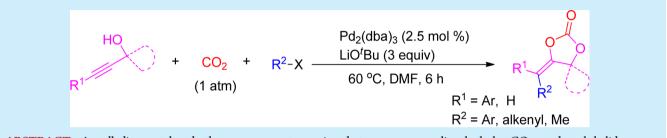


# Palladium-Catalyzed Arylcarboxylation of Propargylic Alcohols with $CO_2$ and Aryl Halides: Access to Functionalized $\alpha$ -Alkylidene Cyclic Carbonates

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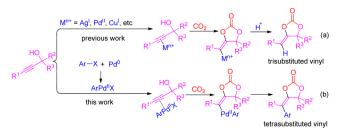
**Supporting Information** 



**ABSTRACT:** A palladium-catalyzed, three-component reaction between propargylic alcohols, CO<sub>2</sub>, and aryl halides was developed whereby a sequential carboxylation, *trans*-oxopalladation of the C $\equiv$ C bond by an ArPdX species, and a reductive elimination procedure afforded a series of functionalized  $\alpha$ -alkylidene cyclic carbonates in moderate to excellent yields. Notably, the configuration of these tetrasubstituted olefins was dominated by the *trans*-oxopalladation step where the aryl group derived from ArX is located *trans* to the oxygen attached in the double bond. This protocol features simultaneous formation of four novel bonds in a one-pot reaction, representing an efficient method for incorporation of CO<sub>2</sub> into heterocycles.

he transformation of CO<sub>2</sub> as a nontoxic, economical, and abundant C1 source toward useful carbonyl-containing compounds,<sup>1-3</sup> especially heterocycles,<sup>4</sup> has emerged as a flourishing research area in terms of the concept of sustainable chemistry. In this field, transition-metal-catalyzed hydrocarboxylation of propargylic alcohols with CO<sub>2</sub> is a particularly appealing approach to assemble important  $\alpha$ -alkylidene cyclic carbonates, which represents an important class of heterocyclic compounds with a wide range of applications in organic synthesis.<sup>5</sup> Generally, these procedures proceed via the carboxylation of propargylic alcohols with  $\overline{CO}_2$  to form the vinyl-M intermediates, which sequentially undergo protonation toward trisubstituted alkenes (Scheme 1a).<sup>6-9</sup> However, these procedures suffer from the requirement of either strong organic bases (often super bases) or high CO<sub>2</sub> pressure (>1 MPa).<sup>10</sup> Furthermore, such successful cases are limited to protonation of

## Scheme 1. Reactions Involving Propargylic Alcohols and $\mathrm{CO}_2$



the vinyl-M intermediates, and approaches using the vinyl-M intermediates for the introduction of new functional groups have scarcely been reported.<sup>11</sup>

According to the elemental reaction, the oxidative addition of aryl halides to  $Pd^0$  would produce the  $ArPd^{II}X$  intermediates. The formed  $Pd^{II}$  species was highly expected to possess similar activity with  $Pd^{II}$  salt to take part in carboxylative cyclization of propargylic alcohols with  $CO_2$ . Therefore, after the sequential intramolecular *trans*-oxopalladation<sup>12</sup> and reductive elimination, a three-component reaction between propargylic alcohols, aryl halides, and  $CO_2$  would afford functionalized  $\alpha$ -alkylidene cyclic carbonates bearing a tetrasubstituted vinyl fragment (Scheme 1b). Herein, we report our study in this regard.

Initially, we tested the reaction of 2-methyl-4-phenylbut-3yn-2-ol **1a** (0.2 mmol) and iodobenzene **2a** (0.3 mmol) under an atmospheric pressure of CO<sub>2</sub> (Table 1). This threecomponent reaction took place in the presence of Pd-(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (5 mol %) and K<sub>2</sub>CO<sub>3</sub> (0.6 mmol) in DMF at 60 °C, producing 5-(diphenylmethylene)-4,4-dimethyl-1,3-dioxolan-2-one **3a** in 52% yield (Table 1, entry 1). Among the bases tested, LiO'Bu (75%) was superior to Cs<sub>2</sub>CO<sub>3</sub> (<5%), KO'Bu (trace), and NaO'Bu (65%, Table 1, entries 1–5). Pd(OAc)<sub>2</sub> (86%) and PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub> (83%) also worked well (Table 1, entries 5–7). However, the reaction efficiency increased dramatically to 92% by using 2.5 mol % of Pd<sub>2</sub>(dba)<sub>3</sub> (Table

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Table 1. Selected Results for Screening the Optimized Reaction Conditions $^{a}$ 

HO Ph 1a	+ CO <sub>2</sub> +	Ph—I	conditions	$\rightarrow Ph + H$
entry	[Pd]	base	solvent	isolated yield (%)
1	$Pd(PPh_3)_2Cl_2$	K <sub>2</sub> CO <sub>3</sub>	DMF	52
2	$Pd(PPh_3)_2Cl_2$	Cs <sub>2</sub> CO <sub>3</sub>	DMF	<5
3	$Pd(PPh_3)_2Cl_2$	KO <sup>t</sup> Bu	DMF	trace
4	$Pd(PPh_3)_2Cl_2$	NaO <sup>t</sup> Bu	DMF	65
5	$Pd(PPh_3)_2Cl_2$	LiO <sup>t</sup> Bu	DMF	75
6	$Pd(OAc)_2$	LiO <sup>t</sup> Bu	DMF	86
7	$PdCl_2(CH_3CN)_2$	LiO <sup>t</sup> Bu	DMF	83
8	$Pd_2(dba)_3$	LiO <sup>t</sup> Bu	DMF	92
9	$Pd_2(dba)_3$	LiO <sup>t</sup> Bu	DMSO	41
10	$Pd_2(dba)_3$	LiO <sup>t</sup> Bu	THF	trace
11	$Pd_2(dba)_3$	LiO <sup>t</sup> Bu	DMF	51, <sup>b</sup> 71 <sup>c</sup>
12	$Pd_2(dba)_3$	LiO <sup>t</sup> Bu	DMF	43, <sup>d</sup> 89 <sup>e</sup>

<sup>*a*</sup>Reaction conditions: 1a (0.2 mmol), 2a (0.3 mmol), [Pd] (0.01 mmol), base (0.6 mmol), solvent (2.0 mL),  $CO_2$  (1 atm), at 60 °C for 6 h, in a sealed Schlenk tube, unless otherwise noted. <sup>*b*</sup>2a (0.2 mmol). <sup>*c*</sup>2a (0.4 mmol). <sup>*d*</sup>LiO'Bu (0.3 mmol). <sup>*e*</sup>LiO'Bu (1.0 mmol)

1, entry 8). The yield decreased to 41% using DMSO, while THF inhibited the reaction (Table 1, entries 9 and 10). Additionally, changing the ratios of the starting materials and the base decreased the reaction efficiency (51-89%, Table 1, entries 11 and 12).

With the optimized reaction conditions in hand, the scope and limitation of aryl halides was studied as shown in Figure 1. Generally, the reaction efficiency was not sensitive to the electronic property of the groups on the aryl halides as substrates bearing both electron-donating (3b-d, 62%-90%) and electron-withdrawing groups (3f-k, 77%-95%) worked well with good to excellent yields. However, a substrate bearing an ortho substituent resulted in a lower yield (3e, 45%). Notably, a series of functional groups, such as fluoro (89%, 3f), chloro (92%, 3g), trifluoromethyl (94%, 3h), ethoxycarbonyl (95%, 3i), formyl (92%, 3j), and acetyl (77%, 3k) groups, which are suitable for potentially further functionalization, survived well in these reactions. Additionally, disubstituted aryl halides also worked well to generate 3l and 3m in 88% and 90% yields, respectively. However, the more bulky 1,2,4-trichloro-5iodobenzene gave poor results (6%, 3n). 1-Iodonaphthalene, 2iodothiophene, and (E)-(2-bromovinyl)benzene also ran smoothly under the standard conditions to afford 30, 3p, and 3q in 56%, 80%, and 78% yields, respectively. In particular, iodomethane served as reaction partners in this reaction (31%, 3r). Importantly, only one Z/E isomer was detected by GC-MS and NMR analysis, while the configuration of double bond was unambiguously confirmed by X-ray crystal study, where the aryl derived from ArX is located trans to the oxygen attached in the C=C double bond.<sup>13</sup>

Next, the scope and limitations of propargylic alcohols were also investigated. Generally, as shown in Figure 2, the reaction efficiency was not sensitive to the electronic property of the groups on the phenyl ring of propargylic alcohols as substrates bearing both electron-donating (4a-c, 82%-88%) and electron-withdrawing groups (4d-f, 81%-84%) worked well with good to excellent yields. 2-Methyl-4-(thiophene-2-yl)but-

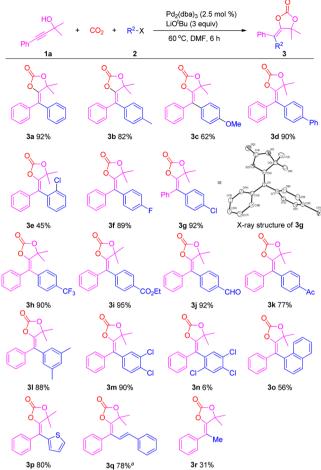


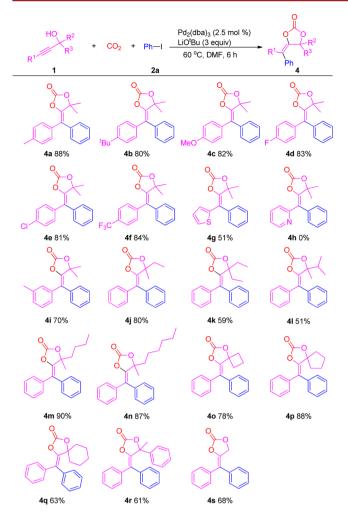
Figure 1. Scope of aryl halides. Reaction conditions: 1a (0.2 mmol), 2 (0.3 mmol),  $Pd_2(dba)_3$  (0.005 mmol, 4.6 mg),  $LiO^tBu$  (0.6 mmol, 48 mg), DMF (2.0 mL),  $CO_2$  (1 atm), at 60 °C for 6 h, in a sealed Schlenk tube, unless otherwise noted. (a)  $Pd(PPh_3)_2Cl_2$  (0.01 mmol, 7.0 mg).

3-yn-2-ol also ran smoothly under the standard conditions to afford 4g in 51% yield. However, 2-methyl-4-(pyridin-2-yl)but-3-yn-2-ol 1h resulted in no reaction. For a substrate with a *meta*-substituent on the phenyl, 4i was isolated in an acceptable 70% yield. Propargylic alcohols with different  $\mathbb{R}^2$  and  $\mathbb{R}^3$  substituents all gave the corresponding products (4j-r) in moderate to excellent yields (51%-90%). Notably, this reaction allowed the construction of spiro compounds 4o-q in 63-88% yields. In particular, this procedure was not limited to tertiary propargylic alcohols, as the primary analogue ran smoothly under the standard conditions, affording 4s in 68% yield. Importantly, 3b,c,f-h,p and 4a,c-g were pairs of Z/E configuration isomers can be accessed by changing the substrate combinations in our procedure.

This procedure was also applicable to the terminal propargylic alcohols, providing 5-(diphenylmethylene)-4,4-dimethyl-1,3-dioxolan-2-one 3a in 55% yield (Scheme 2a). Meanwhile, further transformation of 3a was studied, and the reaction of cyclic carbonate 3a with hexan-1-amine afforded carbamate 5 in 69% yield (Scheme 2b).

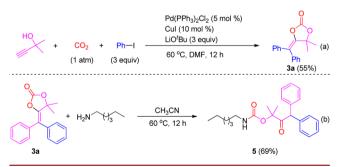
Some control experiments were conducted to gain insight into this transformation. First, 2-methyl-4-phenylbut-3-yn-2-ol 1a was subjected to the standard conditions, and (Z)-5-

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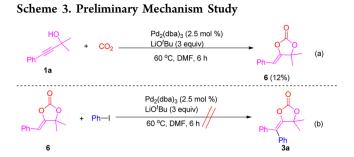
**Figure 2.** Substrate scope of propargylic alcohols. Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol),  $Pd_2(dba)_3$  (0.005 mmol, 4.6 mg), LiO<sup>t</sup>Bu (0.6 mmol), DMF (2.0 mL), CO<sub>2</sub> (1 atm), at 60 °C for 6 h, in a sealed Schlenk tube, unless otherwise noted.

Scheme 2. Reaction of 2-Methylbut-3-yn-2-ol,  $CO_2$ , and Iodobenzene and Further Transformation of 3a

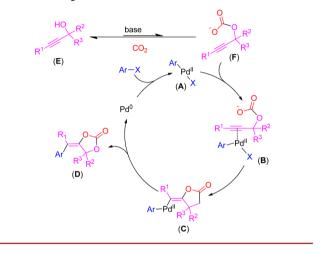


benzylidene-4,4-dimethyl-1,3-dioxolan-2-one **6** was isolated in about 12% yield, indicating  $ArPd^{II}X$  derived from the oxidative oxidation of aryl halides to  $Pd^0$  species served as a promoter for this three-component reaction<sup>14</sup> (Scheme 3a). On the other hand, the presumed intermediate **6** did not work under the procedure, which ruled out the possibility of the Heck reaction pathway (Scheme 3b).

On the basis of these experimental results, a proposed mechanism is outlined in Scheme 4. The reaction is initiated by oxidative addition of  $Pd^0$  to aryl halides to afford  $ArPd^{II}X$ 



Scheme 4. Proposed Mechanism



species **A**. Then, with the assistance of base, the propargylic alcohol **E** reacts with  $CO_2$  rapidly, leading to carbonate **F**. After the coordination of the triple bond in **F** with **A**, an intramolecular *trans*-oxopalladation takes place to afford intermediate **C**. Finally, reductive elimination of **C** delivers the desired functionalized  $\alpha$ -alkylidene cyclic carbonates **D**, along with the regeneration of Pd<sup>0</sup>. In the case of terminal propargylic alcohols, a Sonogashira reaction is involved before the sequential carboxylation, *trans*-oxopalladation of the C $\equiv$ C bond by ArPd<sup>II</sup>X, and reductive elimination procedure.

In conclusion, we have developed a palladium-catalyzed, three-component reaction between propargylic alcohols, an atmospheric pressure of CO<sub>2</sub>, and aryl halides whereby a sequential carboxylation, intramolecular *trans*-oxopalladation of the C=C bond by ArPd<sup>II</sup>X, and reductive elimination procedure affords a series of functionalized  $\alpha$ -alkylidene cyclic carbonates in moderate to excellent yields. Notably, the configuration of these tetrasubstituted olefins was dominated by the *trans*-oxopalladation step, where the aryl derived from ArX was located *trans* to the oxygen attached to the double bond. This protocol features simultaneous formation of four novel bonds in a one-pot reaction, representing an efficient method for incorporation of CO<sub>2</sub> into heterocycles.

### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.or-glett.7b00111.

Experimental procedures and NMR spectra (PDF)

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#### Notes

The authors declare no competing financial interest.

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