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Synthesis and application of atropisomeric dihydrobenzofuran-based bisphosphine (BICMAP)

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ABSTRACT

A new atropisomeric dihydrobenzofuran-based bisphosphine ligand **1** was easily prepared from 1,4dibromo-2-fluorobenzene. This racemic bisphosphine (\pm) -**1** was used as a ligand for the palladium-catalyzed Suzuki–Miyaura reaction of aryl chloride with arylboronic acids and Hartwig–Buchwald amination of aryl bromides with aniline derivatives. The optical resolution of (\pm) -**1** was also carried out by HPLC with a chiral stationary phase column.

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Chiral phosphines are important molecules that affect asymmetric inductions as ligands for transition metal catalysts.¹ Atropisomeric biaryls are also well established as one important class of ligands for asymmetric metal-catalyzed reactions by the discovery and the application of BINAP.² Recently many new chiral biarylphosphines have been reported, such as MeO-BIPHEP,³ BIBFUP,⁴ BI-FAP,⁵ BICAP,⁶ SEGPHOS,⁷ and SYNPHOS.⁸ We herein report the synthesis of a new atropisomeric bisphosphine ligand bearing a dihydrobenzofuran (coumaran) core, hereafter named BICMAP ((\pm)-1), and its use in the palladium-catalyzed Suzuki–Miyaura reaction⁹ and Hartwig–Buchwald amination.^{10,11} The optical resolution of (\pm)-1 was also carried out by use of HPLC with a chiral stationary phase column.

Dihvdrobenzofuran-based bisphosphine ligand **1** was easily prepared from inexpensive reagent 1,4-dibromo-2-fluorobenzene (2) $(\sim 1/g)^{12}$ via 6-diphenylphosphino-2,3-dihydrobenzofuran (5) (Scheme 1). A nucleophilic aromatic substitution (S_NAr) reaction of 1,4-dibromo-2-fluorobenzene (2) and ethylene glycol with potassium *tert*-butoxide gave corresponding alcohol **3**¹³ that was converted into bromide **4** using CBr₄–PPh₃ in good yield.¹⁴ 6-Diphenylphosphino-2,3-dihydrobenzofuran (5) was prepared by intramolecular alkylation and phosphination with chlorodiphenylphosphine via double lithium-bromide exchange of 4 with two equivalents of *n*-butyllithium.¹⁵ After oxidation of the phosphine atom by hydrogen peroxide in chloroform, ortholithiation of phosphine oxides 6^{16} and further oxidative coupling with anhydrous ferric chloride furnished bisphosphine oxide (±)-7 in good yield.¹⁷ This bisphosphine oxide (±)-7 was converted into racemic bisphosphine ligand (±)-1 using trichlorosilane-triethylamine in good yield.¹⁸ We successfully conducted single-crystal X-ray diffraction analysis of (\pm) -1, and the ORTEP diagram of (\pm) -1 is shown in Figure 1. The optical resolution of (\pm) -1 was efficiently carried out by HPLC with a chiral stationary phase column (Chir-



Scheme 1. Preparation of diphosphine ligand 1.





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Figure 1. ORTEP diagram of (±)-1.

alpak IA) of a semi-preparative scale. Optically active (+)-1 and (-)-1 were obtained in an enantiomerically pure form.¹⁹

We investigated the ability of bisphosphine (\pm) -**1** as a ligand for the palladium-catalyzed Suzuki–Miyaura reaction of aryl chlorides **8** with arylboronic acids **9**. This reaction was carried out in the presence of 2.5 mol % of Pd₂dba₃, 7.5 mol % of (\pm) -**1**, and CsCO₃ as a base in dioxane (Table 1).²⁰ When the reaction was carried out using 1-chloro-4-nitrobenzene with phenylboronic acid, 4-nitrobiphenyl (**10a**) was obtained in good yield (Table 1, entry 1). The effect of various aryl chlorides and arylboronic acids in the Suzuki-Miyaura reaction was investigated (Table 2, entries 2–5). The reaction gave corresponding products **10b–e** in moderate to good yields.

We also investigated the ability of bisphosphine (\pm) -1 as a ligand for the palladium-catalyzed Hartwig–Buchwald amination of aryl bromides **11** with aniline derivatives **12**. This reaction was carried out in the presence of 1 mol % of Pd₂dba₃, 2 mol % of (\pm) -1, and CsCO₃ as a base in PhMe (Table 2).²¹ The reaction of various aryl bromides and aniline derivatives gave corresponding products **13a–d** with good yields. When (\pm) -BINAP was used instead of (\pm) -1 as a ligand, the yield of **13a** was slightly decreased (Table 2, entry1 vs entry 2).

To investigate the nature of the catalyst structure of palladium complex with (±)-1, a single-crystal of palladium complex 14 was obtained from the reaction of (±)-1 and $PdCl_2(MeCN)_2$.²² The

Table 1

Palladium-catalyzed Suzuki-Miyaura reaction using (±)-1ª



Entry	R ¹	R ² Reaction time (h) Proc		Product	ict Yield ^b (%)	
1	NO_2	Н	24	10a	91	
2	NO_2	OMe	24	10b	88	
3	Ac	Н	24	10c	59	
4	Ac	OMe	48	10d	80	
5	CN	OMe	48	10e	94	

^a The reactions were carried out on 0.20 mmol scale of **8** with 1.5 equiv of **9** and 2.0 equiv of Cs₂CO₃ in the presence of Pd₂(dba)₃ (2.5 mol %) and ligand (±)-1 (7.5 mol %) in dioxane (0.6 mL) at 80 °C under Ar.

^b Isolated yields.

Table 2

Palladium-catalyzed Hartwig-Buchwald amination using (±)-1^a



Entry	R ¹	R ²	Product	Yield ^b (%)
1	NO ₂	Me	13a	98
2 ^c	NO ₂	Me	13b	93
3	Ac	Me	13c	93
4	CN	Me	13d	92
5	NO ₂	OMe	13e	91

^a The reactions were carried out on 0.25 mmol scale of **11** with 1.2 equiv of **12** and 1.4 equiv of Cs_2CO_3 in the presence of $Pd_2(dba)_3$ (1 mol %) and ligand (±)-**1** (3 mol %) in PhMe (1.0 mL) at 100 °C for 18 h under Ar. ^b Isolated yields.

^c This reaction was carried out using (\pm) -BINAP instead of (\pm) -1.



Figure 2. ORTEP diagram of palladium complex 14 (one molecule of chloroform omitted for clarity).

X-ray analysis of **14** showed that the two phosphine atoms are coordinated to palladium (Fig. 2), the bite angle of P–Pd–P is 92.5°, and the dihedral angle of the biaryl atropisomeric backbone is 62.5°. This dihedral angle is significantly narrower than that of BINAP-PdCl₂ complex (70.2°).²³

In summary, a new atropisomeric dihydrobenzofuran-based bisphosphine ligand (±)-1 was prepared, and the resolution of these isomers was achieved using HPLC with a chiral stationary phase column. We described the use of an efficient ligand for the palladium-catalyzed Suzuki–Miyaura reaction and Hartwig–Buchwald amination. Further studies to explore the scope of chiral ligand 1 in asymmetric catalytic reactions are currently underway.

References and notes

- (a)Catalytic Asymmetric Synthesis; Ojima, I., Ed.; VCH: New York, 2000; (b)Comprehensive Asymmetric Catalysis; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; (c) Noyori, R. Asymmetric Catalysis in Organic Synthesis; John Wiley & Sons: New York, 1994.
- (a) Takaya, H.; Akutagawa, S.; Noyori, R. Org. Synth. 1989, 67, 20; (b) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. J. Org. Chem. 1986, 51, 629; (c) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. J. Am. Chem. Soc. 1980, 102, 7932.
- (a) Schmid, R.; Cereghetti, M.; Heiser, B.; Schönholzer, P.; Hansen, H.-J. Helv. Chim. Acta 1988, 71, 897; (b) Schmid, R.; Foricher, J.; Cereghetti, M.; Schönholzer, P. Helv. Chim. Acta 1991, 74, 370; (c) Schmid, R.; Broger, E. A.; Cereghetti, M.; Crameri, Y.; Foricher, J.; Lalonde, M.; Müller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. Pure Appl. Chem. 1996, 68, 131.

- (a) Laue, C.; Schroeder, G.; Arlt, D.; Grosser, R. (Bayer AG), EP643.065, 1995; *Chem. Abstr.* **1995**, *123*, 112406b.; (b) Namyslo, J. C.; Kaufmann, D. E. *Chem. Ber.* **1997**, 1327.
- Sollewijn Gelpke, A. E.; Kooijman, H.; Spek, A. L.; Hiemstra, H. Chem. Eur. J. 1999, 2472.
- Botman, P. N. M.; Fraanje, J.; Goubitz, K.; Peschar, R.; Verhoeven, J. W.; van Maarseveen, J. H.; Hiemstra, H. Adv. Synth. Catal. 2004, 346, 743.
- (a) Saito, T.; Sayo, N.; Xiaoyaong, Z.; Yokozawa, T. (Takasago International Corporation), EP 0850945, 1998.; (b) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. Adv. Synth. Catal. 2001, 343, 264.
- (a) Pai, C.-C.; Li, Y.-M.; Zhou, Z.-Y.; Chan, A. S. C. Tetrahedron Lett. 2002, 43, 2789; (b) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. Tetrahedron Lett. 2003, 44, 823.
- For reviewes, see: (a) Miyaura, N.; Suzuki, A. Chem. Rev. 1995, 95, 2457; (b) Stanforth, S. P. Tetrahedron 1998, 54, 263; (c) Suzuki, A. In Metal-Catalyzed Cross-Coupling Reactions; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 49–97; (d) Suzuki, A. J. Organomet. Chem. 1999, 576, 147; (e) Llord-Williams, P.; Giralt, E. Chem. Soc. Rev. 2001, 30, 145.
- For reviewes, see: (a) Hartwig, J. F. Angew. Chem., Int. Ed. 1998, 37, 2046; (b) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. Acc. Chem. Res. 1998, 31, 805; (c) Yang, B. Y.; Buchwald, S. L. J. Organomet. Chem. 1999, 576, 125.
- Shekhar, S.; Ryberg, P.; Hartwig, J. F.; Mathew, J. S.; Blackmond, D. G.; Strieter, E. R.; Buchwald, S. L. J. Am. Chem. Soc. 2006, 128, 3584.
- 12. Price: \$91, 100 g, Matrix Scientific Inc.
- Song, Z. J.; Zhao, M.; Frey, L.; Li, J.; Tan, L.; Chen, C. Y.; Tscaen, D. M.; Tillyer, R.; Grabowski, E. J. J.; Volante, R.; Reider, P. J.; Kato, Y.; Okada, S.; Nemoto, T.; Sato, H.; Akao, A.; Mase, T. *Org. Lett.* **2001**, *3*, 3357.
- Preparation of 2-bromoethoxy-1,4-dibromobenzene (4): To the mixture of 3 (6.33 g, 21.4 mmol), triphenylphosphine (6.18 g, 23.5 mmol) in acetonitrile (29.4 mL) was added carbon tetrabromide (7.82 g, 23.5 mmol) at room temperature. After stirring for 3.5 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 8/1): 7.04 g, 19.6 mmol, 92%; white solid; mp 57-59 °C; ¹H NMR (CDCl₃) &: 3.68 (t, *J* = 6.4 Hz, 2H), 4.32 (t, *J* = 6.4 Hz, 2H), 7.00–7.03 (m, 2H), 7.40 (d, *J* = 8.8 Hz, 1H); ¹³C NMR (CDCl₃) &: 3.58 (f, 11.4, 117.2, 121.5, 125.7, 134.4, 155.2; El-MS m/z (rel intensity) 358 (M^{*}, 19).
- Preparation of 6-diphenylphosphino-2,3-dihydrobenzofuran (5): To the solution of bromide 4 (0.356 g, 1.00 mmol) in THF (2 mL) was added slowly n-BuLi in hexane (0.60 mL, 1.00 mmol, 1.66 M) at -80 °C for 10 min under an Ar atmosphere. After the mixture was stirred for 2 h, n-BuLi in hexane (0.60 mL, 1.00 mmol, 1.66 M) was added slowly at -80 °C for 10 min again. After the mixture was stirred for 1.5 h, chlorodiphenylphosphine (0.20 mL, 1.10 mmol) was added, and stirring was continued for 23 h at -80 °C. The mixture was quenched with satd NH₄Cl ag at 0 °C and diluted with ethyl acetate at room temperature. The organic layer was washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 20/1): 0.201 g, 0.66 mmol, 66%; white solid; mp 76–78 °C; ¹H NMR (CDCl₃) δ ; 3.20 (t, J = 8.7 Hz, 2 H), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz), 4.55 (t, J = 8.7 Hz, 2 Hz), 5.5 (t, J = 8.7.6 and 8.7 Hz, 1H), 7.17 (dd, I = 0.8 and 7.5 Hz, 1H), 7.24–7.35 (m, 10H); ¹³C $MMR (CDG13) \delta: 29.6, 71.1, 114.1 (d, J = 16.7 Hz), 124.9 (d, J = 16.7 Hz), 126.5 (d, J = 24.9 Hz), 128.4 (d, J = 7.1 Hz, C \times 4), 128.6 (s, C \times 2), 133.6 (d, J = 19.5 Hz, C \times 4), 137.0 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz, C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d, J = 10.8 Hz), C \times 2), 160.4 (d, J = 10.8 Hz), 137.3 (d,$ I = 7.7 Hz; ³¹P NMR (CDCl₃) δ ; -4.1; EI-MS m/z (rel intensity): 304 (M⁺, 100); HRMS (FAB-MS) *m/z* calcd for C₂₀H₁₇OP 304.1017, found 304.0995.
- 16. Preparation of 6-diphenylphosphinyl-2,3-dihydrobenzofuran (6): To the solution of phosphine 5 (0.304 g, 1.00 mmol) in chloroform (5 mL) was added slowly 30% aqueous H₂O₂ (2.0 mL) then stirred for 2 h. After this, water was added to the mixture and the organic layer was separated. The organic layer was dided over MgSO₄, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 1/3): 0.317 g, 0.99 mmol, 99%; white solid; mp 127–128 °C; ¹H NMR (CDCl₃) δ: 3.26 (t, *J* = 8.8 Hz, 2H), 4.59 (t, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 12.4 Hz, 1H), 7.18–7.32 (m, 2H), 7.41–7.57 (m, 6H), 7.62–7.72 (m, 4H); ¹³C NMR (CDCl₃) δ: 29.6, 71.3, 112.4 (d, *J* = 12.2 Hz), 124.8 (d, *J* = 10.1 Hz), 125.1 (d, *J* = 14.7 Hz), 128.4 (d, *J* = 12.0 Hz, C × 4), 131.7 (d, *J* = 2.6 Hz), 131.8 (d, *J* = 2.8 Hz, C × 2), 132.0 (d, *J* = 10.0 Hz, C × 4), 133.1, 133.3 (s, C × 2), 160.1, (d, *J* = 17.2 Hz); ³¹P NMR (CDCl₃) δ: 30.0; EI-MS m/z (rel intensity): 320 (M*, 54); HRMS (FAB-MS) m/z calcd for C₂₀ H₁₇O₂P+H 321.1044, found 321.1039.
- Preparation of 2,2'-diphenylphosphinyl-1,1'-bi-5,6-dihydrobenzofuran $((\pm)-7)$: To 17. the solution of phosphine oxide ${\bf 6}~(0.961~{\rm g},~3.00~{\rm mmol})$ in THF (24 mL) was added slowly t-BuLi in pentane (2.1 mL, 3.34 mmol, 1.59 M) at $-80\ ^\circ C$ for 10 min under an Ar atmosphere. After the mixture was stirred for 3 h, ferric chloride (FeCl₃) (0.593 g, 3.60 mmol) in THF (2 mL) was added. After the mixture was stirred for 13 h at room temperature, it was concentrated under reduced pressure. The residue was added to 6 M HCl aq (10 mL) and chloroform. The organic layer was washed with 6 M NaOH aq (10 mL) and brine, dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with chloroform/ methanol = 40/1): 0.549 g, 0.86 mmol, 57%; white solid; mp 156–158 °C; ¹H NMR (CDCl₃) δ: 2.92–3.18 (m, 4H), 3.78 (dd, J = 8.7 and 18.7 Hz, 2H), 4.17–4.28 (m, 2H), 6.76 (dd, J = 7.6 and 13.8 Hz, 2H), 7.03 (dd, J = 2.6 and 7.7 Hz, 2H), 7.23-7.31 (m, 4H), 7.32-7.51 (m, 8H), 7.57-7.66 (m, 4H), 7.68-7.76 (m, 4H); ¹³C NMR (CDCl₃) δ : 29.8 (s, C × 2), 70.5 (s, C × 2), 121.6 (d, *J* = 3.2 Hz, C × 2), 123.8 (d, *J* = 15.8 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 126.4 (d, *J* = 12.7 Hz, C × 2), 127.8 (d, *J* = 12.2 Hz, 123.9 (d, *J* = 10.4 Hz, C × 2), 128.4 (d, *J* = 12.7 Hz, C × 2), 128.4 (d, *J* = 12.2 Hz, 129.9 (d, *J* = 10.4 Hz, C × 2), 128.4 (d, *J* = 12.7 Hz, C × 2), 128.4 (d, *J* = 12.2 Hz, 129.9 (d, *J* = 10.4 Hz, C × 2), 128.4 (d, *J* = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), 128.4 (d, J = 12.4 Hz, C × 2), $C \times 8$), 130.2 (d J = 105.2 Hz, $C \times 2$), 130.3 (d, J = 2.6 Hz, $C \times 2$), 130.9 (d,

J = 9.7 Hz, C × 4), 132.2 (d, *J* = 9.7 Hz, C × 4), 132.3 (d, *J* = 10.0 Hz, C × 4), 133.9 (d, *J* = 35.5 Hz, C × 2), 135.3 (d, *J* = 36.2 Hz, C × 2), 158.7 (d, *J* = 15.2 Hz, C × 2); ³¹P NMR (CDCl₃) δ : 29.9; FAB-MS *m/z* (rel intensity): 639 (M*+1, 14); HRMS (FAB-MS) *m/z* calcd for C₄₀H₃₂O₄P₂+H 639.1854, found 639.1886.

- 18 Preparation of (\pm) -2,2'-diphenylphosphino-1,1'-bi-5,6-dihydrobenzofuran $((\pm)$ -BICMAP, (±)-1): To a mixture of phosphine oxide (±)-7 (232.5 mg, 0.364 mmol) and triethylamine (1.82 mL, 13.1 mmol) in *m*-xylene (4.9 mL) was added trichlorosilane (1.10 mL, 10.9 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred for 6 h at 110 °C. After being cooled to room temperature, the mixture was quenched with 6 M NaOH aq (10 mL) and diluted with chloroform and water. The organic layer was dried over MgSO₄, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 10/1): 116.7 mg, 0.192 mmol, 53%; white solid; mp 229–231 °C; ¹H NMR (CDCl₃) δ : 2.90–3.04 (m, 2H), 3.06–3.22 (m, 2H), 3.74 (dd, J = 8.8 and 18.7 Hz, 2H), 4.24–4.36 (m, 2H), 6.60 (dt, J = 1.7 and 7.6 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 7.13–7.34 (m, 2OH); ¹³C NMR (CDCl₃) δ : 29.8 (s, C × 2), 70.7 (s, $C \times 2$), 124.0 (t, J = 2.2 Hz, $C \times 4$), 124.7 (s, $C \times 2$), 126.7 (s, $C \times 2$), 127.8 (d, J = 1.2 Hz, C × 2), 127.9 (t, J = 3.5 Hz, C × 4), 128.0 (s, C × 2), 128.1 (t, J = 3.1 Hz, C × 4), 133.3 (t, J = 10.3 Hz, C × 4), 134.0 (t, J = 10.5 Hz, C × 4), 137.3 (dd, J = 3.6, 4.6 Hz, C × 2), 137.7 (dd, J = 5.4 Hz, C × 2); ³¹P NMR (CDCl₃) δ: –13.0; El-MS *m/z* (rel intensity): 606 (M^+ , 0.08); HRMS (FAB-MS) m/z calcd for $C_{40}H_{32}O_2P_2+H$ 607.1956, found 607.1953; HPLC: Daicel CHIRALPAK[®] IA (0.46 $\phi \times 25$ cm, UV 254 nm, hexane/ethanol = 97: 3, 0.3 mL/min), $t_{\rm R}$ = 22.3 (CD: $\lambda_{\rm ext}$ ($\Delta \varepsilon$) 254 (–)) and 25.9 min (CD: λ_{ext} ($\Delta \varepsilon$) 254 (+)); X-ray diffraction analysis data of (±)-1. Colorless prismatic crystals from hexane/CHCl₃, orthorhombic space group Pnc2, a = 12.1145(12) Å, b = 14.5546(15) Å, c = 8.9488(9) Å, α = 90°, β = 90°, γ = 90°, V = 1577.9(3) Å³, Z = 4, ρ = 1.277 g/cm³, μ (Mo Kα) = 1.73 cm⁻¹. The structure was solved by the direct method of full-matrix least-squares, where the final R and Rw were 0.0338 and 0.0863 for 2118 reflections.
- 19. Optical resolution of (\pm) -BICMAP ((\pm) -1): Chiral HPLC was carried out with a Daicel CHIRALPAK[®] IA column (10 mm $f \times 250$ mm) with hexane/ ethanol = 98:2 eluent. A solution of 2.9 mg of (\pm) -1 in 2 mL of hexane was injected for each batch with flow rate of 0.8 mL/min. Enantiomers were eluted at 45.5 and 51.0 min: (+)-1; 0.79 mg, 27%; >99% ee; $[\alpha]_D^{20}$ +38 (c 0.0275, EtOH); HPLC (Daicel CHIRALPAK[®] IA, 0.46 $\phi \times 25$ cm, UV 254 nm), t_R = 21.0 min (hexane/ethanol = 97:3, 0.3 mL/min) (CD: λ_{ext} ($\Delta \epsilon$) 254 (-)); (-)-1: 0.87 mg, 30%; 98.6% ee; $[\alpha]_D^{20}$ -37 (c 0.0230, EtOH); HPLC (Daicel CHIRALPAK[®] IA, 0.46 $\phi \times 25$ cm, UV 254 nm), t_R = 23.5 min (hexane/ethanol = 97:3, 0.3 mL/min) (CD: λ_{ext} ($\Delta \epsilon$) 254 (-)); (-)-1: 0.87 mg, 20%; 98.6% ee; $[\alpha]_D^{20}$ -37 (c 0.0230, EtOH); HPLC (Daicel CHIRALPAK[®] IA, 0.46 $\phi \times 25$ cm, UV 254 nm), t_R = 23.5 min (hexane/ethanol = 97:3, 0.3 mL/min) (CD: λ_{ext} ($\Delta \epsilon$) 254 (-)).
- 20. General procedure for the palladium-catalyzed Suzuki-Miyaura reaction: To a test tube, arylchloride 8 (0.20 mmol), arylboronic acid 9 (0.30 mmol), Pd₂(dba)₃ (0.005 mmol, 4.6 mg), ligand (±)-1 (0.015 mmol, 9.1 mg), Cs₂CO₃ (0.40 mmol, 130.3 mg) and dioxane (0.60 mL) were added under an Ar atmosphere. The mixture was stirred at 80 °C. After 24 or 48 h, the reaction mixture was diluted with ethyl acetate and water. The organic layer was washed with brine and dried over MgSO₄. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography (elution with *n*-hexane/ ethyl acetate = 100-20/1). All prepared compounds 10 were known and identified by ¹H NMR, ¹³C NMR, and MS.
- 21. General procedure for the palladium-catalyzed Hartwig-Buchwald amination: To a test tube, arylbromide **11** (0.25 mmol), aniline **12** (0.3 mmol), $Pd_2(dba)_3$ (0.0025 mmol, 2.3 mg), ligand (±)-1 (0.0075 mmol, 4.6 mg), Cs₂CO₃ (0.35 mmol, 114.1 mg) and PhMe (1.0 mL) were added under an Ar atmosphere. The mixture was stirred at 100 °C. After 18 h, the reaction mixture was diluted with ethyl acetate and water. The organic layer was washed with brine and dried over MgSO₄. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography (elution with *n*-hexane/ethyl acetate = 6:1). All prepared compounds **13** were known and identified by ¹H NMR, ¹³C NMR, and MS.
- 22. Preparation of palladium complex (±)-14. To a solution of PdCl₂(MeCN)₂ (7.78 mg, 0.03 mmol) in a CHCl₃ (2.0 mL) was added (±)-1 (18.2 g, 0.03 mmol) in a CHCl₃ (2.0 mL) at room temperature and stirred for 2 h. The reaction mixture was evaporated under reduced pressure. The residue was purified by silica gel chromatography (elution with CHCl₃/MeOH = 20:1): 25.5 mg, 0.0282 mmol, 94%; yellow solid; mp 258–259 °C; ¹H NMR (CDCl₃) δ : 2.71–2. 87(m, 2H), 2.93–3.09 (m, 2H), 4.31–4.51 (m, 4H), 6.45 (dd, *J* = 7.8 and 11.9 Hz, 2H), 6.72 (dd, *J* = 1.9 and 7.8 Hz, 2H), 7.27–7.48 (m, 12H), 7.63–7.75 (m, 4H), 7.87–8.08 (m, 4H); ¹³C NMR (CDCl₃) δ : 29.4 (s, C × 2), 71.2 (s, C × 2), 118.6 (dd, *J* = 4.4 Hz, C × 2), 127.8 (dd, *J* = 11.7, 29.3 Hz, C × 8), 128.6 (d, *J* = 5.4 Hz, C × 2), 125.0 (d, *J* = 6.21 Hz, C × 2); 130.8 (d, *J* = 2.9 Hz, C × 2), 135.0 (d, *J* = 1.0 4 Hz, C × 4), 135.6 (s, C × 2), 135.8 (s, C × 2), 135.6 (dd, *J* = 1.0 and 12.3 Hz, C × 2); ³¹P NMR (CDCl₃) δ : 26.9; FAB-MS *m*/z (rel intensity) 747([M–Cl]⁺, 5); HRMS (FAB-MS) *m*/z calcd for C₄₀H₃₂O₂ClP₂Pd 747.0601, found 747.0557; X-ray diffraction analysis data of 14 (Fig. 2): Yellow plate crystals from hexane/CHCl₃, C₄₀H₃₂O₂ClP₂Pd-CHCl₃, *α* = 90°, *β* = 92.8320(10)°, γ = 90°, *V* = 3728.7(4) Å³, *Z* = 4, *ρ* = 1.609 g/cm³, *μ* (Mo Kα) = 9.79 cm⁻¹. The structure was solved by the direct method of full-matrix least-squares, where the final *R* and *Rw* were 0.0367 and 0.0837 for 8391 reflections.
- Mikami, K.; Aikawa, K.; Kainuma, S.; Kawakami, Y.; Saito, T.; Sayo, N.; Kumonayashi, H. Tetrahedron: Asymmetry 2004, 15, 3885.