

New Hg²⁺-Selective Chromo- and Fluoroionophore Based upon 8-Hydroxyquinoline

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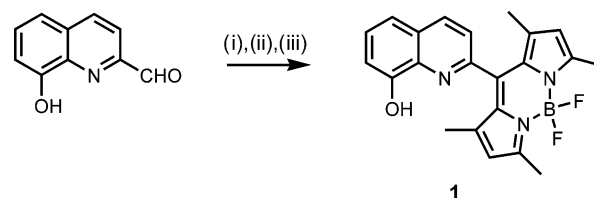
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Abstract: A new 8-hydroxyquinoline derivative having an appended boron–dipyrromethene function has been prepared, and its metal ion sensing properties were investigated. The designed compound exhibited pronounced Hg²⁺-selective on–off-type fluoroionophoric properties among the representative transition- and heavy-metal ions in aqueous dioxane solution. The fluorescence was efficiently quenched more than 98% with 5 equiv of Hg²⁺ ions, and the detection limit was found to be 5×10^{-6} M in a dioxane–water (1:3, v/v) solvent system. The ionophore also showed a selective chromogenic behavior toward Hg²⁺ ions by changing the color of the solution from light amber to red, which can be detected with the naked eye.

Much attention has been focused on the development of chemosensors for the selective and efficient detection of chemically and biologically important ionic species.¹ For the design of selective and sensitive sensors for the target guests, generally, conjugation of a well-established and efficient binding site with a suitable signaling moiety is the most rewarding approach.² As a signaling unit, fluorophores generally have many desirable characteristics in both sensitivity and ease of signal transduction. Among many of the fluorophores, the boron–dipyrromethene (BDP) moiety is a very attractive functional group for the construction of molecular sensors because of its high luminescence intensity and relatively longer wavelength characteristics.³ When this versatile signaling unit is utilized, a variety of compounds having selective fluoroionophoric properties toward alkali- and alkaline-earth-metal ions,⁴ heavy-metal ions,⁵ transition-

SCHEME 1^a



^a(i) 2,4-Dimethylpyrrole, (ii) *p*-chloranil, (iii) NEt₃, BF₃–OEt₂.

metal ions,⁶ monosaccharides,⁷ solution pH,^{3,8} and chiral amines⁹ have been developed. The toxic effects of Hg²⁺ ions in the environment have been well-documented, and a number of selective and sensitive sensors for the determination of Hg²⁺ ions in varying chemical systems have been continually devised.¹⁰ In this case, the design of molecules that can induce prominent spectroscopic changes upon selective binding of Hg²⁺ ions is highly desirable for ease of quantifications and signal transductions. The 8-hydroxyquinoline moiety has valuable structural characteristics of ionophores and is frequently employed as a platform for the construction of functional ionophores for the recognition of a variety of metal ions.¹¹ Here, we report the synthesis of a new ionophore having a BDP function based upon the well-established molecular framework of 8-hydroxyquinoline. The prepared ionophore exhibited highly efficient Hg²⁺-selective chromogenic and definite on–off-type fluoroionophoric switching properties in aqueous dioxane solution.

The BDP derivative was synthesized by the reaction of 8-hydroxyquinoline-2-carboxaldehyde¹² with 2,4-dimethylpyrrole (Scheme 1). The condensation product obtained from the aldehyde and pyrrole was first oxidized with *p*-chloranil, followed by neutralization with NEt₃, and subsequently treated with BF₃–OEt₂ to afford the desired BDP compound **1** (23%). The resulting compound showed a strong greenish-yellow fluorescence in common organic solvents of chloroform, THF, and dioxane.

The ionophoric properties of **1** were investigated by the fluorescence measurements. After a preliminary survey with various solvent systems, we have focused our

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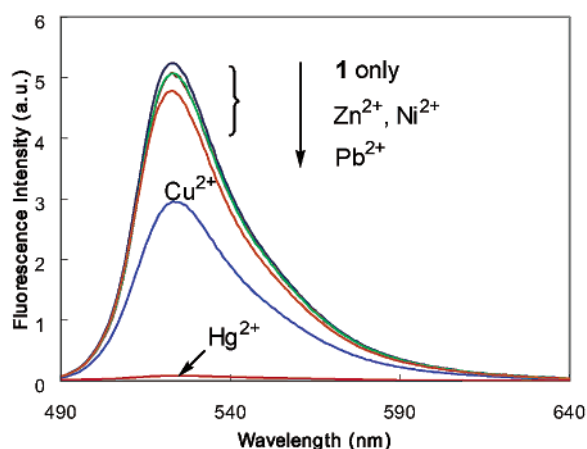


FIGURE 1. Fluorescence spectra of free **1** and **1** in the presence of 10 equiv of Zn^{2+} , Ni^{2+} , Pb^{2+} , Cu^{2+} , and Hg^{2+} ions. $[\mathbf{1}] = 5.0 \times 10^{-5}$ M in dioxane:water = 1:3, v/v.

attention on aqueous dioxane for possible applications of the present system in the metal ion analysis of biological samples.

Ionophore **1** showed an intense greenish-yellow fluorescence around 524 nm, which is typical of the BDP moiety, in aqueous dioxane solution ($\lambda_{\text{ex}} = 480$ nm, dioxane:water = 1:3, v/v). Treatment of **1** (5.0×10^{-5} M) with 10 equiv of varying metal ions (transition-metal ions of Co^{2+} , Ni^{2+} , Cu^{2+} , and Zn^{2+} and heavy-metal ions of Pb^{2+} , Cd^{2+} , and Hg^{2+} in perchlorates) resulted in diverse fluorescence behaviors (Figure 1). Especially with Hg^{2+} ions, the intense fluorescence of **1** around 524 nm was almost completely quenched. In fact, the fluorescence was highly efficiently quenched by the treatment of even less than 1 equiv of Hg^{2+} ions, and the intensity was reduced down to less than 2% of the original value in the presence of 5 equiv of Hg^{2+} ions. Over 80% of the total fluorescence quenching was effected within the concentration range of 3 equiv of Hg^{2+} ions (1.5×10^{-4} M). The quenching efficiency estimated from the ratio of the fluorescence intensity of **1** in the absence and presence of 10 equiv of Hg^{2+} ions was about 63-fold.

Among the other metal ions tested, Cu^{2+} and Pb^{2+} ions also showed some quenching effects on **1**; however, the degrees of quenching are more insignificant compared to Hg^{2+} ions and at best less than 44% and 9% in the presence of 10 equiv of Cu^{2+} and Pb^{2+} ions, respectively. The observed almost complete fluorescence quenching of **1** by Hg^{2+} ions seems to be very attractive for the design of other signaling devices of functional supramolecular systems such as on-off-type molecular switches and molecular logic gates.¹³

The stoichiometry of the **1**– Hg^{2+} complex system was determined by the changes in fluorogenic responses of **1** in the presence of varying concentrations of Hg^{2+} ions at 524 nm. Interestingly, the result obtained indicates the formation of a 1:1 complex. In the present **1**– Hg^{2+} system, the BDP unit of **1** adopts a nearly orthogonal conformation⁶ with the 8-hydroxyquinoline moiety because of the presence of methyl groups on the pyrrole

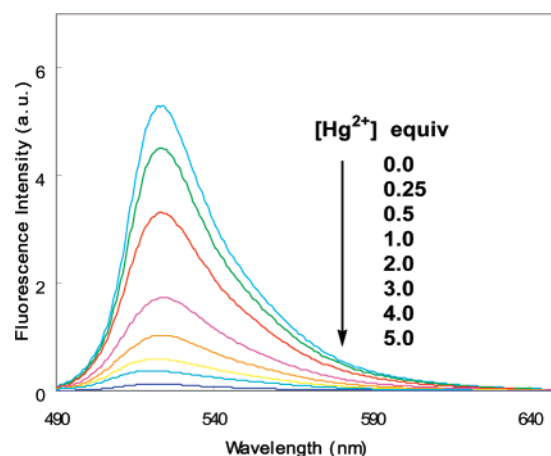


FIGURE 2. Fluorescence spectra of **1** as a function of $[\text{Hg}^{2+}]$. $[\mathbf{1}] = 5.0 \times 10^{-5}$ M in dioxane:water = 1:3, v/v.

rings, and that secures the binding site of 8-hydroxyquinoline for the accommodation of incoming guest metal ions. The molecular modeling studies with HyperChem¹⁴ also suggest that the complex formation having 1:1 (host **1**:guest Hg^{2+} ion) stoichiometry seems to be more appropriate because 2:1 stoichiometry might be unreasonable in terms of the steric requirements around the binding site for the guest metal ions.

The association constant K_{assoc} for the interaction of **1** with Hg^{2+} ions was estimated by the nonlinear curve-fitting procedure of the fluorescence titration data (Figure 2).¹⁵ The K_{assoc} values of the 1:1 complex formation for **1**– Hg^{2+} and the next responding **1**– Cu^{2+} system were found to be 7.41×10^4 and 2.42×10^3 M^{-1} , respectively. The detection limit of the ionophore **1** as a fluorogenic sensor for the analysis of Hg^{2+} ions was also determined from the plot of the fluorescence intensity as a function of the concentration of added metal ions.¹⁶ The ionophore was found to have a detection limit of 5×10^{-6} M for Hg^{2+} ions in the employed aqueous solvent system, which is sufficiently low for the detection of the submillimolar concentration range of Hg^{2+} ions in many chemical and biological systems.

To have further insight into the ionophoric behavior, we also tried to find the possibility of practical applicability of this ionophore in the analysis of biological samples by investigating the Hg^{2+} -selective response of the ionophore in the presence of background metal ions of physiologically important Na^+ (0.1 M), K^+ (0.1 M), Mg^{2+} (0.001 M), and Ca^{2+} ions (0.001 M).¹⁷ The ionophore **1** showed a selective response toward Hg^{2+} ions and was found to have an almost identical response and detection limit comparable with the results obtained in the absence of any other background metal ions.

On the basis of the above-mentioned Hg^{2+} -selective fluorogenic behavior of the ionophore **1**, we next inves-

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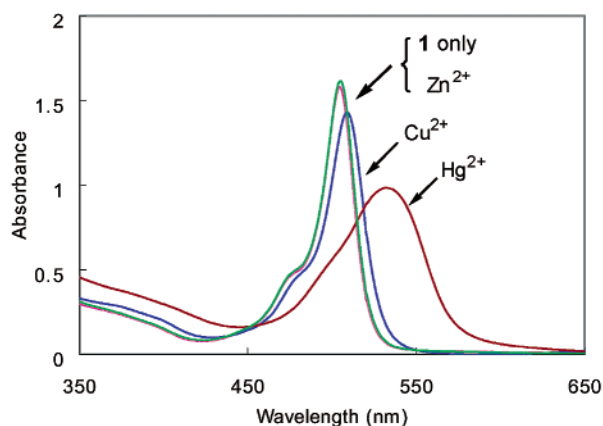


FIGURE 3. Absorption spectra of free host **1** and host **1** in the presence of 100 equiv of metal ions. $[1] = 1.0 \times 10^{-4}$ M in dioxane:water = 1:3, v/v.

tigated the chromogenic responses toward Hg^{2+} ions in the same solvent system. The ionophore **1** showed a sharp and strong absorption band around 504 nm in an aqueous solvent system (1.0×10^{-4} M, dioxane: H_2O = 1:3, v/v). Upon interaction with 100 equiv of metal ions (transition-metal ions of Co^{2+} , Ni^{2+} , Cu^{2+} , and Zn^{2+} and heavy-metal ions of Pb^{2+} , Cd^{2+} , and Hg^{2+} in perchlorate), a distinct change in the absorption spectrum of **1** was observed again exclusively for Hg^{2+} ions (Figure 3). Upon interaction with Hg^{2+} ions, the absorption band of **1** at 504 nm was bathochromic shifted to 534 nm ($\Delta\delta = 30$ nm), and the color of the solution changed from somewhat light amber of free **1** into red, which can be detected even by the naked eye.¹⁸

Among the tested metal ions, Cu^{2+} ions also induced some chromogenic behavior but to a much lesser degree than Hg^{2+} ions to yield a faint red color with only a slight bathochromic shift ($\Delta\delta = 5$ nm). Other metal ions that were employed (Ni^{2+} , Zn^{2+} , Pb^{2+} , and Cd^{2+} ions) induced negligible spectral changes, again manifesting a good chromogenic selectivity of **1** toward Hg^{2+} ions in aqueous media. The selective response toward Hg^{2+} ions was hardly affected by the competitive experiments performed in the presence of physiologically important metal ions as the background.

The high selectivity of **1** toward Hg^{2+} ions is not completely unexpected because the selective responses of Hg^{2+} by hydroxyquinoline moieties have been reported

previously. Prodi et al.^{10b} and Winkler et al.^{11c} showed that compounds containing the 8-hydroxyquinoline group displayed selective fluorescent responses to Hg^{2+} . In the present system, the selective binding of Hg^{2+} ions by the 8-hydroxyquinoline moiety was believed to be the result of efficient fluorescence quenching, by both the well-known quenching behavior of the complexed Hg^{2+} ions¹⁹ and the phenol/phenolate-dependent on-off-type quenching^{3a} of the BDP-phenol compounds.

In conclusion, we have devised a new chromo- and fluorogenic ionophore by conjugating a well-known ion-binding unit of 8-hydroxyquinoline and an efficient signaling handle of BDP. The prepared ionophore showed a selective and sensitive on-off-type fluorescence signaling behavior in addition to a significant chromogenic behavior that makes possible the "naked-eye detection" of Hg^{2+} ions in aqueous chemical and biological samples.

Experimental Section

Synthesis of BDP-Appended 8-Hydroxyquinoline 1. Into a solution of 2,4-dimethylpyrrole (0.19 g, 2.0 mmol) and 8-hydroxyquinoline-2-carboxaldehyde (0.15 g, 0.86 mmol) in N_2 -flushed dichloromethane (50 mL) was added trifluoroacetic acid (6.6 μL , 0.086 mmol). The yellow solution was stirred for 3 h at room temperature under N_2 . A solution of *p*-chloranil (0.21 g, 0.86 mmol) in dichloromethane (20 mL) was then added. After stirring for 30 min, NEt_3 (2 mL) and $\text{BF}_3 \cdot \text{OEt}_2$ (2 mL) were added until a bright-green fluorescence was observed. The solution was washed with water, and the organic phase was evaporated. The residue was purified by silica gel column chromatography (ethyl acetate-hexane, 1:10) to yield 77 mg (23%) of **1** as brown-green solids: mp 218 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 8.33 (d, 1H, $J = 8.4$ Hz), 8.03 (s, 1H), 7.60–7.54 (m, 2H), 7.44 (d, 1H, $J = 8.4$ Hz), 7.27 (d, 1H, $J = 7.2$ Hz), 6.01 (s, 2H), 2.59 and 1.21 (s, 6H each); ^{13}C NMR (CDCl_3 , 75 MHz) δ 157.0, 152.7, 152.0, 143.5, 142.9, 138.6, 131.6, 129.2, 128.0, 122.7, 121.6, 119.1, 118.1, 111.3, 14.8, 13.9. FAB MS (*m*-NBA) m/z calcd for $\text{C}_{22}\text{H}_{20}\text{BF}_2\text{N}_3\text{O}$ 391.2, found 391.0 $[\text{M}]^+$. Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{BF}_2\text{N}_3\text{O}$: C, 67.54; H, 5.15; N, 10.74. Found: C, 67.35; H, 5.27; N, 10.70.

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Supporting Information Available: Fluorogenic and chromogenic behavior of **1** and fluorescence titration spectra of **1** with Hg^{2+} ions in the presence of physiological background metal ions. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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