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Formal Oxidative Addition of a C-H Bond by a 16e Iridium(I) Complex involves Metal-Ligand Cooperation

Amit Kumar, Moran Feller, Yehoshoa Ben-David, Yael Diskin-Posner and David Milstein*

First example of oxidative addition of a C-H bond to a square planar d8-Iridium complex, without any external additive, such as an acid, is described. Our mechanistic investigations show that metal-ligand cooperation through aromatization-dearomatization of the lutidine backbone is involved in this process, and that the actual C-H activation step occurs by an Ir(III) intermediate.

Oxidative addition of a C-H bond is perhaps one of the most characteristic steps in functionalization of hydrocarbons.1,2 There has been intense interest in C-H oxidative addition as it is a key step in the design of environmentally benign and atom-economic catalytic transformations of readily available hydrocarbon substrates.2,3 A substantial part of this research has been carried using iridium, although the very common, 16e square planar iridium(I) complexes have received scant attention.7 In fact, the majority of C-H oxidative addition by Ir(I) relies on the generation of reactive 3-coordinate complexes through ligand dissociation, which form upon C-H oxidative addition a five-coordinate Ir(III) complex.8-15 The direct oxidative addition of a C-H bond to a 16e square planar iridium(I) complex is unfavorable. This is because C-H oxidative addition to metal complexes requires the availability of empty orbitals on the metal that facilitates the side-on interaction of the C-H bond, and as the theoretical calculation of Hoffmann indicate, the generation of such empty orbital for a square planar iridium(I) complex requires the geometry of the complex to distort from planar to tetrahedral, which requires high activation energy.16 Early reports on direct C-H oxidative addition to a four-coordinate d8 complex by Chatt (M = Ru),17 Ittel (M = Fe),18 Herskovitz19 and Marder (M = Rh, Ir)20 involve starting complexes which were significantly distorted from planarity. Interestingly, Goldman has recently reported that the oxidative addition of an alkyne C-H bond to the square planar pincer complex (PCP)Ir(CO) is catalysed by addition of a Bronsted acid catalyst (Scheme 1).21 Based on the proposed mechanism (PCP)Ir(CO) first gets protonated by the acid catalyst to generate a highly active five-coordinate Ir(III) cationic intermediate, which then forms a phenylacetylene adduct which subsequently gets deprotonated to produce the oxidative addition product. Interestingly, the reaction does not occur in the absence of acid, even upon heating at 125°C for six months. This mechanism is similar to that reported by Brookhart for the acid catalyzed oxidative addition of H2 to a square planar Ir(I) complex.22 We herein report for the first time the oxidative addition of a C-H bond to a square planar 16e Ir(I) complex without using any additive such as Bronsted acid (Scheme 1). Our mechanistic investigation shows that the metal-ligand cooperation (MLC)23-25 through the aromatization-dearomatization of the lutidine-based ligand backbone plays a crucial role in facilitating this process.

Scheme 1. Acid catalyzed oxidative addition of C-H bond reported by Goldman (1). Oxidative addition of C-H bond by 16e Ir(I) square-planar complex as reported here (2).

A few years ago we reported the trans rather than the expected cis oxidative addition of H2 to (PNP)Ir(phenyl) complex 1 (Scheme 2).26,27 Based on experimental mechanistic studies and DFT calculations we proposed that the Ir(I) complex 1 exists in equilibrium with the dearomatized (PNP*)Ir(III) hydridophenyl complex A (PNP* is dearomatized PNP with a deprotonated sidearm) which oxidatively adds...
hydride to give the complex I. Indeed, treatment of 1 with CO resulted in trapping of A as the corresponding carbonyl complex II (Scheme 2).\textsuperscript{26} We now report the reactivity of complex 1 towards C-H oxidative addition of alkynes.

Reaction of 1 or 2 equivalents of phenylacetylene with complex 1 in toluene-\textit{d}_{6} for 2 hours at room temperature resulted in the formation of a new complex 2 in quantitative yield by NMR spectroscopy (Scheme 3). Complex 2 showed a signal at \( \delta -10.85 \) ppm (t, \( ^{2}J_{\text{HP}} = 18.9 \text{ Hz} \)) in the \( ^{3}H \) NMR spectrum corresponding to the Ir-H. \( ^{31}P\{^{1}H \} \) NMR spectroscopy showed a signal at \( \delta 40.1 \) ppm (s) suggesting that the pyridine ring is now aromatized, making the phosphines equivalent. The structure of the product was unambiguously confirmed by a single crystal X-ray diffraction that showed an octahedral iridium complex with the acetylide and hydride ligands located \( \text{trans} \) to each other, and the phenyl ligand located \( \text{trans} \) to the pyridine ring (Figure 1). There are only few examples in the literature of crystallographically characterized complexes in which an acetylide ligand is \( \text{trans} \) to a terminal hydride. In case of iridium, the only other example of such a complex is reported by Goldman (Scheme 1).\textsuperscript{21} The other examples bearing this feature are reported with platinum, ruthenium and cobalt. \textsuperscript{28-34} The Ir-\{CCPh\} bond length in complex 2 \( [2.075(3) \text{ Å}] \) is slightly longer than that observed by Goldman \( [2.047(5) \text{ Å}] \).\textsuperscript{21}

The facile oxidative addition of a C-H bond by a 16e iridium(I) complex without the presence of any external additive is unprecedented and therefore we pursued the mechanistic details of this reaction. We carried the reaction of complex 1 with PhCCD (2-5 equivalents) at room temperature. Interestingly, \( ^{1}H \) NMR spectrum of the reaction mixture after 2 hours showed the formation of an \( \text{IrH} \) signal at \( \delta -10.85 \) (t, \( ^{2}J_{\text{HP}} = 18.9 \text{ Hz} \)). We suggest that the hydride ligand on iridium arises from the pyridylic “arm” through the metal-ligand cooperation. This was further confirmed by the \( ^{2}H \) NMR spectroscopy that showed a signal at \( \delta 3.70 \) (br) corresponding to the CHD signal at the pyridylic “arm” suggestive of the incorporation of deuterium from PhCCD on the arm. Additionally, a signal at \( \delta -10.85 \) (br) was also observed corresponding to the IrD moiety. In order to quantify the IrH and IrD signals, we carried two separate reactions of complex 1 with PhCCD in Young’s NMR tubes containing sealed capillaries filled with the known concentration of CH\(_{3}\)Cl or CO\(_{2}\)Cl as internal standards (See SI for full details, Figures S8-S10) and followed the reactions by NMR spectroscopy. \( ^{1}H \) and \( ^{2}H \) NMR spectroscopy after two hours showed that the ratio of signals corresponding to IrH and IrD is approximately 30:1.

Figure 1. Single crystal X-ray structure of complex 2. Atoms are presented as thermal ellipsoids at 50% probability level and hydrogen atoms except the Ir-H are omitted for clarity. Ir-H is presented as a white sphere. Selected bond distances (Å) and angles (deg) for complex 2: Ir1-P1, 2.3072(9); Ir1-P2, 2.3158(9); Ir1-C24, 2.074(3); Ir1-C30, 2.075(3); Ir1-N1, 2.132(3); P1-Ir1-P2, 161.16(3); C24-Ir1-C30, 95.68(13).

Scheme 3. Reaction of complex 1 with phenylacetylene.

Scheme 4. (i) Reaction of PhCCD with 1, (ii) reaction of PhCH with 1D, (iii) proposed mechanism for the overall oxidative addition.

Formation of \( \text{IrH} \) complex in more than 95% yield from the oxidative addition of PhCCD by 1 indicated the involvement of metal-ligand cooperation (MLC) and therefore we propose for the overall oxidative addition process a two-step pathway: (a) reversible conversion of complex 1 to a dearomatized iridium(III) hydride complex A as previously proposed by us,\textsuperscript{26} and (b) C-H activation of PhCH by the iridium(III) intermediate A (Scheme 4ii). Formation of \( \text{IrD} \) can be explained if the conversion of A to 2 is reversible; however as
the signal corresponding to IrD complex indicates less than 5% yield, we suggest that the reverse reaction is very slow. However, we can’t discount the incorporation of deuterium on iridium by the traces of residual DO present in PhCCD. The involvement of MLC was further indicated by the reaction of 1D with 2 equivalents of PhCCD where deuterium and proton/hydride scrambling were observed on both the metal and the arm (Scheme 4ii).

In order to further investigate the C-H oxidative addition of the alkyne, we studied the kinetics by systematically varying the concentrations of both PhCCD and (PNP)Ir(Ph) (1) and monitoring the initial rates of disappearance of complex 1 and the appearance of complex 2 at 298 K. The kinetics demonstrated first order dependence on both [PhCCD] and [complex 1], similar to that observed by Goldman for the acid catalysed oxidative addition of the alkyne, where first-order dependence on [(PCP)IrCO], [PhCCD], and the buffer [HNEt$_2$]$_2$B(C$_6$F$_5$)$_2$ was observed, while zero order dependence was observed on [NET$_3$].$^{21}$ Studying the rate of oxidative addition of alkynes bearing electron-withdrawing and electron-donating substituents by complex 1 using $^1$H NMR spectroscopy we found that the rate of oxidative addition is slightly faster for the alkyne bearing an electron-donating group (Table 1).

Table 1. Rate constants of oxidative addition of alkynes by complex 1.

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<tr>
<th>Alkyne</th>
<th>Rate constant (k), s$^{-1}$</th>
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<tbody>
<tr>
<td>F(C$_6$H$_5$)CCH</td>
<td>6.5x10$^{-3}$ ± 2.0x10$^{-5}$</td>
</tr>
<tr>
<td>PhCCCH</td>
<td>7.2x10$^{-3}$ ± 1.1x10$^{-5}$</td>
</tr>
<tr>
<td>MeO(C$_6$H$_5$)CCH</td>
<td>11.1x10$^{-3}$ ± 3.7x10$^{-5}$</td>
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Based on these observations we propose the mechanism outlined in Scheme 5 for the C-H oxidative addition by the (PNP)Ir(I) complex 1. We suggest that 1 exists in equilibrium with the [(PNP)*Ir(III)(Ph)] intermediate A through MLC via dearomatization of the pyridine backbone. This equilibrium has been previously proposed by us for the same system and was found to be facilitated by the presence of traces of water. $^{27, 35}$ PhCCD then coordinates to the Ir(III) complex A, resulting in formation of an octahedral intermediate B. Migration of a proton from the bound alkyne of B to the arm via MLC results in the formation of the oxidative addition product 2. As the kinetic experiments indicate first order rate dependence on both PhCCD and complex 1, we suggest that either alkyne coordination or the C-H activation of alkyne is the rate determining step.

Scheme 5. Suggested mechanism for formation of the C-H oxidative addition product 2 from the Ir(I) complex 1 through metal-ligand cooperation, P = PBu$_3$. The actual C-H activation is by the Ir(III) intermediate A.

In conclusion, we have uncovered a facile C-H oxidative addition of terminal alkynes by a 16e square planar iridium(I) complex. Our mechanistic investigations show that metal-ligand cooperation via aromatization/dearomatization of the lutidine-based backbone facilitates this process by generating a reactive deaeromatized iridium(III) intermediate that undergoes the C-H activation of the alkyne to produce the desired oxidative addition product. The reaction occurs at room temperature without the presence of an external additive. Further mechanistic insight via DFT calculations is planned.

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Conflicts of interest

There are no conflicts to declare.

References

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Metal-ligand cooperation through the aromatization-dearomatization of the pyridine backbone enables the facile oxidative addition of a C-H bond by a 16e (PNP)Iridium(I) complex.