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# Catalytic Diboration of Aldehydes via Insertion into the Copper−Boron Bond

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A copper(I) boryl complex, the first of its kind to be characterized, reacts with carbon dioxide under remarkably mild conditions to form carbon monoxide plus a copper(I) borate.[1,2] The identity of the initial product of $CO_2$ insertion remains elusive, because CO is generated fairly rapidly even at −60 °C. To explore the reactivity of the copper−boron bond toward other substrates containing the C═O group, we have investigated the insertion of aldehydes. Insertion reactions of alkynes,[3a−c] α,*β*-unsaturated ketones[3c] and alkenes[3d] into metal−boron bonds have been studied, but 1,2-insertion products derived from carbonyl substrates had not been described.[4]

A further goal of this effort was the development of new catalytic borylation reactions using aldehyde substrates. Organoboron compounds are valuable reagents in organic synthesis, because of the synthetic versatility of the carbon−boron bond.[5] An important class of borylation reactions involves the catalytic addition of diboron reagents[6] across unsaturated organic substrates such as alkenes,[7] alkynes,[8] allenes,[9] and α,*β*-unsaturated ketones.[10] The 1,2-diboration of carbon−heteroatom double bonds is rare, but has been achieved in the case of aldimines[11] and thioketones.[12] The use of aldehyde substrates has given rise to complex reactivity,[13] and the isolation of 1,2-diboration products from these reactions has not been reported.

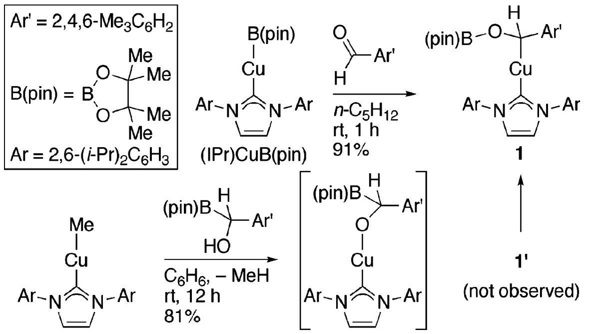
We now report the insertion of an aldehyde carbonyl group into a metal−boron bond, leading to metal−carbon *σ*-bond formation. Subsequent reaction with a diboron reagent in the presence of additional aldehyde results in carbon−boron bond formation and catalytic turnover. A closely related system catalyzes the efficient 1,2-diboration of a range of aldehydes, forming potentially useful α-hydroxyalkyl anion equivalents.[14]

Mesitaldehyde reacts rapidly with (IPr)CuB(pin) (IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene, pin = pinacolate, 2,3-dimethyl-2,3-butanediolate) in $C_6D_6$ solution, forming the single product **1** as judged by NMR spectroscopy (Scheme 1). The $^{11}B$ NMR shift of **1** (21.8 ppm) is consistent with the presence of a neutral boron center bound to three oxygen atoms.[15] The X-ray crystal structure of **1** confirmed the formation of Cu−C and B−O bonds (Figure 1a). The $Cu-C_{alkyl}$ bond distance of 1.9473(19) Å is similar to those in the previously reported $(IPr)CuCH_3$ (1.913(6) Å)[16] and $(IPr)CuCH(Ph)CH_2B(pin)$ (1.948(3) Å).[3d] Benzene solutions of **1** are stable for days at ambient temperature.

Monitoring the aldehyde insertion by $^1H$ NMR spectroscopy, we observed no evidence for formation of the alternative regioisomer **1′**, containing a [Cu−O−C−B] linkage. An attempt to synthesize this isomer independently[17] (Scheme 1) afforded **1** as the sole observed product complex. We cannot conclude, therefore, that the 1,2-insertion of mesitaldehyde into the Cu−B bond forms **1** directly, because rearrangement of **1′** to **1** is apparently facile. Further studies are in progress.

Complex **1** reacts very slowly with a diboron reagent to form a new carbon−boron bond and regenerate the copper boryl, with 10% conversion observed by $^1H$ NMR spectroscopy after 20 h at room temperature. In the presence of both diboron reagent and mesitaldehyde (5 equiv of each), however, **1** acts as a competent precatalyst, with 4.5 equiv of the mesitaldehyde 1,2-diboration product **2** formed after 24 h. The $^{11}B$ NMR spectrum of **2** displays resonances at 22.6 ppm, characteristic of a borate ester, and at 32.7 ppm, characteristic of a boronate ester.[15] Complex **1** is essentially the only IPr-containing complex observed (∼95% of ligand resonances in the $^1H$ NMR spectrum) during this reaction.

***Scheme 1.*** Syntheses of an (α-Boroxy)benzylcopper Complex[a]



[a] (IPr)CuB(pin) generated in situ from (IPr)CuO*t*-Bu and (pin)B−B(pin). α-Borobenzyl alcohol prepared by selective hydrolysis of **2**, vide infra.

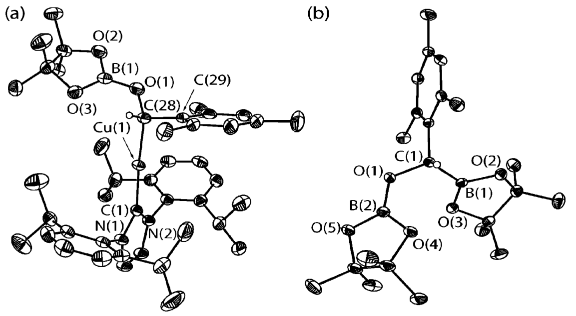


***Figure 1.*** (a) X-ray crystal structures of **1** (a) and **2** (b), shown as 50% ellipsoids. For each, one enantiomer of the racemic mixture is shown. Selected bond distances (Å) and angles (deg) for **1**: Cu(1)−C(28) 1.9473(19), Cu(1)−C(1) 1.8975(18), C(28)−O(1) 1.464(2), O(1)−B(1) 1.352(3), C(1)−Cu(1)-C(28) 175.46(8), Cu(1)−C(28)−O(1) 118.74(14), Cu(1)−C(28)−C(29) 101.94(12).

The smaller ICy (1,3-dicyclohexylimidazol-2-ylidene) proved a more effective supporting ligand for catalysis. The reaction between mesitaldehyde and (pin)B−B(pin), using 2.3 mol % (ICy)CuO*t*-Bu precatalyst, was complete after 22 h at room temperature, and **2** was isolated in 73% yield. The structure of **2** was confirmed by X-ray crystallography (Figure 1b).

The catalytic diboration procedure developed for mesitaldehyde works effectively for a variety of aldehyde substrates (Table 1). Benzaldehydes substituted with electron-donating (entries 2 and 3) and electron-withdrawing groups (entries 4−6) react in high yield, and the [(ICy)Cu] catalyst system tolerates ortho-substitution well

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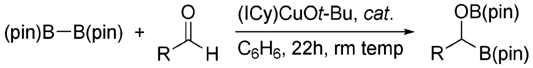
***Table 1.*** Copper-Catalyzed Diboration of Aldehydes



| entry | R = | yield (%)[a,b] | entry | R = | yield (%)[a,b] |
|---|---|---|---|---|---|
| 1 | C$_6$H$_5$ | 88 | 8 | 2,4,6-Me$_3$C$_6$H$_2$ | 73 |
| 2 | 4-MeOC$_6$H$_4$ | 86 | 9 | *n*-butyl | 94 |
| 3 | 4-MeC$_6$H$_4$ | 94 | 10 | *iso*-butyl | 95 |
| 4[c] | 4-BrC$_6$H$_4$ | 80 | 11[d] | *tert*-butyl | 71 |
| 5[c] | 4-ClC$_6$H$_4$ | 81 | 12 | cyclohexyl | 97 |
| 6[c] | 4-CF$_3$C$_6$H$_4$ | 87 | 13[e] | 3-pyridyl | 66 |
| 7 | 2-MeOC$_6$H$_4$ | 91 | 14 | 2-thienyl | 95 |

[a] Conditions: unless otherwise noted, 1 mol % (ICy)CuO*t*-Bu, 1 equiv aldehyde, 1 equiv bis(pinacolato)diboron, 22 h. [b] Isolated yield, average of two runs. [c] Reaction run using 2.3 mol % (ICy)CuO*t*-Bu. [d] Product was isolated as α-hydroxyneopentyl(pinacol)boronate after column chromatography on silica gel. [e] Reaction run using 10 mol % (ICy)CuO*t*- Bu.

(entries 7 and 8). Halogen substituents such as chloride and bromide do not interfere with the reaction. Aliphatic aldehydes bearing primary, secondary, and tertiary alkyl substituents react in excellent yield (entries 9−12). The diboration products can generally be isolated pure by filtration and reconcentration of their solutions in hydrocarbons, or by recrystallization. In the case of the oily product of pivaldehyde diboration (entry 11), an attempt at chromatographic purification on silica gel resulted in B−O bond cleavage, and the product was isolated as the α-hydroxyneopentylboronate ester. This selective hydrolysis also afforded the α-borobenzyl alcohol used in the attempted synthesis of **1′** described above.

Certain aldehydes derived from aromatic heterocycles form 1,2-diboration products in good yield (entries 13, 14). The substrate 2-pyridinecarboxaldehyde, however, undergoes reductive coupling to form a 1,2-dipyridyl-1,2-bis(pinacolboroxy)ethane as the major reaction product; the reason for this change in selectivity is currently unknown. The reaction of 4-pyridinecarboxaldehyde with (pin)B−B(pin) results in reductive coupling even in the absence of copper catalyst. Analogous reactions have been observed for sterically unencumbered aldimines.[11,18]

In the solid state, the aldehyde diboration products are stable for weeks when protected from air and light. No decomposition was observed in benzene solutions, even those saturated with water, after several days at ambient temperature. Exposure to dioxygen results in slow oxidation, regenerating the aldehydes and forming [(pin)B]$_2$O. This reaction occurs more rapidly for benzylic than for aliphatic diboration products.

In conclusion, the insertion of an aldehyde C═O group into a copper−boron bond leads to the formation of a metal−carbon *σ*-bond. The product complex undergoes further reaction with a diboron reagent in the presence of aldehyde, resulting in carbon−boron bond formation. These key processes form the basis of a versatile catalytic 1,2-diboration of aldehydes. The products of this reaction are potentially useful as masked α-hydroxyalkyl anions for organic synthesis.

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**Supporting Information Available:** Experimental procedures and characterization for all products; crystallographic data (also available as a CIF) and structure refinement details for **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

## References

(1) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196−17197.
(2) Copper(I) boryl complexes as likely intermediates: (a) Ito, H.; Yamanaka, H.; Tateiwa, J.-i.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821−6825. (b) Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47−53. (c) Ramachandran, P. V.; Pratihar, D.; Biswas, D.; Srivastava, A.; Ram Reddy, M. V. *Org. Lett.* **2004**, *6*, 481−484. (d) Ito, H.; Kawakami, C.; Sawamura, M. *J. Am. Chem. Soc*. **2005**, *127*, 16034−16035.
(3) (a) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713−720. (b) Clark, G. R.; Irvine, G. J.; Roper, W. R.; Wright, L. J. *Organometallics* **1997**, *16*, 5499−5505. (c) Onozawa, S.-y.; Tanaka, M. *Organometallics* **2001**, *20*, 2956−2958. (d) Laitar, D. S.; Tsui, E. Y.; Sadighi, J. P. *Organometallics* **2006**, *25*, 2405−2408.
(4) Selected aldehyde insertions into metal−silicon bonds: (a) Si−C/Ta−O bond formation, Arnold, J.; Tilley, T. D. *J. Am. Chem. Soc.* **1987**, *109*, 3318−3322. (b) Mn−C/Si−O bond formation, Johnson, D. L.; Gladysz, J. A. *Inorg. Chem.* **1981**, *20*, 2508−2515.
(5) (a) *Organoboranes for Syntheses*; Ramachandran, P. V., Brown, H. C., Eds.; ACS Symposium Series 783; American Chemical Society: Washington, DC, 2001. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483.
(6) For reviews, see (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1999**, *5*, 63−73. (b) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271−280.
(7) See for example (a) Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1336−1338. (b) Nguyen, P.; Coapes, R. B.; Woodward, A. D.; Taylor, N. J.; Burke, J. M.; Howard, J. A. K.; Marder, T. B. *J. Organomet. Chem.* **2002**, *652*, 77−85.
(8) See for example (a) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018−11019. (b) Iverson, C. N.; Smith, M. R., III. *Organometallics* **1996**, *15*, 5155−5165. (c) Thomas, R. L.; Souza, F. E. S.; Marder, T. B. *J. Chem. Soc*., *Dalton Trans*. **2001**, 1650−1656 and references therein.
(9) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328−16329.
(10) See for example Bell, N. J.; Cox, A. J.; Cameron, N. R.; Evans, J. S. O.; Marder, T. B.; Duin, M. A. Elsevier, C. J.; Baucherel, X.; Tulloch, A. A. D.; Tooze, R. P. *Chem. Commun.* **2004**, 1854−1855 and references therein.
(11) Mann, G.; John, K. D.; Baker, R. T. *Org. Lett.* **2000**, *2*, 2105−2108.
(12) Carter, C. A. G.; Vogels, C. M.; Harrison, D. J.; Gagnon, M. K. J.; Norman, D. W.; Langler, R. F.; Baker, R. T.; Westcott, S. A. *Organometallics* **2001**, *20*, 2130−2132.
(13) Carter, C. A. G.; John, K. D.; Mann, G.; Martin, R. L.; Cameron, T. M.; Baker, R. T.; Bishop, K. L.; Broene, R. D.; Westcott, S. A. Bifunctional Lewis Acid Reactivity of Diol-Derived Diboron Reagents. In *Group 13 Chemistry/From Fundamentals to Applications*; Shapiro, P. J., Atwood, D. A., Eds.; ACS Symposium Series 822; American Chemical Society: Washington, DC, 2002; pp 70−87.
(14) Use of α-silylalkyl-Li or -Mg reagents, followed by Si−C bond oxidation, for this purpose: (a) Tamao, K.; Iwahara, T.; Kanatani, R.; Kumada, M. *Tetrahedron Lett.* **1984**, *25*, 1909−1912. (b) Tamao, K.; Kanatani, R.; Kumada, M. *Tetrahedron Lett.* **1984**, *25*, 1913−1916.
(15) Kennedy, J. D. In *Multinuclear NMR*; Mason, J., Ed.; Plenum Press: New York, 1987; pp 221−258.
(16) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191−1193.
(17) (IPr)CuMe + ROH: Goj, L. A.; Blue, E. D.; Munro-Leighton, C.; Gunnoe, T. B.; Petersen, J. L. *Inorg. Chem.* **2005**, *44*, 8647−8649.
(18) These products have been prepared previously by McMurry-type couplings: Clerici, A.; Porta, O. *Tetrahedron* **1983**, *39*, 1239−1246.

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