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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 6079–6082

# Fluorescent anion chemosensors using 2-aminobenzimidazole receptors

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Received 18 May 2005; revised 30 June 2005; accepted 1 July 2005
Available online 20 July 2005

**Abstract**—Simple and easy-to-make fluorescent anion chemosensors using 2-aminobenzimidazole moieties as binding subunits showed selective anion-induced fluorescent changes. The receptors effectively recognized fluoride, chloride, bromide, acetate, dihydrogen phosphate ions with a 1:1 stoichiometry.


The design and synthesis of receptors capable of binding and sensing anions selectively have drawn considerable attention because anions play a major role in many chemical and biological processes.[1] Over the last decade, there have been many reports on fluorescent anion sensors.[2,3] Especially, fluorescent anion chemosensors are of great importance because of their high sensitivity and low detection limit.[2] A typical fluorescent anion sensor consists of a fluorophore and a receptor unit. The receptor–anion interaction induces a signaling process, which modifies the emission of the fluorophore leading to an anion specific fluorescent emission spectrum.

Anion recognition motifs are often structurally complicated and require an elaborate and sophisticated synthetic process.[1,2] Therefore, the development of simple and easy-to-make chemosensors for anions is strongly desired. Some research efforts have been made on developing simple and easy-to-make chemosensors using urea/thiourea and thiouronium as a binding site.[4]

In this work, we designed and synthesized anion chemosensors **1** and **2** by employing 2-aminobenzimidazole as a recognition site, which is connected by a methylene spacer to anthracene, a fluorophore (Fig. 1). The design is mainly based on the idea that N–H bonds in the receptors **1** and **2** align parallel to effectively make a complex with anions, and also that anion recognition on N–H bonds of 2-aminobenzimidazole moiety would be efficiently communicated to the fluorophore in the form of anthracene to detect easily a signaling effect in the system. Surprisingly, although N–H in heterocyclic compounds such as pyrrole derivatives has been employed frequently as anion receptors,[5] as far as we know, no receptors based on 2-aminobenzimidazole have ever been reported.[6]

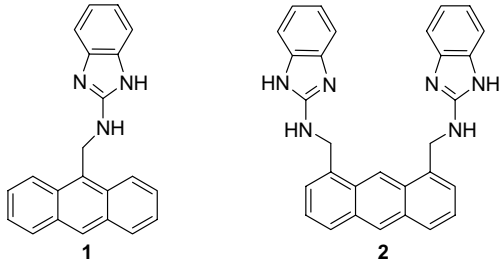


**Figure 1.** Fluorescent anion receptors **1** and **2**.

The synthesis of **1** was carried out by condensing 9-anthraldehyde with 2-aminobenzimidazole in the presence of toluenesulfonic acid, followed by reduction with $NaBH_4$ in MeOH (Scheme 1). The reaction mixture was poured into water and the solid precipitated was chromatographed on silica gel ($CH_2Cl_2$/MeOH, 19:1). The receptor **2** was similarly prepared from 1,8-anthracenedicarboxaldehyde[7,8] following the same method

*Keywords*: Fluorescence; Fluorescent sensor; Anion; Anion recognition; Hydrogen bonding.
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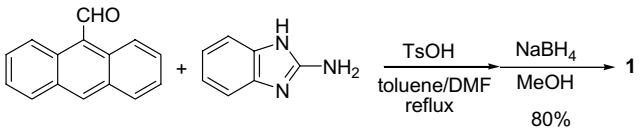
doi:10.1016/j.tetlet.2005.07.002




**Scheme 1.** The synthesis of anion receptor **1**.

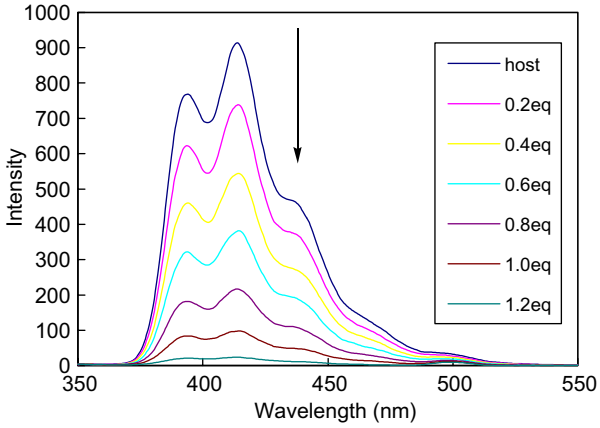



**Figure 2.** The change of fluorescence spectra of **1** (1 μM) in $CH_3CN$ at 25 °C excited at 365 nm upon addition of $Bu_4NF$.

that was applied in the synthesis of **1**. IR, $^1H$, $^{13}C$ NMR, and EA were consistent with the structure of **1** and **2**.[9]

The receptor **1** displayed strong fluorescence emission in acetonitrile as shown in Figure 2. The associations between the receptor **1** and the spherically shaped halides were investigated by fluorescence titration. The fluorescence change of the receptor **1** was monitored in acetonitrile, and the typical spectral changes are shown in Figure 2. The intensity of the emission spectrum from 1 μM solution of the receptor **1** decreased as the concentration of tetrabutylammonium fluoride was increased, which indicates an association between the receptor **1** and $F^-$. No significant spectral changes in absorption spectra were observed. These spectroscopic observations confirm that fluorescence quenching of the receptor **1** takes place via a photoinduced electron transfer (PET) mechanism. It is known that in a system where a fluorophore and a binding site are separated, anion binding to N–H hydrogens causes an increase in reduction potential of N–H bonds, thus increasing the affinity of fluorescence quenching via PET.[2a] Similar spectra were observed when $Cl^-$ and $Br^-$ were added. The stoichiometry between the host and the guest was determined by fluorescence Job's plot, which showed an evident 1:1 stoichiometry.[10] A Benesi–Hildebrand plot by use of change in the 413 nm fluorescence intensity gave association constants.[11] In the experiments, the receptor **1** showed the highest association constant $(2.06 \pm 0.32) \times 10^5\ M^{-1}$ for $F^-$. The order of association constants for halides was $F^- > Cl^- > Br^-$. The results are summarized in Table 1. As shown in the table, it is clear that the association constants of the receptor **1** for halides follow the diameter and basicity of the halide ions. The smallest size and the largest basicity of the fluoride ion allowed a much better fit into the binding site of the receptor **1** as well as the formation of shorter and stronger hydrogen bonds. For **1**, about 42-folds selectivity for fluoride over bromide was observed.

**Table 1.** Binding constants ($M^{-1}$) for the receptors **1** and **2** with various anions in $CH_3CN$ at 25 °C

| | **1** | **2** |
|---|---|---|
| $F^-$ | $(2.06 \pm 0.32) \times 10^5$ | $(2.75 \pm 0.06) \times 10^5$ |
| $Cl^-$ | $(8.95 \pm 0.75) \times 10^3$ | $(2.31 \pm 0.01) \times 10^4$ |
| $Br^-$ | $(4.92 \pm 0.98) \times 10^3$ | $(9.20 \pm 0.33) \times 10^3$ |
| $AcO^-$ | $(1.00 \pm 0.26) \times 10^5$ | $(2.60 \pm 0.40) \times 10^6$ |
| $H_2PO_4^-$ | — | $(2.01 \pm 0.19) \times 10^5$ |

We also investigated the binding of acetate and dihydrogen phosphate with the receptor **1** with fluorescence titration. While the Job's plot of carboxylate in $CH_3CN$ showed a 1:1 binding stoichiometry, the Job's plot of dihydrogen phosphate was not symmetric and showed maximum concentration of the complex when the mole fraction of the host was 0.71, which indicates a mixed stoichiometry. Therefore, we were unable to obtain an accurate association constant for dihydrogen phosphate. The calculated association constant of acetate was $(1.00 \pm 0.26) \times 10^5\ M^{-1}$.

The associations between various anions and the receptor **2** were investigated under the same conditions as the receptor **1** (Fig. 3). The Job's plot showed a 1:1 binding stoichiometry for halides, acetate, and dihydrogen phosphate. The association constants of the receptor **2** for halides were slightly increased compared with the association constants of the receptor **1** for halides. However, the association constants showed a large increase for acetate and dihydrogen phosphate since four hydrogen bondings are involved cooperatively in the binding event. The association constants of **2** for fluoride, acetate, and dihydrogen phosphate were comparable to those of receptors containing urea/thiourea and thiouronium as binding sites.[4]

To examine the nature of interaction between anions and the receptor **2**, we performed a standard $^1H$ NMR titration experiment in DMSO-$d_6$ using a constant host concentration (2 mM) and an increasing concentration of acetate (1–5 equiv).[12] Whereas the N–H protons of 2-aminobenzimidazole moiety shifted downfield dramatically upon addition of acetate from 10.89 to 13.00 ppm with 5 equiv of acetate, no significant shift was observed in the position of the methylene protons and aromatic rings. The N–H protons at benzylic position in **2** appeared at 7.16 ppm in DMSO-$d_6$. Upon addition of acetate to the solution of **2**, the protons shifted to 8.55 ppm with 5 equiv of acetate. The changes in N–H protons of imidazole rings are shown in Figure 4 as a function of the equivalents of acetate. The association constant calculated by WinEQNMR was found to be $1.56 \times 10^3\ M^{-1}$ for acetate.[13] These results suggest that the anion recognition takes place through hydrogen bondings between anions and N–H bonds of 2-aminobenzimidazole moieties (Fig. 5).

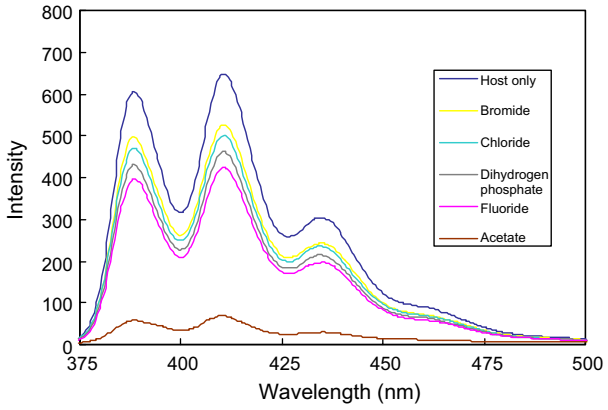



**Figure 3.** The change of fluorescence spectra of **2** (1 μM) in $CH_3CN$ at 25 °C excited at 365 nm upon addition of TBAF, TBACl, TBABr, TBAOAc, and $TBAH_2PO_4$ (1 equiv each) in $CH_3CN$.

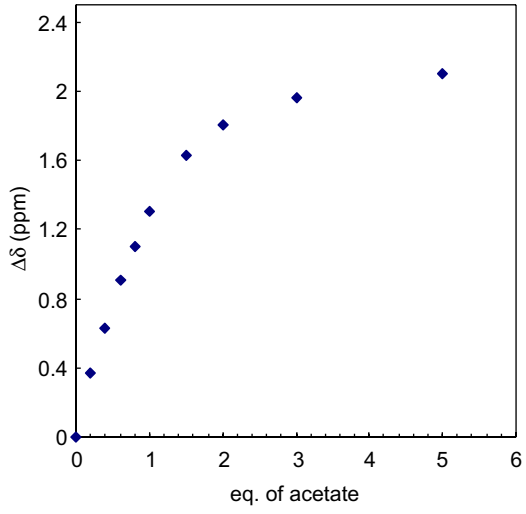



**Figure 4.** $^1H$ NMR titration of **2** with TBAOAc in DMSO-$d_6$.

In conclusion, we developed simple and easy-to-make fluorescent anion chemosensors **1** and **2** using 2-aminobenzimidazole moiety. The receptor **1** effectively recognized fluoride, chloride, bromide, and acetate ions with a 1:1 stoichiometry. The binding selectivity of **1** for fluoride is 42 times as high as that for bromide. The host **2** showed stronger interactions with anions than the receptor **1** since four hydrogen bondings participated in the binding events. We believe that 2-aminobenzimidazole moiety may able to serve as a binding subunit for construction of various chemosensors. Further studies along this line are being planned.

## Acknowledgements

This work was supported by Center for Bioactive Molecular Hybrids.

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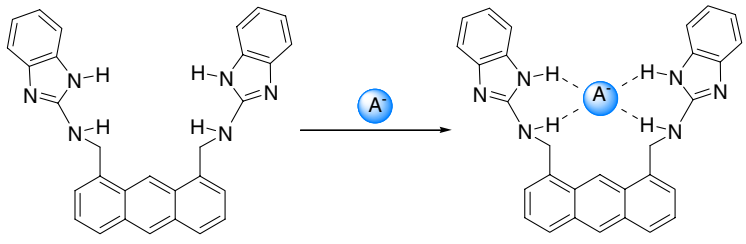


**Figure 5.** Proposed binding mode of **2** with anions.

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9. Compound **1**: mp 274–276 °C; IR (KBr) 3349, 2887, 1592, 1467, 1263, 738 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$ 5.50 (d, $J = 4.2$ Hz, 2H), 6.87 (t, $J = 7.5$ Hz, 2H), 6.96 (t, $J = 7.5$, 2H), 7.07 (s, 1H, NH) 7.15 (d, $J = 7.5$ Hz, 1H), 7.30 (d, $J = 7.5$ Hz, 1H), 7.52–7.62 (m, 4H), 8.14 (d, $J = 7.5$ Hz, 2H), 8.48 (d, $J = 7.5$ Hz, 2H), 8.65 (s, 1H), 10.42 (s, 1H); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 38.6, 108.8, 114.8, 118.4, 119.9, 124.5, 125.1, 126.2, 127.2, 128.8, 130.1, 131.1, 133.9, 143.7, 155.3; Anal. Calcd for $C_{22}H_{17}N_3$: C, 81.71; H, 5.30; N, 12.99. Found: C, 81.87; H, 5.12; N, 12.91. Compound **2**: mp 203–205 °C; IR (KBr) 3394, 3046, 1591, 1463, 1263, 877, 742 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$ 5.16 (d, $J =$ 5.0 Hz, 2H), 6.85 (t, $J = 8.1$ Hz, 4H), 7.14 (t, $J = 8.1$ Hz, 4H), 7.30 (s, NH), 7.45–7.55 (m, 4H), 8.02 (d, $J = 8.1$ Hz, 2H), 8.65 (s, 1H), 9.18 (s, 1H) 10.42 (s, NH); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 43.9, 108.6, 114.6, 118.2, 119.9, 124.1, 125.1, 127.3, 129.2, 131.2, 133.9, 135.9, 143.7, 155.6; Anal. Calcd for $C_{30}H_{24}N_6$: C, 76.90; H, 7.23; N, 16.05, Found: C, 76.72; H, 7.16; N, 16.04.
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