

Synthetic Methods

Copper-Catalyzed Borylation of α -Alkoxy Allenes with Bis(pinacolato)diboron: Efficient Synthesis of 2-Boryl 1,3-Butadienes**

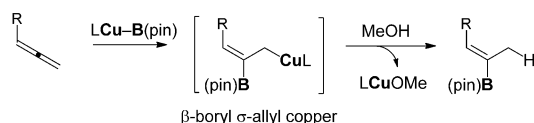
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Organoboranes are useful synthetic intermediates in organic synthesis, with utility in carbon–carbon^[1] and carbon–heteroatom^[2] bond-forming reactions. The hydroboration^[3] of carbon–carbon unsaturated bonds is one of the most powerful methods available for the synthesis of a wide variety of organoboranes. We recently reported the copper-catalyzed selective hydroboration of allenes by the use of bis(pinacolato)diboron ($B_2(\text{pin})_2$) as a borylation reagent.^[4] In the reaction, a β -boryl σ -allyl copper intermediate was cleanly generated by the insertion of an allene into a boryl copper catalytic species (Scheme 1 a).^[4a] On the basis of the pioneering studies by Ito, Sawamura, and co-workers on the copper-catalyzed borylation of substrates containing oxygen-based leaving groups,^[5] we anticipated that 2-boryl 1,3-butadienes could be efficiently synthesized by the borylation of allenes

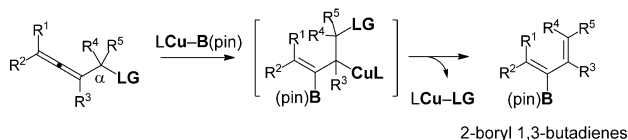
bearing a suitable leaving group at the α -position (Scheme 1 b).

Boryl-substituted 1,3-butadiene derivatives are potentially useful building blocks.^[6] 1-Boryl 1,3-butadienes can be readily synthesized by the hydroboration of 1,3-enynes and then employed as useful boryl compounds.^[7] In sharp contrast, the synthetic methods available to date for the synthesis of 2-boryl 1,3-butadienes are not so efficient.^[8] For example, elaborate methods, including the enyne metathesis of alkynyl boranes^[8a–c] (Scheme 2 a), palladium-catalyzed cross-coupling reactions of (*Z*)-1-halo 1-alkenyl boranes^[8d] or 1,1-diboryl 1-alkenes^[8e] (Scheme 2 b), reactions of alkynyl

a) Hydroboration of allenes^[4a]

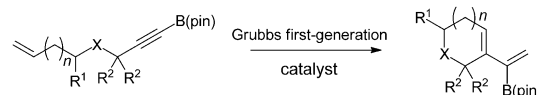


b) Efficient synthesis of 2-boryl 1,3-butadienes

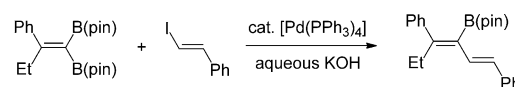


Scheme 1. Approaches to the synthesis of 1,3-dienyl boranes from allenes. LG = leaving group.

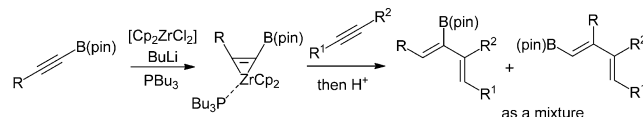
a) Enyne metathesis of alkynyl boranes^[8a,b]



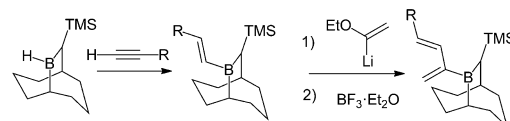
b) Cross-coupling reaction of a 1,1-diboryl 1-alkene^[8e]



c) Reaction of alkynyl boranes with alkynes^[8f]



d) Hydroboration followed by a migration reaction^[8g]



Scheme 2. Previously reported approaches to 2-boryl 1,3-butadiene derivatives. TMS = trimethylsilyl.

boranes with alkynes^[8f] (Scheme 2 c), and hydroboration followed by migration^[8g] (Scheme 2 d), have been reported; however, the variety of available 2-boryl 1,3-butadienes has remained quite limited. Thus, more efficient and general synthetic methods are highly desirable. Herein, we report the straightforward copper-catalyzed borylation^[9] of α -alkoxy allenes with $B_2(\text{pin})_2$ to afford 2-boryl 1,3-butadienes with various substitution patterns.

We investigated the borylation of $\text{Me}_2\text{C}=\text{C}=\text{CCH}_2\text{OBn}$ (**1a**) with $B_2(\text{pin})_2$ in THF at room temperature in the

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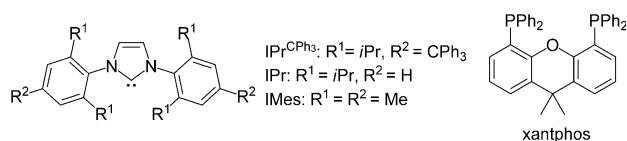
Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201306843>.

Table 1: Optimization of the reaction conditions for the copper-catalyzed borylation of **1a**.^[a]

Entry	L	OR	Yield of 2a [%] ^[b]
1	IMes	OBn (1a)	81
2	IPr	OBn (1a)	92
3	IPr ^{CPh3}	OBn (1a)	95 (89) ^[c]
4	xantphos	OBn (1a)	38
5	IPr ^{CPh3}	O(<i>n</i> -C ₆ H ₁₃) (1a1)	94
6	IPr ^{CPh3}	OCO ₂ Me (1a2)	96
7	IPr ^{CPh3}	OAc (1a3)	8

[a] Reaction conditions: [LCuCl] (0.0050 mmol, 2.0 mol %), KOtBu (0.025 mmol, 10 mol %), B₂(pin)₂ (0.28 mmol), an allene (0.25 mmol), THF (0.50 mL), room temperature, 30 min. [b] The yield was determined by GC with an internal standard. [c] The yield of isolated **2a** is given in parentheses. Bn = benzyl.

presence of copper catalysts (Table 1, entries 1–4). First, commercially available copper complexes bearing an N-heterocyclic carbene (NHC) ligand were evaluated as catalysts. The corresponding 1,1-disubstituted 2-boryl 1,3-butadiene **2a** was obtained in 81 % yield with the catalyst [(IMes)CuCl] and in 92 % yield with [(IPr)CuCl] (Table 1, entries 1 and 2; see Scheme 3 for the structures of ligands used in this study). A bulky NHC complex, [(IPr^{CPh3})CuCl], was found to be a better catalyst. It promoted the formation



Scheme 3. Structures of the ligands used in this study.

of **2a** in 95 % yield and enabled the isolation of pure **2a** in 89 % yield (Table 1, entry 3). However, with [(xantphos)CuCl] as the catalyst, the yield decreased to 38 % (Table 1, entry 4). As leaving groups for the allene, –O(*n*-C₆H₁₃) and –OCO₂Me were found to be effective (entries 5 and 6). In contrast, with the leaving group –OAc, **2a** was formed in only 8 % yield (Table 1, entry 7). Owing to the ease of synthesis and good stability of the corresponding allene substrates, OBn was chosen as the preferred leaving group.^[10]

The reaction was carried out with various allenes bearing an α-OBn leaving group under the optimized reaction conditions (Table 2). When the 1,1-disubstituted allene **1b** was used, **2b** was isolated in pure form in 85 % yield (Table 2, entry 1). The 3-butyl- and 3-phenyl-substituted allenes **1c** and **1d** afforded the corresponding 3-substituted 2-boryl 1,3-butadienes **2c** and **2d** selectively in high yields (Table 2, entries 2 and 3). The α,α-disubstituted allenes **1e** and **1f** were converted selectively into the 2-boryl butadienes **2e** and **2f** containing two substituents at the 4-position in 59 and 62 % yield, respectively (Table 2, entries 4 and 5 in parentheses). In these reactions, [(IPr)CuCl] also showed good catalytic

Table 2: Synthesis of various 2-boryl 1,3-butadienes.^[a]

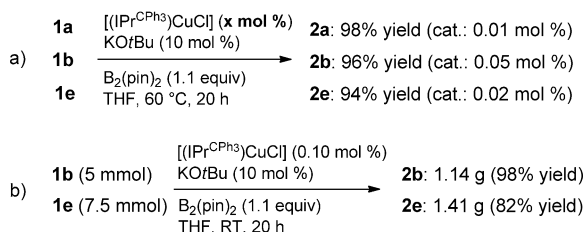
Entry	Substrate	Product	Yield [%] ^[b]
1	1b	2b	85
2	1c	2c	71
3	1d	2d	90
4	1e	2e	59 (67) ^[c]
5	1f	2f	62 (78) ^[c,d]
6	1g	2g	67
7	1h	2h	82
8	1i	2i	87
9 ^[e]	1j	2j	99
10 ^[f]	1k	2k	63 ^[g]
11 ^[h]	1l	2l	96 ^[i]
12 ^[j]	1m	2m	76 ^[k]

[a] Reaction conditions: [(IPr^{CPh3})CuCl] (0.0050 mmol, 2.0 mol %), KOtBu (0.025 mmol, 10 mol %), B₂(pin)₂ (0.28 mmol), an allene (0.25 mmol), THF (0.50 mL), room temperature, 30 min. [b] Yield of the isolated product. [c] The catalyst [(IPr)CuCl] (0.0050 mmol, 2.0 mol %) was used instead of [(IPr^{CPh3})CuCl]. [d] The reaction was carried out at 10 °C. [e] The reaction was carried out at 60 °C for 14 h. [f] The reaction was carried out at 0 °C for 11 h. [g] *E/Z* 96:4. [h] The reaction was carried out at –40 °C for 17 h. [i] *E/Z* 90:10. [j] The catalyst [(xantphos)CuCl] (0.0050 mmol, 2.0 mol %) was used instead of [(IPr^{CPh3})CuCl]. [k] *Z/E* 96:4.

activity (Table 2, entries 4 and 5). *N*-tert-butoxycarbonyl (*N*-Boc) and ketal moieties were tolerated under these reaction conditions, with the formation of **2g** and **2h** in 67 and 82 % yield, respectively (Table 2, entries 6 and 7), and the highly substituted 2-boryl 1,3-butadienes **2i** and **2j** were obtained successfully in high yield from **1i** and **1j** (Table 2, entries 8 and 9). It was anticipated that the borylation of unsymmetri-

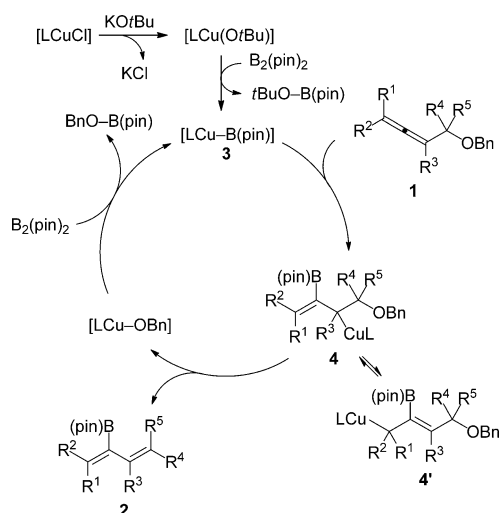
cally α,α -disubstituted allenes, such as **1k** and **1l**, would be challenging, since *E/Z* stereoisomeric mixtures could be produced. However, in practice, (*E*)-**2k** and (*E*)-**2l** were obtained in 63 and 96% yield, respectively, with high stereoselectivity (*E/Z* 96:4 and 90:10; Table 2, entries 10 and 11). Furthermore, the allene **1m** bearing a secondary alkyl substituent at the 1-position was successfully transformed into (*Z*)-**2m** in 76% yield with high stereoselectivity (*Z/E* 96:4) by the use of [(xantphos)CuCl] as the catalyst (Table 2, entry 12). Surprisingly, the products shown in Table 2, including rather simple compounds, are all new compounds, which highlights the impracticality of current methods for the preparation of 2-boryl 1,3-butadienes with various substitution patterns. Furthermore, the reactions proceeded smoothly with much lower catalyst loadings: 0.01–0.05 mol % of [(IPr^{CPh3})CuCl] (Scheme 4a). Gratifyingly, the procedure is amenable to scale-up, as shown by two reactions carried out on a gram scale (Scheme 4b).

A possible catalytic cycle is shown in Scheme 5. First, a boryl copper species **3** is generated in situ by the reaction of



Scheme 4. a) Reactions carried out with low catalyst loadings.
b) Gram-scale synthesis.

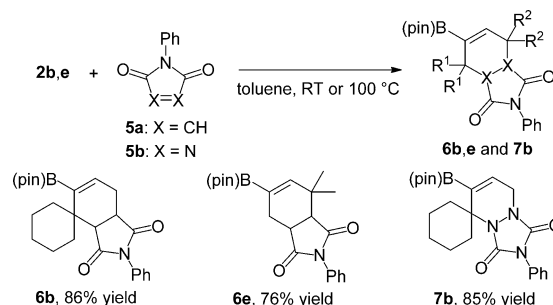
a copper alkoxide with B₂(pin)₂.^[11] As shown previously,^[4a] **3** inserts into an allene to afford σ -allyl copper intermediates **4** and **4'**. Although the distribution of **4** and **4'** would depend on the substituents on the allene, they can exchange by a fast η^1 – η^3 interconversion.^[13] β -Elimination^[14] of the benzyloxy moiety from **4** occurs to give 2-boryl 1,3-butadienes **2** and



Scheme 5. A possible catalytic cycle.

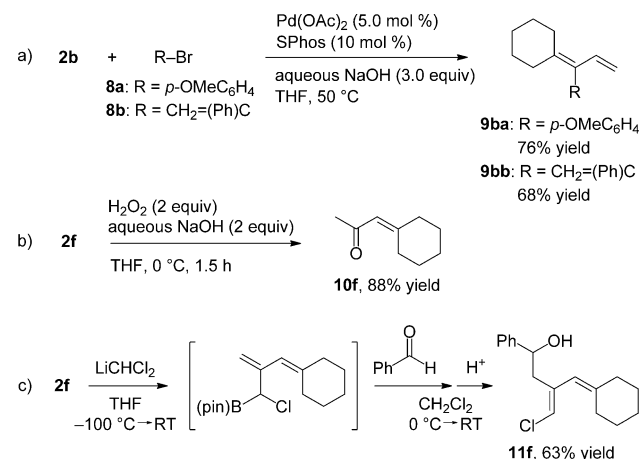
a copper alkoxide ([LCuOBn]).^[15] Finally, σ -bond metathesis of [LCuOBn] with B₂(pin)₂ regenerates a boryl copper species **3**, and the catalytic cycle is closed.

To date, the synthetic utility of 2-boryl 1,3-butadienes **2** has not been fully examined owing to the paucity of these compounds. Diels–Alder reactions^[18a,h,16] of **2b** and **2e** with **5a** afforded cyclic vinyl boranes **6b** and **6e** in high yield (Scheme 6). Furthermore, the hetero-Diels–Alder reaction of **2b** with **5b** proceeded smoothly to give the boryl-substituted heterocycle **7b** in 85% yield. Suzuki–Miyaura



Scheme 6. Diels–Alder reactions of **2**.

coupling of **2b** with **8a** and **8b** afforded the trisubstituted 1,3-butadiene **9ba** and the triene **9bb** in good yield (Scheme 7a). The α,β -unsaturated ketone **10f** was obtained by the treatment of **2f** with H₂O₂ (Scheme 7b), and the functionalized 1,3-diene **11f** was obtained in 63% yield from **2f** by



Scheme 7. Further transformations of the 2-boryl 1,3-butadienes **2**. SPhos = 2-dicyclohexylphosphanyl-2',6'-dimethoxybiphenyl.

homologation^[17] followed by the allylboration of benzaldehyde (Scheme 7c).

In conclusion, we have developed an efficient and general method for the synthesis of 2-boryl 1,3-butadienes by the copper-catalyzed borylation of α -alkoxy allenes with B₂(pin)₂. The reaction can be conducted with low catalyst loadings and on a gram scale. 2-Boryl 1,3-butadienes are useful intermedi-

ates for the synthesis of cyclic vinyl boranes, α,β -unsaturated ketones, and functionalized multisubstituted dienes.

Experimental Section

Typical procedure: [(IPr^{CPh₃})CuCl] (4.9 mg, 0.0050 mmol, 2.0 mol %) and B₂(pin)₂ (71 mg, 0.28 mmol) were placed in an oven-dried 20 mL Schlenk flask, and the flask was evacuated for 30 min. The flask was evacuated and backfilled with argon three times. THF (0.50 mL) and KOrBu (25 μ L of a 1.0 M solution in THF, 10 mol %) were added, and the resulting mixture was stirred at room temperature for 5 min. An allene (0.25 mmol) was then added, and the mixture was stirred at room temperature for 30 min. After the reaction, the mixture was filtered through a pad of Celite and silica gel, and all volatiles were removed in vacuo. The product was obtained by silica-gel column chromatography (eluent: hexane/Et₂O).

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