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Substrate-Controlled Regio- and Stereoselective Synthesis of Boron-Substituted 1,4-dienes via Copper-Catalyzed Boryl-Allylation of Alkynes with Allyl Phosphates and Bis(pinacolato)diboron

Huai-Yu Bin,[†] Xiao Wei,[†] Jing Zi,[†] Ya-Jie Zuo,[†] Tian-Chi Wang,[‡] and Chong-Min Zhong[†,‡]*

[†]Department of Applied Chemistry, College of Science, Northwest A&F University, Yangling 712100, PR China

[‡]Department of Chemistry, College of Chemistry and Chemical Engineering, Harbin Normal University, Harbin 150025, PR China

ABSTRACT: Boron-substituted 1,4-diene is a versatile building block for the synthesis of 1,4-diene (skipped alkene), which is a common motif in bioactive natural products, due to its utility in the Suzuki−Miyaura coupling reaction and conjugate additions. A method for the synthesis of boron-substituted 1,4-dienes has been developed through a copper-catalyzed boryl-allylation of alkyne with allyl phosphate and bis(pinacolato)diboron. The regioselectivity with respect to the alkyne and ally phosphate depended on the structures of both the alkyne and allyl phosphates. For alkynes bearing at least one aryl substituent, the addition of borylcopper to the alkyne mainly generated a β-boryl-α-aryl-α-alkenylcopper species, whose subsequent reaction with secondary

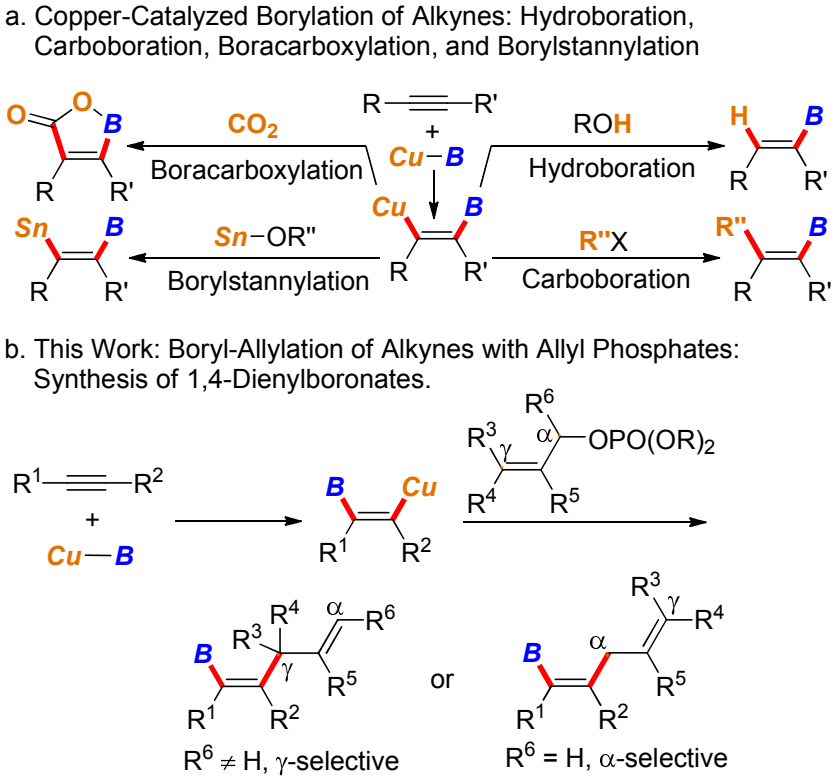
ally phosphates provided γ-(4*E*)-selective boron-substituted 1,4-dienes, and with primary allyl phosphates provided α-selective boron-substituted 1,4-dienes. On the other hand, the α-boryl-α-aryl-β-alkenylcopper species formed as a minor intermediate from arylalkylacetylene and β-borylalkenylcopper formed from dialkylacetylene show poor regioselectivity with respect to the secondary allyl phosphate and produces a mixture of α- and γ-selective boron-substituted 1,4-dienes. However, their reactions with the primary allyl phosphate are highly γ-selective. For all α-selective reactions, the configuration of the C=C bond of the allyl phosphate was retained in the products. The palladium-catalyzed cross-coupling of boron-substituted 1,4-dienes and aromatic, alkenyl, and alkynyl halides gave polyenes or enynes in 68%–95% yields, demonstrating a versatile building block for the synthesis of 1,4-dienes.

KEYWORDS: copper catalysis, carboboration, alkyne, allyl phosphate, 1,4-dienylboronate.

1. INTRODUCTION

Organoboron compounds are important reagents in organic chemistry, enabling many chemical transformations, and the development of efficient strategies for their stereoselective synthesis is an important goal. Alkenylboronates play an important role in organic synthesis due to their utility in the Suzuki−Miyaura coupling reaction[1] and conjugate additions.[2] Metal-catalyzed borylation of alkynes is the most direct method to access these alkenylboronates. Palladium- and nickel-catalyzed carboborations of alkynes have been reported by Suginome et al.[3] However, the use of functionalized alkynes and unusual boron sources in these transformations limits their application in organic synthesis. In addition, Yoshida et al. have reported a silver-catalyzed hydroboration of alkynes;[4] however, only terminal alkynes were investigated in their work. Recently, copper-catalyzed borylation of alkynes has emerged as a more general method for the

synthesis of alkenylboronates. The β-borylalkenylcopper species generated from the *syn*-addition of borylcopper to alkynes are strong carbon nucleophiles and can be reacted with various electrophiles to form more complex alkenylboronates by the concomitant formation of new C–H, C–C, or C–heteroatom bonds (Scheme 1a). It can be protonated by alcohols to produce the corresponding hydroboration compounds of alkynes.[5] Also, the carboboration reaction of alkynes is becoming an important method for the synthesis of tri- and tetrasubsituted alkenlboronates,[6] and β-borylalkenylcopper can also be captured by CO_2 to form cyclic alkenylboronates.[7] Furthermore, *vic*-borylstannylalkenes can be obtained by the cross-coupling reaction between β-borylalkenylcopper and tin alkoxide.[8]



Scheme 1. Reactions of β-Borylalkenylcopper with Electrophiles. (a) Previously Reported Borylation of Alkynes. (b) This Work.

The 1,4-diene framework is a common motif in bioactive natural products.[9] Herein, we report a novel method for the synthesis of boron-substituted 1,4-dienes through a copper-catalyzed three-component coupling reaction of bis(pinacolato)diboron, an alkyne, and an allyl phosphate (Scheme 1b).[10] To make the coupling reaction proceed both regio- and stereoselectively is a challenging task, because there are four possible regioisomers (two for the alkyne if an unsymmetrical alkyne is used, and two for the allyl phosphate), and more isomers may be formed if stereoisomers of the double bond are also considered. Other side-reactions include the hydroboration of the alkyne and boryl substitution of the allyl phosphate.[11]

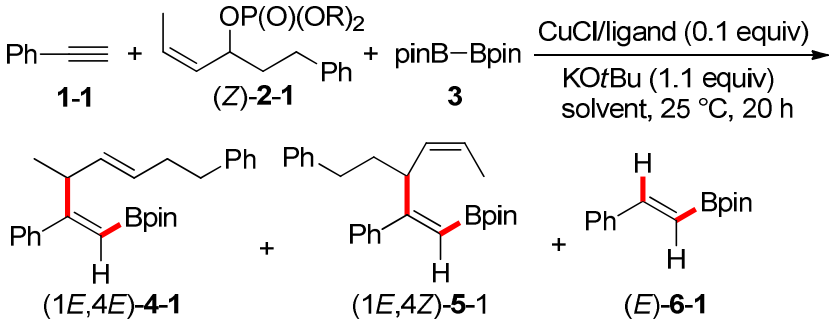
The method reported herein is highly regio- and stereoselective. Furthermore, the boron-substituted 1,4-dienes can be derivatized to form more complex 1,4-diene unit-containing polyenes with a tri- or tetra-substituted double bond.

2. RESULTS AND DISCUSSION

Condition Optimization and Substrate Scope for the Copper-Catalyzed γ-(4*E*)-Selective Coupling Reaction between a Terminal Alkyne and a Secondary Allyl Phosphate. Different reaction conditions were screened using phenylacetylene (**1**-**1**), secondary allyl phosphate (*Z*)-**2**-**1**, and diborane **3** as substrates in the presence of a CuCl/ligand catalytic system at 25 °C. As shown in Table 1, in addition to the desired γ-(4*E*)-selective product [(1*E*,4*E*)-**4**-**1**], α-product (1*E*,4*Z*)-**5**-**1** and the hydroboration product of phenylacetylene [(*E*)-**6**-**1**] were also detected by ^{1}H NMR spectra. Ligand screening (Table 1, entries 1–8) shows that (±)-binap, PCy_3, and PPh_3 give better combined yields of **4**-**1**, **5**-**1**, and **6**-**1** (Table 1, entries 4–6, 71%–82%), and higher selectivities for (1*E*,4*E*)-**4**-**1** (Table 1, entries 4–6, 91%–94%) when using an ethyl group in the phosphate moiety.[12]

To further improve the yield and selectivity and to suppress the hydroboration reaction, the R group in the phosphate was optimized using a CuCl/(±)-binap system (Table 1, entries 9–13). An excellent yield (95%) and γ-selectivity (>99%) are obtained when the *s*-butyl group is present in the leaving group (Table 1, entry 11). The level of hydroboration product is also suppressed to 3% in the isolated products. The presence of the larger (2-ethyl)hexyl group in the leaving group results in a slight decrease in the yield (Table 1, entry 12). The presence of the bulky cyclohexyl group in the leaving group reduces both the yield and selectivity (Table 1, entry 13). The combination of a leaving group bearing s-butyl in the allyl phosphate with a CuCl/PPh_3 or CuCl/PCy_3 catalyst leads to a decrease in both yield and selectivity (Table 1, entries 14 and 15). The use of (*E*)-**2**-**1** instead of (*Z*)-**2**-**1** as the allyl phosphate also produces (1*E*,4*E*)-**4**-**1**, but with reduced yield and selectivity (Table 1, entry 16). Interestingly, the reaction proceeds stereoconvergently with respect to the double bond of the allyl phosphate. Conducting the reaction in toluene decreases both the yield and selectivity, but increases the hydroboration of phenylacetylene (Table 1, entry 17). The double bond configuration of **4**-**1** was determined to be (1*E*,4*E*) by NOESY analysis (see Supporting Information for details). The reaction is highly stereoselective for the formation of the (4*E*) double bond, and the ratio of (1*E*,4*E*)-**4**-**1** to (1*E*,4*Z*)-**4**-**1** is *ca.* 99:1 under the optimal reaction conditions.

Table 1. Condition Screening for the Copper(I)-Catalyzed γ-(4*E*)-Selective Synthesis of Boron-Substituted 1,4-Dienes from Terminal Alkyne[a]



entry	R	ligand	solvent	yield (%)[b]	**4-1**:**5-1**[c](**6-1**%)[d]
1	Et	dppm	THF	27	-
2	Et	Xantphos	THF	45	91:9(35)
3	Et	dppf	THF	66	92:8(36)
4	Et	(±)-Binap	THF	71	94:6(19)
5	Et	PCy_3	THF	80	92:8(12)
6	Et	PPh_3	THF	82	91:9(6)
7	Et	$P[N(CH_3)_2]_3$	THF	77	95:5(27)
8	Et	SIMes·HCl	THF	61	93:7(32)
9	*n*-Pr	(±)-Binap	THF	83	>99:<1(7)
10	*i*-Pr	(±)-Binap	THF	96	>99:<1(7)
11	*s*-Bu	(±)-Binap	THF	95	>99:<1(3)
12	2-ethylhexyl	(±)-Binap	THF	86	>99:<1(3)
13	Cyclohexyl	(±)-Binap	THF	70	97:3(2)
14	*s*-Bu	PPh_3	THF	87	97:3(4)
15	*s*-Bu	PCy_3	THF	63	99:1(19)
16[e]	*s*-Bu	(±)-Binap	THF	83	94:6(14)
17	*s*-Bu	(±)-Binap	toluene	54	99:1(31)

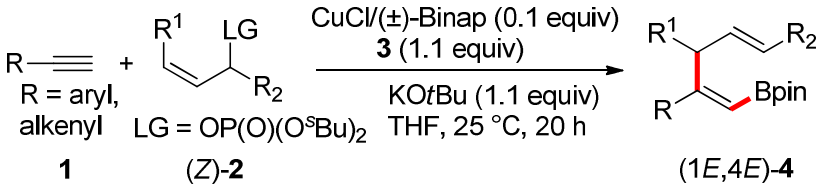
[a]Reaction conditions: **1-1** (0.3 mmol), **2-1** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), ligand, (0.1 equiv for bidentate phosphine or NHC carbene ligand, 0.2 equiv for monodentate phosphine ligand), KO*t*Bu (0.33 mmol), solvent (1.0 ml), 25 °C, 20 h. Cy = cyclohexyl. [b]The combined isolated yields of **4-1**, **5-1** and **6-1**. [c]The molar ratio of **4** and **5** in the isolated product, determined by ^{1}H NMR. **4**, **5** and **6** can not be separated by silica gel column chromatography. [d]The molar percentage of **6** in the isolated product, determined by ^{1}H NMR spectroscopy. [e](*E*)-**2-1** was used, and (1*E*,4*E*)-**5-1** is formed instead of (1*E*,4*Z*)-**5-1**.

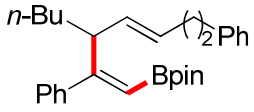
Using these optimal reaction conditions (Table 1, entry 11), the substrate scope was then examined using terminal alkynes and a variety of allyl phosphates (Table 2). Phenylacetylene (**1-**

1) was reacted with various allyl phosphates to synthesize corresponding products **4-2** to **4-6** in 56%–82% yields with good γ-(4*E*)-selectivities. The terminal allyl phosphate, which exhibits higher reactivity toward borylcopper catalytic species, affords the desired product (1*E*,4*E*)-**4-4** at 77% yield with >99% γ-selectivity (4*E*:4*Z* = 95:5). The electronic effects of the γ-$BnOCH_2$ and γ-trimethylsilyl substituents in allyl phosphates do not influence the reactions, and products (*E*)-**4-5** and (1*E*,4*E*)-**4-6** are afforded in 56% and 82% yields, respectively.[13] The products resulting from various terminal aryl alkynes bearing an electron-donating group (EDG) ((1*E*,4*E*)-**4-7** and (1*E*,4*E*)-**4-8**) or an electron-withdrawing group (EWG) at the *para* ((1*E*,4*E*)-**4-9** to **4-12**), *meta* ((1*E*,4*E*)-**4-13**), and *ortho* ((1*E*,4*E*)-**4-14**) positions are obtained in 43%–83% yields with >99% γ-selectivity. It seems that alkynes bearing an EDG give higher concentrations of hydroboration product **6** (ca. 10%). In addition to the arylacetylenes, an alkenylacetylene can also be utilized to produce the corresponding product (1*E*,4*E*)-**4-15** in 84% yield with 89% γ-selectivity. Alkyl-substituted terminal alkynes exhibit poor α/γ regioselectivity and high level of hydroboration (see Supporting information for details).

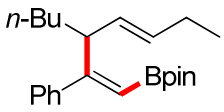
For the terminal alkyne, decreasing the catalyst loading results in a dramatic decrease in yield ((1*E*,4*E*)-**4-3**, 5 mol% CuCl, 11% yield; 2 mol% CuCl, 0% yield).

Table 2. Copper(I)-Catalyzed γ-(4*E*)-Selective Synthesis of Boron-Substituted 1,4-Dienes from Terminal Alkynes, Secondary Allyl Phosphates, and Bis(pinacolato)diboron[a]

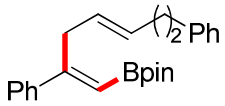




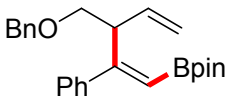
(1*E*,4*E*)-4-2
75% (>99:<1, 6%)



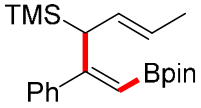
(1*E*,4*E*)-4-3
79% (91:9, 7%); 11%[b]; 0%[c]



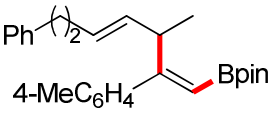
(1*E*,4*E*)-4-4
(4*E*:4*Z* = 95:5)
77% (>99:<1, 2%)



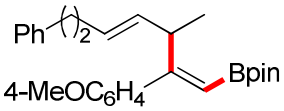
(*E*)-4-5
56% (92:8, 3%)



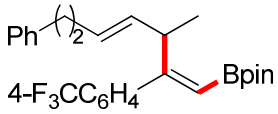
(1*E*,4*E*)-4-6
82% (85:15, 5%)



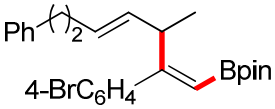
(1*E*,4*E*)-4-7
75% (99:1, 10%)



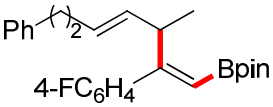
(1*E*,4*E*)-4-8
74% (>99:<1, 9%)



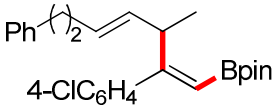
(1*E*,4*E*)-4-9
77% (>99:<1, <1%)



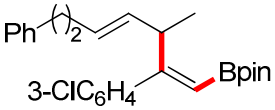
(1*E*,4*E*)-4-10
83% (>99:<1, <1%)



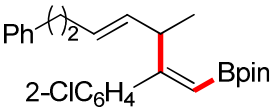
(1*E*,4*E*)-4-11
57% (>99:<1, <1%)



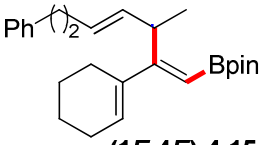
(1*E*,4*E*)-4-12
43% (>99:<1, <1%)



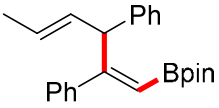
(1*E*,4*E*)-4-13
64% (>99:<1, <1%)



(1*E*,4*E*)-4-14
61% (>99:<1, <1%)



(1*E*,4*E*)-4-15
84% (89:11, 3%)



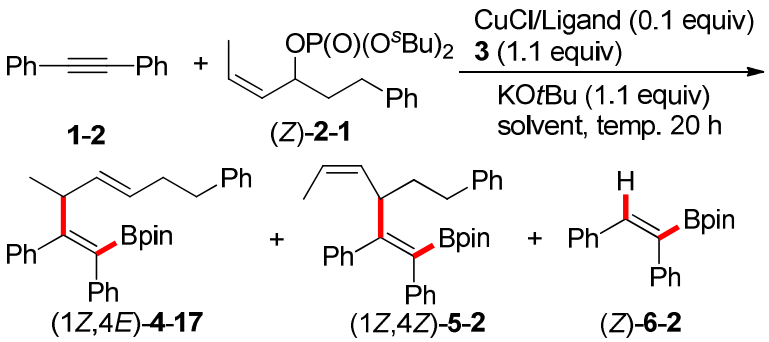
(1*E*,4*E*)-4-16
71% (>99:<1, 5%)

[a]Conditions: **1** (0.3 mmol), (*Z*)-**2** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), (±)-binap (0.03 mmol), KO*t*Bu (0.33 mmol), THF (1.0 ml), 25 °C, 20 h. The yields are combined isolated yields of **4**, **5** and **6**. The molar ratio of **4** and **5,** and molar percentage of **6** in the isolated product, determined by ^{1}H NMR spectroscopy, is shown in parentheses. [b]5 mol% catalyst loading. [c]2 mol% catalyst loading.

In all the investigated examples shown in Table 2, <1%–10% (molar percentage) hydroboration products (**6**) of the terminal alkynes are present in the isolated products. The hydroboration products probably result from the protonation of the borylcopper-alkyne adducts by the acidic protons of the terminal alkynes.

γ-(4*E*)-Selective Coupling Reaction between a Symmetrical Diarylacetylene and a Secondary Allyl Phosphate. We next explored the borylative alkenyl–allyl coupling reaction using symmetrical diarylacetylenes, which have been rarely used in borylative alkenyl–methyl coupling studies.[6c] However, under the reaction conditions optimized for the terminal alkynes, the reaction between diphenylacetylene, (*Z*)-**2-1**, and **3** affords a complex mixture of γ- and α-selective products (Table 3, entry 1). The γ-selectivity is greatly improved to 96% when the reaction is carried out in toluene at 30 °C, though the yield is decreased to 63% (Table 3, entry 2). Yields of 90%–95% and γ-selectivity of 99% are achieved when the reaction temperature is increased to 50–65 °C (Table 3, entries 3 and 4). Further increase in temperature results in a slight decreases in yield and selectivity (Table 3, entry 5). The CuCl/PPh_3 catalytic system is inferior to the CuCl/(±)-binap catalytic system in both yield and selectivity (Table 3, entry 3 *cf.* entry 6). Again, the use of (*E*)-**2-1** instead of (*Z*)-**2-1** results in a poor yield (56%) with 94% γ-selectivity (Table 3, entry 7). Under the newly optimized reaction conditions (Table 3, entry 4), the formation of hydroboration product (*Z*)-**6-2** of diphenylacetylene is limited to a nondetectable level in the ^{1}H NMR spectrum.

Table 3. Reaction Optimization for the Copper(I)-Catalyzed γ-(4*E*)-Selective Synthesis of Boron-Substituted 1,4-Dienes from Symmetrical Diarylacetylenes[a]



entry	solvent	ligand	temp.(°C)	yield (%)[b]	**4-17**:**5-2**[c](**6-2%**)[d]
1	THF	(±)-Binap	25	91	48:52(12)
2	toluene	(±)-Binap	30	63	96:4(<1)
3	toluene	(±)-Binap	50	95	99:1(1)
4	toluene	(±)-Binap	65	90	99:1(<1)
5	toluene	(±)-Binap	80	87	98:2(2)
6	toluene	PPh_3	50	80	98:2(2)
7[e]	toluene	(±)-Binap	65	56	94:6(<1)

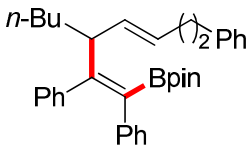
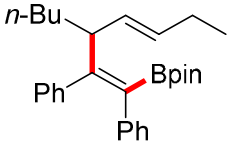
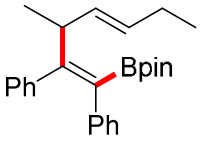
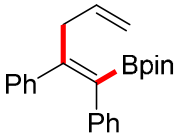
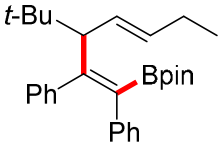
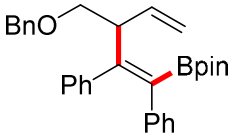
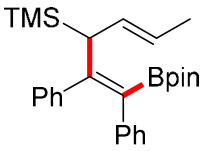
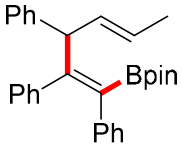
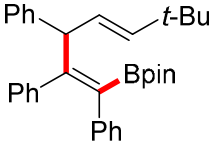
[a]Conditions: **1-2** (0.3 mmol), (*Z*)-**2-1** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), (±)-binap (0.03 mmol), PPh_3 (0.06 mmol), KO*t*Bu (0.33 mmol), solvent (1.0 ml), 25 °C, 20 h. [b]The combined isolated yields of **4-17**, **5-2** and **6-2**. [c]The molar ratio of **4-17** and **5-2** in the isolated product, determined by ^{1}H NMR spectroscopy. **4-17**, **5-2** and **6-2** can not be separated by silica gel column chromatography. [d]The molar percentage of **6** in the isolated product, determined by ^{1}H NMR spectroscopy. [e](*E*)-**2-1** was used instead of (*Z*)-**2-1** and (1*Z*,4*E*)-**5-2** is produced instead of (1*Z*,4*Z*)-**5-2**.

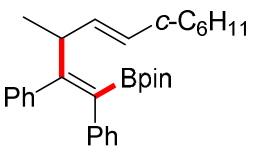
Using the optimized reaction conditions (Table 3, entry 4) for internal alkynes, diphenylacetylene was reacted with various allyl phosphates (Table 4, **4-18** to **4-30**). In most syntheses, the γ-isomeric purity of products **4** is >94%, except for (1*Z*,4*E*)-**4-20** and (*Z*)-**4-30**, where 9% and 59% α-isomers, respectively, are present in the isolated products. γ-Alkyl-substituted allyl phosphates give the corresponding products in moderate to good yields (**4-18**, 82**%**; **4-19**, 71**%**; **4-20**, 74**%**), whereas poor yields are obtained from terminal allyl phosphate (*Z*)-**4-21** (53%), probably due to its higher reactivity toward borylcopper species at higher reaction temperatures.[14] Interestingly, the presence of a bulky γ-*tert*-butyl group in the allyl phosphate does not hinder the reaction, but gives the desired product (1*E*,4*Z*)-**4-22** in 94% yield and 99% γ-selectivity. The electronic effects of γ-$BnOCH_2$, γ-TMS, and γ-phenyl substituents in the allyl phosphates do not influence the selectivities of the reaction (the γ-selectivity is 94% for (*Z*)-**4-23**, 99% for (1*Z*,4*E*)-**4-24**, and 99% for (1*Z*,4*E*)-**4-25**). The allyl phosphates bearing bulky α-*tert*-butyl and α-cyclohexyl groups also react smoothly with excellent selectivities ((1*Z*,4*E*)-**4-26** to **4-28** show >94% γ-selectivity). The cyclic allyl phosphate affords the corresponding

product in excellent yield ((*Z*)-**4-29**, 91% yield). The diaryl alkynes, symmetrically substituted with EDGs (*para*-methyl or *para*-methoxy) or EWGs (*para*-fluoro or *para*-trifluoromethyl), react with (*Z*)-**2-1** to give good yields of the products with an γ-isomeric purity of >94% ((1*Z*,4*E*)-**4-31** to **4-34**). Unfortunately, the reaction gives a mixture of four isomers, *i.e.*, (γ,4*E*), (γ,4*Z*), (α,4*E*), and (α,4*Z*), when a terminal secondary allyl phosphate is used ((1*Z*,4*E*)-**4-35**).

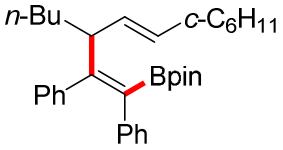
In contrast to the terminal alkyne, the catalyst loading can be reduced to as low as 2 mol% for the synthesis of (1*Z*, 4*E*)-**4-19** using diphenylacetylene (Table 4).

Table 4. Copper(I)-Catalyzed γ-(4*E*)-Selective Synthesis of Boron-Substituted 1,4-Dienes from Symmetrical Diarylacetylenes, Allyl Phosphates and Bis(pinacolato)diboron[a]

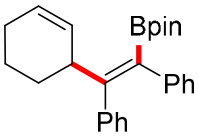
 **(1*Z*,4*E*)-4-18** 65 °C, 20 h 82% (99:1)	 **(1*Z*,4*E*)-4-19** 65 °C, 20 h 71% (98:2); 75% (99:1)[b]; 78% (99:1)[c]	 **(1*Z*,4*E*)-4-20** 65 °C, 20 h 74% (91:9)
 **(*Z*)-4-21** 65 °C, 20 h 53%	 **(1*Z*,4*E*)-4-22** 80 °C, 20 h 94% (99:1)	 **(*Z*)-4-23** 65 °C, 20 h 53% (94:6)
 **(1*Z*,4*E*)-4-24** 80 °C, 20 h 93% (99:1)	 **(1*Z*,4*E*)-4-25** 50 °C, 16 h 75% (99:1)	 **(1*Z*,4*E*)-4-26** 65 °C, 20 h 63% (94:6)



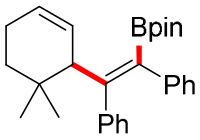
(1*Z*,4*E*)-4-27
65 °C, 12 h
62% (99:1)



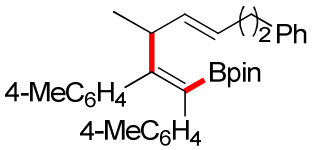
(1*Z*,4*E*)-4-28
65 °C, 8 h
73% (99:1)



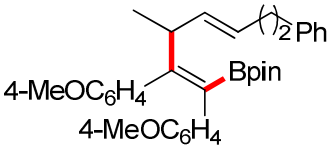
(*Z*)-4-29
65 °C, 20 h
91%



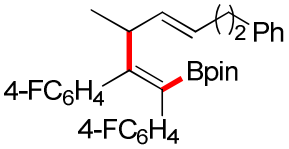
(*Z*)-4-30
80 °C, 20 h
83% (41:59)



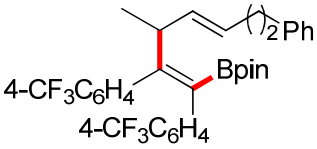
(1*Z*,4*E*)-4-31
65 °C, 4 h
65% (99:1)



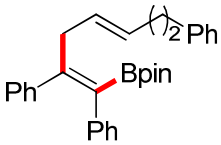
(1*Z*,4*E*)-4-32
65 °C, 4 h
80% (98:2)



(1*Z*,4*E*)-4-33
65 °C, 4 h
89% (94:6)



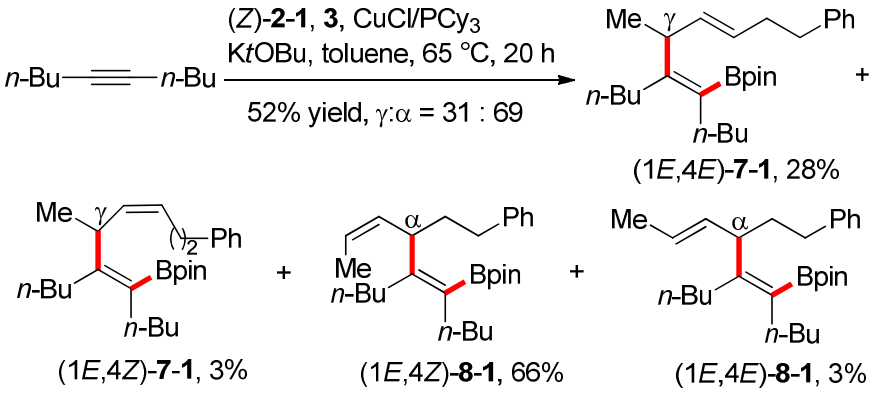
(1*Z*,4*E*)-4-34
50 °C, 3 h
82% (98:2)



(1*Z*,4*E*)-4-35
4*E*:4*Z* = 68:32
40 °C, 20 h
44% (37:63)

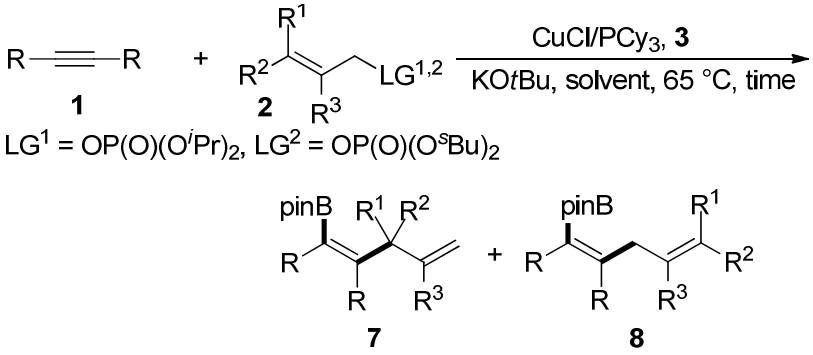
[a]Conditions: **1** (0.3 mmol), (*Z*)-**2** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), (±)-binap (0.03 mmol), KO*t*Bu (0.33 mmol), toluene (1.0 ml). The yields are combined yields of **4** and **5**. The molar ratio of **4** and **5** in the isolated product, determined by ^{1}H NMR spectroscopy, is shown in parentheses. [b]5 mol% catalyst loading. [c]2 mol% catalyst loading.

Reaction of Dialkylacetylene with Allyl Phosphates. Thus far, the alkynes used in the cross-coupling reaction bear one or two aryl substituents. However, polyenes bearing only alkyl chains are often found in natural products.[15] Therefore, dialkylacetylene was also reacted with secondary and primary allyl phosphates. The electron-rich dibutylacetylene reacts smoothly with secondary allyl phosphate (*Z*)-**2-1** to afford a mixture of two regioisomers (Scheme 2, **7-1**:**8-1** = 31:69).[16] In contrast, the reaction of dibutylacetylene with primary allyl phosphate (*Z*)-**2-2** in toluene affords the γ-selective product (*E*)-**7-2** in 41% yield with 99% isomeric purity (Table 5, entry 1). The reaction carried out in DMF leads to a decrease in regioselectivity (Table 5, entry 2, **7**:**8** = 88:12).

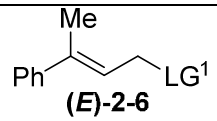


Scheme 2. The Reaction of Dibutylacetylene with Allyl Phosphates

Table 5. The Reaction of Dialkylacetylene with Primary Allyl Phosphates[a]



entry	R	allyl phosphate	solvent	product	yield (%)[b]	**7**:**8**[c]
1[d]	*n*-Bu	*n*-C_6H_{13}, LG^2 **(*Z*)-2-2**	Toluene	(*E*)-**7-2**	41	99:1
2			DMF		35	88:12
3	*n*-Bu	*t*-Bu, LG^2 **(*Z*)-2-3**	Toluene	(*E*)-**7-3**	19	98:2
4			DMF		31	95:5
5[d]	*n*-Bu	Ph, LG^1 **(*Z*)-2-4**	Toluene	(*E*)-**7-4**	57	99:1
6			DMF		64	95:5
7	*n*-Bu	Ph, LG^1 **(*E*)-2-4**	Toluene	(*E*)-**7-4**	61	96:4
8	*n*-Bu	Ph, Me, LG^1 **(*E*)-2-5**	Toluene	(*E*)-**7-5**	51	95:5

9	*n*-Bu	 **(*E*)-2-6**	DMF	(*E*)-**7**-**6**	0	–
10	Et	(*Z*)-**2**-**4**	Toluene	(*E*)-**7**-**7**	43	99:1
11	Et	(*E*)-**2**-**5**	Toluene	(*E*)-**7**-**8**	35	98:2

[a]Conditions: **1** (0.3 mmol), **2** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), PCy_3 (0.06 mmol), KO*t*Bu (0.33 mmol), solvent (1.0 ml), reaction time (20 h in toluene, 10 h in DMF). [b]Combined isolated yields of **7** and **8**. [c]Determined by ^{1}H NMR spectroscopy. [d]The reaction were carried out at 50 °C.

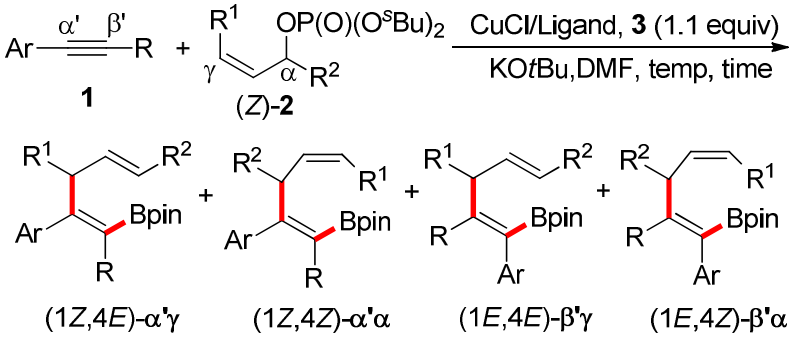
The presence of a bulky γ-*tert*-butyl group in the primary allyl phosphate hinders the reaction and affords the desired product (*E*)-**7**-**3** in 19% yield and 98% γ-selectivity (Table 5, entry 3). Dibutylacetylene reacts with γ-phenyl-substituted (*Z*)-**2**-**4** and (*E*)-**2**-**4** in toluene to afford (*E*)-**7**-**4** in 57% yield and 99% γ-selectivity (Table 5, entry 5), and 61% yield and 96% γ-selectivity (Table 5, entry 7), respectively. β,γ-disubstituted allyl phosphate (*E*)-**2**-**5** also reacts with dibutylacetylene to afford (*E*)-**7**-**5** in 51% yield and 95% γ-selectivity (Table 5, entry 8). However, γ,γ-disubstituted allyl phosphate (*E*)-**2**-**6** does not react with dibutylacetylene (Table 5, entry 9). The reactions of diethylacetylene with monosubstituted (*Z*)-**2**-**4** and disubstituted (*E*)-**2**-**5** show similar regioselectivities to those with dibutylacetylene, but result in decreased yields (Table 5, entries 10 and 11).

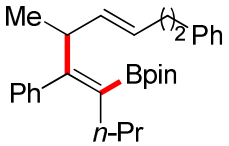
γ-(4*E*)-Selective Coupling Reaction between an Arylalkylacetylene and a Secondary Allyl Phosphate. The addition of borylcopper to unsymmetrical arylalkylacetylenes usually shows poor regioselectivity.[6c] Moon's study[17] shows that the relative size of the aryl and alkyl groups determines the direction when the alkyne is inserted into Cu-B, with boron adding to the less bulky side. Indeed, the reaction between (*Z*)-**2**-**1** and phenylpropylacetylene in DMF produces ca. 5% β′-regioisomers (Table 6, entry 1). When the sterically demanding *tert*-butylphenylacetylene reacts with (*Z*)-**2**-**1**, the regioselectivity for the alkyne is completely inverted,[5g] and the reaction

affords the corresponding product (1*Z*,4*E*)-**β′γ-1** in 64% yield and 99% γ-isomeric purity (Table 6, entry 2).[18] No *anti*-addition products with respect to the alkyne are observed in the ^{1}H NMR spectra.[5b] The reaction of (4-trifluoromethyl)phenylbutylacetylene with (*Z*)-**2-1** also affords 12% of the β′-regioisomer (Table 6, entry 3), even though there is an EWG on the phenyl ring, which is expected to direct the copper to the α′-position by stabilizing the carbon anion during the insertion reaction. It is interesting to note that the two regioisomers (β′γ and β′α) produced from the reaction between (α-alkyl)alkenylcopper and secondary allyl phosphates show similarly poor selectivities (Table 6, entry 1, 2% β′γ and 3% β′α; Table 6, entry 3, 6% β′γ and 6% β′α) as the reaction between dibutylacetylene and secondary allyl phosphate (Scheme 2, 32% γ and 68% α). It is also important to note that the configuration of the double bond in allyl phosphate (*Z*)-**2-1** is retained in the two α-regioisomers ((1*Z*,4*Z*)-**α′α** and (1*Z*,4*Z*)-**β′α**).

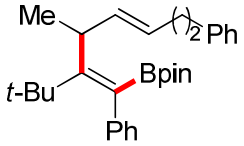
Further examples show that α′- and β′-regioselectivities of the products are also strongly influenced by the structures of the allyl phosphates (Table 6, entries 4 to 9). The β′-regioisomers produced from the reactions of (4-trifluoromethyl)phenylbutylacetylene with allyl phosphates can be limited to a non-detectable level in the ^{1}H NMR spectrum (Table 6, entries 4 to 9). These results show that the reaction between alkenylcopper and allyl phosphate is the rate-determining step for the complete catalytic cycle, and the higher reactivity of (α-aryl)alkenylcopper than (α-alkyl)alkenylcopper results in the high α′-selectivity.

Table 6. Copper(I)-Catalyzed γ-(4*E*)-Selective Synthesis of Boron-Substituted 1,4-Dienes from Arylalkylacetylenes, Secondary Allyl Phosphates and Bis(pinacolato)diboron[a]

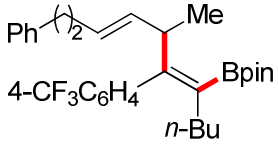




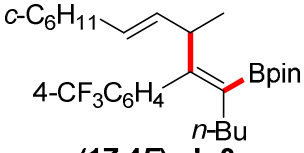
(1*Z*,4*E*)-α'γ-1
Entry 1
PPh_3, 25 °C, 20 h
60%, (83:12:2:3)



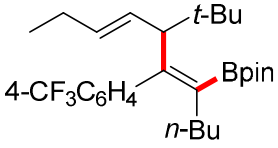
(1*Z*,4*E*)-β'γ-1
Entry 2
PPh_3, 65 °C, 20 h
64%, (0:0:99:1)



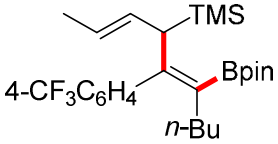
(1*Z*,4*E*)-α'γ-2
Entry 3
PPh_3, 25 °C, 20 h
92%, (85:3:6:6)



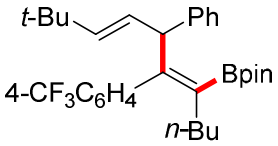
(1*Z*,4*E*)-α'γ-3
Entry 4
(±)-Binap, 50 °C, 15 h
89%, (91:9:<1:<1)



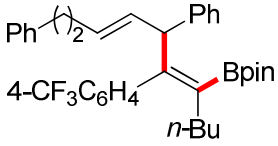
(1*Z*,4*E*)-α'γ-4
Entry 5
(±)-Binap, 50 °C, 20 h
82%, (99:1:<1:<1)



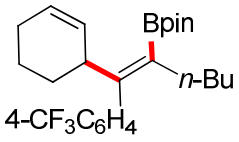
(1*Z*,4*E*)-α'γ-5
Entry 6
(±)-Binap, 50 °C , 20 h
49%, (99:1:<1:<1)



(1*Z*,4*E*)-α'γ-6
Entry 7
(±)-Binap, 50 °C, 20 h
65%, (99:1:<1:<1)



(1*Z*,4*E*)-α'γ-7
Entry 8
PPh_3, 50 °C, 20 h
74%, (99:1:<1:<1)



(*Z*)-α'γ-8
Entry 9
(±)-Binap, 50 °C, 20 h
93%

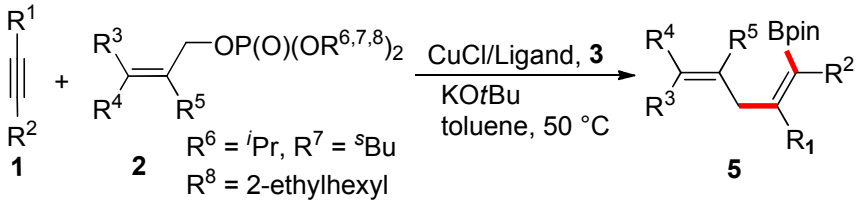
[a]Conditions: **1** (0.3 mmol), (*Z*)-**2** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), (±)-binap (0.03 mmol), PPh_3 (0.06 mmol), KO*t*Bu (0.33 mmol), DMF (1.0 ml). The combined isolated yields of **4** and **5** are shown in table. The molar ratio of **4** and **5** in the isolated product, determined by ^{1}H NMR spectroscopy , is shown in parentheses.

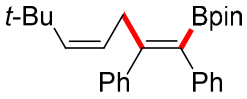
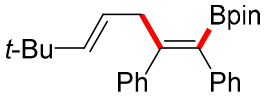
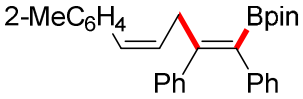
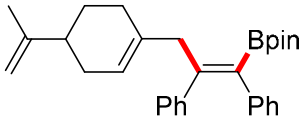
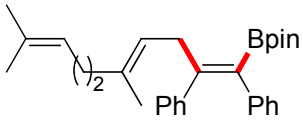
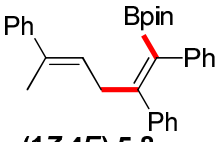
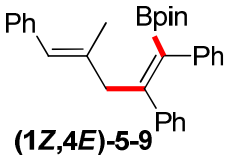
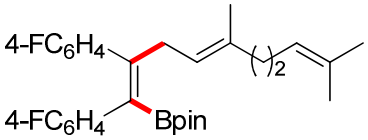
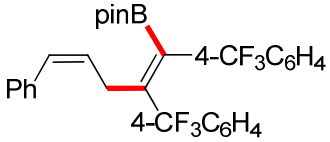
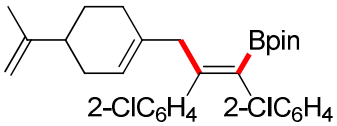
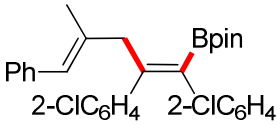
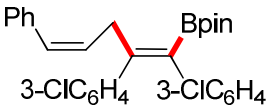
***α*-Selective Coupling between an Alkyne and a Primary Allyl Phosphate**. All the allyl phosphates that we tested were formed from secondary allyl alcohols, except for those in (*Z*)-**4-21** and (*Z*)-**4-23**), and they react with alkynes to produce γ-*E*-selective boron-substituted 1,4-

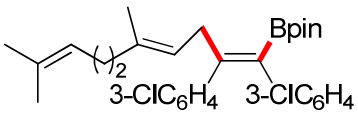
dienes. However, preliminary studies showed that reactions using primary allyl phosphates exhibited reversed regioselectivity, giving primarily α-selective products. The reaction conditions were further screened to improve the α-selectivity; the results showed that the CuCl/PCy_3 and CuCl/(±)-binap catalytic systems in toluene at 50 °C give good results. Diphenylacetylene was first reacted with primary allyl phosphates of various substitution patterns (Table 7). α-Selective products (1Z,4Z)-5-3 and (1Z,4E)-5-4 are produced in 68%–71% yields with >98% α-isomeric purity, and the configurations of the double bonds in the allyl phosphates are completely reserved in the products.[19] The allyl phosphate bearing a bulky γ-(o-methyl)phenyl substituent affords (1*Z*,4*Z*)-**5-5** in 51% yield with 99% α-isomeric purity. Primary allyl phosphates bearing γ,γ-disubstituents and β,γ-disubstituents afford the products in 67%–71% yields with 80%–94% α-isomeric purity ((*Z*)-**5-6**, 90%; (1*Z*,4*E*)-**5-7**, 90%; (1*Z*,4*E*)-**5-8**, 94%; (1*Z*,4*E*)-**5-9**), 80%). The reactions of primary allyl phosphates with symmetrical diarylacetylenes bearing EWGs (*para*-fluoro, *para*-trifluoromethyl, and *ortho*-, *meta*-, and *para*-chloro) afford α-selective products in good yields with >88% α-selectivity ((1*Z*,4*E*)-**5-10**, **5-12**–**5-17**),[20] except for (1*Z*,4*Z*)-**5-11**, where the moderate α-selectivity (79%) was probably due to the less hindered γ-phenyl substituent. The reaction of an unsymmetrical alkyne with primary allyl phosphates also proceeds smoothly and affords the α-selective product in 61%–87% yield and >90% α-selectivity ((1*Z*,4*E*)-**5-18**, (*Z*)-**5-19**, (1*Z*,4*E*)-**5-20** and (1*Z*,4*E*)-**5-21**). The results in Table 7 show that the steric effect of substituents on primary allyl phosphates exerts the main influence on the regioselectivity of allyl phosphates, with bulky γ-substituents showing good α-selectivity ((1*Z*,4*E*)-**5-8** *cf.* (1*Z*,4*E*)-**5-9**). Though copper-catalyzed γ-selective couplings between a carbon nucleophile and a primary allyl phosphate are common,[21] the corresponding α-selective coupling reaction is rare.[22]

For the α-selective reaction, 2 mol% catalyst loading results in no obvious decrease in yield, but with a little yet significant improvement in α-selectivity (Table 7, (1*Z*,4*E*)-**5**-**18**).

Table 7. α-Selective Coupling between an Alkyne and a Primary Allyl Phosphate[a]



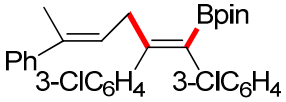
 **(1*Z*,4*Z*)-5-3** R[7], PCy_3, 12 h[b] 71%, (98:2)	 **(1*Z*,4*E*)-5-4** R[7], PCy_3, 12 h[b] 68%, (99:1)	 **(1*Z*,4*Z*)-5-5** R[6], PCy_3, 4 h 51%, (99:1)
 **(*Z*)-5-6** R[7], (±)-Binap, 20 h 69%, (90:10)	 **(1*Z*,4*E*)-5-7** R[8], PPh_3, 12 h 67%, (90:10)	 **(1*Z*,4*E*)-5-8** R[6], PCy_3, 12 h 68%, (94:6)
 **(1*Z*,4*E*)-5-9** R[6], PCy_3, 12 h 71%, (80:20)	 **(1*Z*,4*E*)-5-10** R[7], (±)-Binap, 4 h 62%, (99:1)	 **(1*Z*,4*Z*)-5-11** R[6], PCy_3, 2 h 60%, (79:21)
 **(*Z*)-5-12** R[7], (±)-Binap, 4 h 88%, (93:7)	 **(1*Z*,4*E*)-5-13** R[6], PCy_3, 3 h 77%, (99:1)	 **(1*Z*,4*Z*)-5-14** R[6], PCy_3, 3 h 73%, (88:12)



(1*Z*,4*E*)-5-15

R^7, PCy_3, 3 h

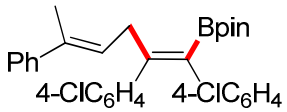
65%, (99:1)



(1*Z*,4*E*)-5-16

R^6, (±)-Binap, 4 h

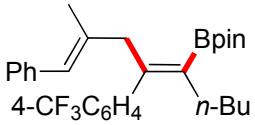
79%, (99:1)



(1*Z*,4*E*)-5-17

R^6, PCy_3, 3 h

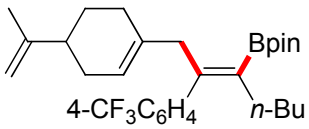
76%, (97:3)



(1*Z*,4*E*)-5-18

R^6, (±)-Binap, 8 h[c]

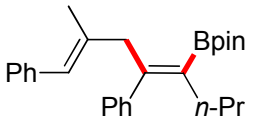
67%, (93:7); 62%, (99:1)[d]; 63%, (98:2)[e]



(*Z*)-5-19

R^7, (±)-Binap, 8 h[c]

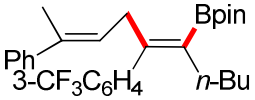
87%, (96:4)



(1*Z*,4*E*)-5-20

R^6, PCy_3, 10 h

62%, (94:6)



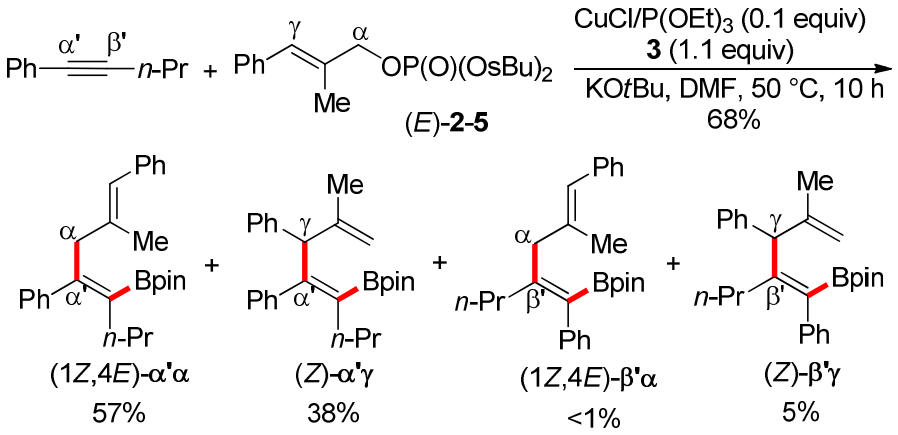
(1*Z*,4*E*)-5-21

R^6, PCy_3, 8 h

61%, (99:1)

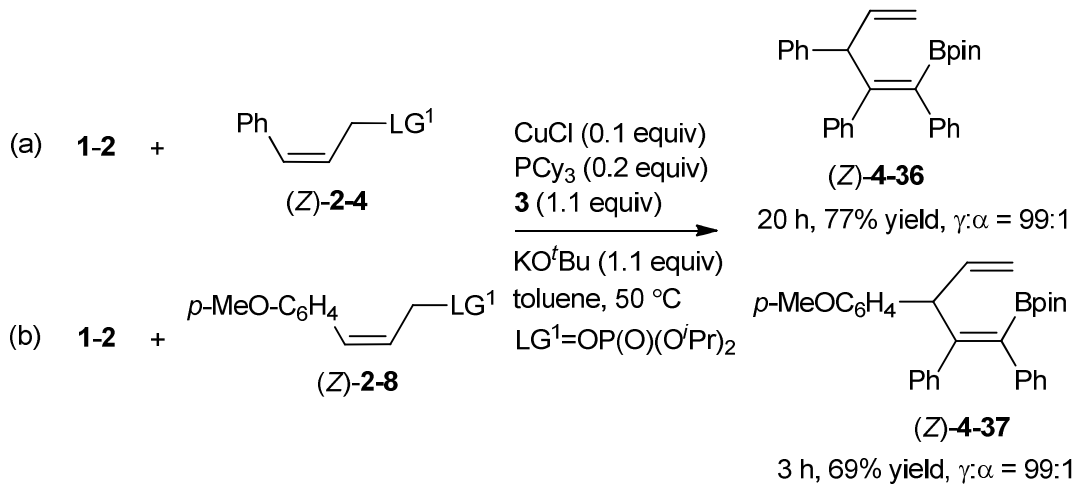
[a]Conditions: **1** (0.3 mmol), **2** (0.45 mmol), **3** (0.33 mmol), CuCl (0.03 mmol), (±)-binap (0.03 mmol), PCy_3 (0.06 mmol), KO*t*Bu (0.33 mmol), toluene (1.0 ml), 50 °C. The combined isolated yields of **5** and **4** are shown in table. The molar ratio of **5** and **4** in the isolated product, determined by ^{1}H NMR spectroscopy, is shown in parentheses. [b]The reactions were carried out at 65 °C. [c]The reactions were carried out in DMF (1.0 ml). [d]5 mol% catalyst loading. [e]2 mol% catalyst loading.

Even though the β′-isomers are produced only in a little amount when phenylpropylacetylene is reacted with primary allyl phosphate (*E*)-**2**-**5**, the high β′γ-selectivity is interesting (Scheme 3, 5% (*Z*)-**β′γ**, <1% (1*Z*,4*E*)-**β′α**). It seems that α-boryl-α-aryl- β -alkenylcopper species formed as a minor intermediate from arylalkylacetylene and β-borylalkenylcopper formed from dialkylacetylene show similar regio- and stereoselectivity towards primary and secondary allyl phosphates.



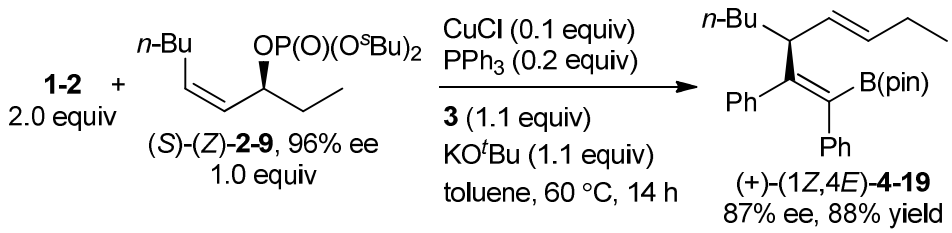
Scheme 3. Regioselectivity of β-Borylalkenylcopper towards Primary Allyl Phosphate

The Substitutent Effects on the Regioselectivity of γ-Monoaryl-Substituted Primary Allyl Phosphates. The electronic and steric factors have complicated effects on the regioselectivity of γ-monoaryl-substituted primary allyl phosphates. When diphenyl acetylene (**1**-**2**) were reacted with γ-phenyl- and γ-4-methoxy-phenyl-substituted primary allyl phosphates ((*Z*)-**2**-**4** and (*Z*)-**2**-**8**), the reactions afford corresponding γ-selective products ((*Z*)-**4**-**36** and (*Z*)-**4**-**37**) in good yields (Scheme 4a and 4b). However, a 2-methyl substitutent on the γ-phenyl ring of the allyl phosphate reversed the regioselectivity (Scheme 4 *cf.* Table 7, (1*Z*,4*Z*)-**5**-**5**)), indicating that the regioselectivity of the γ-monoaryl-substituted primary allyl phosphates is highly sensitive to the size of the γ-substitutent. On the other hand, the introduction of substitutens on the phenyl ring of **1**-**2** also strongly influences the regioselectivity of (*Z*)-**2**-**4**, with EWG groups result in α-selectivity (Table 7, (1*Z*,4*Z*)-**5**-**11** and (1*Z*,4*Z*)-**5**-**14**). The alkynes' substitutents effect on regioselectivity probably works through the ligand effect of the alkenyl group in β-borylalkenylcopper intermediate.



Scheme 4. The Steric and Electronic Effects on Regioselectivity. (a) γ-Selective Reaction of (*Z*)-γ-phenyl allyl phosphate. (b) γ-Selective Reaction of (*Z*)-γ-(4-methoxyphenyl) allyl phosphate.

Chirality Transfer. The boron-substituted 1,4-dienenes produced from γ-substituted allyl phosphates bear a stereogenic center at C3. To obtain optically active product, we investigated the chirality transfer of an optically active allyl phosphate (Scheme 5). Allyl phosphate (*S*)-(*Z*)-**2-7** (96% ee) was reacted with diphenyl acetylene (**1-2**) and diboron **3** in the presence of CuCl (0.1 equiv), PPh_3 (0.2 equiv), and KO*t*Bu in toluene at 60 °C. (+)-(1*Z*,4*E*)-**4-19** was obtained at 87% ee and 88% yield. This result provides a possible route to produce enantiomeric pure boron-substituted 1,4-dienenes from optically active allyl phosphates. Further work to asymmetrically synthesize boron-substituted 1,4-dienenes by chirality transfer and chiral catalyst is in progress.

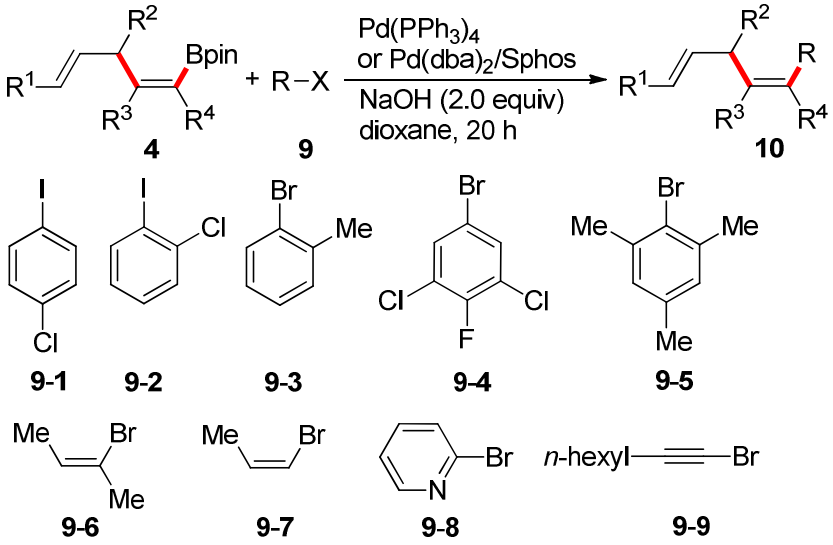


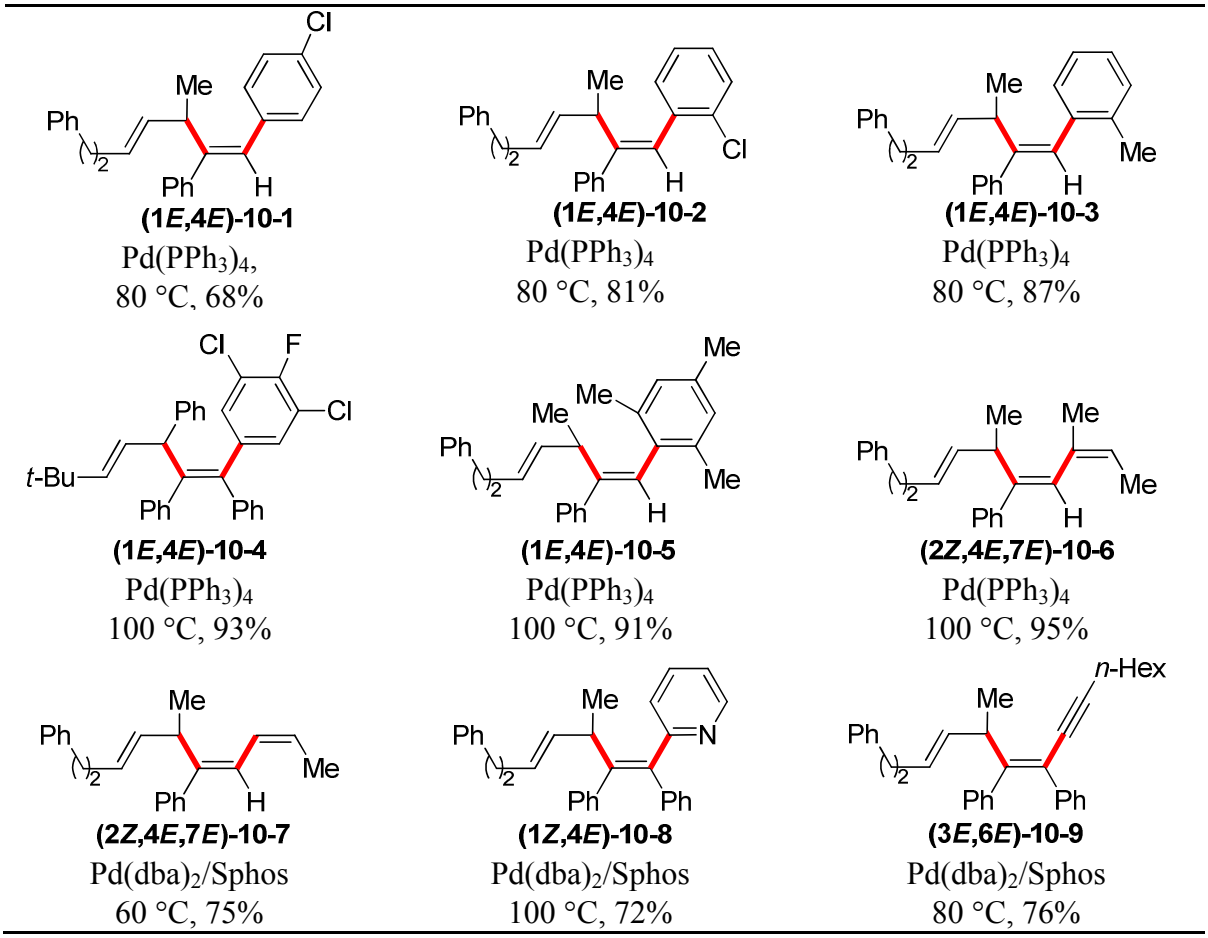
Scheme 5. Chirality Transfer

Palladium-Catalyzed Cross-Coupling Reactions of Boron-Substituted 1,4-Dienes and Halides. The polyenes and conjugated enynes are an important class of compounds occurring in a number of natural products and synthetic molecules.[23] The coupling reaction of boron-substituted 1,4-dienes with alkenyl, aryl, and alkynyl halides provides a convenient route to these compounds. Firstly, the cross-coupling of boron-substituted 1,4-dienes and halides was carried out in the presence of $Pd(PPh_3)_4$ and NaOH (2.0 equiv) in dioxane (Table 8). Both iodides (**9-1** and **9-2**) and bromides (**9-3** and **9-4**) react with boron-substituted 1,4-diene **4** at moderate temperature (80−100 °C) to form the corresponding coupling products (1*E*,4*E*)-**10-1** to **10-4** in 68%–93% yields.[24] Interestingly, the sterically demanding aromatic bromide **9-5** also reacts with (1*E*,4*E*)-**4-1** efficiently and gives coupling product (1*E*,4*E*)-**10-5** in 91% yield. Secondary alkenyl bromide **9-6** reacts with (1*E*,4*E*)-**4-1** to give coupling product (2*Z*,4*E*,7*E*)-**10-6** in 95% yield.

The $Pd(dba)_2$/Sphos catalyst system is also effective for the cross-coupling reaction between boron-substituted 1,4-dienes **4** and halides. (1*E*,4*E*)-**4-1** reacts with (*Z*)-1-bromopropene (**9-7**) to provide triene (2*Z*,4*E*,7*E*)-**10-7** in 75% yield. Heteroaryl bromide **9-8** reacts with (1*E*,4*Z*)-**4-17** to give (1*Z*,4*E*)-**10-8** in 72% yield. Besides the commonly used coupling partners (aryl and alkenyl halides), 1-bromooctyne (**9-9**) also reacts with boron-substituted 1,4-diene (1*E*,4*Z*)-**4-17** to form the conjugated enyne (3*E*,6*E*)-**10-9** in 76% yield.

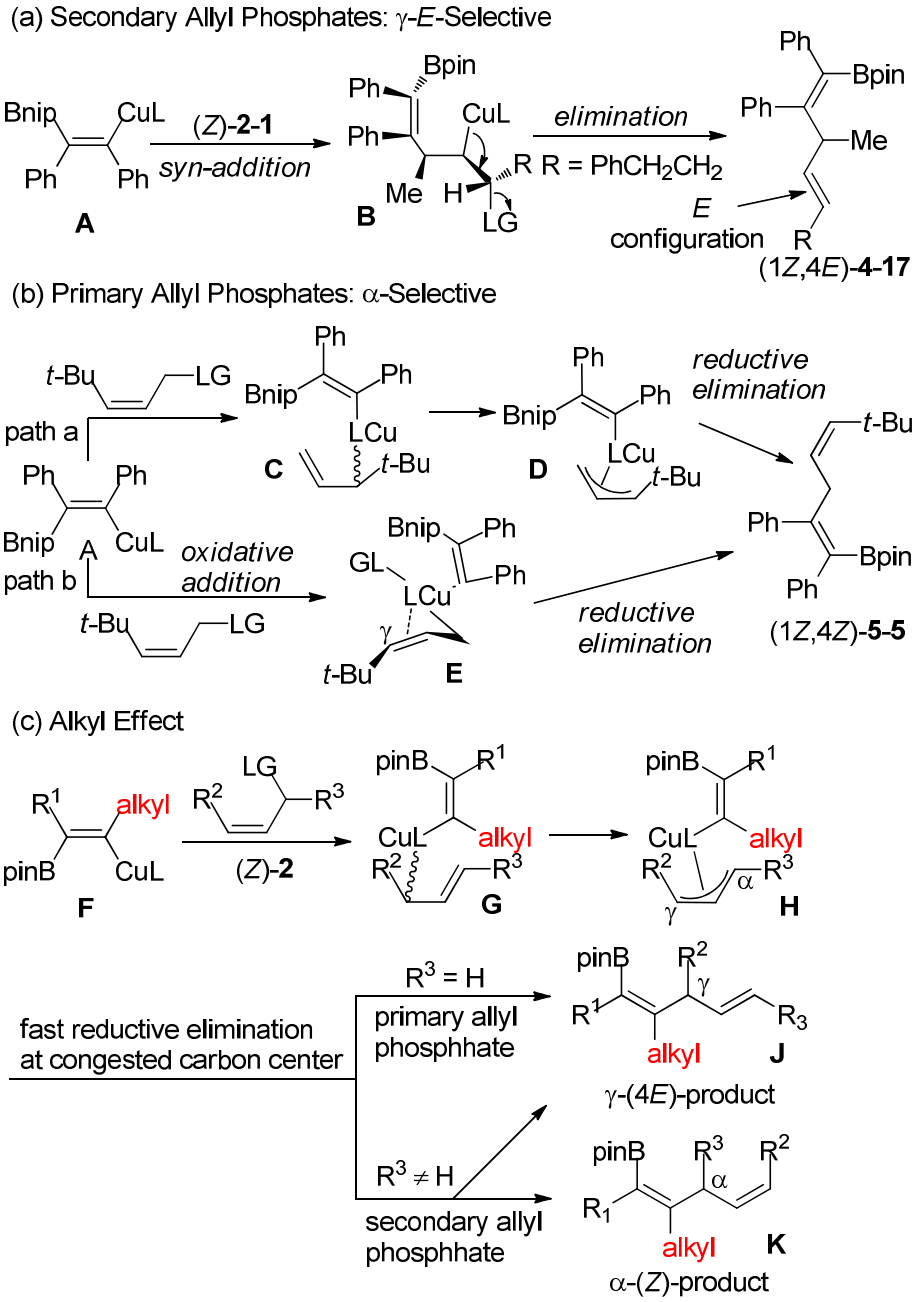
Table 8. Palladium-Catalyzed Cross-Coupling Reactions of Boron-Substituted 1,4-Dienes and Halides[a]





[a]Conditions: **4** (0.1 mmol), **9** (0.15 mmol, 1.5 equiv), NaOH (2 M aqueous, 100 μL, 0.2 mmol, 2.0 equiv), $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol, 0.1 equiv), $Pd(dba)_2$ (5.8 mg, 0.01 mmol, 0.1 equiv), Sphos (4.1 mg, 0.01 mmol, 0.1 equiv). Isolated yields of **10** is shown in table

Mechanistic Consideration. Based on DFT studies by Nakamura *et al*.,[25] the typically proposed mechanism for the copper-catalyzed coupling reaction between a carbon nucleophile and an allyl phosphate proceeds via allylic oxidative-addition and reductive elimination.[21d, 21e, 21h, 21i, 26] Sawamura and Ohmiya *et al*. have also proposed an addition-elimination mechanism to explain the observed high γ-selectivity.[26a, 27] For the γ-*E*-selective coupling reaction between **1**-**2** and (*Z*)-**2**-**1**, an addition–elimination mechanism, similar to that proposed by Sawamura and Ohmiya *et al*., is proposed (Scheme 4(a)). Firstly, (β-boryl)alkenylcopper(I) **A**, formed from the *syn*-addition of borylcopper(I) to the alkyne, is added across the C=C bond of (*Z*)-**2**-**1** to form species **B**. Species **B** affords (1*E*,4*Z*)-**4**-**17** through stereoselective β-elimination. The elimination process may be *syn*- or *anti*-periplanar, as reported by Tsuji *et al*.[10a]



Scheme 6. Possible Reaction Mechanism. (a) γ-*E*-Selective Reaction of Secondary Allyl Phosphates. (b) α-Selective Reaction of Primary Allyl Phosphates. (c) The Possible Ligand Effect of α-Alkyl in Alkenylcopper Species on the Regioselectivity of Primary and Secondary Allyl Phosphates.

A possible mechanism for the formation of α-selective products is shown in Scheme 4(b). Path "a" is a route similar to that proposed by Hirano and Miura.[22] The nucleophilic attack of (β-boryl)alkenylcopper(I) **A** on the primary (*Z*)-allyl phosphate proceeds in an S_N2' manner. The formed complex **C** undergoes a rapid σ–π conversion to give the π-allyl copper species **D**. The σ–π conversion would need to be much faster than rotation around the σ bond for the stereochemistry of the starting (*Z*)-allyl phosphate to be reserved in the product. Reductive elimination of **D** at the least hindered carbon center provides (1*Z*,4*Z*)-**5**-**5**.

Path "b" is another possible route. The primary (*Z*)-allyl phosphate undergoes S_N2-type oxidative-addition over the copper center to form **E.** Subsequent reductive elimination results in the formation of the α-selective product (1*Z*,4*Z*)-**5**-**5**, with the retention of the double bond configuration.

The study shows that the (α-alkyl)alkenylcopper formed from the alkyne (*e.g.*, dibutylacetylene) and borylcopper exhibits a different regioselectivity. Its reaction with secondary allyl phosphates provides a mixture of α- and γ-selective products (Scheme 2, Table 6, entries 1 and 3,). However, its reaction with primary allyl phosphates shows high γ-selectivity (Table 5 and Scheme 3). This regioselectivity probably results from the electron-donating effect and small size of the alkyl substituent. A possible mechanism is shown in Scheme 4(c). (α-Alkyl)alkenylcopper **F** reacts with (*Z*)-**2** in an S_N2' manner to form intermediate **G**, followed by a rapid σ–π conversion to form π-allyl copper species **H**. The subsequent fast reductive elimination occurs at the more hindered carbon center. For primary allyl phosphates (*i.e.*, R^3 = H), **H** eliminates at the γ-position and gives γ-(*E*)-products **J**. For secondary allyl phosphates (*i.e.*, $R^3 \neq$ H), the elimination occurs at both the γ- and α-positions due to their similar steric environments, and leads to a mixture of the γ-(*E*)-product (**J**) and the α-(*Z*)-product (**K**).

It should be noted that the stereo configuration of the C=C bond in allyl phosphates is retained in all α-selective products.

3. CONCLUSIONS

A synthetic method for the production of a diverse range of boron-substituted 1,4-dienes through a copper-catalyzed highly regio- and stereoselective boryl-allylation of alkynes with allyl phosphates and bis(pinacolato)diboron is developed and optimized. The system works well with diverse alkynes, including terminal arylacetylenes, symmetrically diaryl-substituted acetylenes, symmetrically dialkyl-substituted acetylenes, and aryl- and alkyl-substituted acetylenes, and primary and secondary allyl phosphates with diverse substitutents. The β-borylalkenylcopper species, formed by the *syn*-addition of borylcopper to the alkyne, is the key catalytic species. For β-borylalkenylcopper species with copper adds to the aryl side of alkynes bearing at least one aryl group, their reactions with secondary allyl phosphates exhibit γ-(4*E*)-selectivity, and their reactions with primary allyl phosphates exhibit α-selectivity. In contrast, for β-borylalkenylcopper species with copper adds to the alkyl chain side of alkynes, their reactions with secondary allyl phosphates produce a mixture of α- and γ-selective products, and their reactions with primary allyl phosphates show high γ-selectivity. The regioselectivity of the unsymmetrically disubstituted acetylene in the products depends on both the intrinsic regioselectivity when the alkyne is inserted into Cu-B and the relative reactivity of (1-aryl)alkenylcopper and (1-alkyl)alkenylcopper towards allyl phosphates. It seems that the reaction between alkenylcopper and allyl phosphate is, to some extent, the rate-determining step. The boron-substituted 1,4-dienes are excellent reactants in the palladium-catalyzed Suzuki-Miyaura cross-coupling reaction, demonstrating a versatile building block for the synthesis of

1,4-dienes. Further experimental study using chiral catalysts and enantiomeric pure allyl phosphates are in progress.

ASSOCIATED CONTENT

Details of synthetic procedures and characterization of compounds by ^{1}H-NMR, ^{13}C-NMR, NOESY, and HRMS. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* E-mail: zhongcm@nwsuaf.edu.cn.

Notes

The authors declare no competing financial interest.

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(10) Recently the copper-catalyzed allyl-allyl coupling reaction between allene and allyl phosphates has been reported by Tsuji and Hoveyda etal. In contrast to the secondary β-borylalkenylcopper species formed from the *syn*-addition of borylcopper to alkyne, an β-borylallylcopper species was formed in their study, see: (a) Semba, K.; Bessho, N.; Fujihara, T.; Terao, J.; Tsuji, Y. *Angew. Chem. Int. Ed.*, **2014**, *53*, 9007−9011. (b) Meng, F. K.; McGrath, P.;

Hoveyda, A. H. *Nature*, **2014**, *513*, 367–374. Yoshida and co-workers have reported one example of copper-catalyzed synthesis of boron-substituted 1,4-diene, see ref. 6b.

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(12) In this study, the compounds **4**, **5** and **6** show the same Rf value on silica TLC plate and they cannot be separated by silica column chromatography. So the molar ratio of them in the combined isolated products is the same as that in the crude products.

(13) For the copper-catalyzed borylation of γ-silyl-substituted allyl carbonates, see ref. 11b.

(14) For the copper-catalyzed γ-selective borylation of allyl carbonates, see ref. 11c and 11d.

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(18) The configuration of the C_4 double bond in (1*Z*,4*E*)-**β'γ-1** was determined by NOESY. See supporting information for more details.

(19) The configurations of the C_4 double bonds in (1*Z*,4*Z*)-**5-3** and (1*Z*,4*E*)-**5-4** were determined by NOESY. See supporting information for more details.

(20) The configurations of the C_4 double bonds in (1*Z*,4*E*)-**5-13**, (1*Z*,4*Z*)-**5-14**, (1*Z*,4*E*)-**5-16** and (1*Z*,4*E*)-**5-17** were determined by NOESY. See supporting information for more details.

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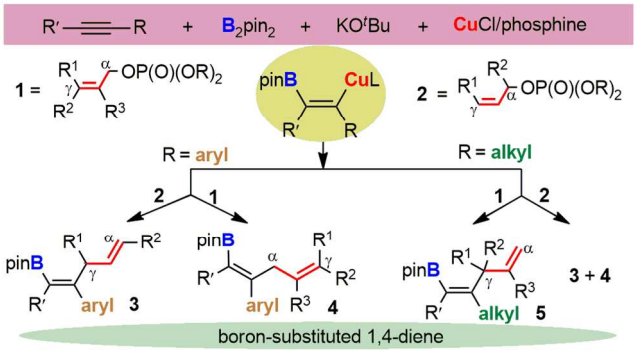

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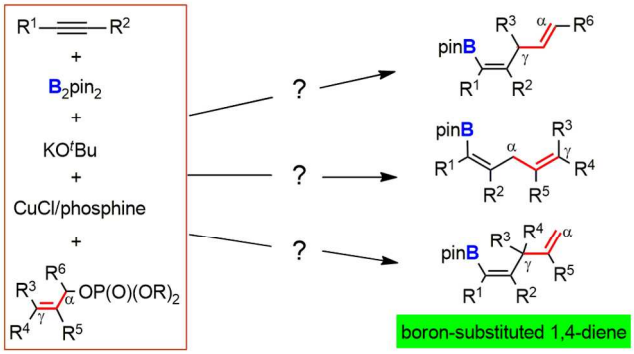
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γ R4 R5
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γ R1 R2
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R1 R2 R5
pinB R3 R4 α
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boron-substituted 1,4-diene