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Showcasing the work from Dr Hiroto Yoshida’s Group, Faculty of Engineering, Department of Applied Chemistry, Hiroshima University, Japan.

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

Borylstannylation of terminal alkynes proceeds with inverse regioselectivity to those of the previous borylstannylations by utilizing a masked diboron as a boron source under copper catalysis.


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

H. Yoshida,*a b Y. Takemotoa and K. Takakia

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

Transition metal-catalyzed dimetallation of alkynes has commanded considerable attention1 because it provides a convenient and direct method for constructing regio- and stereo-defined dimetallated alkenes, whose carbon–metal bonds are utilisable for carbon–carbon bond-forming processes2 to give multisubstituted alkenes, which constitute an important class of biologically and pharmaceutically active molecules. One of the most valuable dimetallation reactions would be borylstannylation, in which the resulting hetero-dimetallic moieties can undergo chemoselective cross-coupling reactions (Suzuki–Miyaura3 and Migita–Kosugi–Stille coupling4) in tandem with high functional group compatibility under controlled reaction conditions. Since the pioneering work reported by Tanaka,5 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 the 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), and thus we have focused our attention on the reversal of regioselectivity, which thereby broadens the synthetic utility of the borylstannylation. Herein we report that the use of a masked diboron9 in the copper-catalyzed three-component borylstannylation of terminal alkynes completely inverts the regioselectivity, and that this method provides a convenient and direct access 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-diaminato11) and tributyltin methoxide in THF 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.
Communication

Table 1 Ligand effect on Cu-catalyzed borylstannylation of 1-octyne*  

Entry | Cu catalyst | Time (h) | Yieldb (%) | 2a: 2a’
--- | --- | --- | --- | ---
1 | (SIPr)CuCl | 7 | 74 | 96:4
2 | (SIMes)CuCl | 2 | 81 | 90:10
3 | (Bu-SIPr)CuCl | 20 | 69 | 94:6
4 | (IPr)CuCl | 5 | 75 | 96:4
5 | (IPr*’’’’’)CuCl | 11 | 80 | 94:4
6 | P(Bu)3 | 2 | 81 | 93:7
7 | P(Bu)3 | 48 | 75 | 44:56
8 | PCy3 | 14 | 60 | 84:16
9 | (SIPr)CuCl | 10 | 86 | 96:4

*General procedure: 1a (0.30 mmol, 1 equiv.), (pin)B–B(dan) (0.36 mmol, 1.2 equiv.), Bu3SnOMe (0.60 mmol, 2 equiv.), Cu catalyst (6.0 μmol, 2 mol%), THF (1 mL).

The borylstannylation was further expanded by application to 1,7-octadiyne17 (1n) and allenes18 (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)-2-stannyll-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)diboron6 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 alkylene

Scheme 2 Borylstannylation of a diyne and allenes.
into the Cu–B(dan) bond, which produces a β-borylalkenylcopper species (borylcupration, step B), followed by capturing with tin methoxide furnishes the product (step C). 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. Hence, the B(dan) moiety is solely installed into the internal carbon of terminal alkynes, which results in the inverse regioselectivity in the present borylstannylation.

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 a convenient and potent approach to diverse cis-boryl(stannyl)alkenes bearing the masked boryl moiety at the internal carbons. Moreover, the 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 using a masked diboron as well as on the details of the mechanism are in progress.

Notes and references


We have already verified that an alkenylcopper species is facilely captured with a Tin methoxide to produce an alkenylstannane. See ref. 6a.

The reaction of ethyl propiolate did not produce the borylstannylation product at all.

The alkyne (1a) had already been consumed at the time indicated in Table 1, and thus the yields would not change if the reactions are left longer.


A boryl moiety is selectively installed into a terminal carbon of 1-octyne in the borylstannylation with bis(pinacolato)diboron under the Cu–PCy3 catalysis, which is in marked contrast to the results described herein. See ref. 6a.


14 2-Selectivity hydroboration of terminal alkynes with (pin)B(pin) proceeds in the presence of a copper catalyst coordinated by a sterically demanding ligand [Pf(Bu)3, SIMes or SIPr], however, the substrate scope is limited to propargyl-functionalized and electron-deficient aryl ones, being in marked contrast to the results described herein. See: A. L. Moure, P. Mauleón, R. G. Arrayáis and J. C. Carretero, Org. Lett., 2013, 15, 2054. See also ref. 21c.