Supporting Information

Enantioselective Rhodium(I)-Catalyzed Hydrogenation of Trifluoromethyl Ketones

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Experimental Section

General Methods. Melting points are uncorrected. Optical rotations were measured at 589 nm using a 1.0-dm cell with a total volume of 1 ml. Infrared spectra were taken either neat or in KBr pellets. ^{1}H NMR spectra were recorded at 200 MHz and expressed in parts per million (ppm) downfield from TMS as the internal standard (δ). ^{19}F NMR spectra were measured at 188 MHz and given in parts per million (ppm) upfield from CCl_3F as the internal standard. Coupling constants are in hertz. Low- and high-resolution mass spectral analyses were performed at 70 eV electron-impact (EI).

General Procedure for the Hydrogenation of Trifluoromethyl Ketones. Toluene was distilled from sodium ketyl. In a glove box a solution of $[Rh(COD)OCOCF_3]_2$ (6.5 mg, 0.01 mmol) and (*S*)-Cy,Cy-oxoProNOP (11.2 mg, 0.022 mmol) in toluene (1 mL) was stirred for 15 min. The resulting catalyst solution (500 μL) was transferred to a 100 mL stainless steel autoclave. A solution of the trifluoromethyl ketone (2.0 mmol) in toluene (3 mL) was transferred to the autoclave, then hydrogen (20 atm) was introduced, and the reaction mixture was magnetically stirred at 30 °C. After the desired reaction time, hydrogen was removed and the solution was concentrated in vacuo. The crude residue was analyzed by GLC and chromatographed to give the hydrogenation product.

(*R*)-1,1,1-Trifluoro-2-decanol: 97% ee; a colorless oil; $[\alpha]_D^{24}$ +22.5 (*c* 1.07, $CHCl_3$); IR (neat) 3392, 2927, 1470, 1169, 1141, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.12-1.80 (m, 14H), 2.11 (d, *J* = 6.2 Hz, 1H), 3.79-4.01 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -80.58 (d, *J* = 6.8 Hz, 3F); MS *m/z* 212 (M^+), 194, 141, 69; MRMS (DIEI) Calcd for $C_8H_{19}F_3O$ (M^+) 212.1383, found 212.1387.

(*R*)-2,2,2-Trifluoro-1-phenylethanol: 73% ee; a colorless oil; $[\alpha]_D^{26}$ -21.9 (*c* 1.17, $CHCl_3$); IR (neat) 3396, 1267, 1127, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.74 (d, *J* = 4.6 Hz, 1H), 5.03 (dq, *J* = 6.6, 4.6 Hz, 1H), 7.35-7.52 (m, 5H); ^{19}F NMR ($CDCl_3$) δ -78.83 (d, *J* = 6.6 Hz, 3F); MS *m/z* 176 (M^+), 107, 69; MRMS (DIEI) Calcd for $C_8H_7F_3O$ (M^+) 176.0449, found 176.0450.

(*R*)-1,1,1,2,2-Pentafluoro-3-dodecanol: 97% ee; a colorless oil; $[\alpha]_D^{25}$ +18.4 (*c* 1.18, $CHCl_3$); IR (neat) 3371, 2927, 1470, 1197, 726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.1 Hz, 3H), 1.11-1.98 (m, 17H), 3.91-4.02 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -82.00 (s, 3F), -124.57 (dd, *J* = 276.2, 6.6 Hz, 1F), -131.01 (dd, *J* = 276.2, 15.5 Hz, 1F); MS *m/z* 276 (M^+) 258, 157, 69; MRMS (DIEI) Calcd for $C_{12}H_{21}F_5O$ (M^+) 276.1507, found 276.1512.

(*R*)-1,1,1-Trifluoro-2-octanol: [α] 97% ee; a colorless oil; $[\alpha]_D^{26}$ +26.3 (*c* 1.04, $CHCl_3$); IR (neat) 3370, 2932, 1279, 1170, 695 cm^{-1}; ^1H NMR ($CDCl_3$) d 0.90 (t, *J* = 7.0 Hz, 3H), 1.20-2.10 (m, 11H), 3.82-4.00 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -80.61 (d, *J* = 6.2 Hz, 3F); MS *m/z* 183 (M^+-1), 166, 97, 69; MRMS (DIEI) Calcd for $C_8H_{14}F_3O$ (M^+-H) 183.0993, found 183.0998.

(*R*)-2,2,2-Trifluoro-1-cyclohexylethanol: 97% ee; a colorless oil; $[\alpha]_D^{26}$ +18.9 (*c* 1.11, $CHCl_3$); IR (neat) 3386, 1453, 1275, 1125, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-2.20 (m, 12H), 3.62-3.81 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -76.14 (d, *J* = 7.8 Hz, 3F); MS *m/z* 182 (M^+), 164, 95, 83, 69; MRMS (DIEI) Calcd for $C_8H_{13}F_3O$ (M^+) 182.0919, found 182.0923.

1-Cyclohexyl-3,3,3-trifluoro-2-propanol: 98% ee; colorless needles; mp 37.6-38.2 °C; $[\alpha]_D^{25}$ +30.8 (*c* 1.03, $CHCl_3$); IR (KBr) 3356, 1452, 1132, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75-2.12 (m, 14H), 3.90-4.12 (m, 1H); ^{19}F NMR ($CDCl_3$) δ -80.78 (d, *J* = 6.6 Hz, 3F); MS *m/z* 196 (M^+), 178, 83, 69; MRMS (DIEI) Calcd for $C_9H_{15}F_3O$ (M^+) 196.1075, found 196.1080.

3-Phenyl-1,1,1-trifluoro-2-propanol: 97% ee; a colorless oil; $[\alpha]_D^{25}$ +47.0 (*c* 1.22, $CHCl_3$); IR (neat) 3405, 1275, 1168, 703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05-2.30 (brs, 1H), 2.85 (dd, *J* = 14.3, 10.1

Hz, 1H), 3.07 (dd, *J* = 14.3, 3.1 Hz, 1H), 4.15 (ddq, *J* = 10.1, 6.5, 3.1 Hz, 1H), 7.20-7.42 (m, 5H); ^{19}F NMR ($CDCl_3$) δ -80.12 (d, *J* = 6.5 Hz, 3F); MS *m/z* 190 (M^+), 172, 103, 91, 69; MRMS (DIEI) Calcd for $C_9H_9F_3O$ (M^+) 190.0606, found 190.0609.

1,1,1-Trifluoro-4-phenyl-2-butanol: 96% ee; colorless needles; mp 57.3-58.7 °C; $[\alpha]_D^{26}$ +36.4 (*c* 0.76, $CHCl_3$); IR (KBr) 3374, 1456, 1264, 1108, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.85-2.15 (m, 2H), 2.12-2.25 (brs, 1H), 2.68-3.02 (m, 2H), 3.80-4.01 (m, 1H), 7.19-7.39 (m, 5H); ^{19}F NMR ($CDCl_3$) δ -80.44 (d, *J* = 6.3 Hz, 3F); MS *m/z* 204 (M^+), 186, 117, 91, 69; MRMS (DIEI) Calcd for $C_{10}H_{11}F_3O$ (M^+) 204.0762, found 204.0758.

1-(Benzyloxy)-3,3,3-trifluoro-2-propanol: 86% ee; a colorless oil; $[\alpha]_D^{26}$ +8.5 (*c* 0.97, $CHCl_3$); IR (neat) 3427, 1455, 1274, 1144, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.90-3.02 (brs, 1H), 3.62-3.79 (m, 2H), 4.01-4.27 (m, 1H), 4.61 (s, 2H), 7.29-7.42 (m, 5H); ^{19}F NMR ($CDCl_3$) δ -77.76 (d, *J* = 7.0 Hz, 3F); MS *m/z* 220 (M^+), 107, 91, 69; MRMS (DIEI) Calcd for $C_{10}H_{11}F_3O$ (M^+) 220.0711, found 220.0716.

1-(4-Chlorophenyl)-2,2,2-trifluoroethanol: 38% ee; a colorless oil; IR (neat) 3386, 1496, 1269, 1129, 811 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.64 (brs, 1H), 5.01 (q, *J* = 6.6 Hz, 1H), 7.30-7.46 (m, 4H); ^{19}F NMR ($CDCl_3$) δ -79.06 (d, *J* = 6.6 Hz, 3F); MS *m/z* 212 (M^+), 210 (M^+), 143, 141, 77, 69; MRMS (DIEI) Calcd for $C_8H_6ClF_3O$ (M^+) 210.0060, found 210.0062.

1-(4-Metoxyphenyl)-2,2,2-trifluoroethanol: 83% ee; a colorless oil; $[\alpha]_D^{26}$ -26.8 (*c* 0.98, $CHCl_3$); IR (neat) 3440, 1614, 1517, 1127, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.03 (brs, 1H), 3.82 (q, *J* = 7.0 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H); ^{19}F NMR ($CDCl_3$) δ -79.07 (d, *J* = 7.0 Hz, 3F); MS *m/z* 206 (M^+), 137, 109, 77, 69; MRMS (DIEI) Calcd for $C_9H_9F_3O$ (M^+) 206.0555, found 206.0557.

Synthesis of (*R*)-Trifluorolactic Acid.

3,3,3-Trifuoro-2,2-dihydroxypropananilide: 2,2-Dianilino-3,3,3-trifluoropropananilide was prepared from hexafluoropropene oxide and aniline according to reference 11. To a dioxane solution (100 mL) of 2,2-dianilino-3,3,3-trifluoropropananilide (19.0 g, 49.35 mmol), 35% aqueous HCl (9 mL) was added at 0°C. The mixture was stirred for 3h at room temperature, poured into water (10 mL), and extracted with ether. The combined extracts were washed with saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. After the evaporation of solvents, a recrystallization of the residue from ether-hexane afforded 3,3,3-trifuoro-2,2-dihydroxypropananilide (10.47 g) in 90% yield.

(*R*)-3,3,3-Trifluoro-2-hydroxypropananilide: In a glove box a solution of $[Rh(COD)OCOCF_3]_2$ (6.5 mg, 0.01 mmol) and (*S*)-Cy,Cy-oxoProNOP (11.2 mg, 0.022 mmol) in toluene (1 mL) was stirred for 15 min. The resulting catalyst solution (150 μL) was transferred to a 100 mL stainless steel autoclave. A solution of 3,3,3-trifuoro-2,2-dihydroxypropananilide (705 mg, 3.0 mmol) in toluene (3 mL) was transferred to the autoclave, then hydrogen (10 atm) was introduced, and the reaction mixture was magnetically stirred at 70 °C. After a 20-h stirring, hydrogen was removed and the solution was concentrated in vacuo. The residue was purified by silica gel column chromatography to give the hydrogenated product **4** (579 mg, 77% ee, 88% yield) [enantiomeric excess determined by HPLC analysis with CHIRALCEL AS]. After a recrystallization from toluene, (*R*)-**4** of 97% ee was obtained by concentration of the mother liquid. And one more recrystallization from EtOAc-hexane afforded enantiopure (*R*)-**4** in 43% overall yield.

(*R*)-Trifluorolactic Acid: The mixture of (*R*)-**4** (150 mg, 0.685 mmol, >99% ee) and conc HCl (1 mL) was stirred at 80°C for 20h, cooled to room temperature, alkalinized with 1N NaOH, and extracted with ether. The separated aqueous solution was acidified with conc. HCl and extracted with ether. The combined extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give trifluorolactic acid (83 mg, 84% yield) as crystals. The obtained trifluorolactic acid was esterified with CH_2N_2, analyzed by GLC with a CP Cyclodex β-236M capillary column, and determined to be >99% ee.