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Boration of an α,β-enone using a diboron promoted by a copper(I)–phosphine mixture catalyst

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Abstract

The Cu(I)-catalyzed boration of an α , β -enone using a diboron is described. Combination of a Cu(I) salt and tributylphosphine is an effective catalyst system, though the individual use of Cu(I) and tributylphosphine is not active for the reaction. © 2000 Elsevier Science Ltd. All rights reserved.

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The addition of the compounds possessing an M–M and M–M' bond (M, M' = Si, B, Sn, Ge, S) to C–C multiple bonds catalyzed by a transition metal has been an extensively studied topic during the past decade.¹ For example, Miyaura and co-workers reported a number of studies for the Pt- and Pd-catalyzed reactions of diborons accompanied with B–B bond cleavage.² While much interest has been focused on the group 10 metals as a versatile catalyst for these reactions, few examples using other metals have been reported.³ We recently found the conjugate addition of Si–Si compounds to α , β -enones catalyzed by a Cu(I) salt.⁴ This result indicates that the Cu(I) salt would be a new promising catalyst in this area. Here we describe an unprecedented reaction of a diboron with an α , β -enone by means of a Cu(I) catalyst.⁵

We first examined the reaction between bis(pinacolato)diboron **1a** and chalcone **2a** in the presence of a catalytic amount of $(CuOTf)_2 \cdot C_6H_6$ (0.05 equiv., 0.10 equiv. for an α,β -enone as a Cu(I) salt) at room temperature (Table 1). However, no reaction products were detected (entry 1). Next, a mixture of a catalytic amount of $(CuOTf)_2 \cdot C_6H_6$ (0.05 equiv.) and tributylphosphine (0.11 equiv.) was employed. By this modified catalyst system, the reaction was dramatically improved to give boration product **3a** in good yield after hydrolysis (entry 2).⁶ It is noteworthy that the reaction temperature of this Cu(I) catalysis is lower than that of the Pt-catalyzed reaction.⁷ Addition of a phosphine is essential for the reaction (entry 2) and a less donative

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phosphine resulted in moderate yield (entry 3). In the absence of a Cu(I) salt, the addition reaction scarcely proceeded (entries 4, 5). The ratio of a phosphine ligand to a Cu(I) salt and its chelation ability affected the activity of the catalyst. Excess use of tributylphosphine decreased the yield of product (entry 6). A bidentate phosphine, such as 1,3-bis(diphenylphosphino)propane, also retarded the addition reaction, and higher temperature was needed to obtain the product (entry 7). Copper(I) chloride, a more easily accessible Cu(I) salt than air-sensitive CuOTf, was also effective in the presence of tributylphosphine, although a slightly longer reaction time was needed (entries 8, 9). DMF was a good solvent for the promotion of the reaction and a less polar solvent (THF, CH_2Cl_2 , toluene) was also useful (entries 10–13).

	1a , 1.2 equiv.	+ Ph Ph 2a	cat. CuX ligand solvent	H ₃ O⁺ →	O _B O B	o ↓ Ph
	Cu(I) salt	phosphine		temp.	time	yield ^b of 3a
entry ^a	/ equiv.	/ equiv.	solvent	/°C	/ h	1%
1	CuOTf, 0.10	-	DMF	rt	14	0
2	CuOTf, 0.10	Bu ₃ P, 0.11	DMF	rt	10	96
3	CuOTf, 0.10	Ph ₃ P, 0.11	DMF	rt	24	50
4	-	Bu ₃ P, 0.11	DMF	rt	24	7
5	-	-	DMF	rt	24	0
6	CuOTf, 0.10	Bu ₃ P, 0.22	DMF	rt	10	79
7	CuOTf, 0.10	dppp ^c , 0.11	DMF	rt	13	O^d
8	CuCl, 0.10	Bu ₃ P, 0.11	DMF	rt	15	83
9	CuCl, 0.10	-	DMF	rt	24	0
10	CuOTf, 0.10	-	THF	rt	10	0
11	CuOTf, 0.10	Bu ₃ P, 0.11	THF	rt	5	77
12	CuOTf, 0.10	Bu ₃ P, 0.11	CH_2Cl_2	rt	5	68
13	CuOTf, 0.10	Bu ₃ P, 0.11	Toluene	rt	5	63

 $Table \ 1 \\ Cu(I)\mbox{-catalyzed reactions of a diboron $1a$ to an α,β-enone $2a$ under various conditions}$

^aA mixture of a diboron **1a** (0.24 mmol), an α , β -unsaturated compound (0.2 mmol), a Cu(I) salt (0-0.02 mmol) and tributylphosphine (0-0.022 mmol) was stirred in a solvent (0.4 ml). ^bIsolated yield. c1,3-Bis(diphenylphosphino)propane. ^dProduct **3a** was obtained in 36 % yield by additional reaction time at 60 °C for 12 h.

The generality of this Cu(I) salt-catalyzed addition was demonstrated by the reaction with various α , β -enones (Table 2). Although the less-hindered substrates gave good yields (entries 1–5), the tetra-substituted enone **2g** furnished the product in a disappointing yield.

Table 2 Reactions of a diboron **1a** and α , β -unsaturated carbonyl compound **2** in the presence of a copper(I) catalyst



^aA mixture of a diboron **1a** (0.24 mmol), an α , β -unsaturated compound (0.2 mmol), a Cu(I) salt (0-0.02 mmol) and tributylphosphine (0-0.022 mmol) was stirred in a solvent (0.4 ml). ^bIsolated yield.

Oxidation of the product **3a** to the corresponding β -hydroxy ketone **4a** represents the utility of the Cu(I)-catalyzed boration for the synthesis of β -hydroxy ketones (Scheme 1). Bis(catecholato)diboron **1b** was also useful for the Cu(I)-catalyzed reaction, though the isolation of the corresponding borylated ketone from the reaction mixture was not successful. One-pot reactions of the copper(I)-catalyzed addition and oxidation gave the product **4a**, **4d** in moderate yield (Scheme 2).



Scheme 1. Oxidation of 3a with hydrogen peroxide



Scheme 2. Synthesis of β -hydroxyketone 4 by one-pot reaction of Cu(I)-catalyzed boration and oxidation

We also examined the reaction between equimolar amounts of CuCl, tributylphosphine and diboron **1a** in the absence of α,β -enones in THF under similar conditions; however, no products were observed by GC. That is, in contrast to the similar reaction of Pt complex, in which B–B bond cleavage proceeded with the oxidative addition of the diboron to the Pt metal, the copper(I) salt itself did not consume the diboron in the absence of an α,β -enone.^{2b}

We considered the coordination of the phosphine to Cu(I) to be the most important factor for the reaction. If the dominant role of the phosphine is activation of the diboron by coordination to the B atom, excess use of the phosphine should enhance the reaction. However, the opposite results were obtained (Table 1, entries 5, 6). The ³¹P NMR measurements also supported this assumption.⁸ The ³¹P NMR (109.3 MHz, DMF- d_7) spectroscopy revealed that the chemical shift of tributylphosphine (δ –30.7) was only slightly changed in the presence of an equimolar diboron **1a** (δ –31.4). On the contrary, the mixture of tributylphosphine and CuCl exhibited a significant down-field shift (δ –14.2). These results suggest that the degree of the coordination of tributylphosphine to Cu(I) is greater than that between tributylphosphine and the diboron **1a**. We assumed the complexation between a ligand and Cu(I) metal reduced the aggregation of the Cu(I) salt in a solvent and this de-aggregation would enhance the catalytic activity.

In conclusion, we have described Cu(I) salt-catalyzed boration of an α , β -enone using a diboron with cleavage of the B–B bond. These findings disclose a new catalytic ability of the Cu(I) salt as well as a new pathway for the synthesis of boron-containing compounds.

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References

 (a) Beletskaya, I.; Moberg, C. Chem. Rev. 1999, 99, 3435–3461. (b) Sharma, H. K.; Pannell, K. H. Chem. Rev. 1995, 95, 1351–1374. (c) Horn, K. A. Chem. Rev. 1995, 95, 1317–1350. (d) Irvine, G. J.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittell, G. R.; Wright, L. J. Chem. Rev. 1998, 98, 2685–2722.

- (a) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. J. Am. Chem. Soc. 1993, 115, 11018–11019. (b) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. Organometallics 1996, 15, 713–728.
 (c) Ishiyama, T.; Yamamoto, M.; Miyaura, N. Chem. Commun. 1997, 689–690. (d) Ishiyama, T.; Kitano, T.; Miyaura, N. Tetrahedron Lett. 1998, 39, 2357–2360. (e) Ishiyama, T.; Miyaura, N. J. Synth. Org. Chem., Japan 1999, 57, 503–511, and references cited therein.
- 3. Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. Angew. Chem., Int. Ed. Engl. 1995, 34, 1336-1338.
- 4. Ito, H.; Ishizuka, T.; Tateiwa, T.; Sonoda, M.; Hosomi, A. J. Am. Chem. Soc. 1998, 120, 11196–11197.
- 5. This work was partly published in the 78th Annual Meeting of Chemical Society of Japan, March 2000, 1F534, Preprint II p. 1052. During the course of our work, an analogous addition of diboron 1a to α,β-enones promoted by CuCl/KOAc was reported. See: Takahashi, K.; Ishiyama, T.; Miyaura, N. The 78th Annual Meeting of Chemical Society of Japan, March 2000, 3F405, Preprint II p. 1029. We thank Professor Norio Miyaura for sending a manuscript prior to publication which was recently accepted in *Chem. Lett.*
- 6. Representative procedure was described as follows: In a glove box, $(CuOTf)_2 \cdot C_6H_6$ (25 mg, 0.05 mmol) was weighed and placed in a two-necked round bottomed flask (30 ml) equipped with a magnetic stirring bar, a rubber septum and a reflux condenser. The reaction tube was removed from the glove box and connected with a nitrogen line. After the addition of DMF (2.0 ml) and tributylphosphine (22 mg, 0.11 mmol), the mixture was stirred for 10 min. To another reaction vessel which was dried and filled with nitrogen, the catalyst solution (0.4 ml) was transferred with a syringe and **1a** (60.9 mg, 0.24 mmol) and **2a** (41.6 mg, 0.2 mmol) were added. After the mixture was stirred for 10 h at room temperature, water (1.0 ml) was added and the resulting mixture was extracted by ethyl acetate (10 ml×3). The combined organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography (SiO₂) to give **3a** (64.6 mg, 96%). The spectral data was identical with the literature.⁷
- 7. Lawson, Y. G.; Lesley, M. J.; Marder, T. B.; Norman, N. C.; Rice, C. R. Chem. Commun. 1997, 2051–2052.
- 8. Phosphoric acid (85% solution in water) was used for external standard.