JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Enantio- and Diastereoselective Synthesis of 1,2-Hydroxyboronates through Cu-Catalyzed Additions of Alkylboronates to Aldehydes

Matthew V. Joannou, Brandon S. Moyer, and Simon J. Meek*

Department of Chemistry, The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-3290, United States

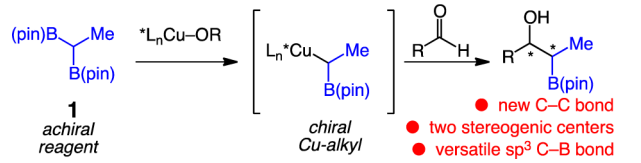
Supporting Information

ABSTRACT: The first catalytic enantio- and diastereoselective synthesis of 1,2-hydroxyboronates is reported. Reactions are promoted by a readily available chiral monodentate phosphoramidite−copper complex in the presence of an alkyl 1,1-diboron reagent. Products contain two contiguous stereogenic centers and are obtained in up to 91% yield, >98:2 d.r., and 98:2 e.r. The reaction is tolerant of aryl and vinyl aldehydes, and the 1,2-hydroxyboronate products can be transformed into versatile derivatives. Mechanistic experiments indicate control of absolute stereochemistry of the α-boryl component.

Enantiomerically pure chiral boron-containing molecules provide enabling platforms for chemical synthesis.[1] Direct catalytic enantioselective preparation of chiral alkyl sp^3 carbon−boron-containing compounds can be achieved by a number of reported methods, for example, hydroboration,[2,3] diboration,[4] allylic substitution,[3,5] conjugate boron addition,[6] and arylborylation.[7] These methods directly generate C−B bonds, while an alternative approach is through the use of chiral α-boron-containing nucleophiles; such reagents do not involve the direct formation of a new C−B bond but rather a C−C bond. α-Boron−carbon nucleophiles can be generated in a number of ways: (1) Through the formation of stoichiometric copper reagents, (2) deprotonation of alkyl boronates, and (3) the activation of 1,1-diboronates. α-Boron substituted alkyl cuprates, developed by Knochel, readily undergo C−C bond formation with a variety of electrophiles, providing an effective stoichiometric method for the installation of alkyl α-boron units.[8] In addition, alkylation methods that employ boron-stabilized carbanions generated through deprotonation of alkyl boronate esters and boranes are limited due to the requirement of strong alkyl or amide lithium bases.[9] Alternatively, reactive α-boryl species can be conveniently accessed through deborylation by treatment of 1,1-diboronates with an alkoxide base.[4h,10] The emerging utility of alkyl 1,1-diboron reagents for chemical synthesis has recently been demonstrated in Suzuki cross-coupling reactions.[11] More recently, Morken and co-workers reported efficient enantioselective Pd-catalyzed Suzuki couplings of alkyl 1,1-diboronates with aryl and vinyl halides.[12]

Herein, we disclose a protocol for the enantio- and diastereoselective generation of 1,2-hydroxyboronates through the Cu-catalyzed addition of sp^3 1,1-diboron reagents to aryl and vinyl aldehydes (Scheme 1). Reactions are promoted by 7.5−10 mol % of a readily available Cu(I) salt and chiral monodentate phosphine in conjunction with an alkoxide base; products are delivered in up to 91% yield, 98:2 e.r., and >98:2 d.r., and the chiral 1,2-hydroxyboronate building blocks can be further elaborated to directly access functionalized small molecules.

Scheme 1. Strategy for the Synthesis of 1,2-Hydroxyboronates

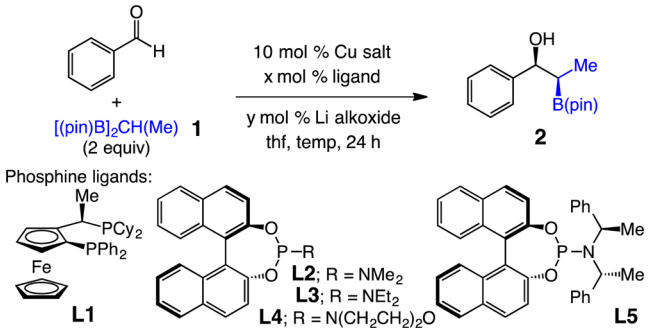


Initial studies of catalytic reaction conditions identified Cu salts in conjunction with monodentate phosphines as effective promoters for the addition of 1,1-diboryl reagents to aldehydes.[13] The data illustrated in Table 1 summarize the optimization of Cu-phosphine conditions. As entry 1 shows, there is no background addition of **1** to benzaldehyde with LiO*t*-Bu at 45 °C. Conversely, use of sodium or potassium alkoxides lead to a significant nonselective background reaction. Of note, catalytic quantities of LiO*t*-Bu were found not to be effective in promoting the reaction, while increasing the amount of base (>1.3 equiv) leads to >98% consumption of aldehyde but low conversion to product. We found bidentate phosphine−Cu complexes to be ineffective (for example, (*R*)-binap, (*R*)-DTBM-segphos, and **L1**, entries 2−4, Table 1), but discovered that a monodentate phosphine−Cu complex can deliver the desired 1,2-hydroxyboronate **2**. Treatment of benzaldehyde and **1** with 10 mol % of the Cu-phosphine complex derived from $Cu(OTf)_2$ and ligand **L2** with LiO*t*-Bu at 45 °C affords **2** (65% conv) in favor of the syn-diastereoisomer (91:9 d.r., and 88:12 e.r.). Steric modification of the lithium alkoxide base revealed that LiO*t*-Am (entry 6) is an equally efficient (64% conv) but more stereoselective activator (91:9 d.r. and 94:6 e.r.) for the formation of **2**.[14] Catalytic 1,2-additions in the presence of various Cu(I) and Cu(II) salts (entries 7−9) revealed $Cu(NCMe)_4PF_6$ to be the most effective promoter, delivering **2** in 66% conversion, 92:8 d.r., and 94:6 e.r (entry 9).[15] The reaction efficiency was found to further improve upon conducting the reaction at 22 °C for 48 h (entry 10); **2** is generated in 92% conversion, 92:8 d.r., and 94:6 e.r. Further efforts to increase reaction selectivity through modification of the phosphoramidite N-$(alkyl)_2$ moiety (**L3**−**5**) results in a decrease in reaction efficiency and stereoselectivity (entries 11−13).[16]

Received: April 2, 2015
Published: April 23, 2015

DOI: 10.1021/jacs.5b03477
J. Am. Chem. Soc. 2015, 137, 6176−6179

Table 1. Evaluation of Cu Complexes[a]



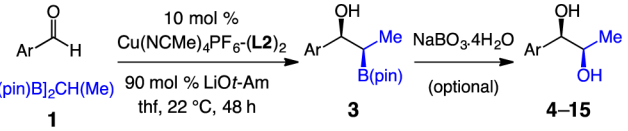
entry	Cu salt	ligand; mol %	Li alkoxide; mol %	temp (°C)	conv (%)[b]	d.r.[b]	e.r.[c]
1	–	–	LiO*t*-Bu; 130	45	<2	–	–
2	$Cu(OTf)_2$	(*R*)-binap; 10	LiO*t*-Bu; 130	45	<2	–	–
3	$Cu(OTf)_2$	(*R*)-segphos; 10	LiO*t*-Bu; 130	45	<2	–	–
4	$Cu(OTf)_2$	**L1**; 10	LiO*t*-Bu; 130	45	<2	–	–
5	$Cu(OTf)_2$	**L2**; 20	LiO*t*-Bu; 130	45	65	91:9	88:12
6	$Cu(OTf)_2$	**L2**; 20	LiO*t*-Am; 90	45	64	91:9	94:6
7	$Cu(OMe)_2$	**L2**; 20	LiO*t*-Am; 90	45	62	92:8	96:4
8	CuCl	**L2**; 20	LiO*t*-Am; 90	45	67	85:15	81:19
9	$Cu(NCMe)_4PF_6$	**L2**; 20	LiO*t*-Am; 90	45	66	92:8	94:6
10[d]	**$Cu(NCMe)_4PF_6$**	**L2; 20**	**LiO*t*-Am; 90**	**22**	**92**	**92:8**	**94:6**
11[d]	$Cu(NCMe)_4PF_6$	**L3**; 20	LiO*t*-Am; 90	22	57	88:12	91:9
12[d]	$Cu(NCMe)_4PF_6$	**L4**; 20	LiO*t*-Am; 90	22	77	87:13	91:9
13[d]	$Cu(NCMe)_4PF_6$	**L5**; 20	LiO*t*-Am; 90	22	30	92:8	67:33

[a]Reactions performed under a N_2 atmosphere. [b]Conversion to **2**; values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with HMDS as internal standard. [c]Determined by $NaBO_3$ oxidation to diol and HPLC analysis; see the Supporting Information for details. [d]48 h reaction.

The monodentate phosphine-Cu-catalyzed 1,2-addition can be used for the enantio- and diastereoselective preparation of synthetically valuable sp^3 organoboron molecules in good yield; representative examples are illustrated in Table 2. Transformations proceed in the presence of 10 mol % Cu catalyst at 22 °C within 48 h. The resulting 1,2-hydroxyboronate products demonstrate variable stability toward elimination during column chromatography. For ease of isolation and enantiomeric ratio determination, the products were oxidized to the corresponding diols. For utilization and functionalization of 1,2-hydroxyboronate products, vide infra. Benzaldehyde derived syn-diol **4** (entry 1) is isolated in 67% yield (92:8 d.r.) and in 94:6 e.r. after oxidation ($NaBO_3$–$4H_2O$). Aryl aldehydes incorporating halogens may be used (entries 2–3); 10 mol % Cu complex delivers **5** (77% yield, 94:6 e.r.) and **6** (91% yield, 95:5 e.r.) in 48 h at 22 °C after oxidation. Cu-catalyzed 1,2-additions to aryl aldehydes containing an electron-donating *p*-MeO group work effectively (entry 4), generating **7** in 69% yield (97:3 d.r. and 93:7 e.r.). Conversely, the presence of electron-withdrawing *p*-NO_2 (entry 5) or *m*-NO_2 (entry 6) substituents delivers **8** and **9** in lower conversion (42% and 37%) but with high enantioselectivity (95:5 e.r. **8**, and 95:5 e.r. **9**). Aldehydes containing *m*-methyl (entry 7) and *m*-trifluoromethyl (entry 8) substituents are also tolerated; diols **10** and **11** are delivered in yields of 76% (92:8: d.r., 98:2 e.r.) and 59% (90:10 d.r., 94:6 e.r.), respectively. Sterically hindered aryl aldehydes participate to afford the desired 1,2-hydroxyboronates with complete diastereocontrol; for example both **12** (68% yield, entry 9) and **13** (65% yield, entry 10) are formed in >99:1 d.r. and 93:7 e.r. and 93:7 e.r., respectively. The reaction protocol is not sensitive to N- and O-containing heteroaryl aldehydes (entries 11–12). However, products are formed in diminished diastereoselectivity; treatment with 10 mol % Cu and **L2** furnish **14** in 55% yield (86:14 d.r., 95:5 e.r.) and **15** in 68% yield (83:17 d.r., 90:10 e.r.).

α,β-Unsaturated aldehydes react in the presence of 7.5 mol % phosphine–Cu complex with 60–80 mol % LiO*t*-Am to afford functional organoboron compounds bearing allylic alcohols

Table 2. Cu-Catalyzed 1,2-Additions of 1 to Aryl Aldehydes[a]



entry	substrate; product	conv(%)[b]	yield (%)[c]	d.r.[b]	e.r.[d]
1	Ar = C_6H_5; **4**	92	67	92:8	94:6
2	Ar = *p*-FC_6H_4; **5**	93	77	92:8	94:6
3	Ar = *p*-BrC_6H_4; **6**	>98	91	93:7	95:5
4	Ar = *p*-$OMeC_6H_2$; **7**	79	69	97:3	93:7
5	Ar = *p*-$NO_2C_6H_4$; **8**	42	34	93:7	95:5
6	Ar = *m*-$NO_2C_6H_4$; **9**	37	35	84:16	95:5
7	Ar = *m*-MeC_6H_4; **10**	82	76	92:8	98:2
8	Ar = *m*-$CF_3C_6H_4$; **11**	65	59	90:10	94:6
9	Ar = *o*-MeC_6H_4; **12**	78	68	>99:1	93:7
10	Ar = mesityl; **13**	>98	65	>99:1	93:7
11	Ar = furyl; **14**	64	55	86:14	95:5
12	Ar = 3-pyridyl; **15**	76	68	83:17	90:10

[a]Reactions performed under a N_2 atmosphere; see the Supporting Information for details. [b]Conversion to 1,2-hydroxyboronate; values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with HMDS as internal standard. [c]Yields of the corresponding purified diol. [d]Determined by HPLC analysis of the diol; see the Supporting Information for details.

DOI: 10.1021/jacs.5b03477
J. Am. Chem. Soc. 2015, 137, 6176–6179

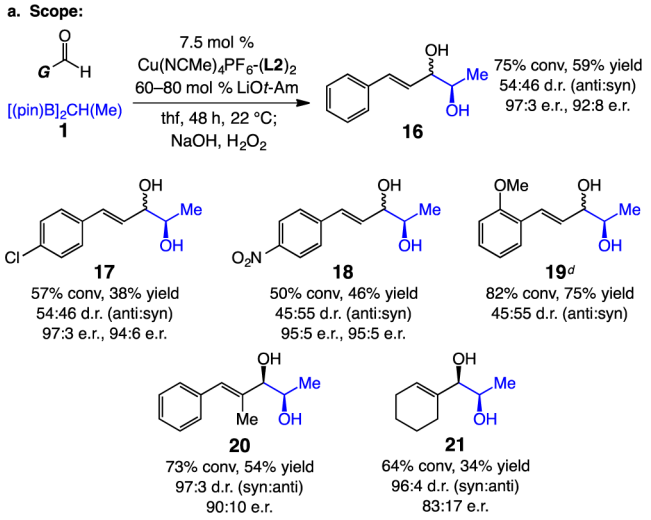
(Scheme 2).[17] Cu-catalyzed addition to sterically unhindered cinnamaldehyde affords diol **16** (59% yield) in low diastereoselectivity (54:46 d.r., anti:syn) in slight favor of the anti diastereoisomer; however, both isomers are formed in high enantioselectivity (97:3 e.r. anti, and 92:8 syn). Electron-withdrawing groups are tolerated: *p*-Cl and *p*-NO_2 cinnamaldehyde derived diols **17** and **18** are generated in low diastereoselectivity (54:46 and 45:55 d.r. anti:syn), but the diastereoisomers are formed in high enantioselectivity (97:3–95:5 e.r. anti, and 94:6–95:5 e.r. syn). Aryl groups bearing electron-donating ortho-substituents are compatible as demonstrated by the formation of **19** in 75% yield, 45:55 d.r.[18] α-Substituted vinyl aldehydes lead to restoration of syn diastereoselectivity without significant loss in enantioselectivity; **20** is delivered in 73% conversion (54% yield) and 97:3 d.r. and 90:10 e.r. Cyclohexene derived vinyl aldehydes undergo smooth diastereoselective 1,2-addition (96:4 syn:anti) to afford **21** in 64% conversion but in an 83:17 enantiomeric ratio.

To address which stereogenic center is set in high enantioselectivity (allylic versus homoallylic) in the cases of low diastereoselectivity observed with vinyl aldehydes, the allylic secondary alcohol in diol **16** was removed. As shown in Scheme 3, diol **16** was first converted to the allylic carbonate with CDI (60% yield), followed by 2 mol % Pd-catalyzed allylic reduction (Et_3N, HCO_2H),[19] and subsequent hydrogenation to the corresponding secondary alcohol **22** (50% two steps).[20] The enantiomeric purity of **22** was determined to be 92:8 e.r., corresponding to the secondary boronate stereogenic center being formed in high enantioselectivity in both anti and syn diastereoisomers. These data suggest a mechanism where the α-boryl nucleophile is formed with high stereopurity through catalyst controlled stereodifferentiation of the two B(pin) groups in achiral diboron **1**. The low diastereoselectivity observed for sterically unhindered alkenyl aldehydes is therefore likely a result of poor facial discrimination of the C=O by the Cu catalyst.

To determine whether lithium alkoxides lead to deborylation of **1** and formation of a boron-stabilized carbanion, as shown to occur with NaO*t*-Bu,[10] activation of **1** with LiO*t*-Bu was followed by ^1H and ^{11}B NMR. As shown in Scheme 4, treatment of **1** with 1.7 equiv of LiO*t*-Bu in d_8-THF at 22 °C for 2.5 h results in 21% formation of borate **23** and <2% conversion to carbanion **24**.[21] Furthermore, warming the mixture to 50 °C for 2.5 h causes no change in the amount of borate **23** (21%) generated but leads to 15% conversion to the proteo-deborylated product, EtB(pin), by ^1H NMR. The ^{11}B NMR shows <10% conversion to an unidentified upfield signal (δ 3.55 ppm), which likely corresponds to deprotonated **1** responsible for the formation of EtB(pin) (see Supporting Information for details).

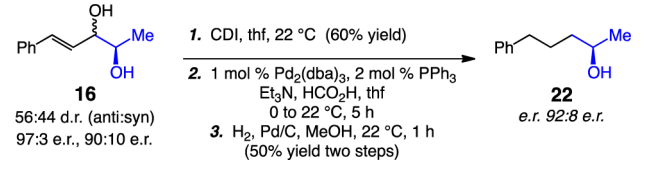
The 1,2-hydroxyboronates synthesized through this Cu-catalyzed manifold can be elaborated to generate useful functional molecules (Scheme 5). In addition to oxidation, 1,2-hydroxyboronate **2** (isolated in 53% yield on 1 mmol scale; 89:11 d.r. and 93:7 e.r.) can be converted to the TBS ether (76% yield) followed by homologation to afford alkyl organoboron **25** in 75%

Scheme 2. Cu(I)-Catalyzed Addition of 1 to Alkenyl Aldehydes[a,b,c]

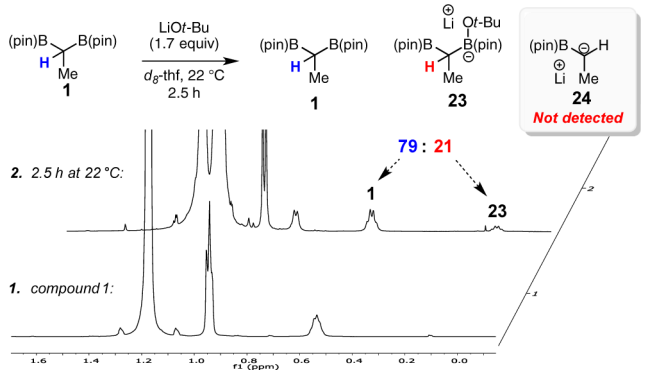


[a]See Table 1 footnote a. [b]See Table 1 footnote b. [c]See Table 1 footnote c. [d]1,2-Diol **19** slowly decomposes precluding HPLC analysis.

Scheme 3. Control of C–B Stereogenic Center

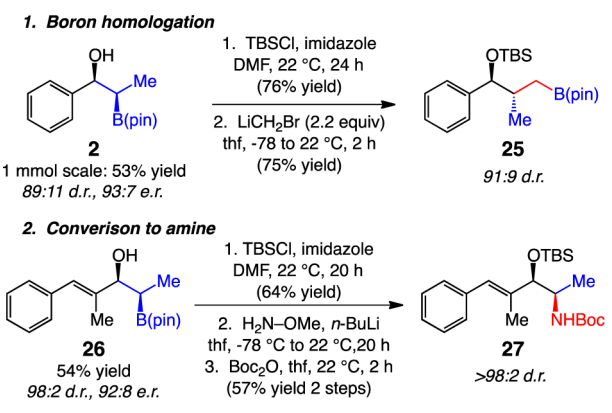


Scheme 4. ^1H and ^{11}B NMR Boron Activation Experiments[a]



[a]^{11}B NMR shows only two signals: **1** (δ 32.3 ppm) and **23** (δ 6.9 ppm).

Scheme 5. Representative Functionalizations of 1,2-Hydroxyboronates



DOI: 10.1021/jacs.5b03477
J. Am. Chem. Soc. 2015, 137, 6176–6179

yield and 91:9 d.r. In a similar manner, allylic 1,2-hydroxyboronate **26** (isolated in 54% yield; 98:2 d.r. and 92:8 e.r.) can be protected as the silyl ether (64% yield), and then treated with lithiated methoxyamine[22] to cause stereospecific C−B to C−N conversion to deliver amino alcohol **27** (57% yield) after Boc protection.

These studies present the first catalytic protocol for the enantio- and diastereoselective synthesis of 1,2-hydroxyboronates. The efficiency of the transformation is demonstrated by the concomitant generation of a new C−C bond and two vicinal stereogenic centers, while retaining a versatile C−B bond. The method is applicable to aryl and alkenyl aldehyde substrates. Mechanistic experiments indicate control of absolute stereochemistry at the α-boryl component even in cases of low aldehyde facial selectivity. A key aspect of the sp^3 B-containing secondary alcohols is the stereospecific transformations (e.g., homologation and amination) made available by the alkyl B(pin) unit of the corresponding silyl protected hydroxyboronate products. Further mechanistic studies, as well as development of additional catalytic enantioselective reactions of alkyl 1,1-diboron reagents, are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and spectral and analytical data for all products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b03477.

■ AUTHOR INFORMATION

Corresponding Author

*sjmeek@unc.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support was provided by the University of North Carolina at Chapel Hill and an Eli Lilly New Faculty Award.

■ REFERENCES

(1) *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, Germany, 2000.

(2) For reviews on catalytic enantioselective hydroboration, see: (a) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695−4712. (b) Carroll, A.- M.; O'Sullivan, T. P.; Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609−631. For recent examples, see: (b) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160−3161. (c) Noh, D.; Chea, H.; Ju, J.; Yun, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6062−6064. (d) Smith, S. M.; Takacs, J. M. *J. Am. Chem. Soc.* **2010**, *132*, 1740−1741. (e) Sasaki, Y.; Zhong, C.; Sawamura, M.; Ito, H. *J. Am. Chem. Soc.* **2010**, *132*, 1226−1227. (f) Corberán, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079−7082. (g) Feng, X.; Jeon, H.; Yun, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 3989−3992. (h) Lee, H.; Lee, B. Y.; Yun, J. *Org. Lett.* **2015**, *17*, 764−766.

(3) For a recent review on Cu-catalyzed boryl addition reactions, see: Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Tetrahedron* **2015**, *71*, 2183−2197.

(4) For a review on catalytic enantioselective diboration, see: (a) Burks, H. E.; Morken, J. P. *Chem. Commun.* **2007**, 4717−4725. For recent examples, see: (b) Burks, H. E.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 9134−9135. (c) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234−18235. (d) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210−13211. (e) Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222−11231. (f) Toribatake, K.; Nishiyama, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 11011−11015. (g) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386−390. (h) Coombs, J. R.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 16140−16143.

(5) For recent examples on catalytic allylic boration, see: (a) Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856−14857. (b) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634−10637. (c) Ito, H.; Kunii, S.; Sawamura, M. *Nat. Chem.* **2010**, *2*, 972−976. (d) Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133*, 2410−2413.

(6) For recent examples of metal-catalyzed enantioselective conjugate boron additions, see: (a) Lee, J.-E.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 145−147. (b) Chen, I.-H.; Yin, L.; Itano, W.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 11664−11665. (c) Chea, H.; Sim, H.-S.; Yun, J. *Adv. Synth. Catal.* **2009**, *351*, 855−858. (d) Park, J. K.; Lackey, H. H.; Rexford, M. D.; Kovnir, K.; Shatruk, M.; McQuade, D. T. *Org. Lett.* **2010**, *12*, 5008−5011. (e) Chen, I.-H.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2010**, *12*, 4098−4101. (f) Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nat. Chem.* **2011**, *3*, 894−899. For recent examples of metal-free enantioselective conjugate boron additions, see: (g) O'Brien, J. M.; Lee, K.-S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630−10633. (h) Wu, H.; Radomkit, S.; O'Brien, J. M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 8277−8285. (i) Radomkit, S.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2014**, *53*, 3387−3391.

(7) Nelson, H. M.; Williams, B. D.; Miró, J.; Toste, F. D. *J. Am. Chem. Soc.* **2015**, *137*, 3213−3216.

(8) Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431−7433. (b) Waas, J. R.; Sidduri, A. R.; Knochel, P. *Tetrahedron Lett.* **1992**, *33*, 3717−3720. (c) Sakai, M.; Saito, S.; Kanai, G.; Suzuki, A.; Miyaura, N. *Tetrahedron* **1996**, *52*, 915−924.

(9) (a) Matteson, D. S.; Moody, R. J. *J. Am. Chem. Soc.* **1977**, *99*, 3196−3197. (b) Matteson, D. S.; Arne, K. *J. Am. Chem. Soc.* **1978**, *100*, 1325−1326. (c) Matteson, D. S.; Moody, R. J. *Organometallics* **1982**, *1*, 20−28. (d) Pelter, A.; Singaram, B.; Williams, L.; Wilson, J. W. *Tetrahedron Lett.* **1983**, *24*, 623−626.

(10) Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581−10584.

(11) (a) Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. *J. Am. Chem. Soc.* **2010**, *132*, 11033−11035. (b) Endo, K.; Ohkubo, T.; Shibata, T. *Org. Lett.* **2011**, *13*, 3368−3371. (c) Endo, K.; Ohkubo, T.; Ishioka, T.; Shibata, T. *J. Org. Chem.* **2012**, *77*, 4826−4831.

(12) (a) Sun, C.; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534−6537. (b) Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 17918−17921.

(13) Reactions of more substituted 1,1-diboron reagents result in low conversions to product; the result of these studies will be reported shortly.

(14) Application of lithium alkoxide bases containing smaller alkyl groups than *t*-Bu (e.g., methyl) leads to <5% conversion.

(15) $Cu(OMe)_2$ results in inconsistent conversion.

(16) Reactions performed with 10 mol % $Cu(NCMe)_4PF_6$ and 10 mol % **L2** result in decreased conversion to product.

(17) The allylic alcohol products demonstrate variable stability to purification, particularly when electron-donating substituents are present on the aryl ring.

(18) *p*-OMe cinnamaldehyde is converted to the corresponding 1,2-hydroxyboronate in 75% yield; however, the corresponding 1,2-diol product is unstable to purification.

(19) Palimkar, S. S.; Uenishi, J. *Org. Lett.* **2010**, *12*, 4160−4163.

(20) Pd-catalyzed allylic reduction affords mixtures that contained the over-reduced product **22** that could not be separated.

(21) The reaction mixture is homogeneous.

(22) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449−16451.

DOI: 10.1021/jacs.5b03477
J. Am. Chem. Soc. 2015, 137, 6176−6179