Supporting Information

A mitochondria-targeted BODIPY-Ir(III) conjugate as a photoinduced ROS generator for the oxidative destruction of triple-negative breast cancer cells

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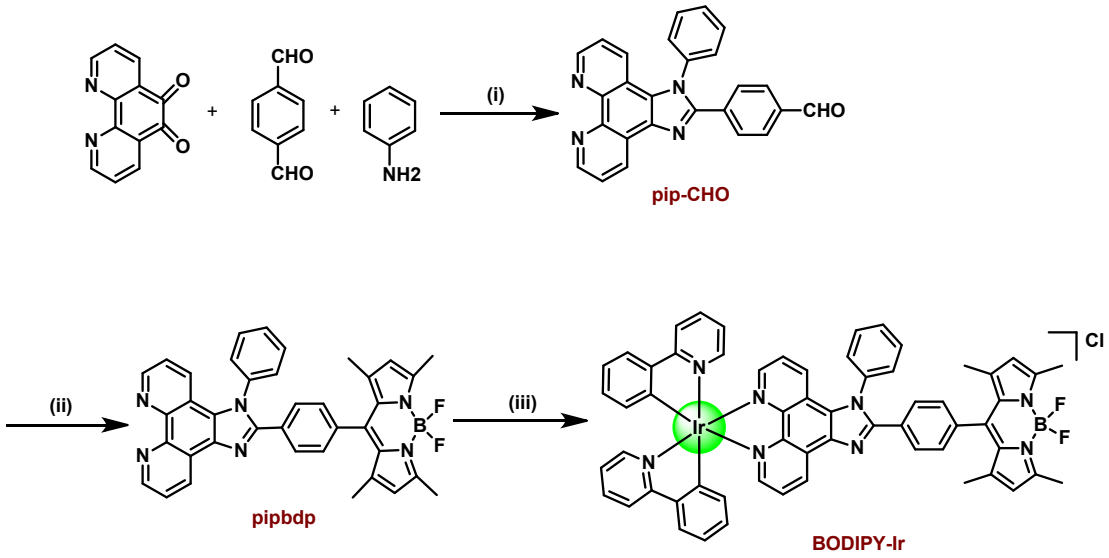
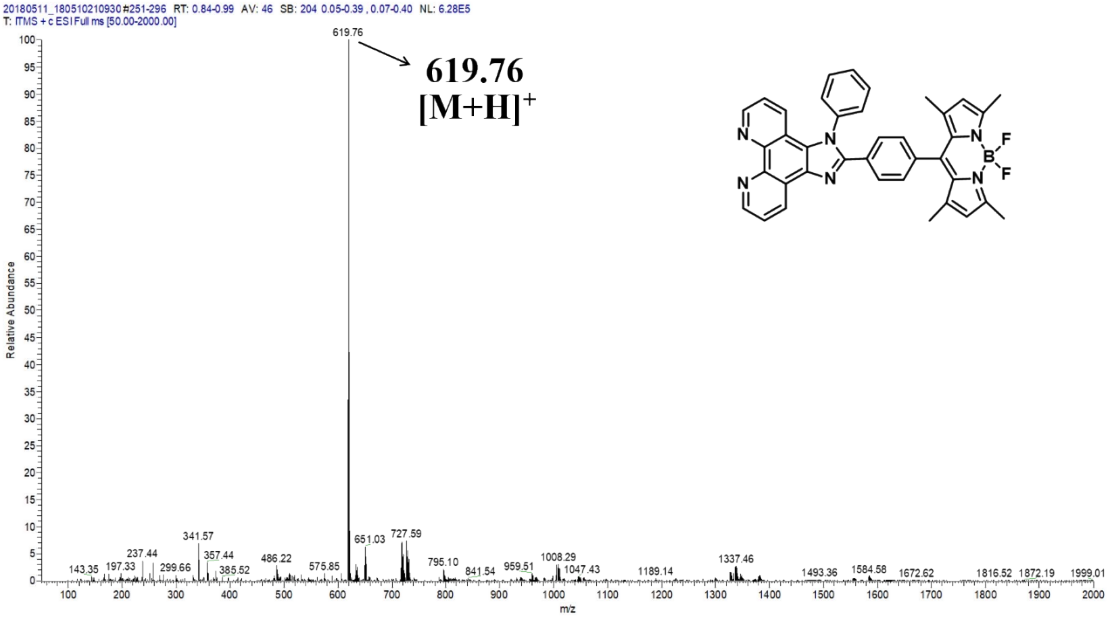
Synthesis



Scheme S1. Synthetic routes for **BODIPY-Ir**. (i) AcOH, reflux overnight. (ii) DCM, 2,4-dimethylpyrrole, TFA, DDQ, TEA, $BF_3 \cdot Et_2O$, RT. (iii) $[Ir(ppy)_2Cl]_2$, DCM/MeOH, reflux, 12h

Supporting Figures and Tables



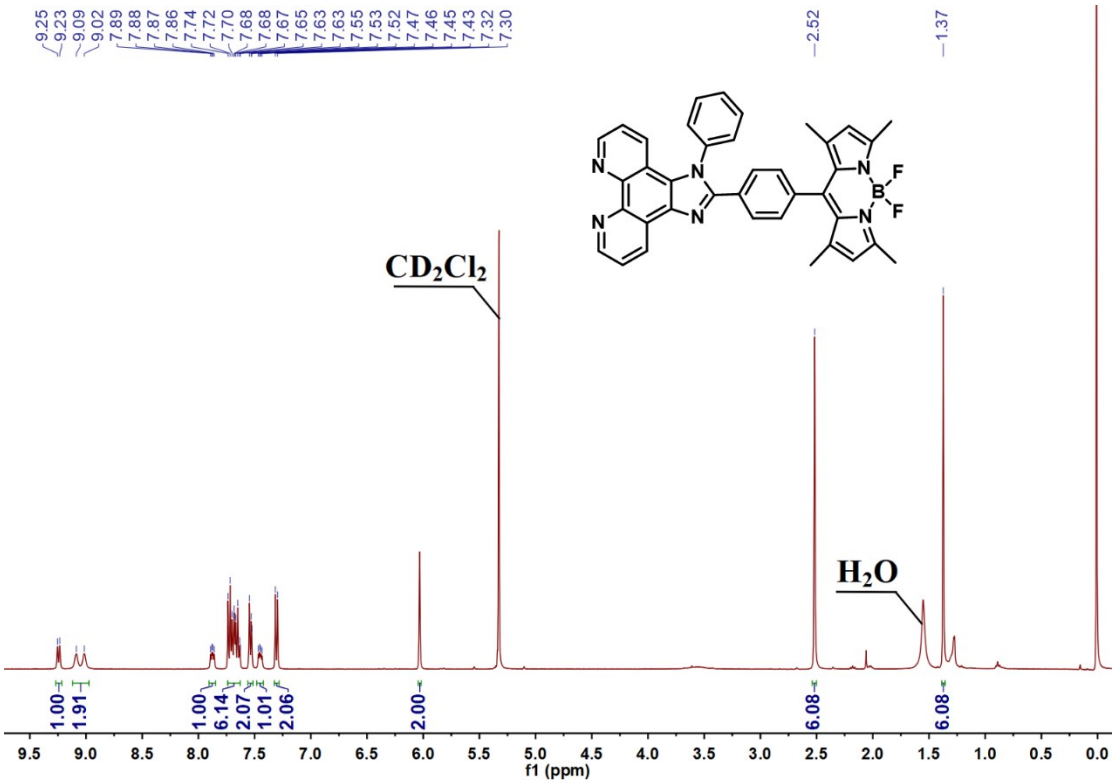
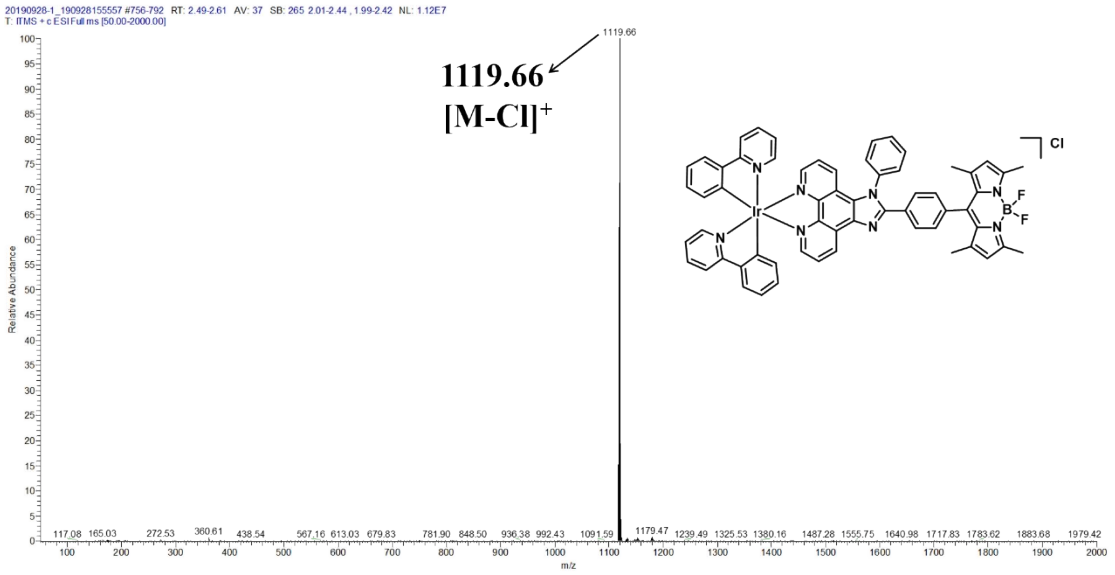


Fig. S1 ESI-MS spectrum, ^{1}H NMR spectrum of **pipbdp**



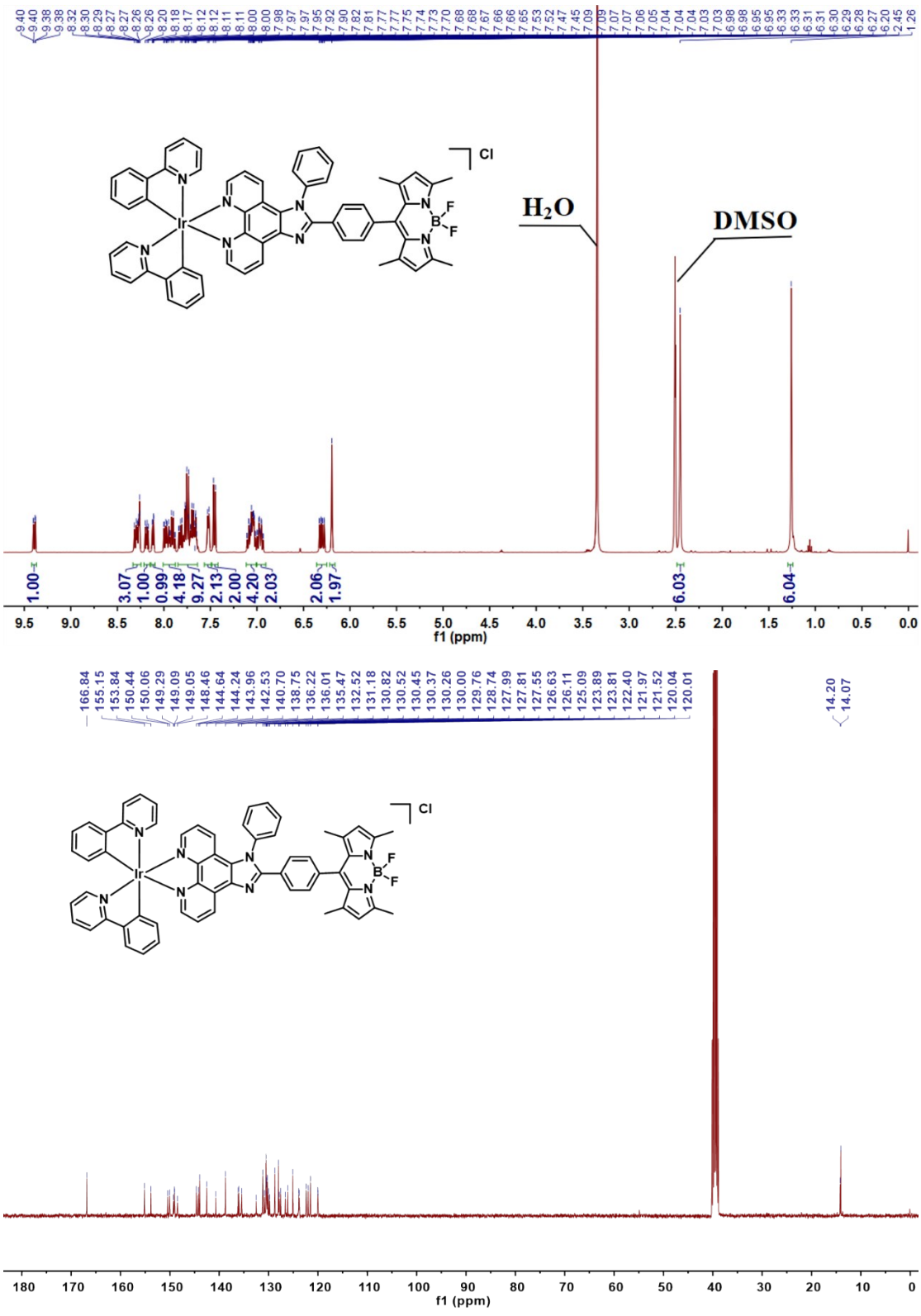


Fig. S2 ESI-MS spectrum, ^{1}H NMR and ^{13}C NMR spectrum of **BODIPY-Ir**

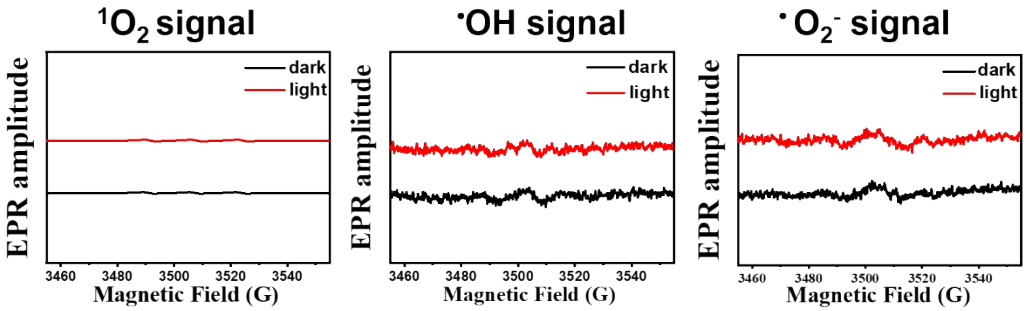


Fig. S3 EPR spectra of the blank (i.e., free ROS trappers): TEMP in MeOH (a), DMPO in H_2O (b) and DMPO in MeOH (c) in the absence/presence of irradiation (λ_{ex} = 405 nm).

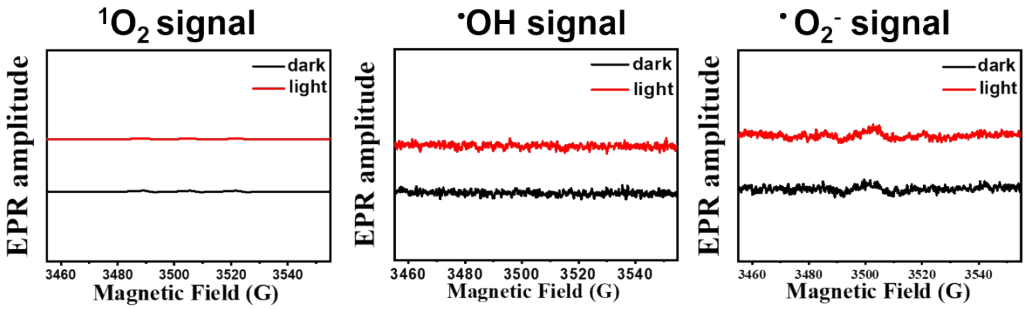


Fig. S4 EPR spectra of the blank (i.e., free ROS trappers): TEMP in MeOH (a), DMPO in H_2O (b) and DMPO in MeOH (c) in the absence/presence of irradiation (λ_{ex} = 500 nm).

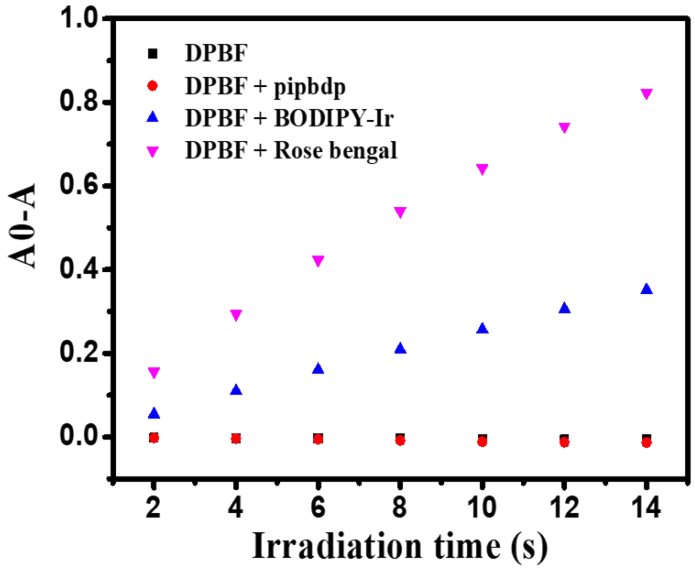


Fig. S5 Photooxidation of DPBF by **pipbdp** and **BODIPY-Ir**, respectively, in aerated MeOH under irradiation at 500 nm. Changes in absorbance of DPBF at 418 nm was plotted. Rose Bengal (Φ = 0.80) was used as the reference.

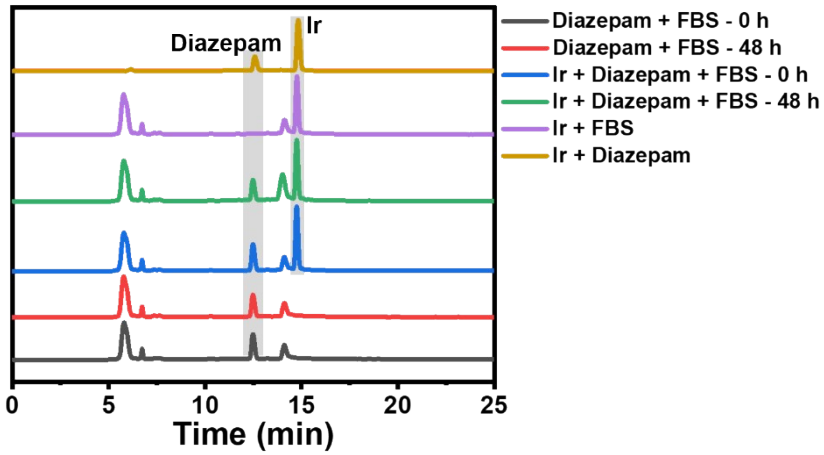


Fig. S6 HPLC analysis of **BODIPY-Ir** incubated in FBS for 0 h or 48 h.

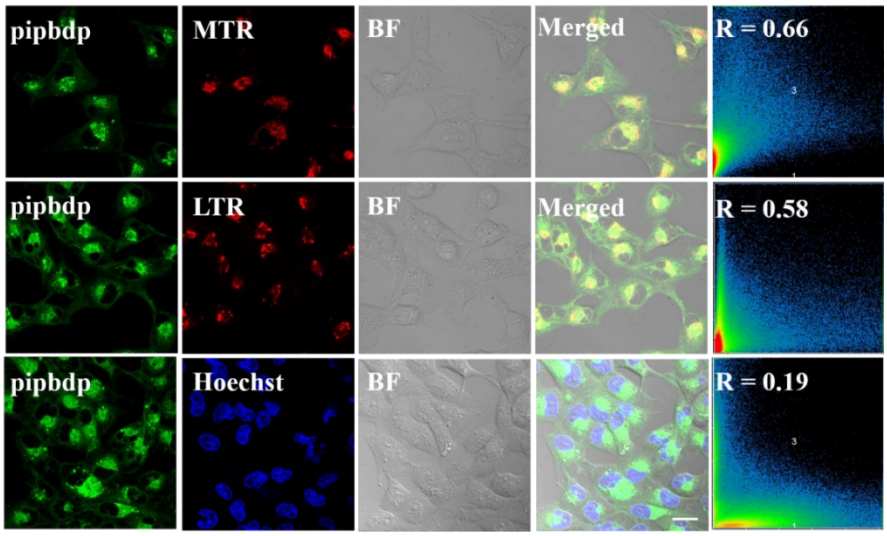


Fig. S7 Subcellular distribution in MDA-MB-231 cells of **pipbdp** (100 nM, 4 h) by confocal co-localization imaging. The respective Pearson's co-localization coefficient (R) of **pipbdp** (λ_{ex} = 488 nm, λ_{em} = 515 ± 20 nm) with MTR (λ_{ex} = 561 nm, λ_{em} = 644 ± 20 nm), LTR (λ_{ex} = 561 nm, λ_{em} = 590 ± 20 nm), and Hoechst 33342 (λ_{ex} = 405 nm, λ_{em} = 460 ± 20 nm) is provided in the rightmost column (scale bar: 20 μm).

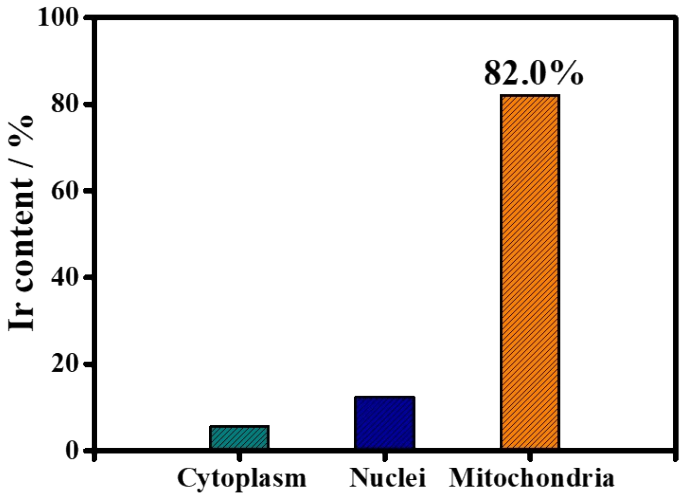


Fig. S8 ICP-MS quantification of the internalized Ir by the MDA-MB-231 cells. MDA-MB-231 cells were treated with **BODIPY-Ir** (100 nM) at 37 °C for 4 h in the dark. Nuclei (Nuc.), mitochondria (Mito.) and cytoplasm (without Nuclei and mitochondria, Cyto.) were extracted using mitochondrial and nuclear isolation kits.

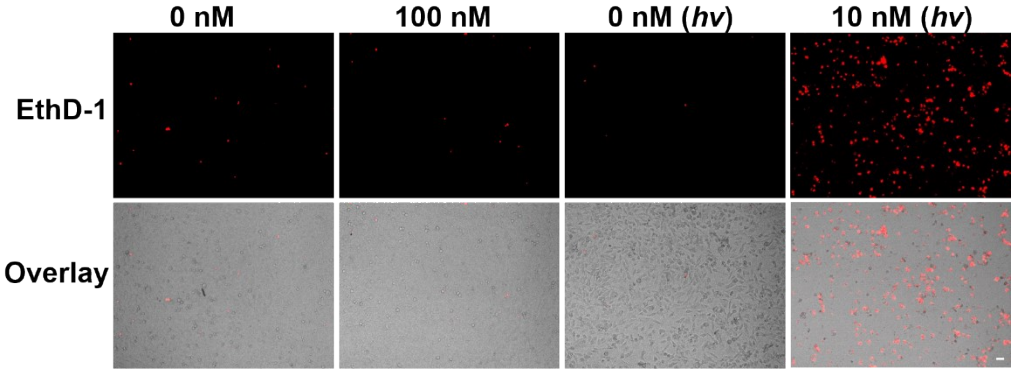


Fig. S9 Live/Dead cell staining of MDA-MB-231 cells pretreated with **BODIPY-Ir** (10 nM) with/without PDT treatment (500 nm, 6 J cm^{-2}). Insert scale bar: 50 μm.

Table. S1 Crystal data and refinement for **BODIPY-Ir**

Empirical formula	$C_{127}H_{99}B_2Cl_2F_4Ir_2N_{16}$
Formula weight	2402.14
Temperature/K	150.0
Crystal system	Triclinic
Space group	$P\bar{1}$
a/Å	17.6837(15)
b/Å	18.1876(18)
c/Å	20.173(2)
α/°	93.911(5)
β/°	92.383(5)
γ/°	104.711(4)
Volume/Å^3	6249.3(10)
Z	2
ρ_{calc}g/cm^3	1.277
μ/mm^{-1}	2.228
F(000)	2414.0
Crystal size/mm^3	0.07 × 0.03 × 0.025
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.028 to 49.998
Index ranges	$-14 \le h \le 21$, $-21 \le k \le 21$, $-23 \le l \le 23$
Reflections collected	49526
Independent reflections	21312 [R_{int} = 0.0946, R_{sigma} = 0.1732]
Data/restraints/parameters	21312/1027/1396
Goodness-of-fit on F^2	1.139
Final R indexes [I>=2σ (I)]	R_1 = 0.0981, wR_2 = 0.2586
Final R indexes [all data]	R_1 = 0.1755, wR_2 = 0.2829
Largest diff. peak/hole / e Å^{-3}	1.77/-1.51

Table. S2 Selected bond lengths (Å) and angles (°) for **BODIPY-Ir**

Bond length (Å)	Ir1-N1	2.049(8)
	Ir1-N2	2.057(8)
	Ir1-N3	2.138(10)
	Ir1-N4	2.162(9)
	Ir1-C1	2.004(12)
	Ir1-C12	2.014(11)
Bond angles (°)	N1-Ir1-N2	173.5(4)
	N1-Ir1-N3	97.3(4)
	N1-Ir1-N4	88.4(3)
	N2-Ir1-N3	88.4(3)
	N2-Ir1-N4	95.8(3)
	N3-Ir1-N4	77.0(4)
	C1-Ir1-N1	79.9(4)
	C1-Ir1-N2	94.5(4)
	C1-Ir1-N3	175.9(4)
	C1-Ir1-N4	99.9(4)
	C1-Ir1-C12	85.4(5)
	C12-Ir1-N1	95.8(4)
	C12-Ir1-N2	80.4(4)
	C12-Ir1-N3	97.9(4)
	C12-Ir1-N4	173.8(4)

Table S3. Photophysical properties of the compounds in MeOH[a]

Compound	λ_{abs} [b]/nm (ε [c])	λ_{em}/nm	Φ (%)[d]	Φ ($^1O_2$)[e]
pipbdp	270 (3.97), 500 (5.87)	510	44.2	0
BODIPY-Ir	270 (8.19), 380 (1.47), 500 (6.49)	513	10.4	0.35

[a] Data recorded in MeOH solution, and the excitation wavelength is 480 nm, 298 K.

[b] λ_{abs} denotes the wavelength corresponding to absorption maximums.

[c] Molar absorption coefficient at the absorption maxima (x 10^4 M^{-1} cm^{-1}).

[d] Luminescent quantum yield, BODIPY was used as the standard (Φ_L = 0.72 in THF)[1, 2].

[e.] Singlet oxygen quantum yield, Rose Bengal (0.80) was used as the reference[1].

References

1. W. Wu, J. Sun, X. Cui and J. Zhao, *J. Mater. Chem. C*, 2013, **1**, 4577.
2. W. Wu, J. Zhao, J. Sun and S. Guo, *J. Org. Chem.*, 2012, **77**, 5305.