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Regioselective copper-catalyzed aminoborylation of styrenes with bis(pinacolato)diboron and diazo compounds†

[illegible],[a] Z[illegible][a] [illegible]*[ab]

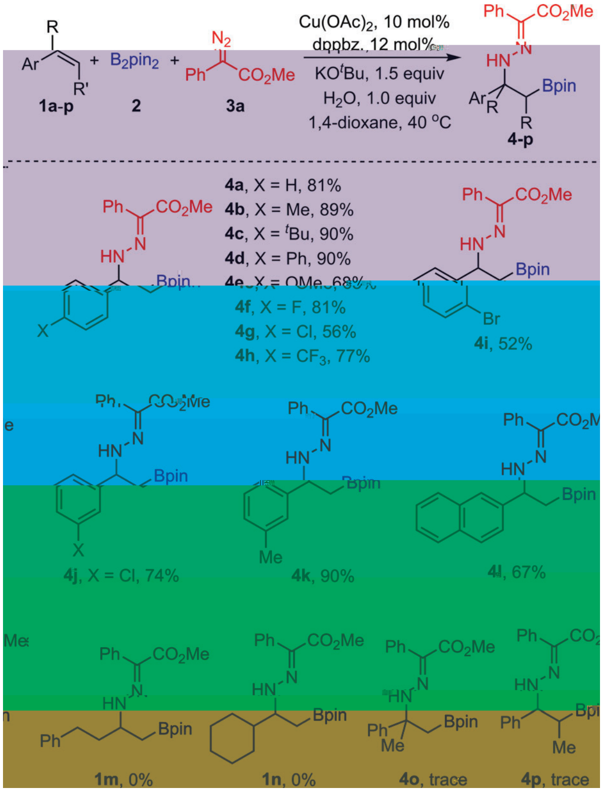
A Cu(I)-catalyzed aminoborylation reaction of styrenes is reported.

Cui and co-workers reported a Fe-catalyzed hydroamination of olefin with diazo compounds for the synthesis of hydrazone.[11] As a continuation of our efforts in the development of transformations of diazo compound, herein we report a Cu(I)-catalyzed aminoborylation of styrenes using bis(pinacolato)diboron (B_2pin_2) as the nucleophilic boryl source and diazo compounds as the electrophilic amination agents. The reaction is under mild conditions and is highly regioselective, affording various borylated hydrazone products.

We began the optimization studies with 1-methyl-4-vinylbenzene **1a**, bis(pinacolato)diboron (pinB-Bpin) **2**, and methyl α-diazophenylacetate **3a** as the model substrates. Initially, the aminoboration reaction was conducted in the presence of $Cu(MeCN)_4PF_6$/dppe catalytic system using NaO^tBu as base in THF at 80 °C. The desired product **4a** was formed in only 18% yield. Study of the effect of base indicated that the counter ions of the *tert*-butoxide bases had significant influence on the reaction, and the use of KO^tBu increased the yield to 42% (entries 1–3). Further examination of solvent effects revealed that 1,4-dioxane gave **4a** in highest yield (entries 4–7). The effect of temperature was also investigated. Reducing the reaction temperature from 80 °C to 40 °C led to an increase in the yield (entries 8–9). However, the yield diminished at room temperature (entry 10). Thus, the reaction at 40 °C offered the optimal result. The desired product **4a** could be obtained in 66% yield in 1,4-dioxane at 40 °C when using KO^tBu as the base (Table 1).

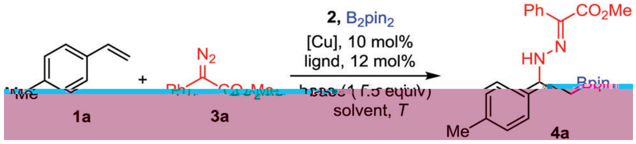
Although Cu(I) is likely the active form of the catalyst, Cu(II) complexes may be used as pre-catalyst because they can be reduced by the diazo substrates. Therefore, Cu(II) complexes were next examined in combination with the dppe ligand. While $CuCl_2$ impaired the reaction outcomes (entry 12), higher yield was observed with $Cu(OAc)_2$ as the catalyst (entry 13). With $Cu(OAc)_2$ some typical bidentate ligands were further screened (entries 14–16). The reaction with dppbz as the ligand afforded **4a** in high yield of 82% (entry 16). Finally, we reasoned that introduction of proton source to the reaction could be beneficial, and we thus carried out the reaction by adding one equivalent of H_2O. The yield of the reaction was indeed improved to 90% (entry 17).

With the optimized conditions in hand, we then investigated the scope of the styrenes using **3a** as the electrophilic nitrogen source. A variety of styrenes bearing different substituents on the aromatic rings was reacted smoothly, affording the corresponding borylated hydrazones in moderate to good yields (Scheme 2, **4a–l**). Both electron-withdrawing groups and electron-donating groups at the *para*-position of styrenes have little influence on the reactions (Scheme 2, **4b–h**). Substituents at the *ortho-* or *meta*-position of styrenes were also tolerated under the optimized reaction conditions (Scheme 2, **4i–k**). The naphthyl substituted substrate also worked in this reaction, giving the product **4l** in 67% yield. However, α-olefins such as 4-phenyl-1-butene **1m** and cyclohexylethene **1n** did not yield the corresponding products under identical conditions. The reaction of sterically hindered α-methylstyrene **1o** and *trans*-β-methylstyrene **1p** produced the aminoborylation products in only trace yield.



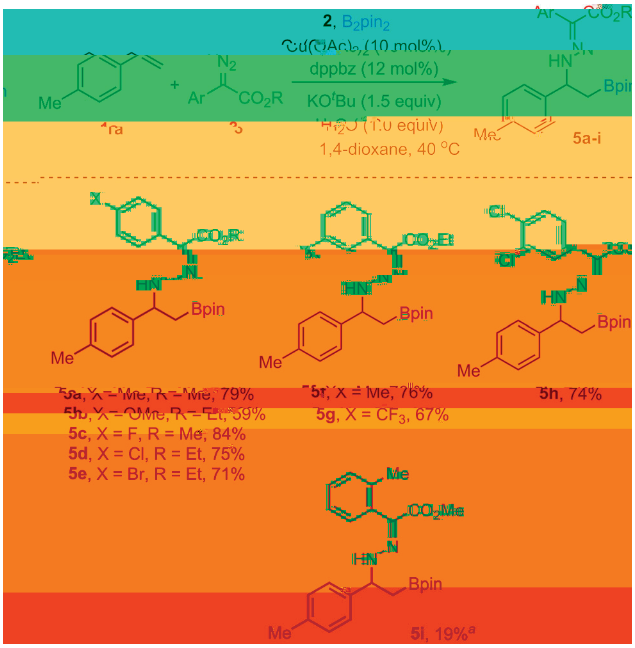
Scheme 2 **1** (0.1), **2** (0.15), **3a** (0.15), ( )$_2$ (10 %), z (12 %), ^{t} (1.5 .), $_2$ (1.0 .) 1,4- (1) 40 ° 3 ,

Table 1 z^{a}



Entry	[Cu]	Ligand	Base	Solvent	T (°C)	Yield^{b} (%)
1	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	THF	80	18
2	$Cu(MeCN)_4PF_6$	dppe	LiO^tBu	THF	80	11
3	$Cu(MeCN)_4PF_6$	dppe	KO^tBu	THF	80	42
4	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	Toluene	80	32
5	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	Dioxane	80	43
6	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	MeCN	80	2
7	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	DCE	80	30
8	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	THF	60	31
9	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	THF	40	39
10	$Cu(MeCN)_4PF_6$	dppe	NaO^tBu	THF	rt	24
11^{c}	$Cu(MeCN)_4PF_6$	dppe	KO^tBu	Dioxane	40	66
12^{c}	$CuCl_2$	dppe	KO^tBu	Dioxane	40	58
13^{c}	$Cu(OAc)_2$	dppe	KO^tBu	Dioxane	40	74
14^{c}	$Cu(OAc)_2$	dppf	KO^tBu	Dioxane	40	23
15^{c}	$Cu(OAc)_2$	Xantphos	KO^tBu	Dioxane	40	40
16^{c}	$Cu(OAc)_2$	dppbz	KO^tBu	Dioxane	40	82
17^{c,d}	$Cu(OAc)_2$	dppbz	KO^tBu	Dioxane	40	90

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), **3a** (0.15 mmol), catalyst (10 mol%), ligand (12 mol%), base (1.5 equiv.) and 1,4-dioxane (1 mL) under nitrogen at 40 °C for 10 h. [b] Determined by ^1H NMR analysis using nitromethane as the internal standard. [c] Reaction time was 3 h. [d] H_2O (1.0 equiv.) was added.

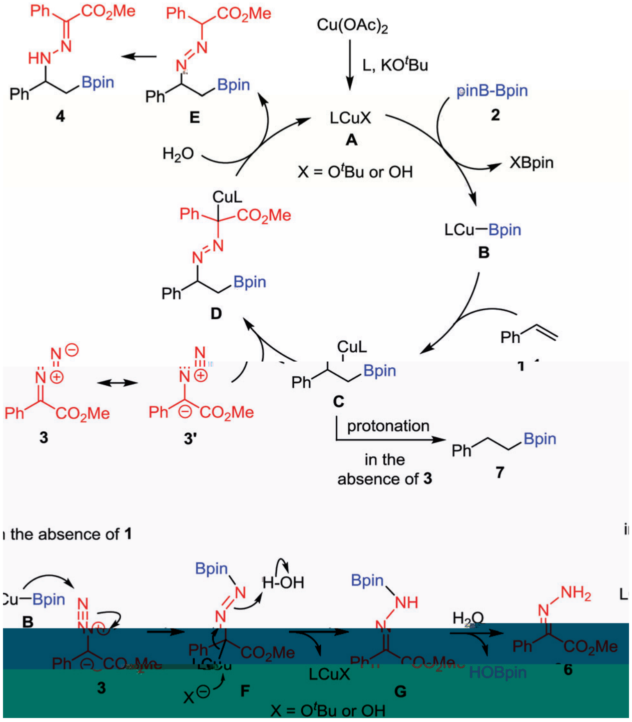


Scheme 3 z 1 (0.1), 2 (0.15), **3a** (0.15), ( )$_2$ (10 %), z (12 %), ^{t} (1.5), $_2$ (1.0) 1,4- (1) 40 ° 3 , ^{a} ^{1}

Next, we explored the reaction scope with various diazo compounds. Methyl-substituted aryl diazoesters at *para*-position and *meta*-position proceeded well to give similar yields (Scheme 3, **5a** and **5f**). However, the reaction with *ortho*-substituted aryl diazoesters only afforded the product in low yield (Scheme 3, **5i**). Importantly, both electron-donating and electron-withdrawing substrates could provide satisfactory results. Moreover, halogen-substituted aryl diazoesters with *p*-F, *p*-Br, *p*-Cl and *m*,*p*-Cl_2 substituents also provided excellent yields (Scheme 3, **5c–h**).

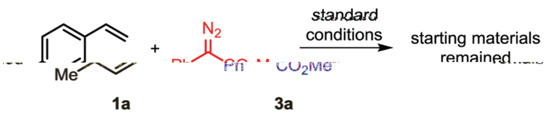
To gain insights into the reaction mechanism, we performed the following control experiments. Firstly, when the reaction was conducted in the absence of B_2pin_2, 4-methylstyrene **1a** and methyl α-diazophenylacetate **3a** remained completely unchanged (eqn (1)). Next, in the absence of 4-methylstyrene **1a**, α-diazophenylacetate **3a** was converted to hydrazone **6** under the standard conditions, and no other products could be observed except the recovery of unreacted **3a** (eqn (2)). Finally, reaction of 4-methylstyrene **1a** and B_2pin_2 in the absence of diazo substrate afforded the hydroborative product **7** in 90% yield (eqn (3)).

Based on the results of the control experiments, and also according to our understanding of diazo chemistry and the literature precedents, a plausible mechanism was proposed as shown in Scheme 4. In the presence of ligand and LiO^{t}Bu, $Cu(OAc)_2$ is initially reduced, generating the active catalyst Cu(I) species **A.**[12] **A** undergoes transmetalation with B_2pin_2 to give borylcopper(I) species **B**. *syn*-Addition of **B** to the styrene affords benzylcopper species **C**, which reacts as a nucleophile trapped by nitrogen electrophile such as diazo compounds to afford intermediate **D**. Protonation of **D** by H_2O followed by



Scheme 4

rapid isomerization of **E** furnishes the borylated hydrazone products. In the absence of styrene **1**, the diazo ester **3** is reduced to hydrazone **6** (eqn (2)) through intermediates **F** and **G**. In striking contrast to this, in the absence of diazo substrate **3** the intermediate **C** will be protonated to give hydroborative product **7** (eqn (3)).



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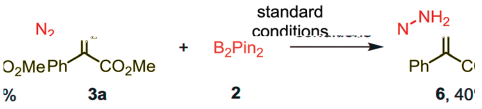

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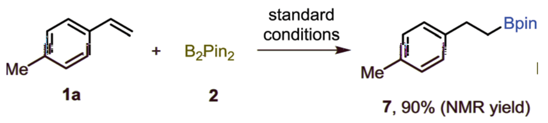

(3)

In summary, we have developed a copper-catalyzed regioselective aminoborylation of styrenes. In contrast to previous aminoborylation of alkenes, this reaction utilizes diazo compounds as the electrophilic amination agent, producing diverse borylated hydrazones which are difficult to access by other means. This protocol features mild reaction conditions and a broad range of functional groups are tolerated. Further extensions of this work, including the *in situ* transformation of the aminoborylation products, and asymmetric version of the reaction are currently underway in our laboratory.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

1 For reviews, see: (*a*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; (*b*) T. Hayashi and K. Yamasaki, *Chem. Rev.*, 2003, **103**, 2829; (*c*) N. Miyaura, *Bull. Chem. Soc. Jpn.*, 2008, **81**, 1535.

20For selected reviews, see: (*() f2.2220T(,)--.020212AngT.1Tf.8302hem.TJF111Tf-0.3.3,2uTf*