Pronounced effects of substituents on the iridium-catalyzed borylation of aryl C–H bonds[†][‡]

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Iridium trisboryl complexes containing bisphosphine and bipyridine ligands and pinacolate and catecholate substituents on boron are reported. A large difference in reactivity towards the borylation of C–H bonds is observed for this series of trisboryl complexes, and this difference is attributed to the electron-donating properties of the pinacolate vs. catecholate groups, and the steric and electronic properties of bipyridine vs. bisphosphine ligands.

Metal-catalyzed borylations of aryl C–H bonds^{1–8} have become a selective and convenient method to generate arylboronate esters from arenes and either pinacolborane or bis-pinacolato diboron reagents.^{9–11} The most active catalyst for this process is generated from the combination of an iridium(1) precursor and di-*tert*-butylbipyridine (dtbpy) as a ligand,¹⁰ and the most effective reagents for Ir-catalyzed C–H borylation contain pinacolate groups (pin) on boron. Detailed mechanistic studies have shown that the reactions catalyzed by Ir(1) and dtbpy occur by generation of iridium-trisboryl complexes and reaction of these trisboryl complexes with arenes to form arylboronate esters in the turnover-limiting step.^{12,13}

We have begun to assess the origins of the effect of the substituents at boron and the dative ligands on the metal on the composition, structure and reactivity of the catalytic intermediates in this borylation process. We report our initial results from these studies on intermediates containing a substituted catecholboryl group, rather than a pinacolboryl group, and di-*tert*-butylbipyridine or an alkylbisphosphine as the dative ligand. These changes in boron substituents and dative ligands, relative to those in the previously characterized [Ir(dtbpy)(Bpin)₃(cyclooctene)], create remarkable changes in structure, reactivity and energetics, which are reported here.

We previously isolated the trisboryl complex $[Ir(dtbpy)(Bpin)_3-(cyclooctene)]$ (1a), which readily dissociates cyclooctene (COE) to form the 16-electron species $[Ir(dtbpy)(Bpin)_3]$, which is an intermediate in the catalytic borylation of arenes.¹³ Although the reaction of $[Ir(COD)(OMe)]_2$ (COD = 1,5-cyclooctadiene), dtbpy, HBpin and COE to form 1a occurred in high yield, analogous reactions conducted with catecholboranes did not lead

to the analogous trisboryl complexes. Thus, we sought an alternative route to complexes of the type $[Ir(dtbpy)[B(OR)_2]_3$ -(cyclooctene)], and we found that the reaction of dtbpy with $[Ir(p-xylene)(Bcat^*)_3]$ (Bcat^{*} = 4-*tert*-butylcatecholboryl),⁴ and 10 equiv. of COE formed [Ir(dtbpy)(Bcat^{*})_3(cyclooctene)] (**1b**) in 86% isolated yield (eqn (1)). This complex contained resonances for the bound COE at 5.11 and 1.51 ppm, and one set of catecholate groups (*vide infra*). The ¹¹B NMR spectrum consisted of a single broad resonance at 34 ppm.



Free COE exchanges with the bound COE in **1b** on the NMR timescale. A solution of **1b** and 3 equiv. of COE in methylcyclohexane- d_{14} contained a single set of resonances for the free and bound olefin. At -25 °C, resonances for both free (δ 5.61) and bound COE (δ 4.78) were observed. This exchange process occurs on a timescale similar to that of the exchange of free COE with the bound COE in pinacolboryl complex **1a**.¹³ This process with **1a** was shown to be dissociative,¹³ and a similar dissociation from **1b**, followed by site exchanges within the resulting five-coordinate intermediates, would account for the equivalence of the Bcat groups *cis* and *trans* to the COE ligand in **1b**.

An ORTEP diagram of complex **1b** is shown in Fig. 1. The structural parameters about the metal center in both **1a** and **1b** are provided in Table 1. The structures of **1a** and **1b** are closely related. Both complexes are pseudooctahedral with a facial orientation of the three boronate groups. The Ir–N bond lengths and the Ir–B bond lengths for the boryl group *trans* to COE in **1a** and **1b** are within 0.005 Å of each other. The Ir–B bond lengths to the two boronate groups *trans* to the bipyridine ligand in **1b** are only 0.021 and 0.028 Å shorter and the two Ir–olefin bonds in **1b** are, on average, only 0.028 Å longer than those in **1a**.

To begin to assess the origin of the differences in reactivity of the bipyridine and bisphosphine catalysts, we prepared trisboryl complexes containing bisphosphine ligands. The reaction of $[Ir(p-xylene)(Bcat^*)_3]$ with 1,2-bis(diisopropylphosphino)ethane (dippe) or 1,2-bis(dicyclohexylphosphino)ethane (dcpe) in the presence or absence of COE formed the bisphosphine-ligated trisboryl complexes **3a** and **3b** (eqn (2)). In contrast to **1a** and **1b**, these complexes were 16-electron, five-coordinate species $[Ir(L_2)(Bcat^*)_3]$ lacking a COE ligand. Thus, these complexes are phosphine analogs of the unsaturated bipyridine intermediates in the borylation of arenes catalyzed by $[Ir(COD)(OMe)]_2$ and dtbpy. Complexes **3a** and **3b** do not bind COE to form stable complexes.

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Fig. 1 ORTEP drawing of complex **1b** with atomic numbering. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at the 35% probability level.

Table 1 Ir-X bond distances in 1a, 1b, and 3a

	$L1/\text{\AA}$	$L2/\text{\AA}$	$B1/{\rm \AA}$	$B2/\text{\AA}$	$\mathbf{B3}/\mathbf{\mathring{A}}$	$C1/\text{\AA}$	$C2/\text{\AA}$
1a 1b 3a	2.177(4) 2.173(4) 2.368(1)	2.221(4) 2.222(4) 2.365(1)	2.055(7) 2.051(6) 1.979(5)	2.057(6) 2.029(6) 2.075(5)	2.027(6) 2.006(6) 2.070(5)	2.318(5) 2.348(5)	2.318(5) 2.344(5)
5 a	2.506(1)	2.505(1)	1.979(3)	2.075(5)	2.070(3)		

Addition of 5 equiv. of COE to these species did not affect the shape or position of the olefinic resonances in the ¹H NMR spectrum.



An ORTEP diagram showing the structure of five-coordinate, bisphosphine complex 3a is shown in Fig. 2, and the structural parameters are included in Table 1. Complex 3a adopts a square pyramidal structure with a facial orientation of the three boronate groups. The bond lengths of the boryl groups *trans* to the ligand are 0.058 and 0.053 Å longer than the average of these bond lengths in complex 1b. Most striking, the Ir–B distance for the boryl group *trans* to the open coordination site in 3a is 0.072 Å shorter than that for the boryl group *trans* to the Ir–B distance for the boryl groups *trans* to the open coordination site in 3a is 0.072 Å shorter than that for the boryl group *trans* to the COE ligand in 1b and about 0.1 Å shorter than the Ir–B distance for the boryl groups *trans* to the phosphine groups.

The effect of these structural changes on the catalytic reactions was evaluated. The presence of the open coordination site on **3a** and **3b** might lead one to expect that complexes generated from the dippe and dcpe ligands in **3a** and **3b** would be active catalysts. However, consistent with the prior lower reactivity of complexes of other bisphosphines as catalysts, ^{11,14} the reaction of HBpin with benzene catalyzed by the combination of $[Ir(COD)(OMe)]_2$ and dcpe formed PhBpin in a low 24% yield, even after heating at 120 °C for 24 h. Moreover, complex **3b** was stable in benzene. Even heating of **3b** in benzene at 80 °C for 4 h led to little conversion, and heating at



Fig. 2 ORTEP drawing of complex **3a** with atomic numbering. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at the 35% probability level.

100 °C for 16 h led to the formation of just one equivalent of PhBcat* per iridium.

Consistent with the lack of published borylations of arenes with the common catecholate-substituted diboron reagent B_2cat_2 , the reaction of B_2cat_2 with benzene in the presence of 2.5 mol% [Ir(COD)OMe]₂ and 5 mol% dtbpy required 120 °C for 24 h, even in neat arene, to occur to completion, as summarised in eqn (3).

+
$$B_2cat_2$$
 $\frac{[Ir(COD)(OMe)]_2, dtbpy}{neat, 120 °C, 24 h}$ (3)

This lower reactivity of the catecholate complexes could result from faster decomposition of the catalyst in the presence of by-products¹⁵ formed from these reagents, or reduced reactivity of the trisboryl complex with the C–H bonds of arenes. To distinguish between these possibilities, we compared the reactions of benzene with isolated, dtbpy-ligated tris-Bpin and tris-Bcat* complexes **1a** and **1b**.

The tris-Bpin complex **1a** was previously shown to react with benzene solvent to form three equivalents of PhBpin at room temperature.¹³ In contrast, the tris-Bcat* complex **1b** is stable for several hours in benzene at room temperature. At 50 °C over 2 h, 1.95 mol (65% yield per Bcat* group on the iridium complex) of PhBcat* was formed per mol of trisboryl complex (eqn (4)). Moreover, the profile for this reaction was far from first order and suggests that the reaction occurs with an induction period or with autocatalysis that will be the subject of future studies.



This difference in reactivity between Bpin and Bcat* complexes **1a** and **1b** can be explained by differences in electron

density at the metal center. The chemical shift of the bound olefinic carbons in Bcat* complex **1b** is 4.78 ppm, which is 0.85 ppm downfield of those in the tris-Bpin complex **1a**. This difference is consistent with a less electron-rich metal center in the tris-Bcat* complex. In addition, the two carbonyl complexes [Ir(dtbpy)(Bpin)₃(CO)] **(4a)** and [Ir(dtbpy)(Bcat*)₃(CO)] **(4b)** were prepared, and, consistent with the two alkene chemical shifts, the ν_{CO} value of the tris-Bcat* complex **4b** (2017 cm⁻¹) is 30 wavenumbers higher than that (1987 cm⁻¹) for the tris-Bpin complex **4a**. This difference in electron density at the metal also agrees with calculations recently reported by Marder *et al.*¹⁶ on the σ -donating properties of Bpin and Bcat ligands.

To understand how the differences in structures and electronic properties between complexes **1a**, **1b**, and **3b** affect C–H bond cleavage, we calculated the enthalpies for oxidative addition of benzene to the dtbpy-ligated Bpin compound **1a** (previously studied theoretically by Sakaki *et al.*¹⁷) and the Bcat compounds **1b** and **3b** (eqn (5)). The pinacolate group was truncated to an ethylene glycolate group (eg), and the *tert*-butyl groups on both the bipyridine ligand and the substituted catechols were replaced by hydrogen (**1a**' and **1b**'). The bisphosphine was truncated to 1,2-bis(dimethylphosphino)-ethane (dmpe).



The ΔH for the oxidative addition of benzene to catecholboryl complex 1b' was computed to be 14.3 kcal mol⁻¹, which is 2.6 kcal mol⁻¹ higher than the 11.7 kcal mol⁻¹ value computed for oxidative addition to the Beg complex 1a'. This less favorable enthalpy for the addition of benzene to 1b' is consistent with the lower reactivity of the catecholboryl complex 1b observed experimentally. The computed enthalpies for addition to the dmpe-ligated Bpin complex (10.9 kcal mol^{-1}) and to the dmpe-ligated Bcat complex (14.6 kcal mol⁻¹) were similar to those for addition to the analogous bpy complexes. However, the dippe and dcpe ligands in the experimental work are much more sterically demanding than dmpe; thus, the actual enthalpies for reactions of the dippe and dcpe complexes are certainly much larger. Thus, these computed enthalpies are also consistent with the observed trends in reactivity.

In conclusion, we have shown that the substituents on the oxygen of dioxaborolane ligands have a strong effect on the reactivity of trisboryl complexes that are intermediates in the catalytic borylation of arenes, and that complexes of hindered bisphosphines are much less reactive toward arenes than complexes of bipyridine, despite the presence of an open coordination site in the bisphosphine complex. We propose that the effect of the substituents on boron results from differences in electron density of the metal center, which affects the enthalpy for the oxidative addition of benzene. Although a determination of the origin of the lack of reactivity of the unsaturated phosphine complexes awaits further studies, the computed energetics imply that this lack of reactivity results from a combination of increased steric hindrance in the absence of stronger electron donation by the phosphine ligand *vs*. the bipyridine ligand that would favor oxidative addition of the arene C–H bond.^{18,19}

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