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# Copper-Catalyzed Carboxylation of Alkylboranes with Carbon Dioxide: Formal Reductive Carboxylation of Terminal Alkenes

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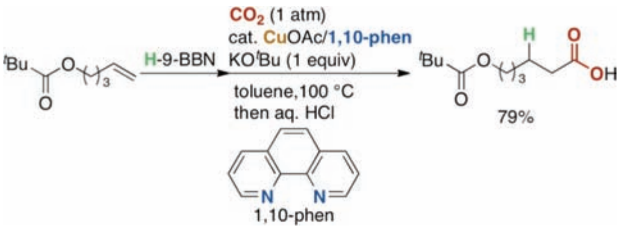
## ABSTRACT



**Carboxylation of alkylboron compounds (alkyl-9-BBN) with $CO_2$ proceeded in the presence of catalytic amounts of CuOAc/1,10-phenanthroline and a stoichiometric amount of KO$^t$Bu. The alkylboranes are easily and widely available through the alkene hydroboration, and thus the overall process represents a reductive carboxylation of alkenes with $CO_2$. The broad functional group compatibility and the inexpensiveness of the Cu/1,10-phenathoroline catalyst system are attractive features of this protocol.**

Incorporation of carbon dioxide ($CO_2$), which is an abundant and renewable C1 source, into organic molecules has emerged as an area of attractive research in recent organic chemistry.[1] In this regard, various carbon−carbon bond formation reactions using $CO_2$ have been achieved under the influence of transition metal catalysts.[2−9] Among them, the transition-metal-catalyzed carboxylations of less basic organometallic reagents such as organostannane, zinc, or boron compounds with $CO_2$ offer versatile methods for the synthesis of functionalized carboxylic acid derivatives.[2−4] Specifically, allylstannane reagents were used for

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(1) For reviews, see: (a) Behr, A. *Angew. Chem., Int. Ed.* **1988**, *27*, 661–678. (b) Gibson, D. H. *Chem. Rev.* **1996**, *96*, 2063–2095. (c) Arakawa, H.; Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; DuBois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nichoras, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953–996. (d) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365–2387. (e) Correa, A.; Martîn, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 6201–6204.

(2) For Pd-catalyzed carboxylations of allylstannane compounds with carbon dioxide, see: (a) Johansson, R.; Wendt, O. F. *Dalton Trans.* **2007**, 488–492. (b) Shi, M.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 5057–5058.

(3) For Ni-catalyzed carboxylations of alkylzinc compounds with $CO_2$, see: (a) Ochiai, H.; Jang, M.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 2681–2683. (b) Yeung, C. S.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 7826–7827.

(4) For transition-metal (Rh or Cu)-catalyzed carboxylations of aryl- and alkenylboron compounds with carbon dioxide, see: (a) Ukai, K.; Aoki, M.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2006**, *128*, 8706–8707. (b) Takaya, J.; Tadami, S.; Ukai, K.; Iwasawa, N. *Org. Lett.* **2008**, *10*, 2697–2700. (c) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 5792–5795.

(5) For transition-metal-free carboxylation of organozinc compounds, see: Kobayashi, K.; Kondo, Y. *Org. Lett.* **2009**, *11*, 2035–2037.

(6) For Cu- or Au-catalyzed carboxylations of (hetero)arenes, see: (a) Boogaerts, I. I. F.; Nolan, S. P. *J. Am. Chem. Soc.* **2010**, *132*, 8858–8859. (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*, 8674–8677. (c) Zhang, L.; Cheng, J.; Ohishi, T.; Hou, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 8670–8673. (d) Boogaerts, I. I. F.; Nolan, S. P. *Chem. Commun.* **2010**, Advance Articles, DOI: 10.1039/c0cc03890c.

10.1021/ol103128x

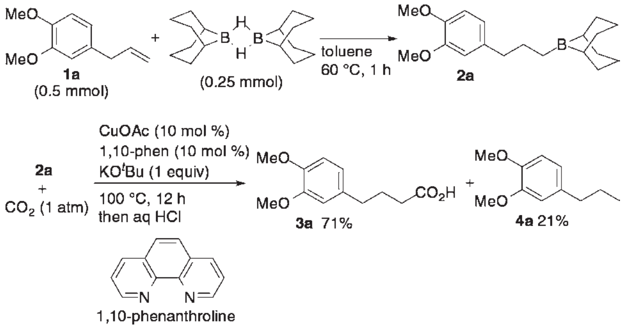
the palladium-catalyzed carboxylations.[2] More recently, nickel- and palladium-catalyzed carboxylations of aryl- (Ni, Pd) or alkylzinc (Ni) reagents have been developed.[3]

The organoboron compounds are particularly attractive reagents due to their broad availability and functional group compatibility. Iwasawa and co-workers developed a rhodium-catalyzed carboxylation of aryl- and alkenylboronates.[4a] Copper-catalyzed reactions were also reported by Iwasawa and co-workers and Hou and co-workers.[4b,c] However, alkylboron compounds have not been used for the transition-metal-catalyzed carboxylation.[3,5,10]

Earlier, we showed that alkylcopper species can catalytically be formed from alkylboron compounds (alkyl-9-BBN) through B/Cu transmetalation in the copper-catalyzed allylic substitution reaction with allylic phosphates and conjugate addition to imidazolyl α,*β*-unsaturated ketones.[11a,12] Here we report an extension of our work to copper-catalyzed carboxylation of alkylboron compounds with CO$_2$ to produce alkanoic acids.[11,12] The wide and easy availability of alkylboranes *via* the established alkene hydroboration is an attractive feature of this transformation, and thus the overall molecular transformation represents a formal reductive carboxylation of terminal alkenes with CO$_2$.[8e,9] A variety of functional groups are tolerated in the alkenes.

Specifically, a solution of alkylborane in toluene was prepared via hydroboration of alkene (**1a**) (0.5 mmol) with a 9-borabicyclo[3.3.1]nonane (9-BBN-H) dimer (**1a**/B 1:1) at 60 °C (Scheme 1). Subsequently, the solution was added to a vial containing CuOAc (10 mol %), 1,10-phenanthroline (1,10-phen) (10 mol %), and KO$^t$Bu (1 equiv to **1**, 0.5 mmol) under an atomospheric pressure of CO$_2$ (balloon), and the resulting reddish brown opaque solution was heated at 100 °C for 12 h. As the reaction proceeded, a small amount of black solid was precipitated. Hydrolytic workup afforded carboxylic acid **3a** in 71% isolated yield (based on **1a**). A smaller amount of deborylated product **4a** (21%) was also obtained as a side product.

**Scheme 1**



Ligand screening showed that 1,10-phenanthroline was most effective. Other diamines such as 2,2′-bipyridyl (7%) and TMEDA (5%) and phosphine ligands such as PPh$_3$ (0%) and DPPE (19%) were much less efficient. The reaction occurred without a ligand but with a decreased product yield (31%). The reaction with CuCl(IPr) (10 mol %)/KO$^t$Bu (1.1 equiv)/toluene at 100 °C resulted in a 35% yield [IPr: 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene].[10]

Several observations concerning the optimum reaction conditions are to be noted. Controlling the reaction temperature was crucial for the reproducibility in the product yield; the reaction temperature over 100 °C (oil bath temp) resulted in the formation of a significant amount of the deborylated product **4a**. Cheaper CuCl was as effective as CuOAc, giving **3a** in 61% yield. The use of Cu(OAc)$_2$ resulted in a lower reaction efficacy (56%). No carboxylation occurred in the absence of KO$^t$Bu.

The formal reductive carboxylation protocol can transform various terminal alkenes into the corresponding alkanoic acids. Functional groups such as methoxy, siloxy, ester, acetal, phthalimide, bromo, and benzyloxy groups were tolerated (Table 1, entries 1−7 and 10). The terminal alkene **1d** bearing a tertiary alkyl substituent served as a substrate to afford the corresponding carboxylic acid in a reasonable yield. The *β*-branched alkylboranes **2j** and **2k** prepared from 1,1-diphenylethylene (**1i**) and **1k** also underwent carboxylation, giving the corresponding branched carboxylic acids (entries 9 and 10). Notably, the carboxylation of styrene (**1i**) afforded hydrocinnamic acid (**3i**): the regioselectivity is complementary to that of the Ni-catalyzed carboxylation of styrenes developed by Rovis and co-workers.[8e] The use of secondary alkylborane reagents prepared from internal alkenes resulted in no reaction (data not shown).

Two reaction pathways for the carboxylation of alkylboranes can be postulated as illustrated in Scheme 2 (paths a and b). In path a, a trialkyl(alkoxo)borate **B** is initially formed by the stoichiometric reaction beween an alkylborane **2** and KO$^t$Bu.[13] Subsequently, the B/Cu transmetalation

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(7) For Cu-catalyzed reactions with carbon dioxide, 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*, 2694–2695. (c) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196–17197. (d) Zhang, W.-Z.; Li, W.-J.; Zhang, X.; Zhou, H.; Lu, X.-B. *Org. Lett.* **2010**, *12*, 4748–4751. (e) Fujihara, T.; Xu, T.; Semba, K.; Terao, J.; Tsuji, Y. *Angew. Chem., Int. Ed.* **2011**, *50*, Early view, DOI: 10.1002/anie.201006292. See also refs 4b, c.

(8) For other examples on transition-metal-catalyzed carboxylations with carbon dioxide, see: (a) Takimoto, M.; Kawamura, M.; Mori, M.; Sato, Y. *Synlett* **2005**, 2019–2022. (b) Takimoto, M.; Nakamura, Y.; Kimura, K.; Mori, M. *J. Am. Chem. Soc.* **2004**, *126*, 5956–5957. (c) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008–10009. (d) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *14*, 15188–15189. (e) Williams, C. M.; Johnson, J. B.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14936–14937. (f) Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2008**, *130*, 15254–15255. (g) Correa, A.; Martîn, R. *J. Am. Chem. Soc.* **2009**, *131*, 15974–15975.

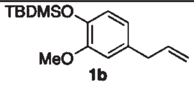
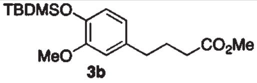
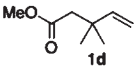
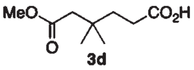
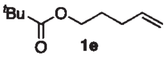
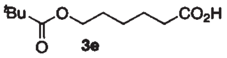
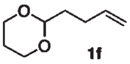
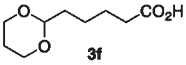
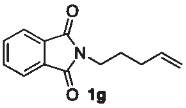
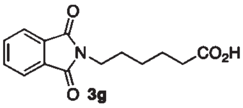
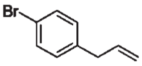
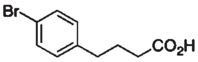
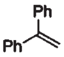
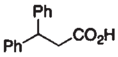
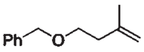
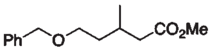
(9) (a) Hoberg, H.; Gross, S.; Milchereit, A. *Angew. Chem., Int. Ed.* **1987**, *26*, 571–572. (b) Hoberg, H.; Peres, Y.; Krüger, C.; Tsay, Y.-H. *Angew. Chem., Int. Ed.* **1987**, *26*, 771–773. (c) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C38–C40.

(10) Hou and co-workers presented the carboxylation of alkyl-9-BBN derivatives with carbon dioxide catalyzed by an *N*-heterocyclic carbene−copper complex: Ohishi, T.; Nishiura, M.; Hou, Z. The 90th Annual Meeting of Chemical Society of Japan, Osaka, March 26−30, 2010, 1F1−46.

(11) For Cu-catalyzed *γ*-selective and stereospecific allyl−alkyl and allyl−aryl couplings with organoboron compounds, see: (a) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895–2897. (b) Ohmiya, H.; Yokokawa, N.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438–2440. (c) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216–3218.

(12) For Cu-catalyzed conjugate additions with alkylboron compounds (alkyl-9-BBN) to imidazol-2-yl α,*β*-unsaturated ketones, see: Ohmiya, H.; Yoshida, M.; Sawamura, M. *Org. Lett.* **2010**, *12*, ASAP, DOI: 10.1021/ol102819k.

**Table 1.** Cu-Catalyzed Carboxylation[a]

| entry | alkene | product | yield (%)[b] |
|---|---|---|---|
| 1[c] |  **1b** |  **3b** | 64 |
| 2[c] |  **1c** |  **3c** | 73 |
| 3 |  **1d** |  **3d** | 63 |
| 4 |  **1e** |  **3e** | 79 |
| 5 |  **1f** |  **3f** | 32 |
| 6 |  **1g** |  **3g** | 58 |
| 7 |  **1h** |  **3h** | 47 |
| 8 |  **1i** |  **3i** | 72[d] |
| 9 |  **1j** |  **3j** | 54 |
| 10[c] |  **1k** |  **3k** | 49 |

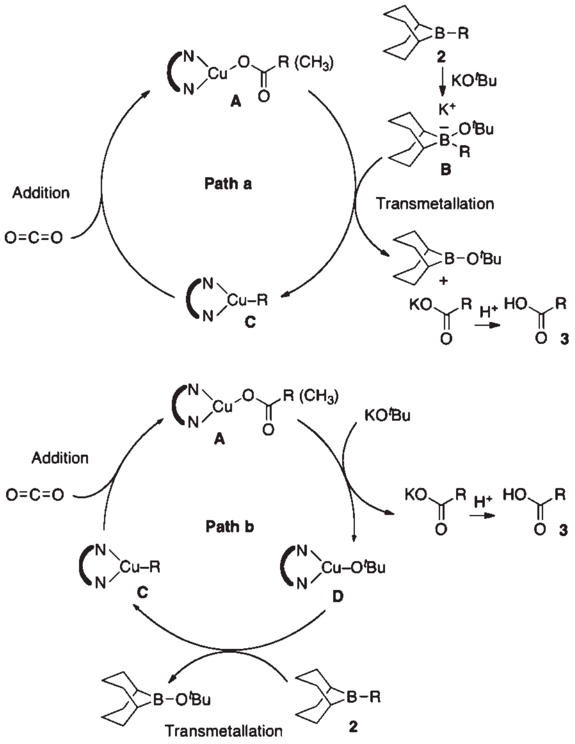
[a] The reaction was carried out with $CO_2$ (1 atm, balloon), alkylborane **2** (0.5 mmol), CuOAc (10 mol %), 1,10-phen (10 mol %), and KO$^t$Bu (1 equiv to **1**, 0.5 mmol) in toluene at 100 °C for 12 h. Alkylborane **2** was prepared in advance by hydroboration of **1** with 9-BBN dimer in toluene at 60 °C for 1 h and used without purification. [b] Isolated yield. [c] After hydrolytic workup and methylation with $TMSCHN_2$, the product was isolated as its methyl ester. [d] NMR yield.

between the borate **B** and a 1,10-phenanthroline-ligated copper carboxylate **A** (or an alkoxocopper **D** shown in path b for the initial cycle) occurs to form an alkylcopper(I) species **C** in the same way as the recently reported Cu-catalyzed allyl−*alkyl* coupling between allylic phosphates and *alkyl*boranes.[11a] Finally, the addition of the alkylcopper species **C** across the C=O bond of $CO_2$ (in place of the C=C bond of the allylic phosphates) occurs to afford the carboxylate complex **A**.

In path b, the reaction of the copper carboxylate **A** and KO$^t$Bu initially gives an alkoxocopper **D**.[4c] Next, the transmetalation between the alkylborane **2** and the alkoxocopper **D** forms the alkylcopper **C**. The addition of the Cu−C bond of **C** across the C=O bond of $CO_2$ affords the carboxylate complex **A**.

At present, neither pathways can be ruled out. Nevertheless, the former (path a) seems to be more plausible because

**Scheme 2.** Possible Reaction Pathways



the coexistence of the alkylborane **2** and KO$^t$Bu as in path b is improbable. In fact, when a toluene-$d_8$ solution of $PhCH_2CH_2$-9-BBN was treated with *t*-BuOK (1:1) at 100 °C for 10 min, a complete conversion of the borane $PhCH_2CH_2$-9-BBN ($\delta$ 87.5, rt) into a tetravalent borate (**B**) occurred as confirmed by $^{11}B$ NMR spectroscopy ($\delta$ −1.6, rt). Subsequent mixing of the borate (1:1) with CuOAc/1,10-phen at 100 °C for 1 h resulted in the formation of 9-BBN-O$^t$Bu ($\delta$ 54.7, rt).[13]

In summary, we have developed a copper-catalyzed carboxylation of alkylboron compounds (alkyl-9-BBN) with $CO_2$ to afford alkanoic acids.[10] The alkylboranes are easily and widely available through the alkene hydroboration, and thus the overall process represents a reductive carboxylation of alkenes with $CO_2$.[8e,9] The broad functional group compatibility and the inexpensiveness of the Cu/1,10-phen catalyst system are attractive features of this protocol.

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**Supporting Information Available.** Experimental details and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) See Supporting Information for details of the NMR studies. In addition, the $^{11}B$ NMR study in our previous work on the Cu-catalyzed allyl−*alkyl* coupling between allylic phosphates and *alkyl*boranes supports the formation of the borate **B** (path a) (see ref 11a). Thus, the reaction of $PhCH_2CH_2$-9-BBN with *t*-BuOK (1:1) in THF-$d_8$ at rt for 5 min resulted in a complete conversion of $PhCH_2CH_2$-9-BBN ($\delta$ 65.7) into a tetravalent borate ($\delta$ −1.4). Subsequent treatment of the solution with CuOAc (B/Cu 1:1) afforded 9-BBN-O$^t$Bu ($\delta$ 55.1).