

Available online at www.sciencedirect.com



Tetrahedron Letters 46 (2005) 4941–4944

Tetrahedron Letters

CuI/Dabco as a highly active catalytic system for the Heck-type reaction

Jin-Heng Li,* De-Ping Wang and Ye-Xiang Xie

Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research, College of Chemistry and Chemical Engineering, Hunan Normal University, Changsha 410081, China

> Received 21 January 2005; revised 24 May 2005; accepted 25 May 2005 Available online 9 June 2005

Abstract—An efficient catalytic system using CuI/Dabco (triethylenediamine) for the Heck-type cross-coupling reaction was developed. In the presence of 10 mol % of CuI and 20 mol % of Dabco, the coupling of various aromatic iodides and 1-((Z)-2-bromovinyl)benzene with olefins was carried out efficiently and selectively to afford the corresponding internal olefins in moderate to good yields.

© 2005 Elsevier Ltd. All rights reserved.

The Heck cross-coupling reaction represents one of the most valuable methods for carbon-carbon bond formation in organic synthesis.^{1–5} As a result, a number of efficient and selective catalytic systems were developed for the Heck cross-coupling reaction.^{1–5} Of these catalytic systems, the palladium complexes, which are employed efficiently in controlling the reactivity and selectivity, are the most popular.^{1,2} In recent years, the applications of complexes with other transition metals have been attracting much attention,^{3,4} including Ni, Co, Rh, Ir and Cu. However, only one paper on CuX-catalyzed Heck-type cross-coupling reaction has been reported.^{4,5} In the presence of 0.1-1 equiv of CuX (X = Br, I), only moderate yields were obtained when treatment of aromatic iodides with olefins was proceeded in NMP under an elevated reaction temperature (150 °C). Thus, the development of mild and efficient copper catalytic systems for the Heck-type cross-coupling reaction still remains a challenging area for organic chemists. Here, we report an inexpensive and efficient CuI/Dabco catalytic system for the Heck-type reactions of aromatic iodides and 1-((Z)-2-bromovinyl)benzene with olefins (Eq. 1).⁶



The efficiency of CuI/Dabco for the Heck-type crosscoupling reaction of 1-iodo-4-methylbenzene (1a) with tert-butyl acrylate (2a) was first evaluated, and the results are summarized in Table 1. The results showed that Dabco was an effective ligand for the copper-catalyzed Heck-type reaction. Without any ligand, only a 11% yield of the corresponding cross-coupled product 3 was isolated in the presence of 10 mol % of CuI and 2 equiv of K_2CO_3 (entry 1), whereas the yield of 3 was increased dramatically to 65% when 10 mol % of Dabco was added (entry 2). A 91% yield of 3 was obtained when the amount of Dabco was increased to 20 mol % (entry 3). The yield was decreased slightly upon further increasing of Dabco to 40 mol % (entry 4). TMEDA and PPh₃ were also tested as the ligands. The results indicated that they were less effective (entries 5 and 6). The use of solvents for the Heck reaction was also investigated, and EtOH gave the highest yield (entries 3 and 8-13). The results also demonstrated that higher reaction temperatures favored the reaction (entries 3 and 7). Finally, the loadings of CuI were tested. The desired yields were obtained in the presence of 1-5 mol % of CuI after prolonged heating (entries 14 and 15).

Typical experimental procedure for the copper/Dabcocatalyzed Heck-type cross-coupling reactions is as

Keywords: CuI; Dabco; The Heck-type cross-coupling reaction; ArI; Olefins.

^{*} Corresponding author. Tel.: +86 731 8872530; fax: +86 731 8872531; e-mail: jhli@hunnu.edu.cn

^{0040-4039/\$ -} see front matter @ 2005 Elsevier Ltd. All rights reserved. doi:10.1016/j.tetlet.2005.05.106

Table 1. CuI/Dabco-Catalyzed Heck reaction of 1a with 2a^a

	$Me - H + COOC(Me)_3 \xrightarrow{Cul/L} Me - H + H + H + H + H + H + H + H + H + H$					
	1a 2a	3				
Entry	Ligand	Solvent	Yield (%) ^b			
1	_	EtOH	11			
2 ^c	Dabco	EtOH	65			
3	Dabco	EtOH	91			
4 ^d	Dabco	EtOH	88			
5	TMEDA	EtOH	37			
6	PPh ₃	EtOH	80			
7 ^e	Dabco	EtOH	79			
8	Dabco	DMF	55			
9	Dabco	THF	21			
10	Dabco	Toluene	33			
11	Dabco	MeCN	42			
12	Dabco	Dioxane	65			
13	Dabco	Acetone	41			
14 ^f	Dabco	EtOH	86			
15 ^g	Dabco	EtOH	75			

^a Under otherwise indicated, the reaction conditions were as follows: 1a (1.0 mmol), 2a (1.5 mmol), CuI (10 mol %), ligand (20 mol %), K₂CO₃ (2 equiv), and solvent (3 mL) for 20 h at 80 °C under N_2 . ^b Isolated yield.

^c Dabco (10 mol %).

^d Dabco (40 mol %).

^e At 50 °C.

^fCuI (5 mol %) at 100 °C for 48 h.

^gCuI (1 mol %) at 100 °C for 48 h.

Table 2. The Heck-type reactions of aryl iodides with olefins catalyzed by CuI/Dabco catalytic system^a

$R \xrightarrow{I \qquad H} R' I \qquad I \qquad$								
Entry	ArX	Olefin	Time (h)	Product	Yield (%) ^b			
1	0 ₂ N-(1b)	COOC(Me) ₃ (2a)	20	O_2N H $COOC(Me)_3$ H (4)	91			
2	NO_2 (1c)	(2a)	40	H H H (5) NO ₂	68			
3	(1d)	(2a)	30	H COOC(Me) ₃ H (6)	90			
4	Me (1e)	(2a)	36	H COOC(Me) ₃ H (7) Me	61			
5	MeO	(2 a)	34	MeO	88			
6	(1f)	COO ⁿ Bu (2b)	30	MeO	81			
7	(1f)	Ph (2c)	30	MeO H H H (10)	78			

Table 2 (continued)							
Entry	ArX	Olefin	Time (h)	Product	Yield (%) ^b		
8	(1 f)	(2d)	36	MeO-(11)	45		
9	Br (1g)	(2b)	40	H H COOC(Me) ₃ (12)	52		
10 ^c	Br (1g)	(2b)	40	COOC(Me) ₃ (12)	88		
11 ^d	O ₂ N-Br (1h)	(2a)	36	O ₂ N H COOC (Me) ₃ H (4)	28		
12 ^{c,d}	(1h)	(2a)	36	O ₂ N-COOC(Me) ₃ H (4)	30		
13 ^d	MeO-Br (1i)	(2a)	36	MeO-H (8)	<5		

^a Under otherwise indicated, the reaction conditions were as follows: **1** (1.0 mmol), **2** (1.5 mmol), CuI (10 mol%), Dabco (20 mol%), K₂CO₃ (2 equiv) and EtOH (3 mL) at 80 °C under N₂.

^b Isolated yield.

^cCuI (1 equiv).

^d At 100 °C.

follows: A mixture of aryl iodide **1a** (1.0 mmol), olefin **2a** (1.5 mmol), CuI (10 mol %), Dabco (20 mol %), K_2CO_3 (2 equiv) and EtOH (3 mL) was added to a tube. Then, the tube was sealed with septum under N₂, and the mixture was then stirred at 80 °C for an appropriate period of time until there was complete consumption of the starting material, as monitored by TLC. After the mixture was filtered and evaporated, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the desired coupled products.

As shown in Table 2, the treatment of various aryl iodides (1b-f) or 1-((Z)-2-bromovinyl)benzene (1g) with olefins (2a-d), CuI (10 mol %) and Dabco (20 mol %) was carried out efficiently and selectively to afford the corresponding cross-coupled products 4–12 in moderate to good yields. The results indicated that the CuI/Dabco catalytic system is remarkably active and tolerant of a range of functionalities. For example, treatment of aryl iodides 1b with 2a afforded 91% yields of the corresponding cross-coupled product 4 in the presence of 10 mol% of CuI and 20 mol% of Dabco (entry 1). For the coupling of substrates 1c-e with 2a, the corresponding coupled products 5-7 were obtained in 68%, 90% and 61% yields, respectively (entries 2-4). Moderate to good yields were obtained when deactivated aryl iodide 1e coupled with 2a-d, respectively, in the presence of 10 mol % of CuI and 20 mol % of Dabco (entries 5-8). The reaction of 1-((Z)-2-bromovinyl)benzene (1g) with 2a was also carried out smoothly to afford 52%

yield of the desired product 12 in the presence of 10 mol % of CuI and 20 mol % of Dabco (entry 9). The yield of 12 was increased to 88%, when 1 equiv of CuI and 200 mol % of Dabco were added (entry 10). Unfortunately, the CuI/Dabco catalytic system was less effective for the reaction of aryl bromides (entries 11–13). The treatment of activated aryl bromide 1h with 2a afforded a lower yield of 4 even in the presence of 1 equiv of CuI (entries 11 and 12). Attempt to couple 1-bromo-4-methoxybenzene 1i with 2a was not successful (entry 13).

A possible mechanism was proposed as shown in Scheme 1.^{2,5b} The reaction of intermediate **3**, a four-centered transition state proposed by Castro and Stephens,⁷ with ArI afforded intermediate **4**. Then, the complex of intermediate **4** with olefin form intermediate **5**, followed by a reductive elimination of intermediate **5**, gave the coupled product **2** and regenerated the active copper(I) complex **3**.

In summary, an efficient CuI/Dabco catalytic system for the Heck-type cross-coupling reaction has been developed. In the presence of CuI and Dabco, coupling of various aryl iodides with olefins were carried out efficiently and selectively to afford the desired products in moderate to excellent yields. Currently, further efforts to extend the application of this catalytic system and this protocol in organic synthesis are underway in our laboratory.



Scheme 1. A possible mechanism for the copper-catalyzed Heck reaction.

Acknowledgements

We thank the National Natural Science Foundation of China (No. 20202002) for financial support.

References and notes

- (a) Mizoroki, T.; Mori, K.; Ozaki, A. Bull. Chem. Soc., Jpn. 1971, 44, 581; (b) Heck, R. F. Org. React. 1982, 27, 345.
- For reviews on the palladium-catalyzed Heck cross-coupling reaction, see: (a) Heck, R. F. Chem. Soc. Rev. 1979, 12, 146; (b) Crisp, G. T. Chem. Soc. Rev. 1998, 27, 427; (c) Beletskaya, I. P.; Cheprakov, A. V. Chem. Rev. 2000, 100, 3009; (d) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. Tetrahedron 2001, 57, 7449; (e) Diederich, F.; Stang, P. J. Metal-Catalyzed Cross-coupling Reactions; Wiley-VCH:

Weinheim, 2002; (f) Miyaura, N. Cross-Coupling Reaction;
Springer: Berlin, 2002; (g) Hegedus, L. S. In Organometallics in Synthesis; Schlosser, M., Ed.; J. Wiley & Sons: Chichester, 2002; p 1123; (h) Larhed, M.; Hallberg, A. In Handbook of Organopalladium Chemistry for Organic Synthesis; Negishi, E., Ed.; Wiley-Interscience: New York, 2002; (i) van der Boom, M. E.; Milstein, D. Chem. Rev. 2003, 103, 1759; (j) Dounay, A. B.; Overman, L. E. Chem. Rev. 2003, 103, 2945; (k) Dupont, J.; Pfeffer, M.; Spencer, J. Eur. J. Inorg. Chem. 2001, 1971; (l) Benford, R. B. Chem. Commun. 2003, 1787; (m) Litter, A. F.; Fu, G. C. Angew. Chem., Int. Ed. 2002, 41, 4176; (n) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Betrand, G. Chem. Rev. 2000, 100, 39; (o) Tang, S.; Liang, Y.; Liu, W.-J.; Li, J.-H. Chin. J. Org. Chem. 2004, 24, 1133.

- For selected papers on other transient metal complexescatalyzed Heck-type cross-coupling reaction, see: (a) Boldini, G. P.; Savoia, D.; Tagliavani, E.; Trombini, C.; Umani Ronchi, A. J. Organomet. Chem. 1986, 301, C62; (b) Lebedev, S. A.; Lopatina, V. S.; Petrov, E. S.; Beletskaya, I. P. J. Organomet. Chem. 1988, 344, 253; (c) Sustman, R.; Hopp, P.; Holl, P. Tetrahedron Lett. 1989, 30, 689; (d) Iyer, S. J. Organomet. Chem. 1995, 490, C27.
- 4. For the paper on CuI-catalyzed Heck-type cross-coupling reaction, see: Iyer, S.; Ramesh, C.; Sarkar, A.; Wadgaon-kar, P. P. *Tetrahedron Lett.* **1997**, *38*, 8113.
- For recent selected papers on CuX-catalyzed reaction of aryl and vinyl iodides with alkynes and other carbon nucleophiles, see: (a) Lindley, J. *Tetrahedron* 1984, 40, 1433; (b) Okuro, K.; Furuune, M.; Enna, M.; Miura, M.; Nomura, M. J. Org. Chem. 1993, 58, 4716; (c) Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. J. Org. Chem. 1993, 58, 7606; (d) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. Org. Lett. 2001, 3, 4315; (e) Ma, D.; Liu, F. Chem. Commun. 2004, 1934.
- 6. For a representative paper on Dabco-palladium catalysts for the Suzuki–Miyaura cross-coupling reaction, see: Li, J.-H.; Liu, W.-J. Org. Lett. **2004**, *6*, 2809.
- 7. Stephens, R. D.; Castro, C. E. J. Org. Chem. 1963, 28, 2163.