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Benzimidazole-Based Tripodal Receptor: Highly Selective Fluorescent Chemosensor for Iodide in Aqueous Solution

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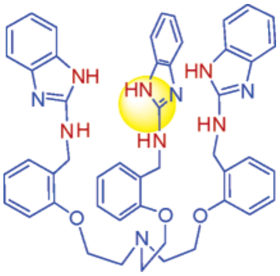
ABSTRACT



We synthesized a novel tripodal fluorescent receptor bearing benzimidazole motifs as recognition sites in the pods of the receptor. The recognition behavior of the receptor toward various anions was evaluated in CH_3CN/H_2O (9:1, v/v) solution. The receptor showed changes in fluorescent intensity only with I^-, but it showed no significant changes on addition of other anions such as F^-, Cl^-, Br^-, HSO_4^-, NO_3^-, CH_3COO^-, and $H_2PO_4^-$.

The design and synthesis of receptors capable of sensing anions selectively have provided important tools of detecting biologically and environmentally important analysts.[1] Iodide plays an important role in several biological activities such as neurological activity and thyroid function. Hence the iodide content of urine and milk is often required for nutritional, metabolic, and epidemiological studies of thyroid disorder.[2] Moreover, elemental iodine has been frequently used in many areas of chemistry for synthesizing valuable molecules such as drugs and dyes. Therefore, developing receptors that can bind iodide selectively is strongly desired.

Spectroscopic or electrochemical tools have been used to observe anion binding to a receptor, and the fluorescent sensing of anions has drawn much attention for its high sensitivity and selectivity.[3] Nevertheless, there are few reports on the fluorescent recognition of iodide,[4] and in-depth research has not been done on the estimation of iodide in

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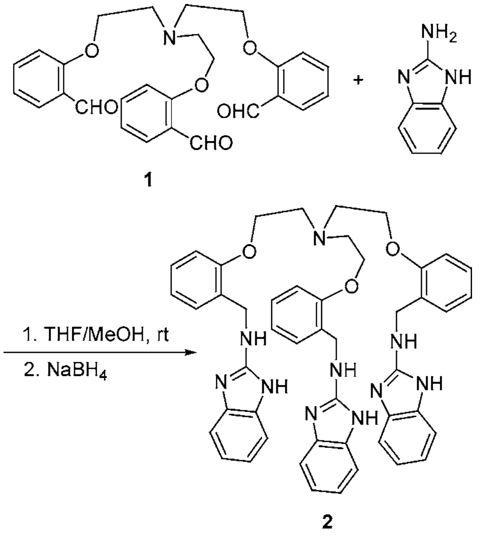
the presence of other anions, i.e., selective estimation of iodide.

As part of our ongoing studies on simple and easy-to-make receptors for anion recognition,[5] here we present the synthesis and anion binding studies of a new flexible tripodal receptor containing three benzimidazole groups as recognition sites for iodide. To date, there have been no reports in which a benzimidazole-based tripodal receptor is used for recognition of any anions.

The strategy for the design of the receptor is based upon two ideas. First, N−H bonds in the receptor aligned in parallel may effectively make a complex with an anion. Second, the flexibility of the receptor would allow encapsulation of large anions such as iodide.

The receptor **2** was prepared by applying the condensation reaction of tripodal aldehyde **1** with 2-aminobenzimidazole in a THF and MeOH solvent mixture in the presence of a catalytic amount of toluenesulfonic acid (Scheme 1).[6] Upon completion of the reaction, the imine linkages of the product were reduced with $NaBH_4$.

Scheme 1. Synthesis of Receptor **2**



The receptor **2** displayed a maximum at 495 nm in its fluorescence spectrum that was recorded with its 10 μM concentration in CH_3CN/H_2O (9:1, v/v) at neutral pH (HEPES buffer) when excited at 346 nm. The changes in fluorescence intensity of **2** upon addition of a particular anion are shown in Figure 1, and the fluorescence ratio $(I_o - I)/I_o$ is displayed in Figure 2. As can be seen from Figures 1 and 2, it is clear that there was marked quenching upon addition of iodide, and no significant quenching was observed upon addition of any F^-, Cl^-, Br^-, HSO_4^-, NO_3^-, CH_3COO^-, and $H_2PO_4^-$.

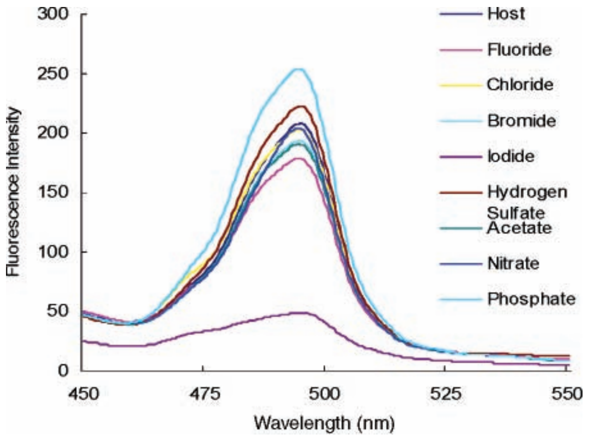


Figure 1. Changes in fluorescence intensity of **2** (10 μM) upon addition of 5.0 equiv of a particular tetrabutylammonium anion salt in CH_3CN/H_2O (9:1, v/v) (10 mM HEPES buffer, pH = 7.0) with excitation at 346 nm.

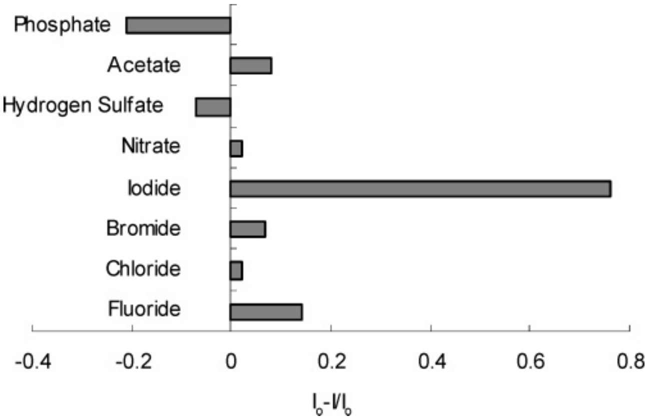


Figure 2. Fluorescence ratio $(I_o - I/I_o)$ of **2** (10 μM) at 495 nm upon addition of 5.0 equiv of a particular tetrabutylammonium anion salt in HEPES buffered (10 mM, pH = 7.0) CH_3CN/H_2O (9:1, v/v).

The preference for iodide suggests that the flexible pods in **2** are more compatible to the size of iodide than to the size of other anions. The higher binding of F^- among halides on the basis of its basicity has been known, and anions tend to bind in the order of $F^- > Cl^- > Br^- > I^-$.[7] However, there are many examples where other halides (with the exception of F^-) bind predominantly because of the complementary size of the pseudocavity formed by the receptor binding sites.[8] Thus, we think that it is better to encapsulate the iodide according to its size, not according to its basicity.

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(4) For some examples of molecular recognition of iodide: (a) Rodriguez-Docampo, Z.; Pascu, S. I.; Kubik, S.; Otto, S. *J. Am. Chem. Soc.* **2006**, *128*, 11206−11210. (b) Kim, H.; Kang, J. *Tetrahedron Lett.* **2005**, *46*, 5443−5445. (c) Ariga, K.; Kunitake, T.; Furuta, H. *J. Chem. Soc., Perkin Trans. 2* **1996**, 667−672.

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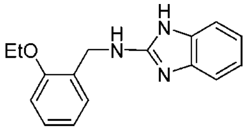
To confirm our point and to rule out the possibility of heavy atomic effects due to iodide, we designed another compound **3** (Scheme 2), which resembles the single pod of receptor **2**. We selected a 30 μM concentration of compound **3** (a 30 μM concentration of **3** has approximately the same number of binding sites as that of a 10 μM concentration of **2**) and then studied the quenching activity by iodide. No significant changes in the fluorescence intensity were observed in the typical experiment. This proved that although **2** and **3** have the same type of binding sites only an appropriate size of the pseudocavity of **2** can bind iodide, and iodide is believed to be bound cooperatively in the cavity of **2**.

Scheme 2. Structure of **3**



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To learn more about the properties of **2** as a receptor for iodide, fluorescence titration was carried out. The fluorescence intensity of a 10 μM solution of **2** decreased as the concentration of tetrabutylammonium iodide salt increased as shown in Figure 3. The receptor **2** exhibited a high sensitivity toward iodide, quenching 75% of its fluorescence intensity with 3.0 equiv of iodide. The association constant K_a of **2** for iodide was calculated on the basis of Benesi−Hildebrand plot,[9] and it was found to be 2.2×10^5 M^{-1}. The Stern−Volmer plot (plot of I_o/I vs concentration of guest) is a straight line. This confirmed the formation of one type of complex between **2** and iodide.[10] The stoichiometry of the complex formed was determined by Job's plot,[11] and it was found to be 1:1. There were no significant changes in the fluorescence intensity of **2** upon addition of F^-, Cl^-, Br^-, HSO_4^-, NO_3^-, CH_3COO^-, and $H_2PO_4^-$. This shows that the receptor **2** is highly selective in its response to iodide in comparison to other anions. Thus, the receptor **2** can be used for selective recognition of iodide, and it can detect iodide up to a low concentration of 2.1 μM.[12]

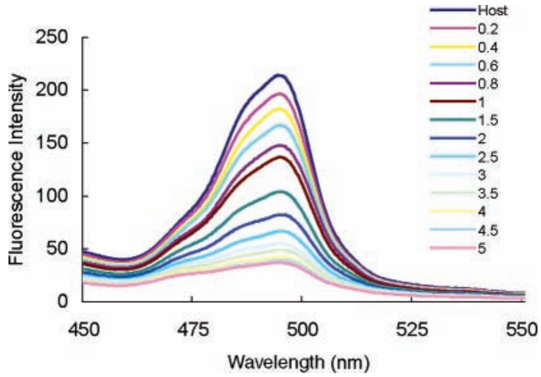

Figure 3. Fluorescence spectra changes of **2** (10 μM) upon addition of tetrabutylammonium iodide (0−50 μM) in HEPES buffered (10 mM, pH = 7.0) CH_3CN/H_2O (9:1, v/v).

The system was further extended to estimate the iodide in the presence of other anions, which may interfere in estimation (Figure 4). Experiments were performed to measure the fluorescence intensity in a series of solutions containing the receptor **2**, different amounts of iodide, and other anions having a concentration 10 times greater than the concentration of iodide in CH_3CN/H_2O (9:1, v/v).

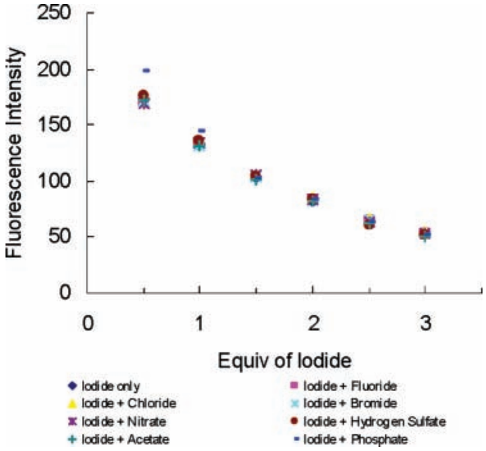

Figure 4. Estimation of I^- in the presence of F^-, Cl^-, Br^-, HSO_4^-, NO_3^-, CH_3COO^-, and $H_2PO_4^-$ in HEPES buffered (10 mM, pH = 7.0) CH_3CN/H_2O (9:1, v/v).

The fluorescence titration of **2** for iodide in aqueous solution was carried out in the presence of F^-, Cl^-, Br^-, HSO_4^-, NO_3^-, CH_3COO^-, and $H_2PO_2^-$. The fluorescence intensity was almost identical to that obtained in the absence

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of anions with the exception of $H_2PO_2^-$. $H_2PO_4^-$ caused a small interference when the sample contained a very small amount of iodide (up to 4 μM), whereas other anions did not cause any interference in the estimation of iodide.

Finally, an ^{1}H NMR titration experiment was performed to understand the character of the receptor−anion interactions. The series of ^{1}H NMR spectra of receptor **2** upon addition of increasing amounts of tetrabutylammonium iodide in DMSO-d_6 are shown in Figure 5. Upon addition of 0.5 equiv of iodide salt, the signal of N−H at the benzylic position split into two signals. The benzylic N−H signal of pure receptor **2** at 6.60 ppm shifted to 6.48 ppm upon addition of 1 equiv of iodide salt. This is a significant shift in the benzylic N−H signal of receptor **2** which shows that this binding site plays a vital role in the binding mode of iodide.

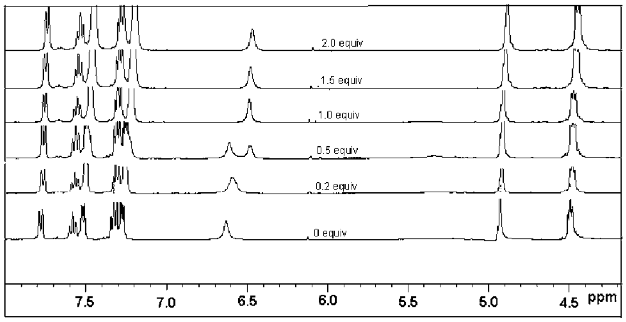

Figure 5. Plot of ^{1}H NMR spectra of receptor **2** on addition of tetrabutylammonium iodide in DMSO-d_6.

In conclusion, we have synthesized an easy-to-make neutral tripodal fluorescent anion receptor **2** based upon benzimidazole moieties and investigated its binding properties toward iodide. It showed an extremely high selectivity for iodide over a wide range of anions. The receptor acts as a selective sensor for iodide even in the presence of other ions in 10% aqueous CH_3CN without any interference.

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Supporting Information Available: Synthesis, characterization data, experimental procedures, NMR spectra, and fluorescence data. This material is available free of charge via the Internet at http://pubs.acs.org.

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