Supporting Information

Photodynamic Therapy with Mitochondria-targeted Biscyclometalated Ir(III) Complexes. Multi-action Mechanism and Strong influence of the Cyclometallating Ligand

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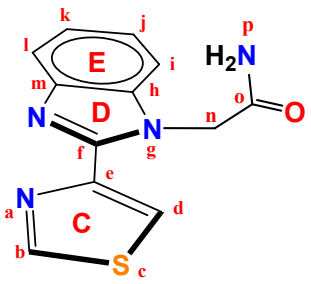
Table of Contents

1.- Synthesis and characterization of the ligands

Synthesis of L1



In a 100 mL Schlenk flask, K_2CO_3 (0.3288 g, 1.990 mmol) was added to a solution of 2-(4-Thiazolyl)benzimidazole (thiabendazole, TBZ) (0.4008 g, 1.992 mmol) in DMF (11 mL). The mixture/suspension was stirred at room temperature for 30 minutes. 2-bromoacetamide (0.2748 g, 1.992 mmol) was then added. The stirring was extended for 22 hours at room temperature. The solvent was removed under vacuum and the residue was redissolved in DMSO (5 mL). Water (10 mL) was added to precipitate a white solid that was filtrated, redissolved in ethanol (15 ml) and took to dryness (2 times) and then redissolved in toluene (15 ml) and took to dryness. The white solid was dried under vacuum. Yield: 0.3848 g (1.490 mmol, 75%). **M_r ($C_{12}H_{10}N_4OS$)** = 258.30 g/mol. **Anal. Calcd for $C_{12}H_{10}N_4OS((CH_3)_2SO)_{0.15}$:** C 54.71; H 4.07; N 20.75; **Found:** C 54.45; H 3.87; N 21.10. **^{1}H NMR (400 MHz, DMSO-d_6, 25 ºC)** δ 9.30 (dd, J = 2.1, 0.6 Hz, 1H, H^d), 8.51 (dd, J = 2.1, 0.6 Hz, 1H, H^b), 7.69-7.66(m, 2H, H^p, H^i), 7.55 – 7.48 (m, 1H, H^l), 7.29 – 7.22 (m, 2H, H^j, H^k), 7.20 (s, 1H, H^p), 5.46 (s, 2H, H^n, H^n) ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 25 ºC)** δ 168.76, 155.14, 147.17, 146.93, 142.33, 136.39, 122.66, 122.21, 122.13, 118.89, 110.54, 47.07 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3305 (w, ν_{N-H}), 3099 (w, ν_{Car-H}), 1603-1573 (m, $\nu_{C=C+C-N}$), 1421 (w, $\nu_{C=N}$), 1164 (m, ν_{C-C}), 1072 (m, δ_{C-Hip}), 735 (vs, δ_{C-Hoop}). **HR ESI+ MS (DCM/DMSO, 4:1):** m/z_{exp} = 259.0651 (m/z_{calcd} $[M+H^+]$ = m/z_{calcd} $[C_{12}H_{11}N_4OS]^+$= 259.0654). **Solubility:** soluble in dichloromethane, methanol, chloroform, dimethylformamide, dimethyl sulfoxide and acetone. Partially soluble in water.

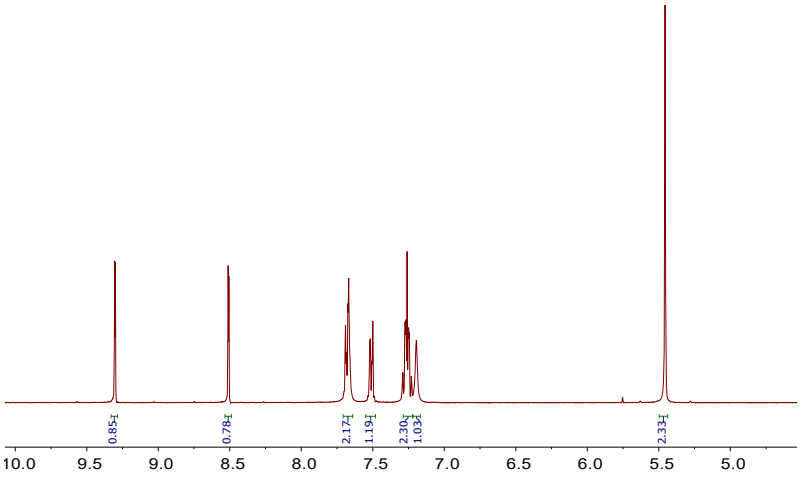


Figure SI1. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **L1**.

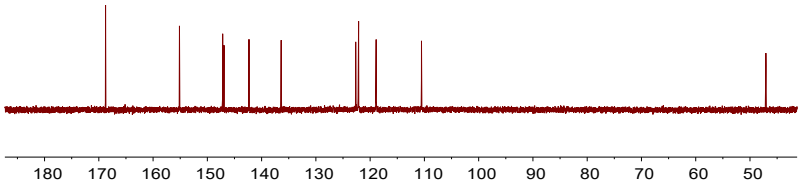


Figure SI2. $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **L1**.

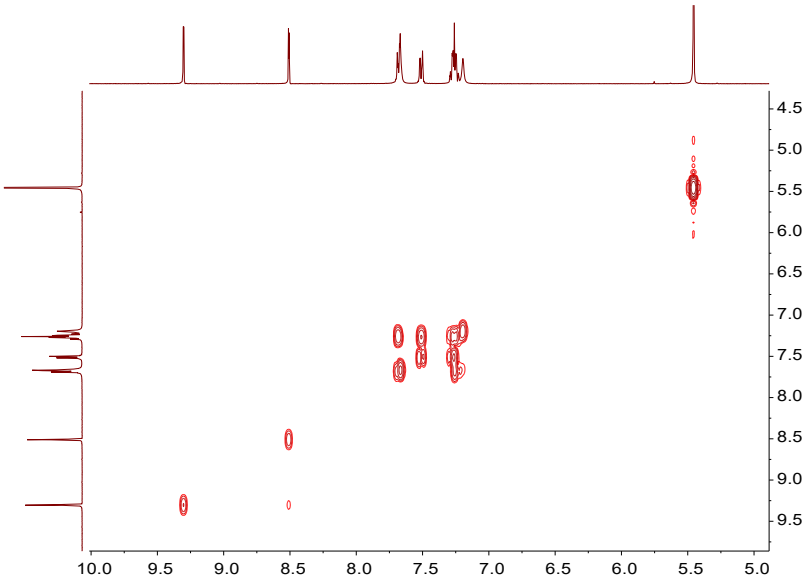


Figure SI3. COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **L1**.

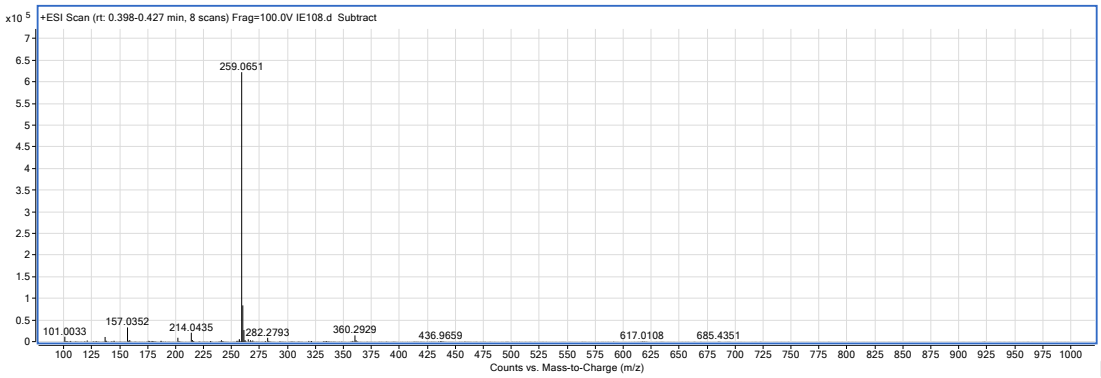
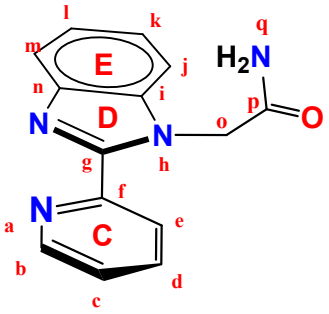


Figure SI4. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **L1**.

Synthesis of L2



In a 100 mL Schlenk flask, K_2CO_3 (0.4236 g, 2.564 mmol) was added to a solution of 2-(2-Pyridyl)benzimidazole (pybzim) (0.5001 g, 2.562 mmol) in DMF (7 mL). The mixture/suspension was stirred at room temperature for 30 minutes. 2-bromoacetamide (0.4241 g, 3.074 mmol) was then added. The stirring was extended for 22 hours at room temperature. The solvent was removed under vacuum and the residue was tried to redissolve with ethanol (15 mL), dichloromethane (15 mL) and methanol (10 mL), which is not possible, but while there is a white-yellow solid, the solution is brown-orange coloured so it is filtered and the solid is washed with water (3 mL). The pale brown solid is dried under vacuum. Yield: 0.5007 g (1.985 mmol, 77%). **M_r ($C_{14}H_{12}N_4O$)** = 252.27 g/mol. **Anal. Calcd for $C_{14}H_{12}N_4O((CH_3)_2SO)_{0.15}$:** C 65.06; H 4.93; N 21.22; **Found:** C 65.05; H 4.77; N 21.50. **^{1}H NMR (400 MHz, DMSO-d_6, 25 ºC)** δ 8.70 – 8.65 (m, 1H, H^e), 8.38 – 8.32 (m, 1H, H^b), 7.99 (td, J = 7.9, 1.8 Hz, 1H, H^c), 7.73 (dd, J = 7.0, 1.5 Hz, 1H, H^m), 7.65 (s, 1H, H^q), 7.59 – 7.54 (m, 1H, H^j), 7.49 (ddd, J = 7.6, 4.9, 1.3 Hz, 1H, H^d), 7.33 – 7.25 (m, 2H, H^k, H^l), 7.15 (s, 1H, H^q), 5.54 (s, 2H, H^o) ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 25 ºC)** δ 169.04, 150.13, 149.60, 148.56, 141.97, 137.36, 137.29, 124.16, 123.93, 123.18, 122.34, 119.42, 110.73, 47.71 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3317 (w, ν_{N-H}), 3147 (w, ν_{Car-H}), 1593-1584 (m, $\nu_{C=C+C-N}$), 1415 (w, $\nu_{C=N}$), 1171 (m, ν_{C-C}), 1045 (m, δ_{C-Hip}), 748 (vs, δ_{C-Hoop}). **HR ESI+ MS (DCM/DMSO, 4:1):** m/z_{exp} = 253.1087 (m/z_{calcd} [M+H$^+$] = m/z_{calcd} [$C_{14}H_{13}N_4O$]$^+$= 253.1089). **Solubility:** soluble in dichloromethane, methanol, chloroform, dimethylformamide, dimethyl sulfoxide and acetone. Partially soluble in water.

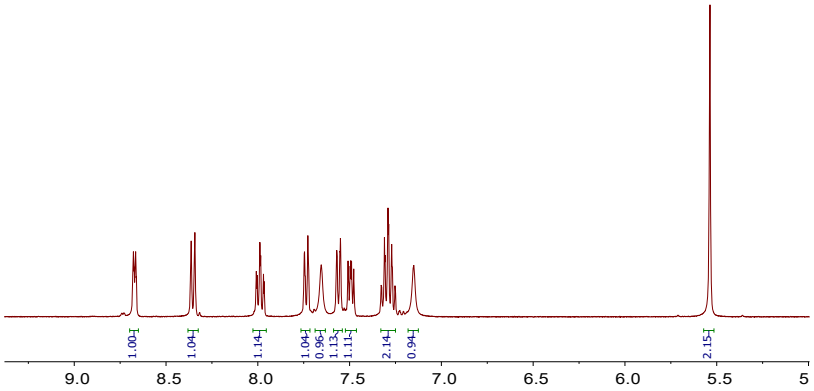


Figure SI5. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **L2**.

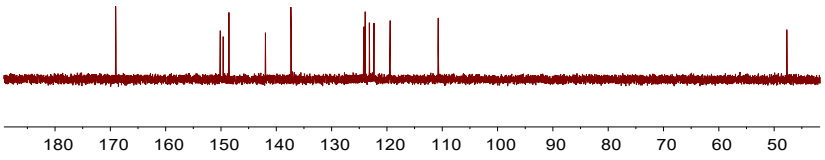


Figure SI6. $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **L2**.

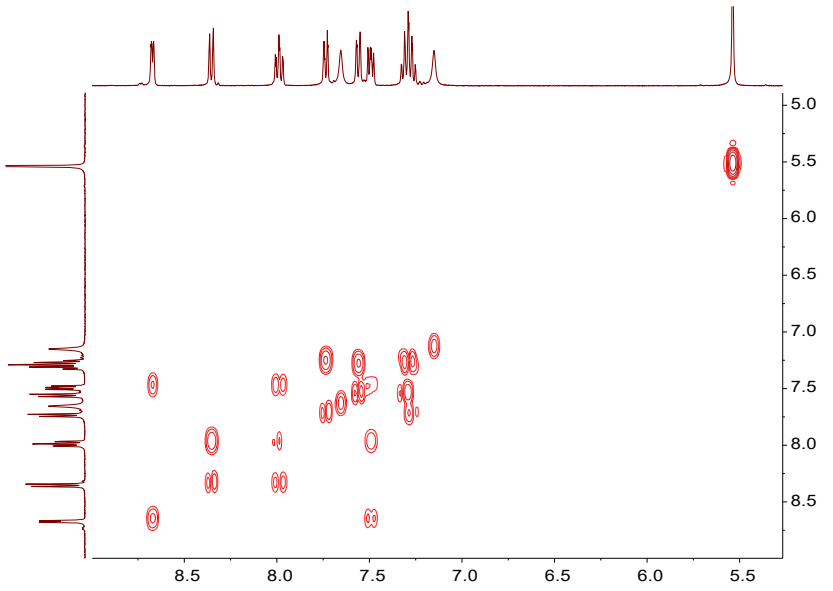
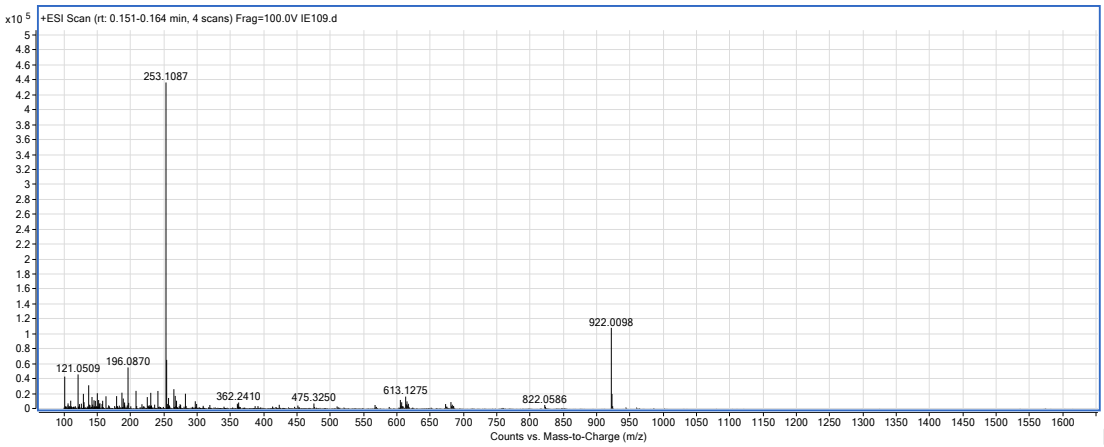


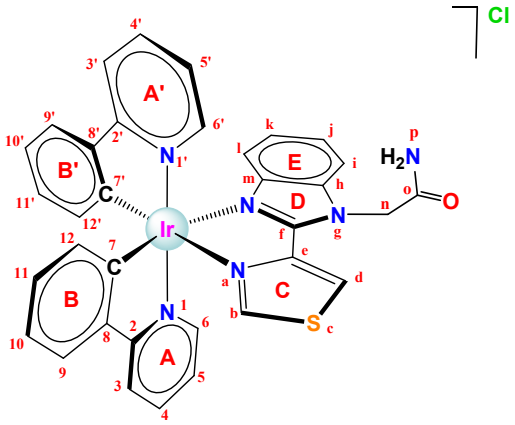
Figure SI7. $^{1}H,^{1}H$-COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **L2**.



igure SI8. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **L2**.

2.- Synthesis and characterization of the Ir(III)-complexes

Synthesis of $[Ir(ppy)_2(L1)]Cl$: [1a]Cl



In a 100 mL Schlenk flask, previously purged with nitrogen, the ancillary ligand L^x (0.0542 g, 0.210 mmol) was added to a solution of $[Ir(\mu\text{-}Cl)(ppy)_2]_2$ (0.1003 g, 0.094 mmol) in a mixture of dichloromethane (8 mL) / methanol (10 mL), and the mixture was stirred at 60 ºC for 24 hours under a N_2 atmosphere. The resulting solution was concentrated to half the volume under vacuum and diethyl ether (15 mL) was added to precipitate a crude solid that was isolated by filtration and washed with diethyl ether (2×5 mL). The product was dried under vacuum to produce a yellow powder. Yield: 0.1182 g (0.149 mmol, 80%). **M_r ($C_{34}H_{26}ClIrN_6OS$)** = 794.34 g/mol. **Anal. Calcd for $C_{34}H_{26}ClIrN_6OS{\cdot}(CH_2Cl_2)_{1.04}$:** C 47.68; H 3.21; N 9.52; **Found:** C 47.70; H 3.30; N 9.32. **^{1}H NMR (400 MHz, DMSO-d_6, 25 ºC)** δ 8.97 (s, 1H, H^d), 8.51 (s, 1H, H^b), 8.31 (s, 1H, H^{NH}), 8.26 (d, J = 8.1 Hz, 1H, H^3), 8.21 (d, J = 8.0 Hz, 1H, $H^{3'}$), 7.96 – 7.86 (m, 5H, H^i, H^4, $H^{4'}$, H^9, $H^{9'}$), 7.73 (d, J = 5.8 Hz, 1H,$H^{6'}$), 7.70 (d, J = 5.8 Hz, 1H, H^6), 7.64 (s, 1H, H^{NH}), 7.36 (t, J = 7.8 Hz, 1H, H^j), 7.19 (t, J = 6.8 Hz, 1H, H^5), 7.13 (t, J = 6.1 Hz, 1H, $H^{5'}$), 7.06 (t, J = 7.2 Hz, 1H, H^{10}), 7.01 (t, J = 7.5 Hz, 2H, $H^{10'}$, H^k), 6.92 (t, J = 7.6 Hz, 1H, H^{11}), 6.89 (t, J = 7.5 Hz, 1H, $H^{11'}$), 6.32 (d, J = 7.5 Hz, 1H, H^{12}), 6.25 (d, J = 7.5 Hz, 1H, $H^{12'}$), 6.15 (d, J = 8.2 Hz, 1H, H^l), 5.64 – 5.52 (AB system, 2H, H^n) ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 25 ºC)** δ 167.12, 167.00, 158.58, 149.23, 148.86, 148.46, 147.30, 144.55, 144.42, 143.31, 138.63, 138.57, 138.43, 136.27, 131.73, 131.27, 129.85, 129.53, 126.07, 125.06, 124.86, 124.75, 124.40, 123.65, 122.06, 121.98, 119.86, 119.50, 116.61, 112.20, 47.30 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3319 (w, $\nu_{N\text{-}H}$), 3038 (w, $\nu_{Car\text{-}H}$), 1604-1581 (m, $\nu_{C=C\,+\,C\text{-}N}$), 1426 (w, $\nu_{C=N}$), 1161 (m, $\nu_{C\text{-}C}$), 1062 (m, $\delta_{C\text{-}Hip}$), 754-739 (vs, $\delta_{C\text{-}Hoop}$). **HR ESI+ MS (DCM/DMSO, 4:1):** m/z_{exp} = 759.1513 (m/z_{calcd} [M^+] = m/z_{calcd} [$C_{34}H_{26}IrN_6OS]^+$ = 759.1518);

501.0935 (m/z_{calcd} $[M^+-L1]$ = m/z_{calcd} $[C_{22}H_{16}IrN_2]^+$ = 501.0943). **Solubility:** soluble in dimethyl sulfoxide, dichloromethane, methanol, acetonitrile, acetone, dimethylformamide, tetrahydrofuran. Partially soluble in water.

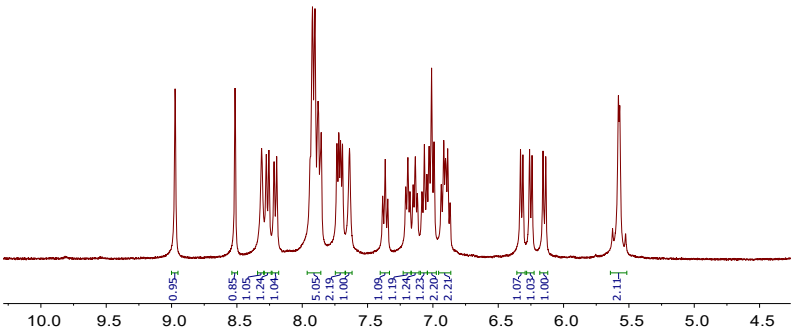


Figure SI9. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[1a]Cl**.

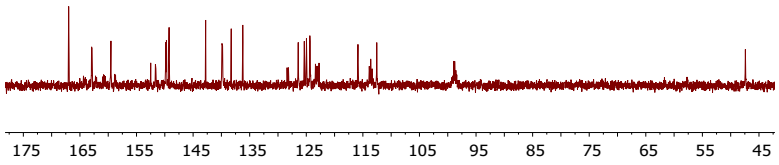


Figure SI10. $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **[1a]Cl**.

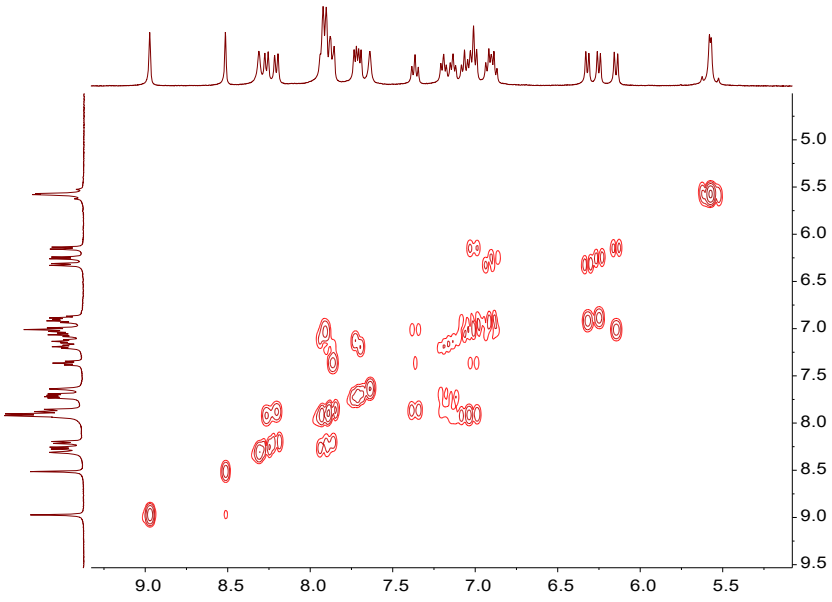


Figure SI11. $^{1}H,^{1}H$-COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[1a]Cl**.

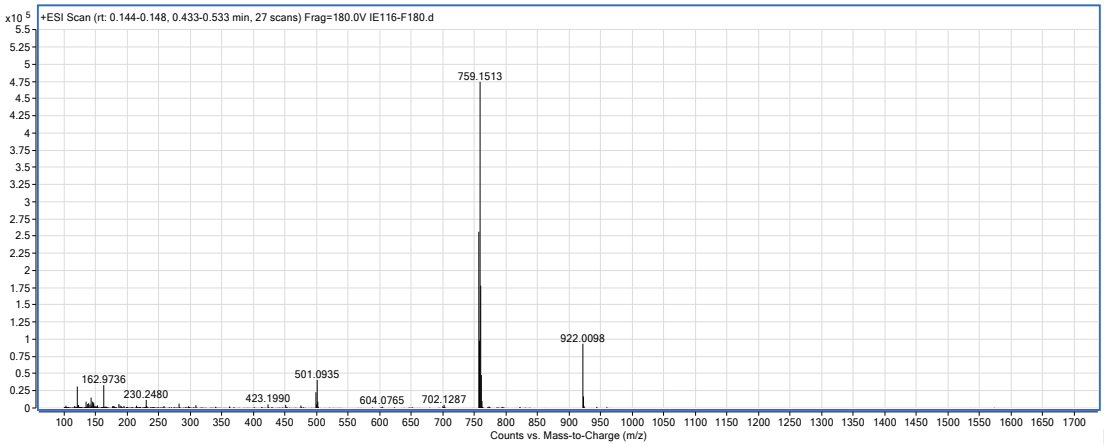
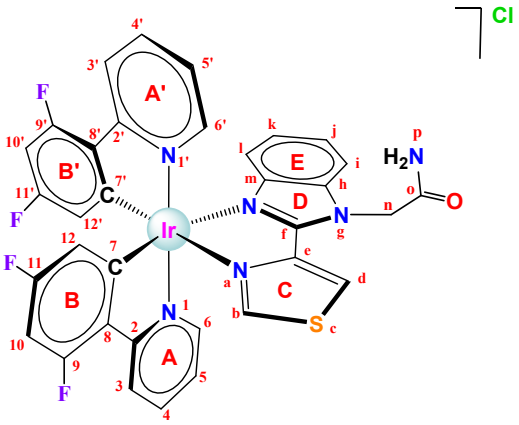


Figure SI12. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **[1a]Cl**.

Synthesis of [Ir(dfppy)$_2$(L1)]Cl: [1b]Cl



In a 100 mL Schlenk flask, previously purged with nitrogen, the ancillary ligand L^x (0.0473 g, 0.183 mmol) was added to a solution of [Ir(μ-Cl)(dfppy)$_2$]$_2$ (0.1001 g, 0.082 mmol) in a mixture of dichloromethane (8 mL) / methanol (10 mL), and the mixture was stirred at 60 ºC for 24 hours under a N_2 atmosphere. The resulting solution was concentrated to half the volume under vacuum and diethyl ether (15 mL) was added to precipitate a crude solid that was isolated by filtration and washed with diethyl ether (2×5 mL). The product was dried under vacuum to produce a yellow powder. Yield: 0.0848 g (0.098 mmol, 60%). **M$_r$ ($C_{34}H_{22}ClF_4IrN_6OS$)** = 866.31 g/mol. **Anal. Calcd for $C_{34}H_{22}ClF_4IrN_6OS{\cdot}(CH_2Cl_2)_{0.90}$:** C 44.46; H 2.54; N 8.91; **Found:** C 44.54.49; H 2.60; N 9.20. **^{1}H NMR (400 MHz, DMSO-d$_6$, 25 ºC)** δ 9.01 (s, 1H, H^d), 8.73 (s, 1H, H^b), 8.30 (d, J = 7.6 Hz, 1H, H^3), 8.29 (s, 1H, H^{NH}), 8.24 (d, J = 8.7 Hz, H$^{3'}$), 8.03 (t, J= 8.1 Hz, 1H, H^4), 7.99 (t, J = 8.1 Hz, 1H, H$^{4'}$), 7.91 (d, J = 8.3 Hz, 1H, H^i), 7.79 (d, J = 5.8 Hz, 1H, H^6), 7.75 (d, J = 5.7 Hz, 1H, H$^{6'}$), 7.65 (s, 1H, H^{NH}), 7.42 (t, J = 7.9 Hz, 1H, H^j), 7.28 (t, J = 6.8 Hz, 1H, H$^{5'}$), 7.24 (t, J = 6.8 Hz, 1H, H^5) 7.18 (t, J = 7.7 Hz, 1H, H^k), 7.09 – 6.91 (m, 2H, H^{10}, H$^{10'}$), 6.21 (d, J = 8.2 Hz, 1H, H^l), 5.76 (d, J_{H-F}= 6.6 Hz, 1H, H^{12} or H$^{12'}$), 5.66 (d, J_{H-F} = 8.5 Hz, 1H, H^{12} or H$^{12'}$), 5.58 (AB system 2H, H^n) ppm. **^{19}F NMR (376 MHz, DMSO-d$_6$, 25 ºC)** δ -107.01 (c, J = 9.8 Hz, 1F, F^{11} or F$^{11'}$), -107.04 (c, J = 9.5 Hz, 1F, F^{11} or F$^{11'}$), -109.12 (t, J = 11.0 Hz, 1F, F^9 or F$^{9'}$), -109.19 (t, J = 11.6 Hz, 1F, F^9 or F$^{9'}$)ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$, 25 ºC)** δ 166.99, 162.93, 162.86, 161.65, 161.08, 159.50, 152.50, 151.58, 149.79, 149.24, 142.78, 139.91, 139.79, 138.26, 136.22, 128.39, 128.15, 127.57, 126.39, 125.35, 124.96, 124.34, 123.57, 123.14, 115.91, 115.82, 113.84, 112.56, 109.55, 99.19, 47.39 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3069 (w, ν_{Car-H}), 1601-1574 (m, $\nu_{C=C+C-N}$), 1429 (w, $\nu_{C=N}$), 1163 (m, ν_{C-C}), 1070 (m, δ_{C-Hip}), 745 (vs, δ_{C-Hoop}). **HR ESI+ MS (DCM/DMSO, 4:1):** m/zexp = 831.1136 (m/zcalcd [M$^+$] = m/z$_{calcd}$ [$C_{34}H_{22}F_4IrN_6OS$]$^+$ = 831.1141); 573.0556 (m/z$_{calcd}$ [M$^+$-L1] = m/z$_{calcd}$ [$C_{22}H_{12}F_4IrN_2$]$^+$ = 573.0566). **Solubility:** soluble in dimethyl sulfoxide, dichloromethane, methanol, acetonitrile, acetone, dimethylformamide, tetrahydrofuran. Partially soluble in water.

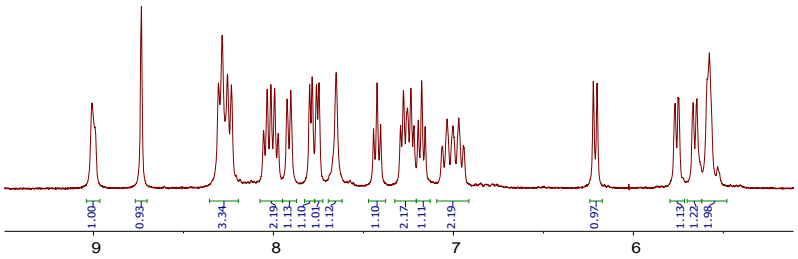


Figure SI13. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[1b]Cl**.

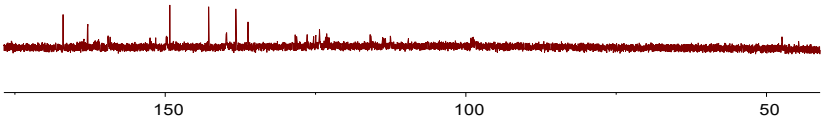


Figure SI14. ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **[1b]Cl**.

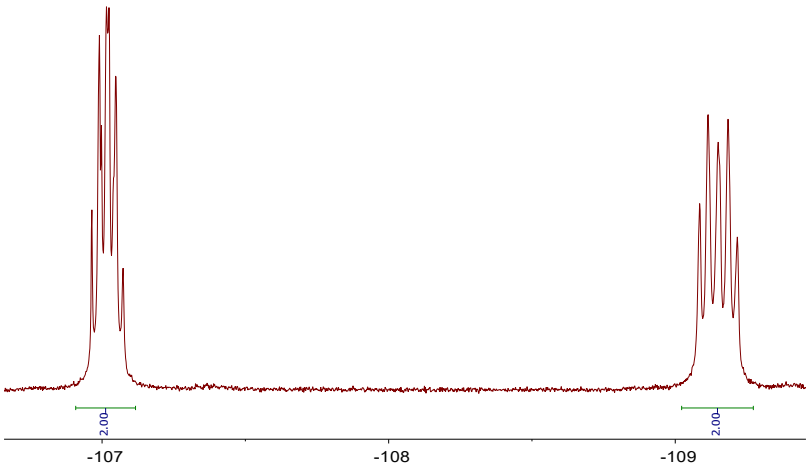


Figure SI15. ^{19}F NMR (376 MHz, DMSO-d_6, 25 °C) spectrum of **[1b]Cl**.

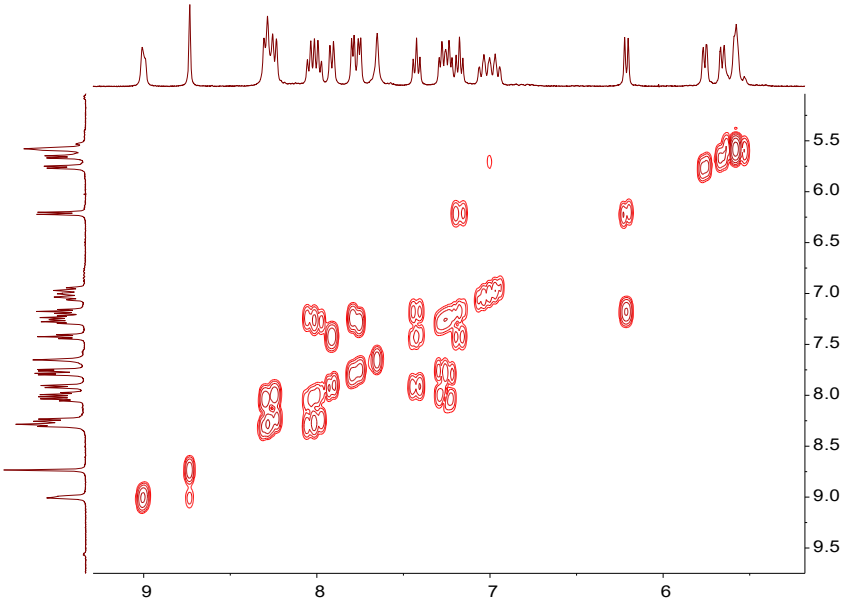
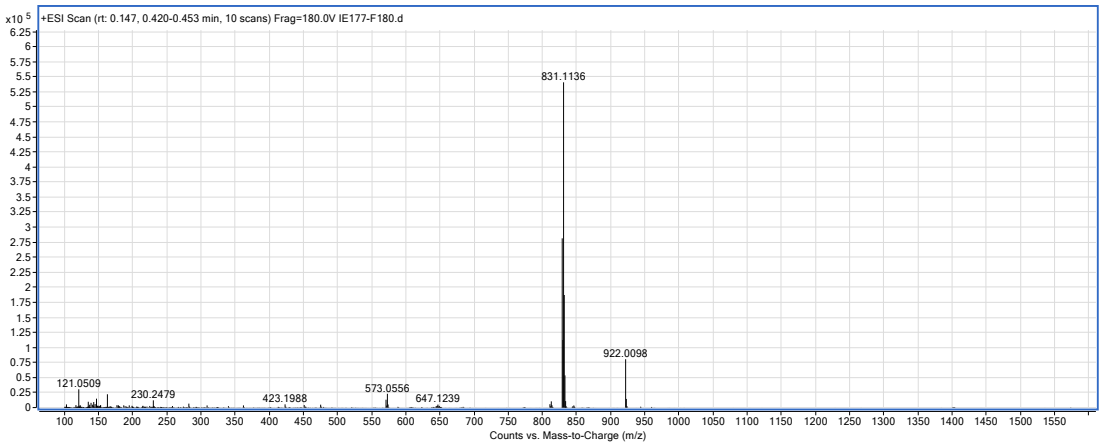


Figure SI16. $^{1}H,^{1}H$-COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[1b]Cl**.



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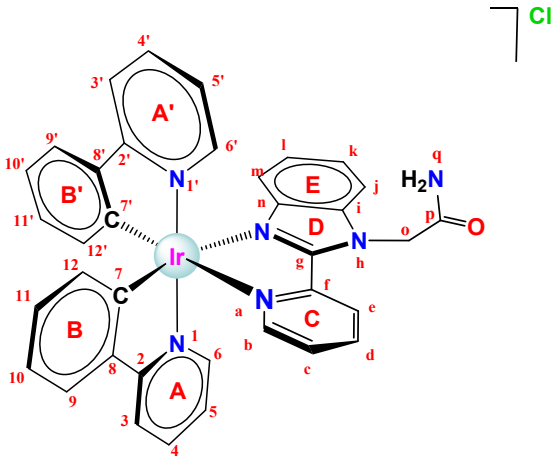
igure SI17. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **[1b]Cl**.

Synthesis of [Ir(ppy)$_2$(L2)]Cl: [2a]Cl



In a 100 mL Schlenk flask, previously purged with nitrogen, the ancillary ligand L^x (0.0537 g, 0.213 mmol) was added to a solution of [Ir(μ-Cl)(ppy)$_2$]$_2$ (0.1004 g, 0.094 mmol) in a mixture of dichloromethane (8 mL) / methanol (10 mL), and the mixture was stirred at 60 ºC for 24 hours under a N_2 atmosphere. The resulting solution was concentrated to half the volume under vacuum and diethyl ether (15 mL) was added to precipitate a crude solid that was isolated by filtration and washed with diethyl ether (2×5 mL). The product was dried under vacuum to produce a orange powder. Yield: 0.1036 g (0.131 mmol, 70%). **M$_r$ (C$_{36}$H$_{28}$ClIrN$_6$O)** = 788.32 g/mol. **Anal. Calcd for C$_{36}$H$_{28}$ClIrN$_6$O·(CH$_2$Cl$_2$)$_{0.80}$:** C 51.62; H 3.48; N 9.81; **Found:** C 51.64; H 3.56; N 9.78. **^{1}H NMR (400 MHz, DMSO-d$_6$, 25 ºC)** δ 8.47 (d, J = 8.2 Hz, 1H, H^e), 8.32 – 8.19 (m, 4H, H^d, H^3, H$^{3'}$, H^{NH}), 7.97-7.86 (m, 6H, H^b, H^j, H^9, H$^{9'}$, H^4, H$^{4'}$), 7.71-7.66 (m, 3H, H^c, H^{NH}, H^6), 7.60 (d, J = 5.5 Hz, 1H, H$^{6'}$), 7.43 (t, J = 7.8 Hz, 1H, H^k), 7.16-7.01 (m,, 5H, H^5, H$^{5'}$, H^{10}, H$^{10'}$, H^l), 6.93 (t, J= 6.7 Hz, 1H, H^{11}), 6.91 (t, J = 6.8 Hz, 1H, H$^{11'}$),, 6.29 (d, J = 7.3 Hz, 1H, H^{12}), 6.22 (d, J = 7.7 Hz, 1H, H^m), 6.20 (d, J = 7.0 Hz, 1H, H$^{12'}$) H^m), 5.69 (s, 2H, H^o, H^o) ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$, 25 ºC)** δ 167.41, 167.09, 166.94, 153.51, 151.46, 150.99, 149.28, 149.02, 147.53, 146.90, 144.43, 144.13, 139.59, 138.67, 138.64, 138.48, 136.85, 131.76, 130.89, 130.31, 129.65, 128.67, 125.86, 125.40, 125.16, 124.89, 124.84, 123.76, 123.68, 122.26, 122.13, 119.98, 119.65, 116.99, 112.40, 48.10 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3310 (w, ν_{N-H}), 3029 (w, ν_{Car-H}), 1606-1581 (m, $\nu_{C=C\ +\ C-N}$), 1436 (w, $\nu_{C=N}$), 1143 (m, ν_{C-C}), 1064 (m, δ_{C-Hip}), 761-742 (vs, δ_{C-Hoop}). **HR ESI+ MS (DCM/DMSO, 4:1):** m/z$_{exp}$ = 753.1949 (m/z$_{calcd}$ [M$^+$] = m/z$_{calcd}$ [C$_{36}$H$_{28}$IrN$_6$O]$^+$ = 753.1954); 501.0934 (m/z$_{calcd}$ [M$^+$-L2] = m/z$_{calcd}$ [C$_{22}$H$_{16}$IrN$_2$]$^+$ = 501.0943). **Solubility:** soluble in dimethyl sulfoxide, dichloromethane, methanol, acetonitrile, acetone, dimethylformamide, tetrahydrofuran.

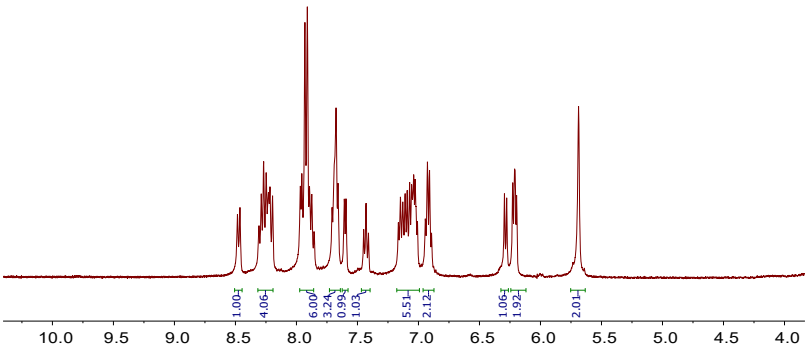


Figure SI18. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[2a]Cl**.

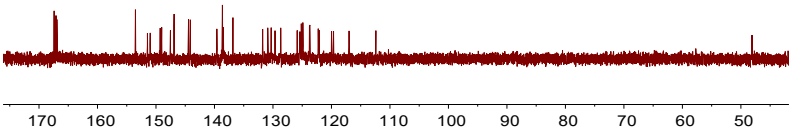


Figure SI19. $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **[2a]Cl**.

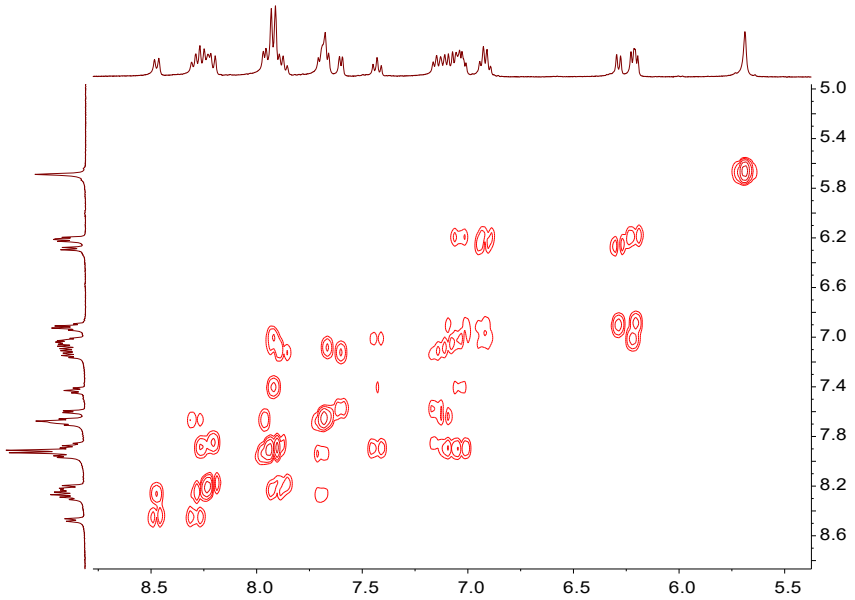


Figure SI20. $^{1}H,^{1}H$-COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[2a]Cl**.

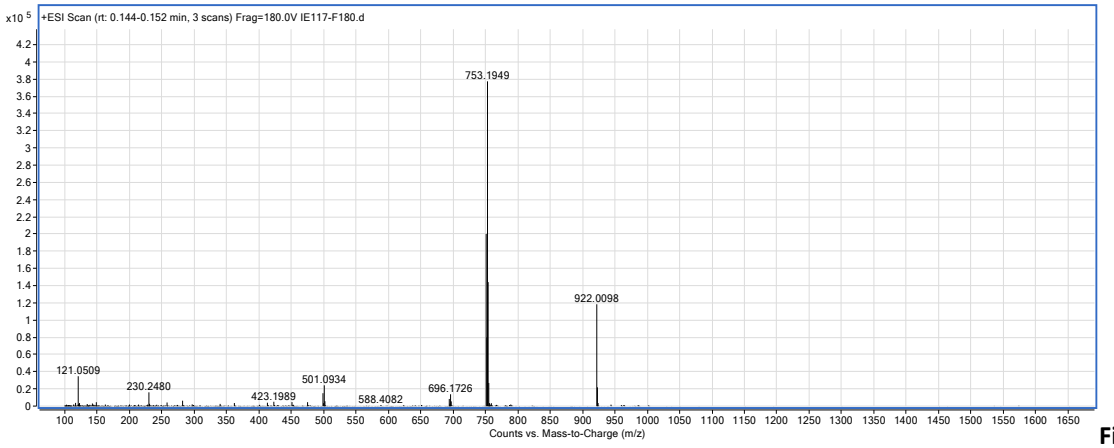
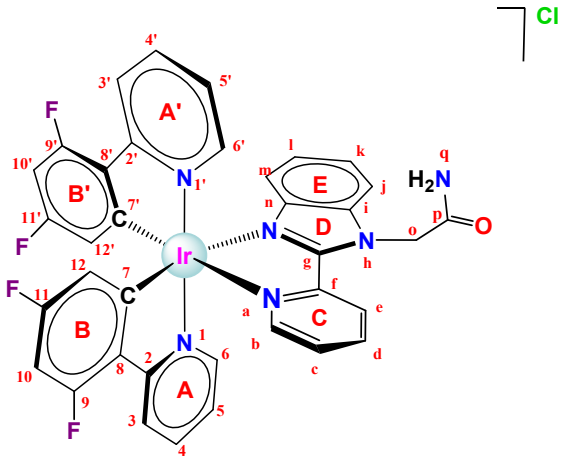


Figure SI21. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **[2a]Cl**.

Synthesis of $[Ir(dfppy)_2(L2)]Cl$: [2b]Cl



In a 100 mL Schlenk flask, previously purged with nitrogen, the ancillary ligand L^x (0.0417 g, 0.165 mmol) was added to a solution of $[Ir(\mu\text{-}Cl)(dfppy)_2]_2$ (0.1002 g, 0.082 mmol) in a mixture of dichloromethane (8 mL) / methanol (10 mL), and the mixture was stirred at 60 ºC for 24 hours under a N_2 atmosphere. The resulting solution was concentrated to half the volume under vacuum and diethyl ether (15 mL) was added to precipitate a crude solid that was isolated by filtration and washed with diethyl ether (2×5 mL). The product was dried under vacuum to produce a yellow powder. Yield: 0.0720 g (0.084 mmol, 51%). **M_r ($C_{36}H_{24}ClF_4IrN_6O$)** = 860.28 g/mol. **Anal. Calcd for $C_{36}H_{24}ClF_4IrN_6O\cdot(CH_2Cl_2)_{1.6}$:** C 45.34; H 2.75; N 8.44; **Found:** C 45.37; H 2.80; N 8.60. **^{1}H NMR (400 MHz, DMSO-d_6, 25 ºC)** δ 8.55 (d, J = 6.9 Hz, 1H, H^e), 8.36-8.29 (m, 3H, H^d, H^{NH}, H^3 or $H^{3'}$), 8.24 (d, J = 7.9 Hz, 1H, H^3 or $H^{3'}$), 7.99 (m, 4H, H^b, H^4, $H^{4'}$, H^j), 7.80 – 7.63 (m, 4H, H^c, H^6, $H^{6'}$, H^{NH}), 7.48 (t, J = 8.7 Hz, 1H, H^k), 7.26-7.18 (m, 3H, H^5, H^l, $H^{5'}$), 7.04 (t, $J_{H\text{-}F}$ = 8.7 Hz, 1H, H^{10} or $H^{10'}$), 6.98 (t, $J_{H\text{-}F}$ = 8.7 Hz, 1H, H^{10} or $H^{10'}$)6.27 (d, J = 8.3 Hz, 1H, H^m), 5.74 (m, 3H, $2H^o$, H^{12}), 5.62 (d, $J_{H\text{-}F}$ = 7.7 Hz, 1H, $H^{12'}$) ppm. **^{19}F NMR (376 MHz, DMSO-d_6, 25 ºC)** δ -106.49 (q, J = 9.3 Hz, 1F, F^{11} or $F^{11'}$), -106.92 (q, J = 9.6 Hz, 1F, F^{11} or $F^{11'}$), -108.62 (t, J = 11.9 Hz, 1F, F^9 or $F^{9'}$), -109.11 (t, J = 11.2 Hz, 1F, F^9 or $F^{9'}$) ppm. **^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 25 ºC)** δ 167.28, 164.23, 163.65, 162.87, 162.11, 161.69, 161.11, 159.53, 159.40, 159.23, 158.48, 155.46, 155.39, 153.53, 151.86, 151.80, 151.54, 149.76, 146.48, 140.19, 139.96, 138.27, 136.78, 129.18, 128.26, 126.08, 125.68, 124.37, 123.26, 123.09, 116.25, 113.83, 112.96, 112.77, 99.07, 48.17 ppm. **FT-IR (KBr, cm^{-1}) selected bands:** 3065 (w, $\nu_{Car\text{-}H}$), 1601-1575 (m, $\nu_{C=C\,+\,C\text{-}N}$), 1429 (w, $\nu_{C=N}$), 1163 (m, $\nu_{C\text{-}C}$), 1069 (m, $\delta_{C\text{-}Hip}$), 745 (vs, $\delta_{C\text{-}Hoop}$). **HR ESI+ MS (DCM/DMSO, 4:1):** m/z_{exp} = 825.1575 (m/z_{calcd} $[M^+]$ = m/z_{calcd} $[C_{36}H_{24}F_4IrN_6O]^+$ = 825.1577); 573.0556 (m/z_{calcd} $[M^+\text{-}L2]$ = m/z_{calcd} $[C_{22}H_{12}F_4IrN_2]^+$ = 573.0566). **Solubility:** soluble in dimethyl sulfoxide, dichloromethane, methanol, acetonitrile, acetone, dimethylformamide, tetrahydrofuran.

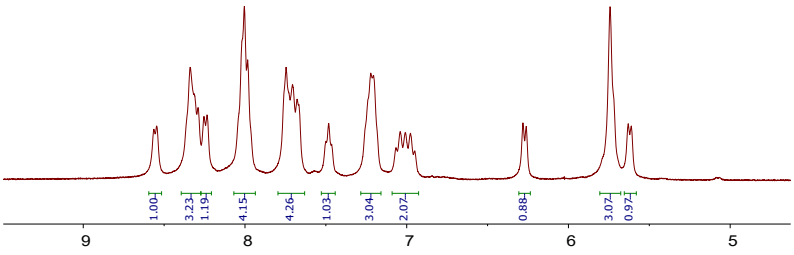


Figure SI22. ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[2b]Cl**.

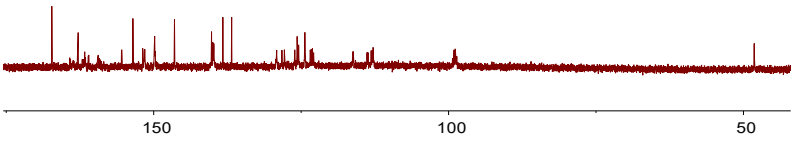


Figure SI23. $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 25 °C) spectrum of **[2b]Cl**.

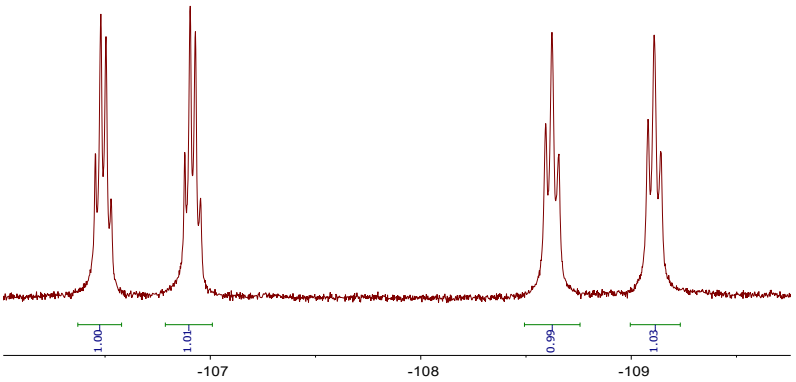


Figure SI24. ^{19}F NMR (376 MHz, DMSO-d_6, 25 °C) spectrum of **[2b]Cl**.

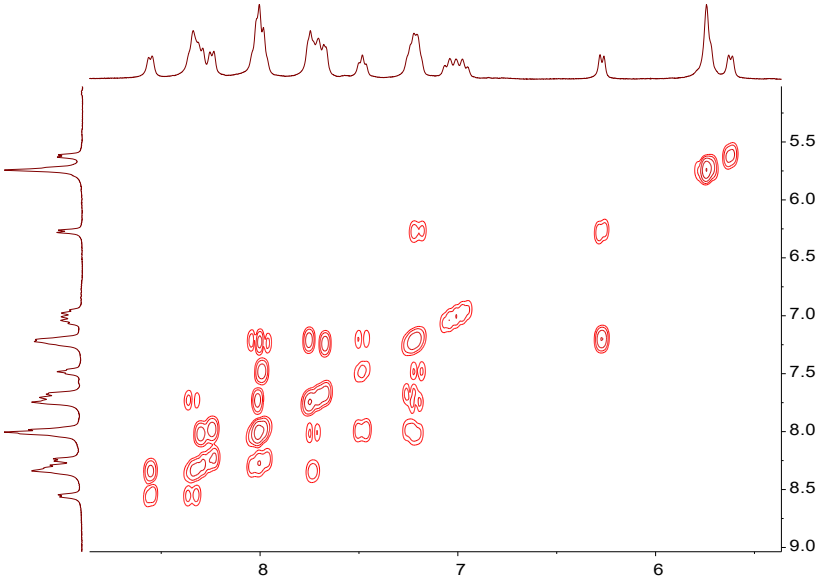


Figure SI25. $^{1}H,^{1}H$-COSY NMR (400 MHz, DMSO-d_6, 25 °C) spectrum of **[2b]Cl**.

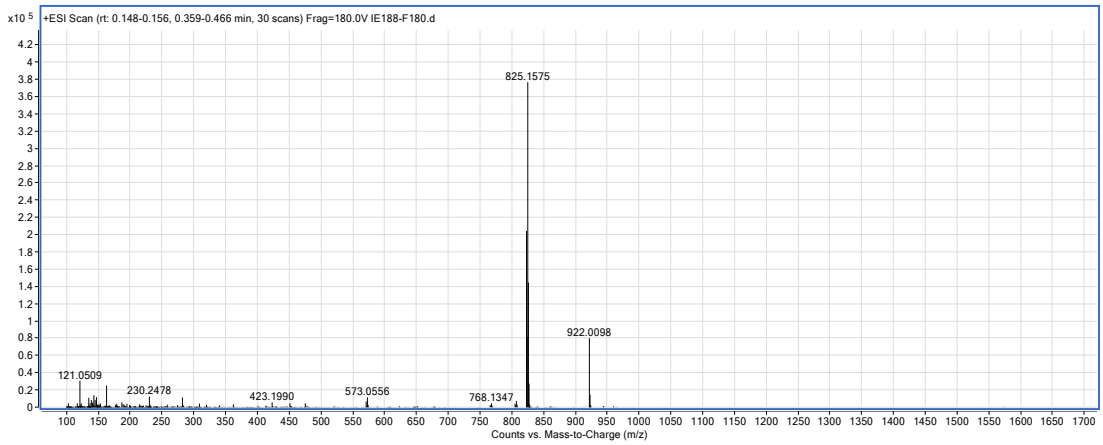


Figure SI26. HR ESI+ MS (DCM/DMSO, 4:1) spectrum of **[2b]Cl**.

3.- X-Ray diffraction. Crystallographic parameters

Table SI1. Bond Lengths (Å) and Angles (º) for **[1a]PF_6** and **[2a]PF_6.**

[1a]PF_6			
Bond Lengths		**Angles (º)**	
Ir1- N3	2.148(9)	N1- Ir1- N2	175.0(3)
Ir1- N5	2.163(8)	C22- Ir1- N5	172.9(4)
Ir1- N1	2.053(5)	C11- Ir1- N3	172.7(3)
Ir1- C22	2.001(11)	C31- S1- C32	90.0(6)
Ir1- N2	2.052(9)	O1- C34- C33	122.7(13)
Ir1- C11	2.002(6)	O1- C34- N6	121.6(13)
S1- C32	1.700(12)	N6- C34- C33	115.6(13)
S1- C31	1.668(13)	C11-Ir1-N1	80.4(3)
O1- C34	1.207(17)	C22-Ir1-N2	80.3(4)
N4- C33	1.445(13)	N3-Ir1-N5	75.7(3)
N6- C34	1.333(17)		
[2a]PF_6			
Ir1- N3	2.121(13)	N2- Ir1- N1	174.4(4)
Ir1- N1	2.032(6)	C11- I r1- N3	173.2(5)
Ir1- N5	2.186(14)	C22- Ir1- N5	173.7(5)
Ir1- N2	2.031(8)	O1- C35- N6	125.1(16)
Ir1- C11	2.035(8)	O1- C35- C34	120.5(16)
Ir1- C22	2.021(8)	N6- C35- C34	114.4(14)
O1- C35	1.22(2)	C11-Ir1-N1	80.0(4)
N4- C34	1.46(2)	C22-Ir1-N2	80.3(4)
N6- C35	1.31(2)	N3-Ir1-N5	75.3(5)

Table SI2. Crystal data and structure refinement for [1a]PF_6 and [2a]PF_6.

Identification code	**[2a]PF_6 x 0.25H_2O**	**[2a]PF_6x0.5CH_3OHx0.25H_2O**
Empirical formula	$C_{34}H_{26.5}F_6IrN_6O_{1.25}PS$	$C_{36.5}H_{30.5}F_6IrN_6O_{1.75}P$
Formula weight	908.34	918.34
Temperature/K	216(2)	180(2)
Wavelength/Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	C 2/c	P 2_1/c
a/Å	20.828(10)	8.7979(12)
b/Å	13.963(7)	38.644(6)
c/Å	24.739(13)	10.9895(16)
α/°	90	90
β/°	105.879(19)	102.083(4)
γ/°	90	90
Volume/Å^3	6920(6)	3653.5(9)
Z	8	4
ρ_{calc}g/cm^3	1.744	1.670
μ/mm^{-1}	4.037	3.770
F(000)	3556	1806
Crystal size/mm^3	0.15 x 0.10 x 0.08	0.08 x 0.06 x 0.01
Index ranges	-24≤ h≤ 24 -16≤ k≤ 16 -29≤ l≤ 29	-10 ≤ h ≤ 10 -45 ≤ k ≤ 45 -12 ≤ l ≤ 12
Reflections collected	46642	64453
Independent reflections	5822 [R(int) = 0.1084]	6235 [R(int) = 0.1160]
Data/restraints/parameters	5822 / 0 / 429	6235 / 1 / 400
Goodness-of-fit on F^2	1.071	1.238
Final R indexes [I>2σ (I)]	R1 = 0.0634 wR2 = 0.1469	R1 = 0.0943 wR2 = 0.2082
Largest diff. peak/hole / e Å^{-3}	1.686 / -2.323	3.581 / -4.797

4.-Photostability of the Iridium complexes

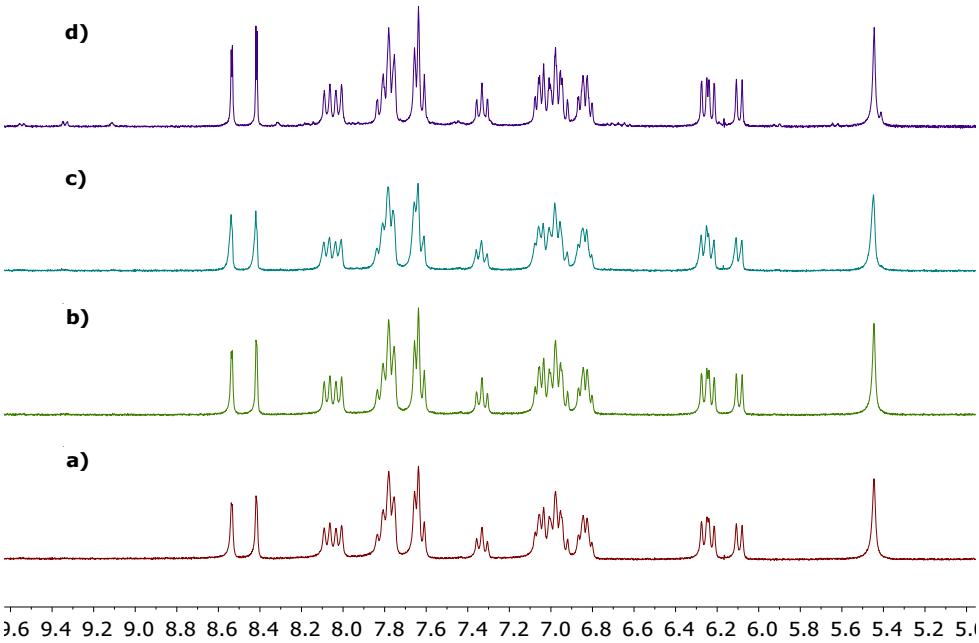


Figure SI27. Aromatic Area of ^{1}H NMR (400 MHz) spectra of **[1a]Cl** in DMSO:Water (3:2) ($1.4 \cdot 10^{-2}$ M) at 25 °C after irradiation with Blue LED light (λ=460 nm): a) t= 0, b) t= 1 h, c) t= 4 h and d) t= 24 h.

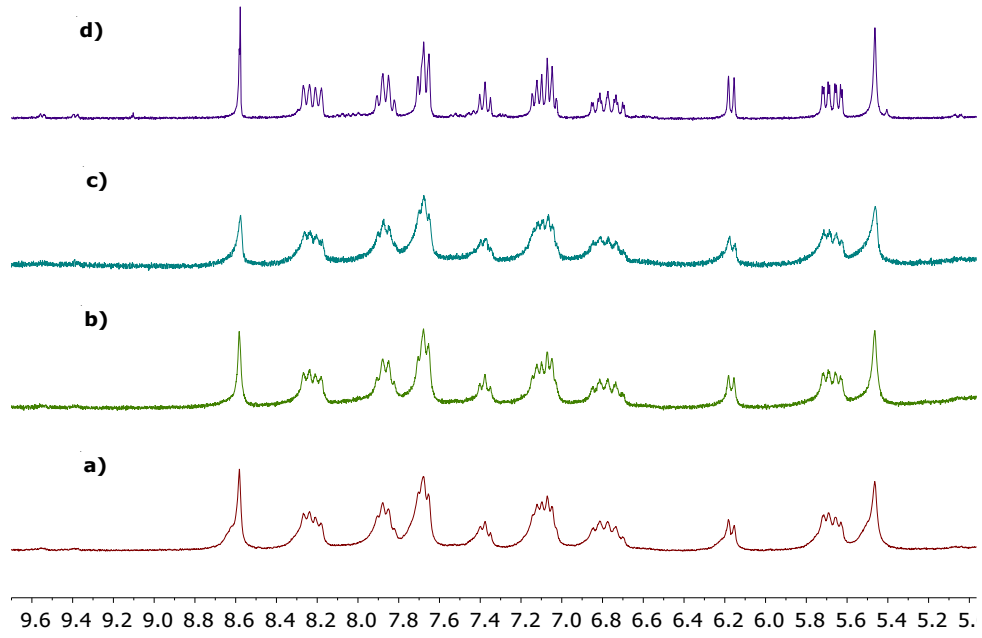


Figure SI28. Aromatic Area of ^{1}H NMR (400 MHz) spectra of **[1b]Cl** in DMSO:Water (3:2) ($1.4 \cdot 10^{-2}$ M) at 25 °C after irradiation with Blue LED light (λ=460 nm): a) t= 0, b) t= 1 h, c) t= 4 h and d) t= 24 h.

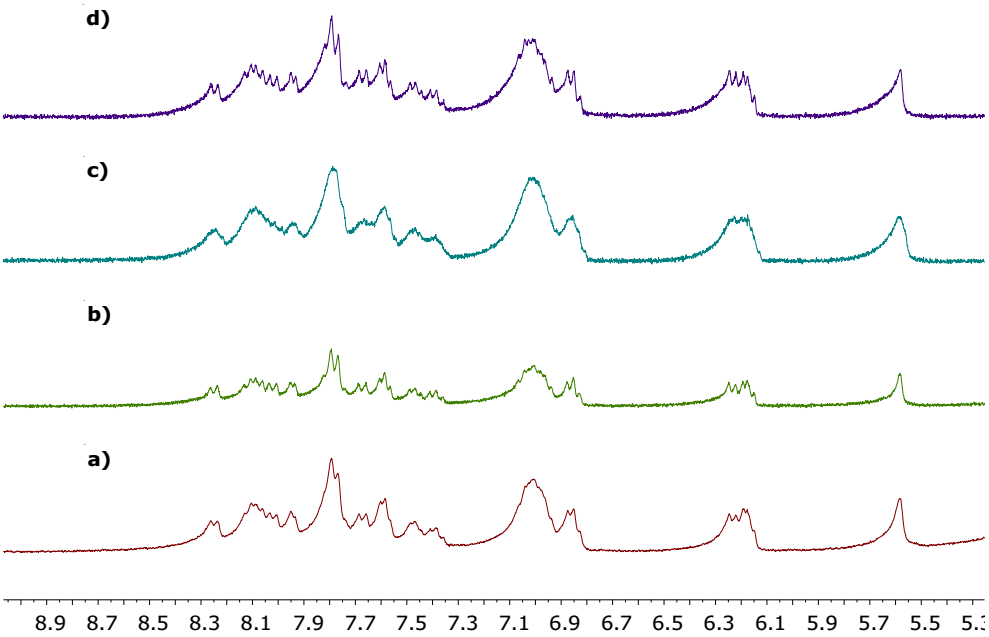


Figure SI29. Aromatic Area of ^{1}H NMR (400 MHz) spectra of **[2a]Cl** in DMSO:Water (3:2) ($1.4 \cdot 10^{-2}$ M) at 25 °C after irradiation with Blue LED light (λ=460 nm): a) t= 0, b) t= 1 h, c) t= 4 h and d) t= 24 h.

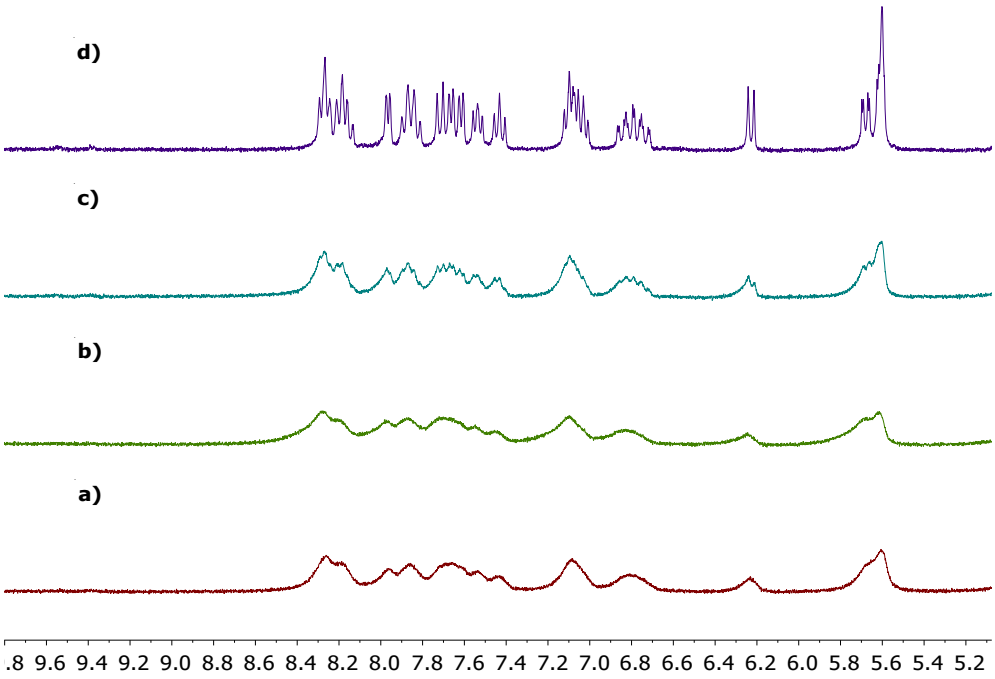


Figure SI30. Aromatic Area of ^{1}H NMR (400 MHz) spectra of **[2b]Cl** in DMSO:Water (3:2) ($1.4 \cdot 10^{-2}$ M) at 25 °C after irradiation with Blue LED light (λ=460 nm): a) t= 0, b) t= 1 h, c) t= 4 h and d) t= 24 h.

5. CV of the Ir(III) complexes.

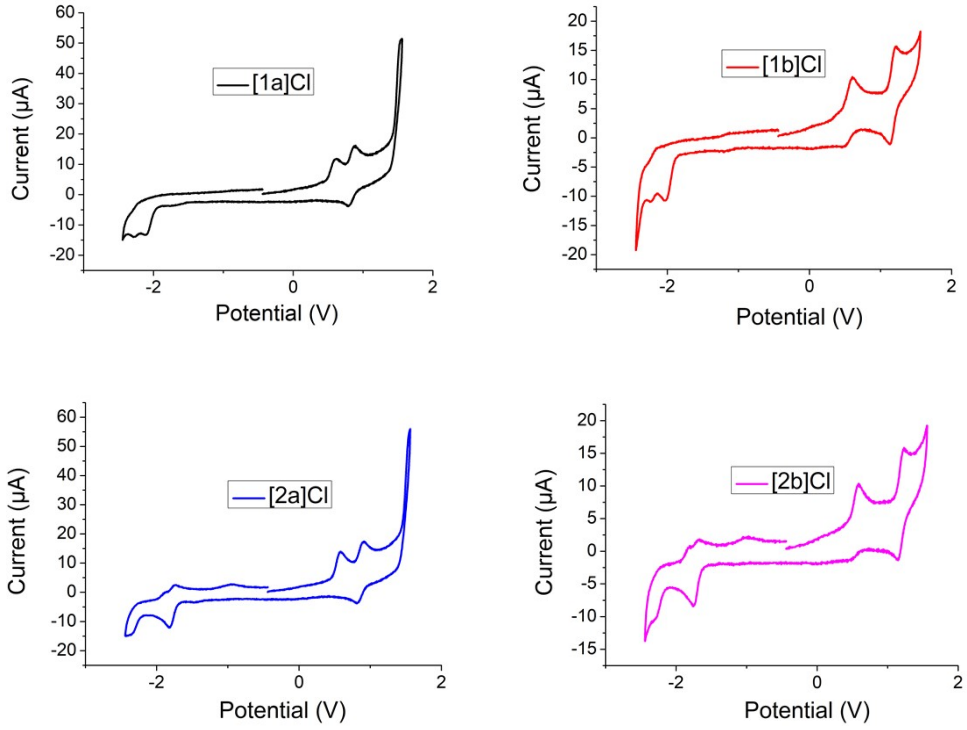


Figure SI31. Cyclic voltammograms of the iridium complexes.

6. UV-Vis spectra

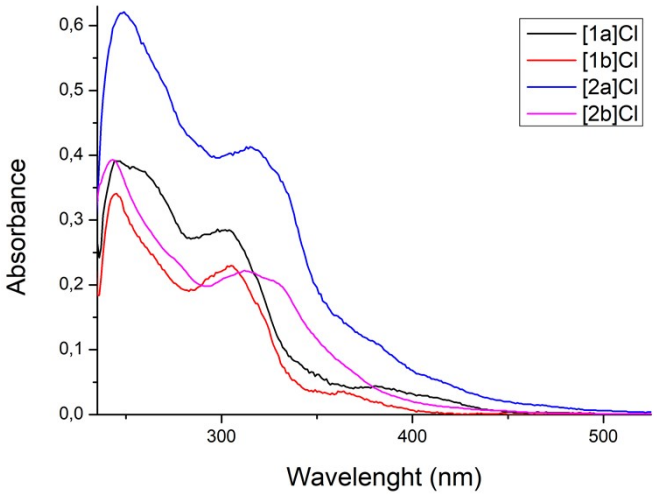


Figure SI32. Overlaid UV-Vis spectra of complexes **[1a]Cl**, **[1b]Cl**, **[2a]Cl** and **[2b]Cl** (10^{-5} M) in DMSO/Water (6:94) at 25 °C.

7. **Determination of the ability for the generation of $^1O_2$**

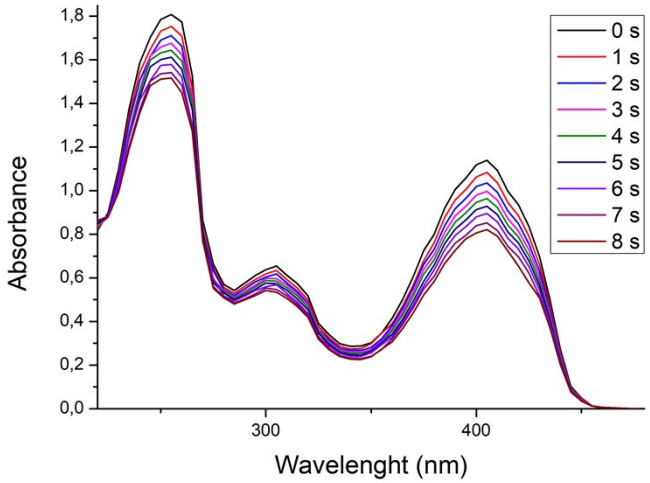


Figure SI33. Photocatalytic oxidation of DPBF in the presence of **[1a]Cl** in acetonitrile.

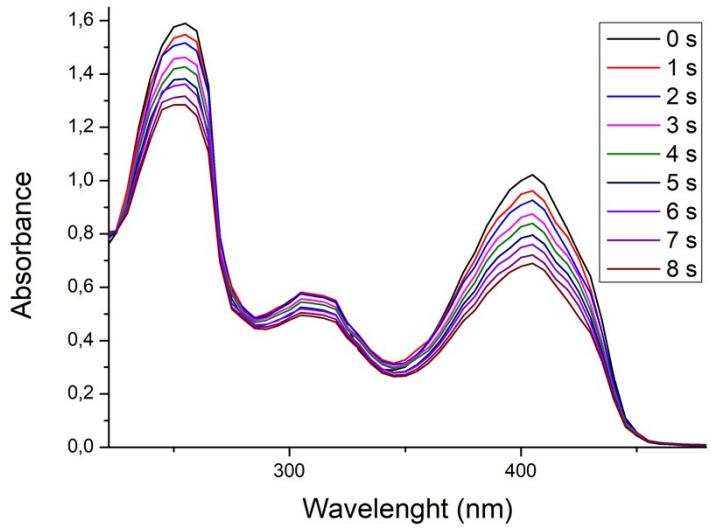


Figure SI34. Photocatalytic oxidation of DPBF in the presence of **[2a]Cl** in acetonitrile.

8. Photo-oxidation of NADH

Control experiments:

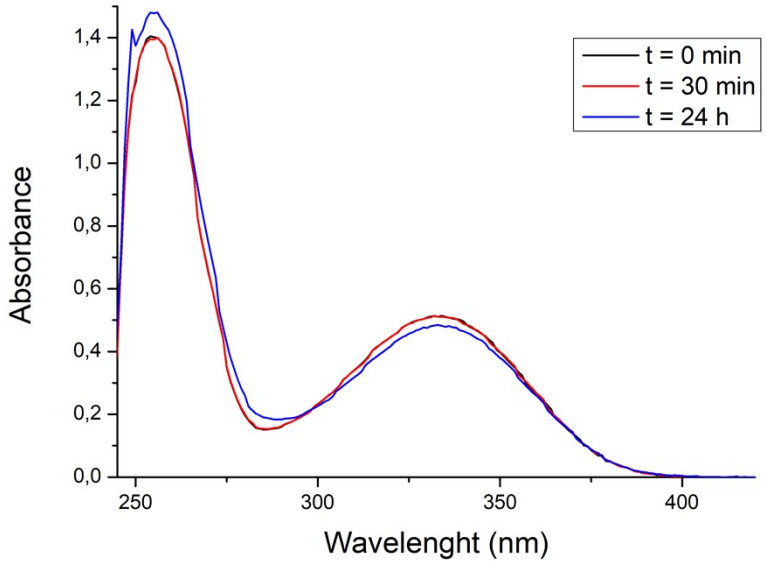


Figure SI35. UV-vis spectra for the photocatalytic oxidation of NADH (100 µM) without catalyst in a mixture of H_2O/MeOH 50/50 (v/v) under blue light irradiation (460 nm).

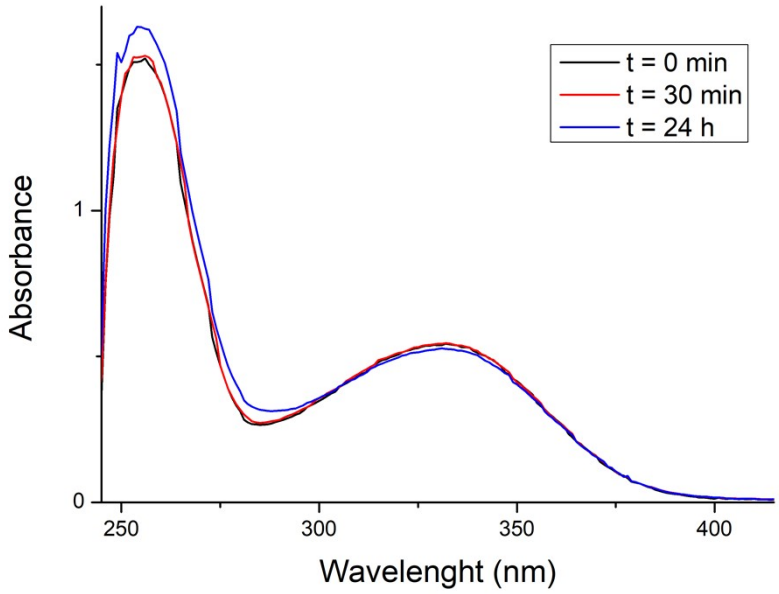


Figure SI36. UV-vis spectra for the photocatalytic oxidation of NADH (100 µM) by complex **[1a]Cl** (5 µM) in a mixture of H_2O/MeOH 50/50 (v/v) in the dark.