Palladium-catalyzed decarboxylative cross-coupling reaction of cinnamic acid with aryl iodide†

Zhiyong Wang,[a] Qiuping Ding,[a] Xiaodan He[a] and Jie Wu*[a,b]

Received 5th December 2008, Accepted 5th January 2009
First published as an Advance Article on the web 14th January 2009
DOI: 10.1039/b821870f

A highly effective decarboxylative cross-coupling reaction of cinnamic acid with aryl iodide catalyzed by the combination of palladium chloride and CyJohnPhos in the presence of Ag_2CO_3 as an additive is described. The desired carbon-carbon bond formation proceeds efficiently with good functional-group tolerance.

Recently, the decarboxylative cross-coupling reaction has attracted much attention since it opens a new avenue for carbon-carbon formation. As highlighted by Baudoin,[1] this method has several advantages over the conventional transition metal-catalyzed cross-coupling reactions and the direct arylation through C–H activation, concerning the regioselectivity as well as atom and step economy issues. Nilsson reported the first example of transition-metal mediated decarboxylative biaryl coupling,[2] and breakthrough was achieved by Myers,[3] Goossen,[4] and others[5,6] in the development of Pd-catalyzed decarboxylative cross-coupling reactions. For instance, Myers reported a versatile decarboxylative Heck-type reaction between arenecarboxylic acids and olefins under palladium catalysis.[3] Goossen and co-workers have described the efficient preparation of biaryls or ketones *via* a Pd-catalyzed decarboxylative coupling of arenecarboxylic acids and aryl halides.[4] The group of Forgione and Bilodeau reported Pd-catalyzed arylation of heteroaromatic carboxylic acids.[5d] Becht and co-workers presented Pd-catalyzed couplings of arenecarboxylic acids with aryl iodides or diaryliodonium triflates.[6a,d] As part of a continuing effort in our laboratory on C–C bond formation,[7] we became interested in developing a novel and efficient method *via* transition metal catalyzed decarboxylative coupling of carboxylic acids with aryl halides. Although decarboxylative coupling of arenecarboxylic acids has been described recently,[3–6] there is only one report[4b] of decarboxylative coupling of vinyl carboxylic acids (one substrate). However, the reaction procedure was tedious and the reaction was performed at 170 °C. Herein, we disclose our recent efforts on the synthesis of 1,2-diaryl olefins *via* a decarboxylative cross-coupling reaction of cinnamic acid with aryl iodides.

To verify our hypothesis of decarboxylative coupling of cinnamic acid, a set of experiments was carried out using cinnamic acid **1a** and 4-methoxyphenyl iodide **2a** as model substrates. This preliminary survey, carried out in the presence of a palladium catalyst, allowed us to evaluate and optimize the most efficient catalytic system (Table 1). Gratifyingly, in an initial experiment, we observed the formation of the desired product **3a** in 10% yield when the reaction was catalyzed by $PdCl_2$ (10 mol%) in the presence of Ag_2CO_3 as an additive in DMA (Table 1, entry 1). No reaction occurred without this additive (Table 1, entry 2). Different ligands were then screened in the reaction. The yield could be increased to 36% when (*R*)-BINAP was utilized as a ligand in the catalytic system (Table 1, entry 3). A better result was generated when PPh_3 was added as a replacement (50% yield, Table 1, entry 4). The addition of 1,10-phenanthroline or bipyridine in the reaction gave rise to product **3a** in 20% or 38% yield, respectively (Table 1, entries 5 and 6). *N*-Heterocyclic carbene[8] ligands were also effective, leading to the final product in moderate yield (Table 1, entries 7 and 8). Similar results were observed when the reaction was performed in the presence of $P(C_6F_5)_3$, Ph_3As, PCy_3, or XPhos (Table 1, entries 9, 13, 16, and 17). Only a trace amount of product **3a** was detected when other phosphine ligands such as $P(2\text{-furanyl})_3$, $P(o\text{-Tol})_3$, $P(1\text{-Nap})_3$, and DPPF were screened (Table 1, entries 10–12, 14). To our delight, we found that the yield could be dramatically improved when ligand CyJohnPhos[9] was utilized in the reaction (77% yield, Table 1, entry 15). Further investigation revealed that DMA was the best choice of solvent (Table 1, entries 18 and 19). Inferior results were displayed when other palladium catalysts were used in the reaction (Table 1, entries 20–24). The Ag_2CO_3 additive was also replaced by other salts and no better results were generated (Table 1, entries 25–28). Decreasing the reaction temperature or reducing the amount of catalyst produced the product **3a** in moderate yield (Table 1, entries 29 and 30).

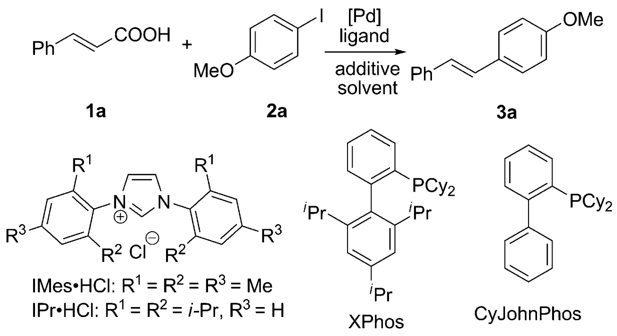
With this promising result in hand, to demonstrate the generality of this method, we investigated the scope of this decarboxylative coupling reaction under the optimized reaction conditions [$PdCl_2$ (10 mol%), CyJohnPhos (20 mol%), Ag_2CO_3 (3.0 equiv), DMA, 150 °C], and the results are shown in Table 2. From Table 2, it was found that all reactions proceeded smoothly to afford the desired product **3** in moderate to good yields. Additionally, the reaction of cinnamic acid with aryl iodide was found to tolerate a range of different groups with different electronic demands on the aromatic rings involving electron-donating and electron-withdrawing groups. For instance, cinnamic acid **1a** reacted with phenyl iodide **2b** leading to (*E*)-1,2-diphenylethene **3b** in 78% yield (Table 2, entry 2). When 4-fluorophenyl iodide **2c** was employed in the reaction, the corresponding product **3c** was generated in 73% yield (Table 2, entry 3). Reaction of cinnamic acid **1a** with 3-methoxyphenyl iodide **2d** gave rise to olefin **3d** in 67% yield

---

[a] *Department of Chemistry, Fudan University, 220 Handan Road, Shanghai, 200433, China. E-mail: jie_wu@fudan.edu.cn; Fax: +86 21 6510 2412; Tel: +86 21 5566 4619*
[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai, 200032, China*

† Electronic supplementary information (ESI) available: General experimental procedures, characterization data and NMR spectra of compounds **3a–q**. See DOI: 10.1039/b821870f

Table 1 Screening conditions for decarboxylative cross-coupling reaction of cinnamic acid **1a** with 4-methoxyphenyl iodide **2a**.[a]



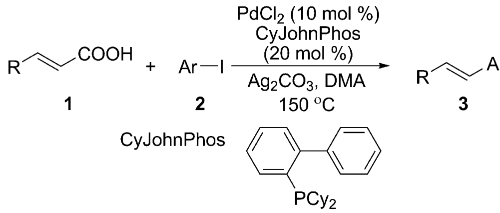
Entry	[Pd]	ligand	additive	solvent	yield (%)[b]
1	$PdCl_2$	—	Ag_2CO_3	DMA	10
2	$PdCl_2$	—	—	DMA	NR
3	$PdCl_2$	(*R*)-BINAP	Ag_2CO_3	DMA	36
4	$PdCl_2$	PPh_3	Ag_2CO_3	DMA	50
5	$PdCl_2$	1,10-phenanthroline	Ag_2CO_3	DMA	20
6	$PdCl_2$	bipyridine	Ag_2CO_3	DMA	38
7	$PdCl_2$	IPr·HCl	Ag_2CO_3	DMA	41
8	$PdCl_2$	IMes·HCl	Ag_2CO_3	DMA	49
9	$PdCl_2$	$P(C_6F_5)_3$	Ag_2CO_3	DMA	34
10	$PdCl_2$	$P(2\text{-furanyl})_3$	Ag_2CO_3	DMA	trace
11	$PdCl_2$	$P(o\text{-Tol})_3$	Ag_2CO_3	DMA	trace
12	$PdCl_2$	$P(1\text{-Nap})_3$	Ag_2CO_3	DMA	trace
13	$PdCl_2$	Ph_3As	Ag_2CO_3	DMA	36
14	$PdCl_2$	DPPF	Ag_2CO_3	DMA	trace
15	$PdCl_2$	CyJohnPhos	Ag_2CO_3	DMA	77
16	$PdCl_2$	PCy_3	Ag_2CO_3	DMA	36
17	$PdCl_2$	XPhos	Ag_2CO_3	DMA	49
18	$PdCl_2$	CyJohnPhos	Ag_2CO_3	DMF	60
19	$PdCl_2$	CyJohnPhos	Ag_2CO_3	mesitylene	trace
20	$Pd(OCOCF_3)_2$	CyJohnPhos	Ag_2CO_3	DMA	40
21	$Pd(OAc)_2$	CyJohnPhos	Ag_2CO_3	DMA	44
22	$PdCl_2(PhCN)_2$	CyJohnPhos	Ag_2CO_3	DMA	46
23	$PdCl_2(PPh_3)_2$	CyJohnPhos	Ag_2CO_3	DMA	43
24	$PdCl_2(dppf)_2$	CyJohnPhos	Ag_2CO_3	DMA	50
25	$PdCl_2$	CyJohnPhos	$Cu(OAc)_2$	DMA	trace
26	$PdCl_2$	CyJohnPhos	$CuCl_2$	DMA	trace
27	$PdCl_2$	CyJohnPhos	AgOAc	DMA	20
28	$PdCl_2$	CyJohnPhos	Cs_2CO_3	DMA	31
29[c]	$PdCl_2$	CyJohnPhos	Ag_2CO_3	DMA	49
30[d]	$PdCl_2$	CyJohnPhos	Ag_2CO_3	DMA	55

[a] Reaction conditions: cinnamic acid **1a** (0.3 mmol), 4-methoxyphenyl iodide **2a** (0.36 mmol, 1.2 equiv), palladium catalyst (10 mol%), ligand (20 mol%), additive (3.0 equiv), solvent (2.0 mL), 150 °C. [b] Isolated yield based on cinnamic acid **1a**. [c] The reaction was carried out at 110 °C. [d] In the presence of $PdCl_2$ (5 mol%) and **A** (10 mol%).

(Table 2, entry 4), while reaction of acetyl- or trifluoromethyl-substituted aryl iodide **2e** or **2f** afforded olefin **3e** or **3f** in 60% or 50% yield, respectively (Table 2, entries 5 and 6). Methyl 2-iodobenzoate **2h** was also a good substrate in the reaction of cinnamic acid **1a**, and the product **3h** was isolated in 56% yield (Table 2, entry 8). With respect to other cinnamic acids, as expected both electron-rich and electron-poor acrylic acids are suitable partners in this process, and the desired products were isolated in good yields. Thus, 4-nitrocinnamic acid **1b** reacted with 4-methoxyphenyl iodide **2a**, leading to the formation of compound **3i** in 86% yield (Table 2, entry 9). A similar result was obtained when 3-nitrocinnamic acid **1c** was utilized as a replacement (80% yield, Table 2, entry 10). Chloro-, cyano-, or fluoro-substituted cinnamic acid also worked well in the reaction with 4-methoxyphenyl iodide **2a** (Table 2, entries 11–14). Reaction of (*E*)-3-(furan-2-yl)propenoic acid **1g** with 4-methoxyphenyl iodide **2a** proceeded smoothly to give the desired product **3o** in 55% yield (Table 2, entry 15). Good isolated yields were observed for reactions of 4-methylcinnamic acid **1h** with various aryl iodides (Table 2, entries 16–19). Besides aryl iodides, we also tested the reactions of aryl bromides. However, no reaction occurred under the standard conditions shown in Table 2.

In conclusion, we have described a highly effective decarboxylative cross-coupling reaction of cinnamic acid with aryl iodide catalyzed by the combination of palladium chloride and CyJohnPhos in the presence of Ag_2CO_3 as additive. The desired carbon-carbon bond formation proceeds efficiently with good functional-group tolerance.

Table 2 Palladium-catalyzed decarboxylative cross-coupling reaction of cinnamic acid **1** with aryl iodide **2**.[10]



Entry	R	Ar	product	yield (%)[a]
1	C_6H_5 **1a**	4-MeOC_6H_4 **2a**	**3a**	77
2	C_6H_5 **1a**	C_6H_5 **2b**	**3b**	78
3	C_6H_5 **1a**	4-FC_6H_4 **2c**	**3c**	73
4	C_6H_5 **1a**	3-MeOC_6H_4 **2d**	**3d**	67
5	C_6H_5 **1a**	4-AcC_6H_4 **2e**	**3e**	60
6	C_6H_5 **1a**	3-$CF_3C_6H_4$ **2f**	**3f**	50
7	C_6H_5 **1a**	4-MeC_6H_4 **2g**	**3g**	62
8	C_6H_5 **1a**	2-Me$O_2CC_6H_4$ **2h**	**3h**	56
9	4-$NO_2C_6H_4$ **1b**	4-MeOC_6H_4 **2a**	**3i**	86
10	3-$NO_2C_6H_4$ **1c**	4-MeOC_6H_4 **2a**	**3j**	80
11	4-ClC_6H_4 **1d**	4-MeOC_6H_4 **2a**	**3k**	65
12	4-CNC_6H_4 **1e**	4-MeOC_6H_4 **2a**	**3l**	55
13	4-FC_6H_4 **1f**	4-MeOC_6H_4 **2a**	**3m**	60
14	4-FC_6H_4 **1f**	4-MeC_6H_4 **2g**	**3n**	71
15	2-Furanyl **1g**	4-MeOC_6H_4 **2a**	**3o**	55
16	4-MeC_6H_4 **1h**	4-MeOC_6H_4 **2a**	**3p**	65
17	4-MeC_6H_4 **1h**	C_6H_5 **2b**	**3g**	82
18	4-MeC_6H_4 **1h**	4-FC_6H_4 **2c**	**3n**	71
19	4-MeC_6H_4 **1h**	2-Me$O_2CC_6H_4$ **2h**	**3q**	60

[a] Isolated yield based on cinnamic acid **1**.

Acknowledgements

Financial support from National Natural Science Foundation of China (20772018), Shanghai Pujiang Program, and Program for New Century Excellent Talents in University (NCET-07-0208) is gratefully acknowledged.

Notes and references

1 O. Baudoin, *Angew. Chem., Int. Ed.*, 2007, **46**, 1373.

2 M. Nilsson, *Acta Chem. Scand.*, 1966, **20**, 423.

3 (*a*) A. G. Myers, D. Tanaka and M. R. Mannion, *J. Am. Chem. Soc.*, 2002, **124**, 11250; (*b*) D. Tanaka and A. G. Myers, *Org. Lett.*, 2004, **6**, 433; (*c*) D. Tanaka, S. P. Romeril and A. G. Myers, *J. Am. Chem. Soc.*, 2005, **127**, 10323.

4 (*a*) L. J. Goossen, G. Deng and L. M. Levy, *Science*, 2006, **313**, 662; (*b*) L. J. Goossen, N. Rodriguez, B. Melzer, C. Linder, G. Deng and L. M. Levy, *J. Am. Chem. Soc.*, 2007, **129**, 4824; (*c*) L. J. Goossen and B. Melzer, *J. Org. Chem.*, 2007, **72**, 7473; (*d*) L. J. Goossen, F. Rudolphi, C. Oppel and N. Rodriguez, *Angew. Chem., Int. Ed.*, 2008, **47**, 3043. For review, see: L. J. Goossen, N. Rodriguez and K. Goossen, *Angew. Chem., Int. Ed.*, 2008, **47**, 3100.

5 (*a*) G. Lalic, A. D. Aloise and M. D. Shair, *J. Am. Chem. Soc.*, 2003, **125**, 2852; (*b*) S. Lou, J. A. Westbrook and S. E. Schaus, *J. Am. Chem. Soc.*, 2004, **126**, 11440; (*c*) D. K. Rayabarapu and J. A. Tunge, *J. Am. Chem. Soc.*, 2005, **127**, 13510; (*d*) P. Forgione, M.-C. Brochu, M. St-Onge, K. H. Thesen, M. D. Bailey and F. Bilodeau, *J. Am. Chem. Soc.*, 2006, **128**, 11350.

6 (*a*) J.-M. Becht, C. Catala, C. Le, Drian and A. Wagner, *Org. Lett.*, 2007, **9**, 1781; (*b*) S. R. Waetzig and J. A. Tunge, *J. Am. Chem. Soc.*, 2007, **129**, 14860; (*c*) A. A. Yeagley and J. J. Chruma, *Org. Lett.*, 2007, **9**, 2879; (*d*) J.-M. Becht and C. L. Drian, *Org. Lett.*, 2008, **10**, 3161; (*e*) A. Voutchkova, A. Coplin, N. E. Leadbeaterb and R. H. Crabtree, *Chem. Commun.*, 2008, 6312.

7 (*a*) L. Zhang and J. Wu, *J. Am. Chem. Soc.*, 2008, **130**, 12250; (*b*) L. Zhang, T. Meng and J. Wu, *J. Org. Chem.*, 2007, **72**, 9346; (*c*) L. Zhang, T. Meng, R. Fan and J. Wu, *J. Org. Chem.*, 2007, **72**, 7279; (*d*) Z. Wang, R. Fan and J. Wu, *Adv. Synth. Catal.*, 2007, **349**, 1943.

8 (*a*) For selected examples, see: F. Glorius, (Eds.), *N-Heterocyclic Carbenes in Transition Metal Catalysis*, Springer, Berlin, 2007; (*b*) W. A. Herrmann, *Angew. Chem., Int. Ed.*, 2002, **41**, 1290; (*c*) O. Navarro, R. A. Kelly, III and S. P. Nolan, *J. Am. Chem. Soc.*, 2003, **125**, 16194; (*d*) G. A. Grasa and S. P. Nolan, *Org. Lett.*, 2001, **3**, 119; (*e*) M. R. Fructos, T. R. Belderrain, M. C. Nicasio, S. P. Nolan, H. Kaur, M. M. Diaz-Requejo and P. J. Perez, *J. Am. Chem. Soc.*, 2004, **126**, 10846; (*f*) C. Yang, H. M. Lee and S. P. Nolan, *Org. Lett.*, 2001, **3**, 1511; (*g*) R. Singh, M. S. Viciu, N. Kramareva, O. Navarro and S. P. Nolan, *Org. Lett.*, 2005, **7**, 1829; (*h*) G. A. Grasa, A. C. Hillier and S. P. Nolan, *Org. Lett.*, 2001, **3**, 1077; (*i*) M. S. Viciu, R. F. Germaneau, O. Navarro-Fernandez, E. D. Stevens and S. P. Nolan, *Organometallics*, 2002, **21**, 5470.

9 For selected examples, see: (*a*) D. S. Surry and S. L. Buchwald, *J. Am. Chem. Soc.*, 2007, **129**, 10354; (*b*) E. R. Strieter and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2006, **45**, 925; (*c*) E. P. Gillis and M. D. Burke, *J. Am. Chem. Soc.*, 2007, **129**, 6716; (*d*) E. McNeill, T. E. Barder and S. L. Buchwald, *Org. Lett.*, 2007, **9**, 3785; (*e*) A. Joncour, A. Decor, S. Thoret, A. Chiaroni and O. Baudoin, *Angew. Chem., Int. Ed.*, 2006, **45**, 4149; (*f*) M. L. Meketa and S. M. Weinreb, *Org. Lett.*, 2006, **8**, 1443; (*g*) J. P. Wolfe, R. A. Singer, B. H. Yang and S. L. Buchwald, *J. Am. Chem. Soc.*, 1999, **121**, 9550.

10 General procedure for palladium-catalyzed decarboxylative cross-coupling reaction of cinnamic acid **1** with aryl iodide **2**.: A mixture of cinnamic acid **1** (0.30 mmol), aryl iodide **2** (0.36 mmol, 1.2 equiv), Ag_2CO_3 (0.90 mmol, 247 mg, 3.0 equiv), CyJohnPhos (0.06 mmol, 21 mg, 0.2 equiv), and $PdCl_2$ (0.03 mmol, 5.3 mg, 0.1 equiv) in DMA (2.0 mL) was stirred at 150 °C under nitrogen for 12 h. After completion of the reaction as indicated by TLC, the mixture was cooled and filtered with Celite. After adding ethyl acetate (10 mL) to the filtrate, the organic phase was washed with saturated NH_4Cl, dried with $MgSO_4$, and concentrated under reduced vacuum. The residue was then purified by flash chromatography on silica gel to afford product **3**(for details, please see Electronic Supplementary Information†).