Mechanistic Investigations of the Iridium(III) Catalyzed Aerobic Oxidations of Primary and Secondary Alcohols.

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Supporting Information

Materials and Methods. Reactions were performed open to the environment as stated or in a Nitrogen filled Glove-box as stated. Oxygen uptake experiments were performed in glass lined stainless steel Parr 4592 50 mL Micro Bench Top Reactor under O_2. Solvents were degassed, and purified with a Mbraun-SPS solvent purification system prior to use. [Cp*IrCl(μ-Cl)]$_2$ was purchased from Strem Chemicals and used as received. Substrates were purchased from VWR or Aldrich and used as received. Oxygen was purchased from Airgas, National Welders. The complexes μ-Chloro-μ-hydrido-bis[chloro(pentamethylcyclopentadienyl)-iridium, **2**, and Di-μ-hydrido-bis(pentamethylcyclopentadienyl)-iridium, **3**, were synthesized according to published procedures.[1] NMR spectra were recorded on Varian 300 instruments. Mass spectrometry was performed by the North Carolina State University Mass Spectrometry Center using an Agilent Technologies 6210LC-TOF mass spectrometer (GC/MS). GC was performed on Varian 3800 Gas Chromatograph with a Varian VF-53ms column.

General Procedure for Kinetic Studies. All reactions were performed in a glass lined stainless steel Parr 4592 50 mL Micro Bench Top Reactor connected to a Cole-Palmer high-accuracy pressure transducer (0.15%) at 80°C. The pressure of O_2 was monitored in ten minute intervals with a Monarch Instrument paperless recorder. The reactor was filled with 10 mL of toluene, 1.0 mL (0.96 M) of benzyl alcohol, 25 μL (0.018 M) of triethylamine and 100 mg of [Cp*IrCl(μ-Cl)]$_2$ (12.6 mM). The reactor was purged with O_2 and filled with 14.7 psi (1 atm) O_2. The data was analyzed using the Kaleidograph$^{\circledR}$ software package. The observed rate constants k_{obs} were obtained from nonlinear least squares fitting of P_t to: $P_t = \Delta P \exp(-k_{obs} t) + P_\infty$ where $\Delta P = P_0 - P_\infty$
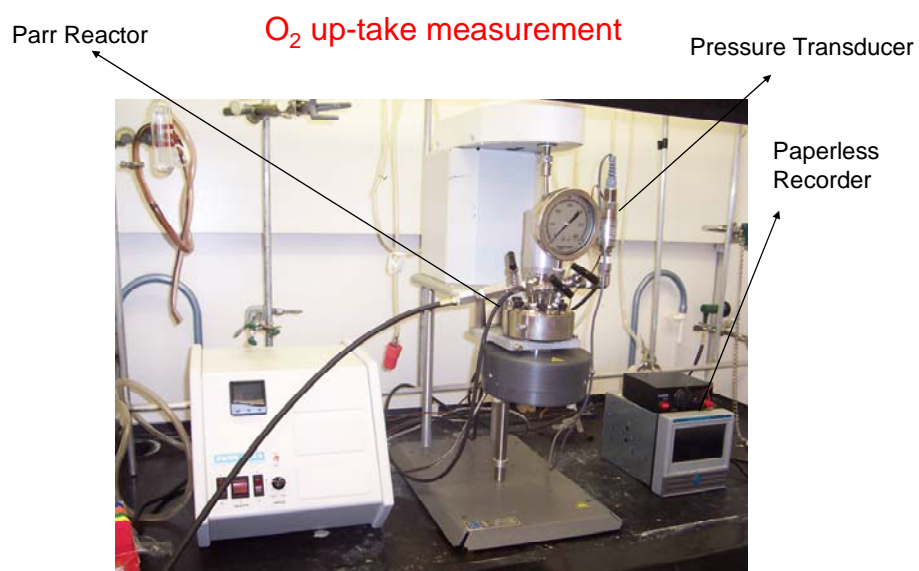
Figure S1. Apparatus for oxygen uptake and kinetic studies.

Measurement of Deuterium Kinetic Isotope Effect. k_{obs} of benzyl alcohol and benzyl alcohol-α,α-d$_2$ were obtained following procedures above. $k_H/k_D = k_{obs}$ (benzyl alcohol) / k_{obs} (benzyl alcohol-α,α-d$_2$) = 0.9(1).
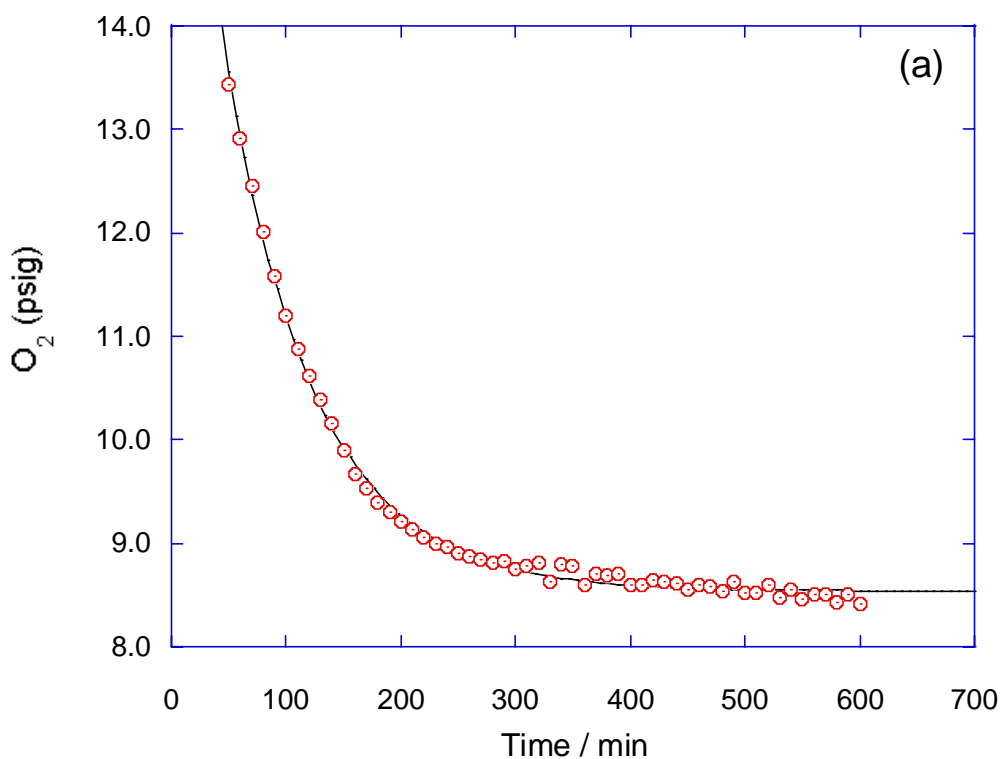
Figure S2. Pressure of O_2 versus time profile for the oxidation of benzyl alcohol (1.0 M) with O_2 (14.7psig), Et$_3$N (0.018 M) and **1** (12.6 mM) in toluene at 353 K. The observed rate constant (k_{obs}) is 0.0128(2) / min^{-1}, R^2=0.997. The observed rate constants (k_{obs}) were obtained from nonlinear least squares fitting of P$_t$ to: [P$_t$] = ΔP exp($-k_{obs}$ t) + P$_\infty$ where ΔP = P$_0$ -P$_\infty$
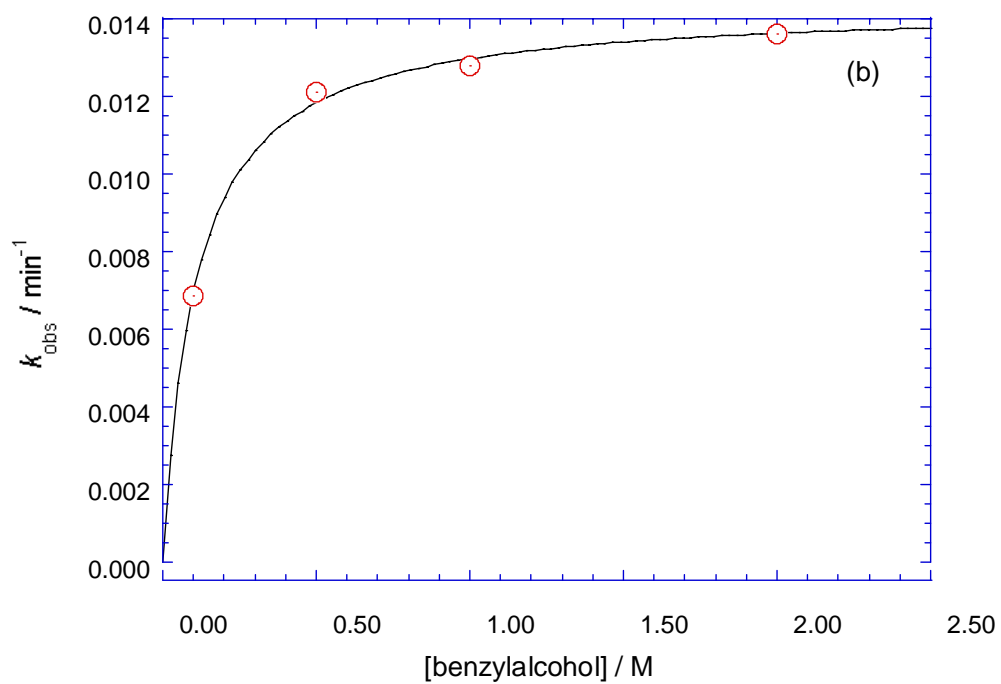
Figure S3. Plot of the k_{obs} versus [benzyl alcohol] with O_2 (14.7 psig), Et_3N (0.018 M) and **1** (12.6 mM). Rate measurements were carried out in toluene at 353 K.

Entry	Benzyl alcohol / M	k_{obs} / min^{-1}
1	0.1	0.00686
2	0.5	0.01210
3	1.0	0.01280
4	2.0	0.01360
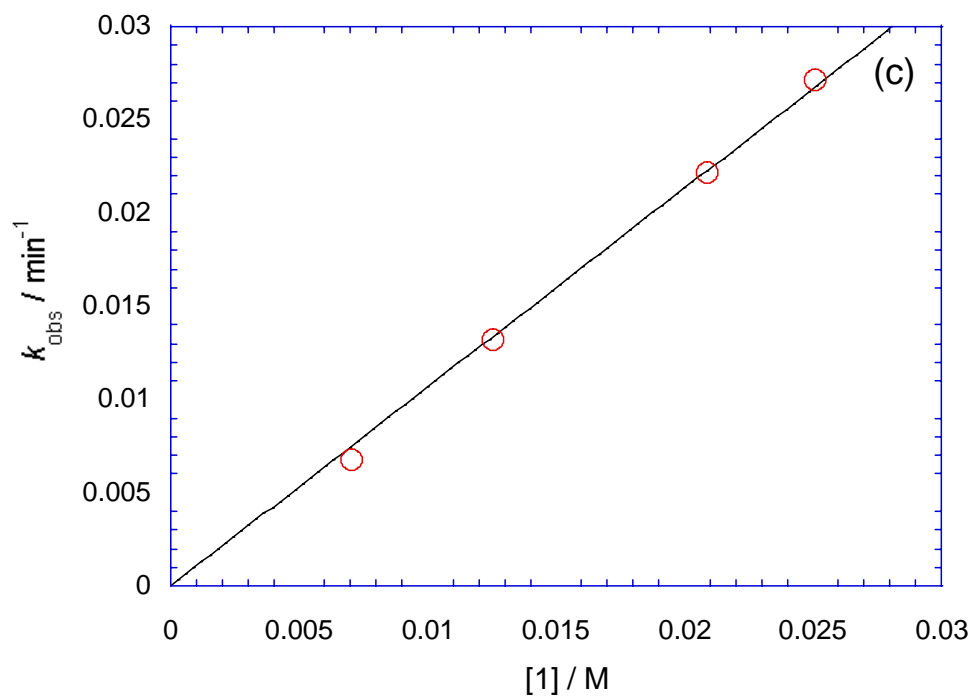
Figure S4. Plot of the k_{obs} versus [**1**] with benzyl alcohol (1M), O_2 (14.7 psig), Et_3N (0.018 M). Rate measurements were performed in toluene at 353 K.

Entry	Catalyst / M	K_{obs} / min^{-1}
1	0.00703	0.00681
2	0.01255	0.01320
3	0.02092	0.02215
4	0.02510	0.02719
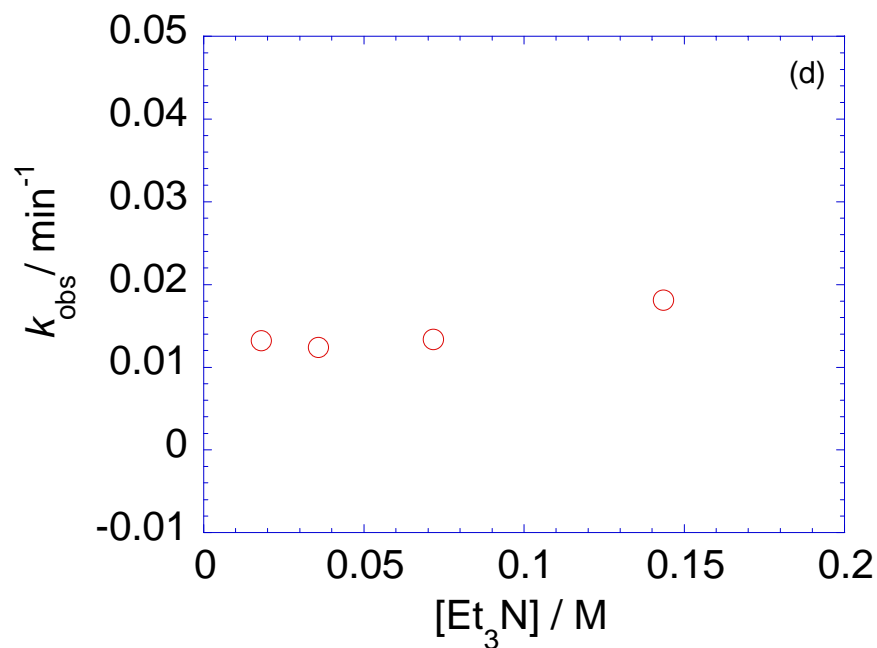
Figure S5. Plot of k_{obs} versus concentration of Et$_3$N with catalyst **1** (12.6 mM), benzyl alcohol (1M), O$_2$ (14.7 psig) in toluene at 353 K.

Entry	TEA / M	K_{obs} / min^{-1}
1	0.01794	0.01322
2	0.03587	0.01238
3	0.07175	0.01334
4	0.14350	0.01810

Figure S6. Pressure of O_2 versus time profile for the oxidation of benzyl alcohol (1.0 M), with O_2 (14.7psig), Et_3N (0.018 M) and **2** (12.6 mM) in toluene at 353 K. The observed rate constant (k_{obs}) is 0.0199(2) / min^{-1}, R^2=0.994.

Table S1. Aerobic Oxidations of Primary and Secondary Alcohols Catalyzed by **1**.[a]

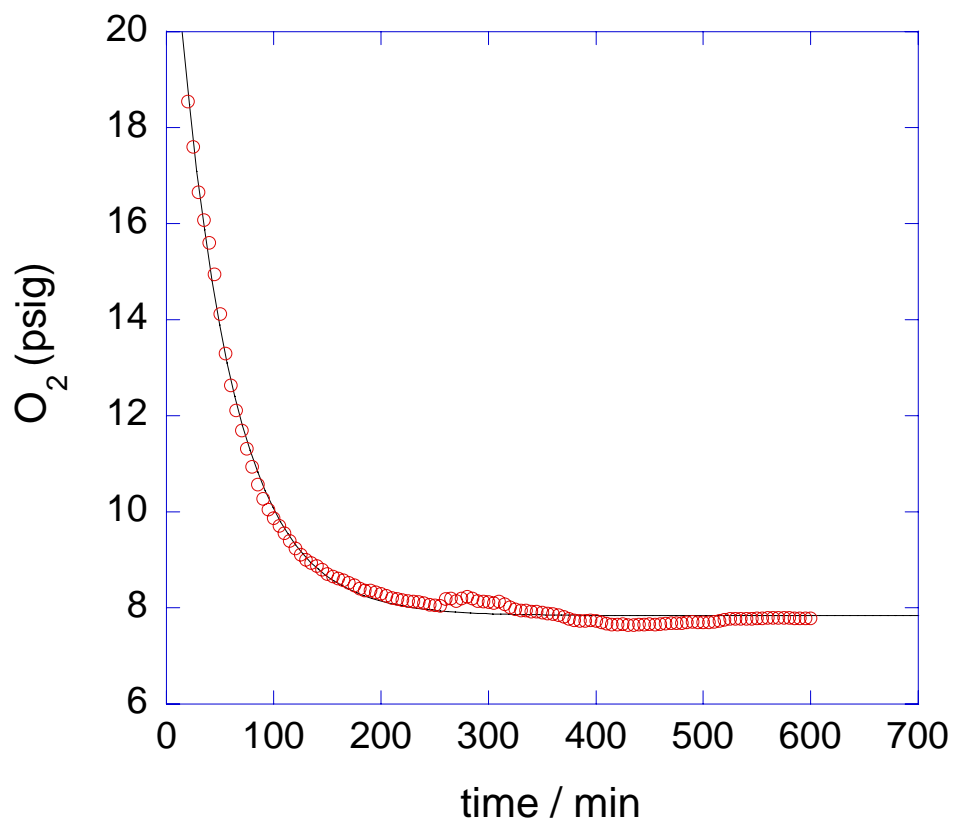| Entry	Substrate	Time (hrs)	Conv[b] (%)	Yield[c] (%)	TON[d]
1	4-methoxybenzyl alcohol	12	90(5)	82(8)	18
2	4-methylbenzyl alcohol	12	87(7)	81(5)	17
3	benzyl alcohol	12	82(4)	76(4)	16
4	4-chlorobenzyl alcohol	24	84(7)	79(6)	17
5	4-(methythio)benzyl alcohol	24	86(3)	81(4)	17
6	4-nitrobenzyl alcohol	12	46(2)	39(2)	9.2
7	cyclohexanol	12	94(5)	86(3)	19
8	2-propanol	12	82(4)	74(4)	16

[a]Reaction Conditions: 5 mol % **1**, substrate (0.5-1M). [b]Conversion by GC with respect to alcohol. [c]Yield by GC with respect to aldehyde. [d]TON with respect to alcohol.

A solution of alcohol (0.05M), catalyst 1 (2.5mM), TEA (0.018M) in toluene (10ml) was purged with O_2 and stirred under constant O_2 (14.7psig) at 80°C for 12 hours. 1mL of toluene solution was collected and 0.1 mL of octane was added to the solution as internal standard.   The products were analyzed by GC. Calibration curves for each substrate and product were made with octane as an internal standard. Conversions and yields were obtained based on the calibration curves.

Synthesis of [Cp*IrCl]₂HCl, 2.   [Cp*IrCl]$_2$HCl is synthesized according to published procedure. A solution of [Cp*IrCl(μ-Cl)]$_2$ (0.30g (0.377mmol)) and KBH$_4$ (0.05g (0.927mmol)) in isopropyl alcohol (10ml) was stirred at room temperature (20°C)

for 4 hours. The solvent was removed on a rotary evaporator to leave a red residual. It was extracted with toluene (30ml), filtered, and reduced to small volume. Hexanes was added and red-purple crystals of the hydrido-complex (**2**) were obtained. Yield (52 %).^{1}H NMR (300MHz, Toluene-d$_8$): δ1.62 (s, 30H, η^5-C$_5$Me$_5$), -13.85 (s, 1H, Ir-*H*); ^{13}C NMR (300MHz, Toluene-d$_6$): δ 88.98 [s, C$_5$-(CH$_3$)$_5$, -*C*=*C*-], 10.15 [s, C$_5$-(CH$_3$)$_5$, -*CH*$_3$].

Synthesis of [Cp*IrCl(μ-H)]$_2$, 3. [Cp*IrCl(μ-H)]$_2$ is synthesized by the same procedure above with the reaction time extended to 12 hours to give di-hydrido complex **3**. Yield (90%). ^{1}H NMR (300MHz, Toluene-d$_6$): δ1.48 (s, 30H, η^5-C$_5$Me$_5$), -13.67 [s, 2H, Ir(*H*)$_2$]; ^{13}C NMR (300MHz, Toluene-d$_8$): δ 88.98 [s, C$_5$-(CH$_3$)$_5$, -*C*=*C*-], 10.15 [s, C$_5$-(CH$_3$)$_5$, -*CH*$_3$].

Catalytic oxidation of 4-methoxyl benzyl alcohol under Oxygen, air and nitrogen atmosphere. In three J-Young NMR tubes, each was charged with [Cp*IrCl(μ-Cl)]$_2$ (3.6 mg, 4.52E-3mmol), 4-methoxyl benzyl alcohol (22 μL, 0.180mmol), triethylamine (22 μL,0.163mmol) and toluene-d$_8$ (1mL). Three NMR tubes were freeze-pump-thaw three times and back filled with A) oxygen; B) air and C) nitrogen. The NMR tubes were heated to 80oC in oil bath and NMR spectrum was monitored periodically. In all three tubes, the solution was red before heating, but 2 minutes after heating to boil, the solution turns to dark red clear solution without any precipitate, which is due to the formation of the intermediate [[Cp*IrCl]2HCl] (resonance at 1.62 ppm is observed, which is due to the CH$_3$ of Cp* ligand). After 12 hours, 95.65% of 4-methoxyl benzyl alcohol was converted to 4-methoxyl benzaldehyde in tube A (TON = 38.26) and

conversion is 24.24% (TON = 9.6) for tube B and 11.5% (TON = 4.6) for tube C, respectively.

[[Cp*IrCl]₂HCl] and Et₃NHCl in O₂ or N₂ at 80°C. Two J-young NMR tubes were charges with [[Cp*IrCl]₂HCl] (5 mg, 6.56E-3 mmol) and Et₃NHCl (2.6 mg, 0.026 mmol) and toluene-d_8, respectively. Freeze-pump-thaw three times of both NMR tubes and tube A is back-filled with O_2, while tube B is back-filled with N_2. The two tubes were heated in a 80°C oil bath and NMR spectrum were monitored periodically. For tube A, after 4 hours, a new resonance grew at 1.58 ppm, instead the resonance due to Cp* CH_3 of [[Cp*IrCl]₂HCl] decreased. After 16 hours, [[Cp*IrCl]₂HCl] was disappeared and only the unidentified new resonance was observed (see NMR spectrum shown below); for tube B, [[Cp*IrCl]₂HCl] resonances was observed even after 16 hours heating.
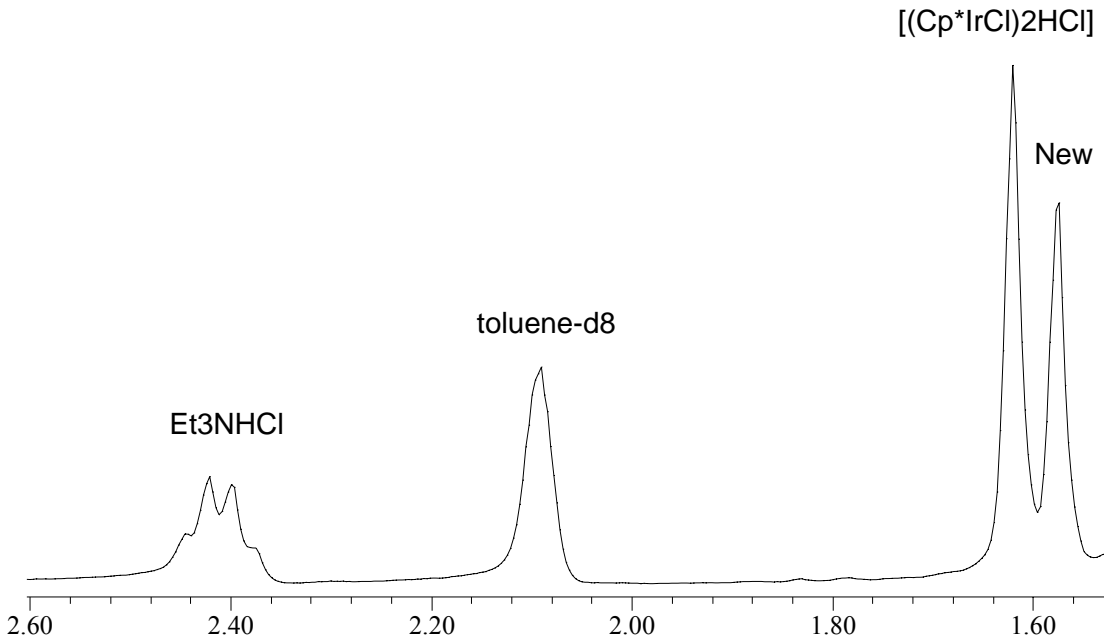
Oxygen atmosphere: 4 hours

Figure S7. NMR spectrum of [[Cp*IrCl]₂HCl] and Et₃NHCl in O_2 after 4 hours.

Oxygen atmosphere: 16 hours
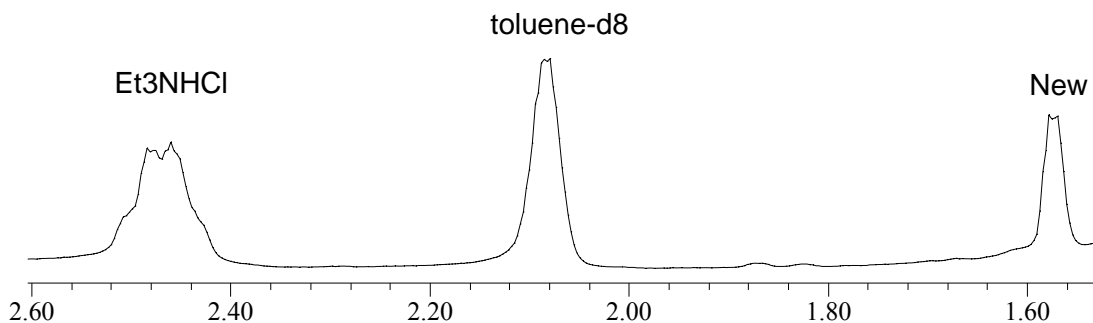
[Cp*IrCl)2HCl] at 1.62 ppm disappeared

Figure S8. NMR spectrum of [[Cp*IrCl]$_2$HCl] and Et$_3$NHCl in O$_2$ after 16 hours.

Reaction of [[Cp*IrCl]$_2$HCl] and benzaldehyde: A J-young NMR tube was charged with [[Cp*IrCl]$_2$HCl] (5 mg, 6.56E-3 mmol), Et$_3$NHCl (3.61 mg, 0.026 mmol), benzaldehyde (13.6 uL, 0.131 mmol) and benzene-d_6 (0.5 mL). The NMR tube was freeze-pump-thaw three times and back-filled with N$_2$. The tube was heated to 80°C in a oil bath and NMR spectrum was monitored. After 2 hours, the formation of benzyl alcohol was observed with the ratio of benzaldehyde : benzyl alcohol = 1.3 : 1. After 12 hours, the ratio of benzaldehyde : benzyl alcohol = 1:1.

Reaction of [Cp*IrCl(μ-Cl)]$_2$, benzyl alcohol and Et$_3$N in toluene-d_8 at room temperature. A regular NMR tube was charged with [Cp*IrCl$_2$]$_2$ (5 mg, 6.28E-3 mmol), benzyl alcohol (13.0 uL, 0.125 mmol) and toluene-d_8 (0.5 mL), and NMR spectrum was monitored periodically. No reaction was observed after 12 hours at room temperature. Et$_3$N (3.48 uL, 0.025 mmol) was added to the NMR tube and NMR spectrum was taken immediately, resonances (δ 9.60 (s, 1H, -C*H*O), 7.48 (d, 2H, *ortho*-phenyl), 7.09 (t, 1H,

para-phenyl), 7.01 (t, 2H, *meta*-phenyl)) due to benzyl aldehyde (10% from NMR integration) and resonances [δ1.62 (s, 30H, η^5-C$_5$Me$_5$), -13.85 (s, 1H, Ir-*H*)] due to [(Cp*IrCl)$_2$HCl] were observed from NMR spectrum.

Reaction of [Cp*IrCl₂]₂, benzyl alcohol and Et₃N at room temperature monitored by UV-Vis spectroscopy. Four methylene chloride solutions were prepared 1) [Cp*IrCl₂]₂ (0.628 mM), 2) [Cp*IrCl₂]₂ (0.628 mM) with benzyl alcohol (0.628 mM), 3) [Cp*IrCl₂]₂ (0.628 mM) with benzyl alcohol (0.628 mM) and TEA (0.628 mM), 4) [Cp*IrCl₂]HCl (0.314 mM) and UV-Vis spectrum were taken of these four solutions (shown below). There is no reaction of [Cp*IrCl]₂ and benzyl alcohol (same UV absorption shown) and the reaction of [Cp*IrCl₂]₂, benzyl alcohol and TEA forms [[Cp*IrCl2]HCl] immediately (same UV absorption, except different concentration).
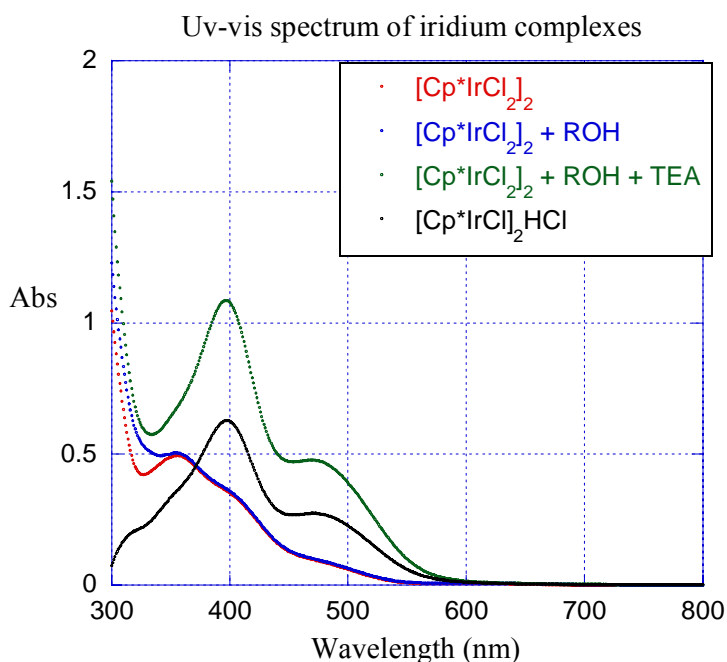

Figure S9. UV spectrum were taken in the order of [Cp*IrCl₂]₂ (0.628 mM)(red line), [Cp*IrCl₂]₂ (0.628 mM) with benzyl alcohol (0.628 mM)(blue line), [Cp*IrCl₂]₂ (0.628

mM) with benzyl alcohol (0.628 mM) and TEA (0.628 mM)(green line), [Cp*IrCl$_2$]HCl (0.314 mM)(black line) (solvent: CH$_2$Cl$_2$).

Reaction of [Cp*IrCl(μ-H)]$_2$ and Et$_3$NHCl: A J-young NMR tube was charged with [Cp*IrCl(μ-H)]$_2$ (5 mg, 6.87E-3 mmol), Et$_3$NHCl (3.72 mg, 0.027 mmol) and benzene-d_6 (0.5 mL). The NMR tube was freeze-pump-thaw three times and back-filled with O$_2$. The tube was heated to 80°C in a oil bath and NMR spectrum was monitored. After 12 hours, [Cp*IrClH]$_2$ decomposed to several unidentified complexes.

Reaction of [Cp*IrCl(μ-H)]$_2$, benzyl alcohol and Et$_3$N: A J-young NMR tube was charged with [Cp*IrCl(μ-H)]$_2$ (5 mg, 6.87E-3 mmol), Et$_3$N (3.62 uL, 0.026 mmol), benzyl alcohol (14.2 uL, 0.137 mmol) and benzene-d_6 (0.5 mL). The NMR tube was freeze-pump-thaw three times and back-filled with O$_2$. The tube was heated to 80°C in a oil bath and NMR spectrum was monitored. After 12 hours, 10% benzyl aldehyde was formed with TON=2.

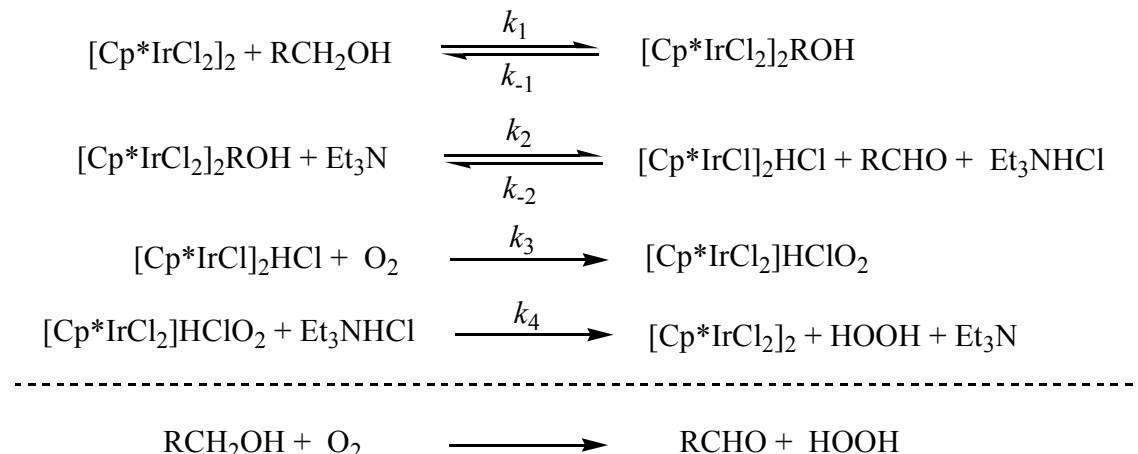**Reaction of [Cp*IrCl(μ-Cl)]$_2$, 4-methoxy benzyl alcohol and Et$_3$N at room temperature under N$_2$:** A J-young NMR tube was charged with [Cp*IrCl(μ-Cl)]$_2$ (5 mg, 6.28E-3 mmol), Et$_3$N (3.48 uL, 0.025 mmol), 4-methoxy benzyl alcohol (38.7 uL, 0.314 mmol) and toluene-d_8 (0.5 mL). The NMR tube was freeze-pump-thaw three times and back-filled with N$_2$. The tube was warmed to room temperature and NMR spectrum was monitored. After 2 hours, the formation of **2** and **3** were observed with the ratio of **2** : **3** = 6 : 1.

Reaction of [[Cp*IrCl]$_2$HCl], 4-methoxy benzyl alcohol and Et$_3$N at room temperature: A regular NMR tube was charged with **2** (5 mg, 6.56E-3 mmol), Et$_3$N

(3.62 uL, 0.026 mmol), 4-methoxy benzyl alcohol (40.5 uL, 0.328 mmol) and toluene-d_8

(0.5 mL). After 1 hour, **3** was formed with a yield of 10%.

Rate law derivations

The following mechanism accounts for the experimental observations.

$$[Cp*IrCl_2]_2 + RCH_2OH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Cp*IrCl_2]_2ROH$$

$$[Cp*IrCl_2]_2ROH + Et_3N \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [Cp*IrCl]_2HCl + RCHO + Et_3NHCl$$

$$[Cp*IrCl]_2HCl + O_2 \overset{k_3}{\longrightarrow} [Cp*IrCl_2]HClO_2$$

$$[Cp*IrCl_2]HClO_2 + Et_3NHCl \overset{k_4}{\longrightarrow} [Cp*IrCl_2]_2 + HOOH + Et_3N$$

$$RCH_2OH + O_2 \longrightarrow RCHO + HOOH$$

The rate of dioxygen uptake is described by the following rate law.

$$\text{Rate} = \frac{-d\text{P}(O_2)}{dt} = k_3[[Cp*IrCl]_2HCl][O_2] \tag{1}$$

$$[[Cp*IrCl_2]_2]_T = [Cp*IrCl_2]_2 + [[Cp*IrCl_2]_2ROH] + [[Cp*IrCl_2]_2HCl] \tag{2}$$

We assume [[Cp*IrCl_2]_2ROH] are vanishingly small and does not contribute significantly to the steady state [Ir], based on the following experimental observations: Treatment of **1** with benzylalcohol at room temperature does not result in a change in the ^{1}H NMR or UV spectrum of **1**. However treatment of this solution with Et_3N results in the immediate formation of a stoichiometric amount of benzaldehyde and **2.** This suggests that [Cp*IrCl_2]_2ROH does not build up appreciably in concentration during the catalytic reaction. Equations 3-9 assume **1** reacts with RCH_2OH in a prior equilibrium step, to

form an adduct prior to Et_3N induced β-hydrogen elimination and the formation of **2**. A kinetically indistinguishable rate expression is also obtained if one also assumes a steady state [[Cp*IrCl$_2$]$_2$ROH]]

$$[[Cp*IrCl_2]_2]_T \quad = \quad [Cp*IrCl_2]_2 + [[Cp*IrCl_2]_2HCl] \tag{3}$$

According to the steady-state approximation for [[Cp*IrCl$_2$]$_2$HCl]],

$$k_2 [[Cp*IrCl_2]_2ROH]] [Et_3N] = k_{-2}[[Cp*IrCl_2]_2HCl]] [RCHO] [Et_3NHCl]$$

$$+ k_3 [[Cp*IrCl]_2HCl] [O_2] \tag{4}$$

$$K_1 = k_1/k_{-1} = [Cp*IrCl_2]_2ROH/[[Cp*IrCl_2]_2][RCH_2OH] \tag{5}$$

Substitute (5) into (4),

$$[[Cp*IrCl_2]_2HCl] \quad = \quad \frac{K_1k_2[RCH_2OH][Et_3N][[Cp*IrCl_2]_2]_T}{k_{-2}[RCHO][Et_3NHCl] + k_3[O_2] + K_1k_2[RCH_2OH][Et_3N]} \tag{6}$$

Substitute (6) into (1),

$$\text{Rate} = \frac{-d\text{P}(O_2)}{dt} = \frac{K_1k_2k_3[RCH_2OH][Et_3N][[Cp*IrCl_2]_2]_T[O_2]}{k_{-2}[RCHO][Et_3NHCl] + k_3[O_2] + K_1k_2[RCH_2OH][Et_3N]} \tag{7}$$

From Figure **1a**, it is observed experimentally that the reaction is 1st order in $[O_2]$, Equation (7) predicts a 1st order dependence on $[O_2]$ when $k_3[O_2] \ll k_{-2}[RCHO][Et_3NHCl] + k_1k_2[RCH_2OH][Et_3N]$ in the denominator in equation (7). Kinetic data were acquired with the following conditions: benzyl alcohol (1M) with O_2 (14.5 psig), Et_3N (25.1 mM) and **1** (12.6 mM) in toluene at 353 K. The solubility of O_2 in toluene at 353 K is $\approx$ 10 mM,[2] $\therefore$ under the conditions for the kinetic runs, $[O_2] \ll [RCHO][Et_3NHCl] + [RCH_2OH][Et_3N]$ and equation (7) reduces to:

$$\text{Rate} = \frac{-d\text{P(O}_2)}{dt} = \frac{K_1 k_2 k_3 [\text{RCH}_2\text{OH}][\text{Et}_3\text{N}][[\text{Cp*IrCl}_2]_2]_\text{T}[\text{O}_2]}{k_{-2}[\text{RCHO}][\text{Et}_3\text{NHCl}] + K_1 k_2 [\text{RCH}_2\text{OH}][\text{Et}_3\text{N}]} \tag{8}$$

From Figure **1b**, saturation kinetics is observed for $[\text{RCH}_2\text{OH}]$. This is consistent with and predicted by equation (8). Equation (8) also predicts a 1st order dependence in $[\text{Ir}]_\text{T.}$ This is observed experimentally, (Figure **1c**). Finally equation (8) predicts no dependence on $[\text{Et}_3\text{N}]$ when $k_{-2}[\text{RCHO}][\text{Et}_3\text{NHCl}] \ll k_1 k_2 [\text{RCH}_2\text{OH}][\text{Et}_3\text{N}]$ and equation 8 reduces to:

$$\text{Rate} = \frac{-d\text{P(O}_2)}{dt} = k_3 [[\text{Cp*IrCl}_2]_2]_\text{T}[\text{O}_2] \tag{9}$$

Kinetic data acquired for Figure **1d** with the following conditions: $[\text{Et}_3\text{N}]$ (0.018M - 0.143M) O_2 (14. 5psig), [**1**] (12.6mM), benzyl alcohol (1M) in toluene at 353K, $\therefore$ under the conditions for the kinetic runs, $[\text{RCHO}][\text{Et}_3\text{NHCl}] \ll [\text{RCH}_2\text{OH}][\text{Et}_3\text{N}]$ and equation (8) reduces to equation (9). This is observed experimentally (Figure **1d**).

References

1. White, C; Oliver, A. J.; Maitlis, P. M., *J. Chem. Soc., Dalton Trans.*, **1973**, 1901 – 1907

2. (a) Battino, R., Ed. *Solubility Data Series, Vol. 7: Oxygen and Ozone*; Pergamon: New York, **1981**. (b) Fischer, K.; Wilken, M. *J. Chem. Thermodyn. **2001**, 33, 1285-1308.