

Synthesis of Allenes via Palladium-Catalyzed Hydrogen-Transfer Reactions: Propargylic Amines as an Allenyl Anion Equivalent

Hiroyuki Nakamura,^{*,†} Takaya Kamakura,[†] Makoto Ishikura,[†] and Jean- François Biellmann[‡]

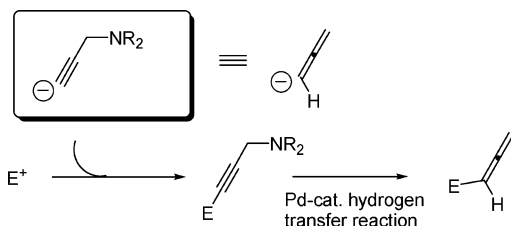
Department of Chemistry, Faculty of Science, Gakushuin University, Mejiro, Toshima-ku, Tokyo 171-8588, Japan, and Institute of Chemistry, Academia Sinica, Nankang Taipei, Taiwan

Received October 22, 2003; E-mail: hiroyuki.nakamura@gakushuin.ac.jp

Recently, much attention has been paid to allenes as building blocks for organic synthesis.¹ Especially transition metal-catalyzed reactions using allenes, such as C–C bond formations of allenes with pronucleophiles² or electrophiles,³ [4+2] and [2+2] cycloadditions,^{4,5} allenes cross-metathesis,⁶ and polymerizations⁷ have broadened the synthetic utility of allenes. Therefore, development of versatile methods for the preparation of allenes has been of great importance.⁸

Allenes can be generally prepared from propargyl alcohol derivatives by S_N2'-type displacement with organocopper species.⁹ Other preparation methods, including the homologation of 1-alkynes,¹⁰ the stereoselective reduction of alkynes,¹¹ asymmetric allylations,^{12,13} β-eliminations by Horner–Emmons–Wadsworth¹⁴ or sulfinyl radical¹⁵ reactions, and palladium-catalyzed hydrogenolysis¹⁶ or coupling reactions of allenylstannanes¹⁷ and allenylindiums,¹⁸ have been recently reported. We report a palladium-catalyzed transformation of allenes from the propargylic amines. In the current transformation, propargylic amines can be handled as an allenyl anion equivalent, which would react with various electrophiles to be transformed into allenes via palladium-catalyzed hydrogen-transfer reactions (Scheme 1).

Scheme 1. Concept of an Allenyl Anion Equivalent



The results are shown in Scheme 2 and Table 1. We first examined the synthesis of phenylallene **4a** from various 3-phenylprop-2-ynylamines (**3aa–3ae**), which were readily prepared from iodobenzene **1a** and propargylic amines (**2a–e**) by Sonogashira coupling in 64–92% yields. The allene transformation reaction of *N,N*-diethyl-3-phenylprop-2-ynylamine **3aa** proceeded in the presence of Pd₂dba₃·CHCl₃/(C₆F₅)₃P catalyst at 100 °C in dioxane for 24 h, giving phenylallene **4a** in only 12% yield (entry 1).¹⁹ Although *N,N*-dibenzyl-3-phenylprop-2-ynylamine **3ab** gave **4a** in 40% yield, the reaction of *N,N*-diisobutyl-3-phenylprop-2-ynylamine **3ac** afforded **4a** in 76% yield (entries 2 and 3). The best result was obtained in the case of *N,N*-diisopropyl-3-phenylprop-2-ynylamine **3ad**, and **4a** was obtained quantitatively (entry 4). The use of the cyclic amine **3ae** was not effective for the allene transformation reaction (entry 5). We also examined the reactions under various phosphine ligands, such as Ph₃P, dppe, dppf, and (PhO)₃P; however, **4a** was obtained in very low yields (9–16%).

Scheme 2

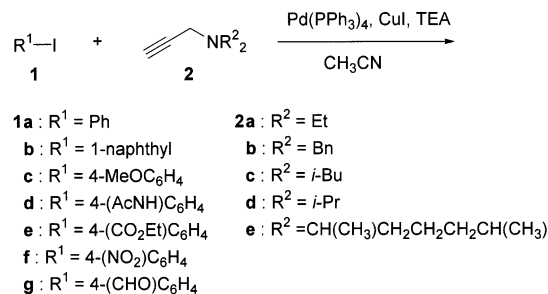


Table 1. Synthesis of Allenes **4** from Various Aromatic Iodides **1** and Propargylic Amines **2** through Sonogashira Coupling^a Followed by Hydrogen-Transfer^b Reactions

entry	R ¹ -I, 1	amine, 2	3 (yield, %) ^c	4 (yield, %) ^c
1	1a	2a	3aa (64)	4a (12) ^d
2	1a	2b	3ab (76)	4a (40) ^d
3	1a	2c	3ac (92)	4a (76) ^d
4	1a	2d	3ad (86)	4a (99) ^d
5	1a	2e	3ae (77)	4a (43)
6	1b	2d	3bd (98)	4b (67)
7	1c	2d	3cd (95)	4c (99)
8	1d	2d	3dd (89)	4d (74)
9	1e	2d	3ed (99)	4e (96)
10	1f	2d	3fd (95)	4f (75)
11	1g	2d	3gd (60)	4g (66)

^a The reactions were carried out in the presence of Pd(PPh₃)₄ (3 mol %), CuI (9 mol %), and TEA (150 mol %) in CH₃CN at 60 °C under Ar (see Supporting Information). ^b The reactions were carried out in the presence of Pd₂dba₃·CHCl₃ catalyst (2.5 mol %) and (C₆F₅)₃P (20 mol %) in dioxane at 100 °C for 24 h under Ar. ^c Isolated yields. ^d Yields were determined by GC analysis using hexadecane as an internal standard.

Once suitable conditions for the palladium-catalyzed hydrogen-transfer reaction were established, we next investigated the synthesis of various allenes (**4b–g**) from the corresponding iodides (**1b–g**) with *N,N*-diisopropylprop-2-ynylamine **2d**. The reaction of **3bd**, which was prepared from 1-iodonaphthalene **1b** in 98% yield, was completed in 24 h to give 1-allenylnaphthalene **4b** in 67% yield (entry 6). The propargylic amines, which have an electron-donating group such as MeO (**3cd**) and AcNH (**3dd**) substituted on the aromatic ring of molecules, underwent the hydrogen-transfer reaction to give the corresponding allenes **4c** and **4d** in 99% and 74% yields, respectively (entries 7 and 8). Not only the electron-rich propargylic amines but also the electron-deficient propargylic amines **3ed–gd** underwent the allene transformation reaction. The reaction of **3ed**, prepared from **1e** in 99% yield, proceeded smoothly to give the corresponding allene **4e** in 96% yield (entry

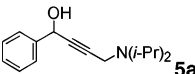
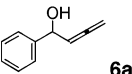
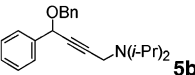
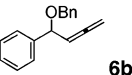
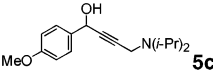
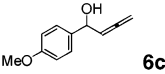
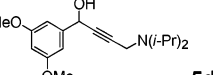
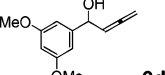
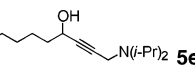
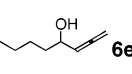
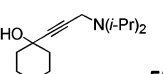
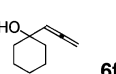
[†] Gakushuin University.

[‡] Academia Sinica.

9). The reactions of propargylic amines **3fd** and **3gd** also gave **4f** and **4g** in 75% and 66% yields, respectively (entries 10 and 11).

Propargyl diisopropylamines, as an allenyl anion equivalent, can be introduced into carbonyl compounds. Various propargylic alcohols and the benzyl ether (**5a–f**) containing a diisopropylaminomethyl group were synthesized by the addition of a lithium acetylide of **2d** to aldehydes and a ketone. The results are summarized in Table 2. The allene transformation reaction of **5a**, which was prepared from benzaldehyde and **2d**, proceeded in the presence of Pd₂dba₃·CHCl₃/(C₆F₅)₃P at 80 °C in dioxane for 13 h, giving the corresponding allene **6a** in 64% yield (entry 1). The benzyl ether **5b**, however, afforded **6b** in a higher yield (91%; entry 2). The propargylic alcohols **5c–e**, derived from 4-anisaldehyde, 3,5-dimethoxybenzaldehyde, and hexanal, respectively, underwent the transformation reaction to give the corresponding allenes **6c–e** in 56–92% yields (entries 3–5). The reaction of **5f**, derived from cyclohexanone, also proceeded to give **6f** in 86% yield (entry 6).

Table 2. Palladium-Catalyzed Hydrogen-Transfer Reaction of **5**

entry	5	time, h	allenes 6	yield, % ^b
1		13		64
2		23		91
3		14		92
4		14		70
5		12		56
6		9		86

^a The reactions were carried out in the presence of Pd₂dba₃·CHCl₃ catalyst (2.5 mol %) and (C₆F₅)₃P (20 mol %) in dioxane at 80 °C under Ar.
^b Isolated yields.

A representative procedure for the palladium-catalyzed hydrogen migration reaction is as follows. To a solution of **3cd** (0.4 mmol) in dry dioxane (1 mL) were added Pd₂dba₃·CHCl₃ (0.01 mmol) and (C₆F₅)₃P (0.08 mmol). The mixture was stirred at 100 °C for 24 h. The reaction progress was monitored by GC. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography with hexane to give **4c** quantitatively.

We developed a novel transformation of allenes using propargylic amines as an allenyl anion equivalent. The use of (C₆F₅)₃P is essential for the palladium-catalyzed hydrogen-transfer reaction. Although mechanisms based upon either Pd(0)²⁰ or Pd(II) could be envisaged (details are discussed in the Supporting Information), hydrogen transfer from a C–H bond adjacent to nitrogen to an alkyne moiety via a hydride–palladium would give the allenes **4**. Further extension of the catalytic allene transformation using propargylic amines as an allene equivalent is now in progress.

Supporting Information Available: Experimental details, mechanisms, and characterization data for compounds **3**, **4b–g**, and **6a–f** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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