

Novel Ratiometric Fluorescent Sensor for Silver Ions

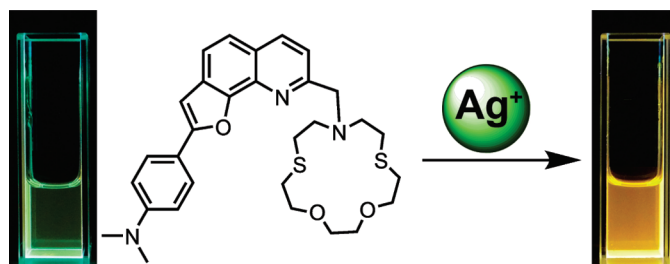
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ABSTRACT



Incorporating azacrown[N,S,O] into furoquinoline fluorophore yields a novel ratiometric fluorescent sensor FQ-crown for silver ions. UV–vis absorption and fluorescence emission investigations indicate that FQ-crown bears the features of a large Stokes shift, about 173 nm, and red-shift up to 50 nm in the emission spectra and high affinity for silver ions ($\log K = 7.21$) in ethanol in comparison with other competitive d^{10} metal ions.

Due to the widespread applications and the broad prospects of silver in the electronic industry and photographic and imaging industry, much attention has been paid to the negative impact of silver ions on the environment, especially on organisms. It is believed that silver ions can bind to various metabolites and enzymes such as inactivate sulphydryl enzymes.¹ Many approaches² such as fluorescence,

UV–vis absorption, atomic absorption, and ICP atomic emission spectroscopy have been employed to measure trace amounts of silver ions. Among these methodologies, fluorescence spectroscopy is widely used because of its high sensitivity and facile operation. More importantly, most fluorescent sensors are ready for in vivo and in vitro cellular imaging to make the fluorescence approach superior to other analytical methods. Therefore, much effort has been devoted

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(1) (a) Zhang, X. B.; Han, Z. X.; Fang, Z. H.; Shen, G. L.; Yu, R. Q. *Anal. Chim. Acta* **2006**, 562, 210. (b) Ratte, H. T. *Environ. Toxicol. Chem.* **1999**, 18, 89.

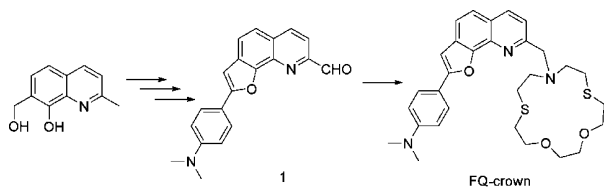
(2) (a) Schildkraut, D.; Dao, P.; Twist, J.; Davis, A.; Robillard, K. *Environ. Toxicol. Chem.* **1998**, 17, 642. (b) Ceresa, A.; Radu, A.; Peper, S.; Bakker, E.; Pretsch, E. *Anal. Chem.* **2002**, 74, 4027. (c) Kimura, K.; Yajima, S.; Tatsumi, K.; Yokoyama, M.; Oue, M. *Anal. Chem.* **2000**, 72, 5290. (d) Chung, S.; Kim, W.; Park, S. B.; Yoon, I.; Lee, S. S.; Sung, D. D. *Chem. Commun.* **1997**, 965. (e) Zeng, X. S.; Weng, L. H.; Chen, L. X.; Leng, X. B.; Ju, H. F.; He, X. W.; Zhang, Z. Z. *J. Chem. Soc., Perkin Trans.* **2001**, 545. (f) Amendola, V.; Esteban-Gómez, D.; Fabbri, L.; Licchelli, M.; Monzani, E.; Sancenón, F. *Inorg. Chem.* **2005**, 44, 8690.

(3) Selective examples: (a) Minta, A.; Kao, J. P. Y.; Tsien, R. Y. *J. Biol. Chem.* **1989**, 264, 8171. (b) Komatsu, H.; Miki, T.; Citterio, D.; Kubota, T.; Shindo, Y.; Kitamura, Y.; Oka, K.; Suzuki, K. *J. Am. Chem. Soc.* **2005**, 127, 10798. (c) Dong, X.; Yang, Y.; Sun, J.; Liu, Z.; Liu, B.-F. *Chem. Commun.* **2009**, 3883. (d) Kiyose, K.; Kojima, H.; Urano, Y.; Nagano, T. *J. Am. Chem. Soc.* **2006**, 128, 6548. (e) Chang, C. J.; Jaworski, J.; Nolan, E. M.; Sheng, M.; Lippard, S. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, 101, 1129. (f) Ko, S.-K.; Yang, Y.-K.; Tae, J.; Shin, I. *J. Am. Chem. Soc.* **2006**, 128, 14150. (g) Nolan, E. M.; Lippard, S. J. *J. Am. Chem. Soc.* **2003**, 125, 14270. (h) Royzen, M.; Dai, Z.; Canary, J. W. *J. Am. Chem. Soc.* **2005**, 127, 1612. (i) Yu, M.; Shi, M.; Chen, Z.; Li, F.; Li, X.; Gao, Y.; Xu, J.; Yang, H.; Zhou, Z.; Yi, T.; Huang, C. *Chem.—Eur. J.* **2008**, 14, 6892.

to design various fluorescent sensors for versatile objectives. Thus, a number of fluorescence sensors have been successfully applied to monitor metal ions such as calcium,^{3a–c} zinc,^{3d,e} mercury,^{3f,g} and copper,^{3h,i} both in solution and in cells. However, fluorescent sensors, in particular, ratiometric sensors for silver ions,⁴ have remained rare up to now because silver ions usually quench fluorescence emission via the electron transfer and intersystem crossing (isc) processes.⁴ⁱ In addition, a quantitative determination of analyte can be realized by ratiometric measurement that rules out extraneous influence factors including membrane permeability, incubation time, and temperature for biological systems. Thus, it is highly desirable to propose a novel sensor with ratiometric module for silver ions. Nevertheless, development of a ratiometric fluorescent sensor for silver still faces tremendous challenges. In this context, we present a novel ratiometric fluorescent sensor on the basis of the internal charge transfer (ICT) mechanism.

Recently, our group reported a ratiometric fluorescent sensor (FQ1) for zinc,⁵ which possesses a large Stokes shift and red-shift in the emission spectra due to ICT. The findings encouraged us to prepare a new ratiometric sensor **FQ-crown** comprised of furoquinoline and azacrown[N,S,O] for silver ions on the basis of a similar mechanism to that of FQ1 (Scheme 1). We envisaged that the crown moiety will display

Scheme 1. Synthesis of **FQ-crown**



high affinity for thio- or aminophilic metal ions such as silver ions, and the furoquinoline moiety acts not only as a fluorophore but as an auxiliary ligand for silver ions as observed for FQ1, where the crystal structure reveals the furoquinoline group participating in the coordination to the zinc ion. It turns out that **FQ-crown** is an effective ratiometric fluorescent sensor for silver ions and bears the features of a large Stokes shift, about 173 nm, red-shift up to 50 nm in the emission spectra, and high affinity for silver ions ($\log K = 7.21$) in ethanol in comparison with other competitive d¹⁰ metal ions.

(4) (a) Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. *J. Am. Chem. Soc.* **2000**, *122*, 968. (b) Liu, L.; Zhang, D.; Zhang, G.; Xiang, J.; Zhu, D. *Org. Lett.* **2008**, *10*, 2271. (c) Chatterjee, A.; Santra, M.; Won, N.; Kim, S.; Kim, K. J.; Kim, B. S.; Ahn, H. K. *J. Am. Chem. Soc.* **2009**, *131*, 2040. (d) Yang, R.-H.; Chan, W.-H.; Lee, A. W. M.; Xia, P.-F.; Zhang, H.-K.; Li, K. *J. Am. Chem. Soc.* **2003**, *125*, 2884. (e) Schmitt, M.; Lin, H. *Inorg. Chem.* **2007**, *46*, 9139. (f) Rathore, R.; Chebny, V. J.; Abdelwahed, S. H. *J. Am. Chem. Soc.* **2005**, *127*, 8012. (g) Ikeda, M.; Tanida, T.; Takeuchi, M.; Shinkai, S. *Org. Lett.* **2000**, *2*, 1803. (h) Sessler, J. L.; Tomat, E.; Lynch, V. M. *J. Am. Chem. Soc.* **2006**, *128*, 4184. (i) Akkaya, E. U.; Coskun, A. *J. Am. Chem. Soc.* **2005**, *127*, 10464. (j) Lyoshi, S.; Taki, M.; Yamamoto, Y. *Inorg. Chem.* **2008**, *47*, 3946. (k) Joseph, R.; Ramanujam, B.; Acharya, A.; Rao, C. P. *J. Org. Chem.* **2009**, *74*, 8181.

(5) Xue, L.; Liu, C.; Jiang, H. *Chem. Commun.* **2009**, 1061.

The spectroscopic properties of **FQ-crown** were evaluated in ethanol solution. As shown in Figure 1, **FQ-crown**

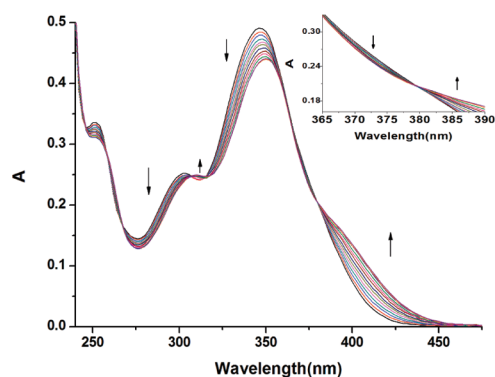


Figure 1. UV–vis spectra of **FQ-crown** (12.5 μM) upon titration of Ag^+ (0–1.2 equiv) in ethanol. Inset: UV–vis absorption bands of **FQ-crown** at 365–390 nm.

exhibits a maximal absorption at 346 nm. Upon addition of silver ions (0–1.2 equiv), the absorbance at 346 nm decreases gradually, and simultaneously, a significant absorption band like a shoulder at 405 nm increases, accompanying several isosbestic points at 380, 322, 307, 267, and 258 nm. Moreover, the absorbance at 405 nm remains constant in the presence of more than 1 equiv of silver ions, indicating the formation of a 1:1 complex between the **FQ-crown** and silver ion, which is in good agreement with 1:1 stoichiometry for the silver complex determined by the Job's plot yielded from UV–vis absorption (Figure S1, Supporting Information).

As depicted in Figure 2, the fluorescence emission spectra of **FQ-crown** display an emission band centered at 519 nm

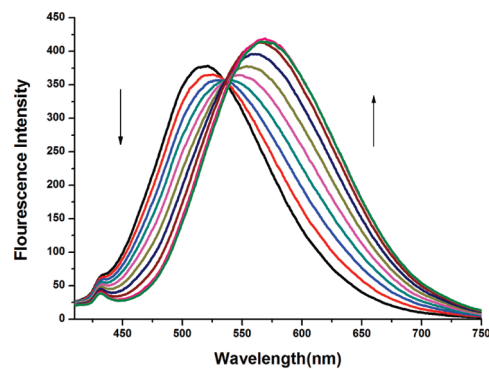


Figure 2. Fluorescence emission spectra ($\lambda_{\text{ex}} = 380 \text{ nm}$) of **FQ-crown** (5 μM) upon addition of Ag^+ (0–1 equiv) in ethanol.

when excited at the isosbestic point 380 nm. Upon addition of various concentrations of silver ions, the emission band centered at 519 nm decreases, and a new emission peak gradually appears at longer wavelength (568 nm) with a

bathochromic shift of about 49 nm. The quantum yield of the complex in ethanol was calculated to be 0.18, which is slightly higher than that of the free ligand ($\Phi = 0.14$). To achieve a reliable binding constant (K) via fluorescence titration,⁶ the titrations were conducted in a very dilute solution (1.0×10^{-6} M). The binding constant was found to be $\log K = 7.21 \pm 0.07$ via a nonlinear least-squares treatment of the fluorescence titration profiles (Figure S3, Supporting Information).

Subsequently, we evaluated the response of **FQ-crown** to other metal ions. The fluorescence emission spectrum of **FQ-crown** demonstrates that only silver ions cause a bathochromic shift ($\Delta\lambda_{em} = 49$ nm) with slight fluorescence intensity enhancements as depicted in Figure 3. In sharp

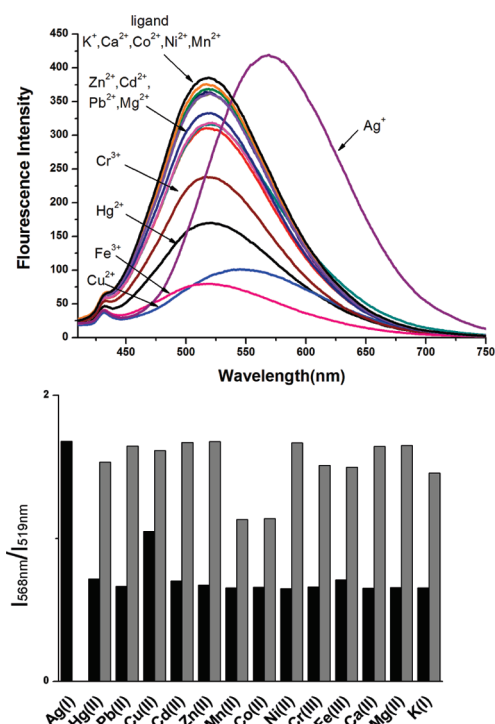


Figure 3. Fluorescence emission spectra of **FQ-crown** (5 μM) in the presence of various metal ions in ethanol (Top). Black bars represent the ratio I_{568nm}/I_{519nm} of **FQ-crown** (5 μM) in the presence of 1 equiv of Mn²⁺, Fe³⁺, Co²⁺, Ni²⁺, Cu²⁺, Cd²⁺, Hg²⁺, and Pb²⁺ and 100 equiv of Mg²⁺, Ca²⁺, and K⁺. Gray bars represent the ratio of I_{568nm}/I_{519nm} of **FQ-crown** (5 μM) in the presence of the indicated metal ions, followed by 1 equiv of silver ion (Bottom).

contrast, other metal ions quench the emission in various extent upon addition of 1 equiv of Cr³⁺, Fe³⁺, Cu²⁺, Hg²⁺, Zn²⁺, Cd²⁺, and Pb²⁺, whereas Ca²⁺, Mg²⁺, Co²⁺, Ni²⁺, K⁺, and Mn²⁺ slightly depress the fluorescence intensity.

To further gauge selectivity for silver ions over other transition metal ions, we also examined transition metal/silver coexisted systems. By monitoring the ratio of fluorescence intensities at 568 and 519 nm, silver ions could be distin-

guished apparently from other metal ions. Furthermore, only Mn²⁺ and Co²⁺ have a little impact on the I_{568nm}/I_{519nm} value of the silver complex. The results imply the sensor bears high selectivity for silver ions in the presence of other competitive metal ions.

The survey of emission responses of **FQ-crown** in the presence of various ions indicates that the nitrogen atom in the furoquinoline moiety got involved in the coordination with silver ions, which induces an ICT process similar to that of FQ1,⁵ that is, the interaction between the silver ion and the nitrogen atom in the furoquinoline moiety enhances the electron-withdrawing ability of furoquinoline that leads to an ICT process and consequently results in a large red shift. We therefore conclude that the silver ion is bound to the crown ether moiety and the furoquinoline fluorophore.

To seek further detailed information on the coordination, we also carried out ¹H NMR titration experiments in CD₃OD. As shown in Figure 4, upon increasing the amount of silver

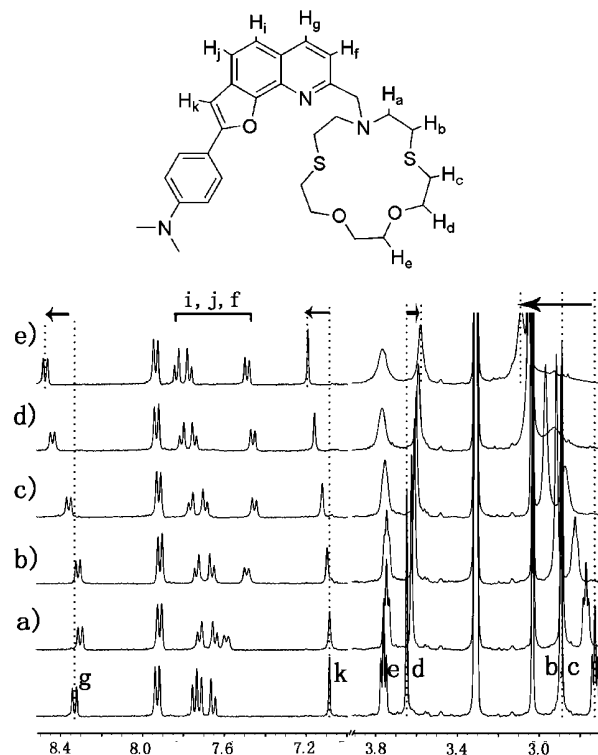


Figure 4. Partial ¹H NMR (400 MHz) spectral changes of **FQ-crown** (20 mM) in CD₃OD upon addition of (a) 0.2 equiv, (b) 0.4 equiv, (c) 0.6 equiv, (d) 0.8 equiv, and (e) 1.0 equiv of AgNO₃ at 298 K.

ions dissolved in D₂O, considerable changes are exhibited in the chemical shifts of protons in **FQ-crown** especially in the crown moiety. In details, the proton H_a displays a dramatic downshift from $\delta = 2.64$ to 3.09 ppm up to $\Delta\delta = 0.45$ ppm. H_b and H_c at $\delta = 2.90$ ppm also demonstrate a similar but weak downshift to 3.09 ppm with $\Delta\delta = 0.19$ ppm, while H_d and H_e show a slight change. On the other hand, protons H_f, H_i, and H_j in furoquinoline, aggregating

(6) Boiocchi, M.; Boca, D. L.; Gómez, E. D.; Fabbriizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507.

in the absence of silver ions, spread over a large chemical shift of $\Delta\delta = 0.32$ ppm, while 1 equiv of silver ions was introduced. The other aromatic protons such as Hg and Hk also experienced downfield shifts. These data further confirm the conclusion that both crown ether moiety and furoquinoline fluorophore are involved in the coordination with silver ions as envisaged. Additionally, all proton chemical shifts remain constant when the amount of silver ions is beyond 1 equiv, suggesting high affinity for the silver ion.

In summary, we have prepared a ratiometric fluorescence sensor **FQ-crown** for silver ions in ethanol, which demonstrates a large Stokes shift of 173 nm and gives rise to bathochromic shift of about 50 nm in fluorescence emission spectra upon addition of silver ions. In addition, **FQ-crown**

shows high affinity and selectivity for silver ions over other competitive metal ions. We expect that **FQ-crown** may have wide applications for quantitative measurement of silver through its ratiometric module.

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Supporting Information Available: Synthetic procedures, characterization of **FQ-crown**, and additional spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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