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Intermolecular Aerobic Oxidative Allylic Amination of Simple Alkenes with Diarylamines Catalyzed by the $Pd(OCOCF_3)_2/NPMoV/O_2$ System

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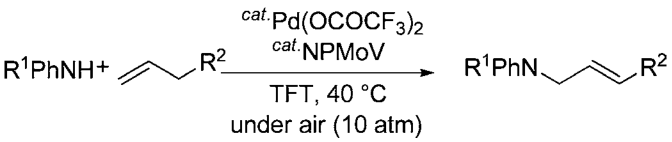
ABSTRACT



Intermolecular aerobic oxidative allylic amination of simple alkyl alkenes with simple amines such as diphenylamine was induced by a $Pd(OCOCF_3)_2$/NPMoV catalytic system, leading to the corresponding (*E*)-allylamines in good yield and selectivity through the formation of (η^3-allyl)palladium(II) trifluoroacetate species as a possible key intermediate.

A selective allylic C−H bond functionalization of alkenes through allylic oxidation reactions is an important methodology for the direct installation of functionality into hydrocarbon frameworks.[1] In particular, Pd(II)-catalyzed oxidative allylic amination is an efficient methodology for preparing nitrogen-containing unsaturated compounds such as enamines and allylic amines.[2] However, there have been limited works on the reaction with nonsubstituted simple alkenes. Recently, White and co-workers reported that Pd(II)-sulfide/Cr(III)-catalyzed oxidative allylic amination of the simple alkenes with tosylamides using 2 equiv of benzoquinone as a reoxidant affords allylamides.[3] Thereafter, the same group presented that the Pd(II)/sulfoxide-catalyzed allylic amination was promoted with dialkylamine bases.[4] In addition, Liu and co-workers reported the Pd(II)-catalyzed aerobic oxidative allylic amination of the simple alkenes with tosylamides under 6 atm of O_2 pressure.[5] On the other hand, Stahl and co-workers reported a Pd(II)-catalyzed aza-Wacker-type reaction of simple alkenes with imides or sulfamate esters affording enamides as products.[6] However, these previous reports are limited to the reaction with nonbasic amides and imides as nitrogen nucleophiles. Therefore, the development of an innovative method for the intermolecular aerobic oxidative allylic amination of simple alkenes with simple amines under mild conditions is highly desired.[7]

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(1) (a) Hansson, S.; Heumann, A.; Rein, T.; Åkermark, B. *J. Org. Chem.* **1990**, *55*, 975. (b) Heumann, A.; Reglier, M.; Waegell, B. *Angew. Chem., Int. Ed.* **1982**, *21*, 366. (c) Heumann, A.; Åkermark, B. *Angew. Chem., Int. Ed.* **1984**, *23*, 453. (d) McMurry, J. E.; Kocovsky, P. *Tetrahedron Lett.* **1984**, *25*, 4187. (e) Åkermark, B.; Larsson, E. M.; Oslob, J. D. *J. Org. Chem.* **1994**, *59*, 5729. (f) Macsari, I.; Szabo, K. J. *Tetrahedron Lett.* **1998**, *39*, 6345. (g) Yu, J.-Q.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, *125*, 3232. (h) Mitsudome, T.; Umetani, T.; Nosaka, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew Chem., Int. Ed.* **2006**, *45*, 481. *Angew. Chem.* **2006**, *118*, 495. (i) Chen, M. S.; White, M. C. *J. Am. Chem. Soc.* **2004**, *126*, 1346. (j) Chen, M. S.; Prabagaran, N.; Labenz, N. A.; White, M. C. *J. Am. Chem. Soc.* **2005**, *127*, 6970. (k) Fraunhoffer, K. J.; Bachovchin, D. A.; White, M. C. *Org. Lett.* **2005**, *7*, 223.

(2) Examples of intramolecular oxidative allylic amination: (a) Wu, L.; Qiu, S.; Liu, G. *Org. Lett.* **2009**, *11*, 2707. (b) Scarborough, C. C.; Bergant, A.; Sazama, G. T.; Guzei, I. A.; Spencer, L. C.; Stahl, S. S. *Tetrahedron.* **2009**, *65*, 5084. (c) Yu, H.; Fu, Y.; Guo, Q.; Lin, Z. *Organometallics,* **2009**, *28*, 4507. (d) Fraunhoffer, K. J.; White, M. C. *J. Am. Chem. Soc.* **2007**, *129*, 7274, and references cited therein.

(3) Reed, S. A.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 3316.

(4) Reed, S. A.; Mazzotti, A. R.; White, M. C. *J. Am. Chem. Soc.* **2009**, *131*, 11701.

(5) Liu, G.; Yin, G.; Wu, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4733.

(6) (a) Rogers, M. M.; Kotov, V.; Chatwichien, J.; Stahl, S. S. *Org. Lett.* **2007**, *9*, 4331. (b) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868.

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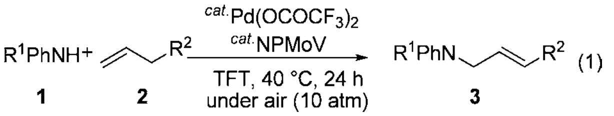


(1)

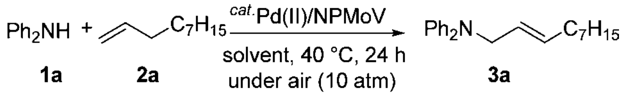
We have recently found that the $PdCl_2(PhCN)_2$/molybdovanadophosphate salt (NPMoV) system[8] catalyzes efficiently the aza-Wacker-type reaction of simple amines such as diphenylamine with electron-deficient alkenes such as acrylates to afford enamines which have been difficult to obtain as products so far.[9]

In this study, we would like to report $Pd(OCOCF_3)_2$/NPMoV-catalyzed intermolecular aerobic oxidative allylic amination of simple aliphatic alkenes with simple amines such as diphenylamine, leading to the corresponding (*E*)-allylamines in good yields with high regio- and stereoselectivity (eq 1).

The reaction of diphenylamine (**1a**) with 1-decene (**2a**) was chosen as a model reaction and carried out under various conditions (Table 1). For instance, **1a** (1 mmol) was reacted with **2a** (7 mmol) in the presence of $Pd(OCOCF_3)_2$ (0.1 mmol) and $(NH_4)_5H_4PMo_6V_6O_{40}{\cdot}23H_2O$ (NPMoV) (0.02 mmol) in trifluorotoluene (TFT) (1 mL) under air (10 atm) at 40 °C for 24 h to give (*E*)-1-diphenylamino-2-decene (**3a**) in good yield (73%) in 78% conversion of **1a** (entry 1). The reaction proceeded with high stereo- and regioselectivity to afford the *E* isomer, exclusively. In addition, no aza-Wacker-type product was detected at all under these conditions. The yield of **3a** was high for the reaction of **1a** when an excess (7 equiv) of **2a** was employed (entry 1). However, even if the reaction of **1a** with **2a** was allowed to take place in a 1:3 molar ratio, the yield of **3a** was still moderate (entry 2). Removal of NPMoV from the catalytic system resulted in a sluggish reaction (entry 3).

Needless to say, no reaction was induced in the absence of Pd(II) catalyst. The reaction under argon resulted in a low yield of **3a** because of difficulty of regenerating Pd(II) from the reduced Pd(0) during the reaction (entry 4). The reaction proceeded under atmospheric oxygen (1 atm) and gave **3a** in moderate yield (entry 5). This is in sharp contrast to the previously reported oxidative aminations with alkyl alkenes which requires relatively high O_2 pressure (4−6 atm).[5,6a] It is important to note that $Pd(OCOCF_3)_2$ showed the highest catalytic activity. In contrast, $Pd(OAc)_2$ and $Pd(acac)_2$, which showed good catalytic performance in the Pd(II)/NPMoV/O_2 catalytic system reported previously,[8] resulted in lower catalytic activity in the present reaction (entries 6−9). The yield of **3a** was considerably decreased when molybdovanadophospholic acids (HPMoV) such as $H_4PMo_{11}VO_{40}{\cdot}23H_2O$ and $H_7PMo_8V_4O_{40}{\cdot}25H_2O$ were used as reoxidation catalysts of the reduced Pd(0) because of the formation of an amine salt of HPMoV with **1a** (entries 10 and 11). This shows that molbdovanadophosphate (NPMoV) partly replaced by ammonium cation of the HPMoV provides an efficient reoxidation system in this reaction.

Table 1. Pd(II)/NPMoV-Catalyzed Oxidative Allylic Amination of Diphenylamine (**1a**) with 1-Decene (**2a**) under Various Conditions[a]



entry	Pd catalyst	solvent	yield of **3a**/%[b,c]
1	$Pd(OCOCF_3)_2$	TFT	73 (62)
2[d]	$Pd(OCOCF_3)_2$	TFT	41
3[e]	$Pd(OCOCF_3)_2$	TFT	15
4[f]	$Pd(OCOCF_3)_2$	TFT	15
5[g]	$Pd(OCOCF_3)_2$	TFT	60
6	$Pd(OAc)_2$	TFT	4
7	$PdCl_2(PhCN)_2$	TFT	n.d.[h]
8	$Pd(acac)_2$	TFT	n.d.[h]
9	$PdCl_2$	TFT	n.d.[h]
10[i]	$Pd(OCOCF_3)_2$	TFT	19
11[j]	$Pd(OCOCF_3)_2$	TFT	37
12	$Pd(OCOCF_3)_2$	perfluorohexane	73
13	$Pd(OCOCF_3)_2$	FC-72[k]	74
14	$Pd(OCOCF_3)_2$	toluene	55
15	$Pd(OCOCF_3)_2$	DMF	35
16	$Pd(OCOCF_3)_2$	DME	6
17	$Pd(OCOCF_3)_2$	PhCN	7
18	$Pd(OCOCF_3)_2$	ᵗBuOH	30

[a] Conditions: **1a** (1 mmol) was allowed to react with **2a** (7 mmol) in the presence of Pd catalyst (10 mol %) and NPMoV (2 mol %) in solvent (1 mL) under air (10 atm) at 40 °C for 24 h. [b] GC yields based on **1a** used. The number in parentheses shows the isolated yield. [c] In this reaction, 2-decanone (5−20% based on **2a** used) was obtained as byproduct. [d] **1a** (1 mmol) and **2a** (3 mmol) were used. [e] Reaction was performed in the absence of NPMoV. [f] Reaction was performed under Ar. [g] Reaction was performed under O_2 (1 atm). [h] Not detected by GC. [i] $H_4PMo_{11}VO_{40}{\cdot}23H_2O$ was used as a reoxidation catalyst. [j] $H_7PMo_8V_4O_{40}{\cdot}25H_2O$ was used as a reoxidation catalyst. [k] Perfluorohexanes, 3 M Company, St Paul, MN.

Among solvents examined in this reaction, fluorous solvents such as TFT, perfluorohexane, and FC-72 were found to be suitable for the formation of **3a**, while the reaction in toluene, DMF, DME, PhCN, and ᵗBuOH under these reaction conditions afforded **3a** in low yields (entries 12−18).

Under optimized conditions, reactions of various diarylamines (**1**) with aliphatic alkenens (**2**) afforded the corresponding allylamine derivatives in good yields (Table 2). Thus, 1-octene (**2b**), 1-dodecene (**2c**), allylcyclohexane (**2d**), allylbenzene (**2e**), and 4-phenyl-1-butene (**2f**) were allowed to react with **1a** affording the corresponding (*E*)-allyamine derivatives (**3b−f**) in good yields (entries 1−5). An alkene bearing ester group, methyl 5-hexenoate (**2g**) also reacted with **1a** to give the corresponding product (**3g**) in good yield (entry 6). Secondary aromatic amines such as 3-methyldiphenylamine (**1b**) and 3-fluorodiphenylamine (**1c**) are tolerated as substrates in the reaction with **2a** to afford the corresponding oxidative allylic amination products in moderate to good yield (entries 7 and 8). Unfortunately, the reaction with aliphatic amines such as hexylamine, dibutylamine, and primary aromatic amines such as anilines were sluggish due to the deactivation of palladium and NPMoV species by strong coordination of these amines.

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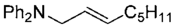
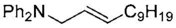
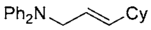
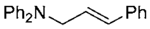
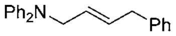
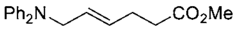
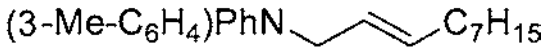
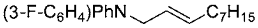
(7) Examples of allylic amination with hydroxyl amines: (a) Hogan, G. A.; Gallo, A. A.; Nicholas, M. M.; Srivastava, R. S. *Tetrahedron Lett.* **2002**, *43*, 9505. (b) Adam, W.; Krebs, O. *Chem. Rev.* **2003**, *103*, 4131.

(8) Examples of the Pd/NPMoV/O_2-catalyzed reactions: (a) Yokota, T.; Fujibayashi, S.; Nishiyama, Y.; Sakaguchi, S.; Ishii, Y. *J. Mol. Catal. A: Chem.* **1996**, *114*, 113. (b) Yokota, T.; Sakakura, A.; Tani, M.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2002**, *43*, 8887. (c) Yokota, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2002**, *67*, 5005.

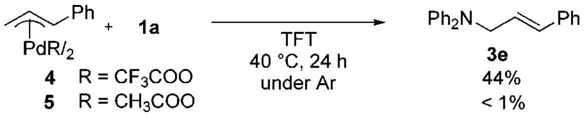
(9) Obora, Y.; Shimizu, Y.; Ishii, Y. *Org. Lett.* **2009**, *11*, 5058.

Table 2. $Pd(OCOCF_3)_2$/NPMoV-Catalyzed Oxidative Allylic Amination of **1** and **2** Leading to Allylamine Derivatives (**3**)[a,b]

entry	amine(**1**) R^1	alkene(**2**) R^2	product (**3**)
1	Ph(**1a**)	C_5H_{11} (**2b**)	 72 (52) (**3b**)
2	**1a**	C_9H_{19} (**2c**)	 (53) (**3c**)
3	**1a**	Cy(**2d**)	 75 (73) (**3d**)
4	**1a**	Ph(**2e**)	 78 (75) (**3e**)
5	**1a**	CH_2Ph (**2f**)	 (67) (**3f**)
6	**1a**	$(CH_2)_2CO_2Me$ (**2g**)	 55 (40) (**3g**)
7	3-Me-C_6H_4 (**1b**)	**2a**	 67 (45) (**3h**)
8	3-F-C_6H_4 (**1c**)	**2a**	 46 (44) (**3i**)

[a] Conditions: **1** (1 mmol) was allowed to react with **2** (7 mmol) in the presence of $Pd(OCOCF_3)_2$ (0.1 mmol) and NPMoV (0.02 mmol) in TFT (1 mL) under air (10 atm) at 40 °C for 24 h. [b] GC yields. The numbers in parentheses show isolated yields.

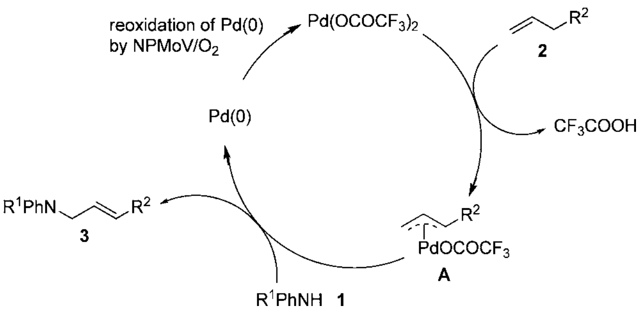
It is known that the reaction of alkenes with Pd(II) forms an η^3-allylpalladium intermediate through allylic C−H bond activation.[3−5] To obtain further insight of the Pd species in this reaction, (η^3-cinnamyl)palladium trifluoroacetate dimer (**4**) and (η^3-cinnamyl)palladium acetate dimer (**5**) were independently prepared as model intermediates and the stoichiometric reaction with **1a** was carried out (eq 2). As a result, the reaction of **4** with **1a** produced **3e** in substantial yield along with unreacted **1a**,[10] while almost no coupling product was obtained by the reaction with **5**. These results indicate that the electrophilicity of the η^3-allylpalladium species is an important factor to facilitate the present reaction. It seems that the formation of more electrophilic η^3-allylpalladium trifluoroacetate is suitable for the present reaction,[11] which would be the key step in the reaction.



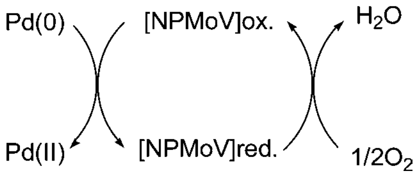
4 R = CF_3COO
5 R = CH_3COO
(2)

Therefore, although a detailed reaction mechanism is not confirmed at this stage, a plausible path is shown in Scheme 1. First, Pd(II) reacts with alkene (**2**) to form an η^3-allylpalladium intermediate **A** through the allylic C−H bond activation.[3−5] Then, the **A** is subjected to the nucleophilic attack of amine (**1**) to afford the oxidative allylic amination product **3** and Pd(0). Finally, Pd(0) is reoxidized by the NPMoV/O_2 system to generate Pd(II) (Scheme 2).[8]

Scheme 1. A Plausible Reaction Mechanism



Scheme 2. A Mechanism of Regeneration of Pd(II) from Pd(0) under the Influence of NPMoV and O_2



Unfortunately, the isolation of the expected palladium−amine adducts and the direct observation of the amine coordinating species by NMR are not successful at this point. Therefore, another reaction pathway through aminopalladation/β-hydride elimination (aza-Wacker process) cannot be ruled out completely (Figure S1, Supporting Information).

In conclusion, we reported the Pd(II)/NPMoV/O_2-catalyzed oxidative allylic amination of simple alkenes with simple amines to afford (*E*)-allylamines.

Further study on the detailed investigation of the scope and the reaction mechanism is currently under investigation.

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Supporting Information Available: Experimental procedure and compound characterization data (^1H NMR, ^{13}C NMR, IR, and MS) of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The yield of **3e** was not improved even if the reaction was carried out under air (10 atm) in the presence of NPMoV.

(11) (a) Obora, Y.; Ogawa, Y.; Imai, Y.; Kawamura, T.; Tsuji, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10489. (b) Hegedus, L. S.; Åkermark, B.; Zetterberg, K.; Olsson, L. F. *J. Am. Chem. Soc.* **1984**, *106*, 7122.