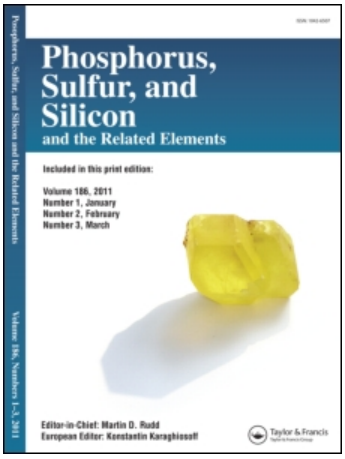

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis and Anion Recognition Properties of Thiosemicarbazone Based Molecular Tweezers

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To cite this Article Zhang, You-Ming , Wang, Dan-Dan , Lin, Qi and Wei, Tai-Bao(2008) 'Synthesis and Anion Recognition Properties of Thiosemicarbazone Based Molecular Tweezers', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 1, 44 — 55
To link to this Article: DOI: 10.1080/10426500701555777
URL: http://dx.doi.org/10.1080/10426500701555777

Phosphorus, Sulfur, and Silicon, 183:44–55, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701555777

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Synthesis and Anion Recognition Properties of Thiosemicarbazone Based Molecular Tweezers

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A series of novel thiosemicarbazone based molecular tweezers were synthesized and studied as anion-binding receptors. Contrasting our former work, some of these receptors not only have considerable selectivity to $H_2PO_4^-$, as well as F^- and CH_3COO^-. When adding F^-, CH_3COO^- and $H_2PO_4^-$ anions to their solutions respectively, the color has shown striking changes from colorless to yellow or dark yellow. The binding abilities of the receptors are according with the acidities of the N-H groups on the thiourea moiety, which are determined by the electronegativity of subgroups on them. Job plot indicated that 1:1 stoichiometry complex are formed between receptors and anions.

Keywords Anion recognition; molecular tweezers receptor; thiosemicarbazone

INTRODUCTION

Anions recognition has been growing in the field of host-guest chemistry due to biological and environmental significance.[1–8] Recently, more and more considerable attentions have focused on the design and synthesis of anion receptors, such as fluorescence chemosensors and colorimetric sensors.[3,5,9–19] Up to now, much of the literature has reported that receptors employing thiourea groups could recognize various anions in organic, inorganic and mixture solvents.[16–21] It is known that receptors

Received May 5, 2007; accepted June 5, 2007.
This work is supported by NSFC (No. 20671077), the Key Project of Chinese Ministry of Education (No. 205161), Gansu Provincial Natural Science Found of China (No. 3ZS061-A25-027), Scientific Research Fund for youth of Gansu province in China (No. 3YS051-A25-010), Scientific Research Fund of Gansu Provincial Education Department (No. 0601-24), and Key Laboratory of Eco-Environment-Related Polymer Materials (Northwest Normal University) Ministry of Education.

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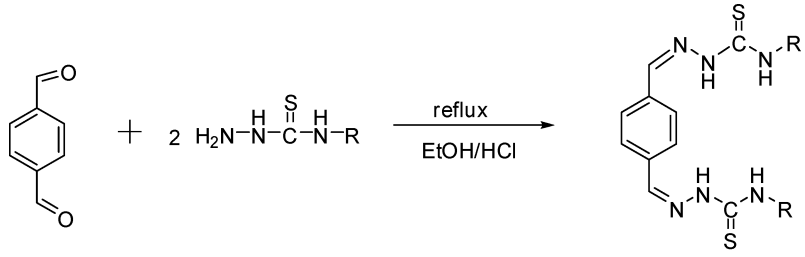
bearing thiourea moieties bind anions through hydrogen bonding; furthermore, among a variety of possible H-bond donor groups, thiourea moieties have been proven especially efficient in the design of anion binding receptors. Interestingly, some of them have been observed the changing from one color to another on addition of anions, which provide an approaching to detect anions just with naked eyes using colorimetry. In our previous work, we have reported that isophthalic aldehyde derivatives bearing two thiourea groups bind F^- and CH_3COO^- in DMSO strongly and selectively, which is due to that the cooperative action of two thiourea groups for anions could effectively enhance the stability of the resultant complexes.[21] In view of these observations and in continuation of our work on the development of anion recognition receptors,[21–25] we combined terephthalic aldehyde with thiosemicarbazide unit to produce a series thiosemicarbazone based molecular tweezers receptors (**1**∼**4**). Herein, we report the synthesis and anion recognition properties of these receptors. Fortunately, we found that the compounds **2**, **3**, and **4** can recognize F^- and CH_3COO^-anions, and besides this, the receptors **2** and **4** have beautiful selectivity to $H_2PO_4^-$ in DMSO. Moreover, a clear color change was observed from colorless to dark yellow upon addition of F^- and CH_3COO^- to the solution of the receptors **2**, **3**, and **4** in DMSO, but the same phenomenon took place only for **4** in the present of $H_2PO_4^-$. After investigating the fluorescence properties of these compounds, we found all of these receptors have strong fluorescence intensity in DMSO, while the fluorescence emission spectra of receptors have not change markedly upon addition of various anions. This may be because there was no ground state interaction between the fluorophore and the receptor's binding spots.

RESULTS AND DISCUSSION

Receptors **1**∼**4** were synthesized by the reaction of terephthalic aldehyde with thiosemicarbazide or N^4-arylthiosemicarbazide in high yields. The synthetic route is shown in Scheme 1. These compounds were characterized by IR,^{1}H NMR, ^{13}C NMR and elemental analysis.

UV-Vis Absorption Spectra

The binding and recognition abilities of receptors **1**∼**4** towards various anions (tetrabutylammonium were used for counter cations) in DMSO were studied via UV-Vis absorption spectrophotometry. As shown in Figure 1a, the spectral changes for receptor **1** which exhibited weak



1: R=H; **2**: R=C_6H_5; **3**: R=4-$OCH_3C_6H_4$; **4**: R=O-ClC_6H_4

SCHEME 1

binding ability in the presence of anions was so small that it was worthless of recognition. In confront to receptor **1**, host **4** exhibited selective recognition for F^-, $CH_3COO^-$and$H_2PO_4^-$ in DMSO (Figure 1b), however, addition of Cl^-, Br^-, I^-, HSO_4^-, NO_3^- scarcely showed spectral changes. Compared to our previous work on isophthalic aldehyde bis-arylthiosemicarbazone receptors—which had a better selectivity of F^- and CH_3COO^-[21]—receptors **2** and **4** had an excellent selectivity of $H_2PO_4^-$ in this report. This is due to the molecular tweezers cavum of current receptors is larger than those have reported, which means that the size of the tweezers cavum of these receptors is able to match up to the spatial structure of $H_2PO_4^-$. The receptor **3** could not recognize $H_2PO_4^-$, which ascribing to the weak acidity of receptor **3** and the alkalescency of the $H_2PO_4^-$ anion. It was observed that when added F^- and CH_3COO^- to the solution of receptors **2**, **3**, and **4** in DMSO,

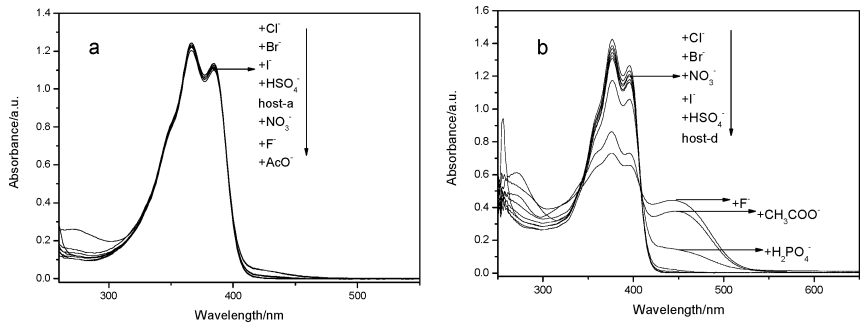


FIGURE 1 (a) UV-Vis absorption of receptor **1** and (b) receptor **4** in the presence of 50 equiv of various anions in DMSO at 298 K. [receptor] = 2.0×10^{-5} mol L^{-1}.

respectively, a color stroke from colorless to dark yellow immediately, and the change could be detected via the naked-eyes. While on addition of $H_2PO_4^-$ the same phenomenon only took place for receptor **4**. The result indicated that there was better recognition action to F^- and CH_3COO^- for receptors **2**, **3** and **4** but $H_2PO_4^-$ only for receptor **2** and **4**.

The UV-Vis absorption titration of receptor **4** for F^-, CH_3COO^- and $H_2PO_4^-$ is depicted in Figure 2. With gradual increasing of the concentration of F^-, the intensity of absorption band at around 376 nm and 392 nm were decreased until the peak disappeared and a new absorption band appeared with a maximum absorption at 453 nm along with two isosbestic points at 347 nm and 404 nm, respectively. The absorbance at 453 nm increased with the increasing concentration of F^- anions with a small bathochromic occurred from 453 to 459, which indicated that the host-guest complex could further promote the intermolecular change transport.[25] The receptors **2** and **3** showed similar spectral changes as **4** through isosbestic points at 345 nm and 403 nm as upon addition of F^- anions. However, the absorption change of receptor

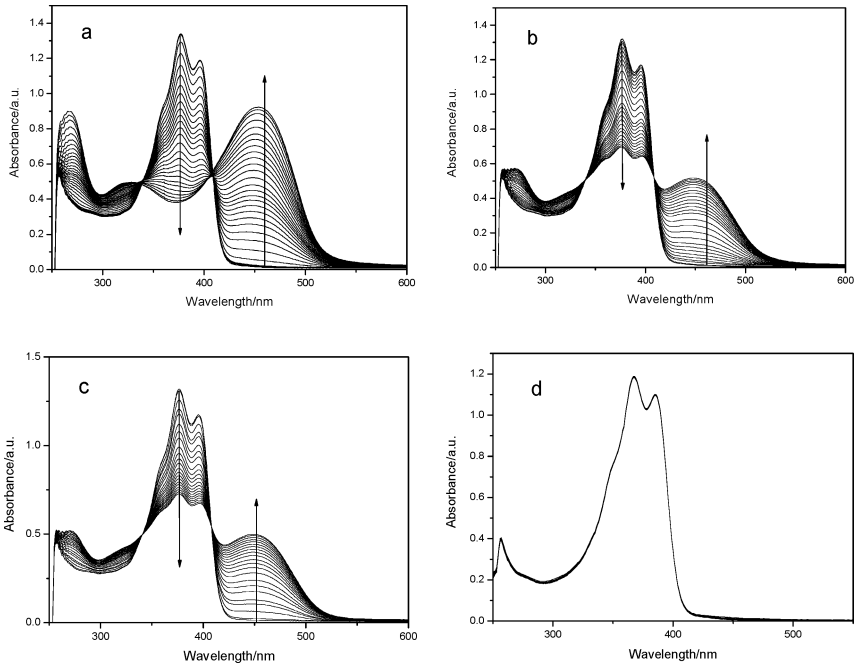


FIGURE 2 (a) The changes in absorption spectra of receptor **4** (2.0×10^{-5} mol L^{-1}) upon addition of 183 equiv of F^-, (b) 200 equiv of CH_3COO^-, and (c) 210 equivalent of $H_2PO_4^-$. (d) Receptor **1** upon addition of 50 equiv of F^- in DMSO.

1 with the addition of F^- anions was very little as shown in Figure 2d. The absorbance of **4** at 376 nm and 392 nm decreased on addition of CH_3COO^-through isosbestic points at 347 nm and 404 nm similar to the titration with F^-. Fortunately, upon addition of F^- and CH_3COO^- beyond 3×10^{-4} mol L^{-1} to receptor **4** and 6×10^{-4} mol $L^{-1}$to receptors **2** and **3** shown color changes which were perceptible to the naked eyes and addition of $H_2PO_4^-$ beyond 8×10^{-4} mol L^{-1} to receptor **4**.

The color change can be attributed to the appearance of the new long wavelength peak. It was interesting that the spectra and color recovered when introduced protic solvent such as methanol into the anion and receptor solution. This may be owed to the competing between protic solvents and thiourea groups for anions. There was no new peak in the visible range and no color change appeared when adding F^-, CH_3COO^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^- into receptor **1**, adding Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, NO_3^- into receptor **3,** or adding Cl^-, Br^-, I^-, HSO_4^-, NO_3^- into receptors **2** and **4**.

Evidence for 1:1 complex formation is provided in Job plot. The Job plot of the two anions with receptors **2**, **3**, and **4** had the same result and one of all was reported in Figure 3. The association constants and correlation coefficients can be obtained by the nonlinear least-squares

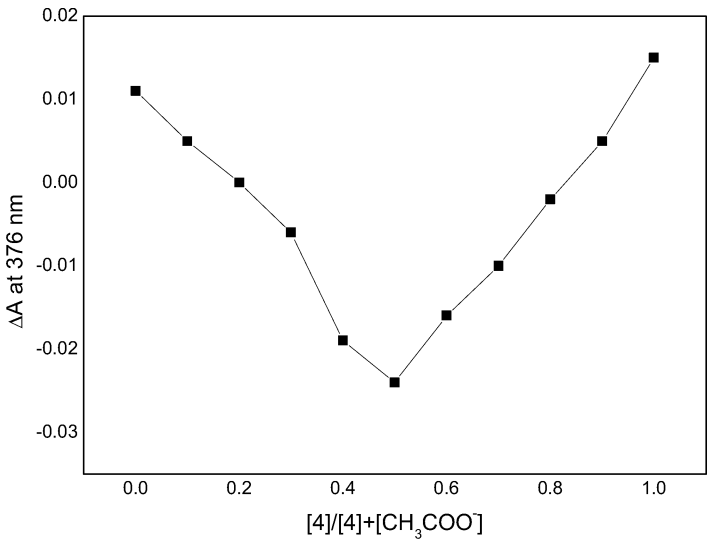


FIGURE 3 Job plot for receptor **4** with TBAA (tetrabutylammonium acetate salt) at a total concentration of 4.0×10^{-5} mol L^{-1} in DMSO, which indicates the formation of the 1:1 complex [**4**-CH_3COO^-].

TABLE I Association Constants *K*s (mol L^{-1}) and Correlation Coefficients *R* of Receptors 2, 3 and 4 with Guest Anions in DMSO

	Receptor **2**		Receptor **3**		Receptor **4**	
Anion	Ks	R	Ks	R	Ks	R
F^-	1960	0.9980	1760	0.9936	4380	0.9921
CH_3COO^-	2810	0.9928	2590	0.9925	2920	0.9936
$H_2PO_4^-$	1520	0.9946	—	—	2560	0.9962

method according to the cure fitting equation and the results were summarized in Table I.

From Table I, we found that all correlation coefficients were larger than 0.99, which also illustrated the formation of 1:1 stoichiometry complex between receptors and the corresponding anions, respectively (Figure 4).

The order of the association constants of receptors **2** and **3** for anions was $H_2PO_4^- < F^- < CH_3COO^-$, which can be rationalized on the basis of the guest basicity in polar protic organic solvent and shapes of anions. But there is a different result for receptor **4** which had an excellent ability to form complex with F^- rather than CH_3COO^-. In addition, the

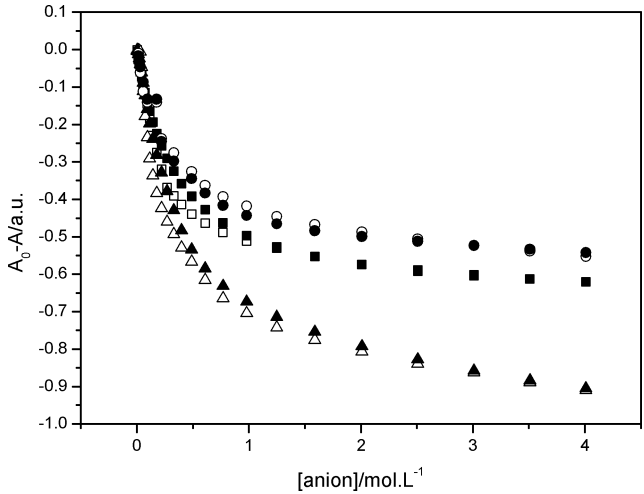
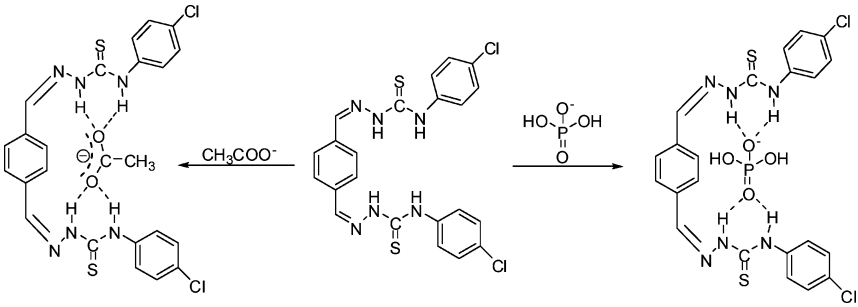


FIGURE 4 The plot of the absorbance of receptor **4** at 376 nm upon the addition of F^- (▲-calc, △-obs), AcO^-(■-calc, □-obs), $H_2PO_4^-$ (●-calc, ○-obs) in DMSO, [**4**] = 2.0×10^{-5} mol L^{-1}, the correlation coefficient are 0.9921, 0.9936, and 0.9962, respectively.

association constants of **4** were larger than those of **2** and **3** owing to higher acidity thiourea NH's of **4** which is related to the electron withdrawing groups such as chlorine on the phenyl increasing the binding affinities. On the other hand, host **1** did not show obviously absorption change after adding 50 equivalent of anions. It is predicated that the prominent abilities to form complexes with F^- and CH_3COO^- for receptors **2**, **3**, and **4** in comparison with receptor **1** are contributed to higher acidity of thiourea NH's of these receptors, which are in conjugation with the phenyl groups. On the basis of the known thiourea-guest anions hydrogen-bonding mode, the interaction between thiourea moiety in **4** and guest anions is indicated in Scheme 2.



SCHEME 2

Fluorescence Emission Spectra

Since receptors **1**∼**4** are fluorescent, the binding affinities of these compounds for various anions (tetrabutylammonium salts of F^-, Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, NO_3^-) were further examined using the fluorescence emission spectra in DMSO. Unfortunately, we did not find excellent changes of the fluorescence spectra of hosts upon addition of 50 equivalent anions, even though we completed this experiment several times (Figure 5). This may be indicated that the conjugative system of C=N with phenyl groups were fluorescent, but the complexation between two thiourea groups of receptors and guest anions could not aroused to any influence on the conjugative system. As shown in Table II, it is easy to find that the emission intensity of these compounds was trend to the order: receptor **4** > **3** > **2** > **1**, which indicated that the larger the conjugative system, the stronger the intensity of the receptor.

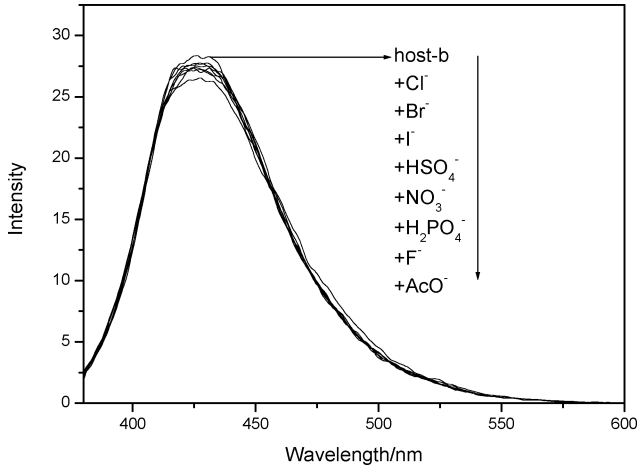


FIGURE 5 Fluorescence spectra changes of receptor **2** upon addition of 50 equiv various anions in DMSO at 298 K with 1%T. [receptor 2] $= 2.0 \times 10^{-6}$ mol L^{-1}.

^{1}H NMR Spectra

To investigate this hydrogen bonding interaction further, we also monitored the changes in the ^{1}H NMR spectra of DMSO-d_6 solutions of **2**, **3**, and **4** upon addition F^-, Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$, HSO_4^-, NO_3^- (as their tetrabutylammonium salts). It was noticed in Figure 6 that on addition of 0.5 equiv F^- to the receptor **4** in DMSO-d_6, the amide NH protons signals were low field shifted from δ10.20 to δ10.25, δ11.99 to δ12.03, receptively. In the meaning time, the integral area became smaller than the receptor alone. The concentration of F^- exceeding one times to the receptor **4** have caused the disappearance of

TABLE II Fluorescence Emission Intensity of Receptors 1∼4 in the Present of Anions under 1%T at 424 nm in DMSO

	Receptor **1**	Receptor **2**	Receptor **3**	Receptor **4**
Receptor only	27.02	27.55	30.66	30.72
$+F^-$	26.40	26.35	30.10	28.00
$+Cl^-$	26.78	27.17	30.50	29.74
$+Br^-$	26.72	27.41	30.78	30.20
$+I^-$	26.52	27.31	30.68	28.73
$+AcO^-$	26.35	26.97	29.77	28.42
$+HSO_4^-$	26.89	27.37	30.22	29.81
$+NO_3^-$	26.96	27.36	30.23	28.85

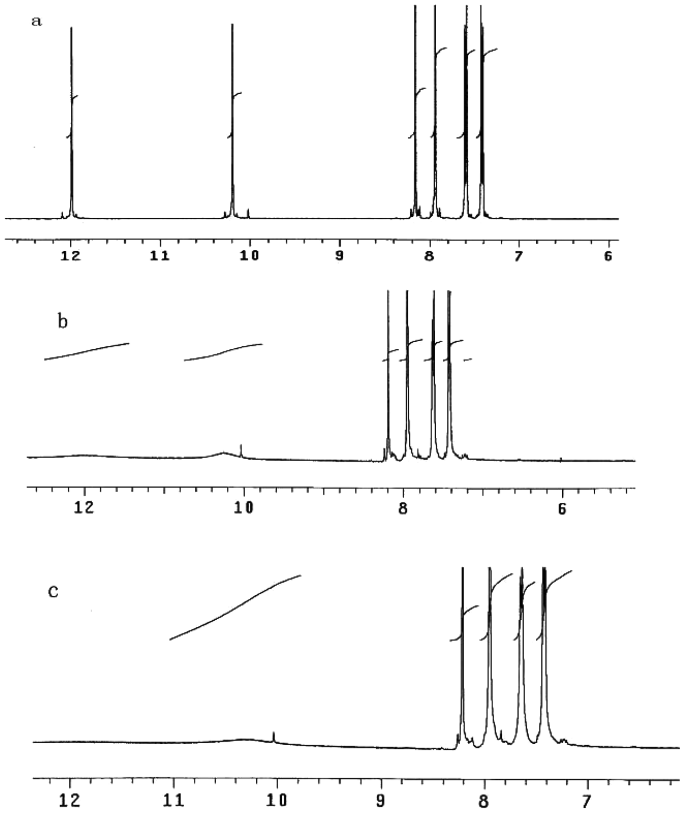


FIGURE 6 ^{1}H NMR spectra on titration of receptor **4** with F^- in DMSO-d_6 at 298 K. (a) receptor **4** only; (b) receptor **4** and 0.5 equiv of F^-; (c) receptor **4** and 1 equiv of F^-.

the signal for amide NH protons. Similar phenomenon was observed in the ^{1}H NMR spectra of the receptor **4** in the presence of CH_3COO^- and $H_2PO_4^-$. These observations clearly supported the hydrogen bonding interaction between the receptors and anions involving the thiourea NH groups. Other five anions displayed no such variations in ^{1}H NMR spectra.

CONCLUSION

In summary, we have synthesized a series of thiosemicarbazone based receptors by an efficient method. Their properties of anion recognition were studied by UV-Vis, fluorescence and ^{1}H NMR spectroscopy. The results showed that receptors **2**, **3**, and **4** can form 1:1 complex with F^-, $CH_3COO^-$and $H_2PO_4^-$ (not for **3**) by multiple hydrogen bonding

interactions. Furthermore, we present effective receptors for the F^-, CH_3COO^- and $H_2PO_4^-$ relative to other anions. The UV-Vis spectra didn't change upon addition of anions for receptor **1**, which the acidity of amino NH was weak.

In addition, we also found there was strong emission intensity of these compounds while the fluorescence spectra could not be used to detect the interaction between receptors with anions. A highly specific colorimetric reaction in the presence of F^-, CH_3COO^-, and $H_2PO_4^-$ has been found in the solution with naked-eyes, which holds promise to be used as optical chemosensors for these anions.

EXPERIMENTAL

Materials and Methods

The N^4-arylthiosemicarbazide has been prepared according to literature.[26] DMSO was dried and distilled before use according to standard practice. All other commercially available reagents were used without further purification. The tetrabutylammonium salts were used as anionic substrates. Melting points were measured on an X-4 digital melting-point apparatus (uncorrected). The infrared spectra were performed on a Digilab FTS-3000 FT-IR spectrophotometer. Elemental analyses were determined by a PE-2400CHN elemental auto analyzer. ^{1}H NMR was recorded on a Varian Mercury plus-400 MHz spectrometer. UV-Vis spectra were taken on a Shimadzu-2550 spectrometer and fluorescence spectra were taken on an LS-55 spectrometer.

Synthesis of the Title Compounds

Bis-thiosemicarbazone **1** was prepared from a mixture of 1.65 g (5 mmol) of terephthalic aldehyde, 0.91 g (10 mmol) of thiosemicarbazide and 0.02 ml of concentrated hydrochloric acid in 15 ml ethanol with refluxing 3–5 h at 70°C. We observed yellow turbid liquid when the reaction finished, and the products were obtained from solvent evaporation. The precipitate was filtered and recrystallized with DMF and EtOH in water bath. By this simple treatment, pure products suitable for characterization were obtained. The synthesis of receptors **2**, **3**, and **4** were similar to **1**.

1

Yield 89%, m.p. >300°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.54 (s, 2H, NH), 8.26 (s, 2H, HC=N), 8.10 (d, 4H, NH_2), 7.41~7.82 (m, 4H, ArH); IR (KBr, cm^{-1}) v: 3372, 3264, 3179 (N-H), 1596 (C=N), 1525

(C=C), 1466 (C=C), 1282 (C=S); Anal. calcd. for $C_{10}H_{12}N_6S_2$: C 42.84, H 4.31, N 29.97; found C 42.73, H 4.45, N 29.76.

2

Yield 88%, m.p. >300°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.51 (s, 2H, NH), 10.14 (s, 2H, NH), 8.26 (s, 2H, HC=N), 7.82 (m, 14H, ArH); IR (KBr, cm^{-1}) v: 3424, 3322, 3130 (N-H), 1595 (C=N), 1544, 1507, 1445 (C=C), 1262 (C=S); Anal. calcd. for $C_{22}H_{20}N_6S_2$: C 61.09, H 4.66, N 19.43; found C 59.83,H 4.45, N 19.46.

3

Yield 86%, m.p. >300°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.84 (s, 2H, NH), 10.08 (s, 2H, NH), 8.15 (s, 2H, HC=N), 6.93~7.94 (m, 12H, ArH), 3.46 (q, 6H, —O—CH_3); IR (KBr, cm^{-1}) v: 3445, 3322, 3136 (N—H), 1597 (C=N), 1539, 1517 (C=C), 1246 (C=S), 1190 (Ar—O—CH_3); Anal. calcd. for $C_{24}H_{24}N_6O_2S_2$,: C 58.52, H 4.91, N 17.06; found C 58.43,H 4.72, N 17.25.

4

Yield 85%, m.p. >300°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.99 (s, 2H, NH), 10.20 (s, 2H, NH), 8.17 (s, 2H, HC=N), 7.41~7.95 (m, 12H, ArH); IR (KBr,cm^{-1})v: 3454, 3305, 3133 (N—H), 1588 (C=N), 1541 (C=C), 1501 (C=C), 1266 (C=S); Anal. calcd. for $C_{22}H_{18}Cl_2N_6S_2$: C 52.69, H 3.62, N 16.67; found C 52.73, H 3.54, N 16.49.

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