Catalytic Asymmetric Hydrogenation of Heteroaromatic Compounds, Indoles
Ryoichi Kuwano, Koji Sato, Takashi Kurokawa, Daisuke Karube, and Yoshihiko Ito*

*Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering,
Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan*

Supporting Information

General and Materials. Specific rotations were measured with a JASCO P-1020 polarimeter. NMR spectra were measured with either Varian GEMINI-2000 (7.0 T magnet) or VXR-200 (4.7 T magnet) spectrometer. Flash column chromatographies and preparative TLCs were performed with silica gel 60 (230–400 mesh, Merck) and silica gel 60 PF₂₅₄ (Merck), respectively. All reactions were carried out under nitrogen atmosphere unless otherwise noted. 2-Propanol was distilled from CaH₂ under nitrogen. 2-Substituted *N*-acetylindoles **1a–c**, **e–h** were prepared according to the literature procedures.¹

Methyl Indoline-2-carboxylate Hydrochloride. Thionyl chloride (21.2 g, 0.18 mol) was added dropwise to MeOH (50 ml) at 0 °C for 20 min. After 10 min, racemic indoline-2-carboxylic acid (8.16 g, 50 mmol) was added to the solution in small portions for 5 min. The mixture was stirred at room temperature for 21 h, then evaporated. The residue was crystallized in Et₂O, giving 9.75 g (91%) of methyl indoline-2-carboxylate hydrochloride: white crystal; ¹H NMR (200 MHz, CD₃OD) δ 3.51 (dd, *J* = 7.6, 16.4 Hz, 1H), 3.71 (dd, *J* = 9.4, 16.4 Hz, 1H), 3.89 (s, 3H), 5.09 (dd, *J* = 7.6, 9.4 Hz, 1H), 7.37–7.54 (m, 4H).

Methyl *N*-Acetylindoline-2-carboxylate. Triethylamine (4.65 g, 46 mmol) was added to a suspension of methyl indoline-2-carboxylate hydrochloride (4.27 g, 20 mmol) in THF (20 ml) at room temperature. After 10 min, acetic anhydride (2.46 g, 24 mmol) and DMAP (24.4 mg, 0.20 mmol) were added to the suspension. The mixture was stirred at room temperature for 10 h, and at 40 °C for 3 h. After dilution with H₂O, the mixture was extracted with EtOAc. The organic layer was washed with 10% citric acid aq, with saturated Na₂CO₃ aq, then with brine, dried over Na₂SO₄, and evaporated. The residue was recrystallized from hexane–EtOAc, giving 3.89 g (89%) of methyl *N*-acetylindoline-2-carboxylate: white crystal; ¹H NMR (200 MHz, CDCl₃, TMS) δ 2.18 and 2.49 (a pair of br s, 3H), 3.00–3.67 (br m, 2H), 3.77 and 3.74 (a pair of br s, 3H), 4.84–4.98 and 5.10–5.23 (a pair of br m, 1H), 7.03 (t, *J* = 7.9 Hz, 1H), 7.09–7.31 (m, 2H), 8.22 (br d, *J* = 7.8 Hz, 1H).

Methyl *N*-Acetylindole-2-carboxylate (1d**).** A mixture of methyl *N*-acetylindoline-2-carboxylate (3.89 g, 18 mmol) and DDQ (6.03 g, 27 mmol) in toluene (90 ml) was refluxed for 24 h. After cooling to room temperature, the mixture was filtered, and evaporated. The residue was purified with a flash column chromatography (hexane/EtOAc), giving 3.27 g (85%) of **1d**: pink solid; ¹H NMR (200 MHz, CDCl₃, TMS) δ 2.62 (s, 3H), 3.95 (s, 3H), 7.29 (ddd, *J* = 1.0, 7.1, 7.8 Hz, 1H), 7.33 (d, *J* = 0.7 Hz, 1H), 7.45 (ddd, *J* = 1.4, 7.1, 8.5 Hz, 1H), 7.63 (ddd, *J* = 0.7, 1.4, 7.8 Hz, 1H), 8.13 (dd, *J* = 1.0, 8.5 Hz, 1H).

Methyl Indole-2-carboxylate. Thionyl chloride (21.2 g, 0.18 mol) was added dropwise to MeOH (50 ml) at 0 °C for 40 min. After 10 min, indole-2-carboxylic acid (8.05 g, 50 mmol) was added to the solution in small portions for 30 min. The mixture was stirred at room temperature for 18 h, and evaporated. The residue was diluted with saturated Na₂CO₃ aq, and then extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, and evaporated. The residue was recrystallized from EtOAc, giving 8.13 g (93%) of methyl indole-2-carboxylate: brown powder; ¹H NMR (300 MHz, CDCl₃, TMS) δ 3.95 (s, 3H), 7.15 (ddd, *J* = 1.2, 6.9, 8.0 Hz, 1H), 7.23

(dd, $J = 0.8, 2.0$ Hz, 1H), 7.31 (dd, $J = 1.2, 8.4$ Hz, 1H), 7.41 (ddd, $J = 1.0, 6.9, 8.4$ Hz, 1H), 7.70 (dd, $J = 1.0, 8.0$ Hz, 1H), 8.85–9.13 (br, 1H).

Methyl *N*-tert-Butoxycarbonylindole-2-carboxylate (3). Di-*tert*-butyl dicarbonate (2.40 g, 11 mmol) was added to a solution of methyl indole-2-carboxylate (1.75 g, 10 mmol) and DMAP (61.4 mg, 0.50 mmol) in MeCN (10 ml) at room temperature. The mixture was stirred for 1 h, and evaporated. The residue was diluted with H₂O, and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO₄, and evaporated. The residue was purified with a flash column chromatography (hexane/EtOAc), giving 2.70 g (98%) of **3**: white solid; ¹H NMR (300 MHz, CDCl₃, TMS) δ 1.63 (s, 9H), 3.92 (s, 3H), 7.11 (s, 1H), 7.27 (ddd, $J = 0.7, 7.2, 8.1$ Hz, 1H), 7.42 (ddd, $J = 1.3, 7.2, 8.4$ Hz, 1H), 7.61 (d, $J = 8.1$ Hz, 1H), 8.10 (dd, $J = 0.7, 8.4$ Hz, 1H).

***N*-Acetyl-3-methylindole (5).** Acetic anhydride (2.72 g, 27 mmol) and triethylamine (2.90 g, 29 mmol) were added to a solution of 3-methylindole (2.91 g, 22 mmol) and DMAP (270 mg, 2.2 mmol) in MeCN (30 ml) at room temperature. The mixture was stirred at room temperature for 20 h, at 60 °C for 3 h, and evaporated. The residue was diluted with H₂O, and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO₄, and evaporated. The residue was purified with a flash column chromatography (hexane/EtOAc), giving 2.30 g (60%) of **5**: white solid; ¹H NMR (200 MHz, CDCl₃, TMS) δ 2.29 (d, $J = 1.4$ Hz, 3H), 2.60 (s, 3H), 7.18 (br s, 1H), 7.23–7.57 (m, 3H), 8.42 (d, $J = 7.4$ Hz, 1H).

General Procedure of Catalytic Asymmetric Hydrogenation of 1, 3, and 5. A mixture of [Rh(nbd)₂]SbF₆ (2.6 mg, 5.0 μ mol) and (*S,S*)-(*R,R*)-PhTRAP (4.2 mg, 5.3 μ mol) 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 **1** (0.50 mmol) and Cs₂CO₃ (16.2 mg, 50 μ mol) were placed beforehand. Hydrogen was introduced into the reaction vessel until the pressure gauge indicated 5.0 MPa. The reaction mixture was stirred at 60 °C for 2 h. After the solvent was evaporated, the residue was purified by a flash column chromatography (hexane/EtOAc) to give **2**.

(*R*)-*N*-Acetyl-2-butyldoline (2a): pale yellow oil; $[\alpha]_D^{20} = -94.0$ (c 1.00, CHCl₃); ¹H NMR (300 MHz, CDCl₃, TMS) δ 0.80–0.99 (br, 3H), 1.19–1.41 (br, 4H), 1.51–1.79 (br, 2H), 2.28 and 2.38 (a pair of br s, 3H), 2.57–2.88 (br m, 1H), 3.12–3.40 (br m, 1H), 4.16–4.41 and 4.63–4.90 (a pair of br, 1H), 7.02 (t, $J = 7.5$ Hz, 1H), 7.05–7.28 (m, 2H), 8.14 (br d, $J = 6.9$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 13.9, 22.5, 23.3 and 24.3 (a pair of s), 27.2, 33.8 and 32.7 (a pair of s), 35.0, 60.6 and 59.8 (a pair of s), 117.8 and 115.1 (a pair of s), 123.8, 124.7 and 126.0 (a pair of s), 127.4, 130.6 and 133.4 (a pair of s), 142.4 and 141.4 (a pair of s), 168.4; Anal. Calcd for C₁₄H₁₉NO: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.38; H, 8.93; N, 6.24.

***N*-Acetyl-2-(2-methylpropyl)indoline (2b):** pale yellow oil; $[\alpha]_D^{20} = -79.5$ (c 1.00, CHCl₃); ¹H NMR (300 MHz, CDCl₃, TMS) δ 0.94 (d, $J = 6.3$ Hz, 3H), 1.01 (br d, $J = 6.3$ Hz, 3H), 1.18–1.80 (br m, 3H), 2.27 and 2.37 (a pair of br s, 3H), 2.56–2.88 (br m, 1H), 3.11–3.40 (br m, 1H), 4.23–4.46 and 4.73–5.01 (a pair of br, 1H), 7.02 (t, $J = 7.4$ Hz, 1H), 7.14–7.36 (m, 2H), 8.14 (br d, $J = 6.9$ Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 21.3, 23.3, 23.7, 24.6, 33.7 and 32.9 (a pair of s), 43.9 and 42.7 (a pair of s), 59.1 and 58.4 (a pair of s), 117.8 and 115.3 (a pair of s), 123.7, 124.9 and 126.0 (a pair of s), 127.4, 130.4 and 133.4 (a pair of s), 142.2 and 141.5 (a pair of s), 168.1; Anal. Calcd for C₁₄H₁₉NO: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.39; H, 8.96; N, 6.50.

***N*-Acetyl-2-phenylindoline (2c):** pale yellow oil; $[\alpha]_D^{20} = -148.1$ (c 1.00, CHCl₃); ¹H NMR (300 MHz, CDCl₃, TMS, at 50 °C) δ 1.57–2.40 (br, 3H), 2.96 (br d, $J = 16.0$ Hz, 1H), 3.76 (br dd, $J = 10.2, 16.0$ Hz, 1H), 5.14–5.64 (br, 1H), 7.03 (t, $J = 7.5$ Hz, 1H), 7.08–7.45 (m, 7H), 8.02–8.51 (br, 1H); ¹³C NMR (75 MHz, CDCl₃, at 50 °C) δ 24.0, 38.8, 63.5, 117.0, 124.0, 124.9, 125.1, 127.8,

129.1, 143.3, 143.4, 169.4; Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.69; H, 6.25; N, 5.82.

Methyl (S)-N-Acetylundoline-2-carboxylate (2d): white solid; $[\alpha]_D^{20} = -126.1$ (c 1.00, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS) δ 2.18 and 2.49 (a pair of s, 3H), 3.27 and 3.11 (a pair of br d, $J = 17.1$ Hz and 16.5 Hz, 1H), 3.38–3.69 (br m, 1H), 3.77 and 3.74 (a pair of s, 3H), 4.92 and 5.17 (a pair of br d, $J = 10.5$ Hz and 7.8 Hz, 1H), 7.03 (t, $J = 7.7$ Hz, 1H), 7.10–7.32 (m, 2H), 8.23 (br d, $J = 8.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5 and 24.4 (a pair of s), 33.4 and 31.4 (a pair of s), 52.8 and 52.3 (a pair of s), 61.3 and 60.1 (a pair of s), 117.3 and 113.8 (a pair of s), 124.0 and 123.4 (a pair of s), 124.2 and 125.7 (a pair of s), 127.9, 128.4 and 130.8 (a pair of s), 142.6 and 141.3 (a pair of s), 168.9 and 168.5 (a pair of s), 171.9; HRMS (FAB) Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0892 (M^+).

N-Acetyl-2-butyl-5-methylindoline (2e): pale yellow oil; $[\alpha]_D^{20} = -98.2$ (c 1.00, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.77–0.97 (br, 3H), 1.17–1.76 (br m, 6H), 2.26 and 2.37 (a pair of br s, 3H), 2.30 (s, 3H), 2.52–2.80 (br m, 1H), 3.08–3.35 (br m, 1H), 4.18–4.32 and 4.67–4.82 (a pair of br, 1H), 6.88–7.06 (m, 2H), 8.01 (br d, $J = 8.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 20.9, 22.5, 23.1 and 24.2 (a pair of s), 27.1, 33.7 and 32.5 (a pair of s), 34.9 and 33.4 (a pair of s), 60.7 and 59.8 (a pair of s), 117.4 and 114.8 (a pair of s), 125.4 and 126.7 (a pair of s), 127.8, 130.7, 133.4, 140.0 and 139.2 (a pair of s), 168.0; Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.65; H, 9.37; N, 6.05.

N-Acetyl-2-butyl-5-(trifluoromethyl)indoline (2f): pale yellow oil; $[\alpha]_D^{20} = -61.6$ (c 1.00, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS, at 50 °C) δ 0.90 (br t, $J = 6.6$ Hz, 3H), 1.21–1.46 (br, 4H), 1.46–1.74 (br, 2H), 2.31 (s, 3H), 2.83 (br d, $J = 16.0$ Hz, 1H), 3.34 (br dd, $J = 9.0, 16.0$ Hz, 1H), 4.15–4.74 (br, 1H), 7.41 (s, 1H), 7.46 (d, $J = 8.4$ Hz, 1H), 7.76–8.52 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, at 50 °C) δ 13.8, 22.4, 23.3, 27.0, 33.4, 34.9, 60.9, 117.3, 121.9, 124.4 (q, $J = 272$ Hz), 125.2, 125.7 (q, $J = 32$ Hz), 131.3, 145.2, 168.8; Anal. Calcd for $C_{15}H_{18}NOF_3$: C, 63.15; H, 6.36; N, 4.91. Found: C, 63.29; H, 6.36; N, 4.92.

N-Acetyl-2-butyl-6-(trifluoromethyl)indoline (2g): pale yellow oil; $[\alpha]_D^{20} = -45.0$ (c 1.01, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS, at 50 °C) δ 0.90 (br t, $J = 6.8$ Hz, 3H), 1.15–1.46 (br m, 4H), 1.46–1.74 (br, 2H), 2.30 (s, 3H), 2.83 (br d, $J = 15.8$ Hz, 1H), 3.34 (br dd, $J = 8.9, 15.8$ Hz, 1H), 4.16–4.66 (br, 1H), 7.17–7.36 (m, 2H), 8.11–8.66 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, at 50 °C) δ 13.8, 22.4, 23.2, 27.0, 33.7, 35.0, 60.9, 114.6, 120.8, 124.3 (q, $J = 273$ Hz), 124.9, 129.9 (q, $J = 32$ Hz), 134.6, 142.8, 168.7; Anal. Calcd for $C_{15}H_{18}NOF_3$: C, 63.15; H, 6.36; N, 4.91. Found: C, 63.22; H, 6.40; N, 4.93.

N-Acetyl-2-butyl-6-methoxyindoline (2h): pale yellow oil; $[\alpha]_D^{20} = -54.8$ (c 1.01, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.79–0.95 (br, 3H), 1.17–1.40 (br, 4H), 1.51–1.74 (br, 2H), 2.27 (br s, 3H), 2.72 (br d, $J = 14.7$ Hz, 1H), 3.05–3.32 (br m, 1H), 3.80 (s, 3H), 4.18–4.39 (br, 1H), 6.58 (br dd, $J = 2.0, 7.9$ Hz, 1H), 7.05 (br d, $J = 7.9$ Hz, 1H), 7.77–7.90 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.5, 23.3, 27.2, 33.0, 35.0, 55.5, 61.5, 103.7, 110.1, 122.4, 124.8, 143.5, 159.4, 168.5; Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.58; H, 8.64; N, 5.68.

Methyl (S)-N-tert-Butoxycarbonylundoline-2-carboxylate (4): colorless oil; $[\alpha]_D^{20} = -57.7$ (c 0.99, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$, TMS) δ 1.50 and 1.59 (a pair of br s, 9H), 3.11 (dd, $J = 4.5, 16.5$ Hz, 1H), 3.50 (dd, $J = 11.4, 16.5$ Hz, 1H), 3.75 (s, 3H), 4.79–5.00 (br, 1H), 6.94 (dt, $J = 0.9, 7.5$ Hz, 1H), 7.11 (d, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 1H), 7.42–7.61 and 7.79–8.01 (a pair of br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2, 32.6, 52.2, 60.3, 81.2, 114.7, 122.6, 124.4, 127.9, 128.7, 142.6, 151.6, 172.5; Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.92; H, 6.90; N, 5.01.

N-Acetyl-3-methylindoline (6): white solid; ^1H NMR (300 MHz, CDCl_3 , TMS) δ 1.36 (d, J = 6.6 Hz, 3H), 2.22 (s, 3H), 3.26–3.67 (m, 2H), 4.21 (t, J = 9.3 Hz, 1H), 7.04 (t, J = 7.4 Hz, 1H), 7.08–7.25 (m, 2H), 8.20 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 20.1, 24.1, 34.7, 56.9, 116.9, 123.4, 123.7, 127.7, 136.3, 142.4, 168.7. The enantiomeric excess of **6** was determined by HPLC analysis of CHIRALCEL OC.

Assignment of the Absolute Configurations of 2a, 2d, and 4. The absolute configurations of **2a**, **2d**, and **4** were assigned by comparison in chiral HPLC analysis of the authentic samples, which were derived from (*S*)-indoline-2-carboxylic acid (Scheme S-1).

Scheme S-1

Methyl (*S*)-Indoline-2-carboxylate Hydrochloride (7). Thionyl chloride (2.6 ml, 36 mmol) was added carefully to MeOH (10 ml) at $-10\text{ }^\circ\text{C}$. After stirring for 10 min, (*S*)-indoline-2-carboxylic acid (1.63 g, 10.0 mmol) was added to the solution. The mixture was stirred at room temperature for 53 h, and evaporated. The residue was crystallized in Et_2O , giving 2.12 g (99%) of (*S*)-**7**: ^1H NMR (200 MHz, CD_3OD) δ 3.51 (dd, J = 7.6, 16.4 Hz, 1H), 3.71 (dd, J = 9.4, 16.4 Hz, 1H), 3.89 (s, 3H), 5.09 (dd, J = 7.6, 9.4 Hz, 1H), 7.37–7.54 (m, 4H).

Methyl (*S*)-N-Acetylindoline-2-carboxylate (2d). Triethylamine (2.54 g, 25 mmol) was added to a suspension of (*S*)-**7** (2.12 g, 9.9 mmol) in THF (10 ml) at room temperature. After stirring for 0.5 h, acetic anhydride (1.19 g, 12 mmol) was added to the mixture at $0\text{ }^\circ\text{C}$. The mixture was stirred at $0\text{ }^\circ\text{C}$ for 10 min, and at room temperature for 17 h. After dilution with water, the mixture was extracted with EtOAc. The organic layer was washed with 10% HCl aq, with saturated Na_2CO_3 aq, then with brine, dried over Na_2SO_4 , and evaporated. The residue was purified by a flash column chromatography (hexane/EtOAc), giving 1.86 g (86%) of (*S*)-**2d**: ^1H NMR (200 MHz, CDCl_3 , TMS) δ 2.18 and 2.49 (a pair of br s, 3H), 3.00–3.67 (br m, 2H), 3.77 and 3.74 (a pair of s, 3H), 4.84–4.98 and 5.10–5.23 (a pair of br m, 1H), 7.03 (t, J = 7.9 Hz, 1H), 7.09–7.31 (m, 2H), 8.22 (br d, J = 7.8 Hz, 1H). The retention time of the authentic (*S*)-**2d** in chiral HPLC analysis with CHIRALPAK AS revealed the absolute configuration of **2d** obtained from the asymmetric hydrogenation of **1d** using (*S,S*)-(*R,R*)-PhTRAP to be *S*.

(*S*)-N-Acetyl-2-(hydroxymethyl)indoline (8). Lithium borohydride (205 mg, 9.4 mmol) was added to a solution of (*S*)-**2d** (1.37 g, 6.2 mmol) in THF (6.2 ml) at room temperature. After stirring for 5 h, the mixture was carefully diluted with 10% HCl aq, and extracted with EtOAc. The organic phase was washed with saturated Na_2CO_3 aq, then with brine, and dried over Na_2SO_4 , and evaporated. The residue was purified with a flash column chromatography (hexane/EtOAc), giving

890 mg (74%) of (*S*)-**8**: ^1H NMR (200 MHz, CDCl_3 , TMS) δ 2.18–2.54 (br s, 3H), 2.54–2.96 (br m, 1H), 3.34 (dd, $J = 9.5, 16.5$ Hz, 1H), 3.43–3.85 (m, 2H), 4.35–4.67 and 4.81–5.09 (a pair of br, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 7.11–7.34 and 7.92–8.12 (br, 3H).

(*S*)-*N*-Acetyl-2-(1-butenyl)indoline (9**).** A solution of dimethyl sulfoxide (78 mg, 1.0 mmol) in CH_2Cl_2 (0.25 ml) was added dropwise to a solution of oxalyl chloride (70 mg, 0.55 mmol) in CH_2Cl_2 (0.5 ml) at -60°C for 30 min. After stirring for 5 min, a solution of (*S*)-**8** (95.6 mg, 0.50 mmol) in CH_2Cl_2 (0.25 ml) was added dropwise to the solution for 5 min. After 15 min, triethylamine (250 mg, 2.5 mmol) was added. After 5 min, the mixture was warmed to room temperature, and stirred for 10 min. The mixture was diluted with water, and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , and evaporated. To a solution of the residue in Et_2O (1.5 ml) was added a suspension of the phosphonium ylide, which was prepared by mixing triphenylpropylphosphonium bromide (202 mg, 0.52 mmol) and potassium *tert*-butoxide (73 mg, 0.65 mmol) in Et_2O (1.5 ml) at 0°C for 2.5 h, at -78°C . After 1 h, the reaction mixture was warmed to room temperature and stirred for 24 h. After dilution with Et_2O , the mixture was filtered, then evaporated. The residue was purified with a preparative TLC (hexane/EtOAc), giving 1.6 mg (1.5%) of (*S*)-**9**: ^1H NMR (200 MHz, CDCl_3 , TMS) δ 1.06 (t, $J = 7.5$ Hz, 3H), 2.08–2.32 (br, 5H), 2.79 (br d, $J = 15.4$ Hz, 1H), 3.56 (br dd, $J = 10.4, 15.4$ Hz, 1H), 5.00–5.18 (br, 1H), 5.36–5.56 (m, 2H), 7.02 (dt, $J = 0.9, 7.5$ Hz, 1H), 7.11–7.29 (m, 2H), 8.20 (br d, $J = 7.6$ Hz, 1H).

(*R*)-*N*-Acetyl-2-butyldoline (2a**).** A mixture of (*S*)-**9** (1.6 mg, 7.4 μmol) and palladium on carbon (5%) (1.3 mg) in MeOH (1.0 ml) was stirred at room temperature and 5.0 MPa of hydrogen pressure for 3h. The mixture was filtered through a pad of Celite[®], and evaporated. The residue was passing through a short column (hexane/EtOAc = 1/1), giving (*R*)-**2a**. The retention time of the authentic (*R*)-**2a** in chiral HPLC analysis with CHIRALPAK AD revealed the absolute configuration of **2a** obtained from the asymmetric hydrogenation of **1a** using (*S,S*)-(*R,R*)-PhTRAP to be *R*.

Methyl (*S*)-*N*-*tert*-Butoxycarbonyl-2-carboxylate (4**).** Triethylamine (213 mg, 2.1 mmol) was added to a solution of (*S*)-**7** (214 mg, 1.0 mmol) in CH_2Cl_2 (2.0 ml) at room temperature. After stirring for 20 min, di-*tert*-butyl dicarbonate (240 mg, 1.1 mmol) was added dropwise to the solution for 10 min. The mixture was stirred for 7 h at room temperature. After dilution with saturated NaHCO_3 aq, the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , and evaporated. The residue was purified by a preparative TLC (hexane/EtOAc), giving 159 mg (57%) of (*S*)-**4**: ^1H NMR (200 MHz, CDCl_3 , TMS) δ 1.51 and 1.59 (a pair of br s, 9H), 3.11 (dd, $J = 4.5, 16.6$ Hz, 1H), 3.51 (dd, $J = 11.4, 16.6$ Hz, 1H), 3.75 (s, 3H), 4.78–4.98 (br, 1H), 6.94 (t, $J = 7.5$ Hz, 1H), 7.11 (d, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 1H), 7.39–7.66 and 7.75–8.00 (a pair of br, 1H). The retention time of the authentic (*S*)-**4** in chiral HPLC analysis with CHIRALCEL OD-H revealed the absolute configuration of **4** obtained from the asymmetric hydrogenation of **3** using (*S,S*)-(*R,R*)-PhTRAP to be *S*.

References

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Figure S-1. ¹H NMR (300 MHz, CDCl₃, TMS) spectrum of 2d.

Figure S-2. ¹³C{¹H} NMR (75 MHz, CDCl₃) spectrum of 2d.