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Design, synthesis and photophysical studies of simple fluorescent anion PET sensors using charge neutral thiourea receptors

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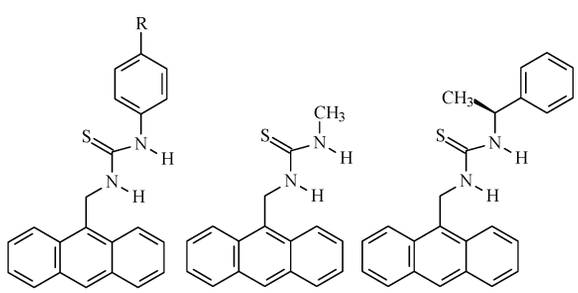
The synthesis of four fluorescent photoinduced electron transfer (PET) chemosensors **1**–**4** for anions is described. These are all based on a simple design employing charge neutral aliphatic or aromatic thiourea anion receptors connected to an anthracene fluorophore *via* a methylene spacer. Here the anion recognition occurred through 1 : 1 hydrogen bonding between the thiourea protons and the anion, as demonstrated by observing the changes in the ^{1}H NMR in DMSO-d_6 where the two thiourea protons were shifted downfield upon addition of anions. Whereas **1**–**3** were designed for the detection of anions such as fluoride, acetate or phosphate, **4** was made for the recognition of *N*-protected amino acids. All the sensors showed 'ideal' behaviour where only the fluorescence emission was quenched upon anion recognition, due to enhanced efficiency of electron transfer quenching from the receptor to the excited state of the fluorophore. By simply varying the nature of the thiourea substituent it was possible to modulate, or tune, the acidity of the thiourea receptor moiety, altering the sensitivity of the anion recognition. For **1**, the anion selectivity and the degree of the fluorescence quenching were in the order of $F^- > AcO^- > H_2PO_4^-$, with Cl^- or Br^- not being detected.

Introduction

Anions play a major role in many biological processes and in biological structures, such as amino acids, neurotransmitters, enzyme substrates, co-factors and nucleic acids.[1] They are also important components in a variety of industries, such as in the production of fertilisers, in food additives and in the water supply.[1] Consequently, many anions are also major pollutants both industrially and environmentally. The recognition and sensing of anions are of current interest in the field of supramolecular chemistry.[2–8] Whereas the sensing of cations is a well established field of research,[2] it is only recently that the same can be said for anion sensing.[3–5] This stems from the fact that in contrast to biologically important cations, such as Na^+, Ca^{2+} or NH_4^+, anions often exhibit a variety of structures and conformations, and are often highly pH sensitive as well as hydroscopic.[6] In view of this fact, the recognition of anions frequently requires the use of structurally complicated hosts, furnished with anion recognition motifs[7] that often require elaborate and lengthy synthesis,[3,8] or the use of metal ion coordination centres.[9] All of these features have to be carefully considered and implemented in the design strategy of efficient anion recognition motifs. Due to these drawbacks the development of simple luminescent sensors for anions has only recently been explored.[10] We are interested in the design of luminescent devices, and we have developed fluorescent[11] as well as lanthanide luminescent[12] chemosensors, switches and logic-gate mimics. We are particularly interested in the development of luminescent sensors for anions and have developed several simple lanthanide based sensors for the detection of carboxylates.[13] Having developed several photoinduced electron transfer (PET) sensors for cations,[11] we set out to develop simple and easy to make PET anion sensors,[10] based on the use of the *fluorophore–spacer–receptor* motif developed by de Silva.[2] Even though Fabbrizzi *et al.*[14] and Czarnick *et al.*[15] have developed PET sensors for anions using positively charged receptors, to the best of our knowledge, no fluorescent PET sensors using charge neutral receptors have been developed. Our aim was thus to demonstrate the feasibility of such sensing, where the anion recognition would give rise to ideal PET anion sensing, *i.e.* only the quantum yield (Φ_F) and the fluorescence lifetime would be affected upon ion recognition.[16,17] Hence, no other spectral changes such as exciplex or excimer emission or changes in the absorption spectra should be observed.[18] Here we give a full account of our investigation, where we developed the charge neutral PET sensors **1**–**3**, for the detection of simple anions such as halides, acetates or phosphates.[10] Furthermore, we describe a chiral PET sensor **4** aimed at the enantioselective sensing of carboxylates such as *N*-acetyl protected amino acids. Even though we were unable to achieve enantioselectivity, we demonstrate the potential feasibility of such sensing, as the fluorescence of **4** was highly modulated upon addition of *N*-acetyl protected amino acids.



1 R = H
2 R = CF_3
3
4

Results and discussion

Design and synthesis of 1–4

We chose to use thiourea as a receptor moiety with the aim of demonstrating anion PET sensing. Thioureas and ureas are well known hydrogen bonding donors and have been used by several researchers as anion recognition sites for anion detection,[16,17,19] or in organic synthesis as catalysts.[20] They are easily made from commercially available isocyanates or isothiocyanates, raising the possibility of developing a range of (thio)urea receptors where the acidity of the hydrogen bonding donor can be tuned.

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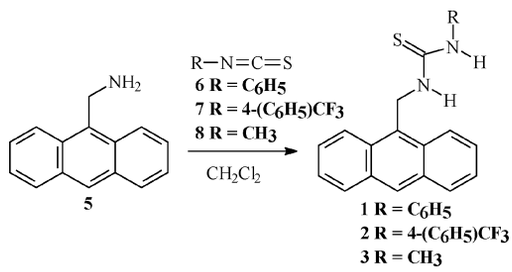
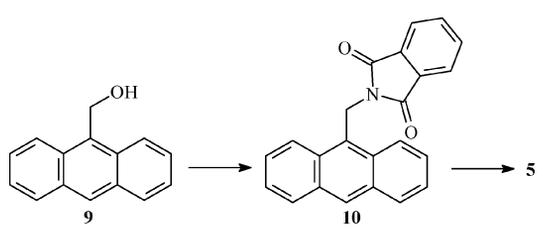
This would lead to different *receptor:anion* stabilities and subsequently provide different affinity and selectivity.[10] To demonstrate such PET sensing we chose to use anthracene as a fluorophore, as this moiety had been used previously by several researchers to demonstrate PET sensing.[1,14,15,21] All the sensors contain the thiourea receptor connected to the anthracene *via* a methyl spacer, giving rise to a *fluorophore–spacer–anion receptor* motif. Scheme 1 shows the synthesis of **1**–**3**, which was carried out in dry CH_2Cl_2 at room temperature. All the sensors were easily made from 9-(aminomethyl)anthracene **5** (see discussion below) and an equimolar amount of 4-(trifluoromethyl)phenyl- (**7**), phenyl- (**6**) and methyl isothiocyanate (**8**) respectively. The resulting products all precipitated upon formation (instantly), but stirring was continued for 12 hours. After reducing the volume, the precipitates were isolated by filtration and recrystallised from hot $CHCl_3$, giving **1** and **2** in 84% and 77% yield respectively. For **3**, the final product was purified by silica flash chromatography with 100% ethyl acetate as the eluent, giving **3** in 67% yield.



Scheme 1 Synthesis of the anion PET sensors **1**–**3**, from 9-(aminomethyl)anthracene **5**, and phenyl-, 4-(trifluoromethyl)phenyl-, and methyl isothiocyanates, giving **1**, **2** and **3** respectively. Carried out in dry CH_2Cl_2 at room temperature for 12 hours.

The synthesis of **5** is worthy of comment. A previously reported preparation of 9-(aminomethyl)anthracene employed the Gabriel synthesis (Scheme 2).[22] 9-Anthraldehyde was reduced with $NaBH_4$ to the corresponding methyl alcohol **9**, which was then converted to 9-(chloromethyl)anthracene using thionyl chloride. Treatment with potassium phthalimide gave **10**, and reaction with NH_2NH_2 in DMF gave **5**. However, this method is both lengthy and low yielding due to the poor solubility of **10**. Consequently we set out to improve the yield of **5**, using two alternative methods.



Scheme 2 Synthesis of the 9-methylamine anthracene **5**, using the classical Gabriel amine synthesis.

We firstly carried out numerous attempts to reduce the commercially available 9-cyanoanthracene to **5**, using reagents such as $NaBH_4$, $LiAlH_4$ or B_2H_6 in solvents such as THF or DMF at either room temperature or at elevated temperatures. Of the different methods employed, the use of B_2H_6 (using borane–THF complex) in either refluxing THF or DMF gave **5** in the best yields of 68% and 65% respectively, after aqueous acid–base workup. However, the yield of **5** was highly dependent on the quality of the borane–THF complex. Consequently, another method was investigated, which involved the transformation of 9-(bromo- or 9-(chloromethyl)anthracene[23] with hexamethylenetetramine[24] in dry $CHCl_3$ at 60 °C. This amine is cheap and easy to use. It reacted readily with 9-(halomethyl)anthracene in $CHCl_3$ to yield an insoluble amine complex, which was isolated by filtration and dispersed in a solution of ethanol, water and concentrated HCl in a ratio of 20 : 4 : 5. The complex dissolved on heating to 70 °C and was refluxed for a subsequent hour. After this time a precipitate of the HCl salt began to form. Once removed from the heat the solution was then allowed to stand at room temperature overnight and the product was isolated by filtration in *ca.* 90% yield.

The three sensors were characterised using conventional methods. The ^{1}H NMR of **2** when recorded in DMSO-d_6 is shown in Fig. 1, clearly demonstrating the C_2 symmetry of the anthracene moiety. Here the three most characteristic resonances are the two thiourea hydrogens marked as **a** and **b**, at 9.62 ppm and 8.36 ppm respectively and the methylene spacer marked as **c**, at 5.72 ppm. It can be seen that the methylene resonance appears as a doublet, coupling to the adjacent thiourea proton **b**. Similar results were observed for **1** and **3**. The ^{13}C NMR of **2** also clearly demonstrated the presence of the thiourea carbon, appearing at 179.6 ppm. We were however unable to characterise these sensors using ESMS due to fragmentation.

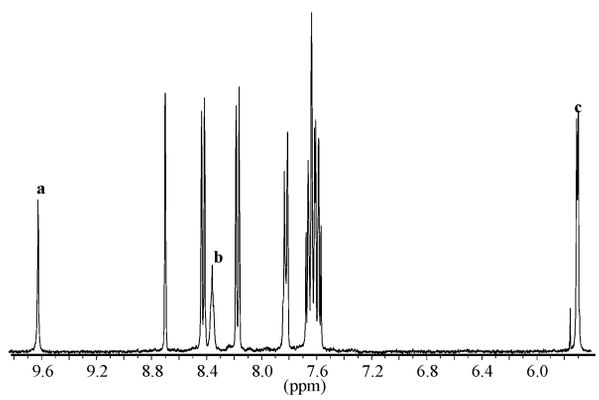
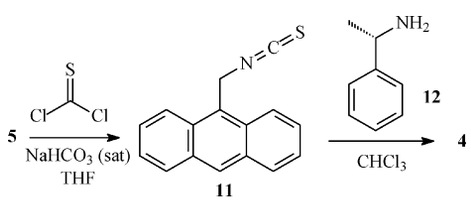


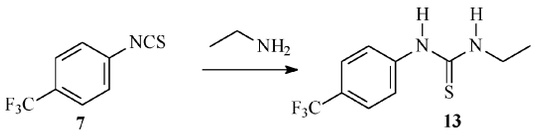
Fig. 1 The ^{1}H NMR (400 MHz, DMSO-d_6) of **2**. The two resonances corresponding to the thiourea protons are marked as **a** and **b** and the methylene spacer as **c**. The remaining resonances can be assigned to the aromatic receptor and the anthracene protons.

In the case of **4**, we firstly made 9-(isothiocyanatomethyl)-anthracene **11**, which was then reacted with the enantiomerically pure (*S*)-1-phenylethylamine **12**, in dry $CHCl_3$ at room temperature, Scheme 3. The isothiocyanate **11** has recently been made by Suzuki *et al.*[25] We made **11** from **5**, by reacting it with thiophosgene in a biphasic mixture of saturated $NaHCO_3$ and THF. The product was obtained as an oil and was subjected to purification on neutral flash silica using ethyl acetate–hexane (9 : 1) as the eluent, after which **11** was obtained as an orange solid in 20% yield.



Scheme 3 Synthesis of the chiral sensor **4**.

The chemosensor **4** was obtained as a yellow powder that precipitated upon reacting **11** with **12**, under conditions similar to those described above for **1**–**3**. The ^{1}H NMR of **4** had characteristic resonances for the two thiourea protons at 6.24 ppm and 6.22 ppm, the latter of these appearing as a doublet due to the coupling to the benzylic proton. As in the case of **1**–**3**, we were unable to obtain HRMS of this product as it fragmented in the ESMS. To investigate the effect of the anion recognition on the receptor moieties themselves, we also synthesised **13**, Scheme 4, which mimics the structural



Scheme 4 Synthesis of the anion receptor **13**.

features of the receptor used in **2**. This was achieved in a similar manner to that of **1**–**3**, by reacting 4-(trifluoromethyl)phenyl isothiocyanate with ethylene amine (2 M in THF) in anhydrous CH_2Cl_2 at room temperature.

Photophysical evaluation of 1–3 in DMSO

The photophysical properties of **1**–**3** were initially measured in DMSO. We first investigated the ground state properties of **2** (1×10^{-5} M) upon anion recognition in HPLC grade DMSO, using tetrabutylammonium acetate (TBAOAc). In accordance with *ideal* PET sensor design, we did not expect to see many changes in the ground state properties for the anthracene moiety of **2** upon anion recognition on the receptor site as stated above. The absorption spectra of the free sensor **2** gave rise to typical anthracene absorption bands at 390, 370, 352 and 336 nm respectively. These transitions appear at almost identical positions to that of 9-methylanthracene. The changes in the absorption spectra of **2** upon addition of AcO^- are shown in Fig. 2. As can be seen from this titration, only minor changes occur in the anthracene absorption spectra. However there are some changes occurring at short wavelength, which are due to the thiourea receptor. Hence upon anion recognition, through hydrogen bonding, Scheme 5, the charge density of the aromatic moiety is substantially affected as the anion increases the reduction potential of the receptor. To investigate this further we carried out an identical absorption titration using AcO^- and **13**. This confirmed that the changes at shorter wavelengths, as in the spectra of **2** were indeed due to the hydrogen bonding interactions of the anion with the thiourea protons. These results confirm that there are no significant ground state interactions between the anthracene fluorophore and the thiourea receptor, as the methylene spacer prevents any π–π or n–π interactions between the two moieties. We also investigated the effect of the addition of several other anions such as F^-, Cl^-, Br^-, and $H_2PO_4^-$ (as their TBA salts) upon the absorption spectra of **2**. Similar results were observed for these anions as for AcO^-. In an analogous way the absorption spectra of **1** and **3** were also recorded. As for **2**, no significant changes were seen in the absorption spectra of these compounds upon titration with any of the aforementioned anions. Hence, the ground state results fulfilled the PET criteria that there should be no significant changes in the absorption spectra.

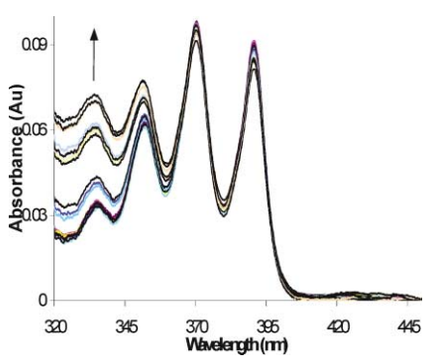
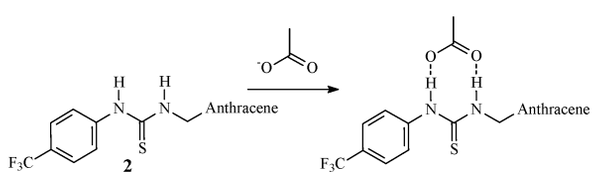


Fig. 2 The changes in the absorption spectra of **2** upon titration with TBAOAc (0 ⟶ 32 mM) in DMSO.



Scheme 5 The formation of linear hydrogen bonding between the thiourea protons of the receptor of **2** with AcO^- in DMSO.

We next investigated the effect of the excited state of **1**–**3** upon titration of several anions. This was carried out in an identical way to that described above for the ground state investigation in DMSO. In contrast to the above results, the changes in the fluorescence emission spectra of **1**–**3** were very different. In the case of **2**, significant fluorescence emission was observed upon excitation at 370 nm. Here a typical anthracene emission was observed, with emission bands at 443 nm, 419 nm and 397 nm, and a shoulder at 473 nm respectively. Using 9-methylanthracene as a reference,[26] the quantum yield of fluorescence (Φ_F) was determined as 0.104. In comparison, the Φ_F of 9-methylanthracene, which lacks the anion receptor was 0.284 in DMSO. This would indicate that some quenching is occurring in **2**, which might suggest that there was an active quenching of the anthracene exited state by the receptor moiety *via* photoinduced electron transfer prior to any anion recognition. Upon addition of AcO^- (0 ⟶ 32 mM), Fig. 3, the intensity of the anthracene emission bands gradually decreased with *no* other spectral changes being observed *i.e.* no spectral shifts or formation of new emission bands, such as red shifted exciplex formation. Teramae *et al.*[16] have recently shown that pyrene based chemosensors having aliphatic thiourea anion receptors (similar to **3**) give rise to long wavelength emission bands. These were due to the formation of intramolecular exciplex emission after anion recognition, hence these related examples can be considered as a ratiometric anion indicator.[16] In our case, using PET nomenclature, the emission can be said to have been approximately 70% (at 419 nm) '*switched off*' with $\Phi_F = 0.0070$. The fluorescent excited state lifetime of the free ligand, or in the presence of AcO^-, was unfortunately too short for us to obtain an accurate estimate.

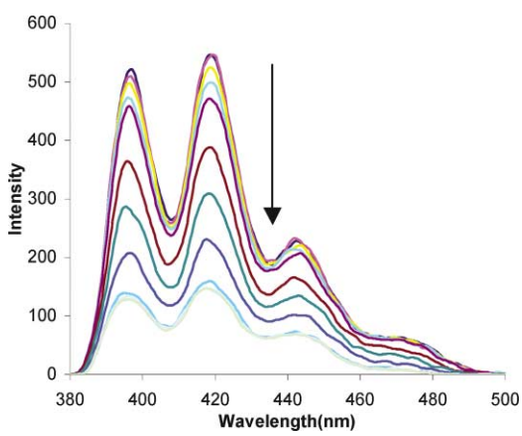


Fig. 3 Changes in the fluorescence emission spectra of **2** upon addition of TBAOAc (0 ⟶ 32 mM) in DMSO.

In a similar way to that described above, the fluorescence emission was also substantially affected upon titrating **2** with $H_2PO_4^-$ and F^-, Figs. 4 and 5 respectively, whereas neither Cl^- nor Br^- gave rise to any substantial changes in the fluorescence emission (less than 5%). As for the AcO^- titration, only the emission intensities of **2** are affected upon anion recognition. The changes in the fluorescence spectra vary significantly. For $H_2PO_4^-$ the fluorescence emission was quenched by approximately 50% ($\Phi_F = 0.0156$), whereas for F^- the quenching (at 443 nm) was much more pronounced, being *ca.* 90% ($\Phi_F = 0.0011$) quenched. For Cl^- ($\Phi_F = 0.108$) or Br^- ($\Phi_F = 0.088$) the quenching is poor, ruling out any quenching by heavy atom effect. We propose that this difference in quenching between these anions is due to their ability to form strong *receptor:anion* complexes with **2**. F^- is a small spherical anion with high charge

Table 1 [a]

Sensor	1			2			3		
	Φ_F [b]	% F_{red} [c]	Log β [d]	Φ_F [b]	% F_{red} [c]	Log β [d]	Φ_F [b]	% F_{red} [c]	Log β [d]
Free	0.187			0.108			0.340		
AcO^-	0.16	73	2.15	0.007	75	2.33	0.200	43	1.75
$H_2PO_4^-$	0.101	46	1.82	0.0156	50	2.05	0.110	38	2.05
F^-	0.067	64	2.90	0.0011	90	3.35	0.230	55	2.37
Cl^-	0.173	8	—[e]	0.108	7	—[e]	0.300	12	—[e]
Br^-	0.172	7	—[e]	0.088	12	—[e]	0.250	14	—[e]

[a] All measurements carried out in DMSO at room temperature. [b] We estimate the error in these measurements to be ± 5%. [c] The % of fluorescent quenching (reduction). [d] We estimate the error in these measurements to be ± 0.1. [e] These changes were too small for the determination of accurate binding.

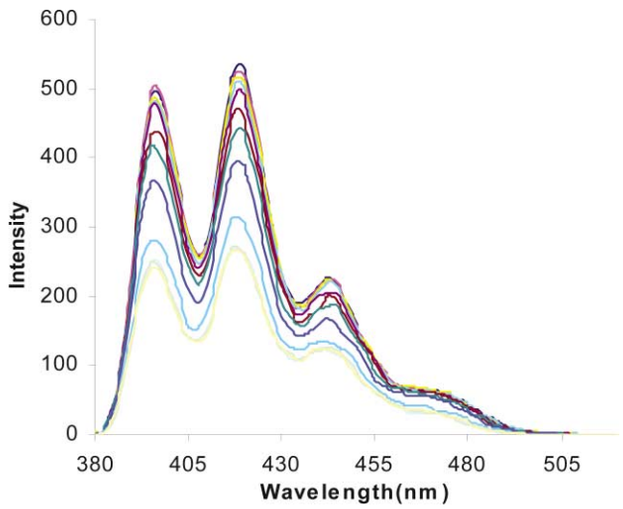


Fig. 4 Changes in the fluorescence emission spectra of **2** upon addition of TBA H_2PO_4 (0 ⟶ 32 mM) in DMSO.

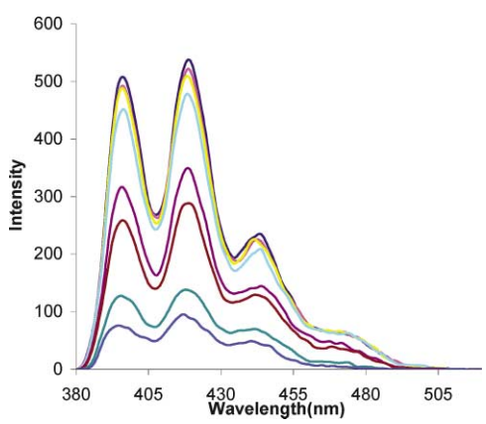


Fig. 5 Changes in the fluorescence emission spectra of **2** upon addition of TBAF (0 ⟶ 32 mM) in DMSO.

density and can hydrogen bond strongly to the receptor, whereas AcO^- can form a stronger linear-directed hydrogen bonding complex than $H_2PO_4^-$. The results obtained for the other halides are simply explained due to size exclusion, and smaller charge density than for F^-, *e.g.* these ions are too big to give rise to strong hydrogen bonding to the thiourea. We propose that these hydrogen bonding *receptor:anion* complexes affect the reduction potential of the thiourea receptor, which in turn will enhance the free energy of PET (ΔG_{PET}) quenching. Hence the rate of PET from the HOMO of the receptor to the anthracene excited state, is greatly increased as the reduction potential of the thiourea is increased upon anion recognition. This will thus cause the fluorescence emission to be more quenched, or *'switched off'*. These systems operate in reverse to the classical PET cation sensing,[2,11] where the oxidation potential of the receptor is increased causing the emission to be *'switched on'*, as the thermodynamic pathway for PET is removed.

To investigate the sensitivity and the selectivity of **2** towards the above anions we investigated the intensity changes as a function of the anion concentration. This is shown in Fig. 6, where the relative intensity at 419 nm has been plotted as a function of the −log [Anion]. From these changes, it is obvious that the binding profiles for AcO^-, $H_2PO_4^-$ and F^- are all sigmoidal, whereas no significant changes are seen for Cl^- and Br^-. Moreover, as quenching occurs over *ca.* two log units, it can be deduced that the sensing is due to a simple equilibrium and 1 : 1 binding, both features that are commonly seen for PET cation sensors. From the equation: log $[(I_{max} - I_F)/(I_F - I_{min})]$ = log [anion] − log β, these were evaluated to be 3.35 (±0.05) for F^-, 2.55 (±0.05) for AcO^- and 2.05 (±0.05) for $H_2PO_4^-$. These results are summarised in Table 1 for all the sensors. Importantly, even though the structure of the receptor of **2** is simple it shows good anion selectivity with AcO^- over $H_2PO_4^-$, both anions representing families of biologically important anions. The fact that **2** shows higher affinity and more efficient quenching for F^- than AcO^- is not surprising, since fluoride's high charge density and small size enable it to form strong hydrogen bonds with the thiourea receptor, as previously discussed.

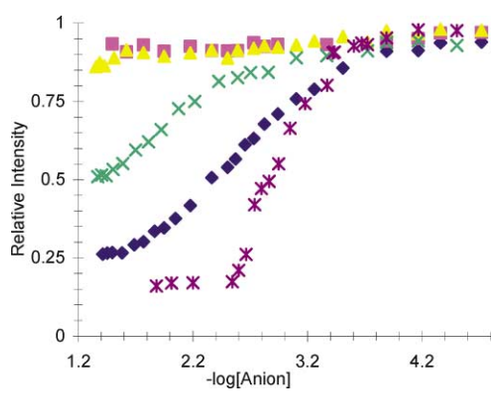


Fig. 6 Changes in the relative fluorescence emission at 419 nm of **2** upon addition of TBAOAc (◆); TBA H_2PO_4 (×); TBAF (*); TBACl (▲) and TBABr (■) in DMSO.

We carried out identical titrations to those described above using **1** and **3**. As expected, the binding affinity for the anions of these sensors was not as strong relative to that of **2** due to the lower electron withdrawing ability of the skeleton groups of **1** and **2**. Furthermore, these results demonstrated that although using simple thiourea moieties, we were able to 'tune' the sensitivity of the ion recognition. The absorption and fluorescence spectra were similar to that of **2** shown above, due to the common anthracene ring with only a slight shift in the absorption λ_{max} *ca.* ~2 nm for **1** and **3** respectively. Furthermore, similar changes in the emission and absorption effects were observed for **1** and **3** as seen for the titrations of **2** with the various TBA

salts *i.e.* no significant changes were seen in the absorption spectra. Whereas the fluorescence emission was quenched for both upon anion recognition, with no other spectral changes being observed. Hence, as in the case of **2**, both sensors behaved like *ideal* PET sensors, as only the intensity or the Φ_F was modulated. For these, the Φ_F was measured to be 0.187 and 0.34 for the two sensors respectively prior to the anion sensing. This clearly supports our earlier findings that the emission is quenched prior to the anion recognition, as the magnitude of Φ_F follows the same order as the ability of the receptors to participate in PET, hence, the electron density of the receptors is **2** > **1** > **3**. We attempted to evaluate the changes in the reduction potentials of the receptor **13**, as a function of [AcO^-] using cyclic voltammetry with the aim of evaluating ΔG_{PET}. Unfortunately, the CV measurements on **13** showed two irreversible oxidative waves, and hence accurate ΔG_{ET} could not be determined from these measurements.

The changes in the relative fluorescence emission of **1** and **3** as a function of −log [anion] are shown in Figs. 7 and 8 respectively. As can be seen from these titration profiles, all gave rise to sigmoidal curves over two log units, which as discussed before, signify the formation of 1 : 1 binding. From the changes shown in Fig. 7 and Fig. 8, we were able to determine log β in an analogous way to that described above for **2**. These results are summarised in Table 1, as well as the degree of quenching (% F_{QUE}) and Φ_F. It is also interesting to see that for all of these sensors the quenching was most pronounced for F^-, giving rise to *ca.* 73% and 43% '*switching off*' for **1** and **3** respectively, followed by AcO^- (which in the case of **1** is close to that of F^-) and $H_2PO_4^-$. The binding of Cl^- and Br^- was, however, in both cases too weak to be measurable. Figs. 6, 7 and 8 demonstrate the above trend for **1**–**3**, where the magnitude of the fluorescence quenching correlates well with the order of the binding

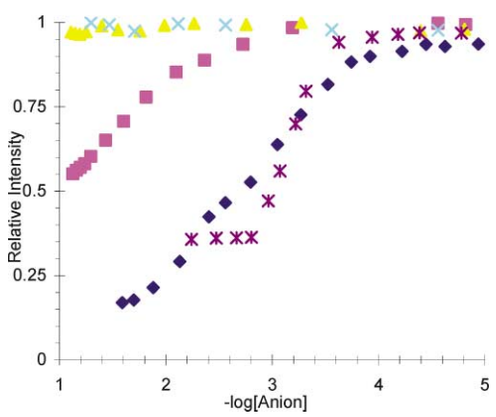


Fig. 7 Changes in the relative fluorescence emission at 419 nm of **1** upon addition of TBAOAc (*); TBA H_2PO_4 (■); TBAF (◆); TBACl (▲) and TBABr (×) in DMSO.

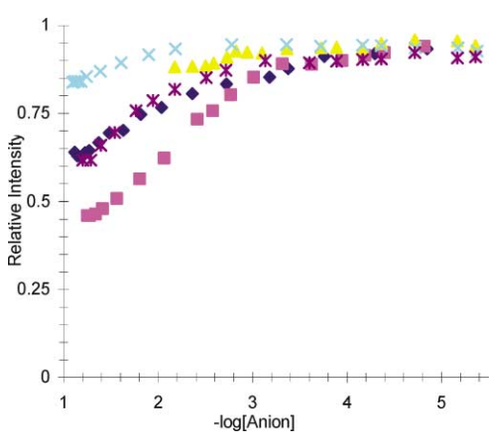


Fig. 8 Changes in the relative fluorescence emission at 419 nm of **3** upon addition of TBAOAc (◆); TBA H_2PO_4 (*); TBAF (■); TBACl (▲) and TBABr (×) in DMSO.

affinity. Only for **3** is the binding affinity trend not so clear. This demonstrates clearly the inability of the aliphatic thiourea in **3** to inflict any significant degree of selectivity, possibly due to steric as well as electronic effects. Hence we believe that the above results support the hypothesis that the affinities of the anion binding can be manipulated by simply changing the acidity of the thiourea protons even in such simple PET sensors. Hence the more electron withdrawing the thiourea substituent the stronger the binding, furthermore, the more electron rich receptors give rise to a larger degree of quenching.

We also investigated the PET affect in other solvents. When the fluorescence titrations of **1**–**3** were carried out in CH_3CN, CH_3CO_2Et or THF, the emission was also quenched upon addition of AcO^- but the degree of quenching was somewhat smaller. In ethanol, which is a highly competitive hydrogen bonding solvent, no binding was observed between **2** and AcO^-, whereas there was a notable degree of quenching observed when CH_3CN was used. The binding was found to be reversible by simply adding ethanol to either the CH_3CN or the DMSO solutions. Whereas $CHCl_3$ has been extensively used for anion recognition studies,[27] it was not employed in the current studies as the sensors were only soluble upon heating.

Investigating the anion recognition using ^{1}H NMR

To investigate the nature of the anion sensing we also evaluated the anion recognition using ^{1}H NMR in DMSO-d_6 and AcO^-. As discussed earlier, the thiourea protons can be used to observe the hydrogen bonding interactions between the receptor and the anion, giving useful information on the structure of the *receptor:anion* complex. Furthermore, the information within the ^{1}H NMR spectra can give details of the rate of association and dissociation as well as conformational changes that can occur upon binding.[28]

All the sensors were analysed and all showed that the anion binding was a fast exchange process, where both the thiourea resonances were shifted down field upon anion recognition. As previously stated, the ^{1}H NMR of **2** in DMSO-d_6 showed two sharp signals at 9.62 ppm and 8.36 ppm for the thiourea hydrogens. The changes in the resonance of the thiourea proton adjacent to the aromatic ring are shown in Fig. 9, as a function of the equivalents of AcO^-. Here the main resonance shifts were observed between 0 ⟶ 1 equivalents of AcO^-, signifying the formation of a 1 : 1 complex. From these changes a binding constant of K_{ass} of 1507 M^{-1} was determined.[29] Whereas the thiourea protons were significantly shifted upon anion recognition, the position of the methylene protons and the resonances for the aromatic protons were only slightly affected, however all the resonances did become significantly broad upon anion binding. This suggests that the anion recognition indeed occurs at the thiourea moiety through hydrogen bonding and that there are no interactions with the anthracene ring, confirming the results obtained from the absorption spectra shown in Fig. 2. This further confirms that the changes seen in

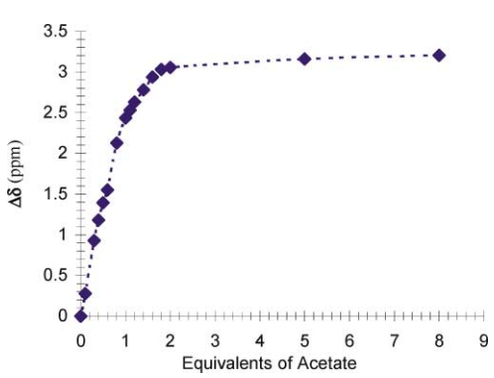


Fig. 9 The changes in the thiourea resonance (appearing at 9.62 ppm in the free sensor) upon titration with AcO^- in DMSO-d_6.

the fluorescence emission spectra of these sensors are due to the modulation of the electronic properties of the receptor after recognition of the anions, which gives rise to enhanced through space PET quenching. Similar effects were observed when the other two sensors were employed.

Evaluation of 4 for the enantioselective recognition of *N*-protected amino acids

The recognition of *N*-protected amino acids has recently been explored by several researchers.[30] However, these often involve the use of structurally complicated hosts. As the fluorescence of sensors **1**–**3** was on all occasions substantially quenched upon sensing of AcO^-, we considered using our simple design to attempt the chiral recognition of such *N*-acetal protected amino acids. With this in mind we synthesised **4** as described above. In this first generation of such chiral sensors, only a single asymmetric carbon was introduced into the receptor.

The absorption spectrum of **4** was similar to that seen for **1**–**3** above, with typical anthracene absorption bands at 335 nm, 351 nm, 370 nm and 390 nm respectively. Upon titration with AcO^- or TBA alanine no significant changes were observed in the absorption spectra, demonstrating no ground state interactions. In contrast to these results, the fluorescence emission spectra, with emission bands at 395 nm, 417 nm, 442 nm, and a shoulder at 469 nm respectively, were significantly affected. As discussed above no other spectral changes were observed and this quenching can be assigned to PET from the chiral receptor to the anthracene excited state. However, as can be seen from Fig. 10, for the change in the 419 nm transition as a function of $-\log [AcO^-]$ the binding is weak in comparison to **1** and **2**, but of a similar magnitude to that seen for **3**. We next evaluated the sensing of (*S*)- and (*R*)-*N*-acetylalanine as their TBA salts in DMSO. As in the case of AcO^- the fluorescence emission of **4** was substantially quenched for both of these amino acids. However, as can be clearly seen from Fig. 10, the chiral recognition of these amino acids was not achieved efficiently. Furthermore, as the receptor is aliphatically based, the thiourea protons are not acidic enough to give rise to strong hydrogen bonding and hence the sensitivity of the sensing is rather low. These results, however, are encouraging and clearly demonstrate that the potential recognition of such amino acids should be feasible, as the fluorescence was on both occasions reduced by *ca.* 60%. Hence the design of more enantioselective receptors is necessary. We are currently working towards developing such systems using receptors that have two stereogenic centres as part of their design.

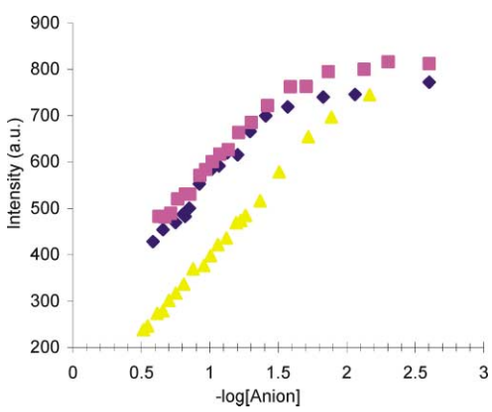


Fig. 10 The changes in the fluorescent emission at 419 nm for **4** upon titration of TBAOAc (▲); TBA L-Ala (■); TBA D-Ala (◆).

Conclusion

In this paper we have demonstrated the feasibility of anion sensing using fluorescent PET sensors, using the simple fluorophore–spacer–receptor design. For all of these, the receptor was either an aryl (**1** and **2**) or an aliphatic (**3** and **4**) based thiourea moiety. All the sensors were characterised using conventional methods. Investigation into the ground and excited state properties of the anthracene fluorophore of **1**–**4** clearly showed that in several solvents these sensors behaved as ideal PET sensors, *i.e.* only the fluorescent quantum yield was affected upon the anion sensing. No other significant spectral changes were observed, and there was no evidence for any charge transfer complex formation between the fluorophore and the thiourea receptor or the *anion:receptor* complex. Analysis of the recognition process using ^1H NMR indeed confirmed that the recognition process was due to 1 : 1 hydrogen bonding binding between the anion and the receptor. We propose that this will increase the reduction potential of the receptor, which consequently gives rise to increased quenching through PET from the *anion:receptor* complex to the anthracene excited state. We also demonstrated that by simply tuning the acidity of the thiourea protons, the strength of this hydrogen bonding interaction could be modulated and hence, the sensitivity of the anion sensing, *i.e.* **2** showed stronger binding than **1**, which gave stronger binding than **3**. We further demonstrated that the anion sensing followed the trend that F^- was most strongly bound and gave rise to the most efficient quenching. This was followed by AcO^- and $H_2PO_4^-$ respectively, but the sensing of Cl^- and Br^- was not feasible using this simple design. We also attempted to apply our simple design to the enantioselective sensing of *N*-protected amino acids. While this was not successful, the anion recognition indeed gave rise to PET quenching which strongly supports that such selective sensing is possible, provided that more enantioselective receptors are employed, *i.e.* the introduction of another chiral centre is necessary.

From the above combined measurements it is clear that the anion recognition occurs through hydrogen bonding of the thiourea receptors to the anions. This gives rise to quenching of the excited state. From these fluorescence changes an accurate binding constant can be determined for ions such as AcO^-, $H_2PO_4^-$ and F^-. Similarly, the change in the ^1H NMR provides us with information about the nature of the binding as well as the strength of these interactions. The final analytical method employed to investigate this sensing, the ground state investigation, however, gives only very minor information as the changes only occur at short wavelengths. Hence, only in the case of **1**, **2** and **4**, where the aromatic receptors absorb do we observe any significant spectral changes, *e.g.* no such changes occur in **3**.

The above results demonstrate the fluorescent PET sensing of biologically important anions using charge neutral receptors. To the best of our knowledge these were the first examples of such anion PET sensors that gave rise to ideal PET behaviour. We are currently working towards modifying our systems for use in more competitive environments, as well as developing more anion enantioselective and sensitive fluorescent PET sensors.

Experimental

General

Reagents (obtained from Aldrich) and solvents were purified using standard techniques. Solvents were dried over the appropriate drying agent before use using standard procedures. Melting points were determined using a GallenKamp melting point apparatus. Infrared spectra were recorded on a Mattson Genesis II FTIR spectrophotometer equipped with a Gateway 2000 4DX2-66 workstation. Oils were analysed using NaCl plates, solid samples were dispersed in KBr and recorded as clear pressed discs. ^1H NMR spectra were recorded at 400 MHz using a Bruker Spectrospin DPX-400 instrument. ^{13}C NMR were recorded at 100 MHz using a Bruker Spectrospin DPX-400 instrument. Fluorescent measurements were made

on a Perkin Elmer LS 50B and on a Varian Cary Eclipse fluorimeter. UV-Vis absorption spectra were recorded at room temperature using a Shimadzu UV-2401PC.

Synthesis of 1–4

Improved synthesis of: 9-(aminomethyl)anthracene, 5. 9-(Bromomethyl)anthracene (1 g, 3.68 mmol) was dissolved in anhydrous $CHCl_3$ (15 mL). This solution was added drop-wise to a solution of hexamethylenetetramine (0.515 g, 3.68 mmol) in 10 mL of anhydrous $CHCl_3$. The resulting solution was refluxed for 5 hours with vigorous stirring. The precipitate was removed by filtration and washed several times with water. The precipitate was added to a mixture of ethanol, water and concentrated HCl (20 : 4 : 5), 29 mL. This mixture was heated at 70 °C, after 1 hour the precipitate had completely dissolved, the solution was kept stirring at 70 °C overnight. Once removed from the heat the solution was then allowed to stand at room temperature overnight and the product precipitated out of solution as a HCl salt. This salt was washed with 10% $KHCO_3$ (10 mL) and extracted into $CHCl_3$ (35 mL). The organic layer was dried over $MgSO_4$. Excess solvent was removed under reduced pressure and the residue was dried over P_2O_5 overnight to give a pale yellow solid (0.708 g, 93%). mp 102 °C (dec.); δ_H(400 MHz, $CDCl_3$): 8.43 (s, 1H, Ar-10H), 8.39 (d, 2H, J = 9.0 Hz, Ar-8H, Ar-1H), 8.06 (s, 2H, J = 8.0 Hz, Ar-4H, Ar-5H), 7.58 (d, 2H, J_1 = 7.5 Hz, J_2 = 7.5 Hz, Ar-2H, Ar-7H), 7.50 (d, 2H, J_1 = 7.5 Hz, J_2 = 8.0 Hz, Ar-3H, Ar-6H), 4.88 (s, 2H, −15H); δ_C(100 MHz, $CDCl_3$): 132.0, 130.9, 130.2, 129.7, 127.7, 126.0, 123.7, 122.9, 35.1; MS *m*/*z* (ES): 207 ($[M]^+$).

9-[4-(Trifluoromethyl)phenyl-thioureidomethyl]anthracene, 2. 9-(Aminomethyl)anthracene, **5** (0. 1 g, 0.483 mM) was dissolved in 20 mL of dry CH_2Cl_2. To this solution was added 4-(trifluoromethyl)phenyl isothiocyanate, **7** (0.098 g, 0.485 mM, 1.01 equiv.). A creamy yellow precipitate was immediately formed upon addition of the isothiocyanate. The reaction was allowed to stir vigorously overnight at room temperature. The resulting precipitate was removed by filtration, washed with dry $CHCl_3$ and dried over P_2O_5, followed by recrystallisation from $CHCl_3$ (0.166 g, 84% yield). mp 197–198 °C; CHN calculated for $C_{23}H_{17}F_3N_2S$: C, 67.30%; H, 4.17%; N 6.82%; found C, 67.28%; H, 4.17%; N, 6.86%; δ_H(400 MHz, $CDCl_3$): 8.53 (s, 1H, 10-H), 8.32 (d, 2H, J = 8.5 Hz, Ar-8H, Ar-1H), 8.09 (s, 2H, Ar-4H, Ar-5H), 7.63 (d, 2H, J_1 = 6.5 Hz, J_2 = 8.5 Hz, Ar-2H, Ar-7H), 7.54 (d, 2H, J_1 = 7.5 Hz, J_2 = 7.5 Hz, Ar-3H, Ar-6H), 7.45 (d, 2H, J = 8.5 Hz, 19-H, 20-H,), 7.16 (d, 2H, J = 8.0 Hz, 18-H, 21-H), 5.83 (s, 2H, 15-H); δ_C(100 MHz, $CDCl_3$): 179.6, 139.56, 131.5, 130.5, 129.5, 127.2, 127.0, 126.6, 123.5, 123.2, 42.7; δ_F(D_6-DMSO, 376.46 MHz); −63.16; IR (KBr) cm^{-1} 3241, 3056, 1542, 1333, 1114, 728.

9-(Phenyl-thioureidomethyl)anthracene, 1. 9-(Aminomethyl)-anthracene, **5** (0.1 g, 0.483 mM) was dissolved in 20 mL of dry CH_2Cl_2. To this solution was added phenyl isothiocyanate, **6** (59 µl, 0.483 mM, 1 equiv.). The resulting solution was stirred overnight at room temperature. The resulting precipitate was removed by filtration, washed with cold CH_2Cl_2 and dried over P_2O_5 and was then recrystallised from $CHCl_3$ (0.127 g, 77% yield). mp 205–207 °C; CHN calculated for $C_{22}H_{18}N_2S$: C, 77.16%; H, 5.30%; N 8.18%; found C, 77.20%; H, 5.29%; N, 8.18%; δ_H(400 MHz, $CDCl_3$): 8.49 (s, 1H, Ar-10H), 8.31 (d, 2H, J = 9.0 Hz, Ar-1H, Ar-8H), 8.05 (d, 2H, J = 8.5 Hz, Ar-4H, Ar-5H), 7.61 (t, 2H, J_1 = 7.5 Hz, J_2 = 7.5 Hz, Ar-2H, Ar-7H), 7.5 (t, 2H, J_1 = 8.5 Hz, J_2 = 7.5 Hz, Ar-3H, Ar-6H), 7.18 (t, 1H, J_1 = 7.5 Hz, J_2 = 8.0 Hz, 20H), 7.10 (d, 1H, J = 7.5 Hz, 18H), 7.04 (d, 1H, J = 7.5 Hz, 19H), 5.82 (d, 2H, J_1 = 4 Hz, 15-H); δ_C(100 MHz, $CDCl_3$): 180.05 (C=S), 139.53, 131.61, 130.26, 129.44, 128.67, 128.43, 126.42, 125.15, 123.92, 129.50, 67.41 (CH_2); IR (KBr) cm^{-1} 3412, 2922, 1509, 1495, 1345, 1256, 717.

9-(Methyl-thioureidomethyl)anthracene, 3. 9-(Aminomethyl)-anthracene, **5** (0.3 g, 1.45 mM) was dissolved in 20 mL of dry CH_2Cl_2. To this solution was added methyl isothiocyanate, **8** (0.18 g, 2.6 mM, 1.8 equiv.). The reaction was allowed to stir vigorously overnight at room temperature. The excess solvent was removed under reduced pressure. The residue was purified by silica flash chromatography with 100% ethyl acetate as the eluent (R_f 0.67). The product was dried over P_2O_5 followed by recrystallisation from $CHCl_3$ (0.155 g, 67% yield). mp 190 °C dec; CHN calculated for $C_{17}H_{16}N_2S$: C, 72.82%; H, 5.75%; N, 9.99%; found C, 72.79%; H, 10.01%; N, 9.98%; δ_H(400 MHz, $CDCl_3$): 8.49 (s, 1H, 10-H), 8.30 (d, 2H, J = 8.5 Hz, Ar-1H, Ar-8H), 8.05 (d, 2H, J = 8.0 Hz, Ar-4H, Ar-5H), 7.59 (t, 2H, J_1 = 6.5 Hz, J_2 = 8.5 Hz, Ar-2H, Ar-7H), 7.51 (t, 2H, J_1 = 7.0 Hz, J_2 = 8.0 Hz, Ar-3H, Ar-6H), 5.66 (s, 2H, 15-H), 2.85 (s, 3H, 17-H); δ_C(100 MHz, $CDCl_3$): 129.1, 128.5, 126.8, 125.16, 123.63, 42.0, 30.2; IR (KBr) cm^{-1} 3204, 3056, 1545, 1333, 1114, 738.

9-(Isothiocyanatomethyl)anthracene 11. 9-(Aminomethyl)-anthracene (600 mg, 2.46 mmol) was added to a biphasic solution of THF (10 mL) and sat. $NaHCO_3$ (10 mL) that was cooled in an ice bath. The mixture was stirred at 0 °C for 20 min. Stirring was stopped and the layers were allowed to separate. Thiophosgene (0.20 mL, 2.66 mmol) was added *via* syringe into the organic phase in one portion. The cool reaction mixture (0 °C) was stirred for a subsequent 3 h to ensure the reaction had gone to completion. The layers were then separated and the aqueous phase was extracted with chloroform (3 × 10 mL). The organic layers were combined and dried over Na_2SO_4, filtered and evaporated to dryness. The crude product was purified by column chromatography on silica gel (9 : 1 hexane–ethyl acetate) to yield the desired product as a yellow solid in 20% yield. The experimental results were in accordance with reference 25. δ_H($CDCl_3$, 400 MHz): 8.55 (s, 1H, An-10H), 8.26 (d, 2H, J = 8.8 Hz, An-8H and An-1H), 8.09 (d, 2H, J = 8.8 Hz, An-4H and An-5H), 7.65 (m, 2H, An-2H and An-7H), 7.54 (m, 2H, An-3H and An-6H), 5.61 (s, 2H, CH_2); δ_C($CDCl_3$, 100 MHz): 132.2, 130.9, 129.5, 128.9, 128.94, 126.8, 124.8, 124.1, 122.5, 40.9.

1-Anthracen-9-ylmethyl-3-(1-phenyl-ethyl)thiourea 4. 9-(Isothiocyanatomethyl)anthracene (2.33 g, 9.36 mmol) was added to anhydrous THF (20 mL). The mixture was stirred at room temperature under an inert environment. (*S*)-(−)-1-phenylethylamine (1.5 mL, 11.6 mmol) was added to the mixture dropwise. The mixture was then refluxed for 12 h, after which a yellow precipitate had formed. The precipitate was isolated by filtration and was washed with THF (3 × 7 mL) to remove any unreacted starting material. The yellow solid was dissolved in chloroform and washed with 1 M HCl (3 × 10 mL) and water (3 × 5 mL), dried over $NaHCO_3$, filtered and concentrated. The desired product was isolated as a yellow solid (310 mg) and did not require any further purification. δ_H(D_6-DMSO, 400 MHz): 8.36 (s, 1H, An), 8.11 (d, J = 8.2 Hz, 2H, An), 7.59 (d, J = 6.8 Hz, 2H, An), 7.55 (m, 4H, 2 × An and 2 × Ar), 7.22 (m, 5H, 2 × An and 3 × Ar), 6.29 (m, 1H, NH), 6.24 (d, J = 7.5 Hz, 1H, NH), 5.19 (m, 2H, CH_2), 4.77 (m, 1H, CH), 1.26 (d, J = 6.8 Hz, 3H, CH_3); δ_C(D_6-DMSO, 100 MHz): 157.2, 145.5, 131.1, 129.6, 128.9, 128.3, 127.1, 126.5, 126.3, 125.6, 125.3, 124.3, 48.7, 35.3, 23.3; IR ν_{max} (cm^{-1}): 3340, 3303, 2360, 2343, 1616, 1571, 1240, 731, 696.

1-Ethyl-3-(4-trifluoromethyl-phenyl)thiourea 13. 4-(Trifluoromethyl)phenyl isothiocyanate (130 mg, 0.64 mmol) was added to anhydrous DCM (5 mL). The mixture was stirred at room temperature under an inert environment. Ethylamine (2 M in THF, 0.5 mL) was added dropwise to the mixture. The reaction was stirred at room temperature overnight after which time TLC of the reaction mixture confirmed reaction of the starting isocyanate. The reaction was washed with 1 M HCl (2 × 15 mL) and extracted with DCM. The organic layer was dried over

$MgSO_4$, filtered and concentrated. The desired product was isolated by precipitation from chloroform as a white solid (100 mg, 63%). *Anal.* Calc. for $C_{10}H_{11}F_3N_2S$: C, 48.38; H, 4.47; N, 11.28. Found: C, 48.42; H, 4.37; N, 11.37%. δ_H(D_6-DMSO, 400 MHz): 9.80 (br s, 1H, NH), 8.06 (br s, 1H, NH), 7.68 (d, J = 8.52 Hz, 4H, Ar), 3.49 (m, 2H, CH_2), 1.14 (t, J = 7.04 Hz, CH_3); δ_C(D_6-DMSO, 100 MHz): 179.9, 143.4, 125.8, 123.3, 121.7, 39.4, 13.9; δ_F(D_6-DMSO, 376.46 MHz): −60.8.

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References

1 *Chemical Sensors and Biosensors for Medical and Biological Applications*, U. S. Spichiger-Keller, Wiley-VCH, Weinheim, Germany, 1998; C. F. Mason, *Biology of Freshwater Pollution*, 2nd edn., Longman, New York, 1991.

2 A. P. de Silva, B. McCaughan, B. O. F. McKinney and M. Querol, *Dalton Trans.*, 2003, 1902; K. Rurack and U. Resch-Genger, *Chem. Soc. Rev.*, 2002, **31**, 116; K. Rurack, *Spectrochim. Acta, Part A*, 2001, **57**, 216; A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515.

3 R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419; C. Suksai and T. Tuntulani, *Chem. Soc. Rev.*, 2003, **32**, 192. *See special issue on anion recognition*: *Coord. Chem. Rev.*, 2003, **240**.

4 P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181.

5 P. D. Beer, *Chem. Commun.*, 1996, 689.

6 E. Bianchi, K. Bowman-James and E. Gracía-Espanña, Eds., *Supramolecular Chemistry of Anions*, Wiley-VCH, New York, 1997.

7 A. Metzger and E. V. Anslyn, *Angew. Chem., Int. Ed.*, 1998, **37**, 649; F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; J. Scheerder, J. F. J. Engersen and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas*, 1996, **115**, 307; J. L. Atwood, K. T. Holman and J. W. Steed, *Chem. Commun.*, 1996, 1401.

8 A. P. Davis, J. F. Gilmer and J. J. Perry, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1312; A. J. Ayling, M. N. Pérez-Payán and A. P. Davis, *J. Am. Chem. Soc.*, 2001, **123**, 12716.

9 P. D. Beer, *Coord. Chem. Rev.*, 2000, **205**, 197.

10 For an earlier communication on this work see: T. Gunnlaugsson, A. P. Davis and M. Glynn, *Chem. Commun.*, 2001, 2556.

11 T. Gunnlaugsson, T. C. Lee and R. Parkesh, *Org. Biomol. Chem.*, 2003, **1**, 3265; T. Gunnlaugsson, B. Bichell and C. Nolan, *Tetrahedron Lett.*, 2002, **43**, 4989; T. Gunnlaugsson, M. Nieuwenhuyzen, L. Richard and V. Thoss, *J. Chem. Soc., Perkin Trans. 2*, 2002, 141.

12 T. Gunnlaugsson, J. P. Leonard, K. Senechal and A. J. Harte, *Chem. Commun.*, 2004, 781; T. Gunnlaugsson, J. P. Leonard, K. Senechal and A. J. Harte, *J. Am. Chem. Soc.*, 2003, **125**, 12062; T. Gunnlaugsson and J. P. Leonard, *Chem. Commun.*, 2003, 2424; T. Gunnlaugsson, D. A. Mac Dónaill and D. Parker, *J. Am. Chem. Soc.*, 2001, **123**, 12866; T. Gunnlaugsson, *Tetrahedron Lett.*, 2001, **42**, 8901; T. Gunnlaugsson, D. A. Mac Dónaill and D. Parker, *Chem. Commun.*, 2000, 93; O. Reany, T. Gunnlaugsson and D. Parker, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1819.

13 T. Gunnlaugsson, A. Harte, J. P. Leonard and M. Nieuwenhuyzen, *Supramol. Chem.*, 2003, **15**, 505; T. Gunnlaugsson, A. Harte, J. P. Leonard and M. Nieuwenhuyzen, *Chem. Commun.*, 2002, 2134; R. S. Dickens, T. Gunnlaugsson, D. Parker and R. D. Peacock, *Chem. Commun.*, 1998, 1643.

14 L. Fabbrizzi, M. Licchelli, G. Rabaioli and A. Taglietti, *Coord. Chem. Rev.*, 2000, **205**, 85.

15 D. H. Vance and A. W. Czarnick, *J. Am. Chem. Soc.*, 1994, **116**, 9397; M. E. Huston, E. U. Akkaya and A. W. Czarnick, *J. Am. Chem. Soc.*, 1989, **111**, 8735.

16 S. Nishizawa, H. Kaneda, T. Uchida and N. Teramae, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2325.

17 Several other researchers have developed luminescent anion sensors using a range of different receptors. Examples include: N. Marcotte and A. Taglietti, *Supramol. Chem.*, 2003, **15**, 617; A. P. de Silva, G. D. McClean and S. Pagliari, *Chem. Commun.*, 2003, 2010; E. J. Cho, J. W. Moon, S. W. Ko, J. Y. Lee, S. K. Kim, J. Yoon and K. C. Nam, *J. Am. Chem. Soc.*, 2003, **125**, 12376; Y. Kubo, S. Ishihara, M. Tsukahara and S. Tokita, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1455; D. H. Lee, H. Y. Lee and J. P. Hong, *Tetrahedron Lett.*, 2002, **34**, 7273; S. O. Kang, S. Jeon and K. C. Nam, *Supramol. Chem.*, 2002, **14**, 405; P. E. Kruger, P. R. Mackie and M. Nieuwenhuysen, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1079; Y. Kubo, M. Tsukahara, S. Ishihara and S. Tokita, *Chem. Commun.*, 2000, 653; P. Anzenbacher, Jr., K. Jursíková and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 9350; H. Miyaji, P. Anzenbacher, Jr., J. L. Sessler, E. R. Bleasdale and P. A. Gale, *Chem. Commun.*, 1999, 1723; H. Xie, S. Yi, X. Yang and S. Wu, *New J. Chem.*, 1999, **23**, 1105; C. B. Blake, B. Andrioletti, A. C. Try, C. Ruiperez and J. L. Sessler, *J. Am. Chem. Soc.*, 1999, **121**, 10438; C. R. Cooper, N. Spencer and T. D. James, *Chem. Commun.*, 1998, 1365; R. S. Dickens, T. Gunnlaugsson, D. Parker and R. D. Peacock, *Chem. Commun.*, 1988, 1643.

18 Since the publication of our communication (ref. 10) several PET anion sensors have been reported: T. Gunnlaugsson, P. E. Kruger, T. Clive Lee, R. Parkesh, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett.*, 2003, **35**, 6575; K. Kim, N. J. Singh, S. J. Kim, H. G. Kim, J. K. Kim, L. W. Lee, K. S. Kim and J. A. Yoon, *Org. Lett.*, 2003, **54**, 2083; A. Coskun, B. T. Baytekin and E. U. S. Akkaya, *Tetrahedron Lett.*, 2003, **35**, 5649; K. Kim and J. T. Yoon, *Chem. Commun.*, 2002, 770; T. Gunnlaugsson, A. P. Davis, J. E. O'Brien and M. Glynn, *Org. Lett.*, 2002, **4**, 2449; S. Sasaki, D. Citterio, S. Ozawa and K. S. Suzuki, *J. Chem. Soc., Perkin Trans. 2*, 2001, 2309 (See also reference 25 for PET sensors).

19 K. H. Choi and A. D. Hamilton, *Coord. Chem. Rev.*, 2003, **240**, 101; K. Kumamoto, Y. Misawa, S. Tokita, Y. Kubo and H. Kotsuki, *Tetrahedron Lett.*, 2003, **44**, 1035; B. R. Linton, M. S. Goodman, E. Fan, S. A. van Arman and A. D. Hamilton, *J. Org. Chem.*, 2001, **66**, 7313; C. K. Lam and T. C. W. Mak, *Tetrahedron*, 2000, **56**, 6657; B. R. Linton, M. S. Goodman and A. D. Hamilton, *Chem. Eur. J.*, 2000, **6**, 2449; T. Hayashita, T. Onodera, R. Kato, S. Nishizawa and N. Teramae, *Chem. Commun.*, 2000, 775; J. L. J. Blanco, J. M. Benito, C. O. Mellet and J. M. G. Fernandez, *Org. Lett.*, 1999, **1**, 1217; A. Casnati, L. Pirondini, N. Pelizzi and R. P. Ungaro, *Supramol. Chem.*, 2000, **12**, 53; K. P. Xiao, P. Buhlmann and Y. Umezawa, *Anal. Chem.*, 1999, **71**, 1183; J. W. M. Nissink, H. Boerrigter, W. Verboom, D. N. Reinhoudt and J. H. van der Maas, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2623; S. Nishizawa, R. Kato, T. Hayashita and N. Teramae, *Anal. Sci.*, 1998, **14**, 595; P. Bühlmann, S. Nishizawa, K. P. Xiao and Y. Umezawa, *Tetrahedron*, 1997, **53**, 1647; J. Scheerder, J. F. J. Engbersen, A. Casnati, R. Ungaro and D. N. Reinhoudt, *J. Org. Chem.*, 1995, **60**, 6448.

20 D. J. Maher and S. J. Connon, *Tetrahedron Lett.*, 2004, **45**, 130; T. Okino, Y. Hoashi and Y. Takemoto, *Tetrahedron Lett.*, 2003, **44**, 2817; P. R. Schreiner and A. Wiikopp, *Chem. Eur. J.*, 2003, 407; P. Vachal and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 10012; M. S. Sigmam and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1998, **120**, 4901.

21 A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *Nature*, 1993, **364**, 42; A. P. de Silva and S. A. de Silva, *J. Chem. Soc., Chem. Commun.*, 1986, 1709; A. P. de Silva and R. A. D. D. Rupasinghe, *J. Chem. Soc., Chem. Commun.*, 1985, 1669.

22 T. M. Fyles and V. V. Suresh, *Can. J. Chem.*, 1994, **72**, 1246.

23 M. Bullpitt, W. Kitching, D. Dodrell and W. Adcock, *J. Org. Chem.*, 1976, **41**, 760.

24 C. V. Kumar and L. M. Tolosa, *J. Phys. Chem.*, 1993, **97**, 13914; B. Alpha, E. Anklam, R. Deschenaux, J. M. Lehn and M. Pietraskiewicz, *Helv. Chim. Acta*, 1988, **71**, 1043.

25 S. Sasaki, D. Cirterio, S. Ozawa and K. Suzuki, *J. Chem. Soc., Perkin Trans. 2*, 2001, 2309.

26 D. F. Eaton, *Pure Appl. Chem.*, 1988, **60**, 1107.

27 A. J. Ayling, S. Broderick, J. P. Clare, A. P. Davis, M. N. Pérez-Payán, M. Lahtinen, M. J. Nissinen and K. Rissanen, *Chem. Eur. J.*, 2002, **8**, 2197.

28 H.-J. Schneider and A. Yatsimirsky, in: *Principles and Methods in Supramolecular Chemistry*, Wiley, UK, 2000.

29 These changes were fitted using a non-linear least squares regression algorithm.

30 Recent examples: M. V. Rekharsky, H. Yamamura, M. Kawai and Y. Inoue, *J. Org. Chem.*, 2003, **68**, 5228; J. V. Hernandez, A. I. Oliva, L. Simon, F. M. Muniz, A. A. Mateos and J. R. Moran, *J. Org. Chem.*, 2003, **68**, 7513; L. Siracusa, F. M. Hurley, S. Dresen, L. J. Lawless, M. N. Pérez-Payán and A. P. Davis, *Org. Lett.*, 2002, **4**, 4639; S. Rossi, G. M. Kyne, D. L. Turner, N. J. Wells and J. D. Kilburn, *Angew. Chem., Int. Ed.*, 2002, **41**, 4233; N. M. Maier, S. Schefzick, G. M. Lombardo, M. Feliz, K. Rissanen, W. Lindner and K. B. Lipkowitz, *J. Am. Chem. Soc.*, 2002, **124**, 8611; L. J. Lawless, A. G. Blackburn, A. J. Ayling, M. N. Pérez-Payán and A. P. Davis, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1329.