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ABSTRACT: In the last 15 years, copper-catalyzed borylative transformations utilizing boryl–copper have been established as a powerful activation mode in organic synthesis and catalysis, enabling direct transformations of various π-systems. Although many of these transformations use NHC ligands (NHC = N-heterocyclic carbene), these studies have been almost exclusively limited to the derivatives of imidazol-2-yldienes. However, the molecular properties of N-aryl-imidazol-2-yldienes, such as IPr (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene), are limited by (1) the high degree of heteroatom stabilization, and (2) symmetrical substitution of the nitrogen atoms. Herein, we report a study on Cu(I)-thiazol-2-yldienes, thia- zole analogues of imidazol-2-yldienes, which (1) feature distinct half-umbrella shape of the coordinating ligand, and (2) exhibit lower heteroatom stabilization of the ancillary ligand through reduced π donation from sulfur. We present the development of a family of stable Cu(I)-thiazol-2-yldienes, where the combined steric of thiazol-2-yldienes lead to monomers [Cu(NHC)X] or bridged-halo dimers [Cu(NHC)(μ-X)]2, their crystallographic characteristics, and application to the hydrobor a tion of alkynes to afford substituted vinylboronates by β-hydroboration of internal alkynes or terminal vinylboronates by β-hydroboration of terminal alkynes. Application to the late-stage modification and detailed mechanistic studies on the catalyst structure and activation are presented. Most crucially, Cu(I)-thiazol-2-yldienes show much higher β-selectivity in hydroboration of alkynes than classical imidazol-2-yldienes, affording vinylborons in excellent yields at ambient conditions. The unique ‘half-umbrella’ shape of thiazol-2-yldienes reverses the α:β regioselectivity observed with imidazol-2-yldienes in hydroboration of terminal alkynes. Kinetic studies demonstrate that Cu(I)-thiazol-2-yldienes supersedes imidazol-2-yldienes. Considering the significant utility of borylative transformations of π-systems, we anticipate that Cu(I)-thiazol-2-yldienes will advance the synthetic transformations of boryl–copper in organic synthesis and catalysis.

KEYWORDS: copper catalysis, thiazol-2-yldiene, N-heterocyclic carbenes, hydroboration, DFT studies

Introduction

Organoboron compounds are one of the most important motifs in organic synthesis. The versatile reactivity as organoborons as precursors to a plethora of molecules bearing diverse functional groups has spurred an array of methodologies for the synthesis of C–B bonds.1–4 Among the methods developed, one of the most powerful are Cu-catalyzed functionalizations of π-systems (Figure 1A).5

These reactions enable to install a boronate and an electrophile in a programmed fashion across unsaturated systems and can be engaged in sequential and cooperative processes, resulting in a significant utility in the preparation of organoborons.6 To date, this reactivity platform has been shown to be uniquely effective with a variety of π-systems and electrophiles, including alkynes, allenes, alkenes, heterocycles as well as polar derivatives, such as ketones, aldehydes, acid halides, imines and epoxides.7 Mechanistically, these reactions involve generation of boryl–copper species, which adds across π-unsaturation to give organocopper that participates in subsequent transformations.8
A. Cu-Catalyzed Borylcupration of $\pi$-Systems: Essential Reactivity Platform

\[
\begin{align*}
\text{R} - \text{R} & \xrightarrow{\text{Cu(I)}} \text{[Cu]} - \text{R} + \text{Bpin} \\
\text{[Cu]} - \text{R} & \xrightarrow{\text{E}^*} \text{[Cu]} - \text{R} - \text{Bpin}
\end{align*}
\]

- valuable organoboranes
- electrophile trapping ($>20$ electrophile classes)
- $\pi$-systems ($>10$ generic substrate classes)
- transmetalation (cooperative catalysis/cross-coupling)
- common feature: Cu-NHC catalysis

B. Cu-Thiazol-2-ylidene: Non-Classical N-Heterocyclic Carbenes (this study)

![Image](image_url)

**Figure 1.** (A) Cu(I)-catalyzed borylcupration of $\pi$-systems. (B) Cu(I)-thiazol-2-ylidene: non-classical, sterically- and electronically-unique Cu(I)-NHCs for borylcupration of $\pi$-systems (this study).

Since the seminal studies by Hoveyda,\(^9\) Cu(I)-NHCs (NHC = N-heterocyclic carbenes) are a major direction in the development of new transformations of boryl-copper species. Studies by Sadighi,\(^10\) Tsuji\(^11\) and others\(^12\) have shown the stabilization of NHC-ligated boryl-copper and its role as an active species in this particularly useful borylcuprative reactivity platform. While many of these transformations use NHC ligands, these studies have been almost exclusively limited to the derivatives of imidazol-2-ylidenes.\(^13\) However, the properties of N-aryl-imidazolylidenes, such as IPr (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene), are limited by (1) the symmetrical substitution of the nitrogen atoms, and (2) high degree of heteroatom stabilization.\(^14\) To fully exploit the potential of NHC ligands in borylcupration of $\pi$-systems it is critical that new active NHC ligands are identified to expand the reactivity of imidazol-2-ylidene.

Herein, we report the first study on Cu(I)-thiazol-2-ylidenes, thiazole analogues of imidazol-2-ylidenes (Figure 1B). These thiazole-based ligands (1) feature distinct half-umbrella shape of the coordinating ligand, which leads to a differential steric impact during the migratory insertion of the copper-boryl species to $\pi$-systems, and (2) exhibit lower degree of heteroatom stabilization of the ancillary ligand through reduced $\pi$-donation from sulfur, which results in higher kinetic reactivity of the catalyst system, while maintaining the beneficial effect of the NHC ligand.\(^15\)

The following features of our study are noteworthy: (1) the development of a family of stable Cu(I)-thiazol-2-ylidenes, where the combined steric of thiazol-2-ylidenes lead to monomers [Cu(NHCX)J or bridged-halo dimers [Cu(NHC)(µ-X)]; (2) application to the valuable hydroboration of alkynes to afford trisubstituted vinylboronates by $\beta$-hydroboration of internal alkynes or terminal vinylboronates by $\beta$-hydroboration of terminal alkynes, including late-stage modification; (3) DFT studies on catalyst structure, activation and borylation selectivity. Most crucially, Cu(I)-thiazol-2-ylidene show high activity in hydroboration of alkynes, affording vinylboronors in excellent yields at ambient conditions. The unique 'half-umbrella' shape of thiazol-2-ylidene reverses the $\alpha$-$\beta$ selectivity observed with imidazol-2-ylidene in hydroboration of terminal alkynes. We fully expect that Cu(I)-thiazol-2-ylidene will advance the synthetic transformations involving boryl-copper in organic synthesis and catalysis.

**Results and Discussion**

**Design.** As part of our program in catalysis, we sought to expand the chemical space of NHC ligands for organic transformations.\(^16\) Cognizant of the properties of symmetrical and nitrogen-stabilized imidazol-2-ylidene, we proposed that improvements in catalytic activity could be achieved by exploring unsymmetrical and less heteroatom stabilized thiazol-2-ylidene. These thiazole analogues of classical imidazol-2-ylidene are inherently reactive in organocatalysis,\(^17\) where they stabilize enol Breslow intermediates, including keyl radicals, through dispersive delocalization;\(^18\) however, this class of ligands is vastly unexplored in transition-metal-catalysis.\(^16\),\(^19\)

The molecular shape of thiazol-2-ylidene presents a unique opportunity that can be defined as 'half-umbrella' shape (cf. 'umbrella' shape of classical imidazol-2-ylidene, Figure 1B), while the lack of substitution at the sulfur atom renders thiazol-2-ylidene geometrically similar to protic NHCs. Electronically, thiazol-2-ylidene are more electrophilic than imidazol-2-ylidene owing to the large radius of sulfur and reduced $\pi$ donation from sulfur.

It is important to note that the 'half umbrella' shape refers to the lack of substituent on the sulfur atom, which creates an unsymmetrical environment and is in contrast to imidazol-2-ylidene.\(^20\) The presence of methyl groups on the thiazol-2-ylidene backbone hinders the rotation of the N-Ar wingtip, providing a defined catalytic pocket. This shape is also distinct from CAAC ligands featuring a quaternary carbon atom adjacent to the carbene carbon.\(^18\) A recent study demonstrated [(CAAC)CuOTf] complexes to selectively promote dehydrogenative borylation of C(sp)–H bonds at room temperature, $\sigma$-Bis(copper) acetylide and copper hydride complexes were identified as catalytic species.\(^18\)

Our study commenced with probing the synthesis of Cu(I)-thiazol-2-ylidene (Scheme 1). Prior to our study, Cu(I)-N-aryl-thiazol-2-ylidene had not been reported, thus at the beginning it was not clear if the complexes would be stable to standard handling and isolation, factors that are critical for a successful use in catalysis.

**Synthesis.** After very extensive optimization, we identified conditions for the synthesis of Cu(I)-thiazol-2-ylidene (Scheme 1, CuCl, 1.1 equiv; KOBu, 1.0 equiv, THF, 25 °C), which afforded the desired [Cu(NHC)Cl] complexes 4a-4c in 59-70% yields. Note that the synthesis of 4a has been
previously reported.\textsuperscript{20} We also prepared the analogous iodo complexes 5\textit{a}–5\textit{c} (Cu, 1.0 equiv; K\textsubscript{2}CO\textsubscript{3}, 2.0 equiv, CH\textsubscript{3}CN, 25 °C) in 73–98% yields. Interestingly, these complexes exist as monomers [Cu(NHC)\textsubscript{2}] or bridged-halo dimers [Cu(NHC)(μ-I)] in the solid state depending on the steric properties of the thiazol-2-ylidene ligand (\textit{vide infra}).

It should be noted that N-aryl thiazolium precursors are easily available on multigram scale (Scheme 1, 1–3), providing facile entryway to study the properties of thiazol-2-ylidenes in transition-metal catalysis.\textsuperscript{17,20} Furthermore, we also probed the synthesis of an IMes analogue of thiazol-2-ylidene; however, this less sterically-hindered Cu(I) complex was found unstable.\textsuperscript{16} The synthesized complexes represent thiazole analogues of IPr in 3-aryl-4,5-dimethylthiazol-2-ylidene scaffold. The following abbreviations are used: 3\textit{a}: Me\textsuperscript{2}TPr (Me\textsuperscript{2}IPrS) 3\textit{b}: t\textsuperscript{2}TPr (t\textsuperscript{2}IPrS).

\textbf{Scheme 1. Synthesis of Cu(I)–Thiazol-2-ylidene Complexes}\textsuperscript{9}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{Scheme1.png}
\caption{Synthesis of Cu(I)–Thiazol-2-ylidene Complexes}
\end{figure}

\textsuperscript{9}Conditions: CuCl (1.1 equiv), KOtBu (1.0 equiv), THF, 25 °C, 16 h. 4\textit{a}: 59%; 4\textit{b}: 63%; 4\textit{c}: 70%; Cu(1.0 equiv), K\textsubscript{2}CO\textsubscript{3} (2.0 equiv), CH\textsubscript{3}CN, 25 °C, 16 h; 5\textit{a}: 98%; 5\textit{b}: 73%; 5\textit{c}: 82%.

\textbf{Crystallographic Characterization. All Cu(I)–thiazol-2-ylidene complexes 4\textit{a}–4\textit{c} and 5\textit{a}–5\textit{c} were found to be air- and moisture-stable. All complexes 4\textit{a}–4\textit{c} and 5\textit{a}–5\textit{c} were characterized by X-ray crystallography (Figure 2). Note that the crystal structure of 4\textit{a} has been previously reported.\textsuperscript{20} The analysis is included for comparison purposes. Complexes 4\textit{a}–4\textit{c} and 5\textit{a} are monomeric (4\textit{a}: C\textsubscript{(NHC)}–Cu–Cl, 177.0°; C–Cu, 1.871 Å; 4\textit{b}: C\textsubscript{(NHC)}–Cu–Cl, 175.6°; C–Cu, 1.869 Å; 4\textit{c}: C\textsubscript{(NHC)}–Cu–Cl, 177.2°; C–Cu, 1.868 Å; 5\textit{a}: C\textsubscript{(NHC)}–Cu–I, 176.0°; C–Cu, 1.883 Å. Complexes 5\textit{b}–5\textit{c} are symmetrical bridged halo dimers (5\textit{b}: C\textsubscript{(NHC)}–Cu–I, 107.1°, 141.9°; C–Cu, 1.911 Å; 5\textit{c}: C\textsubscript{(NHC)}–Cu–I, 117.7°, 132.3°; C–Cu, 1.922 Å). The geometry of copper in [Cu(NHC)(μ-I)]\textsubscript{2} (5\textit{b}–5\textit{c}) is trigonal planar, the bond lengths of C\textsubscript{(NHC)}–C: 1.911–1.922 Å and Cu–I: 2.475–2.739 Å are significantly longer than in the mono-mer [Cu(NHC)I] (5\textit{a}): C\textsubscript{(NHC)}–C: 1.883 Å, Cu–I: 2.385 Å. These values can be compared with the imidazol-2-ylidene complex, [Cu(IPrCl): C\textsubscript{(NHC)}–Cu–I, 176.6°; C–Cu, 1.881 Å.

A clear distinctive feature of all Cu(I)–thiazol-2-ylidene complexes 4\textit{a}–5\textit{c} is the geometry of the thiazole ring with ‘half-umbrella’ substitution and ring distortion (Figure 3), C–S–C\textsubscript{(carbene)}: 93.8–94.6°; C–N–C\textsubscript{(carbene)}: 116.3–117.9°; N–C\textsubscript{(carbene)}: 106.7–107.3°; which can be compared with symmetrical C–N–C\textsubscript{(carbene)}: 111.5° and smaller N–C\textsubscript{(carbene)}–N: 104.3° in the imidazol-2-ylidene complex, [Cu(IPrCl]. The overall effect is a unique unsymmetrical and closer impact of the N-Ar wingtip on the catalytic pocket in thiazol-2-ylidene. The linear monomeric [Cu(NHC)Cl] complexes 4\textit{a}–4\textit{c} were analysed using the method by Cavallo\textsuperscript{21} to evaluate catalytic pocket (Figure 4). The % buried volume (%\(\text{Vol}_{\text{bur}}\)) of

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{Figure2.png}
\caption{X-ray crystal structures of Cu(I) complexes (A) 4\textit{a}–5\textit{a}; (B) 4\textit{b}–5\textit{b}; (C) 4\textit{c}–5\textit{c} 50% ellipsoids. Hydrogen atoms have been omitted for clarity. CCDC 2117739 (4\textit{a}); CCDC 2117744 (4\textit{b}); CCDC 2117741 (4\textit{c}); CCDC 2117740 (5\textit{a}); CCDC 2117745 (5\textit{b}); CCDC 2117743 (5\textit{c}). Selected bond lengths [Å] and angles [°]: 4\textit{a}: Cu–Cl, 1.871(2); Cu–Cl, 2.094(7); C1–N1, 1.338(2); C1–S1, 1.700(2); C6–N1, 1.460(3); C1–N1, 1.402(3); S1–C2, 1.723(2); C1–Cu–Cl, 176.9(7); N1–C1–S1, 107.3(1); C6–N1–C1, 121.3(2); C3–N1–C1, 117.0(2); C2–S1–Cl, 94.5(1); 4\textit{b}: Cu–Cl, 1.869(4); Cu–Cl, 2.086(1); C6–N1, 1.338(5); C16–S1, 1.698(4); C1–N1, 1.452(5); N1–Cl6, 1.400(4); S1–C12, 1.724(4); C6–Cu–Cl, 175.6(1); N1–C1–S1, 107.3(1); C1–N1–C16, 120.2(3); C8–N1–C16, 116.3(3); C12–S1–C16, 93.8(2); 4\textit{c}: Cu–Cl, 1.868(3); Cu–Cl, 2.086(1); C10–N1, 1.348(5); C10–S1, 1.695(5); C4–N1–Cl6, 1.402(4); S1–C6–172.9(4); C6–Cu–Cl, 177.2(4); N1–C10–S1, 107.0(3); C4–N4–C10, 119.9(3); C8–N1–C10,
Steric Effect. To eliminate impact from steric packing, the percent buried volume (%V\textsubscript{bur}) was calculated from the optimized structures of [Cu(NHC)Cl] complexes 4a–4c and IPr at the B3LYP 6-311++g(d,p) level (Figure 5). These studies determined the %V\textsubscript{bur} of NHC in [Cu(NHC)Cl] (4a) as 35.8% (SW, 49.2%; NW, 49.2%; NE, 22.4%; SE, 22.4%), in (4b) as 53.5% (SW, 49.1%; NW, 48.2%; NE, 22.4%; SE, 22.4%) and in (4c) as 35.7% (SW, 50.0%; NW, 48.2%; NE, 22.4%; SE, 22.4%). These values can be compared with the %V\textsubscript{bur} of 42.6% (SW, 46.2%; NW, 42.6%; NE, 42.6%; SE, 42.6%) for standard imidazol-2-ylidine complex [Cu(IPr)Cl].

The optimized geometry clearly points at (1) tightening of the C–S–C(carbene) angle (4a–4c, avg. 93.9°), which can be compared with the analogous C–N–C(carbene) angle of 111.4° from [Cu(IPr)Cl] and (2) opening of the C–N–C(carbene) and N–C(carbene)–S angles in 4a–4c (avg. 117.3° and 107.5°), which can be compared with the analogous angles of 114.4° and 104.0° in [Cu(IPr)Cl]. The outcome is a much tighter control of the catalytic pocket by the N-Ar wingtip in thiazol-2-ylidenes 4a–4c than in classical imidazol-2-ylidenes (N-Ar(C\textsubscript{2}Ph))–Cu: 3.289 Å vs. 3.378 Å in [Cu(IPr)Cl]; N-Ar(C\textsubscript{2}Ph)–Cu: 3.982 Å vs. 4.205 Å in [Cu(IPr)Cl].
The scope of this Cu(I)-catalyzed hydroboronation of alkynes

With the optimized conditions in hand, we next determined the scope of this Cu(I)-catalyzed hydroboronation of alkynes using Cu(I)-thiazol-2-ylidene complex (5a) (Table 2). As shown, the scope of this hydroboronation is broad and compatible with a wide range of internal and terminal alkynes. As such, various internal alkynes were found to be excellent substrates for this reaction, delivering β-hydroboronation products as single Z isomers with >95:5 selectivity (7a–7j).

Importantly, we found that this thiazol-2-ylidene catalyst system is compatible with halides (7e), electrophilic carbenoids (7f) and both electron-rich (7g) and electron-deficient (7h) heterocycles, providing handles for further functionalization and furnishing valuable trisubstituted boronates for medicinal chemistry research. Furthermore, this protocol could be applied to terminal alkynes to deliver β-vinylboronates (7i–7l). In all cases, the products were formed as single regioisomers (β:α >95:5). Notably, this regioselectivity is reversed to the protocols using Cu(I)-imidazol-2-ylidene complexes, which deliver α-vinylboronors,9b and clearly originates from a differential steric impact of the thiazol-2-ylidene scaffold (vide infra). We found that the scope of this hydroboronation of terminal alkynes is very broad and accommodates a variety of phenylacetylenes was various steric hindrance (7k–7p) and electronic nature of the substituents (7l–7q) and the substrate being derived from estrone and 4-methylumbelliferone delivered the desired β-hydroboronation products in excellent yields with >95:5 regioselectivity, highlighting the attractive potential of thiazol-2-ylidenes in medicinal chemistry.

![Figure 6](image)

To gain further insight into the reactivity of Cu(I)-thiazol-2-ylidenes, kinetic studies were conducted (Figure 6). As shown, the thiazol-2-ylidene based catalyst 5a outperformed the standard PPr-based [Cu(IPr)] in hydroborvation of 1-phenyl-1-propyne. It is worthwhile to note that the side-by-side comparison is done between catalysts bearing the same halogen in both starting complexes. [Cu(IPr)] gives approx. 10% faster conversions than [Cu(IPr)Cl] under the same conditions. Our ongoing studies are directed at determining the effect of throw-away ligands on thiazol-2-ylidene-metal complexes on their reactivity. Furthermore, the thiazol-2-ylidene based 5a showed favorable reactivity in the hydroboration of phenylacetylene. Note that the latter process leads to different regioselectivity with thiazol-2-ylidine (β-product, >98:2) vs. imidazol-2-ylidenes (α:β product, IMes, 50:50; SiMes, 77:23; IPr, 40:60).9b In general, symmetrical imidazol-2-ylidene-copper give α or mixed selectivity of terminal alkynes depending on steric of N-wingtip. The use of different metals affects the regioselectivity.9b,7,13 Importantly, the kinetic studies are consistent with the high reactivity of Cu(I)-thiazol-2-ylidenes in the

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#Conditions: 1-Phenyl-1-propyne (1.0 equiv), Bpin (1.1 equiv), base (30 mol %), Cu(I)-NHC (1-10 mol%), ROH (2.0 equiv), solvent (0.5 M), 25 °C, 16 h. CPME: cyclopentyl methyl ether. See SI for details.

Monomeric complexes 4a–4c, 5a showed in general higher reactivity than the dimeric complexes 5b–c, suggesting that dimer dissociation might be a kinetically relevant step in this process. Further screening revealed that catalyst loading could be decreased to 2.5 mol% without a significant decrease in the reaction efficiency (Table 1, entries 7–9). An extensive evaluation of different solvents identified CPME (cyclopentyl methyl ether) as the preferred solvent for this reaction (Table, entries 10–17). Furthermore, we determined that a base selection had an important impact with NaOtBu providing the optimum yield (Table 1, entries 18–23). Finally, we screened different proton sources and found that MeOH is the most suitable for capturing the organocopper under these conditions (Table 1, entries 24–25). It is worth noting that the product of this hydroboronation is a trisubstituted vinylboronate formed by β-hydroboronation with >95:5 regio and Z-selectivity, indicating high steric control over the borolycupration and electrophilic trapping steps by the thiazol-2-ylidene scaffold.

With the optimized conditions in hand, we next determined the scope of this Cu(I)-catalyzed hydroboronation of alkynes using Cu(I)-thiazol-2-ylidene complex (5a) (Table 2). As shown, the scope of this hydroboronation is broad and compatible with a wide range of internal and terminal alkynes. As such, various internal alkynes were found to be excellent substrates for this reaction, delivering β-hydroboronation products as single Z isomers with >95:5 selectivity (7a–7j).

Importantly, we found that this thiazol-2-ylidene catalyst system is compatible with halides (7e), electrophilic carbenoids (7f) and both electron-rich (7g) and electron-deficient (7h) heterocycles, providing handles for further functionalization and furnishing valuable trisubstituted boronates for medicinal chemistry research. Furthermore, this protocol could be applied to terminal alkynes to deliver β-vinylboronates (7i–7l). In all cases, the products were formed as single regioisomers (β:α >95:5). Notably, this regioselectivity is reversed to the protocols using Cu(I)-imidazol-2-ylidene complexes, which deliver α-vinylboronors,9b and clearly originates from a differential steric impact of the thiazol-2-ylidene scaffold (vide infra). We found that the scope of this hydroboronation of terminal alkynes is very broad and accommodates a variety of phenylacetylenes was various steric hindrance (7k–7p) and electronic nature of the substituents (7l–7q) and the substrate being derived from estrone and 4-methylumbelliferone delivered the desired β-hydroboronation products in excellent yields with >95:5 regioselectivity, highlighting the attractive potential of thiazol-2-ylidenes in medicinal chemistry.

To gain further insight into the reactivity of Cu(I)-thiazol-2-ylidenes, kinetic studies were conducted (Figure 6). As shown, the thiazol-2-ylidene based catalyst 5a outperformed the standard PPr-based [Cu(IPr)] in hydroborvation of 1-phenyl-1-propyne. It is worthwhile to note that the side-by-side comparison is done between catalysts bearing the same halogen in both starting complexes. [Cu(IPr)] gives approx. 10% faster conversions than [Cu(IPr)Cl] under the same conditions. Our ongoing studies are directed at determining the effect of throw-away ligands on thiazol-2-ylidene-metal complexes on their reactivity. Furthermore, the thiazol-2-ylidene based 5a showed favorable reactivity in the hydroboration of phenylacetylene. Note that the latter process leads to different regioselectivity with thiazol-2-ylidine (β-product, >98:2) vs. imidazol-2-ylidenes (α:β product, IMes, 50:50; SiMes, 77:23; IPr, 40:60).9b In general, symmetrical imidazol-2-ylidene-copper give α or mixed selectivity of terminal alkynes depending on steric of N-wingtip. The use of different metals affects the regioselectivity.9b,7,13 Importantly, the kinetic studies are consistent with the high reactivity of Cu(I)-thiazol-2-ylidenes in the

5
Table 2. Scope of Cu(I)-Thiazol-2-ylidene-Catalyzed β-Hydroboration of Alkynes

<table>
<thead>
<tr>
<th>Alkyne Type</th>
<th>Product Structures</th>
<th>Percent Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal alkynes</td>
<td><img src="Image" alt="Internal alkynes" /></td>
<td>7a 90%, 7b 96%, 7c 72%, 7d 68%, 7e 68%, 7f 58%, 7g 63%, 7h 76%, 7i 88%</td>
</tr>
<tr>
<td>Terminal alkynes</td>
<td><img src="Image" alt="Terminal alkynes" /></td>
<td>7j 98%, 7k 96%, 7l 98%, 7m 97%, 7n 95%, 7o 98%, 7p 98%, 7q 91%</td>
</tr>
</tbody>
</table>

Late-Stage Functionalization

| ![Late-Stage Functionalization](Image) | 8, 93% | ![Late-Stage Functionalization](Image) | 9, 89% |

*aConditions: alkyn (1.0 equiv), B2pin2 (1.1 equiv), NaOEtBu (30 mol%), Cu(I)-NHC (5a) (2.5 mol%), MeOH (2.0 equiv), CPME (0.5 M), 25 °C, 16 h.

rate determining borylcupration step *(vide infra)*.

Computational Studies. To gain insight into this intriguing class of Cu(I)-thiazol-2-ylidene, density functional theory (DFT) computations based on two catalysts including [Cu(1Pr)Cl] (series A) and Cu(I)-thiazol-2-ylidene (series B) were conducted (Figure 7). The starting point for DFT calculations is LCu–Bpin. For [Cu(1Pr)Cl] or Cu(I)-thiazol-2-ylidene, alkyn Re1 coordinates to Cu center, giving the coordination complexes 1a and 1b via TS1 and TS1, respectively, depending on the two coordination modes. The free energies of activation for TS1 and TS1 are 18.8, 16.3 and 14.7, 13.2 kcal/mol series A and B, respectively. Subsequent to alkyn coordination, the alkyn group inserts to the Cu-B bond by crossing the transition states (TS2 and TS2), affording the intermediates (2a and 2b), respectively. Vibrational frequency calculations were carried out at the B3LYP/6-31G(d) level of theory to characterize all the stationary points as either minima (the number

Figure 6. Kinetic profile using thiazol-2-ylidene 5a. Conditions: 1-Phe

nyl-1-propyne (1.0 equiv), B2pin2 (1.1 equiv), NaOEtBu (30 mol%), Cu(I)-NHC (2.5 mol%), MeOH (2.0 equiv), CPME (0.5 M), 25 °C, 0-2 h.
of imaginary frequencies (NIMAG=0) or transition states (NIMAG=1). The calculation results show that all transition states have only one imaginary frequency. The number of imaginary frequencies are given in the supporting information. Relative to LCu-B(pin), the insertions overcome barriers of 17.3, 20.8 and 13.4, 19.3 kcal/mol for series A and B, respectively. These steps are exerogenic by -23.1, -32.9 and -32.6, -38.6 kcal/mol series A and B, respectively. According to our calculation results, the free energies of activation for series B is lower than that of series A. Furthermore, the differences of free energies of activation between α and β selectivity are 2.0 and 4.5 kcal/mol for series A and B, respectively, which indicates that Cu(I)-thiazol-2-yldenedes should have significantly enhanced regioselectivity and activity than [Cu(I)PrCl].

Conclusions
In summary, transformations involving boryl-copper rank among the most important processes in catalytic functionalization of π-systems. In this study, we have established Cu(I)-thiazol-2-yldenedes as a novel class of catalysts for borylcupration of alkyne. This process exploits unusual thiazol-2-yldenedes as unsymmetrical sulfur-based ‘half-umbrella’ shaped and less heteroatom stabilized NHC ligands.

We have reported the synthesis of catalysts, their crystallographic characterization and high activity in hydroboration of internal and terminal alkyne. The hydroboration of internal alkyne using Cu(I)-thiazol-2-yldenedes affords valuable trisubstituted vinylboronates by β-hydroboration. Terminal alkyne afford β-vinylboronates with excellent regioselectivity, which is opposite to the regioselectivity observed with classical imidazol-2-yldenedes. This hydroboration occurs under mild conditions, in high yields and with excellent regioselectivity, including late-stage modification of complex substrates. Structural and DFT studies have been conducted to gain insight into the catalyst structure, activation and regioselectivity of borylcupration. The high reactivity of Cu(I)-thiazol-2-yldenedes makes it clear that this class of catalysts will be useful in advancing the borylcupration platform in organic synthesis and catalysis.

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The authors declare no competing financial interest.
ASSOCIATED CONTENT
Supporting Information
Experimental procedures, characterization data, computational details, cif files, coordinates and energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES


