

Communications

Efficient One-Pot Synthesis of the Unsymmetrical Diarylalkynes from Two Different Aryl Bromides and Propiolic Acid by Using Pd(PPh₃)₄ Catalyst

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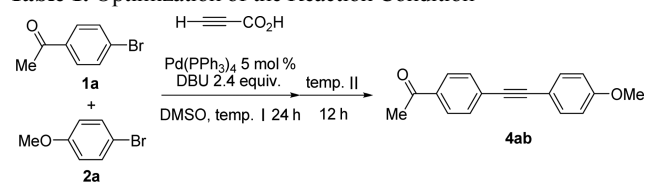
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Unsymmetrical diarylalkynes have attracted much attention, as the molecule structure, having an internal alkyne of two different aromatics, is a core in materials encountered π -conjugated systems.¹ Palladium catalyzed Sonogashira reaction is the most commonly used method for the arylation of terminal alkynes.² Instead of the terminal alkynes, the decarboxylative Sonogashira reaction is used from the alkyne carboxylic acids has several advantages, including a depreciable process for the treatment of the carbon dioxide as a reaction waste released after the complete conversion, and is stable for handling and storage.³ We reported a method for unsymmetrical coupling products from the site selective reaction of propiolic acid with aryl iodides and aryl bromides combinations.⁴ Unlike trimethylsilylacetylene and 2-methylbut-3-yn-ol, Propiolic acid as an alkyne source is very efficient for unsymmetrical coupling products, because a multi-step process is not needed in the method. Buchwald reported the selective Sonogashira reaction of propiolic acid with aryl bromides, which is cost effective, unlike aryl iodides, despite the low reactivity by using sulfonated XPhos as a ligand.⁵ Goossen reported the method for the synthesis of unsymmetrical diarylalkynes with the combination of two different aryl bromides in the presence of SPhos.⁶ Recently, we reported that the Pd(PPh₃)₄ catalyzed a selective Sonogashira reaction with aryl bromides at low temperature.⁷ Instead of the previous reports of the one pot reaction procedures for the synthesis of unsymmetrical diarylalkynes, we carried out an additional experiment due to the simplicity of the non-sequential addition of aryl bromides and non-column purification.

To investigate the method for the synthesis of unsymmetrical diarylalkynes, we screened ratios of **1a**, **2a**, propiolic acid, and arylation temperature, as summarized in Table 1. When all reactants had reached equal amounts, **3ab** showed 26% yield (entry 1). However, in the case of adding more amounts of **1a** or **2a** than the others showed no yields (entry 2 and entry 3). The case of adding lower amounts of **1a** or **2a** than the others showed 23% and 33%, respectively (entry 4 and entry 5). When adding more propiolic acid than either

Table 1. Optimization of the Reaction Condition^a



Entry	Amount (mmol) ^b	Temp. (°C)		Yield (%) ^c
		I	II	
1	0.5/0.5/0.5	35	90	26
2	0.6/0.5/0.5	35	90	0
3	0.5/0.6/0.5	35	90	0
4	0.6/0.5/0.6	35	90	23
5	0.5/0.6/0.6	35	90	33
6	0.5/0.5/0.6	35	90	57
7	0.5/0.5/0.6	35	60	68
8	0.5/0.6/0.6	35	120	0

^aReaction Condition: **1a**, **2a** and propiolic acid as indicated amount, Pd(PPh₃)₄ (0.025 mmol), DBU (1.2 mmol) in DMSO (1 mL). ^b**1a**/**2a**/propionic acid. ^cYield was determined by GC.

1a or **2a**, the product showed 57% yield (entry 6). When the temperature for the second reaction was 60 °C, **3ab** showed 68% yield (entry 7). However, when the temperature for the second reaction was 120 °C, **3ab** showed no yield (entry 8).

Finally, unsymmetrical coupling of propiolic acid with two different of aryl bromides was carried out with the optimized condition. The results are summarized in Table 2. As expected, **1a** with **2a** afforded a corresponding product 60% yield (entry 1). The products coupled with propiolic acid, **1a** and *m*- or *o*-methoxy bromobenzene showed 62% and 51% yield, respectively (entry 2 and entry 3). The combination of **1a** with **2d**, **2e**, **2f** or **2g** showed 68%, 53%, 56%, and 58% yields, respectively (entry 4-7). The combination of **2a** with **1b**, **1c**, **1d** or **1e** showed 66%, 48%, 45%, and 40% yields, respectively (entry 8-11). **1b** with **2h** afforded the desired product of 61% yield (entry 12).

In conclusion, an efficient method for the synthesis of

Table 2. Synthesis of Unsymmetrical Diarylalkynes^a

Entry	ArBr		Yield (%) ^b
	A	B	
1			60
2			62
3			51
4			68
5			53
6			56
7			58
8			66
9			48
10			45
11 ^c			40
12			61

^aAryl bromide (A) (3.0 mmol), aryl bromide (B) (3.0 mmol), propiolic acid (3.6 mmol), Pd(PPh₃)₄ (0.15 mmol), DBU (2.4 mmol), DMSO (6 mL), 35 °C 24 h and 60 °C 12 h. ^bisolated yields. ^c35 °C 24 h and 90 °C 12 h.

unsymmetrical diarylalkynes from the Pd-catalyzed Sonogashira reaction with propiolic acid and two different aryl

bromides has been developed. The various combinations of two different aryl bromides showed good yields. In addition, the column chromatography purification process is not needed in this method.

Experimental Section

Experimental Procedure. Aryl bromide A (3.0 mmol), aryl bromide B (3.0 mmol), propiolic acid (252.2 mg, 3.6 mmol), Pd(PPh₃)₄ (173.2 mg, 0.15 mmol) and DBU (1.09 g, 7.2 mmol) was mixed with DMSO (6 mL). The mixture was stirred at 35 °C for 24 h and 60 °C for 12 h. The resulting solution was poured to H₂O and extracted Et₂O. The organic layer dried over by MgSO₄ and filtered. The solvent was removed under reduced pressure, and the resulting crude product was purified by recrystallization with warm hexane.

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References

- (a) Liu, J.; Lam, J. W. Y.; Tang, B. Z. *Chem. Rev.* **2009**, *109*, 5799-5867. (b) Tykwinski, R. P. *Angew. Chem. Int. Ed.* **2003**, *42*, 1566-1568.
- (a) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979-2017. (b) Yin, L.; Liebscher, J. *Chem. Rev.* **2007**, *107*, 133-173.
- (a) Moon, J.; Jang, M.; Lee, S. *J. Org. Chem.* **2009**, *74*, 1403-1406. (b) Kim, H.; Lee, P. H. *Adv. Synth. Catal.* **2009**, *351*, 2827-2832. (c) Zhang, W.-W.; Zhang, X.-G.; Li, J.-H. *J. Org. Chem.* **2010**, *75*, 5259-5264. (d) Park, K.; Bae, G.; Park, A.; Kim, Y.; Choe, J.; Song, K. H.; Lee, S. *Tetrahedron Lett.* **2011**, *52*, 576-580. (e) Pyo, A.; Kim, J. D.; Choi, H. C.; Lee, S. *J. Organomet. Chem.* **2013**, *724*, 271. (f) Reddy, P. V.; Srinivas, P.; Annapurna, M.; Bhargava, S.; Wagler, J.; Mirzadeh, N.; Kantam, M. L. *Adv. Synth. Catal.* **2013**, *355*, 705-710. (g) Pyo, A.; Kim, Y.; Park, H. K.; Kim, G. C.; Choi, H. C.; Lee, S. *Appl. Organometal. Chem.* **2012**, *26*, 650-654. (h) Li, X.; Yang, F.; Wu, Y. *J. Org. Chem.* **2013**, *78*, 4543-4550.
- (a) Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, *10*, 945-948. (b) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2010**, *75*, 6244-6245. (c) Lee, H. J.; Park, K.; Bae, G.; Choe, J.; Song, K. H.; Lee, S. *Tetrahedron Lett.* **2011**, *52*, 5064-5067.
- Anderson, K. W.; Buchwald, S. L. *Angew. Chem.* **2005**, *117*, 6329-6333.
- Tartaggia, S.; De Lucchi, O.; Goossen, L. J. *Eur. J. Org. Chem.* **2012**, 1431-1438.
- Park, K.; You, J.-M.; Jeon, S.; Lee, S. *Eur. J. Org. Chem.* **2013**, 1973-1978.