Electronic Supplementary Information

BODIPY-based probes for trivalent cations detection in aqueous environments

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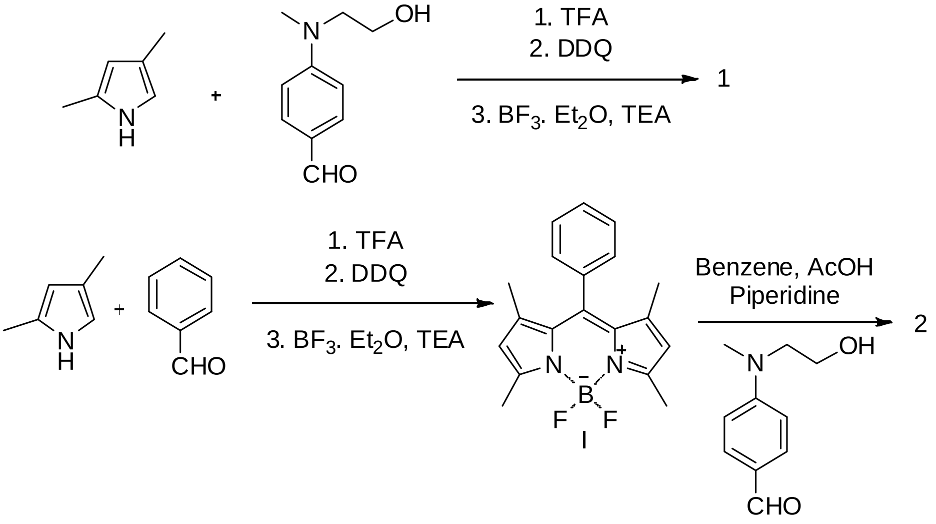


Scheme S-1. Synthetic routes for BODIPY dyes **1** and **2**.

Experimental section

General remarks

CH_2Cl_2 and CH_3CN were distilled from P_2O_5 under Ar prior to use. Benzene was distlled from CaH_2 under Ar proir to use. All other solvents and starting materials were purchased from comercial sources when available, and were used without purification. Colum chromatography was performed on silica gel. ^{1}H NMR, ^{13}C NMR (300 MHz) spectra were determined on a Bruker AV 300 spectrometrer. Chemical shifts are reported in parts per million (ppm), calibrated to the solvent peak set.

Synthesis and characterization of BODIPY derivatives.

4,4-difluoro-8-(4-((2-hydroxyethyl)(methyl)amino)phenyl)-1,3,5,7-tetramethyl -4-bora-3a,4a-diaza-s-indacene. (**1**)
2,4-Dimethylpirrole (2,2 mL; 21,3 mmol) and *N*-methyl-*N*-(2-hydroxyethyl)-4-aminobenzaldehyde (1,90 g; 10,65 mmol) were dissolved in 80 mL of CH_2Cl_2. Trifluoroacetic acid (82 µL; 1,06 mmol) was added, and the solution was stirred at room temperature for 50 min. A solution of DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone, 2,61g; 10,65 mmol) in CH_2Cl_2 (15 mL) was added. Stirring was continued for 50 min, followed by the addition of 20 mL of triethylamine. After stirring for 30 min, $BF_3.OEt_2$ (29 mL) was added. The mixture was stirred for 75 min at rt. After the evaporation of the solvents under reduced pressure, the crude product was purified by silica gel column chromatography with AcOEt/Hexane (2:1) to give the compound **1** as red crystals in 36% yield (1.528 g). ^{1}H NMR (300 MHz, DMSO) δ 7.10 – 7.01 (m, 2H), 6.84 (t, *J* = 5.8 Hz, 2H), 6.15 (s, 2H), 4.73 (t, *J* = 5.3 Hz, 1H), 3.58 (q, *J* = 5.8 Hz, 2H), 3.44 (t, *J* = 6.0 Hz, 2H), 2.98 (s, 3H), 2.43 (s, 6H), 1.45 (d, *J* = 8.5 Hz, 6H).^{13}C NMR (75 MHz, DMSO) δ 154.41 , 149.96 , 143.04 , 128.88 , 120.95 ,112.08, 58.38, 54.54, 41.43, 38.97, 14.64 HRMS (EI): m/z (%) calc for $C_{22}H_{26}BF_2N_3O$: 398.2107 $[M+1]^+$found: 398.2225. UV-Vis (CH_3CN) λ_{max} 496.5 nm.

4, 4-difluoro-1,3,5,7-tetramethyl-8-phenyl-4-bora-3a, 4a-diaza-s-indacene. (**I**)
2, 4-Dimethylpirrole (1 mL; 10 mmol) and benzaldehyde (0.5 mL; 5 mmol) were dissolved in 50 mL of CH_2Cl_2. Trifluoroacetic acid (39 µL; 0.5 mmol) was added, and the solution was stirred at room temperature for 50 min. A solution of DDQ (1.2 g; 5 mmol) in CH_2Cl_2 was added. Stirring was continued for 50 min, followed by the addition of 10 mL of triethylamine. After stirring for 30 min, $BF_3{\cdot}OEt_2$ (10 mL) was added. The mixture was stirred for 45 min at room temperature. After the evaporation of solvents under reduced pressure, the crude product was purified by silica gel column chromatography with AcOEt/Hexane (1:2) to give the compound **I** as green crystals in 40 % yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, *J* = 1.8 Hz, 1H), 7.47 (t, *J* = 2.4 Hz, 2H), 7.30 – 7.26 (m, 2H), 5.98 (s, 2H), 2.56 (s, 6H), 1.37 (s, 6H). UV-Vis (CH_3CN) λ_{max} 507 nm; emission (CH_3CN) λ_{max} 516 nm.

(E)-4,4-difluoro-5-(4-((2-hydroxyethyl)(methyl)amino)styryl)-1,3,7-trimethyl-8-phenyl-4-bora-3a,4a-diaza-s-indacene.(**2**)
Compound **I** (600 mg; 1.85 mmol) and *N*-methyl-*N*-(2-hydroxyethyl)-4-aminobenzaldehyde (330 mg; 1.85 mmol) were dissolved in a mixture of benzene (80 mL), acetic acid (5.3 mL) and piperidine (5.8 mL; 59.2 mmol). Any water formed during the reaction was removed azeotropically by heating in a Dean-Stark apparatus for 3 h. The reaction mixture was concentrated under reduced pressure and then subjected to silica gel column chromatography with AcOEt/Hexane (2:1) to yield the desired product **2** as blue crystals in 43 % yield (387 mg). ^{1}H NMR (300 MHz, DMSO) δ 7.55(dd, *J* = 9 Hz, 3H), 7.47 (d, *J* = 16.4 Hz, 1H), 7.41 (d, *J* = 9 Hz, 2H), 7.38(dd, *J* = 7.0, 2.6 Hz, 2H), 7.22 (d, *J* = 16.3 Hz, 1H), 6.91 (s, 1H), 6.76 (d, *J* = 9.0 Hz, 2H), 6.11 (s, 1H), 4.75 (t, *J* = 5.3 Hz, 1H), 3.58-3.52 (m, 2H), 3.47 (d, *J* = 4.8Hz, 2H), 3.01 (s, 3H), 2.45 (s, 3H), 1.37 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 155.58 153.63 152.41,150.51, 150.37 , 143.29 , 141.86 ,140.44 ,139.44 , 138.73 , 138.28 , 137.75 , 134.37 , 132.51 ,132.37 , 130.54 ,130.05 ,129.77 ,129.50 , 129.08 , 128.18 , 123.11 ,

120.36 , 118.28 , 112.30 ,112.10 ,112.24 ,111.89 , 58.12 , 53.91 ,41.02 , 39.10 , 30.65 ,14.25 , 14.18 , 13.77 . HRMS (EI): m/z (%) calc for $C_{29}H_{30}BF_2N_3O$: 486.3824 $[M+1]^+$ found: 486.2541. UV-Vis (CH_3CN) λ_{max} 601 nm.

Spectroscopic Measurements.

Metal cations (Fe^{+3}, Fe^{+2} Cu^{+2}, Zn^{+2}, Cd^{+2}; Co^{+2}, Ni^{+2}, Li^+, Hg^{+2},Cr^{+3} ,Al^{+3}, Na^+, K^+, Ca^{2+}, Mg^{2+} and Ag^+) as nitrate or perchlorate salts were used to obtain solutions of concentration of 10^{-3}M in CH_3CN. Uv-Vis spectra were recorded using a Shimadzu UV-2600 spectrometer. Fluorescence spectra were recorded using a Varian Cary Eclipse fluorometer. Titrations were performed by adding aliquots of M^{+3}(10^{-3} M in CH_3CN) in a solution of ligand (**1** and **2**) (10^{-5} M) in water:CH_3CN (80:20 v/v for **1** and 40:60 v/v for **2**). The relative fluorescence quantum yields were obtained by comparing the area under the corrected emission spectrum of test sample with that of a solution of Fluorescein (0.1 M in NaOH ϕ= 0,85).[1]

Competition experiments.

Firstly, a solution of ligand (**1** or **2**) (10^{-5} M) in water:CH_3CN (80:20 v/v for **1** and 40:60 v/v for **2**) was mixed with 5 equivalents of various metal ions (Cu^{2+}, Zn^{2+}, Cd^{2+},Ru^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Li^+, Hg^{2+},Na^+, K^+, Ca^{2+}, Mg^{2+} and Ag^+) followed by adding 1 eq. of Al^{3+}, Fe^{3+} or Cr^{3+}. Even in presence of other metal ions, Al^{3+}, Fe^{3+} and Cr^{3+} ($Al^{3}$and Cr^{3+} with **2**) could still coordinate with the ligand and cause a strong response.

^{1}H NMR spectroscopic titrations.

A Bruker AV400 NMR spectrometer was used to measure the ^{1}H NMR shifts of the complexes. NMR titrations were performed by adding aliquots of Al^{+3}(10^{-1} M in CD_3CN) in to a solution of **1** (or **2**) (1, 26 x 10^{-2} M) in CD_3CN.

LOD determination.

To the corresponding receptor in water/acetonitrile (10^{-5}M) increasing amounts of the corresponding cation (in acetonitrile) were added. The Uv-vis and fluorescence spectra were recorded in 1-cm path length cells at 25 ºC (termostatted). Representation of absorbance/ fluorescence at the appropriate wavelength vs. concentration of cation allowed the detection limit to be calculated.

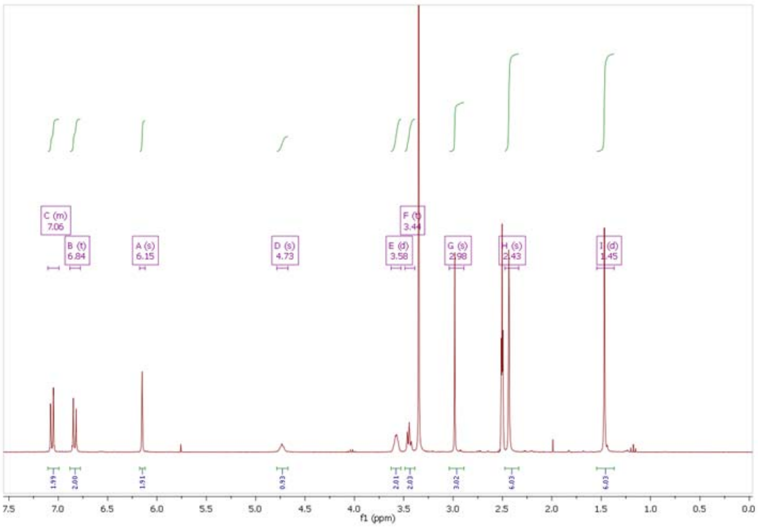


Figure S-1. ^{1}H NMR spectrum of compound **1** (DMSO)

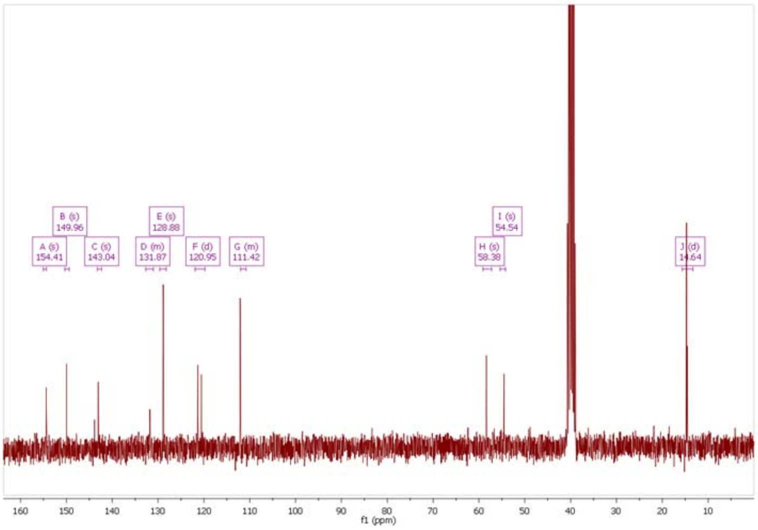


Figure S-2. ^{13}C NMR spectrum of compound **1** (DMSO)

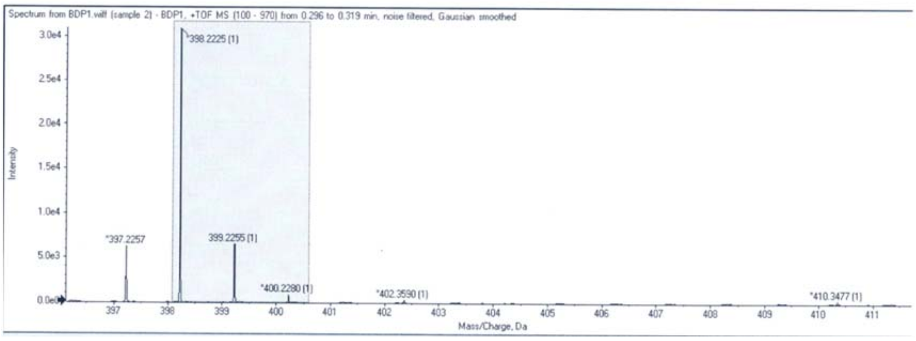


Figure S-3. MS of compound **1**

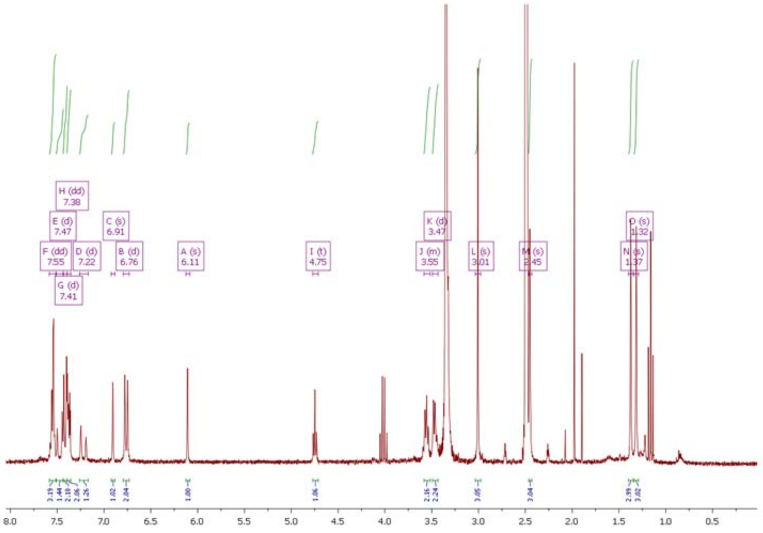


Figure S-4. ^{1}H NMR spectrum of compound **2** (DMSO)

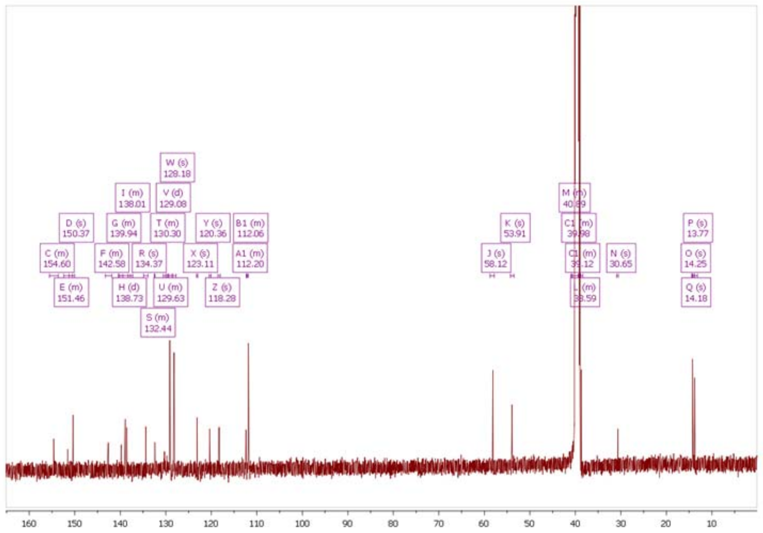


Figure S-5. ^{13}C NMR spectrum of compound **2** (DMSO)

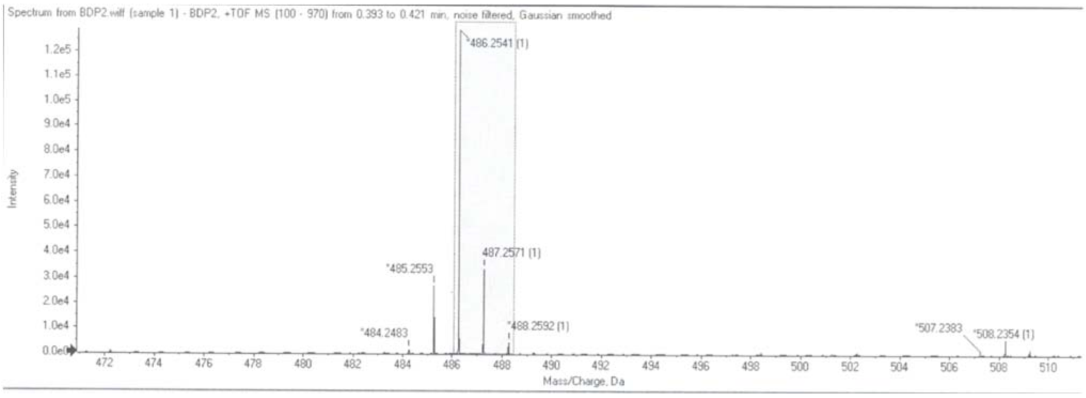


Figure S-6. MS of compound **2**

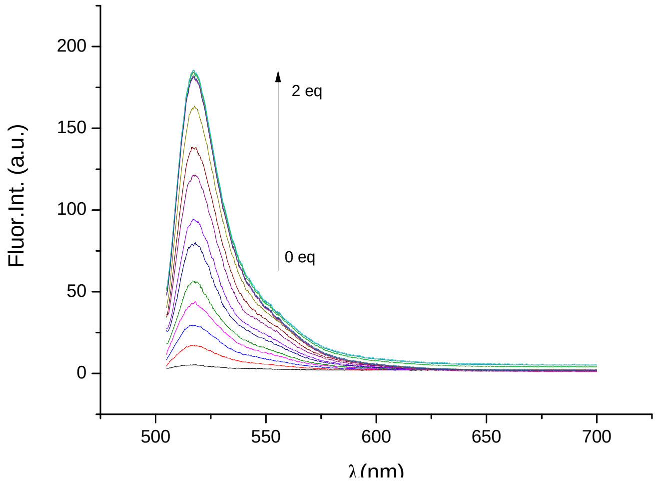


Figure S-7. Fluorescence titration (λ_{ex}= 480 nm) of **1** (10^{-5} M) with Fe^{3+} in water:CH_3CN (80:20 v/v).

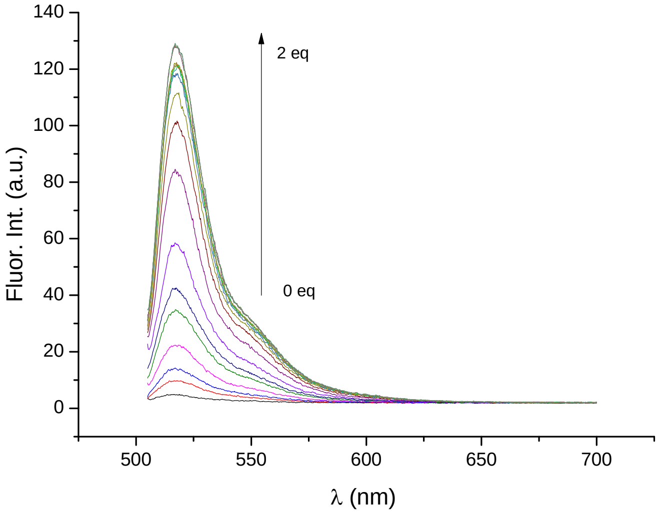


Figure S-8. Fluorescence titration (λ_{ex}= 480 nm) of **1**(10^{-5} M) with Cr^{3+} in water:CH_3CN (80:20 v/v).

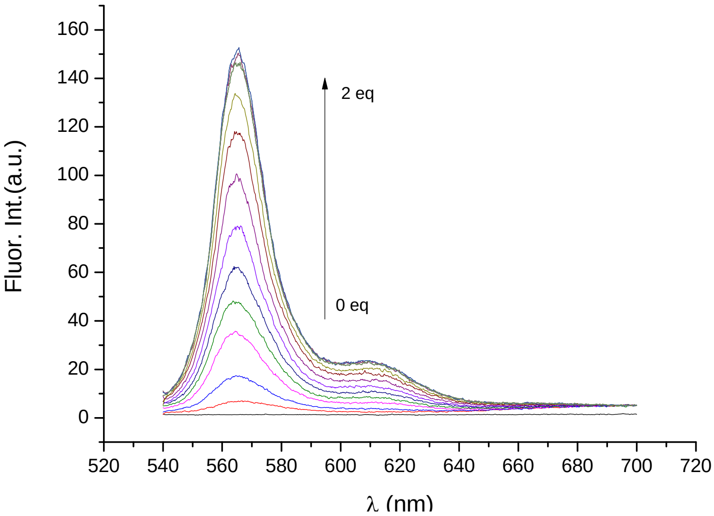


Figure S-9. Fluorescence titration (λ_{ex}= 530 nm) of **2** (10^{-5} M) with Cr^{3+} in water:CH_3CN (40:60 v/v).

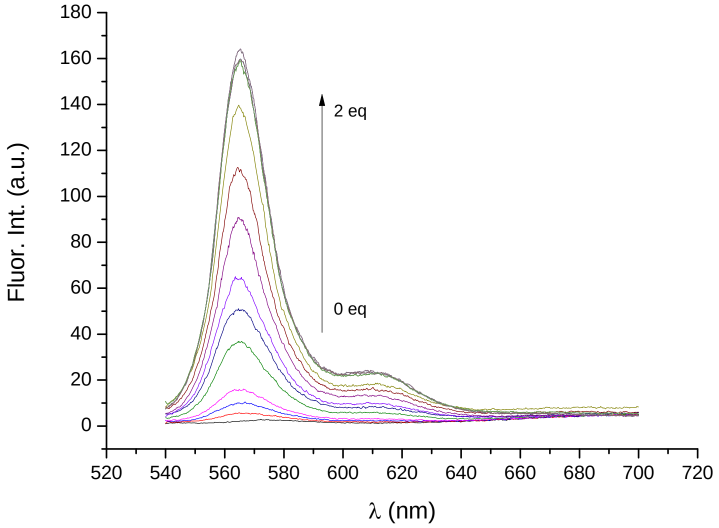


Figure S-10. Fluorescence titration (λ_{ex}= 530 nm) of **2** (10^{-5} M) with Al^{3+} in water:CH_3CN (40:60 v/v).

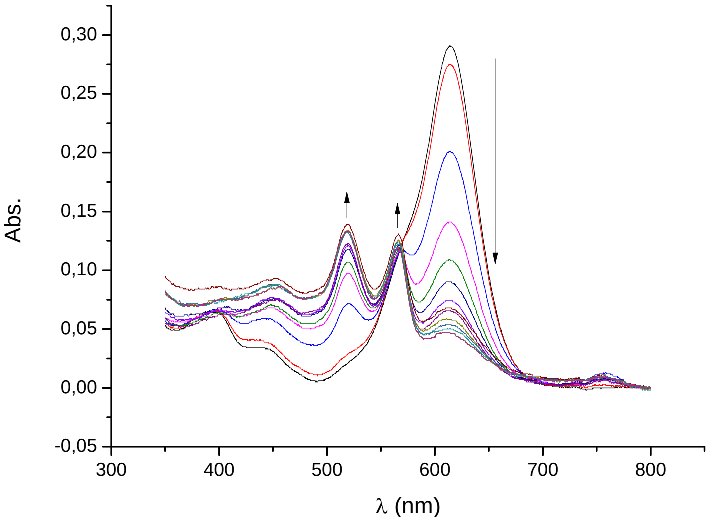


Figure S-11. UV titration of **2** (10^{-5} M) with Cr^{3+} in water:CH_3CN (40:60 v/v).

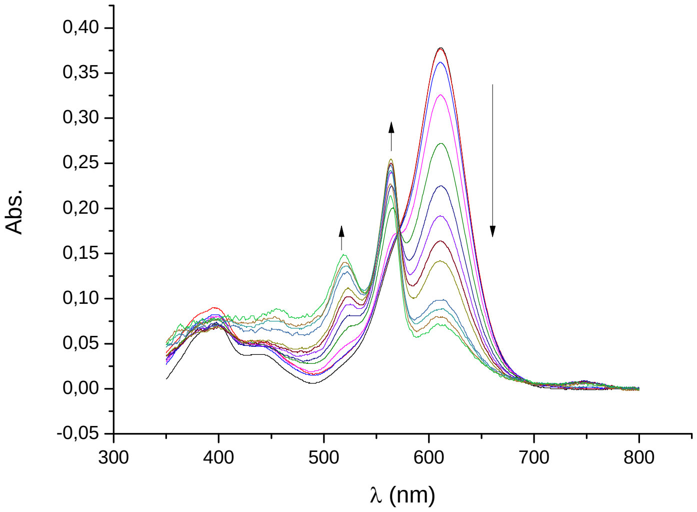


Figure S-12. UV titration of **2**(10^{-5} M) with Al^{3+} in water:CH_3CN (40:60 v/v).

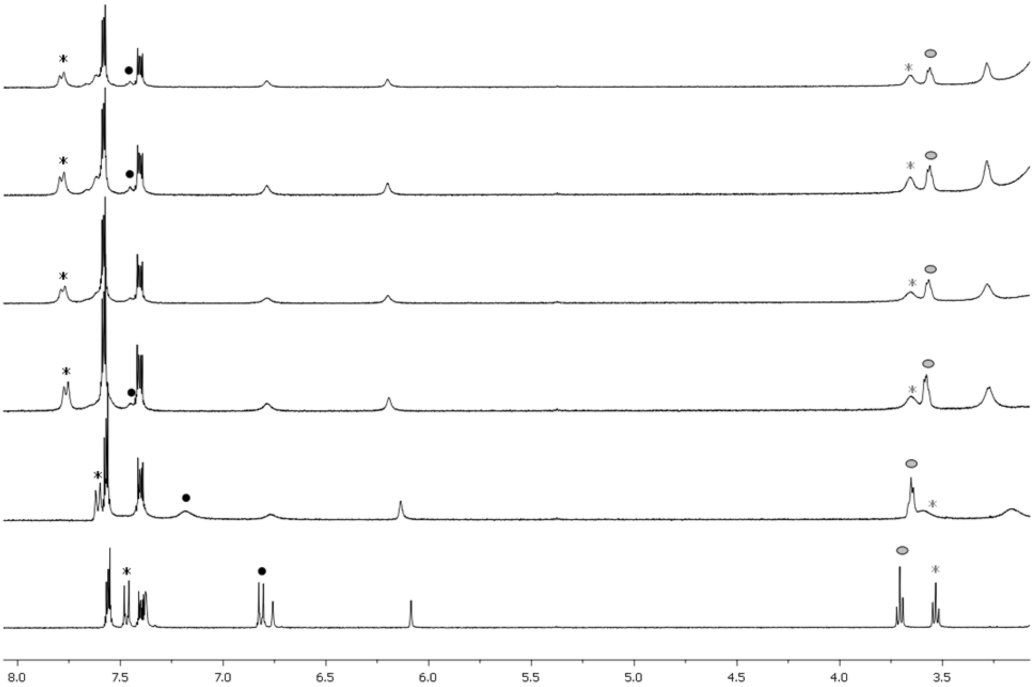


Figure S-13. ^{1}H NMR spectra of compound **2** alone and in the presence of increasing amounts of Al^{3+} in CD_3CN.

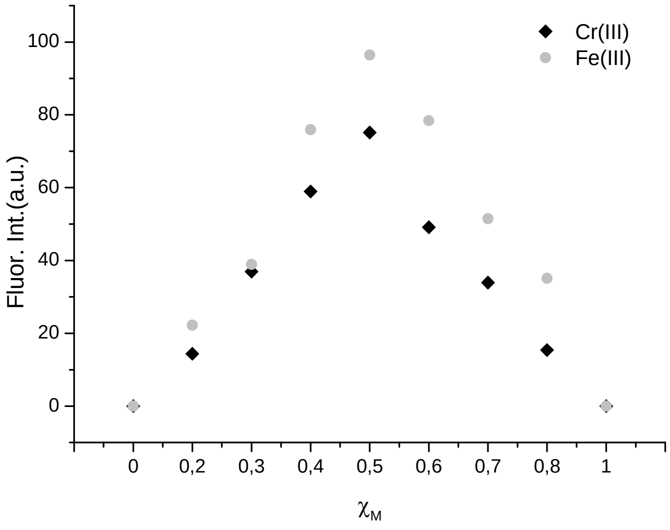


Figure S-14. Job´s Plot of **1** from fluorescence data.

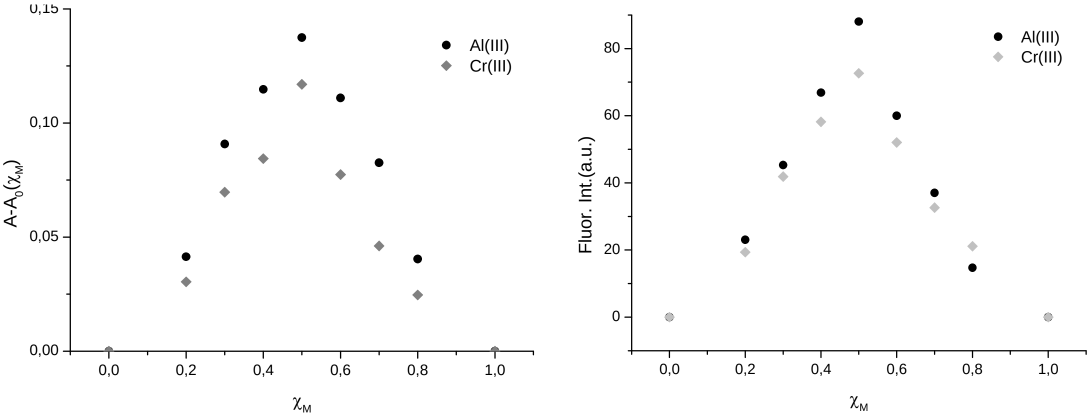
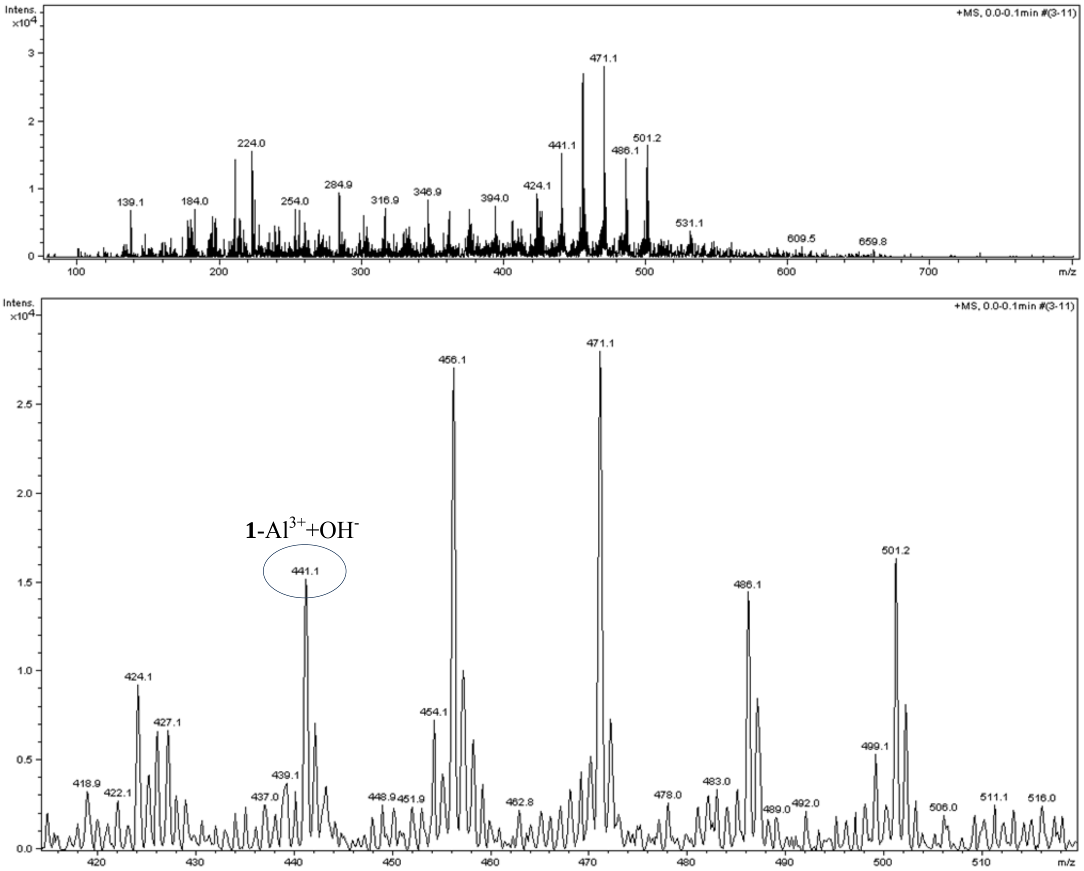
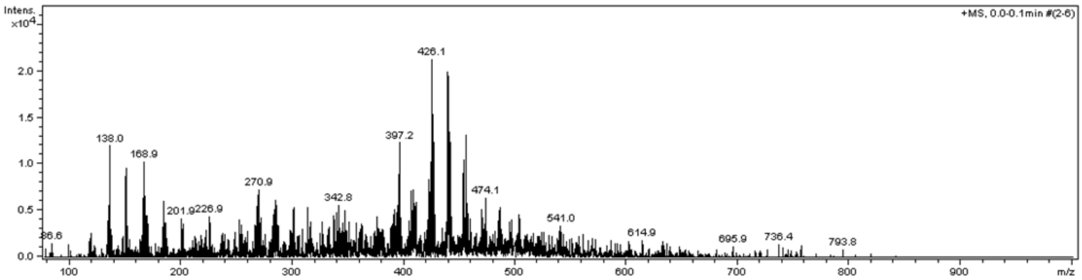


Figure S-15. Job´s Plot of **2** from Uv-Vis data (left) and fluorescence data (right)**.**

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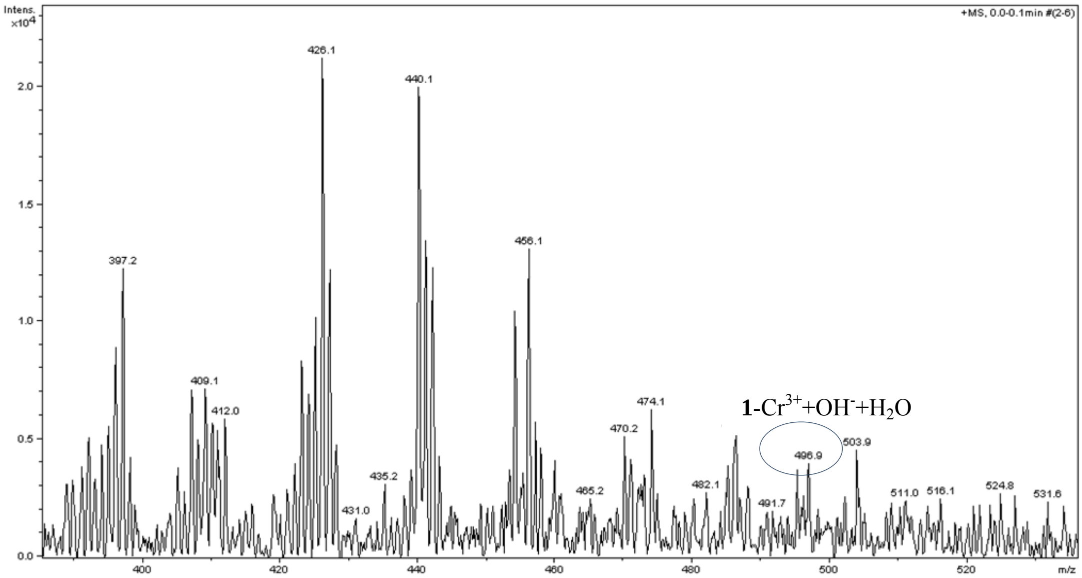
736.4
793.8
m/z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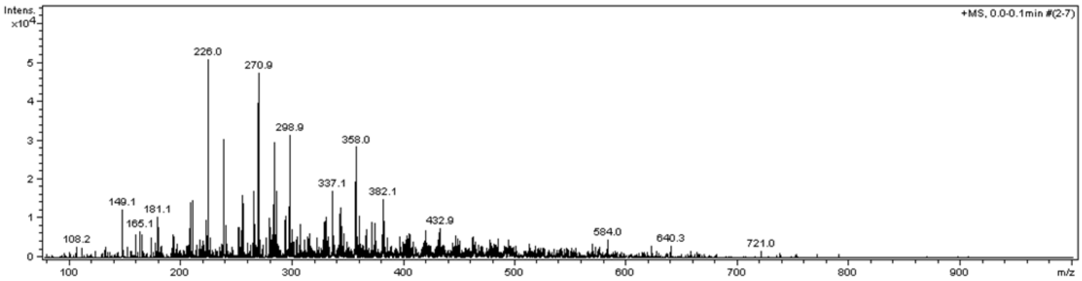
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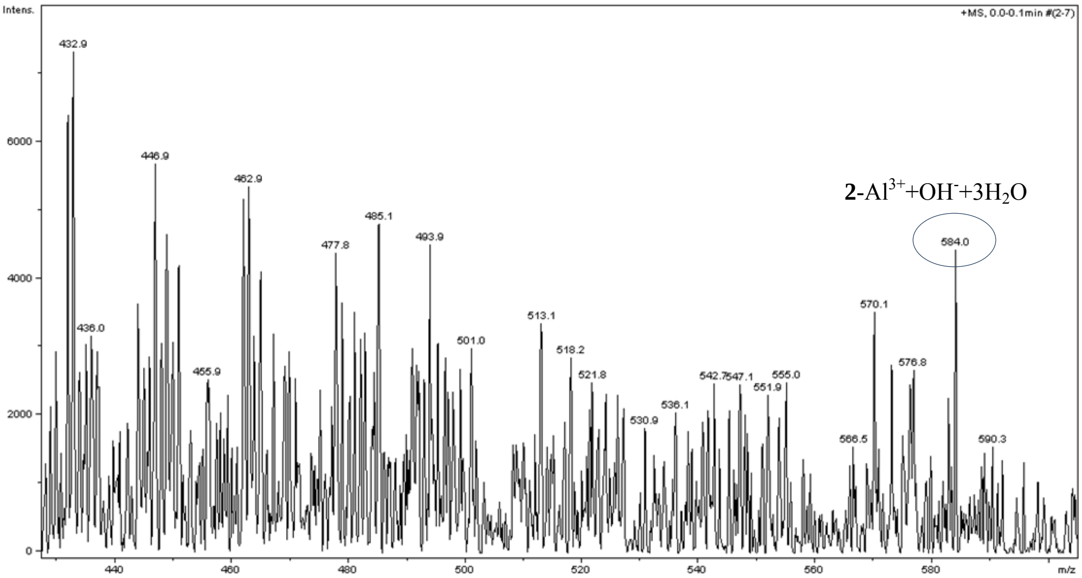
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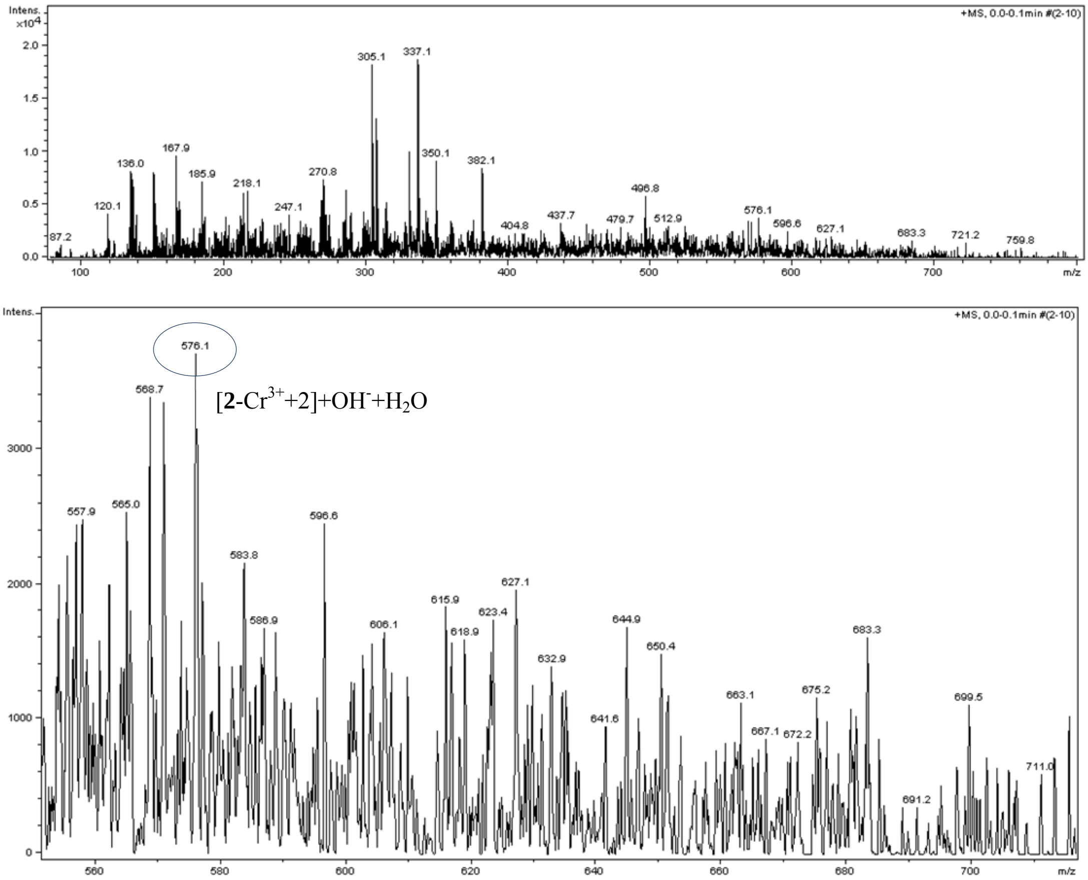


[**2**-Cr^{3+}+2]+OH^-+H_2O

Figure S-16. MS data of complexes formed with 1 and 2 and Al^{3+} and Cr^{3+} showing a 1:1 stoichiometry

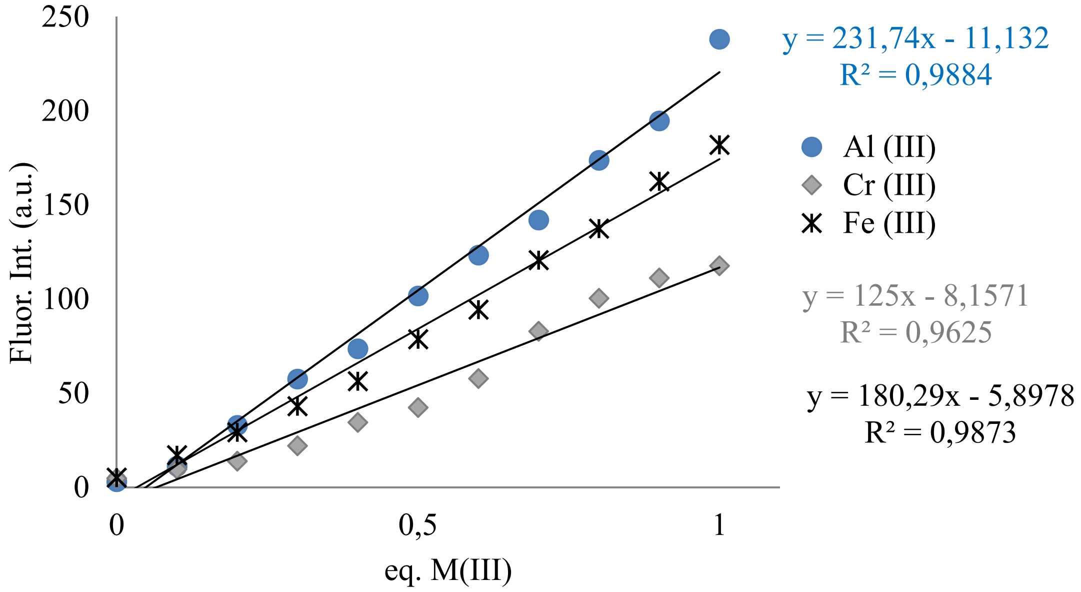


Figure S-17. A plot of **1** vs. cations concentration at 560 nm in CH_3CN:water (80:20 v/v).

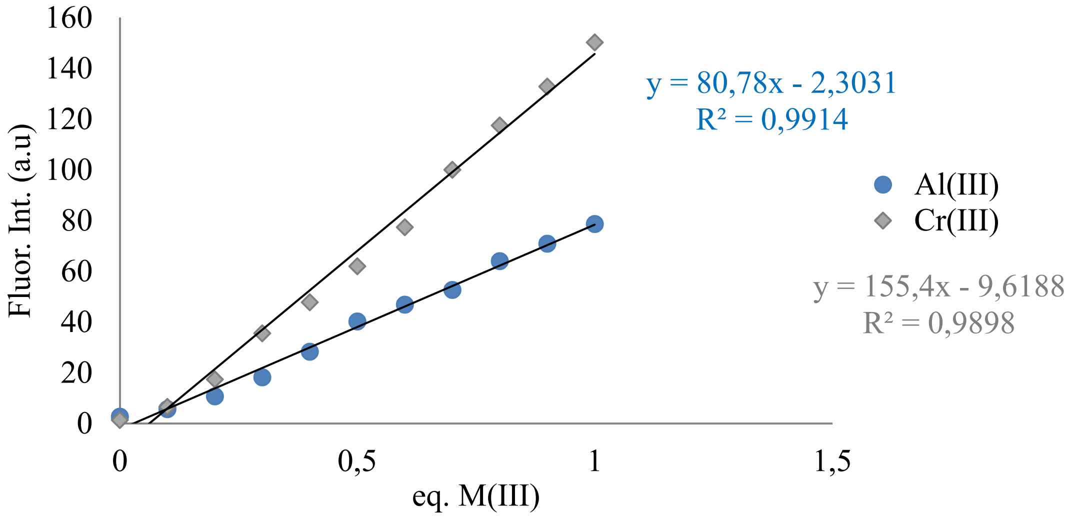


Figure S-18. A plot of **2** vs. cations concentration at 563 nm in CH_3CN:water (40:60 v/v).

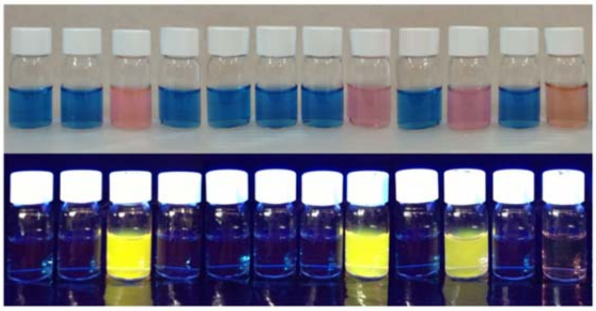


Figure S-19. Color change (top, under ambient light) and fluorescence response (bottom, irradiated with 254 nm by using a UV lamp) of acetonitrile solutions of 2 in the presence of different metal cations. (2, Hg^{2+}, Al^{3+}, Li^{+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Cr^{3+}, Fe^{2+}, Fe^{3+}, Co^{2+} and Cu^{2+}).

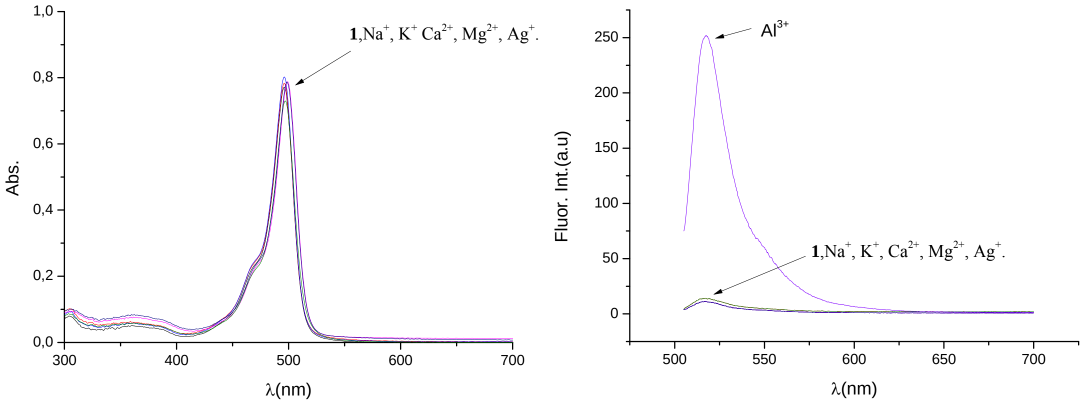


Figure S-20. UV-Vis spectra (a) and fluorescence emission spectra (λ_{ex} = 480 nm) (b) of **1** (10^{-5} M) upon addition of 10 eq of Na^{+}, K^{+}, Ca^{2+}, Mg^{2+}, Ag^{+} and 1 eq of Al^{3+} in water:CH_3CN (80:20 v/v).

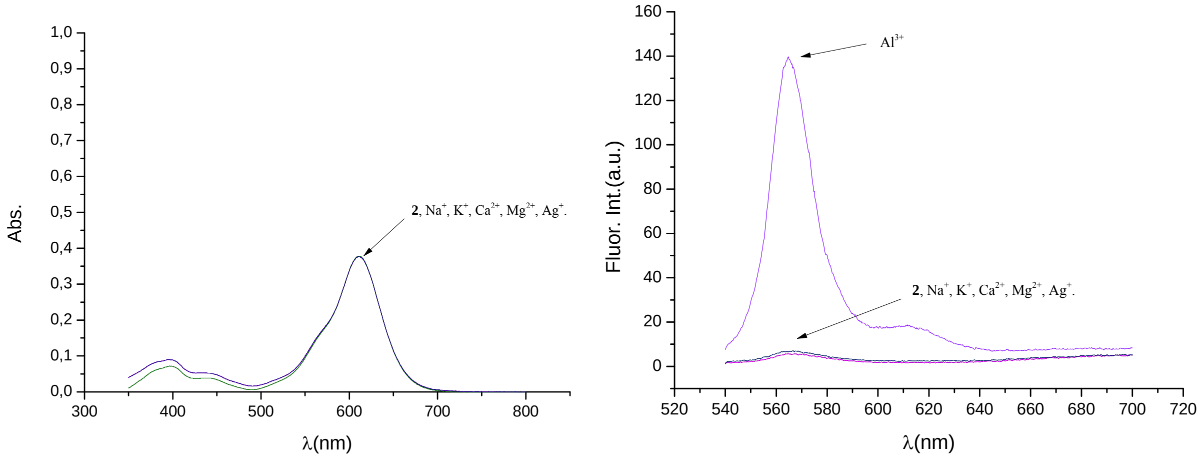


Figure S-21. UV-Vis spectra (a) and fluorescence emission spectra (λ_{ex} = 530 nm) (b) of **2** (10^{-5} M) upon addition of 10 eq of Na^+, K^+, Ca^{2+}, Mg^{2+}, Ag^+ and 1 eq of Al^{3+} in water:CH_3CN (40:60 v/v).

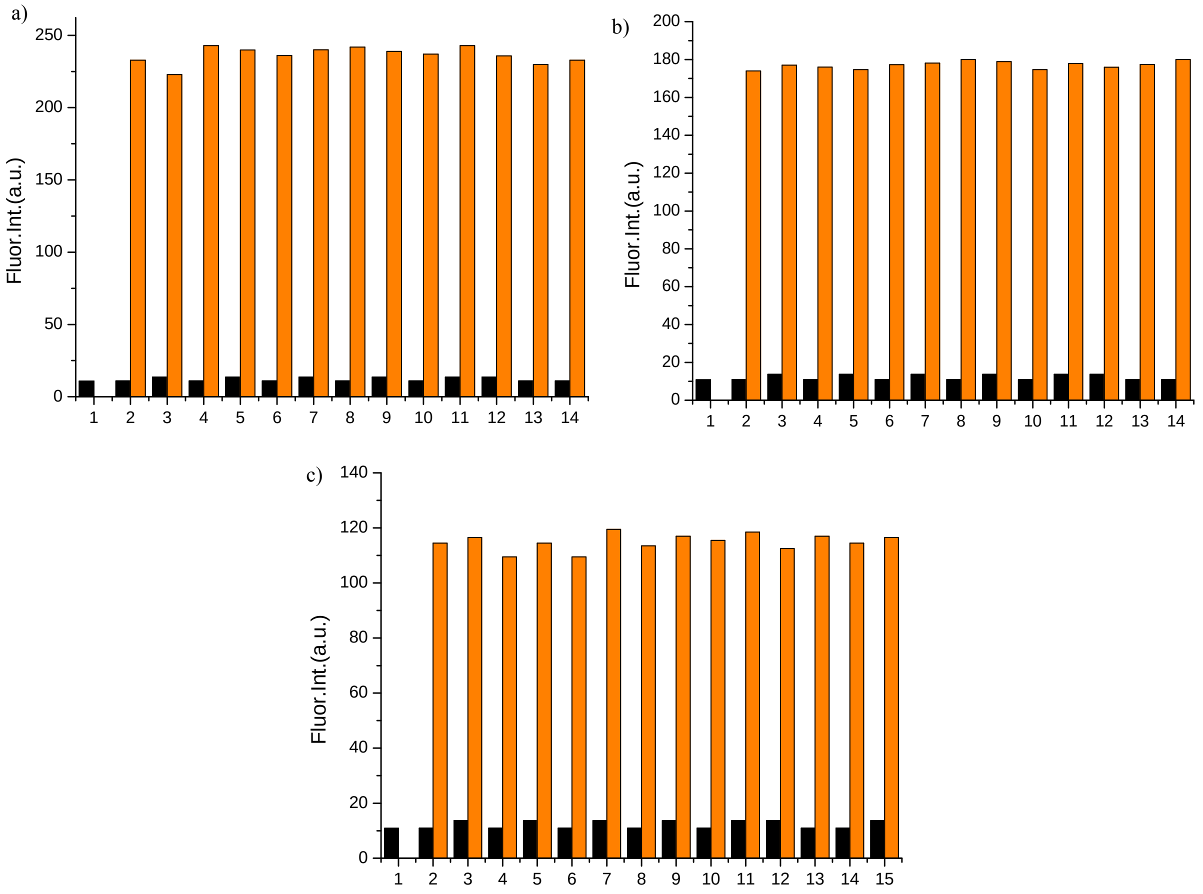


Figure S-22. The fluorescent response of **1** (10^{-5}M in water:CH_3CN; 40:60 v/v) (λ_{ex}=480nm; λ_{em}=515nm) in the presence of a) Al^{3+}; b) $Fe^{3+}$and c) Cr^{3+} and the interfering ions. The black bars represent the addition of 5 eq. appropriate metal ions to a solution of **1**. The orange bars represent the subsequent addition of 1 eq. a) Al^{3+}; b) $Fe^{3+}$and c) Cr^{3+} to the above solution. 1-15 represent, **1**, Cu^{2+}, Zn^{2+}, Cd^{2+},Ru^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Li^+, Hg^{2+},Na^+, K^+, Ca^{2+}, Mg^{2+} and Ag^+.

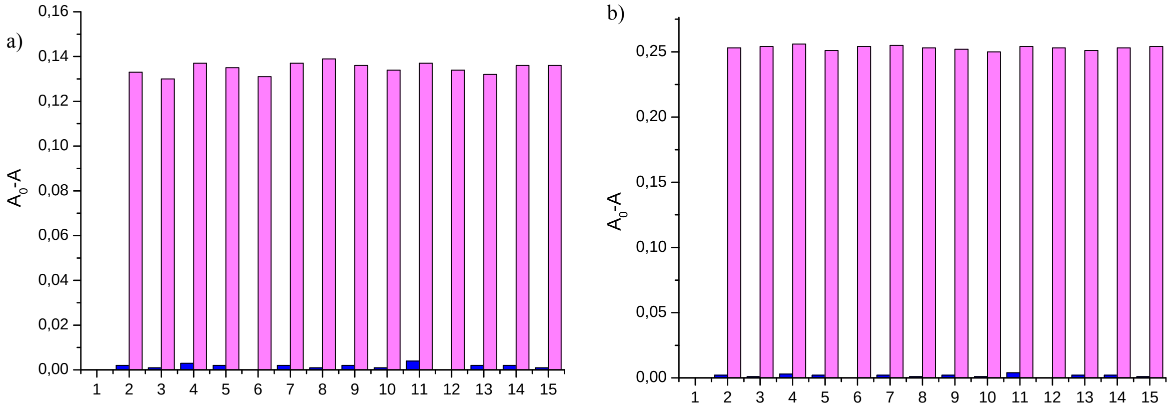


Figure S-23. The Uv-Vis. response of **2** (10^{-5}M in water:CH$_3$CN; 20:80 v/v) in the presence of a) Al^{3+}and b) Cr^{3+} and the interfering ions. The blue bars represent the addition of 5 eq. appropriate metal ions to a solution of **2**. The magenta bars represent the subsequent addition of 1 eq. a) Al^{3+}and b) Cr^{3+} to the above solution. 1-15 represent, **2**, Cu^{2+}, Zn^{2+}, Cd^{2+},Ru $^{3+}$, Fe^{2+}, Co^{2+}, Ni^{2+}, Li^{+}, Hg^{2+},Na^{+}, K^{+}, Ca^{2+}, Mg^{2+} and Ag^{+}.

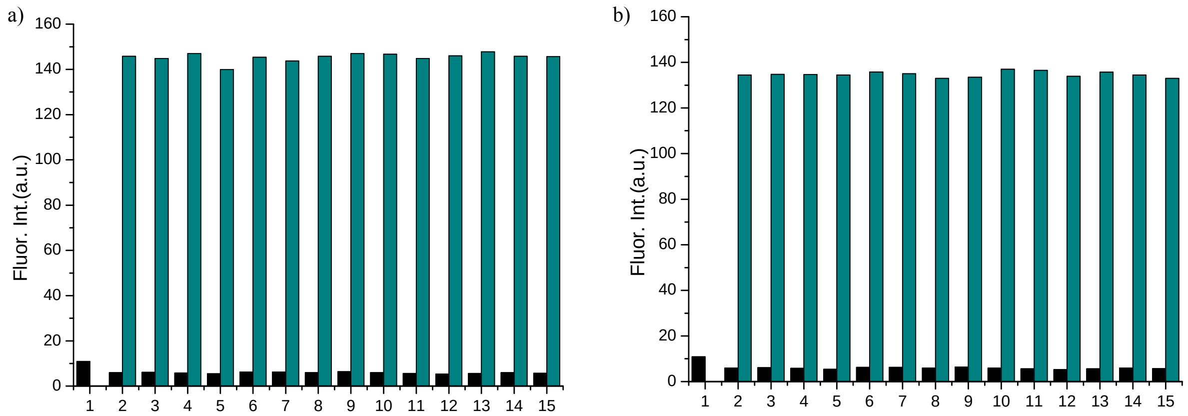
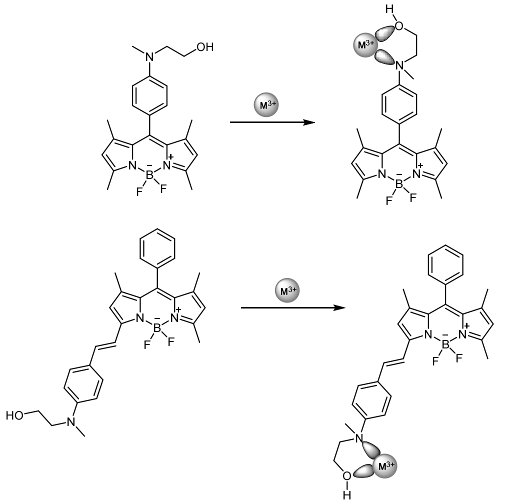


Figure S-24. The fluorescent response of **2** (10^{-5}M in water:CH$_3$CN; 20:80 v/v) (λ_{ex}=530nm; λ_{em}=563nm) in the presence of a) Al^{3+}and b) Cr^{3+} and the interfering ions. The black bars represent the addition of 5 eq. appropriate metal ions to a solution of **2**. The blue bars represent the subsequent addition of 1 eq. a) Al^{3+}and b) Cr^{3+} to the above solution. 1-15 represent, **2**, Cu^{2+}, Zn^{2+}, Cd^{2+}, Ru^{3+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Li^{+}, Hg^{2+},Na^{+}, K^{+}, Ca^{2+}, Mg^{2+} and Ag^{+}.



Scheme S-2. Proposed interaction of compounds **1** and **2** with trivalent cations.

Reference: J. Umberger and V. K. LaMer, J. *Am. Chem. Soc*., 1945, **67**, 1099-1109.