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Simple hydrazide-based fluorescent sensors for highly sensitive and selective optical signaling of Cu^{2+} and Hg^{2+} in aqueous solution

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ABSTRACT

Two new water-soluble hydrazide-based fluorescent probes of poly 3-{[1-(2-hydrazino-2-oxoethyl)piperidin-4-ylidene]methyl}thiophene hydrochloride (**PM1·HCl**) and poly 3-{[1-(3-hydrazino-3-oxopropyl)piperidin-4-ylidene]methyl}thiophene hydrochloride (**PM2·HCl**) have been designed and synthesized. **PM1·HCl** selectively recognizes Cu^{2+} and Hg^{2+} in aqueous solution with different emission characteristics (blue-shifted for Cu^{2+} and red-shifted for Hg^{2+}) and color changes, and the color response of the sensory materials can be tuned for detection with the naked eye. Detection limits of sensor **PM1·HCl** for Cu^{2+} and Hg^{2+} were estimated to be 2.0×10^{-10} M and 2.0×10^{-9} M, respectively. Fluorescence sensor **PM2·HCl** also showed high sensitivity toward Cu^{2+} in aqueous media, and the detection limit was measured to be as low as 2.0×10^{-10} M. Upon addition of Hg^{2+} to the **PM2·HCl** aqueous solution, no significant changes of the fluorescence spectra were observed.

1. Introduction

The design and synthesis of fluorescent chemosensors with high selectivity and sensitivity for cations have received considerable attention as cations play an important role in living systems. Of particular interest is the development of fluorescent sensors for heavy transition metal ions such as Hg^{2+} and Cu^{2+}, due to their biological and environmental importance [1]. Among the various transition metal ions, mercury and its compounds are a particular concern worldwide because of their highly poisonous character [2,3], and the maximum contaminant level of mercury was set by the United States Environmental Protection Agency (EPA) for drinking water (2 ppb, or 1×10^{-8} M) [4]. Mercury ions have high affinity for thiol groups in proteins, leading to the malfunction of cells and consequently causing many health problems in the brain, kidney, and central nervous system. Its accumulation in the body results in a wide variety of diseases, such as prenatal brain damage; serious cognitive and motion disorders; and Minamata disease [5]. Similarly, copper ions are significant environmental pollutants and copper is an essential trace element in biological systems [6]. The unregulated Cu^{2+} ions can lead to oxidative stress, and their concentration in the neuronal cytoplasm may cause the etiology of Alzheimer's or Parkinson's disease [7]. Copper ions play a critical role as catalytic cofactors for a variety of metalloenzymes, including superoxide dismutase, cytochrome coxidase and tyrosinase. Therefore, it is of utmost interest to develop highly sensitive and selective assays for both Cu^{2+} and Hg^{2+}.

Many fluorescent sensors for mercury and copper detection have been reported, but most of them are based on small molecules [8–10]. Moreover, most of them can only work in organic solvents which limit their potential application in environment and biological systems. Although heavy-metal ions are relatively easy to chelate and detect in organic solvents, they are rather difficult to recognize directly in aqueous environments due to their strong hydrations.

In the past few years, water-soluble conjugated polyelectrolytes (CPEs) are an interesting class of organic macromolecules with π-conjugated backbones and charged side chains, which combine the unique optoelectronic properties of traditional conjugated polymers with aqueous solubility and electrostatic behaviors of polyelectrolytes [11–13]. When modified hydrophilic and functional pendant substituents with fine structure to the conjugated main chain, the polymers have showed great potential applications in

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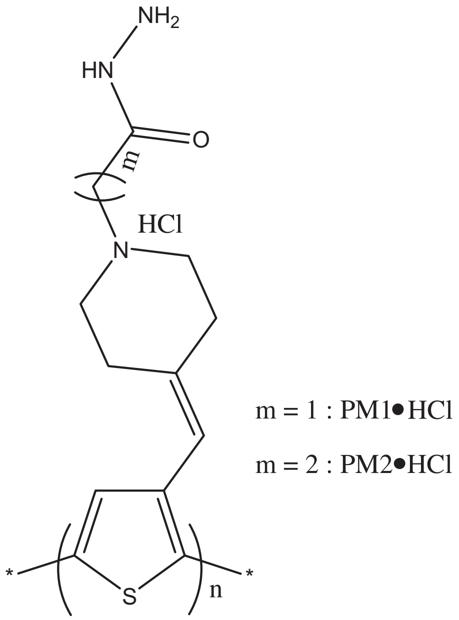

Scheme 1. Structure of **PM1·HCl** and **PM2·HCl**.

many fields [14–19]. We designed and synthesized in this work two water soluble fluorescent chemosensor poly 3-{[1-(2-hydrazino-2-oxoethyl)piperidin-4-ylidene]methyl}thiophene hydrochloride (**PM1·HCl**) and poly 3-{[1-(3-hydrazino-3-oxopropyl)piperidin-4-ylidene]methyl}thiophene hydrochloride (**PM2·HCl**) (Scheme 1) with a hydrazide and a amino hydrochloride group in the repeat unit. The hydrazide group is thought to be a good receptor due to its strong ability to coordinate with heavy and transition metal ions, and the amino hydrochloride group can offer good solubility in water. The new hydrazide based fluorescent sensor **PM1·HCl** for naked-eye detection and quantification of Cu^{2+} and Hg^{2+}, respectively, indicating the potential application of **PM1·HCl** as a highly selective and sensitive chemosensor for Hg^{2+} and Cu^{2+} in aqueous solution. To further study the properties of this class of compounds, another hydrazide-based fluorescent sensor **PM2·HCl** was designed, and the difference of the structure between **PM1·HCl** and **PM2·HCl** is very small, **PM2·HCl** than **PM1·HCl** over a methylene between hydrazide and piperidine, but there is big difference in property.

2. Experimental

2.1. Materials

Unless otherwise stated, solvents and reagents were of analytical grade from commercial suppliers and were used without further purification. The solutions of cations were prepared from their chloride or nitrate salts. 4-(thiophen-3-ylmethylidene)piperidine (compound **1**) was prepared as reported previously [20]. Double distilled water was used throughout the experiment.

2.2. Measurements

UV–vis spectra was recorded on a Shimadzu 3100 spectrometer absorption and fluorescence measurements were carried out on a Edinburgh Instruments Ltd. FLS920 fluorescence spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV III 400 MHz NMR spectrometer. Fluorescence spectra of **PM1·HCl** and **PM2·HCl** were measured at an excitation wavelength of 397 nm and 410 nm. FT-IR of the polymer (films) was carried out on KBr disks using a Perkin Elmer 1750 or Spectrum One spectrophotometer. The gel permeation chromatography (GPC) measurements were performed with a Waters 2410 refractive-index detector at 35 °C, and THF was used as eluent at a flow rate of 1.0 ml/min. Photographs of the polymer solutions were taken using a Canon EOS 400D digital camera under a hand-held UV-lamp with λ_{max} = 365 nm. The fluorescence quantum yields of the polymers were determined in aqueous solution using quinine sulfate ($\sim 1 \times 10^{-5}$ M solution in 1.0 M H_2SO_4, having Φ_F of 54.6%) as the standard by excitation at 397 and 410 nm, respectively [21].

2.3. Sample preparation

All tests described in this paper were carried out at room temperature, in deionized water. In the titration experiments all the cations being added to the **PM1·HCl** and **PM2·HCl** solution were prepared from their chloride and nitrate salts, and the concentration of the salts solution used in the titration with various anions were all 0.01 mM. The concentration of **PM1·HCl** and **PM2·HCl** for both colorimetric and fluorometric experiments were 0.1 mM.

2.4. Synthesis of methyl [4-(thiophen-3-ylmethylidene)piperidin-1-yl]acetate (compound **2**)

Compound **1** (4.0 g, 22.3 mmol) and $NaHCO_3$ (5.62 g, 66.9 mmol) were mixed in acetonitrile (80 ml), the mixture was stirred for 30 min, and then methyl chloroacetate (2.71 g, 24.5 mmol) was added dropwise. The mixture was stirred at room temperature for 12 h. After the reaction was over, the solvent was evaporated under vacuum and then 50 ml of water was added to the residue. The aqueous solution was extracted with $CHCl_3$ (3 × 40 ml). The extract was dried over $MgSO_4$. After removal of the solvent the crude product was purified by chromatography on silica gel eluting with a mixture of ethyl acetate and *n*-hexane (3:1, v/v) (4.7 g, Yield: 85%). ^{1}H NMR ($CDCl_3$, ppm, δ): 7.23 (m, 1H), 7.0 (s, 1H), 6.98 (d, 1H), 6.17 (s, 1H), 3.69 (s, 3H), 3.22 (s, 2H), 2.55 (m, 2H), 2.40 (t, 2H). FTIR (KBr, cm^{-1}): 1731 (C=O), 1640 (C=C), 1141 (C—O—C).

2.5. Synthesis of 2-[4-(thiophen-3-ylmethylidene)piperidin-1-yl]acetohydrazide (compound **3**)

Compound **2** (3.6 g, 14.3 mmol) and hydrazine monohydrate (4.58 g, 143 mmol) were dissolved in ethanol (25 ml). The mixture was stirred at room temperature for 5 h. The solvent was evaporated under vacuum and the crude product was purified by chromatography on silica gel eluting with a mixture of ethanol and triethylamine (4:1, v/v) (2.8 g, Yield: 78%) [22]. ^{1}H NMR ($CDCl_3$, ppm, δ): 8.36 (s, 1H), 7.20 (m, 1H), 6.96 (s, 1H), 6.93 (d, 1H), 6.14 (s, 1H), 3.10 (s, 2H), 2.52 (m, 2H), 2.31 (t, 2H), 1.99 (d, 2H). ^{13}C NMR ($CDCl_3$, ppm, δ): 29.37, 31.46, 36.12, 53.45, 118.72, 122.28, 125.15, 128.62, 138.11, 147.21, 172.98. FTIR (KBr, cm^{-1}): 3104 (NH), 1728 (C=O), 1676 (C=C).

2.6. Synthesis of poly 3-{[1-(2-hydrazino-2-oxoethyl)piperidin-4-ylidene]methyl}thiophene (**PM1**)

Anhydrous ferric chloride (0.97 g, 5.95 mmol) was suspended in 30 ml dry chloroform and stirred for 30 min under the atmosphere of nitrogen, and then the compound **3** (0.30 g, 1.19 mmol) dissolved in dry chloroform (15 ml) was added dropwise. The mixture was stirred at 0 °C for 24 h. Treatment of the reaction mixture with methanol (10 ml) resulted in the precipitation of the polymer and then filtered. The filter cake and 30 ml ammonia water were mixed in 50 ml chloroform and stirred overnight, and then the organic