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Highly Selective Ratiometric Fluorescence Determination of Ag$^+$ Based on a Molecular Motif with One Pyrene and Two Adenine Moieties

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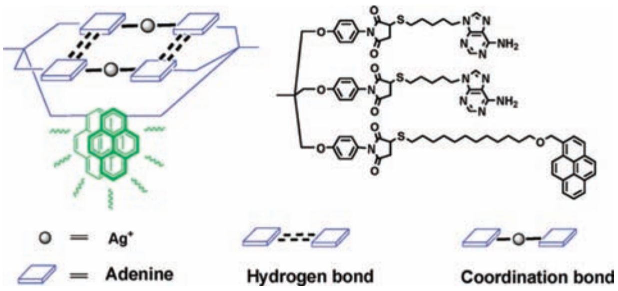
ABSTRACT



A highly selective ratiometric fluorescence sensor for Ag$^+$ was developed with a molecular motif containing one pyrene and two adenine moieties.

Silver and its compounds are widely used in electrical industry, photographic and imaging industry, and pharmacy. However, silver ions inactivate sulfhydryl enzymes and combine with amine, imidazole, and carboxyl groups of various metabolites. There are also many reports on silver bioaccumulation and toxicity.[1] Thus, development of sensitive and selective methods for the determination of trace amounts of silver ions (Ag$^+$) in various media is of considerable importance for the environment and human health.

Various approaches,[2] such as atomic absorption spectroscopy and inductively coupled plasma-mass spectroscopy, have been described for the trace-quantity (down to ppb range) determination of Ag$^+$. Potentiometric methods for Ag$^+$ assay based on ion-selective electrodes are also reported with detection limit reaching 10^{-8} M range. But, most of these methods are expensive and time-consuming in practice. In comparison, sensitive and selective optical sensors for Ag$^+$ with simple instrumental implementation and easy-operation

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(1) (a) Ratte, H. T. *Environ. Toxicol. Chem.* **1999**, *18*, 89–108. (b) Ganjali, M. R.; Norouzi, P.; Alizadeh, T.; Adib, M. *J. Braz. Chem. Soc.* **2006**, *17* (7), 1217–1222. (c) Zhang, X. B.; Han, Z. X.; Fang, Z. H.; Shen, G. L.; Yu, R. Q. *Anal. Chim. Acta* **2006**, *562*, 210–215. (d) Peng, H. Q.; Brooks, B. W.; Chan, R.; Chyan, O.; Point, T. W. L. *Chemosphere* **2002**, *46*, 1141–1146. (e) Kazuyuki, M.; Nobuo, H.; Takatoshi, K.; Yuriko, K.; Osamu, H.; Yashihisa, I.; Kiyoko, S. *Clin. Chem.* **2001**, *47*, 763–766. (f) Wan, A. T.; Conyers, R. A.; Coombs, C. J.; Masterton, J. P. *Clin. Chem.* **1991**, *37*, 1683–1687.

(2) (a) Ceresa, A.; Radu, A.; Peper, S.; Bakker, E.; Pretsch, E. *Anal. Chem.* **2002**, *74*, 4027–4036. (b) Kimura, K.; Yajima, S.; Tatsumi, K.; Yokoyama, M.; Oue, M. *Anal. Chem.* **2000**, *72*, 5290–5294. (c) Mazloum, M.; Niassary, M. S.; Chahooki, S. H. M.; Amini, M. K. *Electroanalysis* **2002**, *14*, 376–380. (d) Shervedani, R. K.; Babadi, M. K. *Talanta* **2006**, *69*, 741–746. (e) Javanbakht, M.; Ganjali, M. R.; Norouzi, P.; Badiei, A.; Hasheminasab, A. *Electroanalysis* **2007**, *19*, 1307–1314. (f) Chung, S.; Kim, W.; Park, S. B.; Yoon, I.; Lee, S. S.; Sung, D. D. *Chem. Commun.* **1997**, 965–966. (g) Teixidor, F.; Flores, M. A.; Escriche, L.; Viñas, C.; Casabó, J. *Chem. Commun.* **1994**, 963–964. (h) 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. 2* **2001**, 545–549.

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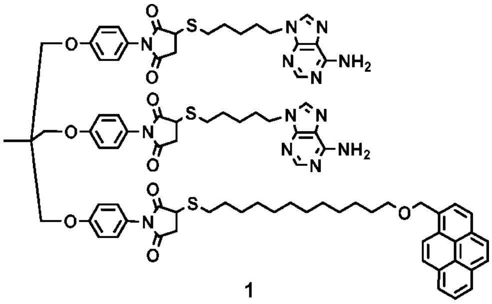
have received a lot of attention.[3] To the best of our knowledge, ratiometric fluorescent sensors for Ag^+, especially with fluorescence enhancement technique, still remain rare.[3f,g] Herein, we describe a selective ratiometric fluorescent sensor for Ag^+ based on a molecular motif with one pyrene and two adenine moieties (compound **1**, Scheme 1).

Scheme 1. Chemical Structure of Compound **1**



Our design employs coordination between Ag^+ and nucleobases to induce pyrene excimer emission. Recent results have revealed that the nucleobases offer a versatile platform for metal ion coordinations.[4] For instance, thymine can bind Hg^{2+} specifically, and by making use of this feature a sensitive and selective "turn on" fluorescent chemosensor for Hg^{2+} ion based on a pyrene−thymine dyad has been described by our group recently.[5] 9-Substituted adenine offers three main coordination sites (N1, N3, and N7).[6] While most of the complexes of adenine with metal ions exhibit mono- and bidentate coordination modes, the 3N (μ-N1, N3, N7) coordination mode for 9-substituted adenine has been observed in silver−adenine metallaquartets.[7] When compound **1** is allowed to react with Ag^+, an extended complex is expected to form; formation of such complex would induce the pyrene moiety in **1** to be adjacent to each other, and accordingly result in pyrene excimer emission. The results show that compound **1** can indeed selectively bind Ag^+ inducing the gradual enhancement of the pyrene excimer emission and the simultaneous decrease of the monomer emission of the pyrene moiety. Therefore, highly selective ratiometric fluorescence determination of Ag^+ is realized with compound **1**.

The synthesis of **1** started from 1,1,1-tris (hydroxymethyl) ethane which was converted to trisulfonate **2** by reaction with benzenesulfonyl chloride. After reaction with 4-nitrophenol in the presence of K_2CO_3, compound **2** was transformed into compound **3**. Reduction of **3** and further reaction with maleic anhydride led to trimaleimide **5**. Reaction of trimaleimide **5** with thiol **6** afforded **7** exclusively by controlling the amount of **6** added to the reaction mixture. In situ reaction of bis-maleimide **7** with thiol **8** yielded the desired compound **1**.[8]

Figure 1 shows the fluorescence spectrum of compound **1** and those in the presence of different amounts of $AgClO_4$ in THF. Compound **1** shows typical monomeric emission bands of pyrene unit around 376 and 395 nm (λ_{ex} = 344 nm);[9] the emission in the range of 450−600 nm was rather

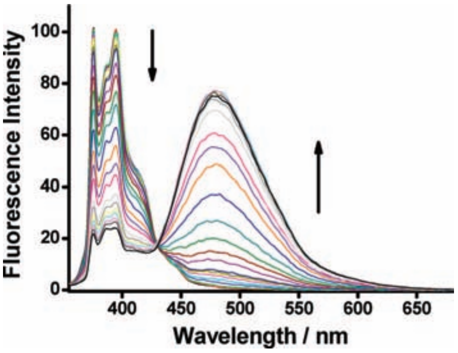


Figure 1. Fluorescence spectra of compound **1** (2.0×10^{-5} M in THF) in the presence of increasing amounts of $AgClO_4$ (from 0 to 27 μM).

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[3] See, for example: (a) Kwon, O.-S.; Kim, H.-S. *Supramol. Chem.* **2007**, *19*, 277–281. (b) Akkaya, E. U.; Coskun, A. *J. Am. Chem. Soc.* **2005**, *127*, 10464–104651. (c) Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. *J. Am. Chem. Soc.* **2000**, *122*, 968–969. (d) Chen, J. L.; Zhu, C. Q. *Anal. Chim. Acta* **2005**, *546*, 147–153. (e) Tong, H.; Wang, L. X.; Jing, X. B.; Wang, F. S. *Macromolecules* **2002**, *35*, 7169–7177. (f) Paker, J.; Glass, T. E. *J. Org. Chem.* **2001**, *66*, 6505–6512. (g) Yang, R. H.; Chan, W. H.; Lee, A. W. M.; Xia, P. F.; Zhang, H. K.; Li, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 2884–2885.

[4] (a) Lippert, B. *Coord. Chem. Rev.* **2000**, *200−202*, 487–516. (b) Navarro, J. A. R.; Lippert, B. *Coord. Chem. Rev.* **1999**, *185−186*, 653–667. (c) Martin, R. B. *Acc. Chem. Res.* **1985**, *18*, 32–38. (d) Schreiber, A.; Lüth, M. S.; Erxleben, A.; Fusch, E. C.; Lippert, B. *J. Am. Chem. Soc.* **1996**, *118*, 4124–4132. (e) Sigel, H. *Chem. Soc. Rev.* **1993**, *22*, 255–267. (f) García-Terán, J. P.; Castillo, O.; Luque, A.; García-Couceiro, U.; Román, P.; Lezama, L. *Inorg. Chem.* **2004**, 4549–4551.

[5] Wang, Z.; Zhang, D. Q.; Zhu, D. B. *Anal. Chim. Acta* **2005**, *549*, 10–13. (a) Other chemical sensors for Hg^{2+} have been also reported: (a) Lee, J.-S.; Han, M. S.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4093–4096. (b) Ono, A.; Togashi, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 4300–4302. (c) Tang, Y. L.; He, F.; Yu, M. H.; Feng, F. D.; An, L. L.; Sun, H.; Wang, S.; Li, Y. L.; Zhu, D. B. *Macromol. Rapid Commun.* **2006**, *27* (6), 389–392. (d) Liu, B.; Tian, H. *Chem. Commun.* **2005**, 3156–3158. (e) Zhang, H.; Han, L. F.; Zachariasse, K. A.; Jiang, Y. B. *Org. Lett.* **2005**, *7* (19), 4217–4220. (f) Guo, X. F.; Qian, X. H.; Jia, L. H. *J. Am. Chem. Soc.* **2004**, *126*, 2272–2273. (g) Nolan, E. M.; Lippard, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 14270–1427.

[6] (a) Arpalahti, J.; Klika, K. D.; Molander, S. *Eur. J. Inorg. Chem.* **2000**, 1007–1013. (b) De Meester, P.; Goodgame, D. M. L.; Skapski, A. C.; Warnke, Z. *Biochem. Biophys. Acta* **1973**, *324*, 301–303.

[7] (a) Purohit, C. S.; Verma, S. *J. Am. Chem. Soc.* **2006**, *128*, 400–401. (b) Purohit, C. S.; Mishra, A. K.; Verma, S. *Inorg. Chem.* **2007**, *46*, 8493–8495. (c) Purohit, C. S.; Verma, S. *J. Am. Chem. Soc.* **2007**, *129*, 3488–3489.

[8] Characterization data of compound **1**: mp 138 °C dec; ^1H NMR (600 MHz, $CDCl_3$, ppm) δ 8.35−8.38 (m, 3H), 8.12−8.18 (m, 4H), 8.00−8.05 (m, 4H), 7.79 (s, 2H), 7.16−7.19 (m, 6H), 6.98 (d, J = 8.7 Hz, 6H), 5.84 (br, 4H), 5.21 (s, 2H), 4.17−4.20 (m, 4H), 4.08 (s, 6H), 3.78−3.80 (m, 3H), 3.59−3.60 (m, 2H), 3.22−3.27 (m, 3H), 3.09−3.11 (m, 2H), 2.92−2.93 (m, 3H), 2.76−2.80 (m, 3H), 2.60−2.65 (m, 3H), 1.91−1.93 (m, 5H), 1.64−1.67 (m, 12H), 1.40−1.44 (m, 4H), 1.37−1.39 (m, 6H), 1.20−1.25 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.73, 174.67, 173.0, 172.8, 158.0, 154.4, 151.9, 149.1, 139.5, 130.9, 130.25, 130.18, 129.8, 128.3, 126.64, 126.57, 126.4, 126.3, 125.9, 124.9, 124.1, 123.9, 123.6, 123.5, 122.5, 118.6, 114.2, 70.4, 69.6, 69.2, 44.8, 42.6, 39.5, 38.1, 38.0, 35.2, 35.0, 30.9, 30.5, 28.8, 28.4, 28.1, 28.0, 27.8, 27.3, 25.2, 24.6, 16.2, 7.6; MALDI-TOF $(M + 2H)^+$, 1541.7, $(M + Na + H)^+$, 1563.7; HRMS (MALDI-TOF) calcd for $C_{84}H_{94}N_{13}O_{10}S_3^+$ $(M + H)^+$ 1540.6403, found 1540.6388. COSY, HMBC, HSQC, and TOCSY spectra are provided in the Supporting Infromation.

[9] Bodenant, B.; Fages, F.; Delville, M. H. *J. Am. Chem. Soc.* **1998**, *120*, 7511–7519.

weak. However, after addition of $AgClO_4$, the emission bands at 376 and 395 nm attributed to the monomeric emission of pyrene unit became gradually weak and simultaneously a new broad featureless band with $\lambda_{max} = 478$ nm, typical of pyrene excimer emission, emerged.[10] The intensity of this new emission band increased by increasing the amounts of $AgClO_4$ added to the solution of **1** as displayed in Figure 1. The variation of the monomeric emission (reduction of the intensity) and the excimer emission (enhancement of the intensity) of pyrene moiety of **1** after addition of $AgClO_4$ led to an isoemission point at 430 nm. Similar fluorescnce spectral variation was observed for **1** after addition of Ag(I) salts with different anions (NO_3^-, PF_6^-, $CF_3SO_3^-$, AsF_6^-, and BF_4^-) (see Figure S8, Supporting Information).

Since an aqueous solution of $AgClO_4$ was used for the fluorescence measurement, the possibility that the pyrene excimer emission is due to aggregation of **1** exists. But, addition of the same volume of water to the THF solution of **1** did not lead to the pyrene excimer emission; thus, this control experiment ruled out such possibility. Also, the competitive experiments with other metal ions, to be discussed below, support this conclusion.

Figure 2 shows the variation of the fluorescence intensity ratio (I_{478}/I_{395}) between the emission band at 478 nm and that at 395 nm vs the concentration of $AgClO_4$. Although the monomeric and excimer emissions started to decrease and increase, respectively, upon addition of Ag^+, the fluorescence intensity ratio (I_{478}/I_{395}) was small and was enhanced just slightly when the concentration of Ag^+ in the solution of **1** was below 10 μM; but, it was enhanced significantly if more Ag^+ was added to the solution of **1**. A nearly linear plot of I_{478}/I_{395} vs the concentration of Ag^+ resulted ($I_{478}/I_{395} = 0.21[Ag^+]-2.51$, $r = 0.999$, $n = 12$) as shown in Figure 2.

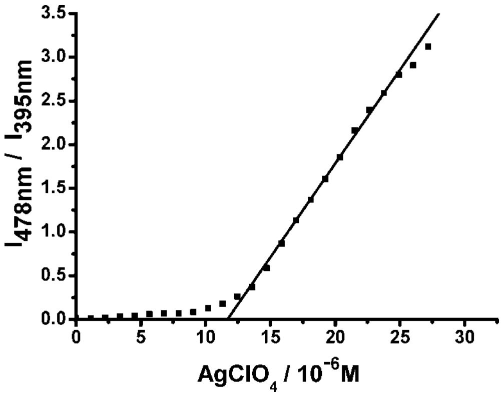
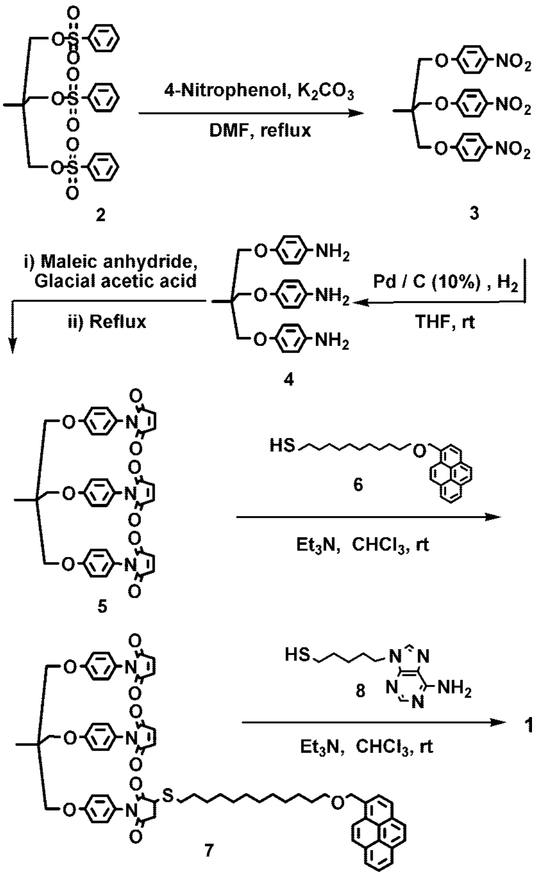


Figure 2. Plot of the fluorescence intensity ratio (I_{478}/I_{395}) between excimer emission band at 478 nm and monomer emission band at 395 nm vs the concentration of $AgClO_4$.

Scheme 2. Synthetic Approach for Compound **1**



It should be noted that the enhancement of the excimer emission intensity around 478 nm became rather small while the monomeric emission band continued to decrease if more Ag^+ ($[Ag^+] > 2.5 \times 10^{-5}$ M) was present in the solution of **1**; further addition of Ag^+ led to the reduction of both monomeric and excimer emission bands. This can be attributed to fluorescence quenching by silver ions[3c,11] that bind to coordination sites (N1, N3, N7) in compound **1**. It is expected that more Ag^+ would bind adenine moiety if more Ag^+ is present.

In addition, absorption and ^1H NMR spectral studies also clearly indicated the coordination of **1** with Ag^+. As shown in Figure S5 (Supporting Information), the absorption intensities of **1** in the range of 225−242 and 281−318 nm increased while those in the range of 249−269 nm decreased upon on adition of Ag^+. Moreover, the absorption bands around 250 and 340 nm were slightly red-shifted. These absorption spectral changes indicated the binding of **1** with Ag^+ and formation the coordination complexes, according to previous report.[12] ^1H NMR spectra of **1** in the presence

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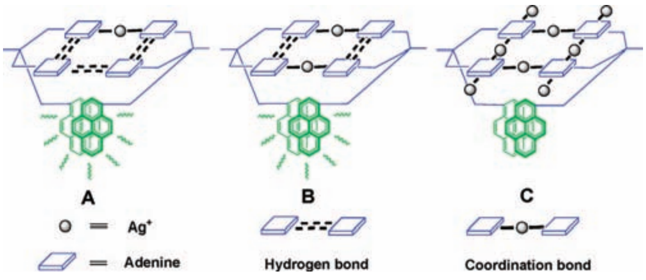
(10) (a) Nishizawa, S.; Kato; Teramae, N. *J. Am. Chem. Soc.* **1999**, *121*, 9463–9464. (b) Sahoo, D.; Narayanaswami, V.; Kay, C. M.; Ryan, R. O. *Biochemistry* **2000**, *39*, 6594–6601. (c) Kim, J. S.; Choi, M. G.; Song, K. C.; No, K. T.; Ahn, S.; Chang, S.-K. *Org. Lett.* **2007**, *9*, 1129–1132. (d) Choi, J. K.; Kim, S. H.; Yoon, J.; Lee, K.-H.; Bartsch, R. A.; Kim, J. S. *J. Org. Chem.* **2006**, *71*, 8011–8015. (e) Yuasa, H.; Miyagawa, N.; Izumi, T.; Nakatani, M.; Izumi, M.; Hashimoto, H. *Org. Lett.* **2004**, *6*, 1489–1492.

(11) Shamsipur, M.; Alizadeh, K.; Hosseini, M.; Caltagirone, C.; Lippolis, V. *Sens, Actuator B-Chem.* **2006**, *113*, 892–899.

(12) Rubina, A. Y.; Rubin, Y. V.; Sorokin, V. A.; Shukla, M. K.; Leszczynski, J. *Pol. J. Chem.* **2005**, *79*, 1873–1882.

of different amounts of Ag^+ were recorded, and the signals at 7.66 and 7.70 ppm due to protons linked to C-2 and C-8 of adenine units were gradually downfield shifted by increasing the amounts of Ag^+ (see Figure S7, Supporting Information). This provided further support for the coordination of **1** with Ag^+. In fact, a TOF/MS signal at 1648.3 (*m*/*z*) corrsponding to $[\mathbf{1}\cdot Ag]_2^{2+}$ was detected for the sample of **1** with 1.0 equiv of Ag^+.

Scheme 3. Illustration of the Binding Modes of Compound **1** with Ag^+



Based on the above studies, the possible stepwise binding of **1** with Ag^+ is illustrated in Scheme 3. Initially, two molecules of **1** are associated through the coordination of two adenine moieties with one Ag^+ and the "dimer" may be further stabilized by the H-bonding among the adenine moieties (A in Scheme 3); as a result, the two pyrene moieties are brought close to induce pyrene excimer emission. When more Ag^+ is present in the solution, coordination of another Ag^+ with another two adenine moieties would occur and accordingly the "dimer" would be further stabilized (B in Scheme 3). As mentioned, adenine offers at least three coordination sites, thus further coordination of **1** with Ag^+ can occur as illustrated in Scheme 3C. As a result, the pyrene moieties would be surrounded by more Ag^+, which would cause the quenching of both monomeric and excimer emission of pyrene moieties since Ag^+ is an effective fluorescence quencher.

The fluorescence spectrum of **1** was investigated in the presence of other perchlorate metal ions, including Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cs^+, Cu^{2+}, Er^{3+}, Fe^{3+}, Fe^{2+}, Gd^{3+}, Hg^{2+}, K^+, Mg^{2+}, Mn^{2+}, Na^+, Nd^{3+}, Ni^{2+}, Pb^{2+}, and Zn^{2+}, under identical conditions. As shown in Figure 3, variation of the fluorescence intensity ratio (I_{478}/I_{395}) was rather small (compared to that in the presence of Ag^+) after addition of these metal ions, even for Hg^{2+} which is usually difficult to be distinguished from Ag^+ by available methods. These results clearly indicate that compound **1** shows good selectivity toward Ag^+ and that other competitive metal ions, such as Pb^{2+}, Hg^{2+}, Fe^{3+}, and Cd^{2+}, will induce a rather low interfering effect on this ratiometric fluorescence assay for Ag^+.

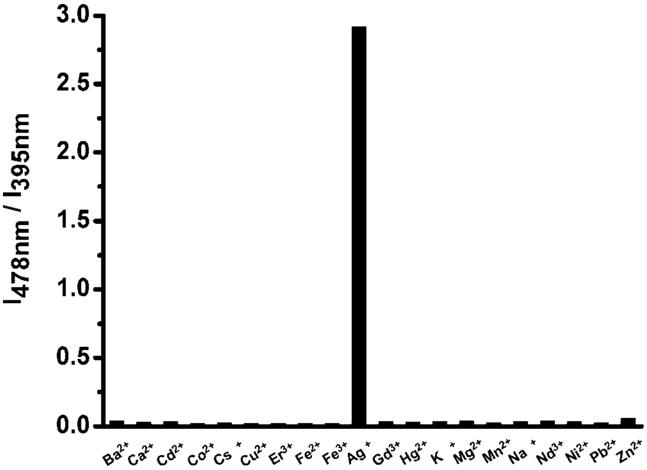


Figure 3. Fluorescence intensity ratio (I_{478}/I_{395}) between the excimer emission band at 478 nm and the monomeric emission band at 395 nm of compound **1** (1.0×10^{-5} M in THF) in the presence of various metal ions (1.25×10^{-5} M).

In summary, compound **1** was designed with a view to developing new fluorescent sensors for Ag^+ by making use of the binding of adenine with Ag^+ to induce excimer emission. Fluorescent spectral results clearly indicate that compound **1** can be used as ratiometric fluorescent sensor for Ag^+ with good selectivity and sensitivity. Further studies include the design of new analogues of **1** with good solubility in water which will enable the practical application of this type of Ag^+ sensor to be implemented.

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Supporting Information Available: Synthesis and characterization data; fluorescence and absorption spectra of compound **1** under different conditions; ^1H NMR and TOF/MS spectra of **1** in the presence of Ag^+. This material is available free of charge via the Internet at http://pubs.acs.org.

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