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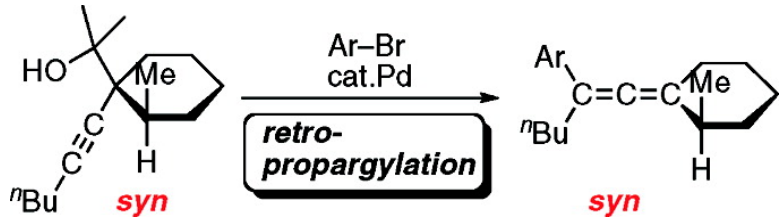

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Synthesis of Arylallenes by Palladium-Catalyzed Retro-Propargylation of Homopropargyl Alcohols

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Allenes are a class of compounds that have interesting reactivity due to the two orthogonal π-bonds[1] and have been found in many natural products.[2] Transition-metal-catalyzed cross-coupling reaction of aryl halides with allenylmetals is one of the most convenient ways to prepare arylallenes.[3] In the case of palladium catalysis, allenylzinc and allenylcopper reagents have been mainly used. These reagents can easily undergo transmetalation with the arylpalladium halide intermediates formed in situ through oxidative addition of aryl halides to palladium. However, the preparation of these allenylmetals requires multiple steps, and they should be handled carefully because of their high reactivity. Moreover, they are in equilibrium with the corresponding propargylmetals[4] so that the control of regioselectivity in the coupling reaction can be difficult.

Here we report a new allenylation reaction of aryl halides with homopropargyl alcohols as allenylmetal equivalents. During our recent studies on palladium-catalyzed regio- and stereospecific allyl transfer from homoallyl alcohols to aryl halides via retro-allylation,[5] we expected the retro-allylation would be extended to retro-propargylation outlined in Scheme 1. If retro-propargylation from intermediate **B** occurs via a cyclic transition state to provide σ-allenyl(aryl)palladium **C** and subsequent reductive elimination proceeds faster than isomerization of **C** to π-allenyl- or propargylpalladium, regioselective allenylated product **3** can be obtained. It is noteworthy that tertiary homopropargyl alcohols are stable to air and moisture. In addition, they are readily accessible in short steps.

Treatment of bromobenzene (**2a**) with homopropargyl alcohol **1a** in the presence of *N*,*N*-dimethylacetamide (DMA) and potassium hydroxide under palladium catalysis in refluxing toluene provided arylallene **3a** in good yield (Table 1, entry 1).[6] In the reaction, no propargylated product was detected. This result is strongly suggestive of our hypothesis. A wide range

Scheme 1. Working Hypothesis

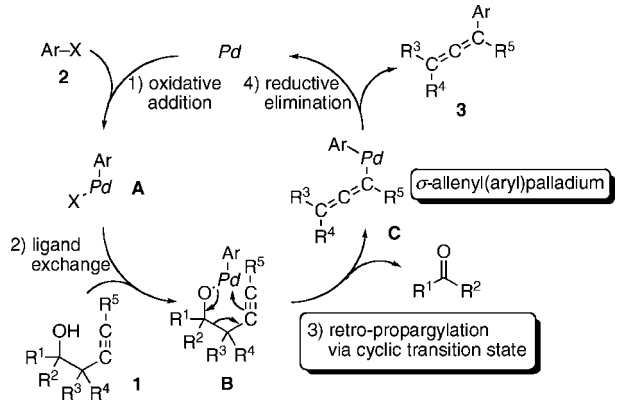
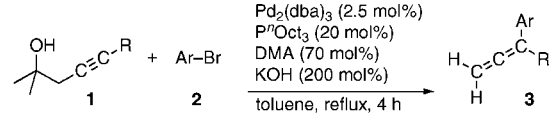
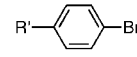
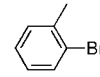
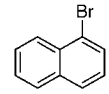
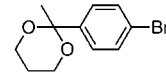
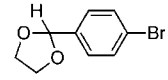


Table 1. Palladium-Catalyzed Allenylation of Aryl Bromides **2** with Homopropargyl Alcohols **1** via Retro-Propargylation[a]



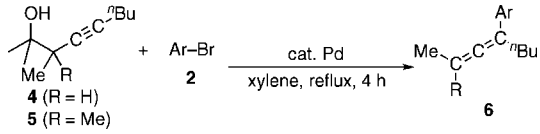
entry	R 1	Ar–Br 2		3, yield[b](%)
1	^{n}Bu **1a**		**2a:** R' = H	**3a**, 74
2			**2b:** Me	**3b**, 67
3			**2c:** Ph	**3c**, 68
4			**2d:** F	**3d**, 62
5			**2e:** CF_3	**3e**, 63
6			**2f :** ^{t}BuCO	**3f**, 85
7			**2g:** OMe	**3g**, 63[c]
8			**2h**	**3h**, 65
9			**2i**	**3i**, 64
10			**2j**	**3j**, 82
11			**2k**	**3k**, 69
12	–$(CH_2)_3$Ph **1b**		**2a**	**3l**, 81
13	–$(CH_2)_4OCH_2$Ph **1c**		**2a**	**3m**, 56[d]
14	^{i}Pr **1d**		**2j**	**3n**, 62
15	^{t}Bu **1e**		**2a**	**3o**, 0

[a] A mixture of $Pd_2(dba)_3$ (0.010 mmol), P(^{n}Oct)$_3$ (0.080 mmol), DMA (0.28 mmol), KOH (0.80 mmol), **1** (0.48 mmol), and **2** (0.40 mmol) was boiled in toluene (6.0 mL) for 4 h. [b] Isolated yields. [c] With 2.0 equiv of **1a**. [d] Xylene was used instead of toluene.

of *p*-substituted aryl bromides including electron-deficient as well as electron-rich ones could be employed (entries 2–7). Sterically demanding **2h** and **2i** also participated in the allenylation reaction. Aryl bromides that possess carbonyl groups except for **2f** decomposed under the strongly basic conditions. Instead, acetal-protected substrates such as **2j** and **2k** gave good results (entries 10 and 11). Scope of the substituents at the alkyne terminus was then examined. Not only primary but also secondary alkyl groups did not interfere with the reaction (entries 12–14). Notably, allenylation of **2a** with **1c** proceeded to furnish **3m**, leaving the benzyl ether moiety untouched. Unfortunately,

10.1021/ja800986m CCC: $40.75

Table 2. Synthesis of Tri- and Tetrasubstituted Arylallenes[a]



entry	alcohol	2	**6**, yield[b] (%)
1	**4**	**2a**	**6a**, 68
2		**2b**	**6b**, 64
3		**2d**	**6c**, 60
4		**2f**	**6d**, 62
5		**2j**	**6e**, 71
6		**2k**	**6f**, 63
7	**5**	**2a**	**6g**, 68
8		**2f**	**6h**, 80
9		**2j**	**6i**, 79

[a] The reaction conditions are the same as those in Table 1 except for the use of xylene instead of toluene. [b] Isolated yields.

Scheme 2

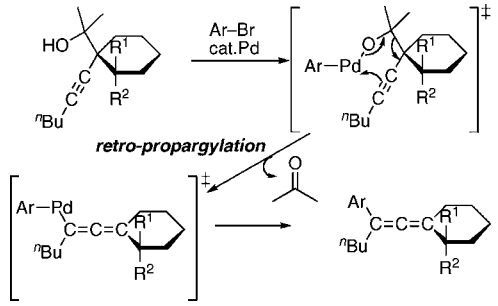
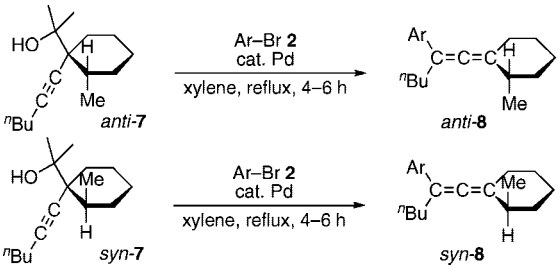


Table 3. Stereospecific Synthesis of Tetrasubstituted Arylallenes[a,b]



entry	**7**	**2**	**8**, yield[c] (%)
1	*anti*	**2a**	*anti*-**8a**, 77
2	*syn*	**2a**	*syn*-**8a**, 77
3	*anti*	**2c**	*anti*-**8b**, 82
4	*syn*	**2c**	*syn*-**8b**, 62
5	*anti*	**2d**	*anti*-**8c**, 72
6	*syn*	**2d**	*syn*-**8c**, 50
7	*anti*	**2j**	*anti*-**8d**, 72
8	*syn*	**2j**	*syn*-**8d**, 77

[a] The reaction conditions were the same as those in Table 2. Both diastereomers were racemic. [b] Relative configurations of alcohol **7** and allene **8** were assigned by X-ray crystallographic analysis. See Supporting Information. [c] Isolated yields. Isomeric purity >99:1.

the bulky *tert*-butyl group of **1e** suppressed the reaction (entry 15).[7]

Homopropargyl alcohols having one or two methyl groups at the propargylic position were converted to tri- or tetrasubstituted arylallenes, respectively (Table 2). Although higher temperature was required, a variety of aryl halides reacted with **4** and **5** to produce the corresponding allenes **6** in moderate to good yields.

Finally, we attempted diastereoselective synthesis of tetrasubstituted arylallenes as depicted in Scheme 2. Taking advantage of the retro-propargylation that would proceed in a concerted fashion via a cyclic transition state, the stereochemical information of homopropargyl alcohols would be transferred to the corresponding allenes through C−C bond cleavage.[8] The reaction of diastereomerically pure homopropargyl alcohol *anti*-**7** with bromobenzene (**2a**) provided tetrasubstituted allene **8a** in good yield with perfect *anti* selectivity (Table 3, entry 1). On the other hand, *syn*-**8a** was obtained as the sole product in the reaction of *syn*-**7** (entry 2). Other aryl bromides also underwent the stereospecific allenylation reaction with both diastereomers (entries 3–8).

In conclusion, we have developed a new method for the generation of σ-allenylpalladium from homopropargyl alcohols via retro-propargylation and applied it to the highly regioselective synthesis of *gem*-di-, tri-, and tetrasubstituted arylallenes. The details of the reaction mechanism and the development of other reactions using the retro-propargylation strategy are under investigation.

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Supporting Information Available: Experimental details, a process for optimizing reaction conditions, characterization data for new compounds, and stereochemical assignments of *anti*-**7** and *anti*-**8b**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Ma, S. In *Modern Allene Chemistry*; Krause, N., Hashimi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; pp 595–699. (b) Murakami, M.; Matsuda, T. In *Modern Allene Chemistry*; Krause, N., Hashimi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; pp 727–815.

(2) (a) Krause, N.; Hoffmann-Röder, A. In *Modern Allene Chemistry*; Krause, N., Hashimi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; pp 997–1039. (b) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196–1216. (c) Wan, Z.; Nelson, S. G. *J. Am. Chem. Soc.* **2000**, *122*, 10470–10471.

(3) (a) Ruitenberg, K.; Kleijn, H.; Meijer, J.; Oostveen, E. A.; Vermeer, P. *J. Organomet. Chem.* **1982**, *224*, 399–405. (b) Russell, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943–949. (c) de Graaf, W.; Boersma, J.; van Koten, G.; Elsevier, C. J. *J. Organomet. Chem.* **1989**, *378*, 115–124. (d) Mukai, C.; Takahashi, Y. *Org. Lett.* **2005**, *7*, 5793–5796.

(4) Tsutsumi, K.; Ogoshi, S.; Nishiguchi, S.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *120*, 1938–1939.

(5) (a) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 2210–2211. (b) Iwasaki, M.; Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 4463–4469. (c) Iwasaki, M.; Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2007**, *63*, 5200–5203. (d) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 12650–12651.

(6) Although the exact role of DMA is not clear at this stage, its coordination to the palladium catalysts could enhance the catalytic activity. See Supporting Information for details of reaction optimization studies.

(7) The reactions with homopropargyl alcohols, the substituent R at the alkyne terminus of which is H, Si^{t}BuMe$_2$, or Ph, resulted in no formation of the desired products.

(8) Reviews for palladium-catalyzed C−C bond cleavage of tertiary alcohols: (a) Muzart, J. *Tetrahedron* **2005**, *61*, 9423–9463. (b) Nishimura, T.; Uemura, S. *Synlett* **2004**, 201–216. (c) Satoh, T.; Miura, M. *Top. Organomet. Chem.* **2005**, *14*, 1–20. Cross-coupling reactions of organic halides with tertiary alcohols via β-carbon elimination: (d) Nakano, M.; Satoh, T.; Miura, M. *J. Org. Chem.* **2006**, *71*, 8309–8311. (e) Terao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2001**, *123*, 10407–10408. (f) Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **1999**, *121*, 11010–11011. (g) Larock, R. C.; Reddy, C. K. *Org. Lett.* **2000**, *2*, 3325–3327. (h) Chow, H.-F.; Wan, C.-W.; Low, K.-H.; Yeung, Y.-Y. *J. Org. Chem.* **2001**, *66*, 1910–1913.

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