Supporting information for

BODI-Pt, a green-light activatable and carboplatin-based platinum(IV) anticancer prodrug with enhanced activation and cytotoxicity

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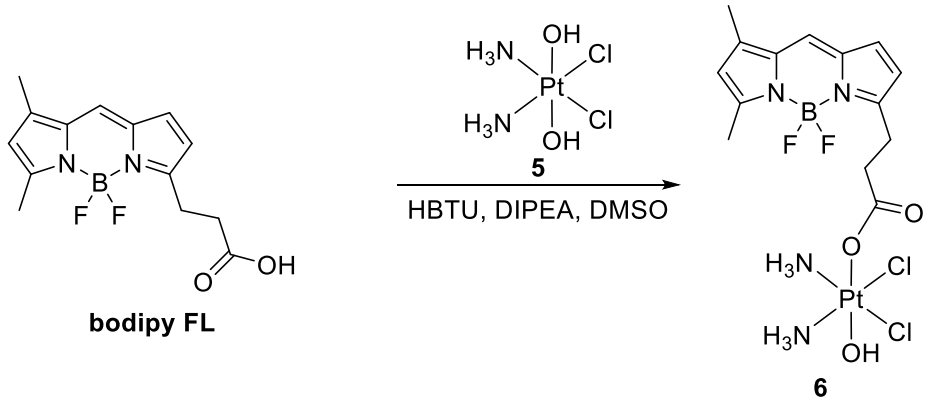


Scheme S1. Synthesis of compound **6**.

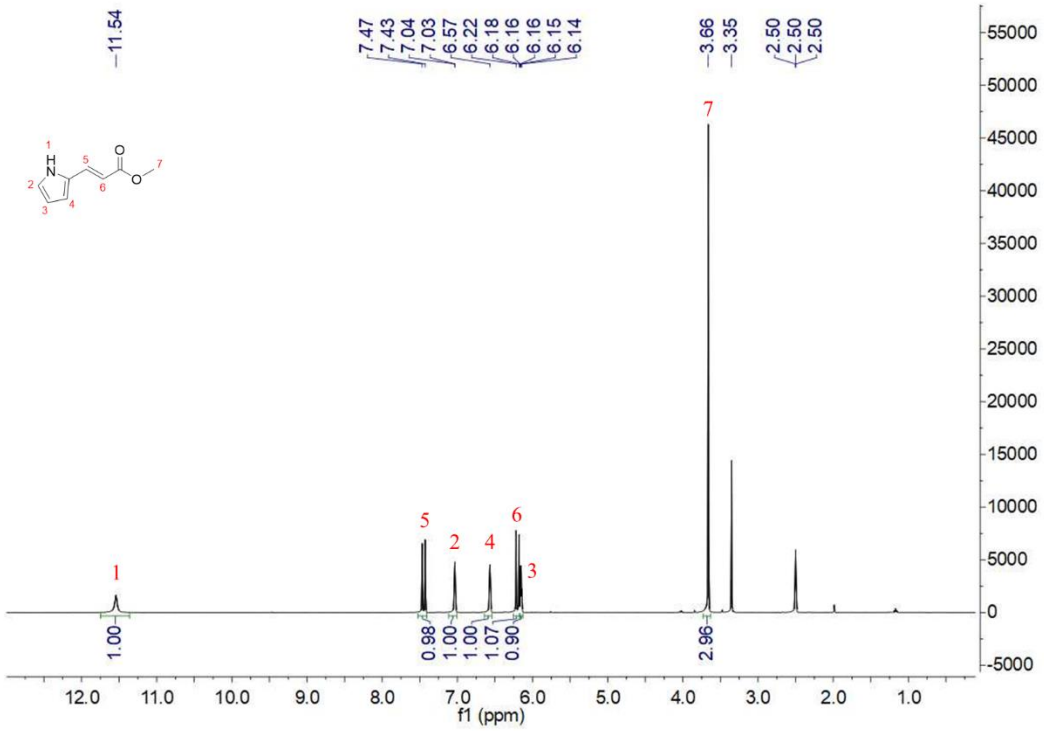


Figure S1. [1]H-NMR spectrum of compound **1** in DMSO-d_6.

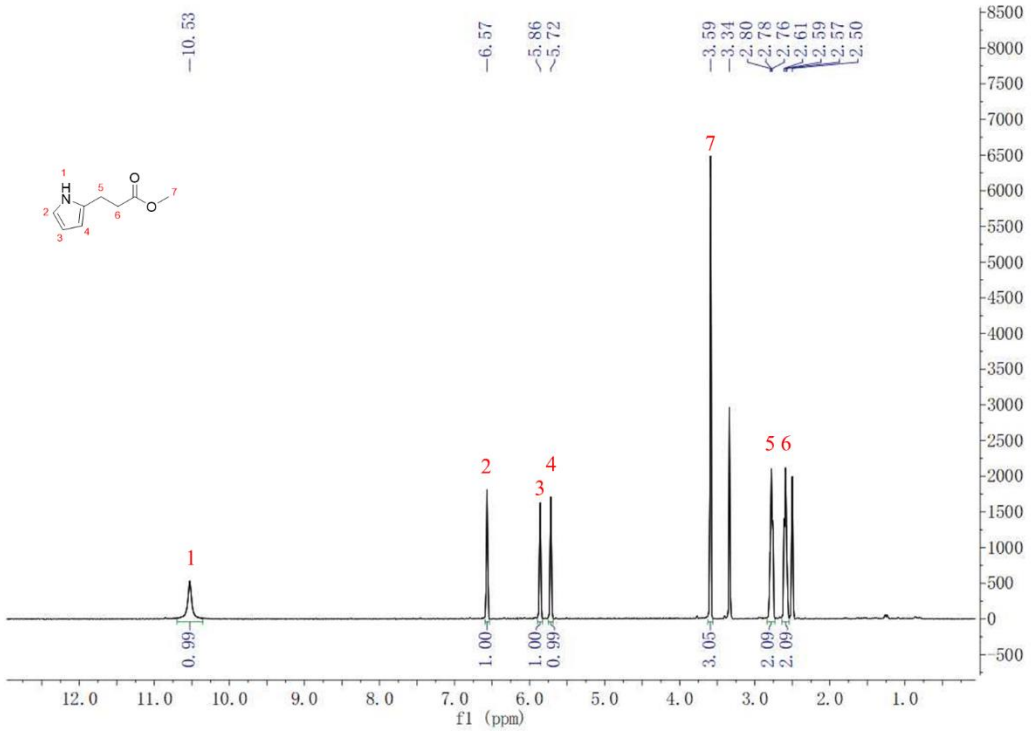


Figure S2. [1]H-NMR spectrum of compound **2** in DMSO-d_6.

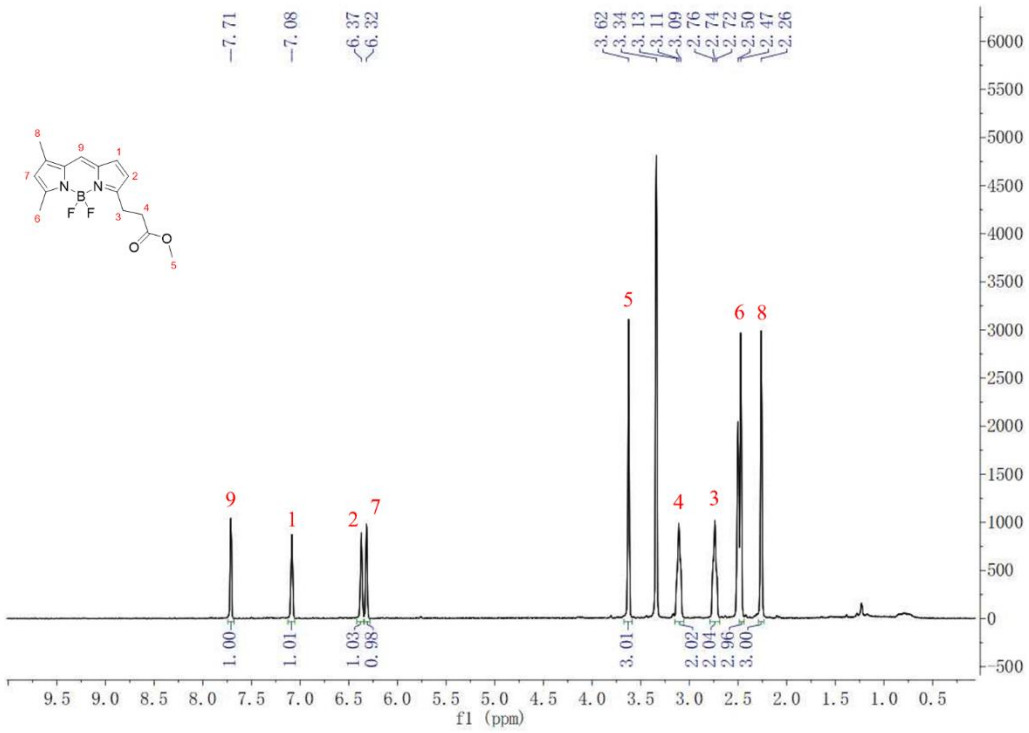


Figure S3. ^{1}H-NMR spectrum of compound **3** in DMSO-d_6.

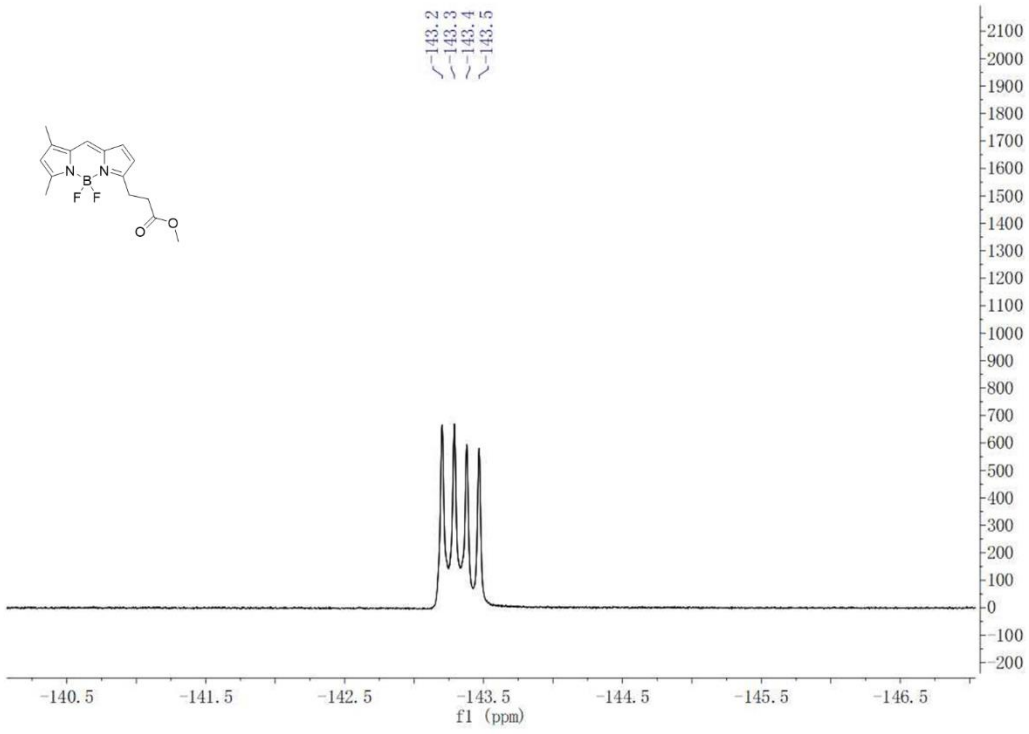


Figure S4. ^{19}F-NMR spectrum of compound **3** in DMSO-d_6.

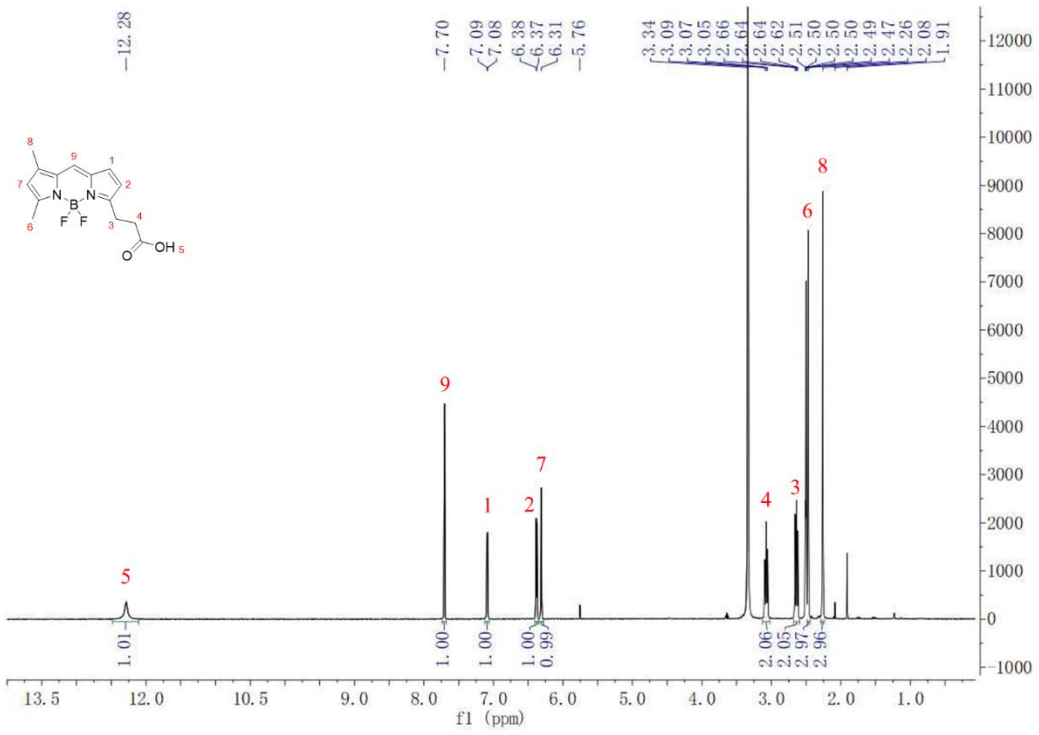


Figure S5. ^{1}H-NMR spectrum of bodipy FL in DMSO-d_6.

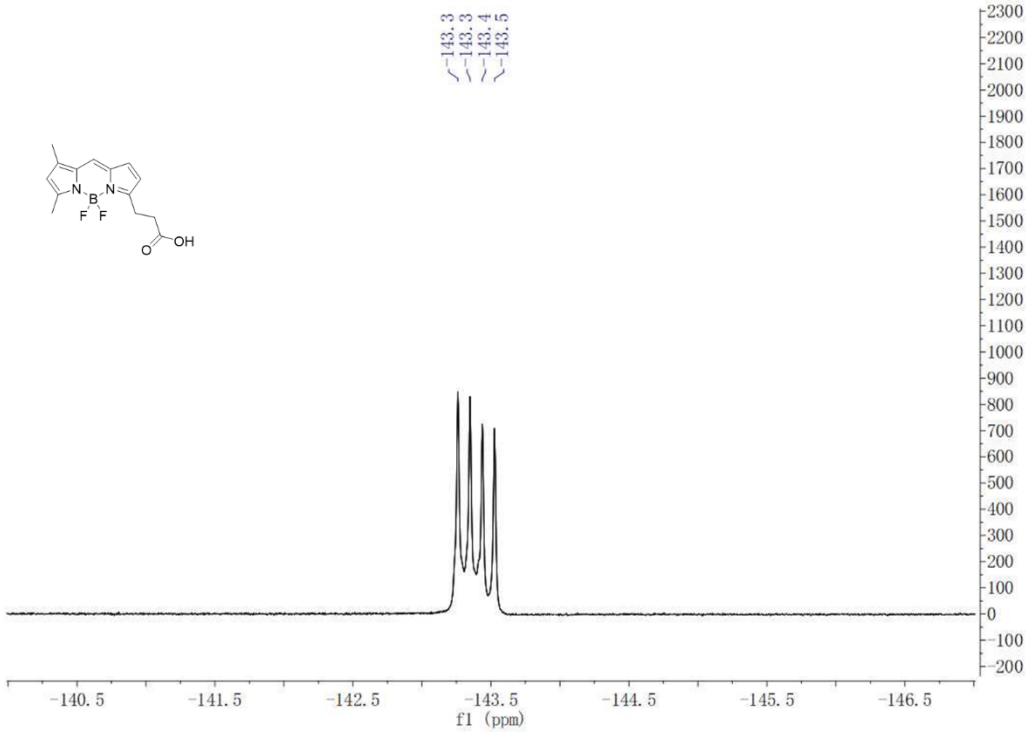


Figure S6. ^{19}F-NMR spectrum of bodipy FL in DMSO-d_6.

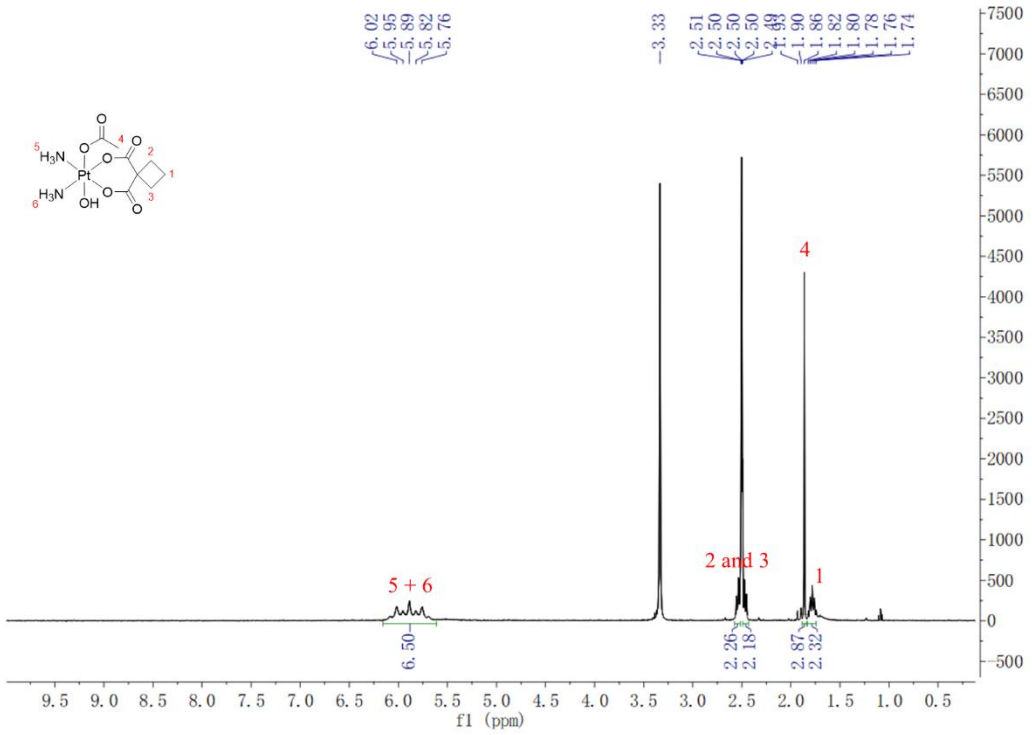


Figure S7. ^{1}H-NMR spectrum of compound **4** in DMSO-d_6.

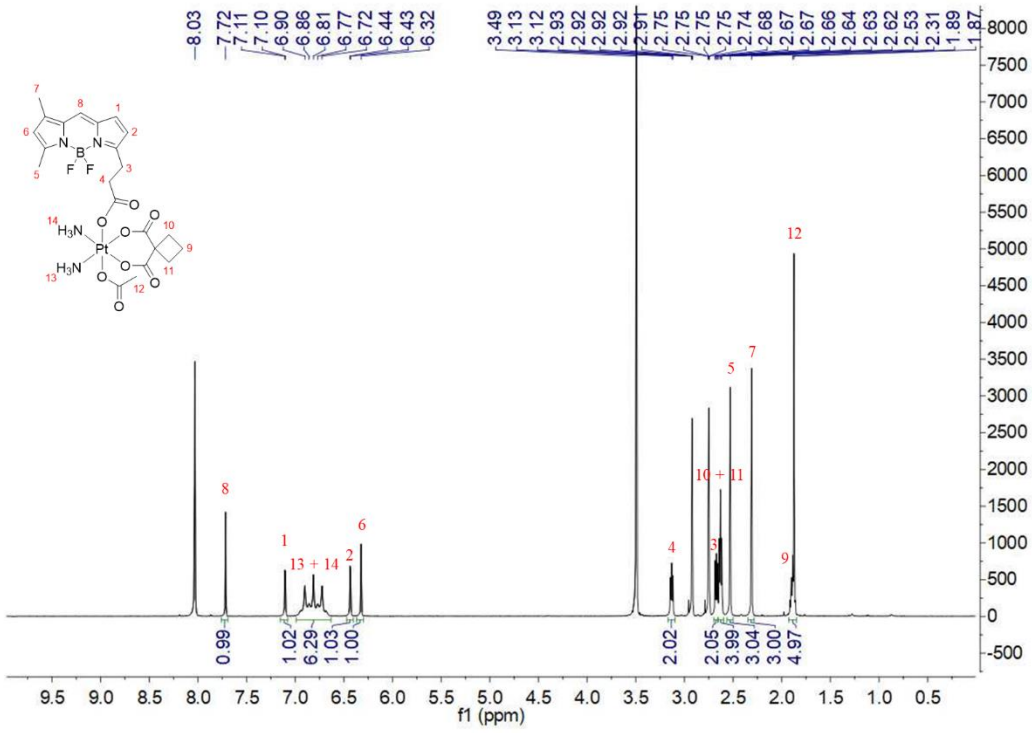


Figure S8 ^{1}H-NMR spectrum of BODI-Pt in DMF-d_7.

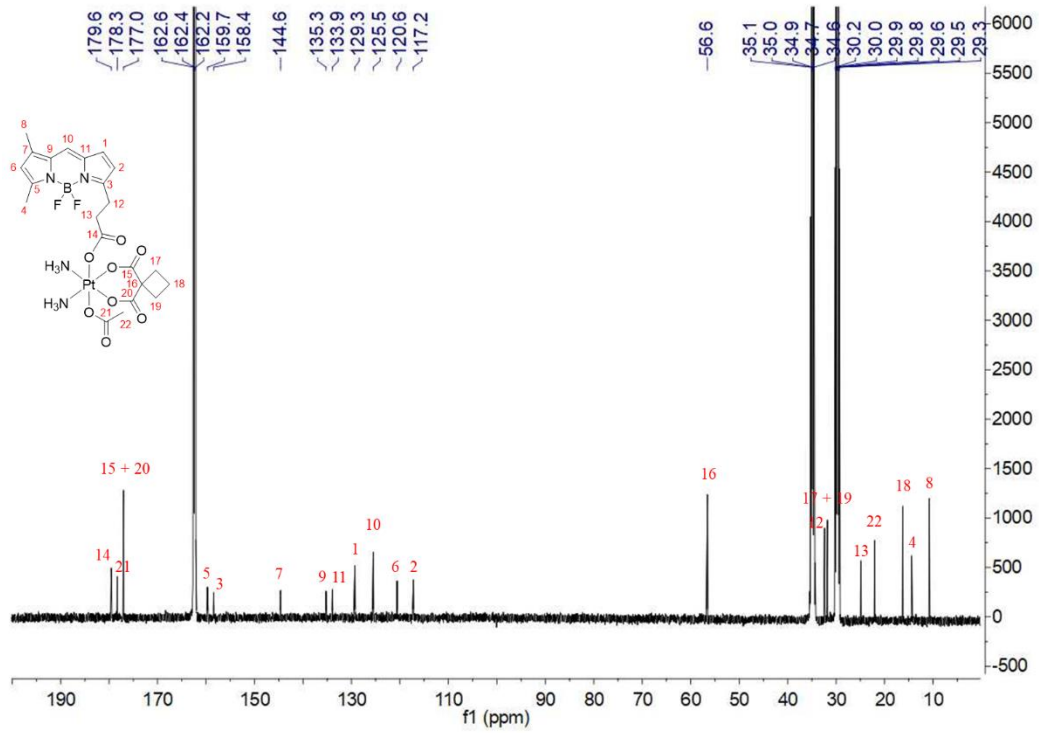


Figure S9. ^{13}C-NMR spectrum of BODI-Pt in DMF-d_7.

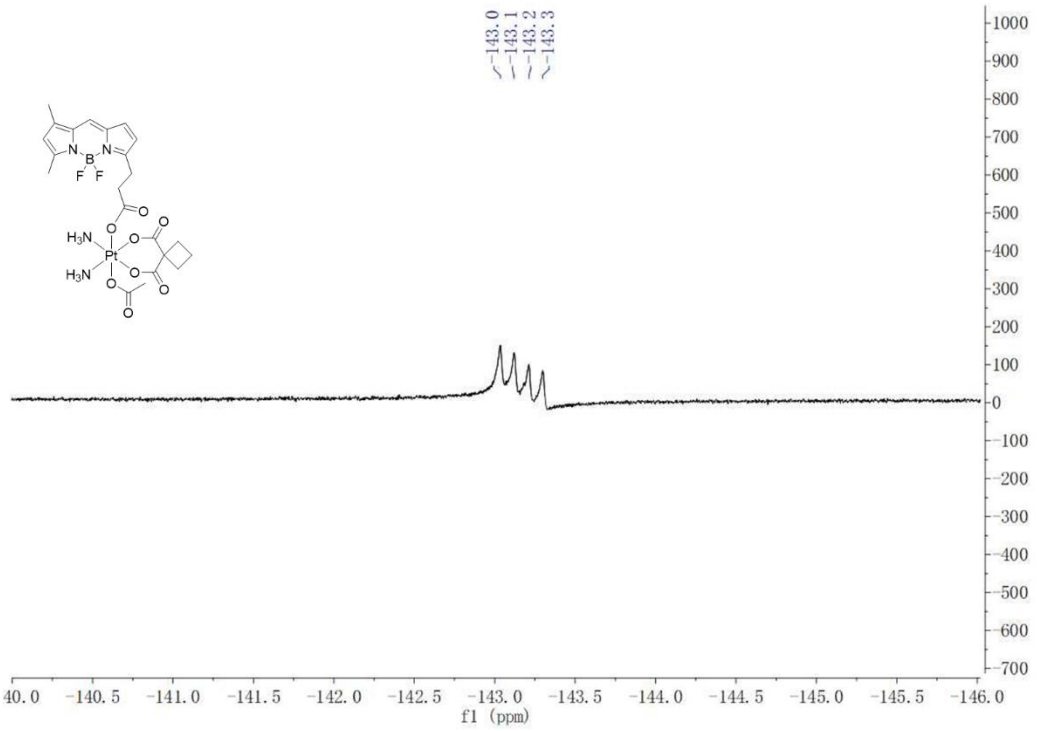


Figure S10. ^{19}F-NMR spectrum of BODI-Pt in DMSO-d_6.

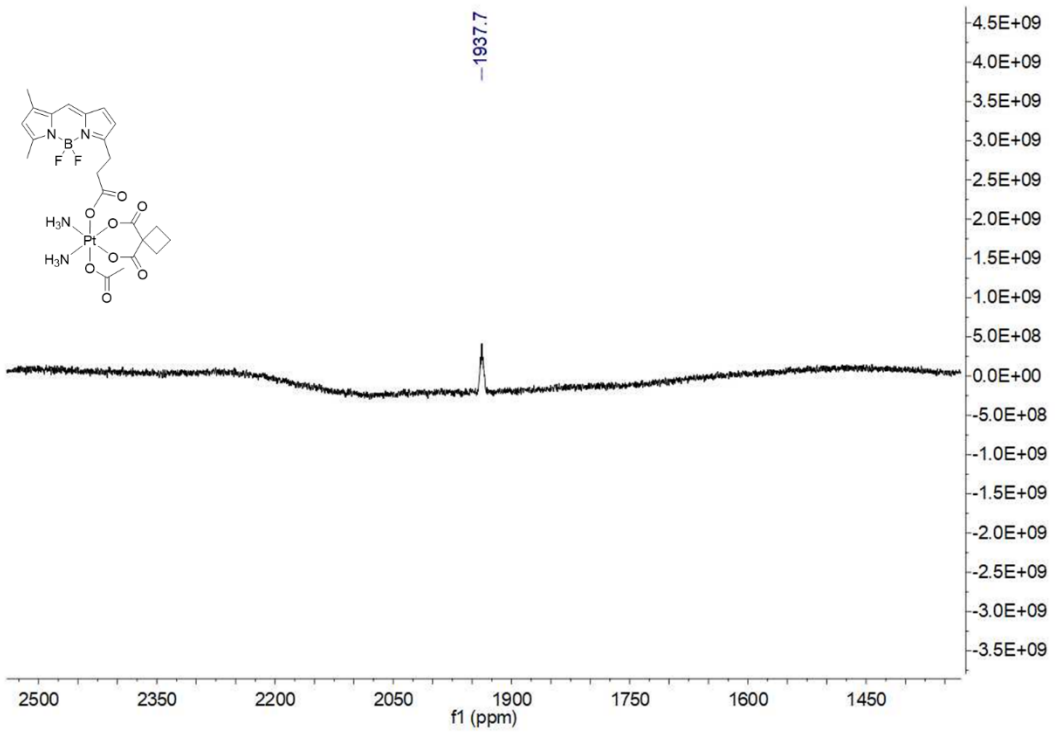


Figure S11. ^{195}Pt-NMR spectrum of BODI-Pt in DMF-d_7.

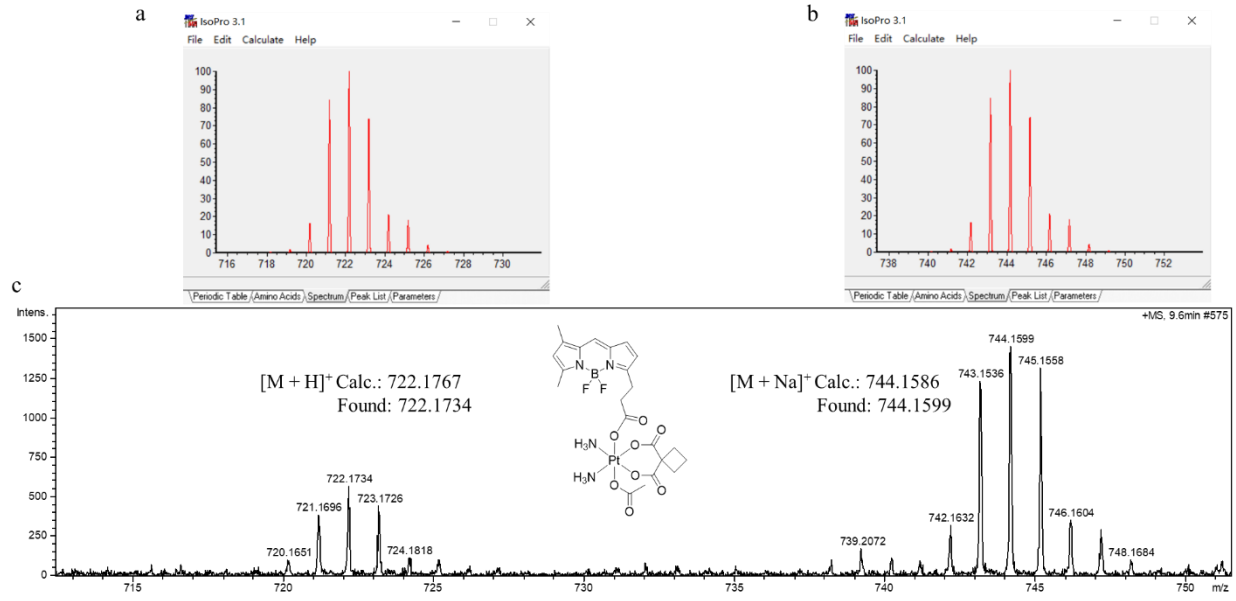


Figure S12. HR-MS of BODI-Pt, positive mode in methanol. Inserted (a) and (b) are the estimated $[M + H]^+$ and $[M + Na]^+$ spectrum of BODI-Pt, respectively.

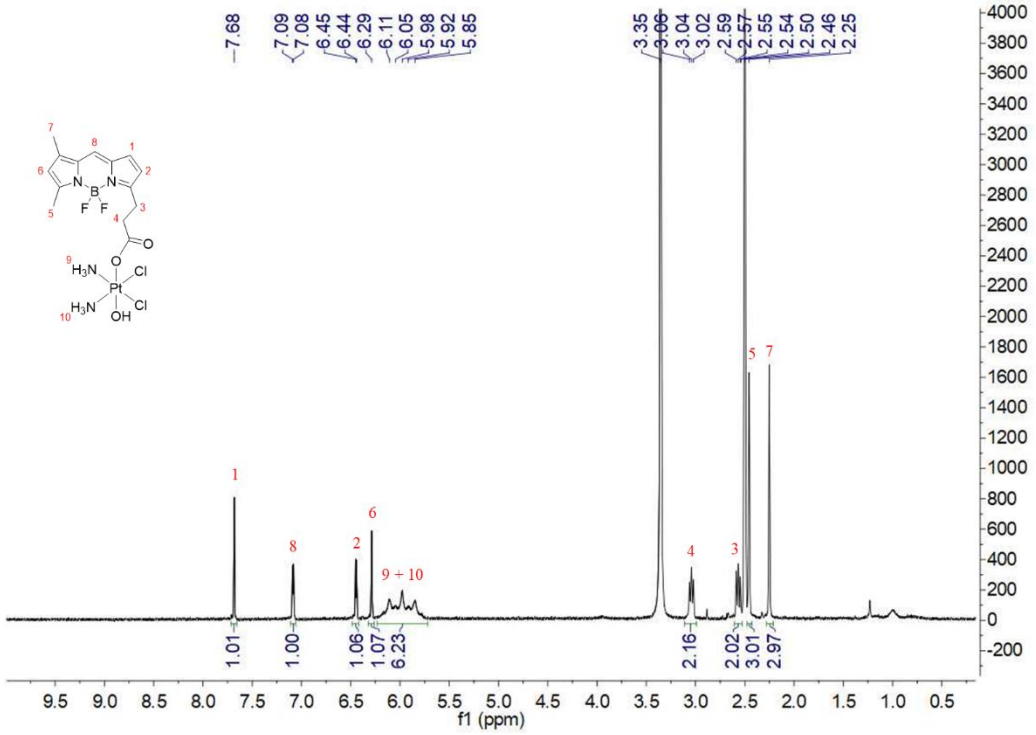


Figure S13. ^{1}H NMR spectrum of compound **6** in DMSO-d_6.

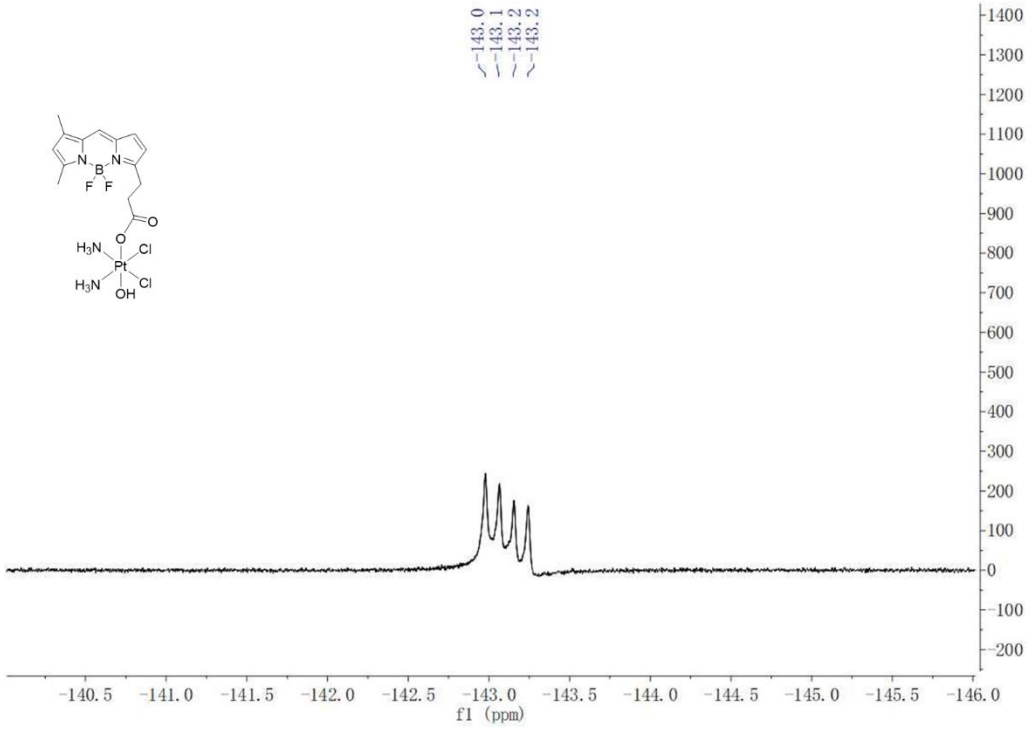
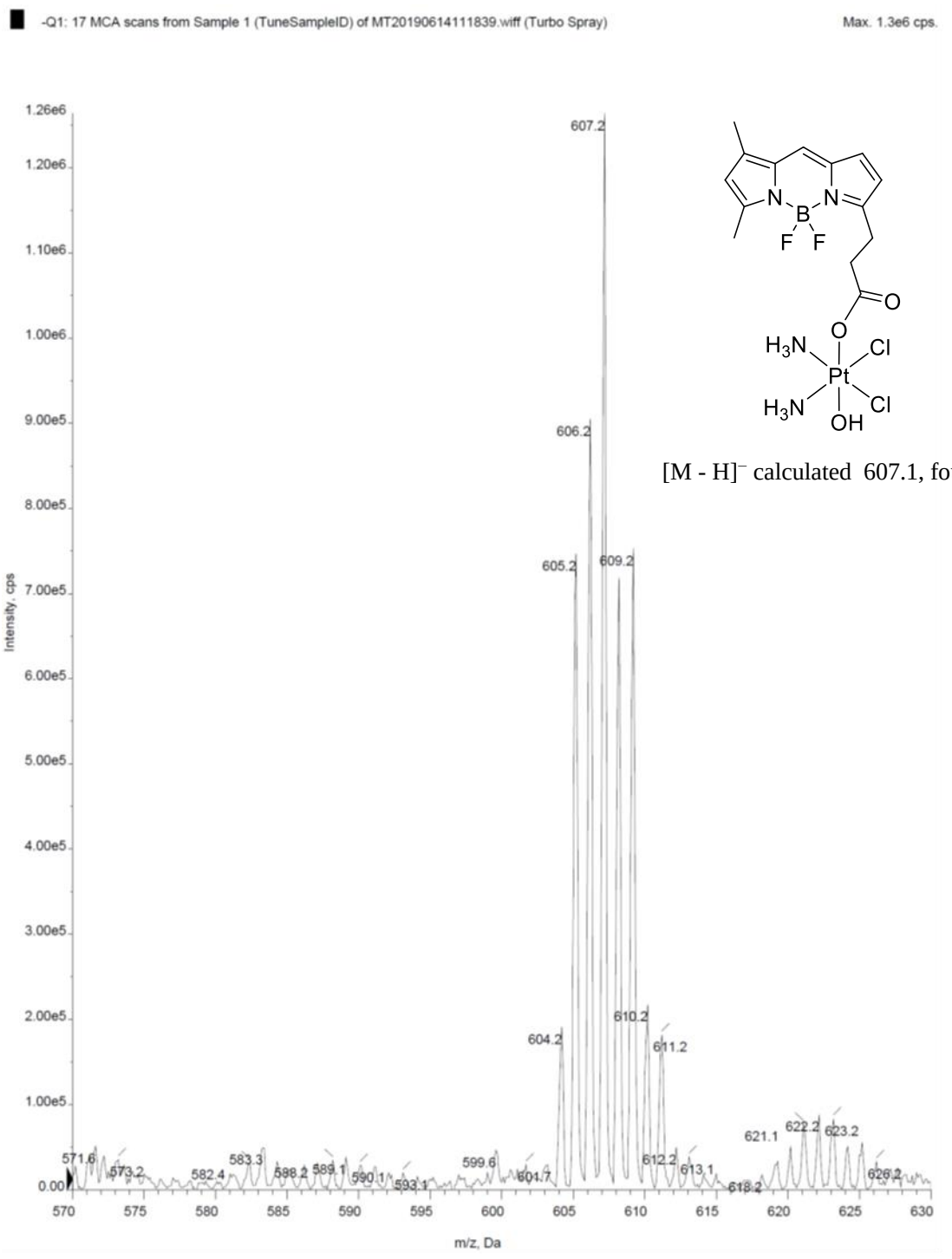


Figure S14. ^{19}F NMR spectrum of compound **6** in DMSO-d_6.



[M - H]$^-$ calculated 607.1, found 607.2

Figure S15. ESI-MS of compound **6**, negative mode in methanol.

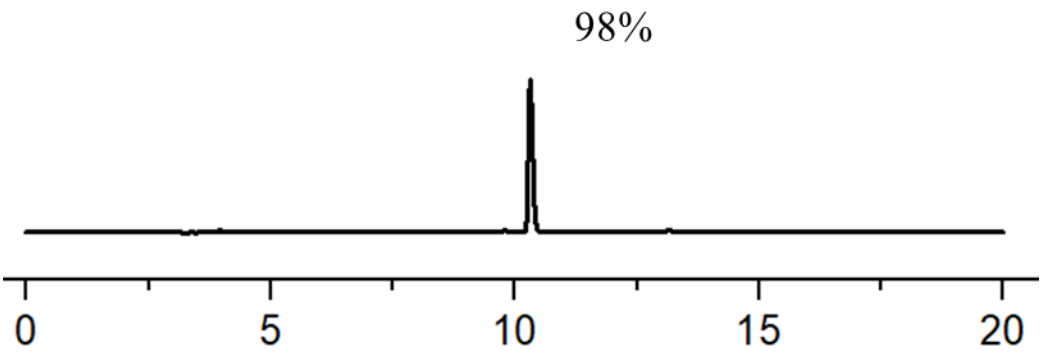


Figure S16. Purity of BODI-Pt by HPLC. HPLC condition: 0 - 3 - 16 - 17 - 20 min, 10 - 50 - 63 - 10 - 10% acetonitrile with 0.1% HCOOH. Flow rate: 1 mL/min. wavelength: 504 nm.

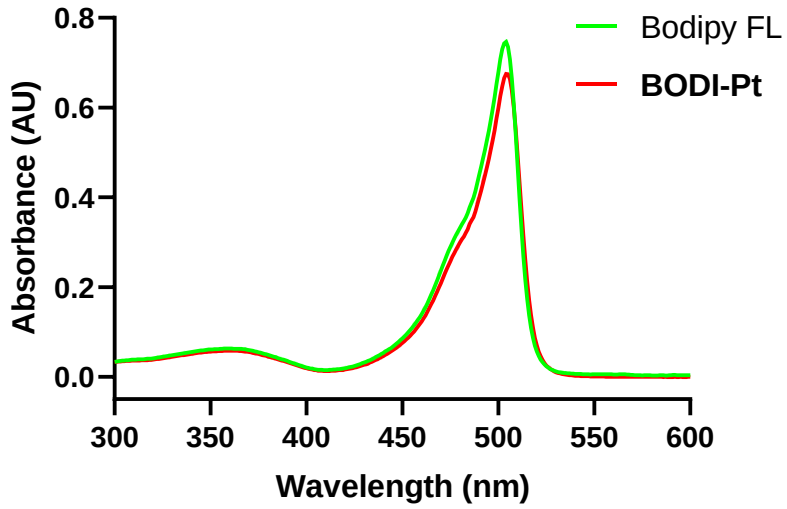


Figure S17. Absorbance of BODI-Pt and bodipy FL recorded by a UV-Vis spectrophotometer. 10 μM compounds were dissolved in a PBS buffer (pH 7.4) with 1% DMF.

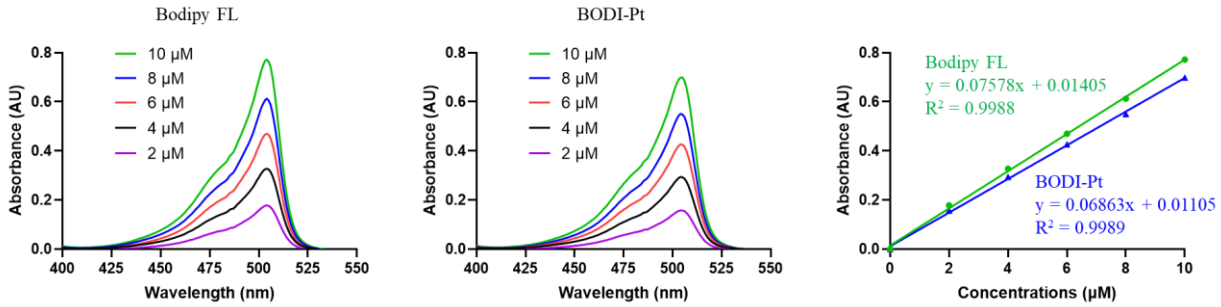


Figure S18. Molar extinction coefficient of BODI-Pt and bodipy FL. 10, 8, 6, 4, and 2 μM of compounds were dissolved in a PBS buffer (pH 7.4) with 1% DMF. The absorbances were recorded by a UV-Vis spectrophotometer. The maximum absorbances at each concentration were plotted with the concentrations of compounds.

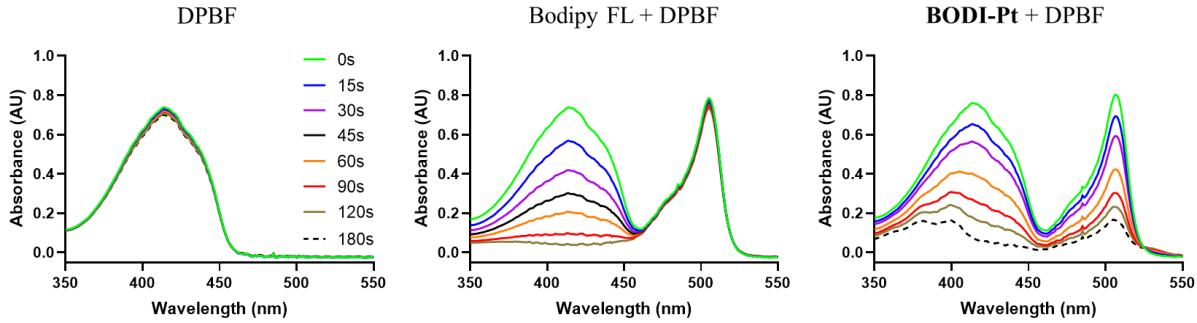


Figure S19. ROS generation of BODI-Pt and bodipy FL by the detection of 1,3-Diphenylisobenzofuran (DPBF). 10 μM of compounds were mixed with 50 μM of DPBF in 3 mL DMF. The mixtures were irradiated under a green light (13 mW/cm^2). The absorbance of DPBF and compounds was recorded by a UV-Vis spectrophotometer at different time points.

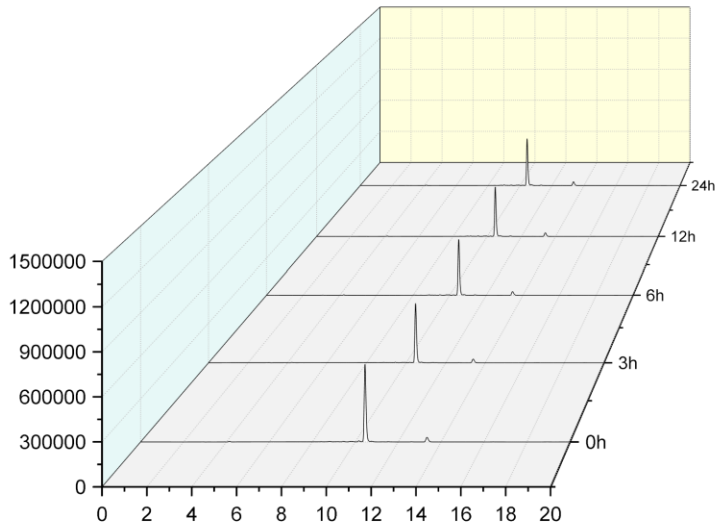


Figure S20. Stability of BODI-Pt in a PBS buffer (pH 7.4) at 37 ℃ in the dark. HPLC condition: 0 - 3 - 16 - 17 - 20 min, 10 - 50 - 63 - 10 - 10% acetonitrile with 0.1% HCOOH. 1 mL/min. wavelength: 504 nm.

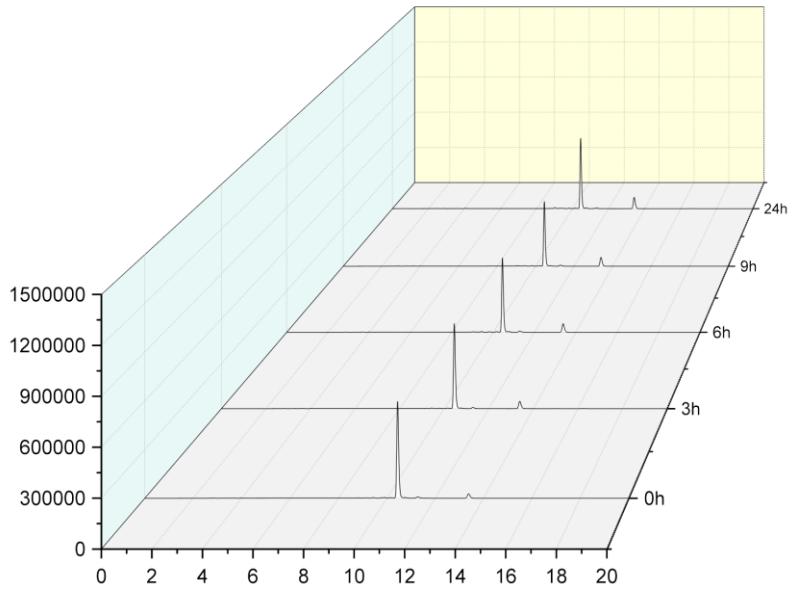


Figure S21. Stability of BODI-Pt in a PBS buffer (pH 7.4) containing 1 mM sodium ascorbate at 37 ℃ in the dark.

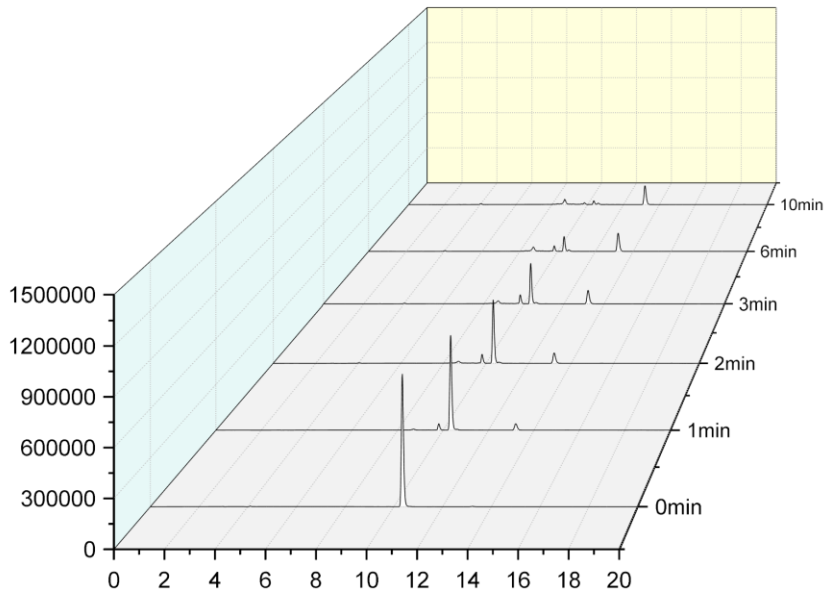


Figure S22. Stability of BODI-Pt in a PBS buffer (pH 7.4) under green light (13 mW/cm^2).

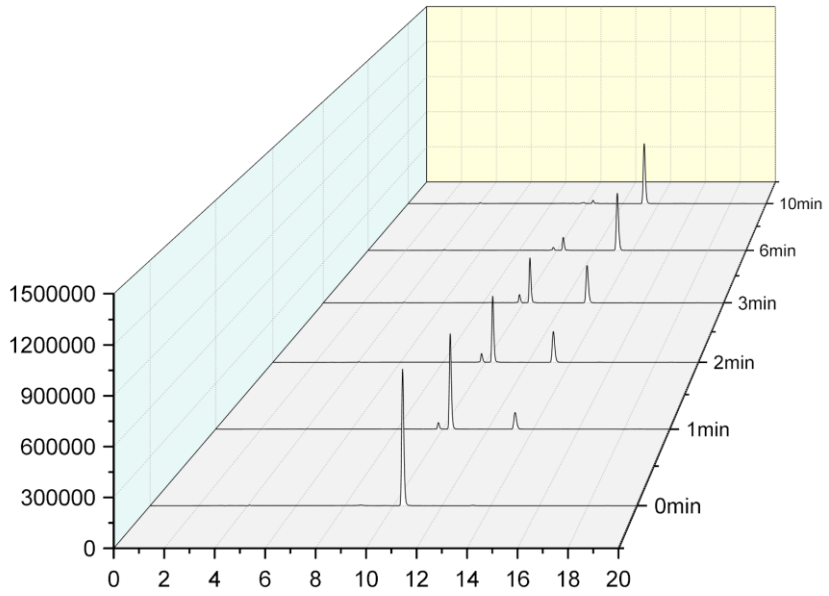


Figure S23. Stability of BODI-Pt in a PBS buffer (pH 7.4) with 1 mM sodium ascorbate under green light (13 mW/cm^2).

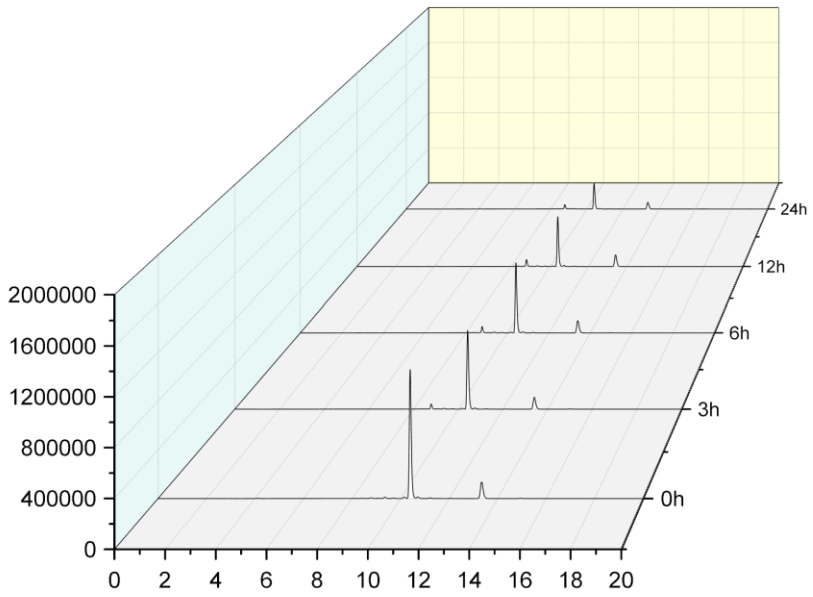


Figure S24. Stability of compound **6** in a PBS buffer (pH 7.4) at 37 ℃ in the dark.

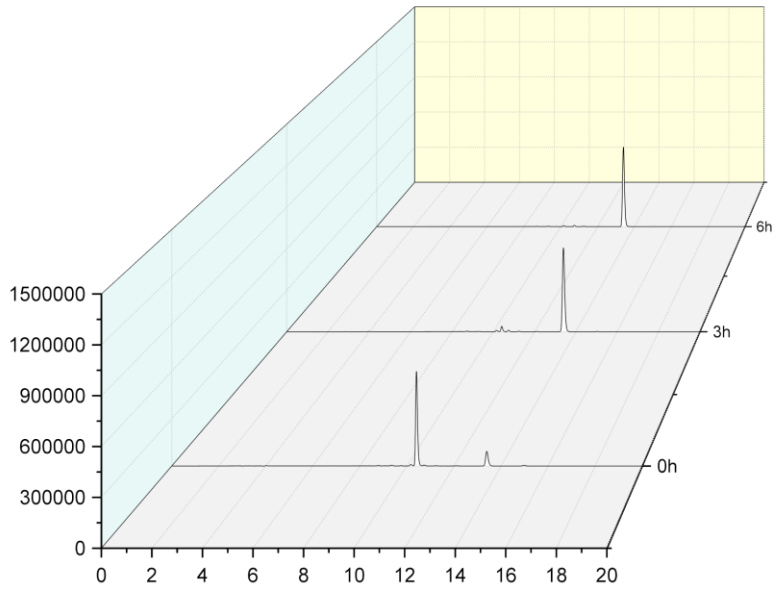


Figure S25. Stability of compound **6** in a PBS buffer (pH 7.4) with 1 mM sodium ascorbate at 37 ℃ in the dark.

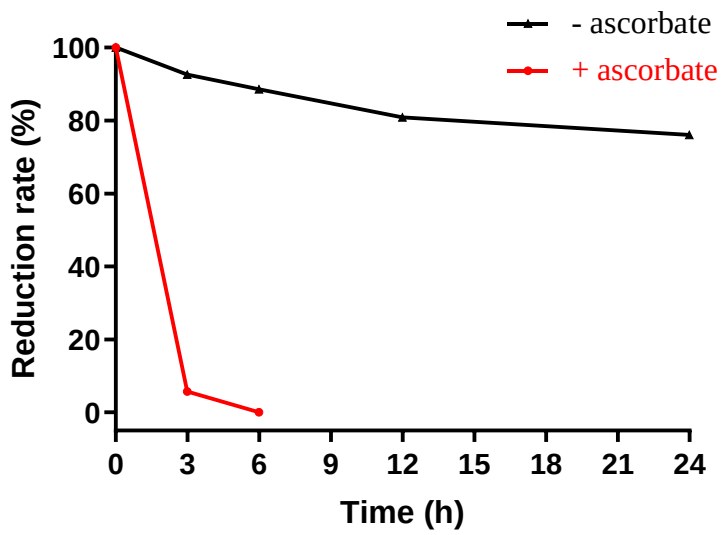


Figure S26. Summary of the stability of compound **6** in a PBS buffer (pH 7.4) with (+) or without (-) 1 mM sodium ascorbate at 37 ℃ in the dark.

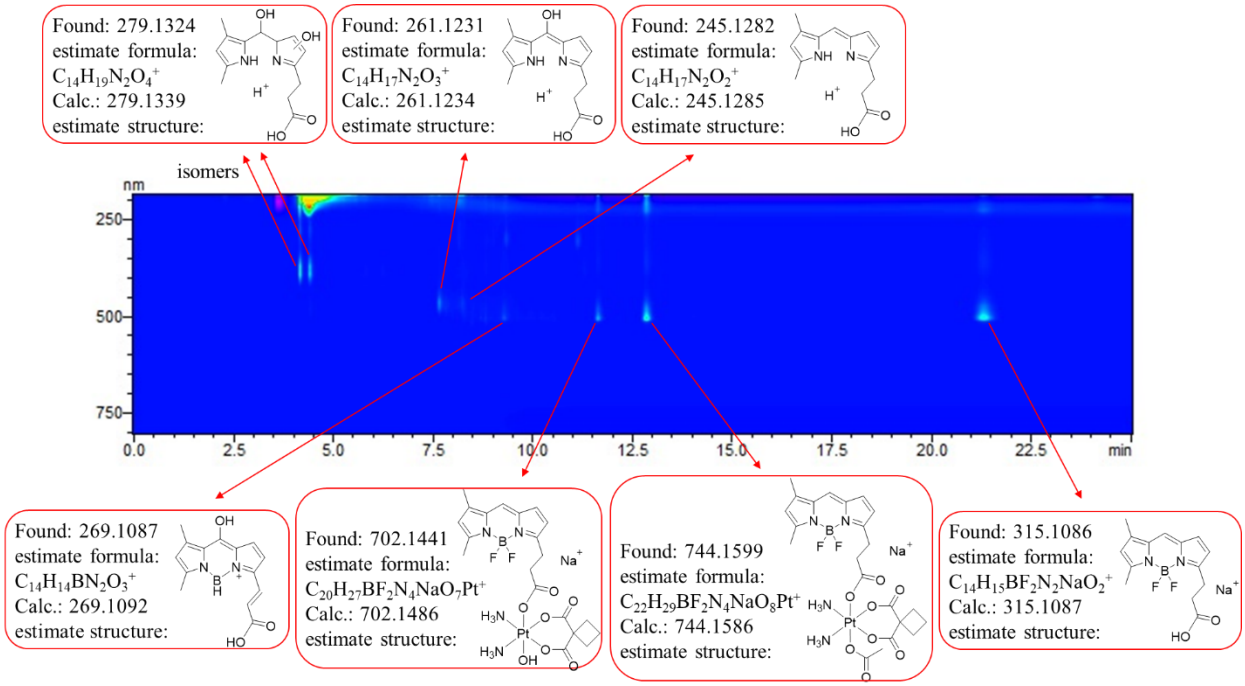


Figure S27. HPLC contour view of 200 µM BODI-Pt under irradiation by a green light (13 mW/cm^2) for 1 h in a PBS buffer (pH 7.4) with 1% DMF. The structures were proposed based on the m/z found in LC-HRMS and the corresponding proposed chemical formula. HPLC condition: 0 - 3 - 21 - 22 - 25 min, 10 - 40 - 40 - 10 - 10% acetonitrile with 0.1% HCOOH. 1 mL/min.

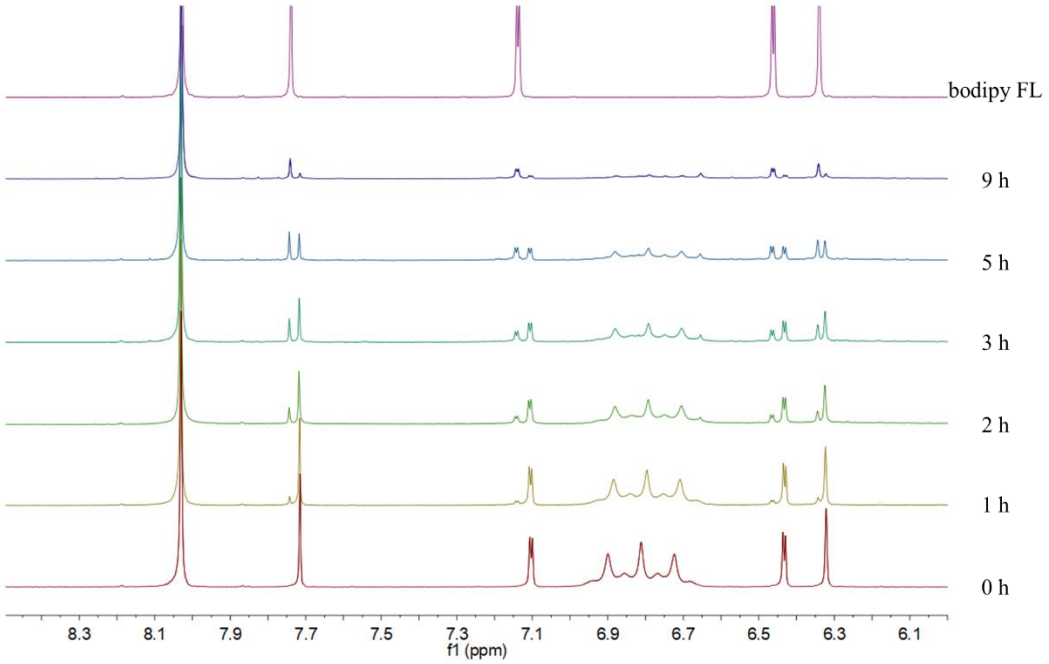


Figure S28. ^{1}H-NMR spectra of 14 mM BODI-Pt that irradiated under a white light (4 mW/cm^{2}) in DMF-d_7 (low field).

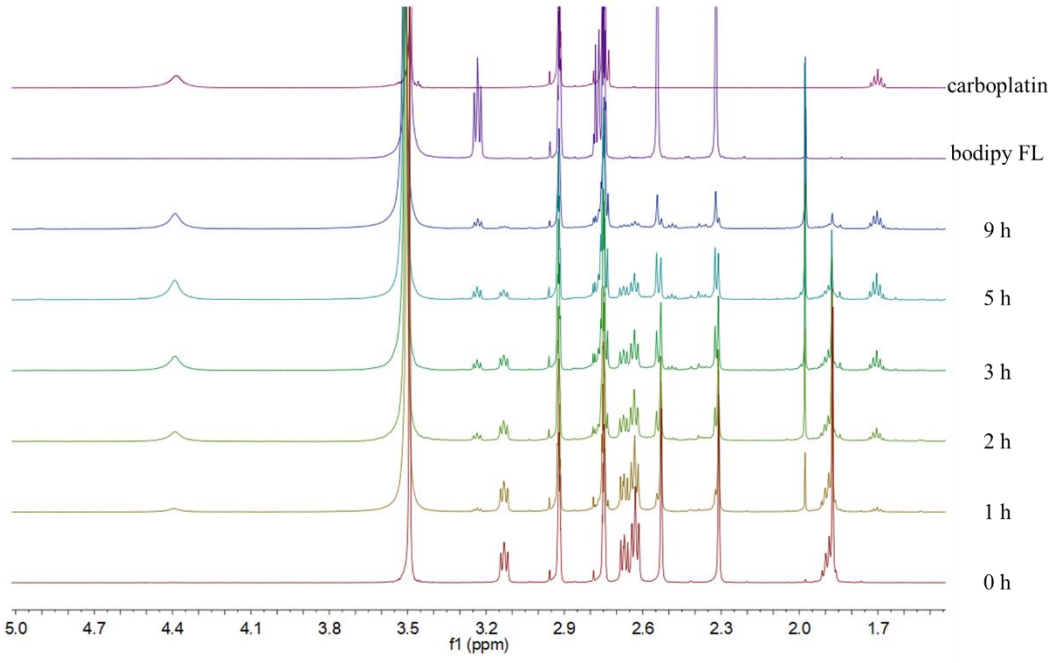


Figure S29. ^{1}H-NMR spectra of 14 mM BODI-Pt that irradiated under a white light (4 mW/cm^{2}) in DMF-d_7 (high filed).

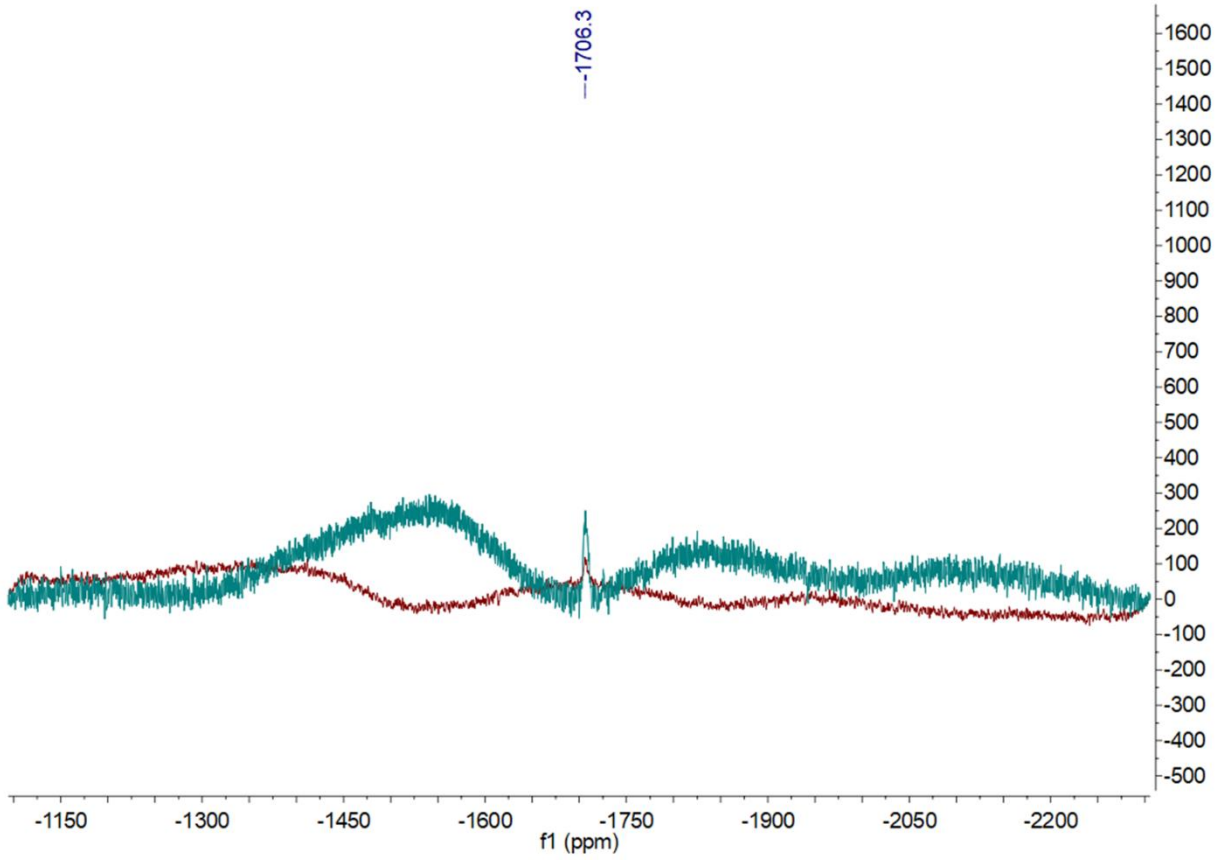


Figure S30. ^{195}Pt-NMR spectra of carboplatin (red line) and that formed from the activation of BODI-Pt (green line). BODI-Pt (14 mM) was irradiated under a white light (4 mW/cm^2) for 5 h in DMF-d_7.

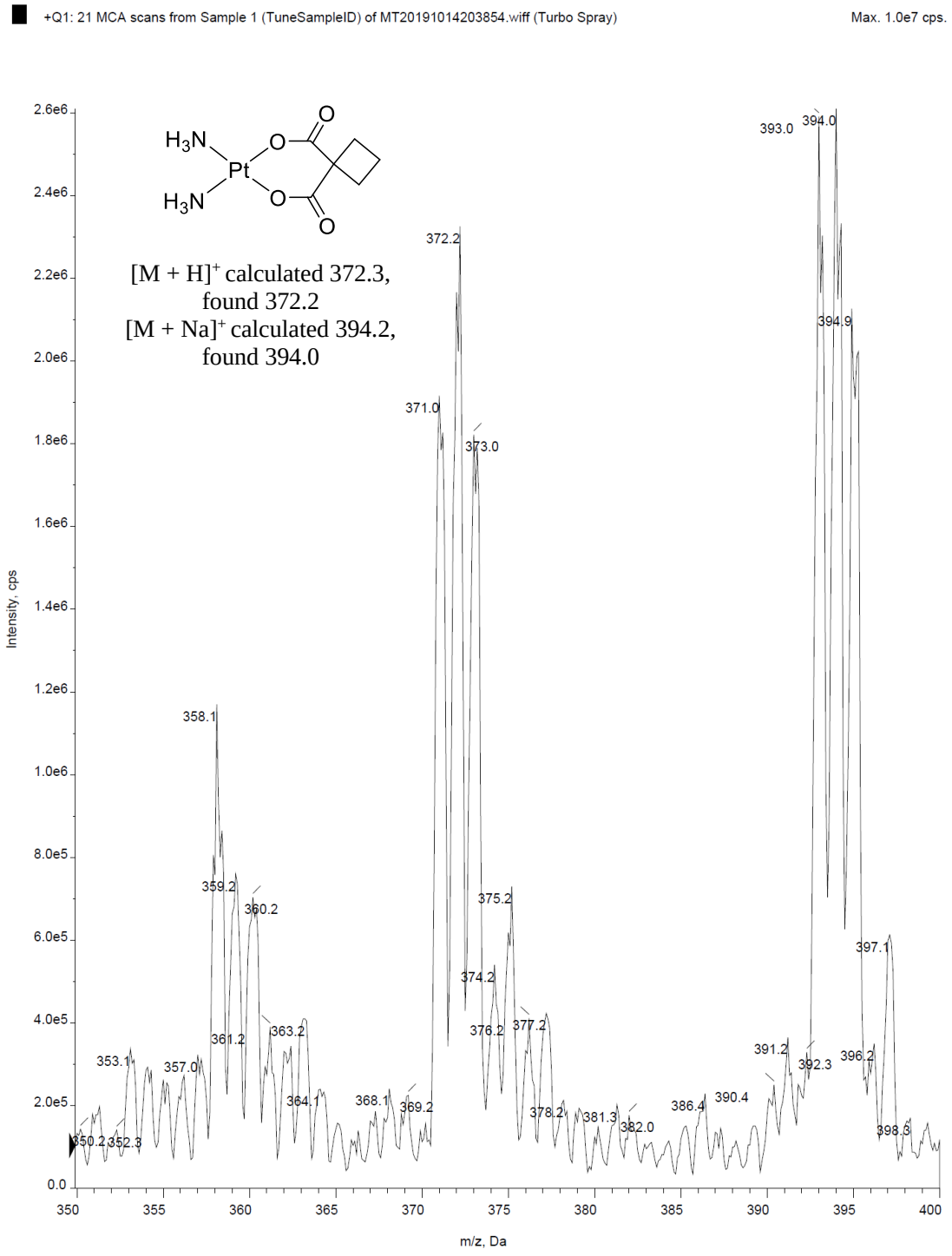


Figure S31. ESI-MS spectrum of carboplatin that formed from BODI-Pt after irradiation under a white light (4 mW/cm^2) for 9 h, positive mode in methanol.

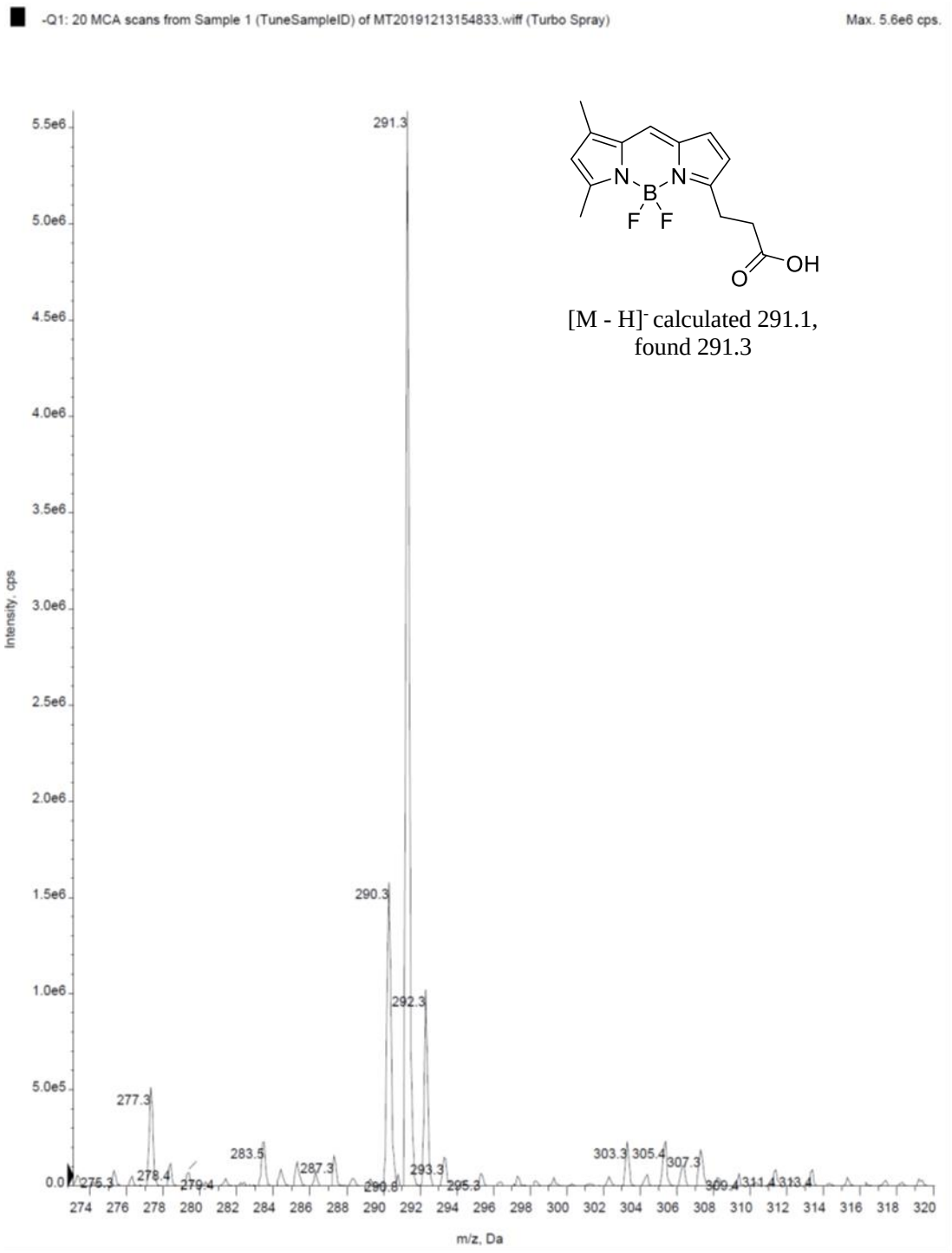


Figure S32. ESI-MS spectrum of bodipy FL that formed from BODI-Pt after irradiation under a white light (4 mW/cm^2) for 9 h, negative mode in methanol.

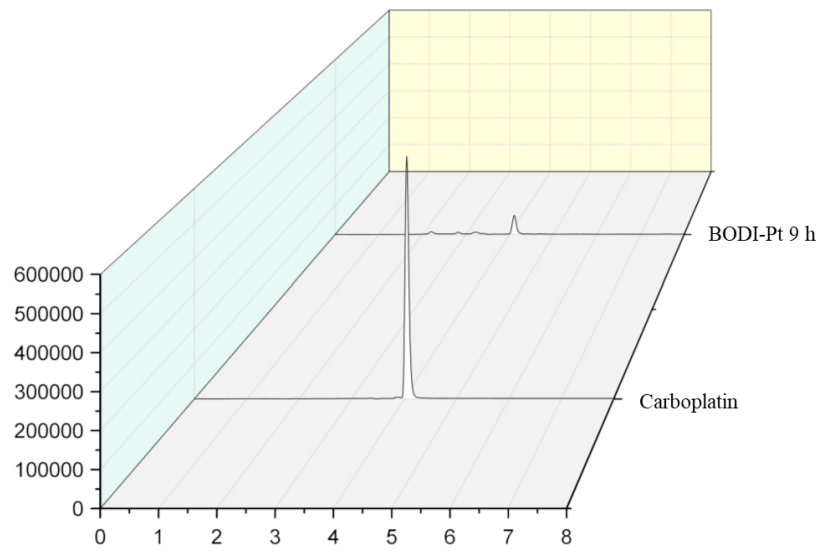


Figure S33. HPLC chromatograms of carboplatin and that formed from the activation of 14 mM BODI-Pt under a white light (4 mW/cm^2) for 9 h. HPLC condition: isocratic 5% ACN with 0.1% HCOOH for 8 min. 1 mL/min. Wavelength: 254 nm.

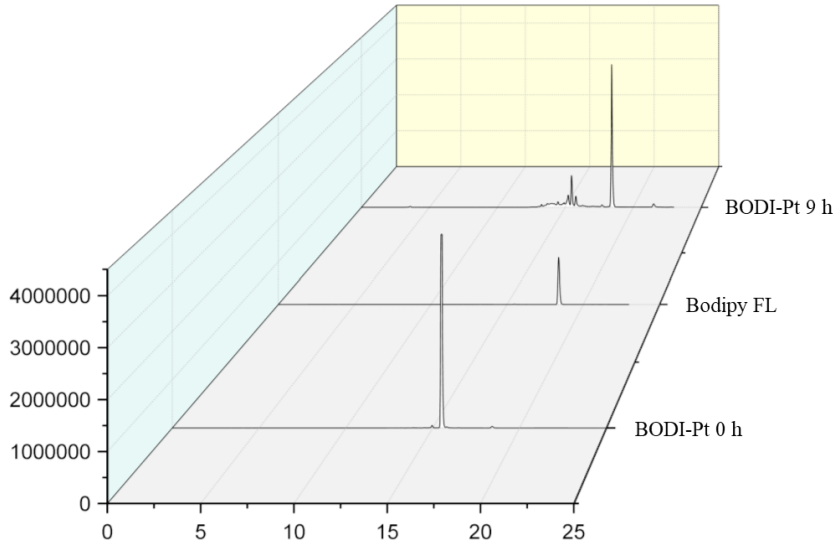


Figure S34. HPLC chromatograms of bodipy FL ligand and that formed from the activation of 14 mM BODI-Pt under a white light (4 mW/cm^2) for 9 h. HPLC condition: 0 - 5 - 7 - 20 - 21 - 25 min, 5 - 5 - 50 - 63 - 5 - 5% ACN with 0.1% HCOOH. 1 mL/min. Wavelength: 504 nm.

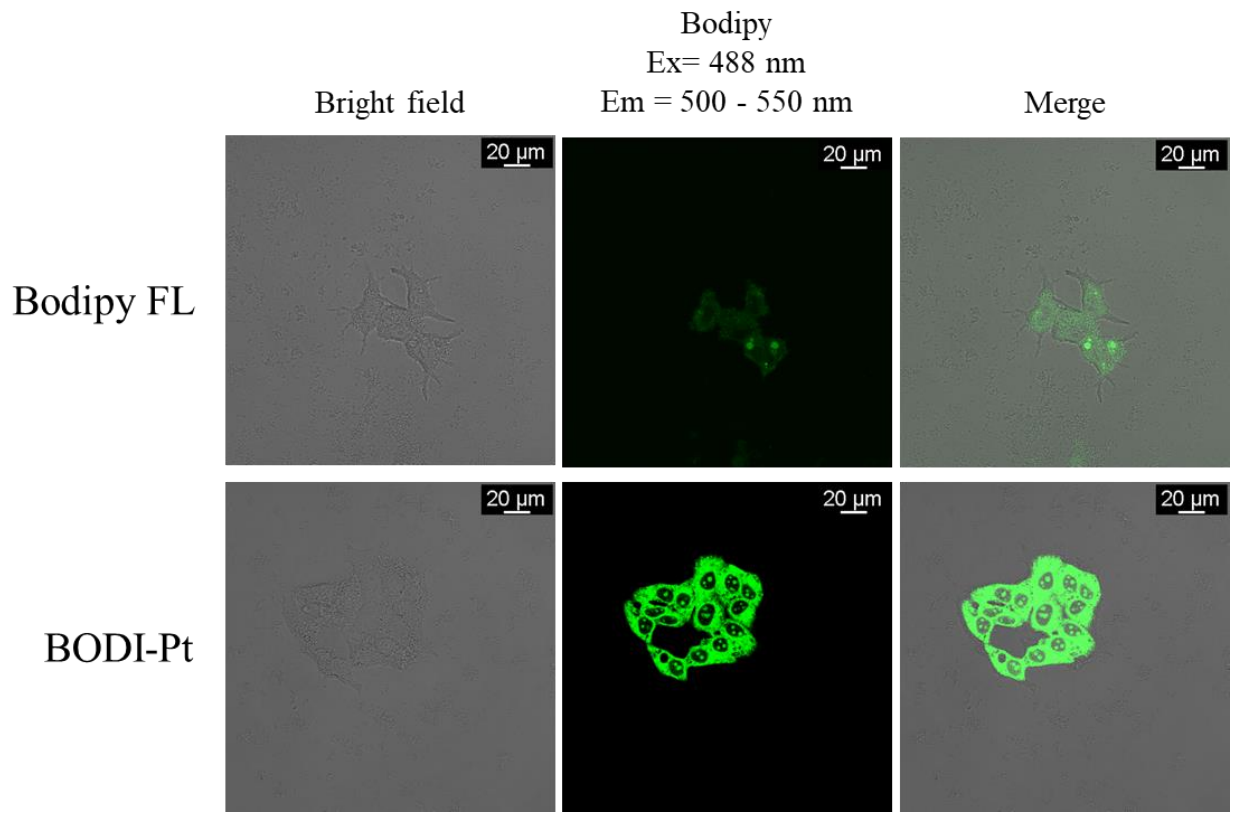


Figure S35. Confocal images of MCF-7 cells treated with bodipy FL and BODI-Pt (10 µM) for 6 h.

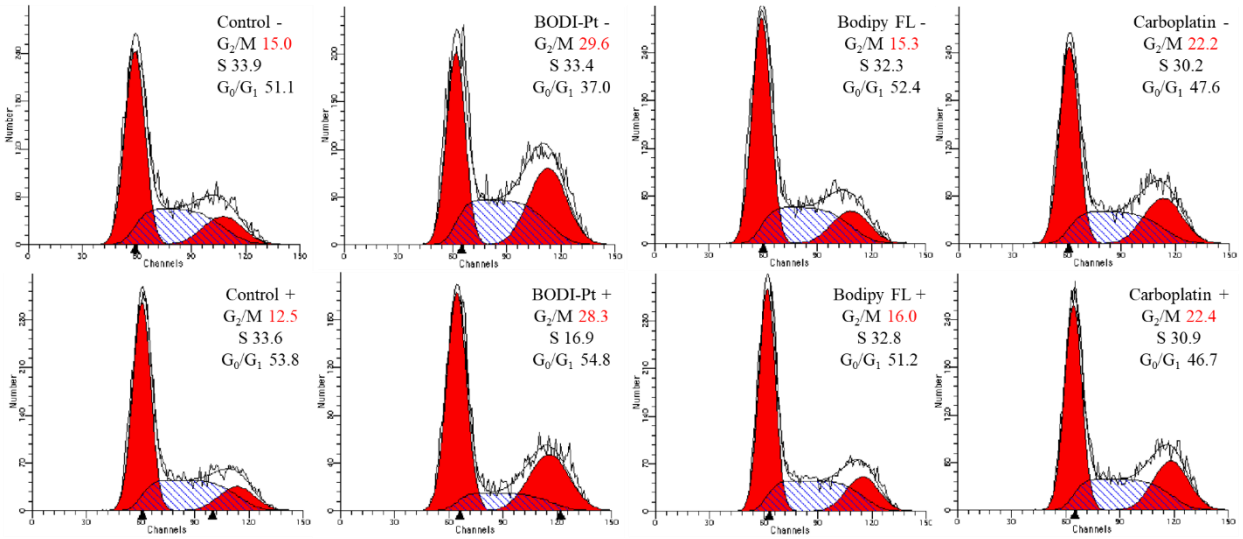


Figure S36. Cell cycle distribution of MCF-7 cells treated with BODI-Pt, carboplatin, and bodipy FL at 30 μM for 12 h before irradiation under green light (13 mW/cm^2) (+) or kept in the dark (-) for 30 min and then incubation in fresh media for another 24 h. Cells with medium only were used as the control group.

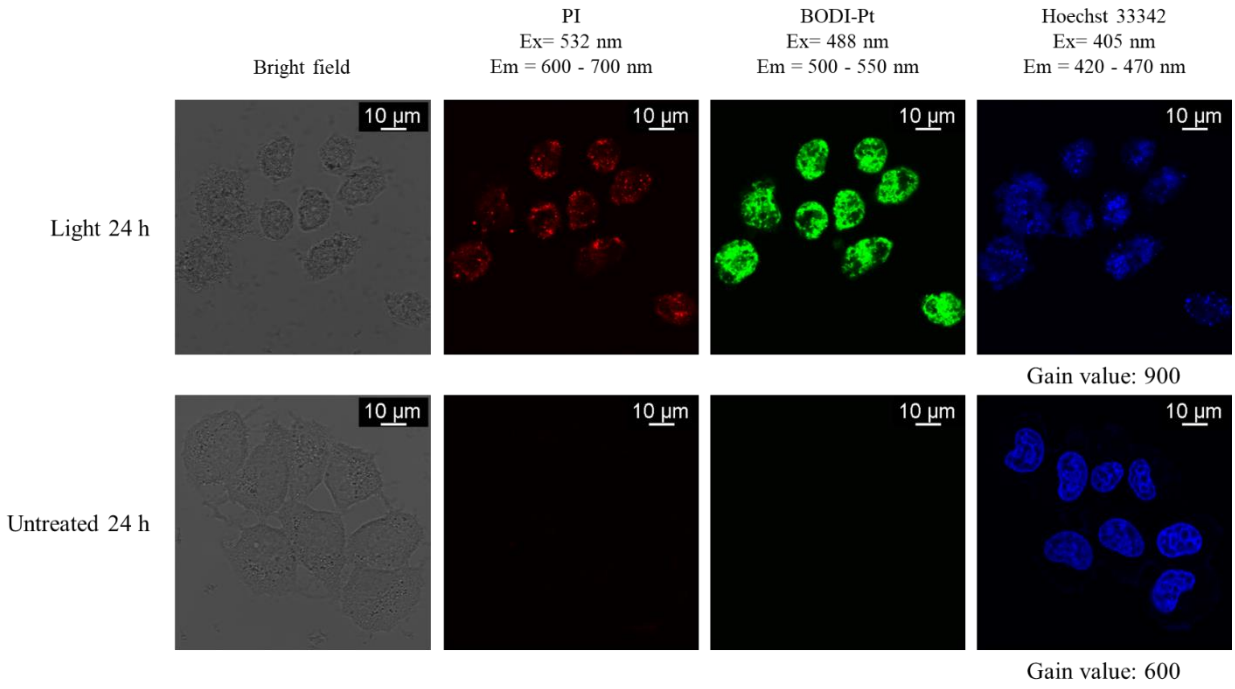


Figure S37. Confocal images of MCF-7 cells treated 30 μM BODI-Pt for 12 h, irradiated under green light (13 mW/cm^2) for 30 min and then incubated in fresh media for another 24 h, followed by staining with PI (1 μg/mL) and Hoechst 33342 (1 μg/mL) for 30 min. Cells without treatment were used as controls.

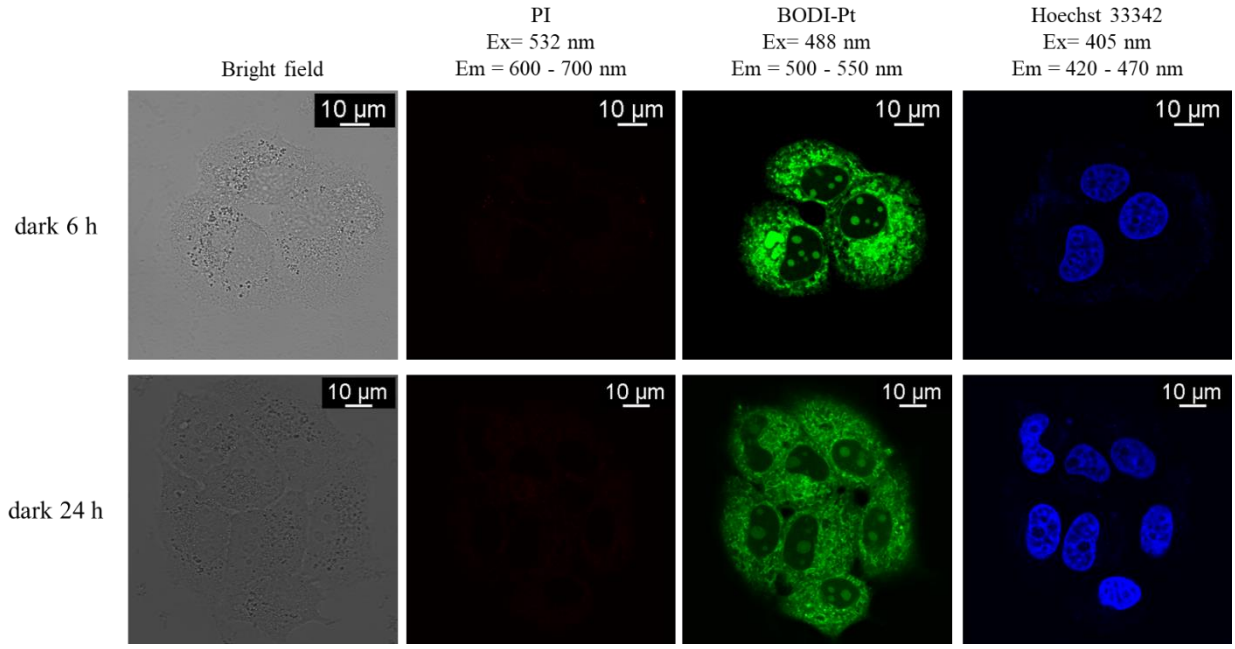


Figure S38. Confocal images of MCF-7 cells treated with 30 μM BODI-Pt for 12 h and then incubated in fresh media for another 6 or 24 h, followed by stained by PI (1 μg/mL) and Hoechst 33342 (1 μg/mL) for 30 min.

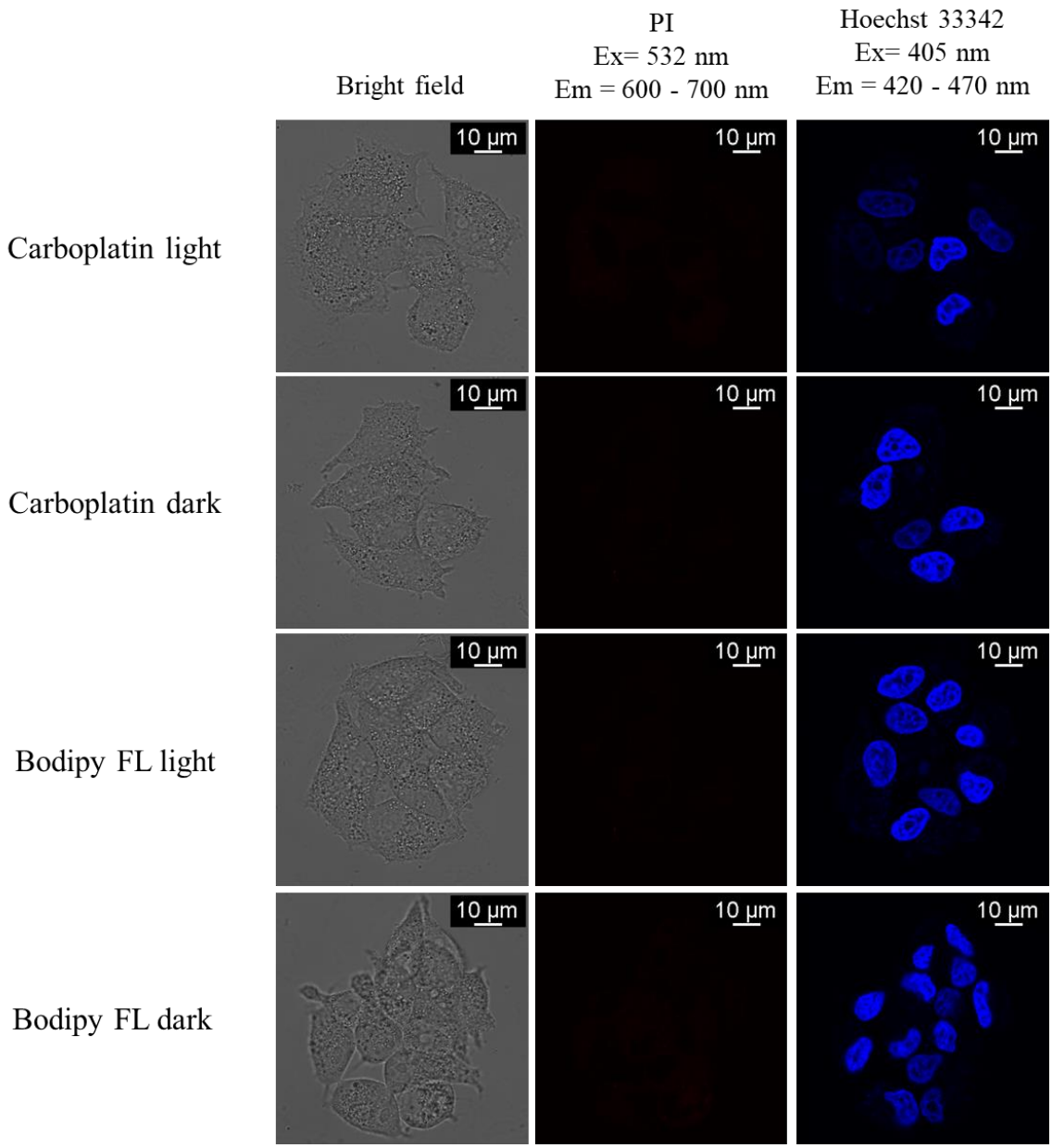


Figure S39. Confocal images of MCF-7 cells treated with 30 µM carboplatin or bodipy FL ligand for 12 h, irradiated under green light (13 mW/cm^2) for 30 min and then incubated in fresh media for another 6 h, followed by staining with PI (1 µg/mL) and Hoechst 33342 (1 µg/mL) for 30 min. Cells kept in the dark were used as controls.

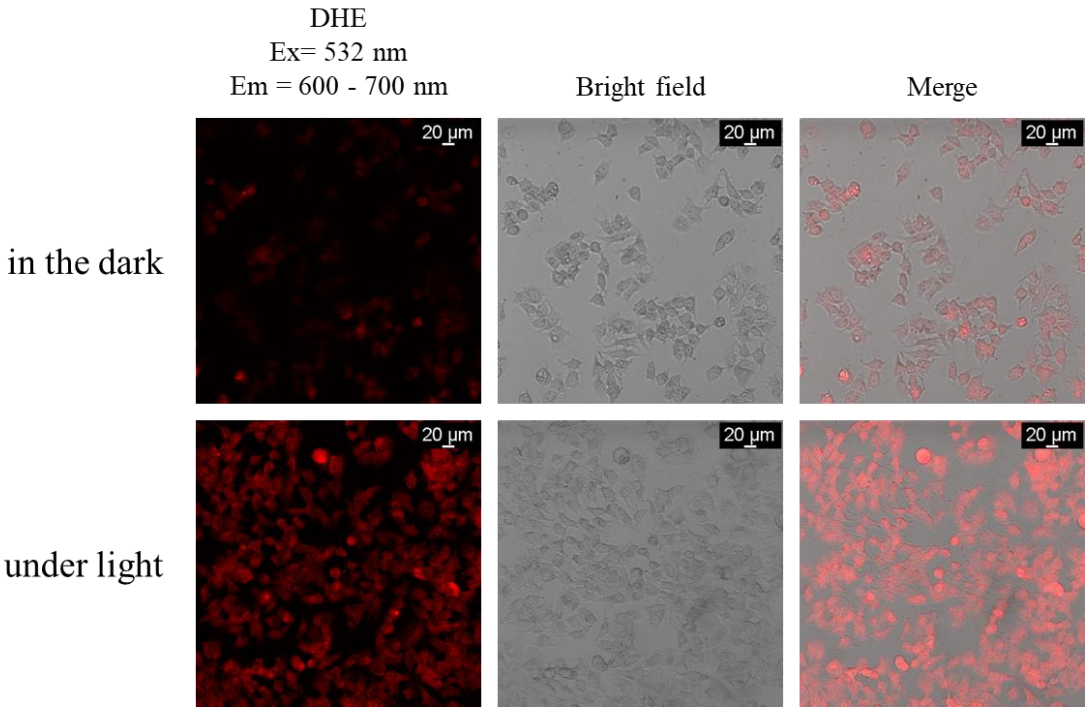


Figure S40. Confocal images of MCF-7 cells treated 30 μM BODI-Pt for 6 h and stained with 10 μM DHE for 15 min before irradiation under green light (13 mW/cm^2) or kept in the dark for 30 min.

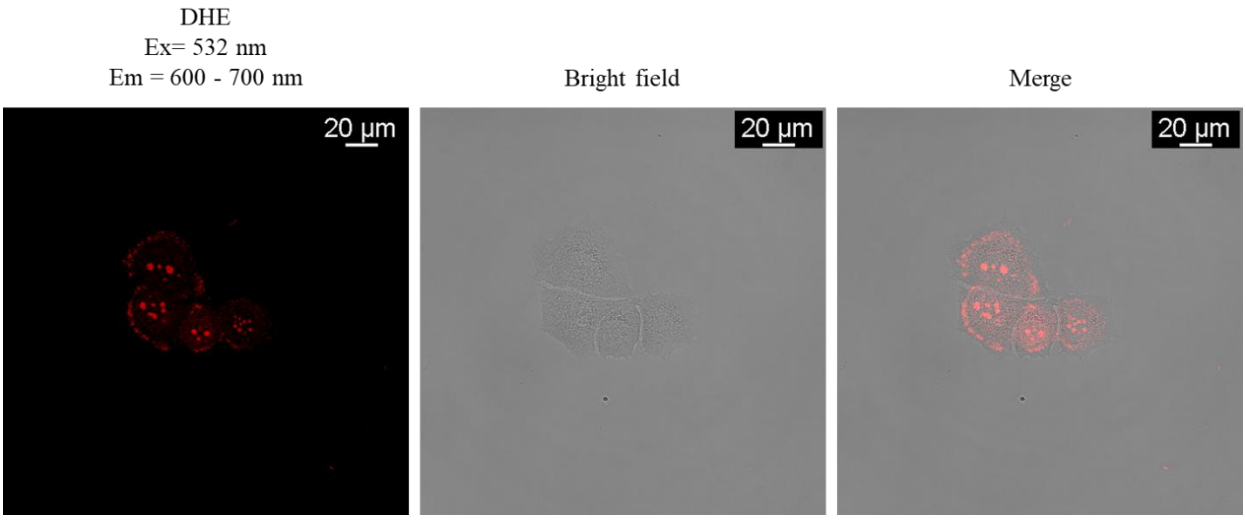


Figure S41. Enlarged confocal images of MCF-7 cells treated 30 μM BODI-Pt for 6 h and stained with 10 μM DHE for 15 min before irradiation under green light (13 mW/cm^2) for 30 min.

Table S1. The ct-DNA binding ratio of cisplatin, BODI-Pt, and carboplatin (10 μM) in a PBS buffer (pH = 7.4) after irradiation under green light (13 mW/cm^2) for 30 min and incubation at 37 ℃ for 24 h. +: Under light. -: In the dark.

Groups	Cisplatin	BODI-Pt	Carboplatin
Light (+)	83.7 ± 9.7	30.2 ± 2.2	4.6 ± 0.2
Dark (-)	85.9 ± 1.7	5.9 ± 0.8	5.7 ± 0.4

Table S2. Time-dependent accumulation of 10 μM BODI-Pt and carboplatin in MCF-7 cells.

Time (h)	Pt concentration (ng Pt/ 10^6 cells)	
	BODI-Pt	Carboplatin
0	0	0
3	3.9 ± 0.4	2.7 ± 0.4
6	8.4 ± 0.9	3.9 ± 0.3
12	15.5 ± 1.7	6.1± 0.7
24	19.9 ± 1.5	9.5 ± 0.7

Table S3. IC_{50} (μM) of bodipy FL ligand on different cell lines.

Cell Lines	Bodipy FL	
	Light (+)	Light (-)
MCF-7	> 200	>200
MDA-MB-231	> 200	> 200
SKOV3	> 200	> 200
A2780	198.5	> 200
HeLa	>200	>200
A549	> 200	> 200
WI-38	-	>200

Cells were treated with bodipy FL at different concentrations for 12 h before irradiation under the green light (13 mW/cm^2) (+) or keep in the dark (-) for 30 min and then incubation in fresh media for another 72 h.

Table S4. Pt binding levels of BODI-Pt and carboplatin in the genomic DNA of MCF-7 cells after treatment at 30 μM for 12 h, irradiation under green light (13 mW/cm^2) for 30 min and culture for another 8 h.

Groups	Pt concentration (ng Pt/ μg DNA)	
	BODI-Pt	Carboplatin
Light	0.92 ± 0.19	0.19 ± 0.04
Dark	0.29 ± 0.07	0.25 ± 0.02

Table S5. Cell cycle distribution of MCF-7 cells treated with BODI-Pt, carboplatin, and bodipy FL.

Groups	G_0/G_1	S	G_2/M
Control -	51.1	33.9	15.0
Control +	53.8	33.6	12.5
BODI-Pt -	37.0	33.4	29.6
BODI-Pt +	54.8	16.9	28.3
Carboplatin -	47.6	30.2	22.2
Carboplatin +	46.7	30.9	22.4
Bodipy FL -	52.4	32.3	15.3
Bodipy FL +	51.2	32.8	16.0

Cells were treated with compounds at 30 μM for 12 h before irradiation under green light (13 mW/cm^2) (+) or keep in the dark (-) for 30 min and then incubation in fresh media for another 24 h. Cells with medium only were used as the control group.