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Original article

Design of quinoline-based fluorescent probe for the ratiometric detection of cadmium in aqueous media

Qing Liu [a,b], Guo-Ping Li [a,b], Dong-Jian Zhu [a,b], Lin Xue [a,*], Hua Jiang [a,*]

[a] *Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Photochemistry, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190 China*
[b] *University of Chinese Academy of Sciences, Beijing 100049, China*

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ABSTRACT

A new fluorescent probe, DQCd2, based on 4-piperidinoquinoline has been synthesized as a fluorescent probe for Cd^{2+}. It can ratiometrically respond to Cd^{2+} in PBS buffer by a remarkable emission intensity enhancement (88-fold) and wavelength shift (70 nm).

1. Introduction

With the development of industrial production, many highly toxic heavy metal ions have entered the environment and the human food chain. Among them, cadmium has caught growing attention because of its bioaccumulation and pathogenicity [1]. Hence, both the EPA (United States Environmental Protection Agency) and the WHO (World Health Organization) have provided strict safety standards for drinking water [2]. It is rather essential to develop facile and efficient analytical methods to detect and monitor Cd level in drinking water or other environmental samples.

Owing to the simplicity, high sensitivity and real-time detection, fluorescent sensors/probes have been regarded as excellent candidates to selectively recognize and quantify metal ions [3]. Up to now, only a few Cd^{2+}-selective fluorescent probes have been realized [4], partially because the detection of Cd^{2+} could be seriously interfered by Zn^{2+}, which has similar chemical properties to Cd^{2+} [5]. Moreover, most of these probes report a sensing event merely based on the variation of emission intensity, which might be affected by sample environment, dye concentration, photo-bleaching and so forth [6]. In contrast, ratiometric fluorescent probes, which have a built-in calibration based on the ratio of two excitation/emission wavelengths for extrinsic factors, can, in principle, address the issue of accuracy and quantitative measurements [7].

In our previous work [8], we have developed a quinoline scaffold for the design of ratiometric metal ion-selective probes, such as DQCd1, DQZn1-4, and DQAg, in aqueous solutions based on inhibition of resonance charge transfer. Although DQCd1 exhibits remarkable ratiometric response to Cd^{2+} with high sensitivity, it still requires a masking agent, nitrilotriacetic acid (NTA), to improve the specificity for Cd^{2+}. On the other hand, Qian et al. have recently reported that the water soluble polyamide is an efficient Cd^{2+} receptor to develop fluorescent Cd^{2+}-selective probes [9]. These results prompted us to design a highly selective ratiometric probe for Cd^{2+} by combining our ratiometric quinoline-based sensing scaffold with this polyamide Cd^{2+}-receptor. Therefore, in this contribution, we report the synthesis and photophysical evaluation of DQCd2 as a ratiometric Cd^{2+}-probe in aqueous solution (Scheme 1).

2. Experimental

Unless otherwise noted, the chemicals were purchased from Alfa Aesar (China) and used as received. All solvents were purified and dried by standard methods prior to use. Pure water (18.2 Ω) was used to prepare all aqueous solutions. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE-400 spectrometer. All chemical shifts are reported in the standard notation of parts per million using residual solvent protons as an internal standard. Mass spectra (ESI) were obtained on a Bruker Apex IV Fourier

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* Corresponding authors.
E-mail addresses: zinclin@iccas.ac.cn (L. Xue), hjiang@iccas.ac.cn (H. Jiang).

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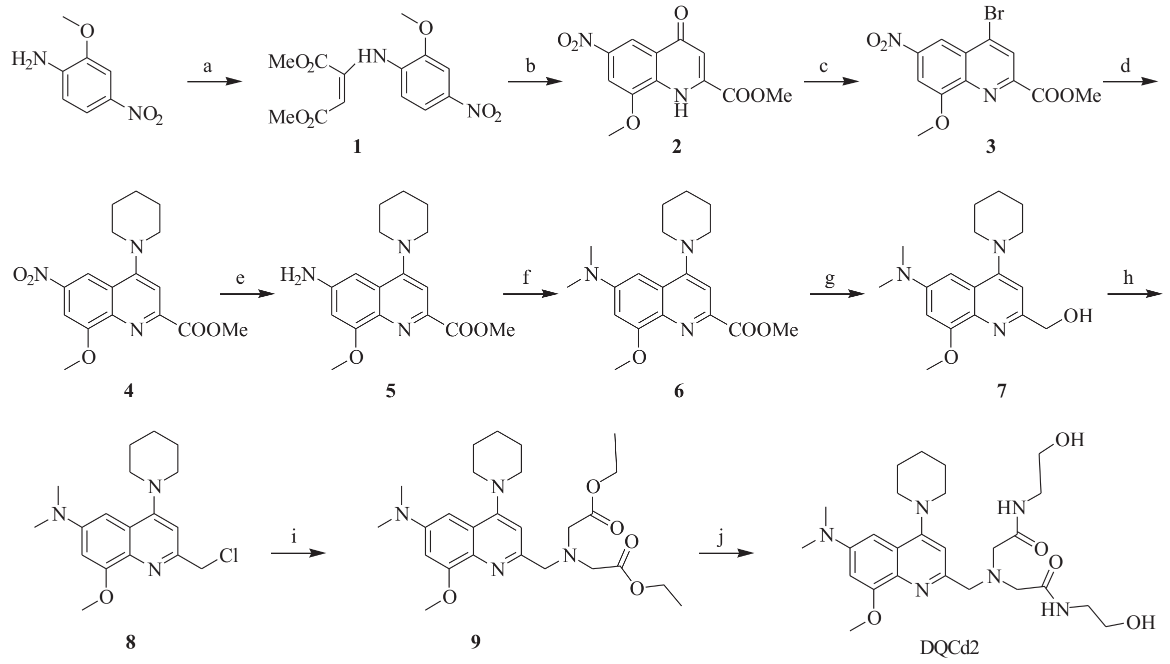

Scheme 1. Synthesis of probe DQCd2. Reagents and conditions: (a) Ethyl acetoacetate, MeOH, reflux, 64%. (b) Diphenyl oxide, 250 °C, 68%. (c) $POBr_3$, THF, 60 °C, 75%. (d) Piperidine, dioxane, 80 °C, 80%. (e) H_2, Pd/C, EA, 95%. (f) Paraformaldehyde, $NaBH_3(CN)$, AcOH, r.t., 92%. (g) $NaBH_4$, MeOH/THF, 65 °C, 88%. (h) $SOCl_2$, DCM, 0 °C. (i) Diethyl iminodiacetate, K_2CO_3, KI, acetonitrile, r.t. (j) Ethanolamine, acetonitrile, reflux, 48%.

transform mass spectrometer. UV–vis absorption spectra were obtained using a Shimadzu UV-2550 spectrometer. Fluorescence spectra were obtained using a Hitachi F-4600 spectrometer. The path length was 1 cm with a cell volume of 3.0 mL. All of the spectroscopic measurements were carried out in PBS buffer (10 mmol/L phosphate, 8 g/L NaCl, 0.2 g/L KCl, pH 7.0) at 25 °C. The solutions were allowed to equilibrate at 25 °C for 3 min after each addition. Quinine sulfate in 0.1 mol/L H_2SO_4 ($\Phi = 0.54$) was used as the standard for quantum yield measurements [10].

The synthetic procedures are outlined in Scheme 1. Compound **7** was prepared according to our previous procedures [8]. Chlorination of **7** gave compound **8**, which was further reacted with diethyl iminodiacetate under basic conditions to give compound **9**. The probe DQCd2 was then obtained by the aminolysis of the ethyl ester **9**.

3. Results and discussion

As a routine procedure, we initially measured the fluorescence spectra of DQCd2 in the aqueous solution over pH 2.5–10. The fluorimetric titration curve shows two distinct pH changing ranges, from which two apparent pK_a values of 7.19 and 2.66 were obtained (Fig. S1). According to previous reports, [8,11] we reasoned that the quinolinic nitrogen, methoxyl oxygen and tertiary nitrogen constitute a proton binding pocket, leading to the combined pK_{a1} of 7.19 and a partial reduction of the photo-induced electron transfer (PeT) quenching by the tertiary nitrogen from ion binding receptor. Hence, the pK_{a2} of 2.66 is assigned to the dimethylamino nitrogen atom. These data suggest DQCd2 can be well protonated in neutral aqueous media. Therefore, a phosphate buffered saline solution (PBS) at pH 7.0 containing 10 mmol/L phosphate, 8 g/L NaCl, 0.2 g/L KCl was chosen for measurements.

In PBS solution, free DQCd2 showed a clear charge-transfer band around 380–450 nm in the absorption spectra resulting from its mono-protonated species (Fig. 1). Upon the addition of Cd^{2+}, this band gradually decreased with the appearance of a new absorption band around 270–370 nm and four distinct isosbestic points at 380, 358, 278, 265 nm. These spectral changes can be well

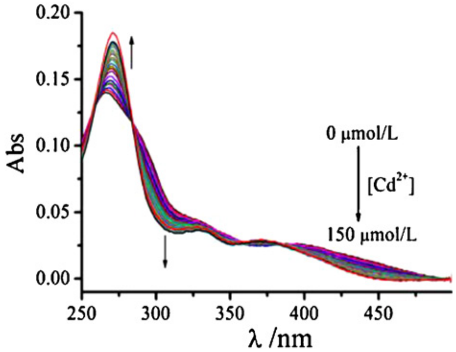

Fig. 1. Absorption spectra of 5 μmol/L DQCd2 upon titration of Cd^{2+} (0–150 μmol/L) in PBS buffer.

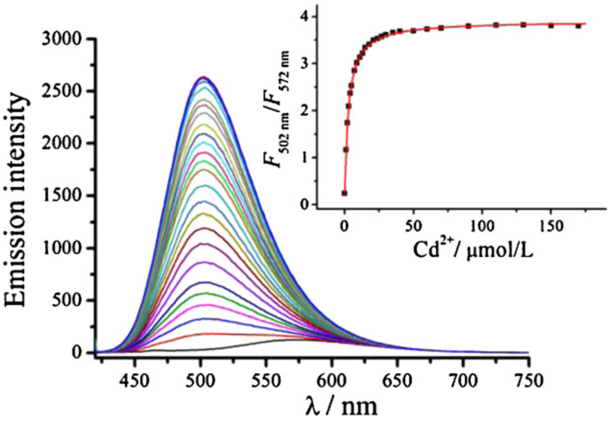

Fig. 2. Fluorescence spectra ($\lambda_{ex} = 402$ nm) of 5 μmol/L DQCd2 upon titration of Cd^{2+} (0–170 μmol/L) in PBS buffer. Inset: ratio (F_{502nm}/F_{572nm}) changes as a function of the Cd^{2+} concentration.

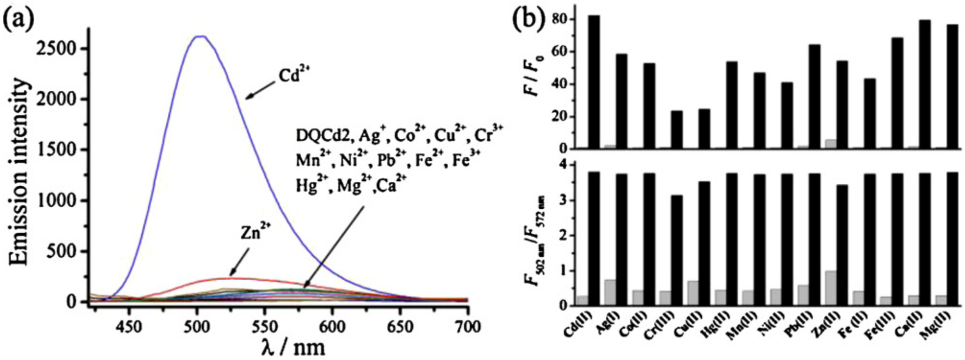

Fig. 3. (a) Fluorescence spectra of DQCd2 (5 μmol/L) in the presence of various metal ions (100 μmol/L Cd^{2+}, Ag^{+}, Co^{2+}, Cr^{3+}, Cu^{2+}, Hg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, Fe^{2+}, Fe^{3+}, Ca^{2+} and Mg^{2+}) in PBS buffer, λ_{ex} = 402 nm. (b) Gray bars represent the fluorescence intensity (top) and ratio calibration (bottom) responses of DQCd2 (5 μmol/L) in the presence of various metal ions. Black bars represent the responses of DQCd2 in the presence of the indicated metal ions, followed by 100 μmol/L Cd^{2+}.

explained as a result of the Cd-coordination induced liberation of the proton at quinolinic site and subsequent inhibition of resonance [8]. As shown in Fig. 2, DQCd2 displayed relatively weak emission at 572 nm in the absence of Cd^{2+} ($\Phi_0 = 0.07$). Upon the addition of Cd^{2+}, the emission peak gradually shifted to 502 nm with remarkable fluorescence enhancements ($\Phi_{Cd} = 0.49$; $F/F_0 = 88$, F measured at 502 nm), also indicating that the Cd-induced inhibition of resonance occurred. Meanwhile, the ratios (F_{502}/F_{572nm}) of the fluorescence intensities at 502 nm and 572 nm varied from 0.2 to 3.8 with the continuous addition of Cd^{2+}. Further, Job's plot suggested that DQCd1 chelated Cd^{2+} with 1:1 binding stoichiometry (Fig. S2). By measuring the ratios of emission intensity (F_{502}/F_{572nm}) at different concentrations of Cd^{2+} in PBS buffer, the dissociation constant (K_d) of DQCd2 was determined to be 1.2×10^{-5} mol/L (Fig. 2, inset). These data clearly indicate that DQCd2 is an excellent turn-on and ratiometric fluorescent Cd^{2+}-selective probe ($F/F_0 = 88$, and $R/R_0 = 19$).

Next, the selectivity profiles of DQCd2 were examined by titrations with various, potentially competing, metal ions. As depicted in Fig. 3a, the addition of Cd^{2+} to a solution of DQCd2 resulted in a significant blue-shifted and enhanced emission, whereas other metal ions, including Ag^{+}, Co^{2+}, Cr^{3+}, Cu^{2+}, Hg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+}, Ca^{2+} and Mg^{2+}, gave rise to no fluorescent turn-on signal. It is worth mentioning that Zn^{2+}, which bears many properties similar to those of Cd^{2+}, only induced slight fluorescent enhancement. Then, we performed ion-competition experiments to further evaluate the metal ion selectivity of DQCd2. In the presence of other indicated metal ions, DQCd2 still exhibited excellent response to Cd^{2+} based on both fluorescence intensity and ratiometric calibration (Fig. 3b). In addition, pH variations (6–8) did not affect the sensing properties as well (Fig. S3). Therefore, DQCd2 can be used for ratiometric detection of Cd^{2+} in aqueous solution without the adverse influence of other metal ions and pH variations.

4. Conclusion

In conclusion, we have designed and synthesized a new fluorescent probe, DQCd2, based on the mechanism of inhibition of resonance. It is able to detect Cd^{2+} with significant turn-on and ratiometric signal output. Moreover, DQCd2 also has the good selectivity and pH-independency in the biological pH range (6–8), providing an efficient method for detecting Cd^{2+} in aqueous media.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.cclet.2013.04.002.

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