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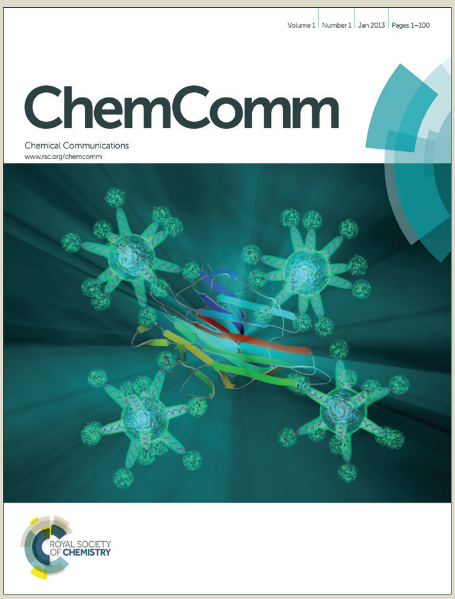

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COMMUNICATION

Borylstannylation of alkynes with inverse regioselectivity: Copper-catalyzed three-component coupling using a masked diboron

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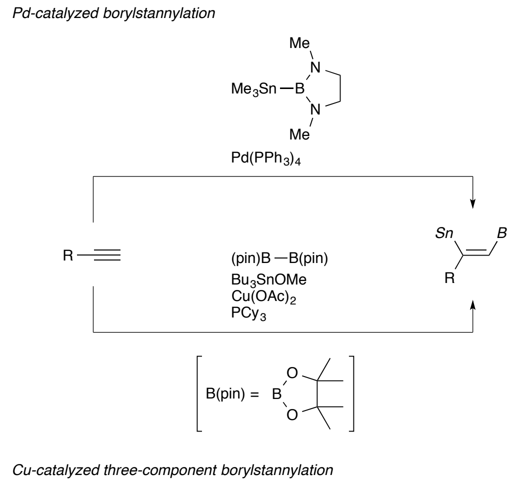
A variety of terminal alkynes are facilely convertible into *cis*-boryl(stannyl)alkenes with regioselectivity inverse to those of the previous borylstannylation by the copper-catalyzed three-component reaction using a masked diboron. Synthetic utility of the resulting boryl(stannyl)alkenes has been demonstrated by chemoselective coupling reactions.

Transition metal-catalyzed dimetallation of alkynes has commanded considerable attention,[1] because it provides convenient and direct method for constructing regio- and stereo-defined dimetallated alkenes, whose carbon–metal bonds are utilizable for carbon–carbon bond-forming processes[2] to give multisubstituted alkenes, which constitute an important class of biologically and pharmaceutically active molecules. One of the most valuable dimetallations would be borylstannylation, in which the resulting hetero-dimetallic moieties can tandemly undergo chemoselective cross-coupling reactions (Suzuki–Miyaura[3] and Migita–Kosugi–Stille coupling[4]) with high functional group compatibility under controlled reaction conditions. Since the pioneering work was reported by Tanaka,[5a] the borylstannylation has hitherto been achieved by direct insertion of alkynes into a B–Sn bond of borylstannanes under palladium catalysis.[5] On the other hand, we have recently disclosed a different mode of the borylstannylation by a copper-catalyzed three-component coupling using a diboron and a tin alkoxide.[6-8] Irrespective of the catalytic systems and the reaction modes, terminal alkynes exclusively accept regioselective addition of the boryl group at the terminal carbon and the stannyl group at the internal carbon in a *cis* fashion to give (*Z*)-1-boryl-2-stannyl-1-alkenes

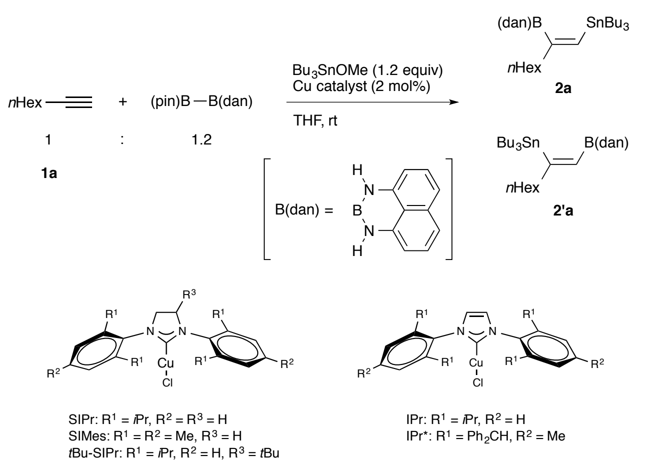


Scheme 1 Reported borylstannylation of terminal alkynes.

(Scheme 1), and thus we have focused our attention on reversal of regioselectivity, which increases structural diversity of *vic*-boryl(stannyl)alkenes and thereby broadens the synthetic utility of the borylstannylation. Herein we report that the use of a masked diboron[9] in the copper-catalyzed three-component borylstannylation of terminal alkynes completely inverts the regioselectivity, and that this method provides convenient and direct entry to unprecedented hetero-dimetallated alkenes having masked boryl and stannyl moieties.[10]

First we conducted the reaction of 1-octyne (**1a**) with a masked diboron ((pin)B–B(dan), pin: pinacolato, dan: naphthalene-1,8-diaminato[11]) and tributyltin methoxide in THF

Table 1 Ligand effect on Cu-catalyzed borylstannylation of 1-octyne[a]



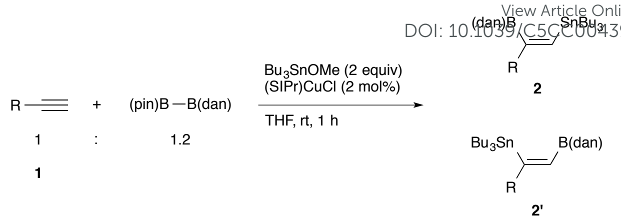
Entry	Cu catalyst	Time (h)	Yield (%)[b]	**2a**:**2'a**[c]
1	(SIPr)CuCl	7	74	96:4
2	(SIMes)CuCl	2	81	90:10
3	(*t*Bu-SIPr)CuCl	20	69	94:6
4	(IPr)CuCl	5	75	96:4
5	(IPr*)CuCl	11	80	96:4
6[d]	P(*t*Bu)$_3$, CuCl	2	81	93:7
7	(PPh$_3$)$_3$CuCl	48	75	44:56
8[d]	PCy$_3$, CuCl	14	60	84:16
9[e]	(SIPr)CuCl	10	86	96:4

[a] General procedure: **1a** (0.30 mmol, 1 equiv), (pin)B–B(dan) (0.36 mmol, 1.2 equiv), Bu$_3$SnOMe (0.36 mmol, 1.2 equiv), Cu catalyst (6.0 μmol, 2 mol%), THF (1 mL). [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] Ligand = 4 mol%. [e] Bu$_3$SnOMe = 2 equiv.

at room temperature in the presence of an *N*-heterocyclic carbene (NHC)-coordinated copper complex ((SIPr)CuCl), and found that the *cis*-borylstannylation took place with regioselectivity inverse to those of the previous borylstannylation (74% yield, **2a**:**2'a** = 96:4), leading to the introduction of the boryl group at the internal carbon and the stannyl group at the terminal carbon (Table 1, entry 1). It is noteworthy that the B(dan) moiety was solely installed in the product, and a borylstannylation product having the B(pin) moiety was not formed at all. The regioselectivity for the formation of **2a** was generally high with bulky ligands (SIMes, *t*Bu-SIPr, IPr, IPr*[12] and P(*t*Bu)$_3$) (entries 2–6), whereas the use of triphenylphosphine ((PPh$_3$)$_3$CuCl) led to the formation of regioisomeric mixtures (**2a**:**2'a** = 44:56, entry 7). In addition, the reaction with PCy$_3$, used for the previous borylstannylation with bis(pinacolato)diboron,[6a] also afforded **2a** preferentially (**2a**:**2'a** = 84:16, entry 8), which reveals that the choice of a diboron as well as a ligand is the key for the present regioselectivity.[13] Since the increase in an amount of tributyltin methoxide resulted in the increase in the yield with the highest regioselectivity (86% yield, entry 9), we selected the conditions for further studies.[14]

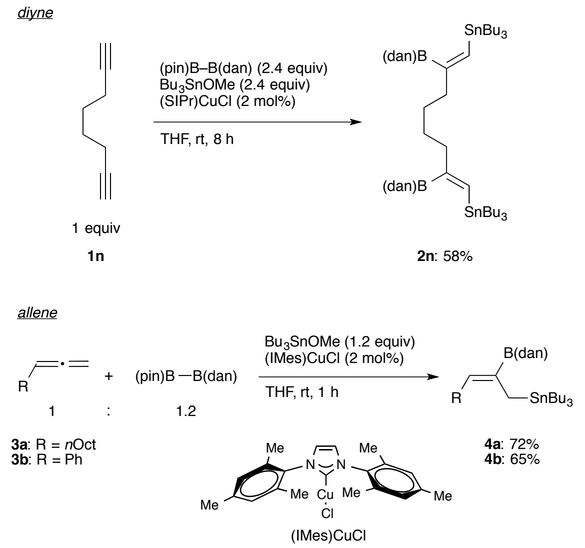
With the optimum conditions in hand (Table 1, entry 9), the substrate scope on alkynes was next investigated (Table 2). Such aliphatic terminal alkynes as 1-hexyne (**1b**), 4-methyl-1-pentyne (**1c**) and 4-phenyl-1-butyne (**1d**) also underwent the

Table 2 NHC–Cu-catalyzed borylstannylation of terminal alkynes[a]



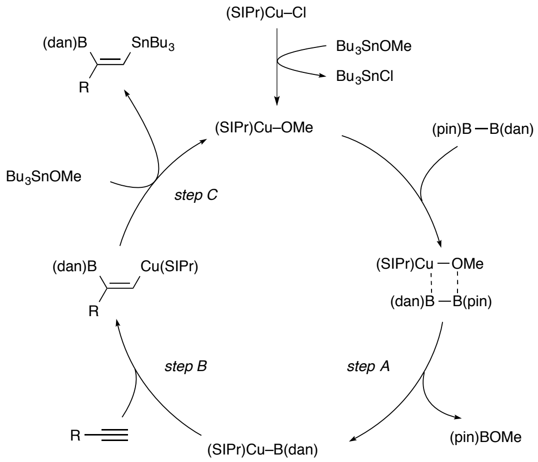
Entry	R	Yield (%)[b]	**2**:**2'**[c]	Products
1	*n*Bu (**1b**)	78	94:6	**2b**, **2'b**
2	*i*Bu (**1c**)	81	99:1	**2c**, **2'c**
3	Ph(CH$_2$)$_2$ (**1d**)	74	94:6	**2d**, **2'd**
4	Br(CH$_2$)$_2$ (**1e**)	87	99:1	**2e**, **2'e**
5	NC(CH$_2$)$_3$ (**1f**)	79	95:5	**2f**, **2'f**
6	1-Cyclohexenyl (**1g**)	81	99:1	**2g**, **2'g**
7	Ph (**1h**)	73	99:1	**2h**, **2'h**
8	MeOCH$_2$ (**1i**)	66	>99:1	**2i**
9	BnOCH$_2$ (**1j**)	66	>99:1	**2j**
10	THPOCH$_2$ (**1k**)	66	>99:1	**2k**
11	Et$_2$NCH$_2$ (**1l**)	69	>99:1	**2l**
12	Me$_3$Si (**1m**)	75	>99:1	**2m**

[a] General procedure: **1** (0.30 mmol, 1 equiv), (pin)B–B(dan) (0.36 mmol, 1.2 equiv), Bu$_3$SnOMe (0.60 mmol, 2 equiv), (SIPr)CuCl (6.0 μmol, 2 mol%), THF (1 mL). [b] Isolated yield. [c] Determined by ^{1}H NMR.

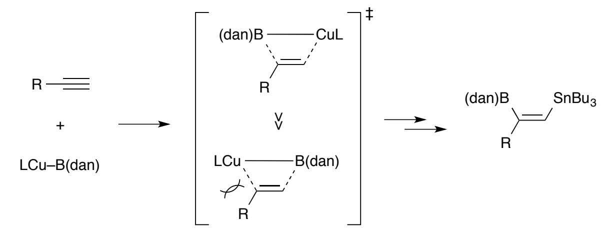


Scheme 2 Borylstannylation of a diyne and allenes.

borylstannylation with high degrees of regioselectivity to give **2b**, **2c** and **2d** in 78, 81 and 74% yield (entries 1–3). The functional group compatibility of the reaction was sufficiently high, and thus a C–Br bond[15] in **1e** and a cyano group in **1f** remained intact throughout the reaction (entries 4 and 5). The present regioselectivity was also observed by using enyne **1g** and phenylacetylene **1h** (entries 6 and 7), and furthermore the reaction of propargyl ethers (**1i** and **1j**) or a THP-protected propargyl alcohol (**1k**) resulted in the exclusive formation of **2i**–**2k** (entries 8–10). In addition, propargyl amine **1l** and trimethylsilylacetylene **1m** accepted the addition of the B(dan) moiety at their internal carbon with perfect regioselectivity (entries 11 and 12).[16] The versatility of the borylstannylation



Scheme 3 A plausible catalytic cycle for borylstannylation.



Scheme 4 Regioselectivity in the borylcupration.

was further expanded by application to 1,7-octadiyne[17] (**1n**) and allenes[18] (**3a** and **3b**): both of the triple bonds were convertible regioselectively into the borylstannylalkenes in the former case, and the regio- and stereoselective reaction proceeded to provide (*Z*)-1-stannyl-2-boryl-2-alkenes (**4a** and **4b**) as the single product, although the regioselectivity is similar to that of the previous borylstannylation with bis(pinacolato)diboron[6b] in the latter case (Scheme 2).

Similarly to the previous copper-catalyzed borylstannylation with bis(pinacolato)diboron,[6] generation of a borylcopper species, Cu–B(dan), from Cu–OMe and a masked diboron commences the reaction (Scheme 3, step A). Subsequent insertion of an alkyne into the Cu–B(dan) bond which produces a β-borylalkenylcopper species (borylcupration, step B),[19] followed by capturing with a tin methoxide furnishes the product (step C).[20] The formation of Cu–B(dan) (*vs*. Cu–B(pin)) can be rationally explained by selective interaction between the Lewis acidic B(pin) moiety of (pin)B–B(dan) and the methoxy moiety of Cu–OMe in step A, leading to the exclusive introduction of the masked boryl moiety across the triple bond of alkynes. The orientation of a borylcopper species in the borylcupration step entirely governs the regiochemical outcome of the borylstannylation (Scheme 4), and the mode of the borylcupration with Cu–B(dan) would simply be controlled by steric repulsion between a substituent on alkynes and a bulkier copper moiety as was the case with the hydroboration.[10a] Hence, the B(dan) moiety is solely installed into the internal carbon of terminal alkynes,[21,22] which results in the inverse regioselectivity in the present borylstannylation.

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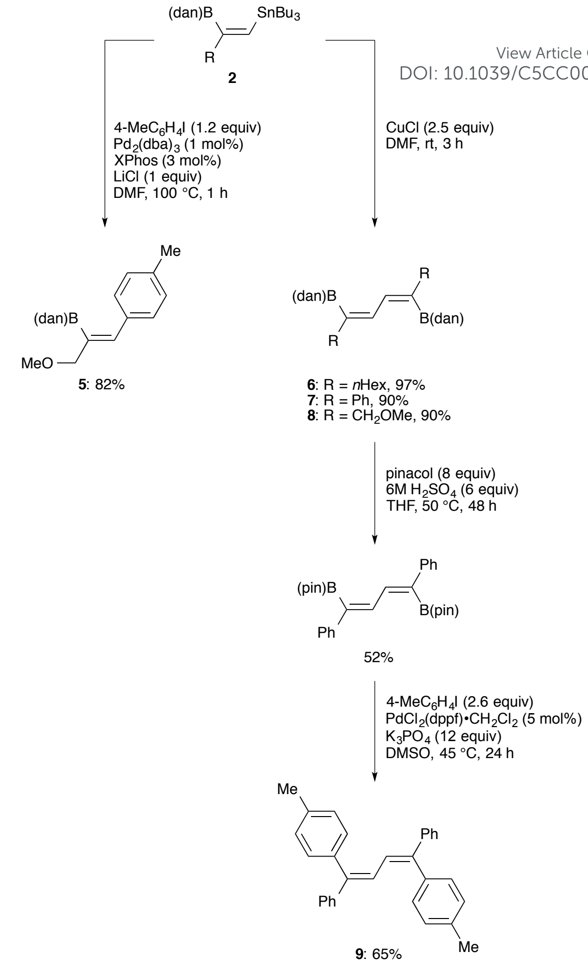

Scheme 5 Transformation of borylstannylation products.

Synthetic utility of the boryl(stannyl)alkenes was demonstrated by the chemoselective cross-coupling: a C–Sn bond of **2i** was solely convertible into a C–C bond by the palladium-catalyzed Migita–Kosugi–Stille reaction to provide an 82% yield of **5** with a masked boryl moiety remaining intact (Scheme 5). Furthermore, the masking enabled the copper-mediated oxidative homocoupling to take place at the C–Sn bond selectively, affording 1,4-diboryl-1,3-butadienes (**6**–**8**) stereoretentively in high yield. Unmasking of the resulting 1,4-diboryl-1,3-butadiene, followed by the Suzuki–Miyaura reaction with 4-iodotoluene furnished 1,1,4,4-tetraarylbutadiene **9**.

In conclusion, we have disclosed that the borylstannylation of terminal alkynes proceeds with inverse regioselectivity by the copper-catalyzed three-component reaction using a masked diboron, which gives us convenient and potent approach to diverse *cis*-boryl(stannyl)alkenes bearing the masked boryl moiety at the internal carbons. Moreover, synthetic versatility of the resulting boryl(stannyl)alkenes has been shown by the chemoselective coupling reactions depending on the difference in the reactivity between the masked boryl and the stannyl moieties. Further studies on copper-catalyzed borylation reactions by use of a masked diboron as well as on details of the mechanism are in progress.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures and characterization data. See DOI: 10.1039/c000000x/

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