Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

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Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Iridium-Catalyzed *Ortho*-C–H Borylation of Aromatic Aldimine Derived from Pentafluoroaniline with Bis(pinacolate)diboron†

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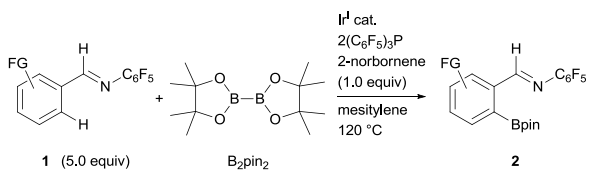
Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

The development of an Ir-catalyzed *ortho*-C–H borylation with aromatic aldimines derived from pentafluoroaniline is reported. This reaction proceeded at 120 °C to afford the corresponding borylated products in high yield with good regioselectivity using an Ir complex formed *in situ* from [Ir(OMe)(cod)]$_2$/2(C_6F_5)$_3$P in the presence of 2-norbornene.

Arylboronic acids and their derivatives are versatile synthetic intermediates.[1] The most straightforward and attractive method for the synthesis of arylboronic acid derivatives is the direct C–H borylation of arenes.[2] Recently, we have developed the regioselective *ortho*-C–H borylation of various benzoates or aryl ketones using the complex [Ir(OMe)(cod)]$_2$/[3,5-(CF_3)$_2$$C_6H_3$]$_3$P or ($C_6H_5$)$_3$As.[3] At the same time, several groups have also reported similar borylations of functionalized arenes.[4] The regioselectivity of these reactions is probably derived from the interaction between the coordinating O atoms in the directing group and the transition metal center. However, benzaldehyde derivatives are not amenable to these directed borylation due to the poor chemical stability of the formyl group.[5] Very recently, Sawamura's and Lassaletta's groups reported directed *ortho* borylations using imidazolidines[6] or *N*,*N*-dimethylhydrazones[7] as the coordinating groups which are the synthetic equivalent of an aldehyde. Although these reactions produced the desired products in high yields with excellent regioselectivities, the formation of diborylated side products and the use of hazardous hydrazine might hamper the industrial application of these reactions.

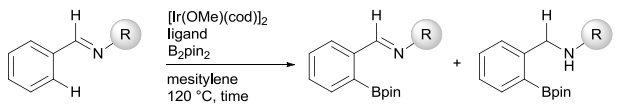
Herein, we describe the *ortho*-C–H borylation of stable aromatic aldimines **1** with B_2pin_2, catalyzed by *in-situ*-generated Ir complexes consisting of readily available [Ir(OMe)(cod)]$_2$ and (C_6F_5)$_3$P in mesitylene as the solvent. The reaction proceeds regioselectively at 120 °C in the presence of 2-norbornene (1.0 equiv) to give the corresponding aromatic boron compounds **2** in high yields without the formation of diborylated side products (Scheme 1). The synthetic utility of this procedure is demonstrated by the subsequent formation of biphenyl carbaldehyde.



Scheme 1. *Ortho*-C–H borylation of aromatic ardimines **1** with B_2pin_2

To find an aldimine moiety suitable for the *ortho*-C–H borylation, the borylation of various aromatic aldimines (5.0 equiv) was examined using [Ir(OMe)(cod)]$_2$ (1.5 mol%) and a number of ligands (Table 1, entries 1–11). Consequently, the pentafluorophenyl-substituted aldimine **1a**, which is very stable towards air and moisture, reacted smoothly with B_2pin_2 using tris(pentafluorophenyl)phosphine (C_6F_5)$_3$P[8] (6.0 mol%) as the ligand to produce the desired product **2a** in 120% yield as judged by ^{1}H NMR based on B_2pin_2 (entry 1). No diborylated side products were observed under these reaction conditions; however, a reduction side product **3a** was obtained in 25% yield. The borylation of *N*-aryl (**1b**–**1d**), alkyl **1e**, sulfonyl **1f** or hydroxyl **1g** aldimines did not proceed (entries 2–7). We then screened possible ligands (entries 8–11). No reaction occurred when using [3,5-(CF_3)$_2$$C_6H_3$]$_3$P or ($C_6H_5$)$_3$As, which can weakly coordinate to the Ir metal center like (C_6F_5)$_3$P (entries 8 and 9).

Table 1. Optimization of the *N*-substitution of the imine and reaction conditions using various aromatic aldimines[a]



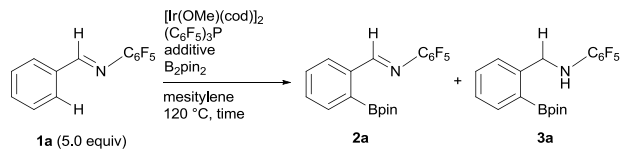
entry	R	ligand	time (h)	yield (%)[b] 2	3
1	C_6F_5 (**1a**)	(C_6F_5)$_3$P	3	120	25
2	4-$CF_3C_6H_4$ (**1b**)	(C_6F_5)$_3$P	24	0	0
3	4-$MeOC_6H_4$ (**1c**)	(C_6F_5)$_3$P	24	0	0
4	C_6H_5 (**1d**)	(C_6F_5)$_3$P	24	0	0
5	*t*-Bu (**1e**)	(C_6F_5)$_3$P	24	0	0
6	Ts (**1f**)	(C_6F_5)$_3$P	24	0	0
7	OH (**1g**)	(C_6F_5)$_3$P	24	0	0
8	C_6F_5 (**1a**)	[3,5-(CF_3)$_2$$C_6H_3$]$_3$P	24	0	0
9	C_6F_5 (**1a**)	(C_6H_5)$_3$As	24	0	0
10	C_6F_5 (**1a**)	(C_6H_5)$_3$P	24	0	0
11	C_6F_5 (**1a**)	(C_6H_5O)$_3$P	24	0	0
12	C_6F_5 (**1a**)	—	24	0	0
13[c]	C_6F_5 (**1a**)	(C_6F_5)$_3$P	3	112	23
14[d]	C_6F_5 (**1a**)	(C_6F_5)$_3$P	3	91	11
15[e]	C_6F_5 (**1a**)	(C_6F_5)$_3$P	24	29	n.d.

[a]The reactions were carried out using aldimines (**1a**–**g**) (1.625 mmol), B_2pin_2 (0.325 mmol), [Ir(OMe)(cod)]$_2$ (0.0049 mmol), and (C_6F_5)$_3$P (0.0196 mmol). [b] ^{1}H NMR yields based on B_2pin_2 using 1,1,2,2-tetrachloroethane as an internal standard. [c] [Ir(OMe)(cod)]$_2$ (0.0049 mmol), and (C_6F_5)$_3$P (0.0098 mmol) was used. [d] [Ir(OMe)(cod)]$_2$ (0.0049 mmol), and (C_6F_5)$_3$P (0.0294 mmol) was used. [e] 1.0 equiv of **1a** was used.

Other phosphine ligands also did not result in borylation (entries 10 and 11). The reaction did not produce **2a** without $(C_6F_5)_3P$ (entry 12). The use of 3 mol % and 9 mol % of $(C_6F_5)_3P$ did not improve the yield of borylated product **2a** (entries 13 and 14). The yield of **2a** significantly decreased using one equivalent of **1a**, indicating the excess use (5 equiv) of **1a** is necessary to obtain the products in high yield. (entry 15).

Although the desired borylated product could be obtained in high yield, separation of the imine **2a** from the reduction side product **3a** was very difficult. We thus screened various additives to suppress the reduction (Table 2). Addition of 1-hexanol or H_2O, which can consume HBpin via hydrolysis, to the standard conditions described above (Table 1, entry 1) resulted in disappointing yields (Table 2, entries 1 and 2). Alkene derivatives were good inhibitors for the reduction while maintaining the high catalytic activity (entries 3–7).[9] For acyclic alkenes such as 1-octene, 1,7-octadiene and 3,3-dimethyl-1-butene, the undesired formation of **3a** was partially inhibited to less than 11% (entries 3–5). Use of 2-norbornene successfully inhibited the reduction of **2a** to **3a**, providing **2a** in the highest yield of 131% by ^{1}H NMR and in 90% isolated yield (entry 6). A trace amount of **3a** was detected with a reduced yield of **2a** (126%) when 0.5 equivalent of 2-norbornene was used (entry 7).

Table 2. Optimized reaction conditions using various additives[a]

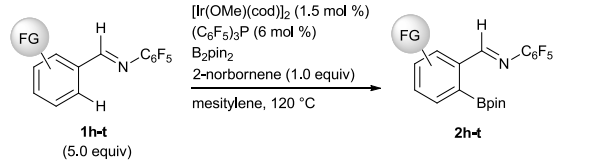


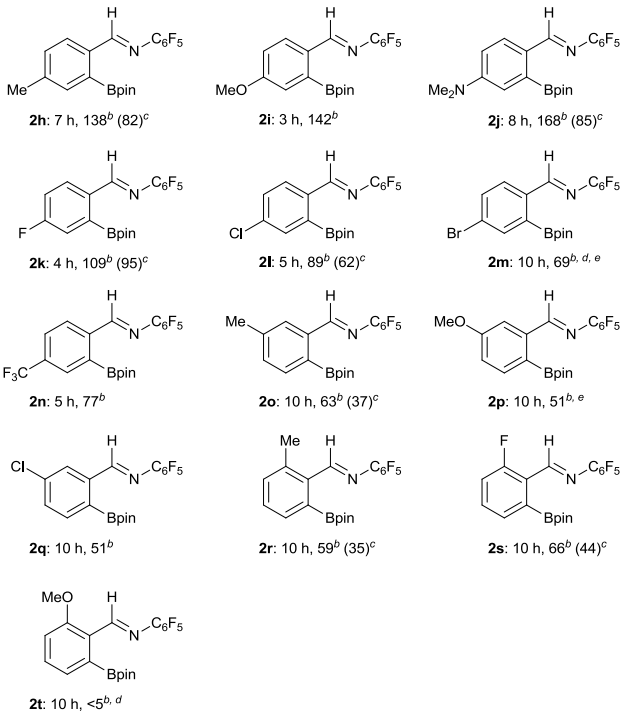
entry	additive (equiv)	time (h)	yield (%)[b] 2a	3a
1	1-hexanol (1.0)	3	trace	trace
2	H_2O (1.0)	3	20	trace
3	1-octene (1.0)	3	108	11
4	1,7-octadiene (1.0)	3	102	11
5	3,3-dimethyl-1-butene (1.0)	3	106	<5
6	2-norbornene (1.0)	4	131(90)[c]	0
7	2-norbornene (0.5)	3	126	trace

[a] The reactions were carried out by using aldimine **1a** (1.625 mmol), B_2pin_2 (0.325 mmol), $[Ir(OMe)(cod)]_2$ (0.0049 mmol), and $(C_6F_5)_3P$ (0.0196 mmol). [b] ^{1}H NMR yields based on B_2pin_2 using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield.

The Ir catalyst system [Ir/$(C_6F_5)_3$P/2-norbornene] was applied to various aromatic aldimines derived from non-hazardous $C_6F_5NH_2$ and aromatic aldehydes with electron-donating or electron-withdrawing groups. The results are listed in Table 3. The *para*-substituted aldimines bearing an electron-donating group such as methyl (**1h**), methoxy (**1i**) and dimethylamino (**1j**) reacted smoothly with B_2pin_2 to afford the desired products in high yields without the formation of diborylated side products (**2h**: 138%, **2i**: 142%, **2j**: 168%). Although transition-metal catalysis often exhibit high reactivity toward C–X bonds (X: F, Cl, Br), the halogenated aldimines **1k**, **1l** and **1m** underwent chemo- and regio-selective borylation at the *ortho*-C–H bond, in moderate to high yields, without any evidence of side reactions involving the C–X bonds (**2k**: 109%, **2l**: 89%, **2m**: 69%). The reaction of CF_3-containing aldimine **1n** also afforded the corresponding **2n** in 77% yield. The reaction of *meta*- substituted aldimine derivatives (**1o**–**1q**) proceeded, whereas the corresponding products were obtained in low yields (**2o**: 63%, **2p**: 51%, **2q**: 51%). Steric hindrance around the reaction site generated by the *meta*-substituent most probably caused the low yields for **2o**–**2q**. The borylated products were also obtained in low yields when *ortho*-substituted aldimines (**1r**–**1t**) were used (**2r**: 59%, **2s**: 66%,**2t**: >5%).

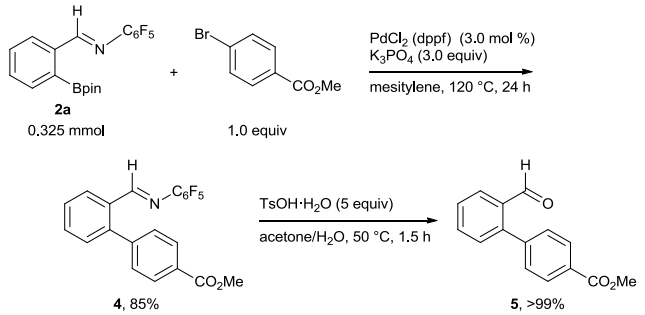
Table 3. *Ortho*-C–H borylation of various aldimines with $B_2(pin)_2$[a]





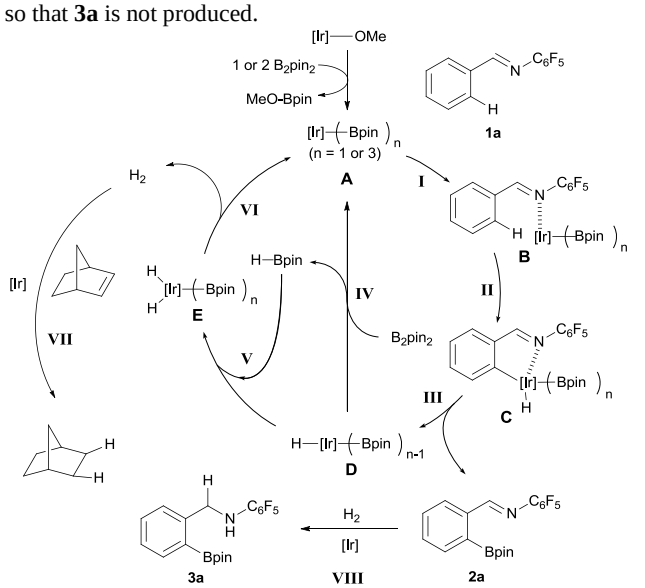
[a] The reactions were carried out by using aldimines **1h-t** (1.625 mmol), B_2pin_2 (0.325 mmol), $[Ir(OMe)(cod)]_2$ (0.0049 mmol), and $(C_6F_5)_3P$ (0.0196 mmol). [b] ^{1}H NMR yields based on B_2pin_2 using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield. [d] $[Ir(OMe)(cod)]_2$ (2.5 mol %) and $(C_6F_5)_3P$ (10 mol %) were used. [e] The reaction was conducted in the absence of 2-norbornene.

The utility of these borylated aldimines was demonstrated by the transformation to 2-formylbiphenyl compound **5** (Scheme 2).[10] The cross-coupling reaction of arylboronate **2a** with methyl 4-bromobenzoate (1.0 equiv) in the presence of $PdCl_2$(dppf) (3 mol%), and K_3PO_4 (3.0 equiv), in mesitylene at 120 °C for 24 h afforded the desired product **4** in 85% isolated yield. The product **4** was then treated with TsOH·H_2O (5.0 equiv) in acetone/H_2O (1:1) at 50 °C for 1.5 h, to give the hydrolyzed product **5** in >99% isolated yield. This procedure should be applicable for other borylated products as a useful method to obtain these potentially bioactive compounds.



Scheme 2. Synthetic utility of **2a** and recovery of the aldehyde functionality

A plausible mechanism for this reaction is shown in Scheme 3. The mono- (n = 1) or tris- (n = 3) boryliridium complexes **A** are first produced by reaction of the Ir(I) precursor with B_2pin_2.[11] Next, the electron-donating nitrogen atom in the imino group coordinates to the Ir metal center (Path I, **B**). Oxidative addition of the *ortho*-C–H bond to **B** then produces the pseudo metallacycle **C** (Path II). After reductive elimination, the Ir–hydride complexes **D** and the product **2a** are produced (Path III). Finally, subsequent oxidative addition of B_2pin_2 (Path IV) or HBpin (Path V) to **D**, followed by reductive elimination of HBpin or H_2, regenerates **A**. 2-Norbornene acts as a H_2 scavenger in this reaction (Path VII), inhibiting the reduction pathway (Path VIII) so that **3a** is not produced.



Scheme 3. A plausible mechanism for the *ortho*-selective C–H borylation

In summary, an iridium complex formed from $[Ir(OMe)(cod)]_2$ and $(C_6F_5)_3P$ was found to be an efficient catalyst with B_2pin_2 for the *ortho*-C–H borylation of stable aromatic aldimines derived from non-hazardous pentafluoroaniline in the presence of 2-norbornene. The borylation produced the corresponding arylboronates in high yields with regioselectivity without the formation of diborylated side products. This report is the first example using 2-norbornene in C–H borylation as a H_2 scavenger. The borylation of substrates containing halogens such as F, Cl and Br afforded the corresponding products in high yields with good chemoselectivity. Additionally, we demonstrated the utility of **2a** by the transformation to the biphenyl carbaldehyde **5**.

This work was supported by a Grant-in-Aid for Scientific Research (B) (No. 21350049) from the Ministry of Education, Culture, Sports, Science and Technology, Japan, and the Funding Program for Next Generation World-Leading Researchers (NEXT Program, GR002).

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† Electronic Supplementary Information (ESI) available: experimental procedures and spectral analyses. See DOI: 10.1039/b000000x/

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