Highly Enantioselective Synthesis of Chiral 3-Substituted Indolines by Catalytic Asymmetric Hydrogenation of Indoles

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Supporting Information

General and Materials. Specific rotations were measured with a JASCO P-1020 polarimeter. NMR spectra were measured with Varian GEMINI-2000 (7.0 T magnet) or Bruker AVANCE 400 (9.4 T magnet) spectrometer. Flash column chromatographies were performed with silica gel 60 (230–400 mesh, Merck).

All reactions were conducted under nitrogen atmosphere. 2-Propanol and DMF were distilled from CaH₂ under nitrogen atmosphere. CH₂Cl₂ was distilled from P₂O₅. THF and toluene were distilled from sodium benzophenone ketyl. [Rh(nbd)₂][SbF₆],¹ (*S,S*)-(*R,R*)- and (*R,R*)-(*S,S*)-PhTRAP,² **5**,³ and **7**⁴ were prepared according to literatures. Sodium bis(2-methoxyethoxy)aluminum dihydride was purchased from TCI.

General procedure of the catalytic asymmetric hydrogenation of 3-Substituted Indoles: A mixture of [Rh(nbd)₂][SbF₆] (2.6 mg, 5.0 μmol) and (*S,S*)-(*R,R*)-PhTRAP (4.0 mg, 5.0 μmol) in 2-propanol (2.0 ml) was stirred vigorously at room temperature for 10 min. The mixture was transferred by a cannula to a nitrogen-filled stainless steel autoclave, in which 3-substituted indole **1** (0.50 mmol) and Cs₂CO₃ (16.2 mg, 50 μmol) were placed beforehand. Hydrogen was introduced into the reaction vessel until the pressure gauge indicated 50 kg/cm². The reaction mixture was stirred at 80 °C for 24 h. After the solvent was evaporated, the residue was purified by flash column chromatography on silica gel (hexanes/EtOAc) to obtain the desired 3-substituted indoline **2**.

(*S*)-3-Methyl-1-(*p*-toluenesulfonyl)indoline (2c**) (Table 1, Entry 4).** The general procedure was followed with 3-methyl-1-(*p*-toluenesulfonyl)indole (**1c**) (143 mg, 0.50 mmol) to give (*S*)-**2c** (138 mg, 96%). The enantiomeric excess of the product was determined to be 98% ee by HPLC analysis with a chiral stationary phase column, CHIRALCEL OD-H (4.6 mm φ × 25 cm, 4% 2-propanol in hexane): colorless solid; [α]_D²⁰ = +29.4 (*c* 1.06, CHCl₃); ¹H NMR (300 MHz, CDCl₃, TMS) δ 1.11 (d, *J* = 7.0 Hz, 3H), 2.36 (s, 3H), 3.19 (double quintet, *J* = 8.6, 7.0 Hz, 1H), 3.42 (dd, *J* = 7.0, 10.4 Hz, 1H), 4.08 (dd, *J* = 8.6, 10.4 Hz, 1H), 6.96–7.08 (m, 2H), 7.16–7.26 (m, 3H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H); ¹³C {¹H} NMR (75 MHz, CDCl₃) δ 19.4, 21.4, 34.6, 57.5, 114.9, 123.8, 124.0, 127.4, 127.9, 129.7, 134.1, 136.9, 141.6, 144.1; Anal. Calcd for C₁₆H₁₇NO₂S: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.84; H, 5.96; N, 4.73.

(*R*)-3-Methyl-1-(*p*-toluenesulfonyl)indoline (2c**).** The general procedure was followed with 3-methyl-1-(*p*-toluenesulfonyl)indole (**1c**) (285 mg, 1.00 mmol) and (*R,R*)-(*S,S*)-PhTRAP to give (*R*)-**2c** (280 mg, 98%). The enantiomeric excess of the product was determined to be 98% ee by HPLC analysis with a chiral stationary phase column, CHIRALCEL OD-H (4.6 mm φ × 25 cm, 4% 2-propanol in hexane): colorless solid; [α]_D²⁵ = –32.4 (*c* 1.54, CHCl₃).

(+)-3-(2-Propyl)-1-(*p*-toluenesulfonyl)indoline (2f**) (Table 2, Entry 1).** The general procedure except amount of solvent (1 ml) and reaction time (48 h) was followed with 3-(2-propyl)-1-(*p*-toluenesulfonyl)indole (**1f**) (157 mg, 0.50 mmol) to give **2f** (152 mg, 94%). The enantiomeric excess of the product was determined to be 97% ee by HPLC analysis with a chiral stationary phase column,

CHIRALCEL OD-H (4.6 mm $\phi \times 25$ cm, 20% 2-propanol in hexane): colorless oil; $[\alpha]_D^{20} = -19.1$ (c 1.06, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 0.63 (d, $J = 6.8$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H), 1.87 (doublet, $J = 4.8, 6.8$ Hz, 1H), 2.37 (s, 3H), 3.11 (dt, $J = 10.5, 5.2$ Hz, 1H), 3.73 (dd, $J = 5.5, 10.5$ Hz, 1H), 3.81 (dd, $J = 10.0, 10.5$ Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H), 7.06 (d, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 8.0$ Hz, 1H), 7.23 (d, $J = 8.0$ Hz, 2H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 2H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 17.3, 20.0, 21.5, 31.3, 45.8, 51.7, 114.1, 123.2, 125.0, 127.3, 127.9, 129.6, 133.9 (2C), 142.2, 144.0; Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{S}$: C, 68.54; H, 6.71; N, 4.44. Found: C, 68.47; H, 6.70; N, 4.39.

(+)-3-Phenyl-1-(*p*-toluenesulfonyl)indoline (2g) (Table 2, Entry 2). The general procedure was followed with 3-phenyl-1-(*p*-toluenesulfonyl)indole (**1c**) (174 mg, 0.50 mmol), $[\text{Rh}(\text{nbd})_2]\text{SbF}_6$ (5.2 mg, 10 μmol), and (*S,S*)-(*R,R*)-PhTRAP (8.3 mg, 10.5 μmol) to give **2c** (163 mg, 93%). The enantiomeric excess of the product was determined to be 96% ee by HPLC analysis with a chiral stationary phase column, CHIRALCEL OD-H (4.6 mm $\phi \times 25$ cm, 20% 2-propanol in hexane): colorless solid; $[\alpha]_D^{25} = +88.9$ (c 1.01, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.39 (s, 3H), 3.74–3.82 (m, 1H), 4.31–4.38 (m, 2H), 6.84–6.89 (m, 3H), 6.97 (t, $J = 7.5$ Hz, 1H), 7.17–7.28 (m, 6H), 7.68 (d, $J = 8.0$ Hz, 2H), 7.74 (d, $J = 8.0$ Hz, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 21.6, 46.2, 58.5, 114.9, 124.0, 125.6, 127.1, 127.4, 127.7, 128.3, 128.7, 129.7, 133.8, 134.8, 142.1, 142.4, 144.1; Anal. Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}_2\text{S}$: C, 72.18; H, 5.48; N, 4.01. Found: C, 71.96; H, 5.46; N, 3.90.

(+)-3-[2-(*tert*-butyldimethylsilyloxy)ethyl]-1-(*p*-toluenesulfonyl)indoline (2h) (Table 2, Entry 3). The general procedure was followed with 3-[2-(*tert*-butyldimethylsilyloxy)ethyl]-1-(*p*-toluenesulfonyl)indole (**1d**) (215 mg, 0.50 mmol) to give **2d** (202 mg, 94%). The enantiomeric excess of the product was determined to be 98% ee by HPLC analysis with a chiral stationary phase column, Ceramospher RU-1 (4.6 mm $\phi \times 25$ cm, methanol): colorless solid; $[\alpha]_D^{20} = +9.70$ (c 1.18, CHCl_3); ^1H NMR (300 MHz, CDCl_3 , TMS) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.32–1.45 (m, 1H), 1.70–1.82 (m, 1H), 2.32 (s, 3H), 3.14–3.27 (m, 1H), 3.57 (dd, $J = 6.6, 10.8$ Hz, 1H), 3.58 (t, $J = 6.0$ Hz, 2H), 3.99 (dd, $J = 9.0, 10.8$ Hz, 1H), 6.94 (dt, $J = 0.8, 7.4$ Hz, 1H), 7.02 (d, $J = 7.4$ Hz, 1H), 7.12–7.21 (m, 3H), 7.58–7.66 (m, 3H); ^{13}C $\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ -5.5, 18.1, 21.4, 25.8, 37.2, 37.5, 56.0, 60.7, 114.9, 123.7, 124.4, 127.4, 128.0, 129.7, 134.1, 135.7, 141.8, 144.0; Anal. Calcd for $\text{C}_{23}\text{H}_{33}\text{NO}_3\text{SSi}$: C, 64.00; H, 7.71; N, 3.24. Found: C, 64.27; H, 7.86; N, 3.33.

(+)-3-[2-(*tert*-butoxycarbonyl)ethyl]-1-(*p*-toluenesulfonyl)indoline (2i) (Table 2, Entry 4). The general procedure was followed with 3-[2-(*tert*-butoxycarbonyl)ethyl]-1-(*p*-toluenesulfonyl)indole (**1e**) (201 mg, 0.50 mmol) to give **2e** (187 mg, 93%). The enantiomeric excess of the product was determined to be 97% ee by HPLC analysis with a chiral stationary phase column, CHIRALPAK AD (4.6 mm $\phi \times 25$ cm, 4% 2-propanol in hexane): colorless solid; $[\alpha]_D^{20} = +15.6$ (c 1.06, CHCl_3); ^1H NMR (300 MHz, CDCl_3 , TMS) δ 1.43 (s, 9H), 1.47–1.60 (m, 1H), 1.79–1.92 (m, 1H), 2.16 (t, $J = 7.7$ Hz, 2H), 2.36 (s, 3H), 3.08–3.20 (m, 1H), 3.58 (dd, $J = 5.9, 10.4$ Hz, 1H), 3.97 (dd, $J = 9.0, 10.4$ Hz, 1H), 6.99 (dt, $J = 0.9, 7.5$ Hz, 1H), 7.09 (d, $J = 7.5$ Hz, 1H), 7.18–7.26 (m, 3H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.69 (d, $J = 8.1$ Hz, 2H); ^{13}C $\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 21.4, 28.0, 29.7, 32.5, 39.0, 55.2, 80.6, 114.8, 123.7, 124.6, 127.3, 128.2, 129.7, 133.8, 134.7, 141.7, 144.2, 172.2; Anal. Calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_4\text{S}$: C, 65.81; H, 6.78; N, 3.49. Found: C, 66.03; H, 6.82; N, 3.50.

(+)-3-[2-{*N*-(*tert*-butoxycarbonyl)amino}ethyl]-1-(*p*-toluenesulfonyl)indoline (2j) (Table 2, Entry 5). The general procedure was followed with 3-[2-{*N*-(*tert*-butoxycarbonyl)amino}ethyl]-1-(*p*-toluenesulfonyl)indole (**1f**) (208 mg, 0.50 mmol) to give **2e** (148 mg, 71%). The enantiomeric excess of the product was determined to be 95% ee by HPLC analysis with a chiral stationary phase column, CHIRALCEL OC (4.6 mm $\phi \times 25$ cm, 20% 2-propanol in hexane): colorless solid; $[\alpha]_D^{20} = +9.0$ (c 1.02, CHCl_3); ^1H NMR (300 MHz, CDCl_3 , TMS) δ 1.32–1.55 (m, 1H), 1.44 (s, 9H), 1.67–1.80 (m, 1H), 2.37 (s, 3H), 3.05–3.20 (m, 3H), 3.61 (dd, $J = 5.9, 10.6$ Hz, 1H), 4.00 (dd, $J = 9.2, 10.6$ Hz, 1H), 4.48 (br s, 1H), 6.99 (t, $J = 7.4$ Hz, 1H), 7.08 (d, $J = 7.4$ Hz, 1H), 7.17–7.26 (m, 3H), 7.65 (d, $J = 8.1$ Hz, 1H),

7.69 (d, $J = 8.4$ Hz, 2H); ^{13}C { ^1H } NMR (75 MHz, CDCl_3) δ 21.4, 28.3, 29.6, 35.3, 37.6, 38.2, 55.4, 114.9, 123.8, 124.4, 127.4, 128.2, 129.7, 133.9, 134.9, 141.7, 144.2, 155.9; Anal. Calcd for $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4\text{S}$: C, 63.44; H, 6.78; N, 6.73. Found: C, 63.71; H, 6.83; N, 6.60.

Removal of *N*-Tosyl Group from 2c. Sodium bis(2-methoxyethoxy)aluminum dihydride (*ca.* 70% in toluene) (1.10 g, 3.8 mmol) was added to a solution of (*R*)-**2c** (273 mg, 0.95 mmol) in toluene (2.0 ml). The mixture was stirred under reflux for 14 h. After the reaction was quenched with 1 *N* HCl aq (2 ml), the mixture was stirred for 1 h at room temperature. After filtration through Cerite, the filtrate was extracted three times with 1 *N* HCl aq. The combined aqueous layer was basified with Na_2CO_3 and was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4 and was evaporated, giving (*R*)-3-methylindoline (82 mg, 65%) as colorless oil: $[\alpha]_{\text{D}}^{25} = -38.8$ (*c* 1.04, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.32 (d, $J = 6.9$ Hz, 3H), 3.10 (t, $J = 8.6$ Hz, 1H), 3.2–4.0 (br s, 1H), 3.36 (sextet, $J = 7.5$ Hz, 1H), 3.69 (t, $J = 8.7$ Hz, 1H), 6.64 (d, $J = 7.7$ Hz, 1H), 6.73 (t, $J = 7.7$ Hz, 1H), 7.02 (t, $J = 7.6$, 1H), 7.08 (d, $J = 7.3$ Hz, 1H); ^{13}C { ^1H } NMR (100.5 MHz, CDCl_3) δ 18.6, 36.6, 55.4, 109.5, 118.7, 123.3, 127.2, 134.3, 151.2. The enantiomeric excess of the indoline was determined to be 98% ee by HPLC analysis of its acetamide with a chiral stationary phase column, CHIRALCEL OC (4.6 mm $\phi \times 25$ cm, 20% 2-propanol in hexane).

***N*-Methanesulfonyl-2-iodo-5-methoxyaniline (6).**⁵ Methanesulfonylchloride (3.78 g, 33 mmol) was added dropwise for 10 min to a mixture of 2-iodo-5-methoxyaniline (**5**) (7.47 g, 30 mmol) and pyridine (2.61 g, 33 mmol) in CH_2Cl_2 at 0 °C, and the mixture was stirred at room temperature for 16 h. After water was added, the mixture was extracted with EtOAc. The organic layer was washed with brine, was dried with Na_2SO_4 , and was evaporated. The residue was purified by a flash column chromatography on silica gel (hexanes/EtOAc), giving the desired product **6** (8.13 g, 83%) as a pale brown solid: ^1H NMR (400 MHz, CDCl_3 , TMS) δ 3.01 (s, 3H), 3.81 (s, 3H), 6.56 (dd, $J = 3.0, 8.6$ Hz, 1H), 6.52 (br s, 1H), 7.26 (d, $J = 3.0$ Hz, 1H), 7.66 (d, $J = 8.6$ Hz, 1H); ^{13}C { ^1H } NMR (100.5 MHz, CDCl_3) δ 39.9, 55.5, 80.0, 107.9, 113.8, 138.3, 139.3, 161.0.

***N*-Methanesulfonyl-6-methoxy-3-[(triisopropylsilyloxy)methyl]indole (8).** Trimethyl[3-(triisopropylsilyloxy)-1-propynyl]silane (**7**) (4.27 g, 15 mmol) was added to a mixture of **6** (1.64 g, 5.0 mmol), NaHCO_3 (2.10 g, 25 mmol), LiCl (212 mg, 5.0 mmol), and palladium acetate (56 mg, 0.25 mmol) in DMF (100 ml). After 4.5 h of stirring at 100 °C, the mixture was diluted with EtOAc and saturated NH_4Cl aq., and then the aqueous layer was saturated with NaCl. After the mixture was filtered through Celite, the filtrate was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4 and was evaporated. A mixture of the black oily residue, potassium acetate (2.45 g, 25 mmol), and tetrabutylammonium chloride (1.39 g, 5.0 mmol) in DMF (90 ml) was stirred at 100 °C for 4 h. The mixture was diluted with EtOAc and saturated NH_4Cl aq., and then the aqueous layer was saturated with NaCl. After the mixture was filtered through Celite, the filtrate was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4 and was evaporated. The residue was purified by a flash column chromatography on silica gel (hexanes/EtOAc), giving the desired product **8** (1.25 g, 61%) as brown oil: ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.09 (d, $J = 6.6$ Hz, 18H), 1.13–1.24 (m, 3H), 3.04 (s, 3H), 3.88 (s, 3H), 4.93 (s, 2H), 6.94 (dd, $J = 2.3, 8.7$ Hz, 1H), 7.25 (s, 1H), 7.44 (d, $J = 2.3$ Hz, 1H), 7.51 (d, $J = 8.7$ Hz, 1H); ^{13}C { ^1H } NMR (100.5 MHz, CDCl_3) δ 12.0, 18.0, 40.1, 55.8, 58.4, 97.4, 112.6, 120.8, 121.3, 123.2, 123.5, 136.6, 158.3; Anal. Calcd for $\text{C}_{20}\text{H}_{33}\text{NO}_4\text{SSi}$: C, 58.36; H, 8.08; N, 3.40. Found: C, 58.66; H, 8.20; N, 3.29.

(+)-*N*-Methanesulfonyl-6-methoxy-3-[(triisopropylsilyloxymethyl)]indoline (9). The general procedure of the asymmetric hydrogenation of was followed with **8** (412 mg, 1.00 mmol) to give the desired product **9** (355 mg, 87%). The enantiomeric excess of the product was determined to be 93% ee by HPLC analysis with a chiral stationary phase column, CHIRALCEL OD-H (4.6 mm $\phi \times 25$ cm,

10% 2-propanol in hexane): colorless oil; $[\alpha]_D^{25} = +27.0$ (c 1.05, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 0.99–1.14 (m, 21H), 2.88 (s, 3H), 3.44–3.53 (m, 1H), 3.73 (dd, $J = 7.6, 9.6$ Hz, 1H), 3.80 (s, 3H), 3.84 (dd, $J = 5.8, 9.6$ Hz, 1H), 3.94 (dd, $J = 5.1, 10.7$ Hz, 1H), 4.02 (dd, $J = 9.1, 10.7$ Hz, 1H), 6.57 (dd, $J = 2.4, 8.5$ Hz, 1H), 7.02 (d, $J = 2.4$ Hz, 1H), 7.12 (d, $J = 8.5$ Hz, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 11.9, 17.9, 34.3, 42.4, 54.0, 55.6, 65.7, 100.0, 109.0, 123.8, 125.6, 143.4, 160.5; Anal. Calcd for $\text{C}_{20}\text{H}_{35}\text{NO}_4\text{SSi}$: C, 58.07; H, 8.53; N, 3.39. Found: C, 57.87; H, 8.54; N, 3.32.

(+)-*N*-Methanesulfonyl-6-methoxy-3-(hydroxymethyl)indoline. A solution of **9** (549 mg, 1.33 mmol) in THF (2 ml), H_2O (2 ml), and trifluoroacetic acid (0.67 ml) was stirred at 50 °C for 5 h. The mixture was diluted with brine, and was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4 , and was evaporated. The residue was purified by a flash column chromatography on silica gel (hexanes/EtOAc), giving the desired product (274 mg, 80%) as pale blue oil: $[\alpha]_D^{25} = +22.4$ (c 0.90, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.98 (br s, 1H), 2.90 (s, 3H), 3.44–3.52 (m, 1H), 3.75 (dd, $J = 6.0, 11.2$ Hz, 1H), 3.77 (dd, $J = 5.6, 11.2$ Hz, 1H), 3.79 (s, 3H), 3.95 (dd, $J = 5.0, 10.9$ Hz, 1H), 4.06 (dd, $J = 9.1, 10.9$ Hz, 1H), 6.59 (dd, $J = 2.4, 8.3$ Hz, 1H), 7.02 (d, $J = 2.4$ Hz, 1H), 7.13 (d, $J = 8.3$ Hz, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 34.5, 41.7, 53.8, 55.6, 64.6, 100.2, 109.2, 123.1, 125.4, 143.6, 160.6; Anal. Calcd for $\text{C}_{11}\text{H}_{15}\text{NO}_4\text{S}$: C, 51.35; H, 5.88; N, 5.44. Found: C, 51.31; H, 5.88; N, 5.46.

(+)-*N*-Methanesulfonyl-6-methoxy-3-(acetoxymethyl)indoline (4**).** Acetic anhydride (84 mg, 0.82 mmol) and triethylamine (90 mg, 0.89 mmol) was added to a mixture of (+)-*N*-methanesulfonyl-6-methoxy-3-(hydroxymethyl)indoline (191 mg, 0.74 mmol) and DMAP (4.5 mg, 37 μmol) in CH_2Cl_2 (0.4 ml). After 3 h of stirring at room temperature, the mixture was diluted with 1 *N* HCl aq. and was extracted three times with EtOAc. The combined organic layer was washed with brine, was dried with Na_2SO_4 , and was evaporated. The residue was purified by a flash column chromatography on silica gel (hexanes/EtOAc), giving the desired product (208 mg, 94%) as pale yellow oil: $[\alpha]_D^{25} = +30.0$ (c 1.09, CHCl_3); ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.08 (s, 3H), 2.91 (s, 3H), 3.59–3.67 (m, 1H), 3.80 (s, 3H), 3.87 (dd, $J = 5.3, 10.7$ Hz, 1H), 4.03–4.12 (m, 2H), 4.26 (dd, $J = 5.4, 11.1$ Hz, 1H), 6.59 (dd, $J = 2.6, 8.6$ Hz, 1H), 7.03 (d, $J = 2.6$ Hz, 1H), 7.12 (d, $J = 8.6$ Hz, 1H); ^{13}C $\{^1\text{H}\}$ NMR (100.5 MHz, CDCl_3) δ 20.8, 34.6, 38.9, 54.2, 55.6, 65.9, 100.2, 109.4, 122.2, 125.6, 143.3, 160.9, 170.8; Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_5\text{S}$: C, 52.16; H, 5.72; N, 4.68. Found: C, 51.93; H, 5.75; N, 4.69.

Assignment of Absolute Configuration of **2c.** The absolute configuration of **2c** obtained from the asymmetric hydrogenation of **1c** using (*S,S*)-(*R,R*)-PhTRAP was assigned to be *S* as follows: (1) **2c** was converted into *N*-benzyl-3-methylindoline. (2) The specific rotation of the sample derived from **2c** was compared to the value of specific rotation of (*R*)-**2c** in the literature.⁶

***N*-Benzyl-3-methylindoline.** Sodium bis(2-methoxyethoxy)aluminum dihydride (*ca.* 70% in toluene) (324 g, 1.12 mmol) was added to a solution of (*R*)-**2c** (72 mg, 0.25 mmol) in toluene (0.5 ml). The mixture was stirred under reflux for 5 h. After dilution with H_2O and EtOAc, the mixture was filtered through Cerite. The filtrate was extracted three times with EtOAc. The combined organic layer was dried with Na_2SO_4 and was evaporated. Benzyl chloride (48 mg, 0.38 mmol) was added to a solution of the residue, K_2CO_3 (57 mg, 0.41 mmol), and KI (4.5 mg, 27 μmol) in DMF (0.5 ml). After 5 h of stirring at 100 °C, the mixture was diluted with H_2O , and was extracted ten times with hexanes. The combined organic layer was washed with H_2O , was dried with Na_2SO_4 , and was evaporated. After passing through a column on silica gel, the residue was purified by medium-pressure liquid chromatography (hexanes/EtOAc) with C.I.G. pre-packed column CPS-223L-1 (Kusano, Tokyo, Japan), giving the desired compounds (21 mg, 38 %) as pale yellow oil: $[\alpha]_D^{25} = +66.4$ (c 0.51, CH_2Cl_2), lit.⁶ $[\alpha]_D^{20} = -49.7$ (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 { ^1H } 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.

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