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N,B-Bidentate Boryl Ligand-Supported Iridium Catalyst for Efficient Functional-Group-Directed C−H Borylation

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Supporting Information

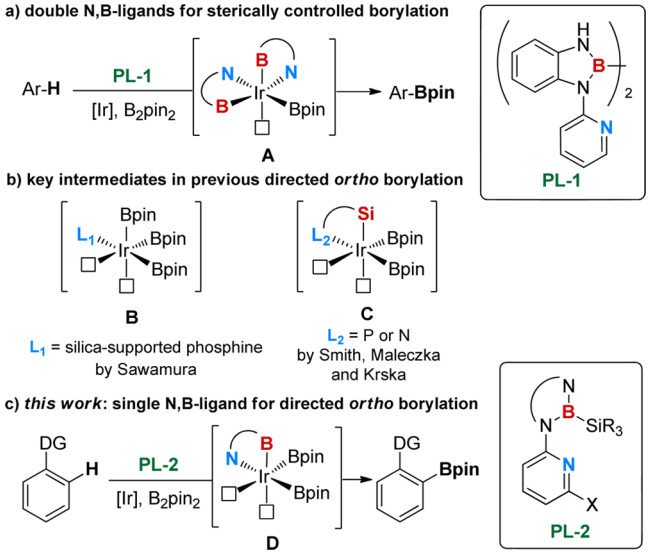
ABSTRACT: Convenient silylborane precursors for introducing N,B-bidentate boryl ligands onto transition metals were designed, prepared, and employed in ready formation of iridium(III) complexes via Si−B oxidative addition. A practical, efficient catalytic *ortho*-borylation reaction of arenes with a broad range of directing groups was developed using an *in situ* generated catalyst from the silylborane preligand **3c** and $[IrCl(COD)]_2$.

Boryl ligands, formally with a negatively charged sp^2-hybridized boron as the coordinating atom, are isoelectronic with carbene ligands.[1] In sharp contrast to the broad applications of carbene ligands, boryl ligands have been rarely used as supporting ligands in transition-metal catalysis. The utilization of metal-boryl catalysts have been challenging because (1) methods for introducing boryls onto metals in a convenient and reliable way are limited and (2) the resulting B−M bonds are highly reactive, often leading to loss of the boryl groups in subsequent steps.

In order to overcome these problems, X−B−X type pincer boryl ligands with a well-defined rigid framework have been reported.[2] Indeed, efficient catalytic reactions have been reported based on P−B−P ligand-supported transition-metal catalysts.[3] In comparison, bidentate boryl ligands may have a more flexible coordination sphere and still good stability as supporting ligands.[4] However, the application of bidentate boryls in catalysis had no precedence prior to our recent work.[5] We prepared a symmetric pyridine-tethered tetraaminodiborane(4) compound and used it as a convenient precursor (**PL-1**, Scheme 1a) to simultaneously introduce two N,B-ligands onto iridium via B−B oxidative addition. The *in situ* generated catalyst by heating the precursor together with $[Ir(OMe)(cod)]_2$ was shown to be highly effective in the borylation of various (hetero)arenes. The regioselectivity was mainly governed by steric hindrance.

To utilize bidentate boryl ligands in other reactions, however, a method for selectively introducing a single N,B-ligand would be needed.[4g] In this communication, we describe our efforts in design and synthesis of a new type of readily accessible, air insensitive, and structurally tunable precursors of N,B-bidentate ligands. Applying these preligands in catalysis culminated in a broad-scope iridium-catalyzed functional-group-directed C−H borylation reaction.

Scheme 1. Design of N,B-Bidentate Ligands for Directed Borylation



Organoboron compounds are versatile intermediates in synthetic chemistry and have been extensively used in syntheses of drugs, agrochemicals, and organic materials.[6] To facilitate the preparation of arylboron compounds, catalytic C−H borylation reactions have received significant research interest and found broad applications.[7] In particular, several approaches for catalytic *ortho* C−H borylation have been developed using catalysts based on Rh, Ir, Pd, Ru, etc.[8] Among them, two iridium-based catalytic systems have been effective for substrates with a broad range of directing groups. Sawamura's heterogeneous catalysts featured silica-supported monophosphine ligands.[8b−d] Smith, Maleczka, and Krska used a novel P,Si- or N,Si-anionic ligand to support a homogeneous iridium catalyst.[8p] Mechanistically, both systems might have created electron-rich iridium intermediates containing two vacant coordination sites, one for the directing group and the other for C−H cleavage (Scheme 1b).[9] Inspired by these works and our previous results,[5] we envisioned that an N,B-bidentate ligand might be employed for selective *ortho* borylation. We hypothesized that silylboranes of generic structure **PL-2**

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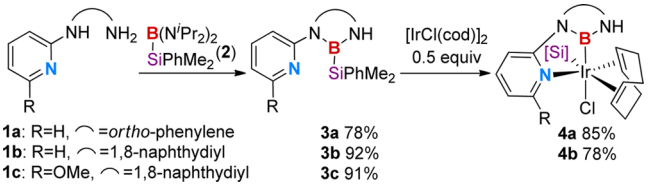
(Scheme 1c) might be suitable precursors of N,B-ligands due to three considerations. First, the Si−B bond may undergo oxidative addition with a low-valent transition metal. Second, the redundant silyl group may be selectively removed by either reductive elimination or ligand exchange.[10] Third, the sterically demanding silyl group might suppress introduction of two N,B-ligands on the metal, while hydroboranes or diboranes have been known to form double X,B-ligated complexes.[4g,5]

The syntheses of silylborane preligands and their iridium complexes are shown in Scheme 2. Treatment of *N*-(2-pyridyl)-

Scheme 2. Preparation of Preligand 3 and Their Iridium Complexes



phenylenediamine (**1a**) with 1.3 equiv of the known silylborane **2**[11] in toluene gave a new silylborane **3a** (^{11}B NMR: 32.1 ppm) in 78% isolated yield. To our delight, when a solution of **3a** and 0.5 equiv of $[IrCl(cod)]_2$ in *n*-hexane was heated at 70 °C, complex **4a** (^{11}B NMR: 38.6 ppm) was quantitatively formed based on NMR spectroscopic analysis and isolated in 85% yield. A single crystal of **4a** suitable for X-ray analysis was obtained from CH_2Cl_2/*n*-hexane solution (Figure 1). Using the same

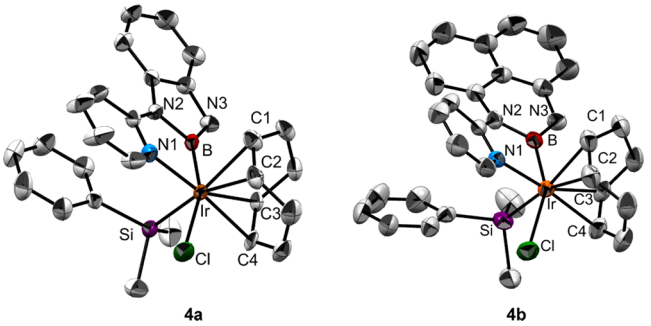
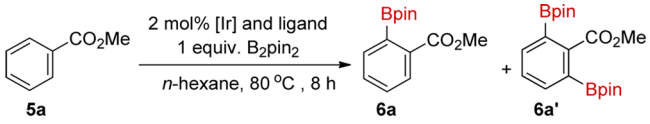


Figure 1. Molecular structures of **4a** and **4b** (50% thermal ellipsoids; hydrogen atoms were omitted for clarity).

method, we have prepared silylboranes **3b** (92%, ^{11}B NMR: 35.1 ppm) and **3c** (91%, ^{11}B NMR: 33.7 ppm) featuring a 1,8-naphthyldiamine backbone. An Ir^{III} complex **4b** based on **3b** was also obtained in good isolated yield. In **4a** and **4b**, the central Ir^{III} atom was surrounded by a N,B-bidentate boryl, a silyl, a chloride, and a 1,5-cyclooctadiene (cod) ligand in a distorted octahedral framework. The Si−Ir−Cl angles are smaller than 90° (88.9° in **4a** and 85.1° in **4b**), suggesting potentially facile Si−Cl reductive elimination. Unfortunately, the reaction of **3c** with $[IrCl(cod)]_2$ produced a complicated mixture based on NMR spectroscopy.

We then sought to test iridium-catalyzed *ortho* C−H borylation using methyl benzoate (**5a**) as the substrate and B_2pin_2 (1.0 equiv) as the borylating reagent. The effects of preligands, iridium precursors, and preformed Ir−B complexes were studied, and selected results are shown in Table 1. The combination of ligands and metal salts was crucial. A high conversion (89%) was observed when preligand **3a** and

Table 1. Catalyst Screening for *ortho* Borylation[a]



entry	precatalyst	conv. (%)[b]	yield (%)[b]	Ratio of *o*/(*m* + *p*)[b]
1	**3a**/$[Ir(OMe)(cod)]_2$	89	4 (**6a**)	5:95
2	**3a**/$[IrCl(cod)]_2$	7	–	–
3	complex **4a**	4	–	–
4	**3b**/$[Ir(OMe)(cod)]_2$	58	36 (**6a**) + 4 (**6a′**)	69:31
5	**3b**/ $[IrCl(cod)]_2$	22	19 (**6a**) + 1 (**6a′**)	91:9
6	complex **4b**	43	35 (**6a**) + 3 (**6a′**)	91:9
7	**3c**/$[IrCl(cod)]_2$	84	70 (**6a**) + 13 (**6a′**)	>99:1
8	**3c**/$[Ir(OMe)(cod)]_2$	20	7 (**6a**)	35:65

[a]Reaction conditions: methyl benzoate **5a** (0.5 mmol), B_2pin_2 (0.5 mmol), $[Ir(X)(cod)]_2$ (0.005 mmol), preligand (0.01 mmol) or complex (0.01 mmol) in 1.0 mL of *n*-hexane, 80 °C, 8 h. [b]Conversions, yields, and ratio were based on ^{1}H NMR analyses of the crude products with **5a** as the limiting reagent.

$[Ir(OMe)(cod)]_2$ were used as the catalyst. However, the regioselectivity was poor and only a trace amount of *ortho*-borylated product was formed (entry 1). The combination of **3a** with $[IrCl(cod)]_2$ or preformed complex **4a** showed low activity in this reaction (entries 2 and 3). In comparison, preligand **3b** containing a 1,8-naphthyldiamine backbone displayed dramatically improved selectivity favoring *ortho*-borylation (entries 4−6). The chlorine ligand in the iridium precursor also showed a significant positive effect over the methoxy counterpart (entries 5 and 6 vs 4). Finally, preligand **3c** that incorporates the 6-methoxy group on the pyridine moiety, in combination with $[IrCl(cod)]_2$, further improved both reactivity and selectivity. The *ortho*-borylation products were formed in high conversion and yields with excellent selectivity ($o/(m + p)$ > 99:1) (entry 7). $[Ir(OMe)(cod)]_2$ again, when combined with **3c**, led to inferior results (entry 8).

Encouraged by the preliminary results, we explored the substrate scope of alkyl arenoates (Table 2). Under the above established conditions, the catalyst **3c**/$[IrCl(cod)]_2$ demonstrated generally high activity and excellent *ortho*-selectivity for a wide range of substituted arenoates. The ratio of monoborylation vs diborylation could be improved when bulkier ester groups are used (**6a**−**6d**). Thus, *tert*-butyl benzoate cleanly afforded monoborylation product **6d** in good yield and no diborylation was observed. With this method, borylated arenoates with various substituents were readily prepared (**6e**−**6p**). When the isopropyl ester of adapalene was used, a separable mixture of α and β monoborylation products was obtained in 87% yield (**6q**). Moreover, heterocyclic compounds such as 2-methoxycarbonyl-benzofuran (**6r**) or -benzothiophene (**6s**) could be borylated at the sterically hindered 3-position.

Next we evaluated arene substrates with different directing groups (Table 3). Aryl acetates are readily available phenol derivatives and challenging substrates in a previous catalytic system.[8d] Herein under standard conditions aryl acetates could be *ortho*-borylated with good efficiency probably via a six-membered iridacycle intermediate (**8a**−**8d**). The *o*-boryl

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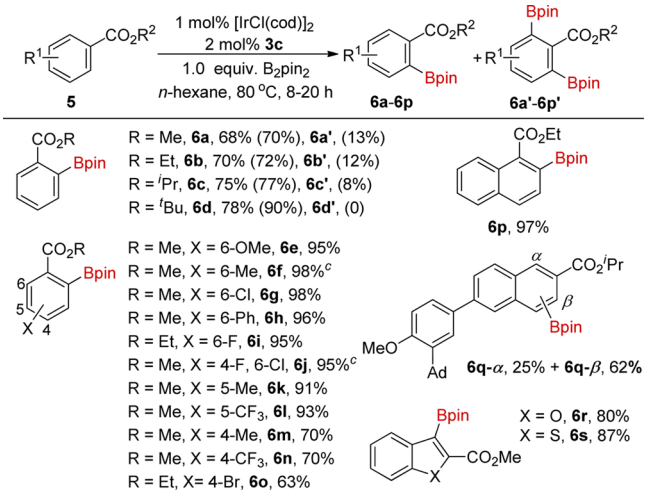
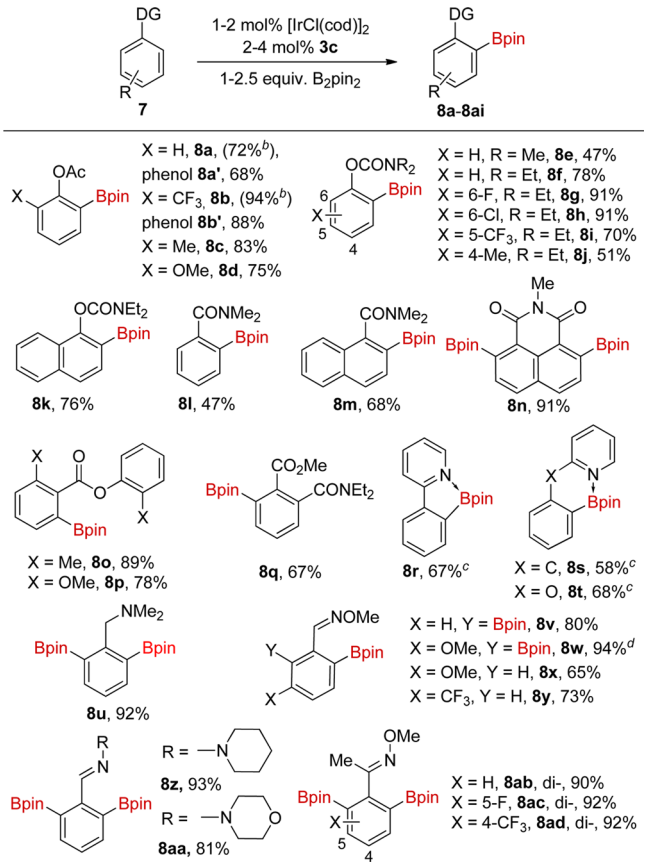
Table 2. Scope of *ortho*-Borylation of Arenoates[a,b]



[a]See SI for reaction conditions. [b]Yields calculated with **5** as the limiting reagent; NMR yields shown in parentheses. [c]5% 5-borylation product.

Table 3. Borylation with 3c/$[IrCl(cod)]_2$ Catalyst[a]

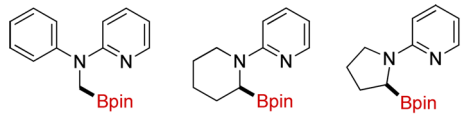


[a]See SI for experimental details; isolated yields shown. [b]NMR yields. [c]Reaction temperature 40 °C. [d]2.7 equiv of B_2pin_2 used.

acetates were deacetylated upon silica gel chromatography, and the corresponding phenols (**8a'**, **8b'**) could be obtained in good yields. Aryl carbamates were also viable substrates (**8e**–**8k**). Compared to *N*,*N*-dimethylcarbamate (**8e**, 47%), *N*,*N*-diethylcarbamate (**8f**, 78%) showed higher reactivity. *N*,*N*-Dimethylbenzamide was moderately reactive under the standard conditions (**8l**, 47%), but naphthalene-derived amides gave higher yields of the desired products (**8m**, **8n**). The competition between different directing groups could lead to chemoselective borylation. Thus, aryl benzoates were selectively borylated on the carbonyl side instead of the phenol side (**8o**, **8p**). Interestingly, borylation selectively (10:1) took place at *ortho* position to the ester group instead of the amide group (**8q**), contrasting the more prevailing directing effect observed by Smith et al.[8p] Nitrogen-based directing groups were also effective in this system.[8g] Substrates containing a pyridine moiety reacted at 40 °C and afforded monoborylation products in moderate isolated yields (**8r**–**8t**). Borylation of *N*,*N*-dimethylbenzylamine using excess B_2pin_2 generated **8u** in excellent yield. Oxime ethers and hydrazones derived from aldehydes or a ketone all gave high yields of the corresponding borylation products (**8v**–**8ad**).

Furthermore, using **3c**/$[IrCl(cod)]_2$ as the catalyst in a preliminary study, the sp^3 C–H borylation of 2-aminopyridine compounds was achieved (Table 4).[12] N-adjacent primary and

Table 4. C(sp^3)–H Borylation Using Preligand 3c[a,b]



[a]Reaction conditions: B_2pin_2 (1.0 equiv), $[IrCl(cod)]_2$ (2 mol %), **3c** (4 mol %), 60 °C. [b]Yields based on isolated materials, and NMR yields shown in parentheses.

secondary alkyl groups were selectively borylated under mild conditions, affording the monoborylation products in high yields (**9a**–**9c**). Remarkably, the potentially more reactive phenyl group in **9a** was not borylated.

Finally, to demonstrate the practicality of the borylation reaction in the synthesis of *ortho*-functionalized arenes, **6e** was prepared in 90% isolated yield from methyl *o*-methoxybenzoate (10 mmol) using 0.35 mol % of $[IrCl(cod)]_2$ and 0.7 mol % of **3c** as the catalyst. By utilizing the versatility of the C–B bond in chemical transformations, a variety of *ortho*-functionalized benzoates could be prepared in one step and good to excellent yields from **6e** without optimizations (see Supporting Information (SI)).

In conclusion, we have designed and prepared new pyridine-tethered silylboranes and demonstrated their utility as convenient precursors for introducing a single N,B-bidentate ligand onto iridium via B–Si oxidative addition. The preligands are structurally modifiable. Based on these preligands, we have developed a highly effective and practical catalyst system for directed C(sp^2)–H and C(sp^3)–H borylation of a broad range of substrates.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b11867.

Detailed experimental procedures, spectral data of products (PDF)

X-ray crystallographic data for **4a** (CIF)

X-ray crystallographic data for **4b** (CIF)

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Notes

The authors declare no competing financial interest.

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