Organic & Biomolecular Chemistry

RSC Publishing

PAPER

View Article Online
View Journal | View Issue

From nonconjugation to conjugation: novel *meso*-OH substituted dipyrromethanes as fluorescence turn-on Zn^{2+} probes†

Cite this: *Org. Biomol. Chem.*, 2013, **11**, 2685

Yubin Ding,[a] Tong Li,[a] Xin Li,[b] Weihong Zhu[a] and Yongshu Xie*[a]

Received 21st January 2013,
Accepted 25th February 2013

DOI: 10.1039/c3ob40121a

www.rsc.org/obc

Most reported Zn^{2+} probes suffer from the interference of background fluorescence originated from the conjugated structures of commonly utilized fluorophores. In this work, three novel *meso*-hydroxyl group substituted dipyrromethanes **DPMOH1–DPMOH3** were synthesized and found to be colourless and nonfluorescent due to the interruption of the conjugated π system by an sp^3 carbon between the two pyrrolic units. Interestingly, only the addition of Zn^{2+} to the solutions of **DPMOH1–DPMOH3** promoted their oxidation to dipyrrin forms, and bright fluorescence "turn on" was observed due to the formation of corresponding dipyrrin complexes with the dipyrrin : zinc stoichiometry of 2 : 1. Zn^{2+} detection mechanism was investigated by UV-Vis, fluorescence, ^1H NMR and HRMS analyses, which can be ascribed to the CHEF type fluorescence enhancement, resulting from good rigidity of the dipyrrin complexes. Hence, **DPMOH1–DPMOH3** can be used as fluorescence turn-on Zn^{2+} probes with the advantage of no background fluorescence.

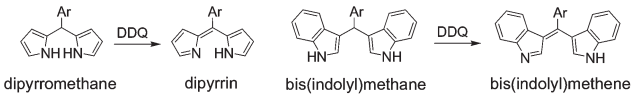
Introduction

Zinc is one of the most important cations in catalytic centers and structural cofactors of many enzymes and metalloproteins, and it plays vital roles in numerous physiological and pathological processes, including brain activity, gene transcription, and immune function.[1] Thus, the development of Zn^{2+} probes has been receiving considerable attention in recent years.[2] Among various sensing techniques, fluorescence has attracted increasing interest due to its high sensitivity and rapid response.[3] Ratiometric fluorescent probes allow the measurement of emission intensities at two different wavelengths, which would increase the dynamic range of fluorescence measurements. However, design of such probes with a large ratiometric signal remains very challenging.[4] On the other hand, lifetime based probes require the utilization of expensive equipments.[5] Hence, probes based on fluorescence turn-on signaling mechanisms are highly desired, because they are relatively simple to design and synthesize, with the advantages of low cost and easy manipulation.[6] In addition, they are also more desired than fluorescence quenching probes, which may be nonspecific because the quenching process may be caused by a number of factors other than the target analyte.[7] Thus, a number of fluorescence turn-on Zn^{2+} probes have been developed based on various fluorescence enhancing mechanisms such as photoinduced electron-transfer (PET), intramolecular charge transfer (ICT), fluorescence resonance energy transfer (FRET), excimer, aggregation-induced emission (AIE), chelation enhanced fluorescence (CHEF) and chemical reactions.[8] Typical fluorophores employed for these purposes include fluorescein, anthracene, naphthalimide, coumarin, cyanine dyes, rhodamine, and BODIPY.[9] In this respect, we have recently demonstrated that pyrrole derived dipyrrins and tripyrrins can be developed as fluorescence turn-on Zn^{2+} probes.[10] In spite of these excellent results, most of the reported probes suffer from the interference of weak to medium background fluorescence originated from the conjugated structures of the fluorophores, which will decrease the signal-to-noise ratio and thus decrease the probing sensitivity. Hence, it is highly desirable to develop probes without background fluorescence.

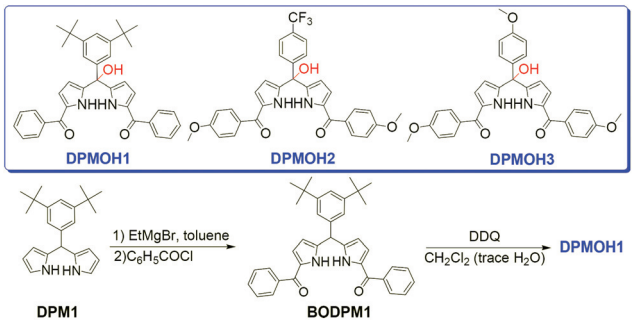
Shao and co-workers reported that bis(indolyl)methane with nitro-substituents can be deprotonated by F^- and then oxidized by air to afford bis(indolyl)methene (Scheme 1), accompanied by vivid colour changes due to the generation of a conjugated structure.[11] Similar F^- promoted deprotonation and oxidation reactions have been reported by Hill and co-workers.[12] Inspired by these results and our work on dipyrrins and tripyrrins, we envisioned that if particularly substituted

[a]*Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai, P. R. China.*
E-mail: yshxie@ecust.edu.cn; Fax: (+86) 21-6425-2758; Tel: (+86) 21-6425-0772
[b]*Department of Theoretical Chemistry and Biology, School of Biotechnology KTH Royal Institute of Technology, Stockholm, Sweden*

†Electronic supplementary information (ESI) available: Full experimental and crystallographic data and Fig. S1 to S30. CCDC 916622. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ob40121a



Scheme 1 Typical oxidation reactions of dipyrromethanes and bis(indolyl)-methanes.



Scheme 2 Structures and synthetic routes for *meso*-OH substituted dipyrromethanes.

dipyrromethanes could react with Zn^{2+} to afford highly fluorescent dipyrrin complexes, it may be possible to develop fluorescence turn-on Zn^{2+} probes without background fluorescence due to the fact that dipyrromethanes are usually colorless and nonfluorescent.[13]

During our systematic work on dipyrromethanes and dipyrrins, we accidentally obtained novel *meso*-OH substituted dipyrromethanes **DPMOH1–DPMOH3** (Scheme 2). Consistent with our expectations, these novel compounds are nonfluorescent, and addition of Zn^{2+} promoted their oxidation to form fluorescent dipyrrin complexes, indicating that they may be applied as a novel prototype of fluorescence turn-on Zn^{2+} probes with the advantage of no background fluorescence. To the best of our knowledge, this is the first report of *meso*-OH substituted dipyrromethanes and Zn^{2+} probes based on dipyrromethanes.

Results and discussion

Synthesis of DPMOH1–DPMOH3

DPMOH1–DPMOH3 were readily synthesized by stirring corresponding dipyrromethanes with 2.0 equiv. of DDQ in CH_2Cl_2 (Scheme 2), followed by separation on silica gel columns. They were fully characterized by ^1H NMR, ^{13}C NMR, and HRMS (Fig. S1–S18†). Generally, oxidation of dipyrromethanes with DDQ would afford corresponding dipyrrins.[14] The generation of **DPMOH1–DPMOH3** instead of common dipyrrins in these reactions may be caused by the reactions of the relatively stable carbonium intermediates with trace amount of water presented in CH_2Cl_2 (See ESI†). For the ^1H NMR spectrum of **DPMOH1** in DMSO-d_6, singlets at 11.65 and 6.62 ppm disappeared upon addition of D_2O (Fig. 1). Thus, they were assigned to pyrrolic-NH and *meso*-OH, respectively. Similar D_2O

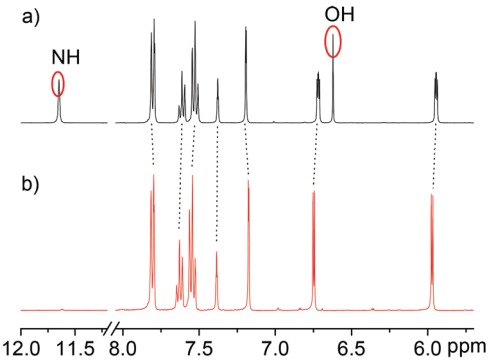


Fig. 1 The low field region of ^1H NMR spectra of **DPMOH1** (400 MHz, 298 K), (a) in DMSO-d_6, (b) in DMSO-d_6 + D_2O.

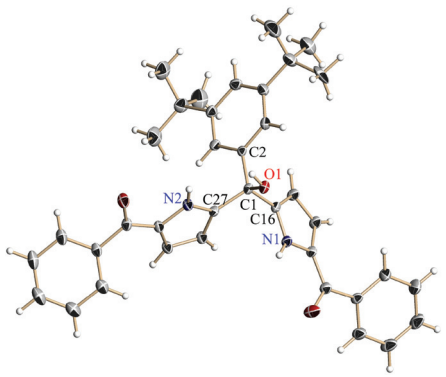


Fig. 2 Crystal structure of compound **DPMOH1** with ellipsoids shown at 20% probability level.

exchange results were observed for **DPMOH2** and **DPMOH3** (Fig. S19, S20†). To further elucidate the molecular structures of these compounds, we tried to grow their single crystals, and fortunately obtained the single crystals of **DPMOH1** by slow evaporation of its solution in a mixture of methanol and H_2O. The molecule of **DPMOH1** really has an OH group attached to the *meso*-C1 atom (Fig. 2). The C1–C2, C1–C16, C1–C27 and C1–O1 bond lengths are 1.538(3), 1.524(3), 1.532(3), and 1.440(3) Å, respectively. These values are typical of C–C and C–O single bonds. The bond angles around C1 lie in the range of 106.3(2)–111.9(2)°, indicating that C1 is an sp^3 carbon atom. Thus, the dipyrrolic unit adopts a nonplanar conformation, with a large dihedral angle of 67.2° between the two pyrrolic units.

Titration study

Due to the interruption of the conjugated system by the *meso*-sp^3 carbon atom between the two pyrrolic units, **DPMOH1–DPMOH3** show no fluorescence. Interestingly, upon addition of Zn^{2+} to their MeOH solutions, strong fluorescence appeared. A titration of **DPMOH1** (10 μM) with Zn^{2+} was carried out to study its detection behavior in detail. As depicted in Fig. 3a, upon addition of 0–6 eq. of Zn^{2+} to the solution of **DPMOH1**,

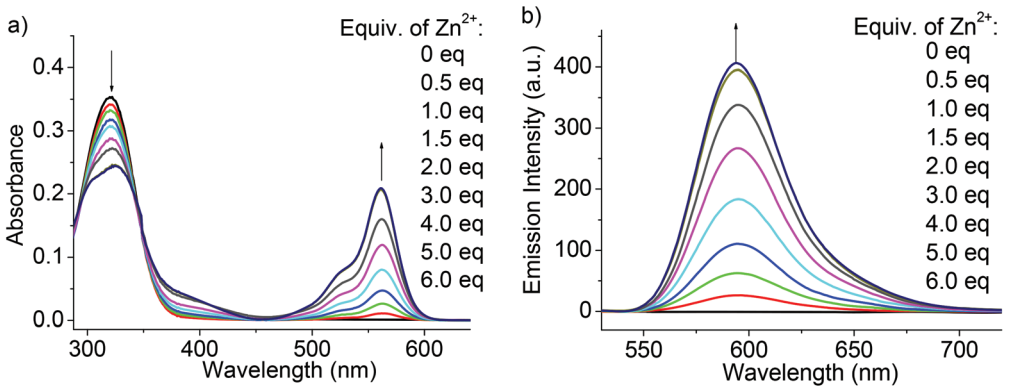


Fig. 3 (a) Absorption spectral changes during a titration of **DPMOH1** (10 μM) with Zn^{2+} (0–6.0 equiv.) in MeOH. (b) Corresponding fluorescence spectral changes with λ_{ex} fixed at 346 nm (one of the isosbestic points).

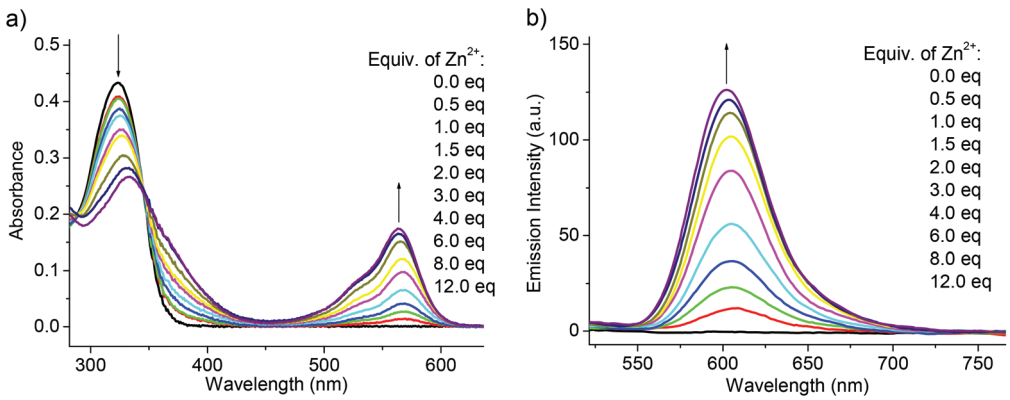


Fig. 4 (a) Absorption spectral changes during a titration of **DPMOH2** (10 μM) with Zn^{2+} (0–12.0 equiv.) in MeOH. (b) Corresponding fluorescence emission spectral changes with λ_{ex} fixed at 345 nm (one of the isosbestic points).

obvious absorption changes were observed. The peak at 320 nm gradually decreased, and a new broad peak developed at about 561 nm, with an isosbestic point observed at 346 nm, which indicates the generation of a well-defined new product. Accompanying with these absorption changes, a sharp fluorescence "turn on" was observed, with the emission peak centered at about 594 nm (Fig. 3b). Similar to the results observed for **DPMOH1**, upon addition of 0–12 eq. of Zn^{2+} to the solution of **DPMOH2**, the peak at 323 nm gradually decreased, and a new broad peak developed at about 564 nm, accompanied with a sharp fluorescence "turn on" at 602 nm (Fig. 4). Similar UV-Vis and fluorescence spectral changes were also observed for **DPMOH3** (Fig. 5). These observations indicated that these compounds may be employed as fluorescence turn-on Zn^{2+} probes. Based on these titration experiments, calibration curves of **DPMOH1–DPMOH3** can be obtained (Fig. S21–S23†). The fluorescence intensity of **DPMOH1** is proportional to the Zn^{2+} concentration in the range of 2.3×10^{-6}–5.7×10^{-5} M. And the dynamic ranges for **DPMOH2** and **DPMOH3** are 6.2×10^{-7}–3.9×10^{-5} and 8.1×10^{-7}–4.9×10^{-5} M, respectively. Respective detection limits for Zn^{2+} calculated from $3\sigma/k$ were found to be 3.2×10^{-7}, 5.0×10^{-7} and 5.5×10^{-7} M, where σ is the standard deviation of the blank solution and k is the slope of the calibration curves (Fig. S21–S23,† inset).[15] These values indicate that probes **DPMOH1–DPMOH3** are sensitive enough for practical detection of Zn^{2+} in biochemical systems.[1b,2b] These results urged us to further investigate the detailed detection mechanisms.

Detection mechanism

As above-mentioned that a well-defined new product was generated during the titration of probes **DPMOH1–DPMOH3** with Zn^{2+}. To understand the product structure, we stirred **DPMOH1** with $Zn(OAc)_2{\cdot}2H_2O$ in a mixture of MeOH and CH_2Cl_2, and successfully obtained a zinc complex **Zn(DP1)$_2$** (Scheme 3) in a yield of 66%, with the structure fully characterized by ^{1}H NMR and HRMS (Fig. S24, S25†). In the NMR spectrum, no OH peak was observed and the pyrrolic hydrogens were shifted downfield due to the generation of a large conjugation system and the coordination of Zn^{2+}. The NH peak also disappeared due to deprotonation and subsequent coordination. In the mass spectrum, a peak appeared at 1143.4764 (m/z), which corresponds to $[\mathbf{Zn(DP1)_2} + H]^+$. Thus, it can be concluded that addition of Zn^{2+} to the solution of **DPMOH1** promoted oxidation of the molecule to its dipyrrin form, and then a complex formed with a dipyrrin : Zn^{2+} stoichiometry of

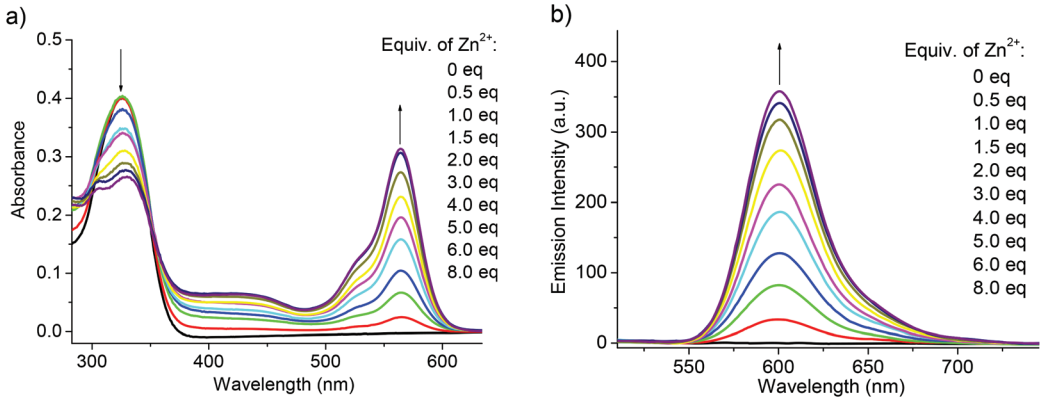
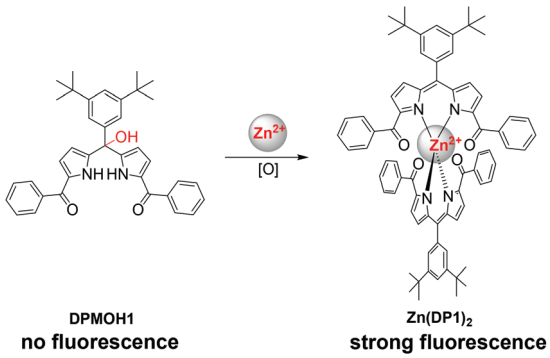


Fig. 5 (a) Absorption spectral changes during a titration of **DPMOH3** (10 μM) with Zn^{2+} (0–8.0 equiv.) in MeOH. (b) Corresponding fluorescence emission spectral changes with λ_{ex} fixed at 350 nm (one of the isosbestic points).



Scheme 3 Proposed detection mechanism of **DPMOH1**.

2 : 1, and the whole oxidation and subsequent coordination processes were completed within *ca.* 2 hours (Fig. S26–S28†). This reaction may be facilitated by the good stability of the resulting complex, which has a relatively large conjugation framework. The resulting strong fluorescence can be ascribed to the CHEF type fluorescence enhancement,[8a,b,16] which results from good rigidity of the dipyrrin complex. In fact, we have observed similar CHEF type fluorescence enhancement for dipyrrins.[10]

Selectivity experiments

Selectivity experiments were carried out in MeOH to indicate whether the detection of Zn^{2+} is interfered by other common cations. As shown in Fig. 6a, only the addition of 3 equiv. of Zn^{2+} to the solution of **DPMOH1** induced a sharp fluorescence "turn on", while other metal cations can not induce obvious fluorescence changes. Competition experiments were also carried out to further elucidate the cation selectivity. When 3 equiv. of various competing cations were added together with 3 eq. of Zn^{2+}, only the presence of Cu^{2+} quenched the fluorescence, but Cu^{2+} is not typically present at high concentrations in biochemical systems.[17] Hence, the interference of Cu^{2+} in the potential applications of these probes in biochemical systems can be neglected. All other cations showed only small interference (Fig. 6b). Similar results were also obtained for compounds **DPMOH2** and **DPMOH3** (Fig. S29, S30†). These results indicate that the probes can be developed as a novel and promising type of selective "turn-on" fluorescent Zn^{2+} probes without background fluorescence.

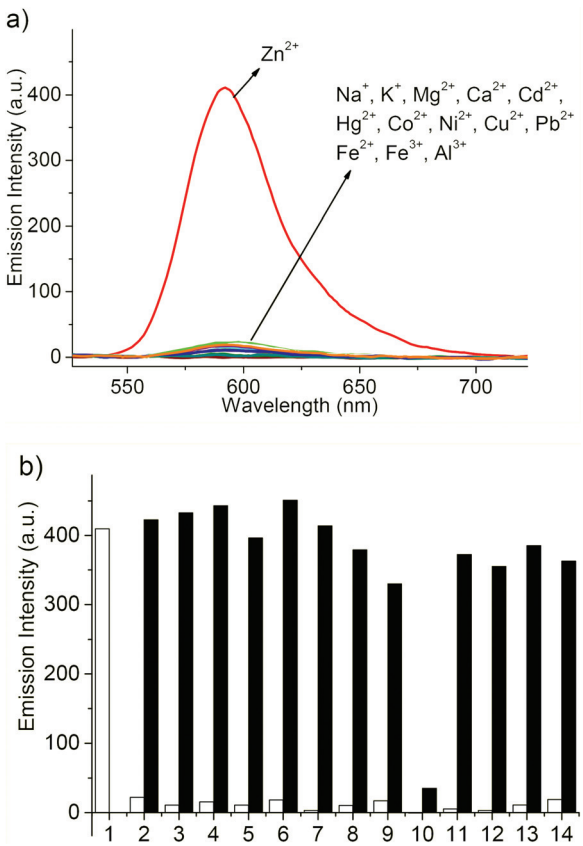


Fig. 6 Relative fluorescence intensity of 10 μM **DPMOH1** in MeOH upon excitation at 346 nm (one of the isosbestic points): (a) In the presence of various metal ions. (b) White bars represent the addition of 3 equiv. of metal ions. Black bars represent the addition of 3 equiv. of Zn^{2+} mixed with 3 equiv. of indicated metal ions. 1–14: Zn^{2+}, Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}, Cd^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+}, Al^{3+}.

Conclusions

In conclusion, three novel nonfluorescent *meso*-OH substituted dipyrromethanes **DPMOH1–DPMOH3** were synthesized. Addition of Zn^{2+} to their solutions induced the generation of strong fluorescence, which may be ascribed to Zn^{2+} promoted oxidation of the compounds to corresponding dipyrrins, followed by coordination with Zn^{2+} to afford 2 : 1 Zn^{2+} complexes. Hence, these nonfluorescent compounds can be employed as fluorescence turn-on Zn^{2+} probes. These results provide examples of a novel strategy for the development of fluorescence turn-on probes without background fluorescence by designing nonfluorescent molecules with nonconjugate structures, which can be converted into conjugate and fluorescent structures upon selective interaction with a specific target analyte under aerobic condition. Further modification of the probes to improve their water solubility and detection behavior is now under way in our lab.

Experimental

General

Commercial available solvents and reagents were used as received. Deuterated solvents for NMR measurements were available from Aldrich. UV-Vis absorption spectra were recorded by a Varian Cary 100 spectrophotometer and fluorescence spectra were recorded on a Varian Cray Eclipse fluorescence spectrophotometer, with a quartz cuvette (path length = 1 cm); both spectrophotometers were standardized. ^{1}H NMR and ^{13}C NMR spectra were obtained using a Bruker AM 400 spectrometer with tetramethylsilane (TMS) as the internal standard. High resolution mass spectra (HRMS) were measured on a Waters LCT Premier XE spectrometer. Elemental analyses were carried out with an Elmentar Vario EL-III analyzer. Column chromatography was carried out in air using silica gel (200–300 mesh). Reactions were monitored by thin-layer chromatography.

UV/Vis absorption spectrum measurements

The absorption spectra of **DPMOH1–DPMOH3** (10 μM) were measured at 25 °C in MeOH. Tested ions Zn^{2+}, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cd^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+} were added as acetate or chloride salts dissolved in MeOH, and Al^{3+} was added as a nitrate salt dissolved in MeOH.

Fluorescence emission spectral measurements

The fluorescence emission spectra of **DPMOH1–DPMOH3** (10 μM) were measured at 25 °C in MeOH, with excitation fixed at λ = 346 nm for **DPMOH1**, 345 nm for **DPMOH2** and 350 nm for **DPMOH3**. The slit width was 5 nm and PMT voltage was 600 V. Tested ions Zn^{2+}, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cd^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+} were added as acetate or chloride salts dissolved in MeOH, and Al^{3+} was added as a nitrate salt dissolved in MeOH.

Preparation of compound BODPM1

A solution of EtMgBr (18.7 mL, 18.7 mmol, 1.0 M solution in THF) was added slowly to a flask containing a solution of **DPM1** (2.5 g, 7.5 mmol) in toluene (150 mL) under nitrogen. The resulting mixture was stirred at room temperature for 30 min. Then, a solution of benzoyl chloride (2.2 mL, 18.7 mmol) in toluene (20 mL) was added over 10 min, and the resulting solution was stirred for 30 min. Then the reaction mixture was poured into saturated aqueous NH_4Cl (200 mL). The organic layer was washed with water for three times, dried (Na_2SO_4), and filtered. The filtrate was concentrated and then purified by a silica gel column (Eluent: dichloromethane (DCM)–petroleum ether (PE) = 4/1 (V : V) then DCM) to afford the crude product of **BODPM1** which was recrystallized from CH_2Cl_2 and *n*-hexane (950 mg, yield: 23.5%). ^{1}H NMR (DMSO-d_6, Bruker 400 MHz, 298 K): δ 12.15 (s, 2H, pyrrolic-NH), 7.77 (d, J = 6.8 Hz, 4H, phenyl-H), 7.60 (t, 2H, phenyl-H), 7.51 (t, 4H, phenyl-H), 7.29 (s, 1H, phenyl-H), 7.18 (d, J = 1.6 Hz, 2H, phenyl-H), 6.72 (d, J = 3.6 Hz, 2H, pyrrolic-βH), 6.08 (d, J = 4.0 Hz, 2H, pyrrolic-βH), 5.72 (s, 1H, *meso*-H), 1.26 (s, 18H, *t*-butyl-H). ^{13}C NMR ($CDCl_3$, Bruker 100 MHz, 298 K): δ 184.4, 151.4, 141.3, 139.1, 138.4, 131.5, 130.9, 129.6, 128.0, 123.0, 121.5, 120.8, 111.2, 53.5, 45.5, 35.0, 31.5. HRMS: obsd 541.2852, calcd for $C_{37}H_{37}N_2O_2$ ($[M - H]^-$): 541.2855.

Preparation of compound DPMOH1

BODPM1 (140 mg, 0.26 mmol) was dissolved in 125 mL of CH_2Cl_2, then DDQ (71 mg, 0.31 mmol) was added. The mixture was stirred at room temperature for 3 hours and then directly purified by a silica gel column (Eluent: CH_2Cl_2–EA = 20/1) to afford the crude product of **DPMOH1** which was recrystallized from CH_2Cl_2 and *n*-hexane (116 mg, yield: 80%). UV-Vis (MeOH) λ_{max} (nm): 320. m.p.: 162–164 °C. IR (KBr pellet, cm^{-1}): 3282 (s), 3228 (s), 2963 (s), 2863 (m), 2253 (m), 1594 (s), 1569 (s), 1478 (m), 1449 (s), 1403 (m), 1358 (m), 1333 (m), 1266 (s), 1229 (s), 1171 (s), 1076 (m), 1042 (m), 881 (s), 835 (w), 798 (m), 781 (m), 727 (m), 694 (m), 615 (m). ^{1}H NMR (DMSO-d_6, Bruker 400 MHz, 298 K): δ 11.65 (s, 2H, pyrrolic-NH), 7.80 (t, 4H, phenyl-H), 7.61 (t, 2H, phenyl-H), 7.53 (t, 4H, phenyl-H), 7.38 (s, 1H, phenyl-H), 7.19 (d, 2H, J = 2.0 Hz, phenyl-H), 6.72 (d, J = 2.4 Hz, 2H, pyrrolic-βH), 6.62 (s, 1H, –OH), 5.94 (d, 2H, J = 2.4 Hz, pyrrolic-βH), 1.25 (s, 18H, *t*-butyl-H). ^{13}C NMR (DMSO-d_6, Bruker 100 MHz, 298 K): δ 183.5, 149.4, 144.6, 143.2, 138.4, 131.7, 130.5, 128.5, 128.4, 121.1, 118.7, 109.9, 74.1, 34.5, 31.2. HRMS: obsd 581.2783, calcd for $C_{37}H_{38}N_2O_3Na$ ($[M + Na]^+$): 581.2780. Anal. Calcd for $C_{37}H_{38}N_2O_3$ (%): C, 79.54, H, 6.86, N, 5.01. Found: C, 79.81, H, 6.75, N, 4.86.

Preparation of compound BODPM2

A solution of EtMgBr (17.3 mL, 17.3 mmol, 1.0 M solution in THF) was added slowly to a flask containing a solution of **DPM2** (2.0 g, 6.9 mmol) in toluene (130 mL) under nitrogen. The resulting mixture was stirred at room temperature for 40 min. A solution of 4-methoxybenzoyl chloride (3.0 g,

17.3 mmol) in toluene (20 mL) was added over 10 min, and the resulting solution was stirred for 35 min. Then the reaction mixture was poured into saturated aqueous NH_4Cl (200 mL). The organic layer was washed by water three times, dried (Na_2SO_4), and filtered. The filtrate was concentrated and then purified by a silica gel column (Eluent: DCM then DCM–ethyl acetate (EA) = 20/1) to afford the crude product of **BODPM2** which was recrystallized from CH_2Cl_2 and *n*-hexane (830 mg, yield: 21.6%). ^{1}H NMR ($CDCl_3$, Bruker 400 MHz, 298 K): δ 12.10 (s, 2H, pyrrolic-NH), 7.68–7.76 (m, 8H, phenyl-H), 6.88 (d, J = 8.8 Hz, 4H, phenyl-H), 6.45 (q, J = 3.6 Hz, 2H, pyrrolic-βH), 5.85 (d, J = 2.8 Hz, 2H, pyrrolic-βH), 5.73 (s, 1H, *meso*-H), 3.85 (s, 6H, –OCH_3). ^{13}C NMR (DMSO-d_6, Bruker 100 MHz, 298 K): δ 182.3, 162.1, 144.6, 141.8, 139.7, 139.6, 130.9, 130.7, 130.4, 128.5, 125.4, 118.9, 113.7, 109.8, 97.3, 55.4, 42.3. HRMS: obsd 559.1843, calcd for $C_{32}H_{26}N_2O_4F_3$ ($[M + H]^+$): 559.1845.

Preparation of compound DPMOH2

BODPM2 (180 mg, 0.32 mmol) was dissolved in 150 mL of CH_2Cl_2, then DDQ (87 mg, 0.38 mmol) was added. The mixture was stirred at room temperature for 2.5 hours and then directly purified by a silica gel column (Eluent: CH_2Cl_2) to afford the crude product of **DPMOH2** which was recrystallized from CH_2Cl_2 and *n*-hexane (145 mg, yield: 78%). UV-Vis (MeOH) λ_{max} (nm): 323. m.p.: 121–126 °C. IR (KBr pellet, cm^{-1}): 3290 (m), 2921 (m), 2847 (m), 1723 (m), 1660 (w), 1604 (s), 1558 (s), 1507 (m), 1472 (m), 1411 (m), 1324 (m), 1255 (s), 1170 (s), 1109 (m), 1034 (m), 972 (w), 885 (m), 839 (m), 802 (m), 765 (m), 706 (w), 648 (w), 623 (w). ^{1}H NMR (DMSO-d_6, Bruker 400 MHz, 298 K): δ 11.62 (s, 2H, Pyrrolic-NH), 7.96 (d, J = 8.8 Hz, 2H, phenyl-H), 7.83 (d, J = 8.8 Hz, 4H, phenyl-H), 7.45 (d, J = 8.8 Hz, 2H, phenyl-H), 7.06 (d, J = 8.8 Hz, 4H, phenyl-H), 6.79 (s, 1H, –OH), 6.73 (dd, J_1 = 2.4 Hz, J_2 = 3.6 Hz, 2H, Pyrrolic-βH), 6.01 (dd, J_1 = 2.8 Hz, J_2 = 3.6 Hz, 2H, Pyrrolic-βH), 3.85 (s, 6H, –OCH_3). ^{13}C NMR (DMSO-d_6, Bruker 100 MHz, 298 K): δ 182.4, 162.2, 147.1, 142.9, 142.6, 131.0, 130.8, 130.7, 127.5, 124.9, 117.9, 113.7, 109.8, 97.2, 73.5, 59.7, 55.4. HRMS: obsd 573.1633, calcd for $C_{32}H_{24}N_2O_5F_3$ ($[M - H]^-$): 573.1637. Anal. Calcd for $C_{32}H_{25}F_3N_2O_5$ (%): C, 66.89, H, 4.39, N, 4.88. Found: C, 67.15, H, 4.48, N, 4.99.

Preparation of compound BODPM3

A solution of EtMgBr (25.0 mL, 25.0 mmol, 1.0 M solution in THF) was added slowly to a flask containing a solution of **DPM3** (2.5 g, 10.0 mmol) in toluene (170 mL) under nitrogen. The resulting mixture was stirred at room temperature for 30 min. A solution of 4-methoxybenzoyl chloride (4.3 g, 25.0 mmol) in toluene (20 mL) was added over 10 min, and the resulting solution was stirred for 35 min. Then the reaction mixture was poured into saturated aqueous NH_4Cl (200 mL). The organic layer was washed by water three times, dried (Na_2SO_4), and filtered. The filtrate was concentrated and then purified by a silica gel column (Eluent: DCM then DCM–EA = 25/1) to afford the crude product of **BODPM3** which was recrystallized from CH_2Cl_2 and *n*-hexane (765 mg, yield: 14.7%). m.p.: 97–99 °C. IR (KBr pellet, cm^{-1}): 3236 (s), 3004 (w), 2954 (m), 2929 (m), 2834 (m), 2046 (w), 1606 (s), 1557 (s), 1511 (s), 1470 (s), 1416 (m), 1337 (m), 1300 (m), 1246 (s), 1171 (s), 1109 (m), 1030 (s), 885 (s), 839 (s), 760 (s), 731 (m), 706 (m), 623 (m), 565 (w), 511 (w). ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ 11.44 (s, 2H, pyrrolic-NH), 7.78 (d, J = 8.8 Hz, 4H, phenyl-H), 7.45 (d, J = 8.4 Hz, 2H, phenyl-H), 6.88–6.93 (m, 6H, phenyl-H), 6.51 (dd, J_1 = 2.4 Hz, J_2 = 3.6 Hz, 2H, pyrrolic-βH), 5.93 (t, 2H, pyrrolic-βH), 5.60 (s, 1H, *meso*-H), 3.85 (s, 6H, –OCH_3), 3.83 (s, 3H, –OCH_3). ^{13}C NMR (DMSO-d_6, Bruker 100 MHz, 298 K): δ 182.2, 162.0, 158.0, 141.1, 133.4, 131.0, 130.6, 130.1, 129.2, 118.9, 113.6, 109.4, 55.4, 55.0. 42.0. HRMS: obsd 519.1923, calcd for $C_{32}H_{27}N_2O_5$ ($[M - H]^-$): 519.1920.

Preparation of compound DPMOH3

BODPM3 (270 mg, 0.5 mmol) was dissolved in 160 mL of CH_2Cl_2, then DDQ (142 mg, 0.6 mmol) was added. The mixture was stirred at room temperature for 3 hours and then directly purified by a silica gel column (Eluent: CH_2Cl_2–EA = 25/1) to afford the crude product of **DPMOH3** which was recrystallized from CH_2Cl_2 and *n*-hexane (210 mg, yield: 74.6%). UV-Vis (MeOH) λ_{max} (nm): 325. m.p.: 131–134 °C. IR (KBr pellet, cm^{-1}): 3290 (m), 2929 (w), 2834 (w), 1603 (s), 1557 (m), 1509 (m), 1470 (m), 1416 (w), 1333 (w), 1304 (w), 1252 (s), 1171 (s), 1113 (w), 1026 (m), 889 (m), 843 (w), 802 (w), 764 (m), 711 (w), 619 (w). ^{1}H NMR (DMSO-d_6, 400 MHz, 298 K) δ 11.5 (s, 2H, pyrrolic-NH), 7.83 (d, J = 8.8 Hz, 4H, phenyl-H), 7.17 (d, J = 8.8 Hz, 2H, phenyl-H), 7.06 (d, J = 8.8 Hz, 4H, phenyl-H), 6.93 (d, J = 8.8 Hz, 2H, phenyl-H), 6.71 (dd, J_1 = 2.8 Hz, J_2 = 4.0 Hz, 2H, pyrrolic-βH), 6.52 (s, 1H, –OH), 5.95 (dd, J_1 = 2.4 Hz, J_2 = 3.6 Hz, 2H, pyrrolic-βH), 3.84 (s, 6H, –OCH_3), 3.76 (s, 3H, –OCH_3). ^{13}C NMR (DMSO-d_6, Bruker 100 MHz, 298 K): δ 182.4, 162.1, 158.7, 144.0, 136.7, 130.7, 130.6, 128.2, 117.9, 113.7, 113.1, 109.7, 73.5, 55.4, 55.1. HRMS: obsd 535.1872, calcd for $C_{32}H_{27}N_2O_6$ ($[M - H]^-$): 535.1869. Anal. Calcd for $C_{32}H_{28}N_2O_6$ (%): C, 71.63, H, 5.26, N, 5.22. Found: C, 71.92, H, 5.14, N, 5.03.

Preparation of compound Zn(DP1)$_2$

A mixture of **DPMOH1** (56 mg, 0.1 mmol) and $Zn(OAc)_2{\cdot}2H_2O$ (22 mg, 0.1 mmol) was dissolved in a mixture of 40 mL MeOH and 10 mL CH_2Cl_2. The solution was stirred at room temperature for 18 h, then poured into 40 mL water. The organic layer was collected, dried and concentrated, and recrystallized from CH_2Cl_2 and *n*-hexane to afford a dark brown solid of **Zn(DP1)$_2$** (38 mg, yield: 66%). UV-Vis (MeOH) λ_{max} (nm): 561. IR (KBr pellet, cm^{-1}): 3361 (w), 2958 (w), 2917 (w), 2847 (w), 1648 (m), 1548 (m), 1449 (w), 1362 (w), 1345 (w), 1251 (s), 1175 (w), 1067 (m), 1003 (s), 876 (w), 835 (m), 806 (w), 723 (w), 690 (w), 673 (w). ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): 7.72 (t, 8H, Ph-H), 7.55 (t, 2H, Ph-H), 7.39 (d, 4H, pyrrolic-βH), 7.34 (t, 4H, Ph-H), 7.18 (t, 8H, Ph-H), 6.56 (q, 8H), 1.43 (s, 36H, –$C(CH_3)_3$). HRMS: obsd 1143.4764, calcd for $C_{74}H_{71}N_4O_4Zn$ ($[M + H]^+$): 1143.4767.

X-ray crystallography and crystal data for DPMOH1

Single crystals suitable for X-ray analyses of **DPMOH1** was obtained by slow evaporation of its methanol–H_2O mixed

solution at room temperature. X-ray diffraction data were collected on a Bruker-AXS APEX diffractometer utilizing MoKR radiation (λ = 0.71073 Å). The structures were solved by direct methods and refined with full matrix least-squares technique. Anisotropic thermal parameters were applied to all non-hydrogen atoms. All of the hydrogen atoms in these structures are located from the differential electron density map and constrained to the ideal positions in the refinement procedure. All calculations were performed using the SHELX-97 software package.[18]

$C_{37}H_{38}N_2O_3$, F_W = 558.69 g mol^{-1}, 0.10 × 0.08 × 0.02 mm^3, Triclinic, $P\bar{1}$, a = 9.9120(6) Å, b = 11.6861(9) Å, c = 15.4195(11) Å, α = 93.9300(10)°, β = 104.033(2)°, γ = 103.177(2)°, V = 1672.6 (2) Å^3, $F(000)$ = 596, ρ_{calcd} = 1.109 Mg m^{-3}, $\mu(Mo_{K\alpha})$ = 0.070 mm^{-1}, T = 298(2) K, 8551 data measured on a Bruker SMART Apex diffractometer, of which 5829 were unique (R_{int} = 0.0470); 448 parameters refined against F_o^2 (all data), final wR_2 = 0.1044, S = 1.063, R_1 ($I > 2\sigma(I)$) = 0.0603, largest final difference peak/hole = 0.160 and −0.167 e Å^{-3}. Structure solution by direct methods and full-matrix least-squares refinement against F^2 (all data) using SHELXTL.

Acknowledgements

This work was financially supported by NSFC (21072060), the Program for Professor of Special Appointment (Eastern Scholar) at Shanghai Institutions of Higher Learning, Program for New Century Excellent Talents in University (NCET), Innovation Program of Shanghai Municipal Education Commission, the Fundamental Research Funds for the Central Universities (WK1013002), and SRFDP (20100074110015).

Notes and references

1 (*a*) C. J. Frederickson, J. Y. Koh and A. I. Bush, *Nat. Rev. Neurosci.*, 2005, **6**, 449–462; (*b*) E. L. Que, D. W. Domaille and C. J. Chang, *Chem. Rev.*, 2008, **108**, 1517–1549; (*c*) E. Tomat and S. J. Lippard, *Curr. Opin. Chem. Biol.*, 2010, **14**, 225–230.

2 (*a*) Z. C. Xu, J. Yoon and D. R. Spring, *Chem. Soc. Rev.*, 2010, **39**, 1996–2006; (*b*) P. Jiang and Z. Guo, *Coord. Chem. Rev.*, 2004, **248**, 205–229; (*c*) E. Manandhar, J. H. Broome, J. Myrick, W. Lagrone, P. J. Cragg and K. J. Wallace, *Chem. Commun.*, 2011, **47**, 8796–8798; (*d*) M. Chen, X. Lv, Y. Liu, Y. Zhao, J. Liu, P. Wang and W. Guo, *Org. Biomol. Chem.*, 2011, **9**, 2345–2349; (*e*) Z. C. Xu, K. H. Baek, H. N. Kim, J. N. Cui, X. H. Qian, D. R. Spring, I. Shin and J. Yoon, *J. Am. Chem. Soc.*, 2010, **132**, 601–610; (*f*) L. Xue, Q. Liu and H. Jiang, *Org. Lett.*, 2009, **11**, 3454–3457; (*g*) Y. Ikawa, M. Takeda, M. Suzuki, A. Osuka and H. Furuta, *Chem. Commun.*, 2010, **46**, 5689–5691.

3 (*a*) T. Ueno and T. Nagano, *Nat. Methods*, 2011, **8**, 642–645; (*b*) B. Valeur and I. Leray, *Coord. Chem. Rev.*, 2000, **205**, 3–40; (*c*) A. P. de Silva, T. S. Moody and G. D. Wright, *Analyst*, 2009, **134**, 2385–2393; (*d*) G. He, X. Zhao, X. Zhang, H. Fan, S. Wu, H. Li, C. He and C. Duan, *New J. Chem.*, 2010, **34**, 1055–1058; (*e*) X. Cheng, S. Li, H. Jia, A. Zhong, C. Zhong, J. Feng, J. Qin and Z. Li, *Chem.–Eur. J.*, 2012, **18**, 1691–1699; (*f*) L. Yuan, W. Lin, B. Chen and Y. Xie, *Org. Lett.*, 2012, **14**, 432–435; (*g*) Y. Chen, L. Wan, X. Yu, W. Li, Y. Bian and J. Jiang, *Org. Lett.*, 2011, **13**, 5774–5777; (*h*) L. Yao, J. Zhou, J. Liu, W. Feng and F. Li, *Adv. Funct. Mater.*, 2012, **22**, 2667–2672; (*i*) J. P. Hill, N. K. Subbaiyan, F. D'Souza, Y. Xie, S. Sahu, N. M. Sanchez-Ballester, G. J. Richards, T. Mori and K. Ariga, *Chem. Commun.*, 2012, **48**, 3951–3953; (*j*) G. R. Deviprasad, B. Keshavan and F. D'Souza, *J. Chem. Soc., Perkin Trans.*, 1998, 3133–3136; (*k*) S. Brovelli, G. Sforazzini, M. Serri, G. Winroth, K. Suzuki, F. Meinardi, H. L. Anderson and F. Cacialli, *Adv. Funct. Mater.*, 2012, **22**, 4284–4291; (*l*) O. Fenwick, J. K. Sprafke, J. Binas, D. V. Kondratuk, F. Di Stasio, H. L. Anderson and F. Cacialli, *Nano Lett.*, 2011, **11**, 2451–2456.

4 (*a*) J. R. Lakowicz, *Topics in Fluorescence Spectroscopy, Volume 4: Probe Design and Chemical Sensing*, Kluwer Academic Publishers, New York, 2002; (*b*) W. Lin, L. Yuan, L. Long, C. Guo and J. Feng, *Adv. Funct. Mater.*, 2008, **18**, 2366–2372.

5 (*a*) Q. Chang, J. R. Lakowicz and G. Rao, *Analyst*, 1997, **122**, 173–177; (*b*) R. Fudala, M. E. Mummert, Z. Gryczynski, R. Rich, J. Borejdo and I. Gryczynski, *J. Photochem. Photobiol., B*, 2012, **106**, 69–73; (*c*) X. D. Wang and O. S. Wolfbeis, *Anal. Chem.*, 2012, **85**, 487–508.

6 (*a*) J. Jo, H. Y. Lee, W. Liu, A. Olasz, C. H. Chen and D. Lee, *J. Am. Chem. Soc.*, 2012, **134**, 16000–16007; (*b*) X. Peng, J. Du, J. Fan, J. Wang, Y. Wu, J. Zhao, S. Sun and T. Xu, *J. Am. Chem. Soc.*, 2007, **129**, 1500–1501; (*c*) A. F. Li, H. He, Y. B. Ruan, Z. C. Wen, J. S. Zhao, Q. J. Jiang and Y. B. Jiang, *Org. Biomol. Chem.*, 2009, **7**, 193–200; (*d*) L. Liu, G. Zhang, J. Xiang, D. Zhang and D. Zhu, *Org. Lett.*, 2008, **10**, 4581–4584; (*e*) K. Huang, H. Yang, Z. Zhou, M. Yu, F. Li, X. Gao, T. Yi and C. Huang, *Org. Lett.*, 2008, **10**, 2557–2560.

7 (*a*) Y. Q. Weng, F. Yue, Y. R. Zhong and B. H. Ye, *Inorg. Chem.*, 2007, **46**, 7749–7755; (*b*) J. Yoshino, N. Kano and T. Kawashima, *J. Org. Chem.*, 2009, **74**, 7496–7503; (*c*) A. P. de Silva, G. D. McClean and T. S. Moody, *Encyclopedia of Supramolecular Chemistry*, 2004, 572–578.

8 (*a*) Y. Zhou, Z. X. Li, S. Q. Zang, Y. Y. Zhu, H. Y. Zhang, H. W. Hou and T. C. W. Mak, *Org. Lett.*, 2012, **14**, 1214–1217; (*b*) M. Mameli, M. C. Aragoni, M. Arca, M. Atzori, A. Bencini, C. Bazzicalupi, A. J. Blake, C. Caltagirone, F. A. Devillanova, A. Garau, M. B. Hursthouse, F. Isaia, V. Lippolis and B. Valtancoli, *Inorg. Chem.*, 2009, **48**, 9236–9249; (*c*) Z. Guo, G. H. Kim, I. Shin and J. Yoon, *Biomaterials*, 2012, **33**, 7818–7827; (*d*) Y. Hong, S. Chen, C. W. T. Leung, J. W. Y. Lam, J. Liu, N. W. Tseng, R. T. K. Kwok, Y. Yu, Z. Wang and B. Z. Tang, *ACS Appl. Mater. Interfaces*, 2011, **3**, 3411–3418; (*e*) F. Sun, G. Zhang,

D. Zhang, L. Xue and H. Jiang, *Org. Lett.*, 2011, **13**, 6378–6381; (*f*) E. M. Nolan, J. Jaworski, K. I. Okamoto, Y. Hayashi, M. Sheng and S. J. Lippard, *J. Am. Chem. Soc.*, 2005, **127**, 16812–16823; (*g*) W. Jiang, Q. Fu, H. Fan and W. Wang, *Chem. Commun.*, 2008, 259–261; (*h*) W. Lin, J. Feng, L. Yuan and W. Tan, *Sens. Actuators, B*, 2009, **135**, 512–515.

9 (*a*) B. Turfan and E. U. Akkaya, *Org. Lett.*, 2002, **4**, 2857–2859; (*b*) D. Maity and T. Govindaraju, *Chem. Commun.*, 2012, **48**, 1039–1041; (*c*) P. N. Basa and A. G. Sykes, *J. Org. Chem.*, 2012, **77**, 8428–8434; (*d*) H. Sasaki, K. Hanaoka, Y. Urano, T. Terai and T. Nagano, *Bioorg. Med. Chem.*, 2011, **19**, 1072–1078; (*e*) X. Lu, W. Zhu, Y. Xie, X. Li, Y. Gao, F. Li and H. Tian, *Chem.–Eur. J.*, 2010, **16**, 8355–8364; (*f*) A. E. Lee, M. R. Grace, A. G. Meyer and K. L. Tuck, *Tetrahedron Lett.*, 2010, **51**, 1161–1165; (*g*) Z. Han, X. Zhang, Z. Li, Y. Gong, X. Wu, Z. Jin, C. He, L. Jian, J. Zhang, G. Shen and R. Yu, *Anal. Chem.*, 2010, **82**, 3108–3113; (*h*) J. J. Du, J. L. Fan, X. J. Peng, H. L. Li and S. G. Sun, *Sens. Actuators, B*, 2010, **144**, 337–341.

10 Y. B. Ding, Y. S. Xie, X. Li, J. P. Hill, W. B. Zhang and W. H. Zhu, *Chem. Commun.*, 2011, **47**, 5431–5433.

11 L. Wang, W. Wei, Y. Guo, J. Xu and S. Shao, *Spectrochim. Acta, Part A*, 2011, **78**, 726–731.

12 A. Shundo, J. P. Hill and K. Ariga, *Chem.–Eur. J.*, 2009, **15**, 2486–2490.

13 (*a*) D. T. Gryko, D. Gryko and C. H. Lee, *Chem. Soc. Rev.*, 2012, **41**, 3780–3789; (*b*) B. J. Littler, M. A. Miller, C. H. Hung, R. W. Wagner, D. F. O'Shea, P. D. Boyle and J. S. Lindsey, *J. Org. Chem.*, 1999, **64**, 1391–1396.

14 (*a*) T. E. Wood and A. Thompson, *Chem. Rev.*, 2007, **107**, 1831–1861; (*b*) Q. Miao, J. Y. Shin, B. O. Patrick and D. Dolphin, *Chem. Commun.*, 2009, 2541–2543.

15 H. T. Niu, D. Su, X. Jiang, W. Yang, Z. Yin, J. He and J. P. Cheng, *Org. Biomol. Chem.*, 2008, **6**, 3038–3040.

16 (*a*) Y. Li, L. Shi, L. X. Qin, L. L. Qu, C. Jing, M. Lan, T. D. James and Y. T. Long, *Chem. Commun.*, 2011, **47**, 4361–4363; (*b*) B. Zhang, K. S. Cao, Z. A. Xu, Z. Q. Yang, H. W. Chen, W. Huang, G. Yin and X. Z. You, *Eur. J. Inorg. Chem.*, 2012, **2012**, 3844–3851.

17 N. C. Lim and C. Bruckner, *Chem. Commun.*, 2004, 1094–1095.

18 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Fundam. Crystallogr.*, 2008, **64**, 112.

