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Electrophilic C−H Activation at {Cp*Ir}: Ancillary-Ligand Control of the Mechanism of C−H Activation

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C−H activation is an extremely important process because of its potential for producing functionalized hydrocarbons.[1,2] Iridium complexes have been extensively used in the study of the mechanisms of C−H activation; in particular, complexes with the {Cp*Ir(I)} fragment undergo oxidative addition of C−H bonds.[1] The Ir(III) complexes [Ir(Me)(X)(PMe_3)Cp*] (X = OTf, B{3,5-$(CF_3)_2C_6H_3$}$_4$) also undergo facile C−H activation with elimination of methane.[3] Computational studies of this reaction have suggested that an oxidative addition pathway is more favorable than a σ-bond metathesis pathway.[4] More recently, Ir(III) acac complexes have been used for catalytic C−H activation, and a new mechanism of "oxidative H migration" has been proposed.[5]

Intramolecular C−H activation can lead to cyclometalated complexes, and such complexes have shown promise in several fields of chemistry, particularly catalysis.[6] Indeed, cyclometalation at Pd^{2+} has been combined with oxidation to give catalytic functionalization of aromatic and sp^3 C−H bonds.[7] In 2003, we reported a room temperature route to cyclometalated complexes of nitrogen donor ligands with [MCl_2Cp^*]$_2$ (M = Ir, Rh) or [$RuCl_2$-(*p*-cymene)]$_2$ in the presence of sodium acetate.[8] More recently, we reported density functional calculations on the cyclometalation of dimethylbenzylamine (DMBA-H) with [$Pd(OAc)_2$].[9] The calculations suggest that the reaction proceeds via an agostic C−H complex, rather than a Wheland intermediate, which is followed by a facile intramolecular H-transfer via a six-membered transition state to coordinated acetate. Thus, the ambiphilic palladium acetate provides electrophilic activation of a C−H bond and acts as an intramolecular base for the deprotonation. The acetate may also play a role in stabilizing the key agostic intermediate through hydrogen bonding. Other computational studies and indeed experimental ones have suggested an important role for hydrogen bonding to acetate in orienting a substrate.[10] We now report density functional calculations[11] that show that intramolecular hydrogen bonding to acetate can provide a low-energy pathway to C−H activation with iridium. The results show that the {Cp*Ir} fragment, usually associated with C−H activation via oxidative addition, is also capable of the *electrophilic* activation of C−H bonds and that the nature of the hydrogen acceptor, as well as the metal, plays a key role in this process. Comparisons are drawn with other mechanisms of C−H activation.

In our previous experimental study on the cyclometalation of DMBA-H with [$IrCl_2Cp^*$]$_2$, [Ir(DMBA-H)(OAc)(Cl)Cp*] was proposed as a key intermediate.[8] From this point, Cl^- dissociation would generate [Ir(DMBA-H)(OAc)Cp*]$^+$ from which C−H activation can occur. Support for this proposal comes from our previous study where the key role of acetate as an intramolecular base was identified.[9] Moreover, continuum solvation calculations (dichloromethane) comparing [Ir(DMBA-H)(OAc)Cp]$^+$ + free Cl^- with [Ir(DMBA-H)(Cl)Cp]$^+$ + free OAc^- indicate the former is more stable by 36 kcal/mol. OAc dissociating and acting as an intermolecular base can therefore be ruled out, and we have used [Ir(DMBA-H)(OAc)Cp]$^+$, **1**, as a starting point for the calculations.[12]

A number of different conformations were computed for [Ir(DMBA-H)(κ^2-OAc)Cp]$^+$, but only one of these, **1a**, was shown to be directly involved in C−H activation and all energies are quoted relative to this species. In **1a**, the DMBA-H ligand is orientated such that one *ortho* C−H bond is well positioned to approach the metal center,[13] and three pathways for C−H activation from this species have been considered (see Figure 1).

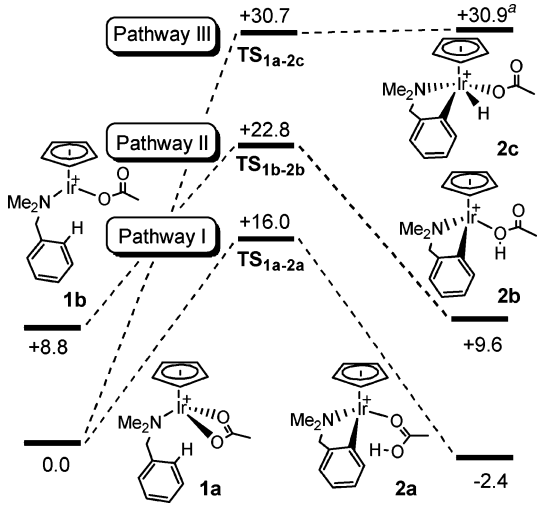

Figure 1. Computed reaction profiles (kcal/mol) for C−H activation in [Ir(DMBA-H)(OAc)Cp]$^+$. [a] **2c** was computed to lie 0.4 kcal/mol below $\mathbf{TS_{1b-2c}}$ prior to the inclusion of the correction for zero-point energies.

Pathway I proceeds via a single, low-energy six-membered transition state ($\mathbf{TS_{1a-2a}}$, E = +16.0 kcal/mol; see Figure 2), which corresponds to displacement of the proximal OAc arm by the incoming C−H bond. IRC and geometry optimization calculations show that $\mathbf{TS_{1a-2a}}$ leads directly to the C−H-activated product (**2a**, E = −2.4 kcal/mol), where H is transferred to the dissociated OAc arm and HOAc is bound through the carbonyl oxygen in the product. Pathway II is initiated by dissociation of the distal OAc arm via $\mathbf{TS_{1a-1b}}$ (E = +13.8 kcal/mol; see Supporting Information) to give formally 16e [Ir(DMBA-H)(κ^1-OAc)Cp]$^+$ (**1b**, E = +8.8 kcal/mol). The vacant site available in **1b** allows the *ortho* C−H bond to move toward the metal, although long Ir···C and Ir···H contacts (2.61 and 2.69 Å) and a short C−H distance (1.09 Å) suggest minimal agostic stabilization. The orientation of the OAc ligand in **1b** means that C−H activation requires a four-membered transition state ($\mathbf{TS_{1b-2b}}$, E = +22.8 kcal/mol) with H transfer to

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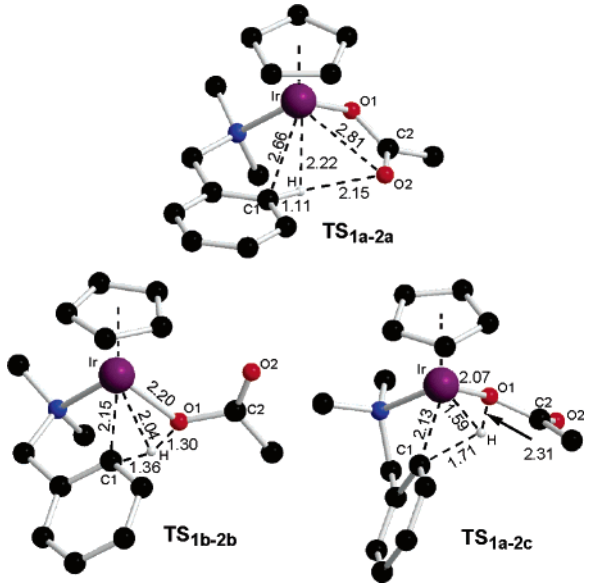

Figure 2. Computed C−H activation transition states (Å) along Pathways I−III. Nonparticipating H atoms are omitted for clarity.

the Ir-bound oxygen. This leads to **2b** (E = +9.6 kcal/mol), and this species is less stable than **2a**, presumably because HOAc is bound through the hydroxyl oxygen. In Pathway III, we considered an oxidative addition process and were able to locate $\mathbf{TS_{1a-2c}}$ (E = +30.7 kcal/mol). This was subsequently shown to link **1a** directly to an Ir(V) product (**2c**, E = +30.9 kcal/mol).

Figure 2 compares key distances in the three C−H activation transition states. The very low energy barrier along Pathway I is remarkable, especially given the very long Ir···C1 and Ir···H contacts. This implies that the metal center is playing a minimal role in activating the C−H bond in this case; indeed only a slight C−H elongation to 1.11 Å is computed. Overall, $\mathbf{TS_{1a-2a}}$ is very similar to that computed previously in $Pd(OAc)_2$(DMBA-H), where an agostic complex was subsequently formed as an intermediate.[9] No such agostic species was located in [Ir(DMBA-H)(OAc)Cp*]$^+$ for which C−H activation occurs in a single step.

Along Pathway II, $\mathbf{TS_{1b-2b}}$ features much greater metal involvement, with short Ir···C1 and Ir···H contacts (2.15 and 2.04 Å). The transferring H lies in the C1−Ir−O1 plane and is roughly equidistant between C1 and O1. The OAc ligand is itself approximately perpendicular to the C−H activation plane (H−Ir−O1−C2 = 111°), and this means that, unlike $\mathbf{TS_{1a-2a}}$, it is the OAc π-system that accepts the transferring H. Overall, the structure of $\mathbf{TS_{1b-2b}}$ is very similar to the "σ-bond metathesis" transition states computed recently for the C−H bond activation of benzene by Ru−[14a] and Ir−OMe[14b] species. However, despite the apparent greater involvement of the metal center, $\mathbf{TS_{1b-2b}}$ lies to significantly higher energy than $\mathbf{TS_{1a-2a}}$.

In the oxidative addition transition state, $\mathbf{TS_{1a-2c}}$, the dissociated OAc arm points away from the *ortho* C−H bond such that this ligand is close to coplanar with the Ir···H vector (H−Ir−O1−C2 = 21°). Both factors effectively deny access to the lower energy Pathways I and II. $\mathbf{TS_{1a-2c}}$ exhibits a very late geometry (C···H = 1.71 Å; Ir−H = 1.59 Å) and as such resembles transition states for oxidative H transfer computed for C−H bond activation of benzene by $Ir(acac)_2Ph$.[5]

Overall, our results show that electrophilic C−H activation is favored in [Ir(DMBA-H)(OAc)Cp*]$^+$, and that the reactivity of the {Cp*Ir} fragment can extend beyond oxidative addition based on the Ir^+/Ir^{3+} and Ir^{3+}/Ir^{5+} couples. Very similar electrophilic cyclometalations with OAc as an intramolecular base have now been characterized for both Ir^{3+} and Pd^{2+}. Hence, this process could be general, with little dependence on the metal center, particularly when oxidative addition is energetically unfavorable.

The preferred pathway for C−H activation with Ir^{3+} alters depending on the other ligands present. Thus, for {Cp* Ir^{3+}} with hydrocarbyl coligands[3] (or indeed poorly orientated OAc, Pathway III) which cannot readily act as proton acceptors, oxidative addition dominates (although with a somewhat less electron-rich metal center, e.g., $Ir(acac)_2Ph$, this becomes oxidative H transfer[5]). With heteroatom coligands bearing lone pairs (e.g., κ^1-OAc in Pathway II or methoxide[14]), less participation of the metal is required and a four-centered mechanism akin to σ-bond metathesis becomes accessible. Finally, ligands, such as κ^2-OAc, can provide both strong basic character and, via arm dissociation, a geometrically convenient route for intramolecular H transfer (Pathway I). In this case, the metal center plays a limited role in the C−H activation transition state. Viewed in this way, rather than being distinct pathways, oxidative addition/H transfer, σ-bond metathesis, and electrophilic activation present a continuum of mechanistic possibilities, the most favorable of which will depend on the coordination environment of the metal center both in terms of the electron density at the metal and the proton acceptor capacity of the coligands.

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Supporting Information Available: Computed Cartesian coordinates and energies of all stationary points. Complete ref 11. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Frisch, M.; et al. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004. Calculations used the BP86 functional. Ir and Cl were described using the Stuttgart RECPs and the associated basis sets. 6-31G** basis sets were used for C, N, O, and H atoms. Energies include corrections for zero-point energy. See Supporting Information for details.
(12) Calculations on key stationary points incorporating Cp* did not result in any significant change in the reaction energetics reported in the text.
(13) Several different conformations of **1** were located, but the most stable was only 3 kcal/mol lower than **1a**. We assume that the barriers associated with the formation of **1a** from this global minimum are small.
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