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Copper(I)-Catalyzed Carboxylation of Aryl- and Alkenylboronic Esters

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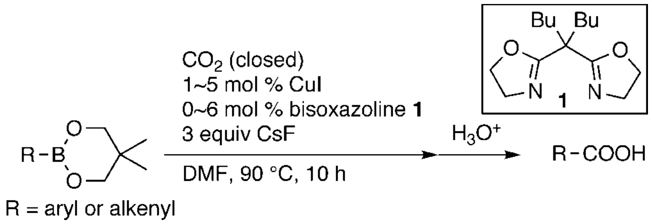
ABSTRACT



The copper(I)-catalyzed carboxylation reaction of aryl- and alkenylboronic esters proceeded smoothly under CO_2 to give the corresponding carboxylic acid in good yield. This reaction showed wide generality with higher functional group tolerance compared to the corresponding Rh(I)-catalyzed reaction.

Transition metal-catalyzed addition reaction of carbon−nucleophile toward CO_2 has attracted much attention not only from the standpoint of development of novel synthetic methodologies but also from that of utilization of CO_2 as an important one-carbon source.[1,2] As an approach toward this goal, we recently reported the Rh(I)-catalyzed carboxylation reaction of aryl- and alkenylboronic esters, which proceeds under mild reaction conditions and allows use of arylboronic esters containing a carbonyl or a cyano group without affecting these functionalities.[3] However, arylboronic esters containing a reactive functional group such as bromo gave a complex mixture of products, and those containing an alkynyl or a vinyl substituent did not give the desired products probably due to the coordination of these functional groups to the rhodium metal, suppressing its catalytic activity or leading to oligomerization. To expand the synthetic utility of this approach, we further examined various transition metal catalysts to promote the carboxylation reaction of aryl- and alkenylboronic esters containing such reactive functional groups. In this paper, we would like to report that copper(I) complexes also promote this type of carboxylation reaction efficiently with wider functional-group compatibility compared to the Rh(I)-catalyzed reaction.[4–6]

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(1) For reviews on transition metal-promoted CO_2-fixation reactions, see: (a) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.* **1988**, *88*, 747. (b) Gibson, D. H. *Chem. Rev.* **1996**, *96*, 2063. (c) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27. (d) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365.

(2) For recent examples of catalytic nucleophilic addition of carbonucleophiles containing a carbon−transition metal bond toward CO_2, see: (a) Shi, M.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 5057. (b) Franks, R. J.; Nicholas, K. M. *Organometallics* **2000**, *19*, 1458. (c) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008. (d) Takimoto, M.; Nakamura, Y.; Kimura, K.; Mori, M. *J. Am. Chem. Soc.* **2004**, *126*, 5956. (e) Takimoto, M.; Kawamura, M.; Mori, M.; Sato, Y. *Synlett* **2005**, 2019. (f) Johansson, R.; Wendt, O. F. *Dalton Trans.* **2007**, 488.

(3) Ukai, K.; Aoki, M.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2006**, *128*, 8706.

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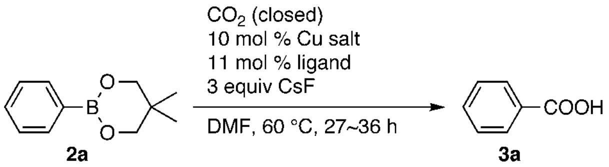
Table 1. Examination of Ligand

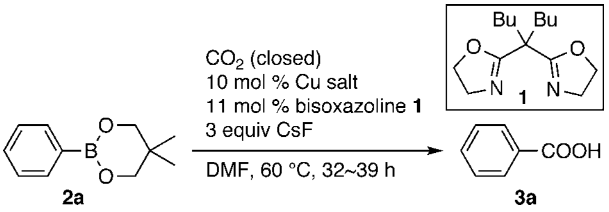


entry	ligand	yield (%)[a]
1	none	36
2	dppp	50
3	dppf	3
4	BINAP	13
5	bpy	49
6	TMEDA	52
7	pyridine	31
8	DMAP	46
9	DBU[b]	31
10	DABCO[b]	49
11	bisoxazoline **1**	74

[a] NMR yield. [b] 21 mol % of ligand was used.

We first examined the Cu(I)-catalyzed carboxylation reaction under several reaction conditions using the neopentyl glycolato ester of phenylboronic acid under CO_2. Examination of various reaction solvents with 10 mol % of CuI, 11 mol % of dppp, and 3 equiv of CsF at 60 °C in a closed system revealed that DMF is the solvent of choice.[7,8] Further examination of several copper complexes including their ligands is summarized in Tables 1 and 2. As shown here, not only dppp but also nitrogen ligands such as bpy, TMEDA, DABCO, etc. showed good catalytic activity, and bisoxazoline ligand **1** gave the best results among the ligands examined.[9] It should be noted that even under ligandless conditions the reaction proceeded to some extent. Several copper salts were also examined in the presence of the bisoxazoline ligand **1**, and CuCl, CuBr, and CuOAc also showed comparable catalytic activity, while Cu(II) complexes such as $CuCl_2$ and $Cu(OTf)_2$ did not promote the reaction at all.

Table 2. Examination of Copper Salts



entry	Cu salt	yield (%)[a]
1	CuI	74
2	CuCl	65
3	CuBr	54
4	CuOAc	68
5	$CuCl_2$	0
6	$Cu(OTf)_2$	0

[a] NMR yield.

The generality of this Cu(I)-catalyzed carboxylation reaction of arylboronic esters was examined by using 5 mol % of CuI, 6 mol % of bisoxazoline ligand **1**, and 3 equiv of CsF in DMF at 90 °C,[10] and the results are summarized in Table 3. In a similar manner to the Rh(I)-catalyzed reaction, arylboronic esters substituted with an electron-donating or -withdrawing group such as methoxy, acetyl, methoxycarbonyl, and cyano groups gave the corresponding benzoic acids in high yield without affecting these functionalities (entries 1−5). More importantly, this Cu(I)-catalyzed reaction allows the use of alkynyl- or vinyl-substituted arylboronic esters, which did not give the product at all in the Rh(I)-catalyzed reaction. Thus, *p*-phenylethynyl-, *p*-octynyl-, and *p*-vinylphenylboronic esters gave the corresponding benzoic acid derivatives in high yield by this protocol (entries 6−8). *p*-Nitrophenylboronic ester, which was another inappropriate substrate in the Rh(I)-catalyzed reaction, also gave the desired product by using this Cu(I)-catalyzed protocol (entry 9). *p*-Bromo- or even *p*-iodophenylboronic ester, which gave a complex mixture of coupling, protonated, and carboxylated products by the Rh(I)-catalyzed reaction, gave the corresponding *p*-bromo- or *p*-iodobenzoic acid in good yield without any of these side products (entries 10 and 11). Heteroarylboronic esters were also applicable to the present reaction without problems (entries 12 and 13). In particular, the reaction of 2-benzothiopheneboronic ester, which gave no carboxylation product in the Rh(I)-catalyzed reaction, proceeded smoothly to afford the corresponding carboxylic acid **3m** in good yield (entry 13). Furthermore, in these reactions of **3*l*** and **3m**, the amount of the catalyst loading could be reduced to 1 mol % even at 60 °C, demonstrating higher activity of Cu-catalysis. As various preparative methods of arylboronic esters that proceed under mild reaction conditions are now available such as the coupling reaction of aryl halides and the direct borylation of aromatic C−H bonds both using bis(neopentyl glycolato)diboron,[11,12] this protocol would be a general method for the preparation of various functionalized arylcarboxlylic acids

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(5) For catalytic carboxylation reactions with carbon dioxide with copper catalyst see: (a) Fukue, Y.; Oi, S.; Inoue, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 2091. (b) Oi, S.; Fukue, Y.; Nemoto, K.; Inoue, Y. *Macromolecules* **1996**, *29*, 2694. (c) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196.

(6) This work was partly presented in the 88th Annual Meeting of Chemical Society of Japan, March 2008, 2H332. An analogous copper-catalyzed carboxylation of aryl- or alkenylboronic esters with CO_2 was reported by Prof. Hou's group at the same meeting. See: Ohishi, T.; Hou, Z. The 88th Annual Meeting of Chemical Society of Japan, March 2008, 2H333. We would like to thank Prof. Hou for discussion on this subject.

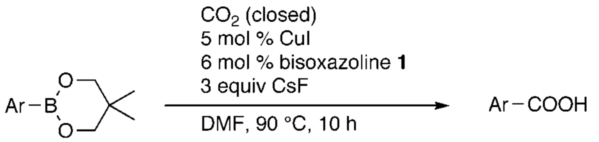
(7) The active catalyst seemed to be sensitive to water and oxygen in the air and decrease of the yield of carboxylation product was often observed in the reaction under 1 atm CO_2 with a balloon. A closed system can achieve good reproducibility.

(8) Other solvent such as toluene, 1,4-dioxane, and acetonitrile resulted in low conversion and only a trace amount of carboxylation product was obtained.

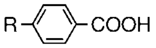
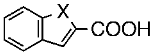
(9) For reactions of bisoxazoline-Cu catalyst, see: (a) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005. (b) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232. (c) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726. (d) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1. (e) McManus, H. A.; Guiry, P. J. *Chem. Rev.* **2004**, *104*, 4151.

(10) Generality of the reaction was examined with 5 mol % of CuI at 90 °C to shorten the reaction time.

Table 3. Generarity of Arylboronic Esters [a,b,c,d]



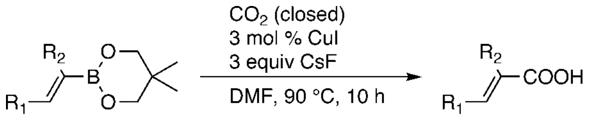
2a-m **3a-m**

entry	product	yield (%)	yield using the Rh-catalyst (%)[c]
			
1	R = H (**3a**)	62	73
2	OMe (**3b**)	72	95
3	Ac (**3c**)	99	74[d]
4	CH_2CN (**3d**)	72	49[d]
5	COOMe (**3e**)	87	67[d]
6	$\equiv$–Ph (**3f**)	86	0
7	$\equiv$–n-C_6H_{14} (**3g**)	84	0
8	-CH=CH_2 (**3h**)	70	0
9[a]	NO_2 (**3i**)	76	0
10	Br (**3j**)	86	complex mixture
11	I (**3k**)	76	–
			
12[b]	X = O (**3l**)	82	59[d]
13[b]	S (**3m**)	78	0

[a] 10 mol % of CuI and 11 mol % of **1** were used. [b] 1 mol % of CuI and 1 mol % of **1** were used at 60 °C. [c] 3 mol % of $[RhOH(cod)]_2$, 7 mol % of dppp, 3 equiv of CsF, dioxane, 60 °C. [d] $Ar_2PCH_2CH_2CH_2PAr_2$ (Ar = p-$MeOC_6H_4$) was used instead of dppp.

Reactions of alkenylboronic esters also proceeded under similar conditions in good yield. Interestingly, ligandless conditions gave the products in higher yield in these cases and the generality of the reaction was examined by using 3 mol % of CuI and 3 equiv of CsF in DMF at 90 °C in a closed system. Not only β-styrylboronic ester **4a** but also β-alkyl-substituted ethenylboronic esters such as **4b** and **4c** reacted smoothly to give α,β-unsaturated carboxylic acids in good yield (entries 1–3). Notably, no further 1,4-addition of alkenylboronic esters to α,β-unsaturated carboxylates, the initial carboxylation products, was observed. Here again, the Cu(I)-catalyzed reaction showed wider applicability compared to the Rh(I)-catalyzed reaction as demonstrated in entries 4 and 5. p-CF_3-substituted β-styrylboronic ester and α-styrylboronic ester, inappropriate substrates for the Rh(I)-catalyzed reaction, gave the corresponding carboxylated products **5d** and **5e** in good yield (Table 4). Since alkenylboronic esters can be easily prepared by hydroboration of alkynes or Pd-catalyzed boration of the corresponding alkenyl halides, this carboxylation protocol provides an easy access to various synthetically useful α,β-unsaturated carboxylic acids.

Table 4. Generarity of Alkenylboronic Esters



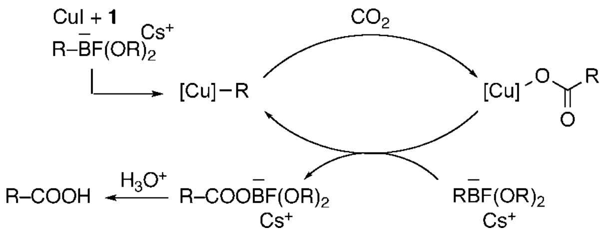
4a-e **5a-e**

entry	R¹	R²	yield (%)	yield using the Rh-catalyst[a] (%)
1	Ph	H	72 (**5a**)	68
2	c-C_6H_{11}	H	73 (**5b**)	
3	t-Bu	H	76 (**5c**)	
4	p-$CF_3C_6H_4$	H	74 (**5d**)	0
5	H	Ph	60 (**5e**)	0

[a] 5 mol % of $[RhCl(nbd)]_2$, 10 mol % of dppp, 3 equiv of CsF, dioxane, 60 °C

We believe that the reaction mechanism of the present reaction (Scheme 1) is similar to that of the Rh-catalyzed carboxylation reaction. Thus, aryl- or alkenylcopper species are generated by transmetalation of the corresponding fluoroborates with Cu(I) salts and undergo carboxylation with carbon dioxide to give Cu-carboxylates, which work as the real active species to further undergo transmetalation and carboxylation catalytically.[13]

Scheme 1. Proposed Reaction Mechanism



In summary, we have succeeded in developing the Cu(I)-catalyzed carboxylation reaction of aryl- and alkenylboronic esters under mild conditions. Use of much less expensive

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(12) (a) Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995. (b) Cho, J.-Y.; Iverson, C. N.; Smith, M. R., III *J. Am. Chem. Soc.* **2000**, *122*, 12868. (c) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III *Science* **2002**, *295*, 305. (d) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390. (e) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 3056. (f) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263. (g) Chotana, G. A.; Rak, M. A.; Smith, M. R., III *J. Am. Chem. Soc.* **2005**, *127*, 10539. (h) Murphy, J. M.; Liao, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 15434. (i) Hata, H.; Yamaguchi, S.; Mori, G.; Nakazono, S.; Katoh, T.; Takatsu, K.; Hiroto, S.; Shinokubo, H.; Osuka, A. *Chem. Asian J.* **2007**, *2*, 849. (j) Paul, S.; Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E., Jr.; Smith, M. R., III *J. Am. Chem. Soc.* **2006**, *128*, 15552.

(13) The reaction did not proceed without CsF. Concerning the effect of CsF, promotion of the transmetalation step by forming arylfluoroborates would be most likely although participation in the carboxylation step by making fluorocuprate might also be possible. Research is now in progress to elucidate the mechanism including the role of CsF and also of the oxazoline ligand.

copper salts and wider generality of the reaction would expand the utility of the reaction to a great extent.

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Supporting Information Available: Experimental procedures and spectral and analytical data for new compounds and copies of ^{1}H and ^{13}C NMR and IR spectra for new compounds and all the carboxylation products. This material is available free of charge via the Internet at http://pubs.acs.org.

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