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## Cobalt-catalyzed carboxylation of propargyl acetates with carbon dioxide

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The cobalt-catalyzed carboxylation of propargyl acetates with CO<sub>2</sub> (1 atm) is described. The reaction proceeds at room temperature with Mn powder as a reducing reagent. Various propargyl acetates are converted to the corresponding carboxylic acids in good to high yields.

Carbon dioxide (CO<sub>2</sub>) is an environmentally friendly raw material and its utilization as a sustainable carbon source is one of the most important challenges in homogeneous transition-metal catalysis.<sup>1</sup> In particular, C–C bond forming reactions using CO<sub>2</sub> are the most promising.<sup>1a</sup> Reactions using highly reactive Grignard and organolithium reagents with CO<sub>2</sub> are fundamental for the C–C bond formation, but chemoselectivity with these reagents is very poor. In contrast, less reactive arylboronic esters<sup>2a–c</sup> and arylzinc compounds<sup>2d,e</sup> were found to react with CO<sub>2</sub> with good chemoselectivity in the presence of a transition-metal catalyst. However, all these organometallic compounds are mainly synthesized from the corresponding aryl halides. Thus, the direct carboxylation of aryl halides is more straightforward and efficient. We recently reported the nickel-catalyzed direct carboxylation of aryl and vinyl chlorides with CO<sub>2</sub> (1 atm) at room temperature,<sup>3a,b</sup> while carboxylations of more reactive aryl bromides<sup>3c</sup> and benzyl chlorides<sup>3d</sup> as well as inert C–O bonds<sup>3e</sup> were also reported.<sup>4</sup>

Reactions of allylic and propargylic compounds with CO<sub>2</sub> afford a variety of unsaturated carboxylic acids. To date, these transformations consume a stoichiometric amount of the corresponding Grignard, organolithium, or other metal reagents.<sup>5</sup> These reactions also have problems in regioselectivity and chemoselectivity.

Therefore, the development of a new selective methodology is highly desirable. Allyl and propargyl esters (typically, acetates or carbonates) are well known as efficient *electrophiles* in transition-metal-catalyzed C–C bond forming reactions.<sup>6</sup> In order to utilize these electrophiles with CO<sub>2</sub>, umpolung<sup>7</sup> reactivity of these esters is crucial. Actually, the reactions of *allyl* esters with CO<sub>2</sub> were carried out under electrochemical conditions in the presence of Pd or Ni catalysts;<sup>8</sup> however, the yields and regioselectivities were low. Furthermore, there is no precedent for the carboxylation of *propargyl* esters with CO<sub>2</sub>.<sup>9</sup> Herein, we report the Co-catalyzed carboxylation of propargyl acetates with CO<sub>2</sub> utilizing Mn powder as a reducing agent. Various propargyl acetates were converted to the corresponding carboxylic acids under 1 atm CO<sub>2</sub> at room temperature.

Table 1 Reaction optimization<sup>a</sup>

Entry	Catalyst System: Change from the Standard Conditions	Yield of <b>2a-Me</b> (%) <sup>b</sup>
1	none	83 (82) <sup>c</sup>
2	Without Co <sub>2</sub> (phen)	0
3	Co <sub>2</sub> in place of Co <sub>2</sub> (phen)	0
4	Without Mn powder	0
5	Mn Powder (0.60 mmol, 1.2 equiv)	74
6	CoBr <sub>2</sub> (phen) in place of Co <sub>2</sub> (phen)	80
7	Co <sub>2</sub> (bpy) in place of Co <sub>2</sub> (phen)	76
8	Co <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> in place of Co <sub>2</sub> (phen)	23
9	Co <sub>2</sub> (dppe) in place of Co <sub>2</sub> (phen)	0
10	Zn in place of Mn	41
11	Mg in place of Mn	57
12 <sup>d</sup>	NiCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> in place of Co <sub>2</sub> (phen)	7

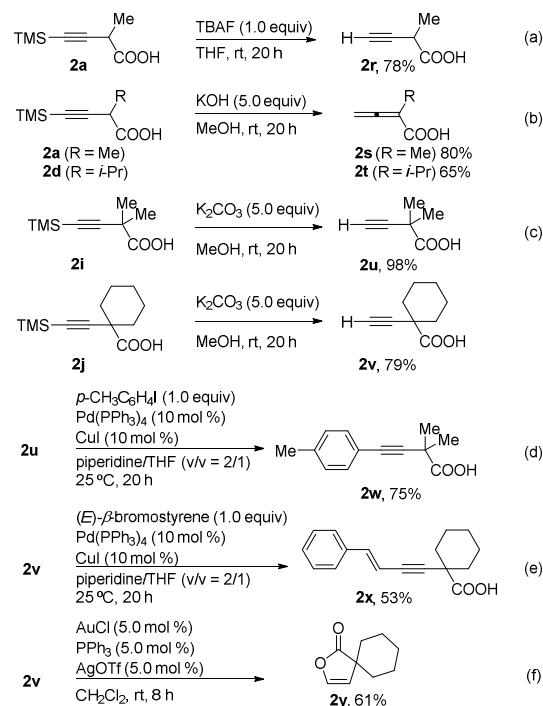
<sup>a</sup> Reaction conditions; **1a** (0.50 mmol), Co<sub>2</sub>(phen) (0.025 mmol, 5.0 mol %), Mn powder (1.5 mmol, 3.0 equiv), CO<sub>2</sub> (1 atm), in DMA (0.50 mL), at room temperature for 20 h. <sup>b</sup> Determined by GC analysis. <sup>c</sup> Isolated yield of **2a**. <sup>d</sup> With Et<sub>3</sub>Ni (0.05 mmol, 10 mol %).

The carboxylation of propargyl acetate **1a** was carried out under CO<sub>2</sub> (1 atm) at room temperature in the presence of Co<sub>2</sub>(phen)<sup>10</sup> (phen = 1,10-phenanthroline) and Mn powder (3.0 equiv) in DMA (*N,N*-dimethylacetamide) (Table 1). The yield of the corresponding carboxylic acid (**2a**) was determined by gas chromatographic (GC) analysis after derivatization to the corresponding methyl ester (**2a-Me**). Under the standard conditions, **2a-Me** was obtained in 83% yield (entry 1). Compound **2a** was isolated from the reaction mixture in 82% yield. Without Co<sub>2</sub>(phen), **2a-Me** was not obtained (entry 2). In the absence of phen (i.e., Co<sub>2</sub> as the catalyst), **1a** was not converted (entry 3). Without the addition of Mn powder, the carboxylation did not proceed at all (entry 4). When the amount of Mn powder was reduced to 1.2 equiv, the yield of **2a-Me** was decreased to 74% (entry 5). CoBr<sub>2</sub>(phen) was also a good catalyst and afforded **2a-Me** in 80% yield (entry 6). Employing Co<sub>2</sub>(bpy) (bpy = 2,2'-bipyridine) as a catalyst, **2a-Me** was obtained in 76% yield (entry 7). Thus, phen and bpy show comparable efficiency as the ligand. In contrast, Co<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> and Co<sub>2</sub>(dppe) (dppe = 1,2-diphenylphosphinoethane) suppressed the carboxylation considerably (entries 8 and 9). Other reducing agents such as Zn

**Table 2** Cobalt-catalyzed carboxylation of various propargyl acetates<sup>a</sup>

Entry	Substrate <b>1</b>	Product <b>2</b>	Yield (%) <sup>b</sup>
1			80
2			75
3			79
4			65
5			85
6			73
7			87
8 <sup>c</sup>			71
9 <sup>c</sup>			80
10 <sup>f</sup>			80
11 <sup>c</sup>			46
12			40
13			88
14			55
15			57
16			26

<sup>a</sup> Reaction conditions; propargyl acetate (**1**, 0.50 mmol), CoI<sub>2</sub>(phen) (0.025 mmol, 5.0 mol %), Mn powder (1.5 mmol, 3.0 equiv), CO<sub>2</sub> (1 atm), in DMA (0.50 mL), at room temperature for 20 h. <sup>b</sup> Isolated yield. <sup>c</sup> CoI<sub>2</sub>(bpy) (0.025 mmol, 5.0 mol %) was used as a catalyst. powder and Mg turnings gave **2a-Me** in only moderate yields

**Scheme 1** Derivatization of carboxylated products.

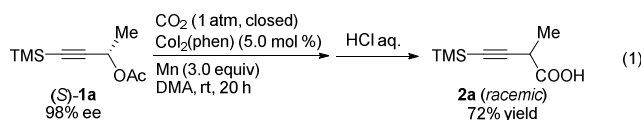
(entries 10 and 11). NiCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, which was an efficient catalyst for the carboxylation of aryl chloride,<sup>3a</sup> did not show good catalytic activity (entry 12). Other nickel catalysts such as NiBr<sub>2</sub>(bpy) and NiI<sub>2</sub>(phen) were not efficient. With regard to the choice of solvent, 1,3-dimethyl-2-imidazolidinone (DMI) and DMF were also suitable, while reactions in THF and toluene afforded **2a-Me** in 26% and 0% yields, respectively (Table S1).<sup>11</sup>

The carboxylation of various propargyl acetates was carried out in the presence of CoI<sub>2</sub>(phen) or CoI<sub>2</sub>(bpy) as a catalyst (Table 2). The carboxylation reaction of acetates of secondary alcohols (**1b-h**) bearing TMS in the R<sup>1</sup> position proceeded smoothly and afforded the corresponding carboxylic acids (**2b-h**) in high isolated yields (entries 1–7). It is noteworthy that ester (**1e**), chloro (**1f**), terminal alkene (**1g**), and furan (**1h**) functionalities were compatible in the reaction (entries 4–7). When the carboxylation of acetates derived from tertiary alcohols was examined with CoI<sub>2</sub>(phen), conversion of starting material remained low. In that case, CoI<sub>2</sub>(bpy) was found to be a good catalyst and provided the carboxylated products (**2i-l**) in good to high yields (entries 8–11). Amide functionality (**1l**) was also tolerated in the reaction (entry 11). The acetate of primary propargylic alcohol (**1m**) also provided the corresponding carboxylic acid (**2m**) in moderate yield (entry 12). A substituent on the alkyne carbon of **1** (R<sup>1</sup>, Table 2) affects the carboxylation considerably. As the substituent R<sup>1</sup> became less bulky, the yields of the carboxylated products (**2**) decreased; **1n** (R<sup>1</sup> = TBS, TBS = *tert*-butyldimethylsilyl), **1o** (R<sup>1</sup> = CMe<sub>2</sub>(OTBS)), **1p** (R<sup>1</sup> = *t*-Bu), and **1q** (R<sup>1</sup> = Cy) afforded the corresponding products (**2n-q**) in 88%, 55%, 57%, and 26% yields, respectively (entries 13–16). Propargyl acetate having phenyl ring (**1**: R<sup>1</sup> = Ph, R<sup>2</sup> = Me, R<sup>3</sup> = H) afforded the product in 9% yield. Substrate bearing terminal alkyne moiety (**1**: R<sup>1</sup> = H, R<sup>2</sup> = Me, R<sup>3</sup> = H) did not provide the carboxylated product.<sup>12</sup>

The TMS group of the products in Table 2 could easily be removed via protodesilylation<sup>13</sup> in the presence of a suitable base. In the case of  $\alpha,\alpha$ -disubstituted carboxylic acids such as **2a**, reaction with tetrabutylammonium fluoride (TBAF, 1.0 M in THF) provided the corresponding carboxylic acid **2r** in 78% yield (Scheme 1a). In

contrast, when **2a** or **2d** were treated with KOH (crushed), carboxylic acids bearing an allenyl moiety (**2s**, **2t**) were selectively obtained in 80% and 65% yields, respectively (Scheme 1b). A similar reaction of **2a** with  $K_2CO_3$  resulted in the formation of a mixture of **2r** and **2s** ( $2r/2s = 1/3$ ). On the other hand,  $\alpha,\alpha,\alpha$ -trisubstituted carboxylic acids such as **2i** and **2j** reacted with  $K_2CO_3$  to give **2u** and **2v** in 98% and 79% yields (Scheme 1c). Aryl and alkenyl carbons were introduced onto the terminal alkyne moiety of **2u** and **2v** by the Sonogashira coupling reaction<sup>14a</sup> (**2w** and **2x**, Scheme 1d and 1e). Moreover, Au-catalyzed intra-molecular cyclization<sup>14b</sup> of **2v** provided unsaturated  $\gamma$ -lactone **2y** smoothly (Scheme 1f). Thus these TMS moieties are very useful for the further derivatization.

When an optically pure (*S*)-**1a** was employed as the substrate in the present carboxylation, a racemic **2a** was obtained in 72% yield (eqn (1)).



A plausible reaction mechanism is shown in Scheme 2. Initially, the reduction of a Co(II) complex with manganese affords a Co(I) catalyst species (**A**). Then, oxidative addition of a propargyl acetate (**1**) takes place via C–O bond cleavage, giving a Co(III) intermediate (**B**) (step a). Subsequent reduction of propargyl Co(III) with manganese gives propargyl cobalt(II) species (**C**) (step b).<sup>3a,b,15</sup> Then, the more nucleophilic<sup>3b</sup> Co(II) species (**C**) reacts with  $CO_2$  to give the carboxylatocobalt intermediate (**D**) (step c). Finally, the reduction of **D** with manganese affords the corresponding manganese carboxylate and the Co(I) catalytic species (**A**) regenerates (step d). Further studies about the reaction mechanism are now in progress.

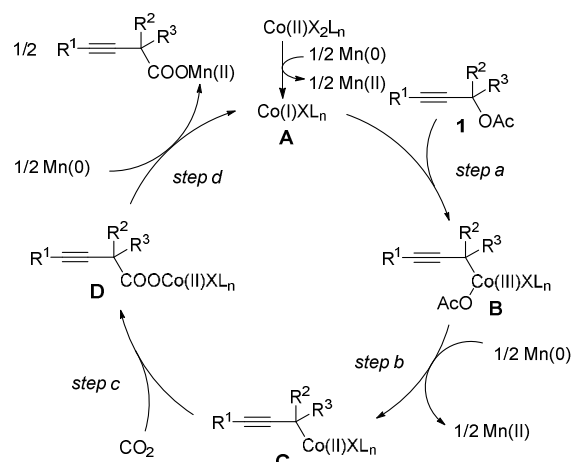
We thank Professors Michinori Sugimoto and Toshimichi Ohmura (Kyoto University) for measuring optical rotations. This work was supported by Grant-in-Aid for Scientific Research on Innovative Areas (“Organic synthesis based on reaction integration” and “Molecular activation directed toward straightforward synthesis”) from MEXT, Japan. K. N. is grateful to a Research Fellowship of JSPS for Young Scientists.

## Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data for all new compounds. See DOI: 10.1039/c000000x/

- For reviews, see: (a) Y. Tsuji and T. Fujihara, *Chem. Commun.*, 2012, **48**, 9956–9964; (b) L. Zhang and Z. Hou, *Chem. Sci.*, 2013, **4**, 3395–3403; (c) K. Huang, C.-L. Sun and Z.-J. Shi, *Chem. Soc. Rev.*, 2011, **40**, 2435–2452; (d) M. Cokoja, C. Bruckmeier, B. Rieger, W. A. Herrmann and F. E. Kühn, *Angew. Chem., Int. Ed.*, 2011, **50**, 8510–8537; (e) S. N. Riduan and Y. Zhang, *Dalton Trans.*, 2010, **39**, 3347–3357.
- (a) K. Ukai, M. Aoki, J. Takaya and N. Iwasawa, *J. Am. Chem. Soc.*, 2006, **128**, 8706–8707; (b) T. Ohishi, M. Nishiura and Z. Hou, *Angew. Chem., Int. Ed.*, 2008, **47**, 5792–5795; (c) J. Takaya, S. Tadami, K. Ukai and N. Iwasawa, *Org. Lett.*, 2008, **10**, 2697–2700; (d) C. S. Yeung and V. M. Dong, *J. Am. Chem. Soc.*, 2008, **130**, 7826–7827; (e) Hd. Ochiai, M. Jang, K. Hirano, H. Yorimitsu and K. Oshima, *Org. Lett.*, 2008, **10**, 2681–2683.



Scheme 2 Plausible catalyst cycle.

- (a) T. Fujihara, K. Nogi, T. Xu, J. Terao, and Y. Tsuji, *J. Am. Chem. Soc.*, 2012, **134**, 9106–9109; (b) F. B. Sayyed, Y. Tsuji and S. Sakaki, *Chem. Commun.*, 2013, **49**, 10715–10717; (c) A. Correa and R. Martin, *J. Am. Chem. Soc.*, 2009, **131**, 15974–15975; (d) T. León, A. Correa and R. Martin, *J. Am. Chem. Soc.*, 2013, **135**, 1221–1224; (e) A. Correa, T. León and R. Martin, *J. Am. Chem. Soc.*, 2014, **136**, 1062–1069.
- For another important C–C bond forming reaction employing  $CO_2$ , i.e., hydro- or heterocarboxylations, see: (a) T. Fujihara, T. Xu, K. Semba, J. Terao and Y. Tsuji, *Angew. Chem., Int. Ed.*, 2011, **50**, 523–527; (b) T. Fujihara, Y. Tani, K. Semba, J. Terao and Y. Tsuji, *Angew. Chem., Int. Ed.*, 2012, **51**, 11487–11490; (c) L. Zhang, J. Cheng, B. Carry and Z. Hou, *J. Am. Chem. Soc.*, 2012, **134**, 14314–14317; (d) S. Li, W. Yuan and S. Ma, *Angew. Chem., Int. Ed.*, 2011, **50**, 2578–2582; (e) C. M. Williams, J. B. Johnson and T. Rovis, *J. Am. Chem. Soc.*, 2008, **130**, 14936–14937; (f) J. Takaya and N. Iwasawa, *J. Am. Chem. Soc.*, 2008, **130**, 15254–15255; (g) J. Takaya, K. Sasano and N. Iwasawa, *Org. Lett.*, 2011, **13**, 1698–1701.
- (a) G. Courtois and L. Miginiac, *J. Organomet. Chem.*, 1974, **69**, 1–44; (b) G. R. Lappin, *J. Am. Chem. Soc.*, 1949, **71**, 3966–3968; (c) N. R. Pearson, G. Hahn and G. Zweifel, *J. Org. Chem.*, 1982, **47**, 3364–3366; (d) B. Miao and S. Ma, *Chem. Commun.*, 2014, **50**, 3285–3287.
- (a) J. Tsuji, *Palladium Reagents and Catalysts*; Wiley: Chichester, UK, 2004; (b) B. M. Trost, *Acc. Chem. Res.*, 1996, **29**, 355–364; (c) B. M. Trost, *Acc. Chem. Res.*, 1980, **13**, 385–393.
- D. Seebach, *Angew. Chem., Int. Ed.*, 1979, **18**, 239–258 and references cited therein.
- (a) S. Torii, H. Tanaka, T. Hamatani, K. Morisaki, A. Jutand, F. Pfluger and J.-F. Fauvarque, *Chem. Lett.*, 1986, 169–172; (b) M. J. Medeiros, C. Pintaric, S. Olivero and E. Dunach, *Electrochimica Acta*, 2011, **56**, 4384–4389.
- Recently, in the Ni-catalyzed carboxylation of benzylic chlorides with  $CO_2$ ,<sup>3d</sup>  $C_6H_5C\equiv CCH_2Cl$  was used as a substrate and afforded  $C_6H_5C\equiv CCH_2COOH$  in only 29% yield; other propargylic substrates were not examined in the reaction.
- $CoI_2(phen)$  was synthesized by a similar method for  $CoBr_2(phen)$ ; G. Hilt, W. Hess, T. Vogler and C. Hengst, *J. Organomet. Chem.*, 2005, **690**, 5170–5181.
- See the Electronic Supplementary Information (ESI) for details.
- In those cases including entries 14–16 in Table 2, most substrates were consumed and some oligomerizations occurred judging from GPC (gel permeation chromatography) analysis of the resulting reaction mixtures.
- (a) C. Cai and A. Vasella, *Helv. Chim. Acta*, 1995, **78**, 732–757; (b) L. T. Scott, M. J. Cooney and D. Johnels, *J. Am. Chem. Soc.*, 1990, **112**, 4054–4055.
- (a) K. Sonogashira, *J. Organomet. Chem.*, 2002, **653**, 46–49; (b) H. Shi, L. Fang, C. Tan, L. Shi, W. Zhang, C.-C. Li, T. Luo and Z. Yang, *J. Am. Chem. Soc.*, 2011, **133**, 14944–14947.
- X. Qian, A. Auffrant, A. Felouat and C. Gosmini, *Angew. Chem., Int. Ed.*, 2011, **50**, 10402–10405.