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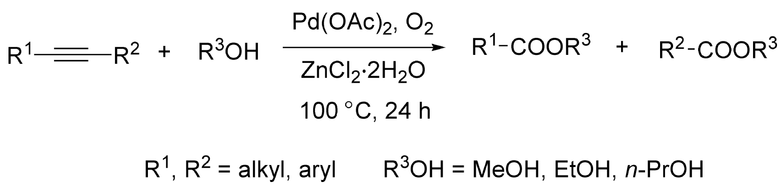

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Palladium-Catalyzed Cleavage Reaction of Carbon−Carbon Triple Bond with Molecular Oxygen Promoted by Lewis Acid

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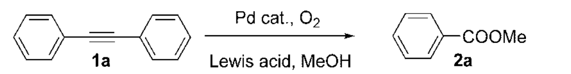
Transition-metal-catalyzed cleavage reactions of carbon−carbon bonds have been recognized as powerful tools in organic transformations.[1] Various unique and useful catalytic processes involving C−C single and double bonds cleavage have recently been developed.[2] What has remained unexplored is the cleavage of C−C triple bond, which is one of the most challenging subjects in modern synthetic organic chemistry.[3] Most studies on alkyne cleavage have focused on stoichiometric organometallic reactions, such as alkyne-ligand scission on metal complexes[4] and oxidative cleavage.[5] Examples for the metal-catalyzed C−C triple bond cleavage reactions are rare, except for metathesis of alkynes.[6] Jun et al. reported catalytic C−C triple bonds cleavage through the rhodium-catalyzed hydroimino-acylation.[7] Yamamoto reported the cleavage of diynes via ruthenium-catalyzed hydroamination.[8] Liu et al. reported catalytic cleavage of alkynes in which ethynyl alcohol is split into alkene and CO by ruthenium complex.[9] Very recently, Liu et al. reported the gold-catalyzed cleavage of C−C triple bonds in (*Z*)-enynols with molecular oxygen.[10] However, there have been no reports in the literature concerning palladium-catalyzed cleavage of C−C triple bond using molecular oxygen.[11,12] Herein, we describe a new Lewis acid promoted and palladium-catalyzed cleavage reaction with molecular oxygen in which alkyne is split into carboxylic ester in various alcohols.

Initially, we employed palladium-catalyzed cleavage reaction of 1,2-diphenylethyne (**1a**) in MeOH at 100 °C as a model for discovery of optimized conditions. As summarized in Table 1, it was found that without oxygen the reaction did not occur (entry 1). A small amount of benzoate **2a**, an oxidative cleavage product, was observed when 7.5 atmospheric pressure of O_2 was used as the oxidant (entry 2). Although the conversion was quite low, it was promising since the result indicated the possibility of catalyzing C−C triple bonds cleavage via palladium-mediated reactions. Further exploration led to a discovery that 88% isolated yield of **2a** was afforded from **1a** if $ZnCl_2 \cdot 2H_2O$ is employed as the additive and O_2 as the oxidant in MeOH (entry 3). We examined several different Lewis acids for the cleavage reaction. $ZnCl_2 \cdot 2H_2O$ was found to be the most effective one (entry 3). Other Lewis acids such as $CuCl_2 \cdot 2H_2O$, $FeCl_3 \cdot 6H_2O$, $MnCl_2 \cdot 4H_2O$, and $AlCl_3 \cdot 6H_2O$, were substantially less effective (entries 4–7). The reaction provided no conversion without palladium catalyst (entry 8). Upon decreasing the temperature to 60 °C, lower yield was obtained (entry 9). Different palladium species were also tested. Both $PdCl_2$ and $Pd_2(dba)_3$ had a comparable catalytic reactivity for this transformation (entries 10, 11). When the dosage of $ZnCl_2 \cdot 2H_2O$ was reduced to 10 mol %, lower yield was obtained (entry 12). Anhydrous $ZnCl_2$ was also found effective for the cleavage reaction (entry 13).

Encouraged by the ease of this reaction, we next focused on expanding the scope of the methodology. Table 2 highlights the broad range of the various alkynes that can be used in the cleavage reaction. 1,2-Di-*p*-tolylethyne provided the desired product **2b** in excellent yield (Table 2, entry 1). The change of methanol to ethanol or *n*-propyl alcohol did not alter the course of the reaction (entries 2, 3). A notable exception was observed when using oct-4-yne as substrate (entry 4); only 18% yield of the cleavage product was obtained, along with the byproduct from cyclotrimerization of oct-4-yne. Unsymmetrical internal alkynes were also included in this study. Compared to the symmetrical internal alkynes, the unsymmetrical internal alkynes were cleaved to two different products (entries 5–9), except for ethyl 3-phenylpropiolate (entry 10). The cleavage reaction of terminal alkynes afforded the corresponding products in good yields (entries 11, 12). Finally, we carried out the cleavage reaction from 1,3-diynes. Under the optimized conditions, the cleavage reaction of 1,4-diphenylbuta-1,3-diyne and hexadeca-7,9-diyne provided the desired products **2a**, and **3e** in 83 and 77% yields, respectively (Scheme 1).

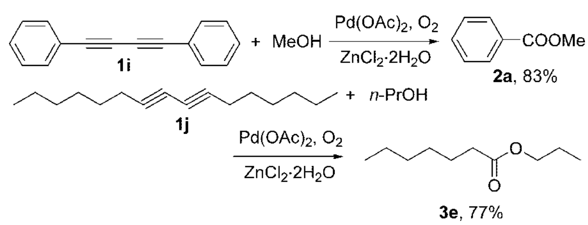
Table 1. Optimization of Reaction Conditions for the Palladium-Catalyzed Triple Bond Cleavage Reaction[a]



entry	O_2 (atm)	catalyst	Lewis acid	temp (°C)	yield[b] (%)
1[c]		$Pd(OAc)_2$		100	0
2	7.5	$Pd(OAc)_2$		100	3
3	**7.5**	**$Pd(OAc)_2$**	**$ZnCl_2 \cdot 2H_2O$**	**100**	**90(88)**
4	7.5	$Pd(OAc)_2$	$CuCl_2 \cdot 2H_2O$	100	43
5	7.5	$Pd(OAc)_2$	$FeCl_3 \cdot 6H_2O$	100	72
6	7.5	$Pd(OAc)_2$	$MnCl_2 \cdot 4H_2O$	100	77
7	7.5	$Pd(OAc)_2$	$AlCl_3 \cdot 6H_2O$	100	73
8	7.5		$ZnCl_2 \cdot 2H_2O$	100	0
9	7.5	$Pd(OAc)_2$	$ZnCl_2 \cdot 2H_2O$	60	43
10	7.5	$PdCl_2$	$ZnCl_2 \cdot 2H_2O$	100	80
11	7.5	$Pd_2(dba)_3$	$ZnCl_2 \cdot 2H_2O$	100	83
12[d]	7.5	$Pd(OAc)_2$	$ZnCl_2 \cdot 2H_2O$	100	77
13	7.5	$Pd(OAc)_2$	$ZnCl_2$	100	89

[a] Reaction conditions: All reactions were performed with 1,2-diphenylethyne (1 mmol), palladium catalyst (2 mol %) and Lewis acid (20 mol %) in 2 mL of MeOH for 24 h. [b] Determined by GC. Number in parentheses is isolated yield. [c] Under N_2 atmosphere. [d] With 10 mol % of $ZnCl_2 \cdot 2H_2O$.

Scheme 1. Cleavage Reaction of 1,3-Diynesx



Although we are unable to determine the detailed pathway of the oxidative cleavage at present, on the basis of 1-methoxy-1,2-diphenylethene **A** detected from GC−MS, we do propose **A** as the key intermediate which undergoes the carbon−carbon cleavage

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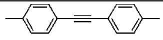
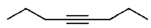
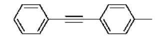
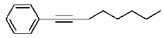
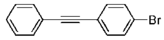
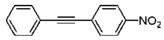
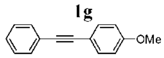
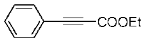
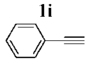
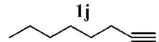
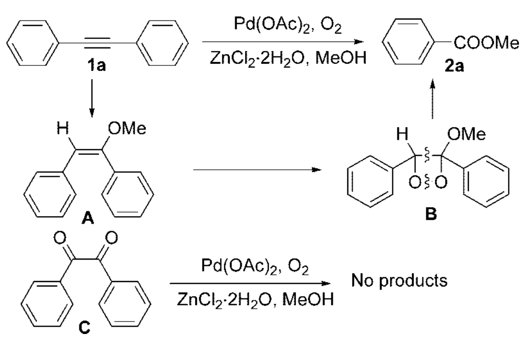
Table 2. Palladium-Catalyzed Triple Bond Cleavage Reaction[a]

$$\underset{\mathbf{1}}{R^1\!-\!\equiv\!-\!R^2} + R^3OH \xrightarrow[ZnCl_2\cdot 2H_2O]{Pd(OAc)_2,\ O_2} \underset{\mathbf{2}}{R^1\text{-}COOR^3} + \underset{\mathbf{3}}{R^2\text{-}COOR^3}$$

Entry	Alkyne	R^3OH	Product(s)	Yield[b] / % 2	3
1	 **1b**	MeOH	**2b**	89	-
2	**1a**	EtOH	**2c**	86	-
3	**1a**	*n*-PrOH	**2d**	79	-
4	 **1c**	MeOH	**2e**	18[c]	-
5	 **1d**	MeOH	**2a**, **2b**	89	89
6	 **1e**	*n*-PrOH	**2d, 3e**	87	87
7	 **1f**	MeOH	**2a,3f**	86	86
8	 **1g**	MeOH	**2a, 3g**	88	88
9	 **1h**	MeOH	**2a, 3h**	85	85
10	 **1i**	MeOH	**2a**	90	-
11	 **1j**	MeOH	**2a**	86	-
12	 **1k**	*n*-PrOH	**3e**	73	-

[a] Reaction conditions: alkyne (1 mmol), $Pd(OAc)_2$ (2 mol %), $ZnCl_2\cdot 2H_2O$ (20 mol %), pressure of O_2 (7.5 atm), alcohol (2 mL), 100 °C, 24 h. [b] Isolated yields. [c] Determined by GC.

Scheme 2. Plausible Reaction Mechanism



involved by oxygen molecule.[13] Furthermore, we rule out diphenyl diketone **C** as a possible intermediate in this reaction, not only because diphenyl diketone was not detected via GC−MS, but also it did not yield any products in $Pd(OAc)_2$-$ZnCl_2\cdot 2H_2O$-O_2 catalytic system and is recovered quantitatively.[14] A plausible mechanism for this cleavage is shown in Scheme 2. In the first step, **1a** is hydroalkoxylated catalyzed by $Pd(OAc)_2$ to form the intermediate **A**,[15] which is subsequently attacked by palladium activated molecular oxygen to generate a cyclic peroxide intermediate **B**. Fragmentation of **B** produces methyl benzoate and benzaldehyde, and benzaldehyde could undergo further oxidation and esterification to yield benzoate.

In summary, we have demonstrated that the palladium-catalyzed cleavage of C−C triple bonds proceeds efficiently using oxygen as a sole oxidant in various alcohols, affording carboxylic esters in good yields. Further investigation of the reaction scope, mechanism, and its applications in organic synthesis is ongoing in our laboratory and will be reported in due course.

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Supporting Information Available: Experimental procedures for **1a**−**k**, **A**, and characterization of compound **2a**−**e**, **3e**−**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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