CH Activation with an O-donor Ir Methoxo Complex

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General Considerations: All air and water sensitive procedures were carried out either in a MBraun inert atmosphere glove box, or using standard Schlenk techniques under argon. Methanol was dried from Mg/I₂, and benzene from sodium/benzophenone ketal. All deuterated solvents (Cambridge Isotopes), and NaOCH₃ (Aldrich) were used as received. Complexes 1 and 1-Cl were prepared as described in the literature.¹ GC/MS analysis was performed on a Shimadzu GC-MS QP5000 (ver. 2) equipped with cross-linked methyl silicone gum capillary column (DB5). The retention times of the products were confirmed by comparison to authentic samples. NMR spectra were obtained on a Varian Mercury-400 spectrometer at room temperature. All chemical shifts are reported in units of ppm and referenced to the residual protonated solvent. All high-resolution mass spectra were obtained by UCLA Pasarow Mass Spectrometry Laboratory on an ESI mass spectrometer. Elemental Analysis was performed by Desert Analytics of Tucson, Arizona.

X-ray Crystallography. Diffraction data for 2-Py and 2-CH₃OH were collected at low temperature (T = 153 K ans 133 K respectively) on a Bruker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The cell parameters for the Ir complex were obtained from the least-squares refinement of the spots (from 60 collected frames) using the SMART program. A hemisphere of the crystal data was collected and the intensity data was processed using the Saint Plus program. All calculations for structure determination were carried out using the SHELXTL package (version 5.1).² Initial atomic positions were located by direct methods using XS, and the structure was refined by least-squares methods using SHELX. Absorption corrections were applied by using SADABS.³ Calculated hydrogen positions were input and refined in a riding manner along with the attached carbons.
Synthesis of \([\text{CH}_3\text{O-Ir(O,acac)}_2(\text{CH}_3\text{OH})]\) (2-\text{CH}_3\text{OH}): To a 30 mL thick-walled ampoule equipped with a high-vacuum valve at top \([\text{acac-Ir(O,acac)}_2]\), 1 (370 mg, 0.38 mmol), sodium methoxide (128 mg, 2.37 mmol), and 30 mL methanol were added. The mixture was heated at 130°C with stirring for 30 min. During this time the color of the solution turned from yellow to dark red. After cooling, the solution was twice filtered through a pad of basic alumina on a medium porosity frit, and purified by centrifugal thin layer chromatography using ethyl acetate: methanol 9:1 on alumina (the material was loaded onto the disk using methylene chloride and washed with methylene chloride for approximately 5 minutes before eluting. The eluent was concentrated under vacuum to yield approximately 74 mg (22%) of title complex as an orange solid. ¹H NMR (CD$_3$OD): $\delta$ 5.50(s, 2H, CH), 2.83(s, 3H, Ir-OCH$_3$), 2.01(s, 12H, CH$_3$). ¹³C¹H NMR (CD$_3$OD): $\delta$ 187.39(C-acac, C=O), 103.9(O-acac, CH), 55.9(OCH$_3$), 27.0(O-acac, CH$_3$). HRMS (ESI): Calculated for C$_{12}$H$_{22}$IrO$_6$ (M+H) 455.1046, found 455.1035. Elemental Analysis: Calculated for C$_{12}$H$_{21}$IrO$_6$: C, 31.78; H, 4.67. Found: C, 31.82; H, 4.53.

Single crystals were grown by slow evaporation of a concentrated sample in chloroform.

Crystal data for 2-\text{CH}_3\text{OH}: a yellow-orange prism-shaped crystal of dimensions 0.29 x 0.05 x 0.03 mm was grown from chloroform by slow evaporation of the solvent. C$_{24}$H$_{40}$Ir$_2$O$_{12}$: orthorhombic, group Pnma, $a = 7.8771(16)$ Å, $b = 11.924(2)$ Å, $c = 16.046(3)$ Å, $V = 1147.1(5)$ Å$^3$, $Z = 2$, $T = 133(2)$ K, $D$$_{calc} = 2.035$ Mg/m$^3$, $R(F) = 6.02$ for 8995 observed reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters.+ Full crystallographic information is given in a separate document in the Supporting Information for this paper.

ORTEP diagram of complex 2-\text{CH}_3\text{OH}, showing ellipsoids at the 50% probability level. A molecule of co-crystallized CHCl$_3$ has been omitted for clarity.
Alternative synthesis of \( \text{[CH}_3\text{O-Ir(O,O-acac)}_2(\text{CH}_3\text{OH})] \) (2): To a 50 mL re-sealable Schlenk tube [Cl-Ir(O,O-acac)]_2 \( \text{1-Cl} \) (250 mg, 0.29 mmol), sodium methoxide (125 mg, 2.32 mmol), and 30 mL methanol were added. The mixture was heated to gentle reflux with stirring for 32 hr. During this time the color of the solution turned from yellow to dark red. The volatiles were removed from the tube under vacuum, and the remaining solids were dissolved in methylene chloride, filtered through a medium porosity frit, and purified by column chromatography using ethyl acetate: methanol 5:1 on alumina. The eluent was concentrated under vacuum to yield 5% of title complex as an orange solid.

Synthesis of \( \text{[CH}_3\text{O-Ir(O,O-acac)}_2(\text{Py})] \) (2-Py): A 15 mL re-sealable Schlenk tube was charged with 2-CH\(_3\)OH (10 mg, 0.022 mmol) and pyridine (7 mL) was added. The Schlenk tube was then sealed, and placed in a 55\(^\circ\)C oil bath for 30 min. The resulting yellow-orange solution was cooled to room temperature, and the volatiles were removed under vacuum, yielding a yellow-orange solid in quantitative yield. The product was recrystallized from dichloromethane.\(^1\)H NMR (CDCl\(_3\)): \( \delta \) 8.25(d, 2H, o-Py), 7.72(t, 1H, p-Py), 7.24(t, 2H, m-Py), 5.32(s, 2H, CH), 3.16(s, 3H, Ir-OCH\(_3\)), 1.94(s, 12H, CH\(_3\)). \(^{13}\)C\(^{1}\)H NMR (CDCl\(_3\)): \( \delta \) 185.2(C-acac, C=O), 152.1(o-Py), 137.5(p-Py), 124.9(m-Py), 102.8(O-acac, CH), 57.9(OCH\(_3\)), 26.9(O-acac, CH\(_3\)). HRMS (MALDI-TOF): Calculated for C\(_{16}\)H\(_{22}\)IrNO\(_5\)Na (M+Na) 524.1025, found 524.1043. Single crystals were grown by slow evaporation of a concentrated sample in chloroform.

Crystal data for 2-Py: a yellow-orange prism-shaped crystal of dimensions 0.35 x 0.32 x 0.10 mm was grown from chloroform by slow evaporation of the solvent. C\(_{16}\)H\(_{22}\)IrNO\(_5\)-CHCl\(_3\): orthorhombic, group \( Pnma \), \( a = 11.2909(8) \) Å, \( b = 13.7659(10) \) Å, \( c = 13.9240(10) \) Å, \( V = 2164.2(3) \) Å\(^3\), \( Z = 4 \), \( T = 133(2) \) K, \( D_{calcd} = 1.903 \) Mg/m\(^3\), \( R(F) = 2.46 \) for 12680 observed reflections. All non-hydrogen atoms were refined with anisotropic displacement parameters. Full crystallographic information is given in a separate document in the Supporting Information for this paper.
ORTEP diagram of complex 2-Py, showing ellipsoids at the 50% probability level. A molecule of co-crystallized CHCl₃ has been omitted for clarity. Selected bond distances (Å): Ir1-O3, 2.024(4); Ir1-N1, 2.048(5).

CH activation reaction between 2 and benzene: To a re-sealable Schlenk tube was added 2 (5 mg, 0.011 mmol), and benzene (1 mL). The resulting suspension was thoroughly degassed before being placed under an atmosphere of argon. The tube was sealed and then heated to 160°C in an oil bath for 10 min. After a few minutes of heating, the solid dissolved to yield a clear orange-yellow solution that lightened over the course of the reaction to clear light yellow. After cooling to room temperature, the solvent was removed to yield a yellow solid which was characterized as the iridium phenyl complex which has been previously reported by our group.¹ ¹H NMR (THF-d8): δ 6.65(m, 3H, Ph), 6.57(m, 2H, Ph), 5.21(s, 2H, CH), 1.77(s, 12H, CH₃), ¹³C{¹H} NMR (THF-d₈): δ 184.5(s, O-acac, C=O), 136.3(s, Ph), 125.3(s, Ph), 122.9(s, Ph), 103.0(s, O-acac, CH), 26.6(s, O-acac, CH₃). Further treatment of this material with pyridine yielded the pyridyl derivative, which has been previously reported by our group.¹ ¹H NMR (CDCl₃): δ 8.52(m, 2H, py), 7.81(m, 1H, py), 7.46(m, 2H, py), 6.99(m, 5H, Ph), 5.14(s, 2H, CH), 1.80(s, 12H, CH₃), ¹³C{¹H} NMR (THF-d₈): δ 184.5(s, O-acac, C=O), 149.7(s, py), 137.3(s, Ph), 135.7(s, py), 131.3(s, Ph), 125.2(s, py), 124.5(s, Ph), 103.2(s, O-acac, CH), 27.2(s, O-acac, CH₃). MS (ESI): Calculated for C₂₁H₂₅IrNO₄(M+H) 548.14, found 548.20.
**CH activation experiment with 2-^{13}C:** To prepare the $^{13}$C labeled complex, a 5 mL screw-cap vial was charged with 2-CH$_3$OH (10 mg, 0.022 mmol) and $^{13}$CH$_3$OH (0.5 mL). The vial was then sealed, and placed in an inert atmosphere (Ar) glovebox for 4 days. The resulting yellow-orange solution was then evaporated under vacuum, yielding a yellow-orange solid. The solid was then transferred to a Schlenk tube, 5 mL of pyridine was added, and the tube was placed in an oil bath regulated at 55°C for 30 min. A yellow-orange solid was obtained after the volatiles were removed under vacuum. The complex was estimated to be 62% $^{13}$C enriched by comparison of the integration of the doublet resulting from the $^{13}$C-labeled methoxide protons to that of the singlet of the remaining unlabeled methoxide. $^1$H NMR (C$_6$D$_6$): δ 8.43(d, 2H, o-Py), 6.58(t, 1H, p-Py), 6.29(t, 2H, m-Py), 5.08(s, 2H, CH), 3.76(d, 3H, Ir-OCH$_3$, J = 140 Hz), 1.67(s, 12H, CH$_3$). $^{13}$C $^1$H NMR (C$_6$D$_6$): δ 185.4(C-acac, C=O), 102.7(O-acac, CH), 57.1(OCH$_3$), 27.3(O-acac, CH$_3$).

To examine the possibility of the reversible generation of a reactive Ir-H via β-hydride elimination, 2-$^{13}$C (10 mg) was heated in C$_6$D$_6$ (1.5 mL) at 180°C for 4 h and the $^{13}$C NMR of the crude reaction mixture was obtained. Only $^{13}$CH$_3$OD was detected as was apparent from the clean singlet resonance for the methyl group. To account for the stoichiometric formation of CH$_3$OH, the Ir-H pathway would be expected to lead to generation of the D$^{13}$CH$_2$OD isotopomer (mechanism shown below) whereas the proposed σ-bond metathesis would lead to $^{13}$CH$_3$OH(D).

**H-D exchange:** Catalytic H-D exchange reactions were quantified by monitoring the increase of deuterium into C$_6$H$_6$ by GC/MS analyses. This was achieved by deconvoluting the mass fragmentation pattern obtained from the MS analysis, using a program developed with Microsoft EXCEL. An important assumption made with this method is that there are no isotope effects on the fragmentation pattern for the various benzene isotopomers. Fortunately, because the parent ion of benzene is relatively stable towards
fragmentation, it can be used reliably to quantify the exchange reactions. The mass range from 78 to 84 (for benzene) was examined for each reaction and compared to a control reaction where no metal catalyst was added. The program was calibrated with known mixtures of benzene isotopomers. The results obtained by this method are reliable to within 5%. Thus, analysis of a mixture of C₆H₆, C₆D₆ and C₆H₅D₁ prepared in a molar ratio of 40: 50: 10 resulted in a calculated ratio of 41.2(C₆H₆): 47.5(C₆D₆): 9.9(C₆H₅D₁). Catalytic H/D exchange reactions were thus run for sufficient reaction times to be able to detect changes >5% exchange. 2 was the catalyst used to carry out the H/D exchange between benzene and deuterium oxide. In a typical experiment, a 5 mL Schlenk tube was charged with 10 mg of 2-CH₃OH, benzene 1 mL, and 0.2 mL of deuterium oxide under an atmosphere of argon. The tube was then placed in a temperature controlled oil-bath maintained at 160 °C, and the H/D exchange was measured as described above. A representative graph of the data from this reaction is shown below.

Theoretical Calculations: All calculations were performed using the hybrid DFT functional B3LYP as implemented by the Jaguar 5.0 and Jaguar 5.5 program packages. This DFT functional utilizes the Becke three-parameter functional (B3) combined with the correlation functional of Lee, Yang, and Parr (LYP), and is known to produce good descriptions of reaction profiles for transition metal containing compounds. The metals were described by the Wadt and Hay core-valence (relativistic) effective core potential (treating the valence electrons explicitly) using the LACVP basis set with the valence double contraction of the basis functions, LACVP**. All electrons were used for all other elements using a modified variant of Pople’s 6-31G** basis set, where the six d functions have been reduced to five. Implicit solvent effects of the experimental benzene medium were calculated with the Poisson-Boltzmann (PBF) continuum approximation, using the parameters ε = 2.284 and rₛolv = 2.602Å. Due to the increased cost of optimizing systems in the solvated phase (increase in computation time by a factor of ~4) solvation effects are calculated here as single point solvation corrections to gas phase geometries. Our previous work on the Ir(acac)₂ system has shown that the total energies, geometries, frequencies and zero point energies were also largely unchanged when the systems were optimized in the solvation phase. All energies here are reported as ΔE + zero point energy corrections at 0K + solvation correction. Relative energies on the ΔH(0K) surface are expected to be accurate to within 3 kcal/mol for stable intermediates,
and within 5 kcal/mol for transition structures. Moreover, relative energies of iso-electronic species (such as regio-isomers) are considerably more accurate, since the errors largely cancel.

Free energies are not included, due to the inadequacies of free energy calculations in solutions. However, a free energy term is implicitly included in the PBF solvation methodology.

All geometries were optimized and evaluated for the correct number of imaginary frequencies through vibrational frequency calculations using the analytic Hessian. Zero imaginary frequencies correspond to a local minimum, while one imaginary frequency corresponds to a transition structure.

To reduce computational time the methyl groups on the acac ligands were replaced with hydrogens. Control calculations show that relative energies of intermediates and transition structures change less than 0.1 kcal/mol when methyl groups are included.