Tetrahedron Letters 49 (2008) 5676–5679

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A molecular half-subtractor based on a fluorescence and absorption dual-modal sensor for copper ions

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ARTICLE INFO

Article history:
Received 30 January 2008
Revised 14 July 2008
Accepted 15 July 2008
Available online 17 July 2008

Keywords:
Half-subtractor
Copper sensor
L-Phenyl alanine
Anthracene

ABSTRACT

A L-phenyl alanine derivative (**L**) could be used as a fluorescence and absorption dual-modal sensor, which was highly sensitive and selective to copper ion at physiological pH. We have drawn attention to the use of its copper complex to acquire a half-subtractor with parallel operating INHIBIT and XOR logic gates, by monitoring, fluorescence and absorbance as output signals, respectively.

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Currently, the ability to reduce the size of silicon-based electronic devices is rapidly reaching its limits due to both technological and physical factors.[1,2] To further extend the process of miniaturization, application of molecular devices for information storage and processing seems to be a solution. In this regard, a variety of molecular logic gates have been fabricated in the past decade.[3–6] However, these simple logic gates must be integrated into combinatorial logic circuits for potential application in future molecular-scale computers. Such reconfigurations are thought to be an attractive and elegant way to enhance the computing power of molecules.[7–13]

The half-subtractor is a combinatorial circuit, which permits subtraction of binary digits. It is composed of INHIBIT and XOR gates operating in parallel to process the two input bits, so that the INHIBIT gate outputs the borrow digits and the XOR gate outputs the difference digits. Whereas the half-adder has parallel AND and XOR gates, which output the carry digits (C) and sum digits (S), respectively. Subtraction operations based on half-subtractor are relatively complicated, as the relative magnitudes of minuend and subtrahend need to be accounted for during performing subtraction algebraic operation. Until recently, the first half-subtractor was demonstrated using a commercially available porphyrin and UV–vis and fluorescence spectrometry.[10] Besides, examples of a molecular system which is able to function as a half-subtractor are rare in the literature.[14–21] Following our previous work,[22] here we report a L-phenyl alanine derivative, *N*-(9-anthrylmethyl)-L-phenyl alanine (**L**), and describe how a simple copper complex Cu**L**$_2$ can be used to demonstrate the operation of a half-subtractor by monitoring the emission intensity and absorbance changes, respectively. To the best of our knowledge, this is the first report of a molecular half-subtractor based on a fluorescence and absorption dual-modal sensor for metal ions.

Compound **L** was synthesized by the condensation reaction of L-phenyl alanine and 9-anthraldehyde, followed by reduction with $NaBH_4$, in 56% total yield (Fig. S1). The structure of **L** was identified by ^1H and ^{13}C NMR, mass spectrum, and elemental analysis.[23]

The changes in fluorescence intensity at the maximum emission wavelength (418 nm) of systems **L** (5 μM) and **L** + Cu^{2+} (1 equiv) with pH values in methanol/H_2O (v/v = 1:9) solution are shown in Figure 1. Under alkali conditions (pH > 8), the fluorescence of **L** is quenched because of a faster process, known as photo-induced electron transfer (PET), in which an electron is transferred to the anthracenyl group from the nitrogen atom separated by a methylene spacer.[22,24] In a wide pH range (pH 3.0–9.0), addition of Cu^{2+} induces an observed fluorescence quenching of **L** due to binding interactions. The fluorescence titration curve of **L** (5 μM) with Cu^{2+} is shown in Figure 2 in aqueous solution (methanol/HEPES buffer, pH 7.0, v/v = 1:9). The intensities of the emission peaks show significant decrease with increasing of Cu^{2+} concentration. The Job's plot indicates that a 1:2 stoichiometry is most possible for the binding mode of Cu^{2+} and **L** (inset in Fig. 2). From the fluorescence titration, the association constant (k_a) is calculated as 1.12×10^6 M^{-2}.[25,26] The molecular structure of Cu**L**$_2$ is proposed to a planar tetracoordinate Cu^{2+} complex with the two coordinated

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doi:10.1016/j.tetlet.2008.07.081

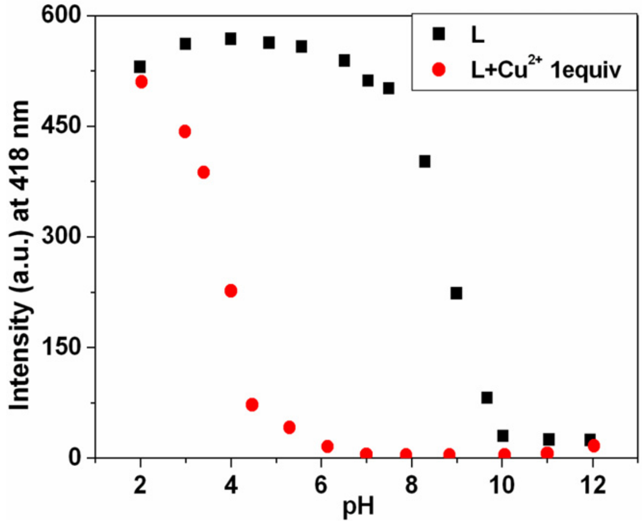


Figure 1. The effect of pH on fluorescence intensity at 418 nm of **L** (5 μM) (■) and **L** (5 μM) + Cu^{2+} (5 μM) (●) systems.

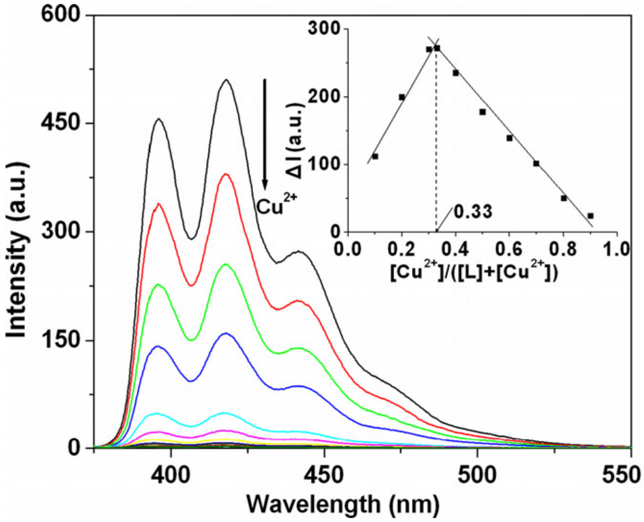


Figure 2. Changes in the fluorescent intensity of **L** (5 μM) in aqueous solution (methanol/HEPES buffer, pH 7.0, v/v 1:9) after addition of 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.5, 5.0, 7.0, 8.0, 9.0, 10.0 μM Cu^{2+}. Inset is the Job's plot of complexation between **L** and Cu^{2+}. Total concentration of **L** + Cu^{2+} is kept constant at 5 μM in methanol/HEPES buffer, pH 7.0, v/v 1:9.

amino groups and the two carboxyl groups in the trans configuration of **L**.[27] The Cu^{2+}-induced quenching effect can be explained as a result of the electron transfer as well as energy transfer from the excited anthracene moiety of **L** to low-lying empty d-orbital of Cu^{2+} ion.[28,29] The NMR resonance signals on its anthracene moiety shift upfield after addition of 1 M equiv of $CuCl_2$ (Fig. 3), which also confirms the process. In addition, the upfield shift of phenyl ring protons may be attributed to π–π stacking interaction between it and anthracene moiety,[22,28] which is most likely to contribute to the formation of a 1: 2 stoichiometry Cu^{2+}–**L** complex. The fluorescence spectra of system **L** (5 μM) upon addition of diverse cations are recorded in aqueous solution (methanol/HEPES buffer, pH 7.0, v/v = 1:9) (Fig. 4). Addition of metal ions except Cu^{2+}, such as Mg^{2+}, Ca^{2+}, Ba^{2+}, Al^{3+}, Ni^{2+}, Zn^{2+}, Co^{2+}, Cd^{2+}, Hg^{2+}, Fe^{3+}, Mn^{2+}, Cr^{3+}, and La^{3+}, do not show noticeable changes, indicating the high selectivity of this chemosensor for Cu^{2+} over the other cations at physiological pH.

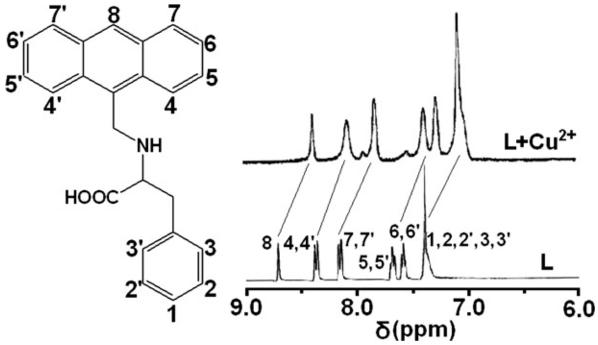


Figure 3. Partial ^1H NMR spectra of **L** and **L** + Cu^{2+} in CD_3OD at pH 7.0.

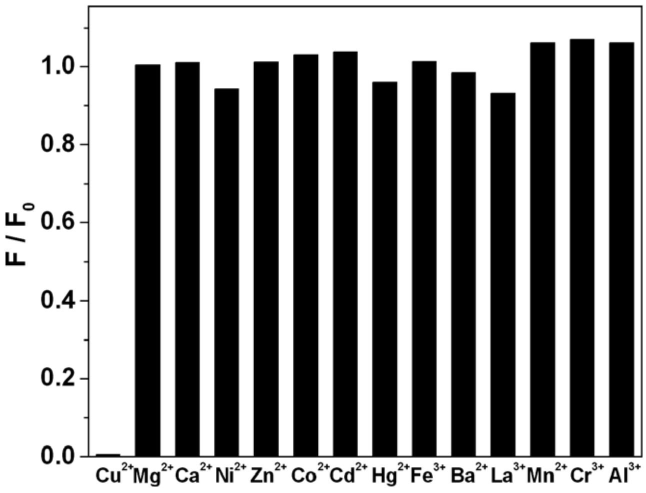


Figure 4. The relative fluorescence intensity at 418 nm of **L** (5 μM) in aqueous solution (methanol/HEPES buffer, pH 7.0, v/v 1:9) upon addition of 5 equiv of various cations, only Cu^{2+} causes a significant fluorescence quenching (λ_{ex} = 368 nm).

Starting with non-fluorescent **L** (5 μM) with $CuCl_2$ (5 μM) at pH 7.0 and monitoring changes of fluorescence as outputs, this system can operate as INHIBIT logic gate if NaOH (0.03 M) and HCl (0.03 M) are regarded as two inputs. Addition of HCl causes $Cu\mathbf{L}_2$ to liberate acidic $\mathbf{L}^+$ with the blue emission at 418 nm and Cu^{2+}, due to the protonation of the coordinated amino groups in receptor **L**. Addition of NaOH causes $Cu\mathbf{L}_2$ to liberate basic $\mathbf{L}^-$ without the blue emission at 418 nm as a result of the formation of $Cu(OH)_2$ precipitation. When both base and acid are added, the chemical inputs annihilate each other, the Cu^{2+} remains bounded to the receptor at neutral pH, and no fluorescence in output signal is observed (Fig. 5a–c). The quantum yields of **L** with Cu^{2+} system have been measured to be 3.67×10^{-3}, 0.368, 1.43×10^{-2}, and 3.61×10^{-3} when two inputs (OH^-, H^+) are (0,0), (0,1), (1,0), and (1,1), respectively, using anthracene in deoxygenated ethanol as standard ($\Phi_{fs} = 0.27$).[30] The fluorescence quantum yields (Φ_f) at output = 1 is more than 25 times higher than that at output = 0. Hence, a characteristic INHIBIT logic gate is obtained, as shown in Figure 5c.

On the other hand, the UV–vis spectrum of **L** is also substantially affected by addition of Cu^{2+}. The absorption spectra of **L** are consisted of an intense band centered at 255 nm and three weaker bands occurring at 340–400 nm. Acid and base show little affect on the absorbance of **L** (Fig. S2). In the presence of increasing Cu^{2+} concentrations at neutral pH, **L**–Cu^{2+} complex is formed, and then charge and energy transfer from anthracene unit to Cu^{2+} can lead to a severe decrease in absorption at 255 nm, while a new weak band centered at 270 nm appears. At the same time, the three

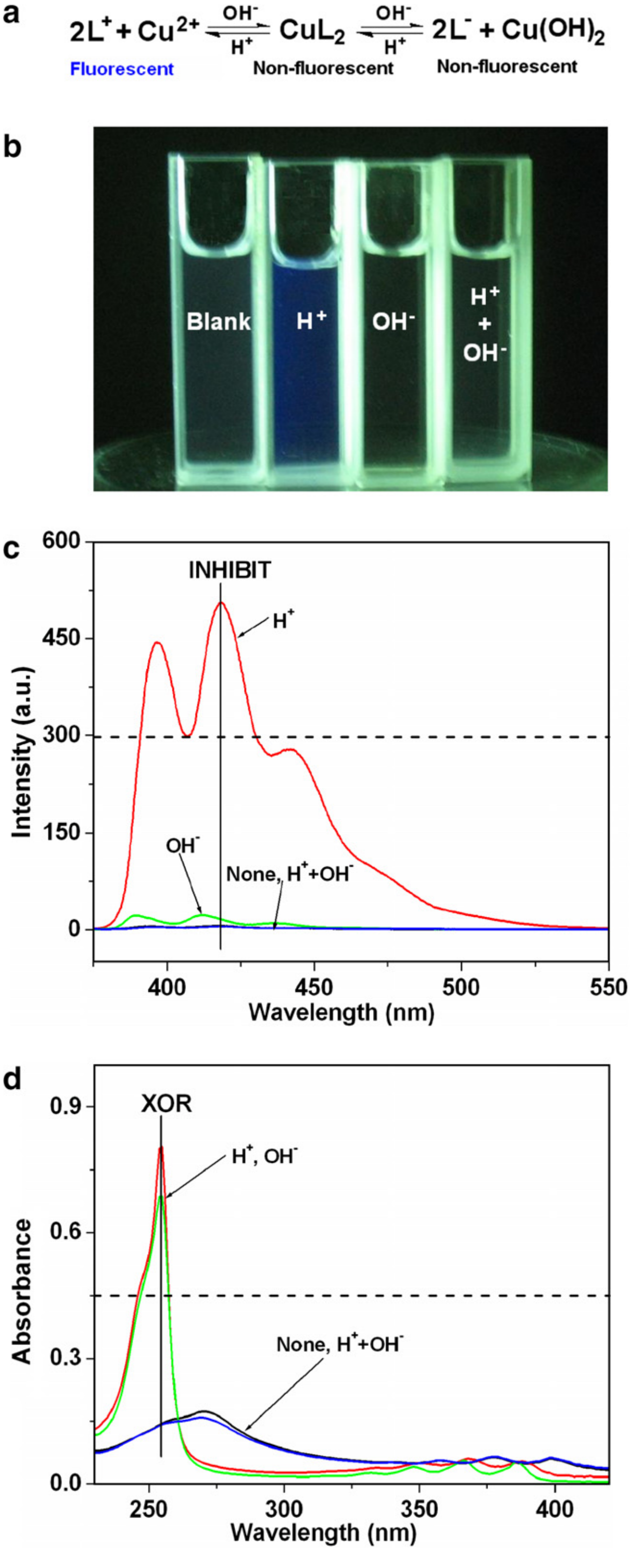
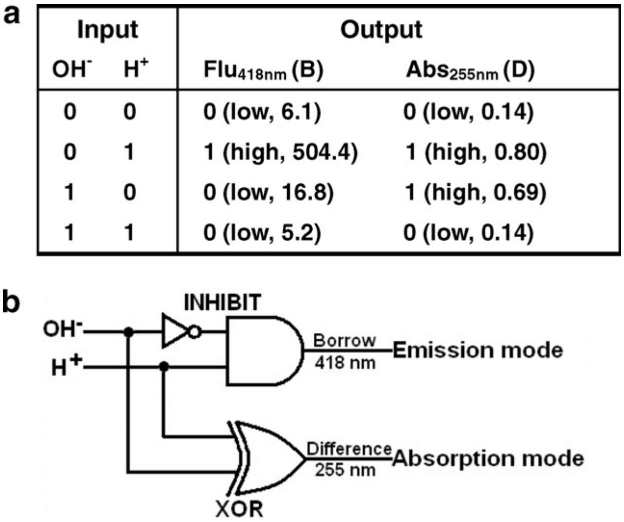


Figure 5. (a) Schematic representation of the interconversion of **L** among different fluorescent states. (b) **L** (5 μM) with Cu^{2+} (5 μM) system in methanol/water (v/v 1:9) solution illuminated with a UV lamp at 365 nm. From left to right: **L**–Cu^{2+} alone (pH 7.0), upon addition of 0.03 M HCl, 0.03 M NaOH, a mixture of 0.03 M HCl and 0.03 M NaOH. (c) Changes in fluorescence intensity of **L** (5 μM) with Cu^{2+} (5 μM) under four different inputs conditions, the INHIBIT function is attributed to the emission band at 418 nm. The dashed line marks the threshold value. (d) Changes in the absorption bands of **L** (5 μM) with Cu^{2+} (5 μM) under four different inputs conditions, the XOR function is derived by monitoring the absorbance at 255 nm. The dashed line marks the threshold value.



Input		Output	
OH^-	H^+	Flu_{418nm} (B)	Abs_{255nm} (D)
0	0	0 (low, 6.1)	0 (low, 0.14)
0	1	1 (high, 504.4)	1 (high, 0.80)
1	0	0 (low, 16.8)	1 (high, 0.69)
1	1	0 (low, 5.2)	0 (low, 0.14)

Figure 6. (a) Truth table for the operation of the molecular half-subtractor **L** (5 μM) with Cu^{2+} (5 μM) system. (b) Logic diagram of the half-subtractor. The 'difference' and 'borrow' outputs are collected in absorption and emission modes, respectively.

weaker absorption bands at 340–400 nm are also red shifted about 10 nm (Fig. S3). The absorption spectra of system **L** (5 μM) with various metal ions are conducted to examine its selectivity in aqueous solution (methanol/HEPES buffer, pH 7.0, v/v = 1:9) (Fig. S4). When Cu^{2+} is added, the spectrum change of **L** is much more significant. Upon addition of 5 equiv of other metal ions, the absorption peaks at 255 nm and 340–400 nm do not shift, and exhibit negligible absorbance changes.

Under the same starting conditions and the two inputs as those in the INHIBIT logic gate, monitoring changes of absorption at 255 nm as outputs, this molecule can operate as XOR logic gate simultaneously. Upon addition of acid or base, likewise, the complex CuL_2 liberates acidic L^+ and base L^-, respectively. As a result, the absorbances at 255 nm are significantly improved. When both acid and base are added, a neutralization reaction occurs, resulting in an absorbance at 255 nm decrease due to Cu^{2+} coordination with **L** at neutral pH, just as the initial state without adding. The resultant changes in maximum absorption at 255 nm can be used to derive a desirable XOR logic gate based on the chemical inputs H^+ and OH^- and absorbance as the output variable (Fig. 5d).

In summary, a highly effective dual-modal molecular sensor **L** was synthesized, which showed a significant quenching of fluorescence as well as a drastic change in the UV–vis spectrum in the presence of Cu^{2+} ions. The copper complex could perform simultaneously the functions of an 'INHIBIT' gate and an 'XOR' gate, capable of operating as a half-subtractor with acid and base as inputs, by monitoring the fluorescence and absorbance modes, respectively (Fig. 6).

Acknowledgment

We thank the National Natural Science Foundation of China for financial support (No. 90210027).

Supplementary data

Synthesis of **L**, the effect of pH on UV–vis absorption spectrum of **L**, **c**hanges in absorption spectra of **L** with various amounts of Cu^{2+} ions, absorption responses of **L** upon addition of various cations. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.07.081.

References and notes

1. Packan, P. A. *Science* **1999**, *285*, 2079.
2. Keyes, R. W. *Proc. IEEE* **2001**, *89*, 227.
3. Balzani, V.; Venturi, M.; Credi, A. *Molecular Devices and Machines—A Journey into the Nanoworld*; Wiley-VCH: Weinheim, 2003.
4. Ball, P. *Nature* **2000**, *406*, 118.
5. Raymo, F. M. *Adv. Mater.* **2002**, *14*, 401.
6. Magri, D. C.; Vance, T. P.; de Silva, A. P. *Inorg. Chim. Acta* **2007**, *360*, 751.
7. Margulies, D.; Melman, G.; Shanzer, A. *J. Am. Chem. Soc.* **2006**, *128*, 4865.
8. de Silva, A. P.; McClenaghan, N. D. *J. Am. Chem. Soc.* **2000**, *122*, 3965.
9. Guo, X. F.; Zhang, D. Q.; Zhang, G. X.; Zhu, D. B. *J. Phys. Chem. B* **2004**, *108*, 11942.
10. Langford, S. J.; Yann, T. *J. Am. Chem. Soc.* **2003**, *125*, 11198.
11. Credi, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5472.
12. Zhao, L.; Sui, D.; Chai, J.; Wang, Y.; Jiang, S. *J. Phys. Chem. B* **2006**, *110*, 24299.
13. Guo, Z. Q.; Zhu, W. H.; Shen, L. J.; Tian, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5549.
14. Margulies, D.; Melman, G.; Shanzer, A. *Nat. Mater.* **2005**, *4*, 768.
15. Margulies, D.; Melman, G.; Felder, C. E.; Arad-Yellin, R.; Shanzer, A. *J. Am. Chem. Soc.* **2004**, *126*, 15400.
16. Coskun, A.; Deniz, E.; Akkaya, E. U. *Org. Lett.* **2005**, *7*, 5187.
17. Suresh, M.; Jose, D. A.; Das, A. *Org. Lett.* **2007**, *9*, 441.
18. Liu, Y.; Jiang, W.; Zhang, H. Y.; Li, C. J. *J. Phys. Chem. B* **2006**, *110*, 14231.
19. Pérez-Inestrosa, E.; Montenegro, J. M.; Collado, D.; Suau, R.; Casado, J. *J. Phys. Chem. C* **2007**, *111*, 6904.
20. Sun, W.; Zheng, Y. R.; Xu, C. H.; Fang, C. J.; Yan, C. H. *J. Phys. Chem. C* **2007**, *111*, 11706.
21. Guo, Z. Q.; Zhao, P.; Zhu, W. H.; Huang, X. M.; Xie, Y. S.; Tian, H. *J. Phys. Chem. C* **2008**, *112*, 7047.
22. Zong, G. Q.; Xian, L.; Lu, G. X. *Tetrahedron Lett.* **2007**, *48*, 3891.
23. Preparation of Compound **L**: L-phenyl alanine (0.83 g, 5 mmol) and KOH (0.28 g, 5 mmol) were dissolved in hot anhydrous ethanol (50 mL), and 9-anthraldehyde (1.0 g, 5 mmol) was added portion-wise under stirring. And then the mixture was stirred at room temperature for 24 h to produce a yellow precipitate. $NaBH_4$ (1.0 g, 25 mmol) was added portion-wise, and the resulting solution was stirred at room temperature for 10 h. After distilling off the solvent under reduced pressure, the residue was treated with 50 mL of water and acidified with 37% HCl to pH 2–3 under stirring. The resultant solid was then filtered and recrystallized from acetone–HCl (aq) and dried in vacuum at 333 K, affording a yellow needle crystal **L**·HCl (1.1 g, yield: 56%). Mp 218–220 °C; ^1H NMR (CD_3OD, 400 MHz) δ (ppm): 8.70–7.37 (m, 14H, Ar*H*), 5.39–5.26 (m, 2H, C*H*$_2$NH), 4.71 (t, *J* = 7.2 Hz, 1H, C*H*COOH), 3.44–3.27 (m, 2H, C*H*$_2C_6H_5$); ^{13}C NMR (CD_3OD, 400 MHz) δ (ppm): 171.2, 135.7, 132.9, 132.5, 131.9, 130.6, 130.5, 130.0, 128.8, 128.7, 126.6, 124.4, 122.4, 62.7, 43.9, 36.9; MS (ESI): 356.4 $[M+H]^+$; Anal. Calcd. for $C_{24}H_{21}NO_2$·HCl: C, 73.56; H, 5.66; N, 3.57. Found: C, 73.2; H, 5.54; N, 3.91.
24. Martinez-Manez, R.; Snacenon, F. *Chem. Rev.* **2003**, *103*, 4419.
25. Connors, K. A. *Binding Constants*; Wiley: New York, 1987.
26. Polster, J.; Lachmann, H. *Spectrometric Titrations*; VCH: Weinheim, 1989.
27. Tao, W. A.; Zhang, D. X.; Nikolaev, E. N.; Cooks, R. G. *J. Am. Chem. Soc.* **2000**, *122*, 10598.
28. Shiraishi, Y.; Tokitoh, Y.; Hirai, T. *Chem. Commun.* **2005**, 5316.
29. Alves, S.; Pina, F.; Albelda, M. T.; Garcia-Espana, E.; Soriano, C.; Luis, S. V. *Eur. J. Inorg. Chem.* **2001**, 405.
30. Demas, J. N.; Crosby, G. A. *J. Phys. Chem.* **1971**, *75*, 991.