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Aminoquinoline-based fluorescent probe for detection of Cu^{2+} and hydrogen sulfide

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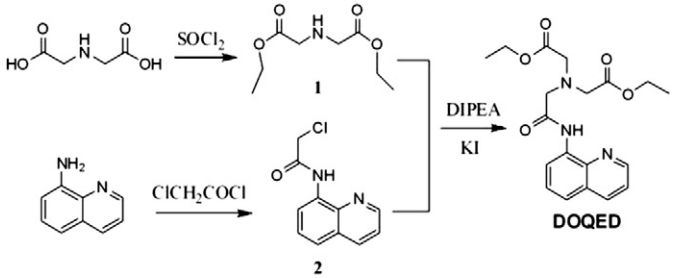
ABSTRACT

Diethyl 2,2′-(2-oxo-2-(quinolin-8-ylamino)ethylazanediyl) diacetate (DOQED), an aminoquinoline-based fluorescent probe, was synthesized, and successfully applied in detection of Cu^{2+} and S^{2-} in an aqueous buffered solution. The emission signal of DOQED was selectively quenched by Cu^{2+}, and was exclusively recovered by subsequent addition of S^{2-}. The formation of a $[Cu(DOQED)]^{2+}$ complex was confirmed by X-ray crystallography.

Exploring functions of biomolecules is critically contingent upon the development of novel assay techniques. Among the various detection methods, fluorescence sensing, due to its high sensitivity, operational simplicity, and biocompatibility, is one of the most powerful and popular tools to visualize complicated biological processes [1]. And thus, the past years have witnessed a burst of interest in developing diverse fluorescent probes in reconigizing biomolecules of interest [2]. Copper, an essential trace element in humans, is a pivotal co-factor for many enzymes, and participates in numerous physiological processes [3]. Its deficiency or over-accumulation may lead to various diseases [4]. Sulfide anion, a traditional toxic pollutant, is widespread in the environment where it is generated from industrial processes or biological metabolism [5]. Recent studies have also demonstrated that protonated sulfide is involved in various physiological processes [6]. For example, together with NO and CO, H_2S has been recognized as the third gaseous transmitter and shown to regulate a variety of physiological/pathophysiological processes. Although, a large number of fluorescent probes have been developed for sensing Cu^{2+} [7] and S^{2-} [8], the probes simultaneously sensing for both species are quite rare [9]. In this work, an aminoquinoline-based fluorescence probe DOQED was synthesized (Scheme 1) and fully characterized (Figs. S1–S9). The emission signal was selectively quenched by Cu^{2+} via forming a $[Cu(DOQED)]^{2+}$ complex, and was exclusively recovered followed by an addition of S^{2-}. This "on–off–on" response provides a convenient and practical way in detection of both Cu^{2+} and S^{2-} in biological samples.

As shown in Fig. 1A, the response of probe DOQED to Cu^{2+} was evaluated by UV–vis absorption titration at first. The free probe DOQED (10 μM) displayed two peaks at 235 nm and 310 nm with molar absorption coefficients of 14,458 cm^{-1} M^{-1} and 3153 cm^{-1} M^{-1}, respectively, the typical absorbance bands of aminoquinoline. Both bands were red-shifted with the addition of Cu^{2+} (0–1.2 equiv.) in the absorption spectrum, accompanying three isosbestic points at 240, 285 and 320 nm, supporting intermediate complex formation.

In order to understand the binding modes of probe DOQED towards Cu^{2+}, fluorescence titration experiments were carried out. In Fig. 1B with the increasing addition of Cu^{2+} (0–1.5 equiv.) to a solution of 10 μM probe DOQED in a PBS buffer (10 mM, pH 7.4), a gradual decrease in the fluorescence intensity at 420 nm was observed. Quenching of fluorescence was due to the coordination of Cu^{2+} to probe DOQED which decreased the electron-donating of nitrogen atom of quinoline and then inhibited the ICT process. Furthermore, the paramagnetic nature of Cu^{2+} commonly leads to fluorescence quenching. There was a good linear correlation between the fluorescence intensity and the concentration of Cu^{2+} in the range from 0 μM to 10 μM, and the fluorescence intensity was retained even if more Cu^{2+} was added ($R^2 = 0.998$, inset



Scheme 1. Synthesis of probe DOQED.

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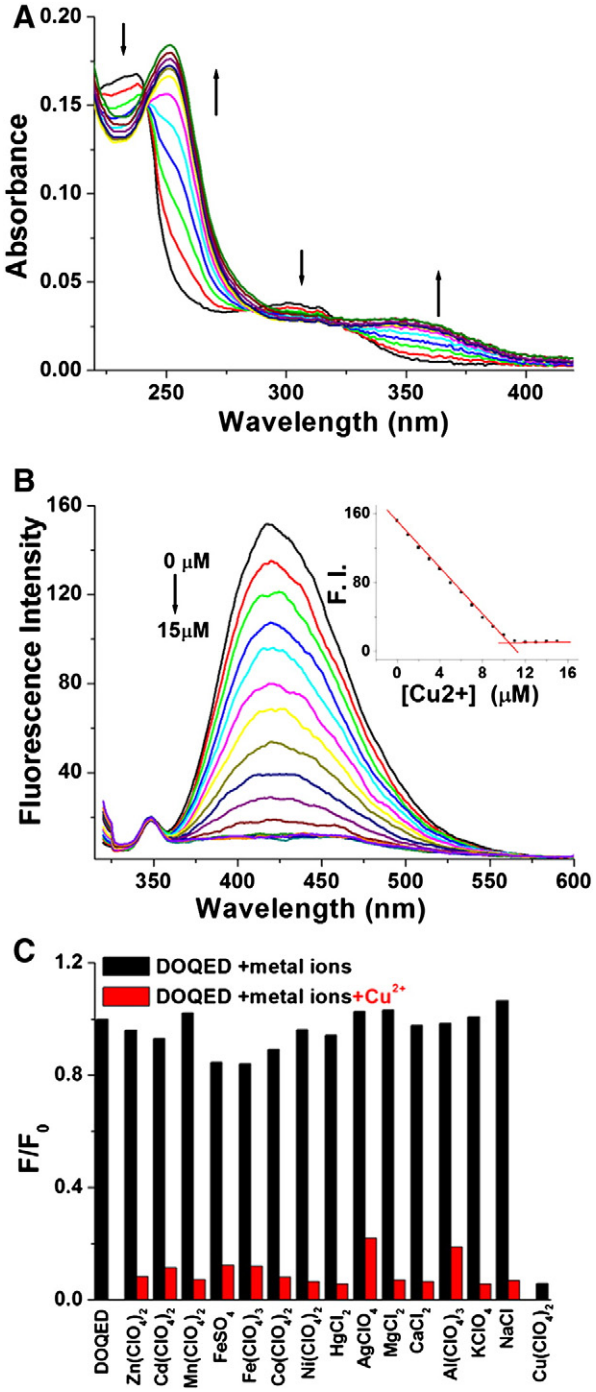

Fig. 1. (A) UV–vis spectra changes of the probe DOQED (10 μM) upon addition of Cu^{2+} (0–12 μM); (B) the fluorescence changes of the probe DOQED (10 μM) upon addition of Cu^{2+} (0–15 μM), Inset: A linear correlation between fluorescence intensity and concentrations of Cu^{2+}; (C) The fluorescence responses of DOQED to various cations. The black bars represent the fluorescence intensity of DOQED (10 μM) in the presence of various cations (100 μM), the red bars represent the changes of fluorescence intensity that occur upon the subsequent addition of Cu^{2+} (10 μM) to above solution.

in Fig. 1B). The results indicated that probe DOQED coordinated with Cu^{2+} with 1:1 stoichiometry, which is consistent with the result from the Job's plot (Fig. S10). Moreover, the single crystal of the $[Cu(DOQED)]^{2+}$ complex [10] was obtained to understand the coordinative geometry between probe DOQED and Cu^{2+}. In Fig. 2, it can be clearly seen that the probe complexes with Cu^{2+} in a 1:1 binding mode, and Cu(II) is hexa-coordinated with two oxygen atoms (O6, O9), three nitrogen atoms (N2, N3, N4) from DOQED, and other nitrogen

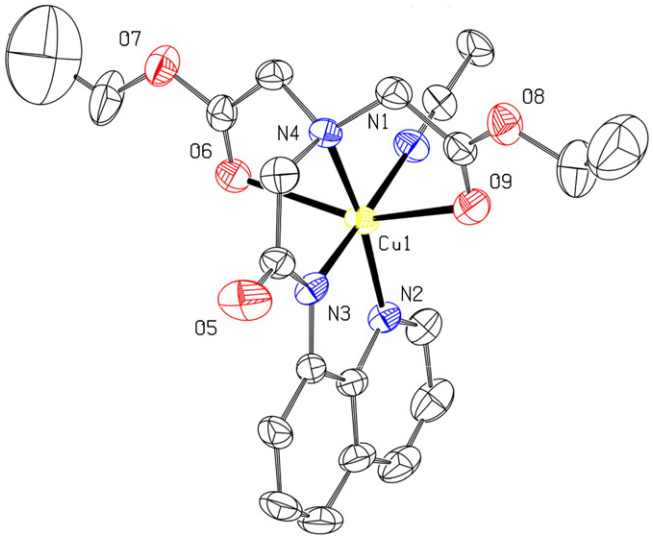

Fig. 2. The crystal structure of $[Cu(DOQED)]^{2+}$ complex (thermal ellipsoid at the 30% probability level). ClO_4^- and H atoms are omitted for clarity.

atom (N1) from acetonitrile. Selected bond lengths and bond angles for $[Cu(DOQED)]^{2+}$ complex are given in Table S1. The absolute quantum yield of DOQED and its Cu^{2+} complex is determined as 0.042 and 0.037. The detection limit of probe DOQED for Cu^{2+} was estimated to be 1.44×10^{-7} according to the reported method [11]. The dissociation constant, K_d, of the $[Cu(DOQED)]^{2+}$ complex was obtained to be 8.0×10^{-5} M from the fluorescence titration by theoretical nonlinear fitting assuming 1:1 stoichiometry [12] (Fig. S11). In addition, the fluorescence intensity of probe DOQED in the absence and presence of Cu^{2+} at various pH conditions was measured for exploitation of practical applications of the probe. The fluorescence responses towards Cu^{2+} can be employed in a wide pH range from 5.0 to 12.0 (Fig. S12).

The fluorescence titration of probe DOQED towards representative metal ions and its selectivity for Cu^{2+} were investigated (Fig. 1C). When probe DOQED was treated with a variety of metal ions, none of them, except $Cu(ClO_4)_2$, caused prominent fluorescence quenching at 420 nm. Furthermore, the competition experiment was carried out by adding 1 equiv. of Cu^{2+} to the solution of probe DOQED (10 μM) in the presence of 10 equiv. of other metal ions. There was little interference from other ions for Cu^{2+} to quench the emission. Taken together, probe DOQED is a highly selective probe for Cu^{2+}.

Since sulfide is known to react with copper ions to form a very stable CuS species, which has a low-solubility product constant $K_{sp} = 6.3 \times 10^{-36}$ [13]. We subsequently examined the fluorescence response of $[Cu(DOQED)]^{2+}$ complex to S^{2-} in a PBS buffer. As shown in Fig. 3A, upon addition of S^{2-} (0–5 equiv.) to a solution of probe DOQED (10 μM) in the presence of 10 μM Cu^{2+}, the fluorescence intensity was gradually recovered. The fluorescence intensity was enhanced by S^{2-} due to the fact that S^{2-} can coordinate with Cu^{2+} to form very stable CuS, and thus release the free probe. We also determined the fluorescence signal of the probe with different anions. As shown in Fig. 3B, complex $[Cu(DOQED)]^{2+}$ (10 μM) showed highly selectivity for S^{2-} (20 μM) over other common anions (100 μM), such as for NaF, NaCl, KBr, KI, Na_2SO_3, $NaHSO_3$, $Na_2S_2O_3$, $NaHSO_4$, Na_2SO_4, NaAc, KNO_3, Na_2CO_3, $NaHCO_3$, $NaNO_2$, Na_3PO_4, KH_2PO_4, NaH_2PO_2, Na_2HPO_4, $KClO_4$, $KBrO_3$. In addition, complex $[Cu(DOQED)]^{2+}$ could detect S^{2-} without interference even in the presence of these common anions. All these result suggest that the $[Cu(DOQED)]^{2+}$ complex is a practical probe for detection of S^{2-} with high selectivity.

In conclusion, the probe DOQED shows high selectivity towards Cu^{2+} via forming a $[Cu(DOQED)]^{2+}$ complex, which can be subsequently used in recognition of S^{2-} without suffering from other anion interference. Since all of our tests were performed in pure aqueous

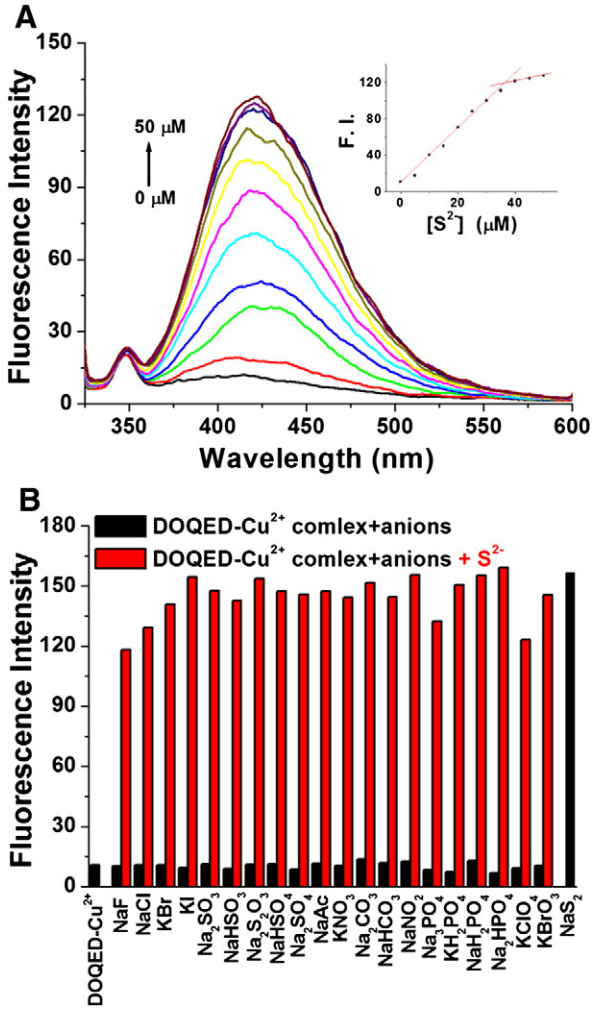

Fig. 3. (A) The fluorescence changes of the $[Cu(DOQED)]^{2+}$ complex (10 μM) upon addition of S^{2-} (0–50 μM), Inset: A linear correlation between fluorescence intensity and concentrations of S^{2-}; (B) The fluorescence responses of the $[Cu(DOQED)]^{2+}$ to various anions. The black bars represent the fluorescence intensity of $[Cu(DOQED)]^{2+}$ complex (10 μM) in the presence of various cations (100 μM), the red bars represent the changes of fluorescence intensity that occurs upon the subsequent addition of S^{2-} (20 μM) to above solution.

solutions, we expect the probe to be a convenient and practical sensor in detection of both Cu^{2+} and S^{2-} in biological samples.

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Appendix A. Supplementary data

Synthetic procedures, characterization data and additional spectroscopic data are available as supporting data. Supplementary data to this article can be found online at doi: http://dx.doi.org/10.1016/j.inoche.2013.07.005.

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