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Colorimetric determination of Hg^{2+} via thiosemicarbazide-to-oxadiazole transformation of a coumarin-benzopyrylium dye

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A B S T R A C T

A dual signaling reaction-based probe derived from a hybrid coumarin-benzopyrylium dye was developed for Hg^{2+} signaling. The probe exhibited selective colorimetric Hg^{2+} signaling via the Hg^{2+}-induced thiosemicarbazide-oxadiazole transformation. Interference from Cu^{2+} ions was successfully circumvented using a citrate buffer as a masking agent. The detection limit for Hg^{2+} ions was found to be 1.88×10^{-7} M. Practical application to Hg^{2+} detection in simulated wastewater was realized using a typical smartphone as a stand-alone data capture and data processing device.

Rapid acceleration of modern industrialization has inevitably resulted in the discharge of large amounts of heavy-metal-containing wastes.[1] In addition to being notoriously toxic, heavy metals are non-biodegradable, thus persisting indefinitely in ecological systems and the food chain.[2] Thus, the development of selective strategies for sensing heavy metals in chemical systems, living systems, and the environment is of immense research importance.[3] Standard instrumental methods such as atomic absorption spectroscopy,[4] inductively coupled plasma-mass spectrometry,[5] and X-ray fluorescence spectroscopy[6] are employed for the routine analysis of trace-level heavy metals. Recently, techniques such as colorimetry[7] and fluorescence spectroscopy[8] have attracted considerable research interest because they are convenient and allow facile device miniaturization, and thus, field application.

The determination of mercurial species is particularly important owing to their well-known toxic impact on the environment,[9] and a number of sophisticated optical sensors and probes have been designed.[10] The Hg^{2+}-induced ring-opening of spirocyclic systems such as rhodamines and fluoresceins is an especially successful strategy for this purpose. Consequently, a number of rhodamine-based hydrazides, hydrazones, and thiosemicarbazides with adjacent ligating groups such as phenol and thio-functionalized units have been developed as excellent Hg^{2+}-selective sensors and probes.[11] Among the many intricately designed rhodamine-hydrazide-based Hg^{2+} probes, those exploiting the conversion of thiosemicarbazide functionalities to 1,3,4-oxadiazoles are particularly noteworthy.[12] This type of transformation has been employed for the signaling of important but toxic Hg^{2+} species[13] as well as biologically important oxidants such as hypochlorous acid[14] and nitric oxide (NO)[15] using rhodamine and rhodol fluorophores.

Benzopyrylium dyes have interesting optical properties and have been used for various applications in chemical and biological fields such as laser dyes,[16] organic dye-sensitized solar cells,[17] solvatochromism,[18] and molecular imaging.[19] In particular, they have attracted research interest as near-IR-absorbing and near-IR-emitting dyes[20] for sensors[21] and red-region fluorescent markers.[22] Recently, a new type of hybrid dye based on the combination of coumarin and benzopyrylium subunits has been developed. However, there are relatively few reports on the use of these hybrid dyes for the construction of probes for chemical species. Two representative examples concern their use as probes for cysteine and homocysteine[23] and for the gasotransmitter hydrogen sulfide.[24] Other probes for detecting sulfite using selective nucleophilic addition to benzopyrylium moiety,[25] H_2O_2 by the conversion to carboxycoumarin via oxidative rearrangement (the Baeyer-Villiger reaction[26]), and hydrazine via spirocyclic ring-opening and ring-closing of rhodamine moiety by hydrazide formation have been reported.[27]

In this paper, we report a coumarin-benzopyrylium hybrid-dye-based dual-signaling probe for the selective and sensitive determination of Hg^{2+}. Signaling is realized by the Hg^{2+}-triggered

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thiosemicarbazide-to-oxadiazole transformation. Interference from coexisting Cu^{2+} is readily suppressed using a citrate buffer as a masking agent. Furthermore, the system was successfully applied to the determination of Hg^{2+} in simulated wastewater using a typical smartphone as a stand-alone signal capture and signal-processing device.

The basic platform of coumarin-benzopyrylium hybrid dye (**CB**) was prepared by the reaction of 2-(4-diethylamino-2-hydroxybenzoyl)benzoic acid with 3-acetyl-7-(diethylamino)coumarin in 42% yield according to the literature procedure (Scheme 1).[28] Treatment of **CB** with $POCl_3$ and subsequent reaction with hydrazine afforded the hydrazide derivative (**CB-hydrazide**) in 89% yield. Condensation of **CB-hydrazide** with acetyl thiocyanate yielded the desired thiosemicarbazide derivative **1** in 86% yield. The structures of compounds **CB**, **CB-hydrazide**, and **1** were characterized by ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry.

Metal-ion-signaling experiments using probe **1** were carried out based on UV–vis and fluorescence measurements. Preliminary results using acetate-buffered solutions showed that probe **1** exhibited undesirable multiple responses toward Hg^{2+}, Cu^{2+}, and Ag^{+} ions (Fig. S1, Supplementary data). To improve the metal-ion selectivity of probe **1**, we assayed standard chelating agents that provide discriminative responses toward specific metal ions over competing background metal ions. Among the masking agents tested, citrate ions were found to be effective. As shown in Fig. 1, the response of **1** toward Cu^{2+} in citrate-buffered solutions was greatly suppressed, allowing exclusive Hg^{2+} signaling to be realized. Meanwhile, solutions containing Ag^{+} became slightly turbid under these conditions, possibly due to the redox reaction with the citrate ions.[29] In citrate-buffered aqueous DMSO solution, signaling was possible under conditions containing larger than 50% water and the signal became more pronounced with increasing water content (Fig. S2, Supplementary data).

The Hg^{2+}-signaling response of **1** was not significantly affected by the presence of commonly encountered environmentally important metal ions (Fig. S3, Supplementary data). The Hg^{2+}-signaling response, expressed as the ratio of the absorbances in the presence and absence of competing metal ions at 665 nm ($A_{(\text{metal ion + Hg(II)})}/A_{\text{Hg(II)}}$), was virtually constant (Fig. 2).

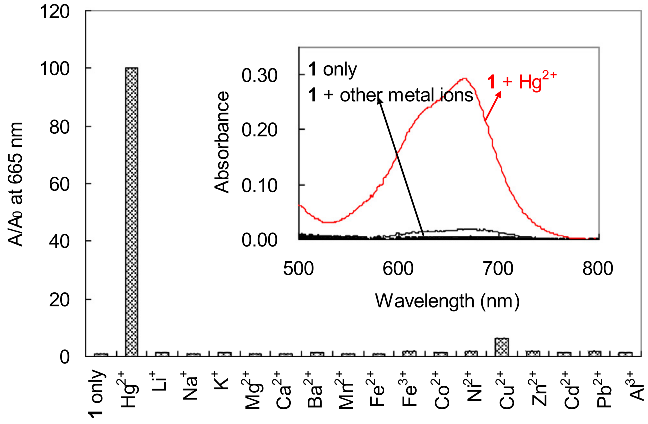


Fig. 1. Hg^{2+}-selective signaling of **1** as expressed by the absorbance ratio (A/A_o) at 665 nm. Inset: UV–vis spectra of **1** in the presence of various metal ions. [**1**] = 1.5 × 10^{-5} M, [M^{n+}] = 1.5 × 10^{-5} M in citrate buffer solution (pH = 6.0, 1.0 × 10^{-2} M) containing 10% DMSO.

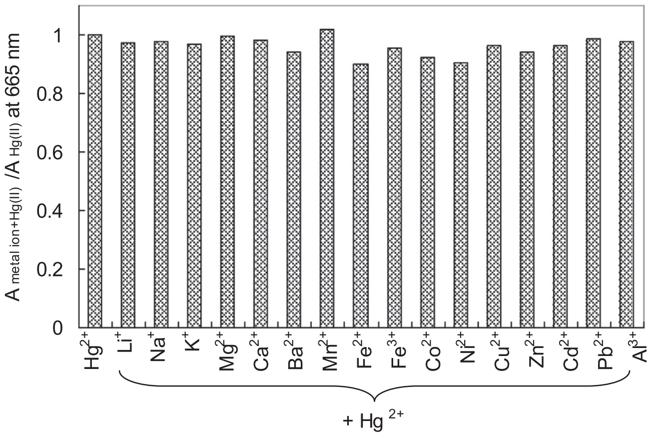
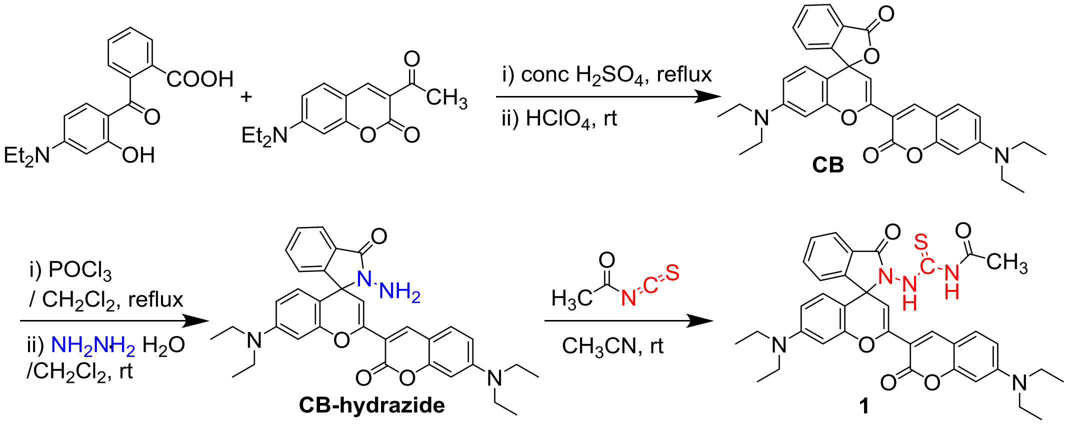


Fig. 2. Hg^{2+}-selective signaling of **1** in the presence of background metal ions as expressed by the absorbance ratio ($A_{(\text{metal ion + Hg(II)})}/A_{\text{Hg(II)}}$) at 665 nm. [**1**] = 1.5 × 10^{-5} M, [Hg^{2+}] = 1.5 × 10^{-5} M, [M^{n+}] = 7.5 × 10^{-5} M in citrate buffer solution (pH = 6.0, 1.0 × 10^{-2} M) containing 10% DMSO.

In the current study, the Hg^{2+} signaling depends on the transformation of the thiosemicarbazide moiety of **1** to the oxadiazole moiety of **2** (Scheme 2). Experimental evidence for this Hg^{2+}-induced conversion was provided by ^{1}H and ^{13}C NMR, FT-IR, and mass measurements. In the ^{1}H NMR spectrum, the resonances for the two NH protons (11.71 and 11.59 ppm) and the benzopyrylium CH proton (6.53 ppm) of **1** were replaced by resonances for a single NH proton (11.71 ppm) and a benzopyrylium CH proton (9.18 ppm) of **2** (Fig. 3). In the ^{13}C NMR spectrum, the resonances of C = S of thiosemicarbazide (183.2 ppm) and C═O of lactam (162.5 ppm) disappeared, while new carbon peaks of oxadiazole (157.9 and 159.3 ppm) emerged (Fig. S4, Supplementary data). The mass spectrum also evidenced the formation of **2** by revealing a prominent



Scheme 1. Preparation of Hg^{2+}-selective thiosemicarbazide-based probe **1**.