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Highly selective colorimetric fluorescence sensor for Cu^{2+}: cation-induced '*switching on*' of fluorescence due to excited state internal charge transfer in the red/near-infrared region of emission spectra

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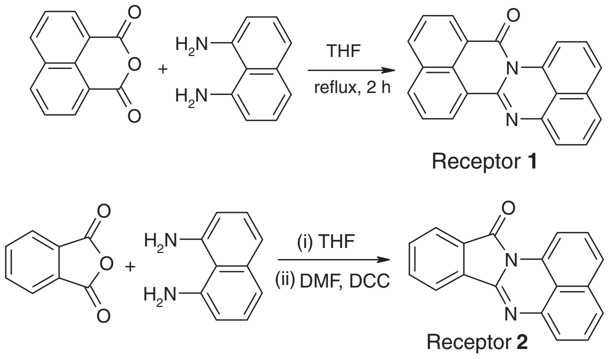
ABSTRACT

A 1,8-naphthalimide-based colorimetric fluorescence perinone dye, receptor **1** is reported herein for the selective detection of Cu^{2+} over the other heavy and transition metal ions. Receptor **1** shows a strong colorimetric change from orange to purple and a dramatic enhancement of fluorescence intensity due to cation-induced excited state internal charge transfer during the sensing event, that is, a dual optical response that would facilitate naked-eye detection of Cu^{2+}.

Development of molecular signaling systems especially for cations, rendering selective changes upon binding analytes either by colorimetric or by fluorescence modulations has received much attention as photonic molecular devices.[1] For the past few decades, fluorescent chemosensors for the detection of Cu^{2+} ion have actively been investigated as copper is a widely used industrial metal and hence it is a significant environmental pollutant at high concentration[2] but at the same time, it is an essential trace element in biological systems. It is well known to all that Cu^{2+} is a notorious fluorescence quencher[3] because of its paramagnetic nature, so most of the classic and early-reported Cu^{2+} sensors undergo fluorescence quenching upon binding of Cu^{2+} either by electron or by energy transfer mechanism.[4] Therefore owing to sensitivity reasons and high order of interference often caused by the chemically closely related metal ions (e.g., Zn^{2+}, Fe^{3+}, and Hg^{2+}) during spectroscopic studies, the development of new highly selective and sensitive colorimetric Cu^{2+} fluoroionophores showing fluorescence enhancement[5] is a continued interesting and challenging task. Fused heterocycles perinone and its derivatives are excellent chromogenic and fluorogenic dyes which are widely used for industrial plastics.[6] Previously, we have mentioned that perimidine core at the top of naphthalene moiety has excellent colorimetric response upon Cu^{2+} complexation via internal charge transfer (ICT) mechanism.[7] Additionally, 1,8-naphthalimide-based fluorescent chemosensors[8] have excellent photophysical properties due to large Stoke-shifted emission band, larger molar extinction coefficient, and high quantum yield. In continuation of our interest in the ICT concept as a promising metal ion-sensing strategy, we now report an easy to access colorimetric '*switching on*' ICT probe, a new 1,8-naphthalimide-based perinone dye for the selective detection of Cu^{2+} ion. The chromophore shows a distinct color change from orange to purple as a result of enhanced ICT and a dramatic enhancement of emission intensity due to excited state charge transfer (CT) in the red/near-infra-red (NIR) region[9] during Cu^{2+} complexation. Successful reports of such chemosensors with copper ion-induced enhancement of fluorescence at $\lambda > 650$ nm in the literature are very scarce.[10] Combination of dual optical responses via either colorimetric or fluorescence modulations raises the sensitivity of the fluoroionophore and thus makes it a particularly effective one for selective detection of Cu^{2+}.

The fused fluoroionophore[11] receptor **1** having six fused rings is synthesized (Scheme 1) in a single step simply by cyclization of 1,8-diaminonaphthalene with 1,8-naphthalic anhydride in dry tetrahydrofuran under refluxing condition and the product was obtained in an excellent yield. The rigid receptor constitutes a perimidine core as an ion recognition unit, which is fused together by fluorescence naphthalene moieties which are certainly



Scheme 1. Synthesis of the receptors.

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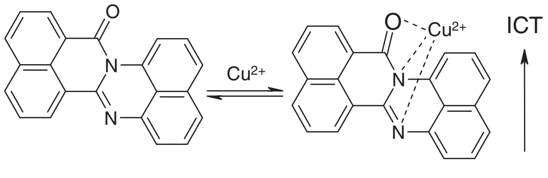
responsible for signal transduction during spectral investigations. The known phthalimide analog perinone, receptor **2** was also synthesized by the reported procedure[12] for comparison of binding and fluorescence sensitivity with Cu^{2+} which thus demonstrated that our designed naphthalimide analog is the most effective fluorescence sensor for Cu^{2+}.

The plausible ICT mechanism for our system is illustrated in Scheme 2. The metal ion chelation at the three potential binding sites, comprising of the perimidine nitrogens and the carbonyl oxygen functions could trigger the enhanced ICT and thus we may anticipate significant photophysical perturbations of the ionophore in the presence of Cu^{2+}. The pronounced spectral variations, particularly the largely red shifted ICT absorption by Cu^{2+} are consistent with the expected increase in the ICT interaction mediated by the electron donation from the probable donor perimidine nitrogens along with amide carbonyl of the naphthalimide subunit, acting as an acceptor. This mode of binding is supported by the IR data. In the IR spectrum of receptor **1** (see Supplementary data), the peaks at 1680 and 1600 cm^{-1} ascribed to the C=O and C=N stretching, respectively, are observed to shift upon Cu^{2+} complexation toward lower wave numbers of 1660 and 1585 cm^{-1}, respectively.[13]

The photophysical behavior of the chemosensor with several guest cations (Li^{+}, Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Ni^{2+}, Co^{2+}, Fe^{3+}, and Mn^{2+}) in CH_3CN/H_2O (90:10, v/v) is investigated by means of UV–vis and fluorescence measurements. All the cations are employed using their perchlorate salts and the titration experiments are carried out at pH 7.1 (35 mM HEPES buffer). The UV–vis absorption spectrum of the metal-free form of receptor **1** ($c = 2.0 \times 10^{-5}$ M) in CH_3CN/H_2O (90:10, v/v) exhibits two λ_{max} peaks at 343 and 359 nm and a low energy broad band at around 470 nm which is possibly attributed to the weak ICT type transition from pyrimidine core to naphthalimide subunit in the ground state level of the dye. Spectroscopic investigations are carried out by using the above-mentioned set of metal cations ($c = 2.0 \times 10^{-4}$ M). From the instrumental read-out, it can easily be concluded that Cu^{2+} promotes remarkable response toward the receptor (Fig. 1a). Upon gradual addition of Cu^{2+} solution to the receptor **1**, the bands at 343 and 359 nm progressively decrease and get slightly blue shifted while the band at 470 nm disappears gradually with simultaneous generation of a new broad band appearing at 557 nm whose intensity increases progressively reaching the maxima when 50 μM of this metal ion is added. The new red shifted low-energy absorption band ($\Delta\lambda = 87$ nm) is observed confirming the efficient charge transfer phenomenon which results in a naked-eye color change from orange to purple (Fig. 1b). Two well-defined isosbestic points at 404 and 514 nm are observed during the spectral titrations, indicating the presence of a unique complex in equilibrium with the receptor.



Scheme 2. Proposed mode of binding with Cu^{2+}.

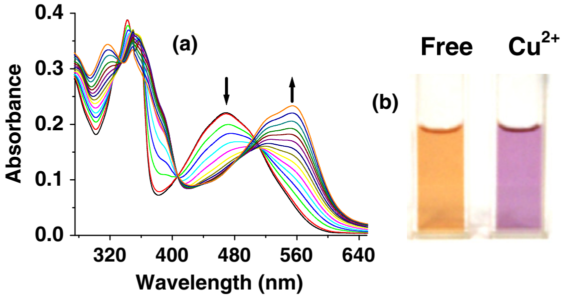


Figure 1. (a) UV–vis absorption spectra of receptor **1** upon addition of 50 μM Cu^{2+} in CH_3CN/H_2O (90:10, v/v). (b) Color changes from orange to purple upon Cu^{2+} complexation.

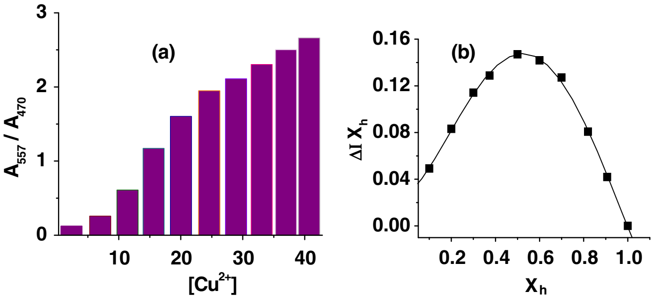


Figure 2. (a) Intensity ratio (A_{557}/A_{470}) as a function of Cu^{2+} concentration (in μM). (b) Job plot diagram of receptor **1** for Cu^{2+} determined by UV–vis method (where X_h is the mole fraction of the host and ΔI indicates the change of absorbance).

The resulting titration isotherm fits nicely with a 1:1 binding model as suggested by the Job plot diagram (Fig. 2b). The association constant (K_a) determined by UV–vis method[14] is found to be 2.16×10^{4} M^{-1} (error <10%). The HRMS mass spectrum of the Cu^{2+} complex of receptor **1** (see Supplementary data) also supports a single mononuclear complex between the metal ion and receptor unit. The $[M-H]^{+}$ and $[M-2H]^{+}$ peaks for the Cu^{2+} complex are calculated at *m*/*z* 382.0722 and 381.0714 which are found at *m*/*z* 382.0720 and 381.0708, respectively.

The addition of other metal ions even in excess such as Li^{+}, Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, Ni^{2+}, Co^{2+}, Fe^{3+}, Mn^{2+}, and Ag^{+} produces insignificant changes in the absorption spectra. In all the cases, a nominal decrease in absorbance intensities is observed. The UV–vis absorption spectra of receptor **2** and its subsequent color change during complexation with Cu^{2+} as a result of ICT are depicted in Figure 3.

The cation-binding properties of the receptor **1** with Cu^{2+} in the excited state are also studied by fluorescence spectroscopic method. Chemosensor in the absence of Cu^{2+} upon excitation at 470 nm shows a very weak fluorescence at 650 nm. This weakly emissive band probably has its origin in the ICT-type excited state. Upon gradual addition of Cu^{2+} solution to the receptor solution, a remarkable enhancement of fluorescence intensity (almost 25-fold increase) is observed and the emission intensity gets slightly red shifted at 675 nm assigning Cu^{2+}-induced enhancement of ICT, which is clearly observed (Fig. 4a).

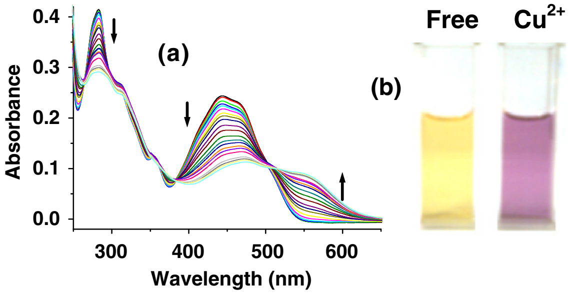


Figure 3. (a) UV–vis absorption spectra of receptor **2** upon addition of 60 μM Cu^{2+}. (b) Color changes from yellow to purple upon Cu^{2+} complexation.

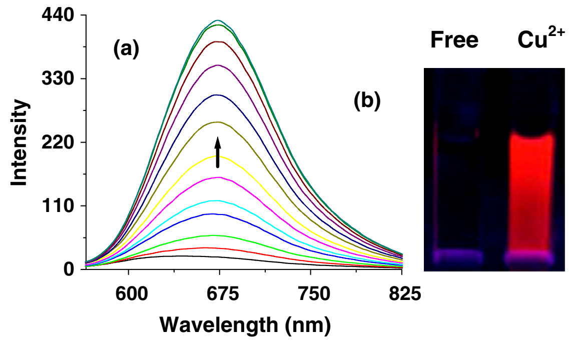


Figure 4. (a) Fluorescence emission spectra of receptor **1** upon gradual addition of Cu^{2+} in CH_3CN/H_2O (90:10, v/v). (b) Red emission as observed during titration experiment with Cu^{2+}.

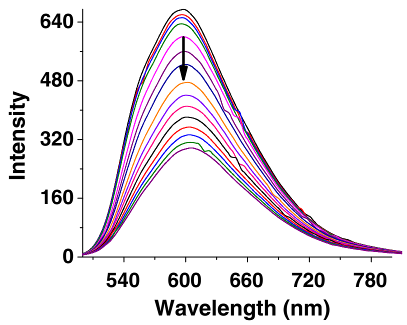


Figure 6. Fluorescence emission spectra of receptor **2** upon gradual addition of Cu^{2+} in CH_3CN/H_2O (90:10, v/v).

It is noteworthy to mention that addition of other metal ions produces insignificant change in emission intensity and only a slight decrease of fluorescence intensity is observed at 650 nm under identical experimental conditions (Fig. 5). Though the nature of the excited states involved in this phenomenon is presently undefined, we assume that two different but distinct emissive channels are involved within the Cu^{2+}-bound state of the fluorophore. Fluorescence enhancement at 675 nm in the present case is probably due to the engagement of different donors and acceptor groups within the proximity during complexation and thereby a tightly bound metal complex is formed due to strong chelation of Cu^{2+} with the receptor unit.[15] Hence, the responsible mechanism of fluorescence quenching via non-radiative pathways prevailing in the free receptor unit might be suppressed that leads to an enhancement of fluorescence in the presence of the Cu^{2+} ion. Another factor for the fluorescence enhancement is that coordination of the amide oxygen with the target metal ion probably increases the electron-withdrawing character of the 1,8-naphthalimide subunit and therefore some degree of efficient excited state ICT occurs between the Cu^{2+}-bound substrate and the conjugated electronic system of the 1,8-naphthalimide acceptor subunit within such a microenvironment of the fluorophore. Hence, a substantial change in the geometry followed by a change in the dipole moment of the probe in the excited state is expected that possibly modulates the fluorescence signal and a slight red shift ($\Delta\lambda = 25$ nm) in fluorescence is observed during Cu^{2+} sensing. Such metal ion-induced fluorescence activation of the donor subunit followed by excited state ICT[16] between the donor and the attached acceptor fluorophore is supported when we compare receptor **2** (single fluorophore system) with receptor **1** (dual fluorophore system) for Cu^{2+} sensing. The phthalimide analog perinone exhibits similar cation-induced enhanced ICT (Fig. 3) but due to its poor stabilizing capacity relative to 1,8-naphthalimide subunit such excited state ICT is possibly prevented and the emission intensity quenched steadily during Cu^{2+} complexation (Fig. 6). Therefore receptor **2** behaves as a '*switched off*' fluorescence probe toward Cu^{2+}.

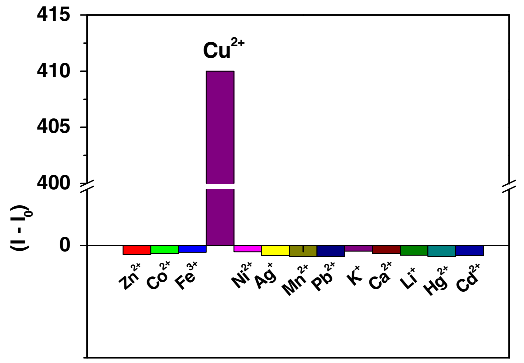


Figure 5. Change of fluorescence intensity of receptor **1** after adding 50 μM of each of the guest cation in CH_3CN/H_2O (90:10, v/v).

Participation of the 1,8-naphthalimide unit in most effective sensor **1** in the excited state probably induces a highly emissive stable CT excited state that strongly amplifies the fluorescence signal emitted by the system upon binding with Cu^{2+}. Since the broad and large Stokes shifted emission bands are in visible region, this visible CT emission allows the sensor to detect Cu^{2+} through naked eye experiment readily and a colorless to promising red fluorescence is observed (Fig. 4b). The association constant as determined by fluorescence titration method following Benesi–Hildebrand equation[14] is found to be $2.54 \times 10^4\ M^{-1}$ (error <10%).

In summary, we have reported here a highly selective and sensitive colorimetric fluoroionophore for Cu^{2+} based on metal triggered enhanced ICT in a six rings annulated structurally rigid perinone dye with efficient cation-induced '*switching on*' of fluorescence in the red/near-infrared spectral region. An important feature of this charge transfer fluoroionophore is that its highly selective fluorescence response toward Cu^{2+} is not only due to the binding preference of the metal ion with perimidine donor subunit (like receptor **2**) but also due to the combined response of the electron donor in the perimidine core, and the conjugated naphthalimide acceptor unit in the excited state provides a new strategy for constructing '*switching on*' ICT fluorophore for Cu^{2+}.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.048.

References and notes

1. (a) James, T. D.; Linnane, P.; Shinkai, S. *Chem. Commun.* **1996**, 281; (b) Beer, P. D. *Chem. Commun.* **1996**, 689; (c) de Silva, A. P.; Gunaratne, H. Q. N.; McVeigh, C.; Maguire, G. E. M.; Maxwell, P. R. S.; O'Hanlon, E. *Chem. Commun.* **1996**, 2191.
2. (a) Krämer, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 772; (b) Linder, M. C.; Hazegh-Azam, M. *Am. J. Clin. Nutr.* **1996**, *63*, 797S–811S; (c) Uauy, R.; Olivares, M.; Gonzalez, M. *Am. J. Clin. Nutr.* **1998**, *67*, 952S–959S; (d) Harris, Z. L.; Gitlin, J. D. *Am. J. Clin. Nutr.* **1996**, *63*, 836S–841S.
3. (a) Kim, H. J.; Park, S. Y.; Yoon, S.; Kim, J. S. *Tetrahedron* **2008**, *64*, 1294; (b) Kim, H. J.; Hong, J.; Hong, A.; Ham, S.; Lee, J. H.; Kim, J. S. *Org. Lett.* **2008**, *10*, 1963; (c)

Lin, W.; Yuan, L.; Tan, W.; Feng, J.; Long, L. *Chem. Eur. J.* **2009**, *15*, 1030; (d) Zheng, Y.; Gattás-Asfura, K. M.; Konka, V.; Leblanc, R. M. *Chem. Commun.* **2002**, 2350.

4. (a) Xie, J.; Ménand, M.; Maisonneuve, S.; Métivier, R. *J. Org. Chem.* **2007**, *72*, 5980; (b) Mu, H.; Gong, R.; Ma, Q.; Sun, Y.; Fu, E. *Tetrahedron Lett.* **2007**, *48*, 5525; (c) Goswami, S.; Chakraborty, R. *Tetrahedron Lett.* **2009**, *50*, 2911; (d) Choi, J. K.; Kim, S. H.; Yoon, J.; Lee, K.-H.; Bartscha, R. A.; Kim, J. S. *J. Org. Chem.* **2006**, *71*, 8011; (e) Park, S. M.; Kim, M. H.; Choe, J.-I.; No, K. T.; Chang, S.-K. *J. Org. Chem.* **2007**, *72*, 3550; (f) Wen, Y.-Q.; Yue, F.; Zhong, Y.-R.; Ye, B.-H. *Inorg. Chem.* **2007**, *46*, 7749.
5. (a) Ghosh, P.; Bharadwaj, P. K. *J. Am. Chem. Soc.* **1996**, *118*, 1553; (b) Li, G.-K.; Xu, Z.-X.; Chen, C.-F.; Huang, Z.-T. *Chem. Commun.* **2008**, 1774; (c) Jung, S.-H.; Park, M.; Han, Y.-D.; Kim, E.; Lee, C.; Ham, S.; Kim, S.-J. *Org. Lett.* **2009**, *11*, 3378; (d) Weng, Z.-C.; Yang, R.; He, H.; Jiang, Y.-B. *Chem. Commun.* **2006**, 106; (e) Xu, Z.; Xiao, Y.; Qian, X.; Cui, J.; Cui, D. *Org. Lett.* **2005**, *7*, 3029; (f) Zhou, Y.; Wang, F.; Kim, Y.; Kim, S.-J.; Yoon, J. *Org. Lett.* **2009**, *11*, 4442; (g) YuFang, X.; Feng, L.; ZhaoChao, X.; TanYu, C.; XuHong, Q. *Sci. China, Ser. B Chem.* **2009**, *52*, 771; (h) Kaur, S.; Kumar, S. *Chem. Commun.* **2002**, 2840; (i) Bhattacharya, S.; Gulyani, A. *Chem. Commun.* **2003**, 1158; (j) Bhattacharya, S.; Thomas, M. *Tetrahedron Lett.* **2000**, *41*, 10313; (k) Zheng, Y.; Huo, Q.; Kele, P.; Andreopoulos, F. M.; Pham, S. M.; Leblanc, R. M. *Org. Lett.* **2001**, *3*, 3277; (l) Zheng, Y.; Cao, X.; Orbulescu, J.; Konka, V.; Andreopoulos, F. M.; Pham, S. M.; Leblanc, R. M. *Anal. Chem.* **2001**, *75*, 1706.
6. (a) Herbst, W.; Hunger, K. *Industrial Organic Pigments*, 3rd ed.; Wiley, 2004.; (b) Hays, B. G.; Bindra, A. P. In *Polymeric Materials Encyclopedia*; Salamone, J. C., Ed.; CRC Press: Boca Raton, 1996; pp 1321–1332; (c) Nagao, Y.; Tsuda, K.; Kozawa, K.; Uchida, T. *Heterocycles* **2001**, *54*, 757.
7. Goswami, S.; Sen, D.; Das, N. K. *Org. Lett.* **2010**, *12*, 856.
8. (a) Guo, X.; Qian, X.; Jia, L. *J. Am. Chem. Soc.* **2004**, *126*, 2272; (b) Xu, Z.; Qian, X.; Cui, J. *Org. Lett.* **2005**, *7*, 3029; (c) Wang, J.; Qian, X. *Chem. Commun.* **2006**, 109; (d) Chovelon, J.-M.; Grabchev, I. *Spectrochim. Acta, Part A* **2007**, *67*, 87; (e) Wang, J.; Xiao, Y.; Zhang, Z.; Qian, X.; Yang, Y.; Xu, Q. *J. Mater. Chem.* **2005**, *15*, 2836; (f) Wen, G.-T.; Zhu, M.-Z.; Wang, Z.; Meng, X.-M.; Hu, H.-Y.; Guo, Q.-X. *Chin. J. Chem.* **2006**, *24*, 1230.
9. (a) Miller, J. N. Long-wavelength and Near-infrared Fluorescence. State of the Art, Future Applications, and Standards. In *Standardization and Quality Assurance in Fluorescence Measurement II. Springer Ser. Fluoresc.*; Resch-Genger, U., Ed.; Springer: Berlin, 2008; Vol. 5, pp 147–162; (b) Li, X.; Shi, W.; Chen, S.; Jia, J.; Ma, H.; Wolfbeis, O. S. *Chem. Commun.* **2009**, 5000.
10. Rurack, K.; Resch-Genger, U.; Bricks, J. L.; Spieles, M. *Chem. Commun.* **2000**, 2103.
11. Thomas, P. Eur. Pat. Appl. EP 780444, Jun 25, 1997. PCT Int. Appl., 2009, 21pp. Chemical Indexing Equivalent to 152:120631(DE). CODEN: PIXXD2 WO 2009127182 A1 20091022 CAN 151:471181 AN 2009: 1289891.
12. Alfredo, N. K.; Likhatchev, D.; Ramirez, S. B.; Vazquez, J. R.; Valverde, G. C.; Alexandrova, L. *Polymer* **2008**, *49*, 3654–3662.
13. Bardez, E.; Devol, I.; Larrey, B.; Valeur, B. *J. Phys. Chem. B* **1997**, *101*, 7786.
14. Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703.
15. (a) Mcfarland, S. A.; Finney, N. S. *J. Am. Chem. Soc.* **2002**, *124*, 1178; (b) Zhang, L.; Clark, R. J.; Zhu, L. *Chem. Eur. J.* **2008**, *14*, 2894; (c) Badugu, R.; Lakowicz, J. R.; Geddes, C. D. *J. Am. Chem. Soc.* **2005**, *127*, 3635.
16. (a) Wen, Z.-C.; Yang, R.; Hea, H.; Jiang, Y.-B. *Chem. Commun.* **2006**, 106; (b) Lee, S. Y.; Kim, H. J.; Wua, J.-S.; No, K.; Kim, J. S. *Tetrahedron Lett.* **2008**, *49*, 6141; (c) Jung, J. H.; Lee, M. H.; Kim, H. J.; Jung, H. S.; Lee, S. Y.; Shin, N. R.; No, K.; Kim, J. S. *Tetrahedron Lett.* **2009**, *50*, 2013; (d) Sumner, J. P.; Westerberg, N. M.; Stoddard, A. K.; Fierke, C. A.; Kopelman, R. *Sens. Actuators, B: Chem.* **2006**, *13*, 760; (e) Rurack, K.; Bricks, J. L.; Schulz, B.; Maus, M.; Reck, G.; Resch-Genger, U. *J. Phys. Chem. A* **2000**, *104*, 6171; (f) Leray, I.; Lefevre, J.-P.; Delouis, J.-F.; Delaire, J.; Valeur, B. *Chem. Eur. J.* **2001**, *7*, 4590.