Dynamic Kinetic Resolution of Primary Amines with a Recyclable Pd Nanocatalyst for Racemization

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Supporting Information

Experimental Section

General Procedure for Racemization of (S)-1a

(S)-1a (24 mg, 0.20 mmol) was added to a suspension of Pd nanocatalyst (1.0 mol%) in dry and degassed toluene (0.10 M). The reaction mixture was stirred and heated to 70 °C under argon. After 12 or 24 h, the reaction mixture was cooled to room temperature and filtered through a glass filter (pore size: 20–30 μm). Filtrate was concentrated and analyzed by ¹H NMR spectroscopy, indicating that all of the substrate was consumed. The % ee was determined by HPLC (Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, UV 217 nm) after converting to the corresponding amide (2a) by treatment with a few drops of acetic anhydride to the vial.

Table 1. Racemization of (S)-1a.

entry	Pd catalyst	time (h)	1a (%) ^a	4 (%) ^a	5 (%) ^a	6 (%) ^a	ee (%) ^b
1	Pd/AIO(OH)	12	99	<1	<1	1	29
2		24	82	11	<1	7	2
3	commercial 5% Pd/Al ₂ O ₃	12	99	<1	<1	<1	94
4		24	99	<1	<1	<1	88

^a Determined by ¹H NMR. ^b Determined by HPLC (Whelk-O1).

General Procedure for Dynamic Kinetic Resolution of Benzyl Amines

Synthesis of *N*–((*R*)-1-phenylethyl)acetamide (2a): A suspension containing **1a** (97 mg, 0.80 mmol), Pd nanocatalyst (1.0 mol%), Novozym–435 (120 mg/mmol), ethyl acetate (3 equiv.), and molecular sieves 4 Å (560 mg) in dry and degassed toluene (0.10 M) was stirred at 70 °C under argon atmosphere. After 3 days, the reaction mixture was cooled to room temperature and filtered through a glass filter (pore size: 20–30 µm). Filtrate was concentrated and analyzed by ¹H NMR spectroscopy, indicating that all of the substrate was consumed. The mixture was subjected to a flash chromatography (silica gel, *n*–hexane/ethyl acetate = 1/1) to provide **2a** (119 mg, 0.73 mmol, 92%, 98% ee).

Synthesis of 2-methoxy-*N*–((*R*)-1-phenylethyl)acetamide (3a): A suspension containing **1a** (39 mg, 0.30 mmol), Pd nanocatalyst (1.0 mol%), Novozym–435 (15 mg/mmol), and ethyl methoxyacetate (1.7 equiv.) in dry and degassed toluene (0.10 M) was stirred at 70 °C under argon atmosphere. After 3 days, the reaction mixture was cooled to room temperature and filtered through a glass filter (pore size: 20–30 µm). Filtrate was concentrated and analyzed by ¹H NMR spectroscopy, indicating that all of the substrate was consumed. The mixture was subjected to a flash chromatography (silica gel, *n*–hexane/ethyl acetate = 1/1) to provide **3a** (57 mg, 0.29 mmol, 98%, 99% ee).

General Procedure for Dynamic Kinetic Resolution of Aliphatic Amines

A suspension containing **1i** (90 mg, 0.60 mmol), Pd nanocatalyst (12 mol%), Novozym–435 (120 mg/mmol) and ethyl acetate (3 equiv.) in dry and degassed toluene (0.20 M) was stirred at 100 °C under H₂ (1 atm). After 4 h, the reaction mixture was cooled to room temperature and filtered through a glass filter (pore size: 20–30 µm). Filtrate was concentrated and analyzed by GC spectroscopy, indicating that all of the substrate was consumed. The mixture was subjected to a flash chromatography (silica gel, *n*–hexane/ethyl acetate = 1/1) to provide **2i** (109 mg, 0.57 mmol, 95%, 98% ee).

General Procedure for Recycling of Pd Nanocatalyst in Racemization of (*S*)–1i

(*S*)–**1i** (30 mg, 0.20 mmol) was added to a suspension of Pd nanocatalyst (8.0 mol%) in dry and degassed toluene (0.20 M). The reaction mixture was stirred and heated to 100 °C under H₂ (1 atm). After 24 h, the reaction mixture was cooled to room temperature and filtered through a glass filter (pore size: 20–30 µm). Filtrate was concentrated and analyzed by ¹H NMR spectroscopy, indicating that all of the substrate

was consumed. The % ee was determined by HPLC (Whelk-O1, *n*-hexane/2-propanol = 85/15, flow rate = 0.50 mL/min, UV 217 nm) after converting to the corresponding amide (**2i**) by treatment with a few drops of acetic anhydride to the vial. The separated catalysts were washed with ethyl acetate and dried in vacuo before reuse.

Table 2. Recycling of catalyst in racemization of (*S*)-**1i**.

(*S*)-**1i**
(30 mg, 0.20 mmol)
>99% ee

$\xrightarrow[\text{Toluene (0.20 M), 100 }^{\circ}\text{C, 24 h}]{\text{H}_2 \text{ (1 atm), Pd/AlO(OH) (8.0 mol \%)}}$

1i

Cycle	1i (%) ^a	byproducts (%) ^a	ee (%) ^b
1 (fresh)	>99	<1	3
2	>99	<1	3
3	>99	<1	3
4	>99	<1	9
5	>99	<1	4
6	>99	<1	5
7	>99	<1	5
8	>99	<1	2
9	>99	<1	9
10	>99	<1	13

^a Determined by GC. ^b Determined by HPLC equipped with a chiral column (Whelk-O1) after converting to amide.

General Procedure for Recycling of Catalysts in DKR

A suspension containing **1i** (30 mg, 0.20 mmol), Pd nanocatalyst (12 mol%), Novozym-435 (120 mg/mmol) and ethyl acetate (3 equiv.) in dry and degassed toluene (0.20 M) was stirred at 100 °C under H₂ (1 atm). After 4 h, the reaction mixture was filtered through a glass filter (20–30 μm) and the products in the filtrate were analyzed by GC and HPLC. The separated catalysts were washed with ethyl acetate and dried in vacuo before reuse.

Table 3. Recycling of catalysts in DKR of **1i**.

<div style="display: flex; align-items: center; justify-content: center;"> <div style="text-align: center;"> <p>1i (30 mg, 0.20 mmol)</p> </div> <div style="text-align: center; margin: 0 20px;"> $\xrightarrow[\text{Toluene (0.20 M), 100 }^{\circ}\text{C, 4 h}]{\begin{array}{l} \text{H}_2 \text{ (1 atm)} \\ \text{Ethyl acetate (53 mg, 3.0 equiv.)} \\ \text{Novozym-435 (24 mg, 120 mg/mmol)} \\ \text{Pd/AIO(OH) (297 mg, 12 mol \%)} \end{array}}$ </div> <div style="text-align: center;"> <p>2i</p> </div> </div>				
Cycle	Convsn. (%) ^a	1i (%) ^a	2i (%) ^a	ee (%) ^b
1 (fresh)	>99	-	>98	99
2	>99	-	>98	99
3	>99	-	>98	98
4	>99	-	>98	97
5	>99	-	>98	96
6	>99	-	>98	95
7	>99	-	>98	94
8	99	1	>98	93
9	93	7	93	93
10	89	11	89	92
11 ^c	>99	-	>98	95

^a Determined by GC. ^b Determined by HPLC equipped with a chiral column (Whelk-O1).

^c After recycling 10 times, Novozym-435 (8 mg, 40 mg/mmol) was added.

Characterization of Products

N-((*R*)-1-Phenylethyl)acetamide (**2a**)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.34 – 7.26 (m, 5H), 5.85 (s, 1H), 5.15 – 5.09 (m, 1H), 1.98 (s, 3H), 1.49 (d, *J* = 6.88 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.5, 143.7, 129.0, 127.7, 126.6, 49.2, 23.8, 22.1

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**2a** = 8.19 min, (*R*)-**2a** = 14.36 min

mp 97 – 100 °C, [α]_D²⁵ +141 (c = 1.0, CHCl₃)

(lit. mp 98 – 100 °C, $[\alpha]_D^{25}$ -140 (c = 0.96, CHCl₃, (*S*)-isomer); Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.)

2-Methoxy-*N*-((*R*)-1-phenylethyl)acetamide (3a)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.37 – 7.25 (m, 5H), 6.76 (s, 1H), 5.23 – 5.13 (m, 1H), 3.89 (dd, J_1 =19.65 Hz, J_2 =14.97 Hz, 2H), 3.39 (s, 3H), 1.51 (d, J =6.93 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.6, 143.0, 128.7, 127.4, 126.1, 72.0, 59.1, 48.0, 21.9

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 2.0 mL/min, UV 217 nm

(*S*)-**3a** = 4.97 min, (*R*)-**3a** = 11.86 min

mp 59 – 60 °C, $[\alpha]_D^{25}$ +85.2 (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 68.37, H 7.82, N 7.25; found C 68.31, H 7.82 N 7.24

***N*-((*R*)-1-*p*-Tolylethyl)acetamide (2b)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.19 (d, J = 8.08 Hz, 2H), 7.11 (d, J = 8.11 Hz, 2H) 6.30 (s, 1H), 5.10 – 4.98 (m, 1H), 2.31 (s, 3H), 1.93 (s, 3H), 1.44 (d, J = 6.85 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.9, 141.0, 137.5, 129.9, 126.7, 49.1, 23.9, 22.4, 21.6

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**2b** = 8.66 min, (*R*)-**2b** = 17.86 min

mp 80 – 81 °C, $[\alpha]_D^{25}$ +146 (c = 1.0, CHCl₃)

(lit. mp 80 – 82 °C, $[\alpha]_D^{25}$ +144 (c = 1.03, CHCl₃); Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.)

2-Methoxy-*N*-((*R*)-1-*p*-tolylethyl)acetamide (3b)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.22 (d, J =8.13 Hz, 2H), 7.15 (d, J =8.08 Hz, 2H), 6.73 (d, J =5.47 Hz, 1H), 5.19 – 5.09 (m, 1H), 3.88 (dd, J_1 =20.46 Hz, J_2 =14.95 Hz, 2H), 3.39 (s, 3H), 2.33 (s, 3H), 1.50 (d, J =6.91 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.5, 140.0, 137.1, 129.3, 126.1, 72.0, 59.1, 47.8, 21.8, 21.0

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 2.0 mL/min. UV 217 nm

(*S*)-**3b** = 5.04 min, (*R*)-**3b** = 14.28 min

mp 44 – 46 °C, $[\alpha]_D^{25}$ +91.8 (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 69.54, H 8.27, N 6.76; found C 69.39, H 8.34, N 6.64

***N*–((*R*)–1–(4–Methoxyphenyl)ethyl)acetamide (2c)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.23 (d, *J* = 8.47 Hz, 2H), 6.85 (d, *J* = 8.38 Hz, 2H), 6.15 (s, 1H), 5.10 – 4.95 (m, 1H), 3.77 (s, 3H), 1.93 (s, 3H), 1.44 (d, *J* = 6.88 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.7, 159.3, 136.0, 128.0, 114.5, 55.9, 48.7, 23.9, 22.3

HPLC condition

Whelk–O1, *n*–hexane/2–propanol = 80/20, flow rate = 1.0 mL/min, UV 217 nm

(*S*)–**2c** = 14.49 min, (*R*)–**2c** = 33.72 min

mp 82 – 83 °C, [α]_D²⁵ +145 (c = 1.0, CHCl₃)

(lit. mp 82 – 84 °C, [α]_D²⁵ +51.2 (c = 0.11, CHCl₃); Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.)

2–Methoxy–*N*–((*R*)–1–(4–methoxyphenyl)ethyl)acetamide (3c)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.25 (d, *J* = 8.49 Hz, 2H), 6.87 (d, *J* = 8.76 Hz, 2H), 6.71 (d, *J* = 6.63 Hz, 1H), 5.18 – 5.09 (m, 1H), 3.88 (dd, *J*₁ = 19.89 Hz, *J*₂ = 14.97 Hz, 2H), 3.79 (s, 3H), 3.39 (s, 3H), 1.50 (d, *J* = 6.93 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.5, 158.9, 135.1, 127.4, 114.0, 72.0, 59.1, 55.3, 47.5, 21.7

HPLC condition

Whelk–O1, *n*–hexane/2–propanol = 80/20, flow rate = 2.0 mL/min, UV 217 nm

(*S*)–**3c** = 7.57 min, (*R*)–**3c** = 26.91 min

mp 53 – 55 °C, [α]_D²⁵ +99.6 (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 64.55, H 7.67, N 6.27; found C 64.47, H 7.74, N 6.22

***N*–((*R*)–1–(4–(Trifluoromethyl)phenyl)ethyl)acetamide (2d)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.60 (d, *J* = 8.19 Hz, 2H), 7.42 (d, *J* = 8.19 Hz, 2H), 5.70 (s, 1H), 5.21 – 5.11 (m, 1H), 2.01 (s, 3H), 1.50 (d, *J* = 6.96 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.2, 147.3, 126.4, 125.6, 125.5, 48.5, 29.7, 23.3, 21.8

HPLC condition

Whelk–O1, *n*–hexane/2–propanol = 80/20, flow rate = 1.0 mL/min, UV 217 nm

(*S*)–**2d** = 8.59 min, (*R*)–**2d** = 16.47 min

mp 103 – 105 °C, [α]_D²⁵ +89.1 (c = 1.0, CHCl₃)

(lit. mp 102 – 104 °C, $[\alpha]_D^{25} -75.0$ (c = 0.12, CHCl₃, (S)-isomer); Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.)

2-Methoxy-N-((R)-1-(4-(trifluoromethyl)phenyl)ethyl)acetamide (3d)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.59 (d, *J*=8.20 Hz, 2H), 7.44 (d, *J*=8.36 Hz, 2H), 6.82 (d, *J*=6.59 Hz, 1H), 5.25 – 5.16 (m, 1H), 3.90 (dd, *J*₁=18.27 Hz, *J*₂=15.03 Hz, 2H), 3.42 (s, 3H), 1.52 (d, *J*=7.00 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.8, 147.2, 126.4, 125.9, 125.7, 122.3, 71.9, 59.2, 47.8, 21.9

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 80/20, flow rate = 2.0 mL/min, UV 217 nm

(S)-**3d** = 6.95 min, (R)-**3d** = 23.26 min

mp 82 – 84 °C, $[\alpha]_D^{25} +67.2$ (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 55.17, H 5.40, N 5.36; found C 55.36, H 5.46, N 5.44

N-((R)-Phenylpropyl)acetamide (2e)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.35 – 7.25 (m, 5H), 5.91 (s, 1H), 4.91 – 4.83 (m, 1H), 1.97 (s, 3H), 1.88 – 1.78 (m, 2H), 0.88 (t, *J* = 7.39 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.5, 142.5, 129.0, 127.7, 127.0, 55.3, 29.4, 23.9, 11.1

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 93/7, flow rate = 1.0 mL/min, UV 217 nm

(R)-**2e** = 16.05 min, (S)-**2e** = 18.94 min

mp 106 – 108 °C, $[\alpha]_D^{25} +123$ (c = 1.0, CHCl₃)

(lit. mp 105 – 107 °C, $[\alpha]_D^{25} +135$ (c = 0.12, CHCl₃); Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.)

2-Methoxy-N-((R)-phenylpropyl)acetamide (3e)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.37 – 7.23 (m, 5H), 6.76 (d, *J*=5.79 Hz, 1H), 4.97 – 4.89 (m, 1H), 3.89 (dd, *J*₁=24.90 Hz, *J*₂=15.00 Hz, 2H), 3.41 (s, 3H), 1.90 – 1.80 (m, 2H), 0.90 (t, *J*=7.38 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.8, 141.9, 128.6, 127.4, 126.6, 72.0, 59.1, 54.1, 29.3, 10.7

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 93/7, flow rate = 1.0 mL/min, UV 217 nm

(R)-**3e** = 8.22 min, (S)-**3e** = 14.13 min

mp 71 – 72 °C, $[\alpha]_D^{25} +79.2$ (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 69.54, H 8.27, N 6.76; found C 69.23, H

8.27, N 6.72

***N*–((*R*)-2,3-Dihydro-1H-inden-1-yl)acetamide (2f)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.25 – 7.19 (m, 4H), 6.29 (s, 1H), 5.41 – 5.33 (m, 1H), 3.00 – 2.75 (m, 2H), 2.53 – 2.47 (m, 1H), 1.95 (s, 3H), 1.80 – 1.73 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 170.1, 143.7, 143.5, 128.4, 127.2, 125.2, 124.4, 55.2, 34.5, 30.6, 23.9

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**2f** = 11.70 min, (*R*)-**2f** = 13.18 min

mp 151 – 153 °C, [α]_D²⁵ +72.4 (c = 1.0, CHCl₃)

(lit. [α]_D²⁵ +74.4 (c = 1.0, CHCl₃); Zhang, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 1774.)

2-Methoxy-*N*–((*R*)-2,3-dihydro-1H-inden-1-yl)acetamide (3f)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.30 – 7.20 (m, 4H), 6.74 (d, *J* = 5.61 Hz, 1H), 5.57 – 5.50 (m, 1H), 3.96 (s, 2H), 3.39 (s, 3H), 3.00 – 2.85 (m, 2H), 2.64 – 2.59 (m, 1H), 1.87 – 1.80 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.3, 143.4, 142.9, 128.0, 126.8, 124.8, 124.0, 72.0, 59.1, 53.9, 34.0, 30.3

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**3f** = 7.68 min, (*R*)-**3f** = 10.98 min

mp 50 – 52 °C, [α]_D²⁵ +44.0 (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 70.22, H 7.37, N 6.82; found C 69.52, H 7.39, N 6.73

***N*–((*R*)-1,2,3,4-Tetrahydronaphthalen-1-yl)acetamide (2g)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.22 – 7.03 (m, 4H), 6.29 (d, *J* = 7.85 Hz, 1H), 5.12 – 5.07 (m, 1H), 2.75 – 2.71 (m, 2H), 2.01 – 1.93 (m+s, 4H), 1.84 – 1.73 (m, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.6, 138.0, 137.1, 129.6, 129.1, 127.7, 126.6, 47.9, 30.5, 29.6, 23.9, 20.3

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, UV 217 nm

(*S*)-**2g** = 29.95 min, (*R*)-**2g** = 34.30 min

mp 148 – 151 °C, [α]_D²⁵ +83.6 (c = 1.0, CHCl₃)

(lit. $[\alpha]_D^{25} +106$ (c = 1.0, CHCl₃); Zhang, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 1774.)

2-Methoxy-*N*-((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)acetamide (3g)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.28 – 7.09 (m, 4H), 6.77 (d, *J*=7.35 Hz, 1H), 5.26 – 5.21 (m, 1H), 3.95 (s, 2H), 3.38 (s, 3H), 2.83 – 2.77 (m, 2H), 2.10 – 2.03 (m, 1H), 1.89 – 1.79 (m, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 168.8, 137.6, 136.5, 129.2, 128.6, 127.3, 126.3, 72.0, 59.1, 46.8, 30.2, 29.2, 20.0

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, UV 217 nm

(*S*)-**3g** = 15.83 min, (*R*)-**3g** = 20.20 min

mp 86 – 87 °C, $[\alpha]_D^{25} +65.8$ (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 71.21, H 7.81, N 6.39; found C 70.51, H 7.75, N 6.37

***N*-((*R*)-3,4-Dihydro-2H-chromen-4-yl)acetamide (2h)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.20 – 7.14 (m, 2H), 6.89 (t, *J* = 7.2 Hz, 1H), 6.82 (d, *J* = 8.13 Hz, 1H), 5.94 (s, 1H), 5.14 – 5.07 (m, 1H), 4.25 – 4.22 (m, 1H), 4.17 – 4.10 (m, 1H), 2.22 – 2.15 (m, 1H), 2.07 – 2.00 (m+s, 4H); ¹³C NMR (300 MHz, CDCl₃, ppm): δ 169.4, 155.1, 129.3, 129.2, 121.9, 120.7, 117.1, 63.1, 43.6, 28.9, 23.3

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**2h** = 10.49 min, (*R*)-**2h** = 14.05 min

mp 189 – 190 °C, $[\alpha]_D^{25} +79.2$ (c = 1.0, CHCl₃)

(lit. $[\alpha]_D^{25} +79.7$ (c = 1.0, CHCl₃); Zhang, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 1774.)

2-Methoxy-*N*-((*R*)-3,4-dihydro-2H-chromen-4-yl)acetamide (3h)

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.21 – 7.16 (m, 2H), 6.91 (t, *J*=7.26 Hz, 1H), 6.86 – 6.82 (d+s, 2H), 5.24 – 5.16 (m, 1H), 4.27 – 4.13 (m, 2H), 3.94 (s, 2H), 3.39 (s, 3H), 2.27 – 2.03 (m, 2H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.0, 155.1, 129.3, 129.2, 121.8, 120.9, 117.2, 71.9, 63.2, 59.1, 43.0, 29.1

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 95/5, flow rate = 0.5 mL/min, UV 217 nm

(*S*)-**3h** = 14.34 min, (*R*)-**3h** = 20.70 min

mp 137 – 138 °C, $[\alpha]_D^{25} +61.6$ (c = 0.5, CHCl₃)

Elemental analysis (VarioEL III CHN): calc. C 65.14, H 6.83, N 6.33; found C 65.06, H 6.83, N 6.31

***N*–((*R*)-4-Phenylbutan-2-yl)acetamide (**2i**)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 7.30 – 7.15 (m, 5H), 5.47 (brs, 1H), 4.10 – 4.00 (m, 1H), 2.67 – 2.62 (m, 2H), 1.93 (s, 3H), 1.79 – 1.71 (m, 2H), 1.17 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.5, 142.0, 128.6, 128.5, 126.1, 45.4, 38.8, 32.7, 23.7, 21.2

HPLC condition

Whelk-O1, *n*-hexane/2-propanol = 85/15, flow rate = 0.50 mL/min, UV 217 nm

(*S*)-**2i** = 23.99 min, (*R*)-**2i** = 27.07 min

[α]_D²⁰ +41.3 (c = 1.0, CH₂Cl₂)

(lit. [α]_D²⁵ +45.5 (c = 1.0, CH₂Cl₂); Paetzold, J.; Bäckvall, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 17620.)

mp 71 – 72 °C

(lit. mp 74 – 75 °C; González-Sabín, J.; Gotor, V.; Rebolledo, F. *Tetrahedron: Asymmetry* **2002**, *13*, 1315.)

***N*–((*R*)-1-Cyclohexylethyl)acetamide (**2j**)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 5.42 (brs, 1H), 3.88 – 3.81 (m, 1H), 1.97 (s, 3H), 1.77 – 1.66 (m, 5H), 1.36 – 1.13 (m, 4H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.01 – 0.93 (m, 2H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.4, 49.6, 43.3, 29.3, 26.6, 26.4, 23.8, 18.1

Chiral GC condition

BETA DEX 120, Supelco, injection temp. 220 °C, detection temp. 300 °C, oven initial temp. 120 °C (30 min), rate 15 °C/min, oven final temp. 220 °C (10 min)

(*S*)-**2j** = 36.60 min, (*R*)-**2j** = 36.77 min

mp 117 – 119 °C, [α]_D²⁰ +19.1 (c = 1.0, CH₂Cl₂)

(lit. mp 101 – 102.5 °C, [α]_D²⁵ +11.7 (c = 5.27, DMF); Mohan, A. T.; Conley, R. T. *J. Org. Chem.* **1969**, *34*, 3259.)

***N*–((*R*)-Octan-2-yl)acetamide (**2k**)**

¹H NMR (300 MHz, CDCl₃, ppm): δ 5.63 (brs, 1H) 4.00 – 3.90 (m, 1H), 1.96 (s, 3H), 1.42 – 1.38 (m, 2H), 1.27 – 1.17 (m, 8H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm): δ 169.5, 45.5, 37.1, 31.9, 29.3, 26.1, 23.6, 22.7, 21.1, 14.2

Chiral GC condition

BETA DEX 120, Supelco, injection temp. 220 °C, detection temp. 300 °C, oven temp. 140 °C

(*S*)-**2k** = 18.83 min, (*R*)-**2k** = 19.57 min

$[\alpha]_D^{20} + 6.6$ (c = 1.0, CH₂Cl₂)

(lit. $[\alpha]_D + 4.4$ (c = 1.0, CH₂Cl₂); Paetzold, J.; Bäckvall, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 17620.)

Not crystallized

(*S*)-2-Acetamido-3-phenylpropanamide (2l)

¹H NMR (300 MHz, DMSO, ppm): δ 8.04 (s, 1H), 7.29 – 7.15 (m, 5H), 4.45 – 4.37 (m, 1H), 3.01 – 2.95 (m, 1H), 2.76 – 2.68 (m, 1H), 1.75 (s, 3H); ¹³C NMR (75 MHz, DMSO, ppm): δ 173.2, 169.0, 138.2, 129.0, 127.9, 126.1, 53.7, 37.6, 22.5

HPLC condition

Chiralcel OD, *n*-hexane/2-propanol = 95/5, flow rate = 1.0 mL/min, UV 217 nm

(*S*)-**2l** = 55.04 min, (*R*)-**2l** = 59.15 min

mp 177 – 179 °C, $[\alpha]_D^{20} + 36.6$ (c = 0.50, MeOH)

(lit. mp 176 – 177 °C, $[\alpha]_D^{25} + 27$ (c = 0.10, MeOH); Huang, H. T.; Foster, R. J.; Niemann, C. *J. Am. Chem. Soc.* **1952**, *74*, 105.)