Supporting Information

DESIGN AND SYNTHESIS OF A C₄SYMMETRIC CHIRAL 1,2-BIS(DIPHENYLPHOSPHINO)BENZENE LIGAND VIA RHODIUM-CATALYZED INTRAMOLECULAR [2+2+2] CYCLOADDITION

Fumiya Mori,¹ Keiichi Noguchi,² and Ken Tanaka¹,*

¹ Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

² Instrumentation Analysis Center, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

I. General

Anhydrous CH₂Cl₂ (No. 27,099-7) and (CH₂Cl)₂ (No. 28,450-5) were obtained from Aldrich and used as received. H₈-BINAP, Segphos, (R)-3-butyne-2-ol [(R)-7] were obtained from Takasago International Corporation. Solvents for the synthesis of substrates were dried over Molecular Sieves 4Å (Wako) prior to use. Alkenes 14a and 14b are commercially available. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring.

II. Synthesis of Achiral Diphosphine 6a

Triyne Diphosphine Oxide 4a

To a solution of 1,4-bis(prop-2-ynyloxy)but-2-yne (5.45 g, 33.6 mmol), CuI (0.213 g, 1.12 mmol) and Et₃N (9.37 mL, 67.2 mmol) in toluene (100 mL) was added chlorodiphenylphosphine (4.95 g, 22.4 mmol), and the mixture was stirred at room temperature for 20 h. The reaction was quenched by the addition of water and extracted with EtOAc. The organic layer was washed with saturated aqueous NH₄Cl and brine, dried over Na₂SO₄, and concentrated. The residue was dissolved in CH₂Cl₂ (80 mL) and 30% H₂O₂ (7 mL) was added to this solution at 0 °C. The mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of water and extracted with CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The crude product was purified by a silica gel column chromatography (EtOAc) afforded 4a (2.12 g, 3.77 mmol, 33% yield based on chlorodiphenylphosphine) as a pale yellow oil. The corresponding mono-diphenylphosphinoyl triyne was also generated in 49% yield.

IR (neat) 3076, 3056, 2895, 2853, 2200, 1205 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 7.88–7.78 (m,
8H), 7.58–7.43 (m, 12H), 4.44 (d, J = 3.0 Hz, 4H), 4.30 (s, 4H), $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 132.7, 132.45, 132.42, 131.8, 130.9, 130.8, 128.7, 128.6, 101.8, 101.6, 82.2, 82.0, 80.7 57.4, 56.83, 56.85, 57.4, $^{31}$P (CDCl$_3$, 121 MHz) δ 8.64; HRMS (ESI) calcd for C$_{34}$H$_{28}$O$_4$P$_2$Na [M+Na]$^+$ 585.1355, found 585.1367.

4,5-Bis(diphenylphosphinoyl)-1,3,6,8-tetrahydro-2,7-dioxo-as-indacene (5a: Table 1, entry 2)

A CH$_2$Cl$_2$ (1.0 mL) solution of rac-BINAP (6.2 mg, 0.010 mmol) was added to a CH$_2$Cl$_2$ (0.5 mL) solution of [Rh(cod)$_2$]BF$_4$ (4.1 mg, 0.010 mmol) at room temperature, and the mixture was stirred for 30 min. H$_2$ was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 1 h, the resulting solution was concentrated to dryness and redissolved in CH$_2$Cl$_2$ (0.5 mL). To this solution was added a solution of 4a (56.3 mg, 0.10 mmol) in CH$_2$Cl$_2$ (1.5 mL) at room temperature. After stirring at room temperature for 21 h, the resulting solution was concentrated and purified by a preparative TLC (EtOAc/MeOH = 70:3), which furnished 5a (52.7 mg, 0.094 mmol, 94% yield) as a pale yellow solid. Mp 165.8–167.1 °C; IR (KBr) 3056, 2850, 1437, 1196 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz) δ 7.42 (dd, J = 12.6, 8.0 Hz, 8H), 7.34 (t, J = 7.4 Hz, 4H), 7.23 (t, J = 7.4 Hz, 8H), 5.00 (s, 4H), 4.75 (s, 4H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 146.95, 146.86, 146.8, 144.6, 144.6, 137.7, 137.6, 133.5, 132.6, 131.9, 131.8, 131.5, 127.9, 127.8, 74.9, 70.8; $^{31}$P (CDCl$_3$, 121 MHz) δ 5.02; HRMS (ESI) calcd for C$_{34}$H$_{28}$O$_4$P$_2$Na [M+Na]$^+$ 585.1355, found 585.1357.

4,5-Bis(diphenylphosphanyl)-1,3,6,8-tetrahydro-2,7-dioxo-as-indacene (6a: Scheme 3)

HSiCl$_3$ (0.670 g, 4.91 mmol) and N,N-dimethylaniline (118.0 mg, 0.97 mmol) was stirred in xylene (10 mL) at room temperature for 30 min. The mixture was added to 5a (100.0 mg, 0.177 mmol) in xylene (4 mL) and stirred at 130 °C for 24 h. After the solution was cooled to room temperature, the reaction was quenched by the addition of 1 M aqueous sodium hydroxide and extracted with EtOAc. The organic layer was washed with brine, dried over Na$_2$SO$_4$, and concentrated. The residue was purified by a preparative TLC (hexane/EtOAc = 1:1), which furnished 6a (39.0 mg, 0.074 mmol, 42% yield) as a colorless solid. Mp 87.2–88.9 °C; IR (KBr) 3067, 3051, 2848, 1583, 1479 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) δ 7.33–7.11 (m, 20H), 4.87 (s, 4H), 4.02 (s, 4H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 145.2, 135.3, 135.2, 132.9, 132.7, 132.6, 128.59, 128.55, 128.51, 128.4, 73.3, 71.2; $^{31}$P (CDCl$_3$, 121 MHz) δ –11.0; HRMS (ESI) calcd for C$_{34}$H$_{28}$O$_2$P$_2$Na [M+Na]$^+$ 553.1457, found 553.1461.
III. Synthesis of Chiral Diphosphine 6b

Triyne Diphosphine Oxide [(R,R)-(+-4b: Scheme 4)

To a stirred suspension of NaH (55% in paraffin oil, 0.231 g, 5.30 mmol) in NMP (10 ml) at 0 °C was added an NMP (5 mL) solution of (R)-7 (0.309 g, 4.41 mmol, 98% ee). The mixture was stirred at the same temperature for 1 h, and then 10 (1.22 g, 4.63 mmol) was added. The cold bath was removed, and the solution was stirred for 18 h. The reaction was quenched by the addition of water and saturated aqueous NH₄Cl and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was dissolved in THF (10 mL) and 1M TBAF (6.17 mL) was added to this solution at room temperature. The mixture was stirred at room temperature for 30 min and concentrated. To the residue was added saturated aqueous NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The crude product was purified by a silica gel column chromatography (hexane/EtOAc = 7:1) afforded (R)-11 (0.393 g, 2.84 mmol, 64% yield) as a pale yellow oil.

³¹H NMR (CDCl₃, 300 MHz) δ 4.44–4.341 (m, 2H), 4.336–4.23 (m, 3H), 2.47 (d, J = 2.0 Hz, 1H), 2.15 (s, 1H), 1.47 (d, J = 6.6 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 84.8, 82.6, 81.2, 73.7, 63.9, 55.9, 51.0, 21.8.

To a solution of (R)-11 (0.393 g, 2.84 mmol), CBr₄ (1.13 g, 3.41 mmol) in CH₂Cl₂ (25 mL) was added PPh₃ (1.12 g, 4.26 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h.
The reaction was quenched by the addition of saturated aqueous NH₂Cl and extracted with CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The crude product was purified by a silica gel column chromatography (hexane/EtOAc = 20:1) afforded (R)-12 (0.429 g, 2.13 mmol, 75% yield) as a pale yellow oil.

¹H NMR (CDCl₃, 300 MHz) δ 4.40 (dt, J = 15.8, 2.1 Hz, 1H), 4.37 (dq, J = 6.6, 2.1 Hz, 1H), 4.30 (dt, J = 15.8 Hz, 2.1 Hz, 1H), 3.95 (t, J = 2.1 Hz, 2H), 2.45 (d, J = 2.1 Hz, 1H), 1.47 (d, J = 6.6 Hz, 3H).

To a stirred suspension of NaH (55% in paraffin oil, 80.6 mg, 1.85 mmol) in DMF (5 ml) at 0 °C was added a DMF (2 mL) solution of (R)-7 (0.108 g, 1.54 mmol). The mixture was stirred at the same temperature for 1 h, and then (R)-12 (0.325 g, 1.62 mmol) was added. The cold bath was removed, and the solution was stirred for 3 h. The reaction was quenched by the addition of saturated aqueous NH₂Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The crude product was purified by a silica gel column chromatography (hexane/EtOAc = 20:1) afforded (R,R)-9 (0.239 g, 1.24 mmol, 81% yield) as a colorless solid.

¹H NMR (CDCl₃, 300 MHz) δ 4.44–4.24 (m, 4H), 4.39 (dq, J = 6.6 Hz, 2.0 Hz, 2H), 2.45 (d, J = 2.0 Hz, 2H), 1.47 (d, J = 6.6 Hz, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 82.7, 82.0, 73.6, 63.8, 56.0, 21.8.

To a solution of (R,R)-(−)-9 (0.100 g, 0.520 mmol), CuI (19.8 mg, 0.104 mmol), and Et₃N (0.47 mL, 3.38 mmol) in toluene (5 mL) was added chlorodiphenylphosphine (0.287 g, 1.30 mmol), and the mixture was stirred at room temperature for 20 h. The reaction was quenched by the addition of saturated aqueous NH₂Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was dissolved in CH₂Cl₂ (8 mL) and 30% H₂O₂ (0.5 mL) was added to this solution at room temperature. The mixture was stirred at the same temperature for 3 h. The reaction was quenched by the addition of water and extracted with CH₂Cl₂. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The crude product was purified by a preparative TLC (EtOAc) to afford (R,R)-(−)-4b (0.237 g, 1.23 mmol, 77% yield) as a pale yellow oil.

[α]D²⁵ +202.0° (CHCl₃, c 0.325); IR (neat) 3234, 3059, 2989, 2935, 2188, 1200 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 7.82 (dd, J = 13.7, 6.9 Hz, 8H), 7.58–7.53 (m, 4H), 7.51–7.45 (m, 8H), 4.57 (dq, J = 6.3, 1.5 Hz, 2H), 4.39–4.34 (m, 2H), 4.29–4.23 (m, 2H), 1.54 (d, J = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 133.0, 132.40, 132.38, 132.0, 130.9, 130.8, 128.7, 128.6, 105.5, 105.3, 82.1, 80.7, 79.4, 64.3, 56.6, 21.1; ³¹P (CDCl₃, 202 MHz) δ 8.59; HRMS (ESI) calcd for C₅₀H₃₂O₄P₂Na [M+Na]+ 613.1668, found 613.1685.

Diastereomeric mixture of 4b (Table 2): ¹H NMR (CDCl₃, 500 MHz) δ 7.90–7.72 (m, 8H), 7.64–7.40 (m, 12H), 4.62–4.52 (m, 2H), 4.43–4.32 (m, 2H), 4.31–4.21 (m, 2H), 1.54 (d, J = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 132.9, 132.40, 132.37, 131.9, 130.9, 130.8, 128.7, 128.6, 105.6, 105.4, 82.1, 80.6, 79.3, 64.25, 64.23, 56.6, 21.1; ³¹P (CDCl₃, 202 MHz) δ 8.74.

4,5-Bis(diphenylphosphinoyl)-3,6-dimethyl-1,3,6,8-tetrahydro-2,7-dioxo-as-indacene [(R,R)-(−)-5b: Scheme 5]
A CH₂Cl₂ (1.0 mL) solution of BIPHEP (39.2 mg, 0.075 mmol) was added to a CH₂Cl₂ (1.0 mL) solution of [Rh(cod)₂]BF₄ (30.5 mg, 0.075 mmol) at room temperature, and the mixture was stirred for 30 min. H₂ was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 1 h, the resulting solution was concentrated to dryness and redissolved in CH₂Cl₂ (5.0 mL). To this solution was added a solution of (R,R)-(+)-4b (0.222 g, 0.376 mmol) in CH₂Cl₂ (20.0 mL) at room temperature. After stirring at room temperature for 24 h, the resulting solution was concentrated and purified by a preparative TLC (EtOAc/MeOH = 20:1), which furnished (R,R)-(+)-5b (0.151 g, 0.256 mmol, 68% yield, 98% ee) as a pale yellow solid.

Mp 154.5–155.8 °C; [α]²⁵D +9.40° (CHCl₃, c 0.68, 98% ee); IR (KBr) 3055, 2972, 2926, 1437, 1194 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 7.56–7.46 (m, 7H), 7.42–7.37 (m, 4H), 7.32–7.26 (m, 3H), 7.18–7.13 (m, 2H), 7.06–7.00 (m, 4H), 5.35 (q, J = 6.3 Hz, 2H), 5.05 (d, J = 13.7 Hz, 2H), 4.93 (d, J = 13.7 Hz, 2H), 1.06 (d, J = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 151.8, 151.7, 151.6, 138.2, 135.3, 134.5, 134.1, 133.3, 133.05, 132.97, 132.25, 132.17, 131.8, 131.3, 128.2, 128.1, 127.4, 127.3, 81.4, 68.9, 22.1; ³¹P (CDCl₃, 202 MHz) δ 36.0; HRMS (ESI) calcd for C₃₆H₃₂O₄P₂Na [M+Na]- 613.1668, found 613.1682; CHIRALPAK AD-H, hexane/2-ProH = 80:20, 1.0 mL/min, retention times: 7.0 min (S,S-isomer) and 20.3 min (R,R-isomer).

Diastereomeric mixture of 5b (Table 2): ¹H NMR (CDCl₃, 300 MHz) δ 7.77–7.68 (m, 20H), 5.73–5.56 (m, 1H), 5.35 (q, J = 6.0 Hz, 1H), 5.06 (d, J = 13.5 Hz, 2H), 4.93 (d, J = 13.5 Hz, 2H), 1.06 (d, J = 6.3 Hz, 3H), 0.94 (d, J = 6.3 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 151.7, 151.6, 151.5, 138.2, 138.1, 135.9, 135.2, 135.0, 134.3, 134.1, 133.2, 132.93, 132.88, 132.8, 132.13, 132.08, 132.06, 131.99, 131.96, 131.8, 131.71, 131.67, 131.31, 131.30, 131.2, 128.11, 128.05, 128.0, 127.96, 127.9, 127.8, 127.7, 127.32, 127.27, 127.2, 81.32, 81.29, 68.7, 68.2, 21.9, 20.8; ³¹P (CDCl₃, 202 MHz) δ 36.6.

4,5-Bis(diphenylphosphanyl)-3,6-dimethyl-1,3,6,8-tetrahydro-2,7-dioxo-as-indacene [(R,R)-(+)-6b: Scheme 5]

HSiCl₃ (0.670 g, 4.91 mmol) and iPr₂NH (0.659 g, 5.44 mmol) was stirred in xylene (8 mL) at room temperature for 30 min. One third of the mixture was added to diphosphine oxide 5b (86.4 mg, 0.146 mmol) in xylene (3 mL) and stirred at 120 °C for 15 h. After the solution was cooled to room temperature, the reaction was quenched by the addition of 1 M aqueous sodium hydroxide and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was purified by a preparative TLC (hexane/Et₃N = 7:1), which furnished diphosphine (R,R)-(+)-6b (20.9 mg, 0.037 mmol, 26% yield, 98% ee) as a yellow solid. The ee
value of 6b was determined after oxidation to 5b.

Mp 123.4–125.0 °C; [α]25D +468.4° (CHCl3, c 0.410, 98% ee); IR (KBr) 3069, 3053, 2971, 2925, 1435 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.54–7.16 (m, 20H), 4.92 (d, J = 13.2 Hz, 2H), 4.76 (d, J = 13.2 Hz, 2H), 3.92 (q, J = 6.1 Hz, 2H), 0.88 (d, J = 6.1 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 148.83, 148.81, 148.77, 137.0, 136.9, 136.8, 136.2, 135.2, 134.34, 134.31, 132.7, 132.62, 132.55, 132.1, 132.0, 131.9, 128.6, 128.53, 128.51, 128.45, 128.14, 128.12, 128.10, 79.1, 68.9, 22.5; ³¹P (CDCl₃, 202 MHz) δ −7.46; HRMS (ESI) calcd for C₃₆H₃₂O₂P₂Na [M+Na]⁺ 581.1770, found 581.1794.

IV. Rh-Catalyzed Asymmetric Hydrogenation of Substituted Alkenes

**General procedure (Table 3):** A (CH₂Cl₂)₂ (0.25 mL) solution of ligand (0.0033 mmol) was added to a (CH₂Cl₂)₂ (0.25 mL) solution of [Rh(nbd)₂]BF₄ or [Rh(cod)₂]BF₄ (0.0033 mmol) at room temperature, and the mixture was stirred at room temperature for 15 min. To this solution was added a solution of 13 (0.065 mmol) in (CH₂Cl₂)₂ (0.5 mL) at room temperature, and the solution was stirred at room temperature for 1 h. Then H₂ was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 16 h, the resulting solution was concentrated and passed through a silica gel plug to remove the catalyst. The ee values of the products 14 were determined by chiral HPLC analyses.

2-Acetylaminopropionic acid methyl ester (14a)¹

\[
\begin{align*}
\text{Me-} & \text{CO₂Me} \\
\text{NHAc} &
\end{align*}
\]

CHIRALPAK AD-H, hexane/2-ProH = 90:10, 1.0 mL/min, retention times: 5.6 min (R-isomer) and 7.0 min (S-isomer).

2-Methylsuccinic acid dimethyl ester (14b)¹

\[
\begin{align*}
\text{Me-} & \text{CO₂Me} \\
\text{CO₂Me} &
\end{align*}
\]

CHIRALPAK OD-H, hexane/2-ProH = 98:2, 1.0 mL/min, retention times: 7.6 min (R-isomer) and 12.3 min (S-isomer).

2-Methylbut-2-enoic acid diphenylamide (13c)

To a stirred solution of (E)-2-methylbut-2-enoic acid (1.00 g, 10.0 mmol) in CH₂Cl₂ (5 mL) was added thionyl chloride (1.1 mL, 15 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h, which furnished the corresponding crude acid chloride. The resulting solution was added to a solution of diphenylamine (1.86 g, 11.0 mmol), pyridine (20 mL), and CH₂Cl₂ (5 mL) at 0 °C, and the resulting mixture was stirred at room temperature for 48 h. The reaction was quenched by the addition of aqueous 1N HCl and extracted with CH₂Cl₂. The organic layer was washed with aqueous 1N NaOH and brine, dried over Na₂SO₄, and concentrated. The residue was purified by a
silica gel column chromatography (hexane/EtOAc = 2:1) to give 17c (0.502 g, 2.00 mmol, 20% yield) as a colorless solid. 
Mp 89.3–90.3 °C; IR (KBr) 3063, 3037, 2971, 2921, 1644 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 7.31 (t, J = 7.7 Hz, 4H), 7.19 (t, J = 6.9 Hz, 2H), 7.13 (d, J = 8.0 Hz, 4H), 6.02 (q, J = 6.9 Hz, 1H); 1.63 (s, 3H), 1.55 (d, J = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 173.2, 143.8, 133.1, 132.6, 129.0, 127.1, 126.1, 13.8, 13.6.; HRMS (ESI) calcd for C₁₇H₁₇NONa [M+Na]+ 274.1202, found 274.1200.

(-)-2-Methyl-N,N-diphenyl-butyramide (14c)

Mp 64.4–65.4 °C; IR (KBr) 3089, 2969, 2930, 2871, 1656 cm⁻¹; [α]_D^{25} –100.6° (CHCl₃, c 0.64, 52% ee); ¹H NMR (CDCl₃, 500 MHz) δ 7.58–7.05 (m, 10H), 2.54–2.45 (m, 1H), 1.84–1.70 (m, 1H), 1.44–1.33 (m, 1H), 1.13 (d, J = 6.9 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 177.1, 143.0, 129.7, 128.7, 127.6, 126.5, 125.9, 39.0, 27.7, 17.9, 12.0; HRMS (ESI) calcd for C₁₇H₁₉NONa [M+Na]+ 276.1359, found 276.1366. CHIRALPAK AD-H, hexane/2-ProOH = 98:2, 0.8 mL/min, retention times: 21.8 min [major isomer with (R,R)-10b] and 23.2 min [minor isomer with (R,R)-10b].

V. Reference

Triyne Diphospine Oxide 4a

\[
\text{Ph}_2(\text{O})\text{P} \equiv \equiv \text{O} \\
\text{O} \equiv \equiv \text{P}(\text{O})\text{Ph}_2
\]
Diphosphine oxide 5a
Diphosphine 6a
Chiral Triyne Diphosphine Oxide (R,R)-(+) -4b

\[
\begin{align*}
\text{Ph}_2\text{(O)}\text{P} & \equiv \\
\equiv \quad \equiv \\
\text{Me} & \equiv \quad \equiv \\
P\text{(O)}\text{Ph}_2 \quad \text{P(O)}\text{Ph}_2
\end{align*}
\]
Chiral Diphosphine Oxide \((R,R)-(+)\)-5b
Chiral Diphosphine \((R,R)-(+)\)-6b