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A retrievable and highly selective fluorescent sensor for detecting copper and sulfide

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ABSTRACT

A new selective fluorescent sensor for Cu^{2+} and S^{2-}, 2-hydroxy-N′-((quinolin-2-yl)methylene)benzohydrazide (**HL**), based on 2-methylquinoline derivative has been designed, synthesized and evaluated. The fluorescence of the sensor **HL** was quenched by Cu^{2+} with a 1:1 binding ratio, behaving as an "on–off" type sensor even in the presence of a wide range of biological cations. Once binding with Cu^{2+}, it can display high selectivity for S^{2-}. Among the various anions, only sulfide anion induces the revival of fluorescence of **HL**, resulting in "off–on" type sensing of sulfide anion. The signal transduction occurs via reversible formation–separation of complex **L**–Cu and CuS. With the addition of Cu^{2+}, sensor **HL** give rise to a colorless to yellow color change. The resulting yellow solution switches to colorless immediately upon the addition of S^{2-}; however, no changes were observed in the presence of other anions, including CN^-, NO_3^-, $P_2O_7^{4-}$, various forms of sulfate, and some other reactive sulfur species (RSS) including SCN^-, L-methionine (L-Me) and L-cysteine (L-Cys). Notably, the color change is so distinct that the recycling process can be seen clearly by the naked eye.

1. Introduction

Developing fluorescent sensors for chemical species which can be used in biological and environmental detection is currently an attractive field for chemists [1]. Specially, heavy metal ions are earned great concern about their toxicity, because they can lead to serious environmental and health problems [1d,2]. As the third most abundant transition metal ions in the human body, Cu^{2+} shows a key point in various biological processes, and its homeostasis is critical for the metabolism and development of living organisms [3]. Among a variety of quantification techniques have been developed, fluorescent measurement have been employed the base standard for sensing Cu^{2+} because of their sensitivity and specificity, and real-time monitoring with fast response time [4]. Cu^{2+} is a typical ion that has a pronounced quenching effect on fluorophores by mechanisms inherent to the paramagnetic species [5]. More interestingly, the Cu^{2+} complex can be applied to sense other substances.

Sulfide anion can be found not only in industrial settings where it is either used as a reactant or produced as a by-product of manufacturing or industrial processes, but also due to the microbial reduction of sulfate by anaerobic bacteria or formed from the sulfur containing amino acids in meat proteins, for example, conversion into sulfur and sulfuric acid, dyes and cosmetic manufacturing, production of wood pulp, etc. [6]. Continuous and high concentration exposure of sulfide would lead to various physiological and biochemical problems. It can irritate the mucous membranes and even cause unconsciousness and respiratory paralysis [7]. Once sulfide anion is protonated, it becomes even more toxic. Thus, the detection of sulfide anion has become very important from industrial, environmental, and biological requirements [8]. A large quantity of tools for recognizing sulfide anions have been designed [9], for example, titration [10], fluorimetry [11], chemiluminescence [12], spectrophotometry [13], inductively coupled plasma atomic emission spectroscopy [14], hydride generation atomic fluorescence spectrometry [15], an electrochemical method [16], and ion chromatography [17]. Considering practicality and convenience, fluorimetry and colorimetry are acceptable. However, the development of selective fluorescent sensors for the detection of sulfide ions has attracted little interest with respect to other widely investigated anions such as fluoride [18], cyanide [19], and other forms of sulfate [20]. Utilization of metal-anion affinity has been described as another method of sensing anions [21]; however, most of them are irreversible. Among the various approaches to sensing sulfide anions, reversible sensors exploiting copper sulfide affinity [9d,21d,22] attracted our extraordinary attention. Sulfide is known to react with copper ions to make a very stable CuS form with a very low solubility product constant $K_{sp} = 6.3 \times 10^{-36}$. Recently, Nagano and Zeng groups reported new approaches for the detection of sulfide in live biological systems through the development of Cu^{2+}

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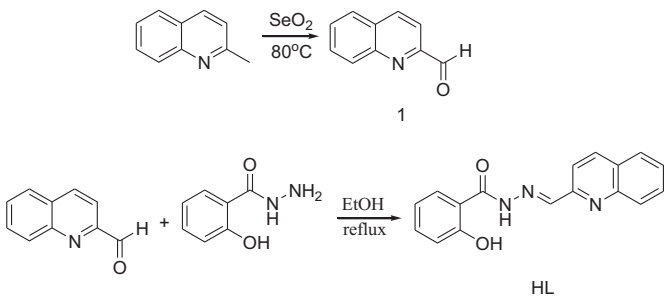

Scheme 1. Synthesis of the fluorescent sensor **HL**.

complex for chemoselective sulfide-responsive fluorescent sensors [9b,23]. The mechanism we expected is that Cu^{2+} would be dragged out from the complex when sulfide binds to copper ion, resulting in fluorescence enhancement. Consequently, the inorganic-reaction based method could be developed and created a platform for discovering new sulfide sensors that may be potentially useful for sulfide detection from industrial, environmental, and biological requirements.

On the basis of this hypothesis, we designed and synthesized a new small molecular fluorescent sensor 2-hydroxy-N′-((quinolin-2-yl)methylene)benzohydrazide (**HL**, Scheme 1) based on 2-methylquinoline derivative. Sensor **HL** demonstrates obvious fluorescence quenching after the addition of Cu^{2+}. Once interacted with Cu^{2+} to form complex **L**–Cu, the new complex showed high sensitivity and selectivity for sulfide over other possible competitive anions, meaning that the sulfide anion may react with the complex and release the sensor **HL**. The synthesis, photophysical characterization of sensor **HL** which is selective for copper ions were described, and the subsequent complex **L**–Cu displays characteristic fluorescence "off–on" behavior for sulfide. Notably, the color change of the system from colorless to yellow and then to colorless was accompanied during the whole course, which would be detected easily by the naked eye.

2. Experimental

2.1. General information and materials

All of the materials for synthesis were purchased from commercial suppliers and used without further purification. ^1H and ^{13}C NMR spectra were taken on a Varian mercury-400 spectrometer in $CDCl_3$ and d_6-DMSO solutions, with tetramethylsilane (TMS) as an internal standard. Fourier transform infrared (FTIR) spectra of the materials were conducted within the 4000–400 cm^{-1} wavenumber range using a Nicolet 360 FTIR spectrometer with the KBr pellet technique. Absorption spectra were determined on a Varian UV-Cary100 spectrophotometer. Mass spectra were obtained on a Bruker esquire 6000 and a Bruker maxis 4G respectively. X-ray diffraction patterns (XRD) were determined with Rigaku-Dmax 2400 diffractometer using Cu Kα radiation. Fluorescence spectra measurements were performed on a Hitachi F-4500 spectrofluorimeter. All pH measurements were made with METTLER TOLEDO EL20 pH meter. Quantum yields were determined by an absolute method using an integrating sphere on Edinburgh Instrument FLS920.

All of the detections of metal ions were operated in HEPES/DMSO (20 mM, pH 7.22, 1:9, v/v). The stock solution of **HL** was prepared in DMSO (10 mM). Stock solutions (10 mM) of the perchlorate salts of Na^+, K^+, Mg^{2+}, Ca^{2+}, Cu^{2+}, Al^{3+}, Hg^{2+}, Zn^{2+}, Cr^{3+}, Cd^{2+}, Ag^+, Fe^{3+}, Mn^{2+}, Co^{2+}, and Ni^{2+} were prepared in ethanol, respectively. Stock solutions (10 mM) of the chloride salt of Cu^+ were prepared in acetonitrile. Stock solutions (10 mM) of the sodium salts of F^-, Cl^-, Br^-, I^-, CO_3^{2-}, NO_2^-, NO_3^-, PO_4^{3-}, HPO_4^{2-}, $H_2PO_4^-$, $P_2O_7^{4-}$, HS^-, HSO_3^{2-}, $S_2O_3^{2-}$, $S_2O_8^{2-}$, SO_3^{2-}, S^{2-}, SO_4^{2-}, CN^- and HSO_4^- were prepared in the second distilled water. Stock solutions (10 mM) of the potassium salts of SCN^- were prepared in the second distilled water. L-Methionine (L-Me) and L-cysteine (L-Cys) were prepared in the second distilled water. The volume of cationic stock solution added was less than 100 μL to remain the concentration of **HL** unchanged. All fluorescence spectra were recorded at 25 °C with the excitation wavelength set at 410 nm.

2.2. Calculation methods

To investigate the interaction mode, we carried out density functional theory (DFT) calculations with B3LYP/6-31G (d) method. The geometry of the molecules was optimized with Gaussian 09 [24] package at the B3LYP/6-31G (d) levels for C, H, O, N atoms and LANL2DZ [25] levels for Cu.

2.3. Synthesis

2.3.1. Synthesis of quinoline-2-carbaldehyde (*1*)

2-Methylquinoline (500 mg, 3.50 mmol) was dissolved in 1,4-dioxane (30 ml), and SeO_2 (805 mg, 7.00 mmol) was added to the solution. The mixture was stirred at 80 °C for 2 h, and then cooled to ambient temperature. The precipitate was filtered off. The solvents were evaporated to give the crude product, which was purified by flash chromatography on silica gel (1:1 petroleum ether/ethyl acetate as eluent) to give **1** (401 mg, 2.56 mmol, 73%) as a yellow solid. IR (KBr disk, cm^{-1}): 1708 (C=O), 1641, 1588, 1566, 1500, 1300, 1263, 1201, 838, 751. ^1H NMR (400 MHz, $CDCl_3$): δ 10.21 (1H, S), 8.22–8.28 (4H, m), 8.99 (2H, d, J = 8.4 Hz), 7.87 (1H, d, J = 8.0 Hz), 7.80 (1H, t), 7.67 (1H, t). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 152.5, 147.9, 137.3, 130.4, 130.4, 130.0, 129.1, 127.8, 117.3. MS (ESI+): m/z 158 $(M+H)^+$.

2.3.2. Synthesis of 2-hydroxy-N′-((quinolin-2-yl)methylene)benzohydrazide (*HL*)

Quinoline-2-carbaldehyde (400 mg, 2.56 mmol) and 2-hydroxybenzohydrazide (389 mg, 2.56 mmol) were mixed in boiling ethanol with stirring for 4 h, then brown precipitates obtained were filtered off, washed with ethanol and dried over P_4O_{10} under vacuum to give **HL** (581 mg, 2.00 mmol, 78%) as an ivory white solid. IR (KBr disk, cm^{-1}): 3437, 1632 (C=O), 1545, 1500, 1457, 1427, 1315, 1231, 1150, 830, 755. ^1H NMR (400 MHz, DMSO): δ 12.12 (1H, S), 11.60 (1H, S), 8.62 (1H, S), 8.45 (1H, d, J = 8.8 Hz), 8.13 (1H, d, J = 8.8 Hz), 8.07–7.01 (2H, m), 7.88 (1H, d, J = 7.6 Hz), 7.81 (1H, t, J = 7.2 Hz), 7.65 (1H, t, J = 7.6 Hz), 7.47 (1H, t, J = 7.2 Hz), 7.02–6.97 (2H, m) (Fig. S1). ^{13}C NMR (100 MHz, DMSO): δ 164.9, 158.6, 153.6, 148.5, 147.4, 136.8, 133.9, 130.1, 128.9, 128.9, 128.0, 127.9, 127.4, 119.0, 117.5, 117.2, 116.5 (Fig. S2). MS (ESI+): m/z 292 $(M+H)^+$ (Fig. S3).

3. Results and discussion

3.1. Fluorescence detection toward Cu^{2+}

After systematically looking for selective signaling toward different metal ions for potential applications, the selectivity of **HL** to various metal ions was examined in DMSO–H_2O (9:1, v/v) solution at pH 7.22 in HEPES buffer. The sensor **HL** exhibits the emission maximum at 468 nm excited at 410 nm with quantum yield (Φ) ca. 0.097. Upon the addition of 1.0 equiv. of Cu^{2+}, a clear fluorescence quench is observed (Φ = 0.059) (Fig. 1). The quench in emission intensity may be attributed to the formation of the **L**–Cu complex. As shown in Fig. 1, all other cations have little effect on the