

Palladium(0)-Catalyzed Carbonylation–Coupling–Cyclization of Allenic Sulfonamides with Aryl Iodides and Carbon Monoxide

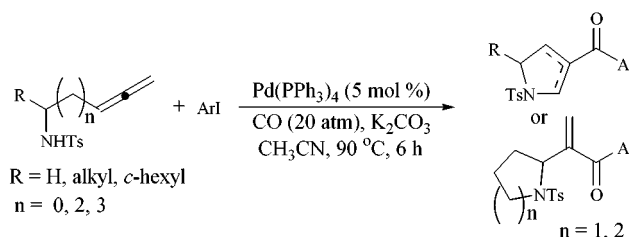
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ABSTRACT



α -Allenic sulfonamides undergo carbonylation–coupling–*endo*-cyclization with aryl iodides in the presence of Pd(PPh₃)₄ (5 mol %), K₂CO₃, and CO (20 atm) to form 3-aryl-2- or 3-pyrrolines. Alternatively the carbonylation–coupling–*exo*-cyclization of γ - and δ -substituted sulfonamides under the same conditions afforded pyrrolidine- or piperidine-substituted enones.

The palladium-catalyzed reaction of allene-substituted amine derivatives to form highly regio- and stereoselective five- and six-membered azacycles has received much attention in recent years.¹ Palladium has been reported to be an effective catalyst for the cyclization of allenes bearing a protected amino group separated from the carbon atom of the allene moiety by one to four carbon atoms.² Although the palladium-catalyzed cyclization of various allenic sulfonamides to yield azacycles has been well-documented, the palladium-

catalyzed carbonylative cyclization of allenic sulfonamides to form heterocycles is rare. Only the palladium(II)-catalyzed cyclization of allenic amine derivatives by carbomethoxylation in the presence of carbon monoxide and methanol to form pyrrolidine or piperidine carboxylic esters is known.³ Alternatively the acylation–cyclization of γ -allenic *p*-toluenesulfonamide by treatment of a stoichiometric amount of acyltetracarbonyl cobalt complexes from alkyl halides, carbon monoxide, and NaCo(CO)₄ to form the pyrrolidine-substituted enones is known.⁴ Herein we wish to report the palladium(0)-catalyzed three-component carbonylation–

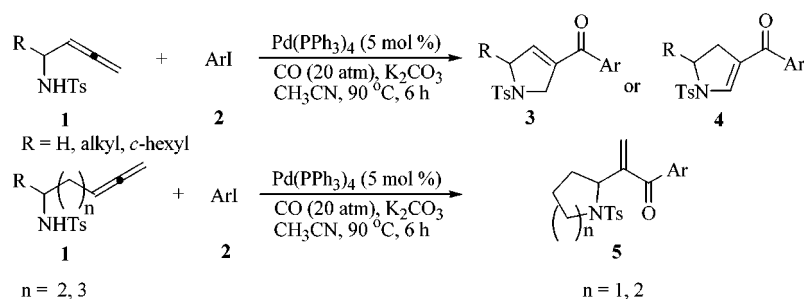
(1) Review: Zimmer, R.; Dinesh, C. U.; Nandan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3257–3282.

(2) (a) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421–5424. (b) Davis, I. W.; Scopes, D. I. C.; Gallagher, T. *Synlett* **1993**, 85–87. (c) Karstens, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **1997**, *38*, 6275–6278. (d) Karstens, W. F. J.; Stol, M.; Rutjes, F. P. J. T.; Hiemstra, H. *Synlett* **1998**, 1126–1128. (e) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4257–4260. (f) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Osawa, E.; Yamaoka, Y.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1999**, *64*, 2992–2993. (g) Rutjes, F. P. J. T.; Tjen, K. C. M. F.; Wolf, L. B.; Karstens, W. F. J.; Schoemaker, H. E.; Hiemstra, H. *Org. Lett.* **1999**, *1*, 717–720. (h) Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 7393–7397. (i) Kang, S.-K.; Baik, T.-G.; Kulak, A. N. *Synlett* **1999**, 324–326.

(3) The palladium-catalyzed methoxycarbonylation of allene-substituted amines to form pyrrolidine or piperidine carboxylic esters was known by Gallagher et al. See: (a) Gallagher, T.; Davies, I. W.; Jones, S. W.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Shaw, R. W.; Vernon, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 433–440. (b) Fox, D. N. A.; Gallagher, T. *Tetrahedron* **1990**, *46*, 4697–4710. (c) Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Am. Chem. Soc.* **1991**, *113*, 2652–2656. (e) Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009–6012.

(4) Bates, R. W.; Rama-Devi, T.; Ko, H.-H. *Tetrahedron* **1995**, *51*, 12939–12954.

Scheme 1



coupling–cyclization reaction of α -, γ -, and δ -allene substituted *p*-toluenesulfonamide with aryl iodides and carbon monoxide to form pyrroles, pyrrolidine, and/or piperidine heterocycles (Scheme 1).⁵

Our initial work began with α -allenic *p*-toluenesulfonamide **1a**⁶ with iodobenzene under CO (atmospheric pres-

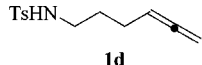
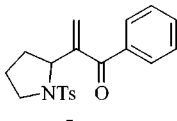
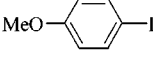
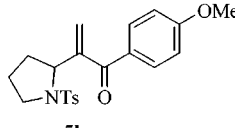
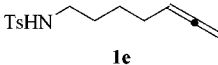
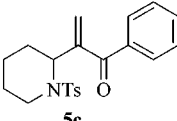
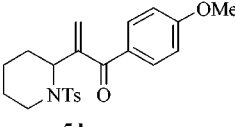
sure) at 90 °C in CH₃CN to obtain the carbonylative cyclization product without success. After a series of experiments we found that the reaction of α -allenic *p*-toluenesulfonamide **1a** with iodobenzene at 90 °C under CO (20 atm) in CH₃CN for 6 h afforded two easily separable compounds, 3-benzoyl-3-pyrroline **3a** (24%) and 3-benzoyl-

Table 1. Pd(0)-Catalyzed Carbonylative Cyclization of α -Allenic Sulfonamide Derivatives

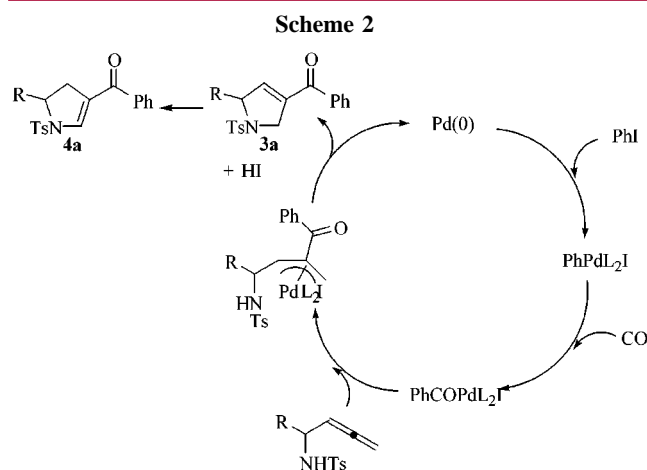
entry	substrate	aryl iodide	product	isolated yield (%)
1		PhI 2a	 + 	81
2	1a		 + 	72
3		2a	 + 	82
4		2a		72
5	1c	2b	 + 	60

^a The abbreviation Mts represents 2,4,6-trimethylbenzenesulfonyl.

Table 2. Pd(0)-Catalyzed Carbonylative Cyclization of γ - and δ -Allenic Sulfonamide Derivatives

entry	substrate	aryl iodide	product	isolated yield (%)
1	 1d	PhI 2a	 5a	83
2	1d	 2b	 5b	91
3	 1e	2a	 5c	61
4	1e	2b	 5d	65

2-pyrroline **4a** (57%) in 81% combined yield (entry 1 in Table 1).^{7–8} Presumably under the conditions with palladium the compound **3a** was isomerized to the thermodynamically more stable compound **4a**. For the formation of **3a** the plausible mechanism is shown in Scheme 2.

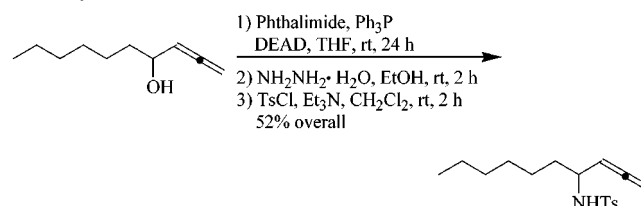


It is presumed that oxidative addition of Pd(0) to ArI is followed by carbonylation to give PhCOPdI, which adds to the central carbon of allene moiety to provide π -allylpalladium complex. Cyclization of this intermediate by the *endo*-mode would give the pyrroline enone **3a** (Scheme 2).⁹ Under

(5) The palladium(0)-catalyzed cyclization–carbonylation–coupling of aryl halides and γ -hydroxyallenes to form aryl(tetrahydrofuran-2-yl)vinyl ketones is known. See: Walkup, R. D.; Guan, L.; Kim, Y. S.; Kim, S. W. *Tetrahedron Lett.* **1995**, *36*, 3805–3808.

the same conditions with *p*-iodoanisole the coupling and cyclization gave the two pyrrolines **3b** and **4b** in 72% combined yield (entry 2). When alkyl-substituted α -allenic mesitylsulfonyl amide **1b** was reacted with iodobenzene, 3-pyrroline derivative **3c** and 2-pyrroline derivative **4c** were afforded in 71% and 11% (total 82%) yields, respectively

(6) The α -allenic *p*-toluenesulfonamide **1a** was prepared from deca-1,2-diene-4-ol by Mitsunobu reaction followed by deprotection and tosylation in 52% yield.



(7) The same reactions and conditions under CO (10 atm) at 90 °C in CH₃CN for 18 h gave **3a** and **4a** in 42% yield. As the solvent, DMF can be used to obtain the similar products and yields.

(8) **Typical Procedure.** A stainless autoclave was charged with α -allenic *p*-toluenesulfonamide **1a** (100 mg, 0.33 mmol), CH₃CN (3 mL), iodobenzene (99.4 mg, 0.49 mmol), K₂CO₃ (179 mg, 1.30 mmol), and Pd(PPh₃)₄ (18.7 mg, 5 mol %) and flushed with 20 atm of CO three times. It was then pressurized to 20 atm, and the reaction mixture was stirred at 90 °C for 6 h. The mixture was cooled and then quenched with saturated NH₄Cl solution. The reaction mixture was extracted with ether (20 mL \times 3), and the organic layer was dried over anhydrous MgSO₄ and evaporated in vacuo. The crude product was separated by SiO₂ column chromatography (hexanes/EtOAc, 6:1) to give 3-pyrroline **3a** (32 mg, 24%) and 2-pyrroline **4a** (76 mg, 57%). Walkup et al. suggested two possible mechanisms for cyclization–coupling between aryl halides and γ -hydroxyallenes (ref 4).

(9) The mechanistic path via an η^3 -allylpalladium(II) complex is considered to be operative for intermolecular coupling nucleophilic reaction with amines. See: (a) Shimizu, I.; Tsuji, J. *Chem. Lett.* **1984**, 233–236. (b) Cazes, B. *Pure Appl. Chem.* **1990**, *62*, 1867–1878. (c) Larock, R. C.; Berrios-Pena, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615–2617. Alper et al. suggested that the initial addition of arylpalladium to allene is followed by nucleophilic attack of the hydroxy group in the carbonylation of *o*-iodophenol with allenes. See: Okuro, K.; Alper, H. *J. Org. Chem.* **1997**, *62*, 1566–1567.

(entry 3). In the case of cyclohexyl-substituted α -allenic sulfonamide **1c**, the same coupling and cyclization with iodobenzene under CO (20 atm) at 90 °C in CH₃CN for 6 h provided 3-benzoyl-2-pyrroline **3d** in 72% as the sole product (entry 4). However, with *p*-iodoanisole as an electrophile two products, **3d** and **4d**, were obtained in 43% and 17% yields, respectively (entry 5). The results of carbonylation–coupling–cyclization of α -allenic sulfonamide derivatives are summarized in Table 1.

Our carbonylation–coupling–cyclization method was extended to γ - and δ -allenic *p*-toluenesulfonamides **1d** and **1e**, and the results are summarized in Table 2. When γ -allenyl *p*-toluenesulfonamide **1d** was treated with iodobenzene under CO, the pyrrolidine-substituted enone **5a** was provided in 83% yield (entry 1). The structure of **5a** was unambiguously confirmed by X-ray crystallography (Figure 1). When *p*-iodoanisole was utilized under the same condi-

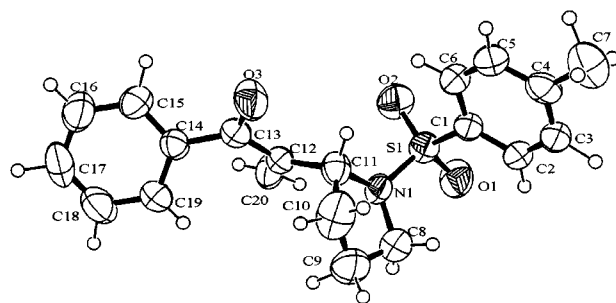
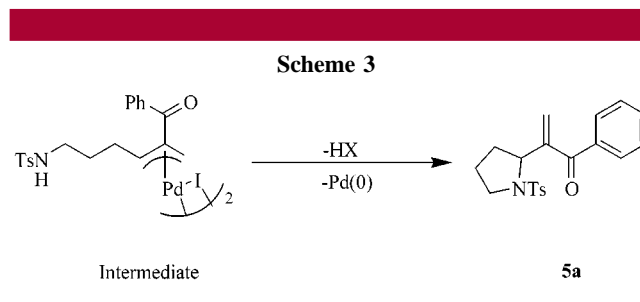


Figure 1. ORTEP drawing of **5a**.

tions, the pyrrolidine **5b** was obtained (entry 2). Alternatively, when δ -allenyl *p*-toluenesulfonamide **1e** was reacted with

iodobenzene, the piperidine-substituted enone **5c** was afforded (entry 3). Finally, for the *p*-iodoanisole, carbonylation gave the *p*-anisole-substituted enone **5d** (entry 4). A plausible mechanism for the formation of **5a** is that this reaction may occur by addition of an arylpalladium intermediate to the allene unit of the allenic *p*-toluenesulfonamide **1e** to produce a η^3 -allylpalladium species, which undergoes nucleophilic attack via the *exo*-mode by *p*-toluenesulfonamide group to produce the cyclized product **5a** (Scheme 3).



In conclusion, the palladium(0)-catalyzed carbonylation–coupling–cyclization of allenic *p*-toluenesulfonamides with aryl iodides under CO (20 atm) to give substituted pyrrolines and pyrrolidine or piperidine enones was accomplished.

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Supporting Information Available: Typical experimental procedures and characterization for **3a–4e** and **5a–d**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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