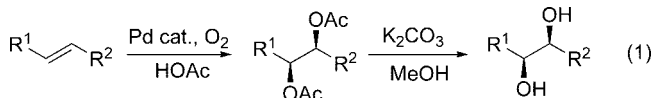# J|A|C|S
COMMUNICATIONS

Palladium-Catalyzed Diacetoxylation of Alkenes with Molecular Oxygen as Sole Oxidant

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Transiton metal catalyzed oxidative difunctionalization of alkenes continues to be a fascinating and useful area of research.[1] One such method is the OsO$_4$-catalyzed *cis*-dihydroxylation of alkenes and its asymmetric version developed by Sharpless et al.[2] Currently, there is considerable interest in the palladium-catalyzed alkene difunctionalization.[3] Muñiz reported Pd-catalyzed intramolecular diamination reactions of alkenes.[4] Sorensen[5] and Stahl[6] reported Pd-catalyzed aminoacetoxylation of alkenes respectively. Very recently, Song reported hydroxyacetoxylation of alkenes using cationic Pd catalysts.[7] One common ground of these reactions is that PhI(OAc)$_2$ was used as an oxidant to oxidize Pd^{II} to Pd^{IV}. However, as a stoichiometric oxidant, PhI(OAc)$_2$ often produces a large amount of byproduct. Oxygen would be a preferred oxidant because it is abundant and environmentally benign. Herein, we report the first examples of Pd-catalyzed diacetoxylation of alkenes using oxygen as the sole oxidant to afford diacetates.[8,9] Noteworthy is that the method may be valuable for the synthesis of *cis*-vicinal diols without use of toxic and expensive osmium catalysts (eq 1).

$$R^1 \diagup\diagdown R^2 \xrightarrow[\text{HOAc}]{\text{Pd cat., O}_2} \underset{\underset{\text{OAc}}{|}}{R^1}\overset{\overset{\text{OAc}}{|}}{}R^2 \xrightarrow[\text{MeOH}]{\text{K}_2\text{CO}_3} \underset{\underset{\text{OH}}{|}}{R^1}\overset{\overset{\text{OH}}{|}}{}R^2 \quad (1)$$

Initially, we tried to seek an effective system for the Pd-catalyzed diacetoxylation of styrene **1a** to produce diacetate **2a** with O$_2$ as the oxidant. As shown in Table 1, a variety of additives were explored to improve the yield. We screened several strong acids with the hope that protonation of O$_2$ would accelerate the reaction.[10] However, strong acid was ineffective for the diacetoxylation of **1a** (entries 2–4). Further investigation on the additive led to the discovery that a halide would promote the reaction (entries 5–10). In particular, when KI was used as the additive, a high yield of **2a** was obtained (entry 10).[11] The Pd source is critical for the success of this reaction. Pd(OAc)$_2$ is superior to any other Pd catalyst so far tested. A small amount of the desired product was obtained when PdCl$_2$, PdCl$_2$(PPh$_3$)$_2$, or Pd$_2$(dba)$_3$ was used as the catalyst (entries 11–13). A lower yield of **2a** was obtained when the reaction was run under 5 atm of pressure of O$_2$ (entry 14). The reaction without O$_2$ or Pd(OAc)$_2$ did not give the desired product at all (entries 15–16). Moreover, a decrease in the temperature led to a decrease in the yield (entries 17–18).

We next explored the scope and the utility of this method with other alkenes. In almost all the cases tested, the diacetoxylation went smoothly, giving a high yield of the desired products. As summarized in Table 2, a series of *para*-substituted styrene derivatives, including 1-fluoro-4-vinylbenzene, 1-chloro-4- vinylbenzene, and 1-methyl-4-vinylbenzene can be converted into their corresponding 1,2-diacetate in 91, 89, and 83% isolated yields respectively (entries 1–3). A very good result was obtained by using
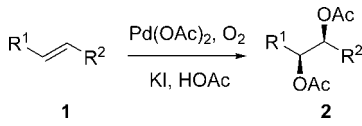
Table 1. Optimization of Reaction Conditions for the Palladium-Catalyzed Diacetoxylaton of Styrene[a]

entry	O$_2$ (atm)	Pd cat.	additive	temp (°C)	yield[b] (%)
1	8	Pd(OAc)$_2$	–	100	trace
2	8	Pd(OAc)$_2$	*p*-TsOH·H$_2$O	100	trace
3	8	Pd(OAc)$_2$	CF$_3$COOH	100	trace
4	8	Pd(OAc)$_2$	CH$_3$SO$_3$H	100	trace
5	8	Pd(OAc)$_2$	NaCl	100	<5
6	8	Pd(OAc)$_2$	LiCl	100	<5
7	8	Pd(OAc)$_2$	NaBr	100	34
8	8	Pd(OAc)$_2$	LiBr	100	38
9	8	Pd(OAc)$_2$	NaI	100	83
10	**8**	**Pd(OAc)$_2$**	**KI**	**100**	**87 (85)**
11	8	PdCl$_2$	KI	100	<5
12	8	PdCl$_2$(PPh$_3$)$_2$	KI	100	<5
13	8	Pd$_2$(dba)$_3$	KI	100	trace
14	5	Pd(OAc)$_2$	KI	100	62
15[c]	–	Pd(OAc)$_2$	KI	100	0
16	8	–	KI	100	0
17	8	Pd(OAc)$_2$	KI	80	71
18	8	Pd(OAc)$_2$	KI	50	trace

[a] Reaction conditions: All reactions were performed with **1a** (1 mmol), Pd catalyst (2 mol %), and additive (20 mol %) in 3 mL of HOAc for 24 h. [b] Determined by GC. Number in parentheses is isolated yield. [c] Under N$_2$ atmosphere.

2-vinylnaphthalene as substrate (entry 4). Allylbenzene and allyl benzyl ether also proceed in high yield (entries 5–6). Notably, very high diastereoselectivity is observed with 1,2-disubstituted alkenes as substrate, affording the diacetates with *syn* diastereoselectivity (>95:5 diastereomeric ratios). *trans*-Stilbene and *cis*-stilbene afforded the corresponding 1,2-diacetate **2h** (77% yield) and **2i** (82% yield) (entries 7–8). Likewise, diacetoxylation of *trans*-methyl cinnamate, *trans*-methyl 3-(thiophen-2-yl)acrylate, and cinnamonitrile provided the desired *syn* diacetate products in good yields (entries 9–11). Furthermore, diacetoxylation of linear aliphatic alkenes was also achieved, giving the corresponding product in 78% yield (entry 12).

On the basis of these results, a possible catalytic cycle for this new transformation is proposed in Scheme 1. First, a Pd^{II} catalyst undergoes *cis*-acetoxypalladation with olefin to afford a organopalladium intermediate **A**;[12] the extremely high diastereoselectivity observed in the diacetoxylation of 1,2-disubstituted alkenes **7**–**11** provides strong evidence in support of this step. Next, the organopalladium intermediate **A** is oxidized by O$_2$ to a Pd^{IV} intermediate **B**.[13] To our knowledge, there is no report concerning direct O$_2$-mediated Pd^{II}/Pd^{IV} oxidation. A control reaction was carried out with stoichiometric Pd(OAc)$_2$ as catalyst, and the

Table 2. Palladium-Catalyzed Diacetoxylaton of Alkenes[a]

entry	alkene	product	d. r.[b] (*syn:anti*)	Yield[c] (%)
1	**1b**	**2b**	-	91
2	**1c**	**2c**	-	89
3	**1d**	**2d**	-	83
4	**1e**	**2e**	-	85
5	**1f**	**2f**	-	84
6	**1g**	**2g**	-	81
7	**1h**	**2h**	98:2	77
8	**1i**	**2i**	99:1	82
9	**1j**	**2j**	97:3	76
10	**1k**	**2k**	96:4	72
11	**1l**	**2l**	98:2	73
12	**1m**	**2m**	-	78

[a] Reaction conditions: alkene (1 mmol), $Pd(OAc)_2$ (2 mol%), KI (20 mol%), pressure of O_2 (8 atm), HOAc (3 mL), 100 °C, 24 h. [b] Diastereomeric ratios were determined after purification from GC and ^{1}H NMR. [c] Isolated yields.

Scheme 1. Plausible Reaction Mechanism
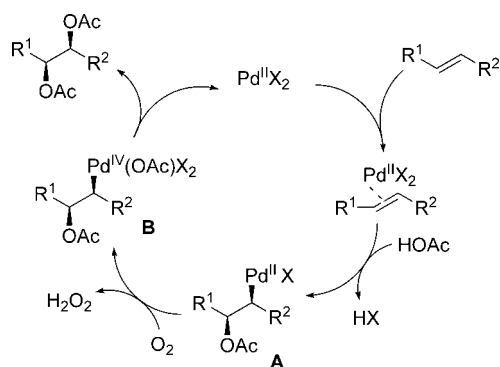
diacetate product was not detected without O_2. Due to this result, an alternative Pd^{II}/Pd^0 cycle result is less probable. Finally, reductive elimination from Pd^{IV} intermediate **B** results in the C—O bond forming and regenerates the Pd^{II} catalyst.

In summary, we have successfully developed a direct dioxygen-coupled Pd^{II}-mediated diacetoxylation of alkenes. This methodology opens up a new avenue for the green synthesis of 1, 2-diacetates, which completely avoids the use of conventional toxic stoichiometric reagents. Furthermore, the extremely high levels of stereoselectivity in the diacetoxylation of 1,2-disubstituted alkenes make this a potentially attractive method in organic synthesis, for example, in the synthesis of *cis*-1,2-diols. Further studies on the reaction mechanism, the scope of the reaction, and the potential for asymmetric induction in the diacetoxylation process are in progress.

Supporting Information Available: Experimental procedure and characterization of compounds **2a−3m**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) A control reaction was carried out with a stoichiometric amount of I_2 as oxidant (without O_2 present), and it was found that the diacetoxylation reaction did not occur. Therefore, I_2 oxidizing Pd^{II} to Pd^{IV} can be excluded.

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