doi:10.1246/cl.2011.913

Paper in Celebration for the 2010 Nobel Prize in Chemistry

# An Improvement of Nickel Catalyst for Cross-coupling Reaction of Arylboronic Acids with Aryl Carbonates by Using a Ferrocenyl Bisphosphine Ligand

Ryoichi Kuwano* and Ryosuke Shimizu
*Department of Chemistry, Graduate School of Sciences, Kyushu University,*
*6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-8581*

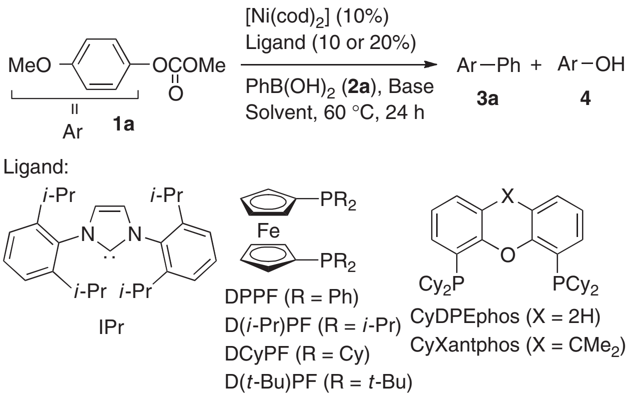
(Received March 9, 2011; CL-110201; E-mail: rkuwano@chem.kyushu-univ.jp)

Aryl carbonates work as electrophilic substrates for the Suzuki–Miyaura reaction in the presence of the nickel catalyst, which is generated from [Ni(cod)$_2$] and ferrocenyl bisphosphine, DCyPF. The nickel catalyst allowed the cross-coupling reaction of arylboronic acids with non-benzo-fused aryl carbonates as well as naphthyl substrates.

Nickel- or palladium-catalyzed cross-coupling reaction of arylmetals with aryl halides is regarded as a powerful method for connecting two aromatic compounds through a C(sp$^2$)–C(sp$^2$) bond.[1] Either iodide or bromide is commonly used as the leaving group of the electrophilic substrate. Chloro-[2] or sulfoxyarene[3] is sometimes chosen as the coupling partner of the organometallic reagent. However, the reactive leaving groups cause toxicity and carcinogenicity of the aryl halides or sulfonates. Furthermore, aryl halides lack environmental biodegradability. Such properties of the electrophilic substrates present a drawback of the cross-coupling reaction. To improve the cross-coupling reaction in usability and environmental friendliness, some research groups including us have recently developed coupling reactions using carboxylates[4–9] as the leaving groups of the electrophilic substrate. Aryl esters can be readily prepared through esterification of phenols. In general, the functionalities themselves do not have a serious impact on animals and the environment. The by-product stemming from the leaving group is easily decomposed by microbes.

Recently, Garg reported the Suzuki–Miyaura reaction of aryl carbonates with [NiCl$_2$(PCy$_3$)$_2$] catalyst.[10,11] However, the use of a carbonate leaving group has been limited to naphthyl substrates. Here, we developed a new catalyst for the reaction of aryl carbonates. The nickel catalysis was enhanced by use of a chelate bisphosphine ligand. The improved catalyst allowed the C–C bond formation between arylboronic acids and non-benzo-fused aryl carbonates.

**Table 1.** Optimization of reaction conditions[a]

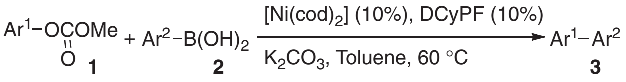


| Entry | Ligand | Solvent | Base | Yield/%[b] | |
|---|---|---|---|---|---|
| | | | | **3a** | **4** |
| 1[c] | PCy$_3$ | Toluene | K$_3$PO$_4$ | 0 | 19 |
| 2[d] | PCy$_3$ | Toluene | K$_3$PO$_4$ | 3 | 33 |
| 3[d] | PCy$_3$ | Toluene | K$_2$CO$_3$ | 1 | 13 |
| 4[d] | IPr | Toluene | K$_2$CO$_3$ | 1 | 12 |
| 5 | DPPF | Toluene | K$_2$CO$_3$ | 0 | 16 |
| 6 | D(*i*-Pr)PF | Toluene | K$_2$CO$_3$ | 11 | 12 |
| 7 | DCyPF | Toluene | K$_2$CO$_3$ | 37 | 11 |
| 8 | CyDPEphos | Toluene | K$_2$CO$_3$ | 0 | 21 |
| 9 | CyXantphos | Toluene | K$_2$CO$_3$ | 0 | 21 |
| 10 | D(*t*-Bu)PF | Toluene | K$_2$CO$_3$ | 0 | 16 |
| 11 | DCyPF | CPME | K$_2$CO$_3$ | 16 | 13 |
| 12 | DCyPF | THF | K$_2$CO$_3$ | 4 | 26 |
| 13 | DCyPF | DMF | K$_2$CO$_3$ | 0 | 65 |
| 14 | DCyPF | *t*-AmOH | K$_2$CO$_3$ | 6 | 35 |
| 15 | DCyPF | Toluene | K$_3$PO$_4$ | 24 | 43 |
| 16 | DCyPF | Toluene | KO(*t*-Bu) | 0 | 21 |
| 17 | DCyPF | Toluene | KHCO$_3$ | 13 | 2 |
| 18 | DCyPF | Toluene | Li$_2$CO$_3$ | 4 | 3 |
| 19 | DCyPF | Toluene | Na$_2$CO$_3$ | 21 | 0 |
| 20 | DCyPF | Toluene | Cs$_2$CO$_3$ | 2 | 20 |
| 21[e] | DCyPF | Toluene | K$_2$CO$_3$ | 25 | 46 |

[a]Reactions were conducted on a 0.20 mmol scale in 0.6 mL of solvent. The ratio of **1a**:**2a**:[Ni(cod)$_2$]:ligand:base was 10:12:1:1:20. [b]GC yields (average of two runs). [c][NiCl$_2$(PCy$_3$)$_2$] was used in place of [Ni(cod)$_2$]–2PCy$_3$ catalyst. [d]The ratio of [Ni(cod)$_2$]:ligand was 1:2. [e]The reaction was conducted at 80 °C.

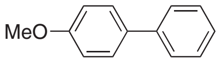
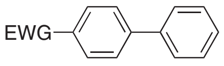
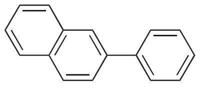
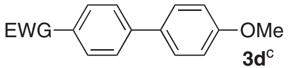
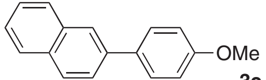
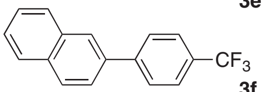
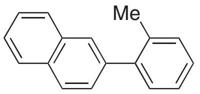
We attempted the reaction of aryl carbonate **1a** with phenylboronic acid (**2a**) at 60 °C in the presence of 10 mol % [NiCl$_2$(PCy$_3$)$_2$]. However, the nickel catalyst failed to produce the unsymmetrical biaryl compound **3a** (Table 1, Entry 1). Thus, a variety of phosphine ligands were examined in the cross-coupling by using [Ni(cod)$_2$] as a catalyst precursor. As with PCy$_3$, the heterocyclic carbene ligand, which is effective for the cross-coupling reaction of aryl pivalate with amines,[12] failed in the desired carbon–carbon bond formation (Entry 4). The formation of **3a** was observed in the reaction using a ferrocene-bridged chelate ligand, D(*i*-Pr)PF or DCyPF[13] (Entries 6 and 7). Choice of the alkyl substituents on phosphorus is crucial for the nickel catalysis. DPPF– and D(*t*-Bu)PF–nickel complexes exhibited no catalytic activity for the cross-coupling of **1a** with **2a** (Entries 5 and 10). The tether of the bisphosphine ligand also strongly affected the catalytic reaction. No cross-coupling reaction took place in the presence of a nickel complex bearing CyDPEphos or CyXantphos (Entries 8 and 9). In most cases, the catalytic reaction accompanied the hydrolytic decomposition of

**Table 2.** Cross-coupling of arylboronic acids with aryl carbonates[a]



**1a:** $Ar^1$ = 4-(MeO)$C_6H_4$
**1b:** $Ar^1$ = 4-(*t*-BuO$_2$C)$C_6H_4$
**1c:** $Ar^1$ = 2-naphthyl

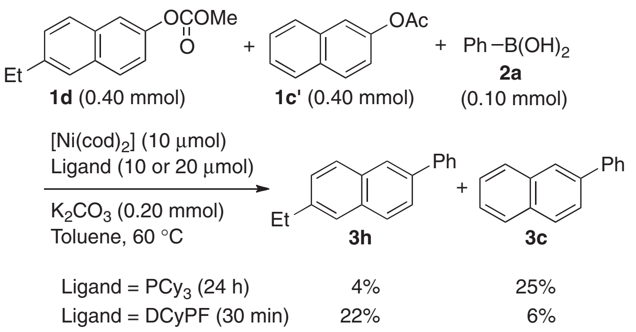
**2a:** $Ar^2$ = Ph
**2b:** $Ar^2$ = 4-(MeO)$C_6H_4$
**2c:** $Ar^2$ = 4-($F_3$C)$C_6H_4$
**2d**: $Ar^2$ = 2-Me$C_6H_4$

| Entry | 1 | 2 | Time/h | Product (3) | Yield/%[b] |
|---|---|---|---|---|---|
| 1 | **1a** | **2a** | 96 |  **3a** | 46 |
| 2 | **1b** | **2a** | 72 |  **3b**[c] | 71 |
| 3 | **1c** | **2a** | 24 |  **3c** | 83 |
| 4[d] | **1c** | **2a** | 96 | | 80 |
| 5[e] | **1b** | **2b** | 72 |  **3d**[c] | 82 |
| 6 | **1c** | **2b** | 48 |  **3e** | 95 |
| 7 | **1c** | **2c** | 48 |  **3f** | 64 |
| 8 | **1c** | **2d** | 96 |  **3g** | 63 |

[a]Reactions were conducted on a 0.50 mmol scale in 1.0 mL of toluene. The ratio of **1**:**2**:[Ni(cod)$_2$]:ligand:base was 10:12:1:1:20. [b]Isolated yields. [c]EWG– = *t*-BuO$_2$C–. [d]The reaction was conducted with 5% catalyst loading. [e]The reaction was conducted on a 0.20 mmol scale.

**1a** to phenol **4**. The side reaction took precedence over the desired cross-coupling, when the reaction was conducted in polar solvent (Entries 11–14) as well as with a stronger and/or more soluble base (Entries 15–20). Raising the reaction temperature also facilitated the undesirable formation of **4** and disfavored the cross-coupling (Entry 21). The cross-coupling product **3a** was obtained in 46% isolated yield from the reaction carried out for 96 h (Table 2, Entry 1).

The [Ni(cod)$_2$]–DCyPF catalyst was applied to the synthesis of various biaryl compounds (Table 2). As with typical cross-coupling reactions, electron-deficient aryl carbonates **1b** and **1c** were more reactive than electron-rich **1a**, affording the coupling products **3b** and **3c** in good yields (Entries 2 and 3). The reaction of **1c** with **2a** proceeded without significant loss of the yield of **3c** when the catalyst loading was reduced to 5 mol % (Entry 4). In contrast to the electrophilic substrate, the reactivity of arylboronic acid was increased by the electron-donating group on the aromatic ring. *p*-Methoxyphenylboronic acid (**2b**) reacted with **1c** to give the product **3e** in 95% yield (Entry 6). Meanwhile, the trifluoromethyl group of **2c** seemed to cause decrease in the yield of cross-coupling product (Entry 7). *o*-Substituted arylboronic acid **2d** worked as a coupling partner of aryl carbonates (Entry 8).



**Scheme 1.** Competitive experiment of the cross-coupling reaction.

In the precedent work,[5,10] PCy$_3$ is the preferable ligand to the nickel-catalyzed cross-coupling reaction involving the cleavage of the inert C(sp$^2$)–O bond. However, the results of Table 1 indicate that the monophosphine is useless for the reaction of aryl carbonates. The aryl carbonates were allowed to couple with the arylboronic acids by using bidentate ligand, DCyPF. In order to clarify the difference in reactivity between PCy$_3$– and DCyPF–nickel catalyst, we conducted a set of competitive experiments using an equimolar mixture of carbonate **1d** and acetate **1c′** (Scheme 1). In the competitive experiment with PCy$_3$, formation of **3c** prevailed over that of **3h**. However, use of DCyPF ligand led to preferential formation of **3h**. The observations indicate that the PCy$_3$–nickel complex is favorable for the C–O bond cleavage of aryl acetates but cannot activate the C–O bond of aryl carbonates. In contrast, coordination of DCyPF ligand enables the nickel catalyst to undergo the oxidative addition of aryl carbonates, but the reaction with the acetates might be restrained by use of the bidentate bisphosphine.[14] Although the detailed mechanism of the reaction is unclear, the chemoselectivities of the nickel catalysts may be governed by the number of phosphorus atoms on the nickel atom in the active catalyst species.[5d]

In summary, we have developed a new effective catalyst for the Suzuki–Miyaura reaction of aryl carbonates. The carbonate electrophiles couple with arylboronic acids through [Ni(cod)$_2$]–DCyPF catalyst, giving biaryl compounds in good yields. The nickel catalyst enables the organoborons to react with non-benzo-fused aryl carbonates.[15]

This work was supported by Grant-in-Aid for the Grobal COE Program, "Science for Future Molecular Systems" from MEXT.

This paper is in celebration of the 2010 Nobel Prize awarded to Professors Richard F. Heck, Akira Suzuki, and Ei-ichi Negishi.

## References and Notes

1 a) *Metal-Catalyzed Cross-Coupling Reactions, Second Completely Revised and Enlarged Edition*, ed. by A. de Meijere, F. Diederich, Wiley-VCH, Weinheim, **2004**, Vols. 1–2. b) *Cross-Coupling Reactions. A Practical Guide*, ed. by N. Miyaura, Springer-Verlag, Berlin, **2002**. c) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359.

2 a) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374. b) S. Saito, M. Sakai, N. Miyaura, *Tetrahedron Lett.* **1996**, *37*, 2993. c) A. F. Littke, G. C. Fu, *Angew. Chem., Int. Ed.* **1998**, *37*, 3387. d) D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 9722.

3 a) W. J. Scott, G. T. Crisp, J. K. Stille, *J. Am. Chem. Soc.* **1984**, *106*, 4630. b) A. Huth, I. Beetz, I. Schumann, *Tetrahedron* **1989**, *45*, 6679.

4 Reviews: a) L. J. Gooßen, K. Gooßen, C. Stanciu, *Angew. Chem., Int. Ed.* **2009**, *48*, 3569. b) D.-G. Yu, B.-J. Li, Z.-J. Shi, *Acc. Chem. Res.* **2010**, *43*, 1486. c) B.-J. Li, D.-G. Yu, C.-L. Sun, Z.-J. Shi, *Chem.—Eur. J.* **2011**, *17*, 1728. d) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346.

5 a) K. W. Quasdorf, X. Tian, N. K. Garg, *J. Am. Chem. Soc.* **2008**, *130*, 14422. b) B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu, Z.-J. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 14468. c) B.-J. Li, Y.-Z. Li, X.-Y. Lu, J. Liu, B.-T. Guan, Z.-J. Shi, *Angew. Chem., Int. Ed.* **2008**, *47*, 10124. d) Z. Li, S.-L. Zhang, Y. Fu, Q.-X. Guo, L. Liu, *J. Am. Chem. Soc.* **2009**, *131*, 8815. e) C.-L. Sun, Y. Wang, X. Zhou, Z.-H. Wu, B.-J. Li, B.-T. Guan, Z.-J. Shi, *Chem.—Eur. J.* **2010**, *16*, 5844. f) G. A. Molander, F. Beaumard, *Org. Lett.* **2010**, *12*, 4022.

6 J. Lindh, J. Sävmarker, P. Nilsson, P. J. R. Sjöberg, M. Larhed, *Chem.—Eur. J.* **2009**, *15*, 4630.

7 a) J.-Y. Yu, R. Kuwano, *Angew. Chem., Int. Ed.* **2009**, *48*, 7217. b) H. W. Lee, F. Y. Kwong, *Synlett* **2009**, 3151.

8 B.-J. Li, L. Xu, Z.-H. Wu, B.-T. Guan, C.-L. Sun, B.-Q. Wang, Z.-J. Shi, *J. Am. Chem. Soc.* **2009**, *131*, 14656.

9 Itoh et al. had reported the cross-coupling reaction of organometals with a highly strained alkenyl carboxylate, diketene: a) K. Itoh, M. Fukui, Y. Kurachi, *J. Chem. Soc., Chem. Commun.* **1977**, 500. b) K. Itoh, T. Yogo, Y. Ishii, *Chem. Lett.* **1977**, 103. c) K. Itoh, T. Harada, H. Nagashima, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3746.

10 K. W. Quasdorf, M. Riener, K. V. Petrova, N. K. Garg, *J. Am. Chem. Soc.* **2009**, *131*, 17748.

11 The cross-coupling reaction of organometals with carbamates: a) S. Sengupta, M. Leite, D. S. Raslan, C. Quesnelle, V. Snieckus, *J. Org. Chem.* **1992**, *57*, 4066. b) A. Antoft-Finch, T. Blackburn, V. Snieckus, *J. Am. Chem. Soc.* **2009**, *131*, 17750.

12 T. Shimasaki, M. Tobisu, N. Chatani, *Angew. Chem., Int. Ed.* **2010**, *49*, 2929.

13 DCyPF: 1,1′-bis(dicyclohexylphosphino)ferrocene: a) T.-J. Kim, Y.-H. Kim, H.-S. Kim, S.-C. Shim, Y.-W. Kwak, J.-S. Cha, H.-S. Lee, J.-K. Uhm, S.-I. Byun, *Bull. Korean Chem. Soc.* **1992**, *13*, 588. b) L. E. Hagopian, A. N. Campbell, J. A. Golen, A. L. Rheingold, C. Nataro, *J. Organomet. Chem.* **2006**, *691*, 4890.

14 The cross-coupling reaction of **2a** with 4-methoxyphenyl acetate was attempted by using the DCyPF–nickel catalyst. However, no formation of **3a** was observed.

15 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.