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A Novel Thiourea-Based Dual Fluorescent Anion Receptor with a Rigid Hydrazine Spacer

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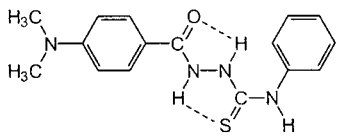
ABSTRACT



A neutral receptor with a rigid hydrazine spacer, *N*-*p*-(dimethylamino)benzamido-*N*′-phenylthiourea, was prepared, and its dual fluorescence in acetonitrile was found to show response toward the presence of anions such as AcO^-, $H_2PO_4^-$, HSO_4^-, Br^-, Cl^-, F^-, and ClO_4^- with high sensitivity and selectivity toward AcO^-.

Recognition and sensing of anions has been a subject of intensive current interest and hydrogen bonding is one of the important recognition elements in anion sensing.[1] Like the cation chemosensor,[2] an anion chemosensor consists of a recognition moiety and a signal reporter that are either directly linked to allow for a highly efficient communication between the recognition moiety and the reporter[3] or connected by a flexible spacer to ensure an optimal approaching of them.[4] Herein reported is a thiourea-based neutral anion receptor, *N*-*p*-(dimethylamino)benzamido-*N*′-phenylthiourea (**1**,[5] Scheme 1), in which the thiourea hydrogen-bonding recognition moiety[6] is linked to the dual fluorescent reporter *p*-dimethylaminobenzamide[7] by a *rigid* hydrazine (−NHNH−) spacer.[8] We found that the dual fluorescence of this receptor in acetonitrile showed response to the presence of anions such as AcO^-, $H_2PO_4^-$, HSO_4^-, ClO_4^-, F^-, Cl^-, and Br^-, with high sensitivity and selectivity toward AcO^-.

The configuration rigidity of the −NHNH− component results from the repulsion of the nonpaired electrons on

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(5) Compound **1** was synthesized by reaction of phenylisothiocynate with **2**. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.98 (6H, s), 6.73 (2H, d, J = 9 Hz), 7.14 (1H, t, J = 8 Hz), 7.31 (2H, t, J = 8 Hz), 7.45 (2H, s), 7.81 (2H, d, J = 9 Hz), 9.57 (1H, s), 9.71 (1H, s), 10.14 (1H, s). ESI-MS: m/z 314.9 (M + H$^+$, MeOH) and 336.8 (M + Na$^+$, ACN). Compound **2** was obtained from reaction of ethyl *p*-dimethylaminobenzoate with hydrazine hydrate. ^{1}H NMR (500 MHz, DMSO-d_6): 2.95 (6H, s), 4.33 (−N*H*, s), 6.68 (2H, d, J = 9 Hz), 7.69 (2H, d, J =9 Hz), 9.36 (−N*H*, s). Compound **3** was synthesized according to ref 7a.

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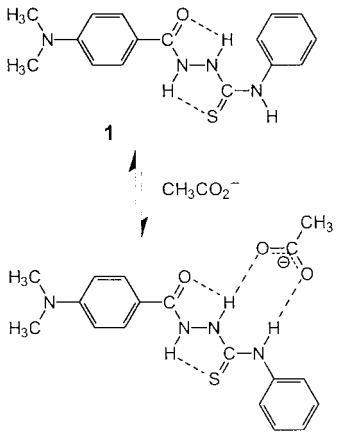
Scheme 1. Molecular Structure of **1** and Its 1:1 Hydrogen-Bonding Interaction with Acetate Anion



neighboring nitrogen atoms[8] and the preferential *Z*-conformation of secondary amide.[9] This rigidity makes it difficult for the thiourea recognition moiety in **1** to approach intramolecularly the dual fluorescent reporter moiety. Indeed, AM1 calculations indicated that the most stable conformation of **1** was the one shown in Scheme 1 with two five-membered ring intramolecular hydrogen bonds. The latter was also supported by the substantial downfield NMR signals of the −N*H* protons.[5] Here, the intramolecular hydrogen-bond network would be of particular significance, since it might open the proton transfer and probably the so-called proton-transfer coupled electron transfer (PCET) channel[10] in the photoexcited state and facilitate the excited-state communication of the receptor with the reporter via hydrogen bonds, making the fluorescent sensing possible.

The dual fluorescence of **1** was observed in highly polar solvents. In acetonitrile (ACN), the dual fluorescence, with a total quantum yield of 0.020, peaked at 370 and 520 nm due to the locally excited (LE) state and charge transfer (CT) state in equilibrium, respectively[7] (Figure 1a). The dual fluorescence was found to be sensitive to the presence of anions such as AcO^-, $H_2PO_4^-$, HSO_4^-, Br^-, Cl^-, F^-, and ClO_4^-. Figure 1a shows the fluorescence spectra of **1** in ACN in the presence of AcO^-. It was found that, whereas the band positions remained unchanged, the introduction of AcO^- resulted in quenching of the long wavelength CT emission while enhancing of the LE emission, with a clear isoemissive point at 425 nm. On the basis of the known thiourea−AcO^- hydrogen-bonding mode,[4,6] this might point to the hydrogen-bonding interaction between thiourea moiety in **1** and AcO^-, as indicated in Scheme 1, that resulted in variation in the dual fluorescence. Absorption spectra monitoring supported the hydrogen-bonding interaction. Figure 1b presents the absorption spectra of **1** in the presence of AcO^-. Introduction of AcO^- into ACN solution of **1** led to a split of the absorption spectrum of **1** originally peaked at 311 nm (ϵ = 3.5×10^4 cm^{-1} mol^{-1} L), and clear isosbestic points at 322, 289, and 240 nm, respectively, were observed. Introducing hydrogen-bonding solvents such as methanol, ethanol, or 2-propanol into the last **1**−AcO^- solution led to the recovery of the absorption spectrum of **1**. No such spectral variations were observed with *p*-(dimethylamino)benzoylhydrazine (**2**) and *p*-dimethylaminobenzamide (**3**) that have the same chromophore as **1** but no thiourea moiety. These observations clearly pointed to the formation of a 1:1 hydrogen-bonding complex, Scheme 1. Further evidence for this 1:1 hydrogen-bonding interaction was obtained from NMR and MS data.[11] In DMSO-d_6, the NMR signals of the thiourea −NH protons in **1** were found to show a downfield shift in the presence of AcO^-,[5,11] and in the ESI mass spectra of the **1**−AcO^- mixture in ACN we observed species of *m*/*z* value 375.1 (1:1 complex + $2H^+$). Acetate anion binding to the thiourea moiety in **1** was also supported by the observation of a smaller binding constant when the thiourea moiety in **1** was replaced by a urea moiety.[12] Similar but smaller variations were observed with F^- and $H_2PO_4^-$,[13] whereas with other anions the variations were found to be much less; see Figure 2.

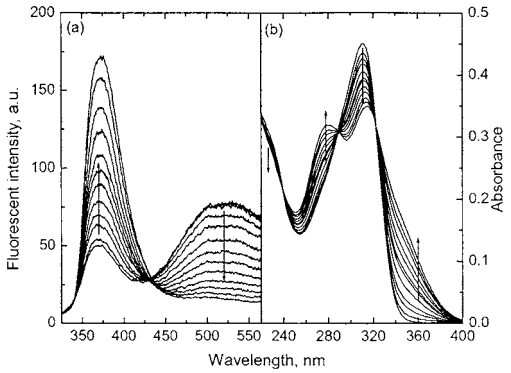


Figure 1. Fluorescence (a) and absorption (b) spectra of **1** in ACN in the presence of increasing concentration of AcO^-. The concentrations of **1** are (a) 8.0×10^{-6} and (b) 1.6×10^{-5} mol L^{-1}, respectively. AcO^- exists in its *n*-Bu_4N^+ salt. Arrows show the increase of AcO^- concentration from 0 to 11×10^{-6} mol L^{-1}. The excitation wavelength is 289 nm, the isosbestic wavelength. ACN was purified to have no fluorescent impurity at the used excitation wavelength.

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(11) ^{1}H NMR titrations were carried out in DMSO-d_6. In the presence of AcO^-, a downfield shift was found for the thiourea −NH ^{1}H NMR signals. The broadening and hence the overlapping of the NMR signals of the three −NH protons in the presence of AcO^- (e.g., 10.58 ppm in the presence of 2 equiv of AcO^-) made it impossible to measure from NMR data the binding constant of **1** with AcO^-. ESI−MS spectra were recorded on a Bruker ESQUIRE-3000$^+$ spectrometer.

(12) It is known that the binding constant of thiourea to the same oxoanion such as AcO^- is higher than that of the urea derivative; see, for example: Linton, B. R.; Goodman, M. S.; Fan, E.; van Arman, S. A.; Hamilton, A. D. *J. Org. Chem.* **2001**, *66*, 7313. The binding constants of AcO^- and $H_2PO_4^-$ with the urea derivative of **1** were measured as 1.4×10^3 and 1.2×10^3 mol^{-1} L, respectively, which were much smaller than those with **1** given later in the text.

(13) The absorption and fluorescence spectra of **1** in the presence of F^- (Figures 1SA and 1SF) and $H_2PO_4^-$ (Figures 2SA and 2SF) are provided in the Supporting Information.

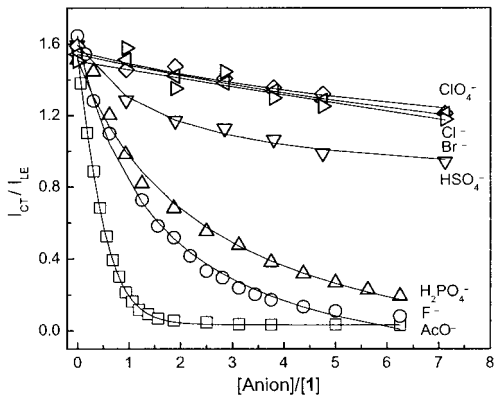

Figure 2. Plots of the CT to LE fluorescence maximum intensity ratio of **1** versus anion concentration. Concentration of **1** is 8.0×10^{-6} mol L^{-1}. All anions exist in the form of the *n*-Bu_4N^+ salt. The lines through the data points are fitted curves for 1:1 complex by the reported methods.[6b,14]

Both the variations of the absorbance at 311 nm (Figure 1b) and the CT to LE maximum intensity ratio (Figure 2) were used to evaluate the binding constants of **1** with anions, following the reported methods by assuming a 1:1 binding stoichiometry.[6b,14] Nice fittings (Figure 2) supported the 1:1 binding stoichiometry. The fitted binding constants are $(1.6 \pm 0.3) \times 10^5$ mol^{-1} L (abs), $(4.8 \pm 0.1) \times 10^5$ mol^{-1} L (flu) (AcO^-); $(4.9 \pm 0.4) \times 10^4$ mol^{-1} L, $(2.1 \pm 0.4) \times 10^5$ mol^{-1} L (F^-); $(1.3 \pm 0.2) \times 10^4$ mol^{-1} L, $(4.7 \pm 0.1) \times 10^4$ mol^{-1} L ($H_2PO_4^-$); and $(2.3 \pm 0.3) \times 10^3$ mol^{-1} L, $(8.7 \pm 0.4) \times 10^3$ mol^{-1} L (HSO_4^-), respectively, and are too small for Br^-, Cl^-, and ClO_4^- to be accurately determined, which vary in general in the order of the anion basicity. It is obvious that the present neutral receptor shows a high selectivity in acetonitrile for AcO^- over other anions, and in particular, its binding constant to AcO^- is close to that ($>10^6$ mol^{-1} L) of a positively charged thiourea-based repector.[4b]

It is interesting to note that the substantial change in the dual fluorescence intensity ratio of **1** upon anion binding is not accompanied by any change in the CT emission band position. With similar dual fluorescent molecules, experimental data have shown that the CT emission shifted to the red or blue when the electron donor/acceptor strength was enhanced or weakened.[7a,15,16] It hence follows that no change in the electron-withdrawing ability occurs with the acceptor in **1** upon anion binding. The fluorescence response observed here might not be accounted for within the classic PET (photoinduced electron transfer) mechanism either,[2a,4d] since that would lead to the same quenching of both the LE and CT emission with their intensity ratio remained unchanged. The fact that no fluorescence quenching was found when up to 10 equiv of AcO^- was added to the 1:1 mixture of **2** and *N*,*N*′-diphenylthiourea of 9.0×10^{-6} mol L^{-1}, a model system for **1**, ruled out the possibility that the change in the CT to LE fluorescence intensity ratio of **1** in the presence of AcO^- was due to different quenching of the LE and CT emission by the thiourea-AcO^- bound moiety in the **1**−AcO^- complex. This observation therefore suggested that the intramolecular hydrogen-bond network in **1** is important in facilitating the sensing. Indeed, we found that the absorption spectrum of **1** in ACN showed a 25 nm red shift with respect to the sum of the spectra of **2** and *N*,*N*′-diphenylthiourea, pointing out the contribution of the intramolecular hydrogen bonding in **1**. The excitation spectra of **1** in the absence of AcO^- obtained by monitoring the LE and CT fluorescence respectively were found to be almost the same and close to its absorption spectrum. In the presence of AcO^-, the LE-related excitation spectrum underwent a variation profile similar to that of the absorption spectrum (Figure 1b), whereas the CT related excitation spectrum remained the same as that in the absence of AcO^-. This implied that, in the presence of AcO^-, charge transfer from the LE state be accompanied by a new process that led to a CT species similar to that in the absence of AcO^-. A change in the hydrogen bond network of the receptor−anion complex (Scheme 1) might be assumed as being responsible for the fluorescence response. This actually suggested the occurrence of an excited-state proton transfer or probably a PCET process[10] within this network so that the LE to CT equilibrium was shifted, as was also evident from the appearance of an isoemissive point in the dual fluorescence variations (Figure 1a). The fact that the CT to LE intensity ratio of the 1:1 receptor−anion complex is in general lower with the anion of higher basicity (Figure 2) is in line of this assumption. The detailed mechanism, however, remains to be further clarified. Detailed work is now underway in this laboratory.

In summary, we reported a novel thiourea-based dual fluorescent neutral receptor for anions in which the recognition site was linked to the fluorophore reporter via a rigid spacer that affords an intramolecular hydrogen bond network. It was found that the response in the dual fluorescence by a substantial decrease in the CT to LE intensity ratio was not due to the change in the reduction potential of the electron acceptor upon anion binding. The response mechanism would be of use in designing novel receptors for anions that base mainly on hydrogen-bonding interactions.

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Supporting Information Available: Absorption and fluorescence spectra of **1** in acetonitrile in the presence of F^- (Figures 1SA and 1SF) and $H_2PO_4^-$ (Figures 2SA and 2SF). This material is available free of charge via the Internet at http://pubs.acs.org.

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