Electronic Supporting Information Materials

Highly cytotoxic, cyclometalated iridium(III)-5-fluoro-8-quinolinol complexes as cancer cell mitochondriotropics agents

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Table S1. Crystal data and structure refinement details for **Ir-1**.

Empirical formula	$C_{31}H_{21}FIrN_3O$
Formula weight	662.71
Temperature/K	273.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.4485(7)
b/Å	9.3218(6)
c/Å	23.3115(14)
α/°	90
β/°	92.268(2)
γ/°	90
Volume/Å^3	2485.9(3)
Z	4
ρ_{calc}g/cm^3	1.771
μ/mm^{-1}	5.409
F(000)	1288.0
Crystal size/mm^3	0.403 × 0.177 × 0.089
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.86 to 55.04
Index ranges	$-14 \le h \le 14$, $-12 \le k \le 12$, $-30 \le l \le 30$
Reflections collected	38204
Independent reflections	5704 [R_{int} = 0.0469, R_{sigma} = 0.0332]
Data/restraints/parameters	5704/0/334
Goodness-of-fit on F^2	1.134
Final R indexes [I>=2σ (I)]	R_1 = 0.0280, wR_2 = 0.0663
Final R indexes [all data]	R_1 = 0.0434, wR_2 = 0.0796
Largest diff. peak/hole / e Å^{-3}	0.80/-1.41

[a] $R_1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|$; [b] $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^2)^2]^{1/2}$.

Table S2. Selected bond lengths (Å) for **Ir-1**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ir1	O1	2.146(2)	C9	C10	1.387(6)
Ir1	N1	2.033(3)	C10	C11	1.395(5)
Ir1	N2	2.132(3)	C12	C13	1.405(6)
Ir1	N3	2.040(3)	C12	C17	1.404(6)
Ir1	C11	2.003(4)	C13	C14	1.387(6)
Ir1	C12	2.015(4)	C14	C15	1.369(8)
F1	C31	1.362(5)	C15	C16	1.379(8)
O1	C28	1.307(4)	C16	C17	1.408(6)
N1	C1	1.335(5)	C17	C18	1.441(6)
N1	C5	1.378(5)	C18	C19	1.383(6)
N2	C23	1.327(5)	C19	C20	1.350(8)
N2	C27	1.367(4)	C20	C21	1.385(8)
N3	C18	1.368(5)	C21	C22	1.379(6)
N3	C22	1.349(5)	C23	C24	1.401(6)
C1	C2	1.370(5)	C24	C25	1.349(6)
C2	C3	1.384(6)	C25	C26	1.422(5)
C3	C4	1.359(6)	C26	C27	1.401(5)
C4	C5	1.384(5)	C26	C31	1.392(5)
C5	C6	1.465(5)	C27	C28	1.434(5)
C6	C7	1.385(6)	C28	C29	1.401(5)
C6	C11	1.411(6)	C29	C30	1.398(5)
C7	C8	1.362(7)	C30	C31	1.363(6)
C8	C9	1.377(7)			

Table S3. Selected bond angles (°) for **Ir-1**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	Ir1	O1	93.56(11)	C9	C10	C11	121.9(4)
N1	Ir1	N2	92.06(11)	C6	C11	Ir1	114.6(3)
N1	Ir1	N3	174.17(12)	C10	C11	Ir1	128.7(3)
N2	Ir1	O1	78.12(10)	C10	C11	C6	116.5(4)
N3	Ir1	O1	89.37(10)	C13	C12	Ir1	128.4(3)
N3	Ir1	N2	93.47(13)	C17	C12	Ir1	113.9(3)
C11	Ir1	O1	172.11(12)	C17	C12	C13	117.6(4)
C11	Ir1	N1	80.78(14)	C14	C13	C12	121.1(5)
C11	Ir1	N2	96.50(13)	C15	C14	C13	120.4(6)
C11	Ir1	N3	96.77(14)	C14	C15	C16	120.4(5)
C11	Ir1	C12	91.72(15)	C15	C16	C17	120.0(5)
C12	Ir1	O1	94.18(12)	C12	C17	C16	120.4(5)
C12	Ir1	N1	94.16(15)	C12	C17	C18	115.8(4)
C12	Ir1	N2	170.40(13)	C16	C17	C18	123.7(4)

C12	Ir1	N3	80.59(16)	N3	C18	C17	114.6(4)
C28	O1	Ir1	112.0(2)	N3	C18	C19	118.7(5)
C1	N1	Ir1	124.3(3)	C19	C18	C17	126.6(5)
C1	N1	C5	119.8(3)	C20	C19	C18	121.5(5)
C5	N1	Ir1	115.8(3)	C19	C20	C21	120.1(5)
C23	N2	Ir1	128.2(3)	C22	C21	C20	117.5(5)
C23	N2	C27	118.8(3)	N3	C22	C21	122.6(5)
C27	N2	Ir1	112.7(2)	N2	C23	C24	122.3(4)
C18	N3	Ir1	115.1(3)	C25	C24	C23	119.9(4)
C22	N3	Ir1	125.3(3)	C24	C25	C26	119.4(4)
C22	N3	C18	119.5(4)	C27	C26	C25	117.6(4)
N1	C1	C2	122.3(4)	C31	C26	C25	124.8(4)
C1	C2	C3	118.6(4)	C31	C26	C27	117.6(4)
C4	C3	C2	119.6(4)	N2	C27	C26	121.9(3)
C3	C4	C5	120.9(4)	N2	C27	C28	115.8(3)
N1	C5	C4	118.8(4)	C26	C27	C28	122.2(3)
N1	C5	C6	113.5(3)	O1	C28	C27	120.5(3)
C4	C5	C6	127.6(4)	O1	C28	C29	123.0(3)
C7	C6	C5	123.6(4)	C29	C28	C27	116.4(3)
C7	C6	C11	121.4(4)	C30	C29	C28	121.4(4)
C11	C6	C5	115.0(4)	C31	C30	C29	120.1(4)
C8	C7	C6	120.0(4)	F1	C31	C26	118.3(4)
C7	C8	C9	120.8(4)	F1	C31	C30	119.6(4)
C8	C9	C10	119.4(5)	C30	C31	C26	122.2(4)

Table S4. Crystal data and structure refinement details for **Ir-2**.

Empirical formula	$C_{33}H_{25}FIrN_3O$
Formula weight	690.76
Temperature/K	273.15
Crystal system	monoclinic
Space group	C2/c
a/Å	20.4836(17)
b/Å	16.3026(14)
c/Å	15.6214(13)
α/°	90
β/°	100.056(3)
γ/°	90
Volume/Å^3	5136.4(7)
Z	8
ρ_{calc}g/cm^3	1.787
μ/mm^{-1}	5.239
F(000)	2704.0

Crystal size/mm^3	0.333 × 0.264 × 0.148
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.886 to 55.112
Index ranges	-26 ≤ h ≤ 26, -21 ≤ k ≤ 21, -20 ≤ l ≤ 20
Reflections collected	52961
Independent reflections	5921 [R_{int} = 0.0364, R_{sigma} = 0.0216]
Data/restraints/parameters	5921/0/354
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0210, wR_2 = 0.0476
Final R indexes [all data]	R_1 = 0.0309, wR_2 = 0.0513
Largest diff. peak/hole / e Å^{-3}	0.75/-0.78

[a] $R_1 = \Sigma\, ||F_o| - |F_c||/\Sigma|F_o|$; [b] $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{½}$.

Table S5. Selected bond lengths (Å) for **Ir-2**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ir1	O1	2.162(2)	C10	C11	1.390(5)
Ir1	N1	2.042(2)	C11	C12	1.401(4)
Ir1	N2	2.144(2)	C13	C14	1.395(4)
Ir1	N3	2.038(2)	C13	C18	1.420(4)
Ir1	C12	1.997(3)	C14	C15	1.381(5)
Ir1	C13	1.992(3)	C15	C16	1.365(6)
F1	C28	1.367(4)	C16	C17	1.382(6)
O1	C25	1.306(4)	C17	C18	1.396(5)
N1	C1	1.345(4)	C18	C19	1.471(5)
N1	C6	1.368(4)	C19	C20	1.410(4)
N2	C30	1.371(4)	C20	C21	1.509(6)
N2	C33	1.320(4)	C20	C22	1.388(6)
N3	C19	1.359(4)	C22	C23	1.349(6)
N3	C24	1.344(4)	C23	C24	1.371(5)
C1	C2	1.372(5)	C25	C26	1.394(4)
C2	C3	1.355(5)	C25	C30	1.432(4)
C3	C4	1.385(5)	C26	C27	1.394(5)
C4	C5	1.503(5)	C27	C28	1.356(5)
C4	C6	1.417(5)	C28	C29	1.399(5)
C6	C7	1.474(5)	C29	C30	1.424(4)
C7	C8	1.395(4)	C29	C31	1.400(5)
C7	C12	1.419(5)	C31	C32	1.351(5)
C8	C9	1.379(5)	C32	C33	1.400(5)
C9	C10	1.367(5)			

Table S6. Selected bond angles (°) for **Ir-2**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	Ir1	O1	89.81(9)	C10	C11	C12	122.1(3)
N1	Ir1	N2	96.86(9)	C7	C12	Ir1	115.9(2)
N2	Ir1	O1	77.64(9)	C11	C12	Ir1	126.9(2)
N3	Ir1	O1	95.80(9)	C11	C12	C7	117.1(3)
N3	Ir1	N1	171.15(9)	C14	C13	Ir1	127.4(2)
N3	Ir1	N2	91.04(9)	C14	C13	C18	117.1(3)
C12	Ir1	O1	95.64(10)	C18	C13	Ir1	115.2(2)
C12	Ir1	N1	79.72(11)	C15	C14	C13	121.9(3)
C12	Ir1	N2	172.55(10)	C16	C15	C14	120.6(4)
C12	Ir1	N3	92.88(11)	C15	C16	C17	119.6(3)
C13	Ir1	O1	172.01(9)	C16	C17	C18	120.9(3)
C13	Ir1	N1	95.29(11)	C13	C18	C19	114.5(3)
C13	Ir1	N2	95.60(10)	C17	C18	C13	119.9(3)
C13	Ir1	N3	79.90(11)	C17	C18	C19	125.4(3)
C13	Ir1	C12	91.33(11)	N3	C19	C18	112.4(2)
C25	O1	Ir1	112.88(18)	N3	C19	C20	119.0(3)
C1	N1	Ir1	122.5(2)	C20	C19	C18	128.5(3)
C1	N1	C6	120.6(3)	C19	C20	C21	123.7(4)
C6	N1	Ir1	116.8(2)	C22	C20	C19	117.5(3)
C30	N2	Ir1	112.80(19)	C22	C20	C21	118.6(3)
C33	N2	Ir1	128.1(2)	C23	C22	C20	122.1(3)
C33	N2	C30	119.1(3)	C22	C23	C24	118.7(4)
C19	N3	Ir1	116.9(2)	N3	C24	C23	121.1(4)
C24	N3	Ir1	121.0(2)	O1	C25	C26	123.5(3)
C24	N3	C19	121.3(3)	O1	C25	C30	119.9(3)
N1	C1	C2	122.2(3)	C26	C25	C30	116.6(3)
C3	C2	C1	118.6(4)	C27	C26	C25	121.3(3)
C2	C3	C4	121.3(3)	C28	C27	C26	120.8(3)
C3	C4	C5	117.8(3)	F1	C28	C29	117.4(3)
C3	C4	C6	118.7(3)	C27	C28	F1	120.0(3)
C6	C4	C5	123.5(4)	C27	C28	C29	122.6(3)
N1	C6	C4	118.5(3)	C28	C29	C30	116.2(3)
N1	C6	C7	113.0(3)	C28	C29	C31	125.9(3)
C4	C6	C7	128.4(3)	C31	C29	C30	117.9(3)
C8	C7	C6	126.2(3)	N2	C30	C25	116.7(3)
C8	C7	C12	119.8(3)	N2	C30	C29	120.8(3)
C12	C7	C6	113.9(3)	C29	C30	C25	122.6(3)
C9	C8	C7	120.9(3)	C32	C31	C29	120.0(3)
C10	C9	C8	120.4(3)	C31	C32	C33	119.5(3)
C9	C10	C11	119.6(3)	N2	C33	C32	122.7(3)

Table S7. Crystal data and structure refinement details for **Ir-3**.

Empirical formula	$C_{35}H_{21}FIrN_3O$
Formula weight	710.77
Temperature/K	293(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	21.5039(6)
b/Å	16.6692(5)
c/Å	14.8357(4)
α/°	90
β/°	101.136(3)
γ/°	90
Volume/Å^3	5217.8(3)
Z	8
ρ_{calc}g/cm^3	1.810
μ/mm^{-1}	5.161
F(000)	2768.0
Crystal size/mm^3	0.381 × 0.273 × 0.168
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.724 to 58.58
Index ranges	-28 ≤ h ≤ 29, -22 ≤ k ≤ 21, -20 ≤ l ≤ 20
Reflections collected	18790
Independent reflections	6270 [R_{int} = 0.0639, R_{sigma} = 0.0925]
Data/restraints/parameters	6270/0/370
Goodness-of-fit on F^2	0.999
Final R indexes [I>=2σ (I)]	R_1 = 0.0448, wR_2 = 0.0516
Final R indexes [all data]	R_1 = 0.0966, wR_2 = 0.0624
Largest diff. peak/hole / e Å^{-3}	1.26/-0.96

[a] $R_1 = \Sigma\, ||F_o| - |F_c||/\Sigma|F_o|$; [b] $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{½}$.

Table S8. Selected bond lengths (Å) for **Ir-3**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ir1	O1	2.146(3)	C7	C8	1.387(7)
Ir1	N1	2.128(4)	C10	C11	1.388(7)
Ir1	N2	2.044(4)	C11	C12	1.354(7)
Ir1	C3	2.012(5)	C12	C13	1.390(7)
Ir1	C4	2.000(6)	C13	C14	1.421(7)
Ir1	N5	2.060(4)	C13	C21	1.390(7)
F1	C1AA	1.362(7)	C14	C15	1.353(7)
O1	C1	1.303(6)	C15	C16	1.417(7)
N1	C8	1.313(6)	C16	C17	1.411(7)

N1	C9	1.382(6)	C16	C20	1.406(6)
N2	C10	1.334(5)	C17	C18	1.357(8)
N2	C21	1.373(6)	C18	C19	1.401(7)
C3	C19	1.381(6)	C20	C21	1.424(6)
C3	C20	1.404(6)	C22	C23	1.408(7)
C4	C22	1.391(7)	C23	C24	1.363(8)
C4	C33	1.416(7)	C24	C25	1.408(7)
N5	C31	1.332(6)	C25	C26	1.421(8)
N5	C32	1.365(6)	C25	C33	1.410(7)
C1	C2	1.392(7)	C26	C27	1.340(8)
C1	C9	1.442(7)	C27	C28	1.431(8)
C2	C0AA	1.388(8)	C28	C29	1.404(8)
C0AA	C1AA	1.340(8)	C28	C32	1.396(7)
C1AA	C5	1.398(7)	C29	C30	1.354(8)
C5	C6	1.410(7)	C30	C31	1.402(7)
C5	C9	1.405(7)	C32	C33	1.416(7)
C6	C7	1.357(7)			

Table S9. Selected bond angles (°) for **Ir-3**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
N1	Ir1	O1	78.24(15)	N1	C8	C7	122.5(6)
N2	Ir1	O1	93.54(15)	N1	C9	C1	115.6(5)
N2	Ir1	N1	93.57(16)	N1	C9	C5	122.0(5)
N2	Ir1	N5	171.55(19)	C5	C9	C1	122.4(5)
C3	Ir1	O1	172.99(18)	N2	C10	C11	121.0(5)
C3	Ir1	N1	97.25(19)	C12	C11	C10	120.2(5)
C3	Ir1	N2	81.31(18)	C11	C12	C13	120.3(6)
C3	Ir1	N5	95.80(18)	C12	C13	C14	126.1(6)
C4	Ir1	O1	96.91(17)	C21	C13	C12	117.5(5)
C4	Ir1	N1	173.69(18)	C21	C13	C14	116.3(5)
C4	Ir1	N2	90.7(2)	C15	C14	C13	121.5(6)
C4	Ir1	C3	87.9(2)	C14	C15	C16	122.2(6)
C4	Ir1	N5	81.2(2)	C17	C16	C15	125.5(6)
N5	Ir1	O1	89.95(14)	C20	C16	C15	118.6(5)
N5	Ir1	N1	94.66(18)	C20	C16	C17	115.9(5)
C1	O1	Ir1	112.9(3)	C18	C17	C16	120.3(6)
C8	N1	Ir1	128.5(4)	C17	C18	C19	122.3(6)
C8	N1	C9	118.5(5)	C3	C19	C18	120.6(6)
C9	N1	Ir1	113.0(4)	C3	C20	C16	124.9(5)
C10	N2	Ir1	126.6(4)	C3	C20	C21	117.6(4)
C10	N2	C21	119.1(5)	C16	C20	C21	117.5(5)

C21	N2	Ir1	114.1(3)	N2	C21	C13	121.8(5)
C19	C3	Ir1	131.7(4)	N2	C21	C20	114.4(5)
C19	C3	C20	116.0(5)	C13	C21	C20	123.7(5)
C20	C3	Ir1	112.3(3)	C4	C22	C23	122.7(6)
C22	C4	Ir1	133.1(5)	C24	C23	C22	121.4(6)
C22	C4	C33	114.5(5)	C23	C24	C25	119.2(6)
C33	C4	Ir1	112.4(4)	C24	C25	C26	123.0(7)
C31	N5	Ir1	127.0(4)	C24	C25	C33	118.2(6)
C31	N5	C32	119.0(5)	C33	C25	C26	118.8(6)
C32	N5	Ir1	114.0(4)	C27	C26	C25	121.3(7)
O1	C1	C2	124.1(5)	C26	C27	C28	122.5(7)
O1	C1	C9	120.2(5)	C29	C28	C27	126.4(7)
C2	C1	C9	115.7(6)	C32	C28	C27	116.1(6)
C0AA	C2	C1	122.1(6)	C32	C28	C29	117.5(7)
C1AA	C0AA	C2	120.3(6)	C30	C29	C28	119.8(6)
F1	C1AA	C5	117.0(6)	C29	C30	C31	120.1(6)
C0AA	C1AA	F1	120.1(6)	N5	C31	C30	121.3(6)
C0AA	C1AA	C5	122.9(7)	N5	C32	C28	122.3(6)
C1AA	C5	C6	126.2(6)	N5	C32	C33	114.8(5)
C1AA	C5	C9	116.6(6)	C28	C32	C33	123.0(6)
C9	C5	C6	117.1(6)	C25	C33	C4	124.0(6)
C7	C6	C5	119.3(6)	C25	C33	C32	118.4(6)
C6	C7	C8	120.5(6)	C32	C33	C4	117.5(6)

Table S10. Crystal data and structure refinement details for **Ir-4**.

Empirical formula	$C_{29}H_{27}FIrN_5O_3$
Formula weight	704.75
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.7444(8)
b/Å	22.9897(12)
c/Å	10.6487(6)
α/°	90
β/°	96.221(6)
γ/°	90
Volume/Å^3	2614.8(3)
Z	4
ρ_{calc}g/cm^3	1.790
μ/mm^{-1}	5.155
F(000)	1384.0
Crystal size/mm^3	0.356 × 0.257 × 0.175

Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.716 to 58.392
Index ranges	$-13 \leq h \leq 14$, $-31 \leq k \leq 31$, $-13 \leq l \leq 13$
Reflections collected	20028
Independent reflections	6202 [R_{int} = 0.0606, R_{sigma} = 0.0780]
Data/restraints/parameters	6202/0/356
Goodness-of-fit on F^2	0.995
Final R indexes [I>=2σ (I)]	R_1 = 0.0435, wR_2 = 0.0853
Final R indexes [all data]	R_1 = 0.0746, wR_2 = 0.0972
Largest diff. peak/hole / e Å^{-3}	1.50/-1.62

[a] $R_1 = \Sigma \, ||F_o| - |F_c|| / \Sigma |F_o|$; [b] $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^2)^2]^{1/2}$.

Table S11. Selected bond lengths (Å) for **Ir-4**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ir1	O1	2.180(4)	C5	C6	1.367(8)
Ir1	N2	2.009(5)	C7	C8	1.351(9)
Ir1	N3	2.145(5)	C8	C9	1.392(8)
Ir1	N5	2.029(4)	C10	C11	1.406(9)
Ir1	C1	1.999(6)	C11	C12	1.360(10)
Ir1	C18	2.016(7)	C13	C14	1.375(9)
F1	C22	1.358(8)	C13	C18	1.414(8)
O1	C19	1.338(8)	C14	C15	1.377(11)
N1	N2	1.361(7)	C15	C16	1.369(11)
N1	C12	1.359(8)	C16	C17	1.389(9)
N1	C13	1.408(8)	C17	C18	1.397(9)
N2	C10	1.330(8)	C19	C20	1.397(9)
N3	C26	1.316(8)	C19	C27	1.429(10)
N3	C27	1.371(8)	C20	C21	1.402(10)
N4	N5	1.363(7)	C21	C22	1.354(10)
N4	C6	1.407(8)	C22	C23	1.412(10)
N4	C7	1.353(7)	C23	C24	1.407(10)
N5	C9	1.333(7)	C23	C27	1.393(9)
C1	C2	1.390(8)	C24	C25	1.350(10)
C1	C6	1.402(7)	C25	C26	1.412(9)
C2	C3	1.380(9)	O2	C28	1.418(10)
C3	C4	1.392(8)	O3	C29	1.354(12)
C4	C5	1.384(9)			

Table S12. Selected bond angles (°) for **Ir-4**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N2	Ir1	O1	91.10(18)	C6	C5	C4	118.6(6)
N2	Ir1	N3	93.91(19)	C1	C6	N4	114.6(5)
N2	Ir1	N5	171.8(2)	C5	C6	N4	120.8(5)
N2	Ir1	C18	80.3(2)	C5	C6	C1	124.6(6)
N3	Ir1	O1	77.96(19)	C8	C7	N4	109.0(6)
N5	Ir1	O1	95.32(18)	C7	C8	C9	105.6(6)
N5	Ir1	N3	92.39(18)	N5	C9	C8	109.8(6)
C1	Ir1	O1	172.26(19)	N2	C10	C11	110.0(7)
C1	Ir1	N2	94.2(2)	C12	C11	C10	105.7(6)
C1	Ir1	N3	96.0(2)	N1	C12	C11	107.8(7)
C1	Ir1	N5	80.0(2)	N1	C13	C18	114.1(6)
C1	Ir1	C18	91.3(2)	C14	C13	N1	122.7(6)
C18	Ir1	O1	95.2(2)	C14	C13	C18	123.1(7)
C18	Ir1	N3	171.0(2)	C13	C14	C15	119.0(7)
C18	Ir1	N5	94.0(2)	C16	C15	C14	120.2(7)
C19	O1	Ir1	111.0(4)	C15	C16	C17	120.6(8)
N2	N1	C13	116.6(5)	C16	C17	C18	121.5(7)
C12	N1	N2	110.1(6)	C13	C18	Ir1	114.0(5)
C12	N1	C13	133.3(6)	C17	C18	Ir1	130.5(5)
N1	N2	Ir1	115.0(4)	C17	C18	C13	115.5(6)
C10	N2	Ir1	138.4(5)	O1	C19	C20	122.0(7)
C10	N2	N1	106.5(5)	O1	C19	C27	120.9(6)
C26	N3	Ir1	126.7(4)	C20	C19	C27	117.0(7)
C26	N3	C27	119.5(6)	C19	C20	C21	120.7(8)
C27	N3	Ir1	113.6(5)	C22	C21	C20	121.0(7)
N5	N4	C6	116.0(5)	F1	C22	C23	118.0(8)
C7	N4	N5	108.7(5)	C21	C22	F1	120.7(7)
C7	N4	C6	135.2(6)	C21	C22	C23	121.3(7)
N4	N5	Ir1	114.6(4)	C24	C23	C22	124.0(7)
C9	N5	Ir1	138.4(4)	C27	C23	C22	117.7(8)
C9	N5	N4	106.9(5)	C27	C23	C24	118.3(7)
C2	C1	Ir1	130.6(4)	C25	C24	C23	118.8(7)
C2	C1	C6	114.6(6)	C24	C25	C26	120.7(7)
C6	C1	Ir1	114.7(4)	N3	C26	C25	121.0(7)
C3	C2	C1	122.9(6)	N3	C27	C19	116.1(6)
C2	C3	C4	119.8(7)	N3	C27	C23	121.6(7)
C5	C4	C3	119.6(6)	C23	C27	C19	122.4(7)

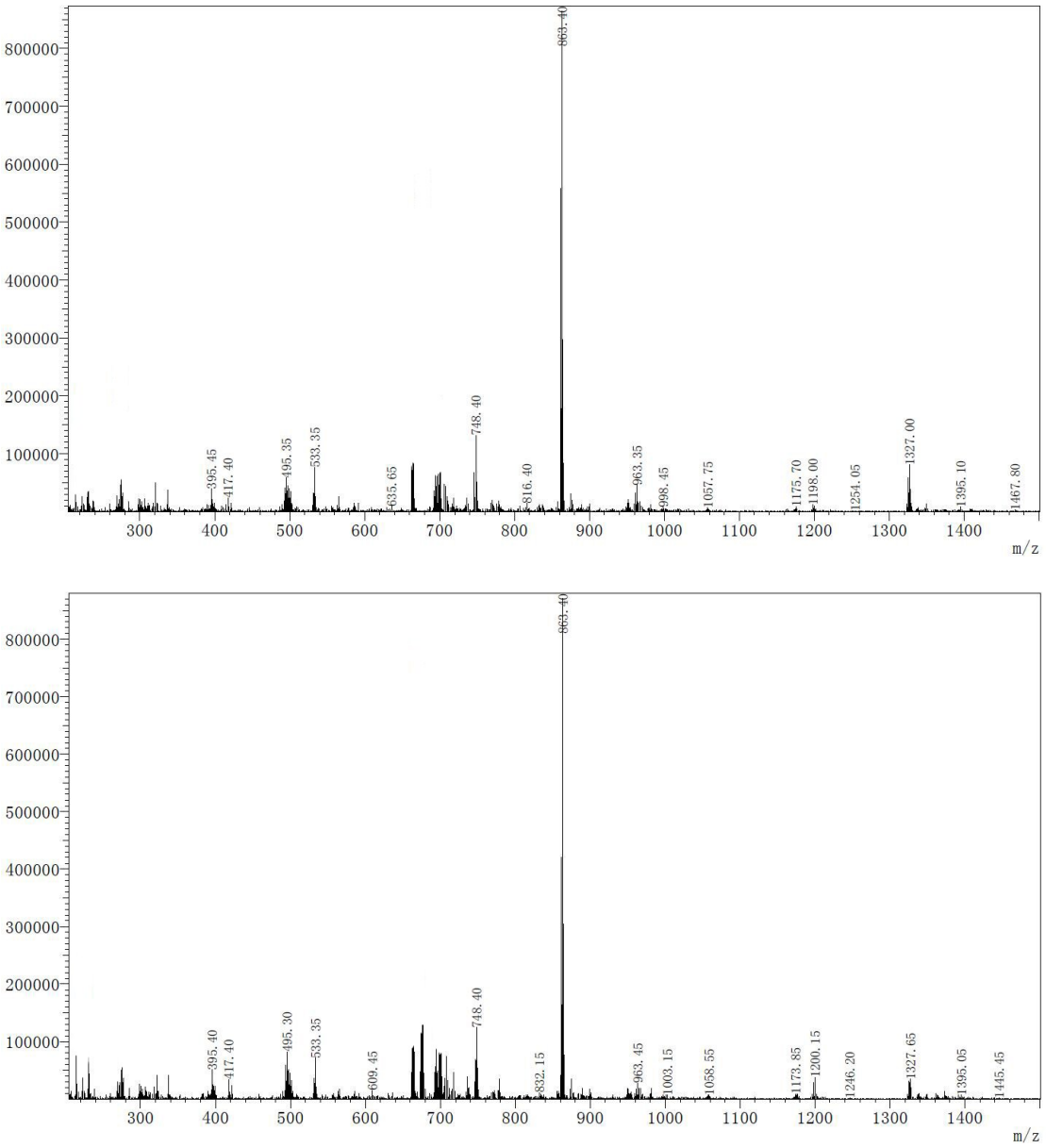

Fig. S1. The mass spectra of **Ir1** in Tris-HCl buffer solution (containing 1% DMSO) for 0 h (top) and 48 h (down), respectively.

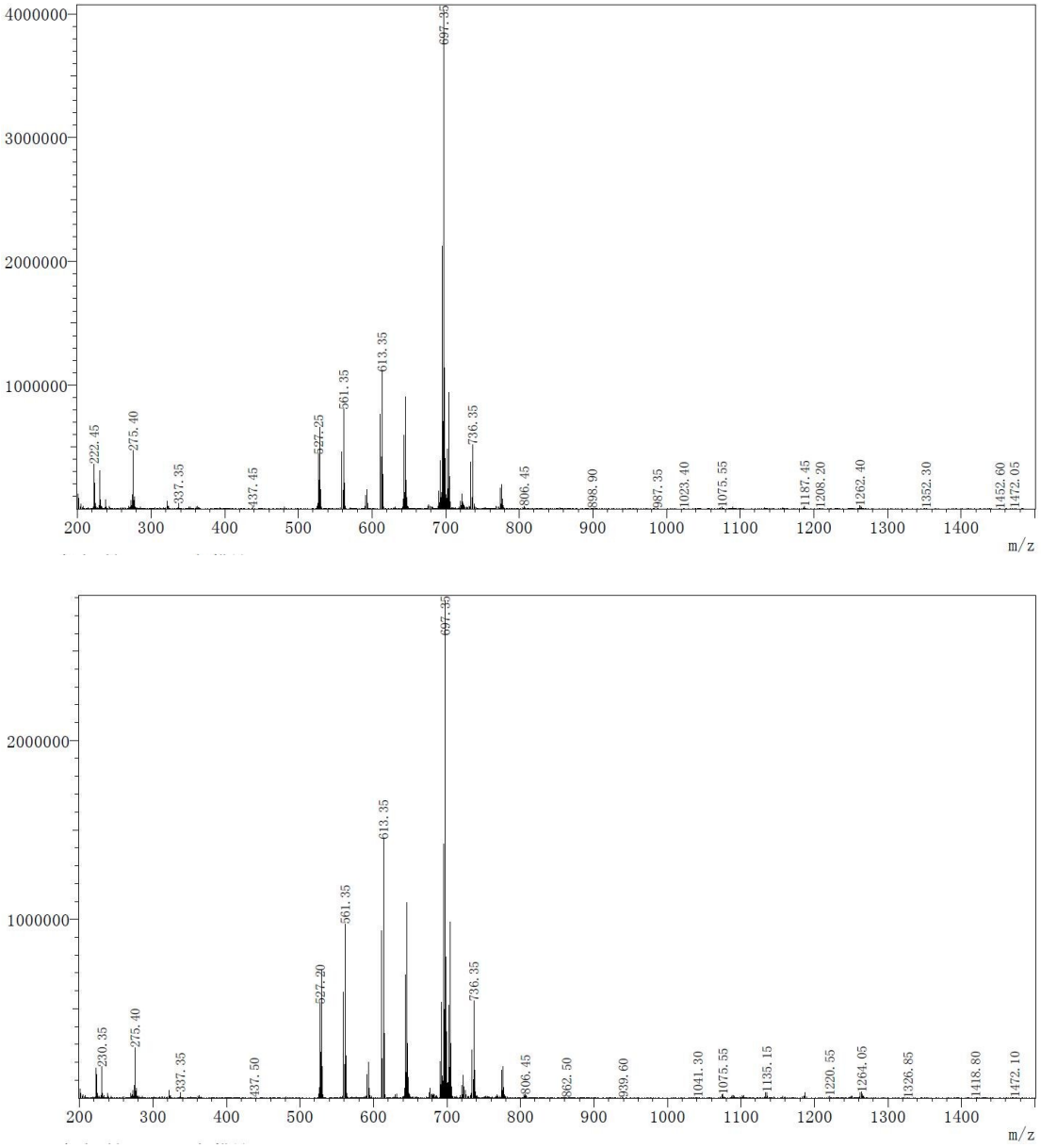

Fig. S2. The mass spectra of **Ir2** in Tris-HCl buffer solution (containing 1% DMSO) for 0 h (top) and 48 h (down), respectively.

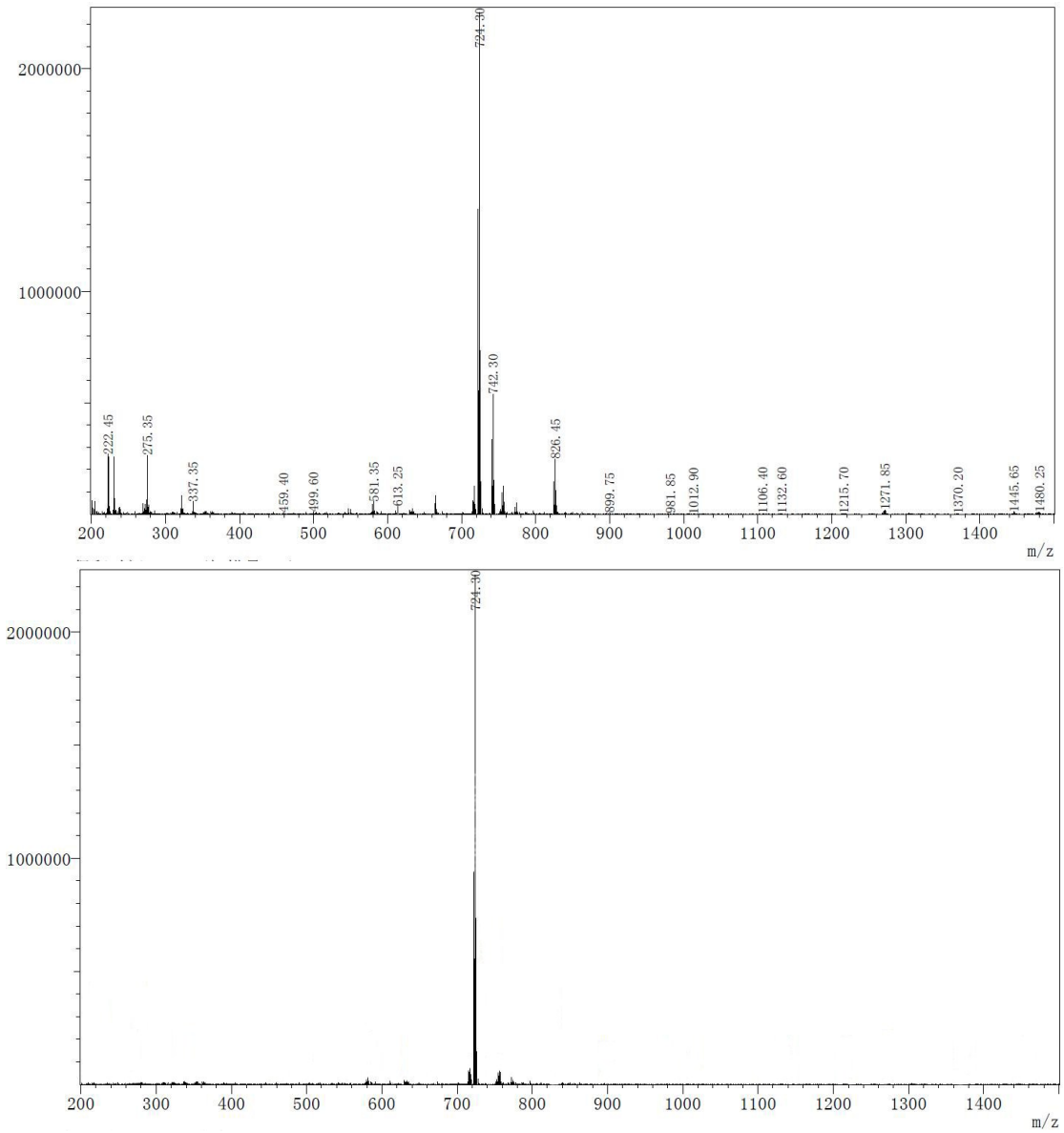

Fig. S3. The mass spectra of **Ir3** in Tris-HCl buffer solution (containing 1% DMSO) for 0 h (top) and 48 h (down), respectively.

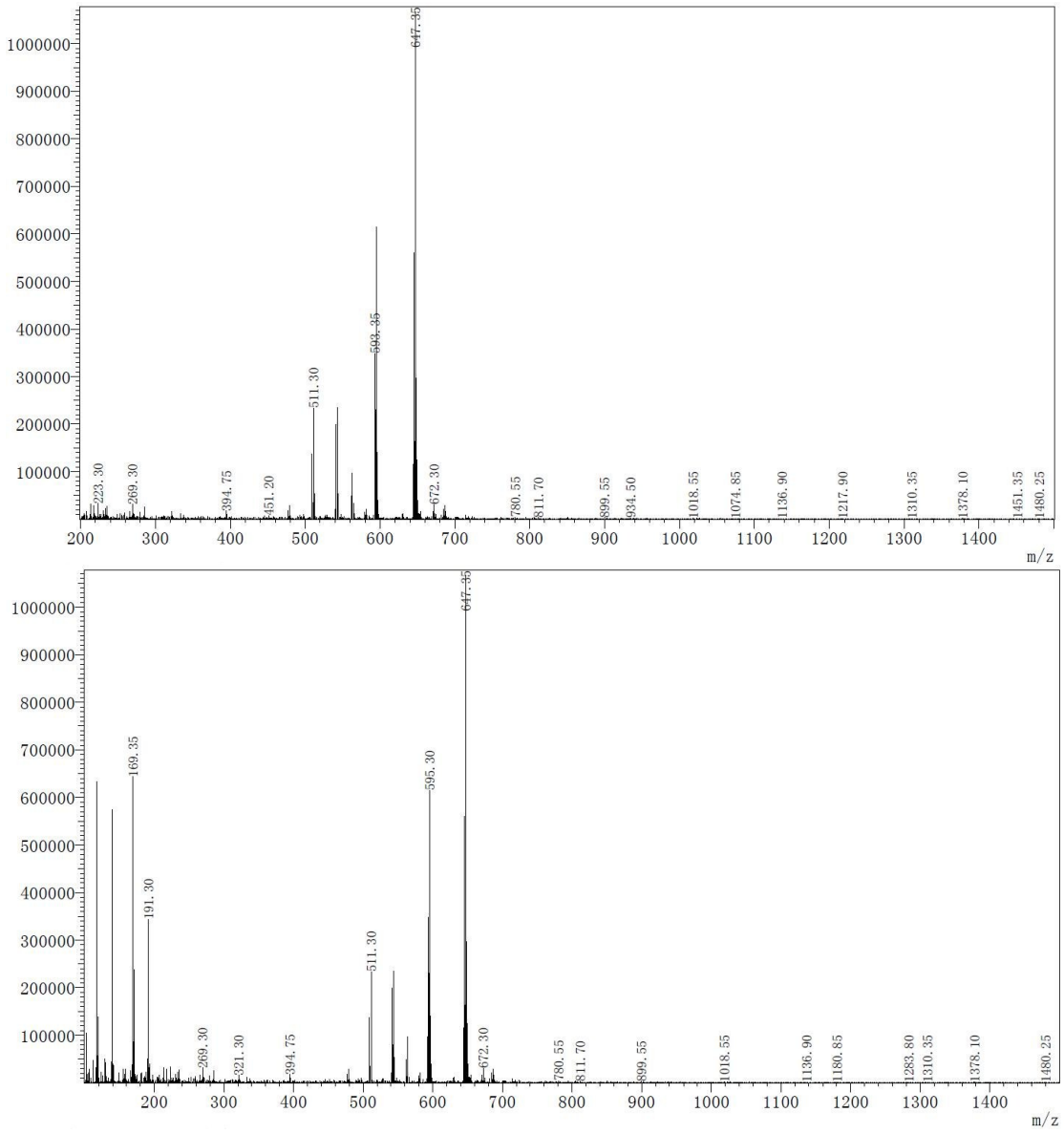

Fig. S4. The mass spectra of **Ir4** in Tris-HCl buffer solution (containing 1% DMSO) for 0 h (top) and 48 h (down), respectively.

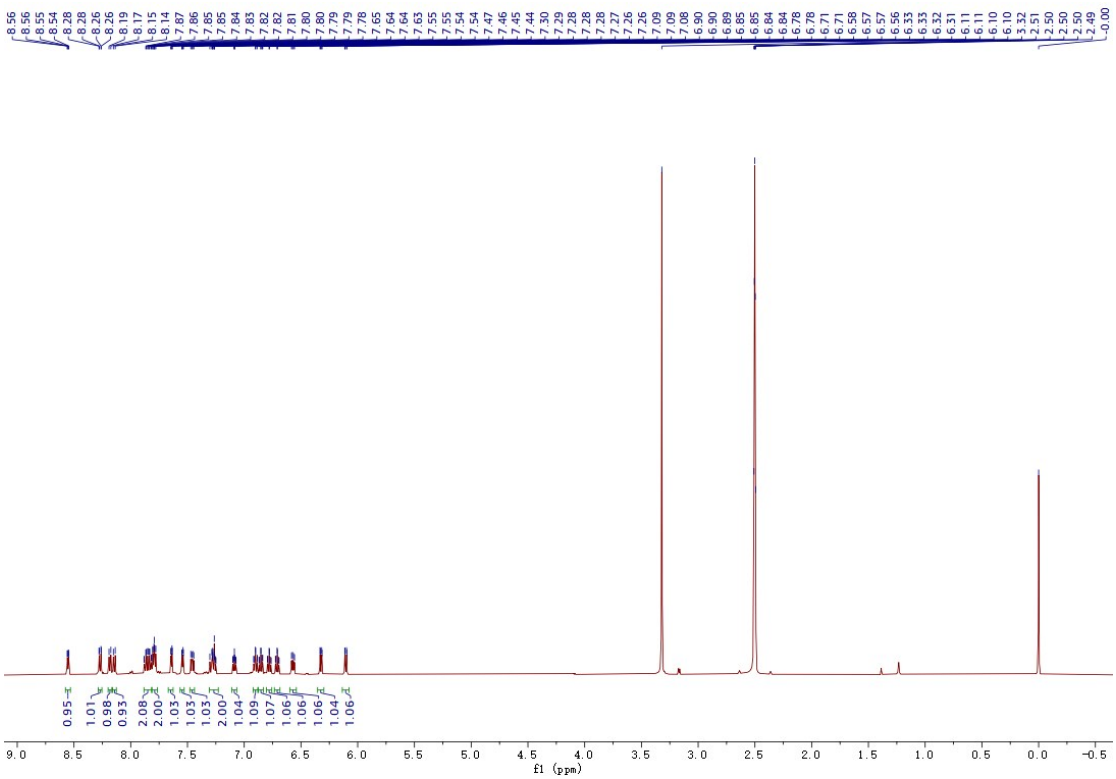

Fig. S5. ^{1}H NMR (500MHz, DMSO-d_6) for complex **Ir-1**.

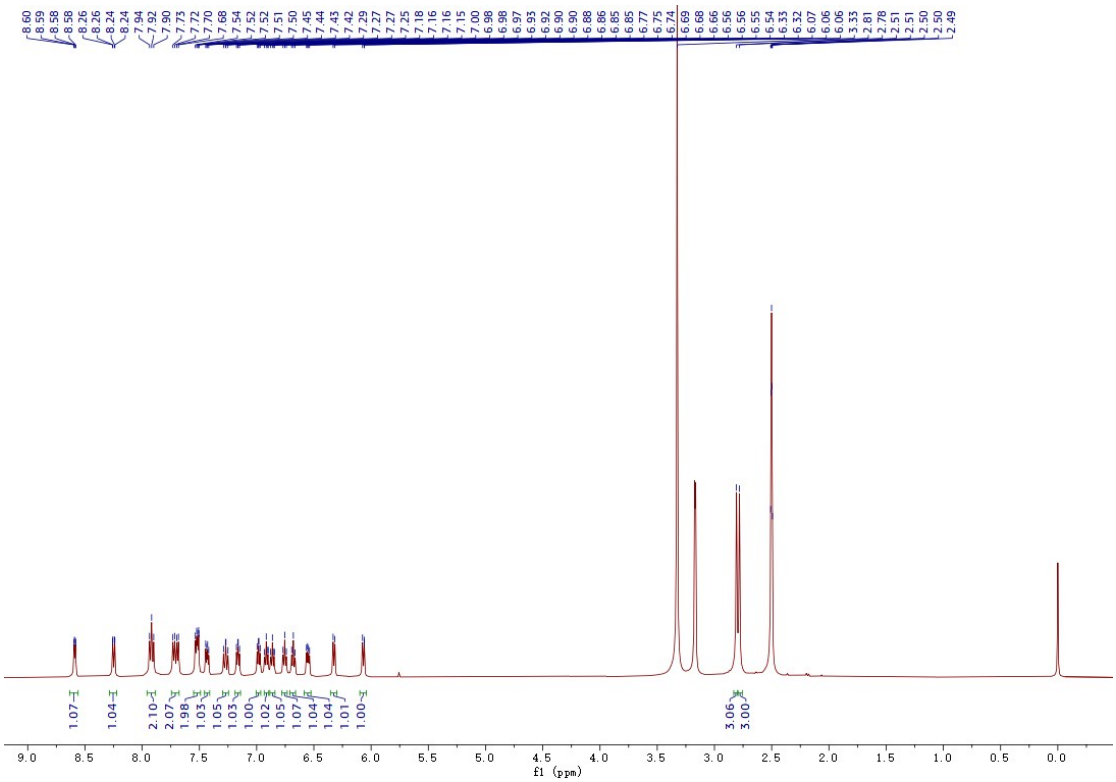

Fig. S6. ^{1}H NMR (500MHz, DMSO-d_6) for complex **Ir-2**.

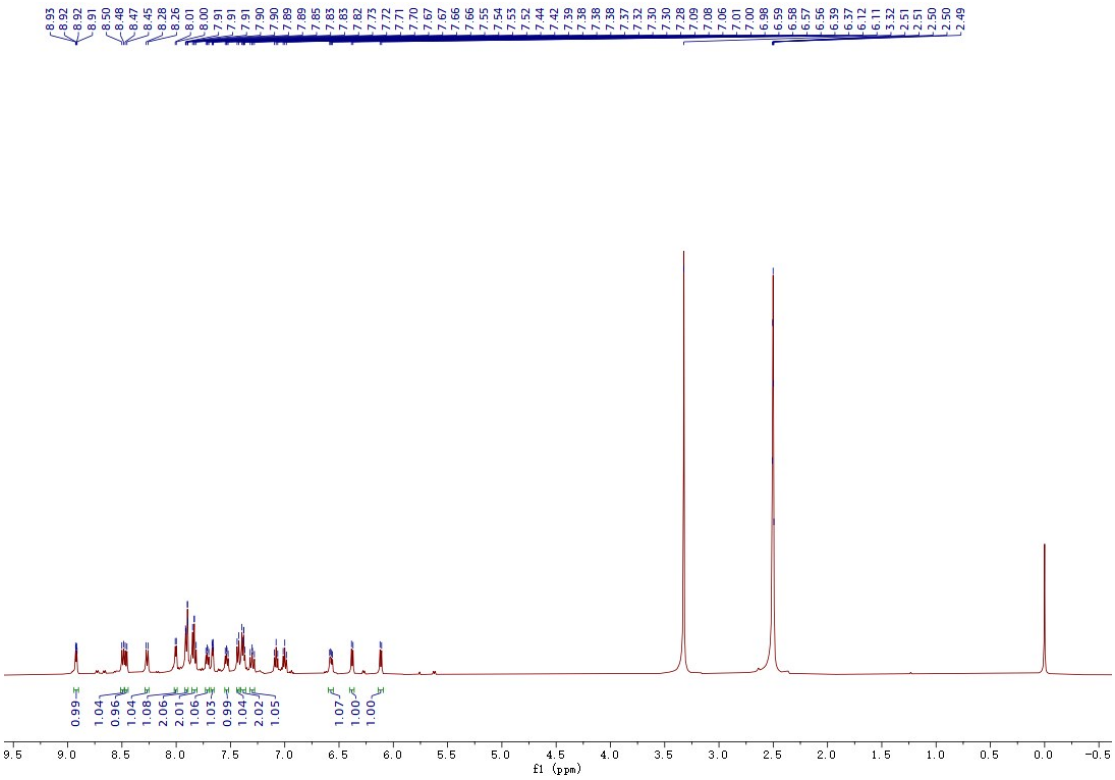

Fig. S7. ^{1}H NMR (500MHz, DMSO-d_6) for complex **Ir-3**.

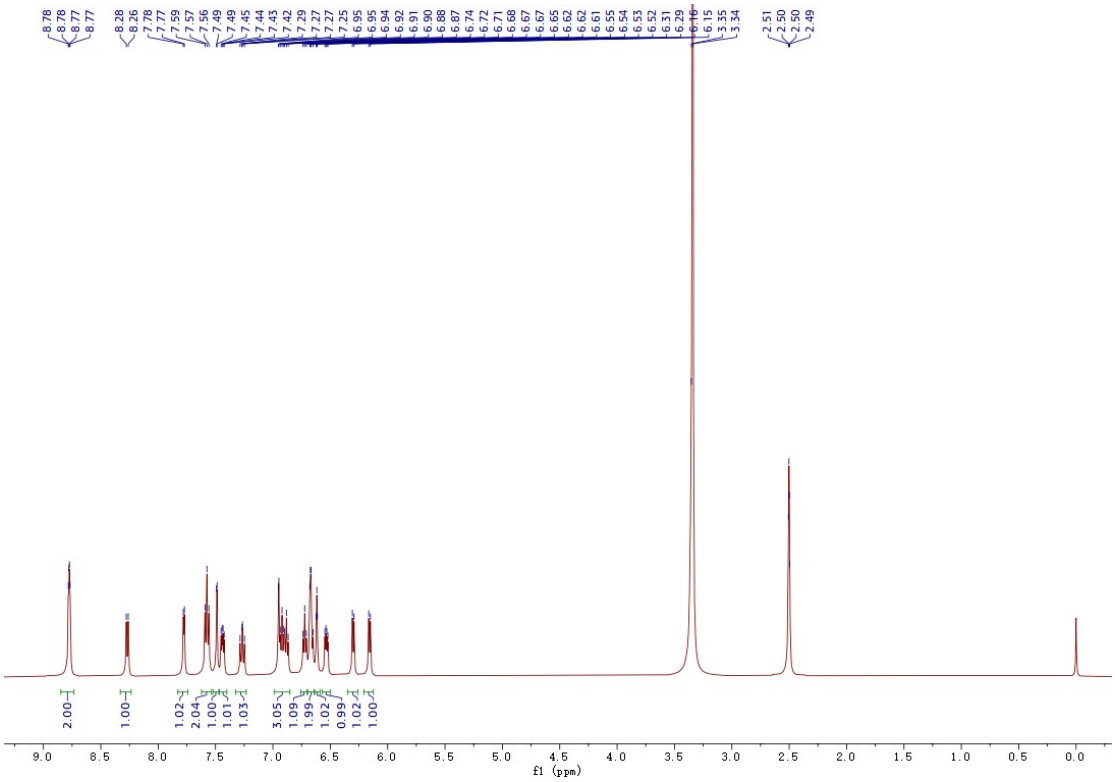

Fig. S8. ^{1}H NMR (500MHz, DMSO-d_6) for complex **Ir-4**.

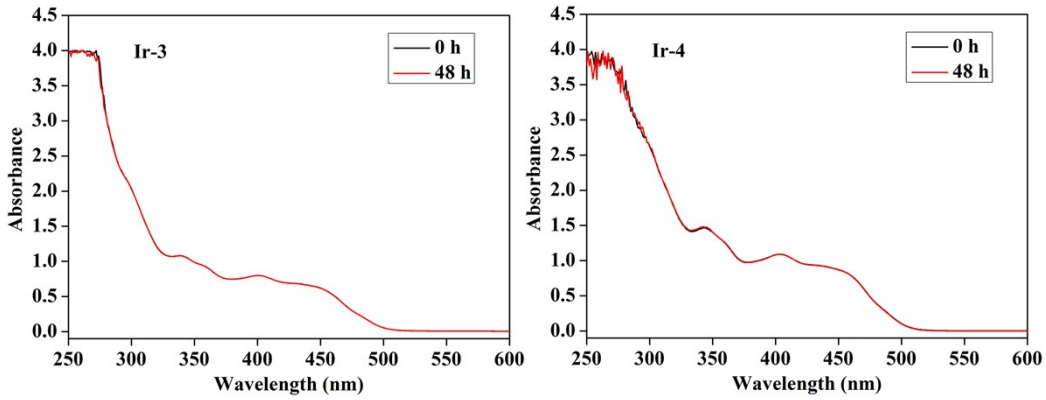

Fig. S9. Absorption spectra of **Ir-3** and **Ir-4** (2.0×10^{-5} M) measured in 10 mM pH 7.35 Tris-HCl solution containing DMSO (1% v/v).

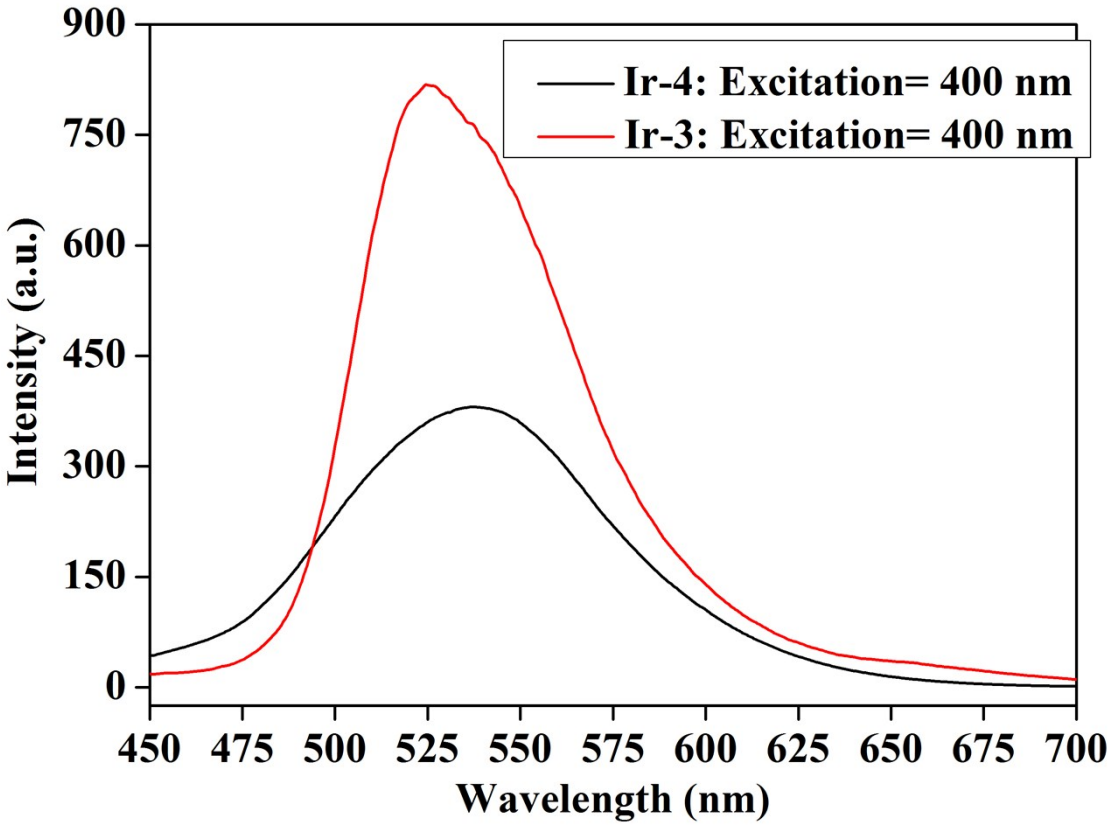

Fig. S10. Fluorescence spectra of **Ir-3** and **Ir-4** (2.0×10^{-5} M) recorded in 10 mM pH 7.35 Tris-HCl solution containing DMSO (1%v/v) followed by excitation at 400 nm.

Table S13. Cellular distribution of **Ir-3** (170 nM) and **Ir-4** (35 nM) in HeLa cancer cells after 24 h of incubation.

	total	nuclear fraction	mitochondrial fraction
Ir-3	(4.32±0.09 nmol of Ir)/10^6 cells	(0.83 nmol of Ir)/10^6 cells	(2.94 nmol of Ir)/10^6 cells
Ir-4	(5.64±0.12 nmol of Ir)/10^6 cells	(0.97 nmol of Ir)/10^6 cells	(3.24 nmol of Ir)/10^6 cells

Experimental section

Materials

The Tris, gel loading buffer, RNase A, 5-fluoro-8-quinolinol (H-FQ) and 2-phenylpyridine (H-L1), 3-methyl-2-phenylpyridine (H-L2), 7,8-benzoquinoline (H-L3), 1-phenylpyrazole (H-L4) and propidium iodide (PI) were purchased from Sigma. The antibody bcl-2, bax, cytochrome c (cyto C), apaf-1 and caspase-9/-3 were purchased from Abcam. The tumor cell lines cervical (HeLa), cisplatin-resistant SK-OV-3 cells (SK-OV-3/DDP), and normal hepatocyte-HL-7702 were obtained from the Shanghai Institute for Biological Science (China).

Instruments

Elemental analyses (C, H and N) were carried out on a PerkinElmer series II CHNS/O 2400 elemental analyzer. Infrared spectra (IR) was obtained on a PerkinElmer FT-IR spectrometer. The NMR spectra were recorded on a Bruker AV-500 NMR spectrometer. ESI-MS spectra was performed on Thermofisher Scientific

Exactive LC-MS spectrometer (Thermal Elctronic, USA). The MTT assay was performed on M1000 microplate reader (Tecan Trading Co. Ltd., Shanghai, China). Apoptosis assay, JC-1 and the cellular localization behavior analysis were recorded on confocal microscopy (Zeiss 710).

X-ray Crystallography

The data collection of single crystals of **Ir-1−Ir-4** was performed on a SuperNova CCD diffractometer equipped with graphite monochromated Mo Kα radiation (λ = 0.710 73 Å) at room temperature. The structures were solved with direct methods and refined using SHELX-97 programs. The nonhydrogen atoms were located in successive difference Fourier synthesis. The final refinement was performed by full-matrix leastsquares methods with anisotropic thermal parameters for no-hydrogen atoms on F_2. The hydrogen atoms were added theoretically and riding on the concerned atoms. The paramerters used intensity collection and refinements are summarized in Tables S1–S12 together with the crystal data.

Cell Culture

The cell culture was maintained in RPMI-1640 medium supplemented with 10.0% fetal bovine serum (FBS), 100.0 U/mL penicillin, and 100.0 μg/mL streptomycin in 25.0 cm^2 culture flasks at 37 °C in a humidified atmosphere with 5% CO_2. All the cells to be tested in the following assays had a passage number of 5.0.

MTT assays

The cells were seeded in 96 well plates at the density of 5000-8000 cells per well for 24 h, then incubated with different concentrations of each complex for 24.0 h. And then these cell medium was discarded and MTT (1.0 mg/mL) was added. 4.0 h later, MTT solution was removed and DMSO was added. And obtained the results by a M1000 microplate reader (Tecan Trading Co. Ltd., Shanghai, China) at 570 nm.

Apoptotosis and JC-1 staining assays

Annexin V-FITC staining of the membranes was performed by using the Annexin-V and PI. The cells were incubated with each complex for 24.0 h, then the cells were harvested after another 24h, stained with Annexin-V and PI, and then analyzed by flow cytometry or confocal microscopy (Zeiss 710). Similar procedure was used for JC-1 staining assay.

Western Blot

The cells were incubated with each complex for 24.0 h, and then the cells harvested from each well of the culture plates were lysed in 150 μL of extraction buffer consisting of 149 μL of RIPA lysis buffer and 1 μL of PMSF (100 mM). The suspension was centrifuged at 10 000 rpm at 4 °C for 10 min, and the supernatant (10μL for each sample) was loaded onto 10% polyacrylamide gel and then transferred to a microporous polyvinylidene difluoride (PVDF) membrane. Western blotting was performed using each anti-apoptotic antibody, or anti-β-actin primary antibody and horseradish-peroxidase-conjugated anti-mouse or anti-rabbit secondary antibody. The protein bands were visualized using chemiluminescence substrate.

Statistical Analysis

The experiments have been repeated from three to five times, and the results obtained are presented as means ± standard deviation (SD). Significant changes were assesses by using Student's *t* test for unpaired data, and *p* values of <0.05 were considered significant.