Carbon Dioxide Fixation

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Carboxylation of Alkylboranes by N-Heterocyclic Carbene Copper Catalysts: Synthesis of Carboxylic Acids from Terminal Alkenes and Carbon Dioxide**

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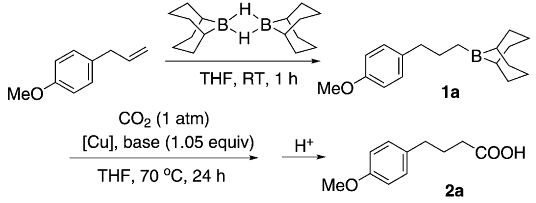
The use of carbon dioxide (CO_2) as a C1 building block for C–C bond-formation reactions such as carboxylation has recently received much attention.[1–4] Among the most promising and attractive substrates for the carboxylation reaction with CO_2 are alkylboron compounds given their ease of availability, functional group tolerance, and substrate scope. However, the catalytic carboxylation of alkylboranes with CO_2 has hardly been explored to date, which is in contrast with recent successful carboxylation of aryl- and alkenylboronic esters catalyzed by various transition-metal catalysts.[2g–i] The fewer number of reports on carboxylation of alkylboranes could probably be because of the difficulty in generating a transition metal–alkyl species that has the appropriate stability and high activity (toward CO_2) from an alkylborane compound. Indeed, although alkylboron compounds have been used for various transition-metal-catalyzed cross-coupling reactions, information on the interaction between an alkylboron compound and a transition-metal species has remained very limited.[5,6] The isolation of a structurally characterizable intermediate in the transmetalation of an organoboron compound to a transition metal is scarce.[7]

We report herein that N-heterocyclic carbene (NHC) copper complexes can serve as excellent catalyst systems for the carboxylation of alkylboron compounds with CO_2. The reaction can be carried out easily in one pot by hydroboration of terminal alkenes with 9-borabicyclo[3.3.1]nonane (9-BBN-H) and subsequent carboxylation of the resulting alkylboranes with CO_2 in the presence of a NHC–copper complex. More remarkably, a novel copper methoxide/alkylborane adduct and its subsequent CO_2 insertion product have been isolated and structurally characterized, thus providing new insight into the mechanistic aspect of the catalytic process. Some preliminary results of this work were disclosed in 2010.[8] During the preparation of this manuscript, the carboxylation of alkylboranes catalyzed by a CuOAc/1,10-phenanthroline system was reported by Sawamura and co-workers.[8,9]

At first, the reaction of an alkylborane compound **1a**, which was generated in situ from the hydroboration reaction of 3-(4- methoxyphenyl)propylene with 9-BBN-H, was examined using [(IPr)CuCl] (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) as a catalyst.[2i] In the presence of 1 mol% [(IPr)CuCl], 1.05 equivalents of *t*BuOK, and CO_2 (1 atm) in THF at 70 °C, the carboxylation product 4-(4-methoxyphenyl)butanoic acid (**2a**) was obtained in 35% yield after 24 hours (Table 1, entry 1). This yield is much lower than those (almost quantitative) obtained in the analogous carboxylation of aryl- and alkenylboronic esters under similar reaction conditions,[2i] thus showing that alkylborane is less effective for the carboxylation with CO_2. The use of MeOLi, a less bulky base, instead of *t*BuOK gave a notably higher yield (Table 1, entry 4). To our delight, when 3 mol% [(IPr)CuCl] was used in the presence of 1.05 equivalents of LiOMe, the carboxylation product **2a** was obtained in almost quantitative yield (Table 1, entry 5). MeONa and MeOK are also as effective as LiOMe (Table 1, entries 6 and 7). The use of a less

Table 1: Carboxylation of alkylborane **1a** with carbon dioxide.[a]



Entry	[Cu] (mol%)	Base	Yield [%][b]
1	[(IPr)CuCl] (1)	*t*BuOK	35
2	[(IPr)CuCl] (1)	–	–
3	–	*t*BuOK	–
4	[(IPr)CuCl] (1)	MeOLi	42
5	[(IPr)CuCl] (3)	MeOLi	97
6	[(IPr)CuCl] (3)	MeONa	97
7	[(IPr)CuCl] (3)	MeOK	81
8	[(IMes)CuCl] (3)	MeOLi	41
9	[(IPr)Cu(OAc)$_2$](3)	MeOLi	97
10	[(IPr)CuCl] (3)	MeOLi[c]	37

[a] Reaction conditions: **1a** (1 mmol), [Cu] (mol%), base (1.05 mmol), CO_2 (1 atm), THF (5 mL), 70 °C, 24 h, unless otherwise noted. [b] Yield of isolated product. [c] 0.5 mmol of MeOLi was used.

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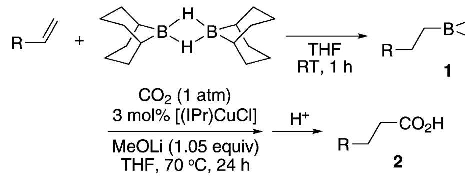
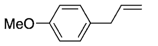
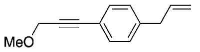
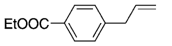
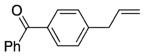
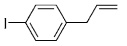
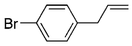
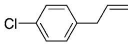
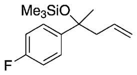
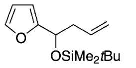
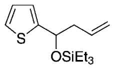
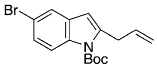
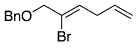
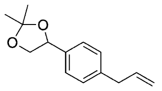
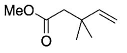
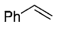
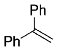
bulky copper catalyst such as [(IMes)CuCl] (IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) instead of [(IPr)CuCl] led to a much lower yield (41 %) of **2a** (Table 1, entry 8), probably owing to lower stability (or shorter lifetime) of the resultant active species. The Cu^{II} complex $[(IPr)Cu(OAc)_2]$ was also effective (Table 1, entry 9). The use of 0.5 mmol of MeOLi did not result in completion of the reaction (Table 1, entry 10). In a control experiment, the carboxylation reaction was not observed in the absence of either [(IPr)CuCl] or the base under the same reaction conditions (Table 1, entries 2 and 3, respectively).

We then examined the reactions of various functionalized alkylboranes with CO_2 by using [(IPr)CuCl] as the catalyst. The results are summarized in Table 2. A wide variety of reactive functional groups, such as propargyl, carbonyl, halide (I, Br, Cl, F), and vinyl bromide survived the reaction conditions (Table 2, entries 2–8 and 12–13). Synthetically useful protecting groups, such as silyl ethers, *N-tert*-butoxycarbonyl, benzyl ether, and isopropylidene can also be utilized under the present reaction conditions (Table 2, entries 8–13). Alkylboranes with heteroaromatic motifs are also applicable (Table 2, entries 9–11). In all the cases, the reaction took place selectively to give the corresponding carboxylation products in high yields (81–99 %) upon isolation. In the case of a tertiary substituent (Table 2, entry 14), the carboxylation product was obtained in 60 % yield at 70 °C, but was increased to 70 % at a higher temperature (100 °C). The one-pot reaction of styrene with 9-BBN-H and CO_2 afforded the β-carboxylated product **2o** in 65 % yield upon isolation (Table 2, entry 15). 1,1-Diphenylethylene was not suitable for this reaction probably owing to steric bulk (Table 2, entry 16).

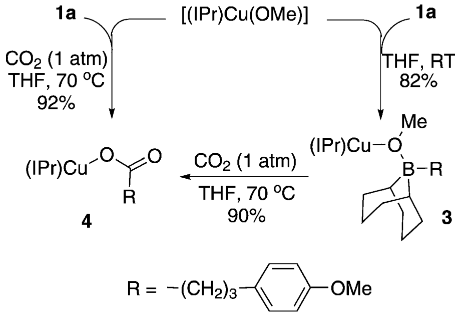
Table 2: [(IPr)CuCl]-catalyzed carboxylation of various alkylboranes with CO_2.



Entry	Alkene	Product 2[a]
1		**2a** (97)
2		**2b** (92)
3		**2c** (94)
4		**2d** (91)
5		**2e** (90)
6		**2f** (91)
7		**2g** (82)
8		**2h** (99)
9		**2i** (97)
10		**2j** (81)
11		**2k** (92)
12		**2l** (95)
13		**2m** (87)
14		**2n** (70)[b]
15		**2o** (65)[c]
16		–

[a] Yield of isolated product. [b] Hydroboration was carried out at 70 °C, and the subsequent carboxylation was carried out at 100 °C in toluene. The carboxylation at 70 °C in THF gave a lower yield (60 %). [c] The hydroboration reaction was carried out at 70 °C in THF. Boc = *tert*-butoxycarbonyl.

To elucidate the mechanism of the current catalytic process, several stoichiometric reactions were examined (Scheme 1). When [IPrCu(OMe)],[10a] which was prepared by the reaction of [IPrCuCl] with MeOLi, was mixed with alkylborane **1a** in THF at room temperature, the adduct **3** was obtained almost instantly. Single crystals suitable for X-ray crystallographic studies were obtained from THF/*n*-hexane (1:1) at −30 °C. It was determined that **3** is formed by the interaction between the oxygen atom of the methoxy group in [IPrCu(OMe)] and the boron atom in **1a** (Figure 1). The Cu−O bond distance in **3** (1.859(2) Å) is significantly longer than those in [IPrCu(OEt)] (1.799(3) Å)[5e] and [IPrCu(O*t*Bu)] (1.8104(13) Å),[10b] apparently owing to the coordination of the MeO group to the boron atom in **3**. The B−O bond distance (1.572(3) Å) in **3** is shorter than that found in a 1-boraadamantane·THF adduct (1.637(2) Å).[10c] When **3** was heated to 70 °C in $[D_6]C_6H_6$, 3-(4-methoxyphenyl)propylene was formed as shown by ^1H NMR spectroscopy.[11] However, when **3** was exposed to a CO_2 atmosphere at 70 °C, the carboxylate complex **4** was obtained in 90 % yield (Scheme 1 and Figure 2), thus suggesting that a 3-(4-methoxyphenyl)-propyl copper intermediate might be formed by transfer of the alkyl group from the B atom to the Cu atom in **3**.[12] Alternatively, the carboxylate complex **4** could also be obtained in 92 % yield by the reaction of [IPrCu(OMe)] and **1a** under a CO_2 atmosphere. [IPrCu(OMe)], **3**, and **4** all



Scheme 1. Some stoichiometric reactions.

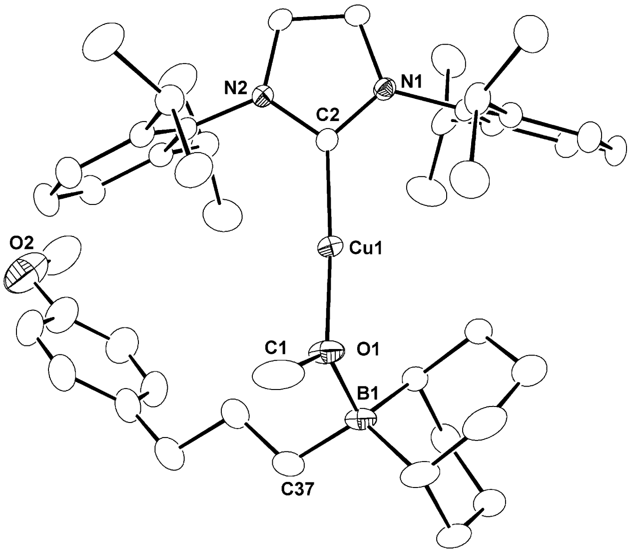


Figure 1. ORTEP structure of **3**. Thermal ellipsoids are shown at 30% probability. Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Cu(1)–O(1) 1.859(2), O(1)–B(1) 1.572(3), B(1)–C(37) 1.631(4); Cu(1)-O(1)-B(1) 126.4(2), Cu(1)-O(1)-C(1) 116.2(2), C(1)-O(1)-B(1) 117.0(2).[14]

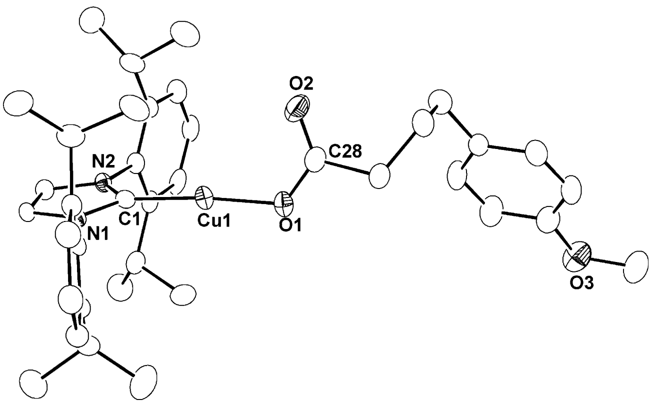
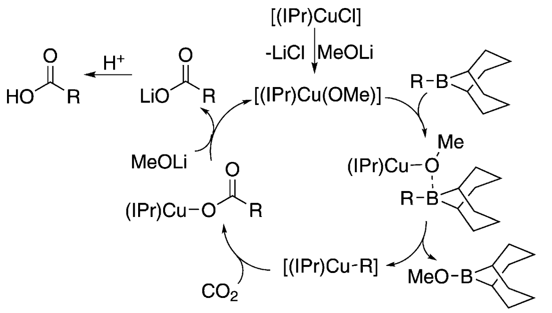


Figure 2. ORTEP structure of **4**. Thermal ellipsoids are shown at 30% probability. Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Cu(1)–C(1) 1.857(4), Cu(1)–O(1) 1.836(3), O(1)–C(28) 1.286(5), O(2)–C(28) 1.216(5), C(1)–Cu(1)-O(1) 174.2(2); Cu(1)-O(1)-C(28) 122.0(3), O(1)-C(28)-O(2) 124.5(4).[14]

showed high catalytic activity for the carboxylation of **1a** under the reaction conditions shown in Table 2, thereby suggesting that these complexes are true active catalyst species. The interaction between a metal alkoxide or hydroxide base with an organoboron compound has been thought to be critically important in many transition-metal-catalyzed cross-coupling reactions employing organoboron compounds,[13] however, this work demonstrates unambiguously for the first time that such a bonding interaction does take place as shown in **3**.

On the basis of these studies, a catalytic cycle for the carboxylation of alkylboranes with CO_2 is proposed as shown in Scheme 2. The metathesis reaction between [(IPr)CuCl] and MeOLi should give straightforwardly the methoxide complex [(IPr)Cu(OMe)], which on reaction with an alkylborane gives the adduct **3** through interaction between the methoxy group and the boron atom. The subsequent transmetalation of the alkyl group to the copper atom would generate the alkylcopper complex [(IPr)CuR]. Nucleophilic addition of the alkyl group to CO_2 should yield the carboxylate [(IPr)Cu(OCOR)], which upon metathesis with MeOLi could regenerate [(IPr)Cu(OMe)] and release the lithium carboxylate RCO_2Li. The latter would yield the carboxylic acid RCO_2H after hydrolysis.



Scheme 2. A possible mechanism for [(IPr)CuCl]-catalyzed carboxylation of alkylboranes with CO_2.

In summary, we have demonstrated that the combination of [(IPr)CuCl] with MeOLi can serve as an excellent catalyst system for the carboxylation of alkylboranes with CO_2, leading to the efficient synthesis of various functionalized carboxylic acids. The isolation of the copper methoxide/alkylborane adduct complex **3** and its CO_2 insertion product **4** has provided important information for understanding the mechanistic details. These results may also offer new insight into other catalytic cross-coupling reactions involving metal/organoboron compounds; in particular reactions for the transmetalation of organoboron compounds.

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[14] CCDC 782839 (**3**) and 782840 (**4**) contains 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.