ORGANIC LETTERS

2005
Vol. 7, No. 9
1781−1783

Palladium-Catalyzed Intermolecular Three-Component Coupling of Aryl Iodides, Alkynes, and Alkenes To Produce 1,3-Butadiene Derivatives

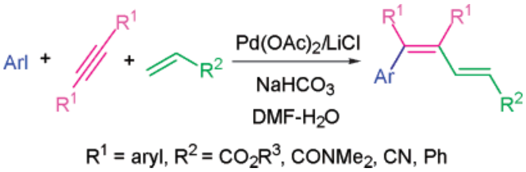
Kana Shibata, Tetsuya Satoh,* and Masahiro Miura*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

satoh@chem.eng.osaka-u.ac.jp; miura@chem.eng.osaka-u.ac.jp

Received February 22, 2005

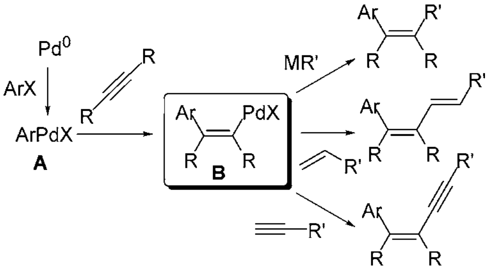
ABSTRACT



The sequential three-component coupling of aryl iodides, diarylacetylenes, and monosubstituted alkenes effectively proceeds in the presence of $Pd(OAc)_2$, LiCl, and $NaHCO_3$ as catalyst, promoter, and base, respectively, in DMF–H_2O to produce the corresponding 1,3-butadiene derivatives.

Transition-metal-catalyzed domino coupling is now recognized to be a powerful tool for constructing rather complex molecules from simple starting materials by a single treatment.[1] Among such potential reactions is the palladium-catalyzed sequential three-component coupling of aryl halides, internal alkynes, and various terminators including organometallic reagents, alkenes, and terminal alkynes.[2] The reaction proceeds via a key vinylpalladium intermediate **B**, which is generated by carbopalladation on an alkyne with an arylpalladium species **A**, as illustrated in Scheme 1. The intermediate **B** is *living* and, thus, undergoes further coupling with the terminators.[2a]

Scheme 1



While the reactions via intramolecular cyclization with alkynylhaloarenes followed by intermolecular termination or the reverse with substrates such as alkenylhaloarenes and alkynes have been studied extensively,[2,3] the fully intermolecular versions to afford π-conjugated acyclic compounds have been less explored.[4,5] As one of the rare but efficient

---

[1] (a) Wender, P. A. *Chem. Rev.* **1996**, *96*, 1. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (d) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (e) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271. (f) Malacria, M. *Chem. Rev.* **1996**, *96*, 289. (g) Negishi, E.-I.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365. (h) Battistuzzi, G.; Cacci, S.; Fabrizi G. *Eur. J. Org. Chem.* **2002**, 2671. (i) Balme, G.; Bossharth, E.; Monteiro, N. *Eur. J. Org. Chem.* **2003**, 4101.

[2] (a) Tsuji, J. *Palladium Reagents and Catalysts*, 2nd ed.; John Wiley & Sons: Chichester, U.K., 2004; pp 201−265. (b) Bräse, S.; de Meijere, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002; Vol. 1, Chapter IV.3, pp 1369−1429.

[3] For recent example, see: (a) Huang, Q.; Larock, R. C. *Org. Lett.* **2002**, *4*, 2505. (b) Huang, Q.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 7342. (c) Kressierer, C. J.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5997. (d) D'Souza, D. M.; Rominger, F.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 153. (e) Bour, C.; Suffert, J. *Org. Lett.* **2005**, *7*, 653.

10.1021/ol0503743 CCC: $30.25

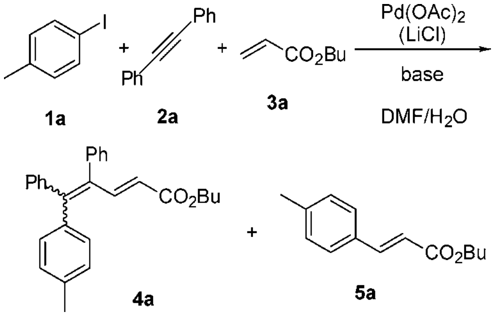
examples, Larock and co-workers recently reported that involving the Suzuki−Miyaura coupling with organoboron reagents in the termination step.[4a] We also demonstrated that two molecules of alkynes can be inserted between aryl halides and arylboronic acids to produce the corresponding 1:2:1 coupling products, 1,4-diaryl-1,3-butadienes, when using a suitable base such as silver carbonate.[6]

During the course of our further study of the catalytic arylation of alkynes,[6,7] we observed that the 1:1:1 coupling of aryl halides, diarylacetylenes, and monosubstituted alkenes can take place selectively under palladium catalysis by employing appropriate conditions. This is a novel example for the above *intermolecular* three-component coupling involving the Mizoroki−Heck reaction with alkenes in the termination.[8]

In an initial attempt, 4-iodotoluene (**1a**) was treated with diphenylacetylene (**2a**) (1 equiv) and butyl acrylate (**3a**) (1 equiv) under conditions similar to those employed for the reaction of **1a** with **2a** and arylboronic acids.[6] In the presence of $Pd(OAc)_2$ (5 mol %) and Ag_2CO_3 (1 equiv) in 1-propanol/H_2O (9:1) at 120 °C for 20 h, butyl 5-(4-methylphenyl)-4,5-diphenyl-2,4-pentadienoate (**4a**) was formed in 16% yield along with a normal Mizoroki−Heck-type product, butyl 3-(4-methylphenyl)-2-propenoate (**5a**), in 25% yield (Table 1, entry 1). In this case, a trace amount of 1:2 coupling product, methyl(tetraphenyl)naphthalene, was also detected by GC−MS.[7d] The reaction was found to be enhanced significantly by using DMF/H_2O as solvent (entry 2). Various bases could be used in place of Ag_2CO_3 (entries 3−7), and among those examined, relatively weak and less expensive $NaHCO_3$ gave the best result (entry 7). As expected, the use of excess **2a** (4 equiv) improved the selectivity for the desired three-component coupling product **4a** (entry 4 vs 3). When the reaction was conducted with the addition of LiCl (0.7 equiv) as promoter at 130 °C, **4a** was obtained in a further improved yield of 72% with a suppressed amount of **5a** (entry 9). The NMR spectra of **4a** isolated in entry 9 indicated that it consists of two geometrical isomers ((2*E*,4*E*)/(2*E*,4*Z*) = 1.2:1).[9] Either decreasing and increasing the amount of LiCl resulted in a reduction in the yield of **4a** (entries 10 and 11). 4-Bromotoluene could be used in place of **1a** with the addition of P(*p*-tolyl)$_3$ (0.2 mmol) as ligand (entry 13).

As expected, the reaction using the substrate combination of an aryl iodide and a diarylacetylene, in which same aryl groups are contained, with **3a** gave the corresponding butyl 4,5,5-triaryl-2,4-pentadienoate as the predominant product. Thus, dienes **6a−d** were obtained from **1a−d** and **2a−d** (Scheme 2).

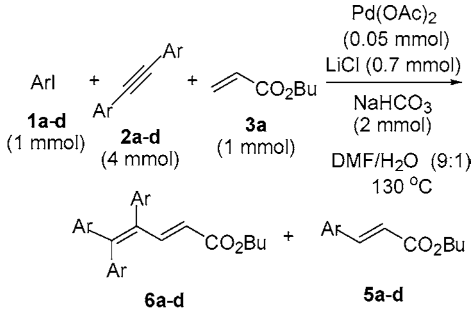
Table 1. Reaction of 4-Iodotoluene (**1a**) with Diphenylacetylene (**2a**) and Butyl Acrylate (**3a**)[a]



entry	base (mmol)	LiCl (mmol)	T (°C)	time (h)	% yield[b] 4a	5a
1[c,d]	Ag_2CO_3(1)		120	20	16	25
2[c]	Ag_2CO_3(1)		120	2	20	36
3[c]	Cs_2CO_3(2)		120	0.5	29	58
4	Cs_2CO_3(2)		120	0.5	53	40
5	Na_2CO_3(2)		120	2	53	28
6	NaOAc (2)		120	0.5	51	35
7	$NaHCO_3$(2)		120	2.5	60	31
8	$NaHCO_3$(2)	0.7	120	1.5	64	28
9	$NaHCO_3$(2)	0.7	130	1	72 (50)[e]	12
10	$NaHCO_3$(2)	0.5	130	1	53	15
11	$NaHCO_3$(2)	1.0	130	2	63	12
12[f]	$NaHCO_3$(2)	0.7	130	0.5	70	14
13[f,g]	$NaHCO_3$(2)	0.7	130	4	58	24

[a] Reaction conditions: **1a** (1 mmol), **2a** (4 mmol), **3a** (1 mmol), $Pd(OAc)_2$ (0.05 mmol), and $NaHCO_3$ in DMF/H_2O (9:1, 5 mL) under N_2. [b] GC yield based on the amount of **1a** used. Value in parentheses indicates yield after purification. [c] **2a** (1 mmol) was used. [d] In 1-propanol/H_2O (9:1, 5 mL). [e] (2*E*,4*E*)/(2*E*, 4*Z*) = 1.2:1. [f] With P(*p*-tolyl)$_3$ (0.2 mmol). [g] 4-Bromotoluene (1 mmol) was used in place of **1a**.

Scheme 2[a]



Ar	substrates	time (h)	products, %yield[a]
Ph	**1b**, **2a**	1.5	**6a**, 65 (47); **5b**, 26
4-MeC_6H_4	**1a**, **2b**	0.5	**6b**, 55 (42); **5a**, 25
4-ClC_6H_4	**1c**, **2c**	1	**6c**, 60 (35); **5c**, 21
2-thienyl	**1d**, **2d**	1.5	**6d**, 30 (18); **5d**, 6

[a] Determined by GC (the value in parentheses indicates yield after purification).

The reaction of **1b** and **2a** with alkenes other than **3a** was next examined (Scheme 3). The alkenes with an electron-

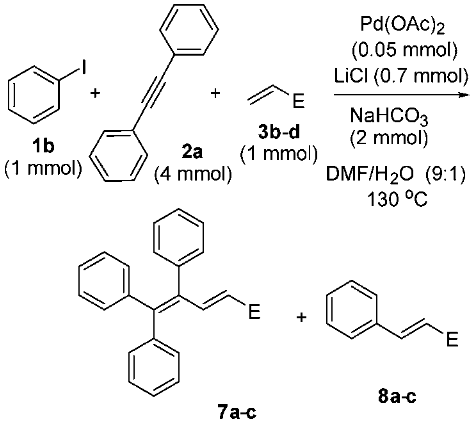
---

(4) Intermolecular reaction with organoboron reagents: (a) Zhou, C.; Emrich, D. E.; Larock, R. C. *Org. Lett.* **2003**, *5*, 1579. (b) Zhang, X.; Larock, R. C. *Org. Lett.* **2003**, *5*, 2993. See also: (c) Thadani, A. N.; Rawal, V. H. *Org. Lett.* **2002**, *4*, 4317.

(5) Intermolecular reaction with terminal alkynes: (a) Pal, M.; Parasuraman, K.; Subramanian, V.; Dakarapu, R.; Yeleswarapu, K. R. *Tetrahedron Lett.* **2004**, *45*, 2305. (b) Pottier, L. R.; Peyrat, J.-F.; Alami, M.; Brion, J.-D. *Synlett* **2004**, 1503.

(6) Satoh, T.; Ogino, S.; Miura, M.; Nomura, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5063.

Scheme 3[a]



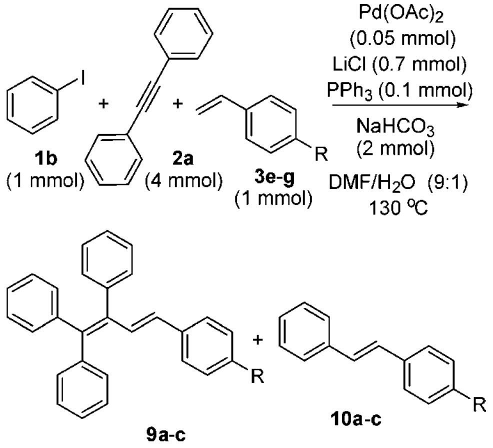
E	alkene	time (h)	products, %yield[a]
CO_2Et	**3b**	1.5	**7a**, 62 (46); **8a**, 20
$CONMe_2$	**3c**	3.5	**7b**, 55 (50); **8b**, 21
CN	**3d**	1	**7c**, 60 (53); **8c**, 10

[a] Determined by GC (the value in parentheses indicates yield after purification).

withdrawing group such as ethyl acrylate (**3b**), *N*,*N*-dimethylacrylamide (**3c**), and acrylonitrile (**3d**) smoothly reacted to produce the corresponding dienes **7a**−**c**.

Styrene (**3e**) also reacted with **1b** and **2a** to afford 1,1,2,4-tetraphenyl-1,3-butadiene (**9a**) (Scheme 4). In this case, the addition of PPh_3 (0.1 mmol) was found to improve the yield of **9a**. The use of 4-methyl- and 4-chlorostyrenes **3f** and **3g** afforded the corresponding dienes **9b** and **9c**.

Scheme 4[a]



R	alkene	PPh_3	time (h)	products, %yield[a]
H	**3e**	-	2.5	**9a**, 44; **10a**, 14
H	**3e**	+	2	**9a**, 63 (45); **10a**, 8
Me	**3f**	+	5	**9b**, 55 (50); **10b**, 3
Cl	**3g**	+	4	**9c**, 69 (52); **10c**, 6

[a] Determined by GC (the value in parentheses indicates yield after purification).

In summary, we have demonstrated that the three-component coupling reaction of aryl iodides with diarylacetylenes and monosubstituted alkenes can be performed under palladium catalysis to selectively give the corresponding 1:1:1 coupling products. The reaction provides a straightforward route to butadienes having multiple aryl groups, which are of interest for their photo- and electrochemical and biological properties.[10]

Supporting Information Available: Reaction procedures and product characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0503743

---

(7) (a) Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941. (b) Pivsa-Art, S.; Satoh, T.; Miura, M.; Nomura, M. *Chem. Lett.* **1997**, 823. (c) Yasukawa, T.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2002**, *124*, 12680. (d) Kawasaki, S.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 6836. (e) Terao, Y.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2004**, *69*, 6942.

(8) Intermolecular coupling of acetic acid, alkynes, and alkenes has been reported: Zhao, L.; Lu, X. *Org. Lett.* **2002**, *4*, 3903.

(9) The formation of the isomers implies that (*E*)−(*Z*) isomerization occurs in the corresponding intermediate **B**. See: Dyker, G.; Kellner, A. *Tetrahedron Lett.* **1994**, *35*, 7633.

(10) For recent papers, see: (a) Hünig, S.; Kemmer, M.; Wenner, H.; Barbosa, F.; Gescheidt, G.; Perepichka, I. F.; Bäuerle, P.; Emge, A.; Peters, K. *Chem. Eur. J.* **2000**, *6*, 2618. (b) Kim, J.-H.; Noh, S.; Kim, K.; Lim, S.-T.; Shin, D.-M. *Synth. Met.* **2001**, *117*, 227. (c) Suzuki, T.; Higuchi, H.; Ohkita, M.; Tsuji, T. *Chem. Commun.* **2001**, 1574. (d) Davis, R.; Mallia, V. A.; Das, S. *Chem. Mater.* **2003**, *15*, 1057. (e) Gage, J. L.; Kirst, H. A.; O’Neil, D.; David, B. A.; Smith, C. K., II; Naylor, S. A. *Bioorg. Med. Chem.* **2003**, *11*, 4083.