Homogeneous Catalysis

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Carboxylation of Organoboronic Esters Catalyzed by N-Heterocyclic Carbene Copper(I) Complexes **

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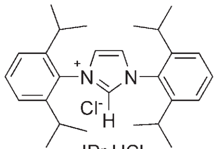
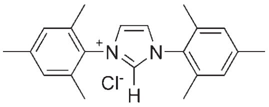
Carbon dioxide (CO_2) is an attractive, cheap, and nontoxic C_1 source.[1] However, because of its high thermodynamic stability and low reactivity, the use of CO_2 as a C_1 source for C–C bond formation usually requires highly nucleophilic organometallic reagents, such as alkyllithium compounds and Grignard reagents. Less nucleophilic organoboron compounds, though easily available, usually do not react with CO_2. Recently, transition-metal-catalyzed addition of carbon nucleophiles to CO_2 has attracted much attention.[2,3] In this context, Iwasawa and co-workers have reported the catalytic carboxylation of aryl- and alkenylboronic esters with CO_2 in the presence of a rhodium(I) compound and additives.[3b] This reaction is potentially useful for the synthesis of functionalized carboxylic acid derivatives because of the easy availability of various functionalized organoboronic esters.[4] Unfortunately, however, the Rh catalyst systems showed only limited tolerance toward functional groups. Although carbonyl and cyano groups survived the reaction conditions, more reactive functional moieties, such as bromo, iodo, and vinyl groups, seemed intolerant. Moreover, little information about the active catalyst species and the reaction mechanism was available because of the complexity of the catalyst systems. These difficulties have limited the application scope of the Rh catalyst systems. The search for new catalysts for more efficient, selective CO_2 transformation as well as the clarification of the catalytic process is therefore of interest and importance. We report herein an excellent N-heterocyclic carbene copper(I) catalyst system for the carboxylation of aryl- and alkenylboronic esters with CO_2. This Cu catalyst system not only showed higher functional-group tolerance, but could also afford structurally characterizable active catalyst species, thus offering unprecedented insight into the mechanistic aspects of the catalytic process.[5]

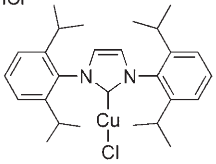
Copper complexes bearing N-heterocyclic carbene (NHC) ligands have been reported to act as efficient catalysts for the transformation of various carbonyl compounds,[6] such as conjugate reduction of α,β-unsaturated carbonyl compounds,[6b] hydrosilylation of ketones,[6c] and also for the reduction of CO_2.[7] In addition, many copper compounds have also been reported to promote nucleophilic addition of organoboron compounds to electrophiles, such as α,β-unsaturated carbonyls and allylic carbonates.[8] These results encouraged us to examine the carboxylation of organoboronic esters with CO_2 by use of N-heterocyclic carbene copper complexes as catalysts. At first we examined the reaction of 4-methoxyphenylboronic acid 2,2-dimethyl-1,3-propanediol ester (**1a**) with CO_2 using N-heterocyclic carbene copper species generated in situ from CuCl, IPr·HCl[9] and *t*BuOK. In the presence of 5 mol% of CuCl with 5 mol% of IPr·HCl and 2 mmol of *t*BuOK in THF 70 °C, the reaction of **1a** (1 mmol) with CO_2 (1 atm) took place smoothly to afford the carboxylation product 4-methoxybenzoic acid **2a** almost quantitatively after acidic hydrolysis (Table 1, entry 1). The reaction did not occur in the absence of CuCl or an NHC ligand or *t*BuOK under the same conditions. The use of a less bulky NHC ligand, such as IMes·HCl, instead of IPr·HCl led to a lower yield of **2a** (Table 1, entry 4). CuBr, CuI, and the Cu^{II} compounds $CuCl_2$ and $Cu(OAc)_2$ were less effective than CuCl (Table 1, entries 5–9). Further screening revealed that the isolated carbene copper(I) chloride complex [(IPr)CuCl][6b,c] could also show high activity for this reaction, and the catalyst loading could be reduced to 1 mol% with 1.05 mmol of *t*BuOK (Table 1, entries 9 and 10).



IPr·HCl



IMes·HCl



[(IPr)CuCl]

We then examined the reactions of various functionalized organoboronic esters with CO_2 by using [(IPr)CuCl] as a catalyst precursor. Representative results are summarized in Table 2. A wide range of aryl- and alkenylboronic esters could be used in this reaction. The reaction was not affected by either electron-donating (e.g., OMe) or electron-withdrawing (e.g., NO_2 and CF_3) groups (Table 2, entries 1, 15, 16). A variety of reactive functional groups, such as vinyl, propargyl

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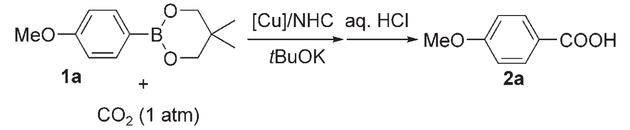
Table 1: Carboxylation of an arylboronic ester with CO_2 by various Cu catalysts.[a]

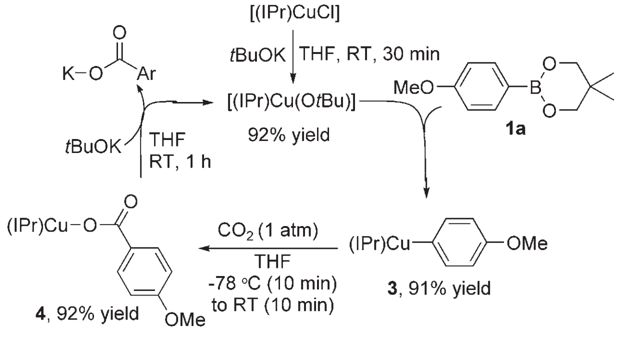


Entry	{Cu}	NHC	Yield [%][b]
1	CuCl	IPr·HCl	96
2	–	IPr·HCl	–
3	CuCl	–	–
4	CuCl	IMes·HCl	81
5	CuBr	IPr·HCl	80
6	CuI	IPr·HCl	58
7	$CuCl_2$	IPr·HCl	70
8	$Cu(OAc)_2$	IPr·HCl	83
9	[(IPr)CuCl]	–	96
10	[(IPr)CuCl]	–	97[c]

[a] Conditions: **1a** (1 mmol), {Cu} (0.05 mmol), *t*BuOK (2 mmol), CO_2 (1 atm), THF (5 mL), 70 °C, 12 h, unless otherwise noted. [b] Yield of isolated product. [c] The reaction was carried out by use of 1 mol% of [(IPr)CuCl] and 1.05 mmol of *t*BuOK for 24 h.

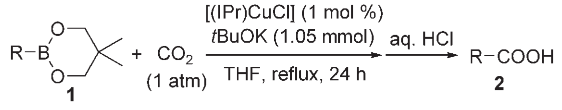
ether, epoxy, carbonyl, and halides (F, Cl, Br, I), survived in these reactions (Table 2, entries 3–14). Boronic esters with sterically demanding aryl groups (e.g., 2,4,6- $Me_3C_6H_2$), heteroaromatic derivatives, and alkenyl substituents were also applicable (Table 2, entries 17, 19–21, 24–26). In all the cases, the reaction took place selectively to give the corresponding carboxylation products in high yields.

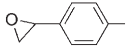
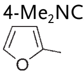
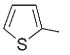
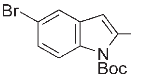
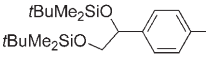
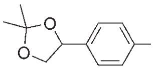
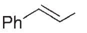
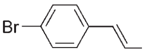
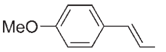
To gain information on the mechanistic aspects of the catalytic process, several stoichiometric reactions were examined. The reaction of [(IPr)CuCl] with 1 equivalent of *t*BuOK in THF at room temperature under N_2 gave the known copper alkoxide complex [(IPr)Cu(O*t*Bu)] isolated in 92 % yield.[10] Further reaction of [(IPr)Cu(O*t*Bu)] with 1 equivalent of the arylboronic ester **1a** afforded the corresponding arylcopper complex **3** isolated in 91 % yield (Scheme 1). In contrast, no reaction was observed between [(IPr)CuCl] and **1a** under the same conditions. Recrystallization of **3** in THF/toluene yielded colorless single crystals suitable for X-ray analysis. This investigation revealed that **3** adopts a monomeric structure, in which the NHC ligand, the Cu atom, and the aryl unit are oriented almost linearly with ∢C8-Cu1-C1 = 177.27(16)° (Figure 1).[11] Exposure of the aryl complex **3** to CO_2 in THF at room or lower temperatures rapidly afforded the carboxylate complex **4** isolated in 92 % yield. X-ray analysis revealed that the carboxylate unit in **4** is bonded to the metal center in an η^1-fashion rather than an η^3-form, probably owing to the steric hindrance from the NHC ligand (Figure 2).[11,12] Treatment of the carboxylate complex **4** with 1 equivalent of *t*BuOK in THF regenerated the alkoxide [(IPr)Cu(O*t*Bu)], with quantitative release of potassium 4-methoxybenzoate as a white precipitate (Scheme 1). Hydrolysis of the potassium salt afforded 4-methoxybenzoic acid quantitatively. It is also noteworthy that, similar to the chloride complex [(IPr)CuCl], the alkoxide complex [(IPr)Cu(O*t*Bu)], the aryl complex **3** and the carboxylate complex **4** all showed high catalytic activity for the carboxylation of **1a** with CO_2 in the presence of *t*BuOK, affording **2a** in 95 %, 95 %, and 96 % yields, respectively.



Scheme 1. Stoichiometric reactions of [(IPr)CuCl].

Table 2: {(IPr)Cu}-catalyzed carboxylation of aryl- and alkenylboronic esters with CO_2.



entry	R	**2** [%][a]
1	$4\text{-}MeOC_6H_4$	**2a** (97)
2	4-*t*BuC_6H_4	**2b** (88)
3	$4\text{-}PhC_6H_4$	**2c** (97)
4	$4\text{-}(CH_2{=}CH_2)C_6H_4$	**2d** (93)
5	$4\text{-}(MeOCH_2C{\equiv}C)C_6H_4$	**2e** (94)
6		**2f** (77)
7	$4\text{-}HCOC_6H_4$	**2g** (97)
8	$4\text{-}PhCOC_6H_4$	**2h** (99)
9	$4\text{-}MeOOCC_6H_4$	**2i** (89)
10	$4\text{-}NCC_6H_4$	**2j** (88)
11	$4\text{-}FC_6H_4$	**2k** (89)
12	$4\text{-}ClC_6H_4$	**2l** (92)
13	$4\text{-}BrC_6H_4$	**2m** (99)
14	$4\text{-}IC_6H_4$	**2n** (85)
15	$4\text{-}F_3CC_6H_4$	**2o** (92)
16	$3\text{-}O_2NC_6H_4$	**2p** (79)
17	$2,4,6\text{-}Me_3C_6H_2$	**2q** (98)
18	$4\text{-}Me_2NC_6H_4$	**2r** (87)[b]
19		**2s** (73)
20		**2t** (83)
21[c]		**2u** (82)
22		**2v** (86)
23		**2w** (73)
24		**2x** (85)
25		**2y** (92)
26		**2z** (89)

[a] Yield of isolated product. [b] Yield of the methyl ester derivative. [c] Boc = *tert*-butoxycarbonyl.

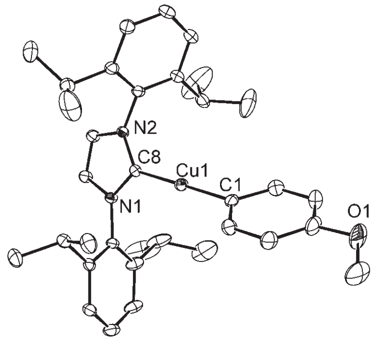


Figure 1. ORTEP structure of **3**.Thermal ellipsoids set at 30% probability. Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angle [°]: Cu1–C8 1.903(4), Cu1–C1 1.913(4); C8-Cu1-C1 177.27(16).

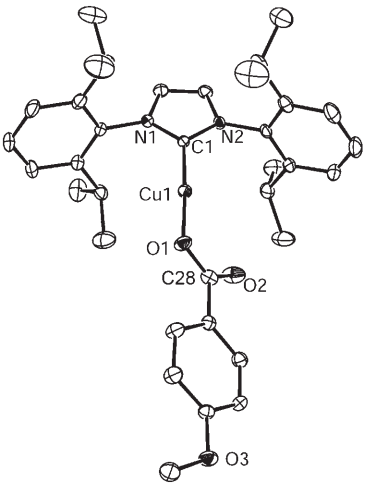
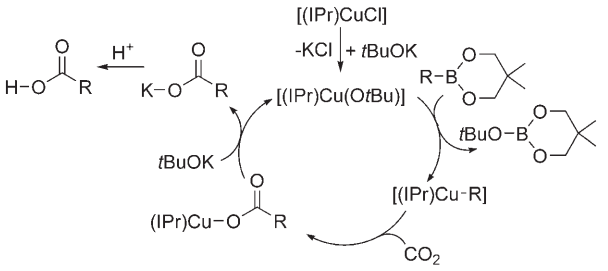


Figure 2. ORTEP structure of **4**. Thermal ellipsoids set at 30% probability. Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angle [°]: Cu1-O1 1.861(2), Cu1-C1 1.869(3), O1-C28 1.287(4), O2-C28 1.235(4); C1-Cu1-O1 176.9(1).

On the basis of the above experimental results, a catalytic cycle for the carboxylation of organoboronic esters with CO_2 could be proposed as shown in Scheme 2. The metathesis reaction between [(IPr)CuCl] and *t*BuOK should give straightforwardly the alkoxide complex [(IPr)Cu(O*t*Bu)] which, on reaction with an organoboronic ester, would give the corresponding organocopper complex [(IPr)CuR]. Nucleophilic addition of [(IPr)CuR] to CO_2 should yield the carboxylate [(IPr)Cu(OCOR)], which on metathesis with *t*BuOK could regenerate [(IPr)Cu(O*t*Bu)] and release the potassium salt RCOOK. The potassium salt would yield the carboxylic acid RCOOH after hydrolysis.



Scheme 2. A possible mechanism for (IPr)Cu-catalyzed carboxylation of organoboronic esters with CO_2.

In summary, we have demonstrated that the combination of [(IPr)CuCl] with *t*BuOK can serve as an excellent catalyst system for the carboxylaton of aryl- and alkenylboronic esters with CO_2, leading to selective formation of various functionalized carboxylic acid derivatives. Some key reaction intermediates, such as the copper(I) alkoxide complex [(IPr)Cu(O*t*Bu)], the aryl complex **3**, and the carboxylate complex **4,** have been isolated and structurally characterized, and have also been confirmed to be active species in this catalytic process. Further studies on catalytic fixation of CO_2 with other substrates are under progress.

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Keywords: boronic esters · carbene ligands · carbon dioxide · carboxylation · copper catalysts

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[1] Reviews: a) T. J. Marks, et al., *Chem. Rev.* **2001**, *101*, 953–996(see Supporting Information); b) A. Behr, *Angew. Chem.* **1988**, *100*, 681–698; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 661–678.

[2] Recent Reviews: a) Z. Hou, T. Ohishi in *Comprehensive Organometallic Chemistry III*, *Vol. 10* (Eds.: R. H. Crabtree, D. M. P. Mingos, I. Ojima), Elsevier, Oxford, **2007**, pp. 537–555, and references therein; b) T. Sakakura, J.-C. Choi, H. Yasuda, *Chem. Rev.* **2007**, *107*, 2365–2387; c) J. Louie, *Curr. Org. Chem.* **2005**, *9*, 605–623; d) X. Yin, J. R. Moss, *Coord. Chem. Rev.* **1999**, *181*, 27–59; e) D. Walther, M. Ruben, S. Rau, *Coord. Chem. Rev.* **1999**, *182*, 67–100.

[3] For examples, see: a) R. Johansson, O. F. Wendt, *Dalton Trans.* **2007**, 488–492; b) K. Ukai, M. Aoki, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2006**, *128*, 8706–8707; c) M. Takimoto, M. Kawamura, M. Mori, Y. Sato, *Synlett* **2005**, 2019–2022; d) M. Takimoto, Y. Nakamura, K. Kimura, M. Mori, *J. Am. Chem. Soc.* **2004**, *126*, 5956–5957; e) M. Takimoto, M. Mori, *J. Am. Chem. Soc.* **2002**, *124*, 10008–10009; f) R. J. Franks, K. M. Nicholas, *Organometallics* **2000**, *19*, 1458–1460; g) M. Shi, K. M. Nicholas, *J. Am. Chem. Soc.* **1997**, *119*, 5057–5058; h) S. Oi, Y. Fukue, K. Nemoto, Y. Inoue, *Macromolecules* **1996**, *29*, 2694–2695; i) Y. Fukue, S. Oi, Y. Inoue, *J. Chem. Soc. Chem. Commun.* **1994**, 2091.

[4] a) N Miyaura, Y. Yamamoto in *Comprehensive Organometallic Chemistry III*, *Vol. 9* (Eds.: R. H. Crabtree, D. M. P. Mingos), Elsevier, Oxford, **2007**, pp. 145–244; b) D. G. Hall, *Boronic Acids*, Wiley-VCH, Weinheim, **2005**.

[5] A portion of this work was reported at the 88th Annual Meeting of Chemical Society of Japan, March **2008**, 2H3-33. The catalytic carboxylation of aryl- and alkenylboronic esters by copper(I) complexes with bisoxazoline ligands was reported by Prof. N. Iwasawa and co-workers at the same meeting. See: S. Tadami, K. Ukai, Takaya, N. Iwasawa, The 88th Annual Meeting of Chemical Society of Japan, March **2008**, 2H3-32, *Org. Lett.*, in press. We would like to thank Prof. Iwasawa for discussion on this subject and for communication of unpublished results.

[6] a) S. Díez-González, S. P. Nolan, *Synlett* **2007**, 2158–2167; b) V. Jurkauskas, J. P. Sadighi, S. L. Buchwald, *Org. Lett.* **2003**, *5*, 2417–2420; c) H. Kaur, F. K. Zinn, E. D. Stevens, S. P. Nolan, *Organometallics* **2004**, *23*, 1157–1160.

[7] D. S. Laitar, P. Muller, J. P. Sadighi, *J. Am. Chem. Soc.* **2005**, *127*, 17196 – 17198.

[8] For examples, see: a) R. Wada, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 8910 – 8911; b) R. Wada, T. Shibuguchi, S. Makino, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2006**, *128*, 7687 – 7691; c) K. Takahashi, T. Ishiyama, N. Miyaura, *Chem. Lett.* **2000**, 982 – 983; d) H. Ito, H. Yamanaka, J. Tateiwa, A. Hosomi, *Tetrahedron Lett.* **2000**, *41*, 6821 – 6825; e) K. Takahashi, T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* **2001**, *625*, 47 – 53; f) P. V. Ramachandran, D. Pratihar, D. Biswas, A. Srivastava, M. V. Ram. Reddy, *Org. Lett.* **2004**, *6*, 481 – 484; g) H. Ito, C. Kawakami, M. Sawamura, *J. Am. Chem. Soc.* **2005**, *127*, 16034 – 16035; h) S. Mun, J. E. Lee, J. Yun, *Org. Lett.* **2006**, *8*, 4887 – 4889; i) D. S. Laitar, E. Y. Tsui, J. P. Sadighi, *J. Am. Chem. Soc.* **2006**, *128*, 11036 – 11037; j) H. Ito, S. Ito, Y. Sasaki, K. Matsuura, M. Sawamura, *J. Am. Chem. Soc.* **2007**, *129*, 14856 – 14857; k) J. E. Lee, J. Kwon, J. Yun, *Chem. Commun.* **2008**, 733 – 734; l) J. E. Lee, J. Kwon, *Angew. Chem.* **2008**, *120*, 151 – 153; *Angew. Chem. Int. Ed.* **2008**, *47*, 145 – 147.

[9] Purchased from Strem Chemicals, Inc. For preparation of IPr·HCl, see: A. J. Arduengo III, R. Krafczyk, R. Schmutzler, *Tetrahedron* **1999**, *55*, 14523 – 14534.

[10] N. P. Mankad, D. S. Laiter, J. P. Sadighi, *Organometallics* **2004**, *23*, 3369 – 3371.

[11] CCDC 685031 (**3**) and 685032 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] An analogous acetate complex [(IPr)CuOAc] was reported previously. See: T. G. David, D. S. Laiter, J. P. Sadighi, *Organometallics* **2004**, *23*, 1191 – 1193.