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Palladium-Catalyzed Arylcarboxylation of Propargylic Alcohols with CO_2 and Aryl Halides: Access to Functionalized α-Alkylidene Cyclic Carbonates

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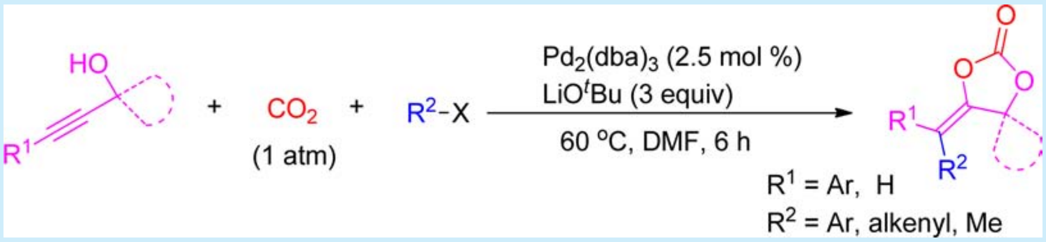
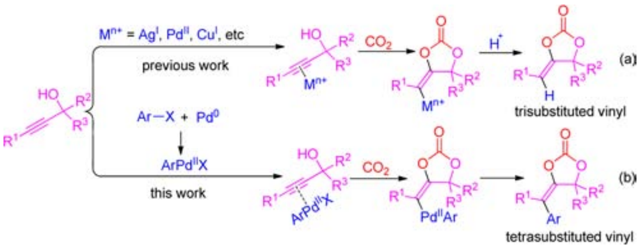
Supporting Information



ABSTRACT: A palladium-catalyzed, three-component reaction between propargylic alcohols, CO_2, and aryl halides was developed whereby a sequential carboxylation, *trans*-oxopalladation of the C≡C bond by an ArPdX species, and a reductive elimination procedure afforded a series of functionalized α-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_2 into heterocycles.

The transformation of CO_2 as a nontoxic, economical, and abundant C1 source toward useful carbonyl-containing compounds,[1−3] especially heterocycles,[4] 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_2 is a particularly appealing approach to assemble important α-alkylidene cyclic carbonates, which represents an important class of heterocyclic compounds with a wide range of applications in organic synthesis.[5] Generally, these procedures proceed via the carboxylation of propargylic alcohols with CO_2 to form the vinyl-M intermediates, which sequentially undergo protonation toward trisubstituted alkenes (Scheme 1a).[6−9] However, these procedures suffer from the requirement of either strong organic bases (often super bases) or high CO_2 pressure (>1 MPa).[10] Furthermore, such successful cases are limited to protonation of the vinyl-M intermediates, and approaches using the vinyl-M intermediates for the introduction of new functional groups have scarcely been reported.[11]

Scheme 1. Reactions Involving Propargylic Alcohols and CO_2



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[12] and reductive elimination, a three-component reaction between propargylic alcohols, aryl halides, and CO_2 would afford functionalized α-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-3-yn-2-ol **1a** (0.2 mmol) and iodobenzene **2a** (0.3 mmol) under an atmospheric pressure of CO_2 (Table 1). This three-component reaction took place in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol %) and K_2CO_3 (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^tBu (75%) was superior to Cs_2CO_3 (<5%), KO^tBu (trace), and NaO^tBu (65%, Table 1, entries 1−5). $Pd(OAc)_2$ (86%) and $PdCl_2(CH_3CN)_2$ (83%) also worked well (Table 1, entries 5−7). However, the reaction efficiency increased dramatically to 92% by using 2.5 mol % of $Pd_2(dba)_3$ (Table

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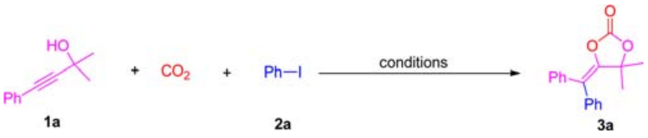
Table 1. Selected Results for Screening the Optimized Reaction Conditions[a]



entry	[Pd]	base	solvent	isolated yield (%)
1	$Pd(PPh_3)_2Cl_2$	K_2CO_3	DMF	52
2	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMF	<5
3	$Pd(PPh_3)_2Cl_2$	KO^tBu	DMF	trace
4	$Pd(PPh_3)_2Cl_2$	NaO^tBu	DMF	65
5	$Pd(PPh_3)_2Cl_2$	LiO^tBu	DMF	75
6	$Pd(OAc)_2$	LiO^tBu	DMF	86
7	$PdCl_2(CH_3CN)_2$	LiO^tBu	DMF	83
8	$Pd_2(dba)_3$	LiO^tBu	DMF	92
9	$Pd_2(dba)_3$	LiO^tBu	DMSO	41
10	$Pd_2(dba)_3$	LiO^tBu	THF	trace
11	$Pd_2(dba)_3$	LiO^tBu	DMF	51,[b] 71[c]
12	$Pd_2(dba)_3$	LiO^tBu	DMF	43,[d] 89[e]

[a] 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. [b] **2a** (0.2 mmol). [c] **2a** (0.4 mmol). [d] LiO^tBu (0.3 mmol). [e] LiO^tBu (1.0 mmol)

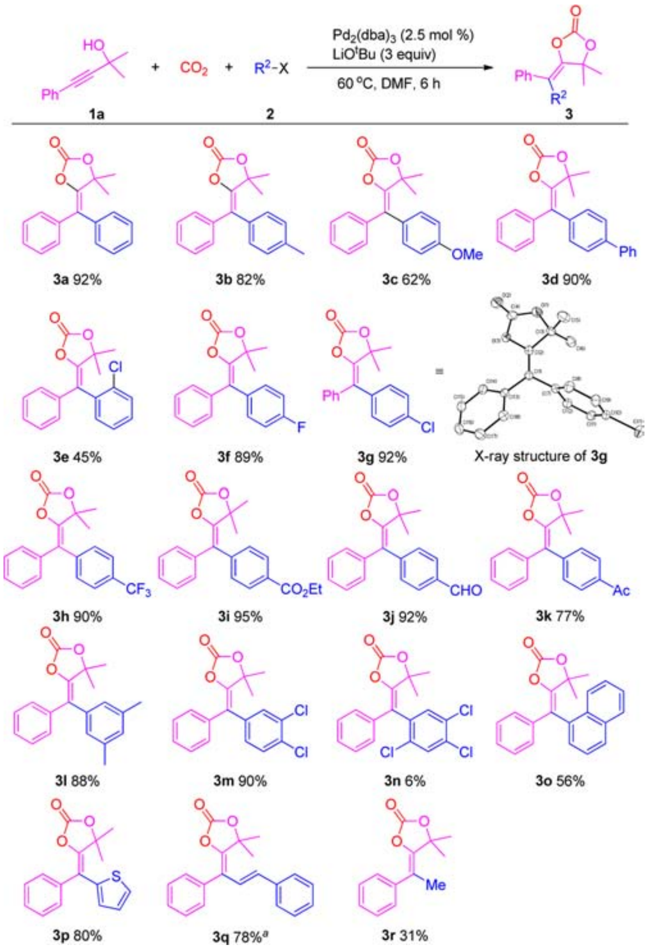


Figure 1. Scope of aryl halides. Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol), $Pd_2(dba)_3$ (0.005 mmol, 4.6 mg), LiO^tBu (0.6 mmol, 48 mg), DMF (2.0 mL), CO_2 (1 atm), at 60 °C for 6 h, in a sealed Schlenk tube, unless otherwise noted. (a) $Pd(PPh_3)_2Cl_2$ (0.01 mmol, 7.0 mg).

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-5-iodobenzene gave poor results (6%, **3n**). 1-Iodonaphthalene, 2-iodothiophene, and (*E*)-(2-bromovinyl)benzene also ran smoothly under the standard conditions to afford **3o**, **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.[13]

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-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 R^2 and 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 about the C═C bond. Namely, both *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-

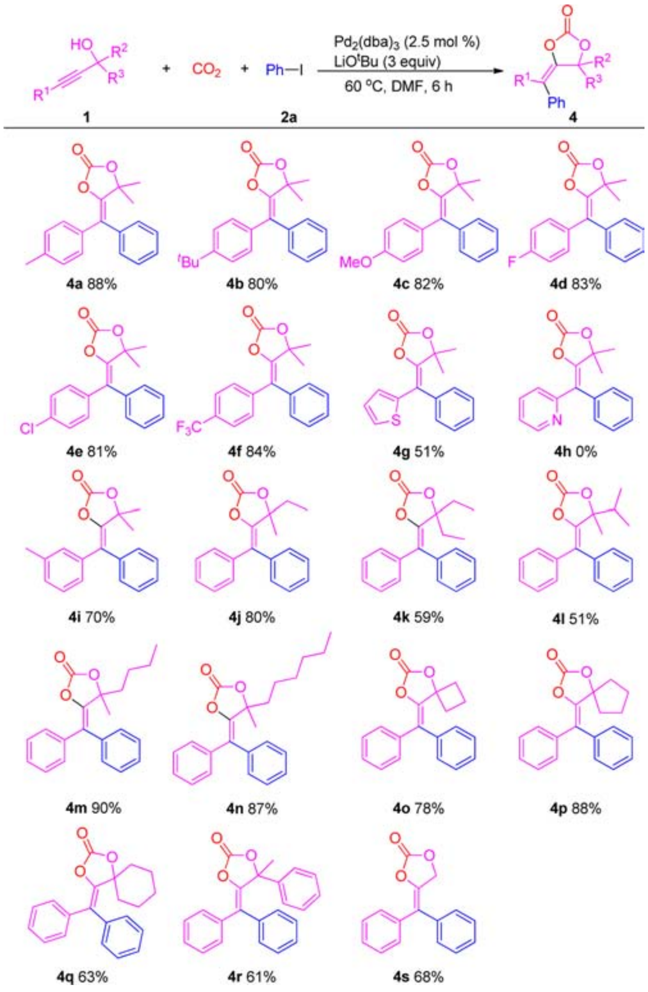
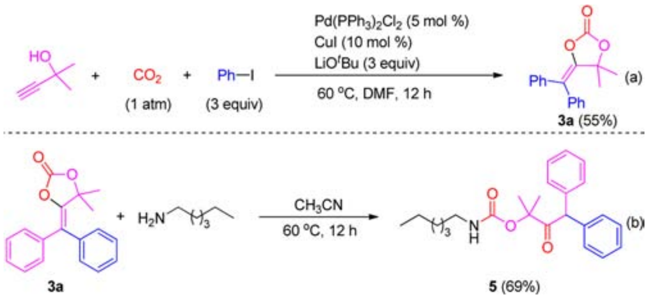
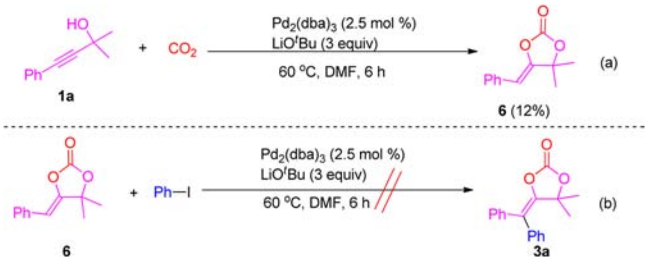


Figure 2. Substrate scope of propargylic alcohols. Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), Pd$_2$(dba)$_3$ (0.005 mmol, 4.6 mg), LiO^{t}Bu (0.6 mmol), DMF (2.0 mL), CO$_2$ (1 atm), at 60 °C for 6 h, in a sealed Schlenk tube, unless otherwise noted.

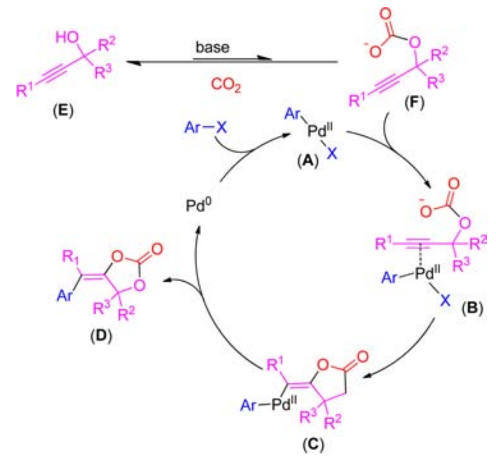
Scheme 2. Reaction of 2-Methylbut-3-yn-2-ol, CO$_2$, and Iodobenzene and Further Transformation of 3a



Scheme 3. Preliminary Mechanism Study



Scheme 4. Proposed Mechanism



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[14] (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 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 α-alkylidene cyclic carbonates **D**, along with the regeneration of Pd^0. In the case of terminal propargylic alcohols, a Sonogashira reaction is involved before the sequential carboxylation, *trans*-oxopalladation of the C≡C bond by ArPd^{II}X, and reductive elimination procedure.

In conclusion, we have developed a palladium-catalyzed, three-component reaction between propargylic alcohols, an atmospheric pressure of CO$_2$, and aryl halides whereby a sequential carboxylation, intramolecular *trans*-oxopalladation of the C≡C bond by ArPd^{II}X, and reductive elimination procedure affords a series of functionalized α-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$_2$ into heterocycles.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

Experimental procedures and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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