

Supporting Information

**Mitochondria-localized dinuclear iridium(III) complexes for
two-photon photodynamic therapy**

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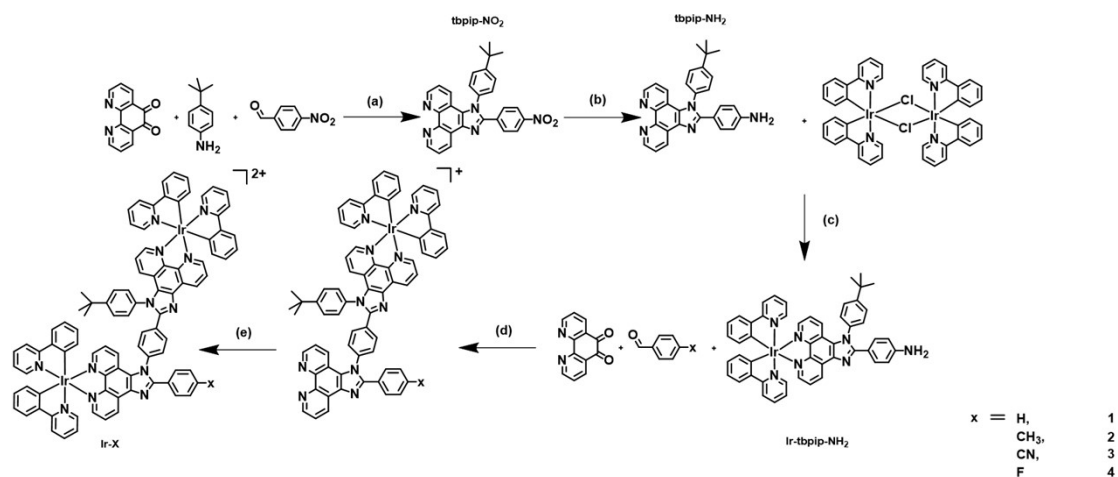


Fig. S1 Synthetic route of the **Ir(III)** complexes. (a) NH₄OAc, HOAc, 120 °C, 12 h; (b) Pd/C, EtOH, H₂O₂, 65°C, 12 h; (c) DCM/MeOH(1:1, v/v), Ar, 85 °C, 6 h; (d) NH₄OAc, HOAc, 135 °C, 12 h; (e) DCM/MeOH(1:1, v/v), Ar, 85 °C, 6 h.

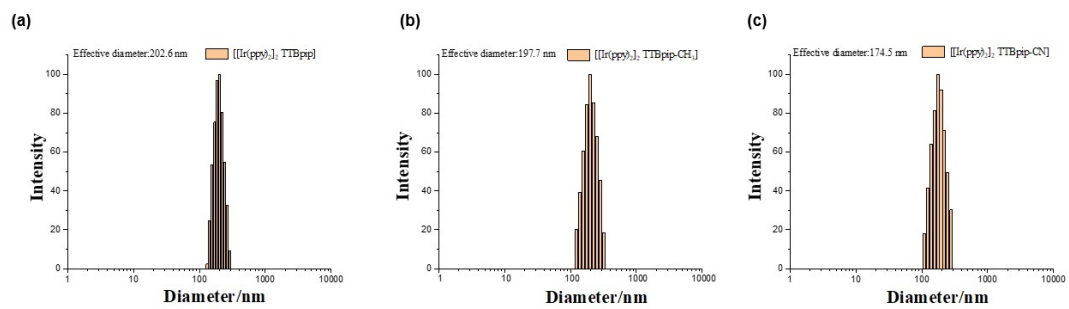


Fig. S2 Size distribution of (a) N-Ir1, (b) N-Ir2, (c) N-Ir3 determined by dynamic light scattering.

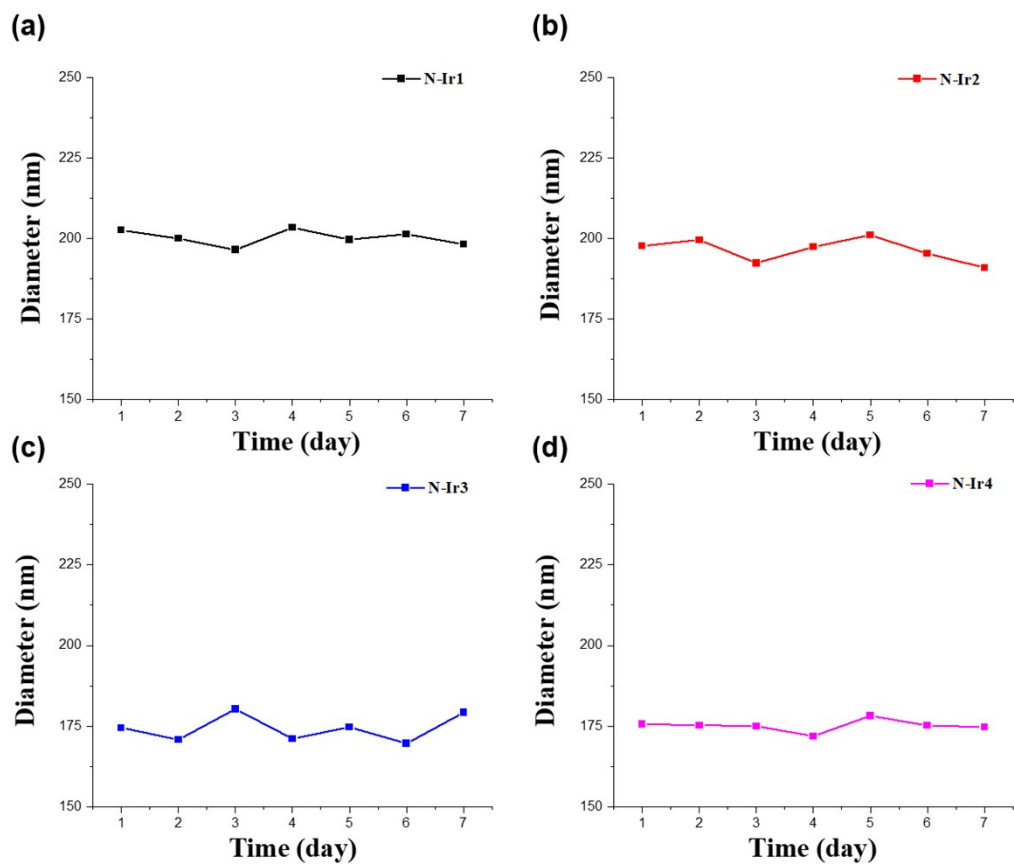


Fig. S3 Long-term stability evaluation for different nanoparticles. (a) N-Ir1, (b) N-Ir2, (c) N-Ir3, (d) N-Ir4.

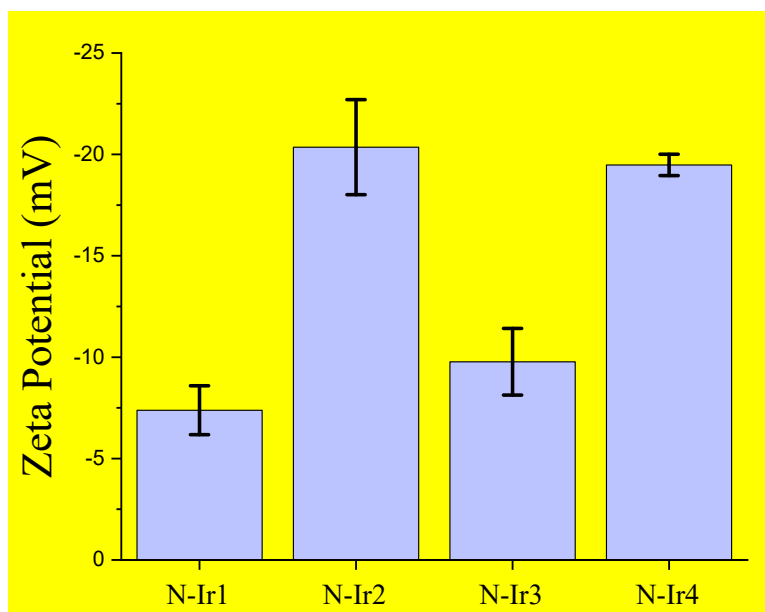


Fig. S4 Zeta potentials of N-Ir1-4 in physiological pH aqueous solution.

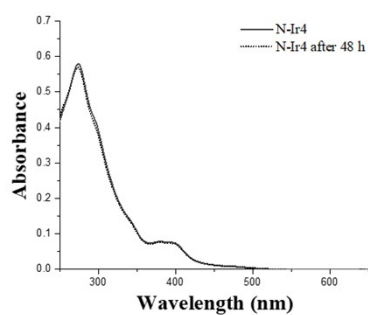
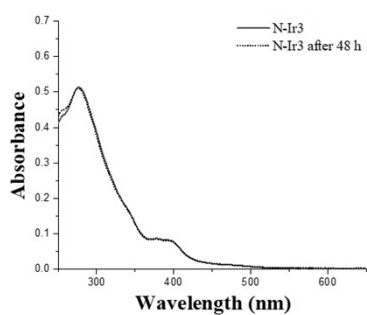
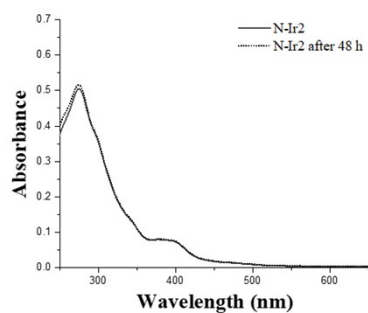
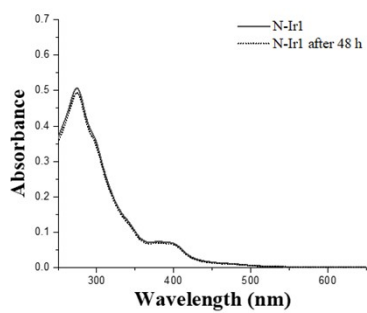


Fig. S5 UV-Vis spectra of the N-Ir1-4 in PBS for 48 h.

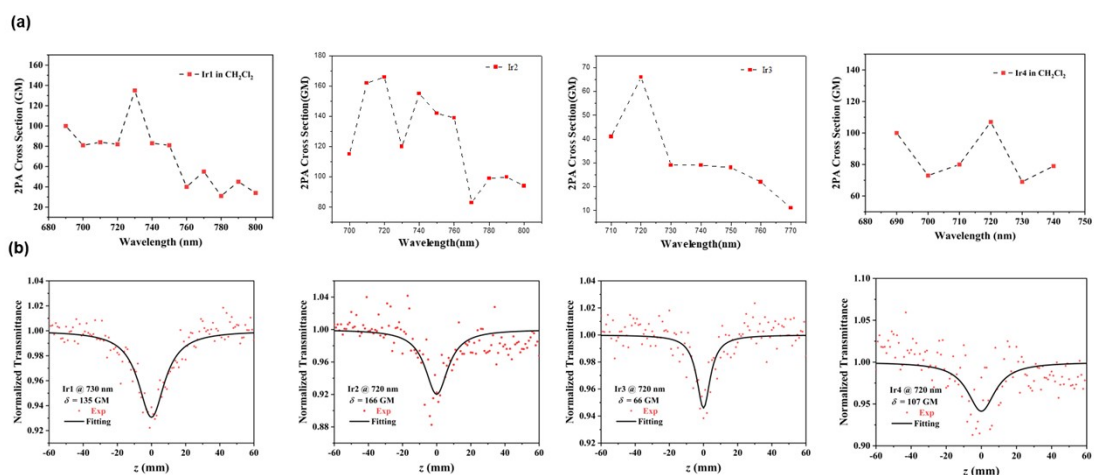


Fig. S6 (a) Two-photon absorption cross section of **Ir1-4** in dichloromethane ($c \sim 1.0 \times 10^{-2}$ M). (b) OA Z-scan data of **Ir1-4**. Open scattered symbols represent experimental data and solid lines are fits resulting from 2PA, The solid lines represent the fits for 2PA.

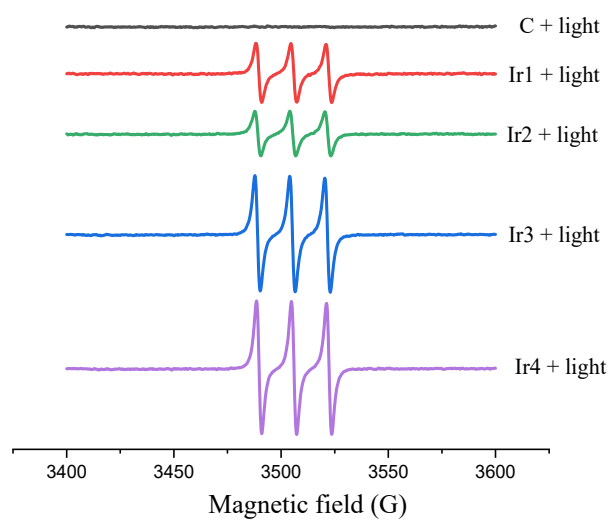


Fig. S7 ESR spectra of **Ir1-4** in the presence of TEMP.

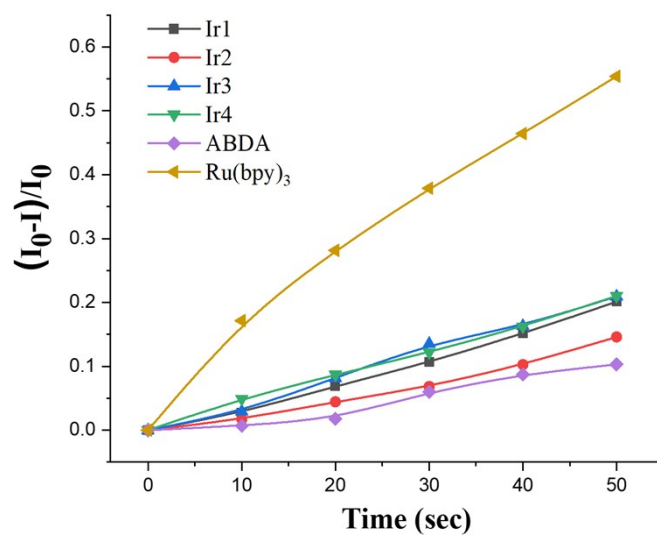


Fig. S8 Plots of the cumulative decrease in optical density of ABDA (100 μ M) at 378 nm along irradiation time ($\lambda_{\text{irr}}=405$ nm) in the presence of the indicated complexes. $[\text{Ru}(\text{bpy})_3]^{2+}$ as the standard.

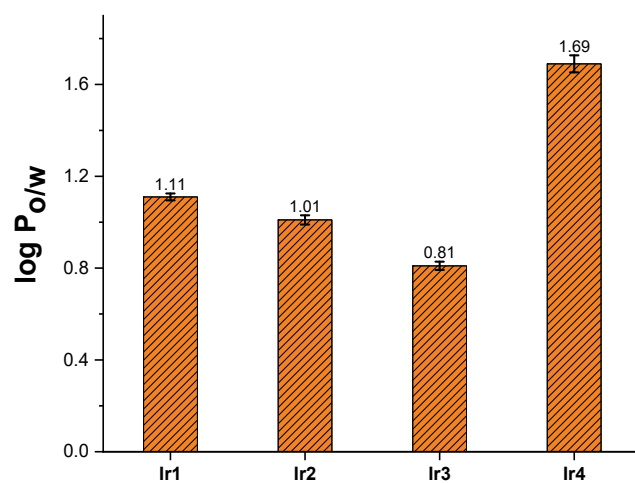


Fig. S9 Partition coefficient ($\log P_{o/w}$) of the indicated complexes. All the experiments were performed as duplicates of triplicates ($n = 3$ independent experiments). The error bars represent the standard deviation (SD).

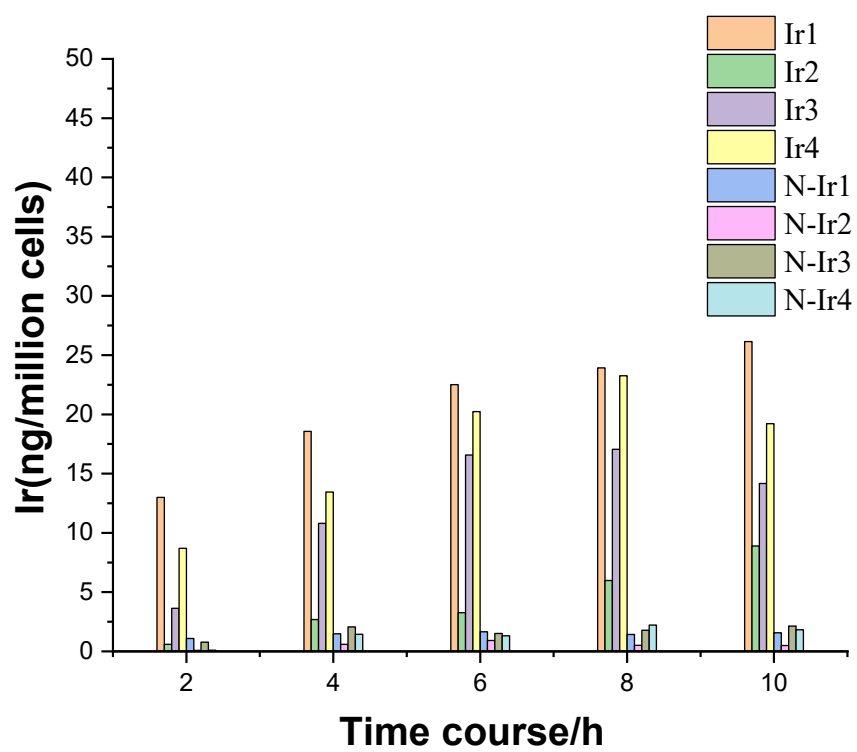


Fig. S10 Time-dependent ICP-MS of A375 cells pre-incubated with **Ir1-4** and **N-Ir1-4** (4 μ M).

20241129_241202090227 #1500 RT: 3.37 AV: 1 SB: 217 2.24-2.72 NL: 1.39E7
T: FTMS + c ESI Full ms [50.00-1000.00]

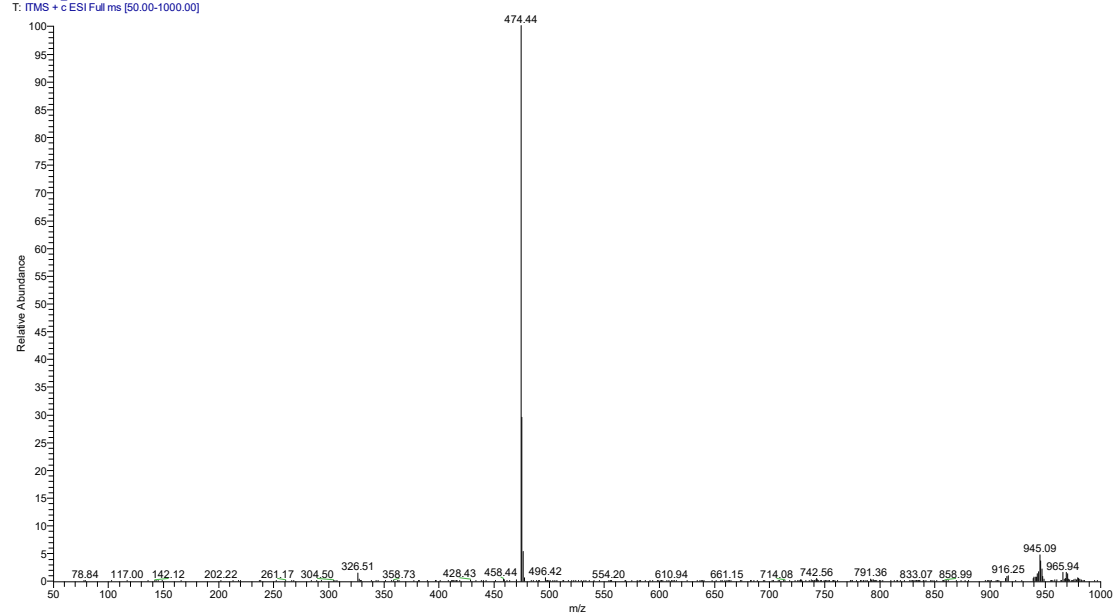


Fig. S11 MS spectrum of the ligand tbpip-NO_2

20241129_241202090227#1000 RT: 2.25 AV: 1 SB: 49 0.29-0.40 NL: 1.60E7
T: FTMS + c ESI Full ms [50.00-1000.00]

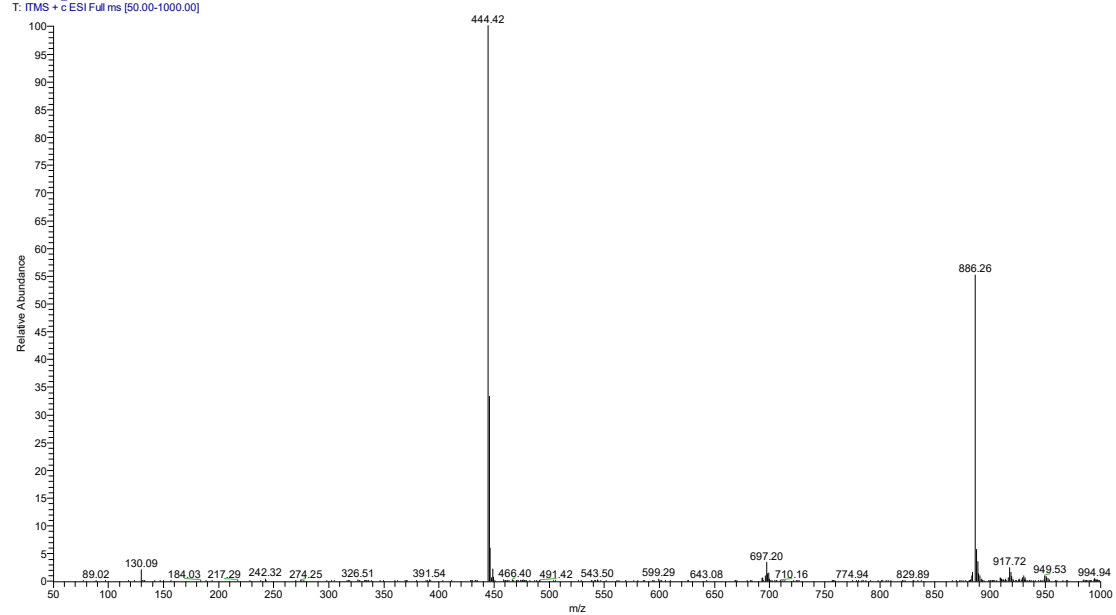


Fig. S12 MS spectrum of the ligand tbpip-NH_2

111111_241206182642 #167 RT: 0.54 AV: 1 SB: 40 0.29-0.42 NL: 4.33E6
T: FTMS + c ESI Full ms [100.00-2000.00]

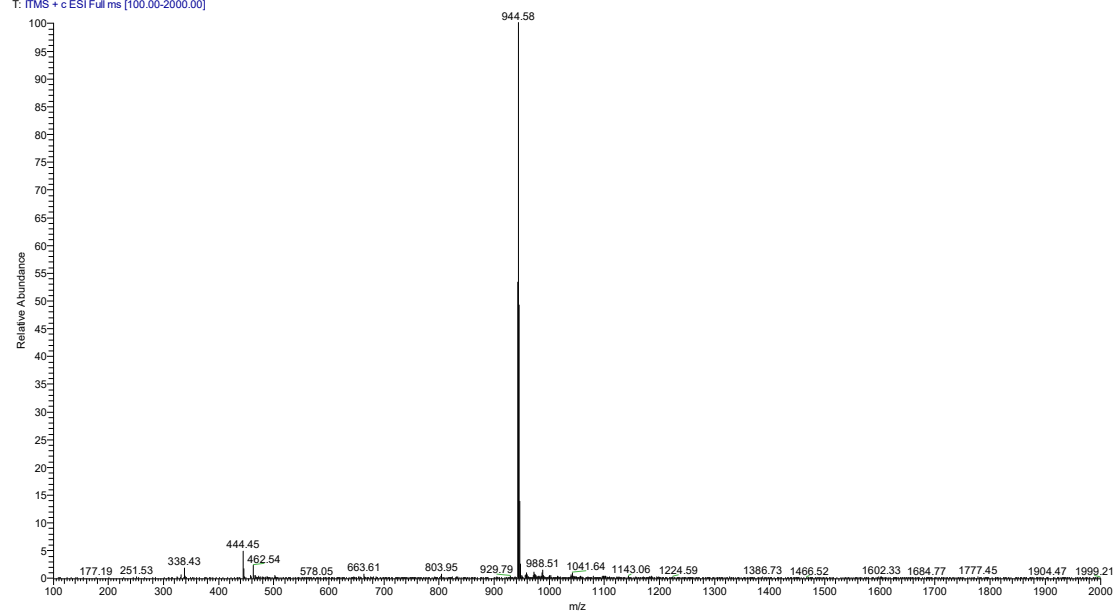


Fig. S13 MS spectrum of Ir-tbpip-NH₂

20241017-HPC_241018091155#1205 RT: 3.95 AV: 1 SB: 71 2.77-2.99 NL: 6.85E6
T: FTMS + c ESI Full ms [50.00-2000.00]

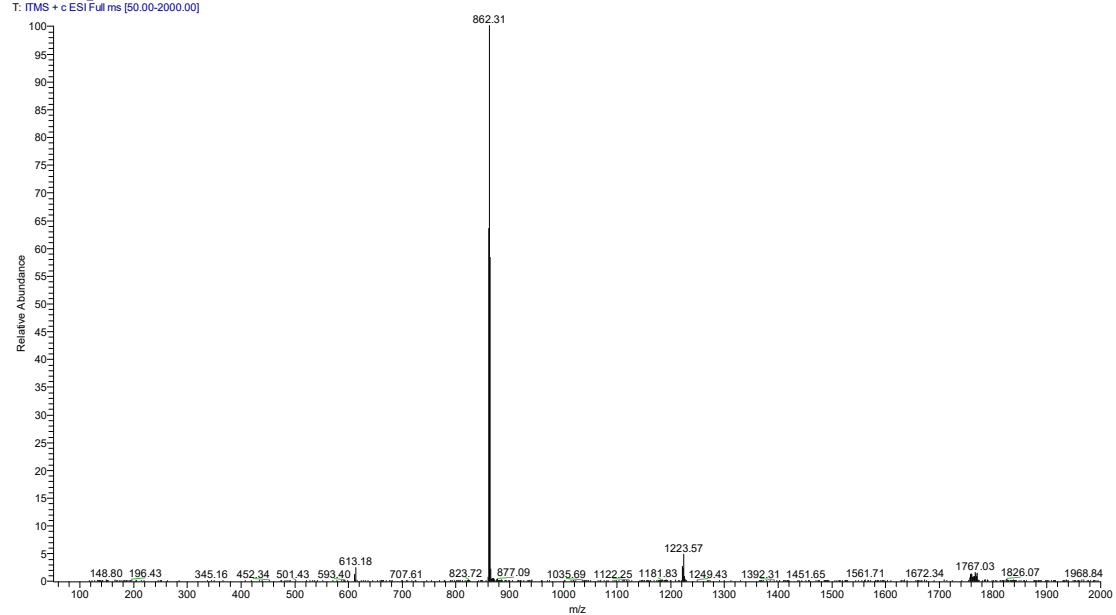


Fig. S14 MS spectrum of Ir1

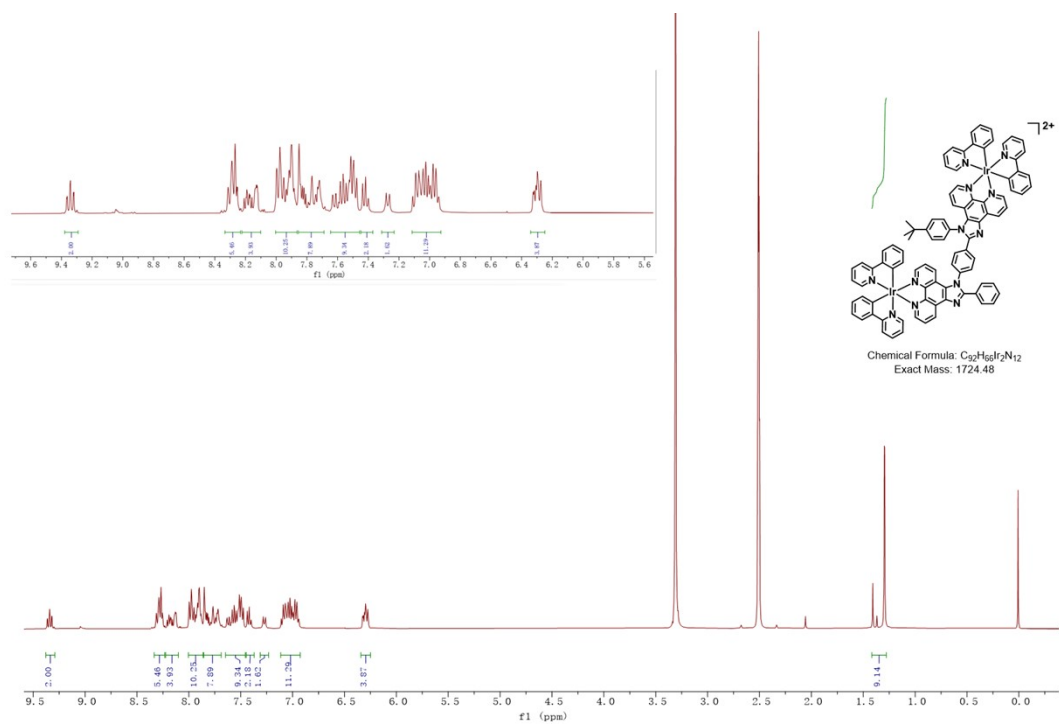


Fig. S15 ¹H NMR spectrum of Ir1

20241017-HPC_241018091155#1876 RT: 6.17 AV: 1 SB: 71 2.77-2.99 NL: 1.63E7
T: FTMS + c ESI Full ms [50.00-2000.00]

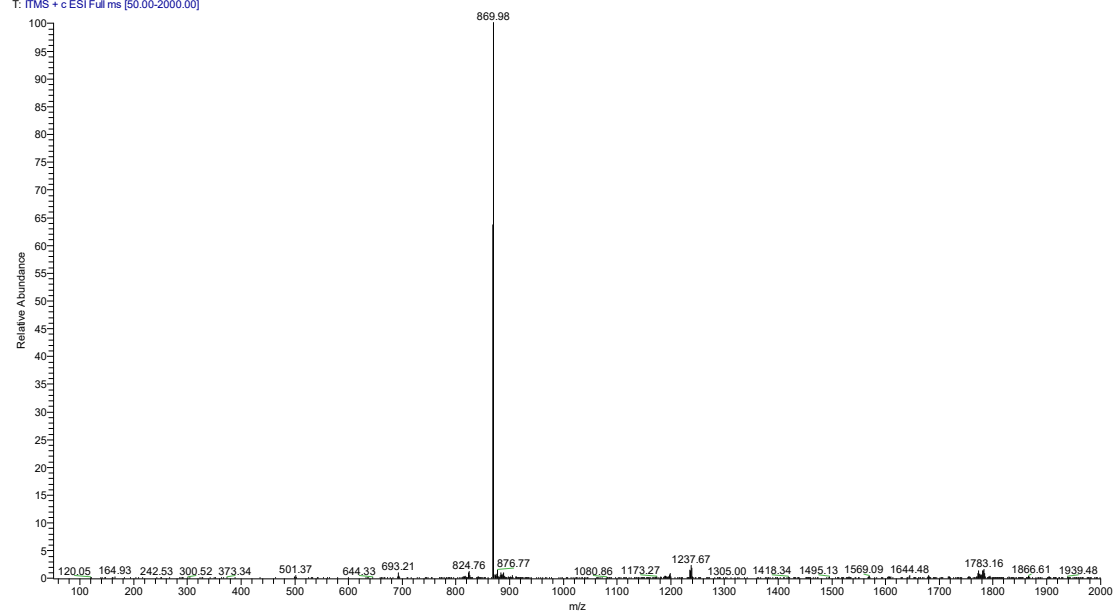


Fig. S16 MS spectrum of Ir2

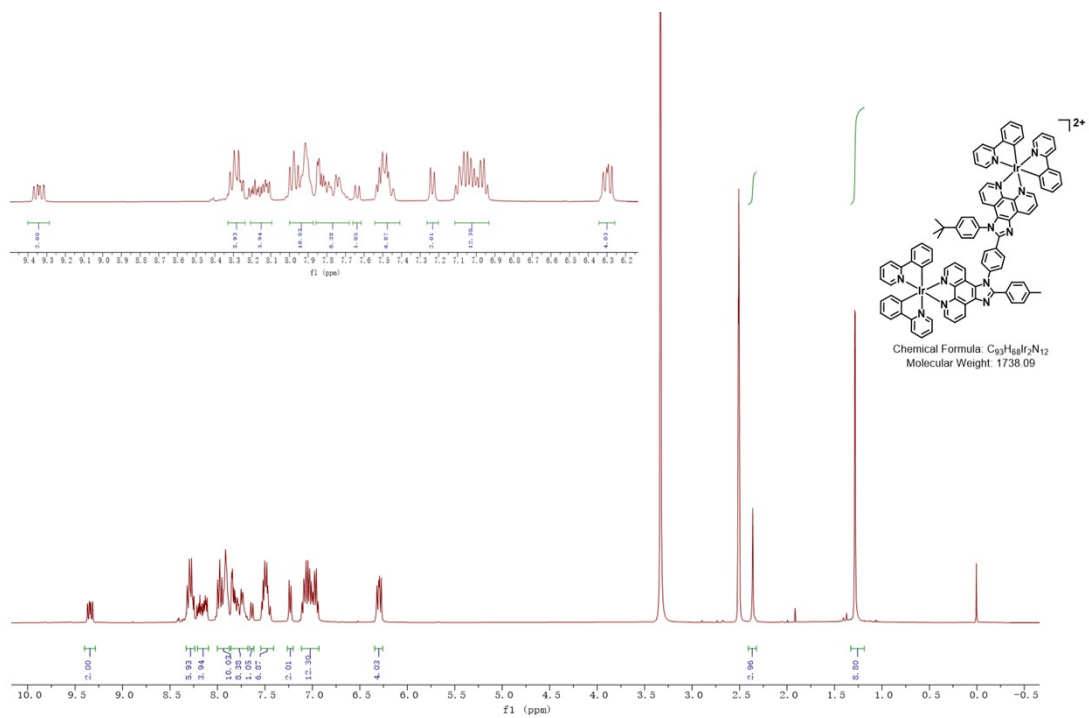


Fig. S17 ^1H NMR spectrum of Ir2

20241017-HPC_241018091155#3111 RT: 10.23 AV: 1 SB: 71 2.77-2.99 NL: 1.27E7
T: FTMS + c ESI Full ms [50.00-2000.00]

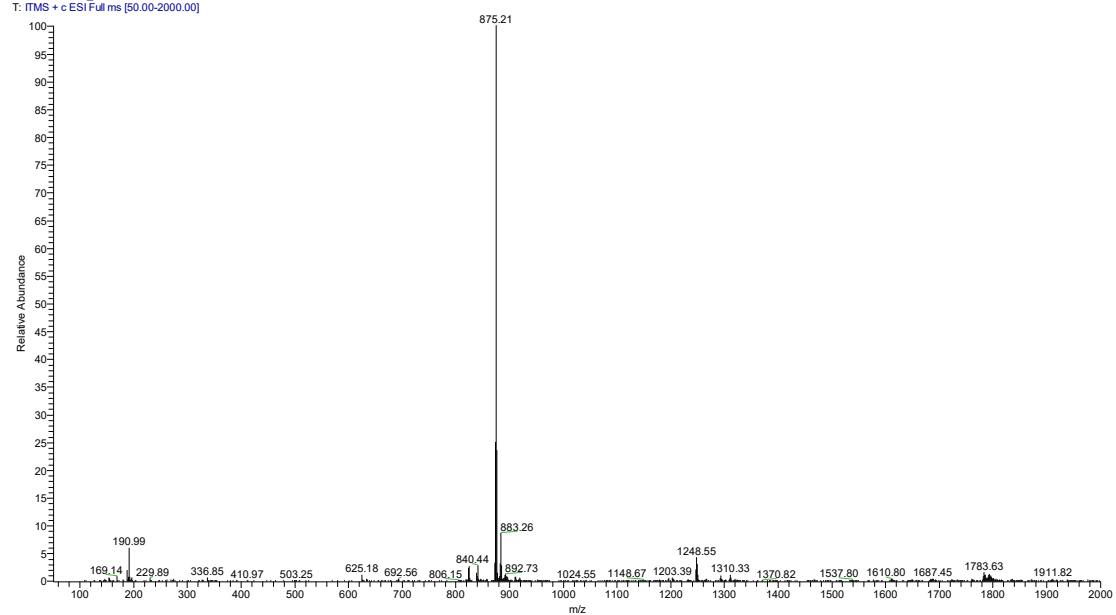


Fig. S18 MS spectrum of Ir₃

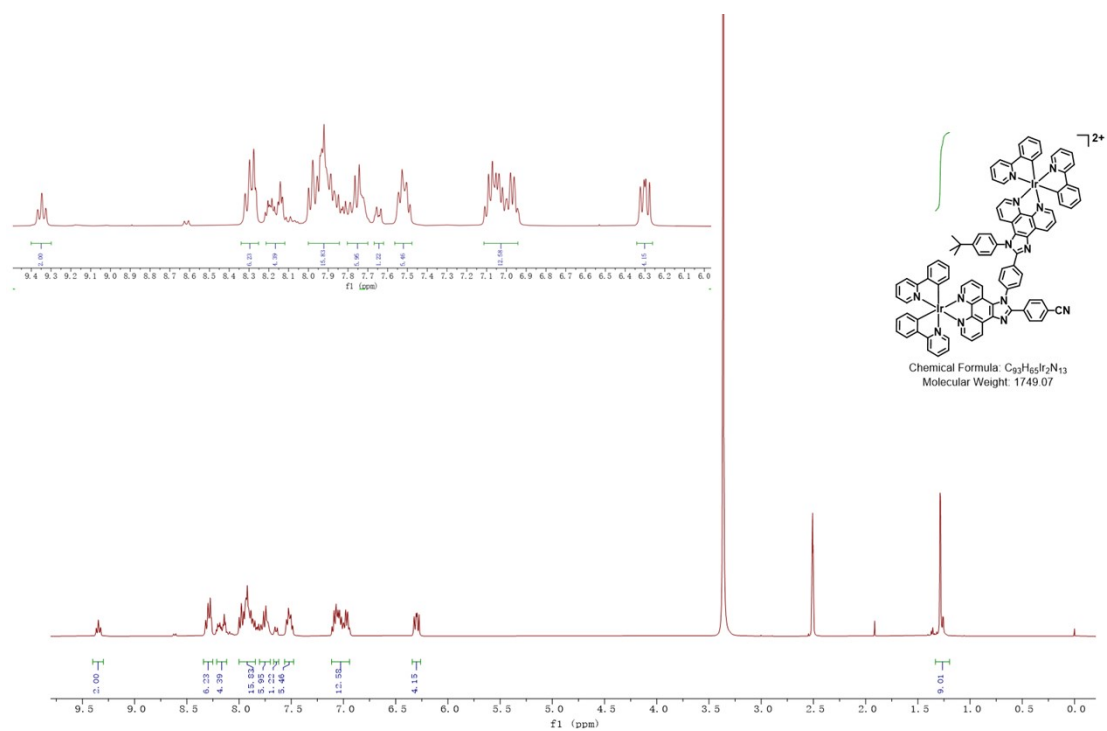


Fig. S19 1H NMR spectrum of Ir3

20241017-HPC_241018091155 #2318 RT: 7.63 AV: 1 SB: 71 2.77-2.99 NL: 5.99E7
T: FTMS + c ESI Full ms [50.00-2000.00]

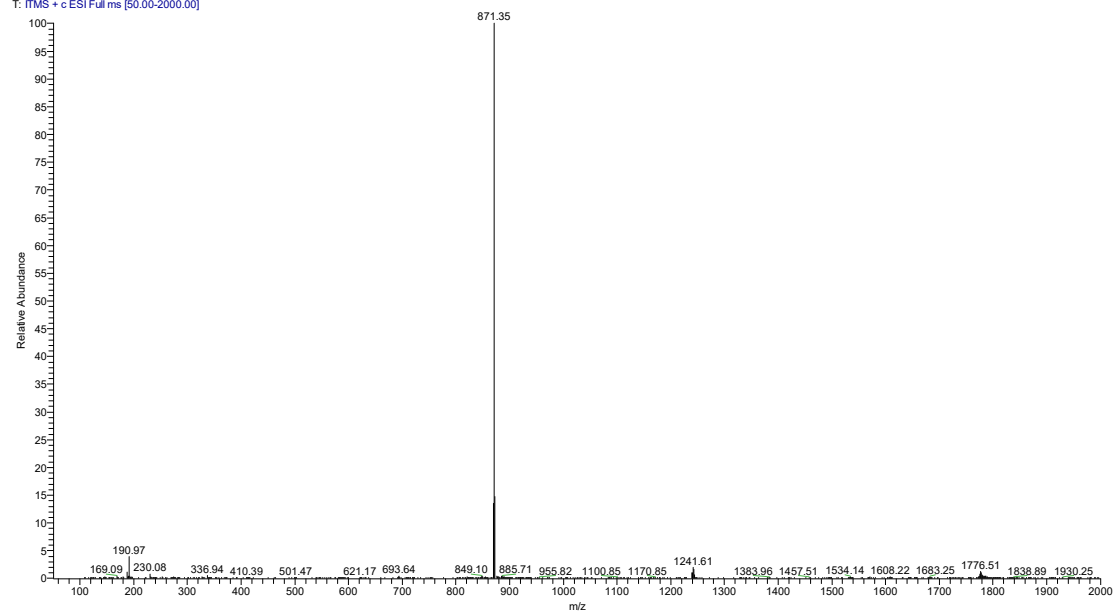


Fig. S20 MS spectrum of Ir4

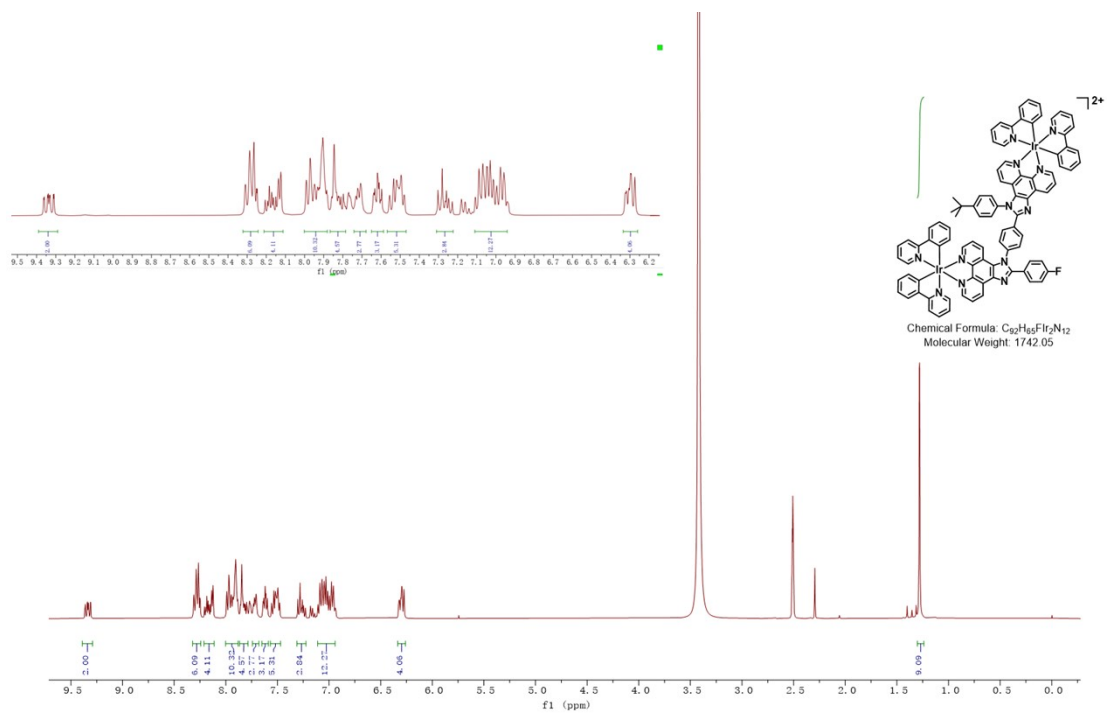


Fig. S21 1H NMR spectrum of Ir4

Table S1 Photophysical properties of designed compounds

Compd	$\lambda_{\text{abs}}/\text{nm}$ ($\epsilon, \times 10^3 \text{ M}^{-1} \cdot \text{cm}^{-1}$)	$\lambda_{\text{em}}/\text{nm}$	$\Phi_{\text{u}}(\text{air})$	τ/ns
Ir1	275, 385, 404	568	0.0198	203
Ir2	274, 385, 404	569	0.0182	201
Ir3	275, 383, 401	570	0.0187	201
Ir4	273, 385, 403	570	0.0193	200

Wavelength/nm	690	700	710	720	730	740	750	760	770	780	790	800
Ir1 δ_{2PA}/GM	100	81	84	82	135	83	81	40	55	31	45	34
Ir2 δ_{2PA}/GM	--	115	162	166	120	155	142	139	83	99	100	94
Ir3 δ_{2PA}/GM	--	--	41	66	29	29	28	22	11	--	--	--
Ir4 δ_{2PA}/GM	100	73	80	107	69	79	--	--	--	--	--	--

Table S2. 2PA cross sections of Ir1-4 with different excitation wavelengths.

Table S3 Single oxygen quantum yields of complexes.

Compd	Ru(bpy)₃²⁺	Ir1	Ir2	Ir3	Ir4
Φ_{Δ}	0.81	0.31	0.22	0.32	0.31