**Asymmetric Mannich Reactions of β -Keto Esters with Acyl Imines
Catalyzed by Cinchona Alkaloids**

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Supporting Information

General Information. All ^1H NMR, and ^{13}C NMR spectra were recorded using Varian Unity Plus 400 (93.94 kG, ^1H 400 MHz) or Varian Gemini 300 (70.5 kG, ^{13}C 75 MHz) spectrometers at ambient temperature in CDCl_3 . Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, and integration. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR ESP spectrophotometer. High-resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory on a Finnegan MAT-90 spectrometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm, and were reported as $[\alpha]_D$ (concentration in grams/100 mL solvent). Analytical thin layer chromatography was performed using EMD 0.25 mm silica gel 60-F plates. Flash column chromatography was performed on Sorbent Technologies 60 Å silica gel. Chiral HPLC analysis was performed using an Agilent 1100 series HPLC with a diode array detector and either a Chiralcel® OD (Chiral Technologies Inc., 24cm×4.6mm I.D.) or a (R,R)-Whelk-O 1 (Regis® Technologies Inc., 25cm×4.6mm I.D.) column. All reactions were performed under nitrogen atmosphere, in oven dried glassware with magnetic stirring, unless otherwise noted. Reaction solvents were obtained from a dry solvent system (alumina) and used without further drying. All acyl imines were prepared according to the published procedure.¹ (+)-Cinchonine, quinine, quinidine and other reagents were used as supplied by Sigma-Aldrich, Alfa Aesar, Lancaster, or Acros unless otherwise noted.

General asymmetric mannich reaction procedure of allyl acetoacetate (3a) to acyl imines(6). In an oven dried 17×110 mm round bottom reaction vessel, (+)-cinchonine (15 mg, 0.05 mmol) was dissolved in 1.00 mL CH_2Cl_2 . The solution was cooled down to $-35\text{ }^\circ\text{C}$. The imine (6, 0.50 mmol) and allyl acetoacetate (0.070 mL, 0.50 mmol) were added successively. The solution was stirred at $-35\text{ }^\circ\text{C}$ for 16 h. The reaction mixture was then passed through a plug of silica gel and eluted with 5 mL of ethyl acetate. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography over silica gel (elution with 15%-30% ethyl acetate in hexanes) to afford 7a'-7j'.

General Pd⁰ promoted decarboxylation procedure. An oven dried 17×110 mm round bottom reaction vessel was charged with allyl palladium chloride dimer (3.6 mg, 0.010 mmol) and (±)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((±)DIOP)² (10 mg, 0.020 mmol). The Pd catalyst and ligand were dissolved in CH₂Cl₂ (0.5 mL) and stirred at room temperature for 10 minutes. Methyl acetoacetate (0.045 mL, 0.40 mmol) and isolated product (**7a'** - **7j'**, 0.20 mmol) were added successively. The reaction solution was stirred at room temperature for 3 h and subjected directly to flash chromatography over silica gel (elution with 30%-50% ethyl acetate in hexanes) to afford **7a - 7j**.

2-((*R*)-Methoxycarbonylamino-phenyl-methyl)-3-oxo-butyl ester (**5c** or **7a'**)

Yield: 151 mg, 99%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.33-7.22 (m, 10H), 6.30 (br, 1H), 5.92 (br, 1H), 5.81-5.67 (m, 2H), 5.56 (br, 1H), 5.45 (t, *J* = 8.0 Hz, 1H), 5.28-5.11 (m, 4H), 4.55 (d, *J* = 5.6 Hz, 2H), 4.52 (m, 2H), 4.05 (m, 2H), 3.62 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H), 2.13 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₄H₂₁O₂: 305.1263; found: 305.1257.

(*R*)-(3-Oxo-1-phenyl-butyl)-carbamic acid methyl ester (**7a**).

Yield: 35 mg, 80%. **ee:** 92%.

HPLC analysis, *t_r* minor: 14.6 min, *t_r* minor: 21.3 min, [(*R, R*)-Whelk-O 1 column, Hexanes:IPA 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.31-7.19 (m, 5H), 5.65 (br, 1H), 5.10 (dd, *J* = 13, 6.0 Hz, 1H), 3.61 (s, 3H), 3.06-3.00 (dd, *J* = 16, 5.0 Hz, 1H), 2.91-2.86 (dd, *J* = 16, 11 Hz, 1H), 2.05 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 208.2, 156.2, 141.2, 128.7, 127.5, 126.2, 52.2, 51.5, 49.0, 30.6.

IR (thin film, cm⁻¹): 3328, 3030, 2952, 1712, 1700, 1538, 1455, 1360, 1258, 1057, 700.

HRMS: calc'd for (M+H)⁺ C₁₂H₁₅NO₃: 222.1085; found: 222.1154.

[α]_D²³ = + 33.7° (c = 1.0, CHCl₃).

2-[(*R*)-(4-Chloro-phenyl)-methoxycarbonylamino-methyl]-3-oxo-butyrac acid allyl ester (7b')

Yield: 158 mg, 93%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.25 (m, 8H), 6.33 (br, 1H), 6.03 (br, 1H), 5.72 (m, 2H), 5.50 (br, 1H), 5.40 (t, 1H), 5.21 (m, 4H), 4.57 (dd, *J* = 6.0, 1.2 Hz, 2H), 4.53 (t, *J* = 6.0 Hz, 2H), 4.02 (br, 1H), 3.95 (br, 1H), 3.65 (s, 3H), 3.63 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H).

(*R*)- [1-(4-Chloro-phenyl)-3-oxo-butyl]-carbamic acid methyl ester (7b)

Yield: 41 mg, 80%. **ee**: 83%.

HPLC analysis, *t_r* minor: 14.0 min, *t_r* major: 23.2 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.25 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 5.71 (br, 1H), 5.03 (dd, *J* = 14, 6.0 Hz, 1H), 3.61 (s, 3H), 3.04-2.99 (dd, *J* = 17, 6.0 Hz, 1H), 2.90-2.84 (dd, *J* = 17, 6.0 Hz, 1H), 2.06 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.3, 156.2, 139.8, 128.7, 127.6, 52.2, 50.8, 48.6, 30.6.

IR (thin film, cm⁻¹): 3328, 2962, 1715, 1695, 1544, 1404, 1347, 1260, 1090, 1060, 1015, 800.

HRMS: calc'd for (M)⁺ C₁₂H₁₄ClNO₃: 255.0662; found: 255.0684.

[α]_D²³ = + 21.1° (c = 1.0, CHCl₃).

2-[(R)-(4-Fluorophenyl)-methoxycarbonylamino-methyl]-3-oxo-butyrac acid allyl ester (7c')

Yield: 158 mg, 98%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.26 (m, 4H), 6.99 (m, 4H), 6.34 (d, *J* = 8.0 Hz, 1H), 6.04 (d, *J* = 8.4 Hz, 1H), 5.75 (m, 2H), 5.51 (br, 2H), 5.41 (t, *J* = 7.2 Hz, 1H), 5.20 (m, 4H), 4.55 (d, *J* = 5.2 Hz, 2H), 4.51 (m, 2H), 4.01 (d, *J* = 5.6 Hz, 1H), 3.96 (br, 1H), 3.64 (s, 3H), 3.62 (s, 3H), 2.30 (s, 3H), 2.14 (s, 3H).

(R)-[1-(4-Fluorophenyl)-3-oxo-butyl]-carbamic acid methyl ester (7c)

Yield: 46 mg, 97%. **ee:** 93%.

HPLC analysis, *t_r* minor: 14.3 min, *t_r* major: 20.8 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.23 (dd, *J* = 7.0, 2.0 Hz, 2H), 6.97 (dd, *J* = 9.0, 2.0 Hz, 2H), 5.67 (br, 1H), 5.05 (dd, *J* = 14, 6.0 Hz, 1H), 3.61 (s, 3H), 3.05-2.99 (dd, *J* = 17, 6.0 Hz, 1H), 2.90-2.84 (dd, *J* = 15, 6.0 Hz, 1H), 2.06 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.5, 156.2, 137.1, 128.0, 127.8, 115.6, 115.3, 52.2, 50.9, 48.8, 30.6.

IR (thin film, cm⁻¹): 3326, 1713, 1698, 1542, 1274, 1160, 1058, 822.

HRMS: calc'd for (M+H)⁺ C₁₂H₁₄FNO₃: 240.0991; found: 240.1036.

[α]_D²³ = + 29.5° (c = 0.6, CHCl₃).

2-[(*R*)-(3-Fluoro-phenyl)-methoxycarbonylamino-methyl]-3-oxo-butyrac acid allyl ester (7d')

Yield: 158 mg, 98%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.27 (t, *J* = 8 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.93 (t, *J* = 8.8 Hz, 1H), 6.12 (d, *J* = 7.2 Hz, 1H), 5.80 (m, 1H), 5.44 (t, 1H), 5.26 (d, *J* = 16.8 Hz, 1H), 5.23 (d, *J* = 10 Hz, 1H), 4.58 (d, *J* = 5.6 Hz, 2H), 4.04 (d, *J* = 4.8 Hz, 1H), 3.64 (s, 3H), 2.14 (s, 3H).

(*R*)- [1-(3-Fluoro-phenyl)-3-oxo-butyl]-carbamic acid methyl ester (7d)

Yield: 40 mg, 84%. **ee:** 91%.

HPLC analysis, *t_r* minor: 12.9 min, *t_r* major: 17.7 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.26 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 9.6 Hz), 6.92 (t, *J* = 8.4 Hz), 5.74 (br, 1H), 5.09 (dd, *J* = 14, 6.0 Hz), 3.64 (s, 3H), 3.06-3.03 (dd, *J* = 17, 6.0 Hz, 1H), 2.93-2.87 (dd, *J* = 17, 6 Hz, 1H), 2.08 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.2, 155.8, 143.4, 129.8, 121.4, 114.0, 112.9, 51.8, 50.4, 48.0, 30.3.

IR (thin film, cm⁻¹): 3326, 1717, 1697, 1592, 1538, 1451, 1363, 1258, 1058, 695.

HRMS: calc'd for (M)⁺ C₁₂H₁₄FNO₃: 239.0958; found: 239.0940.

[α]_D²³ = + 18.4 ° (c = 0.9, CHCl₃).

2-((*R*)-Methoxycarbonylamino-m-tolyl-methyl)-3-oxo-butyrac acid allyl ester (7e')

Yield: 153 mg, 96%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.18 (m, 2H), 7.05 (m, 6H), 6.35 (d, J = 8.8 Hz, 1H), 6.21 (d, J = 8.8 Hz, 1H), 5.74 (m, 2H), 5.53 (m, 1H), 5.41 (t, J = 7.2 Hz, 1H), 5.18 (m, 4H), 4.55 (d, J = 5.2 Hz, 2H), 4.53 (d, J = 6.4 Hz, 2H), 4.03 (d, J = 7.2 Hz, 1H), 4.00 (d, J = 4.0 Hz, 1H), 3.64 (s, 3H), 3.62 (s, 3H), 2.30 (s, 3H), 2.29 (s, 6H), 2.13 (s, 1H).

(R)- (3-Oxo-1-m-tolyl-butyl)-carbamic acid methyl ester (7e)

Yield: 38 mg, 81%. **ee:** 96%.

HPLC analysis, t_r minor: 13.0 min, t_r major: 22.6 min, [(*R,R*)-Whelk-O 1 column, Hexanes: IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.19 (t, J = 18 Hz, 1H), 7.05 (m, 3H), 5.57 (br, 1H), 5.08 (dd, J = 14, 6.0 Hz, 1H), 3.63 (s, 3H), 3.04-3.00 (dd, J = 15, 4.0 Hz, 1H), 2.92-2.86 (dd, J = 16, 7.0 Hz), 2.31 (s, 3H), 2.08 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.2, 156.0, 138.4, 128.6, 128.3, 126.9, 123.1, 52.2, 51.4, 49.0, 30.6, 21.5.

IR (thin film, cm⁻¹): 3326, 2954, 1720, 1700, 1533, 1362, 1262, 1193, 1159, 1060, 787, 704.

HRMS: calc'd for (M)⁺ C₁₃H₁₇NO₃: 235.1208; found: 235.1208.

$[\alpha]_D^{23}$ = + 25.7 ° (c = 0.75, CHCl₃).

2-[(R)-Methoxycarbonylamino-(3-trifluoromethyl-phenyl)-methyl]-3-oxo-butyrac allyl ester (7f')

Yield: 188 mg, 99%.

¹H NMR (400 MHz, CDCl₃, both diastereomers were reported): δ 7.52 (m, 6H), 7.45 (m, 2H), 6.48 (d, J = 8.8 Hz, 1H), 6.27 (d, J = 9.2 Hz, 1H), 5.74 (m, 2H), 5.62 (dd, J = 9.2, 4 Hz, 1H),

5.51 (br, 1H), 5.26-5.12 (m, 4H), 4.56 (d, $J = 4.8$ Hz, 2H), 4.52 (d, $J = 6$ Hz, 2H), 4.09 (d, $J = 6$ Hz, 1H), 4.02 (d, $J = 4.4$ Hz, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 2.33 (s, 3H), 2.17 (s, 3H).

(R)- [3-Oxo-1-(3-trifluoromethyl-phenyl)-butyl]-carbamic acid methyl ester (7f)

Yield: 46 mg, 83%; **ee:** 90%.

HPLC analysis, t_r minor: 9.2 min, t_r major: 12.6 min, [(*R,R*)-Whelk-O 1, Hexanes:IPA, 85:15, 1.5 mL/min].

^1H NMR (400 MHz, CDCl_3): δ 7.48 (m, 4H), 5.78 (br, 1H), 5.15 (m, 1H), 3.64 (s, 1H), 3.10-3.06 (dd, $J = 14, 5.2$ Hz, 1H), 2.97-2.91 (dd, $J = 14, 5.2$ Hz, 1H), 2.09 (s, 3H).

^{13}C NMR (75.0 MHz, CDCl_3): δ 206.4, 156.1, 142.4, 129.8, 129.1, 124.3, 122.9, 52.3, 51.0, 49.9, 48.5, 30.7.

IR (thin film, cm^{-1}): 3340, 1715, 1695, 1540, 1328, 1270, 1165, 1106, 1061.

HRMS: calc'd for (M) $^+$ $\text{C}_{13}\text{H}_{14}\text{F}_3\text{NO}_3$: 289.0926; found: 289.0953.

$[\alpha]_D^{23} = +15.0^\circ$ ($c = 1.0$, CHCl_3).

2-((R)-Benzo[1,3]dioxol-5-yl-methoxycarbonylamino-methyl)-3-oxo-butyric acid allyl ester (7g')

Yield: 166 mg, 95%.

^1H NMR (400 MHz, CDCl_3 , both diastereomers reported): δ 6.76 (m, 2H), 6.72 (m, 4H), 6.29 (d, $J = 7.6$ Hz, 1H), 5.92 (s, 2H), 5.91 (s, 2H), 5.77 (m, 2H), 5.43 (br, 1H), 5.33 (t, $J = 8.0$ Hz, 1H), 5.27-5.17 (m, 4H), 4.55 (m, 4H), 3.99 (d, $J = 6.0$ Hz, 1H), 3.93 (br, 1H), 3.63 (s, 3H), 3.61 (s, 3H), 2.28 (s, 3H), 2.15 (s, 3H).

(R)- (1-Benzo[1,3]dioxol-5-yl-3-oxo-butyl)-carbamic acid methyl ester (7g)

Yield: 43 mg, 81%. **ee:** 80%.

HPLC analysis, t_r minor: 27.1 min, t_r major: 44.3 min[(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

^1H NMR (400 MHz, CDCl_3): δ 6.75 (s, 1H), 6.71 (d, $J = 1.0$ Hz, 2H), 5.90 (s, 2H) 5.54 (br, 1H), 4.98 (dd, $J = 14$, 6.0 Hz, 1H), 3.61 (s, 3H), 3.02-2.96 (dd, $J = 16.5$, 6.0 Hz, 1H), 2.87-2.81 (dd, $J = 17$, 6.0 Hz, 1H), 2.07 (s, 3H).

^{13}C NMR (75.0 MHz, CDCl_3): δ 209.6, 156.3, 119.5, 108.3, 106.9, 101.1, 52.2, 51.2, 48.9, 30.6.

IR (thin film, cm^{-1}): 3332, 2923, 1714, 1697, 1504, 1490, 1444, 1358, 1242, 1038, 930.

HRMS: calc'd for $(\text{M}+\text{H})^+$ $\text{C}_{13}\text{H}_{15}\text{NO}_5$: 265.0950; found: 265.0955.

$[\alpha]_D^{23} = +13.0^\circ$ ($c = 0.8$, CHCl_3).

2-((R)-Furan-2-yl-methoxycarbonylamino-methyl)-3-oxo-butyl allyl ester (7h')

Yield: 120 mg, 81%.

^1H NMR (400 MHz, CDCl_3 , both diastereomers reported): δ 7.28 (d, $J = 6.8$ Hz, 2H), 6.28 (m, 2H), 6.20 (m, 2H), 6.09 (d, $J = 9.6$ Hz, 1H), 5.91 (d, $J = 8.8$ Hz, 1H), 5.84 (m, 2H), 5.60 (dd, $J = 10$, 4.4 Hz, 1H), 5.53 (dd, $J = 8.4$, 6 Hz, 1H), 5.24 (m, 4H), 4.60 (d, $J = 6.4$ Hz, 4H), 4.18 (d, $J = 5.6$ Hz, 1H), 4.13 (d, $J = 4.0$ Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 2.30 (s, 3H), 2.23 (s, 3H).

(R)-(1-Furan-2-yl-3-oxo-butyl)-carbamic acid methyl ester (7h)

Yield: 40 mg, 96%; **ee:** 93%.

HPLC analysis, t_r minor: 29.0 min, t_r minor: 30.5 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.28 (d, *J* = 2.0 Hz, 1H), 6.27 (dd, *J* = 3.1, 2.0 Hz, 1H), 6.16 (d, *J* = 3.4 Hz, 1H), 5.58 (br, 1H), 5.17 (dd, *J* = 14, 6.0 Hz, 1H), 3.64 (s, 3H), 3.09-3.05 (dd, *J* = 16, 5.0 Hz, 1H), 2.94-2.88 (dd, *J* = 17, 6.0 Hz, 1H), 2.12 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.5, 153.5, 141.8, 110.5, 106.2, 52.2, 46.1, 45.6, 30.3.

IR (thin film, cm⁻¹): 3324, 2950, 1708, 1693, 1290, 1257, 1237, 1047, 1014, 926, 737.

HRMS: calc'd for (M)⁺ C₁₀H₁₃NO₄: 211.0845; found: 211.0816.

[α]_D²³ = + 49.1° (c = 0.44, CHCl₃).

2-((*R*)-Methoxycarbonylamino-thiophen-2-yl-methyl)-3-oxo-butyrac acid allyl ester (7i')

Yield: 130 mg, 84%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.19 (m, 2H), 6.90 (m, 4H), 6.29 (d, *J* = 8.8 Hz, 1H), 6.08 (d, *J* = 4.0 Hz, 1H), 5.78 (m, 3H), 5.71 (m, 1H), 5.30-5.19 (m, 4H), 4.60 (m, 4H), 4.13 (m, 1H), 4.09 (d, 7.2 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 2.32 (s, 3H), 2.22 (s, 3H).

(*R*)-(1-Oxo-1-thiophen-2-yl-butyl)-carbamic acid methyl ester (7i)

Yield: 37 mg, 82%. **ee**: 92%.

HPLC analysis, *t*_r minor: 31.9 min, *t*_r minor: 37.0 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.16 (t, *J* = 3.2 Hz, 1H), 6.90 (d, *J* = 2.8 Hz, 2H), 5.70 (br, 1H), 5.36 (dd, *J* = 14, 6.0 Hz, 1H), 3.65 (s, 3H), 3.15-3.09 (dd, *J* = 17, 5.0 Hz, 1H), 3.01-2.95 (dd, *J* = 17, 6.0 Hz, 1H), 2.14 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 206.6, 156.2, 126.9, 126.1, 124.5, 52.2, 48.8, 47.4, 30.5.

IR (thin film, cm⁻¹): 3328, 2952, 1715, 1697, 1540, 1350, 1269, 1160, 1060.

HRMS: calc'd for (M)⁺ C₁₀H₁₃NO₃S: 227.0620; found: 227.0616.

$[\alpha]_D^{23} = +19.3^\circ$ ($c = 0.6$, CHCl_3).

2-((R)-Methoxycarbonylamino-naphthalen-2-yl-methyl)-3-oxo-butylric acid allyl ester (7j')

Yield: 160 mg, 96%.

^1H NMR (400 MHz, CDCl_3 , major diastereomer reported): δ 7.83 (m, 3H), 7.77 (s, 1H), 7.49 (m, 2H), 4.41 (d, $J = 8.4$ Hz, 1H), 6.22 (d, $J = 8.8$ Hz, 1H), 5.82 (m, 1H), 5.67 (m, 1H), 5.23 (m, 2H), 4.60 (d, $J = 4.8$ Hz, 2H), 4.20 (d, $J = 5.6$ Hz, 1H), 3.67 (s, 3H), 2.16 (s, 3H).

(R)-(1-Naphthalen-2-yl-3-oxo-butyl)-carbamic acid methyl ester (7j)

Yield: 46 mg, 83%. **ee:** 95%.

HPLC analysis, t_r minor: 18.3 min, t_r minor: 21.1 min, Chiralcel[®] OD Column, Hexanes : IPA = 90 : 10, 1.5 mL/min.

^1H NMR (400 MHz, CDCl_3): δ 7.79 (m, 3H), 7.72 (s, 1H), 7.44 (m, 2H), 7.39 (d, $J = 8.8$ Hz, 1H), 5.77 (br, 1H), 5.27 (dd, $J = 14$, 6.0 Hz, 1H), 3.64 (s, 3H), 3.14-3.11 (dd, $J = 17$, 5.0 Hz, 1H), 3.02-2.95 (dd, $J = 17$, 6.0 Hz, 1H), 2.07 (s, 3H).

^{13}C NMR (75.0 MHz, CDCl_3): δ 207.1, 156.4, 138.6, 133.2, 132.7, 128.6, 128.0, 127.6, 126.4, 126.1, 125.0, 124.4, 52.5, 51.5, 48.8, 30.7.

IR (thin film, cm^{-1}): 3336, 2953, 1712, 1706, 1533, 1362, 1249, 1057, 744.

HRMS: calc'd for $(\text{M}+\text{H})^+$ $\text{C}_{16}\text{H}_{17}\text{NO}_3$: 272.1242; found: 272.1261.

$[\alpha]_D^{23} = +40.7^\circ$ ($c = 1.1$, CHCl_3).

Preparation of racemic β -amino ketones 7a - 7j. An oven dried 17×110 mm round bottom reaction vessel was charged with YbCl_3 (7.0 mg, 0.025 mmol). The metal salt was flamed dried under high vacuum and purged with nitrogen. The vessel was cooled to room temperature. $\text{Pd}_2(\text{dba})_3$ (11.4 mg, 0.0125 mmol) and $(\pm)\text{-DIOP}$ ² (25 mg, 0.050 mmol) were added. The solids were taken up in 1.0 mL CH_2Cl_2 . The solution was stirred at room temperature for 30 min. Imine (**6**, 0.50 mmol) and allyl acetoacetate (1.25 mmol) were added successively. The solution was stirred at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure and subjected directly to flash chromatography over silica gel (elution with 30%-50% ethyl acetate in hexanes) to give the β -amino ketones (**7a - 7j**).

The absolute configuration of (+)-3-Oxo-1-phenyl-butyl)-carbamic acid methyl ester was determined to be *R* isomer by comparing the optical rotation and chiral HPLC with the authentic sample.

(*R*)-Acetic acid 2-methoxycarbonylamino-2-phenyl-ethyl ester. To a suspension of sodium percarbonate (636 mg, 4.0 mmol) in CH_2Cl_2 was added trifluoroacetic anhydride (924 mg, 4.4 mmol) over 3 min. The mixture was stirred at room temperature for 15 min. The solution became slightly cloudy and was transferred via syringe to the solution of (*R*)-(3-Oxo-1-phenyl-butyl)-carbamic acid methyl ester (86 mg, 0.37 mmol) in CH_2Cl_2 (3 mL). The reaction mixture was stirred overnight until the starting material was not detectable by TLC. The reaction was quenched by the addition of saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution (5 mL). The organic layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was further purified by flash chromatography on silica gel (elution with 30% ethyl acetate in hexanes) to give the product 50 mg (58% yield).

Yield: 50 mg, 58%. **ee:** 86%.

HPLC analysis, t_r minor: 15.1 min, t_r major: 20.6 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

^1H NMR (400 MHz, CDCl_3): δ 7.33-7.22 (m, 5H), 5.43 (br, 1H), 4.97 (br, 1H), 4.30 (dd, J = 11, 6.0 Hz, 1H), 4.24-4.20 (dd, J = 11, 6.0 Hz, 1H), 3.63 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (75.0 MHz, CDCl_3): δ 170.9, 156.2, 138.5, 128.7, 127.9, 126.4, 66.3, 54.3, 52.2, 20.7.

IR (thin film, cm^{-1}): 3328, 3030, 2952, 1712, 1700, 1538, 1455, 1360, 1258, 1057, 700.

HRMS: calc'd for (M+H)⁺ C₁₂H₁₅NO₄: 238.1035; found: 238.1076.

[α]_D²³ = + 37.5 (c = 1.1, CHCl₃).

(R)-Acetic acid 2-methoxycarbonylamino-2-phenyl-ethyl ester. To a solution of (*R*)-2-amino-2-phenylethanol (137 mg, 1.0 mmol) in 2 mL CH₂Cl₂ was added a solution of methyl chloroformate (0.070 mL, 0.80 mmol) in 1 mL CH₂Cl₂. The reaction was stirred at room temperature for 2 h and was quenched by the addition of saturated NaHCO₃ aqueous solution (5 mL). The organic layer was extracted with CH₂Cl₂ (3×10 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (elution with 40% ethyl acetate in hexanes) to give the (2-Hydroxy-1-phenyl-ethyl)-carbamic acid methyl ester (135 mg, 70% yield). The product (60 mg, 0.30 mmol) was treated with acetic anhydride (0.036 mL, 0.36 mmol) and stirred in 2 mL pyridine until the alcohol was not detectable by TLC. The reaction solution was subjected directly to flash chromatography on silica gel (elution with 30% ethyl acetate in hexanes) to give the product (52 mg, 71% yield).

HPLC analysis, *t*_r: 19.5 min, [(*R,R*)-Whelk-O 1 column, Hexanes:IPA, 85:15, 1.5 mL/min].

¹H NMR (400 MHz, CDCl₃): δ 7.33-7.22 (m, 5H), 5.43 (br, 1H), 4.97 (br, 1H), 4.30 (dd, *J* = 11, 6.0 Hz, 1H), 4.24-4.20 (dd, *J* = 11, 6.0 Hz, 1H), 3.63 (s, 3H), 2.01 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 170.9, 156.2, 138.5, 128.7, 127.9, 126.4, 66.3, 54.3, 52.2, 20.7.

IR (thin film, cm⁻¹): 3328, 3030, 2952, 1712, 1700, 1538, 1455, 1360, 1258, 1057, 700.

HRMS: calc'd for (M+H)⁺ C₁₂H₁₅NO₄: 238.1035; found: 238.1076.

[α]_D²³ = + 40.6 (c = 1.0, CHCl₃).

General asymmetric mannich reaction procedure of methyl acetoacetate to acyl imines. In an oven dried 25 mL round bottom flask, (+)-cinchonine (15mg, 0.050 mmol) was dissolved in 1.0 mL CH₂Cl₂. The solution was cooled down to -35 °C. The imine (**6**, 0.50 mmol) and methyl acetoacetate (0.060 mL, 0.50 mmol) were added successively. The reaction mixture was stirred at -35 °C for 16 h. The solution was then passed through a plug of silica gel and eluted with 5 mL ethyl acetate. The filtrate was concentrated under reduced pressure and the residue was

purified by flash chromatography on silica gel (elution with 15-30% ethyl acetate in hexanes) to give the product **8a'** - **8h'**.

The *anti* diastereoselectivity was determined by ^1H -NMR analogy of 6-methyl-2-oxo-4-phenyl-[1,3]oxazinane-5-carboxylic acid methyl ester with known compounds³.

(4R, 5S, 6R)-6-Methyl-2-oxo-4-phenyl-[1,3]oxazinane-5-carboxylic acid methyl ester. The compound **7k** (558mg, 2.0 mmol) was dissolved in 12 mL CH_2Cl_2 and cooled to $-78\text{ }^\circ\text{C}$. Cyclohexene (0.812 mL, 12 mmol) was added. Then a solution of $\text{Zn}(\text{BH}_4)_2$ in ether⁴ (16 mL, 0.15 M, 2.4 mmol) was added in dropwise. The solution was stirred at $-78\text{ }^\circ\text{C}$ for 30 min. The reaction mixture was warmed up to $-45\text{ }^\circ\text{C}$ and stirred for 1h, warmed up to $-15\text{ }^\circ\text{C}$ and stirred for 1 h. The reaction was quenched by the addition of saturated ammonium chloride solution (8 mL). The mixture was transferred to 80 mL saturated NH_4Cl solution and extracted with CH_2Cl_2 ($3 \times 80\text{ mL}$). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (elution with 40% ethyl acetate in hexanes) to give the major diastereomer, (2*S*, 3*R*)-3-Hydroxy-2-((*R*)-methoxycarbonylamino-phenyl-methyl)-butyric acid methyl ester (510 mg), minor diastereomer (15 mg). (95%yield, dr = 34 : 1)

A 5 mL round bottom flask was charged with hexamethyldisilazane (0.316mL, 1.5 mmol) and cooled to $0\text{ }^\circ\text{C}$. *n*-BuLi (0.94 mL, 1.6 M) was added. The solution was diluted with an additional 0.9 mL THF. The 3-Hydroxy-2-(methoxycarbonylamino-phenyl-methyl)-butyric acid methyl ester (422 mg, 1.5 mmol) was dissolved in 2 mL THF and cooled to $-20\text{ }^\circ\text{C}$. LiHMDS solution was added to the methyl ester THF solution dropwise. The reaction mixture was stirred at $-20\text{ }^\circ\text{C}$ for 5 minutes and was quenched with 4 M HCl (20 mL). The organic layer was extracted with CH_2Cl_2 ($3 \times 30\text{ mL}$). The collected organic layers were combined and dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (elution with 10-20% ethyl acetate in hexanes) to give the 6-Methyl-2-oxo-4-phenyl-[1,3]oxazinane-5-carboxylic acid methyl ester (346 mg, 82% yield).

(2*S*, 3*R*)-3-Hydroxy-2-((*R*)-methoxycarbonylamino-phenyl-methyl)-butyric acid methyl ester

Yield: 510 mg, 91%;

¹H NMR (400 MHz, CDCl₃): δ 7.33-7.21(m, 5H), 5.78 (d, *J* = 8.4 Hz, 1H), 5.21 (t, *J* = 8 Hz, 1H), 4.11 (br, 1H), 3.62 (s, 3H), 3.51 (s, 3H), 2.91 (t, *J* = 7.2 Hz, 1H), 2.20 (br, 1H), 1.20 (d, *J* = 6 Hz, 3H);

HRMS: calc'd for (M+H)⁺ C₁₄H₁₉NO₅: 282.1297 ; found: 282.1341;

(4*R*, 5*S*, 6*R*)-6-Methyl-2-oxo-4-phenyl-[1,3]oxazinane-5-carboxylic acid methyl ester

Yield: 346 mg, 82%;

¹H NMR (400 MHz, CDCl₃): δ 7.36-7.34 (m, 2H), 7.31-7.23 (m, 3H), 5.15 (s, 1H), 4.78 (d, *J* = 10.4 Hz, 1H), 4.60 (m, 1H), 3.55 (s, 3H), 2.68 (t, *J* = 10.4 Hz, 1H), 1.37 (d, *J* = 6 Hz, 3H);

¹³C NMR (75.0 MHz, CDCl₃): δ 169.8, 153.2, 138.1, 128.9, 126.3, 74.2, 58.0, 53.7, 52.1, 19.0;

HRMS: calc'd for (M+H)⁺ C₁₃H₁₅NO₄: 250.1035 ; found: 250.1099;

General procedure for the preparation of (*Z*)-enamines (8a – 8h). An oven dried 17×110 mm round bottom reaction vessel was charged with Yb(OTf)₃ (2.0 mg, 0.003 mmol). This metal salt was flamed dried under high vacuum and purged with nitrogen. The vessel was cooled to room temperature and the product (**8a' – 8h'**) (0.30 mmol) was added. Trimethyl orthoformate (1 mL) and benzyl amine (0.070 mL, 0.60 mmol) were added successively. The solution was stirred for 4.0 h. The reaction mixture was subjected directly to the flash chromatography over silica gel (elution with 15-20% ethyl acetate in hexanes) to give the enamines (**8a – 8h**). The (*Z*) configuration of enamines (**8a – 8h**) were determined by ¹H-NMR analogy of reported compounds.⁵

(*S*) - 2-((*R*)-Methoxycarbonylamino-phenyl-methyl)-3-oxo-butiric acid methyl ester (5d or 8a')

Yield: 139 mg, 99%.

¹H NMR (400 MHz, CDCl₃, major diastereomer reported): δ 7.28 (m, 5H), 6.08 (br, 1H), 5.45 (m, 1H), 4.07 (d, *J* = 4.0 Hz, 1H), 3.68 (s, 3H), 3.63 (s, 3H), 2.12 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₄H₁₇NO₅: 279.1107; found: 279.1084.

(Z)-3-Benzylamino-2-((S)-methoxycarbonylamino-phenyl-methyl)-but-2-enoic acid methyl ester (8a)

Yield: 105 mg, 95%. **ee:** 94%.

HPLC analysis, *t_r* major: 12.8 min, *t_r* minor: 16.2 min, Chiralcel[®]OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.90 (br, 1H), 7.36-7.15 (m, 10H), 5.95 (s, 2H), 4.48 (d, *J* = 6.0 Hz, 2H), 3.70 (s, 3H), 3.43 (s, 3H), 2.19 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 170.1, 161.6, 157.0, 143.3, 138.3, 128.8, 127.9, 127.4, 126.8, 126.1, 125.4, 94.3, 52.2, 52.0, 50.1, 47.4, 15.4.

IR (thin film, cm⁻¹): 3447, 3395, 2950, 1719, 1649, 1594, 1453, 1247, 1191, 1090.

HRMS: calc'd for (M)⁺ C₂₁H₂₄N₂O₄: 368.1736; found: 368.1725.

[α]_D²³ = - 52.4 ° (c = 1.0, CHCl₃).

(S)-2-[(R)-(4-Chloro-phenyl)-methoxycarbonylamino-methyl]-3-oxo-butyric acid methyl ester (8b')

Yield: 126 mg, 81%.

¹H NMR (400 MHz, CDCl₃, major diastereomer reported): δ 7.33-7.19 (m, 4H), 6.17 (d, *J* = 9.6 Hz, 1H), 5.38 (t, *J* = 6.6 Hz, 1H), 4.00 (d, *J* = 5.6 Hz, 1H), 3.66 (s, 3H), 3.61 (s, 3H), 2.13 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₄H₁₆ClNO₅: 313.0717; found: 313.0715.

(Z)-3-Benzylamino-2-[(S)-(4-chloro-phenyl)-methoxycarbonylamino-methyl]-but-2-enoic acid methyl ester (8b)

Yield: 100 mg, 83%. **ee:** 81%.

HPLC analysis, *t_r* major: 12.4 min, *t_r* minor: 16.4 min, Chiralcel[®] OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.88 (br, 1H), 7.33 (m, 3H), 7.26 (m, 3H), 7.20 (m, 2H), 7.14 (m, 2H), 5.88 (s, 2H), 4.48 (d, *J* = 7.0 Hz, 2H), 3.69 (s, 3H), 3.42 (s, 3H), 2.18 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 169.9, 161.8, 156.9, 142.0, 138.1, 131.8, 128.9, 128.0, 127.5, 126.9, 126.8, 93.9, 52.2, 51.9, 50.2, 47.5, 15.5.

IR (thin film, cm⁻¹): 3446, 3388, 2950, 1719, 1650, 1594, 1490, 1453, 1247, 1190, 1091, 1012.

HRMS: calc'd for (M)⁺ C₂₁H₂₃ClN₂O₄: 402.1346; found: 402.1344.

[α]_D²³ = - 87.1 ° (*c* = 0.66, CHCl₃).

(S)-2-[(R)-(4-Fluoro-phenyl)-methoxycarbonylamino-methyl]-3-oxo-butyric acid methyl ester (8c')

Yield: 129 mg, 87%.

¹H NMR (400 MHz, CDCl₃, major diastereomer reported): δ 7.24 (m, 2H), 6.95 (m, 2H), 6.12 (d, *J* = 9.1 Hz, 1H), 5.40 (t, *J* = 6.6 Hz, 1H), 3.65 (s, 3H), 3.61 (s, 3H), 2.13 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₄H₁₆FNO₅: 297.1013; found: 297.0998.

(Z)-3-Benzylamino-2-[(S)-(4-fluorophenyl)-methoxycarbonylamino-methyl]-but-2-enoic acid methyl ester (8c)

Yield: 95 mg, 82%. **ee:** 91%.

HPLC analysis, t_r major: 11.2 min, t_r minor: 14.5 min, Chiralcel[®] OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.89 (br, 1H), 7.32 (m, 2H), 7.26 (m, 3H), 7.18 (t, J = 6.0 Hz, 2H), 6.92 (t, J = 6.0 Hz, 2H), 5.91 (s, 2H), 4.47 (d, J = 6.0 Hz, 2H), 3.69 (s, 3H), 3.44 (s, 3H), 2.18 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 169.9, 161.6, 156.9, 138.9, 138.1, 128.8, 127.4, 127.0, 126.9, 126.7, 114.7, 114.4, 94.0, 52.0, 51.7, 50.1, 47.3, 15.4.

IR (thin film, cm⁻¹): 3448, 3390, 2950, 1719, 1650, 1593, 1495, 1454, 1248, 1220, 1190, 1089, 1027.

HRMS: calc'd for (M+H)⁺ C₂₁H₂₃FN₂O₄: 386.1642; found: 386.1654.

$[\alpha]_D^{23}$ = - 85.5 ° (c = 1.0, CHCl₃).

2-[(R)-(3-Fluoro-phenyl)-methoxycarbonylamino-methyl]-3-oxo-butyrac acid methyl ester (8d')

Yield: 148 mg, 99%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.18 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 10 Hz, 2H), 6.85 (m, 2H), 6.41 (d, J = 9.2 Hz, 1H), 6.32 (d, J = 8.8 Hz, 1H), 5.48 (m, 1H), 5.37 (t, J = 7.6 Hz, 1H), 3.99 (m, 2H), 3.567 (s, 3H), 3.560 (s, 3H), 3.554 (s, 3H), 3.534 (s, 3H), 2.20 (s, 3H), 2.09 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₄H₁₆FN₂O₅: 297.1013; found: 297.1012.

(Z)-3-Benzylamino-2-[(S)-(3-fluoro-phenyl)-methoxycarbonylamino-methyl]-but-2-enoic acid methyl ester (8d)

Yield: 95 mg, 82%. **ee:** 92%.

HPLC analysis, t_r major: 12.3 min, t_r minor: 16.1 min, Chiralcel[®]OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.89 (br, 1H), 7.34 (m, 2H), 7.27 (m, 3H), 7.19 (t, J = 6.0 Hz, 1H), 7.00 (d, J = 8 Hz, 1H), 6.94 (d, J = 10 Hz, 1H), 6.84 (t, J = 8.8 Hz, 1H), 5.91 (s, 2H), 4.50 (d, J = 6.0 Hz, 2H), 3.70 (s, 3H), 3.43 (s, 3H), 2.19 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 169.4, 161.3, 156.5, 146.1, 137.7, 128.9, 128.4, 127.0, 126.4, 120.6, 112.4, 93.6, 51.7, 49.7, 46.9, 14.9.

IR (thin film, cm⁻¹): 3446, 3390, 2951, 1720, 1650, 1591, 1499, 1453, 1253, 1193, 1090.

HRMS: calc'd for (M)⁺ C₂₁H₂₃FN₂O₄: 386.1642; found: 386.1649.

$[\alpha]_D^{23}$ = - 72.3 ° (c = 1.0, CHCl₃).

2-((R)-Methoxycarbonylamino-m-tolyl-methyl)-3-oxo-butyric acid methyl ester (8e')

Yield: 129 mg, 88%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.17 (m, 2H), 7.06 (m, 6H), 6.31 (br, 1H), 6.01 (br, 1H), 5.49 (m, 1H), 5.40 (t, J = 7.2 Hz, 1H), 4.02 (d, J = 6.4 Hz, 1H), 3.97 (br, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 3.63 (s, 3H), 3.63 (s, 3H), 2.317 (s, 3H), 2.310 (s, 3H), 2.296 (s, 3H), 2.12 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₅H₁₉NO₅: 293.1263; found: 293.1287.

(Z)-3-Benzylamino-2-((S)-methoxycarbonylamino-m-tolyl-methyl)-but-2-enoic acid methyl ester (8e)

Yield: 110 mg, 96%. **ee:** 90%.

HPLC analysis, t_r major: 14.5 min, t_r minor: 18.0 min, Chiralcel[®]OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.91 (br, 1H), 7.35 (m, 2H), 7.27 (m, 3H), 7.15 (t, J = 8.0 Hz, 1H), 7.05 (s, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8 Hz, 1H), 5.93 (dd, J = 14.4, 10 Hz, 2H), 4.49 (d, J = 5.6 Hz, 2H), 3.71(s, 3H), 3.45(s, 3H), 2.31(s, 3H), 2.19(s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 170.1, 161.6, 156.9, 143.1, 138.8, 137.4, 128.8, 127.8, 127.4, 126.9, 126.8, 126.2, 122.5, 94.3, 52.1, 50.1, 47.3, 21.5, 15.4.

IR (thin film, cm⁻¹): 3451, 3390, 2949, 1719, 1651, 1593, 1497, 1454, 1251, 1192, 1090, 1028.

HRMS: calc'd for (M)⁺ C₂₂H₂₆N₂O₄: 382.1893; found: 382.1899.

$[\alpha]_D^{23}$ = - 15.5 ° (c = 1.0, CHCl₃).

2-((R)-Furan-2-yl-methoxycarbonylamino-methyl)-3-oxo-butyric acid methyl ester (8f')

Yield: 111 mg, 83%.

¹H NMR (400 MHz, CDCl₃, major diastereomers reported): δ 7.30 (m, 1H), 6.28 (dd, J = 3.2, 1.6 Hz, 1H), 6.19 (d, J = 6.4 Hz, 1H), 6.09 (d, J = 9.2 Hz, 1H), 5.59 (dd, J = 9.6, 4.0 Hz, 1H), 4.11 (d, J = 4.0 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 2.29 (s, 3H).

(Z)-3-Benzylamino-2-((S)-furan-2-yl-methoxycarbonylamino-methyl)-but-2-enoic acid methyl ester (8f)

Yield: 90 mg, 84%. **ee:** 90%.

HPLC analysis, t_r major: 14.2 min, t_r minor: 18.8 min, Chiralcel[®] OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.89 (br, 1H), 7.32 (m, 2H), 7.25 (m, 4H), 6.23 (dd, J = 3.6, 2.0 Hz, 1H), 5.98 (d, J = 3.2 Hz, 1H), 5.92 (t, J = 10 Hz, 2H), 4.45 (d, J = 6 Hz, 2H), 3.67(s, 3H), 3.55(s, 3H), 2.18 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 169.7, 161.4, 156.2, 155.4, 140.6, 137.7, 128.4, 127.0, 126.4, 109.8, 104.2, 91.7, 51.6, 49.8, 47.7, 46.9, 14.8.

IR (thin film, cm⁻¹): 3447, 3390, 2950, 1720, 1650, 1595, 1498, 1454, 1260, 1192, 1090, 1008.

HRMS: calc'd for (M)⁺ C₁₉H₂₂N₂O₅: 358.1529; found: 358.1541.

$[\alpha]_D^{23}$ = - 28.6 ° (c = 1.0, CHCl₃).

2-((R)-Methoxycarbonylamino-thiophen-2-yl-methyl)-3-oxo-butyrac acid methyl ester (8g')

Yield: 122 mg, 86%.

¹H NMR (400 MHz, CDCl₃, both diastereomers reported): δ 7.23 (t, J = 4.8 Hz, 1H), 7.14 (m, 2H), 6.94 (t, J = 3.6 Hz, 1H), 6.88 (m, 2H), 6.28 (d, J = 8.0 Hz, 1H), 6.13 (d, J = 8.0 Hz, 1H), 5.74 (m, 1H), 5.67 (t, J = 8.0 Hz, 1H), 4.11 (m, 2H), 3.67(s, 3H), 3.65(s, 3H), 3.63(s, 3H), 3.61(s, 3H), 2.27(s, 3H), 2.19 (s, 3H).

HRMS: calc'd for (M)⁺ C₁₂H₁₅NO₅S: 285.0671; found: 285.0662.

(Z)-3-Benzylamino-2-((S)-methoxycarbonylamino-thiophen-2-yl-methyl)-but-2-enoic acid methyl ester (8g)

Yield: 99 mg, 88%. **ee:** 93%.

HPLC analysis, t_r major: 11.9 min, t_r minor: 15.1 min, Chiralcel[®]OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.89 (br, 1H), 7.31 (m, 2H), 7.22 (m, 3H), 7.06 (d, J = 4.8 Hz, 1H), 6.85 (t, J = 4.8 Hz, 1H), 6.73 (d, J = 3.2 Hz, 1H), 6.05 (m, 2H), 4.45 (d, J = 6.4 Hz, 2H), 3.66 (s, 3H), 3.51 (s, 3H), 2.15 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 170.1, 161.6, 156.6, 149.3, 138.2, 128.8, 127.5, 126.7, 123.5, 122.7, 94.5, 52.1, 50.3, 49.8, 47.3, 15.2.

IR (thin film, cm⁻¹): 3450, 3317, 2951, 1717, 1652, 1594, 1497, 1455, 1254, 1080.

HRMS: calc'd for (M+H)⁺ C₁₉H₂₂N₂O₃S: 375.1334 ; found: 375.1419.

$[\alpha]_D^{23}$ = - 26.0 ° (c = 1.0, CHCl₃).

(S)-2-((R)-Methoxycarbonylamino-naphthalen-2-yl-methyl)-3-oxo-butyric acid methyl ester (8h')

Yield: 156 mg, 95%.

¹H NMR (400 MHz, CDCl₃, major diastereomer reported): δ 7.78 (m, 4H), 7.37(m, 3H), 6.20 (br, 1H), 5.62 (br, 1H), 4.14 (br, 1H), 3.69 (s, 3H), 3.65 (s, 1H), 2.12 (s, 1H).

HRMS: calc'd for (M)⁺ C₁₈H₁₉NO₅: 329.1263; found: 329.1240.

(Z)-3-Benzylamino-2-((S)-methoxycarbonylamino-naphthalen-2-yl-methyl)-but-2-enoic acid methyl ester (8h)

Yield: 120 mg, 96%.ee: 94%.

HPLC analysis, t_r major: 22.0 min, t_r minor: 29.7 min, Chiralcel[®]OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 9.97 (br, 1H), 7.77 (m, 4H), 7.66 (s, 1H), 7.45-7.35 (m, 5H), 7.30 (m, 2H), 6.07 (dd, *J* = 20, 10 Hz, 2H), 4.53 (d, *J* = 6.0 Hz, 2H), 3.75(s, 3H), 3.41(s, 3H), 2.25 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 170.2, 161.8, 157.0, 140.8, 138.3, 133.2, 132.2, 128.9, 127.8, 127.6, 127.5, 127.4, 126.8, 125.8, 125.3, 124.5, 123.7, 94.2, 52.4, 52.1, 50.2, 47.4, 15.5.

IR (thin film, cm⁻¹): 3446, 3395, 2949, 1717, 1651, 1593, 1497, 1455, 1239, 1089.

HRMS: calc'd for (M)⁺ C₂₅H₂₆N₂O₄: 418.1893; found: 418.1891.

[α]_D²³ = - 77.9 ° (c = 0.68, CHCl₃).

Preparation of racemic (Z)-enamines (8a – 8h). An oven dried 17×110 mm round bottom reaction vessel was charged with Yb(OTf)₃ (7 mg, 0.025 mmol). The metal salt was flamed dried under high vacuum, purged with nitrogen and dissolved in CH₂Cl₂ (1.0 mL). Imine (**6**, 0.50 mmol) and methyl acetoacetate (**3b**, 0.50 mmol) were added in successively. The solution was stirred at room temperature for overnight. The benzyl amine (1.50 mmol) was added and the reaction was stirred at room temperature for an additional 15 hours. The reaction mixture was subjected directly to the flash chromatography over silica gel (elution with 15-20% ethyl acetate in hexanes) to give the product (**8a – 8h**).

2-((R)-Allyloxycarbonylamino-phenyl-methyl)-3-oxo-butyric acid methyl ester (9). In an oven dried 100 mL round bottom flask, (+)-cinchonine (294mg, 1.0 mmol) was dissolved in 40 mL CH₂Cl₂. The solution was cooled to -35 °C. Benzylidene-carbamic acid allyl ester (1.89g, 10 mmol) and the solution of methyl acetoacetate (1.08 mL, 10 mmol) in CH₂Cl₂ (10 mL) were added successively. The solution was stirred at -35 °C for 15 h. The reaction mixture was then passed through a plug of silica gel and eluted with ethyl acetate (150 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography over silica gel (elution with 15-30% ethyl acetate in hexanes) to give **5e** (2.95g, 97% yield).

An oven dried 100 mL round bottom flask was charged with Pd(PPh₃)₄ (115 mg, 0.10 mmol) and 1,3-dimethylbarbituric acid (780 mg, 5.0 mmol). A solution of 2-(allyloxycarbonylamino-phenyl-methyl)-3-oxo-butyric acid methyl ester (1.52 g, 5.0 mmol) in 20 mL CH₂Cl₂ and benzyl

isocyanate (680 μ L, 5.0 mmol) were added successfully. The solution was stirred at room temperature for 30 min. The reaction mixture was then passed through a plug of silica gel and eluted with ethyl acetate (100 mL). The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography over silica gel (elution with 30-70% ethyl acetate in hexanes) to give the urea intermediate (1.5g, 85% yield).

The 2-[(*R*)-(3-Benzyl-ureido)-phenyl-methyl]-3-oxo-butyric acid methyl ester (1.06g, 3.0 mmol) was dissolved in 2.5 mL ethanol and 7.5 mL acetic acid. The solution was subjected to microwave irradiation (300W) at 120 $^{\circ}$ C for 10 min. The solvent was removed under reduced pressure and residue was purified by flash chromatography over silica gel (elution with 30% ethyl acetate in hexanes) to give compound **9** (0.90 g, 90% yield).

5e

Yield: 2.95 g, 97%.

^1H NMR (400 MHz, CDCl_3 , both diastereomers reported): δ 7.35-7.24 (m, 10H), 6.42 (d, J = 9.2 Hz, 1H), 6.15 (d, J = 8.4 Hz, 1H), 5.87 (m, 2H), 5.71 (dd, J = 9.2, 3.6 Hz, 1H), 5.48 (dd, J = 8.8, 6.0 Hz, 1H), 5.28 (m, 2H), 5.20 (m, 2H), 4.55 (s, 2H), 4.54 (s, 2H), 4.06 (d, J = 5.6 Hz, 1H), 4.02 (d, J = 3.6 Hz, 2H), 3.67 (s, 3H), 3.62 (s, 3H), 2.12 (s, 3H), 2.02 (s, 3H).

2-[(*R*)-(3-Benzyl-ureido)-phenyl-methyl]-3-oxo-butyric acid methyl ester.

Yield: 1.5 g, 85%.

^1H NMR (400 MHz, CDCl_3 , both diastereomers reported): δ 7.28 (m, 20H), 6.17 (d, J = 10 Hz, 1H), 5.82 (d, J = 9.2 Hz, 1H), 5.78 (dd, J = 9.2, 4.4 Hz, 1H), 5.61 (dd, J = 9.2, 8.4 Hz, 1H), 4.84 (m, 2H), 4.35 (m, 4H), 4.06 (m, 2H), 3.66 (s, 3H), 3.58 (s, 3H), 2.37 (s, 3H), 2.13 (s, 3H).

HRMS: calc'd for $(\text{M}+\text{H})^+$ $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_4$: 355.1613 ; found: 355.1690.

(S)-1-Benzyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid methyl ester (9).

Yield: 0.9 g, 90%. **ee:** 90%.

HPLC analysis, t_r major: 27.8 min, t_r minor: 36.6 min, Chiralcel[®] OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min.

¹H NMR (400 MHz, CDCl₃): δ 7.29-7.22 (m, 8H), 7.10 (d, J = 7.2 Hz, 2H), 5.64 (s, 1H), 5.42 (d, J = 3.2 Hz, 1H), 5.17 (d, J = 14.8 Hz, 1H), 4.87 (d, J = 14.8 Hz, 1H), 3.61 (s, 3H), 2.43 (s, 3H).

¹³C NMR (75.0 MHz, CDCl₃): δ 166.5, 153.8, 149.3, 142.9, 137.8, 128.7, 128.6, 127.9, 127.2, 126.4, 126.3, 99.9, 53.9, 51.4, 46.0, 16.5.

IR (thin film, cm⁻¹): 3234, 2948, 1685, 1623, 1456, 1387, 1257, 1203, 1164, 1106, 696.

HRMS: calc'd for (M+H)⁺ C₂₀H₂₀N₂O₃: 336.1; found: 336.1.

$[\alpha]_D^{23}$ = - 29.8 ° (c = 1.0, CHCl₃).

The (±)-1-Benzyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid methyl ester was made according to a published procedure.⁶

The synthesis of the following lactam was performed to compare the enantiomer and diastereomer 9 to a known compound.⁷

(2S, 3R)-2-((R)-Amino-phenyl-methyl)-3-hydroxy-butyric acid methyl ester (10) An oven dried 50 mL round bottom flask was charged with 4 Å molecular sieve (200 mg) and flame dried under high vacuum, purged with nitrogen. (2S, 3R)-3-Hydroxy-2-((R)-methoxycarbonylamino-phenyl-methyl)-butyric acid methyl ester (200 mg, 0.71 mmol), dry acetonitrile (10 mL), and indotrimethylsilane (0.22 mL, 1.56 mmol, 2.2 equiv.) were added successively. The solution were stirred at room temperature for 45 min and concentrated under reduced pressure. The residue was dissolved in anhydrous methanol (10 mL). The solution was stirred at room temperature for 25 min. The solvent was removed under reduced pressure and the residue was

treated with CHCl_3 (1 mL). The white precipitate was filtered and washed with hexane to give the desired product **10** (184 mg, 90% yield).

^1H NMR (400 MHz, d_6 -DMSO): δ 7.39 (m, 5H), 7.25 (d, J = 2.1 Hz, 2H), 4.54 (d, J = 9.6 Hz, 1H), 4.00 (dd, J = 6.3, 9.0 Hz, 1H), 3.48 (s, 1H), 3.30 (s, 3H), 2.92 (t, J = 9.0 Hz, 1H), 1.12 (d, J = 6.3 Hz, 3H).

^{13}C NMR (75.0 MHz, d_6 -DMSO): δ 172.0, 129.6, 129.2, 128.4, 67.7, 56.3, 56.2, 52.3, 22.5.

IR (thin film, cm^{-1}): 3429, 3043, 2952, 1733, 1608, 1457, 1255, 1112, 848, 763, 700.

LRMS: calc'd for $(\text{M})^+$ $\text{C}_{12}\text{H}_{17}\text{NO}_3$: 223.1; found: 223.9.

$[\alpha]_D^{23} = +36^\circ$ (c = 1.5, CHCl_3).

(3*S*, 4*R*)-3-[(*R*)-1-(tert-Butyl-dimethyl-silanyloxy)-ethyl]-4-phenyl-azetidin-2-one (Lactam formation). To a solution of β -amino alcohol **9** (100 mg, 0.44 mmol) in DMF 3 mL, imidazole (60 mg, 0.88 mmol) and tert-butyldimethylsilyl chloride (75 mg, 0.44 mmol) were added. The solution was stirred at room temperature for 20 h. The mixture was diluted with diethyl ether (10 mL) and successively washed with 5% aqueous HCl (5 mL) and distilled water (5 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give the crude (2*S*, 3*R*)-2-((*R*)-Amino-phenyl-methyl)-3-(tert-butyl-dimethyl-silanyloxy)-butyric acid methyl ester. This material was used in next step without further purification. The ^1H -NMR spectra data was in agreement with literature value.⁷ **^1H NMR** (400 MHz, CDCl_3): δ 7.20 – 7.34 (m, 5H), 4.3 (m, 1H), 4.18 (d, J = 9.6 Hz, 1H), 3.30 (s, 3H), 2.85 (dd, J = 6.8, 9.6 Hz, 1H), 1.31 (d, J = 6.3 Hz, 3H), 0.91 (s, 3H), 0.14 (s, 3H), 0.11 (s, 3H).

In a round bottom flask, diisopropylamine (67.1 mg, 0.66 mmol) was dissolved in 3 mL THF. *n*-BuLi (0.388 mL, 1.6 M, 0.62 mmol) was added at 0°C . The mixture was stirred for 10 minutes and cooled to -78°C . TBS ether (70 mg, 0.20 mmol) in 1 mL THF was added. The reaction mixture was stirred at -78°C for 10 h and was quenched by the addition of saturated aqueous sodium bicarbonate solution (0.5 mL). The mixture was filtered and the filtrate was concentrated under reduced pressure and residue was purified on silica gel to give the desired lactam (56 mg, 75% yield for two steps). The analytical data was in agreement with the literature value.⁷

^1H NMR (400 MHz, CDCl_3): δ 7.19-7.36 (m, 5H), 4.25 (m, 1H), 3.85 (d, J = 10.5 Hz, 1H), 2.69 (dd, J = 9.4, 10.5 Hz, 1H), 1.17 (d, J = 6.3 Hz, 3H), 0.97 (s, 9H), 0.35 (s, 6H).

^{13}C NMR (75.0 MHz, CDCl_3): δ 171.9, 151.6, 128.8, 128.2, 127.3, 71.0, 68.2, 59.0, 25.5, 22.1, 19.3, -1.4.

LRMS: calc'd for $(\text{M})^+$ $\text{C}_{17}\text{H}_{27}\text{NO}_2\text{Si}$: 305.2; found: 305.1.

$[\alpha]_D^{23} = +85^\circ$ (c = 1.0, CHCl_3).

The spectral data of the synthetic material was identical to the reported compound.⁷

References and Notes

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Table 2, entry 1: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.556	MM	0.6829	4404.67969	107.49847	51.1525
2	22.121	MM	0.9436	4206.20264	74.28988	48.8475
Totals :				8610.88232	181.78835

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.625	MM	0.5482	444.59094	13.51624	4.0792
2	21.343	MM	0.9499	1.04543e4	183.43141	95.9208
Totals :				1.08989e4	196.94765	

Table 2, entry 2: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.130	MM	0.8806	2031.91418	38.45496	51.1212
2	25.569	MM	1.2791	1942.78455	25.31450	48.8788
Totals :				3974.69873	63.76947

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.035	MM	0.5839	392.62192	11.20608	8.4508
2	23.239	MM	1.0631	4253.35791	66.68427	91.5492
Totals :				4645.97983	77.89034	

Table 2, entry 3: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.948	MM	0.8287	4394.27637	88.37822	51.5085
2	20.427	MM	1.0463	4136.88330	65.89849	48.4915
Totals :				8531.15967	154.27671

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.399	MM	0.5918	229.68318	6.46809	3.5636
2	20.840	MM	0.9812	6215.50537	105.57628	96.4364
Totals :				6445.18855	112.04437	

Table 2, entry 4: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.932	MM	0.7002	9043.82910	215.25920	50.2325
2	18.240	MM	0.9023	8960.12793	165.49834	49.7675
Totals :				1.80040e4	380.75754

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.886	MM	0.5063	764.06006	25.15283	4.4035
2	17.707	MM	0.8336	1.65871e4	331.64175	95.5965
Totals :				1.73511e4	356.79458	

Table 2, entry 5: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.583	MM	0.6801	1.69600e4	415.62628	51.5750
2	21.643	MM	1.0203	1.59241e4	260.12759	48.4250
Totals :				3.28841e4	675.75388

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.997	MM	0.4488	134.63843	5.00036	1.5053
2	22.452	MM	0.9465	8809.60156	155.12576	98.4947
Totals :				8944.23999	160.12613	

Table 2, entry 6: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.765	MM	0.4712	4932.40527	174.45830	49.8464
2	13.446	MM	0.6067	4962.80615	136.32362	50.1536
Totals :				9895.21143	310.78192

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.212	MM	0.2979	342.13422	19.14143	4.7909
2	12.632	MM	0.5015	6799.26953	225.96758	95.2091
Totals :				7141.40375	245.10901	

Table 2, entry 7: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.551	MM	1.2713	4109.57178	53.87682	50.2065
2	44.563	MM	1.9160	4075.76465	35.45387	49.7935
Totals :				8185.33643	89.33068

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.136	MM	1.1838	553.88745	7.79830	9.2198
2	44.300	MM	2.0258	5453.68945	44.86845	90.7802
Totals :				6007.57690	52.66675	

Table 2, entry 8: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 90 : 10, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.753	MF	1.1169	6209.71680	92.66091	48.3405
2	32.336	FM	1.2613	6636.07568	87.68997	51.6595
Totals :				1.28458e4	180.35088

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.017	MF	0.6992	564.23328	13.45017	3.5455
2	30.502	FM	1.2320	1.53497e4	207.65182	96.4545
Totals :				1.59139e4	221.10200	

Table 2, entry 9: (R, R)-WheIk-O 1 Column, Hexanes : IPA, 90 : 10, 1.0 mL/min, 230 nm

(±)- 7i

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.204	MM	1.3592	5772.26318	70.78181	49.2490
2	37.640	MM	1.5344	5948.30908	64.60970	50.7510
Totals :				1.17206e4	135.39150

7i

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.900	MM	1.1000	802.53784	12.15927	4.2313
2	36.976	MM	1.5390	1.81643e4	196.71086	95.7687
Totals :				1.89668e4	208.87013	

Table 2, entry 10: Chiralcel[®]OD Column, Hexanes : IPA = 90 : 10, 1.5 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.541	MM	0.8992	3.33675e4	618.49164	50.2328
2	21.070	MM	1.0305	3.30582e4	534.66614	49.7672
Totals :				6.64257e4	1153.15778

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.345	MM	0.9062	7018.48145	129.08740	97.3067
2	21.100	MM	0.6985	194.25874	4.63530	2.6933
Totals :				7212.74019	133.72270	

Table 3, entry 1: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

(±)- 8a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.192	MM	0.6166	2.04968e4	554.00671	49.9467
2	16.407	MM	0.6661	2.05405e4	513.93530	50.0533
Totals :				4.10374e4	1067.94202

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

8a

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.798	MM	0.6366	2.32012e4	607.39606	97.0301
2	16.171	MM	0.5767	710.14117	20.52411	2.9699
Totals :				2.39113e4	627.92016	

Table 3, entry 2: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

(±)- 8b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.979	MM	0.6062	5.35072e4	1470.99768	48.7296
2	16.402	MM	0.7639	5.62972e4	1228.27808	51.2704
Totals :				1.09804e5	2699.27576

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

8b

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.371	MM	0.5725	2.46353e4	717.19672	90.3750
2	16.456	MM	0.5877	2623.67334	74.40260	9.6250
Totals :				2.72590e4	791.59932	

Table 3, entry 3: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.894	MM	0.5541	2908.90137	87.49238	48.5660
2	16.490	MM	0.6530	3080.68359	78.63310	51.4340
Totals :				5989.58496	166.12548

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.226	MM	0.4830	2.96862e4	1024.28711	95.4101
2	14.532	MM	0.4653	1428.11658	51.14992	4.5899
Totals :				3.11143e4	1075.43703

Table 3, entry 4: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

COC(=O)N[C@@H](C(=O)Nc1ccccc1)C(=O)c2cc(F)ccc2

(±)- 8d

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.298	MM	0.5714	1.33096e4	388.22281	50.3694
2	16.176	MM	0.6425	1.31144e4	340.17441	49.6306
Totals :				2.64240e4	728.39722

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

COC(=O)N[C@H](C(=O)Nc1ccccc1)[C@H](C(=O)c2cc(F)ccc2)C

8d

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.336	MM	0.6415	3.09609e4	804.33331	95.9288
2	16.111	MM	0.7014	1313.99219	31.22369	4.0712
Totals :				3.22749e4	835.55700	

Table 3, entry 5: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

(±)- 8e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.307	MM	0.7435	1.72483e4	386.67041	49.5863
2	17.397	MM	0.8241	1.75361e4	354.64133	50.4137
Totals :				3.47844e4	741.31174

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

8e

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.525	MM	0.8142	1.72689e4	353.51062	95.2443
2	18.017	MM	0.6867	862.26129	20.92840	4.7557
Totals :				1.81312e4	374.43902	

Table 3, entry 6: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

(±)- 8f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.526	MM	0.6399	1.29630e4	337.64926	49.7385
2	18.745	MM	0.7573	1.30993e4	288.29373	50.2615
Totals :				2.60623e4	625.94299

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

8f

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.174	MM	0.6631	5.03164e4	1264.64771	95.1790
2	18.803	MM	0.6214	2548.61792	68.35530	4.8210
Totals :				5.28650e4	1333.00301	

Table 3, entry 7: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

(±)- 8g

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.962	MM	0.5925	1.16607e4	327.99448	50.0900
2	14.986	MM	0.6084	1.16188e4	318.26312	49.9100
Totals :				2.32794e4	646.25760

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

8g

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.941	MM	0.5874	1.65062e4	468.30508	96.5220
2	15.140	MM	0.6241	594.76373	15.88237	3.4780
Totals :				1.71009e4	484.18745	

Table 3, entry 8: Chiralcel®OD Column, Hexanes : IPA = 95 : 5, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.349	MM	1.1527	2.14123e4	309.59421	49.8221
2	27.615	MM	1.2343	2.15653e4	291.20346	50.1779
Totals :				4.29776e4	600.79767

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.993	MM	1.3539	6.90514e4	850.04169	96.7175
2	29.739	MM	1.1464	2343.54883	34.07155	3.2825
Totals :				7.13949e4	884.11324	

Determination of absolute stereochemistry: (*R, R*)-Whelk-O 1 Column, Hexanes : IPA, 85 : 15, 1.5 mL/min, 210 nm

enantiomeric pure form

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.466	PB	0.9401	5.23272e4	807.40204	100.0000
Totals :				5.23272e4	807.40204

86% ee

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.144	MM	0.5146	721.48029	23.36738	7.0531
2	20.617	MM	0.8559	9507.75488	185.14413	92.9469

Compound **9**, Chiralcel[®] OD Column, Hexanes : IPA = 90 : 10, 1.0 mL/min, 210 nm

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.140	MM	1.2311	8422.36621	114.02174	49.5711
2	35.747	MM	1.6668	8568.12500	85.67381	50.4289
Totals :				1.69905e4	199.69554	

(±)-**9**

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.804	MM	1.3213	3.76392e4	474.79144	95.3736
2	36.641	MM	1.4674	1825.80640	20.73677	4.6264
Totals :				3.94650e4	495.52821	

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