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Ligand-Free Ag(I)-Catalyzed Carboxylation of Terminal Alkynes with CO_2

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ABSTRACT

A convenient approach to selectively prepare a wide range of functionalized propiolic acids was developed by AgI-catalyzed carboxylation of terminal alkynes using carbon dioxide as carboxylative agent under ligand-free conditions.

The development of efficient catalytic processes for CO_2 transformation into useful fine chemicals is of great interest and has been a long-standing goal for chemists, since CO_2 is an abundant, inexpensive, and renewable C1 feedstock.[1] One of the most promising reactions in this field is the direct carboxylation of organic compounds with CO_2 to afford carboxylic acids and derivatives. Although the direct carboxylation of highly reactive organolithium and Grignard reagents with CO_2 can be easily carried out, it is impossible to synthesize functionalized carboxylic acids. On the contrary, transition-metal-catalyzed carboxylation of less reactive carbon[2−4] and other nucleophiles[5]

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(4) For carboxylation of organozinc reagents with CO_2, see: (a) Yeung, C. S.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 7826. (b) Ochiai, H.; Jang, M.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 2681. (c) Kobayashi, K.; Kondo, Y. *Org. Lett.* **2009**, *11*, 2035.

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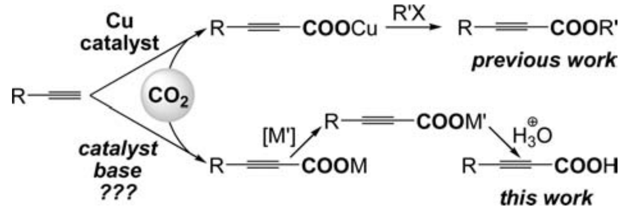
10.1021/ol200638z

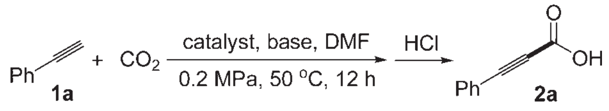
with CO_2, which shows highly catalytic efficiency, broad substrate scope, and good applicability, offers an attractive access to various functionalized carboxylic acids and derivatives.[6] Recently, a more economical method was reported with regard to copper- or gold-catalyzed direct carboxylation of relatively active C–H bonds with CO_2.[7] However, because of the inherently thermodynamical and kinetical stability of CO_2, the above-mentioned catalytic reactions usually encounter the use of high-energy organometallic reagents or rather rigorous reaction conditions. Furthermore, those transition-metal-catalyzed carboxylation reactions inevitably use expensive or complex ligands to guarantee selectivity and catalytic efficiency. Therefore, the development of a simple and efficient catalytic system for the direct carboxylation reaction using CO_2 under mild condition is highly desirable.

Scheme 1. Carboxylative Coupling and Direct Carboxylation of Teminal Alkynes Using CO_2



Recently, we developed a highly selective copper-catalyzed carboxylative coupling reaction of terminal alkynes, allylic chlorides, and CO_2,[8] wherein CO_2 could rapidly insert into a sp-hybridized carbon–copper bond and formed copper(I) carboxylate intermediate then reacted with allylic chloride compounds to afford allylic 2-alkynoates. We envisioned that with judicious choice of catalyst and base, various functionalized propiolic acids[9] could be conveniently prepared by the direct carboxylation of terminal alkynes with CO_2 via the acidification of the formed metal propiolate (Scheme 1). This straightforward strategy has obvious advantages over traditional accesses to propiolic acids such as carboxylation of air- and moisture-sensitive alkynylmagnesium or -lithium reagents, oxidation of propargylic alcohols or aldehydes, and hydrolysis of corresponding derivatives.[10] More recently, Goossen and Zhang reported nitrogen or N-heterocyclic carbene ligand-assisted copper-catalyzed direct carboxylation of terminal alkynes with CO_2.[11] Herein, we report a convenient ligand-free silver-catalyzed direct carboxylation of terminal alkynes using CO_2 as carboxylative agent affording a variety of functionalized propiolic acids.

Table 1. Carboxylation of Phenylacetylene with CO_2[a]



entry	catalyst (mol %)	base	yield[b] (%)
1[c,d]	(IPr)CuCl (10)	K_2CO_3	39
2[c,d]	CuCl (20)	K_2CO_3	35
3[c,d]	CuI (20)	K_2CO_3	46
4[c]	CuI (20)	Cs_2CO_3	60
5	CuI (1)	Cs_2CO_3	75
6[c]	AgI (20)	Cs_2CO_3	83
7	AgI (1)	Cs_2CO_3	94
8[c]	AgI (0.1)	Cs_2CO_3	68
9[e]	AgI (1)	Cs_2CO_3	79
10		Cs_2CO_3	6
11	AgF (1)	Cs_2CO_3	53
12	AgCl (1)	Cs_2CO_3	74
13	AgBr (1)	Cs_2CO_3	82
14	AgOAc (1)	Cs_2CO_3	90
15	$AgNO_3$ (1)	Cs_2CO_3	92
16	Ag_2CO_3 (1)	Cs_2CO_3	86
17	$AgBF_4$ (1)	Cs_2CO_3	82
18	$AgSbF_6$ (1)	Cs_2CO_3	89
19	$AgPF_6$ (1)	Cs_2CO_3	95
20	AgI (1)	KO^tBu	59
21[f]	AgI (1)	Cs_2CO_3	
22[g]	AgI (1)	Cs_2CO_3	92
23[h]	AgI (1)	Cs_2CO_3	79

[a] Reaction conditions: **1a** (2 mmol), base (3 mmol), 20 mL of DMF. [b] Isolated yield. [c] 1.5 MPa, 24 h. [d] 60 °C. [e] CO_2 was bubbled into the reaction system. [f] In the absence of CO_2. [g] In the presence of 1 mol % of PPh_3. [h] In the presence of 1 mol % of PCy_3.

Initial investigations of direct carboxylation of phenylacetylene (**1a**) with CO_2 were carried out to screen the optimized reaction conditions (Table 1). The catalytic system used in the previous carboxylative coupling reaction (10 mol % of (IPr)CuCl as catalyst and K_2CO_3 as base) gave a poor but encouraging yield of 39% for phenylpropiolic acid (**2a**) formation (entry 1). Surprisingly, a slightly improved yield was obtained when 20 mol % of CuI was used as catalyst (entry 3). Hu disclosed that Cs_2CO_3 was a superior base for the direct

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(7) (a) Boogaerts, I. I. F.; Nolan, S. P. *J. Am. Chem. Soc.* **2010**, *132*, 8858. (b) Boogaerts, I. I. F.; Fortman, G. C.; Furst, M. R. L.; Cazin, C. S. J.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2010**, *49*, 8674. (c) Zhang, L.; Cheng, J.; Ohishi, T.; Hou, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 8670. (d) Boogaerts, I. I. F.; Nolan, S. P. *Chem. Commun.* **2011**, *47*, 3021. (e) Mizuno, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 1251.

(8) Zhang, W.-Z.; Li, W.-J.; Zhang, X.; Zhou, H.; Lu, X.-B. *Org. Lett.* **2010**, *12*, 4748.

(9) (a) Donets, P.; Van der Eycken, E. V. *Org. Lett.* **2007**, *9*, 3017. (b) Liu, C.-R.; Yang, F.-L.; Jin, Y.-Z.; Ma, X.-T.; Cheng, D.-J.; Li, N.; Tian, S.-K. *Org. Lett.* **2010**, *12*, 3832. (c) Bararjanian, M.; Balalaie, S.; Rominger, F.; Movassagh, B.; Bijanzadeh, H. R. *J. Org. Chem.* **2010**, *75*, 2806. (d) Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, *10*, 945. (e) Jia, W.; Jiao, N. *Org. Lett.* **2010**, *12*, 2000. (f) Feng, C.; Loh, T.-P. *Chem. Commun.* **2010**, *46*, 4779. (g) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee., S. *J. Org. Chem.* **2010**, *75*, 6244. (h) Ranjit, S.; Duan, Z.; Zhang, P.; Liu, X. *Org. Lett.* **2010**, *12*, 4134.

(10) (a) Lyons, T. W.; Sanford, M. S. *Tetrahedron* **2009**, *65*, 3211. (b) Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **1999**, *64*, 2564. (c) Lee, A. S.-Y.; Hu, Y.-J.; Chu, S.-F. *Tetrahedron* **2001**, *57*, 2121. (d) Koster, F.; Dinjus, E.; Dunach, E. *Eur. J. Org. Chem.* **2001**, 2507.

(11) During preparation of this manuscript, similar ligand-assisted Cu(I)-catalyzed reactions were reported: (a) Goosen, L. J.; Rodriguez, N.; Manjolinho, F.; Lange, P. P. *Adv. Synth. Catal.* **2010**, *352*, 2912. (b) Yu, D.; Zhang, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20184.

carboxylation of aromatic heterocycles with CO_2.[6f] Base also plays an important role in the catalyst systems. When the base was changed into Cs_2CO_3, moderate yield was achieved at the decreased temperature (entry 4). It is well-known that besides copper(I) catalyst, silver(I) salt and complexes were also established as powerful catalysts for alkynylation reaction.[12,13] It was found that 20 mol % of AgI as catalyst without any ligand together with Cs_2CO_3 gave 83% yield of **2a** (entry 6). To our surprise, an excellent yield (94%) of **2a** was obtained using 1 mol % loading of AgI (entry 7). The increased catalyst loading resulting in the lower yield of product might be tentatively ascribed to the decarboxylative activity of Cu(I) or Ag(I) salt (entries 4 and 6).[14,15] Notably, the catalyst system proved to be efficient even in a very low catalyst loading of 0.1 mol % (entry 8) and/or at a low CO_2 pressure of bubbling CO_2 into the reaction system (entry 9). It is noteworthy that the reaction with 1.5 equiv Cs_2CO_3 without any transition-metal catalyst afforded only 6% yield of product (entry 10). These clearly certified the catalytic role of copper(I) and silver(I) salt.

The catalytic activities of various simple silver(I) salts were also tested at the same conditions. These silver(I) salts all exhibited moderate to high activity (entries 11−19). Among them, $AgPF_6$ is more efficient in catalyzing this reaction (entry 19). In view of the complicated manipulation of hygroscopic $AgPF_6$, we chose AgI as catalyst in subsequent investigations.

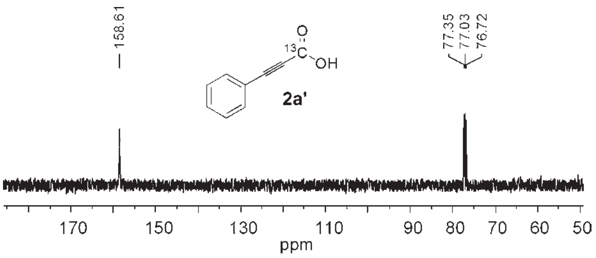


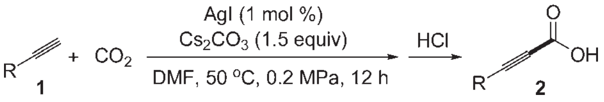
Figure 1. ^{13}C NMR spectrum of $^{13}C_{carbonyl}$-labeled phenylpropiolic acid (**2a′**).

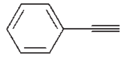
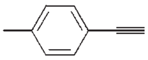
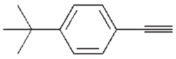
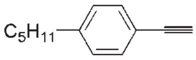
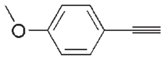
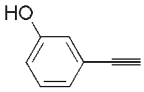
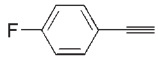
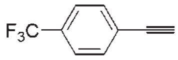
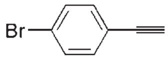
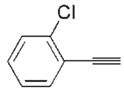
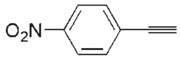
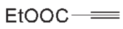
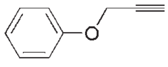
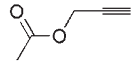
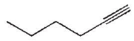
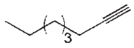
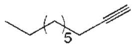
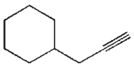
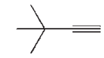
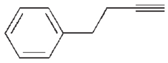
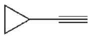
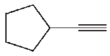
When KO^{t}Bu was used as base, the carboxylation reaction afforded 59% yield of **2a** (entry 20). It is worthwhile noting here that no carboxylation product was observed when the reaction proceeded in the absence of CO_2 (entry 21). When phenylacetylene reacted with ^{13}C-labeled CO_2, $^{13}C_{carbonyl}$-labeled phenylpropiolic acid (**2a′**) was obtained in excellent yield (Figure 1 and Supporting Information). These results demonstrated that the CO_2 unit in carboxylation product came from free CO_2, rather than carbonate salts.

Interestingly, the addition of a ligand has a negative effect on catalyst activity (entries 22 and 23). For example, the presence of 1 mol % of PCy_3 resulted in an obvious decrease of the yield from 94% to 79% (entry 23).

The scope with respect to terminal alkyne substrates was then explored under the optimized reaction conditions: 1 mol % of AgI, 1.5 equiv of Cs_2CO_3, 0.2 MPa CO_2, DMF, 50 °C. As shown in Table 2, various aryl- and alkyl-substituted terminal alkynes smoothly underwent the carboxylation reaction and were converted into the corresponding propiolic acids in moderate to excellent yield.

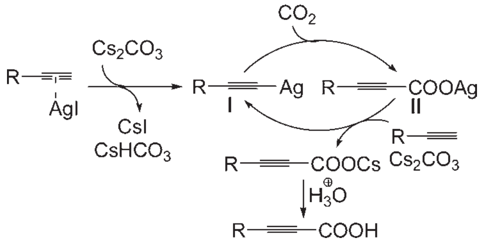
Table 2. Ag(I)-Catalyzed Carboxylation of Terminal Alkynes with CO_2[a]



entry	alkyne		yield (%)[b]
1		**1a**	94 (**2a**)
2		**1b**	85 (**2b**)
3		**1c**	87 (**2c**)
4[c]		**1d**	91 (**2d**)
5		**1e**	88 (**2e**)
6		**1f**	64 (**2f**)
7		**1g**	81 (**2g**)
8[c]		**1h**	83 (**2h**)
9[c]		**1i**	78 (**2i**)
10[c]		**1j**	76 (**2j**)
11[c]		**1k**	74 (**2k**)
12[c]		**1l**	70 (**2l**)
13		**1m**	81 (**2m**)
14		**1n**	44 (**2n**)
15		**1o**	65 (**2o**)
16		**1p**	81 (**2p**)
17		**1q**	88 (**2q**)
18		**1r**	74 (**2r**)
19[c]		**1s**	55 (**2s**)
20[c]		**1t**	90 (**2t**)
21[c]		**1u**	74 (**2u**)
22[c]		**1v**	96 (**2v**)

[a] Reaction conditions: **1** (2 mmol), 20 mL of DMF. [b] Isolated yield. [c] 24 h.

Scheme 2. Possible Reaction Mechanism



Both electron-donating and electron-withdrawing group substituted phenylacetylenes were successfully carboxylated with CO_2 (entries 1–11). The reactions were compatible with aryl-OMe, OH, F, CF_3, Br, Cl, and NO_2 groups.

Ethyl propiolate bearing an ester group was also found to be a suitable substrate (entry 12). A variety of alkyl-substituted terminal alkynes could be carboxylated, and phenyl ether, cyclopropane, and cyclopentane groups were tolerable (entries 13–22). Thus, this ligand-free Ag(I)-catalyzed direct carboxylative approach showed wide generality for the synthesis of various functionalized propiolic acids.

To probe the mechanistic aspects, silver phenylacetylide and silver phenylpropiolate were prepared and directly used as catalyst (1 mol % loading) for the carboxylation of phenylacetylene, and 80% and 86% yields of phenylpropiolic acid were obtained, respectively. On the basis of the above experimental results, a possible catalytic cycle for the Ag(I)-catalyzed direct carboxylation of terminal alkynes with CO_2 is proposed as shown in Scheme 2. First, terminal alkyne coordinates to the silver(I) salt and the acidity of the alkyne C–H bond is enhanced. Then the deprotonation reaction of terminal alkyne by Cs_2CO_3 eventually affords silver(I) acetylide **I**, which is generally proposed as key intermediate in the silver(I)-catalyzed alkynylation reaction[12] and silver-cocatalyzed Sonogashira reaction.[16] The insertion of CO_2 into sp-hybridized carbon–silver bond forms silver propiolate intermediate **II**, which subsequently reacts with another terminal alkyne and Cs_2CO_3 releasing cesium propiolate, meanwhile regenerating silver(I) acetylide **I**. The acidification of cesium propiolate after reaction affords propiolic acid product.

In summary, we have developed a ligand-free Ag(I)-catalyzed direct carboxylation of terminal alkynes with CO_2, which represents a convenient method to straightforwardly synthesize functionalized propiolic acids in good yield. Further exploration of these in situ generated silver propiolate as nucleophiles for building new organic compounds is in progress in our laboratory.

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Supporting Information Available. Experimental procedure and characterization of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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