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PAPER

Synthesis and evaluation of thiosemicarbazones functionalized with furyl moieties as new chemosensors for anion recognition†

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A family of heterocyclic thiosemicarbazone dyes (**3a–f** and **4**) containing furyl groups was synthesized in good yields, characterized and their response in acetonitrile in the presence of selected anions was studied. Acetonitrile solutions of **3a–f** and **4** showed absorption bands in the 335–396 nm range which are modulated by the electron donor or acceptor strength of the heterocyclic systems appended to the thiosemicarbazone moiety. Fluoride, chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulphate, nitrate, acetate and cyanide anions were used in recognition studies. From these anions, only sensing features were seen for fluoride, cyanide, acetate and dihydrogen phosphate. Two clearly different chromofluorogenic behaviours were observed: (i) a small shift of the absorption band due to the coordination of the anions with the thiourea protons and (ii) the appearance of a new red shifted band due to deprotonation. For the latter effect, a change in the colour of solution from pale yellow to purple was observed. Fluorescence studies were also in agreement with the different effects observed in the UV/Vis titrations. In this case, hydrogen bonding interactions were visible through the enhancement of the emission band, whereas deprotonation induced the appearance of a new red-shifted emission. Logarithms of stability constants for the two processes (complex formation + deprotonation) for receptors **3a–f** in the presence of fluoride and acetate anions were determined from spectrophotometric titrations using the HypSpec V1.1.18 program. Semi-empirical calculations to evaluate the hydrogen-donating ability of the receptors and a prospective electrochemical characterization of compound **3b** in the presence of fluoride were also performed.

Introduction

The development of new molecular systems for the detection of anions, cations or neutral molecules has gained prime importance in recent years due to the significance of detecting target species in biological and environmental samples. In this area, designed receptors are able to transform, upon coordination, host–guest interactions into a measurable signal which allows analyte recognition and sensing through optical or electrochemical responses.[1] In particular, optical outputs are attractive given the possibility of using low-cost, widely available instrumentation. Apart from the development of fluorescent probes, chromogenic recognition has drawn attention because it offers the possibility of straightforward semiquantitative "naked-eye" detection.[2] Moreover, the colorimetric probes showing a simple displacement of the absorption band allow one to develop ratiometric methods, thus avoiding the use of an internal reference. Optical detection for metal cations was developed more than two decades ago,[3] yet anionic chromogenic receptors have only recently been investigated.[4] The latter focus on anions are mainly due to the more challenging chemistry of host–anion interactions, the lower stability constants observed with anionic species when compared with metal cations, the complex and varied shapes found for anions, their possible dependence on pH and the strong competition of water usually found for receptor–anion complexes based on hydrogen-bonding interactions.[5]

Despite these setbacks, the supramolecular chemistry of anions has advanced a great deal in the last few years mainly due to the progress made in the knowledge of how the formation of host–anion complexes operates. Based on these advances, a number of receptors for anion binding have been developed,

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most of which are based on hydrogen bonding and electrostatic interactions.[6] In contrast to purely electrostatic interactions, which are only distance-dependent, hydrogen bonds offer the advantage of being directional which allows one to discriminate between anions of different geometries or hydrogen-bonding requirements.[7] Among the neutral anion binding groups, thioureas and thiourea-containing fragments have been widely used for the formation of complexes with anions because the hydrogen-bonding ability of these functional groups commonly results in the formation of quite stable complexes, and also because they can be easily synthesized from commercially available reagents by a single-step procedure.[8] In fact, thiourea derivatives have been the subject of intense research given their performance in the development of anion receptors and, for instance, thioureas (and also ureas) have been demonstrated as good coordinating groups for Y-shaped anions such as carboxylates.[9] Moreover, the hydrogen-bonding ability of the thiourea moiety depends on the acidity of the thioureido NH protons and the number of binding sites. A means of tuning this acidity is to introduce electron-donating or electron-withdrawing substituents.[10] Additionally, experimental and theoretical studies have demonstrated that replacing the benzene ring of a chromophore bridge with easily delocalizable five-member heteroaromatic rings, such as thiophene, pyrrole and thiazole, results in enhanced intramolecular electronic delocalization.[11]

On the other hand, among the molecules containing thiourea fragments, the use of thiosemicarbazones has recently gained interest as potential receptors. Schiff base compounds containing thiosemicarbazone groups have also grown in the biology and chemistry areas due to ample biological activity,[12] such as antitumoural, fungicidal, bactericidal, or antiviral, and nonlinear optical properties.[13] Moreover, thiosemicarbazones have also gained attention recently as anion receptors due to their easy synthesis. Also, thiosemicarbazones will be easily included in aromatic frameworks functionalized with acceptor and donor moieties in order to fine tune the acidity of the NH protons. In fact, we and others have recently demonstrated that π-conjugated heterocyclic derivatives, containing thiosemicarbazone moieties, are suitable systems for the colorimetric and fluorimetric sensing of anions.[14] Following this previous work on the synthesis and evaluation of thiosemicarbazones as binding groups, and by also considering our interest in the development of new probes for anion recognition, we report herein the synthesis and the characterization of new *N*-phenylthiosemicarbazones. As a special feature, these newly reported derivatives additionally contain heteroaromatic π-conjugated systems (instead of the more commonly used benzene rings) because anion chemosensors containing phenylthioureas functionalized with heterocyclic moieties are still unusual. The new reported receptors contain furan (instead of thiophene as we have reported recently)[14] as aromatic rings. The underlying idea of the present paper was to evaluate the effect in the binding efficiency of the thiosemicarbazone moiety upon functionalization with furan groups.

Results and discussion

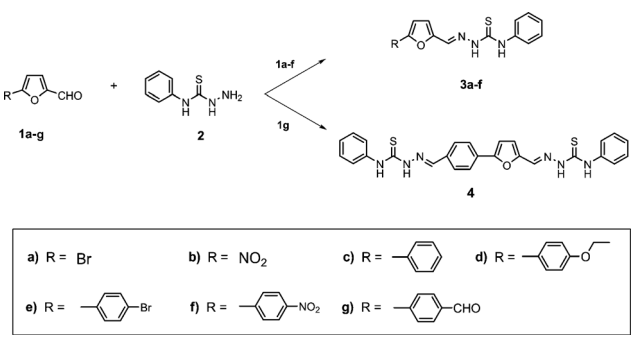
Synthesis and characterization

Different formyl precursors **1a–g** containing several substituents, such as bromo, nitro and alkoxy, linked to different π conjugating bridges were used to evaluate the influence of the structure modification (*i.e.*, donating and accepting strength of these groups, and the nature and length of the π-conjugated bridge) on the optical properties of prepared *N*-phenylthiosemicarbazones **3a–f** and **4**. The new compounds containing furan and arylfuran π-conjugated bridges were synthesized in good yields (76–96%) through the Schiff-base condensation of heterocyclic aldehydes **1a–g** with 4-phenyl-3-thiosemicarbazide in methanol at room temperature (see Scheme 1).

Aldehydes **1a–c** and **1e–f** are inexpensive and commercially available, and 5-(4′-ethoxyphenyl)furan-2-carbaldehyde **1d**[15] and the precursor 5-(4′-formylphenyl)furan-2-carbaldehyde **1g** were easily prepared in good yields (75–91%) through Suzuki cross-coupling reactions of 5-bromofuran-2-carbaldehyde with 4-ethoxyphenylboronic acid or 4-formylphenylboronic acid, respectively, using the synthetic procedure previously reported by us.[11a] All the compounds were completely characterized by ^{1}H and ^{13}C NMR, IR, MS, EA or HRMS, and the data obtained were in full agreement with the proposed formulation (see Experimental section). The ^{1}H NMR spectra of this family of thiosemicarbazones show the most characteristic signals for N–H and CH═N protons. ^{1}H NMR studies using deuterated *N*,*N*-dimethylsulphoxide (DMSO) displayed resonances due to the CH═N protons in the 7.99–8.16 ppm interval, whereas thiourea N–H protons were found in the 9.88–10.18 and 11.84–12.23 ppm range for the N–H groups adjacent to the monosubstituted phenyl ring and for the N–H adjacent to the CH═N moiety, respectively. When the whole family of compounds was considered, the highest variations in δ were found for the N–H protons located in the vicinity of the CH═N moiety adjacent to the furan ring functionalized with electron withdrawing or electron donor groups ($\Delta\delta$ = 0.39 ppm). Additionally, the CH═N protons were the least affected by the substituents located in their vicinity ($\Delta\delta$ = 0.17 ppm), whereas the N–H protons adjacent to the monosubstituted phenyl ring showed an interval of $\Delta\delta$ = 0.30 ppm.

Spectroscopic behaviour of 3a–f and 4

Acetonitrile solutions (C = 1.2 × 10^{-5} mol dm^{-3} at 25 °C) of thiosemicarbazone-functionalised receptors **3a–f** and **4** showed an intense absorption band (log $\varepsilon \approx$ 4.4) in the 335–396 nm region (see Table 1 for spectroscopic data). Compound **3a**, containing the thiosemicarbazone moiety surrounded by a



Scheme 1 Synthesis of furyl-thiosemicarbazone receptors **3a–f** and **4**.

Table 1 Spectroscopic data for compounds **3a–f** and **4**

Receptor	λ_{ab} LH (nm)	λ_{ab} L^{-} [a] (nm)	Log ε (LH)	λ_{em} LH (nm)	λ_{em} L^{-} [a] (nm)	Φ	$\Delta\lambda_{ab\text{-}em}$ LH (nm)	$\Delta\nu_{ab\text{-}em}$ LH (cm^{-1})
3a	335	391	4.55	421	431	0.0016	86	6097.78
3b	383	540	4.27	422	409	0.0006	39	2412.98
3c	362	416	4.59	426	491	0.0226	64	4150.13
3d	366	410	4.01	432	462	0.0644	66	4174.26
3e	364	423	4.61	429	476	0.0183	65	4162.50
3f	396	489	4.31	586	546	0.0259	190	8187.68
4	359	443	4.53	486	467	0.0363	127	7279.02

[a] Measured upon addition of 100 equiv. of the fluoride anion.

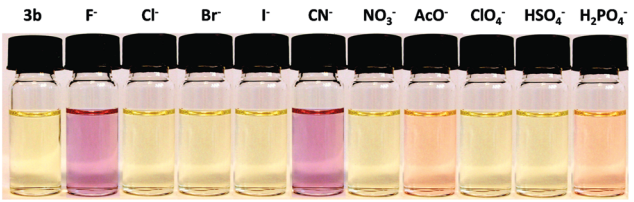


Fig. 1 Colour changes of the **3b** solution (1.2×10^{-4} mol dm^{-3}) seen in the presence of 10 equiv. of F^{-}, Cl^{-}, Br^{-}, I^{-}, CN^{-}, NO_3^{-}, AcO^{-}, ClO_4^{-}, HSO_4^{-} and $H_2PO_4^{-}$.

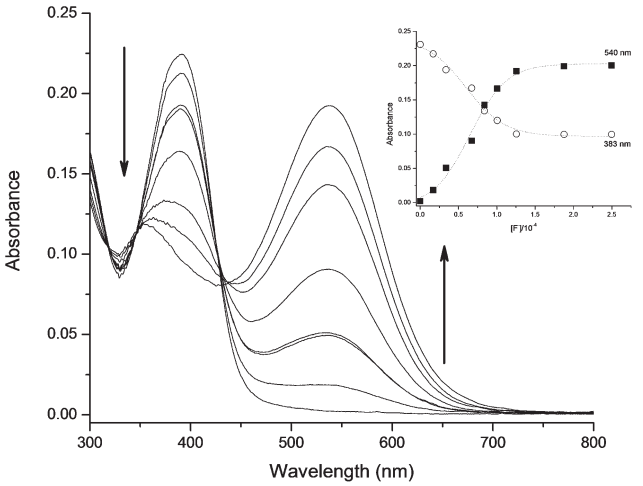


Fig. 2 UV-Vis titration of receptor **3b** (1.2×10^{-5} mol dm^{-3}) with F^{-} anion (0–10 equiv.) in acetonitrile. Inset: Absorbance of a solution of **3b** at 383 and 540 nm *versus* concentration of F^{-} anion (mol dm^{-3}).

phenyl and a furyl ring functionalized with a bromo group, presented an absorption band at 335 nm, whereas changing the bromo substituent for a better electron acceptor moiety, such as a nitro group (receptor **3b**), induced a pronounced red shift from 335 to 383 nm. The coupling of an additional aromatic ring with the framework of **3a** or **3b** (receptors **3e** and **3f**, respectively) induced a significant bathochromic shift of the band (from 335 to 364 nm and from 383 to 396 nm, respectively), this being a direct consequence of the extension of the conjugation.

UV-Vis studies involving anions

The UV-Vis behaviour of receptors **3a–f** and **4** in acetonitrile solutions ($C = 1.2 \times 10^{-5}$ mol dm^{-3}) was studied at 25 °C in the presence of selected anions of different sizes and shapes such as fluoride, chloride, bromide, iodide, cyanide, nitrate, acetate, perchlorate, hydrogen sulphate and dihydrogen phosphate. For all the receptors, addition of increasing quantities (up to 10 equiv.) of chloride, bromide, iodide, nitrate, perchlorate and hydrogen sulphate induced negligible changes in the UV-Vis bands, which clearly indicates that no coordination occurs. Much more relevant results were observed in the presence of those anions showing a basic character in acetonitrile, such as fluoride, cyanide, acetate, and dihydrogen phosphate (see Fig. 1). The changes in colour observed upon addition of basic anions were almost immediate (see ESI† for the kinetic profile of changes in the 390 nm band of **3b** in the presence of the fluoride anion).

In most cases, UV-Vis titration experiments with receptors **3a–f** and **4** and fluoride showed similar behaviour; *i.e.*, intensity decreased and there was a slight hypsochromic shift of the absorption band, together with simultaneous growth of a new red-shifted band. However, it was clearly apparent from the titration profiles that both the position of the new band and the relative intensity of the absorption band of the receptor in relation to the red-shifted band upon addition of fluoride were dependent on the receptor used. Acetonitrile solutions of **3b** were yellow due to the presence of a band at 383 nm. Upon addition of increasing quantities of the fluoride anion, this band progressively decreased, while a new absorption at 540 nm ($\Delta\lambda$ = 157 nm) increased in intensity with a clear isosbestic point at 429 nm (see Fig. 2). The formation of this new visible band induced a change in colour from pale yellow to purple (see Fig. 1).

Fluoride and cyanide anions were able to induce UV-Vis changes for all the receptors tested, whereas acetate and hydrogen phosphate displayed a poorer response with all the receptors (see Fig. 3).

The selectivity of receptors **3a–b** and **4** for the most basic anions (F^{-}, CN^{-}, AcO^{-} and $H_2SO_4^{-}$) was demonstrated by further UV-Vis experiments. Fig. 4 shows that addition of 10 equiv. of fluoride anion to acetonitrile solutions of receptor **3b** induced the appearance of an absorbance band at 540 nm. The same red-shifted band with identical absorbance was obtained upon addition of a mixture of anions (10 equiv. of fluoride, chloride, bromide, iodide, perchlorate, hydrogen sulfate and nitrate). Similar chromogenic behaviors were observed for CN^{-} and AcO^{-} in mixtures with other anions (*i.e.* chloride, bromide, iodide, perchlorate, hydrogen sulfate and nitrate).

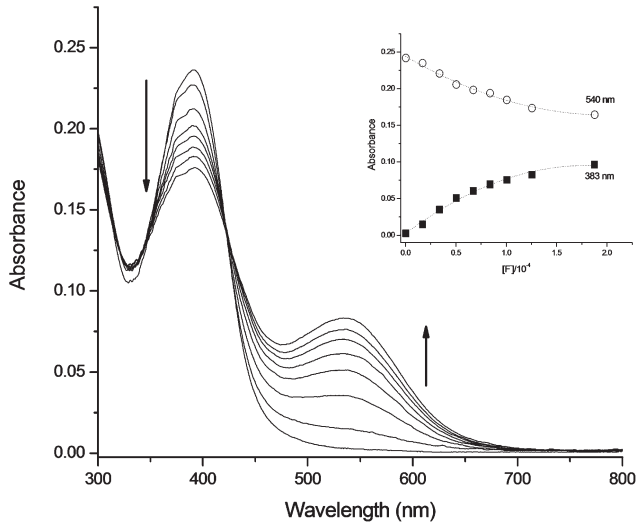


Fig. 3 UV-Vis titration of receptors **3b** (1.2×10^{-5} mol dm^{-3}) with AcO^- anion (0–10 equiv.) in acetonitrile. Inset: Absorbance of acetonitrile solutions of receptor **3b** at 383 and 540 nm *versus* concentration of AcO^- anion (mol dm^{-3}).

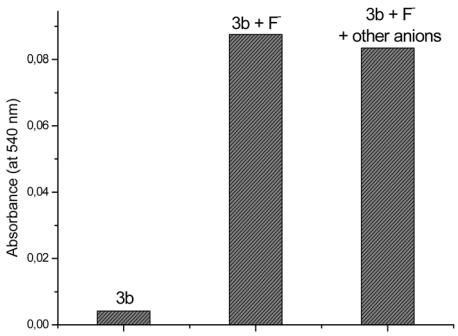


Fig. 4 Absorbance at 540 nm of receptor **3b** (1.0×10^{-5} mol dm^{-3}) alone and upon addition of 10 equiv. of F^- and 10 equiv. of F^-, Cl^-, Br^-, ClO_4^-, HSO_4^-, I^- and NO_3^- anions.

Once the selectivity of this family of receptors was determined, the limits of detection (LOD) were estimated. In all cases LOD values of *ca.* 10 μM were determined for fluoride and cyanide anions.

Moreover the interaction of **3a–f** and **4** with basic anions in water and acetonitrile–water mixtures (1 : 1, 5 : 1 and 10 : 1 v/v) was also tested. Unfortunately in all cases neither changes in colour nor in fluorescence were observed. This was most likely due to the reduced basicity of the anions in aqueous environments due to solvation and the poor acidity of the receptors when compared with other reported ligands (*vide infra*).

On the whole, the changes observed in acetonitrile are in agreement with the expectation that the interaction between an electron-rich anion and a donor group in a push–pull system will induce a bathochromic shift. In fact, similar shifts in the presence of fluoride have also been reported to occur using other amide-, urea-, thiourea-, or pyrrole-containing hosts.[16] This interaction is attributed to the formation of strong hydrogen-bonding complexes between these groups and to the highly basic F^- anion that is eventually able to originate the deprotonation of the binding site.[17] In fact, we believe that this dual complex + deprotonation process is active in all of our receptors in the presence of fluoride: a first step consisting in the formation of a hydrogen-bonding complex and a second step in which the receptor is deprotonated by the anion. Usually the formation of hydrogen-bonding complexes, *via* receptor-interactions, is reflected in relatively minor variations in the absorption band of the receptor, whereas the deprotonation processes are revealed with the clear appearance of a new absorption band at longer wavelengths.[18] From a more physical viewpoint, the negative charge generated upon deprotonation induces an increase in the intensity of the electrical dipole that results in a substantial red shift of the absorption band. In most cases, the observation of complexation or/and deprotonation depends on a delicate balance between the acidity of the N–H protons of the receptor and the basicity of the anion. In our case, a close look at the results indicated that the final response of receptors **3a–f** and **4** to the tested basic anions strongly depends on the chemical nature of the functional groups attached to the thiosemicarbazone framework, which modulated the acidity of the N–H protons; *i.e.* for a certain anion (fluoride) at a given concentration, the development of the band due to deprotonation grew more or less in intensity depending on the receptors used.

When comparing the behaviour of similar compounds **3a–f**, it was apparent that the presence of electron-withdrawing moieties, such as a nitro group in **3b** and **3f**, induced an increase in the acidity of the N–H protons of the thiosemicarbazone, thus favouring the interaction with the fluoride and cyanide anions and deprotonation, whereas the presence of electron-donor groups, such as bromo (**3a**) and ethoxy (**3d**), respectively induced a certain decrease in acidity and the red-shifted band due to deprotonation developed to a lesser extent.

Stability constants

As stated above in the interaction of basic anions with semithiocarbazone-containing receptors **3a–f** and **4**, two different behaviours could be expected; *i.e.*, (i) hydrogen-bonding interactions and (ii) deprotonation (see eqn (1) and (2)).

$$LH + A^- \rightleftarrows LH\cdots A^- \quad (1)$$

$$LH\cdots A^- + A^- \rightleftarrows L^- + A_2H^- \quad (2)$$

In order to complete the characterization of the interaction of receptors **3a–f** and **4** with anions, the strength of both processes (coordination and deprotonation) was studied *via* the evaluation of the corresponding stability constants, which were determined by the UV-Vis spectroscopic titrations between receptors **3a–f** and **4** and fluoride and acetate anions using the HypSpec software V1.1.18. The data set was adjusted to the two consecutive equilibriums in eqn (1) and (2); the results are shown in Table 2.

In all cases, the formation of anion–ligand 2 : 1 complexes shown in eqn (2) was confirmed for the method of continuous variation (Job's plots). As an example Fig. 5 shows the studies for the interaction of **3b** with fluoride. It is noticeable that

Table 2 Logarithms of the stability constants measured for the interaction of receptors **3a–f** with fluoride and acetate

	F^-		AcO^-	
	$LH + A^- \rightleftarrows LH\cdots A^-$	$LH\cdots A^- + A^- \rightleftarrows L^- + A_2H^-$	$LH + A^- \rightleftarrows LH\cdots A-$	$LH\cdots A^- + A^- \rightleftarrows L^- + A_2H^-$
3a	3.46(6)	2.48(7)	3.40(6)	0.31(8)
3b	4.56(2)	4.24(4)	3.91(1)	1.53(4)
3c	4.20(5)	3.51(8)	3.60(1)	0.13(4)
3d	4.23(4)	3.81(8)	—[a]	—[a]
3e	4.37(1)	3.57(7)	3.56(8)	0.31(2)
3f	4.47(7)	4.47(1)	4.56(8)	1.64(1)

[a] No reliable results were obtained.

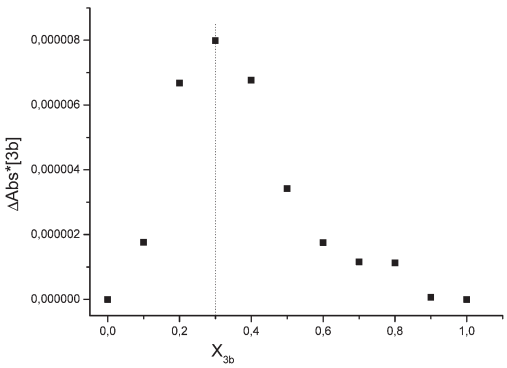


Fig. 5 Job's plot for complexation of **3b** with the fluoride anion determined by UV-Vis spectrophotometry in acetonitrile at 540 nm and $[\mathbf{3b}] + [F^-] = 1.2 \times 10^{-4}$ mol dm^{-3}.

despite the presence of two potential binding sites in **4**, this receptor showed the same response as **3a–f**, namely the formation of 2 : 1 anion–ligand stoichiometry complexes.

Table 2 shows that, as a general trend, the logarithms of the stability constants measured for both equilibriums with fluoride were higher than those obtained for acetate. This is in agreement with the more basic character of fluoride in acetonitrile when compared with acetate. The logarithms of the stability constants for the formation of the Y-shaped hydrogen-bonding complexes were about one order of magnitude larger than the logarithms of the stability constants for the deprotonation for fluoride, and about three orders of magnitude larger for acetate. It is also apparent in Table 2 that the deprotonation logarithms of constants for all the receptors were more important for fluoride than for acetate.

The stability constants for the formation of the corresponding hydrogen-bonding complexes remained approximately the same for both anions. It is noteworthy that the logarithms of stability constants determined in this study for thiosemicarbazones were generally lower than those reported for the other urea/thiourea receptors functionalized with benzene rings containing electron withdrawing moieties. This is a clear consequence of the reduced acidity of the receptors studied herein when compared with other reported ligands. For instance, compound 1,3-bis-(4-nitrophenyl)urea has also been reported to display the two-step process (coordination + deprotonation) upon addition of fluoride with logarithms of the stability constants for the formation of the complex and for the deprotonation of 7.38 and 6.37 respectively.[19] Another urea-based receptor (1-nitrobenzo[1,2,5]oxadiazol-4-yl)-3-(4-nitrophenyl)urea showed logarithm values higher than 6 for the formation of the hydrogen-bonding complexes and 4.2 for the deprotonation step.[20] Finally, the thiourea receptor 1-(2-methyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-3-phenylthiourea also underwent a first coordination step and a second proton transfer process with the basic anions, with a logarithm of stability constants 5.7 and 5.5 for fluoride, and 6.02 and 3.23 for acetate.[21]

Fluorogenic studies involving anions

It is widely known that fluorescence, despite being a less extended technique in some cases, is much more sensitive to intermolecular interactions than colour changes. Therefore, fluorescence studies in acetonitrile solutions of the receptors upon addition of increasing amounts of the corresponding anion were carried out. Receptors were excited in the pseudo-isosbestic points observed in the course of UV-Vis titrations. In all cases, the emission consisted in a broad, unstructured band. Quantum yields in acetonitrile (see Table 1) ranged from quite low (receptor **3a**, $\Phi = 0.0016$) to medium (compound **3d**, $\Phi = 0.0644$). For all the receptors tested (*i.e.*, **3a–f** and **4**), addition of the anions chloride, bromide, iodide, hydrogen sulphate and nitrate induced negligible changes in the emission intensity profiles. In contrast, the fluorescence emission in the presence of fluoride, cyanide, acetate and dihydrogen phosphate changed significantly.

A different general behaviour was found depending on the anion and the receptor used in the studies. As a general trend, and in the presence of fluoride, all the receptors **3a–f** and **4** showed enhanced fluorescence intensity upon the addition of moderate amounts of fluoride followed by a quenching of the emission band at higher anion concentrations and the growth of a new band at longer wavelengths (λ_{em} in the 421–586 nm range, see Table 1).

In order to interpret this behaviour, we made a comparison between the changes observed in the emission and absorption spectra. A typical example is that shown in Fig. 6, namely the behaviour found for ligand **3e** in the presence of fluoride. As seen, for small quantities of the fluoride anion, while the intensity of the absorption band at 364 nm remains unaltered, the fluorescence intensity at 429 nm progressively increased until 10 equiv. of fluoride had been added. Moreover, upon addition of larger amounts of fluoride, the intensity of the emission band at 429 nm diminished, suggesting the formation of a new compound that emits at longer wavelengths ($\lambda_{em} = 476$ nm). Thus, fluorescence measurements suggest that the interaction of the receptors with fluoride took place in two steps, as found in the UV-Vis studies. In the first step, the anion coordinates with the acidic NH protons of the thiourea moiety through hydrogen-bonding interactions and led to an increase in the donor capacity of the binding site. Upon addition of more equivalents of the anion, deprotonation of the receptor occurred. This deprotonation process induced the appearance of the red-shifted visible and emission bands.

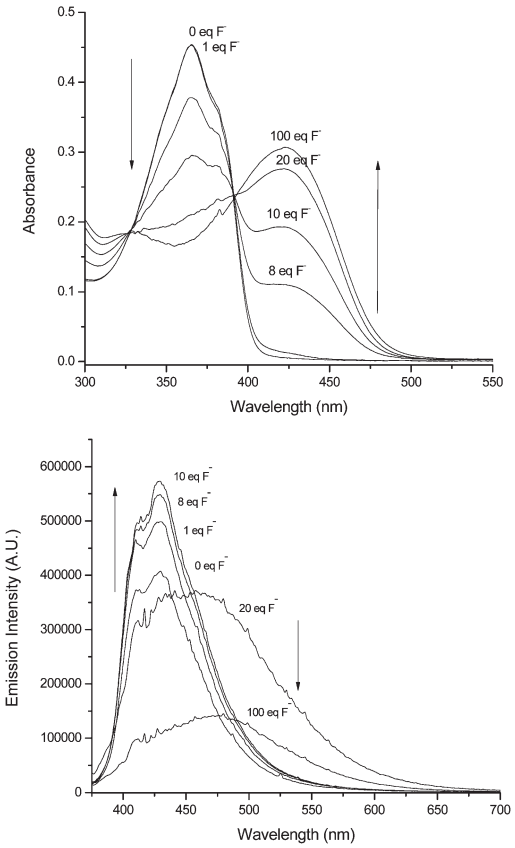


Fig. 6 Interaction of receptor **3e** (1.2×10^{-5} mol dm^{-3}) with F^- anion (top): absorption spectra and (bottom): emission spectra of receptor in the presence of 0, 1, 8, 10, 20 and 100 equiv. of F^- anion.

The overall shape and intensity of the emission band for a certain receptor–anion pair depends on the LH/LH···A^-/L^- ratios. For instance, a closer look at the titration experiments with fluoride indicated that in order to induce the appearance of the red-shifted emission band, larger amounts of fluoride are required for receptor **3e** (functionalized with bromophenylfuryl) than for receptor **3f** (functionalized with nitrophenylfuryl), which is in agreement with the larger acidity of **3f** *versus* **3e**.

Fig. 7 shows the emission and absorption spectra for receptor **3e** in the presence of acetate. The emission intensity was enhanced upon the addition of increasing quantities of the acetate anion. This enhancement in the emission intensity was assigned to the formation of the Y-shaped hydrogen-bonding complex between the NH thiourea protons of the receptor and the acetate anion. However in this case, no significant deprotonation occurred and no red-shifted absorptions or emission bands were observed.

^{1}H-NMR spectroscopic studies in the presence of anions

As seen previously, the UV-Vis and fluorescence data of thiosemicarbazone receptors **3a–f** and **4** in the presence of anions displayed a varied response related with the presence of hydrogen-bonding interactions and the deprotonation of the receptors. In particular, the colorimetric behaviour observed for these receptors depends on the deprotonation tendencies of the thiosemicarbazone units in receptors **3a–f** and **4** and on the proton affinities of the anions.

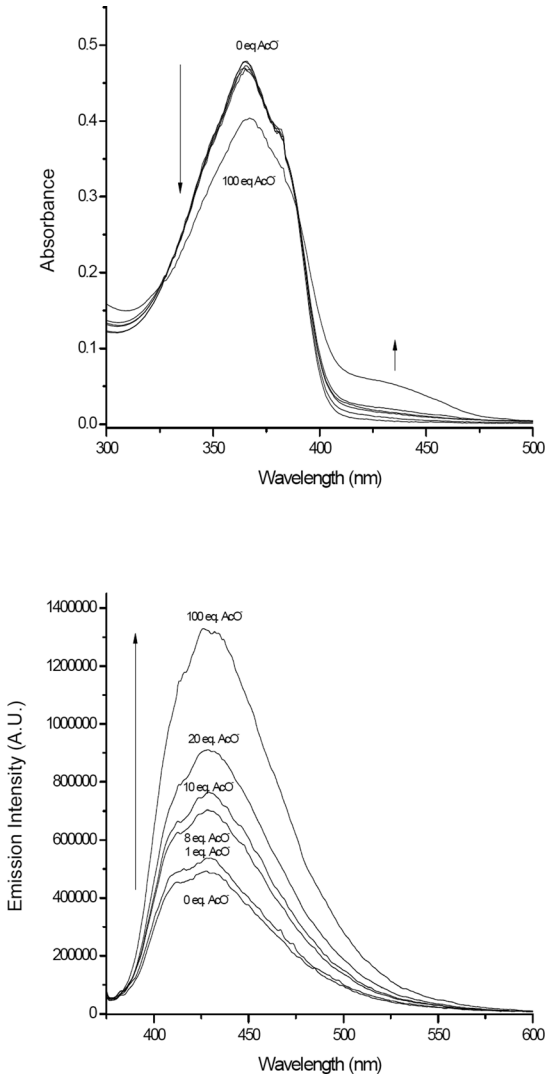


Fig. 7 Interaction of receptor **3e** (1.2×10^{-5} mol dm^{-3}) with AcO^- anion (top): absorption spectra and (bottom): emission spectra of the receptor in the presence of 0, 1, 8, 10, 20 and 100 equiv. of AcO^- anion.

In order to study the coordination/deprotonation processes in these systems in more detail, the interaction of receptor **3b** with the fluoride anion was investigated by means of ^{1}H NMR titration experiments in DMSO-d_6. Deuterated DMSO was selected as the solvent due to the poor solubility of **3b** in deuterated acetonitrile.

The ^{1}H NMR spectrum of **3b** showed the expected signals in the aromatic zone due to the presence of one benzene ring and one furan heterocycle. The monosubstituted benzene ring showed resonances at 7.21–7.26 (1H, multiplet, H_p), 7.39 (2H, broad triplet, H_m), 7.52–7.56 (2H, multiplet, H_o) ppm, whereas the protons of the 2,5-disubstituted furan ring (H_d and H_c) appeared as a broad doublet at 7.50 (H_d) and at 7.83 (H_c) ppm. Finally, the imine proton (–C*H*═N) was a broad singlet at 8.08 (H_e) ppm, and the N–*H* protons of the thiosemicarbazone group were also broad singlets at 10.18 (H_g) and 12.23 (H_f) ppm (Scheme 2).

In a first step, we studied the shifts of the protons of receptor **3b** upon addition of increasing quantities of the fluoride anion. The most important fact was the disappearance of the H_f and H_g protons upon addition of 1 equiv. of fluoride. Additionally, the

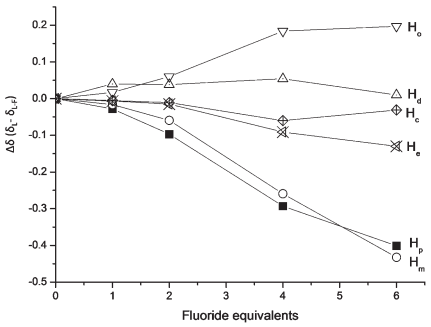


Fig. 8 ^{1}H NMR shifts for the protons of receptor **3b** in the presence of increasing quantities of F^- anion (DMSO-d_6).

variation in the chemical shifts $\Delta\delta$ (ppm) for other protons in **3b** during the titration with fluoride is shown in Fig. 8.

As seen, protons H_c, H_d and H_e showed negligible changes in their position in the NMR spectrum. In contrast, remarkable shifts were noted for H_o, H_m and H_p, suggesting that deprotonation took place in the N–H group closer to the phenyl group. It has been reported that upon the deprotonation of the N–H group, two effects might become active: (i) an increase in the electron density in the phenyl ring according to a π-mechanism, which should induce a shielding effect (an upfield shift of the C–H signals is expected), and (ii) a polarization of the C–H bonds induced by a through-space electrostatic mechanism, which is expected to cause a deshielding effect. Fig. 8 shows how the H_o protons underwent important downfield shifts, indicating strong electrostatic effects due to the proximity of a negatively charged thiourea nitrogen atom. Protons H_m and H_p underwent upfield shifts as a result of the through-bond effect which, in this case, dominated (through-space effects vanished with distance). Fabbrizzi *et al.* and ourselves have observed a similar behaviour in closely related thioureas; *i.e.*, deprotonation apparently occurred in the protons of the nitrogen attached to the phenyl ring.[22]

Quantum mechanical studies

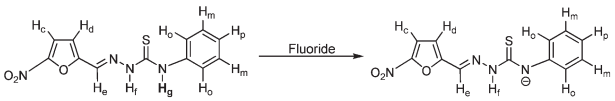
One way of describing the hydrogen bond-donating or -accepting ability of a molecule in a particular group can be accessed by gas-phase deprotonation energy studies determined by quantum chemical calculations by subtracting the energy of the receptor alone from that of the deprotonated form. For these studies, receptors **3a–f** containing furyl heterocycles were selected in order to obtain data that would be comparable. Calculations were carried out using a PM3 semi-empirical model. These thiosemicarbazone receptors contained two N–H groups and the deprotonation studies were performed by assuming that both protons could be eliminated. The data in Table 3 strongly suggest that the most acidic one was that attached to the imine carbon directly bonded to the furyl heterocycle (the more negative the value of the difference, the stronger the hydrogen-bond donor character). However, these results obtained from theoretical calculations contrast with the apparent conclusion of the ^{1}H NMR titrations, which suggested that deprotonation occurred at the H_g proton. The literature describes similar contradictory results obtained from the theoretical and experimental NMR data.[14]

Despite this apparent contradiction, the theoretical calculations roughly agree with the chromogenic behaviour observed for the

Table 3 Stabilization energy of the deprotonation for receptors

	$E_{(L)} - E_{(LH)}$ (kcal mol^{-1})	
Receptor	R = N-NH-C(S)-*N*-Ph[a]	R = N-*N*-C(S)-NH-Ph[b]
3a	−5.87	−13.66
3b	−5.18	−14.56
3c	−6.16	−14.93
3d	−6.35	−14.33
3e	−6.84	−14.67
3f	−10.20	−18.86

[a] Deprotonation at the H_g proton (see Scheme 2). [b] Deprotonation at the H_f proton (see Scheme 2).



Scheme 2 Proposed mode for fluoride-induced deprotonation of receptor **3b**.

receptors. Among the compounds studied using a PM3 semi-empirical model, we can observe that the presence of an extra phenyl ring next to the furyl moiety (compounds **3c–3f**) made the receptors more acidic when compared with derivative **3a**. Moreover, the quantum mechanical studies indicate that derivative **3f** was the most acidic one. In fact, the acidity of the studied receptors followed this order **3f** > **3c** ~ **3e** ~ **3b** ~**3d** > **3a** (see Table 3). Basically, these data are in agreement with the chromofluorogenic behaviour of the receptors and with the expected basicity of anions in acetonitrile (*i.e.*, $F^- > CN^- > AcO^- > H_2PO_4^-$, Cl^-, HSO_4^-, SCN^-, NO_3^-, Br^-, I^-). Thus, the most basic anions fluoride and cyanide induced substantial spectroscopic changes for all the receptors, whereas acetate generally showed more minor changes in the optical properties of the receptors.

Electrochemical studies in the presence of fluoride

The electrochemical behaviour of receptor **3b** was studied alone (5×10^{-4} mol dm^{-3}) and in the presence of fluoride anion in acetonitrile using platinum as the working electrode and $[Bu_4N][ClO_4]$ as the supporting electrolyte (see Fig. 9). Receptor **3b** showed a poorly defined irreversible oxidation band sweeping to anodic potentials at 0.7 V. Addition of 1 equiv. of fluoride induced an intensity increase, a small shift of the original oxidation band (band 1) and the appearance of a new oxidation band (band 2) at 0.2 V. Addition of 10 equiv. of fluoride enhanced the intensity of both bands. The fact that band 1 did not completely disappear with excess fluoride suggests the presence of a complex electrochemical mechanism involving both electrochemical and chemical reactions.

Moreover, Fig. 10 shows the plot showing the current of band 1 *versus* the equivalents of the fluoride added in the **3b** receptor. As observed, an almost linear increase took place up to 2 equiv. This behaviour is in agreement with fluoride reaction with **3b**, inducing deprotonation and the formation of the F_2H^- species.

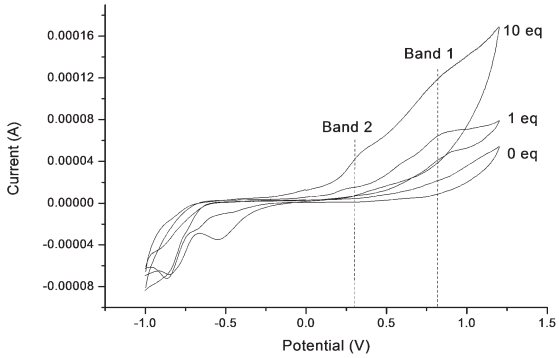


Fig. 9 Cyclic voltammogram of receptor **3b** (5×10^{-4} mol dm^{-3}) in a solution of 1×10^{-2} mol dm^{-3} $[Bu_4N][ClO_4]$/acetonitrile alone (left) with 1 (centre) and 10 (right) equiv. of F^- anion at the scan rate of 20 mV s^{-1}.

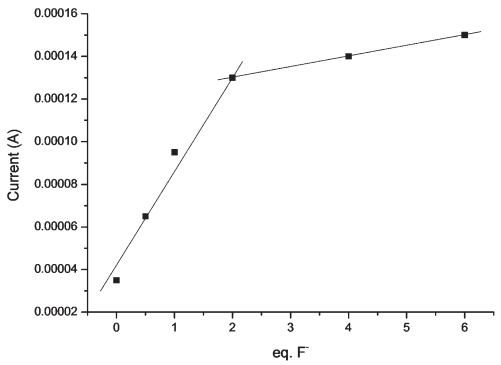


Fig. 10 Current (A) of oxidation band 1 of **3b** *versus* the equivalents of F^- added.

Conclusions

A family of novel heterocyclic thiosemicarbazones containing furyl moieties (derivatives **3a–f** and **4**) has been prepared and characterized, and their interactions with anions have been studied *via* UV-Vis and fluorescence titrations, quantum chemical calculations and electrochemical techniques. The thiosemicarbazone dyes show a modulation of their donor hydrogen-bonding abilities as a function of the electronic nature of the attached chemical groups. Two distinctive chromo-fluorogenic behaviours in the presence of anions in acetonitrile solutions are observed. The more basic anions fluoride and cyanide are capable of inducing dual coordination–deprotonation for all the receptors studied, whereas acetate and dihydrogen phosphate display poorer coordination ability, and deprotonation is observed only upon the addition of large amounts of anion. Coordinative hydrogen-bonding interactions result in a slight bathochromic shift, while deprotonation is indicated by the appearance of a new band at *ca.* 400–450 nm. The fluorescence studies evidence that hydrogen-bonding interactions become visible through the enhancement of the emission band, whereas deprotonation induces the appearance of a new red-shifted emission. The PM3 studies are basically in agreement with the experimental behaviour. The electrochemical studies carried out with receptor **3b** show an irreversible oxidation process at 0.7 V, whereas the addition of fluoride also induces the growth of a new oxidation band at 0.2 V. The observed response toward basic anions of the receptors described in this paper clearly resembles that obtained with other derivatives containing hydrogen bonding binding sites (ureas, thioureas and amides). The selectivity trend is the same and only basic anions were able to induce a chromo-fluorogenic response. Despite the lack of response of these receptors in aqueous environments, the ease of synthesis of thiosemicarbazones opens the possibility to design more complex and pre-organized neutral receptors for anions with enhanced selectivity and applicability in aqueous environments.

Experimental section

Materials and methods

Thin-layer chromatography was carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel 60F_{254}). All the melting points were measured on a Gallenkamp melting point apparatus. NMR spectra were obtained on a Varian Unity Plus Spectrometer at an operating frequency of 300 MHz for ^{1}H and 75.4 MHz for ^{13}C or with a Bruker Avance III 400 at an operating frequency of 400 MHz for ^{1}H and 100.6 MHz for ^{13}C, using the solvent peak as an internal reference. Solvents are indicated in parentheses before the chemical shift values (δ relative to TMS and given in ppm). The IR spectra were run on a FTIR Perkin-Elmer 1600 spectrophotometer in Nujol. The elemental analyses were carried out on a Leco CHNS 932 instrument. Mass spectrometry analyses were performed at the C.A.C.T.I. – Unidad de Espectrometria de Masas of the University of Vigo, Spain, in a Hewlett Packard 5989 A spectrometer for low resolution spectra and in a VG Autospec M spectrometer for high resolution mass spectra. All the solvents were of spectrophotometrical grade. Air-/water-sensitive reactions were performed in flame-dried glassware under argon. Aldehydes **1a–c**, **1e–f** and 4-phenyl-3-thiosemicarbazide **2** were purchased from Sigma-Aldrich and were used without further purification.

General procedure for the synthesis of formyl-furans 1d and 1g through Suzuki cross-coupling

5-Bromofuran-2-carbaldehyde (1.2 mmol) was coupled with 4-ethoxyphenylboronic acid or with 4-formylphenylboronic acid (1.6 mmol), in a mixture of DME (15 mL) and aqueous 2 mol dm^{-3} Na_2CO_3 (1 mL) and $Pd(PPh_3)_4$ (6 mol%) at 80 °C in an argon atmosphere for 5–12 h. After cooling, the mixture was filtered. Ethyl acetate and a saturated solution of NaCl were added and the phases were separated. The organic phase was washed with water (3 × 50 mL) and with an aqueous solution of NaOH (10%). The organic phase obtained was dried ($MgSO_4$), filtered and solvent removal gave a crude mixture which was submitted to column chromatography on silica with increasing amounts of diethyl ether in light petroleum as an eluent, thus affording the coupled products.

5-(4′-Ethoxyphenyl)furan-2-carbaldehyde (1d).[15] Yellow solid (75%). Mp: 120.1–122.3 °C. IR (Nujol) ν 1670 (C═O), 1608, 1291, 1254, 1119, 1041, 1029, 959, 919, 838, 797, 772 cm^{-1}.

^{1}H NMR ($CDCl_3$) δ 1.39 (t, 3H, J = 7.2 Hz, CH_3), 4.02 (q, 2H, J = 7.2 Hz, CH_2), 6.66 (d, 1H, 3H, J = 3.6 Hz, 4-H), 6.89 (dd, 2H, J = 6.4 and 2.0 Hz, H3′ and H5′), 7.25 (d, 1H, J = 3.6 Hz, H3), 7.69 (dd, 2H, J = 6.4 and 2.0 Hz, H2′ and H6′), 9.54 (s, 1H, C*H*O). ^{13}C NMR ($CDCl_3$) δ 14.54 (*C*H$_3$), 63.46 (*C*H$_2$), 106.10 (C4), 114.17 (C3′ and C5′), 121.38 (C5), 124.32 (C3), 126.78 (C2′ and C6′), 151.37 (C2), 159.72 (C1′), 160.12 (C4′), 176.60 (*C*HO). MS (EI) m/z (%): 216 (M^+, 100), 188 (93), 187 (35), 160 (33), 131 (43), 77 (17). HRMS: (EI) m/z (%) for $C_{13}H_{12}O_3$; calcd 216.079; found 216.078.

5-(4′-Formylphenyl)furan-2-carbaldehyde (1g). Orange solid (91%). Mp: 124.6–126.0 °C. IR (Nujol) ν 1659 (C═O), 1602, 1309, 1157, 1117, 1093, 1020, 966, 946, 810, 722 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.01 (d, 1H, J = 3.6 Hz, H4), 7.36 (d, 1H, J = 3.6 Hz, H3), 7.98 (m, 4H, H2′, H6′, H3′ and H5′), 9.72 (s, 1H, C*H*O), 10.05 (s, 1H, C*H*O). ^{13}C NMR ($CDCl_3$) δ 110.0 (C4), 123.0 (C3), 125.6 (C2′ and C6′), 130.3 (C3′ and C5′), 134.1 (C1′), 136.5 (C4′), 152.7 (C2), 157.4 (C5), 177.5 (*C*HO), 191.3 (C*H*O). MS (EI) m/z (%): 200 (M^+, 100), 199 (84), 171 (18), 143 (23), 115 (56). HRMS: (EI) m/z (%) for $C_{12}H_8O_3$; calcd 200.047; found 200.048.

General procedure for the synthesis of heterocyclic phenylthiosemicarbazones 3–4

Equal amounts (0.4 mmol) of the appropriate aldehyde and thiosemicarbazide were dissolved in MeOH (30 mL) at room temperature. A solution was obtained, which was stirred overnight. Compounds were precipitated as microcrystalline solids, and were collected by suction filtration, washed with cold MeOH and diethyl ether, then dried by vacuum. Further recrystallizations using $CHCl_3$–petroleum ether mixtures were performed when was necessary.

1-((5-Bromofuran-2-yl)methylene)-4-phenylthiosemicarbazone. 3a was obtained as a yellow solid (76%). Mp: 149.5–150.8 °C. ^{1}H NMR (DMSO-d$_6$): δ = 6.76 (d, J = 3.9 Hz, 1H, H3′), 7.10 (d, J = 3.9 Hz, 1H, H4′), 7.15–7.21 (m, 1H, H4), 7.34 (br t, J = 7.2 Hz, 2H, H3 and H5), 7.55 (br d, J = 7.2 Hz, 2H, H2 and H6), 7.99 (s, 1H, –C*H*═N), 9.88 (s, 1H, S═C–N*H*), 11.85 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d$_6$): δ = 114.5 (C3′), 115.6 (C4′), 124.3 (C5′), 125.3 (C4), 125.5 (C2 and C6), 128.1 (C3 and C5), 131.67 (–*C*H═N), 138.9 (C1), 151.4 (C2′), 175.8 (*C*═S) ppm. IR (Nujol) ν 3332, 3132, 1593, 1558, 1538, 1515, 1448, 1274, 1266, 1205, 1125, 1016, 920, 781, 739, 689 cm^{-1}. $C_{12}H_{10}BrN_3OS$ (322.97): calcd C 44.46, H 3.11, N 12.96, S 9.89; found C 44.33, H 3.12, N 12.93, S 9.81.

1-((5-Nitrofuran-2-yl)methylene)-4-phenylthiosemicarbazone. 3b was obtained as a yellow solid (81%). Mp: 188.0–188.7 °C. ^{1}H NMR (DMSO-d$_6$): δ = 7.20–7.25 (m, 1H, H4), 7.38 (br t, J = 7.8 Hz, 2H, H3 and H5), 7.49–7.55 (m, 3H, H3′, H2 and H6), 7.82 (d, J = 3.9 Hz, 1H, H4′), 8.07 (s, 1H, –C*H*═N), 10.18 (s, 1H, S═C–N*H*), 12.23 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d$_6$): δ = 113.5 (C3′), 115.2 (C4′), 125.7 (C4), 125.9 (C2 and C6), 128.2 (C3 and C5), 130.2 (–C*H*═N), 138.7 (C1), 151.6 (C5′), 152.6 (C2′), 176.3 (C═S) ppm. IR (Nujol) ν 3313, 3135, 1554, 1529, 1514, 1344, 1251, 1188, 1098, 1015, 964, 810, 760, 741, 693 cm^{-1}. $C_{12}H_{10}N_4O_3S$ (290.05): calcd C 49.65, H 3.47, N 19.30, S 11.05; found C 49.24, H 3.53, N 19.18, S 11.11.

4-Phenyl-1-((5-phenylfuran-2-yl)methylene)thiosemicarbazone. 3c was obtained as a yellow solid (76%). Mp: 176.0–176.8 °C. ^{1}H NMR (DMSO-d$_6$): δ = 7.14 (d, J = 3.3 Hz, 1H, H3′), 7.18–7.23 (m, 2H, H4 and H4′), 7.32–7.47 (m, 5H, H3″, H4″, H5″, H3 and H5), 7.58 (br d, J = 7.5 Hz, 2H, H2 and H6), 7.83 (br d, J = 6.9 Hz, 2H, H2″ and H6″), 8.09 (s, 1H, –C*H*═N), 9.93 (s, 1H, S═C–N*H*), 11.89 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d$_6$): δ = 108.5 (C3′), 115.8 (C4′), 124.0 (C2″ and C6″), 125.3 (C4), 125.7 (C2 and C6), 128.1 (C3 and C5), 128.3 (C4″), 129.0 (C3″ and C5″), 129.5 (C1″), 132.4 (–*C*H═N), 139.0 (C1), 148.9 (C5′), 154.8 (C2′), 175.6 (*C*═S) ppm. IR (Nujol) ν 3270, 3147, 1622, 1595, 1553, 1530, 1491, 1259, 1188, 1092, 1026, 980, 922, 908, 754, 685 cm^{-1}. $C_{18}H_{15}N_3O_5S$ (321.09): calcd C 67.27, H 4.70, N 13.07, S 9.98; found C 67.19, H 4.76, N 12.91, S 9.65.

1-((5-(4-Ethoxyphenyl)furan-2-yl)methylene)-4-phenylthiosemicarbazone. 3d was obtained as a yellow solid (78%). Mp: 178.8–179.9 °C. ^{1}H NMR (DMSO-d$_6$): δ = 1.32 (t, J = 7.2 Hz, 3H, OCH$_2$C*H*$_3$), 4.05 (q, J = 7.2 Hz, 2H, OC*H*2CH3), 6.96–7.01 (m, 3H, H3′, H3″ and H5″), 7.13 (d, J = 3.6 Hz, 1H, H4′), 7.17–7.23 (m, 1H, H4), 7.37 (br t, J = 7.2 Hz, 2H, H3 and H5), 7.58 (br d, J = 7.2 Hz, 2H, H2 and H6), 7.76 (dd, J = 6.9 and 2.1 Hz, 2H, H2″ and H6″), 8.01 (s, 1H, –C*H*═N), 9.89 (s, 1H, S═C–N*H*), 11.84 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d$_6$): δ = 14.6 (OCH$_2$*C*H$_3$), 63.2 (O*C*H$_2$CH$_3$), 106.7 (C3′), 114.8 (C3″ and C5″), 116.2 (C4′), 122.2 (C1″), 125.3 (C4), 125.6 (C2 and C6), 125.7 (C2″ and C6″), 128.1 (C3 and C5), 132.5 (–*C*H═N), 139.0 (C1), 148.1 (C5′), 155.2 (C2′), 158.7 (C4″), 175.5 (*C*═S) ppm. IR (Nujol) ν 3339, 3133, 1621, 1606, 1548, 1505, 1269, 1251, 1219, 1176, 1116, 1037, 975, 919, 833, 786, 740 cm^{-1}. $C_{20}H_{19}N_3O_2S$ (365.12): calcd C 65.73, H 5.24, N 11.50, S 8.77; found C 65.23, H 5.21, N 11.49, S 8.69.

1-((5-(4-Bromophenyl)furan-2-yl)methylene)-4-phenylthiosemicarbazone. 3e was obtained as a yellow solid (87%). Mp: 197.3–198.7 °C. ^{1}H NMR (DMSO-d$_6$): δ = 7.18–7.23 (m, 3H, H3′, H4′ and H4), 7.37 (br t, J = 8.0 Hz, 2H, H3 and H5), 7.58 (br d, 1H, J = 8.0 Hz, 2H, H2 and H6), 7.63 (dd, J = 6.4 and 2.0 Hz, 2H, H2″ and H6″), 7.78 (dd, J = 6.4 and 2.0 Hz, 2H, H3″ and H5″), 8.08 (s, 1H, –C*H*═N), 9.92 (s, 1H, S═C–N*H*), 11.89 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d$_6$): δ = 109.2 (C3′), 115.8 (C4′), 121.2 (C4″), 125.3 (C4), 125.7 (C2 and C6), 125.9 (C3″ and C5″), 128.1 (C3 and C5), 128.6 (C1″), 131.9 (C2″ and C6″), 132.2 (–*C*H═N), 139.0 (C1), 149.3 (C5′), 153.6 (C2′), 175.7 (*C*═S) ppm. IR (Nujol) ν 3287, 3143, 1683, 1667, 1594, 1552, 1504, 1445, 1265, 1197, 1974, 1021, 1008, 926, 822, 785, 766, 735 cm^{-1}. MS (ESI): m/z (%) = 402 (M + H + ^{81}Br, 100), 400 (M + H + ^{79}Br, 100), 399 (M+, 82), 370 (41), 368 (41). HRMS (ESI): calcd for $C_{18}H_{15}{}^{81}BrN_3OS$ 402.00929, found 402.00905; calcd for $C_{18}H_{15}{}^{79}BrN_3OS$ 400.0114, found 400.0111.

1-((5-(4-Nitrophenyl)furan-2-yl)methylene)-4-phenylthiosemicarbazone. 3f was obtained as a yellow solid (96%). Mp: 205.4–206.8 °C. ^{1}H NMR (DMSO-d$_6$): δ = 7.19–7.25 (m, 1H,

H4), 7.28 (d, J = 3.9 Hz, 1H, H3′), 7.38 (br t, J = 7.8 Hz, 2H, H3 and H5), 7.48 (d, J = 3.9 Hz, 1H, H4′), 7.57 (br d, J = 7.8 Hz, 2H, H2 and H6), 8.05–8.11 (m, 3H, H2″, H6″ and –C*H*═N), 8.28 (dd, J = 7.2 and 2.1 Hz, 2H, H3″ and H5″), 9.99 (s, 1H, S═C–N*H*), 12.00 (s, 1H, C═N–N*H*) ppm. ^{13}C NMR (DMSO-d_6): δ = 112.6 (C3′), 115.7 (C4′), 124.4 (C3″ and C5″), 124.6 (C2″ and C6″), 125.5 (C4), 125.8 (C2 and C6), 128.2 (C3 and C5), 131.8 (–*C*H═N), 135.2 (C1″), 138.9 (C1), 146.3 (C4″), 151.0 (C5′), 152.4 (C2′), 175.8 (*C*═S) ppm. IR (Nujol) ν 3316, 3135, 1600, 1592, 1552, 1510, 1341, 1265, 1212, 1201, 1114, 1084, 1029, 809, 849, 798, 711, 693, 637 cm^{-1}. $C_{18}H_{14}N_4O_3S$ (366.08): calcd C 59.01, H 3.85, N 15.29, S 8.75; found C 58.39, H 3.92, N 15.25, S 8.77.

1,1-((5-Phenylfuran-2-yl)methylene)-bis-4-phenylthiosemicarbazone. 4 was obtained as a yellow solid (90%). Mp: 203.9–204.8 °C. ^{1}H NMR (DMSO-d_6): δ = 7.18–7.23 (m, 3H, 2 × (H4 and H4′)), 7.27 (d, J = 3.6 Hz, 1H, H3′), 7.37 (br t, J = 7.9 Hz, 4H, 2 × (H3 and H5)), 7.55–7.62 (m, 4H, 2 × (H2 and H6)), 7.88 (d, J = 8.4 Hz, 2H, H2″ and H6″), 7.97 (d, J = 8.4 Hz, 2H, H3″ and H5″), 8.10 (s, 1H, –C*H*═N), 8.16 (s, 1H, –C*H*═N), 9.96 (s, 1H, S═C–N*H*), 10.15 (s, 1H, S═C–N*H*), 11.86 (s, 1H, C═N–NH), 11.91 (s, 1H, C═N–NH) ppm. ^{13}C NMR (DMSO-d_6): δ = 109.7 (C3′), 115.9 (C4′), 124.1 (C2″ and C6″), 125.3 (C4), 125.4 (C4), 125.5 (C2 and C6), 126.0 (C2 and C6), 128.0 (C3 and C5), 128.1 (C3 and C5), 128.2 (C3″ and C5″), 130.5 (C1″), 132.2 (–*C*H═N), 133.7 (C4″), 138.9 (C1), 139.0 (C1), 142.2 (–*C*H═N), 149.4 (C2′), 154.3 (C5′), 175.6 (*C*═S), 176.0 (*C*═S) ppm. IR (Nujol) ν 3322, 3300, 3158, 1598, 1559, 1524, 1449, 1329, 1261, 1195, 1096, 1024, 943, 919, 747, 693 cm^{-1}. MS (ESI): m/z (%) = 499 (M + H+, 100), 467 (24), 437 (14), 415 (25), 350 (16), 298 (9). HRMS (ESI): calcd for $C_{26}H_{22}N_6OS_2$ 499.1369, found 499.1364.

Spectroscopic studies

Stock solutions of the anions (F^-, Cl^-, Br^-, I^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, AcO^-, BzO^-, CN^- as tetrabutylammonium salts) were prepared at 10^{-2} and 10^{-3} mol dm^{-3} in acetonitrile. The concentrations of ligands used in these measurements were *ca.* 1.2 × 10^{-4} and 1.2 × 10^{-5} mol dm^{-3}. We took care that the maximum addition of anion solutions did not exceed 5% of the volume of the receptor to avoid significant changes in the solution concentration. In the experiments that required the addition of excess of anion (50 equiv.), corrections of the volume and concentration were made. The UV-Vis titrations were carried out at room temperature (~25 °C).

In fluorimetric titrations, all receptors were excited at wavelengths of the pseudo-isosbestic points observed in the course of UV-Vis titrations with fluoride anion. The electronic absorption spectra were obtained on a Perkin Elmer Instruments Lambda 35 UV/visible spectrometer and fluorescence spectra were recorded on a Quanta Master 40 steady state fluorescence spectrofluorometer from Photon Technology Internation (PTI) all in quartz cuvettes (1 cm). ^{1}H NMR titration spectra were acquired with a Varian 300 spectrometer.

Electrochemical studies were carried out in a GPES V 4.9 Autolab 30 system using platinum as the working and reference electrodes, a [Bu_4N][ClO_4] solution (1.0 × 10^{-2} mol dm^{-3}) as the supporting electrolyte and a scan rate of 20 mV s^{-1} in a thermostated cell at 25 °C.

Theoretical studies

Quantum chemical calculations at the semi-empirical level (PM3, within restricted Hartree–Fock level) were carried out in vacuum with the aid of Hyperchem V6.03. The Polar–Ribiere algorithm was used for optimization. The convergence limit and the RMS gradient were set to 0.01 kcal mol^{-1}. Stability constants were estimated with the HypSpec Software V1.1.18 using the data of the titration of receptors with selected anions.

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