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Room temperature borylation of arenes and heteroarenes using stoichiometric amounts of pinacolborane catalyzed by iridium complexes in an inert solvent†

Tatsuo Ishiyama,*[a] Yusuke Nobuta,[a] John F. Hartwig[b] and Norio Miyaura*[a]

[a] *Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan. E-mail: ishiyama@org-mc.eng.hokudai.ac.jp; Fax: +81-11-706-6562; Tel: +81-11-706-6562*

[b] *Department of Chemistry, Yale University, P.O. Box 208107, New Haven, Connecticut 06520-8107, USA*

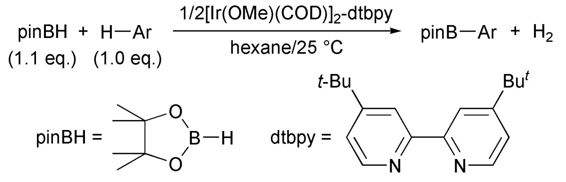
Received (in Cambridge, UK) 12th September 2003, Accepted 8th October 2003
First published as an Advance Article on the web 22nd October 2003

Aromatic C–H borylation of arenes and heteroarenes using stoichiometric amounts of pinacolborane was catalyzed by an iridium complex generated from $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ and 4,4′-di-*tert*-butyl-2,2′-bipyridine at room temperature in hexane and afforded the corresponding aryl- and heteroarylboronates in high yields with excellent regioselectivities.

Aryl- and heteroarylboron derivatives have been applied to various fields of chemistry.[1] Traditional methods for their synthesis are based on the reactions of trialkylborates with arylmagnesium or -lithium reagents derived from haloarenes, which are the most common and convenient for large-scale preparations.[2] However, two milder catalytic methods have been developed recently. First, catalytic coupling of aryl and heteroaryl halides with tetra(alkoxy)diboron[3] or di(alkoxy)borane[4] reagents produces arylboronates without magnesium or lithium intermediates. Second, catalytic borylation of arenes and heteroarenes leads to arylboronates without any halogenated arene.

Previous work has demonstrated the reaction of arenes and heteroarenes with bis(pinacolato)diboron (pin$_2$B$_2$, pin = Me$_4$C$_2$O$_2$) or pinacolborane (pinBH) in the presence of various transition metal complexes to form arylboronates.[5–11] Most of these studies have been conducted with an excess of substrate, and the methods have required the use of pin$_2$B$_2$ instead of pinBH to obtain high yields. No reactions of a 1 : 1 ratio of substrate and the readily accessible and inexpensive pinBH, instead of the expensive pin$_2$B$_2$, have been reported. We disclose the culmination of several steps toward the development of such an aromatic C–H borylation process. With modest loadings of $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ (COD = 1,5-cyclooctadiene) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy), the reaction of pinBH with many arenes and heteroarenes in a 1 : 1 ratio occurs in an inert solvent at room temperature (Scheme 1).

To achieve the borylation of arenes and heteroarenes at room temperature with equimolar amounts of pinBH and substrate, several combinations of Ir(I) precursors (0.03 mmol of Ir) and ligands (0.03 mmol) were investigated as catalysts for the reaction of pinBH (1.1 mmol) with 1,3-dichlorobenzene (1.0 mmol) in hexane (6 mL) at 25 °C for 8 h. Of the precursors and ligands examined, the combination of $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ and dtbpy[12] efficiently catalyzed the borylation to form isomerically pure 5-boryl-1,3-dichlorobenzene in 86% yield.



Scheme 1

The choice of catalyst precursor was crucial for reactions to be observed at room temperature. Although the combination of $\frac{1}{2}$[Ir(OAc)(COD)]$_2$ and dtbpy produced the borylated product in 42% yield after 8 h, the combination of dtbpy and either $\frac{1}{2}$[IrCl(COD)]$_2$ or [Ir(COD)$_2$]BF$_4$ formed no borylated product.

The effects of steric and electronic properties of bipyridine ligands were evaluated using $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ as a catalyst precursor. Catalysts bearing 2,2′-bipyridine (bpy), 4,4′-di-Me-bpy, and 5,5′-di-Me-bpy displayed moderate or good reactivity, but catalysts bearing 3,3′-di-Me-bpy or 6,6′-di-Me-bpy displayed little activity. These results indicated the importance of a parallel arrangement of two pyridine rings and a relatively unhindered coordination sphere at iridium. Reactions catalyzed by complexes containing electron-rich derivatives of bpy generated more active catalysts than those containing electron-poor derivatives. Catalysts containing 4,4′-di-Me$_2$N-bpy produced the highest yields (88%). We evaluated reactions catalyzed by $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ and dtbpy for studies on reaction scope because of the high solubility of the catalyst and the commercial availability of the ligand.

The choice of inert solvent was also important to observe efficient borylation. The reactions were faster in non-polar solvents, such as hexane, than in more polar and coordinating solvents. The order of reactivity in different solvents was hexane > mesitylene > DME > DMF.

Reactions of equimolar amounts of pinBH with arenes and heteroarenes catalyzed by the combination of $\frac{1}{2}$[Ir(OMe)(COD)]$_2$ and dtbpy at room temperature in hexane are summarized in Table 1. In contrast to the control of regioselectivity of electrophilic and nucleophilic substitution of arenes by the electronic properties of substituents, the regiochemistry of C–H borylation of arenes is primarily controlled by the steric effects of these substituents. Reactions occurred at C–H bonds located *meta* or *para* to a substituent in preference to those located in the *ortho* position. Thus, 1,2- 1,4-, and 1,3-dichlorobenzenes gave a single product (Entries 1–3), but the 1,4-isomer reacted slowly (Entry 2). In addition, the borylation of 1,3-disubstituted arenes containing two different substituents at the 1 and 3 positions produced isomerically pure arylboronates in excellent yields (Entries 4–9). In the case of five-membered heteroarenes, the electronegative heteroatom causes the C–H bonds at the α-positions to be active[13] so that the borylation of indole, benzo[*b*]furan, and benzo[*b*]thiophene selectively occurred at the α-positions to form single isomers in high yields (Entries 10–12).

Functional group tolerance of the borylation is higher than that of boronate synthesis through magnesium or lithium reagents. The reaction occurred with substrates possessing Cl, Br, I, CF$_3$, and OMe groups, but also with the more reactive CO$_2$Me and CN. The aryl iodide and bromide underwent borylation at the C–H bond (Entries 4, 6, and 7) without C–X

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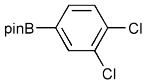
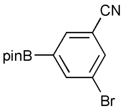
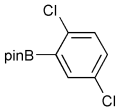
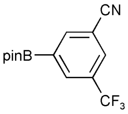
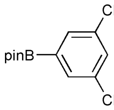
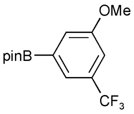
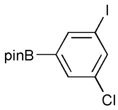
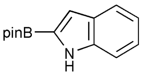
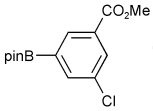
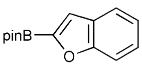
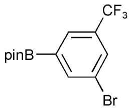
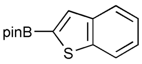
† Electronic supplementary information (ESI) available: experimental procedures and spectral analyses of products. See http://www.rsc.org/suppdata/cc/b3/b311103b/

DOI: 10.1039/b311103b

Table 1 C–H borylation of arenes and heteroarenes[a]

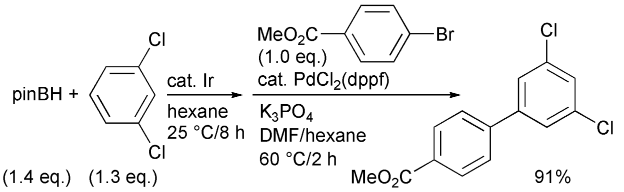
Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
1		73% (8 h)	7		74% (2 h)
2		22% (24 h)	8		83% (1 h)
3		86% (8 h)	9		73% (24 h)
4		67% (8 h)	10		99% (0.5 h)
5		70% (24 h)	11		90% (1 h)
6		80% (8 h)	12		99% (2 h)

[a] All reactions were carried out at 25 °C with pinacolborane (1.1 mmol), arene or heteroarene (1.0 mmol), $[Ir(OMe)(COD)]_2$ (0.015 mmol), dtbpy (0.03 mmol), and hexane (6 mL). [b] GC yields based on arenes or heteroarenes. Reaction times are in parentheses.

bond cleavage.[14] Electron-withdrawing substituents activated the arene for the borylation process.

The mechanism of the catalytic borylation of arenes and heteroarenes with pinBH may proceed through an Ir(III)–Ir(V) cycle.[10–12,15] Generation of a $(pinB)_3Ir(III)$ intermediate[10,11a,16] by the reaction of an Ir(I) complex with pinBH, oxidative addition of a C–H bond to the $(pinB)_3Ir(III)$ intermediate to yield an $(Ar)(H)(pinB)_3Ir(V)$ species, and reductive elimination of pinB–Ar from the $(Ar)(H)(pinB)_3Ir(V)$ species to give a $(H)(pinB)_2Ir(III)$ complex would be followed by oxidative addition of pinBH and reductive elimination of H_2 to regenerate the $(pinB)_3Ir(III)$ intermediate.

The direct preparation of aryl- and heteroarylboronates from pinBH and the corresponding arenes or heteroarenes creates an efficient, one-pot, two-step procedure for the synthesis of unsymmetrical biaryls. The biaryl shown in Scheme 2 was produced in 91% yield by sequential generation of 5-boryl-1,3-dichlorobenzene from pinBH (1.43 mmol) and 1,3-dichlorobenzene (1.3 mmol) in hexane (2 mL), followed by reaction of the resulting arylboronate with added methyl 4-bromobenzoate (1.0 mmol), $PdCl_2(dppf)$ (0.03 mmol), K_3PO_4 (3.0 mmol), and DMF (4 mL) at 60 °C.[17]



Scheme 2

In summary, aromatic C–H borylation of arenes and heteroarenes with pinBH without an excess of substrate or reagent provides a convenient, economical, and environmentally benign route to regiodefined aryl- and heteroarylboronates. Further investigations to survey the scope and limitation of this C–H borylation, including that of monosubstituted arenes, other heteroarenes, alkenes, and alkanes, as well as the application of this catalyst system to other types of C–H functionalizations, are in progress.

This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 14078101, “Reaction Control of Dynamic Complexes”) from the Ministry of Education, Culture, Sports, Science and Technology, Japan and by the National Science Foundation (JFH). T.I. thanks the Itoh Science Foundation and The Akiyama Foundation for support of a part of his work.

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