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Palladium(II)-Catalyzed Tandem Reaction of Intramolecular Aminopalladation of Allenyl *N*-Tosylcarbamates and Conjugate Addition

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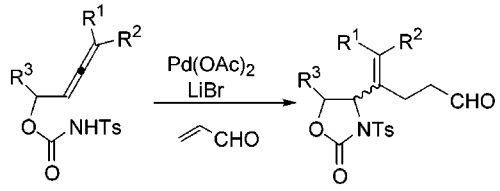
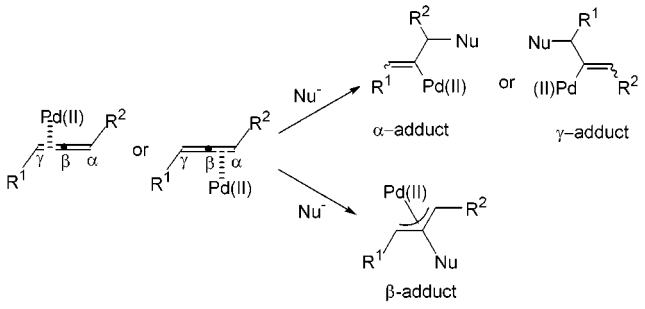
ABSTRACT



A divalent palladium-catalyzed tandem cyclization–coupling reaction of allenyl *N*-tosylcarbamates and acrolein was developed. The reaction gave aldehyde-functionalized 2-oxazolidinones in one step with high regioselectivity. A mechanism involving intramolecular aminopalladation of allene, followed by insertion of alkene and C–Pd bond protonolysis, is proposed.

The vinylic palladium species is a versatile reactive intermediate in palladium-catalyzed coupling reactions.[1] Besides the well-studied oxidative addition of vinylic halides or triflates to Pd(0), which generates the vinylic palladium species,[1] it can be also obtained from the addition of a nucleophile to the divalent palladium-coordinated alkynes[1,2] or allenes.[1a,3] There are two kinds of pathways for the reaction of Pd(II)-coordinated allenes with nucleophiles: (1) the nucleophile attacks the α- or γ-carbon atom to form a vinylic palladium species (α-adduct or γ-adduct); (2) the nucleophile attacks the β-carbon atom to form a π-allylic palladium species (β-adduct) (Scheme 1).[3]

Scheme 1



A number of Pd(II)-catalyzed reactions of allenes with nucleophiles have been reported in the literature. However, in most of these reactions, some oxidant (e.g., Cu(II) salts or quinones) must be used to regenerate Pd(II) from Pd(0) in order to achieve a catalytic reaction.[4] To our knowledge, nucleophilic addition reactions of allenes catalyzed by

(1) (a) Tsuji, J. *Palladium reagents and Catalysis: Innovations in Organic Synthesis*; John Wiley: Chichester, 1995. (b) Soderberg, B. C. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: 1995; Vol. 12, Chapter 3.5, p 241.

(2) (a) Maitlis, P. M. *The Oragnic Chemistry of Palladium*; Academic Press: New York, 1971; Vol. 1, p 79. (b) Maitlis, P. M. *Acc. Chem. Res.* **1976**, *9*, 93−99. (c) Kaneda, K.; Uchiyama, T.; Fujiwarka, Y.; Teranishi, S. *J. Org. Chem*. **1979**, *44*, 55. (d) Yanagihara, N.; Lambert, C.; Iritani, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc*. **1986**, *108*, 2753. (e) Lu, X.; Zhu, G.; Wang, Z. *Synlett*. **1998**, 115. (f) Lu, X.; Ma, S. New Age of Divalent Palladium Catalysis. In *Transition Metal Catalyzed Reaction*; Murahashi, S.-I., Davies, S. G., Eds.; Blackwell Science, Oxford, 1999; Chapter 6, p 133. (g) Zhang, Q.; Lu, X. *J. Am. Chem. Soc*. **2000**, *122*, 7604.

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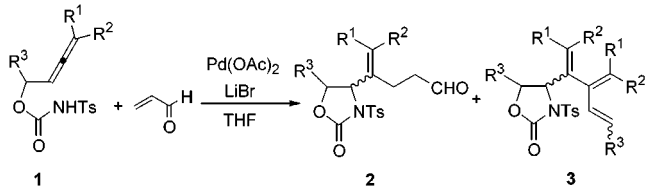
divalent palladium without additional oxidants have not been widely reported.[5] In our previous work, we studied the protonolysis reaction of the carbon−palladium bond in the presence of excess halide ions and found it to be an effective method to quench the carbon−palladium bond and regenerate Pd(II) species.[6] These results prompted us to explore the possibility of a Pd(II)-catalyzed nucleophilic addition reaction of allenes using C−Pd bond protonolysis as the Pd(II) regeneration step. Herein, we report the development of a novel Pd(II)-catalyzed tandem cyclization−conjugate addition reaction of allenyl *N*-tosylcarbamates to acrolein by applying this principle.

We first investigated the reaction of allenyl *N*-tosylcarbamate **1c** ($R^1 = R^2 = H$, $R^3 = i$-Pr, 0.5 mmol) with acrolein (2.5 mmol) in the presence of $Pd(OAc)_2$ (5 mol %) and NaI (2 mmol) in THF (5 mL) (Scheme 2). The reaction

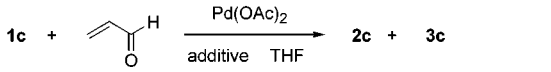
Scheme 2



was complete within 12 h and gave the expected cyclization−conjugate addition product **2c** (yield: 46%), as well as another product, **3c**, formed from cyclization and coupling with another molecule of **1** (yield: 47%) (entry 1, Table 1).

When LiCl or LiBr was used in place of NaI, the reaction also proceeded smoothly, giving similar results (entries 2 and 3, Table 1). In the absence of halide ions, no coupling reaction occurred, but a Pd black precipitate appeared within a few minutes (entry 4, Table 1). Addition of HOAc did not improve the yield of the reaction (entry 5, Table 1), and surprisingly, no reaction occurred when neat HOAc was used as the solvent (entry 6, Table 1). The yield of **2c** can be improved by using a higher concentration of acrolein and slow addition of **1** (entries 7−9, Table 1). Further, in a control experiment with only **1c** as the substrate and no acrolein, the reaction finished within 1 h at room temperature and gave **3c** as the main product in good yield (79%),[7] confirming that **3c** is the self-coupling product of **1c**. Finally, the standard procedure was carried out by adding a THF solution of allenyl *N*-tosylcarbamate **1** dropwise to a mixture of $Pd(OAc)_2$, LiBr, and acrolein in THF over 3 h and then stirring the mixture for an additional 2 h. A series of allenyl *N*-tosylcarbamates with different R^1, R^2, and R^3 substituents was coupled with acrolein using the standard procedure. The results are shown in Table 2.

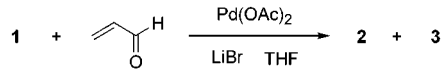
Table 1. Reactions of **1c** with Acrolein Catalyzed by Pd(II) Species[a]



entry	acrolein:**1c** (molar ratio)	additive	solvent	time (h)	yield (%)[b] **2c**	**3c**
1	5	NaI	THF	12	46	47
2	5	LiCl	THF	2	41	47
3	5	LiBr	THF	2	55	35
4[c]	5	none	THF	4	no reaction	
5	5	LiBr	THF/HOAc (v/v: 4/1)	4	47	26
6	5	LiBr	HOAc	12	no reaction	
7	20	LiBr	THF	2	66	23
8	15	LiBr	THF	3[d]	79	13
9	15	LiBr	THF	5[e]	86	trace

[a] All reactions were carried out using **1c** (0.5 mmol), $Pd(OAc)_2$ (0.025 mmol), additive (2 mmol), and acrolein in the specified solvent (5 mL) at room temperature. [b] Isolated yield. [c] A black precipitate appeared within several minutes. [d] A solution of **1c** in THF was added dropwise into a solution of $Pd(OAc)_2$, LiBr, and acrolein in THF in 1 h, and then the mixture was stirred for another 2 h. [e] A solution of **1c** in THF was added dropwise into a solution of $Pd(OAc)_2$, LiBr, and acrolein in THF in 3 h, and then the mixture was stirred for another 2 h.

Table 2. Reactions of Allenyl *N*-Tosylcarbamates **1** with Acrolein Catalyzed by Pd(II)[a]



entry	**1**	R^1	R^2	R^3	yield of product (%)[b] **2** (*trans*:*cis*)[c]	**3**
1	**1a**	H	H	H	**2a** 74	**3a**, 17
2	**1b**	H	H	Et	**2b** 67 (2.8:1)	**3b**, 10
3	**1c**	H	H	Pr^i	**2c** 86 (>97:3)	trace
4	**1d**	H	H	Pr^n	**2d** 60 (2.4:1)	**3d**, 17
5	**1e**	H	H	n-C_5H_{11}	**2e** 73 (4.4:1)	trace
6[d]	**1f**	H	H	Ph	**2f** 84 (>97:3)	trace
7	**1g**	Me	Me	H	**2g** 85	trace
8	**1h**	Me	Me	Et	**2h** 71 (1.7:1)	trace

[a] All reaction were carried out using **1** (0.5 mmol) at room temperature. A solution of **1** in THF (3 mL) was added to a mixture of $Pd(OAc)_2$ (0.025 mmol), LiBr (2 mmol). and acrolein (7.5 mmol) in THF (5 mL) over 3 h, and the mixture was stirred for another 2 h. [b] Isolated yield. [c] The *cis*:*trans* ratio was determined by the ^1H NMR spectra of the product mixture. [d] Compound **1f** is unstable, was synthesized from allenyl alcohol with TsNCO, and was used in situ without purification.

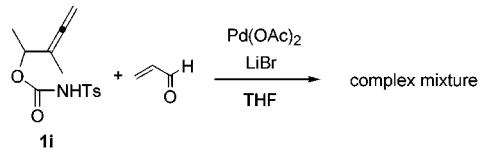
The cyclization is highly regioselective, giving five-membered ring products (oxazolidinones). For the substrate **1** with a bulky R^3 group, only *trans*-**2** was obtained, showing

(4) (a) Alper, H.; Hartstock, F. H.; Despeyrous, B. *J. Chem. Soc., Chem. Commun*. **1984**, 905. (b) Hegedus, L. S.; Kambe, N.; Ishii, Y.; Mori, A. *J. Org. Chem*. **1985**, *50*, 2240. (c) Walkup, R. D.; Mosher, M. D. *Tetrahedron Lett*. **1987**, *28*, 1023. (d) Walkup, R. D.; Mosher, M. D. *Tetrahedron*. **1993**, *49*, 9285. (e) Gallagher, T.; Davis, I.W.; Jones, S. W.; Lathbury, D.; Mahon, M. F.; Molly, K. F.; Shaw, R. W.; Vernon, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 433. (f) Kimura, M.; Saeki, N.; Uchida, S.; Harayama, H.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett*. **1993**, *34*, 7611. (g) Bäckvall, J.-E.; Jonasson, C. *Tetrahedron Lett*. **1997**, *38*, 291. (h) Jonasson, C.; Howath, A.; Bäckvall, J.-E. *J. Am. Chem. Soc*. **2000**, *122*, 9600.

(5) (a) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett*. **1988**, *29*, 4257. (b) Kimura, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem*. **1992**, *57*, 6377. (c) Kimura, M.; Tanaka, S.; Tamaru, Y. *J. Org. Chem*. **1995**, *60*, 3764. (d) Ma, S.; Gao, W. *Tetrahedron Lett*. **2000**, *41*, 8933.

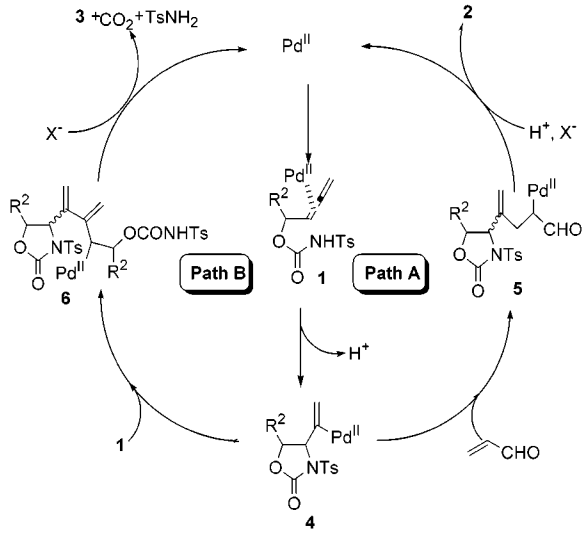
that the reaction is stereoselective (entries 3 and 6, Table 2). The stereoselectivity decreases with less bulky R^3 groups (entries 2, 3, 4, and 8, Table 2). The coupled products **2a**−**2h** were characterized by ^{1}H NMR, IR, MS, and elemental analyses or HRMS. The stereoconfigurations were determined by NOESY spectra and compared with the literature data.[5c] For substrates with a substituent at the allene carbon where the cyclization occurs (e.g., compound **1i**), the reaction gave a complex mixture (Scheme 3).

Scheme 3



The following mechanism was proposed: First, the nucleophile intramolecularly attacks the Pd(II)-coordinated allene **1** to form the vinylic palladium intermediate **4**. This is followed by the insertion of the acrolein into the vinylic palladium bond to yield intermediate **5** and then the newly formed carbon−palladium bond is protonized in the presence of halide ions to give **2** (Scheme 4, path A). However,

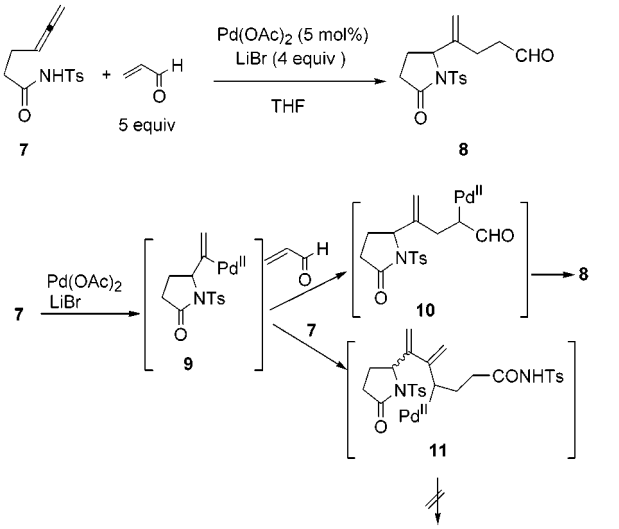
Scheme 4



because allenes are more reactive than alkenes,[3] **1** can compete favorably to insert into the vinylic palladium bond of **4** to yield **6**, which undergoes β-heteroatom elimination to give product **3**, CO_2, and $TsNH_2$ and regenerate the Pd(II) species (Scheme 4, path B). Here, the halide ion plays a very important role in inhibiting the β-H elimination of both **5** and **6**,[8] making the reaction proceed with high catalytic efficiency and good selectivity. In this reaction, the proton needed for protonolysis may come from the dissociation of the acidic N−H in **1**. A related observation is that the reaction is completely shut down in neat HOAc (entry 6, Table 1). This is possibly due to suppression of the N−H dissociation, which is imperative for aminopalladation to occur.

To examine the generality of the present reaction, as well as to develop synthetic methods for other nitrogen-containing heterocyclic compounds, e.g., functionalized lactams, we prepared **7** and tested its reaction with acrolein under the standard conditions. To our delight, product **8** was obtained as the single product in very high yield (95%) (Scheme 5).

Scheme 5



It is not clear why **7** gives a higher yield and selectivity than **1**. A possible explanation is that the relative rate for the insertion of acrolein versus insertion of allene (path A versus path B, Scheme 4) is higher for the vinylic palladium intermediate **9** formed from **7** than that for **4**. Another possibility is that the insertion of allene to the vinylic palladium is reversible, so when β-heteroatom elimination becomes impossible for the allyl palladium intermediate **11**, the reaction will solely give acrolein-coupled product **8** via path A.

In summary, we have developed a divalent palladium catalyzed coupling reaction of allenyl *N*-tosylcarbamates or *N*-tosyl allenamide with acrolein. Functionalized 2-oxazolidinones and lactams can be synthesized with high regioselectivity in one step. The reaction mechanism involves

(6) (a) Wang, Z.; Lu, X. *Chem. Commun.* **1996**, 535. (b) Wang, Z.; Lu, X. *J. Org. Chem.* **1996**, *61*, 2254. (c) Wang, Z.; Lu, X. *Tetrahedron Lett.* **1997**, *38*, 5213. (d) Wang, Z.; Lu, X.; Lei, A.; Zhang, Z. *J. Org. Chem.* **1998**, *63*, 3806. (e) Xie, X.; Lu, X. *Synlett* **2000**, 707. (f) Lu, X.; Wang, Z. *Polyhedron* **2000**, *19*, 577. (g) Lei. A.; Lu, X. *Org. Lett.* **2000**, *2*, 2699.

(7) Toluenesulfonamide, $TsNH_2$, was isolated as a byproduct.

(8) In the Pd(II)-mediated conjugate addition reaction, the halide ion can block the β-H elimination of a (2-oxoalkyl)palladium species, giving preferentially the protonolysis product, see: Wang, Z.; Zhang, Z.; Lu, X. *Organometallics* **2000**, *19*, 775. Zhang, Z.; Lu, X.; Xu, Z.; Zhang, Q.; Han, X. *Organometallics* **2001**, *20*, 3724.

intramolecular aminopalladation of allene, acrolein insertion, and halide-assisted protonolysis to regenerate Pd(II) species without using oxidants.

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Supporting Information Available: Spectroscopic data for new compounds **2a**−**2h**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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