Supporting Information

Nickel-Catalyzed Enantioselective Umpolung Hydrogenation for the Synthesis of β-Amido Esters

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Experimental procedures

Table of Contents

I. General

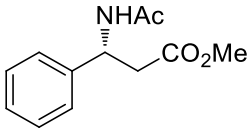
All NMR spectra were acquired on Bruker AV 500 MHz, BBFO 400 MHz NMR spectrometers. ^{1}H NMR (500 MHz) chemical shifts were recorded relative to $SiMe_4$ (δ 0.00) or residual protiated solvents ($CDCl_3$: δ 7.26). Multiplicities were given as: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The number of protons (n) for a given resonance was indicated by nH. Coupling constants were reported as a *J* value in Hz. ^{13}C NMR (125 MHz) chemical shifts were recorded relative to solvent resonance ($CDCl_3$: δ 77.16).

Glassware was dried at 120 ^{o}C for at least 3 h before use. Dry THF was freshly distilled from sodium/benzophenone under argon before use and stored in an argon filled glove box. Anhydrous 1,4-dioxane (Aldrich) was stored over activated 4 Å molecular sieve beads in an argon-filled glove box. Dry toluene was collected from a solvent purification system containing a column of activated alumina (1 m x 2) under argon. Methanol, ethanol and isopropanol were degassed and stored over dried molecular sieve in an argon-filled glove box before use. All anhydrous solvents were stored in Schlenk tubes in the glove box.

Unless noted otherwise, commercially available chemicals were used as received without purification. The GC internal standard, *n*-$C_{12}H_{26}$ and *n*-$C_{14}H_{30}$ was degassed with argon and dried over activated 4Å molecular sieve beads before use. Flash chromatography was performed using Merck 40-63D 60Å silica gel. Gas chromatography (GC) analysis was performed on a Shimadzu GC-2010 instrument with Agilent J & W GC column DB-5MS-UI. GC/MS analysis was conducted on a Thermo Scientific DSQ II single quadrupole GC/MS instrument with Agilent J & W GC column DB-5MS-UI. ESI/MS analysis was conducted on a Thermo Finnigan LCQ Fleet MS spectrometer. High resolution mass spectral analysis (HRMS) was performed on Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiracel columns at 25°C and a mixture of HPLC-grade hexanes and isopropanol as eluent. Optical rotation was measured using a JASCO P-1030 Polarimeter equipped with a sodium vapor lamp at 589 nm and the concentration of samples was denoted as *c*.

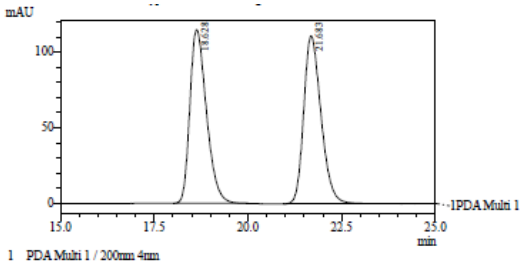
II. Nickel-catalyzed asymmetric Umpolung hydrogenation of (*Z*)-*β*-amidoacrylates

A general procedure: In an argon-filled glove box, $Ni(OAc)_2$ (1.1 mg, 0.006 mmol), (*S*)-binapine (4.4 mg, 0.006 mmol), tetra-*n*-butylammonium iodide (14.8 mg, 0.04 mmol), indium powder (25.2 mg, 0.22 mmol, Alfa Aesar, 100 mesh, 99.9% purity) and dry methanol (0.6 mL) were charged into a 10-mL Schlenk tube. After stirring for 15 min, (*Z*)-*β*-acylamidoacrylate (0.2 mmol) and acetic acid (35 μL, 0.6 mmol, 3 equiv) were added. The reaction mixture was heated with stirring in an oil bath maintained at 60 ^{o}C, until almost full conversion as monitored by GC. After the reaction mixture was cooled to room temperature, solid $NaHCO_3$ was added to basify the mixture. After addition of silica gel and evaporation of the solvent on a rotary evaporator, the residue was dry loaded on a silica gel column and then purified by flash chromatography using ethyl acetate and hexanes as eluent. The enantioselectivity of the purified product was determined by chiral HPLC analysis with Daicel Chiralcel columns. The use of Schlenk tubes and a vacuum manifold gave similar results as the procedure using a glove box. All the products herein with CAS numbers have been isolated and fully characterized previously.[1]



(*R*)-Methyl 3-acetamido-3-phenyl-propanoate 2a [67654-57-3].

The reaction was complete in 36 h at 60 ^{o}C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 43 mg, 97% yield. Ee: 91%. $[\alpha]^{23}_{D}$ = +25.6˚ (*c* = 0.52, $CDCl_3$). Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



PeakTable

PDA Ch1 200nm 4nm

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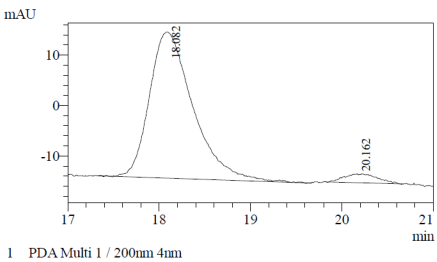

PeakTable

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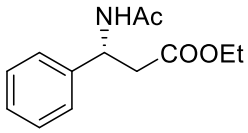
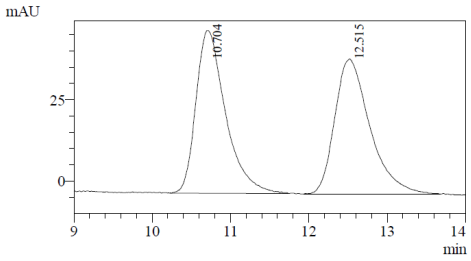
1	18.082	957107	95.484
2	20.162	45272	4.516
Total		1002379	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.13 (m, 5H), 6.68 (d, *J* = 7.5 Hz, NH), 5.50-5.39 (m, 1H), 3.63 (s, 3H), 2.95 (dd, *J* = 15.7, 6.0 Hz, 1H), 2.85 (dd, *J* = 15.7, 6.0 Hz, 1H), 2.03 (s, 3H). GC-MS (EI) m/z: Calcd for $C_{12}H_{15}NO_3$ M^+: 221.1. Found: 221.0.



(*R*)-Ethyl 3-acetamido-3-phenyl-propanoate 2b [609849-87-8].

The reaction was complete in 36 h at 60 °C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 46 mg, 97% yield. Ee: 96%. $[\alpha]^{23}_{D}$ = +37.4° (*c* = 0.3, $CDCl_3$). Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



1 PDA Multi 1 / 200nm 4nm

PeakTable

PDA Ch1 200nm 4nm

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2	12.515	1294335	49.585
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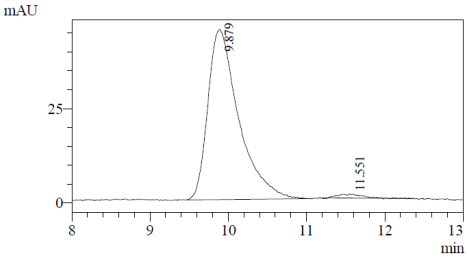


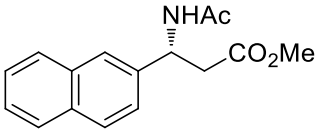
1 PDA Multi 1 / 200nm 4nm

PeakTable

PDA Ch1 200nm 4nm

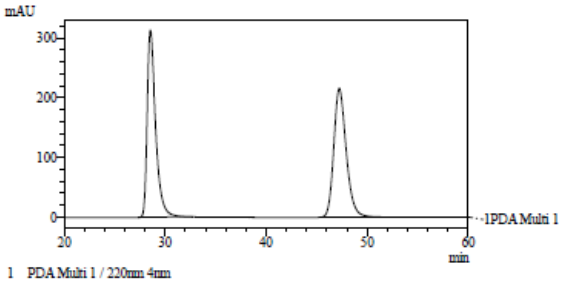
Peak#	Ret. Time	Area	Area %
1	9.879	1238150	98.041
2	11.551	24738	1.959
Total		1262888	100.000

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.18 (m, 5H), 6.66 (d, *J* = 7.6 Hz, NH), 5.57-5.36 (m, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 2.91 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.81 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.01 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). GC-MS (EI) m/z: Calcd for $C_{13}H_{17}NO_3$ M^+: 235.1 Found: 235.1.



(*R*)-Methyl 3-acetamido-3-(2-naphthyl)propanoate 2c [1642872-44-3].

The reaction completed in 36 h at 60 °C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 52 mg, 96% yield. Ee: 92%. $[\alpha]^{2}_{D}$ = +64.4 ° (*c* = 0.48, $CDCl_3$).
Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

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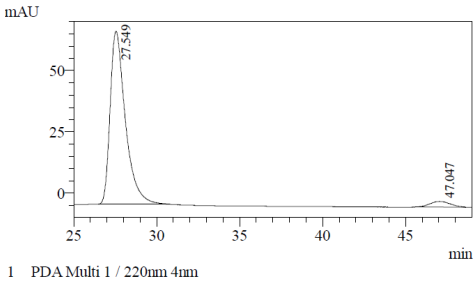
1	28.527	18264693	49.817
2	47.243	18398972	50.183
Total		36663664	100.000



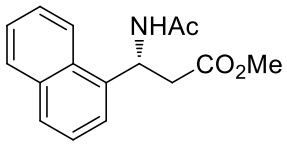
1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

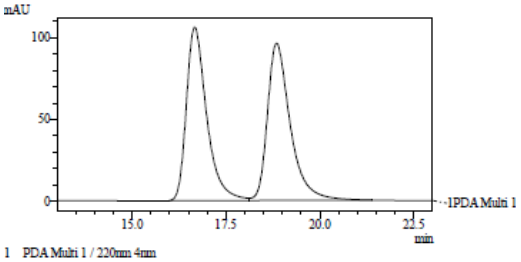
Peak#	Ret. Time	Area	Area %
1	27.549	4506221	95.901
2	47.047	192604	4.099
Total		4698824	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.76 (m, 3H), 7.73 (s, 1H), 7.57-7.44 (m, 2H), 7.43-7.31 (m, 1H), 6.82-6.54 (br s, NH), 5.67-5.46 (m, 1H), 3.60 (s, 3H), 3.03 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.93 (dd, *J* = 15.8, 6.0 Hz, 1H), 2.02 (s, 3H). GC-MS (EI) m/z: Calcd for $C_{16}H_{17}NO_3$ M^+: 271.1. Found: 271.0.



(*R*)-Methyl 3-acetamido-3-(1-naphthyl)propanoate 2d [1642855-01-3].

The reaction was finished in 24 h at 60 °C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 50 mg, 92% yield. Ee: 84%. $[\alpha]^{23}_{D}$ = +27.4 ° (*c* = 0.32, $CDCl_3$). Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

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1	16.661	4004906	49.593
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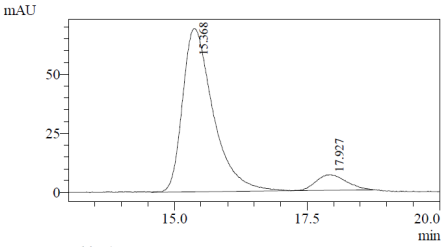
Total		8075474	100.000



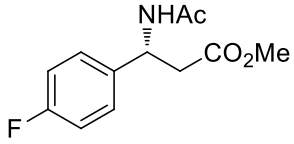
1 PDA Multi 1 / 200nm 4nm

PeakTable

PDA Ch1 200nm 4nm

Peak#	Ret. Time	Area	Area %
1	15.368	2773474	91.232
2	17.927	266545	8.768
Total		3040020	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.90-7.83 (m, 1H), 7.83-7.76 (m, 1H), 7.63-7.46 (m, 2H), 7.46-7.36 (m, 2H), 6.50 (d, *J* = 8.0 Hz, NH), 6.31-6.15 (m, 1H), 3.59 (s, 3H), 3.10-2.96 (m, 2H), 1.98 (s, 3H). GC-MS (EI) m/z: Calcd for $C_{16}H_{17}NO_3$ M^+: 271.1. Found: 271.0.

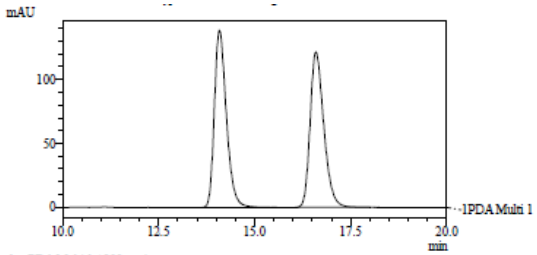


(*R*)-Methyl 3-acetamido-3-(4-fluorophenyl)propanoate 2e [844439-54-9].

The reaction completed in 36 h at 60 °C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 46 mg, 96% yield.

$[\alpha]^{23}_{D}$ = +22.3 ° (*c* = 0.52, $CDCl_3$).

Ee: 94%. Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



1 PDA Multi 1 / 200nm 4nm

PeakTable

PDA Ch1 200nm 4nm

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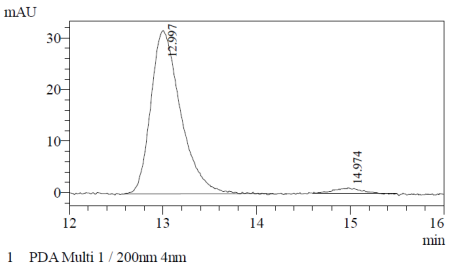
2	16.592	3015794	49.965
Total		6035805	100.000



1 PDA Multi 1 / 200nm 4nm

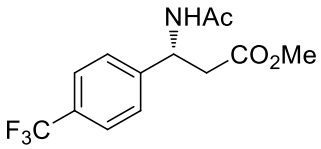
PeakTable

PDA Ch1 200nm 4nm

Peak#	Ret. Time	Area	Area %
1	12.997	696938	96.917
2	14.974	22173	3.083
Total		719111	100.000

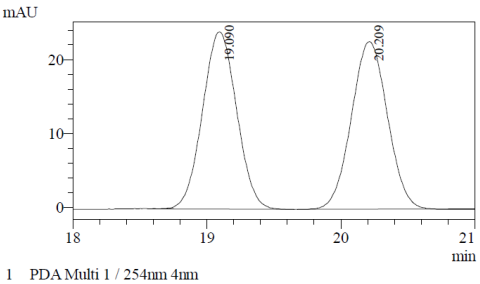
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.18 (m, 2H), 7.06-6.94 (m, 2H), 6.66 (d, *J* = 7.7 Hz, NH), 5.51-5.29 (m, 1H), 3.61 (s, 3H), 2.90 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.81 (dd, *J* = 15.8, 5.9 Hz, 1H), 2.01 (s, 3H).

GC-MS (EI) m/z: Calcd for $C_{12}H_{14}FNO_3$ $(M)^+$: 239.1. Found: 239.0.



(*R*)-Methyl 3-acetamido-3-[4-(trifluoromethyl)phenyl]propanoate 2f [1642855-02-4].

The reaction was complete in 36 h at 60 °C. The product was isolated by flash chromatography (EA/hexane 1:1 to 2:1) as white solid. 55 mg, 95% yield. Ee: 89%. $[\alpha]^{23}_D$ = +11.3 ° (*c* = 0.32, $CDCl_3$). Daicel Chiralcel OD-H, n-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

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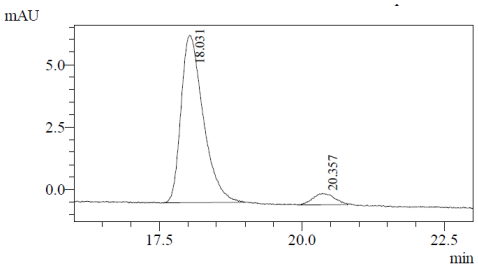
Total		848846	100.000



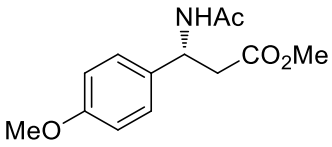
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

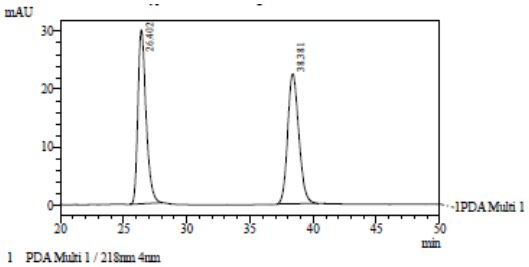
Peak#	Ret. Time	Area	Area %
1	18.031	181668	94.020
2	20.357	11555	5.980
Total		193223	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, NH), 5.60-5.38 (m, 1H), 3.63 (s, 3H), 2.94 (dd, *J* = 16.1, 5.9 Hz, 1H), 2.87 (dd, *J* = 16.0, 5.8 Hz, 1H), 2.06 (s, 3H). GC-MS (EI) m/z: Calcd for $C_{13}H_{14}F_3NO_3$ M^+: 289.1. Found: 289.0.



(*R*)-Methyl 3-acetamido-3-(4-methoxyphenyl)propanoate 2g [810670-02-1].

The reaction completed in 24 h at 60 °C. The product was isolated by flash chromatography (EA/hexanes 1:1 to 2:1) as white solid. 48 mg, 96% yield. Ee: 92%. $[\alpha]^{23}_D$ = +65.6 ° (*c* = 0.43, $CDCl_3$). Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



PeakTable

PDA Ch1 218nm 4nm

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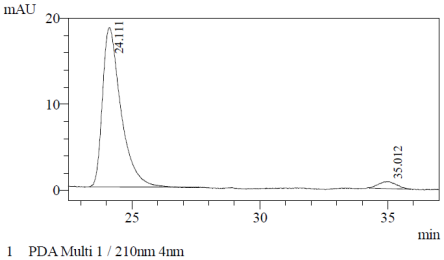
2	38.381	1369508	50.343
Total		2720348	100.000

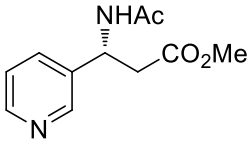


PeakTable

PDA Ch1 210nm 4nm

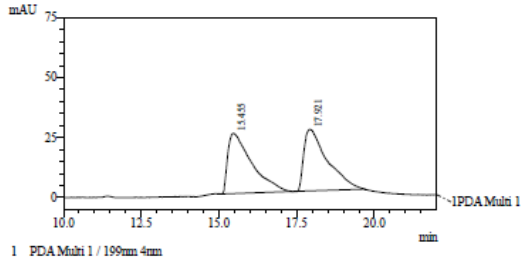
Peak#	Ret. Time	Area	Area %
1	24.111	929651	96.068
2	35.012	38048	3.932
Total		967698	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 6.60 (br s, NH), 5.47-5.23 (m, 1H), 3.76 (s, 3H), 3.60 (s, 3H), 2.90 (dd, J = 15.6, 6.0 Hz, 1H), 2.78 (dd, J = 15.7, 6.3 Hz, 1H), 1.97 (d, J = 0.8 Hz, 3H). GC-MS (EI) m/z: Calcd for $C_{13}H_{17}NO_4$ M^+: 251.1. Found: 251.0.



(*R*)-Methyl 3-acetamido-3-(3-pyridyl)propanoate 2h [1642855-03-5].

The reaction was complete in 36 h at 60 °C. The product was isolated by flash chromatography (MeOH/DCM 1:10) as yellow solid. 41 mg, 92% yield. Ee: 98%. $[\alpha]^{23}_D$ = +43.2° (c = 0.6, $CDCl_3$). Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



PeakTable

PDA Ch1 199nm 4nm

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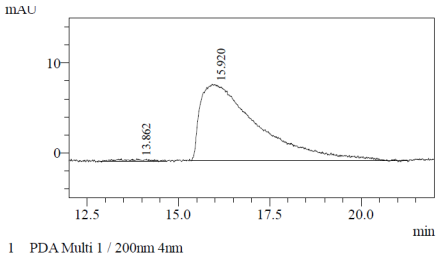
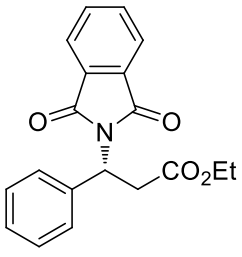


PeakTable

PDA Ch1 200nm 4nm

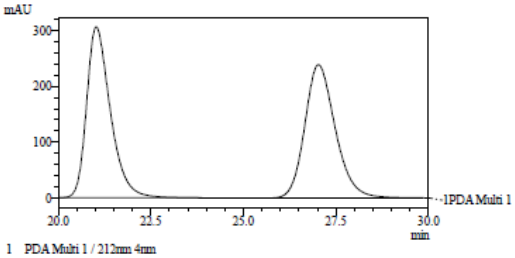
Peak#	Ret. Time	Area	Area %
1	13.862	8922	0.942
2	15.920	938391	99.058
Total		947312	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.49 (d, J = 4.0 Hz, 1H), 7.67-7.58 (m, 1H), 7.26-7.20 (m, 1H), 6.95 (d, J = 8.1 Hz, NH), 5.62-5.23 (m, 1H), 3.62 (s, 3H), 2.94 (dd, J = 16.1, 5.8 Hz, 1H), 2.96 (dd, J = 16.1, 5.8 Hz, 1H), 2.02 (s, 3H). GC-MS (EI) m/z: Calcd for $C_{11}H_{14}N_2O_3$ M^+: 222.1. Found: 222.0.



(*R*)-Ethyl 3-phthalimido-3-phenylpropanoate 2i [1204518-31-9].

The product was isolated by flash chromatography (EA/hexane 1:3) as white solid. 62 mg, 96% yield. Ee: 88%. $[\alpha]^{23}_{D}$ = +10.3 ° (*c* = 0.42, $CHCl_3$). Daicel Chiralcel OJ-H, n-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.

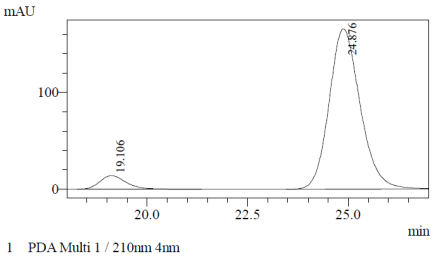


1 PDA Multi 1 / 212nm 4nm

PeakTable

PDA Ch1 212nm 4nm

Peak#	Ret. Time	Area	Area %
1	21.021	13661903	50.053
2	27.023	13632928	49.947
Total		27294831	100.000



1 PDA Multi 1 / 210nm 4nm

PeakTable

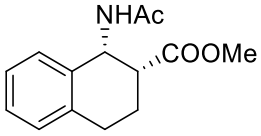
PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	19.106	647414	6.755
2	24.876	8936670	93.245
Total		9584083	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.76 (m, 2H), 7.72-7.64 (m, 2H), 7.56-7.44 (m, 2H), 7.38-7.24 (m, 3H), 5.84 (dd, *J* = 10.2, 5.7 Hz, 1H), 4.22-4.39 (m, 2H), 3.79 (dd, *J* = 16.4, 10.3 Hz, 1H), 3.24 (dd, *J* = 16.4, 5.7 Hz, 1H), 1.14 (t, *J* = 7.1 Hz, 3H). GC-MS (EI) m/z: Calcd for $C_{19}H_{17}NO_4$ M^+: 323.1. Found: 323.1.

III. Nickel-catalyzed asymmetric umpolung hydrogenation of cyclic *β*-amidoacrylates

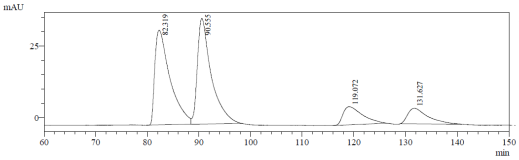
A general procedure: In an argon-filled glove box, $Ni(OAc)_2$ (1.8 mg, 0.01 mmol), (*R*)-QuinoxP* (4.0 mg, 0.012 mmol), indium powder (34.4 mg, 0.3 mmol, Alfa Aesar, 100 mesh, 99.9% purity) and dry methanol (0.8 mL) were charged into a 10-mL Schlenk tube. After stirring for 15 min, cyclic *β*-amidoacrylate (0.2 mmol) and acetic acid (35 μL, 0.6 mmol, 3 equiv) were added. The reaction mixture was heated with stirring in an oil bath maintained at 80 °C for 60 h. After the reaction mixture was cooled to room temperature, solid $NaHCO_3$ was added to basify the mixture. After addition of silica gel and evaporation of the solvent on a rotary evaporator, the residue was dry loaded on a silica gel column and purified by flash chromatography using ethyl acetate and hexanes as eluent. The ratio of diastereomers was determined by GC and confirmed by GCMS and they were separable on silica gel. The enantioselectivity of the main isomer was determined by chiral HPLC analysis with Daicel Chiralcel columns. All the products (main isomers) herein with CAS numbers have been isolated and fully characterized previously.



(1*R*,2*R*)-Methyl 1-acetamidotetralin-2-carboxylate 4a [126662-34-8].

The reaction was completed after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 44 mg, 89% yield. 96/4 dr. Ee: 95%. $[\alpha]^{20}_{D}$ = +52.7°(*c* = 1.3, $CHCl_3$).

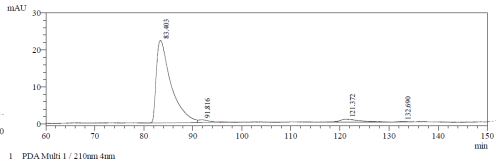
Daicel Chiralcel AD-H, *n*-hexane/isopropanol 98/2, flow rate = 0.5 mL/min. Fractions of racemic samples were used containing high percentages of the trans-isomers (with greater retention times).



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	82.319	6768268	40.125
2	90.555	6959510	41.259
3	119.072	1650014	9.782
4	131.627	1490205	8.835
Total		16867997	100.000

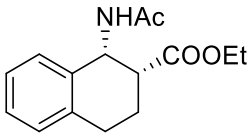


PeakTable

PDA Ch1 210nm 4nm

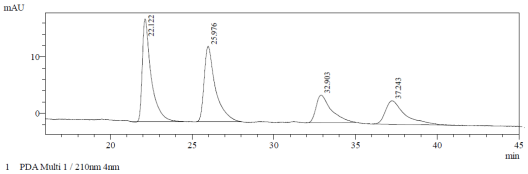
Peak#	Ret. Time	Area	Area %
1	83.403	4619840	93.356
2	91.816	119507	2.415
3	121.372	199844	4.038
4	132.690	9445	0.191
Total		4948636	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.27 (m, 1H), 7.19-7.15 (m, 2H), 7.10-7.06 (m, 1H), 6.24 (d, J = 9.3 Hz, NH), 5.55 (ψq, J = 4.8 Hz, 1H), 3.69 (s, 3H), 3.07-3.03 (m, 1H), 2.88-2.74 (m, 2H), 2.19-2.07 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 169.6, 136.0, 135.7, 129.0, 128.2, 127.5, 126.7, 52.0, 48.0, 44.0, 27.1, 23.6, 22.8. HRMS (ESI) m/z: Calcd for $C_{14}H_{18}NO_3$ $[M+H]^+$: 248.1286; Found: 248.1290.



(1*R*,2*R*)-Ethyl 1-acetamidotetralin-2-carboxylate 4b

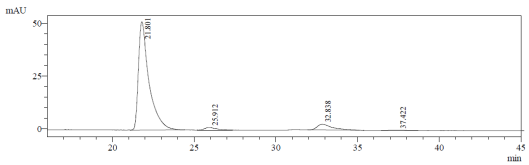
The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 48 mg, 91% yield. Ee: 95%. 93/7 dr. $[\alpha]^{20}_D$ = +62.5°(*c* = 0.9, $CHCl_3$). Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	22.122	683051	34.340
2	25.976	648100	32.583
3	32.903	311384	15.655
4	37.243	346558	17.423
Total		1989093	100.000

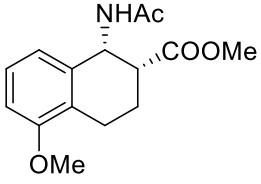


PeakTable

PDA Ch1 210nm 4nm

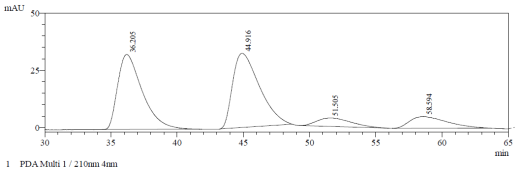
Peak#	Ret. Time	Area	Area %
1	21.801	2313614	90.438
2	25.912	57581	2.251
3	32.838	177609	6.943
4	37.422	9423	0.368
Total		2558227	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.27 (m, 1H), 7.18-7.14 (m, 2H), 7.09-7.05 (m, 1H), 6.29 (d, J = 9.6 Hz, NH), 5.55 (ψq, J = 4.9 Hz, 1H), 4.17-4.09 (m, 2H), 3.05-3.01 (m, 1H), 2.88-2.73 (m, 2H), 2.18-2.07 (m, 2H), 2.00 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.5, 169.6, 136.2, 135.7, 128.9, 128.1, 127.4, 126.6, 60.9, 47.9, 44.0, 27.1, 23.6, 22.9, 14.3. HRMS (ESI) m/z: Calcd for $C_{15}H_{20}NO_3$ $[M+H]^+$: 262.1443; Found: 262.1449.



(1*R*,2*R*)-Methyl 5-methoxy-1-acetamidotetralin-2-carboxylate 4c

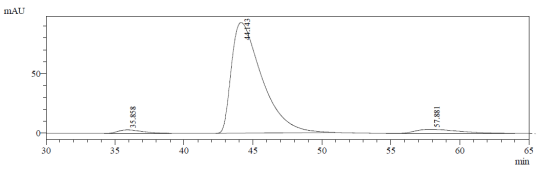
The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 52 mg, 93% yield. Ee: 95%. 95/5 dr. $[\alpha]^{20}_D$ = +62.7°(*c* = 1.1, $CHCl_3$). Daicel Chiralcel AD-H, *n*-hexane/isopropanol 96/4, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	36.205	4235156	40.399
2	44.916	4575977	43.650
3	51.505	669698	6.388
4	58.594	1002557	9.563
Total		10483388	100.000

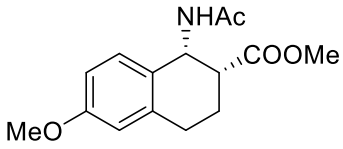


PeakTable

PDA Ch1 210nm 4nm

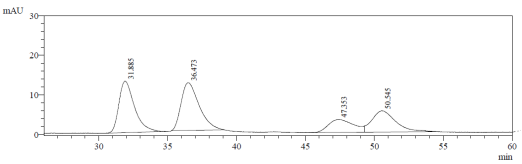
Peak#	Ret. Time	Area	Area %
1	35.858	349065	2.278
2	44.143	14247792	92.991
3	57.881	724895	4.731
Total		15321751	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (t, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 1H), 6.30 (d, *J* = 9.2 Hz, NH), 5.51 (ψq, *J* = 4.6 Hz, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 3.00-2.96 (m, 1H), 2.74-2.58 (m, 2H), 2.15-2.02 (m, 2H), 1.98 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 169.5, 156.9, 137.1, 127.0, 124.8, 120.0, 108.5, 55.4, 51.9, 48.0, 43.6, 23.5, 22.1, 21.2. HRMS (ESI) m/z: Calcd for $C_{15}H_{20}NO_4$ $[M+H]^+$: 278.1392; Found: 278.1399.



(1*R*,2*R*)-Methyl 6-methoxy-1-acetamidotetralin-2-carboxylate 4d

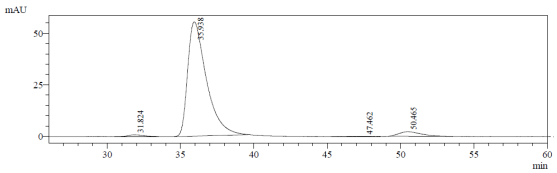
The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 46 mg, 83% yield. Ee: 97%. 96/4 dr. $[\alpha]^{20}_D$ = +79.1°(*c* = 0.9, $CHCl_3$). Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	31.885	1028886	32.330
2	36.473	1094461	34.390
3	47.353	415511	13.056
4	50.545	643598	20.223
Total		3182455	100.000

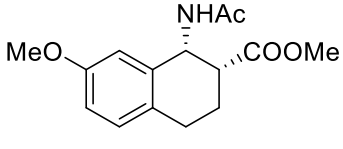


PeakTable

PDA Ch1 210nm 4nm

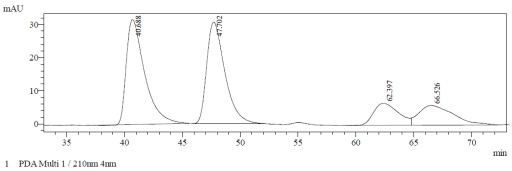
Peak#	Ret. Time	Area	Area %
1	31.824	64362	1.227
2	35.938	4949650	94.332
3	47.462	2279	0.043
4	50.465	230755	4.398
Total		5247047	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.58 (d, *J* = 2.6 Hz, 1H), 6.18 (d, *J* = 9.5 Hz, NH), 5.48 (ψq, *J* = 4.8 Hz, 1H), 3.75 (s, 3H), 3.67 (s, 3H), 3.01-2.97 (m, 1H), 2.84-2.69 (m, 2H), 2.10-2.05 (m, 2H), 1.98 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.9, 169.5, 158.9, 137.1, 129.6, 128.2, 113.4, 113.0, 55.3, 52.0, 47.5, 44.2, 27.6, 23.5, 22.4. HRMS (ESI) m/z: Calcd for $C_{15}H_{20}NO_4$ $[M+H]^+$: 278.1392; Found: 278.1395.



(1*R*,2*R*)-Methyl 7-methoxy-1-acetamidotetralin-2-carboxylate 4e

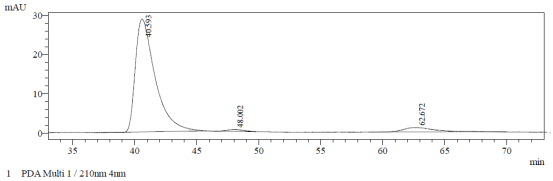
The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 50 mg, 90% yield. Ee: 97%. 94/6 dr. $[\alpha]^{20}_D$ = +42.3°(*c* = 1.2, $CHCl_3$). Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 96/4, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	40.688	3498423	38.606
2	47.702	3344046	36.902
3	62.397	1001079	11.047
4	66.526	1218362	13.445
Total		9061909	100.000

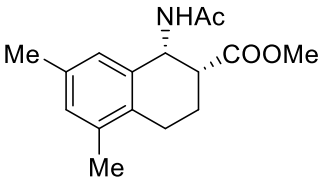


PeakTable

PDA Ch1 210nm 4nm

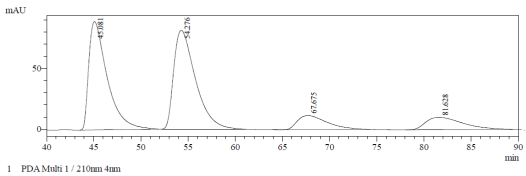
Peak#	Ret. Time	Area	Area %
1	40.593	3192103	92.844
2	48.002	44932	1.307
3	62.672	201089	5.849
Total		3438124	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, *J* =8.4 Hz, 1H), 6.79 (d, *J* = 2.4 Hz, 1H), 6.73 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.28 (d, *J* = 9.5 Hz, NH), 5.48 (ψq, *J* = 4.8 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.04-3.00 (m, 1H), 2.79-2.65 (m, 2H), 2.16-2.03 (m, 2H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 169.6, 158.3, 137.0, 130.0, 127.7, 114.0, 112.6, 55.4, 52.0, 48.2, 44.0, 26.3, 23.5, 23.0. HRMS (ESI) m/z: Calcd for $C_{15}H_{20}NO_4$ $[M+H]^+$: 278.1392; Found: 278.1384.



(1*R*,2*R*)-Methyl 5,7-dimethyl-1-acetamidotetralin-2-carboxylate 4f

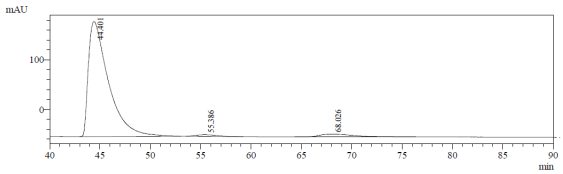
The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 50 mg, 90% yield. Ee: 97%. 96/4 dr. $[\alpha]^{21}_D$ = +62.9°(*c* = 1.0, $CHCl_3$). Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 98/2, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	45.081	12150754	39.920
2	54.276	13033101	42.819
3	67.675	2502708	8.222
4	81.628	2750956	9.038
Total		30437519	100.000

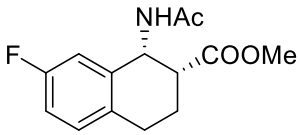


PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	44.401	32120919	94.663
2	55.386	452508	1.334
3	68.026	1358525	4.004
Total		33931953	100.000

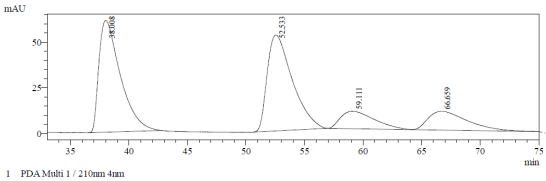
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97 (s, 1H), 6.90 (s, 1H), 6.14 (d, *J* = 9.5 H, NH), 5.52 (dd, J = 9.6, 4.6 Hz, 1H), 3.69 (s, 3H), 2.99 (ψq, J = 5.7 Hz, 1H), 2.72-2.51 (m, 2H), 2.26 (s, 3H), 2.18 (s, 3H), 2.15-2.09 (m, 2H), 2.01(s, 3H). ^{13}C NMR (76 MHz, $CDCl_3$): δ 174.1, 169.5, 136.4, 135.9, 135.7, 131.2, 130.2, 126.5, 52.0, 48.3, 43.7, 24.5, 23.7, 22.4, 21.0, 19.6. HRMS (ESI) m/z: Calcd for $C_{23}H_{33}O_2$ $[M+H]^+$: 276.1599; Found: 276.1591.



(1*R*,2*R*)-Methyl 7-fluoro-1-acetamidotetralin-2-carboxylate 4g

The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 46 mg, 86% yield. Ee: 95%. 93/7 dr. $[\alpha]^{20}_{D}$ = +17.7°(*c* = 1.1, $CHCl_3$). Crystals were obtained from slow evaporation of a solution in a mixture of hexane and ethyl acetate. Crystals that were suitable for single-crystal X-ray diffraction was obtained from slow evaporation of a solution in a concentrated soluton of hexane and DCM at rt. The configuration of the main isomer was determined to be cis.

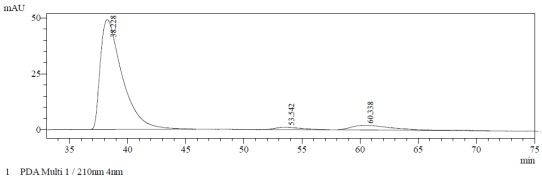
Daicel Chiralcel OD-H, *n*-hexane/isopropanol 96/4, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	38.008	7763482	39.119
2	52.533	7832104	39.465
3	59.111	1903093	9.589
4	66.659	2347222	11.827
Total		19845900	100.000



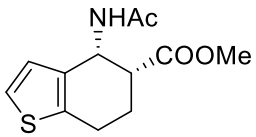
PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	38.228	6422136	90.847
2	53.542	161149	2.280
3	60.338	485876	6.873
Total		7069160	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03-6.95 (m, 2H), 6.85 (td, *J* = 8.4, 2.7 Hz, 1H), 6.43 (d, *J* = 9.0 Hz, NH), 5.48 (ψq, *J* = 4.9 Hz, 1H), 3.68 (s, 3H), 3.09-3.05 (m, 1H), 2.74 (*t*, *J* = 6.5 Hz, 2H), 2.24-2.15 (m, 1H), 2.13-2.06 (m, 1H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.9, 169.8, 161.5 ($J_{C\text{-}F}$ = 244.3 Hz), 138.1 ($J_{C\text{-}F}$ = 6.7 Hz), 131.1 ($J_{C\text{-}F}$ = 3.1 Hz) 130.4 ($J_{C\text{-}F}$ = 7.8 Hz), 114.6 ($J_{C\text{-}F}$ = 21.5 Hz), 113.9 ($J_{C\text{-}F}$ = 21.9 Hz), 52.1, 48.0, 43.6, 29.8, 26.1, 23.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ -116.2.

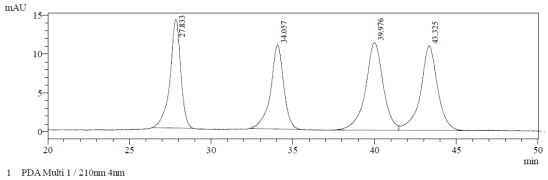
HRMS (ESI) m/z: Calcd for $C_{14}H_{17}FNO_3$ $[M+H]^+$: 266.1192; Found: 266.1198.



(4*R*,5*R*)-Methyl 4-acetamido-4,5,6,7-tetrahydrobenzo[b]thiophene-5-carboxylate 4h

The reaction was complete after 60 h at 80 °C. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 46 mg, 91% yield. Ee: 94%. 97/3 dr. $[\alpha]^{21}_{D}$ = +82.6°(*c* = 1.0, $CHCl_3$).

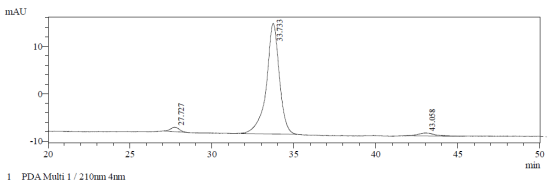
Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min.



PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	27.833	637992	22.132
2	34.057	603645	20.940
3	39.976	850033	29.488
4	43.325	790996	27.440
Total		2882666	100.000

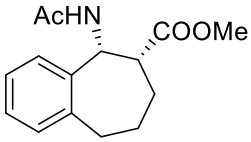


PeakTable

PDA Ch1 210nm 4nm

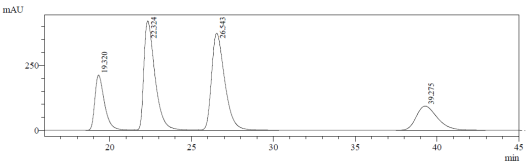
Peak#	Ret. Time	Area	Area %
1	27.727	34081	2.570
2	33.733	1283047	94.275
3	43.058	42928	3.154
Total		1360956	100.000

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.07 (d, *J* = 5.2 Hz, 1H), 6.86 (d, *J* = 5.2 Hz, 1H), 6.15 (d, *J* = 9.2 Hz, NH), 5.48 (q, *J* = 4.8 Hz, 1H), 3.68 (s, 3H), 3.01 (q, J = 5.4 Hz, 1H), 2.90-2.70 (m, 2H), 2.17-2.11 (m, 2H), 1.96 (s, 3H). ^{13}C NMR (76 MHz, $CDCl_3$): δ 173.7, 169.4, 136.9, 135.1, 126.6, 123.4, 52.0, 45.6, 44.0, 23.5, 23.3, 23.2. HRMS (ESI) m/z: Calcd for $C_{12}H_{16}NO_3S$ $[M+H]^+$: 254.0851; Found: 254.0846.



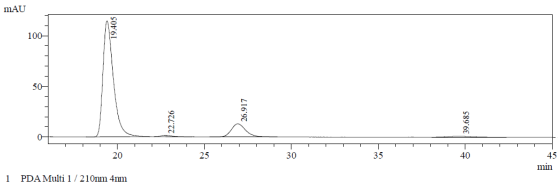
(5*R*,6*R*)-Methyl 5-acetamidobenzocycloheptene-6-carboxylate 4i

The conversion was incomplete after 72 h at 80 °C using 10 mol% nickel catalyst. The product was isolated by flash chromatography (hexanes/EA 2:1) as white solid. 34 mg, 65% yield. Ee: 97%. 86/14 dr. $[\alpha]^{20}_D$ = +81.1˚(*c* = 0.7, $CHCl_3$). Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



PeakTable
PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	19.320	8730132	15.099
2	22.324	19877137	34.379
3	26.543	20874957	36.105
4	39.275	8335520	14.417
Total		57817746	100.000



PeakTable
PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area %
1	19.405	4790031	84.174
2	22.726	60129	1.057
3	26.917	747888	13.143
4	39.685	92556	1.626
Total		5690605	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.21 (m, 1H), 7.18-7.14 (m, 2H), 7.11-7.08 (m, 1H), 5.94 (d, *J* = 7.2 Hz, NH), 5.51 (Ψt, *J* = 7.8 Hz, 1H), 3.63 (s, 3H), 3.00 (s, 3H), 2.93-2.79 (m, 2H), 2.18-2.08 (m, 1H), 2.02 (s, 3H), 1.94-1.81 (m, 2H), 1.69-1.59 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 169.1, 140.8, 138.5, 130.2, 128.1, 126.7, 54.9, 51.8, 47.5, 35.1, 28.8, 24.6, 23.5. HRMS (ESI) m/z: Calcd for $C_{15}H_{20}NO_3$ $[M+H]^+$: 262.1443; Found: 262.1440.

VI. Reference

1. Yang, P.; Xu, H.; Zhou, J. S. *Angew. Chem., Int. Ed.* **2014,** *53*, 12210-3.

V. X-ray measurement and thermal ellipsoid plots of crystal structures

Intensity data of **4g** were collected at 100(2)K using a Bruker X8 diffractometer with fine-focus sealed tube Mo source. The structures were solved by Intrinsic Phasing (SHELXTL XT-2014) and refined by full-matrix least squares methods on F^2 (Sheldrick, G. M. (2015). *Acta Cryst.* A**71**, 3-8). All non-hydrogen atoms were subjected to anisotropic refinement. The hydrogen atoms were generated geometrically and allowed to ride in their respective parent atoms; they were assigned appropriate

isotropic thermal parameters and included in the structure-factor calculations.

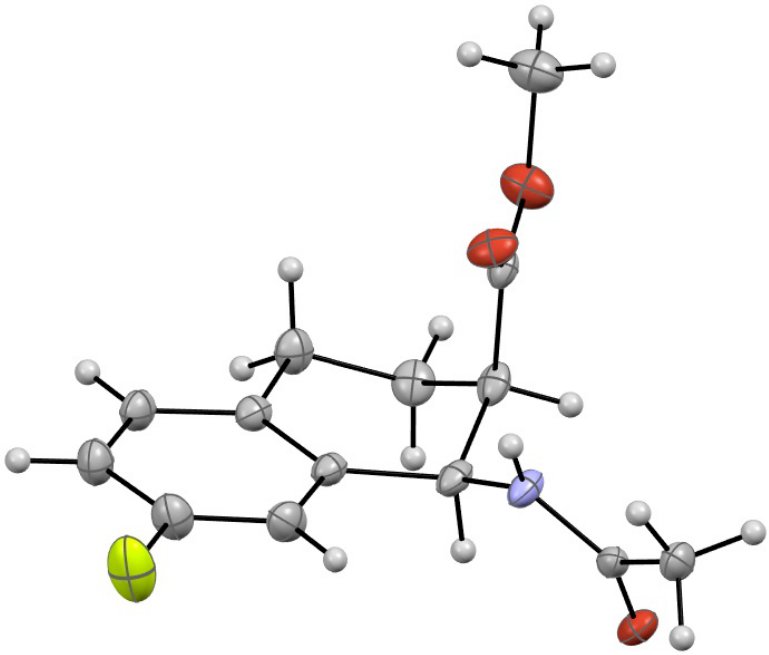


Fig S1. Thermal ellipsoid plot for crystal structure of compound **4g** (ellipsoid contour at 60% probability)