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SUPPORTING INFORMATION

Experimental and Theoretical Investigation of Cyclometalated Phenylpyridine Iridium (III) Complex Based on Flavonol and Ibuprofen Ligands as Potent Antioxidant

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Synthesis of the Complex [Ir(ppy)(Ibu)(Fla)]

To a solution of $IrCl_3 \cdot 3H_2O$ (0.30 mmol, 105.78 mg) in 2-ethoxyethanol/water (2:1, v/v) (20 mL), were added 2-phenylpyridine (0.32 mmol, 49.66 mg), ibuprofen (0.32 mmol, 66.01 mg), 3-hydroxyflavone (0.32 mmol, 76.23 mg) and NaOH (1.60 mmol, 63.95 mg). The solution was put in a microwave reactor (maximum pressure: 5 bar; maximum power: 350 W) at 130 ºC for 45 min. The solvent was then evaporated under reduced pressure and the crude product was collected and purified by column chromatography on silica gel (9:2 DCM: hexane) to afford the title complex as a yellow solid (148.4 mg, 0.30 mmol, 62.7% yield). ^{1}H NMR (DMSO-d_6): δ 8.62 (d, 2H, H-Ar, J = 7.6 Hz), 8.29 (d, 1H, H-Ar, J = 7.6 Hz), 8.11 (d, 1H, H-Ar, J = 7.6 Hz), 7.70-7.92 (m, 2H, H-Ar), 7.65-7.69 (m, 3H, H-Ar), 7.49-7.56 (m, 3H, H-Ar), 7.32-7.39 (m, 3H, H-Ar), 7.20 (d, 2H, H-3b, J = 7.6 Hz), 7.02-7.09 (m, 2H, H-Ar), 6.92 (t, 1H, H-Ar, J = 7.6 Hz), 6.34 (d, 1H, IrC=C*H*, J = 7.6 Hz), 3.13 (q, 1H, OOCC*H*(CH3), J = 6.0 Hz), 2.32 (d, 2H, CH_2CH(CH_3)$_2$, J = 6.0 Hz), 1.84-1.93 (m, 1H, CH$_2$C*H*(CH_3)$_2$), 1.10 (d, 3H, OOC-CHCH_3, J = 7.6 Hz), 0.81 (d, 6H, CH$_2$CH(CH_3)$_2$, J = 6.0 Hz). ^{13}C NMR (DMSO-*d6*): δ 176.8 (C=O), 173.6 (C=O), 165.2 (Ar), 159.3 (Ar), 153.0 (Ar), 148.8 (Ar), 145.8 (Ar), 142.1 (Ar), 136.9 (Ar), 131.5 (Ar), 129.2 (Ar), 127.1 (Ar), 124.9 (Ar), 122.1 (Ar), 120.0 (Ar), 116.2 (Ar), 46.1 (CH (C35), CH_2 (C32)), 30.0 (CH (C31)), 24.1 (CH_3 (C36,37)), 17.0 (CH_3 (C42)). Anal. Calc. (%) for $C_{39}H_{34}IrNO_5$ (789.2066): C, 59.38; H, 4.34; N, 1.78; Found (%): C, 59.34; N, 1.75. TOF-MS: 790.2144 $[M + H]^+$.

Stability test

The stability of the Ir (III) complex was tested by dissolving the complex in PBS buffer/1% DMSO and keeping the solution at 37 °C for 3 days. Briefly, a 12 µL of the solution was injected into an HPLC system (Thermo, USA) connected to a UV-Vis spectrophotometer with 254 nm UV detector at room temperature. The mobile phase was 0-100 % linear gradient of hexane in chloroform over 20 min with flow rate 0.5 mL.mn^{-1}. A Hypersil Gold Dim (100 × 2.1 mm, Thermo, USA) reversed-phase column was used at a flow rate of 0.5 mL.mn^{-1}.

DPPH•, HO•, NO•, and ABTS•+ Radicals Scavenging Assay

DPPH•

The DPPH• assay was carried out using the reported method with slight modifications.[1,2] To a 0.1 mM solution of DPPH• in MeOH (1 mL), was added a 25-150 μM solution of the inquired antioxidant in methanol (3 mL) and the reaction mixture was shaken vigorously. The reduction of DPPH• absorbance was followed by monitoring at 517 nm every 5 min for about 35 min. As a control, the absorbance of the blank solution of DPPH• was also registered at 517 nm.

ESR spin trapping were applied to detect the DPPH• radical scavenging activity by potential antioxidant compounds as previously described.[2,3] A solution of 25-150 μM of inquired antioxidant in MeOH (60 μL) was added to a 0.1 mM solution of DPPH in MeOH (60 μL). After mixing vigorously for 10 s, the solution was transferred into a 100 μL quartz capillary tube, and the spin adduct was measured after 2 mn. Trolox (Sigma-Aldrich) was used as positive control.

HO•

Hydroxyl radical (HO•) scavenging activity was investigated based on the method reported in the literature. [2,4] Briefly, different concentrations of (25-150 μM) of the inquired antioxidant (20 μL) were added to the reaction mixture containing 8 mM $FeSO_4$ (0.25 mL), 6 mM H_2O_2 (0.4 mL), 0.25 mL distilled water and 20 mM sodium salicylate (0.1 mL) (final concentration 1 mM). Then the reaction system was incubated at 37 ºC for 1 h. Absorbance value was measured at 562 nm.

For HO• scavenging assay by ESR spectroscopy, the Fenton reagents were used to test the ability of antioxidants. [2,5] The reaction mixture contained 10 mM DMPO, 100 μM $FeSO_4$, 10 mM H_2O_2 with and without the presence of the studied antioxidant at different concentrations (25-150 μM). After stirring for 5 s, 50 μL of the mixture were transferred into a 100 μL disposal capillary tube. The ESR spectrum was recorded after 2.5 minutes. Ascorbic acid was used as positive control.

NO•

Nitric oxide radical (NO•) scavenging activity was investigated based on the method reported in the literature. [6,7] Briefly, 5 mM sodium nitroprusside (2 mL) in 0.2 M phosphate buffer (pH 7.4), was incubated with different concentrations (25–150 μM, 0.5 mL) of the inquired antioxidant (dissolved in methanol) at 25 ºC for 150 min. Griess reagent was prepared by mixing equal volume of 1% sulphanilamide in 2% phosphoric acid and 0.1% N-(1-naphthyl) ethylenediamine

dihydrochloride. To 0.5 mL of incubated antioxidant solution was added immediately 0.5 mL of Griess reagent and the absorbance were immediately recorded at 546 nm.

The $NO^{\bullet}$ scavenging assay was studied by ESR as the method reported in literature.[8] The nitric oxide radical was generated from S-nitroso-N-acethylpenicillamine, and an iron–dithiocarbamate complex [$(MGD)_2$–Fe^{2+}] was used as the trapping agent. Spin trap iron–dithiocarbamate complex [$(MGD)_2$–Fe^{2+}] was prepared by reacting 25 mM of MGD with 5 mM of Fe_2SO_4. Iron sulfate solution was freshly prepared in distilled water for each experiment. The reaction mixture was mixed in sequence starting with 5 μL of 5 mM SNAP, 5 μL of [$(MGD)_2$–Fe^{2+}], and 80 μL of deionized water, followed by addition of 10 μL of test compound to give a total volume of 100 μL. The inquired antioxidant was prepared in methanol (25–150 μM). After mixing, the solution was incubated at 37 °C in a water bath for 10 min and then transferred into a 100 μL disposal capillary tube of the ESR spectrometer. Hemoglobin (Sigma-Aldrich) was used as positive control.

$ABTS^{\bullet+}$

$ABTS^{\bullet+}$ radical scavenging activity was performed based on the reported method.[2,9] Briefly, ABTS powder (54.2 mg) was dissolved in 10 mL of phosphate buffer (5 mM, pH 7.0). To that mixture, 1.0 g of MnO_2 was added and the resulting solution was incubated at room temperature for 30 min to generate a green color $ABTS^{\bullet+}$ solution. The solution was centrifuged for 5 min and filtered to remove all excess of MnO_2. The filtrate was diluted with phosphate buffer until the absorbance of solution measured at 723 nm equal to 0.70 ± 0.01 (final concentration 1 mM). Different concentrations (5-15 μM) of the inquired antioxidant (20 μL) were added to 2 mL of $ABTS^{\bullet+}$ solution and the solution was incubated at room temperature for 10 min. The absorbance was monitored at 734 nm after 10 min.

For $ABTS^{\bullet+}$ radicals scavenging assay by ESR, a solution of different concentrations (25–150 μM) of the inquired antioxidant in EtOH (50 μL) was added to a 50 μM solution of $ABTS^{\bullet+}$ in EtOH (50 μL). After mixing vigorously for 5 s, the solution was transferred into a 100 μL quartz capillary tube, and the spin adduct was measured after 3 minutes.

For all assays by UV–Vis spectroscopy, the radical scavenging activity (RSA) was calculated using the following equation:

$$RSA(\%) = \left(1 - \frac{A}{A_0}\right) \times 100$$

where A_0 is the absorbance of the control, and A is the absorbance of test sample.

For all assays by ESR, the radical scavenging activity (RSA) was calculated using the following equation:

$$RSA(\%) = \left(1 - \frac{H}{H_0}\right) \times 100$$

where H and H_0 were the height of the third resonance peak for test sample and the control, respectively.

Cell culture

The A549 (human non-small cell lung carcinoma), A2780 (human ovarian carcinoma), and A2780*cis* (subline resistant to *cis*-platin) cancer cell lines were obtained from the American Type Culture Collection (ATCC, USA). All reagents and cell culture media were purchased from Sigma-Aldrich. The cells were maintained in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% FBS, 100 IU mL^{-1} of penicillin, 100 µg mL^{-1} of streptomycin and 2 mM of Glutamax at 37 ˚C in a humidified incubator at 5% CO_2. The adherent cultures were grown as monolayers and were passaged once in 4-5 days by trypsinizing with 0.25% Trypsin-EDTA.

Cytotoxicity

The growth inhibitory effect towards tumor cells was evaluated by means of the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tetrazolium reduction assay.[10] Stock solutions of free ligands and Ir (III) complex were prepared by dissolving the compounds in DMSO (0.1%) and for *cis*-platin by dissolving in 0.9% NaCl aqueous solution. The stocks were further diluted with the respective medium containing 10% FBS (0.02–10 µM) before addition to the cells. Cells were trypsinized with 0.25% trypsin-EDTA and counted with 0.4% trypan blue. The cells were seeded at a concentration of (3-8) × 10^3 cells/well, dependent upon the growth characteristics of the cell line, and grown at 37 °C for 24 h in a humidified incubator. After 24 h, the medium was removed and replaced with fresh medium containing the compound to be studied at the appropriate concentration. Triplicate cultures were established for each treatment. After 48 h, each well was treated with 10 µl of a 5 mg/mL MTT saline solution, and, following 5 h of incubation, 100 µl of

a sodium dodecylsulfate solution in HCl (0.01 M) was added. The optical absorbance of each well (96-well plates) was quantified using EnVision multilabel plate readers (PerkinElmer, Waltham, MA, USA) at 570 nm wavelength. The mean absorbance for each drug dose was expressed as a percentage of the control, untreated well absorbance and plotted *vs*. drug concentration. The data exported to Graphpad Prism version 6.0 for Windows and plotted in the logarithmic form to determine the IC_{50} values. The IC_{50} value was calculated as the concentration reducing the proliferation of the cells by 50% and is presented as a mean (±SE) of three independent experiments each with triplicates. $P < 0.05$ was considered to be statistically significant.

Due to the stability of the Ir (III) complex under physiological like conditions and its great potential antioxidant activity, the cytotoxicity of this complex was screened against a panel of different cancer cell lines, including A549 (human non-small cell lung carcinoma), A2780 (human ovarian carcinoma), and A2780*cis* (subline resistant to *cis*-platin). The cytotoxic activity of the Ir (III) complex was compared with free ligands and *cis*-platin as reference drug under the same experimental conditions (Table S5). The free ligands flavonol, ibuprofen, and phenylpyridine revealed very low cytotoxic activity after 48 hours of incubation and did not show IC_{50} values in the used concentration range (up to 100 μM) in the studied cell lines. Remarkably, the IC_{50} values of the Ir (III) complex were found to be in the low μM range. The Ir (III) complex presented IC_{50} values ranging from 0.48 to 1.37 μM for cancer cell lines A2780 and A2780*cis*, respectively. Also, the IC_{50} value for Ir (III) complex was 7.24 μM on A549 cell lines, which is 2-fold more active than *cis*-platin (18.90 μM). Overall, the Ir (III) complex was more potent than *cis*-platin on A549 (2.6-fold), A2780 (6.75-fold) and A2780*cis* (20.9-fold) cancer cell lines (Table S7 and Figure S9).

Reactive oxygen species (ROS) production

The A549 cells (3×10^4/mL) were plated in 96-well tissue culture plates and test Ir (III) complex and pyocyanin were added at 300 μM concentration one day later of incubation at 37 °C, 5% CO_2 and 95% humidity in the dark for 24 or 48 h. A 0.1% solution of NBT (50 μL/well) in PBS was added to the cells after centrifugation (300 g, 5 min, 4 °C) and removal of the medium. After another 4 h of incubation the microplates were centrifuged and the supernatant NBT solution was discarded. The reduced formazen were dissolved sequentially in 120 μL of 2M KOH followed by 100 μL of DMSO and read at 620 nm using KOH/DMSO as a blank. Results were expressed as means of at least three replicates ± standard error.

Oxidative stress increases the intracellular concentration of reactive oxygen species (ROS) that cause damage to lipids, proteins and DNA. However, antioxidants with ROS scavenging ability play an important role in the prevention of oxidative stress. [11] To explore the effect of new compound on ROS production, the A549 cancer cells were treated with the Ir (III) complex with incubation time from 24 to 48 hours. The pyocyanin was also tested as ROS positive control. The Ir (III) complex induced an obvious intracellular ROS production in A549 cancer cell lines after 24 or 48 hours of incubation, which is about 8.5-fold or 1.5-fold higher than the control group or pyocyanin, respectively (Figure S10). Increasing the incubation time from 24 to 48 hours also increased the ROS level about 1.5-fold, induced by Ir (III) complex. This study suggested that the new Ir (III) complex is a potent ROS generator and the ROS production can be responsible for cytotoxic activity by this complex.

Statistical Analyses

Statistical analyses were carried out using ANOVA and a Student's t-test and the Kruskal–Wallis and Mann–Whitney U-test (SPSS for Windows version 10.0). Data's were represented as means ± SEM and differences were considered statistically significant at $p<0.05$.

Chemical stability of Ir (III) complex

The Ir (III) complex is air-stable and soluble in methanol, ethanol, DMF and DMSO. In order to confirm the stability of Ir (III) complex in biological media and in solution, the stability test was directed in a solution phase (DMSO/PBS, 1:99 v/v) solution by HPLC-UV at 37 ºC over a period of 72 h. There was no evident change in retention time during the three days of observation, indicating that Ir (III) complex is stable under physiological conditions (Figure S4).

Calculation of thermochemical properties

H is the total enthalpy of the studied species at 298.15 K and 1 atm and usually estimated from the following expression:

$$H = E_0 + ZPE + H_{trans} + H_{rot} + H_{vib} + RT$$

where E_0 was the total energy at 0 K, ZPE was the zero-point vibrational energy, H_{trans}, H_{rot} and H_{vib} were translational, rotational and vibrational contributions to the enthalpy. The enthalpy value for hydrogen atom ($H^{\bullet}$) was calculated at the same level of theory as for the complex, while the enthalpies in the gas phase of proton and of electron were taken as 1.4811 and 0.7519 kcal/mol,

values widely accepted in the literature.[12] The enthalpies of proton and of electron in solvent were calculated by assuming the hydration of a proton or an electron with a molecule of solvent using the polarizable continuum model with integral equation formalism variant IEF-PCM. Water and pentylethanoate (PEA) were used as solvents in order to consider the influence of lipid media on the reactivity of the studied compounds by placing the solute in a cavity within the solvent reaction field (SCRF method). The Polarizable Continuum Model (PCM) using the integral equation formalism variant (IEFPCM) as default were used.[13, 14]

- *Hydrogen atom transfer (HAT)*:

$R–H \rightarrow R^{\bullet} + H^{\bullet}$, (BDE) (R1)

$BDE = H(R^{\bullet}) + H(H^{\bullet}) – H(R–H)$ (eq.1)

- *Proton loss (PL)*:

$R–H \rightarrow R^{-} + H^{+}$, (PA) (R2)

$PA = H(R^{-}) + H(H^{+}) – H(R–H)$ (eq.2)

- *Single electron transfer (SET)*:

$R–H \rightarrow (R–H)^{+\bullet} + e^{-}$, (IP) (R3)

$IP = H(R–H^{+\bullet}) + H(e^{-}) – H(R–H)$ (eq.3)

$R–H + e^{-} \rightarrow (R–H)^{-\bullet}$, (EA) (R4)

$EA = H(R–H) + H(e^{-}) – H(R–H^{-\bullet})$ (eq.4)

- *Proton transfer step of SETPT mechanism*:

$(R–H)^{+\bullet} \rightarrow R^{\bullet} + H^{+}$, (PDE) (R5)

$PDE = H(R^{\bullet}) + H(H^{+}) – H(R–H^{+\bullet})$ (eq.5)

- *Electron transfer step of SPLET mechanism*:

$R^{-} \rightarrow R^{\bullet} + e^{-}$, (ETE) (R6)

$ETE = H(R^{\bullet}) + H(e^{-}) – H(R^{-})$ (eq.6)

- *Hydration of proton*:

$H^{+}_{gas} + H_2O_{aq} \rightarrow H_3O^{+}_{aq}$ (R7)

$\Delta H(H^{+})_{aq} = H(H_3O^{+})_{aq} – H(H_2O)_{aq} – H(H^{+})_{gas}$ (eq.7)

- *Hydration of electron*:

$e^{-}_{gas} + H_2O_{aq} \rightarrow H_2O^{-\bullet}_{aq}$ (R8)

$\Delta H(e^{-})_{aq} = H(H_2O^{-\bullet})_{aq} – H(H_2O)_{aq} – H(e^{-})_{gas}$ (eq.8)

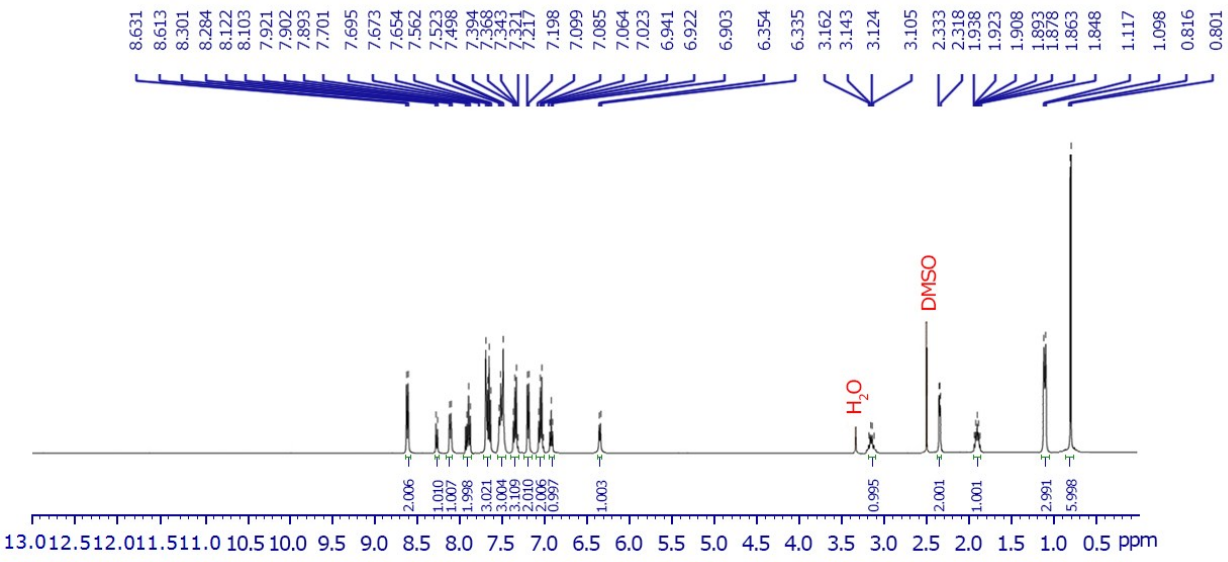

Figure S1. ^{1}H-NMR spectrum of Ir (III) complex (DMSO-d_6).

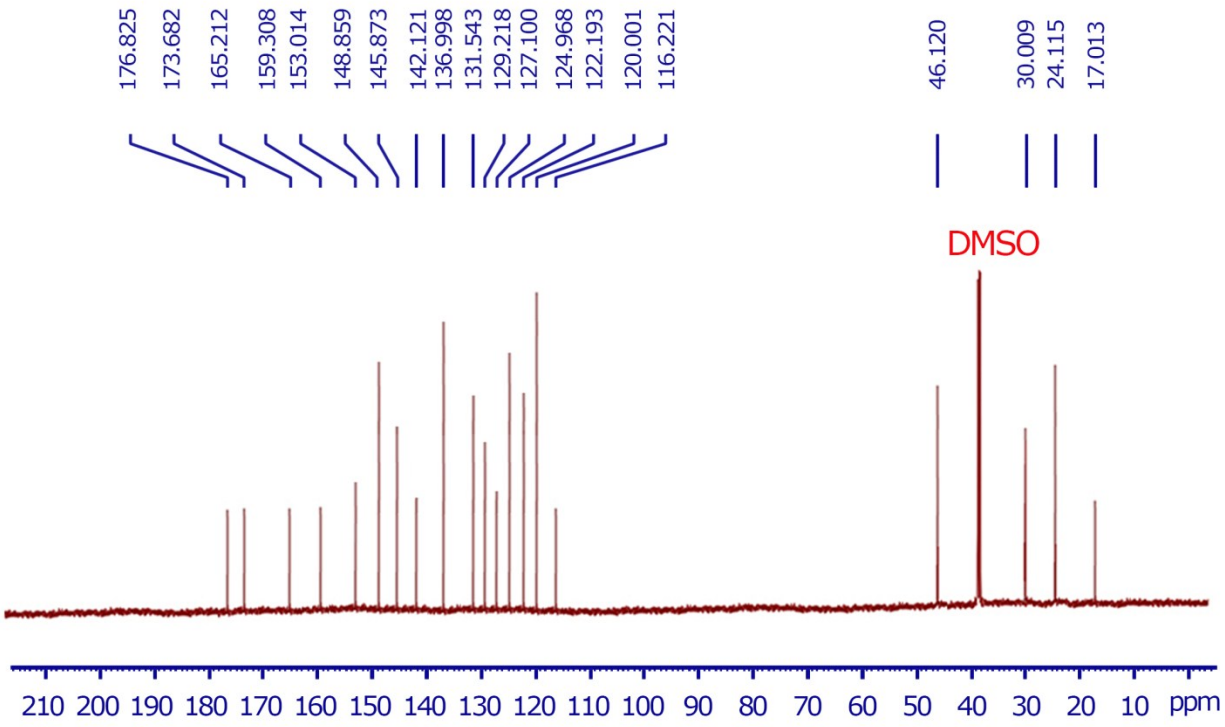

Figure S2. ^{13}C-NMR spectrum of Ir (III) complex (DMSO-d_6).

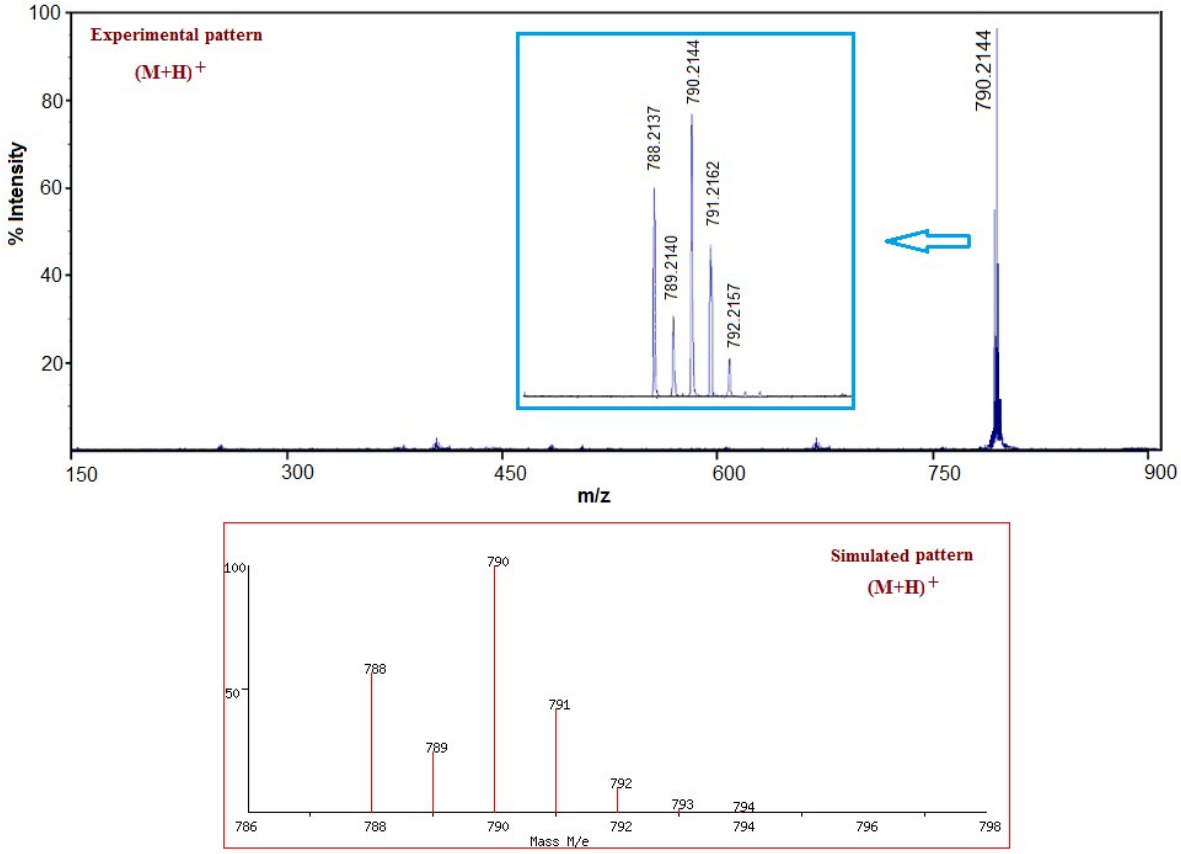

Figure S3. TOF-MS spectrum of Ir (III) complex.

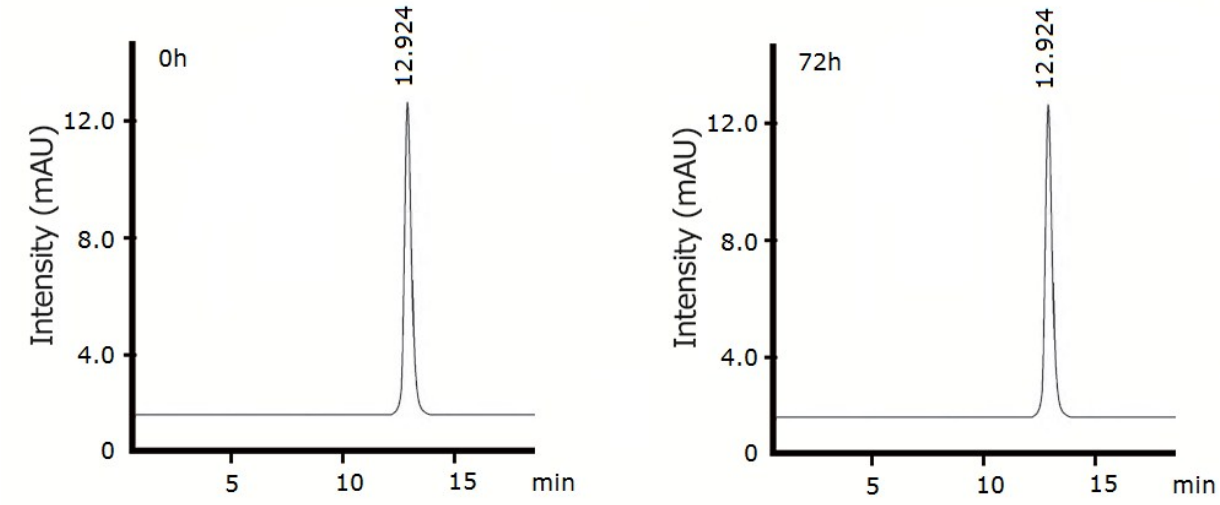

Figure S4. HPLC chromatogram of the Ir (III) complex in PBS/DMSO (1%) solution before and after incubation time (72h) at 37 ºC.

Table S1. Cartesian coordinates of molecules and transition states of HAT and RAF reactions

N^0	**Compound**		
1	Ir (III) complex		
	0 1		
	O	4.90684400	1.54367000	1.31787200
	O	1.99301800	-0.50827000	0.65985200
	O	1.60342800	1.51190100	-1.04211200
	C	3.58757300	2.63280700	-0.37038500
	C	4.03692900	0.48734400	1.41242600
	C	4.71146000	2.57929300	0.47307500
	C	4.46810700	-0.50455100	2.39563800
	C	2.89128100	0.45817900	0.61573000
	C	2.64992200	1.54549600	-0.30381200
	C	3.43541600	3.74159300	-1.23402500
	C	5.67328700	3.60031800	0.46944700
	C	5.67404800	-0.31719400	3.10684300
	C	3.70610700	-1.66350900	2.66033000
	C	4.38056500	4.74925600	-1.24072900
	C	5.50134400	4.67601000	-0.38579400
	C	6.09963100	-1.25202200	4.04403700
	C	4.14451100	-2.59273000	3.60123200
	C	5.33806800	-2.39629100	4.29776000
	H	2.56475100	3.77271700	-1.88023900
	H	6.52721400	3.52462600	1.13448500
	H	6.27423000	0.56502800	2.91917800
	H	2.78005200	-1.81772100	2.12383500
	H	4.26397300	5.60111400	-1.90382600
	H	6.24010700	5.47225000	-0.39659800
	H	7.03099800	-1.08672400	4.57920700
	H	3.54396900	-3.47854900	3.79046700
	H	5.67288900	-3.12531600	5.03081600
	Ir	0.45380900	-0.19584700	-0.68794400
	O	-1.21086100	0.47258000	-1.78043500
	O	-1.20137400	1.23467200	0.28622900
	C	-8.84399600	0.46724000	1.83669600
	C	-7.70267900	-0.51549200	1.44617200
	C	-6.49149600	0.10209600	0.77632700
	C	-4.22655500	1.28132600	-0.47685600
	C	-3.03292900	1.93744000	-1.16489000
	C	-8.39808100	1.50181300	2.87963300
	C	-9.47341800	1.15134500	0.61490400
	C	-5.40035300	0.56510100	1.52794700
	C	-6.41571700	0.22799900	-0.61737200
	C	-4.28939300	1.14669500	0.91814400
	C	-5.30487000	0.80727600	-1.23265400
	C	-2.88519100	3.42435600	-0.78107200

C	-1.74705400	1.18479600	-0.85042600
H	-9.62068700	-0.15789400	2.30218300
H	-8.12791700	-1.28057800	0.78294000
H	-7.38108500	-1.03823100	2.35701400
H	-3.17816800	1.85939200	-2.24681500
H	-7.62546300	2.16665900	2.47682500
H	-7.98993800	1.01792900	3.77576400
H	-9.24398600	2.12497000	3.19352600
H	-10.32501800	1.77359400	0.91491000
H	-8.75098700	1.79839200	0.10432300
H	-9.83798000	0.41594300	-0.11315700
H	-5.41864400	0.46340900	2.61095000
H	-7.23341600	-0.14018700	-1.23286900
H	-3.45343300	1.48266600	1.52420000
H	-5.27410800	0.88636600	-2.31705400
H	-3.80651000	3.96716100	-1.01651000
H	-2.68021900	3.53018900	0.28763700
H	-2.05875400	3.88660100	-1.33263100
C	-0.11835300	-3.02496200	-0.96746200
C	-0.71954900	-4.26358800	-0.70937200
C	-1.73181300	-4.36444400	0.23689300
C	-2.14432200	-3.21945100	0.92388600
C	-1.51947500	-2.01339000	0.63900100
C	0.93581500	-2.74698500	-1.93761900
C	1.49389700	-3.70453700	-2.79961800
C	2.47324800	-3.33035400	-3.71305300
C	2.89142700	-1.99467100	-3.76995500
C	2.34194300	-1.03632600	-2.91658100
H	-0.38842900	-5.13969300	-1.25550600
H	-2.19820700	-5.32514800	0.43561100
H	-2.93649500	-3.25197300	1.66361400
H	-1.79235400	-1.08461800	1.12646100
H	1.16275500	-4.73962000	-2.76415700
H	2.90651800	-4.06963900	-4.38076800
H	3.65295600	-1.69999700	-4.48858800
H	2.67135100	-0.00362200	-2.98338600
N	-0.53373000	-1.91950900	-0.27380200
C	1.35973100	-1.39214200	-1.98191300

Zero-point correction= 0.640598 (Hartree/Particle)
Thermal correction to Energy= 0.680988
Thermal correction to Enthalpy= 0.681933
Thermal correction to Gibbs Free Energy= 0.562057
Sum of electronic and zero-point Energies= -2041.662603
Sum of electronic and thermal Energies= -2041.622212
Sum of electronic and thermal Enthalpies= -2041.621268

	Sum of electronic and thermal Free Energies= -2041.741144
2	TS-IrC32-OOH
	0 2 O 5.43582400 -0.14743800 -1.45453400 O 2.08494400 0.76308300 -0.41695600 O 2.27295200 -1.71683900 0.54935400 C 4.48072200 -2.01299100 -0.27789700 C 4.31032500 0.61988600 -1.28955200 C 5.53871700 -1.40713400 -0.97860300 C 4.44199300 1.94223500 -1.89788800 C 3.21044100 0.10029100 -0.60527100 C 3.28215300 -1.24398400 -0.08155600 C 4.64508500 -3.33443300 0.19634100 C 6.74230500 -2.08918200 -1.21100500 C 5.64624700 2.30940400 -2.53841600 C 3.38594700 2.87916400 -1.86629300 C 5.82914400 -4.00943800 -0.03007300 C 6.87882700 -3.38284700 -0.73572100 C 5.78710500 3.56282100 -3.12361700 C 3.54053200 4.13184800 -2.45614000 C 4.73533700 4.48270900 -3.08677600 H 3.82228800 -3.79168400 0.73541200 H 7.53638600 -1.58945800 -1.75593900 H 6.46948500 1.60594200 -2.57347500 H 2.45822400 2.61016400 -1.38022100 H 5.95597400 -5.02447100 0.33415600 H 7.80675700 -3.92001900 -0.90994300 H 6.72301000 3.82326300 -3.61096700 H 2.71577000 4.83871500 -2.42154400 H 4.84783800 5.46162400 -3.54513100 Ir 0.69740900 -0.34595400 0.64206500 O -0.74655400 -1.70916400 1.34233100 O -0.52867700 -1.79113300 -0.85210400 C -8.19955000 0.12221300 -1.32452100 C -6.71799100 0.16765400 -1.72249100 C -5.67400100 -0.73886200 -1.21402800 C -3.49215800 -2.36088600 -0.34632800 C -2.28509600 -3.14736900 0.15207500 C -8.85878000 -1.16127100 -1.87055800 C -8.52105400 0.30560200 0.16993700 C -4.66989900 -1.17784900 -2.10894100 C -5.54493000 -1.13703000 0.13484600 C -3.60793000 -1.96819300 -1.69034300 C -4.48237300 -1.93400400 0.55005000 C -1.95199900 -4.38477300 -0.69952800 C -1.10267600 -2.17945700 0.19886700

H	-8.65531300	0.97164600	-1.85352600
H	-6.30523400	1.38467600	-1.40270600
H	-6.63933400	0.26635400	-2.81191700
H	-2.47939600	-3.45612600	1.18376400
H	-8.43123200	-2.05081700	-1.39367500
H	-8.71502900	-1.25722200	-2.95283700
H	-9.93758700	-1.15408600	-1.67228200
H	-9.58508500	0.53968900	0.29384700
H	-8.32759000	-0.60620700	0.74442000
H	-7.93731700	1.11852000	0.61374600
H	-4.73234900	-0.88169600	-3.15357300
H	-6.26042500	-0.79731700	0.87284100
H	-2.84512300	-2.26067200	-2.40441100
H	-4.40437100	-2.21117700	1.59848900
H	-2.82166300	-5.04642700	-0.77047500
H	-1.64358200	-4.09829800	-1.70816300
H	-1.12716000	-4.94543700	-0.24662200
C	-0.68731200	1.94865100	1.75850400
C	-1.66501700	2.94253400	1.89012500
C	-2.69688500	3.03317100	0.96337200
C	-2.74074400	2.13610700	-0.10720200
C	-1.74362300	1.17561300	-0.20288500
C	0.42984700	1.69058500	2.66424800
C	0.70222400	2.43710000	3.82092600
C	1.77492600	2.09143100	4.63653200
C	2.57297100	0.99170700	4.29919100
C	2.30912000	0.24325200	3.15021300
H	-1.61698700	3.62737900	2.72966000
H	-3.47598000	3.78117200	1.07245700
H	-3.54574900	2.16858600	-0.83316900
H	-1.71962800	0.44020500	-0.99820800
H	0.07789400	3.28614100	4.08859900
H	1.98742400	2.66993000	5.53124500
H	3.40809700	0.71597500	4.93938000
H	2.93337100	-0.61324100	2.91302900
N	-0.75115100	1.07950400	0.70402900
C	1.23992900	0.57977900	2.30901400
O	-5.93936600	2.56372300	-1.28634500
O	-6.09134000	2.88216000	0.08401800
H	-6.93234600	3.37685600	0.08277900

Zero-point correction= 0.651606 (Hartree/Particle)
Thermal correction to Energy= 0.695193
Thermal correction to Enthalpy= 0.696137
Thermal correction to Gibbs Free Energy= 0.569683
Sum of electronic and zero-point Energies= -2192.523243

	Sum of electronic and thermal Energies= -2192.479656 Sum of electronic and thermal Enthalpies= -2192.478712 Sum of electronic and thermal Free Energies= -2192.605166
3	TS-IrC35-OOH
	0 2 O -4.46365200 2.70037300 0.08958600 O -2.56683400 -0.36328500 -0.29693000 O -0.63585200 1.37102400 0.32405600 C -2.14137600 3.20501400 0.45226000 C -4.21176500 1.37142800 -0.13014900 C -3.48935400 3.59591500 0.36432900 C -5.42798600 0.61111000 -0.41303800 C -2.90116500 0.89600100 -0.07024000 C -1.83566100 1.81735900 0.24227600 C -1.16296800 4.18530400 0.73620300 C -3.87426100 4.93048400 0.55764400 C -6.68247200 1.26012200 -0.41309700 C -5.38813800 -0.77315100 -0.68823400 C -1.53808600 5.50136700 0.92520400 C -2.89724500 5.87179000 0.83654900 C -7.84936200 0.55169000 -0.67722000 C -6.56490200 -1.47136300 -0.95020400 C -7.79873600 -0.81875100 -0.94742500 H -0.12526100 3.87492000 0.79325600 H -4.92379200 5.19497000 0.48256900 H -6.73565700 2.32183800 -0.20422700 H -4.43378300 -1.28139600 -0.69348700 H -0.78729200 6.25563200 1.13980600 H -3.18344300 6.90885800 0.98616800 H -8.80349100 1.07191800 -0.67199700 H -6.51362100 -2.53652500 -1.15962200 H -8.71218900 -1.37000000 -1.15382800 Ir -0.53934200 -0.67575200 -0.06055600 O 1.55673400 -0.72057300 -0.17470000 O 0.63053800 -0.12289300 -2.07658600 C 8.68365400 1.15904900 1.36435300 C 7.74732800 -0.07707500 1.50008000 C 6.52587400 -0.08691300 0.60570200 C 4.22448500 -0.09502300 -1.08344900 C 3.04169900 -0.04277600 -1.98014100 C 9.31301400 1.26854600 -0.03165000 C 7.98906000 2.46936700 1.76124000 C 6.56143700 -0.66497400 -0.67122600 C 5.31042900 0.48052500 1.02331900 C 5.44322300 -0.66192100 -1.50172300

C	4.18826500	0.48187900	0.20399300
C	3.17710400	-0.57551000	-3.40171900
C	1.68798300	-0.31727100	-1.38703500
H	9.49907100	0.98584100	2.08243900
H	7.42439600	-0.14333400	2.54747600
H	8.34461900	-0.97672000	1.30057000
H	2.82837600	1.25392500	-2.22033100
H	8.55190000	1.45005900	-0.79912400
H	9.85079800	0.35130700	-0.30239400
H	10.02906400	2.09810800	-0.06968600
H	8.69739700	3.30602300	1.73573100
H	7.16663900	2.70828500	1.07733400
H	7.57598800	2.41301900	2.77606200
H	7.47881600	-1.13383300	-1.01968800
H	5.24226600	0.92415200	2.01374100
H	5.51749500	-1.12745200	-2.47889800
H	3.26666700	0.92573700	0.56294100
H	4.06569600	-0.16537600	-3.88942500
H	3.25389400	-1.67215300	-3.41363300
H	2.30475700	-0.28838000	-3.99175500
C	-0.87440800	-3.46471000	0.66406700
C	-0.98265200	-4.85090900	0.49153500
C	-0.81694600	-5.41240800	-0.76818300
C	-0.53964400	-4.58215100	-1.85825200
C	-0.44110000	-3.21502000	-1.64186700
C	-1.00992100	-2.72241800	1.91286100
C	-1.23910500	-3.31223800	3.16629500
C	-1.32571500	-2.51627400	4.30304600
C	-1.17708100	-1.12822400	4.18848300
C	-0.94865300	-0.53322600	2.94636600
H	-1.19730500	-5.47865300	1.34898700
H	-0.90166400	-6.48708900	-0.90118000
H	-0.40132100	-4.98049300	-2.85736300
H	-0.22432300	-2.51008200	-2.43660300
H	-1.34468700	-4.39042300	3.25854100
H	-1.50303500	-2.97039800	5.27374700
H	-1.23926500	-0.50570600	5.07818800
H	-0.82571000	0.54370600	2.87971400
N	-0.60603600	-2.67268600	-0.42013200
C	-0.86496500	-1.31539700	1.78665300
O	2.32744000	2.34890600	-2.46346700
O	1.43979400	2.10171200	-3.51492300
H	0.76489000	1.53378200	-3.07224400

Zero-point correction= 0.651605 (Hartree/Particle)
Thermal correction to Energy= 0.694909

	Thermal correction to Enthalpy= 0.695853 Thermal correction to Gibbs Free Energy= 0.569138 Sum of electronic and zero-point Energies= -2192.530388 Sum of electronic and thermal Energies= -2192.487085 Sum of electronic and thermal Enthalpies= -2192.486141 Sum of electronic and thermal Free Energies= -2192.612855
4	TS-IrC32-OH
	0 2 O -5.18285000 1.39436900 -1.29187400 O -2.18610800 -0.53896800 -0.64851200 O -1.83524700 1.53099700 1.00122800 C -3.87013400 2.56725200 0.34465500 C -4.27873800 0.36711100 -1.38054000 C -5.00762700 2.45549200 -0.47454500 C -4.69399700 -0.66171400 -2.33222100 C -3.11742500 0.39648300 -0.60688300 C -2.89670500 1.51174700 0.28323700 C -3.74036300 3.70017600 1.18021300 C -6.00450200 3.44225200 -0.47438700 C -5.91909800 -0.53208200 -3.02324800 C -3.89780600 -1.80004000 -2.58544000 C -4.72004000 4.67429200 1.18339700 C -5.85388300 4.54262700 0.35302100 C -6.33018300 -1.50258300 -3.93012800 C -4.32197900 -2.76550800 -3.49585800 C -5.53470900 -2.62601300 -4.17270800 H -2.85916400 3.77635800 1.80813400 H -6.86797900 3.32172600 -1.12018200 H -6.54559500 0.33338800 -2.84380300 H -2.95690500 -1.91028100 -2.06419800 H -4.62074400 5.54464000 1.82492800 H -6.61978600 5.31280300 0.36099200 H -7.27675000 -1.38165900 -4.45022700 H -3.69520000 -3.63472300 -3.67671500 H -5.85827000 -3.38302800 -4.88203600 Ir -0.63703200 -0.14559700 0.66392500 O 1.02013900 0.60223000 1.71673000 O 0.96449400 1.32225800 -0.36548300 C 8.74390800 0.71186900 -1.74187000 C 7.49868100 -0.18578700 -1.55509100 C 6.28978400 0.39115900 -0.87626800 C 3.99062400 1.50254900 0.37212400 C 2.77771400 2.12340900 1.05706900 C 8.43211500 1.88708900 -2.68663400 C 9.35377100 1.20141300 -0.42193700

	C	5.16611700	0.77660900	-1.62746300
	C	6.22650600	0.55008200	0.51809300
	C	4.04129100	1.33098100	-1.01960000
	C	5.09759800	1.09568200	1.12790000
	C	2.56938700	3.59560700	0.64464400
	C	1.51945000	1.31443000	0.76710000
	H	9.49154000	0.07578000	-2.23639900
	H	7.88926700	-1.10080100	-0.91397100
	H	7.21895800	-0.62557200	-2.52079600
	H	2.93409900	2.07280100	2.13896100
	H	7.68425500	2.55753900	-2.24789800
	H	8.04706500	1.53791800	-3.65238200
	H	9.33928600	2.47227400	-2.87899500
	H	10.29020300	1.73848100	-0.61356300
	H	8.67923000	1.88893400	0.10120200
	H	9.57059500	0.35842000	0.24221500
	H	5.17860800	0.64614900	-2.70735900
	H	7.06161900	0.21965100	1.12906800
	H	3.18427100	1.61453200	-1.62277000
	H	5.07318000	1.20047600	2.21013000
	H	3.47017100	4.17914500	0.86122000
	H	2.35119300	3.67152300	-0.42397500
	H	1.72994400	4.03530800	1.19467900
	C	0.03086200	-2.94833500	0.99390300
	C	0.66323700	-4.17407300	0.74836800
	C	1.65417100	-4.26648900	-0.22094800
	C	2.01428000	-3.12568000	-0.94383200
	C	1.36090100	-1.93246700	-0.66915500
	C	-1.00982800	-2.68069100	1.98106600
	C	-1.51770300	-3.63431000	2.87785600
	C	-2.48891000	-3.26947600	3.80360100
	C	-2.94935700	-1.94698000	3.83793600
	C	-2.45007500	-0.99247500	2.95007600
	H	0.37186800	-5.04715400	1.32130600
	H	2.14381600	-5.21733400	-0.41084700
	H	2.78647200	-3.15273000	-1.70470100
	H	1.59213500	-1.00733200	-1.18437900
	H	-1.15368500	-4.65871400	2.85976300
	H	-2.88329300	-4.00565400	4.49824100
	H	-3.70451100	-1.65949200	4.56608400
	H	-2.81145300	0.03041300	2.99964800
	N	0.39627200	-1.84673800	0.26675100
	C	-1.47691900	-1.33964100	2.00294200
	O	8.28719900	-2.06194900	0.06949700
	H	7.39958000	-2.18095700	0.46576700

	Zero-point correction= 0.647832 (Hartree/Particle) Thermal correction to Energy= 0.690386 Thermal correction to Enthalpy= 0.691330 Thermal correction to Gibbs Free Energy= 0.565611 Sum of electronic and zero-point Energies= -2117.381780 Sum of electronic and thermal Energies= -2117.339226 Sum of electronic and thermal Enthalpies= -2117.338282 Sum of electronic and thermal Free Energies= -2117.464001
5	TS-IrC35-OH
	0 2 O -5.32454000 0.97904400 -1.07817400 O -2.16317300 -0.70582800 -0.53083000 O -1.68394000 1.67520000 0.57702500 C -3.84601700 2.50532800 0.04540000 C -4.39013200 -0.02376200 -1.09200500 C -5.08597900 2.19583500 -0.54117700 C -4.88783400 -1.24268000 -1.72722900 C -3.12899100 0.19701000 -0.53691700 C -2.83850100 1.48104500 0.05424000 C -3.65244300 3.79478800 0.59169900 C -6.12307900 3.13867200 -0.59127400 C -6.20966800 -1.29186700 -2.22258600 C -4.07734400 -2.39100900 -1.86145400 C -4.67149700 4.72643100 0.54417500 C -5.90865600 4.39503300 -0.04916600 C -6.69997800 -2.44406200 -2.82698000 C -4.58133700 -3.53937100 -2.46818200 C -5.88942000 -3.57570300 -2.95383700 H -2.69208500 4.02352900 1.04118000 H -7.06616100 2.86392000 -1.05197400 H -6.84864700 -0.42192900 -2.12970400 H -3.06288500 -2.36569500 -1.48817400 H -4.52349100 5.71707500 0.96315000 H -6.70475400 5.13321700 -0.08266400 H -7.72032000 -2.45904400 -3.20078300 H -3.94202800 -4.41318400 -2.56187300 H -6.27502100 -4.47489500 -3.42675300 Ir -0.46550500 -0.00991400 0.41227600 O 1.28719200 0.98625500 1.01779500 O 0.90454700 1.23349700 -1.13828100 C 8.92646100 -0.39036700 -1.03624000 C 7.53706100 -1.06214700 -1.23740400 C 6.32945300 -0.18281100 -0.98463000 C 4.07963500 1.48682000 -0.50427000 C 2.86325200 2.34510100 -0.23163800

	C	9.16792000	0.76529400	-2.01756100
	C	9.15823800	0.05877600	0.41337500
	C	5.75586000	0.57818600	-2.01302600
	C	5.74580900	-0.09568400	0.28924600
	C	4.65557700	1.40370300	-1.78044900
	C	4.64486400	0.72220100	0.52922400
	C	2.65654500	3.54738500	-1.14716600
	C	1.61151400	1.48480200	-0.13092400
	H	9.66397100	-1.17517700	-1.26166100
	H	7.48669800	-1.93787800	-0.57664800
	H	7.49298300	-1.44482000	-2.26592700
	H	3.00634300	2.77513700	0.88699600
	H	8.46793900	1.59018400	-1.84217700
	H	9.04918600	0.43959500	-3.05857900
	H	10.18427300	1.16143700	-1.90638300
	H	10.17487500	0.44973200	0.53942800
	H	8.45848100	0.85096800	0.70291400
	H	9.03190500	-0.77373500	1.11669300
	H	6.17289700	0.52103300	-3.01596900
	H	6.16340100	-0.67654700	1.10837100
	H	4.23686200	1.97331100	-2.60431600
	H	4.22924800	0.80379100	1.52853600
	H	3.57575100	4.13591000	-1.22338100
	H	2.35223200	3.22737900	-2.14968000
	H	1.86345800	4.19080300	-0.75353500
	C	0.38824500	-2.66716700	1.20023500
	C	1.03800400	-3.90508600	1.11473600
	C	1.87930200	-4.17870100	0.04337600
	C	2.07220900	-3.20727500	-0.94268300
	C	1.40716000	-1.99543700	-0.81933500
	C	-0.50686100	-2.21766600	2.26200000
	C	-0.82679900	-2.97080000	3.40288800
	C	-1.66591500	-2.43740900	4.37510000
	C	-2.18188400	-1.14576800	4.21068500
	C	-1.86963200	-0.38953400	3.07932500
	H	0.87828900	-4.64482400	1.89106800
	H	2.38306600	-5.13880000	-0.02226700
	H	2.72610500	-3.37715400	-1.79077800
	H	1.51408300	-1.19364700	-1.54107500
	H	-0.41857700	-3.96945400	3.53776400
	H	-1.91434700	-3.01863900	5.25849700
	H	-2.83304900	-0.72561000	4.97383600
	H	-2.27148000	0.61391700	2.97446600
	N	0.58685100	-1.73538800	0.21670500
	C	-1.03273000	-0.91061700	2.08340500
	O	2.93112600	2.95721900	2.23572000

	H 2.23256900 2.27916700 2.36528900 Zero-point correction= 0.647316 (Hartree/Particle) Thermal correction to Energy= 0.689580 Thermal correction to Enthalpy= 0.690524 Thermal correction to Gibbs Free Energy= 0.565495 Sum of electronic and zero-point Energies= -2117.385891 Sum of electronic and thermal Energies= -2117.343627 Sum of electronic and thermal Enthalpies= -2117.342683 Sum of electronic and thermal Free Energies= -2117.467713
6	TS-IrC12-OOH
	0 2 O -4.80850600 -1.59969800 0.41851700 O -1.83403400 0.46514900 0.51898000 O -1.37326000 -0.97833100 -1.67030000 C -3.41224100 -2.18499500 -1.45455000 C -3.92560600 -0.64781400 0.87763900 C -4.57978700 -2.34417700 -0.68689400 C -4.37317000 0.02088600 2.06263900 C -2.73636000 -0.41704000 0.15547600 C -2.46237200 -1.19348000 -1.02672600 C -3.23080400 -2.99483000 -2.59747300 C -5.55719300 -3.28415700 -1.04220900 C -5.52933900 -0.49447600 2.77098700 C -3.69638200 1.13708900 2.60647900 C -4.19140800 -3.92517100 -2.94928300 C -5.35678100 -4.06738200 -2.16862700 C -6.11086900 0.31385700 3.80657900 C -4.21444900 1.80865500 3.70241500 C -5.44027000 1.40932700 4.29065000 H -2.32551700 -2.86346400 -3.18044800 H -6.44992600 -3.37551500 -0.43191700 H -6.19666600 -1.14731900 2.22210000 H -2.78501500 1.47780500 2.13524800 H -4.05129200 -4.54754800 -3.82782000 H -6.10951900 -4.79790300 -2.45080800 H -7.05120900 -0.00484200 4.24613100 H -3.68637300 2.67268600 4.09573400 H -5.85658800 1.98804200 5.11108900 Ir -0.21531500 0.50549100 -0.76773700 O 1.49659700 0.13841100 -1.92065100 O 1.34601000 -1.19964600 -0.17962900 C 8.89697600 -1.21270100 1.92460600 C 7.79664800 -0.12002100 1.79711900 C 6.61694600 -0.46308300 0.90965800

	C	4.41156400	-1.13008400	-0.75782500
	C	3.25098800	-1.50784900	-1.67399400
	C	8.37345500	-2.50111000	2.57488800
	C	9.58651200	-1.51108700	0.58579900
	C	5.47436300	-1.09210000	1.42803900
	C	6.62317000	-0.16047300	-0.45873400
	C	4.39196700	-1.42356200	0.61384300
	C	5.54152200	-0.48841500	-1.27758600
	C	3.05108900	-3.03518500	-1.76139600
	C	1.96324500	-0.83664700	-1.21861400
	H	9.65470700	-0.78616200	2.59883300
	H	8.27223500	0.79645600	1.42299100
	H	7.43076000	0.10983700	2.80682000
	H	3.46449700	-1.11653600	-2.67352800
	H	7.61543800	-2.98463800	1.94810500
	H	7.92082100	-2.30123700	3.55412200
	H	9.18908800	-3.21842200	2.72518900
	H	10.40911200	-2.22290100	0.72375700
	H	8.88551100	-1.94727100	-0.13504300
	H	10.00484000	-0.60089200	0.13819400
	H	5.42916000	-1.32234600	2.49032100
	H	7.48291800	0.34695200	-0.89040800
	H	3.51552700	-1.89715300	1.04582200
	H	5.57507500	-0.23669100	-2.33525200
	H	3.97485100	-3.51615300	-2.09917700
	H	2.77873600	-3.44712200	-0.78598700
	H	2.25176800	-3.28164000	-2.46935600
	C	0.43671600	3.26840700	-0.17092500
	C	1.04702300	4.35254600	0.47233200
	C	1.99295400	4.13175900	1.46589800
	C	2.32926500	2.82067600	1.81310800
	C	1.69865000	1.77624700	1.15140200
	C	-0.55774600	3.32858600	-1.23814300
	C	-1.03470300	4.51750400	-1.81246300
	C	-1.96300900	4.46590600	-2.84678000
	C	-2.41123200	3.22360800	-3.31280100
	C	-1.94206200	2.03639300	-2.74724200
	H	0.77506500	5.36252800	0.18704500
	H	2.46643900	4.97299500	1.96391300
	H	3.06724400	2.60397200	2.57737200
	H	1.91517200	0.73553800	1.36274800
	H	-0.68010900	5.48285300	-1.45955200
	H	-2.33323000	5.38479200	-3.29246800
	H	-3.13243100	3.18266800	-4.12597500
	H	-2.29242800	1.08216800	-3.12951200
	N	0.77815600	1.99324700	0.19271000

	C -1.01269300 2.06488600 -1.69888900 O -3.99886900 -2.71162300 3.05539100 H -4.64155500 -3.35495400 2.69866200 O -4.80573600 -1.85764400 3.82136900 Zero-point correction= 0.655896 (Hartree/Particle) Thermal correction to Energy= 0.699262 Thermal correction to Enthalpy= 0.700206 Thermal correction to Gibbs Free Energy= 0.572988 Sum of electronic and zero-point Energies= -2192.525154 Sum of electronic and thermal Energies= -2192.481788 Sum of electronic and thermal Enthalpies= -2192.480844 Sum of electronic and thermal Free Energies= -2192.608062
7	TS-IrC13-OOH
	0 2 O -4.80323500 1.43127200 -1.25433300 O -1.90625300 -0.52616300 -0.29991500 O -1.44284400 1.74290000 1.01441500 C -3.43470400 2.76429900 0.21131400 C -3.94850200 0.35405000 -1.19424500 C -4.57747500 2.58727900 -0.58900000 C -4.40865800 -0.77056500 -1.96273900 C -2.78204600 0.44647400 -0.41255100 C -2.50795000 1.66846700 0.30479500 C -3.25313400 3.99591400 0.87923100 C -5.52843300 3.60715200 -0.73095000 C -5.64527700 -0.72198800 -2.64296000 C -3.58704400 -1.95661700 -2.12372400 C -4.18899600 5.00417500 0.74202500 C -5.32816000 4.80657100 -0.06544400 C -6.12546200 -1.82849400 -3.32988000 C -4.18928000 -3.12552900 -2.70025800 C -5.40360000 -3.04780200 -3.33505200 H -2.36772500 4.12065800 1.49335400 H -6.39819700 3.43552600 -1.35647500 H -6.24098700 0.18240200 -2.60105900 H -2.77505400 -2.08929300 -1.42134200 H -4.04927600 5.95074300 1.25518500 H -6.06005600 5.60242900 -0.16947200 H -7.08292500 -1.76674500 -3.83978000 H -3.61774700 -4.04830500 -2.69736300 H -5.82410700 -3.91861800 -3.83060600 Ir -0.31354100 -0.01195800 0.91277300 O 1.39380900 0.80448300 1.81620900

	O	1.30102300	1.21476300	-0.34440900
	C	8.86421500	0.09548400	-2.06305600
	C	7.73360800	-0.79230400	-1.46790900
	C	6.55724600	-0.05503100	-0.85998500
	C	4.35680800	1.34572900	0.27355500
	C	3.19853100	2.12330500	0.89240200
	C	8.38128300	0.94914800	-3.24413700
	C	9.55105400	0.96349100	-0.99915500
	C	5.43768000	0.29219900	-1.63191800
	C	6.54300000	0.30078000	0.49547100
	C	4.35799800	0.98158700	-1.08121100
	C	5.46370400	0.98883600	1.05204700
	C	3.04405900	3.52814300	0.27369400
	C	1.89607000	1.34696600	0.76046900
	H	9.61537100	-0.60938300	-2.44983700
	H	8.18134500	-1.44338400	-0.70522000
	H	7.36879100	-1.45358000	-2.26530000
	H	3.38962200	2.22319400	1.96538900
	H	7.63130100	1.68225400	-2.92584500
	H	7.93169300	0.32932500	-4.02989000
	H	9.21723400	1.49983000	-3.69173300
	H	10.39424500	1.51391100	-1.43329300
	H	8.85675300	1.69766500	-0.57457900
	H	9.94026800	0.35390500	-0.17410000
	H	5.40801600	0.01246400	-2.68278700
	H	7.38424500	0.02834500	1.12879900
	H	3.49896000	1.22372600	-1.69962600
	H	5.48059600	1.24669800	2.10863400
	H	3.97831300	4.08946000	0.37798200
	H	2.79469400	3.45845800	-0.78850800
	H	2.24512700	4.08666500	0.77437800
	C	0.26408700	-2.75781900	1.64558600
	C	0.84825800	-4.02858800	1.57504500
	C	1.80808100	-4.30230800	0.60821100
	C	2.18410200	-3.29857100	-0.28805700
	C	1.57878900	-2.05398900	-0.18310900
	C	-0.74321700	-2.30717600	2.60177200
	C	-1.26053800	-3.09647100	3.64101400
	C	-2.20006900	-2.56323600	4.51699600
	C	-2.61932600	-1.23647400	4.35810600
	C	-2.10977300	-0.44447000	3.32728100
	H	0.54455300	-4.79400100	2.28026800
	H	2.26079300	-5.28819100	0.55384300
	H	2.93233000	-3.46825300	-1.05417400
	H	1.82543100	-1.22754700	-0.83930400
	H	-0.92876800	-4.12351500	3.77254400

	H -2.60147100 -3.17247400 5.32184700 H -3.34955300 -0.81715000 5.04660100 H -2.43849600 0.58575800 3.22666300 N 0.64592700 -1.79305300 0.75224800 C -1.16789700 -0.96328000 2.42866600 O -2.99943100 -1.22877500 -4.64981700 H -3.29342900 -0.30038200 -4.57064100 O -2.36617700 -1.45429300 -3.42563400 Zero-point correction= 0.655747 (Hartree/Particle) Thermal correction to Energy= 0.699156 Thermal correction to Enthalpy= 0.700101 Thermal correction to Gibbs Free Energy= 0.572779 Sum of electronic and zero-point Energies= -2192.524127 Sum of electronic and thermal Energies= -2192.480718 Sum of electronic and thermal Enthalpies= -2192.479774 Sum of electronic and thermal Free Energies= -2192.607096
8	TS-IrC12-OH
	0 2 O -4.85748500 -1.59079800 0.81572300 O -1.89972100 0.48135700 0.55150100 O -1.46457200 -1.28948300 -1.39520800 C -3.48063600 -2.46738000 -0.94973400 C -3.98027600 -0.57635100 1.08958900 C -4.63507300 -2.51009600 -0.14660000 C -4.42893500 0.27270200 2.18091800 C -2.80365300 -0.45446200 0.34394000 C -2.53802200 -1.41106000 -0.70726400 C -3.30441600 -3.45579400 -1.94539600 C -5.60247400 -3.51163100 -0.31681900 C -5.65072100 -0.02863800 2.84887600 C -3.68049100 1.38526300 2.61949400 C -4.25584200 -4.44218300 -2.11697100 C -5.40608700 -4.46810400 -1.29849800 C -6.11464400 0.80196400 3.88318600 C -4.14928800 2.18133400 3.66256900 C -5.36523100 1.89703900 4.29937700 H -2.41055400 -3.41337200 -2.55844900 H -6.47573900 -3.51619700 0.32670100 H -6.29218300 -0.80541900 2.46033600 H -2.74221900 1.61274000 2.13273200 H -4.12124900 -5.20214600 -2.88067300 H -6.14784100 -5.24937100 -1.43733200 H -7.05793200 0.56195500 4.36384200 H -3.55902000 3.03647300 3.98097100

	H	-5.72004400	2.52879500	5.10894400
	Ir	-0.31236400	0.33643800	-0.76991700
	O	1.38259800	-0.19710200	-1.88613100
	O	1.28772200	-1.23329900	0.05420400
	C	8.86952600	-0.82276300	1.98352800
	C	7.75159800	0.22224200	1.70189800
	C	6.56188100	-0.27342000	0.90447800
	C	4.33781200	-1.22612400	-0.59103600
	C	3.16674300	-1.75901100	-1.41173400
	C	8.37614000	-1.99334900	2.84563000
	C	9.53872700	-1.32803500	0.69753800
	C	5.43915900	-0.82714800	1.53915000
	C	6.53850200	-0.19224200	-0.49441800
	C	4.34795500	-1.29819600	0.80995600
	C	5.44776700	-0.66041000	-1.22873800
	C	2.98712000	-3.28275500	-1.24950900
	C	1.87758500	-1.03776100	-1.04421100
	H	9.63323700	-0.28356400	2.56377800
	H	8.20756100	1.07125500	1.17527600
	H	7.39994000	0.60870000	2.66795100
	H	3.35694200	-1.53087200	-2.46506900
	H	7.61332100	-2.58061200	2.32176000
	H	7.93915800	-1.64114800	3.78838100
	H	9.20424000	-2.66785400	3.09395000
	H	10.37376000	-1.99862800	0.93287600
	H	8.83096600	-1.88364300	0.07174100
	H	9.93579800	-0.49849300	0.09923600
	H	5.41677900	-0.88612600	2.62522800
	H	7.38197600	0.25139200	-1.01856700
	H	3.48711300	-1.70857300	1.32911600
	H	5.45818000	-0.57942300	-2.31338000
	H	3.91145700	-3.80149200	-1.52392000
	H	2.73769700	-3.53608600	-0.21562100
	H	2.17907300	-3.64839700	-1.89308100
	C	0.29950600	3.16844700	-0.64101500
	C	0.90535600	4.35089600	-0.19724000
	C	1.88426800	4.30653100	0.78768800
	C	2.25868200	3.07273900	1.32679700
	C	1.63068700	1.92647300	0.86001600
	C	-0.72291000	3.04165600	-1.67484400
	C	-1.23942600	4.11634900	-2.41616100
	C	-2.19091000	3.88557400	-3.40364000
	C	-2.62260200	2.57716200	-3.65568300
	C	-2.11420400	1.50287300	-2.92325700
	H	0.60444400	5.29797200	-0.63074400
	H	2.35452600	5.22384300	1.13021300

	H 3.02441500 2.99216300 2.09029200 H 1.87595800 0.93614100 1.22576600 H -0.89754600 5.13148600 -2.22945600 H -2.59190800 4.71562200 -3.97833300 H -3.36203200 2.39524000 -4.43236600 H -2.45326700 0.49445000 -3.14136300 N 0.67710200 1.97290700 -0.08993500 C -1.16086800 1.71265700 -1.91748100 O -4.96162900 -1.71309800 4.13346100 H -4.31186900 -1.17344200 4.62774200 Zero-point correction= 0.651078 (Hartree/Particle) Thermal correction to Energy= 0.693747 Thermal correction to Enthalpy= 0.694691 Thermal correction to Gibbs Free Energy= 0.568792 Sum of electronic and zero-point Energies= -2117.381789 Sum of electronic and thermal Energies= -2117.339121 Sum of electronic and thermal Enthalpies= -2117.338177 Sum of electronic and thermal Free Energies= -2117.464075
9	TS-IrC13-OH
	0 2 O 4.84703100 1.53937300 1.24417800 O 1.96522300 -0.52039200 0.48574100 O 1.54512400 1.56440800 -1.12139200 C 3.51999600 2.67673500 -0.40834200 C 3.98272000 0.47358700 1.30357800 C 4.64436100 2.60036800 0.43349100 C 4.41490700 -0.54405700 2.24503600 C 2.84032000 0.45966600 0.49686600 C 2.58987500 1.58154400 -0.38291100 C 3.36056600 3.81386200 -1.23305800 C 5.59876000 3.62788500 0.46522200 C 5.66845300 -0.43770800 2.88503600 C 3.58578800 -1.65943300 2.56045700 C 4.29880100 4.82741900 -1.20474400 C 5.41970000 4.73144800 -0.35227500 C 6.10346500 -1.42061100 3.76782100 C 4.05976700 -2.65652000 3.43594400 C 5.30283100 -2.53944000 4.04487800 H 2.48959300 3.86158600 -1.87785600 H 6.45269000 3.53566600 1.12813400 H 6.30398200 0.41428100 2.67561400 H 2.67382700 -1.80743000 2.00361400 H 4.17653300 5.70117700 -1.83754200

	H	6.15303700	5.53257200	-0.33460500
	H	7.07702900	-1.31971200	4.24017300
	H	3.42155000	-3.50957300	3.64349600
	H	5.65452200	-3.30621700	4.72949000
	Ir	0.39967100	-0.15897900	-0.81579600
	O	-1.28392900	0.53991300	-1.85428000
	O	-1.23386000	1.23242300	0.23502000
	C	-8.83800100	0.41119900	1.93227100
	C	-7.70902600	-0.55974800	1.48101400
	C	-6.51232300	0.07853800	0.80456300
	C	-4.27511200	1.29736600	-0.45976800
	C	-3.09763300	1.97745500	-1.15253200
	C	-8.36458300	1.40750300	3.00010000
	C	-9.49355800	1.13936300	0.75038200
	C	-5.40151800	0.51081800	1.54557600
	C	-6.47032200	0.25506100	-0.58509400
	C	-4.30385400	1.11174800	0.93046700
	C	-5.37297200	0.85382600	-1.20587900
	C	-2.94421500	3.45175100	-0.72425700
	C	-1.80403300	1.21919000	-0.89022400
	H	-9.60556300	-0.22813300	2.39361100
	H	-8.15193400	-1.30050300	0.80188100
	H	-7.36749600	-1.11433500	2.36532000
	H	-3.26621600	1.93372100	-2.23303400
	H	-7.59920500	2.08396700	2.60285400
	H	-7.93739400	0.89160100	3.86905200
	H	-9.20087000	2.02151300	3.35514500
	H	-10.33576500	1.75291300	1.09195400
	H	-8.78095500	1.80201200	0.24607200
	H	-9.87754100	0.43096400	0.00571100
	H	-5.39319900	0.36917000	2.62416600
	H	-7.30397400	-0.08855400	-1.19336600
	H	-3.45224200	1.42294900	1.52790100
	H	-5.36849100	0.97258900	-2.28711100
	H	-3.87149700	3.99925900	-0.92235500
	H	-2.71678200	3.52338300	0.34273500
	H	-2.13073200	3.93379900	-1.27818700
	C	-0.18581300	-2.97313200	-1.19286000
	C	-0.78091100	-4.22033000	-0.96599000
	C	-1.75769500	-4.35940400	0.01253500
	C	-2.13942000	-3.24478500	0.76365600
	C	-1.52327300	-2.02799700	0.50629300
	C	0.84087800	-2.65727500	-2.18159500
	C	1.36931200	-3.57857000	-3.09955600
	C	2.32823400	-3.17011900	-4.02036100
	C	2.75593400	-1.83649300	-4.02791700

C	2.23537200	-0.91375300	-3.11863500
H	-0.47195600	-5.07336700	-1.55957500
H	-2.21897100	-5.32705500	0.18805700
H	-2.90034700	-3.30840200	1.53342400
H	-1.77268600	-1.12116400	1.04470400
H	1.03114100	-4.61196400	-3.10196600
H	2.73822800	-3.88156900	-4.73160200
H	3.50151200	-1.51501400	-4.75175400
H	2.57100500	0.11880500	-3.14742200
N	-0.57480500	-1.89725100	-0.44052100
C	1.27351500	-1.30464800	-2.17722300
O	2.22094000	-0.75281900	4.03423800
H	2.92812100	-0.50389600	4.66337500

Zero-point correction= 0.650993 (Hartree/Particle)
Thermal correction to Energy= 0.693658
Thermal correction to Enthalpy= 0.694603
Thermal correction to Gibbs Free Energy= 0.568974
Sum of electronic and zero-point Energies= -2117.380288
Sum of electronic and thermal Energies= -2117.337623
Sum of electronic and thermal Enthalpies= -2117.336679
Sum of electronic and thermal Free Energies= -2117.462307

Table S2. Natural population charges of heavy atoms in the Ir (III) complex calculated at the B3LYP/Lanl2dz/6-31G(d) level of theory.

Atom	No	Natural charge	Natural population			
			Core	Valence	Rydberg	Total
O	1	-0.45846	1.99959	6.44749	0.01138	8.45846
O	2	-0.61384	1.99974	6.60081	0.01329	8.61384
O	3	-0.55395	1.99972	6.54097	0.01326	8.55395
C	4	-0.18042	1.99879	4.16765	0.01397	6.18042
C	5	0.32149	1.99867	3.65817	0.02167	5.67851
C	6	0.36529	1.99859	3.61443	0.02169	5.63471
C	7	-0.11352	1.99887	4.09909	0.01555	6.11352
C	8	0.25047	1.99861	3.72541	0.0255	5.74953
C	9	0.44655	1.99876	3.52403	0.03066	5.55345
C	10	-0.1786	1.99894	4.16524	0.01442	6.1786
C	11	-0.26738	1.99889	4.25406	0.01443	6.26738
C	12	-0.20551	1.99894	4.19341	0.01317	6.20551
C	13	-0.19542	1.99894	4.18304	0.01344	6.19542
C	14	-0.24464	1.99895	4.2318	0.01389	6.24464
C	15	-0.20685	1.99897	4.19408	0.01379	6.20685
C	16	-0.23571	1.99895	4.22268	0.01408	6.23571
C	17	-0.2347	1.99895	4.22174	0.01401	6.2347
C	18	-0.22188	1.99894	4.20904	0.0139	6.22188
Ir	28	0.6957	67.976	8.29888	0.02942	76.3043
O	29	-0.5983	1.99974	6.58586	0.01271	8.5983
O	30	-0.66801	1.99974	6.65001	0.01826	8.66801
C	31	-0.24249	1.99908	4.23153	0.01189	6.24249
C	32	-0.46507	1.99911	4.45184	0.01411	6.46507
C	33	-0.04279	1.99887	4.02759	0.01633	6.04279
C	34	-0.03654	1.99885	4.02025	0.01744	6.03654
C	35	-0.34767	1.99893	4.33279	0.01596	6.34767
C	36	-0.6761	1.99927	4.66788	0.00895	6.6761
C	37	-0.67595	1.99927	4.66773	0.00895	6.67595
C	38	-0.22753	1.99888	4.21509	0.01356	6.22753

C	39	-0.22555	1.99888	4.21325	0.01342	6.22555
C	40	-0.22731	1.99888	4.21456	0.01387	6.22731
C	41	-0.21828	1.99887	4.20593	0.01348	6.21828
C	42	-0.65948	1.99928	4.65114	0.00905	6.65948
C	43	0.84744	1.99904	3.09859	0.05493	5.15256
C	61	0.24887	1.99887	3.73253	0.01972	5.75113
C	62	-0.24436	1.9989	4.23318	0.01228	6.24436
C	63	-0.18883	1.99896	4.17562	0.01425	6.18883
C	64	-0.27623	1.99895	4.26352	0.01376	6.27623
C	65	0.06019	1.99904	3.92098	0.0198	5.93981
C	66	-0.12739	1.99877	4.11379	0.01483	6.12739
C	67	-0.19566	1.99891	4.18423	0.01253	6.19566
C	68	-0.25699	1.99895	4.24368	0.01436	6.25699
C	69	-0.20664	1.99895	4.19366	0.01403	6.20664
C	70	-0.25687	1.99885	4.24333	0.01469	6.25687
N	79	-0.38662	1.99911	5.37051	0.017	7.38662
C	80	-0.0446	1.99851	4.01775	0.02833	6.0446
	Total	0	157.93128	233.26342	0.80531	392

Table S3. DPPH$^{\bullet}$ radical scavenging activity of flavonol, ibuprofen and Ir (III) complex with reference to ascorbic acid as standard.

Concentration (μM)	% DPPH radical scavenged			
	Flavonol	Ibuprofen	Ir (III) complex	Ascorbic acid
25	12.10 ± 0.05	12.35 ± 0.10	38.45 ± 0.10	25.28 ± 0.15
50	31.15 ± 0.10	22.52 ± 0.20	63.20 ± 0.30	46.50 ± 0.10
125	54.16 ± 0.05	37.42 ± 0.10	88.15 ± 0.10	75.42 ± 0.20
150	62.45 ± 0.15	45.15 ± 0.05	98.95 ± 0.20	96.10 ± 0.05
	IC_{50} (μM)			
	85.32 ± 0.10	143.55 ± 0.20	8.32 ± 0.05	14.25 ± 0.18

[a] Data are shown as means ±SEM (n = 3).

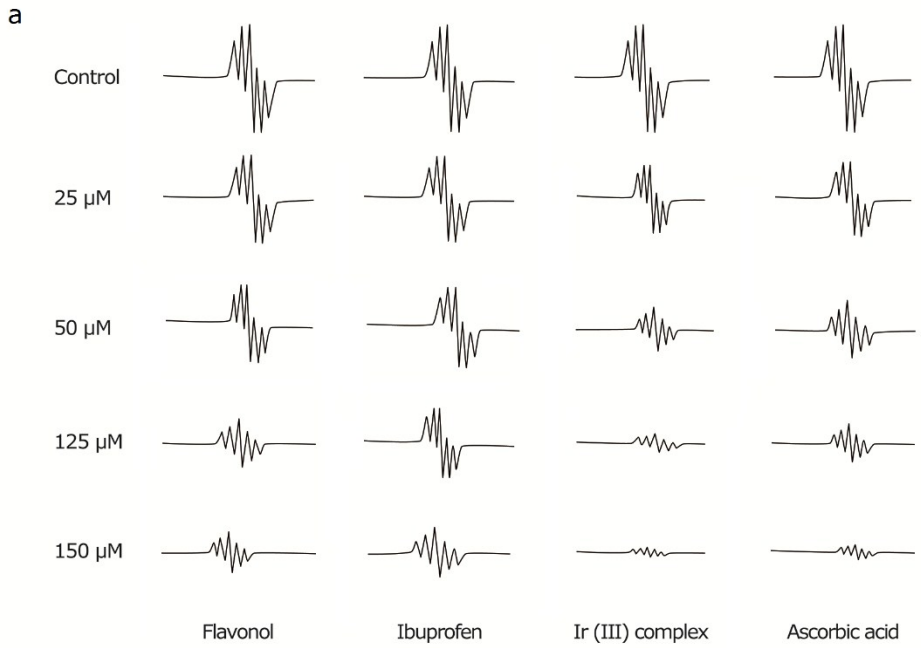

Figure S5. ESR spectra of DPPH• radical according to dose of flavonol, ibuprofen, Ir (III) complex and ascorbic acid (25 µM -150 µM). Trolox was used as positive control.

Table S4. OH• radical scavenging activity of flavonol, ibuprofen and Ir(III) complex with reference to ascorbic acid as standard

Concentration (µM)	% OH radical scavenged			
	Flavonol	Ibuprofen	Ir (III) complex	Ascorbic acid
25	11.75 ± 0.12	14.17 ± 0.12	22.31 ± 0.05	18.24 ± 0.10
50	17.22 ± 0.10	25.17 ± 0.10	31.42 ± 0.09	33.18 ± 0.06
125	46.31 ± 0.15	43.14 ± 0.10	79.27 ± 0.12	66.42 ± 0.05
150	53.18 ± 0.10	58.17 ± 0.05	92.35 ± 0.10	78.21 ± 0.13
	IC_{50} (µM)			
	138.24 ± 0.12	105.23 ± 0.05	19.32 ± 0.05	28.12 ± 0.10

[a] Data are shown as means ±SEM (n = 3).

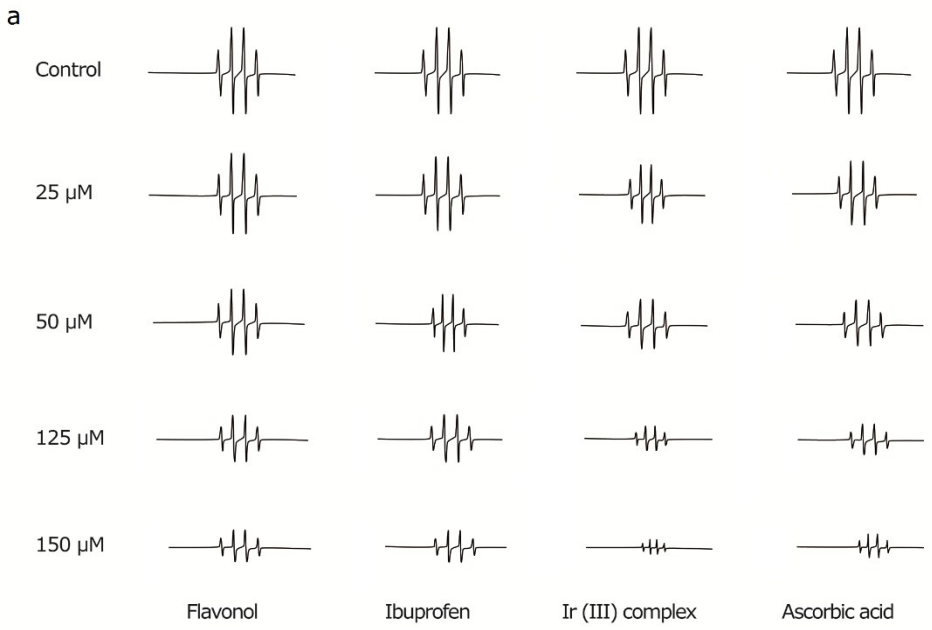

Figure S6. ESR spectra of $OH^{\bullet}$ radical according to dose of flavonol, ibuprofen, Ir(III) complex and ascorbic acid (25 µM -150 µM). Ascorbic acid was used was used as positive control.

Table S5. $NO^{\bullet}$ radical scavenging activity of flavonol, ibuprofen and Ir(III) complex with reference to ascorbic acid as standard.

Concentration (µM)	% NO radical scavenged			
	Flavonol	Ibuprofen	Ir (III) complex	Ascorbic acid
25	10.31 ± 0.10	8.27 ± 0.07	23.17 ± 0.05	31.11 ± 0.10
50	16.24 ± 0.10	19.12 ± 0.03	38.25 ± 0.08	49.25 ± 0.05
125	55.21 ± 0.05	35.13 ± 0.10	71.31 ± 0.10	64.21 ± 0.05
150	62.32 ± 0.12	49.21 ± 0.12	89.20 ± 0.05	73.31 ± 0.10
	IC_{50} (µM)			
	97.27 ± 0.12	127.13 ± 0.05	25.42 ± 0.05	43.27 ± 0.14

[a] Data are shown as means ±SEM (n = 3).

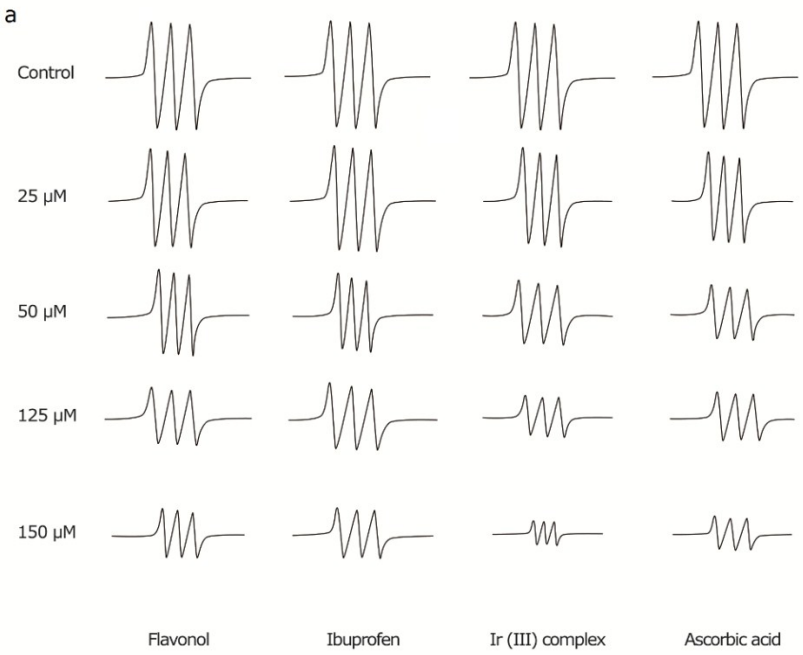

Figure S7. ESR spectra of [$(MGD)_2$-Fe^{2+}-NO] adduct in the presence of antioxidant according to dose of flavonol, ibuprofen, Ir (III) complex and ascorbic acid (25 μM -150 μM). Hemoglobin was used as positive control.

Table S6. $ABTS^{\bullet+}$ radical scavenging activity of flavonol, ibuprofen and Ir (III) complex with reference to ascorbic acid as standard. [a]

Concentration (μM)	% ABTS•+ radical scavenged by			
	Flavonol	Ibuprofen	Ir (III) complex	Ascorbic acid
25	9.17 ± 0.07	13.27 ± 0.06	33.21 ± 0.10	37.26 ± 0.10
50	27.31 ± 0.12	26.82 ± 0.10	57.12 ± 0.12	42.44 ± 0.07
125	56.28 ± 0.05	69.28 ± 0.10	79.32 ± 0.05	82.16 ± 0.05
150	62.84 ± 0.11	80.18 ± 0.08	96.12 ± 0.14	89.27 ± 0.15
		IC_{50} (μM)		
	110.74 ± 0.12	76.25 ± 0.10	10.14 ± 0.10	65.31 ± 0.15

[a] Data are shown as means ±SEM (n = 3).

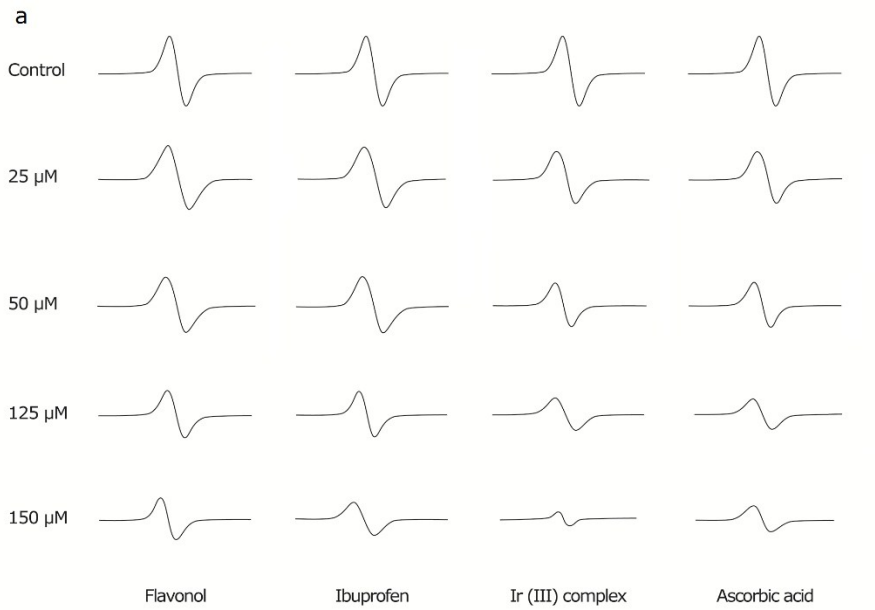

Figure S8. ESR spectra of $ABTS^{\bullet+}$ in the presence of antioxidant according to dose of flavonol, ibuprofen, Ir (III) complex and ascorbic acid (25 µM -150 µM).

Table S7. *In vitro* antitumor activity of Ir (III) complex and two ligands towards A549, A2780 and A2780*cis* cells. *Cis*-platin was used as reference.

Compounds	**IC_{50} ± SD[a] (µM)**		
	A549	**A2780**	**A2780*cis***
Flavonol	> 100	> 100	> 100
Ibuprofen	> 100	> 100	> 100
Ir (III) complex	7.24 ± 0.11	0.48 ± 0.10	1.37 ± 0.12
***Cis*-platin**	18.90 ± 0.15	3.24 ± 0.13	28.63 ± 0.12

[a] The Ir (III) complex was dissolved in 0.1% of DMSO and diluted with water and *cis*-platin was dissolved in 0.9%NaCl. Cells were treated for 48 h with increasing concentrations of tested compounds. IC_{50} values are calculated as mean values obtained from three independent experiments and presented with their standard deviations.

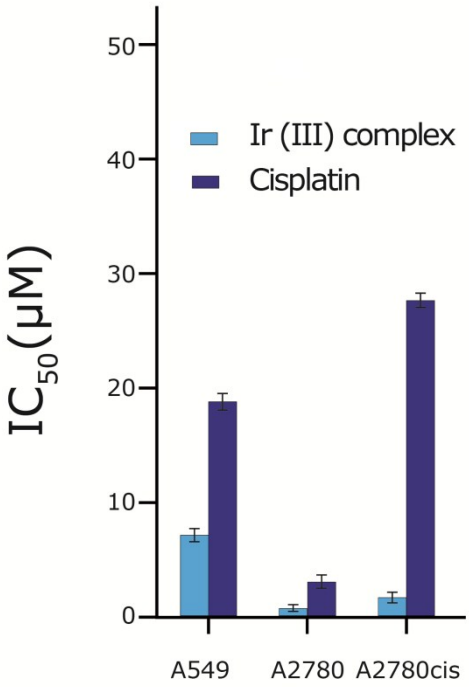

Figure S9. Comparative plots of the cytotoxicity (IC_{50} concentrations) of Ir (III) complex and *cis*-platin against A549, A2780 and A2780*cis* cancer cell lines.

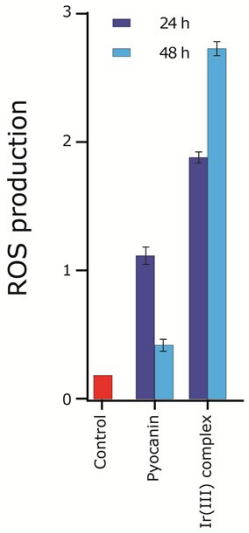

Figure S10. ROS levels in A549 cells as determined by NBT assays. Results were expressed as means of at least three replicates ± standard error.

Table S8. Enthalpy and Gibbs free energy (kcal/mol) of the principal reactions for free radical scavenging by ibuprofen

ΔH^0 (kcal/mol)															
	Gas					**Water**					**PEA**				
Radical	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**
SET-ed	184.0	189.4	230.9	118.2	35.7	63.4	76.6	119.4	43.7	31.2	87.8	99.5	141.8	62.0	32.2
SET-ea	390.9	297.1	248.9	177.5	253.5	266.6	181.3	130.4	98.5	113.6	292.4	205.4	154.6	115.5	143.7
PL (C35)[a]	218.4	204.7	250.5	134.7	-	96.3	92.0	131.6	53.1	-	121.4	115.2	156.4	70.9	-
HAT (C35)[b]	-30.5	1.4	75.2	-26.6	-	-31.6	5.7	71.9	5.9	-	-31.3	1.1	72.5	5.9	-
RAF (C13)[c]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ΔG^0 (kcal/mol)															
	Gas					**Water**					**PEA**				
Radical	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**
SET-ed	183.4	188.6	230.2	117.0	34.3	62.5	75.5	118.4	42.4	28.8	87.2	98.6	141.1	60.9	30.8
SET-ea	390.3	296.7	248.4	176.9	253.1	266.0	180.9	130.0	98.2	113.8	291.8	205.0	154.8	114.9	143.3
PL (C35)[a]	218.2	205.8	250.1	135.5	-	96.3	93.3	131.4	54.1	-	121.2	116.3	156.0	71.7	-
HAT (C35)[b]	-31.4	1.2	73.9	4.8	-	-32.8	5.3	70.3	5.1	-	-32.3	1.0	71.2	5.4	-
RAF (C13)[c]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

[a]The PL reaction is considered at C35 as: $AntioxH + R^{\bullet} \rightarrow (Antiox)^{-} + RH^{\bullet+}$

[b]The HAT reaction is considered at C35 as: $AntioxH + R^{\bullet} \rightarrow (Antiox)^{\bullet} + RH$

[c]The RAF reaction is considered at C13 as: $Antiox + R^{\bullet} \rightarrow (AntioxR)^{\bullet}$

Table S9. Enthalpy and Gibbs free energy of the principal reactions for free radical scavenging by flavonol

ΔH^0 (kcal/mol)															
	Gas					**Water**					**PEA**				
Radical	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**
SET-ed	170.7	176.1	217.5	104.9	22.3	52.3	65.5	108.3	32.6	20.1	76.2	87.9	130.2	50.5	20.6
SET-ea	355.6	261.9	213.6	142.2	218.2	234.1	148.7	97.9	66.0	81.1	259.1	172.1	121.3	82.1	110.4
PL (C35)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HAT (C35)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RAF (C13)	-32.3	2.0	-9.9	-	-	-27.4	4.0	-5.9	-	-	-28.7	3.7	-	-	-
ΔG^0 (kcal/mol)															
	Gas					**Water**					**PEA**				
Radical	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**	**HO•**	**HOO•**	**NO•**	**DPPH•**	**ABTS•+**
SET-ed	170.7	175.9	217.5	104.3	21.6	52.4	65.4	108.2	32.3	18.7	76.3	87.7	130.2	49.9	19.9
SET-ea	355.3	261.8	213.4	142.0	218.1	233.7	148.5	97.7	65.9	81.5	258.8	172.0	121.8	81.9	110.3
PL (C35)	x	x	x	x	x	x	x	x	x	x	-	-	-	-	-
HAT (C35)	x	x	x	x	x	x	x	x	x	x	-	-	-	-	-
RAF (C13)	-21.4	14.3	-4.5	x	x	-16.6	16.2	-2.8	x	x	-17.8	16.0	-	-	-

[a]The PL reaction is considered at C35 as: $AntioxH + R^{\bullet} \rightarrow (Antiox)^{-} + RH^{\bullet+}$

[b]The HAT reaction is considered at C35 as: $AntioxH + R^{\bullet} \rightarrow (Antiox)^{\bullet} + RH$

[c]The RAF reaction is considered at C13 as: $Antiox + R^{\bullet} \rightarrow (AntioxR)^{\bullet}$

Table S10. Reaction enthalpies (ΔH^0, kcal/mol) and Gibbs free energies (ΔG^0, kcal/mol) at 298.15 K for the HAT reactions with HOO• and HO• at the most favorable positions calculated in the gas phase.

Radical	Position	ΔH (kcal/mol)		ΔG (kcal/mol)	
		Ibuprofen	Complex	Ibuprofen	Complex
HOO•	C32	9.6	9.7	9.2	10.0
	C35	1.4	1.2	1.2	1.3
HO•	C32	-22.2	-22.1	-23.5	-22.7
	C35	-30.5	-30.6	-31.4	-31.4

Table S11. Imaginary frequencies of TS structures.

Reaction	Radical	TS	Imaginary frequency
HAT	HO•	Ir-C32	-294.96
		Ir-C35	-731.46
		Ibu-C32	-298.17
		Ibu-C35	-650.40
	HOO•	Ir-C32	-1706.56
		Ir-C35	-1842.90
		Ibu-C32	-1727.59
		Ibu-C35	-1761.97
RAF	HO•	Ir-C12	-78.38
		Ir-C13	-120.88
		Flav-C12	-324.91
		Flav-C13	-345.42
	HOO•	Ir-C12	-535.30
		Ir-C13	-535.35
		Flav-C12	-573.22
		Flav-C13	-466.38

Table S12. Energy of the optimized structures of TSs for the RAF reaction with HOO• radical calculated for all possible positions by PM6 and at B3LYP/Landl2dz//6-31G(d) level of theory

Position		PM6 (hartree)		B3LYP/Lanl2dz//6-31G(d) (hartree)
		Ligand	Ir-complex	Ir-complex
Flavonol	C4	-0.0399		
	C6	-0.042247		
	C7	-0.04945		
	C10	-0.05075		
	C11	-0.04909		
	C12	-0.050954	0.699252	-2192.481788
	C13	-0.057518	0.673692	-2192.480718
	C14	-0.048889		
	C15	-0.047006		
	C16	-0.049386		
	C17	-0.051174	0.694146	-2192.477514
	C18	-0.050108		
Ibuprofen	C33	-0.143151		
	C34	-0.143451		
	C38	-0.147874	0.693739	-2192.482106
	C39	-0.146232		
	C40	-0.149567	0.693937	-2192.482688
	C41	-0.147465	0.695079	-2192.475865
2-phenylpyridine	C61	0.107393	0.677233	-2192.478553
	C62	0.108888		
	C63	0.111759		
	C64	0.108973		
	C66	0.113866		
	C67	0.109046		
	C68	0.109506		
	C69	0.109034		
	C70	0.109563		
	C80	0.107448		Ir bonding
	N79	0.108351		

Table S13. Reaction enthalpy and Gibbs free energy of the RAF reaction between Ir (III) complex and HOO• radical calculated for all possible positions at B3LYP/Landl2dz//6-31G(d) level of theory.

Position	ΔH (kcal/mol)	ΔG (kcal/mol)
C12	***8.7***	***20.5***
C13	***6.6***	***18.5***
C17	13.6	26.2
C38	10.8	24.0
C40	10.7	23.0
C41	12.3	23.9
C61	12.6	25.2
C66	16.7	28.8

Table S14. Reaction enthalpies (ΔH^0, kcal/mol) and Gibbs free energies (ΔG^0, kcal/mol) at 298.15 K for the RAF reactions at C12 and C13 calculated in the gas phase at the B3LYP/Lanl2dz//6-31G(d) level of theory.

Radical	Position	ΔH (kcal/mol)		ΔG (kcal/mol)	
		Flavonol	Complex	Flavonol	Complex
HOO•	C12	9.5	8.7	21.2	20.5
	C13	2.0	6.6	14.3	18.5
HO•	C12	-30.2	-22.2	-19.8	-11.7
	C13	-21.6	-32.3	-21.4	-11.2

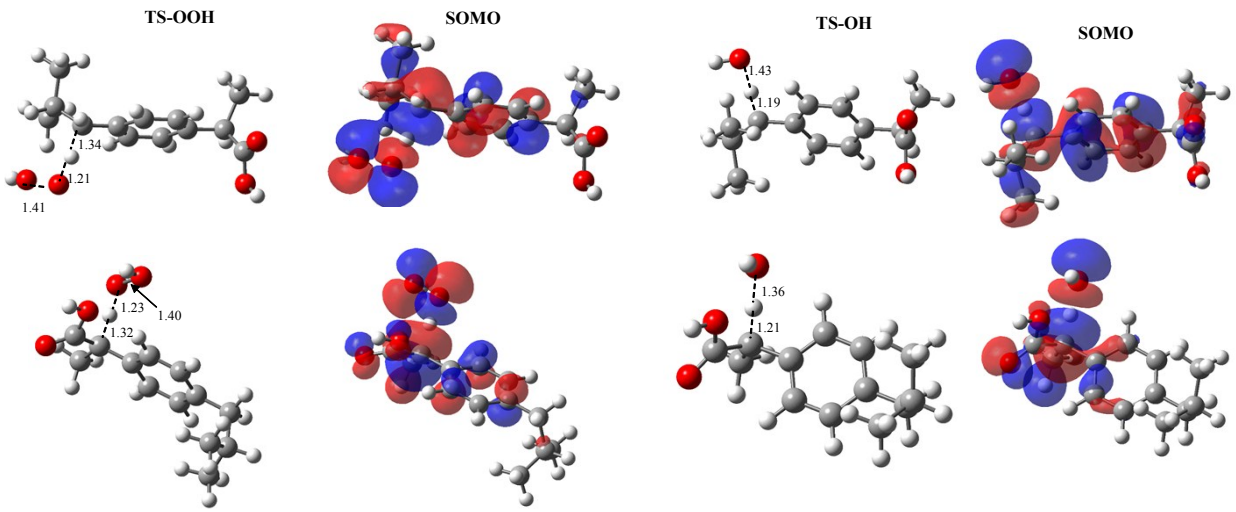

Figure S11. TS and SOMO orbitals of HAT reaction between Ibuprofen and HO•/HOO• radicals occurred at the corresponding positions to C32 and C35 positions of Ir (III) complex.

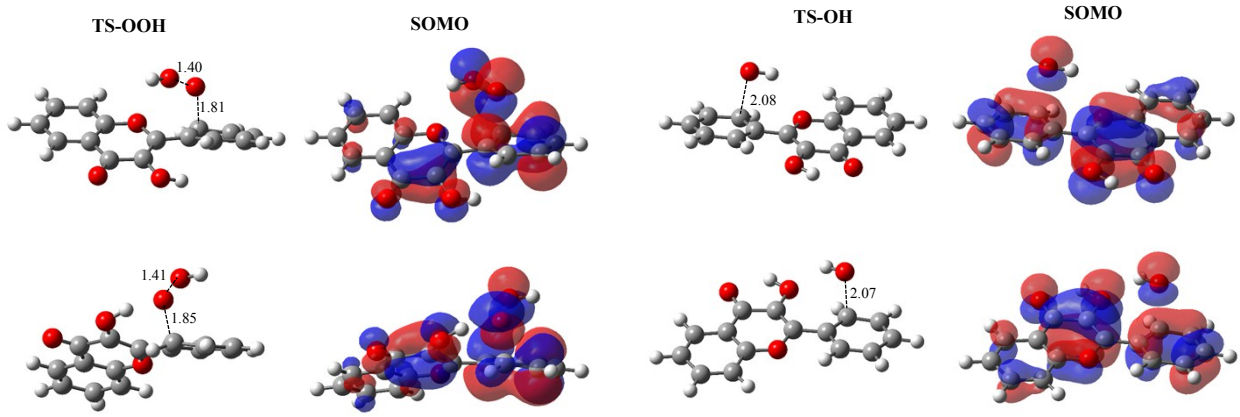

Figure S12. TS and SOMO orbitals of RAF reaction between flavonol and HO•/HOO• radicals occurred at the corresponding positions to C12 and C13 positions of Ir (III) complex.

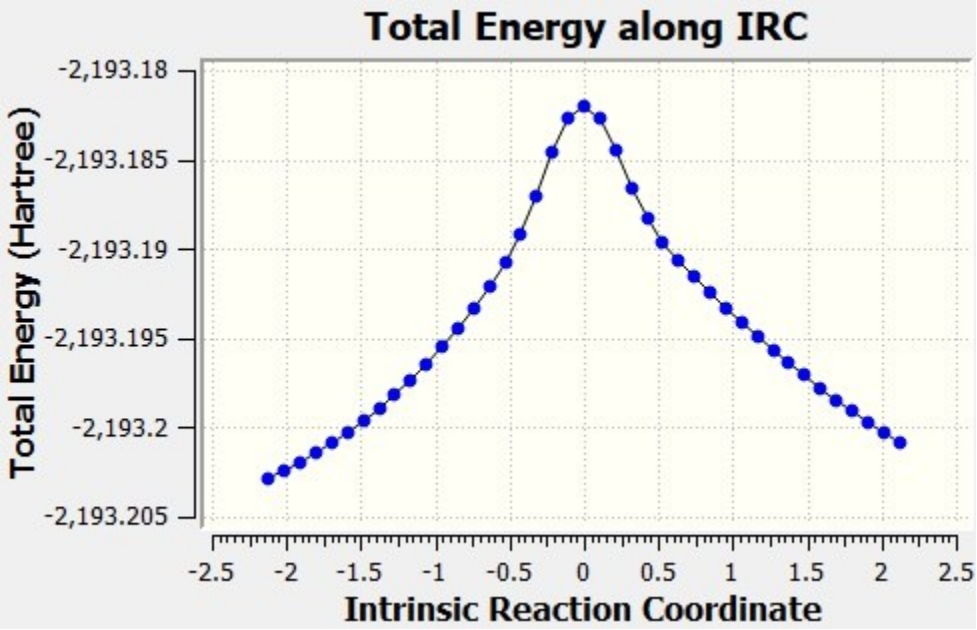

Figure S13. IRC plot of HAT reaction between Ir (III) complex and HOO• radical at C35 position

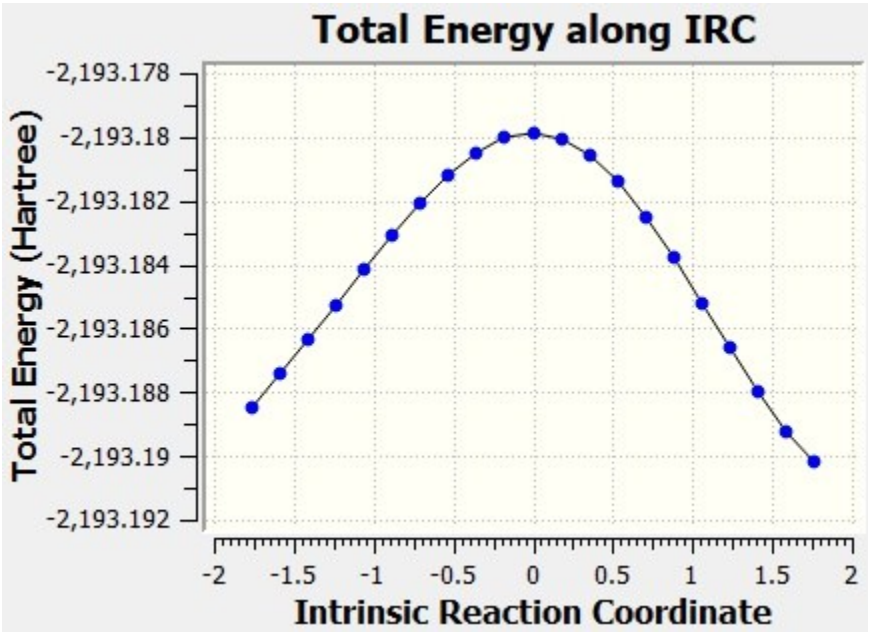

Figure S14. IRC plot of RAF reaction between Ir (III) complex and HOO• radical at C13 position.

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