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## Practical, efficient, and broadly applicable synthesis of readily differentiable vicinal diboronate compounds by catalytic three-component reactions



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#### ABSTRACT

A practical, efficient and broadly applicable catalytic method for synthesis of easily differentiable vicinal diboronate compounds is presented. Reactions are promoted by a combination of  $PCy_3$  or  $PPh_3$ ,  $PCV_3$  or  $PCV_3$  or

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## 1. Introduction

Organoboron compounds that contain vicinal C-B(pin) (pin = pinacolato) bonds are of considerable value in chemical synthesis and may be accessed through diboron additions to alkenes catalyzed by Pd- or Pt-based complexes, metal alkoxides or carbohydrate-based diboron species.<sup>3</sup> A primary C–B bond may be induced to undergo cross-coupling reactions site selectively because of activation provided by the neighboring, more substituted C—B(pin) unit. In 2009 we showed that vicinal diboronate compounds may be synthesized through exceptionally site-selective (<2% geminal diboronate) and stereoselective (syn) Cu-B(pin) addition to alkenyl-B(pin) moiety; the resulting Cu-C bond was then reacted with deuterio-methanol in situ, affording ii with complete diastereoselectivity (>98% retention of stereochemistry; Scheme 1a).<sup>5</sup> More recently, we envisioned that three-component fusion of an alkenyl-B(pin) with (dan)B-B(pin)  $(dan = naphthalene-1,8-diaminato)^6$ and an allyl electrophile (in place of MeOH) might deliver, through site-selective Cu–B(dan) addition/allylic substitution, valuable easy-to-differentiate vicinal diboronate products (e.g., viii, Scheme 1b). Specifically, we surmised that the intermediate copperalkoxide (**iii**, Scheme 1b) should favor interaction with the more Lewis acidic B(pin) unit (**iv**), which would afford a Cu-B(dan) complex (**v**) along with products containing a terminal B(dan) and an internal B(pin) group (**vi**). Differentiation of a B(pin) and a B(dan) moiety would be easier [vs two B(pin) groups]; as a result, the method would offer a distinct advantage, especially when selective functionalization at the typically less reactive secondary C–B bond is desired [e.g., internal B(pin) and a terminal B(dan) group]. Alternatively, a sequence involving an alkenyl–B(dan) substrate and  $B_2(pin)_2$  would furnish the complementary diboron isomer [i.e., primary C–B(pin) and secondary C–B(dan)]. Herein, we disclose the realization of these objectives.

### 2. Results and discussion

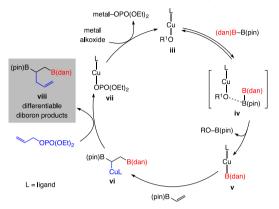
We first probed the possibility of a three-component process with vinyl—B(pin), allylphosphate and (dan)B—B(pin) (Table 1).<sup>8</sup> With NaOt-Bu as the base but without a ligand there was near complete (~95%) disappearance of the limiting reagent [(vinyl—B(pin)] but **1a** was obtained in 39% yield (entry 1). Efficiency improved substantially with the addition of 11.0 mol % PPh<sub>3</sub>, as vicinal diboronate **1a** was isolated in 78% yield (entry 2). Evaluation of other alkali metal alkoxides (entries 3—4) and several mono- and bidentate phosphines with distinct steric and electronic attributes (entries 5—9) indicated that the combination of PCv<sub>3</sub> and LiOt-Bu is

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a. Previous work: Catalytic protylboron addition to alkenyl-B(pin) compounds

b. Basis for this work: Catalytic three-component process involving vinyl-B(pin):



**Scheme 1.** Related previous work and the basis for the present studies.

**Table 1** Examination of different Cu complexes.<sup>a</sup>

entry	ligand	alkoxide	conv (%) <sup>b</sup>	yield (%) <sup>€</sup>
1	none	NaOt-Bu	93	39
2	$PPh_3$	NaOt-Bu	>98	78
3	$PPh_3$	LiOt-Bu	>98	81
4	$PPh_3$	KOt-Bu	91	58
5	$P(nBu)_3$	LiOt-Bu	96	77
6	$PCy_3$	LiOt-Bu	>98	84
7	phos-1	LiOt-Bu	50	19
8	phos-2	LiOt-Bu	43	21
9	rac-binap	LiOt-Bu	74	61
10	imid-1	LiO <i>t</i> -Bu	86	18

<sup>&</sup>lt;sup>a</sup> Performed under N<sub>2</sub> atm.

optimal (>98% conv, 84% yield; entry 6, Table 1). Reactions with N-heterocyclic carbene (NHC) complexes of copper were less efficient (e.g., entry 10), probably arising from competitive reaction of the Cu–B(dan) with allylphosphate to afford allyl–B(dan)<sup>9</sup> (i.e., lower chemoselectivity).

A variety of 2-substituted allylic phosphates, including those that contain a versatile allyl silyl ether (1c), an alkenyl silyl group (1e), a furyl moiety (1f), or a chloride or bromide that might be used in catalytic cross-coupling (1g, 1h), may be used (Scheme 2).

Products containing a primary C–B(dan) bond and a secondary C–B(pin) moiety were generated with complete selectivity: <2% of the alternative isomer could be detected based on <sup>1</sup>H NMR spectra of the unpurified mixtures. The identity of the products was ascertained by determination of X-ray structures of **1d** and **1f** (Scheme 2).

As the transformation in Eq. (1) illustrates, the method is applicable to the formation of a boron-substituted quaternary carbon center.  $^{10}$  Thus, diboronate **3** was obtained in 87% yield after four hours at room temperature. Conversion of the commercially available 1,2-disubstituted alkenylboronate **4** to 5, isolated in 83% yield, further highlights the utility of the method (Eq. (2)). This latter transformation is especially notable; although longer reaction time was needed (14 vs 1–4 h), site- and diastereoselectivity levels were high [>98:2 vicinal:geminal, 89:11 diastereomeric ratio (dr)]. Similarly noteworthy is the transformation with vinyl—B(dan) (Eq. (3)), accessible in a single step from vinyl—B(pin), leading to the formation (>98% conv, 1 h) of the transposed diboronate product **6** in 88% yield, the identity of which was confirmed by X-ray crystallography.

Reactions are scalable, as illustrated by the example in Eq. (4). The transformations were performed with 2.5 mol % of the phosphine—copper complex (vs 10 mol % used above), although this required a longer reaction time (12 vs 2 h).

The C-B(pin) bond of the bis-boronate products can be site selectively oxidized to afford the corresponding alcohol products (e.g., **7** and **8**, Scheme 3). The remaining C-B(dan) bond can then be converted to a C-C bond, <sup>11</sup> as the examples in Scheme 3 illustrate,

<sup>&</sup>lt;sup>b</sup> Determined by analysis of <sup>1</sup>H NMR spectra of unpurified mixtures; conv. ( $\pm 2\%$ ) refers to disappearance of vinyl–B(pin).

 $<sup>^{</sup>c}$  Yields of isolated and purified products ( $\pm5\%$ ). See the Supporting Information for details. Abbreviations: pin, pinacolato; Mes, 2,4,6-(Me) $_{3}$ C $_{6}$ H $_{2}$ , dan = naphthalene-1,8-diaminato.

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