Ruthenium-Catalyzed Asymmetric Hydrogenation of *N*-Boc-Indoles

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Supporting Information

General and Materials. Optical rotations were measured with a JASCO P-1020 polarimeter. NMR spectra were measured with a Bruker AVANCE 400 (9.4 T magnet) spectrometer. IR spectra were measured with a Nicolet Magna 560. ESI-MS spectrum was measured with a Perkin-Elmer Sciex API 300 triple-quadrupole mass spectrometer in the positive detection mode. Elemental analyses were performed by Service Centre of Elementary Analysis of Organic Compounds in Kyushu University. Flush column chromatographies and medium-pressure liquid chromatographies (MPLC) were performed with silica gel 60 (230–400 mesh, Merck) and C.I.G. pre-packed column CPS-223L-1 (Kusano, Tokyo, Japan), respectively.

2-Propanol, acetonitrile, *N,N*-dimethylformamide (DMF), triethylamine, diisopropylamine were dried with calcium hydride. Methanol, ethanol, and dichloromethane were dried with Mg(OMe)₂, Mg(OEt)₂, and P₂O₅, respectively. These solvents and reagents were distilled under nitrogen atmosphere. THF (HPLC grade, without inhibitor) was deoxidized by purging with nitrogen for 30 min and dried with an alumina column system (GlassContour Co.). Indoles were commercially available unless otherwise noted, and were used without further purification. (*S,S*)-(*R,R*)-PhTRAP,¹ [RuCl₂(*p*-cymene)]₂,² [RuCl₂(benzene)]₂,² Ru(η^3 -2-methylallyl)₂(cod),³ and **1h**⁴ were prepared according to literature procedures. These ruthenium catalyst precursors were purchasable from STREM or Aldrich. All other materials were commercially available and were used without further purification.

Preparations of *N*-Boc-Indoles.

***N*-(*tert*-Butoxycarbonyl)-2-methylindole (**1a**).**⁵ Compound **1a** was prepared by modified Gilchrist's procedure.⁵ Under nitrogen atmosphere, (Boc)₂O (*d* 0.95 g/ml, 13.7 ml, 60 mmol) was added to a solution of 2-methylindole (7.17 g, 55 mmol) and 4-(*N,N*-dimethylamino)pyridine (DMAP) (195 mg, 1.6 mmol) in dry acetonitrile (10 ml) at room temperature. The solution was stirred at room temperature for 22 h, and then was evaporated under reduced pressure. After water was added, the resulting mixture was extracted twice with EtOAc. The combined organic layer was washed with brine, was dried with MgSO₄, and was evaporated under reduced pressure. The residue was purified with a flush column chromatography (EtOAc/hexane = 1/50) to give **1a** (9.85 g, 78%) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.68 (s, 9H), 2.59 (s, 3H), 6.31 (s, 1H), 7.15–7.24 (m, 2H), 7.43 (d, *J* = 7.1 Hz, 1H), 8.10 (d, *J* = 8.1 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 17.1, 28.3, 83.6, 107.9, 115.4, 119.5, 122.5, 123.1, 129.4, 136.5, 137.8, 150.7.

***N*-(*tert*-Butoxycarbonyl)-5-methoxy-2-methylindole (1b).** The procedure for the preparation of **1a** was followed with 5-methoxy-2-methylindole (645 mg, 4.0 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/10) to give **1b** (901 mg, 98%) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.67 (s, 9H), 2.57 (s, 3H), 3.83 (s, 3H), 6.24 (s, 1H), 6.82 (dd, *J* = 2.6, 9.0 Hz, 1H), 6.91 (d, *J* = 2.6 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 17.2, 28.3, 55.6, 83.4, 102.4, 107.8, 111.4, 116.2, 130.2, 131.2, 138.5, 150.6, 155.7; IR (thin film) 1729 cm⁻¹; Anal. Calcd for C₁₅H₁₉NO₃: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.09; H, 7.30; N, 5.43.

***N*-(*tert*-Butoxycarbonyl)-5-fluoro-2-methylindole (1c).**⁶ The procedure for the preparation of **1a** was followed with 5-fluoro-2-methylindole (1.49 g, 10 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/20) to give **1c** (2.44 g, 98%) as a pale yellow solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.67 (s, 9H), 2.58 (s, 3H), 6.27 (s, 1H), 6.93 (dt, *J* = 2.6, 9.2 Hz, 1H), 7.07 (dd, *J* = 2.6, 8.8 Hz, 1H), 8.04 (dd, *J* = 4.7, 9.1 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 17.2, 28.2, 83.9, 104.9 (d, *J* = 24 Hz), 107.7 (d, *J* = 4 Hz), 110.5 (d, *J* = 25 Hz), 116.3 (d, *J* = 9 Hz), 130.2 (d, *J* = 10 Hz), 132.8, 139.5, 150.4, 159.2 (d, *J* = 159 Hz).

***N*-(*tert*-Butoxycarbonyl)-2-butylinidole (1d).**⁷ The procedure for the preparation of **1a** was followed with 2-butylinidole⁸ (867 mg, 5.0 mmol). The crude product was purified with a flush column chromatography (hexane) to give **1d** (1078 mg, 79%) as pale yellow oil: ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.97 (t, *J* = 7.3 Hz, 3H), 1.44 (sextet, *J* = 7.4 Hz, 2H), 1.63–1.74 (m, 2H), 1.68 (s, 9H), 3.00 (t, *J* = 7.6 Hz, 2H), 6.34 (s, 1H), 7.15–7.24 (m, 2H), 7.44 (d, *J* = 7.1 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 14.0, 22.5, 28.2, 29.9, 31.0, 83.6, 106.9, 115.5, 119.6, 122.5, 123.1, 129.4, 136.6, 142.5, 150.6.

***N*-(*tert*-Butoxycarbonyl)-2-cyclohexylinidole (1e).** Under nitrogen atmosphere, diisopropylamine (610 mg, 6.0 mmol) and cyclohexylacetylene (660 mg, 6.1 mmol) was added to a solution of 2-bromonitrobenzene (1013 mg, 5.0 mmol), CuI (9.6 mg, 50 μmol), PdCl₂(MeCN)₂ (25.9 mg, 0.10 mmol), and tri(*tert*-butyl)phosphonium tetrafluoroborate (58.0 mg, 0.20 mmol) in dry THF (5 ml) at room temperature. The solution was stirred at room temperature for 24 h. After 1 *N* HCl *aq.* was added, the resulting mixture was extracted five times with EtOAc. The combined organic layer was washed with brine, was dried with Na₂SO₄, and was evaporated under reduced pressure. Hydrazine monohydrate (7.83 g, 156 mmol) was added dropwise for 30 min to a suspension of the residue, FeCl₃·6H₂O (150 mg, 0.56 mmol), and activated carbon (1.43 g) in methanol (70 ml) under reflux. After 10 min, the boiling mixture was filtered. The filtrate was evaporated under reduced pressure. The residue was purified with a flush column chromatography (EtOAc/hexane = 1/20) to give 2-(2-cyclohexylethynyl)aniline (973 mg, 97%): ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.34–1.92 (m, 10H), 2.68 (tt, *J* = 4.0, 8.8 Hz, 1H), 7.38 (dt, *J* = 1.5, 7.8 Hz, 1H), 7.51 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.57 (dd, *J* = 1.5, 7.8 Hz, 1H), 7.96 (dd, *J* = 1.2, 8.3 Hz, 1H). Under nitrogen atmosphere, the resulting product (973 mg, 4.9 mmol) was diluted with dry THF (10 ml), and then sodium tetrachloroaurate dihydrate (99 mg, 0.25 mmol) was added to the THF solution. The solution was stirred under reflux for 1.5 h. After the mixture was filtered through a Celite pad, the filtrate was evaporated under reduced pressure. The residue was purified with a flush column chromatography (EtOAc/hexane = 1/50) to give 2-cyclohexylinidole (751 mg, 77%): ¹H NMR

(400 MHz, CDCl₃, TMS) δ 1.22–1.53 (m, 5H), 1.72–1.79 (m, 1H), 1.82–1.89 (m, 2H), 2.05–2.12 (m, 2H), 2.72 (tt, J = 11.1, 3.3 Hz, 1H), 6.23 (t, J = 1.0 Hz, 1H), 7.06 (dt, J = 1.2, 7.5 Hz, 1H), 7.11 (dt, J = 1.4, 7.5 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.90 (br s, 1H). The procedure for the preparation of **1a** was followed with the resulting indole (751 mg, 3.8 mmol). The crude product was purified with a flush column chromatography (hexane) to give **1e** (943 mg, 84%) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.21–1.53 (m, 5H), 1.69 (s, 9H), 1.73–1.89 (m, 3H), 2.07–2.14 (m, 2H), 3.35 (tt, J = 3.0, 11.4 Hz, 1H), 6.37 (s, 1H), 7.14–7.24 (m, 2H), 7.45 (d, J = 6.9 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 26.4, 26.6, 28.3, 33.7, 37.4, 83.6, 104.8, 115.5, 119.8, 122.5, 123.1, 129.4, 136.7, 148.0, 150.6; IR (thin film) 1732 cm⁻¹; Anal. Calcd for C₁₉H₂₅NO₂: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.16; H, 8.41; N, 4.72.

N-(tert-Butoxycarbonyl)-2-phenylindole (1f).⁹ The procedure for the preparation of **1a** was followed with 2-phenylindole (1.93 g, 10.0 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/50) to give **1f** (2.94 g, quant.) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.30 (s, 9H), 6.55 (s, 1H), 7.25 (t, J = 7.4 Hz, 1H), 7.30–7.44 (m, 6H), 7.55 (d, J = 7.7 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 27.5, 83.4, 109.9, 115.2, 120.4, 122.9, 124.3, 127.5, 127.8, 128.7, 129.2, 135.0, 137.4, 140.5, 150.2.

N-(tert-Butoxycarbonyl)-2-(4-fluorophenyl)indole (1g). The procedure for the preparation of **1a** was followed with 2-(4-fluorophenyl)indole (2.11 g, 10.0 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/20) to give **1g** (3.11 g, quant.) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.35 (s, 9H), 6.53 (s, 1H), 7.09 (t, J = 8.7 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 7.30–7.41 (m, 3H), 7.54 (d, J = 7.6 Hz, 1H), 8.20 (d, J = 8.3 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 27.7, 83.6, 110.2, 114.8 (d, J = 22 Hz), 115.3, 120.4, 123.0, 124.4, 129.1, 130.4 (d, J = 8 Hz), 131.0 (d, J = 3 Hz), 137.3, 139.3, 150.1, 162.4 (d, J = 247 Hz); IR (thin film) 1728 cm⁻¹; Anal. Calcd for C₁₉H₁₈NO₂F: C, 73.29; H, 5.83; N, 4.50. Found: C, 73.23; H, 5.83; N, 4.55.

N-(tert-Butoxycarbonyl)-3-methylindole (4a).¹⁰ The procedure for the preparation of **1a** was followed with 3-methylindole (1.31g, 10 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/50) to give **4a** (2.32 g, quant.) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.66 (s, 9H), 2.27 (d, J = 1.2 Hz, 3H), 7.24 (dt, J = 0.9, 7.4 Hz, 1H), 7.31 (dt, J = 1.3, 7.7 Hz, 1H), 7.35 (br s, 1H), 7.49 (d, J = 7.7 Hz, 1H), 8.11 (br d, J = 7.7 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 9.6, 28.2, 83.1, 115.1, 116.3, 118.9, 122.3, 122.8, 124.2, 131.4, 135.4, 149.8.

N-(tert-Butoxycarbonyl)-3-phenylindole (4b).¹¹ The procedure for the preparation of **1a** was followed with 3-phenylindole¹² (1.50 g, 7.8 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/20) to give **4b** (1.73 g, 76%) as a colorless solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.69 (s, 9H), 7.29 (dd, J = 1.0, 7.5 Hz, 1H), 7.33–7.39 (m, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.65 (dd, J = 1.1, 8.1 Hz, 2H), 7.71 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 28.2, 83.8, 115.4, 119.9, 122.2, 122.8, 122.9, 124.6, 127.1, 127.9, 128.8, 129.0, 133.9, 135.9, 149.7.

N-(tert-Butoxycarbonyl)-2,3-dimethylindole (6).¹⁰ The procedure for the preparation of **1a** was followed with 2,3-dimethylindole (1.45 g, 10 mmol). The crude product was purified with a flush column chromatography (EtOAc/hexane = 1/30) to give **6** (2.37 g, 97%) as a colorless solid: ¹H NMR

(400 MHz, CDCl₃, TMS) δ 1.67 (s, 9H), 2.18 (s, 3H), 2.52 (s, 3H), 7.18–7.25 (m, 2H), 7.38–7.43 (m, 2H), 8.06–8.11 (m, 2H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 8.7, 13.9, 28.3, 83.2, 113.7, 115.3, 117.7, 122.3, 123.2, 130.8, 132.8, 135.6, 150.8.

Preparation of [RuCl(*p*-cymene)]{(*S,S*)-(*R,R*)-PhTRAP}Cl (3**).**

Under nitrogen atmosphere, dry ethanol (6.4 ml) and dry dichloromethane (2.2 ml) was added to a mixture of [RuCl₂(*p*-cymene)]₂ (30.6 mg, 50 μ mol) and (*S,S*)-(*R,R*)-PhTRAP (71.8 mg, 90 μ mol). The resulting suspension was stirred at 50 °C for 1 h. After cooled to room temperature, the mixture was filtered through a Celite pad. The filtrate was evaporated under reduced pressure to give **3** (99.1 mg, quant.) as a brown amorphous solid: ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.73 (d, *J* = 6.8 Hz, 3H), 0.80 (s, 3H), 1.02 (dd, *J* = 12.4, 6.8 Hz, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.58 (dd, *J* = 12.0, 7.3 Hz, 3H), 2.29 (septet, *J* = 6.8 Hz, 1H), 2.67 (d, *J* = 4.5 Hz, 1H), 2.74 (m, 1H), 3.32 (quintet, *J* = 6.3 Hz, 1H), 3.69 (s, 1H), 4.00 (quintet, *J* = 7.0 Hz, 1H), 4.05 (s, 1H), 4.13 (s, 5H), 4.24 (s, 5H), 4.32 (s, 2H), 4.52 (s, 1H), 4.77 (s, 1H), 4.92 (t, *J* = 5.0 Hz, 1H), 6.00 (s, 1H), 7.10–9.10 (br m, 19H), 8.10 (t, *J* = 7.5 Hz, 1H); ³¹P {¹H} NMR (162 MHz, 85% H₃PO₄) δ 9.0 (d, *J* = 42 Hz), 25.1 (d, *J* = 42 Hz).

The ESI-MS spectrum of **3** is shown in Figure S-1. The spectrum exhibited the base peak at *m/z* = 1065.0, which is identified as [RuCl(*p*-cymene)]{(*R,R*)-(*S,S*)-PhTRAP}]⁺ (*M_w* = 1065.1). The observed isotope distribution pattern was almost consistent with the calculated pattern for the cationic ruthenium species.

As with **3**, the enantiomeric [RuCl(*p*-cymene)]{(*R,R*)-(*S,S*)-PhTRAP}]Cl (**3'**) was prepared from [RuCl₂(*p*-cymene)]₂ and (*R,R*)-(*S,S*)-PhTRAP.

Asymmetric Hydrogenation of *N*-Boc-Indoles.

General Procedure for Screening of Catalyst Precursors for Asymmetric Hydrogenation of **1a (Table 1).** Under nitrogen atmosphere, a mixture of a catalyst precursor (5.0 μ mol), (*S,S*)-(*R,R*)-PhTRAP (4.4 mg, 5.5 μ mol), and cesium carbonate (16.3 mg, 50 μ mol) in dry 2-propanol (1.0 ml) was stirred at room temperature for 10 min. The resulting suspension was transferred by a cannula to **1a** (0.50 mmol). The mixture was moved into a nitrogen-filled 50 mL stainless steel autoclave. Hydrogen was introduced into the autoclave until the pressure gauge indicated over 50 atm, and then the pressure was carefully released to 1 atm. This procedure was repeated four times, and finally the inside of the autoclave was pressurized with hydrogen to 50 atm. The reaction mixture was stirred at 60 °C for 2 h. The resulting mixture was evaporated under reduced pressure. The residue was analyzed with ¹H NMR in order to determine the yield of **2a**, and was passed through a short silica gel column (EtOAc/hexane = 1/10) to remove the catalyst. When the residue contained a lot of **1a**, it was purified with MPLC. The enantiomeric excess of **2a** was determined by HPLC analysis with CHIRALCEL OC (4.6 mm ϕ $\times$ 250 mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*S*) *t*₁ = 14.3 min, (*R*) *t*₂ = 15.7 min.

General Procedure for Catalytic Asymmetric Hydrogenation of *N*-Boc-indoles. Under nitrogen atmosphere, a mixture of **3** (5.5 mg, 5.0 μ mol) and cesium carbonate (16.3 mg, 50 μ mol) in methanol or 2-propanol (1.0 ml) was transferred by a cannula to **1** (0.50 mmol). The mixture was moved into a

nitrogen-filled 50 mL stainless steel autoclave. Hydrogen was introduced into the autoclave until the pressure gauge indicated over 50 atm, and then the pressure was carefully released to 1 atm. This procedure was repeated four times, and finally the inside of the autoclave was pressurized with hydrogen to 50 atm. The reaction mixture was stirred at 60 °C for 2 h. The resulting mixture was evaporated under reduced pressure. The residue was purified with a short silica gel column (EtOAc/hexane) to give **2**. The enantiomeric excess of **2** was determined by HPLC analysis.

(R)-N-(tert-Butoxycarbonyl)-2-methylindoline (2a) (Table 2, entry 1).¹³ The general procedure was followed with **1a** (116 mg, 0.50 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/10) to give **2a** (116 mg, 99%) as colorless oil: $[\alpha]_D^{25} = -44.6$ (*c* 0.52, CHCl₃), lit.¹³ $[\alpha]_D^{25} = +39$ (*c* 0.0101, CHCl₃) for 97% ee (*S*); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.29 (d, *J* = 6.3 Hz, 3H), 1.57 (s, 9H), 2.60 (dd, *J* = 2.1, 15.9 Hz, 1H), 3.34 (dd, *J* = 9.6, 15.9 Hz, 1H), 4.50 (br, 1H), 6.93 (dt, *J* = 0.9, 7.4 Hz, 1H), 7.11–7.19 (m, 2H), 7.72 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 21.1, 28.5, 35.7, 55.2, 80.6, 115.3, 122.2, 124.9, 127.3, 130.0, 141.6, 152.3. The enantiomeric excess of **2a** was determined to be 95% ee by HPLC analysis with CHIRALCEL OC.

(-)-N-(tert-Butoxycarbonyl)-5-methoxy-2-methylindoline (2b) (Table 2, entry 2). The general procedure was followed with **1b** (131 mg, 0.50 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/5) to give **2b** (128 mg, 97%) as colorless oil: $[\alpha]_D^{25} = -43.3$ (*c* 1.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.27 (d, *J* = 6.3 Hz, 3H), 1.56 (s, 9H), 2.56 (dd, *J* = 1.7, 16.1 Hz, 1H), 3.32 (dd, *J* = 9.6, 16.1 Hz, 1H), 3.76 (s, 3H), 4.49 (br, 1H), 6.63–6.78 (m, 2H), 7.70 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 21.1, 28.5, 35.9, 55.3, 55.6, 80.2, 111.3, 111.9, 115.6, 131.4, 135.4, 152.2, 155.4; IR (neat) 1694 cm⁻¹; Anal. Calcd for C₁₅H₂₁NO₃: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.38; H, 8.00; N, 5.25. The enantiomeric excess of **2b** was determined to be 91% ee by HPLC analysis with CHIRALCEL OC (4.6 mm φ × 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) *t*₁ = 14.0 min, (–) *t*₂ = 16.4 min.

(-)-N-(tert-Butoxycarbonyl)-5-fluoro-2-methylindoline (2c) (Table 2, entry 3). The general procedure was followed with **1c** (125 mg, 0.50 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/10) to give **2c** (121 mg, 96%) as colorless oil: $[\alpha]_D^{27} = -33.3$ (*c* 1.03, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.28 (d, *J* = 6.3 Hz, 3H), 1.56 (s, 9H), 2.57 (dd, *J* = 1.5, 16.2 Hz, 1H), 3.33 (dd, *J* = 10.2, 16.2 Hz, 1H), 4.51 (br, 1H), 6.81–6.87 (m, 2H), 7.70 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 21.1, 28.4, 35.7, 55.6, 80.6, 112.1 (d, *J* = 24 Hz), 113.4 (d, *J* = 23 Hz), 115.8 (d, *J* = 8 Hz), 131.8, 137.8, 152.1, 158.7 (d, *J* = 234 Hz); IR (neat) 1701 cm⁻¹; Anal. Calcd for C₁₄H₁₈NO₂F: C, 66.91; H, 7.22; N, 5.57. Found: C, 66.69; H, 7.24; N, 5.50. The enantiomeric excess of **2c** was determined to be 90% ee by HPLC analysis with CHIRALCEL OB-H (4.6 mm φ × 250 mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) *t*₁ = 15.9 min, (–) *t*₂ = 19.6 min.

(S)-N-(tert-Butoxycarbonyl)-2-butyldindoline (2d) (Table 2, entry 4).¹² The general procedure was followed with **1d** (137 mg, 0.50 mmol). (*R,R*)-(*S,S*)-PhTRAP–ruthenium complex **3'** was used as a catalyst in order to achieve complete separation in the chiral HPLC analysis. The crude product was purified with a short silica gel column (EtOAc/hexane = 1/15) to give **2d** (130 mg, 94%) as colorless oil: $[\alpha]_D^{29} = +54.1$ (*c* 1.09, CHCl₃), lit.¹² $[\alpha]_D^{26} = -46.3$ (*c* 1.04, CHCl₃) for 77% ee (*R*); ¹H NMR (400 MHz,

CDCl₃, TMS) δ 0.89 (t, J = 6.9 Hz, 3H), 1.20–1.41 (m, 4H), 1.46–1.62 (m, 1H), 1.56 (s, 9H), 1.70–1.81 (m, 1H), 2.72 (dd, J = 2.1, 16.0 Hz, 1H), 3.26 (dd, J = 9.7, 16.0 Hz, 1H), 4.37 (br, 1H), 6.92 (t, J = 7.4 Hz, 1H), 7.10–7.17 (m, 2H), 7.69 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 14.1, 22.6, 27.2, 28.5, 33.3, 34.3, 59.4, 80.6, 115.3, 122.2, 124.8, 127.2, 130.5, 142.2, 152.4. The enantiomeric excess of **2d** was determined to be 92% ee by HPLC analysis with CHIRALCEL OB-H (4.6 mm ϕ $\times$ 250 mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (*R*) t_1 = 11.5 min, (*S*) t_2 = 15.6 min.

(+)-*N*-(*tert*-Butoxycarbonyl)-2-cyclohexylindoline (2e) (Table 2, entry 5). The general procedure was followed with **1e** (150 mg, 0.50 mmol). (*R,R*)-(*S,S*)-PhTRAP–ruthenium complex **3'** was used as a catalyst in order to achieve complete separation in the chiral HPLC analysis. After the reaction was carried out for 48 h, the resulting mixture was evaporated under reduced pressure. After passing through a short silica gel column (EtOAc/hexane = 1/10), the residue was purified with MPLC (EtOAc/hexane = 1/10) to give **2e** (139 mg, 92%) as colorless oil: $[\alpha]_D^{27}$ = +63.5 (c 1.02, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.79–0.91 (m, 1H), 1.02–1.08 (m, 4H), 1.40–1.90 (m, 6H), 1.56 (s, 9H), 2.83 (dd, J = 2.0, 16.2 Hz, 1H), 3.15 (dd, J = 10.0, 16.2 Hz, 1H), 4.32 (br, 1H), 6.91 (dt, J = 0.8, 7.4 Hz, 1H), 7.08–7.16 (m, 2H), 7.62 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 26.0, 26.3, 26.4, 26.5, 28.5, 28.8, 30.1, 41.8, 63.7, 80.7, 115.3, 122.3, 124.2, 127.1, 131.5, 143.0, 152.8; IR (neat) 1701 cm⁻¹; Anal. Calcd for C₁₉H₂₇NO₂: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.66; H, 8.98; N, 4.61. The enantiomeric excess of **2e** was determined to be 87% ee by HPLC analysis with CHIRALCEL OF (4.6 mm ϕ $\times$ 250 mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (–) t_1 = 18.3 min, (+) t_2 = 19.6 min.

(+)-*N*-(*tert*-Butoxycarbonyl)-2-phenylindoline (2f) (Table 2, entry 6).⁵ The general procedure was followed with **1f** (147 mg, 0.50 mmol). (*R,R*)-(*S,S*)-PhTRAP–ruthenium complex **3'** was used as a catalyst in order to achieve complete separation in the chiral HPLC analysis. After the reaction was carried out for 24 h, the resulting mixture was evaporated under reduced pressure. The residue was purified with a short silica gel column (EtOAc/hexane = 1/10) to give **2f** (146 mg, 99%) as a colorless solid: $[\alpha]_D^{25}$ = +20.8 (c 1.08, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.31 (br s, 9H), 2.95 (dd, J = 3.2, 16.3 Hz, 1H), 3.67 (dd, J = 10.7, 16.3 Hz, 1H), 5.36 (br, 1H), 6.97 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 7.3 Hz, 1H), 7.16–7.30 (m, 6H), 7.90 (m, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 28.1, 37.8, 62.6, 80.7, 114.6, 122.5, 124.8, 125.2, 127.1, 127.6, 128.5, 129.2, 143.1, 144.6, 152.3. The enantiomeric excess of **2f** was determined to be 95% ee by HPLC analysis with CHIRALCEL AD-H (4.6 mm ϕ $\times$ 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (–) t_1 = 12.8 min, (+) t_2 = 16.3 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-2-(4-fluorophenyl)indoline (2g) (Table 2, entry 7). The general procedure was followed with **1g** (156 mg, 0.50 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/10) to give **2g** (149 mg, 95%) as a colorless solid: $[\alpha]_D^{24}$ = –69.4 (c 1.02, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.34 (br s, 9H), 2.92 (dd, J = 3.2, 16.3 Hz, 1H), 3.67 (dd, J = 10.7, 16.3 Hz, 1H), 5.35 (br, 1H), 6.92–7.01 (m, 3H), 7.10–7.19 (m, 3H), 7.23 (t, J = 7.8 Hz, 1H), 7.89 (br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 28.2, 37.7, 61.9, 80.9, 114.7, 115.3 (d, J = 21 Hz), 122.7, 124.8, 126.9 (d, J = 8 Hz), 127.7, 129.0, 140.4, 142.8, 152.2, 161.9 (d, J = 245 Hz); IR (neat) 1704

cm⁻¹; Anal. Calcd for C₁₉H₂₀NO₂F: C, 72.82; H, 6.43; N, 4.47. Found: C, 72.97; H, 6.46; N, 4.69. The enantiomeric excess of **2g** was determined to be 93% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ϕ $\times$ 250 mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) t_1 = 26.0 min, (–) t_2 = 34.9 min.

Methyl (S)-N-(tert-Butoxycarbonyl)indolin-2-carboxylate (2h) (Table 2, entry 8).⁴ The general procedure was followed with **1h** (138 mg, 0.50 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/5) to give **2h** (132 mg, 95%) as colorless oil: $[\alpha]_D^{28} = -69.7$ (c 0.87, CHCl₃), lit.⁴ $[\alpha]_D^{20} = -57.7$ (c 0.99, CHCl₃) for 78% ee (S); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.50 and 1.60 (a pair of br, s, 9H), 3.11 (dd, J = 4.3, 16.4 Hz, 1H), 3.50 (dd, J = 11.7, 16.4 Hz, 1H), 3.75 (s, 3H), 4.87 (br, 1H), 6.94 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.90 and 7.49 (a pair of br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 28.2, 32.6 and 31.9 (a pair of s), 52.3, 60.3, 81.2 and 82.3 (a pair of s), 114.6, 122.5, 124.3 and 124.7 (a pair of s), 127.8, 128.8, 142.5 and 141.6 (a pair of s), 151.5 and 152.6 (a pair of s), 172.4. The enantiomeric excess of **2h** was determined to be 90% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ϕ $\times$ 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (R) t_1 = 23.3 min, (S) t_2 = 28.4 min.

(S)-N-(tert-Butoxycarbonyl)-3-methylindoline (5a).⁵ The general procedure was followed with **4a** (124 mg, 0.54 mmol). After the reaction was carried out at 40 °C for 24 h, the resulting mixture was evaporated under reduced pressure. The residue was purified with a flush column chromatography (EtOAc/hexane = 1/10) to give **5a** (116 mg, 92%) as colorless oil: $[\alpha]_D^{26} = +25.1$ (c 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.32 (d, J = 6.9 Hz, 3H), 1.57 (br s 9H), 3.38 (sextet, J = 6.9 Hz, 1H), 3.50 (br, 1H), 4.14 (br t, J = 10.1 Hz, 1H), 6.95 (dt, J = 0.7, 7.4 Hz, 1H), 7.12 (d, J = 7.4 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.83 and 7.46 (a pair of br, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 20.2, 28.4, 34.0, 55.6, 80.4 and 81.2 (a pair of br), 114.6, 122.2, 123.5, 127.5, 136.1 and 136.7 (a pair of br), 142.4 and 141.6 (a pair of br), 152.5. The enantiomeric excess of **5a** was determined to be 87% ee by HPLC analysis with CHIRALCEL OD-H (4.6 mm ϕ $\times$ 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (R) t_1 = 12.3 min, (S) t_2 = 17.4 min.

To assign the absolute configuration of (+)-**5a**, the hydrogenation product was transformed into *N*-benzyl-3-methylindoline, whose correlation between the absolute configuration and specific rotation had been established.¹⁴

Concentrated HCl aq. (0.5 ml) was added to a solution of (+)-**7** (86% ee, 117 mg, 0.50 mmol) in EtOAc (1.5 ml) at 0 °C. The two-phase solution was vigorously stirred at 0 °C for 3 h, and then at room temperature for 1 h. The resulting mixture was extracted twice with water. The combined aqueous layer was basified to pH 10 with saturated Na₂CO₃ aq., and then was extracted five times with EtOAc. The combined organic layer was dried with Na₂SO₄, and then was evaporated under reduced pressure. Under nitrogen atmosphere, benzyl chloride (100 mg, 0.79 mmol) was added to a suspension of the residue (61 mg, 0.46 mmol), K₂CO₃ (113 mg, 0.82 mmol), and KI (8.8 mg, 53 mmol) in dry DMF (1.0 ml). The mixture was stirred at 100 °C for 1 h. After water was added, the resulting mixture was extracted ten times with hexane. The combined organic layer was dried with Na₂SO₄, and then evaporated under reduced pressure. After passing through a short silica gel column (EtOAc/hexane = 1/10), the residue was purified with MPLC (EtOAc/hexane = 1/10) to give *N*-benzyl-3-methylindoline

(72 mg, 65%) as pale yellow oil: $[\alpha]_D^{26} = +56.5$ (c 1.15, CH_2Cl_2), lit.¹⁴ $[\alpha]_D^{20} = -49.7$ (c 1, CH_2Cl_2) for 87% ee (*R*); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.30 (d, $J = 6.5$ Hz, 3H), 2.83 (t, $J = 8.5$ Hz, 1H), 3.30 (sextet, $J = 7.5$ Hz, 1H), 3.50 (t, $J = 8.5$ Hz, 1H), 4.11 (d, $J = 15.1$ Hz, 1H), 4.36 (d, $J = 15.1$ Hz, 1H), 6.51 (d, $J = 8.0$ Hz, 1H), 6.70 (t, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.0$ Hz, 2H), 7.24–7.36 (m, 5H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 18.6, 35.2, 53.4, 61.6, 107.0, 117.7, 123.2, 127.0, 127.4, 127.9, 128.4, 135.0, 138.5, 152.1.

(–)-*N*-(*tert*-Butoxycarbonyl)-3-phenylindoline (5b). The general procedure was followed with **4b** (148 mg, 0.50 mmol). (*R,R*)-(*S,S*)-PhTRAP–ruthenium complex **3'** was used as a catalyst in order to achieve complete separation in the chiral HPLC analysis. After the reaction was carried out at 40 °C for 24 h, the resulting mixture was evaporated under reduced pressure. The residue was purified with a flush column chromatography (EtOAc/hexane = 1/20) to give **5b** (126 mg, 85%) as a colorless solid: $[\alpha]_D^{26} = -69.0$ (c 1.02, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.56 (s, 9H), 3.88 (br, 1H), 4.40 (t, $J = 10.8$ Hz, 1H), 4.53 (dd, $J = 7.4, 10.1$ Hz, 1H), 6.89–6.96 (m, 2H), 7.17–7.35 (m, 6H), 7.92 and 7.53 (a pair of br, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.4, 46.0, 56.8, 80.6, 114.7, 122.5, 125.2, 127.0, 127.9, 128.0, 128.8, 134.2 and 134.9 (a pair of br, 1H), 142.9, 143.6, 152.4; IR (neat) 1703 cm^{-1} ; Anal. Calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 76.96; H, 7.18; N, 4.63. The enantiomeric excess of **5b** was determined to be 94% ee by HPLC analysis with CHIRALPAK AD-H (4.6 mm $\phi \times 250$ mm): 0.4% 2-propanol in hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 19.7$ min, (–) $t_2 = 26.1$ min.

(–)-*cis-N*-(*tert*-Butoxycarbonyl)-2,3-dimethylindoline (7).⁵ The general procedure for screening of catalyst was followed with **6** (123 mg, 0.50 mmol). $\text{Ru}(\eta^3\text{-2-methylallyl})_2(\text{cod})$ (1.6 mg, 5.0 μmol) was used as a catalyst precursor and triethyl amine (5.5 mg, 54 μmol) was used in place of cesium carbonate. After the reaction was carried out at 80 °C for 72 h, the resulting mixture was evaporated under reduced pressure. After passing through a short silica gel column (EtOAc/hexane = 1/15), the residue was purified with MPLC (EtOAc/hexane = 1/15) to give **7** (73 mg, 59%) as colorless oil: $[\alpha]_D^{27} = -29.4$ (c 1.05, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.10 (d, $J = 6.6$ Hz, 3H), 1.29 (d, $J = 7.2$ Hz, 3H), 1.57 (s, 9H), 3.51 (quintet, $J = 7.3$ Hz, 1H), 4.51 (br, 1H), 6.96 (dt, $J = 0.9, 7.4$ Hz, 1H), 7.09 (d, $J = 7.4$ Hz, 1H), 7.16 (t, $J = 7.7$ Hz, 1H), 7.66 (br, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 12.0, 13.9, 28.5, 37.5, 59.9, 80.6, 115.1, 122.4, 123.1, 127.4, 135.4, 141.2, 152.1. The enantiomeric excess of **7** was determined to be 72% ee by HPLC analysis with CHIRALPAK AD-H (4.6 mm $\phi \times 250$ mm): hexane, 0.5 ml/min flow, at 35 °C, UV 254 nm detection, (+) $t_1 = 24.5$ min, (–) $t_2 = 27.3$ min.

Although the NMR spectra of the hydrogenation product was consistent with that of *cis*-**7** reported by Gilchrist,^[5] we confirmed the relative geometry of **7** further by comparison between the ^1H NMR spectra of deprotected indoline and *trans*-2,3-dimethylindoline.¹⁵

Concentrated HCl *aq.* (0.2 ml) was added to a solution of **7** (52 mg, 0.21 mmol) in EtOAc (0.6 ml) at 0 °C. After stirred at room temperature for 0.5 h, the mixture was extracted three times with water. The combined aqueous layer was basified to pH 10 with saturated Na_2CO_3 *aq.*, and then was extracted five times with EtOAc. The combined organic layer was dried with Na_2SO_4 , and then was evaporated under reduced pressure. After passing through a short silica gel column (EtOAc/hexane = 1/1), the residue was purified with MPLC (EtOAc/hexane = 1/1) to give 2,3-dimethylindoline (16 mg, 53%) as

pale yellow oil: $[\alpha]_D^{26} = +19.3$ (c 0.30, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.13 (d, $J = 6.6$ Hz, 3H), 1.18 (d, $J = 7.2$ Hz, 3H), 3.26 (quintet, $J = 7.3$ Hz, 1H), 3.63 (br s, 1H), 3.94 (dq, $J = 8.1, 6.6$ Hz, 1H), 6.61 (d, $J = 7.7$ Hz, 1H), 6.72 (t, $J = 7.3$ Hz, 1H), 7.01 (t, $J = 7.6$ Hz, 1H), 7.06 (d, $J = 7.1$ Hz, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 13.6, 16.3, 39.4, 58.3, 109.3, 118.7, 123.8, 127.2, 134.2, 150.1.

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Figure S-1. (a) The ESI-MS spectrum of **3** from $m/z = 900$ to 1120. (b) The observed isotope distribution pattern of the base peak. (c) The calculated pattern for $[\text{RuCl}(p\text{-cymene})(\text{PhTRAP})]^+$.

Figure S-2. The ^1H NMR spectrum of **2a**.

Figure S-3. The ¹³C NMR spectrum of **2a**.

Figure S-4. The ^1H NMR spectrum of **5a**.

Figure S-6. The ¹H NMR spectrum of 7.

Figure S-7. The ¹³C NMR spectrum of 7.