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Copper-Catalyzed Decarboxylative C-P Cross-Coupling of Arylpropiolic Acids with Dialkyl Hydrazinylphosphonates Leading to Alkynylphosphonates

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Abstract

A facile and novel copper-catalyzed decarboxylative coupling of various arylpropiolic acids with readily available dialkyl hydrazinylphosphonates has been developed, providing an attractive synthetic tool for the synthesis of valuable alkynylphosphonates with operational simplicity and mild reaction conditions.



KEYWORDS: Decarboxylative coupling, arylpropiolic acids, dialkyl

hydrazinylphosphonates, alkynylphosphonates

INTRODUCTION

The phosphorus-containing compounds are of great importance in organic synthesis, pharmaceuticals, and bioactive products.^[1-5] Among them, alkynylphosphonates have attracted intense attention over the past decades, since they are an important class of triple bond-containing, extremely valuable chemicals in modern synthesis chemistry, which are extensively used as the key precursors for biologically active molecules in medicinal chemistry and for synthesizing structurally diverse phosphorus-containing products through hydrations, reductions, metallacycle formation, conjugate-addition reactions and cycloaddition reactions.^[6] However, synthetic approaches to such useful frameworks are so far limited. The traditional methods for the synthesis of alkynylphosphonates mainly employ readily hydrolyzable Ph₂P(O)Cl and Li or Mg acetylides as the substrates, suffering from poor tolerance of functional groups.^[6a] In recent years, the transition-metal-catalyzed C-P bond forming reactions have emerged as one of the most reliable and robust tools for the preparation of alkynylphosphonates, including Pd-catalyzed cross-coupling of 1,1-dibromo-1-alkenes with H-phosphites,^[7] Cu-catalyzed oxidative coupling of terminal alkynes with H-phosphonates,^[8] and the other approaches^[9] Despite their usefulness, almost all of these methods have common problems such as relatively strict reaction conditions, excess reagents, poor substrate scope or unsatisfactory vields. Thus, the development of more simple and efficient methods to prepare alkynylphosphonates is still desirable.

In the past few years, the decarboxylative coupling reaction as a new synthetic strategy has wide applications in the construction of C-C and C-heteroatom bonds.^[10-19] Among these couplings, as a practical alternative, using arylpropiolic acids instead of terminal alkynes as the coupling partner is safer and more promising since arylpropiolic acids are usually solid-state without unpleasant smell and easy to prepare, store, and transport.^[20] Following this viewpoint, in 2011, Yang's group first reported the Pd/Cu cocatalyzed decarboxylative coupling of arylpropiolic acid with H-phosphonate for the synthesis alkynylphosphonates. However, this reaction did not work well for the dialkyl H-phosphonate.^[21] In 2014, Wu's group improved the above method and developed an efficient Cu-catalyzed decarboxylative coupling of arylpropiolic acids with dialkyl H-phosphonates leading to alkynylphosphonates.^[22] Although the reaction could proceed smoothly under air, this method required 2.0 equivalent of copper catalyst, 2.5 equivalent of ligand, 2.0 equivalent of K₃PO₄ and 3.0 equivalent of additive, thus increasing the cost and limiting their applications. As we know, the dialkyl H-phosphonate is not stable, tend to decompose to phosphorous acid and alcohol. In contrast, dialkyl hydrazinylphosphonates is more stable and easily available, which can be conveniently prepared according to the known literature.^[23] Therefore, using dialkyl hydrazinylphosphonates instead of H-phosphonates might make the coupling reaction easier to operate. In this context, we attempt to develop a mild, simple, and green protocol for the copper-mediated oxidative decarboxylative coupling of arylpropiolic acids with dialkyl hydrazinyl phosphonates. Herein, we described a convenient and practical Cu-catalyzed oxidative decarboxylative coupling of

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various arylpropiolic acids with dialkyl hydrazinylphosphonates for the preparation of alkynylphosphonates through using a simple catalysis system. To the best of our knowledge, this transformation has not been reported to date.

RESULTS AND DISCUSSION

As the outset of our studies, we chose phenylpropiolic acid (1a) as the model substrate to optimize the reaction conditions (Table 1). Initially, the coupling reaction was performed with diethyl hydrazinylphosphonate (2a) in the presence of CuSO₄ (30 mol%) in N,N'-dimethyl formamide (DMF) at 70 °C for 12 h. Gratifyingly, the desired product was obtained in 50% yield (entry 1). Encouraged by this result, we further optimized the reaction conditions. A screening of various bases illustrated that pyridine was the best base for this reaction (entries 2-6) and the use of pyridine (10 mol%) could significantly enhance the product yield to 90% (entry 4), demonstrating the base plays a crucial role in this catalytic system. Subsequently, using pyridine as base, we evaluated different copper catalysts but no better results were obtained (entries 7-9). The transformation could not proceed without the participation of CuSO₄, revealing that CuSO₄ catalyst was essential to achieve a high yield of product 2a. To advance the process further, the effect of solvents was also investigated, such as CH₃CN, 1, 4-dioxane and toluene, however, no desired product was observed (entries 10-12). Subsequent survey on the role of oxidants disclosed H_2O_2 or tert-butyl hydroperoxide (TBHP) could not promote this reaction (entries 13-14). Decreasing the loading of $CuSO_4$ or **2a** led to the yield reduction (entries 15-16). When

decreasing the reaction temperature to 60°C, however, it also gave a decreased yield of 56% (entry 17). Moreover, when rasing the temperature to 80°C, it only afforded a trace amount of desired compounds (entry 18). After a series of detailed investigations, the reaction conditions were eventually optimized as shown in Table 1, entry 4.

With the optimized conditions in hand, we next explored the scope of the substrates and generality of the method by varying the structures of the arylpropiolic acids. The results are summarized in Table 2. Various valuable alkynylphosphonates could be conveniently obtained by this novel copper-catalyzed decarboxylative C-P cross-coupling of arylpropiolic acids with dialkyl hydrazinylphosphonates, and the corresponding oxidative coupling products were produced in 20% to 90% yields. Some electron-rich and electron-deficient arylpropiolic acids were suitable for this method. Thus, a variety of functionalities, such as methyl, nitro, trifluoromethyl, fluoro and cyano groups, were all tolerated under the present reaction conditions. Generally, arylpropiolic acids with both electron-rich and electron-neutral functional groups have a relatively high reactivity, affording the corresponding products in higher yield (Table 2, 5-11). In contrast, electron-poor arylpropiolic acids afforded the products in relatively low yields, along with the generation of divnes as the byproducts. The results indicated that electronic effect had an obvious influence on this decarboxylative coupling. For example, 3-(4-tolyl)propiolic

acid **1b** could well be coupled with diethyl hydrazinylphosphonate **2a** to afford the desired product in a good yield of 70%, but 3-(4-nitrophenyl)propiolic acid **1m** having a strong

electron-withdrawing nitro group could only generate the desired product in a low yield of 20% (Table 2, entry 13). Nevertheless, the substrates **1e** and **1i** bearing the electron-withdrawing cyano and trifluoromethyl groups, respectively, were also good coupling partners for this oxidative coupling reaction, giving the corresponding products in moderate yields (3e, 3i, 61%, 45%, respectively, entries 5 and 9). Notably, the 3-(p-tolyl)propiolic acid 1b and meta-substituted counterpart 1c afforded similar yields of 70% and 61%, respectively, but sterically demanding 3-(o-tolyl)propiolic acid only gave a very low yield of 9%, illustrating that this coupling reaction is sensitive to steric hindrance (entries 2 and 3). Interestingly, fluoro group substituted substrates such as 1f, 1g and 1h could well be coupled with diethyl hydrazinylphosphonate 2a, affording the desired products in moderate yields (Table 2, entries 6-8). However, 3-(3-cyanophenyl)propiolic acid(1j), 3-(3-bromophenyl)propiolic acid (1k) and 3-(m-tolyl)propiolic acid (1l) only afforded the corresponding products in lower yields of 37%, 30% and 31%, respectively (Table 2, entries 10-12). To gain more insight into the substrate scope of the reaction, in addition to **1a**, the alkynylation of diisopropyl hydrazinylphosphonate (**1b**) and P,P-diphenylphosphinic hydrazide were also detected. Unfortunately, diisopropyl hydrazinylphosphonate (2b) and dibutyl hydrazinylphosphonate (2c) only afforded the desired products in a lower yield of 35% and 43%, respectively, probably owing to the steric hindrance of bulky isopropyl and butyl substituents (Table 2, entries 14-15). In addition, P,P-diphenylphosphinic hydrazide was not suitable for this protocol and gave no product.

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On the basis of the above experimental results and previous reports,^[8a,24] a possible mechanism is proposed (Scheme 2). First, dialkyl hydrazinylphosphonate **2** released one molecule N₂ and H₂O to form copper phosphate **B** in the presence of Cu(II) and O₂. Meanwhile, the decarboxylative reaction of **1** occurred with the assistance of Cu(I) to produce alkynyl copper intermediate **A**, which was observed as a yellow precipitate at the very beginning of the reaction and completely disappeared at the end of the reaction. Indeed, (phenylethynyl)copper (0.2 mmol) did react with **2a** (0.8 mmol) in DMF (1 mL) at 70 °C for 12 h under dry air to give **3a** in 47% yield. The subsequent coordination of **B** to **A** led to the formation of intermediate **C**. Finally, **C** reacted with **1** and O₂ leading to the generation of the desired product **3** and catalytically active Cu species to fulfill the catalytic cycle. However, the details of the mechanism are not clear at present.

EXPERIMENTAL

Diaryl hydrazinylphosphonate (1.2 mmol), arylpropiolic acids (0.3 mmol) and CuSO₄ (30 mol%) were dissolved in DMF (1 mL) and stirred at 70 °C for 12 h under dry air. The resulting mixture was concentrated under vacuum and the crude product was purified by silica gel chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

CONCLUSION

In conclusion, we have developed the first copper-catalyzed decarboxylative coupling of various arylpropiolic acids with dialkyl hydrazinylphosphonates to access alkynylphosphonates. Importantly, the reaction is performed without excess catalysts, ligands, bases and additives, and various products can be conveniently obtained in a one-pot process. In addition, in view of the following desirable features, such as cheap catalysts, readily available materials, operation simplicity and mild reaction conditions, this method provides an attractive synthetic tool for simple synthesis of valuable P-alkynylated motifs. Further mechanistic investigations and synthetic applications are currently underway.

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SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on publisher's website.

REFERENCES

1. Mcmanus, H. A.; Guiry, P. J. Chem. Rev. 2004, 104, 4151-4152.

- 2. Kolla, L.; Keglevich, G. Chem. Rev. 2010, 110, 4257-4302.
- 3. Chou, H. H.; Hong, C. H. Adv. Mater. 2010, 22, 2468-2471.
- 4. Lassaux, P.; Hamel, M.; Gulea, M.; Gulea, M.; Delbrück, H.; Mercuri, P. S.; Horsfall,

L.; Dehareng, D.; Kupper, M.; Frère, J-M.; Hoffmann, K.; Galleni, M.; Bebrone, C. J. Med.

Chem. 2010, 53, 4862-4876.

5. Bae, Y.; Yoon, T. J. Appl. Polym. Sci. 2012, 123, 3298-3308.

 Some selected publications: (a) Iorga, B.; Eymery, F.; Carmichael, D.; Savignac, P. *Eur. J. Org. Chem.* 2000, 3103-3115. (b) Ashburn, B. O.; Carterand R. G.; Zakharov, L. N. *J. Am. Chem. Soc.* 2007, *129*, 9109-9116. (c) Nishida, G.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem. Int. Ed.* 2007, *46*, 3951-3954. (d) Kee, J. M.; Villani, B.; Carpenter, L. R.; Muir, T. W. *J. Am. Chem. Soc.* 2010, *132*, 14327-14329. (e) Kettles, T. J.; Cockburn, N.; Tam, W. *J. Org. Chem.* 2011, *76*, 6951-6957. (f) Li, X. B.; Hu, G. B.; Luo, P.; Tang, G.; Gao, Y. X.; Xu P. X.; Zhao, Y. F. *Adv. Synth. Catal.* 2012, *354*, 2427-2432. (g) Kocsis, L. S.; Benedetti, E.; Brummond, K. M. *Org. Lett.* 2012, *12*, 4430-4433. (h) Mo, J.; Kang, D. J.; Eom, D.; Kimand, S. H.; Lee, P. H. *Org. Lett.* 2013, *15*, 26-29.

7. Lera, M.; Hayes, C. J. Org. Lett. 2000, 2, 3873-3875.

Selected recent publications: (a) Gao, Y. X.; Wang, G.; Chen, L.; Xu, P. X.; Zhao, Y.
 F.; Zhou Y. B.; Han, L. B. *J. Am. Chem. Soc.* 2009, *131*, 7956-7957. (b) Liu, P.; Yang, J.;
 Li, P. H.; Wang, L. *Appl. Organometal. Chem.* 2011, *25*, 830-835. (c) Bernoud, E.; Alayrac,
 C.; Delacroix, O.; Gaumont, A. C. *Chem. Commun.* 2011, *47*, 3239-3241. (d) Jouvin, K.;

Heimburger, J.; Evano, G. Chem. Sci. 2012, 3, 756-760. (e) Jouvin, K.; Veillard, R;

Theunissen, C.; Alayrac, C.; Gaumont, A. C.; Evano, G. Org. Lett. 2013, 15, 4592-4595.

9. (a) Honga, J. E.; Leea, C. W.; Kwona, Y.; Oha, D. Y. Synth. Commun. 1996, 26,

1563-1567. (b) Lecerclé, D.; Mothes, C.; Taran, F. Synth. Commun. 2007, 37, 1301-1311.

(c) Yatsumonji, Y.; Ogata, A.; Tsubouchi, A.; Takeda, T. *Tetrahedron Lett.* **2008**, 49, 2265-2267.

 Weaver, J. D.; Recio, A.; Grenning, A. J.; Tunge, J. A. Chem. Rev. 2011, 111, 1846-1913.

- 11. Song, B.; Knauber, T.; Gooßen, L. J. Angew. Chem. Int. Ed. 2013, 52, 2954-2958.
- 12. Hu, P.; Shang, Y. P.; Su, W. Angew. Chem. Int. Ed. 2012, 51, 5945-5949.
- 13. Shard, A.; Sharma, N.; Bharti, R.; Dadhwal, S.; Kumar, R.; Sinha, A. K. Angew.

Chem. Int. Ed. 2012, 51, 12250-12253.

- 14. Burger, E. C.; Tunge, J. A. J. Am. Chem. Soc. 2006, 128, 10002-10003.
- 15. Yin, F.; Wang, Z. T.; Li, Z. D.; Li, C. Z. J. Am. Chem. Soc. 2012, 134, 10401-10404.
- 16. Bhadra, S.; Dzik, W. I.; Goossen, L. J. J. Am. Chem. Soc. 2012, 134, 9938-9941.
- 17. Wang, C.; Isabel, P.; Glorius, F. J. Am. Chem. Soc. 2009, 131, 4194-4195.
- 18. Bi, H. P.; Zhao, L.; Liang, Y. M.; Li, C. J. Angew. Chem. Int. Ed. 2009, 48, 792-795.
- 19. Selected recent reviews: (a) Gooßen, L. J.; Rodríguez, N.; Gooßen, K. Angew. Chem.,
- Int. Ed. 2008, 47, 3100. (b) Rodríguez, N.; Gooßen, L. J. Chem. Soc. Rev. 2011, 40, 5030.
- (c) Weaver, J. D.; Recio, A.; Grenning, A. J.; Tunge, J. A. Chem. Rev. 2011, 111, 1846.

Selected recent papers: (d) Shang, R.; Fu, Y.; Li, J.-B.; Zhang, S.-L.; Guo, Q.-X.; Liu, L. J.

Am. Chem. Soc. 2009, 131, 5738. (e) Ranjit, S.; Duan, Z.; Zhang, P.; Liu, X. Org. Lett.

2010, 12, 4134; (f) Li, X.; Yang, F.; Wu, Y. J. Org. Chem. 2013, 78, 4543. (g) Priebbenow,

D. L.; Becker, P.; Bolm, C. Org. Lett. 2013, 15, 6155; (h) Li, X.; Yang, F.; Wu, Y. RSC Adv.

2014, *4*, 13738.

20. Selected recent papers on decarboxylative reactions of propionic acids: (a) Park, K.;

Lee, S. RSC Adv. 2013, 3, 14165. (b) Gooßen, L. J.; Rodríguez, N.; Manjolinho, F.; Lange,

P. P. Adv. Synth. Catal. 2010, 352, 2913. (c) Yu, D.; Zhang, Y. Green Chem. 2011, 13,

1275. (d) Zhang, X.; Zhang, W.-Z.; Ren, X.; Zhang, L.-L.; Lu, X.-B. Org. Lett. 2011, 13,

2402. (e) Arndt, M.; Risto, E.; Krause, T.; Goossen, L. J. ChemCatChem 2012, 4, 484. (f)

Yu, D.; Tan, M.-X.; Zhang, Y. Adv. Synth. Catal. 2012, 354, 969. (g) Park, K.; You, J.-M.; Jeon, S.; Lee, S. Eur. J. Org. Chem. 2013, 1973.

21. Hu, J.; Zhao, N.; Yang, B.; Wang, G.; Guo, L. N.; Liang, Y. M.; Yang, S. D. *Chem. Eur. J.* **2011**, *17*, 5516.

- 22. Li, X.; Yang, F.; Wu, Y.; Wu, Y. Org. Lett. 2014, 16, 992-995.
- 23. Verner, J.; Potáček, M. Molecules 2006, 11, 34-42.
- 24. (a) Hu, G.; Gao, Y.; Zhao, Y. Org. Lett. 2014, 16, 4464-4467. (b) Wei, W.; Liu, C.;

Yang, D.; Wen, J.; You, J.; Suo, Y.; Wang, Hua. Chem. Commun. 2013, 49, 10239. (c) Xu,

W.; Hu, G.; Xu, P.; Gao, Y.; Yin, Y.; Zhao, Y. Adv. Synth. Catal. 2014, 354, 969.

\bigcirc	— — —соон +	O ⊢ EtO−P−NHNH₂ - OEt	catalyst, base solvent, oxidar temperature	nt,	
	1a	2a			3a
entry	catalyst	base	solvent	yield $(\%)^b$	
1	CuSO ₄	-	DMF	50	
2	CuSO ₄	DPPE	DMF	66	
3	CuSO ₄	Et ₃ N	DMF	44	\sim
4	CuSO ₄	pyridine	DMF	90 C	
5	CuSO ₄	TMEDA	DMF	37	
6	CuSO ₄	K ₂ CO ₃	DMF	trace	
7	CuI	pyridine	DMF	15	
8	CuO	pyridine	DMF	13	
9	Cu(OAc) ₂	pyridine	DMF	31	
10	CuSO ₄	pyridine	CH ₃ CN	0	
11	CuSO ₄	pyridine	Dioxane	0	
12	CuSO ₄	pyridine	Toluene	0	
13 ^c	CuSO ₄	pyridine	DMF	0	
14^d	CuSO ₄	pyridine	DMF	0	
15^e	CuSO ₄	pyridine	DMF	83	
16 ^f	CuSO ₄	pyridine	DMF	43	
17 ^g	CuSO ₄	pyridine	DMF	56	
18 ^{<i>h</i>}	CuSO ₄	pyridine	DMF	trace	

Table 1. Optimization of the Reaction Conditions^a

^{*a*} **1a** (0.3 mmol), **2a** (1.2 mmol), CuSO₄ (0.09 mmol), pyridine (0.03 mmol), DMF (1 mL), 70 °C, 12 h, under dry air. ^{*b*} Isolated yield. ^{*c*} using 30% H₂O₂ (0.6 mmol) in water. ^{*d*} using 70% TBHP (0.6 mmol) in water. ^{*e*} **2a** (0.9 mmol). ^{*f*} CuSO₄ (0.05 mmol). ^{*g*} At 60 °C. ^{*h*} At 80 °C.

Table 2. Copper-catalyzed decarboxylative coupling of arylpropiolic acids with dialkyl hydrazinylphosphonate^{*a*}





^a Reaction conditions: diethyl hydrazinylphosphonate (1.2 mmol), arylpropiolic acids (0.3 mmol), CuSO₄ (30 mol%), pyridine (10 mol%), DMF (1 mL), 70 °C, 12 h, under dry air.
^b diisopropyl hydrazinylphosphonate (1.2 mmol). ^c Isolated yield.



