

# Efficient Diacetoxylation of Alkenes via Pd(II)/Pd(IV) Process with Peracetic Acid and Acetic Anhydride

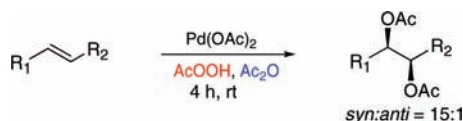
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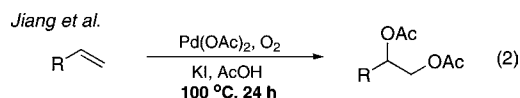
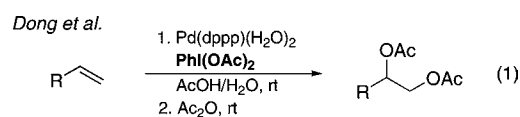
## ABSTRACT



A palladium-catalyzed diacetoxylation of alkenes in the presence of peracetic acid and acetic anhydride was developed to produce diacetates efficiently and diastereoselectively. Due to its mild conditions, this method was suitable for a broad range of substrates encompassing conjugated and nonconjugated olefins.

The Pd-catalyzed dioxygenation of alkenes is an important difunctionalization method in organic synthesis due to its efficiency, safety, and economy,<sup>1</sup> although osmium catalysts have been widely used for dioxygenation reactions.<sup>2</sup> Sigman proposed a Pd(II)-catalyzed aerobic dialkoxylation of styrene derivatives requiring an *o*-phenol to facilitate the formation of a quinone methide intermediate.<sup>1b</sup> On the other hand, we envisioned an alternative Pd(II)/Pd(IV) mechanism for dioxygenation and embarked on the development of efficient processes for alkene diacetoxylation via peracetic acid as an oxidant. During the course of our research, Dong<sup>3a</sup> and

Jiang<sup>3b</sup> reported olefin diacetoxylation catalyzed by palladium complexes in the presence of either  $\text{PhI(OAc)}_2$  or molecular oxygen as an oxidant (eqs 1 and 2).



These olefin dioxygenations would presumably occur by a distinct Pd(II) to Pd(IV) process, which is significantly broad in its application toward various alkenes.<sup>4</sup> However, the use of  $\text{PhI(OAc)}_2$  as a stoichiometric oxidant produces a large amount of byproduct, while the use of molecular oxygen as an oxidant requires high pressure, temperature, and long reaction time. Therefore, our newly developed Pd(II)/Pd(IV) processes using peracetic acid can provide practical improvements over the previously reported reaction conditions.

Our initial studies included the identification of appropriate conditions and the understanding of the possible mechanism

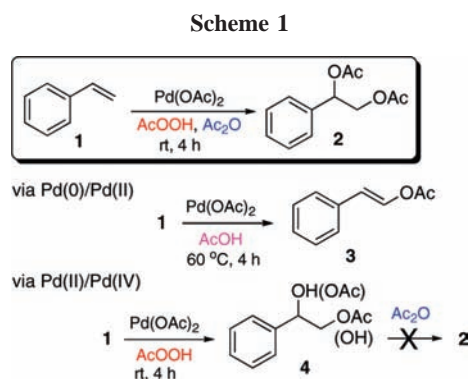
(1) (a) Chevrin, C.; Le Bras, J.; Henin, F.; Muzart, J. *Synthesis* **2005**, 2615–28618. (b) Schultz, M. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 1460–1463. (c) Thiery, E.; Chevrin, C.; Le Bras, J.; Harakat, D.; Muzart, J. *J. Org. Chem.* **2007**, *72*, 1859–1862. (d) Zhang, Y.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3076–3077. (e) Jensen, K. H.; Sigman, M. S. *Org. Biomol. Chem.* **2008**, *6*, 4083–4088.

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for the oxygenation using a palladium catalyst. As representatively shown in Scheme 1, diacetoxylation was facile



in the presence of a combination of peracetic acid and acetic anhydride with palladium acetate, converting styrene (**1**) to diacetate **2** at room temperature efficiently. To validate the possibility of Pd(II)/Pd(IV) process, we compared similar conditions without peracetic acid or acetic anhydride. When the reaction was carried out with only acetic acid, styrene underwent acetoxylation and  $\beta$ -hydride elimination to furnish the vinyl acetate **3** presumably via a Pd(0)/Pd(II) process. However, when the reaction was performed in the presence of peracetic acid as the oxidant at an ambient temperature, hydroxyacetoxylated products (**4**) were produced, implying a Pd(II)/Pd(IV) process instead of Pd(0)/Pd(II). In addition, when acetic anhydride was added to the mixture of **4** under similar conditions, conversion of **4** to **2** was not observed by  $^1\text{H}$  NMR spectra. Therefore, diacetoxylation would require both peracetic acid and acetic anhydride, and further investigation was carried out.

As shown in Table 1, we examined the correlation between product selectivity and the ratio of peracetic acid and acetic

**Table 1.** Diacetoxylation of Styrene with Pd(OAc)<sub>2</sub><sup>a</sup>

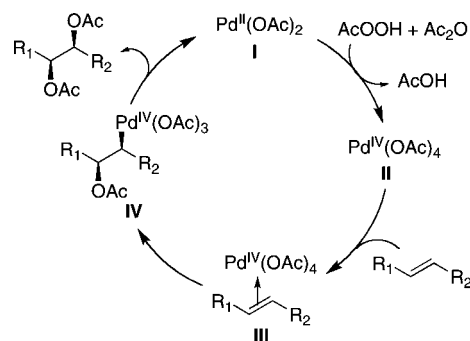
entry	time (h)	AcO <sub>2</sub> H <sup>b</sup> (mmol)	Ac <sub>2</sub> O (mmol)	conversion <sup>c</sup> (%)		
				<b>1</b>	<b>4</b>	<b>2</b>
1	4	0.13	0	41	53	6
2	4	0.26	0	12	78	10
3	4	0.26	1.3	4	79	17
4	4	0.26	2.6	0	62	38
5	4	0.26	5.2	0	21	79
6	4	0.26	7.8	0	6	94

<sup>a</sup> All reactions were carried out with styrene (0.26 mmol) and Pd(OAc)<sub>2</sub> (0.026 mmol) in acetic acid (500  $\mu\text{L}$ ). <sup>b</sup> 35.5 wt % in AcOH. <sup>c</sup> The conversions were determined by  $^1\text{H}$  NMR in the presence of an internal standard.

anhydride. In the presence of only peracetic acid as an oxidant (entries 1 and 2), dioxygenation of styrene proceeded

to give hydroxyacetoxylated product (**4**) preferably along with small amounts of diacetate **2**. Upon the addition of acetic anhydride, the chemoselectivity for the diacetoxylation product (**2**) improved significantly (entries 3–6), and its yield was proportional to the amount of acetic anhydride. Optimal results were obtained when styrene was added to the premixed solution of AcO<sub>2</sub>H and Ac<sub>2</sub>O at 0 °C and the reaction mixture was slowly warmed to room temperature (see the Supporting Information).

On the basis of these results, it can be suggested that Pd(OAc)<sub>2</sub> could be oxidized to Pd(IV)(OH)(OAc)<sub>3</sub> without acetic anhydride or Pd(IV)(OAc)<sub>4</sub> with acetic anhydride. Keeping in mind this possibility, we propose a mechanism for the diacetoxylation of an alkene (Figure 1). The Pd(IV)



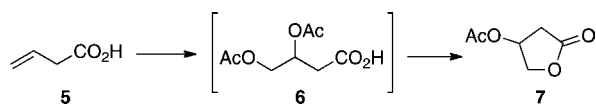
**Figure 1.** Plausible Pd(II)/Pd(IV) pathway.

species **II** (palladium tetraacetate), generated from Pd(OAc)<sub>2</sub> and peracetic acid/acetic anhydride, is suggested to be the starting point of alkene acetoxylation.<sup>5</sup> The highly reactive Pd(IV) species would then undergo *syn*-addition onto the alkene to generate palladium intermediate **IV**, while maintaining the Pd(IV) oxidation state. This is followed quickly by reductive elimination to afford the diacetoxylation product from Pd(IV) center and regenerate Pd(OAc)<sub>2</sub>. The most notable feature of the proposed catalysis is its ability to facilitate diacetoxylation under mild conditions such as ambient temperature and a short reaction time.

Next, we screened various olefins using the optimal conditions. First, we examined 3-butenic acid as a representative nonconjugated olefin to afford diacetate product **6**, which was anticipated to cyclize to the valuable lactone **7**.<sup>6</sup> In the absence of palladium catalysts, only a trace amount of lactone compound was observed, and most of the unreacted 3-butenic acid was recovered (Table 2, entry 1).

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(6) (a) Ahmed, M. M.; Berry, B. P.; Hunters, T. J.; Tomcik, D. J.; O'Doherty, G. A. *Org. Lett.* **2005**, 7, 745–748. (b) Wu, Y.; Guan, M. *Indian J. Chem., Sec. B: Org. Chem. Med. Chem.* **1998**, 37B, 844–846. (c) Brzezinski, L. J.; Rafel, S.; Leahy, J. W. *J. Am. Chem. Soc.* **1997**, 119, 4317–4318. (d) Tiecco, M.; Testaferri, L.; Tingoli, M. *Tetrahedron* **1993**, 49, 5351–5358. (e) Uchiyama, H.; Kobayashi, Y.; Sato, F. *Chem. Lett.* **1985**, 467–470.

**Table 2.** Pd-Catalyzed Diacetoxylation of 3-Butenoic acid.<sup>a</sup>

entry	catalyst	oxidant	solvent <sup>b</sup>	time (h)	yield <sup>c</sup> (%)
1	none	AcO <sub>2</sub> H	AcOH	12	trace
2	PdCl <sub>2</sub>	AcO <sub>2</sub> H	AcOH	8	10
3	Pd(OAc) <sub>2</sub>	AcO <sub>2</sub> H	AcOH	4	72
4	Pd(OAc) <sub>2</sub>	PhI(OAc) <sub>2</sub>	AcOH	12	trace
5 <sup>d</sup>	Pd(OAc) <sub>2</sub>	AcO <sub>2</sub> H	AcOH/MeCN	4	62
6 <sup>e</sup>	<b>Pd(OAc)<sub>2</sub></b>	<b>AcO<sub>2</sub>H</b>	<b>AcOH</b>	4	<b>92</b>

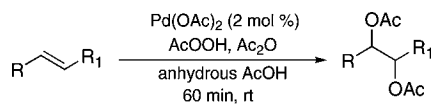
<sup>a</sup> 1.0 mmol scale (0.1 M solution), 5 mol % of Pd catalyst, and 1.2 equiv of oxidant, yield by <sup>1</sup>H NMR data spectra using an internal standard. <sup>b</sup> In entries 1–5, H<sub>2</sub>O was evaporated to afford the cyclized product after reaction. <sup>c</sup> Isolated yields. <sup>d</sup> AcOH/MeCN = 1:1 (wt %). <sup>e</sup> Anhydrous acetic acid.

When PdCl<sub>2</sub> effected the oxidation to a small degree (entry 2), Pd(OAc)<sub>2</sub> facilitated the oxidation and cyclization to offer lactone **7** in a good yield (entry 3). Other oxidants such as PhI(OAc)<sub>2</sub> were also tested, but none of them afforded significant efficiency (entry 4).<sup>7</sup> By varying solvents, we sought optimal conditions. Wet acetic acid (entry 3) and organic solvents (entry 5) were not comparable to the use of anhydrous acetic acid (entry 6), which converted 3-butenic acid completely to the desired lactone **7** in an excellent yield.

Using the developed reaction conditions, we extended the diacetoxylation protocol to a number of olefins to verify the generality of this method. As shown in Table 3, the desired reaction products were synthesized generally in high yields. Terminal aliphatic olefins including 3-butenitrile, 3-methyl-3-butenyl acetate, and allylbenzene afforded their corresponding diacetoxylation products **8**, **9**, and **10**, respectively, in 93%, 90%, and 86% yields (entries 1–3). In the case of the trisubstituted cyclic alkene, 1-methyl-1-cyclohexene underwent diacetoxylation smoothly to give the desired diacetate product **11** in 89% yield along with high diastereoselectivity (*syn/anti* = 15/1) (entry 4). Disubstituted aromatic alkenes also provided the desired vicinal oxygenation products (entries 5–7), and the high *syn*-addition of acetoxy group was confirmed again (entries 6 and 7) (*syn/anti* = 10/1, 12/1, respectively).<sup>3a</sup> Furthermore, the reaction with 1-phenyl-1-cyclohexene as a trisubstituted conjugated olefin took place efficiently to provide the desired compound **15** in 87% yield along with high diastereoselectivity (*syn/anti* = 15/1) (entry 8).

In conclusion, we have successfully developed a highly reactive palladium-catalyzed diacetoxylation for a broad range of alkenes, including conjugated and nonconjugated,

(7) In Song's report (ref 3a), use of excess PhI(OAc)<sub>2</sub> improved the yield and reduced β-hydride elimination.

**Table 3.** Pd-Catalyzed Diacetoxylation of Alkenes<sup>a</sup>

entry	substrate	product	yield <sup>b</sup> ( <i>syn/anti</i> )
1			93%
2			90%
3			86%
4			89% <sup>c</sup> (15 / 1) <sup>c</sup>
5			88%
6 <sup>d</sup>			79% <sup>c</sup> (10 / 1) <sup>c</sup>
7			81% <sup>c</sup> (8 / 1) <sup>c</sup>
8			87% <sup>c</sup> (15 / 1) <sup>c</sup>

<sup>a</sup> 1.0 mmol scale (0.1 M solution), 2 mol % of Pd(OAc)<sub>2</sub>, and 1.2 equiv of CH<sub>3</sub>CO<sub>3</sub>H. <sup>b</sup> Isolated yields. <sup>c</sup> The diastereomeric ratios were determined by <sup>1</sup>H NMR analysis. <sup>d</sup> Reaction temperature was 45 °C.

under ambient temperature and pressure. Mono- to trisubstituted alkenes were compatible with the developed method. In addition, high stereoselectivity as well as functional group tolerance is worthy of note. Overall, our processes are believed to provide a convenient and practical method.

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**Supporting Information Available:** Experimental details for the preparation of compounds and spectral data of these compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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