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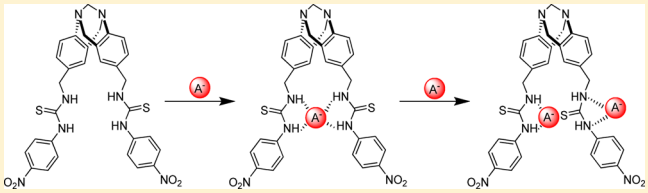
Thiourea Derived Tröger's Bases as Molecular Cleft Receptors and Colorimetric Sensors for Anions

Elaine M. Boyle, Steve Comby, Jennifer K. Molloy, and Thorfinnur Gunnlaugsson*

School of Chemistry, Centre for Synthesis and Chemical Biology and Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin 2, Ireland

Supporting Information

ABSTRACT: Thiourea-functionalized Tröger's base receptors **1** and **2** have been synthesized and evaluated as novel for the recognition of anions. Receptor **2** gave rise to significant changes in the absorption spectrum upon titration with AcO^- and $H_2PO_4^-$ and acted as a colorimetric sensor for F^-, the interaction of which was also evaluated using ^1H NMR spectroscopy.



INTRODUCTION

The recognition of anions via noncovalent interactions is of major interest in host–guest chemistry.[1−3] In particular, molecular clefts have attracted significant attention in supramolecular chemistry due to their ability to allow functional groups to be orientated in defined geometries.[4,5] Specific geometries can also be exploited by arranging the H-bond donors around the acceptors in three-dimensional space, either through the use of single ligands or via a self-assembly formation of more than one such ligand.[6] If the host's preorganized binding cavity complements the guest's geometry, then high selectivity can be achieved, as recently demonstrated by several groups including those of Gale,[7] Steed,[8] Johnson,[9] and Pfeffer.[10] The use of the urea or thiourea moiety in such anion recognition is now well established.[11−14] We have developed many examples of receptors and sensors for anions, using urea and amide functionalities, including employing them into fluorescent emissive structures such as anthracenes[15] and naphthalimides as PET sensors for anions,[16,17] and as colorimetric probes, such as for CO_2 fixation,[18] which was mediated by initial detection of fluoride. Recently, we have also developed Ru(II) polypyridyl[19] and lanthanide[20] complexes possessing such anion recognition systems, and we have developed molecular cleft-type structures, based on pyridyl amidothioureas,[21] and semithiocarbazides[22] with the view of achieving preorganization within such anion recognition moieties. These examples showed very promising properties as hosts for anions, particularly for oxy-anions.

The Tröger's base is a structural motif containing a diazocine ring conjugated to two aromatic moieties, first described by Julius Tröger in 1887,[23] that has more recently become an important building block in supramolecular chemistry.[24] The Tröger's base is chiral, where two aromatic rings fused to the central bicyclic framework, create a rigid, V-shaped, C_2-symmetrical molecular scaffold that places the aryl rings almost 90° to each other. This important shape has played a considerable role in the field of molecular recognition and several receptors for the recognition of carboxylic acids have been developed,[25] and we have recently shown that the Tröger's base building unit can be employed in structures for binding and sensing of nucleic acids and for imaging of cancer cells.[26,27] However, and to the best of our knowledge, their use as a preorganizing unit in the sensing of simple oxy anions has not been explored.[25] With this in mind, we set out to explore the possibility of using the Tröger's base platform for anion recognition and sensing. Herein we report two thiourea-functionalized Tröger's base receptors, **1** and **2**, as "molecular cleft-like" hosts for the recognition of anions. These receptors were easily formed from the Tröger's base benzyl amine **3** in a single step with commercially available isothiocyanates. By incorporating electron-withdrawing moieties into the arylthiourea structures, we demonstrate that the nature of the thiourea moiety greatly affects the sensitivity and the selectivity of the recognition process, which was monitored by using both UV–vis absorption and NMR spectroscopies where the experimental data was analyzed using nonlinear regression analysis, showing that such recognition can occur in both 1:1 and 1:2 (host/guest) stoichiometries. The results from this investigation demonstrate that the Tröger's base motive has a new role to play in anion recognition chemistry; which can also potentially be mapped onto its use in organo-catalysis.[28]

RESULTS AND DISCUSSION

Synthesis of Receptors 1 and 2. The synthesis of receptors **1** and **2** was achieved from **3**, which was formed by using classical organic synthesis, by first reacting potassium phthalimide with 4-nitrobenzyl bromide. Aqueous workup using EtOAC/toluene (2:1) followed by washing with H_2O gave the desired product as white crystals in 64% yield. Reduction of the nitro group was achieved in quantitative yield using Pd/C under 3 atm of H_2, giving the corresponding aniline

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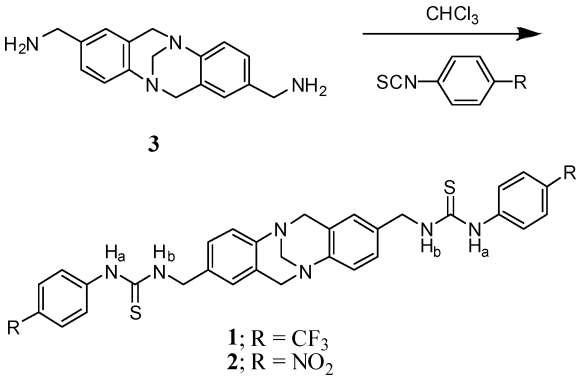
derivative as yellow crystals. Formation of the phthalimide-protected Tröger's base was achieved by using a modified synthesis of that described by Wilcox[23b] by stirring overnight 4-aminobenzylphthalimide with 2 equiv of formaldehyde and TFA, after which the aqueous workup gave the desired phthalimide-based Tröger's base as a brown oil in 30% yield. Deprotection of the phthalimide groups was achieved by stirring with neat hydrazine at 80 °C overnight.[29] The crude product was extracted into $CHCl_3$ and then washed with water, giving **3** as yellow oil in 61% yield. To form **1** and **2**, **3** was simply reacted with the corresponding isothiocyanates in $CHCl_3$ in the presence of triethylamine under reflux overnight, Scheme 1. The crude products were collected by filtration,

Scheme 1. Synthesis of Receptors 1 and 2



followed by trituration with $CHCl_3$, giving compounds **1** in 43% yield as a white solid and **2** as an orange solid in 40% yield. The receptors were fully characterized by 1D and 2D NMR, ^{13}C NMR, mass spectrometry, and elemental analysis; see Figures S1–S4 (Supporting Information). For instance, ^1H NMR (400 MHz, DMSO-d_6, Figures S1 and S3, Supporting Information) of receptors **1** and **2** showed the presence of the two sets of thiourea N–H protons, resonating at 9.84 and 8.35 ppm for the former, while the nitro analogue displayed resonances at 10.15 and 8.58 ppm.

Anion Binding Studies of Receptors 1 and 2. The ability of both **1** and **2** to bind to anions such as acetate, phosphate, chloride, and fluoride as well as "bis-anions" such as pyrophosphate was undertaken in organic solution. The absorption spectrum of receptor **1**, Figure 1, when recorded at room temperature in DMSO shows two main absorption

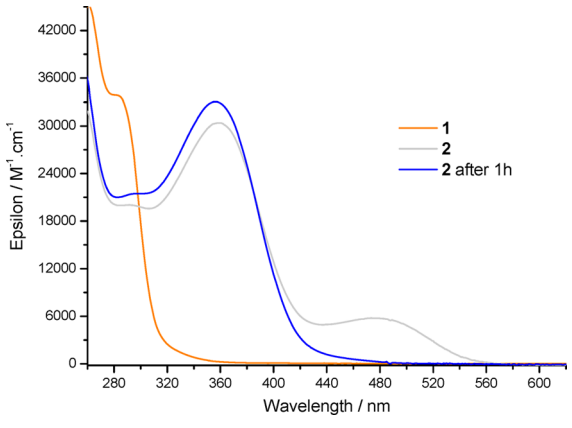


Figure 1. Absorption spectra of receptors **1** and **2** in DMSO.

bands centered at 260 nm and at 284 nm (ε_{284} = 33752 M^{-1} cm^{-1}). In contrast, at high concentrations, the absorption spectrum of receptor **2** displayed three main bands present in the spectrum, at 258, 355 (ε_{355} = 32936 M^{-1} cm^{-1}, calculated after equilibration), and 484 nm, Figure 1. However, over time, the band at 484 nm slowly decreases in absorption before completely disappearing after ca. 1 h standing at room temperature.[30] We attribute this behavior to intermolecular H-bonding occurring in the concentrated stock solution of the receptor as this behavior has already been encountered for bis-thiourea receptors.[31] Excitation at the λ_{max} of each receptor only gave rise to weak fluorescence emission. In fact, X-ray crystal structure analysis of a related structure possessing carboxylic ester developed in our laboratory indeed showed such interactions in the solid state with extended $\pi-\pi$ packing and/or packing of a Tröger's base-cleft within another cleft.[32] Recently, Kruger et al.[32] and Giannis and co-workers[33] have seen similar phenomena in the solid state in their work on Tröger's bases, even though in the latter case the presence of CH–π interactions was triggering the formation of the dimeric species.

The anion-binding abilities of the receptors were evaluated using UV–vis absorption and ^1H NMR spectroscopy. Solutions of $H_2PO_4^-$, AcO^-, F^-, and SO_4^{2-} as their TBA salts in DMSO were titrated against a solution of either **1** or **2** (1×10^{-5} M) in DMSO. All titrations were repeated several times to ensure full reproducibility. Detailed absorption titrations were first carried out with **1** and $H_2PO_4^-$, as Pfeffer et al. had previously shown that cleft-like structures based on the use of preorganized thiourea functionalized [3]polynorbornane receptors give excellent selectivity for phosphate and bis-carboxylate anions.[10] However, to our surprise, the changes in the absorption spectra of **1** were only minor, see Figure S5 (Supporting Information). We thus investigated the binding of the more structurally simple AcO^- and SO_4^{2-} anions to receptor **1**. The absorption spectrum of **1** was mostly unaffected upon addition of the anions, and only minor changes were observed at 284 nm, with a very weak hyperchromic and hypochromic effect for AcO^- (+3%) and SO_4^{2-} (−8%), respectively, Figures S6–S7 (Supporting Information). The minor changes observed in the UV–vis spectrum of **1** upon anion addition are most likely due to the fact that both free and bound species have very similar UV–vis spectra as this behavior has already been observed in other CF_3-containing receptors.[5a]

Conversely, the titration of **1** with F^- did result in significant changes in the absorption spectrum; a new absorption band was observed at 332 nm, while the band at 284 nm decreased in absorbance, resulting in the concomitant formation of an isosbestic point at 300 nm, Figure S8 (Supporting Information). Analysis of these changes showed that these could be attributed to initial hydrogen bonding of the anion to the receptor moieties, rapidly followed by deprotonation and concomitant formation of the stable HF_2^- anion in solution, but such a phenomenon has been well documented.[18]

Similar UV–vis titrations were next performed with receptor **2**. In contrast to that observed for receptor **1**, the absorption spectrum of **2** exhibited significant changes upon binding to $H_2PO_4^-$, Figure 2. The band centered at 355 nm experienced a gradual bathochromic shift to reach a λ_{max} of 370 nm after the addition of 50 equiv of $H_2PO_4^-$. The 15 nm red shift observed for the high energy absorption band was further accompanied by the appearance of a new absorption band at 480 nm.

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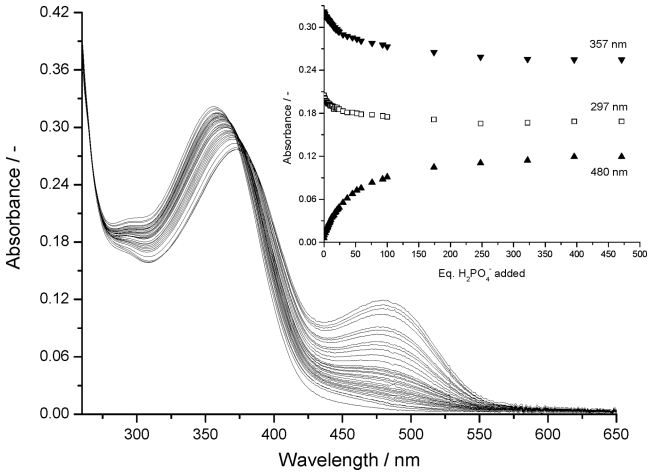

Figure 2. Evolution of the absorption spectrum of receptor **2** (ca. 10 μM) in DMSO upon titration with $H_2PO_4^-$. Inset: Changes observed at 297, 357, and 480 nm as a function of the equivalents of $H_2PO_4^-$ added.

Similarly, upon titration with AcO^-, again the new band at ca. 480 nm appears during the course of the titration and the band at ca. 355 nm also experiences a bathochromic shift similar to that seen for $H_2PO_4^-$, Figure 3. There was no clear

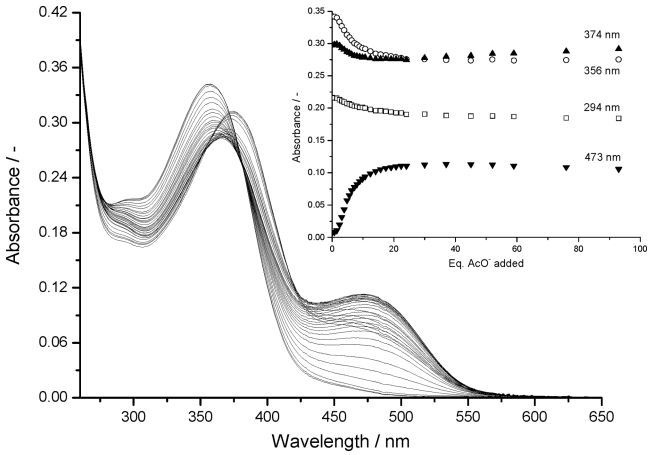

Figure 3. Evolution of the absorption spectrum of receptor **2** (ca. 10 μM) in DMSO upon titration with AcO^-. Inset: Changes observed at 294, 356, 374, and 473 nm as a function of the equivalents AcO^- added.

isosbestic point observed in this titration, but a "pseudo" isosbestic point at ca. 377 nm could be seen. In comparison to the titration with $H_2PO_4^-$, a plateau was reached much earlier, at ca. 20 equivalents of the anion. It can also be seen that at higher concentrations of AcO^-, from ca. 200 eq., absorbance of the bands at 355 and 480 nm undergo a slight increase and decrease respectively, indicating the changes are biphasic.

In contrast to the results obtained for $H_2PO_4^-$ and AcO^-, SO_4^{2-} resulted in no significant modulation of the absorption spectrum of **2**, even at over 400 equiv of the anions, Figure S9 (Supporting Information). The titration of **2** and F^- resulted in significant changes of the absorption spectrum that were accompanied with a color change from colorless to orange, Figure 4A. The absorbance maximum at ca. 355 nm experienced a hypochromism; however, no red shift of this band occurred. The presence of two "pseudo" isosbestic points at ca. 286 and 392 nm can be seen. Nevertheless, a plateau for this titration is not reached until ca. 100 equiv of F^-, Figure 4B. From the observed changes in the UV–vis absorption studies, the binding affinities of each receptor with different anions (**1** vs F^- and **2** vs F^-, AcO^- and $H_2PO_4^-$) were determined using SPECFIT. The binding constants obtained are summarized in Table 1. The data obtained from the titration of **2** with AcO^- and $H_2PO_4^-$ were both best fitted to a 1:1 and 2:1 (guest:host) stoichiometry, indicating identical binding modes for these two oxyanions. As expected from the changes in the UV–vis spectra, similar binding constants were determined for these anions with the values for $H_2PO_4^-$ only marginally higher than that obtained for AcO^-. An excellent fit of the data was obtained for both of these anions, Figure 5A and Figure S10 (Supporting Information).

The speciation distribution diagram demonstrates $H_2PO_4^-$ binds to the receptor with an initial 60% formation of the 1:1 species, forming at lower concentrations before evolving toward the 2:1 species, the latter becoming the most dominant species in solution (ca. 80% formation) at higher equivalents, Figure 5B. At ca. 100 equiv of $H_2PO_4^-$, both species are present in solution in almost equal concentrations. The speciation of the titration with AcO^- was almost identical as shown in Figure S10 (Supporting Information). These interactions are undoubtedly H-bonding between the thiourea moiety of **2** and these anions.

The results obtained for F^- are very similar to that seen for **1** and are most likely due to H-bonding initially, but deprotonation is the main outcome which can be concluded from these titrations. As for the oxyanions, the titration of **2** with F^- was best fitted using a model involving three colored species, namely receptor **2** and 2:1 and 4:1 (guest:host) species, Figure S11 (Supporting Information). The initial formation of a 2:1 (guest:host) species, where each F^- anion is hydrogen-bonded to the thiourea protons that are directly conjugated to the electron-withdrawing NO_2 groups, is followed by the formation of a 4:1 (guest:host) species and subsequent deprotonation and release of HF_2^-. The binding constants obtained for **2** and F^- reflect the higher acidity of the thiourea protons as a result of the highly electron withdrawing NO_2 group compared to the CF_3 derivative.

The varying response of this receptor compared to the CF_3 analogue with the anions studied has provided some very interesting results. Receptor **2** does indeed show H-bonding interactions with AcO^- and $H_2PO_4^-$ with relatively strong binding constants determined for both the 1:1 species (log $K_{1:1}$ = 4.13 ± 0.03 and 4.25 ± 0.05, respectively) and the 2:1 complex (log $K_{2:1}$ = 3.10 ± 0.05 and 3.15 ± 0.07, respectively), while receptor **1** showed no or extremely weak interaction with these anions. Interestingly, neither receptor showed any binding interaction with SO_4^{2-}. The most significant changes occurred between both receptors and F^-. However, due to the presence of the nitro groups, which are more electron-withdrawing than the CF_3 groups of **1**, the N–H protons of **2** are highly acidic and more readily deprotonated. This translates into an overall binding constant log $\beta_{4:1}$ that is more than 1 order of magnitude larger for **2** than for the CF_3 analogue **1**. Interestingly, colorimetric changes have been observed for **2** upon addition of F^- while such changes were not observed for the other anions studied, Figure 4A. Because of these interesting results, we next investigated the anion recognition further using ^{1}H NMR spectroscopy, which will be discussed in the next section.

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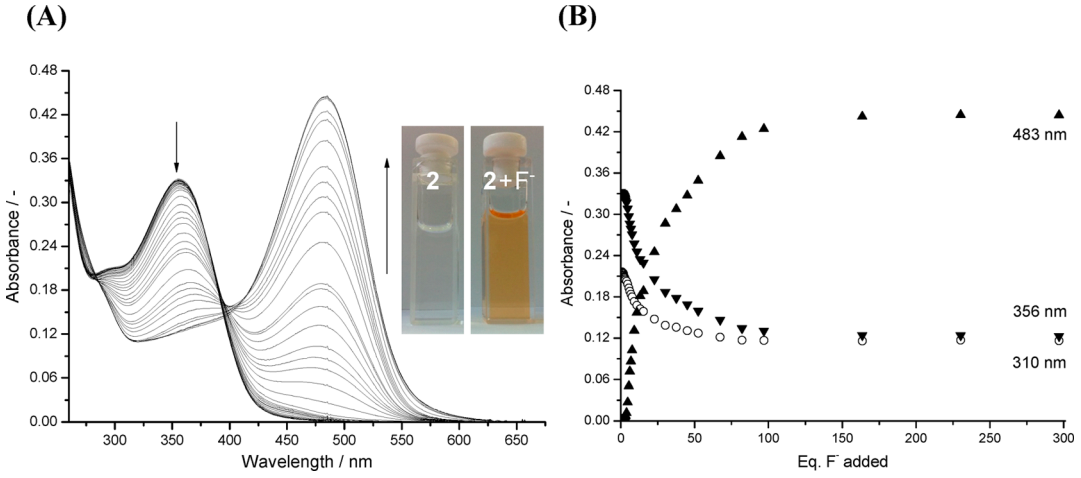

Figure 4. (A) Evolution of the absorption spectrum of receptor **2** (ca. 10 μM) in DMSO upon titration with F^-. Inset: photographs of receptor **2** before and after the addition of F^-. (B) Changes observed at 310, 356, and 483 nm as a function of the equivalents of F^- added.

Table 1. Binding Constants and Binding Modes between Anions and Receptors 1 and 2 as Determined from the Analysis of the UV–vis Titrations Performed in DMSO

receptor	anion	binding mode G_n:L_m	log $\beta_{n:m}$ ± std dev
1	F^-	G_4:L	13.48 ± 0.04
2	AcO^-	G:L	4.13 ± 0.03
		G_2:L	7.23 ± 0.05
2	$H_2PO_4^-$	G:L	4.25 ± 0.05
		G_2:L	7.40 ± 0.07
2	F^-	G_2:L	8.19 ± 0.04
		G_4:L	14.88 ± 0.08

Given our experience in the binding of bis-anions, such as bis-carboxylates and pyrophosphate[5,10b,21] using preorganized calixarene hosts, and inspired by the work of Ghosh et al. and Moriwaki et al.,[25] we also investigated the binding of **1** and **2** to pyrophosphate. We had anticipated that possibly the bis-anion could bridge the cavity of the Tröger's base, binding in a 1:1 stoichiometry. However, while the changes observed in the UV–vis absorption spectra were similar to that observed above, we were unable to obtain reliable binding constants from these changes. It is possible that unlike that demonstrated by Ghosh et al.[25a] the thiourea receptors of **1** and **2** might not facilitate the binding of such bis-anions with the same ease as the changes observed only occurred at higher concentrations of pyrophosphate. We are currently carrying out modifications on **1** and **2**, with the view of achieving such bis-anion binding.

^{1}H NMR Titration of Receptors 1 and 2 with Anions. Having evaluated the ability of **1** and **2** to bind various anions using UV–vis titrations, we next investigated the mode of binding using NMR. The changes in the ^{1}H NMR spectra of **1** and **2** in DMSO-d_6 solutions were monitored upon the addition of AcO^- and $H_2PO_4^-$ as their TBA salts, as these were the two anions that showed the most significant spectral differences between the two receptors. A titration with TBA SO_4^{2-} was also carried out to determine if any interaction between this anion and the receptors occurred at higher concentrations. The chemical shifts of the thiourea protons were monitored after addition of the different anions to evaluate and determine the strength of the interaction taking place with receptors **1** and **2**. The data were plotted as the cumulative changes in chemical shift ($\Delta\delta$) against the equivalents of anion added, where NH_a refers to the thiourea protons that are directly linked to the *para*-substituted phenyl of receptors **1** and **2** and NH_b to the remaining thiourea protons.

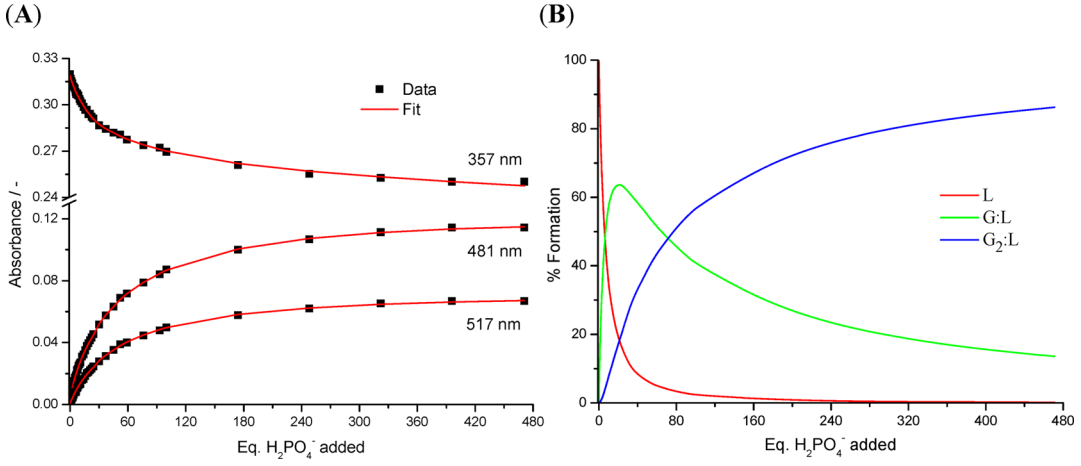

Figure 5. (A) Experimental binding isotherms for the UV–vis titration of **2** (ca. 10 μM) with $H_2PO_4^-$ (0→471 equivalents) in DMSO and their corresponding fit by means of SPECFIT (—). (B) Speciation distribution diagram obtained from the fit of the titration of **2** (L) with $H_2PO_4^-$ (G).

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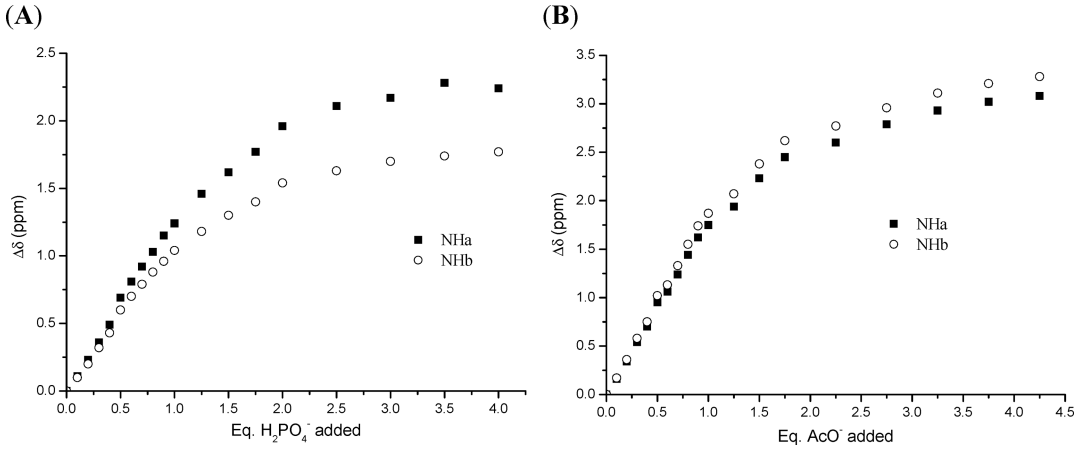

Figure 6. Changes in the thiourea proton resonances NH_a and NH_b of receptor **1** (as $\Delta\delta$) upon titration with $H_2PO_4^-$ (A) and AcO^- (B).

Although no significant changes were observed in the absorption spectrum of **1** upon titration of $H_2PO_4^-$, changes were observed in the ^1H NMR spectrum upon addition of $H_2PO_4^-$, depicted by the binding isotherm in Figure 6A. The anion did interact with the receptor resulting in a chemical shift of ca. 2.2 ppm for the NH_a protons being observed after the addition of 4 equiv of $H_2PO_4^-$ and a smaller shift of ca. 1.7 ppm for the NH_b ones. A plateau was reached after the addition of 2.5−3 equiv of the anion. The doublet assigned to the protons of the phenyl ring *ortho* to the CF_3 group also experienced a downfield shift, but to a much lesser extent ($\Delta\delta \sim 0.4$ ppm). These changes, indicative of H-bonding, were only observed in the NMR studies as the absorption spectrum of **1** displayed only minor changes upon addition of $H_2PO_4^-$, see Figure S5 (Supporting Information). The data obtained from the titration of **1** with AcO^- showed an almost identical trend than for $H_2PO_4^-$, Figure 6B.

The binding of AcO^- to receptor **1** resulted in larger downfield shifts of the thiourea protons (ca. 3 and 3.2 ppm for NH_a and NH_b, respectively) than the ones observed upon binding to $H_2PO_4^-$, Figure 6. This is indicative of a larger perturbation of the magnetic environment of **1** upon binding to AcO^- compared to $H_2PO_4^-$. The doublet assigned to the protons of the phenyl ring *ortho* to the CF_3 group also experienced a small downfield shift as shown in Figure 7. This binding interaction, most likely due to H-bonding, was also not seen during the UV−vis titration of **1** with AcO^-.

The successive addition of $H_2PO_4^-$ to **2** resulted in significant changes in the chemical shifts of the thiourea protons. In the case of NH_a, the resonance became considerably broadened after the addition of ca. 0.5 equiv and progressively disappeared once higher equivalents of $H_2PO_4^-$ were added. Therefore, only the NH_b proton resonance could be followed throughout the course of the titration, Figure 8A. In contrast to the results seen for receptor **1**, the phenyl protons *ortho* to the thiourea shifted downfield, while the protons *ortho* to the NO_2 group shifted upfield, simultaneously experiencing significant broadening. Additionally, the aromatic protons adjacent to the Tröger's base moiety and their multiplicities were clearly resolved up until ca. 1 equiv of the anion before also becoming broadened. A color change from pale yellow to deep orange was observed after the addition of ca. 0.5 equiv of $H_2PO_4^-$. The titration of **2** and AcO^-, a plot of $\Delta\delta$ versus the equivalents of AcO^- added, as shown in Figure 8B, was slightly different from that seen for

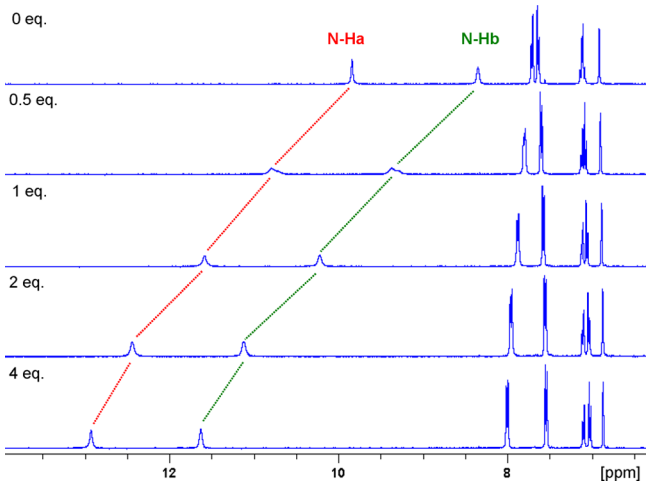

Figure 7. Stack plot of the ^1H NMR (400 MHz, DMSO-d_6) spectra of receptor **1** upon addition of AcO^-.

$H_2PO_4^-$. The two thiourea resonances were clearly visible throughout the entire titration, showing almost identical changes in chemical shifts, with both signals experiencing a downfield shift of over ca. 3 ppm. Similar to what was observed for receptor **1**, the extent of shift is larger than the one seen for $H_2PO_4^-$, which confirms that the binding of AcO^- leads to a stronger difference in the magnetic environment between the free and bound states. The phenyl protons adjacent to the thiourea moiety merged to become one singlet at ca. 2 equiv of the anion, while the other aromatic resonances became more resolved. The binding profile indicates a plateau was reached at ca. 2 equiv of the anion. Again, a drastic color change from pale yellow to deep orange was observed almost immediately after the addition of 0.2 equiv of AcO^-. In direct contrast, the titration of both receptors **1** and **2** with SO_4^{2-} did not result in any perturbation of the thiourea protons or any other resonances in the spectrum, corroborating the results obtained from the UV−vis absorption titrations, Figures S12−S13 (Supporting Information).

The binding constants for the interaction of the different anions with receptors **1** and **2** were determined using *NMRTit HGG*.[34] The cumulative changes in chemical shift plotted against the equivalents of anion added were best fitted following a binding model involving the presence of two main species, namely a 1:1 and 2:1 (guest:host) species. An

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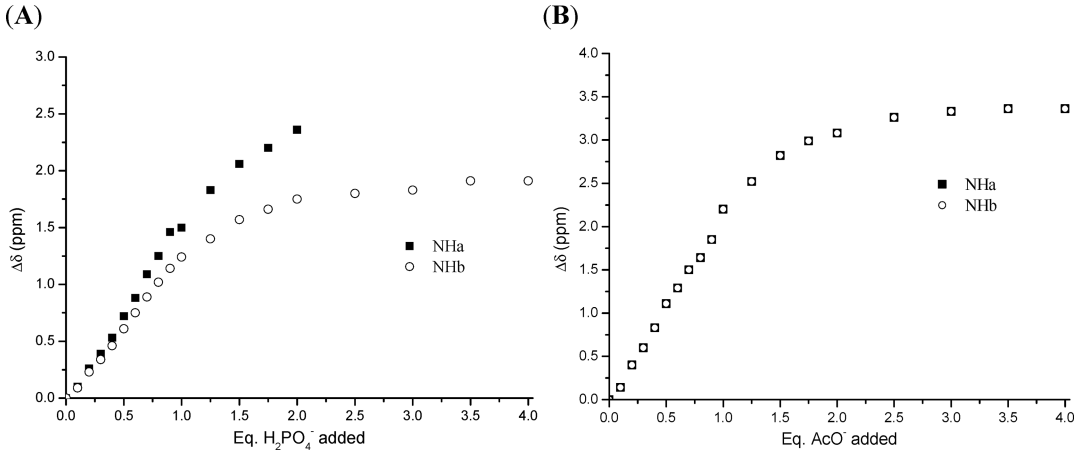

Figure 8. Changes in the thiourea resonances NH_a and NH_b of receptor **2** (as $\Delta\delta$) upon titration with $H_2PO_4^-$ (A) and AcO^- (B).

excellent fit of the NMR data was obtained for **1** and **2** with $H_2PO_4^-$ and AcO^- (Figures S14 and S15, Supporting Information), and the binding constants determined are summarized in Table 2.

Table 2. Binding Constants and Binding Modes between Anions and Receptors 1 and 2 as Determined from the Analysis of the ^{1}H NMR Titrations Performed in DMSO-d_6

receptor	anion	binding mode G_n:L_m	log $\beta_{n:m}$ ± std dev
1	$H_2PO_4^-$	G:L	3.42 ± 0.05
		G_2:L	5.99 ± 0.09
1	AcO^-	G:L	3.18 ± 0.05
		G_2:L	6.25 ± 0.09
2	$H_2PO_4^-$	G:L	4.21 ± 0.06
		G_2:L	7.21 ± 0.11
2	AcO^-	G:L	4.22 ± 0.06
		G_2:L	7.40 ± 0.11

The values obtained for **2** were in good agreement with those determined from the UV−vis titrations. Conversely, the binding constants of receptor **1** with the different anions were found to be lower than those determined for **2**.

The ^{1}H NMR titrations of receptors **1** and **2** gave some interesting results. The studies performed on receptor **1** demonstrated that interactions occurred with $H_2PO_4^-$ and AcO^-. Indeed, contrary to the absorption studies above, it can be concluded that these anions do in fact form H-bonded complexes with the receptor. The results for receptor **2** were found to be in agreement with the UV−vis spectroscopic titrations as the formation of H-bonded complexes with $H_2PO_4^-$ and AcO^- was confirmed. Color changes were also observed upon addition of these anions to **2**. Interestingly, as before, neither receptor was found to interact with SO_4^{2-}.

CONCLUSION

In this paper, we demonstrate that the attachment of thiourea functional groups, capable of forming H-bonds, at the extremities of the Tröger's base skeleton can be used successfully to create synthetic receptors for the recognition of anions. The two receptors were synthesized and fully characterized, and a description of their spectroscopic properties has been described. The anion recognition abilities of both receptors were investigated by absorption and ^{1}H NMR spectroscopy. The presence of H-bonding interactions between the CF_3 derivative **1** and the oxy-anions, AcO^- and $H_2PO_4^-$, were only observed in the ^{1}H NMR studies as addition of these anions resulted in no or extremely weak changes during the UV−vis absorption titrations. Conversely, receptor **1** underwent deprotonation upon titration with F^-. The NO_2 derivative **2** was found to be selective for AcO^- and $H_2PO_4^-$, while acting as a colorimetric sensor for F^-, most likely via deprotonation. Attaching H-bond donor units to a suitable molecular scaffold is a common method for achieving preorganization of the binding cavity and the use of conformationally preorganized receptors have been shown to bind anions very efficiently. The two thiourea functionalized Tröger's base receptors detailed herein are the first example of this unique structural framework being incorporated into synthetic receptors for anions. The results highlight the fact that exceptionally strong complexation can be achieved through the active cooperation of multiple, prepositioned H-bonds in a preorganized binding cavity. We are currently investigating the use of other Tröger's base receptors based on this design as molecular clefts for bis-carboxylates anions and for use in anion-driven supramolecular self-assembly formations.

EXPERIMENTAL SECTION

Starting Materials and General Procedures. All solvents and chemicals were purchased from commercial sources and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded in dimethyl-d_6 sulfoxide (>99.8 atom % D) using either a 400 or 600 MHz NMR spectrometer. Chemical shifts are reported in ppm using deuterated solvents as internal standards. Full assignments of the resonances observed in the ^{1}H NMR spectra of receptors **1** and **2** have been confirmed by measuring ^{13}C−^{1}H and ^{15}N−^{1}H HSQC and HMBC COSY experiments. Midinfrared spectra were recorded using a FT-IR spectrometer equipped with a universal attenuated total reflection (ATR) sampler. Mass spectrometry was carried out using HPLC grade solvents. MALDI Q-ToF mass spectra were carried out on a MALDI Q-ToF Premier, and high-resolution mass spectrometry was performed using Glu-Fib as an internal reference (peak at m/z 1570.6774).

Bis-1-benzyl-3-(4-(trifluoromethyl)phenyl)thiourea[1,5]-diazocene, Receptor 1. 2,8-Bis(methanamine)-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (**3**) (0.246 g, 0.88 mmol) was dissolved in $CHCl_3$ with Et_3N and stirred vigorously while trifluoro-*p*-tolyl isothiocyanate (0.358 g, 1.76 mmol) was added dropwise in $CHCl_3$ over 1 h. The solution was heated at reflux overnight, after which the product was isolated by suction filtration to give a white solid in 43% yield (0.260 g): mp = 211−213 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 9.80 (s, 2H), 8.31 (s, 2H), 7.71 (d, 2H, J = 8.5 Hz),

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7.62 (d, 2H, J = 8.5 Hz), 7.12 (d, 2H, J = 8.4 Hz), 7.09 (d, 2H, J = 8.4 Hz), 6.91 (s, 2H,), 4.61 (d, 2H, J = 16.8 Hz), 4.58 (bs, 4H, CH_2), 4.22 (s, 2H,), 4.09 (d, 2H, J = 16.7 Hz); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C 180.3, 147.1, 143.3, 133.4, 127.8, 126.6, 126.0, 125.6, 125.2, 124.7, 123.5, 121.9, 66.3, 58.3, 46.8; ^{19}F NMR (376 MHz, DMSO-d_6) δ_F −60.8; HRMS (m/z) (MALDI-ToF) calcd for $C_{33}H_{29}N_6F_6S_2$ m/z = 687.1799 $[M + H]^+$, found m/z = 687.1801; IR ν_{max} (cm^{-1}) 3250, 1616, 1543, 1493, 1462, 1422, 1321, 1266, 1209, 1166, 1121, 1066, 1016, 978, 962, 942, 888, 836, 744, 670. Anal. Calcd for $C_{33}H_{28}F_6N_6S_2 \cdot 0.2H_2O$: C, 57.41; H, 4.15; N, 12.17. Found: C, 57.02; H, 4.03; N, 12.44.

Bis-1-benzyl-3-(4-nitrophenyl)thiourea[1,5]diazocene, Receptor 2. Compound **3** (0.19 g, 0.68 mmol) was dissolved in $CHCl_3$ with Et_3N and stirred vigorously while 4-nitrophenyl isothiocyanate (0.26 g, 1.43 mmol) was added dropwise in $CHCl_3$ over 1 h. The solution was heated at reflux overnight at 65 °C, after which the product was isolated by suction filtration to give an orange solid in 40% yield (0.17 g): mp = 215−217 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ_H 10.11 (s, 2H), 8.54 (s, 2H), 8.16 (d, 2H, J = 9.1 Hz), 7.82 (d, 2H, J = 9.2 Hz), 7.13 (d, 2H, J = 8.1 Hz), 7.09 (d, 2H, J = 8.2 Hz), 6.92 (s, 2H,), 4.61 (d, 2H, J = 17.1 Hz), 4.59 (bs, 4H, CH_2), 4.22 (s, 2H), 4.09 (d, 2H, J = 16.8 Hz); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C 180.0, 147.2, 146.3, 141.8, 133.1, 127.9, 126.6, 126.0, 124.7, 124.4, 120.4, 66.3, 58.3, 46.8; HRMS (m/z) (ES$^+$) calcd for $C_{31}H_{29}N_8O_4S_2$ m/z = 641.1753 $[M + H]^+$, found m/z = 641.1740. IR ν_{max} (cm^{-1}) 3295, 3082, 2979, 1597, 1495, 1453, 1327, 1319, 1257, 1231, 1171, 1111, 969, 875, 849, 751, 725, 721. Anal. Calcd for $C_{31}H_{28}N_8O_4S_2 \cdot 0.2H_2O \cdot 0.2CHCl_3$: C, 56.08; H, 4.31; N, 16.77. Found: C, 56.27; H, 4.53; N, 17.01.

Preparation of the Anion Solutions. The TBA salts of the various anions used in the titrations were purchased from a commercial supplier. All TBA salts were dried over P_2O_5 at 313 K under vacuum, except for TBAF·$3H_2O$, which was dried under vacuum at room temperature. The dried salts were then used to prepare the different anion stock solutions required on the day of the titration.

UV−vis Spectrophotometry. UV−vis absorption spectra were measured in 1-cm quartz cuvettes. Baseline correction was applied for all spectra. The DMSO used for the UV−vis studies was of spectroscopic grade (≥99.8%, GC). The temperature was kept at 298 K throughout the measurements by using a thermostated unit block. All stock solutions were freshly prepared prior to measurement. Solutions of **1** and **2** were prepared at a concentration of 10^{-3} M in DMSO before being diluted to the desired concentration before titration (ca. 10^{-5} M). The exact concentration of the host solution in the titration cell was confirmed using the molar absorption coefficient calculated for each host. The solutions of the TBA salts were prepared in DMSO at varying concentrations of ca. 10^{-3}, 5×10^{-3}, and 10^{-2} M. Binding constants of receptors **1** and **2** with the different anions were determined using the nonlinear regression analysis software SPECFIT.

^{1}H NMR Spectroscopy. ^{1}H NMR titrations were carried out on a 400 MHz NMR spectrometer at 298 K. Solutions of **1** and **2** were prepared freshly before titration at a concentration of 7×10^{-3} M in DMSO-d_6. The solutions of the TBA salts were prepared in DMSO-d_6 at varying concentrations such that 2−5 μL would correspond to ca. 0.1 molar equiv of anion. Binding constants of receptors **1** and **2** with the different anions were determined using the program *NMRTit-HGG* (for 1:2 host:guest complexes).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of receptors **1** and **2**; UV−vis absorption titrations and ^{1}H NMR titrations of **1** and **2** and corresponding fits. For each figure, see the main text for reference. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: gunnlaut@tcd.ie.

Notes

The authors declare no competing financial interest.

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