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(CAAC)CuX-catalyzed hydroboration of terminal alkynes with pinacolborane directed by the X-ligand

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ABSTRACT

When X is a basic ligand (CAAC)CuX complexes [CAAC = cyclic (alkyl) (amino)carbene] selectively promote the (*E*)-*β*-hydroboration of terminal alkynes with pinacolborane instead of the dehydrogenative borylation observed with weakly nucleophilic X ligand. This methodology is applicable to a variety of terminal alkynes. Deuterium labeling experiments coupled with stoichiometric reactions give evidence towards a plausible mechanism involving a σ-mono (copper)acetylide complex.

1. Introduction

Due to the importance of the Suzuki-Miyaura cross-coupling reaction, organoboronic esters have found wide applicability as synthons in organic chemistry [1]. Alkenyl derivatives have been prepared via transition metal-catalyzed hydroboration of the corresponding alkynes [2], with only seldom reports involving the use of inexpensive metals such as copper [3–5]]. With this metal, Yun et al. [5] recently described an elegant atom efficient methodology affording selectively the (*E*)-*β*-hydroboration or the (*Z*)-*β*-hydroboration products of terminal alkynes, using 1,8-naphthalenediaminatoborane as the borane partner. There are no extensive investigations detailing the hydroboration of terminal alkynes to afford (*E*)-*β*-hydroboration using pinacolborane and a copper catalyst. However, Hoveyda et al. [3a] demonstrated that both (E)-*β*- and *α*-hydroboration of terminal alkynes can be obtained using bis(pinacolato)diboron (PinBBPin) as the boron partner. Note that this synthetic method requires the presence of an alkoxide, which generates a stoichiometric amount of ROBPin as waste.

Previously, we reported on the role of the X ligand in the mechanism of the (CAAC)CuX-catalyzed [CAAC = cyclic (alkyl) (amino)carbene [6,7]] azide-alkyne cycloaddition (Click reaction) [8]. We showed that basic X ligands favor the metallation step leading to the σ-mono (copper) acetylide complexes **A** [8b] [9], but disfavor the formation of the catalytically active σ,π-bis(copper)acetylide **B** (Fig. 1). Conversely, non-nucleophilic ligands favor the latter but slowly promote the former; this problem could be circumvented, however, in the presence of an external base. Using this knowledge, we recently demonstrated [10] that (CAAC)CuX complexes, featuring a weakly nucleophilic X ligand such as trifluoromethanesulfonate can selectively promote the dehydrogenative borylation of terminal alkynes with pinacol borane [11]. This result is due to the formation of **B** [8] in which the triple bond is protected, and thus cannot participate in classical hydroboration. We hypothesized, that in contrast to **B**, **A** features an unprotected and polarized C—C triple bond and should readily undergo hydroboration. Here we report that indeed a simple modification of the X ligand of (CAAC)CuX complexes allows for switching the selectivity of the reaction of pinacolborane with terminal alkynes from dehydrogenative borylation to (*E*)-*β*-hydroboration.

2. Results and discussion

We started our investigation using a stoichiometric mixture of phenylacetylene **1a** and pinacolborane in C_6D_6 at room temperature for 2 h. We first checked that there was no reaction at room temperature in the absence of catalyst (Table 1, Entry 1). As

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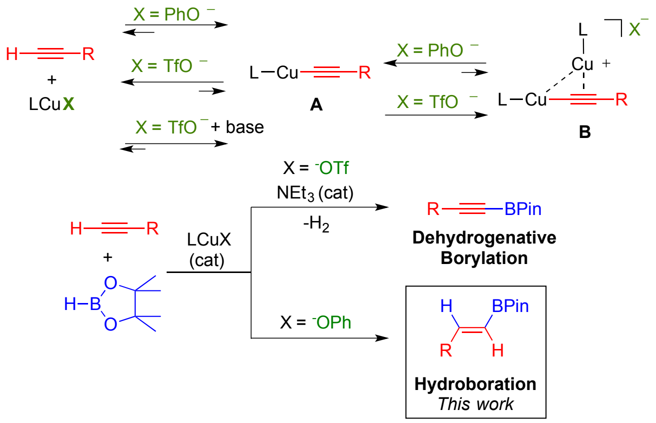
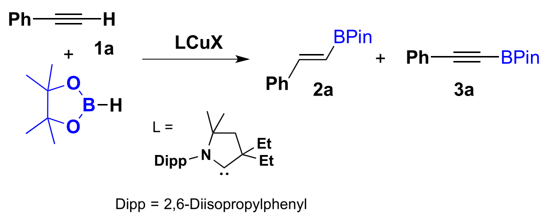


Fig. 1. (CAAC)CuOTf has been shown to promote the dehydrogenative borylation of terminal alkynes due to the formation of **B.** (CAAC)CuOPh should catalyze the hydroboration of terminal alkynes via the copper acetylides **A**.

Table 1
Effect of the X ligand, solvent, and concentration on the β-hydroboration reaction.[a]



Entry	LCuX (mol%) X	Solvent	Conc. (M)	**2a** (%)[b]	**3a** (%)[b]
1	–	C_6D_6	2.3	0	0
2	OTf (2.5)	C_6D_6	2.3	1	6
3	**OTf (2.5)**[c]	**C_6D_6**	**2.3**	**1**	**90**
4	OBz (2.5)	C_6D_6	2.3	30	20
5	OAc (2.5)	C_6D_6	2.3	40	10
6	OPh (2.5)	C_6D_6	2.3	61	0
7	OPh (2.5)	CD_2Cl_2	2.3	85	0
8	OPh (2.5)	THF-d_8	2.3	79	0
9	**OPh (2.5)**	**CD_3CN**	**2.3**	**94**	**0**
10	OPh (2.5)	CD_3CN	1.6	91	0
11	OPh (2.5)	CD_3CN	1.3	77	0
12	OPh (1)	CD_3CN	2.3	81	0
13	OPh (0.5)	CD_3CN	2.3	53	0

Bolded **Entry 3** and **Entry 9** correspond to the best reaction conditions for the selective formation of **3a** and **2a** respectively.

[a] Reactions were carried out for 2 h in a test tube at RT under an argon atmosphere using 0.69 mmol of phenylacetylene and 0.71 mmol of pinacol borane.

[b] Measured by NMR using CH_2Cl_2 or toluene as an internal standard.

[c] 5 mol% Et_3N.

previously reported [10], in the presence of 2.5 mol% of (CAAC)CuOTf no significant reaction occurred which stems for the difficulty of triflate (pK_a = −12) to deprotonate **1a** (Entry 2). However, in the presence of Et_3N (5 mol%), as an additive, selective formation of the dehydrogenative borylation product **3a** was observed (Entry 3). In marked contrast, with the more basic phenoxide anion (pK_a = 10), which favors the formation of **A** at the expense of the dinuclear complex **B**, the (*E*)-β-hydroboronic ester **2a** was obtained with no trace of **3a** (Entry 6). The influence of the basicity of the X ligand was confirmed, using the benzoate (pK_a = 4.2) and the acetate (pK_a = 4.8) (Entry 4–5).

A survey of solvent polarities (Entries 6–9) revealed that the reaction is in all cases very selective for the formation of **2a** with acetonitrile giving the best results (94% NMR yield). We found that decreasing the concentration from 2.3 to 1.6 mol/L had little effect on the selectivity (Entry 10), but further dilution to 1.3 mol/L significantly affects the formation of **2a** (Entry 11). Lastly, decreasing the catalyst loading below 2.5 mol% also proved detrimental to the reaction (Entries 12–13).

Using the optimized conditions, the scope of the hydroboration reaction was then investigated at room temperature in acetonitrile (2.3 ± 0.1 M) using 3.65 mmol of alkyne and 3.74 mmol of borane in the presence of 2.5 mol% (CAAC)CuOPh (Fig. 2). This reaction encompasses a wide range of electronically diverse terminal alkynes. In most cases, the NMR spectra of the crude reaction mixture showed excellent selectivity, and the alkenylboronic esters **2a-m** were isolated in good to excellent yields. Importantly, purification of products **2a-m** is readily achieved in air by filtration through a short plug of silica with pentane as the eluent. This protocol also allows for gram-scale syntheses, as shown with **2a**.

We then turned our attention to the mechanism of the reaction. We previously showed that (CAAC)CuOPh reacts with terminal alkynes to afford the copper acetylide complex **B** with elimination of phenol [8b]. Note that complexes of type **B** can be isolated, and that phenol readily reacts with pinacol borane to afford the catalytically inert PinBOPh (See SI for characterization). In accordance with recent work by Roesky et al., [12]] we postulate that a 1,2-addition of PinB-H across the C (sp)-C (sp) bond of **B** gives rise to a copper alkenyl boronic ester, which could not be isolated. Then, as already observed in the copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC) [8], the alkyne should be acidic enough to induce a protonolysis, which affords **2** and regenerates the copper acetylide complex **B** (Fig. 3). In order to confirm this hypothesis, we performed the catalytic reaction using deuterium labelled phenylacetylene, and as expected, we observed the formation **2a-D** (90% D-incorporation). In addition, when a stoichiometric amount of copper phenylacetylide **Ba** and PinB-H were reacted with a

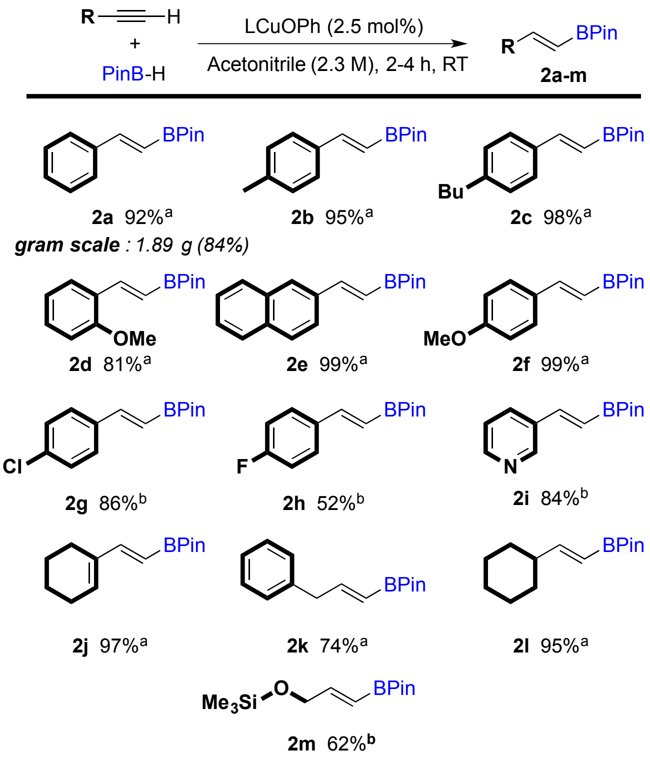


Fig. 2. Scope of the hydroboration of terminal alkynes. **[a]** reaction time 2 h **[b]** reaction time 4 h.

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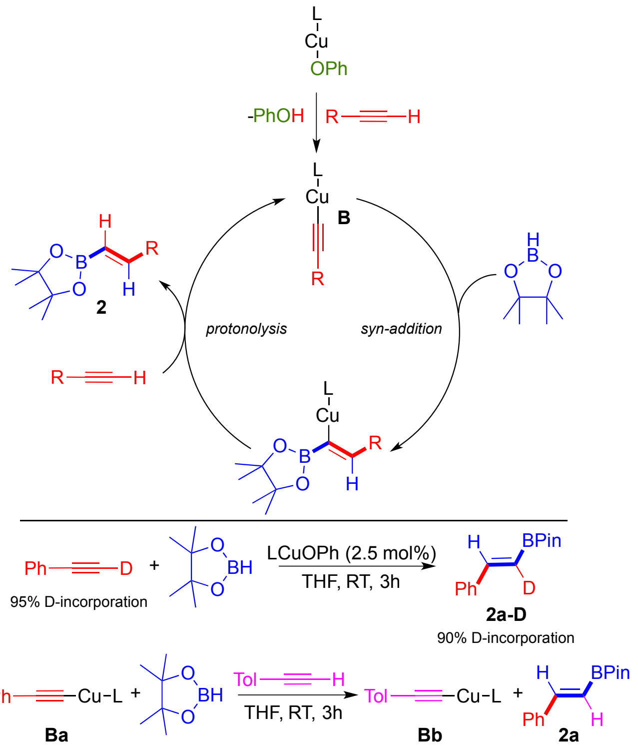

Fig. 3. Proposed mechanism and related experiments for the hydroboration of terminal alkynes.

three-fold excess of tolylacetylene, the copper tolyl acetylide **Bb** and **2a** were isolated.

In summary, we have shown that a simple replacement of a weakly coordinating X ligand by a basic anion allowed for switching the fate of the (CAAC)CuX catalyzed reaction of pinacolborane with terminal alkynes. Whereas with X = OTf a dehydrogenative borylation occurs, with X = OPh (E)-β-hydroboration takes place. Deuterium labeling experiments coupled with stoichiometric reactions suggest that a σ-mono (copper)acetylide is the key catalytic species in the hydroboration. The importance of the X ligand in other copper catalyzed reactions is under active investigation.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2016.09.025.

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