Electronic Supplementary Material (ESI) for Chemical Communications.

Supplementary Information for

Organoiridium-Quinone Conjugates for Facile Hydrogen Peroxide Generation

Huong T. H. Nguyen, Loi H. Do*

Department of Chemistry, University of Houston, Houston, Texas, 77204

TABLE OF CONTENTS **Page(s)**

General Procedures

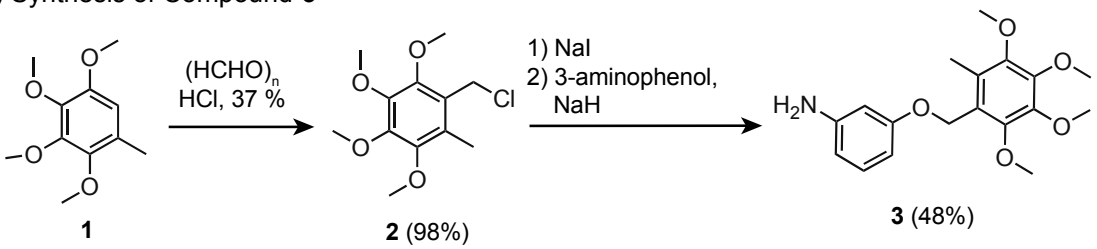
Commercial reagents were used as received without further purification. All air- and water-sensitive manipulations were performed using standard Schlenk techniques or under a nitrogen atmosphere inside a glovebox. NMR samples of iridium-hydride complexes were prepared inside the glovebox and then transferred to J-Young tubes before taken outside. Anhydrous solvents were obtained from an Innovative Technology solvent drying system saturated with Argon. Complex **Ir1, Q1** and **Q2** were prepared as described previously [1,2].

Physical Methods

NMR spectra were acquired using JEOL spectrometers (ECA-400, 500, and 600) at room temperature and referenced using residual solvent peaks. All ^{13}C NMR spectra were proton-decoupled. Gas chromatography-mass spectrometry (GC/GC-MS) was performed using an Agilent 7890 GC/5977A MSD instrument equipped with an HP-5MS capillary column. Cyclic voltammetry (CV) experiments were performed using a BAS Epsilon electroanalytical system. Ultraviolet-visible (UV) absorption spectroscopic studies were performed using an Agilent Cary 60 spectrophotometer. Cyclic voltammograms of the iridium complexes and quinone were recorded at 0.1 V/s in phosphate buffer saline (0.1M, PBS) using a glassy carbon working electrode, a Ag/AgCl reference electrode, and a Pt wire as the auxiliary electrode. All potentials were referenced to NHE.

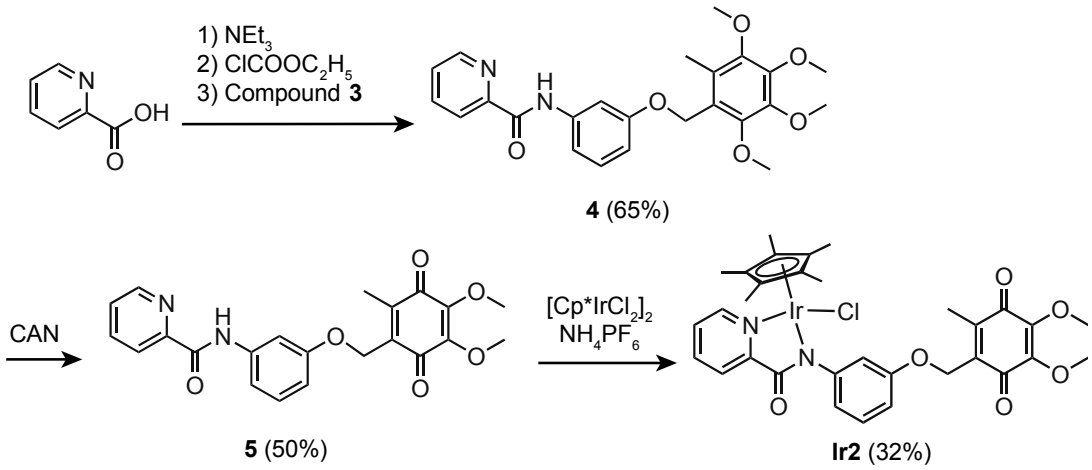
Synthesis and Characterization

A) Synthesis of Compound **3**



1 **2** (98%) **3** (48%)

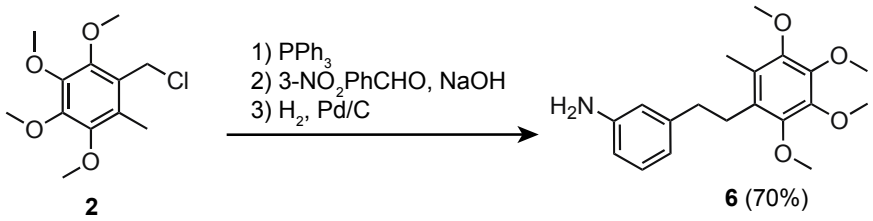
B) Synthesis of Complex **Ir2**



4 (65%) **5** (50%) **Ir2** (32%)

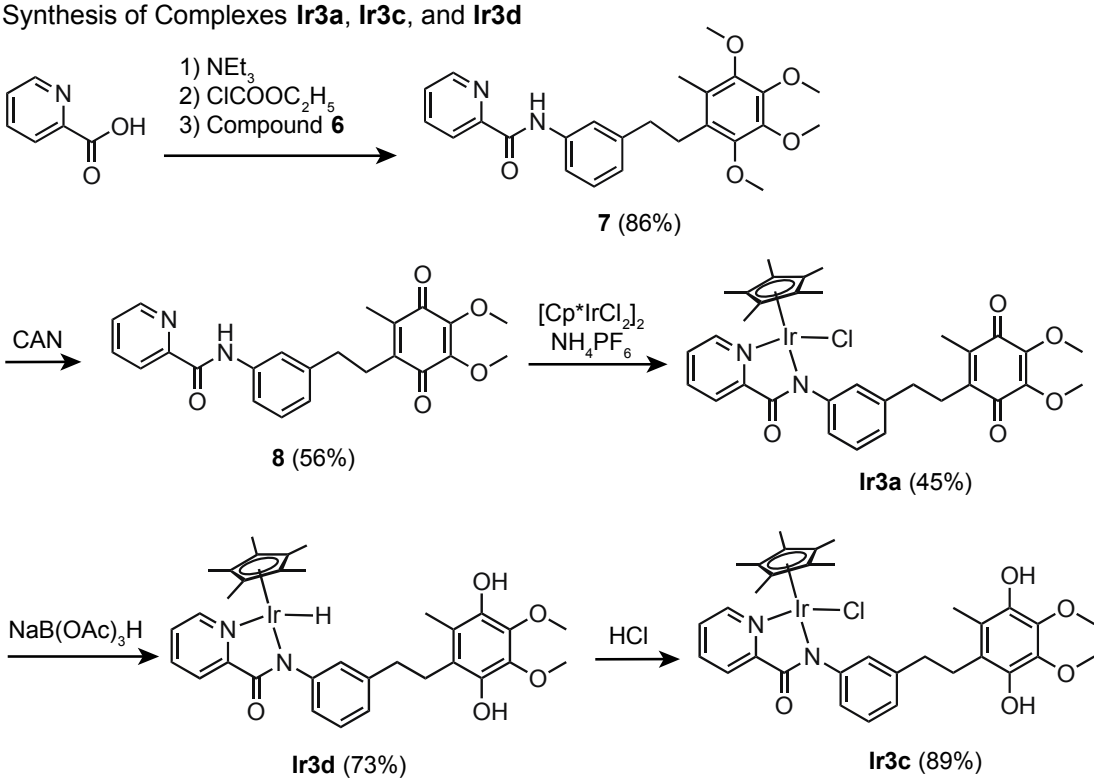
Scheme S1. Synthesis of complex **Ir2**.

A) Synthesis of Compound **6**



2 **6** (70%)

B) Synthesis of Complexes **Ir3a**, **Ir3c**, and **Ir3d**



7 (86%)

8 (56%)

Ir3a (45%)

Ir3d (73%)

Ir3c (89%)

Scheme S2. Synthesis of complexes **Ir3a**, **Ir3c**, and **Ir3d**.

Preparation of Compound 2. To a stirred mixture of 1,2,3,4-tetramethoxytoluene (3.0 g, 14.1 mmol, 1.0 equiv.) and paraformaldehyde (633 mg, 21.1 mmol, 1.5 equiv.) at room temperature, 3 mL of concentrated HCl was added. The mixture was then stirred at 40 °C for 2 h. Water (10 mL) was added and the organic layer was extracted into ethyl acetate (4 x 5 mL). The combined mixture was washed with brine (4 x 5 mL), dried over Na_2SO_4, filtered to removing the drying agent, and then evaporated to obtain a yellow oil **2** (3.6 g, 98%). ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 4.58 (s, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.769 (s, 3H), 2.19 (s, 3H). ^{13}C NMR ($CDCl_3$, 150.91 MHz): δ (ppm) = 148.49, 148.06, 147.72, 144.77, 126.60, 124.85, 61.59, 60.92, 60.57, 60.56, 38.48, 10.98. IR: ν = 1037, 1071, 1195, 1279, 1352, 1406, 1466, 2830 and 2936 cm^{-1}. GC-MS: calc. for $C_{12}H_{17}ClO_4$ $[M]^+$ = 260.0, found 260.1

Preparation of Compound 3. Compound **2** (1.2 g, 4.0 mmol) and NaI (1.2 g, 8.0 mmol) were combined in 25 mL of acetone. In a separate flask, 3-aminophenol (480 mg, 4.4 mmol) and NaH (60% in mineral oil; 240 mg, 6.0 mmol) were stirred in 25 mL of dry THF. These two solutions were stirred separately at room temperature for 2 h before the former was transferred into the latter via syringe. This mixture was stirred at room temperature for ~14 h and was monitored by thin layer chromatography. After the reaction was complete, the solvent was removed, and the organic products were dissolved into DCM and washed with water. The organic layer was separated, evaporated to dryness, and purified by silica gel column chromatography using ethyl acetate:hexane (1:2) to obtain the final product as a colorless oil (640 mg, 48%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.25 (s, 1H), 7.09 (t, J_{HH} = 8.0 Hz, 1H), 6.46 (dd, J_{HH} = 8.0, 2.4 Hz, 1H), 6.36 (t, J_{HH} = 2.0 Hz, 1H), 6.33 (dd, J_{HH} = 8.0, 2.0 Hz, 1H), 4.98 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 150.91 MHz): δ (ppm) = 160.31, 149.15, 148.26, 148.09, 147.60, 144.84, 130.20, 127.76, 123.89, 108.12, 104.74, 101.78, 62.29, 61.99, 61.29, 61.18, 60.79, 11.66 IR: ν = 730, 1010, 1046, 1105, 1158, 1185, 1267, 1353, 1408, 1464, 1495, 1599, 2381, 2936, and 3373 cm^{-1}. GC-MS calc. for $C_{18}H_{23}NO_3$ $[M]^+$ = 333.4, found 333.1.

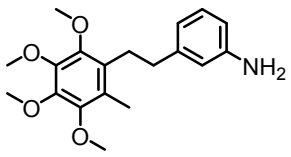
Preparation of Compound 4. In a 100 mL round bottom flask, picolinic acid (431 mg, 3.5 mmol, 1.75 equiv.) was stirred in 20 mL of anhydrous dichloromethane. Trimethylamine (980 μL, 7 mmol, 3.5 equiv.) was added and the reaction mixture was cooled in an ice bath for 10 min. Next, ethyl chloroformate (335 μL, 3.5 mmol, 1.75 equiv.) was added dropwise and the reaction was stirred at 0 °C for another 20 min before warming to RT. After compound **3** (666 mg, 2 mmol, 1.0 equiv.) was added, the reaction was refluxed for 5 h. Finally, the reaction mixture was quenched by the addition of 30 mL of water, extracted into dichloromethane (3×20 mL), dried over sodium sulfate, filtered to remove the salt, and concentrated. The final product was purified by column chromatography (ethyl acetate:hexane 1:1) as a yellow oil (564 mg, 65%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) = 10.05 (s, 1H), 8.63 (d, J_{HH} = 4.0 Hz ,1H), 8.30 (d, J_{HH} = 8.0 Hz, 1H), 7.91 (td, J_{HH} = 6.4, 1.6 Hz, 1H), 7.68 (s, 1H), 7.50-7.48 (m, 1H), 7.30 (d, J_{HH} = 4.4 Hz, 2H), 6.83-6.81 (m, 1H), 5.08 (s, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.84 (s, 3H), 3.81 (s, 3H), 2.26 (s, 2H). ^{13}C NMR ($CDCl_3$, 125.73 MHz): δ (ppm) = 162.10, 159.81, 149.82, 149.21, 148.22, 148.08, 147.67, 144.82, 139.04,

137.82, 129.89, 127.76, 126.61, 123.61, 122.46, 112.24, 111.33, 106.01, 62.37, 62.27, 61.30, 61.20, 60.83, 11.70. IR: ν = 687, 1010, 1046, 1106, 1160, 1185, 1280, 1353, 1408, 1464, 1528, 1597, 1686, 2934, and 3337 cm^{-1}. ESI–MS(+) calc. for $C_{24}H_{26}N_2O_6$ [M+Na]$^+$ = 461.1688, found 461.1690.

Preparation of Compound 5. A solution of compound **4** (1.0 g, 2.3 mmol, 1.0 equiv.) in THF (20 mL) was stirred in an ice bath for 5 min. Ceric ammonium nitrate (3.2 g, 5.75 mmol, 2.5 equiv.) in water (20 mL) was added dropwise into the reaction flask over a 10 min period. After the addition was complete, the mixture turned from colorless to orange. The reaction was allowed to warm up to RT and stirred for an additional 1 h while monitoring by TLC. To workup the reaction, THF was gently removed under vacuum and the crude product was extracted into ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, filtered to remove the salt, and then concentrated. The final product was obtained after purification by silica gel column chromatography (ethyl acetate:hexane, 2:1) as a sticky orange oil (466 mg, 50%).^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) = 10.02 (s, 1H), 8.58 (d, J_{HH} = 5.0 Hz , 1H), 8.26 (d, J_{HH} = 10.0 Hz, 1H), 7.88 (t, J_{HH} = 5.0 Hz, 1H), 7.62 (s, 1H), 7.50-7.47 (m, 1H), 7.25 (s, 2H), 6.71 (d, J_{HH} = 10.0 Hz, 1H), 4.95 (s, 2H), 4.01 (s, 3H), 3.98 (s, 3H), 2.14 (s, 2H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ (ppm) = 184.39, 183.01, 162.13, 159.02, 149.67, 148.08, 144.84, 144.56, 144.24, 139.07, 137.85, 135.79, 129.98, 126.67, 122.48, 112.75, 110.98, 106.21, 61.40, 61.33, 60.41, 12.52. IR: ν = 687, 729, 1041, 1158, 1186, 1268, 1445, 1528, 1607, 1651, 1683, 2948, and 3329 cm^{-1}. ESI–MS(+) calc. for $C_{22}H_{20}N_2O_6$ [M+Na]$^+$ = 431.1219, found 431.1213.

Preparation of Complex Ir2. In a round bottom flask $[Cp^*IrCl_2]_2$ and (40 mg, 0.05 mmol, 1.0 equiv.) and ligand **5** (42.4 mg, 0.105 mmol, 2.1 equiv.) were added into 8 mL of degassed ethanol and stirred for 15 min at 80 °C. The reaction mixture was treated with ammonium hexafluorophosphate (33 mg, 0.225 mmol, 4.5 equiv.) and stirred overnight at 80 °C. The ethanol solvent was removed by rotary evaporation to obtain a dark yellow solid. This crude material was dissolved in a minimal amount of DCM and then mixed with hexanes until a solid precipitate formed, which was isolated by filtration (25 mg, 32%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) = 8.56 (d, J_{HH} = 5.0 Hz, 1H), 8.15 (d, J_{HH} = 5.0 Hz, 1H), 7.92 (t, J_{HH} = 10.0 Hz, 1H), 7.49 (t, J_{HH} = 8.0 Hz, 1H), 7.40 (s, 1H), 7.28-7.22 (m, 1H), 7.21 (t, J_{HH} = 8.0 Hz, 1H), 6.67 (d, J_{HH} = 10.0 Hz, 1H), 4.95-4.84 (m, 2H), 4.02 (s, 3H), 3.99 (s, 3H), 2.12 (s, 3H), 1.42 (s, 15H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ (ppm) = 184.54, 183.10, 168.45, 158.63, 155.80, 149.73, 149.48, 144.75, 144.71, 144.22, 138.67, 136.06, 128.72, 127.46, 126.57, 120.47, 112.70, 111.50, 86.76, 61.36, 60.30, 12.49, 8.56. IR: ν = 686, 726,763, 914, 1030, 1195, 1268, 1376, 1467, 1589, 1632, 1651, 2850, and 2920 cm^{-1}. UV-Vis: λ_{max} = 270 (ε = 25.28×10^3 M^{-1}cm^{-1}), ESI–MS(+) calc. for $C_{32}H_{34}ClIrN_2O_6$ [M+Na]$^+$ = 793.1632, found 793.1664. MP: 83 °C (decompose).

Preparation of Compound 6. A mixture of compound **2** (2.0 g, 7.6 mmol, 1.0 equiv.) and triphenylphosphine (3.0 g, 11.5 mmol, 1.5 equiv.) was refluxed in 65 mL of toluene overnight. The white solid formed was collected by filtration and then dried under vacuum overnight. The phosphonium salt and 3-nitrobenzaldehyde (1.27 g, 8.4 mmol, 1.1 equiv.) were combined in 70



mL of DCM and then treated with a 15 mL a solution of 50 % NaOH in H_2O through dropwise addition (1 drop/sec). The reaction was stirred at room temperature for ~14 h. The organic layer was separated, washed with water (2 x 35 mL), dried over Na_2SO_4, filtered to remove the salt, and concentrated under vacumn. The crude material was purified by silica gel column chromatography (ethyl acetate:hexane, 1:1.5) to afford the desired Wittig product as a colorless oil. This compound was combined with 10% Pd/C (615 mg, 8.6 mmol, 0.1 equiv.) in 150 mL of methanol and stirred for ~14 h under an atmosphere of hydrogen gas at RT. The reaction mixture was then filtered through a pad of celite and the solvent was removed to obtain compound **7** as clear oil (1.7 g, 70%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) = 7.13 (t, J_{HH} = 10 Hz, 1H), 6.79-6.78 (m, 2H), 6.74 (d, J_{HH} = 10 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.85 (s, 3H), 3.79 (s, 3H), 2.86-2.83 (m, 2H), 2.69-2.65 (m, 2H), 2.18 (s, 3H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ (ppm) = 147.88, 145.19, 144.75, 143.89, 143.01, 129.59, 129.51, 129.21, 125.19, 121.04, 117.10, 114.81, 61.24, 61.20, 61.13, 60.79, 36.51, 29.34, 11.73. IR: ν = 693, 877, 1012, 1040, 1069, 1102, 1350, 1405, 1463, 1534, 1685, 2827, 2934, and 3344 cm^{-1}. GC-MS calc. for $C_{19}H_{25}NO_4$ $[M]^+$ = 331.2, found 331.2.

Preparation of Compound 7. The same procedure as that described for the synthesis of compound **4** was followed, except that picolinic acid (431 mg, 3.5 mmol, 1.75 equiv.) and compound **6** (870 mg, 2 mmol, 1 equiv.) were used instead. The product was obtained as a yellow oil (750 mg, 86%). ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) = 10.01 (s, 1H), 8.63-8.61 (m, 1H), 8.30 (dt, J_{HH} = 7.6, 1.5 Hz, 1H), 7.91 (td, J_{HH} = 7.5, 1.5 Hz, 1H), 7.69-7.67 (m, 1H), 7.64 (s, 1H), 7.47 (ddd, J_{HH} = 7.5, 5.0, 1.0 Hz, 1H), 7.31 (t, J_{HH} = 8.0 Hz, 1H), 7.02 (d, J_{HH} = 7.5 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.84 (s, 3H), 3.77 (s, 3H), 2.91-2.88 (m, 2H), 2.79-2.75 (m, 2H), 2.17 (s, 3H). ^{13}C NMR ($CDCl_3$, 150.9 MHz): δ (ppm) = 162.04, 149.92, 148.05, 147.92, 147.85, 145.23, 144.75, 143.51,, 137.81, 129.17, 129.08, 126.55, 125.22, 124.56, 122.46, 119.68, 117.42, 61.24, 61.23, 61.13, 60.79, 36.57, 29.38, 11.76. IR: ν = 692, 882, 1013, 1042, 1070, 1103, 1350, 1406, 1464, 1534, 1686, 1741, 2857, 2930, and 3342 cm^{-1}. ESI–MS(+) calc. for $C_{25}H_{28}N_2O_5$ $[M+Na]^+$ = 459.1896, found 459.1888.

Preparation of Compound 8. The same procedure as that described for the synthesis of **5** was followed, except that compound **7** (750 mg, 1.72 mmol, 1 equiv.) in 20 mL of THF and CAN (2.1 g, 3.4 mmol, 2.0 equiv.) in 10 mL of water were used. The pure product was obtained by silica gel column chromatography (ethyl acetate:hexane, 1:1) as an orange solid (390 mg, 56%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) = 10.01 (s, 1H), 8.62-8.60 (m, 1H), 8.27 (dt, J_{HH} = 7.5, 1.0 Hz, 1H), 7.90 (td, J_{HH} = 7.5, 1.5 Hz, 1H), 7.68 (s, 1H), 7.61-7.58 (m, 1H), 7.48 (ddd, J_{HH} = 7.5, 5.0, 1.0 Hz, 1H), 7.29 (t, J_{HH} = 7.5 Hz, 1H), 6.97 (d, J_{HH} = 7.5 Hz, 1H), 3.98 (s, 3H), 3.98 (s, 3H), 2.81-2.77 (m, 2H), 2.74-2.71 (m, 2H), 1.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 50.91 MHz): δ (ppm) = 184.58, 184.07, 162.01, 149.76, 148.04, 144.51, 144.33, 142.05, 141.55, 139.64, 137.94, 137.94, 137.83, 129.26, 126.60, 124.57, 122.42, 119.77, 117.67, 61.27, 61.24, 34.81, 28.73, 11.98. IR: ν = 692, 739, 844, 1037, 1152, 1205, 1257, 1442, 1526, 1592, 1592, 1609, 1643, 1676, 2948, and 3315 cm^{-1}. ESI–MS(+) calc. for $C_{23}H_{22}N_2O_5$ $[M+Na]^+$ = 429.1426, found 429.1428. MP: 80–82 °C.

Preparation of Complex Ir3a. In a round bottom flask $[Cp^*IrCl_2]_2$ and (160 mg, 0.2 mmol, 1.0 equiv.) and the ligand **8** (170.5 mg, 0.42 mmol, 2.1 equiv.) were added into 20 mL of degassed ethanol and stirred for 15 min at 80 °C. The reaction mixture was treated with ammonium hexafluorophosphate (147 mg, 0.9 mmol, 4.5 equiv.) and stirred overnight at 80 °C. The ethanol solvent was removed by rotary evaporation to obtain a dark yellow solid. The final product was obtained by precipitating the Ir complex out of DCM using hexane (140 mg, 45%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ (ppm) = 8.56 (d, J_{HH} = 5.2 Hz, 1H), 8.13 (d, J_{HH} = 7.6 Hz, 1H), 7.92 (t, J_{HH} = 7.6 Hz, 1H), 7.53-7.46 (m, 3H), 7.25-7.21 (m, 1H), 6.94 (d, J_{HH} = 7.6 Hz, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 2.79-2.77 (m, 2H), 2.71-2.69 (m, 2H), 1.95 (s, 3H), 1.40 (s, 15H). ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ (ppm) = 184.69, 184.14, 168.58, 155.66, 149.79, 148.38, 144.47, 144.40, 141.90, 140.63, 139.63, 138.70, 128.29, 127.57, 126.97, 126.37, 124.94, 86.66, 61.28, 61.26, 34.71, 28.64, 12.08, 8.52. IR: ν = 686, 763, 1030, 1076, 1151, 1204, 1263, 1377, 1447, 1594, 1644, and 2921 cm^{-1}. UV-Vis: λ_{max} = 272 (ε = 20.0×10^3 M^{-1} cm^{-1}), ESI–MS(+) calc. for $C_{33}H_{36}ClIrN_2O_5$ $[M+Na]^+$ = 791.1840, found 791.1850. Anal. Calc for $C_{33}H_{36}ClIrN_2O_5$: MP: 125–126 °C.

Preparation of Complex Ir3d. Inside the glovebox, excess $NaB(OAc)_3H$ (138 mg, 0.66 mmol, 3.0 equiv.) was added to a solution of **Ir3a** (167 mg, 0.22 mmol, 1.0 equiv.) in DCM. The reaction mixture was stirred for 2 h at room temperature. The organic mixture was washed with water three times and then dried under vacuum for 2 h. The final product was obtained as a pale orange solid (118 mg, 73%). ^{1}H NMR (MeOD, 600 MHz): δ (ppm) = 8.77 (d, J_{HH} = 0.6 Hz, 1H), 7.92-7.88 (m, 2H), 7.45-7.43 (m, 1H), 7.28 (t, J_{HH} = 0.9 Hz, 2H), 7.14 (s, 3.79 (s, 6H), 2.90-2.87 (m, 2H), 2.72 (t, J_{HH} = 1.2 Hz, 2H), 2.14 (s, 3H), 1.53 (s, 15H), -11.30 (s, 1H). ^{13}C NMR (MeOD, 150.9 MHz): δ (ppm) = 168.42, 154.96, 151.96, 148.54, 142.98, 140.55, 140.48, 138.70, 136.36, 127.95, 126.63, 126.55, 125.42, 124.24, 123.83, 122.81, 118.10, 88.18, 59.84, 59.76, 35.52, 28.81, 10.42. IR: ν = 684, 823, 956, 1032, 1102, 1380, 1574, 1618, 2034, and 2916 cm^{-1}. UV-Vis: λ_{max} = 269 (ε = 8.5×10^3 M^{-1}cm^{-1}), ESI–MS(+) calc. for $C_{33}H_{39}IrN_2O_5$ $[M+Na]^+$ = 759.2386, found 759.2404. MP: 130 °C (decompose).

Preparation of Complex Ir3c. Inside the glovebox, **Ir3d** (118 mg, 0.18 mmol) was treated with one drop of HCl in Et_2O and stirred in 2 mL of $CDCl_3$ for 2 h. The organic mixture was washed with water 3 times and then dried under vacuum for 2 h. The final product was obtained as a pale orange solid (125 mg, 89%). ^{1}H NMR (MeOD, 600 MHz): δ (ppm) = 8.77 (s, 1H), 8.08-8.05 (m, 1H), 7.99 (d, J_{HH} = 0.6 Hz, 1H), 7.68-7.66 (m, 1H), 7.44 (s, 1H), 7.31-7.25 (m, 2H), 7.07-7.04 (m, 1H), 3.79 (s, 6H), 2.90-2.87 (m, 2H), 2.74-2.71 (m, 2H), 2.14 (s, 3H), 1.37 (s, 13H). ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ (ppm) = 168.31, 153.42, 151.41, 146.42, 143.52, 140.57, 140.49, 139.42, 138.73, 138.46, 128.87, 128.39, 126.08, 125.84, 125.61, 123.06, 122.59, 118.10, 87.75, 59.84, 59.76, 35.39, 28.67, 10.47, 7.16. IR: ν = 685, 731, 760, 955, 1031, 1096, 1378, 1426, 1560, 1589, 1618, and 2930 cm^{-1}. UV-Vis: λ_{max} = 291 (ε = 9.8×10^3 M^{-1} cm^{-1}), ESI–MS(+) calc. for $C_{33}H_{38}ClIrN_2O_5$ $[M+Na]^+$ = 793.1996, found 793.5092. MP: 130 °C (decompose).

Cyclic Voltammetry

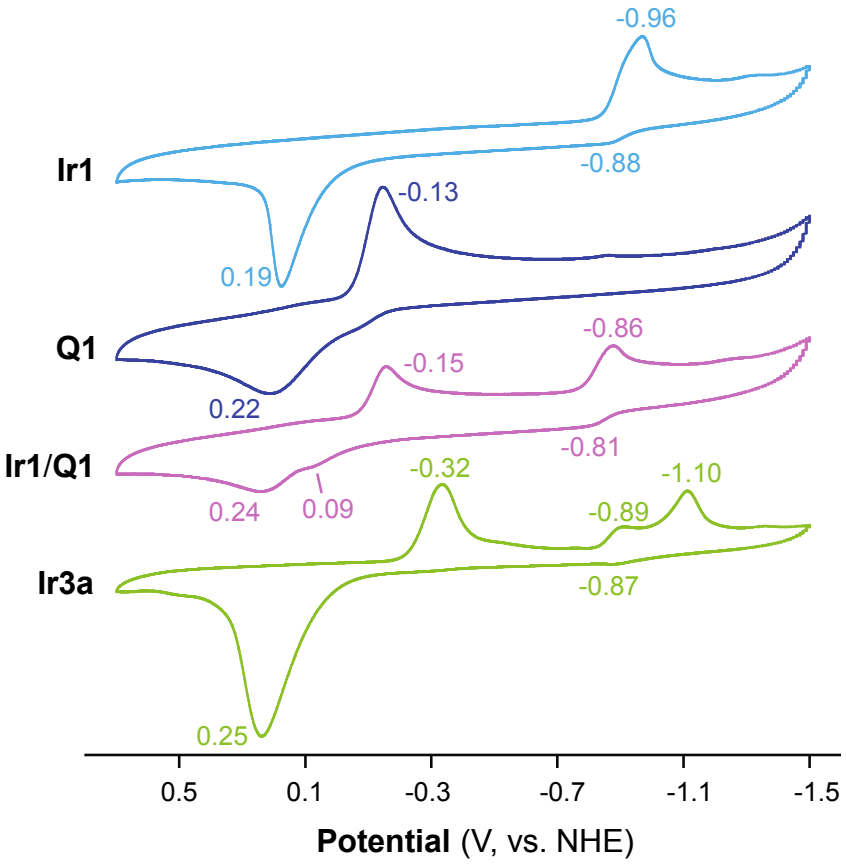


Figure S1. Cyclic voltammograms of iridium complexes (1.0 mM) and quinone (0.5 mM) recorded at 0.1 V/s in 0.1 M phosphate buffer saline (PBS) using a glassy carbon working electrode, Ag/AgCl reference electrode, and Pt wire as the auxiliary electrode. All potentials are referenced to NHE.

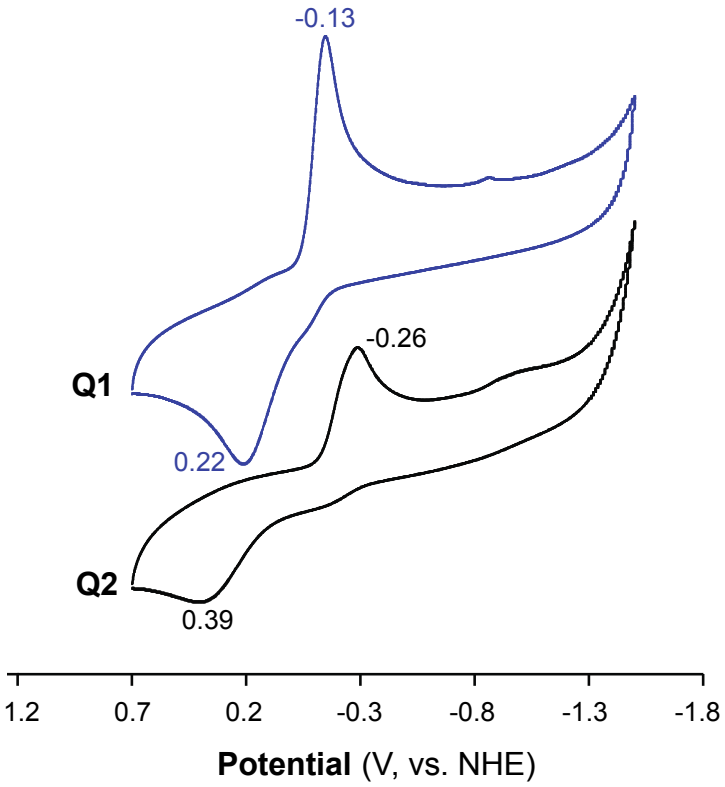


Figure S2. Cyclic voltammograms of **Q1** and **Q2** (0.5 mM) recorded at 0.1 V/s in 0.1 M phosphate buffer saline (PBS) using a glassy carbon working electrode, Ag/AgCl reference electrode, and Pt wire as the auxiliary electrode. All potentials are referenced to NHE.

Determination of H_2O_2 Concentration

Procedure: Stock solutions of **Ir1**, **Ir2**, **Ir3a** and **Q1** were prepared in DMSO at a concentration of 10 mM and stored in the freezer for subsequent use. Solutions containing H_2O_2 and NaHCOO (100 mM) in water were freshly prepared each time. Reactions were performed in 20 mL vials at room temperature. In each experiment, the catalyst and quinone stock solutions were diluted to concentrations ranging from 15 to 50 μM. Additional DMSO was added to maintain a constant co-solvent concentration of 1% in 10 mL of solvent. To 10 mL of this mixture, 20 equiv. of NaHCOO relative to the Ir complex or quinone, was added. The H_2O_2 concentration was monitored using Quantofix H_2O_2 test strips every 1 h. The amount of peroxide present was determined based on the grayscale intensity of the test strip after exposure to the reaction mixture for 30 sec. Each set of experiments was repeated two times to confirm that the trends observed were consistent and reproducible.

Analysis of Peroxide Test Strips: Photos of the original colored test strips were taken using an iPhone Xs Max under normal lab lighting. The colored photos were converted to 8-bit grayscale and the mean gray intensity was determined using the area selection tool in ImageJ. The grayscale intensity was then converted to peroxide concentration using the equation: [peroxide concentration] = 1000880 $e^{(-0.050755 \times \text{intensity})}$, which was obtained from an exponential fit of the intensity data obtained by converting the color scale provided by the manufacturer to grayscale (Figure S1). This method of peroxide concentration determination is meant only to be semi-quantitative since errors associated with inhomogeneous photo lighting, test strip response, and other uncontrolled experimental factors could affect the accuracy of the results.

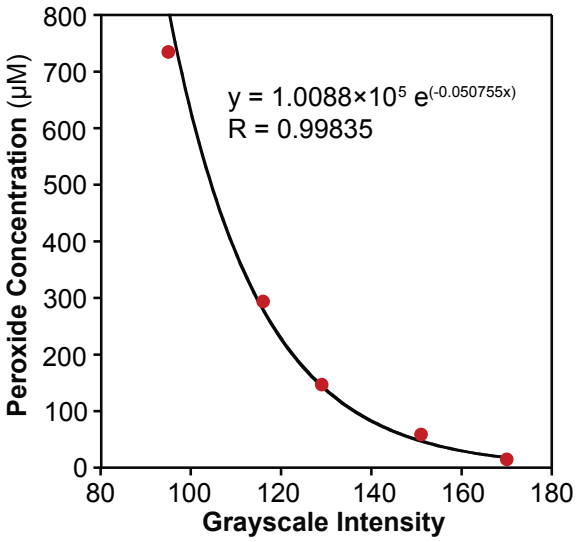


Figure S3. The color scale provided by the test strip manufacturer Quantofix was converted to grayscale and its intensity was plotted vs. concentration. A best fit of the data points provided an exponential equation relating the grayscale intensity with peroxide concentration.

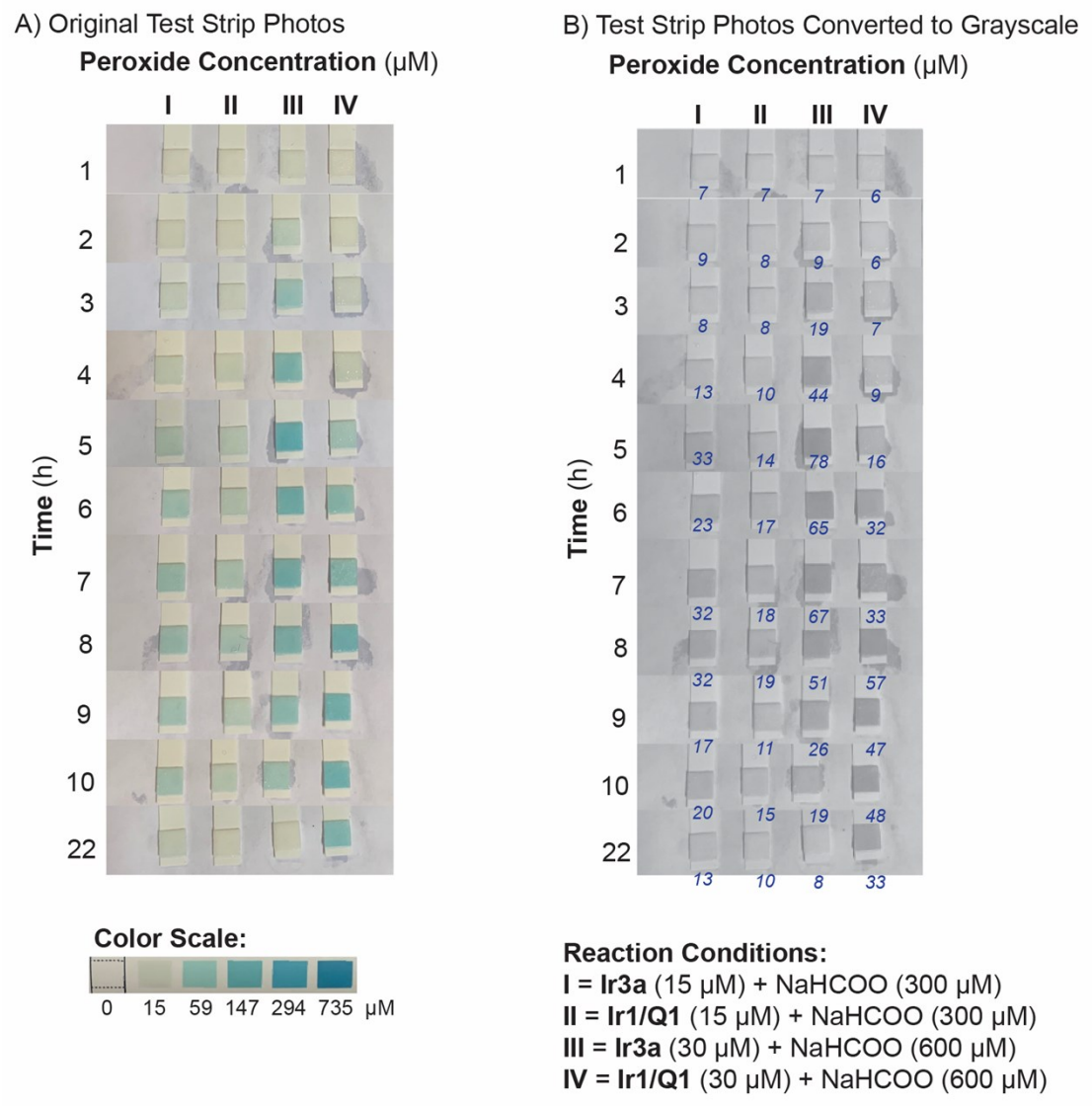


Figure S4. Photos of the test strips obtained from a time study of the formation of hydrogen peroxide by Ir complexes and NaHCOO (Part A: original; Part B: converted to grayscale). The blue numbers in the grayscale image indicate the peroxide concentration of the test area. The reactions were carried out in 10 mL of solvent (1% DMSO in water) using the concentration of reagents given above.

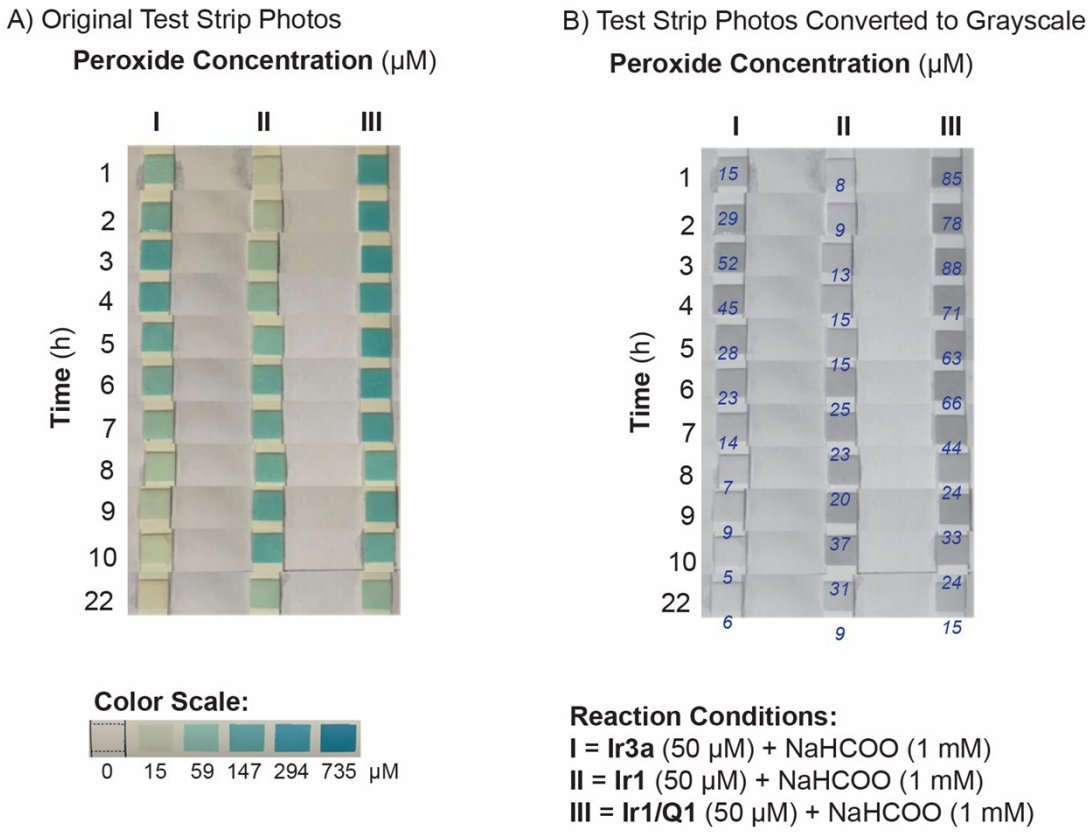


Figure S5. Photos of the test strips obtained from a time study of the formation of hydrogen peroxide by Ir complexes and NaHCOO (Part A: original; Part B: converted to grayscale). The blue numbers in the grayscale image indicate the peroxide concentration of the test area. The reactions were carried out in 10 mL of solvent (1% DMSO in water) using the concentration of reagents given above.

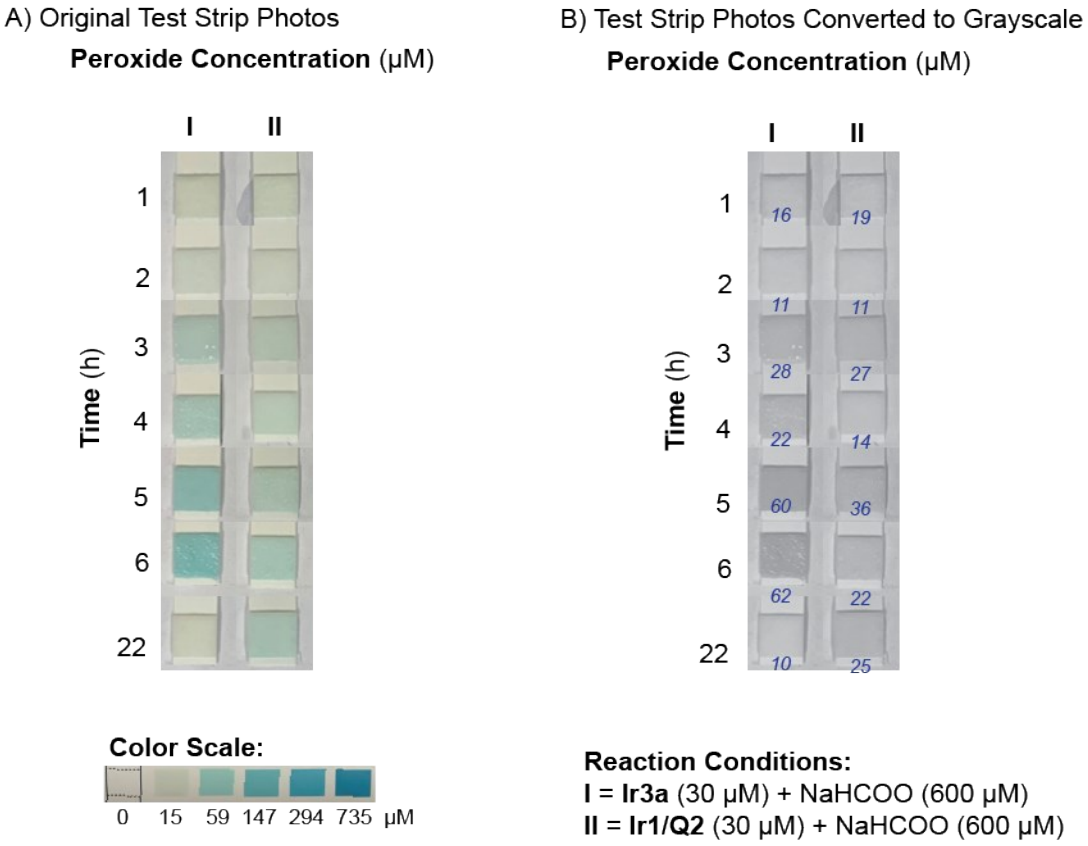


Figure S6. Photos of the test strips obtained from a time study of the formation of hydrogen peroxide by Ir complexes and NaHCOO (Part A: original; Part B: converted to grayscale). The blue numbers in the grayscale image indicate the peroxide concentration of the test area. The reactions were carried out in 10 mL of solvent (1% DMSO in water) using the concentration of reagents given above.

Decomposition of H_2O_2 in the Presence of Ir Complexes: Stock solutions of **Ir1**, **Ir3a**, and **Q1** were prepared as described above and then diluted to 10 µM. Solutions containing 30 µL of either the Ir complex or quinone were treated with H_2O_2 (5 µL). No sodium formate were used in these experiments. The reactions were followed for 22 h by periodically measuring the peroxide concentration using the H_2O_2 test strips. Decrease in the concentration of H_2O_2 was observed over time in the presence of the iridium complexes (Figure S4).

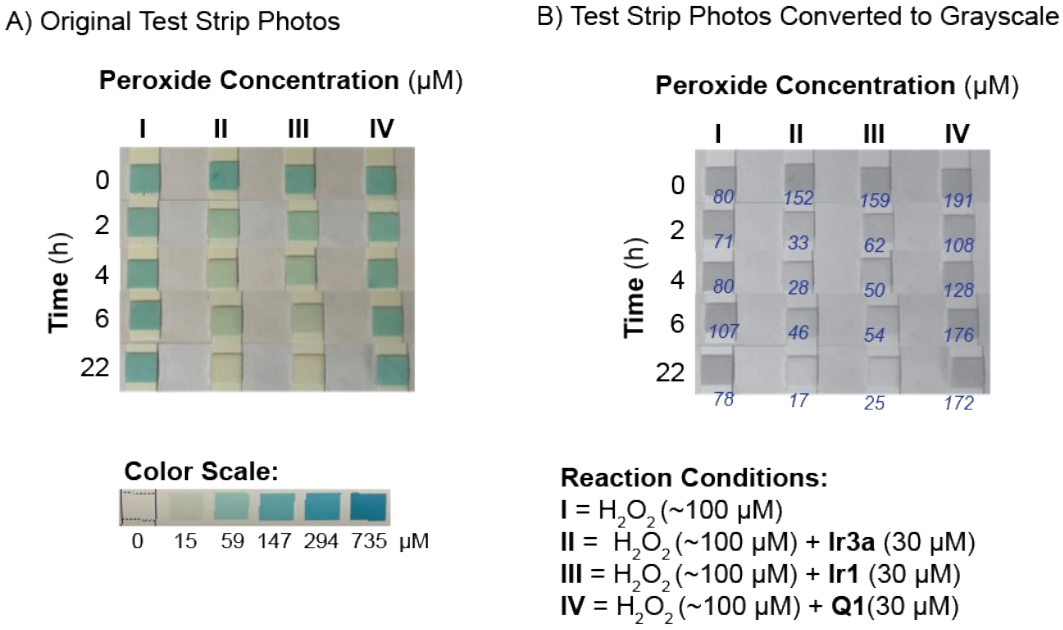


Figure S7. Photos of the test strips obtained from a time study of the decomposition of hydrogen peroxide in the presence and absence of Ir complexes (Part A: original; Part B: converted to grayscale). The blue numbers in the grayscale image indicate the peroxide concentration of the test area. The reactions were carried out in 10 mL of solvent (1% DMSO in water) using the concentration of reagents given above. The wide variation in the starting H_2O_2 concentration (e.g., from 80-191 µM at time = 0 h) was attributed to slightly different amounts of H_2O_2 added since the total volume of H_2O_2 used was very low (~5 µL); however, in these experiments, we were interested in the *relative changes* over time rather than the absolute amounts of H_2O_2 present, which would require more rigorous analytical studies.

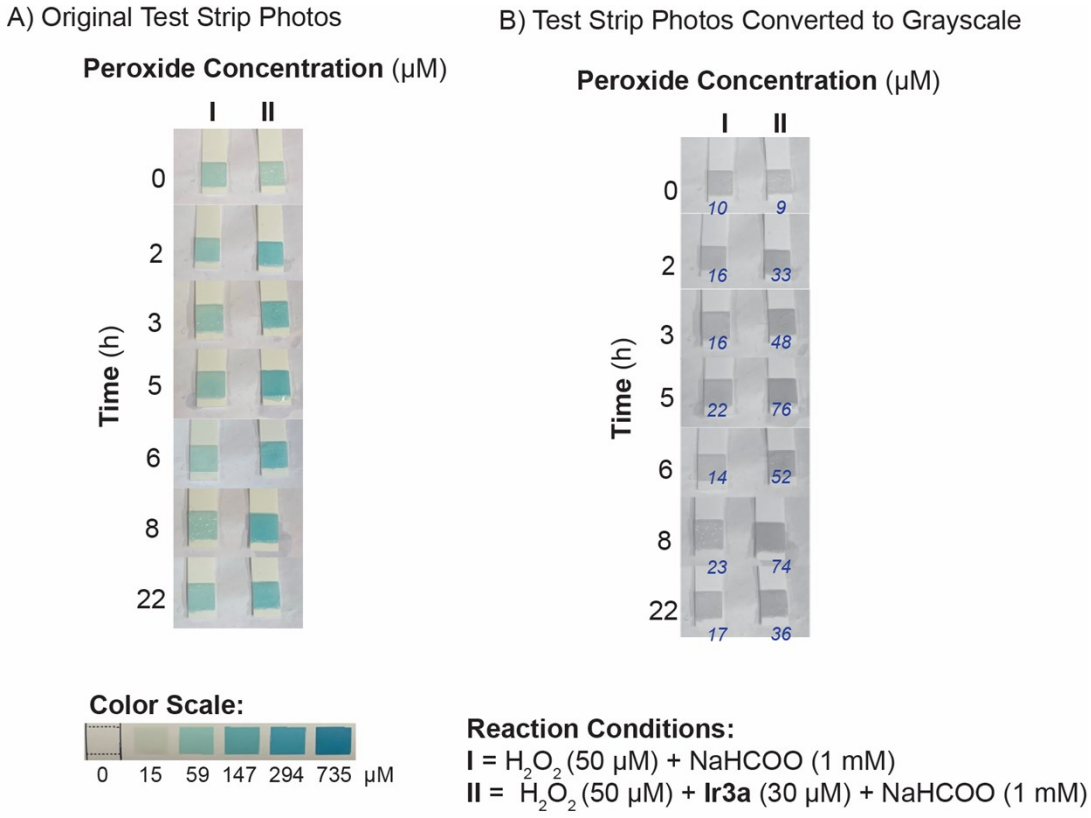


Figure S8. Photos of the test strips obtained from a time study of the decomposition of hydrogen peroxide in the presence and absence of **Ir3a** and NaHCOO (Part A: original; Part B: converted to grayscale). The blue numbers in the grayscale image indicate the peroxide concentration of the test area. The reactions were carried out in 10 mL of solvent (1% DMSO in water) using the concentration of reagents given above.

Reaction Monitoring by NMR Spectroscopy

Procedure for reaction of Ir1 with NaHCOO: A mixture of catalyst **Ir1** (5 mg, 6.5 μmol) and NaHCOO (2.2 mg, 5 equiv.) was prepared in the glove box. A 1.2 mL solution of acetone-d_6 /D_2O (9:1) was used to dissolve this mixture. The NMR spectrum was measured immediately, which showed that NaHCOO was completely consumed. This sample was then divided equally into 2 NMR tubes. One was kept at 40 °C under an inert atmosphere whereas the other was exposed to air. Both samples were then monitored by NMR spectroscopy. The air exposed-sample showed significant **Ir1** decomposition, as indicated by the disappearance of the ^{1}H NMR peaks corresponding to the ether linkage.

Procedure for reaction of Ir3a with NaHCOO: A 100 mM stock solution of **Ir3a** in CD_3OD was prepared in the glovebox. A 25 μL aliquot of this solution was diluted with 450 μL of CD_3OD in a J-Young NMR tube. The NMR tube was cooled to -40 °C inside the spectrometer and then the spectrum of the starting compound was measured. The sample was ejected, treated with a -40 °C solution containing 50 μL of NaHCOO (100 mM) in CD_3OD, and then quickly reinserted back into the NMR spectrometer. The temperature was slowly increased at a rate of 5 °C /10 min up to 15 °C and NMR spectra were recorded at -35, -20, 0, 10, and 15 °C. Finally, the NMR sample was warmed to RT, removed from the instrument, and the solution was exposed to air overnight. This sample was analyzed by NMR spectroscopy to confirm the reduced species was oxidized by air. Alternatively, the final NMR sample was treated with excess sodium formate and then recorded by NMR spectroscopy to observe the formation of **Ir3d**.

Quantification of turnover number: The following reagents from individually prepared stock solutions were combined in a 3 mL scintillation vial: NaHCOO (20 μmol) and methyl benzyl alcohol as an internal standard (10 μmol) in 1 mL of D_2O/DMSO-d_6 (9:1). This solution was stirred for 1 min. The sample was prepared by taking out a 100 μL aliquot of the mixture and combining it with 300 μL of D_2O/DMSO-d_6 (9:1). The Ir catalyst (0.45 μmol) was then added to the vial and the reaction was monitored directly by NMR spectroscopy at 6 and 21 h.

Procedure for reaction of Ir3a with NaHCOO/nPr_2S: The appropriate volumes of stock solutions containing the following reagents were combined in a 20 mL scintillation vial: NaHCOO (100 μmol), **Ir3a** (2 μmol) and *n*Pr_2S (200 μmol) in 10 mL of H_2O/DMSO (95:5). This solution was stirred at room temperature for 18 h. After the reaction was complete, the organic compounds were extracted into dichloromethane (2×1 mL), dried over Na_2SO_4, filtered, to remove the drying agent, and characterized by NMR spectroscopy. A control experiment was set up following the same procedure except *n*Pr_2S was not added. Measurement of the samples by NMR spectroscopy confirmed that *n*Pr_2S did not inhibit the catalyst activity of **Ir3a** since NaHCOO was still consumed.

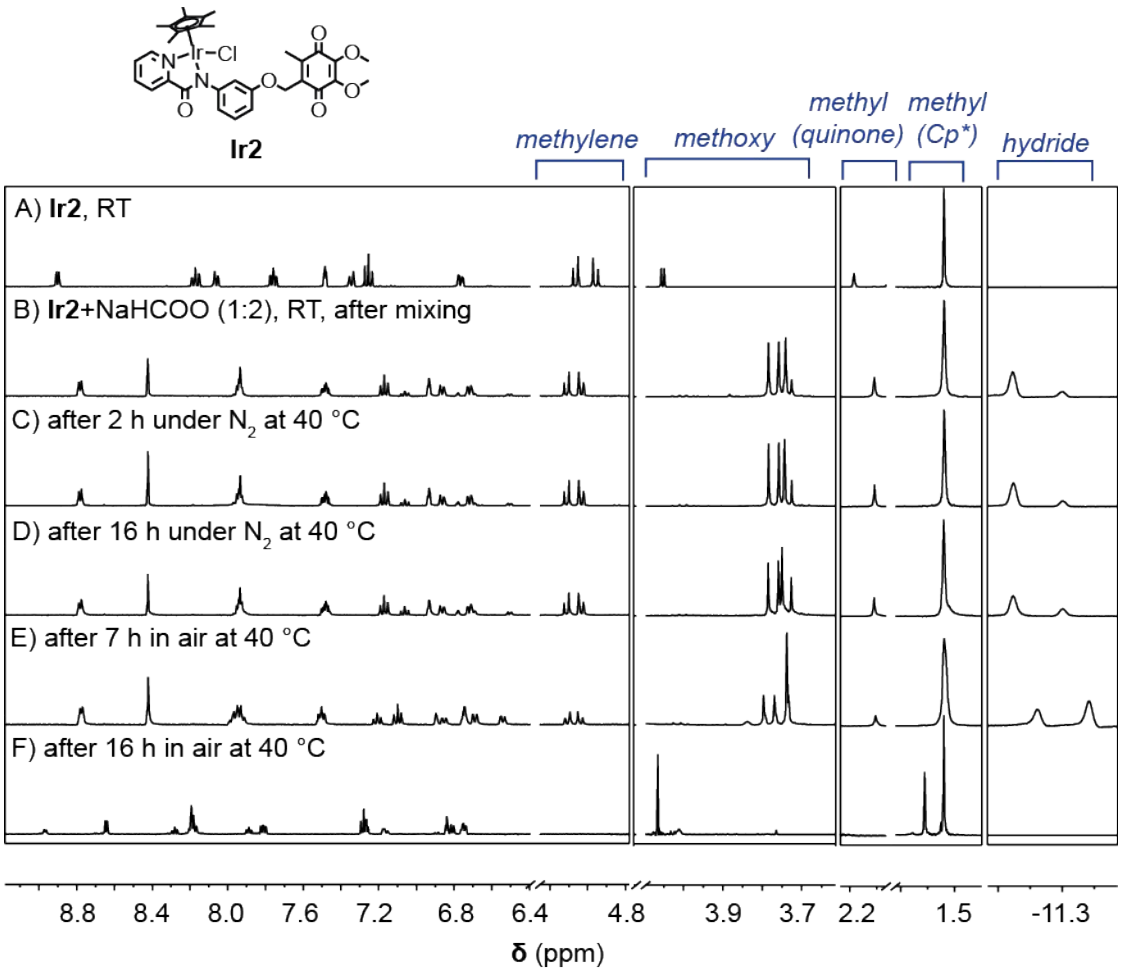


Figure S9. ^{1}H NMR spectra (acetone-d_6 - D_2O 9:1; 400 MHz) obtained from the reaction of **Ir2** with 5 equiv. of NaHCOO. The data show A) complex **Ir2** at RT; B) reaction mixture immediately after treatment with NaHCOO at RT; C) reaction mixture after 2 h under nitrogen at 40 °C; D) reaction mixture after 16 h under nitrogen at 40 °C; E) reaction mixture after 7 h in air at 40 °C; and F) reaction mixture after 16 h in air at 40 °C. The spectrum F clearly showed disappearance of the benzylic (methylene) hydrogen peaks upon exposure to air, suggesting that the ether group had cleaved.

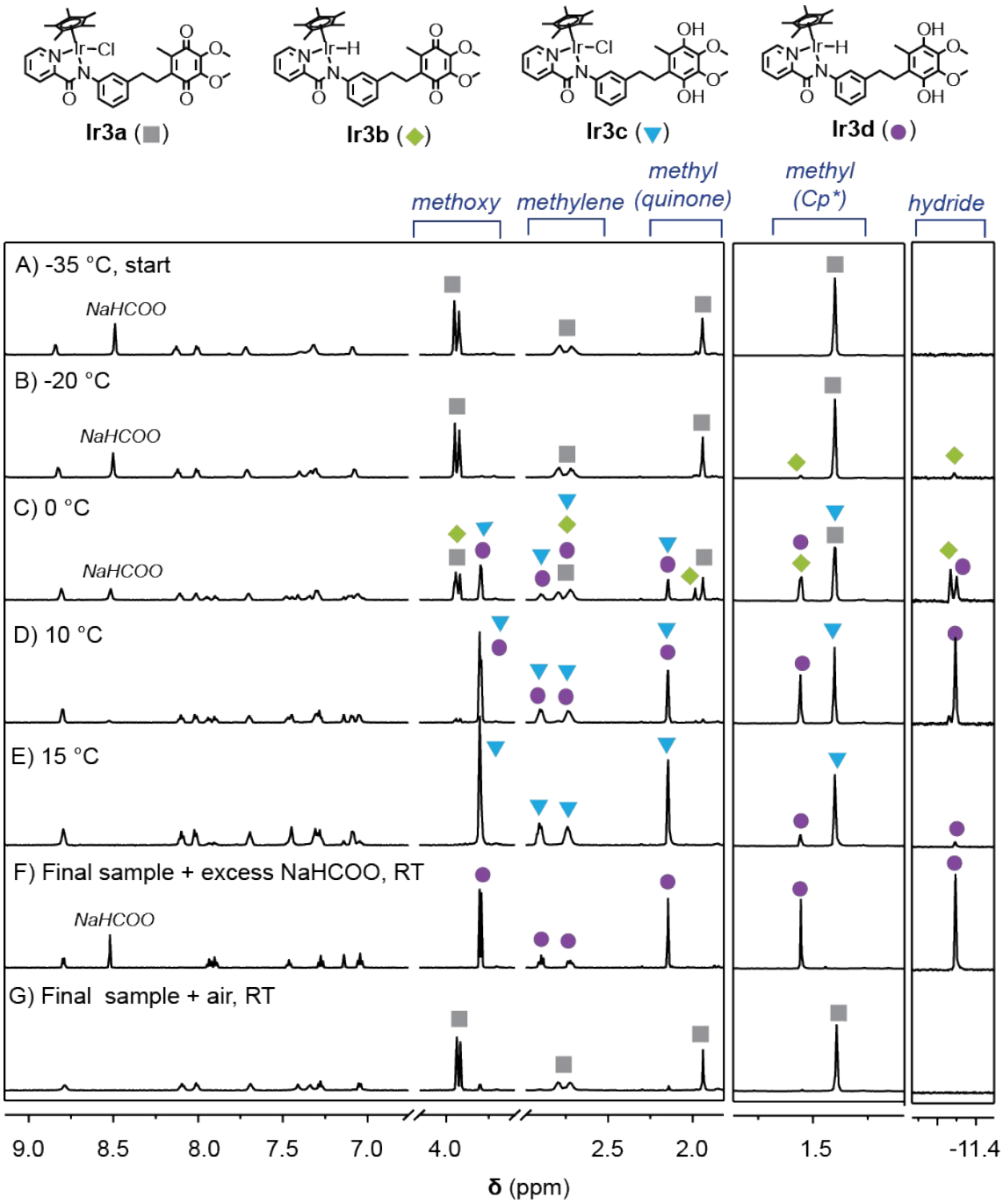


Figure S10. Reaction of **Ir3a** with NaHCOO (2.0 equiv.) in CD_3OD studied by variable temperature ^1H NMR spectroscopy (600 MHz). The peak assignments are indicated by colored shapes corresponding to the chemical structures shown above.

Table S1. ^{1}H NMR Spectral Peak Assignments from Reaction of **Ir3a** with NaHOO[a]

Complex	Hydride	Methyl (Cp*)	Methyl (quinone)	Methylene	Methoxy
Ir3a	none	1.381	1.924	2.686, 2.766	3.907, 3.934
Ir3b	-11.287	1.534	1.967	2.70, 2.88[b]	3.917, 3.927
Ir3c	none	1.379	2.126	2.70, 2.77[b]	3.77, 3.78[b]
Ir3d	-11.309	1.540	2.131	2.707, 2.880	3.779, 3.789

[a]All chemical shift values are reported in ppm. There were minimal peak shifts due to temperature. These data were obtained from the experiment in Figure S6. The peaks for **Ir3a**, **Ir3c**, and **Ir3d** matched those observed in independently prepared complexes. [b]These peaks overlap with those of one or more additional species.

Table S2. Population of Iridium Species at Various Temperatures[a]

Temperature	Ir3a	Ir3b	Ir3c	Ir3d
-35 °C	100%	0	0	0
-20 °C	97%	3%	0	0
0 °C	39%	19%	24%	19%
10 °C	trace	trace	47%	53%
15 °C	0	0	86%	14%

[a]Percentage population determined based on the peak integrations of the various iridium species at the specified temperature. These data were obtained from the reaction of **Ir3a** with NaHCOO shown in Figure S6.

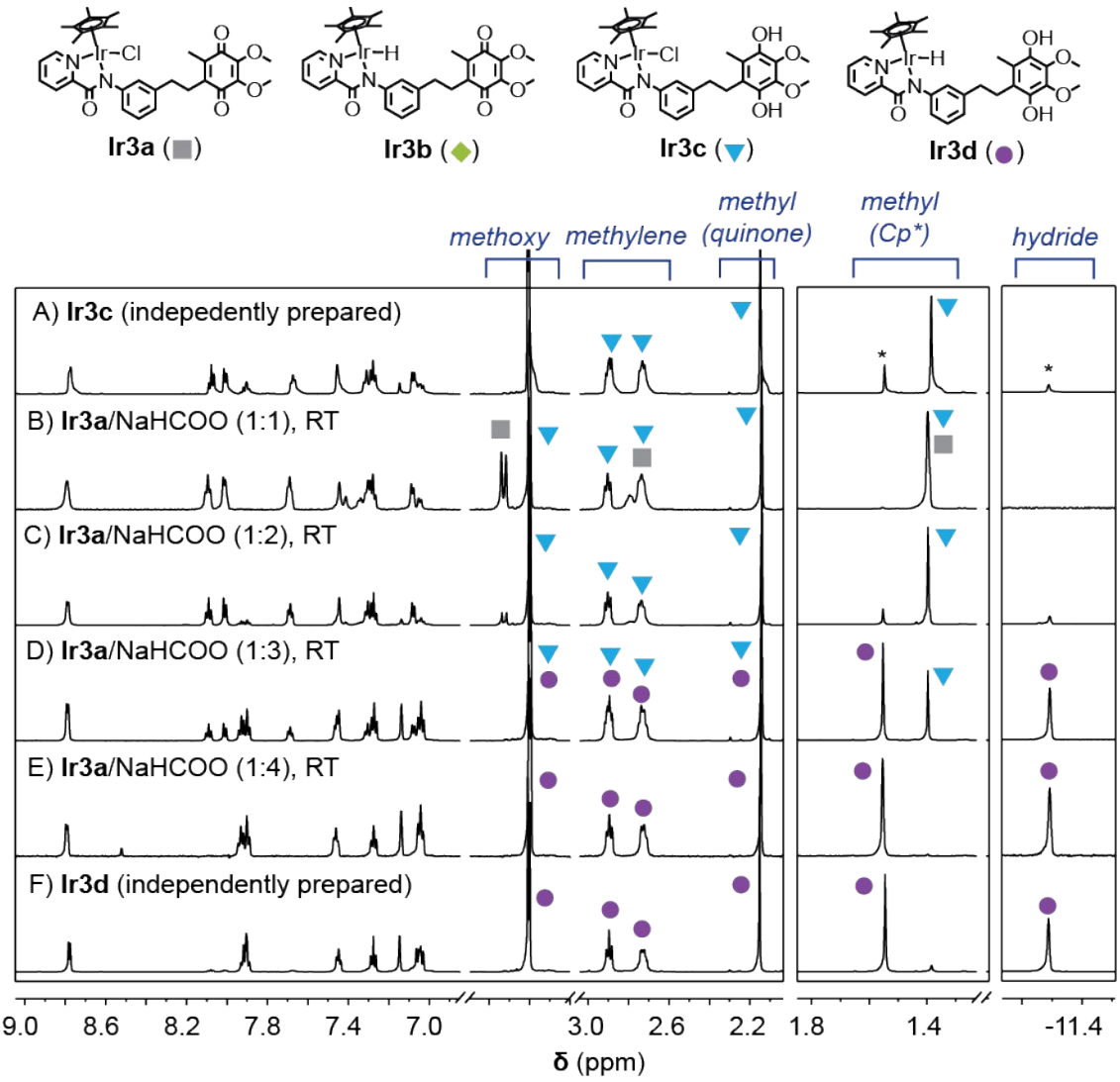


Figure S11. Reaction of **Ir3a** with NaHCOO (1-4 equiv.) in CD_3OD at RT (500 MHz). The peak assignments are indicated by colored shapes corresponding to the chemical structures shown above. A minor amount of **Ir3d** is present in the independently prepared sample of **Ir3c** (part A). Although the equivalence of NaHCOO used do not lead to a clear stoichiometric conversion from **Ir3a** → **Ir3c** → **Ir3d**, the growth of **Ir3d** with greater amounts of reductant added indicates it is the most reduced species.

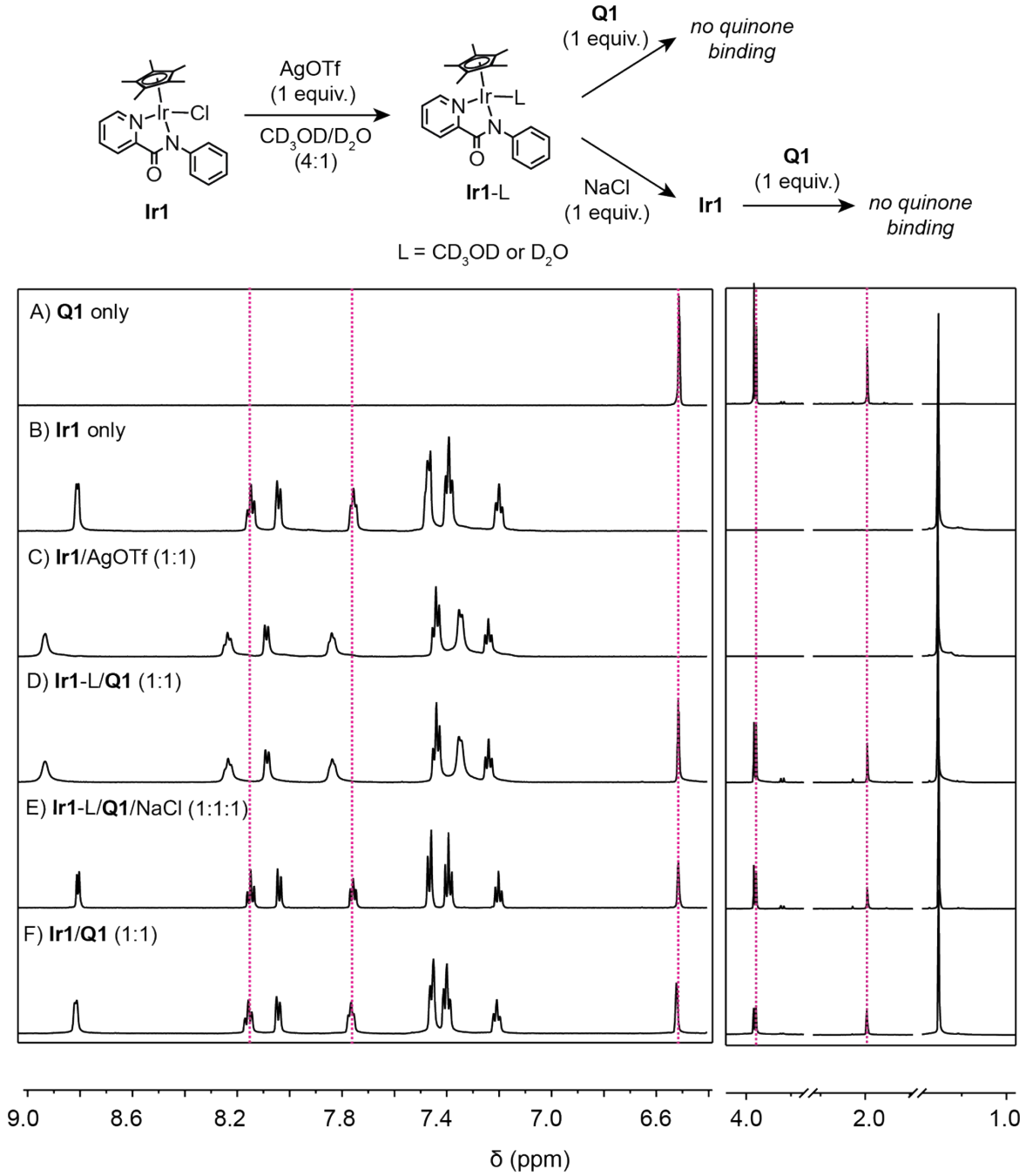


Figure S12. ^{1}H NMR spectra (CD_3OD/D_2O, 4:1, 600 MHz) of A) **Q1** only; B) **Ir1** only; C) **Ir1**/AgOTf (1:1); D) **Ir1**-L/**Q1** (1:1); E)) **Ir1**-L/**Q1**/NaCl (1:1:1); and F) **Ir1**/**Q1** (1:1). These data suggest that even in aqueous solutions, the iridium-chloride species is favored over the iridium-solvato complex. Furthermore, quinone **Q1** does not appear to bind either **Ir1** or **Ir1**-L.

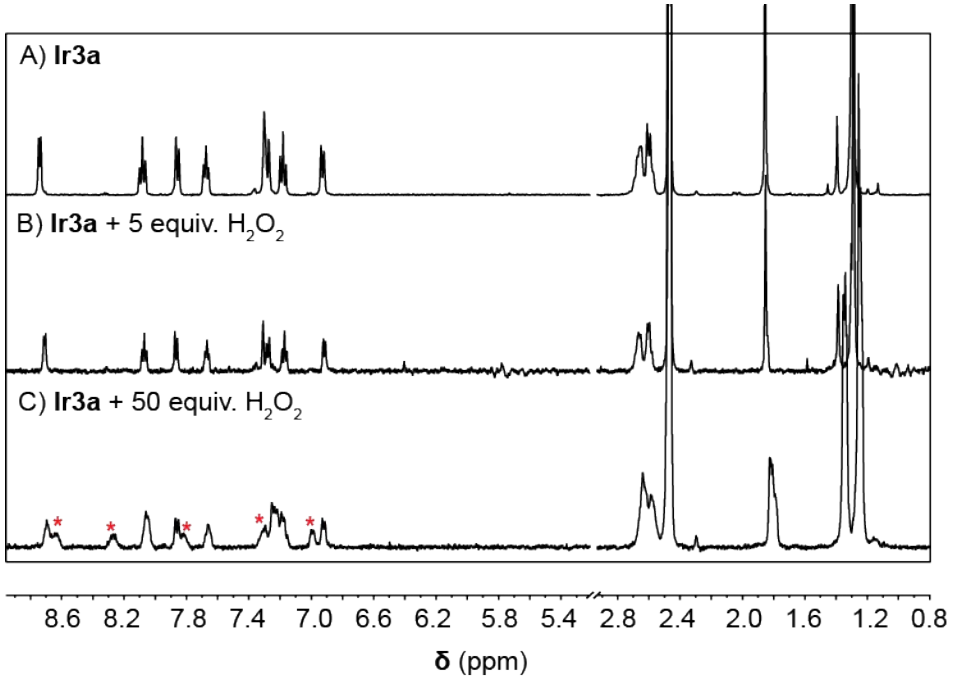


Figure S13. ^{1}H NMR spectra (DMSO-d_6, 400 MHz) of complex **Ir3a** before (A) and after addition of 5 equiv. (B) and 50 equiv. of hydrogen peroxide (C). Spectrum B has diminished signal intensity compared to A and spectrum C contains additional peaks that were assigned to at least one or more decomposition products (marked with red asterisks *). The identity of the decomposed Ir complex could not be determined due to its intractability.

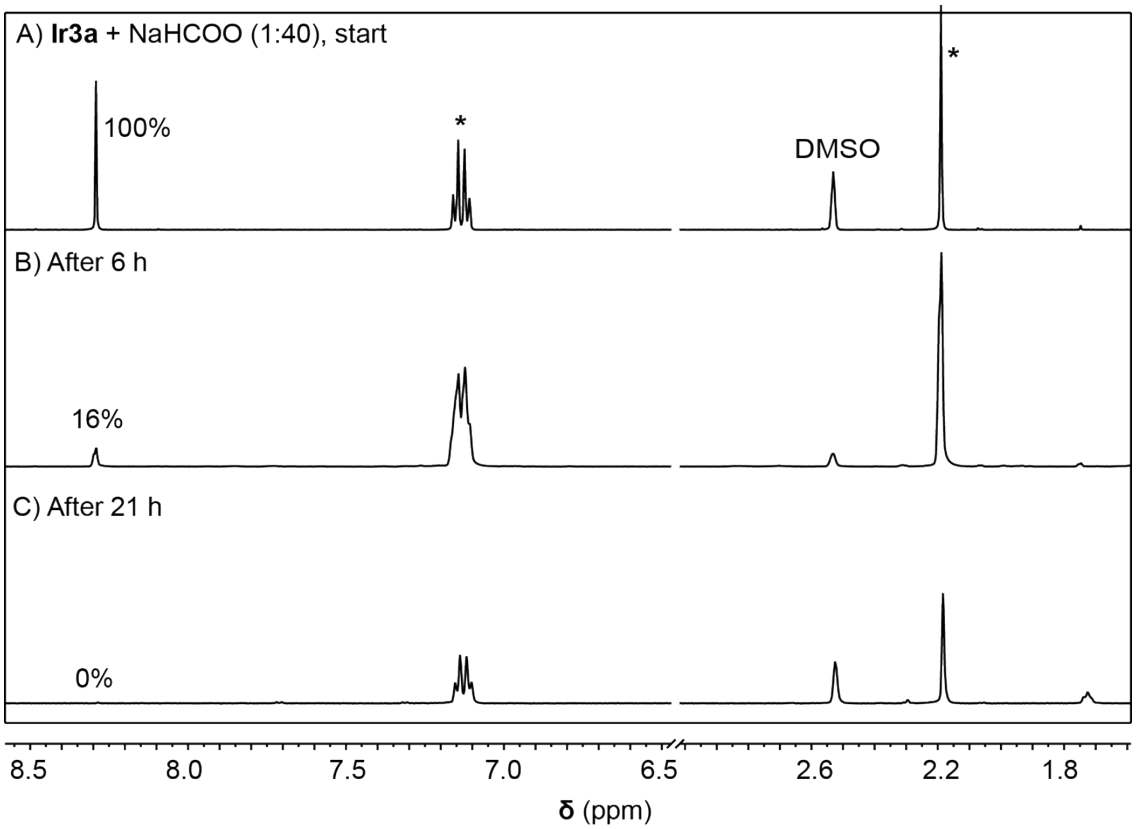


Figure S14. ^{1}H NMR spectra (DMSO-d_6/D_2O, 500 MHz) of the reaction of **Ir3a** (0.5 μmol) with NaHCOO (20 μmol) over the course of 21 h (A-C) in the presence of an internal standard methyl benzyl alcohol (marked with *). After 21 h, complete consumption of NaHCOO was observed, which gave a turnover number (TON) of 40.

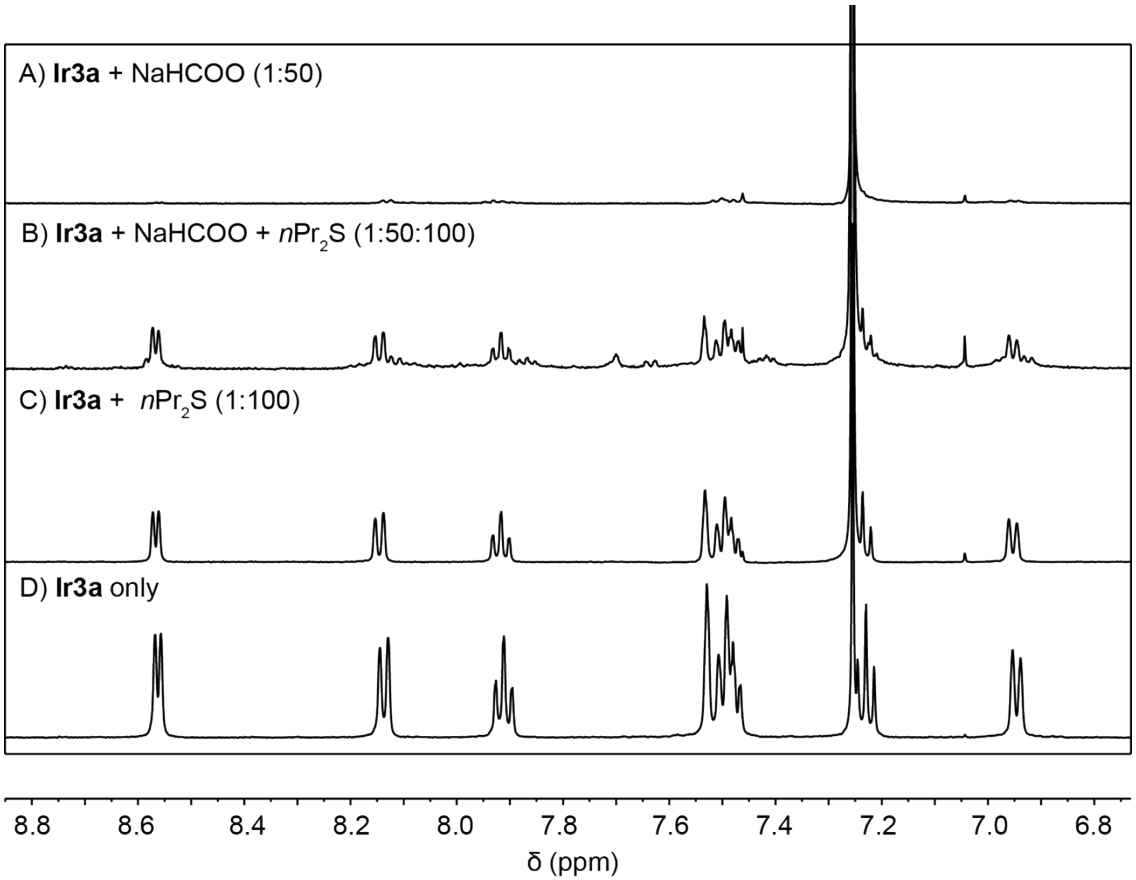


Figure S15. ^{1}H NMR spectra ($CDCl_3$, 500 MHz) of A) **Ir3a** (2 μmol) + NaHCOO (100 μmol); B) **Ir3a** (2 μmol) + NaHCOO (100 μmol) + nPr$_2$S (200 μmol); C) **Ir3a** (2 μmol) + nPr$_2$S (200 μmol); and D) **Ir3a** (2 μmol). Each reaction was performed in 10 mL of DMSO/H_2O (1:19) for 18 h and then the organic products were extracted for NMR spectroscopic analysis. These data showed that propyl sulide can protect the iridium catalysts from oxidiative damage.

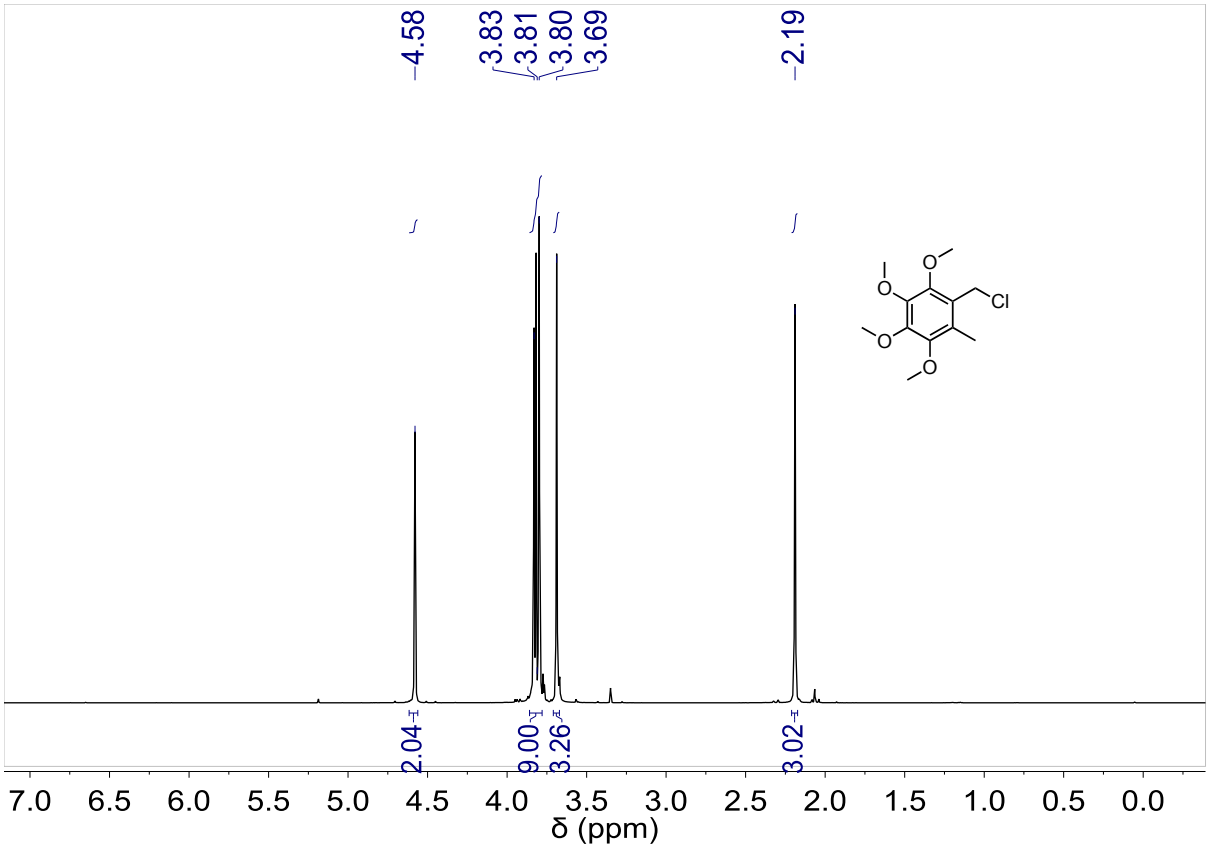


Figure S16. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of compound **2**.

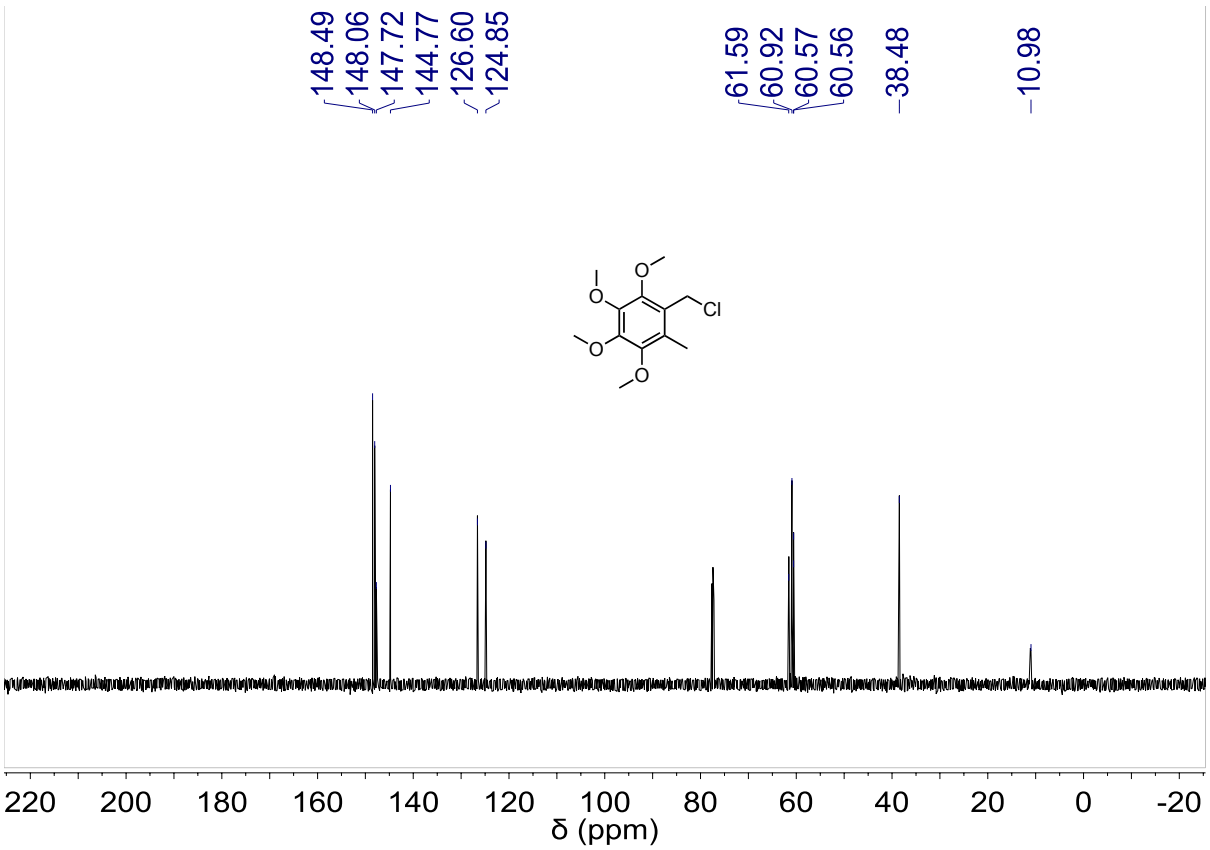


Figure S17. ^{13}C NMR spectrum ($CDCl_3$, 151 MHz) of compound **2**.

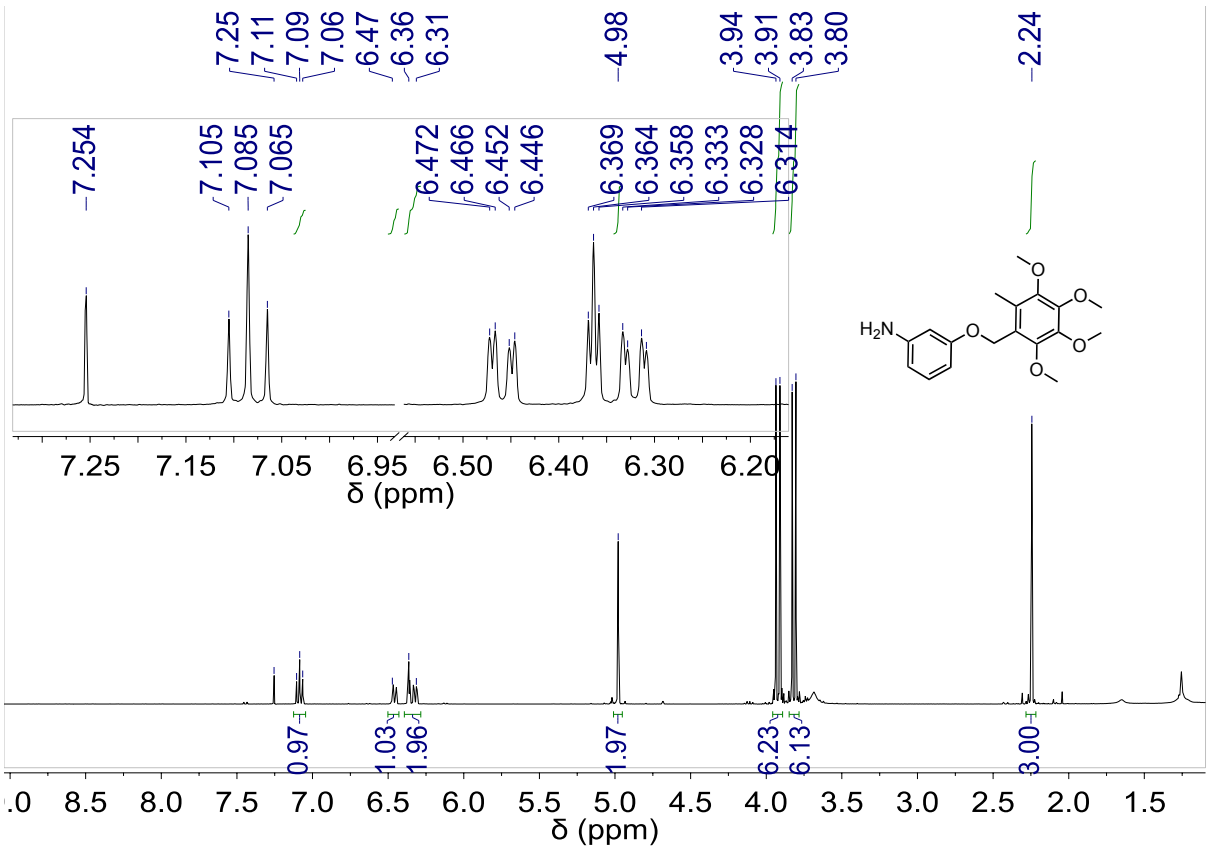


Figure S18. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **3**.

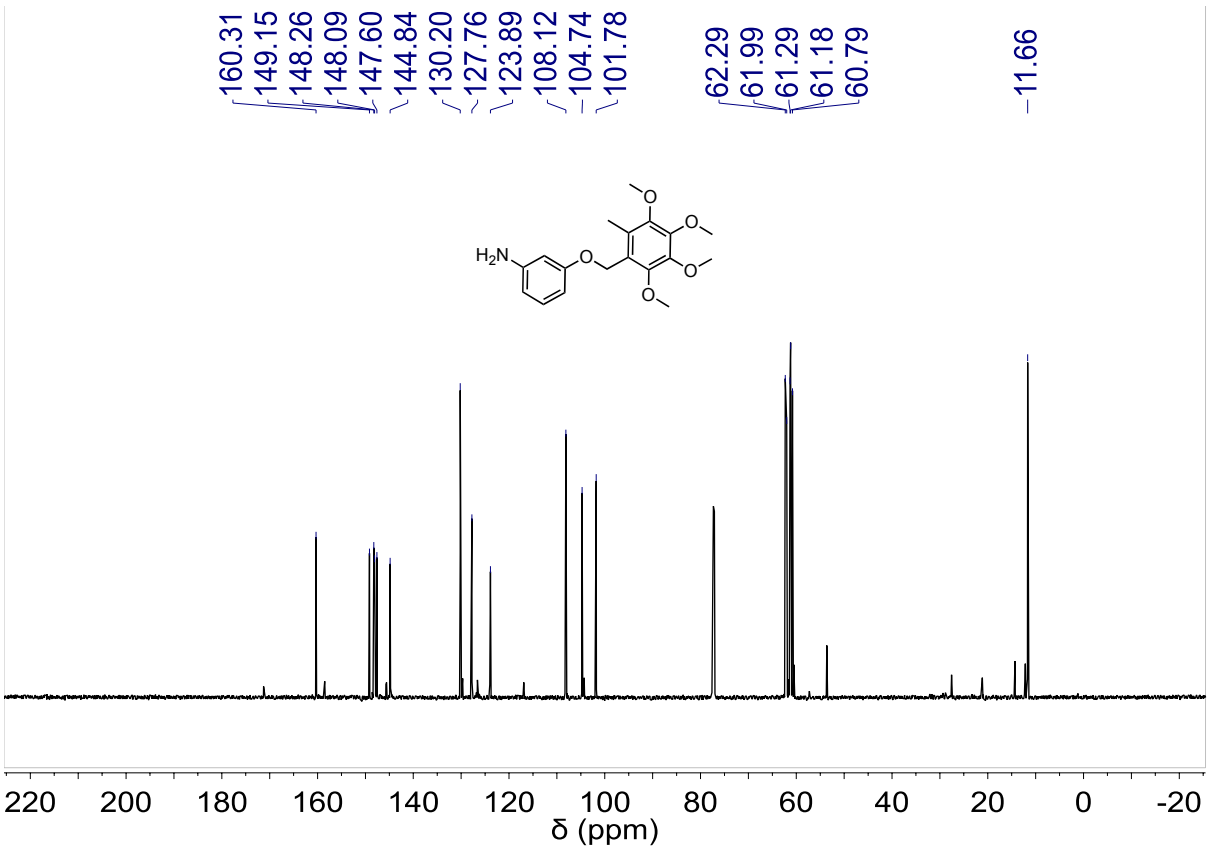


Figure S19. ^{13}C NMR spectrum ($CDCl_3$, 151 MHz) of compound **3**.

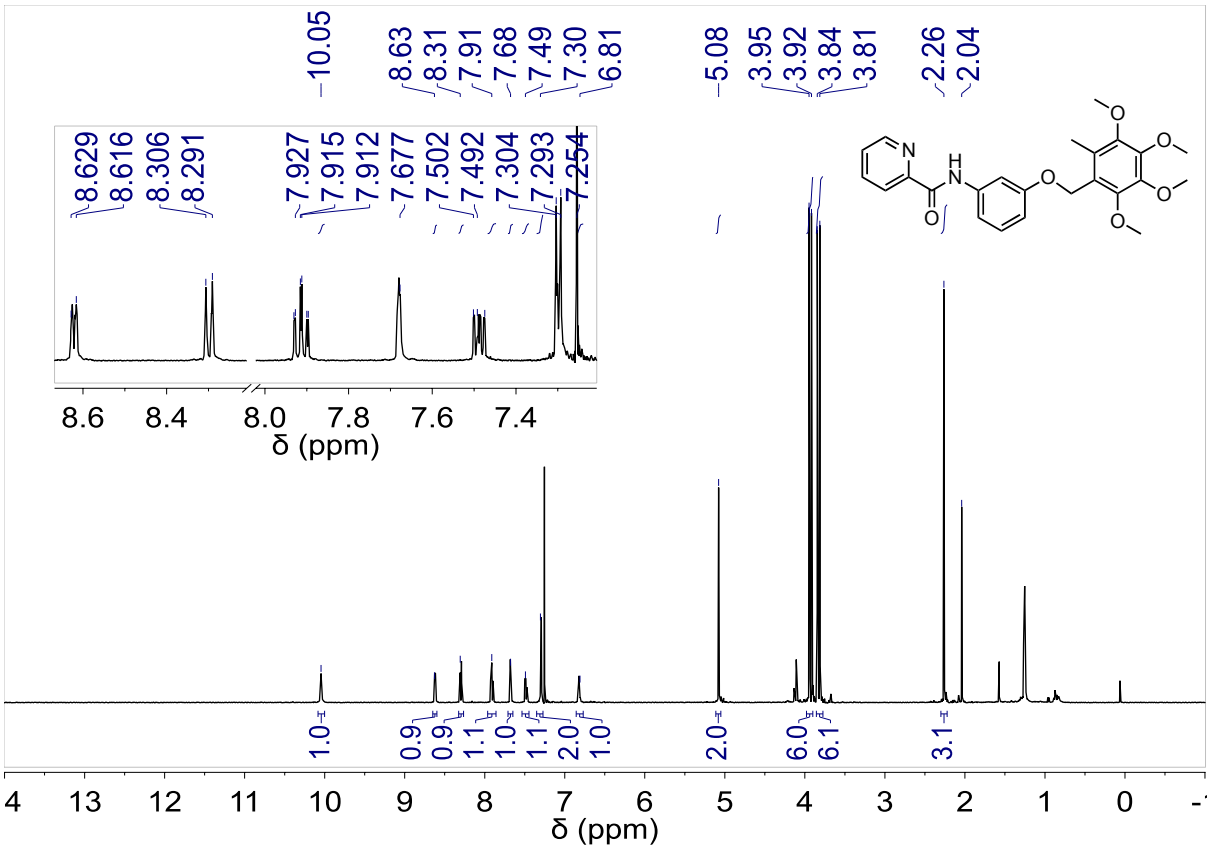


Figure S20. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **4**.

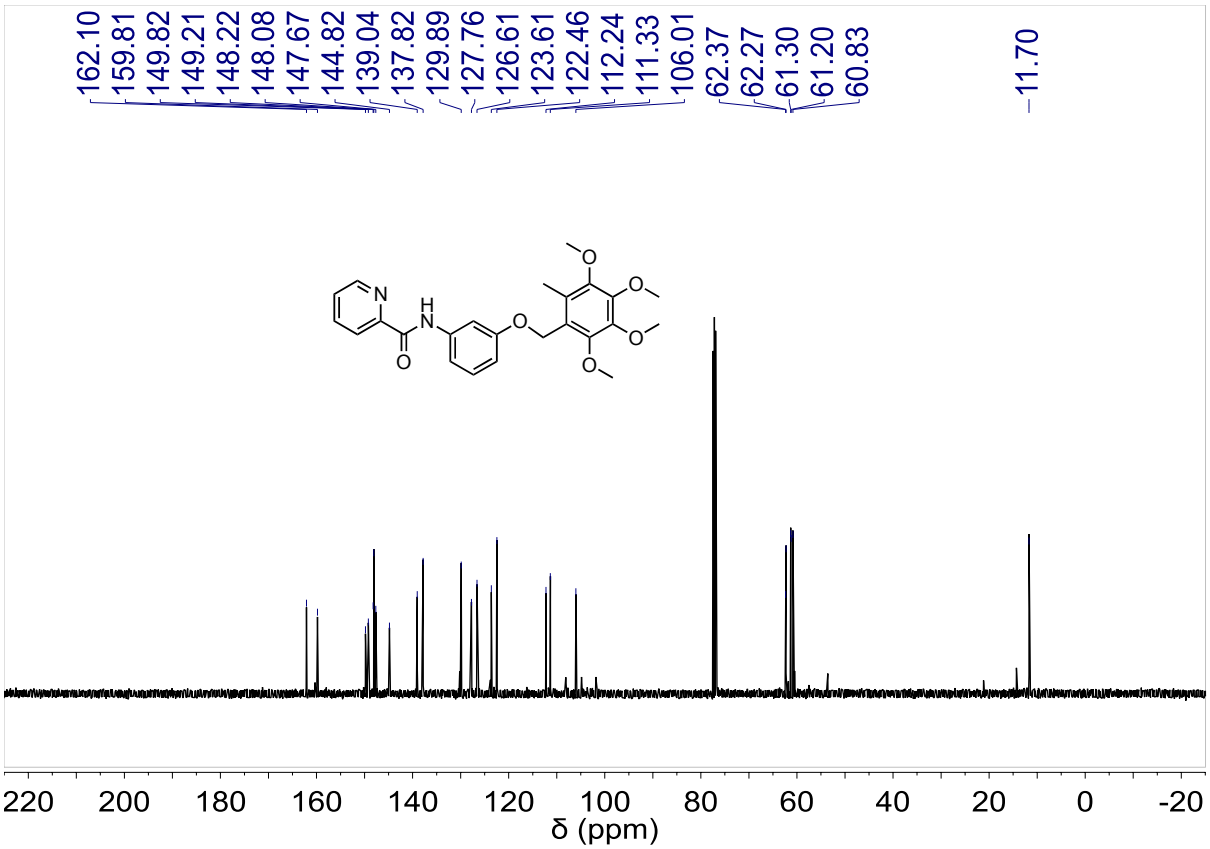


Figure S21. ^{13}C NMR spectrum ($CDCl_3$, 126 MHz) of compound **4**.

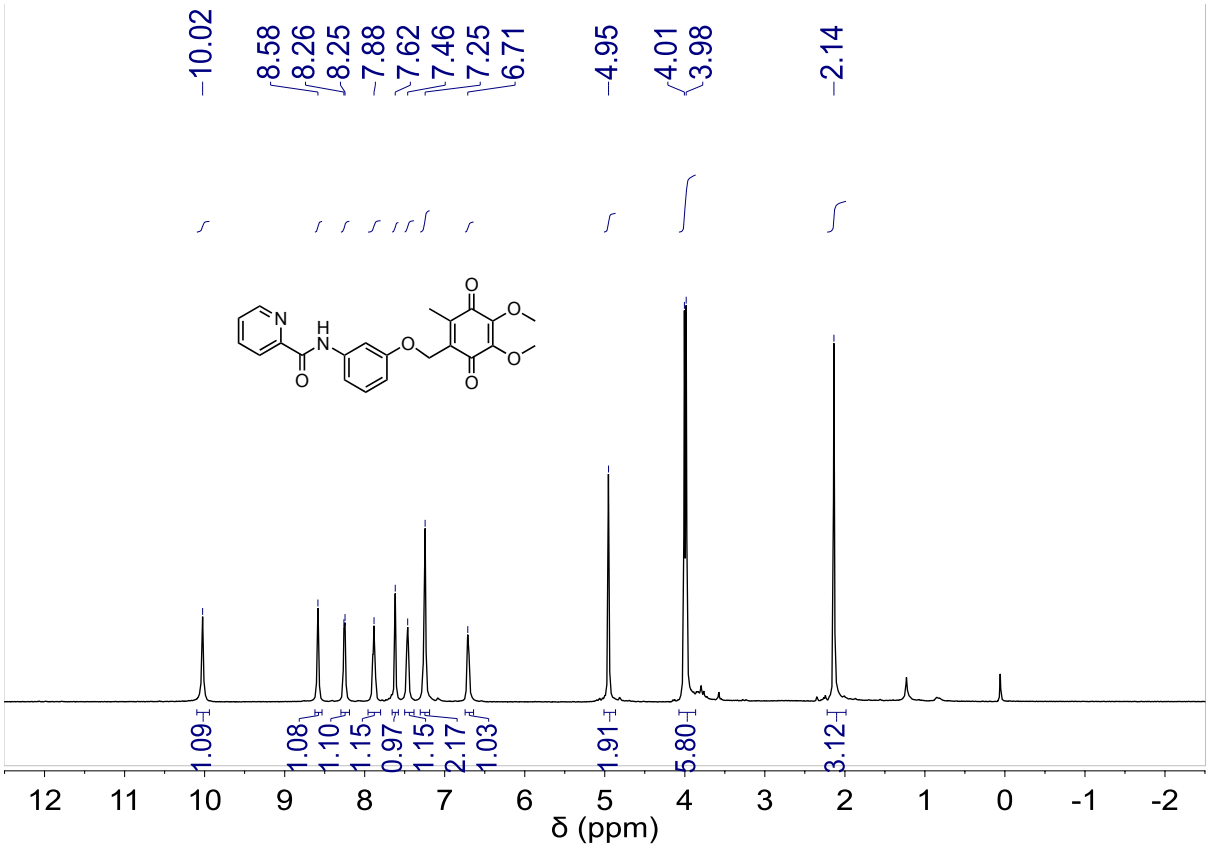


Figure S22. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **5**.

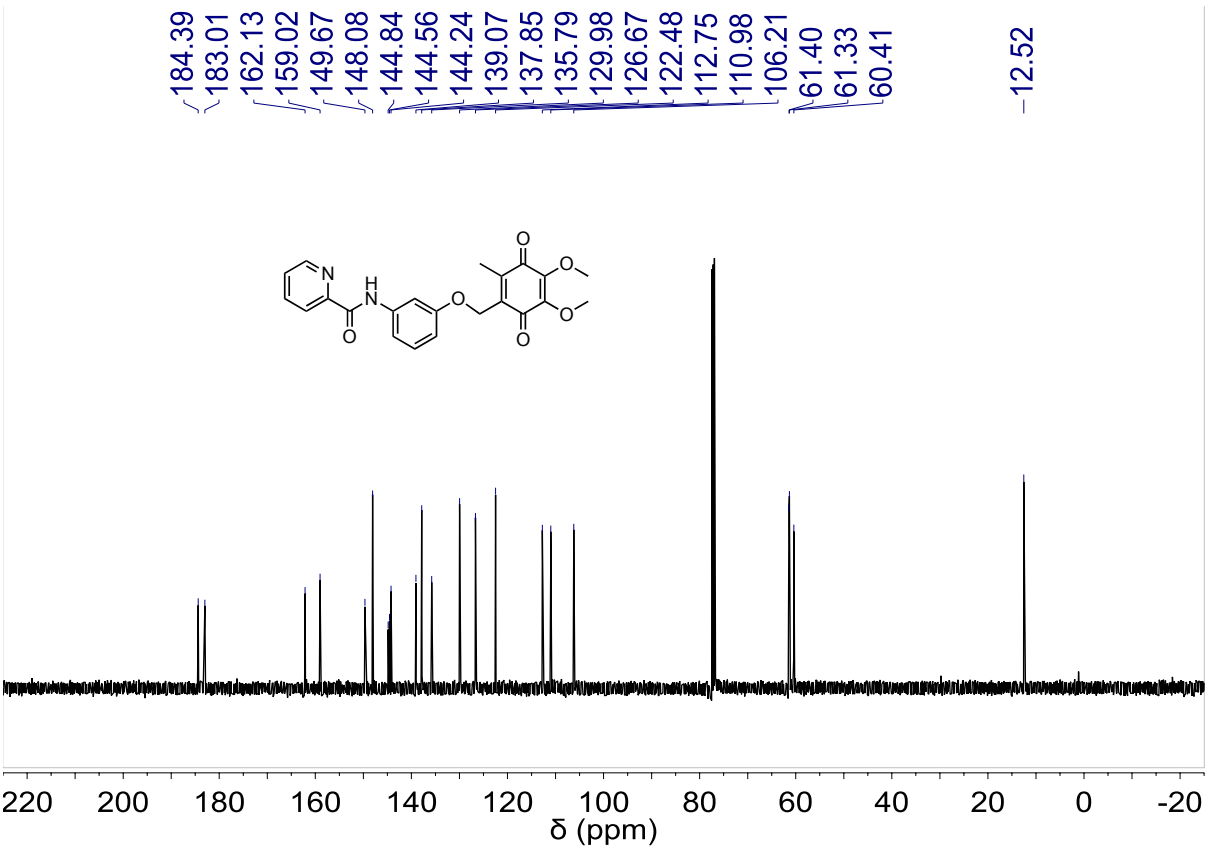


Figure S23. ^{13}C NMR spectrum ($CDCl_3$, 126 MHz) of compound **5**.

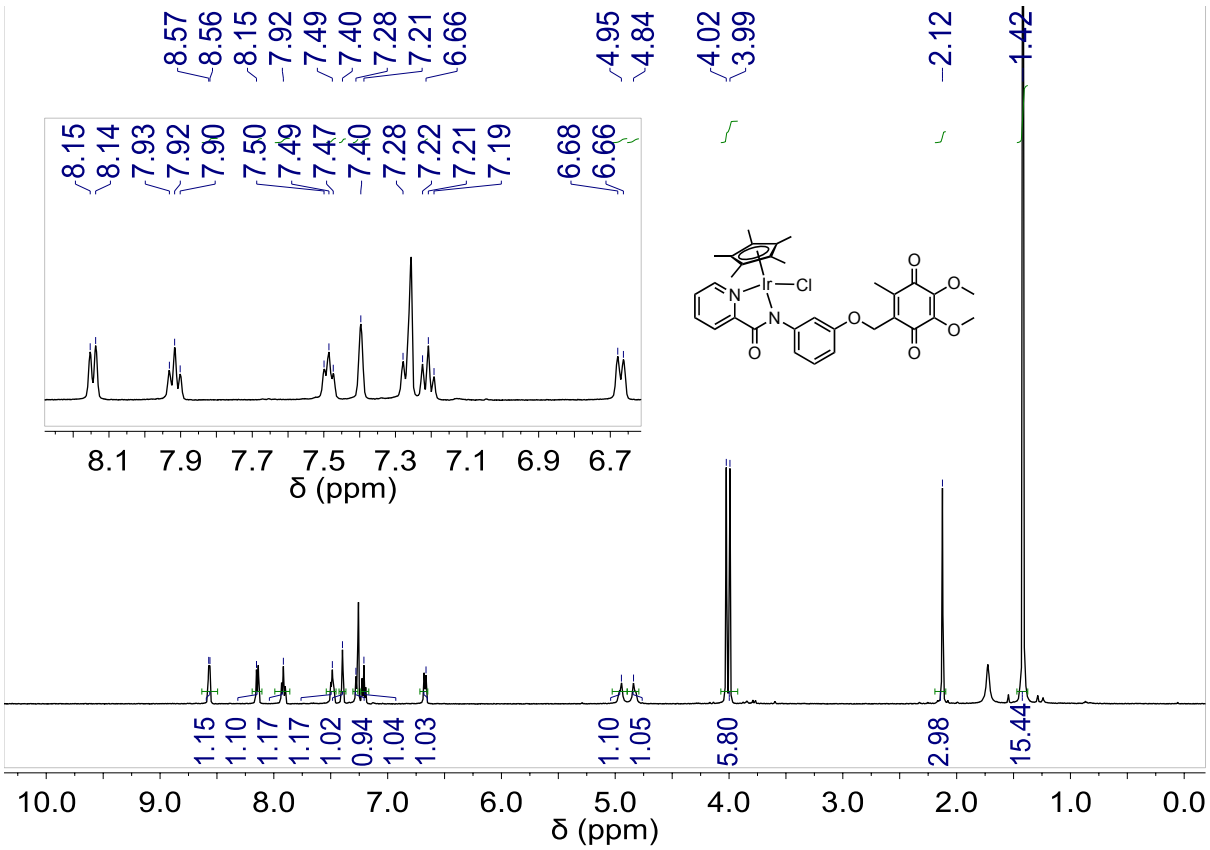


Figure S24. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **Ir2**.

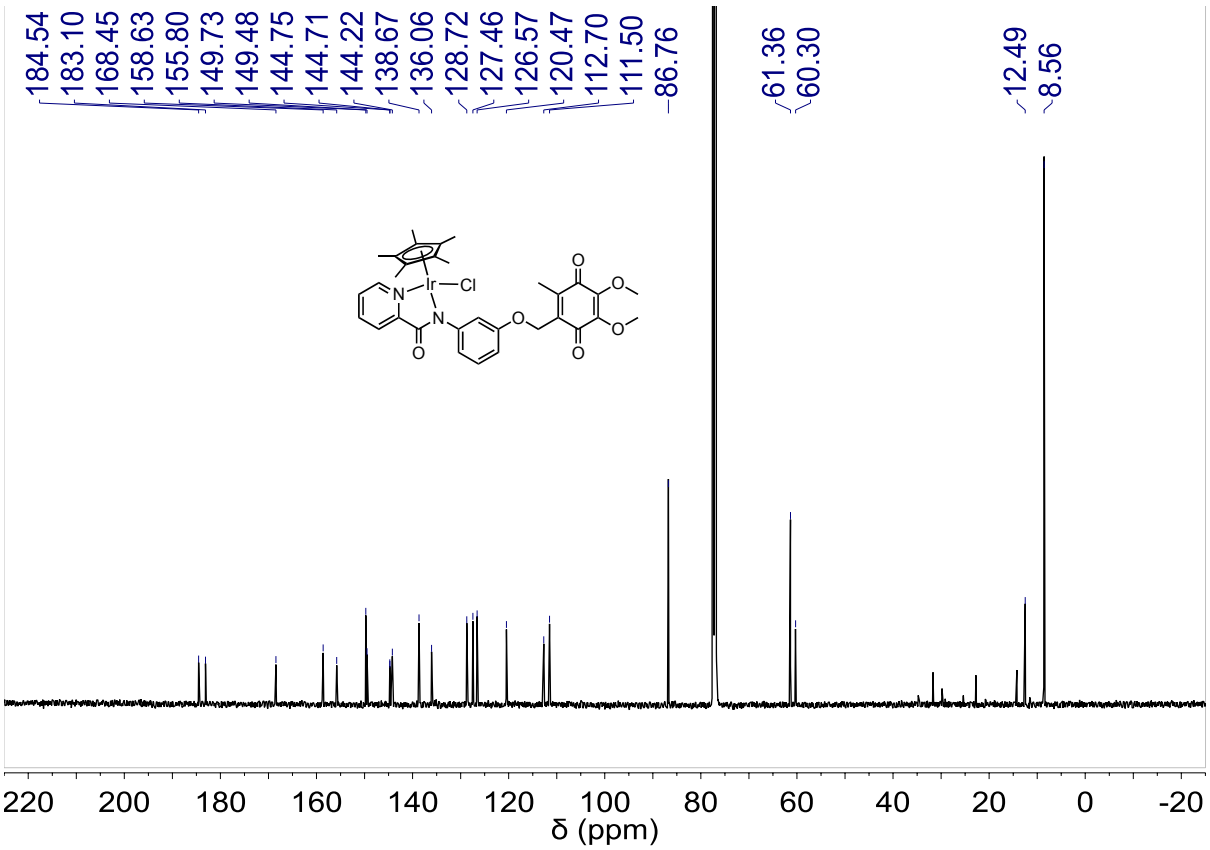


Figure S25. ^{13}C NMR spectrum ($CDCl_3$, 126 MHz) of compound **Ir2**.

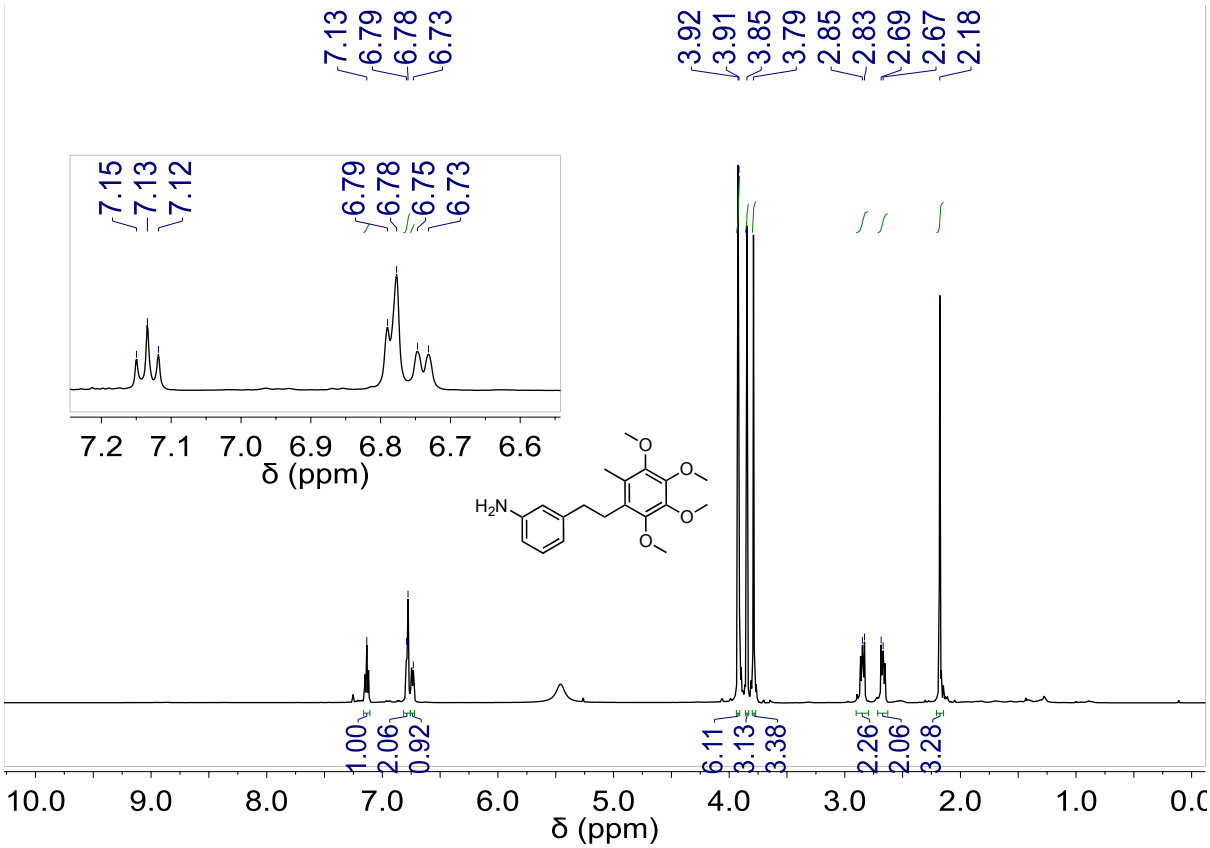


Figure S26. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **6**.

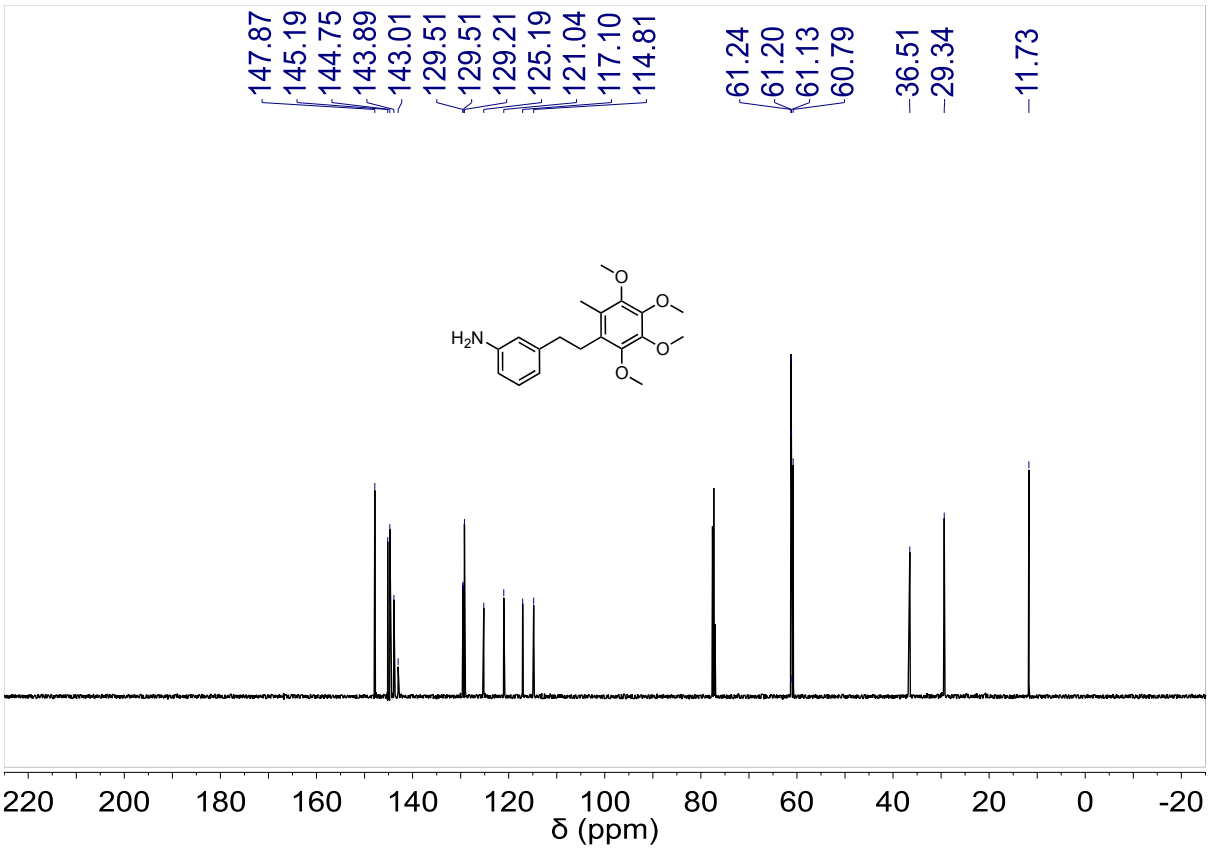


Figure S27. ^{13}C NMR spectrum ($CDCl_3$, 126 MHz) of compound **6**.

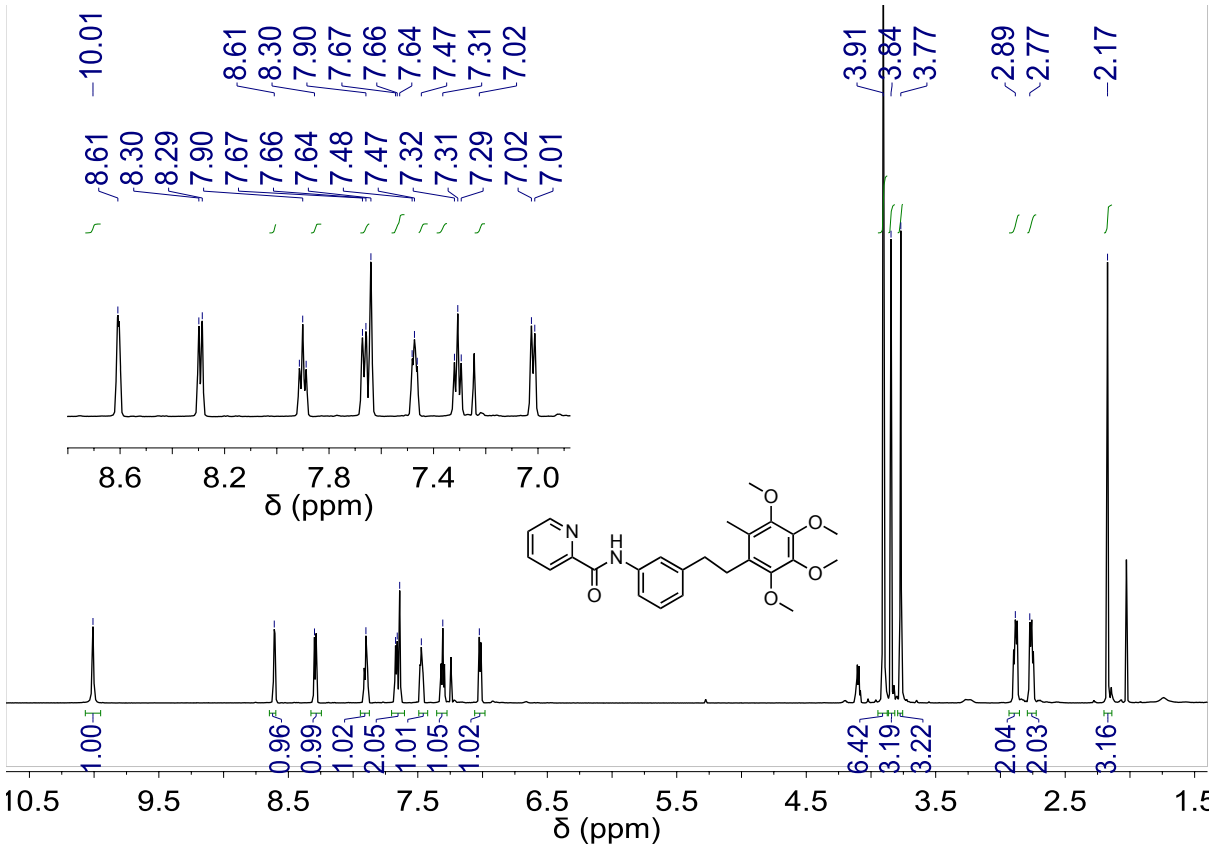


Figure S28. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of compound **7**.

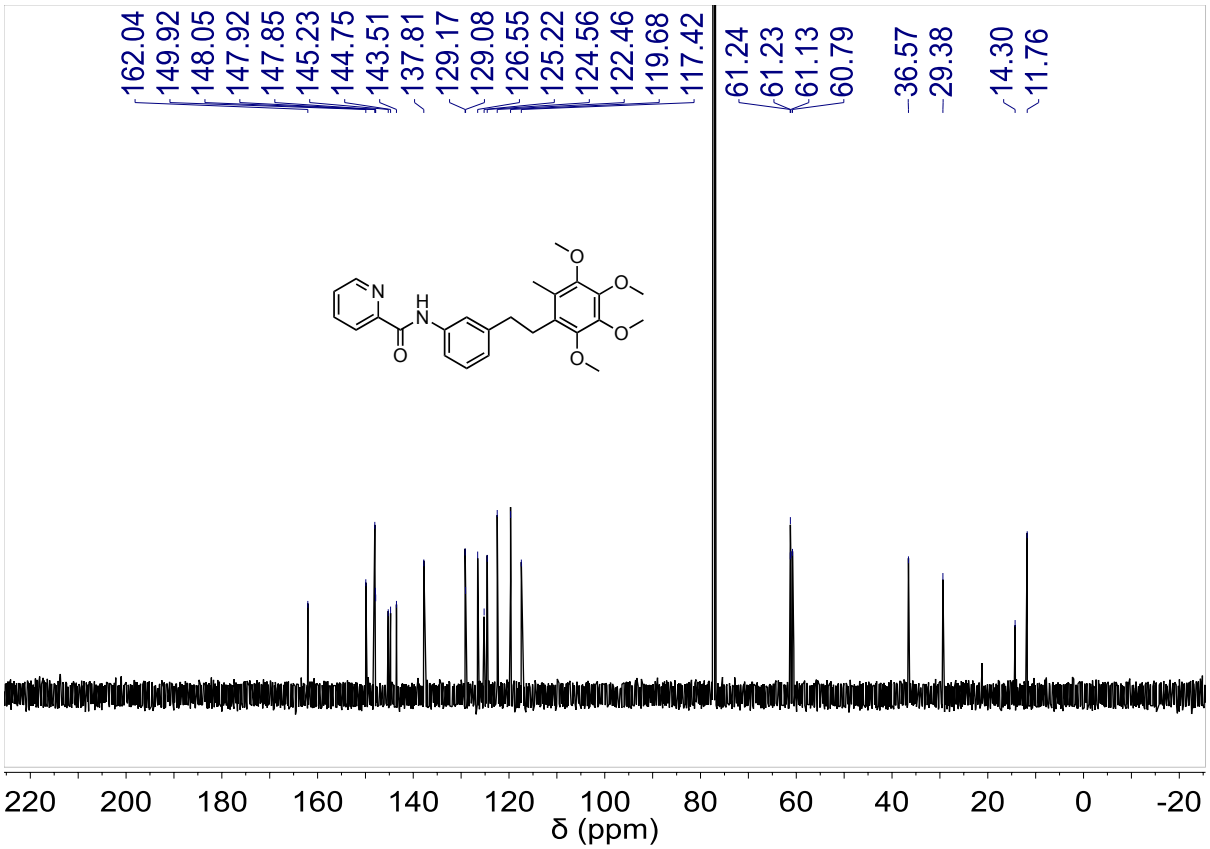


Figure S29. ^{13}C NMR spectrum ($CDCl_3$, 151 MHz) of compound **7**.

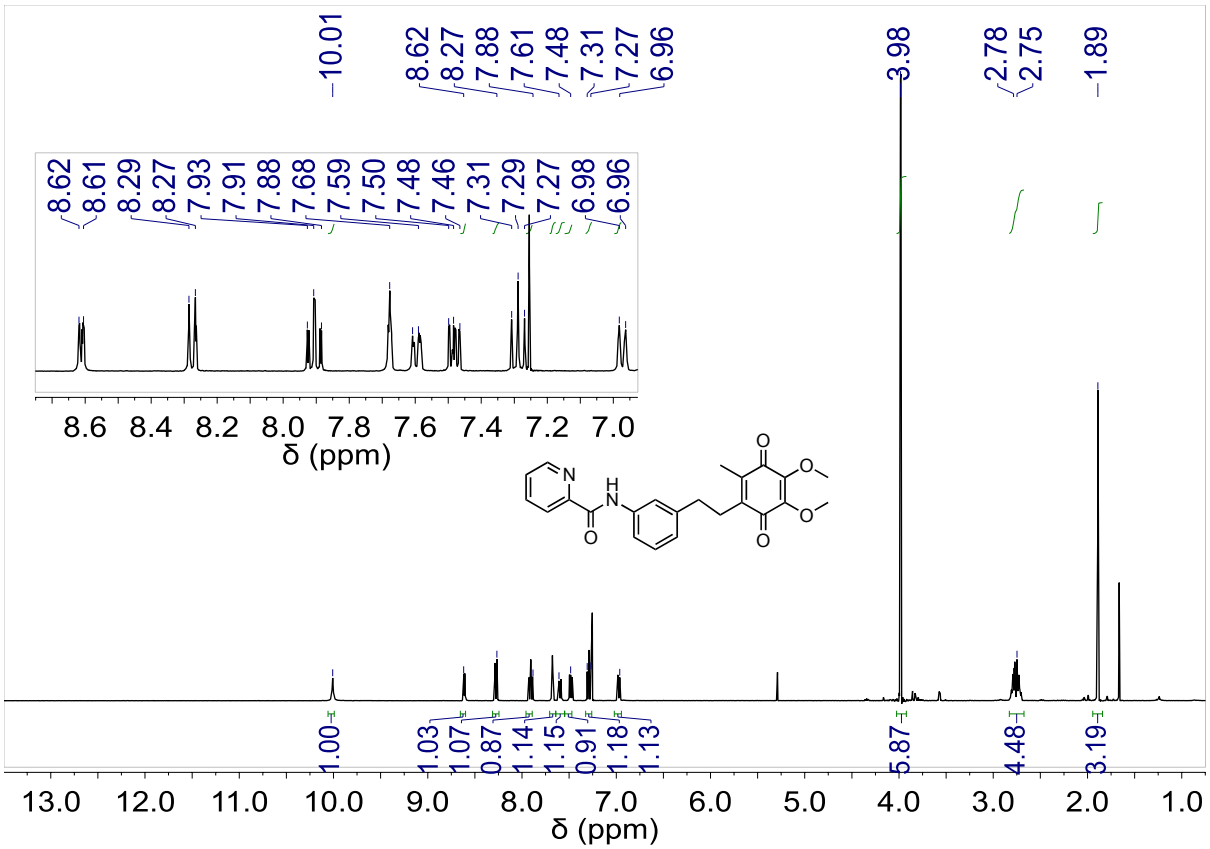


Figure S30. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of compound **8**.

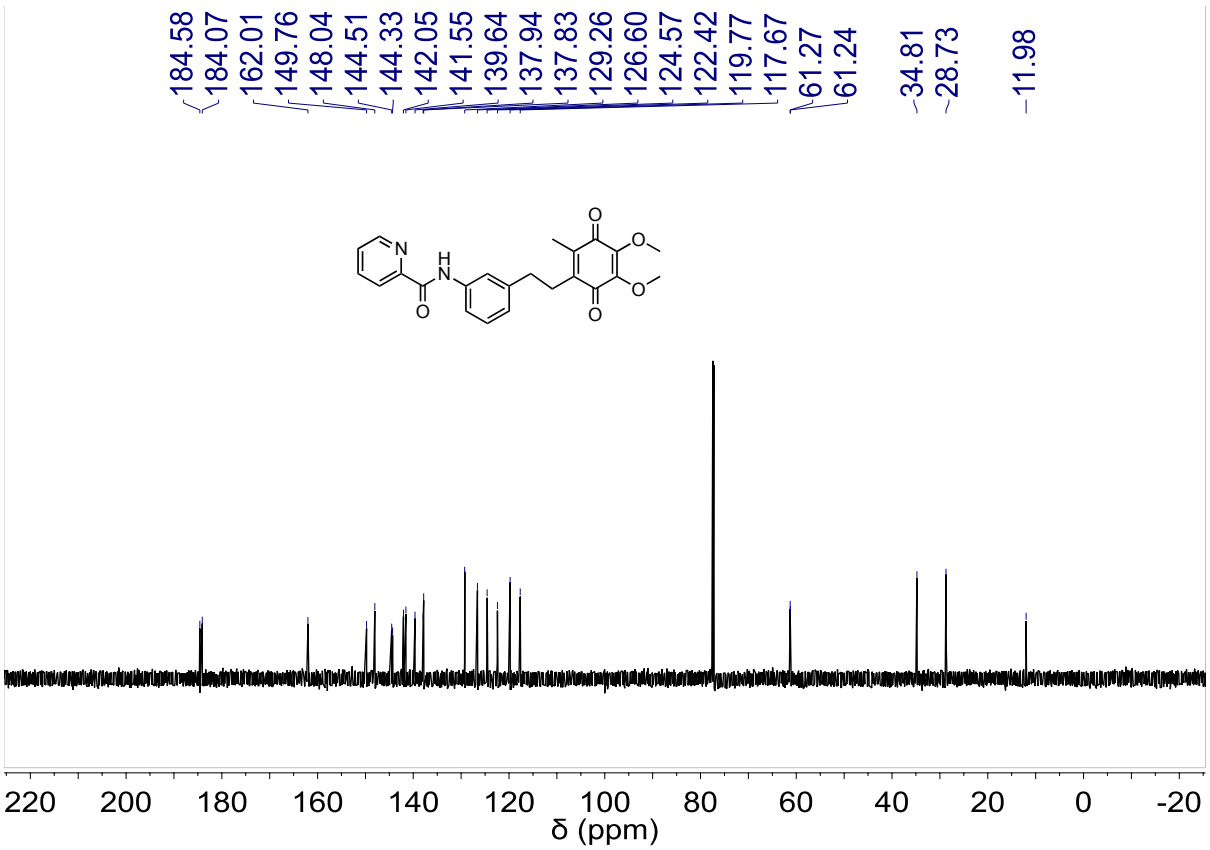


Figure S31. ^{13}C NMR spectrum ($CDCl_3$, 151 MHz) of compound **8**.

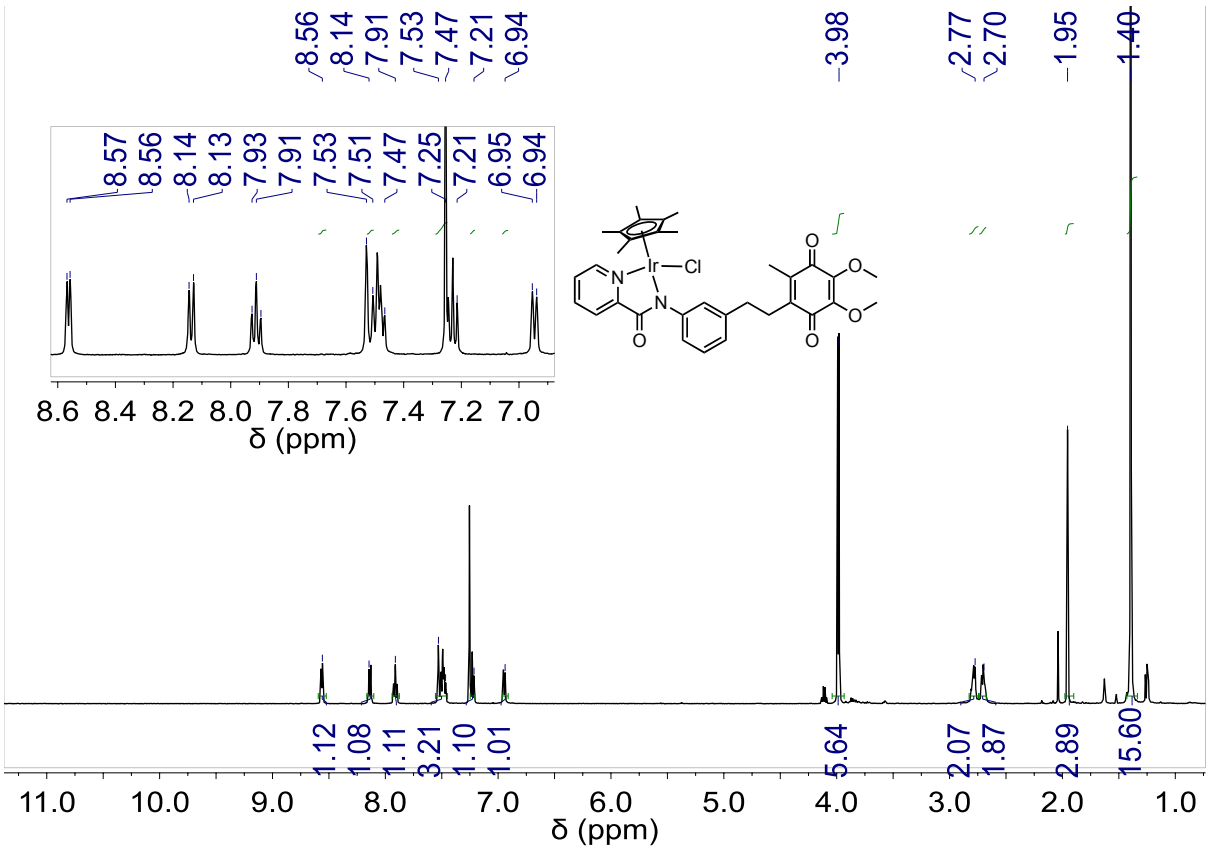


Figure S32. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **Ir3a**.

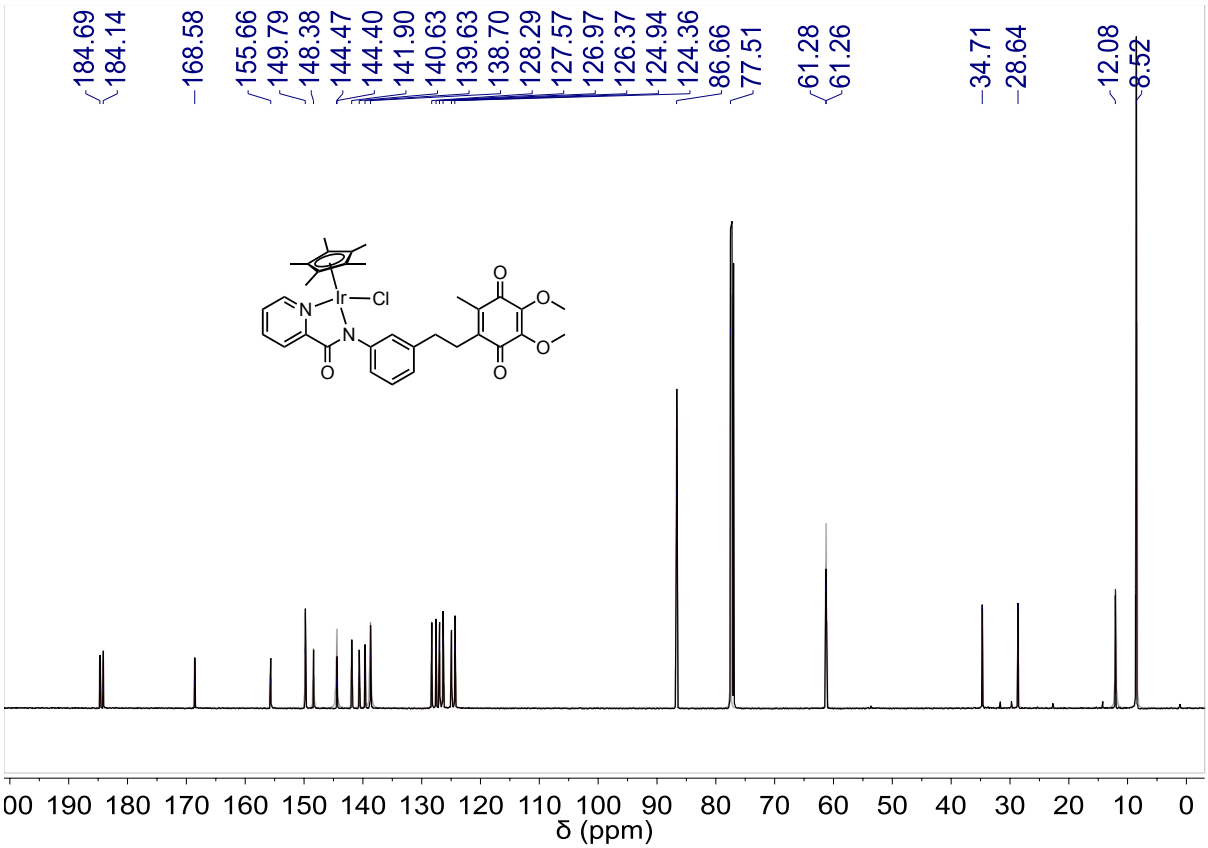


Figure S33. ^{13}C NMR spectrum ($CDCl_3$, 101 MHz) of compound **Ir3a**.

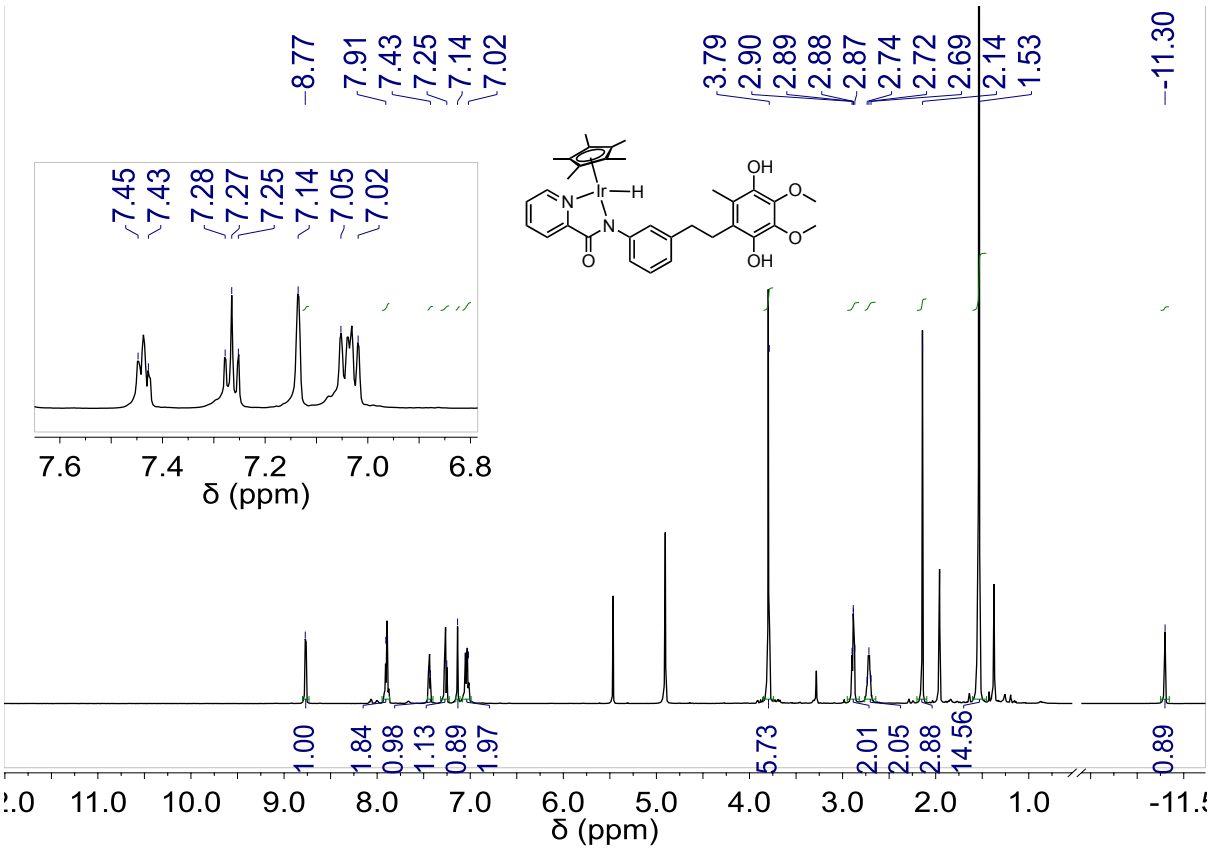


Figure S34. ^{1}H NMR spectrum (CD_3OD, 600 MHz) of compound **Ir3d**.

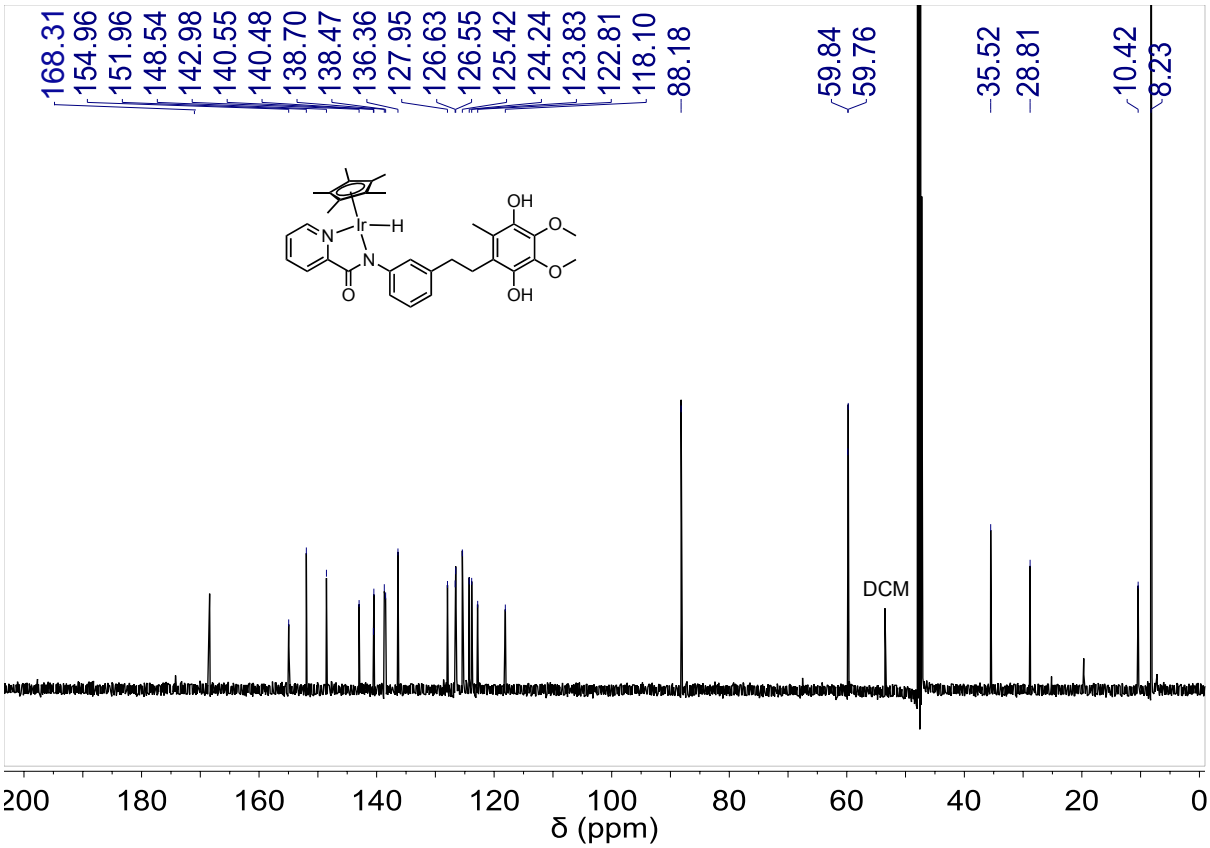


Figure S35. ^{13}C NMR spectrum (CD_3OD, 151 MHz) of compound **Ir3d**.

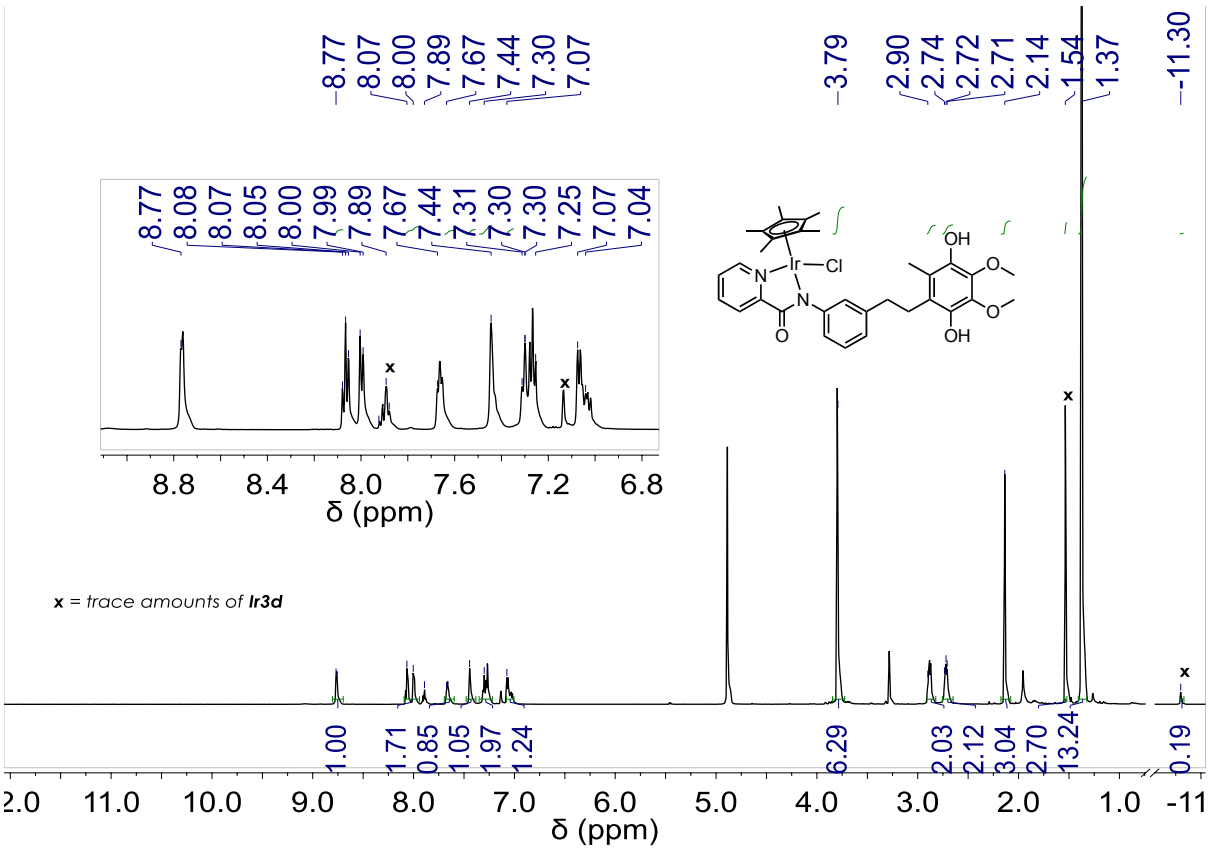


Figure S36. ^{1}H NMR spectrum (CD_3OD, 600 MHz) of compound **Ir3c**. Peaks corresponding to trace amounts of **Ir3d** present are marked with "x."

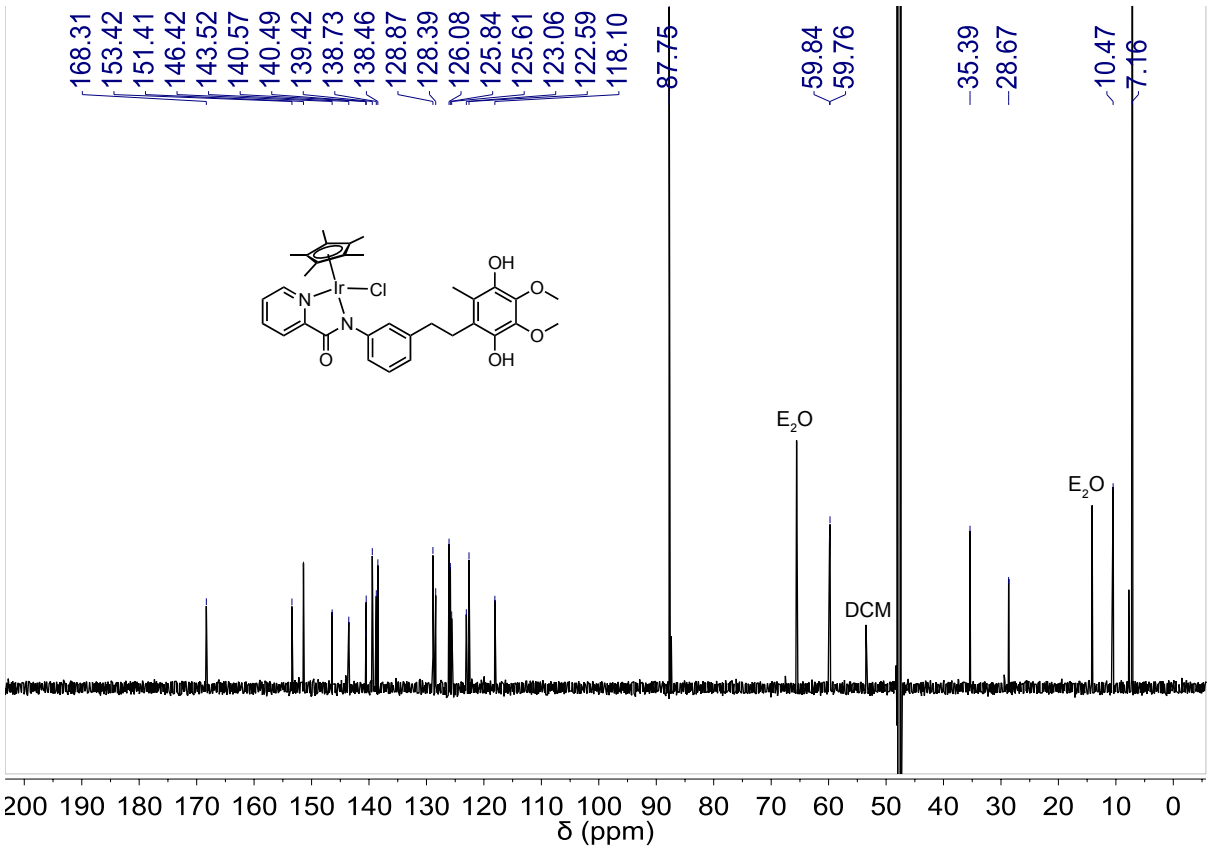


Figure S37. ^{13}C NMR spectrum (CD_3OD, 151 MHz) of compound **Ir3c**.

X-ray Data Collection and Refinement

Single crystals of complex **Ir3a** was grown from vapor diffusion of pentane into a solution of the complex in acetone. The yellow orange crystals were mounted at -150 °C on a Bruker diffractometer equipped with a CCD APEX II detector using Mo-Kα radiation. Data reduction was performed within the APEX II software and empirical absorption corrections were applied using SADABS. The structures were solved by direct methods in SHELXS and refined by full-matrix least squares based on F2 using SHELXL. All non-hydrogen atoms were located and refined anisotropically. Hydrogen atoms were fixed using a riding model and refined isotropically. The acetone solvent molecule was located on an inversion center and was refined with half occupancy using a negative part number to suppress generation of special position constraints and bonds to symmetry-related atoms.

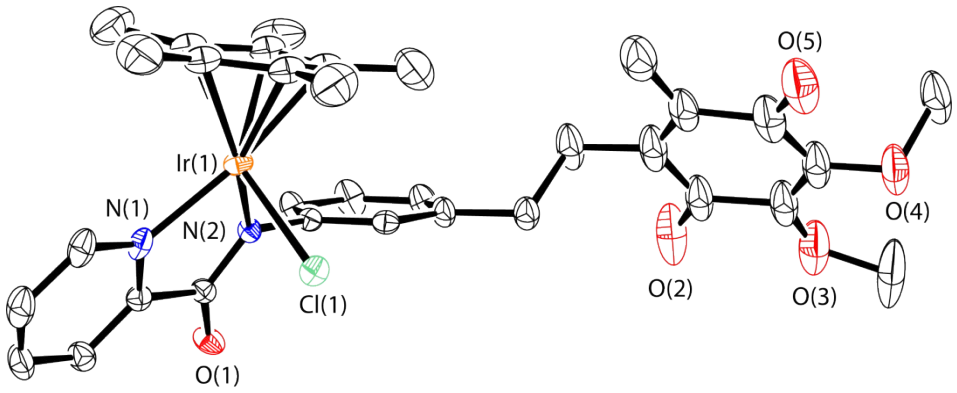


Figure S38. The molecular structure of **Ir3a** shown in ORTEP view with displacement ellipsoids drawn at 50% probability level. The hydrogen atoms and acetone solvent molecule have been omitted for clarity.

Table S3. Crystallographic Table for Complex **Ir3a**

	Ir3a·acetone
Empirical Formula	$(IrC_{33}H_{35}ClN_2O_5)\cdot(C_3H_6O)_{0.5}$
Formula Weight	796.32
Temperature (°C)	-150
Wavelength (Å)	0.71073
Crystal System,	Triclinic,
Space Group	P-1
Unit Cell Dimensions	
a (Å)	7.7989(15)
b (Å)	9.4618(18)
c (Å)	24.171(5)
α (°)	95.058(2)
β (°)	94.646(3)
γ (°)	112.464(2)
Volume ($Å^3$)	1629.0(5)
Z, Calculated Density (Mg/m^3)	2, 1.623
Absorption Coefficient (mm^{-1})	4.225
F(000)	794
Crystal Size (mm^3)	0.20 x 0.17 x 0.1
Theta Range for Data Collection (°)	0.852 to 26.372
Limiting Indices	$-9 \le h \le 8$ $-11 \le k \le 11$ $-21 \le l \le 29$
Reflections Collected/ Unique	8585 / 6530 [R(int) = 0.0114]
Completeness	99.1%
Absorption Correction	Empirical
Max. and Min. Transmission	0.7456 and 0.5454
Refinement Method	Full-Matrix Least–Squares on F^2
Data/ Restraints/ Parameters	6530 / 107 / 356
Goodness of Fit on F^2	1.322
Final R Indices	R_1= 0.0478
[I > 2σ(I)]	wR_2 = 0.1170
R Indices (All Data)*	R_1 = 0.0488
	wR_2 = 0.1188
Largest Diff. Peak and Hole (e $Å^{-3}$)	2.713 and -2.168

*$R_1 = \Sigma\ ||F_o|-|F_o||/\Sigma|F_o|$; $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)_2]]^{1/2}$; GOF = $[\Sigma[w(F_o^2 - F_c^2)_2]/(n-p)]^{1/2}$, where *n* is the number of reflections and *p* is the total number of parameters refined.

References

(1) Yang, L.; Bose, S.; Ngo, A. H.; Do, L. H. *ChemMedChem* **2017**, *12*, 292-299.
(2) Wang, J.; Li, S.; Yang, T.; Zeng, J.-R.; Yang, J. *Chem. Pap.* **2015**, *69*, 486-489.