A New Air-Stable P-Chiral Phosphine Ligand for Highly Enantioselective Transition-Metal-Catalyzed Reactions

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SUPPORTING INFORMATION

General Experimental Procedures

All solvents used in reactions were dried and purified according to standard procedure. NMR spectra were measured with JEOL JMN-GXS-500 (500 MHz) or JEOL JMN-LA-400 (400 MHz) spectrometer in CDCl₃. Chemical shifts were reported in δ ppm. Optical rotations were measured with JASCO DIP-370 polarimeter. Enantiomeric excesses were determined by HPLC analysis using CHIRALCEL AD, OJ, OD-H columns and varying concentrations of 2-propanol/hexane as the mobile phase.

(*R*)-Benzoyloxymethyl(*t*-butyl)methylphosphine–borane (**3**)

To a stirred, cooled (0 °C) solution of (*R*)-*t*-butyl(hydroxymethyl)methylphosphine–borane (92% ee, 2.22 g, 15.0 mmol) in pyridine (10 mL) was added dropwise benzoyl chloride (2.1 mL, 18 mmol), and the mixture was warmed to room temperature. After 1 h, the reaction mixture was diluted with water and was extracted with ether three times. The collected organic layers were washed with 1 M HCl, aq. NaHCO₃, brine, and dried over Na₂SO₄. The solvent was removed, and the residue was purified by chromatography on silica gel (hexane/EtOAc, 3/1). The colorless solid was recrystallized from a mixed solvent of hexane and EtOAc twice to give optically pure benzoyloxy(*t*-butyl)methylphosphine–borane (**3**) (2.34 g, 62 %) as colorless crystal; mp 89–90 °C; [α]_D²² –4.3 (*c* 1.00, CHCl₃); ¹H NMR (395.75 MHz, CDCl₃): δ 0.14–0.84 (br m, 3H), 1.27 (d, *J* = 14.2 Hz, 9H), 1.39 (d, *J* = 10.0 Hz, 3H), 4.71–4.79 (m, 2H), 7.47 (t, *J* = 8.0 Hz, 2H), 7.61 (tt, *J* = 7.6, 1.2 Hz, 1H), 8.04 (dd, *J* = 8.5, 1.0 Hz, 2H); ¹³C NMR (99.45 MHz, CDCl₃): δ 3.42 (d, *J* = 34.6 Hz), 25.51 (d, *J* = 2.4 Hz), 27.57 (d, *J* = 32.1 Hz), 57.85 (d, *J* = 35.5 Hz), 128.61, 128.89, 129.68, 133.58, 165.77 (d, *J* = 4.1 Hz); ³¹P NMR (202.35 MHz, CDCl₃): δ 28.0–29.1 (m); HRMS (FAB) calcd for C₁₃H₂₁BO₂P (M⁺–H) 251.1375, found 251.1378. Anal. Calcd for C₁₃H₂₂BO₂P: C, 61.94; H, 8.80. Found: C, 61.94; H, 8.76.

(*S*)-*t*-Butylmethylphosphine–borane (**4**)

To a stirred solution of benzoyloxymethyl(*t*-butyl)methylphosphine–borane (**3**) (>99% ee, 6.05 g, 24.0 mmol) in ethanol (25 mL) was added a solution of potassium hydroxide (4.0 g, 72 mmol) in water (15 mL) dropwise. After completion of the hydrolysis (ca. 1 h), the reaction mixture was diluted with water and extracted with ether three times. The combined extracts were washed with brine and dried over Na₂SO₄. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography on silica gel (hexane/EtOAc = 3/1) to give (*R*)-*t*-butyl(hydroxymethyl)methylphosphine–borane (**2**). This compound was dissolved in acetone (72 mL) and the solution was slowly added to a vigorously stirred, cooled (0 °C) solution of potassium hydroxide (13.5 g, 240 mmol), potassium persulfate (19.4 g, 72.0 mmol), and ruthenium trichloride trihydrate (624 mg, 2.4 mmol) in water (150 mL). After 2 h, the reaction mixture was neutralized with 3 M HCl and was extracted with ether three times. The combined extracts were washed with brine, and dried over Na₂SO₄. The solvent was removed on a rotary evaporator at room temperature, and the residue was purified by chromatography on silica gel (pentane/ether = 8/1) to give (*R*)-*t*-butylmethylphosphine–borane (**4**) (2.27 g, 80 %).

(*R,R*)-2,3-Bis(*t*-butylmethylphosphino)quinoxaline (**1**)

A solution of *n*-BuLi (1.25 mL of 1.60 M hexane solution, 2.0 mmol) was added dropwise to a stirred solution of *t*-butylmethylphosphine–borane (**4**) (236 mg, 2.0 mmol) in THF (4 mL) at –78 °C under nitrogen. After 15 min, a solution of 2,3-dichloroquinoxaline (133 mg, 0.67 mmol) in THF (4 mL)¹ was added in one portion with vigorous stirring and the mixture was warmed to room temperature during 1 h. After stirring for an additional 3 h, tetramethylethylenediamine (1 mL) was added and stirring was continued for 2 h. The reaction was quenched with 1 M HCl and the mixture was extracted with hexane. The combined extracts were washed with 1 M HCl and brine, and dried over Na₂SO₄. The solvent was removed in vacuum and the residue was purified by chromatography on silica gel (hexane/EtOAc = 30/1) to give 2,3-bis(*t*-butylmethylphosphino)quinoxaline (**1**) (179 mg, 80 %) as an orange solid, which was further purified by recrystallization from hot MeOH (1.7 mL) to give orange cubes; mp 102–103 °C; [α]_D²² –54.3 (*c* 1.00, CHCl₃); ¹H NMR (395.75 MHz, CDCl₃): δ 1.00–1.03 (m, 18H), 1.42–1.44 (m, 6H), 7.70–7.74 (m, 2H), 8.08–8.12 (m, 2H); ¹³C NMR (99.45 MHz, CDCl₃): δ

4.77 (t, $J = 4.1$ Hz), 27.59 (t, $J = 7.4$ Hz), 31.90 (t, $J = 7.4$ Hz), 129.50, 129.60, 141.63, 165.12 (dd, $J = 5.7, 2.4$ Hz); ^{31}P NMR (202.35 MHz, CDCl_3): δ -17.7 (s); IR (KBr) 2950, 1470, 780 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{18}\text{H}_{29}\text{N}_2\text{P}_2$ ($\text{M}^+ + \text{H}$) 335.1809, found 335.1826. Anal. Calcd for $\text{C}_{18}\text{H}_{28}\text{N}_2\text{P}_2$: C, 64.66; H, 8.44. Found: C, 64.57; H, 8.29.

In order to determine the enantiomeric excess of this phosphine ligand, it was converted into diphosphine disulfide derivative (**5**) by treatment with excess sulfur in refluxing hexane for 20 h. The product was isolated by preparative TLC (hexane/AcOEt = 5 : 1) and the ee of the compound was determined to be >99% using HPLC analysis on a CHIRALCEL AD column. $i\text{PrOH/hexane} = 1: 99$, flow rate: 1 mL/min (retention times: 10.3, 17.1 min).

General Procedure for Rhodium-Catalyzed Asymmetric Hydrogenation (Reactions were carried out in a similar procedure described in the literatures.²)

A 50 mL hydrogenation tube was charged with 0.5 mmol of substrate. The tube was connected to the hydrogen tank via stainless steel tubing. The vessel was evacuated and filled with 1 atm of hydrogen gas (Nippon Sanso, 99.9999%). A solution of $[\text{Rh}(\text{nbd})_2]\text{BF}_4$ (1.9 mg, 5.0 μmol) and (*R,R*)-2,3-bis(*t*-butylmethylphosphino)quinoxaline (**1**) (2.0 mg, 6.0 μmol) in degassed MeOH (1 mL) was added via a syringe to the tube, and the hydrogen pressure was increased to 3 atm. The reaction mixture was evaporated and the residue was purified by flash chromatography on silica gel using EtOAc as an eluent. The absolute configurations and ee values of the products were determined by comparison of the retention times with reported values.²

General Procedure for Rhodium-Catalyzed Asymmetric 1,4-Addition of Organoboronic Acid to Enone (Reactions were carried out in a similar procedure described in the literature.³)

A solution of $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ (1.5 mg, 4.5 μmol) and (*R,R*)-2,3-bis(*t*-butylmethylphosphino)quinoxaline (**1**) (3.3 mg, 9.9 μmol) in dioxane (1 mL) was stirred at room temperature for 15 min under nitrogen. To the reaction mixture was added KOH (0.1 mL, 1.5M, 0.15 mmol) in water and the solution was stirred for 15 min. Arylboronic acid (0.60 mmol) and α,β -unsaturated carbonyl compound (0.30 mmol) was added to the solution. After stirring at 40 $^\circ\text{C}$ for 1 h, the reaction mixture was quenched with saturated NaHCO_3 and extracted with ether five times. The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by preparative TLC (silica gel, hexane/EtOAc = 3/1).

The absolute configurations and ee values of the products were determined by comparison

of the retention times with reported values.⁴

General Procedure for the Alkylating Ring Opening of Oxabenzonorbornadiene Derivatives (Reactions were carried out in a similar procedure described in the literature.⁵)

A solution of PdCl₂(cod) (7.1 mg, 0.025 mmol) and (*R,R*)-2,3-bis(*t*-butylmethylphosphino)quinoxaline (**1**) (8.3 mg, 0.025 mmol) in CH₂Cl₂ (1 mL) was stirred at room temperature under nitrogen for 2 h. To the solution was added a solution of oxabenzonorbornadiene (0.5 mmol) in CH₂Cl₂ (15 mL), followed by dimethylzinc (0.75 mL of 1.0 M hexane solution) or diethylzinc (0.75 mL of 1.0 M hexane solution). The resulting solution was stirred at room temperature until completion of the reaction. The reaction was quenched by the addition of a few drops of water and the mixture was passed through a short plug of Celite and then concentrated. The residue was purified by preparative TLC (hexane/EtOAc).

The absolute configurations and ee values of the products were determined by comparison of the retention times with reported values.⁵

References

- (1) Use of diethylene glycol dimehyl ether as the solvent gave a similar result.
- (2) Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 1635–1636; Gridnev, I. D.; Yamanai, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Catal.* **2001**, *343*, 118–136; Gridnev, I. D.; Yasutake, M.; Higashi, N.; Imamoto, T. *J. Am. Chem. Soc.* **2001**, *123*, 5268–5276; Yasutake, M.; Gridnev, I. D.; Higashi, N.; Imamoto, T. *Org. Lett.* **2001**, *3*, 1701–1704.
- (3) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2002**, *125*, 11508–11509.
- (4) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579; Takaya, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron Lett.* **1999**, *40*, 6957–6961.
- (5) Lautens, M.; Renaud, J.-L.; Hiebert, S. *J. Am. Chem. Soc.* **2000**, *122*, 1804–1805.

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