ORGANIC CHEMISTRY
FRONTIERS

RESEARCH ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Org. Chem. Front.*, 2014, **1**, 1116

Copper(I)-catalyzed enantioselective hydroboration of cyclopropenes: facile synthesis of optically active cyclopropylboronates†

Bing Tian,‡[a,b] Qiang Liu,‡[a,b] Xiaofeng Tong,[b] Ping Tian*[a] and Guo-Qiang Lin*[a]

Received 28th May 2014,
Accepted 5th September 2014

DOI: 10.1039/c4qo00157e

rsc.li/frontiers-organic

Copper(I)-catalyzed enantioselective hydroboration of 3-aryl substituted cyclopropene-3-carboxylate is described, providing chiral cyclopropylboronates with excellent enantioselectivities (89–95% ee) in moderate to high yields (55–86%). The non-directing effect of the ester group was observed, and the reaction proceeded with solely *trans*-selectivity. The chiral boronates could be conveniently converted into chiral 1,2-diaryl substituted cyclopropane derivatives.

Introduction

The chiral cyclopropane framework represents the smallest carbocycles existing in a wide range of naturally-occurring compounds,[1] chiral drugs, and insecticides, for instance, (+)-Coronatine,[2] Saxagliptin (Onglyza®),[3] EBC-219,[4] Milnacipran,[5] Deltamethrin,[6] and (+)-Tranylcypromine[7] (Fig. 1). These three-membered carbocycles, due to their unique structural and electronic properties, serve as extremely significant versatile building blocks in organic synthesis.[8] Thus, a few interesting and characteristic transformations have continually emerged.[9] Owing to their important biological activities and wide applications in organic chemistry, much attention has been paid to their efficient enantioselective syntheses.

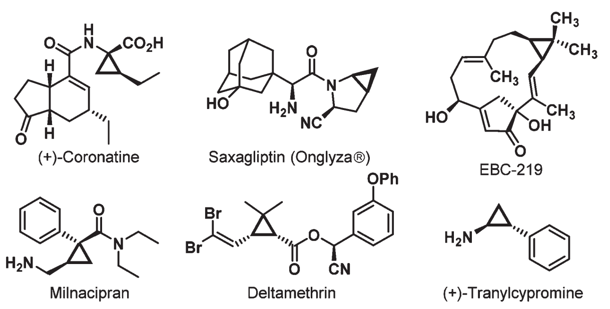
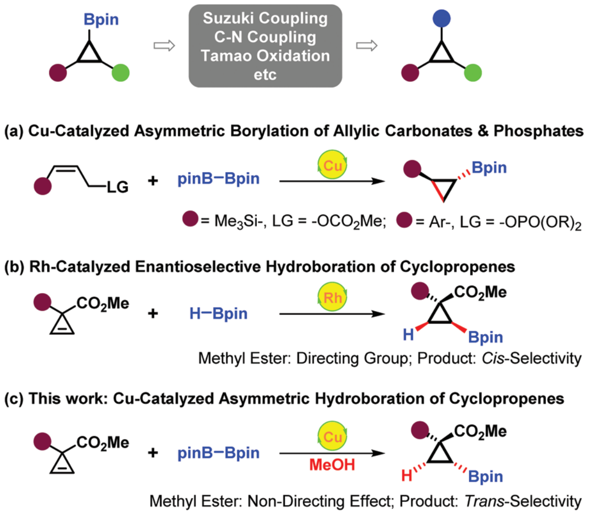

(+)-Coronatine
Saxagliptin (Onglyza®)
EBC-219
Milnacipran
Deltamethrin
(+)-Tranylcypromine

Fig. 1 Cyclopropane-containing natural products, chiral drugs and insecticides.

Through Suzuki–Miyaura coupling, C–N coupling, Tamao oxidation reaction, *etc.*, cyclopropylboronates could be readily converted into structurally and functionally diverse cyclopropanes.[10] Thus, efficient enantioselective synthesis of optically active cyclopropylboronates has gradually become a spotlight. Recently, Ito and co-workers successfully established copper(I)-catalyzed asymmetric cyclopropanation reactions of allylic phosphates and carbonates with bis(pinacolato)diboron (B_2pin_2), affording optically active *trans*-silyl- and *trans*-aryl-substituted cyclopropylboronates (Scheme 1a).[11,12] Gevorgyan


Bpin
Suzuki Coupling
C-N Coupling
Tamao Oxidation
etc
(a) Cu-Catalyzed Asymmetric Borylation of Allylic Carbonates & Phosphates
LG
pinB–Bpin
Cu
Bpin
● = Me3Si-, LG = -OCO2Me; ● = Ar-, LG = -OPO(OR)2
(b) Rh-Catalyzed Enantioselective Hydroboration of Cyclopropenes
CO2Me
H–Bpin
Rh
CO2Me
H
Bpin
Methyl Ester: Directing Group; Product: Cis-Selectivity
(c) This work: Cu-Catalyzed Asymmetric Hydroboration of Cyclopropenes
CO2Me
pinB–Bpin
Cu
MeOH
CO2Me
H
Bpin
Methyl Ester: Non-Directing Effect; Product: Trans-Selectivity

Scheme 1 Enantioselective synthesis of optically active cyclopropylboronates.

---

[a] *Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China. E-mail: tianping@sioc.ac.cn, lingq@sioc.ac.cn; Tel: (+86) 21-54925081*

[b] *Shanghai Key Laboratory of Functional Materials Chemistry, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China*

† Electronic supplementary information (ESI) available: Preparation of substrates, characterization data, ^{1}H, ^{13}C NMR, MS and IR spectra. CCDC 1004894. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4qo00157e

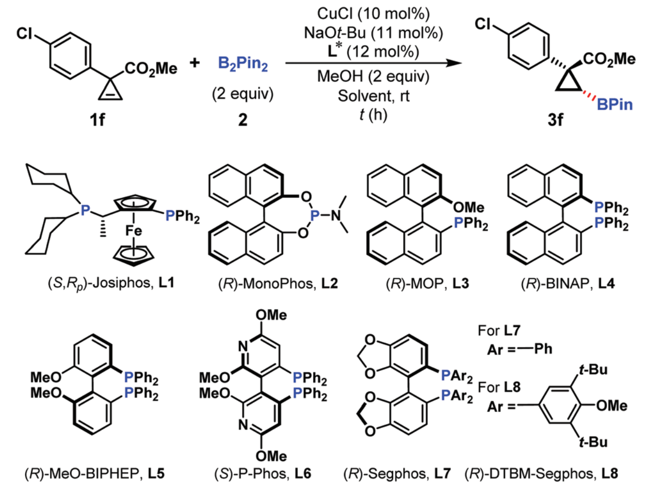
‡ These authors contributed equally to this work.

and co-workers described rhodium-catalyzed asymmetric hydroboration of 3,3-disubstituted cyclopropenes, directly constructing enantiopure 2,2-disubstituted cyclopropylboronates. The directing effect of the ester group was found to be necessary for achieving *cis*-selectivity and high enantioselectivity (Scheme 1b).[13,14] Herein, we present our findings in copper(I)-catalyzed asymmetric hydroboration of 3,3-disubstituted cyclopropenes.[15] Interestingly, the non-directing effect of the ester group was observed in this case, and the reaction proceeded with solely *trans*-selectivity (Scheme 1c).

Results and discussion

At the outset, a set of representative chiral phosphorus ligands were investigated for the Cu-catalyzed asymmetric hydroboration of the cyclopropene substrate **1f**, and the screening results are summarized in Table 1. The chiral bisphosphine ligand, (R,S_p)-Josiphos (**L1**), has been successfully employed in the Cu-catalyzed asymmetric conjugate hydroboration reaction of α,β-unsaturated compounds.[16] However, only 62% yield and 40% ee were observed in our hydroboration (Table 1, entry 1). Phosphoramidite ((*R*)-MonoPhos, **L2**)[17] and (*R*)-MOP (**L3**) ligands were subsequently subjected to this reaction, but no promising outcomes were obtained (Table 1, entries 2 and 3). To our delight, the ligand (*R*)-BINAP (**L4**) could dramatically improve the yield and ee of hydroboration product **3f** to 75% and 94%, respectively (Table 1, entry 4). Several electronically different bisphosphine ligands (**L5–L8**) were applied in this reaction, but no better results were achieved (Table 1, entries 5–8).

Table 1 Initial evaluation of various ligands and solvents[a]


Cl
CO$_2$Me
1f
+
B$_2$Pin$_2$
(2 equiv)
2
CuCl (10 mol%)
NaO*t*-Bu (11 mol%)
L* (12 mol%)
MeOH (2 equiv)
Solvent, rt
t (h)
Cl
CO$_2$Me
BPin
3f
P
PPh$_2$
Fe
(S,R_p)-Josiphos, L1
O
P–N
O
(*R*)-MonoPhos, L2
OMe
PPh$_2$
(*R*)-MOP, L3
PPh$_2$
PPh$_2$
(*R*)-BINAP, L4
MeO
MeO
PPh$_2$
PPh$_2$
(*R*)-MeO-BIPHEP, L5
OMe
N
MeO
MeO
N
OMe
PPh$_2$
PPh$_2$
(*S*)-P-Phos, L6
PAr$_2$
PAr$_2$
For L7
Ar = —Ph
For L8
Ar =
t-Bu
OMe
t-Bu
(*R*)-Segphos, L7
(*R*)-DTBM-Segphos, L8

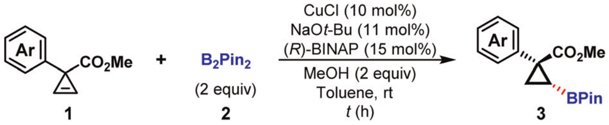
Entry	L*	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	**L1**	Toluene	6	62	40
2	**L2**	Toluene	8	16	22
3	**L3**	Toluene	8	30	51
4	**L4**	Toluene	6	75	94
5	**L5**	Toluene	8	58	93
6	**L6**	Toluene	10	85	−89
7	**L7**	Toluene	12	60	93
8	**L8**	Toluene	16	40	79
9[d]	**L4**	Toluene	24	46	90
10	**L4**	THF	6	44	84
11	**L4**	DCM	6	32	94
12[e]	**L4**	Toluene	6	80	95
13[f]	**L4**	Toluene	6	78	94

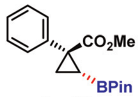
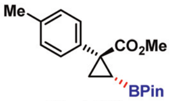
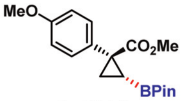
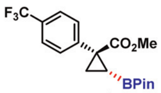
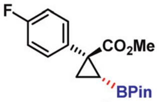
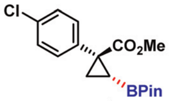
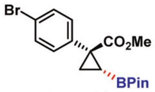
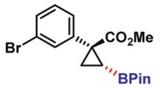
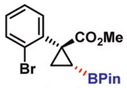
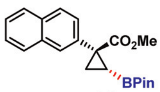
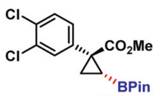
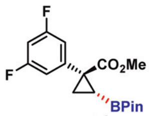
[a] The reaction was carried out with **1f** (0.15 mmol), B_2Pin_2 (**2**, 0.3 mmol), CuCl (10 mol%), chiral ligand (**L***, 12 mol%) and NaO*t*Bu (11 mol%) in anhydrous toluene (1.0 mL) at room temperature under a N_2 atmosphere, unless otherwise noted. [b] Yield of the isolated product. [c] Determined by HPLC analysis using a chiral stationary phase. [d] At 0 °C. [e] **L4** (15 mol%) was used. [f] **L4** (20 mol %) was used. B_2Pin_2 = bis(pinacolato)diboron.

Next, the reaction temperature and the solvent were investigated to further improve the enantioselectivity. Unfortunately, they led to different levels of erosion in yields and ee values (Table 1, entries 9–11). Increasing the ligand loading to 15 mol% resulted in a slight improvement of both yield and ee values (Table 1, entry 12). However, further increasing the ligand loading failed to give better results (Table 1, entry 13).

With the optimal reaction conditions identified, various aryl-substituted cyclopropenes were investigated, and the results are summarized in Table 2. All 4-substituted phenyl substrates, regardless of the electron-donating or electron-

Table 2 Substrate scope of various aryl-substituted cyclopropenes[a]


Ar
CO$_2$Me
1
+
B$_2$Pin$_2$
(2 equiv)
2
CuCl (10 mol%)
NaO*t*-Bu (11 mol%)
(*R*)-BINAP (15 mol%)
MeOH (2 equiv)
Toluene, rt
t (h)
Ar
CO$_2$Me
BPin
3

Entry	Product	Result
1		**3a**, 8 h[b] 66%,[c] 94% *ee*[d]
2		**3b**, 10 h[b] 55%,[c] 94% *ee*[d]
3		**3c**, 12 h[b] 58%,[c] 93% *ee*[d]
4		**3d**, 3 h[b] 86%,[c] 92% *ee*[d]
5		**3e**, 3 h[b] 83%,[c] 95% *ee*[d]
6		**3f**, 6 h[b] 80%,[c] 95% *ee*[d]
7		**3g**, 5 h[b] 75%,[c] 89% *ee*[d]
8		**3h**, 5 h[b] 77%,[c] 93% *ee*[d]
9		**3i**, 5 h[b] 74%,[c] 94% *ee*[d]
10		**3j**, 16 h[b] 59%,[c] 92% *ee*[d]
11		**3k**, 6 h[b] 78%,[c] 92% *ee*[d]
12		**3m**, 3 h[b] 83%,[c] 93% *ee*[d]

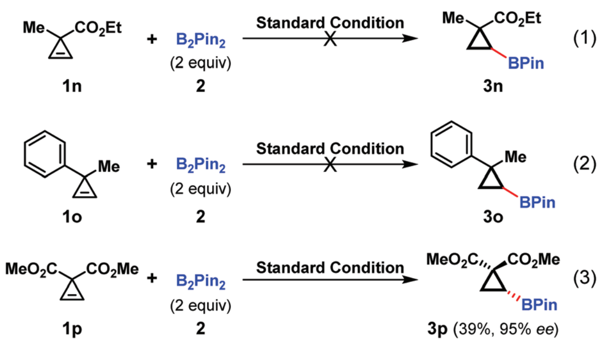
[a] The reaction was carried out with **1** (0.15 mmol), B_2Pin_2 (**2**, 0.3 mmol), CuCl (10 mol%), (*R*)-BINAP (**L4**, 15 mol%) and NaO*t*Bu (11 mol%) in anhydrous toluene (1.0 mL) at room temperature under a N_2 atmosphere. [b] Reaction time. [c] Yield of the isolated product. [d] Determined by HPLC analysis using a chiral stationary phase.

withdrawing properties of the substituent at the phenyl ring, afforded the hydroboration products in moderate to high yields (55–86%) and with high to excellent enantioselectivities (89–95% ee, Table 2, entries 1–7). Interestingly, *p*-, *m*-, and *o*-bromophenyl substituted cyclopropene substrates (**1g**, **1h**, and **1i**) gave almost the same yields with high to excellent levels of enantioselectivities (Table 2, entries 7–9). As for 2-naphthyl and disubstituted phenyl substrates, the hydroboration reaction also proceeded smoothly with high yields and excellent enantioselectivities (Table 2, entries 10–12). In general, cyclopropene substrates bearing electron-withdrawing phenyl substituents provided better yields (Table 2, entries 1–3 *vs.* 4–6, 12).

Given the highly enantioselective nature of this hydroboration reaction, the methyl substituted substrates **1n** and **1o** were tested under the standard conditions. Unfortunately, no desired products were observed, indicating that the α-substituent played an important role in the cyclopropene reactivity (Scheme 2, eqn (1) and (2)). As for the diester substrate **1p**, the hydroboration reaction readily occurred with excellent enantioselectivity, albeit in a lower yield. This was partially attributed to the decomposition of the starting material (Scheme 2, eqn (3)).

The relative configuration of hydroboration products **3** was determined using NOE interactions; for example, the NOE interactions between the aryl group and the boronate group in **3g** and **3j** clearly revealed that both of them were on the same side of the cyclopropane plane (Fig. 2). Thus *trans*-cyclopropylboronates were achieved in this Cu(I)-catalyzed asymmetric hydroboration of cyclopropenes.

To determine the absolute configurations of the hydroboration product **3a** in Table 2,[18] we converted cyclopropylboronate **3a**, through Suzuki–Miyaura coupling with iodobenzene (**4**), into a known compound (1*R*,2*S*)-**5** in almost quantitative yield with no loss of the enantiomeric excess.[19] Thus, the absolute configuration of cyclopropylboronate **3a** was unambiguously assigned as 1*R*,2*R*. The absolute configurations of other hydroboration products in Table 2 were assigned on the basis of their chemical correlation with (1*R*,2*R*)-**3a** (Scheme 3).


Me
CO2Et
+
B2Pin2
(2 equiv)
Standard Condition
Me
CO2Et
BPin
(1)
1n
2
3n
Me
+
B2Pin2
(2 equiv)
Standard Condition
Me
BPin
(2)
1o
2
3o
MeO2C
CO2Me
+
B2Pin2
(2 equiv)
Standard Condition
MeO2C
CO2Me
BPin
(3)
1p
2
3p (39%, 95% ee)

Scheme 2 Cu-catalyzed asymmetric hydroboration of cyclopropenes **1n**, **1o** and **1p**.

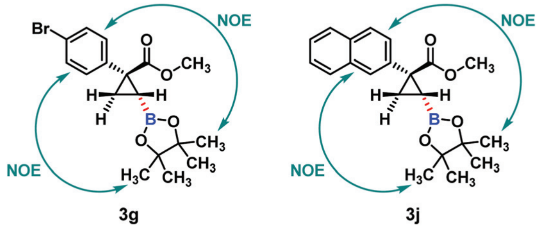
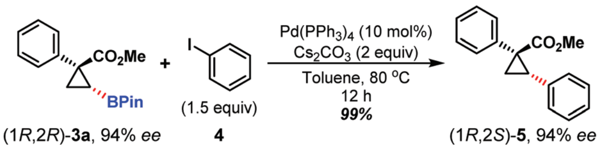

Br
NOE
O
O
CH3
H
H
H
B
O
O
CH3
CH3
H3C
CH3
NOE
3g
NOE
O
O
CH3
H
H
H
B
O
O
CH3
CH3
H3C
CH3
NOE
3j

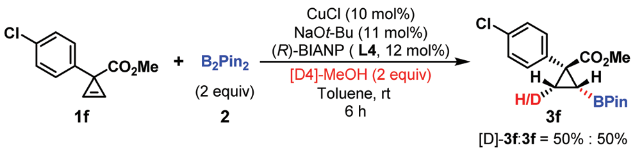
Fig. 2 The NOE interactions between the aryl group and the boronate group in **3g** and **3j**.

To probe the 'hydrogen' source of this hydroboration reaction, [D4]-methanol experiment was investigated. *cis*-Deuterated product **3a** (50%) was observed, suggesting that the proton partially came from methanol and this hydroboration reaction was a *syn*-addition process (Scheme 4).

Piecing together the above details and preceding results,[20] a plausible reaction mechanism is proposed in Fig. 3. Initiation of the reaction through the transmetallation of a (pinacolato)boron group (BPin) from boron to copper species **A** generated the borylated copper **B**, which subsequently underwent *syn*-addition from the aryl group side[21] to the double bond of the cyclopropene substrate **1** to afford the borylated cyclopropyl-copper intermediate **D**. The intermediate **D**


CO2Me
BPin
+
I
Pd(PPh3)4 (10 mol%)
Cs2CO3 (2 equiv)
Toluene, 80 °C
12 h
99%
CO2Me
(1R,2R)-3a, 94% ee
(1.5 equiv)
4
(1R,2S)-5, 94% ee

Scheme 3 Determining the absolute configuration of cyclopropylboronate **3a**.


Cl
CO2Me
+
B2Pin2
(2 equiv)
CuCl (10 mol%)
NaOt-Bu (11 mol%)
(R)-BIANP (L4, 12 mol%)
[D4]-MeOH (2 equiv)
Toluene, rt
6 h
Cl
CO2Me
H
H
H/D
BPin
1f
2
3f
[D]-3f:3f = 50% : 50%

Scheme 4 [D4]-Methanol experiment.

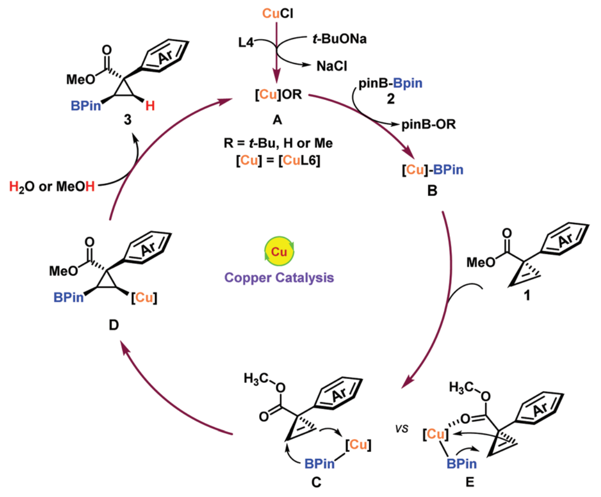

CuCl
L4
t-BuONa
NaCl
[Cu]OR
A
R = t-Bu, H or Me
[Cu] = [CuL6]
pinB-Bpin
2
pinB-OR
[Cu]-BPin
B
MeO
O
Ar
1
H3C
O
O
Ar
BPin
[Cu]
C
vs
H3C
O
[Cu]
O
Ar
BPin
E
MeO
O
Ar
BPin
[Cu]
D
H2O or MeOH
MeO
O
Ar
BPin
H
3
Cu
Copper Catalysis

Fig. 3 Proposed mechanism.

was readily protonated by trace water or methanol to regenerate **A** and liberate the *trans*-product **3**. Due to the bigger steric hindrance of the methyl ester group (**C** *vs.* **E**), the weak coordination between copper and carboxyl groups could not overcome this energy barrier. Therefore, the *cis*-product was not observed.

Conclusions

In summary, copper-catalyzed asymmetric hydroboration reaction of 3-aryl, 3-methylester substituted cyclopropenes has been successfully established. This reaction proceeded smoothly at room temperature, affording optically active *trans*-cyclopropylboronates with excellent enantioselectivities (89–95% ee) in moderate to high yields (55–86%). The non-directing effect of the methylester group was observed and this method was actually complimentary to the earlier reported *cis*-borylated cyclopropane products through rhodium catalysis. The chiral boronates could be readily transformed to chiral 1,2-diaryl substituted cyclopropanes through Suzuki–Miyaura coupling reaction. Further studies on the applications of cyclopropylboronates are in progress in our laboratories.

Experimental section

General information

All solvents were dried before use by following the standard procedures. Unless otherwise indicated, all starting materials purchased from commercial suppliers were used without further purification. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 400 MHz in the indicated solvents. Chemical shifts are reported in δ (ppm) referenced to the internal standard TMS for ^{1}H NMR and to $CDCl_3$ (δ = 77.10 ppm) for ^{13}C NMR. Coupling constants (*J*) are quoted in Hz. Optical rotations were measured on a JASCO P-1030 polarimeter. IR spectra were recorded on a Nicolet iN 10 MX. ESI mass spectra were recorded on an Agilent 1200/G6100A. HRMS of boron-containing compounds is based on ^{10}B. For the preparation of substrates **4a**, see the ESI.†

General procedure for Cu-catalyzed hydroboration of 3,3-disubstituted cyclopropenes

A dried Schlenk flask was charged with CuCl (1.5 mg, 0.015 mmol, 10 mol%), (*R*)-(+)-BINAP (14 mg, 0.0225 mmol, 15 mol%), B_2pin_2 (**2**, 76.2 mg, 0.3 mmol, 2.0 equiv.), NaO*t*Bu (1.6 mg, 0.0165 mmol, 11 mol%) and anhydrous toluene (1.0 mL) under a nitrogen atmosphere. After the mixture was stirred at room temperature for 40 min, a solution of cyclopropene **1** (0.15 mmol) in anhydrous toluene (0.5 mL) was added, followed by anhydrous MeOH (12.2 μL, 0.30 mmol, 2.0 equiv.). The resulting mixture was stirred at room temperature for the time indicated in Table 2, then filtered through Celite®, and concentrated *in vacuo*. The residue was purified by silica gel (300–400 mesh) column chromatography using hexane–ethyl acetate (15 : 1) as an eluent to afford the desired product **3**.

(1*R*,2*R*)-Methyl 1-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3a). Colorless oil. 29.9 mg, 66% yield. $[\alpha]_D^{28}$ −206.8 (*c* 1.0, $CHCl_3$) for 94% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35–7.21 (m, 5H), 3.60 (s, 3H), 1.70 (dd, *J* = 10.4 Hz, 3.2 Hz, 1H), 1.62 (dd, *J* = 8.0 Hz, 3.2 Hz, 1H), 1.28 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H), 1.05 (s, 6H), 0.82 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 174.96, 137.76, 131.17 (2C), 127.87 (2C), 127.15, 83.37 (2C), 52.56, 33.83, 24.89 (2C), 24.44 (2C), 18.78. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 325.1; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{23}{}^{10}BO_4Na^{\oplus}$ 324.1618, found 324.1614; IR (KBr) ν (cm^{-1}) 3451, 3086, 3047, 3027, 2979, 2954, 1961, 1726, 1602, 1429, 1372, 1264, 1166, 1142, 1062, 971, 858, 733, 698, 637, 503; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 6.4 min (*R*,*R*-isomer), 8.2 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-*p*-tolylcyclopropanecarboxylate (3b). Colorless oil. 26.1 mg, 55% yield. $[\alpha]_D^{26}$ −158.5 (*c* 1.0, $CHCl_3$) for 94% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.30–7.21 (m, 2H), 7.07 (d, *J* = 7.6 Hz, 2H), 3.60 (s, 3H), 2.31 (s, 3H), 1.68 (dd, *J* = 10.0 Hz, 3.2 Hz, 1H), 1.58 (dd, *J* = 8.4 Hz, 3.2 Hz, 1H), 1.32–1.20 (m, 1H), 1.06 (s, 6H), 0.84 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.16, 136.74, 134.74, 131.01 (2C), 128.56 (2C), 83.37 (2C), 52.58, 33.43, 24.89 (2C), 24.45 (2C), 21.21, 18.86. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 339.2; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{18}H_{25}{}^{10}BO_4Na^{\oplus}$ 338.1774, found 338.1758; IR (KBr) ν (cm^{-1}) 2978, 2951, 2924, 1723, 1515, 1436, 1410, 1371, 1329, 1285, 1263, 1215, 1165, 1142, 963, 858, 821, 751, 583, 504; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 6.7 min (*R*,*R*-isomer), 7.8 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(4-methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3c). Colorless oil. 28.9 mg, 58% yield. $[\alpha]_D^{26}$ −190.1 (*c* 1.0, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.25 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H), 3.60 (s, 3H), 1.69 (dd, *J* = 10.0 Hz, 3.2 Hz, 1H), 1.57 (dd, *J* = 8.0 Hz, 3.2 Hz, 1H), 1.24 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H), 1.07 (s, 6H), 0.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.08, 158.65, 132.08 (2C), 129.95, 113.20 (2C), 83.26 (2C), 55.26, 52.42, 32.93, 24.87 (2C), 24.36 (2C), 18.62. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + H]^{\oplus}$ 333.3; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{18}H_{25}{}^{10}BO_5Na^{\oplus}$ 354.1724, found 354.1729; IR (KBr) ν (cm^{-1}) 3542, 2979, 2952, 2837, 1723, 1614, 1582, 1517, 1440, 1409, 1331, 1264, 1247, 1165, 1143, 1034, 858, 834, 689, 548; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 9.6 min (*R*,*R*-isomer), 12.4 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(4-(trifluoromethyl)phenyl)cyclopropanecarboxylate (3d). White semisolid. 47.7 mg, 86% yield. $[\alpha]_D^{25}$ −128.2 (*c* 1.0,

$CHCl_3$) for 92% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.54 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 3.62 (s, 3H), 1.76 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.64 (dd, J = 8.4 Hz, 3.2 Hz, 1H), 1.31 (dd, J = 10.0 Hz, 8.4 Hz, 1H), 1.04 (s, 6H), 0.81 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.13, 142.00, 131.58 (2C), 129.45, 124.79 (q, J_{CF} = 3.5 Hz, 2C), 83.54 (2C), 52.68, 33.69, 24.77 (2C), 24.38 (2C), 18.82. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) EI-MS, 370 ($M.^{\oplus}$), 355 ($M^{\oplus} - CH_3$), 312 ($M^{\oplus} - CO_2CH_3$). HRMS (FTMS-EI) calcd for $C_{18}H_{22}{}^{10}BF_3O_4$ ($M.^{\oplus}$) 369.1600, found 369.1597; IR (KBr) ν (cm^{-1}) 3430, 2980, 1726, 1607, 1514, 1437, 1372, 1332, 1287, 1263, 1223, 1165, 1143, 1102, 971, 858, 837, 689, 579, 543; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 99/1; flow rate = 1.0 mL min^{-1}; retention time: 5.4 min (*R*,*R*-isomer), 7.4 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(4-fluorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3e). White semisolid. 39.8 mg, 83% yield. $[\alpha]_D^{26}$ −163.0 (*c* 1.0, $CHCl_3$) for 95% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.32–7.28 (m, 2H), 7.00–6.92 (m, 2H), 3.60 (s, 3H), 1.72 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.58 (dd, J = 8.0 Hz, 3.2 Hz, 1H), 1.26 (dd, J = 10.0 Hz, 8.0 Hz, 1H), 1.07 (s, 6H), 0.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.61, 161.92 (d, J_{CF} = 244.4 Hz), 160.70, 133.61 (d, J_{CF} = 3.0 Hz), 132.66 (d, J_{CF} = 8.4 Hz, 2C), 114.56 (d, J_{CF} = 21.3 Hz, 2C), 83.36 (2C), 52.46, 33.01, 24.81 (2C), 24.34 (2C), 18.86. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + H]^{\oplus}$ 321.0; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{22}{}^{10}BFO_4Na^{\oplus}$ 342.1524, found 342.1519; IR (KBr) ν (cm^{-1}) 2983, 1960, 1720, 1618, 1430, 1392, 1382, 1327, 1296, 1268, 1165, 1141, 1115, 1064, 1018, 877, 837, 765, 608; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 4.5 min (*R*,*R*-isomer), 5.9 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(4-chlorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3f). White semisolid. 40.3 mg, 80% yield. $[\alpha]_D^{26}$ −175.7 (*c* 1.0, $CHCl_3$) for 95% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.29–7.23 (m, 4H), 3.60 (s, 3H), 1.72 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.57 (dd, J = 8.0 Hz, 3.2 Hz, 1H), 1.27 (dd, J = 10.0 Hz, 8.0 Hz, 1H), 1.07 (s, 6H), 0.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.36, 136.35, 132.86, 132.47 (2C), 127.88 (2C), 83.42 (2C), 52.50, 33.16, 24.79 (2C), 24.34 (2C), 18.78. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 359.0; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{22}{}^{10}B^{35}ClO_4Na^{\oplus}$ 358.1228, found 358.1241; IR (KBr) ν (cm^{-1}) 2978, 2955, 1918, 1723, 1490, 1446, 1372, 1337, 1279, 1259, 1192, 1146, 1098, 1067, 1010, 967, 864, 752, 664, 542; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 5.2 min (*R*,*R*-isomer), 6.5 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(4-bromophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3g). White semisolid. 42.9 mg, 75% yield. $[\alpha]_D^{26}$ −79.8 (*c* 1.0, $CHCl_3$) for 89% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.40 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 3.60 (s, 3H), 1.71 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.57 (dd, J = 8.0 Hz, 3.2 Hz, 1H), 1.27 (dd, J = 10.0 Hz, 8.0 Hz, 1H), 1.07 (s, 6H), 0.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.27, 136.87, 132.84 (2C), 130.84 (2C), 120.98, 83.42 (2C), 52.51, 33.25, 24.79 (2C), 24.34 (2C), 18.74. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 403.1; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{22}{}^{10}B^{79}BrO_4Na^{\oplus}$ 402.0723, found 402.0719; IR (KBr) ν (cm^{-1}) 3062, 3045, 2987, 2945, 2848, 1724, 1486, 1424, 1325, 1265, 1193,1141, 1012, 856, 826, 768, 757, 539, 510; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 7.3 min (*R*,*R*-isomer), 9.6 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(3-bromophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3h). White semisolid. 43.9 mg, 77% yield. $[\alpha]_D^{26}$ −152.5 (*c* 1.0, $CHCl_3$) for 93% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.48 (s, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.28–7.25 (m, 1H), 7.14 (t, J = 7.6 Hz, 1H), 3.61 (s, 3H), 1.72 (dd, J = 10.0 Hz, 3.6 Hz, 1H), 1.56 (dd, J = 8.0 Hz, 3.6 Hz, 1H), 1.26 (dd, J = 10.0 Hz, 8.0 Hz, 1H), 1.09 (s, 6H), 0.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.20, 140.19, 134.34, 130.17, 129.70, 129.33, 121.71, 83.46 (2C), 52.56, 33.48, 24.87 (2C), 24.42 (2C), 18.85. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 403.1; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{22}{}^{10}B^{79}BrO_4Na^{\oplus}$ 402.0733, found 402.0723; IR (KBr) ν (cm^{-1}) 3419, 3048, 2983, 2951, 1723, 1597, 1566, 1479, 1404, 1260, 1281, 1260, 1166, 1138, 998, 977, 854, 716, 695, 686, 574, 564; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 5.4 min (*R*,*R*-isomer), 6.9 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(2-bromophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3i). White semisolid. 42.2 mg, 74% yield. $[\alpha]_D^{26}$ −219.3 (*c* 1.0, $CHCl_3$) for 94% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.51 (d, J = 8.0 Hz, 1H), 7.31–7.24 (m, 2H), 7.13–7.11 (m, 1H), 3.62 (s, 3H), 1.79–1.44 (m, 2H), 1.31–1.26 (m, 1H), 1.07 (s, 6H), 0.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.78, 132.28, 128.42, 126.81, 83.18 (2C), 52.59, 35.46, 24.76 (2C), 24.25 (2C), 21.37. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: $[M + Na]^{\oplus}$ 403.0; HRMS (FTMS-ESI): $[M + Na]^{\oplus}$ calcd for $C_{17}H_{22}{}^{10}B^{79}BrO_4Na^{\oplus}$ 402.0723, found 402.0719; IR (KBr) ν (cm^{-1}) 3061, 3018, 2978, 2954, 2931, 1721, 1592, 1567, 1431, 1411, 1332, 1285, 1169, 1143, 993, 860, 759, 666, 561; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; *n*-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 7.9 min (*R*,*R*-isomer), 10.9 min (*S*,*S*-isomer).

(1*R*,2*R*)-Methyl 1-(naphthalen-2-yl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3j). Colorless oil. 31.2 mg, 59% yield. $[\alpha]_D^{26}$ −194.7 (*c* 1.0, $CHCl_3$) for 92% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80–7.73 (m, 4H), 7.50–7.42 (m, 3H), 3.60 (s, 3H), 1.79 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.74 (dd, J = 8.0 Hz, 3.2 Hz, 1H), 1.35 (dd, J = 10.0 Hz, 8.0 Hz, 1H), 1.00 (s, 6H), 0.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.86, 135.28, 133.05, 132.61, 129.58, 129.43, 127.76, 127.50, 127.25, 125.80, 125.65, 83.28 (2C), 52.47, 33.92, 24.73 (2C), 24.27 (2C), 18.94. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: [M + Na]$^{\oplus}$ 375.0; HRMS (FTMS-ESI): [M + Na]$^{\oplus}$ calcd for $C_{21}H_{25}{}^{10}BO_4Na^{\oplus}$ 374.1774, found 374.1771; IR (KBr) ν (cm^{-1}) 2999, 2982, 1724, 1618, 1438, 1410, 1265, 1168, 1147, 1128, 1113, 1070, 1016, 974, 858, 759, 660, 608, 531; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; n-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 8.7 min (R,R-isomer), 12.3 min (S,S-isomer).

(1*R*,2*R*)-Methyl 1-(3,4-dichlorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3k). White semisolid. 43.3 mg, 78% yield. $[\alpha]_D^{26}$ −98.4 (c 1.0, $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.43 (d, J = 1.2 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.17 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 3.62 (s, 3H), 1.74 (dd, J = 10.0 Hz, 3.2 Hz, 1H), 1.54 (dd, J = 8.0 Hz, 3.2 Hz, 1H), 1.30–1.24 (m, 1H), 1.09 (s, 6H), 0.90 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.95, 138.32, 133.38, 131.70, 131.19, 130.57, 129.77, 83.66 (2C), 52.71, 33.16, 24.93 (2C), 24.49 (2C), 19.08. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: [M + Na]$^{\oplus}$ 393.0; HRMS (FTMS-ESI): [M + Na]$^{\oplus}$ calcd for $C_{17}H_{21}{}^{10}B^{35}Cl_2O_4Na^{\oplus}$ 392.0838, found 392.0830; IR (KBr) ν (cm^{-1}) 2979, 2952, 1727, 1558, 1474, 1435, 1411, 1380, 1372, 1333, 1262, 1224, 1193, 1167, 1140, 1104, 1071, 1031, 971, 945, 857, 833, 758, 737, 666, 597; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; n-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 5.2 min (R,R-isomer), 6.5 min (S,S-isomer).

(1*R*,2*R*)-Methyl 1-(3,5-difluorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropanecarboxylate (3m). White semisolid. 42.1 mg, 83% yield. $[\alpha]_D^{26}$ −96.1 (c 1.0, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.89–6.86 (m, 2H), 6.69 (t, J = 9.2 Hz, 1H), 3.62 (s, 3H), 1.73 (dd, J = 10.0 Hz, 3.6 Hz, 1H), 1.55 (dd, J = 8.4 Hz, 3.6 Hz, 1H), 1.27 (dd, J = 10.0 Hz, 8.4 Hz, 1H), 1.10 (s, 6H), 0.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.78, 162.46 (dd, J_{CF} = 246, 12.9 Hz, 2C), 141.81 (t, J_{CF} = 9.1 Hz), 114.30 (dd, J_{CF} = 18.2 Hz, 6.1 Hz, 2C), 102.68 (t, J_{CF} = 25.0 Hz), 83.62 (2C), 52.71, 33.69, 24.93 (2C), 24.46 (2C), 19.02. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: [M + Na]$^{\oplus}$ 361.3; HRMS (FTMS-ESI): [M + Na]$^{\oplus}$ calcd for $C_{17}H_{21}BF_2O_4Na^{\oplus}$ 360.1429, found 360.1434; IR (KBr) ν (cm^{-1}) 3438, 3085, 1981, 1728, 1624, 1599, 1435, 1409, 1372, 1334, 1269, 1216, 1142, 1100, 1077, 990, 966, 857, 759, 736, 685, 532, 511; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; n-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 4.4 min (R,R-isomer), 5.6 min (S,S-isomer).

(*R*)-Dimethyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-cyclopropane-1,1-dicarboxylate (3p). Colorless oil. 16.6 mg, 39% yield. $[\alpha]_D{}^{24}$ −59.8 (c 1.06, $CHCl_3$) for 95% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.73 (s, 3H), 3.71 (s, 3 H), 1.54–1.52 (m, 2H), 1.23 (s, 6H), 1.22 (s, 6H), 1.12–1.08 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.88, 169.23, 83.93 (2C), 52.77, 52.54, 33.71, 24.84 (2C), 24.81 (2C), 18.98. (The carbon directly attached to the boron atom was not detected, likely due to quadrupole relaxation.) ESI-MS: [M + H]$^{\oplus}$ 285.2; HRMS (FTMS-ESI): [M + H]$^{\oplus}$ calcd for $C_{13}H_{22}{}^{10}BO_6{}^{\oplus}$ 285.1504, found 285.15; IR (KBr) ν (cm^{-1}) 2980, 2954, 1735, 1436, 1414, 1381, 1373, 1338, 1290, 1271, 1234, 1208, 1167, 1142, 1079, 971, 879, 858, 835, 772, 758, 669; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 220 nm; n-hexane–i-propanol = 98/2; flow rate = 1.0 mL min^{-1}; retention time: 11.8 min (S-isomer), 12.9 min (R-isomer).

(1*R*,2*S*)-Methyl 1,2-diphenylcyclopropanecarboxylate (5). A mixture of **3a** (30.2 mg, 0.1 mmol), iodobenzene (**4**, 30.6 mg, 0.15 mmol), $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol), and Cs_2CO_3 (97.5 mg, 0.3 mmol) in toluene (1 mL) was stirred at 80 °C under a N_2 atmosphere overnight. After cooling to room temperature, the reaction mixture was filtered and washed with ethyl acetate. The filtrate was concentrated under reduced pressure and purified by flash column chromatography using hexane–ethyl acetate (8 : 1) as an eluent to afford the desired product **5** (25 mg, 99% yield). $[\alpha]_D^{26}$ −38.9 (c 1.0, $CHCl_3$) for 94% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.05–6.94 (m, 8H), 6.70–6.68 (m, 2H), 3.58 (s, 3H), 3.06–3.01 (m, 1H), 2.06 (dd, J = 9.2 Hz, 4.8 Hz, 1H), 1.82–1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.42, 136.42, 134.80, 131.99, 128.40, 128.10, 127.76, 127.09, 126.37, 52.68, 37.45, 33.19, 20.54; ESI-MS: [M + Na]$^{\oplus}$ 275.1; HRMS (FTMS-ESI): [M + Na]$^{\oplus}$ calcd for $C_{17}H_{16}O_2Na^{\oplus}$ 275.1043, found 275.1037; IR (KBr) ν (cm^{-1}) 3648, 3412, 3061, 3086, 3029, 2953, 1966, 1897, 1720, 1602, 1496, 1456, 1447, 1428, 1376, 1342, 1255, 1205, 1189, 1104, 1050, 989, 865, 788, 760, 742, 702, 650, 545; HPLC: OJ-H Column; detected at 214 nm; n-hexane–i-propanol = 95/5; flow rate = 0.7 mL min^{-1}; retention time: 11.5 min (R,S-isomer), 16.3 min (S,R-isomer).

Acknowledgements

Financial support for this work was generously provided by the National Natural Science Foundation of China (NSFC 21372243, 21232009, 21102161), the Shanghai Municipal Committee of Science and Technology (13JC1406900), and the State Key Laboratory of Bioorganic and Natural Products Chemistry. We thank Dr Hanqing Dong (Arvinas Inc.) for his help in the preparation of this manuscript.

Notes and references

1 For selected recent reviews, see: (*a*) D. Y.-K. Chen, R. H. Pouwerb and J.-A. Richardc, *Chem. Soc. Rev.*, 2012, **41**, 4631; (*b*) P. Tang and Y. Qin, *Synthesis*, 2012, 2969.

2 B. J. F. Feys, C. E. Benedetti, C. N. Penfold and J. G. Turner, *Plant Cell*, 1994, **6**, 751.

3 D. J. Augeri, J. A. Robl, D. A. Betebenner, D. R. Magnin, A. Khanna, J. G. Robertson, A. Wang, L. M. Simpkins, P. Taunk, Q. Huang, S.-P. Han, B. Abboa-Offei, M. Cap, L. Xin, L. Tao, E. Tozzo, G. E. Welzel, D. M. Egan, J. Marcinkeviciene, S. Y. Chang, S. A. Biller, M. S. Kirby, R. A. Parker and L. G. Hamann, *J. Med. Chem.*, 2005, **48**, 5025.

4 L. A. Maslovskaya, A. I. Savchenko, E. H. Krenske, C. J. Pierce, V. A. Gordon, P. W. Reddell, P. G. Parsons and C. M. Williams, *Angew. Chem., Int. Ed.*, 2014, **53**, 7006.

5 S. N. Vaishnavi, C. B. Nemeroff, S. J. Plott, S. G. Rao, J. Kranzler and M. J. Owens, *Biol. Psychiatry*, 2004, **55**, 320.

6 D. A. Laskowski, *Rev. Environ. Contam. Toxicol.*, 2002, **174**, 49.

7 W. Zhang, T. Kilicarslan, R. F. Tyndale and E. M. Sellers, *Drug Metab. Dispos.*, 2001, **26**, 897.

8 M. Rubin, M. Rubina and V. Gevorgyan, *Chem. Rev.*, 2007, **107**, 3117.

9 For selected recent examples, see: (*a*) H. Xiong, H. Xu, S.-H. Liao, Z.-W. Xie and Y. Tang, *J. Am. Chem. Soc.*, 2013, **135**, 7851; (*b*) S. M. Wales, M. M. Walker and J. S. Johnson, *Org. Lett.*, 2013, **15**, 2558; (*c*) F. de Nanteuil, E. Serrano, D. Perrotta and J. Waser, *J. Am. Chem. Soc.*, 2014, **136** 6239.

10 (*a*) G.-H. Fang, Z.-J. Yan and M.-Z. Deng, *Org. Lett.*, 2004, **6**, 357; (*b*) S. Bénard, L. Neuville and J. Zhu, *Chem. Commun.*, 2010, **46**, 3393; (*c*) P. B. Brondani, H. Dudek, J. S. Reis, M. W. Fraaije and L. H. Andrade, *Tetrahedron: Asymmetry*, 2012, **23**, 703.

11 (*a*) H. Ito, Y. Kosaka, K. Nonoyama, Y. Sasaki and M. Sawamura, *Angew. Chem., Int. Ed.*, 2008, **47**, 7424; (*b*) C. Zhong, S. Kunii, Y. Kosaka, M. Sawamura and H. Ito, *J. Am. Chem. Soc.*, 2010, **132**, 11440.

12 For selected Cu-catalyzed asymmetric tandem borylation reactions, see: (*a*) H. Ito, T. Toyoda and M. Sawamura, *J. Am. Chem. Soc.*, 2010, **132**, 5990; (*b*) A. R. Burns, J. S. González and H. W. Lam, *Angew. Chem., Int. Ed.*, 2012, **51**, 10827; (*c*) N. Matsuda, K. Hirano, T. Satoh and M. Miura, *J. Am. Chem. Soc.*, 2013, **135**, 4934; (*d*) P. Liu, Y. Fukui, P. Tian, Z.-T. He, C.-Y. Sun, N.-Y. Wu and G.-Q. Lin, *J. Am. Chem. Soc.*, 2013, **135**, 11700.

13 M. Rubina, M. Rubin and V. Gevorgyan, *J. Am. Chem. Soc.*, 2003, **125**, 7198.

14 For other catalyzed hydrometallations, see: (*a*) M. Rubina, M. Rubin and V. Gevorgyan, *J. Am. Chem. Soc.*, 2002, **124**, 11566; (*b*) M. Rubina, M. Rubin and V. Gevorgyan, *J. Am. Chem. Soc.*, 2004, **126**, 3688.

15 For selected Cu-catalyzed asymmetric hydroborations of the aryl- and silyl-substituted alkenes, see: (*a*) Y. Lee and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2009, **131**, 3160; (*b*) R. Corberán, N. W. Mszar and A. H. Hoveyda, *Angew. Chem., Int. Ed.*, 2011, **50**, 7079; (*c*) F. Meng, H. Jang and A. H. Hoveyda, *Chem. – Eur. J.*, 2013, **19**, 3204.

16 For selected examples of Cu-catalyzed conjugate hydroboration, see: (*a*) J.-E. Lee and J. Yun, *Angew. Chem., Int. Ed.*, 2008, **47**, 145; (*b*) H.-S. Sim, X. Feng and J. Yun, *Chem. – Eur. J.*, 2009, **15**, 1939; (*c*) I.-H. Chen, L. Yin, W. Itano, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2009, **131**, 11664; (*d*) J. M. O'Brien, K.-s. Lee and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2010, **132**, 10630; (*e*) I. Ibrahem, P. Breistein and A. Córdova, *Angew. Chem., Int. Ed.*, 2011, **50**, 12036; (*f*) A. L. Moure, R. G. Arrayás and J. C. Carretero, *Chem. Commun.*, 2011, **47**, 6701; (*g*) H. Wu, S. Radomkit, J. M. O'Brien and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2012, **134**, 8277; (*h*) S. Kobayashi, P. Xu, T. Endo, M. Ueno and T. Kitanosono, *Angew. Chem., Int. Ed.*, 2012, **51**, 12763; (*i*) Y. Luo, I. D. Roy, A. G. E. Madec and H. W. Lam, *Angew. Chem., Int. Ed.*, 2014, **53**, 4186; (*j*) Z.-T. He, Y.-S. Zhao, P. Tian, C.-C. Wang, H.-Q. Dong and G.-Q. Lin, *Org. Lett.*, 2014, **16**, 1426.

17 C. Sole, A. Bonet, A. H. M. de Vries, J. G. de Vries, L. Lefort, H. Gulyás and E. Fernández, *Organometallics*, 2012, **31**, 7855.

18 Direct single crystal incubation of hydroboration product **3g** resulted in the production of a dimer compound through deboration and the [2 + 2] reaction process. See ESI† for the details.

19 (*a*) H. M. L. Davies and G. H. Lee, *Org. Lett.*, 2004, **6**, 1233; (*b*) R. Sambasivan and Z. T. Ball, *Angew. Chem., Int. Ed.*, 2012, **51**, 8568.

20 For selected Cu(I)-catalyzed asymmetric additions of cyclopropenes, see: (*a*) X. Liu and J. M. Fox, *J. Am. Chem. Soc.*, 2006, **128**, 5600; (*b*) N. Yan, X. Liu and J. M. Fox, *J. Org. Chem.*, 2008, **73**, 563; (*c*) V. Tarwade, X. Liu, N. Yan and J. M. Fox, *J. Am. Chem. Soc.*, 2009, **131**, 5382; (*d*) V. Tarwade, R. Selvaraj and J. M. Fox, *J. Org. Chem.*, 2012, **77**, 9900.

21 In the cyclopropene substrate **1**, the aryl group was almost vertical to the cyclopropene plane. As a result, the aryl group side was supposed to be less hindered than the methyl ester side.