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Selective Addition to Iridium of Aryl C−H Bonds Ortho to Coordinating Groups. Not Chelation-Assisted

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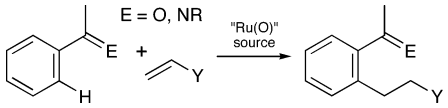
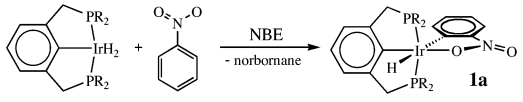
The ability to selectively and catalytically functionalize C−H bonds of a complex organic molecule has tremendous potential utility in organic synthesis. In stoichiometric reactions, transition metal complexes have revealed selectivity patterns toward C−H bonds that offer great promise in this context. Applied to catalysis, perhaps the most useful class of such reactions reported to date is the functionalization of aryl C−H bonds ortho to a coordinating group such as acyl.[1−7] This chemistry has been most extensively developed by Murai and co-workers, who have reported the insertion of olefins into ortho C−H bonds, with 100% regioselectivity (eq 1),[8] as well as other functionalizations at the same position,[9] using Ru(0) catalysts or precursors. It is widely assumed that the role of the coordinating group in such catalyses is to direct the metal center toward the "targeted" C−H bond.[1]



(1)

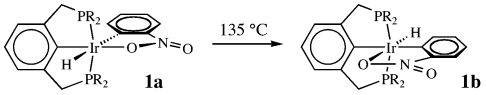
We have previously reported that the pincer-ligated fragment (PCP)Ir (PCP = κ^3-C_6H_3-2,6-$(CH_2P^tBu_2)_2$) adds aryl C−H bonds to give isolable aryl hydrides.[10] Like Ru(0), the Ir(I) center of this fragment has a d^8 electron configuration. In this Communication we report addition of C−H bonds to (PCP)Ir with apparently quantitative selectivity for the position ortho to coordinating groups.[11] We have determined, however, that the coordinating group does *not* direct C−H addition. To the contrary, the functional group is found to actually *hinder* the kinetics of C−H addition; however, after C−H addition, the coordinating group acts to trap the ortho-C−H addition product and form stable chelated complexes.

The reaction of $(PCP)IrH_2$ with norbornene (NBE) in *p*-xylene solvent is known to generate a precursor of the reactive fragment (PCP)Ir.[10] Reaction of $(PCP)IrH_2$ and NBE with 1.5 equiv of nitrobenzene at ambient temperature in *p*-xylene gave the cyclometalated iridium(κ^2-O,C-nitrophenyl)hydride (**1a**) in quantitative yield. **1a** was characterized by ^1H and ^{31}P NMR and single-crystal X-ray diffraction; the structure is shown in eq 2. Most notably, the hydride in **1a** is located trans to the coordinated carbon of the chelating nitrophenyl group. This is not the structure that would be directly obtained if C−H addition occurred after O-coordination, in which case the ortho-carbon and hydride could only be mutually cis.



(2)

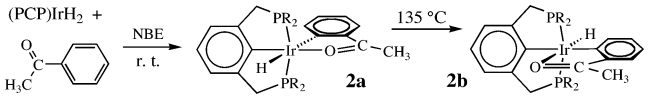
The discrepancy between the expected and actual structures of the product of eq 2 might be rationalized by proposing that the reaction initially gives the *cis*-C−H complex, followed by rearrangement to give **1a**. However, refluxing **1a** in *p*-xylene solution for 5 h gave the *cis*-C−H complex, **1b**, in 95% yield, characterized by NMR and X-ray diffraction. Thus, **1b** is thermodynamically more stable than **1a**, and it is not possible that the formation of **1a** (in reaction 2) proceeds via **1b**.



(3)

Completely analogous results are obtained when (PCP)Ir is reacted with acetophenone instead of nitrobenzene. The reaction of $(PCP)IrH_2$ with NBE and acetophenone at room temperature gave as the kinetic product the iridium(acetylphenyl)hydride, **2a**, in which the hydride and acetylphenyl carbon are mutually trans (NMR, X-ray). Upon refluxing in *p*-xylene solution for 5 h, complex **2a** was converted in 98% yield to complex **2b**, in which the hydride and phenyl carbon are cis (NMR, X-ray) (structures as shown in Scheme 1).

Scheme 1. Reaction of (PCP)Ir with Acetophenone



We believe that the only plausible explanation for the formation of products **1a** and **2a** involves C−H addition prior to O-coordination. This conclusion can be easily rationalized on the premise that C−H addition to three-coordinate d^8 metal centers is generally much more facile than addition to square planar d^8 centers.[12] However, although C−H addition prior to O-coordination is a *necessary* condition to explain these results, it would not appear to be sufficient. If C−H addition were to occur initially and give the aryl hydride rotamer with a nitro or acyl group anti to hydride (Int_B; Scheme 2), the functional group would presumably coordinate to give **1b** or **2b**, respectively (rather than undergoing rotation about the hindered Ir−aryl bond, to give the thermodynamically less stable isomers **1a** and **2a**). Thus, C−H addition selectively gives the rotamer with functional group syn to hydride (Int_A), which undergoes coordination prior to Ir−C rotation. The selective formation of rotamer Int_A strongly implies that the iridium atom approaches the C−H bond from the "side" that is opposite the functional group (Scheme 2, TS_A). In this context, it is worth noting that rotation of unsubstituted (and therefore much less hindered) aryls coordinated to (PCP)Ir has previously been found to be slow on the NMR time scale.[10]

If, in fact, the functional group does not promote C−H addition, as implied by the exclusive formation of complexes **1a** and **2a**, the question then arises as to why there is apparently complete selectivity for the activation of the ortho positions. Low-temperature NMR spectroscopy provides a simple answer to this query, specifically, that *the actual kinetic selectivity is, in fact, quantitative*

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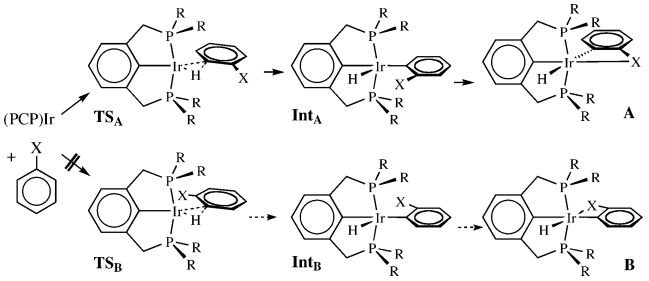
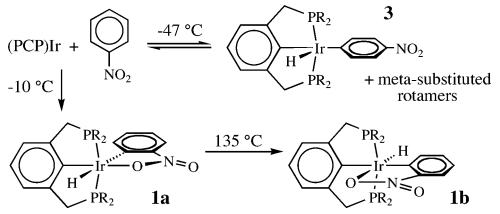
Scheme 2. Reaction of (PCP)Ir with Nitrobenzene or Acetophenone



Scheme 3. Formation of (PCP)Ir(*p*-Nitrophenyl)(H) (and Two Rotameric Forms of *m*-Nitrophenyl Isomer, Not Shown)



for the meta and para C−H bonds. When nitrobenzene is added to solutions of (PCP)IrH_2/NBE at −47 °C, three C−H addition products form immediately upon mixing. In the selectively ^{1}H-decoupled ^{31}P NMR spectrum, doublets appear at δ 67.28, 66.67, and 66.17, respectively, with a ratio of 4.4:1:1. Accordingly, three hydride peaks are observed as triplets in the ^{1}H NMR at δ −45.12, −45.20, and −45.52 ppm in approximately the same ratio. These highly upfield ^{1}H NMR resonances are indicative of five-coordinate species (PCP)Ir(aryl)(H); for example, the corresponding hydride chemical shifts of (PCP)Ir(phenyl)(H) and (PCP)Ir(3,5-dimethyl-4-nitrophenyl)(H) are δ −45.6 and −45.5, respectively (^{31}P NMR, δ 67.5 and 67.0).[10,13]

Electron-withdrawing groups at the aryl para position of (PCP)-Ir(aryl)(H), including NO_2, have been shown to favor the thermodynamics of C−H addition (cf. (PCP)Ir(3,5-dimethyl-4-nitrophenyl)-(H)).[13] Thus, the major product of the low-temperature reaction with nitrobenzene was suspected to be the para-substituted isomer (PCP)Ir(4-nitrophenyl)(H) (**3**, Scheme 3). This assignment was confirmed by the reaction of isotopically labeled nitrobenzene-4-*d* with "(PCP)Ir", conducted as described above with nitrobenzene-d_0. The ^{31}P NMR spectrum comprised the same three signals, but the major signal (δ 67.28) was now a singlet due to the absence of coupling with (protio) hydride. The ^{1}H NMR spectrum revealed the absence of the major peak observed in the reaction with nitrobenzene-d_0 (δ −45.12), but the two other triplets at δ −45.20 and −45.52 were unaffected. The two minor species may be assigned as the meta rotamers (3-nitro group syn and anti to hydride), consistent with their nearly identical spectral parameters and the 1:1 ratio. Upon warming to −10 °C, the five-coordinate nitrophenyl hydrides are converted quantitatively to **1a**. Scheme 3 summarizes the overall behavior of the system.

In summary, (PCP)Ir appears to undergo selective addition of the ortho-C−H bonds of nitrobenzene and acetophenone, giving chelated species **1a** and **2a**. Superficially, these results appear suggestive of chelate-assisted C−H bond activation; however, the structure of **1a** and **2a** is inconsistent with their direct formation via such a pathway. The products expected from chelate-assisted C−H bond activation (**1b** and **2b**) are found to be thermodynamically more stable than the initially observed products; therefore, they cannot be involved as intermediates. The structural results imply that C−H addition is kinetically hindered, rather than assisted, by proximity of the coordinating groups. Low-temperature experiments support this conclusion; addition at the aryl meta and para positions is kinetically more favorable than that at the ortho position, although thermodynamics favor the chelated ortho-C−H addition products. We suggest that these conclusions will prove general at least to three-coordinate d^8 metal centers.[14,15] Computational and experimental work is in progress to test this proposal, and to determine the actual role that chelation plays in systems that catalytically functionalize ortho-C−H bonds.

Acknowledgment. We thank the National Science Foundation (grant CHE-0316575) for support of this work.

Supporting Information Available: Preparative procedures, spectral data, ORTEP diagrams, and crystallographic data for **1a**, **1b**, **2a**, and **2b** (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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