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An AIRE active Schiff base bearing coumarin and pyrrole unit: Cu^{2+} detection in either solution or aggregation states

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ABSTRACT

A new fluorescent molecular probe **1**, derived from 3-(1-aminoiminethyl)-4-hydroxycoumarine and 2-formyl-3,5-dimethyl-1*H*-pyrrole by a simple Schiff base condensation, was designed, synthesised and accurately characterized. The aggregation induced ratiometric emission (AIRE) active probe **1** showed selective interaction with Cu^{2+} in both 1:1 and 9:1 H_2O/DMSO solutions (v:v, buffered by 10 mM HEPES at pH = 7.4). However, the sensing mechanism was found to be different in each media. In H_2O/DMSO 1:1 solution, **1** exhibited a coumarin emission at 525 nm and the addition of Cu^{2+} results in a coordination complex under strong Photoinduced Electron Transfer (PET) process. Conversely, TEM studies revealed that probe **1** organizes itself as mono disperse aggregates in H_2O/DMSO 9:1 solution with the emission at 585 nm, and further disassembly of aggregates was induced by the addition of Cu^{2+}, accomplishing with the fluorescence quenching. The application of the fluorescent sensor in monitoring intracellular Cu^{2+} in HeLa cells was also demonstrated.

1. Introduction

The design and development of selective optical chemosensors for biological important cations has gained considerable attention [1]. Among them, fluorescent sensors for the detection and measurement of Cu^{2+} ions are actively investigated, as this metal ion is a significant environmental pollutant and an essential trace element in biological systems [2,3].

To date, a sizable number of fluorescent chemosensors for Cu^{2+} have been developed based on quinoline [4], coumarin [5,6], dansyl amide [7], naphthalimide [8,9], fluorescein [10], rhodamine [11–18] and other fluorophores [19,20]. However, some of the probes suffer from several limits, such as the poor water solubility, poor fluorescence intensity, poor selectivity and/or sensitivity, long response time and high costs [21,22]. More importantly, fluorescent probes capable of detection for Cu^{2+} in both aqueous and organic systems are very scarce [23], although this characteristic allows extending the application of an analytical method to different matrix systems without the need of sample pre-treatment, leading to easy handling and reducing the number of possible random and systematic errors [24]. Works related to this area are of great challenge.

Recently, luminogens with the feature of aggregation-induced emission (AIE) or aggregation-induced emission enhancement (AIEE) have attracted considerable interest in luminescent materials [25]. Luminogens with AIE/AIEE attributes show little or no emission in dilute solutions but emit intensely when aggregated [26–28]. Based on AIE/AIEE fluorescent signals, chemosensors have been employed for Cu^{2+} detection in water sufficent or pure aqueous solution [23,29,30]. Unfortunately, few of them display aggregation induced ratiometric emission (AIRE), which is highly desired to facilitate the practical applications of AIE-based sensors in different fields [31].

On the other hand, Schiff bases require simple synthesis steps and are applied to numerous optical sensors [32,33] and in AIE applications [27,28]. Noticeably, pyrrole containing Schiff bases generally show higher affinity with Cu^{2+} than with other metal ions [8,22,32,33]. Furthermore, coumarin is often selected as a signaling moiety due to its high quantum yield, large stokes shift and

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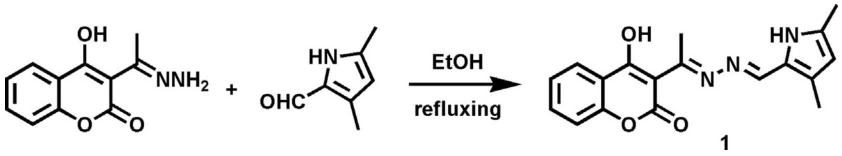

Scheme 1. Synthesis route of the sensor **1**.

low cytotoxicity [5]. Herein, we conjugate pyrrole and coumarin moieties to fabricate a Schiff base **1** (Scheme 1), which did exhibit special AIRE effect via stoke shift from green to orange emissions upon adding water. Surprisingly, both emissions are quenched specifically and significantly by Cu^{2+}; thus, a highly efficient fluorescent chemosensor for Cu^{2+} in both solution and aggregation states is easily established. In addition, the as-synthesised fluorescent probe is applicable to imaging Cu^{2+} in live cells.

2. Experimental section

2.1. Materials and instrumentation

Solvents and starting materials for synthesis were purchased commercially and used as received. Elemental analyses were carried out on an Elemental Vario EL analyzer. ^1H NMR and ^{13}C NMR spectra are recorded on a Bruker AV400 NMR spectrometer in DMSO-d_6 solution. The IR spectra were determined by the KBr pressed disc method on a Bruker V70 FT-IR spectrophotometer. The UV spectra were recorded on a Purkinje General TU-1800 spectrophotometer. Fluorescence spectra were determined on a Varian CARY Eclipse spectrophotometer. ESI–MS spectra were obtained on a Bruker Daltonics Esquire 6000 mass spectrometer. The microstructure was obtained by transmission electron microscope (TEM) on JEOL, JEM-2010F (200 kV). Dynamic light scattering (DLS) experiments were constructed with a HORIBA SZ–100 nano particle analyzer. Fluorescent images were taken on Zeiss Leica inverted epifluorescence/reflectance laser scanning confocal microscope.

2.2. Synthesis of **1**

A quantity of 3-(1-aminoiminethyl)-4-hydroxycoumarine (218 mg, 1 mmol) [34] was added to an EtOH solution (10 mL) containing 2-formyl-3,5-dimethyl-1H-pyrrole (123 mg, 1 mmol). The mixture was refluxed for 3 h with two drops of acetic acid. After cooling to room temperature, the separated solid was filtered, washed with EtOH, and then dried in air. Yield 75%. Anal. Calc. for $C_{18}H_{17}N_3O_3$: C, 66.86; H, 5.30; N, 13.00. Found: C, 66.68; H, 5.48; N, 12.88%. IR (cm^{-1}): 3233, 3160, 1680, 1611, 1562. ^1H NMR (400 MHz, DMSO-d_6), δ (ppm): 16.36 (s, 1H, OH), 11.22 (s, 1H, NH), 8.41 (s, 1H, CH=N), 7.96–7.98 (m, 1H, Ar-H), 7.62–7.67 (m, 1H, Ar-H), 7.27–7.34 (m, 2H, Ar-H), 5.83 (s, 1H, $CH_{pyrrole}$), 2.93 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.19 (s, 3H, CH_3). ^{13}C NMR (400 MHz, DMSO-d_6), δ (ppm): 179.58, 168.78, 161.91, 153.57, 145.90, 136.58, 134.44, 130.07, 125.94, 124.18, 122.22, 120.41, 116.73, 111.73, 95.36, 11.73, 13.35, 11.46. ESI–MS: $m/z = 324.1235$ for $[M+H]^+$ (Calc. 324.13).

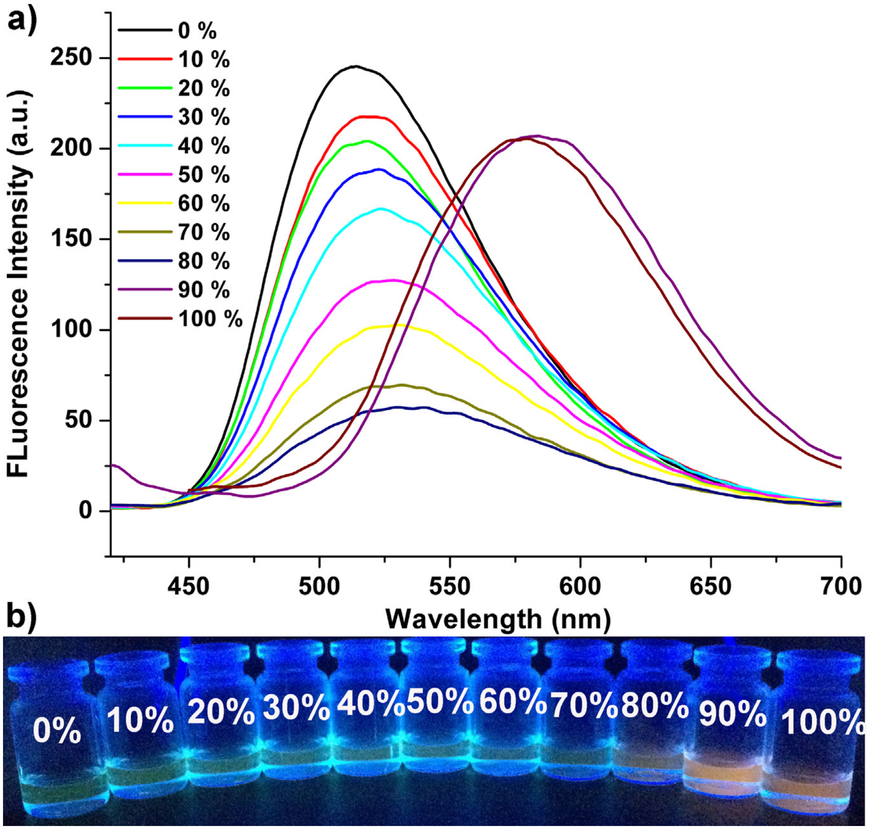

Fig. 1. Fluorescence spectra of **1** (10 μmol L^{-1}) in H_2O/DMSO mixtures with different water fractions, excitation wavelength was 400 nm. Inset: The corresponding fluorescence images of **1** solutions under 365 nm UV lamp.