Benzene C–H Bond Activation in Carboxylic Acids Catalyzed by O-Donor Iridium(III) Complexes: An Experimental and Density Functional Study


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The mechanism of benzene C–H bond activation by [Ir(μ-acac-O-O,C3)(acac-O,O)(OAc)]2 (4) and [Ir(μ-acac-O-O,C3)(acac-O,O)(TFA)]2 (5) complexes (acac = acetylacetonato, OAc = acetate, and TFA = trifluoroacetate) was studied experimentally and theoretically. Hydrogen–deuterium (H/D) exchange between benzene and CD2COOD solvent catalyzed by 4 (ΔH‡ = 28.3 ± 1.1 kcal/mol, ΔS‡ = 3.9 ± 0.3 cal K⁻¹ mol⁻¹) results in a monotonic increase of all benzene isotopologues, suggesting that once benzene coordinates to the iridium center, there are multiple H/D exchange events prior to benzene dissociation. B3LYP density functional theory (DFT) calculations reveal that this benzene isotopologue pattern is due to a rate-determining step that involves acetate ligand dissociation and benzene coordination, which is then followed by heterolytic C–H bond cleavage to generate an iridium-phenyl intermediate. A synthesized iridium-phenyl intermediate was also shown to be competent for H/D exchange, giving similar rates to the proposed catalytic systems. This mechanism nicely explains why hydroarylation between benzene and alkenes is suppressed in the presence of acetic acid when catalyzed by [Ir(μ-acac-O-O,C3)(acac-O,O)(acac-C3)]2 (3) (Matsumoto et al. J. Am. Chem. Soc. 2000, 122, 7414). Benzene H/D exchange in CF3COOD solvent catalyzed by 5 (ΔH‡ = 15.3 ± 3.5 kcal/mol, ΔS‡ = −30.0 ± 5.1 cal K⁻¹ mol⁻¹) results in significantly elevated H/D exchange rates and the formation of only a single benzene isotopologue, (C6H2D).

DFT calculations show that this is due to a change in the rate-determining step. Now equilibrium between coordinated and uncoordinated benzene precedes a single rate-determining heterolytic C–H bond cleavage step.

1. Introduction

In contrast to classic oxidative addition¹ and σ-bond metathesis mechanisms, the recent discovery of 1,2-addition or substitution mechanisms across metal–heterometal bonds offers a new paradigm for transition metal mediated C–H bond activation. Previously, we reported that the iridium(III) acetylacetonato (acac) alkoxide and hydroxo complexes 1a and 1b promote stoichiometric benzene C–H bond activation to generate methanol or water and the corresponding iridium-phenyl complexes (2a,b) by an internal substitution mechanism (IS, Scheme 1a). Recent density functional theory (DFT) and energy decomposition calculations have revealed that the IS transition state involves the interplay between an electrophilic iridium center that


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facilitates iridium–carbon bond formation and a nucleophilic OR group that utilizes a lone pair to bond with hydrogen (Scheme 1b).

Benzene–C–H bond activation by the (acac-O,O)\textsubscript{2}Ir(R)(L) motif\textsuperscript{7} also occurs during the hydroarylation reaction between benzene and alkenes catalyzed by the dinuclear [Ir(μ-acac-O, O,C\textsubscript{3})(acac-C\textsubscript{3})\textsubscript{2}] complex 3 (Scheme 2a,b).\textsuperscript{9} Previous DFT studies have shown that the C–H bond activation in this reaction occurs via an oxidative hydrogen migration\textsuperscript{10} (OHM) transition state (Scheme 2b).\textsuperscript{10,11} The OHM transition state involves exchange of an iridium–R bond for an iridium–phenyl bond without forming an oxidative addition intermediate (Scheme 2b).

In the presence of acetic acid, benzene–alkene hydroarylation is severely suppressed; however, catalytic hydrogen–deuterium (H/D) exchange between deuterated acetic acid and benzene occurs with a turnover frequency (TOF) of 7.6 s\textsuperscript{-1} at 160 °C (Scheme 2c).\textsuperscript{9a} This observation is intriguing because a new acetate/acetate complex is likely formed that does not catalyze hydroarylation, which requires both C–H bond activation and alkene insertion reactions. Previous DFT calculations have suggested that a coordinated acetate group can assist in C–H bond cleavage via a substitution mechanism akin to the IS mechanism (Scheme 2c, acetate-assisted transition state).\textsuperscript{7a,11} A similar transition state was also located for intramolecular cyclometalation of dimethylbenzylmine by the [CpIr(OAc)]\textsuperscript{+} complex (Cp = cyclopentadienyl, OAc = acetate).\textsuperscript{12} Also, we have previously shown that an acetate-assisted mechanism is likely operative for H/D exchange between benzene and trifluoroacetic acid (HTFA) catalyzed by K\textsubscript{2}[Pt(pic)(TFA)\textsubscript{2}]\textsuperscript{11d} (pic = 2-O,O-acetylacetonato, TFA = trifluoroacetate)\textsuperscript{11d} and [Ir(μ-acac-O, O,C\textsubscript{3})(acac-O, O)(O-acetate)]\textsuperscript{2} (Scheme 3).

Here we report an experimental and computational (B3LYP density functional) study of the mechanism of catalytic H/D exchange between benzene and carboxylic acid solvents using (acac-O,O)\textsubscript{2}Ir(R)(L).\textsuperscript{13} Among the most important questions to answer are the following: (1) What is the mechanism and rate-determining step for H/D exchange, benzene coordination, or C–H bond cleavage? (2) What occurs if a more acidic solvent, such as trifluoroacetic acid, is used? (3) Why is hydroarylation inhibited but not benzene–solvent H/D exchange? To answer these questions, we have synthesized the dinuclear Ir(μ-acac-O, O,C\textsubscript{3})(acac-O, O,O)(O-acetate)]\textsuperscript{2} (Scheme 3).
2. Results and Discussion

The mechanism for hydroarylation between benzene and alkenes catalyzed by dinuclear [(acac-O,O)₂Ir(L)]₂ species has been reasonably well established by theory and experiment (Scheme 4). Briefly, the dinuclear complex first disassociates into a coordinatively unsaturated (acac-O,O)₂Ir(L) species that undergoes cis–trans isomerization followed by benzene C–H activation to generate the iridium phenyl intermediate, which then coordinates the alkene. Alkene insertion into the iridium-phenyl bond followed by a second benzene C–H bond activation event releases the product and regenerates the iridium phenyl-intermediate.

In 2000, Matsumoto et al. showed that complex 3 catalyzes hydroarylation between benzene and substituted alkenes. They also reported that addition of acetic acid inhibited hydroarylation; however, facile catalytic CH activation, characterized by H/D exchange between benzene and deuterated acetic acid, was still observed. This intriguing observation was the impetus for our mechanistic investigation. To start, we repeated H/D exchange experiments between benzene and deuterated acetic acid catalyzed by 3. Monitoring deuterium incorporation into benzene in deuterated acetic acid in a 1:1 (v/v) mixture at 180 °C gave a turnover frequency (TOF) of 7.4 s⁻¹. This TOF value is very close to the 7.6 s⁻¹ value reported by Matsumoto and co-workers. The reaction was stopped after 10 min and isolation of the residue and analysis by NMR revealed the formation of a new iridium species.

Previous studies from our group have shown the C₃-bound acac group of 3 is highly labile. We suspected that in acetic acid this acac ligand is readily replaced by acetate. Heating a solution of 3 in neat acetic acid at 100 °C for 1 h followed by in vacuo removal of solvent resulted in a yellow solid in greater than 95% yield (Scheme 5). The ¹H NMR (Figure 1) showed three methyl signals between 1.9 and 2.2 ppm relative to the residual chloroform solvent signal with an integration ratio of 6:12:12 and two methine signals at 5.7 ppm with an integration ratio of 2:2, consistent with an acetate-bound (acac-O,O)₂Ir(III) species. The X-ray crystal structure (Figure 2), ¹³C NMR, HR ESI mass spectrometry, and elemental analysis also confirm this yellow solid to be the dinuclear [Ir₂(acac-O,O,C₃)(acac-O,O)(OAc)]₂ species 4. Complex 4 was also independently synthesized starting with the previously reported (acac-O,O)₂Ir(acac-C₃)(H₂O) complex. Reaction of approximately 100 mg of 4 in a 1:10 mixture of acetic acid and methanol was heated for 10 min at 60 °C to give a yellow, homogeneous solution. Excess solvent was then removed, yielding 4 in 95% yield (Scheme 5). Compound 4 is a dinuclear iridium(III) species with two O-bound acetates, two conventional O-bonded acac ligands, and two bridging acac ligands that connect the two iridium centers via the central carbon on the acac ligand.

With the discrete species 4 synthesized we next compared H/D exchange rates between benzene and deuterated acetic acid using catalysts 3 and 4. Two separate reactions each containing 0.1 mL of benzene in 1 mL of deuterated acetic acid were loaded with 0.5 mol % of either 3 or 4. Monitoring deuterium incorporation into benzene via GC-MS after 30 min at 130 °C showed similar TOF values of (1.6 ± 0.6) × 10⁻³ and (1.8 ± 0.2) × 10⁻³ s⁻¹ for 3 and 4, respectively (Table 1). The similar TOF values suggest that the labile C₃ acac ligands are readily replaced in acetic acid to generate the same in situ catalyst. The slightly lower TOF for 3 is likely the result of a shorter induction period resulting from ligand exchange of acac to acetate.

Next, the thermal stability of 4 was examined. A 3.4 mM solution of 4 in acetic acid was heated to 180 °C in a Schlenk flask with a resealable Teflon valve. In less than one hour, the reaction mixture turned from a bright yellow color to a

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(16) Catalytic reactions were monitored by ¹H NMR, where comparison to a stated internal or external standard was used for relative concentrations of products or by GC-MS and deconvolution of the MS data using a Microsoft Excel program to calculate turnover frequency (TOF) and turnover number (TON) of the reaction. We consider a turnover to be the process of a single C–H cleavage step where one proton is replaced by a deuterium and degenerate exchanges of a proton with a proton and deuterium with a deuterium are not accounted for in our calculations. Turnover frequency (TOF) is defined as [mol of product produced]/[mol of added catalysts] per second. Turnover number (TON) is defined as [mol of product produced]/[mol of added catalysts] when the reaction is stopped. Moles of catalyst for the above calculations are based upon moles of added iridium.

(17) A typical experiment involved loading a 4 mL Schlenk flask with a resealable Teflon valve with 0.5 mol % of the desired catalyst and addition of 1 mL of deuterated acetic acid. The flask was freeze–thawed a minimum of three times, and 0.1 mL of benzene was added to the flask under an argon flow. The flask was sealed and placed in a well-stirred, temperature-controlled, oil bath. After 30 min the flask was removed from the bath and sampled by syringe under argon for analysis by GC-MS.
homogeneous yellow solution. Heating the solution for more than 2 h resulted in a color change from yellow to brown and after 8 h resulted in a black solution and a precipitate on the reaction flask. The black precipitate is likely due to the formation of iridium black. The reaction was monitored by \( ^1\)H NMR over a period of 8 h (Figure 3) by taking 1 mL aliquots and transferring the aliquot to a J-Young NMR tube and removing the solvent in vacuo.18 Then, a 0.6 mL premixed solution of internal standard/NMR solvent was then added to the residue in the J-Young NMR tube under argon. Over 2 h, signals for \( ^1\)H decreased \( \sim \) 50% relative to the added internal standard. At a lower temperature of \( \sim 130^\circ\)C, \( ^1\)H is stable and showed no signs of decomposition with greater than 95% of the catalyst being recovered after heating for a period of seven days as determined by mass balance and comparison of \( ^1\)H and \( ^13\)C NMR spectra. The stability of complex \( ^1\)H was also studied with added benzene-H\( _6\). Heating the mixture at 150 \( ^\circ\)C for \( \sim 6 \) h showed no decomposition and nearly full catalyst recovery. The residue was confirmed to be \( ^1\)H by comparison of \( ^1\)H and \( ^13\)C NMR spectra to an authentic sample. Later kinetic studies were performed at or below 150 \( ^\circ\)C.

To examine the stability of the catalytic system, H/D exchange between benzene-H\( _6\) and deuterated acetic or trifluoroacetic acid catalyzed by \( ^1\)H were monitored for 5 h using catalyst \( ^1\)H. Figure 4 shows a plot turnover number (TON) versus time. The linear correlation shows that catalysis is stable over a period of (18) The solvent mixture was prepared by adding 35 \( \mu\)L (0.55 mmol) of dichloromethane to 10 mL (0.12 mol) of CDCl\( _3\) in a 10 mL volumetric flask.
5 h and results in ~165 turnovers based on moles of added iridium.

Next, the enthalpy and entropy of activation catalyzed by 4 was measured over a temperature range of 80–150 °C by monitoring H/D exchange between benzene and deuterated acetic acid. Figure 5 shows the resulting Eyring plot, which gives an estimated enthalpy of activation of 28.3 ± 1.1 kcal/mol and entropy of activation of 3.9 ± 3.0 cal K⁻¹ mol⁻¹.

Previous studies of the Pt(picolinate)(TFA)₂ and other C–H activation systems showed that increasing the acidity of the solvent resulted in faster H/D exchange rates. 9,11,19 Attempts to use deuterated trichloroacetic acid20 proved difficult because at elevated temperatures (>100 °C) trichloroacetic acid decomposition occurs and post-reaction workup resulted in the isolation of a previously reported bright orange solid that was not active for CH activation. 21 Methanesulfonic acid was also tested. However, background deuterium exchange between solvent and benzene at temperatures greater than 100 °C was too rapid and prohibited monitoring H/D exchange. A successful significant rate increase was found by using trifluoroacetic acid. Monitoring a reaction of 0.1 mL of benzene-H₆ and 1 mL of CF₃COOD at 130 °C catalyzed by 4 resulted in a TOF = (6.92 ± 0.3) × 10⁻³ s⁻¹ (Table 1). This is nearly quadruple the rate of H/D exchange catalyzed by 4 in acetic acid (TOF = (1.8 ± 0.2) × 10⁻³ s⁻¹ at 130 °C).

Control reactions showed that heating 4 for 1 h at 130 °C in HTFA and isolation of the product resulted in substitution of the acetate ligand, as seen by ¹H NMR. In order to understand the effects of ligand substitution (TFA for OAc), we synthesized the corresponding trifluoroacetate complex [Ir(μ-acac-O,O,C₃)(acac-O,O)(TFA)]₂ (5). Heating a solution of 3 in neat trifluoroacetic acid at 100 °C for 1 h followed by in vacuo removal of solvent resulted in a yellow solid in 51% yield (Scheme 6). The ¹H NMR showed two methyl signals between 2.1 and 2.2 ppm relative to the chloroform residual solvent signal with an integration ratio of 12:12 and two methine signals at 5.7 ppm with an integration ratio of 2:2, consistent with a trifluoroacetate-bound (acac-O,O)Ir(III) dinuclear species 5. The ¹⁹F NMR showed a single signal at −75.2 ppm relative to added CFCl₃, consistent with an iridium-bound trifluoroacetate. Reaction of approximately 100 mg of 6 in a 1:10 mixture of trifluoroacetic acid and methanol was heated for 10 min at 60 °C to give a yellow, homogeneous solution. Excess solvent was then removed to give 5 in 95% yield (Scheme 6). The complex was then fully characterized by ¹³C NMR, HR ESI spectrometry, and elemental analysis to definitively confirm the yellow solid to be the dinuclear iridium(III) acac species 5.

Table 1 shows that H/D exchange catalyzed by 5 in deuterated trifluoroacetic acid gives the largest TOF value of (10.7 ± 0.9) × 10⁻³ s⁻¹. This likely indicates that ligand substitution (TFA for OAc) occurs as well as a significant increase in H/D exchange due to the increased solvent polarization and acid strength.


(20) Deuterated trichloroacetic acid was prepared according to literature methods: Kendall, J.; Gross, P. M. J. Am. Chem. Soc. 1921, 43, 1426.

(21) Attempts to synthesize an iridium trichloroacetate complex analogous to 4, by heating 3 in neat, molten trichloroacetic acid at 100 °C for 1 h, resulted in formation of a similar bright orange solid. This species was characterized by ¹H and ¹³C NMR and high-resolution ESI mass spectrometry and determined to be the iridium dichloride species, [Ir(µ-acac-O,O,C₃)(acac-O,O)Cl₂]. Formation of the dichloride species occurred due to decomposition of trichloroacetic acid. Unfortunately, [Ir(µ-acac-O,O,C₃)(acac-O,O)Cl₂] is not active for C–H activation in acidic media and requires added base for C–H activation reactions to proceed.
To quantify the relative activation barriers between acetic and trifluoroacetic acid based systems, the enthalpy of activation for H/D exchange catalyzed by 4 was measured over a temperature range of 100–130 °C by monitoring exchange between benzene and deuterated trifluoroacetic acid by GC-MS (Figure 5). The 15.3 ± 3.5 kcal/mol activation enthalpy is ∼13 kcal/mol lower than the ΔH‡ value when catalyzed by 4 in acetic acid. Not only are the activation enthalpies between the acetic and trifluoroacetic acid systems different, but there is also a significant difference between entropies of activation. The ΔS‡ value for the exchange catalyzed by 4 in acetic acid is 2.9 ± 3.0 cal K⁻¹ mol⁻¹, and that for exchange catalyzed by 5 in trifluoroacetic acid is −30.0 ± 5.1 cal K⁻¹ mol⁻¹ (Table 2).

One possible explanation for the differences in ΔS‡ values could be a change in the rate-determining step. Benzene C–H bond activation may be considered as two steps: (1) ligand decoordination/benzene coordination and (2) benzene C–H bond cleavage. We later report DFT calculations that support this hypothesis. The ΔH‡ and ΔS‡ values were also measured for H/D exchange catalyzed by 4 in HTFA and resulted in intermediate values from those reported in Table 2. We speculate that this is the result of a monitoring time of only 30 min and that there is likely an initial induction period for ligand exchange of OAc to TFA (see Supporting Information).

<table>
<thead>
<tr>
<th>catalyst</th>
<th>solvent</th>
<th>ΔH‡ (kcal/mol)</th>
<th>ΔS‡ (cal K⁻¹ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>CD₃COOD</td>
<td>28.3 ± 1.1</td>
<td>2.9 ± 3.0</td>
</tr>
<tr>
<td>5</td>
<td>CF₃COOD</td>
<td>15.3 ± 3.5</td>
<td>−30.0 ± 5.1</td>
</tr>
</tbody>
</table>

There are three possible resting states of 4: a dinuclear-trans-[Ir(acac-O,O)₂(acac-O,O)(OAc)]₂ (4), a mononuclear-trans-[Ir(acac-O,O)₂(OAc)] (7), and a mononuclear-cis-[Ir(acac-O,O)₂(OAc,L)] (8), species where L is a solvent molecule (Scheme 7). The ability of [Ir(acac-O,O)₂(R)]₂ dinuclear complexes to dissociate to stable five-coordinate square-pyramidal complexes or octahedral mononuclear solveto species in coordinating solvents is also possible. DFT calculations on a related (acac-O,O)₂Ir(OH)(Py)
system have shown that trans to cis isomerization is exothermic and that two cis coordination sites are required for C–H bond activation. To identify the resting state, ~10 mg of complex 4 was dissolved in 0.75 mL of deuterated acetic acid in a J-Young NMR tube. Initial proton NMR spectra at 25 °C showed only the trans-dinuclear species. However, after mild heating (100 °C for 20 min) conversion to the trans-mononuclear species as characterized by two methyl signals and a single methine occurs (Figure 6). Subsequent variable-temperature NMR (VT-NMR) experiments revealed that heating ~10 mg of complex 4 dissolved in 0.75 mL of deuterated acetic acid from 25 to 80 °C revealed conversion to the mononuclear-trans-[(acac-O,O)2Ir(OAc)(L)] as characterized by the conversion of the two methine signals to a single methine and two methyls. Heating the NMR probe to temperatures greater than 80 °C resulted in a mixture of methyl signals that could not be clearly identified due to significant signal broadening and overlap. This could be indicative of both cis and trans complexes being present in equilibrium.

Interestingly, on the basis of the significant change in rate of H/D exchange between 4 and 5 as well as differences in the ΔS‡ values it is plausible that a mechanistic change occurs when switching between 4 in HOAc and 5 in HTFA. We must then consider the possible mechanisms by which the coordination and cleavage steps occur to generate the iridium–phenyl bond via CH activation. As shown in Figure 6, solvation of 4 in acetic acid leads to the trans-(acac-O, O2Ir(OAc)(HOAc) species (7). Scheme 8 shows the two most plausible pathways for the CH activation of benzene by 4 and 5 (see Supporting Information for other considered mechanistic pathways). Path A consists of a trans to cis isomerization to 8 followed by rate-determining opening of the κ2-acetate, leading to an open coordination site (9). A series of fast steps occur including benzene coordination followed by CH cleavage to generate 11. Path B contrasts this by having a rate-determining cleavage step to give 11 preceded by a pre-equilibrium step of benzene coordination. Path A would be zero-order in benzene and first-order in catalyst, while Path B would show first-order dependence on both benzene and catalyst. The order of reactants was determined by monitoring a series of reactions at varying concentrations over several hours for product conversion. All reactants were determined to be first-order except there is an inverse dependence on acetic acid concentration in all cases and H/D exchange involving 4 with benzene, where benzene was determined to be zero-order, consistent with the proposed rate laws in Scheme 8. The suggests that 4 in acetic acid follows a mechanism operating via Path A and 5 in trifluoroacetic acid operates via a mechanism in which facile benzene coordination occurs as shown in Path B.

Kinetic isotope effects (KIE) are often measured to probe the nature of a rate-determining transition state. Differentiation of our two proposed mechanisms could be evaluated by a KIE. If coordination were rate determining, a KIE ≈ 1 would be expected as no cleavage or formation of these bonds occurs prior to the rate determining step (Path A, Scheme 8). Contrasting that with a case in which C–H bond cleavage occurs prior to the rate determining step, a large KIE should be seen (Path B, Scheme 8). However, using deuterated carboxylic acid solvents would contaminate KIE.
values with solvent isotope effect values. Therefore, we used an alternative method based on analysis of benzene isotopologue formation. Figures 7 and 8 show the benzene isotopologue formation patterns analyzed by GC-MS over 2 h at 120 °C for H/D exchange catalyzed by 4 in acetic acid and 4 in trifluoroacetic acid (Scheme 9). In acetic acid, there is a nearly linear increase in all benzene isotopologues formed. C₆H₅D and C₆H₄D₂ both have 10 mmol of deuterium incorporation after 2 h, while other isotopologues are formed in significant amounts, but to a lesser extent based on a statistical distribution. Changing the solvent from acetic acid to trifluoroacetic acid dramatically changes the isotopologue pattern and results in a buildup of only C₆H₅D with ~16.5 mmol of deuterium incorporation after 2 h.

The isotopologue pattern (so-called parallel incorporation) shown in Figure 7 is consistent with a mechanism where once benzene coordinates to the metal center there are multiple H/D exchange events to benzene and the solvent before benzene is released. Considering CH activation consists of coordination and cleavage steps, the rapid deuteration of benzene is indicative of the barrier for substrate coordination being higher in energy than the C–H bond cleavage step. Another possible explanation is that the rate of benzene coordination and rate of C–H cleavage are similar, which leads to the multiple exchanges for each coordination event (Path A). In contrast, Figure 8 shows that in trifluoroacetic acid there is a sequential incorporation isotopologue pattern that results in a Schultz–Flory-type distribution. Here there is the almost exclusive formation of the C₆H₅D isotopologue. This suggests that in trifluoroacetic acid there is a change in the rate-determining step. There is now a rapid equilibrium of coordinated and uncoordinated benzene, and a single H/D exchange event occurs followed by facile benzene release (Path B). This leads to a slow buildup of each isotopologue only after the previous isotopologue has been consumed.

In Matsumoto’s original investigation, the authors used CD₃COOD as the deuterium source for H/D exchange. To decipher whether the deuterium is transferred to benzene from the O–D or CD₃ position of acetic acid, three separate reaction vessels were loaded with CD₃COOD, CD₃COOH, and CH₃COOD solvent isotopologues (Table 3). H/D exchange reactions were performed by using 1 mL of acid, 0.1 mL of benzene-H₆, and ~5 mg (0.5 mol%) of 4 under argon at 130 °C in a well-stirred oil bath for 30 min. Exchange was monitored by GC-MS. For CD₃COOH there was less than 0.7 mmol of deuterium incorporation into benzene, indicating that C–D bond activation does not occur on the methyl group of acetic acid. Using CH₃COOD and CD₃COOD led to 155 mmol of deuterium incorporation into benzene. These results suggest that protonation/deuteration of an iridium phenyl intermediate is the microscopic reverse of a heterolytic substitution-type benzene C–H activation mechanism (see later discussion).

To further explore the origin of differences in isotopologue patterns, we have carried out B3LYP-DFT calculations to characterize the potential energy surfaces for H/D exchange by cis-(acac-O,O)₂Ir(OAc) and cis-(acac-O,O)₂Ir(TFA). Figure 9 shows the energy surface and relative enthalpies for benzene H/D exchange in acetic acid catalyzed by cis-(acac-O, O)₂Ir(OAc). Exploration of several possible HOAc/OAc cis-(acac-O,O)₂Ir(III) complexes revealed that cis-(acac-O, O)₂Ir(κ¹-acetate-O,O), 9A, is lowest in energy. It is possible

Table 3. Deuterium Incorporation Catalyzed by 4 in the Presence of Acetic Acid Solvent Isotopologues (where blue = proton and red = deuterium)

<table>
<thead>
<tr>
<th>entry</th>
<th>acid</th>
<th>D incorporation (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CD₃COOD</td>
<td>155 ± 16</td>
</tr>
<tr>
<td>2</td>
<td>CH₃COOD</td>
<td>155 ± 20</td>
</tr>
<tr>
<td>3</td>
<td>CD₃COOH</td>
<td>0.7 ± &lt; 1</td>
</tr>
</tbody>
</table>

Figure 9. B3LYP/LACVP3P++*/LACVP** enthalpy surface for benzene H/D exchange catalyzed by cis-(acac-O,O)$_2$Ir(OAc) in acetic acid. HX = CD$_3$COOH and DX = CD$_3$COOD. Red line = CH activation pathway. Black dotted line = Substrate release path (ΔH at 298 K, kcal/mol).

for benzene coordination to occur through a two-step dissociative mechanism or a single-step associative mechanism. In the dissociative mechanism, the κ$^2$-acetate Ir–O bond is ruptured prior to benzene coordination. Unfortunately, no transition state could be located for this process because there is a smooth increase in energy as the iridium–oxygen bond is stretched until complete bond dissociation to give the five-coordinate species shown as $9\text{B}$ (23 kcal/mol). We have also previously reported an associative transition state for benzene coordination, which is energetically very close to $9\text{B}$, but is a second-order saddle point and not a true transition state. However, experimental evidence suggests that based on the zero-order dependence of benzene, substrate coordination occurs through a dissociative process via rate-determining opening of the κ$^2$-acetate followed by benzene coordination.

Complexation of benzene to structure $9\text{B}$ gives the endothermic κ$^2$-benzene complex $9\text{C}$ (20 kcal/mol). From $9\text{C}$ only 1 kcal/mol of energy is required to cleave the C–H bond via a six-membered intramolecular substitution transition state, $9\text{TS}1$ (21 kcal/mol), to give the iridium phenyl species $9\text{D}$. Deuterium incorporation into benzene occurs through the microscopic reverse of C–H bond cleavage by intramolecular protonation of the iridium phenyl species by $9\text{TS}2$ after CH$_3$COOH is replaced by solvent CD$_3$COOD to give coordinated C$_6$H$_5$D (9E). At this point the barrier for reinsertion (9F) into a C–H bond of C$_6$H$_5$D is at least 2 kcal/mol lower than the pathway for dissociation, resulting in multiple deuterium atoms incorporated into a single benzene isotope and the experimental observation of the buildup of all benzene isotopologues.

When benzene H/D exchange is carried out with 4 in deuterated trifluoroacetic acid, the coordinated CH$_3$COO$^-$ group is replaced rapidly with CF$_3$COO$^-$ group. Therefore, Figure 10 shows the potential energy surface for C–H activation by cis-(acac-O,O)$_2$Ir(κ$^2$-trifluoroacetate). This potential energy surface is qualitatively different from Figure 9 and features a change in the rate-determining step. From $10\text{A}$ the energy required to generate the five-coordinate species $10\text{B}$ now drops to only 5 kcal/mol, giving a slightly endothermic κ$^2$-benzene complex, $10\text{C}$ (3 kcal/mol). The much lower barrier for decoordination of κ$^2$-TFA (and benzene coordination) is readily understood by the significant charge stabilization of the trifluoroacetate group upon rupturing the iridium–oxygen bond; this stabilization is significant because the transition state is dissociative. Breaking the C–H bond via $10\text{TS}1$ to give the iridium phenyl intermediate $10\text{D}$ requires 10 kcal/mol of energy relative to $10\text{A}$ and is 5 kcal/mol above $10\text{B}$. The activation enthalpy predicted by B3LYP is approximately 5 kcal/mol too low compared to experiment. However, the predicted lowering of the activation barrier by 13 kcal/mol is in accord with the experimental difference of 13 kcal/mol; see Table 2.

After C–H bond activation and CF$_3$COOH is replaced by solvent CF$_3$COOD, deuterium incorporation again occurs via the microscopic reverse of CH activation (10-TS2) to give coordinated C$_6$H$_5$D (10E). Different from the potential energy surface in acetic acid, in trifluoroacetic acid the energy required for benzene dissociation is 5 kcal/mol lower than the energy required for a second CH activation into C$_6$H$_5$D. This computed energy surface is in accord with the observed formation of only C$_6$H$_5$D; decoordination of C$_6$H$_5$D is lower in energy than C–H bond activation, and therefore benzene (and its isotopologues) coordination is in equilibrium prior to C–H bond cleavage.

To further investigate our proposed mechanism and catalytic cycle, several inhibition studies were carried out. To test for water inhibition, multiple H/D exchange reactions catalyzed by 4 were examined with added D$_2$O (0–4.6 mM) to the reaction mixture. Figure 11 plots the observed TOF versus 1/[water] and shows a nearly linear correlation of decreased rate and water concentration. This indicates that catalyst 4 is electrophilic and electron-donating ligands, such as water, likely coordinate to the iridium center. It is important to note that there is only a small retardation in the rate of exchange with added water. DFT calculations predict that a water complex is only ∼2 kcal/mol lower than the (acac-O,O)$_2$Ir(κ$^2$-acetate) ground state (9A).
Next, to confirm that the H/D exchange observed is indeed occurring via coordination catalysis, a mercury drop test was performed to confirm that colloidal metal does not act as a catalyst.\(^{24}\) Catalytic reactions containing 4 with and without Hg\(^0\) resulted in similar turnover frequencies ((1.3 $\pm$ 0.2) x 10\(^{-3}\) and (1.4 $\pm$ 0.2) x 10\(^{-3}\) s\(^{-1}\), respectively) and similar deuterium incorporations (29 $\pm$ 12 and 30 $\pm$ 7 mmol, respectively) over 30 min. A control reaction was also run containing an equimolar excess drop of elemental mercury in the absence of 4, yielding $<2$ mmol of deuterium incorporation. This evidence suggests that colloidal iridium is not acting as the H/D exchange catalyst.

The rate of H/D exchange was also examined with increasing acetate concentration by addition of cesium acetate to a reaction between benzene and deuterated acetic acid using 4. The addition of 20–52 mg (0.097–0.25 M in added CsOAc) of cesium acetate to the reaction mixture lowered the TOF to (6.43 $\pm$ 0.3) x 10\(^{-4}\) s\(^{-1}\). This inhibition is similar to that found for (acac-O,O)\(_2\)Ir(OH)(OH\(_2\)) with added hydroxide\(^{6b}\) and is likely the result of a bisacetato anionic complex [(acac-O,O)\(_2\)Ir(OAc)\(_2\)]\(^{-}\) being formed. A 1/\([\text{OAc}]\) plot showing the rate inhibition is shown in Figure 12. Inhibition by added acetate suggests that dissociation of acetate from iridium is required prior to substrate coordination and C–H bond activation in the case of using 4 as the catalyst, consistent with the proposed mechanism in Scheme 8 (Path A).

We previously reported that several (acac-O,O)\(_2\)Ir(X)Py species, where X = phenyl, hydroxo, or pyridine, showed that the addition of pyridine led to the formation of a stable pyridyl complex.\(^8\) Figure 13 shows a plot of H/D exchange rate (TOF) versus 1/[pyridine]. The addition of just 1 equiv of pyridine results in significant rate inhibition due to one of the two vacant cis sites being occupied by pyridine when both sites are required for CH activation. B3LYP DFT

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(24) (a) Whitesides, G. M.; Hackett, M.; Brainard, R. L.; Lavallee, J. F. M.; Sowinski, A. F.; Izumi, A. N.; Moore, S. S.; Brown, D. W.; Staudt, E. M. *Organometallics* 1985, 4, 1819. (b) Smith, S. E.; Sasaki, J. M.; Bergman, R. G.; Mondloch, J. E.; Finke, R. G. *J. Am. Chem. Soc.* 2008, 130, 1839. (c) Widegren, J. A.; Finke, R. G. *J. Mol. Catal. A: Chem.* 2003, 198, 317. The colloidal Hg(0) test with iridium must be taken in context, as iridium has been known not to form amalgams; however, iridium does have some appreciable solubility in mercury. Therefore, lack of inhibition in rate is negative evidence toward a homogenous catalyst. For a more in-depth explanation on Hg(0) poisoning, please review cited references, specifically 24a and 24c.
Figure 13. Plot of $1/\text{[pyridine (M)]}$ vs TOF for the H/D exchange reaction between acetic acid and benzene using 4 as a catalyst.

Scheme 10. CH Activation Reaction Catalyzed by the Iridium Phenyl Intermediate 2

\[
\begin{align*}
\text{H}_6 + \text{D}_3\text{C} & \quad \rightarrow 2 \\
\text{D}_3\text{H}_6 & + \text{D}_2\text{C} = \text{OH}
\end{align*}
\]

calculations predict that the iridium-pyridyl complex is $\sim 10$ kcal/mol lower in energy than the (acac-O,O)$_2$Ir($\kappa^2$-acetate) species.

A complication of performing $1/\text{[pyridine]}$ studies in the presence of acetic acid is the possible protonation of pyridine to form pyridinium and acetate. Based on the $pK_a$ values of acetic acid (4.76)$^{25}$ and pyridinium (5.17)$^{26}$ in H$_2$O, calculation of $K_{eq}$ gives a value of $K_{eq} = 2.6$. The equilibrium constant suggests that the equilibrium lies on the side of pyridinium in the reaction mixture. At the calculated $K_{eq}$, an equilibrium exists between pyridine and pyridinium, and pyridine will still be present in solution to carry out the proposed reaction and act as a coordinating ligand to bind open sites on the catalyst.

We have also explored H/D exchange catalyzed by the stable iridium-phenyl complex 2. Our group previously synthesized and characterized this intermediate.$^{8a}$ Initial comparison of 2 versus 4 in H/D exchange reactions led to complications from a possible induction period for the breakup of the dinuclear species, 4, versus the mononuclear species, 2. Also, the addition of small quantities of pyridine to the iridium catalyst stock solution requires the accurate measurement of pyridine on the microliter scale which could lead to large induced experimental error. To alleviate such problems, we set out to synthesize a mononuclear iridium-acetate-pyridyl complex. This would allow for direct comparison of relative rates of CH activation between a mononuclear-iridium-acetate species and a proposed iridium-phenyl intermediate.

Synthesis of trans-(acac-O,O)$_2$Ir(OAc)(Pyr) (12) was carried out by heating 503 mg (0.88 mmol) of (acac-O,O)$_2$Ir(C$_3$-acac)(Pyr)$^{8a}$ (13) in a 50 mL Schlenk tube with a resealable Teflon valve and 20 mL of concentrated acetic acid for 1 h at 120 °C in an oil bath (Scheme 11). Removal of the solvent followed by flash chromatography on alumina and elution with a gradient of neat ethyl acetate to 5% methanol yielded 319 mg (68.3% yield) of 12. Compound 12 was characterized by $^1$H and $^{13}$C NMR, elemental analysis, HR MS, and IR. The $^1$H NMR can be characterized by the three pyridyl resonances integrating to 2:1:2 at 8.26, 7.79, and 7.30 ppm, respectively, a single methine signal at 5.35 ppm with an integration of 2, and finally two methyl groups integrating to 3:12 around 2 ppm for the acetate and acac methyl groups.

After the synthesis of 12, initial attempts were made to compare the iridium phenyl intermediate, 2, with the proposed iridium acetate catalyst, 12. Stock solutions of both species were prepared at equivalent concentrations (~5 mM). To a 4 mL Schlenk flask with a resealable Teflon valve containing a magnetic stir bar were added a 1 mL aliquot of the stock solution and 0.1 mL of benzene to the flask under argon. The reactions were then heated at 110 °C in a well-stirred oil bath and monitored by GC-MS over a period of 3 h. However, after analysis of the GC-MS data, results showed that the formation of 2 was orders of magnitude faster than 12 at initial time measurements, and eventually their relative rate of CH activation became equivalent as the reaction progressed. This led us to believe that 12 may suffer from an induction period due to the required loss of pyridine prior to trans to cis isomerization, whereas 2 may undergo rapid protonation of the phenyl group while in the trans isomer, leading to rapid formation of benzene-D$_3$H$_6$. To avoid any induction periods present in either catalytic system, we again prepared ~5 mM stock solutions of both 2 and 12 in two separate 8 mL resealable Schlenk flasks (Scheme 12). The flasks were heated at 130 °C for 2 h in a well-stirred oil bath. The reactions were then cooled and the solvent was removed in vacuo. In both flasks, the residue was redissolved in 3 mL of deuterated acetic acid. Then, 1 mL of the stock solution was transferred to a 4 mL resealable Schlenk flask and 0.1 mL of benzene was added to give our standard H/D exchange conditions. The flasks were heated over a period of 3 h and monitored by GC-MS (Table 4). After 1 h, both reactions had converted $\sim 32 \pm 4$ mmol of benzene-H$_6$ to deuterated benzene at a TOF $\approx (1.0 \pm 0.1) \times 10^{-3}$ s$^{-1}$ and

Scheme 11. Synthesis of trans-(acac-O,O)$_2$Ir(OAc)(Pyr) (12)
~75 ± 10 mmol after 3 h. Also, heating both 2 and 4 under reaction conditions with added pyridine led to conversion and isolation of 12, as confirmed by NMR. This confirms that generation of the iridium-phenyl complex occurs and that species is competent for reversible CH activation under the catalytic conditions of 4, with comparable rates of CH activation.

From the experimental and DFT results above, Scheme 13 shows the proposed overall catalytic cycle for H/D exchange between benzene and acetic acid. Upon solvation, the
trans-dinuclear complex (4) rapidly converts to an equilibrium of 7 and 14. Species 14 can enter into the catalytic cycle via trans to cis isomerization to the six-coordinate κ²-acetate species 8. Following the transition state for loss of acetate and benzene coordination, TS1, to form the η² intermediate 15, the acetate ligand then participates in the C–H bond-breaking process via transition state TS2 by acting as a base to deprotonate benzene via a concerted process. From the iridium-phenyl species 11, CH₃COOH exchanges with CD₃COOD via the five-coordinate intermediate 16 to generate the acetic acid coordinated species 17. Protonation of the iridium–phenyl bond occurs via transition state TS3, the microscopic reverse reaction of CH activation, to give the coordinated η²-benzene isotopologue 18. Finally, benzene is released, regenerating the six-coordinate cis-κ²-acetate complex 8 to complete the catalytic cycle.

Now that the mechanism for H/D exchange has been established, it is possible to briefly explain why hydroarylation does not occur in the presence of acetic acid. Figure 14 compares the potential energy surfaces for H/D exchange and hydroarylation catalyzed by cis-(acac)Ir(CH₃COO) in acetic acid. HX = CD₃COOH and DX = CD₃COOD. Red line = CH activation pathway. Blue line = Hydroarylation pathway (ΔH at 298 K, kcal/mol).

### Table 4. H/D Exchange Data for Comparing H/D Exchange between Catalysts 2 and 11

<table>
<thead>
<tr>
<th>time (min)</th>
<th>catalyst</th>
<th>D incorporation (mmol)</th>
<th>TOF (s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>2</td>
<td>32.0 ± 5.3</td>
<td>(11.1 ± 1.8) x 10⁻⁴</td>
</tr>
<tr>
<td>60</td>
<td>12</td>
<td>32.1 ± 3.9</td>
<td>(9.4 ± 1.2) x 10⁻⁴</td>
</tr>
<tr>
<td>180</td>
<td>2</td>
<td>75.4 ± 12.4</td>
<td>(8.7 ± 1.4) x 10⁻⁴</td>
</tr>
<tr>
<td>180</td>
<td>12</td>
<td>76.7 ± 8.6</td>
<td>(7.5 ± 0.8) x 10⁻⁴</td>
</tr>
</tbody>
</table>

Figure 14. B3LYP/LACV3P++/LACVP** energy surface for benzene H/D exchange and hydroarylation catalyzed by cis-(acac)Ir(CH₃COO) in acetic acid. HX = CD₃COOH and DX = CD₃COOD. Red line = CH activation pathway. Blue line = Hydroarylation pathway (ΔH at 298 K, kcal/mol).

3. Conclusion

In summary, the mechanism of benzene C–H activation by (acac-O,O)₂Ir(III)(R)(L) complexes in acetic and trifluoroacetic acid solvents was studied experimentally and by B3LYP-DFT. In acetic acid, the rate-determining step is loss of the κ²-acetate followed by benzene coordination and rapid H/D exchange via a six-membered acetate-assisted transition state to generate the iridium phenyl intermediate. In contrast, in trifluoroacetic acid, C–H bond cleavage becomes rate-determining, resulting in the formation of only monodeuterated benzene. Hydroarylation in acetic acid is inhibited because the new (acac-O,O)₂Ir(III)(κ²-OAc) species generated raises the barrier for alkene insertion.

4. Experimental Section

4.1. General Procedure. All manipulations were carried out using an argon-filled MBraun glovebox and standard Schlenk techniques. Benzene was used directly from an MBraun solvent purification system after passing through an activated molecular sieves column or via distillation over Na/benzophenone. Reagent-grade chemicals and solvents were purchased from Sigma Aldrich, and IrCl₃·H₂O was from Pressure Chemical. Deuterated solvents were purchased from Cambridge Isotope or Sigma Aldrich and used as is. Deuterated acetic acid and deuterated trifluoroacetic acid were degassed before use by several freeze–pump–thaw cycles and stored under argon. Elemental analyses were performed by Columbia Analytical Services, Tucson, AZ. Fast atom bombardment (FAB +) or electrospray ionization (ESI) mass spectroscopy was performed for alkene insertion and reduces the rate by ~10², in qualitative accord with the observed lowering of the TOF.²⁷

(²⁷) For a detailed catalytic cycle showing the separate hydroarylation and C–H activation pathways and how they are connected, please see the Supporting Information.
at UC Riverside Mass Spec Facility, Riverside, CA, or at the University of Florida Mass Spec Facility, Gainesville, FL. Flash chromatography was performed on a Teledyne Isco CombiFlash(Rf) with pre-packed Teledyne Isco alumina or silica columns using HPLC or better grade solvents. Liquid phase organic products were analyzed with a Shimadzu GC-MS QP5000 (ver. 2) equipped with a cross-linked methyl silicone gum capillary column, DB5, or a Shimadzu GC-MS QP2010S equipped with a cross-linked methyl silicone gum capillary column, RTX-5. Gas measurements were performed using a GasPro column. The retention times of the products were confirmed by known standards. NMR spectra were obtained on a Bruker AC-250 (250.134 MHz for 1H and 62.902 MHz for 13C), a Varian Mercury 400 (400.151 MHz for 1H and 100.623 MHz for 13C), or Bruker Digital Avance III 400 (400.132 MHz for 1H, 100.623 MHz for 13C, and 376.461 MHz for 19F) spectrometer. Chemical shifts are given in ppm relative to residual solvent proton resonances or to a stated internal or external standard. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer. Complexes 3, 8a, and 13 were prepared according to previously reported procedures. 28

4.2. Compounds. [Ir(μ-acac-O,OC=C)(μ-acac-O)(OAc)]2, 4. (Method A) In a Schlenk flask with a resealable Teflon valve, 0.27 g (0.28 mmol) of 3 was dissolved in degassed acetic acid (30 mL, 0.52 mol). The reaction mixture was heated at 100 °C for 1 h. The solvent was then removed in vacuo. After pumping off the solvent, the solid was dissolved in CHCl3 and reprecipitated with hexanes. The solid was collected by vacuum filtration to yield a yellow, fine powder (0.24 g, > 95% yield). (Method B) To 100 mg (0.197 mmol) of 3 in 95% (190 mg) of CD3COOD, 0.5 mol % of catalyst (unless otherwise mentioned). The liquid phase was sampled and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program. 29 An important assumption built into the program is that there are no isotope effects on the fragmentation pattern of benzene. The parent ion peak of benzene is relatively stable toward fragmentation and can be used to quantify the exchange reactions. The mass fragmentation pattern from m/z of 78 to 84 was analyzed for each reaction and compared to control reactions not containing catalyst. The results obtained by this method are accurate within ±5% of deuterium incorporation or loss. Background H-D exchange between solvent and substrate does not occur in acetic acid, and in trifluoroacetic acid, background reactions were subtracted from reported values.

Stability Tests of 4. A 12 mL Schlenk flask with a resealable Teflon valve was charged with 6 mL (0.105 mol) of CD3COOD or CH3COOH and 30 mg (33.4 μmol) of 4. The flask was degassed (freeze, pump, thaw 3 cycles) and placed under an argon atmosphere. Over the course of the reaction, 1 mL aliquots of the reaction mixture were taken every 2 h (t = 0–8 h) under an argon flow. Aliquots were transferred to a J-Young NMR tube, and the solvent was removed in vacuo. To the dry reaction solid, a premixed internal standard/NMR solvent mixture was added. The internal/NMR solvent mixture was prepared by adding 35 μL (0.55 mmol) of dichloromethane to 10 μL (0.12 mol) of CDCl3 in a 10 mL volumetric flask. The reaction was monitored by 1H NMR over a period of 8 h.

Location of Deuterium Incorporation from Acetic Acid. A 4 mL Schlenk flask with a resealable Teflon valve and a magnetic stir bar was charged with 1.0 mL (1.75 × 10−3 mol) of CD3COOD, 5.0 mg (5.56 μmol, 0.50 μmol %) of 4, and 0.10 mL (1.12 mmol) of


benzene-H₆. Simultaneously, another 4 mL Schlenk flask was charged with 1.0 mL of CH₃COOD, 5.0 mg of 4, and 0.10 mL of benzene-H₆. A third 4 mL Schlenk flask was charged with 1.0 mL of CD₃COOH, 5.0 mg of 4, and 0.10 mL of benzene-H₆. The flask was degassed (freeze, pump, thaw 3 cycles) and placed under an argon atmosphere. The flask was heated for 60 min in a well-stirred oil bath maintained at constant temperature (130 °C). The liquid phase was sampled (20 and 60 min) and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program.

**Activation Parameters.** (Acetic acid) A 4 mL Schlenk flask with a resealable Teflon valve and a magnetic stir bar was charged with 1.0 mL (1.75 x 10⁻² mol) of CD₃COOD, 5.0 mg (5.56 μmol, 0.50 mol %) of 4, and 0.10 mL (1.12 mmol) of benzene-H₆. The flask was degassed (freeze, pump, thaw 3 cycles) and placed under an argon atmosphere. The flask was heated for 30 min in a well-stirred oil bath maintained at constant temperature (100–130 °C). The liquid phase was sampled and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program.

(Trifluoroacetic acid) A 4 mL Schlenk flask with a resealable Teflon valve and a magnetic stir bar was charged with 1.0 mL (0.013 mol) of CF₃COOD, 5.0 mg (5.56 μmol, 0.50 mol % or 4.96 μmol, 0.40 mol %) of 4, and 0.10 mL (1.12 mmol) of benzene-H₆. The flask was degassed (freeze, pump, thaw 3 cycles) and placed under an argon atmosphere. The flask was heated for 30 min in a well-stirred oil bath maintained at constant temperature (100–130 °C). The liquid phase was sampled and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program.

1/L Dependence on Pyridine. A 4 mL Schlenk flask with a Teflon valve and a magnetic stir bar was charged with 1 mL (1.75 x 10⁻² mol) of CD₃COOD, 5.0 mg (5.56 μmol, 0.50 mol %) of 4, 0.10 mL (0.96–1.0 M) of benzene-H₆, and 20–60 μL (0.22–0.64 M) of pyridine. The flask was degassed (freeze, pump, thaw 3 cycles) and placed under an argon atmosphere. Reaction flasks were then placed in an oil bath (130 °C) for 1 h. The liquid phase was sampled and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program.

**Comparison between 2 and 12.** Stock solutions (~5 mM) of 2 and 12 were prepared in two separate 8 mL resealable Schlenk flasks and placed under argon. The flasks were heated at 130 °C for 2 h in a well-stirred oil bath. The reactions were then cooled to room temperature, and the solvent was removed in vacuo. In both flasks, the residue was redissolved in 3 mL of deuterated acetic acid (~5 mM) under argon. A 1 mL aliquot of the stock solution was transferred to a 4 mL resealable Schlenk flask and 0.1 mL of benzene added to give our standard H/D exchange conditions. The flasks were heated over a period of 3 h. The liquid phase was sampled and analyzed by GC-MS. The percent deuterium incorporation into benzene was determined by deconvoluting the mass fragmentation pattern for benzene using a Microsoft Excel program.

4.4. Computational Methodology. All calculations were performed using the B3LYP hybrid DFT functional as implemented by the Juguar 7.0 program package. This functional has provided good agreement with experiment for (acac-O)₂Ir(III) (R)L complexes and other reaction profiles of transition metal-containing compounds. Trigonal iridium atoms were described using the Wadt and Hay core–valence (relativistic) effective core potential in the LACVP basis set for geometry optimizations and single-point energies with the LACVP** basis set. Implicit solvent effects of the acetic and trifluoroacetic acid mediums were calculated with the Poisson–Boltzmann (PB) continuum approximation, using the parameters ε = 6.2 and r_solv = 2.247 Å for HOAc and ε = 8.42 and r_solv = 2.479 Å for HTFA. All energies reported are ΔH(298 K). We also note that to be consistent with past computational efforts, the methyl groups on the acac ligands were replaced with hydrogens.

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**Supporting Information Available:** The SI includes DFT coordinates, a CIF file, X-ray data, supporting graphs and pictures, and further experimental details and is available free of charge via the Internet at http://pubs.acs.org.

(36) Previously, we have examined the effect of basis sets on the calculations for Ir(acac) systems. However, it was found that the double-zeta basis set used here correlates with experiment and reduces the computational time relative to larger basis sets. Please see refs 4a, 7, 8c–8e, and Osygaard, J.; Periana, R. A.; Goddard W. A., III. J. Am. Chem. Soc. 2004, 126, 11658 for examples of these previous studies.