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Synthesis and evaluation of fluorimetric and colorimetric chemosensors for anions based on (oligo)thienyl-thiosemicarbazones

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ABSTRACT

A family of heterocyclic thiosemicarbazone dyes (**3a**–**d**) containing thienyl groups has been synthesized, characterized, and their chromo-fluorogenic response in acetonitrile in the presence of selected anions was studied. Acetonitrile solutions of **3a**–**d** show absorption bands in the 338–425 nm range, which are modulated by the groups attached to the thiosemicarbazone moiety. The fluoride, chloride, bromide, iodide, dihydrogen phosphate, hydrogen sulfate, nitrate, acetate, and cyanide anions were used in the recognition studies. Only sensing features were observed for fluoride, cyanide, acetate, and dihydrogen phosphate anions. Two different chromogenic responses were found, (i) a small shift of the absorption band due to coordination of the anions with the thiourea protons and (ii) the appearance of a new red-shifted band due to deprotonation of the receptor. For the latter process changes in the color solutions from pale-yellow to orange-red were observed. Fluorescence studies showed a different emission behavior according to the number of thienyl rings in the π-conjugated bridges. Stability constants for the two processes (complex formation+deprotonation) for receptors **3a**–**d** in the presence of fluoride and acetate anions were determined from spectrophotometric titrations using the HypSpec program. The interaction of **3d** with fluoride was studied through ^{1}H NMR titrations. Semiempirical calculations to evaluate the hydrogen-donating ability of the receptors were also performed.

1. Introduction

The development of new molecular-based receptors able to detect anions, cations, or neutral molecules has recently gained significance due to the importance of detecting some target species in biological and environmental samples. In these systems the receptors are able to transform host-guest interactions into a measurable signal, which allows analyte sensing via electrochemical or optical modulations.[1] In this field, apart from the interest in developing fluorescent probes, chromogenic sensing has gained attention due to the possible semi-quantitative detection to the 'naked-eye' or using very simple instrumentation.[2] Optical chemosensors for metal cations have been developed for more than two decades,[3] whereas in contrast anionic chromogenic probes have only recently been investigated.[4,5] In particular, the supramolecular chemistry of anions has advanced a great deal in the last years and today a number of receptors for anion binding have been described. In most cases they are based on hydrogen bonding, electrostatic interactions or coordination with suitable metal complexes.[6] In this area hydrogen bonding ligands are attractive because show the advantage of being directional allowing discrimination between anions of different hydrogen-bonding requirements or geometries.[7] Among neutral anion binding groups thioureas and thiourea-containing fragments have been widely used for the formation of complexes with anions.[8] In particular thiourea derivatives have been intensively studied as anion receptors and a number of ligands containing different number of thiourea moieties and thioureido NH protons with different acidities have been described.[9] A means of tuning the acidity of thioureido NH protons is to introduce electron-donating or electron-withdrawing substituents.[10] On the other hand, among molecules containing thiourea fragments the use of thiosemicarbazones has gained interest recently as potential receptors. For instance Schiff-base compounds containing thiosemicarbazone groups have also grown in the areas of biology and chemistry due to their fungicidal,

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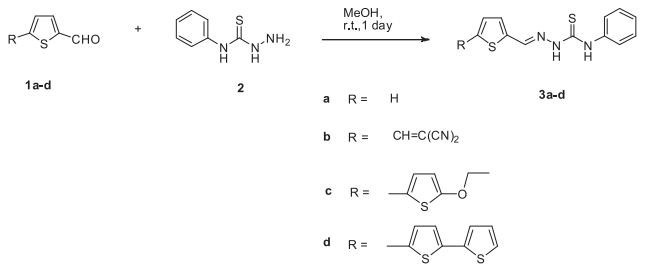
bactericidal, antiviral,[11] and antitumor properties.[12] Recently, we have demonstrated that (oligo)thiophenes, electronically connected to recognition sites, are efficient π-conjugated bridges for the fluorimetric and/or colorimetric sensing of certain anions (e.g., F^-, CN^-) and cations (H^+, Na^+, Pd^{2+}, Cu^{2+}, Zn^{2+}, Hg^{2+}, Ni^{2+}).[13] Moreover recently thiosemicarbazones have also gained attention as anion receptors. 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]

Taking into account our interest in the development of probes for anions and inspired in this previous work on the use of thiosemicarbazones as binding sites we report herein the synthesis and characterization of new (oligo)thienyl-thiosemicarbazones. These derivatives contain heteroaromatic π-conjugated systems (instead of the more commonly used aryl groups) and have been tested as anion chemosensors.

2. Results and discussion

2.1. Synthesis and characterization

The new compounds **3a**–**d** with thiophene, bithiophene, and terthiophene π-conjugated bridges were synthesized in moderate to good yields (41–77%) through Schiff-base condensation of heterocyclic aldehydes **1a**–**d** with 4-phenyl-3-thiosemicarbazide **2** in methanol at room temperature (see Scheme 1).



Scheme 1. Synthesis of the thienyl-thiosemicarbazone receptors **3a**–**d**.

Aldehyde **1a** was commercially available whereas aldehydes **1c** and **1d** were synthesized as reported elsewhere.[15] The 2-((5-formylthien-2-yl)methylene)malononitrile **1b** was synthesized through reaction of thiophene-2,5-dicarbaldehyde with malononitrile in dry DMF with a catalytic amount of piperidine. Purification of the crude product by column chromatography on silica with increasing amounts of diethyl ether in light petroleum as eluent, gave the pure compound in 22% yield. All the compounds were completely characterized by ^1H and ^{13}C NMR, IR, MS, EA or HRMS and the data obtained were in full agreement with the proposed formulation (see Table 1).

The most characteristic signals in the ^1H NMR spectrum of this family of thiosemicarbazones were those corresponding to N–H and CH=N protons. ^1H NMR studies in deuterated chloroform showed CH=N protons in the 7.97–8.14 ppm range whereas thiourea-N–H protons were found in the 9.07–9.11 and 9.35–10.49 ppm interval for N–H adjacent to the phenyl ring and for the N–H adjacent to the CH=N moiety, respectively. When four compounds are considered the highest variation in δ were found for the N–H protons located in the vicinity of the CH=N moiety adjacent to thiophene ($\Delta\delta$=0.94 ppm). Moreover, the N–H protons adjacent to the phenyl ring were the less affected ($\Delta\delta$=0.04 ppm).

2.2. Spectroscopic behavior of 3a–d

Acetonitrile solutions (C=1.2×10^{-5} mol dm^{-3} at 25 °C) of the thiosemicarbazone-functionalized receptors **3a**–**d** showed an intense absorption band ($\log \varepsilon \approx 4.4$) in the 338–425 nm region (see Table 2). Compound **3a** containing thiosemicarbazone moiety surrounded by a phenyl and a thienyl ring, showed an absorption band at 338 nm. The change of a hydrogen at the thienyl ring by a better electron acceptor moiety, such as a dicyanovinyl group (receptor **3b**) induced a red shift from 338 to 425 nm. The presence of one more thienyl group and an electron donor, such as an ethoxy group (receptor **3c**) induced a small red shift when compared with **3a** from 338 to 381 nm. Moreover the presence of two additional thienyl rings on the framework of **3a** (receptor **3d**) induced a bathochromic shift of the band (from 338 to 396 nm), which is most likely a consequence of the extension of the conjugation.

2.3. UV–vis studies involving anions

The UV–vis behavior of receptors **3a**–**d** in acetonitrile solutions (C=1.2×10^{-5} mol dm^{-3}) was studied at 25 °C in the presence of the fluoride, chloride, bromide, iodide, cyanide, nitrate, acetate, perchlorate, hydrogen sulfate, and dihydrogen phosphate anions. For all the receptors the presence (up to 100 equiv) of chloride, bromide, iodide, hydrogen sulfate, and nitrate induced insignificant changes in the UV–vis spectra strongly suggesting that no coordination takes place. This behavior contrasts with that observed in the presence of basic anions, such as fluoride, cyanide, acetate, and dihydrogen phosphate (see Fig. 1).

For instance UV–vis titrations of receptors **3a**–**d** with fluoride showed an intensity decrease and a small bathochromic shift of the absorption band together with a simultaneous growth of a new red-shifted band. Moreover both the position of the new band and the relative intensity of the absorption band of the receptor with respect to the band upon addition of fluoride were dependent on the receptor used. For instance, the behavior observed in the presence of F^- for receptors **3c** and **3d** is shown in Figs. 2 and 3.

Receptor **3c** in acetonitrile was yellow due to the band at 381 nm. Upon addition of increasing quantities of fluoride this band progressively decreased while a new absorption at 515 nm ($\Delta\lambda$=134 nm) increased in intensity (see top of Fig. 2). This induced a color modulation from pale-yellow to orange. This was in agreement with the expectation that the coordination of an anion in a donor group in a push–pull system will induce a bathochromic

Table 1
Yields, ^1H NMR, and IR data of the oligothienyl-thiosemicarbazone receptors **3a**–**d**

Formyl thiophene	Product	Yield (%)	δ_H (ppm)[a]			IR[b] ν(cm^{-1})	
			(CH=N)	(C=N–NH)	(S=C–NH)	(=C–H)	(NH)
1a	**3a**	66	8.14	10.29	9.11	3141	3297
1b	**3b**	77	8.02	9.60	9.07	3122	3341
1c	**3c**	50	8.07	10.49	9.09	3127	3329
1d	**3d**	41	7.97	9.35	9.09	—	3310

[a] For the NH proton of the (oligo)thienyl-thiosemicarbazone receptors **3a**–**d** (300 MHz, $CDCl_3$).
[b] IR was recorded in Nujol.

Table 2
Spectroscopic data for compounds **3a**–**d**

Receptor	λ_{ab} LH (nm)	λ_{ab} L^- (nm)[a]	Log ε (LH)	λ_{em} LH (nm)	$\Delta\lambda_{em}$ L^- (nm)[a]	Φ	$\Delta\lambda_{ab-em}$ LH (nm)	$\Delta\nu_{ab-em}$ LH (cm^{-1})
3a	338	397	4.25	439	447	0.0064	101	6806
3b	425	626	4.35	560	539	0.0019	135	5672
3c	381	515	4.51	483	482	0.065	102	5542
3d	396	503	4.39	489	517	0.088	93	4802

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

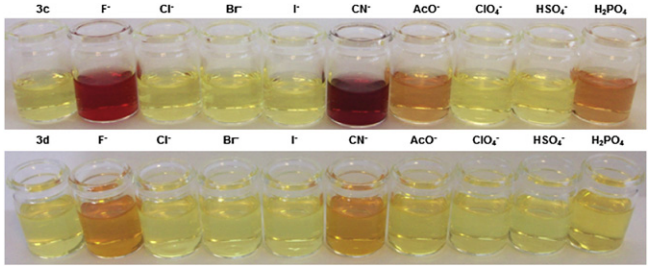


Fig. 1. Color changes of **3c** (top) and **3d** (bottom) solution (5×10^{-4} mol dm^{-3}) seen in the presence of 10 equiv of F^-, Cl^-, Br^-, I^-, CN^-, AcO^-, ClO_4^-, HSO_4^- and $H_2PO_4^-$.

shift. Receptor **3d** showed a similar behavior with fluoride; i.e., the band at 396 nm suffered a small hypochromic effect and a new absorption band at 503 nm ($\Delta\lambda$=107 nm) grew in intensity (see top of Fig. 3). As can be seen, it is apparent from the figure that the ratio between both bands was different for receptors **3c** and **3d**. Also it was clear that for a certain receptor the change observed depends on the anion used in the titration experiments. It was observed that fluoride and cyanide anions induced UV–vis changes for all the receptors whereas acetate and hydrogen phosphate displayed a poorer response and only gave noticeable changes with **3b** and **3c** (see for instance the bottom of Figs. 2 and 3). When receptors **3a** and **3d** were compared it was found that **3a** was able to induce some changes with acetate, although to a much lesser extent than **3b** and **3c**.

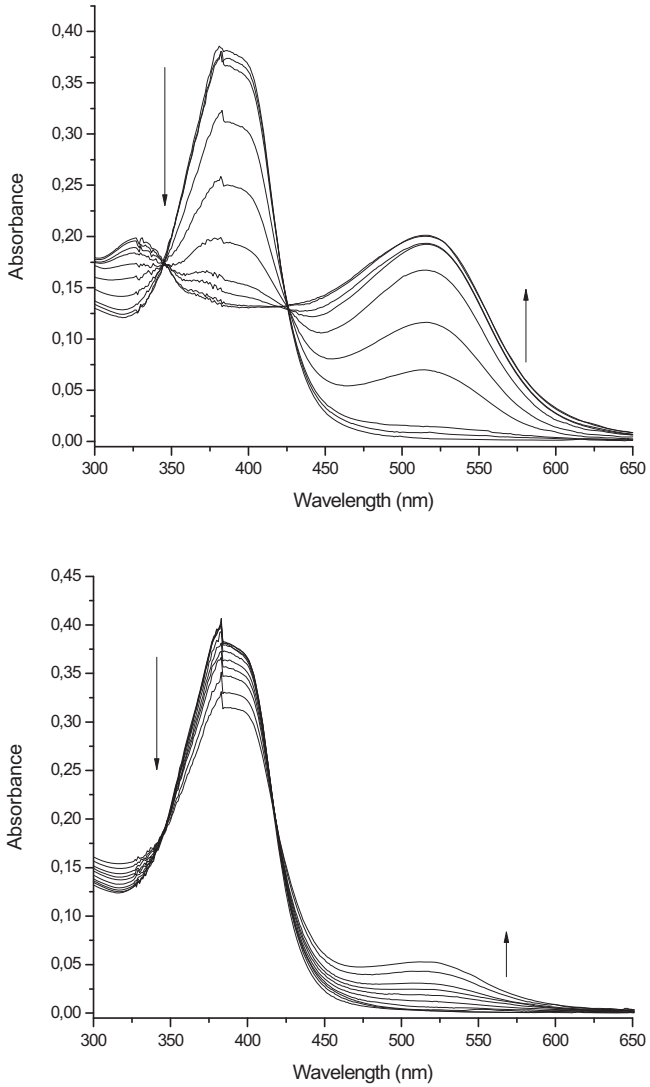


Fig. 2. UV–vis titration of receptors **3c** (1.2×10^{-5} mol dm^{-3}) with fluoride (top) and acetate (bottom) anions (0–30 equiv) in acetonitrile.

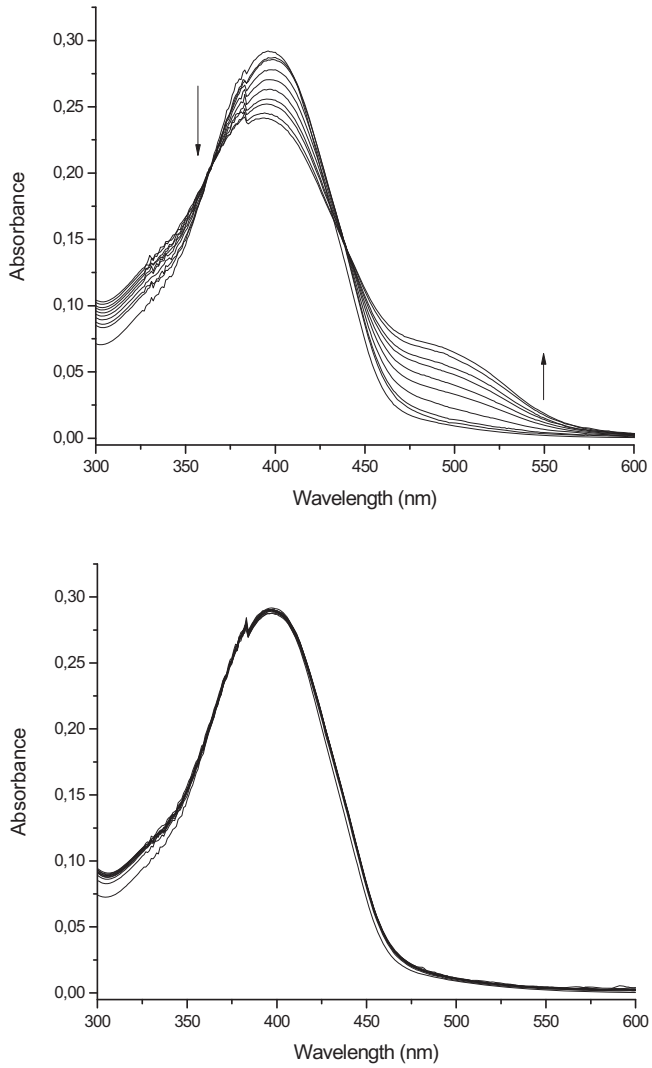


Fig. 3. UV–vis titration of receptors **3d** (1.2×10^{-5} mol dm^{-3}) with fluoride (top) and acetate (bottom) anions (0–30 equiv) in acetonitrile.

The changes observed in the UV–vis spectrum upon fluoride addition were attributed to the formation of hydrogen-bonding complexes with the thiosemicarbazone groups that eventually resulted in a deprotonation.[16,17] The formation of hydrogen-bonding complexes was reflected in relatively small variations in the absorption band of the receptor whereas deprotonation processes was related with the appearance of a new absorption band at longer wavelengths.[18] Moreover a close view of the results indicated that the final response of the receptors **3a**–**d** towards the tested anions is dependent on the functional groups attached to the thiosemicarbazone group that modulated the acidity of the N–H protons. In our case the UV–vis studies suggested that the acidity of the receptors follows the order **3b**>**3c**>**3a**>**3d**. In fact, whereas **3b** and **3c** were able to display color changes (deprotonation) with fluoride, cyanide, acetate and dihydrogen phosphate, receptors **3a** and **3d** only showed significant color modulations in the presence of fluoride and cyanide.

2.4. Stability constants

As stated above, in the interaction of basic anions with the semithiocarbazone-containing receptors **3a**–**d** two different behaviors were observed: (i) hydrogen bonding interactions and (ii) deprotonation (see Eqs. 1 and 2). In order to complete the characterization of **3a**–**d** coordination and deprotonation processes were studied via the evaluation of the corresponding stability constants that were determined by UV–vis spectroscopic titrations between receptors **3a**–**d** and the fluoride and acetate anions, using the software HypSpec V1.1.18. The obtained data were adjusted to two consecutive equilibriums corresponding to coordination and deprotonation (see Eqs. 1 and 2) and the results are shown in Table 3.

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

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

2.5. Fluorogenic studies involving anions

Fluorescence studies in acetonitrile solutions of the receptors upon addition of increasing amounts of the corresponding anion were also carried out. Receptors were excited in the pseudo-isosbestic points observed in the course of UV–vis titrations. All receptors displayed a broad and unstructured emission band. Quantum yields in acetonitrile (see Table 2) ranged from quite low (receptor **3a**, Φ=0.0064) to medium (compound **3d**, Φ=0.088). The addition of chloride, bromide, iodide, hydrogen sulfate, and nitrate anions to receptors **3a**–**d** resulted in negligible changes in the emission intensity profiles. In contrast, the fluorescence emission in presence of fluoride, cyanide, acetate, and dihydrogen phosphate changed significantly.

A different general behavior was found depending on the anion and the receptor used in the studies. Fig. 4 shows the changes observed in the emission of **3a** in the presence of increasing amounts of fluoride or acetate. In presence of fluoride, an enhancement of the fluorescence intensity upon the addition of moderate amounts of fluoride followed by a quenching of the emission band at higher anion concentrations and the shift of the final band at longer wavelengths were observed. This behavior is in agreement with the changes observed in the absorption titrations and the coordination plus deprotonation equilibriums. Thus enhancement of the fluorescence emission is attributed to the formation of the corresponding hydrogen-bonding complex (Eq. 1), whereas further quenching and shift of the band is related with the formation of the deprotonated species.

Fig. 4 (bottom) also shows the emission behavior found for **3a** in the presence of acetate. In this case only an enhancement of the fluorescence was found in agreement with the formation of hydrogen-bonding complex (note that no clear deprotonation was found for **3a** with acetate). A similar emission behavior in the presence of fluoride and acetate was found when using receptor **3b**.

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

	F^-		AcO^-	
	$LH + A^- \leftrightarrows LH\cdots A^-$	$LH\cdots A^- + A^- \leftrightarrows L^- + A_2H^-$	$LH + A^- \leftrightarrows LH\cdots A^-$	$LH\cdots A^- + A^- \leftrightarrows L^- + A_2H^-$
3a	3.46(4)	2.75(3)	1.29(3)	[a]
3b	5.39(8)	4.19(4)	3.46(2)	1.52(7)
3c	3.62(6)	2.06(8)	2.36(5)	0.48(2)
3d	3.55(6)	1.06(6)	[a]	[a]

[a] No reliable results were obtained.

From Table 3 it can be observed that, as a general trend, the logarithms of the stability constants measured for both equilibriums with fluoride were higher than those obtained for acetate when using receptors **3a**, **3b** and **3c**. This was in agreement with the results detailed above and with the more basic character of fluoride in acetonitrile when compared with acetate. It can be observed in Table 3 that the stability constants for the formation of the corresponding hydrogen-bonding complexes were, for fluoride, at least one order of magnitude larger than the stability constants for the deprotonation and about two orders of magnitude for acetate. Table 3 also shows that deprotonation constants were more important for fluoride than for acetate. The stability constants determined in this study are similar than those reported for other thiosemicarbazones receptors but lower than those found for other urea/thiourea receptors functionalized with benzene.[19–21]

This behavior observed for **3a** and **3b** contrasts with the emission behavior found for **3c** and **3d**. For these latter receptors a quenching of the fluorescence was observed in the presence of increasing amounts of both fluoride and acetate. Taking into account that all four receptors showed a similar UV–vis behavior with anions the strong difference in emission properties should most likely be attributed to the presence of two and three thienyl groups in **3c** and **3d** that would favor deactivations paths that were not active in compounds **3a** and **3b**, which contain only one thiophene moiety.

2.6. ^{1}H NMR spectroscopic studies in the presence of anions

UV–vis and fluorescence studies of thiosemicarbazone receptors **3a**–**d** displayed a varied response in the presence of anions related with hydrogen bonding interactions and deprotonation of

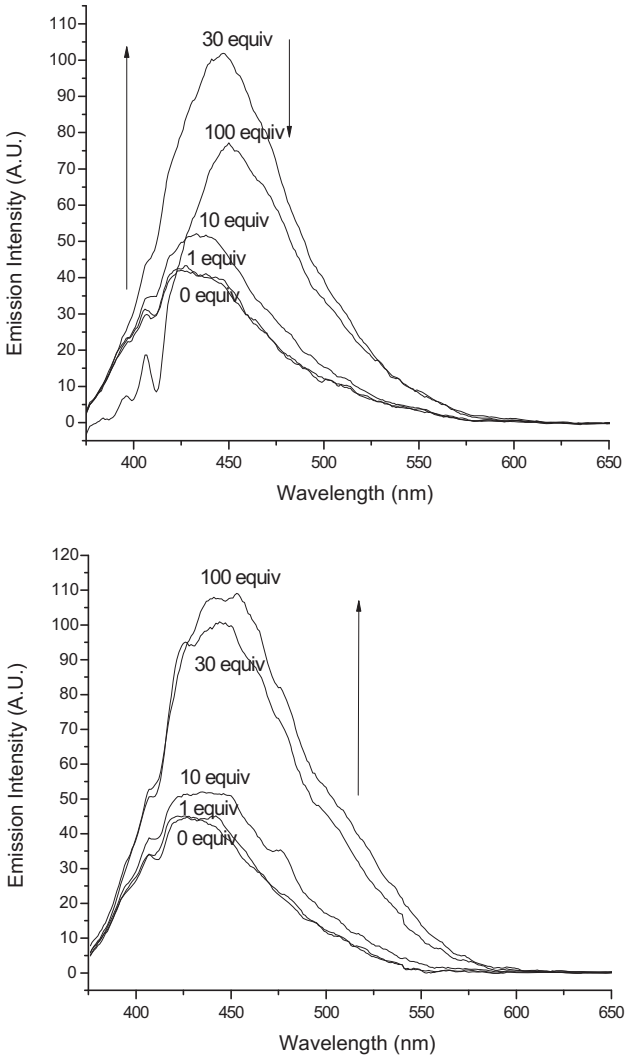
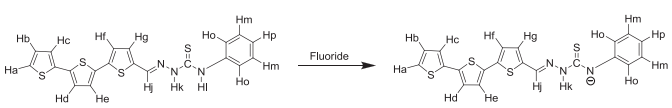


Fig. 4. Emission changes in **3a** (1.2×10^{-5} mol dm^{-3}) in the presence of fluoride (top) and acetate (bottom) anions. Emission spectra of the receptor in the presence of 0, 1, 10, 30 and 100 equiv of the corresponding anion.

the receptors. In order to study in more detail this dual coordination/deprotonation process the interaction of receptor **3d** with fluoride anion was investigated by means of ^{1}H NMR titration experiments in DMSO-d_6.

^{1}H NMR spectrum of **3d** showed resonances for the benzene ring at 7.20 (1H, broad triplet, H_p), 7.39–7.36 (2H, broad multiplet, H_m), 7.58 (2H, broad doublet, H_o) ppm, whereas protons of the two 2,5-disubstituted thiophene rings (H_d, H_e and H_f, H_g) appeared as doublets at 7.31(H_f) and at 7.49 (H_g) ppm for the first ring and as a broad multiplet in the 7.39–7.36 ppm range (H_d and H_e) for the second. Protons of the third 2-monosubstituted thienyl ring appeared as a double doublet at 7.11 (H_b), a doublet at 7.54 (H_c), which overlapped with a doublet at 7.35(H_a). Finally, the imine proton (–C*H*=N) appeared as a broad singlet at 8.30 (H_j) ppm and the N–*H* protons of the thiosemicarbazone group also were broad singlets at 11.88 (H_k) and 9.84 (H_l) ppm (Scheme 2).



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

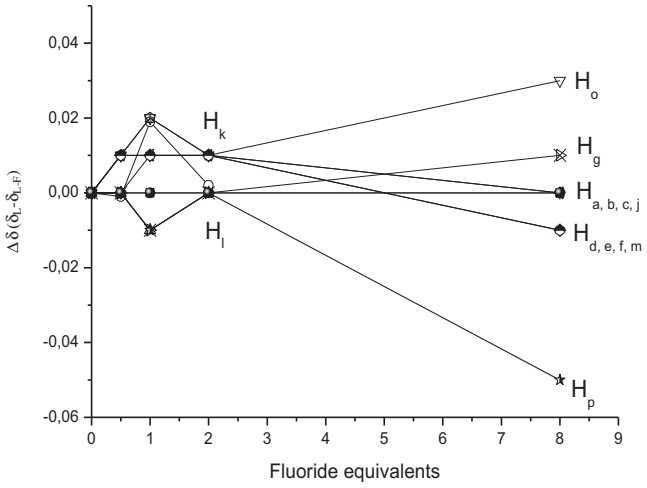


Fig. 5. ^{1}H NMR shifts for the protons of receptor **3d** in the presence of increasing quantities of fluoride anion (DMSO-d_6).

In the presence of fluoride (5 equiv) the most remarkable observation was the disappearance of the H_k and H_l signals. Moreover the observed variation in the chemical shifts $\Delta\delta$ (ppm) over the course of the titration with fluoride for other protons in **3d** is shown in Fig. 5.

As could be seen, H_a–H_g protons showed minor changes, whereas, in contrast, remarkable shifts were observed for H_o and H_p suggesting that deprotonation occurs in the N–H group closer to the phenyl group. Fabbrizzi et al. and ourselves have observed in closely related thioureas a similar behavior; i.e., the deprotonation apparently occurs in the protons of the nitrogen attached to the phenyl ring from NMR studies.[22]

2.7. Quantum mechanical studies

The hydrogen bond donating or accepting ability of a molecule at a particular site can be known by studying the deprotonation energy in gas-phase using quantum chemical calculations via the subtraction of the energy of the receptor alone from that of the deprotonated form. Following this concept, calculations were carried out using a PM3 semiempirical model that was applied to all the receptors **3a**–**d**. As these thiosemicarbazone receptors contain two N–H groups, the deprotonation studies were performed assuming that both protons could be eliminated. The results of this study are shown in Table 4. Data strongly suggests that the most acidic proton is H_k (see Scheme 2). As it can be observed there is not an agreement between the data obtained from the theoretical calculations and ^{1}H NMR titrations that suggested that deprotonation occurs at the H_l proton.

Despite this contradiction, theoretical calculations agree with the chromogenic behavior observed for the receptors. Quantum mechanical studies indicated that the dicyanovinyl derivative **3b** is the most acidic followed by the receptor **3c**. In fact the theoretical studies indicated that the acidity of the receptors follow the order **3b**>**3c**>**3a**>**3d** (see Table 4). This is in agreement with the chromofluorogenic behavior of the receptors (vide ante) 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^-); i.e., the most acidic receptors **3b** and **3c** showed color changes in the presence of fluoride, cyanide, acetate, and dihydrogen phosphate, whereas the less acidic **3a** and **3d** ligands were only able to show a remarkable color modulation in the presence of the most basic anions fluoride and cyanide anions.

Table 4
Stabilization energies calculated for the deprotonation of the receptors **3a**–**d**

Receptors	$E_{(L)}-E_{(LH)}$ (Kcal/mol)	
	R=N–NH–C(S)–*N*–Ph[a]	R=N–N–C(S)–NH–Ph[b]
3a	−4.81	−12.3
3b	−10.54	−19.85
3c	−6.39	−14.19
3d	−0.57	−3.46

[a] Deprotonation at the H_l proton (see Scheme 2).
[b] Deprotonation at the H_k proton (see Scheme 2).

3. Conclusions

A family of novel heterocyclic thiosemicarbazone containing thienyl groups, derivatives **3a**–**b**, has been prepared, characterized and their interactions with anions were studied through UV–vis, fluorescence, ^{1}H NMR and quantum chemical calculations. Two different chromo-fluorogenic behaviors in the presence of anions in acetonitrile were observed. The more basic anions fluoride and cyanide were able to induce dual coordination–deprotonation for all **3a**–**d** receptors studied, whereas acetate and dihydrogen phosphate showed poorer coordination ability and deprotonation was only observed on the more acidic receptors **3b** and **3c**. Hydrogen bonding interactions resulted in a small bathochromic shift, whereas deprotonation was indicated by the appearance of a new band at longer wavelengths. Color changes from pale-yellow to yellow-red were observed. In fluorescence studies it was apparent that hydrogen bonding interactions were visible through the enhancement or the decay of the emission band according to the number of thienyl rings at the π-conjugated bridges. Quantum mechanical studies suggested that the acidity of the receptors follows the order **3b**>**3c**>**3a**>**3d**, which was in agreement with the experimentally observed behavior.

4. Experimental section

4.1. Materials and methods

Thin layer chromatography was carried out on 0.25 mm thick precoated silica plates (Merck Fertigplatten Kieselgel 60F_{254}). All melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. 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 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 internal reference. The solvents are indicated in parenthesis before the chemical shift values (δ relative to TMS and given in parts per million). IR spectra were run on a FTIR Perkin–Elmer 1600 spectrophotometer. 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, on a Hewlett Packard 5989 A spectrometer for low resolution spectra and a VG Autospec M spectrometer for high resolution mass spectra. All the solvents were of spectrophotometrical grade. The aldehyde **1a** and 4-phenyl-3-thiosemicarbazide **2** were purchased from Sigma–Aldrich reagents and used without further purification. The synthesis of the aldehydes **1c** and **1d** was reported elsewhere.[15]

4.2. Synthesis of 2-((5-formylthiophen-2-yl)methylene) malononitrile 1b

To a solution of malononitrile (0.094 g, 1.4 mmol) and thiophene-2,5-dicarbaldehyde (0.2 g, 1.4 mmol) in dry DMF (15 mL), was added piperidine (1 drop). The solution was heated at 120 °C during 2 h. After cooling the mixture the solvent was removed under reduced pressure to give 2-((5-formylthiophen-2-yl)methylene)malononitrile **1b**, which was purified by column chromatography on silica with increasing amounts of diethyl ether in light petroleum as eluent.

*4.2.1. 2-((5-Formylthiophen-2-yl)methylene)malononitrile **1b**.* Orange solid (22%). Mp 161.1–165.3 °C. IR ($CHCl_3$) ν 2221 (CN), 1663 (C=O), 1571, 1432, 1215, 1069, 795 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.83 (br d, 1H, *J*=3.9 Hz, 4-H), 7.80–7.90 (m, 2H, 3-H and=C*H*), 10.03 (s, 1H, C*H*O). MS (EI) *m*/*z* (%): 188 (M^+, 60), 187 (100), 159 (11), 115 (9). HRMS: (EI) *m*/*z* (%) for $C_9H_4N_2OS$; calcd 188.0044; found 188.0049.

4.3. General procedure for the synthesis of heterocyclic phenylthiosemicarbazones 3a–d

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 precipitated as microcrystalline solids, which were collected by suction filtration, washed with cold MeOH and diethyl ether and dried in vacuum. Further recrystallization steps using $CHCl_3$/petroleum ether mixtures were performed if necessary.

4-*Phenyl*-1-((*thiophen*-2-*yl*)*methylene*)*thiosemicarbazone* **3a**[23] was obtained as a yellow solid (66%). Mp 185.6–186.9 °C. ^{1}H NMR ($CDCl_3$): δ=7.07–7.10 (m, 1H, 4′-H), 7.25–7.29 (m, 1H, 4-H), 7.32 (dd, *J*=3.9 and 0.9 Hz, 1H, 3′-H), 7.39–7.48 (m, 3H, 3- and 5- and 5′-H), 7.66 (br d, *J*=9.0 Hz, 2H, 2- and 6-H), 8.11 (s, 1H, –C*H*=N), 9.11 (s, 1H, S=C–N*H*), 10.29 (s, 1H, C=N–N*H*) ppm. IR (Nujol) ν 3297(NH), 3141(=C–H), 1588, 1547, 1521, 1505, 1445, 1386, 1311, 1268, 1220, 1204, 1068, 1041, 922, 855, 817, 784, 763, 742, 726, 712, 701, 687, 622, 541 cm^{-1}. MS (FAB): *m*/*z* (%)=262 ($[M+H]^+$, 100), 228 (3), 168 (17). FAB-HRMS: calcd for $C_{12}H_{11}N_3S_2$ 262.0475; found 262.0467.

1-((5-(2,2-*Dicyanovinyl*)*thiophen*-2-*yl*)*methylene*)-4-*phenylthiosemicarbazone* **3b** was obtained as a red solid (77%). Mp 185.0–186.0 °C. ^{1}H NMR ($CDCl_3$): δ=7.22–7.28 (br t, *J*=7.2 Hz, 1H, 4-H), 7.37 (br d, *J*=7.8 Hz, 2H, 3- and 5-H), 7.52 (br d, *J*=7.2 Hz, 2H, 2- and 6-H), 7.82 (br s, 1H, 4′-H), 7.87 (br s, 1H, 3′-H), 7.96 (s, 1H, –C*H*=N), 8.02 (s, 1H, –C*H*=C($CN)_2$), 9.08 (s, 1H, S=C–N*H*), 9.60 (s, 1H, C=N–N*H*) ppm. IR (Nujol) ν 3341 (NH), 3122 (=C–H), 2223 (CN), 1596, 1579, 1568, 1540, 1517, 1498, 1261, 1198, 1097, 1061, 915, 811, 748, 705, 690, 610 cm^{-1}. MS (FAB): *m*/*z* (%)=338 ($[M+H]^+$, 100), 306 (9). FAB-HRMS: calcd for $C_{16}H_{11}N_5S_2$ 338.0529; found 338.0526.

1-((5-(5-*Ethoxythiophen*-2-*yl*)*thiophen*-2-*yl*)*methylene*)-4-*phenylthiosemicarbazone* **3c** was obtained as a brown solid (50%). Mp 171.3–171.6 °C. ^{1}H NMR ($CDCl_3$): δ=1.44 (t, *J*=7.2 Hz, 3H, OCH_2CH_3), 4.14 (q, *J*=7.2 Hz, 2H, OCH_2CH_3), 6.15 (d, *J*=3.9 Hz, 1H, 4″-H), 6.91 (d, *J*=3.9 Hz, 1H, 3″-H), 6.93 (d, *J*=3.9 Hz, 1H, 3′-H), 7.15 (d, *J*=3.9 Hz, 1H, 4′-H), 7.25–7.32 (m, 1H, 4-H), 7.43 (br t, *J*=7.5 Hz, 2H, 3- and 5-H), 7.67 (br d, *J*=7.5 Hz, 2H, 2- and 6-H), 8.07 (s, 1H, –C*H*=N), 9.09 (s, 1H, S=C–N*H*), 10.50 (s, 1H, C=N–N*H*) ppm. ^{13}C NMR ($CDCl_3$): δ=14.6 (OCH_2CH_3), 69.6 (OCH_2CH_3), 105.7 (C4″), 122.2 (C3″), 122.9 (C3′), 123.0 (C2′), 124.7 (C2 and C6), 126.3 (C4), 128.8 (C3 and C5), 132.4 (C4′), 134.8 (C5′), 137.6 (*C*H=N), 137.8 (C1), 141.7 (C2″), 165.7 (C5″), 175.0 (C=S) ppm. IR (Nujol) ν 3329 (NH), 3127 (=C–H), 1588, 1550, 1509, 1483, 1465, 1384, 1322, 1274, 1245, 1206, 1079, 1039, 912, 873, 779, 764, 743, 729, 703, 692, 614 cm^{-1}. $C_{18}H_{17}N_3OS_3$ (387.54): calcd. C 55.79, H 4.42, N 10.84, S 24.82; found C 56.21, H 4.51, N 10.51, S 25.09.

4-*Phenyl*-1-((5-(5-(*thiophen*-2-*yl*)*thiophen*-2-*yl*)*thiophen*-2-*yl*)*methylene*)*thiosemicarbazone* **3d** was obtained as an orange solid (41%). Mp >216 °C. ^{1}H NMR ($CDCl_3$): δ=7.05–7.18 (m, 8H, 4-H and thienyl-H), 7.21 (t, 2H, 3- and 5-H), 7.70 (d, 2H, 2- and 6-H), 7.97 (s, 1H, –C*H*=N), 9.09 (s, 1H, S=C–N*H*), 9.35 (s, 1H, C=N–N*H*) ppm. ^{13}C NMR (DMSO-d_6): δ=124.6, 124.7, 125.2, 125.3, 125.6, 125.9, 126.1, 128.1, 128.6, 132.3, 134.8, 135.8, 136.3, 137.4, 137.6, 138.3, 139.0, 175.5

(C=S) ppm. IR (Nujol) ν 3310 (NH), 1742, 1586, 1546, 1463, 1456, 1377, 1307, 1270, 1202, 1169, 1156, 1076, 1059, 967, 922, 892, 783, 722, 703, 514 cm^{-1}. MS (FAB): m/z (%)=426 ($[M+H]^+$, 100), 424 (98), 394 (47), 338 (47), 288 (11). FAB-HRMS: calcd for $C_{20}H_{15}N_3S_4$ 426.0221; found 426.0218.

4.4. Physical measurements

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}. ^1H NMR experiments were carried out in DMSO-d_6. At high concentrations the receptors showed low solubility in acetonitrile.

In fluorimetric titrations, all receptors were excited in wavelength 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). ^1H NMR titrations spectra were acquired with Varian 300 spectrometer.

4.5. Theoretical studies

Quantum chemical calculations at semiempirical 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 the optimization. The convergence limit and the rms gradient were set to 0.01 kcal mol^{-1}. The stability constants were estimated with the HypSpec Software V1.1.18 with data of titration of receptors with selected anions.

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