C−H Oxidative Addition to a (PNP)Ir Center and Ligand-Induced Reversal of Benzyl/Aryl Selectivity

Yanjun Zhu, Lei Fan, Chun-Hsing Chen, Shannon R. Finnell, Bruce M. Foxman, and Oleg V. Ozerov*

Department of Chemistry, Brandeis University, MS 015, 415 South Street, Waltham, Massachusetts 02454

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Summary: The (PNP)Ir fragment displays a thermodynamic preference for the oxidative addition of aromatic vs benzylic C−H bonds. However, in the case of the mesitylene activation products, the benzylic isomer is kinetically accessible and can be trapped by an external donor ligand. The preference for the benzylic isomer in the six-coordinate Ir(III) adduct of mesitylene activation is ascribed to steric factors.

Selective activation of C−H bonds by transition-metal complexes remains a focal point, in part owing to the potential benefits of selective functionalization of unreactive C−H bonds.[1–3] Control and discrimination between activation of aromatic C(sp^2)−H bonds on one hand and aliphatic C(sp^3)−H bonds, especially benzylic C−H bonds, on the other hand is an issue for any substrate containing both. As a rule, transition-metal systems typically display both the thermodynamic and kinetic preference for the activation of aromatic C−H bonds. The thermodynamic preference to activate stronger C−H bonds[4] has been traced to the greater differences in M−C bond strengths compared with the case for C−H bond strengths.[5] Selectivity for a product of benzylic activation may come in cases where (a) formation of an aryl−metal product is sufficiently sterically disfavored,[5–7] (b) the benzylic product is stabilized by η^3 coordination,[8,9] or (c) in the sense of kinetic selectivity, the reaction proceeds via homolysis pathways.[10] Eisenberg et al. reported an aryl-to-benzyl rearrangement induced by coordination of ethylene to an Ir(I) center in ($Me_3C_6H_2$)Ir(CO)(dppe),[11] but the mechanistic details were not fully elucidated. Here we report an example where the aryl/benzylic preference is reversed by addition of an external ligand at an Ir(III) center. We provide an analysis of the underlying causes of this preference reversal and report on our investigation of the mechanism of the requisite transformations through kinetic studies. We have previously reported on the selectivity (C−H vs C−Cl) of the oxidative addition of chlorobenzene in this system, where the Ir center is supported by a rigid PNP pincer ligand.[12–15]

(PNP)Ir(H)(Mes) (**1**) served as a synthon for the transient (PNP)Ir species. Thermolysis of **1** in benzene[16] or toluene at 70 °C led to the elimination of mesitylene and formation of **2** or **3**,[17] respectively (Scheme 1). However, when C_6D_6 solutions of **1** were treated with excess pyridine, the anticipated C−H OA of pyridine did not take place. Instead, an entirely different product (**4a**) was isolated after 24 h at ambient temperature (Scheme 1). Similar products were obtained from the reaction of **1** with PMe_3 (**4b**) and thiazole (**4c**). Compounds **4a**−**c** were fully characterized by NMR spectroscopy. For instance, in **4a**, the Ir−CH_2 unit gave rise to characteristic resonances in the ^{1}H (δ 3.67, br t, J_{HP} = 6 Hz) and ^{13}C{^{1}H} (δ −6.6, t, J_{CP} = 2 Hz) NMR spectra. The hydride resonance in **4b** displayed a large $^2J_{HP}$ value of 142 Hz for the coupling with the ^{31}P nucleus in PMe_3, indicative of the trans disposition of PMe_3 and the hydride. In the solid-state structure of **4c** (Figure 1), the N-bound thiazole ligand is also trans to the hydride. The pyridine ligand in **4a** is most likely trans to the hydride as well.

The rate of the transformation of **1** to **4a** in C_6D_6 was found to be independent of the concentration of pyridine in the 0.5−2.2 M range. Notably, **1** does not detectably bind pyridine in solution at 22 °C. This strongly implies that the rate-determining step is

* To whom correspondence should be addressed. E-mail: ozerov@brandeis.edu.

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(16) The thermolysis of **1** in C_6D_6 led to (PNP)Ir(D)(C_6D_5) (**2**-d_6); see the Supporting Information.

(17) **3** and **6** denote mixtures of the corresponding m- and p-tolyls in a ca. 2:1 ratio; see the Supporting Information for details.

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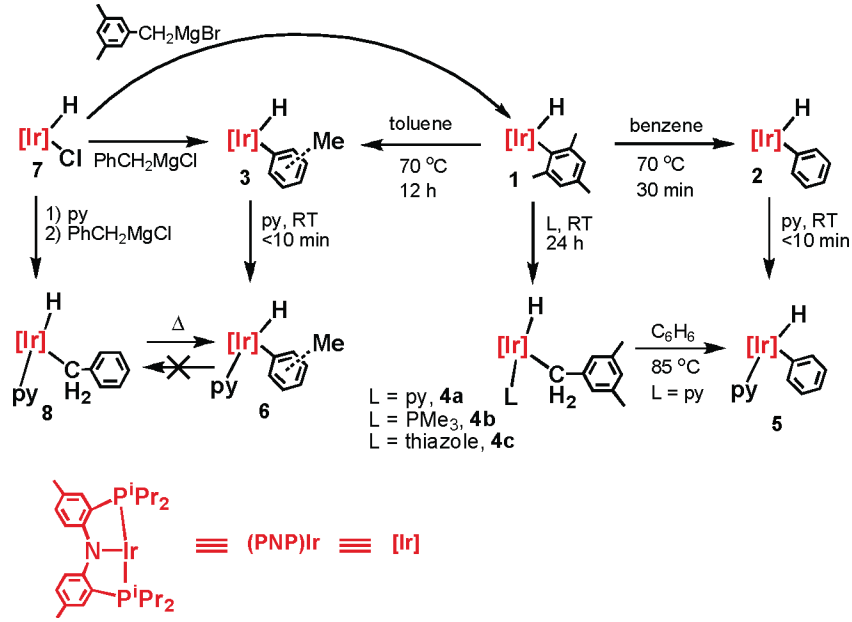
Scheme 1



the transformation of **1** to its benzylic isomer **9** followed by fast trapping of the latter by pyridine. An attempt to isolate **9** by treatment of (PNP)IrHCl (**7**) with 3,5-$Me_2C_6H_3CH_2MgBr$ led to the observation of **1** as the major product (Scheme 1). Thus, for the five-coordinate system, the aryl isomer (**1**) is thermodynamically preferred over the benzylic isomer (**9**), although **9** is kinetically accessible. Addition of pyridine, thiazole, or PMe_3, however, causes the preference to reverse and favor the benzylic products **4a**−**c**.[19]

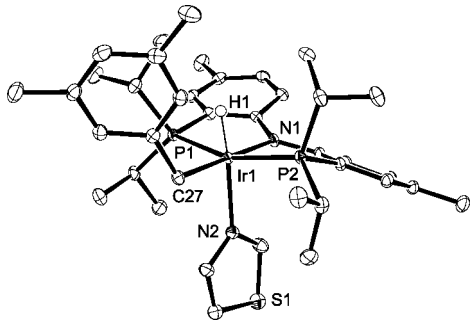


Figure 1. ORTEP drawing[18] (50% probability ellipsoids) of **4c** showing selected atom labeling. Hydrogen atoms (except Ir−H) are omitted for clarity. Selected bond distances (Å) and angles (deg): Ir1−P1, 2.2866(7); Ir1−P2, 2.3026(7); Ir1−N1, 2.137(2); Ir1−N2, 2.213(2); Ir1−C27, 2.135(3); P1−Ir1−P2, 159.33(2); N1−Ir1−N2, 179.12(10).

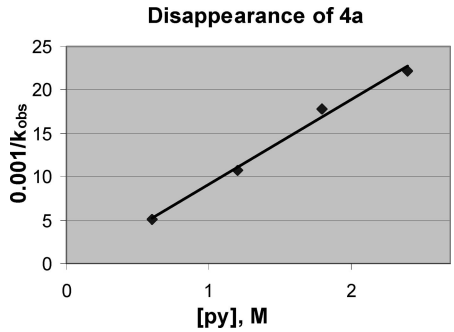


Figure 2. Rate of disappearance of **4a** during thermolysis at 85 °C in C_6D_6 as a function of pyridine concentration.

We set out to investigate the importance of the steric influence in the aryl/benzyl isomerization. In contrast to the case for **1**, the less sterically encumbered aryl complexes **2** and **3** readily coordinated pyridine to give **5** and **6**,[17] respectively (Scheme 1). Neither **3** nor **6** converted to the corresponding benzyl isomers (PNP)Ir(H)(CH_2Ph) (**12**) and **8** upon thermolysis (20 h, 95 °C). On the other hand, the reverse reactions did proceed: (a) **8** converted to **6** upon thermolysis (complete disappearance of **8** after 70 °C, 18 h; unidentified products also observed), and (b) an attempted synthesis of **12** from (PNP)Ir(H)(Cl) and $PhCH_2MgCl$ led to **3**. Thus, unlike the case for the mesityl/3,5-dimethylbenzyl pair, in the tolyl/benzyl pair, the thermodynamic preference for the aryl isomer exists not only for the five-coordinate but also for the six-coordinate case. In a sense, the coordination of pyridine (possible to **1** but not **3**) compensates for the ostensibly unfavorable mesityl-to-3,5-dimethylbenzyl isomerization, but the difference in the energies of binding of pyridine to **3** vs **12** does not override the intrinsic unfavorability of tolyl-to-benzyl isomerization.

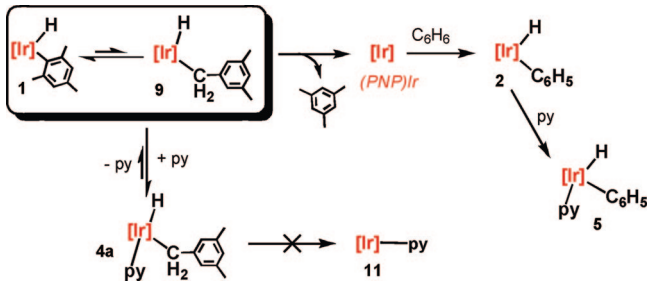
Continued thermolysis of **4a** in C_6H_6 led to the production of **5** via activation of the solvent (Scheme 1).[20] Kinetic studies carried out at 85 °C revealed the inverse dependence of the rate of conversion of **4a** to **5** on the concentration of pyridine (Figure 2). This is consistent with the dissociation of pyridine from **4a** being necessary for the reaction to proceed (Scheme 2). Elimination of mesitylene generates transient (PNP)Ir, which reacts with benzene to give **2**, and the latter is trapped by pyridine to give **5**. A dissociative mechanism for the activation of benzene by **1** is consistent with the previously demonstrated intermediacy of analogous three-coordinate Ir fragments (e.g., (PCP)Ir and Milstein's

(18) ORTEP plots were created using Ortep-3 for Windows: Farrugia, L. *J. Appl. Crystallogr.* **1997**, *30*, 565.

(19) Fryzuk observed benzylic C−H activation of toluene via ostensibly radical pathways (no reaction in the dark) by [$(Ph_2PCH_2SiMe_2)_2N$]Rh(Me)(I) in the presence of MeI. In our case, the transformation of **1** to **4a** proceeds in the dark (see the Supporting Information); radical pathways are unlikely. See: Fryzuk, M. D.; MacNeil, P. A.; McManus, N. T. *Organometallics* **1987**, *6*, 882.

(20) Thermolysis of **4a** in C_6D_6 led to (PNP)Ir(D)(C_6D_5)(py) (5-d_6); see the Supporting Information.

Scheme 2



$[(PN^{pyr}P)Ir]^+$)[21,22] in C−H oxidative addition reactions. The lack of direct reductive elimination from the six-coordinate d^6 complex **4a** dovetails with the findings of Goldberg et al.[23] of the necessity of the five-coordinate intermediate for C−X reductive elimination from six-coordinate Pt(IV) d^6 complexes and the trapping by Goldman et al.[24] of the reductive-elimination-prone d^6 complex (PCP)Ir(H)(Ph) as a robust six-coordinate adduct with CO.

In summary, we have demonstrated that the thermodynamic preference for aryl or benzylic C−H oxidative addition may in certain cases depend on the coordination number of the metal center. A higher coordination number favors a less sterically demanding benzylic product instead of the preference for the mesityl isomer for the lower coordination number.

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Supporting Information Available: Crystallographic information for **19a** and **21** in the form of CIF files, experimental details on the equilibrium and kinetics experiments, and pictorial NMR spectra for select compounds. This material is available via the Internet free of charge at http://pubs.acs.org.

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