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Copper-Catalyzed B(dan)-Installing Allylic Borylation of Allylic Phosphates

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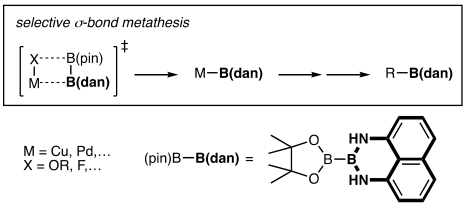
Abstract. γ-Selective B(dan)-installing allylic borylation was found to proceed efficaciously by the reaction of an unsymmetrical diboron, (pin)B–B(dan), with allylic phosphates under copper catalysis. The resulting allyl–B(dan) was convertible into 1,3-, 1,2-, or 1,1-diborylalkanes with different boron-Lewis acidity by B(pin)-installing hydroboration, and its C(sp^3)–B(dan) bond turned out to be preferentially transformed into a C(sp^3)–N bond, leaving the B(pin) intact, despite its well-accepted inertness toward various transformations.

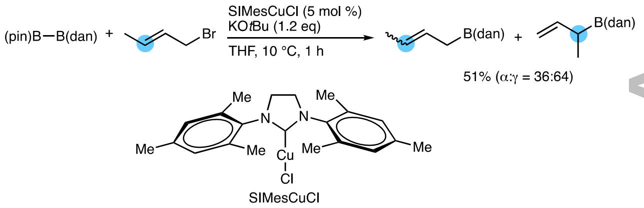
Keywords: Allylic compounds; Boron; Copper; Regioselectivity

Recently, much attention has been focused on the use of unsymmetrical diborons[1] in catalytic boron-installing reactions, aiming at enhanced reactivity/selectivity, unique regioselectivity, etc. In particular, the borylations with (pin)B–B(dan)[2] (dan = naphthalene-1,8-diaminato), which can facilely be prepared by simple substitution of (pin)B–B(pin) with dan,[3] have become increasingly popular, where B(dan) serves as a sole transferable group into organic frameworks. This chemoselective transfer is attributable to contrasting Lewis acidity between B(pin) (Lewis acidic) and B(dan) (less Lewis acidic), leading to preferential generation of M–B(dan) species in σ-bond metathesis step via Lewis acid [B(pin)]–base (X) interaction (Scheme 1).



Scheme 1. B(dan)-Installing Reactions with (pin)B–B(dan).

Since our report on the copper-catalyzed Markovnikov hydroboration of terminal alkynes,[4a] a borylcopper species [Cu–B(dan)] has been the linchpin of the catalytic B(dan)-installing reactions.[4,5] In addition to the well-established addition reactions across unsaturated carbon–carbon bonds such as borylstannylation,[4c] carboboration,[4f] aminoboration[4d] and conjugate addition,[4e] borylative substitution of organic halides[4g,6] also occurs smoothly, demonstrating that Cu–B(dan) can act as a boron nucleophile. Although various R–B(dan) (R = alkyl, alkenyl, aryl and allyl) are directly accessible by the substitution, a representative problem awaiting solution is low α/γ-selectivity in the allylic borylation of allylic halides (Scheme 2), which should result from a radical pathway operative therein. One-electron reduction of a carbon–halogen bond sets off the radical pathway, and therefore we envisaged that use of a one-electron reduction-resistant leaving group instead of halogen[4h] should be promising for regiocontrol. We report herein on the copper-catalyzed γ-selective B(dan)-installing allylic borylation of allylic phosphates, which proceeds not through the radical pathway. Pioneering works on the copper-catalyzed γ-selective allylic borylation of allylic carbonates or ethers with (pin)B–B(pin) have already been reported by Ito and Sawamura.[7,8,9]



Scheme 2. Borylation of (*E*)-Crotyl Bromide.

Our studies were commenced with the reaction of (pin)B–B(dan) (**1a**) with (*E*)-crotyl diethyl phosphate (**2a**) in THF at 30 °C in the presence of Cs_2CO_3 and SIMesCuCl catalyst (Table 1). The allylic borylation

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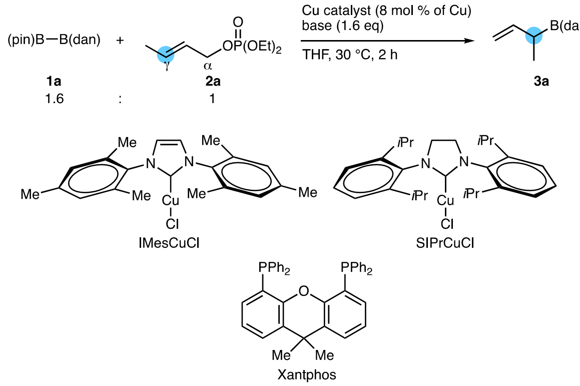
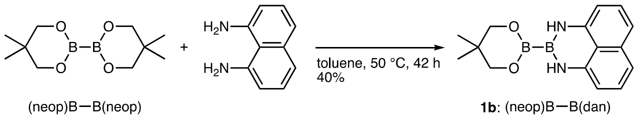
was found to complete within 2 h to give an 80% yield of α-Me-allyl–B(dan) (**3a**) with perfect γ-regioselectivity (Entry 1). The B(dan) moiety was solely installed into the organic framework, indicating that the chemoselective σ-bond metathesis between **1a** and a copper catalyst is operative also in this case (*vide infra*). The reaction became sluggish with other NHC ligands (IMes, SIPr) or Xantphos (Entries 2–4), and monodentate phosphines (PCy$_3$, PPh$_3$) were totally ineffective (Entries 5 and 6). The use of KOAc instead of Cs$_2$CO$_3$ as a basic additive inhibited the reaction progress, and the reaction conducted with KO*t*Bu or toluene resulted in moderate yield (Entries 7–9). It should be noted that the selective B(dan)-installation also took place with a new unsymmetrical diboron, (neop)B–B(dan) (**1b**) (Entry 10), being directly available by treatment of (neop)B–B(neop) with dan in a way similar to the synthesis of **1a** (Scheme 3),[3,10] and finally, **3a** turned out to be generated quantitatively by employing 2 equiv. of **1a** (Entry 11).

Table 1. Optimization of Reaction Conditions.



Entry	Cu catalyst	base	Yield (%)[a]
1	SIMesCuCl	Cs$_2$CO$_3$	80
2	IMesCuCl	Cs$_2$CO$_3$	53
3	SIPrCuCl	Cs$_2$CO$_3$	16
4[b]	Xantphos/CuCl	Cs$_2$CO$_3$	21
5	[Cy$_3$PCuCl]$_2$	Cs$_2$CO$_3$	trace
6	[Ph$_3$PCuCl]$_4$	Cs$_2$CO$_3$	0
7[c]	SIMesCuCl	KOAc	trace
8	SIMesCuCl	KO*t*Bu	43
9[d]	SIMesCuCl	Cs$_2$CO$_3$	59
10[e,f]	SIMesCuCl	Cs$_2$CO$_3$	83
11[f]	SIMesCuCl	Cs$_2$CO$_3$	quant

[a] NMR yield determined using anisole as a standard. [b] Xantphos/CuCl = 1. [c] Reaction time = 24 h. [d] Solvent = toluene. [e] Diboron = **1b**. [f] Diboron (2 eq), Cs$_2$CO$_3$ (1.5 eq), SIMesCuCl (5 mol %).

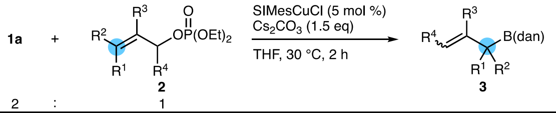


Scheme 3. Synthesis of (neop)B–B(dan).

Although we also examined the reaction of crotyl electrophiles with another leaving group such as methyl carbonate, benzoate or ether, none of them gave **3a** (Table S1, Supporting Information).[11]

Under the optimized conditions, the γ-selective borylation proceeded smoothly with hex-2-en-1-yl phosphate (**2b**), whose stereochemistry affected the reaction efficiency to afford **3b** in 83% (from *Z* isomer) or 51% yield (from *E* isomer) (Entries 1 and 2, Table 2). Functionalized allylic phosphates derived from (*Z*)-but-2-ene-1,4-diol (**2c** and **2d**) were also convertible into the borylated products (**3c** and **3d**) with the intact functional groups (acetal and silylether) (Entries 3 and 4), and the results revealed that only a phosphate moiety acted as a leaving group. In addition, the reaction of allyl (**2e**) or methallyl (**2f**) phosphate provided a 96% or 93% yield of the products (**3e** and **3f**) (Entries 5 and 6), whereas the use of 2-phenylallyly (**2g**) or cyclohex-2-en-1-yl (**2h**) phosphate led to moderate yields (Entries 7 and 8). Although allylic phosphates having an α-substituent (**2i**–**2k**) were also found to undergo the borylation efficaciously, a mixture of *E*/*Z* stereoisomers was formed in each case (Entries 9–11). On the other hand, the stereoselectivity was improved by use of Xantphos as a ligand,[7a] albeit at the expense of the yield (Entry 12).[12] We examined the reaction of cinnamyl (R^2 = Ph, R^1 = R^3 = R^4 = H) or hydroxy-substituted allylic (R^1 = CH$_2$OH, R^2 = R^3 = R^4 = H) phosphates as well, however none of them afforded the desired products.

Table 2. Substrate Scope.[a]



Entry	R^1	R^2	R^3	R^4	3	Yield (%)[b]
1	*n*Pr	H	H	H	**3b**	83
2	H	*n*Pr	H	H	**3b**	51
3	CH$_2$OTHP	H	H	H	**3c**	79
4	CH$_2$OTBS	H	H	H	**3d**	69
5	H	H	H	H	**3e**	91
6	H	H	Me	H	**3f**	93
7	H	H	Ph	H	**3g**	51
8[c]	-CH$_2$*CH$_2$*-	H	H	-*CH$_2$*CH$_2$-	**3h**	50
9	H	H	H	Me	**3i**[d]	70
10	H	H	H	*n*Pent	**3j**[e]	87
11	H	H	H	allyl	**3k**[f]	66
12[g]	H	H	H	*n*Pent	**3j**[h]	49

[a] Conditions: **1a** (0.20 mmol), **2** (0.10 mmol), Cs$_2$CO$_3$ (0.15 mmol), SIMesCuCl (5.0 μmol), THF (1.0 mL). [b] Isolated yield based on **2**. [c] Cyclohex-2-en-1-yl phosphate was used. [d] *major*:*minor* = 57:43. [e] *major*:*minor* = 50:50. [f] *major*:*minor* = 52:48. [g] Catalyst = Xantphos/CuCl. [h] *major*:*minor* = 90:10.

As depicted in Scheme 4, perillyl alcohol or geraniol-derived phosphate (**2l** or **2m**) could be transformed into the respective allyl–B(dan) (**3l** or

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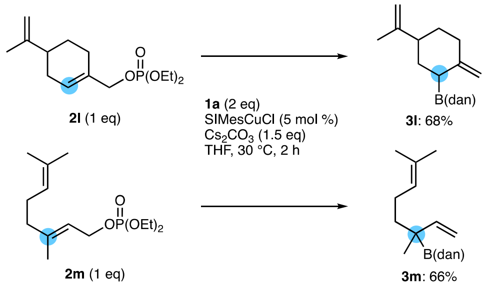
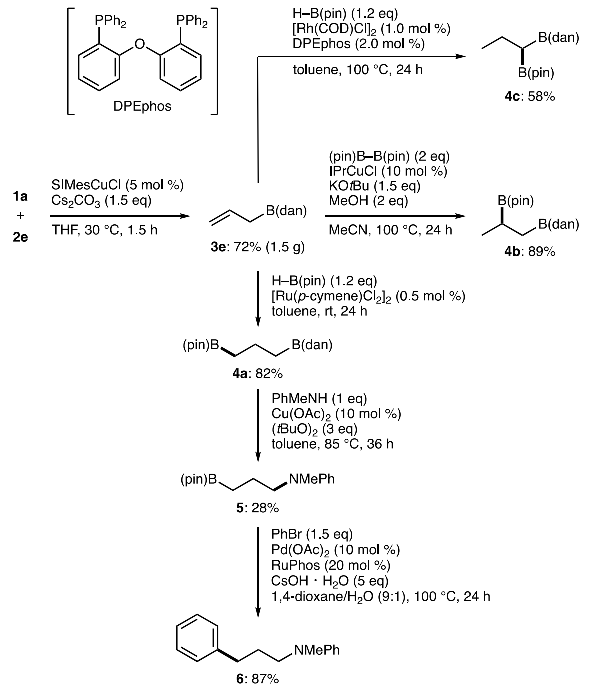
3m) in 68% and 66% yield, showing that disubstitution at the γ-position does not impede the reaction in the latter case. The distal C–C double bonds were not injured thoroughly (also in the case of **2k**), despite the fact that simple aliphatic alkenes undergo the B(dan)-installing reactions under copper catalysis.[4b,d,f]



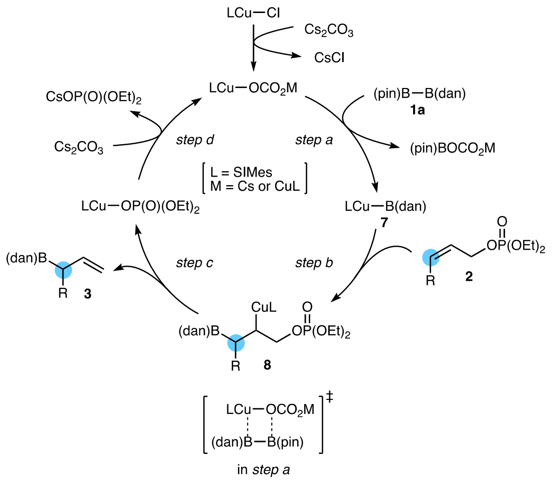
Scheme 4. Borylation of Terpenoid-Derived Phosphates.

Synthetic practicality of the borylation was exemplified by treating **2e** (10 mmol) with **1a** to afford **3e** in a gram-scale (Scheme 5), and furthermore, its C–C double bond could be hydroborated with H–B(pin) in the *anti*-Markovnikov fashion under ruthenium catalysis[13] to give 1,3-diborylpropane **4a** in 82% yield. In addition, a regiocomplementary 1,2-diborylpropane (**4b**) was accessible in 89% yield by the copper-catalyzed formal hydroboration with (pin)B–B(pin).[14] Moreover, **3e** was found to undergo rhodium-catalyzed isomerization–hydroboration, resulting in the formation of 1,1-diborylpropane (**4c**).[15] It should be noted that the C–B(dan) bond of **4a** turned out to be preferentially convertible into a C–N bond by copper-catalyzed Chan–Lam–Evans-type coupling,[16] leaving the C–B(pin) bond intact. Although the yield still remains to be improved,[17] the reaction has demonstrated first that a C–B(dan) bond can become more reactive under certain conditions, being in marked contrast to its inertness toward the cross-coupling because of the diminished Lewis acidity.[18] Finally, the remaining C–B(pin) bond of **5** underwent the cross-coupling to provide **6** in 87% yield.[19]



Scheme 5. Transformation of Allyl–B(dan).

Formation of Cu–B(dan) (**7**) by the selective σ-bond metathesis between a cuprous carbonate and **1a** would trigger the borylation (*step a*, Scheme 6). As proposed in the reaction of allylic carbonates with (pin)B–B(pin), **7** undergoes insertion of an alkene moiety of **2** to provide an alkylcopper species (**8**) (*step b*), which is then transformed into **3** via β-oxygen elimination (*step c*). The exclusive γ-selectivity is ascribable to this insertion–elimination sequence, and a cuprous carbonate is finally regenerated by counteranion exchange with Cs_2CO_3 (*step d*).



Scheme 6. Plausible Catalytic Cycle.

In conclusion, the B(dan)-installing allylic borylation, which proceeds with exclusive γ-selectivity, has been achieved by the reaction of

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allylic phosphates with (pin)B–B(dan) under copper catalysis. Diverse allyl–B(dan) derivatives are straightforwardly accessible from α/β/γ-substituted allylic phosphates, preparable readily from respective allylic alcohols, and furthermore the hydroboration of allyl–B(dan) provides diborylpropanes with different boron-Lewis acidity, whose less Lewis acidic boron moiety (B(dan)) can selectively be transformed into a nitrogen functionality. Further studies on the Chan–Lam–Evans-type coupling of dan-substituted organoboranes as well as the catalytic B(dan)-installing reactions are in progress.

Experimental Section

Typical Procedure for the Copper-Catalyzed B(dan)-Installing Allylic Borylation Using (pin)B–B(dan) (1a) and Allyl Phosphate (2e) (Table 2, Entry 5)

A flame-dried Schlenk tube equipped with a magnetic stirring bar was charged with SIMesCuCl (2.0 mg, 5.0 μmol), THF (1.0 mL) and Cs_2CO_3 (48.9 mg, 0.15 mmol) under an argon atmosphere. Then, the mixture was stirred at room temperature for 15 min before addition of allyl diethyl phosphate **2e** (19.4 mg, 0.10 mmol) and (pin)B–B(dan) **1a** (58.8 mg, 0.20 mmol). After the mixture was stirred at 30 °C for 2 h, the mixture was diluted with ethyl acetate and the organic solution was filtered through a Celite pad. Evaporation of the solvent followed by silica gel-column chromatography (hexane:ethyl acetate = 2:1 as an eluent) gave **3e** as a red oil; yield: 18.9 mg (91%).

Acknowledgements

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[10] The modest yield of **1b** is attributable to concomitant formation of (dan)B–B(dan) (7%) and unidentified side-products.

[11] The reaction of crotyl methyl carbonate with (pin)B–B(pin) under the present conditions also did not give allyl–B(pin). The contrasting result to those reported previously (ref. 7 and 8) should be due to the catalyst system.

[12] We tentatively assigned the stereochemistry of the major isomer as *E*, according to the observed *E* stereoselectivity in the B(pin)-installing allylic borylation catalyzed by a Xantphos–Cu catalyst (ref. 7a).

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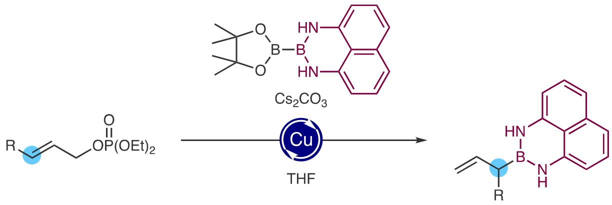

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