Tetrahedron 68 (2012) 3444–3449

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Copper-catalyzed boration of activated alkynes. Chiral boranes via a one-pot copper-catalyzed boration and reduction protocol

Ho-Young Jung, Xinhui Feng, Hyohyun Kim, Jaesook Yun *

Department of Chemistry and Institute of Basic Science, Sungkyunkwan University, Suwon 440-746, Republic of Korea

ARTICLE INFO

Article history:
Received 3 June 2011
Received in revised form 7 July 2011
Accepted 21 July 2011
Available online 26 July 2011

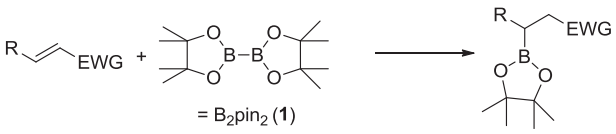
Keywords:
Boration
Conjugate reduction
Copper
Asymmetric synthesis
Vinylboronates

ABSTRACT

Phosphine–copper(I) complexes efficiently catalyzed the mono-boration of electron-deficient alkynes in the presence of MeOH and also catalyzed conjugate reductions of alkenylboronates bearing an electron-withdrawing group. The mono-addition of bis(pinacolato)diboron to alkynes catalyzed by a copper–Xantphos complex produced vinylboronates with high regio and stereoselectivity and asymmetric reduction of the vinylboronates by a chiral copper–bisphosphine catalyst allowed the synthesis of valuable chiral boranes with high enantioselectivity. One-pot boration/asymmetric reduction of α,β-unsaturated alkynoates could be conducted with a single copper–phosphine catalyst.

1. Introduction

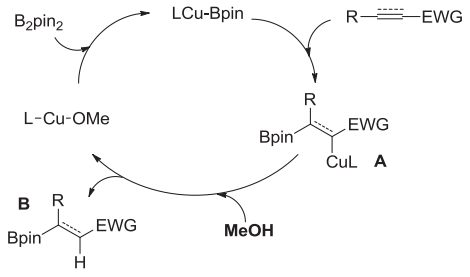
Transition-metal catalyzed boration reactions of unsaturated C–C bonds can provide a variety of organoboron compounds with high levels of regio- and stereocontrol.[1] In recent years, the transition metal-catalyzed addition of diboron reagents, such as bis(pinacolato)diboron (**1**) and bis(catecholato)diboron to electron-deficient C–C multiple bonds has received substantial amounts of attention as an efficient means to prepare functionalized organoboron compounds (Scheme 1).[2]



Scheme 1. β-Boration of α,β-unsaturated (C=C) carbonyl compounds.

Previously, we reported a new copper-catalytic system for the β-boration of various α,β-unsaurated (C=C) carbonyl compounds that included methanol as a reaction promoter.[3] The accelerant role of methanol could be explained by protonolysis of an organocopper intermediate (**A**) to provide a fast catalytic cycle (Scheme 2).[4] As a result of this reaction modification, the substrate scope was greatly extended from enones to less electrophilic ethylenic esters and nitriles.

Vinylboronates are versatile intermediates in organic synthesis,[5] and simple vinylboronates can be easily accessed by either conventional or metal-catalyzed hydroboration reactions of alkynes.[6] However, the preparation of electron-deficient vinylboronates[7] by the hydroboration approach is not trivial; only β-boryl acrylates are available by hydroboration of propiolic acid esters with alkylboranes,[8] thus further conversion using pinacolborane is necessary to obtain stable boronates, and a regioselectivity issue arises with alkynoates possessing a β-substituent.[9] Therefore, the development of a general and efficient method for these highly functionalized compounds is required. We were intrigued by the possibility of utilizing the catalytic mono-boronate addition to α,β-acetylenic (C≡C) substrates to obtain, formally 'hydroborated', β-boryl-α,β-ethylenic products (Scheme 2).[10]

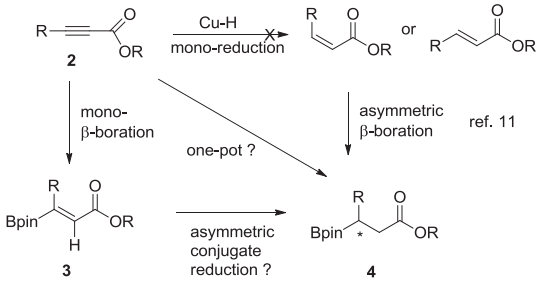


Scheme 2. Proposed catalytic cycle for the copper-catalyzed boration of β-substituted unsaturated carbonyl compounds in the presence of MeOH.

* Corresponding author. E-mail address: jaesook@skku.edu (J. Yun).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.07.061

In addition to the mono-boration of alkynes, further application of the resulting alkenylboronates (**3**) to the synthesis of chiral alkyl organoboron compounds (**4**) is delineated in Scheme 3. For the preparation of chiral boranes, the asymmetric β-boration of α,β-unsaturated carbonyl compounds has become a useful tool and several catalytic systems for asymmetric boration including copper-catalyzed β-borations introduced by our group have been developed.[4a,11] Alternatively, the same types of chiral alkyl organoboronates could be prepared by asymmetric reduction of alkenylboronates **3**.



Scheme 3. Synthetic approaches to chiral alkyl boronates.

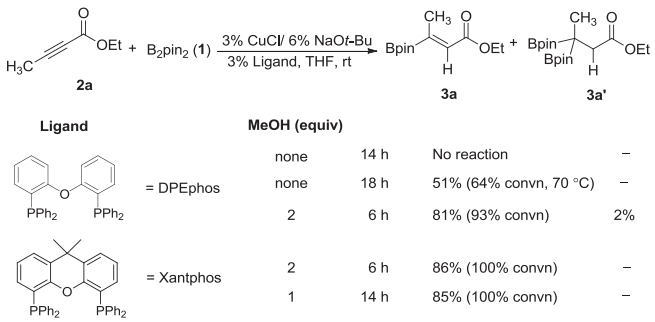
Copper hydride (CuH) catalysis has proven very efficient for conjugate reductions[12] of a variety of α,β-unsaturated substrates.[13] However, the asymmetric conjugate reduction of β-boryl-α,β-unsaturated carbonyl compounds (**3**) has not previously been reported. Since phosphine–copper complexes catalyze both boration and reduction reactions, we initially investigated the conjugate reduction of **3** and then the one-pot reaction to produce the chiral boron compounds **4** from the corresponding alkynes using a single copper-complex as catalyst. In this paper, we present details of our recent studies on these topics.

2. Results and discussion

2.1. Copper-catalyzed mono β-boration of alkynoates; synthesis of electron-deficient alkenylboronates

To check the feasibility of the proposed mono-boron addition approach, we chose ethyl 2-butynoate (**2a**) as a model substrate and DPEphos and Xantphos as ligands on the basis of their efficiency in the β-boration of ethyl crotonate.[3] By employing a catalytic amount of copper salt and ligand in the presence of 1.1 equiv of B_2pin_2 in THF, various reaction conditions were examined (Scheme 4). The reaction without the methanol additive showed no appreciable conversion at room temperature. A moderate conversion (64%) and yield were obtained with an increased reaction temperature(70 °C).

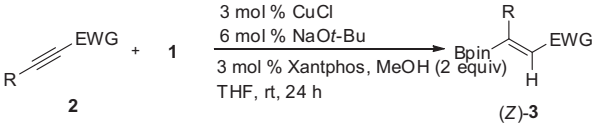
Fortunately, addition of methanol greatly enhanced the reaction rate, and the reactions with either DPEphos or Xantphos ligand proceeded in good conversion at room temperature to give exclusively the *syn* addition product, (*Z*)-**3a**. The Xantphos ligand performed better than the DPEphos ligand, since the latter ligand gave incomplete conversion with concurrent production of ~2% of the diboration product (**3a′**). The formation of **3a′** was even greater with another bidentate phosphine, dppf,[14] under otherwise identical conditions. Using more than 1.2 equiv of B_2pin_2 increased the formation of the diboration product even with the Xantphos ligand.

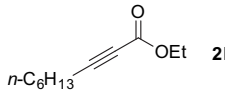
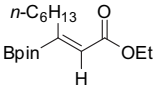
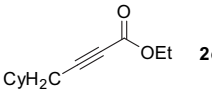
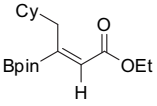
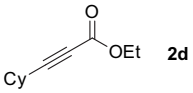
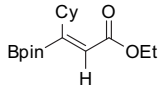
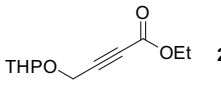
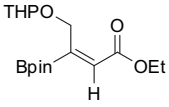
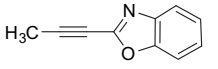
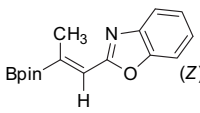
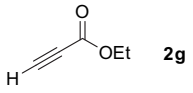
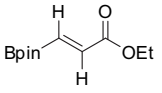
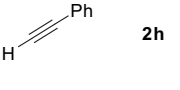
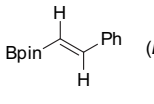
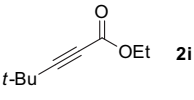


Scheme 4. Optimization.

With an optimal reaction protocol using 1.1 equiv of **1**, 2 equiv of MeOH, and Xantphos ligand, various α,β-alkynyl substrates were examined in the copper-catalyzed β-boration reaction (Table 1). Primary alkyl (**2b**, **2c**, **2e**) and secondary alkyl (**2d**) substituted acetylenic esters were smoothly converted within 24 h exclusively to the corresponding (*Z*)-vinylboronates. Alkyne substrates with benzoxazole (**2f**) or phenyl (**2h**) substitution as the electron-withdrawing group were also suitable substrates for the reaction, yielding addition products with high regio- and stereoselectivity. However, the reaction of ethyl propiolate **2g** furnished the *syn* addition product in 65% yield due to incomplete conversion. While

Table 1
Synthesis of vinylboronates via copper-catalyzed mono-boration of alkynes



Entry	Substrate (**2**)	Product (**3**)	Yield[a] (%)
1	 **2b**	 (*Z*)-**3b**	93
2	 **2c**	 (*Z*)-**3c**	88
3	 **2d**	 (*Z*)-**3d**	99
4[b]	 **2e**	 (*Z*)-**3e**	77
5	 **2f**	 (*Z*)-**3f**	82
6[c]	 **2g**	 (*E*)-**3g**	65
7[d]	 **2h**	 (*E*)-**3h**	99
8	 **2i**	(*Z*)-**3i** + (*E*)-**3i** (34 : 66)	71

[a] Isolated yield.
[b] (*Z*)-**3e**:protodeboronated product=87:13 by GC and NMR analysis.
[c] 90% Conversion.
[d] With DPEphos ligand instead of Xantphos ligand.

the examples shown in Table 1 are highly stereoselective, the *tert*-butyl substituted ester **2b** produced a mixture of (*E*)- and (*Z*)-isomers presumably as a result of equilibration of the copper–enolate intermediates[15] during the catalytic cycle.

Suitable levels of regioselective mono-boration could not be obtained for aryl-substituted alkynoates and alkynones under our reaction conditions, which employed a limited amount of bis(pinacolato)diboron (Fig. 1). Regioselectivity was problematic with aryl-substituted alkynoates and alkynones, and double boration was significant with active alkynones; thus reactions of these substrates furnished mixtures of organoboron products along with unreacted starting material.

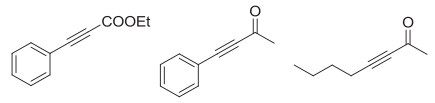
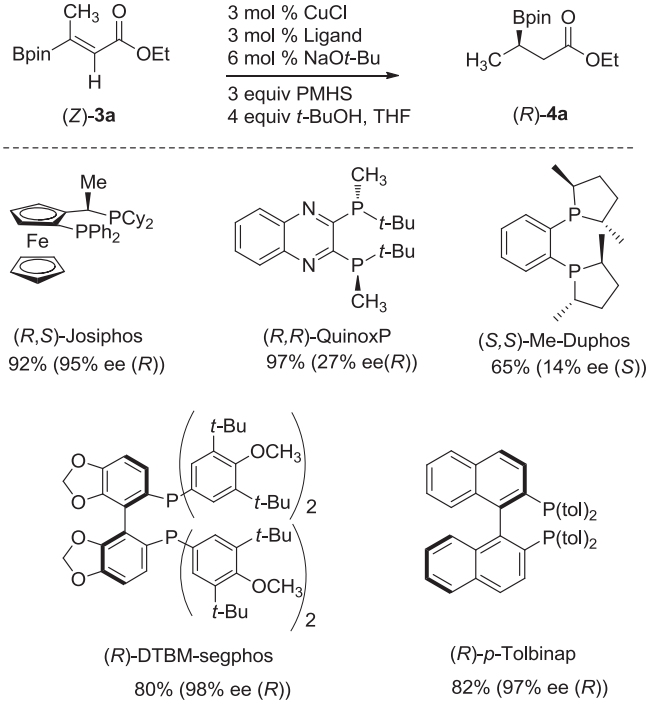


Fig. 1. Some of the unsuitable alkyne substrates for the copper-catalyzed β-boration with MeOH.

2.2. Copper-catalyzed conjugate reduction of alkenylboronates

Chiral boron compounds are valuable building blocks in organic synthesis. C–B bonds can be converted into a C–N or C–O functionality[5a,5d,16] with retention of configuration and their role in asymmetric C–C bond forming reactions[17] has seen a recent significant increase.

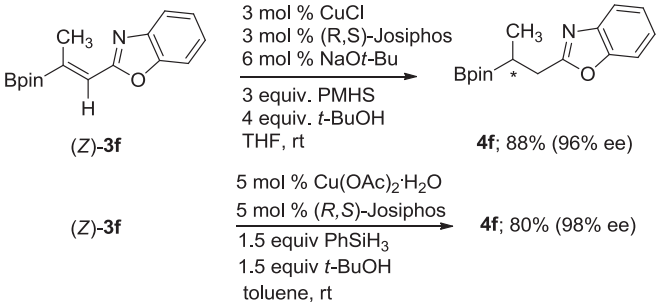
As described in Scheme 3, an alternative strategy for asymmetric β-boration is the conversion of β-borylated-α,β-unsaturated (C=C) carbonyl compounds to chiral boranes using a chiral CuH catalyst. While several asymmetric hydrogenations of vinylboronates using either Rh or Ir catalysts have been reported in the literature,[18] analogous CuH-catalyzed enantioselective reductions have not yet been reported. Starting materials in this investigation should be geometrically pure since the reduction of (*E*)- and (*Z*)-isomers would result in the formation of opposite enantiomers.[13]



Scheme 5. Results using representative chiral bisphosphine ligands with CuH.

Asymmetric hydrosilylations of vinylboronate (*Z*)-**3a** were conducted with an in situ generated catalyst by combining 3 mol % CuCl, 6 mol % NaO*t*-Bu, and 3 mol % ligand in THF, followed by the addition of polymethylhydrosiloxane (PMHS) and *t*-BuOH. Five representative chiral ligands were screened for their effectiveness, and the results are described in Scheme 5.

The enantiomeric excess and absolute stereochemistry of the product (**4a**) from each reaction were determined by converting it to the corresponding β-hydroxy ester by oxidation.[19] The conjugate reductions with (*R*,*R*)-QuinoxP or (*S*,*S*)-Me-Duphos as the ligand were not highly enantioselective for the model substrate, producing the product with only 27% ee and 14% ee, respectively. However, the Josiphos, DTBM-segphos, and *p*-Tolbinap ligands were very effective in forming the chiral boron product **4a** with excellent enantioselelctivities (>95% ee) in good yield. Next, we carried out the reduction of benzoxazole-substituted vinylboronate, (*Z*)-**3f** under the same catalytic conditions in THF using PMHS as the hydrosilane source. The reduction furnished the product **4f** in 96% ee. In comparison, the reaction using 5 mol % $Cu(OAc)_2 \cdot H_2O$ in the presence of $PhSiH_3$ as the stoichiometric reducing agent in toluene[20] gave a similar enantioselectivity, 98% ee (Scheme 6).



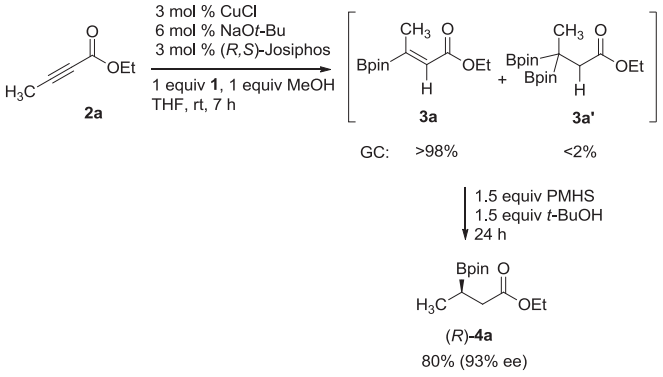
Scheme 6. CuH reductions of **3f**.

2.3. One-pot sequential β-boration/reduction reactions of alkynoates

The success of this reduction approach to prepare chiral boranes increased the likelihood of one-pot sequential β-boration and reduction reactions with a single copper-catalytic species. Since the copper-catalyzed boration produces geometrically pure vinylboronates, no chromatographic purification would be necessary for the subsequent CuH reduction.

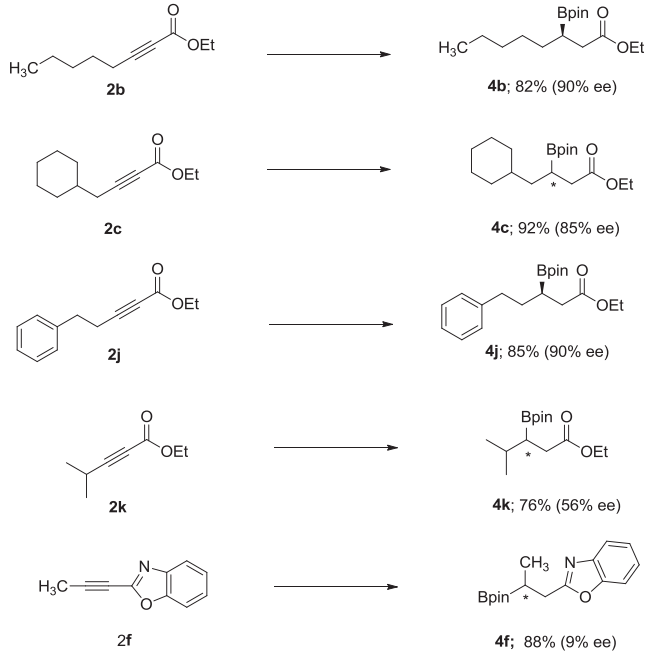
Nonetheless, chiral bisphosphine ligands have not been previously employed for the mono-boration of alkynoates, and thus, we next investigate the proper mono-boration conditions with the active bisphosphine ligands. Fortunately, with a limited amount of MeOH (1 equiv) and B_2pin_2 (1 equiv) in the presence of the Josiphos ligand, the reaction of ethyl 2-butynoate (**2a**) was complete in 7 h, and only a small amount of the diboration product (**3a′**) was detected by GC analysis. The following addition of 1.5 equiv of PMHS and *t*-BuOH to the reaction mixture furnished the desired reduction product in 80% overall yield with 93% enantioselectivity (Scheme 7). In an attempt to improve the selectivity of the boration and to simplify the addition sequence, we employed 4 equiv of *t*-BuOH instead of MeOH; however, only a low conversion of the starting material was observed. Neither the Me-Duphos nor DTBM-segphos ligands gave a good conversion in the second reduction step under these one-pot sequential reaction conditions.

More examples were examined using the chiral Josiphos ligand as the optimal ligand (Scheme 8). After the boration of alkynoates (**2**) was complete (12–24 h), subsequent addition of PMHS and



Scheme 7. One-pot boration/reduction of **2a**.

t-BuOH led to the formation of the desired chiral β-borylated esters **4**. The reaction of primary alkyl-substituted alkynoates (**2b**, **2c**, and **2j**) furnished the products in 24 h with good overall isolated yield and enantioselectivity. The secondary isopropyl substituted substrate **2k** gave a moderate enantioselectivity, reflecting the smaller steric difference between the β-substituents of the alkenylboron intermediates. However, the benzoxazole substituted alkyne **2f** did not proceed in good enantioselectivity in opposition to our expectation. It turned out that the first boration step with the Josiphos ligand gave a mixture of (*Z*) and (*E*)-isomers (56:43) in contrast to the Xantphos ligand, which afforded only the (*Z*)-isomer in a geometrically pure form (entry 5, Table 1).[21] Accordingly, this one-pot sequence is less appropriate for the benzoxazole alkyne than the separate procedures using two different copper catalystic systems with chromatographic separation of the intermediate vinylboronates.



Conditions: 3 mol % CuCl, 6 mol % NaO*t*-Bu, 3 mol % (*R*,*S*)-Josiphos, 1 equiv **1**, 1 equiv MeOH, THF, rt, 12–24 h; then1.5 equiv PMHS, 1.5 equiv *t*-BuOH, 12-24 h

Scheme 8.

3. Conclusions

In summary, we have shown that phosphine–copper(I) complexes efficiently catalyze the mono-boration of electron-deficient alkynes in the presence of MeOH to afford vinylboronates. A copper–Xantphos complex leads to the successful mono-addition of bis(pinacolato)diboron to active alkynes, such as α,β-unsaturated alkynoates with high regio- and stereoselectivity under mild reaction conditions. Copper-hydride catalyzed asymmetric reduction of the resulting vinylboronates has been carried out employing a chiral copper–bisphosphine catalyst, and the one-pot boration/asymmetric reduction of α,β-unsaturated alkynoates has been investigated with a single copper–phosphine catalyst. These reactions furnished valuable chiral boranes with high enantioselectivity.

4. Experimental section

4.1. General information

THF was distilled from sodium benzophenone ketyl under nitrogen. CuCl, NaO*t*-Bu, bis(pinacolato)diboron, and other commercial substrates were purchased from Aldrich and used as received. All reactions were carried out under nitrogen atmosphere, in an oven-dried Schlenk tube and run two or more times. Flash chromatography was performed on silica gel from Fuji Silysia Chemical (70–230 mesh). All ^{1}H NMR spectra were obtained on Varian Mercury 300 systems and reported in parts per million (ppm) downfield from tetramethylsilane. ^{13}C NMR spectra are reported in ppm referenced to deuteriochloroform (77.16 ppm). Infrared spectra (IR) were obtained on Nicolet FT-IR instrument and recorded in cm^{-1}. HPLC and GC analysis were performed on a Younglin Acme 9000 series and Younglin Acme 6000 Series. High resolution mass spectra (HRMS) were obtained at Korea Basic Science Institute (Daegu, Korea) and reported in the form of *m*/*z* (intensity relative to base peak=100). Optical rotations were measured with a Perkin–Elmer 343 plus Polarimeter.

4.2. General procedure for the mono β-boration of alkynoates

CuCl (1.5 mg, 0.015 mmol), NaO*t*-Bu (2.9 mg, 0.03 mmol), and Xantphos ligand (8.7 mg, 0.015 mmol) were placed in an oven-dried Schlenk tube under nitrogen and THF (0.45 mL) were added. The reaction mixture was stirred for 30 min at room temperature and then bis(pinacolato)diboron (127 mg, 0.5 mmol) in THF (0.3 mL) was added. The reaction mixture was stirred for 10 min and α,β-acetylenic ester **2** (0.5 mmol) was added, followed by MeOH (40 μL, 1 mmol). The reaction tube was washed with further THF (0.2 mL), sealed, and stirred until no starting material was detected by TLC. The reaction mixture was filtered through a pad of Celite and concentrated. The product was purified by silica gel chromatography.

*4.2.1. (Z)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (**3a**).* Yield (85%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.45 (1H, s), 4.18 (2H, q, J=6.9 Hz), 2.17 (3H, s), 1.30–1.20 (15H, m); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 166.0, 147.0 (C–B), 130.5, 84.0, 60.0, 24.7, 16.2, 14.2; EIMS *m*/*z* (rel intensity) 241 (M^+, 100), 195 (33), 111 (18).

*4.2.2. (Z)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-enoate (**3b**).* Yield (93%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (1H, s), 4.17 (2H, q, J=7.1 Hz), 2.66 (2H, t, J=7.2 Hz), 1.34–1.27 (23H, m), 0.87 (3H, t, J=6.6 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 165.9, 162.0 (C–B), 129.8, 84.0, 59.6, 31.8, 30.0, 29.6, 29.5, 24.7, 14.3, 14.1; EIMS *m*/*z* (rel

intensity) 311 (M^+, 32), 265 (14), 210 (100), 181 (56), 167 (33), 83 (13).

*4.2.3. (Z)-Ethyl 4-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (**3c**).* Yield (88%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.44 (1H, s), 4.16 (2H, q, J=7.2 Hz), 2.58 (2H, d, J=7.0 Hz), 1.72–1.40 (6H, m), 1.30–1.18 (5H, m), 1.27 (12H, s), 0.98 (3H, t, J=7.2 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 166.0, 151.7 (C–B), 130.4, 84.0, 59.8, 38.9, 37.2, 33.4, 26.6, 26.5, 24.7, 14.3; HRMS (EI^+) m/z calculated for $C_{18}H_{31}BO_4$: 322.2315, found: 322.2318.

*4.2.4. (Z)-Ethyl 3-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (**3d**).* Yield (99%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.24 (1H, s), 4.16 (2H, q, J=7.2 Hz), 1.74–1.65 (5H, m), 1.55–1.48 (6H, m), 1.30–1.25 (15H, m); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 166.1, 158.0 (C–B), 127.9, 83.9, 59.8, 40.0, 31.5, 26.4, 26.1, 24.8, 14.4; EIMS m/z (rel intensity) 309 (M^+, 12), 208 (100), 180 (32), 112 (13).

*4.2.5. (Z)-Ethyl 4-(tetrahydro-2H-pyran-2-yloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (**3e**).* Colorless oil, 77% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (1H, s), 4.81 (1H, dd, J=12.3, 2.1 Hz), 4.71–4.61 (2H, m), 4.17 (2H, q, J=7.2 Hz), 3.96–3.88 (1H, m), 3.57–3.47 (1H, m), 1.90–1.47 (6H, m), 1.42–1.24 (15H, m); irradiation of the vinylic proton at 6.29 ppm resulted in no enhancement of the allylic proton signal; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 165.6, 150.0 (C–B), 128.5, 98.2, 84.0, 65.7, 61.4, 60.1, 30.4, 25.5, 24.7, 19.0, 14.2; HRMS (EI^+) m/z calculated for $C_{17}H_{29}BO_6$: 340.2057, found: 340.2057.

*4.2.6. (Z)-2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-enyl)benzo[d]oxazol (**3f**).* Yellow solid, 82% yield; ν_{max} cm^{-1} 2977, 1200, 1080; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.72 (1H, m), 7.55–7.48 (1H, m), 7.34–7.30 (2H, m), 7.14 (1H, d, J=1.6 Hz), 2.42 (3H, d, J=1.6 Hz), 1.31 (12H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.4, 150.0, 142.0, 126.2, 125.3, 124.4, 120.3, 110.6, 84.2, 24.9, 17.3; HRMS (EI^+) m/z calculated for $C_{16}H_{20}BNO_3$: 285.1536, found: 285.1533.

*4.2.7. (E)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (**3g**).* Yield (65%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (1H, d, J=18.3 Hz), 6.62 (1H, d, J=18.3 Hz), 4.21 (2H, q, J=7.2 Hz), 1.35–1.24 (15H, m); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 166.0, 138.8, 134.1 (C–B), 84.1, 60.6, 24.8, 14.2; EIMS m/z (rel intensity) 227 (M^+, 100), 211 (42), 182 (11), 127 (6), 111 (31).

*4.2.8. (E)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane (**3h**).* Yield (99%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51–7.30 (6H, m), 6.17 (1H, d, J=18.3 Hz), 1.38–1.25 (12H, m); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 149.6, 137.4, 129.0, 128.6, 127.1, 116.2 (C–B), 83.3, 24.8; EIMS m/z (rel intensity) 230 (M^+, 47), 215 (21), 144 (100), 131 (23), 77 (6).

*4.2.9. (E)-Ethyl 4,4-dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-enoate (**3i**).* Yield (71%) ((*E*) and (*Z*)-isomer). The major (*E*)-isomer was characterized as the following; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.23 (1H, s), 4.17 (2H, q, J=7.2 Hz), 1.21–1.29 (24H, m); NOE measurement: irradiation of the vinylic proton at 6.23 ppm resulted in a 3.4% enhancement of the *tert*-butyl proton signal at 1.24 ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.9, 152.0 (C–B), 128.1, 83.7, 60.4, 36.1, 29.6, 25.0, 14.1; HRMS (EI^+) m/z calculated for $C_{15}H_{27}BO_4$: 288.2002, found: 288.2004.

4.3. General procedure for the copper-catalyzed conjugate reduction of alkenylboronates

A mixture of CuCl (1.2 mg, 0.012 mmol), NaO*t*-Bu (2.5 mg, 0.024 mmol), and (*R*,*S*)-Josiphos ligand (7.7 mg, 0.012 mmol) in anhydrous THF (0.5 mL) was stirred for 10 min in a Schlenk tube under an atmosphere of nitrogen. PMHS (72 μL, 1.2 mmol) was added to the reaction mixture and stirring was continued for 10 min at room temperature for catalyst activation. Alkenylboronate (0.5 mmol) was added, followed by *t*-BuOH (153 μL, 1.6 mmol). The reaction tube was washed with further THF (0.4 mL), sealed, and stirred for 24 h. The reaction mixture was quenched with aqueous ammonium chloride (1 mL) for 10 min. The aqueous layer was extracted with diethyl ether (3×5 mL) and the combined organic layers were dried over $MgSO_4$, and concentrated in vacuo. The product was purified by silica gel chromatography.

4.4. General procedure for the one-pot boration/reduction of α,β-acetylenic esters

CuCl (1.5 mg, 0.015 mmol), NaO*t*-Bu (2.9 mg, 0.03 mmol), and (*R*,*S*)-Josiphos ligand (9.6 mg, 0.015 mmol) were placed in an oven-dried Schlenk tube and THF (0.45 mL) were added under nitrogen. The reaction mixture was stirred for 30 min at room temperature and then, bis(pinacolato)diboron (127 mg, 0.5 mmol) and THF (0.3 mL) were added. The reaction mixture was stirred for 10 min and an alkyne (**2**) (0.5 mmol) was added, followed by MeOH (20 μL, 0.5 mmol). The reaction tube was washed with THF (0.2 mmol), sealed, and stirred until no starting material was detected by TLC or GC. PMHS (45 μL, 0.75 mmol) and *t*-BuOH (71.6 μL, 0.75 mmol) were added to the reaction mixture and stirring was continued. After completion, the reaction mixture was quenched with aqueous ammonium chloride (1 mL) and stirred for 10 min. The aqueous layer was extracted with diethyl ether (3×5 mL) and the combined organic layers were dried over $MgSO_4$, and concentrated in vacuo. The product was purified by silica gel chromatography.

*4.4.1. (R)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (**4a**).* Colorless oil, 80% yield; ν_{max} cm^{-1} 2979, 1730, 1200, 1140; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (2H, q, J=7.2 Hz), 2.40 (2H, t, J=7.8 Hz), 1.41–1.34 (1H, m), 1.27–1.22 (15H, m), 1.00 (3H, d, J=7.5 Hz); ^{13}C NMR (75.4 MHz) δ 173.9, 83.4, 60.4, 38.0, 25.1, 25.0, 15.5, 14.7, 13.8 (C–B); Enantiomeric excess and absolute configuration were determined with the corresponding acetate derivative of the β-hydroxy compound obtained by oxidation. 95% ee was determined by GC analysis on a Beta-Dex column; (*S*)-isomer t_R=30.3 min, (*R*)-isomer t_R=30.9 min. $[\alpha]_D^{20}$ +2.29 (*c* 0.1, $CHCl_3$) [lit.[22] $[\alpha]_D^{25}$ +2.9 (*c* 1.0, $CHCl_3$), 98% ee (*R*)].

*4.4.2. (R)-Ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octanoate (**4b**).* Colorless oil, 82% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14–4.06 (2H, m), 2.44–2.35 (2H, m), 1.46–1.22 (24H, m), 0.86 (3H, t, J=7.0 Hz); ^{13}C NMR (75.4 MHz) δ 174.2, 83.2, 60.3, 35.9, 32.1, 30.6, 28.5, 24.9, 24.8, 22.7, 14.4, 14.2; Enantiomeric excess and absolute configuration were determined with the corresponding β-hydroxy compound. 90% ee was determined by HPLC analysis on an OD-H column; (hexane/*i*-PrOH=95:5, λ=210 nm, 0.5 mL/min), (*R*)-isomer t_R=9.00 min, (*S*)-isomer t_R=9.67 min. $[\alpha]_D^{20}$ −22.0 (*c* 0.1, $CHCl_3$). [lit.[23] $[\alpha]_D^{24}$ −21 (*c* 0.99, $CHCl_3$) (*R*)].

*4.4.3. Ethyl 4-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (**4c**).* Colorless oil, 92% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11 (2H, q, J=7.2 Hz), 2.4 (2H, d, J=7.8 Hz), 1.79–1.58 (3H, m), 1.46 (1H, m), 1.28–1.18 (22H, m), 0.84 (3H, t, J=7.2 Hz); ^{13}C NMR (75.4 MHz $CDCl_3$) δ 174.1, 83.2, 60.3, 38.2, 37.2, 36.4, 33.3, 26.5, 25.8, 24.8, 24.0 14.4; HRMS (ESI^+) calculated for $C_{18}H_{33}BO_4$: 324.2472, found: 324.2475; Enantiomeric excess (85%) was determined by HPLC analysis on an OD-H column with the corresponding β-hydroxy compound; (hexane/*i*-PrOH=95:5, λ=210 nm, 0.5 mL/min),

major isomer t_R=8.8 min, minor isomer t_R=9.7 min. $[\alpha]_D^{20}$ −12.7 (*c* 0.54 $CHCl_3$).

*4.4.4. (R)-Ethyl 5-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (**4j**).* Colorless oil, 85% yield; ν_{max} cm^{-1} 2976, 1726, 1143; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.14 (5H, m), 4.11 (2H, q, *J*=7.2 Hz), 2.65 (2H, dd, *J*=7.2, 1.8 Hz), 2.46 (2H, dd, *J*=4.8, 3.6 Hz), 1.83–1.76 (1H, m), 1.70–1.60 (1H, m), 1.47–1.38 (1H, m), 1.29–1.19 (15H, m); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 173.9, 142.6, 128.5, 128.4, 125.8, 83.3, 60.3, 35.8, 35.2, 32.7, 25.0, 24.8, 19.9 (C–B), 14.4; HRMS (ESI^+) calculated for $C_{19}H_{29}BO_4$: 332.2159, found: 332.2162; Enantiomeric excess (90%) was determined by HPLC analysis on an OD-H column with the corresponding β-hydroxy compound; (hexane/*i*-PrOH=95:5, λ=254 nm, 0.5 mL/min), (*S*)-isomer t_R=18.0 min, (*R*)-isomer t_R=20.7 min. $[\alpha]_D^{20}$ −0.9 (*c* 0.8, $CHCl_3$) [lit.[24] $[\alpha]_D^{24}$ +1.3 (*c* 1.0, $CHCl_3$), 98% ee (*S*)].

*4.4.5. Ethyl 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (**4k**).* Colorless oil, 76% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 4.08 (2H, m), 2.45 (1H, dd, *J*=10.7, 5.7 Hz), 2.34 (1H, dd, *J*=10.8, 5.7 Hz), 1.80–1.69 (1H, m), 1.30–1.16 (16H, m), 0.91 (6H, q, 4.0 Hz); ^{13}C NMR (75.4 MHz $CDCl_3$) δ 174.4, 83.1, 60.2, 33.9, 29.2, 27.1, 24.9, 24.7, 22.9, 21.7 (C–B), 14.3; HRMS (ESI^+) calculated for $C_{14}H_{27}BO_4$: 270.2002, found: 270,1997; Enantiomeric excess (56%) was determined by GC Beta-Dex column and optical rotation was measured with the corresponding acetate derivative; minor isomer t_R=45.5 min, major isomer t_R=46.9 min. $[\alpha]_D^{20}$ −12.7 (*c* 0.54 $CHCl_3$).

*4.4.6. 2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)propyl) benzo[d]oxazole (**4f**).* Yellow oil, 86% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69–7.57 (1H, m), 7.50–7.36 (1H, m), 7.32–7.18 (2H, m), 3.06 (1H, dd, *J*=15.8, 7.5 Hz), 2.91 (1H, dd, *J*=15.8, 7.5 Hz), 1.72–1.63 (1H, m), 1.23 (6H, s), 1.21 (6H, s), 1.09 (3H, d, *J*=7.5 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 167.4, 150.8, 141.4, 124.2, 119.4, 110.2, 83.4, 31.7, 24.7, 24.6, 15.3; HRMS (ESI^+) calculated for $C_{16}H_{22}BNO_3$: 287.1693, found: 287.1694; Enantiomeric excess (9%) was determined by HPLC analysis on an OD-H column with the corresponding β-hydroxy compound; (hexane/*i*-PrOH=99:1, λ=254 nm, 0.5 mL/min), minor isomer t_R=24.9 min, major isomer t_R=26.7 min.

Acknowledgements

We thank the National Research Foundation for financial support (R01-2008-000-20332-0, NRF-20090085824 and NRF-20110009533). We are grateful to Solvias for a generous gift of (*R*,*S*)-Josiphos.

References and notes

1. For reviews, see: (a) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320–2354; (b) Irvine, G. J.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittell, G. R.; Wright, L. J. *Chem. Rev.* **1998**, *98*, 2685–2722; (c) *Contemporary Boron Chemistry*; Davison, M. G., Hughes, A. K., Marder, T. B., Wade, K., Eds.; RSC: 2000; (d) *Stereodirected Synthesis with Organoboranes*; Matteson, D. S., Ed.; Springer: 1995; (e) Suginome, M.; Matsuda, T.; Ohmura, T.; Seki, A.; Murakami, M. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, D. M. P., Eds.; Elsevier: 2007; Vol. 10, pp 725–787.
2. (a) Cu: Ito, H.; Yamanaka, H.; Tateiwa, J.-I.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821–6825; (b) Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47–53; (c) Gao, M.; Thorpe, S. B.; Santos, W. L. *Org. Lett.* **2009**, *11*, 3478–3481; (d) Chea, H.; Sim, H.-S.; Yun, J. *Bull. Korean Chem. Soc.* **2010**, *31*, 551–552; (e) Pt: Lawson, Y. G.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R. *Chem. Commun.* **1997**, 2051–2052; (f) Bell, N. J.; Cox, A. J.; Cameron, N. R.; Evans, J. S. O.; Marder, T. B.; Duin, M. A.; Elsevier, C. J.; Baucherel, X.; Tulloch, A. A. D.; Tooze, R. P. *Chem. Commun.* **2004**, 1854–1855; (g) Rh: Kabalka, G. W.; Das, B. C.; Das, S. *Tetrahedron Lett.* **2002**, *43*, 2323–2325; (h) Ni: Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 5031–5033; (i) NHC: Lee, K.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253–7255.
3. Mun, S.; Lee, J.-E.; Yun, J. *Org. Lett.* **2006**, *8*, 4887–4889.
4. For experimental evidence and related DFT calculations, see: (a) Sim, H.-S.; Feng, X.; Yun, J. *Chem.—Eur. J.* **2009**, *15*, 1939–1943; (b) Dang, L.; Lin, Z.; Marder, T. B. *Organometallics* **2008**, *27*, 4443–4454.
5. (a) Shade, R. E.; Hyde, A. M.; Olsen, J.-C.; Merlic, C. A. *J. Am. Chem. Soc.* **2010**, *132*, 1202–1203; (b) Wang, Q.; Finn, M. G. *Org. Lett.* **2000**, *2*, 4063–4065; (c) Jeon, S.-J.; Chen, Y. K.; Walsh, P. J. *Org. Lett.* **2005**, *7*, 1729–1732; (d) Hupe, E.; Marek, I.; Knochel, P. *Org. Lett.* **2002**, *4*, 2861–2863; (e) Schlüter, A. D. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 1533–1556; (f) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623–3658.
6. (a) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991; (b) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485; (c) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127–3128; (d) Pereira, S.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 3283–3286; (e) Wang, Y. D.; Kimball, G.; Prashad, A. S.; Wang, Y. *Tetrahedron Lett.* **2005**, *46*, 8777–8780; (f) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics* **1993**, *12*, 589–592.
7. A palladium-catalyzed cross coupling of diboron with vinyl triflates provides another route to electron-deficient vinylboronates, see: (a) Ishiyama, T.; Takagi, J.; Kamon, A.; Miyaura, N. *J. Organomet. Chem.* **2003**, *687*, 284–290; (b) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006.
8. (a) Negishi, E.-i.; Yoshida, T. *J. Am. Chem. Soc.* **1973**, *95*, 6837–6838; (b) Martinez-Fresneda, P.; Vaultier, M. *Tetrahedron Lett.* **1989**, *30*, 2929–2932.
9. Plamondon, J.; Snow, J. T.; Zweifel, G. *Organomet. Chem. Synth.* **1971**, *1*, 249–252.
10. Lee, J.-E.; Kwon, J.; Yun, J. *Chem. Commun.* **2009**, 5996–5998.
11. For asymmetric catalysis, (a) Cu: Lee, J.-E.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 145–147; (b) Chea, H.; Sim, H.-S.; Yun, J. *Adv. Synth. Catal.* **2009**, *351*, 855–858; (c) Feng, X.; Yun, J. *Chem. Commun.* **2009**, 6577–6579; (d) Feng, X.; Yun, J. *Chem.—Eur. J.* **2010**, *16*, 13609–13612; (e) Lillo, V.; Prieto, A.; Bonet, A.; Díaz-Requejo, M. M.; Ramírez, J.; Pérez, P. J.; Fernández, E. *Organometallics* **2009**, *28*, 659–662; (f) Chen, I.-H.; Yin, L.; Itano, W.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 11664–11665; (g) O'Brien, J. M.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630–10633; (h) Rh: Shiomi, T.; Adachi, T.; Toribatake, K.; Zhou, L.; Nishiyama, H. *Chem. Commun.* **2009**, 5987–5989; (i) Ni: Lillo, V.; Geier, M. J.; Westcott, S. A.; Fernández, E. *Org. Biomol. Chem.* **2009**, *7*, 4674–4676; (j) Phosphine: Bonet, A.; Gulyás, H.; Fernández, E. *Angew. Chem., Int. Ed.* **2010**, *49*, 5130–5134.
12. (a) Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473–9474; (b) Lipshutz, B. H.; Noson, K.; Chrisman, W. *J. Am. Chem. Soc.* **2001**, *123*, 12917–12918; (c) Czekelius, C.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4793–4795; (d) Lee, D.; Kim, D.; Yun, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2785–2787; (e) Yoo, K.; Kim, H.; Yun, J. *Chem.—Eur. J.* **2009**, *15*, 11134–11138; (f) Llamas, T.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 1–5; (g) Desrosiers, J.-N.; Charette, A. B. *Angew. Chem., Int. Ed.* **2007**, *46*, 5955–5957; (h) Deutsch, C.; Krause, N.; Lipshutz, B. H. *Chem. Rev.* **2008**, *108*, 2916–2927.
13. With an alkynoester, double reduction was reported to form the saturated ester derivative with CuH, see: Lipshutz, B. H. *Synlett* **2009**, 509–524.
14. Dppf=1,1-bis(diphenylphosphino)ferrocene. The ratio of **3a** and **3a′** was 77:23 in 90% conversion.
15. (a) Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851–1852; (b) For anti-addition examples in copper-mediate additions when *t*-Bu is involved: Gil, J. M.; Oh, D. Y. *J. Org. Chem.* **1999**, *64*, 2950–2953; (c) Kim, H. R.; Yun, J. *Chem. Commun.* **2011**, 2943–2945.
16. (a) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535–1551; (b) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695–4712.
17. (a) Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024–5025; (b) Ros, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 6289–6292; (c) Ohmura, T.; Awano, T.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 13191–13193; (d) Sandrock, D. L.; Jean-Gérard, L.; Chen, C.; Dreher, S. D.; Molander, G. A. *J. Am. Chem. Soc.* **2010**, *132*, 17108–17110.
18. (a) Ueda, M.; Saitoh, A.; Miyaura, N. *J. Organomet. Chem.* **2002**, *642*, 145–147; (b) Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415; (c) Paptchikhine, A.; Cheruku, P.; Engman, M.; Andersson, P. G. *Chem. Commun.* **2009**, 5996–5998; (d) Copper-catalyzed reduction of β-silylated enoates, see: Lipshutz, B. H.; Tanaka, N.; Taft, B. R.; Lee, C.-T. *Org. Lett.* **2006**, *8*, 1963–1966.
19. Farthing, C. N.; Marsden, S. P. *Tetrahedron Lett.* **2000**, *41*, 4235–4238.
20. (a) Rupnicki, L.; Saxena, A.; Lam, H. W. *J. Am. Chem. Soc.* **2009**, *131*, 10386–10387; (b) Lee, D.; Yun, J. *Tetrahedron Lett.* **2004**, *45*, 5415–5417.
21. For examples of ligand effect on the copper-catalyzed boron addition to internal aryl alkynes: Kim, H. R.; Jung, I. G.; Yoo, K.; Jang, K.; Lee, E. S.; Yun, J.; Son, S. U. *Chem. Commun.* **2010**, 758–760 see also Ref. 15c.
22. Shi, X.-X.; Shen, C.-L.; Yao, J.-Z.; Nie, L.-D.; Quan, N. *Tetrahedron: Asymmetry* **2010**, *21*, 277–284.
23. Nagai, K.; Doi, T.; Sekiguchi, T.; Namatame, L.; Sunazuka, T.; Tomoda, H.; Ōmura, S.; Takahashi, T. *J. Comb. Chem.* **2006**, *8*, 103–109.
24. Sumida, S.; Ohga, M.; Mitani, J.; Nokami, J. *J. Am. Chem. Soc.* **2000**, *122*, 1310–1313.