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Palladium-Catalyzed Regioselective Carbonylation of 2,3-Dienylamines to α-Vinylacrylamides

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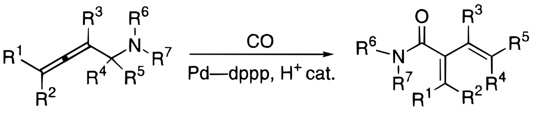
The selective insertion of carbon monoxide into an unactivated carbon−nitrogen bond of an amine to form an amide provides a novel and convenient process for homologation and functionalization of nitrogen-containing organic molecules. Although some nitrogen heterocycles have been found to undergo carbonylative ring expansion efficiently,[1] the palladium-catalyzed homologation of allylamines was the only example involving an acyclic system.[2] More recently, we found that the carbonylation of propargylamines occurs regioselectively in the presence of a catalytic system consisting of tris(dibenzylideneacetone)dipalladium(0), 1,3-bis(diphenylphosphino)propane (dppp), and *p*-toluenesulfonic acid, affording 2,3- or 2,4-dienamides.[3] It was of considerable interest to determine whether amines containing an allenyl unit can be carbonylated using a palladium-based catalytic system. We now wish to report the highly regioselective efficient carbonylation of 2,3-dienylamines[4,5] affording α-vinylacrylamides in 59−84% isolated yield (eq 1).



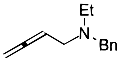
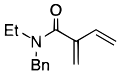
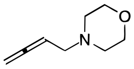
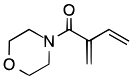
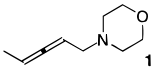
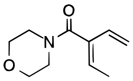
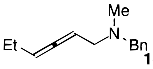
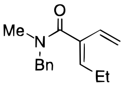
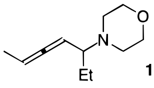
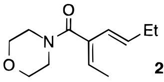
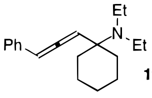
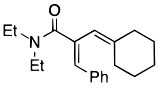
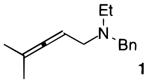
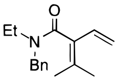
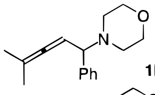
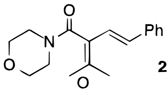
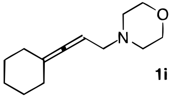
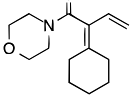
(1)

1 **2**

N-Benzyl-*N*-ethyl-2,3-butadienylamine (**1a**) was carbonylated to *N*-benzyl-*N*-ethyl-2-methylene-3-butenamide (**2a**) in 83% yield, using a catalytic system consisting of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.5 mol %), dppp (1 mol %), and *p*-TsOH (1 mol %) in dichloromethane at 75 °C for 3 h. It is noteworthy that the insertion of carbon monoxide occurred in a regioselective manner at the central sp carbon of the allene unit, and no other isomers were detected. The addition of *p*-TsOH promotes the formation of amide **2a**; in the absence of *p*-TsOH, a longer reaction time is required. The amide **2a** was not formed in the absence of dppp, and use of excess dppp reduced the catalytic activity of palladium. Monodentate phosphines such PPh_3 and PCy_3 are ineffective.

The carbonylation reaction was applied to a series of 2,3-dienylamines, and the results are listed in Table 1.

Table 1. Palladium-Catalyzed Carbonylation of 2,3-Dienylamines to α-Vinylacrylamides[a]

entry	2,3-dienylamine		α-vinylacrylamide[b]		yield,[c] %
1		**1a**		**2a**	83
2		**1b**		**2b**	83
3		**1c**		**2c**	84[e]
4		**1d**		**2d**	78[f]
5		**1e**		**2e**	80[g]
6		**1f**		**2f**	64[d,h]
7		**1g**		**2g**	59[d]
8		**1h**		**2h**	68[d,i]
9		**1i**		**2i**	68[d]

[a] Reaction conditions: 2,3-dienylamine, $Pd_2(dba)_3{\cdot}CHCl_3$ (0.5 mol %), dppp (1 mol %), *p*-TsOH (1 mol %), CH_2Cl_2, 75 °C, 3 h unless otherwise noted. [b] Products were identified by spectroscopic methods [IR, MS, NMR (^1H, ^{13}C)]. [c] Isolated yield. [d] $Pd_2(dba)_3{\cdot}CHCl_3$ (2 mol %), dppp (4 mol %), *p*-TsOH (4 mol %), 6 h. [e] 95:5 (α,*β*-*E*/*Z*). [f] 97:3 (α,*β*-*E*/*Z*). [g] 65:35 (*β*,*γ*-*E*/*Z*); not determined for α,*β*-*E*/*Z*. [h] 98:2 (α,*β*-*E*/*Z*). [i] 97:3 (*β*,*γ*-*E*/*Z*).

Less hindered 2,3-dienylamines, such as nonsubstituted, 4-monosubstituted, and 1,4-disubstituted 2,3-dienylamines **1a**−**e**, were carbonylated smoothly in the presence of 0.5 mol % of palladium catalyst [$Pd_2(dba)_3{\cdot}CHCl_3$], affording the α-vinylacrylamides in 78−84% yield (Table 1, entries 1−5). Highly substituted 2,3-dienylamines, such as 1,1-disubstituted and 4,4-disubstituted 2,3-dienylamines **1f**−**i**, did not undergo carbonylation under the standard reaction conditions. However, carbonylation of these amines can be brought about successfully after 6 h, when 2 mol % of palladium catalyst was used, affording the highly substituted α-vinylacrylamides in 59−68% isolated yield (Table 1, entries 6−9). In all cases, the insertion of carbon monoxide occurred regioselectively at the central sp carbon of the allene unit giving α-vinylacrylamides as the sole product, which may be used in Diels−Alder reactions. The carbonylations of 4-monosubstituted 2,3-dienylamines **1c**−**f** were stereoselective, affording exclusively the α,*β*-*E* isomer of **2c**−**f** as confirmed by NOE experiments. To our knowledge, only two methods have been reported for the direct synthesis of α-vinylacrylamides, including [2 + 2] cycloaddition of *β*-vinylynamines with carbonyl compounds[6] and the dehydrogenation of α,*β*-unsaturated amides *via* immonium chloride.[7]

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(1) For a review, see: Khumtaveeporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414.

(2) Imada, Y.; Nishimura, K.; Murahashi, S.-I. *Tetrahedron* **1994**, *50*, 453.

(3) Imada, Y. Alper, H. *J. Org. Chem.*, in press.

(4) 2,3-Dienylamines were prepared in 34−71% yield by copper-catalyzed Mannich-type reaction[5a] of the corresponding methyl propargyl ether with amines and aldehydes and subsequent $AlCl_3$-mediated reduction with $LiAlH_4$.[5b]

(5) (a) Mornet, R.; Gouin, L. *Bull. Soc. Chim. Fr.* **1974**, 206. (b) Barbot, F.; Dauphin, B.; Miginiac, P. *Synthesis* **1985,** 768.

(6) Kormer, M. V.; Tolchinskii, S. E.; Maretina, I. A.; Petrov, A. A. *Zh. Org. Khim.* **1985**, *21*, 725; *Chem. Abstr.* **1985**, *103*, 141583.

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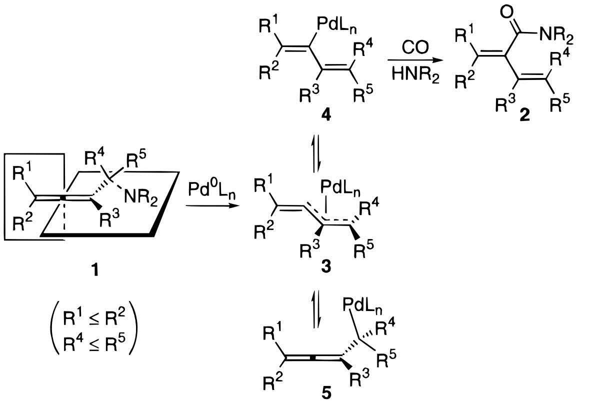
Scheme 1



A possible mechanism for the reaction is outlined in Scheme 1. Palladium(0) undergoes oxidative addition to the central sp carbon of a 2,3-dienylamine **1**, in *anti*-S$_N$2' fashion (as proposed in an allylic system),[8] leading to the π-allylpalladium intermediate **3**. Similar π-allylpalladium intermediates, in which the π-allylpalladium unit is directly connected to the double bond, have previously been proposed for the palladium-catalyzed reaction of 2,3-dienyl alcohols[9] and their esters.[10] The insertion of carbon monoxide occurs selectively *via* the 1,3-dien-2-ylpalladium intermediate **4** rather than the 2,3-dienylpalladium intermediate **5**, giving α-vinylacrylamide **2**. This selectivity is opposite to that of the palladium-catalyzed allylic carbonylations, where carbon monoxide is inserted only at the least substituted terminal carbon of the allyl unit.[11] The high selectivity may be explained in terms of the greater stability of the 1,3-dienyl complex **4** in comparison with the isomeric 2,3-dienyl species **5**, because of the possibility of π-conjugation in the 1,3-dienyl complex **4**.

The stereochemistry of the reaction can also be accounted for using Scheme 1. Palladium attacks at the central sp carbon from the direction of the smaller substituent at C-4 to avoid steric repulsion, forming the π-allylpalladium intermediate (*E*)-**3** and subsequently to the σ-1,3-dien-2-ylpalladium (*E*)-**4**. Insertion of carbon monoxide takes place with retention of stereochemistry to give the (*E*)-α-vinylacrylamide **2** exclusively. When sterically hindered 1,1-disubstituted and 4,4-disubstituted amines are used as the substrates, these substituents block the approach of palladium, resulting in low reactivities of these hindered 2,3-dienylamines.

The carbonylation of 1-monosubstituted 2,3-dienylamines **1e** and **1h** gave the α-vinylacrylamides **2e** and **2h** as a mixture of two stereoisomers concerning β,γ-double bond (Table 1, entries 5 and 8), which are 65:35 and 93:7, respectively. In both cases, the major isomers were determined to be β,γ-*E* on the basis of the coupling constants of those protons in ^{1}H NMR. These selectivities may be governed by the thermodynamic stability of *syn*- and *anti*-π-allylpalladium intermediates.

The following general procedure was used: In a 45-mL autoclave with a glass liner was placed the 2,3-dienylamine (1.0 mmol), $Pd_2(dba)_3 \cdot CHCl_3$ (0.005 mmol), dppp (0.01 mmol), *p*-TsOH (0.01 mmol), and CH_2Cl_2 (5 mL). After being flushed three times with CO, the autoclave was charged to 600 psi, and the mixture was stirred at 75 °C for 3 h. After the mixture was cooled to room temperature and the CO was released, the reaction mixture was passed through a plug of Florisil with CH_2Cl_2 as an eluant to give the amide containing a small amount of dba. The amide was further purified by flash column chromatography on silica gel.

In conclusion, $Pd_2(dba)_3 \cdot CHCl_3$, together with dppp and *p*-TsOH, catalyzes the regioselective carbonylation of 2,3-dienylamines to α-vinylacrylamides. Since the reaction is highly regioselective and stereoselective for the α,β-double bond, this method is useful for the preparation of α-vinylacrylamides. In addition, it demonstrates the selective insertion of carbon monoxide into a carbon−nitrogen bond of acyclic amines.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada for support of this research.

Supporting Information Available: General experimental procedures and characterization data for all starting materials and products; NMR (^{1}H, ^{13}C) spectra for **2a**−**i** (24 pages).

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(7) Da Costa, R.; Gillard, M.; Falmagne, J. B.; Ghosez, L. *J. Am. Chem. Soc.* **1979**, *101*, 4381

(8) Osakada, K.; Chiba, T.; Nakamura, Y.; Yamamoto, T.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1589. See also ref 11.

(9) Piotti, E. M.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1956.

(10) (a) Kleijin, H.; Westmijze, H.; Meijer, J.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 378. (b) Djahanbini, D.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1984**, *25*, 203. (c) Nokami, J.; Maihara, A.; Tsuji, J. *Tetrahedron Lett.* **1990**, *31*, 5629.

(11) Murahashi, S.-I.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *J. Org. Chem.* **1993**, *58*, 1538 and references cited therein.