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N-Aryl indole-derived C–N bond axially chiral phosphine ligands: synthesis and application in palladium-catalyzed asymmetric allylic alkylation

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ABSTRACT

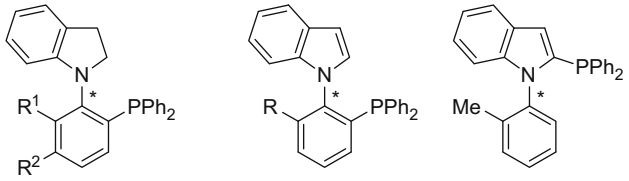
N-Aryl indole-derived C–N bond axially chiral phosphine ligands **2a–c** were obtained by DDQ oxidation of *N*-aryl indoline-derived phosphine oxide followed by silane reduction. Resolution of C–N bond atropisomers was achieved by chiral HPLC. The investigation of the rotation barrier for the C–N bond axial stability of phosphines and the determination of the absolute configuration of **2c** are described. Finally, the ability of the chiral ligand **2c** was demonstrated in a palladium-catalyzed asymmetric allylic alkylation (up to 99% ee).

1. Introduction

Chiral phosphines are important molecules that effect asymmetric inductions as ligands for transition metal catalysts.[1] C(aryl)–C(aryl) bond axially chiral biaryls[2] including BINAP[3] are well established as an important class of ligands for asymmetric metal-catalyzed reactions.[4] For nonbiaryl C–C bond axially chiral ligands, C(aryl)–C(amide carbonyl) bond axially chiral phosphine ligands[5] and C(aryl)–N(amide or imide) bond axially chiral phosphine ligands, such as quinazolinone-containing *N*-anilide[6] and *N*-arylimide[7] type ligands, have been reported. Although the synthesis of C(aryl)–N(amine) bond axially chiral *N*-aryl indoles by the stereoselective S_NAr reaction of planar chiral arene Cr-complex was recently reported by Kamikawa,[8] the discovery of C(aryl)–N(amine) bond axially chiral compounds has rarely been described.[9] Previously, we prepared such compounds using an approach similar to the synthesis of *N*-aryl indoline type C(aryl)–N(amine) bond axially chiral aminophosphine **1**.[10] We herein report the synthesis of *N*-aryl indole type C(aryl)–N(amine) bond axially chiral phosphines **2** and **3**, the investigation of the rotation barrier for C–N bond axial stability, and an application in a palladium-catalyzed asymmetric allylic alkylation.

2. Results and discussion

Phosphine ligands **2a–c** were easily prepared in two steps from phosphine oxides **4a–c**, which were the intermediates of *N*-aryl indoline type C(aryl)–N(amine) bond axially chiral aminophosphines **1a–c**.[10] Oxidation of phosphine oxide **4a** with DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) gave the corresponding *N*-aryl indole-derived phosphine oxide **5a**. This phosphine oxide was converted into desired phosphine ligand (±)-**2a** using trichlorosilane–triethylamine in good yield (Scheme 1). Phosphines (±)-**2b** and (±)-**2c** were easily prepared in the same manner.



On the other hand, phosphine (±)-**3** was prepared from *N*-(*o*-tolyl)-indole **6**[11] via the selective lithiation of indole **6** with *n*-BuLi–TMEDA in cyclopentyl methyl ether (CPME) and then treatment with chlorodiphenylphosphine (Scheme 2).

The X-ray crystallographic analysis of phosphines (±)-**2a**, (±)-**2c**, and (±)-**3** was accomplished. ORTEP drawings of (±)-**2a**, (±)-**2c**, and (±)-**3** are shown in Figures 1–3. In all cases, C–N bonds were twisted between the aryl ring with diphenylphosphine and the indole ring.

To investigate whether C(aryl)–N(amine) bond axial chirality exists in phosphines (±)-**2a–c** and (±)-**3**, we analytically separated

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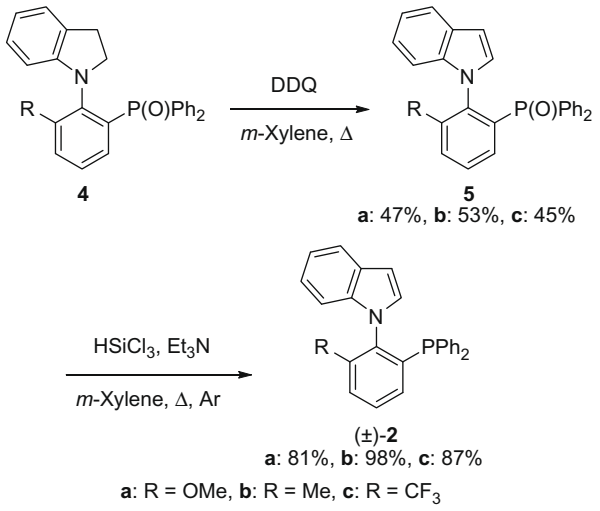
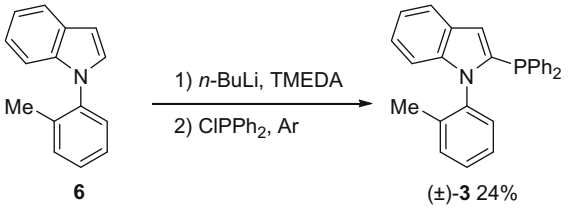


Scheme 1. Preparation of phosphine ligands (±)-**2**.



Scheme 2. Preparation of phosphine ligand (±)-**3**.

these isomers using HPLC with a chiral stationary phase column. As a result, we obtained nearly resolved UV plots for phosphines **2a**–**c** and **3** in addition to a pair of clear positive (+) and negative (−) CD trace signals of HPLC run at 270 ((±)-**2a**) or 254 nm ((±)-**2b**, **2c**, and **3**) (Fig. 4).

This result indicates the existence of a pair of atropisomers in *N*-aryl indole type phosphines (±)-**2a**–**c** and (±)-**3**. Resolution of (±)-**2a**–**c** and (±)-**3** was achieved using a semi-preparative HPLC with a chiral stationary phase column (Daicel CHIRALCEL® OJ). The enantiomeric purities of both **2a**–**c** and **3** were more than 99% ee from chiral HPLC analyses.

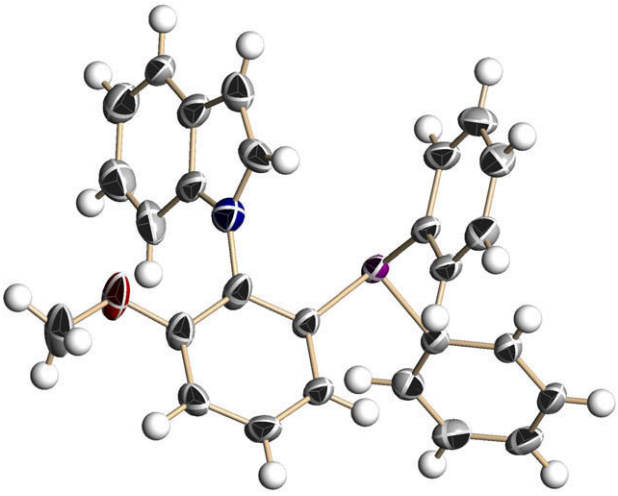


Figure 1. ORTEP drawing of (±)-**2a**.

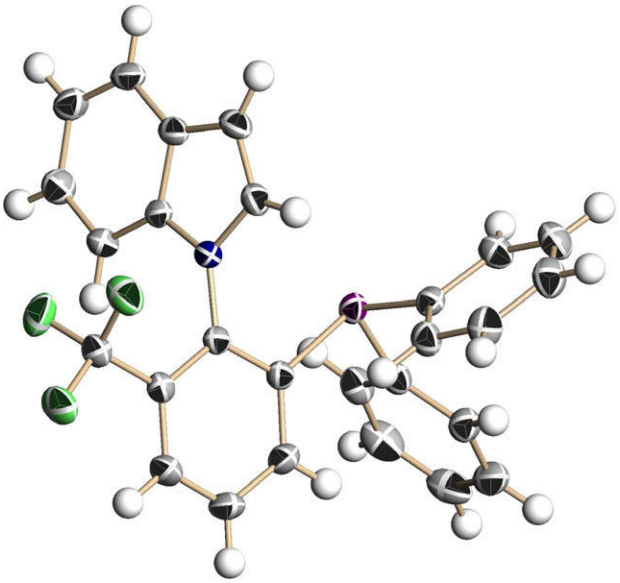


Figure 2. ORTEP drawing of (±)-**2c**.

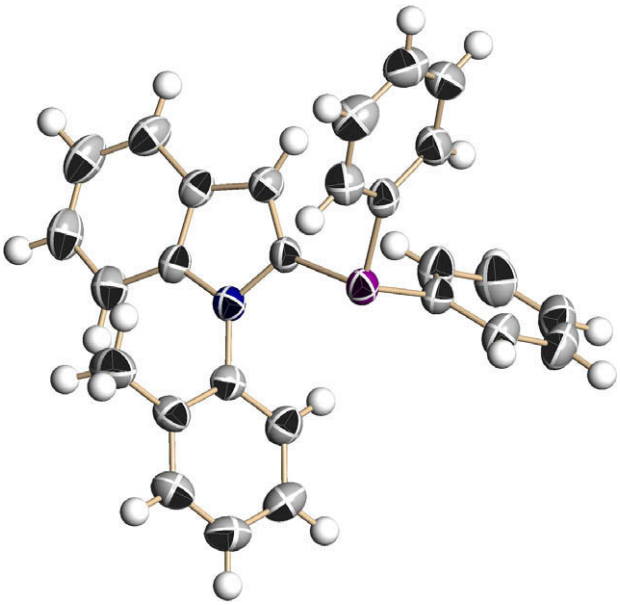


Figure 3. ORTEP drawing of (±)-**3**.

We conducted a study on the thermal racemization of C–N bond axially chiral phosphines **2a**–**c** and **3** and assessed the rate of racemization by following the first-order decay in enantiomeric excess in time at a suitable temperature. A small portion of the solution of optically active **2a**–**c** and **3** in nonane was removed at regular intervals and subsequently analyzed for enantiomeric excesses by chiral HPLC analysis. We repeated the experiment at three temperatures and determined the rate constants (k_{rac}) of **2a**–**c** and **3** at each temperature. For example, the rotational barrier ($\Delta G^{\ddagger}_{rac}$) of **2c** was found to be 36.9 kcal/mol in nonane at 25 °C based on the Arrhenius and Eyring equations.[12] This result corresponds to a half-life of approximately 2.06×10^6 years in nonane at 25 °C (Table 1).

Determination of the absolute configurations of **2** was decided by a preparation of (a*R*)-**2c** from (a*R*)-**1c** (Scheme 3). We attempted the direct preparation of indole type chiral phosphine (a*R*)-**2c** from

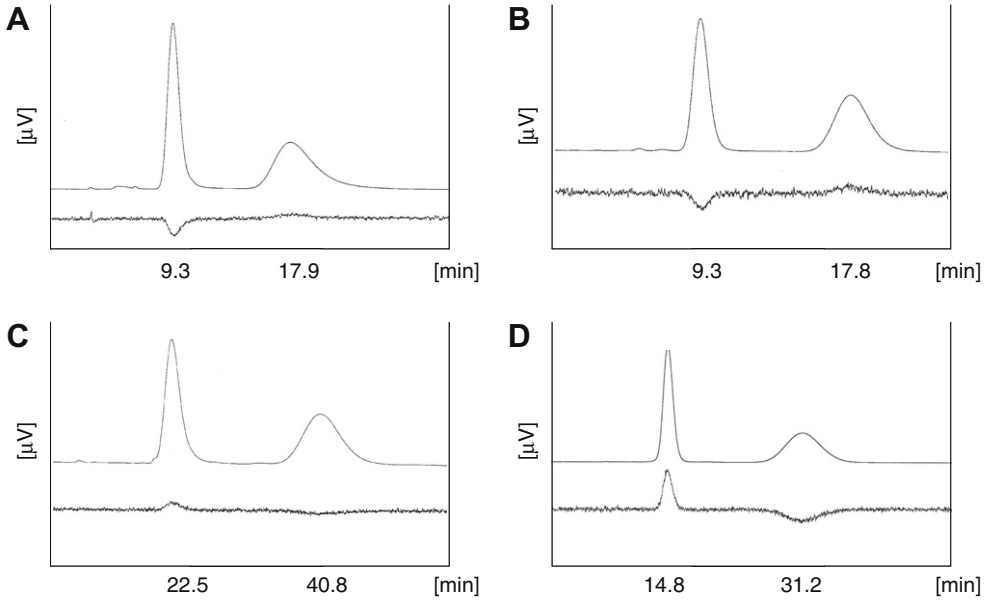


Figure 4. Chiral phase HPLC–UV and –CD charts of (±)-**2a–c** and (±)-**3**. (A) (±)-**2a** (UV 254 nm, CD 270 nm; solvent hexane/EtOH = 70/30; flow 1.0 mL/min). (B) (±)-**2b** (UV 254 nm, CD 254 nm; solvent hexane/EtOH = 95/5; flow 1.0 mL/min). (C) (±)-**2c** (UV 254 nm, CD 254 nm; solvent hexane/EtOH = 97/3; flow 0.5 mL/min). (D) (±)-**3** (UV 254 nm, CD 254 nm; solvent hexane/EtOH = 90/10; flow 0.5 mL/min).

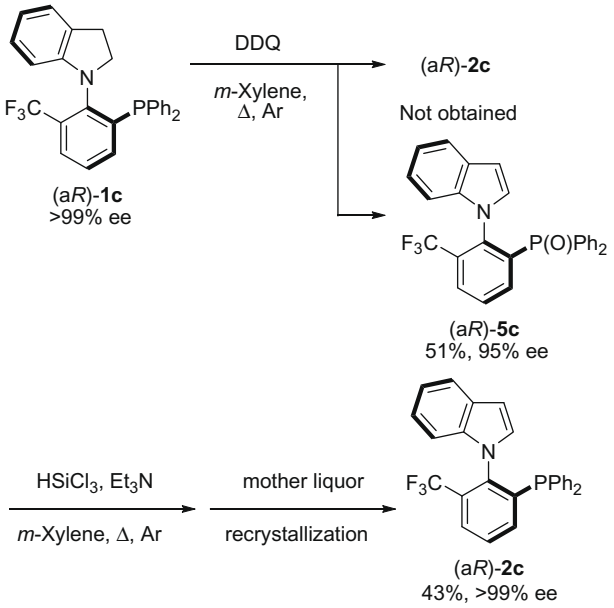
Table 1
Thermodynamic parameters of thermal racemization of optically active **2a–c** and **3**

Thermodynamic parameter at 25 °C	**2a**	**2b**	**2c**	**3**
ΔH (kcal/mol)	28.0	31.7	45.1	24.8
ΔS (cal/mol K)	2.91	−4.67	27.5	−20.1
$\Delta G^{\ddagger}_{rac}$ (kcal/mol)	27.1	33.1	36.9	30.8
Half-life (year)	0.15	3123	2.06×10^6	64

indoline type chiral phosphine (a*R*)-**1c** (>99% ee) by DDQ oxidation of the indoline moiety. Oxidation occurred not only at the indoline moiety but also at the phosphine moiety, and corresponding *N*-aryl indole-derived phosphine oxide (a*R*)-**5c** was obtained instead of chiral phosphine (a*R*)-**2c** with slight racemization (95% ee). This phosphine oxide was converted into the desired phosphine (a*R*)-**2c** (>99% ee: after one recrystallization) using trichlorosilane–triethylamine in a moderate yield. Although the reaction procedure was not optimized, *N*-aryl indole type C(aryl)–N(amine) bond axially chiral phosphine (a*R*)-**2c** was obtained using an alternative synthetic route without HPLC resolution.

We investigated the ability of chiral phosphines **2** and **3** as chiral ligands for palladium-catalyzed asymmetric allylic alkylation[13] using 1,3-diphenyl-2-propenyl acetate **7** with dimethyl malonate **8a**. This reaction was carried out in the presence of 2 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 4 mol % of **2** (Pd:**2** = 1:1) or 8 mol % of **3** (Pd:**3** = 1:2), and a mixture of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and LiOAc[14] as the base (Table 2).

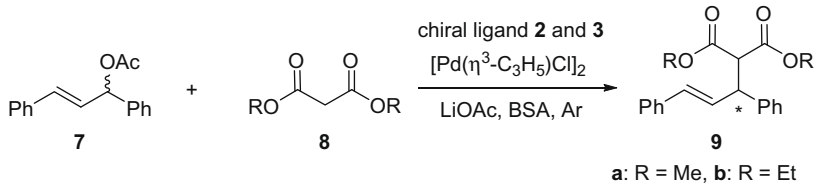
We investigated the ability of ligands **2a–c** in toluene at room temperature (entries 1–3). When the reaction was carried out using (a*R*)-**2c** as the ligand, the enantioselectivity of product (*S*)-**9a** was higher than in the case of chiral ligands **2a** and **2b** with good yield (entry 3 vs entries 1 and 2). With **3** as the chiral ligand, the enantioselectivity and the yield were decreased (entry 4). We examined the effect of solvents using chiral ligand (a*S*)-**2c** (entries 3, and 5–8). When the reaction was carried out in diethyl ether instead of toluene, the enantioselectivity of (*R*)-**9a** slightly increased to 98.9% ee (entry 5). When the reaction was carried out at −20 °C (entry 9), the enantioselectivity of product was not changed (99.0% ee) but the yield dropped dramatically. We also investigated the reaction of diethyl malonate **8b** at room temperature. The reaction gave corresponding product (*R*)-**9b** in high enantioselectivity with high yield (entry 10).



Scheme 3. Preparation of phosphine (a*R*)-**2c** from chiral indoline type phosphine (a*R*)-**1c**.

As a result, (*S*)-product **9** was obtained in a palladium-catalyzed asymmetric allylic alkylation using (a*S*)-**2** as the chiral ligand. On the other hand, we previously reported that the antipodal of product (*R*)-**9** was obtained in this reaction using (a*S*)-**1**.[10] On the palladium-catalyzed asymmetric allylic alkylation using chiral ligand **2c** at −20 °C (entry 9, Table 1), the unreacted acetate **7** was recovered with product **9a**. The kinetic resolution of starting material **7** did not occur (~2% ee). The reaction mechanism using *N*-aryl indole

Table 2
Palladium-catalyzed asymmetric allylic alkylation using **2** and **3**[a]



Entry	Ligand	R	Solv.	Temp (°C)	Time (h)	Yield[b] (%)	ee (%) (config.)[c]
1	(−)-**2a**	Me	PhMe	rt	24	93	94(*R*)
2	(+)-**2b**	Me	PhMe	rt	24	96	97(*S*)
3	(a*S*)-(+)-**2c**	Me	PhMe	rt	24	95	98(*S*)
4[d]	(−)-**3**	Me	PhMe	rt	72	8	50(*R*)
5	(a*R*)-(−)-**2c**	Me	Et_2O	rt	24	96	98.9(*R*)
6	(a*R*)-(−)-**2c**	Me	THF	rt	24	97	98.5(*R*)
7	(a*R*)-(−)-**2c**	Me	DCM	rt	24	95	97(*R*)
8	(a*R*)-(−)-**2c**	Me	MeCN	rt	24	98	98(*R*)
9	(a*R*)-(−)-**2c**	Me	Et_2O	−20	48	46	99.0(*R*)
10	(a*R*)-(−)-**2c**	Et	Et_2O	rt	24	99	99.0(*R*)[e]

[a] The reactions were carried out with 3.0 equiv of **8** and BSA in the presence of LiOAc (4 mol %) and ligand **2** (4 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mol %).
[b] Isolated yields.
[c] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OD-H).
[d] This reaction was carried out using 8 mol % of (−)-**3** and LiOAc.
[e] Determined by HPLC analysis using a chiral column (Daicel CHIRALCEL® OJ).

type ligand **2** was different from the case of *N*-aryl indoline type ligand **1** and resembled the pyrrolidinyl-containing aminophosphines.[15] The π–allyl–Pd complex **10** containing the racemic ligand (±)-**2a** was synthesized upon the successive treatment of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with ligand **2a** (Pd:**2a** = 1:1). Its suitable crystal was obtained from hexane–$CHCl_3$ and single crystal X-ray analysis of **10** was carried out (Fig. 5).

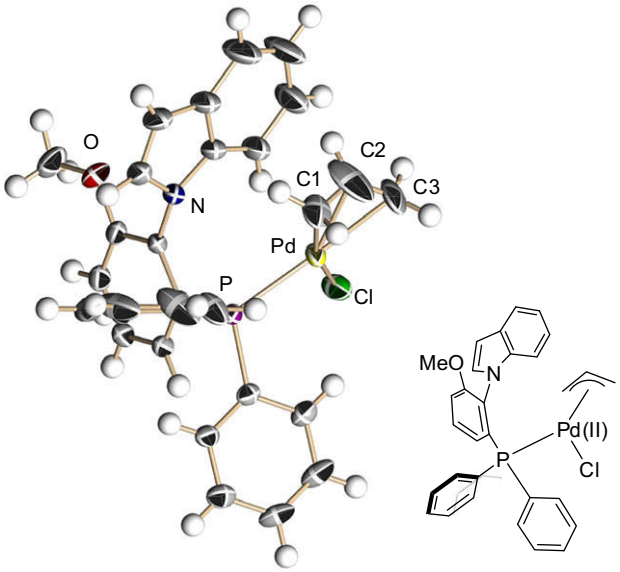


Figure 5. ORTEP drawing of palladium complex **10**. Selected bond lengths (Å) and angles (°): Pd–P, 2.2984(11); Pd–Cl, 2.3796(13); Pd–C(1), 2.117(5); Pd–C(2), 2.128(6); Pd–C(3), 2.190(5); C(1)–Pd–C(3), 67.6(3); Cl–Pd–P, 94.27(4). The unit cell contains one solvent molecule ($CHCl_3$). For the purpose of clarity, the solvent molecule is omitted.

The solid-state structure shows that ligand **2a** is coordinated to palladium atom as the monodentate ligand. The *trans* influence of the ligand is reflected in the lengthening of the Pd–C(3) bond in *trans* disposition to the phosphine atom to the Pd–C(1) distance [2.190(5) vs 2.117(5) Å].

We suggest the plausible asymmetric induction process of palladium-catalyzed AAA reaction of **7** with **8a** using chiral ligand (a*S*)-**2** in Figure 6. There are two candidates, **A** and **B**, which are possible structures formed from chiral ligand (a*S*)-**2**. Intermediate **B** could be obtained from **A** by exchanging the relative positions of the phosphine and the acetate ligands. However, intermediate **B** is unstable because of the steric hindrance between the phenyl rings of allylic substrate and the indole ring of ligand. Therefore, the reaction probably proceeds through an M-type intermediate **A** rather than a W-type intermediate **B**. The nucleophilic attack occurs predominantly at the allyl terminus from the *trans* to the phosphine atom. As a result, the (*S*)-product **9a** was obtained in this reaction using the chiral ligand (a*S*)-**2**.

3. Conclusions

In conclusion, we prepared *N*-aryl indole type C(aryl)–N(amine) bond axially chiral phosphines **2a–c** and **3** which were resolved by HPLC over a chiral stationary phase column. We also obtained (a*R*)-**2c** by an alternative synthetic route without HPLC resolution. Our pilot study disclosed that high enantioselectivity was achieved with these ligands in a palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate **7** (up to 99% ee). Further studies to explore the scope of these ligands in other asymmetric catalytic reactions are currently in progress.

4. Experimental

4.1. Preparation of phosphine oxide 5a

To a mixture of phosphine oxide **4a** (0.153 g, 0.36 mmol) and *m*-xylene (3 mL) was added DDQ (0.152 g, 0.72 mmol) and then heated to 130 °C for 2 h. After cooling to room temperature, the mixture was diluted with ethyl acetate, and filtered though Celite, eluting with additional ethyl acetate. The filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate/triethylamine = 3:3:1): 0.072 g, 0.17 mmol, 47% as a white solid; mp 163–164 °C; ^{1}H NMR ($CDCl_3$) δ 3.60 (s, 3H), 6.32 (d, J = 3.3 Hz, 1H), 6.52 (d, J = 7.7 Hz, 1H), 6.83–7.05 (m, 5H), 7.17–7.49 (m, 10H), 7.60–7.67

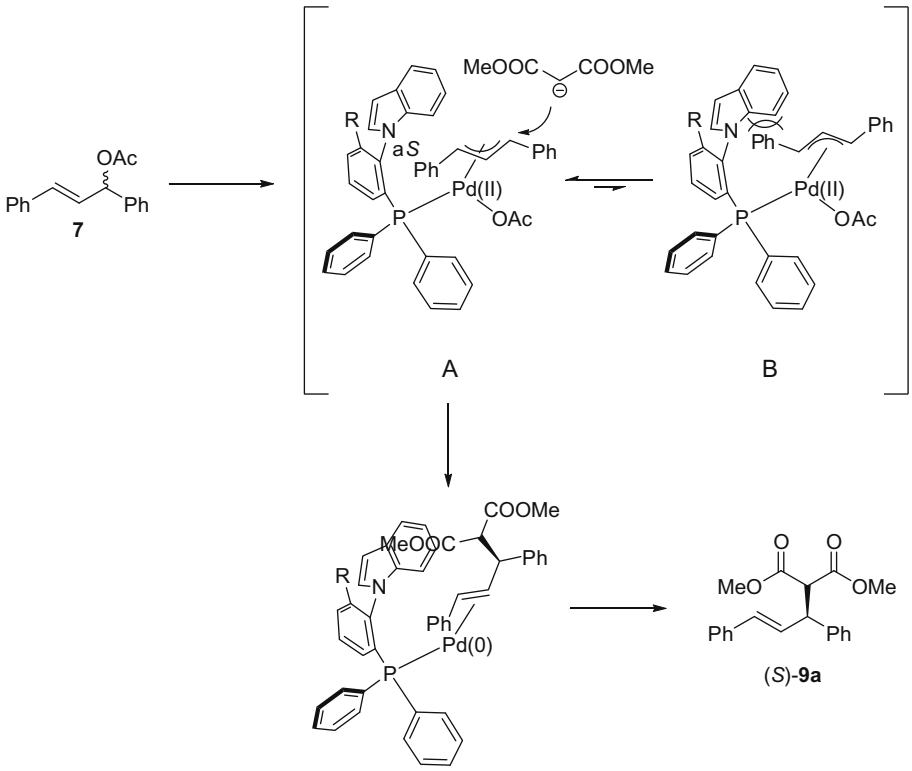


Figure 6. Plausible asymmetric induction process of palladium-catalyzed AAA reaction using chiral ligand (a*S*)-**2**.

(m, 2H); ^{13}C NMR ($CDCl_3$) δ 56.1, 102.3, 110.9, 116.1 (d, J_{CP} = 2.4 Hz), 119.3, 120.0, 120.9, 126.1 (d, J_{CP} = 9.4 Hz), 127.3, 127.4, 127.8, 128.0, 128.2, 129.1 (d, J_{CP} = 13.95 Hz), 130.1, 130.3, 130.4 (d, J_{CP} = 106.8 Hz), 130.6, 130.6 (d, J_{CP} = 5.3 Hz), 130.7 (d, J_{CP} = 2.9 Hz), 131.4 (d, J_{CP} = 2.8 Hz), 131.7, 131.7 (d, J_{CP} = 106.3 Hz), 131.8, 134.5 (d, J_{CP} = 98.8 Hz), 136.9, 157.2 (d, J_{CP} = 10.5 Hz); ^{31}P NMR ($CDCl_3$) δ 26.1; EI-MS *m*/*z* (relative intensity): 423 (M^+, 100); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{22}O_2NP$ + H 424.1466, found 424.1464.

4.2. Preparation of phosphine oxide 5b

To a mixture of phosphine oxide **4b** (0.614 g, 1.50 mmol) and *m*-xylene (5 mL) was added DDQ (1.73 g, 7.5 mmol) and then heated to 130 °C for 5 d. After cooling to room temperature, the mixture was diluted with ethyl acetate, and filtered though Celite, eluting with additional ethyl acetate. The filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate/triethylamine = 6:2:1): 0.324 g, 0.80 mmol, 53% as a white solid; mp 170–171 °C; ^{1}H NMR ($CDCl_3$) δ 1.70 (s, 3H), 6.36 (d, *J* = 3.2 Hz, 1H), 6.42 (d, *J* = 8.1 Hz, 1H), 6.81–6.92 (m, 2H), 6.97–7.11 (m, 3H), 7.16 (d, *J* = 3.3 Hz, 1H), 7.27–7.32 (m, 3H), 7.35–7.44 (m, 4H), 7.48–7.55 (m, 2H), 7.60–7.67 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 17.2 (d, J_{CP} = 1.4 Hz), 102.5, 110.7, 119.5, 120.3, 121.3, 127.4, 127.5, 127.8, 128.0, 128.1 (d, J_{CP} = 13.8 Hz), 128.2, 129.9, 130.3, 130.4, 130.7 (d, J_{CP} = 105.9 Hz), 130.8 (d, J_{CP} = 2.9 Hz), 131.4 (d, J_{CP} = 3.0 Hz), 131.7, 131.7 (d, J_{CP} = 106.1 Hz), 131.8, 132.3, 132.4 (d, J_{CP} = 9.5 Hz), 132.4, 133.6 (d, J_{CP} = 99.8 Hz), 135.0 (d, J_{CP} = 2.2 Hz), 136.3, 139.7 (d, J_{CP} = 6.9 Hz), 140.6 (d, J_{CP} = 4.4 Hz); ^{31}P NMR ($CDCl_3$) δ 26.1; EI-MS *m*/*z* (relative intensity): 407 (M^+, 100); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{22}ONP$ + H 408.1517, found 408.1533.

4.3. Preparation of phosphine oxide 5c

To a mixture of phosphine oxide **4c** (2.38 g, 5.14 mmol) and *m*-xylene (14 mL) was added DDQ (2.34 g, 11.7 mmol) and then heated to 80 °C for 3 h. After cooling to room temperature, the mixture was diluted with ethyl acetate, and filtered though Celite, eluting with additional ethyl acetate. The filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate/triethylamine = 7:4:1): 1.06 g, 2.31 mmol, 45% as a white solid; mp 78–79 °C; ^{1}H NMR ($CDCl_3$) δ 6.33 (dd, *J* = 0.7 and 3.3 Hz, 1H), 6.39 (d, *J* = 8.2 Hz, 1H), 6.79 (td, *J* = 1.0 and 7.1 Hz, 1H), 6.90 (td, *J* = 0.8 and 7.1 Hz, 1H), 7.02 (d, *J* = 3.3 Hz, 1H), 7.08–7.14 (m, 2H), 7.20–7.30 (m, 4H), 7.34–7.41 (m, 3H), 7.47–7.54 (m, 2H), 7.68 (td, *J* = 0.9 and 9.3 Hz, 1H), 7.93–8.03 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 102.9, 110.9, 119.7, 120.0, 121.4, 122.5 (qd, J_{CP} and J_{CF} = 2.3 and 274.8 Hz), 127.4, 127.8 (d, J_{CP} = 12.4 Hz), 128.3 (d, J_{CP} = 12.2 Hz), 128.9 (d, J_{CP} = 11.8 Hz), 129.8 (d, J_{CP} = 107.8 Hz), 130.0, 130.6, 130.7, 130.8, 131.2 (qd, J_{CP} and J_{CF} = 2.3 and 5.0 Hz), 131.5 (d, J_{CP} = 1.7 Hz), 131.6 (d, J_{CP} = 9.5 Hz), 131.8 (d, J_{CP} = 2.8 Hz), 132.1 (d, J_{CP} = 7.9 Hz), 137.7 (d, J_{CP} = 97.2 Hz), 138.2 (d, J_{CP} = 9.0 Hz), 138.8, 140.4 (dq, J_{CP} and J_{CF} = 1.6 and 5.5 Hz); ^{31}P NMR ($CDCl_3$) δ 25.7; FAB-MS *m*/*z* (relative intensity): 461 (M^+, 63); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{19}ONF_3P$ 461.1156, found 461.1182.

4.4. Preparation of (±)-*N*-(2′-diphenylphosphino-6′-methoxy phenyl)indole (±)-2a

To a mixture of phosphine oxide **5a** (0.121 g, 0.3 mmol) and triethylamine (0.25 mL, 1.8 mmol) in *m*-xylene (1 mL) was added trichlorosilane (0.18 mL, 1.8 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was heated to 130 °C for 6 h. After being cooled to room temperature, the mixture was diluted with chloroform and the reaction was quenched with 2 M aqueous NaOH solution. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 15:1): 0.098 g, 0.24 mmol, 81% as a white solid, mp 146–148 °C; ^{1}H NMR ($CDCl_3$) δ 3.65 (s, 3H), 6.51 (d, *J* = 3.2 Hz, 1H), 6.69 (ddd, *J* = 7.7, 3.0 and 1.2 Hz, 1H), 6.77–6.81 (m, 2H), 6.98–7.38

(m, 14H), 7.57–7.60 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 102.1, 110.7, 110.7, 112.5, 119.5, 120.4, 121.5, 125.7, 127.9, 128.1, 128.2, 128.4, 128.5, 128.6, 128.7, 129.4, 129.5, 129.6,131.4 (d, J_{CP} = 3.2 Hz), 133.7, 134.0, 136.5 (d, J_{CP} = 5.3 Hz), 136.5 (d, J_{CP} = 2.3 Hz), 137.1, 140.5 (d, J_{CP} = 2.2 Hz), 156.6 (d, J_{CP} = 0.6 Hz); ^{31}P NMR ($CDCl_3$) δ −16.2; EI-MS *m*/*z* (relative intensity): 407 (M^+, 15); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{22}ONP$ 407.1439, found 407.1461; HPLC Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 70:30, 1.0 mL/min), t_R = 9.3 (CD, λ_{ext} ($\Delta\varepsilon$) 270 (−)) and 17.9 (CD, λ_{ext} ($\Delta\varepsilon$) 270 (+)) min; X-ray diffraction analysis data of (±)-**2a** (Fig. 1). Colorless prismatic crystals from *n*-hexane–chloroform, monoclinic space group $P2_1/n$, a = 12.6654(7) Å, b = 8.0543(5) Å, c = 20.9933(12) Å, α = 90°, β = 98.3380(10)°, γ = 90°, V = 2118.9(2) Å^3, Z = 4, ρ = 1.277 Mg/m^3, μ (Mo Kα) = 1.48 cm^{-1}. The structure was solved by the direct method of full-matrix least-squares, where the final *R* and *Rw* were 0.1050 and 0.2631 for 11517 reflections, respectively.

4.5. Preparation of (±)-*N*-(2′-diphenylphosphino-6′-methylphenyl)indole (±)-2b

To a mixture of phosphine oxide **5b** (0.109 g, 0.27 mmol) and triethylamine (0.23 mL, 1.62 mmol) in *m*-xylene (1 mL) was added trichlorosilane (0.16 mL, 1.62 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was heated to 120 °C for 6 h. After being cooled to room temperature, the mixture was diluted with chloroform and the reaction was quenched with 2 M aqueous NaOH solution. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 15:1): 0.102 g, 0.26 mmol, 98% as a white solid, mp 115–116 °C; ^{1}H NMR ($CDCl_3$) δ 1.84 (s, 3H), 6.53 (d, J = 3.1 Hz, 1H), 6.72–6.74 (m, 2H), 6.95–7.11 (m, 5H), 7.16–7.23 (m, 5H), 7.30–7.33 (m, 5H), 7.61 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 17.2, 102.2, 110.5, 119.7, 120.6, 121.8, 127.8, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7 (d, J_{CP} = 1.8 Hz), 128.8, 131.5, 131.9, 133.7 (d, J_{CP} = 2.3 Hz), 133.9 (d, J_{CP} = 2.8 Hz), 136.5, 136.7, 137.1 (d, J_{CP} = 12.1 Hz), 137.9 (d, J_{CP} = 2.7 Hz), 139.1 (d, J_{CP} = 15.1 Hz); ^{31}P NMR ($CDCl_3$) δ −16.5; FAB-MS *m*/*z* (relative intensity): 391 (M^+, 53); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{22}NP$ 391.1490, found 391.1476; HPLC Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 95:5, 1.0 mL/min), t_R = 9.3 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (−)) and 17.8 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (+)) min.

4.6. Preparation of (±)-*N*-(2′-diphenylphosphino-6′-trifluoro methylphenyl)indole (±)-2c

To a mixture of phosphine oxide **5c** (0.461 g, 1.0 mmol) and triethylamine (0.84 mL, 6.0 mmol) in *m*-xylene (2 mL) was added trichlorosilane (0.61 mL, 6.0 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was heated to 120 °C for 6 h. After being cooled to room temperature, the mixture was diluted with chloroform and the reaction was quenched with 2 M aqueous NaOH solution. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/ethyl acetate = 15:1): 0.388 g, 0.87 mmol, 87% as a white solid, mp 135–136 °C; ^{1}H NMR ($CDCl_3$) δ 6.55 (dd, J = 3.2 and 0.8 Hz, 1H), 6.68 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 3.2 Hz, 1H), 6.96–7.13 (m, 6H), 7.19–7.39 (m, 7H), 7.54 (td, J = 7.8 and 0.6 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.83 (dd, J = 7.9 and 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 102.8, 110.8 (d, J_{CP} = 1.5 Hz), 119.9, 120.5, 122.0, 122.9 (qd, J_{CP} and J_{CF} = 2.2 and 274.2 Hz), 127.7 (q, J_{CF} = 5.1 Hz), 127.7, 128.5 (d, J_{CP} = 6.9 Hz), 128.6 (d, J_{CP} = 7.1 Hz), 129.0, 129.1, 130.0, 130.4 (qd, J_{CP} and J_{CF} = 3.2 and 31.0 Hz), 133.6 (d, J_{CP} = 20.6 Hz), 133.7 (d, J_{CP} = 20.9 Hz), 135.5 (d, J_{CP} = 12.4 Hz), 136.2 (d, J_{CP} = 12.1 Hz), 138.1, 138.6, 141.1 (qd, J_{CP} and J_{CF} = 1.7 and 27.2 Hz), 143.9 (d, J_{CP} = 19.9 Hz); ^{31}P NMR ($CDCl_3$) δ −17.4; FAB-MS *m*/*z* (relative intensity): 445 (M^+, 100); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{19}NF_3P$ 445.1207, found 445.1205; HPLC Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 97:3, 0.5 mL/min), t_R = 22.5 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (+)) and 40.8 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (−)) min; X-ray diffraction analysis data of (±)-**2c** (Fig. 2). Colorless prismatic crystals from *n*-hexane–chloroform, monoclinic space group $P\bar{1}$, a = 9.4193(13) Å, b = 10.7966(14) Å, c = 11.4274(15) Å, α = 109.707(2)°, β = 90.486(2)°, γ = 97.413(2)°, V = 1083.2(2) Å^3, Z = 2, ρ = 1.366 g/cm^3, μ (Mo Kα) = 1.67 cm^{-1}. The structure was solved by the direct method of full-matrix least–squares, where the final *R* and *Rw* were 0.0341 and 0.0891 for 4103, respectively.

4.7. Preparation of (±)-*N*-(2′-methylphenyl)-2-diphenyl phosphinoindole (±)-3

To a mixture of *N*-(2′-methylphenyl)indole **6** (0.609 g, 2.94 mmol) and TMEDA (0.50 mL, 3.31 mmol) in CPME (12 mL) was added dropwise *n*-BuLi in *n*-hexane (2.09 mL, 3.30 mmol, 1.58 M) over 10 min. The mixture was stirred at 50 °C for 3 h then treated with chlorodiphenylphosphine (0.61 mL, 3.30 mmol) and stirring was continued for 20 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl and the reaction mixture was diluted with diethyl ether. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with chloroform/ethyl acetate = 8:1): 0.271 g, 0.69 mmol, 24% as a white solid, mp 124–125 °C; ^{1}H NMR ($CDCl_3$) δ 1.86 (s, 3H), 6.36 (d, J = 0.6 Hz, 1H), 6.83–6.86 (m, 1H), 6.92 (d, J = 7.8 Hz, 1H), 7.06–7.12 (m, 3H), 7.27–7.37 (m, 12H), 7.56–7.59 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.6 (d, J_{CP} = 4.1 Hz), 110.4 (d, J_{CP} = 1.3 Hz), 111.1, 120.0, 120.5, 122.5, 126.3, 127.9 (d, J_{CP} = 1.5 Hz), 128.3, 128.4, 128.9, 128.9, 130.0 (d, J_{CP} = 2.7 Hz), 130.7, 133.7, 134.0, 135.6 (d, J_{CP} = 12.2 Hz), 135.7 (d, J_{CP} = 10.8 Hz), 136.7 (d, J_{CP} = 2.3 Hz), 137.4, 138.6 (d, J_{CP} = 3.2 Hz), 140.3 (d, J_{CP} = 2.8 Hz); ^{31}P NMR ($CDCl_3$) δ −27.2; EI-MS *m*/*z* (relative intensity): 391 (M^+, 32); HRMS (FAB-MS) *m*/*z* calcd for $C_{27}H_{22}NP$ 391.1490, found 391.1486; HPLC Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 90:10, 0.5 mL/min), t_R = 14.8 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (+)) and 31.2 (CD, λ_{ext} ($\Delta\varepsilon$) 254 (−)) min; X-ray diffraction analysis data of (±)-**3** (Fig. 3). Colorless prismatic crystals from hexane–chloroform, monoclinic space group $P2_1/C$, a = 10.488(3) Å, b = 18.091(5) Å, c = 11.346(4) Å, β = 92.23(3)°, V = 2151.2(12) Å^3, Z = 4, ρ = 1.209 g/cm^3, μ (Cu Kα) = 1.21 cm^{-1}. The structure was solved by the direct method of full-matrix least–squares, where the final *R* and *Rw* were 0.038 and 0.139 for 3175 reflections, respectively.

4.8. Resolution of (±)-2a

HPLC resolution of (±)-**2a** (8.0 mg) dissolved in EtOH (2.5 mL) was carried out by successive injections of 0.5 mL on a CHIRALCEL® OJ (1.0 $\varphi \times 25$ cm). A mixture of *n*-hexane/ethanol = 70:30 was used as the eluent working at a flow rate of 1.0 mL/min and with UV monitoring at 254 nm. Enantiomerically pure (−)-**2a** (3.2 mg) and (+)-**2a** (3.1 mg) were, respectively, obtained by evaporation of fractions.

Compound (−)-**2a**: >99% ee; $[\alpha]_D^{20} = -55.4$ (*c* 0.25, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 70:30, 1.0 mL/min), t_R = 7.8 min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2a**.

Compound (+)-**2a**: >99% ee; $[\alpha]_D^{20} = +53.0$ (*c* 0.22, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 70:30, 1.0 mL/min), t_R = 14.0 min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2a**.

4.9. Resolution of (±)-2b

HPLC resolution of (±)-**2b** (10.0 mg) dissolved in ethanol (2.5 mL) was carried out by successive injections of 0.5 mL on a CHIRALCEL® OJ (1.0 $\varphi \times 25$ cm). A mixture of *n*-hexane/ethanol = 90:10 was used as the eluent working at a flow rate of 2.0 mL/min and with UV monitoring at 254 nm. Enantiomerically pure (−)-**2b** (4.8 mg) and (+)-**2b** (4.3 mg) were, respectively, obtained by evaporation of fractions.

Compound (−)-**2b**: >99% ee; $[\alpha]_D^{25} = -125.0$ (*c* 0.50, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 95:5, 1.0 mL/min), $t_R = 7.8$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2b**.

Compound (+)-**2b**: >99% ee; $[\alpha]_D^{25} = +126.9$ (*c* 0.50, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 95:5, 1.0 mL/min), $t_R = 15.1$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2b**.

4.10. Resolution of (±)-2c

HPLC resolution of (±)-**2c** (90.7 mg) dissolved in ethanol (18.0 mL) was carried out by successive injections of 0.5 mL on a CHIRALCEL® OJ (1.0 $\varphi \times 25$ cm). A mixture of *n*-hexane/ethanol = 97:3 was used as the eluent working at a flow rate of 1.0 mL/min and with UV monitoring at 254 nm. Enantiomerically pure (a*S*)-(+)-**2c** (36.3 mg) and (a*R*)-(−)-**2c** (35.3 mg) were, respectively, obtained by evaporation of fractions.

Compound (a*S*)-(+)-**2c**: >99% ee; $[\alpha]_D^{20} = +183.0$ (*c* 0.20, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 97:3, 0.5 mL/min), $t_R = 22.9$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2c**.

Compound (a*R*)- (−)-**2c**: >99% ee; $[\alpha]_D^{20} = -183.4$ (*c* 0.20, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 97:3, 0.5 mL/min), $t_R = 42.8$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2c**.

4.11. Resolution of (±)-3

HPLC resolution of (±)-**3** (20.8 mg) dissolved in ethanol (4.0 mL) was carried out by successive injections of 0.5 mL on a CHIRALCEL® OJ (1.0 $\varphi \times 25$ cm). A mixture of *n*-hexane/ethanol = 90:10 was used as the eluent working at a flow rate of 1.5 mL/min and with UV monitoring at 254 nm. Enantiomerically pure (+)-**3** (6.7 mg) and (−)-**3** (6.4 mg) were, respectively, obtained by evaporation of fractions.

Compound (+)-**3**: >99% ee; $[\alpha]_D^{25} = +2.6$ (*c* 0.96, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 90:10, 0.5 mL/min), $t_R = 15.1$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2c**.

Compound (−)-**3**: >99% ee; $[\alpha]_D^{25} = -2.5$ (*c* 1.00, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 90:10, 0.5 mL/min), $t_R = 34.9$ min; ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**3**.

4.12. Elucidation of the thermal racemization of optically active 2a–c and 3

A small amount of optically active **2** or **3** was dissolved in nonane at room temperature. The solution was kept a constant temperature in the thermostat oil bath, a small portion was taken out several times, and the transitions of enantiomeric excess were measured by chiral HPLC analysis.

4.13. Preparation of (a*R*)-5c

To a mixture of (a*R*)-**1c** (0.107 g, 0.24 mmol, >99% ee) and *m*-xylene (1.0 mL) was added DDQ (0.109 g, 0.48 mmol) and then heated to 80 °C for 1.5 h. After cooling to room temperature, the mixture was diluted with diethyl ether and water. 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/triethylamine = 7:4:1): 0.057 g, 0.12 mmol, 51% as a white solid; 94.9% ee; $[\alpha]_D^{20} = -170.4$ (*c* 0.73, $CHCl_3$); HPLC (Daicel CHIRALCEL® OJ-H (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 92:8, 0.3 mL/min), $t_R = 33.8$ (major) and 54.4 min (minor); ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**5c**.

4.14. Preparation of (a*R*)-(−)-2c

To a mixture of (a*R*)-**5c** (0.048 g, 0.10 mmol, 95% ee) and triethylamine (0.087 mL, 0.62 mmol) in *m*-xylene (0.6 mL) was added trichlorosilane (0.063 mL, 0.62 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was heated to 120 °C for 6 h. After being cooled to room temperature, the mixture was diluted with diethyl ether and the reaction was quenched with 2 M aqueous NaOH solution. 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 = 15:1) and recrystallized in *n*-hexane–chloroform at −20 °C. After filtration, the motherliquor was concentrated with a rotary evaporator: 0.020 g, 0.04 mmol, 43% as a white solid; >99% ee; HPLC Daicel CHIRALCEL® OJ (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/ethanol = 97:3, 0.5 mL/min), $t_R = 32.9$ (minor) and 61.6 (major); ^{1}H NMR and ^{31}P NMR data were identical to those of (±)-**2c**.

4.15. General procedure for the palladium-catalyzed allylic alkylation

To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.004 mmol, 1.46 mg), chiral aminophosphine ligand **2** (0.008 mmol), and LiOAc (0.004 mmol, 0.26 mg) in a solvent (0.4 mL) were added BSA (0.6 mmol, 0.15 mL) and racemic allylic ester **7** (0.2 mmol, 0.050 mg) at room temperature or −20 °C under an Ar atmosphere. After 30 min, malonate **8** (0.6 mmol) was added at the desired temperature. After 24 or 48 h, the reaction mixture was diluted with diethyl ether and water. The organic layer was washed with brine and dried over $MgSO_4$. The filtrate was concentrated with a rotary evaporator and the residue was purified by column chromatography.

4.15.1. (*R*)-Methyl 2-carbomethoxy-3,5-diphenylpent-4-enonate (*R*)-9a[15c] (Table 1, entry 9)

46%; 99.0% ee; $[\alpha]_D^{20} = +19.2$ (*c* 0.50, $CHCl_3$); HPLC (Daicel CHIRALCEL® OD-H (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/2-propanol = 99:1, 0.13 mL/min), $t_R = 66.1$ (major) and 71.4 min (minor); ^{1}H NMR ($CDCl_3$) δ 3.51 (s, 3H), 3.70 (s, 3H), 3.96 (d, $J = 10.9$ Hz, 1H), 4.27 (dd, $J = 8.4$ and 10.9 Hz, 1H), 6.33 (dd, $J = 8.4$ and 15.8 Hz, 1H), 6.48 (d, $J = 15.8$ Hz, 1H), 7.19–7.32 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 49.2, 52.4, 52.6, 57.6, 126.3, 127.1, 127.5, 127.8, 128.4, 128.7, 129.1, 131.8, 136.8, 140.1, 167.7, 168.2.

4.15.2. (*R*)-Ethyl 2-carboethoxy-3,5-diphenylpent-4-enonate (*R*)-9b[15c] (Table 1, entry 10)

99%; 99.0% ee; $[\alpha]_D^{20} = +16.4$ (*c* 0.50, $CHCl_3$); HPLC (Daicel CHIRALCEL® OD-H (0.46 $\varphi \times 25$ cm, UV 254 nm, *n*-hexane/2-propanol = 95:5, 0.7 mL/min), $t_R = 16.9$ (major) and 21.5 min (minor); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, $J = 7.1$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H), 3.90–4.00 (m, 3H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.26 (dd, $J = 8.4$ and 11.0 Hz, 1H), 6.33 (dd, $J = 8.4$ and 15.8 Hz, 1H), 6.48 (d, $J = 15.8$ Hz, 1H), 7.18–7.31 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 13.7, 14.1, 49.2, 57.7, 61.3, 61.5, 126.3, 127.0, 127.5, 127.9, 128.4, 128.6, 129.3, 131.6, 136.8, 140.2, 167.4, 167.8.

4.16. Preparation of palladium complex 10

To a solution of racemic phosphine (±)-**2a** (20.4 mg, 0.05 mmol) in chloroform (2 mL) was added $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.025 mmol, 9.0 mg) at room temperature. After stirred for 20 min, chloroform (1.3 mL) and hexane (4.0 mL) were added to the solution of palladium complex. After 27 h, the crystals were filtered: 71% as a yellow solid; mp 153–155 °C (dec); 0.025 g, 0.036 mmol, ^{1}H NMR ($CDCl_3$) δ 1.69–2.28 (br m, 1H), 2.90–3.50 (br m, 1H), 3.57 (s, 3H), 4.20–5.25 (br m, 2H), 6.36 (d, J = 1.6 Hz, 1H), 6.81 (dt, J = 0.7 and 8.5 Hz, 1H), 6.84–7.20 (br m, 3H), 7.00 (t, J = 7.2 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 6.77–6.81 (m, 2H), 6.98–7.38 (m, 14H), 7.21–7.65 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 56.0, 57.5 and 59.3, 79.6 and 79.9, 102.5, 113.2 (d, J_{CP} = 35.0 Hz), 114.4 (d, J_{CP} = 1.7 Hz), 116.9, 119.7, 119.9, 121.6, 125.8 (d, J_{CP} = 2.3 Hz), 127.8, 128.3 (d, J_{CP} = 10.5 Hz), 128.5 (d, J_{CP} = 10.4 Hz), 129.6 (d, J_{CP} = 8.3 Hz), 130.4 × 2, 130.8 (d, J_{CP} = 12.2 Hz), 131.2, 133.4, 133.8 (d, J_{CP} = 12.8 Hz), 135.1 (d, J_{CP} = 13.0 Hz), 138.2, 157.8 (d, J_{CP} = 8.3 Hz); ^{31}P NMR ($CDCl_3$) δ 18.3 and 17.7; FAB-MS m/z (relative intensity): 554 (M^+−Cl, 78); HRMS (FAB-MS) m/z calcd for $C_{30}H_{27}ClNOPPd$-Cl 554.0865, found 554.0914; X-ray diffraction analysis data of **10**. Yellow prismatic crystals from n-hexane–chloroform, triclinic space group $P\bar{1}$, a = 9.7238(6) Å, b = 12.4329(8) Å, c = 13.7988(9) Å, α = 104.8890(10)°, β = 100.6320(10)°, γ = 102.5920(10)°, V = 1521.40(17) Å^3, Z = 2, ρ = 1.549 Mg/m^3, μ (Mo Kα) = 1.040 mm^{-1}. The structure was solved by the direct method of full-matrix least-squares, where the final R and Rw were 0.0625 and 0.1692 for 6621 reflections, respectively.

References

1. (a) Bessel, C. A.; Aggarwal, P.; Marschilok, A. C.; Takeuchi, K. J. *Chem. Rev.* **2001**, *101*, 997; (b) Lagasse, F.; Kagan, H. B. *Chem. Pharm. Bull.* **2000**, *48*, 315; (c) Buono, G.; Chiodi, O.; Wills, M. *Synlett* **1999**, 377.
2. Rosini, C.; Eranzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503.
3. Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.
4. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994. Chapter 1.
5. Dai, W.-M.; Yeung, K. K. Y.; Liu, J.-T.; Zhang, Y.; Williams, I. D. *Org. Lett.* **2002**, *4*, 1615.
6. Chen, Y.; Smith, M. D.; Shimizu, K. D. *Tetrahedron Lett.* **2001**, *42*, 7185.
7. (a) Dai, X.; Virgil, S. *Tetrahedron Lett.* **1999**, *40*, 1245; (b) Dai, X.; Wong, A.; Virgil, S. C. *J. Org. Chem.* **1998**, *63*, 2597.
8. (a) Kamikawa, K.; Kinoshita, S.; Furusyo, M.; Takemoto, S.; Matsuzaka, H.; Uemura, M. *J. Org. Chem.* **2007**, *72*, 3394; (b) Kamikawa, K.; Kinoshita, S.; Matsuzaka, H.; Uemura, M. *Org. Lett.* **2006**, *8*, 1097.
9. (a) Vorkapic-Furac, J.; Mintas, M.; Kastner, F.; Mannschreck, A. *J. Heterocycl. Chem.* **1992**, *29*, 327; (b) Adams, R.; Joyce, R. M., Jr. *J. Am. Chem. Soc.* **1938**, *60*, 1491; (c) Bock, L. H.; Adams, R. *J. Am. Chem. Soc.* **1931**, *53*, 374.
10. (a) Mino, T.; Wakui, K.; Oishi, S.; Hattori, Y.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2008**, *19*, 2711; (b) Mino, T.; Tanaka, Y.; Hattori, Y.; Yabusaki, T.; Saotome, H.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 7346; (c) Mino, T.; Tanaka, Y.; Hattori, Y.; Tanaka, M.; Sakamoto, M.; Fujita, T. *Lett. Org. Chem.* **2004**, *1*, 67; (d) Mino, T.; Tanaka, Y.; Yabusaki, T.; Okumura, D.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2003**, *14*, 2503.
11. Mino, T.; Harada, Y.; Shindo, H.; Sakamoto, M.; Fujita, T. *Synlett* **2008**, 614.
12. (a) Cooke, A. S.; Harris, M. M. *J. Chem. Soc. C* **1967**, 988; (b) Cagle, F. W., Jr.; Eyring, H. *J. Am. Chem. Soc.* **1951**, *73*, 5628; (c) Eyring, H. *Chem. Rev.* **1935**, *17*, 65.
13. (a) Trost, B. M. *Chem. Pharm. Bull.* **2002**, *50*, 1; (b) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed., 2nd ed.; VCH Publishers: New York, 2000; p 893; (c) Helmchen, G. *J. Organomet. Chem.* **1999**, *576*, 203; (d) Pfaltz, A.; Lautens, M.. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Tokyo, 1999; Vol. 2, p 833. and references cited therein.
14. (a) Mino, T.; Shiotsuki, M.; Yamamoto, N.; Suenaga, T.; Sakamoto, M.; Fujita, T.; Yamashita, M. *J. Org. Chem.* **2001**, *66*, 1795; (b) Mino, T.; Imiya, W.; Yamashita, M. *Synlett* **1997**, 583.
15. (a) Mino, T.; Sato, Y.; Saito, A.; Tanaka, Y.; Saotome, H.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 7979; (b) Mino, T.; Saito, A.; Tanaka, Y.; Hasegawa, S.; Sato, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 1937; (c) Tanaka, Y.; Mino, T.; Akita, K.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2004**, *69*, 6679; (d) Mino, T.; Tanaka, Y.; Akita, K.; Sakamoto, M.; Fujita, T. *Heterocycles* **2003**, *60*, 9; (e) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 2435; (f) Mino, T.; Tanaka, Y.; Akita, K.; Anada, K.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 1677; (g) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Heterocycles* **2000**, *53*, 1485.