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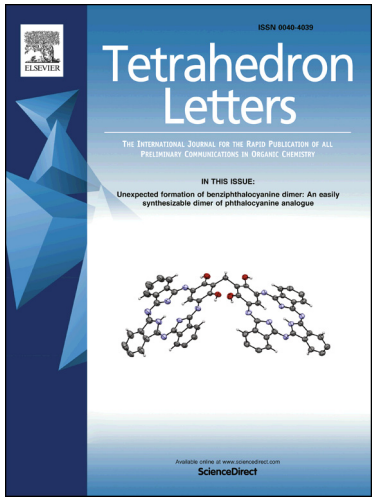

Cu^{2+}-selective turn-on fluorescence signaling based on metal-induced hydrolysis of pyrenecarbohydrazide

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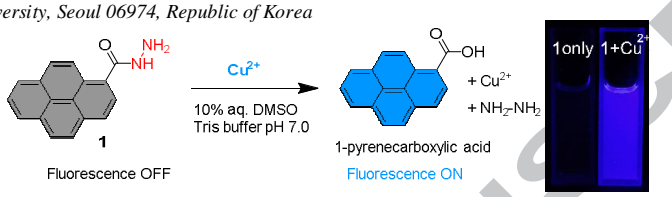

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ABSTRACT

We developed a simple Cu^{2+}-selective turn-on fluorescence signaling probe based on the hydrolysis of 1-pyrenecarbohydrazide (**1**) to 1-pyrenecarboxylic acid. Probe **1** exhibited prominent fluorescence signaling of Cu^{2+} ions in a 10% aqueous Tris-buffered (pH 7.0) DMSO solution with a detection limit of 5.93×10^{-8} M. Signaling with control compounds derived from pyreneacetic acid and pyrenebutyric acid showed that the fluorescence signal became less pronounced as the distance between the hydrazide functionality and the pyrene fluorophore increased. As a practical application, this probe was employed for the determination of Cu^{2+} in a simulated semiconductor wastewater.

The development of selective signaling and visualization systems for biologically and environmentally important species has attracted increasing research interest.[1] In particular, selective and sensitive metal ion signaling is important in chemical, biological, environmental, and industrial applications.[2] Copper, the third most abundant transition metal ion in the body after iron and zinc, is one of the most important metal ionic species in the human body. It plays critical roles in several physiological processes, such as a signal messenger in cell signaling, bone formation, cellular respiration, connective tissue development, and a catalytic cofactor in metalloenzymes.[3] Further, because of its high ductility, malleability, electrical and thermal conductivities, and resistance to corrosion, copper has been one of the most important metals in modern industrial activities.[4] However, copper causes serious diseases, such as Alzheimer's, Parkinson's,[5] Menkes, and Wilson diseases,[6] as well as Indian childhood cirrhosis.[7] Owing to its toxicity, the United States Environmental Protection Agency (USEPA) has recommended a safe limit of 20 μM for Cu^{2+} in drinking water.[8] For this reason, development of selective and sensitive methods for convenient monitoring of Cu^{2+} levels in environmental analytes is a critical challenge.

Quantitative Cu^{2+} determinations have been routinely carried out using standard instrumental methods, such as atomic absorption spectroscopy,[9] inductively coupled plasma mass spectrometry,[10] and inductively coupled plasma atomic emission spectrometry.[11] However, such instrument-based determination techniques require high costs and well-trained personnel and are prone to operational difficulties. For this reason, a number of optical probes have been developed for Cu^{2+} determination, and they tend to exhibit convenient, selective, and sensitive colorimetric and fluorescence changes.[12]

In particular, fluorescence signaling is attractive owing to its high sensitivity and specificity. However, most Cu^{2+}-selective fluorescence sensors show turn-off-type signaling behavior resulting from fluorescence quenching by strongly interacting Cu^{2+} ions.[13] In contrast, well-designed reaction-based probes utilizing specific Cu^{2+}-assisted reactions commonly show more desirable turn-on-type fluorescence signaling. For the construction of Cu^{2+}-selective reaction-based probes, Cu^{2+}-assisted hydrolysis, oxidation, and spirolactam ring-opening processes have been employed.

The most successful approach for designing Cu^{2+} signaling reaction-based probes is based on the spirolactam ring-opening process of a variety of rhodamine hydrazide derivatives, building on the pioneering research of Czarnik.[14,15] Concurrently, Cu^{2+}-assisted hydrolysis reactions involving an acetate of 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY),[16] a picolinate of coumarin,[17] and hydrazones of coumarin and hydroxyquinoline have been successfully employed for the selective determination and visualization of Cu^{2+} ions in various biological and environmental samples.[18] In particular, hydrolysis of 5-(dimethylamino)naphthalene-1-sulfonyl hydrazide[19] and D-luciferin hydrazide[20] was effectively utilized for the determination of Cu^{2+} levels in simulated urine samples and intratumoral imaging of Cu^{2+} ions, respectively. Cu^{2+}-assisted oxidative processes involving coupling reactions between 4-aminoantipyrine and phenol[21] or anilines,[22] and oxidative

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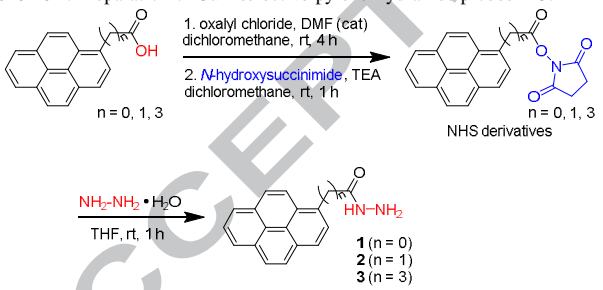
coupling reaction of azoaromatics[23] and *N*-acylhydrazones[24] have also been successfully developed.

However, the majority of the literature focuses mainly on the determination and imaging of Cu^{2+} ions in biological samples. Cu^{2+} determination using optical probes in environmentally important analytes, such as tap water and wastewater, is relatively less exploited. Herein, we report a fluorogenic Cu^{2+}-selective signaling probe based on Cu^{2+}-induced hydrolysis of pyrenecarbohydrazide to pyrenecarboxylic acid. This probe has a simple structure and is easy to synthesize. The effect of spacer length in the probe on the signaling was also elucidated using control compounds with no, methylene, and trimethylene spacers between pyrene and the hydrazide moiety. Finally, the designed probe was used for the determination of Cu^{2+} concentrations in simulated semiconductor wastewater.

The hydrazide-based probes were designed by combining a pyrene moiety as a fluorophore and a fluorescence-quenching hydrazide moiety as a signaling handle. To understand the Cu^{2+}-selective signaling behavior in the Cu^{2+}-assisted hydrolysis of hydrazide, a series of pyrene-hydrazides with various spacers between the two subunits were prepared (Scheme 1). First, *N*-hydroxysuccinimide (NHS)-activated esters were prepared by the reaction of 1-pyrenecarboxylic acid, 1-pyreneacetic acid, or 1-pyrenebutyric acid with oxalyl chloride and subsequent treatment with NHS (dichloromethane, yield: 88.9% for **1**, 92.4% for **2**, and 92.9% for **3**). Then, hydrazides **1**–**3** were synthesized readily by reaction of the activated esters with hydrazine monohydrate (THF, yield: 93.1% for **1**, 90.5% for **2**, and 94.8% for **3**). It was found that cleaner reactions with improved yields were obtained using NHS-activated esters rather than the direct reaction between activated acyl chloride and hydrazine. UV–vis and fluorescence measurements suggest that probe **1** is stable under the photoirradiation conditions (Figure S1, Supporting Information) and in common organic solutions except for water where considerable decreases of absorbance and fluorescence were observed after 24 h storage (Figure S2, Supporting Information).

Scheme 1. Preparation of Cu^{2+}-selective pyrene-hydrazide probes **1**–**3**.



1-Pyrenecarboxylic acid-derived hydrazide **1** exhibited very weak fluorescence emission owing to the PET quenching from acylhydrazide NH_2 to pyrene fluorophore.[18] Suggested quenching process could be confirmed by the observation that the fluorescence emission of probe **1** enhanced under the acidic conditions due to the revival of the PET-suppressed emission of pyrene fluorophore by the protonation of acylhydrazide NH_2 (Figure S3, Supporting Information). Meanwhile, increasing the distance between the pyrene fluorophore and the quenching hydrazide moiety in pyreneacetic acid-based and pyrenebutylic acid-based hydrazides **2** and **3** noticeably increased the residual fluorescence emission (Figures S4 and S5, Supporting Information).[25]

Upon treatment with Cu^{2+}, probes **1**–**3** revealed pronounced fluorogenic signaling behaviors in 10% aqueous Tris-buffered DMSO solution. However, owing to the different residual fluorescence intensities of **1**–**3**, the most pronounced signaling contrast was observed for **1** (signal enhancement (I/I_o): 130 (at 392 nm, for **1**), 13.4 (at 378 nm, for **2**), and 1.62 (at 378 nm, for **3**). Therefore, Cu^{2+} signaling experiments were conducted with probe **1**, which exhibited the strongest fluorogenic signaling behavior. UV–vis measurements, on the other hand, revealed no significant changes in spectral properties of **1** on the addition of Cu^{2+} or other tested metal ions (Figure S6, Supporting Information).

Optimal signaling conditions were obtained by surveying the profile of the fluorescence intensity changes as a function of pH and solvent for probe **1** alone and in the presence of Cu^{2+} ions. As shown in Figure S7 (Supporting Information), the most pronounced off–on fluorescence signaling contrast was observed in 10% aqueous Tris-buffered DMSO solution. In 10% aqueous DMSO solution (Tris-buffered at pH 7.0, final concentration = 10 mM), hydrazide **1** exhibited very weak fluorescence. With the addition of Cu^{2+} ions, probe **1** revealed marked navy-blue emission under UV illumination. The fluorescence enhancement (I/I_0) at 392 nm generated by Cu^{2+} ions was 130-fold (Figure 1). Other tested metal ions (Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, Mn^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Ag^+, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, and Al^{3+}) did not induce any significant changes in the fluorescence spectra, with a relatively small range of fluorescence enhancement ratios (I/I_0) at 392 nm between 1.03 (for Na^+) and 1.82 (for Co^{2+}).

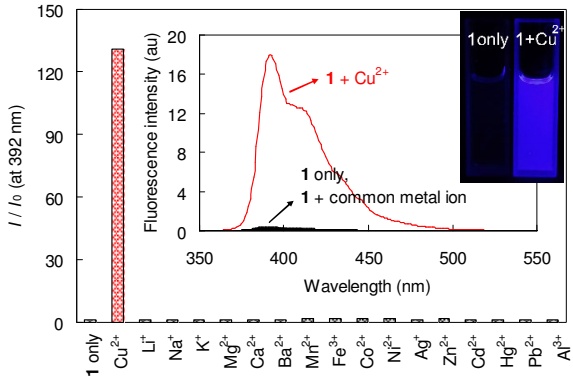


Figure 1. Changes in fluorescence intensity (I/I_0) of **1** at 392 nm in the presence of representative metal ions (M^{n+}). Inset: fluorescence spectra of **1**. [**1**] = 5.0×10^{-6} M, [Cu^{2+}] = [M^{n+}] = 5.0×10^{-5} M in a mixture of Tris-buffer (pH 7.0, final concentration = 10 mM) and DMSO (1:9, *v*/*v*). λ_{ex} = 340 nm.

To develop a probe for a specific metal ion in practical samples, selective signaling of the target metal ion in the presence of coexisting environmentally relevant metal ions is critical. For this reason, the interference of other metal ions in Cu^{2+} signaling was investigated (Figure 2 and Figure S8, Supporting Information). The fluorescence intensity ratio ($I_{1+Cu(II)+metal}/I_{1+Cu(II)}$) of probe **1** at 392 nm was virtually invariant for most metal ions (from 0.97 (for Ni^{2+}) to 1.01 (for Ba^{2+})). In addition, Cu^{2+} signaling by probe **1** was not noticeably affected by environmentally relevant pH conditions (pH 5.0–8.0) (Figure S9, Supporting Information). This pH-dependency of Cu^{2+} signaling of probe **1** is primarily due to the unique fluorescence property of 1-pyrenecarboxylic acid as inferred from the observation that the pH profile of Cu^{2+} signaling of probe **1** is similar to that of 1-pyrenecarboxylic acid (Figure S10, Supporting Information). Specifically, under neutral pH

conditions (pH 7.0 Tris buffer), probe **1** exhibited the greatest Cu^{2+} signaling contrast ($I_{\mathbf{1}+Cu(II)}/I_{\mathbf{1}\ only}$ at 392 nm = 130). In addition, we confirmed that the structural variation of the probes **1**–**3** did not influence the Cu^{2+} signaling (Figure S11, Supporting Information). From this wide pH tolerance, rapid signaling time, and lack of interference from other metal ions, we deduced that probe **1** might be useful for determination of Cu^{2+} ions in environmentally relevant practical samples.

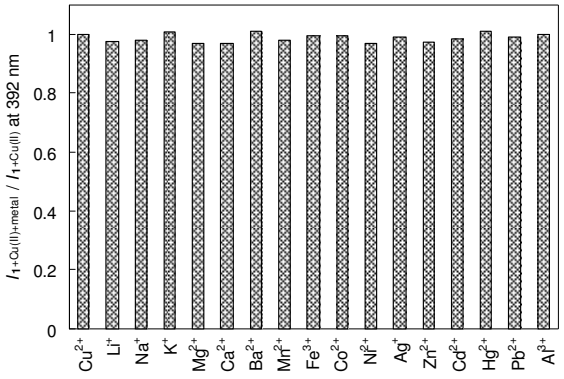
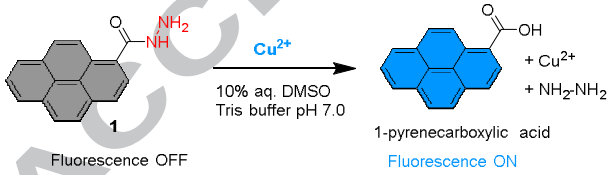


Figure 2. Changes in the fluorescence intensity ratio of **1** at 392 nm during Cu^{2+} signaling in the presence of common metal ions ($I_{\mathbf{1}+Cu(II)+metal}/I_{\mathbf{1}+Cu(II)}$). [**1**] = 5.0×10^{-6} M, $[Cu^{2+}] = [M^{n+}] = 5.0 \times 10^{-5}$ M in a mixture of Tris-buffer (pH 7.0, final concentration = 10 mM) and DMSO (1:9, *v*/*v*). λ_{ex} = 340 nm.

Cu^{2+}-selective fluorescence signaling of **1** is due to Cu^{2+}-induced catalytic hydrolysis of the hydrazide moiety of the probe to its carboxylic acid and hydrazine (Scheme 2).[26,27] The hydrolysis of probe **1** by Cu^{2+} was confirmed by ^{1}H NMR and mass spectroscopy. The ^{1}H NMR spectrum of the purified signaling product was identical to that of 1-pyrenecarboxylic acid (Figure 3). In addition, the mass spectrum revealed a diagnostic peak at *m*/*z* = 245.1 consistent with transformation to the suggested signaling product 1-pyrenecarboxylic acid (calcd for $[C_{17}H_9O_2]^-$, *m*/*z* = 245.06). Also, from the observation of nearly identical fluorescence spectra of a mixture of probe **1** and Cu^{2+} ions (**1** + Cu^{2+}) and fluorescent signaling product 1-pyrenecarboxylic acid (Figure S12, Supporting Information), we further confirmed that the Cu^{2+} signaling of probe **1** is due to the hydrolysis of probe **1** to 1-pyrenecarboxylic acid.

Scheme 2. Cu^{2+} signaling by pyrenecarbohydrazide **1**.



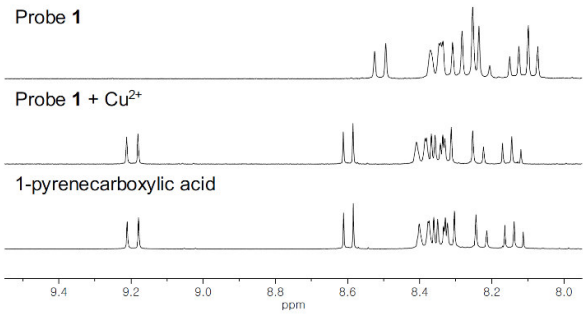


Figure 3. Partial ^{1}H NMR spectra of **1** in the absence and presence of Cu^{2+} ions and 1-pyrenecarboxylic acid. [**1**] = [1-pyrenecarboxylic acid] = 0.01 M in DMSO-d_6. Because of the paramagnetic effect of Cu^{2+} ions, the middle spectrum was obtained after simple purification of the signaling product by passage through a short silica column.

To obtain the detection limit of probe **1** for Cu^{2+} determination, changes of the fluorescence intensity of probe **1** at 392 nm in the presence of varying concentrations of Cu^{2+} ions were analyzed. Although Cu^{2+} signaling of probe **1** is based on the Cu^{2+}-induced catalytic hydrolysis of hydrazide moiety (Scheme 2), we could obtain the quantitative results for Cu^{2+} determination after 20 min of sample preparation, where saturated signalings were observed (Figure S13, Supporting Information). As shown in Figure 4, the fluorescence intensity at 392 nm increased linearly as a function of $[Cu^{2+}]$ in the range of 0–1.0 × 10^{-5} M. From the Cu^{2+}-concentration-dependent fluorescence data, the detection limit of **1** for Cu^{2+} ions was calculated as 5.93×10^{-8} M (0.004 ppm) as per IUPAC recommendation ($3s_{bl}$/m, where s_{bl} is the standard deviation of the blank signal (number of measurements = 16) and m is the calibration sensitivity (Figure S14, Supporting Information).[28]

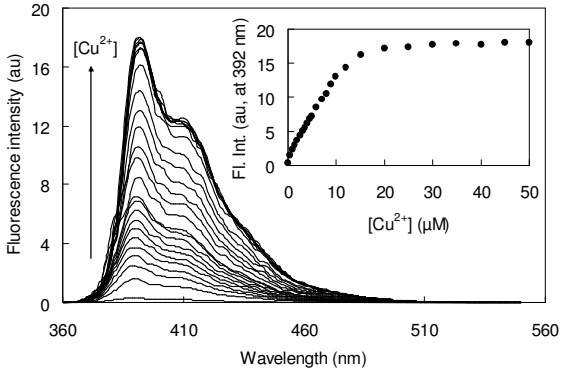


Figure 4. Fluorescence titration of **1** with Cu^{2+}. [**1**] = 5.0×10^{-6} M, $[Cu^{2+}]$ = 0–5.0×10^{-5} M in a mixture of Tris-buffer (pH 7.0, final concentration = 10 mM) and DMSO (1:9, *v*/*v*). λ_{ex} = 340 nm.

Copper is known to be one of the most important metals in semiconductor-related industrial fields.[29] As a practical application of probe **1**, determination of Cu^{2+} ions was conducted in a simulated semiconductor wastewater (Figure 5). The simulated semiconductor wastewater was prepared following the literature.[30] As shown in Figure 5, a satisfactory calibration curve was obtained up to 5.0×10^{-6} M of Cu^{2+}, and the detection limit for Cu^{2+} in the simulated semiconductor wastewater was found to be 6.93×10^{-8} M (0.005 ppm).[28] In addition, we confirmed that the probe could also be used to determine Cu^{2+} ions in tap water samples (Figure S15, Supporting Information).

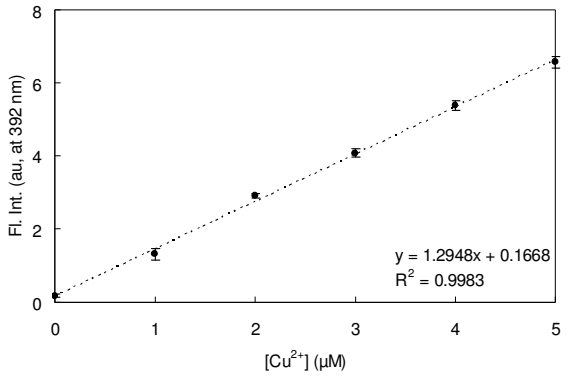


Figure 5. Concentration-dependent fluorescence signaling of Cu^{2+} by probe **1** in simulated semiconductor wastewater. [**1**] = 5.0×10^{-6} M, [Cu^{2+}] = 0–5.0×10^{-6} M in a mixture of Tris-buffered (pH 7.0, final concentration = 10 mM) wastewater and DMSO (1:9, *v*/*v*). λ_{ex} = 340 nm. Error bars were obtained by three measurements.

In summary, a simple Cu^{2+}-selective fluorescence signaling probe based on a hydrazide derivative of pyrene fluorophore was investigated. The designed probe exhibited marked Cu^{2+}-selective turn-on fluorescence signaling behavior via Cu^{2+}-assisted hydrolysis of pyrenecarbohydrazide to pyrenecarboxylic acid. Investigation of related model compounds suggested that the fluorescence signal became less significant as the distance between the hydrazide functionality and the pyrene fluorophore increased. The limit of detection of the probe for Cu^{2+} signaling was 5.93×10^{-8} M (0.004 ppm). Moreover, as a practical application, Cu^{2+} signaling in simulated semiconductor wastewater was achieved with a detection limit of 6.93×10^{-8} M (0.005 ppm).

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:****.

References and notes

1. (a) Yang, Y.; Zhao, Q.; Feng, W.; Li, F. *Chem. Rev*. **2013**, *113*, 192–270; (b) Yuan, L.; Lin, W.; Zheng, K.; He, L.; Huang, W. *Chem. Soc. Rev*. **2013**, *42*, 622–661; (c) Liu, Z.; He, W.; Guo, Z. *Chem. Soc. Rev*. **2013**, *42*, 1568–1600.
2. (a) Nolan, E. M.; Lippard, S. J. *Chem. Rev*. **2008**, *108*, 3443–3480; (b) Carter, K. P.; Young, A. M.; Palmer, A. E. *Chem. Rev*. **2014**, *114*, 4564–4601.
3. (a) Uauy, R.; Olivares, M.; Gonzales, M. *Am. J. Clin. Nutr*. **1988**, *67*, 952S–959S; (b) Lutsenko, S.; Barnes, N. L.; Bartee, M. Y.; Dmitriev, O. Y. *Physiol. Rev*. **2007**, *87*, 1011–1046; (c) Viguier, R. F. H.; Hulme, A. N. *J. Am. Chem. Soc*. **2006**, *128*, 11370–11371; (d) Chan, Y. H.; Chen, J. X.; Liu, Q.; Wark, S. E.; Son, D. H.; Batteas, J. D. *Anal. Chem*. **2010**, *82*, 3671–3678.
4. U.S. Geological Survey. *Minerals Yearbook*. Washington, DC: U.S. Geological Survey.
5. (a) Bush, A. I. *Curr. Opin. Chem. Biol*. **2000**, *4*, 184–191; (b) Barnham, K. J.; Bush, A. I. *Curr. Opin. Chem. Biol*. **2008**, *12*, 222–228.
6. (a) Kaler, S. G.; Holmes, C. S.; Goldstein, D. S.; Tang, J.; Godwin, S. C.; Donasante, A.; Liew, C. J.; Sato, S.; Patronas, N. *N. Engl. J. Med*. **2008**, *358*, 605–614; (b) Ala, A.; Walker, A. P.; Ashkan, K.; Dooley, J. S.; Schilsky, M. L. *Lancet* **2007**, *369*, 397–408.
7. Hahn, S. H.; Tanner, M. S.; Danks, D. M.; Gahl, W. A. *Biochem. Mol. Med*. **1995**, *54*, 142–145.
8. Guidelines for Drinking-water Quality, World Health Organization, Geneva, 1996.
9. Hunt, D. T. E.; Wilson, A. L. In *The Chemical Analysis of Water*; The Royal Society of Chemistry: Oxford, 1986, p. 398.
10. McLaren, J. W.; Jarnis, K. E.; Gray, A. L.; Houk, R. S. In *Handbook of Inductively Coupled Plasma Mass Spectrometry*, eds.; Blackie & Son Ltd.: Glasgow, 1992, p. 266.
11. Dymott, T. M. In *Quality Assurance in Environmental Monitoring*, Subramaniam, G. eds.; VCH: Weinheim, 1995, p. 114.
12. (a) Zhang, X.; Shiraishi, Y.; Hirai, T. *Org. Lett*. **2007**, *9*, 5039–5042; (b) Noh, J. Y.; Park, G. J.; Na, Y. J.; Jo, H. Y.; Lee, S. A.; Kim, C. *Dalton Trans*. **2014**, *43*, 5652–5656; (c) Goswami, S.; Chakraborty, S.; Paul, S.; Halder, S.; Panja, S.; Kanti, S.; Mukhopadhyay, K. *Org. Biomol. Chem*. **2014**, *12*, 3037–3044.
13. (a) Weng, Y. Q.; Yue, F.; Zhong, Y. R.; Ye, B. H. *Inorg. Chem*. **2007**, *46*, 7749–7755; (b) Jung, H. S.; Kwon, P. S.; Lee, J. W.; Kim, J. I.; Hong, C. S.; Kim, J. W.; Yan, S.; Lee, J. Y.; Lee, J. H.; Joo, T.; Kim, J. S. *J. Am. Chem. Soc*. **2009**, *131*, 2008–2012.
14. Dujols, V.; Ford, F.; Czarnik, A. W. *J. Am. Chem. Soc*. **1997**, *119*, 7386–7387.
15. (a) Chen, X.; Ma, H. *Anal. Chim. Acta* **2006**, *575*, 217–222; (b) Yuan, L.; Chen, B.; Xie, Y. *Org. Lett*. **2012**, *14*, 432–435; (c) Fan, J.; Zhan, P.; Hu, M.; Sun, W.; Tang, J.; Wang, J.; Sun, S.; Song, F.; Peng, X. *Org. Lett*. **2013**, *15*, 492–495; (d) Shirasaki, Y.; Kamino, S.; Tanioka, M.; Watanabe, M.; Takeuchi, Y.; Komeda, S.; Enomoto, S. *Chem. Asian J*. **2013**, *8*, 2609–2613; (e) Cheng, X. W.; Zhou, Y.; Fang, Y.; Ruia, Q. Q.; Yao, C. *RSC Adv*. **2015**, *5*, 19465–19469; (f) Liu, K.; Shang, H.; Meng, F.; Liu, Y.; Lin, W. *Talanta* **2016**, *147*, 193–198; (g) Liu, Y.; Su, Q.; Chen, M.; Dong, Y.; Shi, Y.; Feng, W.; Wu, Z.-Y.; Li, F. *Adv. Mater*. **2016**, *28*, 6625–6630.
16. Qi, X.; Jun, E. J.; Xu, L.; Kim, S.-J.; Hong, J. J. S.; Yoon, Y, J.; Yoon, J. *J. Org. Chem*. **2006**, *71*, 2881–2884.
17. Zhou, Z.; Li, N.; Tong, A. *Anal. Chim. Acta* **2011**, *702*, 81–86.
18. (a) Kim, M. H.; Jang, H. H.; Yi, S.; Chang, S.-K.; Han M. S. *Chem. Commun*. **2009**, 4838–4840; (b) Ye, J.-H.; Xu, H.; Bai, Y.; Zhang, W.; He, W. *Tetrahedron Lett*. **2014**, *55*, 6269–6273.
19. Choi, M. G.; Kim, J.; Hong, J. M.; Chang, I. J.; Ahn, S.; Chang, S.-K. *Tetrahedron Lett*. **2016**, *57*, 975–978.
20. Zheng, Z.; Wang, L.; Tang, W.; Chen, P.; Zhu, H.; Yuan, Y.; Li, G.; Zhang, H.; Liang, G. *Biosens. Bioelectron*. **2016**, *83*, 200–204.
21. Kim, H. Y.; Lee, H. J.; Chang, S.-K. *Talanta* **2015**, *132*, 625–629.
22. Hong, J. M.; Jun, J. K.; Kim, H. Y.; Ahn, S.; Chang, S.-K. *Tetrahedron Lett*. **2015**, *56*, 5393–5396.
23. Jo, J.; Lee, H. W.; Liu, W.; Olasz, A.; Chen, C.-H.; Lee, D. *J. Am. Chem. Soc*. **2012**, *134*, 16000–16007.
24. Li, A.-F.; He, H.; Ruan, Y.-B.; Wen, Z.-C.; Zhao, J.-S.; Jiang, Q.-J.; Jiang, Y.-B. *Org. Biomol. Chem*. **2009**, *7*, 193–200.
25. Choi, M. G.; Im, H. G.; Noh, J. H.; Ryu, D. H.; Chang, S.-K. *Sens. Actuat. B Chem*. **2013**, *177*, 583–588.
26. Attanasi, O.; Serra-Zanetti, F. *Synthesis* **1980**, *1980*, 314–315.
27. Kumar, M.; Kumar, N.; Bhalla, V.; Sharma, P. R.; Kaur, T. *Org. Lett*. **2012**, *14*, 406–409.
28. Harris, D. C. In *Quantitative Chemical Analysis*; 8th ed.; Freeman: New York, 2010; pp. 103–105.
29. Zhang, J.; Richardson, H. W. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2016; Ch. Copper compounds.
30. (a) Onundi, Y. B.; Mamun, A. A.; Al Khatib, M. F.; Al Saadi, M. A.; Suleyman, A. M. *Int. J. Environ. Sci. Tech*. **2011**, *8*, 799–806; (b) Wong, Y. C.; Moganaragi, V.; Atiqah, N. A. *Orient. J. Chem*. **2013**, *29*, 1421–1428.

Highlights:

- Cu^{2+}-selective fluorescence probe based on pyrene fluorophore was developed.
- Probe exhibited markedly selective signaling via Cu^{2+}-induced hydrazide hydrolysis.
- Signal became less prominent with increased distance between hydrazide and pyrene.
- Probe could be useful for the determination of Cu^{2+} in a simulated wastewater.