Enantioselectivity

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Enantio- and Diastereoselective 1,2-Additions to α-Ketoesters with Diborylmethane and Substituted 1,1-Diborylalkanes

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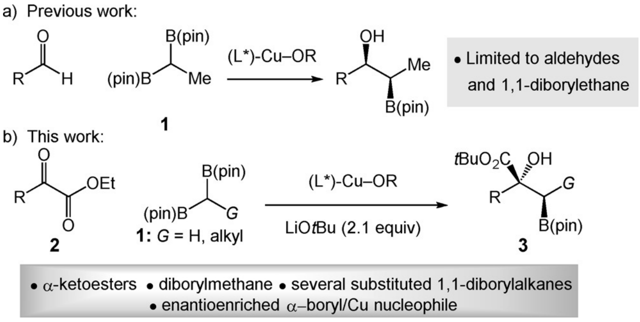
***Abstract:** The catalytic enantioselective synthesis of boronate-substituted tertiary alcohols through additions of diborylmethane and substituted 1,1-diborylalkanes to α-ketoesters is reported. The reactions are catalyzed by readily available chiral phosphine/copper(I) complexes and produce β-hydroxyboronates containing up to two contiguous stereogenic centers in up to 99:1 e.r. and greater than 20:1 d.r. The utility of the organoboron products is demonstrated through several chemoselective functionalizations. Evidence indicates the reactions occur via an enantioenriched α-boryl-copper-alkyl intermediate.*

Tertiary alcohols are valuable functional groups found within many biologically active organic molecules. As a result, the development of efficient and selective methods for their preparation is an important challenge in organic chemistry.[1,2] The catalytic addition of sp^3-carbon-based nucleophiles to ketones provides one of the most efficient strategies to access enantiomerically enriched tertiary alcohols.[3] Nevertheless, despite recent progress in this area, a number of challenges still remain to be addressed. Of particular significance are protocols which deliver nonracemic tertiary alcohols and incorporate chemically versatile functional groups, such as alkyl boronic esters, for further manipulation.[4] Stereoselective synthesis of β-boryl alcohols by the 1,2-addition of α-boryl alkyl nucleophiles provides a direct approach for the generation of such versatile chemical motifs.[5] Catalytic methods of incorporating boronate esters by carbon–carbon bond-formation remain limited, as current stoichiometric protocols involve the use of cuprate reagents[6] and alkylation of reactive dimesityl boron stabilized α-boryl carbanions.[7] More recently, 1,1-organodiboronate esters have been developed as α-boryl carbanions in stereoselective deborylative carbon–carbon bond forming reactions.[8] Furthermore, catalytic enantioselective reactions which employ substituted 1,1-diborylalkanes are scarce.[5a,8d–e,h]

We have shown that α-boryl/Cu species can be accessed through stereoselective deborylative transmetalation of 1,1-diboron compounds with copper-based catalysts. We recently demonstrated that such catalytically generated intermediates engage in 1,2-additions for the enantio- and diastereoselective preparation of secondary alcohols bearing a vicinal boron-containing stereogenic center (Scheme 1).[5] We proposed that a similar strategy could be employed for the synthesis of tertiary alcohols containing 1,2-hydroxyboronates by addition to α-ketoesters. The difficulty of such a catalytic method arises from the ability to efficiently form a new C–C bond between sterically congested vicinal $C(sp^3)$ stereogenic centers.



Scheme 1. a) Previous work: Catalytic enantio- and diastereoselective 1,2-addition of 1,1-diborylethane to aldehydes. b) This work: Catalytic enantio- and diastereoselective 1,2-addition of 1,1-diborylmethane and functionalized 1,1-diborylalkanes to α-ketoesters.

Herein, we report the catalytic enantio- and diastereoselective synthesis of β-boryl tertiary alcohols through the copper-catalyzed additions of α-boryl nucleophiles to α-ketoesters. The utility of the products is illustrated through further alkyl boronate ester functionalizations (e.g., homologation, oxidation, and iodoetherification). Moreover, addition to a symmetrical ketone demonstrates the reaction occurs by the formation of a nonracemic α-borylalkyl-copper intermediate.

We initiated our studies by evaluating the copper-catalyzed enantioselective addition of unsubstituted 1,1-diborylmethane (**5**) to different α-ketoesters (**4a**–**c**; Table 1). We first examined the ability of the chiral copper complex derived from the commercially available monodentate **L1**, which had emerged as the optimal ligand for 1,2-additions involving aldehydes.[5] We found that, with 5 mol% $[Cu(NCMe)_4]PF_6$, 10 mol% **L1**, and 2.05 equivalents of LiO*t*Bu in THF at 22 °C, the reaction proceeds to afford 43% of **6a** (91:9 e.r.) in 24 hours and 24% of the elimination product **7** (entry 1). At lower temperatures formation of **7** is suppressed, and the conversion into, and enantioselectivity of, **6a** increases. For example, **6a** is generated in 92:8 e.r. and 96:4 e.r. at 4 and −10 °C, respectively (entries 2 and 3).[9] As illustrated in entry 4, the copper(I)-catalyzed reaction is less efficient at

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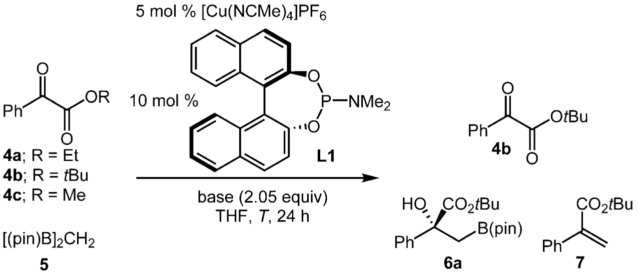
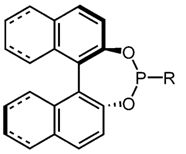
Table 1: Initial examination of chiral copper complexes.[a]



Entry	R	Base	T [°C]	Yield [%][b,c]			e.r.[d]
				4b	**6a**	**7**	**6a**
1	Et	LiO*t*Bu	22	<2	43	24	91:9
2	Et	LiO*t*Bu	4	<2	60	12	92:8
3	Et	LiO*t*Bu	−10	<2	74	<2	96:4
4	Et	LiO*t*Bu	−25	35	51	<2	95:5
5[e]	*t*Bu	LiO*t*Bu	−10	<2	63	<2	94:6
6	Me	LiO*t*Bu	−10	<2	70	<2	93:7
7[e]	Et	LiO*t*Bu	−10	18	26	8	91:9
8	Et	NaO*t*Bu	−10	32	37	<2	81:19

[a] Reactions performed under N_2 atm. [b] In all cases >98% conv. of α-ketoester starting material. [c] Determined by ^{1}H NMR analysis of unpurified mixtures, with DMF as an internal standard, at either 400 or 600 MHz. [d] Determined by $NaBO_3{\cdot}4\,H_2O$ oxidation to diol and HPLC analysis; see the Supporting Information for details. [e] One equivalent of LiO*t*Bu was used. DMF = *N*,*N*-dimethylformamide, THF = tetrahydrofuran.

Other representative findings (**4a**→**6a**): 5 mol % (L)Cu catalyst

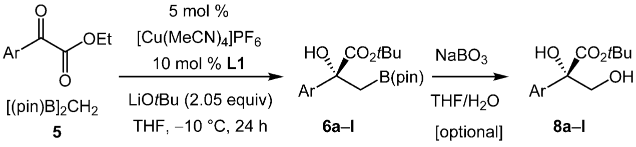


L2: (H_8) R = NMe_2; 43% conv., 83:17 e.r.
L3: R = morpholine; 76% conv., 94:6 e.r.
L4: R = NEt_2; 72% conv., 74:26 e.r.
L5: R = bis[(*R*)-1-phenylethyl]amine; <2 % conv.

L6: (*R*)-binap; <2 conv.
L7: (R)-(S)-Josiphos; 63% conv., 60:40 e.r.
L8: (*R*)-dtbm-SEGPHOS; <2% conv.

−25 °C, thus furnishing **6a** in 51% conversion and in 95:5 e.r.[10] Remarkably, reaction of both the *tert*-butyl and methyl α-ketoesters **4b** and **4c**, respectively, afford **6a** with similar conversions (63% and 70%) and similar enantioselectivities (94:6 and 93:7 e.r.). These data indicate that 1) transesterification of **4a** and **4c**, or the Et and Me ester products, occurs faster than 1,2-addition (entries 3 and 6 versus 5),[9] and 2) C−C bond formation occurs primarily via **4b** (entry 3 versus 6).[11–12] This proposal is further supported by the reaction of **4a** with one equivalent of LiO*t*Bu (entry 7), wherein it proceeds to greater than 98% conversion of **4a** to afford **6a** (26%, 91:9 e.r.), and **4b** (18%).[13] Use of NaO*t*Bu results in a less efficient transformation (entry 8) as **6a** is formed in 37% yield (NMR) and 81:19 e.r. Further reaction optimization using various mono- and bidentate chiral phosphines did not result in a more efficient or stereoselective process (see Table 1). As there is minimal difference in reaction efficiency between **4a–c**, ethyl α-ketoesters were used for the remainder of the study because of their ready availability.

Table 2: Copper(I)-catalyzed 1,2-addition of **1** to aryl α-ketoesters.[a]

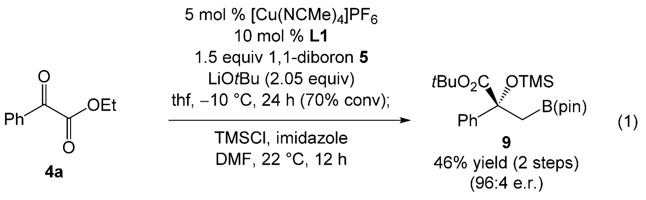


Entry	Product	**6** Yield [%][b,c]	**8** Yield [%][d]	e.r.[e]
1	**8a**; Ar = Ph	74	65	96:4
2	**8b**; Ar = *p*-OMeC_6H_4	72	60	85:15
3	**8c**; Ar = *p*-ClC_6H_4	80	64	97:3
4	**8d**; Ar = *p*-*t*BuC_6H_4	77	70	92:8
5	**8e**; Ar = *p*-$NO_2C_6H_4$	62	46	94:6
6	**8f**; Ar = *p*-$CF_3C_6H_4$	58	54	97:3
7	**8g**; Ar = *m*-MeC_6H_4	76	63	96:4
8	**8h**; Ar = *m*-OMeC_6H_4	82	62	96:4
9	**8i**; Ar = *m*-ClC_6H_4	81	64	97:3
10	**8j**; Ar = 2-napthyl	70	62	96:4
11	**8k**; Ar = *o*-MeC_6H_4	43	27	66:34
12	**8l**; Ar = 3-pyridyl	72	36	97:3

[a] Reactions performed under N_2 atm. [b] In all cases >98% conv. of α-ketoester starting material. [c] Determined by ^{1}H NMR analysis of unpurified mixtures, with DMF as an internal standard, at either 400 or 600 MHz. [d] Yield of the purified diol (average of two runs). [e] Determined by HPLC analysis; see the Supporting Information for details.

We began exploring the scope of the catalytic reaction by synthesizing various unsubstituted hydroxyboronates. Because of the varying stability of unsubstituted hydroxyboronates (e.g., **6a**), the products were oxidized to the corresponding diol. Isolation and non-oxidative workup of the primary alkylboron products can be achieved through hydroxy protection. By using the optimal reaction conditions in Table 1, the catalytic transformations can be performed with various aryl-substituted α-ketoesters (Table 2), including those which carry *para* (**8a–f**) and *meta* (**8g–i**) substituents. Transformations with electron-donating and electron-withdrawing groups proceed with similar ^{1}H NMR yields (58–82%) and high enantioselectivities (92:8–97:3 e.r.) within 24 hours at −10 °C. Only in the presence of *p*-methoxy-substituted phenyl α-ketoesters is a diminution in enantioselectivity observed. The tertiary alcohol **8b** (entry 2), is formed in 72% yield (^{1}H NMR) and 85:15 e.r.[14] The transformation is sensitive to sterically congested α-ketoesters as 2-naphthyl proceeds to 70% and 96:4 e.r. (entry 10), while the *ortho*-methyl-substituted tertiary alcohol **8k** is generated in 43% and 66:34 e.r. (entry 11). Synthesis of pyridyl-substituted product **8l** demonstrates that N-heterocyclic α-ketoesters can serve as effective substrates, albeit oxidation to the corresponding diol proceeds with lower efficiency (entry 12).

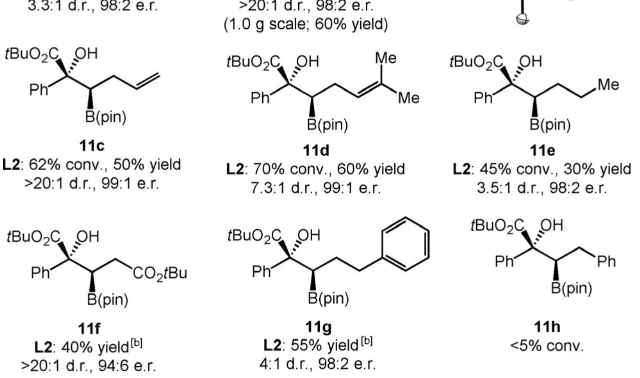
Access to the β-boryl substituted products **6**, can be easily achieved by protection of the tertiary alcohol as the silyl ether product prior to purification. The conversion of **4a** into **9** in Equation (1) (TMS = trimethylsilyl) is representative. Treatment of the crude product **6a** (70% conv) with $(Me)_3SiCl$ and imidazole (DMF, 22 °C, 14 h) affords the alkylboronate **9** in



4a **9** (1)

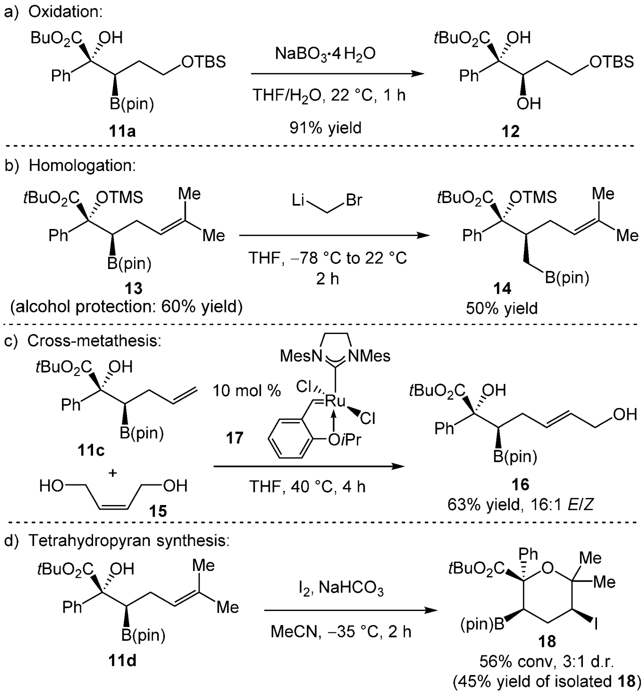
46 % overall yield and 96:4 e.r. after silica gel chromatography.

The copper-catalyzed protocol can be extended to more challenging processes which utilize substituted alkyl 1,1-diboron reagents to afford congested contiguous tertiary and secondary stereogenic centers. Reactions require 5–10 mol % of the copper catalyst derived from either **L1** or **L2** at 22 °C to proceed to good conversion and high enantioselectivity. Notably, the secondary alkyl hydroxyboronate products are stable to silica gel column chromatography. For example, β-boryl tertiary alcohols containing silyl ether (**11a**), alkyl (**11b**,**c**), and alkenyl (**11d**,**e**) functional groups are isolated in up to 64 % yield, greater than 20:1 d.r., and 99:1 e.r. (Scheme 2). The reaction is easily performed on a gram scale as subjection of 1.0 gram of **4a** to **10b** led to the formation of **11b** in 75 % conversion, 60 % yield, greater than 20:1 d.r., and 98:2 e.r. The reaction of a *gem*-diboron reagent which contains an ester (e.g., **11f**), although remarkably diastereo- (> 20:1 d.r.) and enantioselective (94:6 e.r.), results in only 40 % yield (^{1}H NMR) after 24 hours and is likely due to the presence of acidic α-protons.[15] Increasing the size of the substituent proximal to the 1,1-diboron group also results in decreased reactivity. Under optimal reaction conditions the phenethyl-containing **11g** is generated in 55 % yield (4:1 d.r., 98:2 e.r.). The lack of formation (< 5 % conv) of the benzyl-substituted **11h** highlights the sensitivity of the copper-catalyzed protocol to increased steric demand of the substituted nucleophilic components. The absolute and relative stereochemistry of the 1,2-hydroxyboronates synthesized through the copper-catalyzed protocol was determined by X-ray crystallographic analysis of tertiary alcohol **11b** (Scheme 2). The stereochemical assignment of **11b** is (*R*,*R*) with an *anti* relationship between the hydroxy and B(pin) units, thus corresponding to the addition of an *R*-alkyl copper species to the *Si* face of the α-ketoester.[16]



Scheme 2. Enantio- and diastereoselective addition of substituted 1,1-diboronates to α-ketoesters. Reactions performed under N_2 atm. In all cases > 98 % conv. of α-ketoester starting material. The e.r. values were determined after oxidation with $NaBO_3 \cdot 4H_2O$ to the diol by HPLC analysis; see the Supporting Information for details.
[a] $Cu(NCMe)_4PF_6$ (5 mol %), **L1** (10 mol %). [b] Yield determined by ^{1}H NMR spectroscopy.

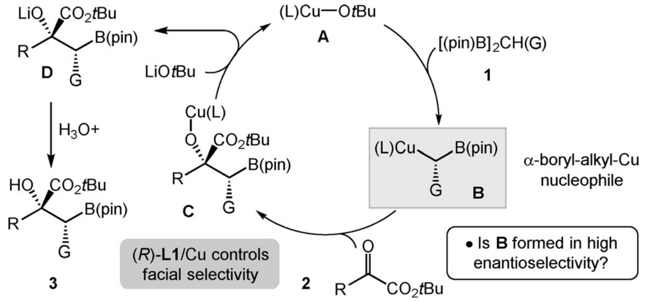
The substituted organoboron compounds formed by the reported catalytic reaction can be transformed to afford a number of valuable enantio- and disastereoenriched molecules (Scheme 3 a–d). Boron oxidation of **11a** delivers the *trans* diol **12** in 91 % yield, and is equivalent to the dihydroxylation of a stereodefined trisubstituted alkene. While the secondary alkyl B(pin) functional groups synthesized through the copper-catalyzed protocol (e.g., **13**) proved to be unsuitable reagents for palladium-catalyzed cross-coupling,[17] they readily participate in metal-free homologations. The sterically hindered secondary alkyl B(pin) silyl ether **13** (formed in 60 % yield) undergoes stereospecific C−B to C−C conversion, to afford the primary alkylboron tertiary silyl ether **14** in 50 % yield. The functional-group-rich organoboron molecules can also be chemoselectively functionalized



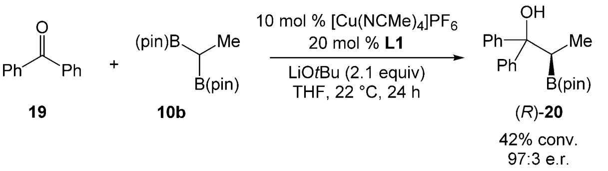
Scheme 3. Representative functionalizations of α-boryl tertiary alcohols. TBS = *tert*-butyldimethylsilyl.

leaving the C(sp^3)−B bond intact. As illustrated in Scheme 3c, the allyl substituted hydroxyboronate **11c** undergoes efficient cross-metathesis.[18] In the presence of 10 mol% of the ruthenium catalyst **17** and 2 equivalents of the *cis*-alkene **15**, the allylic alcohol **16** is formed in 63% yield and 16:1 *E*/*Z*. Additionally, the prenyl-substituted β-boryl tertiary alcohols can be readily converted into tetrahydropyrans by iodoetherification[19] without loss of the B(pin) unit. Treatment of **11d** with I_2 and $NaHCO_3$ at −35 °C in MeCN for 2 hours furnishes the substituted tetrahydropyran **18** in 56% conversion and 3:1 d.r., and silica gel purification delivers **18** as a single diastereoisomer in 45% yield.

A proposed catalytic reaction sequence for the copper-catalyzed process is outlined in Scheme 4. Enantioselective transmetalation between a copper alkoxide (**A**) and the 1,1-diboron **1**, generates the chiral α-boryl-alkyl-copper **B**. Stereoselective 1,2-addition to the α-ketoester **2** affords the copper alkoxide **C**, containing two contiguous stereogenic centers. Reaction with LiO*t*Bu furnishes the lithium alkoxide product **D**, which is converted into **3** after acid workup, and regenerates **A**. While the chiral phosphine/copper catalyst controls addition of the α-boryl/Cu intermediate to the *Si* face of the α-ketoester (**B**→**C**) for diborylmethane, and substituted variants, it is unclear if substituted 1,1-diborons react through an enantioenriched (*R*)-α-boryl-copper-alkyl nucleophile (e.g., **B** R = Me; Scheme 4). To gain insight into the formation of an enantioenriched α-boryl-copper-alkyl intermediate we examined the copper-catalyzed 1,2-addition of **10b** to a symmetrical carbonyl electrophile [Eq. (2)]. Treatment of benzophenone (**19**) with **10b** under optimal reaction conditions (Scheme 2; 10 mol% Cu), affords (*R*)-**20** in 42% yield (^{1}H NMR) and 97:3 e.r.[20] This result indicates that the sterocenter of the α-boryl-copper-alkyl nucleophile is formed with a high e.r., and that the catalyst functions to control both the formation of the copper alkyl and the facial selectivity.[21]



Scheme 4. Working catalytic cycle for copper-catalyzed 1,2-addition.



(2)

In summary, we present the first catalytic protocol for the enantio- and diastereoselective synthesis of β-boryl tertiary alcohols. The approach is applicable to diboroylmethane and other readily accessible substituted 1,1-diborylalkanes and α-ketoesters. Reactions are promoted by a phosphine/Cu complex and proceed by 1,2-addition of α-boryl nucleophiles to generate up to two contiguous stereogenic centers. The versatility of the β-boryl tertiary alcohol products synthesized is underlined by representative stereospecific and chemoselective functionalizations to provide useful chemical fragments. Further mechanistic studies, application to multistep complex molecule syntheses, and the development of related stereoselective catalytic reactions are in progress.

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Keywords: asymmetric catalysis · boron · copper · enantioselectivity · reaction mechanisms

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[1] a) *Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis* (Eds.: J. Christoffers, A. Baro), Wiley-VCH, Weinheim, **2006**.

[2] For recent reviews on catalytic enantioselective additions to ketones, see: a) O. Riant, J. Hannedouche, *Org. Biomol. Chem.* **2007**, *5*, 873; b) M. Shibasaki, M. Kanai, *Chem. Rev.* **2008**, *108*, 2853–2873.

[3] For representative examples of catalytic enantioselective additions of sp^3-carbon-based nucleophiles to ketones, see: a) C. García, L. K. LaRochelle, P. J. Walsh, *J. Am. Chem. Soc.* **2002**, *124*, 10970–10971; b) E. F. DiMauro, M. C. Kozlowski, *J. Am. Chem. Soc.* **2002**, *124*, 12668–12669; c) K. Funabashi, M. Jachmann, M. Kanai, M. Shibasaki, *Angew. Chem. Int. Ed.* **2003**, *42*, 5489–5492; *Angew. Chem.* **2003**, *115*, 5647–5650; d) J. M. Betancort, C. García, P. J. Walsh, *Synlett* **2004**, *5*, 749–760; e) J. Siewert, R. Sandmann, P. von Zezschwitz, *Angew. Chem. Int. Ed.* **2007**, *46*, 7122–7124; *Angew. Chem.* **2007**, *119*, 7252–7254; f) M. Hatano, T. Miyamoto, K. Ishihara, *Org. Lett.* **2007**, *9*, 4535–4538; g) D. K. Friel, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2008**, *130*, 9942–9951; h) A. V. R. Madduri, S. R. Harutyunyan, A. J. Minnaard, *Angew. Chem. Int. Ed.* **2012**, *51*, 3164–3167; *Angew. Chem.* **2012**, *124*, 3218–3221; i) J. Rong, T. Pellegrini, S. R. Harutyunyan, *Chem. Eur. J.* **2016**, *22*, 3558–3570.

[4] a) S. M. Winbush, W. R. Roush, *Org. Lett.* **2010**, *12*, 4344–4347; b) T. P. Blaisdell, T. C. Caya, L. Zhang, A. Sanz-Marco, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 9264–9267; c) T. P. Blaisdell, J. P. Morken, *J. Am. Chem. Soc.* **2015**, *137*, 8712–8715; for a recent in direct approach to 1,2-hydroxyborons, see: d) D. Chen, X. Zhang, W.-Y. Qi, B. Xu, M.-H. Xu, *J. Am. Chem. Soc.* **2015**, *137*, 5268–5271.

[5] a) M. V. Joannou, B. S. Moyer, S. J. Meek, *J. Am. Chem. Soc.* **2015**, *137*, 6176–6179; b) M. V. Joannou, B. S. Moyer, M. J. Goldfogel, S. J. Meek, *Angew. Chem. Int. Ed.* **2015**, *54*, 14141–14145; *Angew. Chem.* **2015**, *127*, 14347–14351.

[6] a) P. Knochel, *J. Am. Chem. Soc.* **1990**, *112*, 7431 – 7433; b) M. Sakai, S. Saito, G. Kanai, A. Suzuki, N. Miyaura, *Tetrahedron* **1996**, *52*, 915 – 924.

[7] A. Pelter, S. Peverall, A. Pitchford, *Tetrahedron* **1996**, *52*, 1085 – 1094.

[8] a) K. Endo, T. Ohkubo, M. Hirokami, T. Shibata, *J. Am. Chem. Soc.* **2010**, *132*, 11033 – 11035; b) K. Endo, T. Ohkubo, T. Shibata, *Org. Lett.* **2011**, *13*, 3368 – 3371; c) K. Endo, T. Ohkubo, T. Ishioka, T. Shibata, *J. Org. Chem.* **2012**, *77*, 4826 – 4831; d) C. Sun, B. Potter, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 6534 – 6537; e) B. Potter, A. A. Szymaniak, E. K. Edelstein, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 17918 – 17921; f) K. Hong, X. Liu, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 10581 – 10584; g) J. R. Coombs, L. Zhang, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 16140 – 16143; h) H. Y. Sun, K. Kubota, D. G. Hall, *Chem. Eur. J.* **2015**, *21*, 1 – 10; i) J. Kim, S. Park, J. Park, S. H. Cho, *Angew. Chem. Int. Ed.* **2016**, *55*, 1498 – 1501; *Angew. Chem.* **2016**, *128*, 1520 – 1523; j) Y. Shi, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2016**, *55*, 3455 – 3458; *Angew. Chem.* **2016**, *128*, 3516 – 3519; k) Z.-Q. Zhang, B. Zhang, X. Lu, J.-H. Liu, X.-Y. Lu, B. Xiao, Y. Fu, *Org. Lett.* **2016**, *18*, 952 – 955; l) J. Park, Y. Lee, J. Kim, S. H. Cho, *Org. Lett.* **2016**, *18*, 1210 – 1213; m) M. Zhan, R.-Z. Li, Z.-D. Mou, C.-G. Cao, J. Liu, Y.-W. Chen, D. Niu, *ACS Catal.* **2016**, *6*, 3381 – 3386; for recent syntheses of 1,1-alkylbisboronate esters, see: n) Z.-Q. Zhang, C.-T. Yang, L.-J. Liang, B. Xiao, X. Lu, J.-H. Liu, Y.-Y. Sun, T. B. Marder, Y. Fu, *Org. Lett.* **2014**, *16*, 6342 – 6345; o) A. S. Batsanov, J. A. Cabeza, M. G. Crestani, M. R. Fructos, P. García-Álvarez, M. Gille, Z. Lin, T. B. Marder, *Angew. Chem. Int. Ed.* **2016**, *55*, 4707 – 4710; *Angew. Chem.* **2016**, *128*, 4785 – 4788; p) A. K. Cook, S. D. Schimler, A. J. Matzger, M. S. Sanford, *Science* **2016**, *351*, 1421 – 1424; q) K. T. Smith, S. Berritt, M. González-Moreiras, S. Ahn, M. R. Smith III, M.-H. Baik, D. J. Mindiola, *Science* **2016**, *351*, 1424 – 1427.

[9] Absolute configuration of the tertiary alcohol **6a** formed with (*R*)-MonoPhos is *R* (see the Supporting Information).

[10] Reactions run for 48 h at −25 °C did not lead to an increase in yield.

[11] Treatment of **4a** with 2 equivalents of LiO*t*Bu (no Cu or **L1**) at −10 °C for 2.5 h results in > 98 % conversion of **4a** and 90 % conversion to **6**. Treatment of **4a** with 2 equivalents of LiO*t*Bu, 5 mol % $[Cu(NCMe)_4]PF_6$, and 10 mol % **L1**) at −10 °C for 2.5 h results in > 98 % conversion of **4a** but only 70 % to **6**.

[12] For an example of copper(I)-catalyzed transesterification, see: C. Munro-Leighton, S. A. Delp, E. D. Blue, T. B. Gunnoe, *Organometallics* **2007**, *26*, 1483 – 1493.

[13] The decreased e.r. value is likely due to reaction with LiOEt.

[14] The lower enantioselectivity of **9b** is not due to partial racemization during purification. Re-subjection of **9b** to silica column chromatography affords **9b** in 85:15 e.r.

[15] Increasing the equivalents of LiO*t*Bu or decreasing the reaction temperature does not improve conversion into **10e**.

[16] For examples of stereoretentive reactions of organocopper alkyls, see: a) M. J. Campbell, J. S. Johnson, *Org. Lett.* **2007**, *9*, 1521 – 1524; b) Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 3160 – 3161; c) C. Zhong, S. Kunii, Y. Kosaka, M. Sawamura, H. Ito, *J. Am. Chem. Soc.* **2010**, *132*, 11440 – 11442; d) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2013**, *135*, 4934 – 4937; e) T. Jia, P. Cao, B. Wang, Y. Lou, X. Yin, M. Wang, J. Liao, *J. Am. Chem. Soc.* **2015**, *137*, 13760 – 13763; f) Y. Yang, S.-L. Shi, D. Niu, P. Liu, S. L. Buchwald, *Science* **2015**, *349*, 62 – 66; for stereoinvertive reactions of organocopper alkyls, see: g) Ref. [16c]; h) K. M. Logan, K. B. Smith, M. K. Brown, *Angew. Chem. Int. Ed.* **2015**, *54*, 5228 – 5231; *Angew. Chem.* **2015**, *127*, 5317 – 5320.

[17] Steric hindrance of the primary and secondary alkyl boronic esters likely inhibits reaction.

[18] S. J. Connon, S. Blechert, *Angew. Chem. Int. Ed.* **2003**, *42*, 1900 – 1923; *Angew. Chem.* **2003**, *115*, 1944 – 1968.

[19] S. Kumar, P. Kaur, A. Mittal, P. Singh, *Tetrahedron* **2006**, *62*, 4018 – 4026.

[20] 24 % unreacted benzophenone. The e.r. value was determined by conversion into the known corresponding diol (see the Supporting Information for details).

[21] Studies to elucidate the boron enantiotopic group-selectivity during transmetalation are ongoing.

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