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Cu/Pd-catalyzed borocarbonylative trifunctionalization of alkynes and allenes: synthesis of β-geminal-diboryl ketones

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Functionalized bisboryl compounds have recently emerged as a new class of synthetically useful building blocks in organic synthesis. Herein, we report an efficient strategy to synthesize β-geminal-diboryl ketones enabled by a Cu/Pd-catalyzed borocarbonylative trifunctionalization of readily available alkynes and allenes. This reaction promises to be a useful method for the synthesis of functionalized β-geminal-diboryl ketones with broad functional group tolerance. Mechanistic studies suggest that the reaction proceeds through borocarbonylation/hydroboration cascade of both alkynes and allenes.

carbonylation, copper/palladium, alkynes/allenes, trifunctionalization, β-geminal-diboryl ketones

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1 Introduction

Alkynes, alkenes, and allenes are prevalent commodity feedstocks and ideal starting materials in organic synthesis, which have been widely used in the production of pharmaceuticals, polymers, as well as fine chemicals [1]. Catalytic functionalization of the carbon-carbon π-bonds in alkynes, alkenes or allenes offers a straightforward strategy for valuable building blocks construction [2]. Multifunctionalized compounds containing three or more functional groups are widely represented in biologically active molecules or natural products [3]. The intrinsic property of alkynes and allenes (have two π-bonds) compared with alkenes make them more attractive, as the potential reactivity of the two π-bonds increases their flexibility in multistep reaction sequences [4]. Although there are numerous methods and options for alkene functionalization, developing a complementary platform for selective multifunctionalization of alkynes or allenes bypassing the synthesis or isolation of alkene intermediates is still desirable, as it would minimize the reaction step count and improve atom-economy.

Organoboron compounds play an important role in modern organic synthesis since they are usually air & moisture stable, easy to operate, non-toxic, and prone to forge new C–C bonds [5]. Numerous strategies that introduce more complexity of molecules have been developed, but most of the examples involve the incorporation of two identical groups. Transition-metal catalyzed borylative difunctionalization of unsaturated π-bonds represents one of the most powerful and straightforward tools to access functionalized organoboranes, which was well developed [6]. However, trifunctionalization processes of unsaturated carbon-carbon bonds to get even highly functionalized organoboranes are relatively rarely reported [7]. As depicted in Figure 1a, the products or intermediates after the initial difunctionalization of alkynes still contain C–C double bond, which means that the remaining double bonds have the potential to proceed with further functionalizations. Moreover, the possibility to functionalize allenes in a 2,3-addition onto one of the two contiguous π systems presents considerable challenges in regioselectivity, since four regioisomers could

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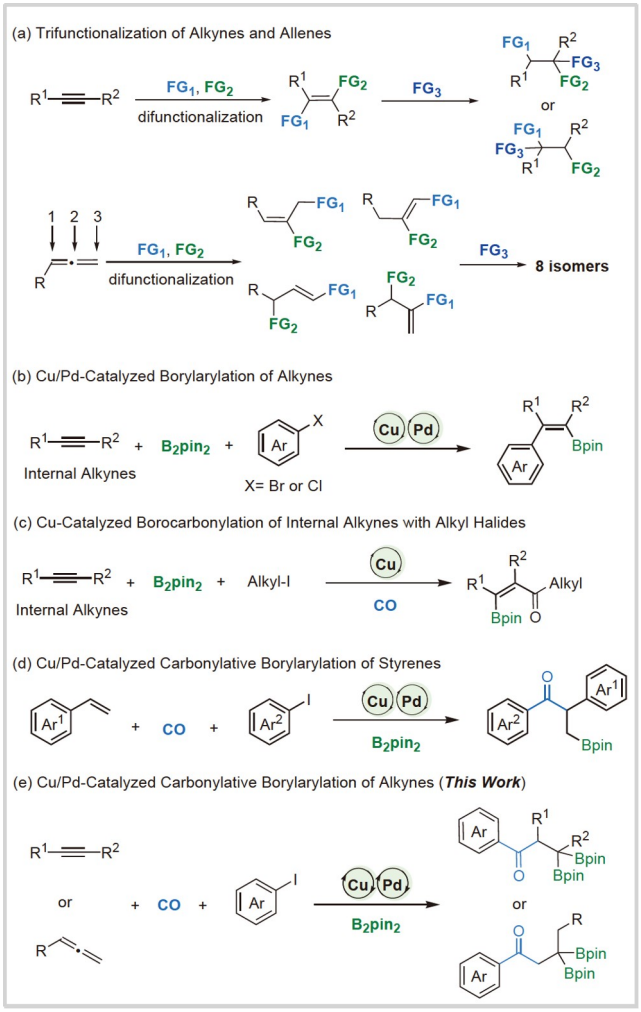


Figure 1 (a) Trifunctionalization of alkynes and allenes; (b) Cu/Pd-Catalyzed borylarylation of alkynes; (c) carbonylative borylation of alkynes with alkyl iodides; (d) carbonylative borylarylation of styrenes; (e) Cu/Pd-catalyzed carbonylative borylarylation of alkynes and allenes (this work) (color online).

be possibly formed [8], and with further functionalization, the isomers would be doubled.

Seminal copper-catalyzed borylarylation of alkynes with aryl iodides was reported by the Brown group [9] in 2014. Later, Cazin *et al*. [10] and Semba and Nakao *et al*. [11] independently developed the three-component arylborylation of alkynes by Cu/Pd cooperative catalysis to synthesize substituted vinyl boronates (Figure 1b). Mankad's group [12] reported a copper-catalyzed borocarbonylation of internal alkynes to produce tetrasubstituted enones (Figure 1c). Recent work from our laboratory [13] described a procedure to synthesize β-boryl ketones *via* Cu/Pd carbonylative borylarylation of styrenes with aryl iodides (Figure 1d). Seeking to further advance of copper/palladium catalysis in borocarbonylative reactions, we here now explored unsaturated π-systems of alkynes and allenes.

Herein, we report a Cu/Pd catalyzed multicomponent borocarbonylative trifunctionalization of alkynes and allenes with aryl iodides (Figure 1e). In contrast to C–C double bond, where carbonylation was accompanied by monoborylation, applying alkynes or allenes as the substrates provided carbonylation and diborylation cascades to furnish β-geminal-diboryl ketones as the trifunctionalized products. Geminal-diboryl compounds, which possess two boronate moieties in one same carbon atom, have recently been deemed as a new class of coupling reagents in organic synthesis [14].

2 Experimental

2.1 General information

All commercial reagents were purchased from Sigma-Aldrich, Strem, Acros, TCI or Alfa Aesar and used as such unless stated otherwise. Solvents (anhydrous and under inert atmosphere) were collected from the solvent purification system by M BRAUN and used under standard schlenk technique.

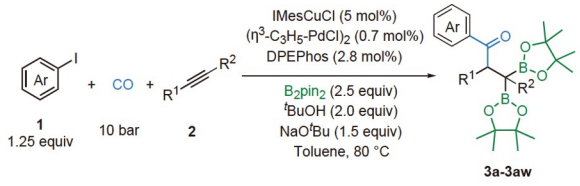
Nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance 300 MHz and Bruker ARX 400 MHz spectrometers (Germany). Multiplets were assigned as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), m (multiplet) and br. s (broad singlet). Coupling constants reported to 0.5 or 1.0 Hz accuracy. Gas chromatography (GC)-yields were calculated using hexadecane as internal standard. All measurements were carried out at room temperature unless otherwise stated. Electron impact (EI) mass spectra were recorded on AMD 402 mass spectrometer (Germany) (70 eV). The data are given as mass units per charge (*m*/*z*). GC analysis was performed on an Agilent HP-7890A instrument (USA) with a FID detector and HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.32 mm i.d., 0.25 μm film thickness) using argon as carrier gas. The products were isolated from the reaction mixture by column chromatography on silica gel 60, 0.063–0.2 mm, 70–230 mesh (Merck). For chiral high performance liquid chromatography (HPLC)-analysis a device Agilent 1100 Series (USA) was used.

2.2 General procedures

2.2.1 General procedure I

A vial (4 mL) was charged with $(\eta^3\text{-}C_3H_5\text{-}PdCl)_2$ (0.7 mol%), DPEPhos (2.8 mol%), IMesCuCl (5.0 mol%), B_2pin_2 (127.0 mg, 2.5 equiv.), NaO^{t}Bu (28.8 mg, 1.5 equiv.), and a stirring bar. The vial was closed by polytetrafluoroethylene (PTFE)/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. Then, toluene (1.0 mL) was injected under argon by using a syringe. After

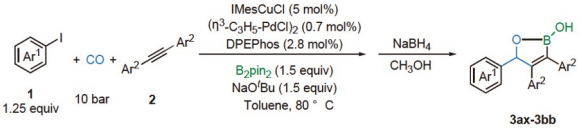
that aryl iodides **1** (0.25 mmol, 1.25 equiv.), alkynes **2** (0.2 mmol, 1.0 equiv.) and *t*BuOH (0.4 mmol, 2.0 equiv.) were added, and the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 10 bar (1 bar $=10^5$ Pa) of CO was adjusted at ambient temperature. Then, the reaction was performed for 12 h at 80 °C. When the reaction was completed, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was then filtered through celite and concentrated *in vacuo*. Finally, the residue was purified by column chromatography to afford the corresponding products **3a**–**3aw** (Reaction 1).



(1)

2.2.2 General procedure II

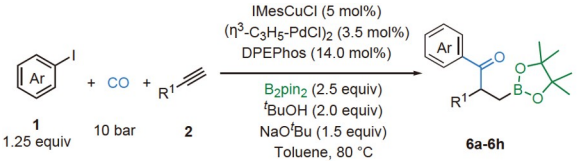
A vial (4 mL) was charged with $(\eta^3\text{-}C_3H_5\text{-}PdCl)_2$ (0.7 mol%), DPEPhos (2.8 mol%), IMesCuCl (5.0 mol%), B_2pin_2 (76.2 mg, 1.5 equiv.), NaO^{t}Bu (28.8 mg, 1.5 equiv.), and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. Then, toluene (1.0 mL) was injected under argon by using a syringe. After that aryl iodides **1** (0.25 mmol, 1.25 equiv.), and internal alkynes **2** (0.2 mmol, 1.0 equiv.) were added, and the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 10 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 12 h at 80 °C. When the reaction was completed, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was then filtered through celite and concentrated *in vacuo*. After that $NaBH_4$ (0.6 mmol, 3 equiv.) and CH_3OH (1.0 mL) were added into the residue, the reaction was stirred at room temperature for 1.0 h, and then the crude reaction mixture was diluted with Et_2O (10 mL) and H_2O (5 mL). The organic phase was separated, and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated on a rotary evaporator. Finally, the residue was purified by silica gel chromatography (hexane/ethyl acetate) to afford the corresponding products **3ax**–**3bb** (Reaction 2).



(2)

2.2.3 General procedure III

A vial (4 mL) was charged with $(\eta^3\text{-}C_3H_5\text{-}PdCl)_2$ (3.5 mol%), DPEPhos (14.0 mol%), IMesCuCl (5.0 mol%), B_2pin_2 (127.0 mg, 2.5 equiv.), NaO^{t}Bu (28.8 mg, 1.5 equiv.), and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. Then, toluene (1.0 mL) was injected under argon by using a syringe. After that aryl iodides **1** (0.25 mmol, 1.25 equiv.), alkynes **2** (0.2 mmol, 1.0 equiv.) and ^{t}BuOH (0.4 mmol, 2.0 equiv.) were added, and the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 10 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 12 h at 60 °C. When the reaction was completed, the autoclave was cooled down with ice water to room temperature and the pressure was released carefully. The solution was then filtered through celite and concentrated *in vacuo*. Finally, the residue was purified by column chromatography to afford the corresponding products **6a**–**6h** (Reaction 3).

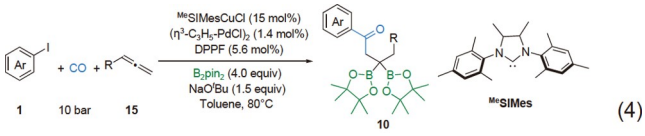


(3)

2.2.4 General procedure IV

A vial (4 mL) was charged with $(\eta^3\text{-}C_3H_5\text{-}PdCl)_2$ (1.4 mol%), DPPF (5.6 mol%), MeSIMesCuCl (15.0 mol%), B_2pin_2 (203.2 mg, 4.0 equiv.), NaO^{t}Bu (28.8 mg, 1.5 equiv.), and a stirring bar. The vial was closed by PTFE/white rubber septum (Wheaton 13 mm Septa) and phenolic cap and connected with atmosphere with a needle. The vial was evacuated under vacuum and recharged with argon for three times. Then, toluene (1.0 mL) was injected under argon by using a syringe. After that aryl iodides **1** (0.20 mmol, 1.0 equiv.), and allenes **15** (0.25 mmol, 1.25 equiv.) were added, and the vial (or several vials) was placed in an alloy plate, which was transferred into a 300 mL autoclave of the 4560 series from Parr Instruments. After flushing the autoclave three times with CO, a pressure of 10 bar of CO was adjusted at ambient temperature. Then, the reaction was performed for 12 h at 80 °C. When the reaction was completed, the auto-

clave was cooled down with ice water to room temperature and the pressure was released carefully. 1.0 mL CH_3OH was added into the residue and stirred for 5 min (to remove the rest of B_2pin_2 and easier for purification). Then, the solution was then filtered through celite and concentrated *in vacuo*. Finally, the residue was purified by column chromatography to afford the corresponding products **10a**–**10k** (Reaction 4).



(4)

3 Results and discussion

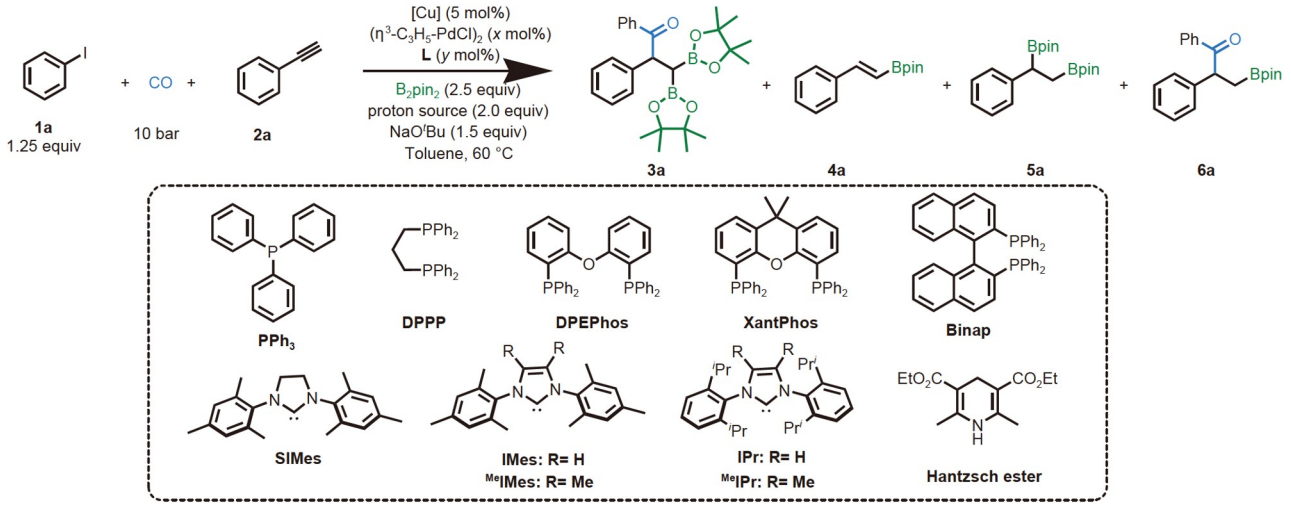
We initiated our studies by examining a model reaction using iodobenzene **1a** (1.25 equiv.) and phenylacetylene **2a** (1.0 equiv.) as the substrates, IMesCuCl as the copper catalyst, allylpalladium chloride dimer and phosphine ligand as the palladium catalyst, NaO^{t}Bu as the base under CO (10 bar) atmosphere. Unexpectedly, we can detect the product **3a** in trace amount, which implies that adventitious water might be the potential proton source to generate **3a**. Indeed, we found that added stoichiometry of ^{t}BuOH as the additional proton source promoted the reaction efficiency and the desired product **3a** was afforded in 11% yield (Table 1, entry 1). The major side products were **4a**, **5a**, and **6a**. Then different monodentate phosphine ligands and bidentate phosphine ligands were tested (Table 1, entries 1–5 and see Supporting Information online for further details). To our delight, when DPEPhos was used, the yield of **3a** can be improved to 48% (Table 1, entry 5). We found the loading of palladium catalyst is also crucial and may ultimately influence the reaction outcomes (Table 1, entries 6–8). Lowering the amount of allylpalladium chloride dimer to 0.7 mol% led to the desired product **3a** in 57% yields (Table 1, entry 6). Interestingly, increasing the palladium loading to 3.5 mol% only gave a trace of **3a**, instead the β-boryl ketone product **6a** was formed in 68% GC yield (Table 1, entry 8). Notably, the yield of **3a** could be further improved to 67% by increasing temperature to 80 °C, and 6% of **6a** was also detected (Table 1, entry 9). Further screening of the *N*-heterocyclic carbene (NHC) ligands, such as SIMes, ^{Me}IMes, IPr, and ^{Me}IPr, did not lead to any improvement (Table 1, entries 10–13). Among the proton sources screening (Table 1, entries 14–18), ^{t}BuOH was the most effective proton source for promoting the yield of diborylated product **3a** (for more details, see the Supporting Information online).

After obtaining the optimized reaction conditions, we systematically investigated the substrate scope of aryl iodides in reactions with phenylacetylene **2a** (Scheme 1). A variety of aryl iodides bearing electron-neutral, electron-rich as well as electron-deficient groups at the *para* position readily participated in this reaction to produce the corresponding 1,1-diboryl ketones **3a**–**3g** in moderate to good yields (53%–72%). Functional group Bpin at the *para* position was compatible, and 51% yield of the desired product **3h** was isolated, affording the product containing three Bpin groups. Additionally, *ortho*- or *meta*-substituted aryl iodides were converted into the corresponding products in reasonable yields as well (**3i**–**3m**). Moreover, di-substituted iodobenzenes also reacted smoothly to furnish the desired products (**3n**–**3p**). The structure of **3n** was confirmed by X-ray crystallography [15]. Importantly, 2-iodothiophene (**3q**), 1-iodonaphthalene (**3r**), and indole-containing (**3s**) substrates also underwent the carbonylative borylarylation successfully to afford the corresponding products. To demonstrate the potential applications, late-stage modification of pharmaceutical derivatives and biologically active molecules were also conducted. Specifically, Clofibrate-, diacetonefructose-, nerol-, and cholesterol-derived **3t**–**3w** were all isolated in good yields.

We then turned our attention to investigate the substrate scope of alkynes, starting with aryl acetylenes and iodobenzene (Scheme 2). In general, good functional group tolerance was observed, and most of aryl acetylenes with regular substituents as well as some reactive functional groups at the *para* position such as halides, ester, ketone can undergo the reaction smoothly to afford the desired 1,1-diboryl ketones in moderate to good yields (**3x**–**3ad**, 39%–76%). *Ortho*, *meta* position substituted phenylacetylenes, and di-substituted phenylacetylene can smoothly be converted into the corresponding products (**3ae**–**3ah**). To our delight, the catalytic system was also successfully used for borocarbonylation of alkylacetylenes with iodobenzene. Different chain length alkylacetylenes and steric bulk alkylacetylenes were all able to deliver the corresponding products (**3ai**–**3ao**). It is worth mentioning that when triethylsilylacetylene was applied as the substrate, desilylation occurred, giving product **3ao** in 51% yield. This catalyst system tolerated a variety of functional groups, including halogen (**3ap**), alkene (**3aq**), and ether (**3ar**).

The generality of this reaction was further evaluated by exploring internal alkynes. Aryl alkyl acetylenes were subjected to the reaction conditions, affording 1,1-diboryl ketones **3as**–**3aw** in good yields and with excellent regioselectivity. Unfortunately, under the current catalytic system, only a trace amount of the desired product was observed with dialkyl-substituted internal alkynes. However, diaryl-substituted internal alkynes could only afford the mono borylated enone products, rather than the targeted 1,1-diboryl ketones, which were reported with poor stability. Hence, upon simple reductive work-up of the enones with $NaBH_4$ in methanol, the reduced five-member ring oxabor-

Table 1 Optimization of the reaction conditions [a)]

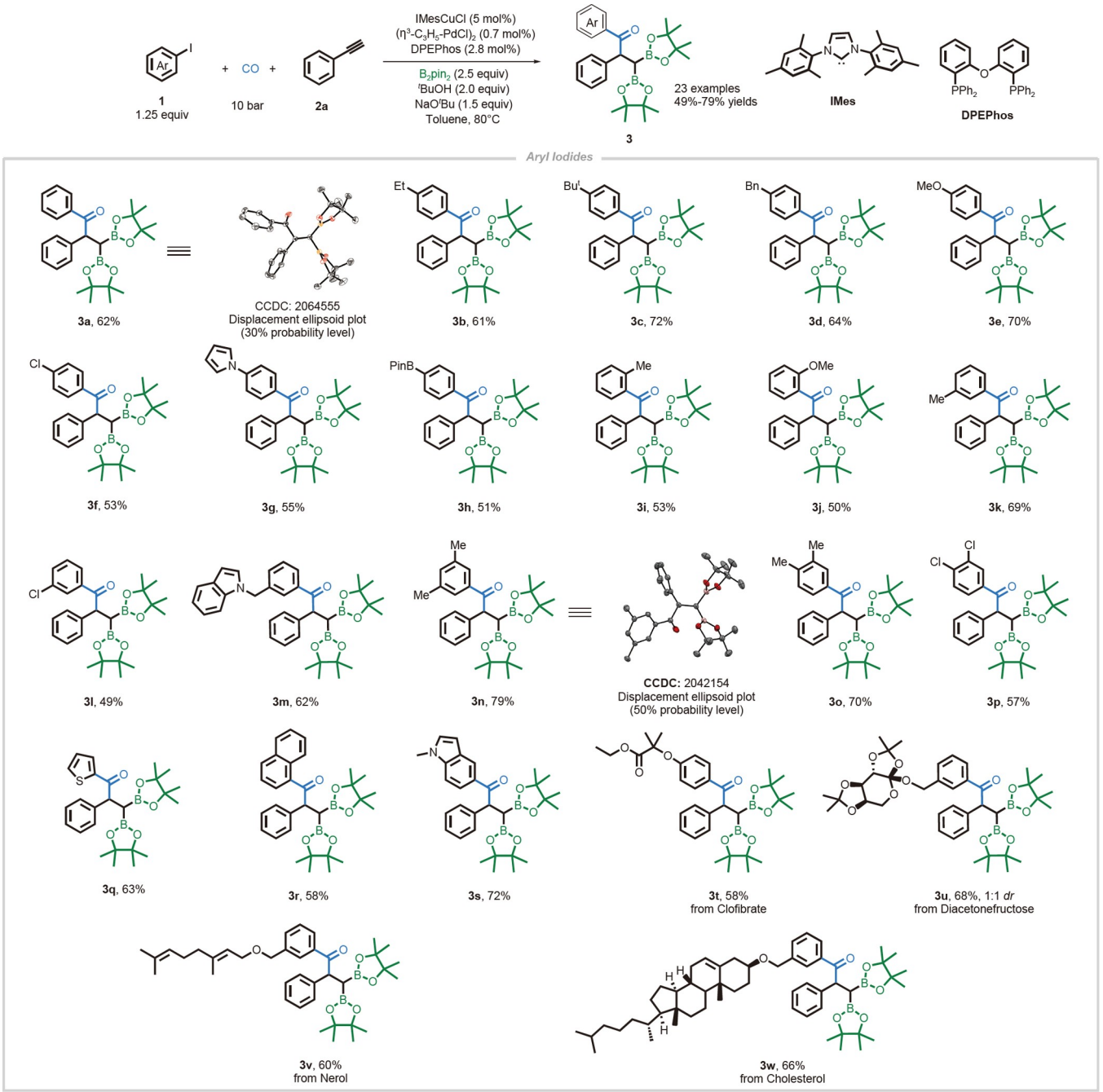


Entry	Ligand	[Pd] (x mol%)	[Cu]	Proton source	Yield (%)			
					3a	**4a**	**5a**	**6a**
1	PPh_3	2.0	IMesCuCl	^{t}BuOH	11	27	29	10
2	DPPP	2.0	IMesCuCl	^{t}BuOH	9	16	11	14
3	XantPhos	2.0	IMesCuCl	^{t}BuOH	20	28	/	6
4	Binap	2.0	IMesCuCl	^{t}BuOH	13	9	16	/
5	DPEPhos	2.0	IMesCuCl	^{t}BuOH	48	10	2	18
6	DPEPhos	1.4	IMesCuCl	^{t}BuOH	57	14	/	10
7	DPEPhos	4.0	IMesCuCl	^{t}BuOH	12	10	/	37
8	DPEPhos	7.0	IMesCuCl	^{t}BuOH	trace	8	/	68 (59) [c)]
9 [b)]	DPEPhos	1.4	IMesCuCl	^{t}BuOH	67 (62) [c)]	10	3	6
10 [b)]	DPEPhos	1.4	SIMesCuCl	^{t}BuOH	47	15	5	18
11 [b)]	DPEPhos	1.4	^{Me}IMesCuCl	^{t}BuOH	60	13	3	8
12 [b)]	DPEPhos	1.4	IPrCuCl	^{t}BuOH	trace	9	16	31
13 [b)]	DPEPhos	1.4	^{Me}IPrCuCl	^{t}BuOH	6	19	17	28
14 [b)]	DPEPhos	1.4	IMesCuCl	CH_3OH	8	11	64	/
15 [b)]	DPEPhos	1.4	IMesCuCl	H_2O	21	72	/	3
16 [b)]	DPEPhos	1.4	IMesCuCl	^{t}AmylOH	52	19	/	12
17 [b)]	DPEPhos	1.4	IMesCuCl	HBpin	4	30	15	1
18 [b)]	DPEPhos	1.4	IMesCuCl	Hantzsch ester	38	18	29	10
19 [b)]	DPEPhos	1.4	/	^{t}BuOH	0	0	0	0
20 [b)]	DPEPhos	/	IMesCuCl	^{t}BuOH	0	0	58	0

a) Reaction conditions: **1a** (0.25 mmol), **2a** (0.2 mmol), B_2pin_2 (2.5 equiv.), proton source (2.0 equiv.), [Pd] (0.7 mol%), ligand (2.8 mol% or 5.6 mol%), [Cu] (5.0 mol%), NaO^{t}Bu (1.5 equiv.), toluene (1.0 mL), CO (10 bar), 60 °C, 12 h; yields were determined by GC analysis using hexadecane as internal standard. b) Under 80 °C. c) Yield of the isolated product.

oles **3ax**–**3bb** can be obtained in 42%–81% yields.

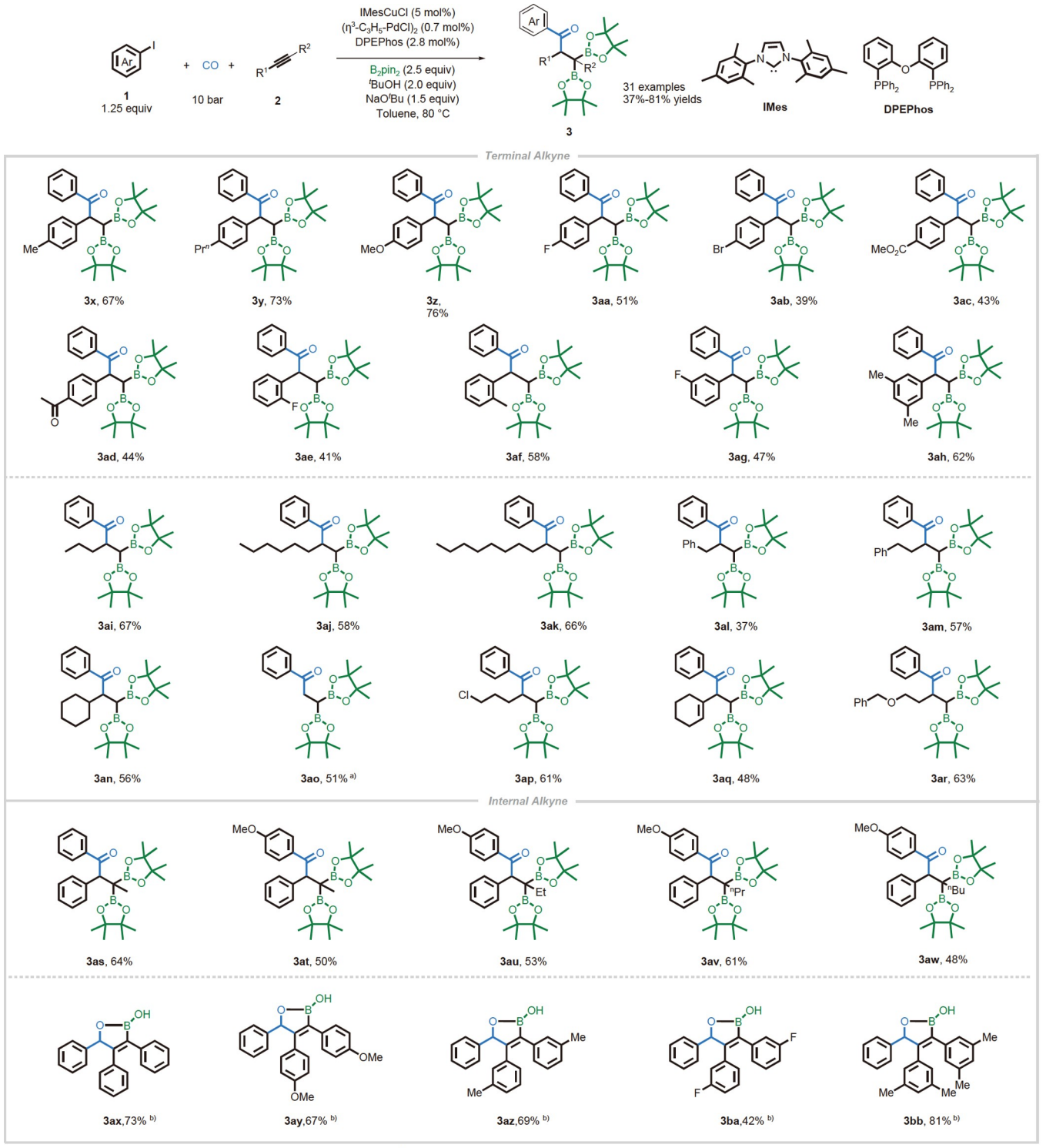
As mentioned above (Table 1, entry 8), product **6a** could be also formed in 68% GC yield under certain reaction conditions. We then turn to explore the scope of substrates, and the results are summarized in Scheme 3. Overall, both iodobenzenes and alkynes worked well in this catalytic system, leading to the corresponding β-boryl ketones in good yields. Especially, alkylacetylenes were also compatible, giving the corresponding products, which could not be synthesized by our previously reported method using alkene as the substrate [13]. However, when aryl alkyl internal acetylenes were used as the substrates under the current reaction conditions, only resulting in a trace amount of the desired products. In order to understand the mechanism for their formation, control experiments were carried out as well. We can only obtain **6a** in 5% or 9% yield after 12 h from



Scheme 1 Substrate scope of aryl iodides. Reaction conditions: **1** (0.25 mmol, 1.25 equiv.), **2a** (0.2 mmol, 1.0 equiv.), B_2Pin_2 (0.5 mmol, 2.5 equiv.), [Cu] (5.0 mol%), [Pd] (0.7 mol%), DPEPhos (2.8 mol%), NaO^{t}Bu (0.3 mmol, 1.5 equiv.), ^{t}BuOH (0.4 mmol, 2.0 equiv.), CO (10 bar), toluene (1.0 mL), 80 °C, 12 h, isolated yields (color online).

product **3a** in the presence of base with or without [Pd]/DPEPhos (Scheme 3a). No effect of copper catalyst could be observed here. Then, we subjected **3as′** into the reaction, but no product **6as** could be detected (Scheme 3b). Additionally, a deuterium incorporation experiment was also conducted by using ^{t}BuOD as the D source (Scheme 3c). Until the current stage, the mechanism for products **6** generation in the reaction is still unclear and further investigations are needed (for details, see the Supporting Information online).

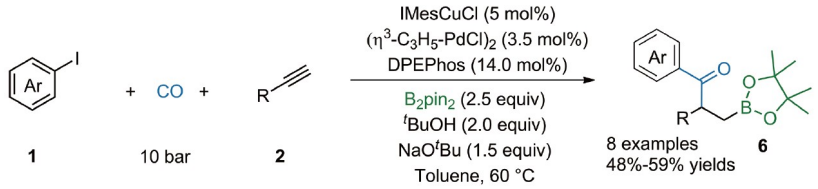
To elucidate the mechanism, control experiments were conducted, as depicted in Figure 2. We first subjected each of the putative intermediates, alkenylBpin (**4a**) and 1,1,2-trisboronates (**7**), to the reaction condition. We found that neither **4a** nor **7** could be converted into the desired product **3a**, only led to **5a** (Figure 2a). These results show that **4a** and **7** are not competent intermediates. Then, we try to isolate the intermediate, using internal alkyne **2as** as the substrate and reducing the stoichiometry of B_2Pin_2 to 1.0 equiv. without

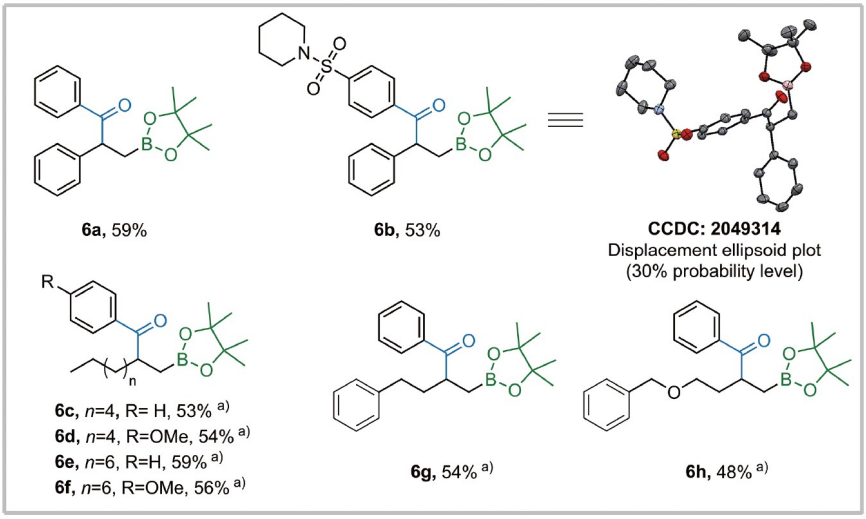


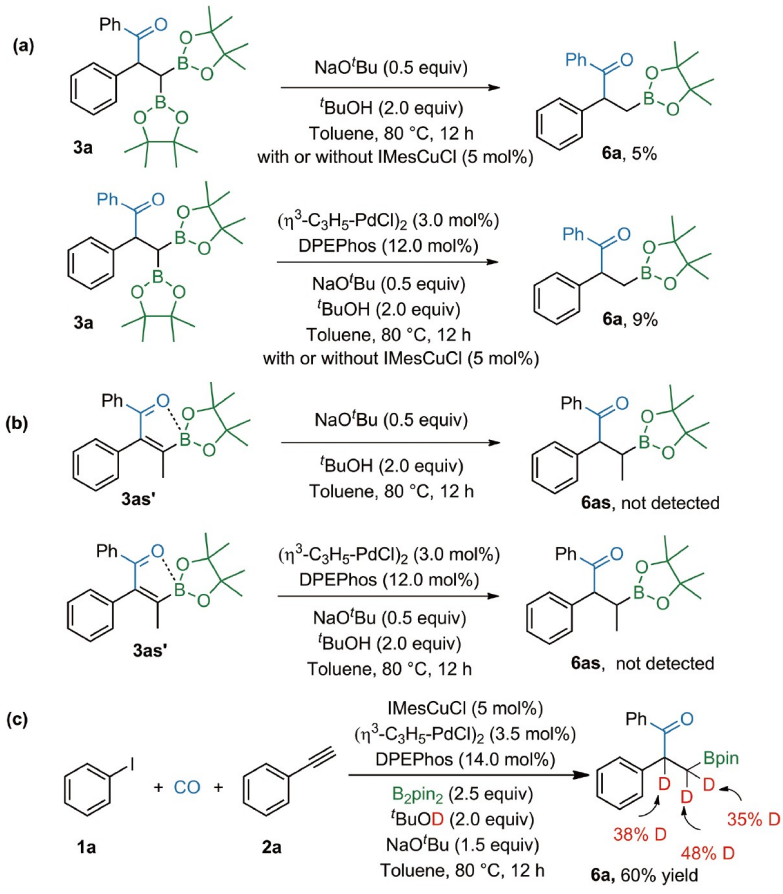
a) Triethylsilylacetylene as substrate; b) With B_2Pin_2 (0.2 mmol, 1.0 equiv.), no ^{t}BuOH, reduced by $NaBH_4$.

Scheme 2 Substrate scope of aryl alkynes. Reaction conditions: **1**(0.25 mmol, 1.25 equiv.), **2a** (0.2 mmol, 1.0 equiv.), B_2Pin_2 (0.5 mmol, 2.5 equiv.), [Cu] (5.0 mol%), [Pd] (0.7 mol%), DPEPhos (2.8 mol%), NaO^{t}Bu (0.3 mmol, 1.5 equiv.), ^{t}BuOH (0.4 mmol, 2.0 equiv.), CO (10 bar), toluene (1.0 mL), 80 °C, 12 h, isolated yields (color online).

^{t}BuOH. Surprisingly, **3as′** can be isolated in 34% yield and a small amount of product **3a** can be also detected. Subsequently, we performed isolated **3as′** to the reaction, which was converted into the desired **3as** (86% yield) smoothly with IMesCuCl as the catalyst after 2.5 h. However, without using IMesCuCl as the catalyst, only less than 5% yield of **3as** can be detected even after 15 h (Figure 2b). The ^{11}B NMR spectrum of **3as′** indicated internal chelation between







a) NaO*t*Bu (0.6 mmol, 3.0 equiv.), *t*BuOH (0.8 mmol, 4.0 equiv.)

Scheme 3 Substrate scope and control experiments. Reaction conditions: **1** (0.25 mmol, 1.25 equiv.), **2a** (0.2 mmol, 1.0 equiv.), B_2Pin_2 (0.5 mmol, 2.5 equiv.), [Cu] (5.0 mol%), [Pd] (3.5 mol%), DPEPhos (14.0 mol%), NaO^{t}Bu (0.3 mmol, 1.5 equiv.), ^{t}BuOH (0.4 mmol, 2.0 equiv.), CO (10 bar), toluene (1.0 mL), 60 °C, 12 h, isolated yields (color online).

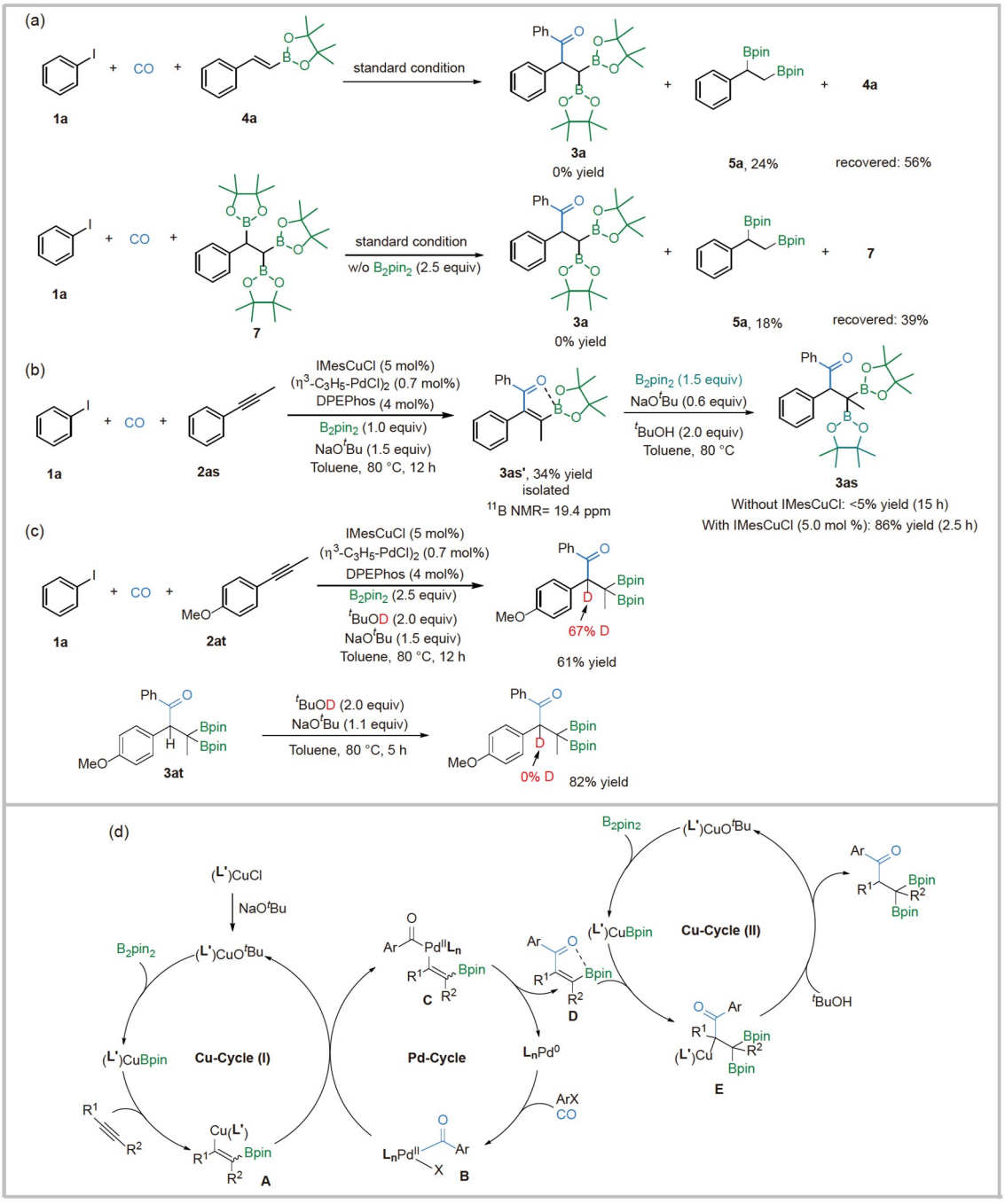
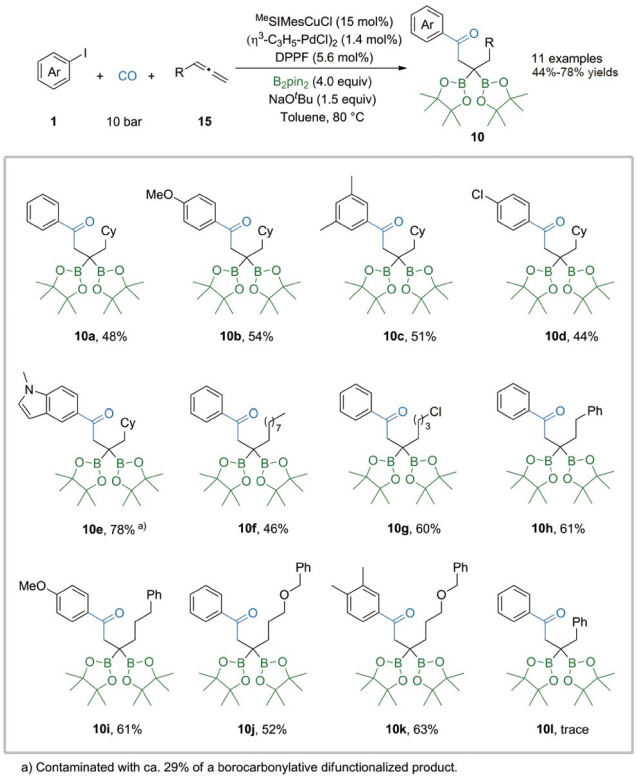


Figure 2 Control experiments and proposed mechanism. (a) Experiments to find potential intermediates; (b) intermediate isolation; (c) deuterium labelling experiment; (d) proposed catalytic cycle (color online).

the carbonyl and Bpin group, and the C=O→Bpin coordination might promote the following hydroboration. A deuterium incorporation experiment was also performed by using ^{t}BuOD as the deuterium source (Figure 2c), resulting in 67% deuterium incorporation at the α-position carbon atom. However, starting from the product in the presence of base in ^{t}BuOD, no deuterated product could be obtained.

Based on the above experiment results and previous literature, we proposed a plausible mechanism. As shown in Figure 2d, in analogy to reported processes involving Cu-catalyzed borylation, the active catalyst is L'Cu-Bpin species, which is generated by addition of B_2pin_2 to L'CuO^{t}Bu [16]. Subsequent borocupration of the alkyne substrate affords the alkenylcopper intermediate **A** (Cu cycle I). At the same time, in the Pd catalytic cycle, the oxidative addition of ArX to $L_nPd(0)$ and subsequent CO insertion would form the acylpalladium species **B**. The transmetalation of the alkenylcopper intermediate **A** with acylpalladium species **B**

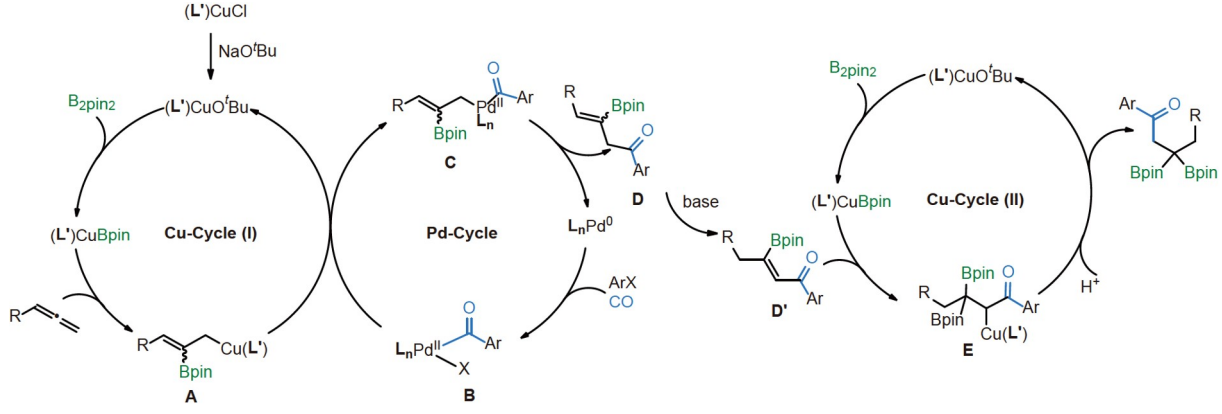


Scheme 4 Substrate scope Cu/Pd-catalyzed borocarbonylative trifunctionalization of allenes and proposed mechanism. Reaction conditions: **1** (0.20 mmol, 1.0 equiv.), **15** (0.25 mmol, 1.25 equiv.), B_2Pin_2 (0.8 mmol, 4.0 equiv.), [Cu] (15.0 mol%), [Pd] (1.4 mol%), DPPF (5.6 mol%), NaO^{t}Bu (0.3 mmol, 1.5 equiv.), CO (10 bar), toluene (1.0 mL), 80 °C, 12 h, isolated yields. See the Supporting Information online (color online).

would generate the palladium complex **C** and L'CuO^{t}Bu. Intermediate **A** was followed by reductive elimination to give intermediate **D** and regenerate $L_nPd(0)$. In the second Cu cycle, the active copper species L'Cu-Bpin undergoes borocupration of **D** again to generate alkyl copper intermediate **E**. Protonation of the alkyl copper species **E** with ^{t}BuOH would afford the desired 1,1-diboryl ketone products (Cu cycle II).

Allenes are of significant utility in chemical synthesis. The active nature imparted by its unique orthogonal cumulative π-system also makes them highly versatile and useful building blocks in organic synthesis [17]. To further assess the synthetic potential of our borocarbonylative trifunctionalization strategy, allenes were also examined. Delightfully, the borocarbonylative trifunctionalization of allenes functions well when ^{Me}SIMesCuCl is employed as the copper catalyst and DPPF used as the ligand, leading to the formation of 3,3-diboryl ketones (Scheme 4). The process is tolerant of a variety of aryl iodides and allenes, providing the corresponding products as a single isomer in moderate yields (**10a**–**10k**). However, phenylallene is not compatible with this catalytic system (**10l**). In the first step of borocarbonylation process, transmetalation of the generated putative allyl copper intermediate with the acylpalladium species occurs at the least-substituted position, followed by hydroboration to provide 2,2,3-trifunctionalized products **10** with exceptional chemo- and regioselectivity. Finally, a possible reaction pathway is proposed which is similar with the previous discussed one for alkynes (Scheme 5). However, one additional step is needed for the isomerization of alkenyl boronate intermediate **D** to α,β-unsaturated ketone intermediate **D′** which can occur easily in the presence of base.

Finally, we rapidly investigated the reactivity of the geminal-diboryl ketone **3a** (Figure 3). For instance, **3a** could be efficiently transformed into **8** in 81% yield by Pd-catalyzed Suzuki-Miyaura cross-coupling reaction. Then, we can acquire **6a** easily in 84% yield from geminal-diboryl ketone **3a**. Under oxidative conditions, **3a** was converted into phenyl benzyl ketone **9** unexpectedly. Here, the formation of compound **9** might go through oxidation of the two Bpin group into OH group and the resulting product is not stable, which will decompose immediately to give the obtained product. The enone **14** was obtained in good yield by $AgNO_3$-catalyzed protodeboration. Similarly, geminal-diboryl ketone **10h** can be easily transformed into **11h** in 90% isolated yield. Oxidation of **11h** with $NaBO_3$ generated the β-



Scheme 5 Proposed mechanism for Cu/Pd-catalyzed borocarbonylative trifunctionalization of allenes (color online).

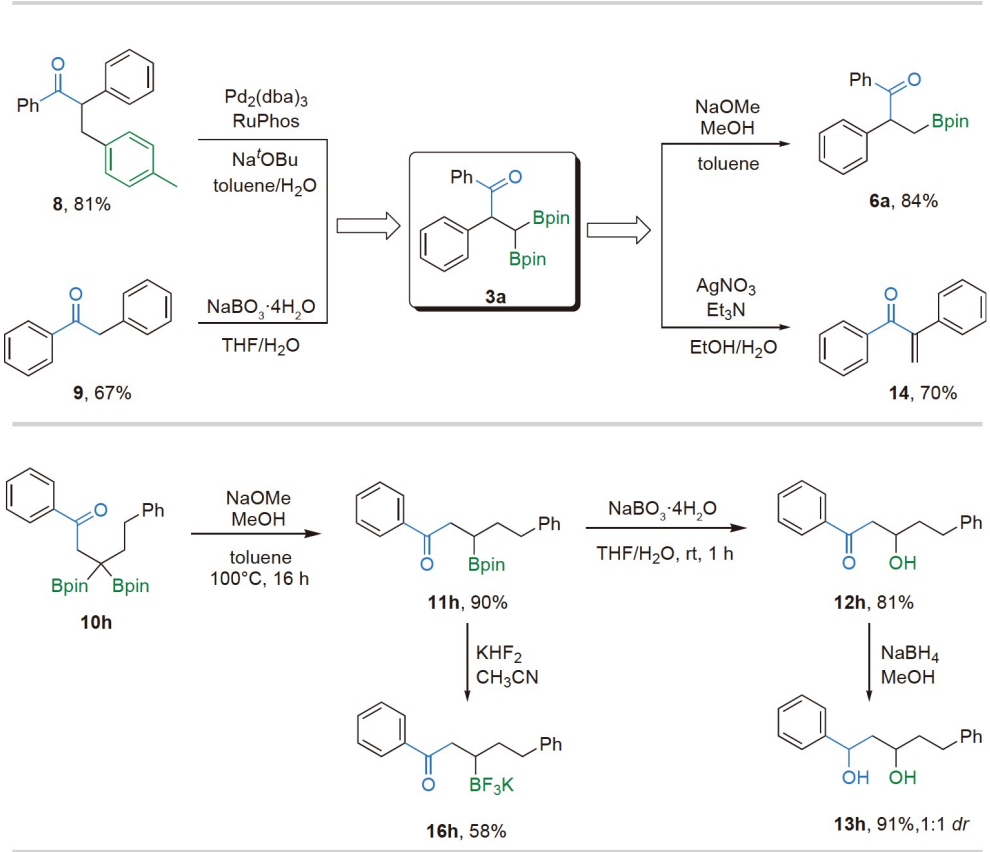


Figure 3 Conversion of the obtained products (color online).

hydroxyketone **12h** in 81% yield. And the compound **12h** could be further reduced to 1,3-diol **13h** in 91% yield with a d.r. value of 1:1. Moreover, **11h** was converted into the trifluoroborate salt **16h** in 58 % yield by using aqueous KHF_2 in acetonitrile.

4 Conclusions

In summary, we have developed a Cu/Pd-catalyzed cascade borocarbonylative trifunctionalization of alkynes to access a range of geminal-diboryl ketones. The method shows a rare example on selective carbonylative trifunctionalization and displays broad functional group tolerance. A rational mechanism involving initial borocarbonylation of alkynes followed by hydroboration of the terminated π-system is provided. Allenes were also successfully used as the substrates under similar catalytic system, producing the corresponding geminal-diboryl ketones with high regioselectivity. It is expected that this general blueprint for catalytic carbonylative trifunctionalization will be possibly applied to more different transformations, thus allowing two π systems compounds (alkynes and allenes) to serve as direct starting material to construct more complexed molecules.

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Conflict of interest The authors declare no conflict of interest.

Supporting information supporting information is available online at http://chem.scichina.com and http://link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accu-racy and content remains entirely with the authors.

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