Synthesis of 1,1-diboronate esters by cobalt-catalyzed sequential hydroboration of terminal alkynes†

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1,1-Organodiboronate esters are valuable synthetic intermediates for preparation of multifunctionalized molecules. Such 1,1-diboryl compounds can be used as coupling reagents for C–C bond formations through Suzuki–Miyaura reactions. Advantages of 1,1-diboronate esters over other 1,1-organo-B bonds of diboron compounds have also been developed for preparation of diboron compounds have also been developed for preparation of diboron compounds have also been developed for preparation of 1,1-diboronates with high regioselectivity, and non-toxicity. In addition, the boronate moiety can be readily converted into alcohol, amine, and other functional groups. Conventional, non-catalytic methods for synthesis of 1,1-diboronate esters involve reactions of lithiated reagents with bis(pinacolato)diboron, or hydroboration of terminal alkynes with a mixture of trichloride and trialkylsilane, followed by treatment with a suitable diol reagent. However, these methods suffer from poor functional-group compatibility, formation of waste inorganic salts, and multiple synthetic sequences. Recently, transition-metal-catalyzed methods have gained attention. For example, copper-catalyzed diborylation of 1,1-dibromoethane with bis(pinacolato) dibor formed 1,1-diborylethene in moderate yield. Platinum-catalyzed enantioselective hydroboration of alkynylboron compounds with a 1,8-naphthalenediaminatoboryl substituent, furnishing 1,1-diboronates with high optical purity. Hartwig reported iridium-catalyzed diborylation of benzylic C–H bonds directed by a hydrosilyl group to form 1,1-benzyl diboron esters. Diamond-catalyzed diborylation of benzyl C–H bonds directed by a hydrosilyl group to form 1,1-benzyl diboron esters. Platinum-catalyzed diborylation of benzyl C–H bonds directed by a hydrosilyl group to form 1,1-benzyl diboron esters. Platinum-catalyzed diborylation of benzyl C–H bonds directed by a hydrosilyl group to form 1,1-benzyl diboron esters.

Due to high atom economy, easy access of starting materials, and mild reaction conditions, the catalytic sequential hydroboration of terminal alkynes is a synthetically useful approach to 1,1-diboronates. However, the sequential, regioselective hydroborations of the alkynylboronate intermediates are rare, and most reactions generate a regioisomeric mixture. In 2009, Shibata reported a rhodium-catalyzed sequential hydroboration of alkynes with pinacolborane to form 1,1-diboronate esters. The reactions proceed under mild conditions with high yields, high regioselectivity, and wide functional group tolerance. The synthetic utility of 1,1-di diboronates is demonstrated by chemoselective monoarylation and stepwise diarylation through palladium-catalyzed Suzuki–Miyaura coupling reactions.
1,1-diboronic esters, but reactions of aryl alkynes yield monoboryl and diboryl mixtures (Scheme 1b).16

Driven by our interest in developing base-metal catalytic systems for alkene hydrofunctionalizations,17 recently we and Lu independently reported iminopyridine-oxazoline (IPO) cobalt17e,18 and iron17c complexes for asymmetric hydroboration/hydrosilylation of 1,1-disubstituted alkenes and ketones. Herein, we report that an IPO cobalt complex catalyses regio- and stereoselective sequential hydroboration of alkyl and aryl alkynes (Scheme 1c). Most reactions occur under mild conditions with high isolated yields. The method exhibits a broad substrate scope and wide functional group tolerance.

We commenced our studies by examining the reaction of 1-hexyne (1a) with HBpin (Table 1). When using 3 mol% of (IPO)FeBr2 (4a) as the catalyst precursor and 6 mol% of NaBHEt3 as the activator, the reaction of 1a with 2 equiv. of HBpin in THF at room temperature after 12 h gave 23% of the desired dual hydroboration product 2a, 28% of trans-monoborylalkane (3α), and 42% of monoborylalkane (3β) (entry 1). However, using the cobalt analogue (IPO)CoCl2, 4b as the precatalyst led to the formation of 2a with very high selectivity and yield (96%) (entry 2). A control experiment with the catalyst activator, but without the precatalyst only gave 4% of 3α (entry 3). To evaluate the role of the ligand, reactions using the related cobalt complexes with bis(imino)pyridine (4c) and bis(oxazoline)pyridine (4d) ligands have been carried out. The former gave the desired product in low yield (11%), along with 39% of 3α and 43% of 3β (entry 5), whereas the latter gave 89% of 2a and 5% of 3β (entry 6). The addition of the catalyst activator is essential for the catalysis (entry 4), but it is not limited to NaBHEt3. The reaction using MeLi as the activator afforded the dual hydroboration product in a yield close to that using NaBHEt3. The reactions proceeded smoothly in other solvents, such as toluene, n-pentane, and diethyl ether, albeit with relatively low yield compared to that in THF (entries 7–10).

We next studied the scope and limitation of the protocol with (IPO)CoCl2 4b as the catalyst precursor, NaBHEt3 as the activator, and THF as the solvent (Table 2). Terminal aliphatic alkynes all reacted with HBpin to form the diboryl products selectively. Simple alkynes with linear and branched alkyl groups were converted to the corresponding 1,1-diboronic esters in high yields (2a–2d). A wide range of functional groups, such as chloride (2e), silicon ether (2f), benzyl ether (2g), amide (2h), ester (2i), and internal olefin (2k), can be tolerated. Phenyl-protected propargyl amine gave the desired product (2l) in moderate yield.

Reactions of terminal aryl alkynes also occurred efficiently. Substrates containing both electron-donating and - withdrawing substituents, such as alkyl (2n and 2o), methoxy (2p), fluoride (2q), and dimethylamino (2r) groups, afforded the 1,1-diboryl products in high isolated yields. Naphthyl- (2s), thienyl- (2t), and ferrocenyl-substituted acetylenes (2u) are suitable substrates for sequential hydroboration with exclusive terminal selectivity.

In situ monitoring of the cobalt-catalyzed reaction of 1-hexyne (1a) with 2 equiv. of HBpin provided insight into the catalytic process. As shown in Fig. 1, the reaction at the early stage gave 2a in low yield, but a substantial amount of 3α (e.g., 15 min, 67% of 3α, 8% of 2a). The intermediate 3α was gradually converted to 2a over the course of the reaction. The transform-
ation was nearly complete in 3 h, furnishing 2a in 91% yield. Except for 2a, 3a, and a trace amount of 3β (<3%), no other products were detected by GC during the whole process. The results indicate that the reaction occurs via formation of trans-monoborylalkene (3α) as the intermediate, which undergoes subsequent hydroboration to give the 1,1-diboryl product.

The synthetic utility of 1,1-diboronate esters was demonstrated by their applications to palladium-catalyzed Suzuki–Miyaura coupling reactions. Seminal work by Shibata showed that the adjacent boron atom in 1,1-diborylalkanes has a beneficial effect on the transmetallation step for coupling reactions. Using Pd[P(ηBu)3]2 as the catalyst and KOH as the base, we found that 1,1-diboryl compound 2j coupled selectively with various aryl bromides at room temperature, giving the monoarylation products in high yields (Table 3). O- and S-containing benzoheterocyclic (5e–5g) and heterocyclic (5h) bromides are also favorable substrates under the reaction conditions. Noteworthily, while the reaction with a p-F-substituted aryl bromide gave the benzyl boronate 5b in 86% isolated yield, under otherwise identical conditions, the coupling with a p-CF3-substituted aryl bromide afforded 80% of the protodeborylation product 6a. Furthermore, with 4-bromo-2-methylpyridine as the substrate, a similar transformation involving the combination of cross coupling and protodeborylation occurred to form 6b in 89% yield.

In addition, using a protocol developed by Crudden, the isolated secondary benzylic boronate esters could undergo

### Table 2 Cobalt-catalyzed sequential hydroboration of various terminal alkynes with HBpin

| R | 2 equiv | HBpin (1.0 mmol) | 4b (3 mol%) | NaBHEt3 (6 mol%) | Isolated yields. 
<table>
<thead>
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<tbody>
<tr>
<td>1</td>
<td>THF, rt, 12 h</td>
<td>4 mol % 4b</td>
<td>6 mol % NaBHEt3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>Bpin</td>
<td>92%</td>
<td>2b, Bpin</td>
<td>95%</td>
<td>2c, Bpin</td>
</tr>
<tr>
<td>2d</td>
<td>83%</td>
<td>2e, 84%</td>
<td>2f, Bpin</td>
<td>89%</td>
<td>2g, Bpin</td>
</tr>
<tr>
<td>2h, 89%</td>
<td>2i, 87%</td>
<td>2j, 96%</td>
<td>2k, 55%</td>
<td>2l, 46%</td>
<td></td>
</tr>
<tr>
<td>2m, 87%</td>
<td>2n, 94%</td>
<td>2o, 87%</td>
<td>2p, 88%</td>
<td>2q, 78%</td>
<td></td>
</tr>
<tr>
<td>2r, 87%</td>
<td>2s, 79%</td>
<td>2t, 72%</td>
<td>2u, 72%</td>
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</table>

*a Reaction conditions: 1 (0.5 mmol), HBPin (1.0 mmol), 4b (3 mol%), and NaBHEt3 (6 mol%) in THF (2 mL) at rt. Isolated yields. 

### Table 3 Coupling of 1,1-diboronate 2j with aryl bromides and the subsequent coupling with aryl iodides

<table>
<thead>
<tr>
<th>Reaction conditions:</th>
<th>2j (0.22 mmol), ArBr (0.2 mmol), Pd[P(ηBu)3]2 (5 mol%), and KOH aq. (40 µL, 10 M in H2O) in dioxane (1 mL) at RT. Isolated yields.</th>
<th>5a (0.2 mmol), ArI (0.24 mmol), Pd2(dba)3 (5 mol%), PPh3 (0.2 mmol), and Ag2O (0.3 mmol) in dioxane (1 mL) at 90 °C. Isolated yields.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ArBr</td>
<td>5 mol % Pd[P(ηBu)3]2</td>
<td>2 KOH</td>
</tr>
<tr>
<td>2 dioxane/H2O</td>
<td>1.5 Ag2O</td>
<td></td>
</tr>
<tr>
<td>rt, 10 h</td>
<td>90 °C, 24 h</td>
<td></td>
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<tr>
<td>6a, 80%</td>
<td>5f, 89%</td>
<td></td>
</tr>
<tr>
<td>6b, 89%</td>
<td>5g, 86%</td>
<td></td>
</tr>
<tr>
<td>6c, 86%</td>
<td>5h, 56%</td>
<td></td>
</tr>
<tr>
<td>6d, 89%</td>
<td>5i, 90%</td>
<td></td>
</tr>
</tbody>
</table>

*a Reaction conditions: 2j (0.22 mmol), ArBr (0.2 mmol), Pd[P(ηBu)3]2 (5 mol%), and KOH aq. (40 µL, 10 M in H2O) in dioxane (1 mL) at RT. Isolated yields. 

**Fig. 1** Profile of sequential hydroboration of 1-hexyne (1a) with 2 equiv. of HBpin catalyzed by 3 mol% 4b and 6 mol% NaBHEt3 in THF at room temperature.
subsequent cross couplings. For example, the reactions of 5a with aryl iodides catalyzed by Pd$_2$(dba)$_3$/PPh$_3$ in the presence of Ag$_2$O afforded the diarylation products (7a–c) in useful yields. Thus, the sequence of dual hydroboration and two-step cross coupling reactions provides a synthetically efficient approach to diarylmethane derivatives from simple alkynes.

In summary, we have developed a cobalt catalyst system for selective synthesis of 1,1-diborones from terminal alkylic and aryl alkynes. Featuring the use of low-cost base–metal catalyst, 100% atom economy, mild reaction conditions, high conversion, wide substrate scope, and broad functional group compatibility, the cobalt-catalyzed alkylne sequential hydroboration could be an attractive route to 1,1-organo diborinate esters. We have also demonstrated that the dual hydroborations products are useful synthetic intermediates for chemoselective Suzuki–Miyaura coupling reactions.

Conflict of Interest The authors declare no competing financial interest.

Acknowledgements

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References


20 Using aryl iodides as the electrophiles, NaOH as the base, THF/H2O as the solvent, Hartwig and co-workers showed that cross coupling with 1,1-benzyldiboronate esters was accompanied by protodeborylation. Also see ref. 10.