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Study on the BODIPY-triazine-based tripod fluorescent systems: various structures from similar procedure

Xin Qi[a1], Sook Kyung Kim[a1], Su Jung Han[b], Li Xu[a], Ah Young Jee[a], Ha Na Kim[a], Chongmok Lee[b], Youngmee Kim[a], Minyung Lee[a,b], Sung-Jin Kim[a,b] and Juyoung Yoon[a,b]*

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We report a small library of fluorophore-triazine tripod fluorescent system that can accommodate a combination of three different functional groups, such as fluorophore (BODIPY), ligand (or ligands) and auxiliary group. Syntheses, photophysical properties as well as binding properties towards metal ions of these BODIPY-triazine derivatives are described.

Keywords: BODIPY; triazine; fluorescent chemosensor; Cu^{2+} sensor

Introduction

Sensors based on the ion-induced changes in fluorescence are particularly attractive owing to their simplicity and the high detection limit of the fluorescence (*1*). Among them, 4,4-difluoro-4-bora-3*a*,4*a*-diaza-*s*-indacene (BODIPY) derivatives have proved to be useful fluorophores on account of their high molar absorptivity, fluorescence quantum yields and stability against light and chemical reactions (*2*). Furthermore, BODIPY dyes can be excited with visible light, and show narrow absorption and emission bands with high peak intensities. In this regard, BODIPY derivatives have been recently reported as fluorescent chemosensors for metal ions (*3*), protons (*4*) or NO (*5*).

Due to the advantage of the temperature-dependent stepwise substitution of its three chlorine atoms by different nucleophiles, cyanuric chloride has been proved to be a very useful template for the synthesis of dendrimers (*6a*), macrocycles (*6b*), calixarene (*6c*) and combinatorial libraries (*6d*). Even though there is a recent example of monosubstituted triazine-BODIPY (*7*), the detailed photophysical properties have not been reported (*7*). Recently, we reported a new design for a fluorophore-triazine tripod fluorescent system that can accommodate a combination of three different functional groups, such as fluorophore (BODIPY), ligand (or ligands) and auxiliary group, as shown in Figure 1 (*8*).

Based on this novel framework, various ligands for binding different types of ions can be attached (one or two at the same time, identical or different) to the BODIPY fluorophore moiety through a triazine linkage utilising similar synthetic procedures. In the case where there is one binding subunit (Figure 1(a)), the third substituted position on the triazine structure allows the introduction of an auxiliary group with different structures, which might not only modify the chemical and/or physical properties of the products, such as solubility or fine-tune of spectrum but also combine the fluorescent behaviour with other research fields such as polymers, nanomaterials and biochemistry, through functional groups attached to it. To some extent, it may be a universal structure for preparing a variety of chemosensors for various applications under similar procedures. In this study, four different classes of BODIPY-triazine tripods were synthesised and their photophysical properties were examined (Figure 2).

Results and discussion

In an earlier study, we reported the synthesis and physical properties of compounds **6**–**9** (*8*). In the present work, four different classes of BODIPY-triazine derivatives, including the above-mentioned four compounds, were prepared (Figure 2), bearing one binding subunit (**1**,**2**), two identical binding subunits (**3**–**5**), one binding subunit and an auxiliary subunit (**6**–**9**), as well as one additional signalling subunit and one binding site (**10**). The detailed syntheses are explained in the Experimental section as well as in Schemes 1–3. Generally, an aldehyde containing a hydroxyl group should react first with cyanuric chloride due to its relatively poor nucleophilicity, and then with the primary amine if needed. Ligands bearing a secondary amine were introduced in the last stage to form intermediates bearing a triazine core and benzaldehyde, which were used for further condensations. All new

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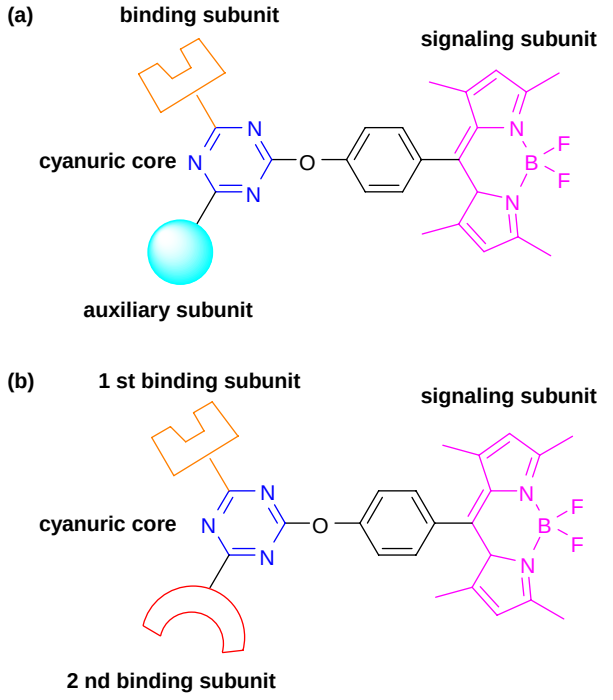


Figure 1. General approaches of the BODIPY-triazine tripod systems.

compounds **1–5** and **10** were fully characterised by ^{1}H and ^{13}C NMR (supporting information) and high-resolution FAB mass.

During our data processing, the Daub group reported a BODIPY structure containing a monosubstituted triazine structure via a condensation reaction between a BODIPY dye bearing a thiol group and cyanuric chloride. Indeed, we first adopted the same methodology in our studies (hydroxyl in this case instead of thiol), but only the above-mentioned monosubstituted derivative was obtained successfully through the type of direct condensation involving the most reactive chlorine atom of cyanuric chloride. Subsequent substitutions of the second and third chlorine atoms on the triazine core from the monosubstituted structure by nucleophiles (ligands used in this report) to explore structure diversity were failed. Similar results were obtained for the condensations between the BODIPY dye with a hydroxyl group and the second or third chlorine atoms on a mono (bis)-substituted cyanuric chloride. It appears that the 4-boron atom on BODIPY structure can also be attacked by the nucleophiles existing in the reaction mixture under high-temperature conditions during those processes as well as the anticipated carbon atom on the substituted cyanuric chloride, which leads to unpredictable complicated mixtures. Similar phenomena were also observed in our other study involving *in situ* formed anions and BODIPY derivatives, wherein series of spots were found on the thin layer chromatography (TLC) plate with the loss of fluorescence (not published). Therefore, we turned to search for other more reliable ways (as reported herein) to fulfil the desired structure diversity (*8*).

The X-ray crystal structures of compounds **1** and **6** are also presented (Figures 3 and 4). In the X-ray structure of **1** (Figure 3), the phenyl and pyrrole rings are planar, with an average deviation of 0.0063 and 0.0359 Å, respectively. The dihedral angle is 89.50°. The triazine and pyridine rings are co-planar with an average deviation of 0.0375 Å, which is almost parallel with pyrrole rings, with a dihedral angle of 4.81°. By intermolecular hydrogen bonds (C25—H25···F2, C6—H62···F1), the molecules of **1** are linked into a three-dimensional network structure (Figure 3).

In the X-ray structure of **6** (Figure 4), the phenyl (C14—C19) and pyrrole rings are planar, with an average deviation of 0.0039 and 0.0919 Å, respectively. The dihedral angle is 87.97°, which is a bit smaller than that in compound **6**. The dihedral angle between the triazine and pyrrole rings (20.20°) is larger than that in compound **6**. The dihedral angles between the triazine and phenyl rings (C35—C40), and two pyridine rings are 41.63°, 75.96° and 81.63°, respectively. One of the pyridine ring (C41—C45, N41) is disordered over two sites (C41–C45, N41; C51—C55, N51). Only one site is shown in Figure 4 for clarity.

Initially, relatively small spectral changes (λ_{max}) in the UV and fluorescent emissions were observed (Figure 5), which were probably due to the long distance between the auxiliary groups and BODIPY as well as the angle (~90°) between the triazine and BODIPY moieties. This was also explained by You et al. (*3j*). However, as shown in the data for compounds **9** and **10**, careful modification of the auxiliary groups or the introduction of a second signalling unit in the tripods can still control the UV absorption as well as the fluorescent emission intensity.

As expected, the introduction of a second BODIPY group (**10**) induced an amplification effect in both the UV and fluorescent spectra. The fluorescence quantum efficiencies were determined in degassed acetonitrile (Table 1). Quantum efficiencies over 0.55 were observed for most structures including as high as 0.81 for compound **4**.

The binding properties of these tripod fluorescent systems were determined using Ag^{+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, Cs^{+}, Hg^{2+}, K^{+}, Mg^{2+}, Mn^{2+}, Na^{+}, Ni^{2+}, Pb^{2+} and Zn^{2+} ions (2 equiv.) to evaluate the metal ion binding properties of these compounds in acetonitrile. For different ligands, compound **1** (Figure 6) bearing one 2-methylpyridine binding unit displayed a highly selective fluorescent quenching effect with only Cu^{2+} among the metal ions examined.

Compound **2** bearing one di-(2-picolyl)amine (DPA) unit also displayed a large and selective CHEQ (chelation-enhanced fluorescence quenching) effect with Cu^{2+}, even though there were relatively small CHEQ effects with Hg^{2+}, Pb^{2+} and Zn^{2+} (Figure S1). There was a small

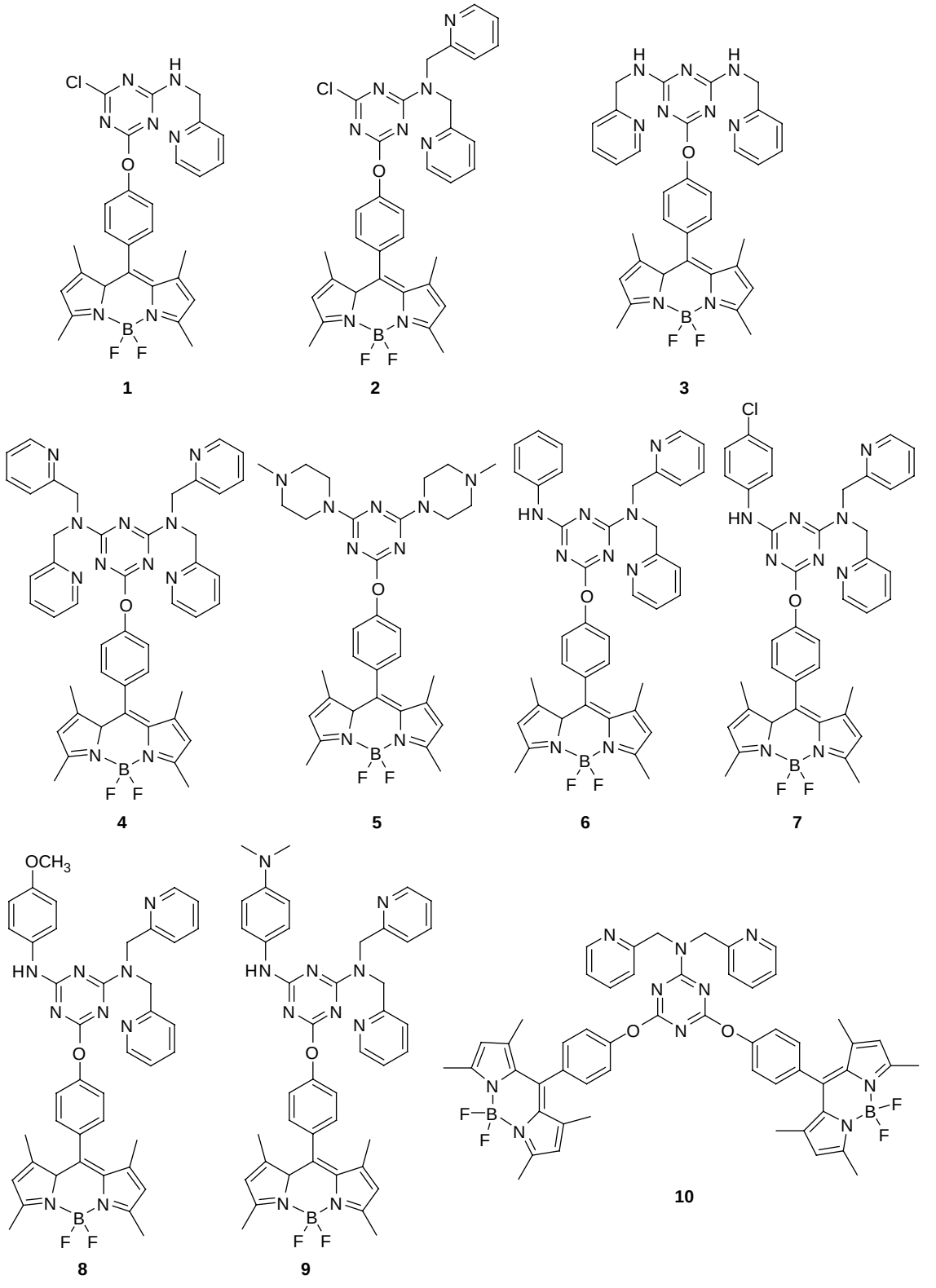
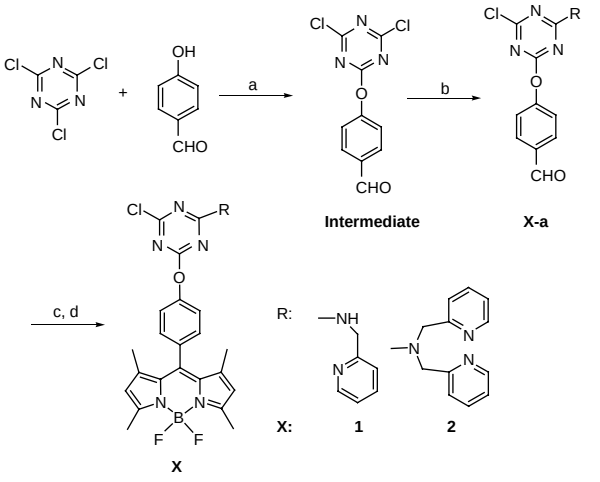


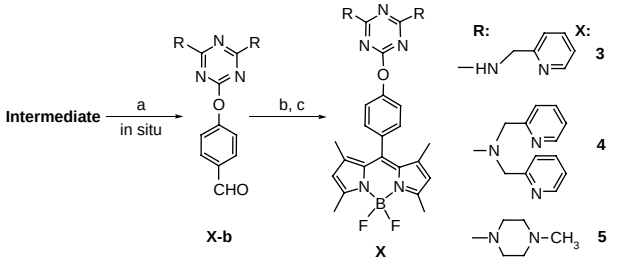
Figure 2. Structures of compounds **1**–**10**.



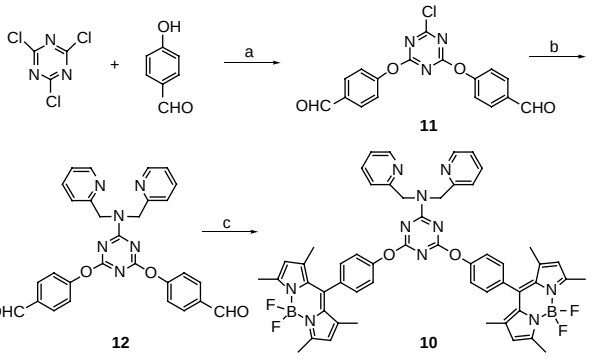
Scheme 1. (a) Methylene Chloride (MC), 4-hydroxybenzaldehyde (1.1 equiv.), diisopropylethylamine (DIEA, 1.2 equiv.), 0–5°C, 20 min. (b) Respective ligand (1.1 equiv.), DIEA (1.2 equiv.), 0–5°C to rt, 2 h (**1a**: 73.5%, **1b**: 73.5%). (c) (i) 2,4-Dimethylpyrrole (1.02 equiv.), trifluoroacetic acid (TFA, catalytic amount), anhydrous MC, rt, 20 h. (ii) 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 1.0 equiv.), MC, rt, 2 h. (d) TEA, MC, rt, BF_3·OEt_2, rt, overnight (**1**: 28.5%, **2**: 21.5%).

(~5 nm) red shift as well as small decrease in the UV absorption spectrum when 2 equiv. of Cu^{2+} was added to the solution of **2** (not shown). Compound **10** bearing two signal BODIPY and one DPA units displayed a large CHEQ effect with Cu^{2+}, and relatively small CHEQ effects with Hg^{2+}, Pb^{2+} and Zn^{2+} (Figure S6).

Compound **5** bearing two piperazine groups did not show any significant fluorescent changes with 2 equiv. of various metal ions (Figure S3). On the other hand, compound **3** (Figure S2) bearing two 2-methylpyridine binding units displayed a highly selective fluorescent quenching effect with only Cu^{2+}, and compound **4** bearing two DPA binding units displayed large CHEQ effects with Co^{2+}, Cu^{2+} and Ni^{2+} (Figure 7).



Scheme 2. (a) Intermediate (1.0 equiv.), DPA (2.0 equiv.), K_2CO_3 (4.0 equiv.), H_2O, 0–5°C to rt, 2 h, then reflux, 5 h (**3b**: 76%, **4b**: 70%, **5b**: 75%). (b) (i) 2,4-Dimethylpyrrole (1.05 equiv.), TFA (catalytic amount), anhydrous THF, rt, 20 h. (ii) DDQ (1.0 equiv.), THF, rt, 2 h. (c) TEA, THF, rt, BF_3·OEt_2, rt, overnight (**3**: 17.8%, **4**: 19.7%, **5**: 39.9%).



Scheme 3. (a) MC, 4-hydroxybenzaldehyde (1.1 equiv.), DIEA (1.2 equiv.), 0–5°C, 20 min, then rt, 4-hydroxybenzaldehyde (1.1 equiv.), DIEA (1.2 equiv.), 2 h, 83%. (b) DPA (2.0 equiv.), aq. potassium carbonate (3.0 equiv.), reflux, 5 h, THF, 72%. (c) (i) 2,4-Dimethylpyrrole (1.0 equiv.), TFA (catalytic amount), anhydrous MC, rt, 20 h. (ii) DDQ (1.05 equiv.), MC, rt, 2 h. (iii) TEA, MC, rt, BF_3·OEt_2, rt, overnight, 26%.

Among the compounds bearing one DPA binding unit and one auxiliary group (**2**, **6**–**9**), large CHEQ effects with Cu^{2+} and Ni^{2+} and small CHEQ effects with Hg^{2+}, Co^{2+}, Zn^{2+} and Pb^{2+} are common features. On the other hand, along with CHEQ effects with Ni^{2+}, Co^{2+} and Cu^{2+}, compound **9** showed a CHEF with Hg^{2+} (Figure 9), which was also explained in our earlier report (*8*). The fluorescent data of compound **9** can be compared to that of compound **7**, as shown in Figure 8.

Fluorescent lifetime measurements are illustrated in Table 2. The fluorescence lifetimes were measured by the time-correlated single-photon counting (TCSPC) system. The fluorescent quenching with Hg^{2+} was also shown in Table 2.

To check the potential application as a fluorescent sensor for metal ions, the fluorescent changes of compound **1** with various metal ions were examined in aqueous solution [acetonitrile-HEPES solution (0.02 M, pH 7.4) (4:1, v/v)]. Under this condition, compound **1** also displayed a selective CHEQ effect only with Cu^{2+} among the metal ions examined. The association constant of **1** with Cu^{2+} was calculated as 190,500 M^{-1} from the fluorescent titration experiment (errors $< 15\%$) (Figure 10) (*9*).

Conclusions

In conclusion, we report tripod fluorescent systems that bear a triazine core for combining three different functional groups, such as fluorophore, ligand and auxiliary group. This novel concept was confirmed through four types of BODIPY-triazine derivatives synthesised under a similar procedure, which revealed different binding behaviours towards metal ions and photophysical properties as a change in the binding and

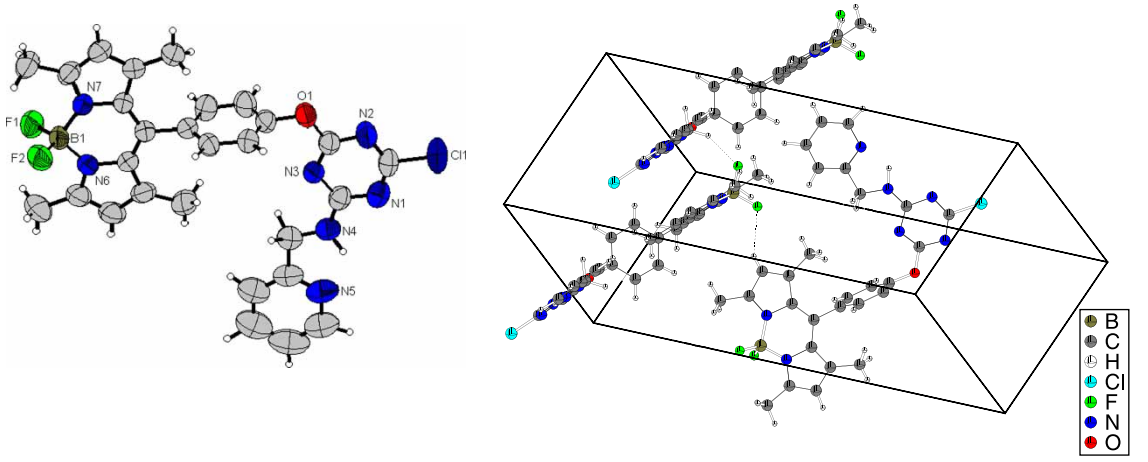


Figure 3. X-ray crystal structure of compound **1** and the packing of compound **1** in the unit cell.

auxiliary subunits. We believe that the flexibility and potential variety of this tripod system can present various applications in the fields of fluorescent chemosensors, organo EL materials, nanomaterials and tagging materials of biological systems. Further research related to this new tripod system is currently under investigation.

Experimental

General methods

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Flash chromatography was carried out on silica gel 60 (230–400 mesh ASTM; Merck). TLC was carried out using Merck 60 F_{254} plates with a thickness of 0.25 mm. Preparative TLC was performed using Merck 60 F_{254} plates with the thickness of 1 mm.

Melting points were measured using a Büchi 530 melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded using Bruker 250 MHz or Varian 500 MHz. Chemical shifts were given in ppm and coupling constants (J) in Hz. UV absorption spectra were obtained on UVIKON 933 double-beam UV/VIS spectrometer. Fluorescence emission spectra were obtained using RF-5301/PC spectrofluorophotometer (Shimadzu).

Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre [deposition no. CCDC 681699 (compound 1), CCDC 681700 (compound 6)]. That data can be obtained free of charge via http://www.ccdc.cam.ac.uk/perl/catreq.cgi (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

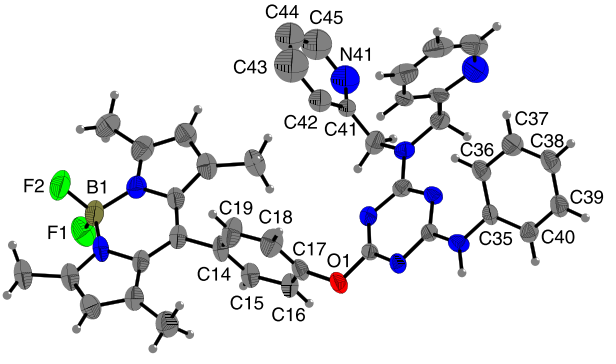


Figure 4. X-ray crystal structure of compound **6**.

*General procedure for **1-a** and **2-a** (Scheme 1)*

To a stirred solution of cyanuric chloride (368.8 mg, 2.0 mmol) in 20 ml of methylene chloride in an ice water bath was added dropwise a solution of 4-hydroxybenzaldehyde (270 mg, 2.2 mmol) and diisopropylethylamine (0.42 ml, 2.4 mmol) in 10 ml of methylene chloride during 30 min. After the addition, the mixture was stirred for another 20 min at 0–5°C until the complete consumption of cyanuric chloride (monitored by TLC, ethyl acetate:hexane 1:8) to afford an intermediate mixture. A mixture of 2-aminomethylpyridine (238 mg, 2.2 mmol) and 0.42 ml of DIEA (2.4 mmol) in 10 ml of MC was added at the same temperature and the ice water bath was then removed. After stirring for 2 h at room temperature (monitored by TLC, ethyl acetate:hexane 1:2), the reactant was passed through a silica gel column (~20 g) and rinsed with ethyl acetate (100 ml). After concentration under vacuum, the crude product was purified by flash chromatography (ethyl acetate:hexane) to afford the products **1-a** and **2-a**.

1-a: Eluent (ethyl acetate:hexane 1:2) to afford product **1-a** (503 mg, 1.47 mmol, 73.5%) as a white solid: mp 137–138°C. ^{1}H NMR ($CDCl_3$): δ 4.55 (d, 1H, $J = 5.2$ Hz), 4.72 (d, 1H, $J = 5.0$ Hz), 6.95–7.30 (m, 3H), 7.54–7.76 (m, 2H), 7.89 (d, 2H, $J = 4.7$ Hz), 8.48 (d, 1H, $J = 4.3$ Hz),

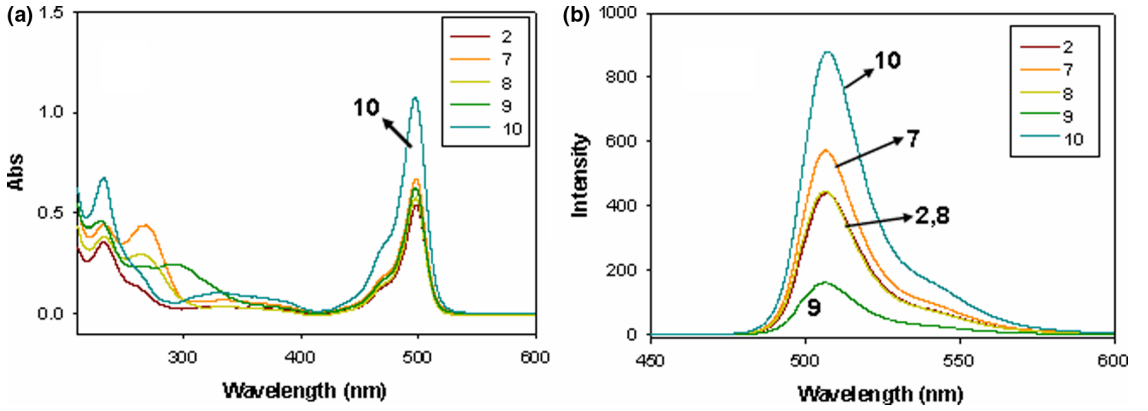


Figure 5. (a) UV absorption spectra of **2**, **7**, **8**, **9** and **10**. (b) fluorescence emission of **2**, **7**, **8**, **9** and **10** in degassed acetonitrile (excitation at 497 nm).

10.0 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 45.6, 121.8, 122.4, 122.8, 131.2, 134.0, 136.9, 148.9, 149.0, 154.6, 156.2, 166.6, 169.9, 170.4, 171.1, 172.0, 190.9; FAB-MS (*m/z*): 342.1 $(M + H)^+$.

2-a: Eluent (ethyl acetate:hexane 1:1 to 4:1) to afford product **2-a** (636 mg, 1.47 mmol, 73.5%) as pale yellow sticky solid. ^{1}H NMR ($CDCl_3$): δ 4.75 (s, 2H), 4.72 (s, 2H), 6.83 (d, 1H, $J = 7.8$ Hz), 7.15–7.30 (m, 5H), 7.52–7.63 (m, 2H), 7.79 (d, 2H, $J = 8.5$ Hz), 8.46–8.52 (m, 2H), 10.0 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 52.1, 52.6, 121.7, 122.3, 122.5, 122.6, 131.0, 133.8, 136.4, 136.7, 149.0, 155.7, 156.3, 166.6, 170.0, 171.5, 190.7; FAB-MS (*m/z*): 433.1$(M + H)^+$.

*General procedure for **1** and **2** (Scheme 1)*

To a stirred solution of pre-dried **1-a** and **2-a** (341 mg, 1.0 mmol) and 2,4-dimethylpyrrole (195 mg, 2.05 mmol) in 30 ml of anhydrous MC was added a catalytic amount of trifluoroacetic acid under nitrogen at room temperature. After stirring of 20 h, a mixture of pre-dried 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (227 mg, 1.0 equiv.) in 20 ml of anhydrous MC was added dropwise during 10 min and the reactant solution was stirred further for 2 h at room temperature. The mixture was passed through an aluminium oxide column (~30 g) and further eluted by $CHCl_3$/MeOH (40:1) to get a dark brown solution. After concentration with aspirator, the residue was dried under vacuum overnight, which was then used directly for further step. Anhydrous MC (30 ml) and triethylamine (5.0 ml) were added consecutively to the flask containing the pre-dried crude product under nitrogen atmosphere at room temperature with stirring, followed by dropwise addition of boron trifluoride diethetate (5.0 ml) during 30 min. The mixture was stirred overnight, then passed through an Al_2O_3 column (~25 g) and rinsed with a mixture of MC/MeOH (50:1). After evaporation of the solvent, the residue was redissolved with MC (80 ml), washed sufficiently with 15% aqueous K_2CO_3 (3 × 150 ml) and water (100 ml) and dried over anhydrous sodium sulphate. The solvent was evaporated by water aspirator and the residue was first separated by flash chromatography on silica gel column (MC to MC/MeOH 50:1), followed by preparative TLC purification (MC/MeOH 50:1) for the brown yellow elution to afford

Table 1. The fluorescence λ_{max} and relative fluorescence quantum efficiencies (QE) in degassed acetonitrile.

Compound	QE[a] (λ_{max})
1	58% (507 nm)
2	73% (508 nm)
3	61% (506 nm)
4	81% (506 nm)
5	66% (506 nm)
10	55% (507 nm)

[a]The relative quantum efficiency was determined using that of fluorescein (0.85) in 0.1 M NaOH as a standard.

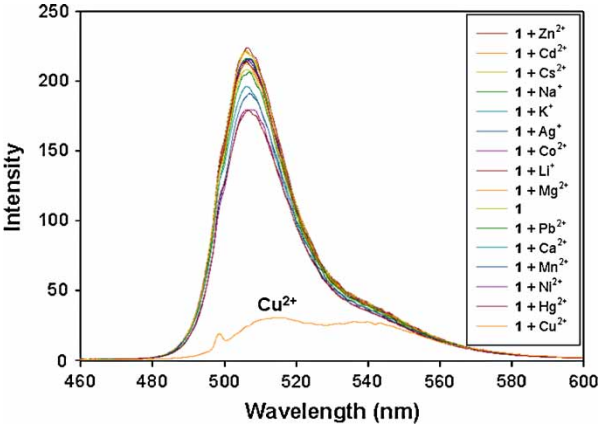


Figure 6. Fluorescence changes of **1** (1 μM) upon addition of various metal ions (2 equiv.) in acetonitrile (excitation at 497 nm).

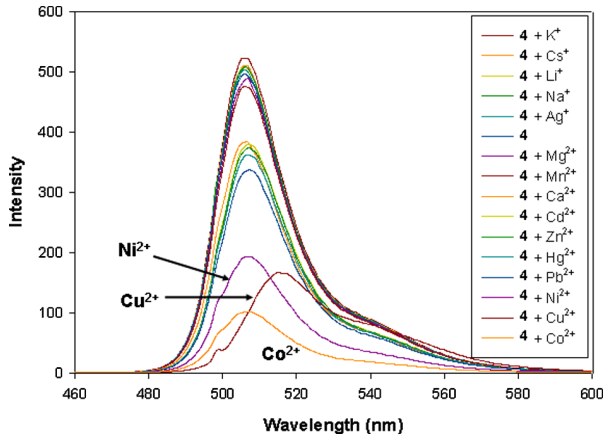


Figure 7. Fluorescence changes of **4** (1 μM) upon addition of various metal ions (2 equiv.) in acetonitrile (excitation at 497 nm).

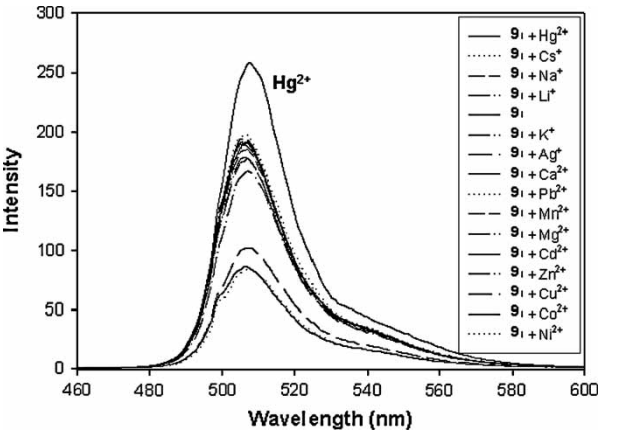


Figure 9. Fluorescent changes of **8** (1 μM) upon addition of metal ions in CH_3CN (excitation at 507 nm).

products **1** and **2**. Analytical sample was received by recrystallisation from ethyl acetate and hexane.

1: Red solid (160 mg, 0.285 mmol, 28.5%): mp > 258°C (Dec.). ^{1}H NMR ($CDCl_3$): δ 1.47 (s, 6H), 2.57 (s, 6H), 4.54 (d, 1H, J = 5.0 Hz), 4.77 (d, 1H, J = 4.9 Hz), 6.00 (s, 2H), 7.14–7.36 (m, 8H), 7.67 (m, 1H), 8.55 (d, 1H, J = 2.9 Hz); ^{13}C NMR ($CDCl_3$): δ 14.8, 41.1, 45.7, 121.7, 122.3, 122.9, 129.5, 131.4, 132.1, 136.7, 137.1, 140.7, 143.1, 149.5, 152.9, 154.8, 155.7, 166.5, 170.5, 171.6; HR-MS (FAB) (*m/z*): 561.2024 $(M + H)^+$, calcd for $C_{28}H_{27}BClF_2N_7O$ 561.2027.

2: Red sticky oil (140 mg, 0.215 mmol, 21.5% yield). ^{1}H NMR ($CDCl_3$): δ 1.40 (s, 6H), 2.62 (s, 6H), 4.88 (s, 2H), 5.10 (s, 2H), 6.03 (s, 2H), 7.13 (d, 1H, J = 7.7 Hz), 7.27 (m, 6H), 7.36 (d, 1H, J = 8.0 Hz), 7.66–7.76 (m, 2H), 8.60 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 14.4, 51.7, 51.9, 121.3. 121.6, 122.5, 129.0, 131.3, 132.4, 136.6, 136.8, 140.4, 142.9, 149.4, 152.2, 155.6, 155.8, 166.8, 170.5, 171.7; HR-MS (FAB) (*m/z*): 651.2372 $(M + H)^+$, calcd for $C_{34}H_{31}BClF_2N_8O$ 651.2377.

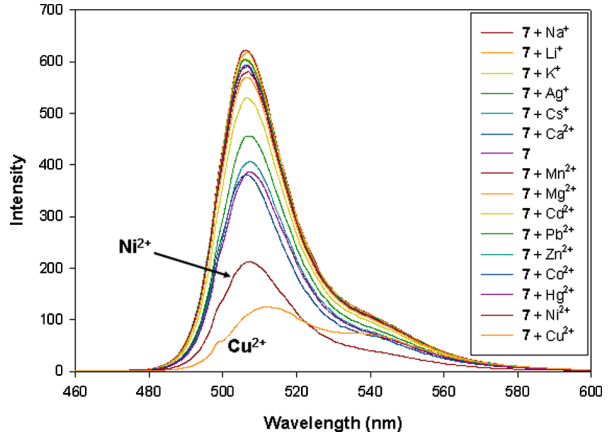


Figure 8. Fluorescence changes of **7** (1 μM) upon addition of various metal ions (2 equiv.) in acetonitrile (excitation at 497 nm).

*General procedure and prepartion for **3-b**, **4-b** and **5-b** (Scheme 2)*

A mixture of DPA (400 mg, 4.0 mmol) in 20 ml of THF and an aqueous solution of potassium carbonate (1.10 g, 8.0 mmol) in 10 ml of water was added consecutively at 0–5°C to the above-mentioned intermediate solution, and the ice water bath was then removed. After stirring for 1 h at room temperature, the mixture was then refluxed for 5 h. After cooling down, the mixture was concentrated to about 20 ml and chloroform (50 ml) was added. The organic layer was washed with water and dried over anhydrous sodium sulphate. After concentration under vacuum, the crude product was purified by flash chromatography (MC/MeOH = 50:1 to 20:1) to afford the products **3-b**, **4-b** and **5-b**.

3-b: White sticky solid (630 mg, 1.52 mmol, 76%). ^{1}H NMR ($CDCl_3$): δ 4.5 (dd, 4H, J = 27.6, 5.4 Hz), 6.45 (s, 1H), 7.19 (m, 6H), 7.60 (t, 2H, J = 7.3), 7.91 (d, 2H, J = 8.3), 8.39 (s, 1H), 8.52 (s, 1H), 10.0 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 46.1, 121.6, 122.3, 122.8, 130.8, 131.1, 133.3, 136.8, 148.9, 157.2, 157.8, 167.2, 191.0; FAB-MS (*m/z*): 414.2 $(M + H)^+$.

Table 2. The fluorescence lifetimes of compounds **7** and **10** in the absence and presence of $Hg(ClO_4)_2$ (5 equiv.) in acetonitrile.

Sample[a]	Lifetimes		$<\tau>$
7	Amp. 1 = 0.31 Amp. 2 = 0.69	τ_1 = 1.34 τ_2 = 3.41	2.7 ns
7 + $Hg(ClO_4)_2$	Amp. 1 = 0.67 Amp. 2 = 0.33	τ_1 = 0.75 τ_2 = 2.57	1.36 ns
10	Amp. 1 = 0.34 Amp. 2 = 0.66	τ_1 = 1.55 τ_2 = 4.43	2.48 ns
10 + $Hg(ClO_4)_2$	Amp. 1 = 0.78 Amp. 2 = 0.22	τ_1 = 0.34 τ_2 = 3.49	1.03 ns

[a] Sample concentration was 5×10^{-5} M.

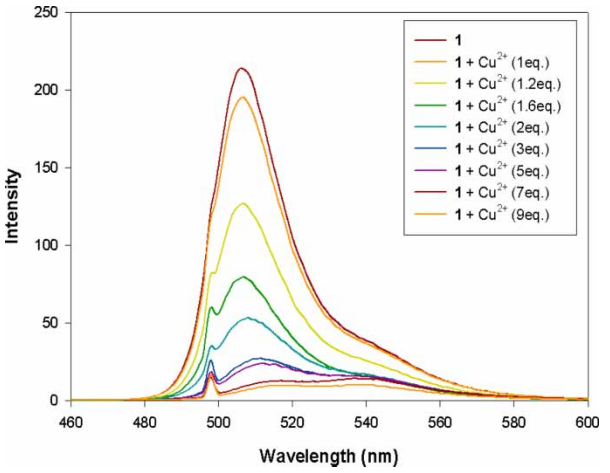


Figure 10. Fluorescent titrations of **1** (1 μM) upon addition of Cu^{2+} in aqueous solution [CH_3CN-HEPES (0.02 M, pH 7.4) (4:1, v/v)] (excitation at 497 nm).

4-b: White sticky solid (833 mg, 1.40 mmol, 70%). ^{1}H NMR ($CDCl_3$): δ 4.88 (d, 8H, $J = 5.8$ Hz), 6.94 (d, 2H, $J = 7.8$ Hz), 7.04–7.21 (m, 8H), 7.35 (dt, 2H, $J = 7.6$, 1.8 Hz), 7.53 (dt, 2H, $J = 7.6$, 1.8 Hz), 7.73 (d, 2H, $J = 8.7$ Hz), 8.41 (m, 2H), 8.47 (m, 2H), 9.93 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 51.7, 52.0, 120.9, 121.4, 121.6, 122.2, 139.2, 132.6, 135.9, 136.0, 148.7, 148.8, 156.7, 156.9, 157.2, 166.5, 170.1, 190.5; FAB-MS (*m/z*): 596.2 $(M + H)^+$.

5-b: White sticky solid (554 mg, 1.50 mmol, 75%). ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 6H), 2.64 (s, 8H), 3.80 (d, 8H, $J = 29$), 7.35 (d, 2H, $J = 8.5$ Hz), 8.22 (d, 2H, $J = 8.2$ Hz, 10.32 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 43.0, 45.6, 54.5, 122.3, 130.6, 132.9, 157.3, 165.6, 170.2, 190.9; FAB-MS (*m/z*): 398.2 $(M + H)^+$.

*General procedure for **3**, **4** and **5** (Scheme 2)*

To a stirred solution of pre-dried **3-b** (260.4 mg, 0.63 mmol), **4-b** (375.2 mg, 0.63 mmol) and **5-b** (238.4 mg, 0.63 mmol) and 2,4-dimethylpyrrole (126 mg, 1.32 mmol) in 30 ml of anhydrous THF was added a catalytic amount of trifluoroacetic acid under nitrogen at room temperature. After stirring of 20 h, a mixture of pre-dried 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (143 mg, 0.63 mmol) in 15 ml of anhydrous THF was added dropwise during 10 min and the solution was stirred further for 2 h at room temperature. The mixture was passed through an aluminium oxide column (~20 g) and further eluted by MC/MeOH (40:1) to get a dark brown solution. After concentration with aspirator, the residue was dried under vacuum overnight, which was then used directly for further step. Anhydrous THF (30 ml) and triethylamine (3.0 ml) were added consecutively to the flask containing the pre-dried crude product under nitrogen atmosphere at room temperature with stirring, followed by dropwise addition of boron trifluoride diethetate (3.0 ml) during 20 min. The mixture was stirred overnight, then passed through an Al_2O_3 column (~20 g) and rinsed with a mixture of MC/MeOH (50:1). After evaporation of the solvent, the residue was redissolved with MC (50 ml), washed sufficiently with 15% aqueous K_2CO_3 (3 × 100 ml) and water (80 ml) and dried over anhydrous sodium sulphate. The solvent was evaporated by water aspirator and the residue was first separated by flash chromatography on silica gel column (MC to MC/MeOH 40:1), followed by preparative TLC purification (MC/MeOH 40:1) for the brown yellow elution to afford products **3**, **4** and **5**.

3: Red sticky oil (74.1 mg, 0.11 mmol, 17.8%). ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 6H), 2.56 (s, 6H), 4.72 (d, 4H, $J = 2.1$ Hz), 5.99 (s, 2H), 6.40 (m, 1H), 6.95 (m, 8H), 7.27 (d, 2H, $J = 6.3$ Hz), 8.39 (s, 1H), 8.53 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 14.5, 40.9, 45.7, 121.2, 121.7, 122.3, 122.9, 128.7, 131.5, 136.7, 140.9, 142.9, 149.0, 152.9, 155.5, 157.3, 157.3, 157.9, 167.2; HR-MS (FAB) (*m/z*): 632.2876 $(M + H)^+$, calcd for $C_{34}H_{33}BF_2N_9O$ 632.2875.

4: Red sticky oil (101.1 mg, 0.12 mmol, 19.7%). ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 6H), 2.51 (s, 6H), 4.85 (s, 4H), 4.92 (s, 4H), 5.90 (s, 2H), 6.93 (d, 2H, $J = 3.8$ Hz), 7.09–7.24 (m, 10H), 7.34 (ddd, 2H, $J = 1.7$, 7.7 Hz), 7.57 (ddd, 2H, $J = 1.7$, 7.6 Hz), 8.40 (m, 2H), 8.48 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 14.2, 14.4, 51.8, 51.9, 121.2, 121.8, 122.1, 122.9, 128.5, 131.4, 136.2, 136.4, 140.9, 143.0, 149.1, 149.2, 152.9, 155.4, 157.4, 157.6, 167.1, 170.8; HR-MS (FAB) (*m/z*): 814.3723 $(M + H)^+$, calcd for $C_{46}H_{43}BF_2N_{11}O$ 814.3721.

5: Red sticky oil (0.155 mg, 0.25 mmol, 39.9%). ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 6H), 2.32 (s, 6H), 2.39 (s, 8H), 2.56 (s, 6H), 3.81 (m, 8H), 5.99 (s, 2H), 7.27 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 14.3, 30.9, 43.1, 46.1, 54.7, 121.2,123.2 128.7, 131.4, 141.1, 142.9, 153.3, 155.5, 165.8, 171.0; HR-MS (FAB) (*m/z*): 616.3512 $(M + H)^+$, calcd for $C_{32}H_{41}BF_2N_9O$ 616.3501.

11 (Scheme 3): A mixture of 4-hydroxybenzaldehyde (270 mg, 2.2 mmol) and 0.42 ml of DIEA (2.4 mmol) in 10 ml of methylene chloride was added at room temperature to the above-mentioned intermediate solution. After stirring for 2 h at the same temperature (monitored by TLC, ethyl acetate:hexane 1:4), the mixture was passed through a silica gel column (~20 g) and rinsed with a mixture of ethyl acetate (100 ml) and hexane (50 ml). The elution was concentrated under vacuum and the crude product was purified by flash chromatography (ethyl acetate:hexane 1:3 to 1:1) to afford product **11** as a white solid (590 mg, 1.66 mmol, 83%). ^{1}H NMR ($CDCl_3$): δ 7.37–7.27 (m, 4H), 8.00–7.89 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 122.3, 122.4, 131.5, 131.6, 134.6, 134.8, 155.6, 155.9, 172.1, 173.4, 174.3, 190.8; FAB-MS (*m/z*): 356.0 $(M + H)^+$.

12 (Scheme 3): An aqueous solution of potassium carbonate (415 mg, 3 mmol) in 5 ml of water was added in several portions to a stirred solution of **11** (355 mg, 1.0 mmol) and DPA (410 mg, 2.0 mmol) in 30 ml of THF while refluxing. After stirring for 5 h, the solvent was evaporated and the residue was redissolved with chloroform (30 ml). The solution was washed with water (2 × 30 ml) and dried over anhydrous sodium sulphate. After concentration under vacuum, the crude product was purified by flash chromatography (ethyl acetate) to afford product **12** as a white sticky solid (373 mg, 0.72 mmol, 72%). ^{1}H NMR ($CDCl_3$): δ 4.86 (s, 4H), 6.92 (d, 2H, $J = 7.8$ Hz), 7.17 (m, 2H), 7.23 (m, 4H), 7.55 (t, 2H, $J = 5.8, 7.7$ Hz), 7.82 (dd, 4H, $J = 2.0, 6.7$ Hz), 8.49 (d, 2H, $J = 4.9$ Hz), 10.0 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 30.9, 52.6, 121.6, 122.0, 122.4, 122.5, 131.0, 131.2, 133.7, 136.6, 149.4, 156.3, 156.6, 167.8, 171.7, 190.8; FAB-MS (*m*/*z*): 519.1 $(M + H)^+$.

10 (Scheme 3): To a stirred solution of pre-dried **12** (241 mg, 0.46 mmol) and 2,4-dimethylpyrrole (189.5 mg, 1.90 mmol) in 30 ml of anhydrous methylene chloride was added a catalytic amount of trifluoroacetic acid under nitrogen at room temperature. After stirring of 20 h, a mixture of pre-dried 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in 20 ml of anhydrous MC was added dropwise during 30 min and the reactant solution was stirred further for 2 h at room temperature. The mixture was passed through an aluminium oxide column (~30 g) and further eluted by MC/MeOH (40:1) to get a dark brown solution. After concentration with aspirator, the crude oil was dried under vacuum overnight, which was then used directly for further step. Anhydrous MC (30 ml) and triethylamine (3.0 ml) were added consecutively to the flask containing the pre-dried crude product under nitrogen atmosphere at room temperature with stirring, followed by dropwise addition of boron trifluoride diethetate (3.0 ml) during 30 min. The mixture was stirred overnight, then passed through an Al_2O_3 column (~20 g) and rinsed with a mixture of MC/MeOH (40:1). After evaporation of the solvent, the crude product was redissolved with MC (50 ml), washed with 15% aqueous K_2CO_3 (3 × 100 ml) and water (100 ml) and dried over anhydrous sodium sulphate. The solvent was evaporated by water aspirator and the residue was first separated by flash chromatography on silica gel column (MC to MC/MeOH 40:1), followed by preparative TLC purification (MC/MeOH 50:1) for the brown yellow elution to afford product **10** as a red sticky solid (113.7 mg, 0.119 mmol, 25.9%). ^{1}H NMR ($CDCl_3$): δ 1.33 (s, 12H), 2.54 (s, 12H), 4.76 (s, 4H), 5.94 (s, 4H), 7.07 (d, 2H, $J = 7.8$ Hz), 7.17–7.29 (m, 10H), 7.57–7.68 (ddd, 2H, $J = 1.7$, 7.6 Hz), 8.48 (d, 2H, $J = 4.0$ Hz); ^{13}C NMR ($CDCl_3$): δ 14.4, 14.5, 30.9, 51.5, 121.3, 121.8, 122.5, 122.7, 129.0, 131.4, 132.1, 136.5, 140.6, 142.9, 149.4, 152.6, 155.6, 167.9, 172.3; HR-MS (FAB) (*m*/*z*): 955.4178 $(M + H)^+$, calcd for $C_{53}H_{49}B_2F_4N_{10}O_2$ 955.4179.

Preparation of fluorometric metal ion titration solutions

Stock solutions (1 mM) of the perchlorate salts of Ag^+, Ca^{2+}, Cd^{2+}, Co^{2+}, Cs^+, Cu^{2+}, Hg^{2+}, K^+, Li^+, Mg^{2+}, Mn^{2+}, Na^+, Ni^{2+}, Pb^{2+}, Rb^+ and Zn^{2+} in acetonitrile were prepared. Stock solution of host (0.1 mM) was also prepared in acetonitrile. Test solutions were prepared by placing 4–40 μL of the probe stock solution into a test tube, adding an appropriate aliquot of each metal stock and diluting the solution to 4 ml with acetonitrile.

For all measurements, excitation wavelength was 497 nm. Both excitation and emission slit widths were either 1.5 or 3 nm.

Fluorescence lifetime measurement

The fluorescence lifetimes were measured by the TCSPC system. The excitation source was a picosecond Nd:YAG laser (Picoquant PDL 800-B) that operates at the 467 nm wavelength at 20 MHz. The TCSPC electronics were from Becker-Hickl (SPC-830). The whole emission was collected via a confocal microscope set-up using dichroic and cut-off filters. The instrument response function was typically *ca.* 250 ps with a solid-state PMT. The decay curves were deconvoluted from the instrument function and fit to the sum of an exponential form $I(t) = \Sigma A_i \exp(-t/\tau_i)$. The average lifetime was defined as $\langle\tau\rangle = \Sigma A_i\tau_i (\Sigma A_i = 1)$. All decay curves exhibit double exponential except for sample 1 that appears to be single. The sample concentration was 5×10^{-5} M and five times higher concentration was used to observe the Hg ion effect.

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Note

1. Contributed equally to this work.

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