RSC Advances

This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This *Accepted Manuscript* will be replaced by the edited, formatted and paginated article as soon as this is available.

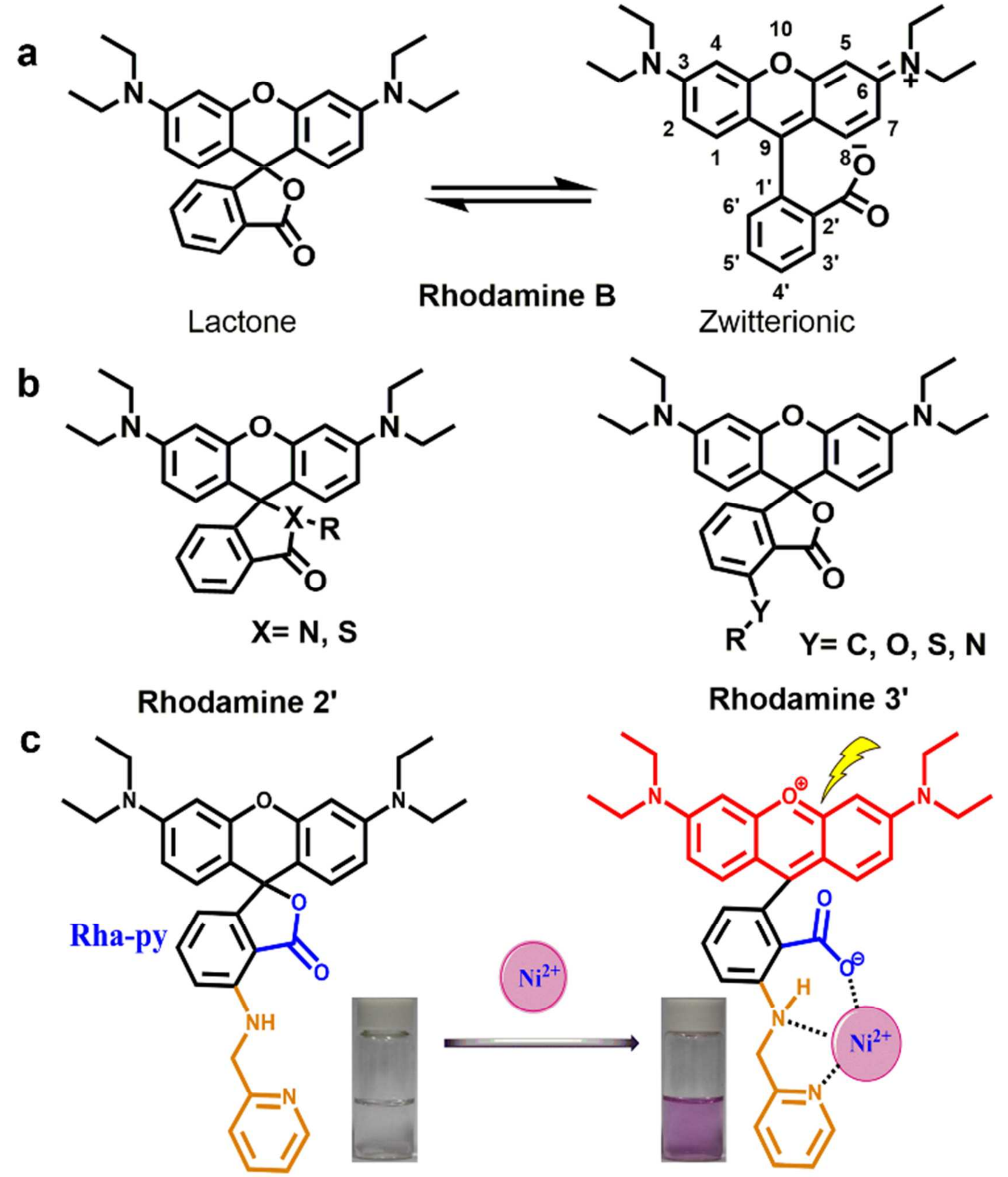
You can find more information about *Accepted Manuscripts* in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

A new spirocyclic rhodamine derivative for colorimetric sensing of Ni^{2+}



RSC Advances Accepted Manuscript

Journal Name

COMMUNICATION

A new rhodamine based chemodosimeter for Ni^{2+} with high sensitivity and selectivity

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Ivan Zhang,[a] Yi Wang,[a] Chao Wan,[b] Zhen Xing,[c] Wen Li,[a] MinjieLi*[a] and Sean Xiao-An Zhang*[a]

A new rhodamine derivative by modifying the ortho-position of carboxylate in benzolate with amino pyridine has been developed, which exhibits high sensitivity and selectivity toward Ni^{2+} with a detection limit lower to 4.6 ppb.

Nickel (Ni) is widely used in various industrial applications such as in electroplating, Ni–Cd batteries, pigments for paints, ceramics, catalysts for hydrogenation, surgical and dental prostheses and as magnetic tapes for computers. Besides, Ni ion is an essential cofactor for a variety of enzymes that play important roles in microorganisms and plants, particularly in energy and nitrogen metabolism. However, excessive Ni ion in our body will result in adverse health effects ranging from allergic dermatitis to lung and nasal sinus cancers.[1] Therefore, the detection of Ni^{2+} is very important. Up to now, various methods have been recently reported for the determination of Ni^{2+} concentration in different biological, industrial and food samples. The mature methods to detect Ni^{2+} are mostly based on time consuming and sophisticated analytical techniques, such as atomic absorption/emission spectrometry, liquid chromatography and voltammetry.[2] Although these methods are accurate, they are not suitable for convenient "in-the-field" detection as they normally require expensive instruments and sample pretreatment, and also have serious influence by the interference of coexisting ions. Therefore, it is very important to develop sensitive, rapid, and simple-to-use methods to sense Ni ions. Meanwhile, colorimetric sensors have also attracted much attention, because the detection can be analyzed by the naked eye. It also allows on-site and real-time detection in an uncomplicated and inexpensive manner, providing qualitative and quantitative information.[3] Unfortunately, colorimetric sensors for Ni^{2+} with high selectivity and sensitivity are rare.[4]

Rhodamine B is a widely used organic dye due to their excellent photophysical properties, such as high extinction coefficients, excellent quantum yields, and relatively long emission wavelengths.[5] But the partial tautomerization from lactone form to zwitterionic form in polar solvent leads to the strong background signal of Rhodamine B, which limits its application in chemosensors (Fig. S1, ESI †).[6] But since Czanik and the co-worker reported the

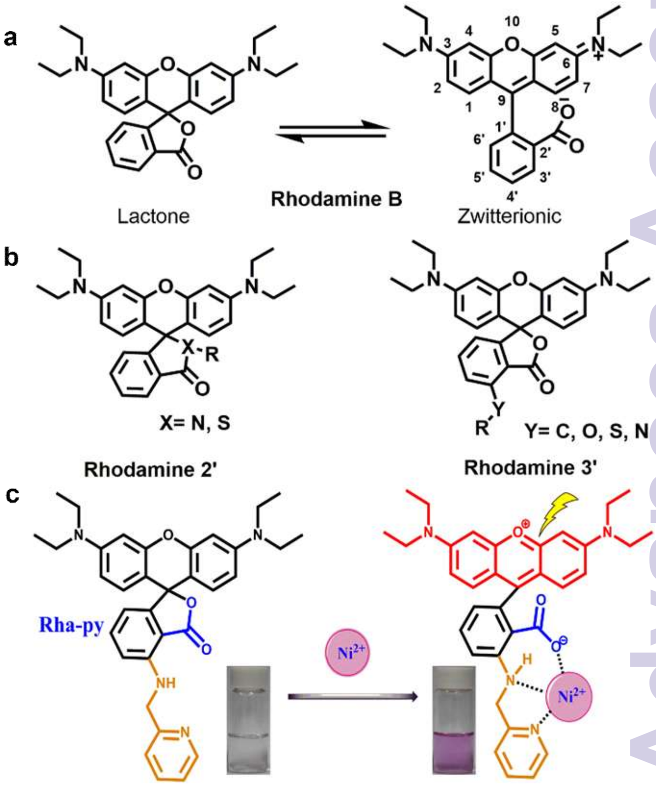


Fig. 1 a) The equilibrium of **Rhodamine B** between neutral lactone form and zwitterion form; b) Conventional rhodamines with modification on 2' (**Rhodamine 2'**) could detect Cu^{2+}, Hg^{2+} and so on; rhodamines with modification on 3' (**Rhodamine 3'**) could response new analytes; c) Molecular structure of **Rha-py** and a proposed mechanism for **Rha-py** in sensing Ni^{2+}. Change in color of **Rha-py** (4 μM) upon addition of Ni^{2+} (40 μM) under ambient light.

---

[a] State Key Lab of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, People's Republic of China. E-mail: liminjie@jlu.edu.cn, seanzhang@jlu.edu.cn; Fax: +86-043185155381
[b] College of Environment and Resources, Jilin University.
[c] College of Life of Science, Jilin University.

† Electronic Supplementary Information (ESI) available: ^{1}HNMR, ^{13}CNMR data, LC-HRMS data, X-ray diffraction data, synthetic details and spectra. SeeDOI: 10.1039/x0xx00000x

This journal is © The Royal Society of Chemistry 20xx

RSC Advances Accepted Manuscript

first modified-rhodamine for detecting Cu^{2+} in 1997, many rhodamine-based probes have been developed.[7] However, the modification in these probes are usually on 2′ position (**Rhodamine 2′**, e.g., the oxygen atom is replaced by nitrogen atom or sulfur atom) and they can only detect some common cations (such as Cu^{2+}, Hg^{2+}, Fe^{3+}, Cr^{3+} and so on) (Fig. 1b left).[8] To our best knowledge, the highly sensitive and selective rhodamine-based probe for Ni^{2+} hasn't been developed yet. The probable reason is that the present **Rhodamine 2′** could not well chelate Ni^{2+} and some new modifications on the skeleton of rhodamine seem particularly important. Here, we put forward a new modification strategy on rhodamine by introducing some proper ligands to ortho-position of carboxylate group in rhodamine (**Rhodamine 3′**, Fig.1 b right) and they would exhibit several advantages: (1) Y atom and R group in the molecular skeleton will be quite variable and they could be expected to detect different analytes by suitable combinations of Y atom and R group; (2) this modification could well maintain carboxylate group to participate in the chelation and finally enhance the recognition ability. As a prototype, we designed and synthesized a new ortho-modified rhodamine derivative of **Rha-py** (Fig. 1c). As we expected, the residual carboxylate group participates in the chelation of Ni^{2+} with other ligands and finally realizes the detection of Ni^{2+} with high selectivity and sensitivity.

Rha-py was facilely synthesized in high yield with only three steps. Detailed synthesis was given in ESI. We first tested the optical properties of **Rha-py** in aqueous solution. **Rha-py** was found that a strong absorption at 550 nm appeared in pure water, indicating that **Rha-py** partially existed in zwitterion form.[9] And the fluorescence of the probe was weak, which is presumably caused by the effect of photo-induced electron transfer (PET) from adjacent electron-donating amine on its benzyl carboxylate structure.[10] In the meanwhile, the thermal dissipation of excitation energy of the probing molecule by strong H bonding with water is another reason for the weak fluorescence. Interestingly, the fluorescence of the probe kept weak in presence of various metal ions (10 equiv) in a series of conventional buffers, and only Ni^{2+} induced an enhancement of less than 2-fold on absorption. But the absorption enhancement is not high enough. This phenomenon is understandable, because the unique properties of water with both the high polarity and H-bond donating and accepting properties of water will effectively decrease capability of coordination from its three built-in functional groups of amine, pyridine and carboxylate, thus metal ions are not easy to be fixed by these coordination groups.

Therefore, further evaluation of the **Rha-py** was then conducted in various mixed solutions of water and CH_3CN, and results indicate that a non-negligible absorption for ring-opened form of **Rha-py** still exist in neutral condition if the percentage of CH_3CN in solution is less than 50%. CH_3CN-H_2O (v/ v=9:1) is finally selected as an ideal test solvent to avoid the background absorption. The absorbance at 550 nm was about 40-fold enhanced in pH range from 4.5 to 7.5 (in HEPES buffer) in presence of 10 equivalents Ni^{2+} (Fig. S2, ESI †), showing obvious pink color from colorless solution. Detailed sensing capability of this probe toward various cations were systematically investigated thereafter with UV-Vis spectroscopy in CH_3CN-H_2O solution (v/ v=9:1) with HEPES buffer at pH=7.1.

Tested cations include Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Mn^{2+}, Ag^+, Hg^{2+}, Al^{3+}, Cr^{3+}, Fe^{3+}, Fe^{2+} and the counter ions are NO_3^- or Cl^-. When 10 equivalents of these cations (c=40 μM) were added to the test solution of **Rha-py** (c=4 μM) at room temperature the solutions remained colorless respectively, except for the Ni^{2+}, Co^{2+} and Cu^{2+}. Upon addition of Ni^{2+}, a dramatic pink color was observed by the naked eye immediately. In corresponding UV-Vis spectra, a new absorption band peaked at about 550 nm was formed herein, which is in good agreement with its color change on Ni^{2+} (Fig. 2). Furthermore, the pink color from this Ni^{2+} sensing still remained after a day. Co^{2+} also resulted in a very weak increment in absorption due possible to the similarity in size with Ni^{2+}. Although Cu^{2+} also induced ring-opening reaction initially with the appearance of pink color, the pink color however disappeared quickly in ten minutes (Fig. 3), but the pink color kept for a rather

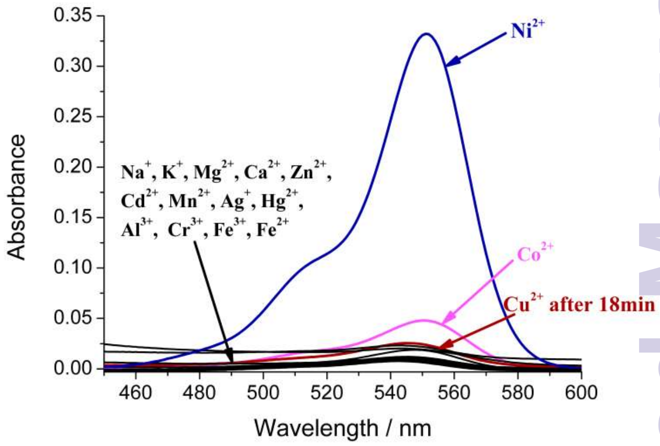


Fig. 2 Absorption spectra of **Rha-py** (4 μM) in CH_3CN buffered with HEPES (9/ 1, v/ v, pH=7.1, 20 mM) after the addition of different metal ions (40 μM) in 3 min, except for copper ion which was detected after 18 min. Metal ions: Na^+, K^+, Mg^{2+}, Ca^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+},Mn^{2+}, Ag^+, Hg^{2+}, Al^{3+}, Cr^{3+}, Fe^{3+} , Fe^{2+}.

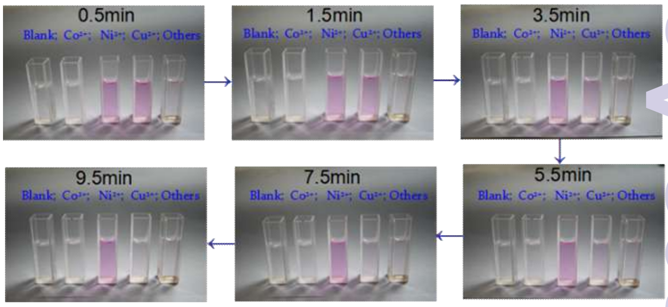


Fig. 3 Gradual color change of the solution of Rha-py (4 μM) after addition of 10 equivalents of various metal ions in CH_3CN buffered with HEPES (9/1, v/v, pH=7.1, 20 mM). Pictures above represent the change with the time in clockwise direction. Respectively, in each picture, the cube containing **Rha-py** and different cations (blank, Co^{2+}, Ni^{2+}, Cu^{2+}, others, from left to right).

RSC Advances Accepted Manuscript

Please do not adjust margins

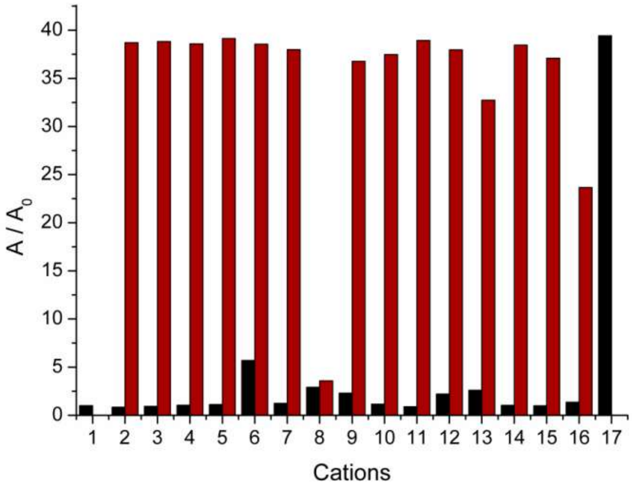


Fig. 4 Absorption spectra bar of **Rha-py** (4 μM) in the presence of 10 equivalents of $Ni^{2+}$with 10 equivalents of various metal ions in CH_3CN buffered with HEPES (9/1, v/v, pH=7.1, 20 mM). The spectra were got in 3 min after the addition of the metal ions, except Cu^{2+} was detected 18 min after the addition. Bars represent absorbance at 550 nm. The black bars represent the addition of the competing metal ions to the solution of **Rha-py**. The red bars represent the addition of competing metal ions and Ni^{2+} to the solution of **Rha-py**: 1, blank; 2 Ag^+; 3, Al^{3+}; 4, Ca^{2+}; 5, Cd^{2+}; 6, Co^{2+}; 7, Cr^{3+}; 8, Cu^{2+}; 9, Fe^{2+}; 10, Fe^{3+}; 11,Hg^{2+}; 12, K^+; 13, Mg^{2+}; 14, Mn^{2+}; 15, Na^+; 16, Zn^{2+}; 17, Ni^{2+}.

long time in presence of Ni^{2+} (Fig. S8, ESI †). In order to find out the reason, LC-MS experiments were carried out (Fig. S11, ESI †), the retention time of **Rha-py** was 2.5 min with its mass signal at 549.3, and the retention time of **Rha-amino** (amino group on the 3' position of Rhodamine B) was 2.7 min with its mass signal at 458.2. However, in the mixture of Cu^{2+} and **Rha-py**, no signal of **Rha-py** or its metal complex with Cu^{2+} was found, but the signal of **Rha-amino**. We presumed **Rha-py** could coordinate with Cu^{2+} well, but Cu^{2+} will catalyze its degradation to generate **Rha-amino**. **Rha-amino** cannot fully coordinate with Cu^{2+} and it exists in colorless lactone form.[11] This distinct difference on color fading time will help to differentiate these two interfering cations in practical sensing. In corresponding fluorescence spectra, Ni^{2+} induced about 5-fold enhancement (Fig S3, ESI †), and Cu^{2+} quenched the fluorescence of the probe, and we presumed it is because their electron configuration of d-orbital and the coordinating effect are different.

An important feature of a sensor is its selectivity toward the analyte relative to other competitive species. Therefore, competition experiments were carried out by adding Ni^{2+} (c=40 μM) to a solution of **Rha-py** (c=4 μM) in the presence of miscellaneous cations (c=40 μM), respectively. These miscellaneous competitive ions did not induce significant absorption changes of **Rha-py** in the absence of Ni^{2+}, except Cu^{2+}, which caused the color change at first and then the color faded in minutes. Upon addition of Ni^{2+} to the above solutions, pink color appeared except for the one with Cu^{2+} in it, which didn't show further color change (Fig. 4). These results revealed that **Rha-py** had a remarkable selectivity toward Ni^{2+} with the only interference of Cu^{2+}, however, by monitoring the time-resolved spectra or color fading rate, Cu^{2+} can be differentiated.

To identify the stoichiometry between Ni^{2+} and **Rha-py**, Job's plot had been drawn (Fig. S4, ESI †). We can find when the molar fraction of Ni^{2+} was 0.5, the absorbance at 550 nm reached a maximum, indicating the formation of a 1:1 complex between **Rha-py** and Ni^{2+}. And the association constant (Ka) of **Rha-py** with Ni^{2+} was determined as 4.87× 10^4 M^{-1} using the Benesi–Hildebrand equation (Fig. S6, ESI †).[12a] The spectroscopic detection limit for Ni^{2+} was 7.8 × 10^{-8} M (Fig. S7, ESI †), calculated with the equation of 3σ/S.[12b] Which is lower than the upper limit 0.04 mg/L (6.8 × 10^{-7} M) recommended by the U. S. Environmental Protection Agency (EPA) for drinking water.[13]

The interaction mechanism of Ni^{2+} with **Rha-py** was further studied with infrared spectroscopy (IR) and MALDI-TOF experiments. From the IR spectra (Fig. S9, ESI †), the stretching vibration absorption peaks of C=O and vibration of pyridine have a significant shift towards lower wavenumbers, and the vibration of carboxyl acid appeared, indicating the complexation with Ni^{2+}.[14] In MALDI-TOF, the number 605.34 stands for the complex of Ni^{2+} and **Rha-py**, which confirmed the coordination ratio was 1:1 (Fig. S10, ESI †).

In order to test the practicality of the **Rha-py** probe, we took the water from South Lake, Changchun as a sample. The sample was filtered to remove organisms and analyzed by the proposed absorption method under optimized conditions, and no Ni^{2+} was detected. Then Ni^{2+} is added to the sample on purpose. The recovery of Ni^{2+} and R.S.D. of probe **Rha-py** are satisfactory (Table S1 ESI †),[15] indicating that the present colorimetric probe of **Rha-py** was applicable for the determination of Ni^{2+} in contaminated water samples.

Conclusions

In summary, we first demonstrate the modification strategy on the 3' position of rhodamine and developed a colorimetric probe for Ni^{2+}. The prototype probe of **Rha-py** based on the strategy shows high sensitivity and selectivity for Ni^{2+}. The probe could respond to Ni^{2+} quickly and distinguish Cu^{2+} with the assistance of time. Unfortunately, Cu^{2+} is an interference for Ni^{2+} detection, however, it can be differentiated by time-resolved spectra or color fading rate. The spectroscopic detection limit is lower than the upper limit recommended by EPA for drinking water. With good performance in analysis of Ni^{2+} in lake water, we believe that this novel Ni^{2+} chemosensor can be used for monitoring Ni^{2+} in contaminated water samples with high sensitivity and selectivity. This work will be a starting point of further research, we will make further effort to modify the 3' position along with the modification on the other position. This will surely inspire more development of chemosensors for environmental and medical applications.

This work was supported by the National Science Foundation of China (Grant No. 51373068) and program for Chang Jiang Scholars and Innovative Research Team in University (No. IRT101713018).

RSC Advances Accepted Manuscript

Please do not adjust margins

Notes and references

1 (a) P. H. Kuck, *Mineral Commodity Summaries: Nickel*, United States Geological Survey, 2006; (b) J. R. Davis, *Uses of Nickel, ASM Specialty Handbook: Nickel, Cobalt, and Their Alloys*, ASM International, 2000, p. 7; (c) E. Denkhaus and K. Salnikow, *Crit. Rev. Oncol. Hematol.*, 2002, **42**, 35; (d) M. E. Rothenberg, *Nat. Immunol.*, 2010, **11**, 781; (e) D. P. Giedroc, A. I. Arunkumar, *Dalton. Trans*., 2007, 3107.

2 (a) S. Carter, A. S. Fisher, M. W. Hinds and S. Lancaster, *J. Anal. At. Spectrom.*, 2012, **27**, 2003; (b) V. K. Gupta, R. N. Goyal, S. Agarwal, P. Kumar and N. Bachheti, *Talanta*, 2007, **71**, 795; (c) V. K. Gupta, R. Prasad, P. Kumar and R. Mangla, *Anal. Chim. Acta*, 2000, **420**, 19; (d) V. K. Gupta, A. K. Singh and M. K. Pal, *Anal. Chim. Acta*, 2008, **624**, 223.

3 (a) D. Xiong and H. Li, *Nanotechnology*, 2008, **19**, 465502; (b) H. Zhu, J. Fan, B. Wang and X. Peng, *Chem. Soc. Rev.*, 2015, **44**, 4337; (c) X. Lou, L. Zhang, J. Qin and Z. Li, *Chem. Commun.*, 2008, 5848; (d) X. M. Liu, Q. Zhao, Y. Li, W. C. Song, Y. P. Li, Z. Chang and X. H. Bu, *Chin. Chem. Lett.*, 2013, **24**, 962.

4 (a) K. P. Carter, A. M. Young and A. E. Palmer, *Chem. Rev*., 2014, **114**, 4564; (b) N. Kaur and S. Kumar, *Chem. Commun.*, 2007, 3069; (c) S. Goswami, S. Chakraborty, A. K. Das, A. Manna, A. Bhattacharyya, C. K. Quah and H. K. Fu, *RSC Adv.*, 2014, **4**, 20922; (d) F. A. Abebe, C. S. Eribal, G. Ramakrishna and E. Sinn, *Tetrahedron Lett.*, 2011, **52**, 5554.

5 (a) M. Beija, C. A. M. Afonso and, J. M. G. Martinho, *Chem. Soc. Rev.*, 2009, **38**, 2410; (b) M. J. Uddin and L. J. Marnett, *Org. Lett.*, 2008, **10**, 4799; (c) T. D. Horvath, G. Kim, R. Kopelman and S. Ashkenazi, *Analyst*, 2008, **133**, 747; (d) F. Yan, L. Chen, X. Yan, F. Ge and E. Duan, *Prog. Chem.,* 2006, **18**, 252.

6 (a) X. Yang, Y. Guo and R. M. Strongin, *Org. Biomol. Chem.*, 2012, **10**, 2739; (b) Y. K. Yang, K. J. Yook and J. Tae, *J. Am. Chem. Soc.*, 2005, **127**, 16760; (c) K. M. K. Swamy, S. K. Ko, S. K. Kwon, H. N. Lee, C. Mao, J. M. Kim, K.-H. Lee, J. H. Kim, I. Shin and J. Yoon, *Chem. Commun.*, 2008, 5915. (d) A. J. Weerasinghe, F. A. Abebe and E. Sinn, *Tetrahedron Lett.*, 2011, **52**, 5648.

7 (a) V. Dujols, F. Ford and A. W. Czarnik, *J. Am. Chem. Soc.*, 1997, **119**, 7386; (b) A. J. Weerasinghe, C. Schmiesing, S. Varaganti, G. Ramakrishna and E. Sinn, *J. Phys. Chem. B*, 2010, **114**, 9413; (c) H. Zheng, X. Q. Zhan, Q. N. Bian and X. J. Zhang, *Chem. Commun.*, 2013, **49**, 429; (d) B. Qiao, S. G. Sun, N. Jiang, S. Zhang and X. J. Peng, *Dalton Trans*., 2014, **43**, 4626; (e) H. N. Kim, M. H. Lee, H. J. Kim, J. S. Kim and J. Y. Yoon, *Chem. Soc. Rev.*, 2008, **37**, 1465.

8 (a) A. J. Weerasinghe, C. Schmiesing and E. Sinn, *Tetrahedron Lett.*, 2009, **50**, 6407; (b) E. M. Nolan and S. J. Lippard, *J. Am. Chem. Soc*., 2007, **129**, 5910; (c) X. Zhang, Y. Xiao and X. Qian, *Angew. Chem., Int. Ed.*, 2008, **47**, 8025; (d) Y. Xiang and A. Tong, *Org. Lett.*, 2006, **8**, 1549; (e) Y. K. Yang, K. J. Yook and J. Tae, *J. Am. Chem. Soc.*, 2005, **127**, 16760; (f) Z. G. Zhou, M. X. Yu, H. Yang, K. W. Huang, F. Y. Li, T. Yi and C. H. Huang, *Chem. Commun.*, 2008, 3387; (g) Y. Koide, Y. Urano, S. Kenmoku, H. Kojima and T. Nagano, *J. Am. Chem. Soc.*, 2007, **129**, 10324; (h) X. D. Lou, Y. Zhang, Q. Q. Li, J. G. Qin and Z. Li, *Chem. Commun.*, 2011, **47**, 3189; (i) S. Wen and H. M. Ma, *Chem. Commun.*, 2008, **16**, 1856; (j) K. B. Li, Y. Zang, H. Wang, J. Li, G. R. Chen, T. D. James, X. P. He and H. Tian, *Chem. Commum.*, 2014, **50**, 11735; (k) Z. X. Han, B. S. Zhu, T. L. Wu, Q. Q. Yang, Y. L. Xue, Z. Zhang and X. Y. Wu, *Chin. Chem. Lett.*, 2014, **25**, 73.

9 N. V. Abrosimova, A. G. Stepanova, I. A. Krasavin, B. V. Parusnikov, *J. Appl. Spect.*, 1988, **48**, 610.

10 (a) C. Munkholm, D. R. Parkinson and D. R. Walt, *J. Am. Chem. Soc.*, 1990, **112**, 2608; (b) A. P. de Silva, T. S. Moody and G. D. Wright, *Analyst*, 2009, **134**, 2385.

11 M. Taki, S. Iyoshi, A. Ojida, I. Hamachi and Y. Yamamoto, *J. Am. Chem. Soc.*, 2010, **132**, 5938.

12 (a) H. A. Benesi, J. H, Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703; (b) IUPAC Commission on Spectrochemical and Other Optical Procedures for Analysis, *Pure. Appl. Chem.*, 1976, **45**, 107.

13 G. Aragay, J. Pons and A. Merkoci, *Chem. Rev.*, 2011, **111**, 3433.

14 (a) G. R. Woodburn, N. R. Lien, A. Hoppe, Y. Jahng and J. R. Telford, *J. Coord. Chem.*, 2010, **63**, 185; (b) X. Liu, Q. Lin, T-B. Wei and Y-M Zhang, *New. J. Chem*., 2014, **38**, 1418.

15 M. Wang, F-Y. Yan, Y. Zou, N. Yang, L. Chen, L-G. Chen, *Spectrochim. Acta, Part A*, 2014, **123**, 216.

RSC Advances Accepted Manuscript

This journal is © The Royal Society of Chemistry 20xx