CONTENTS

(A) Hydrogenation of 2-Acetylfuran

Solid *trans*-$RuCl_2$[(*R*)-xylbinap][(*R*)-daipen] [(*R*,*R*)-**2**] (30.5 mg, 0.025 mmol),[1] was placed in a 1.5-L stainless steel autoclave[2] equipped with a mechanical stirring blade, a pressure gauge, and a gas inlet tube attached to a hydrogen source. Air present in the autoclave was replaced by argon.[3] 2-Acetylfuran (**1a**) (110.1 g, 1.0 mol),[4] 2-propanol (100 mL),[5] and a 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (7.5 mL, 7.5 mmol)[6] were added to the autoclave under a stream of argon. The mixture was degassed by three vacuum–filling with argon cycles. Air present in the gas inlet tube was removed by flushing with a stream of hydrogen.[7] The vessel was pressurized to 50 atm, and then the reaction mixture was vigorously stirred for 22 h at 30 °C. The yield and enantiomeric excess (ee) of (*S*)-1-(2-furyl)ethanol [(*S*)-**3a**] determined by GC analysis were 96 and 99%, respectively. GC (column, HP-INNOWax (polyethylene glycol), df = 0.25 μm, 0.25 mm i.d. x 30 m, Hewlett Packard); carrier gas, helium (55 kPa); column temp, 100 °C; injection temp, 200 °C; split ratio, 20:1); retention time (t_R) of **3a**, 22.4 min (95.8%); t_R of **1a**, 13.2 min (0%); t_R of *n*-pentadecane (internal standard), 13.2 min. Chiral GC (column, Chirasil-DEX CB, df = 0.25 μm, 0.32 mm i.d. x 25 m, CHROMPACK; carrier gas, helium (41 kPa); column temp, 75 °C); t_R of (*R*)-**3a** 31.9 min (0.7%); t_R of *S* isomer, 32.4 min (99.3%). After the hydrogen gas was carefully vented, the solvent was removed under reduced pressure. Distillation of the residue

gave (*S*)-**3a** (92.8 g, 83% yield). Bp 76 °C/18 mmHg. $[\alpha]^{24}_D$ –20.1° (*c* 1.00, $CHCl_3$) (lit.[8] $[\alpha]^{25}_D$ +20.8° (*c* 1.27, $CHCl_3$), *R* alcohol). ^1H NMR (400 MHz, $CDCl_3$) δ 1.52 (d, 3, *J* = 6.0 Hz, CH_3), 2.43 (d, 1, *J* = 4.4 Hz, OH), 4.85 (dq, 1, *J* = 4.4 and 6.0 Hz, C*H*OH), 6.21 (d, 1, *J* = 2.8 Hz, C3 proton of furan ring), 6.31 (dd, 1, *J* = 0.8 and 2.8 Hz, C4 proton of furan ring), 7.35 (d, 1, *J* = 0.8 Hz, C5 proton of furan ring).

Notes

(1) For preparation procedure, see: Supporting Information of Ohkuma, T.; Koizumi, M.; Doucet, H.; Pham, T.; Kozawa, M.; Murata, K.; Katayama, E.; Yokozawa, T.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1998**, *120*, 13529–13530.

(2) For details, see: Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Org. Synth.* **1993**, *71*, 1–13; Takaya, H.; Ohta, T.; Inoue, S.; Tokunaga, M.; Kitamura, M.; Noyori, R. *Org. Synth.* **1994**, *72*, 74–85.

(3) Argon gas (99.998%) was further purified by passing through a BASF catalyst R3-11 column at 80 °C.

(4) The substrate was washed with a 0.1 M KOH solution prior to use. Otherwise catalytic activity is substantially lowered.

(5) Guaranteed-reagent grade 2-propanol was freshly distilled over CaH_2 before use.

(6) Purchased from Aldrich Chemical Co.

(7) Hydrogen of 99.99% purity (Nippon Sanso) was used.

(8) Kobayashi, Y.; Kusakabe, M.; Kitano, Y.; Sato, F. *J. Org. Chem.* **1988**, *53*, 1586–1587.

(B) General Procedure for Asymmetric Hydrogenation[1]

A small-scale reaction was normally conducted in a 100-mL glass autoclave. An example is given by hydrogenation of 3-acetylpyridine (**1k**).

Solid (*R*,*R*)-**2** (1.5 mg, 0.00125 mmol) was placed in a 100-mL glass autoclave equipped with a Teflon-coated magnetic stirring bar, a pressure gauge, and a gas inlet tube attached to a hydrogen source. Air present in the autoclave was replaced by argon.

Ketone **1k** (757 mg, 6.25 mmol), 2-propanol (5 mL), and a 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.01 mmol) which had been degassed by bubbling argon were added to the autoclave under a stream of argon. The mixture was degassed by eight vacuum–filling with argon cycles. Air present in the gas inlet tube was removed by flushing with a stream of hydrogen. Hydrogen was initially introduced into the autoclave at a pressure of 4 atm, before being reduced to 1 atm by carefully releasing the stop valve. After this procedure was repeated three times, the vessel was pressurized to 8 atm. The reaction mixture was vigorously stirred at 25 °C for 12 h. After the hydrogen gas was carefully vented, the solvent was removed under reduced pressure. The yield and ee of (*S*)-1-(3-pyridyl)ethanol [(*S*)-**7**] determined by GC analysis were 100 and 99.6%, respectively. GC (column, Chirasil-DEX CB; 44 kPa; column temp, 120 °C); t_R of (*R*)-**7**, 25.6 min (0.2%); t_R of *S* isomer, 26.0 min (99.8%); t_R of **1k**, 7.7 min (0%). After the solvent was removed under reduced pressure, the residue was purified by bulb-to-bulb distillation to give (*S*)-**7** (728 mg, 95% yield). $[\alpha]^{24}_D$ –56.3° (*c* 1.00, C_2H_5OH) (lit.[2] $[\alpha]^{25}_D$ –30° (*c* 4.92, C_2H_5OH), *S* alcohol). ^1H NMR (270 MHz, $CDCl_3$) δ 1.52 (d, 3, *J* = 6.8 Hz, CH_3), 3.16 (br s, 1, OH), 4.94 (q, 1, *J* = 6.8 Hz, C*H*OH), 7.27 (dd, 1, *J* = 4.9 and 8.1 Hz, C5 proton of pyridine ring), 7.74 (d, 1, *J* = 8.1 Hz, C4 proton of pyridine ring), 8.46 (d, 1, *J* = 4.9 Hz, C6 proton of pyridine ring), 8.56 (s, 1, C2 proton of pyridine ring).

Notes

(1) See Notes of Part A.

(2) Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 3530–3532.

(C) Reaction Conditions of Asymmetric Hydrogenation and Analytical Data of Products

Hydrogenation of 2-acetylfuran (1a). Conditions: (*R*,*R*)-**2** (1.6 mg, 0.00136 mmol), **1a** (750 mg, 6.81 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (4.5 mL), 8 atm H_2, 25 °C, 12 h. **3a** (714 mg, 94% yield, 99% ee). See also Part A. **Hydrogenation of 1-(2-furyl)hexan-1-one (1b)** Conditions: (*R*,*R*)-**2**

(1.5 mg, 0.00125 mmol), **1b** (416 mg, 2.5 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (2.5 mL), 8 atm H_2, 25 °C, 14 h. (*S*)-1-(2-Furyl)hexan-1-ol [(*S*)-**3b**] (392 mg, 93% yield, 98% ee). GC (column, Chirasil-DEX CB; 41 kPa; column temp, 120 °C); t_R of (*R*)-**3b**, 28.9 min (0.9%); t_R of *S* isomer, 26.8 min (99.1%); t_R of **1b**, 11.6 min (0%). $[\alpha]^{20}_D$ –14.3° (*c* 1.03, $CHCl_3$), lit. $[\alpha]^{25}_D$ +13.8° (*c* 1.07, $CHCl_3$), (*R*), Kobayashi, Y.; Kusakabe, M.; Kitano, Y.; Sato, F. *J. Org. Chem.* **1988**, *53*, 1586–1587. **Hydrogenation of 1-(2-furyl)-5-hexen-1-one (1c)** Conditions: (*R*,*R*)-**2** (1.5 mg, 0.00125 mmol), **1c** (411 mg, 5.0 mmol, 96% purity), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (20 μL, 0.020 mmol), 2-propanol (2.5 mL), 8 atm H_2, 25 °C, 2 h. (*S*)-1-(2-Furyl)-5-hexen-1-ol [(*S*)-**3c**] (403 mg, 97% yield, 96% purity). GC (column, HP-5 (95:5 poly(dimethylsiloxane)–poly(diphenylsiloxane)), df = 0.25 μm, 0.25 mm i.d. x 30 m, Hewlett Packard); 55 kPa, column temp, 65 °C); t_R of **3c**, 71.6 min (100%); t_R of **3b**, 75.9 min (0%); t_R of **1c**, 85.8 min (0%). The ee determined by chiral HPLC analysis of its 4-bromobenzoate was 97%: column, CHIRALCEL OJ (4.6 mm i.d. x 250 mm, Daicel Chemical Industries); eluent, 10:90 2-propanol–hexane; temp, 30 °C; flow rate, 0.3 mL/min; detection, 254-nm light; t_R of (*R*)-**3c**, 18.4 min (1.6%); t_R of *S* isomer, 15.8 min (98.4%). $[\alpha]^{18}_D$ –15.6° (*c* 1.02, $CHCl_3$). The absolute configuration was determined by chiral GC analysis after conversion to (*S*)-**3b** by saturation of the terminal olefin, conditions: (*S*)-**3c** (125 mg, 0.75 mmol), $RuCl_2[P(C_6H_5)_3]_3$ (1.0 mg, 0.0005 mmol), CH_3OH (2.5 mL), 8 atm H_2, 25 °C, 21 h. (*S*)-**3b** (117 mg, 93% yield, 100% ee). GC (column, Chirasil-DEX CB; 41 kPa; column temp, 120 °C); t_R of (*R*)-**3b**, 28.9 min (0%); t_R of *S* isomer, 26.8 min (100%). **Hydrogenation of 2-acetylthiophene (1d)** Conditions: (*R*,*R*)-**2** (1.4 mg, 0.00115 mmol), **1d** (749 mg, 5.93 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (4.5 mL), 8 atm H_2, 25 °C, 12 h. (*S*)-1-(2-Thienyl)ethanol [(*S*)-**3d**] (722 mg, 95% yield, 99% ee). GC (column, Chirasil-DEX CB; 44 kPa; column temp, 100 °C); t_R of (*R*)-**3d**, 32.2 min (0.6%); t_R of *S* isomer, 34.2 min (99.4%); t_R of **1d**, 12.6 min (0%). $[\alpha]^{24}_D$ –26.0° (*c* 1.02, $CHCl_3$), lit. $[\alpha]^{25}_D$ +8.33° (*c* 9.6, $CHCl_3$), (*R*), Kasai, M.; Ziffer, H.; Kawai, K.; Kasai, M.; Imuta, M.; Froussios. *J. Org. Chem.* **1983**, *48*,

3017–3021. **Hydrogenation of 3-acetylthiophene (1e).** Conditions: (*R*,*R*)-**2** (1.4 mg, 0.00115 mmol), **1e** (749 mg, 5.93 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (2.5 mL), 8 atm H_2, 25 °C, 5 h. (*S*)-1-(3-Thienyl)ethanol [(*S*)-**4**] (745 mg, 98% yield, 99.7% ee). GC (column, Chirasil-DEX CB; 44 kPa; column temp, 100 °C); t_R of (*R*)-**4**, 35.5 min (0.2%); t_R of *S* isomer, 36.4 min (99.8%); t_R of **1e**, 14.5 min (0%). $[\alpha]^{25}_D$ –44.7° (*c* 1.00, C_2H_5OH). The absolute configuration was determined by single-crystal X-ray analysis of its (1*S*)-camphanoate (See Figure 1 in Part E.). Reaction conditions: **4** (128 mg, 1.0 mmol), (1*S*)-camphanoyl chloride (238 mg, 1.1 mmol), 4-(dimethylamino)pyridine (134 mmol, 1.1 mmol), CH_2Cl_2 (5 mL), 0 °C, 6 h. (*S*)-1-(3-Thienyl)ethyl (1*S*)-camphanoate (253 mg, 82% yield). Recrystallization from ether, mp 88.6–89.7 °C. **Hydrogenation of 2-acetyl-1-methylpyrrole (1f).** Conditions: (*S*,*S*)-**2** (6.1 mg, 0.0050 mmol), **1f** (617 mg, 5.01 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (100 μL, 0.10 mmol), 2-propanol (18 mL), 8 atm H_2, 25 °C, 20 h. The conversion determined by ^{1}H-NMR analysis was 61%. Isolation using a silica-gel column (SiO_2, 31 g) eluted with a 1:2 mixture of ethyl acetate and hexane including 0.5% of $(C_2H_5)_3N$ gave 1-[2-(1-methylpyrrolyl)]ethanol (**3e**) (318 mg, 51% yield). The ee determined by chiral HPLC analysis was 97%: column, CHIRALCEL OJ; eluent, 10:90 2-propanol–hexane; temp, 30 °C; flow rate, 0.2 mL/min; detection, 254-nm light; t_R of **3e**, 36.7 min (1.4%) and 41.0 min (98.6%). $[\alpha]^{25}_D$ –36.3° (*c* 0.55, C_2H_5OH). Absolute configuration was not determined. **Hydrogenation of 2-acetyl-1-(4-toluenesulfonyl)pyrrole (1g).** Conditions: (*R*,*R*)-**2** (1.5 mg, 0.00125 mmol), **1g** (329 mg, 1.25 mmol), 0.1 M *t*-C_4H_9OK in *tert*-butyl alcohol (50 μL, 0.005 mmol), 10:1 2-propanol–DMF (5.5 mL), 8 atm H_2, 25 °C, 18 h. 1-[2-{1-(4-Toluenesulfonyl)}pyrrolyl]ethanol [(*S*)-**3f**] (307 mg, 93% yield). The ee determined by chiral HPLC analysis was 98%: column, CHIRALCEL OJ; eluent, 10:90 2-propanol–hexane; temp, 30 °C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of (*R*)-**3f**, 71.6 min (1.0%); t_R of *S* isomer, 57.3 min (99.0%). $[\alpha]^{23}_D$ –17.3° (*c* 1.06, $CH_3CO_2C_2H_5$), lit. $[\alpha]^{20}_D$ +21.5° (*c* 1.0, $CH_3CO_2C_2H_5$), (*R* based on the Horeau method), Zhou, W.-S.; Wei, D. *Tetrahedron: Asymmetry* **1991**, *2*, 767–770.

Hydrogenation of 2-acetylthiazole (1h). Conditions: (*R*,*R*)-**2** (3.1 mg, 0.0025 mmol), **1h** (636 mg, 5.0 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (20 μL, 0.020 mmol), 0.5 M $B[OCH(CH_3)_2]_3$ in 2-propanol (0.1 mL), 2-propanol (5 mL), 8 atm H_2, 25 °C, 12 h. (*S*)-1-(2-Thiazolyl)ethanol [(*S*)-**5**] (606 mg, 94% yield, 96% ee). GC (column, Chirasil-DEX CB; 41 kPa; column temp, 100 °C); t_R of (*R*)-**5**, 72.9 min (2.2%); t_R of *S* isomer, 74.4 min (97.8%); t_R of **1h**, 8.6 min (0%). $[\alpha]^{27}_D$ –23.2° (*c* 1.64, $CHCl_3$). The absolute configuration was determined by the sign of rotation after conversion to 2-benzyloxy-1-propanal according to the literature, Dondoni, A.; Perrone, D. *J. Org. Chem.* **1995**, *60*, 4749–4754. A reference sample was prepared from (*S*)-ethyl lactate. Reaction conditions: Benzylation; **5** (1.29 g (10 mmol), NaH (60% oil suspension) (606 mg, 15 mmol), benzyl bromide (2.56 g, 15 mmol), THF (20 mL), 0 °C, 1 h. 1-Benzyloxy-1-(2-thiazolyl)ethane (1.86 g, 85% yield). Methylation of the thiazole ring; 1-benzyloxy-1-(2-thiazolyl)ethane (1.86 g, 8.5 mmol), CH_3I (7.7 mL), CH_3CN (40 mL), reflux, 12 h. Reduction of the thiazole ring; a crude 2-(1-benzyloxyethyl)-3-methylthiazolium iodide, $NaBH_4$ (548 mg, 14.5 mmol), CH_3OH (54 mL), 0 °C, 0.5 h. Formylation; a crude 2-(1-benzyloxyethyl)-3-methylthiazolidine, $CuCl_2 \cdot 2H_2O$ (1.74 g (10.2 mmol), CuO (6.32 g (45.9 mmol), 10:1 CH_3CN–H_2O (100 mL), 25 °C, 40 min. 2-Benzyloxy-1-propanal (0.979 g, 70% yield). $[\alpha]^{27}_D$ –63.7° (*c* 2.05, $CHCl_3$). Benzylation; (*S*)-ethyl lactate (1.18 g, 10 mmol) (Kanto Chemical Co., Inc.), NaH (60% oil suspension) (482 mg, 11 mmol), benzyl bromide (1.88 g, 11 mmol), THF (20 mL), 0 °C, 50 min. Reduction of ethoxycarbonyl group; a crude ethyl 2-benzyloxypropionate, 1.0 M DAIBAL-H in hexane (6.6 mL, 6.6 mmol), hexane (25 mL), –78 °C, 25 min. (*S*)-2-Benzyloxy-1-propanal (0.84 g, 51% yield in two steps). $[\alpha]^{26}_D$ –37.7° (*c* 2.26, $CHCl_3$). **Hydrogenation of 2-acetylpyridine (1i).** Conditions: (*R*,*R*)-**2** (3.1 mg, 0.0025 mmol), **1i** (606 mg, 5.0 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (20 μL, 0.020 mmol), 0.5 M $B[OCH(CH_3)_2]_3$ in 2-propanol (0.1 mL), 2-propanol (8 mL), 8 atm H_2, 25 °C, 3 h. (*S*)-1-(2-Pyridyl)ethanol [(*S*)-**6a**] (585 mg, 96% yield). GC (column, HP-INNOWax; 55 kPa, column temp, 120 °C); t_R of **6a**, 24.9 min (99.7%); t_R of **1i**, 12.7 min (0.3%). The ee determined by chiral HPLC analysis was 96%: column,

CHIRALCEL OB-H (4.6 mm i.d. x 250 mm, Daicel Chemical Industries); eluent, 10:90 2-propanol–hexane; temp, 30 °C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of (*R*)-**6a**, 12.6 min (97.9%); t_R of *S* isomer, 14.6 min (2.1%). $[\alpha]^{25}_D$ –58.3° (*c* 0.51, C_2H_5OH), lit. $[\alpha]^{25}_D$ –56.7° (*c* 3.88, C_2H_5OH), (*S*), Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 3530–3532. **Hydrogenation of 1-(2-pyridyl)-2-methylpropan-1-one (1j).** Conditions: (*R*,*R*)-**2** (3.1 mg, 0.00125 mmol), **1j** (373 mg, 2.5 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (2.5 mL), 8 atm H_2, 25 °C, 12 h. (*S*)-1-(2-Pyridyl)-2-methylpropan-1-ol [(*S*)-**6b**] (355 mg, 94% yield). GC (column, HP-INNOWax; 55 kPa, column temp, 120 °C); t_R of **6b**, 32.8 min (100%); t_R of **1j**, 16.4 min (0%). The ee determined by chiral HPLC analysis was 94%: column, CHIRALPAK AS (4.6 mm i.d. x 250 mm, Daicel Chemical Industries) and CHIRALPAK AS (4.6 mm i.d. x 50 mm); eluent, 3:97 2-propanol–hexane; temp, 30 °C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of (*R*)-**6b**, 25.8 min (2.9%); t_R of *S* isomer, 27.9 min (97.1%). $[\alpha]^{17}_D$ –25.2° (*c* 0.96, $CHCl_3$). The absolute configuration was determined by single-crystal X-ray analysis of its (1*S*)-camphanoate (See Figure 2 in Part E.). Reaction conditions: **6b** (151 mg, 1.0 mmol), (1*S*)-camphanoyl chloride (238 mg, 1.1 mmol), 4-(dimethylamino)pyridine (134 mg, 1.1 mmol), CH_2Cl_2 (5 mL), 0 °C, 6 h. (*S*)-1-(2-Pyridyl)-2-methylpropyl (1*S*)-camphanoate (317 mg, 95% yield). Rrecrystallization from 1:10 ethyl acetate–hexane, mp 84.0–84.9 °C. **Hydrogenation of 3-acetylpyridine (1k).** See Part B. **Hydrogenation of 4-acetylpyridine (1l).** Conditions: (*R*,*R*)-**2** (1.5 mg, 0.00125 mmol), **1l** (757 mg, 6.25 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (10 μL, 0.010 mmol), 2-propanol (4.5 mL), 8 atm H_2, 25 °C, 12 h. (*S*)-1-(4-Pyridyl)ethanol [(*S*)-**8**] (754 mg, 98% yield, 99.8% ee). GC (column, Chirasil-DEX CB; 44 kPa; column temp, 120 °C); t_R of (*R*)-**8**, 30.2 min (0.1%); t_R of *S* isomer, 30.6 min (99.9%); t_R of **1l**, 7.1 min (0%). $[\alpha]^{26}_D$ –54.9° (*c* 1.02, C_2H_5OH), lit. $[\alpha]^{25}_D$ –43.4° (*c* 0.5, C_2H_5OH), (*S*), Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 3530–3532. **Hydrogenation of 2,6-diacetylpyridine (9).** Conditions: (*R*,*R*)-**2** (1.4 mg, 0.001 mmol), **9** (1.63 g, 10.0 mmol), 1.0 M *t*-C_4H_9OK in *tert*-butyl alcohol (40 μL, 0.040 mmol), 2-propanol (10 mL), 8 atm H_2, 25 °C, 17 h.

(*S,S*)-2,6-Di(1-hydroxyethyl)pyridine [(*S,S*)-**10**] (1.64 g, 98% yield, 100% ee). GC (column, Chirasil-DEX CB; 80 kPa; column temp, 130 °C); t_R of (*R,R*)-**10**, 34.3 min (0%); t_R of *S,S* isomer, 23.3 min (99.9%); t_R of meso isomer, 26.9 min (0%); t_R of **9**, 12.7 min (0.1%). $[\alpha]^{17}_D$ –28.9° (*c* 3.00, $CHCl_3$), lit. $[\alpha]^{20}_D$ –26.84° (*c* 2.98 $CHCl_3$), (*S,S*), Bailey, D.; O'Hagan, D.; Dyer, U.; Lamont, R. B. *Tetrahedron: Asymmetry* **1993**, 4, 1255–1258. **Hydrogenation of (*E*)-4-(2-thienyl)-3-buten-2-one (11).** Conditions: (*R,R*)-**2** (1.2 mg, 0.00098 mmol), **11** (748 mg, 4.91 mmol), K_2CO_3 (5.4 mg, 0.039 mmol), 2-propanol (8 mL), 8 atm H_2, 25 °C, 17 h. (*S*)-(*E*)-4-(2-Thienyl)-3-buten-2-ol [(*S*)-**12**] (742 mg, 98% yield, 91% ee). GC (column, Chirasil-DEX CB; 41 kPa; column temp, 95 °C); t_R of (*R*)-**12**, 172.2 min (3.9%); t_R of *S* isomer, 178.4 min (96.1%); t_R of 4-(2-thienyl)butan-2-ol, 114.0 min (0%) and 124.1 min (0%); t_R of **11**, 40.3 min (0%). $[\alpha]^{25}_D$ –41.3° (*c* 0.49, $CHCl_3$). The absolute configuration was determined by CD spectrum analysis of its 4-bromobenzoate. Reaction conditions: (*E*)-4-(2-thienyl)-3-buten-2-ol (463 mg, 3.0 mmol), 4-bromobenzoyl chloride (724 mg, 3.3 mmol), 4-(dimethylamino)pyridine (402 mg, 3.3 mmol), CH_2Cl_2 (5 mL), 0 °C, 3 h. 2-[(*E*)-4-(2-Thienyl)-3-butenyl] 4-bromobenzoate (685 mg, 68% yield). CD (CH_3OH), λ_{ext} 252 nm; $\Delta\varepsilon$ +2.59. The positive Cotton effect is correlated with the *S* configuration of the allylic alcohol. See: Gonnella, N. C.; Nakanisni, K.; Martin, V. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 3775–3776. Nakanishi, K.; Berova, N. In *Circular Dichroism: Principles and Applications;* Nakanishi, K.; Berova, N.; Woody, R. W. Eds.; VCH: New York, 1994, Chapter 13.

(D) Hydrogenation of 3-Dimethylamino-1-(2-thienyl)-1-propanone[1]

Solid (*R,R*)-**2** (3.0 mg, 0.0025 mmol) was placed in a 100-mL glass autoclave equipped with a Teflon coated magnetic stirring bar, a pressure gauge, and a gas inlet tube attached to a hydrogen source. Air present in the autoclave was replaced by argon. 2-Propanol (1.5 mL) and a 1.0 M *t*-C_4H_9OK solution in *tert*-butyl alcohol (20 μL, 0.02 mmol) which had been degassed by bubbling argon were added to the autoclave under a stream of argon. The mixture was degassed by five vacuum–filling with argon cycles,

and then was stirred at 25 °C for 40 min under argon atmosphere.[2] To this solution were added 2-propanol (1.5 mL) and 3-dimethylamino-1-(2-thienyl)-1-propanone (**13**) (916 mg, 5.0 mmol) which had been degassed by bubbling argon. The mixture was degassed by five vacuum–filling with argon cycles. Air present in the gas inlet tube was removed by flushing with a stream of hydrogen. Hydrogen was initially introduced into the autoclave at a presence of 5 atm, before being reduced to 2 atm by carefully releasing the stop valve. After this procedure was repeated ten times, the vessel was pressurized to 8 atm. The reaction mixture was vigorously stirred at 25 °C for 7 h. After the hydrogen gas was carefully vented the solvent was removed under reduced pressure to give (*S*)-3-dimethylamino-1-(2-thienyl)propan-1-ol [(*S*)-**14**]. The yield determined by ^{1}H-NMR analysis using methyl propionate (chemical shift of CH_3O, δ = 3.67) as an internal standard was 100%. The residue was purified by buld-to-bulb distillation to give pure (*S*)-**14** (845 mg, 91% yield, 92% ee). $[\alpha]^{22}_D$ –7.72° (*c* 1.03, CH_3OH), lit.[3] $[\alpha]_D$ –7.6° (*c* 1.0, CH_3OH). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.87–2.00 (m, 2, CH_2CH_2N), 2.93 (s, 6, $N(CH_3)_2$), 2.53–2.69 (m, 2, CH_2CH_2N), 5.19 (t, 1, *J* = 6.0 Hz, $CH(OH)CH_2$), 6.92 (d, 1, *J* = 3.6, Hz C3 proton of thiophene ring), 6.97 (dd, 1, *J* = 3.6 and 4.8 Hz, C4 proton of thiophene ring), 7.21 (d, 1, *J* = 4.8 Hz, C5 proton of thiophene ring). HPLC (colum, CHIRALCEL OD (4.6 mm i.d. x 250 mm, Daicel Chemical Industries); eluent, 5:95:0.2 2-propanol–hexane–diethylamine; temp, 30 °C; flow rate, 0.5 mL/min; detection, 254-nm light; t_R of (*R*)-**14**, 18.1 min (4.2%); t_R of *S* isomer, 19.3 min (95.8%).

Notes

(1) See Notes of Part A and B.

(2) This pretreatment diminished the induction period and also minimized β-elimination of **13**.

(3) Deeter, J.; Frazier, J.; Staszak, M.; Weigel, L. *Tetrahedron Letters* **1990**, *31*, 7101–7104.

(E) ORTEP Plots of the Molecular Structures

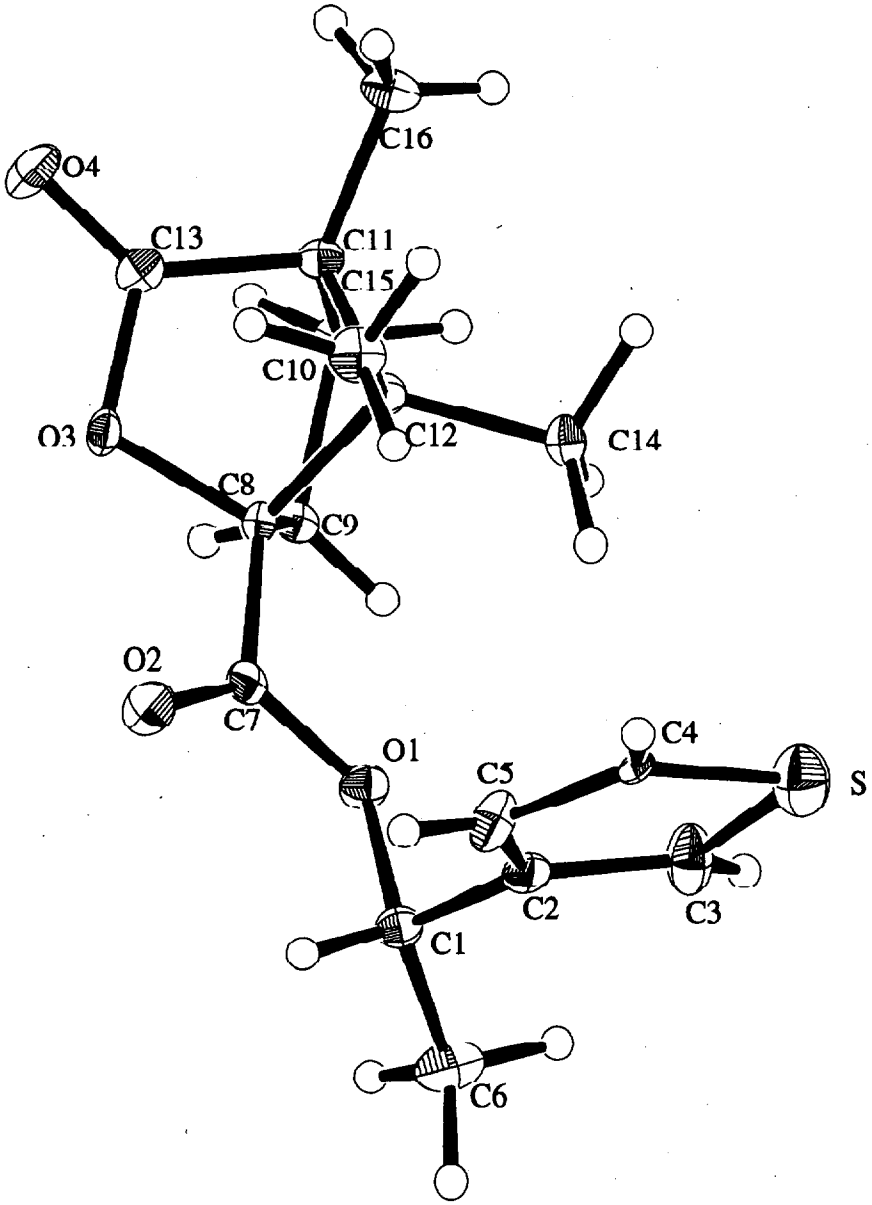

Figure 1. ORTEP plots of the molecular structure of (*S*)-1-(3-thienyl)ethyl (1*S*)-camphanoate. Crystallographic data: $C_{16}H_{20}SO_4$, M_r = 308.39, colorless prism, 0.3 x 0.15 x 0.2 mm, monoclinic, space group $P2_1$ (no. 4), a = 7.228(1), b = 13.159(2), c = 8.1029(3) Å, β = 96.6471(8)°, V = 765.5(2) Å^3, Z = 2, ρ_{calcd} = 1.338 gcm^{-3}, μ(MoKα) = 2.24 cm^{-1}, T = 150 K.

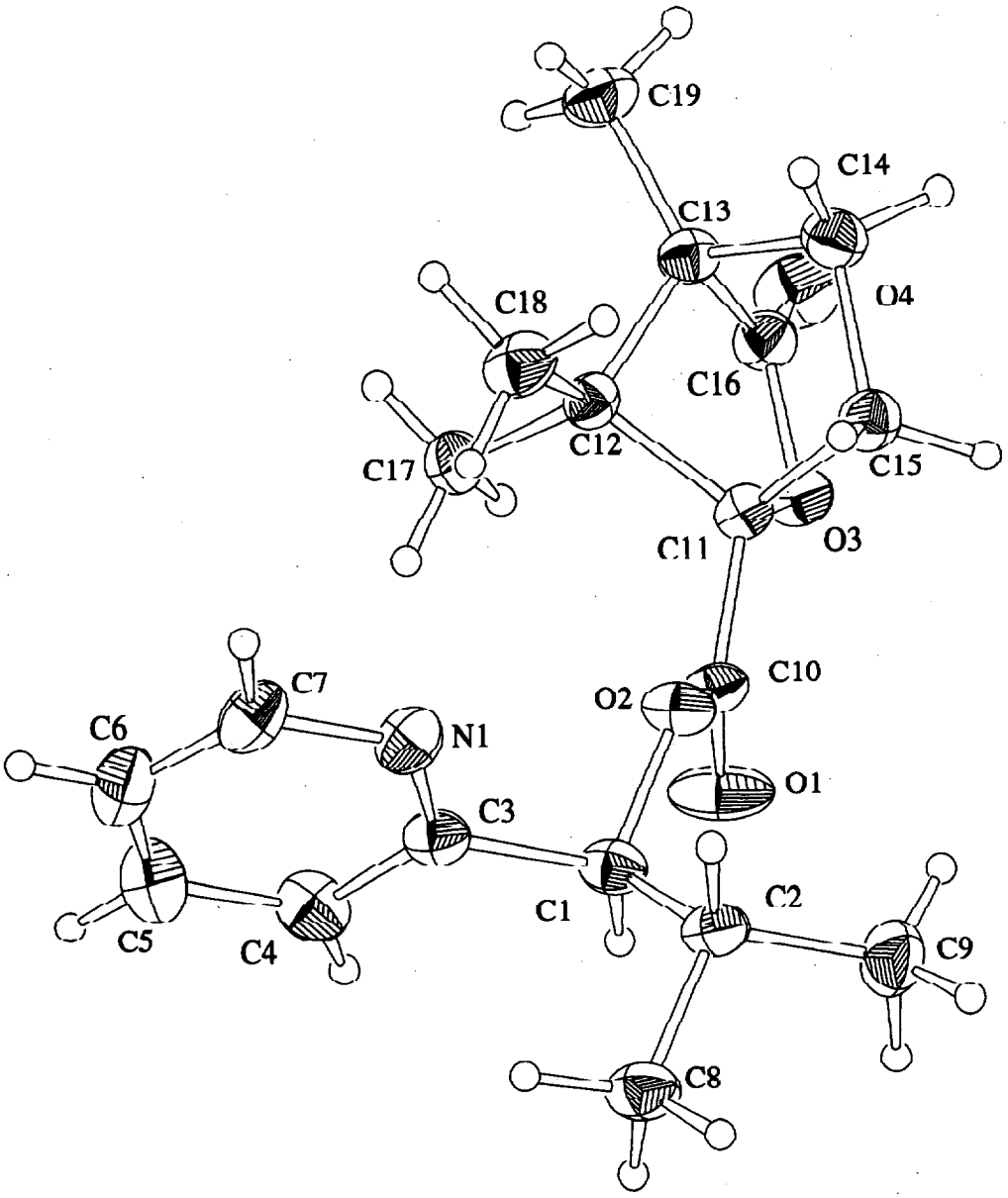

Figure 2. ORTEP plots of the molecular structure of (*S*)-1-(2-pyridyl)-2-methylpropyl (1*S*)-camphanoate. Crystallographic data: $C_{19}H_{25}O_4N$, M_r = 331.41 colorless prism, 0.15 x 0.2 x 0.2 mm, orthorhombic, space group $P2_12_12_1$ (no. 19), a = 7.4500(3), b = 12.1475(4), c = 20.2220(5) Å, V = 1830.1(1) Å^3, Z = 4, ρ_{calcd} = 1.203 gcm^{-3}, $\mu(MoK\alpha)$ = 0.84 cm^{-1}, T = 293 K.