Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary information

BODIPY-picolinium-cation conjugate as a blue-light-responsive caged group

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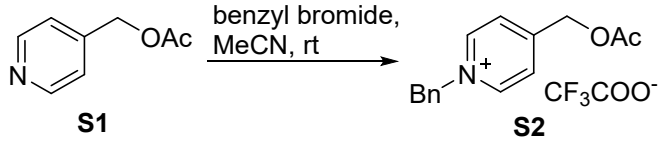
1. General Information

Proton nuclear magnetic resonance spectra (^{1}H NMR) and carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a JEOL JNM-ECZ500R spectrometer. Chemical shifts (δ) are reported in parts per million relative to the internal standard, tetramethylsilane. Elemental analysis was performed with a MICRO CORDER JM11, and all values were within ±0.4 % of the calculated values. Ultraviolet-visible-light absorption spectra were recorded on an Agilent 8453 spectrometer. Fluorescence spectra were recorded on an RF-5300 PC (Shimadzu). Irradiation was conducted with LEDs (CL-1501, Asahi Spectra). All other reagents and solvents were purchased from Aldrich, Tokyo Kasei Kogyo, FUJIFILM Wako Pure Chemical Corp., Nacalai Tesque, Kanto Kagaku, Kishida Kagaku, Junsei Kagaku or Dojindo, and used without purification. Flash column chromatography was performed using Silica Gel 60 (particle size 0.046–0.063 mm) supplied by Taiko-shoji (Kiyosu, Aichi, Japan). Photoirradiation was performed by using the light source of a Xe lamp MAX-302 (Asahi Spectra) or CL-1501 equipped with a 505 nm LED head (Asahi SPectra).

2. Experimental Section

Synthesis of **S2**

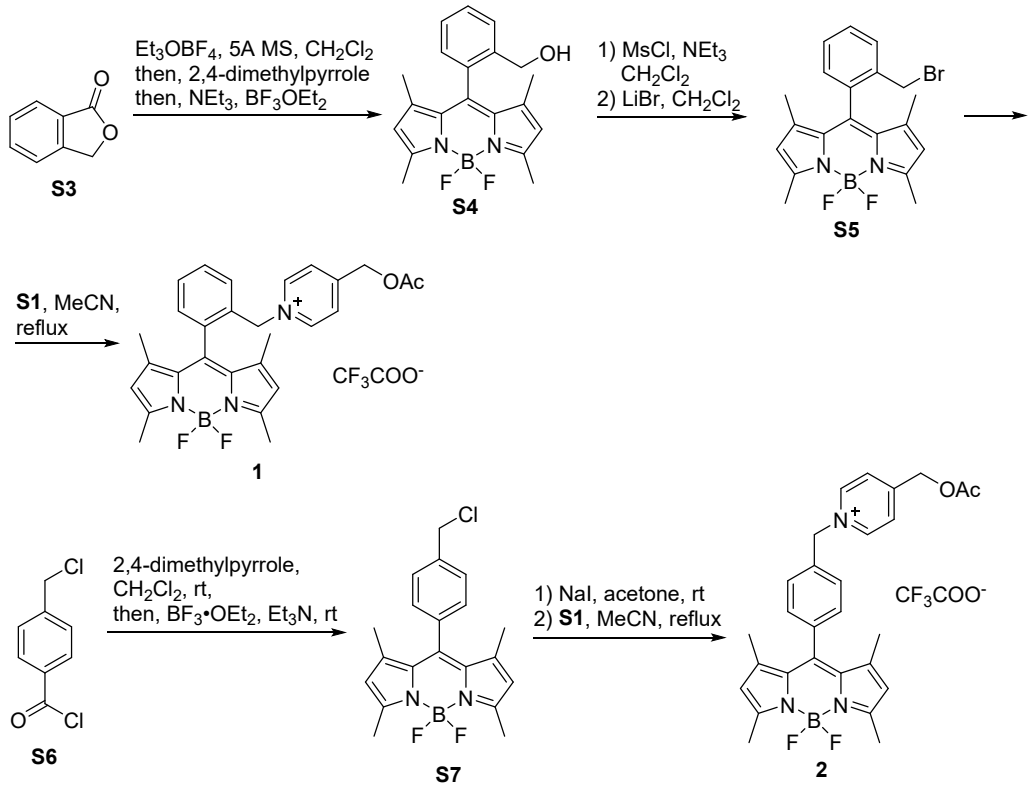


S1 **S2**

Synthesis of **S1**: **S1** was synthesized according to *Tetrahedron Letters* **2020**, *61*, 152123.

Synthesis of **S2**: To a solution of **S1** (148 mg, 0.979 mmol) in MeCN (10 mL) was added benzyl bromide (176 μL, 1.47 mmol, 1.50 equiv.). The reaction mixture was stirred at room temperature for 18 hrs. After evaporation *in vacuo*, the residue was purified by preparative HPLC to afford **S2** (120 mg, 0.353 mmol, 36%) as a white solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 30–100% (0–30 min), 100–100% (30–35 min), 100–30% (35–36 min), 30–30% (36–60 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 2.16 (3H, s), 5.31 (2H, s), 5.78 (2H, s), 7.42 (5H, m), 7.95 (2H, d, J = 6.3 Hz), 8.97 (2H, d, J = 6.4 Hz); ^{13}C-NMR (CD_3OD, 125 MHz, δ; ppm) 20.35, 62.94, 64.78, 125.83, 129.26, 129.89, 130.38, 132.09, 144.39, 157.02, 160.55, 160.85, 170.21; Purity by HPLC: 97% (254 nm); HRMS (ESI^+): calcd: 242.11810; found: 242.11571 $[M]^+$ (–9.90 ppm).

Synthesis of **3**: **3** was synthesized according to *J. Org. Chem.* **2011**, *76*, 7056.



Synthesis of **S4**: To a mixture of **S3** (673 mg, 5.02 mmol) and 5 Å MS (1.0 g) in dry CH_2Cl_2 (5 mL) was added 1 M Et_3OBF_4 in CH_2Cl_2 (5.0 mL, 5.0 mmol, 1.0 equiv.) under an argon balloon at room temperature. The reaction mixture was stirred at room temperature for 22 hrs, then cooled to 0 ºC, and 2,4-dimethylpyrrole (1.56 mL, 15.08 mmol, 3.0 equiv.) was added via a syringe pump (0.15 mL). When the addition was complete, the reaction mixture was allowed to room temperature and stirring was continued for a further 3 hrs. The reaction mixture was cooled to 0 ºC, then Et_3N (4.20 mL, 30.1 mmol, 6.0 equiv., 0.5 mL/min) was added, followed by BF_3OEt_2 (5.67 mL, 45.1 mmol, 9.0 equiv., 0.5 mL/min) via a syringe pump. When the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for a further 1.5 hrs. The mixture was filtered to remove 5 Å MS by washing with CH_2Cl_2 (150 mL), then the filtrate was washed with water (200 mL×2). The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo*, and purification of the residue by MPLC afforded 644 mg of a mixture of **S3** and **S4** as a dark red oil. The mixture was used for the next reaction without further purification.

Synthesis of **S5**: To a solution of the above mixture of **S3** and **S4** (664 mg) in CH_2Cl_2 (10 mL) was added Et_3N (523 µL, 3.75 mmol), followed by methanesulfonyl chloride (218 µL, 2.82 mmol) on ice water bath. The reaction mixture was stirred on ice water bath for 30 min, then the reaction was quenched with sat. $NaHCO_3$ (100 mL) and the mixture was extracted with CH_2Cl_2 three times. The organic layer was dried over Na_2SO_4. Filtration, and evaporation gave a mesylated intermediate, which was dissolved in CH_2Cl_2 (10 mL). To this solution was added lithium bromide (1637 mg, 18.9 mmol). The reaction mixture was stirred at room temperature for 17 hrs, then the reaction was quenched with water (100 mL), and the mixture was extracted with CH_2Cl_2 three times. The organic layer was dried over Na_2SO_4. Filtration, evaporation, and purification of the residue by MPLC gave 189 mg of **S4** as a red solid (9% from phthalide); ^{1}H NMR ($CDCl_3$, 500 MHz, δ;

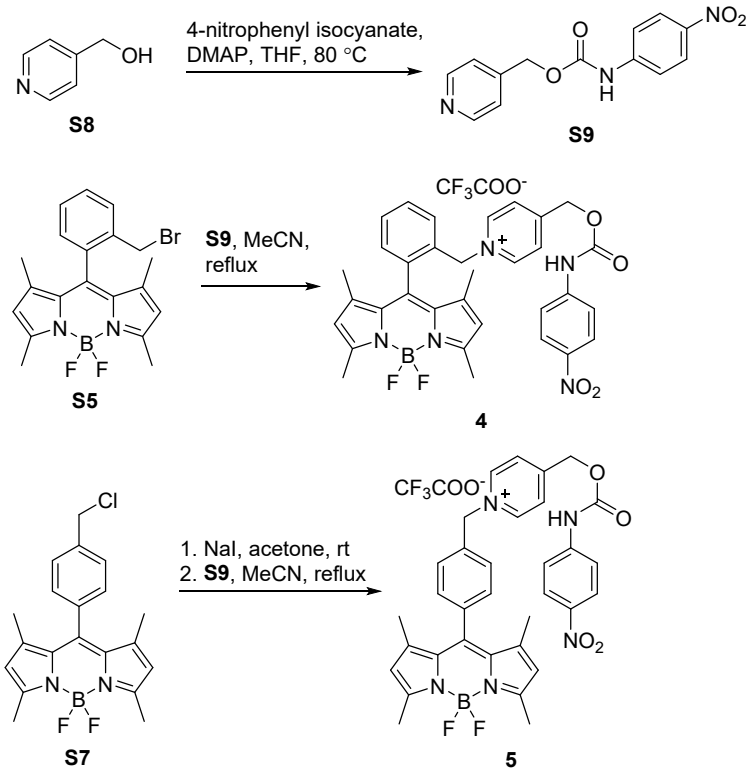
ppm) 7.66 (1H, d, J = 7.4 Hz), 7.50 (1H, ddd, J = 1.3 Hz, 7.5 Hz, 7.5 Hz), 7.43 (1H, ddd, J = 1.2 Hz, 7.6 Hz, 7.6 Hz), 7.21 (1H, dd, J = 1.2 Hz, 7.5 Hz), 5.99 (2H, s), 4.42 (2H, s), 2.57 (6H, s), 1.39 (6H, s); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 14.78, 15.26, 122.07, 129.14, 129.85, 130.58, 131.66, 132.09, 134.76, 135.52, 138.97, 143.62, 156.71; HRMS (ESI^+): calcd: 417.09492; found: 417.09409 $[M]^+$ (–2.01 ppm).

Synthesis of **1**: To a solution of **S5** (22.3 mg, 0.0480 mmol) in MeCN (10 mL) was added **S1** (22.3 mg, 0.147 mmol, 3.07 equiv.). The reaction mixture was refluxed for 17 hrs, then filtered and the filtrate was evaporated *in vacuo*. The residue was purified by preparative HPLC to afford **1** (14.7 mg, 0.0251 mmol, 52%) as a red solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 30–100% (0–30 min), 100–100% (30–35 min), 100–30% (35–36 min), 30–30% (36–60 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 1.14 (6H, s), 2.20 (3H, s), 3.48 (6H, s), 5.30 (2H, s), 5.74 (2H, s), 6.11 (2H, s), 7.47 (1H, dd, J = 1.1 Hz, 7.4 Hz), 7.67 (1H, ddd, J = 1.2 Hz, 7.3 Hz, 7.3 Hz), 7.71 (1H, ddd, J = 1.3 Hz, 7.5 Hz, 7.5 Hz), 7.76 (2H, d, J = 6.8 Hz), 7.79 (1H, d, J = 7.2 Hz), 8.66 (2H, d, J = 6.9 Hz); ^{13}C-NMR (CD_3OD, 125 MHz, δ; ppm) 14.22, 14.72, 62.68, 63.37, 122.35, 124.10, 129.55, 129.89, 131.26, 131.33, 133.72, 135.06, 137.06, 142.62, 144.80, 156.60, 157.23, 169.82; Purity by HPLC: 96% (254 nm); HRMS (ESI^+): calcd: 488.23209; found: 488.23372 $[M]^+$ (3.34 ppm).

Synthesis of **S7**: To a solution of **S6** (201 mg, 1.07 mmol) in dry CH_2Cl_2 (20 ml) was added 2,4-dimethylpyrrole (200 µl, 1.99 mmol, 1.86 equiv.). The reaction mixture was stirred at room temperature under an argon balloon for 16.5 hrs, then Et_3N (697 µl, 5.00 mmol, 4.67 equiv.) was added, followed by BF_3OEt_2 (1.38 ml, 5.12 mmol, 4.79 equiv.). Stirring was continued for a further 30 min at room temperature, then the reaction was quenched with water and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* of the filtrate, and purification of the residue by silica gel flash chromatography (*n*-hexane : AcOEt = 4 : 1) gave **S6** (70.6 mg, 0.190 mmol, 18%) as an orange solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 1.38 (6H, s), 2.55 (6H, s), 4.66 (2H, s), 5.98 (2H, s), 7.29 (2H, d, J = 6.3 Hz), 7.53 (2H, d, J = 6.8 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 15.07, 15.19, 46.20, 95.26, 121.91, 129.01, 129.84, 131.91, 135.68, 139.17, 141.51, 143.61, 156.25, HRMS (ESI^+): calcd: 373.14544; found: 373.14445 $[M]^+$ (–2.64 ppm).

Synthesis of **2**: To a solution of **S7** (44.7 mg, 0.120 mmol) in acetone (10 mL) was added sodium iodide (79.0 mg, 0.527 mmol, 4.39 equiv.). The reaction mixture was stirred at room temperature for 18 hrs, then concentrated. The residue was dissolved into AcOEt and the solution was washed with water. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* of the filtrate gave the iodinated compound as a crude solid (23.9 mg). This was dissolved in MeCN (10 mL), and **S1** (100 µL, 0.737 mmol, 11.8 equiv.) was added to the solution. The reaction mixture was stirred at reflux temperature for 18 hrs, then concentrated *in vacuo*. The residue was purified by preparative HPLC to afford **2** (13.7 mg, 0.0193 mmol, 30%) as a red solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 30–100% (0–

30 min), 100–100% (30–35 min), 100–30% (35–36 min), 30–30% (36–60 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 1.36 (6H, s), 2.21 (3H, s), 2.48 (6H, s), 5.45 (2H, s), 5.94 (2H, s), 6.07 (2H, s), 7.47 (2H, d, *J* = 8.0 Hz), 7.66 (2H, d, *J* = 8.1 Hz), 8.13 (2H, d, *J* = 6.8 Hz), 9.07 (2H, d, *J* = 6.9 Hz); ^{13}C-NMR (CD_3OD, 125 MHz, δ; ppm) 14.60, 14.74, 20.43, 64.41, 64.80, 122.52, 126.28, 126.99, 130.85, 130.95, 132.37, 136.15, 138.05, 142.06, 144.33, 145.91, 157.21, 159.63, 171.73; Purity by HPLC: 96% (254 nm); HRMS (ESI^+): calcd: 488.23209; found: 488.23062 $[M]^+$ (–3.02 ppm).

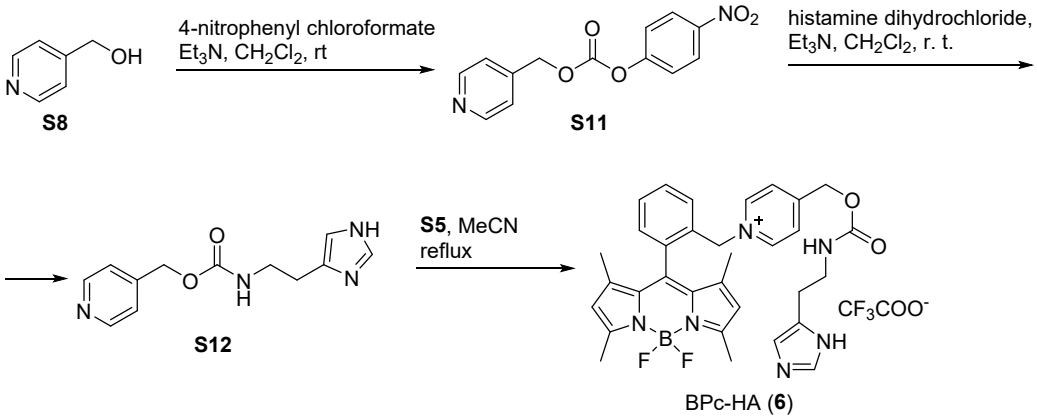


Synthesis of **S9**: To a solution of **S8** (213 mg, 1.96 mmol) in THF (10 mL) were added 4-nitrophenyl isocyanate (316 mg, 1.93 mmol, 0.985 equiv.) and DMAP (240 mg, 1.96 mmol, 1.00 equiv.). The reaction mixture was stirred at room temperature for 19 hrs, then the reaction was quenched with water and the whole was extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* of the filtrate, and purification of the residue by silica gel flash chromatography (AcOEt only) gave **S9** (244 mg, 0.894 mmol, 46%) as a white solid: ^{1}H-NMR (DMSO-d_6, 500 MHz, δ; ppm) 5.27 (2H, s), 7.43 (2H, d, *J* = 6.3 Hz), 7.72 (2H, d, *J* = 9.1 Hz), 8.23 (2H, d, *J* = 9.2 Hz), 8.60 (2H, d, *J* = 5.9 Hz); ^{13}C-NMR (DMSO-d_6, 125 MHz, δ; ppm) 64.61, 117.85, 121.98, 125.17, 141.91, 145.33, 145.46, 149.84, 152.92; HRMS (ESI^+): calcd: 274.08278; found: 274.08260 $[M]^+$ (–0.65 ppm).

Synthesis of **4**: To a solution of **S5** (32 mg, 0.0770 μmol) in MeCN (14 mL) was added **S9** (42 mg, 0.154 mmol, 2.0 equiv.). The reaction mixture was stirred at reflux temperature for 18 hrs, then concentrated. The residue was purified by preparative HPLC to afford **4** (5.1 mg, 9.2 μmol, 12%) as a red solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1%

TFA); B, MeCN (0.1% TFA), gradient; B conc. 30-80 (0-20 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 1.20 (6H, s), 2.51 (6H, s), 5.42 (2H, s), 5.71 (2H, s), 6.01 (2H, s), 7.45 (1H, d, J = 7.3 Hz), 7.77–7.70 (6H, m), 7.94 (1H, d, J = 7.6 Hz), 8.23 (2H, d, J = 9.2 Hz), 8.62 (2H, d, J = 6.5 Hz); ^{13}C-NMR (CD_3OD, 125 MHz, δ; ppm) 14.50, 14.73, 64.25, 64.69, 119.23, 123.43, 125.49, 125.54, 126.06, 131.22, 131.58, 132.65, 134.30, 136.66, 138.55, 144.01, 144.43, 145.84, 146.17, 154.03, 154.04, 158.48, 159.45, 159.51; Purity by HPLC: 95% (254 nm); HRMS (ESI^+): calcd: 610.24372; found: 610.25860 $[M]^+$ (+24.39 ppm).

Synthesis of **5**: To a solution of **S7** (55.0 mg, 0.148 mmol) in acetone (10 mL) was added sodium iodide (152 mg, 1.01 mmol, 6.82 equiv.). The reaction mixture was stirred at room temperature for 18 hrs, then evaporated *in vacuo*. The residue was suspended in AcOEt and the suspension was washed with water. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation *in vacuo* of the filtrate gave the iodinated compound as a crude solid. This was dissolved in MeCN (10 mL), and **S9** (57.2 mg, 0.210 mmol, 1.42 equiv.) was added to the solution. The reaction mixture was stirred at reflux temperature for 18 hrs, then evaporated *in vacuo*. The residue was purified by preparative HPLC to afford **5** (47.0 mg, 0.0664 mmol, 45%) as a red solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 30–100% (0–30 min), 100–100% (30–35 min), 100–30% (35–36 min), 30–30% (36–60 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 1.34 (6H, s), 2.47 (6H, s), 5.57 (2H, s), 5.95 (2H, s), 6.04 (2H, s), 7.44 (2H, d, J = 8.2 Hz), 7.67 (2H, d, J = 8.3 Hz), 7.69 (2H, d, J = 9.3 Hz), 8.17–8.21 (4H, m), 9.11 (2H, d, J = 6.9 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 14.57, 14.68, 64.82, 65.10, 119.14, 122.48, 125.94, 126.82, 130.77, 130.92, 132.32, 136.14, 137.96, 142.01, 144.29, 145.95, 154.09, 157.13, 159.84; Purity by HPLC: 96% (254 nm); HRMS (ESI^+): calcd: 610.24372; found: 610.25858 $[M]^+$ (+24.36 ppm).

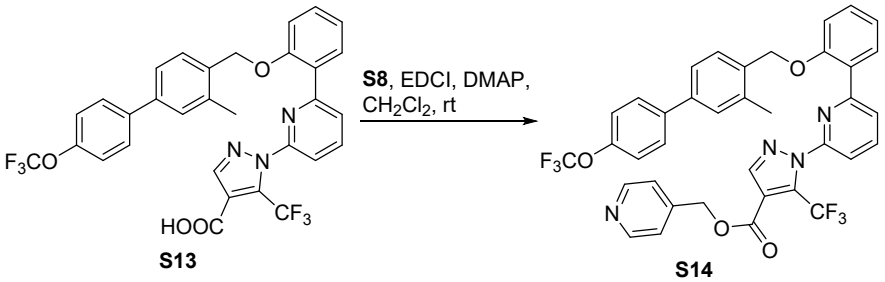


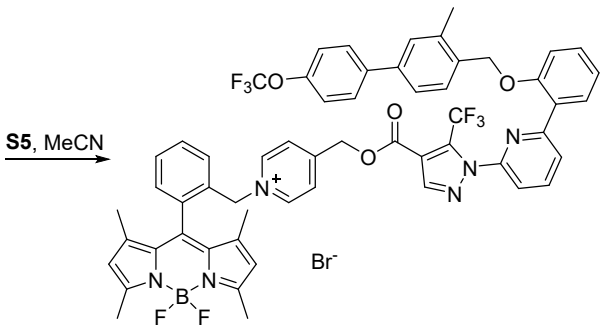
Synthesis of **S11**: To a solution of **S8** (528 mg, 4.85 mmol) in CH_2Cl_2 (10 mL) was added 4-nitrophenyl chloroformate (998 mg, 4.97 mmol, 1.02 equiv.) and Et_3N (693 μL, 5.00 mmol, 1.03 equiv.). The reaction mixture was stirred at room temperature for 18 hrs, then the reaction was quenched with water and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation *in vacuo* of the filtrate, and purification of the residue by silica gel flash chromatography (AcOEt only) gave **S11** (598 mg, 2.18 mmol, 45%) as a yellow solid: ^{1}H-NMR ($CDCl_3$, 500 MHz, δ; ppm) 5.32 (2H,

s), 7.34 (2H, d, J = 5.7 Hz), 7.41 (2H, d, J = 9.2 Hz), 8.30 (2H, d, J = 9.2 Hz), 8.68 (2H, dd, J = 1.7 Hz, 4.5 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 68.76, 121.84, 122.08, 125.52, 143.17, 145.69, 150.47, 152.43, 155.39; HRMS (ESI^+): calcd: 275.06680; found: 275.06727 $[M]^+$ (+1.74 ppm).

Synthesis of **S12**: To a solution of **S11** (78.3 mg, 0.286 mmol) in CH_2Cl_2 (10 ml) were added histamine dihydrochloride (52.5 mg, 0.285 mmol, 1.00 equiv.) and Et_3N (198 μL, 1.43 mmol, 5.00 equiv.). The reaction mixture was stirred at room temperature for 18 hrs. Evaporation *in vacuo*, and purification of the residue by silica gel flash chromatography (AcOEt only) gave **S11** (244 mg, 0.894 mmol, 46%) as a yellow solid; ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 2.79 (2H, t, J = 6.7 Hz), 3.38 (2H, t, J = 7.2 Hz), 5.13 (2H, s), 6.85 (1H, s), 7.36 (2H, d, J = 5.8 Hz), 7.59 (1H, s), 8.49 (2H, d, J = 6.2 Hz); ^{13}C-NMR (CD_3OD, 125 MHz, δ; ppm) 28.24, 41.82, 65.16, 118.00, 123.05, 135.88, 136.06, 149.42, 150.11, 158.21; HRMS (ESI^+): calcd: 247.11950; found: 247.11860 $[M]^+$ (–3.65 ppm).

Synthesis of BPc-HA (**6**): To a solution of **S5** (32.8 mg, 0.0786 mmol) in MeCN (14 mL) was added **S12** (42.2 mg, 0.157 mmol, 2.0 equiv.). The reaction mixture was stirred at reflux temperature for 18 hrs, then evaporated *in vacuo*. The residue was purified by preparative HPLC to afford BPc-HA (**6**, 9.2 mg, 0.0157 mmol, 20%) as a red solid. The HPLC conditions were follows: column; Inertsil ODS-3, 150 mm × Φ 4.6 mm, mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 30-80 (0-20 min); ^{1}H-NMR (CD_3OD, 500 MHz, δ; ppm) 1.20 (6H, s), 2.52 (6H, s), 2.96 (2H, t, J = 6.6 Hz), 3.49 (2H, t, J = 6.9 Hz), 5.25 (2H, s), 5.70 (2H, s), 6.01 (2H, s), 7.38 (1H, s), 7.45 (1H, dd, J = 1.3 Hz, 7.3 Hz), 7.64 (2H, d, J = 6.6 Hz), 7.71 (1H, ddd, J = 1.3 Hz, 7.5 Hz, 7.5 Hz), 7.75 (1H, ddd, J = 1.6 Hz, 7.5 Hz, 7.5 Hz), 7.93 (1H, d, J = 7.1 Hz), 8.57 (2H, d, J = 6.8 Hz), 8.82 (1H, d, J = 1.1 Hz); ^{13}C-NMR ($CDCl_3$, 125 MHz, δ; ppm) 14.52, 14.76, 26.19, 40.79, 64.26, 64.37, 117. 70, 123.43, 125.25, 131.23, 132.04, 132.60, 132.83, 134.32, 135.06, 136.57, 138.58, 144.01, 145.72, 157.44, 158.43, 160.08, 161.46, 161.77; Purity by HPLC: 96% (254 nm); HRMS (ESI^+): calcd: 583.28044; found: 583.28036 $[M]^+$ (–0.14 ppm).





BPc-GSK2181236A (**7**)

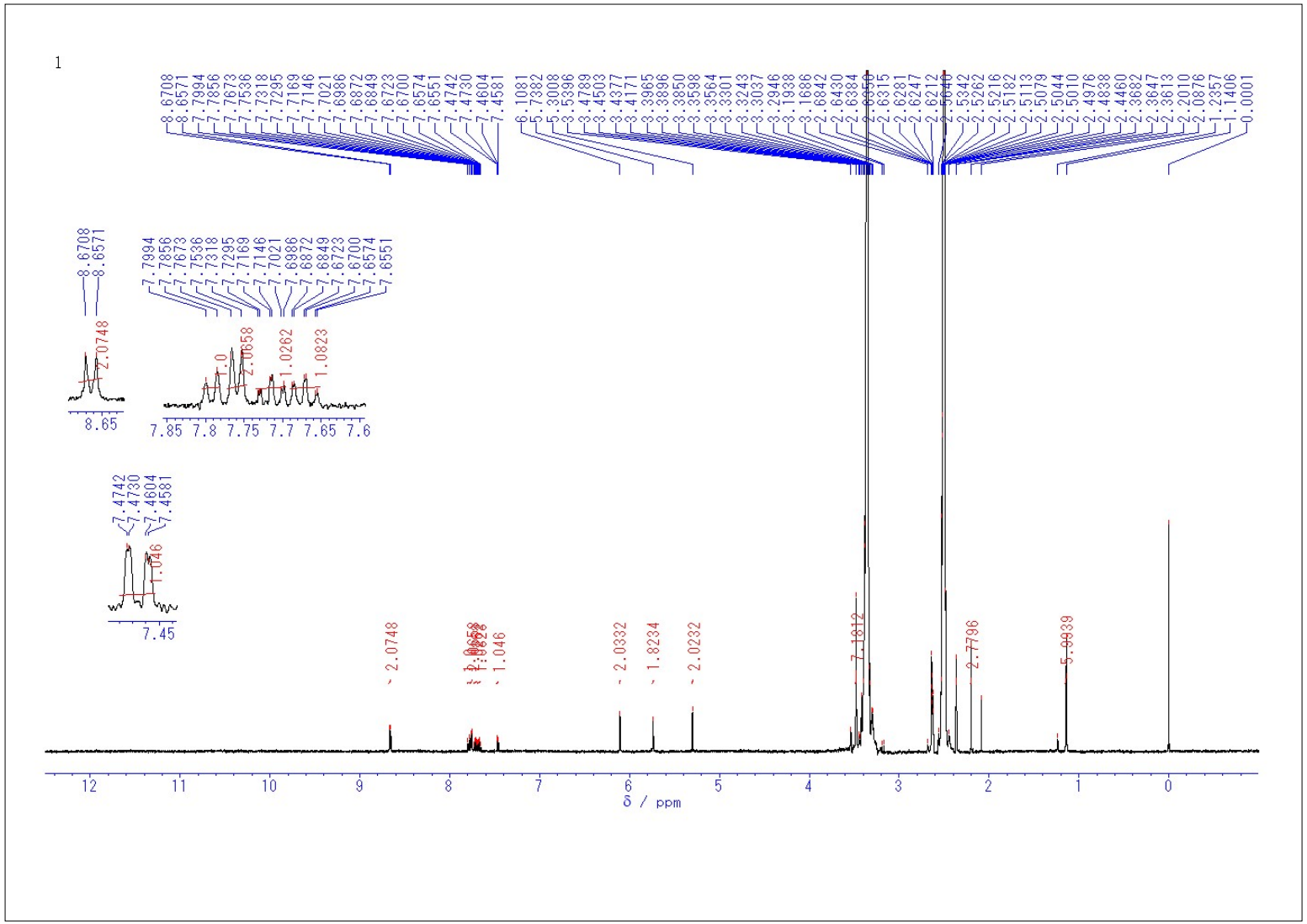
Synthesis of **S13**: **S13** was synthesized according to WO2009071504A1.

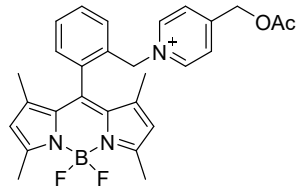
Synthesis of **S14**: To a solution of **S13** (61 mg, 0.0994 mmol), **S8** (13 mg, 0.119 mmol, 1.2 equiv.), and DMAP (12 mg, 0.0982 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL) was added EDCI (21 mg, 0.110 mmol, 1.1 equiv.). The reaction mixture was stirred at room temperature for an hour, then reaction was quenched with sat. NH_4Cl (20 mL) and the mixture was extracted with CH_2Cl_2 three times. The organic layer was washed with brine and dried over Na_2SO_4. Filtration, evaporation, and purification of the residue by MPLC gave 45 mg (64%) of **S14** as a clear oil; ^{1}H NMR ($CDCl_3$, 500 MHz, δ; ppm) 8.56 (2H, d, *J* = 6.3 Hz), 8.28 (1H, s), 8.10 (1H, d, *J* = 8.1 Hz), 7.97 (1H, dd, *J* = 8.0 Hz, 8.0 Hz), 7.83 (1H, dd, *J* = 1.7 Hz, 7.7 Hz), 7.68 (2H, d, *J* = 8.6 Hz), 7.61 (1H, d, *J* = 8.0 Hz), 7.51 (2H, d, *J* = 6.3 Hz), 7.46–7.41 (4H, m), 7.32 (2H, d, *J* = 8.0 Hz), 7.28 (1H, d, *J* = 8.1 Hz), 7.11 (1H, dd, *J* = 7.4 Hz, 7.4 Hz), 5.44 (2H, s), 5.23 (2H, s), 2.34 (3H, s); ^{13}C NMR ($CDCl_3$, 125 MHz, δ; ppm) 19.09, 27.81, 29.79, 65.15, 66.62, 69.15, 83.06, 113.36, 116.66, 116.85, 120.39, 121.32, 121.88, 121.91, 122.05, 124.75, 126.14, 127.65, 128.47, 128.86, 129.18, 130.95, 131.50, 132.72, 134.17, 136.89, 138.63, 139.55, 139.71, 142.68, 144.44, 144.91, 148.77, 150.07, 150.18, 151.01, 153.24, 155.20, 156.61, 160.69; HRMS (ESI^+): calcd: 705.19365; found: 705.19578 $[M]^+$ (+3.02 ppm).

Synthesis of BPc-GSK2181236A (**7**): A solution of **S14** (0.0639 mmol) and **S5** (0.0647 mmol, 1.0 equiv.) in MeCN (2 mL) was stirred at reflux temperature for 15 hrs. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by prep. HPLC (solvent A: 0.1& TFA MilliQ, solvent B: 0.1% TFA MeCN, 0 min, B 20% → 18 min, B 100% → 24 min, B 100% → 25 min, B 20% → 30 min, B 20%) to afford 26 mg (36%) of **7** as a red solid; ^{1}H NMR (CD_3OD, 500 MHz, δ; ppm) 8.63 (2H, d, *J* = 6.9 Hz), 8.39 (1H, s), 8.12 (1H, d, *J* = 8.1 Hz), 8.00 (1H, dd, *J* = 7.8 Hz), 7.93 (1H, d, *J* = 7.0 Hz), 7.84–7.79 (3H, m), 7.77–7.68 (4H, m), 7.64 (1H, d, *J* = 8.1 Hz), 7.47–7.39 (6H, m), 7.33–7.28 (4H, m), 7.10

(1H, dd, J = 6.8 Hz, 6.8 Hz), 6.01 (2H, s), 5.72 (2H, s), 5.57 (2H, s), 2.50 (6H, s), 2.34 (3H, s), 1.20 (6H, s); ^{13}C NMR (CD_3OD, 125 MHz, δ; ppm) 161.16, 158.49, 158.02, 156.83, 152.25, 150.00, 145.95, 144.03, 143.91, 141.25, 140.87, 140.34, 138.66, 138.54, 136.58, 135.78, 134.36, 134.26, 132.63, 132.14, 132.06, 131.60, 131.22, 130.39, 129.98, 129.62, 128.88, 127.64, 125.81, 125.59, 123.41, 123.05, 122.48, 122.41, 121.80, 121.02, 118.50, 117.13, 114.86, 70.32, 64.78, 64.34, 19.10, 14.76, 14.48, 14.18; HRMS (ESI^+): cald. 1041.35458; found 1041.35775 [M^+] (+3.04 ppm); Anal. Calcd. for $C_{57}H_{46}BBrF_8N_6O_4 \cdot 13/4H_2O$: C, 58.01; H, 4.48; N, 7.12. Found: C, 58.37; H, 4.18; N, 6.73.

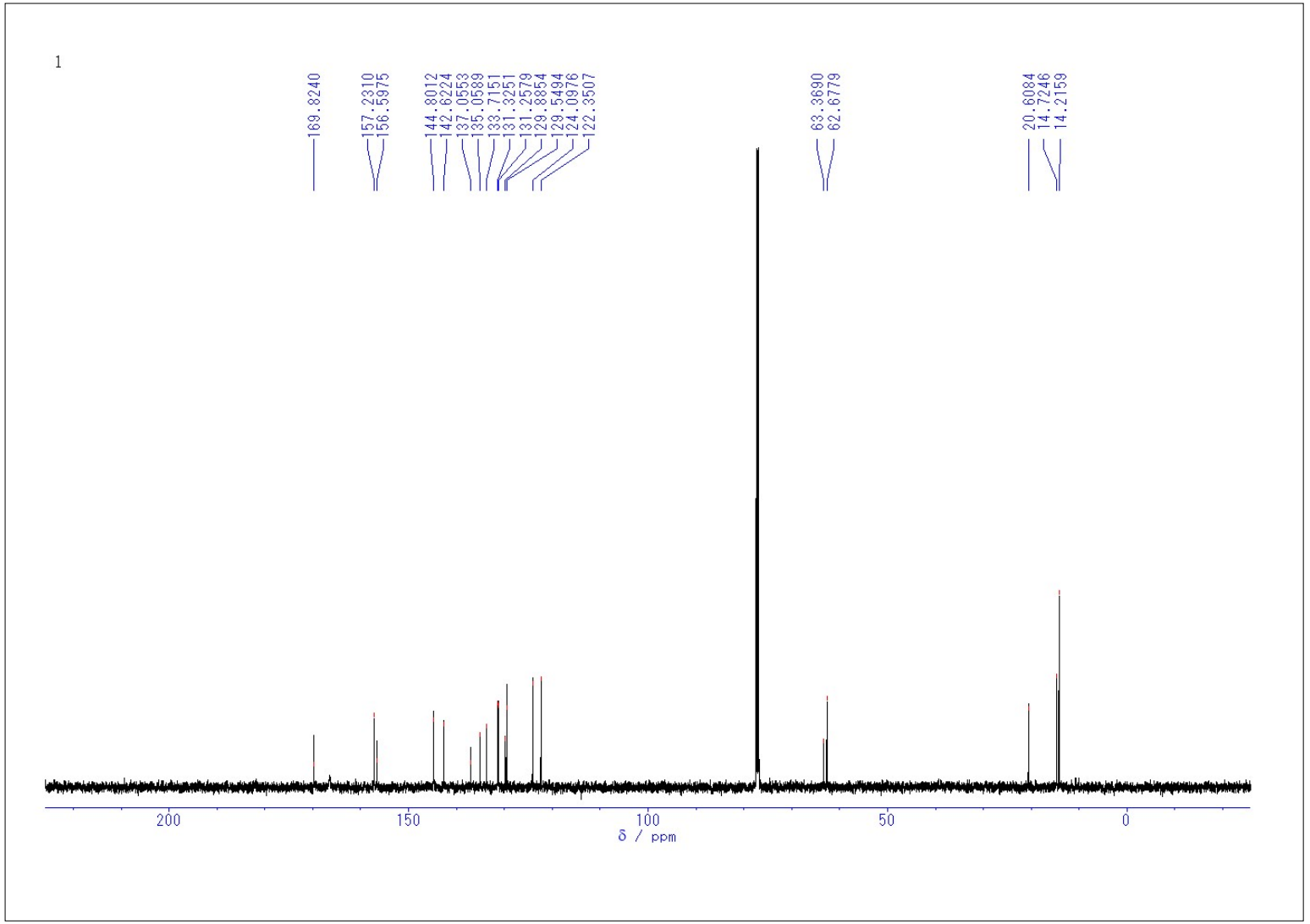
H NMR spectrum of **1**



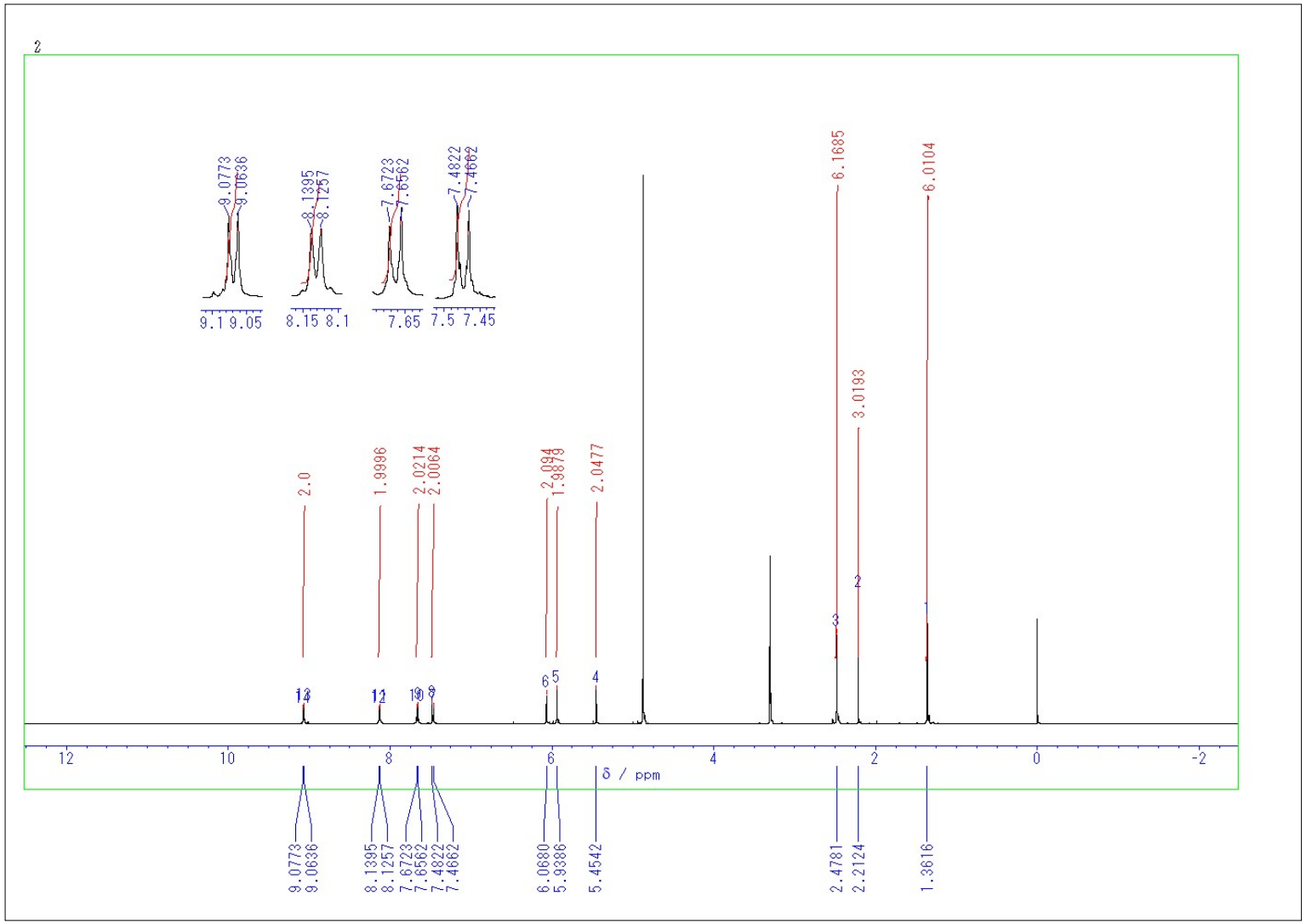


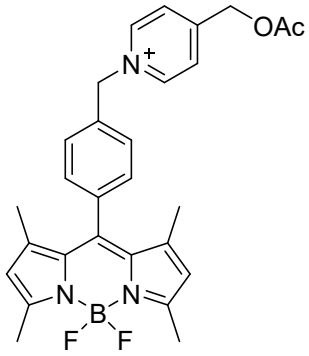
1

C NMR of **1**


1
169.8240
157.2310
156.5975
144.8012
142.6224
137.0553
135.0589
133.7151
131.3251
131.2579
129.8854
129.5494
124.0976
122.3507
63.3690
62.6779
20.6084
14.7246
14.2159
200
150
100
50
0
δ / ppm

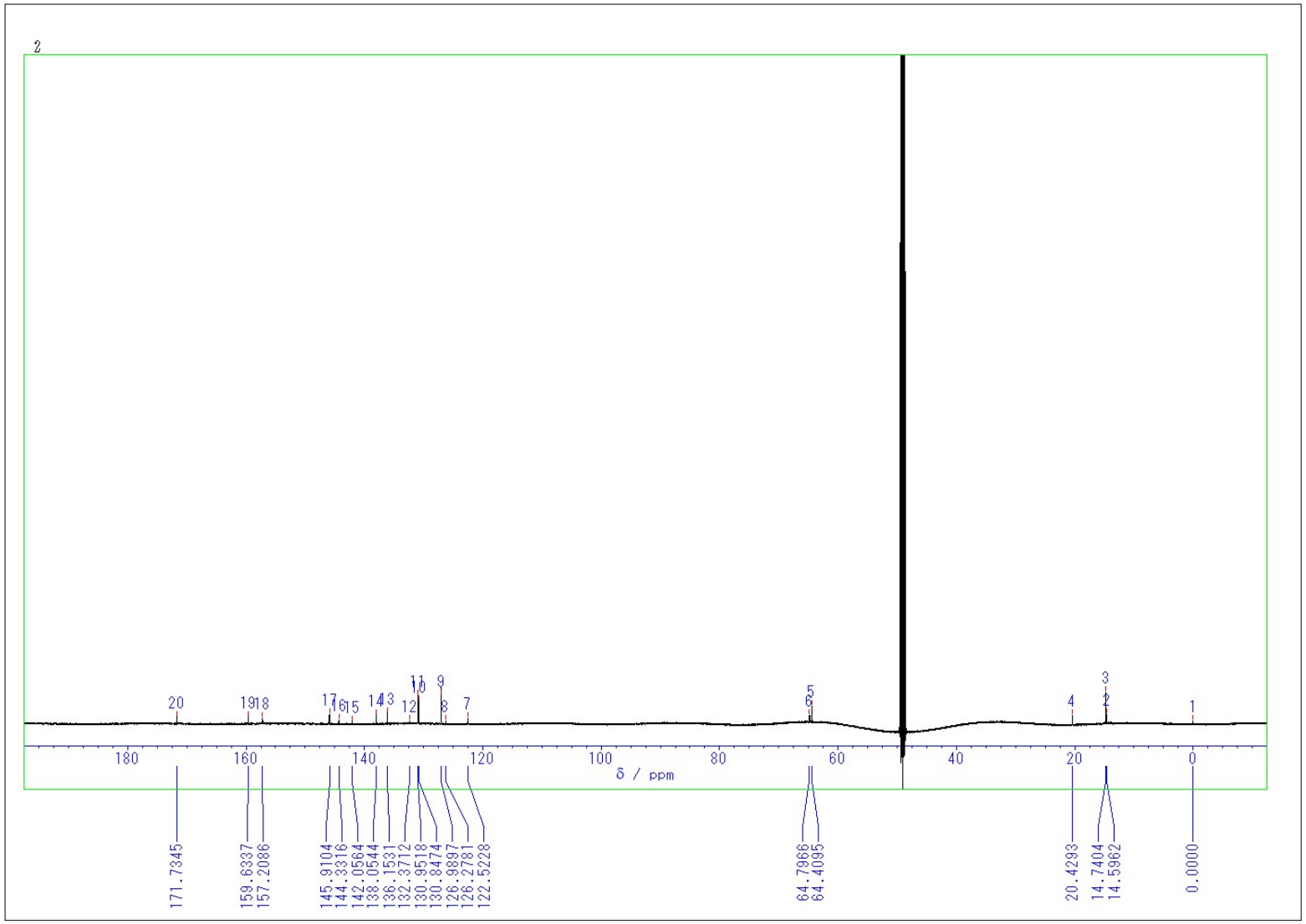
H NMR spectrum of **2**



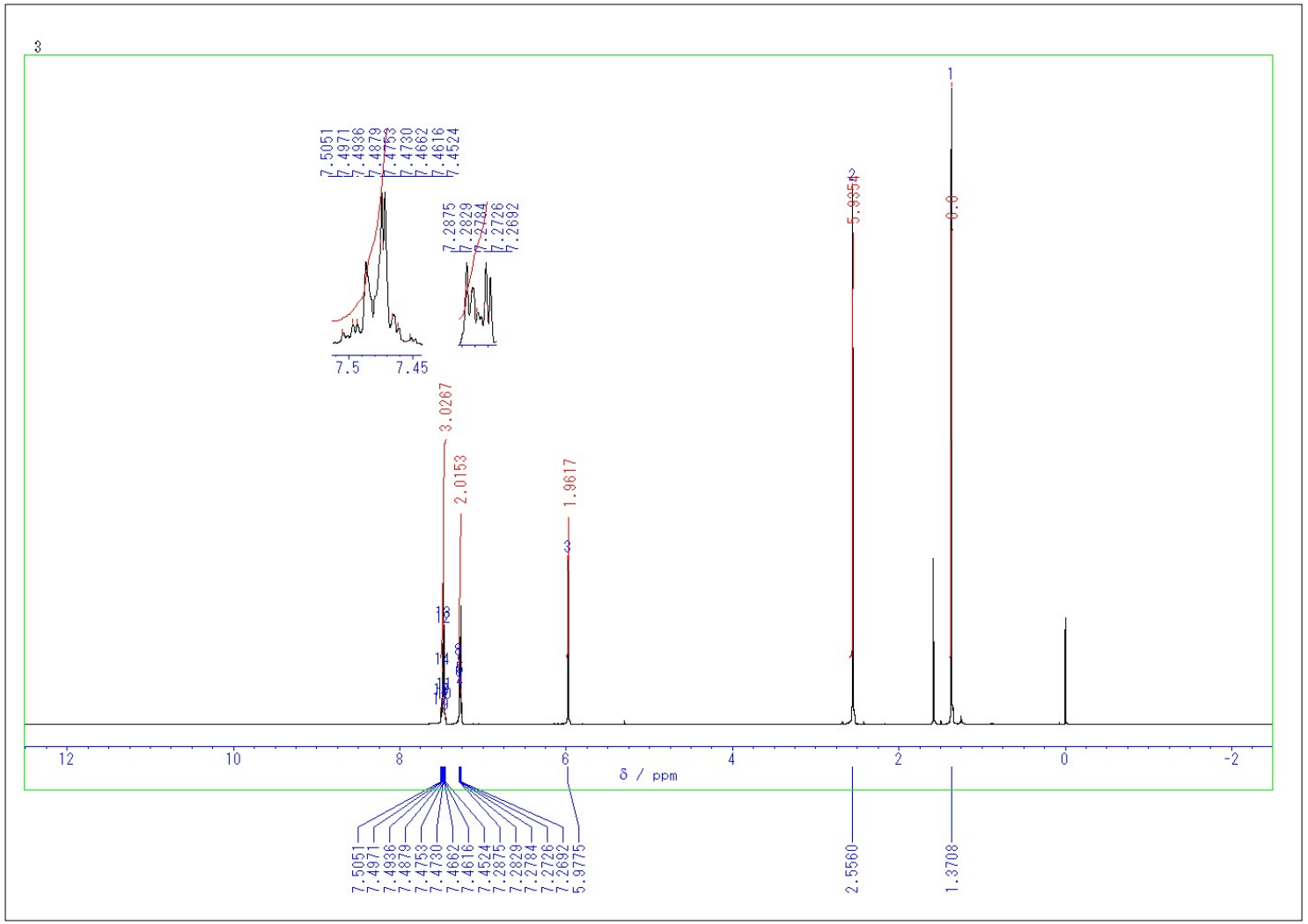


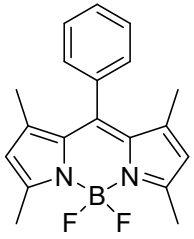
2

C NMR spectrum of **2**



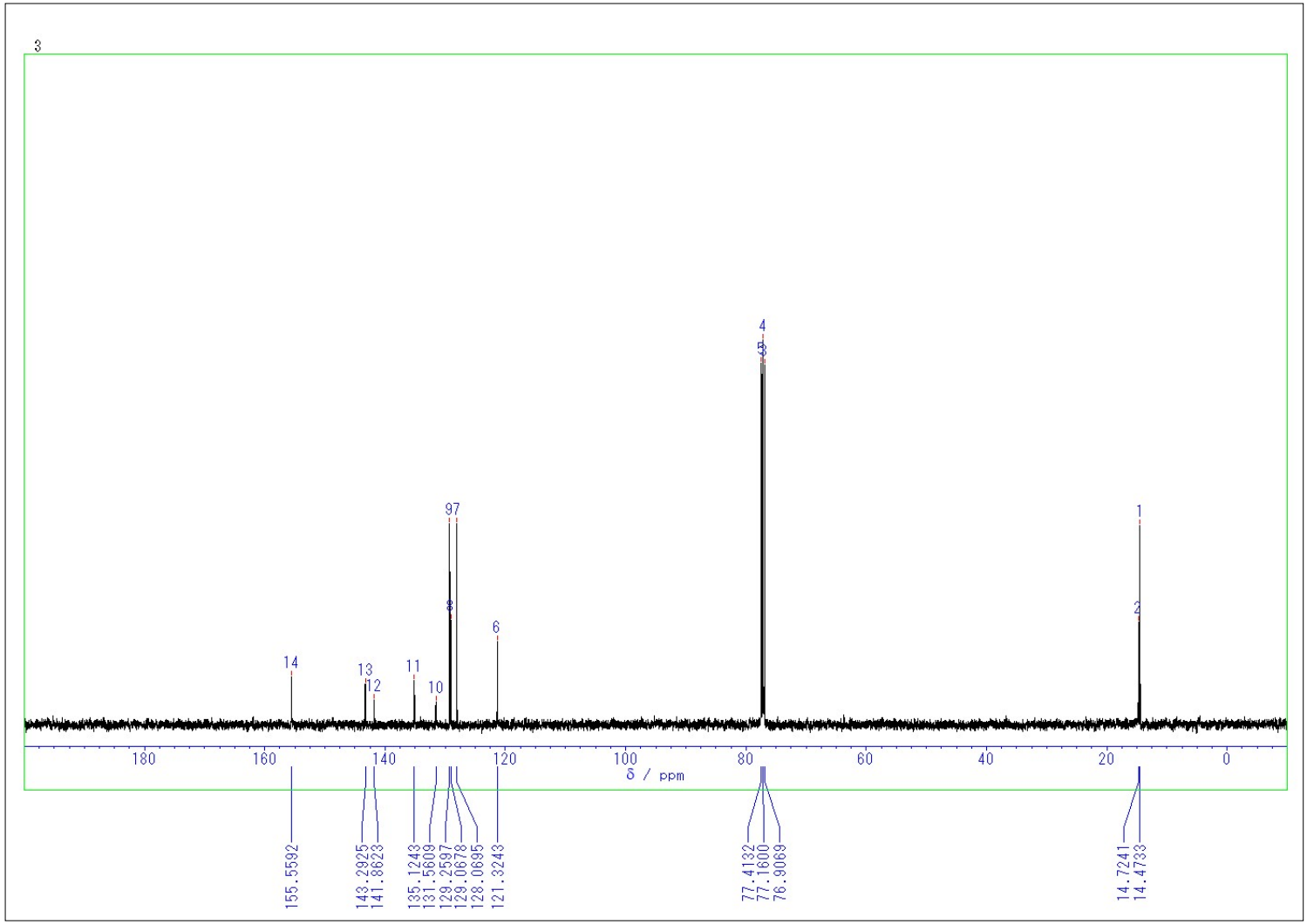
H NMR spectrum of **3**



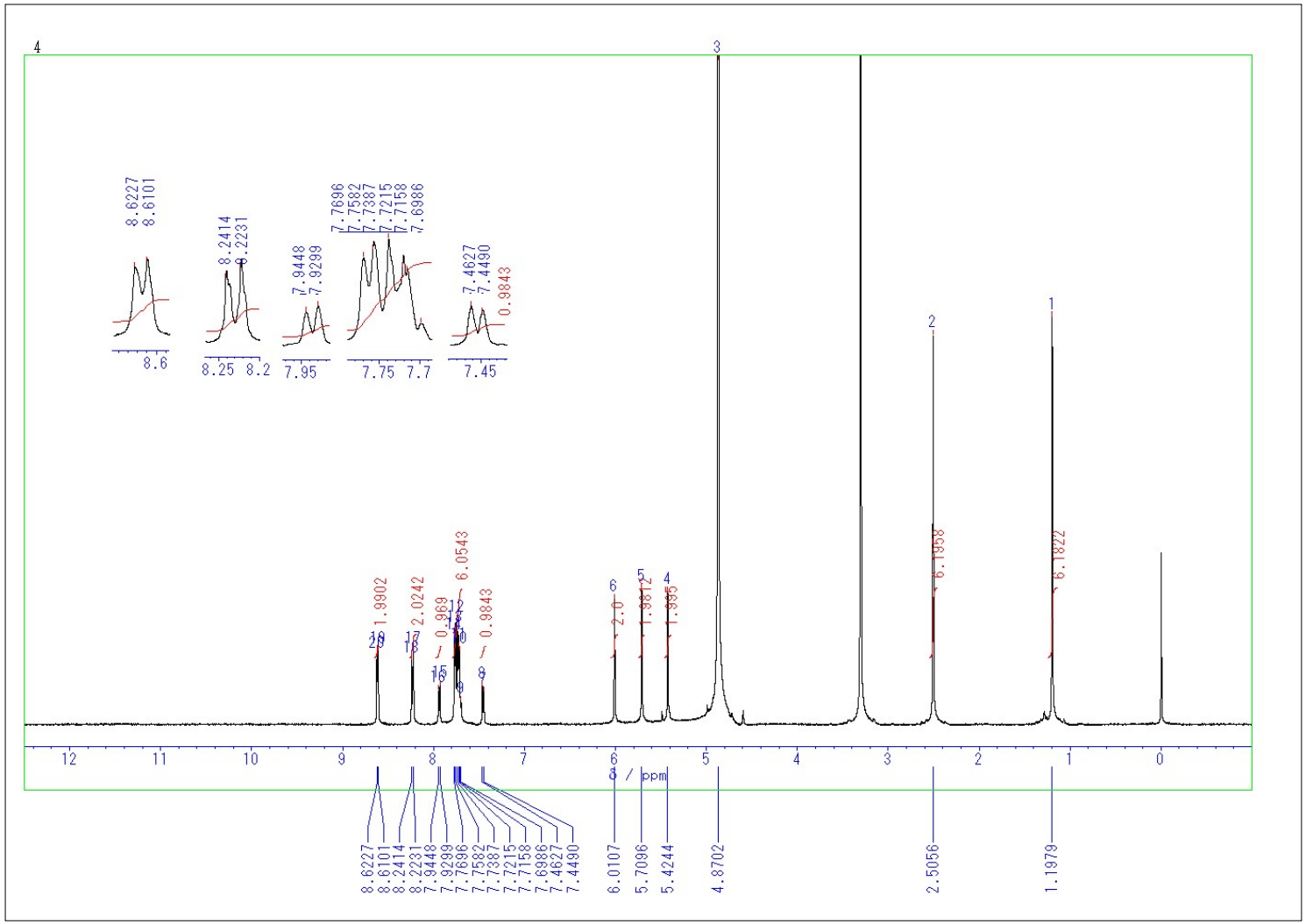


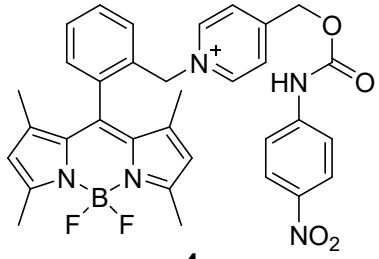
3

C NMR spectrum of **3**



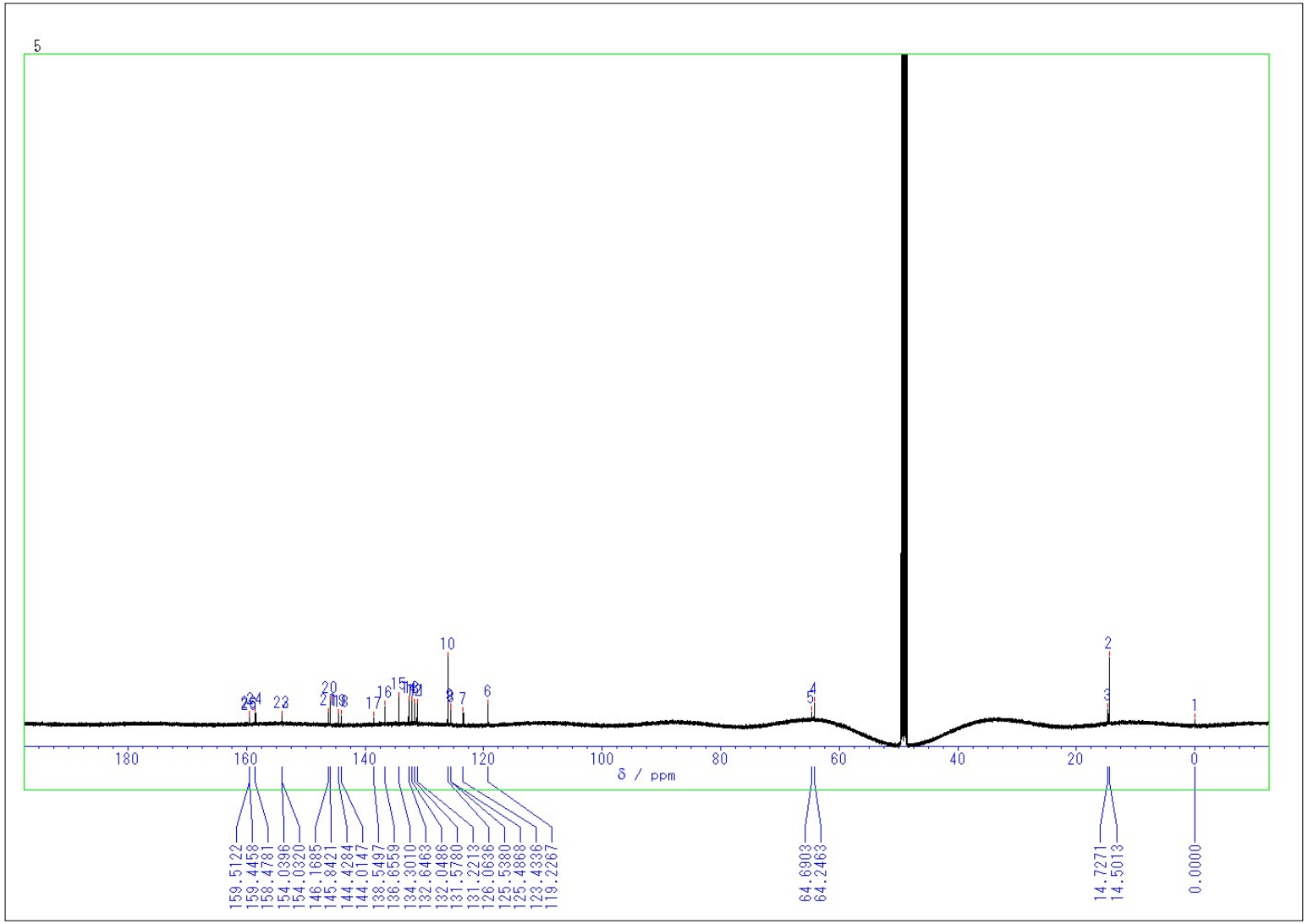
H NMR spectrum of **4**



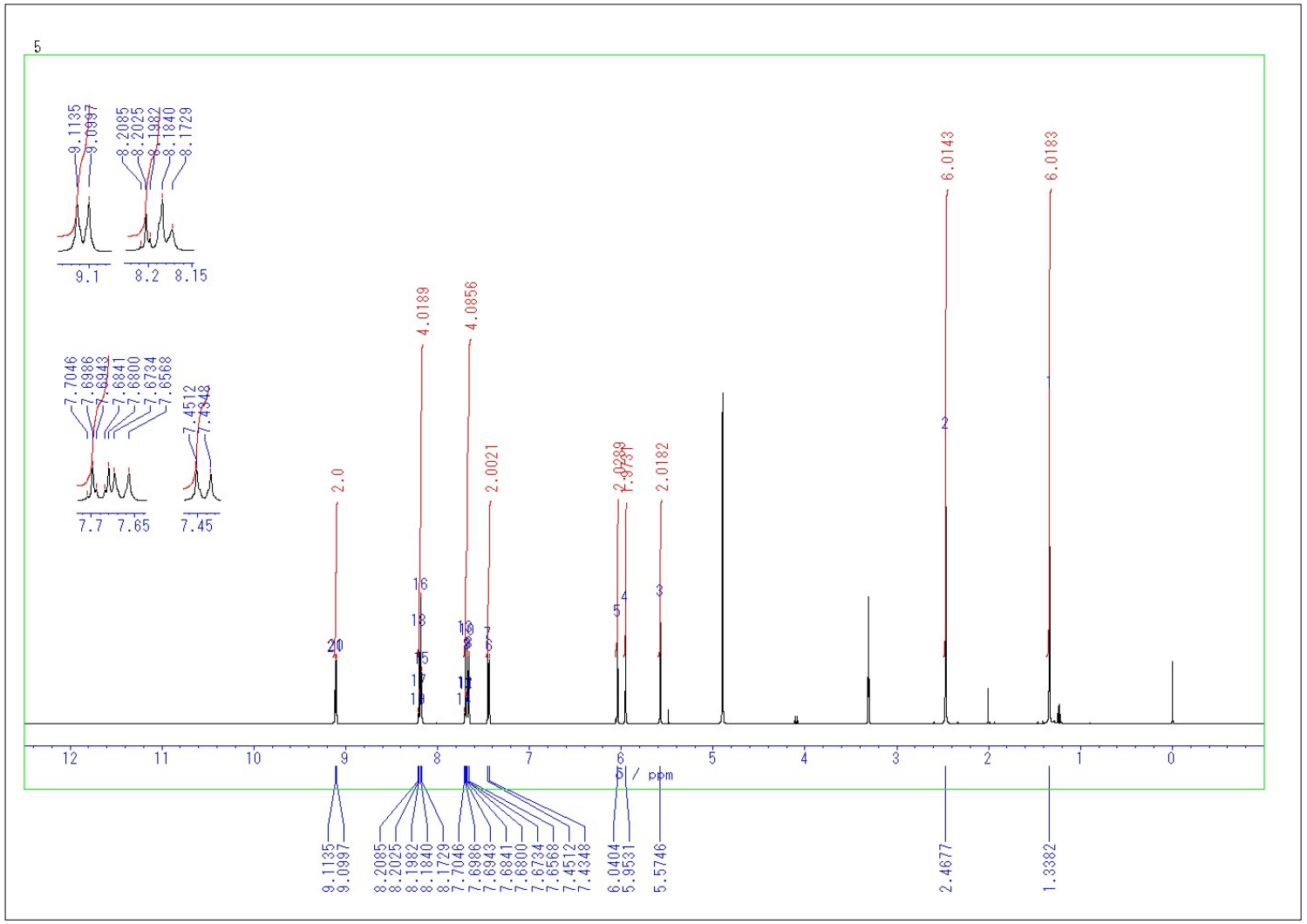


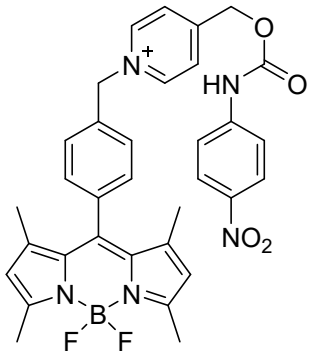
4

C NMR spectrum of **4**



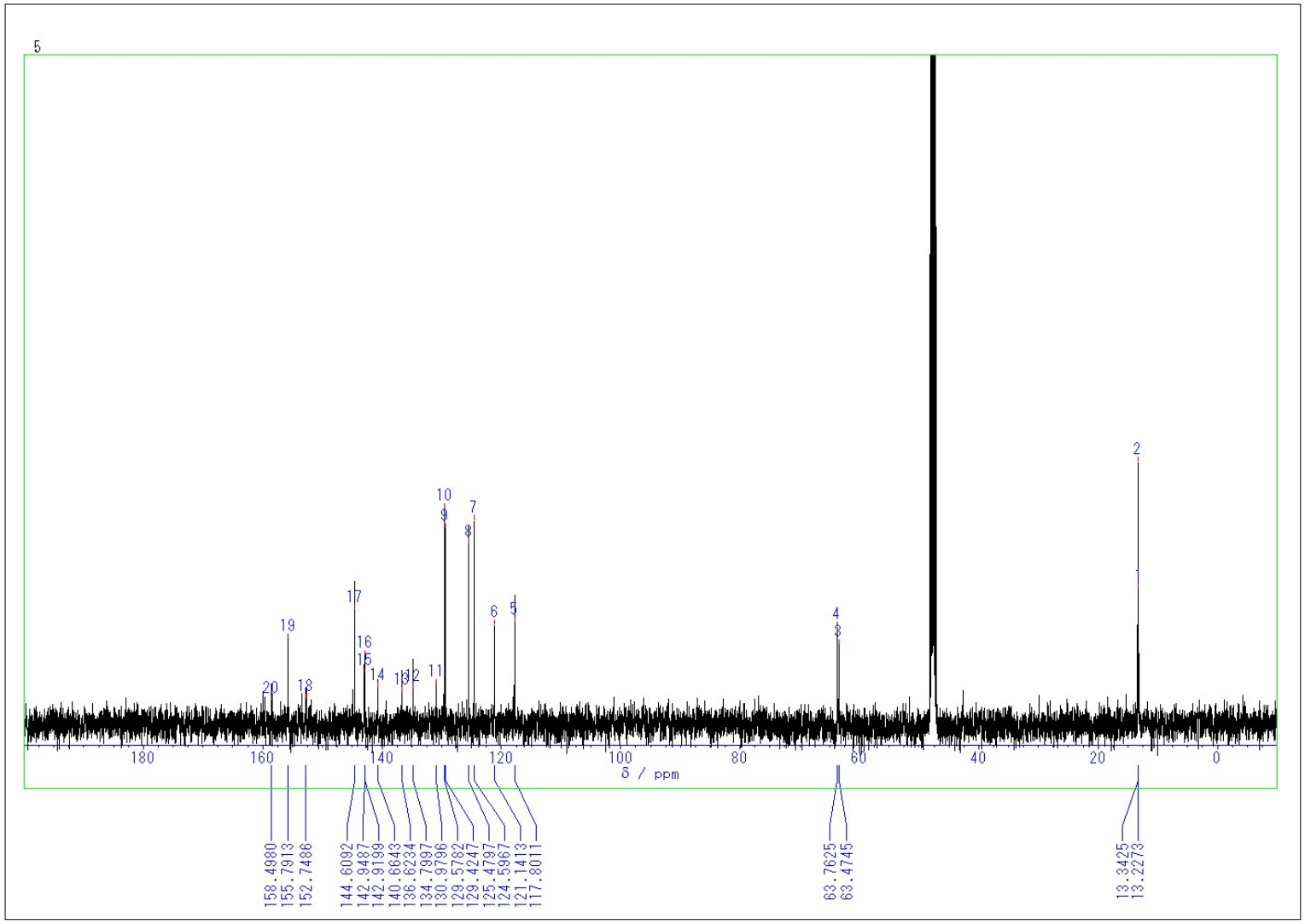
H NMR spectrum of **5**



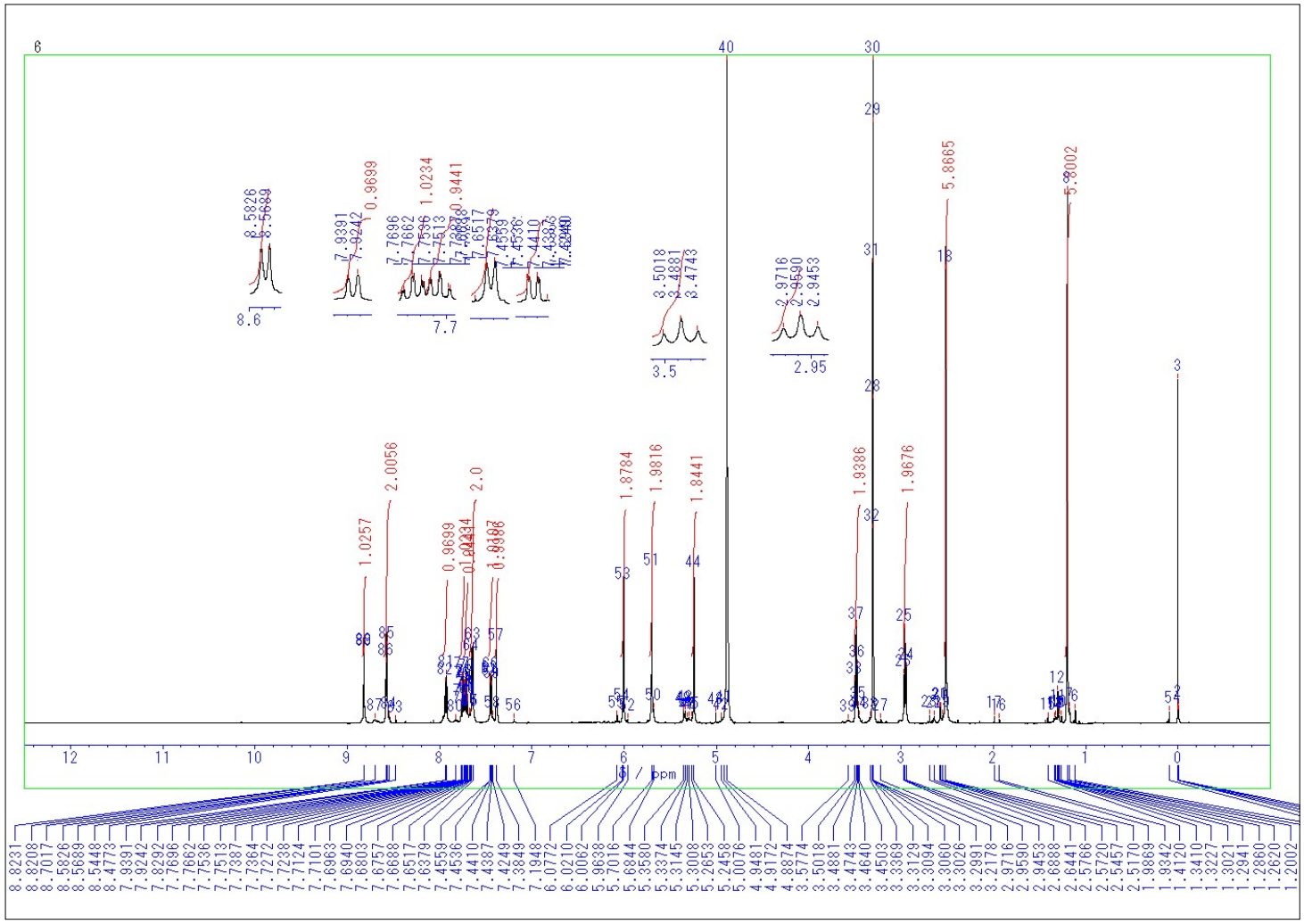


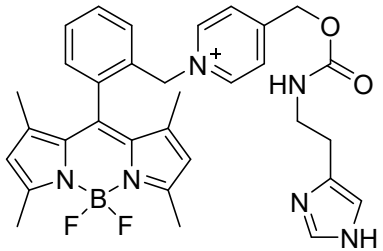
5

C NMR spectrum of **5**



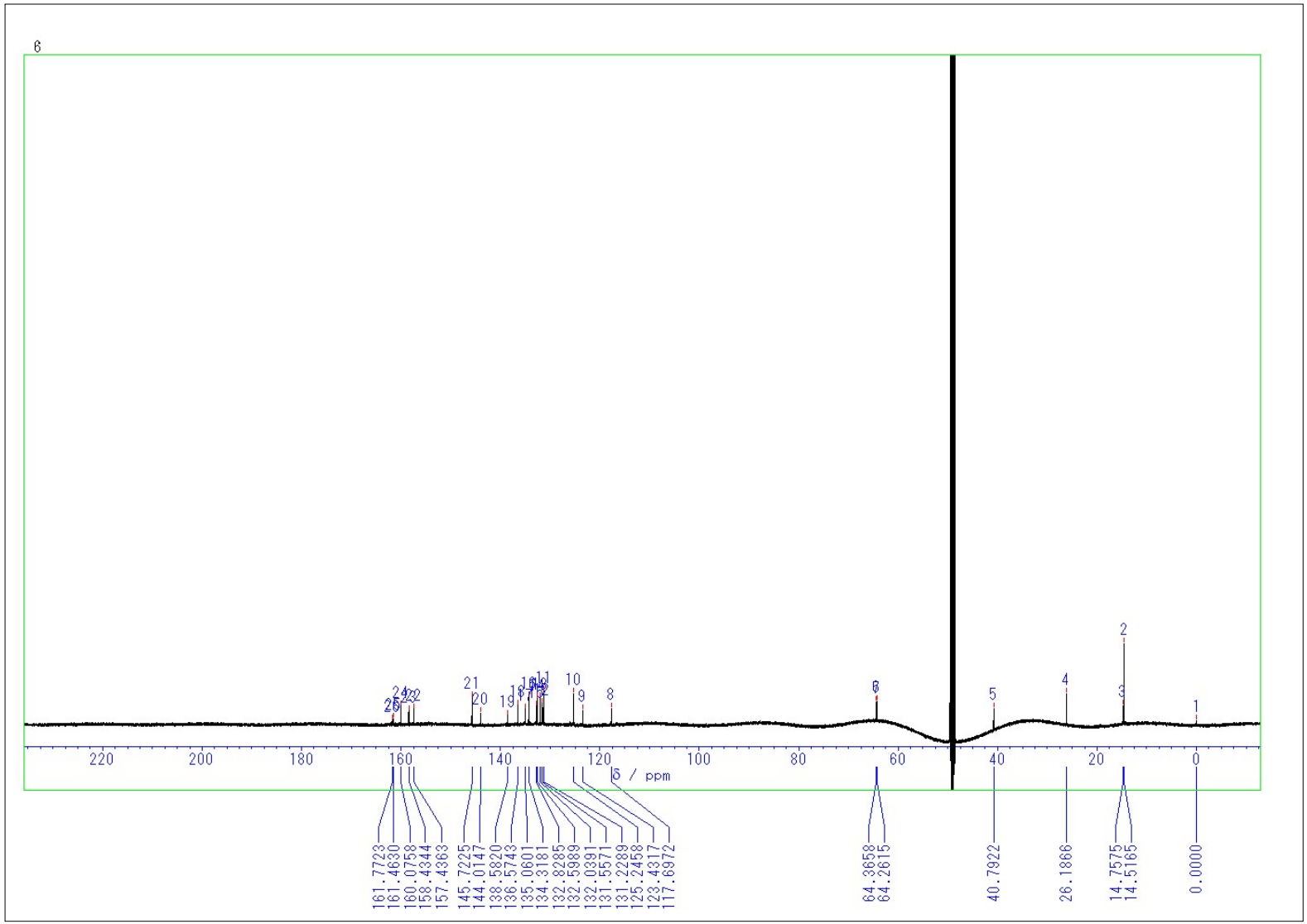
H NMR spectrum of **6**



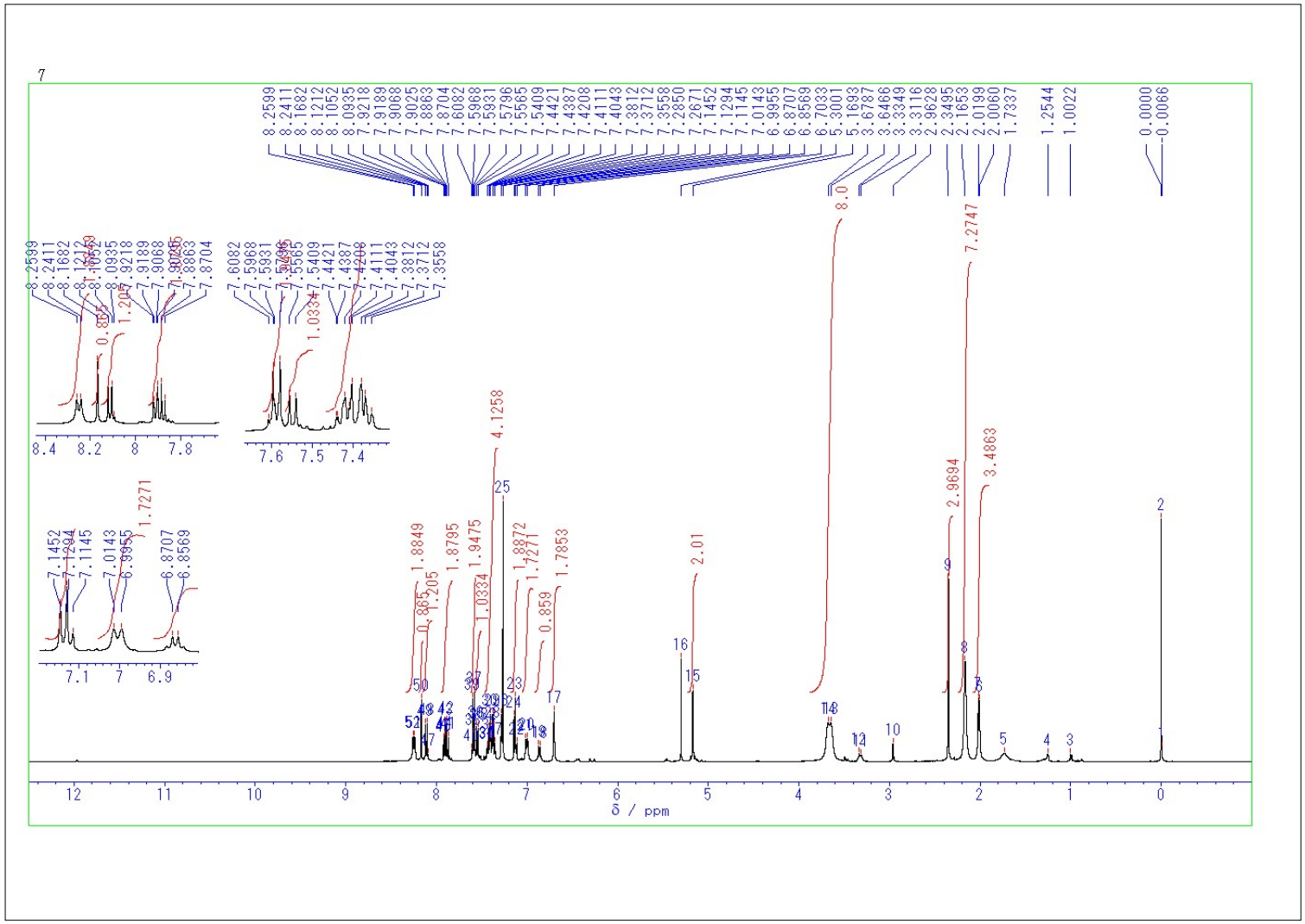


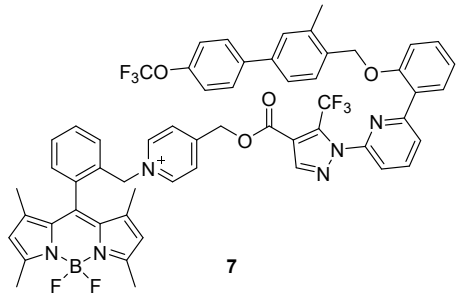
6

C NMR spectrum of **6**



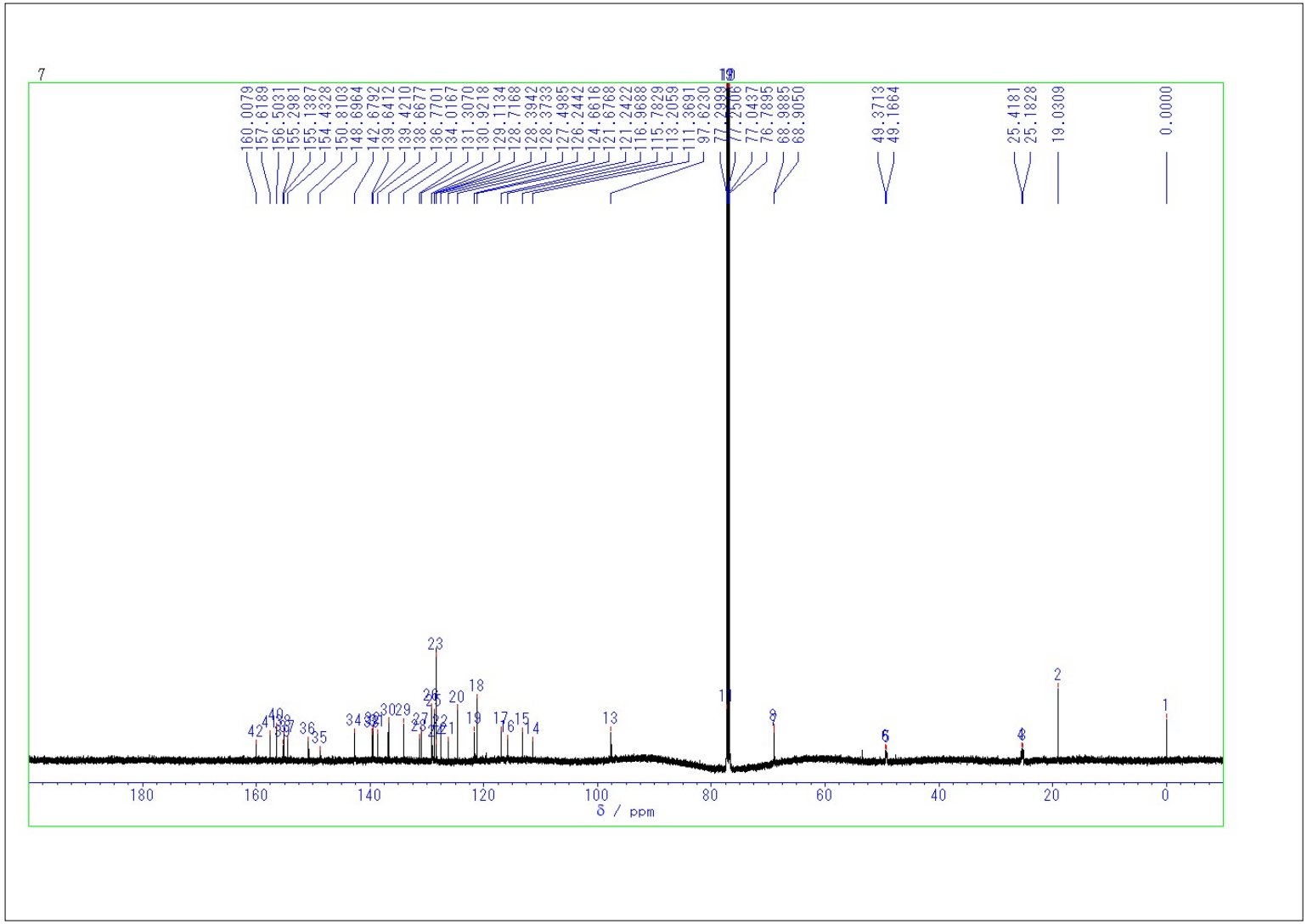
H NMR spectrum of **7**



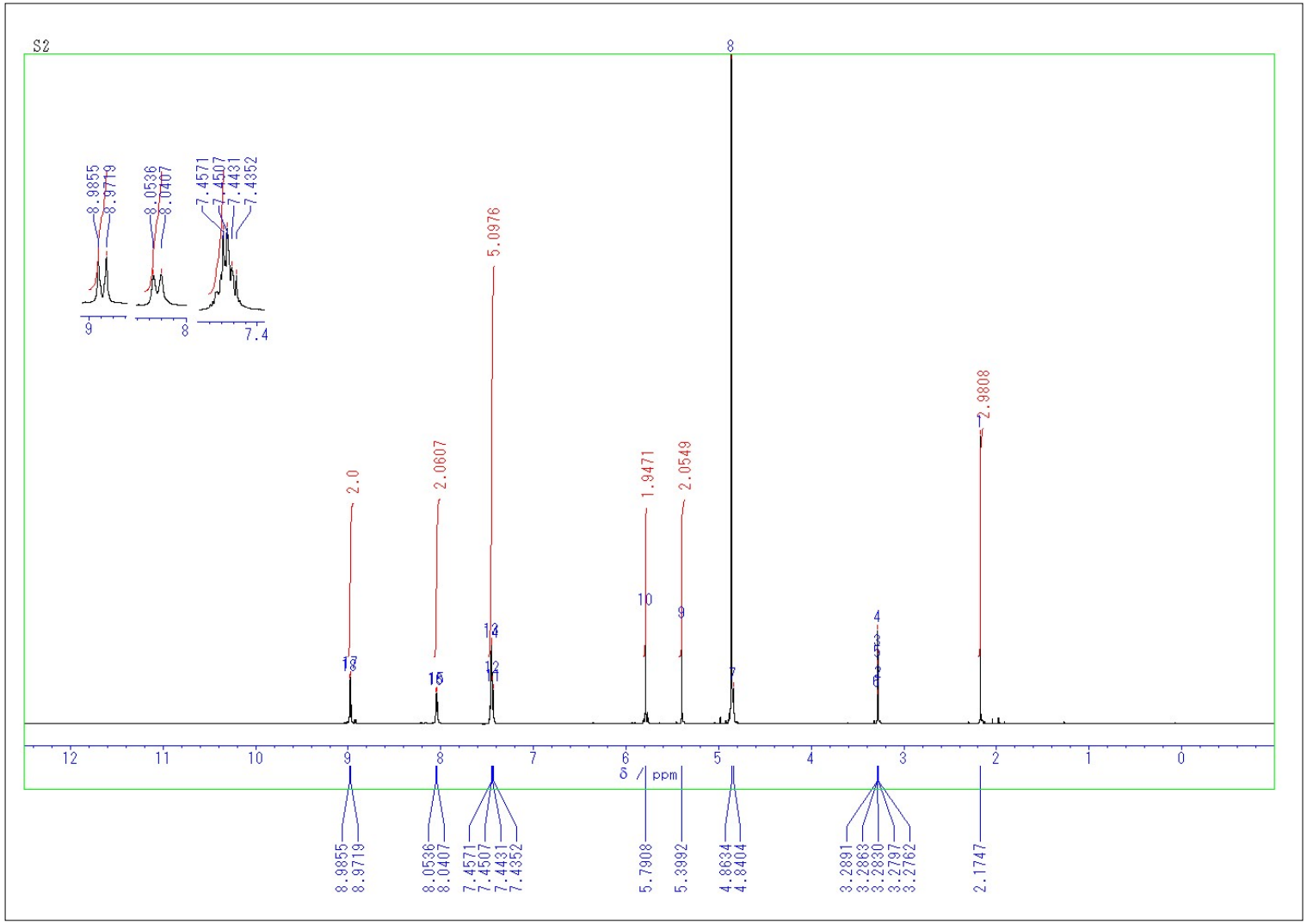


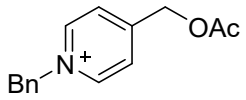
7

C NMR spectrum of **7**

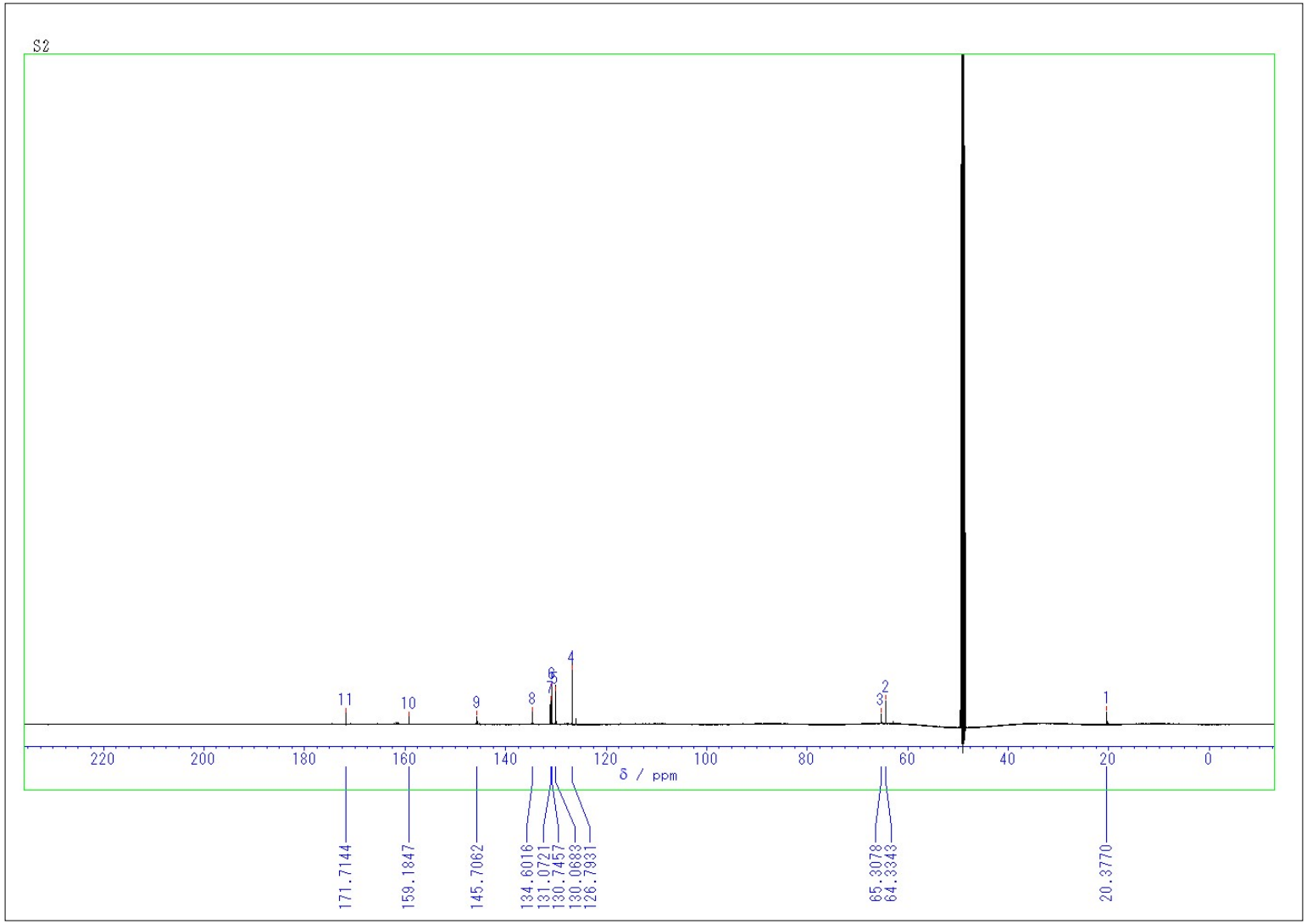


H NMR spectrum of **S2**





C NMR spectrum of **S2**



Cyclic voltammetry

Cyclic voltammetry (CV) was performed on an ALS Electrochemical Analyzer (ALS-612A) using Pt wire electrodes under an argon atmosphere. A solution of **S2** or **3** (1.0 mM) and [*n*-Bu_4N]BF_4 (100 mM) in degassed MeCN (1 mL) was used to measure the redox potential by CV. Ferrocene, whose half-wave potential in the ferrocene/ferrocenium redox couple (Fc/Fc^+) is 0.420 V (vs. SCE), was used as a standard. The CV conditions were as follows: initial potential; 0 V, high potential; 0 V, low potential; –2.0 V, initial scan polarity; negative, scan rate; 0.100 V/sec, sweep segment; 10, sample interval; 0.001 V/sec, quiescence time; 2.0 sec, sensitivity; 5e–6.

HPLC analysis of photodecomposition

A solution (10 mL) of each BODIPY derivative (10 μM) in 100 mM HEPES buffer (pH 7.3, 0.1% DMSO) was irradiated by using a MAX-302 or MAX-303 (Asahi Spectra, Tokyo) with a 470‑530 nm band pass filter for 0, 1, 2, 5, 10 and 20 minutes at 37 °C (79 mW/cm^2 at 500 nm). An aliquot of each solution (20 μL) was loaded onto an Inertsil ODS column (5 μm; 150 × 4.6 mm) fitted on a Shimadzu HPLC system, and the eluates were monitored with an absorption or fluorescence detector. The HPLC conditions were follows: mobile phase; A, MilliQ water (0.1% TFA); B, MeCN (0.1% TFA), gradient; B conc. 5–5% (0–2 min), 5–10% (2–3 min), 10–90% (3–18 min), 90–100% (18–19 min), 100–100% (19–24 min), 100–5% (24–25 min), 5–5% (24–30 min), flow rate; 1.0 mL/min, injection volume; 20 μL, absorbance; 500 nm and 378 nm, fluorescence; ex/em 350/450 nm.

ESR Measurements

A quartz ESR tube (internal diameter: 4.0 mm) containing a deaerated DMSO solution of sample was irradiated in the cavity of the ESR spectrometer with the focused light of a 60 W LED lamp (λ = 405 nm) (Pi Photonics Inc., Japan) at –130 ˚C. ESR spectra in frozen DMSO were measured under non-saturating microwave power conditions using a JEOL X-band spectrometer (JES-X310) with an attached variable temperature apparatus (ES-13060DVT5). The magnitude of modulation was chosen to optimize the resolution and the signal-to-noise (S/N) ratio of the observed spectra when the maximum slope linewidth (ΔH_{msl}) of the ESR signals was unchanged with a larger modulation magnitude. The g values and the hyperfine coupling (*hfc*) constants were calibrated with a Mn^{2+} marker.

Theoretical Calculations

Density functional theory (DFT) calculations were performed with Gaussian09 (Revision C.02, Gaussian, Inc.). The calculations were performed on a 16-processor high performance computer (ForScientist XD1, HPC Systems Inc., Japan).

LC-MS analysis of histamine in an irradiated solution of **6** with fluorescence detection

A solution (5 mL) of **6** (10 μM) in 100 mM HEPES buffer (pH 7.3, 0.1% DMSO) was irradiated (79 mW/cm^2

at 500 nm) by using a MAX-302 (Asahi spectra) with a 470–530 nm band pass filter for 1, 2, 5, 10 and 20 min at 37 ℃. After irradiation, a solution of *o*-phthalaldehyde in DMSO (100 mM, 5 μL) and 2-mercaptoethanol (100 mM, 5 μL) were added to the irradiated solution and the mixture was stirred for 2 min at room temperature. Then, an aliquot of each solution (20 μL) was analyzed under the same conditions as mentioned above.

LC-MS analysis

A solution of **4** (10 μM) in 100 mM HEPES buffer (pH 7.3, 0.1% DMSO) was photoirradiated (85 mW/cm^2) by using a MAX-302 (Asahi Spectra, Tokyo) with a 470–530 nm band pass filter for 1, 2, 5, 10 and 20 min at 37 ℃. An aliquot of the solution (10 μL) loaded on the column was subjected to LC/ESI-MS. LC/ESI-MS was performed with an ion trap mass spectrometer (Quattro Premier XE, Waters Corporation, Milford, MA, USA) equipped with a nanospray ion source. The LC separations were performed on an HPLC system (ACQUITY UltraPerformance LC, Waters Corporation, Milford, MA, USA). The HPLC conditions were follows: column; Inertsil ODS-3, 5 μm : 150 mm × Φ 2.1 mm, mobile phase; A, MilliQ water (0.1% FA); B, MeCN (0.1% FA), gradient; B conc. 10–10% (0–2 min), 10–100% (2–20 min), 100–100% (25–26 min), 100–10% (26–30 min), flow rate; 0.2 mL/min, injection volume; 10 μL, absorbance; 200–800 nm.

Photovasodilation of rat aorta strip

A rat aortic strip was placed in a Magnus tube filled with Krebs buffer at 37 °C. The tension was recorded on a LabChart7 (ADInstruments). The strip was treated with L-NAME (10 μM) before addition of noradrenaline (10 μM). After equilibration, **7** (50 μM), or DMSO (10 μL) was added, and the tube was irradiated with an LED (CL-1501, Asahi Spectra) with a 505 nm LED head (120 mW cm^{-2}) for 3 min.

Supporting Equation, Figure, and Table

$$G_{PeT} = F\{E_{ox}(D) - E_{red}(A)\} - E_{0,0} + C \quad \text{(S1)}$$

F: Faraday constant

E_{ox}(D): oxidation potential of the electron donor (NO-releasing moiety)

E_{red}(A): reduction potential of the electron acceptor (antenna moiety)

$E_{0:0}$: zero vibrational electronic excitation energy of the fluorophore (antenna moiety)

C: Coulombic interaction (negligible in water)

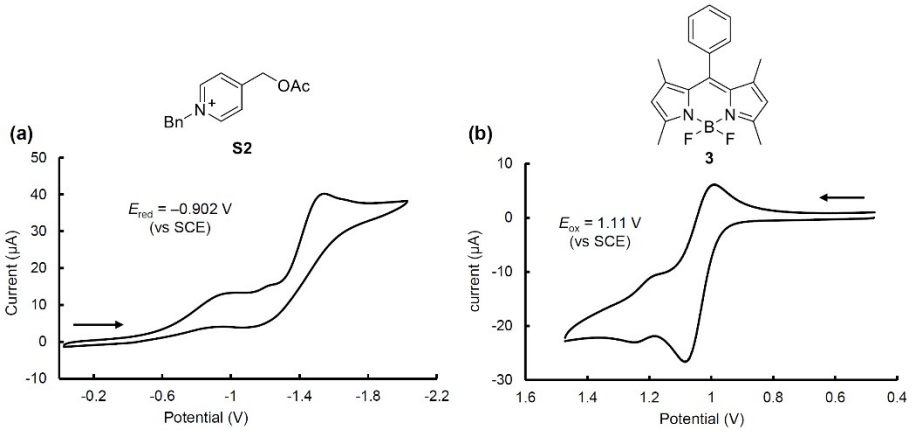
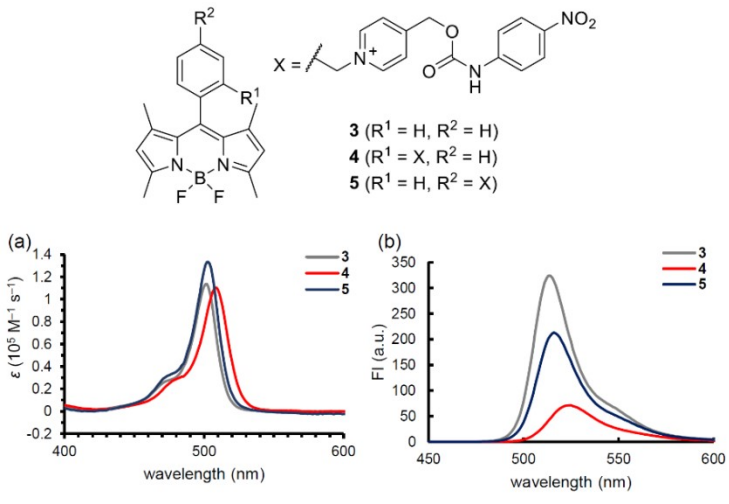


Figure S1 Cyclic voltammogram of a solution of **S2** (a, 1.0 mM) or **3** (b, 1.0 mM) in MeCN/[n-Bu_4N][BF_4] (0.1 M).



	Absorption		Fluorescence	
	λ_{max} (nm)	ε_{max} ($M^{-1}cm^{-1}$)	λ_{em} (nm)	Φ_{fl}
3	502	1.14×10^5	514	0.457
4	508	1.10×10^5	523	0.0206
5	503	1.33×10^5	516	0.180

Figure S2 Absorption (a) and fluorescence (b) spectra of a solution (10 μM) of **3** (gray), **4** (red), or **5** (blue) in

DMSO.

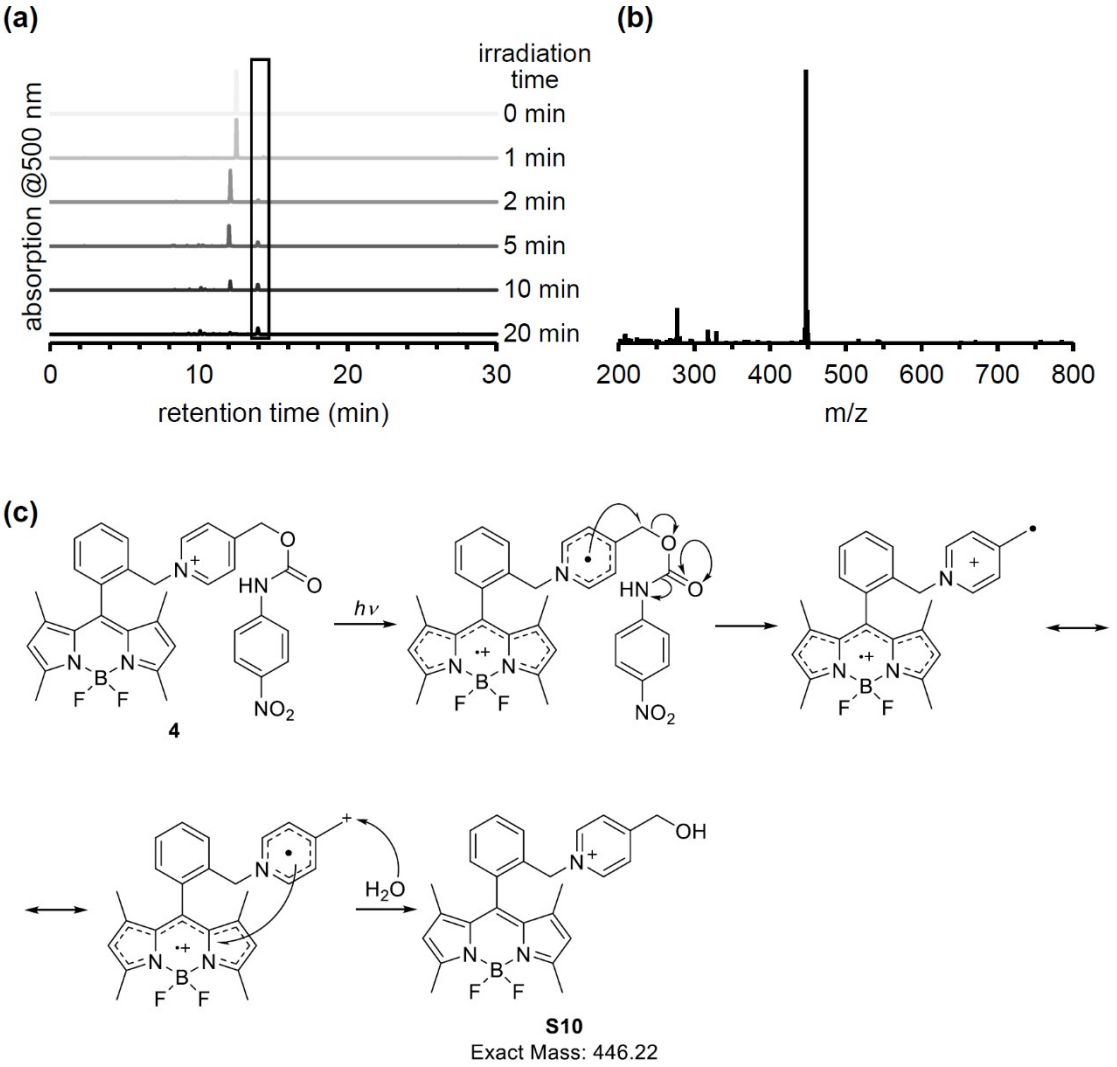


Figure S3 Monitoring the formation of the photodecomposition product of **4**; chromatograms at 500 nm of a solution of **4** during irradiation for the indicated times (a); mass spectrum of the peak surrounded by rectangle in (a) (b); plausible formation mechanism of the hydroxylated product **S10** (c).

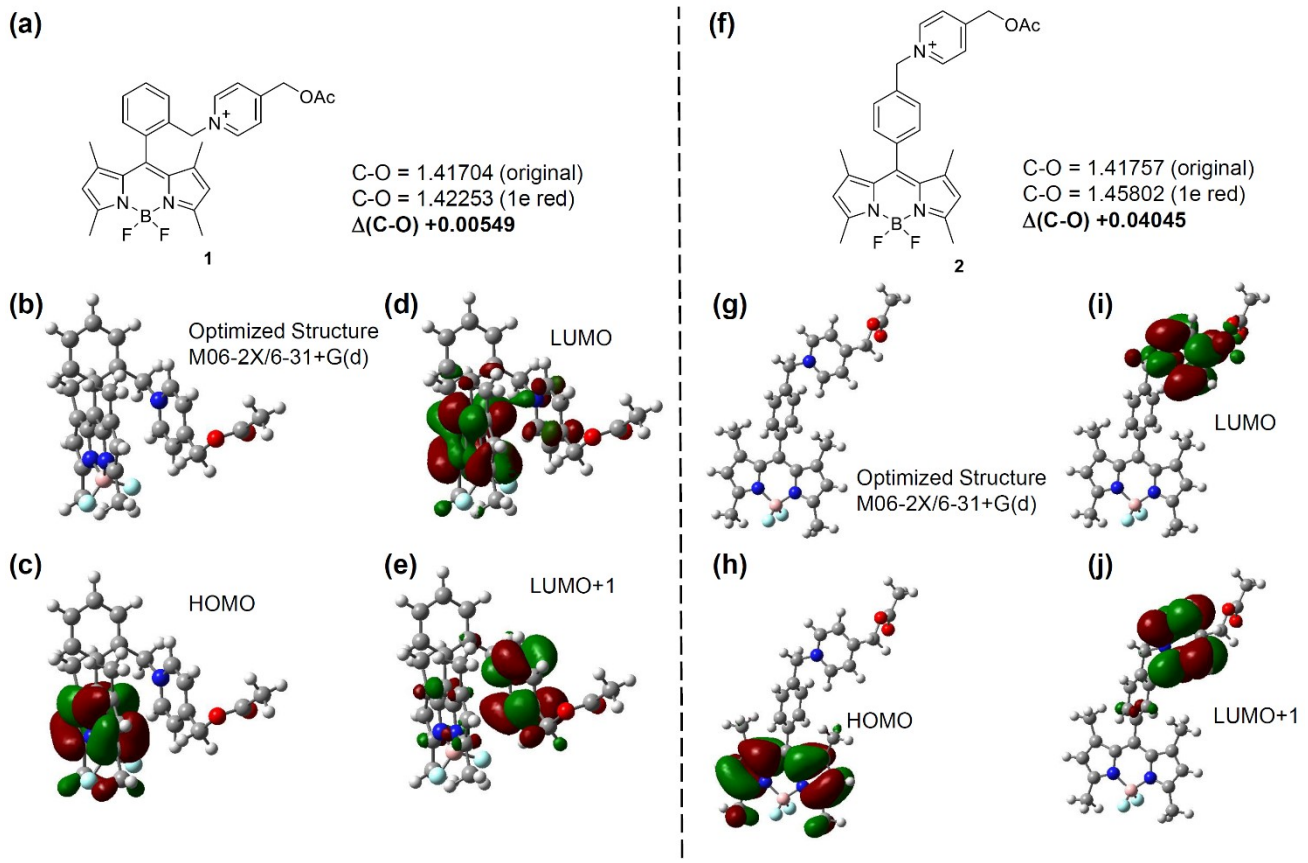
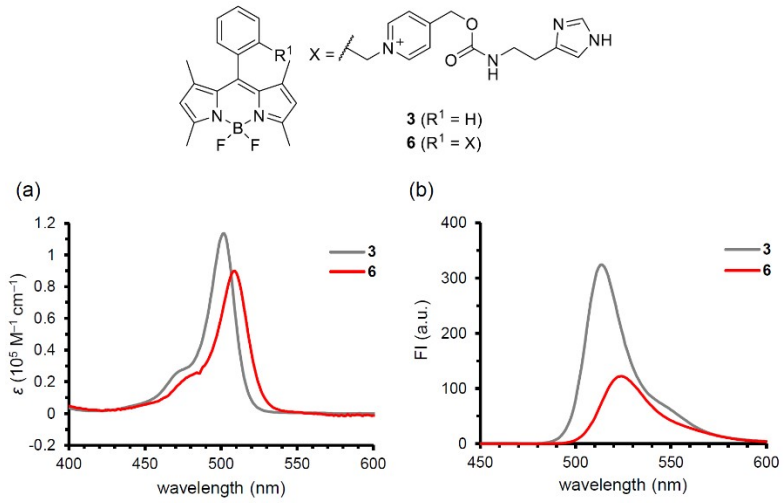
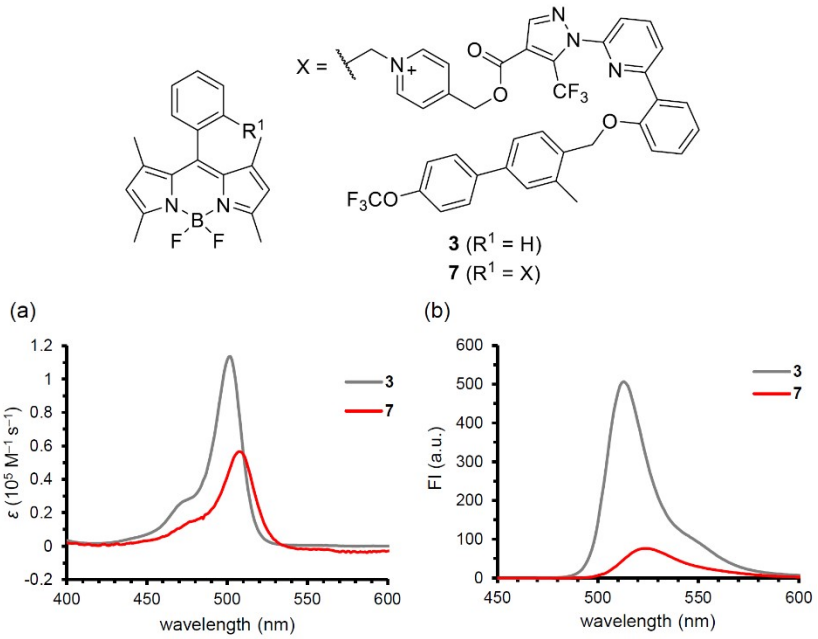


Figure S4 Comparison of C-O bond length between non-reduced and one-electron-reduced forms of **1** (a), and those of **2** (f); optimized structures of **1** (b) and **2** (e); HOMOs of **1** (c) and **2** (h); LUMOs of **1** (d) and **2** (i); LUMO+1s of **1** (e) and **2** (j) calculated at the M06-2X/6-31+G(d) level of theory.



	Absorption		Fluorescence	
	λ_{max} (nm)	ε_{max} (M^{-1} cm^{-1})	λ_{em} (nm)	Φ_{fl}
3	502	1.14×10^5	514	0.457
6	509	8.99×10^4	524	0.0405

Figure S5 Absorption (a) and fluorescence (b) spectra of a solution (10 μM) of **3** (gray), or **6** (red) in DMSO. The spectral data are listed in the table.



	Absorption		Fluorescence	
	λ_{max} (nm)	ε_{max} (M^{-1} cm^{-1})	λ_{em} (nm)	Φ_{fl}
3	502	1.14×10^5	514	0.457
7	508	5.66×10^4	524	0.237

Figure S6 Absorption (a) and fluorescence (b) spectra of a solution (10 μM) of **3** (gray), or **7** (red) in DMSO.

Table S1 Calculation of histamine release quantum yield of **7**

	Irradiated photons (μmol)	Amount of released histamine (μmol)	ε ($M^{-1}cm^{-1}$)	Φ_r	$\varepsilon\Phi_r$ ($M^{-1}cm^{-1}$)
7	4.67	4.72×10^{-4}	8.99×10^4	2.55×10^{-4}	22.9