Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 46 (2005) 8333–8336
Tetrahedron Letters

Synthesis of ene–allenes via palladium-catalyzed hydride-transfer reaction of propargylic amines under mild conditions

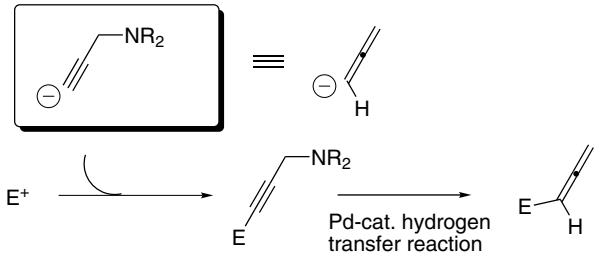
Hiroyuki Nakamura,* Satoshi Tashiro and Takaya Kamakura

Department of Chemistry, Faculty of Science, Gakushuin University, Mejiro, Tokyo, 171-8588, Japan

Received 27 June 2005; revised 22 September 2005; accepted 28 September 2005
Available online 11 October 2005

Abstract—The palladium-catalyzed allene transformation reaction from propargylic amines proceeded in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %) and $(C_6F_5)_2PC_2H_4P(C_6F_5)_2$ (10 mol %) in $CHCl_3$ at room temperature to give the corresponding allenes in good to high yields. Dicyclohexyl groups substituted on the nitrogen of propargylic amines were found to be effective for the current transformation and the conjugated ene–allenes **4** were synthesized from the corresponding propargylic amines **3** under mild conditions.

Allenes are now one of the attractive building blocks for organic synthesis.[1] Although various synthetic methods have been developed for the synthesis of allenes including the S_N2'-type displacement with organocopper species,[2] the homologation of 1-alkynes,[3] the stereoselective reduction of alkynes,[4] asymmetric allylations,[5,6] β-eliminations by Horner–Emmons–Wadsworth[7] or sulfinyl radical[8] reactions, and palladium-catalyzed hydrogenolysis,[9] development of simple protocols for the introduction of an allene moiety into electrophiles is still important subject. In this regard, palladium-catalyzed coupling reactions of aryl halides with allenylstannanes,[10] allenylindiums,[11] and allenylzincs[12] have been reported so far. We recently found that propargylic amines underwent the hydride-transfer reaction in the presence of a palladium catalyst to afford allenes.[13] In this transformation, propargyldiisopropylamine can be handled as an allenyl anion equivalent and introduced into various electrophiles to be transformed into allenes (Scheme 1). Although the transformation can be utilized for the synthesis of heterocyclic allenes,[14] the reactions required relatively high temperatures (80–100 °C), which may cause side-reactions or decomposition of substrates. Actually, the reaction of (*E*)-*N*,*N*-diisopropyl-5-phenylpent-4-en-2-yn-1-amine under the previously reported conditions did not afford the corresponding ene–allene but resulted in the decomposition of compounds. Therefore, development of the allene transformation, which proceeds under mild conditions, has been required for a wide use. In this letter, we found that dicyclohexyl and dicyclopentyl groups substituted on the nitrogen of propargylic amines are potent for the current transformation and succeeded in the synthesis of conjugated ene–allenes via palladium-catalyzed hydride-transfer reaction from propargylic amines at room temperature.



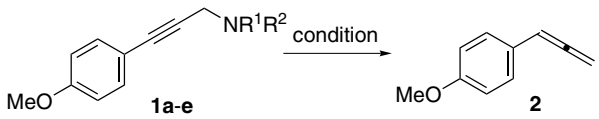
Scheme 1. Allenyl anion equivalent.

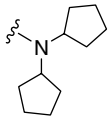
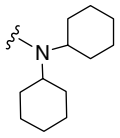
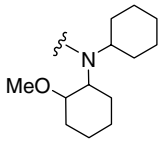
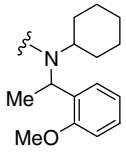
Various amines **1a**–**e** were employed for the allene transformation under palladium-catalyzed conditions as shown in Table 1. The treatment of *N*,*N*-diisopropyl-3-(4-methoxyphenyl)prop-2-ylamine **1a** in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %) and $(C_6H_5)_3P$ (20 mol %) in dioxane at room temperature (Condition A)[13] afforded 4-methoxyphenylallene in 28% conversion with 11% yield, whereas 57% conversion with 58% yield was observed in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$

Keywords: Allene; Palladium catalyst; Propargylic amines; Hydride transfer.
* Corresponding author. Tel.: +81 339 860221x6491; fax: +81 359 921029; e-mail: hiroyuki.nakamura@gakushuin.ac.jp

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.09.169

Table 1. Effect of substituents on the nitrogen of propargylic amines



Entry	NR^1R^2	Condition[a]	Conversion (%)	Yield of[b] **2** (%)
1	 **1a**	A	28	11
		B	57	58
2	 **1b**	A	53	96
		B	71	89
3	 **1c**	A	58	86
		B	67	90
		C	>99	>99
4	 **1d**	A	82	Trace
		B	73	7
5	 **1e**	A	44	98
		B	66	71

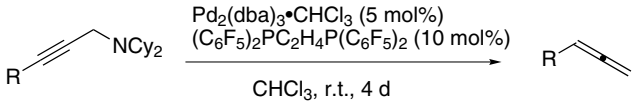
[a] Condition A: $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %) and $(C_6H_5)_3P$ (20 mol %) in dioxane at room temperature for 4 days; Condition B: $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %) and $(C_6F_5)_2PC_2H_4P(C_6F_5)_2$ (10 mol %) in $CHCl_3$ at room temperature for 4 days; Condition C: $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %) and $(C_6F_5)_2PC_2H_4P(C_6F_5)_2$ (10 mol %) in $CHCl_3$ at room temperature for 4 days.
[b] Isolated yield.

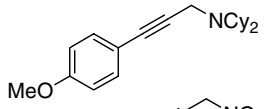
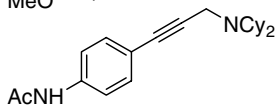
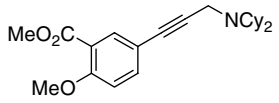
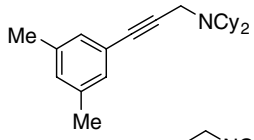
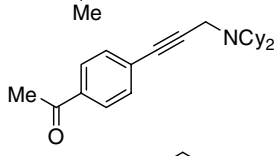
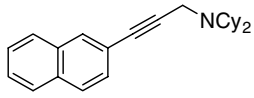
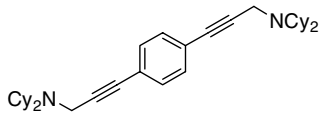
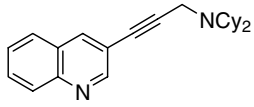
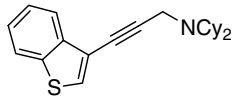
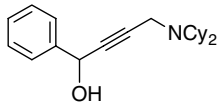
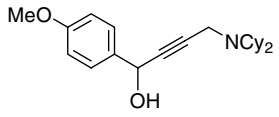
(2.5 mol %) and $(C_6F_5)_2PC_2H_4P(C_6F_5)_2$ (10 mol %) in $CHCl_3$ at room temperature (Condition B).[14] Dicyclopentylamine **1b** and dicyclohexylamine **1c** were more effective for the allene transformation, and 4-methoxyphenylallene was obtained in 71% and 67% conversions with 89% and 90% yields, respectively, under the condition B (entries 2 and 3). Surprisingly, the allene transformation proceeded quantitatively when 5 mol % of $Pd_2(dba)_3{\cdot}CHCl_3$ was employed (Condition C in entry 3). *N*-Cyclohexyl-*N*-(2-methoxycyclohexyl)-3-(4-methoxyphenyl)prop-2-ylamine **1d** and *N*-cyclohexyl-*N*-(1-phenylethyl)-3-(4-methoxyphenyl)prop-2-ylamine **1e**, which would be expected chelation of a palladium through the nitrogen and the oxygen, did not accelerate the reaction rate very much (entries 4 and 5).

We next investigated the synthesis of various allenes from the corresponding propagylic dicyclohexylamines. The results are summarized in Table 2. Propargylic dicyclohexylamines, which have a strong electron-donating group on the phenyl ring, underwent the allene transformation reaction to give the corresponding allenes in good to high yields with high conversion (entries 1–3). 3,5-Dimethylphenyl-, 4-acetylphenyl-, and 2-naphthyl propargyldicyclohexylamines also gave the corresponding allenes in 60–95% yields (entries 4–6). The reaction of 1,4-di-[3-(dicyclohexylamino)prop-1-yl]benzene afforded 1,4-diallenylbenzene in 56% yield along with the monoallene transformation product in 34% yield (entry 7). We also examined the transformation reaction from heterocyclic propargylamines. 3-Allenylquinone and 3-allenylbenzo[*b*]thiophene were obtained in 99% and 77% yields with 46% and 99% conversions, respectively (entries 8 and 9). Propargylic alcohols, which were synthesized from the corresponding aldehydes and the lithium acetylide of *N*,*N*-dicyclohexylpropargylamine, were transformed into the allenylcarbinols in 66–86% yields with high conversions (entries 10 and 11).

The procedure for the current transformation under mild conditions enabled us to synthesize the conjugated ene–allenes, which are labile at high temperatures.[15] The results are shown in Table 3. The conjugated propargylic amine **3a** underwent the allene transformation reaction in $CHCl_3$ at room temperature for 7 days to afford the corresponding conjugated ene–allene **4a** in 88% yield with 75% conversion (entry 1). Various conjugated propargylic amines **3b–e** were employed for the allene transformation at room temperature and the

Table 2. Palladium-catalyzed allene transformation from the propargyldicyclohexylamines at room temperature



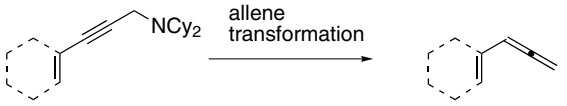
Entry	Propargylic amine	Conversion (%)	Yields[a] (%)
1		>99	>99
2		>99	>99
3		78	79
4		58	95
5		58	79
6		83	60
7		>99	56 (34)[b]
8		46	99
9		>99	77
10		>99	66
11		>99	86

[a] Isolated yield.
[b] The monoallene transformation product was obtained in 34% yield.

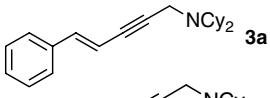
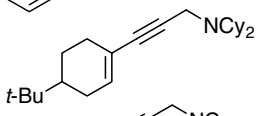
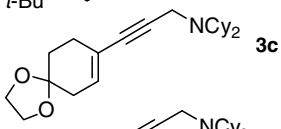
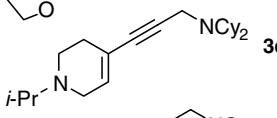
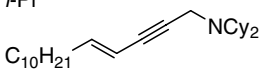
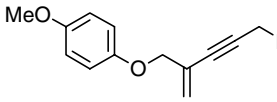
corresponding ene–allenes **4b–e** were obtained in 30–76% yields (entries 2–5). In the case of compound **3f**, the reaction carried at 50 °C gave the better yield than that at room temperature (entry 6).

We succeeded in the synthesis of ene–allenes from the corresponding propargylic amines at room temperature.

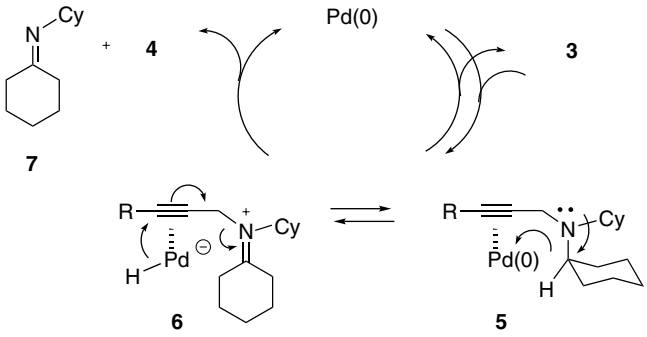
Table 3. Synthesis of the conjugated ene–allenes **4**[a]



3 **4**

Entry	Compound **3**	Conversion (%)	Yield of **4** (%)
1	 **3a**	75	88
2	 **3b**	100	73
3	 **3c**	88	57
4	 **3d**	72	30
5	 **3e**	85	76
6[b]	 **3f**	84	85

[a] Condition: $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %) and $(C_6F_5)_2PC_2H_4P(C_6F_5)_2$ (10 mol %) in $CHCl_3$ at room temperature for 7 days.
[b] The reaction was carried out at 50 °C.



Scheme 2. Proposed mechanism.

Dicyclohexyl groups substituted on the nitrogen of propargylic amines are effective for the current transformation. According to our proposed mechanism as shown in Scheme 2, the imine **7**[16] was generated along with the ene–allenes **4** from **3** via the iminium ion intermediates **6**. Therefore, it is considered that a stable formation of cyclic imines **7** would accelerate the catalytic cycle in the current allene transformation.

References and notes

1. (a) *The Chemistry of Allenes*; Landor, S. R., Ed.; Academic Press: London, 1982; (b) Hoffmann-Roder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 2933;

(c) *Modern Allene Chemistry*; Krause, N., Hashmi, S., Eds.; Wiley-VCH: Weinheim, 2004.
2. (a) *Allenes in Organic Synthesis*; Coppola, G. M., Schuster, H. F., Eds.; Wiley: New York, 1984; (b) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *J. Am. Chem. Soc.* **1990**, *112*, 8042.
3. Searles, S.; Li, Y.; Nassim, B.; Robert Lopes, M.-T.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 747.
4. Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492.
5. (a) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 2089; (b) Zimmermann, M.; Wibbeling, B.; Hoppe, D. *Synthesis* **2004**, 765.
6. Fukuhara, K.; Okamoto, S.; Sato, F. *Org. Lett.* **2003**, *5*, 2145.
7. (a) Tanaka, K.; Otsubo, K.; Fuji, K. *Synlett* **1995**, 993; (b) Brummond, K. M.; Dingess, E. A.; Kent, J. L. *J. Org. Chem.* **1996**, *61*, 6096.
8. Delouvrie, B.; Lacote, E.; Fensterbank, L.; Malacria, M. *Tetrahedron Lett.* **1996**, *40*, 3565.
9. (a) Tsuji, J.; Sugiura, T.; Yuhara, M.; Minami, I. *Chem. Commun.* **1986**, 922; (b) Tsuji, J.; Sugiura, T.; Minami, I. *Synthesis* **1987**, 603.
10. (a) Badone, D.; Cardamone, R.; Guzzi, U. *Tetrahedron Lett.* **1994**, *35*, 5477; (b) Huang, C.-W.; Shanmugasundaram, M.; Chang, H.-M.; Cheng, C.-H. *Tetrahedron* **2003**, *59*, 3635.
11. (a) Lee, K.; Seomon, D.; Lee, P. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3901; (b) Lin, M.-J.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 13042.
12. (a) Ma, S.; He, Q. *Angew. Chem., Int. Ed.* **2004**, *43*, 988; (b) Ma, S.; Zhang, A. *J. Org. Chem.* **1998**, *63*, 9601.
13. Nakamura, H.; Kamakura, T.; Ishikura, M.; Biellmann, J.-F. *J. Am. Chem. Soc.* **2004**, *126*, 5958.
14. Nakamura, H.; Onagi, S.; Kamakura, T. *J. Org. Chem.* **2005**, *70*, 2357.
15. For example, treatment of **3e** in $CHCl_3$ at 80 °C resulted in decomposition of the compound.
16. *N*-Cyclohexylidenecyclohexanamine **7** was detected by GC–MS analysis at the end of the reactions.