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Urea Receptors which Have Both a Fat Brown RR and a Nitrophenyl Group as a Signaling Group

Sung kyu Lee and Jongmin Kang*

*Department of Chemistry, Sejong University, Seoul 143-747, Korea. *E-mail: kangjm@sejong.ac.kr*
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A new colorimetric anion sensor **1** has been synthesized based on both Fat brown RR dye and a nitrophenyl group. This new receptor **1** could recognize the presence of fluoride ion effectively and selectively by the change of color of solution. In addition, receptor **1** shows higher affinity for acetate, dihydrogenphosphate, and hydrogensulfate than the other anions such as chloride, bromide, iodide, perchlorate, and nitrate in acetonitrile.

Key Words: Anion receptor, Urea, Colorimetric receptor, Anion recognition

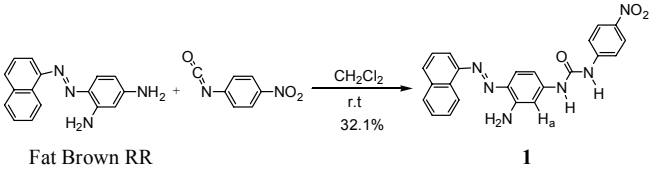
Introduction

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] We have also reported on novel colorimetric receptors containing a nitrophenyl group as chromogenic signaling subunit and urea as binding sites, which were selective for fluoride or acetate ion.[5]

As a part of our efforts to develop more efficient anion receptors, we planned to design a new colorimetric anion sensor **1** utilizing both Fat brown RR dye and nitrophenyl group as chromogenic signaling sites and urea moiety as binding sites.

The receptor **1** was found to be an efficient detector for fluoride ion by the change of UV-Vis, ^{1}H NMR spectra and the naked-eye observation. Receptors **1** was synthesized using the one step reaction of Fat Brown RR and 4-nitrophenyl isocyanate in a reasonably good yield (Scheme 1).[6]

The receptor **1** displayed strong absorption bands at 330 nm and 435 nm in acetonitrile. Figure 1a shows the family of spectra obtained over the course of the titration of the solution **1** with tetrabutylammonium fluoride in acetonitrile. As tetrabutylammonium fluoride was added to the 30 μM solution of **1**, the intensity of absorption spectrum decreased at 330 nm and increased at 383 nm and 435 nm. In addition, λ_{max} of **1** at 330 nm and 435 nm showed red shift, the solution color changes from yellow to red as the concentrations of anions were increased and the clear isosbestic point appears at 356 nm This result suggests that a typical hydrogen bonding complex forms between the receptor and the anion. Assuming 1:1 stoichiometry, a Benesi-Hildebrand plot[7] by use of change in the 385 nm absorption intensity gave association constants. From the experiments, the receptor **1** showed association constants 5.0×10^3 for fluoride. The binding phenomenon could be confirmed by a ^{1}H NMR titration in CD_3CN (Figure 2). As the N-H hydrogen peak became invisible upon addition of fluoride ion, the aromatic signal (H_a, Scheme 1)located next to urea (8.85 ppm) was used for titration. For the receptor **1**, this aromatic signal moved from 8.85 ppm to 9.10 ppm until 5 equivalents of fluoride ion was added. In fact, two effects are expected as a result of hydrogen bond formation between the urea subunit and the anion. (i) A through-bond propagation increases electron density in the phenyl ring, which causes a shielding effect and promotes an upfield shift (ii) A through-space effect increases a polarization of C-H bonds, which causes deshielding and promotes a downfield shift. In this case, the electrostatic effect dominates, and a downfield shift is observed. Analysis of chemical shift utilizing EQNMR[8] gave association constant 4.7×10^3, which is similar value obtained from UV-Vis titration.



Fat Brown RR **1**

Scheme 1. The synthetic procedure for the anion receptor **1**

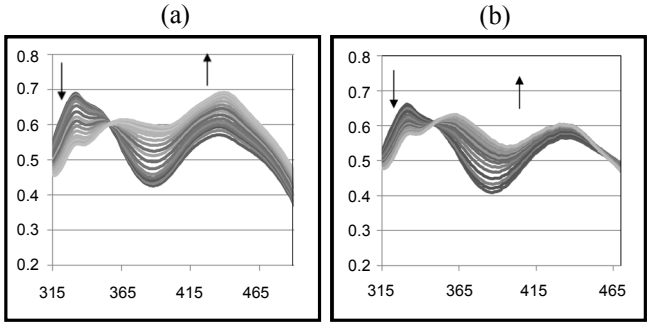


Figure 1. Family of spectra recorded over the course of titration of 30 μM acetonitrile solution of the receptor **1** with a standard solution tetrabutylammonium fluoride (a) and acetate (b).

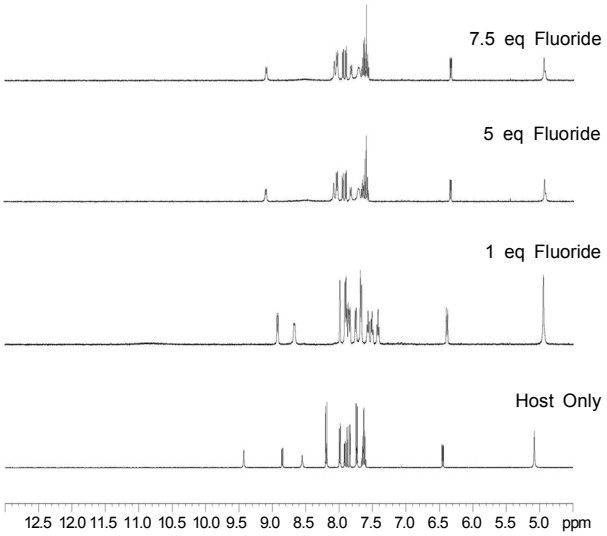


Figure 2. ^{1}H NMR spectra of 2 mM solution of **1** with increased amounts of tetrabutylammonium fluoride in CD_3CN.

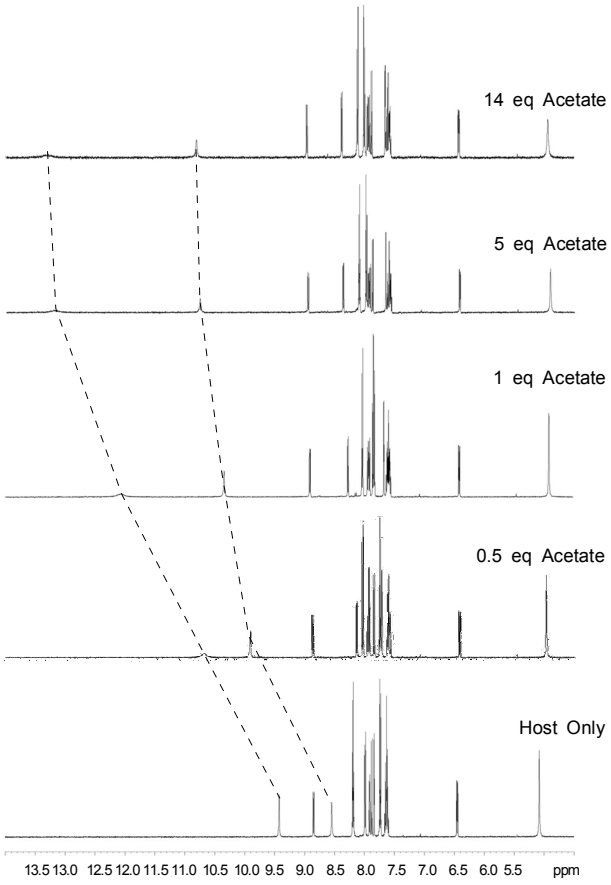


Figure 3. ^{1}H NMR spectra of 2 mM solution of **1** with increased amounts of tetrabutylammonium acetate in CD_3CN. Downfield shift of urea peaks are designated by dotted line.

With acetate, Both UV-Vis titration spectrum and ^{1}H NMR spectrum showed evidence of a discrete hydrogen-bonded complex. In case of UV-Vis titration, as tetrabutylammonium acetate was added to the 30 μM solution of **1**, the intensity of absorption spectrum decreased at 330 nm and increased at 383 nm and 435 nm. In addition, the clear isosbestic point appears at 345 nm (Figure 1b). In case of ^{1}H NMR titration, as tetrabutylammonium acetate was added, two urea peaks moved to downfield (from 9.43 and 8.54 ppm to 13.30 and 10.81 ppm) with broadening of signals, which suggests that the typical hydrogen bonding complex between the receptor and the anion. (Figure 3) The association constants obtained from UV-Vis spectrum and ^{1}H NMR titration were 3.3×10^3 and 4.1×10^3 respectively.

Table 1. The association constants of the receptors **1** with tetrabutylammonium anions in acetonitrile

Anion	Ka from UV-Vis titration	*Ka from ^{1}H NMR titration
F^-	$5.0 \times 10^3 \pm 2.5 \times 10^2$	4.7×10^3
$CH_3CO_2^-$	$3.3 \times 10^3 \pm 1.7 \times 10^2$	4.1×10^3
HSO_4^-	$2.7 \times 10^3 \pm 1.4 \times 10^2$	-
$H_2PO_4^-$	$2.6 \times 10^3 \pm 1.3 \times 10^2$	-
NO_3^-	$2.0 \times 10^3 \pm 1.0 \times 10^2$	-
Cl^-	$1.3 \times 10^3 \pm 6.5 \times 10$	-
Br^-	$1.0 \times 10^3 \pm 5.0 \times 10$	-

*Errors in Ka are estimated in less than 10%

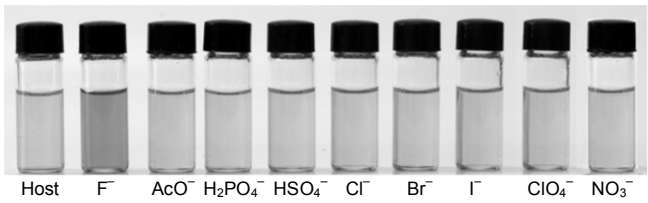


Figure 4. The color changes of the receptor **1** when 50 μM solution of the receptor was treated with 10 equivalents of various anions in acetonitrile.

We also investigated association constants of other anions. Among the anions investigated tetrahedrally shaped anions such as dihydrogenphosphate, and hydrogensulfate have higher affinity than spherically shaped anions such as halides. The binding constants of these anions from UV-Vis titration were summarized in Table 1.

Figure 4 shows the color change of the solutions of the receptor **1** upon additions of various anions in acetonitrile. It can be seen that the color changed from yellow to orange in the presence of fluoride anion with naked eye. Other anions did not induce any color changes even with excess amounts. Probably, as we can see from the NMR titration with fluoride ion, deprotonation of the receptor **1** by the fluoride induces the change of the color.

In summary, we developed a new chromogenic anion receptor **1** with utilizing Fat Brown RR and nitrophenyl group as signaling group. The receptor **1** binds anions *via* hydrogen bonds with a selectivity of $F^- > CH_3CO_2^- > HSO_4^- \sim H_2PO_4^- > NO_3^- > Cl^- \sim Br^-$ and proved to be an efficient naked-eye detector for the fluoride ion.

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6. To a solution of 100 mg (0.38 mmol) of Fat Brown RR in 5 mL of dichloromethane was added 62.4 mg (0.38 mmol) of 4-nitrophenyl isocyanate and the mixture was stirred for 6 hours at room temperature. After the solvent was evaporated from the reaction mixture, the remained solid was washed by dichloromethane. Chromatography on the silicagel (Hexane : Ethyl acetate = 3 : 1) gave 52 mg of red solid product in 32.1% yield ^{1}H NMR (DMSO-d_6) 10.5 (s, 1H), 9.5 (s, 1H), 8.9 (d, J = 8.0, 1H), 8.2 (d, J = 9.0, 2H), 8.0 (m, 3H), 7.9 (d, J = 9.0, 1H), 7.8 (d, J = 9.0, 2H), 7.7 (s, 1H), 7.6 (m, 3H), 6.4 (s, 2H), 6.4 (d, J = 9.0, 1H) LRMS (ES) calculated for $C_{23}H_{18}N_6O_3$, 426.14; found for 426.15.
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