Chapter 6

Alkane C-H Bond Activation by O-Donor Ir Complexes

Gaurav Bhalla, Xiang Yang Liu, Antek Wong-Foy, CJ Jones, Roy A. Periana*

Department of Chemistry, Loker Hydrocarbon Institute, University of Southern California, 837 West 37th Street, LHI 122, Los Angeles, CA 90089-1661

The first examples of well-defined, O-donor ligated, Ir complexes that are competent for alkane C-H activation to generate Ir-alkyl complexes are reported. The O-donor complexes exhibit thermal and protic stability and are efficient catalysts for H/D exchange reactions with alkanes. Somewhat surprisingly, the O-donor Ir alkyl complexes with β-CH bonds are stable to generation of coordinated or uncoordinated olefinic products. Mechanistic studies suggest that while these O-donor Ir-alkyl complexes undergo β-hydride elimination reactions these reactions are reversible and unproductive.

Introduction

Catalysts based on the C-H activation reaction show potential for the development of new, selective, hydrocarbon oxidation chemistry (1). A central consideration in the design of such catalysts is the choice of ligands. The ligands generally acceptable for C-H activation reactions range from C-donor, (e.g. cyclopentadienyl ligands), to mono and multi-dentate P- or N-donor ligands, to chelating NC or PC type ligands (2). While O-donor ligands have been studied with early and late transition metals (3), to our knowledge well-defined, O-ligated, late transition metal complexes that activate alkane C-H bonds have not been reported. We have been particularly interested in O-ligated, late transition metals as such complexes could exhibit protic and oxidant stability given the lower basicity and higher electronegativity of O compared to...
N, C or P. Another key reason for study is that the electronegativity and “hardness” of O-donor ligands could allow access to higher oxidation states during catalysis that could facilitate the oxidative functionalization reactions of M-R intermediates to functionalized RX products in a catalytic cycle. Given these considerations, it was important to establish whether well-defined, O-ligated late transition metal complexes could activate alkane C-H bonds. Herein, we report a well-defined, O-ligated, late transition metal Ir complex that can activate alkane C-H bonds.

Alkane C-H Activation with O-Donor Ir Complex

Recently, we demonstrated that the O-ligated complex, Ph-Ir(III)(acac-O,O)(Py), (acac-O,O = η2-O,O-acetylacetonate, Py = pyridine), 1-Ph, catalyzes the hydroarylation of olefins with arenes to generate alkyl benzenes (4). Herein we report that the Me-Ir(III) derivative, Me-Ir(III)(acac-O,O)(Py), 1-Me, reacts with alkanes (RH) via C-H activation to generate the corresponding alkyl-Ir complexes, Ir-R, (RH = cyclohexane and n-octane). 1-Me was synthesized from Ir(acac-C3)(acac-O,O), I, by treatment with (CH3)2Hg or (CH3)2Zn followed by addition of pyridine, in good yields (70%) as shown in Eq. 1. Complex 1-Me is air stable and was fully characterized by 1H and 13C-NMR spectroscopy and elemental analysis.

Heating 1-Me in neat cyclohexane at 130°C for 3 hrs yielded the corresponding Ir-cyclohexyl complex, 1-C6H11, as shown in Eq. 2. 1H-NMR analysis of the crude reaction mixture showed that the reaction was essentially quantitative. Complex 1-C6H11, could be isolated from the reaction mixture and has been fully characterized by 1H and 13C-NMR spectroscopy and elemental and X-Ray structural analyses. An ORTEP drawing of 1-R (R = C6H11) is shown in Figure 1.
Consistent with the stoichiometry shown in Eq 2, when the reaction is carried out in a sealed NMR tube with cyclohexane-d_{12}, mono-deuterated methane is observed based on gas chromatography-mass spectroscopy (GC-MS) analysis. These observations unambiguously show that complexes based on the O-ligated, (acac-O,O)$_2$Ir(III) motif can activate alkane C-H bonds. To our knowledge, this is the first well-defined, late-metal, O-donor ligated complex that shows this reactivity for alkane C-H activation.

Figure 1. ORTEP drawing of 1-R, R = Cyclohexyl. Thermal ellipsoids are at the 50% probability level. Hydrogen atoms omitted for clarity. Selected bond lengths (Å): Ir1-C4, 2.060(7); Ir1-N1, 2.225(6).

Other hydrocarbon substrates that react by C-H activation with 1-Me are shown in Eq 2. Thus, heating a solution of 1-Me in mesitylene at 130 °C for 3 hr results in the formation of a single new species. $^1$H and $^{13}$C NMR spectroscopy analyses of the crude mixture in CDCl$_3$ show clean formation of the Ir-mesityl species, 1-R, (R = mesityl, Eq 2) in which only the benzylic C-H bond was activated. The reaction with benzene and acetone cleanly provided the corresponding Ir-phenyl and Ir-acetonyl derivatives. These materials have also
been isolated and characterized by \(^1\)H and \(^{13}\)C NMR spectroscopy and elemental analysis. The reaction with n-alkanes, exemplified by n-octane, could not be fully characterized and \(^1\)H and \(^{13}\)C-NMR spectroscopy show that several Ir-octyl products (presumably resulting from \(^1\)o and \(^2\)o C-H bond activation) are produced that could not be separated and quantified.

The alkane C-H activation reactions (Eq 2) in the corresponding alkane solvent are retarded by added free pyridine. As shown in Figure 2, a plausible mechanism for the C-H activation from \(1-R\) can involve initial loss of pyridine, trans to cis isomerization to generate a 5 coordinate, cis-intermediate (cis-2) that cleaves alkane C-H bonds via a 7-coordinate oxidative addition intermediate or transition state (3) or sigma-bond metathesis transition state (not shown) (5).

We are currently carrying out kinetic and theoretical studies of this system to further elucidate the details of these CH activation reactions.

![Figure 2. Proposed Mechanism for the C-H Activation of Alkanes and H/D Exchange Reactions Catalyzed by 1-R](image)

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H-D Exchange of Alkanes Catalyzed with O-Donor Ir Complexes

Having established that O-ligated, late metal complexes can stoichiometrically activate the C-H bonds of alkanes, we have begun to examine the catalytic activity of this class of complexes with hydrocarbons.

$$\text{RH} + \text{DY} \xrightarrow{\text{Cat}} \text{RD} + \text{HY}$$

(3)

Analyses by GC/MS and NMR spectroscopy show that 1-Me efficiently catalyzes H/D exchange between C₆D₆ and hydrocarbons, including alkanes, according to Eq 3, RH = hydrocarbon, Y = C₆D₆ (Table 1, entries 1 – 5). These reactions presumably proceed via the catalytic sequence shown in Figure 2. The reactions are clean and no catalyst decomposition is observed, showing that these systems are thermally stable and activate alkane C-H bonds reversibly. ¹H NMR analysis of the crude reaction mixtures after heating shows that the resting state of the catalyst in the reaction with C₆D₆ is 1-Ph-d₅. Control experiments with added drops of Hg metal (to test for catalysis by reduced metals) show no change in rate. Consistent with the presumption of stoichiometric C-H activation reactions with n-octane, ¹³C NMR analysis of the C₆D₆/n-octane reaction mixture after catalysis shows deuterium incorporation into all the positions of n-octane with higher selectivity for the 1ₒ positions.

Consistent with the expected protic stability of O-donor ligands, preliminary results show that 1-Me is thermally stable (to loss of the O-ligated acac ligands) in protic media such as D₂O, CH₃CO₂D, and CF₃CO₂D and remains active for C-H activation and catalysis in these media. Thus, reaction of 0.1 ml of mesitylene with 1 ml of CF₃CO₂D containing 10 mM of 1-Me shows H/D exchange (according to Eq 3, Y = CF₃CO₂, RH = mesitylene) of only the benzylic C-H bonds with a TOF of ~10⁻³ s⁻¹ at 160°C. These H/D exchange reactions in protic media are being examined in greater detail.

Table 1. H/D exchange With C₆D₆ Catalyzed by 1-Me

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>TON</th>
<th>TOF sec⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cyclohexane</td>
<td>240</td>
<td>0.010</td>
</tr>
<tr>
<td>2</td>
<td>Methane</td>
<td>123</td>
<td>0.0017</td>
</tr>
<tr>
<td>3</td>
<td>n-Octane</td>
<td>43</td>
<td>0.0029</td>
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<tr>
<td>4</td>
<td>Benzene</td>
<td>1210</td>
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<tr>
<td>5</td>
<td>Acetone</td>
<td>72</td>
<td>0.043</td>
</tr>
</tbody>
</table>

a All reactions were carried out at 180°C using 1-Me as the catalyst (2 – 20mM).
Chemistry of O-Donor Ir Alkyl Complexes with β-CH Bonds

The quantitative formation of the Ir cyclohexyl complex, 1-C$_{6}$H$_{11}$, on heating 1-Me in cyclohexane and clean H-D exchange between cyclohexane and benzene catalyzed by 1-Me suggest that the Ir-alkyl products are stable to formation of uncoordinated or Ir-coordinated olefin products that could result from possible β-hydride elimination reactions. However, while 1-C$_{6}$H$_{11}$ is a 6-coordinate, 18e$^-$ complex, as shown in Figure 3, it is likely that the Ir-cyclohexyl species are in equilibrium with 5 coordinate, 16e$^-$ species expected to be required for C-H activation and it could be anticipated that uncoordinated or Ir-coordinated olefinic products could be generated by β-hydride elimination reactions from these intermediates.

![Figure 3](image_url)

**Figure 3.** Plausible Mechanism for Observed Arene C-H Activation and Expected β-Hydride Elimination Products from 1-C$_{6}$H$_{11}$.

To understand why no such olefinic products are observed, we examined the thermal, alkane elimination and arene CH activation chemistry of the Ir-C$_{2}$H$_{5}$
complex in benzene-d₆. This complex was synthesized as shown in Eq 4. Treatment of this complex with benzene-d₆, as in the case of 1-Me, readily leads to quantitative formation of 1-Ph-d₅ and loss of mono-deuteroethane (C₂H₅D) by the stoichiometry shown in Eq 5. These reactions are proposed to proceed via the CH activation reaction mechanism shown in Figure 3 with ethyl replacing the cyclohexyl group. Consistent with the observations of the Ir-cyclohexyl system, GC-MS and NMR analyses of the liquid and gas phases of the reaction mixture show that no uncoordinated or Ir-coordinated ethylene products are produced during loss of ethane.

To examine this reaction of the Ir-ethyl complex more carefully, the ¹³C-labeled complex, Ir-¹³CH₂CH₃, was prepared from the corresponding (¹³CH₂CH₃)₂Zn reagent by an analogous reaction to that shown in Eq 4. This complex was prepared to test the possibility that reversible but unproductive β-hydride elimination to generate cis or trans (acac)Ir(H)(C₂H₄) intermediates could proceed from the five coordinate, 16e⁻ intermediates involved in CH activation (i.e. β-hydride elimination from 1-R could occur reversibly without leading to the productive formation of olefinic products). As shown in Figure 4, if such reversible but unproductive β-hydride reactions did occur with Ir-¹³CH₂CH₃, this could be expected to lead to isomerization of the ¹³C-label from the α to the β-positions with formation of the Ir-CH₃¹³CH₃ regio-isotopomer. Carrying out this reaction in C₆D₆ as the reaction solvent could be expected to lead to two regio-isotopomers of ethane, ¹³CH₃CH₂D and ¹³CH₂DCH₃ (formed by C-D activation of the C₆D₆ solvent and loss of ethane) if reversible β-hydride elimination did occur or only ¹³CH₂DCH₃ if no ¹³C-migration occurred.
Importantly, measurements of the rate of $^{13}$C migration in the $^{13}$C-labelled Ir-C$_2$H$_5$ and/or the relative ratio of the two regio-isotopomers of ethane could both be expected to provide information on the relative rates of reversible β-hydride elimination versus benzene CH activation. Thus, for example, if the reversible β-hydride reaction is fast compared to benzene CH activation, then it could be anticipated that approximately equal amounts of Ir-CH$_2^{13}$CH$_3$ and Ir-$^{13}$CH$_2$CH$_3$ as well as $^{13}$CH$_3$CH$_2$D and $^{13}$CH$_2$DCH$_3$ would be observed upon heating to facilitate the arene CH activation reaction to generate ethane and 1-Ph-d$_5$.

Figure 4. Possible Products Expected from Heating 1-$^{13}$CH$_3$CH$_3$ in C$_6$D$_6$ to Generate Ethane by C-H Activation.
The reaction of 1-13CH2CH3 with C6D6 at 150°C was monitored periodically by 1H and 13C NMR spectroscopy of the liquid phase and GC-MS of the gas and liquid phases. As can be seen in Figure 5, 1H decoupled 13C NMR spectra (with sufficiently long relaxation delay to afford accurate integration of the 13C resonances) of the reaction mixture as the reaction proceeds show that 13C migration from the α-position in 1-13CH2CH3 to the β-position in 1-CH213CH3 does occur. It is also clear from Figure 5, that a steady concentration of the β-isomer, 1-CH213CH3, is attained that is substantially lower than the amount of 1-13CH2CH3 present. This indicates that: A) reversible β-hydride elimination most likely occurs and accounts for the α to β-migration of the 13C-label of 1-13CH2CH3 and B) importantly, the lack of formation of equimolar amounts 1-13CH2CH3 and 1-CH213CH3 as ethane is lost with concomitant CH activation of the benzene solvent, strongly indicates that the α to β-migration of the 13C-label is substantially slower than the CH activation of benzene and formation of ethane and 1-Ph-d5.

![Diagram](image)

**Figure 5.** Time Dependent 13C NMR Spectra of Reaction of 1-13CH2CH3 with C6D6 at 150°C

This result is confirmed by analysis of the dissolved ethane that is produced from arene CH activation. As can be seen, the 13C-resonance of ethane is not a
simple singlet but is composed of a smaller singlet superimposed on a 1:1:1 triplet due to \(^2\)H-\(^{13}\)C coupling. Simulation of this pattern readily shows that the predominant ethane product is \(^{13}\)CH\(_2\)DCH\(_3\) with \(\sim\) 16 mol % of \(^{13}\)CH\(_3\)CH\(_2\)D. Analyses by \(^1\)H NMR, while not as clear as the \(^{13}\)C NMR analyses, confirm these results and show (on the basis of the methyl resonances due to the (acac)$_2$Ir resonances) that 1-Ph-d$_5$ is the only new (acac)$_2$Ir product formed on loss of ethane.

These results strongly indicate that these O-donor Ir-alkyls do undergo reversible β-hydride elimination reactions but that such reactions are unproductive. It is possible that the migration of the \(^{13}\)C-label occurs via a concerted process involving synchronous β-hydrogen and carbon transfers, but initial DFT calculations indicate that such a transition state would be substantially higher in energy than that leading to β-hydride elimination. Interestingly, the results also indicate that the reversible, intramolecular β-hydride elimination reactions are slower than the intermolecular arene CH activation reactions. This is a somewhat unexpected result and it will be important to understand why β-hydride elimination reactions are not highly favorable in these O-donor systems. A likely reason is that with O-donor ligands, the metal is not sufficiently electron-rich to strongly stabilize olefinic intermediates.

### Summary

In summary, we demonstrated that well-defined, late metal, O-ligated complexes are competent for alkane C-H activation, exhibit high thermal and protic stability and are efficient catalysts for H/D exchange reactions with alkanes. \(^{13}\)C-labeling studies show that these O-donor Ir-alkyl complexes may likely undergo reversible β-hydride elimination reactions that are unproductive with respect to stable olefinic products. It will be interesting to further explore and understand the differences between these new O-donor metal complexes and the known Cp, P or N-donor systems for the alkane CH activation reaction. Given the unusual stability of these O-donor CH activation systems, we are currently investigating the oxidative functionalization of O-donor M-R complexes and new O-donor complexes that activate C-H bonds.

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References and Notes


