Turk J Chem
31 (2007) , 327 – 334.

Studies on the Anion Recognition Properties of Synthesized Receptors III: A Novel Thiourea-Based Receptor Constructed by Benzo-15-Crown-5 for Sensing Anions in a Strong Polar Solvent

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Received 17.03.2006

A new series of receptors were designed and synthesized, and their interactions with anions, such as F^-, Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, and NO_3^-, in DMSO solvent were investigated using UV-Vis absorption spectroscopy. The results showed that hydrogen-bonding complexes were formed between the receptors and the tested anions, such as CH_3COO^- and F^-. It was also found that the selectivity of the receptors for anions could be efficiently tuned by changing the place of the substituent group at the *N*-phenyl moiety. The recognition mechanism and binding mode are discussed. These findings were expected to be of significance for designing and developing a novel, highly selective receptor for the acetate anion in a strong polar solvent.

Key Words: Anion recognition, thiosemicarbazone, binding constant.

Introduction

The selective recognition of biologically and/or chemically important anions by means of artificial molecular receptors represents an active field of research with applications spanning analytical chemistry to environmental science, toxicology, and biology.[1] A variety of artificial receptors for anions have been reported, including polyammonium macrocycles,[2] guanidinium,[3] amides,[4] urea/thiourea,[5] and calixarenes.[6] In numerous hydrogen-bonding receptors, thiourea-based compounds have become the focus of the development of neutral anion receptors.[7,8] In addition, many artificial receptors are based on macrocyclic molecules, such as crown ethers, cyclodextrins, and cyclophanes.[9] The substrate selectivity of these simple hosts can be increased by the introduction of additional binding sites.[10,11] Although this strategy has received great attention, to date, only a few neutral anion receptors containing thiourea and crown ethers have been reported.[12]

In view of these points and in continuation of our previous work on the synthesis, crystal structure, anion recognition, and coordination complexes of thiourea and crown ether derivatives,[13−18] we synthesized

a series of potential receptors, **1-3**, composed of crown ether and thiourea groups. The recognition of **1-3** for anions was studied in DMSO and a highly selective receptor for the acetate ion was developed in a strong polar solvent. Moreover, higher sensing properties can be achieved by further chemical modification of synthetic receptors.

Experimental

Materials and methods

The *N*-arylthiosemicarbazide was prepared as described by Shukla et al.[19] DMSO was dried and distilled before using, 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 IR spectra were recorded on a Digilab FTS-3000 FT-IR spectrophotometer. Elemental analyses were determined by a PE-2400 CHN elemental autoanalyzer. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded on a Varian Mercury Plus 400 MHz spectrometer. Mass spectra were recorded on a HP-5988 spectrometer. UV-Vis spectra were recorded on a UV-2550 spectrometer.

Synthesis of receptors

Synthesis of receptors **1-3** was carried out by condensation of 4-acetyl benzo-15-crown-5 with *N*-arylthiosemicarbazide under the condition of microwave irradiation using an acid catalyst (Figure 1).[20] The reaction mixture was cooled to room temperature and then filtered. The solid obtained was washed with ethanol 3 times to give a pure product (see supporting information for detailed data).

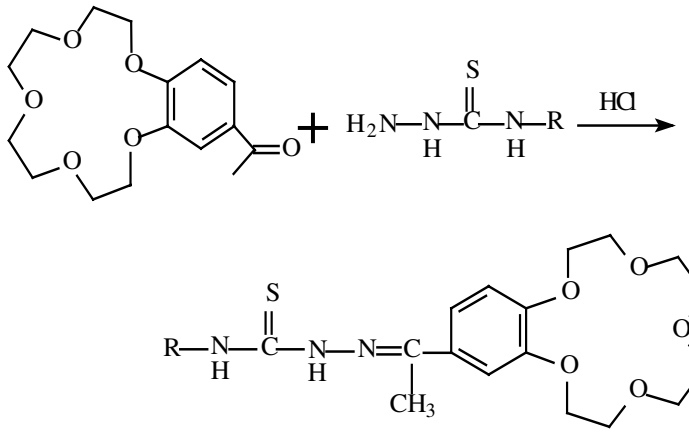

Figure 1. Receptors **1** R=*m*-ClC_6H_4, **2** R=*o*-ClC_6H_4, **3** R=*p*-ClC_6H_4.

Results and Discussion

The UV-Vis absorption spectra were recorded from the solutions of these compounds in the absence or presence of anions, such as F^-, Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, and NO_3^-. In each case the counter cation was tetrabutylammonium. Figure 2 shows the absorption spectra of **1** in the presence of various anions in DMSO. The concentration of the anion is 50-fold that of the receptor. Anion binding was detected

by the spectral perturbation of the *N*-phenyl substituent. The receptors exhibited selective recognition of CH_3COO^- and F^- over other anions, such as Cl^-, Br^-, I^-, HSO_4^-, and NO_3^-, in DMSO.

The observed change in the absorption spectra of receptor **1** upon addition of F^- in DMSO is shown in Figure 3. With increasing F^- concentration, the absorbance of **1** at 330 nm decreased and the presence of 2 isosbestic points at 358 and 307 nm suggested the formation of well-defined binding complexes between **1** and the tested anion. The job plot confirmed the 1:1 binding stoichiometry of $\mathbf{1}F^-$, in which $\mathbf{1}F^-$ represents the receptor-anion complex. Introduction of protic solvents, such as methanol, into the DMSO solution of **1** plus F^- led to a gradual recovery of the absorption spectrum of **1** itself, supported by the hydrogen-bonding nature of the anion-receptor interaction, likely at the thiourea NH sites.

Similar spectra were observed for the titration of **1-3** with each anion (such as F^-, CH_3COO^-). Absorbance values at 330 nm were taken for nonlinear least-squares treatment[21] (i.e. Figure 3 inset); meanwhile, the binding constants (Ka) and free-energy changes (ΔG_0) of these hosts (**1-3**) with guests (F^- and CH_3COO^-) were obtained (Table. All correlation coefficients (R) obtained were larger than 0.995).

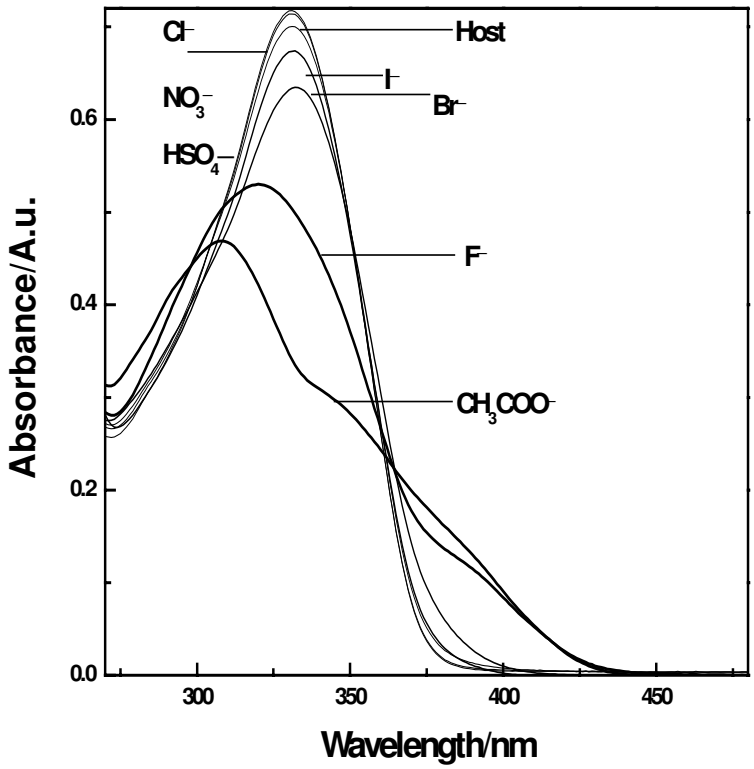

Figure 2. Absorption spectra of **1** in the presence of various anions.

Experimental results showed that F^- was sensed effectively by receptors **1-3** with binding constants of 4.40×10^3, 7.5×10^3, 1.72×10^4 L mol^{-1}, respectively, which was probably due to its special qualities, such as strong basicity, large surface charge density, and small volume. For CH_3COO^-, higher K_a values were observed (Table). In addition, a much more acute response of **1** toward CH_3COO^- in the titration curves was also observed (Figure 4), which illustrated that the receptors had a stronger affinity towards CH_3COO^- than F^-, which was explained by the fact that CH_3COO^-, characterized by a planar triangle form, was a perfect match for the thiourea group of the receptors in steric configuration, which supported

the notion that complementary structure played an important role in anion recognition. The binding modes are illustrated in Figure 5.

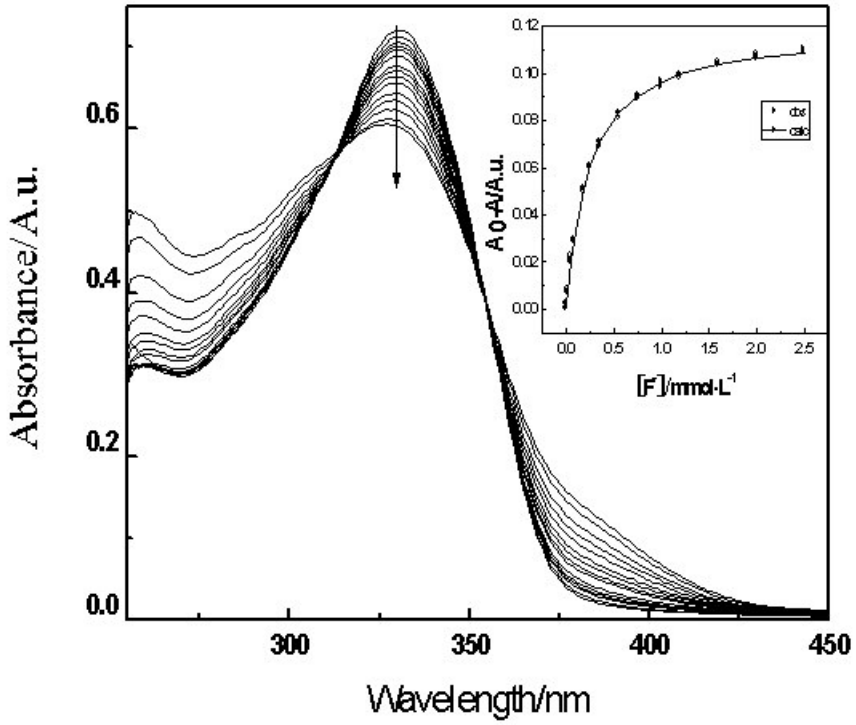

Figure 3. The UV-Vis titration spectra of receptor **1** with F^- in DMSO (298 K). The insets represent the change in absorbance of **1** at 330 nm with varying molar equivalents of anions. **1** = 2×10^{-5} mol L^{-1}.

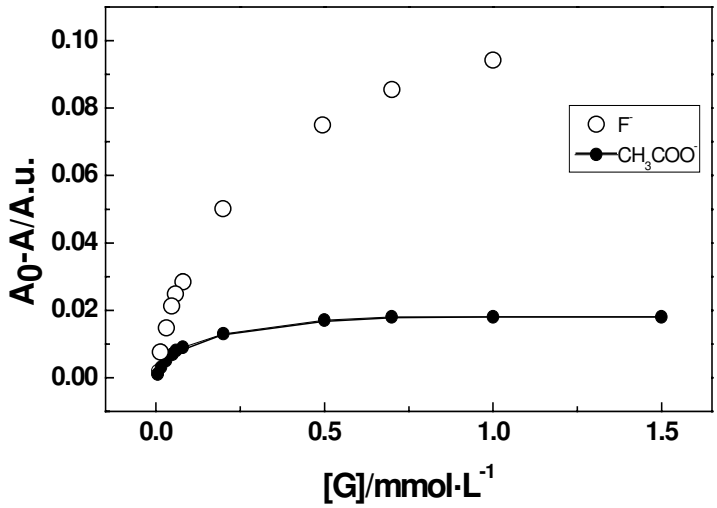

Figure 4. The respective change in absorbance of **1** at 330 nm versus varying molar equivalents of F^- and CH_3COO^-.

Table. Binding constants (K_a) and free-energy of complexation (ΔG_0) for the 1:1 complexes between the hosts (**1**-**3**) and guests (F^- and CH_3COO^-) in DMSO.

Host	Guest	K_a (L mol^{-1})	ΔG_0 (kJ mol^{-1})
1	CH_3COO^-	1.37×10^4	–23.62
	F^-	4.40×10^3	–20.80
2	CH_3COO^-	1.42×10^4	–23.70
	F^-	7.50×10^3	–22.12
3	CH_3COO^-	4.39×10^4	–26.50
	F^-	1.72×10^4	–24.18

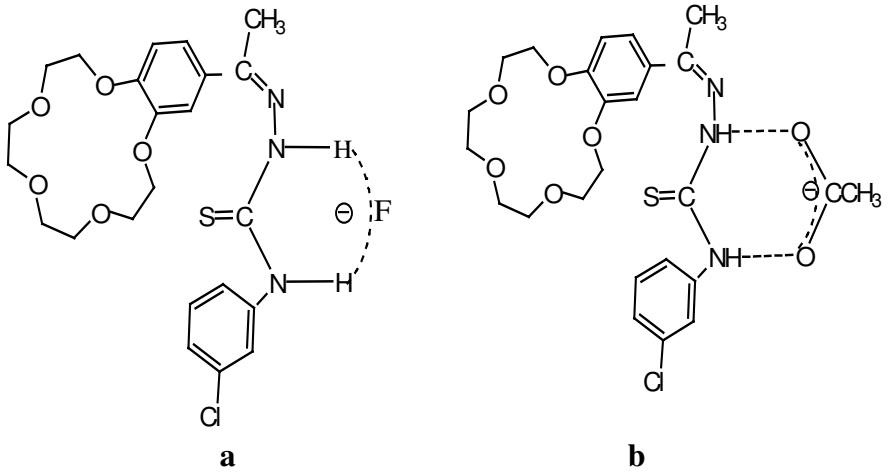

Figure 5. Suggested hydrogen-bonding interaction between the thiourea-based receptor, and F^- (**a**) and CH_3COO^- (**b**).

Figure 6 and Table 1 show that receptor **3** had an excellent ability to complex with the tested anions in comparison to **1** and **2**, which was explained by the nature of hydrogen bonding. The substituent of chlorine attached to N-phenyl as an electron-attracting and ortho-para directing group resulted in the order **1** $<$ **2** and **1** $<$ **3** in the case of the acidity of N-H of thiourea unit, and so it was not surprising that **1** had the poorest hydrogen-bond receptor ability. However, the binding ability of **2** was much less than that of **3**, which was likely due to the steric crowding induced by the adjacent substituent of chlorine.

The poor ability to bind the tested anions of **1** would have, in the normal sense, led to higher anion binding selectivity for CH_3COO^- than for **2** and **3**. With receptors **1**, **2**, and **3**, the binding constants for CH_3COO^- were around 3.1-, 2.5-, and 1.9-fold those for F^-, respectively. The above results illustrated receptor **1** exhibited a higher selectivity of CH_3COO^- than **2** and **3** in the systems containing F^- and CH_3COO^-, which suggested a route for the synthesis of more selective receptors.

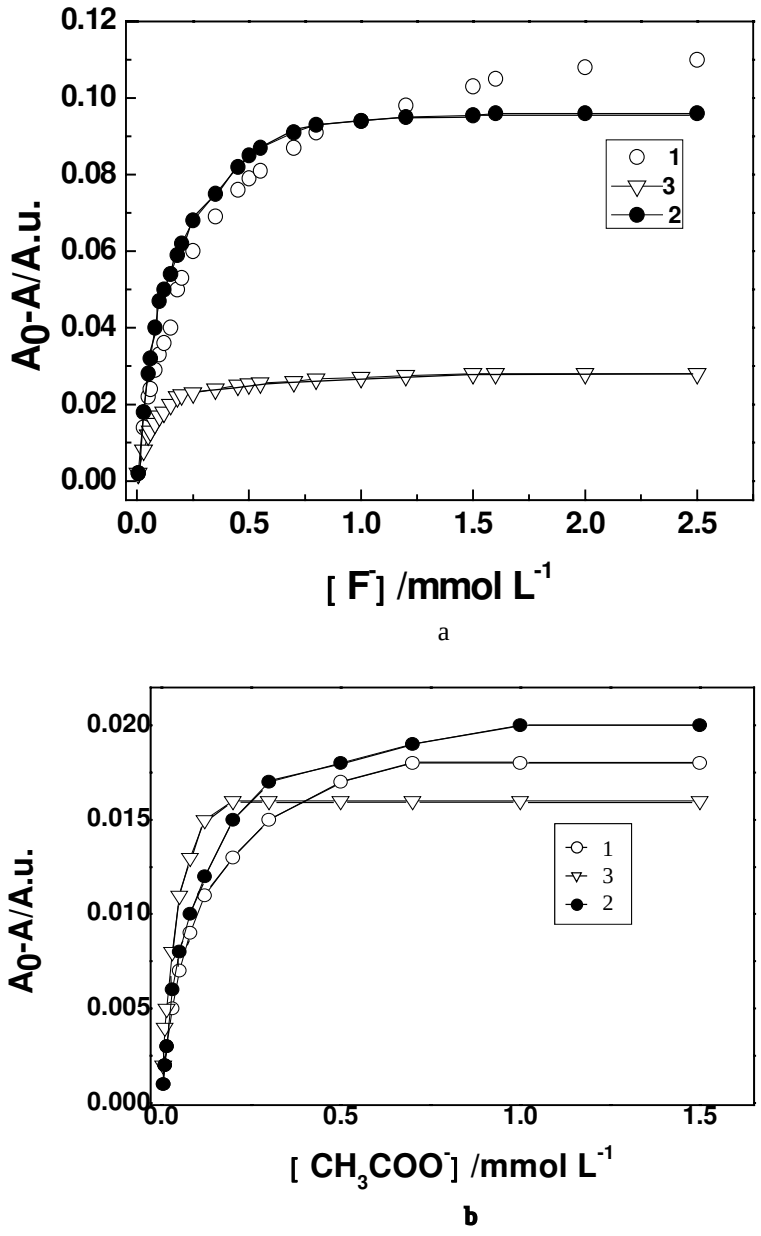

Figure 6. The respective change in absorbance of **1-3** at 330 nm versus varying molar equivalents of F^- (**a**) and CH_3COO^- (**b**).

Conclusion

In summary, we reported 3 receptors, which were synthesized by a simple method. Their properties of anion recognition were studied by UV-Vis spectroscopy. The results showed that receptors **1-3** can form 1:1 complexes with anions, such as F^- and CH_3COO^-, by multiple hydrogen bonding interactions, and that the 3 receptors had strong binding to F^- and CH_3COO^-. The results described in this paper lead us to suggest a new approach to a receptor for selective recognition of the acetate anion in a polar solvent. Most notably, the selectivity of the receptors to anions could be efficiently tuned by changing the place of the

chlorine substituent group at the *N*-phenyl moiety. Of course, other cooperative or allosteric systems could be developed by further modifying these receptors. Extensive efforts are being directed toward this end.

Information for compounds

1. $C_{23}H_{28}N_3O_5SCl$ (**1**): Yield (90%) mp 172 °C° Elemental analysis, found: C 56.02, H 5.63, N 8.61; Calc: C 55.92, H 5.71, N 8.51%. IR (cm^{-1}, KBr): 3437, 3371 (N-H), 3082 (Ar-H), 2922 (CH_3), 2868 (CH_2), 1591 (C=N), 1543,1514 (Ar), 1271, 1056 (Ar-O-CH_2), 1188 (C=S), 1134 (CH_2-O-CH_2). ^{1}H-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 2.507 (s, 3H, CH_3), 3.767-4.163 (m, 16H, OCH_2CH_2O), 6.951-7.809 (m, 7H, Ar-H), 10.074 (s, 1H, NH), 10.669 (s, 1H, NH).^{13}C-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 14.595 (1C, CH_3), 68.269-70.456 (8C, OCH_2CH_2O), 112.447-149.98 (12C, phenyl), 150.292 (1, C=N), 176.546 (1, C=S). MS (FAB), m/z: 366, 308, 127, 169.

2. $C_{23}H_{28}N_3O_5SCl$ (**2**): Yield (93%) mp 182 °C.°lemental analysis, found: C 56.00, H 5.61, N 8.62; Calc: C 55.92, H 5.71, N 8.51%. IR (cm^{-1}, KBr): 3437, 3261 (N-H), 3077 (Ar-H), 2928 (CH_3), 2867 (CH_2), 1597 (C=N), 1543, 1515 (Ar), 1274, 1057 (Ar-O-CH_2), 1185 (C=S), 1130 (CH_2-O-CH_2). ^{1}H-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 2.544 (s, 3H, CH_3), 3.575-4.159 (m, 16H, OCH_2CH_2O), 6.960-8.080 (m, 7H, Ar-H), 10.084 (s, 1H, NH), 10.822 (s, 1H, NH). ^{13}C-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 14.511 (1C, CH_3), 68.261-70.479 (8C, OCH_2CH_2O), 111.769-149.446 (12C, phenyl), 150.330 (1, C=N), 176.599 (1, C=S). MS (FAB) is not available.

3. $C_{23}H_{28}N_3O_5SCl$ (**3**): Yield (92%) mp 165-167. Elemental analysis, found: C 56.04, H 5.63, N 8.64; Calc: C 55.92, H 5.71, N 8.51%. IR (cm^{-1}, KBr): 3460, 3285 (N-H), 3079 (Ar-H), 2923 (CH_3), 2865 (CH_2), 1590 (C=N), 1532, 1513 (Ar), 1273, 1059 (Ar-O-CH_2), 1191 (C=S), 1129 (CH_2-O-CH_2). ^{1}H-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 2.316 (s, 3H, CH_3), 3.614-4.159 (m, 16H, OCH_2CH_2O), 6.944-7.649 (m, 7H, Ar-H), 10.045 (s, 1H, NH), 10.609 (s, 1H, NH). ^{13}C-NMR (400 MHz, in CD_3SOCD_3, ppm), δ: 14.565 (1C, CH_3), 68.269-70.486 (8C, OCH_2CH_2O), 112.432-149.797 (12C, phenyl), 150.277 (1, C=N), 176.691 (1, C=S). MS (FAB), m/z: 366, 308, 127, 169.

Acknowledgments

We gratefully acknowledge the support of the National Natural Science Foundation of China (No. 20671077), the Natural Science Foundation of Gansu Province (3ZS061-A25-027). We also thank Lanzhou Teachers College for the UV-Vis spectrophotometer (UV-2550) made in Japan.

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