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A naphthalene-quinoline based chemosensor for fluorescent "turn-on" and absorbance-ratiometric detection of Al^{3+} and its application in cells imaging

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ABSTRACT

A new naphthalene-quinoline based chemosensor **L** was prepared and structurally characterized. **L** exhibited excellent selectivity and sensitivity to Al^{3+} through distinct fluorescence enhancement (335-fold) and ratiometric detection in DMF/H_2O (v/v, 1/9) based on the combined mechanisms of ESIPT and CHEF. The recognizing behavior of **L** toward Al^{3+} had been investigated in detail through Job's Plot, FT-IR, HNMR, and HRMS analysis. The limit of detection (LOD) for Al^{3+} was as low as and 3.67×10^{-8} M. **L** was successfully applied in real sample detection and construction of molecular logic gate. Moreover, **L** was verified to be of low cytotoxicity and good imaging characteristics for the detection of Al^{3+} in cells HSC.

1. Introduction

Aluminum, the third most abundant metal in the earth's crust (approximately 8% of total mineral components) [1–4], is closely related to people's lives due to its widely use in food additives, cooking utensils, paper and packing materials, textile, clinical drugs and water treatment [5–7]. However, as non-essential element for human, accumulation of excessive amount of Al^{3+} can cause a number of diseases such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, anemia, liver damages and hemochromatosis [8–11]. Furthermore, high concentration of Al^{3+} can hamper plant growth and kill fish in aquatic ecosystems [12,13]. According to the recommendation of world health organization (WHO), average human intake capacity of aluminum is 3–10 mg/day and the permitted level of Al^{3+} in drinking water is 7.4 μM [14]. Thus, the design of chemosensors for detecting Al^{3+} in aqueous medium is of great significance.

Over the past few decades, many modern techniques were employed for the detection of Al^{3+}, such as classical atomic absorption spectrometry, inductively coupled plasma mass spectroscopy, electrochemical methods, hydride generation-atomic, neutron activation analysis and ion chromatography [15–18]. Compared with those detection methods mentioned above, fluorescence detection method has drawn special attention of the researchers attribute to its simple and convenient operation, high selectivity and sensitivity, rapidity, non-destructive and naked-eye recognition [12,19–22]. However, it is still difficult to design a sensitive and selective fluorescent chemosensor for Al^{3+} due to its drawbacks such as lack of spectroscopic characteristics, poor coordination and strong hydration ability [23]. Moreover, compared with the intensity-based probes [12,24–28], ratiometric sensing of an analyte is gaining more and more attention because the ratio of two intensities of absorption or emission wavelength reduces the error (s) which could have been arising from the physical and chemical method. A number of ratiometric Al^{3+} sensors based on various fluorophores and sensing mechanisms have been developed [29–36], but some of them still suffer from the shortcomings such as complicated synthesis, insolubility in water, or interfered by other trivalent metal ion such as Fe^{3+} and Cr^{3+} and lack practical applicability in real samples. Moreover, to our best knowledge, there were few papers concerning the fluorogenic and ratiometric absorbance chemosensor for Al^{3+} based on naphthalene-quinoline [33]. In order to extend our research on the development of Al^{3+} chemosensor [37–39], as show in Scheme 1, we designed and synthesized a novel naphthalene-quinoline chemosensor L. **L** showed excellent selectivity and sensitivity to Al^{3+} through fluorescence enhancement (335-fold) and ratiometric absorption detection in DMF/H_2O (v/v, 1/9). Furthermore, the chemosensor **L** was successfully applied in detection of Al^{3+} in real water samples and the fluorescence signal of chemosensor **L** could be

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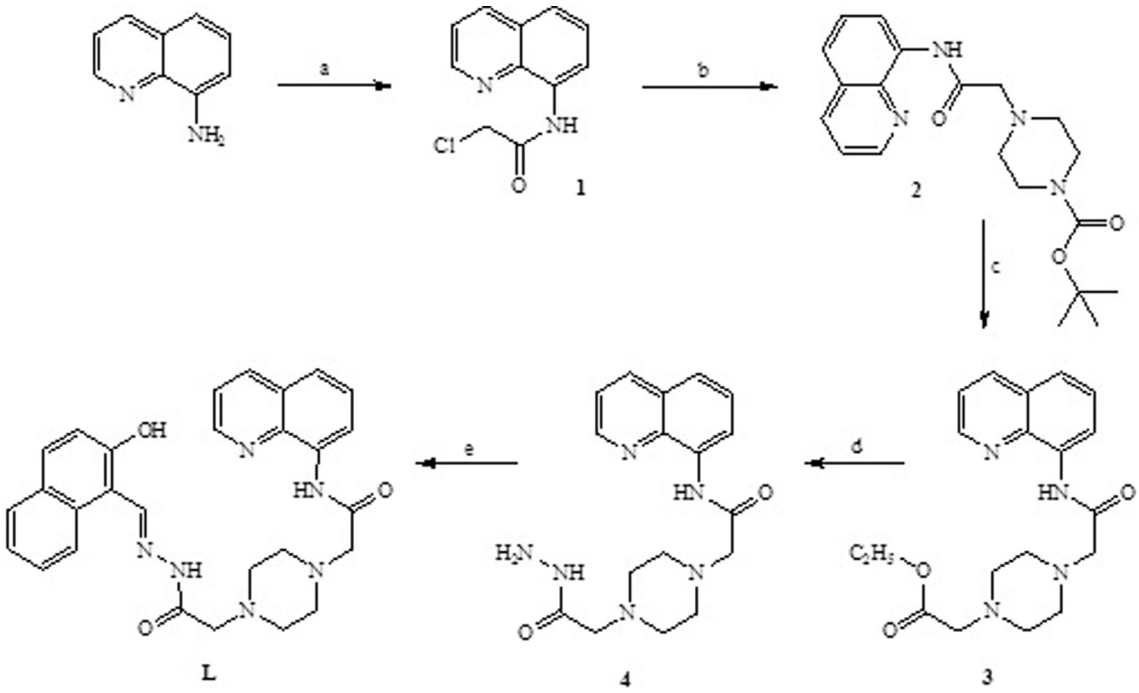

Scheme 1. Synthesis of sensor L. Reagents and conditions: (a) dichloromethane, chloracetyl chloride, triethylamine, reflux; (b) 1-boc-piperazine, K_2CO_3, acetonitrile, reflux; (c) acetonitrile, K_2CO_3, HCl, Ethyl bromoacetate, reflux; (d) hydrazine hydrate, CH_3OH, reflux; (e) CH_3OH, 2-Hydroxy-1-naphthaldehyde, reflux.

used in the construction of molecular logic gate. We also found that the application of **L** for the imaging of Al^{3+} in human stromal cell (HSC) by fluorescence changes was also achieved.

2. Experimental

2.1. Materials and Instruments

Unless otherwise specified, all the solvents and reagents (analytical or spectroscopic grade) were obtained commercially and used without further purification. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruck AV-600 spectrometer. Chemical shifts (δ) are reported in ppm, relative to TMS (tetramethylsilane) and using DMSO d_6 as the solvent. UV–vis spectroscopy measurements were acquired on a Pgeneral TU-1901 and absorption spectra were recorded at 25 °C. Fluorescence measurements were measured on a Perkin Elmer LS55 fluorescence spectrometer. Mass spectra were measured on a Waters Xevo UPLC/G2-SQ Tof MS spectrometer. The melting point was measured on a Beijing XT4-100X microscopic melting point apparatus. The pH measurements were made with a model PHS-3C meter (Shanghai, China). Cell image were collected using laser confocal microscope (Leica, TCS SP2 AOBS).

2.2. Synthesis

The intermediate compounds **1–4** were prepared according to the reported procedure [39–41].

2.2.1. Synthesis of Intermediate Compound *1*

In a 100 mL round bottom flask equipped with dichloromethane (10 mL), 8-aminoquinoline (580 mg, 4 mmol) and TEA (0.3 mL) were added successively. Chloroacetyl chloride (0.15 mL) dissolved in dichloromethane (10 mL) was slowly added to a round bottom flask with a dropping funnel. The solution was stirred at room temperature for 24 h. After the complete consumption of the starting material monitored using TLC, the mixture was extracted with hydrochloric acid (1 M, 20 mL) three times. The dichloromethane layers were dried with anhydrous sodium sulfate and evaporated under vacuum. The crude product was purified by column chromatography on silica gel using dichloromethane as eluent to get white needle-like solid **1** (600 mg, yield: 68.1%); m.p.:148–149 °C. ^{1}H NMR (600 MHz, DMSO d_6) δ (ppm) 10.71 (s, 1H), 9.00–8.93 (m, 1H), 8.65 (d, J = 7.7 Hz, 1H), 8.45 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.68 (dd, J = 8.2, 4.2 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 4.63 (s, 2H).

2.2.2. Synthesis of Intermediate Compound *2*

The 1-boc-piperazine (450 mg, 2.4 mmol) and K_2CO_3 (500 mg, 3.6 mmol) were added to a stirred solution of compound **1** (440 mg, 2 mmol) in acetonitrile (30 mL) and refluxed for 6 h. After the complete consumption of the starting material monitored using TLC, the reaction mixture was allowed to room temperature and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using MeOH/CH_2Cl_2 (v/v, 1/20) to get white solid **2** (520 mg, yield: 70.2%); m.p.:165–166 °C. ^{1}H NMR (600 MHz, DMSO d_6) δ (ppm) 11.30 (s, 1H), 8.97–8.90 (m, 1H), 8.63 (d, J = 7.6 Hz, 1H), 8.39 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.2 Hz, 1H), 7.62 (dd, J = 8.2, 4.2 Hz, 1H), 7.57 (t, J = 7.9 Hz, 1H), 3.48 (s, 4H), 3.27 (s, 2H), 2.54 (m, 4H), 1.40 (s, 9H).

2.2.3. Synthesis of Intermediate Compound 3

The compound **2** (550 mg, 1.5 mmol) and hydrochloric acid (1 M, 3 mL) were dissolved in acetonitrile (20 mL), and the reaction mixture was allowed to reflux for 2 h. After cooling to the room temperature, ethyl bromoacetate (250 mg, 1.5 mmol) and K_2CO_3 (1.38 g, 10 mmol) were directly added to the mixture and refluxed for 5 h. The reaction mixture was cooled and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using MeOH/CH_2Cl_2 (v/v, 1/30) to get compound **3** as yellow oil liquid (336 mg, yield: 63%). ^{1}H NMR (600 MHz, DMSO d_6) δ (ppm) 11.36 (s, 1H), 8.95 (dd, J = 4.2, 1.6 Hz, 1H), 8.65 (dd, J = 7.6, 1.2 Hz, 1H), 8.41 (dd, J = 8.3, 1.6 Hz, 1H), 7.68–7.64 (m, 2H), 7.59 (t, J = 7.9 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.31 (s, 2H), 3.26 (s, 2H), 2.72 (s, 4H), 2.63 (s, 4H), 1.23 (t, J = 7.1 Hz, 3H).

2.2.4. Synthesis of Intermediate Compound *4*

The compound **3** (180 mg, 0.5 mmol) and hydrazine hydrate (100 mg, 2 mmol) were dissolved in methanol (20 mL). Then the