Synthesis, Structure, and Reactivity of O-Donor Ir(III) Complexes: C–H Activation Studies with Benzene

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Abstract: Various new thermally air- and water-stable alkyl and aryl analogues of (acac-O,O)₂Ir(R)(L), R–Ir–L (acac-O,O = \( \kappa^2 \)-O,O-acetylacetonate, –Ir– is the trans-(acac-O,O)₂Ir(III) motif, R = CH₃, C₂H₅, Ph, PhCH₂CH₂, L = Py) have been synthesized using the dinuclear complex \([Ir(acac-O,O,C)\]]; (acac-O,O)Ir(L), [acac-C–Ir]₂, or acac-C–Ir–H₂O. The dinuclear Ir(III) complexes, \([Ir(acac-O,O,C)\]]; (acac-O,O)(R)]₂ (R = alkyl), show fluxional behavior with a five-coordinate, 16 electron complex by a disso-}

1. Introduction

The oxidative conversion of fossilized hydrocarbons to energy and useful materials are foundational technologies. Currently, these conversions operate at high temperatures that ultimately lead to excessive emissions and high costs. Catalysts based on C–H activation⁵ show potential for the development of new hydrocarbon conversion chemistry that can be substantially more efficient than the lower temperature and enhanced selectivity. While many alkane and arene CH activation systems are known, relatively few have been reported to allow efficient catalysis to generate functionalized products.⁶ Some of the most efficient catalysts reported for the low-temperature, selective conversion of hydrocarbons directly to useful products, for example, alcohols, alkyl aranes and carboxylic acids, generally operate by coupling of the CH activation and functionalization steps as shown in Figure 1. Some key challenges to designing effective catalysts that operate via this sequence of reactions are (a) avoiding inhibition of the CH activation reac-

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tion by desirable solvents, products, and reactants; (b) generating functionalized products in a catalytic sequence; and (c) stabilizing the catalysts to the conditions required for functionalization.

Complexes based on Ir are among the most active reported for the CH activation reaction. We have been investigating the design of homogeneous catalysts based on Ir and other late transition metal complexes using O-donor ligands such as acetylacetonate (acac), propylene, aryloxides, catechols, hydroxycetophenone, etc., to stabilize the complexes to the reaction conditions required for generating functionalized products. Compared to the N- or P-donor ligands generally utilized for C–H activation,8 O-donor ligands generally utilized for C–H activation may have the potential for higher thermal, protic, and oxidant stability given the expected covalent character of oxygen–metal bonds with the late transition metals and the lower basicity of oxygen.10

Another key reason for study of these ligands is that the known π-donor11 electron-attracting and “hard” characteristics of O-donor ligands could lead to electronic differences at the metal center that result in significant changes in chemistry compared to complexes based on N- or P-donors. Thus it could be anticipated that O-donor ligands might (a) facilitate access to higher oxidation states, via hard/hard interactions or π-donation during catalysis that may be required for the functionalization step shown in the generalized catalytic cycle; (Figure 1) moderate the electron density, by the interplay of π-withdrawing and π-donating properties at the metal center, and reduce the possibility of the solvent, product, or reactant inhibition that is generally observed with very electron-rich or electron-poor metal centers; and (c) facilitate CH activation reactions with electron-rich, late transition metals that generally take place via “oxidative addition”12 or metal insertion pathways. Recent theoretical and experimental evidence has been presented for CH activation reactions facilitated by π-donation through phenyl–Ir interactions.13 As O-donor ligands directly attached to a metal center can be efficient π-donors, it is likely that O-donor, d5 five-coordinate, square pyramidal motifs would exhibit ground-state destabilization from nonbonding O→Ir to M–Ir, filled–filled repulsions or so-called “π-conflict”11,14 as well as stabilization of the nonbonding O→Ir electrons by bonding interactions (or less repulsion) to the formally empty (or less filled) metal–dπ orbitals when the M–C and M–H bonds are formed by CH activation either in a transition state or as an intermediate (the metal is now formally d4Ir(V)). Figure 2. This stabilization is analogous the pi-donor effects of alkoxide ligands with late transition metals that facilitate binding of CO or oxidative addition to H2 trans to the O-donor ligand as shown by Caulton.15

Recently, we reported a d6 O-donor ligated Ir complex, (acac-O,O)2IrH4(R)(L), (acac-O,O = k2-O,O-acetylacetonate, L = ligand), R–Ir–L, (where –Ir– is understood to be the trans-(acac-O,O)Ir(III) motif throughout this paper unless specified and L is a ligand such as pyridine, Py) that shows stoichiometric and catalytic CH activation and H/D exchange of alkanes and amines as well as catalytic hydroxylation reactions with amines. Some experimental and theoretical studies of this O-donor complex, R–Ir–L, have been reported, and a proposed mechanism for the CH activation and hydroxylation catalysis based on arene CH activation is shown in Figure 3. While O-donor ligands have been utilized with early and late transition metals,16 to our knowledge these are the first, well-defined.
O-ligated, late transition metal complexes that activate alkane and arene C–H bonds. These late metal, O-donor complexes catalyze reactions with hydrocarbons and show significantly higher thermal stability at temperatures above 200 °C to oxidizing, acidic conditions compared to complexes based on C, N, and P ligands. Other unique characteristics are that, unlike more electron rich systems, these O-donor complexes are not severely inhibited by substrates such as olefins and water and do not generate olefinic products that would be expected from β-hydride elimination reactions.

These are intriguing characteristics and, as discussed above, may be related to the α-acceptor and π-donor properties of the O-donor ligands. Given the potentially useful characteristics of these O-donor, bis-acac-O,O, Ir(III) complexes, we embarked on a detailed study of the stoichiometry of this class of compounds. The scope of this work includes the development of a detailed understanding of the reaction chemistry of these complexes, R–Ir–L, with an emphasis on providing a molecular picture of the CH activation and other reactivity of these complexes as examples of the class of late transition metal, O-donor, organometallic complexes. A particular focus of this study is to determine if the CH activation reactions of this novel class of organometallic complexes proceed by inner-sphere or outer-sphere mechanisms.

2. Results and Discussion

2.1. Synthesis and Characterization of (acac-O,O)2Ir(III) Complexes. The various complexes examined in this study were synthesized as shown in Scheme 1. All the complexes were fully characterized by 1H, 13C NMR spectroscopy, elemental analyses, and/or high-resolution mass spectrometry. In selected cases, the compounds were also characterized by X-ray crystallography. These compounds are (both aryl and alkyl, with and without β-CH bonds) stable at room temperature to air and protic solvents such as water and methanol. Importantly, the (acac-O,O)2Ir(III) motif is very stable, and remarkably, refluxing complexes in acid solvents such as acetic or trifluoroacetic acids in air do not lead to loss of the acac-O ligands. This oxidation and protic stability is likely to arise from the octahedral geometry and the lower electropositivity at an Ir center with four electron-donating O-donor ligands.

2.1.1. Dinuclear Complexes, [(acac-O,O)2Ir–R]2. Synthesis of the bis-acac-O,O Ir(III) complexes begins with the mononuclear bis-acac-O,O Ir(III) complex, acac–C–Ir–H2O, that can be obtained in high yield from a modification of the procedure reported by Bennett[10] for the dinuclear complex, [Ir(μ-acac-O,O,C)=acac-O,O(acac-C)=Ir]2[acac–C–Ir]2. Treatment of acac–C–Ir–H2O with ZnR2 or HgR2 (R = alkyl = CH3, CH2CH3, and PhCH2CH2) (Scheme 1) leads to the corresponding dinuclear bis-acac-O,O iridium organometallic complexes [R–Ir]2, in high isolated yields. For example, treatment of acac–C–Ir–H2O in THF with Zn(CH3)2 leads to the formation of the dinuclear complex, [Ir(μ-acac-O,O,C)=acac-O,O(CH3)]2[CH3–Ir]2 in 75% yield. The characteristic bridging acac ligands in these dinuclear iridium complexes is a common feature of these β-diketone complexes.[20]

2.1.2. Mononuclear Complexes, (acac-O,O)Ir(R)(L). The mononuclear complexes R–Ir–Py can be obtained from the corresponding dinuclear complexes, [R–Ir]2, by treatment with pyridine or, in the case of R = acac-C and R = Ph by treatment of the acac–C–Ir–H2O with Py or Ph2Hg followed by Py, respectively. The reactions of the dinuclear alkyl complexes [R–Ir]2, (R = CH3), (R = CH2CH2Ph) and (R = CH2CH3), with pyridine result in the quantitative formation of the corresponding mononuclear complex, R–Ir–Py. The yellow pyridine complexes CH3–Ir–Py, Ph–Ir–Py, Ph2CH2–Ir–Py, and CH3CH2–Ir–Py were all characterized by 1H and 13C NMR spectroscopy, elemental analysis, FAB mass spectrometry, and, in selected cases, single-crystal X-ray crystallography. 1H and 13C NMR spectra of these complexes are consistent with a trans-octahedral geometry. In no cases were any cis-(acac-O,O)Ir(R)(L) complexes isolated in these preparations. FAB mass spectral analyses of CH3–Ir–Py.

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Ph–Ir–Py, PhCH₂CH₂–Ir–Py, and CH₃CH₂–Ir–Py show an M⁺ ion of appreciable intensity. Generally, the most intense fragment is derived from the loss of the pyridine, [M–Py]⁺. These complexes show a general trend of ion peaks for the loss of Py and the hydrocarbyl substituent, i.e., [M⁺], [M–Py]⁺, and [M–Py–R]⁺. For instance, the Ph–Ir–Py complex shows m/z 547.1, 468.1, and 391.1 which correspond to [M⁺], [M–Py]⁺, and [M–Py–Ph]⁺, respectively.

X-ray crystallography of selected complexes was carried out to confirm the structure of these complexes. The ORTEP projections of Ph–Ir–Py and PhCH₂CH₂–Ir–Py are shown in Figures 4 and 5, respectively.

2.2. Dynamic Behavior of Dinuclear Complexes, [(acac-O,O)₂Ir–R]₂. As communicated earlier, both the mononuclear and dinuclear (acac-O,O)₂Ir(III) complexes are active catalysts for C–H activation and olefin hydroarylation with anti-Markovnikov selectivity. There is precedent for catalysis by dinuclear complexes with possible cooperativity between the metal centers. However, given the expected strong trans influence and the weakened Ir(μ-acac-O,O,C⁵) bridging bond in the [R–Ir]₂ dinuclear complexes (where R is alkyl), we anticipated that reactions would be initiated by facile dissociation to generate mononuclear, coordinatively unsaturated, five-coordinate, square pyramidal intermediates, R–Ir–L₀ (where ₀ is used as a symbol for a vacant site throughout this paper). Mechanisms involving C–H activation and olefin insertion are typically inner-sphere, coordination reactions that generally require a vacant coordination site on the metal for coordination of the CH substrate, and substantial evidence can be cited for a dissociative mechanism for octahedral complexes, especially for those of Ir(III). Consistent with these considerations and the observed catalytic activity of these dinuclear complexes for...

Figure 3. Proposed reaction mechanism of H/D exchange and hydroarylation of olefins catalyzed via arene C–H activation by R–Ir–L and [R–Ir]₂ Complexes.
the hydroarylation reaction and catalytic H/D exchange, we find the stability of the dinuclear complexes is highly dependent on the nature of the R group. For example, dinuclear complexes with electron-withdrawing groups such as chloro, or acac-C, are stable at room temperature and show well-defined \(^1\)H NMR resonances for two pairs of methyls

\[ [\text{Acac-C-Ir}]_2 \]

However, dinuclear complexes with more electron donating alkyl groups, such as \([\text{CH}_3\text{-Ir}]_2\), \([\text{CH}_3\text{CH}_2\text{-Ir}]_2\), and \([\text{CH}_3\text{CH}_2\text{CH}_2\text{-Ir}]_2\), are only stable below room temperature and show dynamic behavior by NMR at room temperature that can be best explained by facile formation of the coordinatively unsaturated, five-coordinate intermediates, \(\text{R-Ir} = \square\), as shown in eq 1. It is possible these intermediates could be six-coordinate, solvento complexes, but as will be discussed later, this is not consistent with the chemistry of these complexes.

\[ \text{R-Ph-Ir-H}_2O \]

facile formation of the coordinatively unsaturated, five-coordinate intermediates, \(\text{R-Ir} = \square\), as shown in eq 1. It is possible these intermediates could be six-coordinate, solvento complexes, but as will be discussed later, this is not consistent with the chemistry of these complexes.

\[ \text{R} = \text{CH}_3, \text{Hg-Ph}_2, \text{R} = \text{PhCH}_2\text{CH}_2, [\text{PhCH}_2\text{CH}_2\text{-Ir}]_2 \]

\[ \text{R} = \text{CH}_3, \text{CH}_2\text{-Ir-Py} \]

\[ \text{R} = \text{C}_6\text{H}_5, \text{Ph-Ir-Py} \]

\[ \text{R} = \text{PhCH}_2\text{CH}_2, \text{PhCH}_2\text{CH}_2\text{-Ir-Py} \]

\[ \text{R} = \text{CH}_3\text{CH}_2, \text{CH}_3\text{CH}_2\text{-Ir-Py} \]

Figure 4. ORTEP diagram of complex \(\text{Ph-Ir-Py}\). Selected bond angles (deg): C(6)–Ir(1)–N(1), 180.0; O(1)–Ir(1)–O(2), 95.44(18); O(2)–Ir(1)–N(1), 90.1(2); C(4)–O(2)–Ir(1), 120.7(4).

Figure 5. ORTEP diagram of complex \(\text{PhCH}_2\text{CH}_2\text{-Ir-Py}\). Selected bond lengths (Å) and angles (deg): Ir(1)–C(16), 1.956(13); Ir(1)–N(1), 2.165(7); C(16)–Ir(1)–O(1), 91.7(4); C(16)–Ir(1)–N(1), 176.5(4); O(1)–Ir(1)–N(1), 90.4(3).

The \(^1\)H NMR resonances of the methyl and methine groups in the acac-O,O ligands of the dinuclear complex, \([\text{CH}_3\text{-Ir}]_2\), in tol-\(d_8\) are broad peaks (1.8 and 5.1 ppm, respectively) at room
temperature. At lower temperatures, these signals decoalesce, and at 253 K, the NMR spectrum shows two singlets for two pairs of methyl (1.76 and 1.46 ppm, each 12 H’s) and two methine resonances (5.19 and 5.02 ppm, each 2 H’s) that are consistent with a stable dinuclear complex with bridging acac ligands. Similar dynamic behavior was observed for the alkyl complexes, [PhCH2CH2–Ir]2 and [CH3CH2–Ir]2. Line-broadening analysis was carried out for [CH3–Ir]2 in tol-d8 using the methyl and the methine resonances. The exchange rates were obtained in the slow-exchange region from the width of the NMR signals at half-height.24

The activation parameters, \( \Delta H^\ddagger = 17.8 \pm 1 \text{ kcal/mol} \), \( \Delta S^\ddagger = 12.7 \pm 2 \text{ eu} \), and \( \Delta G^\ddagger (T = 298 \text{ K}) = 14.1 \pm 0.5 \text{ kcal/mol} \), were derived from a linear regression analysis of the Eyring plot using rate data obtained from 253 to 333 K. A qualitative analysis was also carried out using WIND NMR, and the observed and calculated \(^1\text{H} \) NMR spectra of [CH3–Ir]2 are shown in Figure 6. The positive \( \Delta S^\ddagger (>10 \text{ eu}) \) value is consistent with a dissociative reaction mechanism26 of the dinuclear complexes, [R–Ir]2 to presumably generate two coordinatively unsaturated, five-coordinate, square pyramidal species, R–Ir–□.

2.3. Reactions of the Dinuclear Complexes, [(acac–O,O)2–Ir–R]2, with Ligands. As anticipated from the proposed facile dissociation of the dinuclear complexes, these compounds react rapidly at room temperature with added ligands such as pyridine or CH3OH to quantitatively generate the corresponding trans-six-coordinate, mononuclear octahedral complexes on mixing (Scheme 1). This is readily apparent by NMR analysis, as only one methyl (12 H’s) resonance and one methine (2 H’s) resonance are observed upon reaction of the dinuclear complexes with these ligands. While reactions of the dinuclear complexes with strong field ligands such as pyridine lead to six-coordinate, mononuclear octahedral complexes on mixing, six-coordinate mononuclear complexes formed from reaction with weak field ligands such as L = CH3OH can only be observed in solution (by NMR analysis) and are not sufficiently stable to isolate without decomposition back to the dinuclear complexes.

Interestingly, attempts to generate the olefin complexes showed that olefin complexes, R–Ir–L (L = olefin), are also very labile. Thus, treatment of [CH3–Ir]2 in tol-d8 with 1 atm of ethylene shows no reaction by NMR, and only the broad peaks resulting from the dynamic equilibrium between the six-coordinate dinuclear and five-coordinate mononuclear complexes are observed. However, on cooling the reaction mixture to 253 K, in addition to the stable dinuclear complex, a new set of resonances consistent with a trans-six-coordinate, mononuclear olefin complex, CH3–Ir–L (L = C2H4), can be observed by \(^1\text{H} \) and \(^1\text{C} \) NMR. Theoretical calculations show that the coordination of the ethylene only has a \( \Delta H \) of \(-7.5 \) kcal/mol, indicating that the magnitude of the \( \Delta S \) term will control whether the five- or six-coordinate species forms, with increased temperature drastically favoring the five-coordinate complex.

Consistent with the importance of the trans-effect, treatment of the dinuclear complexes with the weaker trans-effect acac-C5 ligand, [acac–C–Ir]2, in CDCl3 with ethylene (2–10 atm) at room temperature does lead to the formation of a stable, trans-six-coordinate, mononuclear, octahedral complex that could be assigned to acac–C–Ir–C2H4. However, as in the case of CH3–Ir–C2H4, all attempts at isolation were unsuccessful, presumably due to facile loss of ethylene. This lack of formation of stable olefinic complexes is in stark contrast to more electron-rich complexes such as those based on more electron-rich Ir(III) complexes with Cp or phosphine ligands that readily form stable olefinic complexes.

While the ease of formation of coordinatively unsaturated intermediates in these dinuclear and mononuclear complexes may be largely due to the strong trans-effect of the strong-field alkyl groups on the stability of the Ir–C2H4 bond or the bridging acac, it is possible that this may also be due to the so-called “cis-effect” resulting from the lone pair effects on the L ligand. Since the generation of coordinative unsaturation is critical to coordination catalysis, this could be an important characteristic of O-donor ligands and we are exploring the magnitude and scope of this possibility.

2.4. Ligand (L) Substitution Chemistry of (acac–O,O)2–Ir–(R)(L) Complexes. Pyridine exchange in the mononuclear complexes, R–Ir–Py, where R is alkyl or phenyl, is quite facile at room temperature. As expected on the basis of the trans-effect and the previous bond length data, the alkyl complexes are significantly more labile than the aryl analogues. Addition of 5 equiv of Py·d5 to a CDCl3 solution of Ph–Ir–Py or CH3–Ir–Py at room temperature leads to rapid Py exchange and formation of Ph–Ir–Py·d5 or CH3–Ir–Py·d5 on mixing, as shown in eq 2. At low temperatures, the rate of exchange is decreased.

\[
\text{[Ph–Ir–Py]} + 5 \text{Py·d5} \rightarrow \text{[Ph–Ir–Py·d5]} + 5 \text{Py}
\]

![Diagram](image)
sufficiently slow on the NMR time scale to allow the reaction kinetics to be followed from the generation of free Py-H₅ at various concentrations of Py-d₅ (under pseudo first order conditions). Kinetic studies, Figure 7, show that the reaction rate is essentially independent of added excess pyridine (52–172 mM) for Ph–Ir–Py as expected for a dissociative process from an octahedral Ir(III) complex. The activation parameters for the rate of exchange for Ph–Ir–Py were estimated to be ΔH° = 22.8 ± 0.5 kcal/mol; ΔS° = 8.4 ± 1.6 eu; and ΔG°²98K = 20.3 ± 1.0 kcal/mol, Figure 8. The pyridine exchange for CH₃–Ir–Py was similarly found to be dissociative, with activation parameters of ΔH° = 19.9 ± 1.4 kcal/mol; ΔS° = 4.4 ± 5.5 eu; and ΔG°²98K = 18.6 ± 0.5 kcal/mol, Figure 8. The previously reported values of ΔH° calculated by DFT methods¹⁷ for the loss of Py from Ph–Ir–Py (20.1 kcal/mol) and CH₃–Ir–Py (17.3 kcal/mol) to generate the coordinatively unsaturated, five-coordinate, square pyramidal complexes, R–Ir–□ are consistent with these experimental values. The generation of these five-coordinate intermediates from the R–Ir–Py complexes by loss of Py is more unfavorable than in the case of the dinuclear complexes, and no dynamic behavior is observed by NMR below 100 °C. These facile exchange reactions of Ir(III), octahedral complexes are unusual, although not unique,²⁸ and, as discussed above, are likely due to the combination of the trans-influence of the hydrocarbyl group on the pyridine and the π-donor, O-ligands cis to the Py.

2.5. Trans–Cis Isomerization of (acac-O,O)₂Ir(R)(Py). As discussed above, the (acac)₂Ir(R)(L) complexes are typically synthesized and isolated only as the trans isomer, and it is this isomer that is utilized in these studies. However, a central premise in the proposed reaction mechanism for hydroxylation and H/D exchange is that the trans-(acac-O,O)₂Ir(R)(L) complexes are capable of isomerization to a cis-configuration that is required for both the olefin insertion and CH activation steps as seen in Figure 3. Related rearrangement has been shown for tris-acac complexes,²⁹ but no data was available on the barriers for such rearrangements with the bis-acac-O,O Ir(III) complexes used in the catalytic studies. Earlier theoretical calculations¹⁷ predicted that the cis-Ph–Ir–Py complex should be more stable than the trans-Ph–Ir–Py isomer (by ~3 kcal/mol) and that the calculated barrier to trans–cis isomerization (ΔH° = 42.0 kcal/mol for Ph–Ir–Py) should be sufficiently high as to preclude the observation of this isomerization at room temperature and typical temperatures and reaction times employed during synthesis.

To show feasibility for the trans–cis isomerization, we investigated the conditions required to generate the cis-Ph–Ir–Py complex from the trans complex, Ph–Ir–Py, eq 3. The reactions were carried out in medium-pressure NMR tubes (with added Ar as an inert gas to prevent solvent refluxing) at 180 °C. To avoid issues of CH activation reactions of the solvent, we examined the reaction of trans-complex, Ph-d₅–Ir–Py, in C₆D₆ where the reactions with the solvent would be kinetically silent. The reaction progress was monitored by ¹H resonances of the methyl groups of the acac-O,O ligands in the starting trans-complex, Ph–Ir–Py, which appear as one peak that integrates to 12 protons relative to two methine protons. Importantly, control experiments showed that conversion of the trans-complex, Ph–Ir–Py to the deuterated trans-complex, Ph-d₅–Ir–Py, which is rapid in C₆D₆, does not change these methyl-acac-O,O resonances. However, as the trans–cis isomerization destroys the C₆ symmetry of the molecule, the formation of the cis-complex should be readily evident from the observation of four new methyl and two new methine resonances in the ¹H NMR.

Importantly, we find that the trans–cis isomerization proceeds cleanly and quantitatively (by NMR analysis) on heating the Ph–Ir–Py complex to 180 °C for 12 h. This shows that, consistent with the theoretical predictions, the cis-Ph–Ir–Py is more stable than the Ph–Ir–Py. To isolate and identify the cis isomer, the reaction was carried out on a preparative scale in C₆H₆. The isolated cis-Ph–Ir–Py complex has been fully characterized by ¹H and ¹³C NMR spectroscopy and elemental analysis. ¹H and ¹³C NMR spectra of the complex are consistent with cis-octahedral geometry.

2.5.1. Mechanism of Trans–Cis Isomerization of (acac-O,O)₂Ir(R)(Py). Given the central importance of this trans–cis isomerization in the CH activation and hydroxylation catalysis of these complexes, we examined the isomerization...
of the Ph–Ir–Py complex in greater detail. In our previous theoretical study of this process,17 two mechanisms were found to be competitive in a study of the olefin complexes, R–Ir–Ol (Ol = olefin); a dissociative mechanism, where trans–cis isomerization occurs with a monomolecular transition state and an associative mechanism, where the trans–cis isomerization is facilitated by coordination of olefin. The first of these related mechanisms for the isomerization of the Ph–Ir–Py complex is shown in Figure 9 (solid line). In this mechanism, the five-coordinate, square pyramidal intermediate, Ph–Ir–Py, generated by reversible, dissociative loss of pyridine, undergoes a unimolecular (U), trans–cis isomerization to generate a five-coordinate cis-intermediate, cis-Ph–Ir–Py, that reacts with free pyridine to generate cis-Ph–Ir–Py (TS1 → TS2 → TS3). An alternative is a direct, bimolecular (B), associative reaction of free pyridine with the five-coordinate trans-complex, Ph–Ir–Py, to directly generate the cis-Ph–Ir–Py (TS1 → TS4).

The predicted rate laws for the two possibilities are shown in Figure 9 (using a pre-equilibrium treatment for the trans-
intermediate, \( \text{Ph-Ir} \rightarrow \square \), and a steady-state approximation for the cis-intermediate, \( \text{cis-Ph-Ir} \rightarrow \square \). As can be seen, only one set of conditions, via the pathway involving a unimolecular, trans–cis isomerization of \( \text{Ph-Ir} \rightarrow \square \) (TS1 → TS2 → TS3) when the formation of the five-coordinate \( \text{cis-Ph-Ir} \rightarrow \square \) intermediate is rate-determining \( (k_3[\text{Py}] > k_{-2}) \), leads to a predicted inverse dependence of the \( k_{\text{obs}} \) on added pyridine. If the formation of the \( \text{cis-Ph-Ir} \rightarrow \square \) is slow but reversible \( (k_{-2} > k_3[\text{Py}]) \) or if the bimolecular pathway (TS1 → TS4) is followed, the reaction rate should be independent of added pyridine. The experimental results are shown in Figures 10 and 11. As can be seen, the rate of isomerization of \( \text{Ph-Ir} \rightarrow \square \) to \( \text{cis-Ph-Ir} \rightarrow \square \) in benzene at 180 °C shows an inverse dependence on added pyridine over a range of 10 to 60 equiv and is consistent with trans–cis isomerization following the unimolecular pathway (TS1 → TS2 → TS3, Figure 9) involving the rate-determining formation of the five-coordinate intermediate, \( \text{cis-Ph-Ir} \rightarrow \square \). As can be seen from the rate law, it is possible that at very low concentrations of pyridine, \( k_{-2} > k_3[\text{Py}] \), reaction via \( \text{cis-Ph-Ir} \rightarrow \square \) could also be expected to be independent of pyridine as under these conditions it is plausible that the unimolecular isomerization of \( \text{cis-Ph-Ir} \rightarrow \square \) back to the trans-intermediate, \( \text{Ph-Ir} \rightarrow \square \), would be faster than trapping by pyridine. The observation that the last data point in Figure 11 (lowest pyridine concentration) deviates significantly from a straight line through the other two points and the origin may indicate the onset of this behavior albeit three data points are not sufficient to establish this trend. Theoretical calculations also show that the barrier for reaction through TS4 is 4.5 kcal/mol lower in energy on the \( \Delta H \) surface, Figure 9 (values in parentheses). However, the \( T^\circ \Delta S \) term is expected to favor the dissociative mechanism, (assuming \( \Delta S(TS2 - TS4) \leq 9.9 \text{ eu at 373 K} \) and the reaction should proceed through TS2 and largely rate-determining formation of the cis-five-coordinate intermediate, \( \text{cis-Ph-Ir} \rightarrow \square \). This energy diagram would lead to the prediction that the rate of exchange of pyridine from the cis-complex, \( \text{cis-Ph-Ir-Py} \), would be expected to be substantially lower than from the trans-complex since exchange of the cis-complex would require generation of \( \text{cis-Ph-Ir} \rightarrow \square \) which is calculated to be \( \sim 20 \text{ kcal/mol} \) higher than the corresponding trans-intermediate. This is indeed the case, and while the trans-complex, \( \text{Ph-Ir-Py} \), exchanges with Py-\( d_5 \) on mixing at room temperature, exchange is only observed with the \( \text{cis-Ph-Ir-Py} \) above 140 °C.

These results suggest that if CH activation reactions with trans-(acac-O,O)\(_2\)Ir(R)(L) complexes require coordination to the cis-intermediate, \( \text{cis-R-Ir} \rightarrow \square \), that the trans–cis isomerization could be expected to be an important contributor to the overall reaction rate in reactions from the trans-complexes. These results are also potentially relevant to design considerations for improved catalysts based on these trans-(acac-O,O)\(_2\)Ir(III) organometallic species. Many reactions require two mutually cis sites for reaction. This geometry is typically achieved through the use of cis-tetradentate or use of tripodal ligands. An alternative strategy is to access this geometry with octahedral metal complexes having cis-bis-bidentate spectator ligands from either the cis- or trans-configurations. However, a fundamental issue with such a strategy that could lead to decreased reactivity is that the trans-configuration could be more stable than the cis and/or the barriers for isomerization can be significant. Before this study, given the known kinetic inertness of Ir complexes, we regarded this to be likely with the trans-(acac-O,O)\(_2\)Ir(III) complexes and considered that the reactivity could be improved by designing cis-restricted bis-acac-O,O ligand motifs. Importantly, however, the observation that the \( \text{cis-(acac-O,O)Ir(Ph)} \rightarrow \text{(Py)} \) complex is more stable than the trans-isomer now indicates that a such a strategy may not lead to improved rates for CH activation for this complex. Indeed, depending on the relative stability of the trans and cis bis-acac-O,O Ir(III) complexes (\( \sim 3 \text{ kcal/mol} \) for the pyridine complexes as discussed above and comparable for the olefin complexes\(^7\) on the basis of theoretical calculations), the cis-complexes could be less active (in the case of the pyridine complex) or comparable (in the case of the olefin complexes) assuming that TS2 and TS3 are comparable in energy. These predictions are being investigated, and preliminary results show that the rate of CH activation of benzene with \( \text{cis-Ph-Ir-Py} \) is slower than that of the corresponding trans-isomer. Thus, while the trans-isomer catalyzes H/D exchange between Tol-\( d_5 \) and C\(_6\)H\(_6\) with a TOF of \( 1 \times 10^{-2} \text{ s}^{-1} \) (TN \( \sim 50 \) after 2 h) at 160 °C, the \( \text{cis-Ph-Ir-Py} \) exhibits a TOF of \( 2 \times 10^{-4} \text{ s}^{-1} \) (TN \( \sim 1 \) after 2 h) under these conditions (Figure 12). This drop in rate is consistent with the predicted ground state differences between trans and the more stable \( \text{cis-Ph-Ir-Py} \). These results are encouraging and suggest that other readily available trans octahedral complexes with bis-bidentate spectator ligands may allow access to two mutually cis sites without significant kinetic penalty. We are currently expanding our study of other bis-bidentate octahedral metal complexes for CH activation and other reactivity studies.\(^30\)

2.6. C–H Activation of Arenes by (acac-O,O)\(_2\)Ir(R)(L).

2.6.1. Rate Laws for Plausible Mechanisms of Arene CH Activation by (acac-O,O)\(_2\)Ir(R)(L). We define the CH activation reaction as a reaction between a CH bond and species MX

that proceeds via coordination chemistry and without the involvement of free radicals to generate M–C intermediates. As a result of the coordination characteristics of the CH activation reaction, it is generally observed to be composed of two steps: coordination of the CH bond to the metal to generate an intermediate alkane or arene complex followed by a CH cleavage step to generate the M–C intermediate.\(^\text{1.3}\) Given the facile rate of ligand exchange with these (acac\(\text{O,O}\))\(_2\)Ir(R)(L) complexes, it is plausible that the CH activation reaction proceeds via the coordinatively unsaturated, trans-five-coordinate intermediate, R–Ir–□. From this intermediate two general pathways for CH activation can be considered.

One possibility is that the benzene coordination occurs before the trans–cis isomerization. In this case, benzene could react directly with the trans-intermediate, R–Ir–□, by coordination and CH cleavage leading to a seven-coordinate, Ir(V), intermediate or transition state that then undergoes rearrangement and loss of RH to generate the Ph–Ir–L product as shown in Figure 13. However, this pathway seems unlikely, as attempts at investigating this pathway by DFT calculations indicate that the intermediate or transition state resulting from CH oxidative addition trans to the R group in the trans-intermediate R–Ir–□ could not be located, with all geometries collapsing back to R–Ir–□. Attempts at constraining pertinent geometry parameters such as Ir–C and/or Ir–H distances all revealed substantial energy increases on the order of >50 kcal/mol. The unfavorable CH activation with this coordinatively unsaturated trans-intermediate, R–Ir–□, is most likely due to a combination of two effects: (A) the destabilizing trans-effect of the R group; (B) the inflexibility of the trans acac ligands, caused by the extended aromatic system generated over the two, six-membered rings, which is necessarily perturbed if the rings are scissored away to make room for an oxidative addition.

The more likely mechanisms for the CH activation reaction from the five-coordinate, trans-intermediate, R–Ir–□ are shown in Figure 14, involving coordination of benzene cis to the R group during the CH cleavage step. The basis of the trans–cis isomerization studies of the Ph–Ir–Py complex, it could be anticipated that the most likely pathway would involve a unimolecular trans–cis isomerization of R–Ir–□ to cis-R–Ir–□, followed by benzene coordination to generate a cis-R–Ir–PhH benzene intermediate complex, CH cleavage, and loss of RH (TS5 \(\rightarrow\) TS6 \(\rightarrow\) TS7 \(\rightarrow\) TS8). Such a pathway is consistent with the observations that the cis-Ph–Ir–Py complex undergoes both Py exchange and CH activation at slower rates than the trans (vide infra), earlier theoretical calculations,\(^\text{17}\) and the studies on CH activation with alkyl-Ir(III) complexes\(^\text{3}\) that show a requirement for cis-orientation for H transfer. However, there is no requirement that cis-benzene coordination is similar to trans–cis isomerization of the Ph–Ir–Py complex, and pathways involving bimolecular reactions, e.g., TS9 and TS10, between benzene and R–Ir–□ can be proposed for the CH activation as shown in Figure 14. In all cases the reaction rates are expected to show an inverse dependence on pyridine, given the low experimentally measured barrier (\(\Delta G = \approx 20\) kcal/mol) for loss of pyridine from R–Ir–Py, while the dependence on benzene can be more complex. These dependences and other aspects of the kinetics of the CH activation reaction were examined in an attempt to distinguish between these possible pathways.

2.6.2. Products of Arene CH Activation with (acac\(\text{O,O}\))\(_2\)Ir(R)(L). As communicated earlier, these thermally protic- and oxidant-stable O-donor Ir(III) complexes readily undergo stoichiometric C–H activation of arenes and alkanes.\(^\text{16}\) The reaction of R–Ir–Py with C\(_6\)D\(_6\) at 130 °C for 1 h leads to irreversible loss of RD and quantitative formation of Ph–d\(_5\)–Ir–Py (based on \(\text{^1H}\) and \(\text{^13C}\) NMR by comparison to independently synthesized and fully characterized Ph–Ir–Py). This reaction is general and can be carried out with Acac–C–Ir–Py, Ph–Ir–Py, CH\(_3\)–Ir–Py, CH\(_2\text{CH}_3\)–Ir–Py, and PhCH\(_2\text{CH}_3\)–Ir–Py as shown in eq 4. Thus, when the reaction of CH\(_3\)–Ir–Py is carried out in C\(_6\)D\(_6\) at 130 °C for 1 h, the quantitative formation of CH\(_3\)D and Ph–d\(_5\)–Ir–Py has been confirmed by GC/MS (of the gas and liquid phase) and \(\text{^1H}\) NMR spectroscopy using trimethoxybenzene as an internal standard. The higher deuterium isotopomers of methane, CH\(_3\)D\(_x\)–Ir–Py, were not observed under the reaction conditions even after longer reaction times. This shows that the generation of methane under these conditions is essentially irreversible (at higher temperatures, reaction with methane can be observed). Indeed, theoretical calculations for the replacement of methyl for phenyl is exothermic by \(\approx 15\) kcal/mol.\(^\text{15.17}\) Similarly, heating other alkyl complexes (PhCH\(_2\text{CH}_3\)–Ir–Py and CH\(_2\text{CH}_3\)–Ir–Py) in neat C\(_6\)D\(_6\) led to the quantitative and irreversible formation of the corresponding monodeuterated hydrocarbons, PhCH\(_2\text{CH}_3\)D and CH\(_2\text{CH}_3\)D, respectively, and Ph–d\(_5\)–Ir–Py. In the case of reaction of PhCH\(_2\text{CH}_3\)–Ir–Py, only the PhCH\(_2\text{CH}_3\)D regioisotomer is formed as determined by \(\text{^1H}\) NMR of the reaction products.

Interestingly, unlike the alkyl-Ir complexes, treating Ph–Ir–Py with tol–d\(_5\) for short times (\(\approx 20\%\) conversion to minimize post H/D scrambling of the benzene product since this reaction is reversible) led to the formation of multiple deuterated isotopomers of benzene rather than only the monodeuterated product, C\(_6\)H\(_5\)D. This observation of multiple deuterium incorporation into the benzene eliminated from

Figure 12. H–D exchange between C\(_6\)H\(_6\) and Tol–d\(_6\) catalyzed by Ph–Ir–Py (•) and cis-Ph–Ir–Py (□) at 160 °C.
Ph–Ir–Py on treatment with tol–d₆ is characteristic of the generation of intermediate arene complexes in a rate-determining step during CH activation reactions.³¹ To examine this possibility and elucidate the details of the CH activation reactions we turned to kinetic studies.

2.6.3. Activation Barrier for CH Activation using CH₃–Ir–Py. The CH₃–Ir–Py complex was used to obtain the barrier for arene CH activation. Due to the poor solubility of the Ph–Ir–Py in benzene and overlapping aromatic resonances in the ¹H NMR, the arene CH activation barrier with this complex could not be accurately obtained. As previous studies¹⁶ showed that the CH activation was inhibited by added pyridine, the activation barriers were obtained at constant pyridine concentrations. The temperature dependence of the reaction was examined over the range 140–180 °C in neat C₆D₆ at a constant pyridine concentration ([Py]/[C₆D₆] = 0.045). The reaction follows clean first-order kinetics, and to determine the reaction rates, ¹H NMR spectroscopy of the methyl resonances of the acac-O,O ligands was used to monitor the irreversible disappearance of the CH₃–Ir–Py starting material and the formation of the Ph–d₅–Ir–Py product for three half-lives. Activation parameters were obtained from an Eyring plot as shown in Figure 15. The activation entropy (ΔS*) was estimated to be 11.5 (±3.0) eu along with a ΔH of 41.1 (±1.1) kcal/mol and ΔGₚ of 37.7 (±1.0) kcal/mol. The PhCH₃CH₂–Ir–Py complex was found to react at essentially the same rates as CH₃–Ir–Py, and as can be seen in Figure 15, the experimentally determined rate for arene CH activation with PhCH₃CH₂–Ir–Py shows similar temperature dependence to that of CH₃–Ir–Py. The previously calculated CH activation barrier¹⁷ for a pathway proceeding via a cis-intermediate was found to be ~43 kcal/mol (ΔHf) for the PhCH₃CH₂–Ir–Py and is consistent with the value obtained in this experimental study.

2.6.4. Dependence of CH Activation on Pyridine Concentration. If the CH activation reaction proceeded, as proposed in Figure 14, from the five-coordinate trans-intermediate, R–Ir–□, then the CH activation should show an inverse dependence on added pyridine as shown in the possible rate laws. To confirm this, the rate of the C–H activation reaction of PhCH₃CH₂–Ir–Py was obtained in the presence of 15 to 44 equiv of pyridine (223 to 669 mM), Figures 16 and 17. The reactions are clean and quantitatively generate the trans-complex, Ph–d₅–Ir–Py. There are very little complications at these concentrations of pyridine with CH activation of the pyridine. The rate of formation of the cis-complexes (R–Ir–Py, R = Ph or Alkyl) is slower than the CH activation reaction at 140 °C and is not observed on the time scale of these experiments.

As can be seen, the rate of CH activation shows an inverse dependence on added pyridine. This is consistent with the CH activation reaction proceeding via the formation of the trans-five-coordinate complex, PhCH₃CH₂–Ir–□, that is formed by prior, rapid, reversible, dissociative loss of pyridine and is consistent with either rate law shown in Figure 14.

2.6.5. Arene Substrate Concentration Dependence. As can be seen in Figure 14 from the various possible mechanisms and associated rate laws for arene CH activation, there is the possibility that the reaction could show a direct dependence, independence, or more complex dependence on the benzene substrate. Both arene dependent and independent kinetics have been reported for arene for CH activation.³²–³³ To begin to distinguish between these possibilities, we examined the dependence of the arene CH activation rate on the arene substrate concentration. A key challenge in carrying out such a study is to identify an inert solvent that could be used as a diluent for the benzene substrate. Due to a combination of reactivity and solubility issues, solvents such as fluoropyridine, hexafluorobenzene, or trifluoroethanol could not be utilized. Instead, we utilized a strategy of carrying out the CH activation reactions in cyclohexane–d₁₂ solvent using the Cy–d₁₁–Ir–Py (where Cy–d₁₁ is the perdeuterated cyclohexyl group), with varying amounts of added excess C₆D₆ (1600–5600 mM to ensure pseudo first-order reaction conditions). Under these conditions, any reactions with the solvent would be degenerate and kinetically silent. The reactions were followed by analyzing the loss of the Cy–d₁₁–Ir–Py relative to trimethoxybenzene as an internal standard at 120 °C, and the results are shown in Figure 18. The Ph–d₅–Ir–Py product was not completely soluble.

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under these reaction conditions, and to ensure that loss of "Cy-d_{11}-Ir-Py" resulted only from formation of "Ph-d_{5}-Ir-Py", CD_{2}Cl_{2} was added after reaction to dissolve all products and the trimethoxybenzene was used as an internal standard to ensure that "Ph-d_{5}-Ir-Py" produced accounted for >95% of the reacted "Cy-d_{11}-Ir-Py". The lack of unreacted "Cy-d_{11}-Ir-Py" after long reaction times ensured that the reaction to generate "Ph-d_{5}-Ir-Py" was irreversible under the reaction conditions, and simple first-order plots could be used to obtain the rate constants.

As can be seen from Figure 18, the CH activation reaction shows a linear dependence on the benzene concentration that indicates that benzene is involved prior to or in the rate-determining step. This observation rules out the unimolecular possibility that \( k_7[\text{PhH}] > > k_{-6}, k_{obs} = k_{sk6}/k_{-5}[\text{Py}] \) (Figure 14), and shows that, unlike the case with isomerization of "Ph-Ir-Py" (at least at the concentrations of benzene examined) the formation of the cis-five-coordinate intermediate, *cis*-"R-Ir-Py", cannot be the rate-determining step and that benzene is involved in the rate-determining step for arene CH activation. Indeed, this observation does not provide any evidence for the formation of a cis-five-coordinate intermediate, *cis*-"R-Ir-Py", or indicate whether an arene complex is formed, if the CH cleavage step is rate-determining or if the CH activation reaction is concerted from the trans-five-coordinate intermediate, "R-Ir-Py". To distinguish between these possibilities, we turned to studies of the kinetic deuterium isotope effects on the CH activation reactions of "R-Ir-Py".

2.6.6. Isotope Effects on the Rate of CH Activation with (acac-O,O)Ir(R)(L) Complexes. As discussed above, the
observation that the reaction of Ph–Ir–Py with tol-d5 leads to multiple deuterated benzenes is most consistent with the CH activation reaction proceeding via the formation of an intermediate arene complex, followed by rapid and reversible CH cleavage before loss of the arene. To examine this possibility in greater detail, we turned to the now classic method, developed by W. Jones, of providing evidence for the intermediacy of arene complexes by comparison of the deuterium kinetic isotope effect (KIE) on the relative rates of CH activation when reactions are carried out with a mixture of C6D6/C6H6 and with 1,3,5-trideuteriobenzene. Three possibilities for the CH activation of benzene with CH3–Ir–Py can be considered with respect to the formation of arene complexes as shown in Figure 19: (A) a concerted process without the involvement of an arene complex (TS5 → TS10), (B) rate-determining CH cleavage proceeding via an arene complex, cis-Ir–Py–PhH, (TS5 → TS9 → TS11 or TS5 → TS6 → TS7 → TS11) that is kinetically indistinguishable by KIE from case A, and (C) rate-determining trans to cis isomerization and benzene coordination followed by rapid CH cleavage (TS5 → TS6 → TS7 → TS8). As can be seen if CH cleavage is rate-determining, case A or B, both the C6D6/C6H6 mixture and neat 1,3,5-C6D3H3 will be expected to show a normal kinetic isotope effect. However, if an arene complex is formed in a rate-determining step and followed by faster CH cleavage (case C), only the reaction with 1,3,5-C6D3H3 will show a normal KIE; the reaction with C6D6/C6H6 will show no KIE.

As discussed above, the reaction of CH3–Ir–Py with C6D6 proceeds quantitatively and irreversibly to produce only CH3D. Thus, analysis of the CH2/CHD ratio produced from CH activation with CH3–Ir–Py provides a convenient method of determining the KIE for CH activation with this complex. The CH activation reaction was carried out by reaction of CH3–Ir–Py at 110 °C with neat 1,3,5-C6H3D3, a 1:1 (molar) mixture of C6D6/C6H6 and neat C6D6 as solvents in separate reactions. In all three cases, the methane generated was analyzed by GC–MS, and the molar ratios of the methane CH2/CHD isotopomers were determined by deconvolution of the mass peaks based on actual response factors and fragmentation patterns from pure samples of CH4 and CH3D. Since it is known that these (acac-O,O)2Ir(R)(L) complexes will catalyze H/D exchange between arenes, the reactions were carried out for three half-lives and GC–MS analysis of the various solvents after reaction confirmed that no significant extent of H/D scrambling had occurred in the C6D6–C6H6 mixture or 1,3,5-C6H3D3 solvents. The results are shown in Table 1.

As discussed above, the observation that only CH3D was produced in the reaction with neat C6D6 ruled out any error that could be introduced from post H–D exchange of the generated methane. Control experiments in neat C6H6 also confirmed that only CH3D is generated. As can be seen, no kinetic isotope effect is observed for the C6D6/C6H6 mixture since a 1:1 ratio of CH3/CH3D is produced. This result effectively rules out pathways via TS10 and TS11 that involve CH cleavage in the rate-determining step. The rather large kinetic isotope effect (considering the temperature of 110 °C) of 3.2 (±0.2) that is observed with 1,3,5-C6H3D3 suggests that the reaction proceeds via TS5 → TS6 → TS7 → TS8 or TS5 → TS9 → TS8 that involve rate-determining coordination of benzene, followed by rapid CH cleavage. These results provide strong evidence that intermediate arene complexes are involved in the CH activation with the O-donor (acac-O,O)2Ir(R)(L) complexes and that CH activation with these O-donor complexes are inner-sphere processes involving substrate coordination.

2.6.7. Does the CH Activation Reaction Proceed via a cis-Five-Coordinate Intermediate? Importantly, these KIE and

(KIE)

(34) Methane can exchange with benzene at elevated temperatures and lead to higher isotopomers of methane as reported, ref 15.
mentally.

tions). This has been examined both theoretically and experi-

cis isomerization for these complexes (obtained when the

1. It may be considered that this specific comparison is not

kinds kinetic studies do not address the question of whether the
formation of these intermediate arene complexes are generated
via the formation of the cis-five-coordinate intermediate cis-

R−Ir−□ (TS5 − TS6 − TS7, Figure 19), or directly, in an
associative step from the trans-five-coordinate intermediate,

R−Ir−□ (TS5 − TS9, Figure 19). The trans−cis isomerization
studies of the Ph−Ir−Py complex provide evidence for the
rate-determining formation of such cis-intermediates, vide
supra. Since the formation of the cis-benzene complex, cis-

R−Ir−PhH, is essentially the same process as the formation of the
cis-pyridine complex, cis-Ph−Ir−Py, it is likely that
formation of the benzene complex also proceeds by formation
of the cis-five-coordinate intermediate, cis-R−Ir−□, and that
this should constitute the bulk of the barrier for the reaction
with benzene. If this is the case, the rate constant for CH
activation should be similar to the rate constant for the trans
cis isomerization for these complexes (obtained when the
reaction rates are corrected for benzene and pyridine concen-
trations). This has been examined both theoretically and experi-
mentally.

Theoretical results for the reaction of CH3−Ir−Py with
benzene, summarized in Figure 20, show that these rate
constants should be comparable as the formation of cis-R−Ir−□
is found to be the slowest step in both reactions. The cis/trans
isomerization has a $\Delta H^\ddagger = 44.6$ kcal/mol, while CH activation
has a $\Delta H^\ddagger = 43.4$ kcal/mol. $\Delta S$ terms are expected to be of
similar magnitude, as the total number of molecules does not
change.

Experimentally, the rates of the trans−cis and CH activation
have been obtained under identical conditions (180 °C and
pyridine to benzene ratio of 0.045) where the trans−cis isomerization
shows an inverse dependence on pyridine, and the
CH activation, a direct dependence on benzene. Taking the
ratio of the appropriate cases of the rate laws, Figure 14, and
assuming these reactions proceed via the formation of the cis-
five-coordinate intermediate, Scheme 2, allow the ratio of the
rate constants for the CH activation, $k_{CH}$, and trans−cis
isomerization, $k_{TC}$, to be compared. As can be seen, this ratio
is $\approx 1$. It may be considered that this specific comparison is not
entirely valid as different complexes, the Ph−Ir−Py and the
CH3−Ir−Py, are utilized in the trans−cis isomerization and
CH activation reactions, respectively. However, extrapolation
of the equilibrium constants for the loss of pyridine from
Ph−Ir−Py and CH3−Ir−Py show that at 180 °C the values
are comparable, $\approx 0.7 \times 10^{-9}$ and $\approx 2.0 \times 10^{-9}$, respectively,
and we anticipate that the trans−cis isomerization steps should
be energetically similar for these complexes. This suggests that
the comparable rate constants for these reactions are consistent
with the CH activation and trans−cis reactions proceeding via
a common intermediate, the cis-five-coordinate intermediate, cis-

R−Ir−□ and that the energetics of benzene coordination to
this species, TS10 and $k_f$ (Figures 13 and 18), do not signifi-
cantly contribute to the activation barrier for CH activation.

A comparison of the rates for trans−cis isomerization and
CH activation via the cis-R−Ir−□ intermediate also explains
why no cis-R−Ir−Py species are detected under typical CH
activation conditions with R−Ir−Py ($\approx 140$ °C and no added

Figure 19. Possible reaction coordinate for reaction of CH3−Ir−Py with 1,3,5-C6D3H3.

Table 1. Methane Isotopomer Ratio Obtained from Reaction of CH3−Ir−Py with Various Solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>CH4</th>
<th>1,3,5-C6H3D3</th>
<th>C6H6/C6D6 (1:1 molar mixture)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH3−Ir−Py</td>
<td>0</td>
<td>76</td>
<td>50</td>
</tr>
<tr>
<td>CH3−D</td>
<td>100</td>
<td>24</td>
<td>50</td>
</tr>
</tbody>
</table>

* See Experimental Section for details.
Py). Under these conditions, the appropriate rate law for the trans–cis isomerization is that shown in Scheme 3, where because of the low concentration of pyridine the reaction is independent of pyridine ($k_{-2} \gg k_{3}[\text{Py}]$, Figure 9) while the rate of CH activation remains inversely dependent on pyridine and directly dependent on benzene ($k_{-6} \ll k_{7}[\text{PhH}$, Figure 14). Thus, assuming that the rate constants $k_{TC}^{\text{cis}}$ for these steps are comparable, at comparable concentrations of complexes the relative rates of trans-cis isomerization to CH activation would be given by $[\text{Py}] / [\text{PhH}]$ which, based on the experimental equilibrium values for pyridine dissociation from $\text{R} - \text{Ir} - \text{Py}$, is $\sim 10^{-6}$. This low value is consistent with the observation that no cis-products are detected after the CH activation reaction is complete. At higher pyridine concentrations, the ratio of these rates would be expected to become comparable (as the rate law changes to those shown in Scheme 2 and both reactions become independent of added pyridine), and the trans–cis isomerization should be observed along with CH activation. This is observed experimentally, and at pyridine concentrations above 1 M, the cis-Ph–Ir–Py is observed during the CH activation of benzene with CH$_3$–Ir–Py. However, clean kinetics could not be obtained under these conditions as the reaction is complicated by CH activation of pyridine.

3. Conclusion

The chemistry of novel (acac-O,O)$_2$Ir(R)(L) organometallic complexes has been examined in detail. The dinuclear, [R–Ir]$_2$, as well as mononuclear complexes, R–Ir–L, have been found to be labile complexes that are in equilibrium, via dissociative processes, with trans-five-coordinate species, R–Ir–□, that are key intermediates in the substitution chemistry of these complexes. These R–Ir–L complexes have also been shown to undergo trans–cis isomerization via a rate-determining, unimolecular isomerization of R–Ir–□ to cis-R–Ir–□, followed by rapid reaction with substrates. Bimolecular pathways involving direct reaction of the substrate with the trans-intermediate, R–Ir–□, are not consistent with the experimental or theoretical results.

Arene CH activation with these O-donor complexes has been shown to occur via an inner-sphere process that involves substrate coordination and intermediate formation of an arene complex, followed by CH cleavage. While ligand exchange reactions readily occur via the trans-five-coordinate intermediate, R–Ir–□, both experimental and theoretical results are consistent with the CH activation reaction requiring further reaction of R–Ir–□ to generate the cis-intermediate, cis-R–Ir–□, before reaction. Experimental and theoretical studies are consistent with the formation of this species constituting the bulk of the barrier for the CH activation reactions and serve to explain why the rates of trans–cis isomerization and CH activation are comparable. Overall the CH activation reaction with R–Ir–Py has been shown to proceed via four key steps:
a pre-equilibrium loss of pyridine that generates a trans-five-coordinate, square pyramidal intermediate. R–Ir–O, (B) a largely rate-determining, unimolecular, isomerization of the trans-five-coordinate to generate a five-coordinate intermediate, cis-R–Ir–O, (C) coordination of benzene to this species to generate a discrete benzene complex, cis-R–Ir–PhH, and (D) a rapid C–H cleavage step. Kinetic isotope effects on the CH activation comparing reaction with a mixture of C₆H₆/C₆D₆ (KIE ≈ 1) and 1,3,5-C₆H₃CHD₃ (KIE ≈ 3) are consistent with the CH activation occurring via rate-determining arene coordination, followed by rapid CH cleavage.

In addition to showing that common O-donor ligands can be utilized in the design of efficient, stable CH activation catalysts capable of functionalization reactions, these studies show that the use of readily available, bis-chelating O-donor ligands, based on the acac-O,O ligands, may be used to access coordination reactions, such as CH activation, that require two mutually cis sites for reaction. These O-donor complexes are effective hydroarylation catalysts, and it will be interesting to rationalize the results of the current studies with the various catalytic steps of the hydroarylation reaction. For example, if mutually cis sites are required for the olefin insertion step, then the rate of the trans–cis isomerization could be expected to be a lower limit for the catalytic rate starting from the trans-complex while the rate for loss of pyridine would be expected to be the lower limit starting from the cis-complex. Other interesting aspects of these complexes, such as why no olefin products are observed in these catalytic reactions, will also be examined.

4. Experimental Section

4.1. General Considerations. Spectroscopy. Liquid phases of the organic products were analyzed by a Shimadzu GC-MS QP5000 (ver. 2) equipped with a cross-linked methyl silicone gum capillary column, DB5. Gas measurements were performed using a GasPro column. The retention times of the products were confirmed by comparison to standards. NMR spectra were obtained on a Bruker AC-250 (250.134 MHz for ¹H and 62.902 MHz for ¹³C), a Bruker AM-360 (360.138 MHz for ¹H and 90.566 MHz for ¹³C), or a Varian Mercury 400 (400.151 MHz for ¹H and 100.631 MHz for ¹³C) spectrometer. Chemical shifts are given in ppm relative to TMS or to residual proton solvent resonances. All carbon resonances are singlets unless otherwise mentioned. Resonances due to pyridine are reported by chemical shift and multiplicity only. All pyridine complexes showed similar coupling constants (J = 5.00 Hz, J' = 1.5 Hz, o-H py; J = 8.0 Hz, J' = 1.5 Hz, p-H py; J = 6.50 Hz, m-H py). The temperature of the probe was monitored using methanol or ethylene glycol solutions with an added trace of concentrated aqueous hydrochloric acid. Errors in reported temperatures are ±2 ℃ at a maximum. Fast atom bombardment (FAB⁺) mass spectrometry was carried out using a VG ZAB-SE, high resolution double-focusing mass spectrometer at PASAROW Mass Spectrometry laboratory at UCLA using nitrobenzene alcohol (NBA) as the matrix.

X-ray diffraction data were collected on a Bruker SMART APEX CCD diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). The cell parameters were obtained from the least-squares refinement of the spots (from 60 collected frames) using the program SMART. A hemisphere of data was collected up to a resolution of 0.75 Å. The intensity data were processed using the program SAINT-Plus. All calculations for the structure determination were carried out using the SHELXTL package (version 5.1). Initial atomic coordinates of the Ir atoms were located by direct methods, and structures were refined by least-squares methods. Empirical absorption corrections were applied using the program SADABS. Calculated hydrogen positions were input and refined in a riding manner along with their attached carbons. A summary of the refinement details and the resulting parameters are given in the Supporting Information.

Materials and Analyses. All manipulations were carried out using glovebox and high vacuum line techniques. Benzene, benzene-d₆, toluene-d₈, and THF were purified by vacuum transfer from sodium benzophenone ketyl. CDCl₃ and pyridine were dried by vacuum transfer from CaH₂. Synthetic work involving iridium complexes was carried out in an inert atmosphere despite the air stability of the complexes. Reagent-grade chemicals and solvents were used as purchased from Aldrich or Sterm. Complex [acac-C–Ir]⁺, acac-C–Ir–H₂O, acac-C–Ir–Py, Ph–Ir–H₂O, Ph–Ir–Py, and ethyl(1-phenyl)mercury were prepared as described in the literature. Elemental analyses were done by Desert Analytical Laboratory, Arizona.

[Ir(µ-acac-O,O,C₃)(acac-O,O)(CH₃)]²⁺ [CH₃–Ir]: Method A: In the glovebox, a Schlenk flask fitted with a Teflon valve was charged with iracac-C–Ir–H₂O (342 mg, 0.675 mmol) and suspended in THF (100 mL). To this, was added a toluene solution of ZnMe₂ (2.0 M, 370 µL, 0.740 mmol). Upon addition, the solution developed a slight orange color. The flask was then sealed, removed from the glovebox, and placed in a 60 ℃ oil bath for 2 h. The resulting slightly cloudy orange solution was cooled to room temperature, whereby a small amount of a white precipitate settled. The solution was poured onto water (200 mL), extracted with CH₂Cl₂ (2 × 100 mL), and then dried over Na₂SO₄. Filtration followed by removal of solvent in vacuo yielded a solid. Addition of acetone and precipitation with ether at ~25 ℃ afforded a bright yellow solid. The clear yellow solution was decanted and the solid dried in vacuo, to afford [CH₃–Ir]⁺ as an analytically pure bright yellow powder (205 mg, 75% yield). Comparable yields were obtained when [acac-C–Ir]⁺ was used.

Method B: A solution of iracac-C–Ir–H₂O (340 mg, 0.674 mmol) in methanol was added to a Schlenk flask fitted with a Teflon valve. To this, dimethylmercury (55 µL, 0.7 mmol) was added through a syringe. The reaction flask was heated to 60 ℃ for 2 h and then cooled to room temperature. The resulting solution was vacuum transferred to leave a crude orange powder. The crude reaction mixture was loaded on a silica gel column and eluted with THF to afford [CH₃–Ir]⁺ as yellow powder (220 mg, 80% yield).

[Ir(µ-acac-O,O,C₃)(acac-O,O(CH₃))][Ir–Ir]: Due to the fluxional nature of the dinuclear complex in CDCl₃ at ambient temperature, the bridging and nonbridging acac resonances are broadened. δ 5.40 (s, 4H, acac-C=O), 1.96 (s, 6H, Ir–CH₃), 1.83 (br s, 24H, acac-CH₂). Ir NMR (CDC₁₅, δ): δ 5.50 (s, 2H, O-acac-C=O), 5.34 (s, 2H, µ-acac-C=O), 1.89 (s, 6H, Ir–CH₃), 1.88 (s, 12H, O-acac-CH₂), 1.77 (s, 12H, µ-acac-CH₂), 1.31 (OH) (27 ℃); δ 191.55 (µ-acac-C=O), 183.14 (O-acac-C=O), 103.79 (O-acac-CH₂), 81.56 (µ-acac-CH₂), 28.53 (µ-acac-CH₂), 27.32 (O-acac-CH₂), 21.31 (Ir–CH₃). 1H NMR (CD₂Cl₂, δ): δ 5.46 (s, 2H, CH₃), 1.76 (s, 12H, acac-CH₂), 1.75 (s, 3H, CH₃). ¹³C(NH) NMR (CD₂Cl₂): δ 184.3 (acac-C=O), 103.8 (acac-CH₂), 26.4 (acac-CH₃), –34.9 (CH₂). Anal. Calcd for C₂₂H₃₄Ir₂O₈: C, 32.58; H, 4.23. Found: C, 31.87; H, 3.94.

[Ir(µ-acac-O,O,C₃)(acac-O,O(CH₃))][Ir–Ir]: [PhCH₂CH₂Ir–Ir]: PHCH₂CH₂Ir–Ir] was synthesized according to Method B with iracac-C–Ir–H₂O (100 mg, 0.197 mmol) in 10 mL of methanol and using bis(2-phenylnethyl)mercury (100 µL, 0.25 mmol). The crude reaction mixture was purified using column chromatography (silica gel) using a gradient solvent (100% THF to 1:1 THF–ether) and recrystallized from a mixture of CH₂Cl₂ and hexanes. The title compound was isolated as an orange powder (60 mg, 60% yield). ¹H NMR (CDCl₃): (−10


pyridine Concentration: A stock solution of Ph-IR−Py and CH3-IR−Py in CDCl3 (5 mM) was made and transferred to four oven-dried NMR tubes. Py-d5 (52−156 mM) was added to these NMR tubes at low temperature and then subjected to precooled (273 K) NMR studies. The intensity of the bound or free pyridine was plotted against time using the Mercury 400 NMR machine.

Kinetics for CH Activation of CD3 with CH3-IR−Py at Constant [CD3/Py]: A stock solution of CH3-IR−Py was made in CD3 (15 mM) with added pyridine-d5 (510 mM) and trimethoxybenzene (5 mg) as internal standard. A 200 µL aliquot of this solution was added to a 5 mm thick J-yard NMR tube fitted with a valve to which argon (100−150 psig) was added. The NMR tube was heated in a well-stirred oil bath maintained at a temperature (140−180 °C) during which the samples were analyzed by 1H NMR spectroscopy. The reaction was monitored for 3 half-lives.

Dependence of Trans−Cis Isomerization of Ph−IR−Py on Pyridine Concentration: A stock solution of Ph−IR−Py in CD3 (15 mM) with trimethoxybenzene (1 mM) as internal standard was added to three 5 mm J-yard NMR tubes fitted with a valve. To each of them, Py-d5, ranging from 0.5 to 2.5 molar equiv., was added. The NMR tube was heated with added argon pressure (100−150 psig) in a well-stirred oil bath maintained at 180 °C during which the samples were analyzed by 1H NMR spectroscopy. The reactions were monitored for 2−3 half-lives.

Dependence of Benzene CH Activation on Pyridine Concentration: A stock solution of PhCH3-IR−Py in CD3 (15 mM) with trimethoxybenzene (1 mM) as internal standard was added to three 5 mm J-yard NMR tubes fitted with a valve. To each of them, Py-d5, ranging from 72 mM to 217 mM was added. The NMR tube were heated with added argon pressure (100−150 psig) in a well-stirred oil bath maintained at 180 °C during which the samples were analyzed by 1H NMR spectroscopy. The reaction was monitored for 3 half-lives.

Arene Concentration Dependence on Rate of C−H Activation of Benzene with Cy-d11−IR−Py: Cy-d11−IR−Py (5 mg) along with trimethoxybenzene (1 mg) as internal standard was added to three 5 mm J-yard NMR tubes fitted with a Teflon valve. To these, varying amounts of Cd3 and Cd3 were added. The NMR tubes were heated with added argon pressure (100−150 psig) in a well-stirred oil bath maintained at 120 °C during which the samples were analyzed by 1H NMR spectroscopy. The reactions were monitored for 3 half-lives. After the reaction, Cd3 was added to dissolve all Ph-d5−IR−Py produced, and the trimethoxybenzene was used as an internal standard to ensure that Ph-d5−IR−Py produced accounted for >95% of the added Cy-d11−IR−Py.

Deuteron Kinetic Isotope Effect on Arene C−H Activation with CH3−IR−Py: Three 2 ml thick glass screw cap vials containing septa were loaded with 5 mg (0.01 mmol) of CH3−IR−Py in parallel. To these vials, 0.5 mL of Cd3, 1,3,5-C6H3D3 and a 1:1 molar mixture of

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C₆H₆ and C₆D₆ were introduced. The vials were freeze—pump—thawed thrice and filled with argon gas. The vials were immersed in a 110 °C oil bath, and the gas phase was sampled for 3 half-lives and analyzed on a GC–MS equipped with a Gas Pro column. The molar ratio of the liberated methanol isotopomers was deconvoluted using a spreadsheet. The solution remained homogeneous throughout the reaction, and no signs of decomposition were observed. The liquid phase was analyzed to make sure that no deuterium scrambling had occurred.

**H—D Exchange between C₆H₆ and Toluene-d₈:** Catalytic H—D exchange reactions were quantified by monitoring the increase of deuterium into C₆H₆ by GC/MS analyses for Ph—Ir—Py and cis-Ph—Ir—Py (5 mM) using toluene-d₈ as the deuterium source at 160 °C. This was achieved by deconvoluting the mass fragmentation pattern obtained from the MS analysis, using a program developed on Microsoft EXCEL. 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%. Catalytic H/D exchange reactions were thus run for reaction times in order to be able to detect changes >5% in exchange.

**Computational Methodology:** All calculations were performed using the hybrid DFT functional B3LYP as implemented in the Jaguar 5.0 or 5.5 program package. 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 iridium was 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-ζ 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 r_solv = 2.602 Å. Due to the increased cost of optimizing systems in the solvated phase (increase in computation time by a factor of ~4) solvation effects were calculated here as single-point solvation corrections to gas-phase geometries, except for cases where a vacant coordination site is created. Allowing relaxation in solvent did not change the relative energies more than 1 kcal/mol for species where the coordination remained constant; however, in cases where the coordination changed, the relaxation can account for up to 4 kcal/mol.

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.

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**Supporting Information Available:** First-order plots and activation parameters for line-broadening analysis, Py exchange, and CH activation, and crystal data for Ph—Ir—Py and Ph—CH₃—CH₂—Ir—Py. This material is available free of charge via the Internet at http://pubs.acs.org.

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