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Acridine-based complex as amino acid anion fluorescent sensor in aqueous solution

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ABSTRACT

Novel acridine-based fluorescence sensors containing alaninol ligands, L1 and D1, were designed and synthesized. The structure of the compound was characterized by IR, ^{1}H NMR, ^{13}C NMR, MS spectra. L1 and D1 possess efficient Cu^{2+} cation ON–OFF selective signaling behavior based on ligand-to-metal binding mechanism at physiological pH condition. Additionally, the L1–Cu(II) and D1–Cu(II) complexes could further serve as reversible OFF–ON signaling sensing ensemble to allow ratiometric response to amino acid anion in aqueous solution.

1. Introduction

As the third abundant trace element in human body, copper plays an important role in the human body and is critical to a variety of physiological processes in living systems such as a critical role as a catalytic cofactor for metalloenzymes, including dismutase, tyrosinase and cytochrome superoxide oxidase. Due to the importance of Cu^{2+} cation, rapid and sensitive recognition of Cu^{2+} cation is of great significance [1]. Amino acids, the basic units of proteins, play a central role in the metabolic processes of living systems. So, the development of amino acid analysis in nutritional analysis [2], and the diagnosis of Alzheimer disease [3] and pancreatitis [4] are of great importance. A number of amino acid analysis methods were performed such as spectroscopic assays [5] or electrochemical [6]. Meanwhile, compared to these traditional techniques, fluorescence for detection of amino acid has received increasing interest due to their high sensitivity, feasibility, and capability of visual detection, etc. [7]. Many efforts have been made to develop artificial fluorescence sensors that recognize amino acid. However, most of these artificial fluorescence sensors have suffered from low sensitivity and selectivity toward amino acids in aqueous solution. Thus, the development of synthetic fluorescence sensors for the recognition of amino acids is highly desirable in aqueous media [8–10]. In this regard, metal–ligand sensors that have a stronger affinity for guest in competitive water are widely used in designing sensors within the past decade [11–15]. To the best of our knowledge, "turn-on" fluorescence sensor that sensitively and selectively detection amino acid anions in aqueous solvents by metal-containing receptors is very scarce [16–18]. This work focus on the synthesis and selective fluorescence recognize of Cu^{2+} cation and its application in discrimination and recognition of amino acids in aqueous solution.

2. Experimental section

2.1. Materials

Optical rotation was taken on a Perkin Elmer Model 341 polarimeter. The IR spectra were performed on a Nicolet 670 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer. Mass spectra were determined by ESI recorded on an Esquire 3000 LC–MS mass instrument. Fluorescence spectra were obtained with an F-7000 FL Spectrophotometer. Purifications by column chromatography were carried out over silica gel (230–400 mesh). The reagents were used of commercial origin without further purification. The anions were used as their tetrabutylammonium salts. 4,5-Bis(bromomethyl)acridine was prepared according to the literature methods [19,20].

2.2. Syntheses

2.2.1. General procedure for the preparation of compounds L1 and D1

4,5-Bis(bromomethyl)acridine (0.37 g, 1.0 mmol) was mixed with potassium carbonate (2.2 mmol) and L- or D-alaninol (2.2 mmol) in 15 mL of acetonitrile. The mixture was then stirred at room temperature overnight and monitored via TLC. The reaction mixture was concentrated under reduced pressure and then it was poured into a separatory funnel over water and extracted with dichloromethane. The combined

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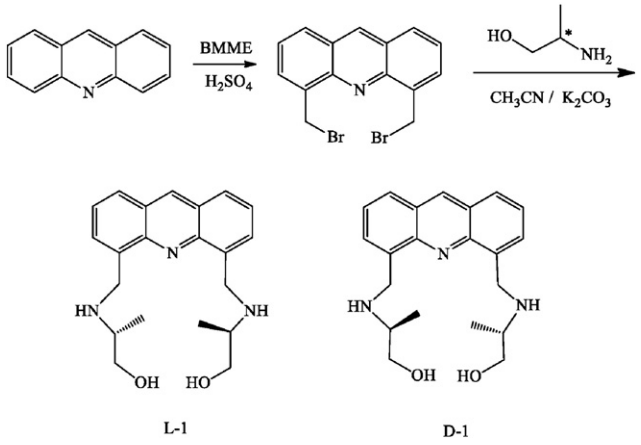

Scheme 1. Synthesis of compounds L1 and D1.

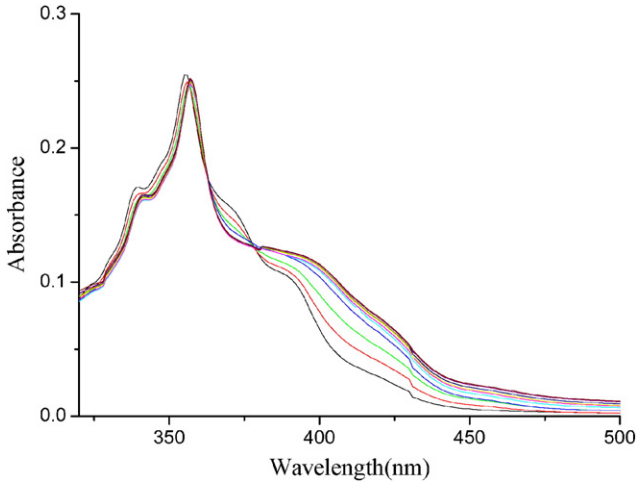

Fig. 1. UV–vis spectra of sensor L1 (3.0×10^{-5} M) upon the addition of Cu^{2+} in HEPES (pH = 7.4). Equivalents o f Cu^{2+}: 0 → 1.0.

organic extracts were rinsed with brine, dried over anhydrous Na_2SO_4. The solution was loaded on a silica gel chromatography and was eluted with dichloromethane/ethanol (5/1) solvent mixture. The product compound was collected from the column. L1**:** 0.24 g, yield, 69%. $[\alpha]_D^{20} = -9.6$ ($c = 0.10$, $CHCl_3$); D1: 0.25 g, yield, 72%, $[\alpha]_D^{20} = +10.1$ ($c = 0.10$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.77 (s, 1H), 7.93(d, $J = 8.0$ Hz, 2H), 7.69(d, $J = 4.0$ Hz, 2H), 7.49–7.45(m, 2H), 4.53(d, $J = 12$ Hz, 2H), 4.43(d, $J = 12$ Hz, 2H), 3.86(d, $J = 12$ Hz, 2H), 3.42(d, $J = 12$ Hz, 2H), 2.84–2.81(m, 2H), 1.27 (s, 2H), 1.10(d, $J = 4.0$ Hz, 6H); ^{13}C NMR ($CDCl_3$): 146.81, 137.02, 136.94, 130.43, 128.04, 126.75, 125.58, 65.06, 54.46, 49.27, 16.43, IR (KBr): 3426, 2926, 1624, 1448, 1380, 1055, 764 cm^{-1}; HRMS m/z: calculated for $C_{21}H_{27}N_3O_2$, $[M + H]^+$ 354.2182, found 354.2177 (Scheme 1).

3. Results and discussion

3.1. UV–vis spectroscopic studies on L1

Fig. 1 showed the UV–vis spectral changes upon addition of Cu^{2+} cation in aqueous solution (0.01 M HEPES, pH = 7.4). Initially, the absorption spectrum of L1 exhibited a characteristic absorption peak of acridine at 356 nm. Within creasing amounts of Cr^{3+} (0–1 equiv.), the main absorption band keeps unchanged, whereas a clear isosbestic point at around 400 was observed. Furthermore, the changes of these absorption peaks were likely due to the coordination of L1 with Cu^{2+} cation [21].

3.2. Fluorescence spectroscopic studies on L1

In order to further evaluate the sensing property of the sensor L1 toward Cu^{2+} cation, fluorescence titration experiment of L1 (3.0×10^{-5} M) with Cu^{2+} cation by using 0–1.0 equiv. in 10 mM HEPES buffer solutions (pH 7.4) was carried out. As shown in Fig. 2a, L1 exhibited strong fluorescence emission at 430 nm. Upon incremental addition of Cu^{2+} cation, the fluorescence emission was gradually decreased. The Fig. 2b showed the dependence of the emission intensity at 430 nm on the Cu^{2+} cation concentration. As a result, L1 exhibited an efficient fluorescence response. The graphs from non-linear curve fitting for L1 interactions with Cu^{2+} cation indicated that the stoichiometry between the sensor L1 and Cu^{2+} cation was 1:1. The association constant (K) was calculated to be 9.2×10^{-4} L mol^{-1} [24,25]. The stoichiometry was also determined by Job's plot method. Fig. 3 indicated that the sensor L1 and Cu^{2+} cation formed of a 1:1 complex in aqueous solution.

In order to investigate the recognition ability of the sensor, the effect of various metal ions such as Li^+, Na^+, K^+, Mg^{2+}, Cu^{2+}, Co^{2+}, Mn^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Al^{3+}, Cr^{3+}, Fe^{3+}, and Eu^{3+} on the fluorescence response were tested in aqueous solution (0.01 M HEPES, pH = 7.4). As shown in Fig. 4, compared to other metal ions that have minimal effects on the fluorescence intensity, Cu^{2+} cation could almost completely quenched the fluorescence of L1 at 430 nm. L1 possesses an efficient Cu^{2+} cation ON–OFF selective signaling behavior at physiological pH condition, which can be used as the selective detection of Cu^{2+} cation by typical ligand-to-metal binding process [22,23].

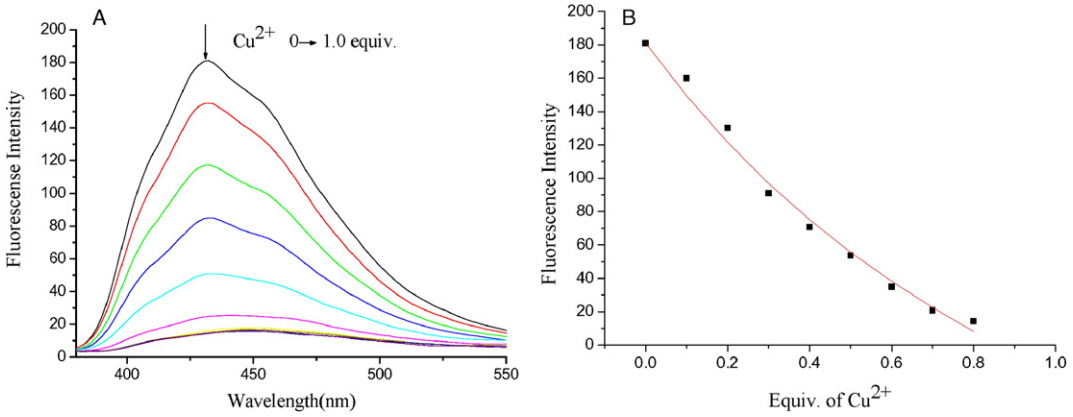

Fig. 2. (a): Fluorescence spectra of sensor L1 (3.0×10^{-5} M) with Cu^{2+} in HEPES (pH = 7.4). Equivalents of anion: 0 → 1.0. $\lambda_{ex} = 356$ nm (EX: 5; EM: 5). (b): changes in the fluorescence intensity of L1 at 430 nm upon addition of Cu^{2+}. The line shown is a line-fitted curve. The correlation coefficient (R) of the non-linear curve fitting is 0.9949.