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Chromogenic and Fluorescent Recognition of Iodide with a Benzimidazole-Based Tripodal Receptor

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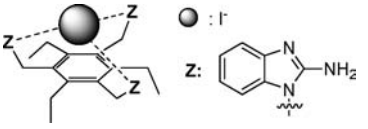
ABSTRACT



A novel 1,3,5-substituted triethylbenzene derivative with a 2-aminobenzimidazole moiety as a binding and signaling subunit was synthesized. The sensor was tested in a buffered CH_3CN/H_2O (99:1, v/v) solution and found to be selective for iodide as demonstrated by the photophysical properties obtained through UV−vis absorption and fluorescence spectroscopy analyses.

The Na^+/I^- symporter (NIS) is an important plasma membrane glycoprotein that mediates active I^- transport in the thyroid gland, which is the first step in thyroid hormone biogenesis.[1] Thyroid hormones are responsible for the regulation of several metabolic processes such as growth and maturation of organ systems.[2] Thus, iodide plays a vital role in many biological activities including neurological activity and thyroid function. Consequently, the iodide content of foodstuff and drinks is often required as part of the nutritional information.[3]

In recent years, chromogenic and fluorescent recognition of anions has received much attention for the estimation of anions because these methods have high sensitivity, low cost, good potential efficiency, and easy operation.[4] Although a number of studies have been published concerning other anions such as fluoride, there are few reports available for the estimation of iodide.[5] Fluoride, which has a small size and high charge density, makes a very strong complex with any anion receptor offering −NH donor sites for the coordination of anions. On the other hand, iodide is a larger anion with a relatively lower charge density, making it an inept candidate for coordination in a receptor pseudocavity.[6] In this context, the design of a receptor should be tailored in such a way that the presence of other anions does not interference in the estimation of iodide. We and

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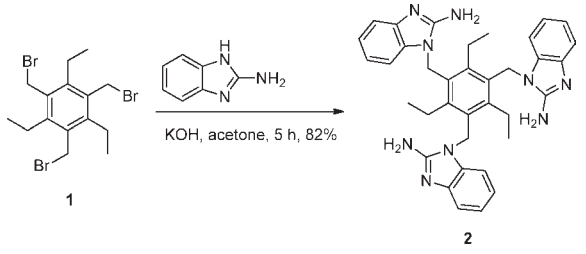
others have previously reported some receptors for iodide recognition.[5] However, the available reports do not focus on the estimation of iodide over a broad concentration range. The concentration range should be free from any interference resulting from other anions.

In continuation of our research focused on the synthesis of benzimidazole-based receptors for the recognition of cation, anions, and biomolecules,[7] we present the development of an iodide sensor capable of analyte estimation over a broad concentration range and without interference from any other anions in this study.

Receptor **2** was synthesized by the series of steps shown in Scheme 1. The tribromide **1** was synthesized by a procedure previously reported in the literature.[8] The reaction of compound **1** with 2-aminobenzimidazole in the presence of KOH afforded receptor **2** in a yield of 82%.

Scheme 1. Synthesis of Receptor **2**



The structure of receptor **2** was established by spectroscopic methods. The ^{1}H NMR spectrum of receptor **2** showed two doublets (3H each) and two triplets (3H each) for the aromatic protons of benzimidazole, confirming the nucleophilic reaction shown in Scheme 1. The possibility of the involvement of the amino ($-NH_2$) group of benzimidazole in the nucleophilic reaction was ruled out as the spectrum showed a broad singlet signal (6H) assigned to $-NH_2$. The pods of receptor **2** may adopt any of the orientations shown in Figure 1. However, the ^{1}H and ^{13}C NMR spectra support conformation **B** as only a single signal was observed for each of $-CH_3$, $-CH_2$, and $-NCH_2$ in both spectra.[9] The orientation **B** is mandatory for the strong encapsulation of any anion. On the other hand, the bulky aromatic platform may authenticate the selective binding of large anions such as iodide.

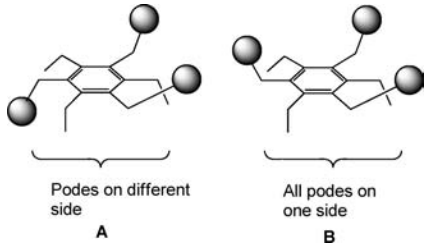


Figure 1. Possible conformations of the 1,3,5-substituted triethylbenzene derivative.

The binding behavior of receptor **2** toward different anions including F^-, Cl^-, Br^-, I^-, HPO_4^-, HSO_4^-, NO_3^-, ClO_4^-, CN^-, and CH_3COO^- was investigated by UV−vis absorption and fluorescence spectroscopy. The absorption spectrum of receptor **2** exhibits a band at λ_{max} = 258 nm in a CH_3CN/H_2O (99:1, v/v, pH = 7.91) HEPES buffer solution, which is expected because of the presence of the benzimidazole moiety. This band was shifted to λ_{max} = 248 nm upon addition of iodide to the solution of receptor **2** in a CH_3CN/H_2O (99:1, v/v, pH = 7.91) HEPES buffer solution (Figure 2A). Upon excitation of receptor **2** at 258 nm, a dual channel emission was observed at λ_{max} = 318 and 408 nm (Figure 2B). The emission at higher wavelength is most likely due to eximer formation. Similar to the anion binding of receptor **2** observed in the UV−vis absorption spectroscopy results, the fluorescence spectroscopy results also established exclusive iodide binding resulting in quenching of the fluorescence intensity of receptor **2**

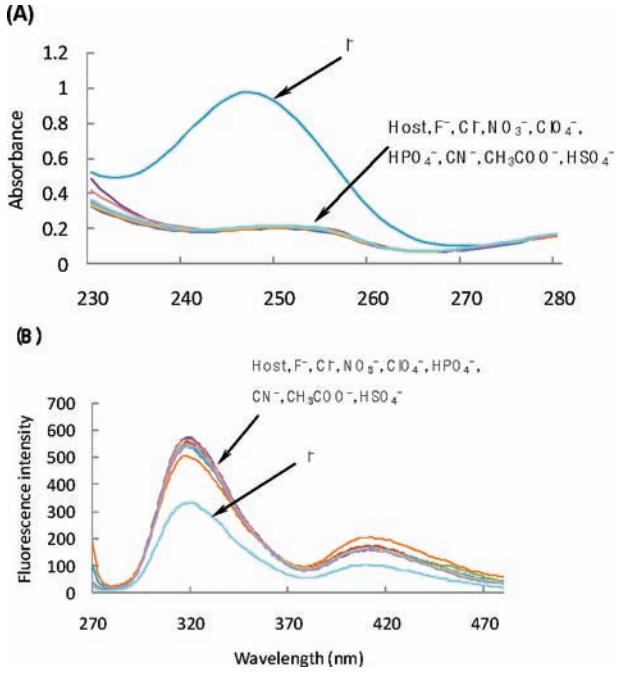


Figure 2. Changes of the photophysical properties of receptor **2** (10 μM) observed by (**A**) UV−vis absorption and (**B**) fluorescence spectroscopy upon addition of anion (50 μM) salt in a CH_3CN/H_2O (99:1, v/v, pH = 7.91) HEPES buffer solution.

The changes in the photophysical properties of receptor **2** upon complexation with iodide observed in the UV−vis absorption and fluorescence spectroscopy results are similar to the findings of Valiyaveettil et al.,[10] who asserted that the changes in photophysical properties are due to the

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"heavy-atom" effect. The latter quenching is of two types: (a) static quenching in which an authenticated complex is formed between a receptor (emitter) and an anion (quencher) and (b) dynamic quenching where the quenching is due to the random collisions between a receptor (emitter) and an anion (quencher).[11] In the present investigation, receptor **2** shows static quenching upon addition of iodide as established by the ^{1}H NMR titration. The family of ^{1}H NMR spectra of receptor **2** obtained by the titration of iodide are shown in Figure 3. The continuous addition of iodide to the solution of receptor **2** caused a downfield shift in the signal corresponding to $-NH_2$. No such significant changes were observed with the other proton signals, showing that iodide is bound to the receptor pseudocavity through hydrogen bonding of $-NH_2$ protons. The complexation through hydrogen bonding was further confirmed by the addition of a polar solvent, H_2O, to the solution containing receptor **2** and iodide. This addition retarded the binding between the host and the guest through competition between iodide and H_2O for the receptor binding sites. This experiment confirmed that iodide experiences authentic binding in the receptor's pseudocavity, thus leading to the static quenching of the fluorescence intensity of receptor **2**. Our belief underlining the pseudocavity of receptor **2** for iodide binding was also confirmed by comparing the binding pattern of receptor **3** (Figure 4), which shows no selective binding for iodide (Figure S1, Supporting Information). Moreover, changing the structure of receptor **2** to **4** (Figure 4), which is lacking $-NH_2$ but, however, providing another hydrogen donor site of $-CH$, shifted the binding pattern from exclusive iodide binding to dominant perchlorate binding. This experiment clearly showed the importance of the $-NH_2$ binding site for iodide recognition (Figure S2, Supporting Information).

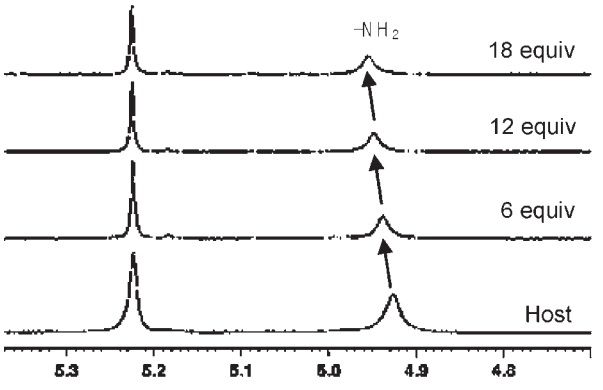

Figure 3. Family of ^{1}H NMR spectra obtained upon continuous addition of tetrabutylammonium iodide to a CD_3CN solution (0.2 mM) containing receptor **2**.

To gain more insight into the use of receptor **2** as a sensor for iodide, a titration was performed with increasing amounts of iodide. Addition of iodide resulted in increases in absorption along with a blue shift of 10 nm. On the other hand, the continuous addition of

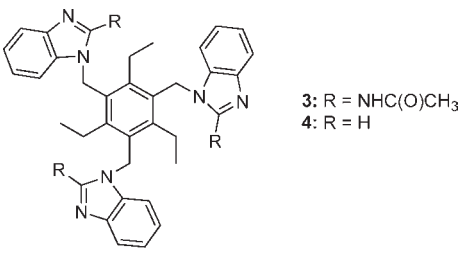

Figure 4. Structure of compounds **3** and **4**.

iodide to receptor **2** led to quenching of the fluorescence intensity at λ_{max} = 318 and 408 nm. The insets in Figure 5 show the Bensei–Hildebrand plots obtained from the UV–vis absorption and fluorescence spectroscopy data.[12] The binding constants were calculated to be $(1.5 \pm 0.2) \times 10^3$ and $(1.3 \pm 0.2) \times 10^3$ M^{-1}, respectively. The detection limit of receptor **2** as a fluorescent sensor for the estimation of iodide was determined from the titration shown in Figure 5B and from the plot of the fluorescence intensity as a function of the iodide concentration. It was found that receptor **2** has a detection limit of 7.45×0^{-6} M^{-1} along with a sufficiently large detection range.[13]

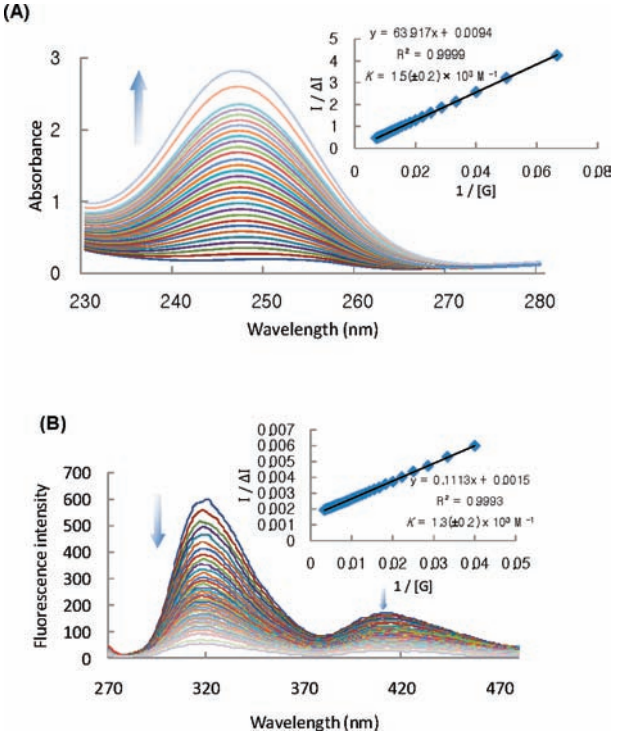

Figure 5. (A) UV–vis absorption spectra and (B) fluorescence spectra of receptor **2** (10 μM) upon addition of tetrabutylammonium iodide in a CH_3CN/H_2O (99:1, v/v, pH = 7.91) HEPES buffer solvent. Insets: Bensei–Hildebrand plots obtained from the UV–vis absorption and fluorescence spectroscopy results.

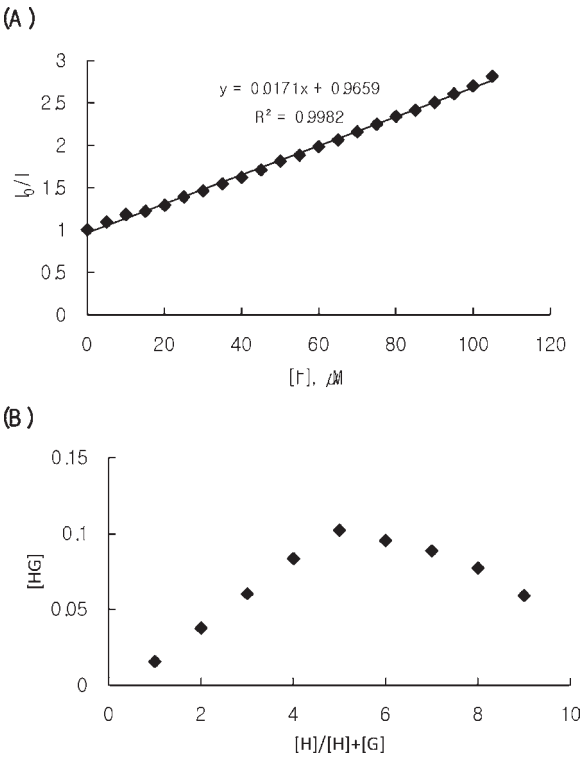

Figure 6. (A) Stern–Volmer plot for **2** in the presence of iodide and (B) Job's plot between receptor **2** and iodide. The concentration of [HG] was calculated as [HG] = $\Delta I/I_o \times$ [H].

The fluorescence quenching interaction between receptor **2** and iodide was further evaluated using the Stern–Volmer equation, $I_o/I = 1 + K_{SV}[Q]^n$, where I_o is the fluorescence intensity of receptor **2**, I is the fluorescence intensity of **2** in the presence of quencher (Q), and K_{SV} is the Stern–Volmer constant derived for a 1:1 complex. The Stern–Volmer plot shown in Figure 6A illustrates an excellent fit in the concentration range of 0–150 μM iodide ($n = 1$), indicating that the most abundant complex formed within this concentration range has a 1:1 (host/guest) stoichiometry.[14] Moreover, the continuous variation method (Job's plot) was also used to prove the 1:1 stoichiometry between the host and guest (Figure 6B).[15]

To test the practical applicability of receptor **2** as an iodide selective sensor, competitive experiments were carried out in the presence of various concentrations of iodide mixed with either F^-, Cl^-, Br^-, HPO_4^-, HSO_4^-, NO_3^-, ClO_4^-, CN^-, or CH_3COO^-. As shown in Figure 7, no significant variation in the fluorescence intensity was observed with and without the other anions except for iodide. This demonstrates that receptor **2** has a high selectivity for iodide ions.

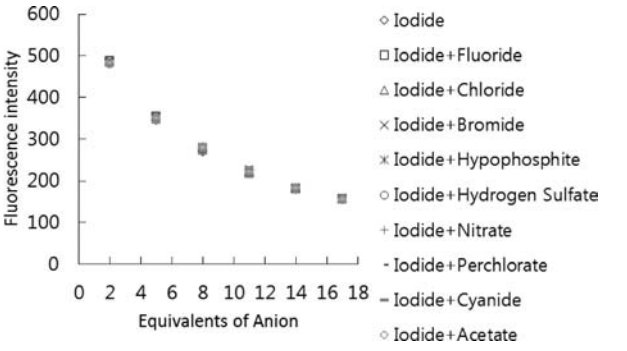

Figure 7. Estimation of iodide with receptor **2** in the presence of various anions in a CH_3CN/H_2O (99:1, v/v, pH = 7.91) HEPES buffer solution as measured by the fluorescence intensity at 318 nm.

In conclusion, a new benzimidazole-based receptor was developed for the estimation of iodide. This receptor was found to be operational over a large iodide concentration range. Moreover, along with such a broad concentration detection range, the system is absolutely free from interference due to the presence of other anions.

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

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