

First bodipy-DOTA derivatives as probes for bimodal imaging

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Experimental Section

General: All the chemicals used to prepare the title compounds including InCl₃, GaCl₃, Cu(NO₃)₂, 2.5 H₂O were purchased from Acros. Tris-*t*-butyl 2,2',2''-(1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetate was obtained from CheMatech[®] and used without further purification. The ¹H and ¹³C NMR spectra were recorded at room temperature or at 330K. NMR spectra were run on BRUKER Avance 300 and 600 spectrometers using perdeuterated solvents as internal standard. Elemental analyses were obtained on EA 1108 CHNS Fisons Instrument. Absorption spectra were recorded on a VARIAN CARY 50. Matrix-Assisted Laser Desorption Ionisation Time-Of-Flight (MALDI-TOF) mass spectrometry was carried out using a Bruker Daltonics Proflex III spectrometer. ESI (Electro Spray Ionisation) High resolution and accurate mass measurements (HRMS) were carried out using a Bruker microTOF-QTM ESI-TOF mass spectrometer. The steady-state fluorescence emission and excitation spectra were obtained by using a Fluorolog-3 instrument. The fluorescence quantum yield (Φ_{exp}) was calculated from equation 1.

$$\Phi_{\text{exp}} = \Phi_{\text{ref}} \frac{F \{1 - \exp(-A_{\text{ref}} \ln 10)\} n^2}{F_{\text{ref}} \{1 - \exp(-A \ln 10)\} n_{\text{ref}}^2}$$

Equation 1

Here, F denotes the integral of the corrected fluorescence spectrum, A is the absorbance at the excitation wavelength, and n is the refractive index of the medium. The reference system used was rhodamine 6G ($\Phi = 0.78$ in H₂O, $\lambda_{\text{exc}} = 488$ nm).ⁱ All the spectrometers were available at the "Plateforme d'Analyse Chimique et de Synthèse Moléculaire de l'Université de Bourgogne" (PACSMUB).

X-ray equipment and refinement: diffraction data were collected on a Nonius Kappa Apex-II CCD diffractometer equipped with a nitrogen jet stream low-temperature system (Oxford Cryosystems). The X-ray source was graphite-monochromated Mo- $K\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) from a sealed tube. The lattice parameters were obtained by least-squares fit to the optimized setting angles of the entire set of collected reflections. No significant temperature drift was observed during the data collections. Data were reduced by using DENZOⁱⁱ software, without applying absorption corrections. The missing absorption corrections were partially compensated by the data scaling procedure in the data reduction. The structure was solved by direct methods using the SIR92ⁱⁱⁱ program. Refinements were carried out by full-matrix least-squares on F^2 using the SHELXL97^{iv} program on the complete set of reflections. Anisotropic thermal parameters were used for non-hydrogen atoms. All H atoms, on carbon atom, were placed at calculated positions using a riding model with C-H = 0.95 \AA (aromatic), C-H = 0.99 \AA (methylene) or 0.98 \AA (methyl) with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{CH})$, $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{CH}_2)$ or $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{CH}_3)$.

Crystal structure determination of 11: *Crystal data.* $\text{C}_{36}\text{H}_{43}\text{BCl}_2\text{F}_2\text{N}_6\text{O}_4$, $M = 743.47$, red prism crystal of dimensions $0.07 \times 0.05 \times 0.05 \text{ mm}^3$, triclinic, space group $P-1$, $a = 9.5109(4) \text{ \AA}$, $b = 12.5631(6) \text{ \AA}$, $c = 16.3648(8) \text{ \AA}$, $\alpha = 101.572(2)^\circ$, $\beta = 103.112(3)^\circ$, $\gamma = 99.345(3)^\circ$, $V = 1820.86(15) \text{ \AA}^3$, $Z = 2$, $T = 115(2) \text{ K}$, $F(000) = 780$, $D_c = 1.356 \text{ g.cm}^{-3}$, $\lambda(\text{Mo-K}\alpha) = 0.71073 \text{ \AA}$, $\mu(\text{Mo-K}\alpha) = 0.237 \text{ mm}^{-1}$, 13572 reflections collected in the range $1.87 \leq \theta \leq 27.54^\circ$, 8217 unique. The maximum and minimum residual electron densities are 0.416 and $-0.955 \text{ e.\AA}^{-3}$. The final agreement factors are $R(F) = 0.0979$ and 0.1499, and $wR(F^2) = 0.1917$ and 0.2229, for $I > 2\sigma(I)$ and all data, respectively. CCDC-785489 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data centre via www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of compound 1^v: *N*-hydroxysuccinimide (54 mg, 0.48 mmol), 4-(dimethylamino)-pyridine (DMAP) (58 mg, 0.48 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (92 mg, 0.48 mmol) were successively added to a solution of 4-carboxyphenyl-1,3,5,7-tetramethyl-2,6-diethyl-4-bora-3a,4a-diaza-s-indacene^{vi} (100 mg, 0.24

mmol) in CH₂Cl₂ (50 mL), and the solution was stirred at room temperature. After total consumption of the starting material (2 hours) followed by TLC (AcOEt/hexane 1:1, R_f = 0.5) the mixture was washed with water (2* 10 mL). The organic phase was dried over MgSO₄ and the solvent was evaporated to give a red oil. The crude product was purified by column chromatography on silica gel (AcOEt/hexane 1:1) to give **1** as a red solid (88 mg, 70%). ¹H NMR (300 MHz, CDCl₃, 300K) δ(ppm): 0.96 (t, 6H, ³J = 7.5 Hz), 1.25 (s, 6H), 2.27 (q, 4H, ³J = 7.5 Hz), 2.51 (s, 6H), 2.92 (s, 4H), 7.47 (d, 2H, ³J = 8.3 Hz), 8.23 (d, 2H, ³J = 8.3 Hz); ¹³C{¹H} NMR (75 MHz, CDCl₃, 300K) δ(ppm): 12.1, 12.7, 14.6, 17.3, 25.7, 125.6, 129.3, 131.2, 133.3, 137.7, 138.0, 138.7, 143.0, 154.6, 161.4, 169.2; ESI-MS: *m/z* = 544.21 [M+Na]⁺; UV-Vis (CH₃CN), λ (nm) (ε, M⁻¹cm⁻¹): 525 (73000), 492 (23200), 378 (7950); Anal.Calcd for C₂₈H₃₀BF₂N₃O₄: C, 68.50; H, 6.67; N, 6.39; found: C, 68.78; H, 6.87; N, 5.95.

Synthesis of compound 2^{vii}: 1-(ethylacetate)-4,7,10-tris(tert-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane^{viii} (11.2 g, 0.018 mol) was dissolved in ethylenediamine (15 mL) and the mixture was stirred at room temperature for 78h. The solvent was evaporated, 200 mL of water was added and the product was extracted with dichloromethane (2*300 mL). The organic phase was dried over MgSO₄ and the solvent was evaporated. The yellow oil was taken in pentane (500 mL) and the impurities were removed by filtration. After evaporation of the solvent, pure compound **2** was obtained as a colorless oil (m = 7.2 g, 65%). ¹H NMR (300 MHz, CDCl₃, 300 K) δ (ppm): 1.35 (s, 18H), 1.36 (s, 9H), 2.41-2.45 (m, 4H), 2.59-2.65 (m, 4H), 2.69-2.65 (t, 2H, ³J = 6.4 Hz), 2.73-2.77 (m, 4H), 2.77-2.81 (m, 4H), 2.98 (s, 2H), 3.15 (s, 4H), 3.18 (s, 2H), 3.20-3.24 (td, 2H, ³J = 6.4 Hz, ³J = 6.5 Hz), 8.63 (bs, 1H, NH); ¹³C{¹H} NMR (75 MHz, CDCl₃, 300 K) δ (ppm): 28.4, 42.3, 42.0, 52.2, 52.6, 53.7, 55.1, 56.4, 57.1, 52.3, 81.0, 81.2, 170.6, 170.8, 172.8; MALDI-TOF: *m/z* = 615.14 [M+H]⁺, 637.14 [M+Na]⁺; Anal.Calcd for C₃₀H₅₈N₆O₇: C, 57.89; H, 9.53; N, 13.47; found: C, 58.07; H, 9.92; N, 13.14.

Synthesis of compound 3: Compound **2** (2 g, 3.2 mmol) was dissolved in 35% HCl (20 mL) and the solution was stirred for 30 min at room temperature. After evaporation of the solvent, acetone was added (20 mL) and the mixture was stirred for 1 hour. Then, the precipitate was filtered, washed with acetone (50 mL), and diethylether (50 mL) to give **3** (+ 3 HCl) as a white solid. (1.5 g, 95 %). ¹H NMR (300 MHz, D₂O+NaOD (pH = 7), 300K) δ(ppm): 2.79-3.00 (m, 4H), 3.05-3.23 (m, 6H), 3.32-3.35 (m, 2H), 3.38-3.42 (m, 2H), 3.43-3.69 (m, 10H),

3.84 (s, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{D}_2\text{O}+\text{NaOD}$ (pD = 7), 300K) $\delta(\text{ppm})$: 36.7, 36.9, 48.4, 48.8, 50.5, 52.2, 56.1, 56.4, 57.3, 170.1, 173.3, 178.9; ESI-MS: $m/z = 447.26$ $[\text{M}+\text{H}]^+$, 893.53 $[2\text{M}+\text{H}]^+$, 915.51 $[2\text{M}+\text{Na}]^+$; Anal. Calcd for $\text{C}_{18}\text{H}_{34}\text{N}_6\text{O}_7, 3\text{HCl}, 1.8\text{H}_2\text{O}$: C, 36.75; H, 14.29; N, 6.95; found: C, 37.20; H, 13.89; N, 7.02.

Synthesis of compound 4: Diisopropylethylamine was added to a solution of **3** (400 mg, 0.7 mmol) in water until pH = 12. A solution of bodipy **1** (330 mg, 0.6 mmol) in CH_3CN (20 mL) was then added and the mixture was stirred at 35°C during 12h, until total consumption of the starting materials was observed by TLC (EtOH/ NH_4OH 9:1, $R_f = 0.4$). The solvent was evaporated, and the resulting red oil was purified by column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{EtOH}/\text{NH}_4\text{OH}$ 2:7:1). Recrystallization from $\text{CH}_2\text{Cl}_2/\text{hexane}$ gave the desired compound as a red solid (m = 230 mg, 45%). ^1H NMR (600 MHz, MeOD, 330K) $\delta(\text{ppm})$: 0.99 (t, 6H, $^3J = 7.5$ Hz), 1.33 (s, 6H), 2.35 (q, 4H, $^3J = 7.5$ Hz), 2.48 (s, 6H), 2.82-3.04 (m, 8H), 3.21-3.33 (m, 8H), 3.35 (s, 4H), 3.49-3.53 (m, 2H), 3.53-3.60 (m, 4H), 3.61-3.65 (m, 2H), 7.44 (d, 2H, $^3J = 8.3$ Hz), 8.09 (d, 2H, $^3J = 8.3$ Hz); ^{11}B NMR (128 MHz, CDCl_3 , 300K): 0.73 ppm (t, $^1J_{\text{B,F}} = 32.8$ Hz); ESI-MS: $m/z = 851.45$ $[\text{M}-\text{H}]^-$, 889.40 $[\text{M}-2\text{H}+\text{K}]^-$; UV-Vis (CH_3CN), λ (nm) (ϵ , $\text{M}^{-1}\text{cm}^{-1}$) 523 (sh, 31000), 492 (sh, 11100), 378 (3700); HRMS ESI: $m/z = \text{calcd for } \text{C}_{42}\text{H}_{59}\text{BF}_2\text{N}_8\text{O}_8-2\text{H}+\text{K}: 889.4010$; found: 889.3922.

Synthesis of compound 5: Indium chloride (25 mg, 0.12 mmol) was added to a solution of **4** (100 mg, 0.12 mmol) in methanol/water (8:2, 10 mL). The mixture was stirred at 35°C for 2h until total consumption of the starting materials was observed by TLC (EtOH/ NH_4OH 8:2, $R_f = 0.3$). The complex was purified by column chromatography over silica gel ($\text{CH}_2\text{Cl}_2/\text{EtOH}/\text{NH}_4\text{OH}$ 1:8:2) to yield compound **5** as a red solid (95 mg, 85%). ^1H NMR (300 MHz, DMSO 300K) $\delta(\text{ppm})$: 0.94 (t, 6H, $^3J = 7.5$ Hz), 1.24 (s, 6H), 2.29 (m, 4H), 2.44 (s, 6H), 2.61-2.92 (m, 10H), 2.97-3.25 (m, 12H), 3.37-3.56 (m, 6H), 7.49 (d, 2H, $^3J = 8\text{Hz}$), 8.03 (d, 2H, $^3J = 8\text{Hz}$), 8.74 (bs, 1H); ^{11}B NMR (128 MHz, CDCl_3 , 300K): 0.60 ppm (t, $^1J_{\text{B,F}} = 33.3$ Hz); UV-Vis (H_2O), λ (nm) (ϵ , $\text{M}^{-1}\text{cm}^{-1}$): 527 (32200), 491 (sh, 14150), 380 (5350); HRMS-MS: m/z : calcd for $\text{C}_{42}\text{H}_{56}\text{BF}_2\text{InN}_8\text{O}_8-\text{H}$: 963.32557; found: 963.32625.

Synthesis of compound 6: Gallium chloride (18 mg, 0.12 mmol) was added to a solution of **4** (100 mg, 0.12 mmol) in methanol/water (8:2, 8 mL). The mixture was stirred at 35°C for 2 hours, during which a precipitate was formed. The precipitate could be isolated by centrifugation, to yield compound **6** as a red solid (100 mg, 92%). UV-Vis (H₂O), λ (nm) (ϵ , M⁻¹cm⁻¹): 523 (33900), 492 (sh, 11350), 378 (3750); HRMS-MS: m/z : calcd for C₄₂H₅₆BF₂GaN₈O₈-H: 917.34725; found: 917.35050; Anal.Calcd for C₄₂H₅₆BF₂GaN₈O₈.CH₃OH: C, 54.28; H, 6.36; N, 11.78; found: C, 53.82; H, 6.72; N, 12.34.

Synthesis of compound 7: Copper nitrate hemipentahydrate (22 mg, 0.09 mmol) was added to a solution of **4** (82 mg, 0.09 mmol) in ethanol (6 mL). The mixture was stirred at 35°C for 2 hours until total consumption of the starting materials was observed by TLC (EtOH/NH₄OH 9:1, R_f = 0.3). The complex was purified by column chromatography over silica gel (EtOH/NH₄OH 9:1) to yield compound **7** as a red solid (69 mg, 84%). UV-Vis (H₂O), λ (nm) (ϵ , M⁻¹cm⁻¹): 523 (30500), 492 (sh, 13400), 378 (6500); HRMS-MS: m/z : calcd for C₄₂H₅₇BF₂CuN₈O₈-H: obtained 912.35513; found: 912.35909; Anal.Calcd for C₄₂H₅₇BF₂CuN₈O₈.NH₃: C, 54.16; H, 6.49; N, 13.54; found: C, 54.62; H, 5.97; N, 13.75.

Synthesis of compound 10: N-hydroxybenzotriazole (180 mg, 1.3 mmol), diisopropylethylamine (DIPEA) (340 mg, 2.6 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (250 mg, 1.3 mmol) and **9** (340 mg, 1.3 mmol) were successively added to a solution of **8** (550 mg, 1.3 mmol) in dry DMF (30 mL), and the solution was stirred at room temperature. After total consumption of the starting material (8 hours) followed by TLC (AcOEt/hexane 6:4, R_f = 0.6), the solvent was evaporated. The solid obtained was washed with water (2* 30 mL) and extracted with dichloromethane (100 mL). The organic phase was dried over MgSO₄ and the solvent was evaporated to give a red oil. The crude product was purified by column chromatography on silica gel (AcOEt/hexane 1:1). Recrystallization in CH₂Cl₂/hexane gave pure **10** as red-green crystals (630 mg, 76%). ¹H NMR (300 MHz, CDCl₃, 300K) δ (ppm): 0.93 (t, 6H, ³J = 7.5 Hz), 1.23 (s, 6H), 2.28 (q, 4H, ³J = 7.5 Hz), 2.51 (s, 6H), 3.34 (dd, 1H, ³J = 13.9 Hz, 6.2 Hz), 3.45 (dd, 1H, J = 13.9 Hz, 5.1 Hz), 3.79 (s, 3H), 5.14 (ddd, 1H, ³J = 7.0 Hz, ³J = 6.2 Hz, ³J = 5.1 Hz), 6.75 (d, 1H, ³J = 7.0 Hz), 7.33 (d, 2H, ³J = 8.7 Hz), 7.40 (d, 2H, ³J = 8.2 Hz), 7.88 (d, 2H, ³J = 8.3 Hz); 8.15 (d, 2H, ³J = 8.7 Hz); ¹³C{¹H} NMR (75 MHz, CDCl₃, 300K) δ (ppm): 11.9, 12.6, 14.6, 17.1,

37.9, 52.8, 53.5, 123.8, 127.7, 129.1, 130.2, 130.3, 133.2, 133.7, 138.1, 138.5, 140.0, 143.7, 147.3, 154.4, 166.2, 171.6; ^{11}B NMR (128 MHz, CDCl_3 , 300K): 0.78 ppm (t, $J_{B,F} = 33.4$ Hz); UV-Vis (CH_3CN), λ (nm) (ϵ , $\text{M}^{-1}\text{cm}^{-1}$): 523 (63000), 492 (21100), 378 (6800); HRMS-ESI m/z : calcd for $\text{C}_{34}\text{H}_{37}\text{BF}_2\text{N}_4\text{O}_5 + \text{H}$: 631.2903; found: 531.2897. Anal. Calcd for $\text{C}_{34}\text{H}_{37}\text{BF}_2\text{N}_4\text{O}_5 + 0.3 \text{CH}_2\text{Cl}_2$: C, 63.56; H, 5.82; N, 8.65; found: C, 63.44; H, 6.25; N, 8.63.

Synthesis of compound 11: A solution of compound **10** (1.7 g, 2.7 mmol) and ethylenediamine (11.3 g, 0.18 mol) in 90 mL of methanol was stirred at 55°C for 48h. The solvent was evaporated, water was added (100 mL) and the product was extracted with dichloromethane (2*300 mL). The organic phase was dried over MgSO_4 and the solvent was evaporated. The crude product was washed with hexane (200 mL), and the solid obtained was purified by column chromatography on silica gel ($\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{NH}_4\text{OH}$ 80:18:2). Recrystallization in $\text{CH}_2\text{Cl}_2/\text{hexane}$ gave pure **11** as red crystals (1.4 g, 79%). ^1H NMR (300 MHz, CDCl_3 , 300K) δ (ppm): 0.95 (t, 6H, $^3J = 7.5$ Hz), 1.22 (s, 6H), 2.27 (q, 4H, $^3J = 7.5$ Hz), 2.51 (s, 6H), 2.64-2.81 (m, 2H), 3.18-3.36 (m, 2H), 4.87 (ddd, 1H, $^3J = 7.0$ Hz, $^3J = 6.2$ Hz, $^3J = 5.1$ Hz), 6.36 (t, 1H, $^3J = 5.5$ Hz, NH), 7.09 (d, 1H, $^3J = 7.0$ Hz, NH), 7.38 (d, 2H, $^3J = 8.2$ Hz), 7.45 (d, 2H, $^3J = 8.5$ Hz); 7.88 (d, 2H, $^3J = 8.2$ Hz), 8.16 (d, 2H, $^3J = 8.5$ Hz); ^{11}B NMR (128 MHz, CDCl_3 , 300K): 0.77 ppm (t, $J_{B,F} = 33.3$ Hz); UV-Vis (CH_2Cl_2), λ (nm) (ϵ , $\text{M}^{-1}\text{cm}^{-1}$): 528 (76500), 493 (23300), 379 (9650); ESI-MS: $m/z = 639.32$ [M-F] $^+$, 659.33 [M+H] $^+$; Anal. Calcd for $\text{C}_{35}\text{H}_{41}\text{BF}_2\text{N}_6\text{O}_4 + 0.7 \text{CH}_2\text{Cl}_2$: C, 59.72; H, 5.95; N, 11.70; found: C, 60.05; H, 5.79; N, 11.34.

Synthesis of compound 13: To a solution of compound **11** (230 mg, 0.34 mmol) and 170 μL of Et_3N (6 equivalents) in dry DMF (25 mL) was added a solution of DOTA-NHS ester **12** (200 mg, 0.28 mmol) in dry DMF (5 mL). The mixture was stirred at room temperature for 12h. Then the solvent was evaporated and the crude product was purified by column chromatography on silica gel ($\text{EtOH}/\text{NH}_4\text{OH}$ 9:1). The solid obtained was washed with hexane (20 mL) and acetonitrile (20 mL). The compound **13** was isolated as a red solid (230 mg, 65%). ^1H NMR (600 MHz, MeOD, 330K) δ (ppm): 1.01 (t, 6H, $^3J = 7.5$ Hz), 1.31 (s, 6H), 2.36 (q, 4H, $^3J = 7.5$ Hz), 2.49 (s, 6H), 2.92-3.02 (m, 4H), 3.05-3.15 (m, 4H), 3.34-3.56 (m, 18H), 3.66-3.77 (m, 4H), 5.01-5.06 (m, 1H), 7.41 (d, 2H, $^3J = 8.2$ Hz), 7.63 (d, 2H, $^3J = 8.5$ Hz); 7.99 (d, 2H, $^3J = 8.2$ Hz), 8.12 (d, 2H, $^3J = 8.5$ Hz); ^{11}B NMR (128 MHz, MeOD, 300K):

0.72 ppm (t, $J_{B,F} = 33.2$ Hz); UV-Vis (DMF), λ (nm) (ϵ , $M^{-1}cm^{-1}$): 523 (64400), 491 (21400), 379 (6800); ESI-MS: $m/z = 1067.49 [M+Na]^+$, 1089.47 $[M+2Na-H]^+$, 1111.46 $[M+3Na-2H]^+$, Anal.Calcd for $C_{51}H_{67}BF_2N_{10}O_{11} + 6.5 H_2O, NH_4$: C, 51.91; H, 7.17; N, 13.06; found: C, 51.75; H, 6.53; N, 12.38.

Synthesis of compound 14: A suspension of compound **13** (50 mg, 47.8 μ mol) and 10 % Pd/C (5mg, 19.2 μ mol) in a mixture of water and ethanol ($H_2O/EtOH$, 90/10, 5 mL) was stirred under H_2 . After consumption of hydrogen, the suspension was eliminated by filtration on Clarcel[®] and the solvent was evaporated. The solid obtained was washed with hexane (10 mL), to give compound **14** as a red solid (45 mg, 95%). 1H NMR (300 MHz, MeOD, 300K) δ (ppm): 0.88 (t, 6H, $^3J = 7.5$ Hz), 1.18 (s, 6H), 2.24 (q, 4H, $^3J = 7.5$ Hz), 2.37 (s, 6H), 2.62-3.05 (m, 8H), 3.20-3.70 (m, 22H), 4.54-4.63 (m, 1H), 6.57 (d, 2H, $^3J = 8.2$ Hz), 6.96 (d, 2H, $^3J = 8.5$ Hz); 7.33 (d, 2H, $^3J = 8.2$ Hz), 7.88 (d, 2H, $^3J = 8.5$ Hz); ^{11}B NMR (128 MHz, MeOD, 300K): 0.71 ppm (t, $J_{B,F} = 33.2$ Hz); UV-Vis (DMF), λ (nm) (ϵ , $M^{-1}cm^{-1}$): 523 (60200), 491 (19200), 379 (5600); ESI-MS: $m/z = 1051.43 [M+K-2H]^-$

Synthesis of compound 15: To a solution of **14** (15 mg, 14.7 μ mol) in H_2O (5 mL) was added at room temperature a solution of thiophosgene (3.5 μ L, 44.3 μ mol) in chloroform (2 mL). The solution was stirred vigorously during 2h. The solvent was evaporated and the residue was lyophilized. The crude product was washed with CH_2Cl_2 (2 mL) and hexane (5 mL) to give **15** as a red solid (13.5 mg, 90%); UV-Vis (DMSO), λ (nm) (ϵ , $M^{-1}cm^{-1}$): 523 (43000), 492 (14400), 378 (4600); ESI-MS: $m/z = 1077.45 [M+Na-2H]^-$; 1093.41 $[M+K-2H]^-$; 1099.42 $[M+2Na-3H]^-$

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Photophysical studies:

Fig. 6: Absorption (____) and emission (.....) of **4** in H_2O

Fig. 7: Absorption (____) and emission (.....) of **5** in H_2O

Fig. 8: Absorption (____) and emission (.....) of **6** in H_2O .

Fig. 9: Absorption (____) and emission (.....) of **7** in H_2O .

X-ray analysis:

Fig. 10: ORTEP view of compound **11**, showing thermal ellipsoid at the 50% probability level.

Fig. 11: ORTEP view of intermolecular H-bond in crystal of **11**, showing thermal ellipsoid at the 50% probability level. For clarity, only hydrogen involved in intermolecular hydrogen bonds are represented by dashed lines.

Table 1: Bond lengths [\AA] and angles [$^\circ$] for **11**.

Table 2: Hydrogen bonds for **11** [\AA and $^\circ$].

Mass Spectrum Report

Analysis Info

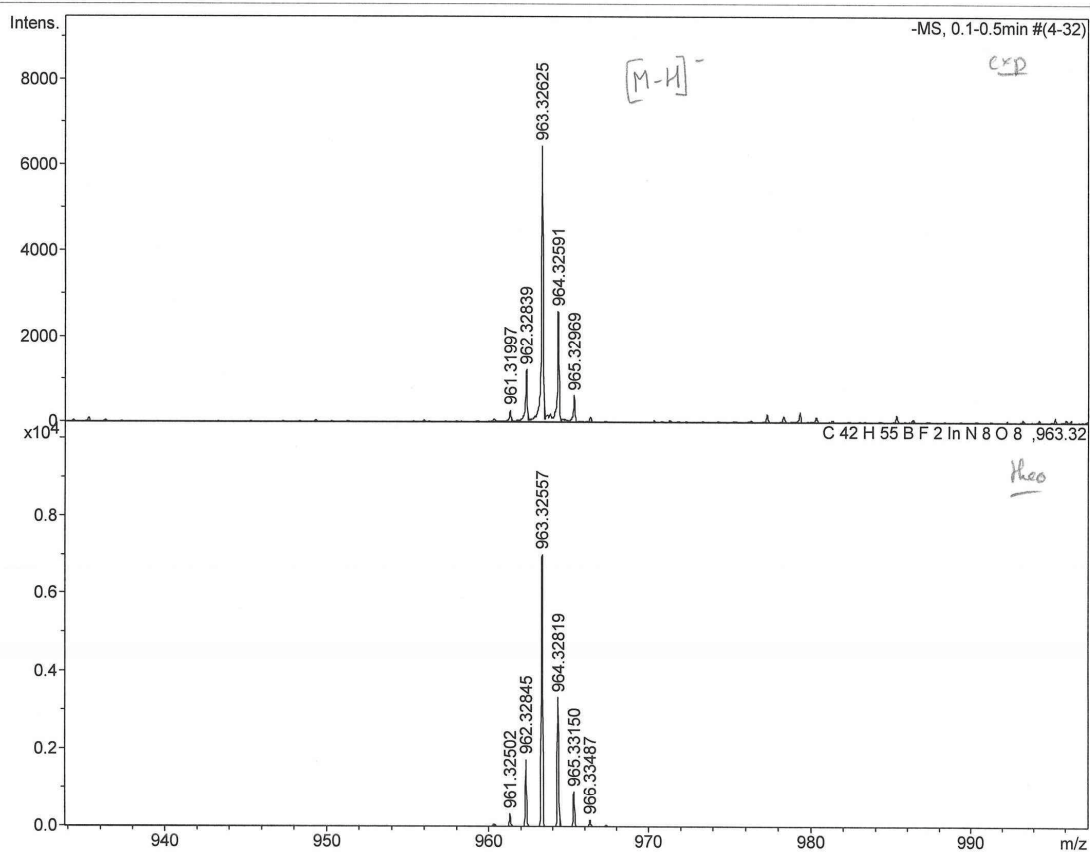
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Acquisition Date 4/15/2010 3:12:47 PM

Operator Marie-José Penouilh
 Instrument micrOTOF-Q 56

Acquisition Parameter

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Scan End	3000 m/z	Set Collision Cell RF	200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSig ma	rdb	e ⁻ Conf	N-R ule
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Fig. 1: HRMS spectrum of **5** (experimental and calculated).

Mass Spectrum Report

Analysis Info

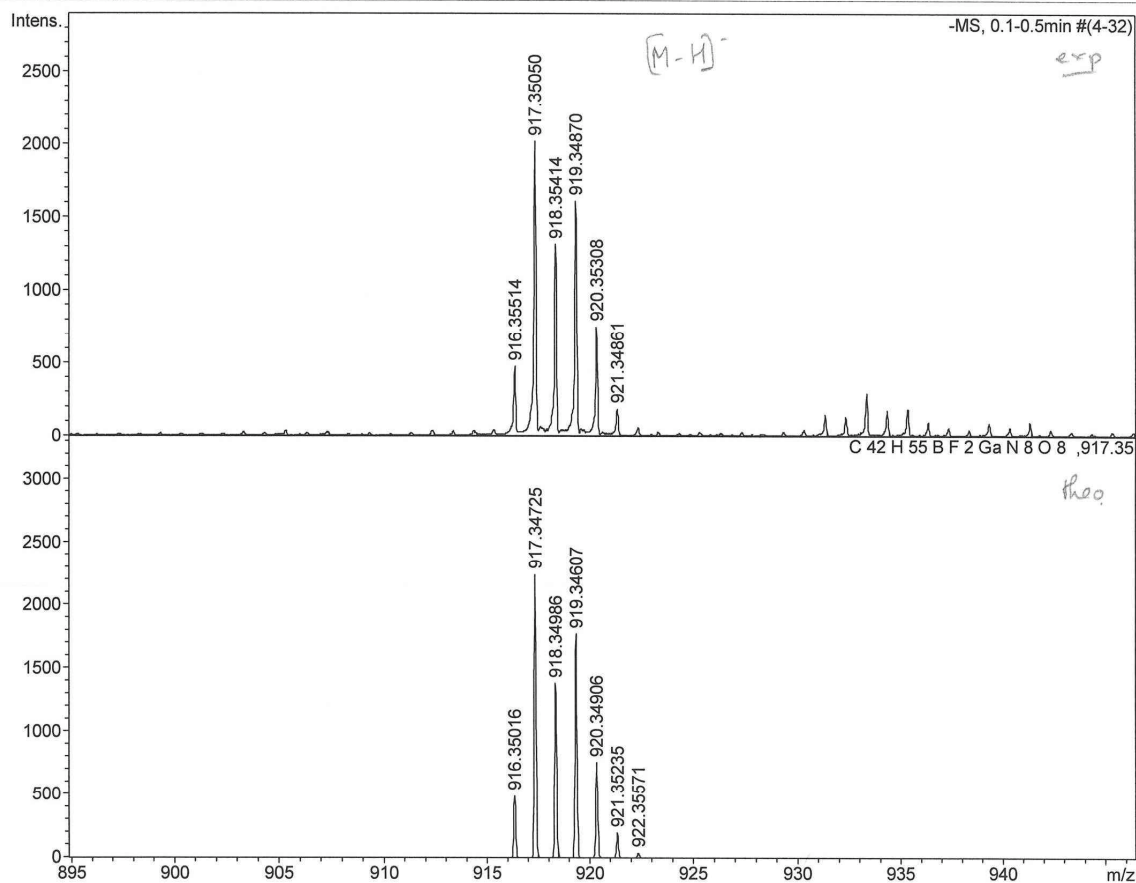
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Acquisition Date 4/15/2010 3:15:56 PM

Operator Marie-José Penouilh
 Instrument micrOTOF-Q 56

Acquisition Parameter

Source Type	ESI	Ion Polarity	Negative	Set Nebulizer	0.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSig ma	rdb	e ⁻ Conf	N-R ule
917.35050	1	C ₄₂ H ₅₅ BF ₂ GaN ₈ O ₈	100.00	917.34724	-3.3	-3.6	408.2	19.5	even	ok

Fig. 2: HRMS spectrum of **6** (experimental and calculated).

Mass Spectrum Report

Analysis Info

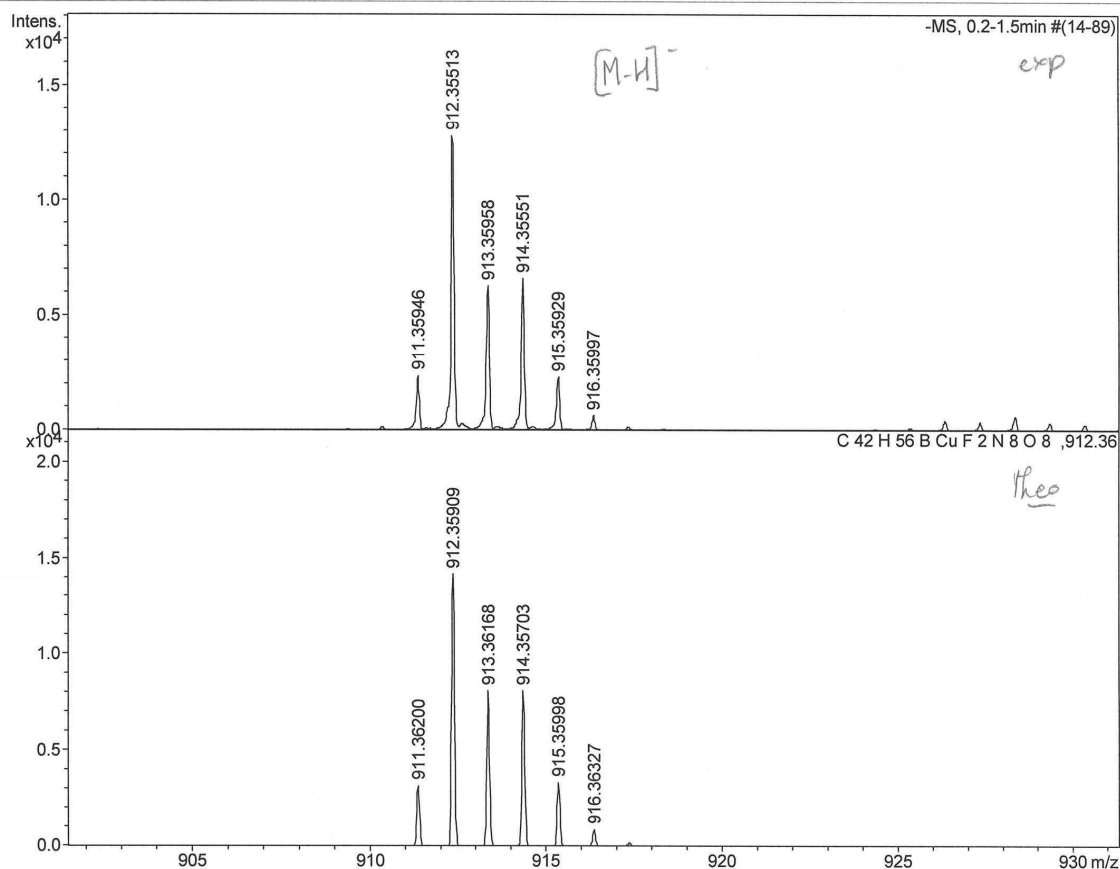
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Operator Marie-José Penouilh
 Instrument micrOTOF-Q 56

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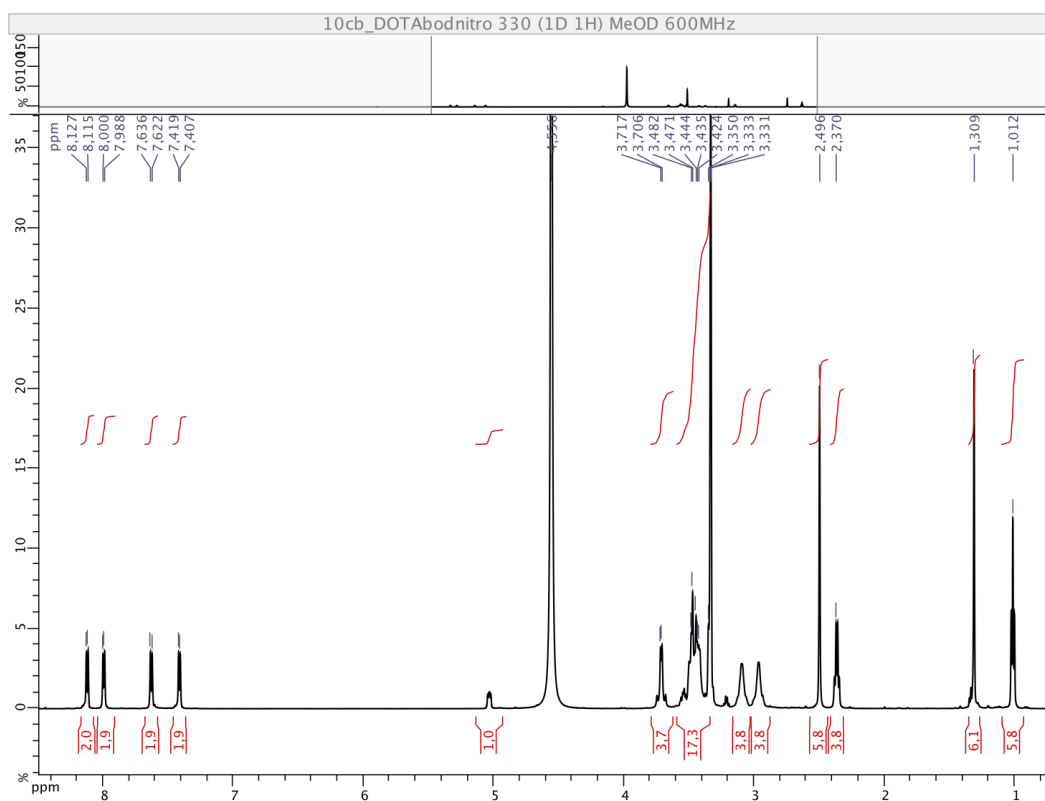
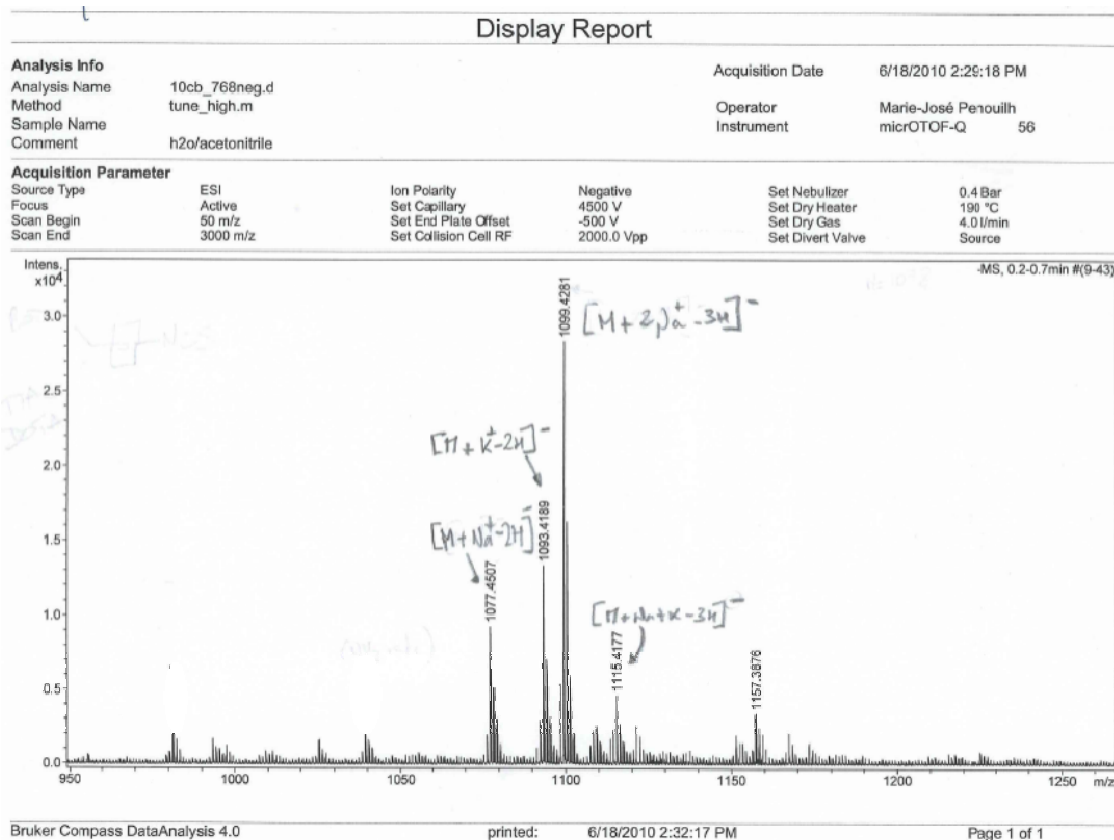
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Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	200.0 Vpp	Set Divert Valve	Source



Meas. m/z	#	Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e ⁻ Conf	N-Rule
912.35513	1	C ₄₂ H ₅₆ BCuF ₂ N ₈ O ₈	100.00	912.35908	3.9	4.3	43.5	18.0	odd	ok

Fig. 3: HRMS spectrum of **7** (experimental and calculated).

I

Fig. 4: ^1H NMR spectrum of **13** (600 MHz, MeOD, 330K).Fig 5: ESI-MS spectrum of **15**

Photophysical studies

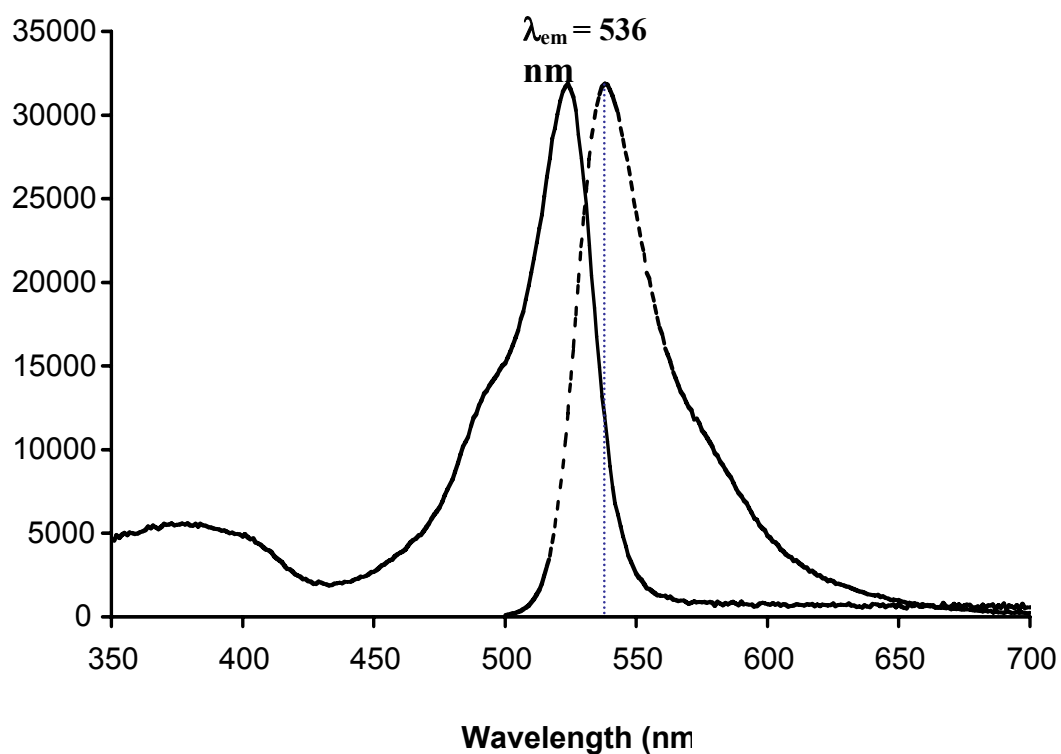


Fig.6: Absorption (—) and emission (---) of **4** in H₂O

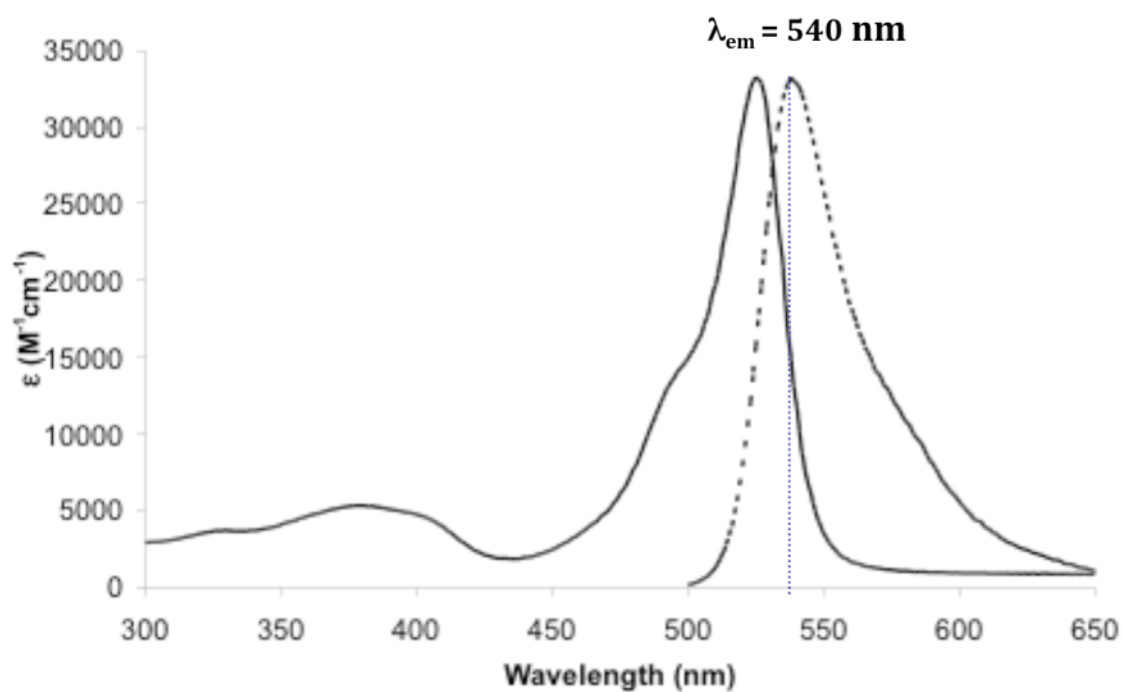


Fig.7: Absorption (—) and emission (---) of **5** in H₂O.

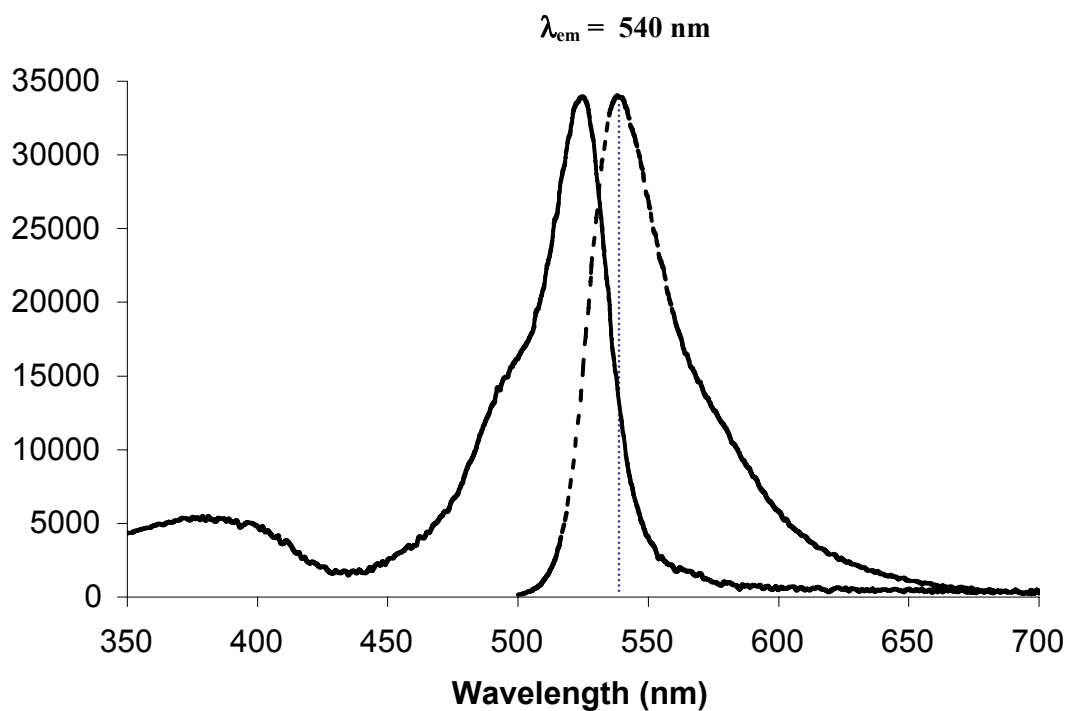


Fig.8: Absorption (—) and emission (---) of 6 in H₂O

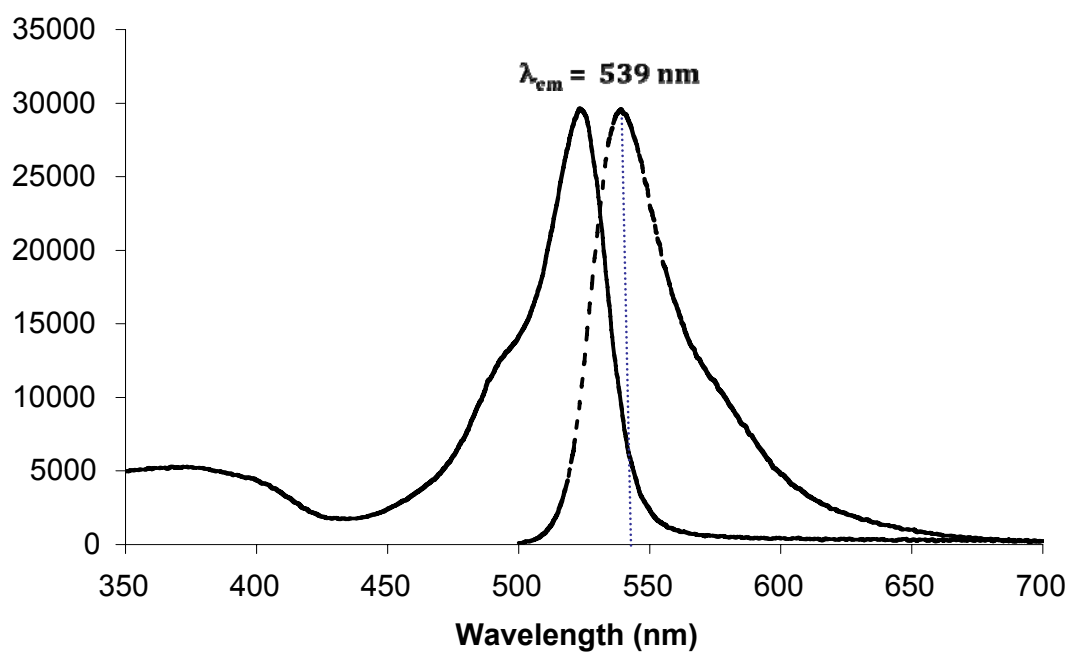


Fig. 9: Absorption (—) and emission (---) of 7 in H₂O.

X-ray analysis:

Ending amine of the ethylenediamine group and dichloromethane are disordered over two positions. The geometric parameters of disordered components in each group were restrained by using EADP constraints.^{iv} In the final stages of refinement, the statistical fractions of the major and minor disordered components were 0.834(3)/0.166(3). Similar Uij constraints were applied within the disordered parts to maintain a reasonable model. An ORTEP view of the compound **11** with disordered part is drawn in **Figure 10**.

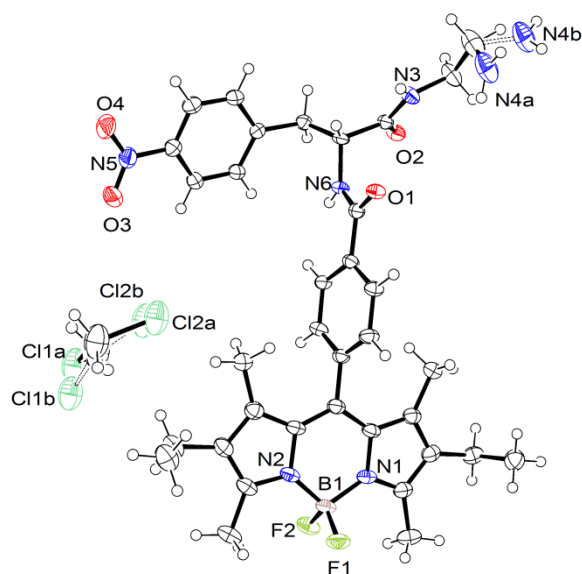


Fig. 10: ORTEP view of compound **11**, showing thermal ellipsoid at the 50% probability level.

Intermolecular hydrogen bonding, between the amide functions of neighboring molecules, involved in the crystal packing are shown in **Figure 11**. Intermolecular N-H...O distances are 2.886(4) Å and 2.941(4) Å for N3-O1 and N6-O2 respectively.

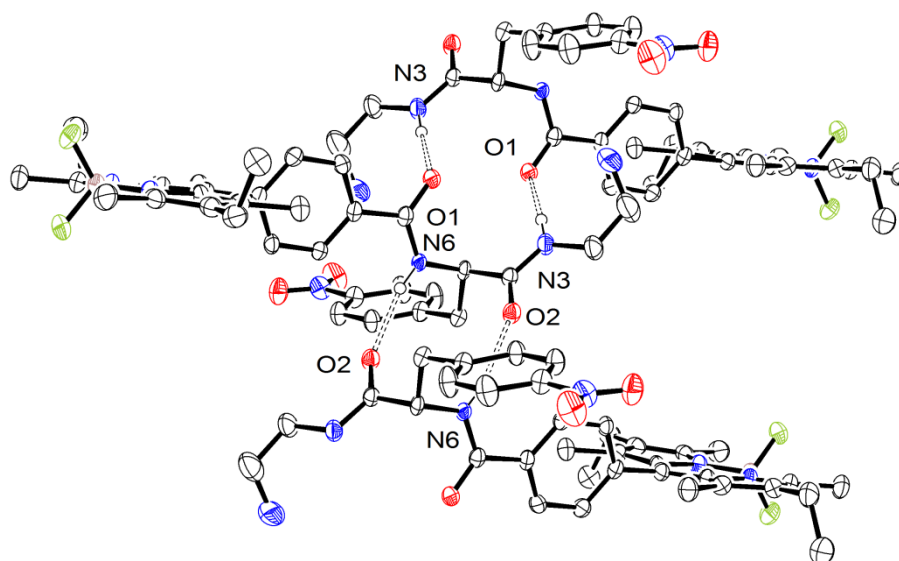


Fig. 11: ORTEP view of intermolecular H-bond in crystal of **11**, showing thermal ellipsoid at the 50% probability level. For clarity, only hydrogen involved in intermolecular hydrogen bonds are represented by dashed lines.

Table 1. Bond lengths [Å] and angles [°]
 for **11**.

C(1)-N(1)	1.355(6)	C(10)-H(10B)	0.9800
C(1)-C(2)	1.406(6)	C(10)-H(10C)	0.9800
C(1)-C(10)	1.495(6)	C(11)-C(12)	1.529(7)
C(2)-C(3)	1.392(6)	C(11)-H(11A)	0.9900
C(2)-C(11)	1.500(6)	C(11)-H(11B)	0.9900
C(3)-C(4)	1.425(6)	C(12)-H(12A)	0.9800
C(3)-C(13)	1.505(6)	C(12)-H(12B)	0.9800
C(4)-C(5)	1.400(6)	C(12)-H(12C)	0.9800
C(4)-N(1)	1.400(5)	C(13)-H(13A)	0.9800
C(5)-C(6)	1.400(6)	C(13)-H(13B)	0.9800
C(5)-C(18)	1.491(5)	C(13)-H(13C)	0.9800
C(6)-N(2)	1.402(5)	C(14)-H(14A)	0.9800
C(6)-C(7)	1.424(6)	C(14)-H(14B)	0.9800
C(7)-C(8)	1.390(6)	C(14)-H(14C)	0.9800
C(7)-C(14)	1.507(6)	C(15)-C(16)	1.516(7)
C(8)-C(9)	1.411(6)	C(15)-H(15A)	0.9900
C(8)-C(15)	1.517(7)	C(15)-H(15B)	0.9900
C(9)-N(2)	1.358(6)	C(16)-H(16A)	0.9800
C(9)-C(17)	1.492(6)	C(16)-H(16B)	0.9800
C(10)-H(10A)	0.9800	C(16)-H(16C)	0.9800
		C(17)-H(17A)	0.9800
		C(17)-H(17B)	0.9800
		C(17)-H(17C)	0.9800

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C(18)-C(23)	1.385(6)	C(36)-N(4B)	1.49(3)
C(18)-C(19)	1.388(6)	C(36)-H(36A)	0.9900
C(19)-C(20)	1.385(5)	C(36)-H(36B)	0.9900
C(19)-H(19)	0.9500	C(37A)-Cl(1A)	1.740(9)
C(20)-C(21)	1.396(6)	C(37A)-Cl(2A)	1.785(12)
C(20)-H(20)	0.9500	C(37A)-H(37A)	0.9900
C(21)-C(22)	1.390(5)	C(37A)-H(37B)	0.9900
C(21)-C(24)	1.504(5)	C(37B)-Cl(2B)	1.68(6)
C(22)-C(23)	1.392(5)	C(37B)-Cl(1B)	1.84(5)
C(22)-H(22)	0.9500	C(37B)-H(37C)	0.9900
C(23)-H(23)	0.9500	C(37B)-H(37D)	0.9900
C(24)-O(1)	1.238(5)	N(1)-B(1)	1.548(6)
C(24)-N(6)	1.343(5)	N(2)-B(1)	1.542(6)
C(25)-N(6)	1.458(4)	N(3)-H(3)	0.8800
C(25)-C(34)	1.533(5)	N(4A)-H(4A1)	0.8800
C(25)-C(26)	1.534(6)	N(4A)-H(4A2)	0.8800
C(25)-H(25)	1.0000	N(4B)-H(4B1)	0.8800
C(26)-C(27)	1.511(6)	N(4B)-H(4B2)	0.8800
C(26)-H(26A)	0.9900	N(5)-O(4)	1.223(5)
C(26)-H(26B)	0.9900	N(5)-O(3)	1.228(5)
C(27)-C(28)	1.393(6)	N(6)-H(6)	0.8800
C(27)-C(32)	1.396(5)	F(1)-B(1)	1.390(5)
C(28)-C(29)	1.372(6)	F(2)-B(1)	1.402(5)
C(28)-H(28)	0.9500		
C(29)-C(30)	1.387(6)	N(1)-C(1)-C(2)	110.3(4)
C(29)-H(29)	0.9500	N(1)-C(1)-C(10)	122.0(4)
C(30)-C(31)	1.380(6)	C(2)-C(1)-C(10)	127.7(4)
C(30)-N(5)	1.460(6)	C(3)-C(2)-C(1)	107.0(4)
C(31)-C(32)	1.373(6)	C(3)-C(2)-C(11)	127.3(4)
C(31)-H(31)	0.9500	C(1)-C(2)-C(11)	125.6(4)
C(32)-H(32)	0.9500	C(2)-C(3)-C(4)	107.2(4)
C(34)-O(2)	1.237(5)	C(2)-C(3)-C(13)	123.6(4)
C(34)-N(3)	1.317(5)	C(4)-C(3)-C(13)	129.2(4)
C(35)-N(3)	1.464(6)	C(5)-C(4)-N(1)	120.0(4)
C(35)-C(36)	1.477(7)	C(5)-C(4)-C(3)	132.0(4)
C(35)-H(35A)	0.9900	N(1)-C(4)-C(3)	107.9(4)
C(35)-H(35B)	0.9900	C(4)-C(5)-C(6)	121.9(4)
C(36)-N(4A)	1.384(8)	C(4)-C(5)-C(18)	118.6(4)

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C(6)-C(5)-C(18)	119.4(4)	C(7)-C(14)-H(14B)	109.5
C(5)-C(6)-N(2)	119.9(4)	H(14A)-C(14)-H(14B)	109.5
C(5)-C(6)-C(7)	132.3(4)	C(7)-C(14)-H(14C)	109.5
N(2)-C(6)-C(7)	107.8(4)	H(14A)-C(14)-H(14C)	109.5
C(8)-C(7)-C(6)	107.2(4)	H(14B)-C(14)-H(14C)	109.5
C(8)-C(7)-C(14)	123.9(4)	C(16)-C(15)-C(8)	113.8(4)
C(6)-C(7)-C(14)	128.8(4)	C(16)-C(15)-H(15A)	108.8
C(7)-C(8)-C(9)	107.3(4)	C(8)-C(15)-H(15A)	108.8
C(7)-C(8)-C(15)	127.2(4)	C(16)-C(15)-H(15B)	108.8
C(9)-C(8)-C(15)	125.5(4)	C(8)-C(15)-H(15B)	108.8
N(2)-C(9)-C(8)	109.7(4)	H(15A)-C(15)-H(15B)	107.7
N(2)-C(9)-C(17)	122.1(4)	C(15)-C(16)-H(16A)	109.5
C(8)-C(9)-C(17)	128.1(4)	C(15)-C(16)-H(16B)	109.5
C(1)-C(10)-H(10A)	109.5	H(16A)-C(16)-H(16B)	109.5
C(1)-C(10)-H(10B)	109.5	C(15)-C(16)-H(16C)	109.5
H(10A)-C(10)-H(10B)	109.5	H(16A)-C(16)-H(16C)	109.5
C(1)-C(10)-H(10C)	109.5	H(16B)-C(16)-H(16C)	109.5
H(10A)-C(10)-H(10C)	109.5	C(9)-C(17)-H(17A)	109.5
H(10B)-C(10)-H(10C)	109.5	C(9)-C(17)-H(17B)	109.5
C(2)-C(11)-C(12)	112.7(4)	H(17A)-C(17)-H(17B)	109.5
C(2)-C(11)-H(11A)	109.1	C(9)-C(17)-H(17C)	109.5
C(12)-C(11)-H(11A)	109.1	H(17A)-C(17)-H(17C)	109.5
C(2)-C(11)-H(11B)	109.1	H(17B)-C(17)-H(17C)	109.5
C(12)-C(11)-H(11B)	109.1	C(23)-C(18)-C(19)	119.7(4)
H(11A)-C(11)-H(11B)	107.8	C(23)-C(18)-C(5)	118.4(4)
C(11)-C(12)-H(12A)	109.5	C(19)-C(18)-C(5)	121.9(4)
C(11)-C(12)-H(12B)	109.5	C(20)-C(19)-C(18)	120.0(4)
H(12A)-C(12)-H(12B)	109.5	C(20)-C(19)-H(19)	120.0
C(11)-C(12)-H(12C)	109.5	C(18)-C(19)-H(19)	120.0
H(12A)-C(12)-H(12C)	109.5	C(19)-C(20)-C(21)	120.5(4)
H(12B)-C(12)-H(12C)	109.5	C(19)-C(20)-H(20)	119.8
C(3)-C(13)-H(13A)	109.5	C(21)-C(20)-H(20)	119.8
C(3)-C(13)-H(13B)	109.5	C(22)-C(21)-C(20)	119.5(4)
H(13A)-C(13)-H(13B)	109.5	C(22)-C(21)-C(24)	122.6(4)
C(3)-C(13)-H(13C)	109.5	C(20)-C(21)-C(24)	117.9(4)
H(13A)-C(13)-H(13C)	109.5	C(21)-C(22)-C(23)	119.6(4)
H(13B)-C(13)-H(13C)	109.5	C(21)-C(22)-H(22)	120.2
C(7)-C(14)-H(14A)	109.5	C(23)-C(22)-H(22)	120.2

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C(18)-C(23)-C(22)	120.7(4)	N(3)-C(34)-C(25)	116.3(3)
C(18)-C(23)-H(23)	119.6	N(3)-C(35)-C(36)	111.3(4)
C(22)-C(23)-H(23)	119.6	N(3)-C(35)-H(35A)	109.4
O(1)-C(24)-N(6)	122.1(3)	C(36)-C(35)-H(35A)	109.4
O(1)-C(24)-C(21)	121.1(4)	N(3)-C(35)-H(35B)	109.4
N(6)-C(24)-C(21)	116.8(3)	C(36)-C(35)-H(35B)	109.4
N(6)-C(25)-C(34)	110.3(3)	H(35A)-C(35)-H(35B)	108.0
N(6)-C(25)-C(26)	109.8(3)	N(4A)-C(36)-C(35)	111.2(5)
C(34)-C(25)-C(26)	108.1(3)	N(4A)-C(36)-N(4B)	78.3(13)
N(6)-C(25)-H(25)	109.5	C(35)-C(36)-N(4B)	120.0(12)
C(34)-C(25)-H(25)	109.5	N(4A)-C(36)-H(36A)	109.4
C(26)-C(25)-H(25)	109.5	C(35)-C(36)-H(36A)	109.4
C(27)-C(26)-C(25)	112.6(3)	N(4B)-C(36)-H(36A)	31.3
C(27)-C(26)-H(26A)	109.1	N(4A)-C(36)-H(36B)	109.4
C(25)-C(26)-H(26A)	109.1	C(35)-C(36)-H(36B)	109.4
C(27)-C(26)-H(26B)	109.1	N(4B)-C(36)-H(36B)	123.1
C(25)-C(26)-H(26B)	109.1	H(36A)-C(36)-H(36B)	108.0
H(26A)-C(26)-H(26B)	107.8	Cl(1A)-C(37A)-Cl(2A)	110.1(5)
C(28)-C(27)-C(32)	118.8(4)	Cl(1A)-C(37A)-H(37A)	109.6
C(28)-C(27)-C(26)	120.4(4)	Cl(2A)-C(37A)-H(37A)	109.6
C(32)-C(27)-C(26)	120.8(4)	Cl(1A)-C(37A)-H(37B)	109.6
C(29)-C(28)-C(27)	121.2(4)	Cl(2A)-C(37A)-H(37B)	109.6
C(29)-C(28)-H(28)	119.4	H(37A)-C(37A)-H(37B)	108.2
C(27)-C(28)-H(28)	119.4	Cl(2B)-C(37B)-Cl(1B)	114(2)
C(28)-C(29)-C(30)	118.5(4)	Cl(2B)-C(37B)-H(37C)	108.8
C(28)-C(29)-H(29)	120.7	Cl(1B)-C(37B)-H(37C)	108.8
C(30)-C(29)-H(29)	120.7	Cl(2B)-C(37B)-H(37D)	108.8
C(31)-C(30)-C(29)	121.7(4)	Cl(1B)-C(37B)-H(37D)	108.8
C(31)-C(30)-N(5)	119.3(4)	H(37C)-C(37B)-H(37D)	107.7
C(29)-C(30)-N(5)	119.1(4)	C(1)-N(1)-C(4)	107.6(4)
C(32)-C(31)-C(30)	119.1(4)	C(1)-N(1)-B(1)	127.0(3)
C(32)-C(31)-H(31)	120.4	C(4)-N(1)-B(1)	125.3(4)
C(30)-C(31)-H(31)	120.4	C(9)-N(2)-C(6)	107.9(4)
C(31)-C(32)-C(27)	120.6(4)	C(9)-N(2)-B(1)	126.7(3)
C(31)-C(32)-H(32)	119.7	C(6)-N(2)-B(1)	125.4(4)
C(27)-C(32)-H(32)	119.7	C(34)-N(3)-C(35)	121.6(4)
O(2)-C(34)-N(3)	123.8(4)	C(34)-N(3)-H(3)	119.2
O(2)-C(34)-C(25)	119.9(3)	C(35)-N(3)-H(3)	119.2

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C(36)-N(4A)-H(4A1)	120.0
C(36)-N(4A)-H(4A2)	120.0
H(4A1)-N(4A)-H(4A2)	120.0
C(36)-N(4B)-H(4B1)	120.0
C(36)-N(4B)-H(4B2)	120.0
H(4B1)-N(4B)-H(4B2)	120.0
O(4)-N(5)-O(3)	122.9(4)
O(4)-N(5)-C(30)	118.8(4)
O(3)-N(5)-C(30)	118.3(4)
C(24)-N(6)-C(25)	121.5(3)
C(24)-N(6)-H(6)	119.3
C(25)-N(6)-H(6)	119.3
F(1)-B(1)-F(2)	108.7(3)
F(1)-B(1)-N(2)	110.6(4)
F(2)-B(1)-N(2)	109.9(4)
F(1)-B(1)-N(1)	110.8(4)
F(2)-B(1)-N(1)	109.4(4)
N(2)-B(1)-N(1)	107.4(3)

Table 2. Hydrogen bonds for **11** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3)...O(1)#1	0.88	2.01	2.886(4)	172.2
N(4B)-H(4B2)...Cl(2B)#1	0.88	2.55	3.31(3)	143.8
N(6)-H(6)...O(2)#2	0.88	2.08	2.941(4)	166.5

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y,-z+3 #2 -x+2,-y,-z+3

Notes

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