Supporting Information for

Ni-Catalyzed Enantioselective *C*-Acylation of α-Substituted Lactams

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Materials and Methods.

Unless otherwise stated, reactions were performed in flame-dried or oven-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. Reaction temperatures were controlled by an IKAmag temperature modulator unless otherwise indicated. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, $KMnO_4$ or PMA (phosphomolybdic acid) staining. Silicycle Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.064 mm) was used for flash column chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralcel OD-H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 254 nm. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralcel (OJ-H) column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 254 nm. ^1H and ^{13}C NMR spectra were recorded on a Varian Inova 500 (500 MHz and 126 MHz, respectively) and are reported in terms of chemical shift relative to $CHCl_3$ (δ 7.26 and δ 77.16, respectively). Data for ^1H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d= broad doublet, app = apparent. Data for ^{13}C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode, or Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL, solvent). Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number.

THF, Et_2O, CH_2Cl_2, toluene, CH_3CN, TBME and dioxane were dried by passage through an activated alumina column under argon. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. Commercially available reagents were purchased from Sigma-Aldrich, Acros Organics, TCI, Oakwood chemicals, Strem, or Alfa Aesar and used as received unless otherwise stated. LiBr was purchased from Aldrich and dried for 3 h at 140 °C in vacuo.

(3-Bromopropoxy)methyl)benzene,[1] 1-bromo-2-butene,[2] (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methylbenzene,[3] (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene,[4] (*E*)-1-(3-chloroprop-1-en-1-yl)-4-fluoro-benzene,[5] (*E*)-3-(thiophen-3-yl)prop-2-en-1-ol,[6] and ((1*E*,3*E*)-5-bromopenta-1,3-dien-1-yl)benzene[7] were prepared by known methods and used without purification. (*E*)-3-(3-Chloroprop-1-en-1-yl)thiophene was prepared from (*E*)-3-(thiophen-3-yl)prop-2-en-1-ol and $SOCl_2$ in CH_2Cl_2 and used without purification.

List of Abbreviations:

ee – enantiomeric excess, dr – diastereomeric ratio, HPLC – high-performance liquid, chromatography, SFC – supercritical fluid chromatography, TLC – thin-layer chromatography, EtOAc – ethyl acetate, THF – tetrahydrofuran, MeOH – methanol, MeCN – acetonitrile, IPA – isopropanol, BINAP – (2,2'–bis(diphenylphosphino)–1,1'–binaphthyl), LHMDS – lithium hexamethyldisilazide, NaHMDS – sodium hexamethyldisilazide, KHMDS – potasium hexamethyldisilazide, PMP – *p*-methoxyphenyl, CAN – ceric ammonium nitrate, TFA – trifluoroacetic acid, *m*-CPBA – *m*-chloroperoxybenzoic acid

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[1] Hasserodt, J.; Janda, K. D.; Lerner, R. A. *J. Am. Chem. Soc.* **1997**, *119*, 5993–5998.

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[6] Kurauchi, D.; Hirano, K.; Kato, H.; Saito, T.; Miyamoto K.; Uchiyama, M. *Tetrahedron* **2015**, *71*, 5849–5857.

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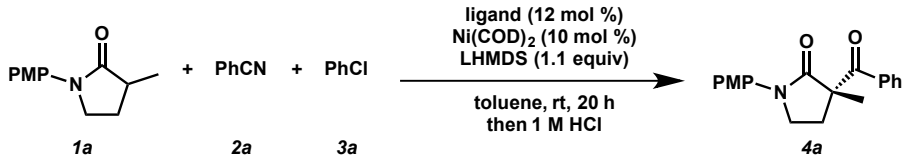
Ligand and Solvent Screen (Table S1 and S2)

Ligand screen (Table S1)[a]



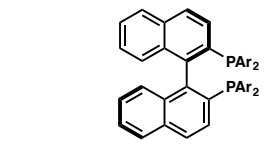
1a *2a* *3a* *4a*

entry	ligand	conversion (%)	ee (%)
1	(*R*)-BINAP	31	7
2	(*R*)-T-BINAP	61	3
3	(*R*)-DM-BINAP	87	7
4	(*R*)-H8-BINAP	73	–2
5	(*R*)-SEGPHOS	1	–31
6	(*R*)-DM-SEGPHOS	59	–1
7	(*R*)-DTBM-SEGPHOS	26	–32
8	(*R*)-DIFLUORPHOS	2	8
9	(*S*)-Xyl-MeOBIPHEP	66	2
10	(R)-BTFM-Garphos	22	–10
11	(*R*)-SYNPHOS	45	–1
12	(*R*)-SOLPHOS	33	–3
13	(*S*)-C_3-TunePhos	53	6
14	(*R*)-P-Phos	19	–5
15	(*R*)-Phanephos	15	–2
16	(*R*)-SDP	16	3
17	(*R*)-Monophos	74	1
18	(*S*)-BINAPINE	8	11
19	CatASiumMN Xyl(*R*)	4	13
20	CatASiumMN Xyl^F(*R*)	6	2
21	(*R,R*)-Chiraphos	0	-
22	(*R,R*)-DIOP	0	-
23	(2*S*,5*S*)-MeBPE	0	-
24	(2*R*,5*R*)-MeDUPHOS	0	-
25	(*R*)-MOP	0	-
26	(*R*)-QUINAP	0	-
27	(*R,R*)-DACH	0	-
28	(*S*)-tBuPHOX	2	10
29	(*S*)-tBu-Me_2-box	0	-
30	(*S*)-iPr-pybox	0	-
31	(*S,S*)-tangphos	3	7
32	(2*S*,5*S*)-Me-Ferocelane	76	–24
33	(2*S*,5*S*)-Et-Ferocelane	25	–6
34	(2*S*,5*S*)-iPr-Ferocelane	1	35
35	(2*S*,5*S*)-Me-f-Ketalphos	63	–56
36	SL-J001-1	80	16
37	SL-J002-1	53	13
38	SL-J003-1	41	5
39	SL-J004-1	54	8
40	SL-J005-1	7	–8
41	SL-J006-1	79	30
42	SL-J007-1	85	–6
43	SL-J008-1	18	–1
44	SL-J009-1	5	1
45	SL-J013-1	32	10
46	SL-J015-1	5	2
47	SL-J212-1	86	12
48	SL-J216-1	4	–5
49	SL-J404-1	37	1
50	SL-J418-1	44	–12
51	SL-J502-1	4	–4
52	SL-J505-1	0	-
53	SL-W001-1	52	20
54	SL-W002-1	64	10
55	SL-W003-1	9	–16
56	SL-W005-1	54	14
57	SL-W006-1	61	18
58	SL-W008-1	19	16
59	SL-W009-1	64	7
60	SL-W022-1	7	–14
61	SL-M001-2	39	35
62	SL-M002-2	0	-
63	SL-M003-2	25	15
64	SL-M004-2	70	59
65	SL-M009-2	71	62
66	SL-M012-2	0	-
67	SL-T001-1	7	34
68	SL-T002-1	0	-
69	SL-F356-2	0	-

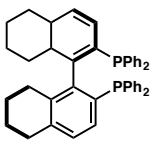
[a] Reaction conditions: lactam (1 equiv), $Ni(COD)_2$ (10 mol %), ligand (12 mol %), LHMDS (1.1 equiv), PhCN (2 equiv), PhCl (2 equiv), toluene (0.2 M), rt, 20 h, then 1 M HCl aq.

The structures of ligands used in table S1 are showed in figure S1

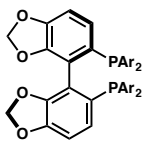
Structures of ligands (Figure S1)



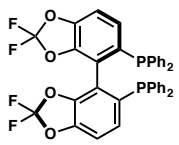
(*R*)-BINAP (Ar = Ph)
(*R*)-T-BINAP (Ar = 4-MePh)
(*R*)-DM-BINAP (Ar = 3,5-Me_2Ph)



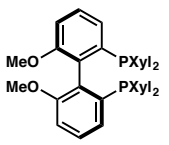
(*R*)-H8-BINAP



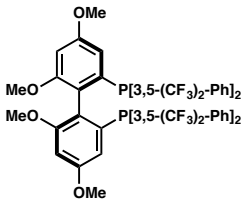
(*R*)-SEGPHOS (Ar = Ph)
(*R*)-DM-SEGPHOS (Ar = 3,5-Me_2Ph)
(*R*)-DTBM-SEGPHOS (Ar = 3,5-*t*Bu_2-4-OMe-Ph)



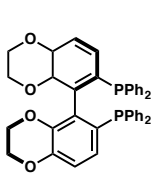
(*R*)-DIFLUORPHOS



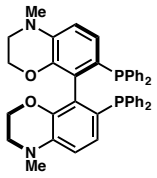
(*S*)-Xyl-MeOBIPHEP



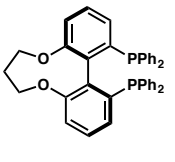
(*R*)-BTFM-Garphos



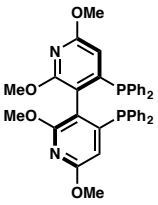
(*R*)-SYNPHOS



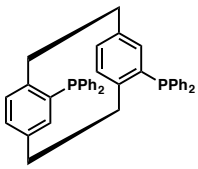
(*R*)-SOLPHOS



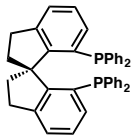
(*S*)-C_3-TunePhos



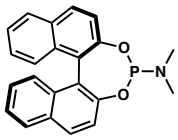
(*R*)-P-PHOS



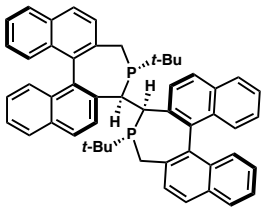
(*R*)-PhanePhos



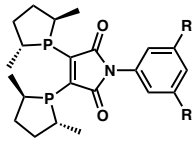
(*R*)-SDP



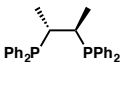
(*R*)-MonoPhos



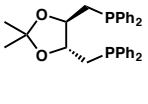
(*S*)-BINAPINE



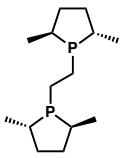
catASium(R) MNXyl (R = Me)
catASium(R) MNXylF (R = CF_3)



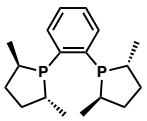
(*R,R*)-Chiraphos



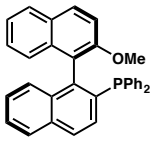
(*R,R*)-DIOP



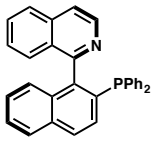
(*S,S*)-Me-BPE



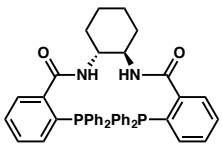
(*R,R*)-Me-DuPHOS



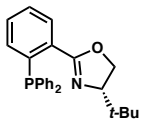
(R)-MOP



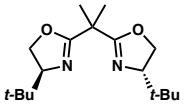
(*R*)-QUINAP



(*R,R*)-DACH



(*S*)-*t*-Bu-PHOX



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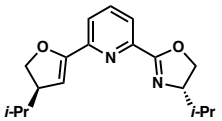
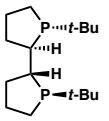
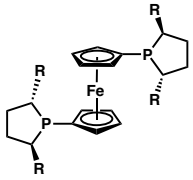


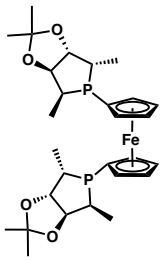
(*S*)-*i*-Pr-pybox



(*S,S*)-TangPhos



(*2S,5S*)-Me-Ferrocelane (R = Me)
(*2S,5S*)-Et-Ferrocelane (R = Et)
(*2S,5S*)-*i*-Pr-Ferrocelane (R = *i*-Pr)



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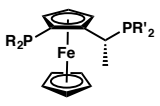
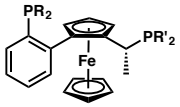
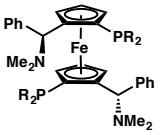


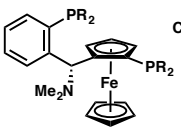
Josiphos



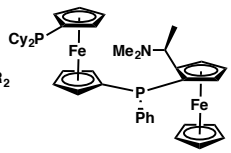
Walphos



Mandyphos



Taniaphos



Chenphos

SL-J001-1 (R,R' = Ph, Cy)
SL-J002-1 (R,R' = Ph, *t*Bu)
SL-J003-1 (R,R' = Cy, Cy)
SL-J004-1 (R,R' = Cy, Ph)
SL-J005-1 (R,R' = Ph, Xyl)
SL-J006-1 (R,R' = Xyl^F, Cy)
SL-J007-1 (R,R' = $MeOMe_2$Ph, Cy)
SL-J008-1 (R,R' = Xyl^F, Xyl)
SL-J009-1 (R,R' = Cy, *t*Bu)
SL-J013-1 (R,R' = $MeOMe_2$Ph, *t*Bu)
SL-J015-1 (R,R' = 2-furyl, Xyl)
SL-J212-1 (R,R' = 2-furyl, *t*Bu)
SL-J216-1 (R,R' = 1-Np, *t*Bu)
SL-J404-1 (R,R' = 1-Np, Xyl)
SL-J418-1 (R,R' = $MeOMe_2$Ph, Xyl)
SL-J502-1 (R,R' = *t*Bu, Ph)
SL-J505-1 (R,R' = *t*Bu, 2-tol)

SL-W001-1 (R,R' = Ph, Xyl^F)
SL-W002-1 (R,R' = Ph, Ph)
SL-W003-1 (R,R' = Ph, Cy)
SL-W005-1 (R,R' = $MeOMe_2$Ph, Xyl^F)
SL-W006-1 (R,R' = Ph, Xyl)
SL-W008-1 (R,R' = Cy, Xyl^F)
SL-W009-1 (R,R' = Xyl, Xyl)
SL-W022-1 (R,R' = Ph, Norbonyl)

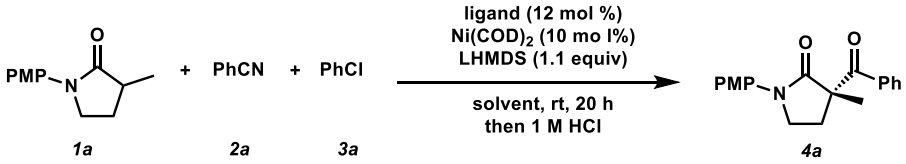
SL-M001-2 (R = Ph)
SL-M002-2 (R = Cy)
SL-M003-2 (R = Xyl^F)
SL-M004-2 (R = $MeOMe_2$Ph)
SL-M009-2 (R = Xyl)
SL-M012-2 (R = 2-tol)

SL-T001-1 (R = Ph)
SL-T002-1 (R = Cy)

(SL-F356-2)

***General Procedure for Ligand and Solvent Screen**:* In a nitrogen-filled glovebox, to a solution of $Ni(COD)_2$ (1.10 mg, 4.00 μmol, 0.100 equiv) and ligand (4.80 μmol, 0.120 equiv) in solvent (0.1 mL) was added a solution of lactam **1a** (8.21 mg, 40.0 μmol, 1.00 equiv), benzonitrile **2a** (8.24 μL, 80.0 μmol, 2.00 equiv), chlorobenzene **3a** (8.13 μL, 80.0 μmol, 2.00 equiv) and LHMDS (7.36 mg, 44.0 μmol, 1.10 equiv) in solvent (0.1 mL) and the reaction mixture was stirred at 25 °C for 20 h. 1M HCl aqueous solution (0.5 mL) was added and the mixture was stirred at ambient temperature for 0.5 h. EtOAc (0.5 mL) was added and the mixture was stirred for 1 min. The organic layer (10 μL) was sampled and diluted to a mixture of hexanes and IPA (8/2, 1 mL). This solution was analyzed for conversion and enantiomeric excess (see Methods for the Determination of Enantiomeric Excess).

Solvent screen (Table S2)[a]



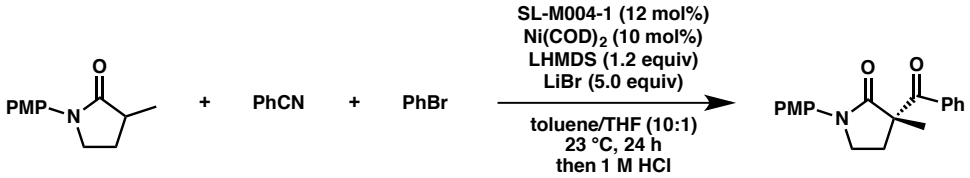
1a *2a* *3a* *4a*

	solvent, conversion / ee					
ligand	toluene	THF	dioxane	TBME	DME	toluene/THF(5/1)
SL-J006-1	79% / 30% ee	26% / 2% ee	52% / 30% ee	74% / 60% ee	37% / 6% ee	54% / 41% ee
SL-M004-2	70% / 59% ee	32% / 15% ee	52% / 47% ee	72% / 51% ee	53% / 25% ee	53% / 52% ee
SL-M009-2	71% / 62% ee	29% / 13% ee	42% / 47% ee	42% / 31% ee	47% / 21% ee	45% / 53% ee

	solvent, conversion / ee		
ligand	methylcyclohexane	nBu_2O	DMF
SL-J006-1	96% / 25% ee	0% / -	0% / -
SL-M009-2	48% / 13% ee	0% / -	0% / -

[a] Reaction conditions: lactam (1 equiv), $Ni(COD)_2$ (10 mol%), ligand (12 mol%), LHMDS (1.1 equiv), PhCN (2 equiv), PhCl (2 equiv), solvent (0.2 M), rt, 20 h.

Effect of lactam stoichiometry (Table S3)[a]

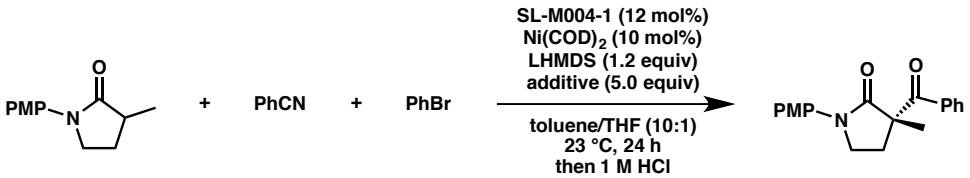


1a *2a* *3b* *4a*

entry	equiv *1a*	conversion (%)	yield (%)	ee (%)
1	2.0	>99	85	88
2	1.8	94	93	86
3	1.6	91	93	nd
4	1.4	85	92	86
5	1.2	89	84	87

[a]Reaction conditions: PhCN (1.0 equiv), PhBr (1.5 equiv), SL-M004-1 (12 mol %), $Ni(COD)_2$ (10 mol%), LHMDS (1.2 equiv), toluene/THF (10:1, 0.09 M), rt, 24 h.

Effect of bromide additives (Table S4)[a]

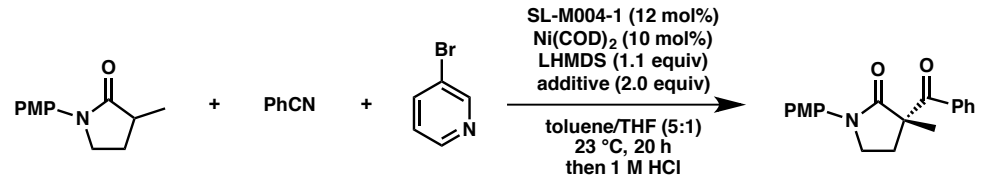


1a *2a* *3b* *4a*

entry	additive	conversion (%)	yield (%)	ee (%)
1	none	>99	67	66
2	LiBr	>99	>99	88
3	NaBr	>99	59	72
4	KBr	>99	66	70
5	TBABr	>99	89	56

[a]Reaction conditions: lactam (2.0 equiv), PhCN (1.0 equiv), PhBr (1.5 equiv), SL-M004-1 (12 mol %), $Ni(COD)_2$ (10 mol%), LHMDS (1.2 equiv), toluene/THF (10:1, 0.09 M), rt, 24 h.

Effect of lithium additives (Table S5)[a]

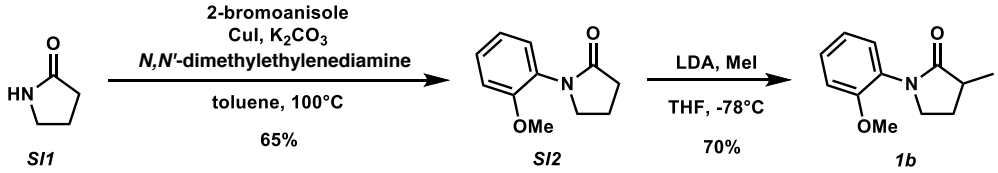


1a *2a* *SI20* *4a*

entry	additive	conversion (%)	ee (%)
1	none	73	63
2	LiBr	60	73
3	LiCl	46	64
4	LiI	20	42
5	LiOAc	65	62

[a]Reaction conditions: lactam (1.0 equiv), PhCN (2.0 equiv), ArBr (2.0 equiv), SL-M004-1 (12 mol %), $Ni(COD)_2$ (10 mol%), LHMDS (1.1 equiv), toluene/THF (5:1, 0.2 M), rt, 20 h.

General Procedure for α-Substituted Lactam Substrates



SI1 *SI2* *1b*

General procedure 1: 1-(2-methoxyphenyl)pyrrolidin-2-one (SI2)

To a suspension of lactam **SI1** (8.17 g, 96.0 mmol, 1.20 equiv), K_2CO_3 (22.1 g, 160 mmol, 2.00 equiv) and CuI (1.52 g, 8.00 mmol, 0.10 equiv) in toluene (80 mL) were added 2-bromoanisole (9.84 mL, 80.0 mmol, 1.00 equiv) and *N,N'*-dimethylethylendiamine (1.68 mL, 16.0 mmol, 0.20 equiv). The reaction mixture was stirred at 100 °C for 18 h then allowed to cool to ambient temperature and filtered through a pad of silica gel eluting with EtOAc (250 mL). The eluate was concentrated under reduced pressure and the residue was purified by flash column chromatography (1:1 EtOAc:hexanes) on silica gel to give lactam **SI2** as a pale yellow oil (9.88 g, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.01 – 6.93 (m, 2H), 3.84 (s, 3H), 3.76 (t, J = 7.0 Hz, 2H), 2.56 (t, J = 8.1 Hz, 2H), 2.23 – 2.14 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 154.8, 128.7, 128.6, 127.2, 120.9, 112.0, 55.6, 49.9, 31.2, 19.0; IR (Neat Film NaCl) 2968, 2889, 2838, 1694, 1504, 1461, 1408, 1304, 1281, 1253, 1023, 755 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{14}NO_2$ $[M+H]^+$: 192.1019, found 192.1019.

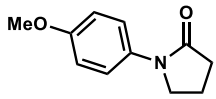
General procedure 2: 1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (1b)

To a solution of diisopropylamine (3.07 mL, 22.0 mmol, 1.10 equiv) in THF (17 mL) was added a solution of *n*-BuLi (8.80 mL, 22.0 mmol, 2.5 M in hexanes, 1.10 equiv) dropwise at -78 °C. After 20 min at -78 °C, a solution of lactam **SI2** (3.82 g, 20.0

mmol, 1.00 equiv) in THF (50 mL) was added dropwise. After an additional 20 min, a solution of methyl iodide (15.0 mL, 30.0 mmol, 2.0 M in TBME, 1.50 equiv) was added and the reaction mixture was stirred at -78 °C for 3 h. Saturated NH_4Cl aqueous solution (50 mL) was added and the mixture was allowed to ambient temperature. The mixture was extracted with EtOAc (100 mL), washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:4 to 1:2 EtOAc:hexanes) on silica gel to give lactam **1b** as a yellow oil (2.86 g, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 6.99 – 6.93 (m, 2H), 3.83 (s, 3H), 3.74 – 3.62 (m, 2H), 2.65 (tq, *J* = 8.7, 7.1 Hz, 1H), 2.37 (dddd, *J* = 12.2, 8.5, 7.3, 3.5 Hz, 1H), 1.82 (dq, *J* = 12.4, 8.5 Hz, 1H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.7, 155.0, 128.8, 128.6, 127.7, 121.0, 112.1, 55.8, 48.1, 37.0, 28.2, 16.4; IR (Neat Film NaCl) 2965, 2932, 2874, 1695, 1504, 1463, 1456, 1403, 1311, 1296, 1277, 1251, 1024, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{16}NO_2$ $[M+H]^+$: 206.1176, found 206.1176.

Spectroscopic Data for N-Protected Lactams

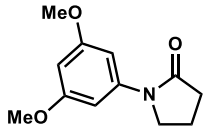
1-(4-Methoxyphenyl)pyrrolidin-2-one (SI3)



SI3

Lactam **SI3** was prepared according to the general procedure 1, using 4-iodoanisole and K_3PO_4 in place of 2-bromoanisole and K_2CO_3 respectively, and isolated by recrystallization in hexanes/EtOAc (4/1) as a white crystal. 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.53 (m, 2H), 6.99 – 6.95 (m, 2H), 3.90 (t, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 2.66 (t, *J* = 8.1 Hz, 2H), 2.27 – 2.19 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 156.5, 132.6, 121.8, 114.0, 55.5, 49.2, 32.5, 18.1; IR (Neat Film NaCl) 2952, 2907, 1683, 1517, 1255, 1226, 1182, 1126, 1032, 829 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{11}H_{14}NO_2$ $[M+H]^+$: 192.1019, found 192.1021.

1-(3,5-Dimethoxyphenyl)pyrrolidin-2-one (SI4)

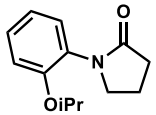


SI4

Lactam **SI4** was prepared according to the general procedure 1, using 1-bromo-3,5-dimethoxybenzene in place of 2-bromoanisole, and isolated by recrystallization in hexanes/EtOAc (5/1) as a white crystal. 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (d, *J* = 2.2 Hz, 2H), 6.31 (t, *J* = 2.2 Hz, 1H), 3.87 (t, *J* = 7.0 Hz, 2H), 3.84 (s, 6H), 2.65 (t, *J* = 8.1 Hz, 2H), 2.19 (p, *J* = 7.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 160.9, 141.3, 98.5, 96.6, 55.5, 49.2, 33.2, 18.0; IR (Neat Film NaCl) 2959,

1694, 1593, 1474, 1455, 1424, 1397, 1276, 1245, 1198, 1152, 1071, 1056, 922, 840, 825, 683 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{16}NO_3$ $[M+H]^+$: 222.1125, found 222.1129.

1-(2-Isopropoxyphenyl)-pyrrolidin-2-one (SI5)

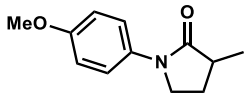


SI5

Lactam **SI5** was prepared according to the general procedure 1, using 1-bromo-2-isopropoxybenzene in place of 2-bromoanisole, and isolated by flash column chromatography (1:2 to 1:1 EtOAc:hexanes) on silica gel as a pale yellow oil. 57% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 2H), 7.03 – 6.96 (m, 2H), 4.58 (hept, *J* = 6.0 Hz, 1H), 3.82 (t, *J* = 6.7 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.28 – 2.16 (m, 2H), 1.38 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 153.1, 128.9, 128.4, 128.4, 120.8, 114.7, 70.8, 49.9, 31.4, 22.2, 19.2; IR (Neat Film NaCl) 2976, 2933, 1697, 1595, 1500, 1456, 1405, 1385, 1304, 1282, 1251, 1125, 1111, 957, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{13}H_{18}NO_2$ $[M+H]^+$: 220.1332, found 220.1328.

Spectroscopic Data for α-Substituted Lactams

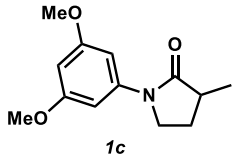
1-(4-Methoxyphenyl)-3-methylpyrrolidin-2-one (1a)



1a

Lactam **1a** was prepared according to the general procedure 2 from **SI3** in place of **SI2**, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a white solid. 82% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.51 (m, 2H), 6.92 – 6.88 (m, 2H), 3.80 (s, 3H), 3.79 – 3.70 (m, 2H), 2.66 (ddq, *J* = 9.4, 8.6, 7.1 Hz, 1H), 2.37 (dddd, *J* = 12.1, 8.5, 7.0, 3.2 Hz, 1H); 1.77 (dq, *J* = 12.5, 8.7 Hz, 1H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 156.4, 133.0, 121.4, 114.0, 55.5, 46.9, 38.1, 27.1, 16.3; IR (Neat Film NaCl) 2952, 2882, 2835, 1682, 1516, 1251, 1225, 1122, 1099, 1030, 829 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{16}NO_2$ $[M+H]^+$: 206.1176, found 206.1177.

1-(3,5-Dimethoxyphenyl)-3-methylpyrrolidin-2-one (1c)

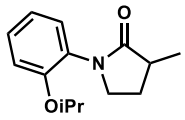


1c

Lactam **1c** was prepared according to the general procedure 2 from **SI4** in place of **SI2**, and isolated by flash column chromatography (1:4 EtOAc:hexanes) on silica gel

as a white solid. 87% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, *J* = 2.2 Hz, 2H), 6.31 (t, *J* = 2.2 Hz, 1H), 3.84 (s, 6H), 3.79 (dd, *J* = 8.8, 5.0 Hz, 2H), 2.78 – 2.66 (m, 1H), 2.45 – 2.35 (m, 1H), 1.86 – 1.74 (m, 1H), 1.35 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 160.8, 141.5, 97.9, 96.5, 55.4, 46.8, 38.6, 26.9, 16.1; IR (Neat Film NaCl) 2964, 1698, 1597, 1474, 1392, 1273, 1246, 1208, 1154, 1071, 927, 834, 682 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{13}H_{18}NO_3$ $[M+H]^+$: 236.1281, found 236.1284.

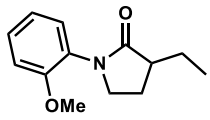
1-(2-Isopropoxyphenyl)-3-methylpyrrolidin-2-one (1d)



1d

Lactam **1d** was prepared according to the general procedure 2 from **SI5** in place of **SI2**, and isolated by flash column chromatography (1:3 to 1:2 EtOAc:hexanes) on silica gel as a pale yellow oil. 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 2H), 7.03 – 6.96 (m, 2H), 4.57 (hept, *J* = 6.1 Hz, 1H), 3.80 – 3.67 (m, 2H), 2.67 (tq, *J* = 8.4, 7.1 Hz, 1H), 2.46 – 2.35 (m, 1H), 1.84 (dq, *J* = 12.3, 8.2 Hz, 1H), 1.37 (d, *J* = 6.1 Hz, 6H), 1.35 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 153.2, 129.0, 128.7, 128.3, 120.8, 114.8, 70.8, 47.9, 36.9, 28.2, 22.2, 16.4; IR (Neat Film NaCl) 2974, 2930, 1701, 1595, 1499, 1457, 1405, 1277, 1249, 1124, 1111, 955, 750 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1489, found 234.1482.

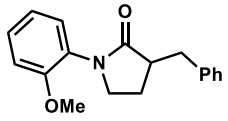
1-(2-Methoxyphenyl)-3-ethylpyrrolidin-2-one (SI6)



SI6

Lactam **SI6** was prepared according to the general procedure 2 using ethyl iodide in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a pale yellow oil. 81% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.19 (m, 2H), 7.01 – 6.92 (m, 2H), 3.82 (s, 3H), 3.76 – 3.69 (m, 1H), 3.69 – 3.60 (m, 1H), 2.53 (qd, *J* = 8.7, 4.3 Hz, 1H), 2.38 – 2.27 (m, 1H), 2.04 – 1.92 (m, 1H), 1.92 – 1.81 (m, 1H), 1.63 – 1.49 (m, 1H), 1.04 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 154.8, 128.7, 128.5, 127.5, 120.8, 112.0, 55.6, 48.2, 43.4, 25.1, 24.2, 11.5; IR (Neat Film NaCl) 2961, 1695, 1596, 1505, 1462, 1404, 1280, 1249, 1024, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{13}H_{18}NO_2$ $[M+H]^+$: 220.1332, found 220.1334.

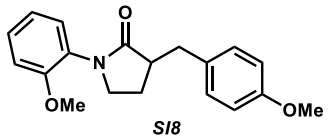
3-Benzyl-1-(2-methoxyphenyl)pyrrolidin-2-one (SI7)



SI7

Lactam **SI7** was prepared according to the general procedure 2 using benzyl bromide in place of methyl iodide, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.08 (m, 7H), 6.99 – 6.90 (m, 2H), 3.80 (s, 3H), 3.63 (dt, *J* = 9.5, 7.7 Hz, 1H), 3.49 (ddd, *J* = 9.5, 8.6, 3.7 Hz, 1H), 3.30 (dd, *J* = 13.7, 4.0 Hz, 1H), 2.93 – 2.83 (m, 1H), 2.77 (dd, *J* = 13.6, 9.7 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.94 – 1.83 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 154.9, 139.8, 129.3, 128.7, 128.65, 128.6, 127.5, 126.4, 121.0, 112.2, 55.7, 48.1, 43.9, 37.1, 25.2; IR (Neat Film NaCl) 2942, 1694, 1596, 1504, 1454, 1407, 1279, 1252, 1025, 753, 701 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{20}NO_2$ $[M+H]^+$: 282.1489, found 282.1491.

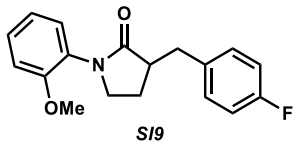
3-(4-Methoxybenzyl)-1-(2-methoxyphenyl)pyrrolidin-2-one (SI8)



SI8

Lactam **SI8** was prepared according to the general procedure 2 using 4-methoxybenzyl chloride in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a pale yellow oil. 59% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 1H), 7.24 – 7.14 (m, 3H), 7.00 – 6.90 (m, 2H), 6.88 – 6.80 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.62 (dt, *J* = 9.5, 7.6 Hz, 1H), 3.47 (ddd, *J* = 9.5, 8.6, 3.8 Hz, 1H), 3.21 (dd, *J* = 13.7, 4.0 Hz, 1H), 2.90 – 2.80 (m, 1H), 2.74 (dd, *J* = 13.8, 9.4 Hz, 1H), 2.20 – 2.09 (m, 1H), 1.93 – 1.81 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 158.1, 154.8, 131.6, 130.1, 128.6, 128.5, 127.4, 120.8, 113.8, 112.1, 55.6, 55.3, 48.1, 43.9, 36.0, 25.0; IR (Neat Film NaCl) 2936, 1696, 1596, 1512, 11506, 1462, 1406, 1300, 1279, 1249, 1179, 1028, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{22}NO_3$ $[M+H]^+$: 312.1594, found 312.1589.

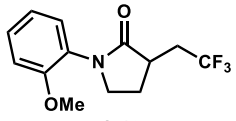
3-(4-Fluorobenzyl)-1-(2-methoxyphenyl)pyrrolidin-2-one (SI9)



SI9

Lactam **SI9** was prepared according to the general procedure 2 using 4-fluorobenzyl bromide in place of methyl iodide, and isolated by flash column chromatography (1:3 to 1:2 EtOAc:hexanes) on silica gel as a pale yellow oil. 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.18 (m, 4H), 7.04 – 6.92 (m, 4H), 3.81 (s, 3H), 3.65 (dt, *J* = 9.6, 7.7 Hz, 1H), 3.50 (ddd, *J* = 9.5, 8.6, 3.6 Hz, 1H), 3.24 (dd, *J* = 13.5, 3.8 Hz, 1H), 2.93 – 2.76 (m, 2H), 2.22 – 2.12 (m, 1H), 1.94 – 1.82 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 161.7 (d, *J* = 243.9 Hz), 154.9, 135.3 (d, *J* = 3.0 Hz), 130.7 (d, *J* = 8.0 Hz), 128.8, 128.6, 127.4, 121.0, 115.3 (d, *J* = 20.9 Hz), 112.2, 55.7, 48.1, 43.8, 36.2, 25.0; IR (Neat Film NaCl) 2942, 1696, 1597, 1507, 1459, 1406, 1252, 1221, 1158, 1025, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{19}FNO_2$ $[M+H]^+$: 300.1394, found 300.1390.

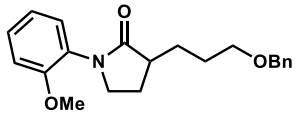
1-(2-Methoxyphenyl)-3-(2,2,2-trifluoroethyl)pyrrolidin-2-one (SI10)



SI10

Lactam **SI10** was prepared according to the general procedure 2 using 2-trifluoroethyl iodide in place of methyl iodide, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a yellow oil. 36% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (ddd, *J* = 8.2, 7.5, 1.7 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.03 – 6.93 (m, 2H), 3.83 (s, 3H), 3.80 – 3.72 (m, 1H), 3.65 (ddd, *J* = 9.7, 8.8, 1.6 Hz, 1H), 3.04 – 2.93 (m, 1H), 2.93 – 2.84 (m, 1H), 2.56 – 2.46 (m, 1H), 2.14 (s, 1H), 2.07 – 1.95 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 154.8, 129.1, 128.6, 127.2 (q, *J* = 276.6 Hz), 127.0, 121.0, 112.1, 55.8, 48.2, 37.1 (q, *J* = 2.5 Hz), 35.7 (q, *J* = 29.0 Hz), 27.0; IR (Neat Film NaCl) 2946, 1703, 1597, 1505, 1462, 1414, 1282, 1252, 1135, 1039, 753, 615 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{13}H_{15}F_3NO_2$ $[M+H]^+$: 274.1049, found 274.1049.

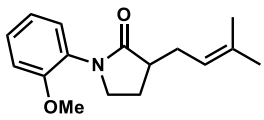
3-(3-(Benzyloxy)propyl)-1-(2-methoxyphenyl)pyrrolidin-2-one (SI11)



SI11

Lactam **SI11** was prepared according to the general procedure 2 using ((3-bromopropoxy)methyl)benzene[1] in place of methyl iodide, and isolated by flash column chromatography (1:3 to 1:2 EtOAc:hexanes) on silica gel as a pale yellow oil. 76% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.32 (m, 4H), 7.28 – 7.24 (m, 1H), 7.23 – 7.19 (m, 1H), 6.98 – 6.90 (m, 2H), 4.50 (s, 2H), 3.80 (s, 3H), 3.72 – 3.59 (m, 3H), 3.57 – 3.48 (m, 2H), 2.58 (qd, *J* = 8.8, 4.6 Hz, 1H), 2.37 – 2.26 (m, 1H), 2.06 – 1.94 (m, 1H), 1.90 – 1.81 (m, 1H), 1.80 – 1.71 (m, 2H), 1.64 – 1.52 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 154.8, 138.6, 128.6, 128.5, 128.4, 127.7, 127.5, 127.4, 120.8, 112.0, 73.0, 70.4, 55.6, 48.2, 41.8, 28.0, 27.5, 25.8; IR (Neat Film NaCl) 2939, 2860, 1697, 1596, 1504, 1454, 1405, 1279, 1252, 1102, 1026, 749, 699 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{26}NO_3$ $[M+H]^+$: 340.1907, found 340.1915.

1-(2-Methoxyphenyl)-3-(3-methylbut-2-en-1-yl)pyrrolidin-2-one (SI12)

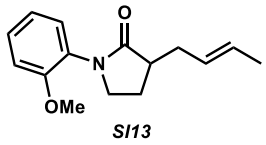


SI12

Lactam **SI12** was prepared according to the general procedure 2 using 1-bromo-3-methyl-2-butene in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a pale yellow oil. 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.20 (m, 2H), 7.01 – 6.92 (m, 2H), 5.24 – 5.16

(m, 1H), 3.83 (s, 3H), 3.73 – 3.59 (m, 2H), 2.69 – 2.53 (m, 2H), 2.33 – 2.22 (m, 2H), 1.91 – 1.80 (m, 1H), 1.74 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 155.0, 133.8, 128.8, 128.6, 127.7, 121.4, 121.0, 112.2, 55.8, 48.3, 42.4, 29.6, 26.0, 25.2, 18.1; IR (Neat Film NaCl) 2913, 1698, 1596, 1505, 1459, 1405, 1279, 1252, 1025, 751 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{16}H_{22}NO_2$ $[M+H]^+$: 260.1645, found 260.1644.

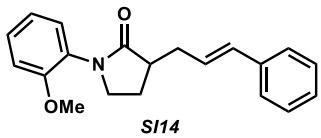
(*E*)-3-(But-2-en-1-yl)-1-(2-methoxyphenyl)pyrrolidin-2-one (SI13)



SI13

Lactam **SI13** was prepared according to the general procedure 2 using 1-bromo-2-butene[2] in place of methyl iodide, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 24% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.21 (m, 2H), 7.01 – 6.92 (m, 2H), 5.62 – 5.43 (m, 2H), 3.83 (s, 3H), 3.73 – 3.58 (m, 2H), 2.68 – 2.53 (m, 2H), 2.32 – 2.19 (m, 2H), 1.95 – 1.82 (m, 1H), 1.72 – 1.66 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 154.8, 128.6, 128.6, 128.6, 128.1, 127.4, 120.9, 112.1, 55.6, 48.2, 42.0, 34.3, 24.8, 18.1; IR (Neat Film NaCl) 2937, 1699, 1596, 1505, 1456, 1436, 1404, 1298, 1279, 1252, 1107, 1046, 1025, 968, 751 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{20}NO_2$ $[M+H]^+$: 246.1489, found 246.1487.

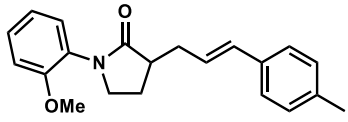
(*E*)-3-Cinnamyl-1-(2-methoxyphenyl)pyrrolidin-2-one (SI14)



SI14

Lactam **SI14** was prepared according to the general procedure 2 using cinnamyl bromide in place of methyl iodide, and isolated by flash column chromatography (1:5 to 1:2 EtOAc:hexanes) on silica gel as a pale yellow oil. 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 2H), 7.36 – 7.17 (m, 5H), 7.02 – 6.93 (m, 2H), 6.51 (d, *J* = 15.7 Hz, 1H), 6.29 (dt, *J* = 15.7, 7.1 Hz, 1H), 3.81 (s, 3H), 3.75 – 3.61 (m, 2H), 2.84 – 2.73 (m, 2H), 2.57 – 2.46 (m, 1H), 2.38 – 2.27 (m, 1H), 2.03 – 1.92 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 154.8, 137.5, 132.2, 128.6, 128.6, 128.5, 127.5, 127.4, 127.1, 126.1, 120.9, 112.0, 55.6, 48.2, 41.9, 34.7, 24.8; IR (Neat Film NaCl) 2941, 1694, 1596, 1504, 1463, 1407, 1253, 1025, 967, 749, 694 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_2$ $[M+H]^+$: 308.1645, found 308.1645.

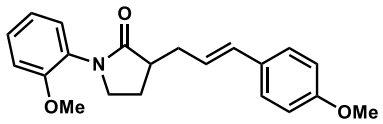
(*E*)-1-(2-Methoxyphenyl)-3-(3-(*p*-tolyl)allyl)pyrrolidin-2-one (SI15)



SI15

Lactam **SI15** was prepared according to the general procedure 2 using (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methylbenzene[3] in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a pale yellow oil. 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 4H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.03 – 6.94 (m, 2H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.24 (dt, *J* = 15.8, 7.1 Hz, 1H), 3.83 (s, 3H), 3.77 – 3.62 (m, 2H), 2.84 – 2.73 (m, 2H), 2.58 – 2.44 (m, 1H), 2.40 – 2.27 (m, 4H), 2.04 – 1.92 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 154.8, 136.9, 134.7, 132.0, 129.2, 128.6, 128.6, 127.4, 126.4, 126.0, 120.9, 112.0, 55.6, 48.2, 41.9, 34.7, 24.8, 21.2; IR (Neat Film NaCl) 2939, 1695, 1596, 1504, 1462, 1405, 1279, 1252, 1181, 1122, 1107, 1045, 1025, 968, 891, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{24}NO_2$ $[M+H]^+$: 322.1802, found 322.1803.

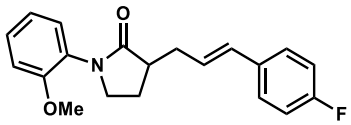
(*E*)-1-(2-Methoxyphenyl)-3-(3-(4-methoxyphenyl)allyl)pyrrolidin-2-one (SI16)



SI16

Lactam **SI16** was prepared according to the general procedure 2 using (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene[4] in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a pale yellow oil. 100% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.18 (m, 4H), 7.02 – 6.94 (m, 2H), 6.94 – 6.82 (m, 2H), 6.45 (dt, *J* = 15.8, 1.4 Hz, 1H), 6.14 (dt, *J* = 15.7, 7.1 Hz, 1H), 3.81 (s, 3H), 3.81 (s, 3H), 3.76 – 3.60 (m, 2H), 2.81 – 2.69 (m, 2H), 2.54 – 2.43 (m, 1H), 2.37 – 2.26 (m, 1H), 2.02 – 1.91 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 158.9, 154.8, 131.5, 130.3, 128.6, 128.6, 127.4, 127.2, 125.2, 120.9, 113.9, 112.0, 55.6, 55.3, 48.2, 42.0, 34.7, 24.8; IR (Neat Film NaCl) 2934, 1694, 1606, 1510,1505, 1463, 1406, 1249, 1175, 1027, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{24}NO_3$ $[M+H]^+$: 338.1751, found 338.1748.

(*E*)-3-(3-(4-Fluorophenyl)allyl)-1-(2-methoxyphenyl)pyrrolidin-2-one (SI17)

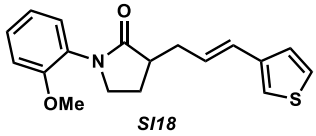


SI17

Lactam **SI17** was prepared according to the general procedure 2 using (*E*)-1-(3-chloroprop-1-en-1-yl)-4-fluorobenzene[5] in place of methyl iodide, and isolated by flash column chromatography (1:3 EtOAc:hexanes) on silica gel as a white solid. 52% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.30 – 7.21 (m, 2H), 7.05 – 6.93 (m, 4H), 6.51 – 6.43 (m, 1H), 6.20 (dt, *J* = 15.8, 7.1 Hz, 1H), 3.81 (s, 3H), 3.75 – 3.61 (m, 2H), 2.83 – 2.73 (m, 2H), 2.56 – 2.45 (m, 1H), 2.38 – 2.27 (m, 1H), 1.96 (ddt, *J* = 12.8, 8.6, 7.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 162.2 (d, *J* = 246.1 Hz), 154.9, 133.8 (d, *J* = 3.4 Hz), 131.1, 128.8, 128.7, 127.7 (d, *J* = 7.8 Hz), 127.4, 127.3 (d, *J* = 2.1 Hz), 121.0, 115.5 (d, *J* = 21.6 Hz), 112.2, 55.7, 48.3, 42.0, 34.8, 25.0; IR (Neat Film NaCl) 2942, 1696, 1597, 1507, 1458, 1405, 1279, 1253,

1225, 1158, 1046, 1025, 968, 839, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{21}FNO_2$ $[M+H]^+$: 326.1551, found 326.1544.

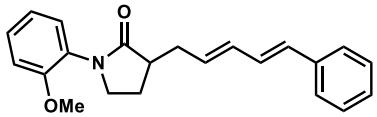
(*E*)-1-(2-Methoxyphenyl)-3-(3-(thiophen-3-yl)allyl)pyrrolidin-2-one (SI18)



SI18

Lactam **SI18** was prepared according to the general procedure 2 using (*E*)-3-(3-chloroprop-1-en-1-yl)thiophene in place of methyl iodide, and isolated by flash column chromatography (1:2 EtOAc:hexanes) on silica gel as a pale yellow oil. 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 4H), 7.10 (dd, *J* = 3.1, 1.2 Hz, 1H), 7.01 – 6.92 (m, 2H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 15.7, 7.1 Hz, 1H), 3.81 (s, 3H), 3.75 – 3.59 (m, 2H), 2.81 – 2.71 (m, 2H), 2.53 – 2.42 (m, 1H), 2.37 – 2.26 (m, 1H), 2.02 – 1.90 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 154.8, 140.1, 128.6, 128.6, 127.3, 127.3, 126.4, 125.9, 125.0, 121.0, 120.9, 112.1, 55.6, 48.2, 41.9, 34.6, 24.9; IR (Neat Film NaCl) 2936, 1694, 1596, 1504, 1463, 1408, 1279, 1252, 1181, 1122, 1046, 1025, 966, 890, 862, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{18}H_{20}NO_2S$ $[M+H]^+$: 314.1209, found 314.1206.

1-(2-Methoxyphenyl)-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-1-yl)pyrrolidin-2-one (SI19)

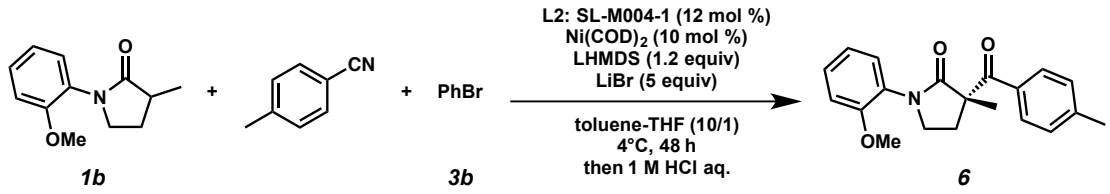


SI19

Lactam **SI19** was prepared according to the general procedure 2 using ((1*E*,3*E*)-5-bromopenta-1,3-dien-1-yl)benzene[7] in place of methyl iodide, and isolated by flash column chromatography (1:2 EtOAc:hexanes) on silica gel as a colorless oil. 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.38 (m, 2H), 7.33 – 7.27 (m, 3H), 7.26 – 7.19 (m, 2H), 7.00 – 6.93 (m, 2H), 6.79 (ddd, *J* = 15.7, 10.4, 0.8 Hz, 1H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.33 (ddd, *J* = 15.1, 10.4, 0.8 Hz, 1H), 5.93 – 5.83 (m, 1H), 3.83 (s, 3H), 3.76 – 3.61 (m, 2H), 2.82 – 2.68 (m, 2H), 2.49 – 2.37 (m, 1H), 2.36 – 2.26 (m, 1H), 1.99 – 1.87 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 154.8, 137.4, 132.8, 132.0, 130.9, 129.0, 128.6, 128.6, 128.6, 127.4, 127.3, 126.2, 120.9, 112.0, 55.6, 48.1, 41.9, 34.6, 25.0; IR (Neat Film NaCl) 2941, 1694, 1596, 1505, 1463, 1407, 1300, 1279, 1252, 1181, 1123, 1107, 1046, 1026, 992, 911, 891, 750, 693 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{24}NO_2$ $[M+H]^+$: 334.1802, found 334.1801.

General Procedure for Ni-Catalyzed *C*-Acylation

*Please note that the absolute configuration was determined only for compound **10** by transforming to a known compound. The absolute configuration for all other products has been inferred by analogy. For respective HPLC and SFC conditions, please refer to Table S3.*

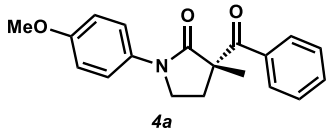


General procedure 3: (*S*)-1-(2-methoxyphenyl)-3-methyl-3-(4-methylbenzoyl) pyrrolidin-2-one (6)

In a nitrogen-filled glovebox, to an oven-dried 4 mL vial equipped with a stir bar was added LHMDS (40.2 mg, 0.240 mmol, 1.20 equiv), LiBr (86.9 mg, 1.00 mmol, 5.00 equiv), a solution of lactam **1b** (82.1 mg, 0.400 mmol, 2.00 equiv) in toluene (1.0 mL) and THF (0.2 mL), bromobenzene (**3b**, 31.5 μL, 0.300 mmol, 1.50 equiv), and *p*-tolunitrile **2a** (23.4 mg, 0.200 mmol, 1.00 equiv). To a separate oven-dried 4 mL vial equipped with a stir bar was added $Ni(COD)_2$ (5.50 mg, 0.0200 mmol, 0.100 equiv), SL-M004-1 (Solvias, 25.3 mg, 0.0240 mmol, 0.120 equiv), and toluene (1.0 mL). Both the lactam suspension and the Ni/ligand solution were stirred at ambient temperature for several minutes and then cooled to 4 °C. The Ni/ligand solution was added to the lactam suspension at 4 °C, and the vial was closed with a PTFE-lined septum cap. *Note*: *Although this effect has not yet been studied in detail, we have observed lower yields when the vial containing the lactam suspension was first closed with a PTFE-lined septum cap, and then the catalyst solution was added through the septum cap.* The reaction mixture was stirred at 4 °C for 48 h and then removed from the glovebox. EtOAc (6 mL) and 1 M HCl aqueous solution (5 mL) were added and the mixture was stirred at ambient temperature for 1 h. The reaction mixture was extracted with EtOAc (24 mL), washed with brine (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:5 EtOAc:hexanes) on silica gel to give lactam **6** as a white solid (59.4 mg, 92% yield, 91% ee). $[\alpha]_D^{25}$ +2.1° (c 1.03, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 2H), 7.33 – 7.20 (m, 4H), 7.03 – 6.95 (m, 2H), 3.94 – 3.87 (m, 1H), 3.85 (s, 3H), 3.84 – 3.78 (m, 1H), 2.94 (ddd, *J* = 12.9, 8.4, 6.4 Hz, 1H), 2.40 (s, 3H), 2.07 (ddd, *J* = 12.8, 8.0, 4.8 Hz, 1H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.4, 174.9, 155.0, 143.2, 133.0, 129.6, 128.98, 128.97, 128.4, 126.9, 120.9, 112.1, 56.6, 55.7, 47.1, 32.5, 21.62, 21.61; IR (Neat Film NaCl) 2973, 2929, 1701, 1696, 1606, 1503, 1459, 1408, 1272, 1255, 1185, 1121, 1023, 1009, 970, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_3$ $[M+H]^+$: 324.1594, found 324.1599.

Spectroscopic Data for Ni-Catalyzed *C*-Acylation Products

(*S*)-3-Benzoyl-1-(4-methoxyphenyl)-3-methylpyrrolidin-2-one (4a)



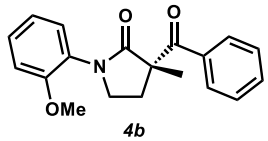
4a

Lactam **4a** was prepared according to the general procedure 3 from **1a** using benzonitrile in place of *p*-tolunitrile, reacting at ambient temperature for 24 h in place of 0 °C for 48 h, and isolated by flash column chromatography (1:10 EtOAc:hexanes) on silica gel as a white solid. 79.9 mg, 86% yield, 88% ee.

Gram-scale reaction

In a nitrogen-filled glovebox, to a solution of LHMDS (1.00 g, 6.00 mmol, 1.20 equiv) in toluene (10 mL) at 23 °C, was slowly added a solution of **1a** (1.33 g, 6.50 mmol, 1.30 equiv) in toluene (13 mL). The flask containing the solution of **1a** was then rinsed with toluene (2 mL), and the rinse was added to the LHMDS/**1a** solution. LiBr (2.17 g, 25.0 mmol, 5.00 equiv) was dissolved in THF (5 mL) and then added to the reaction mixture, followed by benzonitrile (515 μL, 5.00 mmol, 1.00 equiv) and bromobenzene (785 μL, 7.50 mmol, 1.50 equiv). Then, a solution of $Ni(COD)_2$ (138 mg, 0.500 mmol, 0.100 equiv) and SL-M004-1 (632 mg, 0.600 mmol, 1.20 equiv) in toluene (23 mL) was added slowly, followed by a 2 mL toluene rinse. The reaction mixture was stirred at 23 °C for 45 h. The reaction mixture was then removed from the glovebox, EtOAc (150 mL) and 1 M HCl aqueous solution (125 mL) were added, and the mixture was stirred at ambient temperature for 1 h. The reaction mixture was extracted with EtOAc (200 mL), washed with brine (100 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:3 EtOAc:hexanes) on silica gel to give lactam **4a** as an off-white solid. 1.06 g, 69% yield, 90% ee. $[\alpha]_D^{25}$ –27.1° (c 1.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 2H), 7.58 – 7.47 (m, 3H), 7.46 – 7.38 (m, 2H), 6.96 – 6.87 (m, 2H), 3.95 (ddd, *J* = 9.5, 7.9, 6.1 Hz, 1H), 3.86 (ddd, *J* = 9.6, 8.2, 5.1 Hz, 1H), 3.82 (s, 3H), 2.93 (ddd, *J* = 13.0, 8.0, 5.1 Hz, 1H), 2.08 (ddd, *J* = 12.9, 8.3, 6.1 Hz, 1H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 173.3, 157.0, 136.0, 132.58, 132.56, 129.3, 128.5, 121.9, 114.3, 58.4, 55.6, 46.7, 31.8, 22.1; IR (Neat Film NaCl) 1685, 1512, 1399, 1268, 1249, 1182, 1090, 1032, 970, 830, 702 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{20}NO_3$ $[M+H]^+$: 310.1438, found 310.1442.

(*S*)-3-Benzoyl-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (4b)

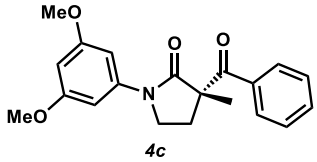


4b

Lactam **4b** was prepared according to the general procedure 3 from **1b** using benzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography

(1:5 EtOAc:hexanes) on silica gel as a white solid. 50.3 mg, 81% yield, 92% ee. $[\alpha]_D^{25}$ +4.0° (c 1.21, $CHCl_3$, 92% ee); ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 – 8.11 (m, 2H), 7.56 – 7.48 (m, 1H), 7.47 – 7.40 (m, 2H), 7.34 – 7.25 (m, 2H), 7.04 – 6.95 (m, 2H), 3.90 (ddd, *J* = 9.6, 8.4, 4.8 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.85 (s, 3H), 2.95 (ddd, *J* = 12.9, 8.4, 6.3 Hz, 1H), 2.08 (ddd, *J* = 12.8, 8.0, 4.8 Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.9, 174.7, 155.0, 135.8, 132.4, 129.4, 129.0, 128.3, 128.3, 126.8, 121.0, 112.1, 56.8, 55.7, 47.1, 32.4, 21.6; IR (Neat Film NaCl) 2974, 2930, 1701, 1697, 1596, 1503, 1459, 1410, 1305, 1270, 1256, 1121, 1023, 1010, 970, 750, 702 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{20}NO_3$ $[M+H]^+$: 310.1438, found 310.1441.

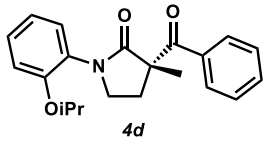
(*S*)-3-Benzoyl-1-(3,5-dimethoxyphenyl)-3-methylpyrrolidin-2-one (4c)



4c

Lactam **4c** was prepared according to the general procedure 3 from **1c** using benzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white solid. 54.5 mg, 80% yield, 85% ee. $[\alpha]_D^{25}$ –30.0° (c 1.04, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 2H), 7.55 – 7.48 (m, 1H), 7.47 – 7.38 (m, 2H), 6.92 (d, *J* = 2.2 Hz, 2H), 6.31 (t, *J* = 2.2 Hz, 1H), 3.97 (ddd, *J* = 9.6, 8.0, 6.0 Hz, 1H), 3.87 (ddd, *J* = 9.6, 8.3, 5.1 Hz, 1H), 3.81 (s, 6H), 2.92 (ddd, *J* = 13.1, 8.0, 5.2 Hz, 1H), 2.07 (ddd, *J* = 12.9, 8.3, 6.0 Hz, 1H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.6, 173.8, 160.9, 141.0, 135.7, 132.6, 129.2, 128.4, 98.3, 97.1, 58.7, 55.5, 46.4, 31.4, 22.0; IR (Neat Film NaCl) 2937, 2840, 1696, 1598, 1480, 1393, 1277, 1249, 1206, 1156, 1067, 972, 834, 722, 699, 682, 661 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_4$ $[M+H]^+$: 340.1543, found 340.1552.

(*S*)-3-Benzoyl-1-(2-isopropoxyphenyl)-3-methylpyrrolidin-2-one (4d)

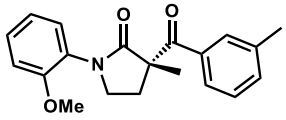


4d

Lactam **4d** was prepared according to the general procedure 3 from **1d** using benzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white solid. 46.7 mg, 69% yield, 86% ee. $[\alpha]_D^{25}$ +9.4° (c 1.01, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.14 (m, 2H), 7.59 – 7.51 (m, 1H), 7.51 – 7.43 (m, 2H), 7.35 – 7.26 (m, 2H), 7.06 – 6.97 (m, 2H), 4.63 (hept, *J* = 6.1 Hz, 1H), 3.98 (ddd, *J* = 9.5, 8.2, 4.9 Hz, 1H), 3.85 (ddd, *J* = 9.6, 8.0, 6.3 Hz, 1H), 3.00 (ddd, *J* = 12.8, 8.2, 6.3 Hz, 1H), 2.10 (ddd, *J* = 12.8, 8.0, 4.9 Hz, 1H), 1.73 (s, 3H), 1.36 (d, *J* = 6.0 Hz, 3H), 1.35 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 174.5, 153.2, 135.9, 132.4, 129.4, 128.8, 128.8, 128.3, 127.7, 120.6, 114.1, 70.4, 56.9, 47.2, 32.6, 22.1, 22.1, 21.6; IR (Neat Film NaCl) 2977, 2930, 1697,

1596, 1500, 1455, 1407, 1281, 1270, 1255, 1124, 954, 750, 701cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{24}NO_3$ $[M+H]^+$: 338.1751, found 338.1744.

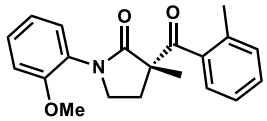
(*S*)-1-(2-Methoxyphenyl)-3-methyl-3-(3-methylbenzoyl)pyrrolidin-2-one (7)



7

Lactam **7** was prepared according to the general procedure 3 from **1b** using *m*-tolunitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 59.1 mg, 91% yield, 93% ee. $[\alpha]_D^{25}$ +5.5° (c 0.52, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 1H), 7.89 – 7.88 (m, 1H), 7.33 – 7.26 (m, 4H), 7.04 – 6.95 (m, 2H), 3.90 (ddd, *J* = 9.6, 8.4, 4.7 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.84 (s, 3H), 2.93 (ddd, *J* = 12.9, 8.4, 6.5 Hz, 1H), 2.40 (s, 3H), 2.11 – 2.02 (m, 1H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 174.8, 155.06, 138.0, 135.8, 133.1, 129.8, 129.0, 128.3, 128.1, 126.9, 126.5, 121.0, 112.1, 56.8, 55.7, 47.1, 32.4, 21.6, 21.5; IR (Neat Film NaCl) 2973, 2931, 1694, 1598, 1504, 1455, 1409, 1276, 1255, 1182, 1121, 1092, 1044, 1024, 976, 905, 789, 754, cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_3$ $[M+H]^+$: 324.1594, found 324.1602.

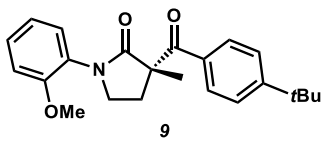
(*S*)-1-(2-Methoxyphenyl)-3-methyl-3-(2-methylbenzoyl)pyrrolidin-2-one (8)



8

Lactam **8** was prepared according to the general procedure 3 from **1b** using *o*-tolunitrile in place of *p*-tolunitrile, reacting with aqueous HCl at 70 °C in place of ambient temperature, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 44.9 mg, 69% yield, 94% ee. $[\alpha]_D^{25}$ –29.6° (c 0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.34 – 7.25 (m, 2H), 7.25 – 7.16 (m, 3H), 7.01 – 6.93 (m, 2H), 3.82 (s, 3H), 3.73 (dd, *J* = 7.6, 6.3 Hz, 2H), 2.82 – 2.73 (m, 1H), 2.33 (s, 3H), 2.14 – 2.05 (m, 1H), 1.59 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.5, 173.8, 154.9, 139.1, 135.6, 130.9, 129.7, 128.9, 128.4, 126.9, 126.0, 125.2, 120.9, 112.1, 58.4, 55.6, 47.2, 31.9, 21.3, 20.1; IR (Neat Film NaCl) 2971, 2932, 1694, 1597, 1505, 1456, 1409, 1305, 1281, 1256, 1122, 1045, 1025, 969, 755 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_3$ $[M+H]^+$: 324.1594, found 324.1601.

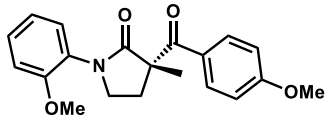
(*S*)-3-(4-(*tert*-Butyl)benzoyl)-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (9)



9

Lactam **9** was prepared according to the general procedure 3 from **1b** using 4-(*tert*-butyl)benzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white solid. 64.7 mg, 89% yield, 92% ee. $[\alpha]_D^{25}$ +6.9° (c 1.04, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.07 (m, 2H), 7.47 – 7.41 (m, 2H), 7.33 – 7.25 (m, 2H), 7.04 – 6.95 (m, 2H), 3.93 – 3.80 (m, 2H), 3.85 (s, 3H), 2.96 (ddd, *J* = 12.9, 8.4, 6.5 Hz, 1H), 2.08 (ddd, *J* = 12.8, 7.9, 4.8 Hz, 1H), 1.69 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.2, 175.0, 156.0, 155.0, 132.7, 129.5, 128.9, 128.4, 126.9, 125.2, 120.9, 112.1, 56.6, 55.7, 47.1, 35.0, 32.5, 31.1, 21.6; IR (Neat Film NaCl) 2963, 1701, 1676, 1603, 1504, 1459, 1406, 1272, 1255, 1121, 1109, 1023, 971, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{28}NO_3$ $[M+H]^+$: 366.2064, found 366.2072.

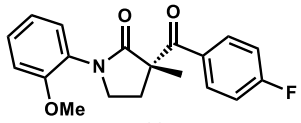
(*S*)-3-(4-Methoxybenzoyl)-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (10)



10

Lactam **10** was prepared according to the general procedure 3 from **1b** using 4-methoxybenzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 57.8 mg, 85% yield, 89% ee. $[\alpha]_D^{25}$ –3.7° (c 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 – 8.17 (m, 2H), 7.32 – 7.27 (m, 2H), 7.03 – 6.88 (m, 4H), 3.93 – 3.87 (m, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 3.83 – 3.77 (m, 1H), 2.97 (ddd, *J* = 12.8, 8.2, 6.2 Hz, 1H), 2.07 (ddd, *J* = 12.9, 8.0, 5.0 Hz, 1H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.8, 175.0, 162.9, 155.0, 132.1, 128.9, 128.3, 128.2, 127.0, 120.9, 113.4, 112.1, 56.6, 55.7, 55.4, 47.2, 32.7, 21.8; IR (Neat Film NaCl) 2971, 2933, 1695, 1600, 1504, 1464, 1456, 1410, 1307, 1259, 1174, 1027, 971, 845, 754, 699, 610 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_4$ $[M+H]^+$: 340.1543, found 340.1547.

(*S*)-3-(4-Fluorobenzoyl)-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (11)

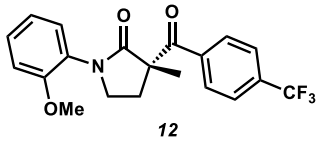


11

Lactam **11** was prepared according to the general procedure 3 from **1b** using 4-fluorobenzonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white solid. 23.3 mg, 36% yield, 93% ee. $[\alpha]_D^{25}$ –1.8° (c 0.77, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 – 8.20 (m, 2H), 7.34 – 7.27 (m, 1H), 7.27 – 7.20 (m, 1H), 7.14 – 7.06 (m, 2H), 7.04 – 6.95 (m, 2H), 3.91 (ddd, *J* = 9.6, 8.3, 5.0 Hz, 1H), 3.83 (s, 3H), 3.80 (ddd, *J* = 9.6, 8.1, 6.2 Hz, 1H), 2.95 (ddd, *J* = 12.8, 8.3, 6.1 Hz, 1H), 2.12 – 2.03 (m, 1H), 1.68 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.1, 174.5, 165.2 (d, *J* = 254.2 Hz), 154.9, 132.4 (d, *J* = 9.1 Hz), 131.9, 129.1, 128.3, 126.7, 121.0, 115.3 (d, *J* = 21.6 Hz), 112.1, 56.9, 55.7, 47.2, 32.5, 21.7; IR (Neat Film NaCl) 2974, 1697, 1684, 1597, 1506, 1457,

1410, 1271, 1256, 1235, 1160, 1024, 972, 848, 754, 609 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{19}FNO_3$ $[M+H]^+$: 328.1343, found 328.1353.

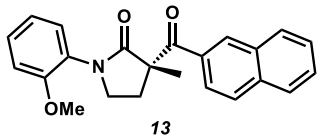
(*S*)-1-(2-Methoxyphenyl)-3-methyl-3-(4-(trifluoromethyl)benzoyl)pyrrolidin-2-one (12)



12

Lactam **12** was prepared according to the general procedure 3 from **1b** using 4-trifluoromethylbenzonitrile in place of *p*-tolunitrile, reacting at ambient temperature for 24 h in place of 0 °C for 48 h, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 21.5 mg, 23% yield, 87% ee. $[\alpha]_D^{25}$ +2.7° (c 0.71, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 – 8.22 (m, 2H), 7.78 – 7.61 (m, 2H), 7.35 – 7.29 (m, 1H), 7.24 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.05 – 6.95 (m, 2H), 3.91 (ddd, *J* = 9.7, 8.3, 5.0 Hz, 1H), 3.84 (s, 3H), 3.83 – 3.77 (m, 1H), 2.93 (ddd, *J* = 12.9, 8.3, 6.2 Hz, 1H), 2.09 (ddd, *J* = 13.0, 8.0, 5.0 Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.4, 174.1, 154.9, 139.0, 133.6 (q, *J* = 32.7 Hz), 129.7, 129.2, 128.3, 126.6, 125.3 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 272.5 Hz), 121.0, 112.1, 57.2, 55.7, 47.2, 32.1, 21.5; IR (Neat Film NaCl) 2975, 2934, 1697, 1505, 1409, 1328, 1316, 1257, 1169, 1127, 1068, 1020, 1009, 973, 858, 753; cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{19}F_3NO_3$ $[M+H]^+$: 378.1312, found 378.1325.

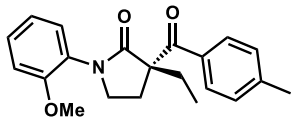
(*S*)-3-(2-Naphthoyl)-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (13)



13

Lactam **13** was prepared according to the general procedure 3 from **1b** using 2-naphthonitrile in place of *p*-tolunitrile, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 47.5 mg, 66% yield, 91% ee. $[\alpha]_D^{25}$ +15.8° (c 0.52, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 1.3 Hz, 1H), 8.14 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.98 – 7.92 (m, 1H), 7.87 (t, *J* = 8.4 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.56 – 7.49 (m, 1H), 7.35 – 7.27 (m, 2H), 7.06 – 6.97 (m, 2H), 3.96 (ddd, *J* = 9.6, 8.3, 4.9 Hz, 1H), 3.90 – 3.81 (m, 1H), 3.84 (s, 3H), 3.04 (ddd, *J* = 12.9, 8.3, 6.2 Hz, 1H), 2.17 – 2.08 (m, 1H), 1.75 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.9, 174.7, 155.0, 135.1, 133.0, 132.4, 131.1, 129.8, 129.0, 128.3, 128.3, 128.0, 127.6, 127.0, 126.5, 125.4, 121.0, 112.2, 57.1, 55.7, 47.2, 32.6, 21.8; IR (Neat Film NaCl) 2930, 1694, 1505, 1463, 1409, 1281, 1255, 1120, 1024, 750 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1594, found 360.1589.

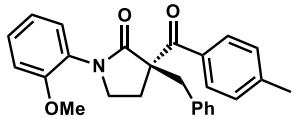
(*S*)-3-Ethyl-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (14)



14

Lactam **14** was prepared according to the general procedure 3 from **SI6**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 33.9 mg, 50% yield, 78% ee. $[\alpha]_D^{25}$ +14.6° (c 0.81, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.3 Hz, 2H), 7.31 – 7.18 (m, 4H), 7.01 – 6.92 (m, 2H), 3.90 (ddd, *J* = 9.5, 8.1, 6.7 Hz, 1H), 3.79 (s, 3H), 3.71 (ddd, *J* = 9.5, 8.7, 4.3 Hz, 1H), 2.95 (ddd, *J* = 13.0, 8.0, 4.2 Hz, 1H), 2.41 – 2.30 (m, 4H), 2.17 – 2.05 (m, 2H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 173.5, 154.9, 143.0, 134.0, 129.5, 128.9, 128.9, 128.4, 127.1, 120.9, 112.1, 61.8, 55.6, 47.5, 29.5, 29.1, 21.6, 8.8; IR (Neat Film NaCl) 2962, 1700, 1606, 1504, 1461, 1253, 1159, 1024, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{24}NO_3$ $[M+H]^+$: 338.1751, found 338.1753.

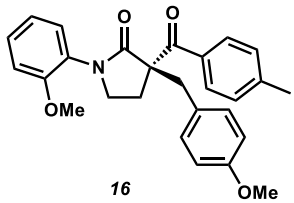
(*S*)-3-Benzyl-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (15)



15

Lactam **15** was prepared according to the general procedure 3 from **SI7**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 48.8 mg, 61% yield, 81% ee. $[\alpha]_D^{25}$ +62.3° (c 0.90, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.06 (m, 2H), 7.31 – 7.16 (m, 8H), 6.93 – 6.83 (m, 3H), 3.77 (s, 3H), 3.62 (td, *J* = 9.1, 4.1 Hz, 1H), 3.53 (d, *J* = 13.7 Hz, 1H), 3.34 (d, *J* = 13.7 Hz, 1H), 2.90 – 2.72 (m, 2H), 2.37 (s, 3H), 2.26 (ddd, *J* = 13.0, 8.4, 4.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 173.1, 154.9, 143.2, 136.7, 133.3, 130.6, 129.7, 129.0, 128.9, 128.4, 127.9, 126.9, 126.7, 120.8, 112.0, 61.4, 55.6, 47.0, 40.9, 28.7, 21.7; IR (Neat Film NaCl) 2928, 1696, 1604, 1502, 1457, 1405, 1240, 1185, 1025, 741, 702 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{26}H_{26}NO_3$ $[M+H]^+$: 400.1907, found 400.1919.

(*S*)-3-(4-Methoxybenzyl)-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (16)

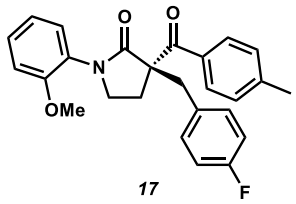


16

Lactam **16** was prepared according to the general procedure 3 from **SI8**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 65.8 mg, 77% yield, 81% ee. $[\alpha]_D^{25}$ +50.4° (c 1.21, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 – 8.09 (m, 2H), 7.30 – 7.18 (m, 5H), 6.99 (dd, *J* = 8.0, 1.8 Hz, 1H),

6.98 – 6.88 (m, 2H), 6.88 – 6.80 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.67 (td, *J* = 9.2, 4.2 Hz, 1H), 3.51 (d, *J* = 13.9 Hz, 1H), 3.32 (d, *J* = 13.9 Hz, 1H), 2.95 (ddd, *J* = 9.4, 8.6, 6.5 Hz, 1H), 2.80 (ddd, *J* = 13.3, 9.0, 6.4 Hz, 1H), 2.40 (s, 3H), 2.27 (ddd, *J* = 13.0, 8.6, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 173.2, 158.7, 154.9, 143.1, 133.4, 131.5, 129.7, 129.0, 128.8, 128.6, 127.9, 126.7, 120.8, 113.7, 112.0, 61.5, 55.6, 55.3, 47.0, 40.1, 28.7, 21.6; IR (Neat Film NaCl) 2930, 1694, 1606, 1505, 1463, 1409, 1301, 1248, 1180, 1028, 832, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{27}H_{28}NO_4$ $[M+H]^+$: 430.2013, found 430.2006.

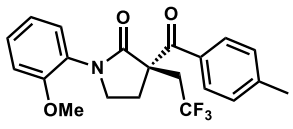
(*S*)-3-(4-Fluorobenzyl)-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (17)



17

Lactam **17** was prepared according to the general procedure 3 from **SI9**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white foam. 63.5 mg, 76% yield, 74% ee. $[\alpha]_D^{25}$ +38.9° (c 3.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 – 8.08 (m, 2H), 7.31 – 7.21 (m, 5H), 7.04 – 6.91 (m, 5H), 3.79 (s, 3H), 3.67 (td, *J* = 9.3, 4.4 Hz, 1H), 3.54 (d, *J* = 13.9 Hz, 1H), 3.34 (d, *J* = 13.9 Hz, 1H), 3.00 (ddd, *J* = 9.5, 8.7, 6.3 Hz, 1H), 2.81 (ddd, *J* = 13.4, 9.1, 6.3 Hz, 1H), 2.41 (s, 3H), 2.26 (ddd, *J* = 13.3, 8.7, 4.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 172.9, 162.1 (d, *J* = 245.2 Hz), 154.8, 143.3, 133.2, 132.4 (d, *J* = 3.4 Hz), 132.0 (d, *J* = 7.7 Hz), 129.6, 129.1, 128.9, 127.8, 126.5, 120.9, 115.2 (d, *J* = 21.1 Hz), 112.0, 61.4, 55.6, 47.0, 40.1, 28.6, 21.7; IR (Neat Film NaCl) 2931, 1697, 1604, 1504, 1465, 1410, 1222, 1185, 1026, 909, 833, 752, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{26}H_{25}FNO_3$ $[M+H]^+$: 418.1813, found 418.1806.

(*R*)-1-(2-Methoxyphenyl)-3-(4-methylbenzoyl)-3-(2,2,2-trifluoroethyl)pyrrolidin-2-one (18)

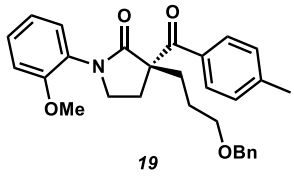


18

Lactam **18** was prepared according to the general procedure 3 from **SI10**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 45.5 mg, 58% yield, 71% ee. $[\alpha]_D^{25}$ +10.3° (c 2.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 – 8.09 (m, 2H), 7.34 – 7.28 (m, 1H), 7.28 – 7.17 (m, 3H), 7.03 – 6.92 (m, 2H), 4.00 (ddd, *J* = 9.6, 7.7, 6.8 Hz, 1H), 3.78 (s, 3H), 3.72 (ddd, *J* = 9.6, 8.7, 3.9 Hz, 1H), 3.34 (dq, *J* = 15.8, 11.1 Hz, 1H), 3.10 – 3.01 (m, 1H), 2.87 (dq, *J* = 15.7, 11.1 Hz, 1H), 2.40 (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 171.5, 154.9, 143.6, 133.2, 129.7, 129.4, 129.3, 128.2, 126.6, 126.5 (q, *J* = 277.8 Hz), 121.1, 112.1, 57.8, 55.7, 47.7, 39.1 (q, *J* = 28.3 Hz), 29.2, 21.8; IR (Neat Film NaCl) 2952, 1703, 1673,

1505, 1464, 1373, 1299, 1260, 1143, 1021, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{21}F_3NO_3$ $[M+H]^+$: 392.1468, found 392.1459.

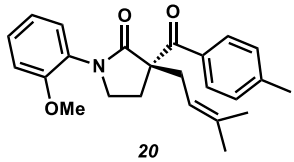
(*S*)-3-(3-(Benzyloxy)propyl)-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin -2-one (19)



19

Lactam **19** was prepared according to the general procedure 3 from **SI11**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a colorless oil. 61.6 mg, 67% yield, 60% ee. $[\alpha]_D^{25}$ +9.3° (c 2.90, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 – 8.10 (m, 2H), 7.35 – 7.27 (m, 6H), 7.25 – 7.19 (m, 3H), 7.01 – 6.92 (m, 2H), 4.45 (d, *J* = 2.3 Hz, 2H), 3.88 (ddd, *J* = 9.5, 8.0, 6.6 Hz, 1H), 3.77 (s, 3H), 3.76 – 3.66 (m, 1H), 3.46 (td, *J* = 6.4, 1.1 Hz, 2H), 2.95 (ddd, *J* = 12.6, 8.0, 4.3 Hz, 1H), 2.44 – 2.36 (m, 4H), 2.19 – 2.07 (m, 2H), 1.77 – 1.58 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 173.4, 154.9, 143.0, 138.5, 133.8, 129.5, 128.9, 128.9, 128.4, 128.3, 127.6, 127.5, 127.0, 120.9, 112.0, 72.8, 70.3, 61.1, 55.6, 47.5, 32.8, 30.0, 24.8, 21.6; IR (Neat Film NaCl) 2935, 1698, 1606, 1504, 1455, 1408, 1302, 1279, 1252, 1185, 1101, 1027, 750, 699 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{29}H_{32}NO_4$ $[M+H]^+$: 458.2326, found 458.2315.

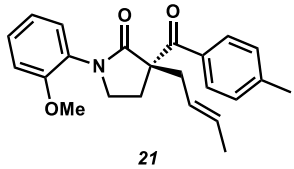
(*S*)-1-(2-Methoxyphenyl)-3-(4-methylbenzoyl)-3-(3-methylbut-2-en-1-yl) pyrrolidin-2-one (20)



20

Lactam **20** was prepared according to the general procedure 3 from **SI12**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 53.2 mg, 71% yield, 76% ee. $[\alpha]_D^{25}$ +29.6° (c 2.15, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.07 (m, 2H), 7.32 – 7.25 (m, 2H), 7.25 – 7.18 (m, 2H), 7.02 – 6.92 (m, 2H), 5.23 – 5.15 (m, 1H), 3.88 (ddd, *J* = 9.5, 8.5, 5.7 Hz, 1H), 3.83 (s, 3H), 3.68 (ddd, *J* = 9.4, 8.7, 5.1 Hz, 1H), 3.02 – 2.93 (m, 1H), 2.89 – 2.73 (m, 2H), 2.39 (s, 3H), 2.14 (ddd, *J* = 13.0, 8.7, 5.7 Hz, 1H), 1.72 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.2, 173.5, 155.0, 142.9, 135.5, 133.8, 129.5, 128.9, 128.9, 128.3, 127.1, 120.9, 118.6, 112.1, 61.1, 55.6, 47.5, 34.5, 29.2, 26.1, 21.6, 18.0; IR (Neat Film NaCl) 2917, 1698, 1606, 1504, 1463, 1408, 1248, 1184, 1123, 1024, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{24}H_{28}NO_3$ $[M+H]^+$: 378.2064, found 378.2060.

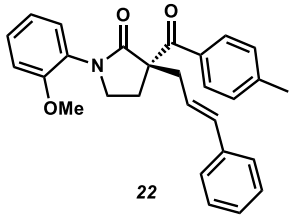
(*S*,*E*)-3-(But-2-en-1-yl)-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (21)



21

Lactam **21** was prepared according to the general procedure 3 from **SI13**, and isolated by flash column chromatography (1:8 EtOAc:hexanes) on silica gel as a pale yellow oil. 51.0 mg, 70% yield, 86% ee. $[\alpha]_D^{25}$ +45.5° (c 2.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.19 (m, 4H), 7.03 – 6.94 (m, 2H), 5.63 – 5.43 (m, 2H), 3.92 – 3.86 (m, 1H), 3.84 (s, 3H), 3.73 – 3.62 (m, 1H), 2.94 – 2.72 (m, 3H), 2.39 (s, 3H), 2.20 (ddd, *J* = 13.2, 8.7, 5.3 Hz, 1H), 1.68 (dq, *J* = 6.3, 1.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 173.5, 155.0, 143.0, 133.7, 129.8, 129.5, 129.5, 128.9, 128.3, 127.0, 125.4, 120.9, 112.1, 60.7, 55.6, 47.4, 39.1, 28.9, 21.6, 18.2; IR (Neat Film NaCl) 2917, 1698, 1606, 1504, 1463, 1408, 1254, 1185, 1122, 1045, 1024, 973, 837, 750 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{26}NO_3$ $[M+H]^+$: 364.1907, found 364.1909.

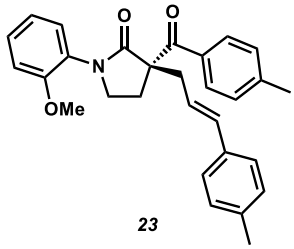
(*S*)-3-Cinnamyl-1-(2-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolidin-2-one (22)



22

Lactam **22** was prepared according to the general procedure 3 from **SI14**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white foam. 51.1 mg, 60% yield, 86% ee. $[\alpha]_D^{25}$ +55.5° (c 0.93, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.06 (m, 2H), 7.37 – 7.34 (m, 2H), 7.32 – 7.27 (m, 3H), 7.26 – 7.20 (m, 4H), 6.99 – 6.94 (m, 2H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.29 (dt, *J* = 15.5, 7.6 Hz, 1H), 3.91 – 3.85 (m, 1H), 3.80 (s, 3H), 3.75 (ddd, *J* = 9.6, 8.7, 5.7 Hz, 1H), 3.08 – 3.03 (m, 2H), 2.85 (ddd, *J* = 13.3, 8.9, 5.8 Hz, 1H), 2.41 (s, 3H), 2.30 (ddd, *J* = 13.5, 8.7, 5.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 173.3, 155.0, 143.1, 137.3, 134.2, 133.5, 129.4, 129.0, 129.0, 128.5, 128.3, 127.4, 126.8, 126.2, 124.8, 121.0, 112.1, 60.7, 55.6, 47.3, 39.4, 28.8, 21.6; IR (Neat Film NaCl) 2961, 1698, 1606, 1504, 1463, 1409, 1279, 1255, 1185, 1025, 971, 911, 742, 694 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{28}H_{28}NO_3$ $[M+H]^+$: 426.2064, found 426.2067.

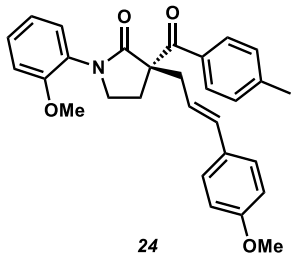
(*S*,*E*)-1-(2-Methoxyphenyl)-3-(4-methylbenzoyl)-3-(3-(p-tolyl)allyl)pyrrolidin-2-one (23)



23

Lactam **23** was prepared according to the general procedure 3 from **SI15**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 74.2 mg, 85% yield, 88% ee. $[\alpha]_D^{25}$ +56.0° (c 2.93, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.25 (m, 2H), 7.25 – 7.19 (m, 4H), 7.14 – 7.08 (m, 2H), 7.00 – 6.93 (m, 2H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.23 (dt, *J* = 15.5, 7.6 Hz, 1H), 3.92 – 3.83 (m, 1H), 3.81 (s, 3H), 3.78 – 3.69 (m, 1H), 3.04 (d, *J* = 7.6 Hz, 2H), 2.85 (ddd, *J* = 13.2, 8.9, 5.8 Hz, 1H), 2.40 (s, 3H), 2.39 – 2.25 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 173.4, 155.0, 143.1, 137.1, 134.5, 134.0, 133.5, 129.4, 129.2, 129.0, 129.0, 128.3, 126.8, 126.1, 123.6, 121.0, 112.0, 60.7, 55.6, 47.4, 39.4, 28.8, 21.6, 21.2; IR (Neat Film NaCl) 2920, 1694, 1606, 1505, 1463, 1409, 1279, 1254, 1184, 1121, 1045, 1025, 974, 911, 838, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{29}H_{30}NO_3$ $[M+H]^+$: 440.2220, found 440.2220.

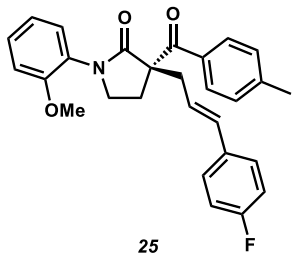
(*S*,*E*)-1-(2-Methoxyphenyl)-3-(3-(4-methoxyphenyl)allyl)-3-(4-methylbenzoyl) pyrrolidin-2-one (24)



24

Lactam **24** was prepared according to the general procedure 3 from **SI16**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a white foam. 62.0 mg, 68% yield, 88% ee. $[\alpha]_D^{25}$ +57.6° (c 1.09, $CHCl_3$, 88% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 – 8.05 (m, 2H), 7.34 – 7.26 (m, 3H), 7.26 – 7.17 (m, 3H), 7.00 – 6.93 (m, 2H), 6.87 – 6.81 (m, 2H), 6.46 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 15.5, 7.5 Hz, 1H), 3.88 (td, *J* = 9.2, 4.9 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.80 – 3.67 (m, 1H), 3.03 (dt, *J* = 7.6, 1.4 Hz, 2H), 2.85 (ddd, *J* = 13.2, 8.9, 5.8 Hz, 1H), 2.40 (s, 3H), 2.35 – 2.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 173.4, 159.0, 155.0, 143.1, 133.5, 130.1, 129.4, 129.0, 128.9, 128.3, 127.4, 126.8, 122.4, 121.0, 113.9, 112.1, 60.8, 55.6, 55.3, 47.4, 39.4, 28.8, 21.6; IR (Neat Film NaCl) 2957, 1699, 1607, 1505, 1464, 1249, 1175, 1027, 838, 752 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{29}H_{30}NO_4$ $[M+H]^+$: 456.2169, found 456.2164.

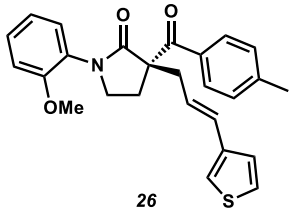
(*S*,*E*)-3-(3-(4-Fluorophenyl)allyl)-1-(2-methoxyphenyl)-3-(4-methylbenzoyl) pyrrolidin-2-one (25)



25

Lactam **25** was prepared according to the general procedure 3 from **SI17**, and isolated by flash column chromatography (1:10 EtOAc:hexanes) on silica gel as a white foam. 55.3 mg, 62% yield, 83% ee. $[\alpha]_D^{25}$ +40.7° (c 0.55, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.05 (m, 2H), 7.34 – 7.27 (m, 3H), 7.25 – 7.19 (m, 3H), 7.02 – 6.94 (m, 4H), 6.51 – 6.44 (m, 1H), 6.20 (dt, *J* = 15.5, 7.6 Hz, 1H), 3.88 (ddd, *J* = 9.6, 8.9, 5.0 Hz, 1H), 3.79 (s, 3H), 3.78 – 3.71 (m, 1H), 3.09 – 2.99 (m, 2H), 2.86 (ddd, *J* = 13.3, 8.9, 5.7 Hz, 1H), 2.41 (s, 3H), 2.37 – 2.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 13C NMR (126 MHz, Chloroform-d) δ 197.9, 173.4, 162.3 (d, *J* = 246.6 Hz), 155.1, 143.3, 133.59 (d, *J* = 2.1 Hz), 133.56, 133.1, 129.6, 129.2, 129.1, 128.3, 127.8 (d, *J* = 7.8 Hz), 126.9, 124.7 (d, *J* = 2.2 Hz), 121.1, 115.6 (d, *J* = 21.6 Hz), 112.2, 60.8, 55.8, 47.5, 39.5, 29.1, 21.8; IR (Neat Film NaCl) 2944, 1693, 1604, 1505, 1460, 1412, 1254, 1228, 1184, 1158, 1045, 1024, 910, 838, 753, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{28}H_{27}FNO_3$ $[M+H]^+$: 444.1969, found 444.1969.

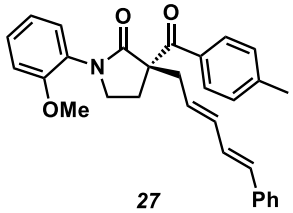
(*S*,*E*)-1-(2-Methoxyphenyl)-3-(4-methylbenzoyl)-3-(3-(thiophen-3-yl)allyl) pyrrolidin-2-one (26)



26

Lactam **26** was prepared according to the general procedure 3 from **SI18**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 65.2 mg, 76% yield, 83% ee. $[\alpha]_D^{25}$ +46.7° (c 1.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.01 (m, 2H), 7.33 – 7.14 (m, 6H), 7.10 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.53 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 15.5, 7.6 Hz, 1H), 3.88 (td, *J* = 9.1, 4.9 Hz, 1H), 3.81 (s, 3H), 3.79 – 3.68 (m, 1H), 3.01 (dd, *J* = 7.7, 1.3 Hz, 2H), 2.85 (ddd, *J* = 13.3, 8.9, 5.8 Hz, 1H), 2.40 (s, 3H), 2.28 (ddd, *J* = 13.5, 8.8, 5.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 173.3, 155.0, 143.2, 139.9, 133.4, 129.4, 129.0, 129.0, 128.4, 128.2, 126.8, 126.0, 125.0, 124.6, 121.5, 121.0, 112.1, 60.7, 55.6, 47.3, 39.3, 28.8, 21.6; IR (Neat Film NaCl) 2958, 1698, 1606, 1504, 1463, 1409, 1302,1279, 1254, 1184, 1122, 1024, 967, 836, 753 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{26}H_{26}NO_3S$ $[M+H]^+$: 432.1628, found 432.1622.

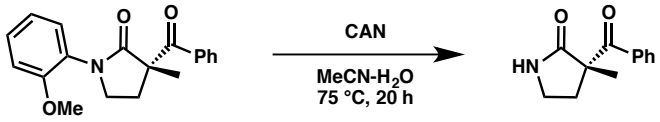
(*S*)-1-(2-Methoxyphenyl)-3-(4-methylbenzoyl)-3-((2*E*,4*E*)-5-phenylpenta-2,4-dien-1-yl)pyrrolidin-2-one (27)



27

Lactam **27** was prepared according to the general procedure 3 from **SI19**, and isolated by flash column chromatography (1:5 EtOAc:hexanes) on silica gel as a pale yellow oil. 31.7 mg, 35% yield, 84% ee. $[\alpha]_D^{25}$ +40.6° (c 1.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.06 (m, 2H), 7.43 – 7.36 (m, 2H), 7.34 – 7.27 (m, 3H), 7.26 – 7.19 (m, 4H), 7.04 – 6.93 (m, 2H), 6.76 (ddd, *J* = 15.7, 10.5, 0.9 Hz, 1H), 6.49 (d, *J* = 15.7 Hz, 1H), 6.40 – 6.27 (m, 1H), 5.87 (dt, *J* = 15.2, 7.7 Hz, 1H), 3.90 (ddd, *J* = 9.5, 8.8, 5.1 Hz, 1H), 3.85 (s, 3H), 3.77 – 3.70 (m, 1H), 3.08 – 2.93 (m, 2H), 2.86 (ddd, *J* = 13.3, 8.8, 5.6 Hz, 1H), 2.40 (s, 3H), 2.25 (ddd, *J* = 13.5, 8.7, 5.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 173.2, 155.0, 143.1, 137.3, 134.8, 133.5, 131.6, 129.5, 129.1, 129.0, 129.0, 128.7, 128.6, 128.4, 127.4, 126.8, 126.3, 121.0, 112.1, 60.8, 55.7, 47.3, 39.3, 29.0, 21.6; IR (Neat Film NaCl) 3024, 1694, 1606, 1505, 1463, 1409, 1304, 1253, 1185, 1122, 1045, 1026, 992, 910, 747, 693 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{30}H_{30}NO_3$ $[M+H]^+$: 452.2220, found 452.2220.

Procedures/Spectroscopic Data for Derivatization of C-Acylation Products

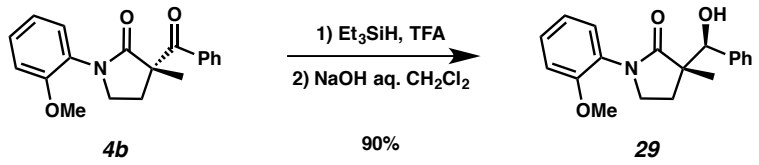


4b 75% *28*

(*S*)-3-Benzoyl-3-methylpyrrolidin-2-one (28)

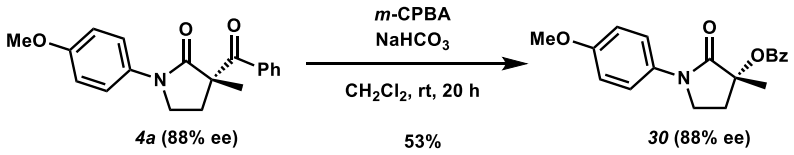
To a solution lactam **4b** (93% ee, 40.0 mg, 0.129 mmol, 1.00 equiv) in MeCN (0.6 mL) and water (0.6 mL) was added CAN (424 mg, 0.774 mmol, 6.00 equiv) and the reaction mixture was stirred at 70 °C for 24 h. The reaction mixture was allowed to cool to ambient temperature and brine (5 mL) was added. The reaction mixture was extracted with EtOAc (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:2 to 2:1 EtOAc:hexanes) on silica gel to give lactam **28** as a white solid (19.6 mg, 75% yield). $[\alpha]_D^{25}$ +25.7° (c 0.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.56 – 7.48 (m, 1H), 7.47 – 7.39 (m, 2H), 5.83 (s, 1H), 3.59 – 3.50 (m, 1H), 3.50 – 3.42 (m, 1H), 2.92 (ddd, *J* = 13.4, 8.1, 5.5 Hz, 1H), 2.08 (ddd, *J* = 13.3, 8.1, 5.5 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.1, 178.3, 135.7, 132.5, 129.1, 128.4, 55.9, 39.6, 34.5, 21.5; IR (Neat Film NaCl) 3246, 2978, 1667, 1595, 1444,

1307, 1265, 1207, 1008, 973, 782, 701, 651 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{12}H_{14}NO_2$ $[M+H]^+$: 204.1019, found 204.1015.



(*S*)-3-((*S*)-Hydroxy(phenyl)methyl)-1-(2-methoxyphenyl)-3-methylpyrrolidin-2-one (29)

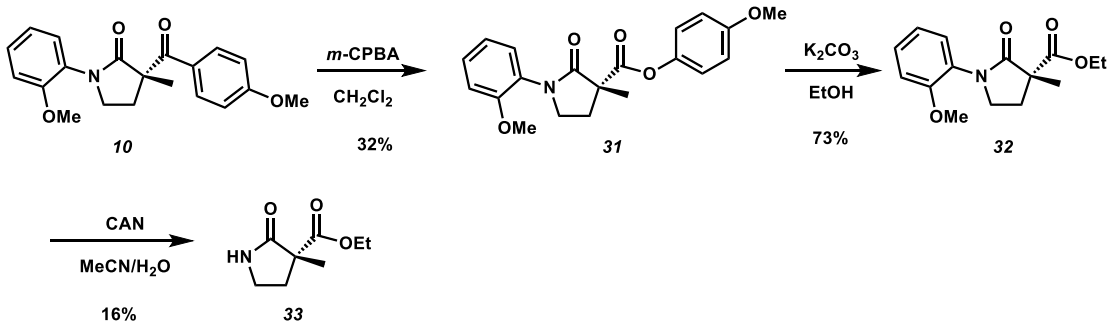
To a solution lactam **4b** (92% ee, 99.5 mg, 0.322 mmol, 1.00 equiv) in TFA (1.6 mL) was added Et_3SiH (0.102 mL, 0.643 mmol, 2.00 equiv) and the reaction mixture was stirred at ambient temperature for 24 h. CH_2Cl_2 (4 mL) and 2 M NaOH aqueous solution (8 mL) was added and the reaction mixture was stirred at ambient temperature for 3 h. The mixture was extracted with CH_2Cl_2 (30 mL, twice), washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:2 EtOAc:hexanes) on silica gel to give lactam **29** as a white solid (90.2 mg, 90% yield). $[\alpha]_D^{25}$ -12.5° (c 1.10, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H), 7.43 – 7.27 (m, 4H), 7.22 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.03 – 6.94 (m, 2H), 5.18 (br s, 1H), 4.99 (s, 1H), 3.84 (s, 3H), 3.69 (td, *J* = 9.4, 6.9 Hz, 1H), 3.54 (ddd, *J* = 9.6, 8.8, 2.2 Hz, 1H), 2.31 (dt, *J* = 12.6, 9.0 Hz, 1H), 1.54 (ddd, *J* = 12.6, 6.9, 2.2 Hz, 1H), 1.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.3, 154.8, 139.4, 129.1, 128.5, 127.9, 127.7, 127.3, 126.5, 120.9, 112.1, 77.8, 55.7, 47.3, 46.9, 30.8, 15.6; IR (Neat Film NaCl) 3400, 2966, 1672, 1596, 1504, 1459, 1413, 1305, 1281, 1256, 1180, 1161, 1121, 1082, 1046, 1026, 917, 885, 753, 725, 703, cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{22}NO_3$ $[M+H]^+$: 312.1594, found 312.1595.



(*R*)-1-(4-Methoxyphenyl)-3-methyl-2-oxopyrrolidin-3-yl benzoate (30)

To a solution lactam **4a** (88% ee, 30.9 mg, 0.100 mmol, 1.00 equiv) in CH_2Cl_2 (1 mL) and were added $NaHCO_3$ (42.0 mg, 0.500 mmol, 5.00 equiv) and *m*-CPBA (75%, 115.0 mg, 0.500 mmol, 5.00 equiv) and the reaction mixture was stirred at ambient temperature for 20 h. 10% $NaHCO_3$ aqueous solution (3 mL) and brine (3 mL) were added and the mixture was extracted with CH_2Cl_2 (30 mL, twice), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:5 EtOAc:hexanes) on silica gel to give lactam **30** as a white solid (17.1 mg, 53% yield, 88% ee). $[\alpha]_D^{25}$ –3.3° (c 0.25, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.03 (m, 2H), 7.63 – 7.53 (m, 3H), 7.47 – 7.40 (m, 2H), 6.96 – 6.89 (m, 2H), 3.96 (td, *J* = 9.6, 3.2 Hz, 1H), 3.82 (s, 4H), 2.83 – 2.74 (m, 1H), 2.40 (ddd, *J*

= 13.3, 8.1, 3.2 Hz, 1H), 1.75 (d, *J* = 0.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 165.5, 156.9, 133.2, 132.5, 129.9, 129.9, 128.3, 121.9, 114.1, 81.2, 55.5, 44.9, 30.6, 23.3; IR (Neat Film NaCl) 2963, 1705, 1512, 1451, 1403, 1317, 1292, 1251, 1136, 1116, 1091, 1072, 1032, 828, 715 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{19}H_{20}NO_4$ $[M+H]^+$: 326.1387, found 326.1381.



(*R*)-4-Methoxyphenyl-1-(2-methoxyphenyl)-3-methyl-2-oxopyrrolidine-3-carboxylate (31)

To a solution of lactam **10** (160 mg, 0.471 mmol, 1.00 equiv) in CH_2Cl_2 (9.4 mL) was added *m*-CPBA (75%, 1.08 g, 4.71 mmol, 10.0 equiv) and the reaction mixture was stirred at ambient temperature for 24 h and then refluxed for 48 h. The reaction mixture was allowed to cool to ambient temperature and 10% Na_2SO_3 aqueous solution (30 mL) and saturated $NaHCO_3$ aqueous solution (10 mL) were added. The mixture was extracted with CH_2Cl_2 (130 mL), washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:5 EtOAc:hexanes) on silica gel to give lactam **31** as a pale yellow oil (54.2 mg, 32% yield). $[\alpha]_D^{25}$ -11.7° (c 0.56, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.09 – 7.02 (m, 2H), 7.02 – 6.93 (m, 2H), 6.93 – 6.85 (m, 2H), 3.92 – 3.75 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 2.84 (ddd, *J* = 12.9, 7.8, 4.5 Hz, 1H), 2.21 (ddd, *J* = 12.9, 8.3, 6.8 Hz, 1H), 1.67 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.6, 157.3, 154.9, 144.3, 129.0, 128.6, 126.9, 122.2, 120.9, 114.4, 112.1, 55.7, 55.6, 51.8, 47.1, 32.1, 20.2; IR (Neat Film NaCl) 2936, 1760, 1699, 1597, 1505, 1463, 1410, 1305, 1251, 1193, 1112, 1088, 1027, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{22}NO_5$ $[M+H]^+$: 356.1492, found 356.1489.

(*R*)-Ethyl-1-(2-methoxyphenyl)-3-methyl-2-oxopyrrolidine-3-carboxylate (32)

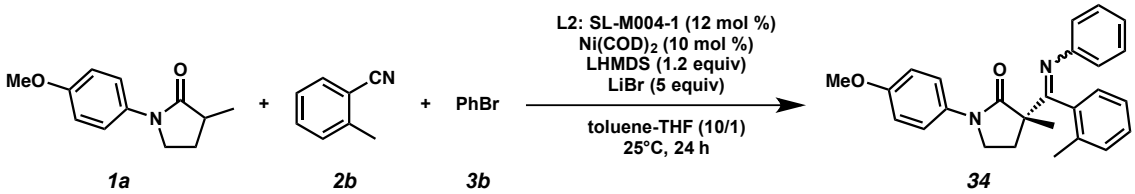
To a solution of lactam **31** (36.0 mg, 0.101 mmol, 1.00 equiv) in EtOH (2.0 mL) was added K_2CO_3 (70.0 mg, 0.506 mmol, 5.00 equiv) and the reaction mixture was stirred at ambient temperature for 30 h. The reaction mixture was concentrated under reduced pressure and brine was added to the residue. The mixture was extracted with EtOAc (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:2 EtOAc:hexanes) on silica gel to give lactam **32** as a pale yellow oil (20.5 mg, 73% yield). $[\alpha]_D^{25}$ -14.6° (c 0.98, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.03 – 6.88 (m, 2H), 4.31 – 4.17 (m, 2H), 3.83 (s, 3H), 3.82 – 3.70 (m, 2H), 2.64 (ddd, *J* = 12.8, 7.0, 4.7 Hz,

1H), 2.14 – 2.04 (m, 1H), 1.55 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 172.6, 154.9, 128.8, 128.5, 127.1, 120.9, 112.1, 61.5, 55.7, 51.6, 47.1, 32.2, 20.3, 14.2; IR (Neat Film NaCl) 2979, 1738, 1699, 1597, 1505, 1456, 1409, 1257, 1195, 1137, 1090, 1024, 754 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{15}H_{20}NO_4$ $[M+H]^+$: 278.1387, found 278.1384.

(*R*)-Ethyl-3-methyl-2-oxopyrrolidine-3-carboxylate (33)

To a solution lactam **32** (20.0 mg, 0.0721 mmol, 1.00 equiv) in MeCN (1.5 mL) and water (1.5 mL) was added CAN (237 mg, 0.433 mmol, 6.00 equiv) and the reaction mixture was stirred at 40 °C for 24 h. The reaction mixture was allowed to cool to ambient temperature and 10% Na_2SO_3 aqueous solution (3 mL) and brine (3 mL) were added. The reaction mixture was extracted with EtOAc (20 mL, twice), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (2:1 EtOAc:hexanes) on silica gel to give lactam **33** as a white solid (2.0 mg, 16% yield). $[\alpha]_D^{25}$ +19.5° (c 0.09, MeOH) (reported data $[\alpha]_D^{25}$ +19.0° (c 2, MeOH))[8]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (br s, 1H), 4.21 (m, 2H), 3.53 – 3.44 (m, 1H), 3.40 – 3.31 (m, 1H), 2.65 (ddd, J = 12.8, 7.8, 4.0 Hz, 1H), 2.05 (ddd, J = 13.0, 8.4, 7.0 Hz, 1H), 1.46 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 172.4, 61.8, 50.6, 39.6, 34.2, 20.2, 14.3; IR (Neat Film NaCl) 3245, 2981, 1703, 1454, 1266, 1196, 1138, 1028 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_8H_{13}NO_3$ $[M]^+$: 171.0968, found 171.0965.

Procedures/Spectroscopic Data for Isolation/Reduction of Imine Intermediates



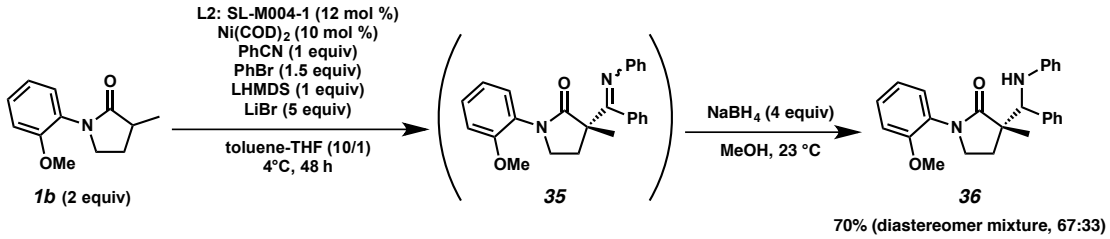
(*S*)-1-(4-Methoxyphenyl)-3-methyl-3-((phenylimino)(*o*-tolyl)methyl)pyrrolidin-2-one (34)

To a suspension of lactam **1a** (82.1 mg, 0.400 mmol, 2.00 equiv), *o*-tolunitrile **2b** (23.4 mg, 0.200 mmol, 1.00 equiv), bromobenzene **3b** (31.5 μL, 0.300 mmol, 1.5 equiv), LHMDS (40.2 mg, 0.240 mmol, 1.20 equiv) and LiBr (86.9 mg, 1.00 mmol, 5.00 equiv) in toluene (1.0 mL) and THF (0.20 mL) were added a solution of $Ni(COD)_2$ (5.50 mg, 0.0200 mmol, 0.100 equiv) and SL-M004-1(Solvias, 25.3 mg, 0.0240 mmol, 0.120 equiv) at 25 °C and the reaction mixture was stirred at 25 °C for

[8] Banerjee, S.; Smith, J.; Smith, J.; Faulkner, F.; Masterson, D. S. *J. Org. Chem*. **2012**, *77*, 10925−10930.

24 h. The reaction mixture was filtered through a pad of silica gel eluting with EtOAc (60 mL). The eluate was concentrated under reduced pressure and the residue was purified by flash column chromatography (1:10 EtOAc:hexanes) on silica gel to give imine **34** as a white foam (62 mg, 77% yield, 60/40 mixture of E/Z isomers). ^{1}H NMR (500 MHz, $CDCl_3$) for major isomer: δ 7.65 – 6.62 (m, 8H), 3.86 (s, 3H), 3.76 (ddd, *J* = 9.3, 8.2, 4.6 Hz, 1H), 3.62 (ddd, *J* = 9.3, 7.9, 6.6 Hz, 1H), 2.68 (ddd, *J* = 12.6, 7.9, 4.6 Hz, 1H), 2.17 (ddd, *J* = 12.8, 8.2, 6.6 Hz, 1H), 2.06 (s, 3H), 1.66 (s, 3H); for minor isomer: δ 7.61 – 6.62 (m, 8H), 4.09 (dt, *J* = 9.1, 7.7 Hz, 1H), 3.85 (s, 3H), 3.82 (td, *J* = 8.8, 3.6 Hz, 1H), 3.15 (ddd, *J* = 12.5, 7.8, 3.6 Hz, 1H), 2.27 – 2.20 (m, 1H), 2.07 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for major and minor isomer: δ 175.1, 174.8, 174.7, 172.2, 156.7, 149.9, 136.1, 135.8, 134.2, 133.3, 132.9, 132.7, 130.1, 129.8, 128.4, 128.3, 128.1, 128.0, 124.8, 124.7, 123.56, 123.4, 122.98, 122.0, 120.59, 120.3, 114.0, 55.8, 55.5, 54.7, 47.0, 46.3, 33.4, 31.2, 22.5, 22.0, 20.5, 20.3; IR (Neat Film NaCl) 2931, 1688, 1512, 1485, 1398, 1289, 1249, 1181, 1090, 1033, 993, 829, 766, 731, 697 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{26}H_{27}N_2O_2$ $[M+H]^+$: 399.2067, found 399.2072.

(S)-1-(2-Methoxyphenyl)-3-methyl-3-(phenyl(phenylamino)methyl)pyrrolidin-2-one (36)



To a suspension of lactam **1b** (82.1 mg, 0.400 mmol, 2.00 equiv), benzonitrile **2a** (20.6 mg, 0.200 mmol, 1.00 equiv), bromobenzene **3b** (31.5 μL, 0.300 mmol, 1.5 equiv), LHMDS (40.2 mg, 0.240 mmol, 1.20 equiv) and LiBr (86.9 mg, 1.00 mmol, 5.00 equiv) in toluene (1.0 mL) and THF (0.20 mL) were added a solution of $Ni(COD)_2$ (5.50 mg, 0.0200 mmol, 0.100 equiv) and SL-M004-1(Solvias, 25.3 mg, 0.0240 mmol, 0.120 equiv) at 0 °C and the reaction mixture was stirred at 0 °C for 48 h. $NaBH_4$ (45.4 mg, 1.20 mmol, 6 equiv), THF (2 mL) and MeOH (2 mL) were added and the reaction mixture was stirred at 25 °C for 2 days. Water was added and the mixture was extracted with EtOAc (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:5 EtOAc:hexanes) on silica gel to give amine **36** as a colorless oil (54.3 mg, 70% yield).

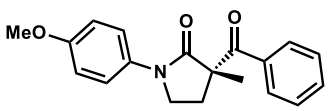
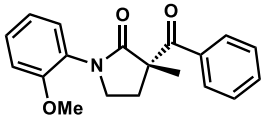
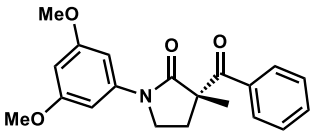
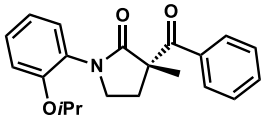
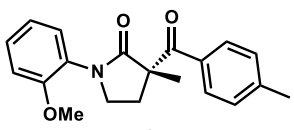
Spectroscopic data for amine **36** was taken after separation of the diastereomers by flash column chromatography on silica gel.

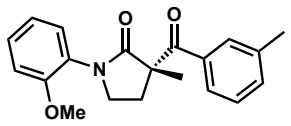
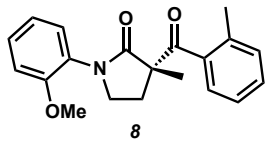
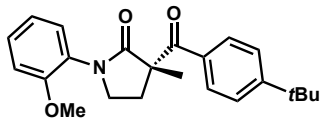
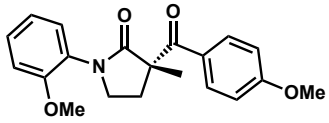
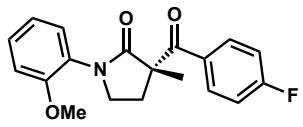
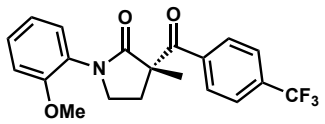
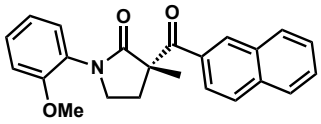
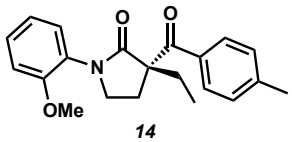
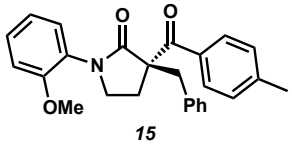
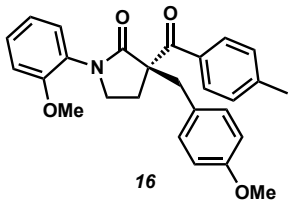
Major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.49 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.23 (m, 2H), 7.12 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.95 (td, *J* = 7.6, 1.3 Hz, 1H), 6.91 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.50 (d, *J*

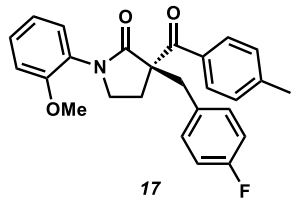
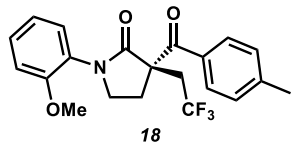
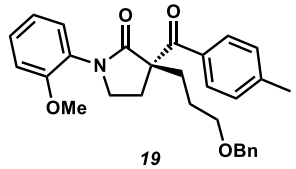
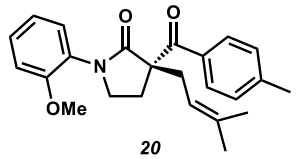
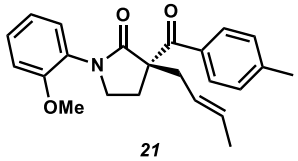
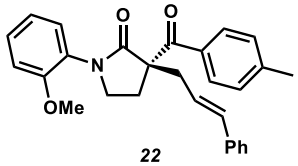
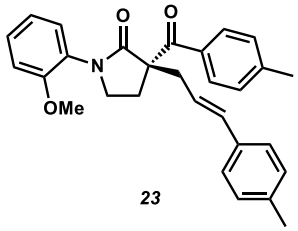
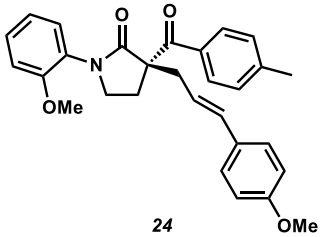
= 7.9 Hz, 2H), 5.51 (s, 1H), 4.53 – 4.48 (m, 1H), 3.60 (s, 3H), 3.59 – 3.50 (m, 2H), 2.42 (ddd, *J* = 12.7, 7.6, 4.7 Hz, 1H), 1.81 (ddd, *J* = 13.0, 8.3, 6.8 Hz, 1H), 1.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.9, 154.9, 148.3, 139.8, 129.0, 128.9, 128.6, 128.6, 128.2, 127.5, 127.0, 120.8, 117.4, 114.1, 112.9, 62.9, 55.4, 47.6, 46.7, 31.0, 19.7; IR (Neat Film NaCl) 3375, 2968, 1678, 1601, 1505, 1455, 1310, 1279, 1260, 1025, 749, 702 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{27}N_2O_2$ $[M+H]^+$: 387.2067, found 387.2070.

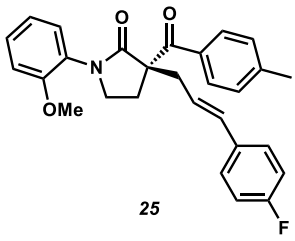
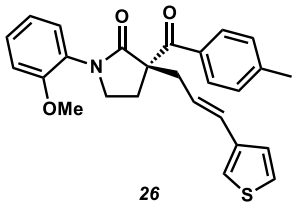
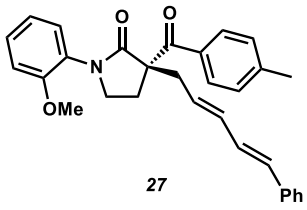
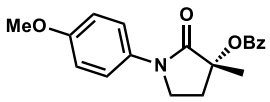
Minor isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 2H), 7.35 – 7.20 (m, 4H), 7.09 – 6.98 (m, 3H), 6.98 – 6.90 (m, 2H), 6.58 – 6.47 (m, 3H), 6.19 (br s, 1H), 4.37 (s, 1H), 3.78 (s, 3H), 3.41 (td, *J* = 9.1, 4.7 Hz, 1H), 2.62 (ddd, *J* = 9.4, 8.4, 6.4 Hz, 1H), 2.27 (ddd, *J* = 13.1, 8.4, 4.7 Hz, 1H), 1.98 (ddd, *J* = 13.0, 8.9, 6.4 Hz, 1H), 1.61 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 154.6, 147.2, 140.6, 129.0, 128.8, 128.3, 128.3, 127.7, 127.5, 126.8, 120.7, 116.4, 112.9, 112.0, 64.5, 55.6, 47.2, 46.8, 30.8, 24.8; IR (Neat Film NaCl) 3375, 2929, 1674, 1600, 1505, 1455, 1418, 1308, 1256, 1026, 748, 704 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{27}N_2O_2$ $[M+H]^+$: 387.2067, found 387.2071.

Determination of Enantiomeric Excess (Table S6)

entry	compound	analytic conditions	ee (%)
1	 *4a*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 10.56, minor 8.06	88
2	 *4b*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 8.55, minor 7.66	92
3	 *4c*	HPLC CHIRALCELL OD, λ = 254 nm 10% IPA/hexanes, 1.0 mL/min t_R(min): major 23.56, minor 16.84	85
4	 *4d*	HPLC CHIRALCELL OD, λ = 254 nm 20% IPA/hexanes, 1.0 mL/min t_R(min): major 7.03, minor 6.39	86
5	 *6*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 10.51, minor 7.66	91

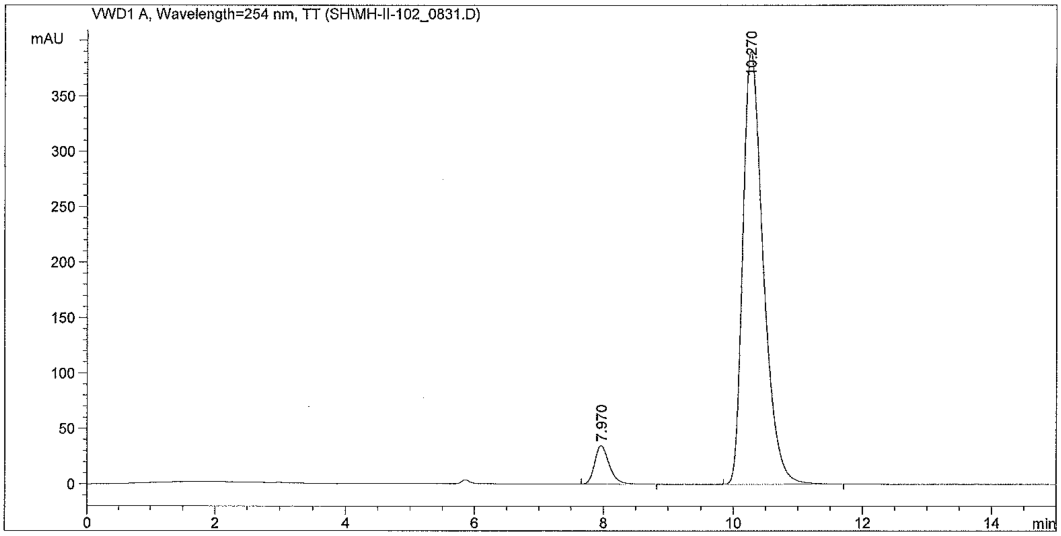
entry	compound	analytic conditions	ee (%)
6	 *7*	SFC Chiralpak OJ-H, λ = 254 nm 15% IPA/CO_2, 2.5 mL/min, t_R(min): major 4.20, minor 5.72	93
7	 *8*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 8.14, minor 6.64	94
8	 *9*	HPLC CHIRALCELL OD, λ = 254 nm 15% IPA/hexanes, 1.0 mL/min t_R(min): major 11.57, minor 9.83	92
9	 *10*	HPLC CHIRALCELL OD, λ = 254 nm 15% IPA/hexanes, 1.0 mL/min t_R(min): major 11.57, minor 9.83	89
10	 *11*	HPLC CHIRALCELL OD, λ = 254 nm 20% IPA/hexanes, 1.0 mL/min t_R(min): major 11.36, minor 9.98	93
11	 *12*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 7.41, minor 6.76	87
12	 *13*	HPLC CHIRALCELL OD, λ = 254 nm 10% IPA/hexanes, 1.0 mL/min t_R(min): major 26.83, minor 23.63	91
13	 *14*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 8.24, minor 6.39	78
14	 *15*	SFC Chiralpak OJ-H, λ = 254 nm 2% IPA/CO_2, 2.5 mL/min, t_R(min): major 7.25, minor 6.34	81
15	 *16*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 11.24, minor 8.72	81

entry	compound	analytic conditions	ee (%)
16	 *17*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 9.40, minor 7.41	74
17	 *18*	HPLC CHIRALCELL OD, λ = 254 nm 20% IPA/hexanes, 1.0 mL/min t_R(min): major 8.40, minor 7.49	71
18	 *19*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 11.38, minor 8.47	60
19	 *20*	HPLC CHIRALCELL OD, λ = 254 nm 20% IPA/hexanes, 1.0 mL/min t_R(min): major 9.61, minor 7.13	76
20	 *21*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 7.31, minor 5.33	86
21	 *22*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 12.63, minor 8.67	86
22	 *23*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 11.30, minor 7.58	86
23	 *24*	HPLC CHIRALCELL OD, λ = 254 nm 40% IPA/hexanes, 1.0 mL/min t_R(min): major 11.68, minor 7.70	88

entry	compound	analytic conditions	ee (%)
24	 *25*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 12.54, minor 8.47	83
25	 *26*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 14.39, minor 8.96	83
26	 *27*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 11.30, minor 7.58	84
27	 *30*	HPLC CHIRALCELL OD, λ = 254 nm 30% IPA/hexanes, 1.0 mL/min t_R(min): major 10.42, minor 7.88	88

HPLC Traces of Enantioenriched and Racemic Compounds

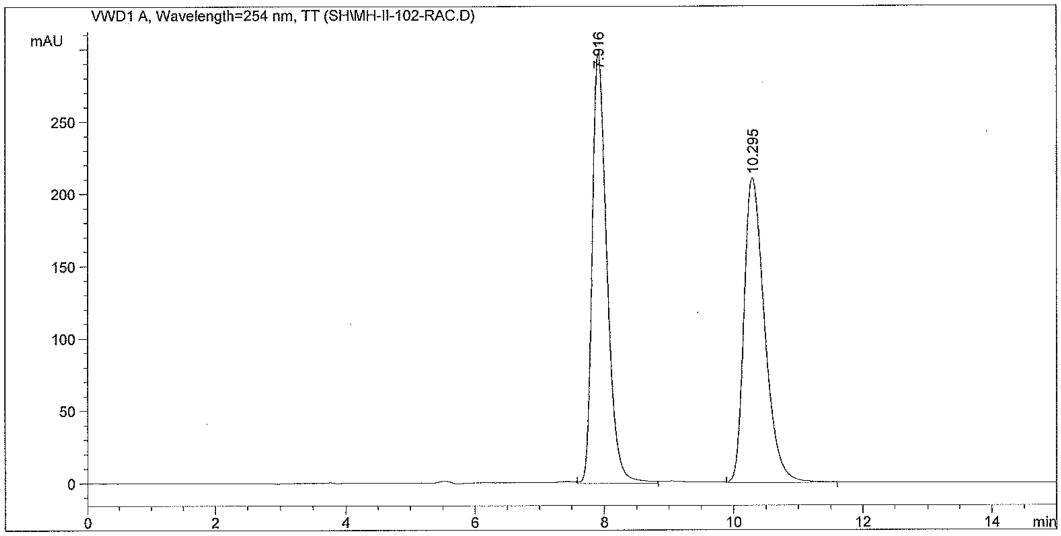
Enantioenriched 4a



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.970	BB	0.2421	546.70709	34.68962	5.9783
2	10.270	BB	0.3360	8598.20117	389.71198	94.0217

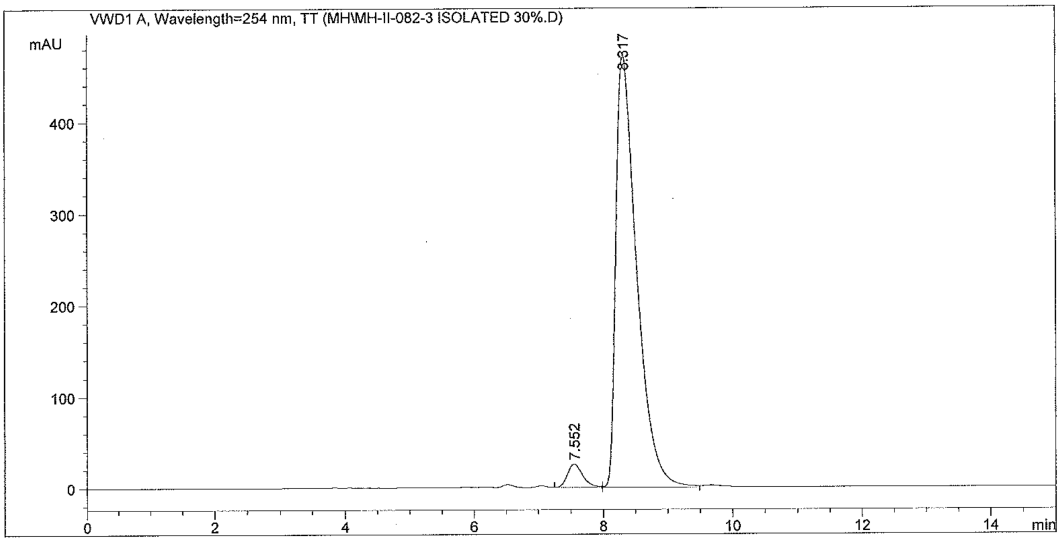
Racemic 4a



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.916	VV	0.2412	4668.71631	297.64624	50.1248
2	10.295	BB	0.3388	4645.46973	210.70407	49.8752

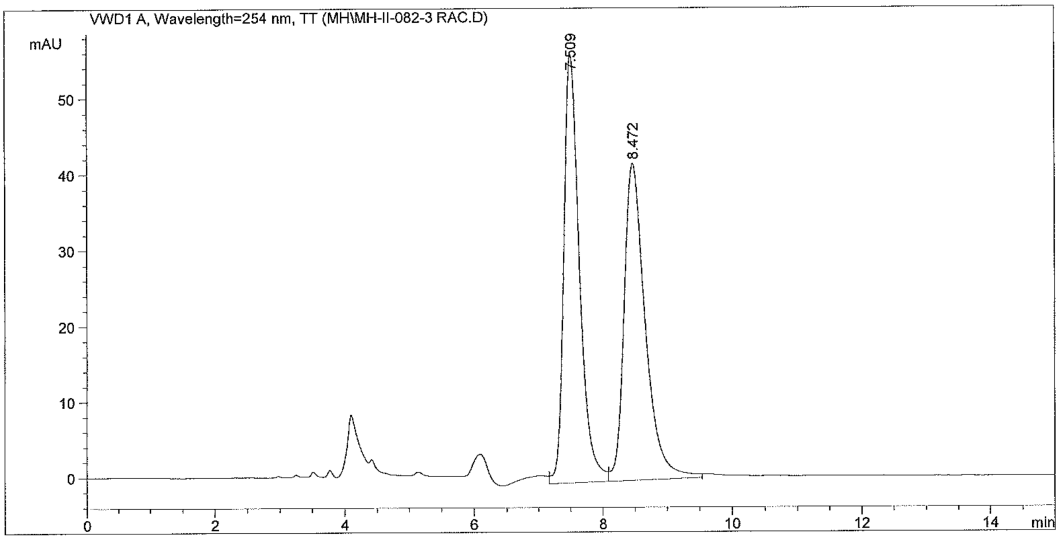
Enantioenriched 4b



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.552	VV	0.2493	419.17737	25.60274	3.8063
2	8.317	VV	0.3400	1.05934e4	472.89438	96.1937

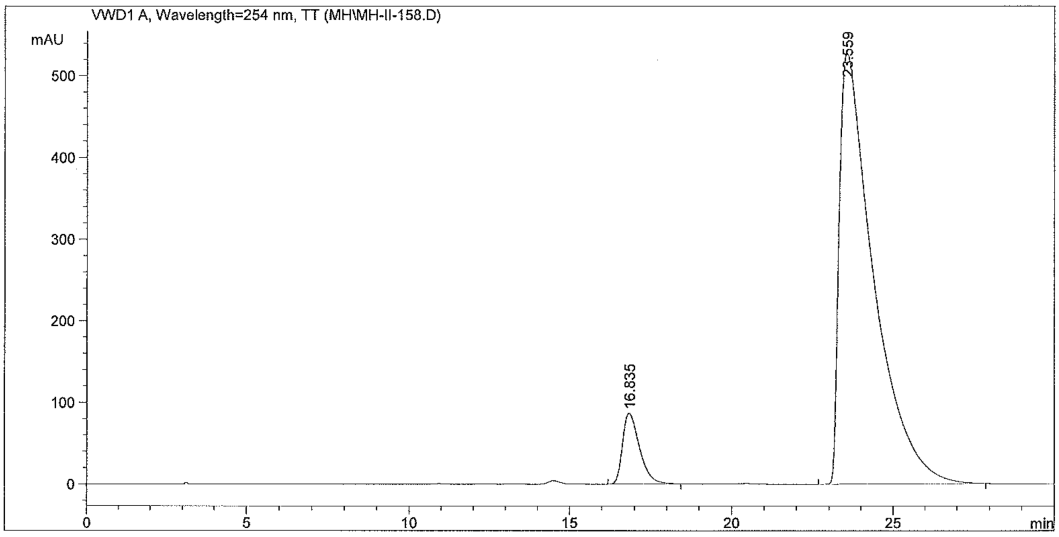
Racemic 4b



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.509	VV	0.2595	962.35553	56.59516	49.9432
2	8.472	VV	0.3475	964.54327	41.84590	50.0568

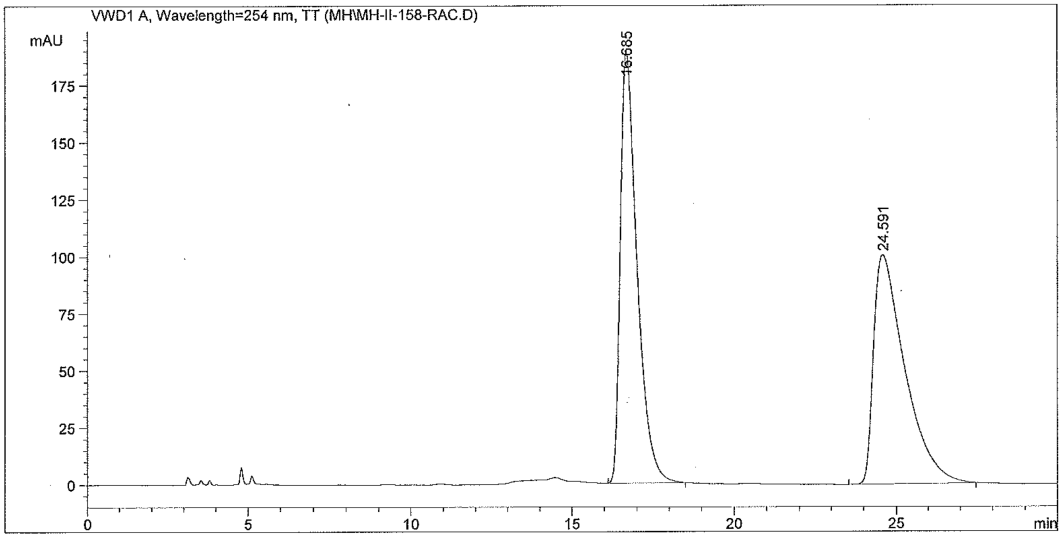
Enantioenriched 4c



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.835	BB	0.5366	3167.57788	86.91119	7.4539
2	23.559	BB	1.0162	3.93278e4	528.31799	92.5461

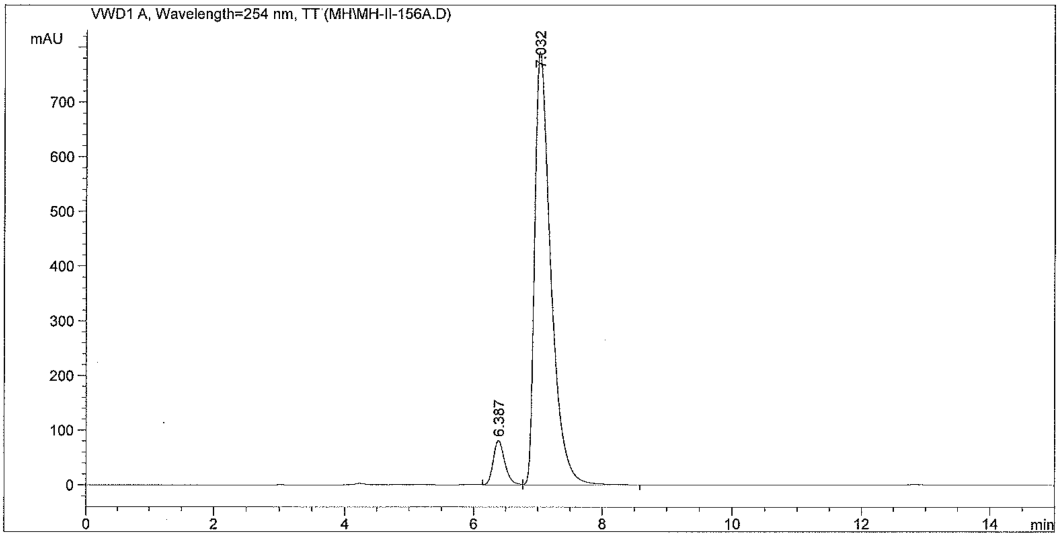
Racemic 4c



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.685	BB	0.5277	6760.87500	188.78192	49.9613
2	24.591	BB	0.9114	6771.34570	100.47928	50.0387

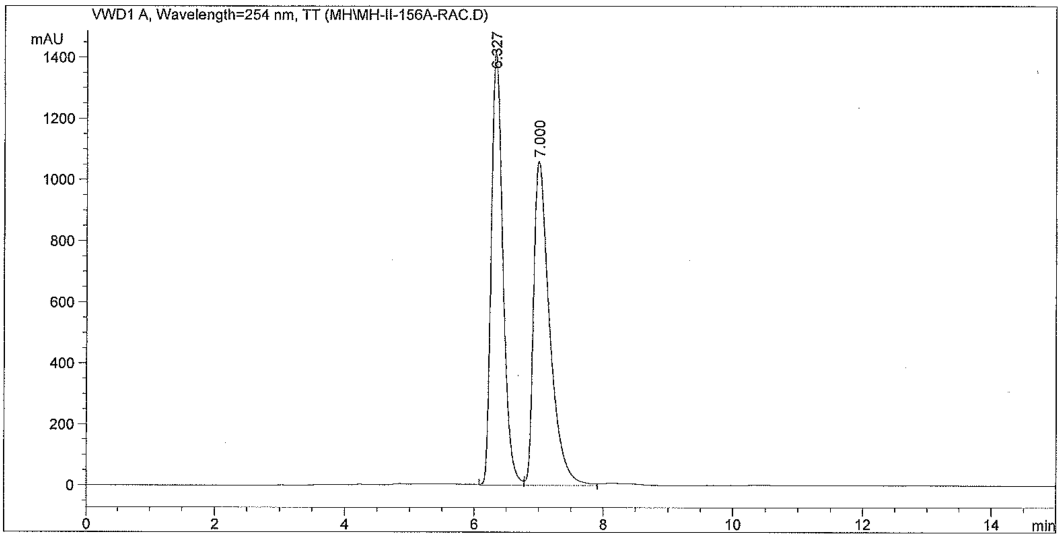
Enantioenriched 4d



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.387	VV	0.1927	1011.20123	80.73458	6.8009
2	7.032	VB	0.2611	1.38574e4	791.45978	93.1991

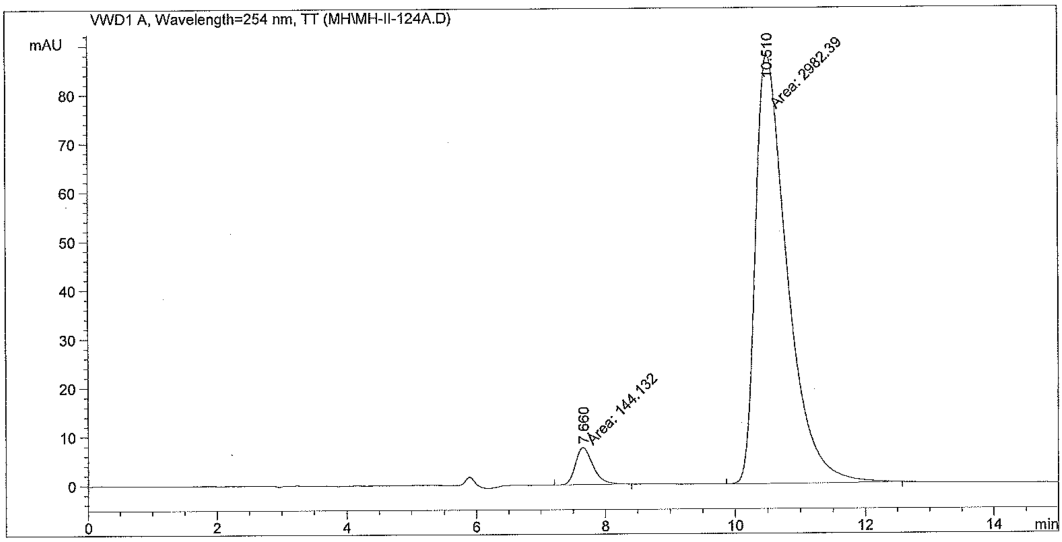
Racemic 4d



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.327	VV	0.1948	1.79902e4	1416.52100	49.4975
2	7.000	VV	0.2563	1.83555e4	1061.55359	50.5025

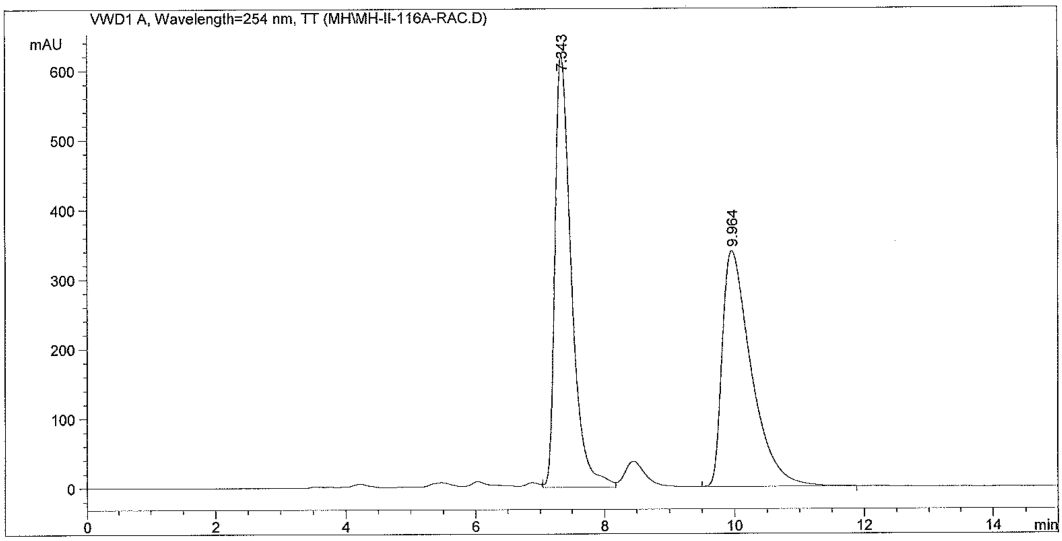
Enantioenriched 6



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.660	MM	0.3166	144.13167	7.58799	4.6100
2	10.510	MM	0.5652	2982.38501	87.94354	95.3900

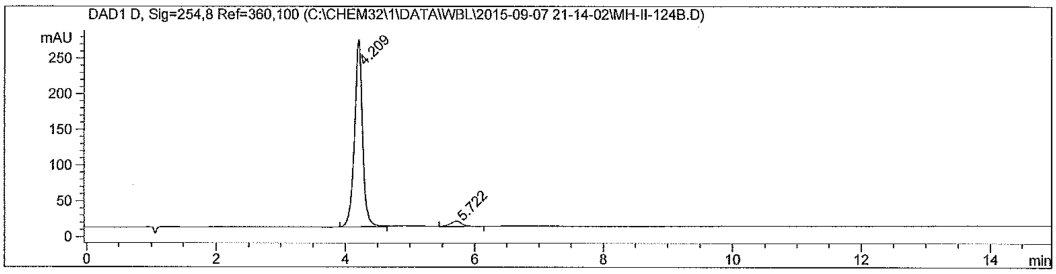
Racemic 6



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.343	VV	0.2678	1.09913e4	620.51941	50.8581
2	9.964	BB	0.4702	1.06204e4	339.16516	49.1419

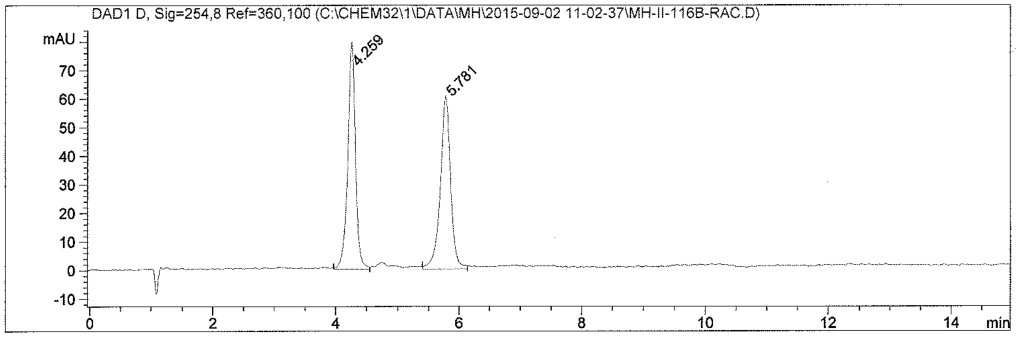
Enantioenriched 7



Signal 1: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4W209	BB	0W1282	2253W46313	262W25006	96W3032
2	5.722	BB	0.1704	86.50503	7.50950	3.6968

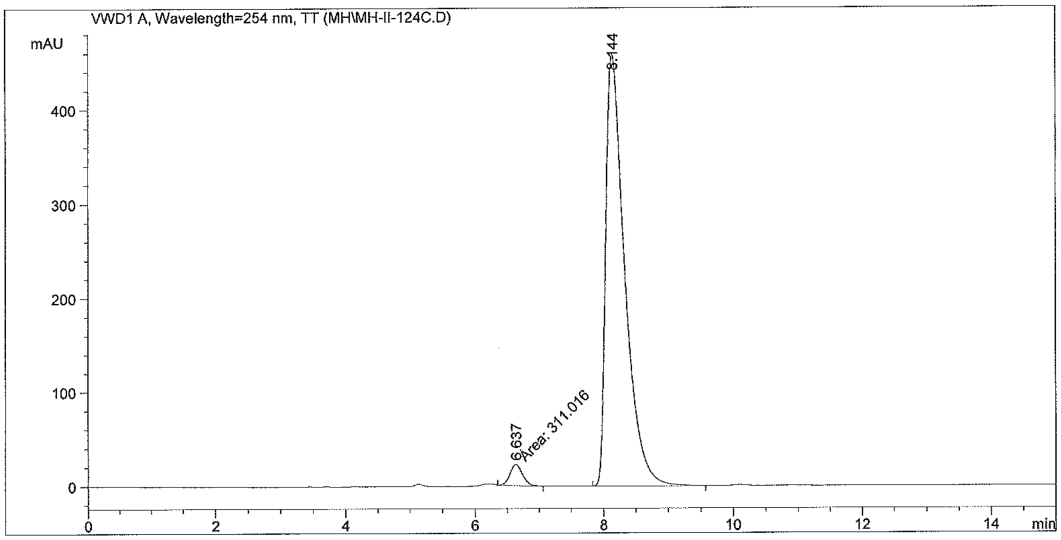
Racemic 7



Signal 1: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.259	VV	0.1298	694.25641	79.58466	49.2289
2	5.781	VB	0.1742	716.00562	60.44555	50.7711

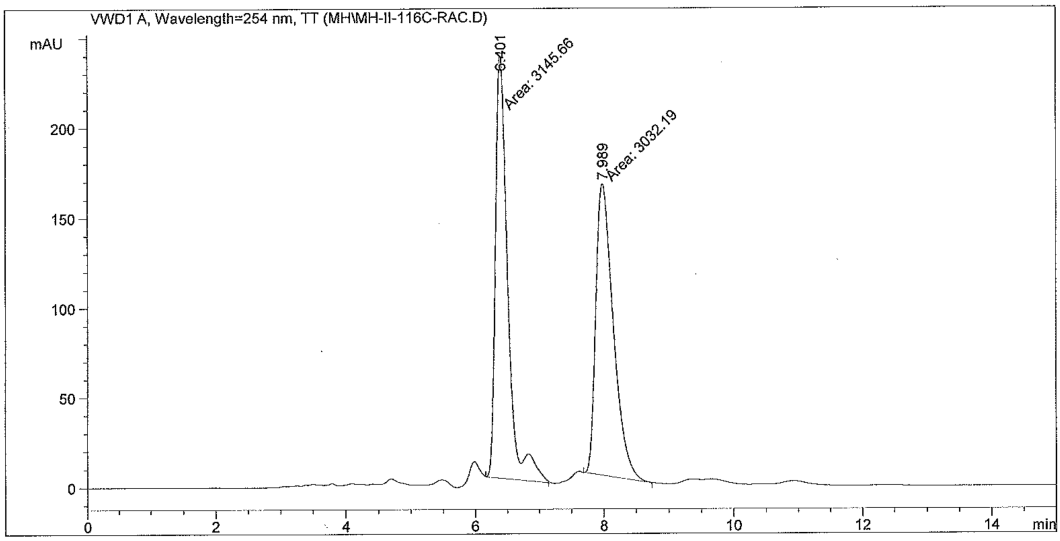
Enantioenriched 8



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.637	MM	0.2295	311.01620	22.58909	3.2230
2	8.144	BB	0.3047	9338.78906	458.28555	96.7770

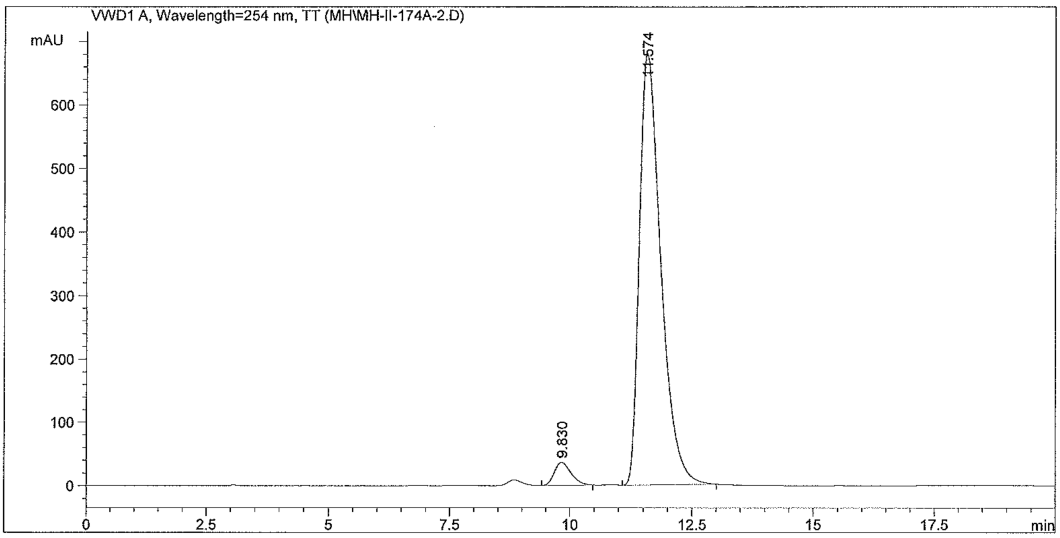
Racemic 8



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.401	MM	0.2226	3145.66260	235.50081	50.9184
2	7.989	MM	0.3119	3032.18726	162.00626	49.0816

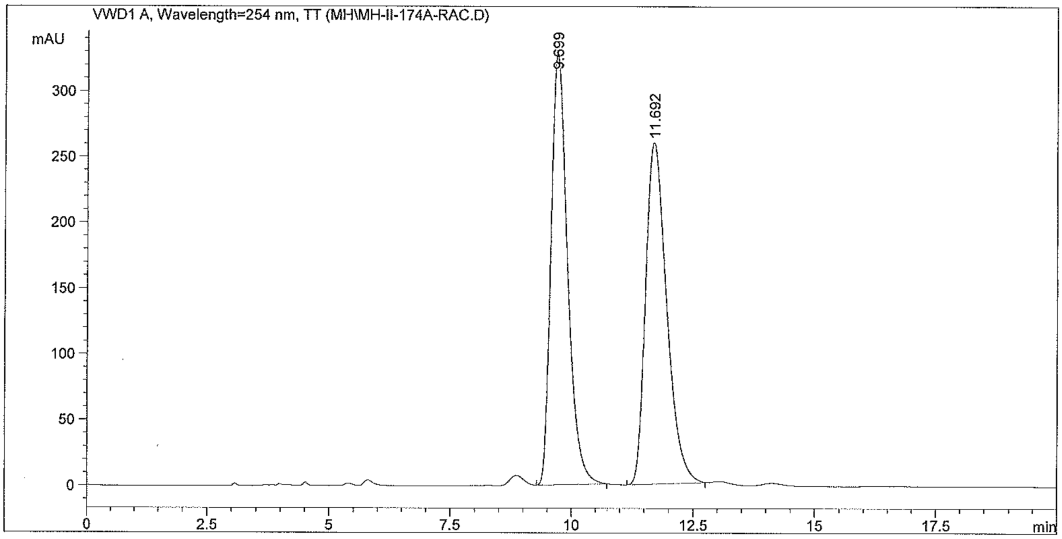
Enantioenriched 9



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.830	BB	0.3083	880.24518	36.35216	4.0655
2	11.574	BB	0.4560	2.07713e4	680.24872	95.9345

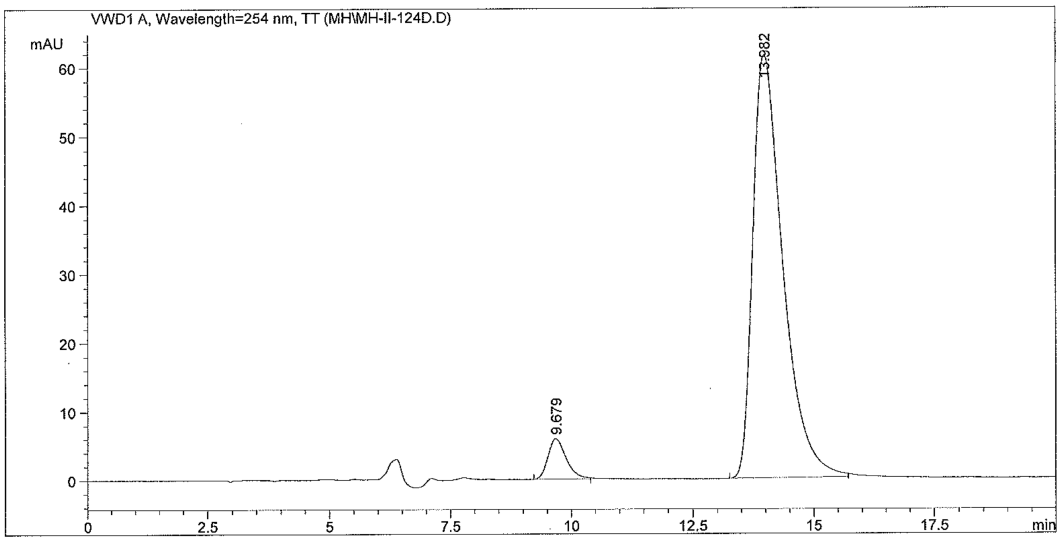
Racemic 9



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.699	VB	0.3601	7834.94385	328.08548	50.2941
2	11.692	BB	0.4416	7743.31348	259.58081	49.7059

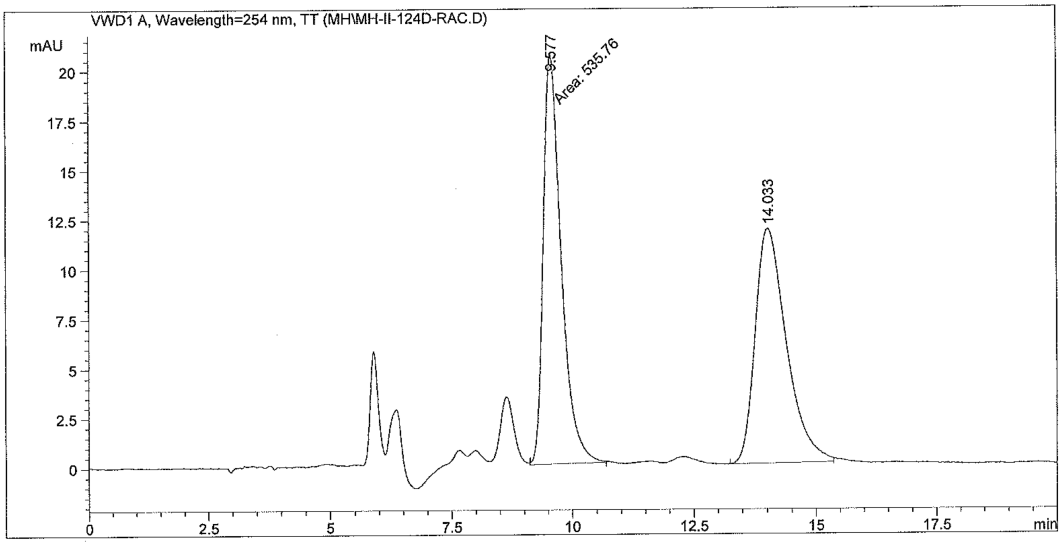
Enantioenriched 10



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.679	BB	0.4039	155.84964	5.90742	5.5248
2	13.982	BB	0.6563	2665.06104	61.58629	94.4752

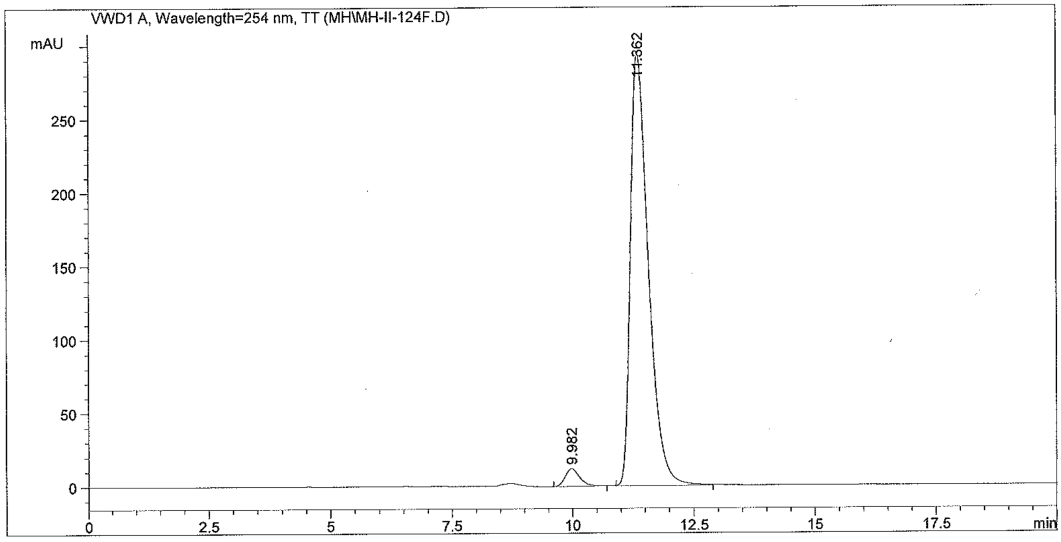
Racemic 10



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.577	MM	0.4335	535.76001	20.59646	50.6705
2	14.033	BB	0.6633	521.58105	11.82115	49.3295

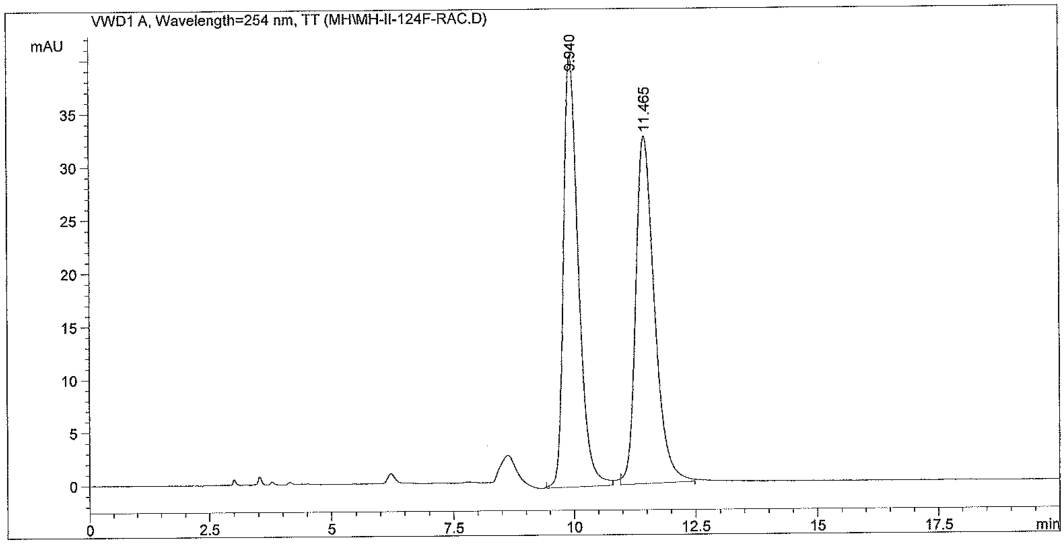
Enantioenriched 11



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.982	BB	0.3287	258.02295	12.03555	3.2743
2	11.362	BB	0.3957	7622.17822	293.95724	96.7257

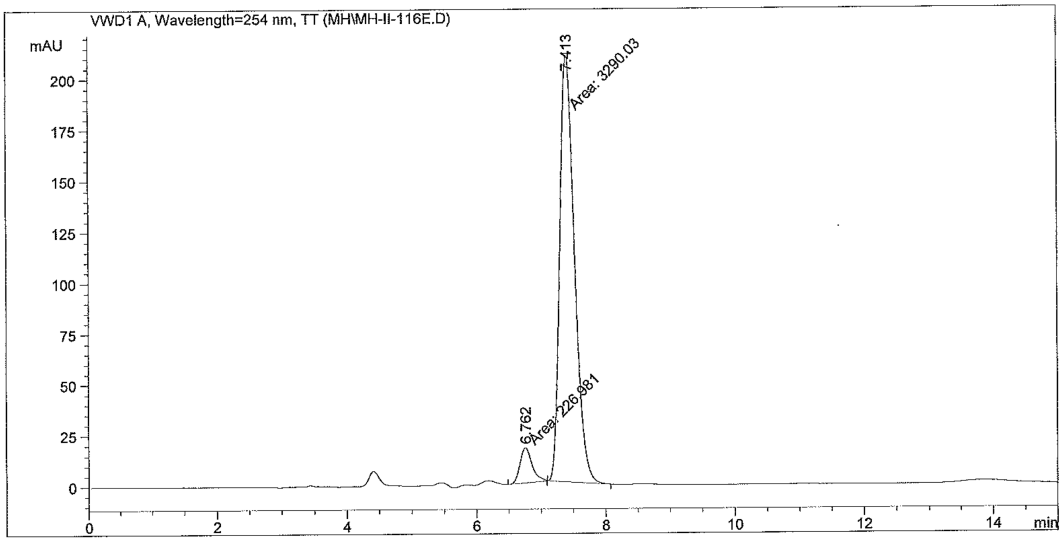
Racemic 11



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.940	BB	0.3240	864.60724	40.63335	49.7122
2	11.465	BB	0.4079	874.61914	32.72326	50.2878

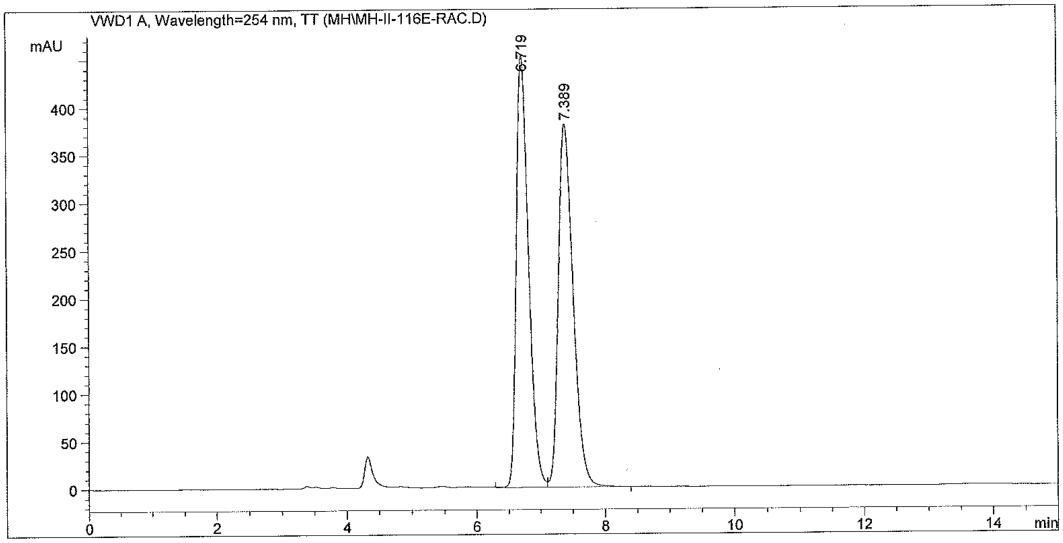
Enantioenriched 12



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.762	MM	0.2198	226.98119	17.20738	6.4538
2	7.413	MM	0.2618	3290.02515	209.46428	93.5462

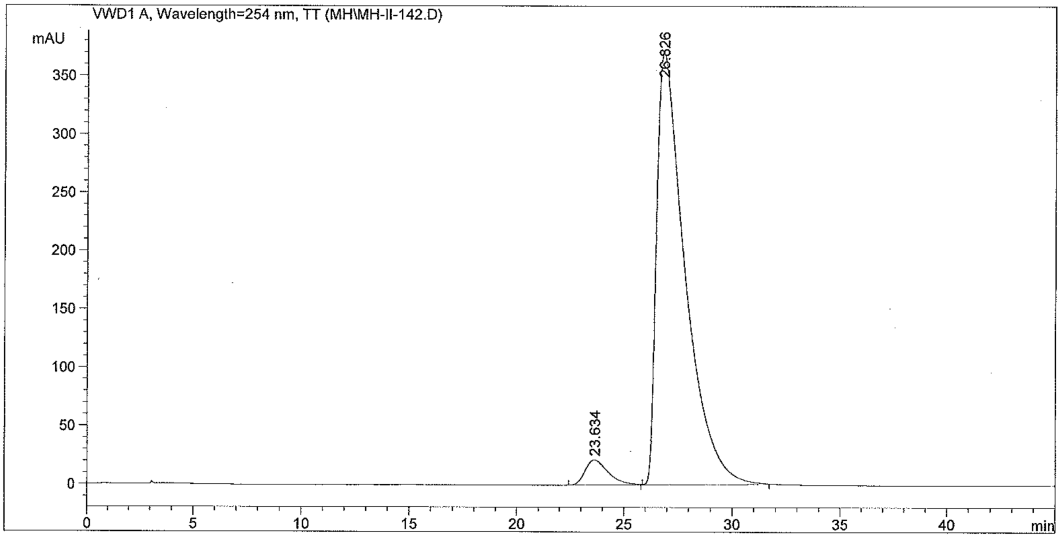
Racemic 12



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.719	VV	0.2045	6015.65381	452.70663	49.6853
2	7.389	VB	0.2480	6091.85986	380.36090	50.3147

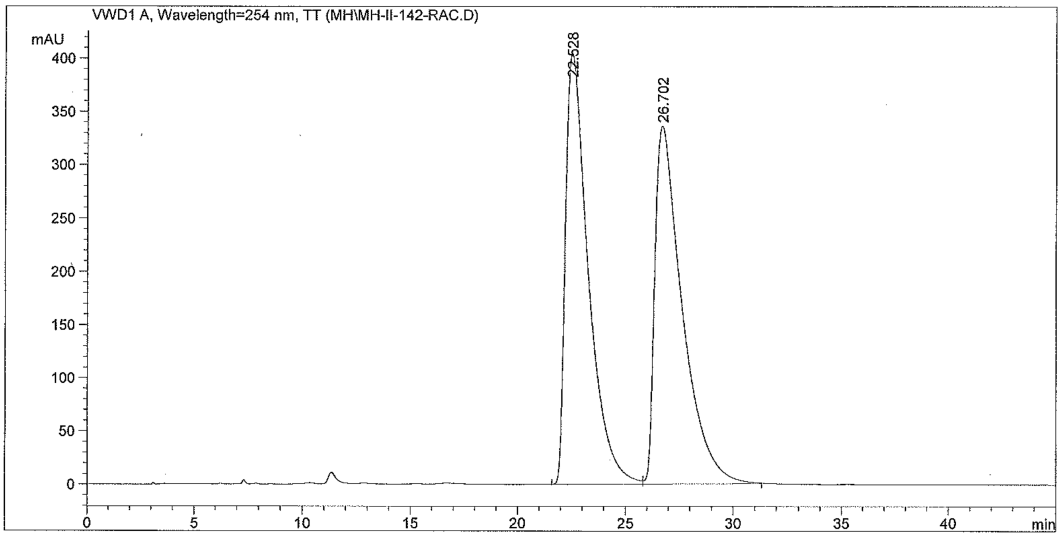
Enantioenriched 13



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.634	BB	1.1265	1615.19861	21.51093	4.5468
2	26.826	BB	1.3489	3.39084e4	369.96021	95.4532

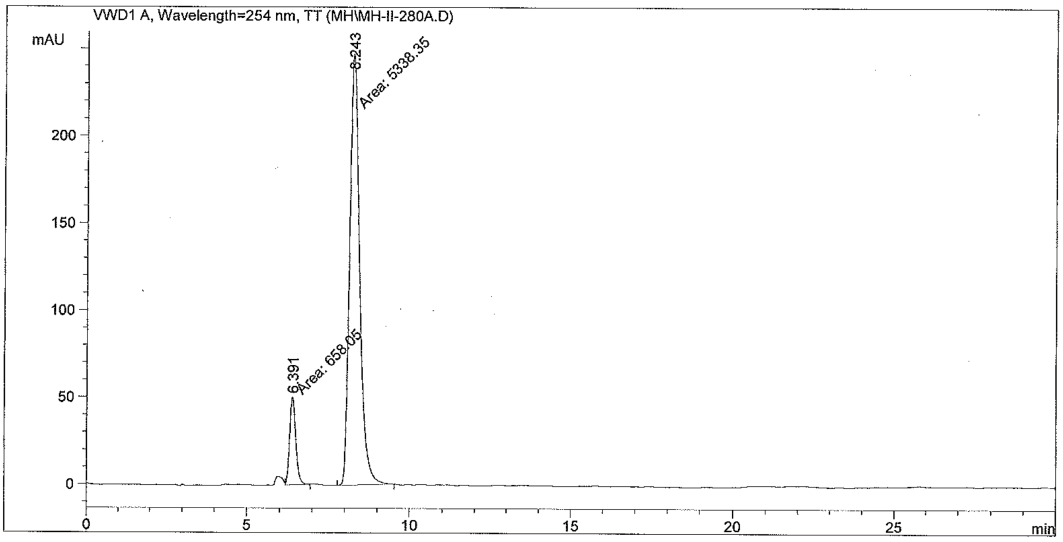
Racemic 13



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	22.528	BV	1.0853	2.95878e4	405.00653	49.7424
2	26.702	VB	1.3034	2.98943e4	335.87433	50.2576

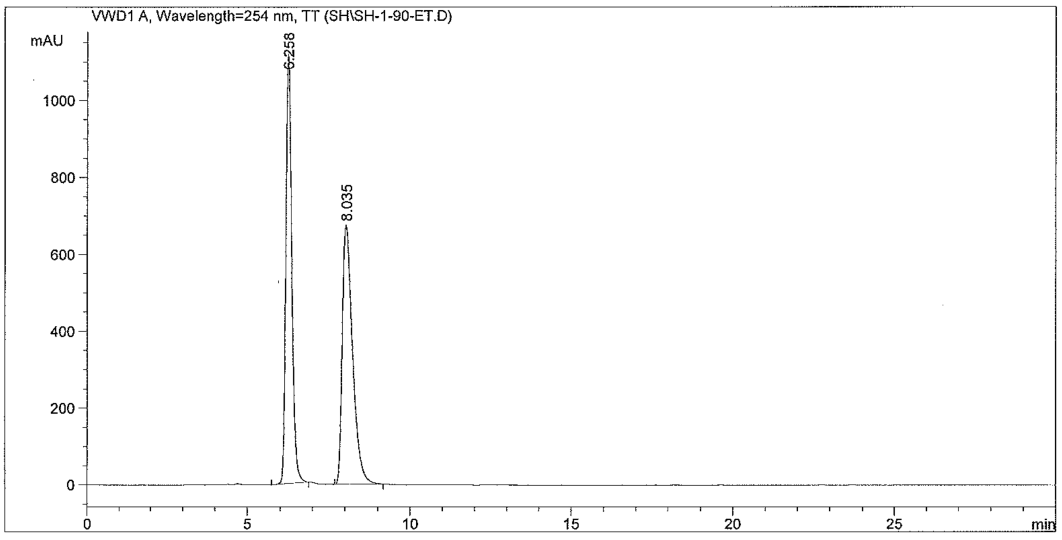
Enantioenriched 14



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.391	FM	0.2183	658.05005	50.24549	10.9741
2	8.243	MM	0.3593	5338.35156	247.60593	89.0259

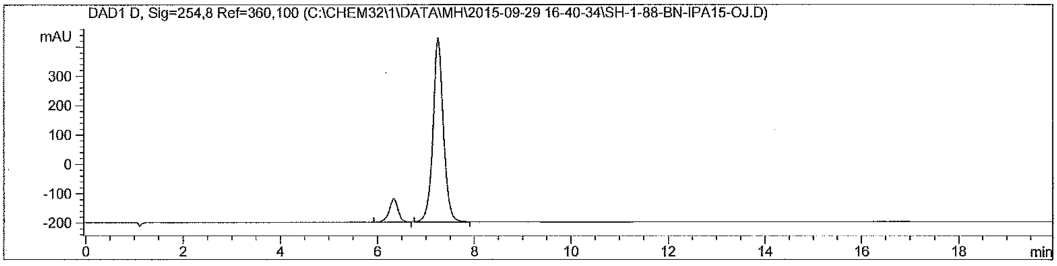
Racemic 14



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.258	BB	0.2004	1.45346e4	1118.64001	50.0252
2	8.035	BB	0.3225	1.45199e4	674.57477	49.9748

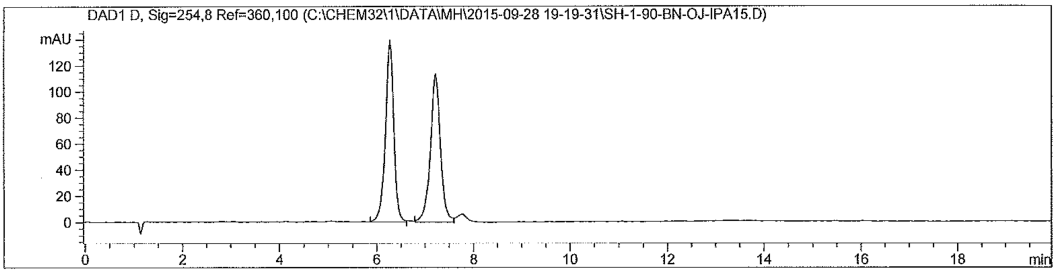
Enantioenriched 15



Signal 1: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.337	BB	0.1875	1003.46246	80.45315	9.6628
2	7.248	BB	0.2202	9381.38672	628.20355	90.3372

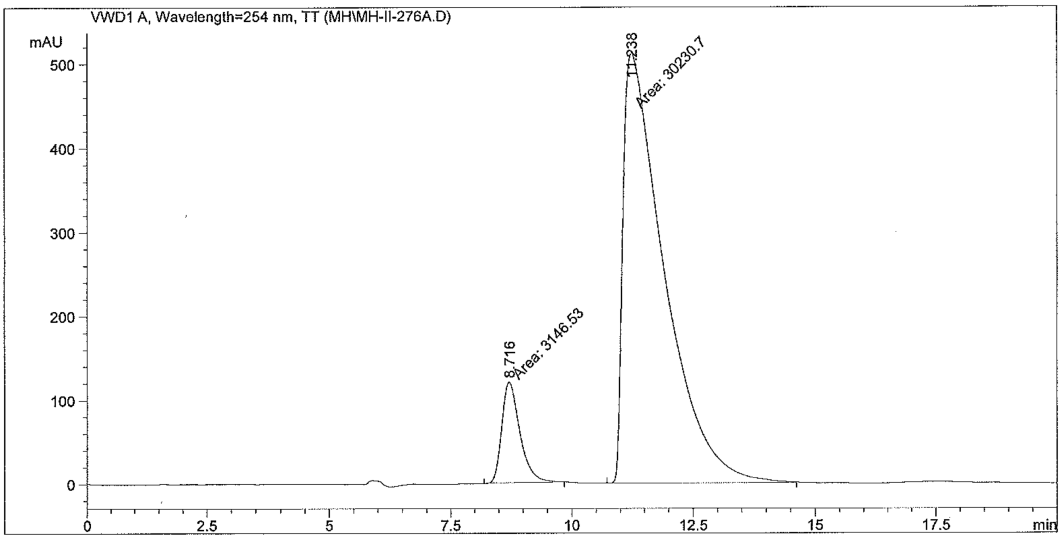
Racemic 15



Signal 1: DAD1 D, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.272	BV	0.1748	1635.60449	139.48480	49.8108
2	7.217	BV	0.2156	1648.03210	113.37238	50.1892

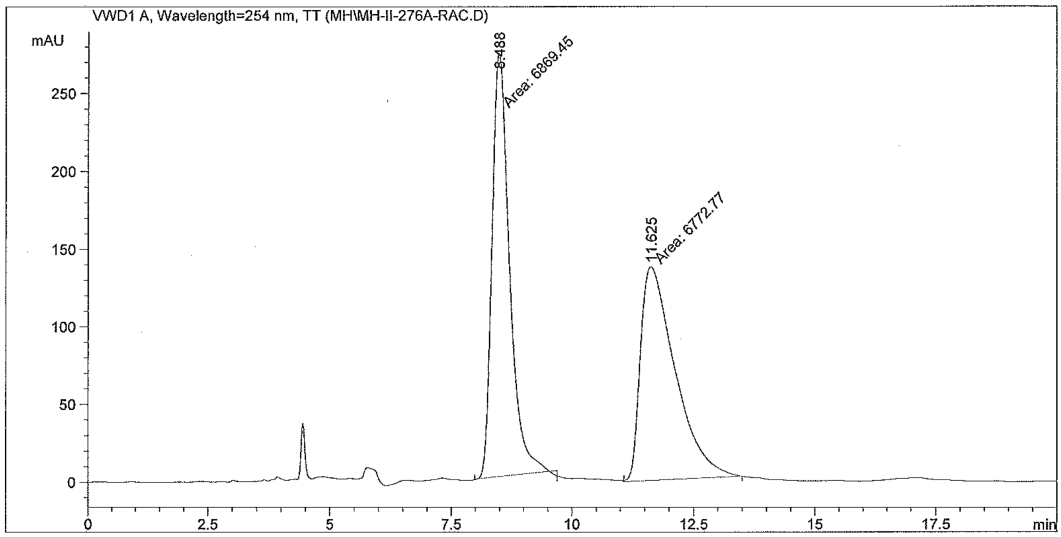
Enantioenriched 16



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.716	MM	0.4361	3146.52881	120.24094	9.4272
2	11.238	MM	0.9849	3.02307e4	511.58353	90.5728

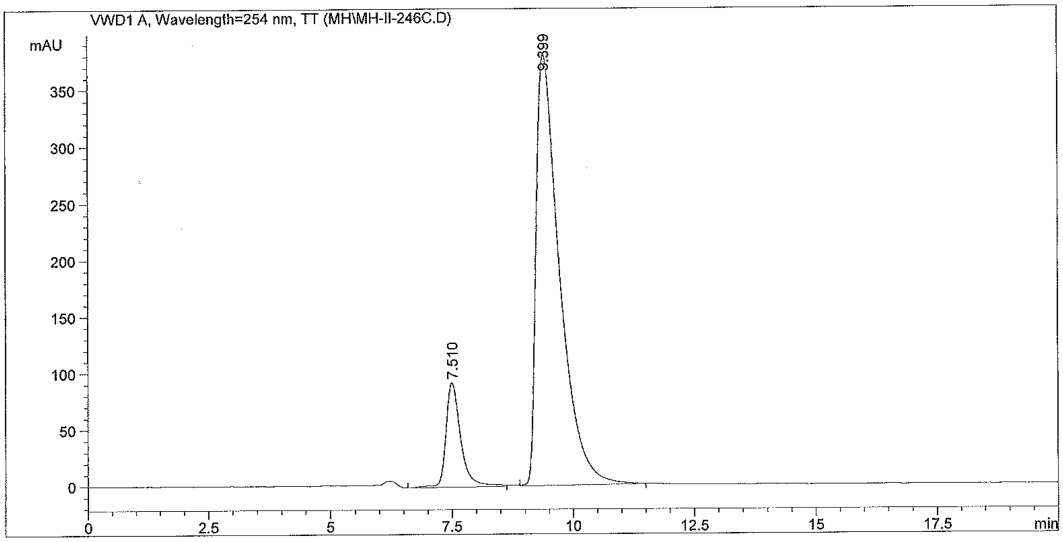
Racemic 16



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.488	MM	0.4203	6869.44971	272.38535	50.3543
2	11.625	MM	0.8194	6772.76904	137.76001	49.6457

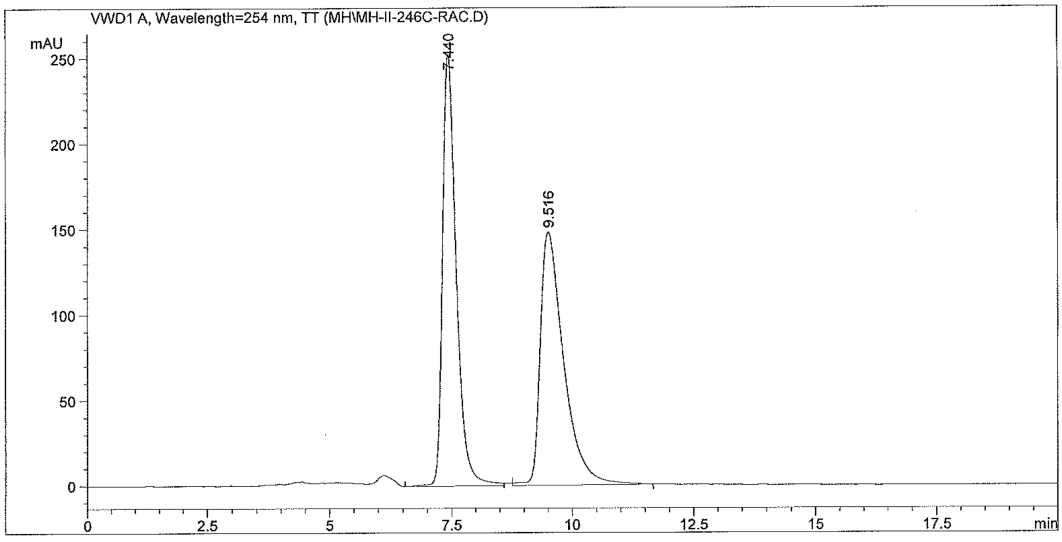
Enantioenriched 17



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.510	VB	0.3194	1960.32910	92.18734	13.2220
2	9.399	BB	0.5009	1.28659e4	380.34464	86.7780

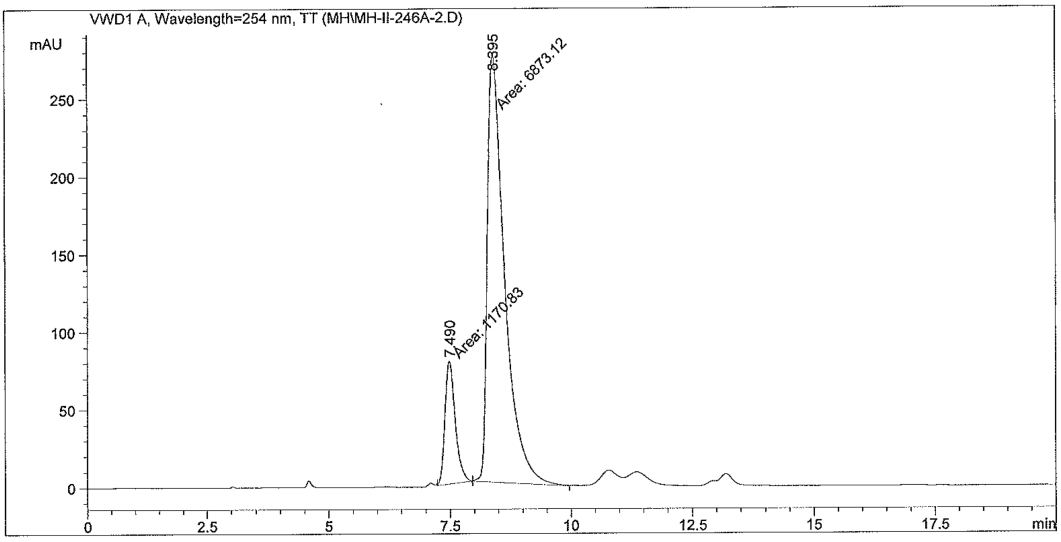
Racemic 17



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.440	VB	0.3011	5004.45313	252.46498	49.9164
2	9.516	BB	0.5046	5021.20752	148.16573	50.0836

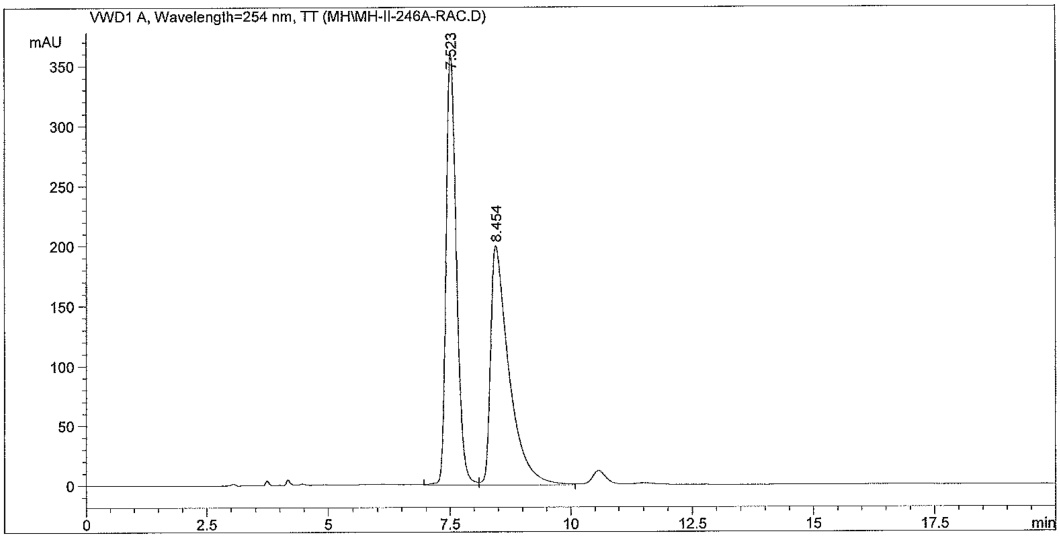
Enantioenriched 18



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.490	MM	0.2468	1170.83386	79.07106	14.5555
2	8.395	MM	0.4170	6873.11572	274.67239	85.4445

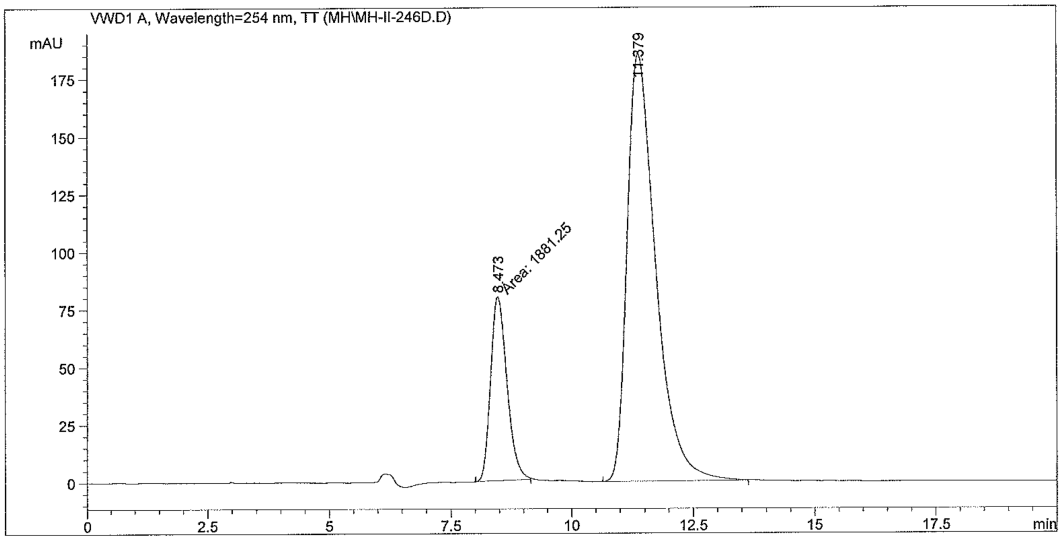
Racemic 18



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.523	BV	0.2278	5321.67188	360.02539	49.8510
2	8.454	VB	0.3872	5353.48389	199.56226	50.1490

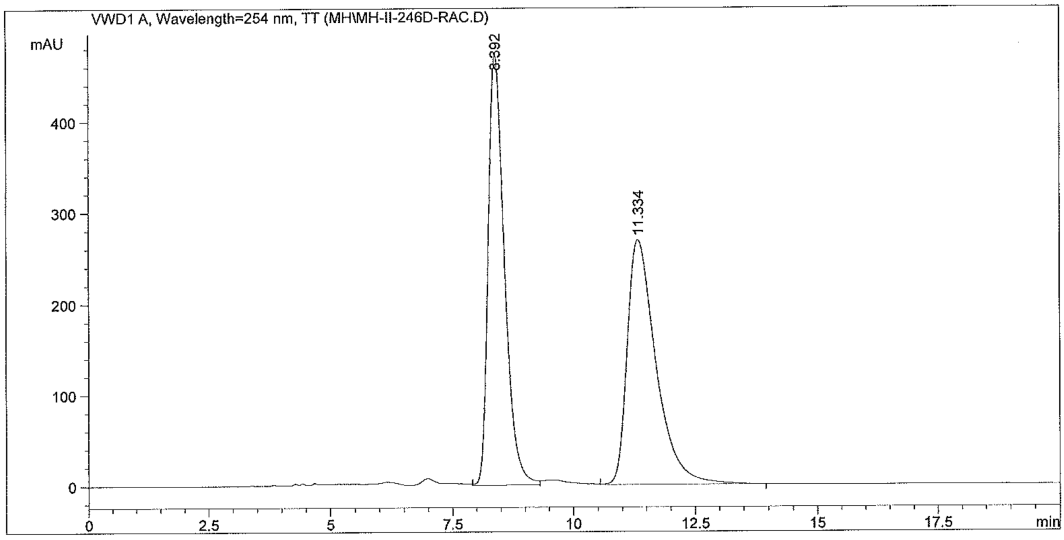
Enantioenriched 19



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.473	MM	0.3933	1881.25317	79.72974	19.8866
2	11.379	BB	0.6331	7578.62891	185.22310	80.1134

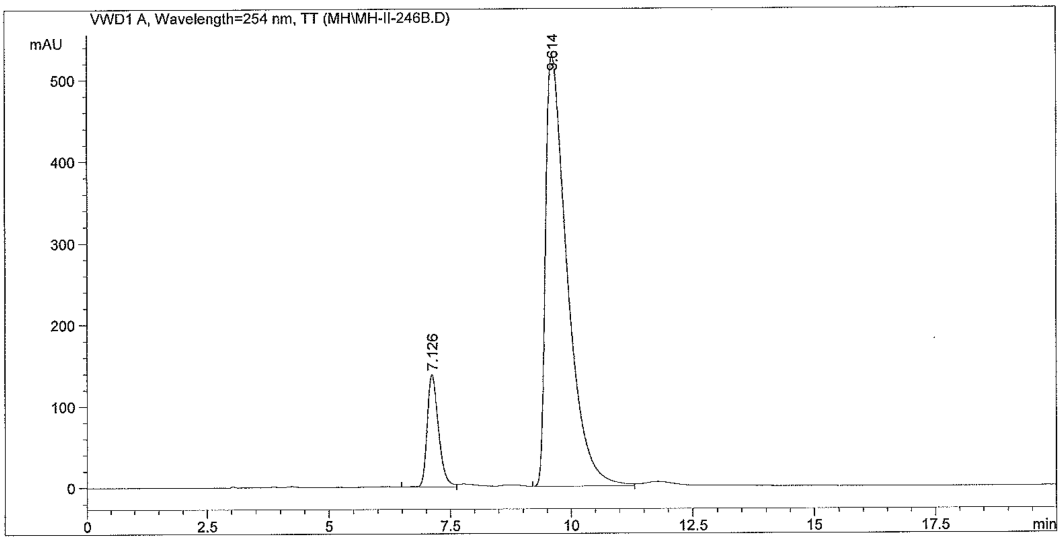
Racemic 19



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.392	VV	0.3593	1.11356e4	472.67834	50.0031
2	11.334	VB	0.6200	1.11342e4	268.84927	49.9969

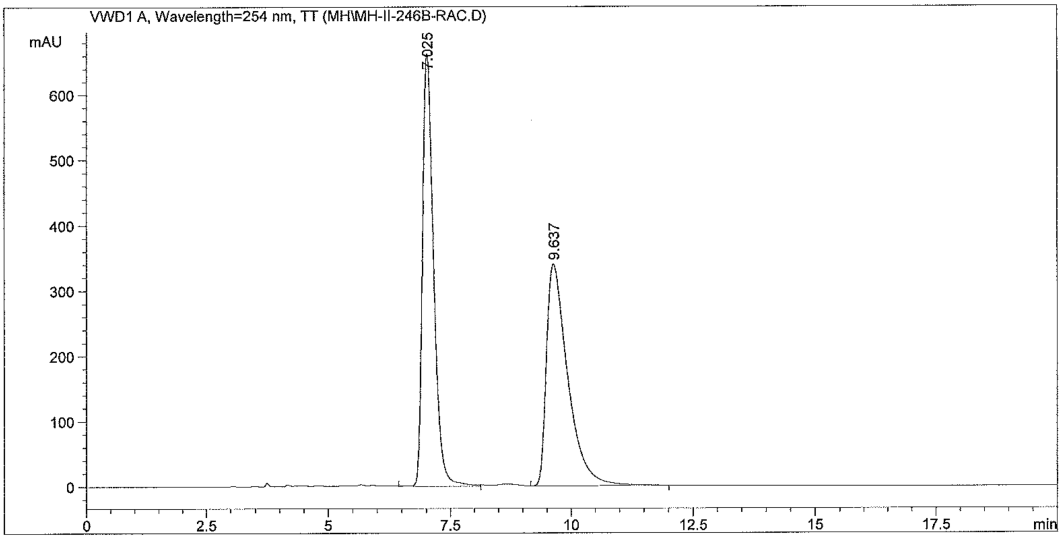
Enantioenriched 20



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.126	VV	0.2498	2245.89282	137.81743	11.9816
2	9.614	VV	0.4672	1.64986e4	528.98590	88.0184

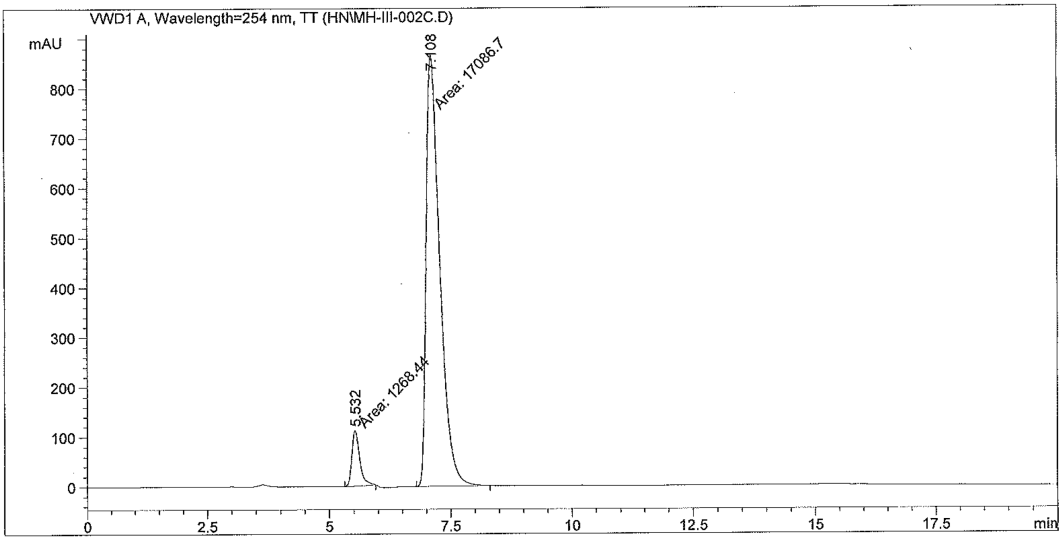
Racemic 20



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.025	VB	0.2449	1.06015e4	662.66174	50.3721
2	9.637	VB	0.4563	1.04449e4	339.70584	49.6279

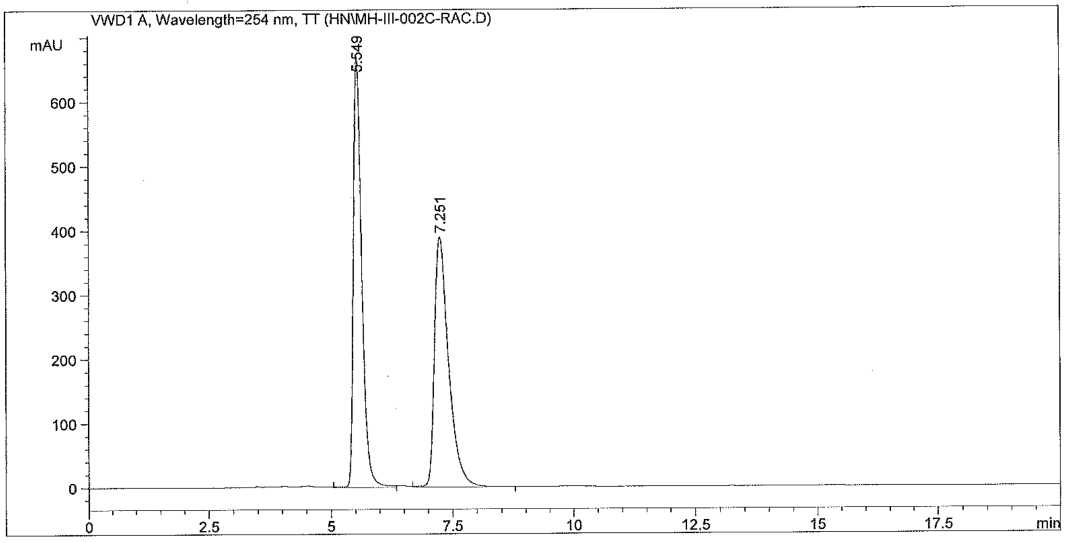
Enantioenriched 21



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.532	MM	0.1900	1268.44031	111.27670	6.9105
2	7.108	MM	0.3285	1.70867e4	866.95087	93.0895

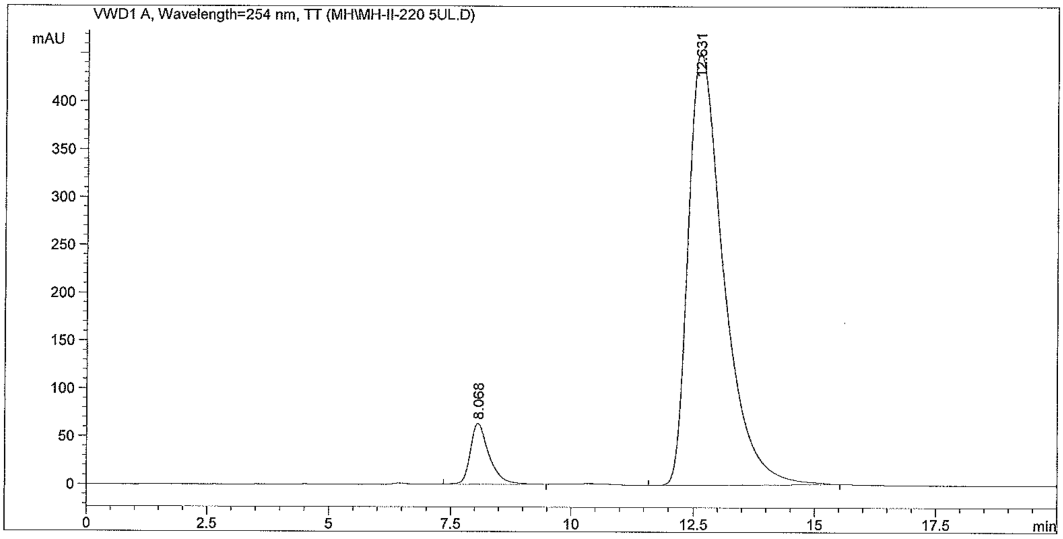
Racemic 21



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.549	VV	0.1845	7924.76514	670.30969	49.9465
2	7.251	VB	0.3080	7941.73828	389.12619	50.0535

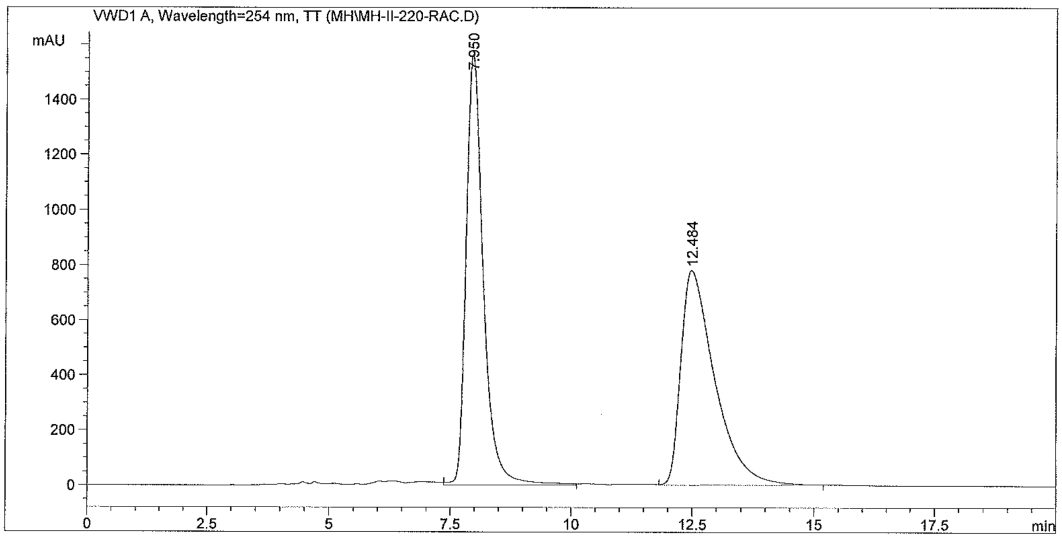
Enantioenriched 22



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.068	VB	0.4006	1716.73059	63.36018	6.9397
2	12.631	VB	0.7519	2.30211e4	450.51941	93.0603

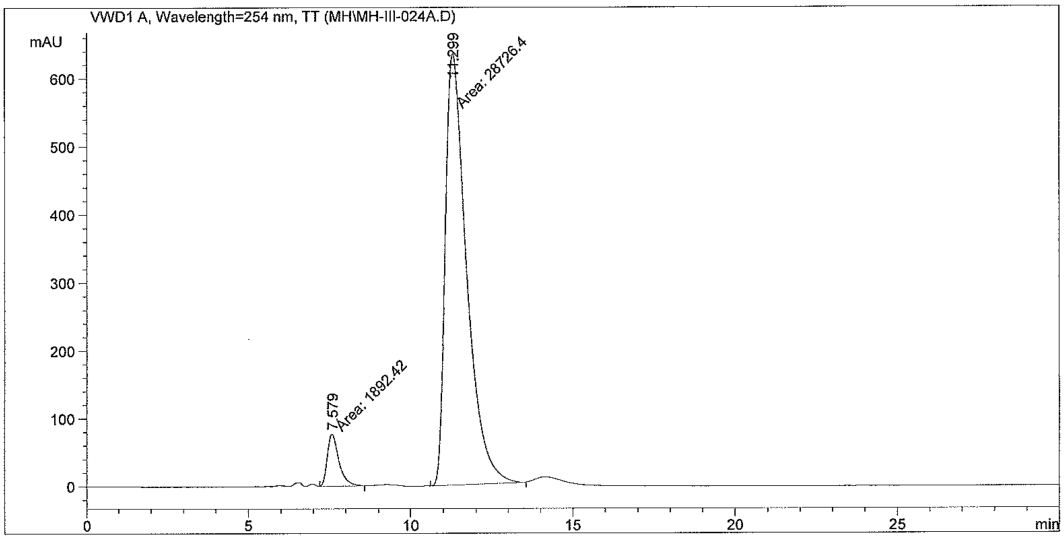
Racemic 22



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.950	VV	0.3737	3.89678e4	1563.95483	50.7303
2	12.484	VB	0.7278	3.78459e4	779.90161	49.2697

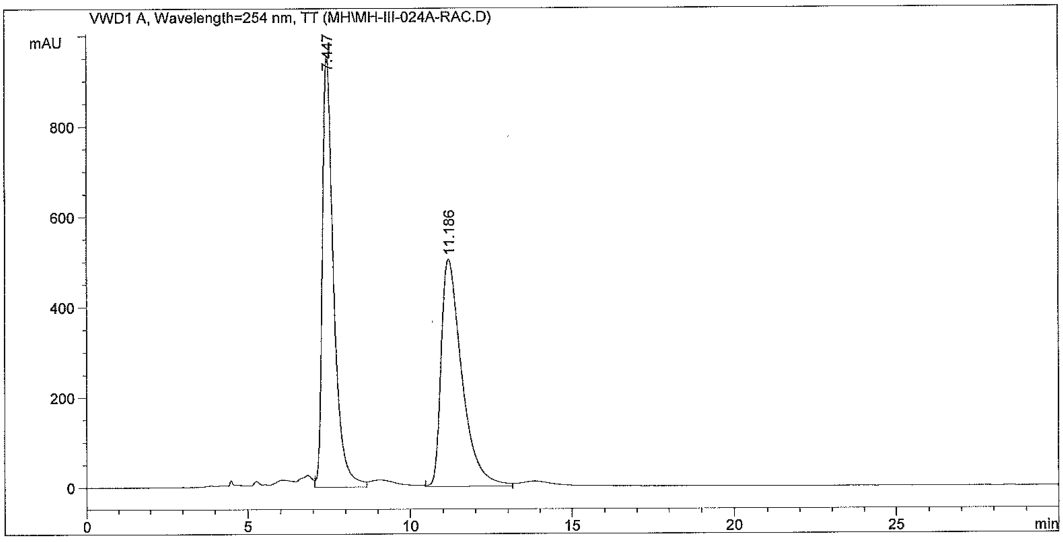
Enantioenriched 23



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.579	MM	0.4115	1892.42041	76.64381	6.1806
2	11.299	MM	0.7545	2.87264e4	634.56439	93.8194

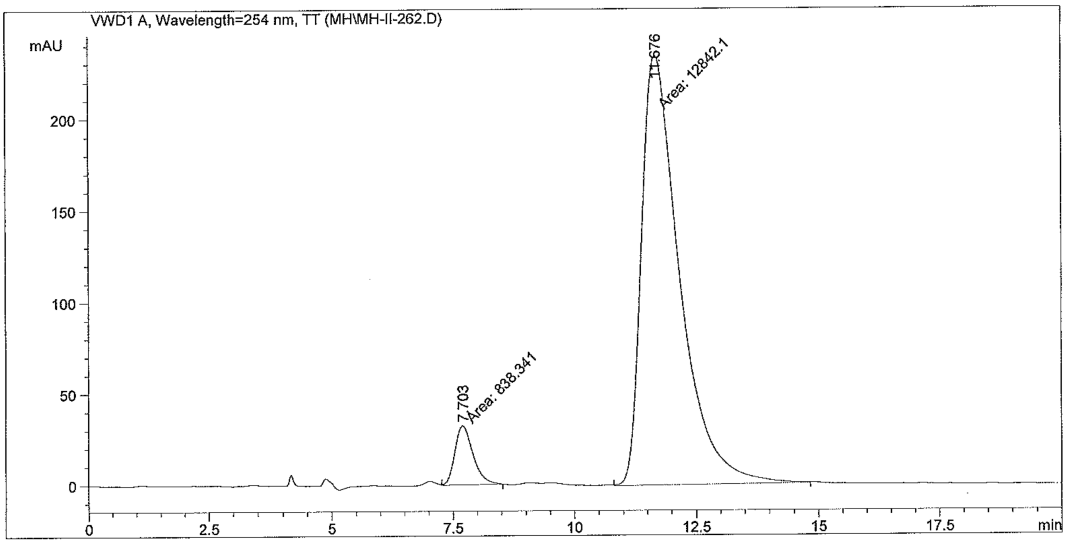
Racemic 23



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.447	VV	0.3618	2.29786e4	956.64764	50.8341
2	11.186	VV	0.6554	2.22245e4	503.59616	49.1659

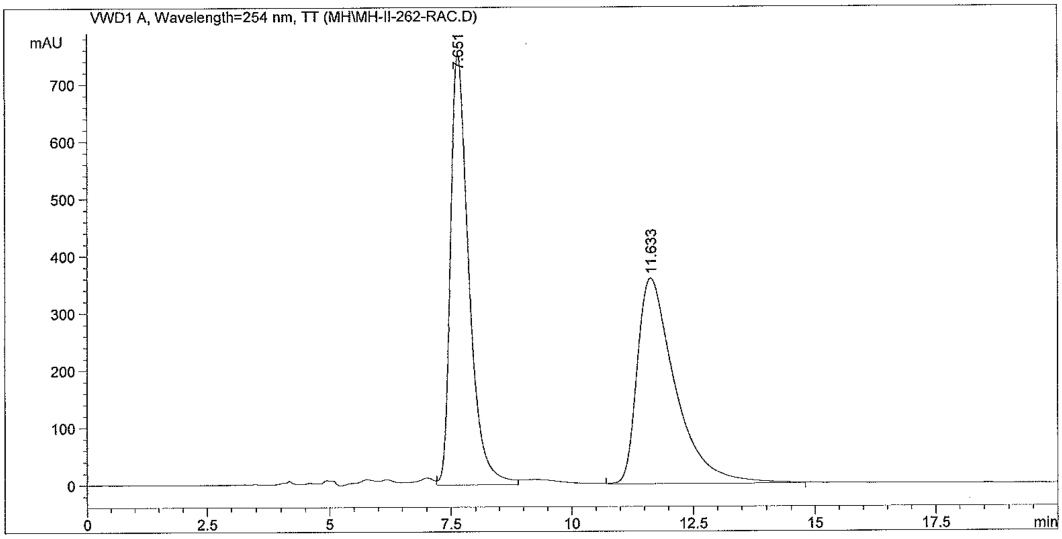
Enantioenriched 24



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.703	MM	0.4346	838.34082	32.15023	6.1280
2	11.676	MM	0.9113	1.28421e4	234.87308	93.8720

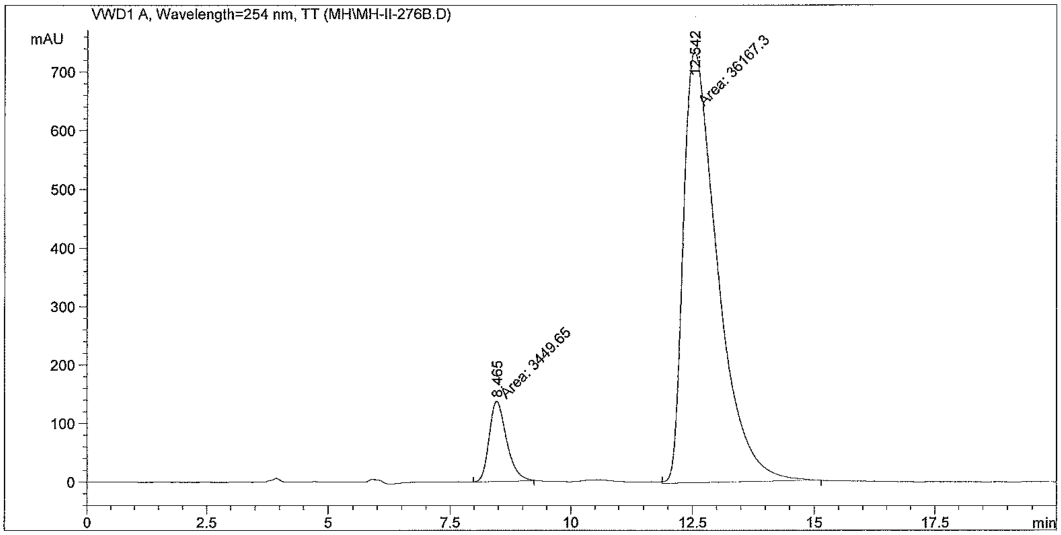
Racemic 24



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.651	VV	0.3944	1.96770e4	753.03821	50.2390
2	11.633	VB	0.7740	1.94898e4	359.32120	49.7610

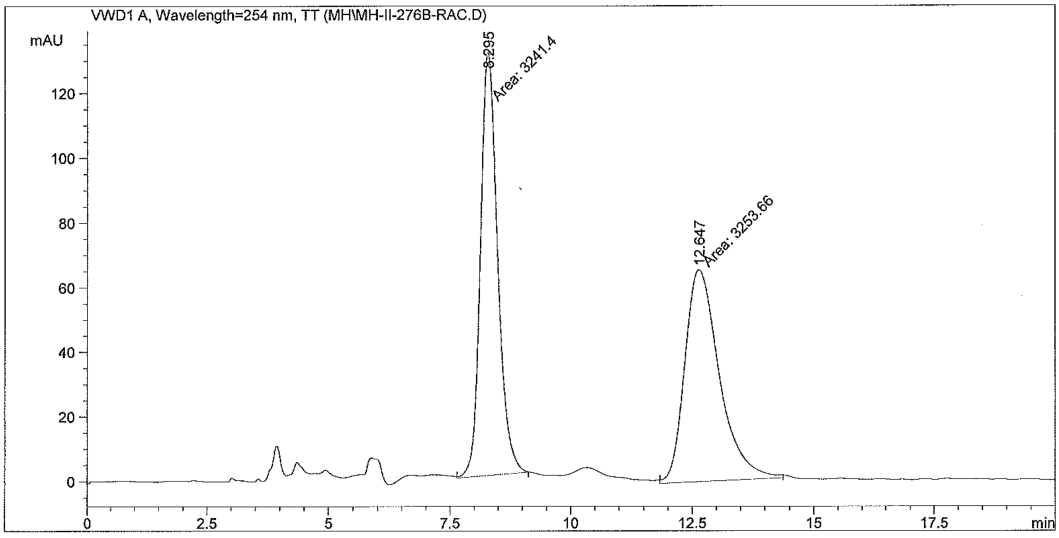
Enantioenriched 25



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.465	MM	0.4194	3449.65381	137.08675	8.7075
2	12.542	MM	0.8187	3.61673e4	736.28906	91.2925

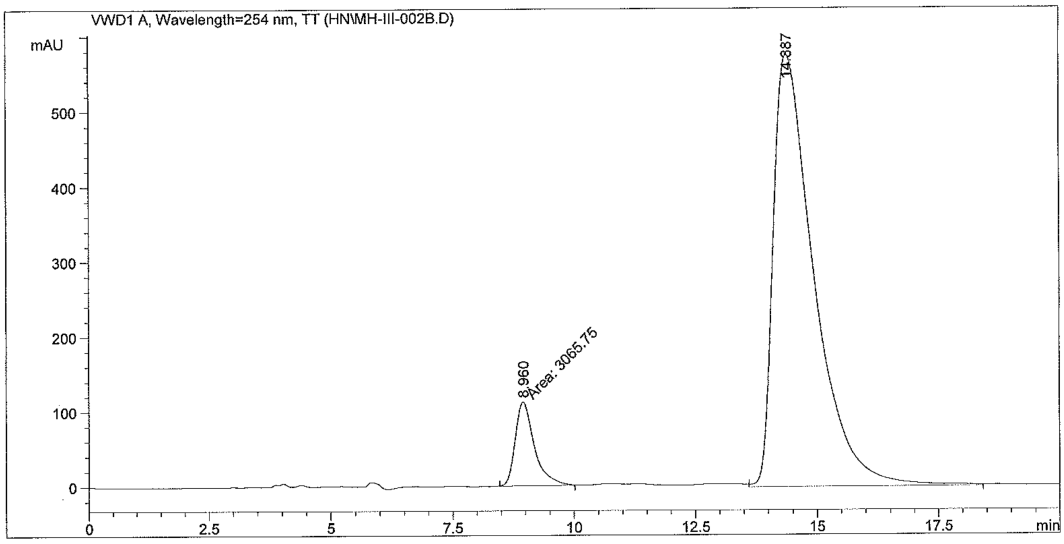
Racemic 25



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.295	MM	0.4129	3241.40137	130.83359	49.9056
2	12.647	MM	0.8269	3253.65771	65.57676	50.0944

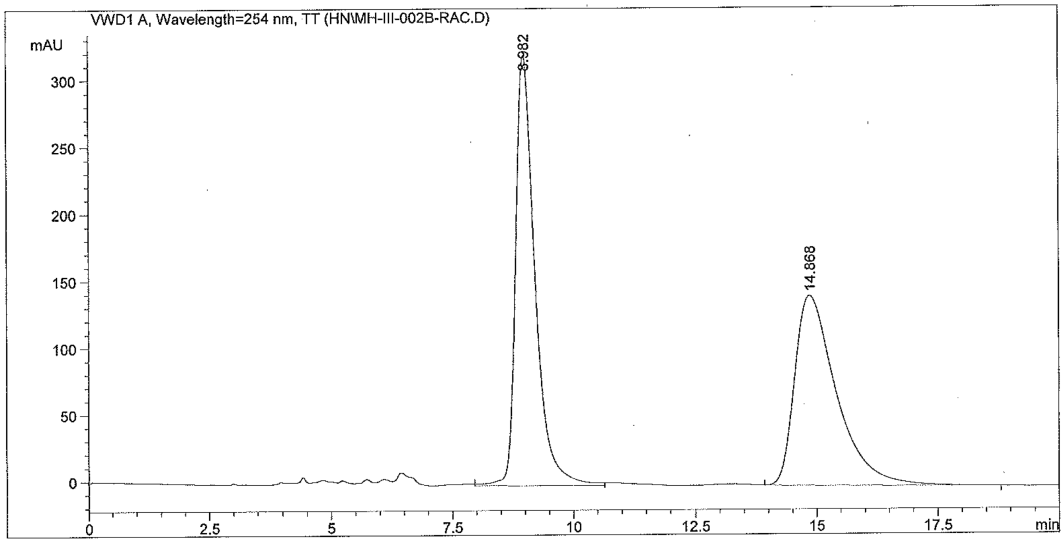
Enantioenriched 26



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.960	MM	0.4562	3065.75293	111.99315	8.4060
2	14.387	VV	0.8581	3.34055e4	575.20129	91.5940

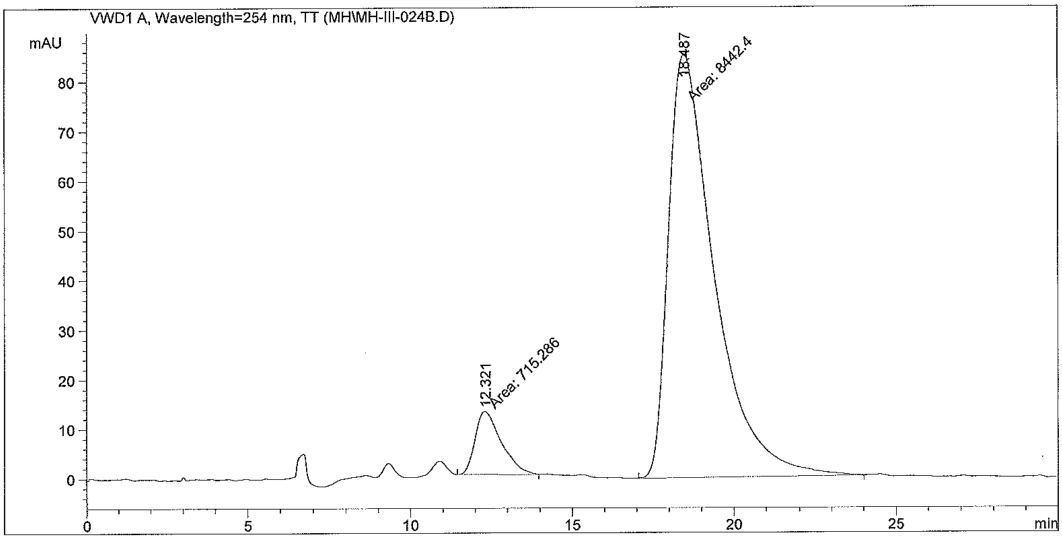
Racemic 26



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.982	VB	0.4267	9035.82129	321.68460	51.3318
2	14.868	VB	0.9000	8566.96777	142.36986	48.6682

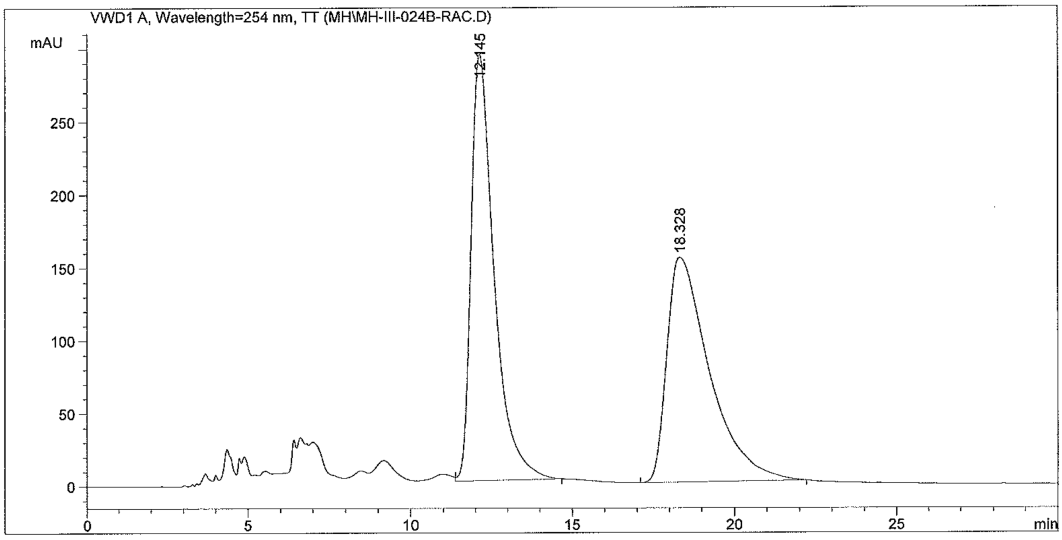
Enantioenriched 27



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.321	MM	0.9359	715.28571	12.73837	7.8108
2	18.487	MM	1.6456	8442.39844	85.50481	92.1892

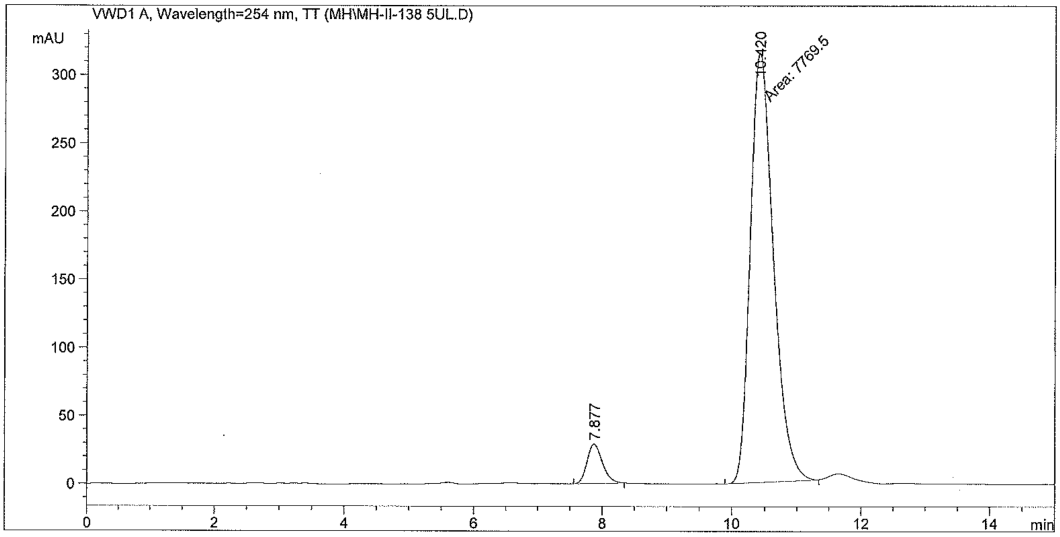
Racemic 27



Signal 1: VWD1 A, Wavelength=254 nm, TT

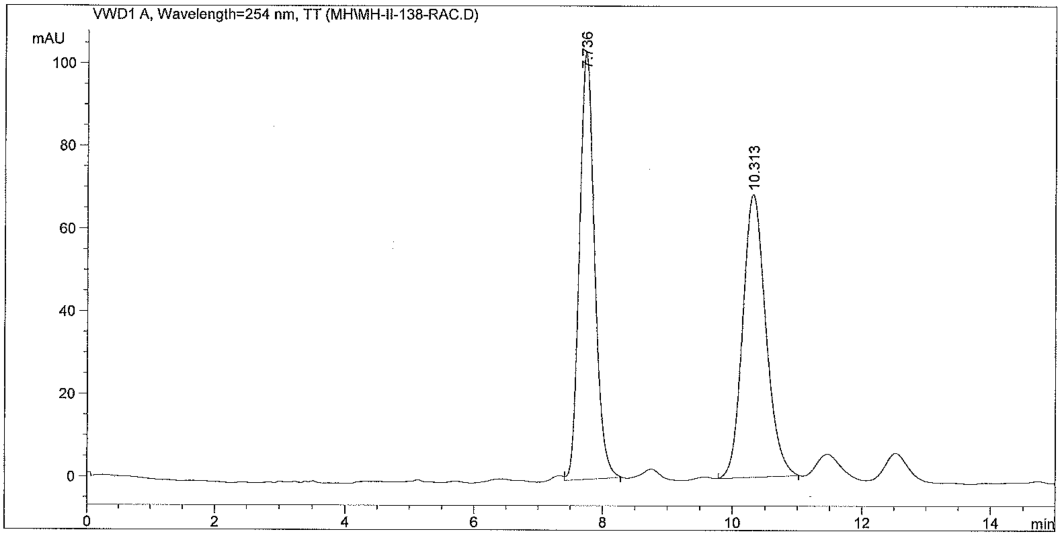
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.145	VB	0.6917	1.45897e4	292.55313	50.8462
2	18.328	BB	1.1879	1.41041e4	154.41762	49.1538

Enantioenriched 30



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.877	BB	0.2456	481.51266	28.90990	5.8358
2	10.420	MM	0.4106	7769.49707	315.38510	94.1642

Racemic 30



Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.736	VB	0.2465	1685.93127	103.27007	49.7714
2	10.313	BB	0.3633	1701.41809	68.33482	50.2286

Crystal Structure Data

Alcohol **29** was recrystallized from EtOAc to provide crystal suitable for X-ray analysis.

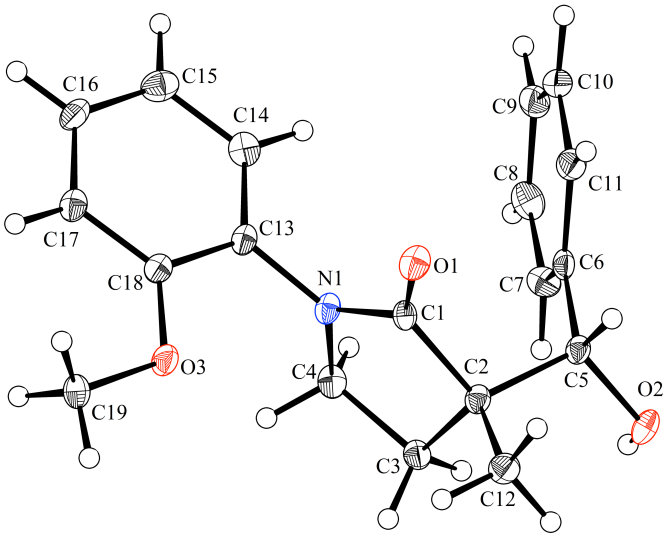


Table S4: Crystal data and structure refinement for alcohol 29.

Empirical formula	C19 H21 N O3	
Formula weight	311.37	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 6.7858(9) Å	α= 112.386(6)°
	b = 7.7709(10) Å	β= 91.911(6)°
	c = 8.1797(10) Å	γ = 96.499(9)°
Volume	394.89(9) $Å^3$	
Z	1	
Density (calculated)	1.309 Mg/m^3	
Absorption coefficient	0.711 mm^{-1}	
F(000)	166	
Crystal size	0.19 x 0.17 x 0.12 mm^3	
Theta range for data collection	5.871 to 72.981°	
Index ranges	-8<=h<=8, -9<=k<=9, -10<=l<=10	
Reflections collected	12444	
Independent reflections	2932 [R(int) = 0.0325]	
Completeness to theta = 67.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9238	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2932 / 3 / 211	
Goodness-of-fit on F^2	1.092	
Final R indices [I>2sigma(I)]	R1 = 0.0285, wR2 = 0.0697	
R indices (all data)	R1 = 0.0296, wR2 = 0.0703	
Absolute structure parameter	0.02(7)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.176 and -0.261 $e.Å^{-3}$	

Table S5. Atomic coordinates (x 10^5) and equivalent isotropic displacement parameters ($Å^2$x 10^4) for alcohol 29. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	70090(20)	62880(20)	34186(18)	178(3)
O(2)	9069(19)	77400(20)	28393(18)	175(3)
O(3)	69940(20)	14730(20)	26787(18)	172(3)
N(1)	50020(20)	43460(20)	43790(20)	137(3)
C(1)	53610(30)	54880(30)	35010(20)	123(4)
C(2)	33840(30)	56260(30)	26220(20)	135(4)
C(3)	19350(30)	40330(30)	27870(30)	149(4)
C(4)	29190(30)	35310(30)	42320(30)	158(4)
C(5)	27750(30)	76160(30)	36140(20)	132(4)
C(6)	28240(30)	82550(30)	56170(20)	138(4)
C(7)	13000(30)	76680(30)	64700(30)	179(4)
C(8)	14580(30)	82500(30)	83020(30)	212(4)
C(9)	31000(30)	94650(30)	93140(30)	206(4)
C(10)	45860(30)	101060(30)	84900(30)	207(4)
C(11)	44560(30)	94920(30)	66480(30)	180(4)
C(12)	36380(30)	53530(30)	6900(20)	175(4)
C(13)	64750(30)	38630(30)	53590(20)	138(4)
C(14)	67970(30)	47950(30)	71850(30)	181(4)
C(15)	81200(30)	42280(30)	81500(30)	208(4)
C(16)	91090(30)	27090(30)	72630(30)	182(4)
C(17)	87950(30)	17540(30)	54260(30)	161(4)
C(18)	74650(30)	23280(30)	44680(30)	137(4)
C(19)	79630(30)	-1260(30)	17620(30)	200(4)

Table S6. Bond lengths [Å] and angles [°] for alcohol 29.

O(1)-C(1)	1.233(2)
O(2)-H(2)	0.8400
O(2)-C(5)	1.428(2)
O(3)-C(18)	1.366(2)
O(3)-C(19)	1.431(2)

N(1)-C(1)	1.346(2)
N(1)-C(4)	1.464(3)
N(1)-C(13)	1.429(2)
C(1)-C(2)	1.535(2)
C(2)-C(3)	1.542(3)
C(2)-C(5)	1.560(2)
C(2)-C(12)	1.531(3)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(3)-C(4)	1.534(3)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5)	1.0000
C(5)-C(6)	1.518(3)
C(6)-C(7)	1.395(3)
C(6)-C(11)	1.393(3)
C(7)-H(7)	0.9500
C(7)-C(8)	1.387(3)
C(8)-H(8)	0.9500
C(8)-C(9)	1.387(3)
C(9)-H(9)	0.9500
C(9)-C(10)	1.381(3)
C(10)-H(10)	0.9500
C(10)-C(11)	1.392(3)
C(11)-H(11)	0.9500
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-C(14)	1.387(3)
C(13)-C(18)	1.399(3)
C(14)-H(14)	0.9500
C(14)-C(15)	1.389(3)
C(15)-H(15)	0.9500
C(15)-C(16)	1.389(3)
C(16)-H(16)	0.9500
C(16)-C(17)	1.395(3)
C(17)-H(17)	0.9500
C(17)-C(18)	1.392(3)

C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800

C(5)-O(2)-H(2)	109.5
C(18)-O(3)-C(19)	116.08(15)
C(1)-N(1)-C(4)	114.79(15)
C(1)-N(1)-C(13)	125.33(16)
C(13)-N(1)-C(4)	119.86(15)
O(1)-C(1)-N(1)	125.46(17)
O(1)-C(1)-C(2)	125.84(17)
N(1)-C(1)-C(2)	108.70(16)
C(1)-C(2)-C(3)	103.50(15)
C(1)-C(2)-C(5)	109.36(15)
C(3)-C(2)-C(5)	113.35(15)
C(12)-C(2)-C(1)	109.59(15)
C(12)-C(2)-C(3)	112.58(16)
C(12)-C(2)-C(5)	108.32(15)
C(2)-C(3)-H(3A)	110.6
C(2)-C(3)-H(3B)	110.6
H(3A)-C(3)-H(3B)	108.7
C(4)-C(3)-C(2)	105.91(16)
C(4)-C(3)-H(3A)	110.6
C(4)-C(3)-H(3B)	110.6
N(1)-C(4)-C(3)	103.61(15)
N(1)-C(4)-H(4A)	111.0
N(1)-C(4)-H(4B)	111.0
C(3)-C(4)-H(4A)	111.0
C(3)-C(4)-H(4B)	111.0
H(4A)-C(4)-H(4B)	109.0
O(2)-C(5)-C(2)	109.80(15)
O(2)-C(5)-H(5)	106.3
O(2)-C(5)-C(6)	112.56(15)
C(2)-C(5)-H(5)	106.3
C(6)-C(5)-C(2)	115.08(15)
C(6)-C(5)-H(5)	106.2
C(7)-C(6)-C(5)	122.89(17)
C(11)-C(6)-C(5)	118.50(17)

C(11)-C(6)-C(7)	118.62(18)
C(6)-C(7)-H(7)	119.9
C(8)-C(7)-C(6)	120.27(19)
C(8)-C(7)-H(7)	119.9
C(7)-C(8)-H(8)	119.7
C(9)-C(8)-C(7)	120.58(19)
C(9)-C(8)-H(8)	119.7
C(8)-C(9)-H(9)	120.2
C(10)-C(9)-C(8)	119.66(19)
C(10)-C(9)-H(9)	120.2
C(9)-C(10)-H(10)	120.0
C(9)-C(10)-C(11)	119.95(19)
C(11)-C(10)-H(10)	120.0
C(6)-C(11)-H(11)	119.6
C(10)-C(11)-C(6)	120.86(19)
C(10)-C(11)-H(11)	119.6
C(2)-C(12)-H(12A)	109.5
C(2)-C(12)-H(12B)	109.5
C(2)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(14)-C(13)-N(1)	120.58(17)
C(14)-C(13)-C(18)	120.32(17)
C(18)-C(13)-N(1)	118.87(16)
C(13)-C(14)-H(14)	119.8
C(13)-C(14)-C(15)	120.44(18)
C(15)-C(14)-H(14)	119.8
C(14)-C(15)-H(15)	120.4
C(14)-C(15)-C(16)	119.17(18)
C(16)-C(15)-H(15)	120.4
C(15)-C(16)-H(16)	119.5
C(15)-C(16)-C(17)	121.02(18)
C(17)-C(16)-H(16)	119.5
C(16)-C(17)-H(17)	120.3
C(18)-C(17)-C(16)	119.50(18)
C(18)-C(17)-H(17)	120.3
O(3)-C(18)-C(13)	115.63(16)

O(3)-C(18)-C(17)	124.81(17)
C(17)-C(18)-C(13)	119.55(17)
O(3)-C(19)-H(19A)	109.5
O(3)-C(19)-H(19B)	109.5
O(3)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S7. Anisotropic displacement parameters ($Å^2$x 10^4) for alcohol 29. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	106(7)	218(7)	248(7)	132(6)	28(5)	16(6)
O(2)	130(7)	229(7)	210(7)	120(6)	18(5)	76(6)
O(3)	184(7)	178(7)	158(6)	52(5)	5(5)	89(6)
N(1)	89(7)	155(8)	196(8)	97(6)	23(6)	25(6)
C(1)	123(9)	120(9)	139(8)	51(7)	40(7)	47(7)
C(2)	113(9)	141(9)	163(9)	70(7)	16(7)	29(7)
C(3)	110(9)	131(9)	205(10)	66(7)	9(7)	7(7)
C(4)	107(9)	160(9)	229(10)	98(8)	41(7)	15(8)
C(5)	98(9)	138(9)	174(9)	73(7)	9(7)	27(7)
C(6)	136(9)	118(9)	177(9)	64(7)	17(7)	54(8)
C(7)	142(10)	175(10)	192(9)	40(8)	29(7)	15(8)
C(8)	227(11)	187(10)	223(10)	67(8)	84(8)	56(9)
C(9)	294(12)	166(10)	145(9)	36(8)	13(8)	68(9)
C(10)	228(11)	152(10)	223(10)	68(8)	-73(8)	0(9)
C(11)	163(10)	168(10)	221(10)	94(8)	-4(8)	6(8)
C(12)	183(10)	188(10)	150(9)	55(8)	19(7)	44(8)
C(13)	103(9)	154(10)	190(10)	102(8)	19(7)	18(8)
C(14)	173(10)	187(10)	194(10)	82(8)	49(8)	33(8)
C(15)	210(11)	255(11)	164(9)	98(8)	3(8)	-9(9)
C(16)	139(10)	219(10)	227(10)	143(8)	-35(8)	-3(8)
C(17)	106(9)	172(10)	235(10)	113(8)	15(7)	15(8)

C(18)	106(9)	158(9)	169(9)	90(7)	15(7)	0(8)
C(19)	195(10)	163(10)	230(10)	42(8)	10(8)	98(8)

Table S8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for alcohol 29.

	x	y	z	U(eq)
H(2)	-19	7232	3229	26
H(3A)	633	4460	3127	18
H(3B)	1722	2930	1646	18
H(4A)	2314	4088	5369	19
H(4B)	2796	2153	3877	19
H(5)	3781	8520	3378	16
H(7)	149	6867	5793	22
H(8)	433	7813	8869	25
H(9)	3203	9854	10568	25
H(10)	5696	10966	9178	25
H(11)	5493	9921	6087	22
H(12A)	4660	6332	653	26
H(12B)	2373	5438	131	26
H(12C)	4042	4116	50	26
H(14)	6107	5828	7781	22
H(15)	8346	4872	9400	25
H(16)	10013	2314	7917	22
H(17)	9484	720	4834	19
H(19A)	7520	-631	495	30
H(19B)	7626	-1091	2242	30
H(19C)	9407	250	1920	30

Table S9. Torsion angles [°] for alcohol 29.

O(1)-C(1)-C(2)-C(3)	167.47(18)
O(1)-C(1)-C(2)-C(5)	-71.4(2)
O(1)-C(1)-C(2)-C(12)	47.2(2)
O(2)-C(5)-C(6)-C(7)	46.8(2)
O(2)-C(5)-C(6)-C(11)	-132.75(18)

N(1)-C(1)-C(2)-C(3)	-12.53(18)
N(1)-C(1)-C(2)-C(5)	108.57(17)
N(1)-C(1)-C(2)-C(12)	-132.83(16)
N(1)-C(13)-C(14)-C(15)	175.12(18)
N(1)-C(13)-C(18)-O(3)	3.4(3)
N(1)-C(13)-C(18)-C(17)	-175.27(17)
C(1)-N(1)-C(4)-C(3)	10.2(2)
C(1)-N(1)-C(13)-C(14)	98.1(2)
C(1)-N(1)-C(13)-C(18)	-87.4(2)
C(1)-C(2)-C(3)-C(4)	18.19(18)
C(1)-C(2)-C(5)-O(2)	-178.29(14)
C(1)-C(2)-C(5)-C(6)	-50.1(2)
C(2)-C(3)-C(4)-N(1)	-17.37(19)
C(2)-C(5)-C(6)-C(7)	-80.1(2)
C(2)-C(5)-C(6)-C(11)	100.4(2)
C(3)-C(2)-C(5)-O(2)	-63.4(2)
C(3)-C(2)-C(5)-C(6)	64.8(2)
C(4)-N(1)-C(1)-O(1)	-178.47(18)
C(4)-N(1)-C(1)-C(2)	1.5(2)
C(4)-N(1)-C(13)-C(14)	-83.8(2)
C(4)-N(1)-C(13)-C(18)	90.7(2)
C(5)-C(2)-C(3)-C(4)	-100.17(17)
C(5)-C(6)-C(7)-C(8)	177.85(18)
C(5)-C(6)-C(11)-C(10)	-179.30(18)
C(6)-C(7)-C(8)-C(9)	2.0(3)
C(7)-C(6)-C(11)-C(10)	1.1(3)
C(7)-C(8)-C(9)-C(10)	0.3(3)
C(8)-C(9)-C(10)-C(11)	-1.8(3)
C(9)-C(10)-C(11)-C(6)	1.0(3)
C(11)-C(6)-C(7)-C(8)	-2.6(3)
C(12)-C(2)-C(3)-C(4)	136.44(16)
C(12)-C(2)-C(5)-O(2)	62.3(2)
C(12)-C(2)-C(5)-C(6)	-169.46(16)
C(13)-N(1)-C(1)-O(1)	-0.3(3)
C(13)-N(1)-C(1)-C(2)	179.70(16)
C(13)-N(1)-C(4)-C(3)	-168.05(16)
C(13)-C(14)-C(15)-C(16)	-0.4(3)
C(14)-C(13)-C(18)-O(3)	177.95(17)

C(14)-C(13)-C(18)-C(17)	-0.7(3)
C(14)-C(15)-C(16)-C(17)	0.2(3)
C(15)-C(16)-C(17)-C(18)	-0.2(3)
C(16)-C(17)-C(18)-O(3)	-178.03(19)
C(16)-C(17)-C(18)-C(13)	0.5(3)
C(18)-C(13)-C(14)-C(15)	0.6(3)
C(19)-O(3)-C(18)-C(13)	-178.57(17)
C(19)-O(3)-C(18)-C(17)	0.0(3)

Symmetry transformations used to generate equivalent atoms: