da. mp: 228–230 °C.

General anion exchange procedure to give 1·BF_4, 2·BF_4 and 3·BF_4
A solution of silver(I) tetrafluoroborate (0.039 g, 0.20 mmol) in acetone (3 mL) was added to a suspension of the appropriate iodide salt (0.101 g, 0.200 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·BF_4: Isolated as golden-yellow crystals, yield: 0.072 g (0.15 mmol, 77%).
^{1}H NMR (d_6-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. ^{19}F NMR (d_6-acetone): –151.2 ppm. IR (inter alia): 1670, 1657 cm^{-1} (C=O stretch). MS (ESI-pos.): 378.1, calc. for $C_{21}H_{20}N_3O_4$, i.e. **1**$^+$ = 378.2; 843.5, calc. for $C_{42}H_{40}BF_4N_6O_8$, i.e. [(**1**$^+$)$_2$·BF_4^-] = 843.3 Da. mp: 211–212.5 °C.

2·BF_4: Isolated as a foamy golden-yellow solid, yield: 0.063 g (0.14 mmol, 68%).
^{1}H NMR (d_6-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, 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. ^{19}F NMR (d_6-acetone): –150.4 ppm. IR (inter alia): 1682, 1662 cm^{-1} (C=O stretch). MS (ESI-pos.): 378.1, calc. for $C_{21}H_{20}N_3O_4$, i.e. **2**$^+$ = 378.2; 843.4, calc. for $C_{42}H_{40}BF_4N_6O_8$, i.e. [(**2**$^+$)$_2$·BF_4^-] = 843.3 Da. mp: decomposition apparent at ~ 222 °C.

3·BF_4: Isolated as pale yellow microcrystals, yield: 0.077 g (0.18 mmol, 88%).
^{1}H NMR (d_6-acetone): 10.19 (s, 2H), 9.80 (d, J = 1.6 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. ^{19}F NMR (d_6-acetone): –150.4 ppm. IR (inter alia): 1682, 1655 cm^{-1} (C=O stretch). MS (ESI-pos.): 346.1, calc. for $C_{21}H_{20}N_3O_2$, i.e. **3**$^+$ = 346.2; 779.5, calc. for $C_{42}H_{40}BF_4N_6O_4$, i.e. [(**3**$^+$)$_2$·BF_4^-] = 779.3 Da. mp: 172.5–174 °C.

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