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A Naked Eye Detection of Fluoride with Urea Receptors Which have both an Azo Group and a Nitrophenyl Group as a Signaling Group

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Anion recognition *via* hydrogen-bonding interactions could be monitored with changes in UV-vis absorption spectra and in some cases easily monitored with naked eye. Urea receptors **1** and **2** connected with both an azo group and a nitrophenyl group as a signaling group for color change proved to be an efficient naked eye receptor for the fluoride ion. The anion recognition phenomena of the receptors **1** and **2** *via* hydrogen-bonding interactions were investigated through UV-vis absorption and ^{1}H NMR spectra.

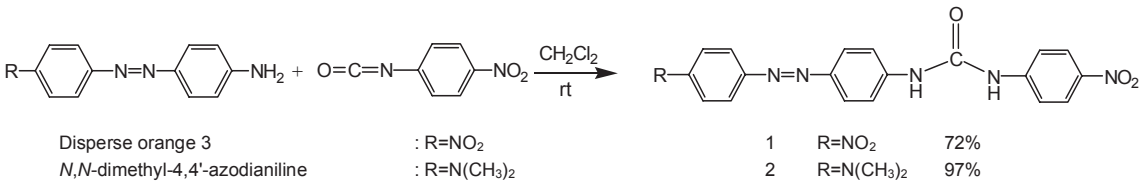
Key Words: Anion receptor, Urea, Naked eye detection

Introduction

Ureas and thioureas participate in bifurcate H-bond interactions and have been used as binding fragments in the design of neutral receptors for anions.[1] Especially, urea or thiourea derivatives connected with a series of chromogenic and fluorogenic substituents proved to be very efficient for the anion sensors.[2] The interaction with anion typically stabilizes the excited state of chromophore and induces red shift of the charge transfer absorption band, thus providing an efficient way for qualitative and quantitative evaluation of anion activity in solution.[3] They can be often easily synthesized from commercially available reagents even by a single step procedure.[4] Previously, we reported on novel colorimetric receptors containing nitrophenyl group as chromogenic signaling subunit and urea as binding sites, which was selective for fluoride or acetate ion.[5] Anion recognition *via* hydrogen-bonding interactions could be monitored with changes in UV-vis absorption spectra and in some cases easily monitored with naked eye.

We'd like to report herein on novel urea receptors with both an azo group and a nitrophenyl group as a signaling group for color change. The anion recognition *via* hydrogen-bonding interactions could be also monitored by changes in UV-vis absorption spectra and ^{1}H NMR.

Receptors **1** and **2** were synthesized using the one step reaction of disperse orange 3 and 4-nitrophenyl isocyanate or *N*,*N*-



Scheme 1. The synthetic procedure for the anion receptors **1** and **2**

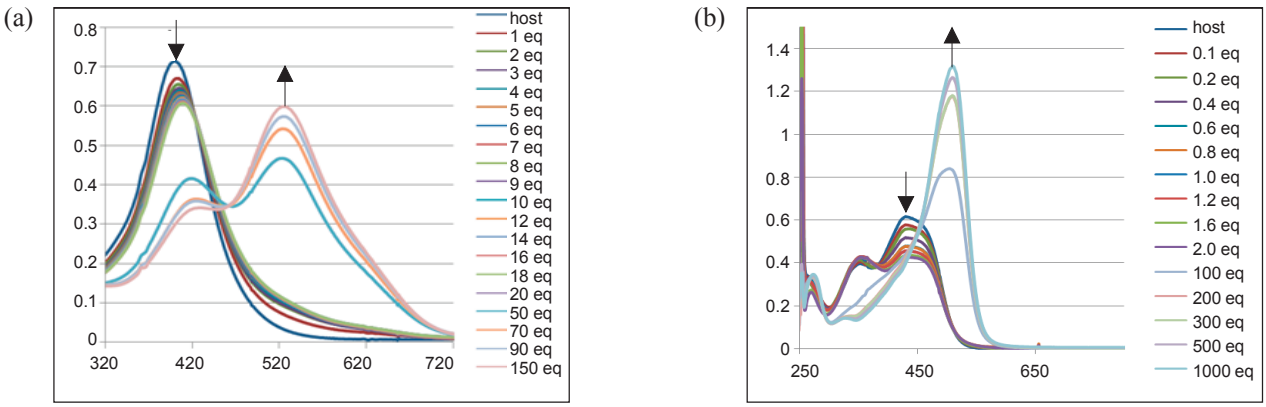


Figure 1. Family of spectra recorded over the course of titration of 20 μM DMSO solution of the receptor **1(a)** and **2(b)** with a standard solution tetrabutylammonium fluoride.

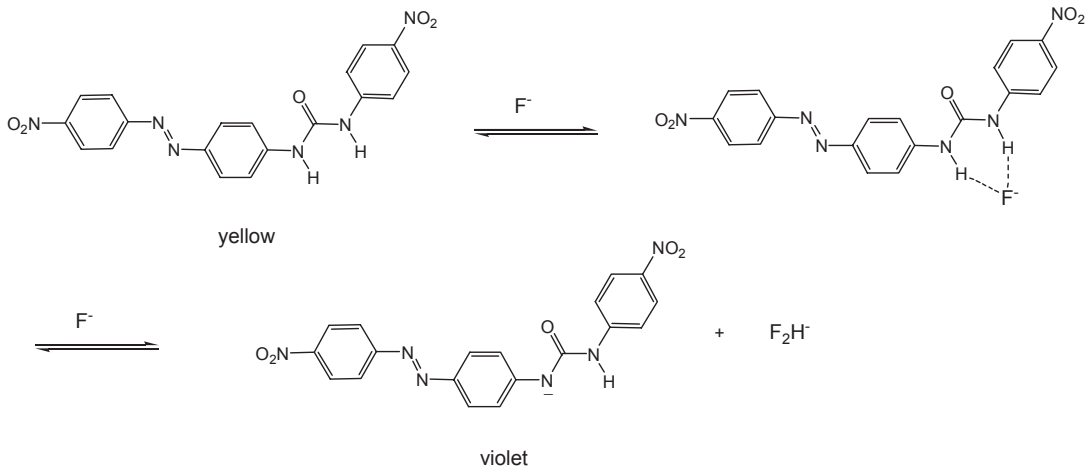


Figure 2. The interaction of receptor **1** and fluoride.

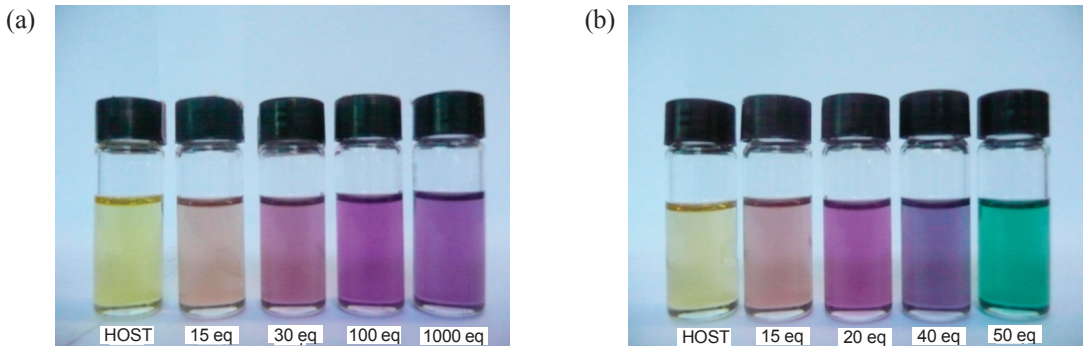


Figure 3. The color changes of the receptor **1** observed upon addition of fluoride ion (a) and hydroxide ion (b) in 20 μM DMSO solution.

dimethyl-4,4'-azodianiline and 4-nitrophenyl isocyanate in a reasonably good yield (Scheme 1).[6]

The receptors **1** and **2** displayed strong absorption bands at 400 nm and 430 nm respectively in DMSO. The intensity of absorption spectrum at these wavelengths decreased and λ_{max} of the spectrum showed red shift as the concentrations of anions were increased. Figure 1 shows the family of spectra obtained over the course of the titration of 20 μM solution **1** and **2** with tetrabutylammonium fluoride in DMSO. In the case of the receptor **1**, until 12 equivalents of fluoride were added to the solution of **1**, λ_{max} of **1** is shifted from 400 nm to 409 nm and spectra showed the clear isosbestic point at 416 nm. This result suggests that a typical hydrogen bonding complex forms between the receptor and the anion. However, when an excess equivalents (more than 50 equivalents) of fluoride ion were added, a new intense absorption bands developed at 523 nm, which were attributed to the deprotonated receptor.[7] In addition, spectra showed a new isosbestic point at 463 nm (Figure 1a). Therefore, fluoride ion initially forms a hydrogen bonded complex, but with excess of added anions, the deprotonation occurs due to formation of the hydrogen bonded anion dimer F_2H^- (Figure 2).[8]

Figure 3a shows the color change of 20 μM solutions of receptors **1** upon addition of fluoride ion in DMSO. It can be seen that the color changes from yellow to dark brown with 15 equivalents of fluoride ion. However with 30 equivalents of fluoride ion the color turns from dark brown to violet. The color change of urea based receptor has been ascribed to the deprotonation of one of N-H fragments of the urea. Therefore it is suggested that the violet compound (new band at 523 nm) pertains to the deprotonated receptor **1**. The dark brown color appears as the

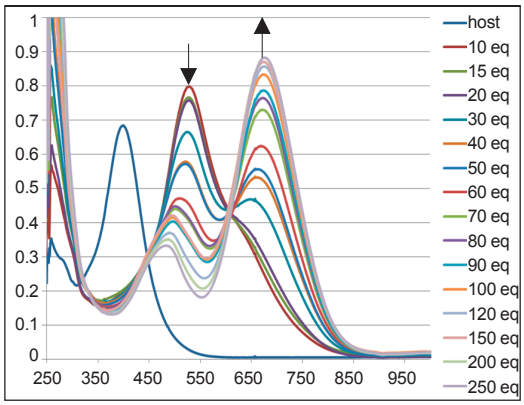


Figure 4. Family of spectra recorded over the course of titration of 20 μM DMSO solution of the receptor **1** with a standard solution tetrabutylammonium hydroxide.

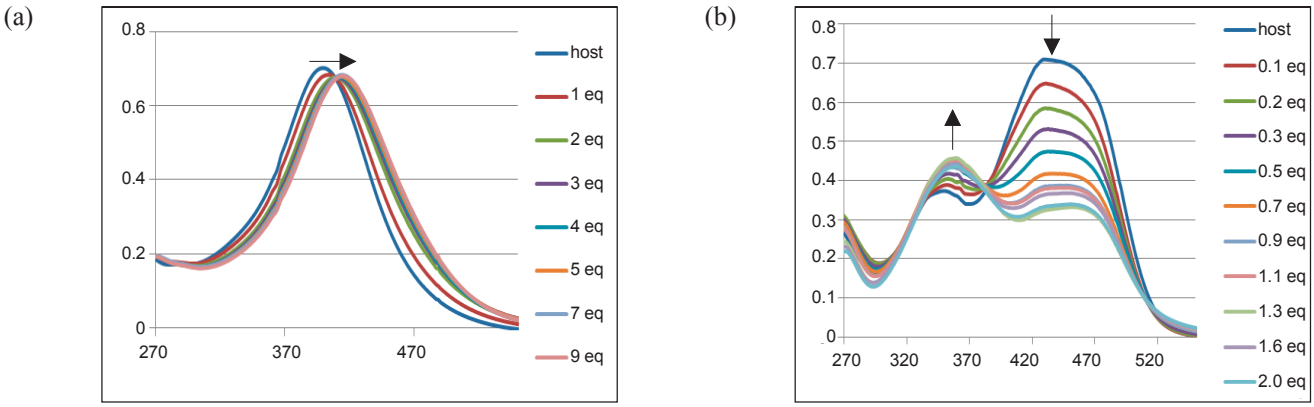


Figure 5. Family of spectra recorded over the course of titration of 20 μM DMSO solution of the receptor **1(a)** and **2(a)** with a standard solution tetrabutylammonium acetate.

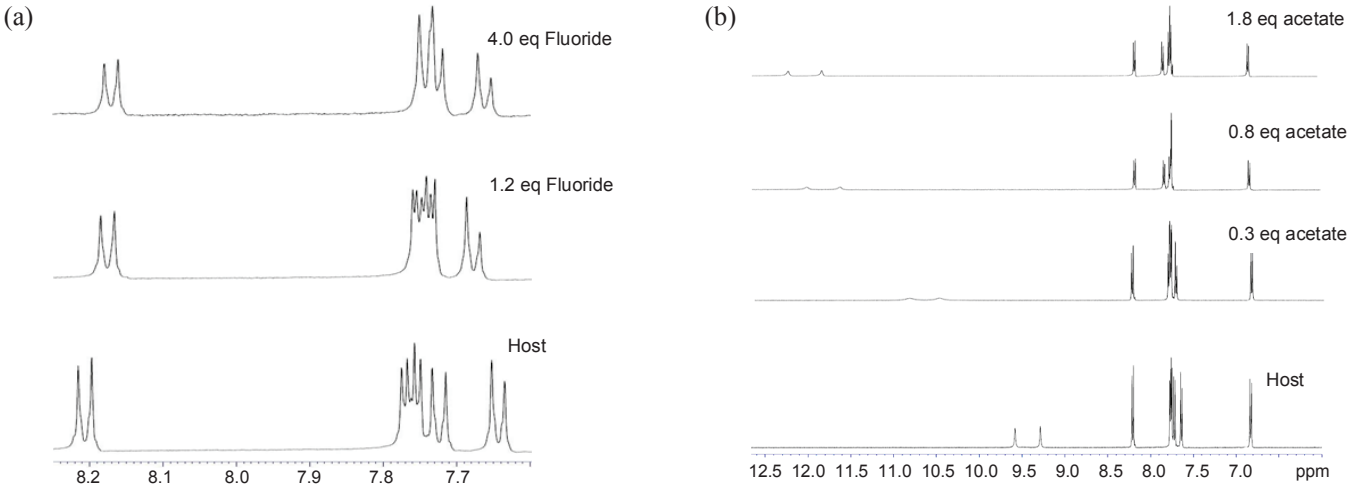


Figure 6. ^{1}H NMR spectra of 2.0 mM **2** in DMSO-d_6 with increased amounts of tetrabutylammonium fluoride (a) and tetrabutylammonium acetate (b).

solution exists as a mixture of hydrogen-bonded complex of receptor **1** and deprotonated receptor **1**. The stepwise deprotonation of the receptor **1** can be seen clearly when the solution of receptor **1** is titrated with tetrabutylammonium hydroxide. With 20 equivalents of hydroxide ion the color turns from yellow to violet and with 50 equivalents of hydroxide ion the color turns from violet to green (doubly deprotonated **1**) (Figure 3b). This result is in accord with consecutive development of new bands at 523 nm (monodeprotonated 1, violet) and 668 nm (doubly deprotonated 1, green) (Figure 4). However, the doubly deprotonated **1** could not be induced even with an excess amount of fluoride ion.

Similar phenomenon was observed for the receptor **2**. The receptor **2** showed hydrogen bonded complex initially with isosbestic point at 376 nm and deprotonated receptor with new bands at 513 nm Figure 1b. The color changed from yellow to orange Figure 7.

The Job plot showed 1:1 stoichiometry between fluoride and receptor **1** or **2**. Therefore a Benesi-Hildebrand plot[9] by use of change in the 400 nm and 523 nm gave association constant for hydrogen bonded complex and equilibrium constant for deprotonation respectively. From the experiments, the receptor **1** showed association constant $3.3 \times 10^4 \pm 2.6 \times 10^2$ and equilibrium constant $2.0 \times 10^3 \pm 8.2 \times 10^2$ for fluoride. In the same way, the association constant and equilibrium constant of the receptor **2** were calculated as $8.6 \times 10^4 \pm 3.4 \times 10^3$ and $1.4 \times 10^2 \pm 8.4$ respectively. With 20 μM solution of the receptor **1** and **2**, acetate only showed a typical spectrum pattern for the formation of hydrogen bonded complex (Figure 5). For acetate, the association constants were $4.6 \times 10^4 \pm 2.8 \times 10^3$ and $7.3 \times 10^4 \pm 5.7 \times 10^3$ for the receptor **1** and **2** respectively.

The binding phenomenon is also confirmed by a ^{1}H NMR titration in DMSO-d_6. For both receptors at the 2 mM solution, the urea N-H hydrogen peak became invisible upon addition of fluoride ion, therefore, one of the aromatic signal was use for titration. For example, In the case of receptor **2**, the signal at 8.22 ppm was used. This aromatic signal moved from 8.22 ppm to 8.17 ppm until 4 equivalents of fluoride ion was added (Figure 6a). In fact, two effects are expected as a result of hydrogen bond formation between the urea subunit and the anion. (i) A through-

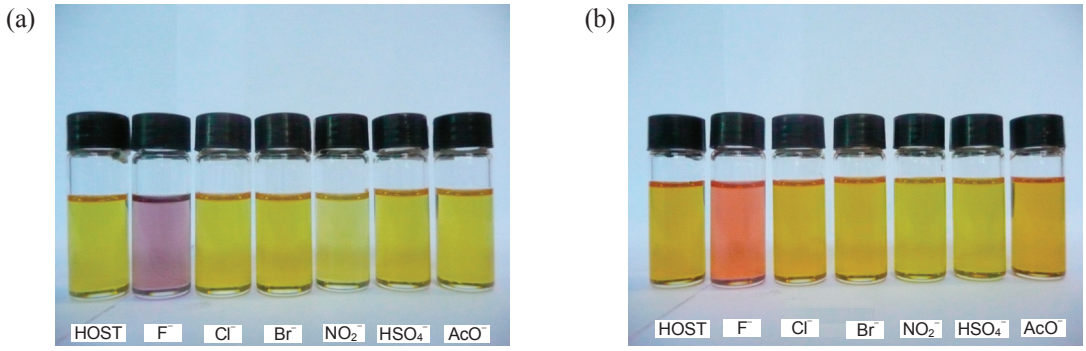


Figure 7. The color changes of the receptors **1**(a) and **2**(b) when 20 μM solutions of both receptors were treated with 25 equivalents in (a) and 50 equivalents in (b) of various anions.

bond propagation, which causes a shielding effect and promotes an upfield shift (ii) A through-space effect, which causes deshielding and promotes a downfield shift. In this case, through-bond propagation effect dominates, and an upfield shift is observed. In case of acetate, the ^{1}H NMR spectrum showed evidence of a discrete hydrogen-bonded complex. As tetrabutylammonium acetate was added, two urea peaks moved to downfield (from 9.58 and 9.29 ppm to 12.22 and 11.83 ppm), which suggests that the typical hydrogen bonding complex between the receptor and the anion Figure 6b. Analysis of chemical shift utilizing EQNMR[10] gave association constant. For fluoride, the association constants were $3.8 \times 10^4 \pm 1.5 \times 10^3$ and $7.8 \times 10^4 \pm 3.1 \times 10^3$ for the receptor **1** and **2** respectively. For acetate, the association constants were $4.1 \times 10^4 \pm 8.2 \times 10^2$ and $7.1 \times 10^4 \pm 4.6 \times 10^3$ for the receptor **1** and **2** respectively. These values are similar with the values obtained from UV-vis titration.

Other anions such as chloride, bromide, iodide, perchlorate, hydrogensulfate, nitrate did not bind to the receptor **1** and **2** in DMSO at all. Therefore, these anions did not induce any color changes Figure 7.

The receptor **1** and **2** only showed minor difference in their binding ability. Probably, nitro group and *N*,*N*-dimethylamino group are too far from the binding site to influence the binding phenomena. However, their change of color with deprotonation showed difference. The deprotonated receptor **1** looked as violet while deprotonated receptor **2** looked as orange.

In summary, we developed new chromogenic anion receptors **1** and **2** with urea which have an azo group and a nitrophenyl group as a signaling group. They formed hydrogen bonded complex. However, when the concentration of anion is basic enough, it deprotonats the receptor. Therefore, they operated based on a hydrogen bonding and an acid-base equilibrium.

In addition, the receptors **1** and **2** proved to be an efficient naked-eye detector for the fluoride ion.

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6. **Compound 1** To a solution of 100 mg of Disperse Orange 3 in 5 mL of dichloromethane was added 67.8 mg of 4-nitrophenyl isocyanate (1 eq, 67.7 mg) and the mixture was stirred for 6 hours at room temperature. After evaporation of the solvent from the reaction mixture, the remained solid was washed by dichloromethane. Recrystallization of the solid in acetone and diethyl ether gave 120 mg of orange solid compound **1** in 72% yields. ^{1}H NMR (DMSO-d_6) 9.6 (s, 1H), 9.5 (s, 1H), 8.4 (d, J = 9.0, 2H), 8.2 (d, J = 9.0, 2H), 8.0 (d, J = 9.0, 2H), 8.0 (d, J = 9.0, 2H), 7.8 (d, J = 9.0, 2H), 7.7 (d, J = 8.5, 2H). Ana. Calcd. for $C_{19}H_{14}N_6O_5$ (406,10): C, 56.16; H, 3.47; N, 20.68; O, 19.69. Found: C, 56.13; H, 3.41; N, 20.54. LRMS (ES) calculated for $C_{23}H_{18}N_6O_3$, 426.14 ; found for 426.15. **Compound 2** To a solution of 100 mg of *N*,*N*-dimethyl-4,4'-azodianiline in 5 mL of dichloromethane was added 82 mg of 4-ni-

trophenyl isocyanate (1 eq, 81.9 mg) and the mixture was stirred for 6 hours at room temperature. The precipitated solid was filtered. Washing with dichloromethane gave 150 mg of yellow solid compound **2** in 97 % yields. ^{1}H NMR (DMSO-d_6) 9.5 (s, 1H), 9.2 (s, 1H), 8.2 (d, J = 9.0, 2H), 7.8 (d, J = 9.0, 2H), 7.8 (d, J = 9.0, 2H), 7.7 (d, J = 9.0, 2H), 7.7 (d, J = 9.0, 2H), 6.8 (d, J = 9.0, 2H), 3.1 (s, 6H). Ana. Calcd. for $C_{21}H_{20}N_6O_3$ (404,16): C, 62.37; H, 4.98; N, 20.78; O, 11.87. Found: C, 62.42; H, 4.91; N, 20.66. LRMS (ES) calculated for $C_{23}H_{18}N_6O_3$, 426.14; found for 426.15.

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