RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2020, **10**, 6109

A coumarin-containing Schiff base fluorescent probe with AIE effect for the copper(II) ion†

Ying Wang,[a] Xiaohui Hao,*[b] Lixun Liang,[a] Luyao Gao,[a] Xumin Ren,[a] Yonggang Wu[a] and Hongchi Zhao *[a]

Received 17th December 2019
Accepted 26th January 2020

DOI: 10.1039/c9ra10632d

rsc.li/rsc-advances

A novel coumarin-derived Cu^{2+}-selective Schiff base fluorescent "turn-off" chemosensor **CTPE** was successfully obtained, which showed an AIE effect. It could identify Cu^{2+} by quenching its fluorescence. The lower limit of detection was 0.36 μM. **CTPE** can act as a highly selective and sensitive fluorescence probe for detecting Cu^{2+}.

The specific detection of transition metal ions has received considerable attention because of their significant roles in the fields of biological, chemical, medical and environmental processes.[1] Among these metal ions, copper(II), acting as one of the most important micronutrients, is of particular interest due to its essential role in a variety of fundamental physiological processes. In spite of the fact that copper(II) is essential in living systems, accumulation of copper(II) can lead to serious environmental and health problems.[2] For instance, the metabolic balance of Cu^{2+} in the body being destroyed can lead to neurodegenerative diseases, such as Alzheimer's, Parkinson's, Menkes, and Wilson's disease.[3–8] Besides, free Cu^{2+} is regarded as a significant environmental pollutant.[9,10] Therefore, an increasingly convenient and fast method to detect Cu^{2+} ion existing in environmental and biological resources is currently of considerably important. By far there existing many methods make it possible to detect and quantify Cu^{2+} ion, such as atomic absorption spectrometry,[11,12] inductively coupled plasma mass spectrometry,[13] inductively coupled plasma-atomic emission spectrometry[14] and voltammetry,[15,16] *etc.* However, these methods require tedious sample preparation procedures and complex instrumentation, which limit their prosperous applications. Alternatively, more and more attention has been attracted to the analytical methods based on fluorescent chemosensors for the detection of the metal ions owing to their high sensitivity, selectivity, and simplicity.[17] As a result, various types of fluorescent probes such as organic dyes, magnetic nanoparticles (MNPs), semiconductor quantum dots (QDs), carbon dots (CDs), fluorescent metal nanoclusters (NCs), and fluorescent metal organic frameworks (MOFs) have been designed and prepared to determine Cu^{2+} ion.[18–27] Since first reported in 2000, MNPs are extensively used in the field of nanotechnology for its nonhazardous feature, strong magnetization values, superparamagnetic property, active surface that can easily assembled of biological soluble structure and targeting, imaging, and therapeutic molecules.[22] Unlike organic fluorescent dyes, QDs are semiconductor particles which exhibit high photochemical stability, excellent resistance to chemical degradation, outstanding photodegradation and extremely large Stokes shift.[23] CDs is a comprehensive term for various nanosized carbon materials including graphene quantum dots (GQDs), carbon nanodots (CNDs), and polymer dots (PDs)[24] which shows excellent properties including high stability, bio-compatibility, low photo bleaching and toxicity and so on.[25] Despite successfully applying in detecting Cu^{2+}, traditional fluorescent probes are still puzzled by the toxicity, poor solubility, "aggregation-caused quenching" (ACQ) effect, *etc.* Thus, preparing fluorescent probes that can compensate for these deficiencies is still imminently desired in the Cu^{2+} ion detection.

Coumarin derivatives are well known excellent fluorophores in the fluorescent probe design and synthesis with the advantages of high fluorescence intensity, excellent solubility, efficient cell permeation, high quantum yield and ease of preparation.[28,29] As a result, an increasing number of papers concerning coumarin derivatives fluorescent chemosensors for copper(II) ion have emerged.[30–33] In 2009, Lee Jin Yong and co-workers developed a novel coumarin-based fluorogenic probe, which can act as a fluorescent chemosensor with high selectivity and suitable affinity in biological systems toward Cu^{2+} (ref. 34). Besides, in 2019, Yin Jiqiu and co-workers obtained a fluorescent chemosensor concerning coumarin derivatives for copper(II) which exhibited good sensitivity, fast response time and high selectivity for Cu^{2+} ion in the presence of other important relevant metal ions.[35]

In 2001, Tang Benzhong and co-workers proposed the concept of "aggregation-induced emission" (AIE).[36] Due to their

---

[a] College of Chemistry and Environmental Science, Hebei University, Baoding, 071002, P. R. China. E-mail: zhc@hbu.edu.cn

[b] College of Physics Science and Technology, Hebei University, Baoding, 071002, P. R. China. E-mail: haoxiaohui@hbu.edu.cn

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c9ra10632d

effective in circumventing the ACQ effect, AIE-active materials provide a new path for the design and synthesis of fluorescent probes. Tetraphenylethene (TPE), one of the most commonly used aggregation-induced emission luminogens (AIEgens), has been widely favored by researchers.[37,38] Owing to its simple structure, simple synthesis, easy modification, and obvious AIE effect, TPE is usually used as an ideal model for construction of various fluorescent sensors.[39] In 2019, Zhao Feng and co-workers designed and synthesized a new tetraphenylethene-based Schiff base ligand with AIE effect, and it could be utilized as optical recording materials.[40] The same year, Ni Zhonghai and co-workers obtained two different polymorphs of a new tetraphenylethene-based Schiff base, which exhibited totally different photochromic and fluorescence properties.[41]

Many Schiff base ligands have been synthesized for the detection of Cu^{2+}, which have general fluorescence characteristics. To solve the ACQ problem, we are going to design and synthesize a Schiff base fluorescent probe with AIE effect. For this purpose, a Schiff base fluorescent probe (**CTPE**) incorporating the TPE group into coumarin framework has been designed and synthesized, which exhibits fast response time, simple synthetic step, lower cost and AIE effect. And it can rapidly recognize Cu^{2+} in a mixed THF/H_2O system.

Scheme 1 was the synthetic route for **CTPE**. Other compounds and intermediates were labelled and displayed in Scheme S1 in the ESI.† As shown in Scheme 1, **CTPE** was prepared in high yield *via* Maillard reaction of 8-formyl-7-hydroxy-4-methylcoumarin (**M1**) and 1-(4′-aminophenyl)-1,2,2-triphenylethene (**TPE-NH₂**) in absolute ethanol. **M1**, **TPE-NH₂** and **CTPE** were prepared according to the literatures.[42,43] Their chemical structures were confirmed by nuclear magnetic resonance (NMR), high resolution mass spectrometry (HRMS) and Fourier transform infrared (FTIR) (Fig. S1–S10, ESI†). In Fig. S10,† compared with **TPE-NH₂** and **M1**, the spectrum of **CTPE** appeared an in-plane bending vibration absorption peak of C═N bond at 1620 cm^{-1}, and a C═O bond stretching vibration absorption peak on the aldehyde group at 1740 cm^{-1}, indicating that **CTPE** has been successfully synthesized.

As an AIE-based fluorescent probe, the AIE effect of **CTPE** was confirmed by its fluorescence spectra in THF/H_2O mixtures with various water contents. **CTPE** was in a good dispersion state in THF solvent, but **CTPE** gradually aggregated as the volume fraction of water (f_w) increased. As shown in Fig. 1A and B, **CTPE** had good dispensability and exhibited weak luminescence in dilute THF solution ($f_w = 0\%$). The weak emissive nature of the luminogens in THF and aqueous mixtures with low f_w values should be ascribed to active intramolecular rotations of the genuinely dissolved compounds, which effectively consumed the energy of the excitons non-radiatively.[44] When f_w increased from 10% to 70%, the fluorescence intensity of **CTPE** gradually decreased, which was attributed to the intramolecular charge transfer (ICT) effect with the increasing polarity of the solution for **CTPE**.[40,45] When f_w was above 70%, **CTPE** displayed a significantly sudden increase in the fluorescence intensity owing to molecular aggregation. The fluorescence intensity at 565 nm was about 60 in THF/H_2O (30/70, v/v) mixtures, while it increased to about 1288 in THF/H_2O (1/99, v/v) mixtures with about 21-fold enhancement. Simultaneously, and the maximum emission wavelength showed a slight red shift from 565 nm to 575 nm with the increase of fluorescence intensity. The fluorescence enhancement phenomenon could be ascribed to the restriction of the intramolecular rotations. In the aggregated state, intramolecular motion (mainly including C═N isomerization and rotation of the benzene ring) was limited, and the attenuation of non-radiative energy was correspondingly blocked, so that a clear enhancement and a slight red shift of the fluorescence of **CTPE** were observed.[40] The above results clearly implied that **CTPE** exhibited a significant AIE effect.

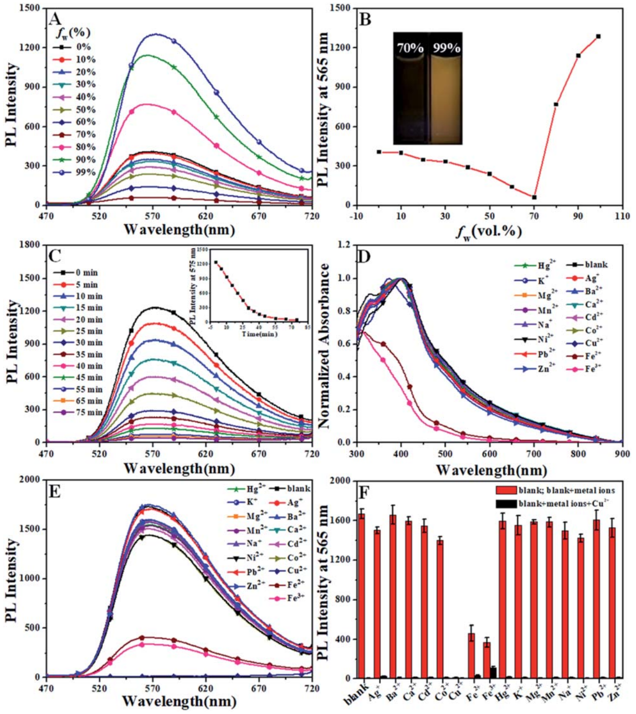
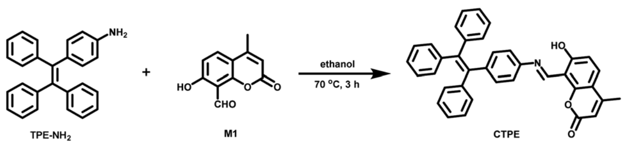


Fig. 1 (A) PL spectra of **CTPE** in THF/H_2O mixtures with different f_w. (B) Plots of PL intensity of **CTPE** *versus* f_w in THF/H_2O mixtures at 565 nm. Inset: photograph of **CTPE** in THF/H_2O mixtures under a hand-held UV lamp illumination ($\lambda_{ex} = 365$ nm). (C) PL spectra of **CTPE** after adding Cu^{2+} in THF/H_2O (1/99, v/v) at different reaction time. Inset: relationship between fluorescence intensities of **CTPE** in THF/H_2O (1/99, v/v) at 575 nm and time of addition of Cu^{2+}. (D) UV-vis absorption and (E) fluorescence spectra of **CTPE** with different metal ions in THF/H_2O (10/90, v/v). (F) Fluorescence responses at 565 nm of **CTPE** to various metal cations in THF/H_2O (10/90, v/v) solution.



Scheme 1 Synthesis and structure of **CTPE**.

The Cu^{2+}-specific binding of **CTPE** with various competitive metal ions was then investigated under the same experimental condition. Different from these AIE sensors that worked in the aggregated state, there was not complete fluorescence quenching even after about 1 h of adding 20 equivalent Cu^{2+} in THF/H_2O (1/99, v/v) solution (shown in Fig. 1C). However, at the moment of adding Cu^{2+}, the fluorescence was immediately quenched in THF/H_2O (10/90, v/v) solution. Therefore the THF/H_2O (10/90, v/v) system was adopted to study the selectivity of **CTPE** to all metal ions.

Metal ion selectivity studies were performed on absorption and fluorescence spectra. Absorption spectra of **CTPE** recorded after the addition of each metal ion (20 eq.) was shown in Fig. 1D. In Fig. 1D, upon addition of a constant amount (20 eq.) of Cu^{2+} ion to **CTPE**, a significant hypsochromic shift from 395 nm to 371 nm in absorption spectrum was observed. No other metal ion induced any change under the identical conditions except Fe^{3+} and Fe^{2+} ions. These results demonstrated the specificity of the **CTPE** for selective binding interaction with Cu^{2+} ion.

To further investigate the selectivity of **CTPE** to Cu^{2+}, we also studied the fluorescence response of **CTPE** in THF/H_2O (10/90, v/v) solution. The behaviour of fluorescence "turn off" merely shown by Cu^{2+} was observed in the Fig. 1E. Surprisingly, the fluorescence was immediately quenched in THF/H_2O (10/90, v/v) solution at the moment of adding Cu^{2+}. And the fluorescence intensities decreased after adding Fe^{3+} and Fe^{2+}, respectively. No obvious changes were observed upon addition of 20 eq. other competitive metal ions. The interferences from the other metal ion with **CTPE** in its response to Cu^{2+} were performed. As shown in Fig. 1F, the red bars represent the emission changes of **CTPE** in the presence of metal ions of interest (all are 20 eq.). The black bars represent the changes of the emission that occurs upon the subsequent addition of Cu^{2+} to the above solution. The fluorescent intensity of **CTPE** in the presence of any of the other metal ions tested after adding Cu^{2+} was decreased significantly, demonstrating little interference from the other metal ions.

Fluorescent titration experiments of **CTPE** in THF/H_2O (10/90, v/v) solution with Cu^{2+} ion were carried out and the changes in the fluorescence intensity at 565 nm of **CTPE** solution with the concentration of Cu^{2+} ion were measured and showed in Fig. 2A. It was found that the fluorescence intensity at 565 nm of **CTPE** solution decreased with the increase in the concentration of Cu^{2+} ion. As showed in Fig. 2B, F_0 and F were the fluorescence intensities at 565 nm without adding Cu^{2+} and adding different concentrations of Cu^{2+}, respectively. In addition, when the Cu^{2+} concentration in the solution to be tested was less than 1.2 μM, the F_0/F of **CTPE** at 565 nm had a good linear relationship with the concentration of Cu^{2+}.

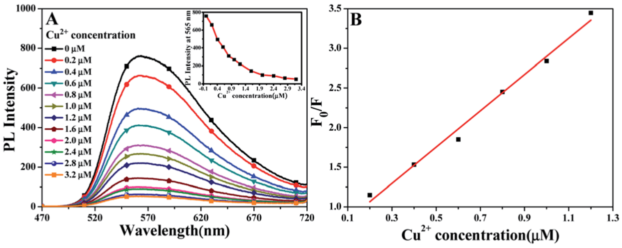


Fig. 2 (A) Fluorescence titration spectra of **CTPE** (10 μM) in THF/H_2O (10/90, v/v) solution. Inset: fluorescence intensities of **CTPE** (10 μM) at 565 nm as a function of Cu^{2+} concentration (0–3.2 μM). (B) Linear relationship between F_0/F and Cu^{2+} concentration.

By taking that change in fluorescence intensity in micro molar range we have calculated the lower limit of detection (LOD) from standard deviation and the slope of calibration plot (Fig. 2B) using the equation.[46] It was deduced from the fluorescence titration profile that the LOD of **CTPE** toward Cu^{2+} ion reached 0.36 μM.

To gain a better understanding the sensing mechanism of **CTPE** towards Cu^{2+}, ^{1}H-NMR titration experiments were performed in DMSO-d_6 at room temperature (Fig. 3A). The ^{1}H-NMR spectra of **CTPE** showed considerable variation with the increasing of Cu^{2+} in DMSO-d_6 solvent. Cu^{2+} is a paramagnetic ion that affects the NMR resonance frequency of protons that are close to the Cu^{2+} binding site.[47] The downfield value of H_a (of –O<u>H</u>) at $\delta = 14.86$ ppm in **CTPE** was due to the intramolecular hydrogen bond between the imine-N atom of **CTPE** with H_a forming a six-membered transition state.[48] On addition of Cu^{2+} ion, the intramolecular hydrogen bonding was disturbed.[49] As Cu^{2+} gradually increased, the proton signal of H_a almost disappeared. The proton signal of H_b (of –C<u>H</u>=N–) at $\delta = 9.16$ ppm significantly decreased indicating the participation of the nitrogen atom in the binding with Cu^{2+} ion. The proton signals of the aromatic ring became broader and weaker with the increasing amount of Cu^{2+}. These results confirmed that Cu^{2+} binded to the **CTPE** chemosensor through the N atom of the imine and the O atom of phenolic hydroxyl, which were directly connected to the aromatic rings.[50] Thus, combined with the FTIR spectra of **CTPE** before and after the addition of Cu^{2+} (Fig. S11†), it was clearly illustrated that the fluorescence "turn

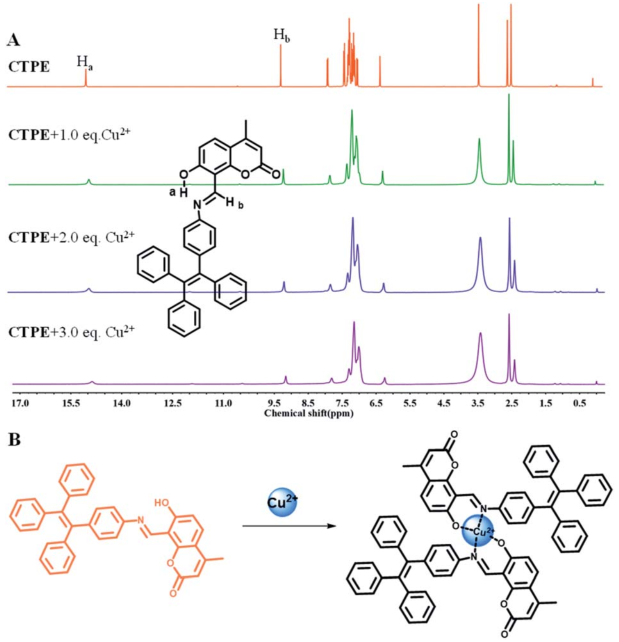


Fig. 3 (A) ^{1}H-NMR data of **CTPE** in DMSO-d_6 solution in the absence and presence of Cu^{2+}. (B) Proposed mechanism for **CTPE** upon addition of Cu^{2+}.

off" of **CTPE** was attributed to the chelation between imine-N atom, phenolic hydroxyl-O atom and Cu^{2+} ion. The possible coordination modes of Cu^{2+} and **CTPE** were shown in Fig. 3B.

In summary, a novel Schiff base fluorescent probe **CTPE** based on coumarin and TPE showing an AIE effect has been successfully synthesized and characterized. The fluorescence of **CTPE** was rapidly quenched by Cu^{2+}, but no significant influence was observed for other metal ions tested. **CTPE** can distinguish Cu^{2+} from other metal ions *via* the fluorescence "turn off". The LOD of **CTPE** for Cu^{2+} can reach 0.36 μM. Recognition mechanism between **CTPE** and Cu^{2+} was given. Therefore, **CTPE** can act as a potential fluorescence probe to selectively and rapidly identify Cu^{2+}.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors thank the financial supports from the Natural Science Foundation of Hebei Province, China (B2018201281, B2019201337).

Notes and references

1 H. Tapiero, D. M. Townsend and K. D. Tew, *Biomed. Pharmacother.*, 2003, **57**, 386.
2 P. G. Welsh, J. Lipton, C. A. Mebane and J. C. A. Marr, *Ecotoxicol. Environ. Saf.*, 2008, **69**, 199.
3 E. Gaggelli, H. Kozlowski, D. Valensin and G. Valensin, *Chem. Rev.*, 2006, **106**, 1995.
4 X. X. He, J. Zhang, X. G. Liu, L. Dong, D. Li, H. Y. Qiu and S. C. Yin, *Sens. Actuators, B*, 2014, **192**, 29.
5 Y. Gao, Y. Z. Li, X. P. Yang, F. F. He, J. M. Huang, M. H. Jiang, Z. H. Zhou and H. J. Chen, *RSC Adv.*, 2015, **5**, 80110.
6 R. I. Khan and K. Pitchumani, *RSC Adv.*, 2016, **6**, 20269.
7 L. Zeng, E. W. Miller, A. Pralle, E. Y. Isacoff and C. J. Chang, *J. Am. Chem. Soc.*, 2006, **128**, 10.
8 E. L. Que and C. J. Chang, *J. Am. Chem. Soc.*, 2006, **128**, 15942.
9 N. Narayanaswamy and T. Govindaraju, *Sens. Actuators, B*, 2012, **161**, 304.
10 K. N. Buck, J. R. M. Ross, A. R. Flegal and K. W. Bruland, *Environ. Res.*, 2007, **105**, 5.
11 T. W. Lin and S. D. Huang, *Anal. Chem.*, 2001, **73**, 4319.
12 M. S. Chan and S. D. Huang, *Talanta*, 2000, **51**, 373.
13 J. S. Becker, A. Matusch, C. Depboylu, J. Dobrowolska and M. V. Zoriy, *Anal. Chem.*, 2007, **79**, 6074.
14 Y. Liu, P. Liang and L. Guo, *Talanta*, 2005, **68**, 25.
15 M. Lin, M. Cho, W. S. Choe, Y. Son and Y. Lee, *Electrochim. Acta*, 2009, **54**, 7012.
16 Y. Oztekin, A. Ramanaviciene and A. Ramanavicius, *Sens. Actuators, B*, 2011, **155**, 612.
17 P. Pathirathna, Y. Y. Yang, K. Forzley, S. P. McElmurry and P. Hashemi, *Anal. Chem.*, 2012, **84**, 6298.
18 Y. B. Shi, Q. Y. Liu, W. Yuan, M. Xue, W. Feng and F. Y. Li, *ACS Appl. Mater. Interfaces*, 2019, **11**, 430.
19 Y. E. Shi, X. M. Zhuang, L. L. Cao, S. Y. Gou, Y. Xiong, W. F. Lai, Z. G. Wang and A. L. Rogach, *ChemNanoMat*, 2019, **5**, 110.
20 C. Fan, X. X. Lv, F. J. Liu, L. P. Feng, M. Liu, Y. Y. Cai, H. Liu, J. Y. Wang, Y. L. Yang and H. Wang, *ACS Sens.*, 2018, **3**, 441.
21 F. Yarur, J. Macairan and R. Naccache, *Environ. Sci.: Nano*, 2019, **6**, 1121.
22 Z. Chen, C. Wu, Z. F. Zhang, W. P. Wu, X. F. Wang and Z. Q. Yu, *Chin. Chem. Lett.*, 2018, **29**, 1601.
23 P. Zhao, Q. Xu, J. Tao, Z. W. Jin, Y. Pan, C. M. Yu and Z. Q. Yu, *Wires Nanomed. Nanobi.*, 2018, **10**, e1483.
24 S. Y. Lu, L. Z. Sui, M. Wu, S. J. Zhu, X. Yong and B. Yang, *Adv. Sci.*, 2019, **6**, 1801192.
25 S. J. Sun, Q. W. Guan, Y. Liu, B. Wei, Y. Y. Yang and Z. Q. Yu, *Chin. Chem. Lett.*, 2019, **30**, 1051.
26 J. Meng, S. E, X. Wei, X. W. Chen and J. H. Wang, *ACS Appl. Mater. Interfaces*, 2019, **11**, 21150.
27 H. Weng and B. Yan, *Anal. Chim. Acta*, 2017, **988**, 89.
28 D. En, Y. Guo, B. T. Chen, B. Dong and M. J. Peng, *RSC Adv.*, 2014, **4**, 248.
29 V. K. Gupta, N. Mergu, L. K. Kumawat and A. K. Singh, *Sens. Actuators, B*, 2015, **207**, 216.
30 X. J. Meng, D. L. Cao, Z. Y. Hu, X. H. Han, Z. C. Li, D. Liang and W. B. Ma, *Tetrahedron Lett.*, 2018, **59**, 4299.
31 H. Q. Li, X. Q. Sun, T. Zheng, Z. X. Xu, Y. X. Song and X. H. Gu, *Sens. Actuators, B*, 2019, **279**, 400.
32 K. S. Mani, R. Rajamanikandan, B. Murugesapandian, R. Shankar, G. Sivaraman, M. Ilanchelian and S. P. Rajendran, *Spectrochim. Acta, Part A*, 2019, **214**, 170.
33 Y. Wang, Q. T. Meng, Q. Han, G. J. He, Y. Y. Hu, H. Feng, H. M. Jia, R. Zhang and Z. Q. Zhang, *New J. Chem.*, 2018, **42**, 15839.
34 H. S. Jung, P. S. Kwon, J. W. Lee, J. I. Kim, C. S. Hong, J. W. Kim, S. H. Yan, J. Y. Lee, J. H. Lee, T. Joo and J. S. Kim, *J. Am. Chem. Soc.*, 2009, **131**, 2008.
35 S. Feng, Q. M. Gao, X. Gao, J. Q. Yin and Y. Jiao, *Inorg. Chem. Commun.*, 2019, **102**, 51.
36 J. D. Luo, Z. L. Xie, J. W. Y. Lam, L. Cheng, H. Y. Chen, C. F. Qiu, H. S. Kwok, X. W. Zhan, Y. Q. Liu, D. B. Zhu and B. Z. Tang, *Chem. Commun.*, 2001, 1740.
37 C. C. Zhou, W. H. Xu, P. B. Zhang, M. J. Jiang, Y. C. Chen, R. T. K. Kwok, M. M. S. Lee, G. G. Shan, R. L. Qi, X. Zhou, J. W. Y. Lam, S. Wang and B. Z. Tang, *Adv. Funct. Mater.*, 2019, **29**, 1805986.
38 T. F. Zhang, Y. Y. Li, Z. Zheng, R. Q. Ye, Y. R. Zhang, R. T. K. Kwok, J. W. Y. Lam and B. Z. Tang, *J. Am. Chem. Soc.*, 2019, **141**, 5612.
39 R. R. Hu, N. L. C. Leung and B. Z. Tang, *Chem. Soc. Rev.*, 2014, **43**, 4494.
40 T. Sun, D. D. Cheng, Y. S. Chai, J. Gong, M. Y. Sun and F. Zhao, *Dyes Pigm.*, 2019, **170**, 107619.
41 H. Sun, S. S. Sun, F. F. Han, Z. H. Ni, R. Zhang and M. D. Li, *J. Mater. Chem. C*, 2019, **7**, 7053.
42 X. G. Zhou and M. S. Peng, *Asian J. Chem.*, 2013, **25**, 4509.
43 S. X. Chen, R. M. Qiu, Q. H. Yu, X. Y. Zhang, M. Wei and Z. Y. Dai, *Tetrahedron Lett.*, 2018, **59**, 2671.

44 H. Z. Gao, D. F. Xu, Y. H. Wang, Y. Wang, X. L. Liu, A. X. Han and C. Zhang, *Dyes Pigm.*, 2018, **150**, 59.

45 L. Zhou, D. F. Xu, H. Z. Gao, A. X. Han, X. L. Liu, C. Zhang, Z. Li and Y. Yang, *Dyes Pigm.*, 2017, **137**, 200.

46 V. Singh and A. K. Mishra, *Sens. Actuators, B*, 2016, **227**, 467.

47 J. T. Yeh, W. C. Chen, S. R. Liu and S. P. Wu, *New J. Chem.*, 2014, **38**, 4434.

48 U. N. Yadav, P. Pant, S. K. Sahoo and G. S. Shankarling, *RSC Adv.*, 2014, **4**, 42647.

49 N. Mergu, M. Kim and Y. A. Son, *Spectrochim. Acta, Part A*, 2018, **188**, 571.

50 S. Dalbera, S. Kulovi and S. Dalai, *ChemistrySelect*, 2018, **3**, 6561.