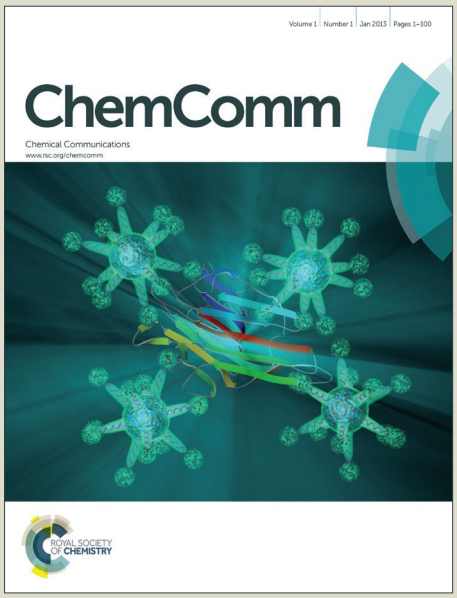
ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: G. Liu, Z. Long, H. Lv, C. Li and G. Xing, *Chem. Commun.*, 2016, DOI: 10.1039/C6CC05116B.



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

ROYAL SOCIETY OF CHEMISTRY View Article Online
DOI: 10.1039/C6CC05116B

Communication

Received 00th January 20xx,

Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Dialdehyde-Diboronate-Functionalized AIE Luminogen: Design, Synthesis and Application for Detection of Hydrogen Peroxide

Guang-Jian Liu, Zi Long, Hai-juan Lv, Cui-yun Li and Guo-wen Xing*

A dialdehyde-diboronate-functionalized tetraphenylethene (TPE-DABF) was reported as a H_2O_2–specific AIE luminogen. TPE-DABF, bearing multiple reductive units (aldehyde, boronate and fructose) in one molecule, afforded an excellent H_2O_2 selectivity over other ROS in biological buffer, and can be used for sensitive detection of glucose under neutral conditions.

The aggregation-induced emission (AIE) effect[1], which is opposite to conventional aggregation-caused quenching (ACQ) phenomenon, features with fluorescence increasing caused by restriction of intramolecular motions.[2] Various AIE luminogens (AIEgens) have been created and successfully used in the field of optoelectronic devices,[3] luminescent sensors,[4] mechanofluorochromic materials,[5] *etc*. Notably, based on electrostatic interaction, coordination binding or chemical reactions between AIEgens and analytes, many new analytic methods utilizing AIE effect have been established for the enzyme assays,[6] screening of inhibitors,[7] detection of ionic species,[8] biomolecules[9] and volatile/explosive organic compounds.[10]

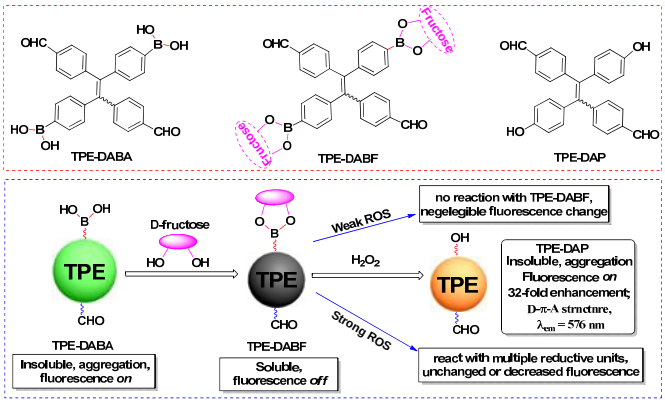
Over last decade, it has been found that the AIEgen sensing systems have the advantages of easy fabrication, facile functionalization, high signal-to-noise ratio and strong photobleaching resistance.[11] However, fewer literatures[12] were reported using AIE probes for the detection of reactive oxygen species (ROS). Hydrogen peroxide (H_2O_2), one of the most important ROS, plays an important physiological and pathological role in human health and aging.[13-14] Although many fluorescent probes for H_2O_2 sensing have been illustrated,[15-21] it still remains a great challenge to design a AIEgen for detection of H_2O_2 over other ROS.

Inspired by the previous findings that sugar-bearing AIE molecules have nearly no luminescence in aqueous solution[22] and aromatic boronic acids could rapidly and reversibly interact with carbohydrates to form boronate complex,[23] herein, we reported a unique sugar-boronic acid complex (TPE-DABF, Scheme 1) as a new AIEgen for highly selective detection of H_2O_2.

TPE-DABF, a complex of D-fructose and dialdehyde-diboronic acid-functionalized tetraphenylethene (TPE-DABA, Scheme 1), not only has lower background fluorescence due to its better water solubility, but also becomes more reactive to H_2O_2 for the boronic ester formation.[24] In addition, TPE-DABF is also an intramolecular charge transfer (ICT) probe upon reacting with H_2O_2, since the oxidation product TPE-DAP (Scheme 1) contains both electron-withdrawing (aldehyde) and electron-donating (phenoic hydroxyl) groups in its TPE core. Remarkably, the multiple reductive units (aldehyde, boronate, double bond and D-fructose) in TPE-DABF should be helpful to increase H_2O_2-selectivity *via* the different oxidation reactions with various ROS (Scheme 1).

To explore our attractive ideas, we prepared the probe TPE-DABA in six steps according to the synthetic route shown in Scheme S1. Firstly, 1,2-bis(4-bromophenyl)-1,2-di-*p*-tolylethene (**3**) was synthesized by McMurry reaction of (4-bromophenyl)(*p*-tolyl)methanone (**2**), following the Friedel-Crafts reaction of 4-bromobenzoyl chloride (**1**). After the bromination and Korublum reaction of **3**, the dialdehyde-dibromo-functionalized TPE (**5**) was obtained. Then palladium-catalyzed Miyaura borylation reaction[25] of **5** proceeded smoothly to furnish bis(pinacolato)diboron TPE **6**. Finally, treatment of **6** with $NaIO_4$ and HCl in the mixture of THF and water gave the desired deprotected product TPE-DABA, which was characterized precisely by NMR and high resolution mass spectroscopy (Fig. S1 in supporting information).

We carried out the pH titration experiments of probe TPE-DABA and its precusor **6** at various pH values in Britton-



Scheme 1 Design of AIEgens for specific detection of H_2O_2 over various ROS.

Department of Chemistry, Beijing Normal University, Beijing 100875, China. E-mail: gwxing@bnu.edu.cn

Electronic supplementary information (ESI) available: Detailed experimental procedures. See DOI: 10.1039/x0xx00000x

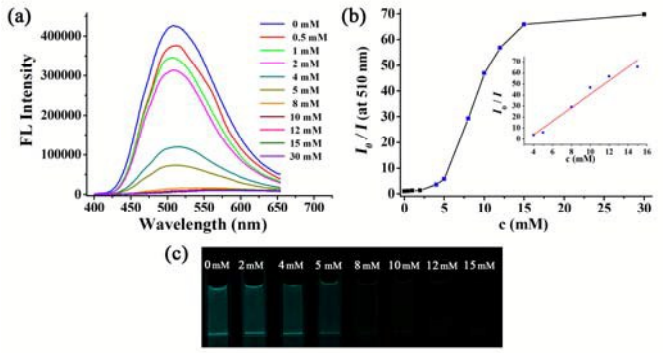


Figure 1. (a) Fluorescence spectra of probe TPE-DABA (50 μM) in the presence of different concentrations of D-fructose in 0.1 M PBS buffer containing 2 vol% DMSO (pH = 7.4, λ_{ex} = 380 nm). (b) Plot of the relative fluorescence intensity ($\boldsymbol{I_0/I}$) at 510 nm versus the concentration of D-fructose. Inset: linearity of the ratio of fluorescence intensity ($\boldsymbol{I_0/I}$) at 510 nm. (c) Photographs of the solutions of TPE-DABA and different concentrations of D-fructose in 0.1 M PBS buffers containing 2 vol% DMSO (pH = 7.4) under UV illumination.

Robinson buffers. As depicted in Fig. S2-S3, the fluorescence intensities of TPE-DABA and **6** were strong under neutral and acid conditions, but decreased dramatically in alkaline medium. Gradual raising the pH from 8 to 12 resulted in a significant decline of the fluorescence emission, indicating that TPE-DABA and **6** were transformed into borate salts and became soluble in the buffers with high pH values. This pH effect was fully consistent with the fact that the boron atom of arylboronic acid could be ionized by OH^- in alkaline aqueous solutions.[9b]

Based on our long-standing interests and studies in the synthesis of complex glycosides and fluorescent detection of oligosaccharides,[26] next, we tested whether the initial strong fluorescence intensity of TPE-DABA under physiological pH conditions could be decreased by binding with sugars through increasing its solubility. Considering that arylboronic acid has a high binding constant with D-fructose,[23] we evaluated the fluorescence responses of TPE-DABA to D-fructose under physiological conditions (0.1 M PBS buffer solutions, pH 7.4). As anticipated, the fluorescence intensity of TPE-DABA decreased gradually upon the addition of D-fructose as shown in Fig. 1, suggesting that the boronic acid TPE-DABA indeed interacted with the diol groups of D-fructose to form TPE-DABA-fructose boronate complex (TPE-DABF). In addition, the relative fluorescence intensity at 510 nm (I_0/I) changed linearly with the concentration of D-fructose in the range of 4-16 mM (Fig. 1b). Due to the good solubility of the sugar-bearing complex TPE-DABF, the fluorescence intensity could be neglected when the concentration of D-fructose reached 30 mM.

Then, we turned our attention to investigate the optical properties of the resulting complex TPE-DABF formed by TPE-DABA (50 μM) and D-fructose (30 mM) towards H_2O_2 in 0.1 M phosphate buffer solution at pH 7.4. To our delight, a red shift in the absorption spectrum and excitation spectrum of the complex TPE-DABF was observed when H_2O_2 was added to the mixture (Fig. S4-S5 in supporting information). Meanwhile, the maximum fluorescence band of the solution of TPE-DBAF and H_2O_2 was red-shifted to 576 nm compared with that of TPE-DABA. The red shifts upon addition of H_2O_2 may be ascribed to the ICT effect caused by the electron-donating and electron-withdrawing units in the oxidative product TPE-DAP.

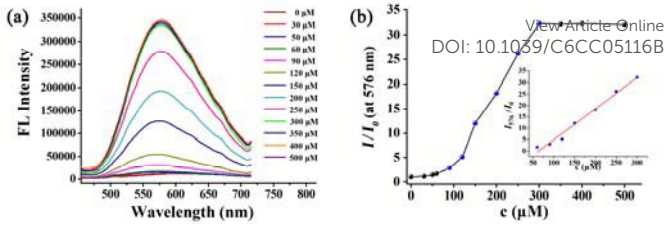


Figure 2. (a) Fluorescence spectra of the TPE-DABF complex (TPE-DABA, 50 μM; D-fructose, 30 mM) upon titration of H_2O_2. (b) Plot of the relative fluorescence intensity ($\boldsymbol{I/I_0}$) at 576 nm versus the concentration of H_2O_2. Inset: linearity of the ratio of fluorescence intensity ($\boldsymbol{I/I_0}$) at 576 nm. λ_{ex} = 430 nm.

To verify the chemospecific H_2O_2-triggered transformation of arylboronates to phenols, we extracted the detection systems with EtOAc and analyzed the extracts by ESI mass spectrometry. The high abundance of the ion at m/z 419.33 in the mass spectrum (Fig. S6) indicated that only the boronate moiety in the TPE-DABF complex was oxidized into phenol by H_2O_2 and the aldehyde moiety remained unchanged. Moreover, we amplified the same reaction in an Erlenmeyer flask and the obtained product was identified with NMR and HRMS spectra, which further indicated the formation of TPE-DAP. As a result, the oxidative product TPE-DAP with electron donor-acceptor structure showed longer-wavelength emission. In addition, the relative fluorescence intensity $\boldsymbol{I}$ (in the presence of H_2O_2)/$\boldsymbol{I_0}$ (in the absence of H_2O_2) of TPE-DABF complex with different concentrations of H_2O_2 at pH 7.4 over time was summarized in Fig. S7. Notable fluorescence changes could be observed within 60 min in most cases, therefore 60 min of reaction time was selected in the following experiments.

As shown in Fig 2a, the fluorescence emission of TPE-DABF was gradually switched on in the presence of H_2O_2. A 32-fold fluorescence enhancement at 576 nm was observed after TPE-DABF was incubated with 300 μM H_2O_2 for 60 min. Moreover, the fluorescence intensity ratio at 576 nm was linearly related to the concentration of added H_2O_2 in the range of 60-300 μM (Fig 2b) and the detection limit of our probe was determined to be ~3.2 μM, indicating that the AIEgen TPE-DABF could sensitively detect micromolar changes of H_2O_2 concentration.

As illustrated in Scheme 1, the detection mechanism of our AIEgen probes TPE-DABA/TPE-DABF was deeply investigated. The existence state, especially, the size of AIEgen probes upon addition of D-fructose and H_2O_2 sequentially was

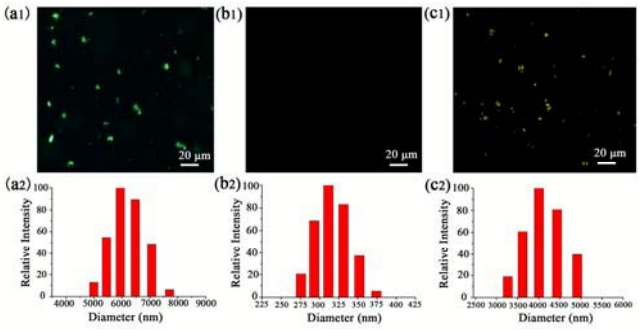


Figure 3. Fluorescence microscopy image of (a1) TPE-DABA (50 μM); (b1) TPE-DABF; (c1) TPE-DABF and H_2O_2 (250 μM); DLS data of (a2) TPE-DABA (50 μM); (b2) TPE-DABF; (c2) TPE-DABF and H_2O_2 (250 μM). TPE-DABF complex was formed with 50 μM TPE-DABA and 30 mM D-fructose *in situ*.

measured by fluorescence microscopy and dynamic light scattering (DLS). It can be seen that probe TPE-DABA was immiscible with water and showed a strong fluorescence in 0.1 M PBS buffer solution (Fig. 3a). The average diameter of the particles measured by DLS was about 6000 nm, which was in accordance with the results obtained by fluorescence microscopy. The aggregate formation restricted the intramolecular rotations of the phenyl rings in TPE-DABA, resulting fluorescence "*on*" at pH 7.4 buffer solution. Owing to the high affinity binding interaction between boronic acid and D-fructose, when D-fructose was added into the solution of TPE-DABA, the suspension became nearly non-fluorescent with concomitant decreasing of the average diameter of the aggregates (Fig. 3b). The results reflected that the intramolecular motions were activated as a radiationless relaxation channel due to the good solubility of the formed TPE-DABF complex. As has been discussed, the addition of H_2O_2 to the solution caused the complex recover its emission (Fig. 3c). This is likely because the hydrophobic property of the oxidation product TPE-DAP induced the formation of aggregates as was borne out by the DLS experiment. Taken

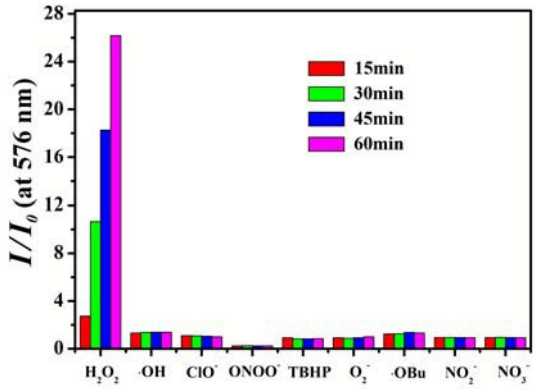


Figure 4. Fluorescence responses of TPE-DABP complex (TPE-DABA, 50 μM; D-fructose, 30 mM) to various reactive oxygen species (ROS) in PBS buffer containing 2 vol% DMSO at pH 7.4. Data shown are for 250 μM of all ROS reagents. Bars represent relative responses at 15 (red), 30 (green), 45 (blue) and 60 (pink) min after addition of each ROS. Fluorescence intensity was collected at 576 nm (λ_{ex} = 430 nm).

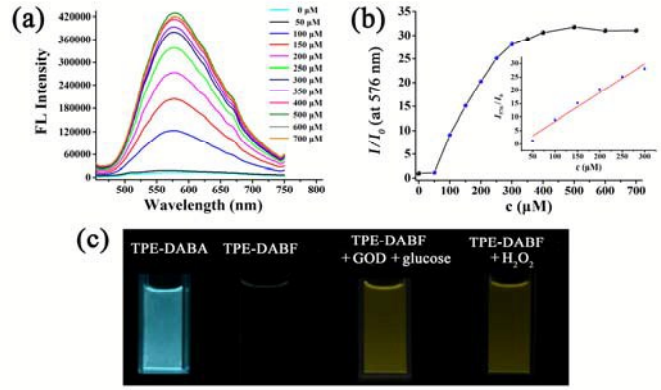


Figure 5. (a) Fluorescence spectra of the aqueous mixture containing TPE-DABF (probe TPE-DABA, 50 μM; D-fructose, 30 mM), GOD (1 U/mL) and different concentrations of glucose. (b) Plot of the relative fluorescence intensity (I/I_0) at 576 nm versus the concentrations of glucose. Inset: linearity of the ratio of fluorescence intensity (I/I_0) at 576 nm. The data were collected in PBS buffer solution containing 2 vol% DMSO (0.1 M PBS, pH 7.4) with excitation at 430 nm. (c) Photographs of the solutions of TPE-DABA (50 μM) before and after addition of D-fructose (30 mM) and H_2O_2 (250 μM) or its alternative (1 U/mL GOD and 250 μM glucose) sequentially; these photographs were taken under UV illumination at 365 nm.

View Article Online
DOI: 10.1039/C6CC05116B

together, these data provided further evidence for the dual AIE and ICT mechanism of the detection system to decipher the significant "*on-off-on*" signal responses as have been observed in the detection process (Scheme 1).

Furthermore, the selectivity of TPE-DABF complex towards other reactive oxygen species at several time points was investigated in pH 7.4 buffer solution. Due to the multiple reductive units (aldehyde, boronate, double bond and D-fructose) in TPE-DABF, even though previous literatures[23a,27] have reported aryl boronic esters can be oxidized into phenols by peroxynitrite ($ONOO^-$), hypochlorite (ClO^-) and superoxide ($O_2^{·-}$) , our probe shows a >20-fold higher fluorescence response to H_2O_2 over other ROS, such as hydroxyl radicals (•OH), hypochlorite (ClO^-), peroxynitrite ($ONOO^-$), *tert*-butyl hydroperoxide (TBHP), superoxide ($O_2^{·-}$), peroxyl radicals (ROO•), nitrite (NO_2^-) and nitrate (NO_3^-) (Fig. 4). As illustrated in Scheme 1, we think that only H_2O_2 could oxidize boronates to phenols selectively and other ROS may either not react with TPE-DABF or react with other reductive units simultaneously. As a result, the incorporation of multiple reductive units into the detecting system was crucial to the good selectivity of TPE-DABF to H_2O_2 over other ROS.

Finally, TPE-DABF was employed for sensitive glucose detection by monitoring the produced hydrogen peroxide in the enzymatic reaction[28] between glucose and glucose oxidase (GOD). Different concentrations of glucose and 1 U/mL GOD were added to the TPE-DABF solution under neutral conditions and the mixture was shaken at 37 ºC for 1 h. As expected, remarkable increasing in the fluorescence of solution was observed upon excitation at 430 nm (Fig. 5a and Fig. S8). The relative fluorescence intensity at 576 nm was increased linearly with the glucose concentration at 50-300 μM, which is indicative of powerful glucose detection (Fig. 5b). Notably, the control experiments indicated that glucose or concomitant product glucolactone could not induce the fluorescence enhancement under the same conditions. More importantly, the changes of the solution before and after addition of H_2O_2 or its alternatives can be easily distinguished with naked eyes under UV illumination as shown Fig. 5c.

In summary, a novel dialdehyde-diboronic acid-functionalized tetraphenylethene derivative (TPE-DABA) was designed and synthesized. Based on the H_2O_2-mediated boronate-to-phenol reaction, we have successfully developed a highly H_2O_2-specific AIEgen TPE-DABF. Due to dual AIE and ICT mechanisms, TPE-DABA displayed an "on-off-on" response companying with concomitant bathochromic shift when treated with D-fructose and hydrogen peroxide sequentially. In addition, TPE-DABF was also used for detection of glucose under neutral conditions by sensing the generated H_2O_2 from the GOD catalyzed oxidation reactions. We believe that the methodology presented in this study should have potential applications to detect substrates related to H_2O_2 generation, and provide a basis for further development of AIEgens for detection of other reactive oxygen species.

The project was financially supported by the National Natural Science Foundation of China (21272027).

Notes and references

1. J. Luo, Z. Xie, J. W. Y. Lam, L. Cheng, H. Chen, C. Qiu, H. S. Kwok, X. Zhan, Y. Liu, D. Zhu and B. Z. Tang, *Chem. Commun.*, 2001, 1740-1741.

2. (a) Y. Hong, J. W. Y. Lam and B. Z. Tang, *Chem. Commun.*, 2009, 4332-4353; (b) X. Fan, J. Sun, F. Wang, Z. Chu, P. Wang, Y. Dong, R. Hu, B. Z. Tang and D. Zou, *Chem. Commun.*, 2008, 2989-2991; (c) J. Shi, N. Chang, C. Li, J. Mei, C. Deng, X. Luo, Z. Liu, Z. Bo, Y. Q. Dong and B. Z. Tang, *Chem. Commun.*, 2012, **48**, 10675-10677.
3. (a) J. Huang, N. Sun, Y. Q. Dong, R. L. Tang, P. Lu, P. Cai, Q. Q. Li, D. G. Ma, J. G. Qin and Z. Li, *Adv. Funct. Mater.*, 2013, **23**, 2329-2337; (b) Z. Zhao, J. W. Y. Lam and B. Z. Tang, *J. Mater. Chem.*, 2012, **22**, 23726-23740; (c) Z. Zhao, C. Y. K. Chan, S. Chen, C. Deng, J. W. Y. Lam, C. K. W. Jim, Y. Hong, P. Lu, Z. Chang, X. Chen, H. S. Kwok, H. Qiu and B. Z. Tang, *J. Mater. Chem.*, 2012, **22**, 4527-4534; (d) J. Huang, X. Yang, J. Wang, C. Zhong, L. Wang, J. Qin and Z. Li, *J. Mater. Chem.*, 2012, **22**, 2478-2484; (e) J. Huang, N. Sun, J. Yang, R. Tang, Q. Li, D. Ma, J. Qin and Z. Li, *J. Mater. Chem.*, 2012, **22**, 12001-12007.
4. (a) Y. Hong, L. Meng, S. Chen, C. W. T. Leung, L.-T. Da, M. Faisal, D.-A. Silva, J. Liu, J. W. Y. Lam, X. Huang and B. Z. Tang, *J. Am. Chem. Soc.*, 2012, **134**, 1680-1689; (b) S. Chen, J. Liu, Y. Liu, H. Su, Y. Hong, C. K. W. Jim, R. T. K. Kwok, N. Zhao, W. Qin, J. W. Y. Lam, K. S. Wong and B. Z. Tang, *Chem. Sci.*, 2012, **3**, 1804-1809; (c) T. Han, J. W. Y. Lam, N. Zhao, M. Gao, Z. Yang, E. Zhao, Y. Dong and B. Z. Tang, *Chem. Commun.*, 2013, **49**, 4848-4850; (d) Y. Yuan, R. T. K. Kwok, G. Feng, J. Liang, J. Geng, B. Z. Tang and B. Liu, *Chem. Commun.*, 2014, **50**, 295-297; (e) D. Ding, J. Liang, H. Shi, R. T. K. Kwok, M. Gao, G. Feng, Y. Yuan, B. Z. Tang and B. Liu, *J. Mater. Chem. B*, 2014, **2**, 231-238; (f) Y. Li, Y. Wu, J. Chang, M. Chen, R. Liu and F. Li, *Chem. Commun.*, 2013, **49**, 11335-11337.
5. (a) Z. Chi, X. Zhang, B. Xu, X. Zhou, C. Ma, Y. Zhang, S. Liu and J. Xu, *Chem. Soc. Rev.*, 2012, **41**, 3878-3896; (b) Z. He, L. Zhang, J. Mei, T. Zhang, J. W. Y. Lam, Z. Shuai, Y. Q. Dong and B. Z. Tang, *Chem. Mater.*, 2015, **27**, 6601-6607; (c) Z. Zhao, T. Chen, S. Jiang, Z. Liu, D. Fang and Y. Q. Dong, *J. Mater. Chem. C*, 2016, **4**, 4800-4804.
6. G. Zhao, C. Shi, Z. Guo, W. Zhu and S. Zhu, *Chin. J. Org. Chem.*, 2012, **32**, 1620.
7. M. Wang, G. Zhang, D. Zhang, D. Zhu and B. Z. Tang, *J. Mater. Chem.*, 2010, **20**, 1858-1867.
8. (a) X. Chen, X. Y. Shen, E. Guan, Y. Liu, A. Qin, J. Z. Sun and B. Z. Tang, *Chem. Commun.*, 2013, **49**, 1503-1505; (b) X. Wang, J. Hu, T. Liu, G. Zhang and S. Liu, *J. Mater. Chem.*, 2012, **22**, 8622-8628; (c) X. Huang, X. Gu, G. Zhang and D. Zhang, *Chem. Commun.*, 2012, **48**, 12195-12197; (d) T. Han, X. Feng, B. Tong, J. Shi, L. Chen, J. Zhi and Y. Dong, *Chem. Commun.*, 2012, **48**, 416-418; (e) F. Sun, G. Zhang, D. Zhang, L. Xue and H. Jiang, *Org. Lett.*, 2011, **13**, 6378-6381.
9. (a) D. Ding, K. Li, B. Liu and B. Z. Tang, *Accounts Chem. Res.*, 2013, **46**, 2441-2453;(b) Y. Liu, C. Deng, L. Tang, A. Qin, R. Hu, J. Z. Sun and B. Z. Tang, *J. Am. Chem. Soc.*, 2011, **133**, 660-663; (c) X. Xu, S. Yan, Y. Zhou, R. Huang, Y. Chen, J. Wang, X. Weng and X. Zhou, *Bioorg. Med. Chem. Lett.*, 2014, **24**, 1654-1656; (d) H. Shi, R. T. K. Kwok, J. Liu, B. Xing, B. Z. Tang and B. Liu, *J. Am. Chem. Soc.*, 2012, **134**, 17972-17981; (e) H. Shi, J. Liu, J. Geng, B. Z. Tang and B. Liu, *J. Am. Chem. Soc.*, 2012, **134**, 9569-9572.
10. (a) J. Liu, J. W. Y. Lam and B. Z. Tang, *J. Inorg. Organomet. Polym.*, 2009, **19**, 249-285;(b) Z. F. An, C. Zheng, R. F. Chen, J. Yin, J. J. Xiao, H. F. Shi, Y. Tao, Y. Qian and W. Huang, *Chem.-Eur. J.*, 2012, **18**, 15655-15661; (c) D. Li, J. Liu, R. T. K. Kwok, Z. Liang, B. Z. Tang and J. Yu, *Chem. Commun.*, 2012, **48**, 7167-7169.
11. (a) Y. Hong, J. W. Y. Lam and B. Z. Tang, *Chem. Soc. Rev.*, 2011, **40**, 5361-5388; (b) Y. Liu, Y. Tang, N. N. Barashkov, I. S. Irgibaeva, J. W. Y. Lam, R. Hu, D. Birimzhanova, Y. Yu and B. Z. Tang, *J. Am. Chem. Soc.*, 2010, **132**, 13951-13953; (c) J. Mei, Y. J. Wang, J. Q. Tong, J. Wang, A. J. Qin, J. Z. Sun and B. Z. Tang, *Chem.-Eur. J.*, 2013, **19**, 613-620; (d) R. Hu, N. L. C. Leung and B. Z. Tang, *Chem. Soc. Rev.*, 2014, **43**, 4494-4562; (e) W. Qin, D. Ding, J. Z. Liu, W. Z. Yuan, Y. Hu, B. Liu and B. Z. Tang, *Adv. Funct. Mater.*, 2012, **22**, 771-779; (f) J. Mei, J. Tong, J. Wang, A. Qin, J. Z. Sun and B. Z. Tang, *J. Mater. Chem.*, 2012, **22**, 17063-17070; (g) D.-M. Li, H. Wang and Y.-S. Zheng, *Chem. Commun.*, 2012, **48**, 3176-3178; (h) D. Wu, L. Shao, Y. Li, Q. Hu, F. Huang, G. Yu and G. Tang, *Chem. Commun.*, 2016, **52**, 541-544; (i) J. Mei, Y. N. Hong, J. W. Y. Lam, A. J. Qin, Y. H. Tang and B. Z. Tang, *Adv. Mater.*, 2014, **26**, 5429-5479; (j) C. W. T. Leung, Y. Hong, S. Chen, E. Zhao, J. W. Y. Lam and B. Z. Tang, *J. Am. Chem. Soc.*, 2013, **135**, 62-65; (k) C. Li, X. Tang, L. Zhang, C. Li, Z. Liu, Z. Bo, Y. Q. Dong, Y.-H. Tian, Y. Dong and B. Z. Tang, *Adv. Optical Mater.*, 2015, **3**, 1184-1190.
12. (a) C. H. Li, T. Wu, C. Y. Hong, G. Q. Zhang and S. Y. Liu, *Angew. Chem. Int. Ed.*, 2012, **51**, 455-459; (b) F. Hu, Y. Huang, G. Zhang, R. Zhao and D. Zhang, *Tetrahedron Lett.*, 2014, **55**, 1471-1474; (c) W. Zhang, W. Liu, P. Li, F. Huang, H. Wang and B. Tang, *Anal. Chem.*, 2015, **87**, 9825-9828.
13. (a) T. Finkel and N. J. Holbrook, *Nature*, 2000, **408**, 239-247; (b) E. A. Veal, A. M. Day and B. A. Morgan, *Mol. Cell*, 2007, **26**, 1-14; (c) B. D'Autreaux and M. B. Toledano, *Nat. Rev. Mol. Cell Biol.*, 2007, **8**, 813-824.
14. (a) K. J. Barnham and C. L. Masters, *Nat. Rev. Drug. Discov.*, 2004, **3**, 205-214; (b) M. T. Lin and M. F. Beal, *Nature*, 2006, **443**, 787-795; (c) M. Giorgio, M. Trinei, E. Migliaccio and P. G. Pelicci, *Nat. Rev. Mol. Cell Biol.*, 2007, **8**, 722-728.
15. (a) M. Onoda, S. Uchiyama, A. Endo, H. Tokuyama, T. Santa and K. Imai, *Org. Lett.*, 2003, **5**, 1459-1461; (b) M. Onoda, H. Tokuyama, S. Uchiyama, K.-i. Mawatari, T. Santa, K. Kaneko, K. Imai and K. Nakagomi, *Chem. Commun.*, 2005, 1848-1850.
16. (a) M. Zhou, Z. Diwu, N. Panchuk-Voloshina and R. P. Haugland, *Anal. Biochem.*, 1997, **253**, 162-168; (b) T. V. Votyakova and I. J. Reynolds, *Arch. Biochem. Biophys.*, 2004, **431**, 138-144.
17. (a) O. S. Wolfbeis, A. Durkop, M. Wu and Z. H. Lin, *Angew. Chem.Int. Ed.*, 2002, **41**, 4495-4498; (b) D. Song, J. M. Lim, S. Cho, S. J. Park, J. Cho, D. Kang, S. G. Rhee, Y. You and W. Nam, *Chem. Commun.*, 2012, **48**, 5449-5451.
18. S. L. Hempel, G. R. Buettner, Y. Q. O'Malley, D. A. Wessels and D. M. Flaherty, *Free Radical Bio. Med.*, 1999, **27**, 146-159.
19. H. Maeda, Y. Futkuyasu, S. Yoshida, M. Fukuda, K. Saeki, H. Matsuno, Y. Yamauchi, K. Yoshida, K. Hirata and K. Miyamoto, *Angew. Chem.Int. Ed.*, 2004, **43**, 2389-2391.
20. (a) A. R. Lippert, G. C. Van de Bittner and C. J. Chang, *Accounts Chem. Res.*, 2011, **44**, 793-804; (b) B. C. Dickinson, C. Huynh and C. J. Chang, *J. Am. Chem. Soc.*, 2010, **132**, 5906-5915; (c) M. C. Y. Chang, A. Pralle, E. Y. Isacoff and C. J. Chang, *J. Am. Chem. Soc.*, 2004, **126**, 15392-15393; (d) E. W. Miller, A. E. Albers, A. Pralle, E. Y. Isacoff and C. J. Chang, *J. Am. Chem. Soc.*, 2005, **127**, 16652-16659; (e) A. E. Albers, V. S. Okreglak and C. J. Chang, *J. Am. Chem. Soc.*, 2006, **128**, 9640-9641; (f) D. Srikun, A. E. Albers, C. I. Nam, A. T. Iavarone and C. J. Chang, *J. Am. Chem. Soc.*, 2010, **132**, 4455-4465; (g) B. C. Dickinson and C. J. Chang, *J. Am. Chem. Soc.*, 2008, **130**, 9638-9639; (h) E. W. Miller, O. Tulyanthan, E. Y. Isacoff and C. J. Chang, *Nat. Chem. Biol.*, 2007, **3**, 263-267; (i) B. C. Dickinson, J. Peltier, D. Stone, D. V. Schaffer and C. J. Chang, *Nat. Chem. Biol.*, 2011, **7**, 106-112; (j) B. C. Dickinson, V. S. Lin and C. J. Chang, *Nat. Protoc.*, 2013, **8**, 1249-1259.
21. M. Abo, Y. Urano, K. Hanaoka, T. Terai, T. Komatsu and T. Nagano, *J. Am. Chem. Soc.*, 2011, **133**, 10629-10637.
22. J.-X. Wang, Q. Chen, N. Bian, F. Yang, J. Sun, A.-D. Qi, C.-G. Yan and B.-H. Han, *Org. Biomol. Chem.*, 2011, **9**, 2219-2226.
23. (a) X. Sun, Q. Xu, G. Kim, S. E. Flower, J. P. Lowe, J. Yoon, J. S. Fossey, X. Qian, S. D. Bull and T. D. James, *Chem. Sci.*, 2014, **5**, 3368-3373; (b) G. Springsteen and B. Wang, *Tetrahedron*, 2002, **58**, 5291-5300; (c) L. Feng, F. Liang, Y. Wang and X. Wang, *Sensor Actuat B-Chem.*, 2012, **173**, 575-579.
24. (a) X. Sun, S.-Y. Xu, S. E. Flower, J. S. Fossey, X. Qian and T. D. James, *Chem. Commun.*, 2013, **49**, 8311-8313; (b) J. Yoon and A. W. Czarnik, *J. Am. Chem. Soc.*, 1992, **114**, 5874-5875.
25. T. Ishiyama, K. Ishida and N. Miyaura, *Tetrahedron*, 2001, **57**, 9813-9816.
26. (a) G. J. Liu, X. T. Zhang and G. W. Xing, *Chem. Commun.*, 2015, **51**, 12803-12806; (b) Z. Y. Gu, J. X. Zhang and G. W. Xing, *Chem.-Asian J.*, 2012, **7**, 1524-1528; (c) X. T. Zhang, S. Wang and G. W. Xing, *Chem.-Asian J.*, 2015, **10**, 2593-2597; (d) X. T. Zhang, S. Wang and G. W. Xing, *ACS Appl. Mater. Interfaces*, 2016, **8**, 12007-12017.
27. (a) A. Sikora, J. Zielonka, M. Lopez, J. Joseph and B. Kalyanaraman, *Free Radic. Biol. Med.*, 2009, **47**, 1401-1407; (b) Q. Xu, K. A. Lee, S. Lee, K. M. Lee, W. J. Lee and J. Yoon, *J. Am. Chem. Soc.*, 2013, **135**, 9944-9949; (c) L. Du, M. Li, S. Zheng and B. Wang, *Tetrahedron Lett.*, 2008, **49**, 3045-3048.
28. (a) K. Wannajuk, M. Jamkatoke, T. Tuntulani and B. Tomapatanaget, *Tetrahedron*, 2012, **68**, 8899-8904; (b) Y. F. Huan, Q. Fei, H. Y. Shan, B. J. Wang, H. Xu and G. D. Feng, *Analyst*, 2015, **140**, 1655-1661.