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A 'turn-on' fluorescent chemosensor for the detection of Zn^{2+} ion based on 2-(quinolin-2-yl) quinazolin-4(3*H*)-one

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Abstract: 2-(Quinolin-2-yl)quinazolin-4(3*H*)-one (**Q**) was synthesized via the Brønsted acid-promoted tandem cyclization/dehydrogenation reaction with a good yield. Compound **Q** is a selective 'turn-on' fluorescent sensor for Zn^{2+} ion without interference by Cd^{2+}. The 1:1 binding model of **Q** to Zn^{2+} was confirmed by the Benesi-Hildebrand analysis, Job's plot analysis and a ultraviolet-visible (UV-Vis) titration experiment. Furthermore, the light-on fluorescent response can be observed by the naked eye under UV-lamp irradiation (365 nm).

Keywords: fluorescent sensor; quinazolinone; Zn^{2+}.

Introduction

The detection of important metal ions using fluorescent chemosensors should be characterized by convenient application and rapid response [1–3]. Zinc ion is involved in many physiological processes such as immune and brain functions [4, 5]. In the human body, zinc ion is mostly complexed and free Zn^{2+} ion is scarce [6, 7]. It has been reported that free Zn^{2+} ion in the human body may cause serious diseases including Alzheimer's disease [8, 9]. Therefore, the development of selective and sensitive fluorescent chemosensors for Zn^{2+} has attracted attention, and numerous fluorescence molecular structures have been designed for the sensing of Zn^{2+} by chelation [10–16]. Unfortunately, the existing sensors are difficult to synthesize and most of them are susceptible to interference from Cd^{2+} [10].

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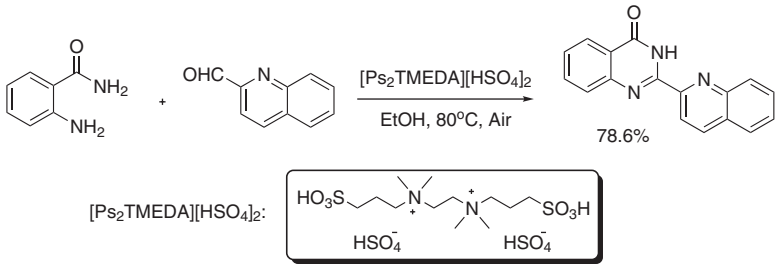
Quinazolinones are good candidates for fluorescent chemosensors in biological systems because of their remarkable biocompatibility [17, 18]. Recently, quinazolinone-based sensors for amine vapors [19] and Cu^{2+} ion [20] have been developed. We report that 2-(quinolin-2-yl)quinazolin-4(3*H*)-one (**Q**, Scheme 1) can be used as a simple and efficient 'turn-on' fluorescent chemosensor for a highly selective and sensitive detection of Zn^{2+}.

Results and discussion

Compound **Q** was synthesized by the treatment of *o*-aminobenzamide with quinoline-2-carboxaldehyde in the presence of $[Ps_2TMEDA][HSO_4]_2$ as a catalyst following the previously reported methodology (Scheme 1) [21]. This catalyst shows stronger acidity than common protic acids including H_2SO_4 and CH_3SO_3H.

The ultraviolet-visible (UV-Vis) absorption spectra of **Q** at various concentrations of Zn^{2+} in acetonitrile-water were recorded (Figure 1). The peaks at 306 nm, 326 nm, 336 nm and 355 nm are due to the UV absorption of quinoline and quinazoline systems of **Q** [22, 23]. The absorption is very weak in the range of 360–400 nm. With the addition of Zn^{2+}, the absorption gradually increases in this range. Consequently, a wavelength of 375 nm was chosen for the excitation experiments.

Next, the fluorescence response of **Q** (10^{-5} M) toward various metal ions including Cu^{2+}, Ni^{2+}, Co^{2+}, Pb^{2+}, Cs^{+}, Ca^{2+}, Cd^{2+}, Ag^{+}, Ba^{2+}, Mg^{2+}, Na^{+}, Mn^{2+}, Hg^{2+}, Fe^{2+}, Al^{3+}, K^{+} and Zn^{2+} were examined (Figure 2A). As can be seen, the maximum emission peak of **Q** shows weak fluorescence at 425 nm. Compound **Q** (10^{-5} M) also exhibits weak fluorescence at 473 nm with a quantum yield $\Phi_f < 0.05$ in a mixture of acetonitrile and water. After the addition of a metal ion including Ag^{+}, Al^{3+}, Ba^{2+}, Ca^{2+}, Co^{2+}, Cr^{3+}, Fe^{3+}, K^{+}, Mg^{2+} or Na^{+}, the emission peak at 473 nm is increased to a small degree due to the weak coordination of **Q** with the metal. By contrast, the fluorescence intensity of **Q** (10^{-5} M) at 473 nm is increased significantly in the presence of Zn^{2+} ion (one equivalent) with a quantum yield Φ_f of 0.43 (Figure 2A). The effects of anions were also tested.



Scheme 1 Synthesis of 2-(quinolin-2-yl)quinazolin-4(3*H*)-one (**Q**).

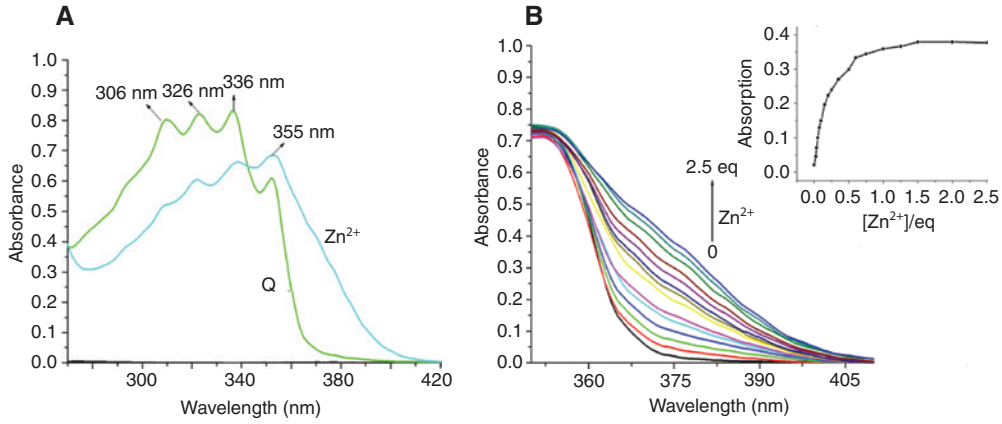


Figure 1 (A) UV-Vis absorption spectra of **Q** (10^{-4} M) and **Q** in the presence of five equivalents of Zn^{2+} ion. (B) UV-Vis absorption spectral changes during titration of **Q** (10^{-4} M) with 0–2.5 equivalents of Zn^{2+}; inset shows absorption as a function of Zn^{2+} ion concentration. All measurements were conducted in a mixture of CH_3CN and water (9:1) at room temperature.

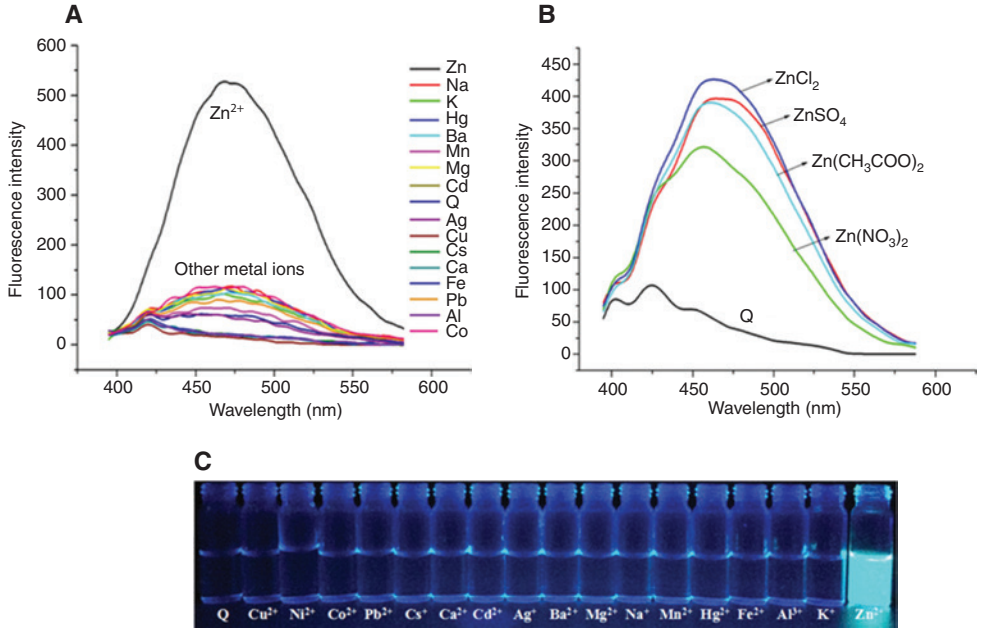


Figure 2 (A) Fluorescence intensity of **Q** (10^{-5} M) in the presence of one equivalent of each of the following metal ions, Cu^{2+}, Ni^{2+}, Co^{2+}, Pb^{2+}, Cs^{+}, Ca^{2+}, Cd^{2+}, Ag^{+}, Ba^{2+}, Mg^{2+}, Na^{+}, Mn^{2+}, Hg^{2+}, Fe^{2+}, Al^{3+}, K^{+} and Zn^{2+}, upon excitation at 375 nm. (B) Fluorescence intensity of **Q** (10^{-5} M) in the presence of one equivalent of various Zn^{2+} salts (Cl^{-}, SO_4^{2-}, CH_3COO^{-}, NO_3^{-}) upon excitation at 375 nm. (C) Visual fluorescence emission of sensor **Q** (10^{-5} M) in the presence of Zn^{2+}; note the lack of visible fluorescence in the presence of other metal ions (one equivalent each); the experiments were conducted in a mixture of acetonitrile and water (9:1) upon excitation at 365 nm using a UV lamp at room temperature.

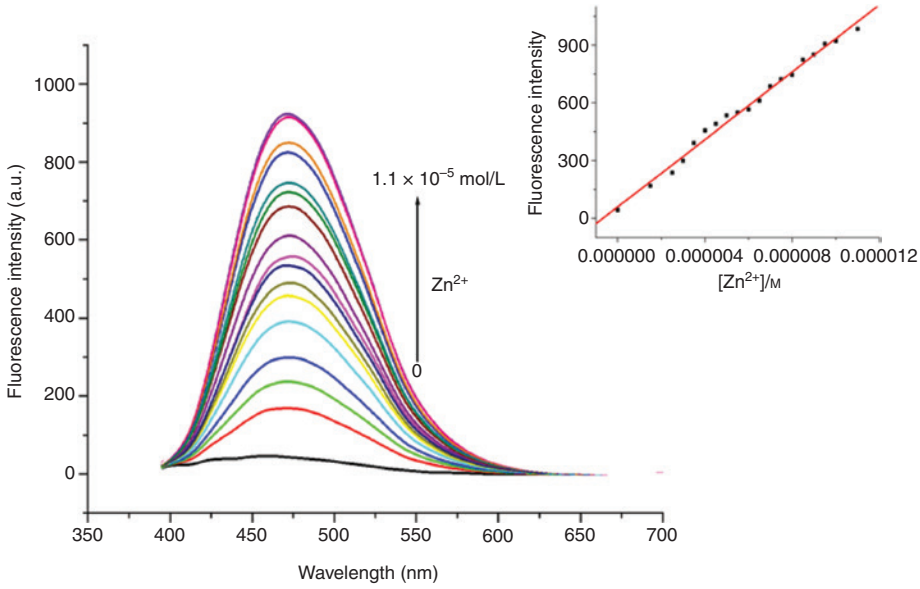


Figure 3 Fluorescence titration of **Q** (5×10^{-6} M), in CH_3CN/H_2O (9:1) upon excitation at 375 nm with successive addition of Zn^{2+} at room temperature. Inset shows fluorescence intensity as a function of Zn^{2+} ion concentration.

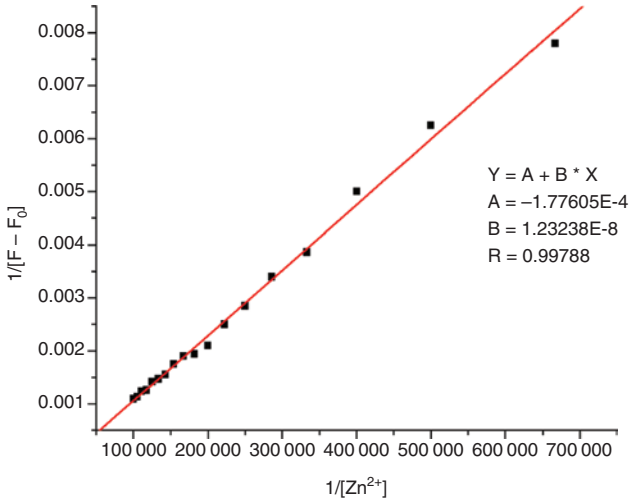


Figure 4 Benesi-Hildebrand plot ($\lambda_{em}=473$ nm) based on a 1:1 binding stoichiometry of **Q** with Zn^{2+}.

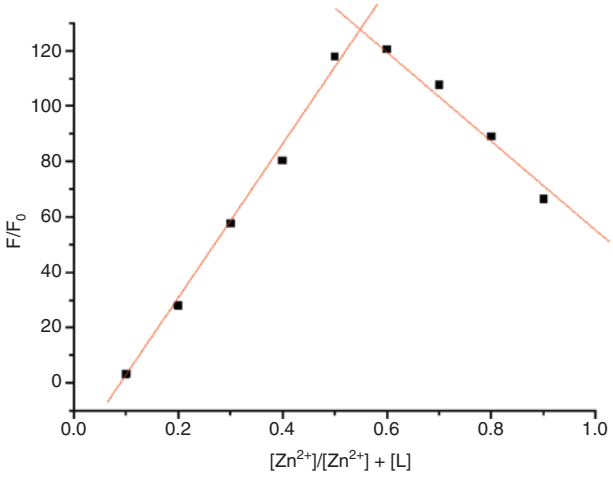


Figure 5 Job's plot for binding of Zn^{2+} to **Q** indicating the 1:1 binding ratio.

The results show that anions have almost no influence on the fluorescence intensity (Figure 2B). The remarkable change of the fluorescence color of **Q** (10^{-5} M) from colorless to blue in the presence of Zn^{2+} (10^{-5} M) upon irradiation with a UV lamp (365 nm) is shown in Figure 2C.

In order to further investigate the selectivity of **Q** toward Zn^{2+}, the competition assays were performed by measuring the fluorescence intensity of **Q** in the presence of Zn^{2+} and an additional metal ion. The results clearly demonstrated that the additional metal ion does not affect the strong fluorescence of **Q** in the presence of Zn^{2+} (not shown).

Finally, the fluorescence titration experiments were conducted to investigate the binding mode between Zn^{2+} and **Q**. With the increase in the concentration of Zn^{2+}, the fluorescence intensity at 473 nm increases linearly (Figure 3). The 1:1 binding mode was confirmed using the Benesi-Hildebrand analysis (Figure 4) [24–26], Job's plot analysis (Figure 5) [27, 28] and UV-Vis titration experiments (Figure 1B). The calculated detection limit (DL) of Zn^{2+} in the presence of **Q** is 8.82×10^{-7} mol L^{-1}, as calculated using the equation $DL=3\sigma/B$ (Figure 6) [29, 30]. The binding constant (K_a) is 8.98×10^{4} M^{-1} using the equation $K_a=B^{-1}\times[F_{max}-F_{min}]^{-1}$ [20].

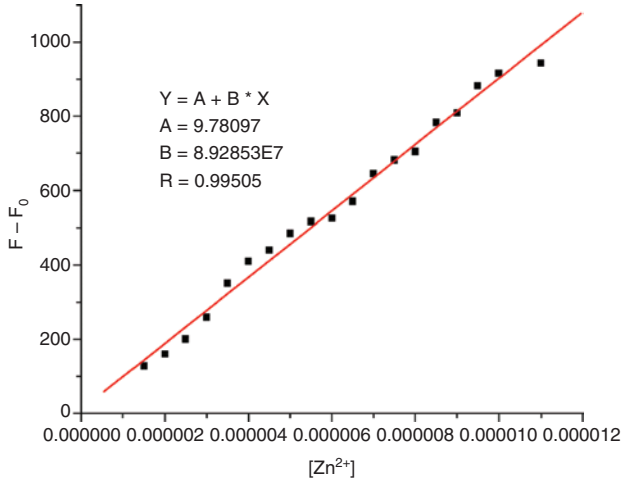


Figure 6 Normalized response of the fluorescence signal to change in Zn^{2+} concentration. The detection limit for Zn^{2+} is 8.82×10^{-7} M.

Conclusions

A new 'turn-on' fluorescent chemosensor for the detection of Zn^{2+} ion based on 2-(quinolin-2-yl)quinazolin-4(3*H*)-one (**Q**) was synthesized. This compound shows a good sensitivity and selectivity for the recognition of Zn^{2+} even in the presence of many other metal ions including Cd^{2+} in a mixture of acetonitrile and water (9:1). The fluorescence quantum yield, $\Phi_f < 0.05$, is dramatically increased to 0.43 in the presence of one equivalent of Zn^{2+} ion. This fluorescent change can be observed by the naked eye under UV-lamp irradiation at 365 nm.

Experimental

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 spectrometer. High resolution mass spectral (HRMS) analysis was performed using electrospray ionization-micro time-of-flight (ESI-microTOF). Solutions of Cu^{2+}, Ni^{2+}, Co^{2+}, Pb^{2+}, Cs^{+}, Ca^{2+}, Cd^{2+}, Ag^{+}, Mn^{2+}, Na^{+}, Mg^{2+}, Fe^{2+}, Al^{3+}, Hg^{2+}, Ba^{2+} and Zn^{2+} were generated from chloride salts using deionized water as a solvent. All spectral measurements were conducted at room temperature. Fluorescence spectra were measured on a Hitachi-F7000 fluorimeter. UV-Vis absorption spectra were measured on a Hitachi-UV3900 spectrophotometer. The width of excitation and emission slits was 5 nm. The fluorescence quantum yields (Φ_f) were measured on an Edinburgh-FLS980 spectrometer.

Synthesis of 2-(quinolin-2-yl)quinazolin-4(3*H*)-one (Q) [21]

A mixture of $[Ps_2TMEDA][HSO_4]_2$ (1 mmol, 555 mg), *o*-aminobenzamide (5 mmol, 681 mg) and 2-quinolinecarboxaldehyde (5 mmol, 786 mg) in ethanol (25 mL) was stirred at 80°C for 3 h, then cooled to room temperature and treated with a solution of sodium bicarbonate (20 mL). The resultant precipitate of **Q** was filtered, washed with deionized water (2×10 mL) and crystallized from ethanol/water: yield 79%, mp 264–226°C (lit. [31] mp 267–268°C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.05 (s, 1H), 8.64 (d, J = 8.8 Hz, 1H), 8.56 (d, J = 8.8 Hz, 1H), 8.26 (m, 2H), 8.13 (m, 1H), 7.91 (m, 3H), 7.76 (m, 1H), 7.63 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.4, 150.4, 149.0, 148.8, 146.8, 138.5, 135.3, 131.2, 129.8, 129.3, 128.9, 128.6, 128.3, 128.1, 126.7, 122.7, 119.1. ESI-HRMS. Calcd for $C_{17}H_{12}N_3O$, $[M+H]^+$: *m/z* 274.0975. Found: *m/z* 274.0953.

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