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Mild Iridium-Catalyzed Borylation of Arenes. High Turnover Numbers, Room Temperature Reactions, and Isolation of a Potential Intermediate

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The simultaneous activation and functionalization of hydrocarbons allows abundant, inert hydrocarbons to serve as direct feedstocks for functionalized compounds.[1−6] The versatility of organoboron compounds in organic synthesis[7,8] makes the borylation of hydrocarbons an attractive goal. One of our groups has developed novel preparations[9] and reactions[10] of arylboronate esters, while the other has developed catalytic conversions of arenes and alkanes to aryl- and alkylboronates.[11,12]

The borylation of both alkanes and benzene by bis(pinacolato)diboron (B_2pin_2, pin = $O_2C_2Me_4$) catalyzed by $Cp^*Re(CO)_3$ under photochemical conditions[11] and by $Cp^*Rh(\eta^4\text{-}C_6Me_6)$ under thermal conditions[12] was reported recently. $Cp^*Rh(\eta^4\text{-}C_6Me_6)$,[12,13] $Cp^*Ir(PMe_3)(H)(Bpin)$,[14,15] $RhCl[P(i\text{-}Pr)_3]_2(N_2)$,[16] and $(Cp^*RhCl_2)_2$ have also been shown to catalyze with variable efficiency the borylation of aromatic substrates by pinacolborane (HBpin). $RhCl[P(i\text{-}Pr)_3]_2(N_2)$[16] and Pd/C[17] catalyze the borylation of benzylic C−H bonds. In all cases, reactions were conducted at elevated temperatures and with limited turnovers. Iridium systems required temperatures between 150 and 200 °C for both catalytic and stoichiometric[18] borylations.

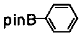
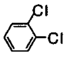
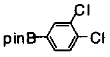
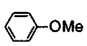
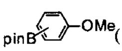
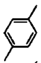
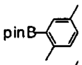
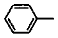
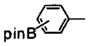
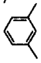
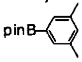
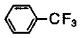
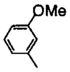
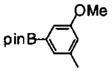
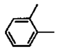
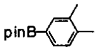
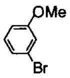
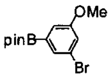
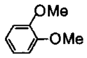
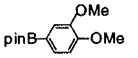
We disclose that air-stable, commercially available iridium(I) precursors in conjunction with simple 2,2′-bipyridine (bpy) ligands form complexes that catalyze the direct borylation of arenes by B_2pin_2 (**1**) to produce pinacol arylboronate esters under mild conditions, including room temperature. All reaction components are air stable and commercially available. The reaction appears to proceed through Ir(III) tris-boryl complexes, which have been isolated and which react rapidly at room temperature to yield the organoboron products (eq 1).

$$\underset{\mathbf{1}}{B_2pin_2} + 2ArH \xrightarrow[\text{room temperature to 80 °C}]{\text{Ir(I)/bpy cat}} 2ArBpin + H_2 \qquad (1)$$

The direct borylation of benzene (60 mmol) by **1** (1.0 mmol) was initially conducted at 80 °C for 16 h while modifying reaction conditions. Iridium(I) complexes comprised of $[IrCl(COD)]_2$ (0.015 mmol) and bpy (0.03 mmol) proved to be active catalysts. Both boryl groups in diboron **1** participated in the reaction to give PhBpin in 95% yield, along with a trace amount of $C_6H_4(Bpin)_2$. Complexes generated from 1,10-phenanthroline also exhibited high catalytic activity and generated the boronate product in 89% yield. Catalysts containing pyridine, TMEDA, PPh_3, and dppe were ineffective. Despite the utility of rhodium(I) or platinum(0) complexes in the related direct metalations of arenes by **1**,[12] disilanes[19] and silanes,[20] the combination of $Pt(dba)_2$ and bpy did not catalyze the reaction, and the combination of $[RhCl(COD)]_2$ and bpy led to formation of PhBpin in only 20% yield and required 150 °C.

Representative results of the direct borylation of arenes by **1** under these conditions are summarized in Table 1. Both electron-rich and electron-poor monosubstituted arenes underwent smooth reaction to produce regioisomeric mixtures of the meta and para borylation products in statistical ratios (ca. 2:1) (entries 2−4). The ortho isomer was not detected in most cases probably due to the steric effect of the substituents.[21] The borylation of benzene in the presence of *o*-, *m*-, or *p*-borylanisole resulted in neither formation of anisole nor isomerization of the borylanisoles. This result indicates that the ratio of isomers was kinetically determined. The nearly statistical ratio of meta and para isomers is inconsistent with a mechanism involving electrophilic C−H activation. Although toluene has weaker benzylic C−H bonds, the reaction occurred only at the aromatic C−H bonds (entry 3).

Table 1. Ir-Catalyzed Direct Borylation of Arenes with **1** (eq 1)[a]

	arene	product	yield/%[b] (o:m:p)[c]		arene	product	yield/%[b] (o:m:p)[c]
1			95	7			83
2			95 (1:74:25)	8			58
3			82 (0:69:31)	9			86
4			80 (0:70:30)	10			72
5			83	11			73
6			86				

[a] All reactions conducted at 80 °C for 16 h with **1** (1.0 equiv), an arene (60 equiv), and $1/2[IrCl(COD)]_2$/bpy (3 mol %) without solvent. [b] GLC yields based on boron atom in **1**. [c] Isomer ratios determined by ^1H NMR.

In contrast, regioselective borylation occurred with disubstituted arenes because the substituents block ortho activation. Both 1,2- and 1,4-disubstituted arenes bearing identical substituents yielded the corresponding boronate ester as a single regioisomer (entries 5−8), although yields for reaction of 1,4-isomers were lower than those for 1,2-isomers due to steric hindrance. The borylation of 1,3-disubstituted arenes occurred only at the common meta position;[13] therefore, regioisomerically pure ester products were obtained even with two distinct substituents on the arene (entries 9−11). Aromatic C−H bonds were selectively borylated in the presence of C−Cl and C−Br bonds, despite the thermodynamic driving force for formation of haloboranes[22] (entries 7 and 11).

The reactions in an equimolar mixture of trifluoromethylbenzene and toluene, trifluoromethylbenzene and anisole, and toluene and anisole afforded the corresponding arylboronate esters in ratios of 90:10, 85:15, and 40:60, respectively. These data indicate that electron-poor arenes are more reactive than electron-rich ones. Inductive effects or coordination of substituents may be influencing the reactivity of arenes because the borylation of anisole was faster than that of toluene.

Monitoring of the reaction of **1** with benzene showed that **1** was completely consumed after 40 min to form PhBpin and HBpin in

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96% yield based on the quantity of **1**. After 4 h, the HBpin was also consumed to form PhBpin in an overall 88% yield based on the number of equivalents of the Bpin unit in **1**. Reaction of HBpin with benzene under the conditions used for the borylation by **1** gave PhBpin in 80% yield (eq 2).

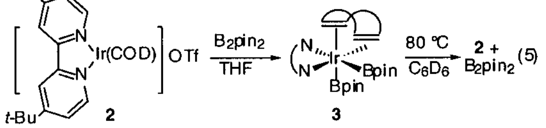
$$\underset{}{\mathrm{HBpin}} + \underset{(60\ \mathrm{equiv})}{\mathrm{PhH}} \xrightarrow[80\ ^\circ\mathrm{C}/16\ \mathrm{h}]{1/2[\mathrm{IrCl(COD)}]_2/\mathrm{bpy}\ (3\ \mathrm{mol}\ \%)} \underset{80\%}{\mathrm{PhBpin}} + \mathrm{H}_2 \quad (2)$$

Careful monitoring by ^{1}H NMR and GC/mass spectroscopy of the early stages of the reaction between benzene-d_6 and **1** at 60 °C revealed an induction period during which the cyclooctadiene ligand was reduced to cyclooctene-d_2. Thus, we evaluated reactions conducted with $[\mathrm{IrCl(COE)_2}]_2$ as precursor. These reactions showed no induction period even when we employed lower reaction temperatures. In fact, the reaction between **1** and benzene in the presence of $[\mathrm{IrCl(COE)_2}]_2$ and 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy), which generates more soluble iridium complexes, produced PhBpin in 83% yield after 4.5 h at room temperature (eq 3). This reaction of **1** with benzene constitutes the first catalytic C−H borylation at room temperature. Moreover, this catalyst system provides remarkably high turnover numbers for a hydrocarbon functionalization process. Reaction of **1** at 100 °C in benzene catalyzed by 0.02 mol % of iridium formed 2 equiv of PhBpin for each diboron reagent in 80% yield (8000 turnovers) (eq 4). This value surpasses previously published catalyst efficiencies by more than an order of magnitude.

$$\mathrm{B_2pin_2} + \underset{(60\ \mathrm{equiv})}{2\mathrm{PhH}} \xrightarrow[\text{room temperature/4.5 h}]{1/2[\mathrm{IrCl(COE)_2}]_2/\mathrm{dtbpy}\ (5\ \mathrm{mol}\ \%)} \underset{83\%}{2\mathrm{PhBpin}} + \mathrm{H}_2 \quad (3)$$

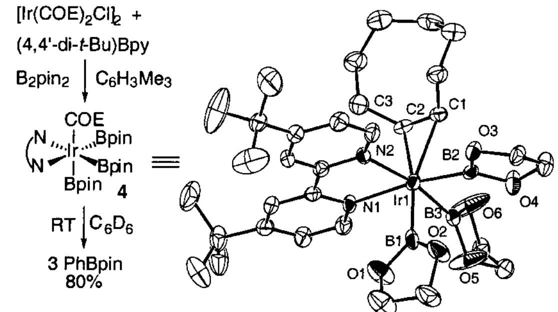
$$\mathrm{B_2pin_2} + \underset{(60\ \mathrm{equiv})}{2\mathrm{PhH}} \xrightarrow[100\ ^\circ\mathrm{C}/16\ \mathrm{h}]{1/2[\mathrm{IrCl(COE)_2}]_2/\mathrm{dtbpy}\ (0.02\ \mathrm{mol}\ \%)} \underset{80\%}{2\mathrm{PhBpin}} + \mathrm{H}_2 \quad (4)$$

Our studies subsequently focused on isolating likely Ir-boryl intermediates. To do so, we generated the dtbpy- and COD-ligated Ir(I) complexes [IrCl(dtbpy)(COD)] and [Ir(dtbpy)(COD)]OTf (**2**). Addition of 1.1 equiv of diboron **1** to the triflate formed the Ir(III) bis-boryl complex *cis*-[Ir(dtbpy)(COD)(Bpin)$_2$]OTf (**3**) (eq 5).[23] Reaction of the chloride did not generate an isolable boryl complex. Although bis-boryl **3** catalyzed the reaction between C_6D_6 and B_2pin_2 to form PhBpin in 80% yield after 5 h at 80 °C, thermolysis of **3** in C_6D_6 in the absence of added diboron regent, a reaction that would complete the catalytic cycle, did not form PhBpin. Instead it simply extruded B_2pin_2 in 75% yield and generated the starting [Ir(dtbpy)(COD)]OTf.[24]



These data underscored the importance of converting the ligated COD to COE and led us to prepare iridium boryl complexes ligated by COE and dtbpy. Monitoring by ^{1}H NMR spectroscopy of a catalytic reaction that contained high catalyst loadings showed a predominant dtbpy-ligated iridium complex. Reaction for 5 h at 50 °C between $[\mathrm{IrCl(COE)_2}]_2$, 2 equiv of dtbpy, and 10 equiv of B_2pin_2 in mesitylene solvent, which dissolved the resulting complex but was unreactive, formed the same species. This complex was isolated in 15% yield as crystals suitable for X-ray diffraction. Spectroscopic and X-ray diffraction methods showed it to be the unusual tris-boryl complex [Ir(dtbpy)(COE)(Bpin)$_3$] (**4**) (Scheme 1).

Scheme 1



Ir-N1=2.177 Å, Ir-N2=2.221 Å, Ir-B1=2.055 Å Ir-B2=2.057 Å, Ir-B3=2.027 Å, Ir-C1=2.308 Å Ir-C2=2.318 Å Pinacol methyl groups and hydrogens have been removed for clarity.

Dissolution of tris-boryl **4** in C_6D_6 generated 3 equiv of C_6D_5-Bpin in 80% yield within minutes at room temperature. Thus, **4** is chemically and kinetically competent to be an intermediate in the catalytic process. Reaction of **4** with a mixture of C_6H_6 and C_6D_6 revealed a kinetic isotope effect of 3.6 ± 0.2. Catalytic reactions conducted in this solvent mixture showed an essentially identical $k_H/k_D = 3.8 \pm 0.4$. Reaction of **4** in a mixture of toluene and trifluoromethylbenzene showed selectivity that was also identical with that of the catalytic reactions. These similar selectivities further substantiated the involvement of **4** in the catalytic process.

In conclusion, Ir(I) complexes containing readily available and air-stable 2,2′-bipyridine catalyze the borylation of arenes by bis(pinacolato)diboron even at room temperature. The method provides a simple and direct route for the synthesis of arylboronates that traditionally have been prepared by transmetalation between aryllithium or arylmagnesium reagents and trialkyl borates.

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Supporting Information Available: Experimental procedures and spectral analyses of all reaction products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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