ORGANIC LETTERS

XXXX
Vol. XX, No. XX
000–000

Palladium-Catalyzed Carboxylative Coupling of Benzyl Chlorides with Allyltributylstannane: Remarkable Effect of Palladium Nanoparticles

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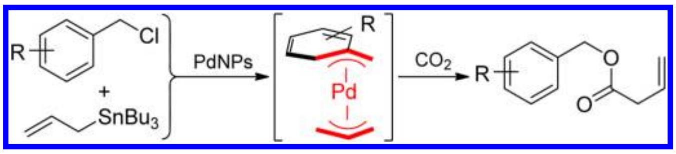
Received November 14, 2012

ABSTRACT



Palladium-catalyzed carboxylative coupling of benzyl chlorides with allyltributylstannane was successfully conducted to produce benzyl but-3-enoates in satisfactory to good yields. The carboxylative coupling reaction occurred smoothly under mild conditions in the presence of palladium nanoparticles in tetrahydrofuran.

The use of carbon dioxide (CO_2) as a nontoxic, renewable, and low-cost carbon source to synthesize commodity chemicals and complex organic molecules has attracted considerable attention. Numerous methods have been developed for CO_2 fixation over the past decades.[1] Among these methods, the transition-metal-catalyzed activation and conversion of CO_2 into valuable chemicals that involve new carbon–carbon bond formation have recently emerged as extremely powerful tools because of their high chemoselectivity, good functional group tolerance, and mild reaction conditions.[2] Palladium catalysts have been successfully utilized in the carboxylation of allylstannanes,[3] allenes,[4] and aryl halides,[5] as well as in the carboxylative coupling of allylstannanes with allyl halides,[6] since the pioneering example of palladium-catalyzed coupling of CO_2 with 1,3-butadiene to form lactones was reported by Inoue et al. in 1976.[7,8] The key to the success of these reactions was the use of appropriate phosphine ligands. The carboxylative coupling of benzyl chlorides with allylstannanes could not occur in the presence of $Pd(PPh_3)_4$ as a catalyst.[6]

We have reported the facile palladium-catalyzed allylative dearomatization and carbonylative coupling reactions of benzyl chlorides **1** with allyltributylstannane.[9,10] These

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(1) For a book, see: (a) *Carbon Dioxide as a Chemical Feedstock*; Aresta, M.; Wiley-VHC: Weinheim, 2010. For a review, see: (b) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365.

(2) For reviews, see: (a) Tsuji, Y.; Fujihara, T. *Chem. Commun.* **2012**, *48*, 9956. (b) Ackermann, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 3842. (c) Correa, A.; Martín, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 6201.

(3) (a) Hruszkewycz, D. P.; Wu, J.; Hazari, N.; Incarvito, C. D. *J. Am. Chem. Soc.* **2011**, *133*, 3280. (b) Wu, J.; Hazari, N. *Chem. Commun.* **2011**, *47*, 1069 and references therein. (c) Hazari, N.; Hruszkewycz, D. P.; Wu, J. *Synlett* **2011**, *13*, 1793.

(4) (a) Takaya, J.; Iwasawa, N. *Organometallics* **2009**, *28*, 6636. (b) Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2008**, *130*, 15254.

(5) (a) Fujihara, T.; Nogi, K.; Xu, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9106. (b) Correa, A.; Martín, R. *J. Am. Chem. Soc.* **2009**, *131*, 15794.

(6) Franks, R. J.; Nicholas, K. M. *Organometallics* **2000**, *19*, 1458.

(7) The pioneering example of palladium-catalyzed coupling of CO_2 with 1,3-butadiene was reported by the Inoue group: Sasaki, Y.; Inoue, Y.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1976**, 605.

(8) The examples of palladium-catalyzed coupling of CO_2 with 1,3-butadiene were reported by other groups: (a) Dai, Y.; Feng, X.; Wang, B.; He, R.; Bao, M. *J. Organomet. Chem.* **2012**, *696*, 4309. (b) Buchemuller, K.; Dahmen, N.; Dinjus, E.; Neumann, D.; Powietzka, B.; Pitter, S.; Schön, J. *Green Chem.* **2003**, *5*, 218. (c) Pitter, S.; Dinjus, E. *J. Mol. Catal. A: Chem.* **1997**, *125*, 39. (d) Behr, A.; He, J.; Jusyak, K. D. *Chem. Ber* **1986**, *119*, 991. (e) Behr, A.; Juszak, K. D.; Keim, W. *Synthesis* **1983**, *7*, 574. (f) Behr, A.; Juszak, K. D. *J. Organomet. Chem.* **1983**, *255*, 263. (g) Musco, A.; Perego, C.; Tartiari, V. *Inorg. Chim. Acta* **1978**, *28*, L147.

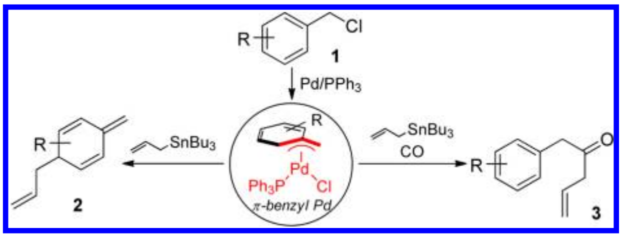
(9) (a) Lu, S.; Xu, Z.; Bao, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 4366. (b) Bao, M.; Nakamura, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 759.

(10) Dai, Y.; Feng, X.; Liu, H.; Jiang, H.; Bao, M. *J. Org. Chem.* **2011**, *76*, 10068.

10.1021/ol303135e

reactions proceeded smoothly via π-benzylpalladium chloride intermediates in the presence of a PPh_3 ligand to produce products **2** and **3** (Scheme 1). The success in achieving carbonylative coupling of benzyl chlorides **1** with allyltributylstannane encouraged us to consider whether carboxylative coupling could also occur in the presence of a novel palladium catalyst system to offer esters.

Scheme 1. Coupling Reactions via π-Benzylpalladium Chloride Intermediates



As illustrated in Scheme 2, we hypothesized that the π-benzyl π-allylpalladium intermediate **B** derived from π-benzylpalladium chloride intermediate **A** could not undergo allylative dearomatization in the absence of the PPh_3 ligand. The π-benzyl and π-allyl carbon-based ligands in intermediate **B** would cause the palladium center to exhibit high basicity, which would facilitate the coordination of CO_2 to form intermediate **C**. The nucleophilicity of the σ-allyl group in intermediate **C** would be enhanced because of the π-benzyl carbon-based ligand, which would function like an *N*-heterocyclic carbene ligand.[11] The nucleophilic addition of the σ-allyl group to CO_2 would take place to afford π-benzylpalladium carboxylate intermediate **D**,[12] which would undergo reductive elimination of the β,γ-unsaturated ester **4** (regenerating the Pd(0) species).

Scheme 2. Palladium-Catalyzed Carboxylative Coupling of Benzyl Chlorides with Allylstannane under Phosphine Ligand-Free Conditions

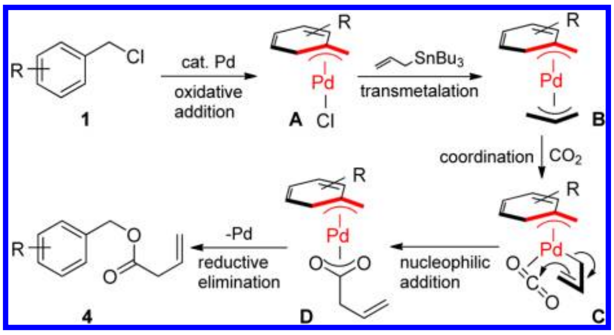
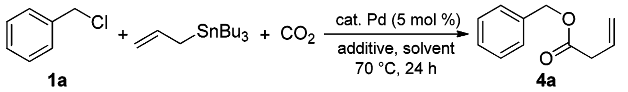


Table 1. Reaction Condition Screening[a]



entry	catalyst	additive	solvent	yield (%)[b]
1	$Pd_2(dba)_3$	TBAB	THF	48
2	$PdCl_2$	TBAB	THF	65
3	$Pd(OAc)_2$	TBAB	THF	69
4	$Pd(acac)_2$	TBAB	THF	86
5	$Pd(acac)_2$	none	THF	NR[c]
6	$Pd(acac)_2$	TBAF	THF	17
7	$Pd(acac)_2$	TBAC	THF	25
8	$Pd(acac)_2$	TBAI	THF	22
9[d]	$Pd(acac)_2$	TBAB	THF	78
10[e]	$Pd(acac)_2$	TBAB	THF	70
11	$Pd(acac)_2$	TBAB	toluene	73
12	$Pd(acac)_2$	TBAB	hexane	44
13	$Pd(acac)_2$	TBAB	dioxane	60
14	$Pd(acac)_2$	TBAB	DMF	49
15[f]	$Pd(acac)_2$	TBAB	THF	83
16[g]	$Pd(acac)_2$	TBAB	THF	78
17[h]	$Pd(acac)_2$	TBAB	THF	24
18[i]	$Pd(acac)_2$	TBAB	THF	70

[a] Reaction conditions: benzyl chloride (**1a**, 0.5 mmol), allyltributylstannane (0.6 mmol), CO_2 (2 MPa), Pd catalyst (5 mol %), additive (1.4 equiv), and solvent (5 mL) at 70 °C for 24 h. [b] Isolated yield. [c] No reaction. [d] 1.2 equiv of TBAB was used. [e] 1.6 equiv of TBAB was used. [f] The reaction was conducted under 1 MPa of CO_2. [g] The reaction was performed under 0.5 MPa of CO_2. [h] The reaction was performed under 0.1 MPa of CO_2. [i] The reaction was conducted for 12 h.

Several palladium catalyst systems were examined to test this hypothesis. Benzyl chloride (**1a**) was used as starting material, and the results are shown in Table 1. Precatalysts $Pd_2(dba)_3$, $PdCl_2$, $Pd(OAc)_2$, and $Pd(acac)_2$ were initially tested in tetrahydrofuran (THF) at 70 °C in the presence of tetrabutylammonium bromide (TBAB). A relatively high yield was obtained using Pd(II) salts as precatalysts, and $Pd(acac)_2$ proved to be the best precatalyst (entries 2–4 vs entry 1). These results indicated that a Pd(0) species generated in situ possessed higher catalytic activity than $Pd_2(dba)_3$. The formation of the Stille coupling and allylative dearomatization products was not observed. No reaction was observed in the absence of TBAB (entry 5). The use of a quaternary ammonium salt as an additive was necessary to avoid palladium black generation. Thus, the quaternary ammonium salts were screened using $Pd(acac)_2$ as the precatalyst in THF (entries 4 and 6–8). Among the tested quaternary ammonium salts [TBAB, tetrabutylammonium fluoride (TBAF), tetrabutylammonium chloride (TBAC), and tetrabutylammonium iodide (TBAI)], the use of TBAB as an additive produced the highest yield of desired product **4a** (entry 4, 86%). The reaction yield was also influenced by the amount of TBAB utilized. A decreased yield of **4a** was obtained when 1.2 or 1.6 equiv of TBAB was employed (entry 9, 78%; entry 10, 70%). The solvents were finally screened using $Pd(acac)_2$ and TBAB as the precatalyst and additive, respectively. Nonpolar

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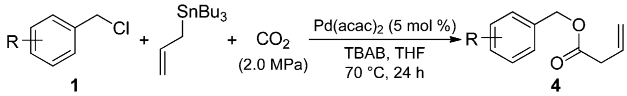
(11) For a book, see: (a) *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006. For a review, see: (b) Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 2768.

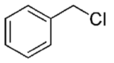
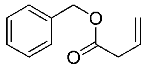
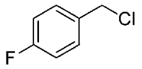
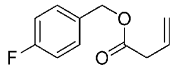
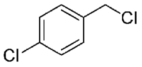
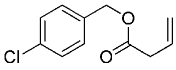
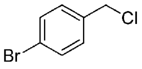
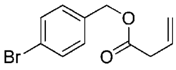
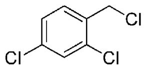
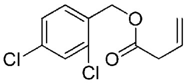
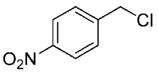
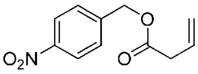
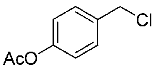
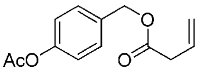
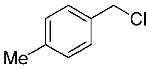
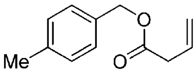
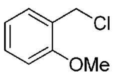
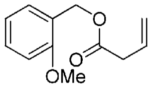
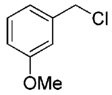
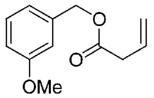
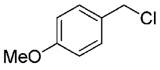
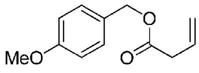
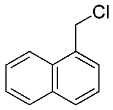
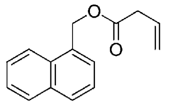
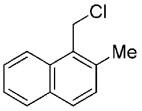
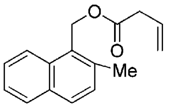
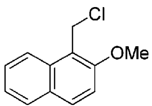
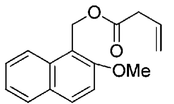
(12) Wu, J.; Green, J. C.; Hazari, N.; Hruszkewycz, D. P.; Incarvito, C. D.; Schmeier, T. J. *Organometallics* **2010**, *29*, 6369.

(toluene and hexane) and polar [THF, dioxane, and *N*,*N*-dimethyl formamide (DMF)] solvents were examined (entries 4 and 11−14). THF proved to be the best solvent (entry 4). Further studies revealed that the yield of product **4a** decreased with a decrease in CO_2 pressure (entry 15: 1 MPa CO_2, 83%; entry 16: 0.5 MPa CO_2, 78%; entry 17: 0.1 MPa CO_2, 24%). The yield of product **4a** decreased (70%) when the reaction time was shortened (12 h, entry 18). Therefore, the subsequent palladium-catalyzed carboxylative couplings of various benzyl chlorides with allyltributylstannane were performed in the presence of $Pd(acac)_2$ as the precatalyst and using TBAB (1.4 equiv) as the additive under 2 MPa of CO_2 pressure in THF for 24 h.

Table 2 shows the results of palladium-catalyzed carboxylative coupling of various benzyl chlorides with allyltributylstannane. Good yields similar to that of **4a** were observed when 4-fluorobenzyl chloride (**1b**), 4-chlorobenzyl chloride (**1c**), and 4-bromobenzyl chloride (**1d**) were examined under optimized reaction conditions (entries 2−4 vs entry 1, 80%−84%). Notably, the Cl and Br atoms linked to the benzene ring were maintained in the structures of products **4c** and **4d** under the carboxylative coupling reaction conditions, which suggests that further manipulation may produce useful compounds. The reaction of the 2,4-dichlorobenzyl chloride (**1e**) with allyltributylstannane also proceeded smoothly to furnish the desired product **4e** in 80% yield (entry 5). Products **4f** and **4g** were obtained in the same moderate yield (64%) from the reactions of benzyl chlorides **1f** and **1g** bearing strong electron-withdrawing groups nitro (NO_2) and acetoxy (AcO) on the *para* position, respectively (entries 6 and 7). The electron density of the π-benzyl carbon-based ligand was strongly decreased by the strong electron-withdrawing groups NO_2 and AcO that were linked to a benzene ring. Thus, the nucleophilic reactivity of the σ-allyl group in intermediate **C** was reduced (Scheme 2). As expected, the reaction of benzyl chloride **1h** that bears an electron-donating group methyl (Me) on the *para* position provided a good yield of product **4h** (entry 8, 82%). Reactions of benzyl chlorides **1i** to **1k** that bear a methoxy (MeO) group on the *ortho*, *meta*, or *para* position provided good yields for products **4i** to **4k** (entries 9−11, 77%−83%). These results indicate that the reactivities of the benzyl chlorides were not influenced by substituent steric effects. Finally, chloromethyl naphthalene substrates **1l**−**1n** were utilized in this type of carboxylative coupling reaction. Products **4l**−**4n** were obtained in 74%−86% yields (entries 12−14).

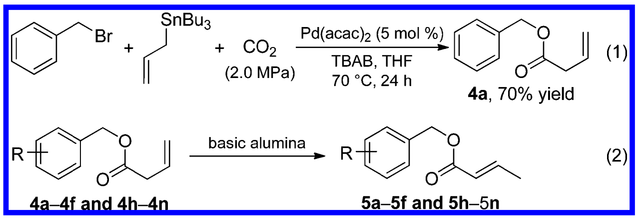
Table 2. Palladium-Catalyzed Carboxylative Coupling of Benzyl Chlorides with Allyltributylstannane[a]



entry	benzyl chloride **1**		product **4**		yield (%)[b]
1		**1a**		**4a**	86
2		**1b**		**4b**	84
3		**1c**		**4c**	80
4		**1d**		**4d**	82
5		**1e**		**4e**	80
6		**1f**		**4f**	64
7		**1g**		**4g**	64
8		**1h**		**4h**	82
9		**1i**		**4i**	83
10		**1j**		**4j**	81
11		**1k**		**4k**	77
12		**1l**		**4l**	86
13		**1m**		**4m**	82
14		**1n**		**4n**	74

[a] Reaction conditions: benzyl chloride (**1**, 0.5 mmol), allyltributylstanane (0.6 mmol), CO_2 (2 MPa), $Pd(acac)_2$ (5 mol %), TBAB (1.4 equiv), and THF (5 mL) at 70 °C for 24 h. [b] Isolated yield.

Carboxylative coupling product **4a** was obtained in 70% yield when benzyl bromide was used as a substrate (eq 1). The β,γ-unsaturated ester products **4** obtained from the palladium-catalyzed carboxylative coupling reaction of benzyl chlorides with allyltributylstannane were very stable under thermal and acidic conditions. However, these products could be easily transformed into the α,β-unsaturated esters **5a**−**5f** and **5h**−**5n** under basic conditions. Equation 2 shows that when the β,γ-unsaturated esters **4** isolated with silica gel column chromatography were passed through a short basic alumina column, the isomerization of **4** easily occurred to provide **5**. The ^1H NMR spectra of **5** clearly showed that the trans-isomer of **5** was exclusively obtained in almost all cases (for details, see Supporting Information).



4a, 70% yield

4a–4f and 4h–4n

5a–5f and 5h–5n

Transmission electron microscopy (TEM) was performed to investigate the reason for the high activity of the palladium catalyst system (Pd/TBAB) in this type of carboxylative coupling. The results are shown in Figure 1. As expected, the TEM image shows the presence of (3.3 ± 1.3)-nm-sized palladium nanoparticles in the reaction mixture. These results reveal that the additive TBAB acted as a stabilizer to disperse the palladium nanoparticles generated in situ by reducing Pd(acac)$_2$ with allyltributylstannane.[13] The palladium nanoparticles generated in situ is known to exhibit higher catalytic activity than a relative molecular catalyst.[14] Therefore, the high activity of the palladium catalyst system employed can be ascribed to the formation of palladium nanoparticles.

In summary, we have developed a new type of palladium-catalyzed carboxylative coupling reaction by utilizing palladium nanoparticles as the catalyst. The mild reaction conditions (low CO$_2$ pressure and temperature), experimental simplicity, and broad substrate scope are features of the novel and general catalytic method proposed in this paper. To the best of our knowledge, the use of metal nanoparticles as a catalyst is the first example reported on the catalytic CO$_2$-fixation reaction. Further studies focusing on the theoretical explanation of the reaction mechanism and the extension of the reaction scope using substituted allyltin reagents are currently underway.

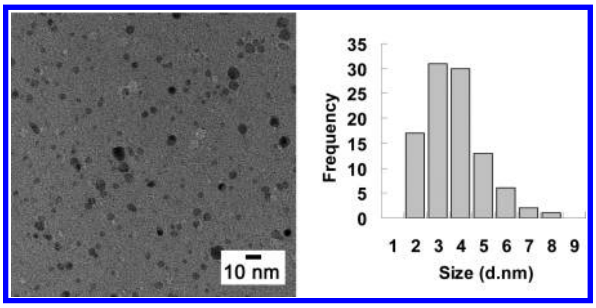


Figure 1. TEM image and size distribution of palladium nanoparticles.

Acknowledgment. We are grateful to the National Natural Science Foundation of China (Nos. 21002010 and 21073025) for their financial support. This work was also supported by the Fundamental Research Funds for the Central Universities [DUT12LK44, DUT13LK03, and DUT11ZD106].

Supporting Information Available. Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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[13] For a review, see: (a) Astruc, D.; Lu, F.; Aranzaes, J. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 7852. For a selected reference, see: (b) Adak, L.; Chattopadhyay, K.; Ranu, B. C. *J. Org. Chem.* **2009**, *74*, 3982.

[14] See: Reference 13a.