OL0002119

Revised

Supporting Information of Asymmetric Transfer Hydrogenation of Benzaldehydes

Issaku Yamada and Ryoji Noyori*

Department of Chemistry and Research Center for Materials Science
Nagoya University
Chikusa, Nagoya 464-8602, Japan

CONTENTS

(A) Typical Procedure for Asymmetric Transfer Hydrogenation with 2-Propanol

Guaranteed-reagent grade 2-propanol was freshly distilled over CaH_2 before use. A solution of $RuCl_2$[(*R*,*R*)-tsdpen](η^6-*p*-cymene) [(*R*,*R*)-**3a**] (31.8 mg, 0.05 mmol) in 2-propanol (100 mL) was placed under Ar atmosphere in a 250-mL round-bottomed flask and stirred at 22 °C for 10 min. To the resulting orange solution benzaldehyde-1-*d* (**1a**) (1.07 g, 10.0 mmol)[1] and a solution of 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (50 μL, 50 μmol) were added. The mixture was stirred at 22 °C for 50 min, neutralized with diluted hydrochloric acid, and concentrated *in vacuo*. The residue was diluted with ethyl acetate, and the organic solution was washed with aqueous $NaHCO_3$ and brine. The orange layer was dried over Na_2SO_4, concentrated under reduced pressure, and distilled to afford (*R*)-benzyl-1-*d* alcohol [(*R*)-**2a**] in 96% ee (1.00 g, 92% yield). $[\alpha]_D^{28}$ –1.39° (neat, d^{24} = 1.052) (lit.[2] $[\alpha]_D^{20}$ +0.68° (*c* 6.7, cyclopentane), *S* alcohol in 39–42% ee). GC (column, HP-INNOWax (polyethylene glycol), df = 0.25 μm, 0.25 mm i.d. x 30 m, Hewlett Packard); carrier gas, helium (350 kPa); column temp, 150 °C; injection temp, 250 °C; split ratio, 20:1); retention time (t_R) of **2a**, 2.78 min (100%); t_R of **1a**, 1.18 min (0%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.78 (br s, 1, OH), 4.65 (m, 1, C_6H_5CDH), 7.1–7.5 (m, 5, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 141.09, 128.68, 127.72, 127.18, 62.25 (t, *J* = 22 Hz). The extent of deuteration of carbinyl proton was judged to be >99% by ^{1}H-NMR analysis. The ee was determind by ^{1}H NMR by comparison of signal intensities of the non-deuterated carbinyl protons of the MTPA ester.[3] ^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-MTPA ester derived from (*S*)-**2a** and (*S*)-MTPA chloride, δ 5.31 (2%); (*R*)-MTPA ester of (*R*)-**2a**, δ 5.35 (98%).

Notes

(1) The substrate in ethyl ether was washed with a 0.1 M KOH solution, dried over Na_2SO_4, concentrated, and distilled (72–74 °C/20 mmHg) before use. C_6H_5CHO was not detected by ^{1}H-NMR analysis.

(2) Reich, C. J.; Sullivan G. R.; Mosher, H. S. *Tetrahedron Lett.* **1973**, *17*, 1505–

1508.

(3) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.

(B) Reaction Conditions of Asymmetric Transfer Hydrogenation of 1 with 2-Propanol and Analytical Data of Products

The reaction was normally carried out using a 0.1 M solution of **1** (1 mmol) in 2-propanol. **Reaction of *p*-methylbenzaldehyde-1-*d* (1b) with (*R*,*R*)-3a.** Conditions: **1b** (121 mg, 1.00 mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h. (*R*)-*p*-Methylbenzyl-1-*d* alcohol [(*R*)-**2b**] (118 mg, 96% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 150 °C); t_R of **2b**, 3.64 min (99%); t_R of **1b**, 1.57 min (1%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3, $C_6H_5CH_3$), 2.58 (br s, 1, OH), 4.62 (m, 1, CDH), 7.13 (d, J = 8 Hz, 2, aromatics), 7.18 (d, J = 8 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 137.89, 137.21, 129.15, 127.12, 64.61 (t, J = 22 Hz), 21.11. The d_1 content was >99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 98%: (*R*)-MTPA ester of (*S*)-**2b**, δ 5.25 (1%); (*R*)-**2b**, δ 5.31 (99%). **Reaction of *p*-methoxylbenzaldehyde-1-*d* (1c) with (*R*,*R*)-3a.** Conditions: **1c** (137 mg, 1.00 mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h. (*R*)-*p*-Methoxylbenzyl-1-*d* alcohol [(*R*)-**2c**] (113 mg, 82% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 180 °C); t_R of **2c**, 3.95 min (87%); t_R of **1c**, 2.17 min (13%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58 (br s, 1, OH), 3.76 (s, 3, OCH_3), 4.51 (m, 1, CDH), 6.84 (d, J = 8 Hz, 2, aromatics), 7.21 (d, J = 8 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.07, 133.19, 128.59, 113.87, 64.31 (t, J = 22 Hz), 55.22. The d_1 content of was >99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 99%: (*R*)-MTPA ester of (*S*)-**2c**, δ 5.23 (0.5%); (*R*)-**2c**, δ 5.30 (99.5%). **Reaction of *p*-bromobenzaldehyde-1-*d* (1d) with (*R*,*R*)-3a.** Conditions: **1d** (186 mg, 1.00

mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h. (*R*)-*p*-Bromobenzyl-1-*d* alcohol [(*R*)-**2d**] (174 mg, 93% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 180 °C); t_R of **2d**, 5.43 min (97%); t_R of **1d**, 1.75 min (3%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.64 (br s, 1, OH), 4.64 (m, 1, CDH), 7.25 (d, J = 8 Hz, 2, aromatics), 7.49 (d, J = 8 Hz, 2, aroamtics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 139.63, 131.51, 128.56, 121.32, 63.86 (t, J = 22 Hz). The d_1 content was >99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 96%: (*R*)-MTPA ester of (*S*)-**2d**, δ 5.26 (2%); (*R*)-**2d**, δ 5.28 (98%). **Reaction of *p*-trifluoromethylbenzaldehyde-1-*d* (1e) with** (*R*,*R*)-**3a**. Conditions: **1e** (175 mg, 1.00 mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h. (*S*)-*p*-Trifluoromethylbenzyl-1-*d* alcohol [(*S*)-**2e**] (170 mg, 96% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 140 °C); t_R of **2e**, 4.71 min (98%); t_R of **1e**, 1.11 min (2%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.77 (br s, 1, OH), 4.66 (m, 1, CDH), 7.41 (d, J = 8.3 Hz, 2, aromatics), 7.58 (d, J = 8.3 Hz, 2H, aromtics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.71, 129.85 (q, J_{C-F} = 32 Hz), 126.92, 125.49 (q, J_{C-F} = 3.6 Hz), 124.26 (q, J_{C-F} = 272 Hz), 64.02 (t, J_{C-D} = 22 Hz). The d_1 content of was >99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 96%: (*R*)-MTPA ester (*S*)-**2e**, δ 5.38 (2%); (*R*)-**2e**, δ 5.36 (98%). **Reaction of *trans*-cinnamaldehyde-1-*d* (5) with** (*R*,*R*)-**3b**. Conditions: **5** (67 mg, 0.5 mmol), (*R*,*R*)-**3b** (3.0 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (30 μL, 30 μmol), 2-propanol (5.0 mL), 28 °C, 15 min. (*R*)-*trans*-Cinnamyl-1-*d* alcohol (65.6 mg, 97% yield). GC (column, HP-INNOWax; carrier gas, helium (350 kPa); column temp, 180 °C); t_R of *trans*-cinnamyl-1-*d* alcohol, 3.97 min (97%); t_R of **5**, 2.21 min (3%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (br s, 1, OH), 4.31 (m, 1, CDH), 6.37 (dd, J = 6 Hz, J = 16 Hz, 1, C*H*=CHC$_6$H$_5$), 6.63 (d, J = 16 Hz, 1, CH=C*H*C$_6$H$_5$), 7.25 (t, J = 7 Hz, 1, aromatics), 7.32 (t, J = 7 Hz, 2, aromatics), 7.39 (d, J = 7 Hz, 2, aromatics). The d_1 content of was

>99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 72%: (*R*)-MTPA ester of (*S*)-*trans*-cinnamyl-1-*d* alcohol, δ 4.94 (14%); (*R*)-*trans*-cinnamyl-1-*d* alcohol, δ 4.96 (86%). **Reaction of dihydrocinnamaldehyde-1-*d* (6) with (*R*,*R*)-3a.** Conditions: **6** (135 mg, 1.00 mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 10 min. (*R*)-Dihydrocinnamyl-1-*d* alcohol (105 mg, 76% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 180 °C); t_R of (*R*)-dihydrocinnamyl-1-*d* alcohol, 2.13 min (90%); t_R of **6**, 1.27 min (10%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (br s, 1, OH), 1.90 (dt, *J* = 7 Hz, *J* = 8 Hz, 2, CH_2), 2.71 (dd, *J* = 8 Hz, *J* = 8 Hz, 2, CH_2), 3.66 (br t, *J* = 7 Hz, 1, CH), 7.15–7.30 (m, 5, aromatics). The d_1 content was >99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 24%: (*R*)-MTPA ester of (*S*)-dihydrocinnamyl-1-*d* alcohol, δ 4.28 (38%); (*R*)-dihydrocinnamyl-1-*d* alcohol, δ 4.33 (62%).

(C) Kinetic Study of Transfer Hydrogenation

Electrospray ionization (ESI) mass analysis of (*R*,*R*)-4 in 2-propanol: $[RuCl(\eta^6\text{-benzene})]_2$ (2.5 mg, 0.005 mmol), (*R*,*R*)-1,2-diphenylethanolamine (2.1 mg, 0.01 mmol), and 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (10 μL, 10 μmol) in 2-propanol (100 mL) was mixted at 28 °C and was stirred for 1h to give (*R*,*R*)-**4**. ESI mass analysis showed an $[M + 1]^+$ peak at 428 (isotope cluster centered around 428).[1]

(1) For detection of a similar Ru–aminoindanol complex using ESI mass, see: Kenny, J. A.; Versluis, K.; Heck, A. J. R.; Walsgrove, T.; Wills, M. *Chem. Commun.* **2000**, 99–100.

Preparation of Ru catalyst (*R*,*R*)-**4**: A mixture of $[RuCl_2(\eta^6\text{-benzene})]_2$ (250 mg, 0.50 mmol), (*R*,*R*)-1,2-diphenylethaolamine (213 mg, 1.00 mmol), and triethylamine (1.0 mL) in 2-propanol (10 mL) was heated at 90 °C for 1.5 h. The orange

solution was concentrated and the solid Ru complex was collected by filtration. The crude material was washed with a small amount of water and dried under reduced pressure to afford RuCl[(*R*,*R*)-OCH(C_6H_5)CH(C_6H_5)NH_2](η^6-benzene) [(*R*,*R*)-**4**] (396 mg, ca. 90% yield, contaminated with 10% of [$RuCl_2$(η^6-benzene)]$_2$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.41 (m, 1, CHO), 4.75 (m, 1, CHN), 5.30 (br s, 6, η^6-C_6H_6), 5.36 (m, 1, NH), 5.49 (m, 1, NH), 6.9–7.5 (m, 10, C_6H_5). FAB-MS (*m/z*): $[M+1]^+$ 428 (isotope cluster centered around 428).

Kinetic experiments: A series of kinetic experiments was conducted at 28 °C using the *para*-substituted 1-deuteriobenzaldehydes. **Asymmetric transfer hydrogenation of *para*-substituted 1-deuteriobenzaldehydes**: A solution of (*R*,*R*)-**4** (2.1 mg, 0.005 mmol) in 2-propanol (10.0 mL) was placed in a 50-mL round-bottomed flask and stirred at 28 °C for 10 min under Ar atmosphere. To the resulting orange solution a benzaldehyde-1-*d* (**1a**–**e**) (1.0 mmol)[1] and a solution of 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol) were added. The mixture was stirred at 28 °C, and small portions of the mixture were sampled after appropriate periods. Conversions were determined by GC analysis using an HP-INNOWax column. The initial rates of reaction of the substituted benzaldehyde-1-*d* (v_X) and the parent aldehyde-1-*d* (v_H) were calculated from 9–23 experiment sets and were first-order-plotted. Correlations between a substrate, $\log(v_X/v_H)$, and σ_p value of substituent are as follows: *p*-methoxybenzaldehyde-1-*d*, –0.26, –0.27; *p*-methylbenzaldehyde-1-*d*, –0.020, –0.17; benzaldehyde-1-*d*, 0, 0; *p*-bromobenzaldehyde-1-*d*, 0.18, 0.23; *p*-trifluoromethylbenzaldehyde-1-*d*, 0.20, 0.54. The ρ value of Hammett plot was determined to be +0.76, although a significant deviation is seen for the *p*-CF_3 derivatives (Figure 1). The ee values of the products were determined by 500-MHz ^{1}H NMR of the (*R*)-MTPA esters.

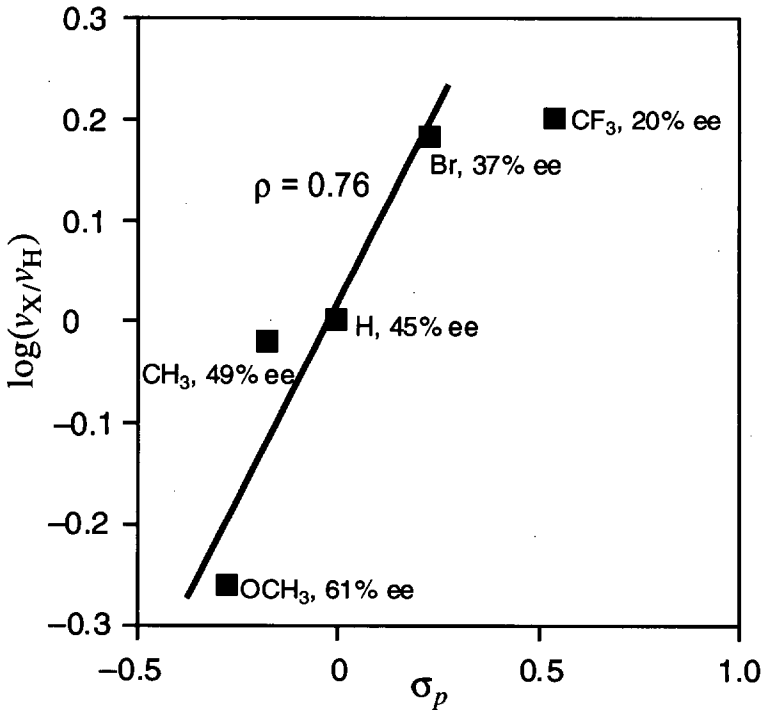

Figure 1. Hammett plots and product ee's in asymmetric transfer hydrogenation of 1-deuteriobenzaldehydes (**1a–e**) in the presence of (*R*,*R*)-**4** ([**1**] = 0.1 M in 2-propanol, **1**:Ru:*t*-C_4H_9OK = 200:1:4, 28 °C).

Reaction Conditions: **Reaction of benzaldehyde-1-*d* (1a) with** (*R*,*R*)-**4**. Conditions: **1a** (107 mg, 1.00 mmol), (*R*,*R*)-**4** (2.1 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h, 49% conversion. The rate of asymmetric transfer hydrogenation of **1a** was 1.32 mol/mol of Ru·min. The ee determined by ^{1}H-NMR analysis was 45%: ^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-MTPA ester derived from (*S*)-**2a** and (*S*)-MTPA chloride, δ 5.31 (27.5%); (*R*)-MTPA ester of (*R*)-**2a**, δ 5.35 (72.5%). **Reaction of *p*-methylbenzaldehyde-1-*d* (1b) with** (*R*,*R*)-**4**. Conditions: **1b** (121 mg, 1.00 mmol), (*R*,*R*)-**4** (2.1 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h, 40% conversion. The rate of asymmetric transfer hydrogenation of **1b** was 1.26 mol/mol of Ru·min. The ee determined by ^{1}H -NMR (500 MHz, $CDCl_3$) analysis was 49%: (*R*)-MTPA ester of (*S*)-**2b**, δ 5.25

(25.5%); (*R*)-**2b**, δ 5.31 (74.5%). **Reaction of *p*-methoxylbenzaldehyde-1-*d* (1c) with (*R*,*R*)-4.** Conditions: **1c** (137 mg, 1.00 mmol), (*R*,*R*)-**4** (2.1 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h, 22% conversion. The rate of asymmetric transfer hydrogenation of **1c** was 0.724 mol/mol of Ru·min. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 61%: (*R*)-MTPA ester of (*S*)-**2c**, δ 5.23 (19.5%); (*R*)-**2c**, δ 5.30 (80.5%). **Reaction of *p*-bromobenzaldehyde-1-*d* (1d) with (*R*,*R*)-4.** Conditions: **1d** (186 mg, 1.00 mmol), (*R*,*R*)-**4** (2.1 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h , 55% conversion. The rate of asymmetric transfer hydrogenation of **1d** was 1.98 mol/mol of Ru·min. The ee determined by ^{1}H -NMR (500 MHz, $CDCl_3$) analysis was 37%: (*R*)-MTPA ester of (*S*)-**2d**, δ 5.26 (31.5%); (*R*)-**2d**, δ 5.28 (68.5%). **Reaction of *p*-trifluoromethylbenzaldehyde-1-*d* (1e) with (*R*,*R*)-4.** Conditions: **1e** (175 mg, 1.00 mmol), (*R*,*R*)-**4** (2.1 mg, 0.005 mmol), 1.0 M *t*-C_4H_9OK in *t*-C_4H_9OH (20 μL, 20 μmol), 2-propanol (10.0 mL), 28 °C, 1 h, 65% conversion. The rate of asymmetric transfer hydrogenation of **1e** was 2.11 mol/mol of Ru·min. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 20%: (*R*)-MTPA ester (*S*)-**2e**, δ 5.38 (40%); (*R*)-**2e**, δ 5.36 (60%).

Notes

(1) The substrate was washed with a 0.1 M KOH solution prior to use.

(D) Typical Procedure for Asymmetric Transfer Hydrogenation with Formic-*d* Acid-*d*

Guaranteed-reagent grade acetonitrile was freshly distilled over CaH_2 before use. A solid Ru complex (*R*,*R*)-**3a** (32 mg, 0.05 mmol), formic-*d* acid-*d* (0.48 g, 10 mmol),[1] triethylamine (1.01 g, 10.0 mmol), and acetonitrile (10.0 mL) was placed in a 50-mL round-bottomed flask, and the mixture was stirred at 28 °C for 10 min under Ar atmosphere. To the orange solution, *p*-methoxybenzaldehude (**7c**)[2] (1.37 g, 10.0 mmol)

was added. The mixture was stirred at 28 °C for 14 h, diluted with water, and then was extracted with ethyl acetate. The organic layer was washed with an aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated under reduced pressure. Bulb-to-bulb distillation afforded (*S*)-*p*-methoxybenzyl-1-*d* alcohol [(*S*)-**2c**] (1.329 g, 96% yield), $[\alpha]_D^{25}$ +0.60° (*c* 10.0, $CHCl_3$). GC (column, HP-INNOWax, 350 kPa; column temp, 180 °C; injection temp, 250 °C); t_R of **2c**, 3.95 min (97%); t_R of **7c**, 2.17 min (3%). ^1H NMR (500 MHz, $CDCl_3$) δ 2.58 (br s, 1, OH), 3.76 (s, 3, OCH_3), 4.51 (m, 1, CDH), 6.84 (d, *J* = 8 Hz, 2, aromatics), 7.21 (d, *J* = 8 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.07, 133.19, 128.59, 113.87, 64.31 (t, *J* = 22 Hz), 55.22. The extent of deuteration of carbinyl proton was judged to be 99% by ^1H-NMR analysis. The ee value determined by ^1H-NMR analysis (500 MHz, $CDCl_3$) using MTPA ester was 99%: (*S*)-MTPA ester obtained from (*S*)-**2c** and (*R*)-MTPA chloride, δ 5.30 (99.5%); (*R*)-**2c**, δ 5.23 (0.5%).

Notes

(1) Purchased from E. Merck and dried with molecular sieve 3A. The deuterium content of formic-*d* acid-*d* was >99.5% by ^1H NMR assay in D_2O.

(2) The substrate was washed with a 0.1 M KOH solution prior to use.

(E) Reaction Conditions of Asymmetric Transfer Hydrogenation of 7 with Formic-*d* Acid-*d* and Analytical Data of Products

The reaction was normally carried out using 10 mmol of **7**. **Asymmetric transfer hydrogenation of benzaldehyde (7a) with** (*R*,*R*)-**3a**. Conditions: **7a** (107 mg, 1.00 mmol), (*R*,*R*)-**3a** (3.2 mg, 0.005 mmol), DCO_2D (48 mg, 1.0 mmol), triethylamine (101 mg, 1.0 mmol), acetonitrile (1.0 mL), 28 °C, 4 h. (*S*)-Benzyl-1-*d* alcohol [(*S*)-**2a**] (98 mg, 90% yield). GC (column, HP-INNOWax; 350 kPa; column temp, 150 °C); t_R of **2a**, 2.78 min (93%); t_R of **7a**, 1.18 min (7%). ^1H NMR (500 MHz, $CDCl_3$) δ 1.78 (br s, 1, OH), 4.65 (m, 1, C_6H_5CDH), 7.1–7.5 (m, 5, aromatics).

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 141.09, 128.68, 127.72, 127.18, 62.25 (t, J = 22 Hz). The d_1 content was 99%. The ee determined by ^1H-NMR (500 MHz, $CDCl_3$) analysis was 98%: (*S*)-MTPA ester of (*S*)-**2a**, δ 5.35 (99%); (*R*)-**2a**, δ 5.31 (1%). **Reaction of *p*-methylbenzaldehyde (7b) with** (*R*,*R*)-**3a**. Conditions: **7b** (1.21 g, 10.0 mmol), (*R*,*R*)-**3a** (32 mg, 0.05 mmol), DCO_2D (0.48 g, 10 mmol), triethylamine (1.01 g, 10 mmol), acetonitrile (10.0 mL), 28 °C, 4 h. (*S*)-*p*-Methylbenzyl-1-*d* alcohol [(*S*)-**2b**] (1.07 g, 87% yield), $[\alpha]_D^{28}$ +1.3° (*c* 4.6, $CHCl_3$). GC (column, HP-INNOWax; 350 kPa; column temp, 150 °C); t_R of **2b**, 3.64 min (92%); t_R of **7b**, 1.57 min (8%). ^1H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3, $C_6H_5CH_3$), 2.58 (br s, 1, OH), 4.62 (m, 1, CDH), 7.13 (d, J = 8 Hz, 2, aromatics), 7.18 (d, J = 8 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 137.89, 137.21, 129.15, 127.12, 64.61 (t, J = 22 Hz), 21.11. The d_1 content was 99%. The ee determined by ^1H NMR (500 MHz, $CDCl_3$) analysis was 98%: (*S*)-MTPA ester of (*S*)-**2b**, δ 5.31 (99%); (*R*)-**2b**, δ 5.25 (1%). **Reaction of *p*-bromobenzaldehyde (7d) with** (*R*,*R*)-**3a**. Conditions: **7d** (1.37 g, 10.0 mmol), (*R*,*R*)-**3a** (32 mg, 0.05 mmol), DCO_2D (0.48 g, 10 mmol), triethylamine (1.01 g, 10 mmol), acetonitrile (10.0 mL), 28 °C, 6 h. (*S*)-*p*-Bromobenzyl-1-*d* alcohol [(*S*)-**2d**] (1.865 g, 99% yield), $[\alpha]_D^{24}$ +1.1° (*c* 15.0, $CHCl_3$). GC (column, HP-INNOWax; 350 kPa; column temp, 180 °C); t_R of **2d**, 5.43 min (99%); t_R of **7d**, 1.75 min (1%). ^1H NMR (500 MHz, $CDCl_3$) δ 1.64 (br s, 1, OH), 4.64 (m, 1, CDH), 7.25 (d, J = 8 Hz, 2, aromatics), 7.49 (d, J = 8 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 139.63, 131.51, 128.56, 121.32, 63.86 (t, J = 22 Hz). The d_1 content was 99%. The ee determined by ^1H-NMR (500 MHz, $CDCl_3$) analysis was 99%: (*S*)-MTPA ester of (*S*)-**2d**, δ 5.28 (99.5%); (*R*)-**2d**, δ 5.26 (0.5%). **Reaction of *p*-trifluoromethylbenzaldehyde (7e) with** (*R*,*R*)-**3a.** Conditions: **7e** (1.21 g, 10.0 mmol), (*R*,*R*)-**3a** (32 mg, 0.05 mmol), DCO_2D (0.48 g, 10 mmol), triethylamine (1.01 g, 10 mmol), acetonitrile (10.0 mL), 28 °C, 2 h. (*R*)-*p*-Trifluoromethylbenzyl-1-*d* alcohol [(*R*)-**2e**] (1.64 g, 92% yield), $[\alpha]_D^{31}$ +1.3° (*c* 12.0, $CHCl_3$). GC (column, HP-

INNOWax; 350 kPa; column temp, 140 °C); t_R of **2e**, 4.71 min (95%); t_R of **7e**, 1.11 min (5%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.77 (br s, 1, OH), 4.66 (m, 1, CDH), 7.41 (d, J = 8.3 Hz, 2, aromatics), 7.58 (d, J = 8.3 Hz, 2, aromatics). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.71, 129.85 (q, J_{C-F} = 32 Hz), 126.92, 125.49 (q, J_{C-F} = 3.6 Hz), 124.26 (q, J_{C-F} = 272 Hz), 64.02 (t, J_{C-D} = 22 Hz). The d_1 content was 99%. The ee determined by ^{1}H-NMR (500 MHz, $CDCl_3$) analysis was 97%: (*S*)-MTPA ester (*S*)-**2e**, δ 5.36 (98.5%); (*R*)-**2e**, δ 5.38 (1.5%).

(F) Confirmation of Absolute Configuration of (*S*)-*p*-Trifluoromethylbenzyl-1-*d* Alcohol[1]

Powdered $CeCl_3 \cdot 7H_2O$ (1.0 g, 2.7 mmol) was placed in a 50-mL round-bottomed flask, heated in vacuo at 140 °C for 2 h, and cooled to room temperature. To the flask THF (10 mL) was added under Ar atmosphere. The suspension was stirred at room temperature for 1 h. The alcohol (*S*)-**2e** obtained in E (59 mg, 0.33 mmol) and $LiAlH_4$ (2.0 g, 53 mmol) were added, and the mixture was stirred at 80 °C for 10 h, diluted with aqueous HCl, and extracted with ether. The organic layer was washed with an aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated under reduced pressure to give an 8:1 of mixture of (*S*)-**2b** and (*S*)-**2e** together with small quantities of mono- and difluorides (34.3 mg, yield of **2b** 71%). The absolute configuration of **2b** was confirmed to be *S* by ^{1}H-NMR analysis (500 MHz, $CDCl_3$) of the MTPA ester obtained from (*R*)-MTPA chloride giving the benzylic proton signal at δ 5.31.

Note

(1) Imamoto, T.; Takeyama, T.; Kusumoto, T. *Chem. Lett.* **1985**, 1491–1492.