Full Paper

Received: 3 April 2013

Revised: 6 May 2013

(wileyonlinelibrary.com) DOI 10.1002/aoc.3020

BiCl₃-catalyzed carbon-carbon cross-coupling of organoboronic acids with aryl iodides

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A procedure for BiCl₃-catalyzed carbon-carbon cross-coupling reaction of organoboronic acids with aryl iodides is described. This protocol has a wide substrate scope and uses an inexpensive and non-toxic catalyst. Copyright © 2013 John Wiley & Sons, Ltd.

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Keywords: carbon-carbon cross-coupling; organoboronic acid; aryl iodide; Bi(III)

Introduction

Metal-catalyzed C–C cross-coupling chemistry has been strenuously developed because of its use in the synthesis of natural products and other biologically active molecules.^[1] In particular, sp²-sp² cross-couplings have had a great impact on drug research and development and the new strategies have transformed pharmaceutical research.^[2] In fact, today metalcatalyzed coupling reactions have become a reliable and indispensable tool for the synthesis of pharmaceuticals and building blocks for natural products synthesis.^[3–6] In particular, palladium-catalyzed cross-coupling reactions are unparalleled because of their spectacular catalytic activity and selectivity.^[7–23] Over the last three decades, the Suzuki coupling reaction has become unarguably the most efficient method for the C-C bond formation. This discovery was honored by awarding the Nobel Prize in Chemistry in 2010.^[24]

In subsequent developments, various inexpensive and environmentally benign catalysts have been developed for C-C cross-coupling reactions. In this regard, transition and nontransition metals such as copper,^[25–27] cobalt,^[28] iron,^[29–34] nickel,^[34–38] zinc,^[39] indium,^[40] solid supported catalyst^[41–44] and nano particles^[45-49] have been used for C-C cross-coupling reactions. Notably, bismuth(III) halides have drawn significant attention during the last three decades as reagents that are inexpensive, relatively non-toxic, environmentally benign and fairly insensitive to moisture.^[50-54] These have been explored as efficient catalysts for various organic transformations, such as oxidation,^[55] allylation,^[56] Mannich reaction,^[57] epoxide-opening reactions^[58] and Diels-Alder reactions.^[59-61] Our continued interest in bismuth chemistry have led us to investigate the catalytic activity of bismuth(III) compounds towards C-C crosscoupling reaction. Herein we report the BiCl₃-catalyzed cross-coupling reaction between organoboronic acids and aryl iodides.

Results and Discussion

C–C Cross-Coupling Reaction

To develop an optimal catalytic system for the C–C cross-coupling, various reaction parameters such as effect of temperature,

catalyst, solvent, ligand and time were studied. In the initial investigation, phenyl iodide and phenyl boronic acid were chosen as model substrates and the reaction was carried out in DMSO at 120°C in the presence of BiCl₃, KOH (as base) and tetramethylethylenediamine (TMEDA) as ligand. Table 1 provides a preliminary summary of the scope and limitation of the bismuth-catalyzed cross-coupling reaction. Our initial experiments were focused on the optimization of the catalyst, and various Bi(III) salts such as BiCl₃, BiBr₃, Bil₃ and Bi(NO₃)₃,5(H₂O) were used. Results revealed that BiCl₃ (10 mol%) was found to be the most effective catalyst, which afforded 80% coupled product (Table 1, entry 2). Among the various bases, KOH (2 equiv.) provided the best results in this reaction (Table 1, entry 2). When 3 equiv. KOH was used, the yield drops to 70% and the increased base concentration reduced the yield. This may be due to the generation of other reaction products upon increasing the KOH concentration. The effect of ligand on the coupling reaction was studied using different nitrogen-based ligands (L1-L4 and neutral L5). The results have shown that the 10 mol% L3 (TMEDA) was the most efficacious ligand for the coupling reaction (Table 2, entry 3).

To analyze the effect of solvent, the reactions were carried out in different solvents such as CH_3NO_2 , CH_3CN , THF, 1,4-dioxane, DMF, DMSO, *N*-methyl-2-pyrrolidone (NMP) and toluene. It was found that the reaction proceeded very well in DMSO and DMF and provided good yields; in fact, a better yield was obtained in the case of DMSO (Table 1, entry 2 vs. 7). Furthermore, polar aprotic NMP provided only 60% desired product (Table 1, entry 13). In the case of toluene the yield was very poor (Table 1, entry 9). To confirm whether in the presence of KOH DMSO plays any crucial role in the coupling reaction,^[62,63] the reaction was carried out in the absence

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Table 1. Optimization of reaction conditions for C–C couplin

Table 1.	optimization of reaction co	nations for c=c coupling			
		+ B(OH) ₂	catalyst (10 mol %) L3 (10 mol %) base (2 equiv.) solvent, 120°C		
Entry	Base	Bi(III) catalyst	Solvent	Time (h) ^a	Yield (%) ^b
1	NaOH	BiCl ₃	DMSO	30	76
2	КОН	BiCl ₃	DMSO	27	80
3	KO- <i>t</i> -Bu	BiCl ₃	DMSO	29	70
4	K ₂ CO ₃	BiCl ₃	DMSO	33	64
5	Cs ₂ CO ₃	BiCl ₃	DMSO	31	67
6	Na ₂ CO ₃	BiCl ₃	DMSO	35	62
7	KOH	BiCl ₃	DMF	27.5	77
8	KOH	BiCl ₃	1,4-Dioxane	34	50
9	КОН	BiCl ₃	Toluene	40	20
10	КОН	BiCl ₃	CH ₃ NO ₂	32	53
11	КОН	BiCl ₃	CH₃CN	33	50
12	КОН	BiCl ₃	THF	35	52
13	КОН	BiCl ₃	NMP	29	60
14	КОН	BiBr ₃	DMSO	27	52
15	КОН	Bil ₃	DMSO	27	55
16	КОН	Bi(NO ₃) ₃ ·5(H ₂ O)	DMSO	27	45
17	КОН	—	DMSO	27	5
18		BiCl ₃	DMSO	27	

^aMonitored using TLC.

^bIsolated yield after column chromatography of the crude product.



of BiCl₃ (Table 1, entry 17) and only 5% coupled product was obtained. In the controlled experiment, when BiCl₃ was used in the absence of KOH, the desired product was not observed (Table 1, entry 18). Furthermore, other Bi(III) salts as catalyst resulted in much lower yield.

After the optimized reaction conditions were determined, to extend the substrate scope of the protocol various aryl iodides were used. We have observed that the electron-donating substrates afford product in a short time with good yields as compared to the electron-withdrawing substrates (Table 3, entries 2–6 vs. entries 8 and 9).

The kinetics of the coupling of phenyl boronic acid and phenyl iodide were studied. High-pressure liquid chromatography (HPLC) was used to determine the various starting materials





Entry	R ₁	R ₂	Time (h) ^a	Yield (%) ^b	Characterization ref.
1	Н	Н	27	80	[64]
2	Me	Н	24	81	[64]
3	C_2H_5	Н	25	80	[65]
4	C(CH ₃) ₃	Н	25	81	[65]
5	2-OMe	Н	28	80	[64]
6	4-OMe	Н	27.5	79	[64]
7	Cl	Н	29	79	[65]
8	F	Н	32	78	[65]
9	COOH	Н	35	77	[66]
10	Н	OMe	29	80	[64]
11	Н	Me	28	82	[64]
12	Н	CF ₃	29	81	[65]
13	Н	2-Naphthyl-B(OH) ₂	30	80	[65]
14	2-Naphthyl-I	Н	35	79	[65]
15	2-Pyridyl-I	Н	40	80	[66]
16	Н	CN	35	79	[66]



Figure 1. Concentration versus time plot for the ${\rm BiCl}_3$ -catalyzed coupling reaction of phenyl iodide and phenyl boronic acid.



At different concentrations, the rate of the reaction was calculated by estimating the slope of the tangent at each point on the concentration curve. From these data, $\log_{10}(\text{rate})$ versus $\log_{10}(\text{concentration})$ was plotted (Fig. 2) and the order (*n*) and rate constant (*k*) were obtained from the slope of the line and its intercept on the \log_{10} (rate) axis. From these figures it is clear that the reaction proceeds with second-order kinetics ($n \approx 2$) and the rate constant is 0.699 l mol⁻¹ h⁻¹.



Figure 2. van't Hoff differential plot for the BiCl₃-catalyzed coupling reaction of phenyl iodide and phenyl boronic acid.

Conclusions

We have demonstrated a simple method for the carbon–carbon cross-coupling reactions between organoboronic acid and aryl iodide. The procedure may be attractive from an environmental point of view.

Experimental

General Considerations

All the aryl halides and boronic acids were purchased from Aldrich and used as received. All the solvents were purchased from Ranchem, India, and purified using standard methods. The products are characterized by recording ¹H and ¹³C NMR using a Bruker Avance 400 MHz instrument. HPLC analysis was done using a Waters HPLC instrument fitted with a Waters 515 pump and a Waters 2487 dual-wavelength absorbance detector. BiCl₃ was purchased from Aldrich (Catalogue No. 224839) and used as received. Inductively coupled plasma mass spectrometry did not indicate the presence of trace palladium or copper impurities.

Typical Procedure for C-C Coupling Reaction

To a suspension of boronic acid (1.2 mmol) and BiCl₃ (10 mol%) in DMSO, aryl iodide (1 mmol) was added, followed by TMEDA (10 mol%) and KOH (2 equiv.). The reaction mixture was heated to 120°C and the reaction progress was monitored using thin-layer chromatography (TLC). The reaction mixture was extracted repeatedly with ethyl acetate. All the volatile organics were removed under reduced pressure. The crude product was purified using column chromatography. The spectral data of the various products matched with the available literature (see Supporting Information).

Supporting Information

Supporting information may be found in the online version of this article.

Acknowledgement

The authors thank the Department of Science and Technology, New Delhi, for financial support.

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