4570 *J. Org. Chem.* **1999,** *64,* 4570−4571

Communications

Palladium/Benzoic Acid Catalyzed Hydroamination of Alkynes

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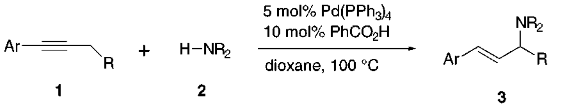
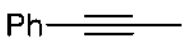
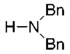
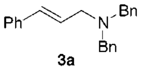
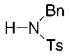
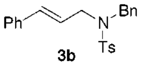
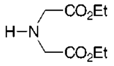
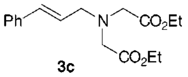
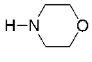
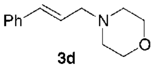
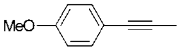
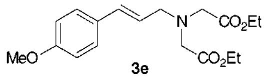
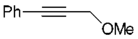
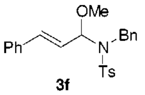
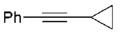
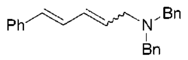
Received March 22, 1999

The hydroamination of C−C multiple bonds has been considered as one of the most efficient methods for the synthesis of organo-nitrogen compounds, because the addition process does not produce a waste element in contrast to the substitution process which inevitably affords a useless byproduct.[1] The palladium-catalyzed intermolecular hydroaminations of 1,3-dienes,[2] allenes,[3] enynes,[4] and methylenecyclopropanes[5] have been developed to realize the ideal C−N bond formation. Recently, we reported that certain alkynes react with carbon pronucleophiles in the presence of palladium/acetic acid catalyst to give the corresponding allylation products (formal hydrocarbonation based on the rearrangement of an alkyne to an allene).[6a] The hydrocarbonation process is similar to the hydroacylation process reported by Trost et al. for the allylation of acetic acid with alkynes which gives allylic acetates.[6b] It occurred to us that the formal hydrocarbonation may be extended to the formal hydroamination to provide a new atom-economical procedure for the synthesis of amines from alkynes.[7] Actually, the reaction of certain aromatic acetylenes **1** with amines **2** in the presence of 5 mol % $Pd(PPh_3)_4$ and 10 mol % $PhCO_2H$ in dioxane at 100 °C gave the corresponding allylic amines **3** in very high to good yields (eq 1).



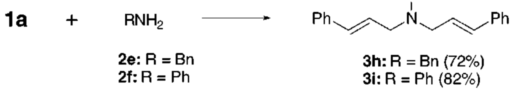
(1)

Table 1. Palladium/Benzoic Acid Catalyzed Hydroamination of Alkynes

entry	alkyne	amine	product	yield (%)[a]
1	 **1a**	 **2a**	 **3a**	98
2	**1a**	 **2b**	 **3b**	98
3	**1a**	 **2c**	 **3c**	77
4	**1a**	 **2d**	 **3d**	94
5	 **1b**	**2c**	 **3e**	82
6	 **1c**	**2b**	 **3f**	61
7	 **1d**	**2a**	 **3g** (E : Z = 85 : 15)	72[b]

[a] Isolated yield. [b] Inseparable mixture of the stereoisomers. The ratio was determined by ^1H NMR analysis.

In an initial experiment, 1-phenyl-1-propyne (**1a**) was treated with 1 equiv of dibenzylamine (**2a**), $Pd(PPh_3)_4$ (5 mol %), and benzoic acid[8] (10 mol %) in dioxane at 100 °C to give the allylic amine **3a** as a sole product in 98% yield (Table 1, entry 1). Similarly, the reactions of **1a** with secondary amines **2b**−**d** gave the allylic amines **3b**−**d**, respectively, in good to high yields (entries 2−4). In all cases, no regio- or stereoisomers were obtained. No reaction took place in the absence of benzoic acid. Other examples with various alkynes are summarized in Table 1. When *p*-methoxyphenylalkyne **1b** was used as a substrate, the yield was slightly increased (see entries 3 and 5). The reaction of substrates which have an electron-withdrawing groups at the para-position gave a messy mixture. A novel *N*,*O*-acetal **3f** was synthesized in good yield by the reaction of propargylic ether **1c** (entry 6). The reaction of cyclopropylphenylacetylene **1d** produced an 85:15 mixture of the *E* and *Z* linear adducts **3g** in 72% yield (entry 7). Aliphatic acetylenes such as 3-hexyne and 1-octyne did not react with amines under the reaction conditions mentioned above. The reaction of primary amines **2e** and **2f** was examined; 3 equiv of **1a** was treated with **2e** and **2f** under the same reaction conditions as above to give the 2:1 adducts **3h** and **3i**, respectively, in good yields (eq 2).



(2)

The reaction of 1-phenyl-1-propyne (**1a**) with dibenzylamine (**2a**) is representative. A mixture of **1a** (75 μL, 0.6 mmol), **2a** (96 μL, 0.5 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), and benzoic acid (6 mg, 0.05 mmol) in dry dioxane (2 mL)

[†] Institute for Chemical Reaction Science.

(1) For recent review of catalytic hydroamination, see: Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−703.

(2) Armbruster, R. W.; Morgan, M. M.; Schmidt, J. L.; Lau, C. M.; Riley, R. M.; Zabrowski, D. L.; Dieck, H. A. *Organometallics* **1986**, *5*, 234−237.

(3) (a) Besson, L.; Goré, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3857−3860. (b) Al-Masum, M.; Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1997**, *38*, 6071−6074. For lanthanoid-catalyzed intramolecular hydroamination of allenes, see: (c) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871−4872.

(4) Radhakrishnan, U.; Al-Masum, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 1037−1040.

(5) Nakamura, I.; Itagaki, H.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 6458−6459.

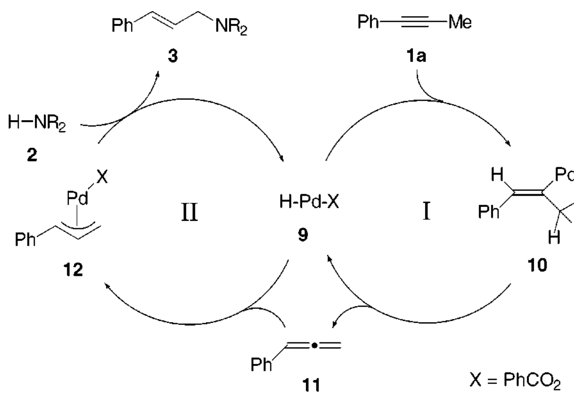
(6) (a) Kadota, I.; Shibuya, A.; Gyoung, Y.-S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 10262−10263. (b) Trost, B. M.; Brieden, W.; Baringhaus, K. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1335−1336. See also ref 9.

(7) For lanthanoid-catalyzed intramolecular hydroamination of alkynes, see: Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 9295−9306 and references therein.

(8) The use of acetic acid gave slightly lower yield.

10.1021/jo990498r CCC: $18.00

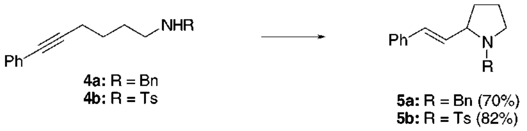
Scheme 1



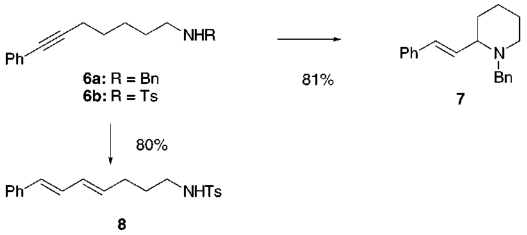
was stirred overnight at 100 °C. The reaction mixture was then filtered through a short silica gel column using ether as an eluent, and the filtrate was concentrated. The residue was purified by a silica gel column chromatography (hexane/EtOAc, 10:1) to give **3a** (154 mg, 98%).

A plausible catalytic cycle of this hydroamination is illustrated in Scheme 1. The initial step would be hydropalladation of **1a** with the hydridopalladium species **9** generated from Pd^0 and benzoic acid (catalytic cycle I).[9] The resulting vinylpalladium species **10** would produce phenylallene **11** and the active catalyst **9** via β-elimination.[10] Hydropalladation of **11** with **9** would give the π-allylpalladium species **12** which would react with amine **2** to give the product **3** along with the hydridopalladium **9** (cycle II).[11]

The usefulness of this transformation is demonstrated by the intramolecular version of the hydroamination reaction. The reaction of the alkynes **4a** and **4b**, having a monoprotected amino group at the terminus of the carbon chain, under the standard conditions mentioned above gave the pyrrolidine derivatives **5a** and **5b**, respectively, in good yields (eq 3). Similarly, the benzylamine derivative **6a** cyclized to produce piperidine **7** in 81% yield (eq 4). Interestingly, the tosylamide counterpart **6b** gave the linear diene **8** in 80% yield. Perhaps, the tosyl group would decrease the nucleophilicity of the nitrogen atom, hampering the cyclization. The diene **8** would be produced from the corresponding π-allylpalladium species via β-elimination.



(3)



(4)

In conclusion, we have developed a simple and efficient method for the synthesis of various acyclic and cyclic allylic amines using palladium/benzoic acid catalyst. Application of this efficient process to alkaloid synthesis is presently under investigation.

Acknowledgment. This work was financially supported by the Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

Supporting Information Available: Characterization data of compounds **3a**−**i**, **5a**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161−3163.

(10) For palladium-catalyzed isomerization of alkynes to allenes, see: (a) Sheng, H.; Lin, S.; Huang, Y. *Tetrahedron Lett.* **1986**, *27*, 4893−4894. (b) Trost, B. M.; Schmidt, T. *J. Am. Chem. Soc.* **1988**, *110*, 2301−2303. (c) Lu, X.; Ji, J.; Ma, D.; Shen, W. *J. Org. Chem.* **1991**, *56*, 5774−5778.

(11) For the allylation of acetic acid with alkynes via a π-allylpalladium intermediate, see ref 6b and Al-Masum, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 3809−3810.