A Chiral Chelating Diene as a New Type of Chiral Ligand for Transition Metal Catalysts. Its Preparation and Use for the Rhodium-Catalyzed Asymmetric 1,4-Addition

Tamio Hayashi,* Kazuhito Ueyama, Norihito Tokunaga, and Kazuhiro Yoshida

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

Supporting Information

General. NMR spectra were recorded on a JEOL JNM LA-500 spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal SiMe_4 standard for ^1H NMR and chloroform- d (δ 77.05) for ^{13}C NMR. Optical rotations were measured on a JASCO DIP-370 polarimeter.

Materials. THF, Et_2O , and dioxane were distilled from sodium benzophenone-ketyl under nitrogen. $\text{PdCl}_2(\text{dppf})$,¹ N -(2-pyridyl)triflimide,² and $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ ³ were prepared according to the reported procedures. Benzylmagnesium bromide was prepared in a standard manner by adding slowly a solution of benzyl bromide in Et_2O to magnesium ribbon that had been dried in a rapid stream of dry nitrogen by flaming. Diisopropylamine, $n\text{-BuLi}$ in hexane, phenyltrimethylstannane (**6m**), and NaOMe were purchased. Phenylboronic acid (**3m**) was purchased and other boronic acids were prepared according to the reported procedures.⁴ 2-Cyclohexenone (**2a**), 2-cyclopentenone (**2b**), and 2-cycloheptenone (**2c**) were purchased and distilled before use. 5-Methyl-3-hexen-2-one (**2d**) was purchased and used without further purification. 2-Propyl 4-methyl-*trans*-2-pentenoate (**2e**) was prepared by esterification of 4-methyl-*trans*-2-pentenoic acid with 2-propanol. (1*R*,2*S*,4*R*,5*S*)-Bicyclo[2.2.1]heptan-2,5-diol (**A**) was prepared from bicyclo[2.2.1]hepta-2,5-diene by the asymmetric hydrosilylation with trichlorosilane catalyzed by the palladium/(*R*)-MeO-MOP complex followed by the hydrogen peroxide oxidation in a manner similar to the reported procedures.⁵ (1*R*,4*R*)-Bicyclo[2.2.1]heptan-2,5-dione (**B**) was prepared from the diol **A** by the Swern oxidation according to the reported procedures.⁶ (1*R*,4*R*)-Spiro[bicyclo[2.2.1]heptan-5-one-2,2'-

[1,3]dioxolane] (**C**) was prepared from (1*R*,4*R*)-diketone **B** according to the reported procedures.⁷

(1*R*,4*R*)-Spiro[5-trifluoromethanesulfonyloxybicyclo[2.2.1]hept-5-ene-2,2'-[1,3]dioxolane] (D**).** LDA was generated by dropwise addition of a 1.59M solution of *n*-BuLi (4.18 mL, 6.64 mmol) in hexane to a -78 °C solution of diisopropylamine (929 µL, 6.63 mmol) in 12 mL of THF. This solution was stirred for additional 20 minutes before a solution of acetal (1*R*,4*R*)-**C** (784 mg, 4.66 mmol) in 8 mL of THF was slowly added at -78 °C. The resulting mixture was stirred at -78 °C for additional 1 hour, before a solution of *N*-(2-pyridyl)triflimide (2.38 g, 6.64 mmol) in 20 mL of THF was slowly added at -78 °C. This mixture was warmed to room temperature while stirred overnight. Ice water (10 mL) was added to quench the reaction and the organic solvent was removed *in vacuo*. The aqueous layer was extracted with Et₂O three times. The combined organic layers were washed with 10% NaOH (5 mL x 2) and then dried over magnesium sulfate. Removal of the solvent gave the crude product, which was purified by chromatography on silica gel column (hexane/CHCl₃ = 1/4) to give 1.40 g (81% yield) of the triflate **D**. ¹H NMR (CDCl₃): δ 1.80-1.86 (m, 2H), 1.97 (dq, *J* = 9.1, 1.8 Hz, 1H), 2.00 (dd, *J* = 12.8, 3.7 Hz, 1H), 2.76 (dq, *J* = 3.5, 1.8 Hz, 1H), 2.91 (br m, 1H), 3.88-4.04 (m, 4H), 5.74 (d, *J* = 3.5 Hz, 1H). ¹³C{¹H} NMR (CDCl₃): δ 39.22, 43.02, 47.86, 49.01, 64.68, 65.08, 117.56, 118.05, 118.58 (q, *J* = 319 Hz), 158.50. Anal. Calcd for C₁₀H₁₁O₅SF₃: C, 40.00; H, 3.69. Found: C, 39.92; H, 3.64.

(1*R*,4*R*)-Spiro[5-benzylbicyclo[2.2.1]hept-5-ene-2,2'-[1,3]dioxolane] (E**).** To a mixture of triflate (1*R*,4*R*)-**D** (97.0 mg, 0.32 mmol) and PdCl₂(dppf) (2.6 mg, 3.6 µmol) in 1.0 mL of Et₂O was added benzylmagnesium bromide (0.58 mL, 1.9M, 1.1 mmol) in Et₂O at room temperature, and the reaction mixture was heated to reflux overnight. After cooled to room temperature, the reaction mixture was quenched with water, and extracted with Et₂O. The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The residue was purified by preparative TLC (silica gel, hexane/EtOAc = 2/1) to give 76.1 mg (97% yield) of **E**. ¹H NMR (CDCl₃): δ 1.38 (dd, *J* = 12.4, 3.1 Hz, 1H), 1.65-1.74 (m, 2H), 1.82 (dd, *J* = 12.4, 3.8 Hz, 1H), 2.57 (br m, 1H), 2.62 (dq, *J* = 2.9, 1.6 Hz, 1H), 3.38 (dd, *J* = 15.8, 1.5 Hz, 1H), 3.51 (d, *J* = 15.8 Hz, 1H), 3.86-3.98 (m, 4H), 5.65 (br m, 1H), 7.17-7.22 (m, 3H), 7.26-7.32 (m, 2H). ¹³C{¹H} NMR (CDCl₃): δ 36.91, 39.85, 43.69, 48.68, 49.99, 64.28, 64.77, 119.44, 126.04, 126.28, 128.31, 128.96, 139.07, 152.49. Anal. Calcd for C₁₆H₁₈O₂: C, 79.31; H, 7.49. Found: C, 79.55; H, 7.62.

(1*R*,4*R*)-2-Benzyl[2.2.1]hept-2-en-5-one (F**).** To a solution of (1*R*,4*R*)-**E** (5.10 g, 21.0 mmol) in 40 mL of THF was added 10 mL of 2.0*N* HCl. The reaction mixture was stirred at room temperature overnight, and neutralized by 10 mL of ca.2*N* NaOH. The organic solvent was removed *in vacuo*, and the residue was extracted with Et₂O three times. The combined organic layers were dried over magnesium sulfate and concentrated under

reduced pressure. The residue was purified by chromatography on silica gel column (hexane/EtOAc = 4/1) to give 3.91 g (94% yield) of **F**. ^1H NMR (CDCl_3): δ 1.63 (dd, J = 16.5, 4.4 Hz, 1H), 1.90 (dd, J = 16.5, 3.3 Hz, 1H), 1.90 (d, J = 8.8 Hz, 1H), 2.15 (dddd, J = 8.8, 4.2, 2.5, 1.5 Hz, 1H), 2.88 (br m, 1H), 2.98 (dq, J = 3.2, 1.6 Hz, 1H), 3.47 (dd, J = 19.1, 1.7 Hz, 1H), 3.50 (dd, J = 19.1, 1.4 Hz, 1H), 5.58 (br m, 1H), 7.16 (d, J = 7.2 Hz, 2H), 7.22 (tt, J = 7.2, 1.4 Hz, 1H), 7.29 (t, J = 7.2 Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 37.14, 37.49, 42.95, 49.93, 56.25, 122.86, 126.48, 128.54, 128.92, 137.54, 156.65, 214.87. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}$: C, 84.81; H, 7.12. Found: C, 85.05; H, 7.36.

(1*R*,4*R*)-2-Benzyl-5-trifluoromethanesulfonyloxybicyclo[2.2.1]hepta-2,5-diene (G). Triflation of (1*R*,4*R*)-**F** was carried out in a manner similar to that of (1*R*,4*R*)-**C**. To a -78 °C solution of diisopropylamine (4.2 mL, 30.0 mmol) in 40 mL of THF was added a 1.58M solution of *n*-BuLi (19.6 mL, 31.0 mmol) in hexane. To this reaction mixture were added a solution of (1*R*,4*R*)-**F** (3.91 g, 19.7 mmol) in 20 mL of THF and a solution of *N*-(2-pyridyl)triflimide (10.7 g, 30.0 mmol) in 40 mL of THF. After work-up, the crude product was purified by chromatography on silica gel column (hexane/EtOAc = 4/1) to give 4.55 g (70% yield) of **G**. ^1H NMR (CDCl_3): δ 2.20 (dt, J = 6.1, 1.8 Hz, 1H), 2.31 (dt, J = 6.1, 1.5 Hz, 1H), 3.22 (br m, 1H), 3.39 (qt, J = 3.1, 1.7 Hz, 1H), 3.52 (dd, J = 15.7, 1.4 Hz, 1H), 3.59 (d, J = 15.7 Hz, 1H), 6.11 (d, J = 3.1 Hz, 1H), 6.35 (dq, J = 3.0, 1.7 Hz, 1H), 7.09 (d, J = 7.2 Hz, 2H), 7.21 (tt, J = 7.2, 1.2 Hz, 1H), 7.28 (t, J = 7.2 Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 37.65, 51.48, 51.50, 71.97, 118.56 (q, J = 320 Hz), 124.87, 126.35, 128.45, 128.93, 133.02, 137.80, 158.05, 167.46. Anal. Calcd for $\text{C}_{15}\text{H}_{13}\text{O}_3\text{SF}_3$: C, 54.54; H, 3.97. Found: C, 55.06; H, 4.07.

(1*R*,4*R*)-2,5-Dibenzylbicyclo[2.2.1]hepta-2,5-diene (1). Grignard cross-coupling of triflate **G** with benzylmagnesium bromide was carried out in a manner similar to that of (1*R*,4*R*)-**D**. To a mixture of triflate (1*R*,4*R*)-**G** (66.2 mg, 0.20 mmol) and $\text{PdCl}_2(\text{dppf})$ (1.5 mg, 2.0 μmol) in 0.5 mL of Et_2O was added benzylmagnesium bromide (0.32 mL, 1.9M, 1.1 mmol) in Et_2O at room temperature, and the reaction mixture was heated to reflux overnight. After work-up, the residue was purified by preparative TLC (silica gel, benzene/ CHCl_3 = 1/4) and GPC to give 24.7 mg (45% yield) of **1**. ^1H NMR (CDCl_3): δ 1.94 (t, J = 1.7 Hz, 2H), 3.14 (dt, J = 3.8, 1.7 Hz, 2H), 3.49 (s, 4H), 6.02 (dt, J = 3.8, 1.6 Hz, 2H), 7.09 (d, J = 7.2 Hz, 4H), 7.18 (tt, J = 7.2, 1.2 Hz, 2H), 7.26 (t, J = 7.2 Hz, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 38.00, 53.17, 71.44, 125.89, 128.17, 128.99, 134.31, 139.16, 156.96. $[\alpha]_D^{20} +217$ (c 1.02, CHCl_3). Anal. Calcd for $\text{C}_{21}\text{H}_{20}$: C, 92.60; H, 7.40. Found: C, 92.47; H, 7.47.

Preparation of $[\text{RhCl}((1*R*,4*R*)-\mathbf{1})_2]$. In an NMR sample tube, $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ (1.8 mg, 9.0 μmol Rh) and (1*R*,4*R*)-**1** (2.7 mg, 9.9 μmol) were charged and CDCl_3 (0.5 mL) was added at 25 °C. Within 1 h, $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ was converted into $[\text{RhCl}((1*R*,4*R*)-\mathbf{1})_2]$. ^1H

NMR (CDCl₃): δ 0.76 (s, 4H), 3.07 (d, J = 14.4 Hz, 4H), 3.50 (s, 4H), 3.75 (d, J = 14.4 Hz, 4H), 3.79 (s, 4H), 7.17-7.47 (m, 20H).

Rhodium-catalyzed asymmetric 1,4-addition of boronic acid **3 or boroxine **4** to enone **2**.** The reaction conditions and results are summarized in Table 1. A typical experimental procedure is shown below: A solution of [RhCl(C₂H₄)₂]₂ (1.8 mg, 9.0 μ mol Rh) and (1*R*,4*R*)-**1** (2.7 mg, 9.9 μ mol) in 1 mL of dioxane was stirred at room temperature for 15 minutes. To this reaction mixture was added KOH (0.1 mL, 1.5M, 0.15 mmol) in water, and the solution was stirred for 15 minutes. Subsequently, phenylboronic acid (**3m**) (73.1 mg, 0.60 mmol) and 2-cyclohexenone (**2a**) (28.8 mg, 0.30 mmol) was added to this solution. After stirring at 30 °C for 1 h, the reaction mixture was quenched with saturated NaHCO₃ in water and extracted with Et₂O five times. The combined organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The residue was purified by preparative TLC (silica gel, hexane/EtOAc = 3/1) to give 49.5 mg (94% yield) of (*R*)-**5am** which is 96% ee. The products **5** obtained by the rhodium-catalyzed asymmetric 1,4-addition were fully characterized by comparison of their spectral and analytical data with those reported in the literature: Ref. 8 for **5am**, **5an**, **5ap**, **5aq**, **5ar**, **5au**, **5bm**, **5bu**, **5cm**, **5dm**. Ref. 9 for **5ao**, **5at**. Ref. 10 for **5as**. Ref. 11 for **5em**.

Rhodium-catalyzed asymmetric 1,4-addition of phenyltrimethylstannane (6m**) to 2-cyclohexenone (**2a**).** [RhCl(C₂H₄)₂]₂ (1.8 mg, 9.0 μ mol) and (1*R*,4*R*)-**1** (2.7 mg, 9.9 μ mol) in 0.5 mL of toluene-*d*₈ was stirred at room temperature for 15 minutes. To this reaction mixture was added NaOMe (1.0 mg, 18.5 μ mol), and the solution was stirred for 15 minutes. Subsequently, phenyltrimethylstannane (**6m**) (79.5 mg, 0.33 mmol) and 2-cyclohexenone (**2a**) (28.8 mg, 0.30 mmol) was added to this solution. The mixture was heated at 60 °C for 22 h. ¹H and ¹³C NMR showed the formation of stannyl enol ether **7**. The reaction mixture was filtered through a short-pass silica gel column. Removal of the solvent gave the hydrolyzed crude product **5am**. Preparative TLC on silica gel (hexane/EtOAc = 3/1) gave 42.0 mg (80% yield) of (*R*)-**5am** which is 95% ee. **(*R*)-3-Phenyl-1-trimethylstannyloxycyclohex-1-ene (**7**):** ¹H NMR (toluene-*d*₈): δ 0.26 ($J_{119\text{Sn-H}} = 58.0$ Hz, $J_{117\text{Sn-H}} = 55.0$ Hz, 9H), 1.39-1.48 (m, 1H), 1.55-1.65 (m, 1H), 1.69-1.78 (m, 1H), 1.84-1.93 (m, 1H), 2.01-2.30 (m, 2H), 3.51-3.56 (m, 1H), 4.52-4.56 (m, 1H), 7.07 (tt, $J = 7.8, 1.3$ Hz, 1H), 7.20 (t, $J = 7.8$ Hz, 2H), 7.27 (d, $J = 7.8$ Hz, 2H). ¹³C{¹H} NMR (toluene-*d*₈): δ -3.88, 22.42, 31.60, 33.80, 42.62, 101.06, 126.03, 128.04, 128.43, 148.96, 158.32.

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