(S)-Selective Dynamic Kinetic Resolution of **Secondary** Alcohols by the Combination of Subtilisin and an Aminocyclopentadienylruthenium Complex as the Catalysts

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Supporting Information

General DKR Procedure

The procedure for the DKR of **1a** is described as a representative. To a Schlenk-type flask was added a solution of potassium *tert*-butoxide (1.0 M in THF, 15 μ L, 0.015 mmol) under argon, followed by the addition of ruthenium complex **3** (0.012 mmol, 7.44 mg). The resulting mixture was dried in vacuo to remove THF and the flask was filled with argon. Then, surfactant-treated subtilisin (7.5mg) and sodium carbonate (63.6 mg) were added under argon. The resulting mixture was dried again in vacuo, followed by the addition of a solution of substrate (36 μ L, 0.3 mmol) in anhydrous THF (1 mL) and acyl donor (2,2,2-trifluoroethylbutyrate, 0.51 mmol, 78 μ L). The resulting red-brown mixture was allowed to stir at 25°C. After the reaction was complete (3 days), the solid materials were filtered off and the filtrate was concentrated. The residue was subjected to flash column chromatography (n-hexane/Et₂O = 10/1) to afford the products. The procedure for the subtilisin-catalyzed DKR of **1i** is identical except that no acyl donor is added. The procedure for the lipase-catalyzed DKR of **1i** is identical except that subtilisin and THF are replaced by lipase PS-C (Amano, 2 mg) and toluene, respectively.

Analytical Data

2a (53mg, 0.276 mmol, 92%): 92% ee by HPLC (Whelk-O1, n-hexane/2-propanol = 95/5, flow rate = 0.5 mL/min, UV = 217 nm); $[\alpha]_D^{25} = -87.3$ (c 1.01, CHCl₃) (lit. +97.9 (c 10, ether, 95 %ee) for (*R*), Kirchner G.; Scollar M. P.; Klivanov A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072); ¹H NMR (300MHz, CDCl₃, ppm) 7.35–7.28 (m, 5H), 5.90 (q, *J* = 6.6 Hz, 1H), 2.31 (t, *J* = 7.4 Hz, 2H), 1.68–1.58 (m, 2H), 1.53 (d, *J* = 6.6 Hz, 3H),

0.92 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 173.6, 142.5, 129.1, 128.4, 126.7, 72.7, 37.2, 23.0, 19.1, 14.3; HRMS (EI+) $\text{C}_{12}\text{H}_{16}\text{O}_2$ calcd 192.1150, found 192.1146.

2b (61mg, 0.269 mmol, 90%): 99% ee by HPLC (Whelk-O1, n-hexane/2-propanol = 95/5, flow rate = 0.5 mL/min, UV = 217 nm); $[\alpha]_D^{25} = -96.0$ (c 1.03, CHCl_3); ^1H NMR (300MHz, CDCl_3 , ppm) 7.33–7.29 (m, 4H), 5.85 (q, $J = 6.6$ Hz, 1H), 2.30 (t, $J = 7.4$ Hz, 2H), 1.68–1.58 (m, 2H), 1.50 (d, $J = 6.6$ Hz, 3H), 0.92 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 172.9, 140.7, 133.8, 128.9, 127.7, 71.5, 36.7, 22.4, 18.6, 13.8; HRMS (EI+) $\text{C}_{12}\text{H}_{15}\text{O}_2\text{Cl}$ calcd 226.0761, found 226.0764.

2c (60.6mg, 0.273 mmol, 91%): 94% ee by HPLC (Whelk-O1, n-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, UV = 217 nm); $[\alpha]_D^{25} = -92.6$ (c 1.01, CHCl_3); ^1H NMR (300MHz, CDCl_3 , ppm) 7.29 (d, $J = 8.6$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.86 (q, $J = 6.6$ Hz, 1H), 3.80 (s, 3H), 2.28 (t, $J = 7.5$ Hz, 2H), 1.68–1.57 (m, 2H), 1.51 (d, $J = 6.6$ Hz, 3H), 0.91 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 173.1, 159.5, 134.2, 127.7, 114.0, 71.9, 55.4, 36.8, 22.2, 18.7, 13.8; HRMS (EI+) $\text{C}_{13}\text{H}_{18}\text{O}_3$ calcd 222.1256, found 222.1257.

2d (47mg, 0.228 mmol, 76%): 97% ee by HPLC (Whelk-O1, n-hexane/2-propanol = 98/2, flow rate = 0.5 mL/min, UV = 217 nm); $[\alpha]_D^{25} = +12.1$ (c 1.00, CHCl_3); ^1H NMR (300MHz, CDCl_3 , ppm) 7.31–7.18 (m, 5H), 5.13 (q, $J = 6.4$ Hz, 1H), 2.92 (dd, $J_1 = 13.6$ Hz, $J_2 = 6.8$ Hz, 1H), 2.76 (dd, $J_1 = 13.6$ Hz, $J_2 = 6.4$ Hz, 1H), 2.22 (t, $J = 7.4$ Hz, 2H), 1.63–1.53 (m, 2H), 1.21 (d, $J = 6.3$ Hz, 3H), 0.88 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 173.8, 138.4, 130.1, 129.0, 127.1, 71.8, 43.0, 37.2, 20.2, 19.1, 14.3; HRMS (FAB+) $\text{C}_{13}\text{H}_{18}\text{O}_2 + \text{H}^+$ calcd 207.1385, found 207.1382.

2e (51.7mg, 0.235mmol, 78%): 98% ee by HPLC (Whelk-O1, n-hexane/2-propanol = 98/2, flow rate = 0.5 mL/min, UV = 217 nm); $[\alpha]_D^{25} = -5.6$ (c 1.15, CHCl_3); ^1H NMR (300MHz, CDCl_3 , ppm) 7.30–7.15 (m, 5H), 4.98–4.92 (m, 1H), 2.68–2.59 (m, 2H), 2.26 (t, $J = 7.4$ Hz, 2H), 1.94–1.78 (m, 2H), 1.70–1.62 (m, 2H), 1.24 (d, $J = 6.3$ Hz, 3H), 0.95 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 174.0, 142.3, 129.1, 129.0, 126.6, 70.9, 38.4, 37.3, 32.5, 20.8, 19.2, 14.4; HRMS (FAB+) $\text{C}_{14}\text{H}_{20}\text{O}_2 + \text{H}^+$ calcd 221.1542, found 221.1545.

2f (44mg, 0.222mmol, 74%): 98% ee by GC (ChiralDEX B-PH, injection temp. 250 °C, FID detection temp. 300 °C, oven initial temp. 60 °C (10 min), rate 2 °C/min, oven final temp. 135 °C (15 min)); $[\alpha]_D^{25} = -1.5$ (c 0.98, CHCl_3); ^1H NMR (300MHz, CDCl_3 , ppm) 4.77–4.68 (m, 1H), 2.26 (t, $J = 7.4$ Hz, 2H), 1.76–1.61 (m, 7H), 1.43–1.41 (m, 1H), 1.25–1.14 (m, 6H), 1.05–0.92 (m, 5H); ^{13}C NMR (300MHz, CDCl_3 , ppm) 174.1, 75.0, 43.3, 37.3, 29.2, 29.1, 27.1, 26.7, 26.6, 19.3, 17.8, 14.4; HRMS (FAB+) $\text{C}_{12}\text{H}_{22}\text{O}_2$

+ H⁺ calcd **199.1698**, found 199.1692.

2g (39.9mg, 0.200 mmol, 67%): 98% ee by GC (Chiraldex B-PH, injection temp. 250 °C, FID detection temp. 300 °C, oven initial temp. 60 °C (10 min), rate 2 °C/min, oven final temp. 104 °C (10 min); $[\alpha]_D^{25} = +5.7$ (c 0.60, CHCl₃) (lit. -7.0 (c 10, ether, 95 %ee) for (*R*), Kirchner G.; Scollar M. P.; Klivanov A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072); ¹H NMR (300MHz, CDCl₃, ppm) 4.95–4.85 (m, 1H), 2.27 (t, *J* = 7.4 Hz, 2H), 1.68–1.58 (m, 2H), 1.56–1.37 (m, 2H), 1.27 (s, 8H), 1.19 (d, *J* = 6.2 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (300MHz, CDCl₃, ppm) 174.1, 71.4, 37.3, 36.7, 32.4, 29.8, 26.1, 23.3, 20.7, 19.3, 14.8, 14.3; HRMS (FAB+) C₁₂H₂₄O₂ + H⁺ calcd **201.1855**, found 201.1853.

2h (58.2mg, 0.271 mmol, 90%): 95% ee by HPLC (Whelk–O1, n-hexane/2–propanol = 98/2, flow rate = 1.0 ml/min, UV = 217nm); $[\alpha]_D^{25} = -235.3$ (c 0.7, CHCl₃); ¹H NMR (300MHz, CDCl₃, ppm) 7.46–7.39 (m, 2H), 7.34–7.22 (m, 3H), 5.70 (q, *J* = 6.7 Hz, 1H), 2.33 (t, *J* = 7.4 Hz, 2H), 1.75–1.63 (m, 2H), 1.58 (d, *J* = 6.7 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (300MHz, CDCl₃, ppm) 172.7, 132.1, 128.7, 128.4, 122.7, 87.9, 84.7, 60.8, 36.5, 21.7, 18.7, 13.7; HRMS (EI+) C₁₄H₁₆O₂ calcd 216.1150, found 216.1152.

2i (*S*)–Isomer (58.7mg, 0.282 mmol, 94%): >99.5% ee by HPLC (Whelk–O1, n-hexane/2–propanol = 90/10, flow rate = 1.0 mL/min, UV = 217 nm); $[\alpha]_D^{25} = -95.4$ (c 1, CHCl₃); ¹H NMR (300MHz, CDCl₃, ppm) 7.20 (t, *J* = 7.9 Hz, 1 H), 6.91 (d, *J* = 7.6 Hz, 1 H), 6.82 (s, 1 H), 6.76 (dd, *J*₁ = 5.5 Hz, *J*₂ = 1.7 Hz, 1 H), 5.83 (q, *J* = 6.6 Hz, 1 H), 2.32 (t, *J* = 7.4 Hz, 2 H), 1.70–1.62 (m, 2 H), 1.51 (d, *J* = 6.6 Hz, 3 H), 0.94 (q, *J* = 7.3 Hz, 3 H); ¹³C NMR (300MHz, CDCl₃, ppm) 174.1, 156.5, 144.2, 130.5, 118.8, 115.5, 113.8, 72.7, 37.3, 22.9, 19.1, 14.3; HRMS (EI+) C₁₂H₁₆O₃ calcd 208.1099, found 208.1101. (*R*)–Isomer (59.3mg, 0.285mmol, 95%); >99.5% ee; $[\alpha]_D^{25} = +95.6$ (lit. +90.7 (c 2, CHCl₃) Kim, M.-J.; Choi, M. Y.; Han, M. Y.; Choi, Y. K.; Lee, J. K.; Park, J. *J. Org. Chem.* **2002**, *67*, 9481); all the NMR data are in good agreement with those for (*S*)–**2i**. The products (*R*_f = 0.23, n-hexane/EtOAc = 4/1) are readily separable from substrates (*R*_f = 0.11, n-hexane/EtOAc = 4/1). Furthermore, almost all substrates are converted to products in the DKR reactions.