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Graphical Abstract

The second-generation synthesis of BICMAP and its derivatives

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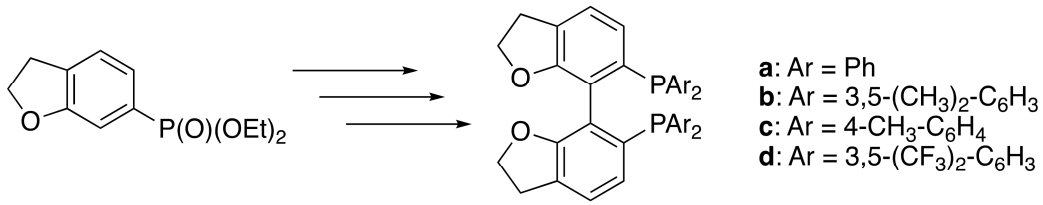

a: Ar = Ph
b: Ar = 3,5-$(CH_3)_2$-C_6H_3
c: Ar = 4-CH_3-C_6H_4
d: Ar = 3,5-$(CF_3)_2$-C_6H_3

BICMAP analogues **1**

The second-generation synthesis of BICMAP analogues

Takashi Mino[a,b]*, Kohei Watanabe[a], Takumu Akiyama[a], Yuki Mizutani[a], Kazuki Miura[a], Masatoshi Hashimoto[a], Yasushi Yoshida[a,b], Masami Sakamoto[a,b]

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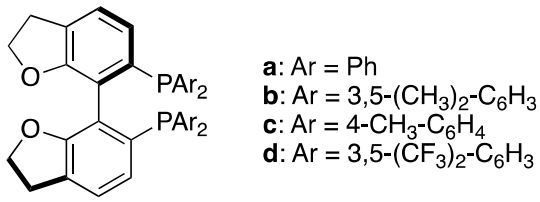
Abstract: We previously reported the synthesis of BICMAP (**1a**) *via* 6-diphenylphosphino-2,3-dihydrobenzofuran as a key intermediate. However, we did not successfully synthesize BICMAP analogues *via* a similar synthetic route. Herein we report the second-generation synthesis of BICMAP and its derivatives *via* diethylphosphonate as a key intermediate.

1. Introduction

Chiral bisphosphines are critical molecules that affect asymmetric inductions as chiral ligands for transition metal catalysts.[1] After the discovery of BINAP,[2] many atropisomeric chiral bisphosphines have been reported, including MeO-BIPHEP,[3] BIBFUP,[4] BIFAP,[5] BICAP,[6] SEGPHOS,[7] and SYNPHOS.[8] We also reported the synthesis of BICMAP,[9] such as an atropisomeric bisphosphine with a dihydrobenzofuran core and its use as a chiral ligand for rhodium-catalyzed asymmetric 1,4-addition[9b,10] and copper-catalyzed propargylic amination.[11] Dihydrobenzofuran core was easily prepared from 1,4-dibromo-2-fluorobenzene (**2**) with ethylene glycol. It seems to be easy to synthesize BICMAP analogues which have modified dihydrobenzofuran core. On the other hand, chiral bisphosphines with diarylphosphino groups instead of the diphenylphosphino group were also reported: For example,

BINAP analogues,[12] MeO-BIPHEP analogues,[13] SEGPHOS analogues,[7a,14] and SYNPHOS analogues.[15] Here we report the synthesis of BICMAP analogues **1** (Figure 1) and their applications to the palladium-catalyzed amination reaction.



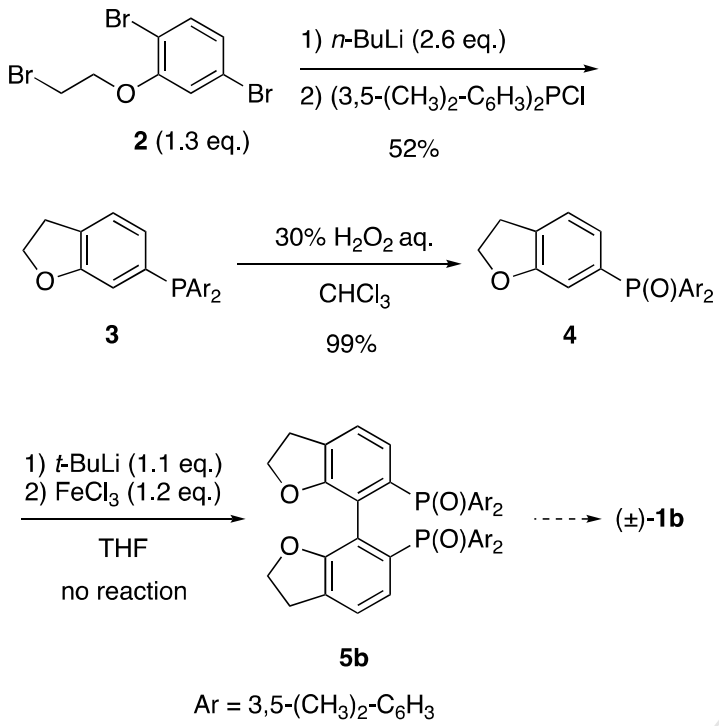
1

Figure 1. (*R*)-BICMAP analogues **1**.

2. Results and discussion

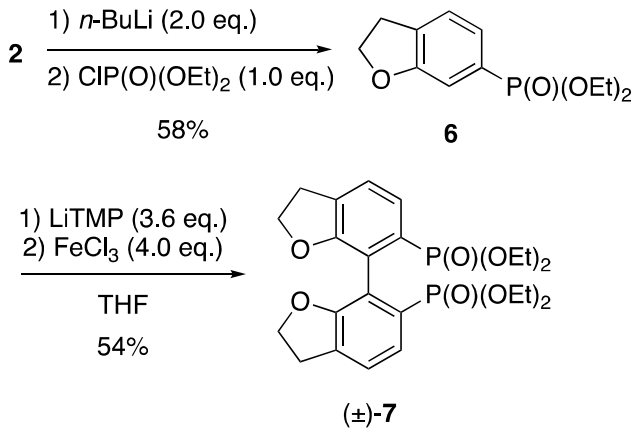
2.1. Synthesis of BICMAP analogues 1

We previously reported the synthesis of BICMAP (**1a**) *via* 6-diphenylphosphino-2,3-dihydrobenzofuran as a key intermediate. First, we tried to synthesize such BICMAP analogues as a 3,5-diMe-BICMAP (**1b**) *via* a similar synthetic route (Scheme 1). The reaction of tribromide **2**[9] with bis(3,5-dimethylphenyl)chlorophosphine using *n*-butyllithium produced corresponding phosphine **3** in 52%. After oxidation of the phosphine atom by hydrogen peroxide in chloroform, we tried the ortholithiation of phosphine oxides **4** and further oxidative coupling with anhydrous ferric chloride. Unfortunately, we failed to obtain the coupling product **5b** under this methodology. The 3,5-dimethylphenyl moiety is more sterically hindered than the phenyl moiety. So, we thought the oxidative coupling of **5b** did not proceed.



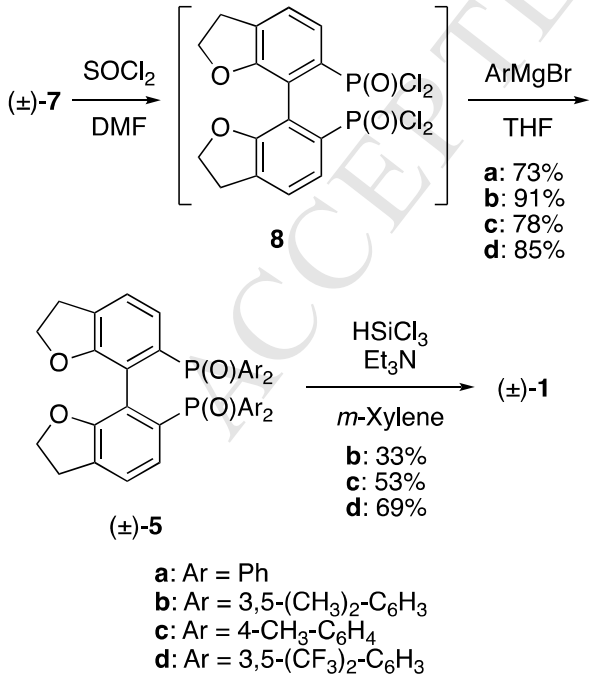
Scheme 1. Synthesis of *rac*-3,5-diMe-BICMAP ((±)-**1b**).

Then, we chose another route for the synthesis of BICMAP analogues **1**. In 2005, the Shibasaki group reported the synthesis of SEGPHOS analogues *via* the corresponding diethylphosphonate derivative as a key intermediate.[14] The Ratovelomanana-Vidal group also reported the synthesis of SYNPHOS analogues using identical methodology.[15] Then we tried a synthesis of BICMAP and its derivatives *via* diethylphosphonate derivative as a key intermediate (Scheme 2). The reaction of tribromide **2** with diethyl chlorophosphate using *n*-butyllithium produced corresponding diethylphosphonate **6** in 58%. The ortholithiation of phosphonate **6** with lithium tetramethylpiperidide (LiTMP) and further oxidative coupling with anhydrous ferric chloride gave bisphosphonate (±)-**7** as a key intermediate in 54%.



Scheme 2. Synthesis of bisphosphonate (±)-**7**.

Subsequently, we tried to synthesize of BICMAP analogues **1** from bisphosphonate (±)-**7** (Scheme 3). The chlorination of bisphosphonate (±)-**7** with thionyl chloride and further arylation with the required aryl Grignard reagents gave corresponding phosphine oxides (±)-**5a-d** in a one-pot, two-step procedure without isolation of chloride **8**. Finally, the reduction of phosphine oxides (±)-**5b-d** with $HSiCl_3$-triethylamine in *m*-xylene gave *rac*-BICMAP analogues ((±)-**1b-d**) under the same manner for the synthesis of BICMAP ((±)-**1a**).[9]



Scheme 3. Synthesis of *rac*-BICMAP analogues ((±)-**1**) from (±)-**7**.

We next tried the optical resolution of BICMAP analogues **1b-d** using HPLC with a semi-preparative chiral stationary phase column. The resolution of (±)-**1b** and (±)-**1c** were efficiently carried out using a chiralpak IE column. We obtained optical active phosphine (+)-**1b** (31%, >99% ee), (–)-**1b** (31%, >99% ee), (+)-**1c** (36%, >99% ee), and (–)-**1c** (38%, >99% ee). On the other hand, we failed to achieve the resolution of (±)-**1d**. Then we tried the optical resolution of (±)-**5d**. Using HPLC with a semi-preparative chiralpak IE column, the resolution of (±)-**5d** was efficiently carried out. We obtained optical active phosphine oxides (+)-**5d** (44%, >99% ee) and (–)-**5d** (44%, >99% ee). The reduction of optical active phosphine oxides (+)-**5d** and (–)-**5d** with $HSiCl_3$-triethylamine in *m*-xylene gave corresponding optical active phosphine (+)-**1d** (56%, 98% ee) and (–)-**1d** (63%, 99% ee), respectively. The determination of the absolute configuration of **1c** was made by a single-crystal X-ray analysis of (*R*)-(+)-**1c** (Figure 2).

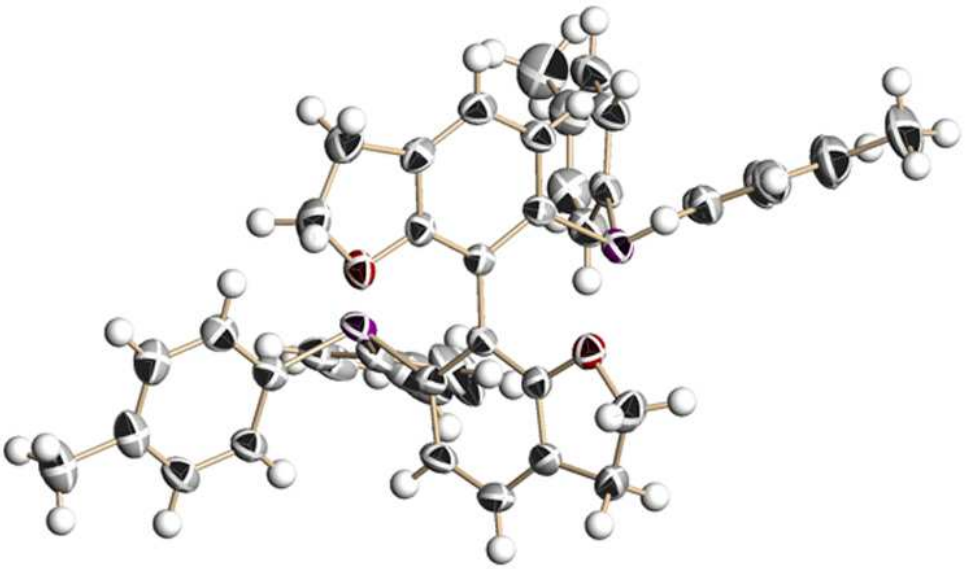
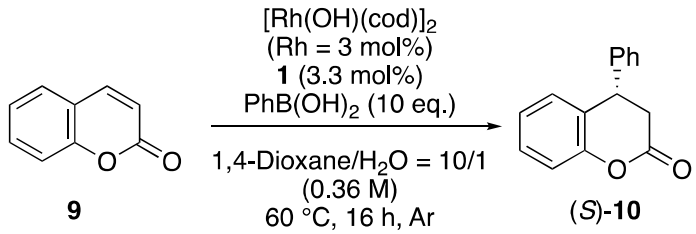


Figure 2. X-Ray structure of (*R*)-(+)-**1c.** Ellipsoids are shown at the 50% probability level.

2.2. Catalytic asymmetric reactions using chiral BICMAP analogues 1 as chiral ligands

We previously reported the (*S*)-BICMAP ((*S*)-**1a**) was useful ligand for the rhodium(I)-catalyzed asymmetric 1,4-addition of phenylboronic acid to coumarin (**9**).[10] So we tried the same reaction using BICMAP analogues such as ligands **1b-d** with $[Rh(OH)(cod)]_2$ (Rh = 3.0 mol%) in 1,4-dioxane/H_2O at 60 °C for 16 h (Scheme 4). Unfortunately, the reaction using them as a chiral ligand gave only low yields of corresponding (*S*)-product **10**. For example, the reaction using (–)-**1d** led to (*S*)-**10** with high enantioselectivity such as 91% ee, but the yield was only 12%.

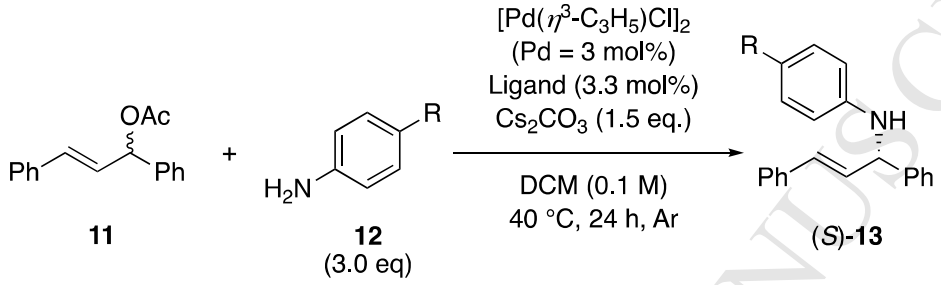


Scheme 4. Rhodium(I)-catalyzed asymmetric 1,4-addition reaction using (*S*)-BICMAP analogues **1**.

On the other hand, we previously also reported the *rac*-BICMAP ((±)-**1a**) was useful ligand for the palladium-catalyzed amination of aryl bromides with anilines.[9a] So, we investigated the palladium-catalyzed asymmetric amination reaction of allylic ester[16] using BICMAP analogues (Table 1). The reaction of the 1,3-diphenyl-2-propenyl acetate (**11**) with aniline (**12a**) using $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (Pd = 3.0 mol%) and (*S*)-BICMAP ((*S*)-**1a**) (3.3 mol%) produced corresponding product (*S*)-**13a** in good enantioselectivity (84% ee) (entry 1). The reaction of *p*-anisidine and *p*-bromoaniline using (*R*)-BICMAP ((*R*)-**1a**) instead of (*S*)-**13a** gave corresponding (*R*)-products ((*R*)-**13b** and (*R*)-**13c**) in moderate enantioselectivities (entry 2 and 3). When we used (–)-**1b** and (*S*)-(–)-**1c** in the reaction of acetate **11** with aniline (**12a**), the reactions generated corresponding (*S*)-products **13a** with high enantioselectivities such as 88% ee (entry 4) and 89% ee (entry 5), respectively. The reaction using (–)-

1d also led to (*S*)-product with moderate enantioselectivity (entry 6). On the other hand, the reaction using (*R*)-Tol-BINAP instead of tolyl type BICMAP (**1c**) gave corresponding (*R*)-product ((*R*)-**13a**) in moderate enantioselectivitiy (entry 5 vs. entry 7). Based on these results, (–)-**1b** and (–)-**1d** estimated the (*S*)-absolute configurations.

Table 1. Palladium-catalyzed asymmetric amination reaction using BICMAP analogues **1**.



Entry	Ligand	R	Yield (%)[a]	Ee (%)[b]
1	(*S*)-**1a**	H	86(**13a**)	84
2	(*R*)-**1a**	OMe	67(**13b**)	–48
3	(*R*)-**1a**	Br	21(**13c**)	–57
4	(–)-**1b**	H	83(**13a**)	88
5	(*S*)-(–)-**1c**	H	78(**13a**)	89
6	(–)-**1d**	H	91(**13a**)	65
7	(*R*)-Tol-BINAP	H	67(**13a**)	–75

[a] Isolated yields.

[b] Determined by HPLC analysis using a chiral column.

3. Conclusions

In conclusion, we found that the second-generation synthesis of BICMAP and its derivatives *via* diethylphosphonate as a key intermediate and these compounds afforded good performance as chiral ligands for the palladium-catalyzed amination reaction in high enantioselectivities (up to 89% ee).

4. Experimental

4.1. General

Melting points were measured on an AS ONE micromelting point apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DPX-300 spectrometer or JEOL ECA500 spectrometer. Chemical shifts of ^{1}H NMR spectra were reported relative to TMS (δ 0.00) and ^{13}C NMR spectra were reported relative to $CDCl_3$ (δ 77.0), as an internal standard. Mass spectra were determined on a Shimadzu GCMS-QP5050A or GCMS-QP2010 using EI or JEOL JMS-T100GCV AccuTOF using FD, and presented as *m*/*z* (% rel intensity). HRMS were recorded on a Thermo Fisher Scientific Exactive (Orbitrap) using ESI or APPI. Analytical high-perfomance liquid chromatography (HPLC) was done with a JASCO GULLIVER 900 or 2000 system coupled with the UV detector using a chiral column. Optical rotations were measured on JASCO P-2100.

4.2. Preparation of 6-bis(3,5-dimethylphenyl)phosphino-2,3-dihydrobenzofuran (3): To the solution of tribromide **2** (0.789 g, 2.2 mmol) in THF (4.4 mL) was added slowly *n*-BuLi in hexane (1.3 mL, 2.2 mmol, 1.72 M) at -80 °C for 10 min under an Ar atmosphere. After the mixture was stirred for 2 h, *n*-BuLi in hexane (1.3 mL, 2.2 mmol, 1.72 M) was added slowly at -80 °C for 10 min again. After the mixture was stirred for 2.5 h, bis(3,5-dimethylphenyl)chlorophosphine (0.474 g, 1.71 mmol) in THF (2 mL) was added, and stirring was continued for 15 h at -80 °C. The mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 20/1): 0.320 g, 0.89 mmol, 52%; yellow solid; mp 130-131 °C; ^{1}H NMR ($CDCl_3$) δ: 2.25 (s, 12H), 3.21 (t, *J* = 8.7 Hz, 2H), 4.55 (t, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 6.9 Hz, 1H), 6.84-6.94 (m, 7H), 7.16 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ: 21.3, 29.6, 71.1, 114.0 (d, *J* = 16.3 Hz), 124.7 (d, *J* = 9.8 Hz), 126.5 (d, *J* = 25.0 Hz), 127.7, 130.5, 131.4 (d, *J* = 19.8 Hz), 137.0 (d, *J* = 9.9 Hz), 137.6 (d, *J* = 11.2 Hz), 137.8 (d, 7.3 Hz), 160.2 (d, *J* = 7.5 Hz); ^{31}P NMR ($CDCl_3$) δ: -3.8; EI-

MS *m/z* (rel intensity): 360 (M^+, 60); HRMS (ESI-MS) *m/z* calcd for $C_{24}H_{25}OP$+H 361.1716, found 361.1699.

4.3. Preparation of 6-bis(3,5-dimethylphenyl)phosphinyl-2,3-dihydrobenzofuran (4): To the solution of phosphine **3** (0.288 g, 0.80 mmol) in chloroform (1 mL) was added slowly 30% aqueous H_2O_2 (3.0 mL) then stirred for 5 h. After the mixture was added water and separated organic layer, the organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was without purification: 0.299 g, 0.79 mmol, 99%; colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.31 (s, 12H), 3.26 (t, *J* = 8.8 Hz, 2H), 4.60 (t, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 12.3 Hz, 1H), 7.14 (s, 2H), 7.22-7.26 (m, 3H), 7.28 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 21.3, 29.7, 71.3, 112.5 (d, *J* = 12.2 Hz), 124.9 (d, *J* = 15.6 Hz), 125.0 (d, *J* = 20.3 Hz), 129.6 (d, *J* = 10.0 Hz), 131.4 (d, *J* = 2.8 Hz), 131.7, 133.1, 133.5 (d, *J* = 2.8 Hz), 138.0 (d, *J* = 12.7 Hz), 160.2 (d, *J* = 55.7 Hz); ^{31}P NMR ($CDCl_3$) δ: 30.6; EI-MS *m/z* (rel intensity): 376 (M^+, 17); HRMS (ESI-MS) *m/z* calcd for $C_{24}H_{25}O_2P$+H 377.1665, found 377.1663

4.4. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(3,5-dimethylphenyl)phosphine oxide) ((±)-5b) in Scheme 1: To the solution of phosphine oxide **4** (0.252 g, 0.67 mmol) in THF (5.4 mL) was added slowly *t*-BuLi in pentane (0.47 mL, 0.74 mmol, 1.59 M) at -80 °C for 10 min under an Ar atmosphere. After the mixture was stirred for 3 h, ferric chloride ($FeCl_3$) (0.130 g, 0.80 mmol) in THF (0.7 mL) was added. After the mixture was stirred for 16 h at room temperature, the mixture was concentrated under reduced pressure. The residue was added 6M HCl aq. (10 mL) and chloroform. The organic layer was washed with 6M NaOH aq. (10 mL) and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude starting material **4** was recovered.

4.5. Preparation of (2,3-dihydrobenzofuran-6-yl)phosphonic acid diethyl ester (6): To the solution of tribromide **2** (5.38 g, 15 mmol) in THF (30 mL) was added slowly *n*-BuLi in hexane (9.1 mL, 15 mmol, 1.64 M) at -80 °C for 10 min under an Ar atmosphere. After the mixture was stirred for 2 h, *n*-BuLi in hexane (9.1 mL, 15 mmol, 1.64 M) was added slowly at -80 °C for 10 min again. After the

mixture was stirred for 2 h, diethyl chlorophosphate (2.2 mL, 15 mmol) was added, and stirring was continued for 18 h at -80 °C. The mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 1/1): 2.21 g, 8.6 mmol, 58%; colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.32 (t, *J* = 7.1 Hz, 6H), 3.26 (t, *J* = 8.8 Hz, 2H), 4.01-4.17 (m, 4H), 4.61 (t, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 13.9 Hz, 1H), 7.28-7.37 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 16.3 (d, *J* = 6.6 Hz), 29.6, 62.0 (d, *J* = 5.4 Hz), 71.2, 112.0 (d, *J* = 11.1 Hz), 124.5 (d, *J* = 10.4 Hz), 125.0 (d, *J* = 18.5 Hz), 127.9 (d, *J* = 186.5 Hz), 132.1 (d, *J* = 3.3 Hz), 160.0 (d, *J* = 20.9 Hz); ^{31}P NMR ($CDCl_3$) δ: 19.7; EI-MS *m/z* (rel intensity): 256 (M^+, 60); HRMS (ESI-MS) *m/z* calcd for $C_{12}H_{17}O_4P$+H 257.0937, found 257.0934.

4.6. Preparation of (±)-tetraethyl (2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(phosphonate) ((±)-7): To the solution of 2,2,6,6-tetramethylpiperidine (4.1 mL, 24 mmol) in THF (12 mL) was added slowly *n*-BuLi in hexane (13.5 mL, 22 mmol, 1.60 M) at -80 °C for 10 min under an Ar atmosphere. After the mixture was stirred for 1 h at -15 °C, the solution of phosphonate **6** (1.54 g, 6.0 mmol) in THF (6 mL) was added at -80 °C. After the mixture was stirred for 5 h, ferric chloride ($FeCl_3$) (3.89 g, 24 mmol) in THF (10 mL) was added. After the mixture was stirred for 18 h at room temperature, the mixture was concentrated under reduced pressure. The residue was added 6M HCl aq. (40 mL) and chloroform (30 mL). The organic layer was washed with 6M NaOH aq. (40 mL) and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with ethyl acetate/methanol = 25/1): 0.828 g, 1.62 mmol, 54%; pale yellow solid; mp 154-155 °C;^{1}H NMR ($CDCl_3$) δ: 1.12 (t, *J* = 7.1 Hz, 6H), 1.19 (t, *J* = 7.1 Hz, 6H), 3.28 (t, *J* = 8.7 Hz, 4H), 3.79-4.01 (m, 8H), 4.45-4.60 (m, 4H), 7.25-7.29 (m, 2H), 7.51 (dd, *J* = 7.6 and 14.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 16.15 (d, *J* = 6.9 Hz), 16.25 (d, *J* = 7.2 Hz), 30.0, 61.3 (d, *J* = 4.8 Hz), 61.5 (d, *J* = 6.0 Hz), 71.1, 120.7 (dd, *J* = 4.2 and 11.4 Hz), 124.1 (d, *J* = 18.0 Hz), 126.1 (d, *J* = 9.6 Hz),

128.0 (d, *J* = 188.3 Hz), 131.3 (d, *J* = 3.6 Hz), 158.6 (d, *J* = 20.4 Hz); ^{31}P NMR ($CDCl_3$) δ: 18.5; EI-MS *m/z* (rel intensity): 510 (M^+, 100); HRMS (ESI-MS) *m/z* calcd for $C_{24}H_{32}O_8P_2$+H 511.1645, found 511.1622; HPLC (Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 300 nm, Hexane : Ethanol = 50 : 50, 0.38 mL / min) t_R = 26.6 and 30.4 min.

4.7.1. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(diphenylphosphine oxide) ((±)-5a):[9a] To the bisphosphonate (±)-**7** (0.255 g, 0.5 mmol) and DMF (0.04 mL) was added thionylchloride (1.1 mL, 15 mmol) under an Ar atmosphere. After the mixture was stirred for 8 h at 75 °C, the mixture was concentrated under reduced pressure. The residue was added THF (5 mL) at room temperature and phenylmagnesium bromide in THF (5 mL, 5.0 mmol, 1.0 M) at -80 °C. After the mixture was stirred for 18 h at room temperature, the mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with ethyl acetate/methanol = 25/1): 0.232 g, 0.36 mmol, 73%; white solid; mp 271-273 °C;^{1}H NMR ($CDCl_3$) δ: 2.97-3.17 (m, 4H), 3.80 (dd, *J* = 8.7, 18.6 Hz, 2H), 4.19- 4.27 (m, 2H), 6.76 (dd, *J* = 7.6 and 13.7 Hz, 2H), 7.03 (dd, *J* = 2.6 and 7.6 Hz, 2H), 7.23-7.49 (m, 12H), 7.58-7.65 (m, 4H), 7.69-7.76 (m, 4H); ^{13}C NMR ($CDCl_3$) δ: 29.7, 70.4, 121.6 (dd, *J* = 4.1 and 8.4 Hz), 123.7 (d, *J* = 16.0 Hz), 126.4 (d, *J* = 12.6 Hz), 127.7 (dd, *J* = 2.1 and 12.2 Hz), 130.1 (d, *J* = 104.4 Hz), 130.2 (d, *J* = 2.6 Hz), 130.81 (d, *J* = 2.4 Hz), 130.84 (d, *J* = 2.4 Hz), 132.1 (d, *J* = 9.5 Hz), 132.3 (d, *J* = 9.8 Hz), 134.4 (d, *J* = 103.3 Hz), 134.8 (d, *J* = 104.4 Hz), 158.7 (d, *J* = 15.3 Hz); ^{31}P NMR ($CDCl_3$) δ: 30.6; EI-MS *m/z* (rel intensity): 638 (M^+, 0.6).

4.7.2 Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(3,5-dimethylphenyl)phosphine oxide) ((±)-5b): To the bisphosphonate (±)-**7** (0.255 g, 0.5 mmol) and DMF (0.04 mL) was added thionylchloride (1.1 mL, 15 mmol) under an Ar atmosphere. After the mixture was stirred for 8 h at 75 °C, the mixture was concentrated under reduced pressure. The residue

was added THF (5 mL) at room temperature and 3,5-dimethylphenylmagnesium bromide in THF (5 mL, 5.0 mmol, 1.0 M) at -80 °C. After the mixture was stirred for 18 h at room temperature, the mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with ethyl acetate/methanol = 25/1): 0.343 g, 0.46 mmol, 91%; white solid; mp 160-162 °C;^{1}H NMR ($CDCl_3$) δ: 2.07 (s, 12H), 2.30 (s, 12H), 2.94-3.16 (m, 4H), 3.99 (dd, *J* = 8.8 and 18.6 Hz, 2H), 4.25-4.33 (m, 2H), 6.90-7.02 (m, 6H), 7.07 (s, 2H), 7.16 (d, *J* = 12.2 Hz, 4H), 7.40 (d, *J* = 12.1 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ: 21.0, 21.3, 29.8, 70.3, 121.6 (dd, *J* = 3.6 and 8.8 Hz), 123.8 (d, *J* = 15.6 Hz), 126.3 (d, *J* = 12.2 Hz), 129.78 (d, *J* = 2.8 Hz), 129.80 (d, *J* = 9.7 Hz), 129.82 (d, *J* = 102.7 Hz), 130.1 (d, *J* = 9.9 Hz), 132.5 (d, *J* = 2.8 Hz), 132.6 (d, *J* = 2.8 Hz), 134.9 (d, *J* = 102.6 Hz), 135.1 (d, *J* = 102.8 Hz), 136.9 (d, *J* = 12.7 Hz), 137.2 (d, *J* = 12.7 Hz), 158.8 (d, *J* = 15.3 Hz); ^{31}P NMR ($CDCl_3$) δ: 31.7; EI-MS *m/z* (rel intensity): 750 (M^+, 3); HRMS (ESI-MS) *m/z* calcd for $C_{48}H_{48}O_4P_2$+H 751.3101, found 751.3086.

4.7.3. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(4-methylphenyl)phosphine oxide) ((±)-5c): To the bisphosphonate (±)-**7** (0.255 g, 0.5 mmol) and DMF (0.04 mL) was added thionylchloride (1.1 mL, 15 mmol) under an Ar atmosphere. After the mixture was stirred for 8 h at 75 °C, the mixture was concentrated under reduced pressure. The residue was added THF (5 mL) at room temperature and 4-methylphenylmagnesium bromide in THF (5 mL, 5.0 mmol, 1.0 M) at -80 °C. After the mixture was stirred for 18 h at room temperature, the mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with ethyl acetate/methanol = 25/1): 0.270 g, 0.39 mmol, 78%; white solid; mp 253-255 °C;^{1}H NMR ($CDCl_3$) δ: 2.29 (s, 6H), 2.36 (s, 6H), 2.29-3.16 (m, 4H), 3.90 (dd, *J* = 8.6 and 18.6 Hz, 2H), 4.21-4.29 (m, 2H), 6.77 (dd, *J* = 7.6 and 13.7 Hz, 2H), 6.99-7.05 (m, 6H), 7.18 (dd, *J* =

2.1 and 7.9 Hz, 4H), 7.42-7.49 (m, 4H), 7.54-7.61 (m, 4H); ^{13}C NMR ($CDCl_3$) δ: 21.5 (dd, *J* = 1.1 and 2.2 Hz), 29.8, 70.4, 123.5 (d, *J* = 15.8 Hz), 121.6 (d, *J* = 3.8 Hz), 126.4 (d, *J* = 12.6 Hz), 128.3 (d, *J* = 12.4 Hz), 128.4 (d, *J* = 12.3 Hz), 130.0 (d, *J* = 2.5 Hz), 130.5 (d, *J* = 104.2 Hz), 131.4 (d, *J* = 105.9 Hz), 131.5 (d, *J* = 106.7 Hz), 132.2 (d, *J* = 15.8 Hz), 132.3 (d, *J* = 16.0 Hz), 140.9 (dd, *J* = 2.9 and 3.0 Hz), 158.7 (d, *J* = 15.2 Hz); ^{31}P NMR ($CDCl_3$) δ: 30.7; EI-MS *m/z* (rel intensity): 694 (M^+, 0.5); HRMS (ESI-MS) *m/z* calcd for $C_{44}H_{40}O_4P_2$+H 695.2475 found 695.2465.

4.7.4. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(3,5-bis(trifluoromethyl)phenyl)phosphine oxide) ((±)-5d): To the bisphosphonate (±)-**7** (0.255 g, 0.5 mmol) and DMF (0.04 mL) was added thionylchloride (1.1 mL, 15 mmol) under an Ar atmosphere. After the mixture was stirred for 8 h at 75 °C, the mixture was concentrated under reduced pressure. The residue was added THF (5 mL) at room temperature and 3,5-bis(trifluoromethyl)phenylmagnesium bromide in THF (5 mL, 5.0 mmol, 1.0 M) at -80 °C. After the mixture was stirred for 18 h at room temperature, the mixture was quenched with sat. NH_4Cl aq. and diluted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with ethyl acetate/methanol = 25/1): 0.501 g, 0.42 mmol, 85%; white solid; mp 115-117 °C; ^{1}H NMR ($CDCl_3$) δ: 2.89-3.05 (m, 2H), 3.13-3.24 (m, 2H), 4.02 (dd, J = 10.0 and 17.0 Hz, 2H), 4.44 (dd, J = 8.9 and 18.1 Hz, 2H), 6.81 (dd, *J* = 7.6 and 14.5 Hz, 2H), 7.16 (dd, *J* = 2.9 and 10.5 Hz, 2H), 7.98 (s, 4H), 8.15 (d, *J* = 11.7 Hz, 4H), 8.25 (d, *J* = 11.5 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ: 29.8, 71.2, 122.9 (dq, *J* = 16.3 and 273.4 Hz), 122.5-122.7 (m), 122.8-123.0 (m), 124.6 (t, *J* = 53.7 Hz), 126.3, 126.9, 130.5, 131.0-132.4 (m), 132.1-132.4 (m), 132.7-133.1 (m), 132.9 (dd, *J* = 2.2 and 4.0 Hz), 139.9 (dd, *J* = 7.7 and 10.5 Hz), 140.3 (dd, *J* = 7.7 and 10.6 Hz), 158.9 (t, *J* = 7.2 Hz); ^{31}P NMR ($CDCl_3$) δ: 24.6; HRMS (ESI-MS) *m/z* calcd for $C_{48}H_{24}O_4F_{24}P_2$+H 1183.0839 found 1183.0848; HPLC (Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : Ethanol = 50 : 50, 0.8 mL / min) t_R = 9.9 and 18.4 min.

4.8.1. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(3,5-dimethylphenyl)phosphine) (*rac*-3,5-diMe-BICMAP, (±)-1b): To a mixture of phosphine oxide (±)-**5b** (75.1 mg, 0.10 mmol) and triethylamine (0.51 mL, 3.6 mmol) in *m*-xylene (1 mL) was added trichlorosilane (0.3 mL, 3.0 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 18 h at 110 °C. After being cooled to room temperature, the mixture was quenched with 2M NaOH aq. (10 mL) and diluted with chloroform and water. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 10/1): 24.0 mg, 0.033 mmol, 33%; white solid; mp 228-230 °C; ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 12H), 2.24 (s, 12H), 3.01-3.25 (m, 4H), 3.95 (dd, *J* = 9.0 and 18.5 Hz, 2H), 4.34-4.42 (m, 2H), 6.65-6.71 (m, 6H), 6.77 (s, 2H), 6.89 (s, 2H), 6.96 (d, *J* = 6.0 Hz, 4H), 7.08 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.26, 21.34, 30.0, 79.6, 124.5, 124.8 (t, *J* = 22.3 Hz), 127.1, 127.5, 129.2, 129.7, 130.9 (tt, *J* = 8.1 and 10.1 Hz), 131.6 (tt, *J* = 8.6 and 10.5 Hz), 136.98 (t, *J* = 3.6 Hz) 137.01 (t, *J* = 3.3 Hz), 137.4 (dd, *J* = 3.7 and 5.8 Hz), 138.2 (dd, *J* = 5.1 and 7.3 Hz), 138.4 (dd, *J* = 5.0 and 7.2 Hz), 158.3 (t, *J* = 6.6 Hz); ^{31}P NMR ($CDCl_3$) δ –12.8; FD-MS *m/z* (rel intensity) 718 (M^+, 100); HRMS (ESI-MS) m/z calcd for $C_{48}H_{48}O_2P_2$+H 719.3202, found 719.3192; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 270 nm, Hexane : DCM = 85 : 15, 0.8 mL / min) t_R = 7.4 and 11.9 min.

4.8.2. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(4-methylphenyl)phosphine) (*rac*-4-Me-BICMAP, (±)-1c): To a mixture of phosphine oxide (±)-**5c** (69.5 mg, 0.10 mmol) and triethylamine (0.51 mL, 3.6 mmol) in *m*-xylene (1 mL) was added trichlorosilane (0.3 mL, 3.0 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 18 h at 110 °C. After being cooled to room temperature, the mixture was quenched with 2M NaOH aq. (10 mL) and diluted with chloroform and water. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 10/1): 35.2 mg, 0.053 mmol, 53%; white solid; mp 202-204 °C; ^{1}H NMR ($CDCl_3$) δ 2.29 (s,

6H), 2.31 (s, 6H), 2.93-3.02 (m, 2H), 3.04-3.20 (m, 2H), 3.82 (dd, *J* = 8.7 and 18.6 Hz, 2H), 4.27-4.35 (m, 2H), 6.61 (dd, *J* = 1.5 and 7.5 Hz, 2H), 6.98-7.07 (m, 14H), 7.14-7.19 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.2 (d, *J* = 3.2 Hz), 29.8, 70.6, 123.9 (t, *J* = 21.6 Hz), 124.5, 126.5 127.4, 128.6 (t, *J* = 3.7 Hz), 128.8 (t, *J* = 3.0 Hz), 133.3 (t, *J* = 10.4 Hz), 133.9 (t, *J* = 10.5 Hz), 134.6 (dd, *J* = 3.5 and 6.1 Hz), 135.0 (dd, *J* = 5.5 and 6.5 Hz), 137.4, 137.6, 137.8 (dd, *J* = 3.9 and 4.8 Hz), 158.4 (t, *J* = 6.1 Hz); ^{31}P NMR ($CDCl_3$) δ –13.9; EI-MS *m/z* (rel intensity) 662 (M^+, 0.2); HRMS (ESI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 663.2576 found 663.2572; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 70 : 30, 0.5 mL / min) t_R = 8.3 and 12.2 min.

4.8.3. Preparation of (±)-(2,2',3,3'-tetrahydro-[7,7'-bibenzofuran]-6,6'-diyl)bis(bis(3,5-bis(trifluoromethyl)phenyl)phosphine) (*rac*-3,5-diCF$_3$-BICMAP, (±)-1d): To a mixture of phosphine oxide (±)-**5d** (47.4 mg, 0.04 mmol) and triethylamine (0.26 mL, 1.8 mmol) in *m*-xylene (0.4 mL) was added trichlorosilane (0.15 mL, 1.5 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at 120 °C. After 24 h, triethylamine (0.26 mL, 1.8 mmol) and trichlorosilane (0.15 mL, 1.5 mmol) was added to the reaction mixture at 0 °C. The reaction mixture was stirred for 24 h at 120 °C again. After being cooled to room temperature, the mixture was quenched with 2M NaOH aq. (10 mL) and diluted with chloroform and water. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ether = 3/1): 31.6 mg, 0.027 mmol, 69%; white solid; mp 196-198 °C; ^{1}H NMR ($CDCl_3$) δ 3.16-3.35 (m, 4H), 4.19 (dd, *J* = 9.7 and 18.0 Hz, 2H), 4.52 (dd, *J* = 9.1 and 16.6 Hz, 2H), 6.57 (dt, *J* = 2.0 and 7.5 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 3.8 Hz, 4H), 7.72 (s, 6H), 7.86 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 29.8, 71.2, 122.9 (dq, *J* = 16.3 and 273.4 Hz), 122.4-122.7 (m), 122.8-123.0 (m), 124.5 (t, *J* = 53.7 Hz), 126.3, 126.9, 130.4, 131.1-132.5 (m), 132.1-132.5 (m), 132.7-133.1 (m), 132.9 (dd, *J* = 2.2 and 4.0 Hz), 139.9 (dd, *J* = 7.7 and 10.5 Hz), 140.3 (dd, *J* = 7.7 and 10.6 Hz), 158.9 (t, *J* = 7.2 Hz); ^{31}P NMR ($CDCl_3$) δ –10.7; HRMS (APPI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 1151.0941 found 1151.0955;

HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 95 : 5, 1.0 mL / min) t_R = 3.5 and 3.8 min.

4.9.1. Optical resolution of (±)-1b: HPLC resolution of (±)-**1b** (44.1 mg, 0.0625 mmol) dissolved in Hexane/DCM (78/22) (5.5 mL) was carried out by successive injections of 0.5-1.5 mL on a CHIRALPAK® IE (1.0 $\phi \times$ 25 cm). A mixture of Hexane : DCM = 78 : 22 was used as the eluent working at a flow rate of 0.5 mL/min and with UV monitoring at 254 nm. Optically active (+)-**1b** and (–)-**1b** were, respectively, obtained by evaporation of fractions.

(+)-**1b**: 13.5 mg, 0.019 mmol, 31%, >99% ee; $[\alpha]^{20}_D$ +123 (*c* 0.5, $CHCl_3$); yellow solid; mp 156-158 °C; ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 12H), 2.24 (s, 12H), 3.01-3.25 (m, 4H), 3.95 (dd, *J* = 9.0 and 18.5 Hz, 2H), 4.34-4.42 (m, 2H), 6.65-6.71 (m, 6H), 6.77 (s, 2H), 6.89 (s, 2H), 6.96 (d, *J* = 6.0 Hz, 4H), 7.08 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.27, 21.35, 30.0, 70.7, 124.4, 124.8 (t, *J* = 22.3 Hz), 127.1, 127.5, 129.2, 129.7, 130.7 (tt, *J* = 8.3 and 10.6 Hz), 131.6 (tt, *J* = 8.6 and 10.5 Hz), 136.97 (t, *J* = 3.9 Hz) 137.03 (t, *J* = 1.9 Hz), 137.4 (dd, *J* = 3.7 and 5.8 Hz), 138.1 (dd, *J* = 5.0 and 7.3 Hz), 138.4 (dd, *J* = 5.0 and 7.2 Hz), 158.3 (t, *J* = 6.6 Hz); ^{31}P NMR ($CDCl_3$) δ –12.9; EI-MS *m/z* (rel intensity) 718 (M^+, 0.2); HRMS (ESI-MS) m/z calcd for $C_{48}H_{48}O_2P_2$+H 719.3202, found 719.3202; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 270 nm, Hexane : DCM = 85 : 15, 0.8 mL / min) t_R = 7.4 (major) and 11.8 min (minor).

(–)-**1b**: 13.9 mg, 0.019 mmol, 31%, >99% ee; $[\alpha]^{20}_D$ –133 (*c* 0.49, $CHCl_3$); yellow solid; mp 154-156 °C; ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 12H), 2.24 (s, 12H), 3.01-3.25 (m, 4H), 3.95 (dd, *J* = 9.0 and 18.5 Hz, 2H), 4.34-4.42 (m, 2H), 6.65-6.71 (m, 6H), 6.77 (s, 2H), 6.89 (s, 2H), 6.96 (d, *J* = 6.0 Hz, 4H), 7.08 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.27, 21.35, 30.0, 70.7, 124.4, 124.8 (t, *J* = 22.3 Hz), 127.1, 127.5, 129.2, 129.7, 130.7 (tt, *J* = 8.3 and 10.6 Hz), 131.6 (tt, *J* = 8.6 and 10.5 Hz), 136.97 (t, *J* = 3.5 Hz) 137.03 (t, *J* = 2.2 Hz), 137.4 (dd, *J* = 3.7 and 5.8 Hz), 138.1 (dd, *J* = 5.0 and 7.3 Hz), 138.4 (dd, *J* = 5.0 and 7.2 Hz), 158.3 (t, *J* = 6.6 Hz); ^{31}P NMR ($CDCl_3$) δ –12.8; EI-MS *m/z* (rel intensity) 718 (M^+,

0.2); HRMS (ESI-MS) m/z calcd for $C_{48}H_{48}O_2P_2$+H 719.3202, found 719.3185; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi\times$ 25 cm, UV 270 nm, Hexane : DCM = 85 : 15, 0.8 mL / min) t_R = 7.4 (minor) and 11.9 min (major).

4.9.2. Optical resolution of (±)-1c: HPLC resolution of (±)-**1c** (83.9 mg, 0.127 mmol) dissolved in Hexane/DCM (70/30) (5.25 mL) was carried out by successive injections of 0.5-1.5 mL on a CHIRALPAK® IE (1.0 $\phi\times$ 25 cm). A mixture of Hexane : DCM = 70 : 30 was used as the eluent working at a flow rate of 0.5 mL/min and with UV monitoring at 254 nm. Optically active (+)-**1c** and (–)-**1c** were, respectively, obtained by evaporation of fractions.

(*R*)-(+)-**1c**: 30.5 mg, 0.046 mmol, 36%, >99% ee; $[\alpha]^{20}_D$ +54.8 (*c* 0.5, $CHCl_3$); white solid; mp 187-189 °C; ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 6H), 2.31 (s, 6H), 2.94-3.02 (m, 2H), 3.04-3.20 (m, 2H), 3.82 (dd, *J* = 8.7 and 18.6 Hz, 2H), 4.27-4.36 (m, 2H), 6.61 (dd, *J* = 1.5 and 7.5 Hz, 2H), 6.99-7.10 (m, 14H), 7.14-7.19 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.3 (d, *J* = 3.1 Hz), 29.8, 70.7, 123.9 (t, *J* = 21.6 Hz), 124.5, 126.5, 127.5, 128.6 (t, *J* = 3.7 Hz), 128.8 (t, *J* = 3.0 Hz), 133.3 (t, *J* = 10.2 Hz), 134.0 (t, *J* = 10.5 Hz), 134.6 (dd, *J* = 4.8 and 6.1 Hz), 135.0 (dd, *J* = 5.5 and 6.5 Hz), 137.4, 137.6, 137.9 (dd, *J* = 5.0 and 8.8 Hz), 158.4 (t, *J* = 6.1 Hz); ^{31}P NMR ($CDCl_3$) δ –14.0; EI-MS *m/z* (rel intensity) 662 (M^+, 0.2); HRMS (ESI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 663.2576 found 663.2572; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi\times$ 25 cm, UV 254 nm, Hexane : DCM = 70 : 30, 0.5 mL / min) t_R = 8.9 (major) and 11.9 min (minor).

X-ray Diffraction Analysis data of (*R*)-(+)-1c: Colorless prismatic plate from hexane/DCM, Monoclinic space group $P2_1$, *a* = 10.9640(5) Å, *b* = 8.4469(4) Å, *c* = 19.1047(8) Å, α = 90.000(0) °, β = 95.410(3) °, γ = 90.000(0) °, *V* = 1761.44(14) Å^3, *Z* = 2, ρ = 1.249 g/cm^3, μ (CuKα) = 1.402 mm^{-1}. Absolute structure parameter: 0.1(0). The structure was solved by the direct method of full-matrix least–squares, where the final *R* and *wR* were 0.0451 and 0.1234 for 12170 reflections. Crystallographic data for (*R*)-(+)-**1c** have been deposited with the Cambridge Crystallographic Data Centre as supplementary

publication number CCDC 1559251. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ ccdc.cam.ac.uk).

(–)-**1c**: 32.2 mg, 0.049 mmol, 38%, >99% ee; $[\alpha]^{20}_{D}$ –54.3 (*c* 0.5, $CHCl_3$); yellow solid; mp 188-189 °C; ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 6H), 2.31 (s, 6H), 2.94-3.02 (m, 2H), 3.04-3.20 (m, 2H), 3.82 (dd, *J* = 8.7 and 18.6 Hz, 2H), 4.27-4.35 (m, 2H), 6.61 (dd, *J* = 1.6 and 7.5 Hz, 2H), 6.98-7.07 (m, 14H), 7.14-7.19 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.2 (d, *J* = 3.0 Hz), 29.8, 70.7, 124.2 (t, *J* = 21.6 Hz), 124.5, 126.5, 127.5, 128.6 (t, *J* = 3.6 Hz), 128.8 (t, *J* = 3.1 Hz), 133.3 (t, *J* = 10.4 Hz), 134.0 (t, *J* = 10.5 Hz), 134.6 (dd, *J* = 5.0 and 6.1 Hz), 135.0 (dd, *J* = 5.7 and 6.8 Hz), 137.4, 137.6, 137.8 (dd, *J* = 3.9 and 4.8 Hz), 158.4 (t, *J* = 6.4 Hz); ^{31}P NMR ($CDCl_3$) δ –14.0; EI-MS *m/z* (rel intensity) 662 (M^+, 0.2); HRMS (ESI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 663.2576 found 663.2572; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 70 : 30, 0.5 mL / min) t_R = 9.9 (minor) and 12.1 min (major).

4.10.1. Optical resolution of (±)-5d: HPLC resolution of (±)-**5d** (143.7 mg, 0.122 mmol) dissolved in Hexane/DCM (50/50) (12 mL) was carried out by successive injections of 1.0-1.5 mL on a CHIRALPAK® IE (1.0 $\phi \times$ 25 cm). A mixture of Hexane : DCM = 50 : 50 was used as the eluent working at a flow rate of 0.7 mL/min and with UV monitoring at 254 nm. Optically active (–)-**5d** and (+)-**5d** were, respectively, obtained by evaporation of fractions.

(–)-**5d**: 62.6 mg, 0.053 mmol, 44%, >99% ee; $[\alpha]^{20}_{D}$ –33.8 (*c* 0.5, $CHCl_3$); white solid; mp 116-118 °C; ^{1}H NMR ($CDCl_3$) δ 2.89-3.05 (m, 2H), 3.13-3.24 (m, 2H), 4.02 (dd, *J* = 10.0 and 17.0 Hz, 2H), 4.44 (dd, *J* = 8.9 and 18.1 Hz, 2H), 6.81 (dd, *J* = 7.6 and 14.5 Hz, 2H), 7.16 (dd, *J* = 2.9 and 10.5 Hz, 2H), 7.98 (s, 4H), 8.15 (d, *J* = 11.7 Hz, 4H), 8.25 (d, *J* = 11.5 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 29.5, 71.0, 120.1 (dd, *J* = 4.4 and 9.4 Hz), 122.7 (dq, *J* = 5.0 and 273.3 Hz), 125.4-125.8 (m), 128.5 (d, *J* = 110.3 Hz), 130.9-132.7 (m), 132.5 (d, *J* = 32.6 Hz), 135.9 (d, *J* = 103.5 Hz), 136.3 (d, *J* = 102.6 Hz), 158.9 (d,

J = 16.0 Hz); ^{31}P NMR ($CDCl_3$) δ 18.5; HRMS (ESI-MS) m/z calcd for $C_{48}H_{24}O_4F_{24}P_2$+H 1183.0839 found 1183.0848; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 50 : 50, 0.85 mL / min) t_R = 14.0 (major) and 33.5 min (minor).

(+)-**5d**: 62.6 mg, 0.053 mmol, 44%, >99% ee; $[\alpha]^{20}_D$ +35.2 (*c* 0.5, $CHCl_3$); white solid; mp 115-117 °C; ^{1}H NMR ($CDCl_3$) δ 2.89-3.01 (m, 2H), 3.13-3.24 (m, 2H), 4.02 (dd, *J* = 10.1 and 17.0 Hz, 2H), 4.40 (dd, *J* = 8.9 and 18.1 Hz, 2H), 6.81 (dd, *J* = 7.6 and 14.5 Hz, 2H), 7.16 (dd, *J* = 2.9 and 7.6 Hz, 2H), 7.98 (s, 4H), 8.14 (d, *J* = 11.6 Hz, 4H), 8.25 (d, *J* = 11.3 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.5, 71.0, 120.1 (dd, *J* = 4.4 and 9.4 Hz), 122.7 (dq, *J* = 5.0 and 273.3 Hz), 125.4-125.8 (m), 128.5 (d, *J* = 110.3 Hz), 130.9-132.7 (m), 132.5 (d, *J* = 32.6 Hz), 135.9 (d, *J* = 103.5 Hz), 136.3 (d, *J* = 102.6 Hz), 158.9 (d, *J* = 16.0 Hz); ^{31}P NMR ($CDCl_3$) δ 18.5; HRMS (ESI-MS) m/z calcd for $C_{48}H_{24}O_4F_{24}P_2$+H 1183.0839 found 1183.0848; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 50 : 50, 0.85 mL / min) t_R = 13.8 (minor) and 33.1 min (major).

4.11.1. Preparation of (+)-3,5-diCF$_3$-BICMAP ((+)-1d): To a mixture of phosphine oxide (+)-**5d** (47.2 mg, 0.04 mmol) and triethylamine (0.26 mL, 1.8 mmol) in *m*-xylene (0.4 mL) was added trichlorosilane (0.15 mL, 1.5 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at 120 °C. After 24 h, triethylamine (0.26 mL, 1.8 mmol) and trichlorosilane (0.15 mL, 1.5 mmol) was added to the reaction mixture at 0 °C. The reaction mixture was stirred for 24 h at 120 °C again. After being cooled to room temperature, the mixture was quenched with 2M NaOH aq. (10 mL) and diluted with chloroform and water. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ether = 3/1): 25.6 mg, 0.022 mmol, 56%, 98% ee; $[\alpha]^{20}_D$ +60.5 (*c* 0.5, $CHCl_3$); white solid; mp 79-81 °C; ^{1}H NMR ($CDCl_3$) δ 3.16-3.35 (m, 4H), 4.19 (dd, *J* = 9.7 and 18.0 Hz, 2H), 4.52 (dd, *J* = 9.1 and 16.6 Hz, 2H), 6.57 (dt, *J* = 2.0 and 7.5 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 3.8 Hz, 4H), 7.72 (s, 6H), 7.86 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 29.8 71.2, 122.9 (dq, *J* = 16.3 and 273.4 Hz), 122.5-122.7 (m), 122.8-123.0

(m), 124.6 (t, *J* = 53.7 Hz), 126.3, 126.9, 130.5, 131.0-132.4 (m), 132.1-132.4 (m), 132.7-133.1 (m), 132.9 (dd, *J* = 2.2 and 4.0 Hz), 139.9 (dd, *J* = 7.7 and 10.5 Hz), 140.3 (dd, *J* = 7.7 and 10.6 Hz), 158.9 (t, *J* = 7.2 Hz); ^{31}P NMR ($CDCl_3$) δ –10.7; HRMS (APPI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 1151.0941 found 1151.0963; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 95 : 5, 1.0 mL / min) t_R = 3.5 (major) and 3.7 min (minor).

4.11.2. Preparation of (–)-3,5-diCF$_3$-BICMAP ((–)-1d): To a mixture of phosphine oxide (–)-**5d** (47.3 mg, 0.04 mmol) and triethylamine (0.26 mL, 1.8 mmol) in *m*-xylene (0.4 mL) was added trichlorosilane (0.15 mL, 1.5 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at 120 °C. After 24 h, triethylamine (0.26 mL, 1.8 mmol) and trichlorosilane (0.15 mL, 1.5 mmol) was added to the reaction mixture at 0 °C. The reaction mixture was stirred for 24 h at 120 °C again. After being cooled to room temperature, the mixture was quenched with 2M NaOH aq. (10 mL) and diluted with chloroform and water. The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ether = 3/1): 28.9 mg, 0.025 mmol, 63%, 99% ee; $[\alpha]^{20}_D$ –60.0 (*c* 0.5, $CHCl_3$); white solid; mp 78-80 °C; ^{1}H NMR ($CDCl_3$) δ 3.16-3.35 (m, 4H), 4.19 (dd, *J* = 9.7 and 18.0 Hz, 2H), 4.52 (dd, *J* = 9.1 and 16.6 Hz, 2H), 6.57 (dt, *J* = 2.0 and 7.5 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 3.8 Hz, 4H), 7.72 (s, 6H), 7.86 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 29.8, 71.2, 122.9 (dq, *J* = 16.3 and 273.4 Hz), 122.4-122.7 (m), 122.8-123.0 (m), 124.5 (t, *J* = 53.7 Hz), 126.3, 126.9, 130.4, 131.1-132.5 (m), 132.1-132.5 (m), 132.7-133.1 (m), 132.9 (dd, *J* = 2.2 and 4.0 Hz), 139.9 (dd, *J* = 7.7 and 10.5 Hz), 140.3 (dd, *J* = 7.7 and 10.6 Hz), 158.9 (t, *J* = 7.2 Hz); ^{31}P NMR ($CDCl_3$) δ –10.7; HRMS (APPI-MS) m/z calcd for $C_{44}H_{40}O_2P_2$+H 1151.0941 found 1151.0949; HPLC **(**Daicel CHIRALPAK® IE-3, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : DCM = 95 : 5, 1.0 mL / min) t_R = 3.5 (minor) and 3.7 min (major).

4.12. General Procedure for the Rhodium(I)-Catalyzed Asymmetric 1,4-Addition Reaction of Phenylboronic Acid to Coumarin.

Under an atmosphere of argon, $[Rh(OH)(cod)]_2$ (1.37 mg, 3.0 μmol) and chiral ligand **1** (6.6 μmol) were added to arylboronic acid (0.244 g, 2.0 mmol) in 1,4-dioxane (0.5 mL) and water (0.05 mL). After stirring the mixture for 1 h at room temperature, coumarin (**9**) (29.3 mg, 0.20 mmol) was added. The reaction mixture was stirred at 60 °C for 16 h. After being cooled to room temperature, the mixture was quenched with sat. $NaHCO_3$ aq. and diluted with EtOAc. The organic layer was washed with water and brine, and dried over Na_2SO_4. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography (elution with *n*-hexane/EtOAc = 8/1): **(*S*)-4-phneylchroman-2-one ((*S*)-10) (Scheme 4 using (–)-1d);** 12% yield (5.3 mg, 0.023 mmol), 91% ee; $[\alpha]_D^{20}$ +34.4 (*c* 0.31, $CHCl_3$); white solid; mp 114-115 °C; ^{1}H NMR ($CDCl_3$) δ 2.99-3.14 (m, 2H), 4.36 (t, *J* = 6.9 Hz, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 7.07-7.18 (m, 4H), 7.26-7.39 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 37.0, 40.6, 117.1, 124.7, 125.7, 127.6, 127.7, 128.3, 128.8, 129.1, 140.2, 151.6, 167.7; EI-MS *m*/*z* (rel intensity) 224 (M^+, 83); HPLC (Daicel CHIRALCEL® OD-H, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : 2-Propanol = 95 : 5, 1.0 mL / min) t_R = 29.0 (major) and 34.7 min (minor).

4.13. General Procedure for the Palladium-Catalyzed Asymmetric Amination Reaction of 1,3-Diphenyl-2-propenyl Acetate with Aniline Derivative.

To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.1 mg, 3 μmol) and chiral ligand (6.6 μmol) in DCM (1 mL) were added to 1,3-diphenyl-2-propenyl acetate (**11**) (50.5 mg, 0.2 mmol) in DCM (1 mL), aniline derivative **12** (0.6 mmol) and Cs_2CO_3 (196 mg, 0.3 mmol) at room temperature under an Ar atmosphere. The reaction mixture was stirred at 40 °C for 24 h. After being cooled to room temperature, the mixture was quenched with sat. $NaHCO_3$ aq. and diluted with ether. The organic layer was washed with water and brine, and dried over Na_2SO_4. The filtrate was concentrated with a rotary evaporator and the residue was purified by preparative thin layer chromatography (elution with *n*-hexane/EtOAc = 40-15/1).

(*R*)-*N*-(1,3-diphenyallyl)-4-methoxyaniline ((*R*)-13b) (Table 1, Entry 2 using (*R*)-1a); 67% yield (42.9 mg, 0.14 mmol), 48% ee; $[\alpha]_D^{20}$ –24.5 (*c* 4.1, $CHCl_3$) (lit. $[\alpha]_D^{25}$ –35.9 (*c* 68.5, $CHCl_3$) (for 81%

ee (*R*)))[16]; orange solid; mp 76-79 °C; ^{1}H NMR ($CDCl_3$) δ 3.72 (s 3H), 3.87 (s, 1H), 5.00 (d, *J* = 6.2 Hz, 1H), 6.39 (dd, *J* = 6.3 and 15.8 Hz, 1H), 6.58-6.65 (m, 3H), 6.71-6.75 (m, 2H), 7.19-7.44 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 55.7, 61.5, 114.7, 114.9, 126.5, 127.2, 127.4, 127.6, 128.5, 128.7, 130.9, 131.1, 136.7, 141.5, 142.3, 152.2; EI-MS *m*/*z* (rel intensity) 315 (M^+, 14); HPLC (Daicel CHIRALPAC® AD-H, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : 2-Propanol = 95 : 5, 0.3 mL / min) t_R = 16.7 (major) and 22.3 min (minor).

(*R*)-4-bromo-*N*-(1,3-diphenyallyl)aniline ((*R*)-13c) (Table 1, Entry 3 using (*R*)-1a); 21% yield (15.1 mg, 0.041 mmol), 57% ee; $[\alpha]_D^{20}$ –29.8 (*c* 1.5, $CHCl_3$) (lit. $[\alpha]_D^{25}$ –37.4 (*c* 72.5, $CHCl_3$) (for 82% ee (*R*)))[16]; yellow oil; ^{1}H NMR ($CDCl_3$) δ 4.16 (s, 1H), 5.03 (d, *J* = 6.0 Hz, 1H), 6.36 (dd, *J* = 6.1 and 15.8 Hz, 1H), 6.47-6.52 (m, 2H), 6.60 (d, *J* = 15.9 Hz, 1H), 7.18-7.42 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 60.6, 109.4, 115.2, 126.5, 127.1, 127.7, 127.8, 128.6, 128.9, 130.1, 131.3, 131.8, 136.4, 141.5, 146.1; EI-MS *m*/*z* (rel intensity) 364 (M^+, 1); HPLC (Daicel CHIRALPAC® AD-H, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : 2-Propanol = 90 : 10, 1.0 mL / min) t_R = 10.2 (major) and 12.8 min (minor).

(*S*)-*N*-(1,3-diphenyallyl)aniline ((*S*)-13a) (Table 1, Entry 5 using (*S*)-(–)-1c); 78% yield (44.4 mg, 0.16 mmol), 89% ee; $[\alpha]_D^{20}$ +51.6 (*c* 0.5, $CHCl_3$) (lit. $[\alpha]_D^{23}$ –46.54 (*c* 1.0, PhMe) (for 98% ee (*R*)))[17]; yellow oil; ^{1}H NMR ($CDCl_3$) δ 4.11 (s, 1H), 5.07 (d, *J* = 6.1 Hz, 1H), 6.38 (dd, *J* = 6.2 and 15.9 Hz, 1H), 6.59-6.63 (m, 3H), 6.70 (t, *J* = 7.3 Hz, 1H), 7.13 (dd, *J* = 7.4 and 8.4 Hz, 2H), 7.18-7.25 (m, 1H), 7.27-7.30 (m, 3H), 7.32-7.37 (m, 4H), 7.41-7.44 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 60.6, 113.5, 117.7, 126.5, 127.2, 127.5, 127.6, 128.5, 128.8, 129.1, 130.6, 131.0, 136.6, 142.0, 147.2; EI-MS *m*/*z* (rel intensity) 285 (M^+, 11); HPLC (Daicel CHIRALPAC® AS-H, 0.46 $\phi \times$ 25 cm, UV 254 nm, Hexane : 2-Propanol = 99 : 1, 0.3 mL / min) t_R = 29.4 (major) and 32.3 min (minor).

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