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Synthesis of 1-bromo-1,4-dienes via palladium-catalyzed bromoallylation of alkynes ☆

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ABSTRACT

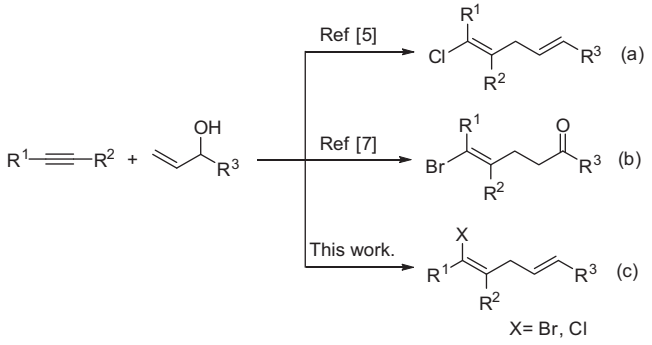
An efficient procedure for the synthesis of a series of 1-bromo-1,4-dienes by a simple Pd-catalyzed intermolecular tandem reaction of alkynes, $CuBr_2$, and allylic alcohol has been developed. The reaction proceeds smoothly under mild condition to give the corresponding products in good to excellent yields.

Transition metal-catalyzed reactions have become powerful tools for the formation of multiple carbon–carbon and carbon–hetero bonds in one transformation, and related approaches have attracted tremendous attention over the past decades.[1] In particular, halopalladation reaction of acetylenes has been demonstrated to be a versatile methodology, owing to its easy access to highly functionalized haloalkenes in a rather efficient and atom economical way.[2] However, in these reported examples, the halopalladation reaction was mainly limited to the addition of allyl halides as allylating reagents[3,9,8a] to capture the vinylpalladium intermediates generated from the halopalladation reaction of alkynes. Obviously, the utilization of allyl alcohols as coupling partners in intermolecular tandem reaction of alkynes would be an appealing approach.

Although allyl alcohols are readily available starting materials, palladium-catalyzed reactions of allyl alcohols in allylating or alkylating reactions have not been well developed.[4] In 2006, we reported a convenient method for the synthesis of 1-chloro-1,4-dienes through Pd-catalyzed coupling of alkynes with allyl alcohols, in which the products of *trans* addition were obtained.[5] Zhu's group[6] implemented an example with the bromopalladation of bromoalkynes as the key step, followed by the addition of allyl alcohols as coupling partners, whereas, phenylacetylene was intact under the reaction conditions.

Very recently, a novel stereo-selective bromoalkylation of internal alkynes and allylic alcohol derivatives has been demonstrated to prepare the δ-bromo γ,δ-unsaturated carbonyl compounds.[7] In a subsequent study of the haloallylation of alkynes with allyl alcohol, we found that alkynes were selectively allylated to give 1-bromo-1,4-dienes. Herein, we wish to report the first synthesis of 1-bromo-1,4-dienes via palladium-catalyzed *cis*-bromoallylation reaction of alkynes and allylic alcohols (Scheme 1).

The reaction of methyl oct-2-ynoate (**1a**) with prop-2-en-1-ol (**2a**) was initially performed in the presence of 5 mol % of $PdCl_2$ and 1.0 equiv of $CuBr_2$ in various solvents (Table 1, entries 1–7). Apparently, the efficiency of this transformation strongly depends



Scheme 1. Three halopalladation-initiated reactions of alkynes.

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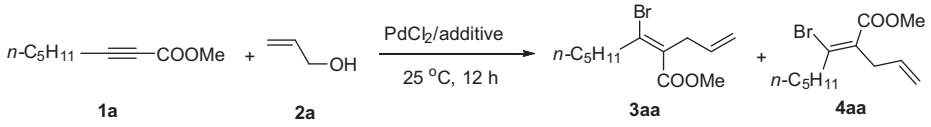
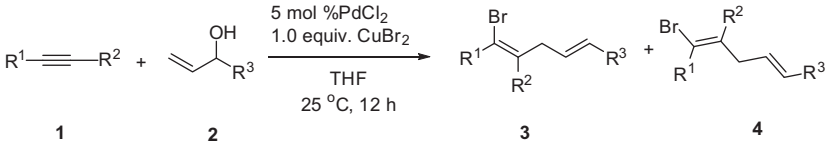
Table 1
Optimization of reaction conditions[a]

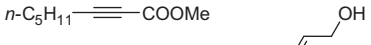
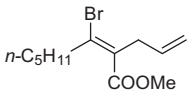
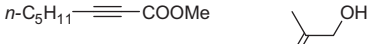
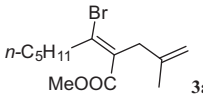
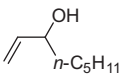
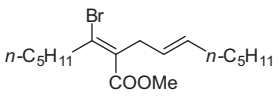
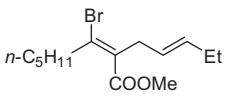
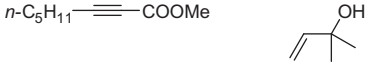
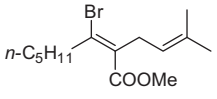
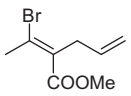


Entry	Solvent	Bromide source	Yield of **3aa**[b] (%)
1	PhMe	$CuBr_2$	40
2	MeCN	$CuBr_2$	10
3	THF	$CuBr_2$	90 (**3aa**/**4aa** 97:3)
4	DMF	$CuBr_2$	23
5	1,4-Dioxane	$CuBr_2$	56
6	1,2-Dichloroethane	$CuBr_2$	34
7	DMSO	$CuBr_2$	n.p.
8[c]	THF	$CuBr_2$	55
9	THF	LiBr	n.p.
10[d]	THF	LiBr/$CuBr_2$	15

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), $PdCl_2$ (5 mol %), and bromide source (1.0 equiv) in 2 mL THF at room temperature for 12 h.
[b] Determined by GC.
[c] 0.5 equiv $CuBr_2$.
[d] 2.0 equiv LiBr, $CuBr_2$ (10 mol %). n.p. = no desired product.

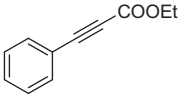
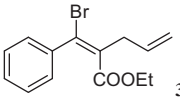
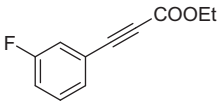
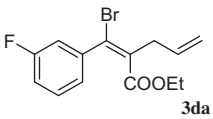
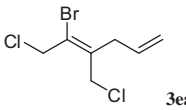
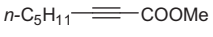
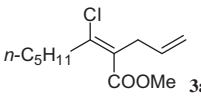
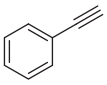
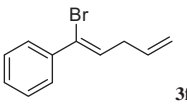
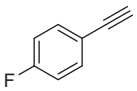
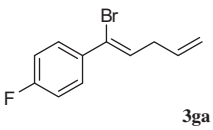
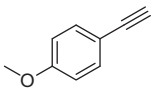
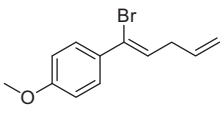
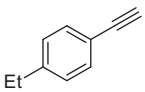
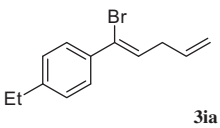
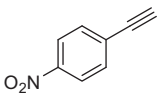
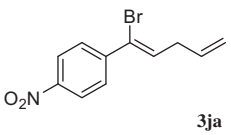
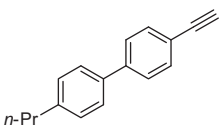
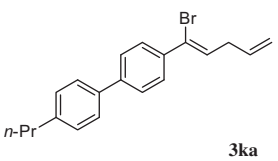
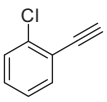
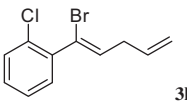
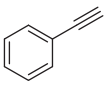
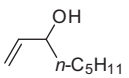
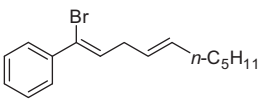
Table 2
Pd-catalyzed allylation of alkynes **1** with allyl alcohols **2**[a]



Entry	Alkynes	Ally alcohol	Major product	3:4[b] (*cis*-add/*trans*-add)	Yield of pure 3[c] (%)
1			 **3aa**	97:3	87
2			 **3ab**	93:7	84
3			 **3ac**	90:10	76
4			 **3ad**	92:8	85
5			 **3ae**	85:15	72
6			 **3ba**	85:15	75

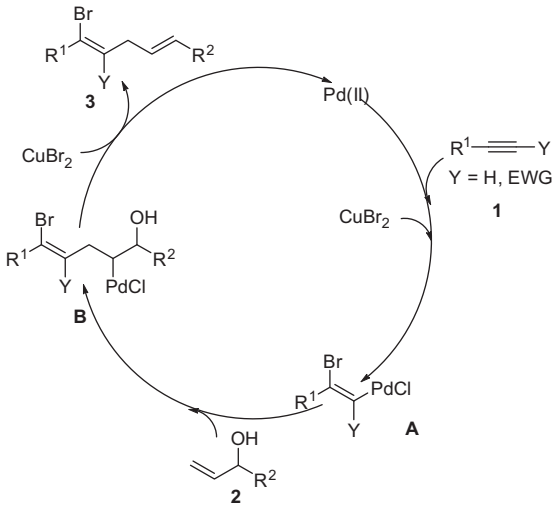
(*continued on next page*)

Table 2 (*continued*)

Entry	Alkynes	Ally alcohol	Major product	3:4[b] (*cis*-add/*trans*-add)	Yield of pure 3[c] (%)
7			 **3ca**	98:2	78
8			 **3da**	91:9	73
9			 **3ea**	88:12	70
10[d]			 **3aa'**	97:3	90
11			 **3fa**	95:5	83
12			 **3ga**	70:30	62
13			 **3ha**	90:10	78
14			 **3ia**	87:13	77
15			 **3ja**	75:25	60
16			 **3ka**	80:20	64
17			 **3la**	96:4	83
18			 **3ma**	92:8	80

[a] Reaction conditions: (1) (1.0 mmol), (2) (1.0 mmol), $PdCl_2$ (5 mol %), and $CuBr_2$ (1.0 equiv) in 2 mL THF at room temperature for 12 h.
[b] Ratio of isomer was determined by GC.
[c] Isolated yields.
[d] 1.0 equiv $CuCl_2 \cdot 2H_2O$ instead of $CuBr_2$.

on the solvent used, and the reaction proceeds smoothly in THF. At room temperature, the reaction afforded the product in 90% yield with good *cis*-add/*trans*-add selectivity (Table 1, entry 3). When 0.5 equiv of $CuBr_2$ was used in this reaction, a lower yield was obtained (Table 1, entry 8). Efforts to further optimize the reaction conditions revealed that $CuBr_2$ was the best bromide source for



Scheme 2. Proposed mechanism.

this reaction. When LiBr was used as the bromide source, no product was obtained (Table 1, entry 9). When the amount of $CuBr_2$ was decreased to 10 mol %, only 15% of the expected product **3aa** was detected (Table 1, entry 10). Therefore, the optimized condition for the haloallylation reaction of alkynes was as follows: 5 mol % of $PdCl_2$ as the catalyst, 1.0 equiv of $CuBr_2$ as the bromide source, and THF as the solvent.

With the optimized reaction conditions in hand (Table 1, entry 3), we proceed to examine the scope of the alkynes and allylic alcohols in this bromopalladation/allylation protocol. Representative results are summarized in Table 2. Firstly, we decided to employ a series of allyl alcohols **2** in this transformation. When primary, secondary, and tertiary allyl alcohols were utilized under the optimal conditions, the desired products were obtained (**3aa**, **3ab**, **3ac**, **3ad**, and **3ae**) in good to excellent yields. Unfortunately aromatic allyl alcohols such as 1-phenylprop-2-en-1-ol, did not obtain the desired products. The scope of the palladium-catalyzed bromoallylation of alkynes leading to 1-bromo-1,4-dienes was further expanded to a range of alkynes **1**. To our delight, not only aliphatic alkynoates but also aromatic alkynoates afford good yields of the desired product (**3aa**, **3ba**, **3ca**, and **3da**). Subsequently, a comparative reaction with $CuCl_2{\cdot}2H_2O$ instead of $CuBr_2$ gave the desired 1,4-diene product to achieve comparable yield (**3aa′**). Inspired by these results, we became interested in further expanding the substrate scope of this methodology to alkynes **1**. It is noteworthy that the standard conditions were compatible with the terminal acetylenes, and the electronic properties of the substituents on the benzene ring do not have significant influence on the reaction efficiency (**3fa**, **3ga**, **3ha**, **3ia**, **3ja**, **3ka**, **3la**, and **3ma**). However, when terminal aliphatic alkyne such as 1-octyne was employed in this transformation, a mixture of *cis*-addition/*trans*-addition was obtained.

The stereochemistry of **3ma** was confirmed by NMR and NOESY methods. NOE enhancements were observed between the olefin proton on C_2 and protons of the benzene ring of **3ma** indicating a *cis*-relationship between these substituents (see Supporting information). The regioselectivity of **3aa** was confirmed by NOESY methods also, which indicated no-relationship between methylenes on C_3 and other methylenes. This result provided an additional proof for the proposed *cis*-halopalladation of the alkyne in Scheme 2.

A plausible mechanism for the allylation of alkynes in THF catalyzed by $PdCl_2$ is shown in Scheme 2. Vinylpalladium intermediate **A** is initially formed by *cis*-halopalladation of the alkyne **1** in THF[8,9] instead of *trans*-halopalladation in aqueous media system in the presence of excess halide ions.[5] Then, the following carbopalladation reaction of vinylpalladium intermediate **A** with allyl alcohol **2** resulted in an alkylpalladium complex **B**.[10] Finally, the β-OH elimination furnished the product **3** and regenerated $PdCl_2$ in the presence of $CuBr_2$.

In conclusion, we have discovered a novel bromoallylation reaction of alkynes using allylic alcohols as alkylating agents. This reaction proceeds via *cis*-bromopalladation and sequential insertions of allylic alcohols. The reactions are operationally simple, and can tolerate a broad range of functional groups. Hence, it is an alternative method for the synthesis of 1-bromo-1,4-dienes.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.05.084.

References and notes

1. (a) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (b) Shi, Z.; Ding, S.; Cui, Y.; Jiao, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 7895–7898; (c) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285–2310; (d) Arai, S.; Sato, T.; Koike, Y.; Hayashi, M.; Nishida, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 4528–4531; (e) Hassan, J.; Svignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1407; (f) Corbet, J.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651–2710; (g) Li, C. *Chem. Rev.* **2005**, *105*, 3095–3166; (h) Sakai, N.; Komatsu, R.; Uchida, N.; Ikeda, R.; Konakahara, T. *Org. Lett.* **2010**, *12*, 1300–1303; (i) Silva, F.; Reiter, M.; Mills-Webb, R.; Sawicki, M.; Klär, D.; Bensel, N.; Wagner, A.; Gouverneur, V. *J. Org. Chem.* **2006**, *71*, 8390–8394; (j) Martínez, C.; Álvarez, R.; Aurrecoechea, J. M. *Org. Lett.* **2009**, *11*, 1083–1086; (k) Liu, R.; Zhang, J. *Chem. Eur. J.* **2009**, *15*, 9303–9306; (l) Li, W.; Zhang, J. *Chem. Commun.* **2010**, 8839–8841; (m) Zhang, X.; Lu, Z.; Fu, C.; Ma, S. *J. Org. Chem.* **2010**, *75*, 2589–2598; (n) Peng, P.; Tang, B.; Pi, S.; Ling, Y.; Li, J. *J. Org. Chem.* **2009**, *74*, 3569–3572; (o) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604–7605; (p) Zhao, L.; Lu, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 4343–4345; (q) Zhao, L.; Lu, X. *Org. Lett.* **2002**, *4*, 3903–3906; (r) Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059–4063; (s) Tang, S.; Peng, P.; Wang, Z.; Tang, B.; Deng, C.; Li, J.; Zhong, P.; Wang, N. *Org. Lett.* **2008**, *10*, 1875–1878; (t) Zhou, P.; Jiang, H.; Huang, L.; Li, X. *Chem. Commun.* **2011**, 1003–1005; (u) Lei, A.; Lu, X. *Org. Lett.* **2000**, *2*, 2699–2702; (v) Shen, Z.; Lu, X. *Tetrahedron* **2006**, *62*, 10896–10899.
2. (a) Kaneda, K.; Kawamoto, F.; Fujiwara, Y.; Imanaka, T.; Teranishi, S. *Tetrahedron Lett.* **1974**, *15*, 1067–1070; (b) Kaneda, K.; Kobayashi, H.; Fujiwara, Y.; Imanaka, T.; Teranishi, S. *Tetrahedron Lett.* **1975**, 2833–2836; (c) Ma, S.; Wu, B.; Zhao, S. *Org. Lett.* **2003**, *5*, 4429–4432; (d) Jiang, H.; Liu, X.; Zhou, L. *Chem. Eur. J.* **2008**, *14*, 11305–11309; (e) Jiang, H.; Qiao, C.; Liu, W. *Chem. Eur. J.* **2010**, *16*, 10968–10970; (f) Zhu, G.; Zhang, Z. *J. Org. Chem.* **2005**, *70*, 3339–3341; (g) Huang, J.; Dong, Y.; Wang, X.; Luo, H. *Chem. Commun.* **2010**, 1035–1037; (h) Tang, S.; Yu, Q.; Peng, P.; Li, J.; Zhong, P.; Tang, R. *Org. Lett.* **2007**, *9*, 3413–3416; (i) Yin, G.; Liu, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 5442–5445; (j) Peng, H.; Liu, G. *Org. Lett.* **2011**, *13*, 772–775; (k) Ye, S.; Gao, K.; Zhou, H.; Yang, X.; Wu, J. *Chem. Commun.* **2009**, 5406–5408; (l) Zhou, P.; Huang, L.; Jiang, H.; Wang, A.; Li, X. *J. Org. Chem.* **2010**, *75*, 8279–8282; (m) Li, Y.; Jardine, K. J.; Tan, R.; Song, D.; Dong, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 9690–9692; (n) Chen, D.; Cao, Y.; Yuan, Z.; Cai, H.; Zheng, R.; Kong, L.; Zhu, G. *J. Org. Chem.* **2011**, *76*, 4071–4074.
3. (a) Chen, X.; Kong, W.; Cai, H.; Kong, L.; Zhu, G. *Chem. Commun.* **2011**, 2164–2166; (b) Cai, H.; Yuan, Z.; Zhu, W.; Zhu, G. *Chem. Commun.* **2011**, 8682–8684; (c) Lu, Z.; Kong, W.; Yuan, Z.; Zhao, X.; Zhu, G. *J. Org. Chem.* **2011**, *76*, 8524–8529; (d) Ma, S.; Lu, X. *J. Org. Chem.* **1991**, *56*, 5120–5125; (e) Ji, J.; Wang, Z.; Lu, X. *Organometallics* **1996**, *15*, 2821–2828.
4. Muzart, J. *Tetrahedron* **2005**, *61*, 4179–4212.
5. Jiang, H.; Zhou, L.; Huang, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 1945–1949.
6. Chen, D.; Chen, X.; Lu, Z.; Cai, H.; Shen, J.; Zhu, G. *Adv. Synth. Catal.* **2011**, *353*, 1474–1478.
7. Wen, Y.; Huang, L.; Jiang, H.; Chen, H. *J. Org. Chem.* **2012**, *77*, 2029–2034.
8. (a) Zhu, G.; Lu, X. *Organometallics* **1995**, *14*, 4899–4904; (b) Zhang, Z.; Lu, X.; Xu, Z.; Zhang, Q.; Han, X. *Organometallics* **2001**, *20*, 3724–3728.
9. (a) Kaneda, K.; Uchiyama, T.; Fujiwara, Y.; Imanaka, T.; Teranishi, S. *J. Org. Chem.* **1979**, *44*, 55–63; (b) Bäckvall, J.-E.; Nilsson, Y. I. M.; Gatti, R. G. P. *Organometallics* **1995**, *14*, 4242–4246; (c) Li, J.; Liang, Y.; Xie, Y. *J. Org. Chem.* **2004**, *69*, 8125–8127.
10. Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265–272.