

Transition State Energy Decomposition Study of Acetate-Assisted and Internal Electrophilic Substitution C–H Bond Activation by (acac-O,O)₂Ir(X) Complexes (X = CH₃COO, OH)

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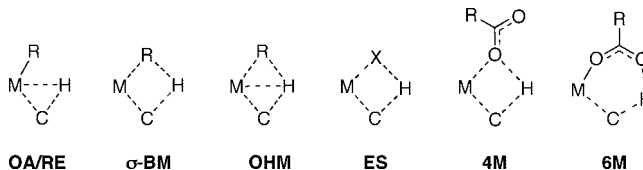
Received July 10, 2008

Chelate-assisted and internal electrophilic substitution type transition states were studied using a DFT-based energy decomposition method. Interaction energies for benzene and methane C–H bond activation by (acac-O,O)₂Ir(X) complexes (X = CH₃COO and OH) were evaluated using the absolutely localized molecular orbital energy decomposition analysis (ALMO-EDA). A ratio of ~1.5:1 for forward to reverse charge-transfer between (acac-O,O)₂Ir(X) and benzene or methane transition state fragments confirms “ambiphilic” bonding, the result of an interplay between the electrophilic iridium center and the internal base component. This analysis also revealed that polarization effects account for a significant amount of transition state stabilization. The energy penalty to deform reactants into their transition state geometry, distortion energy, was also used to understand the large activation energy difference between six-membered and four-membered acetate-assisted transition states and help explain why these complexes do not activate the methane C–H bond.

Introduction

The activation/cleavage of hydrocarbon C–H bonds can occur via several types of transition states (TSs, Scheme 1). Most familiar are the classic oxidative addition/reductive elimination (OA/RE)¹ and σ -bond metathesis (σ -BM) TSs.² Oxidative hydrogen migration (OHM),³ electrophilic substitution (ES),³ and chelate-assisted (4M and 6M)⁴ transition states also provide pathways for C–H bond activation. OHM can mechanistically

Scheme 1. Comparison of Metal (M) Mediated C–H Bond Cleavage Transition States



be considered a concerted transition state that incorporates both oxidative addition and reductive elimination steps. OHM transition states involve a metal–hydrogen interaction, different than σ -BM transition states.⁵ ES involves a metal–heteroatom group (X = OR or NR₂) interacting via a four-membered transition state in a geometry similar to σ -BM. Here the hydrogen is transferred to the heteroatom lone-pair orbital while simultaneously forming a M–C bond. Similar to the ES transition state, is the four-membered, cyclic, chelate-assisted transition state (4M). In this transition state, one of the acetate oxygen atoms participates in the C–H bond substitution event while simultaneously forming M–C and O–H bonds. Alternative to this 4M transition state, is the six-membered (6M) transition state, where the hydrogen is transferred to the pendent acetate oxygen.

The importance of this general chelate-assisted TS design has been experimentally demonstrated by the activation of the benzene C–H bond by (TFA)Pt–N,O-picolinate and (TFA)Pt-bipyrimidine complexes⁶ and the methane C–H bond by the recently synthesized (NNC)Ir(TFA)₂ (NNC = η^3 -6-phenyl-2,2′-

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(1) (a) Bergman, R. G. *Nature* **2007**, *446*, 391. (b) Arndtsen, B. A.; Bergman, R. G. *Science* **1995**, *270*, 1970. (c) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (d) Stoutland, P. O.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 4581. (e) Stoutland, P. O.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5732. (f) Silvestre, J.; Calhorda, M. J.; Hoffmann, R.; Stoutland, P. O.; Bergman, R. G. *Organometallics* **1986**, *5*, 1841. (g) Smith, K. M.; Poli, R.; Harvey, J. N. *Chem.–Eur. J.* **2001**, *7*, 1679.

(2) (a) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (b) DeYonker, N. J.; Foley, N. A.; Cundari, T. R.; Gunnoe, T. B.; Petersen, J. L. *Organometallics* **2007**, *26*, 6604. (c) Zdravkovski, D.; Milletti, M. C. *J. Coord. Chem.* **2006**, *59*, 777. (d) Barros, N.; Eisenstein, O.; Maron, L. *Dalton Trans.* **2006**, *25*, 3052. (e) Sadow, A. D.; Tilley, T. D. *J. Am. Chem. Soc.* **2005**, *127*, 643. (f) Sadow, A. D.; Tilley, T. D. *J. Am. Chem. Soc.* **2003**, *125*, 9462. (g) Niu, S.; Hall, M. B. *J. Am. Chem. Soc.* **1998**, *120*, 6169. (h) Folga, E.; Ziegler, T. *Can. J. Chem.* **1992**, *70*, 333.

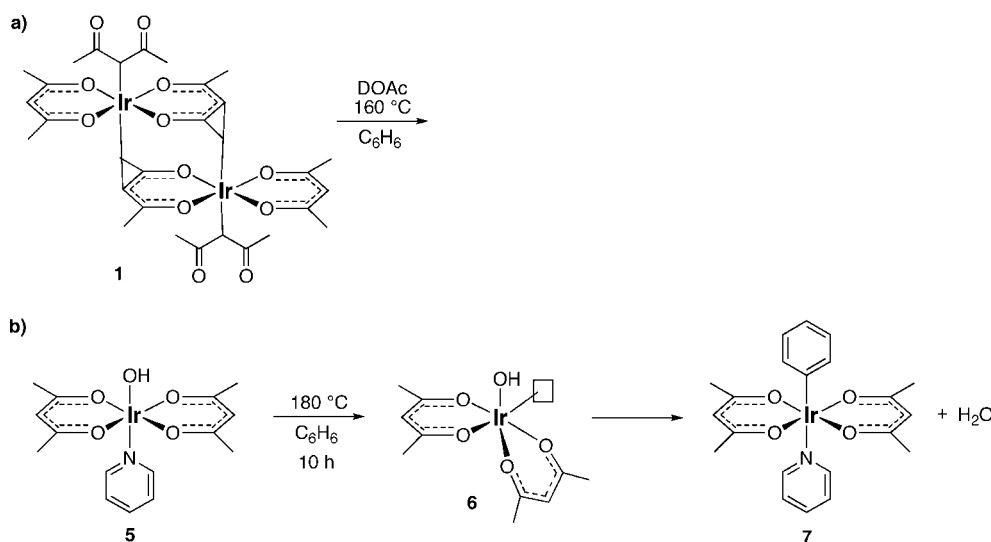
(3) (a) Oxgaard, J.; Muller, R. P.; Goddard, W. A., III.; Periana, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 352. (b) Webster, C. E.; Fan, Y.; Hall, M. B.; Kunz, D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 858. (c) Hartwig, J. F.; Cook, K. S.; Hapke, M.; Incarvito, C. D.; Fan, Y.; Webster, C. E.; Hall, M. B. *J. Am. Chem. Soc.* **2005**, *127*, 2538. (d) Ng, S. M.; Lam, W. H.; Mak, C. C.; Tsang, C. W.; Jia, G.; Lin, Z.; Lau, C. P. *Organometallics* **2003**, *22*, 641. (e) Lam, W. H.; Jia, G.; Lin, Z.; Lau, C. P.; Eisenstein, O. *Chem.–Eur. J.* **2003**, *9*, 2775. In these references, OHM transition states have been referred to as metal-assisted σ -bond metathesis, oxidatively added transition state, and σ -complex assisted metathesis. For a recent review see: (f) Perutz, R. N.; Sabo-Étienne, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 2578.

(4) (a) Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403. (b) Canty, A. J.; van Koten, G. *Acc. Chem. Res.* **1995**, *28*, 406.

(5) Vastine, B. A.; Hall, M. B. *J. Am. Chem. Soc.* **2007**, *129*, 12068.

(6) Ziatdinov, V. R.; Oxgaard, J.; Mironov, O. A.; Young, K. J. H.; Goddard, W. A., III.; Periana, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 7404.

Scheme 2. Reported C–H Activation Reactions and Some Plausible Intermediates



bipyridine) complex.⁷ Chelate-assisted type transition states may also be possible for arene C–H bond activation by rhodium,⁸ palladium/platinum,⁹ and copper¹⁰ acetate complexes.¹¹

Ryabov has generally described chelate-assisted and ES type transition states as either occurring by “electrophilic” or “nucleophilic” C–H activation, that is, describing whether electron density flows to the metal center or to the C–H bond.⁴ Based on Mulliken charges along an intrinsic reaction pathway, we have previously labeled the C–H bond activation of benzene by (acac-O,O)₂Ir(OH), the putative five-coordinate species generated from heating (acac-O,O)₂Ir(OH)(Py), as an “internal electrophilic substitution” mechanism.¹² For chelate-assisted transition states, Davies and Macgregor have reported two seminal foray computational studies describing 6M and 4M transition states for the intramolecular Pd(OAc)₂ and CpIr(OAc) cyclometalation of dimethylbenzylamine.¹³ These investigators suggested that Pd and Ir metal-acetate complexes have “ambiphilic” character due to the electrophilic activation of the intramolecular C–H bond and internal base deprotonation, but also speculated that the metal center plays a limited role in the C–H activation transition state.^{13,14}

Herein we report a quantitative assessment of transition state interaction energies for benzene and methane C–H activation by (acac-O,O)₂Ir(X) complexes (X = CH₃COO and OH) that involve chelate-assisted and ES type transition states. Paramount is the assessment and understanding of possible “ambiphilic” bonding character and the role of the metal center in conjunction with the internal base. We also explore factors controlling relative intermolecular 6M and 4M transition state barriers along with differences between benzene and methane C–H bond substrates. Ultimately, the goal of understanding transition state bonding interactions in these iridium complexes is to further design more active and robust C–H activation catalysts that can be coupled to oxy-functionalization routes.¹⁵

Results and Discussion

In 2000, Matsumoto et al. reported that the dinuclear [Ir(μ -acac-O,O,C³)(acac-O,O)(acac-C³)₂] complex **1** catalyzes rapid H/D exchange between benzene and CH₃COOD with a turnover frequency = 7.6 s⁻¹ at 160 °C (Scheme 2a).¹⁶ Based on previous experimental and computational investigations of the hydroarylation mechanism it is known that the acac ligands first undergo trans to cis isomerization. Extensive exploration of possible OAc

and HOAc ligand complex arrangements revealed that the lowest energy intermediate is the mononuclear κ^2 -cis-(acac)₂Ir(OAc) species **2** (Figure 1a). The alternative *cis*-(acac)₂Ir(OAc)(HOAc) intermediate is ~3 kcal/mol higher in energy. From **2**, there is an associative transition state, **2TS-Benzene** ($\Delta G^\ddagger = 32.6$ kcal/mol, Table 1), that involves breaking one of the Ir–O κ^2 bonds along with stabilization from a weakly coordinated benzene molecule (Ir–C = 3.08 and 3.15 Å).¹⁷ In **2TS-Benzene** and the resulting endergonic π -complex, **3-Benzene** ($\Delta G = 9.4$ kcal/

(7) Young, K. J. H.; Ess, D. H.; Oxgaard, J.; Meier, S. K.; Stewart, T.; Goddard, W. A. III.; Periana, R. A., in preparation.

(8) (a) Ito, J.-i.; Nishiyama, H. *Eur. J. Inorg. Chem.* **2007**, 1114. (b) Hanson, S. K.; Heinekey, D. M.; Goldberg, K. I. *Organometallics* **2008**, *27*, 1454.

(9) (a) Sloopweg, J. C.; Chen, P. *Organometallics* **2006**, *25*, 5863. (b) Bröring, M.; Kleeberg, C. *Chem. Commun.* **2008**, 2777. (c) Biswas, B.; Sugimoto, M.; Sakai, S. *Organometallics* **2000**, *19*, 3895.

(10) Mankad, N. P.; Gray, T. G.; Latar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191.

(11) (a) Musashi, Y.; Sakaki, S. *J. Am. Chem. Soc.* **2000**, *122*, 3867. (b) Musashi, Y.; Sakaki, S. *J. Am. Chem. Soc.* **2002**, *124*, 7588.

(12) Oxgaard, J.; Tenn, W. J., III.; Nielsen, R. J.; Periana, R. A.; Goddard, W. A., III. *Organometallics* **2007**, *26*, 1565.

(13) (a) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754. (b) Davies, D. L.; Donald, S. M. A.; Al-Duaij, O.; Macgregor, S. A.; Pölleth, M. *J. Am. Chem. Soc.* **2006**, *128*, 4210.

(14) Davies, D. L.; Donald, S. M. A.; Al-Duaij, O.; Fawcett, J.; Little, C.; Macgregor, S. A. *Organometallics* **2006**, *25*, 5976.

(15) (a) Klei, S. R.; Tan, K. L.; Golden, J. T.; Yung, C. M.; Thalji, R. K.; Ahrendt, K. A.; Ellman, J. A.; Tilley, T. D.; Bergman, R. G. In *Activation and Functionalization of C–H Bonds*; Goldberg, K. I., Goldman, A. S., Eds.; ACS Symposium Series No. 885; American Chemical Society: Washington D.C., 2004; p 46. (b) Conley, B. L.; Tenn, W. J., III.; Young, K. J. H.; Ganesh, S. K.; Meier, S. K.; Oxgaard, J.; Gonzales, J.; Goddard, W. A., III.; Periana, R. A. *Activation of Small Molecules: Organometallic and Bioinorganic Perspectives*; Tolman, W. B., Ed.; WILEY-VCH: Weinheim, 2006; pp 235–287, and references therein.

(16) (a) Matsumoto, T.; Taube, D. J.; Periana, R. A.; Taube, H.; Yoshida, H. *J. Am. Chem. Soc.* **2000**, *122*, 7414. (b) Periana, R. A.; Liu, X. Y.; Bhalla, G. *Chem. Commun.* **2002**, 3000. (c) Oxgaard, J.; Periana, R. A.; Goddard, W. A., III. *J. Am. Chem. Soc.* **2004**, *126*, 11658. (d) Bhalla, G.; Oxgaard, J.; Goddard, W. A., III.; Periana, R. A. *Organometallics* **2005**, *24*, 3229. (e) Bhalla, G.; Liu, X. Y.; Oxgaard, J.; Goddard, W. A., III.; Periana, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 11372.

(17) Similar associate transition states were found for Pd(OAc)₂ complexes: Biswas, B.; Sugimoto, M.; Sakai, S. *Organometallics* **2000**, *19*, 3895. Also, the transition state orbital interactions between Pd(OAc)₂ and benzene were qualitatively described as a filled sp² C–H bond orbital of benzene interacting with an empty d_σ orbital and a polarized acetate lone pair interacting with the C–H σ* orbital.

(18) *Jaguar*, version 7.0; Schrödinger, LLC: New York, 2007. Gas phase thermodynamic corrections at 298 K were used. Model acac groups were used in all calculations.

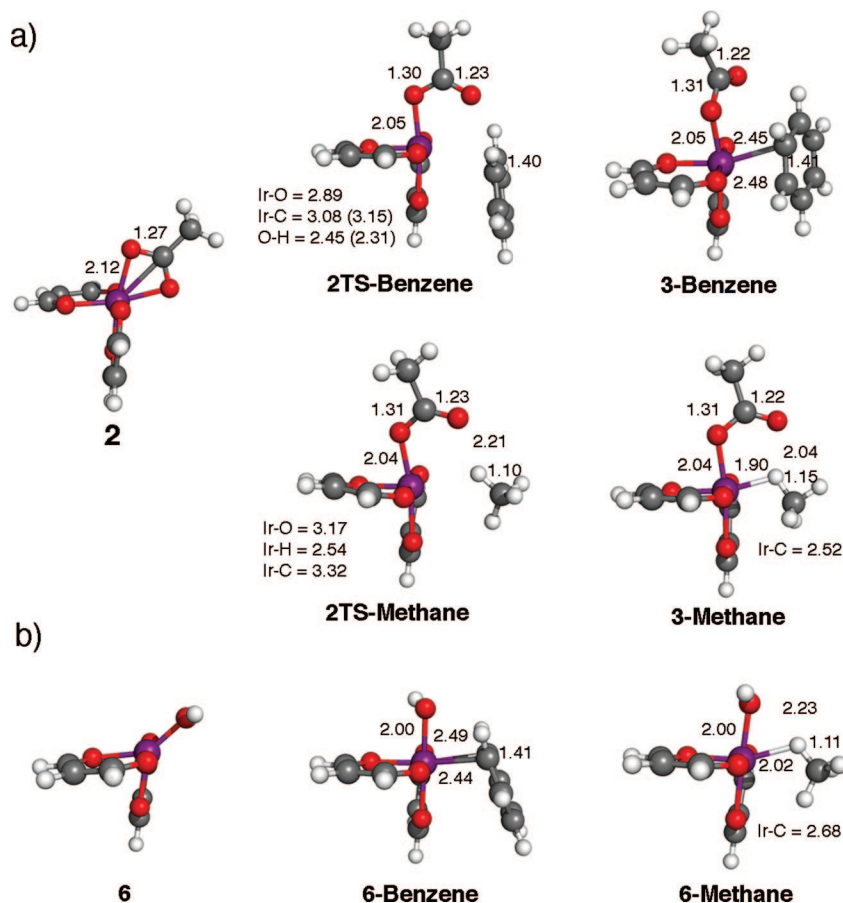


Figure 1. B3LYP/LACVP** optimized intermediates and transition states for (a) benzene coordination and (b) methane coordination.^{18,19} Bond lengths reported in Å.

Table 1. B3LYP/LACV3P++**//LACVP** Electronic Energies (ΔE), Enthalpies (ΔH), Free Energies (ΔG), and Transition State Fragment Distortion Energies (ΔE_d) and Total Interaction Energies (ΔE_i) for Benzene and Methane C–H Bond Activation by *cis*-(*acac*)₂Ir(X) (kcal/mol)^a

species	ΔE	ΔH	ΔG	ΔE_d (<i>acac</i>) ₂ Ir(X)	ΔE_d (CH ₄ or C ₆ H ₆)	ΔE_i
Benzene						
2TS-Benzene ^b	18.5	18.0	32.6			
3-Benzene ^b	13.4	23.7	9.4			
6M-TS-Benzene ^b	15.3	13.1	25.4	27.5 ^b	25.5 ^c	-37.7
4M-TS-Benzene ^b	37.1	32.6	44.7	41.7 ^b	32.3 ^c	-36.9
6 ^c	34.5	33.1	20.8			
6-Benzene ^c	29.2	28.9	28.3			
ES-TS-Benzene ^c	42.7	39.0	39.8	12.4 ^d	24.1 ^e	-6.2
Methane						
2TS-Methane ^b	25.3	24.8	32.6			
3-Methane ^b	16.0	16.7	24.9			
6M-TS-Methane ^b	22.8	20.7	30.2	24.7 ^b	38.5 ^f	-40.4
4M-TS-Methane ^b	44.2	40.1	49.5	39.8 ^b	39.1 ^f	-34.7
6-Methane ^c	39.0	38.2	33.7			
ES-TS-Methane ^c	50.1	46.4	44.3	10.8 ^d	27.4 ^f	-11.9

^a Thermal and entropic corrections (gas phase) use the LACVP** basis set at 298 K. ^b Relative to **2**. ^c Relative to **5**. ^d Relative to **6**. ^e Relative to optimized C₆H₆. ^f Relative to optimized CH₄.

mol), the acetate C–O bond lengths become skewed while the remaining Ir–O bond shortens by 0.07 Å. A similar mechanism is also operative for methane coordination via **2TS-Methane**

(19) The imaginary vibrational frequencies for **2TS-Benzene** are -88.6ν and -4.0ν . The imaginary vibrational frequencies for **2TS-Methane** are -127.8ν and -10.5ν . The second negative force constant could not be eliminated and corresponds to acetate methyl group rotation.

($\Delta G^\ddagger = 32.6$ kcal/mol) to give **3-Methane** ($\Delta G = 24.9$ kcal/mol). The much less stable methane complex compared to the benzene complex is the result of a weaker coordination interaction that slightly stretches the C–H bond length to 1.15 Å (see energy decomposition later).

Figure 2a and b show the benzene and methane²⁰ 6M and 4M C–H bond cleavage transition states. There are large geometrical differences between these 6M and 4M transition states. In the 6M transition states, the acetate group is nearly coplanar with the forming Ir–C and breaking C–H bonds ($\text{IrOCO} = \sim 3^\circ$), whereas in the 4M transition states, the acetate group is nearly perpendicular to the four-membered ring and overlaps with one of the *cis*-*acac* ligands ($\text{IrOCO} = \sim 88^\circ$). Because of the four-membered geometry, the migrating hydrogen in the 4M transition states are ~ 0.2 Å closer to the metal center than in the 6M transition states. 4M transition states have 0.07–0.13 Å longer Ir–OAc bond lengths. There is also a large difference in acetate C–O bond lengths between 6M and 4M TSs. In the benzene 6M transition state, the C–O bond lengths are 1.28 and 1.25 Å, while in the 4M transition states the same bond lengths are 1.36 and 1.21 Å.

The ΔG^\ddagger for **6M-TS-Benzene** is 25.4 kcal/mol. This is 7.2 kcal/mol lower than the coordination barrier. For methane, there is only a 2.4 kcal/mol difference between the coordination barrier (**2TS-Methane**) and the C–H bond cleavage barrier via **6M-TS-Methane** (Table 1). Similar to previous reports,¹³ there are large barrier differences between benzene and methane 6M

(20) Methane H/D exchange has not been observed experimentally for this system.

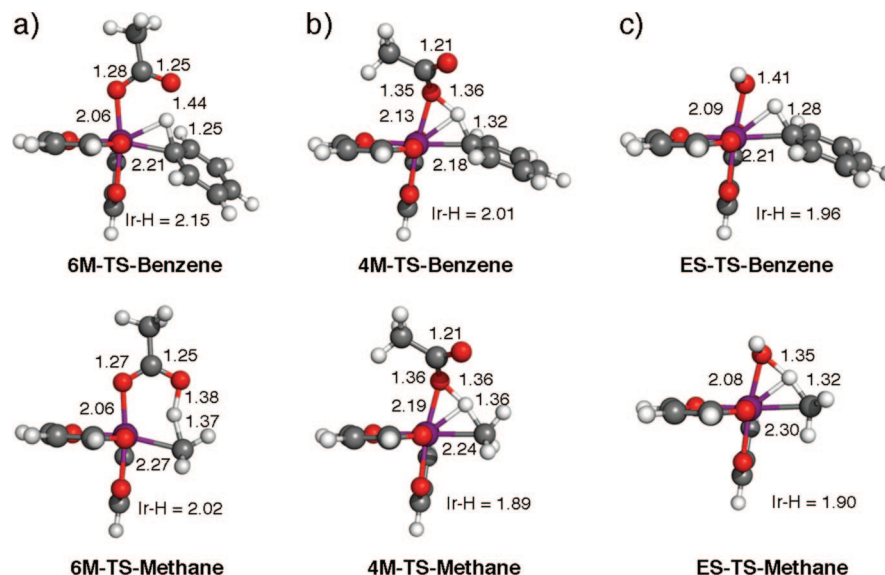


Figure 2. B3LYP/LACVP** benzene and methane (a) 6M, (b) 4M, and (c) ES transition states. Bond lengths reported in Å.

and 4M transition states, $\Delta\Delta G^\ddagger = 20.3$ and 19.3 kcal/mol ($\Delta\Delta E^\ddagger = 19.2$ and 20.0).

In 2006, Tenn et al. showed that the O-donor iridium hydroxide complex (acac-O,O)₂Ir(OH)(Py), **5**, promotes stoichiometric heterolytic C–H activation of benzene to give (acac-O,O)₂Ir(Ph)(Py), **7**, and water (Scheme 2b).²¹ Previous DFT calculations support a reaction mechanism that first involves pre-equilibrium dissociation of pyridine and rate-determining trans to cis acac ligand isomerization to give the five-coordinate intermediate **6**. Subsequent benzene coordination and C–H bond cleavage results in the iridium phenyl water complex **7**. Although the benzene C–H cleavage transition state shown in Figure 1c was initially described as a σ -bond metathesis mechanism,²¹ Oxgaard et al. later showed this transition state to be an example of so-called “internal electrophilic substitution” that utilizes a lone-pair centralized on the oxygen atom to form the O–H bond rather than the breaking M–O bond orbital.¹² Figure 1b shows the five-coordinate species **6** ($\Delta G = 20.8$ kcal/mol) and the resulting benzene and methane coordination complexes that are 28.3 and 33.7 kcal/mol above **5**. Figure 2c also shows the benzene and methane ES C–H bond cleavage transition states, **ES-TS-Benzene** ($\Delta G^\ddagger = 39.8$ kcal/mol) and **ES-TS-Methane** ($\Delta G^\ddagger = 44.3$ kcal/mol). In accord with the predicted ~ 5 kcal/mol higher barrier for breaking the methane versus benzene C–H bond no methane activation was observed by (acac-O,O)₂Ir(OH)(Py). The angles and bond lengths in the benzene and methane ES transition states are very similar to the 4M chelate-assisted transition states except the breaking C–H bonds are slightly shorter.

To understand bonding interactions in these chelate-assisted and ES transition states, as well as the coordination complexes, we have utilized the DFT-based absolutely localized molecular orbital energy decomposition analysis (ALMO-EDA) to dissect the interaction energies into physically meaningful terms.²² In the ALMO-EDA scheme, the TS interaction energy, is partitioned into frozen density (ΔE_{FRZ}), polarization (ΔE_{POL}), and charge-transfer (ΔE_{CT}) contributions. ΔE_{FRZ} is the energy change resulting from

bringing the (acac-O,O)₂Ir(X) complex and benzene or methane into close proximity in their predistorted transition state geometries without orbital relaxation, a combination of Coulombic and exchange interactions. Because the Coulombic and exchange terms are not properly antisymmetrized in this method they cannot be separated. ΔE_{POL} is a result of intramolecular relaxation of the absolutely localized orbitals due to the presence of the other fragment. The ΔE_{CT} term, dissected into directional contributions, is computed from a difference between localized and delocalized molecular orbital energies with correction for basis-set superposition error. This term gives the amount of covalent bonding, largely due to frontier interactions, and is the sum of charge-transfer from the (acac-O,O)₂Ir(X) to benzene or methane and vice versa. Higher-order orbital relaxation effects (ΔE_{HO}), which cannot be assigned to either direction of charge-transfer, are also given. This term is typically small. The sum of these terms gives the overall ALMO-EDA interaction energy, ΔE_{INT} .

Analysis of the bonding between *cis*-(acac)₂Ir and OAc fragments in κ^2 -*cis*-(acac)₂Ir(OAc) reveals that the electrostatic ($\Delta E_{\text{FRZ}} = -71$ kcal/mol) and orbital effects ($\Delta E_{\text{CT}} = -74.9$ kcal/mol) provide nearly the same amount of stabilization (Table 2). Polarization of the metal by O,O-coordination provides another -55 kcal/mol of stabilization. Nearly all of the charge-transfer stabilization is the result of forward bonding between CH₃COO→(acac)₂Ir (-72.7 kcal/mol); back-bonding ((acac)₂Ir→CH₃COO) results in only -2.3 kcal/mol of stabilization.

In the coordination transition states, **2TS-Benzene** and **2TS-Methane**, there is essentially no net stabilization between (acac)₂Ir(OAc) and the hydrocarbon fragments due to nearly equal and opposite ΔE_{FRZ} and ΔE_{CT} terms. Therefore, the large coordination barriers are due to breaking the strong Ir–OAc bond in **2**. In **3-Benzene**, charge transfer stabilization of -31.9 kcal/mol is only slightly larger than the repulsive 28.0 kcal/mol of closed-shell repulsions. However, -13.3 kcal/mol of polarization stabilization results in a net interaction of -17.2 kcal/mol. Benzene coordination to (acac)₂Ir(OAc) in **3-Benzene** is ~ 6 kcal/mol more stabilizing than methane coordination in **3-Methane**. This is due to both larger charge-transfer and polarization stabilization. The charge-transfer stabilization in **3-Benzene** is mainly the result of Benzene→Ir(acac)₂(OAc) interactions worth -24.1 kcal/mol. Back-bonding (Ir(acac)₂(OAc)→Benzene) is worth $\sim 1/3$ of this value (-7.9 kcal/mol).

(21) Tenn, W. J., III.; Young, K. J. H.; Oxgaard, J.; Nielsen, R. J.; Goddard, W. A., III.; Periana, R. A. *Organometallics* **2006**, *25*, 5173.

(22) (a) Shao, Y.; et al. *Q-Chem 3.1*; Q-Chem, Inc.: Pittsburgh, PA, 2007. See Supporting information for full reference. (b) Khaliullin, R. Z.; Cobar, E. A.; Lochan, R. C.; Bell, A. T.; Head-Gordon, M. J. *Phys. Chem. A* **2007**, *111*, 10992.

Table 2. B3LYP/6-31++(d,p) Two-Fragment Absolutely Localized Molecular Orbital Interaction Energy Decomposition Results (kcal/mol)

species	$\Delta E_{(\text{FRZ})}$	$\Delta E_{(\text{POL})}$	$\Delta E_{(\text{CT})}$	(<i>acac</i>) ₂ Ir → CH ₃ COO	CH ₃ COO → (<i>acac</i>) ₂ Ir	$\Delta E_{(\text{HO})}$	$\Delta E_{(\text{INT})}$
2	-71.0	-55.0	-74.9	-2.3	-72.7	9.1	-200.9
				(<i>acac</i>) ₂ Ir(X) → C ₆ H ₆	C ₆ H ₆ → (<i>acac</i>) ₂ Ir(X)		
2TS-Benzene	8.9	-2.6	-6.1	-1.1	-5.0	-0.6	0.1
3-Benzene	28.0	-13.3	-31.9	-7.9	-24.1	-2.0	-17.2
6M-TS-Benzene	73.0	-46.9	-70.5	-27.5	-43.0	-1.8	-44.4
4M-TS-Benzene	100.4	-60.6	-79.1	-26.8	-52.3	1.0	-39.2
6-Benzene	35.7	-15.1	-35.0	-9.8	-25.2	-2.6	-14.4
ES-TS-Benzene	87.0	-47.9	-63.5	-23.2	-40.3	-1.0	-24.5
				(<i>acac</i>) ₂ Ir(X) → CH ₄	CH ₄ → (<i>acac</i>) ₂ Ir(X)		
2TS-Methane	4.7	-1.3	-4.6	-1.1	-3.5	-0.4	-1.2
3-Methane	26.3	-10.8	-26.9	-5.2	-21.6	-0.7	-11.4
6M-TS-Methane	81.7	-50.1	-72.0	-27.9	-44.1	0.1	-40.3
4M-TS-Methane	91.5	-52.3	-72.6	-25.8	-46.8	0.4	-33.4
6-Methane	17.0	-5.5	-15.8	-2.8	-13.0	-0.7	-4.2
ES-TS-Methane	89.8	-46.4	-63.9	-25.2	-38.7	-0.8	-20.5

In the benzene 6M transition state, exchange repulsions ($\Delta E_{(\text{FRZ})}$) cause a 73.0 kcal/mol destabilizing interaction. A total stabilizing interaction of -44.4 kcal/mol is the result of substantial polarization stabilization ($\Delta E_{(\text{POL})} = -46.9$ kcal/mol), due to direct Ir-C bond formation, and charge transfer ($\Delta E_{(\text{CT})} = -70.5$ kcal/mol). Table 1 also gives the $\Delta E_{(\text{CT})}$ term divided into benzene → (*acac*)₂Ir(OAc) and (*acac*)₂Ir(OAc) → benzene occupied → unoccupied interactions. Benzene → Ir(*acac*)₂(OAc) interactions result in -43.0 kcal/mol of stabilizing charge-transfer while the opposite direction (*acac*)₂Ir(OAc) → benzene results in -27.5 kcal/mol of stabilization. This ~1.5:1 ratio of charge-transfer indicates that the benzene C-H cleavage should be regarded as an “ambiphilic” bonding event,¹³ and is the result of an interplay between the electrophilic iridium center and the internal base component. A three-fragment decomposition scheme where the internal base is separated from the metal center is reported later. These results also suggest that the metal- and electron occupation have substantial impact on the total stabilization energy via polarization; intramolecular orbital stabilization is nearly equal to intermolecular orbital stabilization interactions.

Although the benzene 4M transition state has an ~30 kcal/mol more destabilizing $\Delta E_{(\text{FRZ})}$ term, $\Delta E_{(\text{POL})}$ is now much more stabilizing (-60.6 kcal/mol) and the overall charge-transfer is more stable by ~10 kcal/mol ($\Delta E_{(\text{CT})} = -79.1$), due to a shorter forming Ir-C partial bond. All together, the 4M interaction energies result in ~4 kcal/mol less stabilization ($\Delta E_{(\text{INT})} = -39.2$) than in the 6M transition state. This indicates that most of the barrier difference between 6M and 4M TSs is due the energy required to deform the reactants into their transition state geometry, the so-called distortion energy (discussed later), rather than differences in orbital interactions or basicity of the two different oxygen atoms in the pendent acetate group.

The interaction energies for benzene and methane coordination to (*acac*)₂Ir(OH) are approximately equal in magnitude to coordination with (*acac*)₂Ir(OAc). The benzene ES transition state has 87.0 kcal/mol of destabilizing exchange repulsions. The forming Ir-C bond of 2.21 Å is similar to the Ir-C bond length of 2.20 Å in 6M and results in a similar magnitude of polarization stabilization (-47.9 kcal/mol). However, the charge-transfer term only results in -63.5 kcal/mol of stabilization, due to a decrease in both interaction directions, giving a total TS interaction energy of -24.5 kcal/mol.

For the methane transition states, the total interaction energies are ~3–5 kcal/mol smaller. The methane 6M TS has slightly larger charge-transfer (-72.0 kcal/mol) and polarization stabilization (-50.1 kcal/mol), but a larger exchange repulsion term (81.7 kcal/mol) results in $\Delta E_{(\text{INT})} = -40.3$ kcal/mol, 4.1 kcal/mol less stabilizing than the benzene TS. Comparing 4M methane and benzene transition states, the 5.8 kcal/mol lower interaction energy for methane ($\Delta E_{(\text{INT})} = -33.4$ kcal/mol) is the result of smaller

charge-transfer stabilization, mainly in the direction of methane → (*acac*)₂Ir(OAc). Methane and benzene TSs differ in both $\Delta E_{(\text{FRZ})}$ and $\Delta E_{(\text{CT})}$ terms.

To understand the orbital interplay between the metal and acetate/hydroxy groups, the charge-transfer interaction energies for **6M-TS-Benzene**, **6M-TS-Methane**, and **ES-TS-Benzene** were dissected into three fragments: (1) (*acac*)₂Ir, (2) OAc, and (3) C₆H₆ or CH₄. Figure 3 shows the directions and corresponding $\Delta E_{(\text{CT})}$ ALMO-EDA terms. In **6M-TS-Benzene**, the major charge-transfer directions result in (*acac*)₂Ir accepting electron density from benzene and OAc fragments by a similar magnitude, -45.6 and -44.4 kcal/mol, respectively. The acetate fragment also donates electron density to break the C-H bond resulting in a -21.3 kcal/mol stabilizing interaction.¹⁷ In the reverse direction of charge-transfer, back-bonding from Ir to the incoming phenyl group accounts for a meager -5.3 kcal/mol of stabilization while Ir-OAc orbital back-bonding is responsible for only -1.8 kcal/mol of stabilization. The charge-transfer in **6M-TS-Methane** is very similar to **6M-TS-Benzene** except there is an ~6 kcal/mol larger stabilization resulting from the OAc to C₆H₆ interaction. Back-bonding from Ir to the incoming methyl group accounts for -4.7 kcal/mol of stabilization, indicating that the π -system in benzene does not provide an advantage in this type of reaction. **4M-TS-Benzene** and **4M-TS-Methane** transition states have ~6–12 kcal/mol more stabilization from the C₆H₆/CH₄ → (*acac*)₂Ir interaction. In **4M-TS-Benzene** the OAc → C₆H₆/CH₄ interaction is ~5 kcal/mol larger while in **4M-TS-Methane** this interaction is nearly equal in magnitude to the 6M transition state. However, in both **4M-TS-Benzene** and **4M-TS-Methane** the OAc to (*acac*)₂Ir interaction decreases by ~10 kcal/mol, due to the stretched Ir-O bond lengths. The difference between the OH⁻ versus CH₃COO⁻ interaction with (*acac*)₂Ir is shown by ~20 kcal/mol larger stabilization in **ES-TS-Benzene** compared to **6M-TS-Benzene**. Also, the better electron donor OH⁻ does not hinder the capacity of the (*acac*)₂Ir fragment to act as an electrophile. In fact, the charge-transfer between benzene and (*acac*)₂Ir increases by over 5 kcal/mol.

As noted earlier, interaction energies do not account for the difference between 6M and 4M barrier heights. Also, interactions energies only account for approximately half the barrier differences between benzene and methane TSs. The remaining differences are due to the energy penalty to deform the reactants into their transition state geometries, the so-called distortion energy, $\Delta E_{\text{d}}^{\ddagger}$.²³ The distortion energy is directly computed by deletion of one fragment followed by recalculating the energy of the remaining fragment.²⁴ $\Delta E_{\text{d}}^{\ddagger}$ values for Ir(*acac*)₂Ir(OAc) fragments in Table 1 are reported relative to **2** or **5**. Benzene and methane distortion energies are relative to their optimized geometries.

In **6M-TS-Benzene**, 27.5 kcal/mol of energy is required to distort (*acac*)₂Ir(OAc) relative to **2**. Benzene requires 25.5 kcal/mol to stretch the C-H bond and form a pseudo-sp³ hybridized

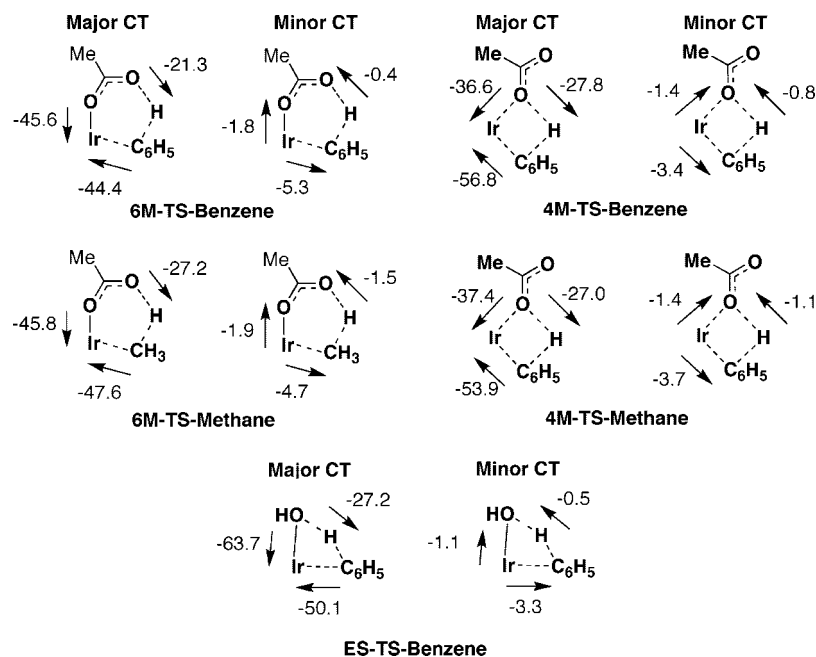


Figure 3. Major and minor charge-transfer stabilizing interactions in benzene and methane chelate-assisted and ES transition states (kcal/mol).

carbon center. In **4M-TS-Benzene**, the (acac)₂Ir(OAc) distortion energy is 14.2 kcal/mol larger than in **6M-TS-Benzene**. Also, benzene now requires an additional 6.8 kcal/mol of distortion energy (32.3 kcal/mol).

Davies and Macgregor previously speculated that a shorter M–OAc bond length is the geometric factor favoring the 6M TS over the 4M TS.¹³ However, starting with the **6M-TS-Benzene** transition state (acac)₂Ir(OAc) fragment, the Ir–O bond length was scanned from 2.07 to 2.13 Å. This scan revealed that stretching the Ir–OAc bond to 2.13 Å (the **4M-TS-Benzene** bond length) requires only a 2.4 kcal/mol energy penalty. Alternatively, we suggest the major difference in (acac)₂Ir(OAc) fragment distortion energies is the result of different acetate C–O bond lengths. Starting with the 4M (acac)₂Ir(OAc) fragment geometry, C–O = 1.35 and 1.21 Å, one C–O bond length was shortened to 1.25 Å and the other was increased to 1.28 Å to give the same bond lengths in the 6M (acac)₂Ir(OAc) TS fragment. This lowered the 4M (acac)₂Ir(OAc) fragment distortion energy by ~13 kcal/mol.²⁵

In **6M-TS-Methane**, 24.7 kcal/mol of energy is required to distort the (acac)₂Ir(OAc) fragment. This is a slightly smaller energy penalty than in the benzene TS. However, methane requires 38.5 kcal/mol to distort into its transition state geometry. The larger methane distortion energy compared to benzene is a consequence of a longer C–H partial bond length (1.37 Å) compared to benzene (1.25 Å) and vicinal H–C–H repulsions from compressed and stretched HCH angles (75, 124, 121, and 111°) required for interaction with the iridium metal (HCIr = 62°).²⁶ As a comparison, the C–H bond in the distorted

benzene fragment was stretched from 1.25 to 1.37 Å. This raised the benzene distortion energy to 35.7 kcal/mol, ~3 kcal/mol less than the computed methane distortion energy.²⁷ Ultimately, the larger methane distortion energy is responsible for no observed C–H bond activation by (acac)₂Ir(X) complexes.

Conclusion

In conclusion, transition state interaction energies for benzene and methane C–H activation by (acac-O,O)₂Ir(X) complexes (X = CH₃COO and OH) were evaluated using a DFT-based localized molecular orbital energy decomposition method. “Ambiphilic” bonding character in these TSs is the result of an electrophilic iridium metal interacting strongly with the incoming methyl or aryl group along with a nearly equivalent amount of covalent bonding resulting from acetate/hydroxide deprotonation. Distortion energies were used to understand energy differences between 6M and 4M TSs and help explain why these complexes do not activate the methane C–H bond.

Acknowledgment. This research was partially supported with funding from Chevron Corporation. The computer systems used were provided by ARO-DURIP and ONR-DURIP. D.H.E. thanks Rustam Khaliullin for help using the ALMO-EDA method.

Supporting Information Available: Cartesian Coordinates, absolute energies, and full Q-Chem 3.1.0.2 reference. This material is available free of charge via the Internet at <http://pubs.acs.org>. OM8006568

(23) (a) Kitaura, K.; Morokuma, K. *Int. J. Quantum Chem.* **1976**, *10*, 325. (b) Ziegler, T.; Rauk, A. *Theor. Chim. Acta* **1977**, *46*, 1. (c) Ziegler, T.; Rauk, A. *Inorg. Chem.* **1979**, *18*, 1755. (d) Bickelhaupt, F. M.; Ziegler, T.; Schleyer, P. v. R. *Organometallics* **1995**, *14*, 2288. (e) Bickelhaupt, F. M. *J. Comput. Chem.* **1999**, *20*, 114. (f) Velde, G. T.; Bickelhaupt, F. M.; Baerends, E. J.; Guerra, C. F.; Gisbergen, S. J. A. V.; Snijders, J. G.; Ziegler, T. *J. Comput. Chem.* **2001**, *22*, 931. (g) Ess, D. H.; Houk, K. N. *J. Am. Chem. Soc.* **2007**, *129*, 10646. (h) Ess, D. H.; Houk, K. N. *J. Am. Chem. Soc.* **2008**, *130*, 10187.

(24) In this type of analysis, the interaction energy can be obtained by taking the difference between the distortion energy and the activation energy. This interaction energy differs from the ALMO interaction energy due to basis set superposition and is not partitioned into physical terms.

(25) The essentially five-coordinate TS species **2TS-Benzene** and **2TS-Methane** have unequal C–O bonds because of κ^1 coordination. However, κ^2 -like coordination in **6M-TS-Benzene** and **6M-TS-Methane** prefer equal C–O bond lengths.

(26) The geminal C–H bond repulsion model is useful for methane but probably not larger alkanes, see: (a) Gronert, S. *J. Org. Chem.* **2006**, *71*, 1209. (b) Wodrich, M. D.; Wannere, C. S.; Mo, Y.; Jarowski, P. D.; Houk, K. N.; Schleyer, P. v. R. *Chem.–Eur. J.* **2007**, *13*, 7731. (c) Mitoraji, M.; Zhu, H.; Michalak, A.; Ziegler, T. *J. Org. Chem.* **2006**, *71*, 9208.

(27) The benzene C–H bond dissociation energy is ~10 kcal/mol larger than methane. For discussion on this topic see: Thompson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schaefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203, and references therein.