

Suzuki–Miyaura Cross Coupling Reactions of B-Allenyl-9-BBN

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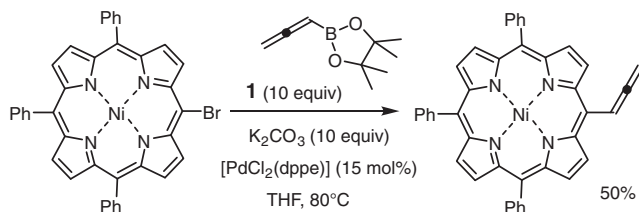
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Despite the tremendously wide scope of the palladium-catalyzed Suzuki–Miyaura cross coupling, boron-based allenylation reactions of aryl halides are virtually unknown. It is now demonstrated that the borate complex formed in situ from B-allenyl-9-BBN and NaOMe in DMF allows aryl- and heteroaryl iodides to be allenylated under mild conditions.

The high reactivity of their orthogonal π -bonds renders allenes highly versatile building blocks for advanced organic synthesis.¹ Recently, the interest in the use of allenes was reinforced by the finding that they are privileged substrates in the realm of π -acid catalysis, most notably in reactions catalyzed by Ag(I+), LAu(I+), or Pt(2+).^{2,3} It was in the context of our investigations in this particular field⁴ that we experienced a need to develop efficient methods for the preparation of allenes in general⁵ and monosubstituted arylallenes in particular.

Although many different procedures for the synthesis of arylallenes have been worked out in the past,¹ a close survey of the literature showed that the cross coupling of aryl halides or triflates with appropriate allenylmetal reagents is not as commonly practiced as one might think in view of the overwhelming success and widespread use of palladium-catalyzed cross coupling reactions in general.⁶ For certain metals, this may be attributed to an unfavorable equilibration between the allenyl and 2-propynyl forms of the reagents in solution by 1,3-metallotropic shifts. Moreover, the allene products themselves may not be indefinitely stable toward the nucleophile and/or the operative catalysts under the reaction conditions.^{7,8} Although scattered reports on the use of allenylmagnesium, -zinc, -copper, and -silver reagents are available,⁹ best results were obtained with the aid of allenylindium¹⁰ and allenyltin species.¹¹ In the latter case, however, the yields are variable and seem to depend strongly on the very substrate and the chosen conditions.

It is particularly surprising, however, that allenylations by the Suzuki–Miyaura cross coupling are essentially unknown, despite the popularity and enormous scope of this venerable transformation.¹² To the best of our knowledge, only a single example has so far been described in the literature (Scheme 1).¹³ It relates to the allenylation of a porphyrin complex, which was



Scheme 1. Literature report on a Suzuki–Miyaura allenylation with allenyl pinacol boronate.¹³

accomplished in 50% yield using a large excess (10 equiv) of allenyl pinacol boronate **1**, K₂CO₃ (10 equiv), and 15 mol % of [PdCl₂(dppe)] in THF at 80 °C overnight.¹³

Following up on our previous investigations into Suzuki–Miyaura reactions,^{14,15} we were keen to probe whether the use of other boron donors would allow us to widen the scope of this arylallene synthesis. To this end, ethyl 4-halobenzoates were reacted with various allenylboron reagents under a variety of experimental conditions. However, neither the use of boronates **1** or **2** nor of trifluoroborate **3**¹⁶ (Chart 1) gave any hit, independent of whether [Pd(PPh₃)₄], [PdCl₂(dppf)], or Pd(OAc)₂ in combination with either phosphane **4**¹⁷ or the NHC-precursor **5**¹⁸ was used as the catalyst. Variation of the base did not change the outcome either (K₃PO₄, Cs₂CO₃, Ba(OH)₂·8H₂O, and NaOMe).

In contrast, the borate complex **8** generated in situ from NaOMe and B-allenyl-9-BBN **7**,¹⁹ which is readily accessible on large scale as described below, promoted the reaction well (Scheme 2). A strong solvent effect was noticed: whereas the allenylation of **9** in THF was unsatisfactory even upon heating, the use of DMF furnished product **10** in 70% yield after a reaction time of 3 h at ambient temperature, provided that a slight excess (1.8 equiv) of the borate complex **8** was used. As the cross coupling proceeded under mild conditions, the degradation of the rather sensitive product was minimized and no 2-propynyl (rather than allenyl) transfer was observed. It is also important to avoid any excess base, since NaOMe in combination with the palladium complex leads to rapid isomerization and degradation of the generated allene product. In contrast to iodide **9**, however, the corresponding bromide and

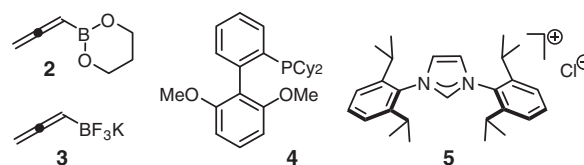
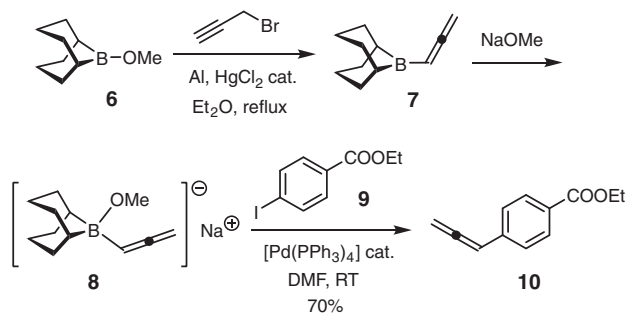


Chart 1.



Scheme 2.

triflate could not be allenylated in preparatively meaningful yields under these conditions.

The new method allowed an assortment of aromatic and heteroaromatic iodides to be allenylated in moderate to good yields, independent of whether they carry electron-withdrawing or -donating substituents (Table 1). As expected, various functional groups remained intact. Surprisingly, however, ethyl *ortho*-iodobenzoate could not be cross coupled (Entry 3), whereas its *para*- and *meta*-congeners reacted smoothly (Entries 1 and 2). Since other *ortho*-substituted iodides were found well suited (Entries 4, 10–12, 14, and 15), this failure is tentatively ascribed to a ligation of the intermediate arylpalladium species by the adjacent carbonyl group, which seems to be sufficiently strong at ambient temperature to prevent transmetalation by the allenyl donor. When dihalobenzene derivatives are used as the substrates, the allenylation occurs exclusively at the iodide group, leaving a bromide, activated chloride or fluoride substituent untouched (Entries 8, 9, 10, and 14). In the heterocyclic series, *N,N*-dibenzyl-5-iodouracil was inert (Entry 13),²⁰ whereas its *O,O*-dimethylated analog shown in Entry 15 was allenylated in respectable yield.

Overall, we conclude that borane **7** in combination with NaOMe is a suitable donor for Suzuki–Miyaura type allenylation reactions. Although the scope of the method still needs to be extended beyond aryl iodides, it compares well to cross coupling reactions using toxic allenyltin reagents or nonmetallic three-carbon donors as the currently most widely practiced alternatives.^{8,11}

Preparation of B-allenyl-9-BBN: A first portion of propargyl bromide (ca. 3 mL) is quickly added to a suspension of Al grit (>97%, 3.33 g, 123 mmol) and HgCl₂ (100 mg) in anhydrous Et₂O (100 mL) and the resulting mixture is stirred at ambient temperature for 15 min under Ar. After that time, a mixture of the remaining 2-propynyl bromide (27.18 g total, 184 mmol) and 9-MeO-9-BBN (18.6 g, 122 mmol) is added over 45 min at such a rate as to maintain gentle reflux. Once the addition is complete, the mixture is refluxed for 3.5 h before insoluble residues are filtered off under Ar. The solvent is carefully distilled off at ambient pressure and the residue purified by distillation under vacuum to give B-allenyl-9-BBN (bp 29–31 °C, 10⁻³ mbar) as a colorless liquid (10.3 g, 52%). ¹H NMR (400 MHz, CDCl₃): δ 5.63 (t, *J* = 6.4 Hz, 1H), 4.64 (d, *J* = 6.4 Hz, 2H), 2.00–1.84 (m, 6H), 1.84–1.68 (m, 6H), 1.38–1.21 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 220.8, 89.0 (br), 68.2, 34.2, 31.0 (br), 23.9; ¹¹B NMR (128 MHz, CDCl₃): δ 80.9.

Representative procedure: B-Allenyl-9-BBN **7** (394 mg, 2.46 mmol), NaOMe (133 mg, 2.46 mmol), and [Pd(PPh₃)₄] (79 mg, 0.068 mmol) are successively added to a solution of ethyl 4-iodobenzoate (**9**) (378 mg, 1.37 mmol) in degassed DMF (5.5 mL) and the resulting mixture is stirred at ambient temperature for 3 h under Ar. For work up, the mixture is diluted with EtOAc (10 mL) and the reaction quenched with sat. aq. NH₄Cl (20 mL). The aqueous phase is extracted with EtOAc (4 × 15 mL), the combined organic layers are washed with brine, dried over Na₂SO₄, and evaporated, and the residue is purified by flash chromatography (pentane/Et₂O, 10:1) to give allene **10** as a pale yellow liquid (180 mg, 70%). ¹H NMR (400 MHz, CDCl₃): δ 7.98 (m, 2H), 7.34 (m, 2H), 6.20 (t, *J* = 6.8 Hz, 1H), 5.20 (d, *J* = 6.8 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ

Table 1. Pd-Catalyzed Suzuki–Miyaura allenylation reactions of aryl iodides with B-allenyl-9-BBN^a

Entry	Substrate	Product	Yield/%
1			70
2			95
3		—	nr
4			89
5			87
6			91
7			51
8			69
9			88
10			93
11			94
12			74
13		—	nr
14			50
15			73

^aAll reactions were performed using **7** (1.8 equiv), NaOMe (1.8 equiv), and [Pd(PPh₃)₄] (5 mol%) in DMF at ambient temperature; nr: no reaction. For characteristic spectral data of the compounds, see the Supporting Information.²¹

210.6, 166.4, 138.9, 129.9, 128.8, 126.5, 93.6, 79.2, 60.8, 14.3; IR (neat): $\tilde{\nu}$ = 2982, 2901, 1939, 1710, 1606, 1436, 1268, 1174, 1100, 1018, 872, 852, 773, 704 cm⁻¹; MS (EI) *m/z* (%): 188 (80) [M⁺], 160 (16), 143 (100), 115 (46); HRMS (ESI) *m/z*: calcd for [C₁₂H₁₂O₂ + Na]⁺: 211.07300; found: 211.07295.

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