Supporting Information

A dual channel sulphur-containing macrocycle functionalised BODIPY probe for the detection of Hg(II) in mixed aqueous solution

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Materials and methods

4-Methoxybenzaldehyde (**I**), 2,4-dimethyl pyrrole (**II**), dry CH_2Cl_2 and dry toluene were purchased from Aldrich and Acros. All commercially available reagents and solvents were used as received. The precursors BODIPY **1b** [1], crown ether **III** [2] and **1a** [3] were synthesized using the experimental procedures reported before. Reaction progress was monitored by thin layer chromatography, 0.25 mm thick pre-coated silica plates (Merck Fertigplatten Kieselgel 60 F254), and spots were visualized under UV light. Purification was achieved by silica gel column chromatography (Merck Kieselgel, 230-400 mesh). NMR spectra were obtained on a Brucker Avance II 400 at an operating frequency of 400 MHz for ^{1}H and 100.6 MHz for ^{13}C, using the solvent peak as internal reference. The solvents are indicated in parenthesis before the chemical shifts values (δ relative to TMS). Peak assignments were made by comparison of chemical shifts, peak multiplicities and *J* values, and were supported by spin decoupling-double resonance and bidimensional heteronuclear HMBC (heteronuclear multiple bond coherence) and HMQC (heteronuclear multiple quantum coherence) techniques. Melting points were determined on a Gallenkamp apparatus and are uncorrected. Infrared spectra were recorded on a BOMEM MB 104 spectrophotometer.

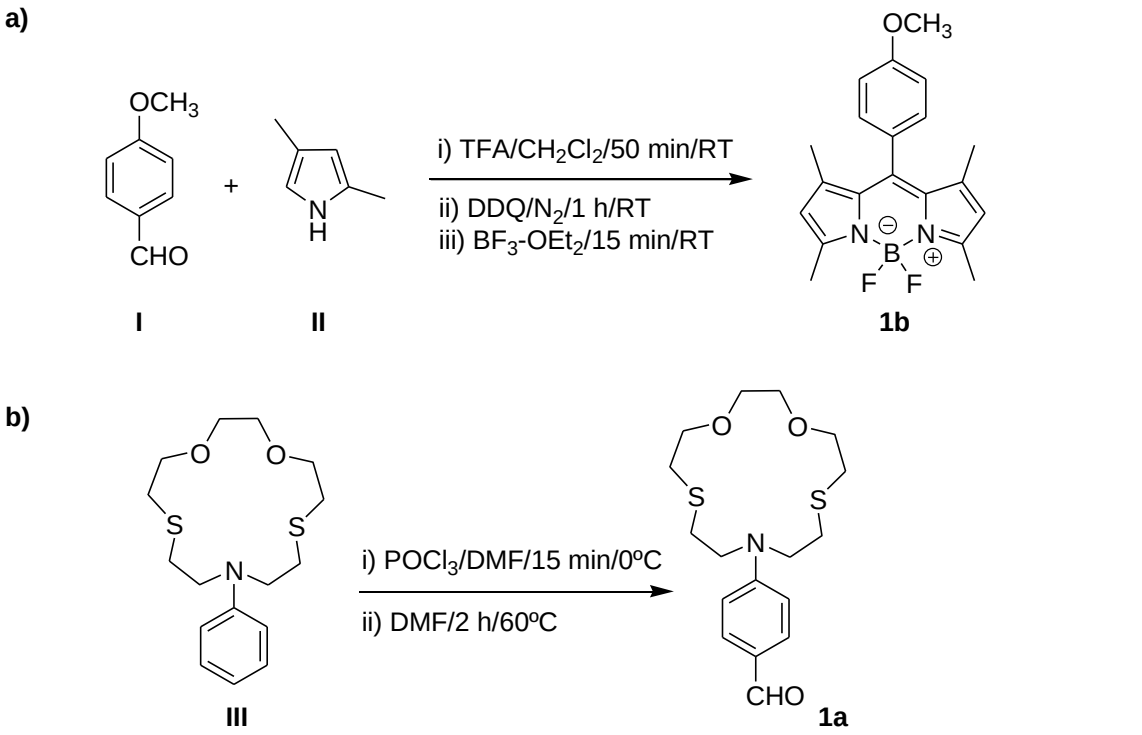
Synthesis of BODIPY derivatives 1b and 1

The precursor BODIPY derivative **1b** was synthesized through reaction of 4-methoxybenzaldehyde (**I**) and 2,4-dimethyl pyrrole (**II**) in the presence of a catalytical amount of TFA, followed by oxidation with DDQ and treatment with BF_3-OEt_2 in 33 % yield. Earlier the synthesis of compound **1b** was reported in in 38 % yield by Boens *et al* [1]. On the other hand, the precursor crown ether **III** was prepared by the Richman-Atkins reaction using the synthetic procedure described by some of us [2], in which the mesylated *N,N´*-phenylethanolamine was initially synthesized by reaction of *N,N'*-phenylethanolamine with methanesulfonyl chloride in 96 % yield. In a second step, the mesylated precursor obtained above reacted with the 3,6-dioxaoctane-1,8-dithiol, yielding the crown ether **III** as a colorless solid in 40 % yield. Vilsmeier formylation of compound **III** with $POCl_3$ in DMF gave the formylated crown ether **1a** [3], in 80 % yield (see Scheme S1).

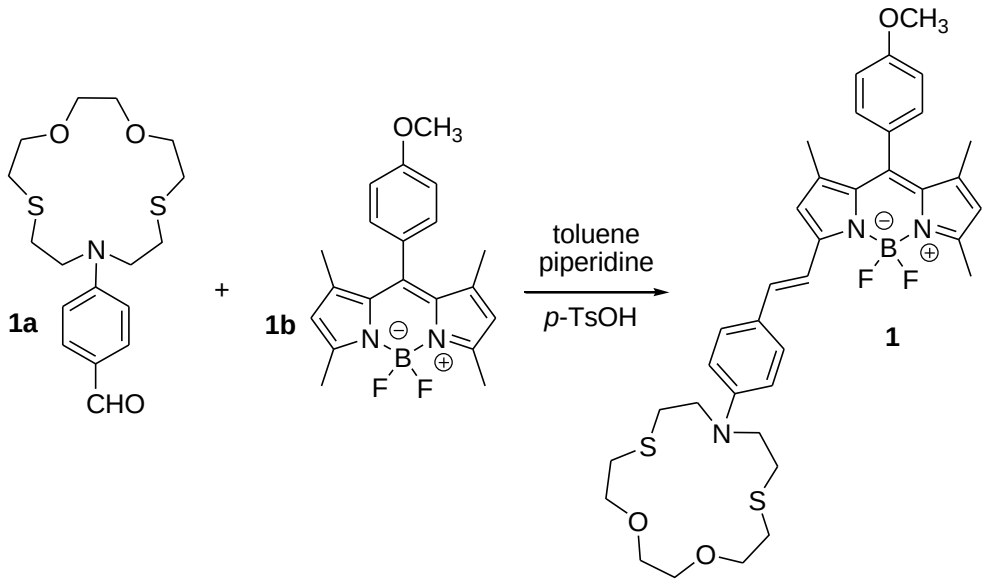
The target BODIPY **1** was prepared by a condensation reaction of **1b** and crown ether **1a**, in toluene, at reflux, under a N_2 atmosphere using piperidine-*p*-toluenesulfonic acid as catalyst (see Scheme S2).

Purification of the crude product **1** by preliminary dry flash chromatography followed by column chromatography on silica, both using ethyl acetate/petroleum ether (1:2) as eluent afford the pure compound as a blue greenish solid in 30% yield. The new BODIPY derivative **1** was completely characterized by the usual spectroscopic techniques.

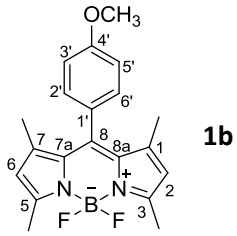
The most characteristic signals in the ^{1}H NMR spectra for compound **1** were those corresponding to the BODIPY nucleus such as the singlets assigned to H-2 and H-6 at 5.97 and 6.59 ppm respectively, and the singlet at 3.88 ppm assigned to the OCH_3 group in 4´ position. Functionalization of the BODIPY **1b** with the crown ether moiety in order to obtained compound **1** can be also confirmed by ^{1}H NMR. Therefore it was observed the substitution of two singlets at 1.44 ppm (s, 6H, CH_3-1 and CH_3-7) and 2.56 ppm (s, 6H, CH_3-3 and CH_3-5) in the ^{1}H NMR spectra of **1b** by three singlets at 1.44, 1.48 and 2.59 ppm assigned to the *N,N*-dimethylamino groups in positions 1, 7 and 3 respectively. Additionally, five new signals at 2.78 ppm (t, *J* = 5.2 Hz, 4H, S-CH_2-CH_2-O), 2.92 ppm (t, *J* = 7.6 Hz, 4H, N-CH_2-CH_2-O), 3.66 ppm (s, 4H, O-$(CH_2)_2$-O), 3.69 ppm (t, *J* = 7.6 Hz, 4H, N-CH_2-CH_2-O) and 3.82 ppm (t, *J* = 5.2 Hz, 4H, S-CH_2-CH_2-O), assigned to the protons of the crown ether moiety were also observed in the ^{1}H NMR spectra of **1**.



Scheme S1. (a) Synthesis of BODIPY **1b** and **(b)** crown ether **1a**.

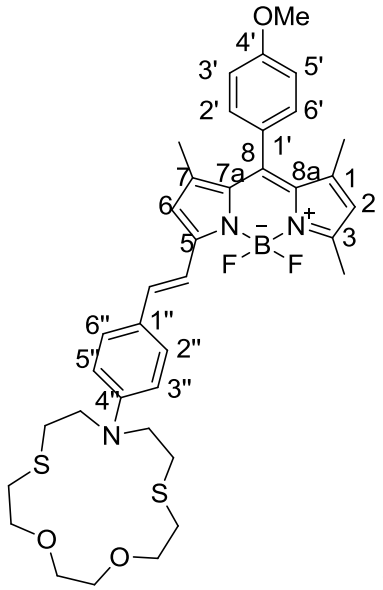


Scheme S2. Synthesis of BODIPY derivative **1**.



1b

*Synthesis of BODIPY **1b***: 2,4-Dimethyl pyrrole (**II**, 559 mg, 5.80 mmol) and 4-methoxybenzaldehyde (**I**, 400 mg, 2.9 mmol) were dissolved in anhydrous dichloromethane (990 mL). One drop of trifluoracetic acid was added in catalytic amount and the mixture was allowed to stir for 50 min at room temperature under N_2 atmosphere. A solution of DDQ (2.62 g, 7.6 mmol) in dichloromethane (50 mL) was added to the mixture. Stirring was continued for another 45 min and then triethylamine (13.3 mL, 95.2 mmol) was added. After stirring for 15 min $BF_3.OEt_2$ (13.3 mL, 161.1 mmol) was added and further stirred for 30 min. The mixture was evaporated under reduced pressure and the crude residue was subjected to a preliminary dry flash chromatography (petroleum ether/ethyl acetate, 4:1), followed by column chromatography on silica gel (petroleum ether/ethyl acetate, 4:1). The compound was obtained as reddish solid (337 mg, 33 %). Mp = 221–223 ºC (lit.[1] 214-216 ^{o}C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 6H, CH_3-1 and CH_3-7), 2.56 (s, 6H, CH_3-3 and CH_3-5), 3.88 (s, 3H, OCH_3), 5.98 (s, 2H, H-2 and H-6), 7.02 (dd, *J* = 7.2 and 2.4 Hz, 2H, H-3'and H-5'), 7.17 (dd, *J* = 7.2 and 2 Hz, 2H, H-2' and H-6') ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.5 (CH_3-1, CH_3-3, CH_3-5 and CH_3-7), 55.3 (OCH_3), 114.5 (C-3' and C-5'), 121.0 (C-2 and C-6), 126.9 (C-1'), 129.2 (C-2' and C-6'), 131.8 (C-7a and C-8a), 141.8 (C-8), 143.1 (C-1 and C-7), 155.2 (C-3 and C-5), 160.1 (C-4') ppm.



1

*Synthesis of BODIPY **1***: The previously prepared BODIPY **1b** (50 mg, 0.14 mmol) was reacted with the formylated crown ether **1a** (50 mg, 0.14 mmol) in dry toluene (10 mL) in a round bottomed flask fitted with a Dean-Stark and a condenser, in the presence of piperidine (0.12 mL, 1.21 mmol) and a trace amount of *p*-toluenesulfonic acid. The reaction mixture was heated at reflux under nitrogen inert atmosphere for 2 h. After cooling, the mixture was transferred to a separation funnel and washed with water (10 mL). The organic phase was dried with anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude residue was subjected to a preliminary dry flash chromatography followed by column chromatography on silica, both using ethyl acetate/petroleum ether (1:2) as eluent. The product was obtained as a blue greenish solid (45 mg, 30 %). Mp = 211–213 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 3H, CH_3-1), 1.48 (s, 3H, CH_3-7), 2.59 (s, 3H, CH_3-3), 2.78 (t, *J* = 5.2 Hz, 4H, S-CH_2-CH_2-O), 2.92 (t, *J* = 7.6 Hz, 4H, N-CH_2-CH_2-O), 3.66 (s, 4H, O-$(CH_2)_2$-O), 3.69 (t, *J* = 7.6 Hz, 4H, N-CH_2-CH_2-O), 3.82 (t, *J* = 5.2 Hz, 4H, S-CH_2-CH_2-O), 3.88 (s, 3H, OCH_3), 5.97 (s, 1H, H-2), 6.59 (s, 1H, H-6), 6.63 (d, *J* = 8.8 Hz, 2H, H-3'' and H-5''), 7.01 (dd, *J* = 8.8 Hz, 2H, H-3' and H-5'), 7.17–7.21 (m, 3H, Hβ, H-2'and H-6'), 7.47–7.51 (m, 3H, Hα, H-2''and H-6'') ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.4 (CH_3-1), 14.6 (CH_3-3), 14.9 (CH_3-7), 29.6 (N-CH_2-CH_2-O), 31.3 (S-CH_2-CH_2-O), 51.9 (N-CH_2-CH_2-O), 55.3 (OCH_3), 70.7 (O-$(CH_2)_2$O), 74.3 (S-CH_2-CH_2-O), 111.8 (C-3'' and C-5''), 114.4 (C-3' and C-5'), 114.6 (Cα), 117.5 (C-6), 120.4 (C-2), 124.8 (C-1''), 127.4 (C-1'), 129.5 (C-2' and C-6'), 129.6 (C-2'' and C-6''), 131.6 (C-8a), 133.4 (C-7a), 137.2 (Cβ), 139.0 (C-8), 140.9 (C-1), 142.8 (C-7), 147.7 (C-4''), 152.9 (C-3), 154.5 (C-5), 160.0 (C-4') ppm. IR (liquid film): υ 2922, 2856, 1737, 1591, 1539, 1520, 1501, 1467, 1413, 1353, 1295, 1247, 1200, 1177, 1119, 1076, 1030, 985, 813 cm^{-1}. HRMS-EI m/z: calcd for $C_{37}H_{44}BF_2N_3O_3S_2$ + H^+: 692.2963; measured: 692.2958.

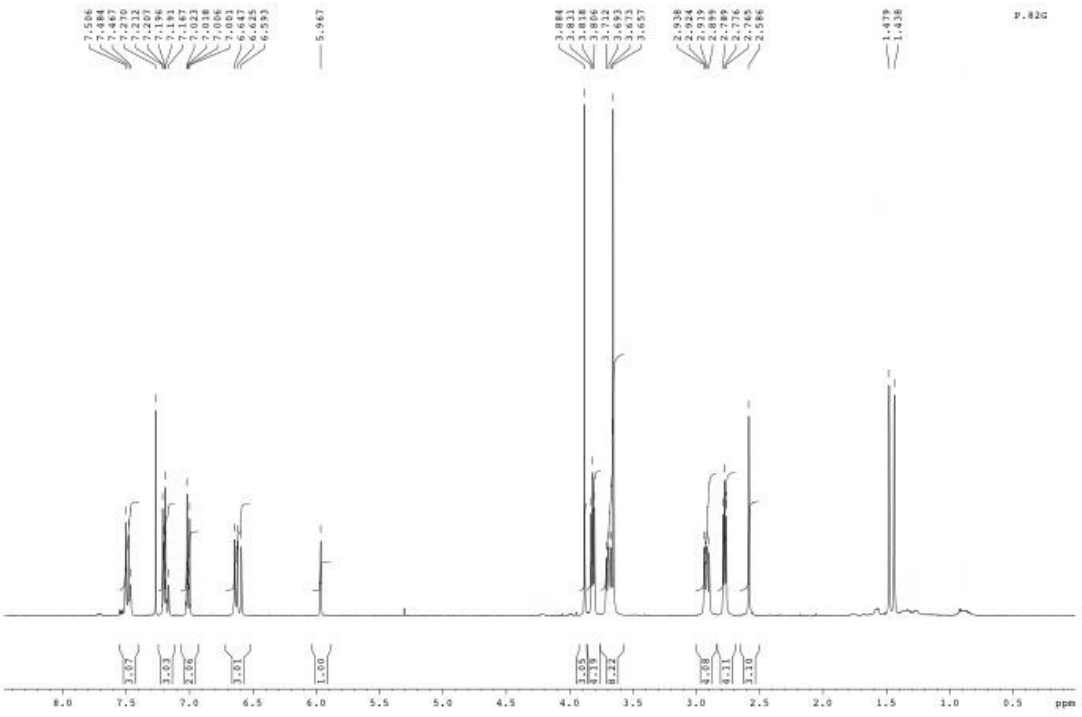


Figure S1. ^{1}H NMR spectrum of probe **1** in $CDCl_3$.

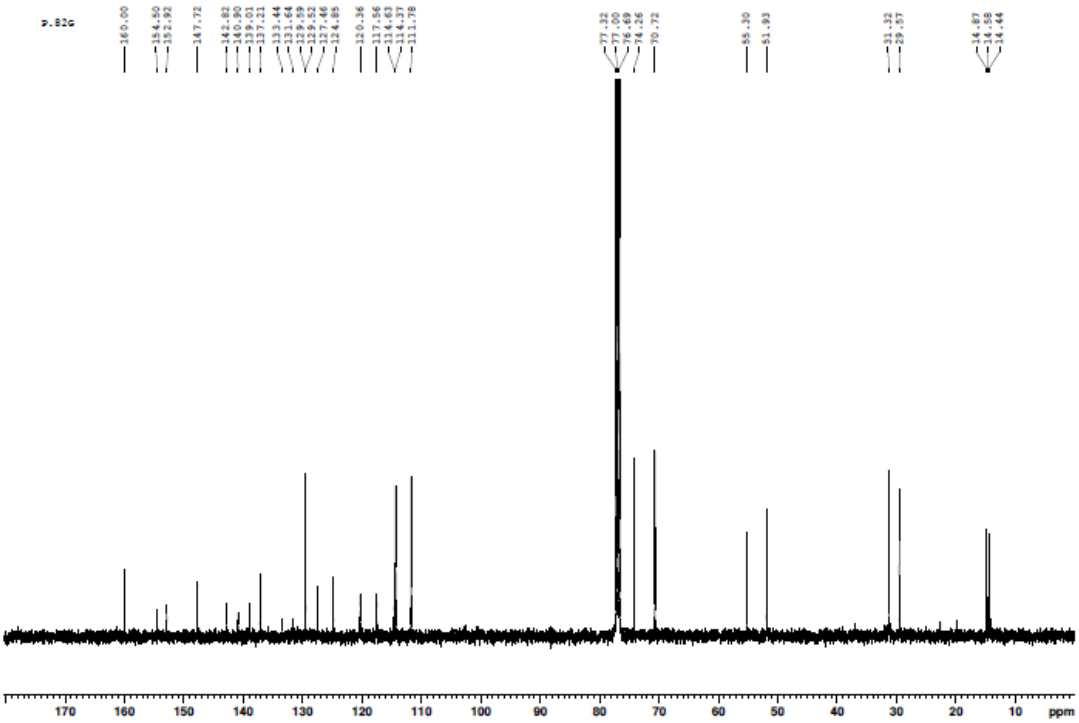


Figure S2. ^{13}C NMR spectrum of probe **1** in $CDCl_3$.

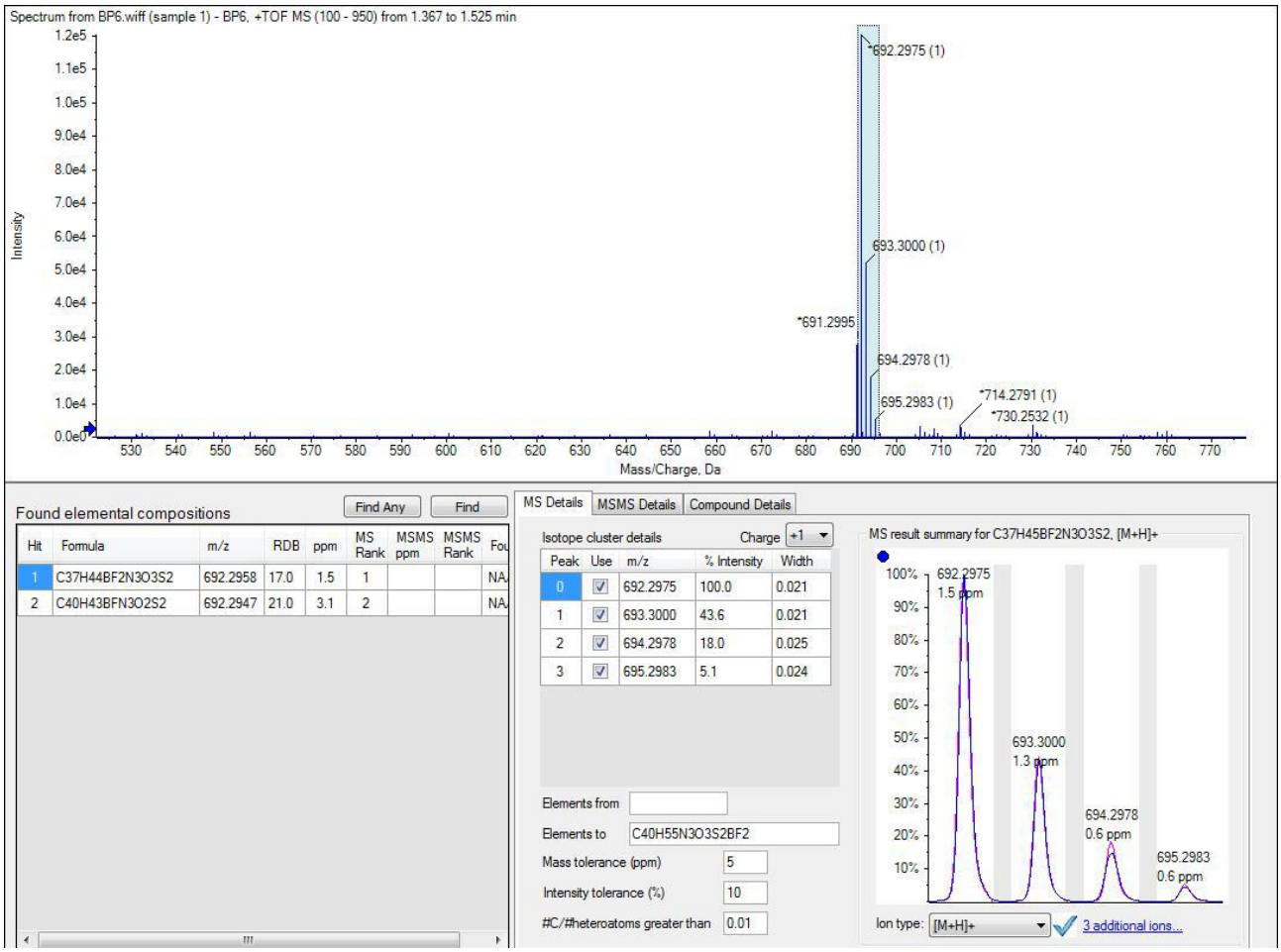


Figure S3. HRMS of probe **1**.

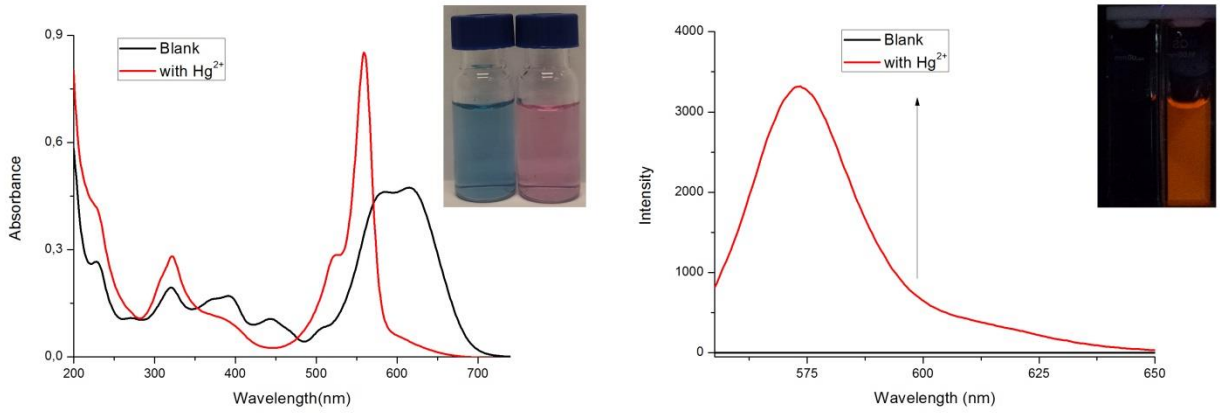


Figure S4. UV-visible and fluorescence spectra of **1** (5.0 x 10^{-5} mol L^{-1}) in water-acetonitrile 95:5 v/v solution at pH 7.0 upon addition of Hg(II) (20 eq.).

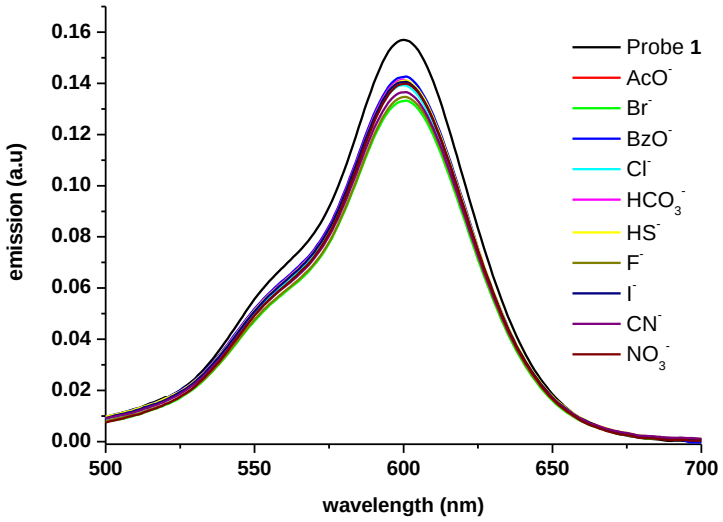


Figure S5. Fluorescence spectra of **1** (5.0 x 10^{-5} mol L^{-1}) in water-acetonitrile 95:5 v/v solution at pH 7.0 upon addition of selected anions (10 eq.).

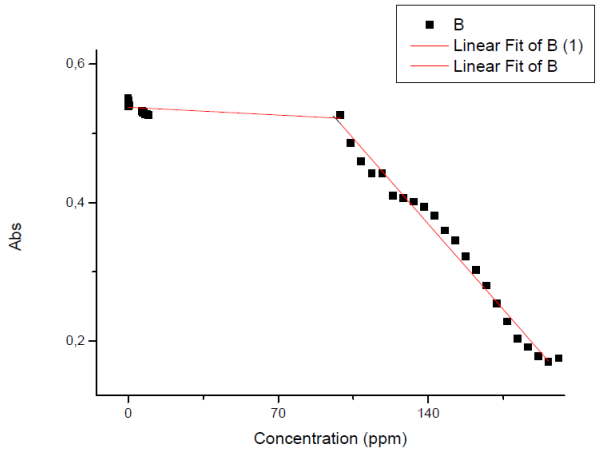


Figure S6. Calibration curve for probe **1** (5.0 x 10^{-5} mol L^{-1}) in water-acetonitrile 95:5 v/v solution at pH 7.0 upon addition of increasing concentrations of Hg(II).

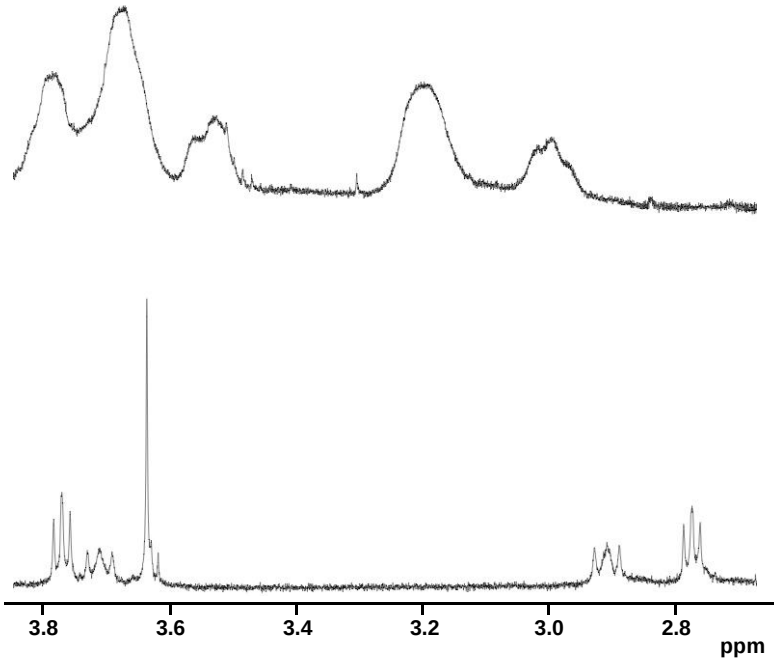


Figure S7. ^{1}H NMR fragment of probe **1** (deuterated acetonitrile) showing the macrocycle signals in the absence (down) and in the presence (up) of Hg(II) cation (1 eq).

References

[1] M. Baruah, W. Qin, C. Flors, J. Hofkens, R. A. L. Valle, D. Beljonne, M. Van der Auweraer, W. M. De Borggraeve, N. Boens, *J. Phys. Chem. A* **2006**, *110*, 5998.

[2] A. B. Descalzo, R. Martínez-Máñez, R. Radeglia, K. Rurack, J. Soto, *J. Am. Chem. Soc.* **2003**, *125*, 3418.

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