Note

The anion recognition of simple-structure molecular tweezers receptors based on acyl-thiourea

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Three title compounds have been designed and synthesized in high yields as novel simple anion receptors. They have a high selectivity for F⁻ and AcO⁻. The binding properties for anions of the receptors have been examined by UV-Vis and ^{1}H NMR spectroscopy. The spectrographic data indicate that a 1:1 stoichiometry complex is formed between the receptors and the anions through hydrogen bonding interactions in DMSO solution.

Keywords: Anion recognition, acyl-thiourea, hydrogen bonds, molecular tweezers.

Nowadays, the research of supramolecular chemistry has focused especially on the anion recognition of simple-structure receptors[1], because the anions play an important role not only in biological processes, but also in chemical processes, the possibilities of applying anion receptors in sensors and molecular self-assembly, even medical and environmental problems[2,3]. Various receptors containing different functional groups for selective binding of F⁻ and AcO⁻ have been reported[1b-5], but the anion recognition of the simple-structure receptors for fluoride ions are seldom[1a]. In recent years, acyl thiourea-based molecular tweezers compounds have received considerable attention in metallomacrocyclic complexes[6], because the multiple hydrogen binding interactions of host can induce high recognition selectivity for guest. To the best of our knowledge, however, the recognition and sensing of simple-structure anion receptors based on acyl-thiourea has not been found in literature.

It is well known that binding strength and anion selectivity depend on structure of the spacers, acidity of H-donors, solvents, shape and size of anions[6]. For construction of anion receptors, it would be crucial to design spacer molecules bearing anion-binding sites. Moreover, receptors bearing two thiourea groups at

suitable sites can bind anions through hydrogen bonding interactions and enhance the stability of the resultant complex and recognition selectivity[7]. In our previous work, we have taken an interest in the research of crown ether and thiosemicarbazide derivatives for anions[8]. In view of these facts and as a part of our work on anion recognition of supramolecular compounds and acyl thiourea-based molecular tweezers receptors, herein we report the synthesis and recognition properties of three novel simple and effective molecular tweezers receptors based on acyl-thiourea. Isophthalyl chloride **1** was prepared from the reaction of isophthalic acid with thionyl chloride, and it was treated with ammonium thiocyanate under the conditions of solid-liquid phase transfer catalysis using 3% polyethylene glycol-400 (PEG-400) as the catalyst to give isophthalyl isothiocyanate **2**. This compound does not need to be isolated and it was treated immediately with substituted aromatic amines to obtain title compounds **3** in good to excellent yields. The synthetic route of receptors is illustrated in

Scheme I. The recognition properties of receptors have been examined by UV-Vis absorption and ^{1}H NMR spectroscopy.

Experimental Section

UV-Vis spectra were obtained on an Agilent-8453 spectrometer. Elemental analyses were performed by a PE-2400 CHN instrument. IR spectra were recorded on a Digilab FTS-3000 FT-IR spectrophotometer (using KBr pellets). ^{1}H NMR and ^{13}C NMR spectra were measured on a Varian Mercury plus-400 MHz spectrometer; DMSO-d_6 was used as solvent and TMS as internal standard. Melting points were determined with an X-4 digital melting-point apparatus and were uncorrected.

Tetrabutylammonium fluoride was commercial product of highest reagent grade and used as received. Tetrabutylammonium acetate was obtained by the neutral reaction of 25% tetrabutylammonium hydroxide and acetic acid, and dried in P_2O_5 drier. DMSO and acetone were analytical pure.

General procedure for the synthesis of receptors 3a-c. 1,3-isophthalyl chloride (1.1 g, 5 mmoles), NH₄SCN (1.2 g, 15 mmoles), PEG-400 (0.18 g, 3% with respect to ammonium thiocyanate) and 20 mL of
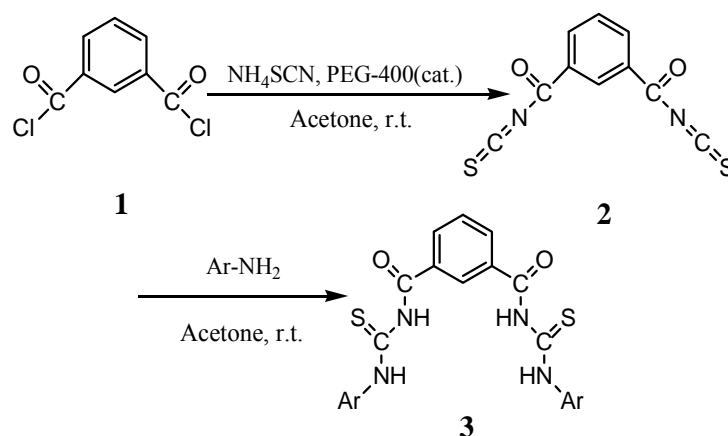
3a. Ar = 4-C$_6$H$_4$CH$_3$; **3b**. Ar = C$_6$H$_5$; **3c**. Ar = β-naphthalene.

Scheme I

acetone were added in a dried round-bottomed flask containing a magnetic stirrer bar and stirred at room temperature for 2 hr, then, aromatic amine (10 mmoles) was added dropwise. The mixture was stirred at room temperature for 1 hr; the precipitate was filtered, washed with water to remove inorganic salts, dried and crystallized from DMF-C$_2$H$_5$OH-H$_2$O to give title compounds. Yield, m.p., elemental analysis, IR and NMR data of the products are as follows.

Receptor **3a** was obtained as a yellow powder after crystallizing from DMF-C$_2$H$_5$OH-H$_2$O in 83.9% yields (2.1 g). m.p. 219-220°C. IR (KBr): 3226, 3166, 3056 (N-H); 1674 (C=O); 1597, 1529 (C=C); 1249, 1137 cm^{-1} (C=S). ^{1}H NMR (DMSO-d_6): δ 12.48 (s, 2H, NHCO), 11.48 (s, 2H, NHAr), 7.23-8.56 (m, 12H, ArH), 2.33 (s, 6H, CH$_3$). ^{13}C NMR (DMSO-d_6): δ 178.49, 166.81, 135.42, 135.13, 132.65, 131.85, 128.74, 128.108, 123.73. Elemental analysis: Calcd for C$_{24}$H$_{22}$N$_4$O$_2$S$_2$: C, 62.34; H, 4.76; N, 12.12. Found: C, 62.37; H, 4.78; N, 12.09.

Receptor **3b** was obtained as a white powder after crystallizing from DMF-C$_2$H$_5$OH-H$_2$O in 80.8% yields (1.9 g). m.p. 197-198°C. IR (KBr): 3298, 3223, 3173, 3033 (N-H); 1700 (C=O); 1599, 1526 (C=C); 1348, 1246, 1145 cm^{-1} (C=S). ^{1}H NMR (DMSO-d_6): δ 12.56 (s, 2H, NHCO), 11.60 (s, 2H, NHAr), 7.28-8.58 (m, 14H, ArH). ^{13}C NMR (DMSO-d_6): δ 178.98, 167.29, 137.92, 133.28, 131.96, 129.14, 128.77, 126.53, 124.51. Elemental analysis: calcd for C$_{22}$H$_{18}$N$_4$O$_2$S$_2$: C, 60.83; H, 4.15; N, 12.90. Found: C, 60.86; H, 4.12; N, 12.86.

Receptor **3c** was obtained as a yellow powder after crystallizing from DMF-C$_2$H$_5$OH-H$_2$O in 86.4%

yields (2.5 g). m.p. 198-199°C. IR (KBr): 3417, 3129 (N-H); 1656, 1535 (C=C); 1401, 1334, 1280, 1239, 1150 cm^{-1} (C=S). ^{1}H NMR (DMSO-d_6): δ 12.73 (s, 2H, NHCO), 11.65 (s, 2H, NHAr), 7.55-8.61 (m, 18H, ArH). ^{13}C NMR (DMSO-d_6): δ 179.21, 162.40, 135.59, 133.37, 132.92, 132.04, 131.44, 129.51, 128.92, 128.31, 127.83, 127.64, 126.70, 126.22, 123.95, 121.88. Elemental analysis: calcd for C$_{30}$H$_{22}$N$_4$O$_2$S$_2$: C, 67.42; H, 4.12; N, 10.49. Found: C, 67.43; H, 4.14; N, 10.46.

Results and Discussion

UV-Vis absorption spectra

UV-Vis spectrometry is associated with the variations of absorption spectra in coordinate systems, and it has been used as an effective and simple measuring method of the association constants of complexes in supramolecular systems.

Titration experiments for anion recognition of receptors **3a-c** were performed using UV-Vis spectroscopy in DMSO. The UV-Vis absorption spectra were obtained from a solution of these receptors in the absence or presence of F$^-$ and AcO$^-$. In each case the counter cation was tetrabutyl-ammonium.

Figure 1 showed the UV-Vis absorption spectra of solution of receptor **3a** (2×10^{-5} mol/L) in the course of the titration with different concentrations of anions in DMSO. During titration with fluoride ions, as shown in **Figure 1a**, the intensity of absorption peak, which is from the benzene moiety, decreased at 270 nm, and a new absorption peak was observed at 322 nm. A noticeable isobestic point appeared at 286 nm. **Figure**

1b shows the absorption spectra of **3a** with adding acetate ions, the peak at 266 nm decreased while the new peak located at 321 nm. Isobestic point appeared at 287 nm. These variations were induced by the formation of the complex between receptor **3a** and fluoride, acetate ions.

Similar to receptor **3a**, the absorption spectra of solution of receptor **3b** (2×10^{-5} mol/L) with different concentrations of anions in DMSO have also been obtained. The absorption spectra of **3b** on adding of fluoride ions showed the new peak at 321 nm, and isobestic point was observed at 283 nm. Similarly, the absorption spectra of **3b** with acetate ions showed the new peak at 322 nm, and isobestic point was observed at 284 nm. Similarly, Receptor **3b** has also shown the selective binding ability for fluoride, acetate ions.
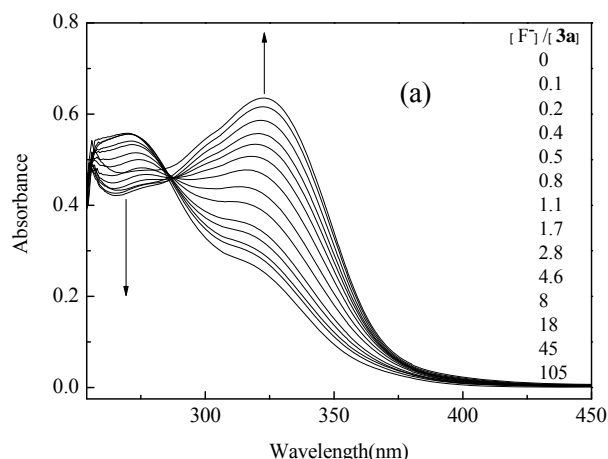
Moreover, **Figure 2a** showed that the variations of the original and new absorption peaks of solution of receptor **3c** with gradual increasing of the concentration of fluoride ions. It was particularly necessary to notice that a discernible bathochromic shift occurred from 262 to 266 nm. The new peak appeared at 328.5 nm. Isobestic point at 292 nm was observed. Similarly, the variations of absorption spectra of **3c** with acetate ions are shown in **Figure 2b**. A bathochromic shift occurred from 260 to 265 nm. Isobestic point appeared at 290 nm. The new peak appeared at 326 nm. These observations clearly show that receptor **3c** has an excellent ability to bind with fluoride, acetate ions in comparison with receptor **3a** and **3b**.

Figure 1a — The UV-Vis absorption spectra of receptor **3a** (2×10^{-5} mol/L, DMSO) with gradual increasing of the concentration of fluoride ions.
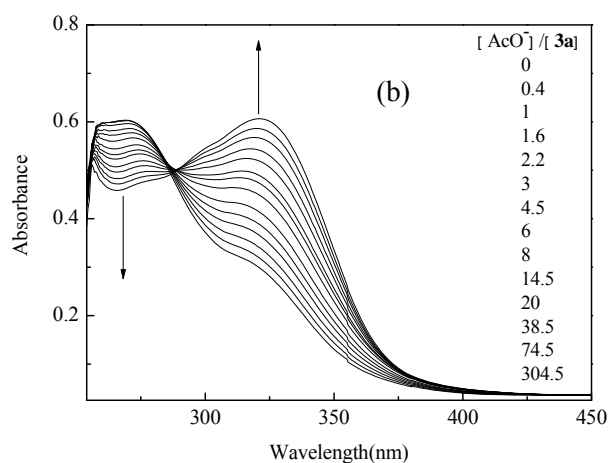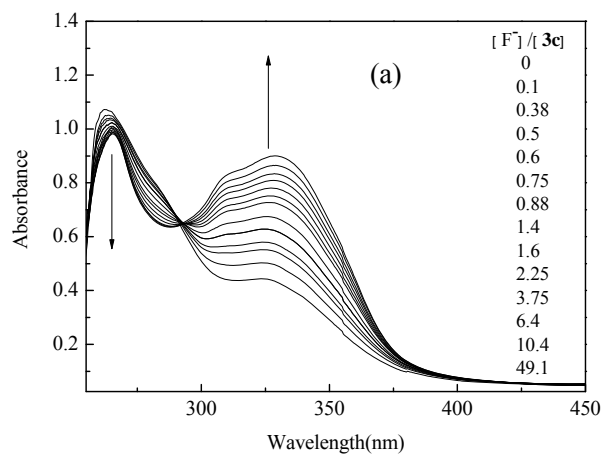

Figure 2a — The UV-Vis absorption spectra of receptor **3c** (2×10^{-5} mol/L, DMSO) with gradual increasing of the concentration of fluoride ions.

Figure 1b — The UV-Vis absorption spectra of receptor **3a** (2×10^{-5} mol/L, DMSO) with gradual increasing of the concentration of acetate ions.
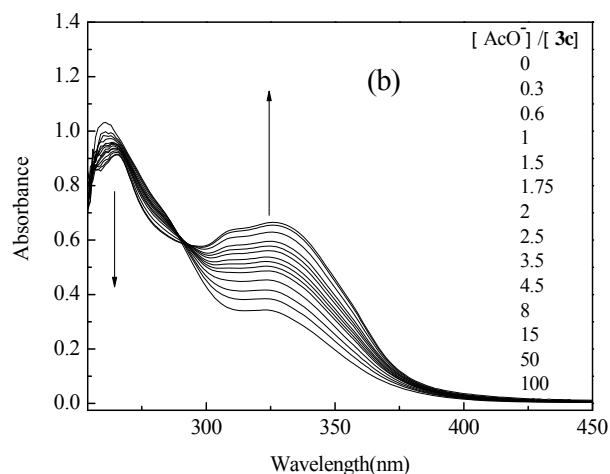

Figure 2b — The UV-Vis absorption spectra of receptor **3c** (2×10^{-5} mol/L, DMSO) with gradual increasing of the concentration of acetate ions.

The Job plot experiment further showed that receptor **3c** formed 1:1 hydrogen-bonding complex with fluoride ions because of $C_F^-/(C_F^-+C_{3c}) = 0.5$. The Job plot of receptor **3c** with acetate ions had the same result. Similarly, Job plot of receptor **3a** and **3b** with fluoride and acetate ions had the same results. The results were obtained from a total concentration of 4.0×10^{-5} mol/L in DMSO.

The association constants Ks $(\text{mol/L})^{-1}$ and correlation coefficients R of receptors 3a-c with fluoride and acetate ions.

The degree of binding ability, as further illustrated by non-linear fitting curve[9], can be seen from **Table I**. The association constants Ks $(\text{mol/L})^{-1}$ of receptors with fluoride and acetate ions are much larger than those with other halide ions, hydrosulfate ions etc. Receptor **3a**, **3b** and **3c** bind fluoride ions

Table I — The association constants Ks $(\text{mol/L})^{-1}$ and correlation coefficients R of receptors with fluoride and acetate ions in DMSO, as further illustrated by non-linear fitting curve.

| Anions		3a	3b	3c
F⁻	Ks	6.7×10^4	7.2×10^4	1.7×10^5
	R	0.9953	0.9989	0.9957
AcO⁻	Ks	1.1×10^4	1.6×10^4	3.9×10^4
	R	0.9990	0.9955	0.9976

preferentially, acetate ion was the other anion bound stably. The observed selectivity for fluoride ions can be rationally explained based on the anion structures. Because the spherical fluoride ion was bound with receptor more easily, however, acetate ion has two oxygen atoms, it may be bound in a different complex structure, and fluoride ion is bound stronger than acetate ion, as known in **Table I**.

Table I show that the association constants Ks of receptors with fluoride and acetate ions are **3c** > **3b** > **3a**. These results explained that the electron-deficient moiety can extend the conjugated system and enhance the acidity of NH protons. In contrast, the electron-rich moiety can decrease the acidity of NH protons of thiourea groups.

Meanwhile, the plot of the absorbance of **3c** *vs* concentration of acetate ions indicated that the experimental association constant Ks is approximate to theoretical constant. The plot of **3c** *vs* concentration of fluoride ions was also obtained by the same step. Similarly, the plots of **3a** and **3b** *vs* concentration of fluoride and acetate ions were also obtained using same conditions.

¹H NMR study

¹H NMR spectroscopy plays an important role in the understanding of receptor-anion interaction and is capable of providing a revealing picture of the details
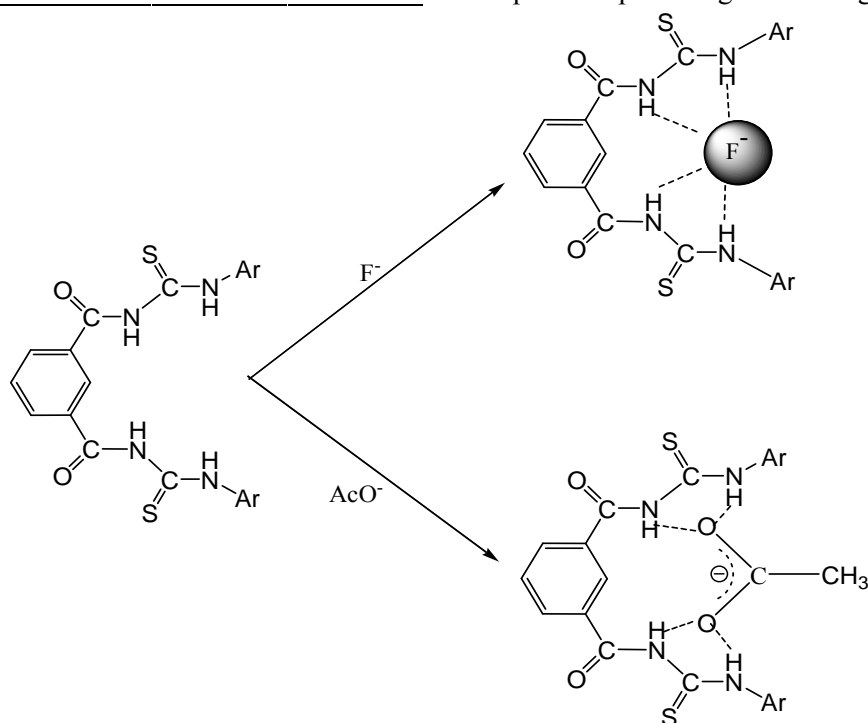
Scheme II — Possible binding structures of receptor **3** with fluoride and acetate ions

of the interaction between receptors and anions and can gave convincing evidence for the existence of intramolecular hydrogen bonds between the NH of thiourea group and anions. The binding ability of the receptor **3c** for fluoride ions is evident in ^{1}H NMR titration experiments in DMSO-d_6. Addition of 1 mol equiv. of tetrabutylammonium fluoride to receptor **3c** in DMSO-d_6 caused complete disappearance of signals for amide NH protons. The variation showed that drastic decreases of the signals for two amide NH protons upon addition of 1 mol equiv. of tetrabutyl-ammonium fluoride. Signals for the amide NH protons at 11.649 ppm (S, 2H) and 12.730 ppm (S, 2H) for **3c** at 80°C completely disappeared. These results indicated that the receptors and the fluoride ions form 1:1 stoichiometry complex by hydrogen-bonding interaction involving the thiourea NH groups. The variations of the signals for receptor **3c** upon addition of 1 mol equiv. of acetate ions can also be observed. Similarly, the variations of the signals for receptor **3a** and **3b** with fluoride and acetate ions can also be observed in the same conditions. However, such similar variations were not observed for other anions such as Cl^-, Br^-, I^-, NO_3^- and HSO_4^-. Due to the above facts, possible structures for the complex of receptor **3** with fluoride and acetate ions are illustrated in **Scheme II**. A more detailed study of the hydrogen bonds between thiourea groups of receptors and other anions is under investigation.

Conclusion

The novel simple and effective receptors **3a, 3b** and **3c** were synthesized in good to excellent yields. The UV-Vis absorption spectroscopy, Job plot and ^{1}H NMR spectroscopy show that the receptors **3a, 3b** and **3c** can form 1:1 stoichiometry complex with F^- and AcO^- by hydrogen-bonding interactions. Receptor **3c** has an excellent ability to recognition with fluoride and acetate ions in comparison with **3a** and **3b**, and these recognition properties of receptor **3c** indicates that receptor **3c** can be considered as an excellent recognition receptor with F^- and AcO^- because of its large conjugated system.

Acknowledgement

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