

Carbocupration of 1-Alkynylphosphines
Followed by Trapping with Electrophiles

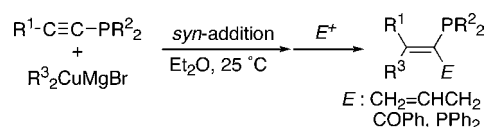
Shigenari Kanemura, Azusa Kondoh, Hideki Yorimitsu,* and Koichiro Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

yori@orgrxn.mbox.media.kyoto-u.ac.jp; oshima@orgrxn.mbox.media.kyoto-u.ac.jp

Received March 19, 2007

ABSTRACT



Treatment of 1-alkynylphosphine with magnesium dialkylcuprate in ether results in regio- and stereoselective syn-carbocupration. The alkenylcopper intermediate reacts with electrophile, which leads to allylation, acylation, and phosphination. The phosphination offers a new route to *gem*-diphosphinoalkene, an interesting phosphorus-based organic structure.

Alkenylphosphines are important not only as ligands in organometallic chemistry¹ but also as reagents in organic synthesis.² Carbometallation³ of 1-alkynylphosphines is likely to be an efficient method for the synthesis of alkenylphosphines.⁴ In 1976, Meijer et al. reported the addition of alkylcopper reagents to ethynyl-diphenylphosphine and diphenyl-(1-propynyl)phosphine.⁵ However, the scope of the addition reaction was not fully investigated. In addition, no attempts to trap the 1-diphenylphosphino-1-alkenylcopper species, generated by the carbocupration, with electrophiles are reported, except for hydrolysis. In the course of our study on the use of 1-alkynylphosphines,⁶ we report herein our detailed examination of the carbocupration of 1-alkynylphosphine. Trapping with electrophiles after the carbocupration was also investigated.

(1) Baya, M.; Buil, M. L.; Esteruelas, M. A.; Oñate, E. *Organometallics* **2005**, *24*, 2030–2038 and references cited therein.

(2) (a) *Organophosphorus Reagents*; Murphy, P. J., Ed.; Oxford University Press: Oxford, UK, 2004. (b) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 2368–2370 and references cited therein.

(3) (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841–870. (b) Lipshutz, L. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135–631.

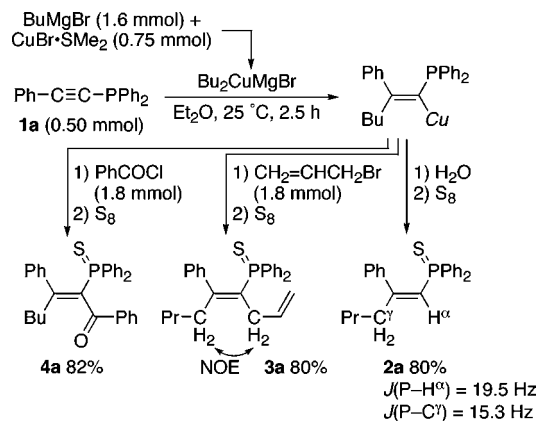
(4) Cross-coupling reaction of alkenyl triflates with secondary phosphines provides an alternative route. (a) Gilbertson, S. R.; Fu, Z.; Starkey, G. W. *Tetrahedron Lett.* **1999**, *40*, 8509–8512. (b) Kazankova, M. A.; Trostyanskaya, I. G.; Lutsenko, S. V.; Beletskaya, I. P. *Tetrahedron Lett.* **1999**, *40*, 569–572.

(5) (a) Meijer, J.; Westmijze, H.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 102–104. (b) Alexakis, A.; Cahiez, G.; Normant, J. F.; Villieras, J. *Bull. Soc. Chim. Fr.* **1977**, 693–698.

(6) (a) Kondoh, A.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 4099–4104. (b) Kondoh, A.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 1383–1385.

Butylmagnesium bromide (1.6 mmol) was added to copper(I) bromide dimethyl sulfide complex (0.75 mmol) in ether at -78 °C to prepare magnesium dibutylcuprate (Bu_2CuMgBr) (Scheme 1).⁷ Diphenyl(phenylethynyl)phos-

Scheme 1



phine (**1a**, 0.50 mmol) was then added to the mixture, and the resulting mixture was stirred for 2.5 h at 25 °C. The reaction was quenched with water under argon. Crystalline

(7) Lipshutz, B. H. In *Organometallics in Synthesis, A Manual*, 2nd ed.; Schlosser, M., Ed.; John Wiley & Sons: Chichester, UK, 2002, Chapter VI/3.2.3.

sulfur was then added to convert the air-sensitive product to stable phosphine sulfide.⁸ Extractive workup and silica gel column purification provided the corresponding phosphine sulfide **2a**. The stereochemistry of **2a** was unambiguously determined by analyzing the characteristic coupling constants.^{2b,6a} Instead of the addition of water, trapping with allyl bromide and benzoyl chloride was successful to yield **3a**⁹ and **4a**, respectively. In each case, the reaction was perfectly regio- and stereoselective. Unfortunately, attempted trapping with benzaldehyde or methyl iodide resulted in failure.

A variety of 1-alkynylphosphines were subjected to the carbocupration reaction followed by allylation (Table 1).

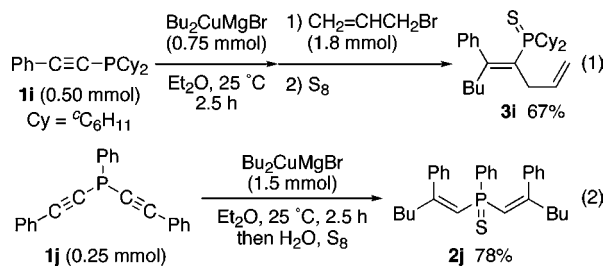
Table 1. Carbocupration of Alkynylbis(diphenylphosphine) **1** with Dibutylcuprate Followed by Trapping with Allyl Bromide

$\text{R}-\text{C}\equiv\text{C}-\text{PPh}_2 \xrightarrow[\text{Et}_2\text{O}, 25^\circ\text{C}, 2.5\text{ h}]{\text{Bu}_2\text{CuMgBr (0.75 mmol)} \quad \begin{matrix} 1) \text{CH}_2=\text{CHCH}_2\text{Br} \\ (1.8\text{ mmol}) \end{matrix}} \text{R}-\text{C}(\text{SPh})=\text{CHCH}_2\text{CH}_3 \quad \text{3}$				
entry	R	1	3	yield (%) ^a
1	C ₆ H ₁₃	1b	3b	80 (88)
2	<i>i</i> Pr	1c	3c	71 (89)
3	<i>t</i> Bu	1d	3d	0
4	H	1e	3e	56 (68)
5	<i>p</i> -MeO-C ₆ H ₄	1f	3f	70 (74)
6	<i>o</i> -MeO-C ₆ H ₄	1g	3g	53 (63)
7	2-pyridyl	1h	3h	59 (85)

^a Isolated yields. Yields based on ³¹P NMR analysis are in parentheses.

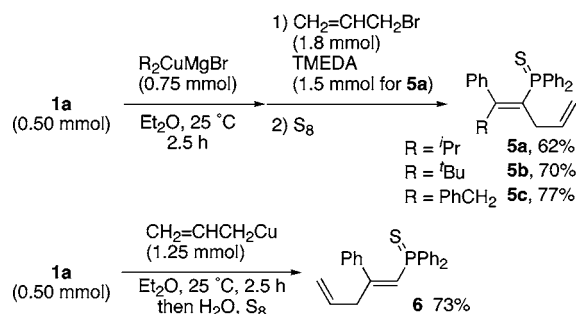
Although a bulky *tert*-butyl group of **1d** completely suppressed the reaction (entry 3), isopropyl- and hexyl-substituted alkynylphosphine **1b** and **1c** underwent the carbocupration (entries 1 and 2). The reaction of ethynylbis(diphenylphosphine) (**1e**) proceeded smoothly to afford **3e** in good yield after allylation with allyl bromide (entry 4). It is worth noting that 2-methoxyphenyl-substituted **1g** as well as 2-pyridyl-substituted **1h** reacted with magnesium dibutylcuprate, without suffering from conceivable adverse effects of the proximal coordinating groups (entries 6 and 7).

Treatment of dicyclohexyl(phenylethynyl)phosphine (**1i**) with magnesium dibutylcuprate followed by addition of allyl bromide provided the corresponding product albeit in modest yield (eq 1). The carbocupration of phenyldi(phenylethynyl)phosphine (**1j**) took place at both of the alkynyl moieties to yield **2j** (eq 2).¹⁰



The scope of organocopper reagents was investigated (Scheme 2). The steric factor of the organocopper reagents

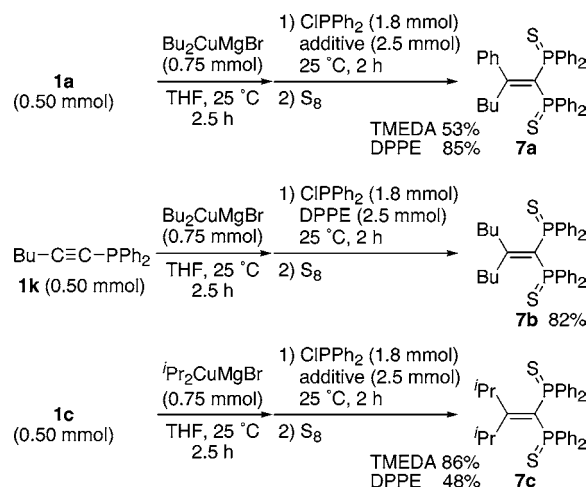
Scheme 2



has little influence on the carbocupration. For instance, the magnesium dialkylcuprates derived from isopropyl- and *tert*-butylmagnesium reagents participated in the carbocupration/allylation reaction. Interestingly, addition of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) was essential to attain a high yield of **5a**.¹¹ Dibenzylcuprate was also reactive. However, phenylation¹² and vinylation did not proceed. Although allylation of **1a** with diallylcuprate provided a complex mixture, allylcopper, derived from equimolar amounts of allylmagnesium bromide and CuBr·SMe₂, was effective for allylcupration of **1a**.^{13,14}

Next we examined trapping the 1-phosphinoalkenylcopper intermediate with chlorodiphenylphosphine (Scheme 3). The

Scheme 3



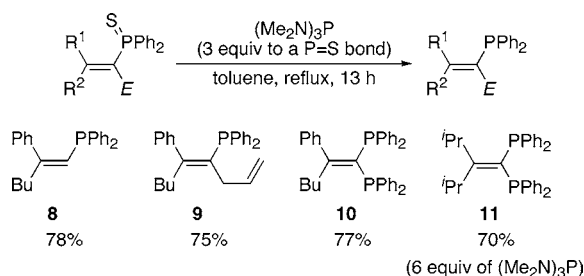
trapping would yield *gem*-diphosphinoalkene derivatives, which are difficult to synthesize despite the interesting structure.¹⁵ Intriguingly, TMEDA or 1,2-bis(diphenylphos-

(8) Without adding sulfur, the results obtained in this paper were not reproducible. The lack of reproducibility originated mainly from formation of the corresponding phosphine oxide during tedious workup and the difficulty in decomplexation of copper–phosphine complexes generated in situ.

phino)ethane (DPPE) proved to be essential as an additive for the trapping. Without the additive, only trace amounts of *gem*-diphosphinoalkenes were formed and the protonated products were mainly obtained. The exact role of the additive is not clear. Not only **7a**¹⁶ but also symmetrical **7b** and **7c** were obtained in high yields.

Finally, desulfidation of the products was investigated. The desulfidation with tris(dimethylamino)phosphine¹⁷ proved to be the best method in our case, which is high-yielding and easy to perform (Scheme 4). Treatment of the phosphine

Scheme 4



sulfides with 3 equiv (to a P=S bond) of tris(dimethylamino)phosphine in boiling toluene for 13 h provided the corresponding trivalent phosphines in high yields.¹⁸ New diphos-

(9) **Experimental procedure:** CuBr·SMe₂ (0.15 g, 0.75 mmol) was placed in a 30-mL reaction flask under argon. Ether (3.0 mL) was added and the mixture was cooled to −78 °C. BuMgBr (1.0 M ether solution, 1.6 mL, 1.6 mmol) was then added. After the mixture was stirred for 1 h at −78 °C, **1a** (0.14 g, 0.50 mmol) was added. The mixture was stirred at 25 °C for 2.5 h. Allyl bromide (0.21 g, 1.8 mmol) was then added. After 1 h, crystalline sulfur (24 mg, 0.75 mmol) was added. The whole mixture was stirred for 30 min, and the reaction was quenched with saturated ammonium chloride solution (10 mL). Extractive workup followed by purification on silica gel provided **3a** (0.17 g, 0.40 mmol, 80%) as a white solid.

(10) Attempts to allylate the corresponding dimetallic species resulted in failure, obtaining mixtures of the non-, mono-, and diallylated compounds.

phines **10** and **11** would be difficult to synthesize by the conventional approach.¹⁵

Acknowledgment. This work was supported by Grants-in-Aid for Scientific Research and COE Research from MEXT and JSPS.

Supporting Information Available: Experimental procedure and characterization data of compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL0706657

(11) Without TMEDA, **5a** was obtained in 31% yield, along with the protonated product in 37% yield. The exact role of TMEDA is not clear.

(12) Lithium diphenylcuprate, derived from PhLi and CuBr·SMe₂, provided a mixture containing triphenylphosphine sulfide, phenylacetylene, and 65% yield of the sulfide of **1a**. In general, magnesium cuprates afforded less complex mixtures in the present reaction than lithium cuprates.

(13) Attempts to trap the corresponding alkenylcopper intermediate with allyl bromide resulted in failure.

(14) Lipshutz, B. H.; Hackmann, C. *J. Org. Chem.* **1994**, *59*, 7437–7444.

(15) (a) Cantat, T.; Ricard, L.; Mézailles, N.; Le Floch, P. *Organometallics* **2006**, *25*, 6030–6038. (b) Bookham, J. L.; Conti, D.; McFarlane, H. C. E.; McFarlane, W.; Thornton-Pett, M. *J. Chem. Soc., Dalton Trans.* **1994**, 1791–1797. (c) Goli, M. B.; Grim, S. O. *Tetrahedron Lett.* **1991**, *32*, 3631–3634.

(16) **Experimental procedure:** The alkenylcopper intermediate was prepared by the same procedure described in ref 8. DPPE (1.0 g, 2.5 mmol) and chlorodiphenylphosphine (0.39 g, 1.8 mmol) were added to the reaction mixture at 25 °C. After the mixture was stirred for 2 h, crystalline sulfur (0.33 g, 10.3 mmol) was added. The whole mixture was stirred for 1 h, and the reaction was quenched with saturated ammonium chloride solution (10 mL). Extraction followed by concentration gave a solid. Purification by gel permeation chromatography provided **7a** (0.25 g, 0.43 mmol, 85%) as a white solid.

(17) Matano, Y.; Miyajima, T.; Nakabuchi, T.; Imahori, H.; Ochi, N.; Sakaki, S. *J. Am. Chem. Soc.* **2006**, *128*, 11760–11761.

(18) **Experimental procedure:** A mixture of **7a** (0.059 g, 0.10 mmol) and tris(dimethylamino)phosphine (0.098 g, 0.60 mmol) in toluene (2.0 mL) was heated at reflux for 13 h under argon. The mixture was then allowed to cool to room temperature. Water (10 mL) was added, and the product was extracted with a mixture of hexane and ethyl acetate (3 × 10 mL). The combined organic layer was dried over sodium sulfate and concentrated in vacuo. Chromatographic purification on silica gel yielded **10** (0.041 g, 0.077 mmol, 77%) as a white solid.