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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 Placeholder

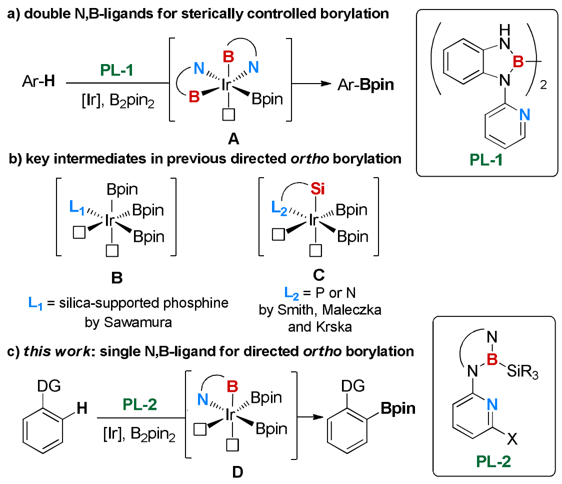
ABSTRACT: Convenient silylborane precursors for introducing N,B-bidentate boryl ligands onto transition-metals were designed, prepared and employed in ready formation of iridium(III) complexes via Si-B oxidative addition. A practical, efficient catalytic *ortho*-borylation reaction of arenes with a broad range of directing groups was developed using *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 following steps.

In order to overcome the problems, X-B-X type pincer boryl ligands with well-defined rigid framework have been reported.[2] Indeed, efficient catalytic reactions have been reported based on P-B-P ligands-supported transition-metal catalysts.[3] In comparison, bidentate boryl ligands may have 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 borylation of various (hetero)arenes. The regioselectivity was mainly governed by steric hindrance.

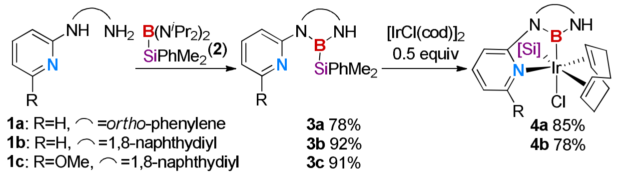
To utilize bidentate boryl ligands in other reactions, however, a method for selectively introducing a single N,B-ligand would be needed.[4g] In this communication, we describe our efforts in design and synthesis of a new type of readily accessible, air insensitive and structurally tunable precursors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

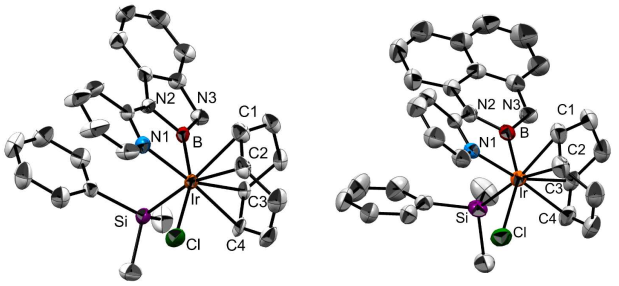
Scheme 1. Design of N,B-Bidentate Ligands for Directed Borylation



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 interests 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-8d] Smith, Maleczka and Krska used novel P,Si- or N,Si-anionic ligand to support a homogenous iridium catalyst.[8p] Mechanistically, both systems might have created electron-rich irdium 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** (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]

Scheme 2. Preparation of Preligand 3 and Their Iridium Complexes





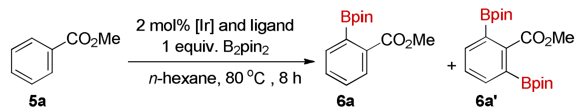
4a **4b**

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

The syntheses of silylborane preligands and their iridium complexes are shown in Scheme 2. Treatment of N-(2-pyridyl)-phenylenediamine (**1a**) with 1.3 equiv. of the known silylbornae **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. Using the same 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 iridium^{III} complex **4b** based on **3b** was also obtained in good isolated yield. In **4a** and **4b**, the central iridium^{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 $[Ir(OMe)(cod)]_2$ were used as the catalyst. However, the regioselectivity was poor and only 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 iridium precursor also showed significant positive effect over the methoxy counterpart (entries 5 and 6 vs 4). Finally, preligand **3c** that incorporates 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, and excellent selectivty ($o/(m+p)$ > 99:1) (entry 7). $[Ir(OMe)(cod)]_2$ again, when combined with **3c**, led to inferior results (entry 8).

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



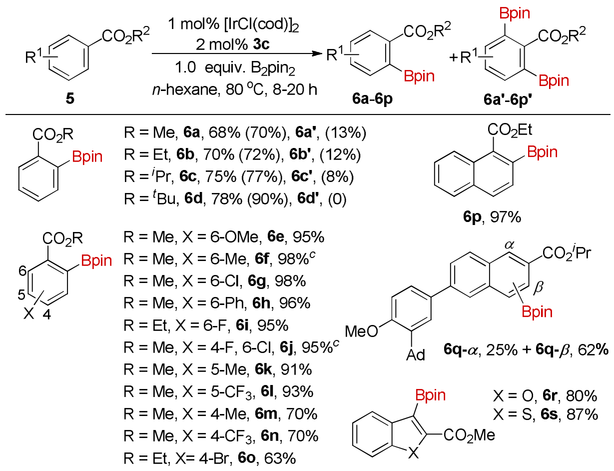
Entry	Precatalyst	Conv. (%)[b]	Yield (%)[b]	Ratio of $o/(m+p)$[b]
1	**3a**/$[Ir(OMe)(cod)]_2$	89	4 (**6a**)	5 : 95
2	**3a**/$[IrCl(cod)]_2$	7	—	—
3	complex **4a**	4	—	—
4	**3b**/$[Ir(OMe)(cod)]_2$	58	36 (**6a**)+4 (**6a'**)	69 : 31
5	**3b**/ $[IrCl(cod)]_2$	22	19 (**6a**)+1 (**6a'**)	91 : 9
6	complex **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.

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 isopropyl ester of adapalene was used, a separable mixture of α and β mono-borylation products was obtained in 87% yield (**6q**). Moreover, heterocyclic compounds such as 2-methoxycarbonylbenzofuran (**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 previous catalytic system.[8d] Herein under standard conditions aryl acetates could be *ortho*-borylated in good efficiency probably via a six-membered iridacycle intermediate (**8a-8d**). The *o*-boryl 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 mono-borylation 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**).

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



R = Me, **6a**, 68% (70%), **6a'**, (13%)
R = Et, **6b**, 70% (72%), **6b'**, (12%)
R = ^{i}Pr, **6c**, 75% (77%), **6c'**, (8%)
R = ^{t}Bu, **6d**, 78% (90%), **6d'**, (0)

R = Me, X = 6-OMe, **6e**, 95%
R = Me, X = 6-Me, **6f**, 98%[c]
R = Me, X = 6-Cl, **6g**, 98%
R = Me, X = 6-Ph, **6h**, 96%
R = Et, X = 6-F, **6i**, 95%
R = Me, X = 4-F, 6-Cl, **6j**, 95%[c]
R = Me, X = 5-Me, **6k**, 91%
R = Me, X = 5-CF_3, **6l**, 93%
R = Me, X = 4-Me, **6m**, 70%
R = Me, X = 4-CF_3, **6n**, 70%
R = Et, X= 4-Br, **6o**, 63%

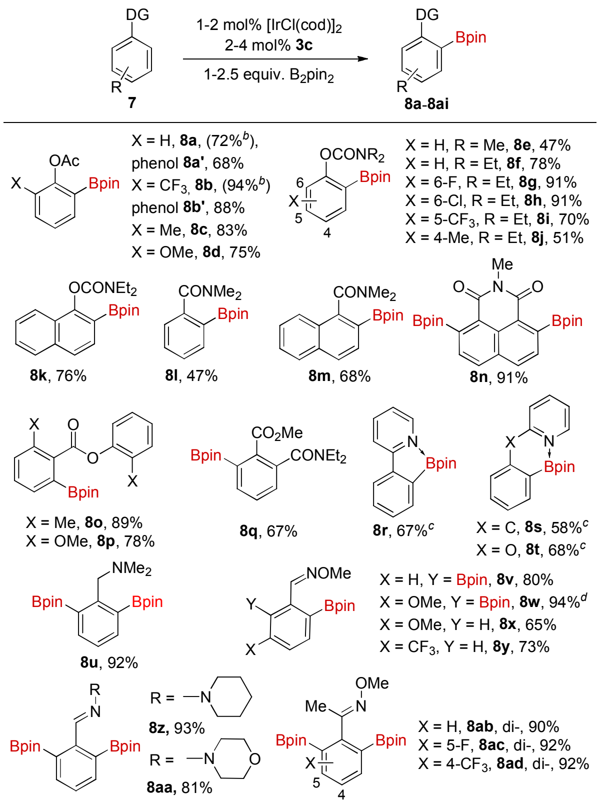
X = O, **6r**, 80%
X = S, **6s**, 87%

[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.

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 secondary alkyl groups were selectively borylated under mild conditions, affording the mono-borylation 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 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. Taking advantage of the versatility of 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 SI).

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



X = H, **8a**, (72%[b]),
phenol **8a'**, 68%
X = CF_3, **8b**, (94%[b])
phenol **8b'**, 88%
X = Me, **8c**, 83%
X = OMe, **8d**, 75%

X = H, R = Me, **8e**, 47%
X = H, R = Et, **8f**, 78%
X = 6-F, R = Et, **8g**, 91%
X = 6-Cl, R = Et, **8h**, 91%
X = 5-CF_3, R = Et, **8i**, 70%
X = 4-Me, R = Et, **8j**, 51%

X = Me, **8o**, 89%
X = OMe, **8p**, 78%

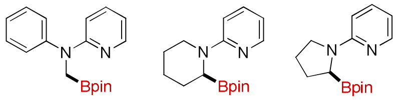
X = C, **8s**, 58%[c]
X = O, **8t**, 68%[c]

X = H, Y = Bpin, **8v**, 80%
X = OMe, Y = Bpin, **8w**, 94%[d]
X = OMe, Y = H, **8x**, 65%
X = CF_3, Y = H, **8y**, 73%

X = H, **8ab**, di-, 90%
X = 5-F, **8ac**, di-, 92%
X = 4-CF_3, **8ad**, di-, 92%

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

Table 4. C(sp^3)-H Borylation using Preligand 3c[ab]



9a, 70% (88%) **9b**, 71% (78%) **9c**, 80% (85%)

[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.

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

Detailed experimental procedures, spectral data of products and X-ray crystallographic data for **4a** and **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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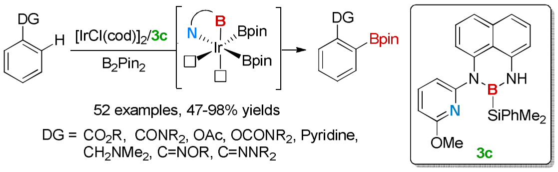
DG
H
[IrCl(cod)]2/3c
B2Pin2
N
B
Bpin
Ir
Bpin
DG
Bpin
52 examples, 47-98% yields
DG = CO2R, CONR2, OAc, OCONR2, Pyridine, CH2NMe2, C=NOR, C=NNR2
N
NH
B
N
SiPhMe2
OMe
3c