Pergamon

Tetrahedron Letters, Vol. 38, No. 34, pp. 6071-6074, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01370-1

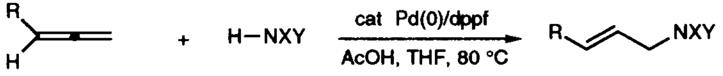
The Two Component Palladium Catalyst System for Intermolecular Hydroamination of Allenes

Mohammad Al-Masum[†], **Masaki Meguro and Yoshinori Yamamoto***

Research Center for Organic Resources and Materials Chemistry, Institute for Chemical Reaction Science
and
Department of Chemistry, Graduate school of Science, Tohoku University,
Sendai 980-77, Japan

Abstract: The combination of acetic acid with $Pd_2(dba)_3.CHCl_3$ and dppf [1.1' - Bis(diphenylphosphino ferrocene)] is a new type of catalytic system, capable of effecting the addition of protected and/or functionalized amines to allenes with high regio- and stereoselectivity.

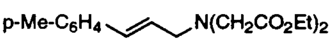
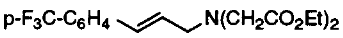
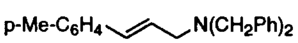
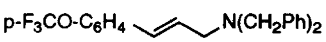
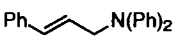
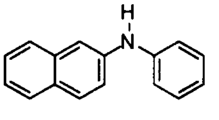
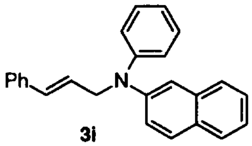
One of the fundamental processes in organic chemistry is to form an amine, enamine or imine by the addition of an H-N bond to an olefin or alkyne.[1,2] Only small number of catalytic intermolecular hydroamination reactions are reported.[3,4] Our recent finding of a hydrocarbonation reaction in the presence of palladium catalyst open up a new era for C-C bond formation reaction.[5] By expanding this palladium chemistry, we found an easy access to intermolecular hydroamination of allenes with protected amines. Cazes's group first reported the intermolecular hydroamination of allenes with aliphatic amines.[6] They found the beneficial effect of adding triethylammonium iodide with palladium catalyst for this transformation. We examined the reaction of phenyl allene **1a** with iminodiacetic acid diethylester **2a** using Cazes's conditions (5 mol% $Pd(dba)_2$, 10 mol% Ph_3P, 30 mol % Et_3NHI, in THF at 65 °C for 22 h), and then 53% yield of **3a** (by NMR) was obtained. But when we ran the same reaction in the presence of $Pd_2(dba)_3.CHCl_3$/dppf with additive acetic acid in THF at 80 °C for 8 h, complete conversion with 98% isolated yield was accomplished. Here we demonstrate that the catalytic system is very effective for the intermolecular hydroamination of various mono-substituted allenes with protected amines. Without acetic acid no satisfactory change was obtained (Table 1, entry 1). The dramatic change was observed when a catalytic amount of acetic acid was introduced into the reaction system (eq 1). Using π-allyl palladium chloride dimer as the palladium source the reaction proceeded but in very low yield. Aromatic allenes reacted faster and gave very high yields of hydroamination products. The results are shown in Table 1, (e.g., entries 2-5). Although phenylethylallene **1d** gave high yield (entry 6), n-octylallene **1e** gave low yield (entry 7). Regardless of EDG and EWG at the para position of the phenyl ring of the allene, γ-selectivity was obtained (entries 4,5). Dibenzylamine **2b** reacted with allenes **1b** and**1f** smoothly and very high yields



1 **2** **3** (eq 1)

2a, X = Y = CH_2CO_2Et
2b, X = Y = CH_2Ph
2c, X = Y = Ph
2d, X = β-Naphthyl, Y = Ph

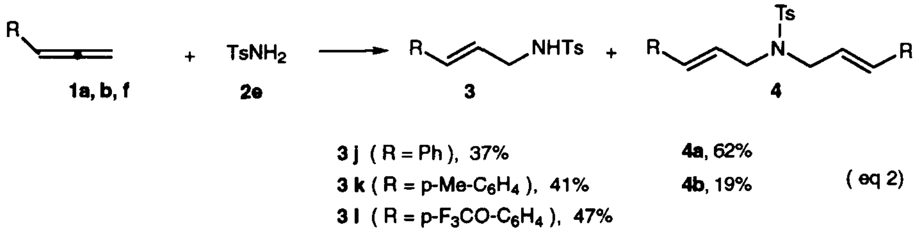
Table 1. Hydroamination of allenes[a]

Entry	R of Allene 1	Amine 2	Product 3	Isolated yield (%)
1	Ph **1a**	H-N(CH_2CO_2Et)$_2$ **2a**	 **3a**	~10[b]
2	**1a**	**2a**	**3a**	98[c]
3	**1a**	**2a**	**3a**	100[d]
4	p-Me-C_6H_4 **1b**	**2a**	 **3b**	73
5	p-F_3C-C_6H_4 **1c**	**2a**	 **3c**	67
6	$PhCH_2CH_2$ **1d**	**2a**	 **3d**	83[e]
7	n-Octyl **1e**	**2a**	 **3e**	32[e]
8	p-Me-C_6H_4 **1b**	H-N(CH_2Ph)$_2$ **2b**	 **3f**	99
9	p-F_3CO-C_6H_4 **1f**	**2b**	 **3g**	75
10	p-Me-C_6H_4 **1b**	H-N(Ph)$_2$ **2c**	 **3h**	67
11	**1a**	 **2d**	 **3i**	62[e]

[a]Optimized conditions were applied. All yields are of pure product isolated by column chromatography. The *E* - stereochemistry is confirmed by NOE experiment. ^1H NMR and high resolution mass spectral (HRMS) data are satisfactory. [b]Without acetic acid. [c]20 mol% acetic acid was added. [d]1.0 equiv acetic acid was added. [e]Reaction time is varied from 20 - 24 h.

were obtained (entries 8,9). Debenzylation can be carried out with β,β,β-trichloroethyl chloformate in acetonitrile followed by treatment with zinc in acetic acid.[7] This deprotection method will not hydrogenate the olefinic double bond. Diphenylamine **2c** and β-naphthylphenylamine **2d** also worked well (entries 10,11). In the case of tosylamine **2e** double amination products **4** along with mono-adducts **3** were obtained (eq 2).[8] Perhaps **3** is more reactive than **2e**. But with p-trifluoromethoxy phenylallene the mono-

-adduct **3l** was obtained as a sole product. This tosyl group can be removed by the usual procedure.[9]

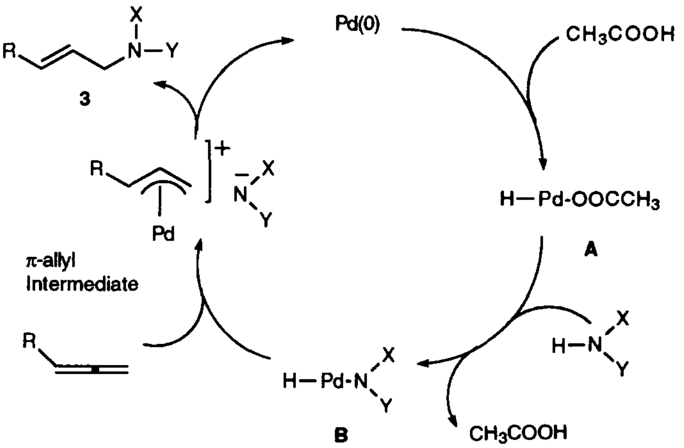


3j (R = Ph), 37% **4a**, 62%
3k (R = p-Me-C_6H_4), 41% **4b**, 19% (eq 2)
3l (R = p-F_3CO-C_6H_4), 47%

The typical procedure for the synthesis of **3a** is as follows: To a reaction vial under argon charged with $Pd_2(dba)_3.CHCl_3$ (0.025 mmol, 26.0 mg) and dppf (0.06 mmol, 33.0 mg) in THF (0.5 ml) were added acetic acid (0.1 mmol, 0.006 ml), phenylallene (0.5 mmol, 58 mg), and iminodiacetic acid diethylester (0.6 mmol, 0.6 ml), and then the mixture was heated at 80 °C for 8 h.[10] The reaction mixture was filtered through a short alumina column or through a celite pad using THF as eluent. The solvent was removed *in vacuo*. The crude product was filtered through silica gel column using hexane/ethylacetate (with ratio 10/1 and then 5/1) as eluent affording the product **3a** in 98% yield.

A possible mechanism for this addition of protected amine to allene is shown in Scheme 1. The oxidative addition of acetic acid to Pd(0) would produce the hydrido palladium species **A** of acetic acid,[11] which then generates acetic acid in the presence of protected amine by the insertion of H-N bond and the intermediate **B** is formed.[12] In fact, Trost et al, recently reported this sort of catalytic system for C-C bond formation reactions.[13] The H-N inserted palladium species forms a π-allylpalladium intermediate with allene which after reductive elimination gives the hydroamination product with γ-selectivity.[14]

By employing various protected amines which can be deprotected easily, this method will be useful for allyl amine synthesis. The mild conditions and easy workup of this new form of palladium catalyst may offer a significant advantage to hydroamination reactions. Furthermore, this method should be of interest for C-N bond formation reaction in synthetic organic chemistry.



Scheme 1

References And Notes

† Research Center for Organic Resources and Materials Chemistry, Institute for Chemical Reaction Science,Tohoku University, Sendai 980-77, Japan

1. a) For a review of additions of amines to alkenes, see: Gase, M. B.; Latties, A.; Perie, J. J. *Tetrahedron* **1983**, *339*, 703. c) For a review of addition of amines to alkynes, see: Jager, V.; Viehe, H. G. Hoben-wel, Methoden der Organischen Chemie, ' Thieme verlag: Stuttgart, Germany, 1977; vol 5/2a, pp 713.
2. a) Brunet, J.-J.; Neibecker, D.; Niedercorn, F. *J. Mol. Catal.* **1989**. *49*, 235-259. b) Hegedus, L. S. *Angew. Chem., Intl. Ed. Engl.* **1988**, *27*, 1113 -1126. c) Trost, B. M.; Verhoeven, T. R. In Comprehensive Organometallic Chemistry; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford. U.K., 1982; Vol. 8, pp 892-895.
3. Intermolecular Hydroamination: a) Haskel, A.; Straub, T; Eisen, M. S. *Organometallics* **1996**, *15*, 3773. b) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708. c) Casalnuovo, A. L.; Calabbreses, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738.
4. a) Organolanthanide-Catalyzed Intramolecular hydroamination: Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 9295-9306. and references therein.
5. a) Yamamoto, Y.; Al-Masum, M.; Fujiwara, N.; Asao, N. *Tetrahedron Lett.* **1995**, *35*, 2811. b) Yamamoto, Y.; Al-Masum, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *113*, 6019. and references therein.
6. Besson, L.; Gore, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3857. and references therein.
7. a) Rawal, V. H.; Jones, R. J.; Cava, M. P. *J. Org. Chem.* **1987**, *52*, 19-28. b) Reinecke, M. C.; Daubert, R. C. *J. Org. Chem.* **1973**, *38*, 3281.
8. In tosyl amine cases, when phenylallene : amine ratio was 1:1, isolated yield for **4a** and **3j** were 62% and 37% respectively and when allene : amine ratio was 2:1, isolated yield for **4a** and **3j** were 61% and 24% respectively.With allenes **1b** and **1f**, 1:1 ratio was used.
9. Protective groups in Organic Synthesis, 2nd Ed.; T. W. Greene and P. G. M. Wuts. John Wiley & Sons, Inc., **1991**, pp 379.
10. It is to be noted that when 1:1 ratio of $Pd_2(dba)_3.CHCl_3$ and dppf was employed **3a** was obtained in lower yield (51%).
11. a) Zudin, V. N.; Chikov, V. D.; Nekipelov, V. M.; Likhholov, V. A.; Yermakov, Y. I. *J. Organomet. Chem.* **1985**, *289*, 425. b) Werner, H.; Bertleff, W. *Chem. Ber.* **1983**, *116*, 823. c) Schunn, R. A. *Inorg. Chem.* **1976**, *15*, 823.
12. Oxidative Addition of H-N Bond in Amides: a) Hursthouse, M. B.; Mazid, M. A.; Robinson, S. D.; Sahajpal, A. *J. Chem. Soc., Chem. Commun.* **1991**, 1146. b) Kurishima, S.; Matsuda, N.; Tamura, N.; Ito, T. *J. chem. Soc.* DALTON TRANS. **1991**, 1135. c) Glueck, D. S.; Wu, J. Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1991**, *113*, 2041. d) Cowan, R. L.; Trogler, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 4750.
13. Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1996**, *118*, 6305. and references therein.
14. One referee suggested that the role of acetic acid is to protonate the Pd-coordinated allene and facilitate nucleophilic attack by the amine.

(*Received in UK* 20 *May* 1997; *revised* 1 *July* 1997; *accepted* 4 *July* 1997)