Inorganic Chemistry Communications 39 (2014) 61–65

Contents lists available at ScienceDirect

Inorganic Chemistry Communications

journal homepage: www.elsevier.com/locate/inoche

An anthracene-based fluorescent sensor for sequential detection of zinc and copper ions

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ARTICLE INFO

Article history:
Received 17 September 2013
Accepted 30 October 2013
Available online 7 November 2013

Keywords:
Anthracene
Fluorescence
Zinc ion
Copper ion
Metal displacement

ABSTRACT

Sequential recognition of Zn^{2+} and Cu^{2+} by a new anthracene-containing dipyridylamine-based receptor **1** (*N*-((anthracen-9-yl)methyl)-*N*-(pyridin-2-yl)pyridin-2-amine) has been achieved. Receptor **1** exhibited highly selective and sensitive fluorescence "off–on" recognition property to Zn^{2+} with a 1:1 binding stoichiometry. The resulting **1**-Zn^{2+} complex displayed high selectivity to Cu^{2+} through the decrease in fluorescence intensity, demonstrating that **1**-Zn^{2+} could detect Cu^{2+} via metal displacement. The sequential recognition of Zn^{2+} and Cu^{2+} via metal exchange suggests that receptor **1** has a potential utility for Zn^{2+} and Cu^{2+} detection.

Fluorescent probes for metal ions have found widespread use not only in environmental monitoring but also in biological studies [1,2] because fluorescence has significant advantages such as generally non-destructive character, high sensitivity, and instantaneous response [2,3].

Zinc is the second most abundant transition metal ion in human body, and it plays a critical role in enzyme regulation structure and function, neural signal transmission, and gene expression [4–7]. Furthermore, Zn^{2+} is mostly trapped within proteins, as a structural or catalytic cofactor [8–11]. However, disorders arising from free zinc metabolism are closely associated with many pathological states, such as Alzheimer's disease, epilepsy, Parkinson's disease, ischemic stroke, and infantile diarrhea [12–19]. Accordingly, developing fluorescent chemosensors with high selectivity for Zn^{2+} has been an active research area [20–28].

Copper is one of the most important metal ions in biological systems. Because of its redox-active nature, copper serves as an essential cofactor by taking an active part in large variety of enzymes, including superoxide dismutase, cytochrome c oxidase, and tyrosinase [28–32]. Thus, daily ingestion of copper is indispensable for our good health. However, under overloading conditions, copper exhibits toxicity in that it causes neurodegenerative disease, such as Menkes and Wilson disease [33–36]. Moreover, copper can also act as a significant environmental pollutant because of its widespread use in industry and agriculture [37–39]. For these reasons, many efforts have devoted to design various fluorescent probes specific for Cu^{2+} detection [40–52].

Over a few years, a number of the researches about fluorescent sensors singly for zinc or copper have been documented. However, reports about pertinent sequential recognition of zinc and copper are relative very rare [53]. Therefore, it is still a challenge to develop sensors that are able to perform the sequential recognition of zinc and copper.

Herein, we report on a new anthracene-based receptor **1**, which displays highly selective and sensitive fluorescence "off–on" recognition to Zn^{2+}, and the resulting **1**-Zn^{2+} complex exhibits highly selective recognition to Cu^{2+} through fluorescence "on-off".

The receptor **1** was synthesized from the coupling reaction of a bidentate metal ion chelator, 2,2-dipyridyl amine [54,55], and a fluorophore, 9-(chloromethyl)anthracene (Scheme 1) [56,57]. Receptor **1** was characterized by ^{1}H NMR, ^{13}C NMR, ESI-mass spectrometry, and elemental analysis.

The fluorescent properties of receptor **1** were primarily investigated in CH_3CN upon addition of various metal ions (Na^+, K^+, Li^+, Ca^{2+}, Mg^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Cr^{3+}, Mn^{2+}, Mg^{2+}, Zn^{2+}, Ag^+, and Hg^{2+}) as their perchlorate salts. Upon the addition of 10 Eq of each cation, only Zn^{2+} induced a distinct fluorescence intensity enhancement (10-fold), while other metal ions showed either no or slight increase in the fluorescence spectra relative to the free receptor **1** at 420 nm with excitation at 369 nm (Fig. 1).

It is a huge challenge to discriminate Zn^{2+} selectively from Cd^{2+} because Zn^{2+} and Cd^{2+} with similar chemical properties often respond together with similar spectral changes [30,31,58–60]. Importantly, the fluorescence enhancement of **1** was little increased in the presence of Cd^{2+}. A better binding selectivity of **1** to Zn^{2+} than Cd^{2+} might be caused by the rigidity of the 2,2-dipyridyl amine moiety [55] that is more suitable for binding to Zn^{2+} with smaller ion radius than that of Cd^{2+}. This result suggests that **1** could act as "turn-on" sensor for Zn^{2+} and discriminate Zn^{2+} particularly from Cd^{2+}. Next, we checked the proton effect on the fluorescence enhancement of **1** because the acid property of metal salts in solution might cause the fluorescent

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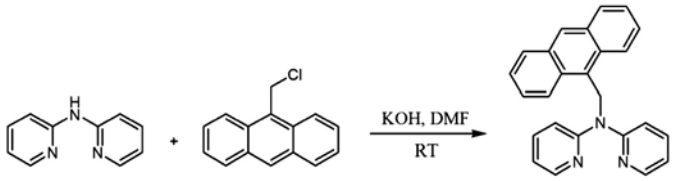
http://dx.doi.org/10.1016/j.inoche.2013.10.049



Scheme 1. Synthesis of receptor **1**.

enhancement of it. As shown in Fig. S1, there is no fluorescence enhancement in the presence of HCl (10 Eq), demonstrating that the proton did not have influence on the fluorescence enhancement of **1**.

To further investigate the chemosensing properties of **1**, fluorescence titration for the complexation of **1** with Zn^{2+} ion was performed. As shown in Fig. 2, the emission intensity of **1** at 420 nm steadily increases until the amount of Zn^{2+} reaches 10 Eq. The photophysical properties of **1** were also examined using UV-vis spectrometry. UV-vis absorption spectrum of **1** showed a broad band at 300 nm and three sharp bands at 348, 367, and 387 nm (Fig. S2). Upon the addition of Zn^{2+} ions to a solution of **1**, the absorption band at 300 nm increased, and the three sharp bands red-shifted to 351, 368, and 388 nm, respectively. Meanwhile, the clear isosbestic points at 361, 369, 380, and 389 nm imply the undoubted conversion of free **1** to a zinc complex.

The Job plot [61] showed a 1:1 complexation stoichiometry between **1** and Zn^{2+} (Fig. S3), which was further confirmed by ESI-mass spectrometry analysis (Fig. 3). The positive-ion mass spectrum indicated that a peak at $m/z = 253.57$ is assignable to $\mathbf{1} + Zn^{2+} + 2CH_3CN$ [calcd, m/z: 253.60]. From the fluorescence titration data, the association constant for **1**-Zn^{2+} complexation was determined as $1 \times 10^5\ M^{-1}$ from a Benesi–Hildebrand plot [62]. This value is within the range of those ($1.0 \sim 1.0 \times 10^7$) reported for Zn^{2+}-binding chemosensors [8,25,63,64].

We also carried out ^1H NMR titration experiments of **1** by adding Zn^{2+} to examine further the binding mode (Fig. 4). On the addition of 0.25 Eq of Zn^{2+}, most protons were slightly shifted. However, more addition (0.5 Eq) of Zn^{2+} showed significant changes in ^1H NMR titration data. The H_a, H_b, H_c, and H_d protons on the pyridine groups began to shift to downfield, and simultaneously the methylene proton (H_e) became shifted to upfield. When 1.0 Eq of Zn^{2+} was added, the H_a, H_b, H_c, and H_d protons on the pyridine groups showed downfield shift by 1.5 ppm, 0.3 ppm, 0.6 ppm, and 0.55 ppm, respectively, while the methylene proton (H_e) showed upfield shift by 0.1 ppm. Further addition of Zn^{2+} did not change ^1H NMR. These results suggest that two nitrogen atoms of the pyridine moieties might be involved in Zn^{2+} coordination. On the basis of the ^1H NMR titration, Job plot, and ESI-mass spectrometry

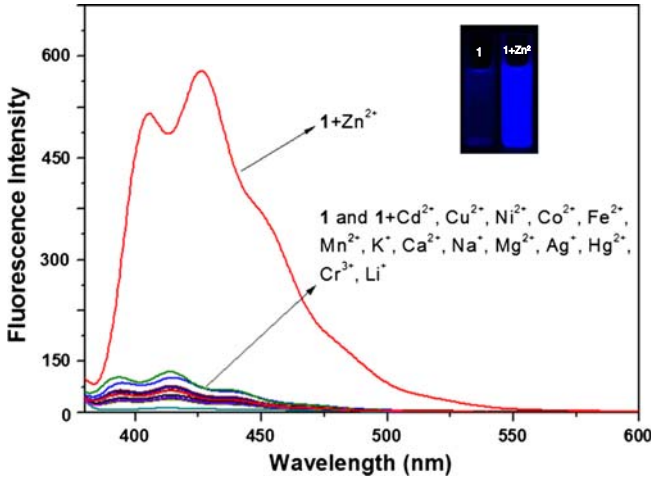


Fig. 1. Fluorescence spectra of **1** (5 μM) in the presence of different metal ions (10 Eq) such as Na^+, K^+, Li^+, Ca^{2+}, Mg^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Cr^{3+}, Mn^{2+}, Mg^{2+}, Ag^+, Hg^{2+}, and Zn^{2+} with an excitation of 369 nm. Inset: Photos of **1** (5 μM) in the absence and presence of Zn^{2+} (50 μM) in CH_3CN.

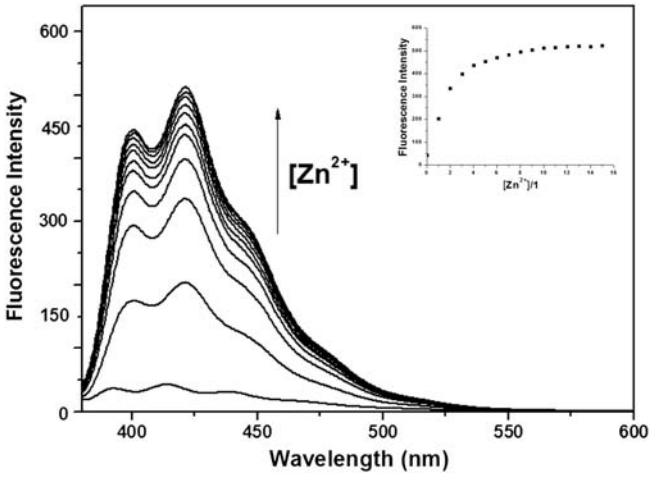


Fig. 2. Fluorescence spectra change of **1** (5 μM) upon the addition of $Zn(ClO_4)_2$ (up to 75 μM) with an excitation of 369 nm. Inset: Fluorescence intensity of **1** at 420 nm as function of Zn^{2+} concentration.

analysis, we propose the structure of a 1:1 complex of **1** and Zn^{2+}, as shown in Scheme 2. For practical purposes, the detection limit of **1** for the analysis of Zn^{2+} ions is also an important parameter. Thus, based on the fluorescence titration measurement, the detection limit [65] of **1** for Zn^{2+} ion was found to be 2.06×10^{-6} M.

To explore the ability of **1** as a fluorescence sensor for Zn^{2+}, competition experiments were performed in the presence of Zn^{2+} (10 Eq) mixed with various metal ions (10 Eq) (Fig. 5). The coexistent metal ions had a small and negligible influence on the fluorescence intensity of the **1**-Zn^{2+} complexation, except for Cu^{2+} that quenched it completely. Interestingly, cadmium ion hardly inhibited the fluorescence intensity of **1**-Zn^{2+}, being capable of distinguishing Zn^{2+} from Cd^{2+}. Hence, these results suggest that **1** could be a good sensor for Zn^{2+}.

Because the results of competition experiments demonstrate that **1**-Zn^{2+} could be inhibited only by Cu^{2+} ion, the sequential recognition study of **1** was paid to our special attention. The fluorescence titration experiment of the **1**-Zn^{2+} complex with Cu^{2+} was first carried out, as shown in Fig. 6. The emission intensity of **1** at 420 nm was quenched upon addition of 1.0 Eq of Cu^{2+}. The fluorescence behavior of **1** clearly demonstrated the on–off switching mechanism, which occurs in response to Cu^{2+} ion displacement in the zinc complex. To further elucidate the displacing property of receptor **1** from Zn^{2+} to Cu^{2+}, UV-vis spectrometry experiments were then examined. UV-vis spectrum of **1**-Zn^{2+} complex exhibited absorption bands at 300, 348, 368, and 388 nm, respectively (Fig. 7). Upon the addition of Cu^{2+} to the solution of **1**-Zn^{2+}, the absorption peak at 300 nm gradually increased, while the

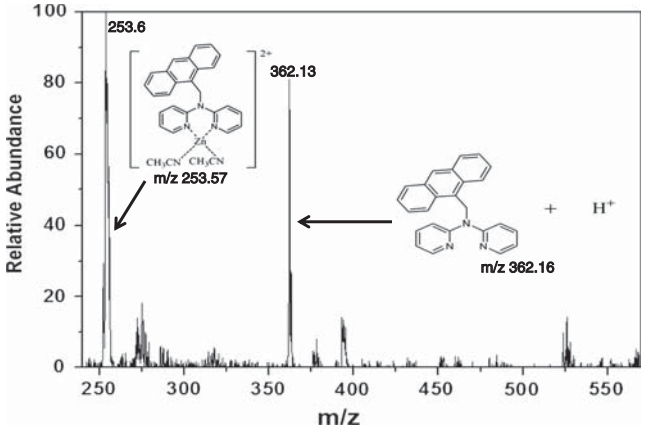


Fig. 3. Positive-ion electrospray ionization mass spectrum of **1** upon addition of $Zn(ClO_4)_2$. (1.0 Eq) in acetonitrile.