Regioselective transformation of alkynes catalyzed by a copper hydride or boryl copper species

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This review summarizes the transformation of alkynes using a copper hydride (Cu-H) or boryl copper (Cu-B) species as the active species. The semihydrogenation, hydrocarboxylation, and hydroboration of alkynes have been developed using Cu-H as the active species. The hydroboration, diboration, carboboration and boracarboxylation of alkynes involve the Cu-B species. These transformations afforded multi-substituted alkenes that are potentially good intermediates in organic synthesis. The key to the regioselective transformation is the addition of the Cu-H or Cu-B species to an alkyne, to afford the corresponding alkenylcopper intermediate regioselectively.

1. Introduction

Copper complexes are highly valuable reagents in organic synthesis.[1] Organocuprates are one of the most versatile synthetic tools in the total synthesis of natural products because their reactions proceed with chemo-, regio-, and stereoselectivity. To date, copper complexes can catalyze diverse organic transformations such as carbon-carbon and carbon-heteroatom bond formation.[1] Similar to the stoichiometric organoquprate system, copper-catalyzed reactions proceeded regio- and stereoselectively. In addition, activity and selectivity of the catalytic reaction can be controlled by ligand employed.

Herein, we reviewed the transformation of alkynes using a copper hydride (Cu-H)[2] or boryl copper (Cu-B)[3] species as the catalytically active species. The key to the successful transformation is the regioselective addition of Cu-H or Cu-B species to an alkyne, giving the corresponding alkenylcopper intermediate (Scheme 1). The regioselectivity can be controlled by directing effects of alkynes and the steric and electronic effect of ligands on the copper. The reactions of the alkenylcopper with various electrophiles such as alcohol, carbon dioxide (CO_2), or alkyl halide afforded the corresponding multi-substituted alkenes that are potentially good intermediate in organic synthesis. The scope and reaction mechanism of these reactions are discussed.
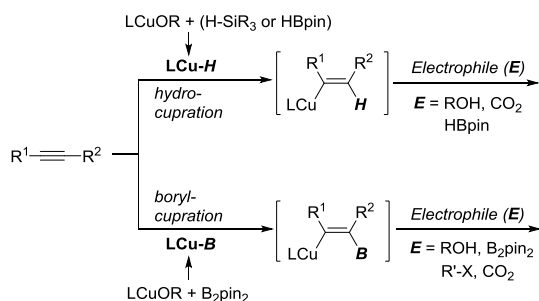

Scheme 1 Generation of alkenylcopper intermediate by the reaction of an alkyne with a copper hydride or a boryl copper species.

2. Reductive transformation of alkynes catalyzed by a copper hydride species

2.1. Synthesis of copper hydride complexes

The first example of a fully characterized copper hydride complex was reported by Churchill and Osborn in 1971.[4] The reaction of a tetrameric copper alkoxide in the presence of triphenylphosphine (PPh_3) afforded a hexameric copper hydride complex [$CuH(PPh_3)$]$_6$ (Scheme 2a). The structure of the complex was established by X-ray diffraction analysis; the six copper atoms were located at each position of an octahedron with an average Cu-Cu bond distance of 2.599 Å. Stryker and co-workers found that the complex effectively worked for the 1,4-reduction of α,β-unsaturated carbonyl compounds.[5] They also reported a conveniet procedure for the multi-gram scale preparation of [$CuH(PPh_3)$]$_6$, and the complex is now commercially available as Stryker's reagent (Scheme 2b).[6] In 2004, Sadighi and co-workers reported a copper complex with an *N*-heterocyclic carbene (NHC)[7] as the ligand; the reaction of IPrCu(O*t*-Bu) with a hydrosilane afforded the corresponding copper hydride complex.[8] The X-ray crystallographic analysis showed that the complex has a dimeric structure bridged by two hydrogen atoms. The ^{1}H NMR signal assigned to the Cu-H appeared at δ 2.36 ppm in benzene-d_6 (C_6D_6). Nolan and co-workers reported (NHC)CuH complexes showed a good catalytic activity in the hydrosilylation of various carbonyl compounds.[9] We found that a copper hydride complex with a bowl-shaped phosphine as the ligand showed the preferential reduction of a bulky ketone in the presence of an aldehyde.[10]
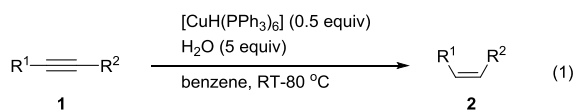
(a), (b), (c)
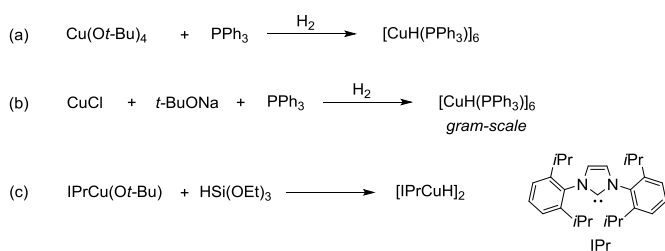
Scheme 2 Synthesis of copper-hydride complexes

2.2. Copper-catalyzed semihydrogenation of alkynes using hydrosilane

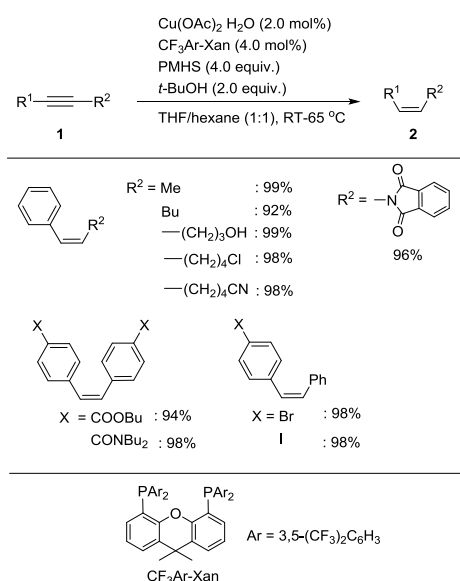The semihydrogenation of internal alkynes is a crucial methodology to afford (Z)-alkenes that are often found in many biologically active compounds. The Lindlar catalyst[11] is well known and most efficient; however, it often suffers from Z/E isomerization, low chemoselectivity, and poor reproducibility. On the other hand, several homogeneous catalysts showed good Z-selectivity in the semihydrogenation of alkynes.[12] Recently, homogeneous palladium catalysts have been extensively developed.[13]

Regarding copper complexes, a pionirring work on the stoichiometric reduction of alkynes usng [CuH(PPh₃)₆] and water was reported by Stryker (Stryker's reagent, eq 1). In the reactions, (Z)-alkenes were selectively obtained in good yields.[14]

$$R^1 \underbar{\quad} R^2 \xrightarrow[\text{benzene, RT-80 °C}]{\substack{[CuH(PPh_3)_6]\ (0.5\ equiv) \\ H_2O\ (5\ equiv)}} \quad (1)$$

We found that the semihydrogenation of alkyne (**1**) proceeded in the presence of a mixture of polymethylhydrosiloxane (PMHS) and *t*-BuOH, as the reducing reagent at room temperature (Scheme 3).[15] Employing Cu(OAc)₂·H₂O and a xantphos ligand bearing 3,5-di-(trifluoromethyl)phenyl moieties (CF₃Ar-Xan), the reaction of 1-phenyl-1-propyne and 1-phenyl-1-hexyne afforded to the corresponding (Z)-alkenes (**2**) in high yields. Diverse functionalities such as hydroxyl, chloro, cyano and phthalimido groups were tolerated in the reaction. Diphenylacetylene was also reduced to *cis*-stilbene in 93% isolated yield without the formation of bibenzyl. To our delight, the bromo and iodo moieties on the aromatic ring were intact; they may undergo the oxidative addition reaction with low-valent transition metal catalyst centers such as Pd(0).[13] The reaction of 6-dodecyne smoothly afforded to the corresponding (Z)-alkene in a good yield and with good regioselectivity.

The selective semihydrogenation of terminal alkynes is known to be difficult owing to their overreduction to the corresponding alkanes. Although Cu(OAc)₂·H₂O/CF₃Ar-Xan catalyst system was not active enough to achieve the complete conversion of terminal alkynes, the catalyst system with NHC ligand (ClIPr or MeIPr) was effective (Scheme 4). The reaction of phenylacetylene afforded styrene in 92% yield without the formation of ethylbenzene. Other aromatic and aliphatic terminal alkynes were also selectively semihydrogenated. Lalic and co-workers also reported the copper-catalyzed semihydrogenation of alkynes using Cu-NHC complexes and hydrosilane as the reducing agent.[16]

Scheme 3 Copper-catalyzed semihydrogenation of internal alkynes
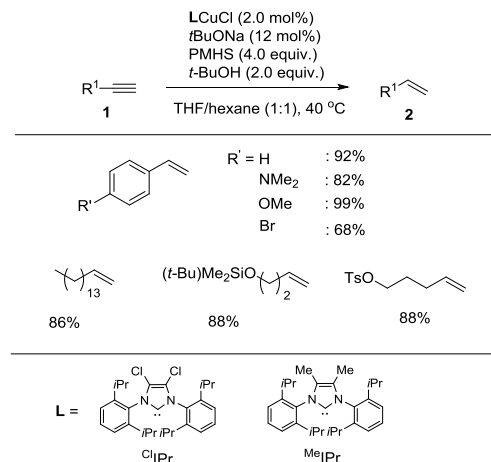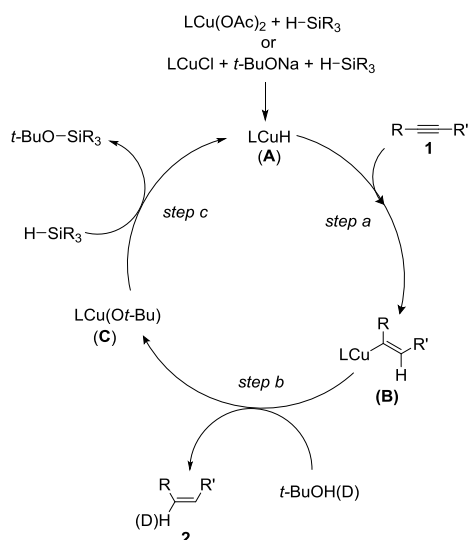

Scheme 4 Copper-catalyzed semihydrogenation of terminal alkynes

A possible catalytic cycle for the copper-catalyzed semihydrogenation of alkynes is shown in Scheme 5. A copper(I) hydride species (**A**) is generated by the reaction of the catalyst precursor with the silane. The addition of **A** to alkynes (**1**) may be much faster than that to alkenes and affords an alkenylcopper intermediate (**B**) stereoselectively via *syn*-addition (step a). Next, the protonation of **B** with *t*-BuOH affords (Z)-alkenes (**2**) selectively with the concomitant formation of LCu(O*t*-Bu) (**C**) (step b). Finally, the σ-bond metathesis of **C** with the silane regenerates **A**, and the catalytic cycle is completed (step c).

2.3. Copper-catalyzed hydrocarboxylation of alkynes using carbon dioxide and a hydrosilane

CO₂ is a readily available and renewable chemical feedstock; however, the thermodynamic stability limits its widespread use in chemical reactions. Transition-metal catalysts are required for effective utilization of CO₂.[17] To realize useful transformations of CO₂, the hydrocarboxylation of carbon-carbon multiple bonds using CO₂ is also very promising.[18,19] In 2008, the first catalytic hydrocarboxylation using CO₂ was independently reported by

Scheme 5 A possible catalytic cycle for the copper-catalyzed semihydrogenation of alkynes.

Iwasawa and Rovis. Iwasawa and co-workers found that a palladium complex with a silyl pincer ligand catalyzed the hydrocarboxylation of allene using triethylaluminum as the reducing agent.[18a] Rovis and co-workers reported the nickel-catalyzed hydrocarboxylation of styrene derivatives using diethylzinc as the reducing agent.[18b]

We reported the first catalytic hydrocarboxylation of alkynes (1) with CO_2 in the presence of a copper catalyst (Scheme 6).[19a] The reactions of alkynes were carried out using $HSi(OEt)_3$ as the reducing agent and LCuF (L = IMes or ^{Cl}IPr) as the catalyst in dioxane or hexane as the solvent. The corresponding α,β-unsaturated carboxylic acids (3) were obtained in good yields with good E-stereochemistry. In the case of diphenylacetylene, the product was obtained in 72% yield. The alkynes bearing both electron-rich and electron-poor aryl moieties afforded the corresponding products in good yields. Importantly, chloro, bromo, and alkoxycarbonyl functionalities were tolerated in the reaction. The reaction of 1-phenyl-1-propyne afforded a mixture of hydrocarboxylated products with moderate regioselectivity in the presence of ^{Cl}IPrCuF (2.5 mol%) in hexane. The reactions of unsymmetrical alkynes with cyclohexyl and t-butyl groups gave the corresponding single regioisomers in good to high yields. Later, Ma and co-workers reported the nickel-catalyzed hydrocarboxylation of alkynes using diethylzinc as the reducing agent.[19b] The reaction was very useful; however, the uses of strong and extremely air-sensitive reducing agents were indispensable in the reactions.

To gain insights into the reaction mechanism, fundamental catalytic steps in the hydrocarboxylation utilizing silanes were examined by performing the stoichiometric reactions (Scheme 7). When ^{Cl}IPrCuF, the catalyst precursor in Scheme 6, was treated with an excess amount (4 equiv) of the silanes such as PMHS or $HSi(OEt)_3$ in C_6D_6, an immediate color change from colorless to bright orange was observed. The ^{1}H NMR spectrum showed clean formation of ^{Cl}IPrCuH (**A**) with a diagnostic proton resonance of Cu-H at δ 2.39 ppm, which is close to the reported value of IPrCuH at δ 2.36 ppm.[8] The reaction of an aromatic alkyne with **A** for 2.5 h at room temperature smoothly afforded the corresponding alkenylcopper complex (**B**). The reaction of **B** with CO_2 (balloon) was very slow at room temperature; however,

the reaction proceeded smoothly at a higher reaction temperature (65 °C) for 12 h. Finally, the reaction of **C** with an excess amount (4 equiv) of $HSi(OEt)_3$ at room temperature cleanly afforded the copper hydride complex (**A**). Based on the results of the stoichiometric reactions, a plausible reaction mechanism is proposed as follows: A copper(I) hydride species is generated in situ from LCuF (L = IMes or ^{Cl}IPr) and a hydrosilane via the strong silicon–fluorine interaction. The *syn* addition of the copper hydride to an alkyne initiates the catalytic cycle and affords the alkenylcopper intermediate stereoselectively. Then, the insertion of CO_2 affords the corresponding copper carboxylate intermediate. Finally, the σ–bond metathesis of **C** with the hydrosilane gives the corresponding silyl ester, and the Cu-H species is regenerated. The insertion of CO_2 required a higher reaction temperature (65 °C), whereas the other stoichiometric reactions proceeded at room temperature. Thus, the insertion of CO_2 must be the rate-determining step.
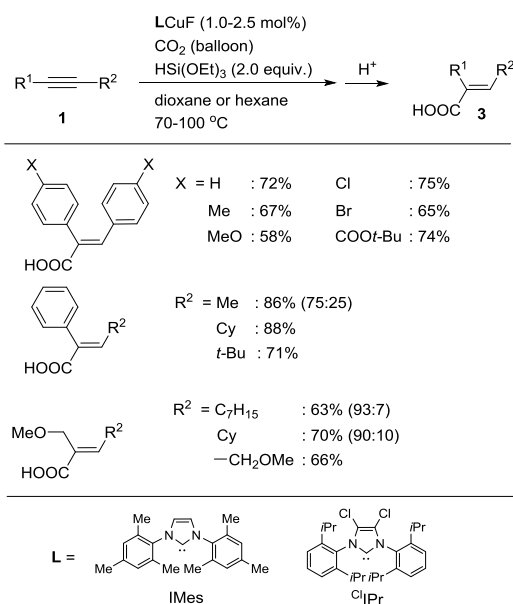
Scheme 6 Copper-catalyzed hydrocarboxylation of alkynes
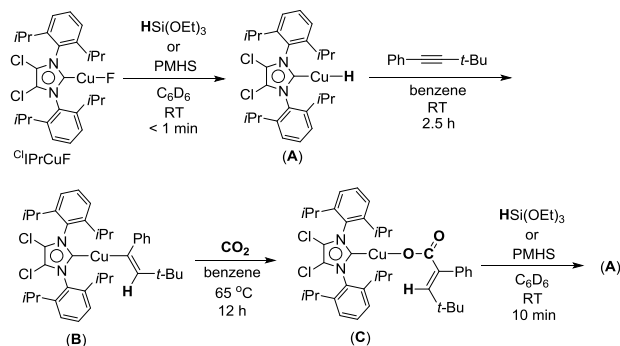

**Scheme 7** Stoichiometric reactions for the relevant to mechanism.

2.4. Copper-catalyzed hydroboration of unsymmetrical internal alkynes using pinacolborane (HBpin)

Hydroboration is a robust and practical synthetic method for the synthesis of organoboranes.[20] In particular, the hydroboration of

alkynes is interesting because the products (alkenyl boranes) are potent starting materials for the Suzuki-Miyaura cross-coupling reaction.[21] It is well known that the hydroboration of terminal alkynes proceeds regio- and stereoselectively.[22] In the case of unsymmetrical internal alkynes as the substrates, position for introducing a boron moiety has to be controlled (eq 2). However, these reactions often suffer from low regioselectivity even in the presence of a catalyst.[23]


(2)
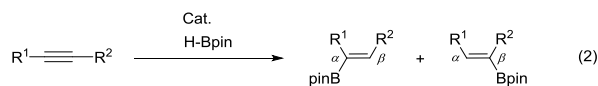
Lipshutz and co-workers reported that a copper complex catalyzed the hydroboration of alkynoates (Scheme 8).[24] The reaction of 1,2-bis(diphenylphosphino)benzene (BDP) ligand (1 mol%) with in situ generated CuH afforded [(BDP)CuH] (Method A, Scheme 8). In addition, the reaction was also carried out with commercially available Stryker's reagent (2 mol%) (Method B, Scheme 9). Both the reactions smoothly afforded the desired products with excellent Z/E ratios.
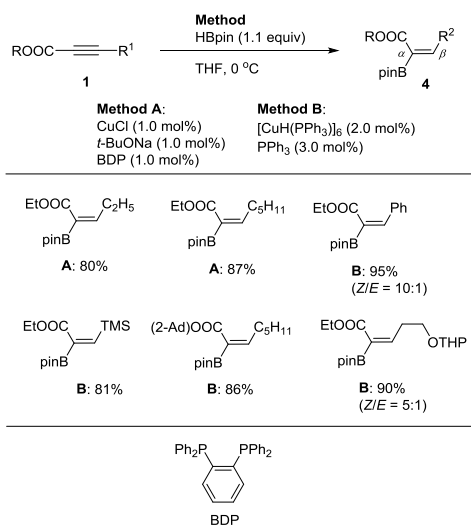

Scheme 8 Copper-catalyzed regioselective hydroboration of alkynoates.

We found that the hydroboration of unsymmetrical internal alkynes (**1**) proceeded when pinacolborane (HBpin) was used in the presence of a copper catalyst system (CuCl/t-BuONa) and xantphos derivatives bearing 3,5-xylyl moieties (MeAr-Xan) (Scheme 9).[25] The reaction of 1-phenyl-1-hexyne afforded the corresponding alkenyl borane (**4**) in 92% overall yield and with high regioselectivity. The reaction of various internal alkynes afforded the corresponding products regioselectively. Both the electron-donating and withdrawing groups on the aryl ring were tolerated while maintaining high yields and regioselectivity. The alkynes with ester and amide functionalities instead of aromatic substituents afforded the corresponding α-products in high yields and with high regioselectivity. Furthermore, the alkynes bearing O and N atoms at the propargylic position provided the corresponding α-products in good yields and with high regioselectivity when CF$_3$Ar-Xan instead of MeAr-Xan was used as the ligand.
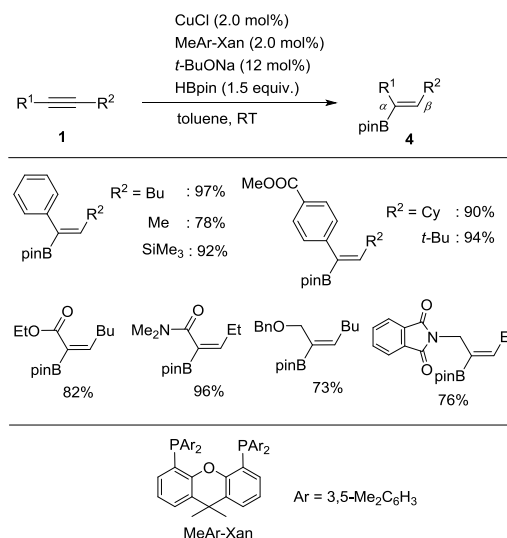

Scheme 9 Copper-catalyzed hydroboration of unsymmetrical internal alkynes employing CuCl/MeAr-Xan.

A possible catalytic cycle for the Cu-catalyzed hydroboration using HBpin is shown in Scheme 10. First, LCu(Ot-Bu) is generated from LCuCl and t-BuONa. As indicated by the clean stoichiometric reaction of [Cl]IPrCu(Ot-Bu) with HBpin, a copper hydride may be the active species in the hydroboration when HBpin is used. The syn addition of the copper hydride to the alkynes affords the alkenylcopper species with high regioselectivity because of the directing effect of the substituent. Finally, the reaction of the alkenylcopper intermediate with HBpin affords the corresponding α-borylated product (**4**) and completes the catalytic cycle by regenerating the active catalytic species, LCu-H (**A**) (step b). In addition, the Xan ligands are effective for the α-borylation reactions because their bulkiness hinders the aggregation of the Cu-H species.[2] In relevance to step b, the reaction an alkenylcopper complex bearing [Cl]IPr ligand with HBpin at 0 °C instantaneously afforded the corresponding hydroboration product in quantitative yield, and the corresponding copper hydride complex was provided cleanly, as confirmed by the ^{1}H NMR measurement (eq. 3).


(3)
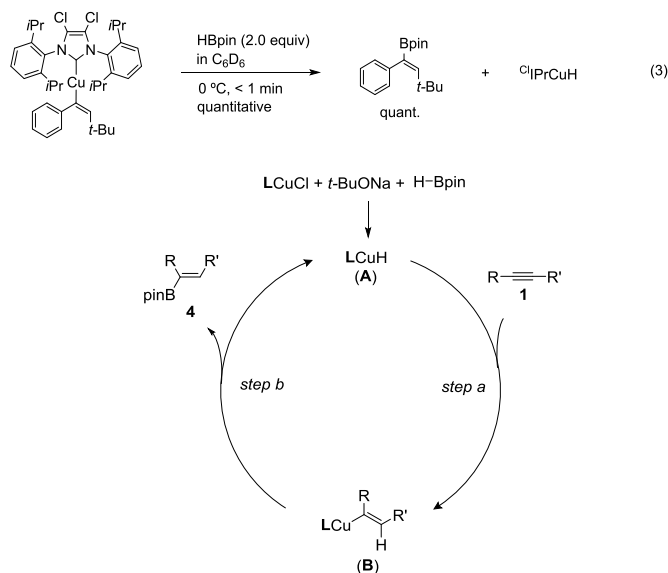
Scheme 10 A possible catalytic cycle for the copper-catalyzed hydroborat ion of unsymmetrical internal alkynes with HBpin.
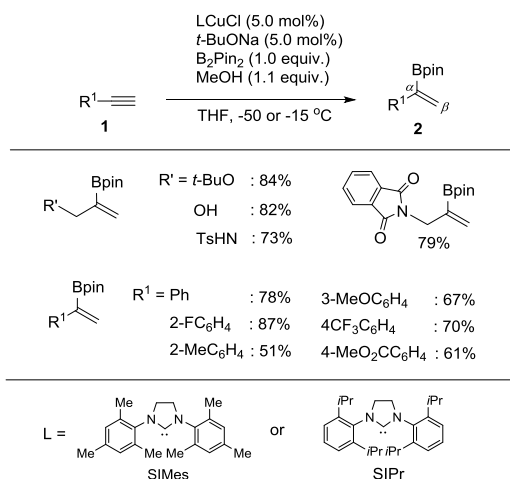
3. Borylative transformation of alkynes catalyzed by a boryl copper species

3.1. Synthesis of boryl copper complexes

Recent studies clearly show that a boryl copper species, generated by the transmetalation of bis(pinacolato)diboron (B_2pin_2) with an alkoxy or acetate copper species, is one of the most efficient borylation reagents.[3,26] In 2005, Sadighi and co-workers reported that the reaction of IPrCu(Ot-Bu) with B_2pin_2 afforded a boryl copper complex, IPrCu(Bpin), and its structure was determined by the X-ray crystallographic analysis.[27] We also determined the crystal structure of a borylcopper complex with ^{Cl}IPr as the ligand (Scheme 11).[28]

[(NHC)Cu(OtBu)]

R = H: IPr
R = Cl: ^{Cl}IPr
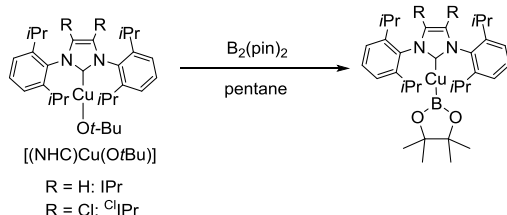
Scheme 11 Synthesis of boryl copper complexes.

3.2. Copper-catalyzed hydroboration of terminal alkynes

As mentioned in Section 2.4., the hydroboration with HBpin is a robust and practical synthetic method for the synthesis of organoboranes.[20] In contrast, B_2pin_2 may be a potentially effective borylation reagent. A pioneering work has been done by Miyaura and co-workers.[26] They carried out the reaction of terminal alkynes with B_2pin_2 in the presence of a stoichiometric amount of CuCl and AcOK in N,N-dimethylformamide (DMF) (Scheme 12). Under the reaction conditions, a mixture of regioisomers of the hydroboration products was obtained. The additives such as LiCl or phosphines affected the yield and regioselectivity of the product.


none	: 63% (92:8)
LiCl	: 90% (91:9)
P(t-Bu)$_3$	: 81% (54:46)
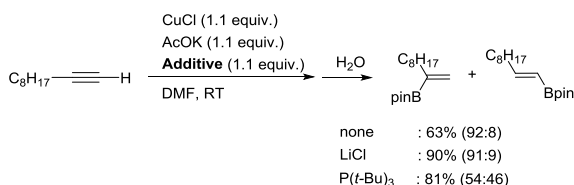
Scheme 12 Copper-mediated hydroboration of 1-decyne.

Hoveyda and co-workers reported the ligand-controlled regioselective borylation of terminal alkynes using a copper catalyst with different NHC ligands (Scheme 13 and 14).[29] When the reaction of *tert*-butyl propargyl ether was carried out with an arylsubstituted NHC ligand (SIMes), α-borylated product was obtained in 84% yield (Scheme 13). Propargyl amine derivatives also afforded the corresponding products in high yields. In the cases of arylacetylenes, α-borylation reaction proceeded in the presence of the copper catalyst bearing SIPr as the ligand.
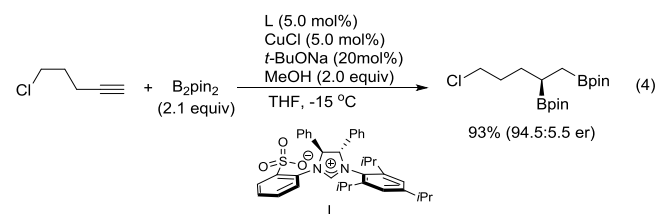

Scheme 13 Copper-catalyzed hydroboration of terminal alkynes, giving α-borylated products.

Interestingly, the regioselectivity of borylation site was switched by using a NHC ligand bearing adamantyl groups (Scheme 14).[29] The reaction of *tert*-butyl propargyl ether at 22 °C successfully afforded the β-borylated product in 80% yield. Strylene derivatibies were also converted to the corresponding β-products in good to high yields. Detailed mechanistic studies indicate that the selectivity arises from the structural and electronic properties of the NHC ligands and the alkyne substrates.
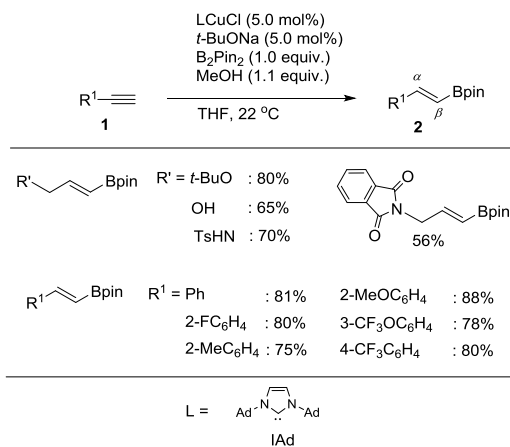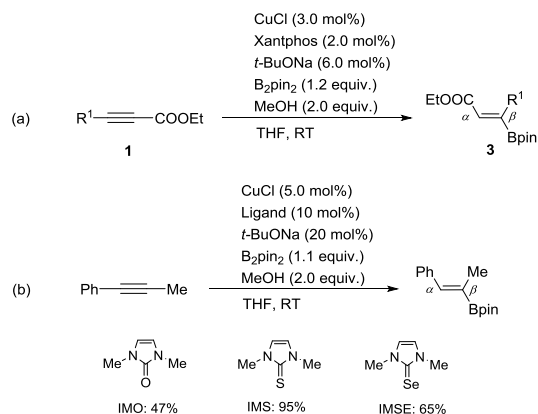

Scheme 14 Copper-catalyzed hydroboration of terminal alkynes, giving β-borylated products.

In addition, Hoveyda and co-workers also reported that vicinal diboronates were obtained by the reaction of terminal alkynes and B_2pin_2 in the presence of CuCl and a chiral NHC ligand (eq 4).[30]
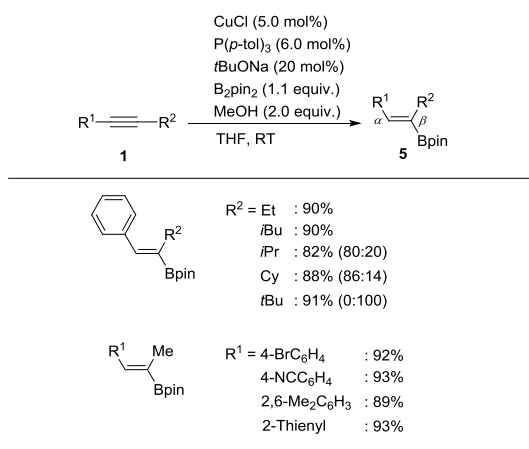
3.3. Copper-catalyzed hydroboration of unsymmetrical internal alkynes

Yun and co-workers achieved the first catalytic hydroboration of activated internal alkynes using a combination of B_2pin_2 and methanol (MeOH) as the borylation reagent (Scheme 15a).[31] The reaction of alkynoates with a catalytic amount of CuCl/t-BuONa/Xan in tetrahydrofuran (THF) at room temperature afforded the corresponding β-functional alkenylboronates in good to high yields and high regioselectivity. They also found that a copper catalyst with an imidazoline-2-thione (IMS) ligand catalyzed the hydroboration of aromatic internal alkynes (Scheme 15b).[32] Although the reaction of 1-phenyl-1-propyne afforded the corresponding product in a high yield and with high regioselectivity, the reaction with 1-pheny-1-hexyne provided the product in a moderate yield and with moderate regioselectivity.
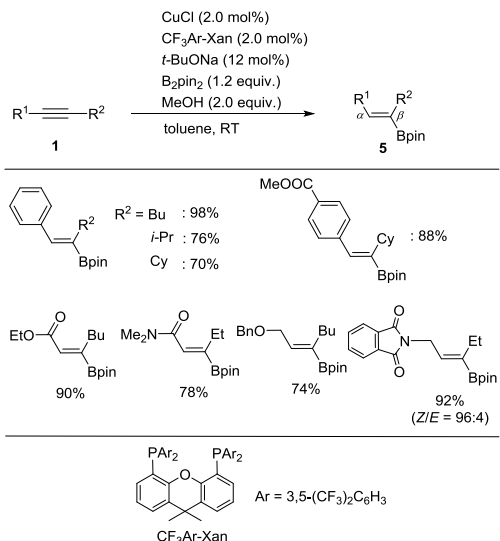

Scheme 15 Copper-catalyzed hydroboration of an alkynoate and 1-phenyl-1propyne employing B_2pin_2 and MeOH.

In 2011, Yun and co-workers reported an improved catalytic system, CuCl/t-BuONa/P(p-tol)$_3$. (Scheme 16).[33] Using this system, the reactions of internal alkynes afforded to the corresponding alkenyl boranes in good to high yields. In the case of unsymmetrical internal alkynes with phenyl and secondary alkyl groups, the corresponding products were obtained in high yields with moderate selectivity. Ma and co-workers also reported the hydroboration of unsymmetrical internal alkynes using CuCl/K_2CO_3/P(p-MeOC$_6$H$_4$)$_3$ catalyst system.[34]

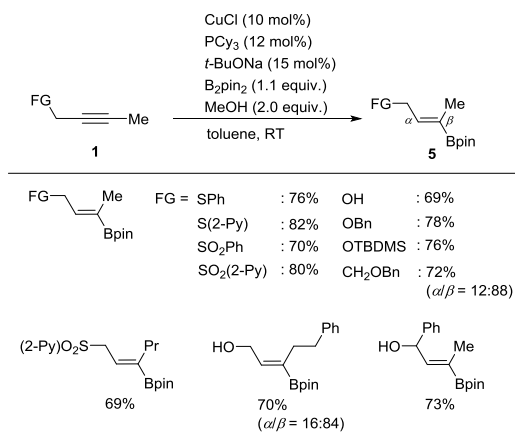**Scheme 16** Copper-catalyzed hydroboration of unsymmetrical internal alkynes employing CuCl/P(o-tol)$_3$.

We developed the regioselective hydroboration of unsymmetrical internal alkynes using a copper catalyst with CF$_3$Ar-Xan as the ligand (Scheme 17).[25] It is noteworthy that even when secondary alkyl moieties were attached to the acetylenic carbon, the regioselectivity of the β-products was high. The alkynes bearing conjugated ester and amide functionalities also afforded the respective β-products in high yields and with high regioselectivity.
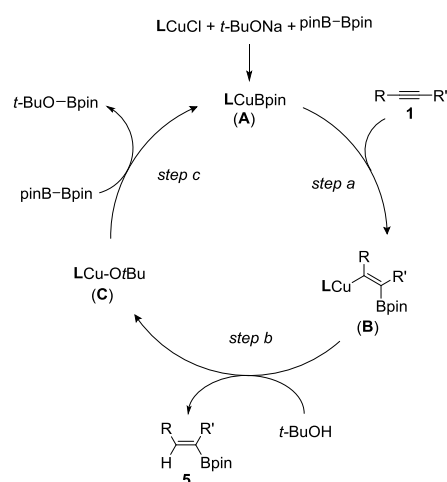

Scheme 17 Copper-catalyzed hydroboration of unsymmetrical internal alkynes employing CuCl/CF$_3$Ar-Xan.

Arrayás and Carretero also reported the regioselective borylation of propargyl-functionalized internal alkynes using a copper catalyst (Scheme 18).[35] The reactions of propargyl-substituted 2-butynes were carried out using CuCl/PCy$_3$/t-BuONa in toluene at room temperature. The reaction of an alkyne bearing a thioether moiety afforded the corresponding product in 76% yield and with high regioselectivity. A sulfonyl-substituted alkyne was converted to the corresponding product in good yield. Interestingly, the reaction of 2-butynol successfully afforded the borylated allylic alcohol. The alkynes bearing a benzylether or silylether moiety provided the corresponding products in good yields and with high regioselectivity. In the case of homopropagylic ether as the functional group, a mixture of hydroborylated products was obtained.

For the hydroboration reactions using B_2pin_2, a boryl copper species (LCu-B) may be generated as the catalytic species (Scheme 19). The addition of the LCu-B species to alkynes (borylcupration)[27] affords a (β-boryl)(alkenyl)copper intermediate with high regioselectivity. Next, the protonation of the alkenylcopper species with MeOH provides a β-borylated product (**5**) efficiently. Finally, the reaction of the resulting LCuOMe with B_2pin_2 regenerates LCu-B, and the catalytic cycle is completed (step c). Through this mechanism, the regioselectivity can be successfully controlled in the borylcupration stage.

**Scheme 18** Copper-catalyzed hydroboration of propagylic substituted alkynes.

Scheme 19 A possible catalytic cycle for the copper-catalyzed hydroboration of alkynes with B_2pin_2/ROH.

3.4. Copper-catalyzed diboration of internal alkynes

As mentioned above, the introduction of one boron moiety can be achieved by the hydroboration with B_2pin_2/ROH. When two boron moieties are introduced onto an alkyne, the product may be a good intermediate for the synthesis of complex molecules. Yoshida and co-workers reported the copper-catalyzed diborylation of internal alkynes using B_2pin_2 and copper catalysts (Scheme 20).[36] The reaction of 4-octyne with B_2pin_2 in the presence of a catalytic amount of Cu(OAc)$_2$ and PCy$_3$ in toluene at 80 °C afforded a *cis*-diborylated product (**6**) in 82% yield. The reaction of diphenylacetylene also gave the corresponding product in 78% yield. Other internal alkynes with various functionalities such as bromo and cyano groups were tolerated. Interestingly, the reaction of a propargyl ether with the Cu(OAc)$_2$/P(*t*-Bu)$_3$ catalyst system afforded a tetraborylated product in a good yield (eq. 5).
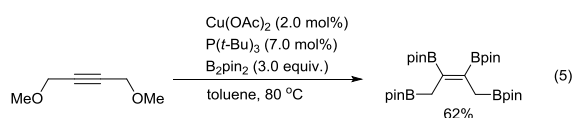
In addition, the catalyst system can be applied to the diborylation of arynes, to afford the 1,2-diborylbenzene derivatives in good to high yields.
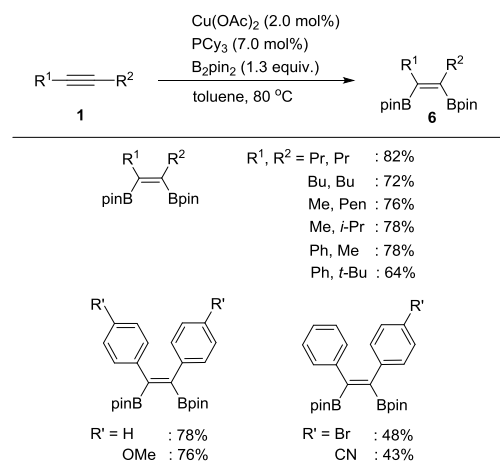
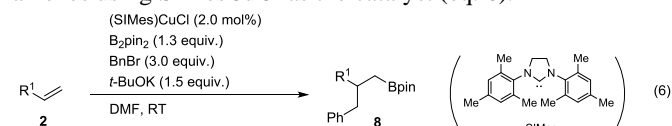**Scheme 20** Copper-catalyzed diborylation of alkynes.

Yoshida and co-workers also developed the stannylboration of internal alkynes using B_2pin_2 as the borylation reagent and alkoxystannanes (Bu$_3$SnOR, R = Me or *t*-Bu) as the stannylation reagent.[37]
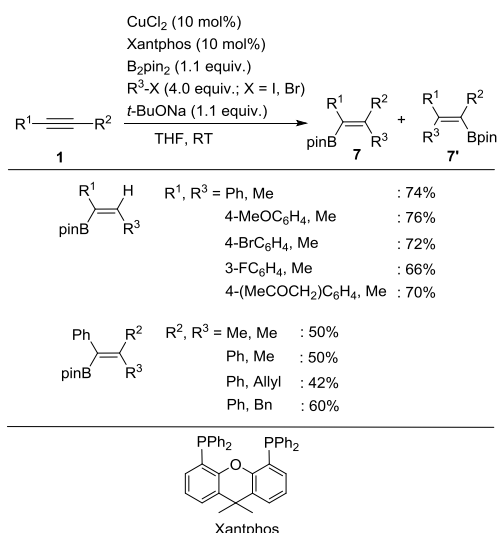
3.5. Copper-catalyzed carboboration of alkynes

The introduction of a boron moiety into an alkyne along with the simultaneous carbon-carbon bond formation is named as the carboboration reaction. The pioneering work has been reported by Suginome and co-workers using palladium or nickel catalysts via the direct activation of a boron-carbon bond.[38] In contrast, Tortosa[39] and Yoshida[40] independently reported the copper-catalyzed carboboration of alkynes using B_2pin_2 and carbon electrophiles such as alkyl halides (Scheme 21 and 22).

Tortosa and co-workers found that the reaction of phenylacetylene, B_2pin_2, and MeI in the presence of *t*-BuONa and a copper catalyst with Xantphos as the ligand afforded the methylborated product (**7**) in 74% yield and with high regioselectivity (Scheme 21).[39] The catalyst system was effective for diverse terminal alkynes with various functional groups such as ester and bromo moieties. The reaction of diphenylacetylene was converted to the corresponding product in a moderate yield. The reaction of 1-phenyl-1-propyne with benzyl bromide as the electrophile afforded a mixture of regioisomers in 55% total yield and with a moderate regioselectivity.

Yoshida and co-workers reported that a mixture of Cu(OAc)$_2$/PCy$_3$ catalyzed the reaction of diphenylacetylene, B_2pin_2, and benzyl chloride in the presence of *t*-BuOK in DMF at 50 °C, to afford the desired carboborated product in 67% yield (Scheme 22).[40] The reaction of diverse internal alkynes gave the corresponding products in good yields. The reaction of 1-phenyl-1-propyne afforded the β-borylated product regioselectively in 54% yield. They successfully established the carboboration of alkenes using SIMesCuCl as the catalyst (eq. 6).
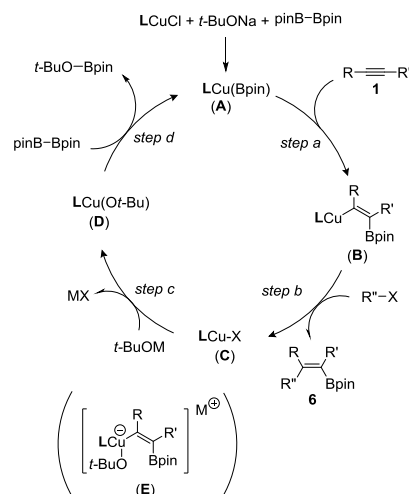
Scheme 21 Copper-catalyzed carboboration of alkynes employing CuCl/Xantphos.
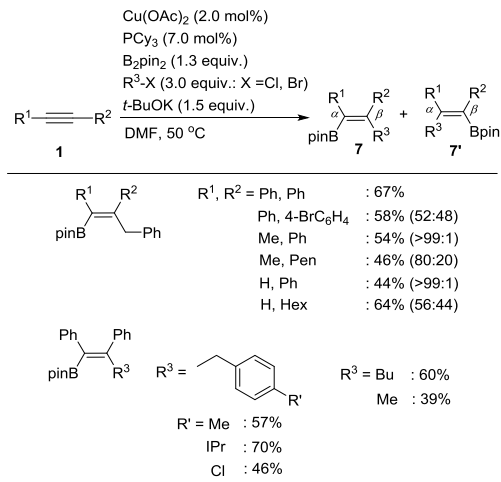
Scheme 22 Copper-catalyzed carboboration of alkynes employing Cu(OAc)$_2$/PCy$_3$.

Scheme 23 shows a plausible mechanism. The reaction of LCu(Ot-Bu) with B$_2$pin$_2$ affords a boryl copper intermediate (**A**). The *syn* addition of **A** to alkynes (borylcupration) affords a (β-boryl)(alkenyl)copper intermediate (**B**). The nucleophilic addition of the alkenylcopper species to a carbon electrophile gives the desired carborated product (**7**) and a copper halide. Finally, the reaction of the copper halide (**C**) and t-BuOM (M = Na or K) affords LCu(Ot-Bu) and the catalytic cycle closes. Yoshida proposed the reaction to proceed via an intermediate **E**, which was formed by the reaction of **B** with alkoxide *in situ*.[40]

Scheme 23 A possible catalytic cycle for the copper-catalyzed carboboration of alkynes with B$_2$pin$_2$ and carbon electrophiles.

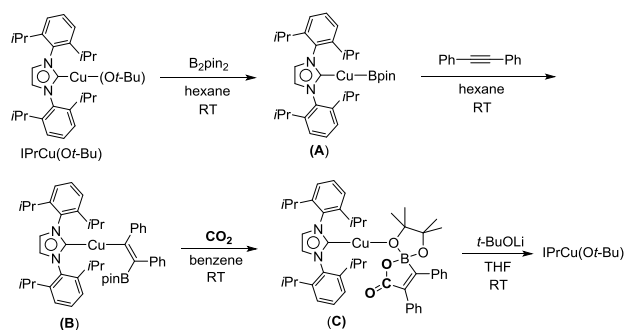### 3.6. Copper-catalyzed boracarboxylation of alkynes

The fixation of CO$_2$ along with the simultaneous introduction of a boron moiety is interesting because of the CO$_2$ fixation and the synthesis of multi-functional conjugated carboxylic acids. Hou and co-workers reported the first catalytic boracarboxylation of alkyne using CO$_2$ and B$_2$pin$_2$ in the presence of a stoichiometric amount of t-BuOLi and a copper catalyst (Scheme 24).[41] The reaction of diphenylacetylene in THF at 80 ºC afforded the boracarboxylated product in 81% yield. Diverse aromatic internal alkynes with different functional groups such as ester and chloro moieties gave the corresponding products in good to high yields.
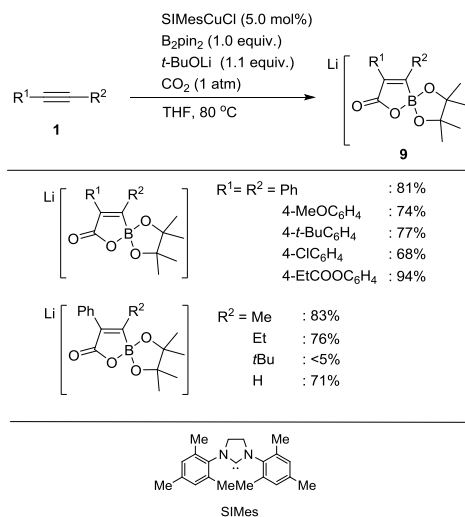
Scheme 24 Copper-catalyzed boracarboxylation of alkynes employing CO$_2$ and B$_2$pin$_2$.

Notably, the structures of all intermediates synthesized by the stoichiometric reactions were determined by X-ray crystallographic analysis (Scheme 25). A possible catalytic cycle is described as follows: First, the reaction of IPrCu(Ot-Bu) with B$_2$pin$_2$ affords a boryl copper complex, IPrCu(Bpin) (**A**). The reaction of **A** with diphenylacetylene gives a (β-

boryl)(alkenyl)copper complex (**B**). The reaction of **B** with CO_2 in THF affords a copper complex **C**. The transmetalation between **C** and *t*-BuOLi regenerates IPrCu(O*t*-Bu).

Scheme 25 Stoichiometric reactions for the copper-catalyzed boracarboxylation of alkynes employing CO_2 and B_2pin_2.

Regarding the heterocarboxylation, we have developed the copper-catalyzed silacarboxylation of alkynes with CO_2 and silylborane, as the silylation reagent, in the presence of a catalytic amount of [CuCl(PCy$_3$)]$_2$/(NaO*t*-Bu) (eq. 7).[42]
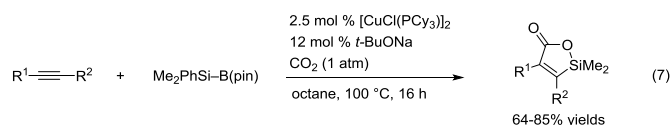
Conclusions

The transformation of alkynes using a copper hydride (Cu-H) or boryl copper (Cu-B) species as the catalytically active species is one of the most efficient methods to afford multi-substituted alkenes. The transformation proceeds via the regioselective addition of the Cu-H or Cu-B species to an alkyne, to afford the corresponding alkenylcopper intermediate. The reactions of the alkenylcopper with various electrophiles such as alcohol, carbon dioxide (CO_2), or alkyl halide afforded the corresponding multi-substituted alkenes that are potentially good intermediate in organic synthesis. The semihydrogenation, hydrocarboxylation, and hydroboration of alkynes have been developed using Cu-H as the active species. The hydroboration, diboration, carboboration and boracarboxylation of alkynes involve the Cu-B species.

Regarding the reductive transformations such as semihydrogenation of hydrocarboxylation, the use of hydrogen gas (H_2) should be one of the most important tasks. In this case, activation of H_2 by a copper catalyst must be a key step. The selective introduction of boron moiety is very important reaction for further organic synthesis. Copper complexes realized the regio- and setereoselective introduction of boron moiety to unsymmetrical internal alkynes. The results would be applicable to other various carbon-carbon multiple bonds. Hopefully, the methodology will contribute to efficient syntheses of many valuable molecules with shorter steps.

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