



Development of recyclable iridium catalyst for C–H borylation

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ABSTRACT

Aromatic C–H borylation using $[\text{IrCl}(\text{COD})]_2$ and 2,2'-bipyridinedicarboxylic acids was studied. 2,2'-Bipyridine-4,4'-dicarboxylic acid was complexed with $[\text{IrCl}(\text{COD})]_2$ in the presence of bis(pinacolato)diboron. The resulting iridium catalyst could be readily separated from the reaction mixture by simple filtration, and the recovered catalyst under a nitrogen atmosphere was still active and could be reused more than 10 times.

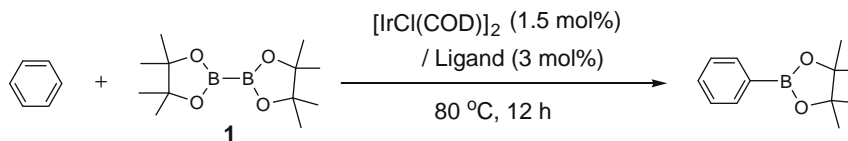
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Arylboryonic acids and their derivatives have been prepared by reacting arylmetal compounds and boronic acid esters.¹ However, these processes involve highly reactive organolithium or organomagnesium reagents. Recently, iridium-catalyzed aromatic C–H borylation has been developed^{2a–i} and the conditions are much safer and milder than the traditional methods. The most effective catalyst developed by Miyaura and Hartwig^{3a–f} was generated from 4,4'-di-*tert*-butyl-2,2'-bipyridine, an iridium complex such as $[\text{IrCl}(\text{COD})]_2$ or $[\text{IrOMe}(\text{COD})]_2$, and a boron reagent such as bis(pinacolato)diboron (Pin_2B_2 , **1**) or pinacolborane (PinBH , **2**). A trisboryl iridium complex, which was the active species in this cat-

alyst system, was isolated and well characterized.⁴ Although a high turnover number was observed for the catalysts in this reaction, it was difficult to recover and reuse the catalysts because they were unstable and highly soluble in organic media. It is highly desirable for industrial-scale processes to develop a new catalyst system that allows easy recovery and reuse of precious iridium catalysts.

In 2007, Zhu et al. reported that iridium(I) salicylaldehydicyclooctadiene complexes could be used for aromatic C–H borylation in the presence of tetra-2-pyridylpyrazine and an ionic liquid. These catalytic systems could be reused at least six times.⁵ However, before the catalyst could be reused, the products first had to be

Table 1
Substitution effect of 2,2'-bipyridinedicarboxylic acids^a



Ligand				
	3	4	5	6
Yield ^b	77%	86%	78%	79%

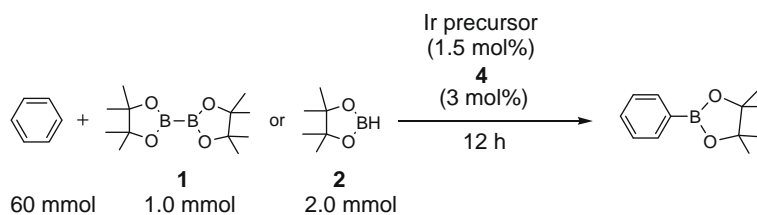
^a All reactions were performed at 80 °C for 12 h with benzene (60 mmol), **1** (1.0 mmol), and $[\text{IrCl}(\text{COD})]_2$ (1.5 mol %), ligand (3 mol %).

^b Yield was determined by GC using 4-ethylbiphenyl as an internal standard.

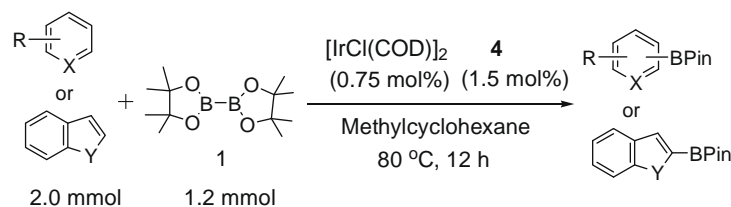
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Table 2

Conditions for the iridium-catalyzed C–H borylation of benzene by bis(pinacolato)diboron and pinacolborane



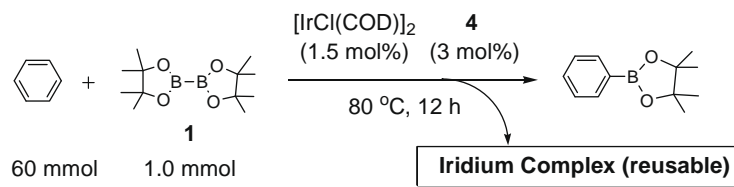
Entry	Ir precursors	Boranes	Temp	Yield ^a
1	$[\text{IrCl}(\text{COD})]_2$	1	80 °C	86%
2	$[\text{IrOMe}(\text{COD})]_2$	1	80 °C	76%
3	$[\text{IrCl}(\text{COD})]_2$	1	25 °C	trace
4	$[\text{IrOMe}(\text{COD})]_2$	1	25 °C	trace
5	$[\text{IrCl}(\text{COD})]_2$	2	80 °C	78%
6	$[\text{IrOMe}(\text{COD})]_2$	2	80 °C	80%

^a Yields based on borylating reagent in **1** or **2** were determined by GC analysis using 4-ethylbiphenyl as an internal standard.**Table 3**Use of other arenes and heteroarenes in an $[\text{IrCl}(\text{COD})]_2$ and **4** system^a

Entry	Arene	Product	Yield ^b (%)
1			20 ^{c,d}
2			76 ^{c,e}
3			64 ^{c,f}
4			83
5			95
6			84
7			86
8			78

^a A mixture of $[\text{IrCl}(\text{COD})]_2$, **4**, and **1** in methylcyclohexane was heated at 80 °C for 5 min. A solution of an arene in methylcyclohexane was added to the mixture and the whole was heated at 80 °C for 12 h.^b Yield was determined by GC using 4-ethylbiphenyl as an internal standard and the isomer ratio was determined by ¹H NMR.^c Isolated yield.^d *o*:*m*:*p* = 6:76:18.^e *m*:*p* = 50:50.^f *m*:*p* = 58:42.3,5-Diborylated compound was obtained in 13% yield based on trifluoromethylbenzene.

Table 4
C–H borylation of benzene catalyzed by recyclable iridium catalyst^{a,b}



Cycle	Yield ^c (%)	Ir leaching ^d (ppm)	Cycle	Yield ^c (%)	Ir leaching ^d (ppm)
1	98	<0.1	6	99	<0.1
2	98	<0.1	7	99	<0.1
3	98	<0.1	8	96	<0.1
4	99	<0.1	9	99	<0.1
5	99	<0.1	10	99	<0.1

^a Iridium complex was prepared under standard C–H borylation conditions and isolated by filtration in a glove box.

^b All reactions were performed at 80 °C for 12 h with benzene (240 mmol), **1** (4.0 mmol), and recycled catalyst.

^c Yield was determined by GC using 4-ethylbiphenyl as an internal standard.

^d Ir leaching into filtrate was checked by ICP analysis.

separated from the reaction mixture by distillation. Thus, a more convenient catalyst that is easier to recover and reuse is still needed.

To develop a new recyclable catalyst, we focused on the feasibility of 2,2'-bipyridinedicarboxylic acids (BPDCA),^{6a–d} such as 2,2'-bipyridine-3,3'-dicarboxylic acid (**3**), 2,2'-bipyridine-4,4'-dicarboxylic acid (**4**)⁷, and 2,2'-bipyridine-5,5'-dicarboxylic acid (**5**), as ligands. Since **3**, **4**, and **5** are less soluble in most organic media than their parent compound, we expect that they might be useful for separating the catalyst from the reaction mixture. Here, we report aromatic C–H borylation using BPDCA as a functional ligand.

We first examined the effect of the positions of carboxyl groups on the 2,2'-bipyridine ring for the C–H borylation of benzene with bis(pinacolato)diboron (**1**) using [IrCl(COD)]₂ as an iridium precursor. The results are shown in Table 1. Borylations were typically carried out in benzene (60 mmol) with bis(pinacolato)diboron **1** (1.0 mmol) in the presence of [Ir(COD)Cl]₂ (0.015 mmol) and BPDCA (0.03 mmol) at 80 °C for 12 h under a nitrogen atmosphere. All reactions with BPDCA, or even its sodium salt, as a ligand proceeded smoothly and gave phenylpinacolborane in good yield. Among the ligands we examined, **4** was most effective and was selected for further survey.

In these reactions, the yellow reaction mixture turned black at around 70 °C. After the reactions were completed, the black iridium complex could be separated by filtration, and evaporation of the colorless filtrate gave the product with high purity (GC >98%). In the filtrates of the reactions using **4** and **5** (entries 2 and 3), iridium metal was not detected by ICP analysis (less than 0.1 ppm). However, 1.0 ppm of iridium metal was observed in the filtrate of the reaction using **3** (entry 1). It seemed that iridium complex prepared from **3** was not sufficiently stable under these reaction conditions.⁸

Next, we surveyed combinations of iridium complex and boron reagents. As shown in Table 2, [IrOMe(COD)]₂ and pinacolborane could be used in the C–H borylation of benzene with **4** as a ligand.

In contrast to Miyaura's catalyst system,^{3d} the reaction using **4** as a ligand did not proceed at room temperature. The active species might not be produced because 2,2'-bipyridine-4,4'-dicarboxylic acid shows very low solubility in benzene at room temperature.

We also used other substrates with the new catalyst system (Table 3). Methylcyclohexane was used as a solvent. To avoid the deactivation caused by coordination of the substrate to the catalyst precursor, substrates were added into the mixture of [Ir(COD)Cl]₂,

4, and **1** which were heated at 80 °C for 5 min. In the reaction of anisole, the borylated product was obtained in low yield. The methoxy group may coordinate with the iridium catalyst because 10 ppm iridium was detected in the filtrate. On the other hand, reactions using other substrates proceeded smoothly and could be tolerated by a wide variety of functionalities, such as Cl, CO₂Me, and CF₃ groups, as with Miyaura's catalyst.^{3b}

Since the iridium complex could be removed from the reaction mixture by filtration, we turned our attention to recycling the catalyst. When the reaction mixture was filtered under air, the iridium complex did not show any catalytic activity. On the other hand, when the iridium complex was filtered under nitrogen in a glove box, the isolated iridium complex could be reused more than 10 times for one week. No iridium was leached into the filtrates. The results are shown in Table 4.⁹

Although we were interested in the structure of this iridium complex, it was difficult to analyze because of its instability under air and its insolubility in organic solvents. At the beginning of the reaction, cyclooctane was observed in the reaction mixture by GC analysis, which indicated the dissociation of cyclooctadiene (COD) from [IrCl(COD)]₂ and hydrogenation to cyclooctane due to the generated hydrogen. On the other hand, cyclooctane was not observed in the reaction using the recycled iridium complex. ICP analysis of the complex showed that it contained both iridium and boron atoms in a molar ratio of 1:2.3–2.5. Based on these results, this complex may have a structure similar to that of the tris(boryl)iridium complex reported by Miyaura and co-workers.^{3b}

In conclusion, we have developed a new recyclable iridium catalyst for C–H borylation. The iridium catalyst was readily separated from the reaction mixture by filtration and the recovered catalyst could be reused more than 10 times. This catalyst system could be applied to an industrial process for C–H borylation.

A more detailed mechanistic study and a structural investigation of the insoluble iridium complex are underway.

Acknowledgments

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- Representative procedure for Table 4; A 50 mL test tube equipped with a magnetic stirring bar and a three-way cock with a septum inlet was charged with [IrCl(COD)]₂ (40.4 mg, 0.06 mmol), 2,2'-bipyridine-4,4'-dicarboxylic acid (29.2 mg, 0.12 mmol), and bis(pinacolato)diboron (1.02 g, 4.0 mmol) and then flushed with nitrogen. Benzene (240 mmol) was added and the mixture was stirred at 80 °C for 12 h in a glove box. The reaction mixture was filtered and the residue was washed twice with 10 mL benzene to give a black powder (89 mg). Combined filtrate and washings were analyzed by GC and GC mass spectroscopy to determine the yield using 4-ethylbiphenyl as an internal standard. The black powder was used for a second run under the same conditions. Leaching of iridium metal was determined by ICP analysis.