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Supplementary Information

Enantioselective construction of cycloalkyl amines via nickel-catalysed alkene desymmetrization

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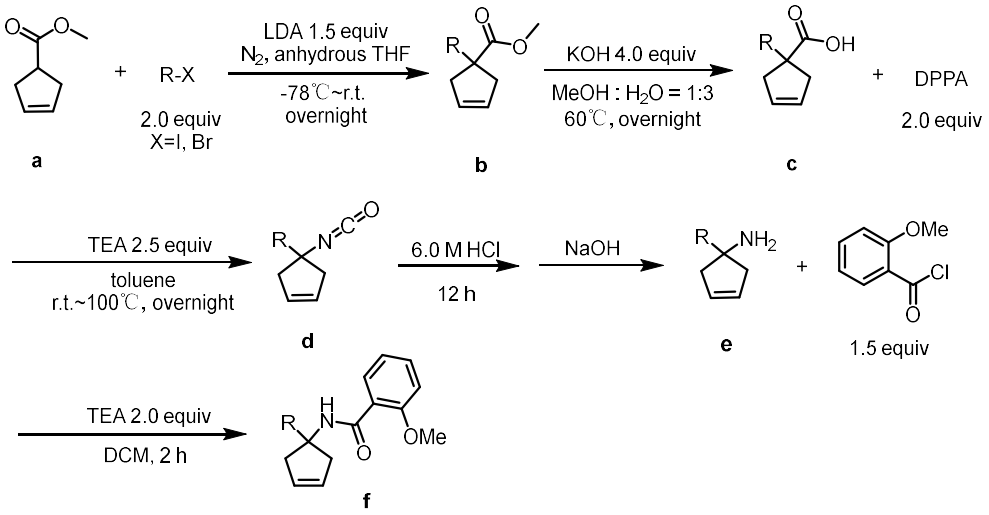
Table of content

General Information

Solvents and all other chemicals used in this article were obtained from Bidepharm, Aladdin, Energy Chemical, Sigma-Aldrich, Alfa-Aesar and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light (254 nm) and Vogel's permanganate. ^{1}H NMR spectra were recorded on BRUKER AVANCE NEO 500 (500MHz) or BRUKER AVANCE NEO Ascend 600 (600 MHz) spectrometers. Data for ^{1}H NMR spectra are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants, and integration. Chemical shifts are reported in parts per million (ppm) referenced to the appropriate solvent signals, for example 7.26 ppm for chloroform-d. Coupling constants, J, are reported in Hertz (Hz). ^{13}C NMR spectra were recorded on BRUKER AVANCE NEO 500 (126 MHz) or BRUKER AVANCE NEO Ascend 600 (151 MHz). Chemical shifts are reported in parts per million (ppm) referenced to the appropriate solvent signals, for example 77.00 ppm for chloroform-d. Optical rotations were measured on a Rudolph Research Analytical Autopol VI automatic polarimeter using a 50 mm path-length cell at 589 nm. The enantiomeric excess was determined on a Hitachi Primaide HPLC system using commercially available columns. High-resolution mass spectra (HRMS) were recorded using LC-MS (Thermo HPLC-orbitrap Elite).

1. Synthesis of substrates



A magnetic stir bar was placed in a 100 mL pear-shaped flask, followed by three cycles of nitrogen purging. Under nitrogen atmosphere, 20 mL of anhydrous THF was introduced and the mixture was cooled to -78°C. Diisopropylamine (1.10 mL, 7.5 mmol) was then injected via syringe, followed by the addition of *n*-butyllithium hexane solution (3.0 mL, 7.5 mmol). After 15 minutes of reaction, methyl cyclopent-3-enecarboxylate (0.61 mL, 5.0 mmol) was introduced into the system and stirred for 45 minutes. The haloalkane R-X (10.0 mmol, 2.0 equiv) was subsequently added dropwise, after which the reaction mixture was warmed to room temperature and stirred overnight. The reaction was quenched with saturated aqueous ammonium chloride solution, and the layers were extracted with ethyl acetate. The combined organic phases were dried over anhydrous sodium sulfate, concentrated under reduced pressure, and purified by column chromatography (98:2 hexane/ethyl acetate) to afford intermediate **b**.

The intermediate **b** was dissolved in methanol, followed by the addition of 3.0 equivalents of potassium hydroxide (pre-dissolved in 15 mL of deionized water). The reaction mixture was heated to 60°C with continuous stirring overnight. After completion, the methanol was removed under reduced pressure. The residue was then dissolved in water, and the aqueous phase was washed with dichloromethane (2-3 times), with the organic layers being discarded. The aqueous phase was subsequently acidified with hydrochloric acid and extracted with dichloromethane. The combined

organic extracts were dried over anhydrous sodium sulfate and concentrated by rotary evaporation to yield the carboxylic acid intermediate **c**.

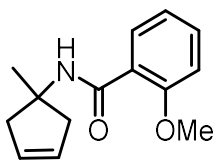
The carboxylic acid intermediate **c** was dissolved in 20 mL of toluene, followed by the gradual addition of Diphenylphosphoryl azide (2.0 equivalents) and triethylamine (2.5 equivalents) at ambient temperature. The resulting mixture was stirred at room temperature for one hour before being heated to 100°C and maintained stirring overnight to provide intermediate **d**, this intermediate was used directly for next step.

10 mL of 6.0 M aqueous hydrochloric acid was directly added to the solution of the last step, and the mixture was stirred for 12 hours. The biphasic system was then separated to isolate the aqueous layer. This aqueous phase was subsequently basified by the addition of sodium hydroxide solution, followed by extraction with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and transferred to a 100 mL flask; this solution of intermediate **e** was used directly for next step.

Under an ice bath, triethylamine (2.0 equiv) was slowly added to the DCM solution of the amine **e**, followed by the dropwise addition of 2-methoxybenzoyl chloride (1.5 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 3 hours. Quenched the reaction by adding pure water, then extracted with DCM. The organic phases were combined and dried over anhydrous sodium sulfate. The solution was filtered and concentrated under vacuum. Purified the concentrated mixture by column chromatography (hexane : ethyl acetate = 91 : 9) to obtain the symmetric cyclopentenyl amine substrate **f**.

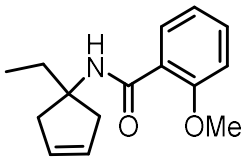
2. Substrates data of 1a to 1af

2-methoxy-N-(1-methylcyclopent-3-en-1-yl)benzamide (1a)



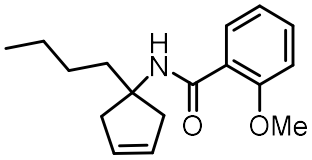
White solid, 474 mg, 41% yield. M.p.: 60-64℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.8, 1.7 Hz, 1H), 8.08 (s, 1H), 7.45 – 7.38 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 5.72 – 5.65 (m, 2H), 3.94 (s, 3H), 2.85 (d, *J* = 14.8 Hz, 2H), 2.51 (d, *J* = 14.7 Hz, 2H), 1.55 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 157.2, 132.4, 131.8, 128.5, 122.2, 121.2, 111.2, 59.4, 55.8, 46.7, 27.3. ESI-HRMS: m/z $[M+H]^+$calcd. For $C_{14}H_{17}NO_2$: 232.1332, found: 232.1331.

N-(1-ethylcyclopent-3-en-1-yl)-2-methoxybenzamide (1v)



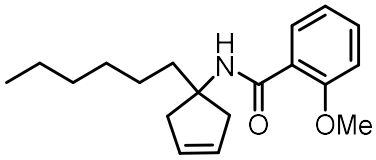
Colorless oil, 441 mg, 36% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.8 Hz, 1H), 7.97 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.73 – 5.62 (m, 2H), 3.95 (s, 3H), 2.78 (d, *J* = 15.7 Hz, 2H), 2.54 (d, *J* = 15.3 Hz, 2H), 1.97 (q, *J* = 7.3 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ164.2, 157.3, 132.4, 131.9, 128.6, 122.5, 121.3, 111.3, 63.2, 56.0, 44.9, 31.3, 8.6. ESI-HRMS: m/z $[M+H]^+$calcd. For $C_{15}H_{19}NO_2$: 246.1489, found: 246.1488.

N-(1-butylcyclopent-3-en-1-yl)-2-methoxybenzamide (1w)



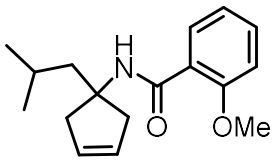
Colorless oil, 475 mg, 35% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.98 (s, 1H), 7.43 – 7.39 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.70 – 5.67 (m, 2H), 3.94 (s, 3H), 2.79 (d, *J* = 15.0 Hz, 2H), 2.54 (d, *J* = 14.9 Hz, 2H), 1.94 (dd, *J* = 13.9, 5.2 Hz, 2H), 1.36 – 1.28 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 157.2, 132.3, 131.9, 128.6, 122.5, 121.3, 111.3, 62.7, 55.9, 45.2, 38.6, 26.7, 23.0, 14.1. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{23}NO_2$: 274.1802, found: 274.1801.

N-(1-hexylcyclopent-3-en-1-yl)-2-methoxybenzamide (1x)



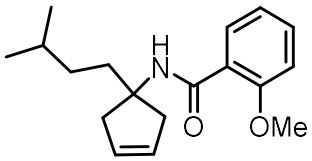
Colorless oil, 241 mg, 16% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.97 (s, 1H), 7.45 – 7.38 (m, 1H), 7.07 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.72 – 5.64 (m, 2H), 3.94 (s, 3H), 2.79 (d, *J* = 15.0 Hz, 2H), 2.54 (d, *J* = 15.0 Hz, 2H), 1.97 – 1.88 (m, 2H), 1.33 – 1.25 (m, 8H), 0.89–0.84 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 157.3, 132.4, 132.0, 128.6, 122.6, 121.4, 111.3, 62.8, 56.0, 45.3, 39.0, 31.9, 29.7, 24.5, 22.6, 14.1. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{27}NO_2$: 302.2115, found: 302.2115.

N-(1-isobutylcyclopent-3-en-1-yl)-2-methoxybenzamide (1y)



Colorless oil, 476 mg, 35% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.97 (s, 1H), 7.45 – 7.36 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.74 – 5.63 (m, 2H), 3.94 (s, 3H), 2.81 (d, *J* = 15.2 Hz, 2H), 2.57 (d, *J* = 15.3 Hz, 2H), 1.94 (d, *J* = 6.1 Hz, 2H), 1.82 – 1.71 (m, 1H), 0.95 (d, *J* = 6.7 Hz, 6H).^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 157.2, 132.4, 132.0, 128.7, 122.6, 121.4, 111.4, 63.3, 55.9, 46.7, 46.3, 25.2, 24.3. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{23}NO_2$: 274.1802, found: 274.1801.

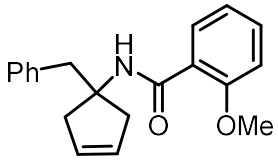
N-(1-isopentylcyclopent-3-en-1-yl)-2-methoxybenzamide (1z)



Colorless oil, 233 mg, 14% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.96 (s, 1H), 7.46 – 7.38 (m, 1H), 7.11 – 7.03 (m, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 5.73 – 5.63 (m, 2H), 3.95 (s, 3H), 2.80 (d, *J* = 14.9 Hz, 2H), 2.53 (d, *J* = 15.0 Hz,

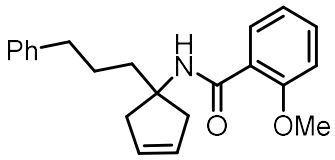
2H), 1.95 – 1.89 (m, 2H), 1.58 – 1.49 (m, 1H), 1.25 – 1.19 (m, 2H), 0.89 (d, J = 6.6 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 157.3, 132.3, 132.0, 128.7, 122.6, 121.4, 111.4, 62.8, 56.0, 45.2, 36.8, 33.5, 28.4, 22.7. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{18}H_{25}NO_2$: 288.1958, found: 288.1958.

N-(1-benzylcyclopent-3-en-1-yl)-2-methoxybenzamide (1aa)



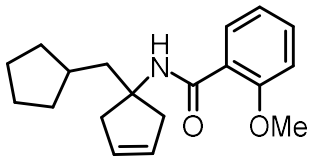
White powder, 245 mg, 16% yield. M.p.: 100-102℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, J = 7.8, 1.6 Hz, 1H), 7.77 (s, 1H), 7.46 – 7.38 (m, 1H), 7.24 – 7.15 (m, 5H), 7.09 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 5.72 (s, 2H), 3.73 (s, 3H), 3.28 (s, 2H), 2.77 (d, J = 15.2 Hz, 2H), 2.62 (d, J = 15.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8, 157.3, 138.5, 132.4, 131.9, 130.5, 128.6, 127.8, 126.1, 122.6, 121.3, 111.5, 63.6, 55.9, 45.1, 42.2. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{20}H_{21}NO_2$: 308.1645, found: 308.1641.

2-methoxy-N-(1-(3-phenylpropyl)cyclopent-3-en-1-yl)benzamide (1ab)



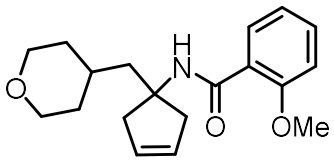
Colorless oil, 324 mg, 19% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, J = 7.8, 1.8 Hz, 1H), 7.96 (s, 1H), 7.43 – 7.38 (m, 1H), 7.25 (t, J = 7.5 Hz, 2H), 7.17 (d, J = 7.8 Hz, 3H), 7.06 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 5.69 – 5.64 (m, 2H), 3.88 (s, 3H), 2.76 (d, J = 15.1 Hz, 2H), 2.62 (t, J = 7.9 Hz, 2H), 2.55 (d, J = 15.1 Hz, 2H), 2.06 – 2.00 (m, 2H), 1.69 – 1.62 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 157.2, 142.6, 132.4, 131.9, 128.6, 128.3, 128.2, 125.6, 122.4, 121.3, 111.3, 62.8, 55.9, 45.4, 38.4, 36.2, 26.8. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{22}H_{25}NO_2$: 336.1958, found: 336.1958.

N-(1-(cyclopentylmethyl)cyclopent-3-en-1-yl)-2-methoxybenzamide (1ac)



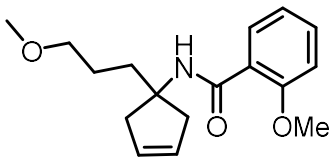
Colorless oil, 362 mg, 24% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.97 (s, 1H), 7.45 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.72 – 5.65 (m, 2H), 3.94 (s, 3H), 2.79 (d, *J* = 15.2 Hz, 2H), 2.58 (d, *J* = 15.2 Hz, 2H), 2.08 (d, *J* = 5.8 Hz, 2H), 1.87 – 1.78 (m, 3H), 1.63 – 1.54 (m, 2H), 1.50 – 1.41 (m, 2H), 1.20 – 1.11 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 157.2, 132.3, 132.0, 128.7, 122.7, 121.4, 111.4, 63.4, 55.9, 45.9, 44.1, 37.2, 34.1, 24.9. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{25}NO_2$: 300.1958, found: 300.1958.

2-methoxy-N-(1-((tetrahydro-2H-pyran-4-yl)methyl)cyclopent-3-en-1-yl)benzamide (1ad)



Colorless oil, 448 mg, 28% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.92 (s, 1H), 7.46 – 7.39 (m, 1H), 7.07 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 5.72 – 5.65 (m, 2H), 3.94 (s, 3H), 3.91 – 3.85 (m, 2H), 3.38 – 3.30 (m, 2H), 2.78 (d, *J* = 15.2 Hz, 2H), 2.58 (d, *J* = 15.3 Hz, 2H), 2.02 (d, *J* = 5.9 Hz, 2H), 1.74 – 1.65 (m, 1H), 1.65 – 1.60 (m, 2H), 1.44 – 1.35 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.1, 132.4, 131.9, 128.6, 122.5, 121.4, 111.4, 68.0, 63.0, 55.9, 46.5, 44.8, 34.3, 32.1. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{25}NO_3$: 316.1907, found: 316.1907.

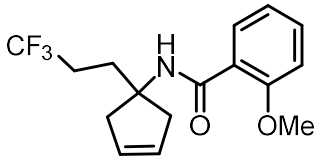
2-methoxy-N-(1-(3-methoxypropyl)cyclopent-3-en-1-yl)benzamide (1ae)



Colorless oil, 273 mg, 19% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.8 Hz, 1H), 8.00 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.72 – 5.64 (m, 2H), 3.94 (s, 3H), 3.38 (t, *J* = 6.7 Hz, 2H), 3.31 (s, 3H), 2.78 (d, *J*

= 15.3 Hz, 2H), 2.57 (d, *J* = 15.3 Hz, 2H), 2.04 – 1.98 (m, 2H), 1.65 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 157.3, 132.4, 131.9, 128.6, 122.3, 121.3, 111.3, 73.0, 62.6, 58.5, 55.9, 45.4, 34.9, 25.0. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{23}NO_3$: 290.1751, found: 290.1750.

2-methoxy-N-(1-(3,3,3-trifluoropropyl)cyclopent-3-en-1-yl)benzamide (1af)

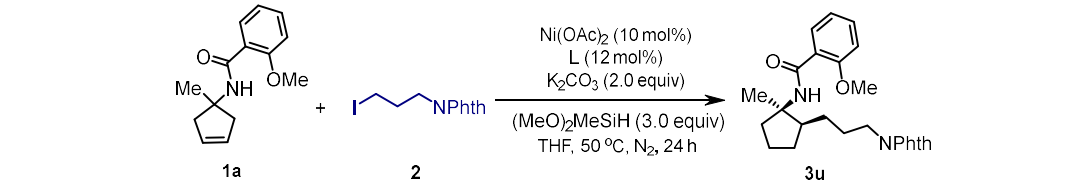


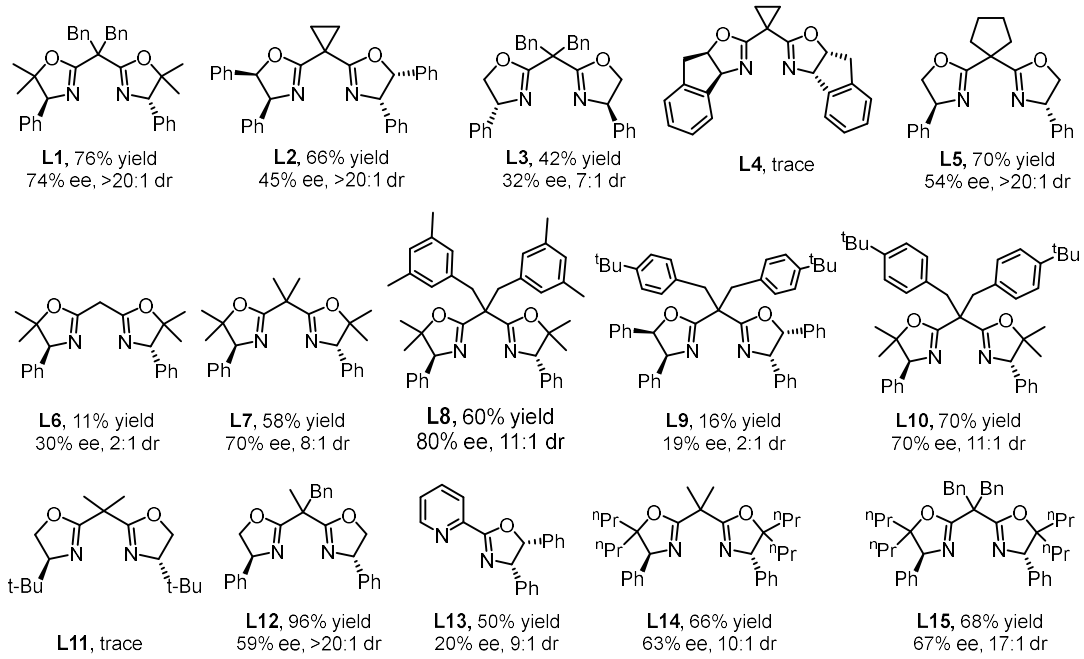
White powder, 166 mg, 11% yield. M.p.: 50-52℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.95 (s, 1H), 7.47 – 7.40 (m, 1H), 7.10 – 7.04 (m, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 5.70 (s, 2H), 3.94 (s, 3H), 2.76 (d, *J* = 15.3 Hz, 2H), 2.59 (d, *J* = 15.3 Hz, 2H), 2.32 – 2.26 (m, 2H), 2.18 – 2.06 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 157.2, 132.7, 131.9, 128.5 (q, *J* = 552.2 Hz), 128.5, 121.9, 121.4, 111.3, 61.9, 55.9, 45.5, 30.4 (q, *J* = 2.7 Hz), 29.8 (q, *J* = 28.8 Hz). ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{16}H_{18}F_3NO_2$: 314.1362, found: 314.1368.

3. Details of screening and substrate scope investigation

3.1 Details of screening

Supplementary Table 1. Ligand screening





L1, 76% yield, 74% ee, >20:1 dr

L2, 66% yield, 45% ee, >20:1 dr

L3, 42% yield, 32% ee, 7:1 dr

L4, trace

L5, 70% yield, 54% ee, >20:1 dr

L6, 11% yield, 30% ee, 2:1 dr

L7, 58% yield, 70% ee, 8:1 dr

L8, 60% yield, 80% ee, 11:1 dr

L9, 16% yield, 19% ee, 2:1 dr

L10, 70% yield, 70% ee, 11:1 dr

L11, trace

L12, 96% yield, 59% ee, >20:1 dr

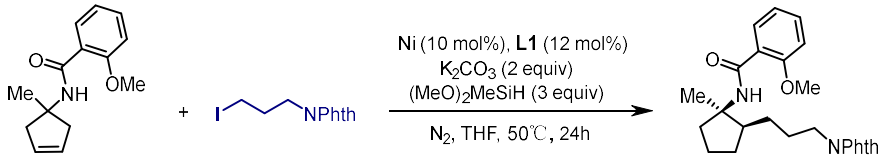
L13, 50% yield, 20% ee, 9:1 dr

L14, 66% yield, 63% ee, 10:1 dr

L15, 68% yield, 67% ee, 17:1 dr

The iodine compound was used in 2.5 equivalents and the reaction was conducted under N_2 atmosphere. The yield was determined by thin layer chromatography. The enantiomeric excess was determined by high-performance liquid chromatography (HPLC) using a chiral stationary phase.

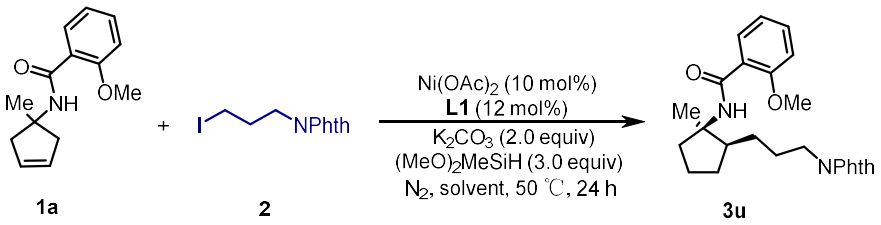
Supplementary Table 2. Nickel catalyst screening



entry	catalyst	yield	ee	dr
1	$Ni(OAc)_2$	76%	-74%	>20:1
2	$NiCl_2(DME)$	65%	74%	>20:1
3	$Ni(OTs)_2$	29%	-75%	13:1
4	$Ni(TFA)_2$	11%	-81%	7.5:1
5	$Ni(OBs)_2$	55%	-76%	>20:1
6	$Ni(OAc)_2(DME)$	25%	-75%	2.5:1
7	$Ni(OTf)_2$	26%	-51%	7:1

The iodine compound was used in 2.5 equivalents and the reaction was conducted under N_2 atmosphere. The yield was determined by thin layer chromatography. The enantiomeric excess was determined by high-performance liquid chromatography (HPLC) using a chiral stationary phase.

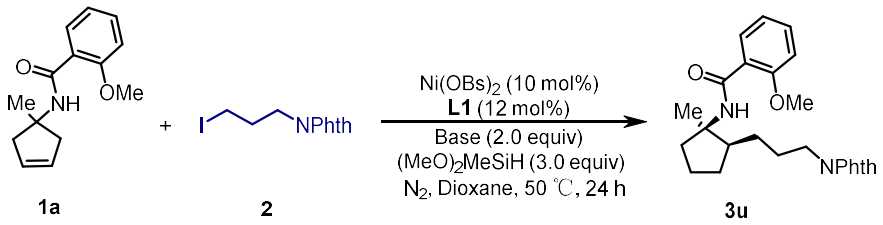
Supplementary Table 3. Solvent screening



entry	solvent	yield	ee	dr
1	THF	76%	-74%	27:1
2	DCM	trace	-	-
3	DMF	none	-	-
4	MeCN	5%	77%	1:1
5	Toluene	trace	-	-
6	DME	25%	-69%	3:1
7	tert-Butyl acetate	20%	-73%	3:1
8	1,4-dioxane	42%	-84%	8:1
9	2-Me-THF	30%	-81%	12:1
10	DMA	trace	-	-

The iodine compound was used in 2.5 equivalents and the reaction was conducted under N_2 atmosphere. The yield was determined by thin layer chromatography. The enantiomeric excess was determined by high-performance liquid chromatography (HPLC) using a chiral stationary phase.

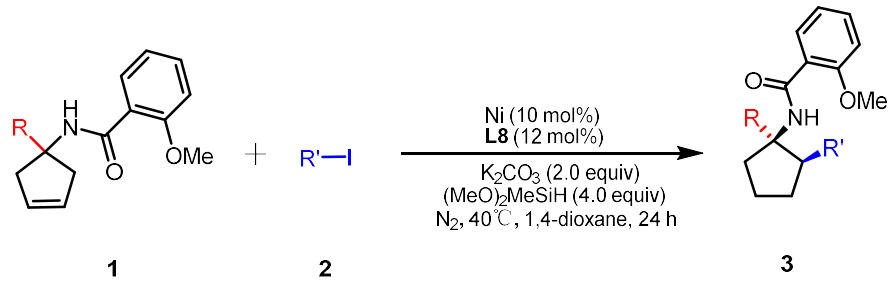
Supplementary Table 4. Base screening



entry	Base	yield	ee
1	K_2CO_3	61%	-90%
2	KF	40%	-92%
3	K_3PO_4	49%	-92%
4	CaF_2	none	-
5	Cs_2CO_3	trace	-
6	Li_2CO_3	trace	-
7	$Ca_3(PO_4)_2$	trace	-
8	Na_2HPO_4	trace	-
9	K_2HPO_4	38%	-89%
10	NaH_2PO_4	none	-
11	KH_2PO_4	trace	-
12	Na_3PO_4	trace	-
13	Na_2CO_3	58%	-88%
14	KOH	none	-

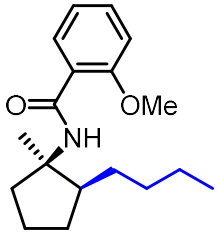
The iodine compound was used in 2.5 equivalents and the reaction was conducted under N_2 atmosphere. The yield was determined by thin layer chromatography. The enantiomeric excess was determined by high-performance liquid chromatography (HPLC) using a chiral stationary phase.

3.2 Substrate scope investigation of 3a to 3af



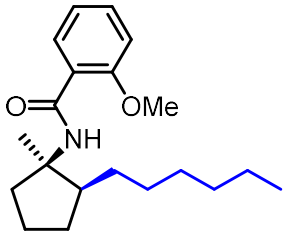
1 2 3

The reaction was carried out in a 4-mL sealed tube under nitrogen atmosphere. A mixture of substrate **1** (0.1 mmol), compound **2** (0.25 mmol to 0.4 mmol), Nickel(II) 2-amino-5-methylbenzenesulfonate (0.01 mmol), ligand **L8** (0.012 mmol), methyldimethoxysilane (0.4 mmol), and potassium carbonate (0.2 mmol) was dissolved in anhydrous 1,4-dioxane (1.0 mL). The resulting solution was stirred at 40°C for 24 hours. After completion, the reaction mixture was concentrated under reduced pressure, and the crude product was purified by preparative thin-layer chromatography to afford the desired compound.



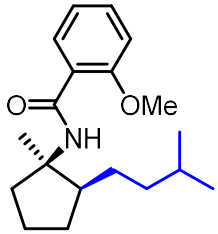
N-((1R,2S)-2-butyl-1-methylcyclopentyl)-2-methoxybenzamide (3a)

Colorless oil, 16 mg, 54% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.90 (s, 1H), 7.44 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.95 (s, 3H), 2.70 – 2.64 (m, 1H), 2.04 – 1.97 (m, 1H), 1.68 – 1.63 (m, 2H), 1.63 – 1.57 (m, 3H), 1.55 (s, 3H), 1.46 – 1.30 (m, 5H), 1.19 – 1.12 (m, 1H), 0.94 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 132.2, 132.0, 123.0, 121.3, 111.3, 62.9, 55.9, 50.9, 37.7, 31.1, 30.1, 29.1, 23.4, 23.2, 20.9, 14.1. $[\alpha]_{20D}$ = +20.0 (c 1.0, CH_3CN). The enantiomeric excess (91% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 35.413 min; t_R (major) = 37.373 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{18}H_{27}NO_2$: 290.2115, found: 290.2114.



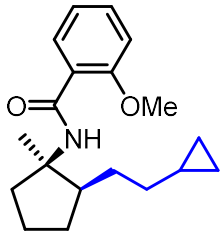
N-((1R,2S)-2-hexyl-1-methylcyclopentyl)-2-methoxybenzamide (3b)

Colorless oil, 19 mg, 61% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.90 (s, 1H), 7.44 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.95 (s, 3H), 2.70 – 2.64 (m, 1H), 2.03 – 1.96 (m, 1H), 1.67 – 1.57 (m, 5H), 1.54 (s, 3H), 1.48 – 1.42 (m, 1H), 1.40 – 1.35 (m, 2H), 1.34 – 1.29 (m, 6H), 1.18 – 1.12 (m, 1H), 0.90 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 132.2, 132.0, 123.0, 121.3, 111.3, 62.9, 55.9, 50.9, 37.7, 31.8, 30.1, 29.8, 29.4, 28.8, 23.4, 22.6, 20.9, 14.1. $[\alpha]_{20D}$ = +24.0 (c 1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 32.313 min; t_R (major) = 34.783 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{20}H_{31}NO_2$: 318.2428, found: 318.2430.



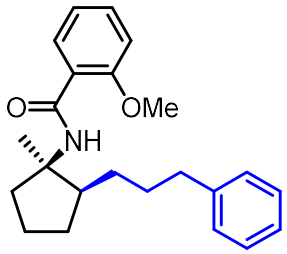
N-((1R,2R)-2-isopentyl-1-methylcyclopentyl)-2-methoxybenzamide (3c)

Colorless oil, 19 mg, 63% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.8 Hz, 1H), 7.90 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 2.72 – 2.66 (m, 1H), 2.04 – 1.97 (m, 1H), 1.69 – 1.63 (m, 2H), 1.62 – 1.57 (m, 3H), 1.55 (s, 4H), 1.40 – 1.30 (m, 2H), 1.25 – 1.20 (m, 1H), 1.18 – 1.10 (m, 1H), 0.93 (dd, *J* = 6.6, 2.3 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 132.2, 132.0, 123.0, 121.3, 111.2, 62.9, 55.9, 51.1, 38.1, 37.6, 30.1, 28.4, 27.0, 23.3, 22.9, 22.3, 20.9. $[\alpha]_{20D}$ = +21.0 (c 1.0, CH_3CN). The enantiomeric excess (89% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 30.950 min; t_R (major) = 34.520 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{29}NO_2$: 304.2271, found: 304.2271.



N-((1R,2R)-2-(2-cyclopropylethyl)-1-methylcyclopentyl)-2-methoxybenzamide (3d)

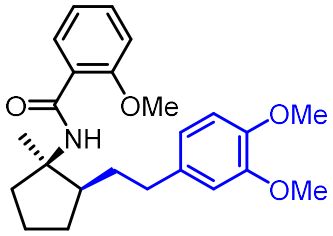
Colorless oil, 18 mg, 58% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.95 (s, 1H), 7.44 – 7.39 (m, 1H), 7.10 – 7.05 (m, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 3.97 (s, 3H), 2.71 – 2.65 (m, 1H), 2.02 – 1.94 (m, 1H), 1.81 – 1.76 (m, 1H), 1.67 – 1.59 (m, 4H), 1.56 (s, 3H), 1.39 – 1.28 (m, 4H), 0.75 – 0.68 (m, 1H), 0.49 – 0.41 (m, 2H), 0.10 – 0.05 (m, 1H), 0.05 – 0.01 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 132.3, 132.0, 123.0, 121.3, 111.2, 62.9, 55.8, 50.7, 37.7, 34.0, 30.2, 29.5, 23.4, 21.0, 11.3, 4.6, 4.3. $[\alpha]_{20D}$ = +9.0 (c 1.0, CH_3CN). The enantiomeric excess (95% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 11.603 min; t_R (major) = 10.717 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{27}NO_2$: 302.2115, found: 302.2114.



2-methoxy-N-((1R,2S)-1-methyl-2-(3-phenylpropyl)cyclopentyl)benzamide (3e)

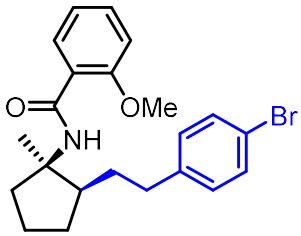
White solid, 22 mg, 62% yield. M.p.: 102-106℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.86 (s, 1H), 7.43 – 7.36 (m, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.15 (m, 3H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 3.74 (s, 3H), 2.80 – 2.73 (m, 1H), 2.69 – 2.57 (m, 2H), 2.05 – 1.97 (m, 1H), 1.85 – 1.76 (m, 1H), 1.70 – 1.56 (m, 6H), 1.55 (s, 3H), 1.40 – 1.31 (m, 1H), 1.22 – 1.14 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.2, 142.3, 132.2, 132.0, 128.4, 128.3, 125.7, 122.8, 121.3, 111.2, 62.9, 55.7, 50.9, 37.6, 36.2, 30.5, 30.0, 28.8, 23.4, 20.8. $[\alpha]_{20D}$ = +11.0 (c

1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 41.950 min; t_R (major) = 44.690 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{23}H_{29}NO_2$: 352.2271, found: 325.2271.



N-((1R,2R)-2-(3,4-dimethoxyphenethyl)-1-methylcyclopentyl)-2-methoxybenzamide (3f)

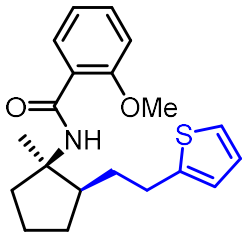
Colorless oil, 28 mg, 71% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.91 (s, 1H), 7.43 – 7.37 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.77 – 6.72 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 2.77 – 2.71 (m, 1H), 2.66 – 2.54 (m, 2H), 2.10 – 2.04 (m, 1H), 2.02 – 1.95 (m, 1H), 1.73 – 1.59 (m, 4H), 1.55 (s, 3H), 1.50 – 1.41 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.1, 148.8, 147.2, 135.0, 132.3, 131.9, 122.8, 121.3, 120.0, 111.5, 111.2, 62.9, 55.9, 55.8, 55.8, 50.2, 37.8, 34.6, 31.8, 30.1, 23.6, 20.9. $[\alpha]_{20D}$ = +30.0 (c 1.0, CH_3CN). The enantiomeric excess (91% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 41.137 min; t_R (major) = 27.157 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{24}H_{31}NO_4$: 398.2326, found: 398.2327.



N-((1R,2R)-2-(4-bromophenethyl)-1-methylcyclopentyl)-2-methoxybenzamide (3g)

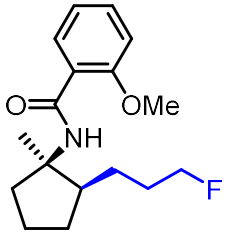
Colorless oil, 32 mg, 77% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 6.7 Hz, 1H), 7.87 (s, 1H), 7.44 – 7.37 (m, 3H), 7.11 – 7.03 (m, 3H), 6.93 (d, *J* = 8.3 Hz, 1H), 3.85 (s, 3H), 2.78 – 2.69 (m, 1H), 2.64 – 2.53 (m, 2H), 2.08 – 1.93 (m, 2H), 1.74 – 1.60

(m, 4H), 1.54 (s, 3H), 1.49 – 1.39 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.1, 141.3, 132.3, 131.9, 131.4, 130.0, 122.8, 121.4, 119.5, 111.2, 62.9, 55.8, 50.1, 37.9, 34.4, 31.5, 30.0, 23.6, 20.9. $[\alpha]_{20D}$ = +34.0 (c 1.0, CH_3CN). The enantiomeric excess (95% ee) was determined by HPLC with a Daicel Chiralpak IJ column (Hexane : EtOH = 90 : 10, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 18.237 min; t_R (major) = 11.637 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{22}H_{26}BrNO_2$: 416.1220, found: 416.1221.



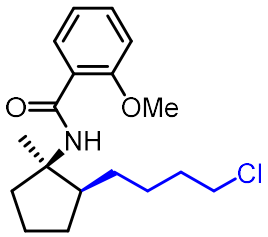
2-methoxy-N-((1R,2R)-1-methyl-2-(2-(thiophen-2-yl)ethyl)cyclopentyl) benzamide (3h)

Colorless oil, 24 mg, 69% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.91 (s, 1H), 7.44 – 7.38 (m, 1H), 7.12 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.08 – 7.04 (m, 1H), 6.96 – 6.90 (m, 2H), 6.84 – 6.81 (m, 1H), 3.91 (s, 3H), 3.03 – 2.97 (m, 1H), 2.90 – 2.82 (m, 1H), 2.68–2.63 (m, 1H), 2.10 – 2.01 (m, 2H), 1.74 – 1.67 (m, 2H), 1.67 – 1.59 (m, 2H), 1.56 (s, 4H), 1.49 – 1.42 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 145.2, 132.3, 132.0, 126.7, 124.1, 123.0, 122.8, 121.3, 111.2, 62.9, 55.9, 50.2, 37.7, 32.0, 29.9, 29.1, 23.5, 20.9. $[\alpha]_{20D}$ = +29.0 (c 1.0, CH_3CN). The enantiomeric excess (94% ee) was determined by HPLC with a Daicel Chiralpak OD-H column (Hexane : i-PrOH = 97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 29.690 min; t_R (major) = 24.167 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{20}H_{25}NO_2S$: 344.1679, found: 344.1680.



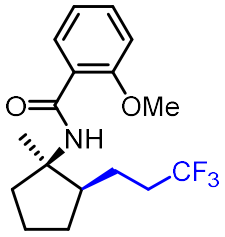
N-((1R,2R)-2-(3-fluoropropyl)-1-methylcyclopentyl)-2-methoxybenzamide (3i)

Colorless oil, 22 mg, 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.94 (s, 1H), 7.44 – 7.38 (m, 1H), 7.09 – 7.04 (m, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 4.61 – 4.40 (m, 2H), 3.96 (s, 3H), 2.67 – 2.60 (m, 1H), 2.05 – 1.97 (m, 1H), 1.93 – 1.82 (m, 1H), 1.78 – 1.61 (m, 6H), 1.56 (s, 3H), 1.46 – 1.38 (m, 1H), 1.38 – 1.30 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.2, 132.3, 131.9, 122.7, 121.3, 111.2, 84.2 (d, *J* = 164.7 Hz), 62.9, 55.9, 50.4, 37.8, 29.9, 29.7 (d, *J* = 19.9 Hz), 25.2 (d, *J* = 4.7 Hz), 23.5, 20.8. $[\alpha]_{20D}$ = +13.0 (c 1.0, CH_3CN). The enantiomeric excess (91% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 14.197 min; t_R (major) = 13.017 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{24}FNO_2$: 294.1864, found: 294.1865.



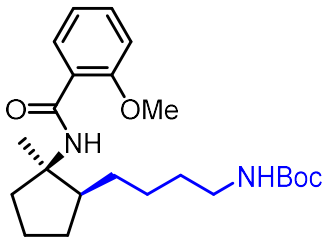
N-((1R,2R)-2-(4-chlorobutyl)-1-methylcyclopentyl)-2-methoxybenzamide (3j)

Colorless oil, 23 mg, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.87 (s, 1H), 7.47 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.57 (t, *J* = 6.6 Hz, 2H), 2.65 – 2.58 (m, 1H), 2.06 – 1.97 (m, 1H), 1.90 – 1.79 (m, 2H), 1.71 – 1.59 (m, 6H), 1.56 (s, 3H), 1.49 – 1.37 (m, 2H), 1.23 – 1.14 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.2, 132.3, 132.0, 122.9, 121.4, 111.3, 62.9, 55.9, 50.6, 44.9, 37.8, 32.9, 29.9, 28.6, 26.0, 23.5, 20.8. $[\alpha]_{20D}$ = +61.0 (c 1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak OD-H column (Hexane : i-PrOH = 97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 20.480 min; t_R (major) = 18.047 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{18}H_{26}ClNO_2$: 324.1725, found: 324.1725.



2-methoxy-N-((1R,2R)-1-methyl-2-(3,3,3-trifluoropropyl)cyclopentyl)benzamide (3k)

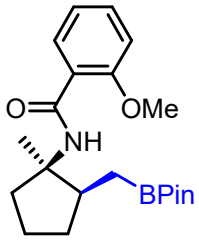
Colorless oil, 26 mg, 80% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.89 (s, 1H), 7.47 – 7.40 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 3.95 (s, 3H), 2.64 – 2.57 (m, 1H), 2.25 – 2.07 (m, 2H), 2.02 – 1.90 (m, 2H), 1.73 – 1.63 (m, 4H), 1.57 (s, 3H), 1.46 – 1.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 157.2, 132.5, 132.0, 127.1 (q, *J* = 277.2 Hz), 122.6, 121.4, 111.3, 62.8, 55.8, 49.5, 37.8, 33.1 (q, *J* = 29.0 Hz), 22.0 (q, *J* = 2.5 Hz), 20.7, 29.6, 23.7. $[\alpha]_{20D}$ = +15.0 (c 1.0, CH_3CN). The enantiomeric excess (93% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : i-PrOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 10.670 min; t_R (major) = 12.887 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{22}F_3NO_2$: 330.1675, found: 330.1674.



tert-butyl (4-((1S,2R)-2-(2-methoxybenzamido)-2-methylcyclopentyl)butyl) carbamate (3l)

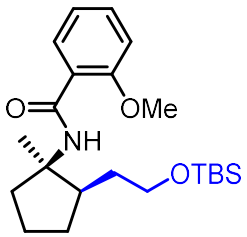
Colorless oil, 20 mg, 50.5% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.87 (s, 1H), 7.45 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 4.59 (s, 1H), 3.96 (s, 3H), 3.19 – 3.09 (m, 2H), 2.66 – 2.57 (m, 1H), 2.04 – 1.95 (m, 1H), 1.70 – 1.56 (m, 6H), 1.54 (s, 3H), 1.52 – 1.46 (m, 2H), 1.44 (s, 9H), 1.40 – 1.32 (m, 2H), 1.21 – 1.14 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.2, 156.0, 132.3, 132.0, 122.9, 121.3, 111.3, 79.0, 62.9, 56.0, 50.7, 40.5, 37.8, 30.6, 30.0, 29.1, 28.4, 26.1, 23.5, 20.8. $[\alpha]_{20D}$ = +13.0 (c 1.0, CH_3CN). The enantiomeric excess (90% ee) was determined by HPLC with a Daicel Chiralpak OJ-H column (Hexane : EtOH =

97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 47.747 min; t_R (major) = 37.183 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{23}H_{36}N_2O_4$: 405.2748, found $[M-Boc+H]^+$: 305.2222.



2-methoxy-N-((1R,2S)-1-methyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentyl)benzamide (3m)

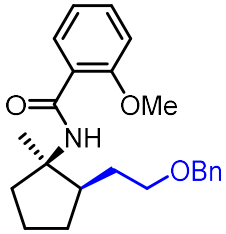
Colorless oil, 21 mg, 57% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 – 8.15 (m, 1H), 7.87 (s, 1H), 7.44 – 7.38 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H), 2.71 – 2.64 (m, 1H), 2.03 – 1.96 (m, 1H), 1.92 – 1.85 (m, 1H), 1.66 – 1.57 (m, 3H), 1.53 (s, 3H), 1.39 – 1.33 (m, 1H), 1.26 (d, *J* = 4.6 Hz, 12H), 1.07 (dd, *J* = 15.0, 3.7 Hz, 1H), 0.64 (dd, *J* = 14.9, 11.5 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 157.3, 132.2, 131.9, 123.1, 121.2, 111.3, 83.2, 63.1, 56.0, 46.6, 37.0, 31.7, 24.9, 24.7, 23.0, 20.7. $[\alpha]_{20D}$ = +16.0 (c 1.0, CH_3CN). The enantiomeric excess (89% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 9.423 min; t_R (major) = 8.597 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{21}H_{32}BNO_4$: 374.2497, found: 374.2500.



N-((1R,2R)-2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-methylcyclopentyl)-2-methoxybenzamide (3n)

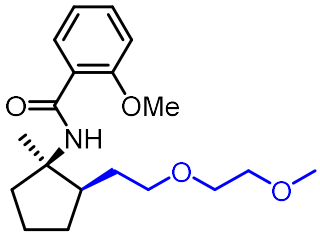
Colorless oil, 23 mg, 58% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.89 (s, 1H), 7.45 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.78 – 3.71 (m, 1H), 3.69 – 3.63 (m, 1H), 2.70 – 2.62 (m, 1H), 2.03 – 1.89 (m, 2H), 1.74 – 1.60 (m, 4H), 1.55 (s, 3H), 1.46 – 1.36 (m, 2H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 157.2, 132.3, 132.0, 122.9, 121.3,

111.3, 63.1, 62.5, 55.9, 47.4, 37.5, 32.9, 30.2, 25.9, 23.4, 21.1, 18.3, -5.3, -5.4. $[\alpha]_{20D}$ = +15.0 (c 1.0, CH_3CN). The enantiomeric excess (96% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 93 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 39.267 min; t_R (major) = 43.353 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{22}H_{37}NO_3Si$: 392.2616, found: 392.2617.



N-((1R,2R)-2-(2-(benzyloxy)ethyl)-1-methylcyclopentyl)-2-methoxybenzamide (3o)

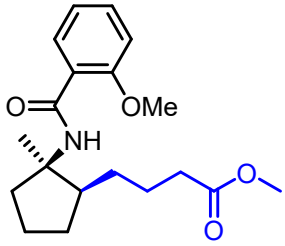
Colorless oil, 21 mg, 56% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.8 Hz, 1H), 7.89 (s, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.35 (s, 2H), 7.34 (s, 2H), 7.31 – 7.26 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 4.57 – 4.48 (m, 2H), 3.93 (s, 3H), 3.63 – 3.51 (m, 2H), 2.61 (t, *J* = 8.3 Hz, 1H), 2.07 – 1.94 (m, 2H), 1.83 – 1.71 (m, 2H), 1.67 (d, *J* = 7.6 Hz, 1H), 1.65 – 1.61 (m, 1H), 1.56 (s, 3H), 1.50 – 1.40 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 157.2, 138.4, 132.3, 131.9, 128.3, 127.6, 127.5, 122.9, 121.3, 111.3, 72.9, 69.6, 63.0, 56.0, 47.5, 37.7, 30.1, 29.6, 23.5, 20.9. $[\alpha]_{20D}$ = +18.0 (c 1.0, CH_3CN). The enantiomeric excess (95% ee) was determined by HPLC with a Daicel Chiralpak OJ-H column (Hexane : EtOH = 90 : 10, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 17.137 min; t_R (major) = 13.413 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{23}H_{29}NO_3$: 368.2220, found: 368.2220.



2-methoxy-N-((1R,2R)-2-(2-(2-methoxyethoxy)ethyl)-1-methylcyclopentyl) benzamide (3p)

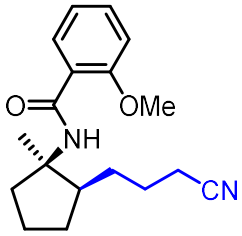
Colorless oil, 23 mg, 70% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.88 (s, 1H), 7.45 – 7.36 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz,

1H), 3.96 (s, 3H), 3.65 – 3.58 (m, 3H), 3.57 – 3.53 (m, 3H), 3.39 (s, 3H), 2.65 – 2.57 (m, 1H), 2.05 – 1.96 (m, 2H), 1.77 – 1.60 (m, 4H), 1.56 (s, 3H), 1.49 – 1.40 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 157.2, 132.3, 131.9, 122.8, 121.3, 111.2, 71.9, 70.7, 70.0, 63.0, 59.0, 56.0, 47.3, 37.6, 30.0, 29.4, 23.5, 20.9. $[\alpha]_{20D}$ = +14.0 (c 1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 17.437 min; t_R (major) = 14.757 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{29}NO_4$: 336.2169, found: 336.2168.



methyl 4-((1R,2R)-2-(2-methoxybenzamido)-2-methylcyclopentyl)butanoate (3q)

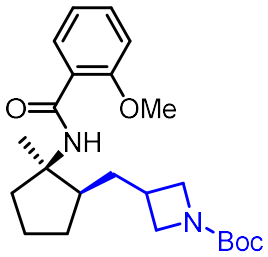
Colorless oil, 25 mg, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.87 (s, 1H), 7.45 – 7.38 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.67 (s, 3H), 2.66 – 2.59 (m, 1H), 2.45 – 2.31 (m, 2H), 2.07 – 1.98 (m, 1H), 1.87 – 1.80 (m, 1H), 1.69 – 1.58 (m, 6H), 1.55 (s, 3H), 1.45 – 1.37 (m, 1H), 1.25 – 1.17 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 164.4, 157.2, 132.3, 132.0, 122.8, 121.3, 111.3, 62.9, 55.9, 51.5, 50.6, 37.7, 34.3, 29.8, 28.9, 24.2, 23.4, 20.8. $[\alpha]_{20D}$ = +22.0 (c 1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 98 : 2, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 27.090 min; t_R (major) = 23.740 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{19}H_{27}NO_4$: 334.2013, found: 334.2011.



N-((1R,2R)-2-(3-cyanopropyl)-1-methylcyclopentyl)-2-methoxybenzamide (3r)

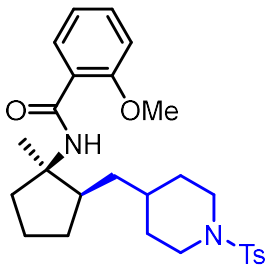
Colorless oil, 21 mg, 70% yield, dr = 5.3:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, 1H), 7.91 (s, 1H), 7.46 – 7.40 (m, 1H), 7.11 – 7.04 (m, 1H), 6.97 (d, *J* = 8.2, 3.7 Hz,

1H), 4.00 (s, 2.56H), 3.97 (s, 0.48H), 2.60 – 2.52 (m, 1H), 2.51 – 2.43 (m, 1H), 2.41 – 2.34 (m, 2H), 2.05 – 1.93 (m, 1H), 1.85 – 1.75 (m, 2H), 1.71 – 1.64 (m, 4H), 1.57 (s, 3H), 1.51 – 1.43 (m, 1H), 1.39 – 1.31 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 157.2, 132.4, 131.9, 122.6, 121.3, 119.6, 111.3, 62.9, 56.1, 50.0, 37.8, 29.8, 28.7, 24.7, 23.7, 20.7, 17.6. $[\alpha]_{20D}$ = +54.0 (c 1.0, CH_3CN). The enantiomeric excess (88% ee) was determined by HPLC with a Daicel Chiralpak AD-H column (Hexane : EtOH = 98 : 2, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 55.507 min; t_R (major) = 69.927 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{18}H_{24}N_2O_2$: 301.1911, found: 301.1910.



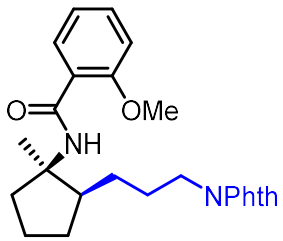
tert-butyl 3-(((1R,2R)-2-(2-methoxybenzamido)-2-methylcyclopentyl)methyl) azetidine-1-carboxylate (3s)

Colorless oil, 26 mg, 65% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.83 (s, 1H), 7.46 – 7.40 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 4.09 – 3.97 (m, 3H), 3.96 (s, 3H), 3.60 – 3.54 (m, 2H), 2.64 – 2.54 (m, 2H), 1.95 – 1.87 (m, 2H), 1.71 – 1.58 (m, 4H), 1.56 (s, 3H), 1.48 – 1.46 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 157.1, 156.4, 132.4, 132.0, 122.8, 121.5, 111.3, 79.3, 62.9, 56.0, 48.9, 37.7, 34.3, 28.4, 28.2, 23.8, 20.9. $[\alpha]_{20D}$ = +32.0 (c 1.0, CH_3CN). The enantiomeric excess (94% ee) was determined by HPLC with a Daicel Chiralpak IH column (Hexane : i-PrOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 17.157 min; t_R (major) = 15.220 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{23}H_{34}N_2O_4$: 403.2591, found $[M\text{-Boc}+H]^+$: 303.2067.



2-methoxy-N-((1R,2R)-1-methyl-2-((1-tosylpiperidin-4-yl)methyl)cyclopentyl) benzamide (3t)

Colorless oil, 26 mg, 54% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.81 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.45 – 7.40 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 3.92 (s, 3H), 3.79 (d, *J* = 11.0 Hz, 2H), 2.64 – 2.55 (m, 1H), 2.43 (s, 3H), 2.29 – 2.19 (m, 2H), 1.93 – 1.84 (m, 1H), 1.82 (d, *J* = 8.7 Hz, 1H), 1.73 (d, *J* = 13.2 Hz, 1H), 1.67 – 1.61 (m, 2H), 1.61 – 1.53 (m, 2H), 1.50 (s, 3H), 1.45 – 1.38 (m, 1H), 1.38 – 1.27 (m, 3H), 1.25 – 1.19 (m, 1H), 1.18 – 1.09 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 157.1, 143.4, 133.1, 132.4, 132.0, 129.5, 127.7, 122.8, 121.4, 111.3, 63.0, 55.9, 47.5, 46.4, 46.4, 37.6, 36.0, 34.1, 32.9, 31.0, 30.4, 23.4, 21.5, 20.9. $[\alpha]_{20D}$ = +2.0 (c 1.0, CH_3CN). The enantiomeric excess (92% ee) was determined by HPLC with a Daicel Chiralpak AD-H column (Hexane : EtOH = 80 : 20, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 13.920 min; t_R (major) = 31.653 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{27}H_{36}N_2O_4S$: 485.2469, found: 485.2470.

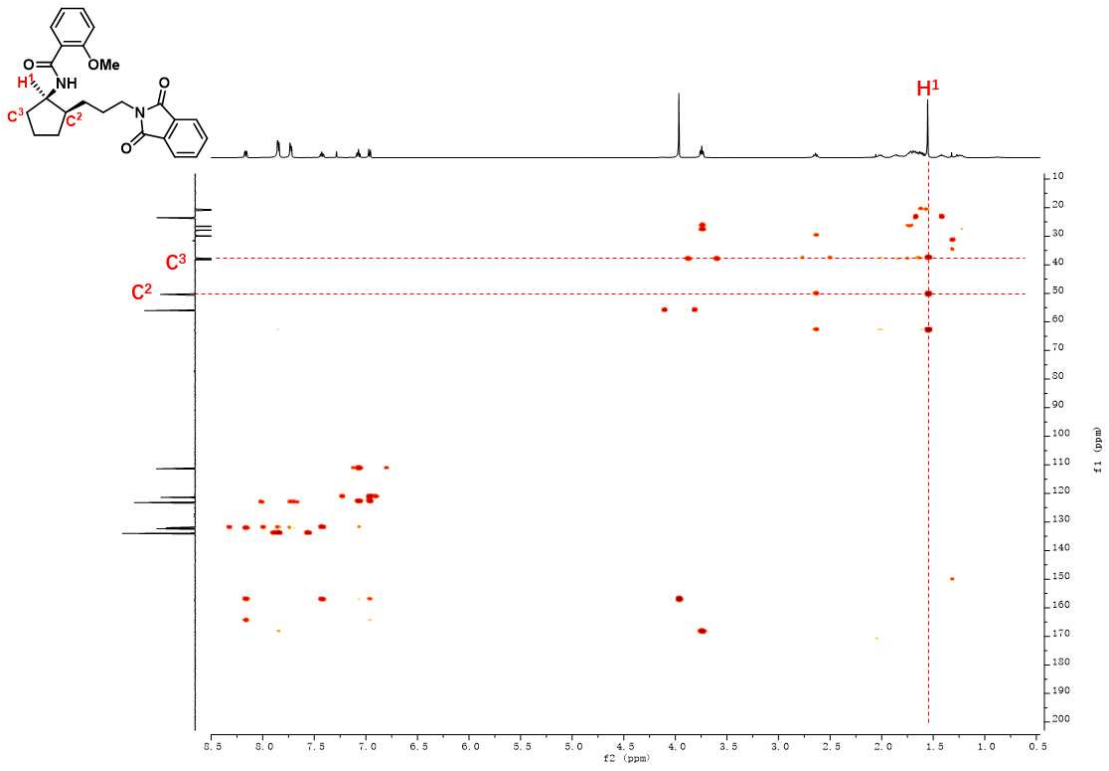


N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-methylcyclopentyl)-2-methoxybenzamide (3u)

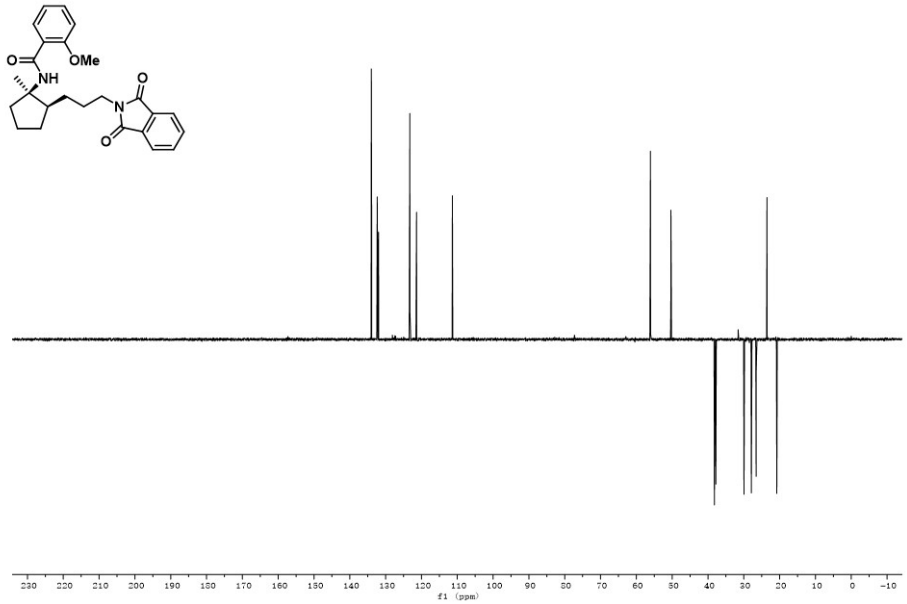
Colorless oil, 29 mg, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.84 (dd, *J* = 5.4, 3.0 Hz, 3H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.48 – 7.38 (m, 1H), 7.06 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 3.95 (s, 3H), 3.73 (t, *J* = 7.1 Hz, 2H), 2.69 – 2.58 (m, 1H), 2.04 – 1.96 (m, 1H), 1.90–1.82 (m, 1H), 1.74 – 1.59 (m, 6H), 1.54 (s, 3H), 1.45 – 1.36 (m, 1H), 1.26 – 1.20 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 164.5, 157.2, 133.9, 132.3, 132.1, 131.9, 123.2, 122.8, 121.3, 111.3, 62.9, 56.0, 50.3, 38.1, 37.7, 29.9, 27.8, 26.5, 23.5, 20.7. $[\alpha]_{20D}$ = +27.0 (c 1.0, CH_3CN). The enantiomeric excess (91% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 75 : 25, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor)

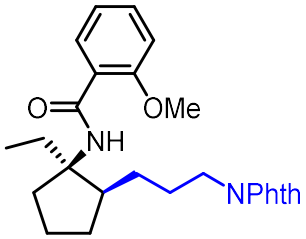
= 45.800 min; t_R (major) = 53.747 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{25}H_{28}N_2O_4$: 421.2122, found: 421.2120.The HMBC and DEPT spectra below indicated that the coupling site was in C^2. The single crystal diffraction pattern of a subsequent product was further verified.

HMBC spectroscopy:



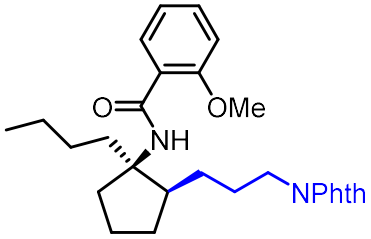
DEPT135 spectroscopy:





N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-ethylcyclopentyl)-2-methoxybenzamide (3v)

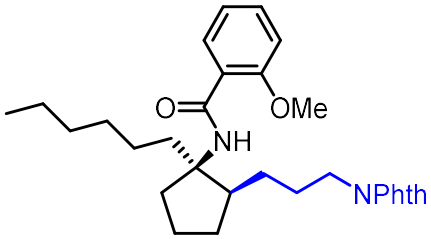
Colorless oil, 24 mg, 55% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.84 – 7.80 (m, 2H), 7.77 (s, 1H), 7.73 – 7.68 (m, 2H), 7.44 – 7.39 (m, 1H), 7.08 – 7.02 (m, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 3.96 (s, 3H), 3.73 – 3.65 (m, 2H), 2.34 – 2.24 (m, 2H), 1.99 – 1.92 (m, 1H), 1.88 – 1.76 (m, 3H), 1.72 – 1.65 (m, 4H), 1.62 – 1.53 (m, 1H), 1.51 – 1.42 (m, 1H), 1.25 – 1.18 (m, 1H), 0.89 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 164.4, 157.2, 133.9, 132.2, 132.1, 132.0, 123.1, 122.9, 121.3, 111.3, 66.4, 56.0, 47.6, 38.2, 35.5, 30.2, 29.1, 27.8, 27.2, 21.2, 9.0. $[\alpha]_{20D}$ = +12.0 (c 1.0, CH_3CN). The enantiomeric excess (83% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : EtOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 80.403 min; t_R (major) = 85.293 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{26}H_{30}N_2O_4$: 435.2278, found: 435.2278.



N-((1R,2R)-1-butyl-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)cyclopentyl)-2-methoxybenzamide (3w)

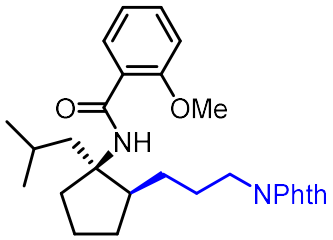
Colorless oil, 22 mg, 47% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.86 – 7.80 (m, 2H), 7.78 (s, 1H), 7.73 – 7.68 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.75 – 3.65 (m, *J* = 6.6 Hz, 2H), 2.43 – 2.33 (m, 1H), 2.24 – 2.15 (m, 1H), 1.99 – 1.91 (m, 1H), 1.88 – 1.80 (m, 2H), 1.79 – 1.76 (m, 1H), 1.73 – 1.63 (m, 4H), 1.62 – 1.52 (m, 1H), 1.50 – 1.40 (m, 1H), 1.31 – 1.19 (m, 5H), 0.86 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 164.3, 157.1, 133.9, 132.2, 132.1, 132.0, 123.1, 123.0, 121.3, 111.3, 66.0, 56.0, 48.0,

38.2, 36.5, 35.9, 30.2, 27.8, 27.1, 26.9, 23.2, 21.3, 14.1. $[\alpha]_{20D}$ = +11.0 (c 1.0, CH_3CN). The enantiomeric excess (81% ee) was determined by HPLC with a Daicel Chiralpak AD-H column (Hexane : EtOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 20.340 min; t_R (major) = 22.673 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{28}H_{34}N_2O_4$: 463.2591, found: 463.2592.



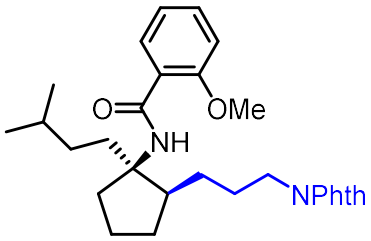
N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-hexylcyclopentyl)-2-methoxybenzamide (3x)

Colorless oil, 22 mg, 45% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 1H), 7.84 – 7.80 (m, 2H), 7.77 (s, 1H), 7.72 – 7.68 (m, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.74 – 3.66 (m, 2H), 2.42 – 2.34 (m, 1H), 2.22 – 2.14 (m, 1H), 1.99 – 1.91 (m, 1H), 1.85 – 1.76 (m, 3H), 1.73 – 1.63 (m, 4H), 1.61 – 1.52 (m, 1H), 1.50 – 1.40 (m, 1H), 1.30 – 1.21 (m, 9H), 0.85 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (201 MHz, $CDCl_3$) δ 168.3, 164.3, 157.1, 133.9, 132.2, 132.1, 132.0, 123.1, 123.0, 121.3, 111.3, 66.0, 56.0, 48.0, 38.2, 36.8, 35.9, 31.8, 30.2, 29.8, 27.8, 27.1, 24.6, 22.6, 21.3, 14.0. $[\alpha]_{20D}$ = +9.0 (c 1.0, CH_3CN). The enantiomeric excess (82% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : i-PrOH = 85 : 15, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 15.370 min; t_R (major) = 12.580 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{30}H_{38}N_2O_4$: 491.2904, found: 491.2908.



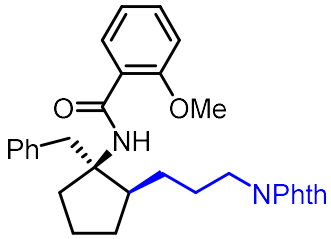
N-((1S,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-isobutylcyclopentyl)-2-methoxybenzamide (3y)

Colorless oil, 19 mg, 42% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.85 – 7.80 (m, 2H), 7.77 (s, 1H), 7.72 – 7.68 (m, 2H), 7.45 – 7.38 (m, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.75 – 3.64 (m, 2H), 2.44 – 2.36 (m, 1H), 2.16 (dd, *J* = 14.3, 5.2 Hz, 1H), 1.98 – 1.89 (m, 1H), 1.86 – 1.77 (m, 3H), 1.75 – 1.67 (m, 4H), 1.64 – 1.57 (m, 1H), 1.54 (dd, *J* = 14.3, 6.4 Hz, 1H), 1.48 – 1.39 (m, 1H), 1.24 – 1.16 (m, 1H), 0.91 (dd, *J* = 6.6, 2.5 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 164.3, 157.1, 133.9, 132.2, 132.1, 132.0, 123.1, 123.1, 121.3, 111.3, 66.3, 56.0, 48.7, 45.0, 38.2, 36.4, 29.7, 27.8, 27.2, 24.8, 24.8, 24.5, 21.2. $[\alpha]_{20D}$ = +44.0 (c 1.0, CH_3CN). The enantiomeric excess (90% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 90 : 10, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 84.023 min; t_R (major) = 77.037 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{28}H_{34}N_2O_4$: 463.2591, found: 463.2592.



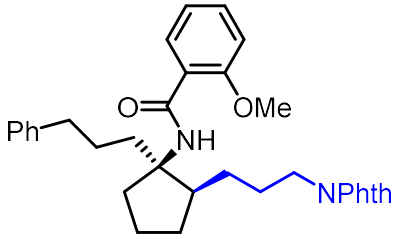
N-((1S,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-isopentylcyclopentyl)-2-methoxybenzamide (3z)

Colorless oil, 31 mg, 64% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.76 (s, 1H), 7.73 – 7.67 (m, 2H), 7.45 – 7.38 (m, 1H), 7.08 – 7.02 (m, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 3.96 (s, 3H), 3.75 – 3.65 (m, 2H), 2.41 – 2.33 (m, 1H), 2.20 (td, *J* = 13.3, 12.8, 4.6 Hz, 1H), 1.99–1.91 (m, 1H), 1.87 – 1.79 (m, 2H), 1.75 – 1.60 (m, 5H), 1.60 – 1.53 (m, 1H), 1.52 – 1.41 (m, 2H), 1.24 – 1.09 (m, 3H), 0.85 (dd, *J* = 8.6, 6.6 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 164.2, 157.1, 133.9, 132.2, 132.1, 132.0, 123.1, 123.0, 121.3, 111.3, 66.0, 56.0, 47.9, 38.2, 35.8, 34.5, 33.6, 30.2, 28.5, 27.8, 27.1, 22.7, 22.6, 21.3. $[\alpha]_{20D}$ = +10.0 (c 1.0, CH_3CN). The enantiomeric excess (80% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : i-PrOH = 90 : 10, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 78.327 min; t_R (major) = 68.937 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{29}H_{36}N_2O_4$: 477.2748, found: 477.2751.



N-(1-benzyl-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)cyclopentyl)-2-methoxybenzamide (3aa)

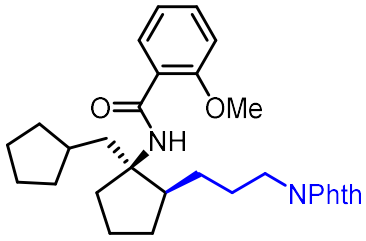
Colorless oil, 14 mg, 25% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.7 Hz, 1H), 7.85 – 7.82 (m, 2H), 7.81 (s, 1H), 7.75 – 7.70 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.13 – 7.07 (m, 5H), 6.99 – 6.93 (m, 2H), 3.88 (s, 3H), 3.62 (t, *J* = 7.1 Hz, 2H), 3.34 – 3.24 (m, 2H), 2.47 – 2.39 (m, 1H), 2.03 – 1.94 (m, 1H), 1.85 – 1.73 (m, 3H), 1.70 – 1.65 (m, 1H), 1.63 – 1.49 (m, 2H), 1.43 – 1.31 (m, 2H), 1.09 – 0.99 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 164.8, 157.3, 138.5, 133.9, 132.4, 132.1, 132.0, 130.4, 127.7, 125.9, 123.1, 122.9, 121.3, 111.4, 66.1, 56.0, 46.9, 41.1, 38.2, 36.2, 30.2, 27.8, 27.3, 21.0. $[\alpha]_{20D}$ = +6.0 (c 1.0, CH_3CN). The enantiomeric excess (84% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 67.290 min; t_R (major) = 60.657 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{31}H_{32}N_2O_4$: 497.2435, found: 497.2431.



N-((1S,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-(3-phenylpropyl)cyclopentyl)-2-methoxybenzamide (3ab)

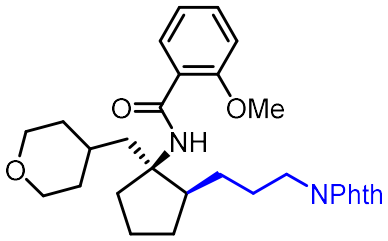
Colorless oil, 24 mg, 51% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.85 – 7.79 (m, 2H), 7.77 (s, 1H), 7.73 – 7.68 (m, 2H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.18 – 7.11 (m, 3H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 3.92 (s, 3H), 3.71 – 3.63 (m, 2H), 2.68 – 2.61 (m, 1H), 2.60 – 2.52 (m, 1H), 2.39 – 2.29 (m, 2H), 1.97 – 1.89 (m, 1H), 1.86 – 1.78 (m, 2H), 1.74 – 1.51 (m, 8H), 1.48 – 1.38 (m, 1H), 1.24 – 1.16 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 164.3, 157.1, 142.7, 133.9, 132.2, 132.1, 132.0, 128.4, 128.2, 125.6, 123.1, 122.9, 121.3, 111.3,

65.9, 56.0, 47.9, 38.2, 36.3, 36.2, 35.9, 30.0, 27.7, 27.1, 26.8, 21.1. $[\alpha]_{20D}$ = +9.0 (c 1.0, CH_3CN). The enantiomeric excess (78% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 96 : 4, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 44.473 min; t_R (major) = 55.670 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{33}H_{36}N_2O_4$: 525.2748, found: 525.2755.



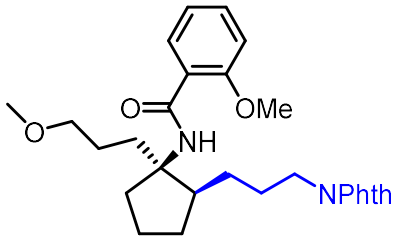
N-((1S,2R)-1-(cyclopentylmethyl)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl) cyclopentyl)-2-methoxybenzamide (3ac)

Colorless oil, 22 mg, 53% yield.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.86 – 7.80 (m, 2H), 7.79 (s, 1H), 7.73 – 7.68 (m, 2H), 7.45 – 7.38 (m, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 3.97 (s, 3H), 3.76 – 3.66 (m, *J* = 7.0, 6.1 Hz, 2H), 2.46 – 2.38 (m, 1H), 2.32 (dd, *J* = 14.0, 4.8 Hz, 1H), 1.98 – 1.90 (m, 1H), 1.85 – 1.68 (m, 10H), 1.63 – 1.51 (m, 3H), 1.45 – 1.36 (m, 3H), 1.24 – 1.18 (m, 1H), 1.17 – 1.05 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 164.3, 157.1, 133.9, 132.2, 132.1, 132.0, 123.1, 123.1, 121.3, 111.3, 66.3, 56.0, 48.3, 42.3, 38.2, 36.8, 36.4, 34.4, 34.3, 29.9, 27.8, 27.2, 25.1, 24.8, 21.2. $[\alpha]_{20D}$ = +17.0 (c 1.0, CH_3CN). The enantiomeric excess (88% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : EtOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 57.697 min; t_R (major) = 54.460 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{30}H_{36}N_2O_4$: 489.2748, found: 489.2751.



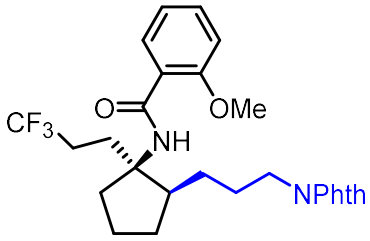
N-((1S,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-((tetrahydro-2H-pyran-4-yl)methyl)cyclopentyl)-2-methoxybenzamide (3ad)

Colorless oil, 24 mg, 48% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.77 – 7.69 (m, 3H), 7.46 – 7.39 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H), 3.87 – 3.81 (m, 2H), 3.74 – 3.67 (m, 2H), 3.31 (t, *J* = 11.6 Hz, 2H), 2.45 – 2.37 (m, 1H), 2.26 (dd, *J* = 14.3, 4.3 Hz, 1H), 1.99 – 1.90 (m, 1H), 1.81 (t, *J* = 10.1 Hz, 3H), 1.76 – 1.68 (m, 3H), 1.63 (d, *J* = 12.5 Hz, 4H), 1.58 – 1.53 (m, 1H), 1.47 – 1.33 (m, 3H), 1.19 (dd, *J* = 13.7, 8.3 Hz, 1H). ^{13}C NMR (201 MHz, $CDCl_3$) δ 168.3, 164.4, 157.0, 133.9, 132.3, 132.0, 132.0, 123.1, 122.9, 121.4, 111.3, 68.1, 67.9, 66.1, 56.0, 49.0, 43.2, 38.1, 36.6, 34.8, 34.6, 31.7, 29.3, 27.7, 27.1, 21.0. $[\alpha]_{20D}$ = +16.0 (c 1.0, CH_3CN). The enantiomeric excess (85% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : i-PrOH = 95 : 5, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 122.860 min; t_R (major) = 138.047 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{30}H_{36}N_2O_5$: 505.2697, found: 505.2699.



N-((1S,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-(3-methoxypropyl) cyclopentyl)-2-methoxybenzamide (3ae)

Colorless oil, 26 mg, 54% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 1H), 7.86 – 7.80 (m, 2H), 7.79 (s, 1H), 7.74 – 7.66 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.74 – 3.64 (m, 2H), 3.40 – 3.32 (m, 2H), 3.29 (s, 3H), 2.38 – 2.31 (m, 1H), 2.29–2.20 (m, 1H), 2.00 – 1.92 (m, 1H), 1.87 – 1.66 (m, 7H), 1.64 – 1.55 (m, 3H), 1.50 – 1.40 (m, 1H), 1.25 – 1.18 (m, 1H). ^{13}C NMR (201 MHz, $CDCl_3$) δ 168.3, 164.4, 157.1, 133.8, 132.3, 132.1, 131.9, 123.1, 122.8, 121.3, 111.2, 73.2, 65.8, 58.5, 56.0, 48.3, 38.2, 36.2, 33.2, 30.0, 27.7, 27.2, 25.1, 21.1. $[\alpha]_{20D}$ = +9.0 (c 1.0, CH_3CN). The enantiomeric excess (74% ee) was determined by HPLC with a Daicel Chiralpak IA column (Hexane : EtOH = 85 : 15, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 32.413 min; t_R (major) = 28.100 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{28}H_{34}N_2O_5$: 479.2541, found: 479.2544.

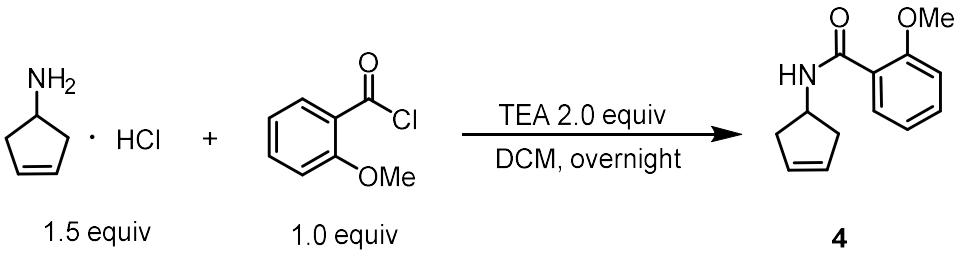


N-(2-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1-(3,3,3-trifluoropropyl)cyclopentyl)-2-methoxybenzamide (3af)

Colorless oil, 26 mg, 52% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.06 (m, 1H), 7.84 – 7.79 (m, 2H), 7.74 (s, 1H), 7.72 – 7.68 (m, 2H), 7.47 – 7.41 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H), 3.70 (t, *J* = 7.1 Hz, 2H), 2.57 – 2.49 (m, 1H), 2.40 – 2.33 (m, 1H), 2.28 – 2.10 (m, 2H), 2.02 – 1.96 (m, 1H), 1.90 – 1.80 (m, 3H), 1.73 – 1.62 (m, 5H), 1.51 – 1.41 (m, 1H), 1.25 – 1.18 (m, 1H). ^{13}C NMR (201 MHz, $CDCl_3$) δ 168.3, 164.7, 157.1, 133.9, 132.6, 132.0, 132.0, 127.4 (q, *J* = 276.1 Hz), 123.2, 122.4, 121.4, 111.3, 65.0, 56.0, 48.9, 37.9, 36.2, 30.0 (q, *J* = 28.8 Hz), 29.5, 29.3, 27.5, 26.9, 20.7. $[\alpha]_{20D}$ = +3.0 (c 1.0, CH_3CN). The enantiomeric excess (53% ee) was determined by HPLC with a Daicel Chiralpak AS-H column (Hexane : EtOH = 93 : 7, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 15.910 min; t_R (major) = 14.330 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{27}H_{29}F_3N_2O_4$: 503.2152, found: 503.2159.

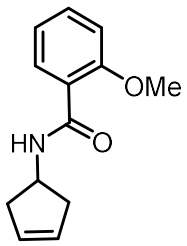
4. The extension of alicyclic substrates without methyl groups

4.1 Substrate synthesis and data of 4, 6, 8



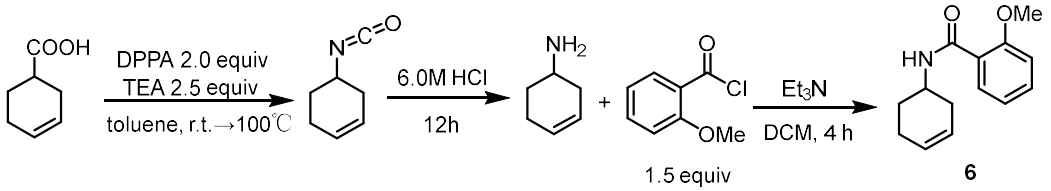
The o-Anisoyl chloride (2.0 mmol, 0.30 mL, 1.0 equiv) was added to the DCM solution of 1-amino-3-cyclopentene hydrochloride (3.0 mmol, 0.36 g, 1.5 equiv) by using a 1.0 mL syringe and stirred at room temperature for overnight. Quenched by saturated water and stratified by DCM extraction. The resulting organic phase was dried

with anhydrous Na_2SO_4, then vacuum concentrated and purified by column chromatography (Hexane : EA= 91 : 9) to obtain the desire compound **4**.



N-(cyclopent-3-en-1-yl)-2-methoxybenzamide (4)

White powder, 434 mg, 100% yield. M.p.: 56-58℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.17 (m, 1H), 8.02 (s, 1H), 7.45 – 7.39 (m, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.80 – 5.73 (m, 2H), 4.81 – 4.72 (m, 1H), 3.92 (s, 3H), 2.86 (dd, *J* = 15.3, 7.8 Hz, 2H), 2.30 (dd, *J* = 15.1, 4.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 157.3, 132.5, 132.1, 128.9, 121.7, 121.2, 111.3, 55.8, 49.0, 40.3. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{13}H_{15}NO_2$: 218.1176, found: 218.1170.

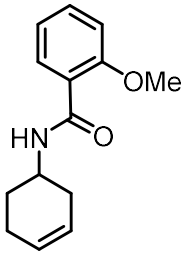


Used a syringe to inject the naphthenic acid (5.0 mmol, 0.58 mL, 1.0 equiv) and toluene (20 mL) into an eggplant-shaped flask with a magnetic stirrer. Added DPPA (10.0 mmol, 2.15 mL, 2.0 equiv) and TEA (12.5 mmol, 1.73 ml, 2.5 equiv) by syringes and stirred 30 mins at room temperature then raised to 100℃ overnight.

Brought the mixture to room temperature, added 6.0 M HCl aqueous solution (10 mL) and stirred for 12 hours. The mixture of toluene and HCl aqueous solution was extracted and stratified to obtain aqueous phase. Added the aqueous NaOH solution until the Ph is greater than 7, and then extracted with DCM, the combined organic layer was dried over anhydrous Na_2SO_4.

Added o-Anisoyl chloride (7.5 mmol, 1.13 mL, 1.5 equiv) dropwise into a solution of the amine and TEA (10.0 mmol, 1.39 mL, 2.0 equiv) in DCM at 0℃. The resulting reaction mixture was allowed to warm to room temperature and stirred for 4 hours.

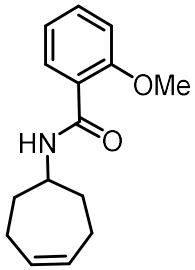
Added pure water and separated the biphasic system. The aqueous phase was extracted with DCM and the organic phases were combined and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purified the residue by column chromatography on silica gel (Hexane : EA = 91 : 9) to afford the desired compound **6**.



N-(cyclohex-3-en-1-yl)-2-methoxybenzamide (6)

Colorless oil, 697 mg, 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 7.8, 1.6 Hz, 1H), 8.05 – 7.94 (m, 1H), 7.46 – 7.39 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 5.79 – 5.72 (m, 1H), 5.70 – 5.64 (m, 1H), 4.41 – 4.34 (m, 1H), 3.93 (s, 3H), 2.48 (d, *J* = 17.3 Hz, 1H), 2.25 – 2.11 (m, 2H), 2.05 – 1.99 (m, 1H), 1.97 – 1.90 (m, 1H), 1.79 – 1.70 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.3, 132.5, 132.1, 127.0, 124.6, 121.9, 121.2, 111.3, 55.9, 44.2, 31.6, 27.6, 23.1. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{14}H_{17}NO_2$: 232.1332, found: 232.1327.

The synthesis of N-(cyclohept-4-en-1-yl)-2-methoxybenzamide is the same as that of N-(cyclohex-3-en-1-yl)-2-methoxybenzamide.

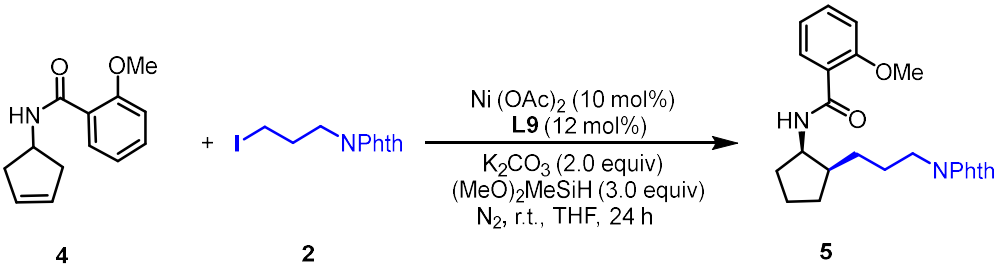


N-(cyclohept-4-en-1-yl)-2-methoxybenzamide (8)

White powder, 492 mg, 56% yield. M.p.: 109-111℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.94 (d, *J* = 6.0 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 5.86 – 5.79 (m, 2H), 4.35 – 4.28 (m, 1H), 3.95 (s, 3H), 2.26 – 2.12 (m, 4H), 2.05 – 1.99 (m, 2H), 1.57 – 1.48 (m, 2H). ^{13}C NMR (126

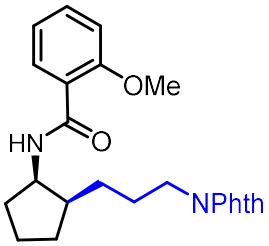
MHz, $CDCl_3$) δ 163.8, 157.4, 132.5, 132.2, 131.9, 121.9, 121.3, 111.3, 55.9, 51.6, 33.1, 24.5. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{15}H_{19}NO_2$: 246.1489, found: 246.1483.

4.2 Substrate investigation and data of 5, 7, 9



4 2 5

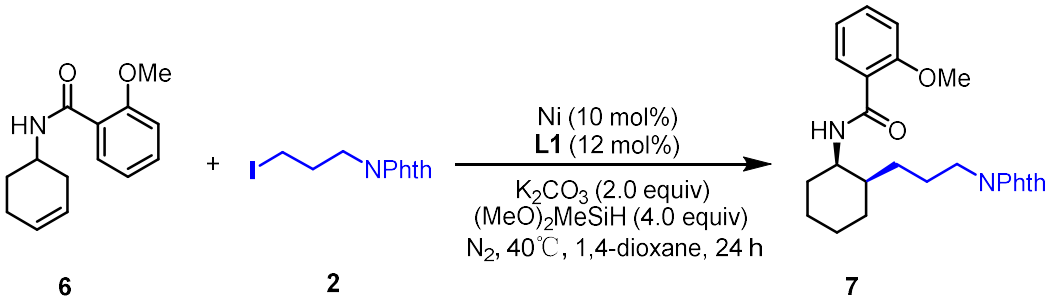
In a nitrogen-filled environment, substrate **4** (0.1 mmol), compound **2** (0.25 mmol), $Ni(OAc)_2$ (0.01 mmol), ligand **L9** (0.012 mmol), methyldimethoxysilane (0.3 mmol), and potassium carbonate (0.2 mmol) were combined in a 4-mL sealed reaction vessel. The reagents were dissolved in anhydrous THF (1.0 mL) and the resulting mixture was stirred at room temperature for 24 hours. Following the reaction, the solution was concentrated under reduced pressure, and the crude product was isolated through preparative thin-layer chromatography to yield compound **5**.



N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)cyclopentyl)-2-methoxybenzamide (5)

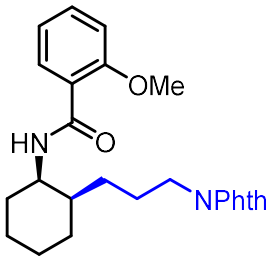
Colorless oil, 13 mg, 31% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 7.7 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.79 – 7.74 (m, 2H), 7.71 – 7.65 (m, 2H), 7.42 (t, J = 7.7 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.57 – 4.51 (m, 1H), 3.95 (s, 3H), 3.70 – 3.61 (m, 2H), 2.08 – 2.01 (m, 1H), 2.01 – 1.95 (m, 1H), 1.94 – 1.87 (m, 1H), 1.78 – 1.70 (m, 3H), 1.69 – 1.66 (m, 1H), 1.53 – 1.46 (m, 1H), 1.37 – 1.28 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 164.6, 157.3, 133.8, 132.4, 132.2, 132.1, 123.1, 121.9, 121.3, 111.3, 56.0, 52.8, 42.7, 38.1, 32.7, 29.7, 27.4, 27.2, 21.7. $[\alpha]_{20D}$ = +3.0 (c 1.0, CH_3CN). The enantiomeric excess (94% ee) was determined by HPLC with

a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 85 : 15, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 19.660 min; t_R (major) = 16.707 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{24}H_{26}N_2O_4$: 407.1965, found: 407.1960.



6 **2** **7**

To a 4-mL sealed tube were added substrate **6** (0.1 mmol), **2** (0.25 mmol), Nickel(II) 2-Amino-5-Methylbenzenesulfonate (0.01 mmol), **L1** (0.012 mmol), methyldimethoxysilane (0.4 mmol) and Potassium carbonate (0.2 mmol) , the mixture was dissolved with anhydrous 1,4-dioxane (1.0 mL) under nitrogen. After stirring for 24 h at 40 ℃, the solution was concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography to give the product **7**.

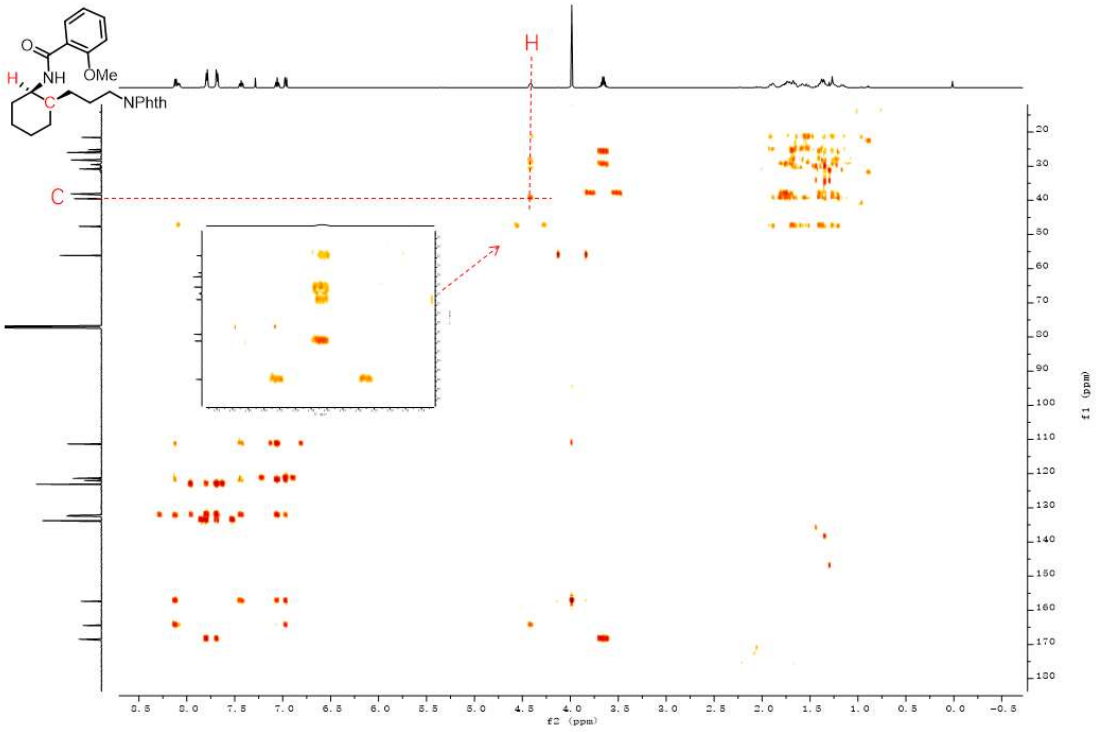


N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)cyclohexyl)-2-methoxybenzamide (7)

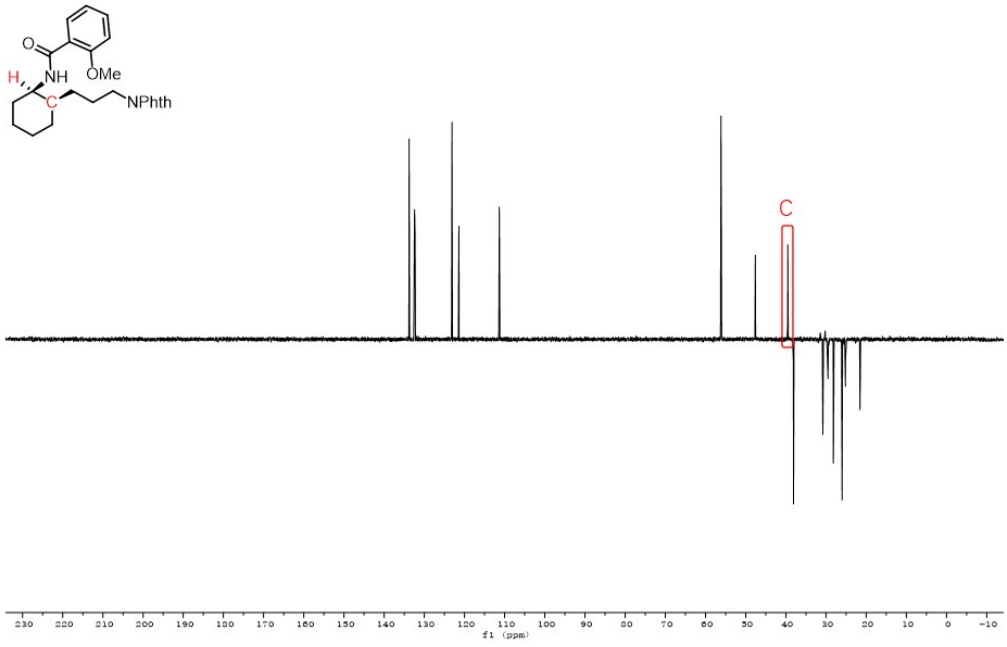
Colorless oil, 19 mg, 46% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.07 (d, *J* = 8.7 Hz, 1H), 7.81 – 7.74 (m, 2H), 7.71 – 7.65 (m, 2H), 7.45 – 7.38 (m, 1H), 7.07 – 7.01 (m, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 4.44 – 4.37 (m, 1H), 3.97 (s, 3H), 3.70 – 3.59 (m, *J* = 7.2 Hz, 2H), 1.92 – 1.87 (m, 1H), 1.81 – 1.64 (m, 5H), 1.61 – 1.48 (m, 2H), 1.42 – 1.33 (m, 3H), 1.25 – 1.20 (m, 1H), 1.19 – 1.10 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 164.4, 157.3, 133.7, 132.4, 132.2, 132.1, 123.0, 122.0, 121.3, 111.3, 56.1, 47.5, 39.5, 38.0, 30.7, 29.5, 28.1, 25.9, 25.1, 21.5. $[\alpha]_{20D}$ = +25.0 (c 1.0, CH_3CN). The enantiomeric excess (72% ee) was determined by HPLC with a Daicel Chiralpak IC column (Hexane : EtOH = 85 : 15, flow rate: 0.8 mL/min, λmax

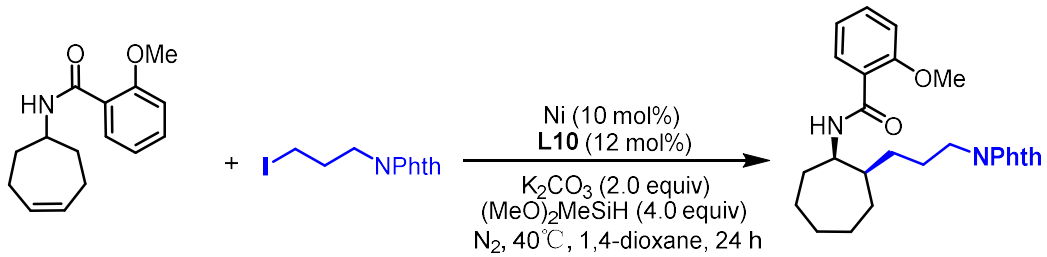
250 nm): t_R (minor) = 53.060 min; t_R (major) = 60.313 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{25}H_{28}N_2O_4$: 421.2122, found: 421.2113.

HMBC spectrum of **7**:



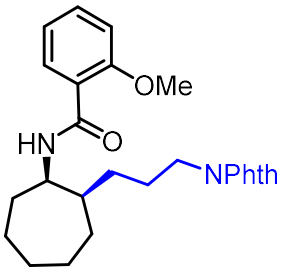
DEPT spectrum of **7**:





8 **2** **9**

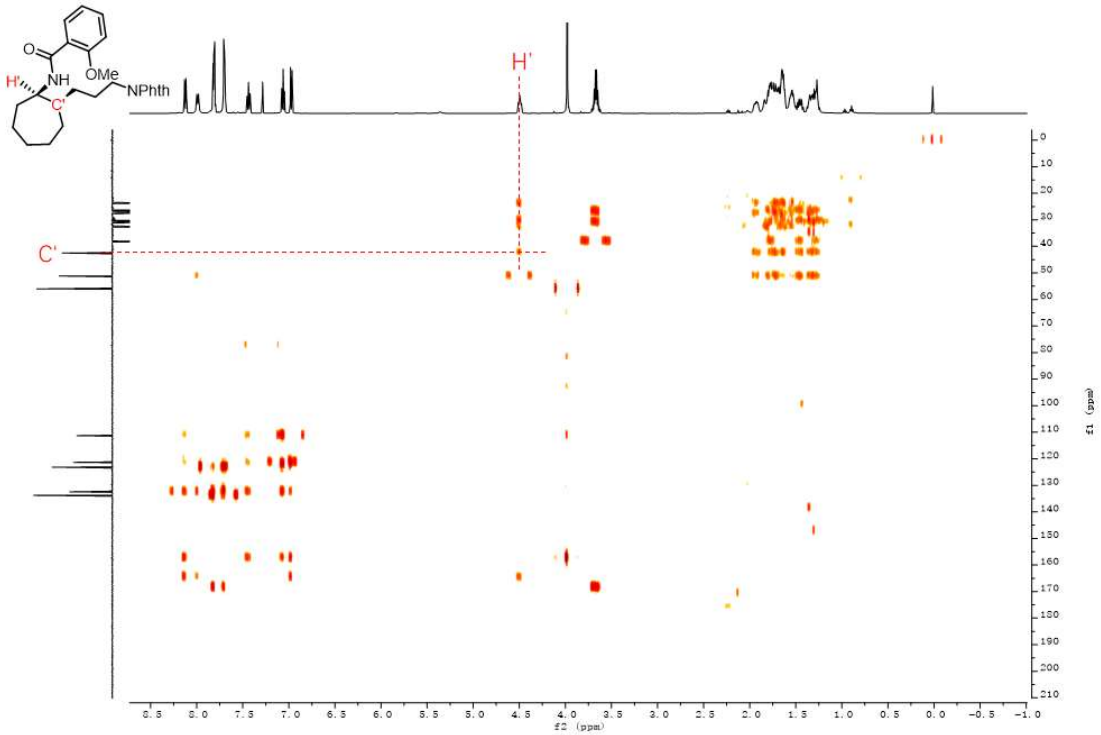
To a 4-mL sealed tube were added substrate **8** (0.1 mmol), **2** (0.25 mmol), Nickel(II) 2-AMino-5-Methylbenzenesulfonate (0.01 mmol), **L10** (0.012 mmol), methyldimethoxysilane (0.4 mmol) and Potassium carbonate (0.2 mmol) , the mixture was dissolved with anhydrous 1,4-dioxane (1.0 mL) under nitrogen. After stirring for 24 h at 40 ℃, the solution was concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography to give the product **9**.



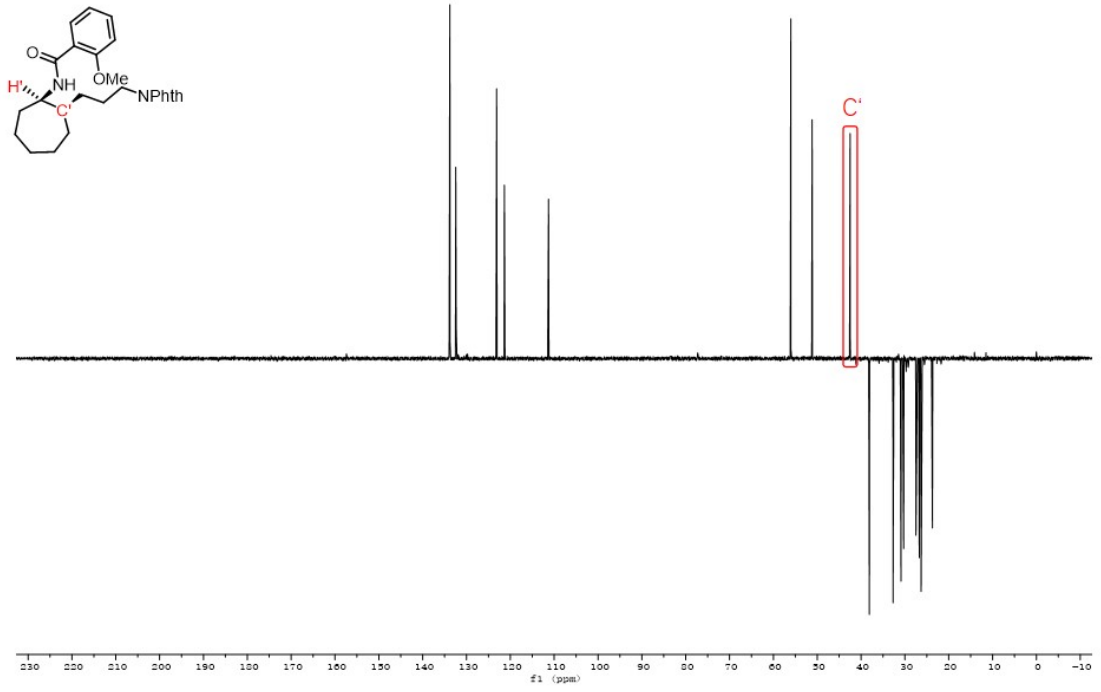
N-((1R,2R)-2-(3-(1,3-dioxoisoindolin-2-yl)propyl)cycloheptyl)-2-methoxybenzamide (9)

Colorless oil, 11 mg, 25% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.7 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 1H), 7.85 – 7.77 (m, 2H), 7.72 – 7.65 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 4.48 (t, *J* = 7.2 Hz, 1H), 3.97 (s, 3H), 3.70 – 3.60 (m, 2H), 1.95 – 1.88 (m, 1H), 1.82 – 1.66 (m, 7H), 1.65 – 1.59 (m, 3H), 1.56 – 1.49 (m, 2H), 1.48 – 1.40 (m, 1H), 1.32 – 1.29 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.4, 164.5, 157.3, 133.7, 132.4, 132.3, 132.2, 123.1, 121.9, 121.3, 111.2, 56.0, 51.1, 42.5, 38.1, 32.7, 30.9, 30.2, 27.4, 26.7, 26.3, 23.7. $[\alpha]_{20D}$ = +18.0 (c 1.0, CH_3CN). The enantiomeric excess (58% ee) was determined by HPLC with a Daicel Chiralpak AD-H column (Hexane : EtOH = 85 : 15, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 55.887 min; t_R (major) = 30.480 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{26}H_{30}N_2O_4$: 435.2278, found: 435.2271.

HMBC spectrum of **9**:



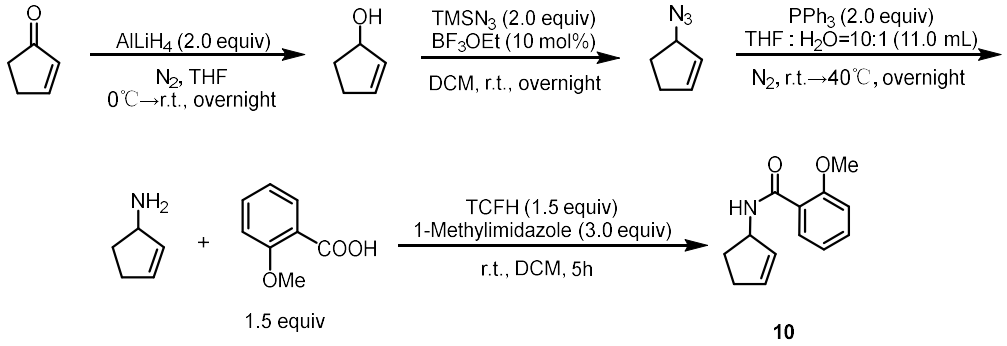
DEPT spectrum of **9**:



5. Mechanistic studies

5.1 Olefin migration experiment

5.1.1 Substrate synthesis and data of 10



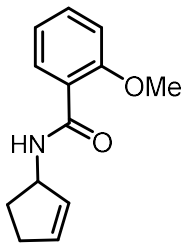
A flask fitted with a magnetic stir bar was purged with nitrogen three times. The reaction was conducted under an ice bath, with THF introduced via syringe as the solvent. Subsequently, 2-Cyclopenten-1-one (0.42 mL, 5 mmol) was added, followed by the dropwise addition of lithium aluminum hydride (4.0 mL, 10 mmol, 2 equiv). The reaction mixture was then allowed to gradually warm to room temperature and stirred overnight. The reaction was quenched by carefully adding a saturated aqueous ammonium chloride solution, followed by extraction with diethyl ether. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure at 30 °C.

A round-bottom flask fitted with a magnetic stir bar was charged with dichloromethane. Cyclopent-2-en-1-ol was dissolved in the solvent via syringe addition, followed by the gradual introduction of azidotrimethylsilane (1.31 mL, 10 equiv). The reaction mixture was initiated by adding boron trifluoride diethyl etherate (61.7 μL, 10 mol%) as catalyst. The solution was maintained under continuous stirring at ambient temperature for 12 hours. Upon completion, the reaction was carefully quenched with water added dropwise. The organic phase was subsequently extracted with dichloromethane, dried over anhydrous sodium sulfate, and concentrated under reduced pressure at 30°C to yield the desired azide intermediate.

Under an inert nitrogen atmosphere, the azide intermediate was dissolved in a 10:1 mixture of THF and water (10 mL THF, 1 mL H_2O). Two equivalents of triphenylphosphine were then introduced, and the reaction mixture was maintained at

40°C for 12 hours. Upon cooling to ambient temperature, 5 mL of 6 M hydrochloric acid was added, followed by continuous stirring for 6 hours. The mixture was subsequently extracted with ethyl acetate, with careful retention of the aqueous layer. The aqueous phase was basified using sodium hydroxide solution and then extracted with dichloromethane to isolate 2-Cyclopenten-1-amine. The final product was dried over anhydrous sodium sulfate, filtered under reduced pressure into a pre-prepared pear-shaped flask containing a magnetic stir bar, and stored for subsequent experimental procedures.

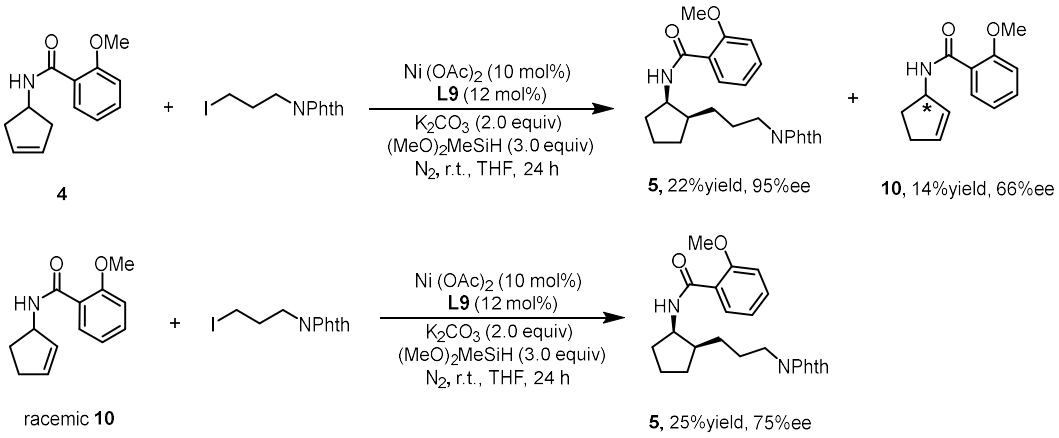
To the prepared solution, 2-methoxybenzoic acid (1.15 g, 1.5 equiv) was introduced, followed by sequential addition of TCFH (2.10 g, 1.5 equiv) and N-methylimidazole (1.20 mL, 3.0 equiv). The reaction mixture was maintained at ambient temperature for 5 hours. The mixture was washed with water and extracted with DCM, The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. Purification by column chromatography employing a PE:EA (90:10) solvent system to provide the product **10**.



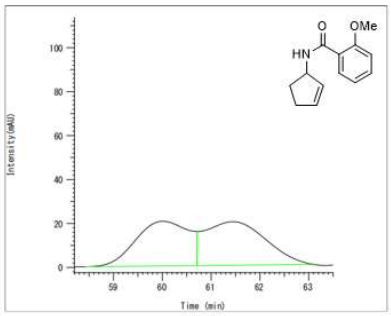
N-(cyclopent-2-en-1-yl)-2-methoxybenzamide (10)

Colorless oil, 195 mg, 18% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.81 (s, 1H), 7.47 – 7.39 (m, 1H), 7.10 – 7.03 (m, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.01 – 5.96 (m, 1H), 5.84 – 5.77 (m, 1H), 5.25 – 5.16 (m, 1H), 3.93 (s, 3H), 2.53 – 2.42 (m, 2H), 2.40 – 2.32 (m, 1H), 1.72 – 1.62 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 157.4, 134.3, 132.5, 132.2, 131.5, 121.7, 121.2, 111.3, 55.8, 55.7, 31.6, 31.2. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{13}H_{15}NO_2$: 218.1176, found: 218.1170.

5.1.2 Control experiment

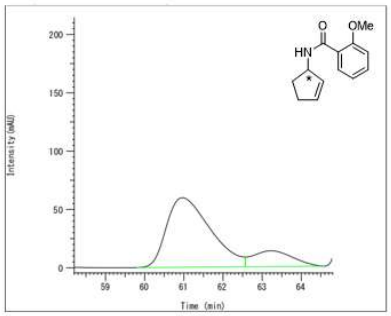


To a 4-mL sealed tube were added olefin substrate (0.1 mmol), Iodinated compound (0.25 mmol), $Ni(OAc)_2$ (0.01 mmol), **L9** (0.012 mmol), methyldimethoxysilane (0.3 mmol) and Potassium carbonate (0.2 mmol) , the mixture was dissolved with anhydrous THF (1.0 mL) under nitrogen. After stirring for 24 h at room temperature, the solution was concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography to give the product.



1410 UV Detector Ch1 SampleID:1 0.5%ACN (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	60.010	1538466	47.268	20351	50.670
2	Peak 2	61.453	1716298	52.732	19813	49.330
			3254764	100.000	40164	100.000

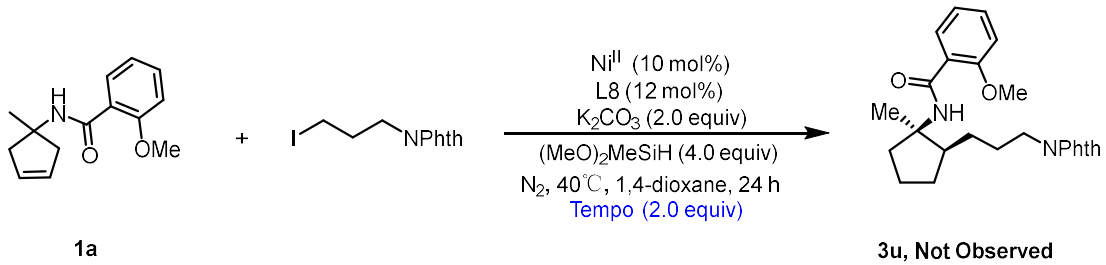


1410 UV Detector Ch1 SampleID:2 0.5%ACN-0.4 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	60.963	4636130	82.917	59627	81.462
2	Peak 2	63.227	955184	17.083	13569	18.538
			5591314	100.000	73197	100.000

Analysis of the unreacted raw material mixture revealed the presence of olefin-migrated alkenyl amines, with this portion of alkenyl amines exhibiting an ee of approximately 66%. This finding demonstrates that the desymmetrization process of symmetrical alkenyl amines involves the step of olefin migration.

5.2 Radical inhibition experiment

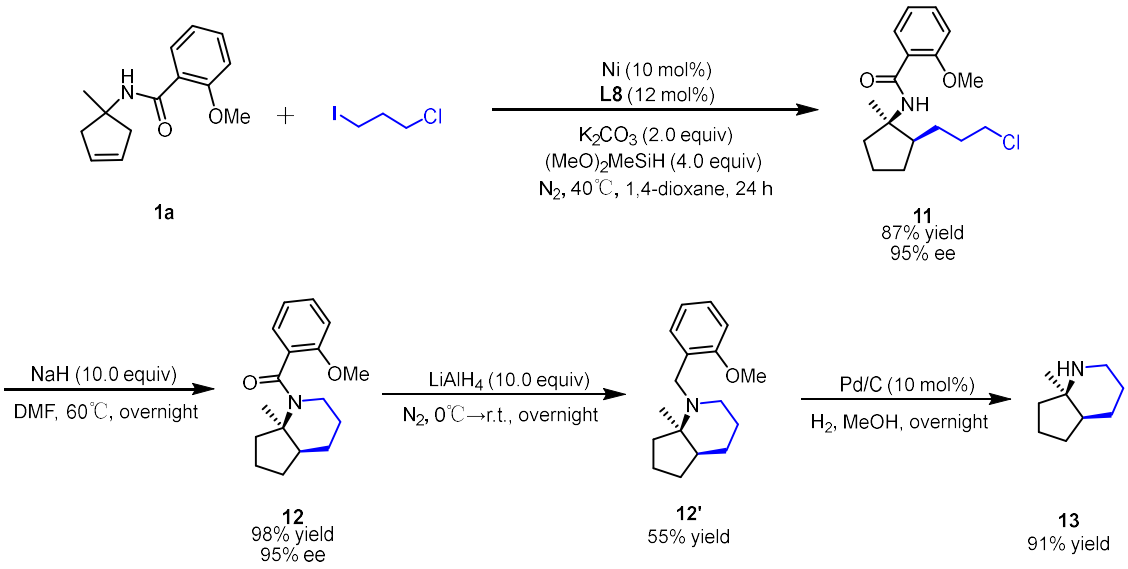


1a

3u, Not Observed

To a 4-mL sealed tube were added substrate **1a** (0.1 mmol), alkyl iodide (0.25 mmol), Nickel(II) 2-AMino-5-Methylbenzenesulfonate (0.01 mmol), **L8** (0.012 mmol), Tempo (0.2 mmol), methyldimethoxysilane (0.4 mmol) and Potassium carbonate (0.2 mmol) . The mixture was dissolved with anhydrous 1,4-dioxane (1.0 mL) under nitrogen. After stirring for 24 h at 40 ℃, the reaction mixture was monitored by TLC, and it was found that only the starting material was remained, no product was detected.

6. Compound synthesis of 13



1a

11
87% yield
95% ee

12
98% yield
95% ee

12'
55% yield

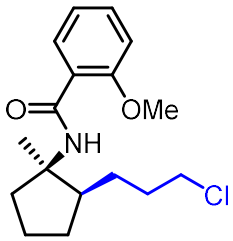
13
91% yield

To a 25-mL sealed tube were added substrate **1a** (1 mmol), 1-Chloro-3-iodopropane (2.5 mmol), Nickel(II) 2-AMino-5-Methylbenzenesulfonate (0.1 mmol), **L8** (0. 12 mmol), methyldimethoxysilane (4 mmol) and Potassium carbonate (2 mmol) , the mixture was dissolved with anhydrous 1,4-dioxane (10.0 mL) under nitrogen. After stirring for 24 h at 40 ℃, the solution was concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography to give the product **11** with a yield of 87% and an ee value of 95%.

Added NaH (348.0 mg, 8.7 mmol) to a solution of **11** (270.0 mg, 0.87 mmol) in DMF, heated to 60°C, and maintained overnight. Quenched the reaction slowly with saturated aqueous ammonium chloride solution in an ice bath. Extracted the mixture using ethyl acetate (EA) and pure water. Dried the obtained organic phase with anhydrous Na_2SO_4, and isolated the product using thin-layer chromatography to yield product **C'** with a yield of 98% and an ee value of 95%.

Under nitrogen protection, dissolved **12** (231.0 mg, 0.85 mmol) in THF and added it to an eggplant-shaped flask equipped with a stir bar. Cooled the temperature to 0°C, then added $LiAlH_4$ (3.4mL, 8.5 mmol, 10 equiv) via a syringe. Allow the temperature to return to room temperature and stirred overnight. Quenched the reaction slowly with saturated aqueous ammonium chloride solution in an ice bath. Extracted the mixture using ethyl acetate (EA) and pure water. Dried the obtained organic phase with anhydrous Na_2SO_4, and isolated the product using thin-layer chromatography to yield product **12'** with a yield of 55%.

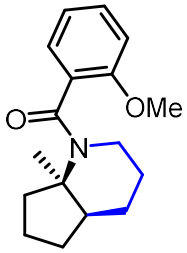
Dissolved **12'** in MeOH and added 10mol% Pd/C into the eggplant-shaped flask, replaced H_2 more than 3 times, then stirred overnight. The TLC monitoring indicated the completion of the reaction. The Pd/C was removed by filtration through diatomaceous earth. The resulting solution was acidified and extracted with DCM and aqueous HCl solution, followed by the removal of DCM. The solution was then basified with aqueous NaOH and extracted with DCM. The organic phase obtained was dried over anhydrous sodium sulfate and concentrated under vacuum at 30°C to yield the product **13**.



N-((1R,2R)-2-(3-chloropropyl)-1-methylcyclopentyl)-2-methoxybenzamide (11)

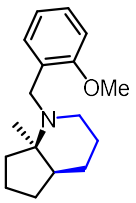
Colorless oil, 270 mg, 87% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 7.8 Hz, 1H), 7.93 (s, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.3 Hz, 1H), 3.98 (s, 3H), 3.69 – 3.63 (m, 1H), 3.60 – 3.53 (m, 1H), 2.68 – 2.61 (m, 1H), 2.03

– 1.96 (m, 1H), 1.94 – 1.88 (m, 1H), 1.87 – 1.72 (m, 3H), 1.70 – 1.62 (m, 3H), 1.56 (s, 3H), 1.47 – 1.36 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 157.2, 132.3, 132.0, 122.7, 121.3, 111.2, 62.9, 56.0, 50.2, 45.5, 37.7, 31.8, 29.9, 26.8, 23.5, 20.8. $[\alpha]_{20D}$ = +11.0 (c 1.0, CH_3CN). The enantiomeric excess (95% ee) was determined by HPLC with a Daicel Chiralpak OD-H column (Hexane : i-PrOH = 97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 23.267 min; t_R (major) = 20.773 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{24}ClNO_2$: 310.1568, found: 310.1570.



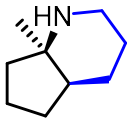
(2-methoxyphenyl)((4aR,7aR)-7a-methyloctahydro-1H-cyclopenta[b]pyridin-1-yl)methanone (12)

White solid, 231 mg, 98% yield, M.p.: 85-88℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 1H), 7.25 – 7.10 (m, 1H), 6.97 – 6.90 (m, 1H), 6.86 (t, *J* = 8.5 Hz, 1H), 3.79 (d, *J* = 3.7 Hz, 3H), 3.19 (s, 1H), 3.12 – 2.92 (m, 1H), 2.54 – 2.31 (m, 2H), 1.93 – 1.70 (m, 4H), 1.65 – 1.60 (m, 1H), 1.56 – 1.48 (m, 2H), 1.46 – 1.38 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.6, 168.7, 155.5, 154.7, 129.5, 129.3, 128.4, 128.2, 126.4, 120.6, 120.4, 110.8, 110.3, 65.8, 65.8, 55.4, 55.0, 45.1, 45.0, 43.0, 42.1, 37.0, 36.6, 28.5, 28.4, 24.2, 24.2, 21.7, 21.5, 21.4, 21.2. $[\alpha]_{20D}$ = -43.0 (c 1.0, CH_3CN). The enantiomeric excess (95% ee) was determined by HPLC with a Daicel Chiralpak IBN-5 column (Hexane : EtOH = 97 : 3, flow rate: 0.8 mL/min, λmax 250 nm): t_R (minor) = 16.297 min; t_R (major) = 15.020 min. ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{23}NO_2$: 274.1802, found: 274.1801.



(4aR,7aR)-1-(2-methoxybenzyl)-7a-methyloctahydro-1H-cyclopenta[b]pyridine (12')

White solid, 144 mg, 55% yield, M.p.: 70.5-72.5℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.4 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 3.81 (s, 3H), 3.69 (d, *J* = 16.1 Hz, 1H), 3.31 (d, *J* = 16.1 Hz, 1H), 2.47 – 2.41 (m, 1H), 2.38 – 2.31 (m, 1H), 2.02 – 1.92 (m, 2H), 1.89 – 1.81 (m, 1H), 1.77 – 1.68 (m, 2H), 1.68 – 1.61 (m, 2H), 1.56 – 1.48 (m, 2H), 1.37 – 1.31 (m, 1H), 1.30 – 1.24 (m, 1H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 129.9, 128.6, 126.8, 120.4, 109.7, 63.4, 55.1, 48.5, 47.3, 46.0, 37.4, 28.1, 23.9, 21.9, 21.4, 16.7. $[\alpha]_{20D}$ = +44.0 (c 1.0, CH_3CN). ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_{17}H_{25}NO$: 260.2009, found: 260.2002.



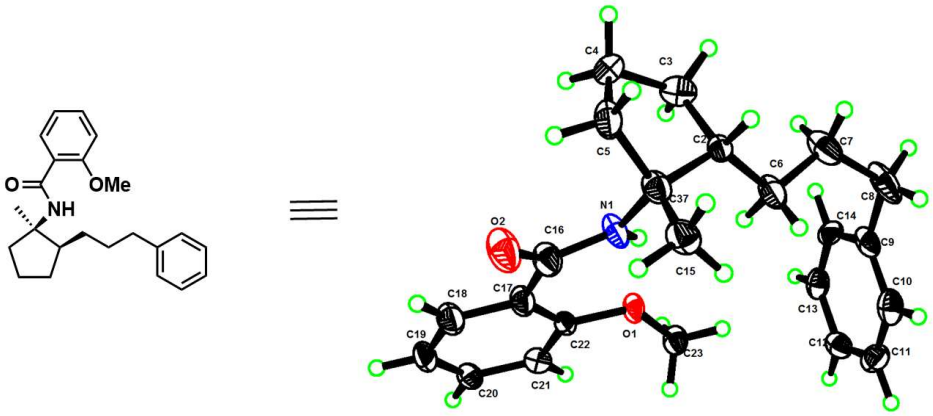
(4aR,7aR)-7a-methyloctahydro-1H-cyclopenta[b]pyridine (13)

Colorless oil, 70 mg, 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.84 – 2.75 (m, 2H), 1.79 – 1.61 (m, 6H), 1.60 – 1.53 (m, 2H), 1.48 – 1.38 (m, 3H), 1.36 – 1.29 (m, 1H), 1.18 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 59.3, 43.0, 41.4, 38.3, 28.4, 25.1, 24.7, 22.9, 20.5. $[\alpha]_{20D}$ = -2.0 (c 1.0, CH_3CN). ESI-HRMS: m/z $[M+H]^+$ calcd. For $C_9H_{17}N$: 140.1434, found: 140.1437.

7. X-ray of 3e

Crystallographic data

A suitable crystal was obtained using hexane/ethyl acetate as the recrystallization solvent and tested on a Bruker APEX-II CCD diffractometer. The crystal was kept at 103.00 K during data collection. Using Olex2, the structure was solved with the SHELXT structure solution program using Intrinsic Phasing to solve the phase problem for single-crystal reflection data expanded to the space group and refined with the SHELXL refinement package using Least Squares minimization for validating and archiving crystal structures.



CCDC-2435261

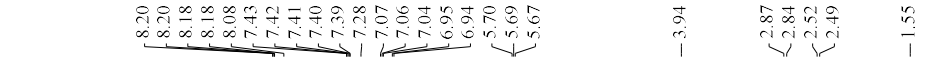
Table 1 Crystal data and structure refinement for mo_20241656_0m.

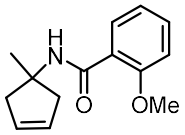
Identification code	mo_20241656_0m
Empirical formula	$C_{23}H_{29}NO_2$
Formula weight	351.47
Temperature/K	103.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	15.6870(6)
b/Å	12.7263(4)
c/Å	20.3517(7)
α/°	90
β/°	104.0370(10)
γ/°	90
Volume/Å^3	3941.6(2)
Z	8
ρ_{calc}g/cm^3	1.185
μ /mm^{-1}	0.075
F(000)	1520.0
Crystal size/mm^3	0.15 × 0.08 × 0.06
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	3.808 to 52.81
Index ranges	$-16 \leqslant h \leqslant 19, -15 \leqslant k \leqslant 15, -23 \leqslant l \leqslant 25$
Reflections collected	38137
Independent reflections	15119 [R_{int} = 0.0764, R_{sigma} = 0.0925]
Data/restraints/parameters	15119/2/973
Goodness-of-fit on F^2	1.025
Final R indexes [I>=2σ (I)]	R_1 = 0.0689, wR_2 = 0.1485
Final R indexes [all data]	R_1 = 0.1026, wR_2 = 0.1722
Largest diff. peak/hole / e $Å^{-3}$	0.76/-0.29
Flack parameter	0.0(9)

^{1}H and ^{13}C NMR Spectra

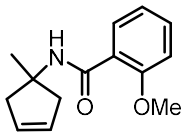
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



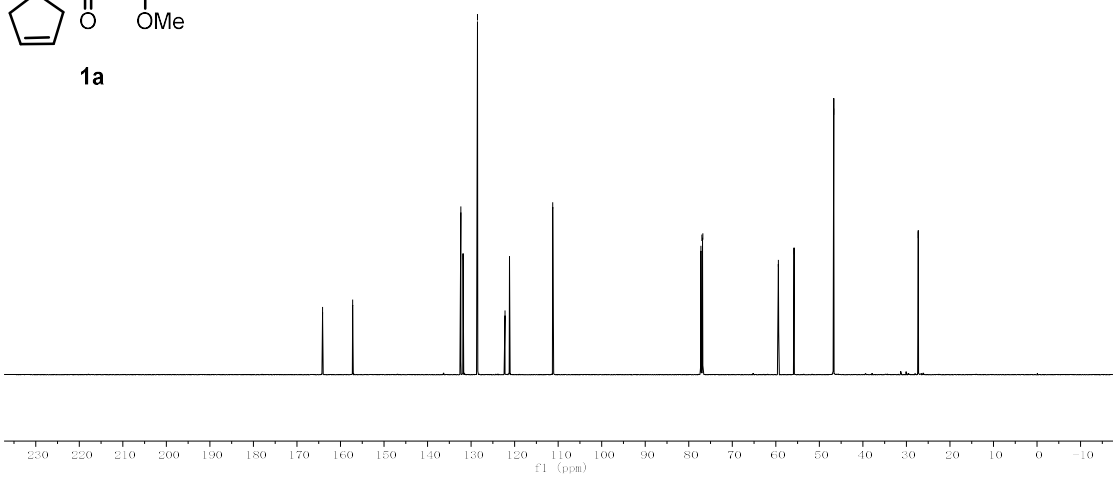


1a

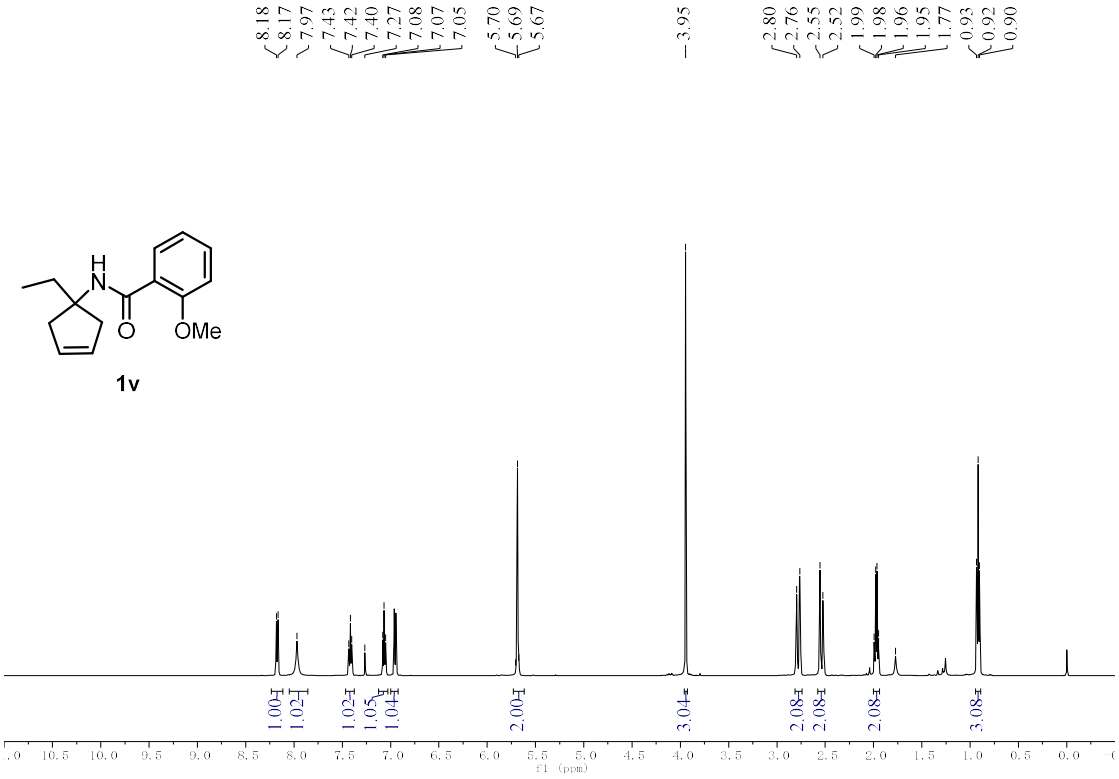
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



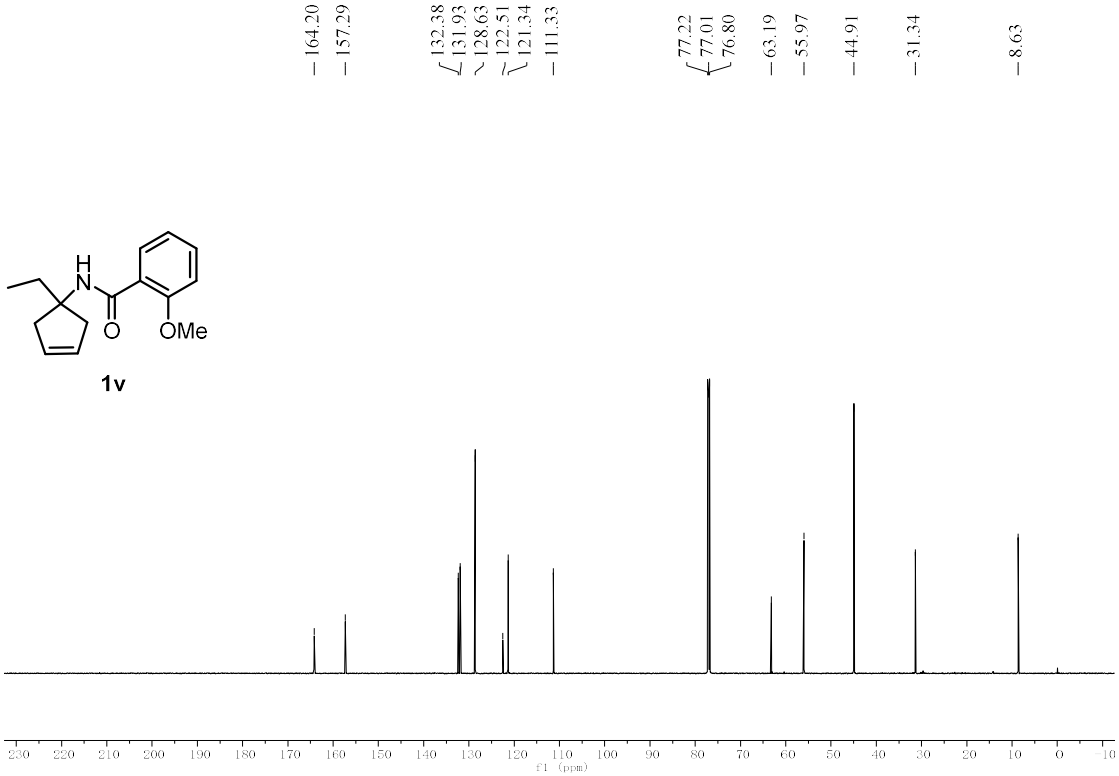
1a



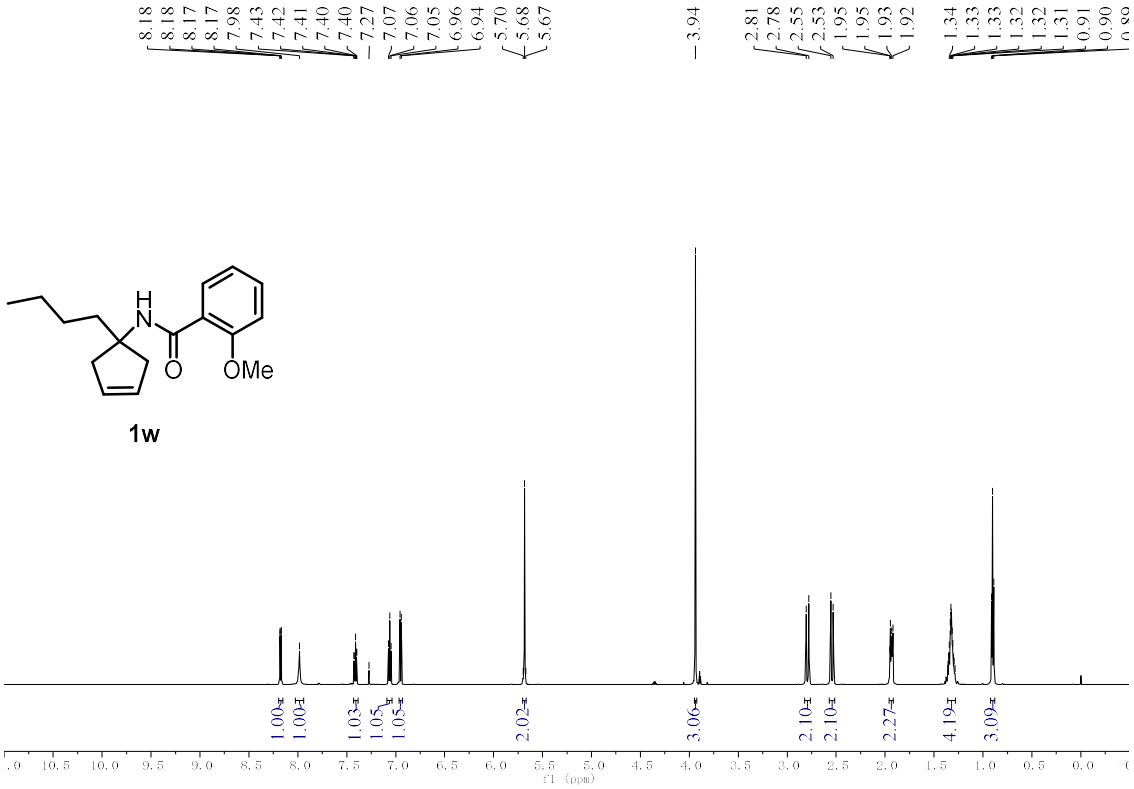
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



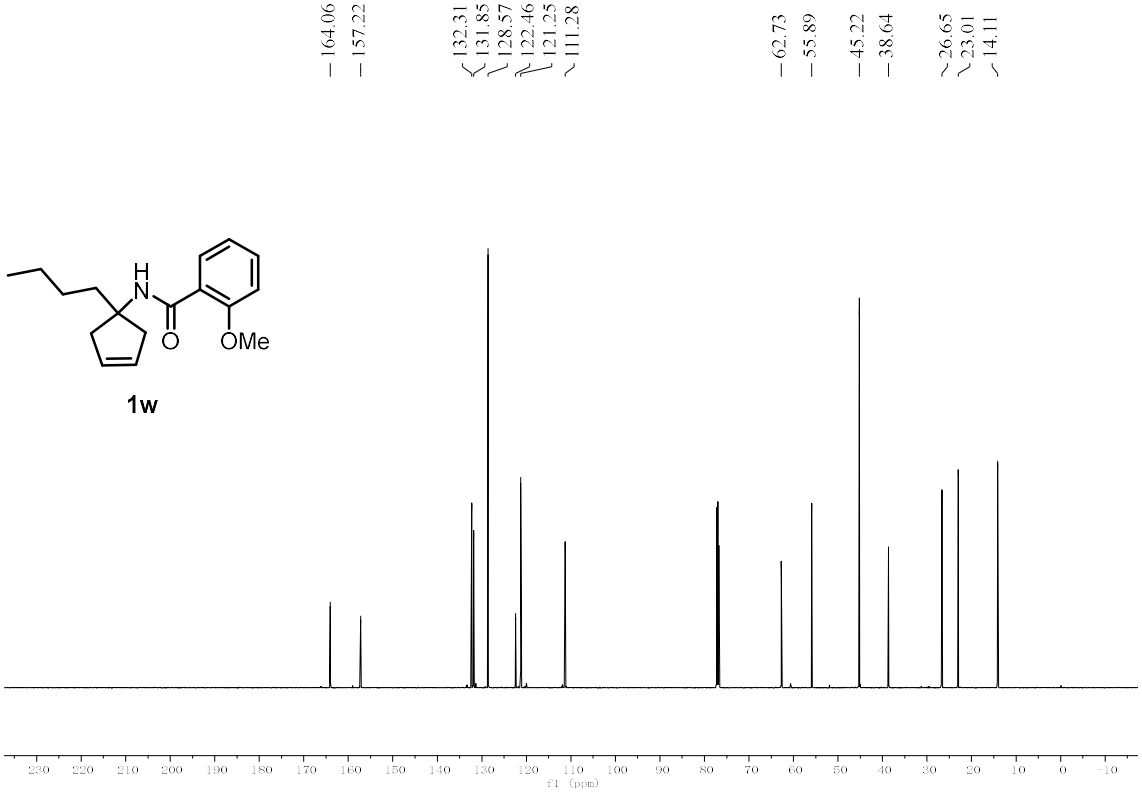
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



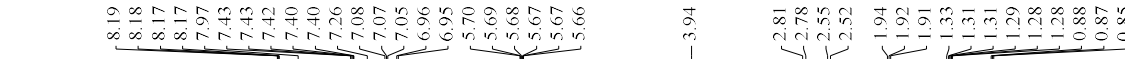
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

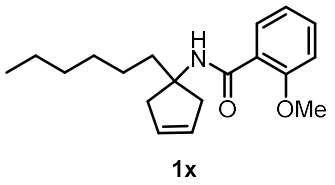


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



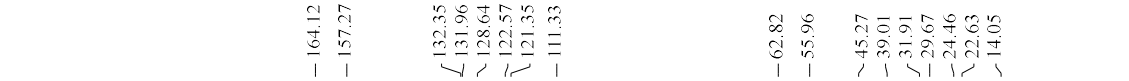
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

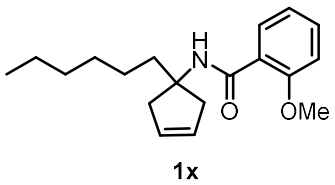




1x

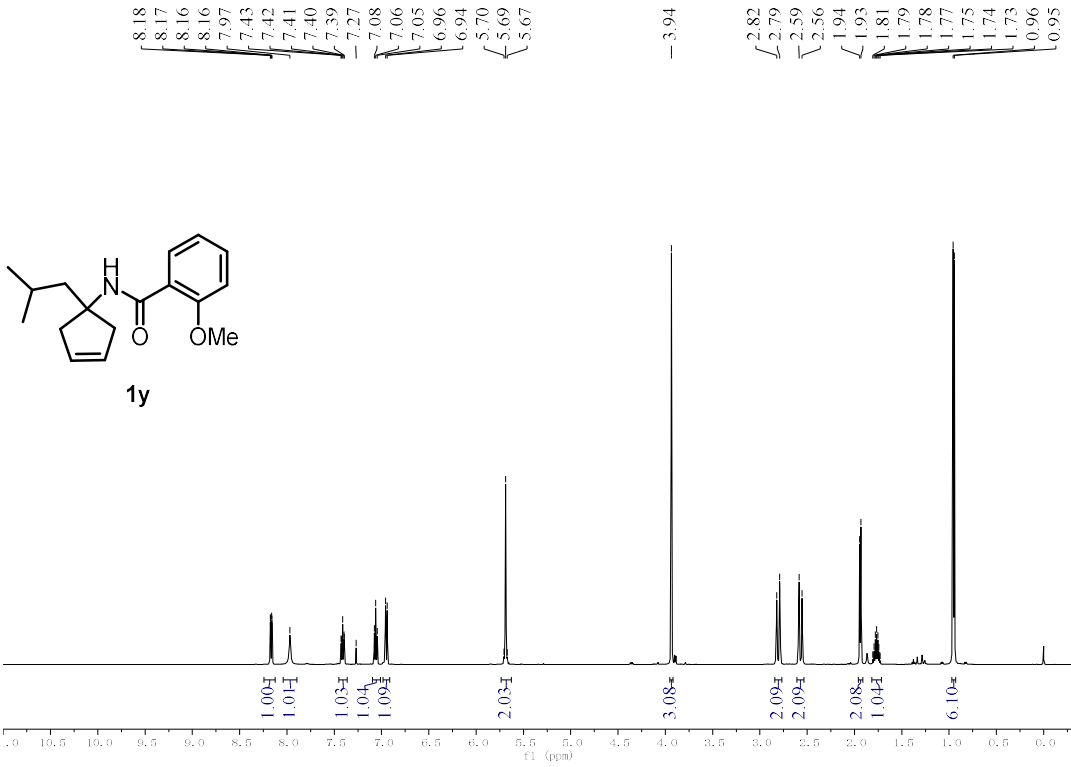
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



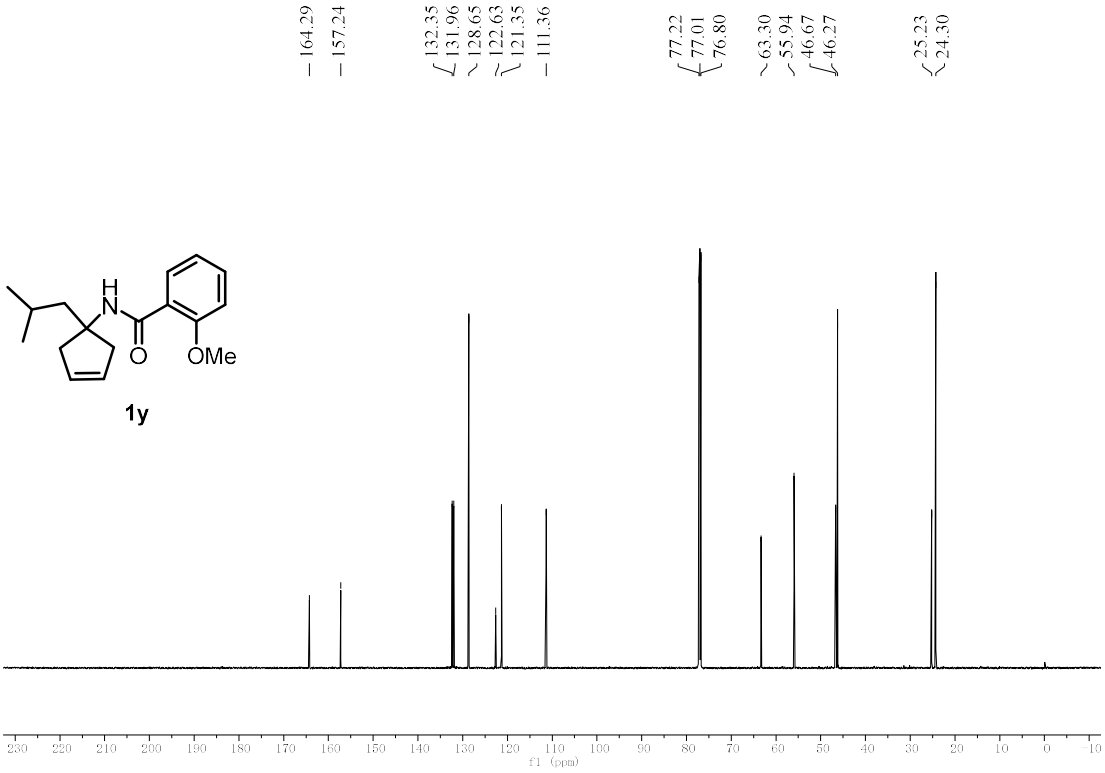


1x

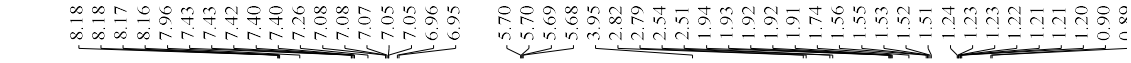
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

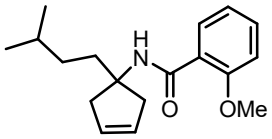


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



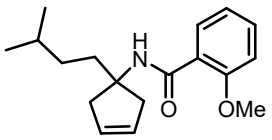
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





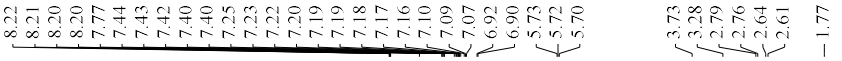
1z

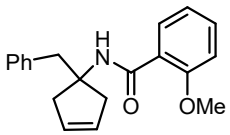
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



1z

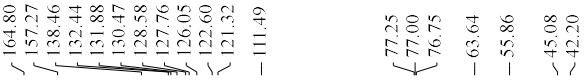
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

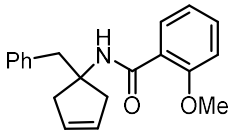




1aa

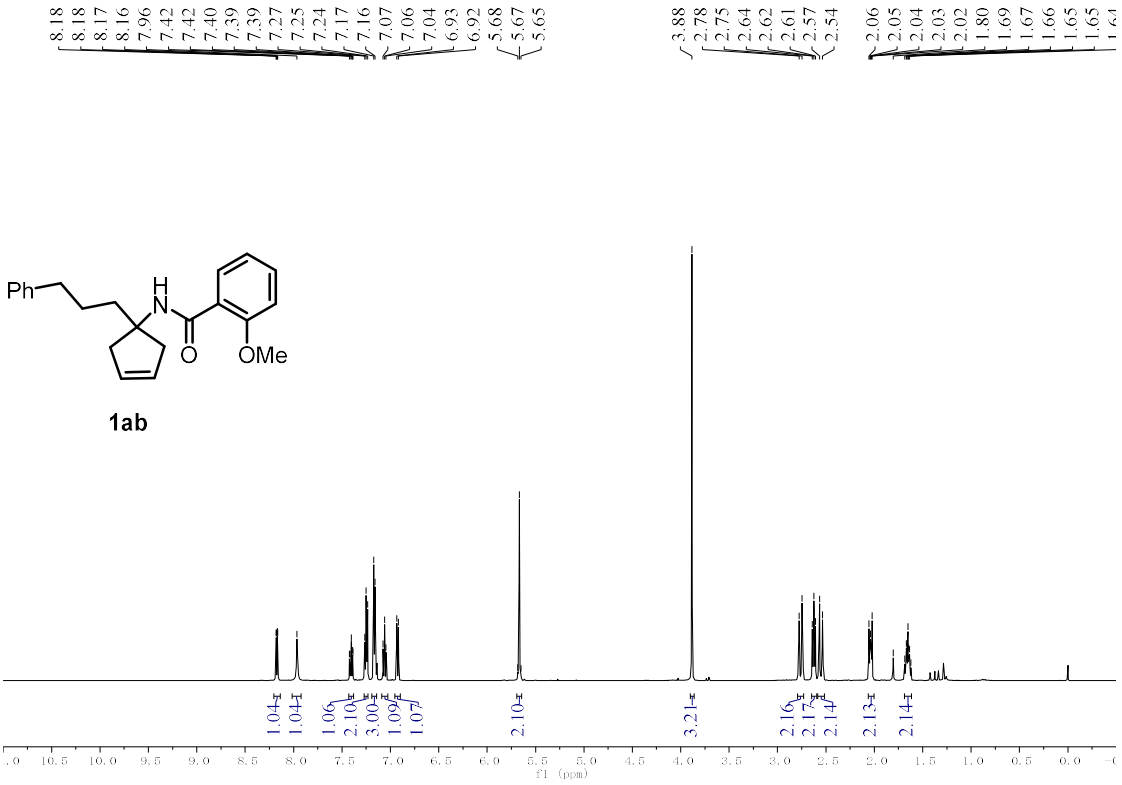
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



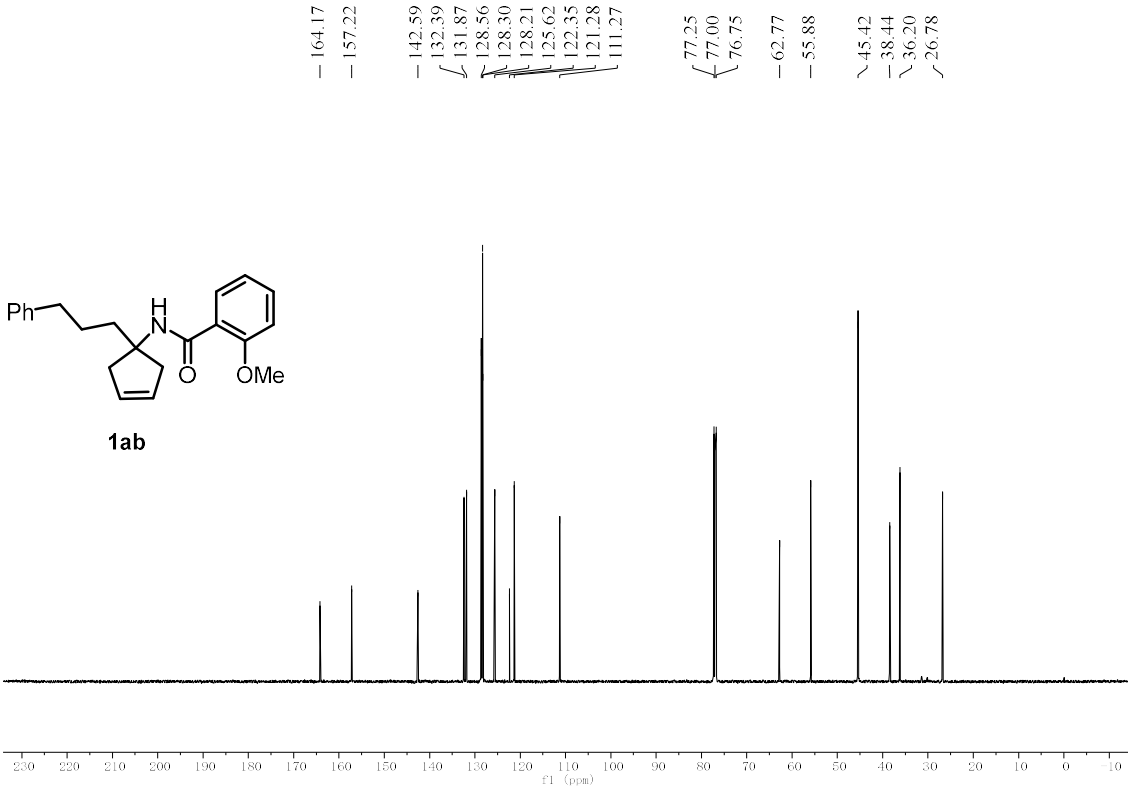


1aa

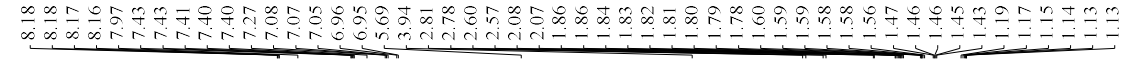
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

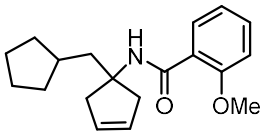


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



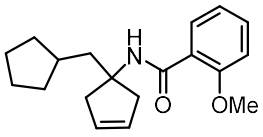
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





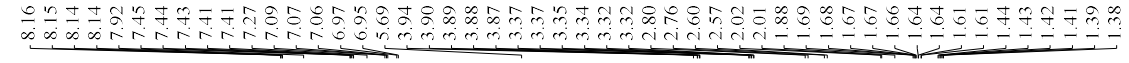
1ac

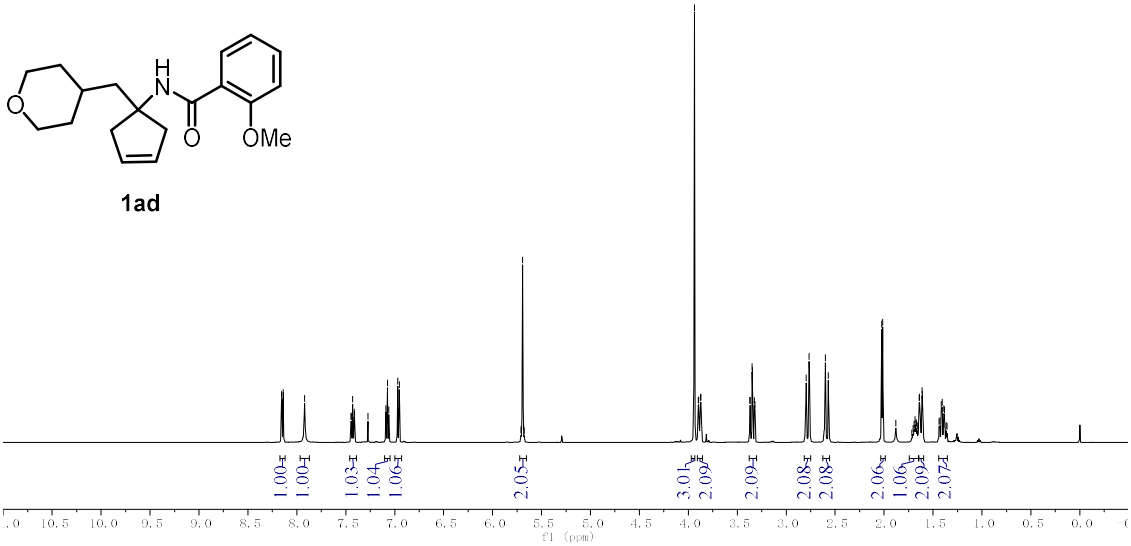
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



1ac

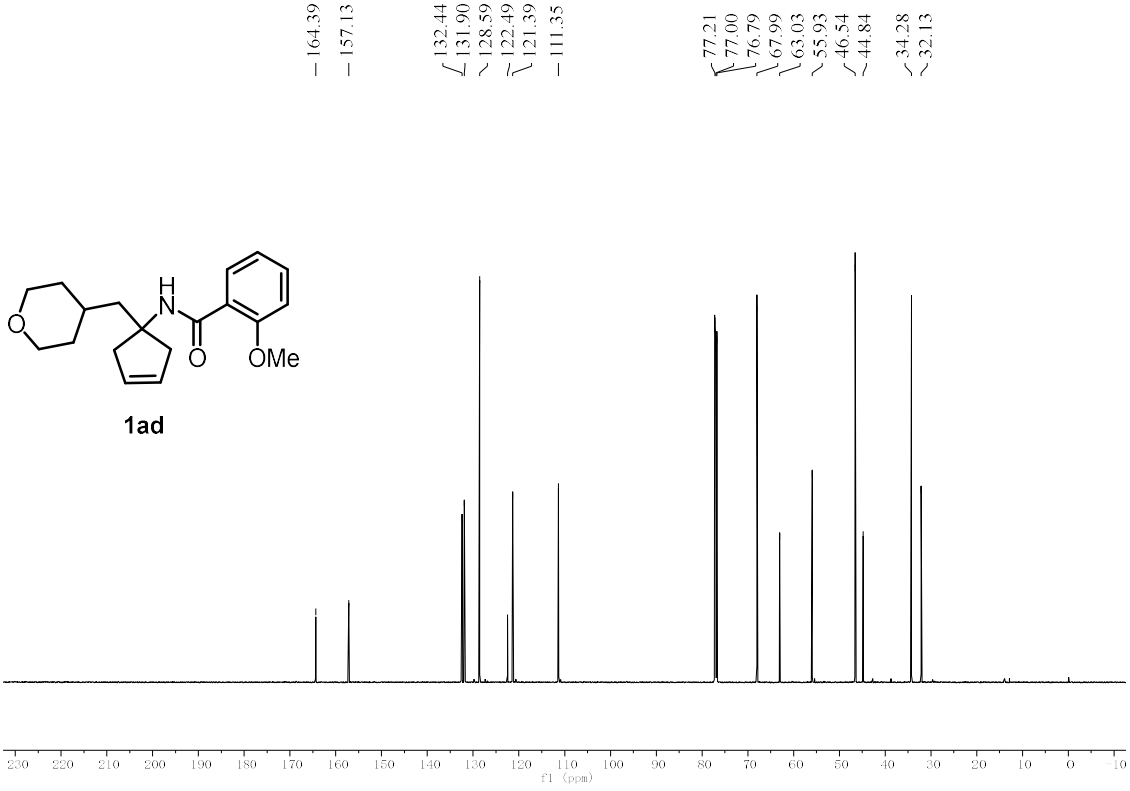
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





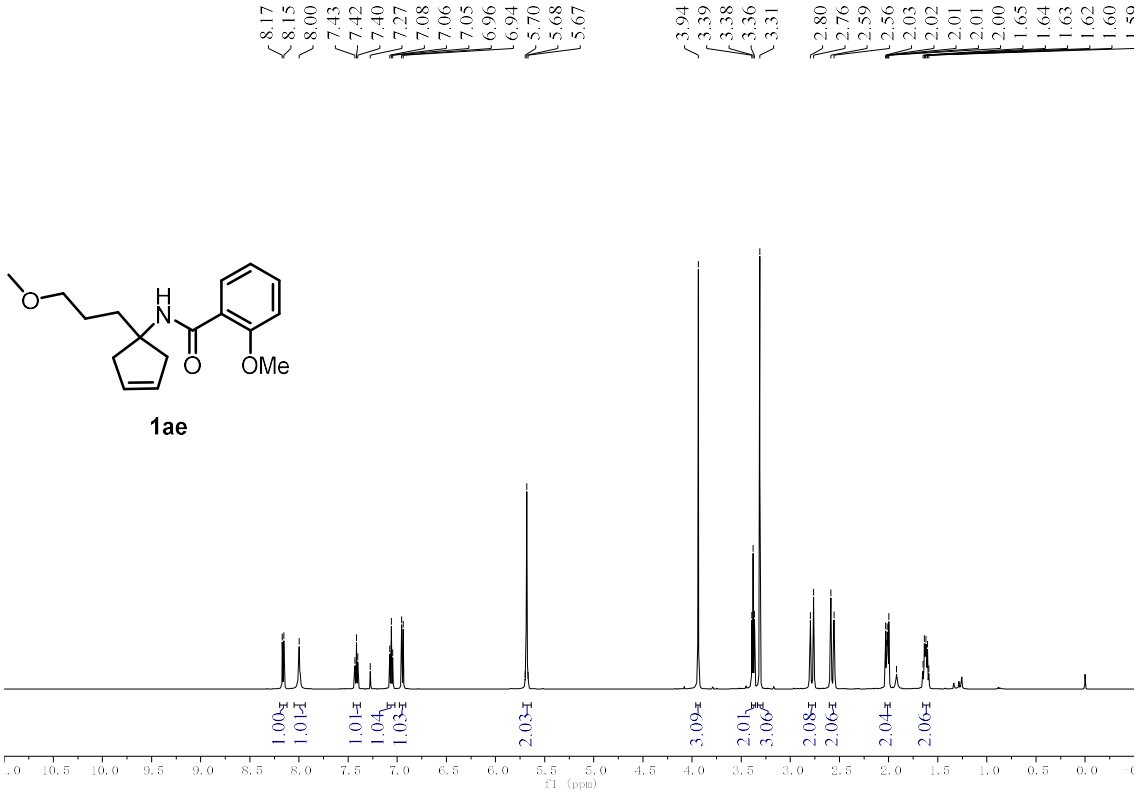
1ad

^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

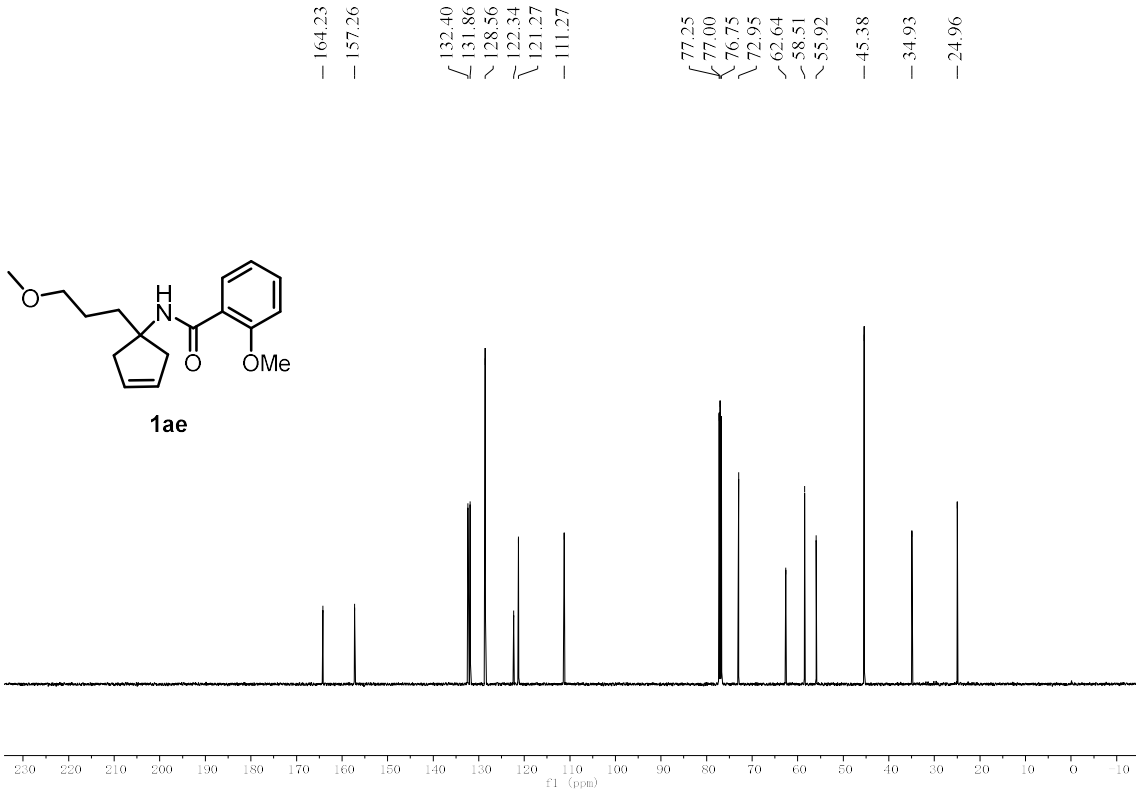


1ad

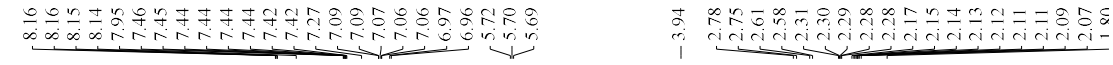
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

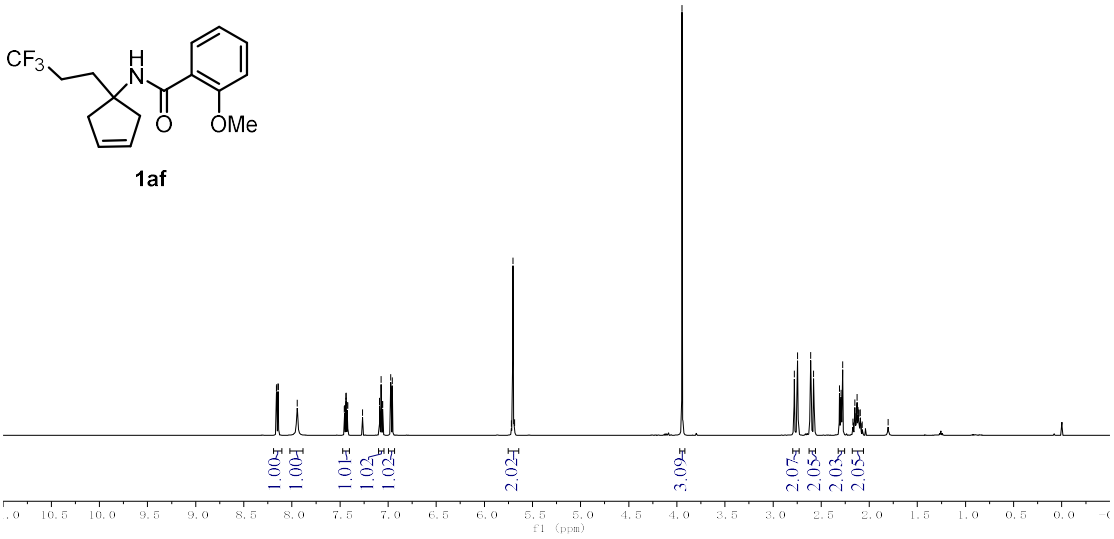


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

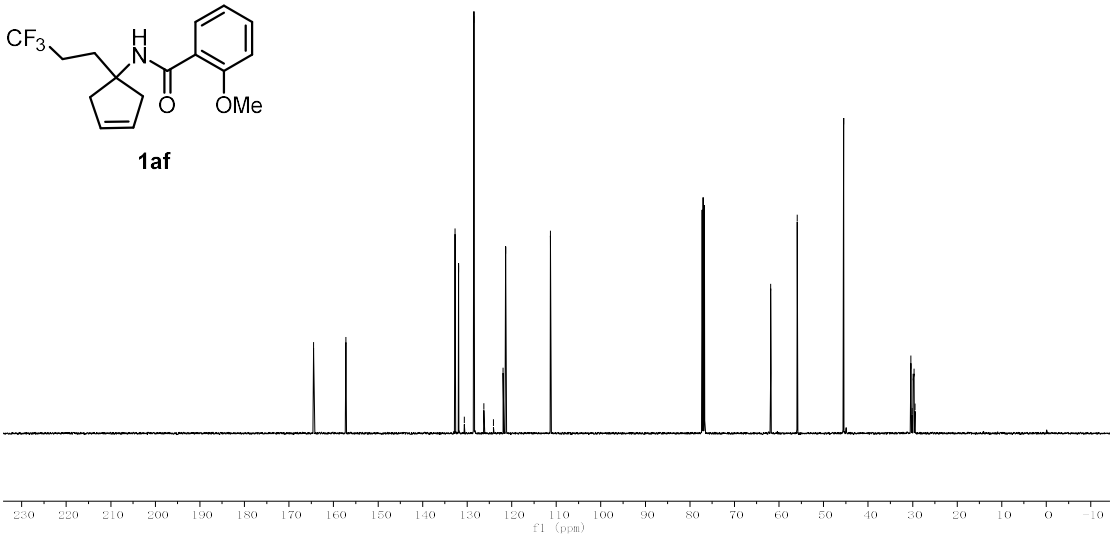


^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

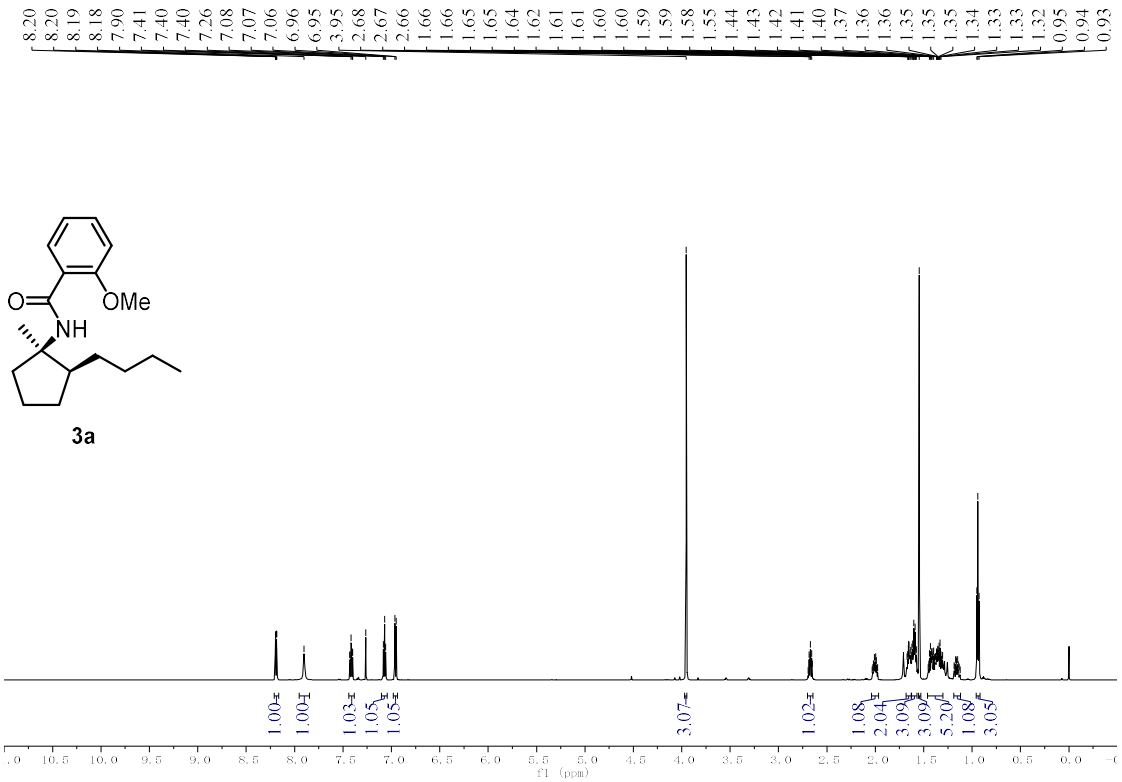




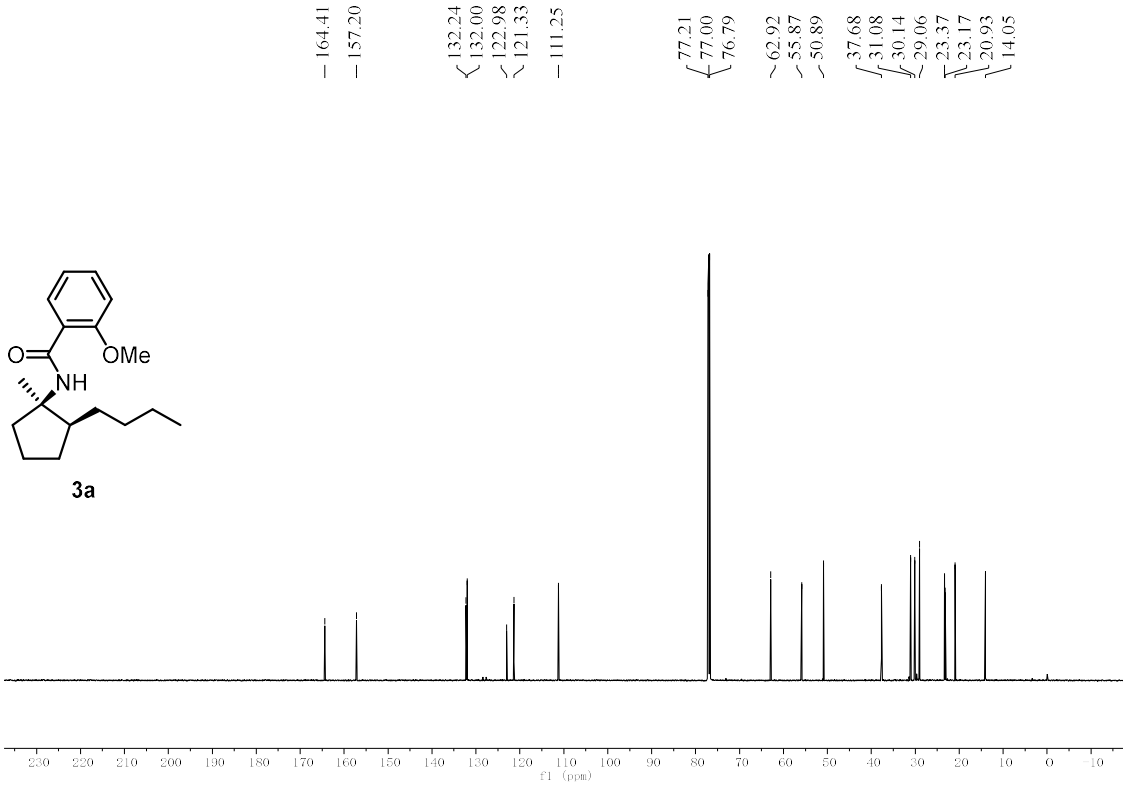
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



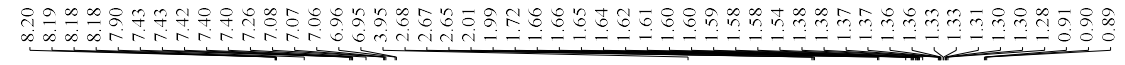
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

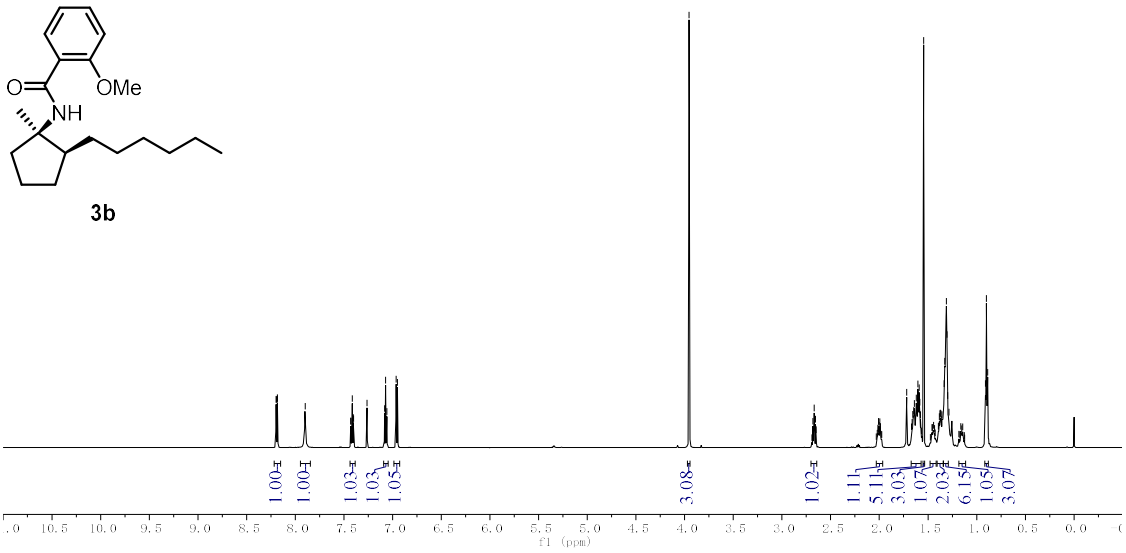


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



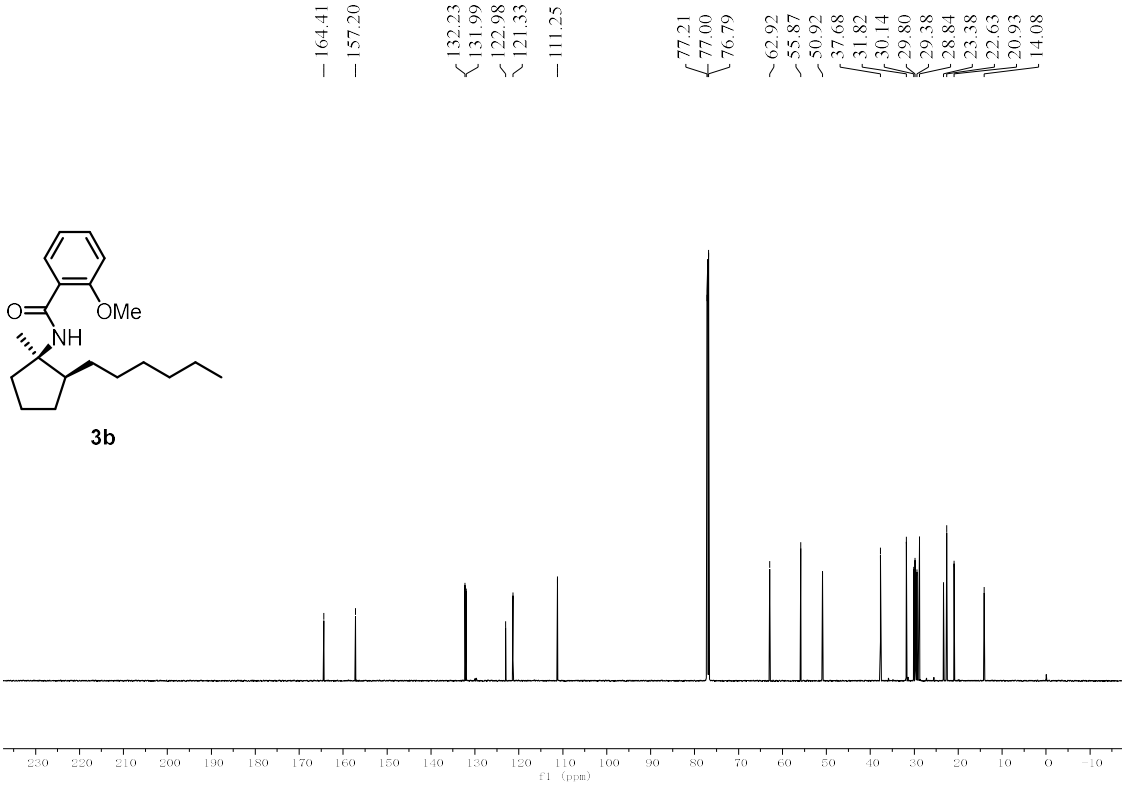
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):





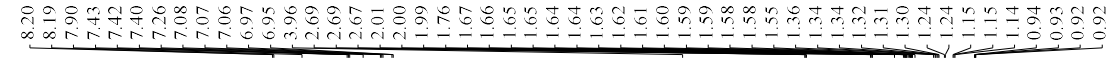
3b

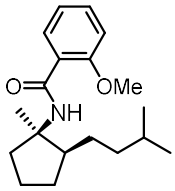
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



3b

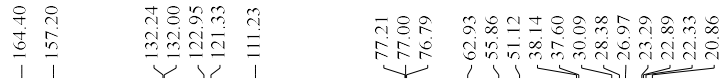
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

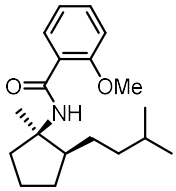




3c

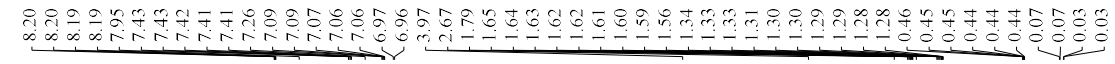
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

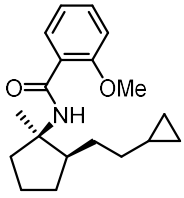




3c

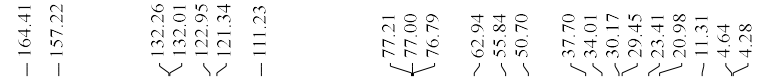
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

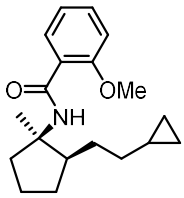




3d

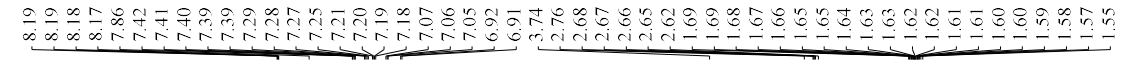
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

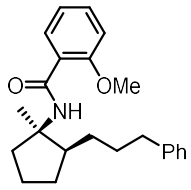




3d

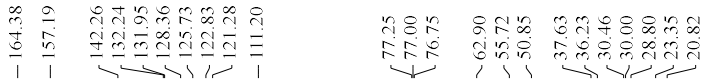
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

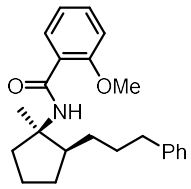




3e

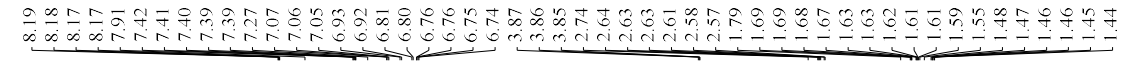
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

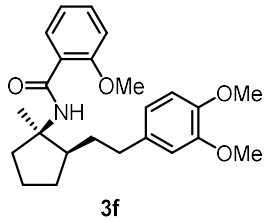




3e

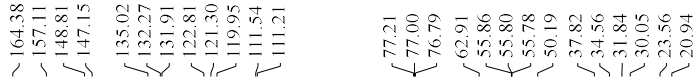
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

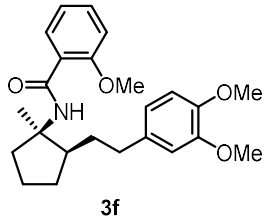




3f

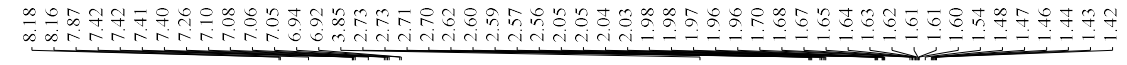
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

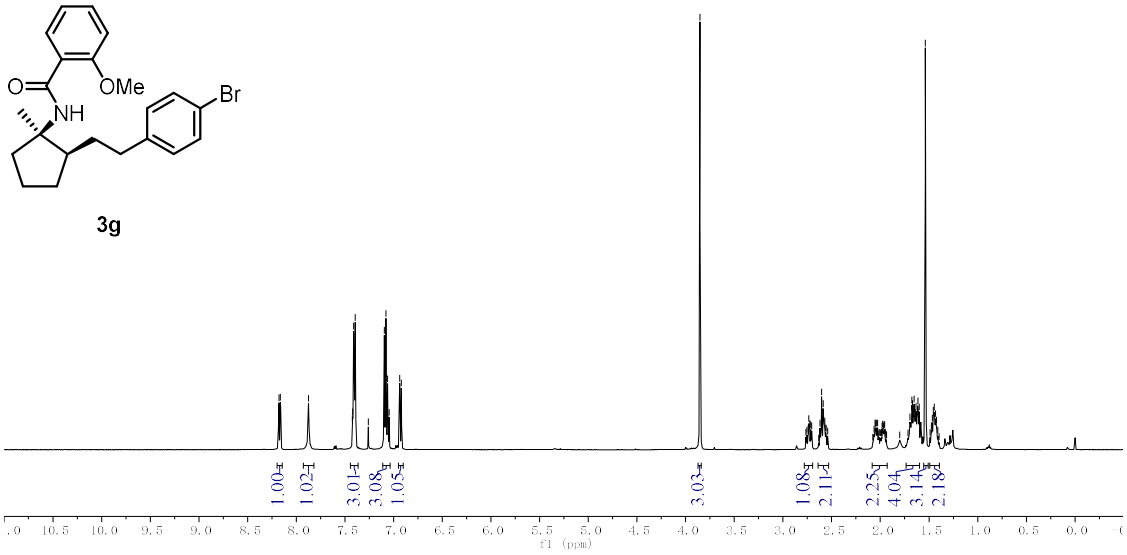




3f

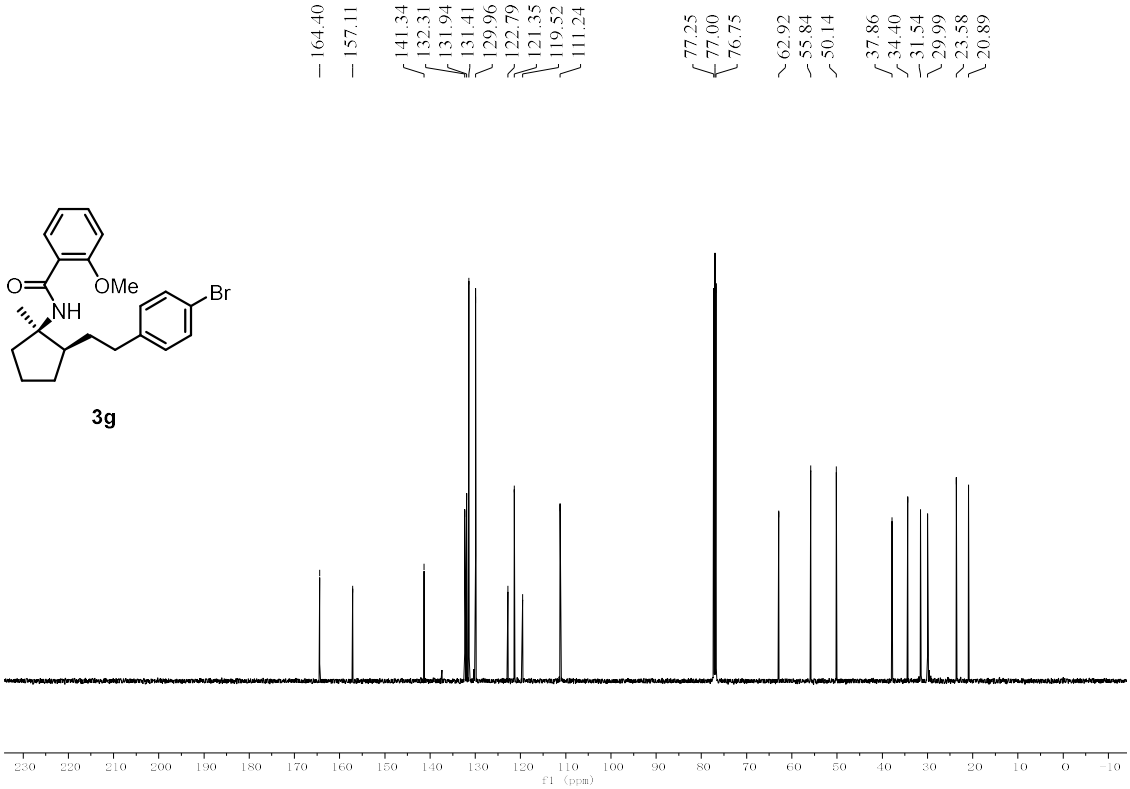
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





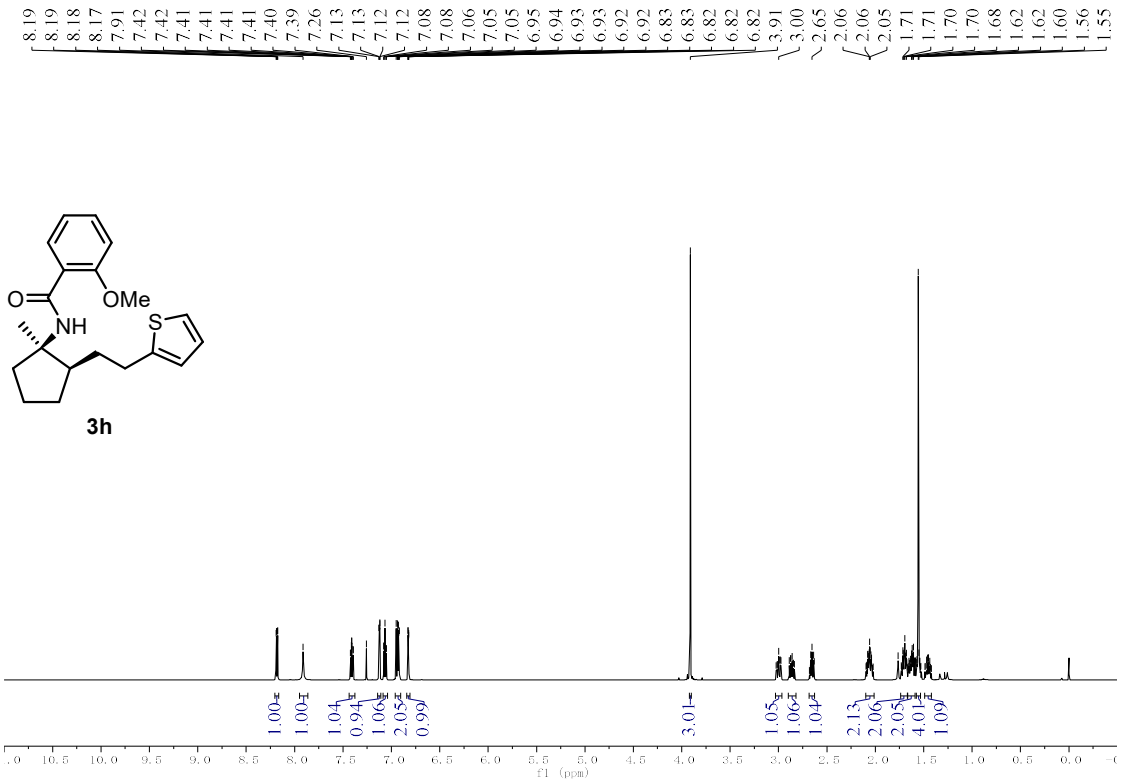
3g

^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

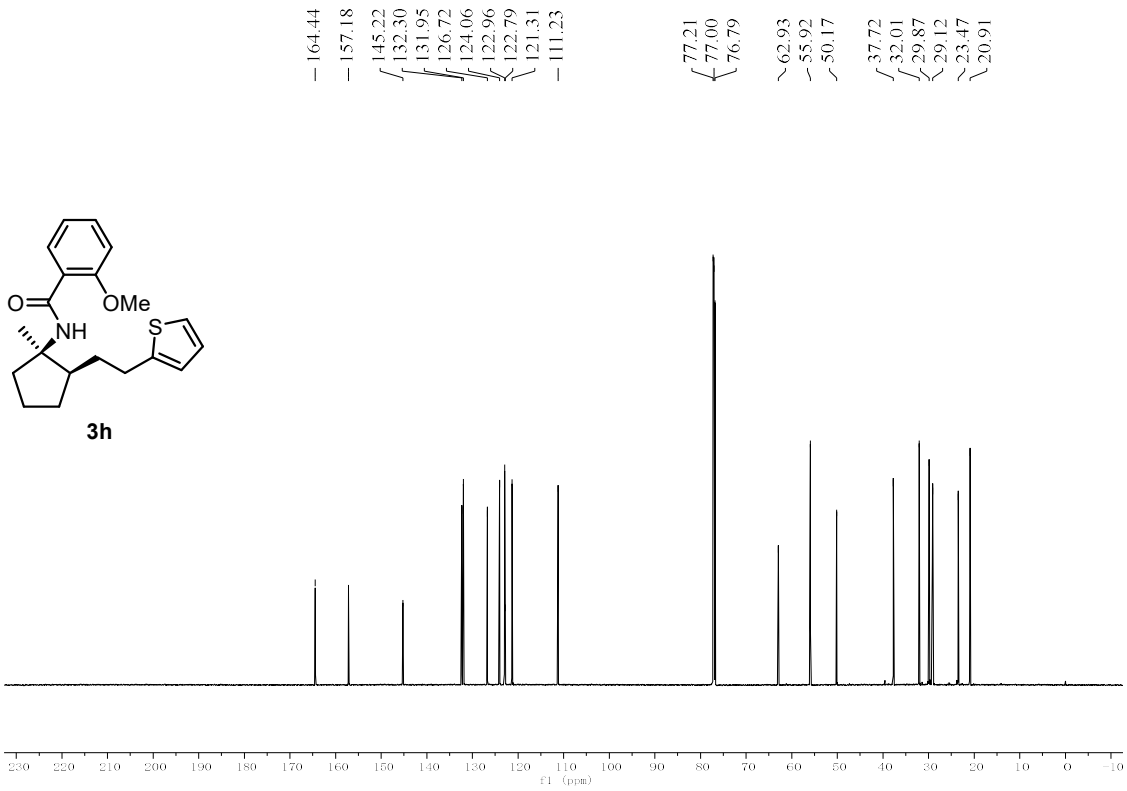


3g

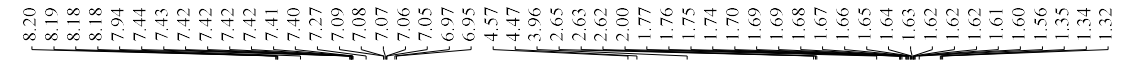
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

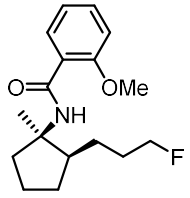


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



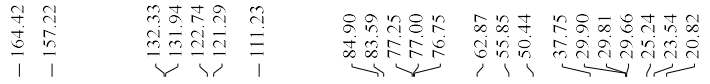
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

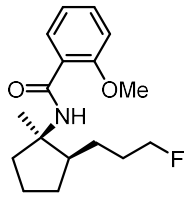




3i

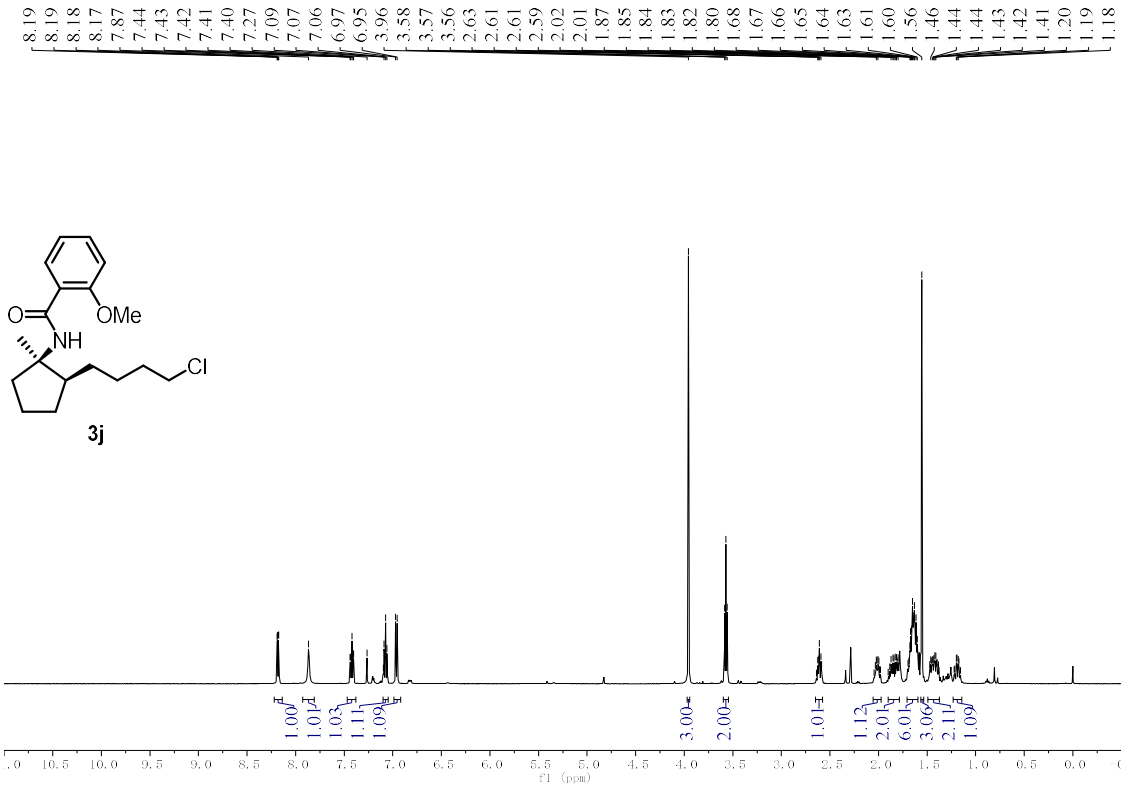
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



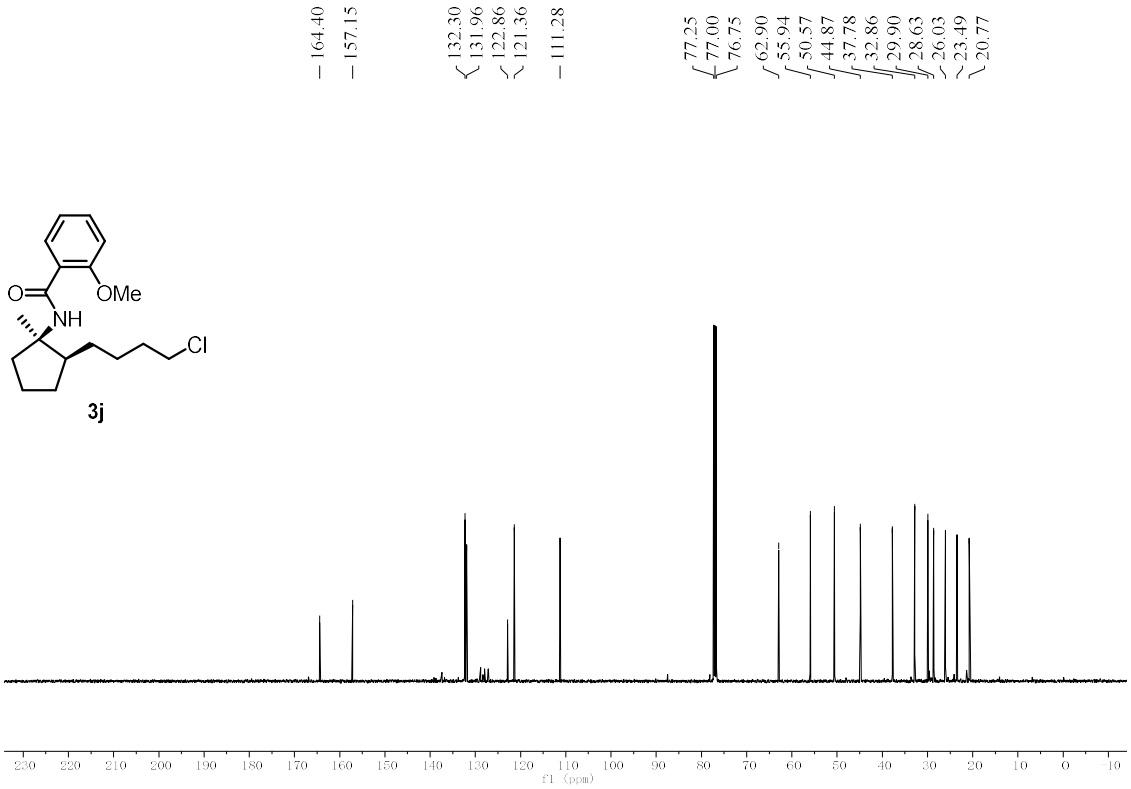


3i

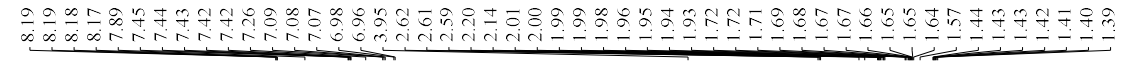
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

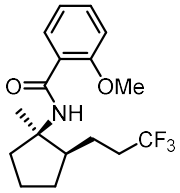


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



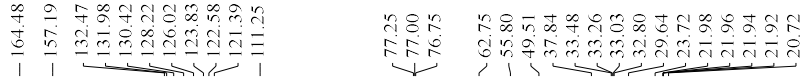
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

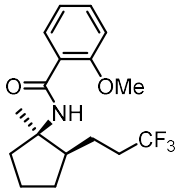




3k

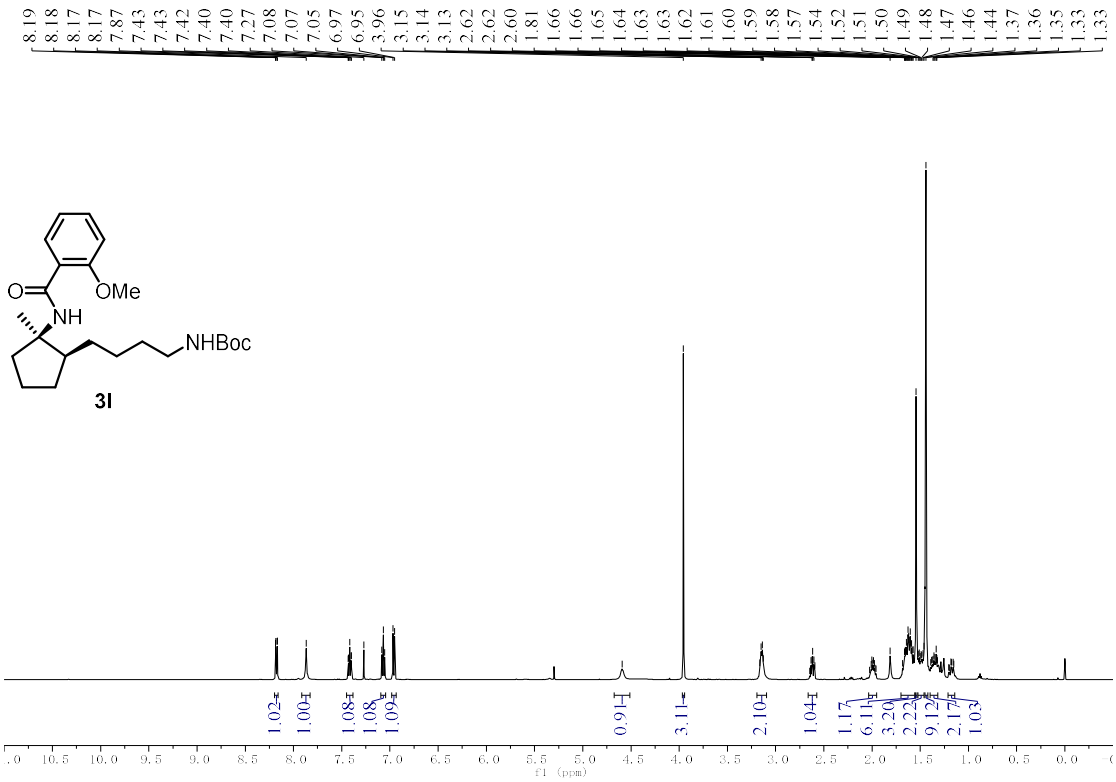
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



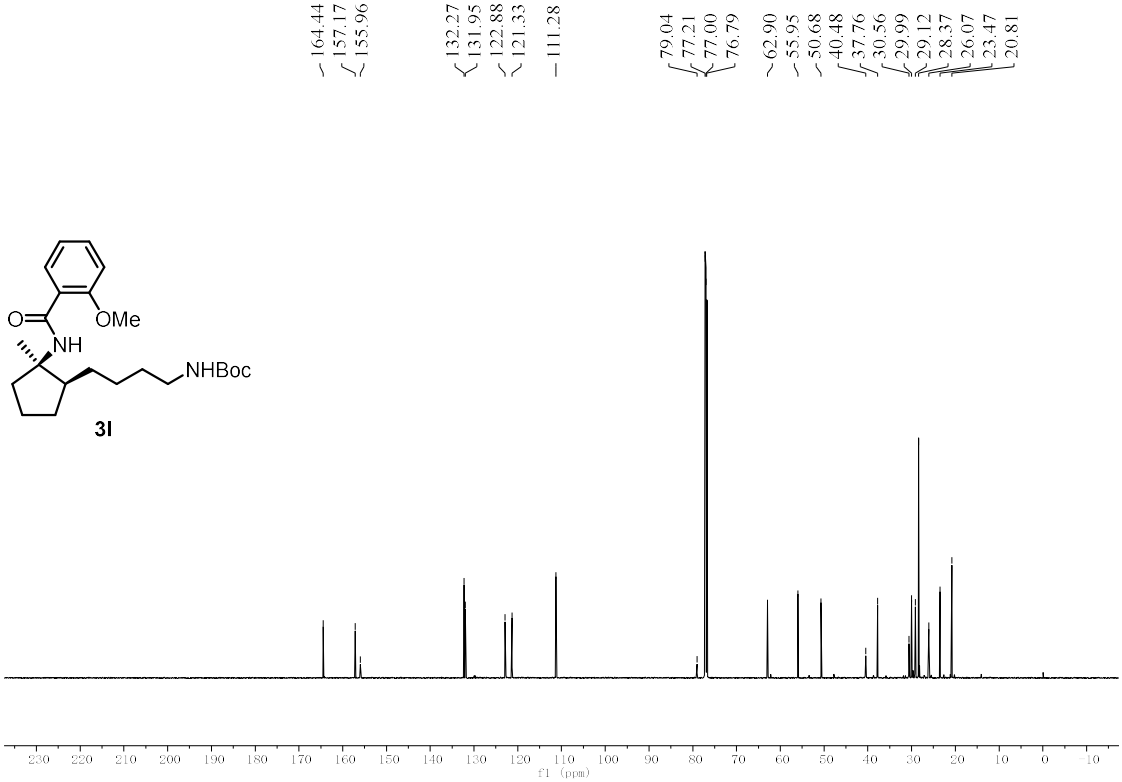


3k

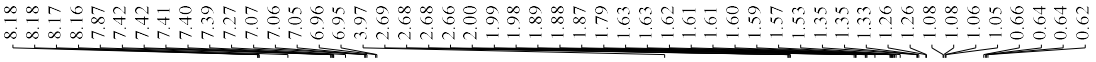
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

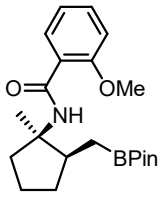


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



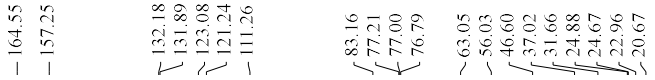
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

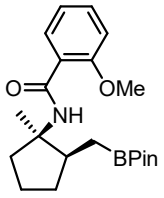




3m

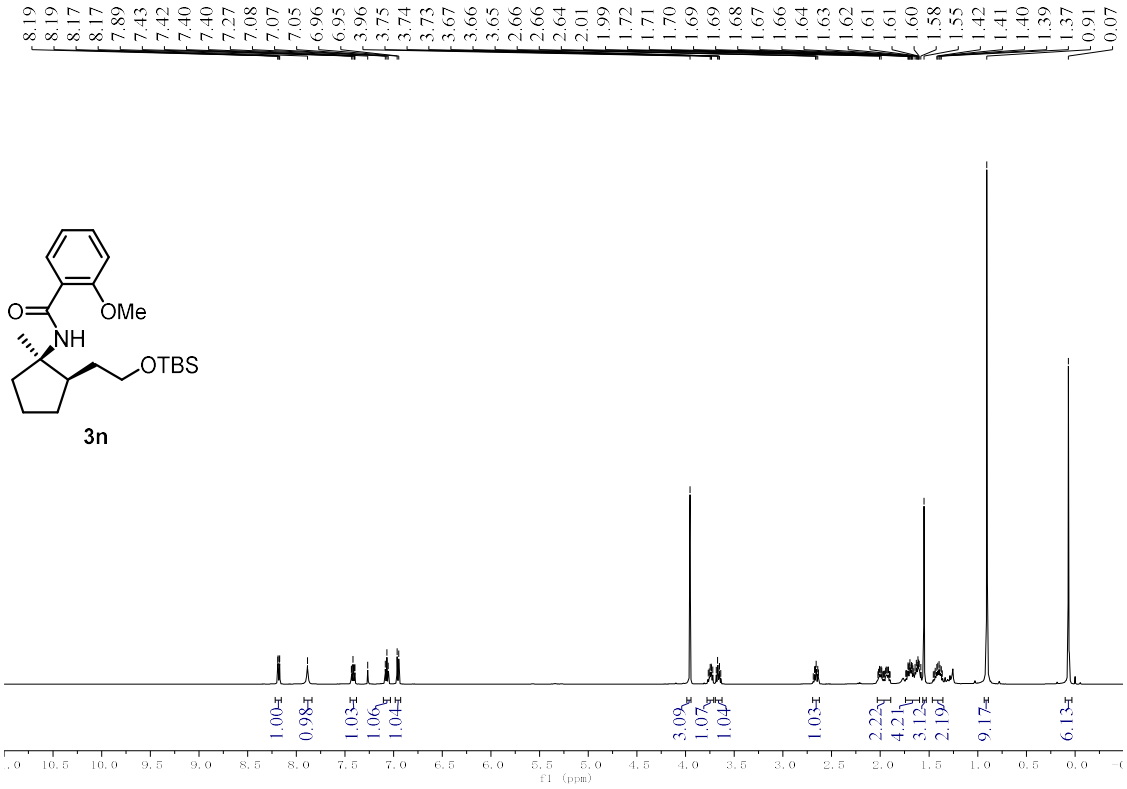
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



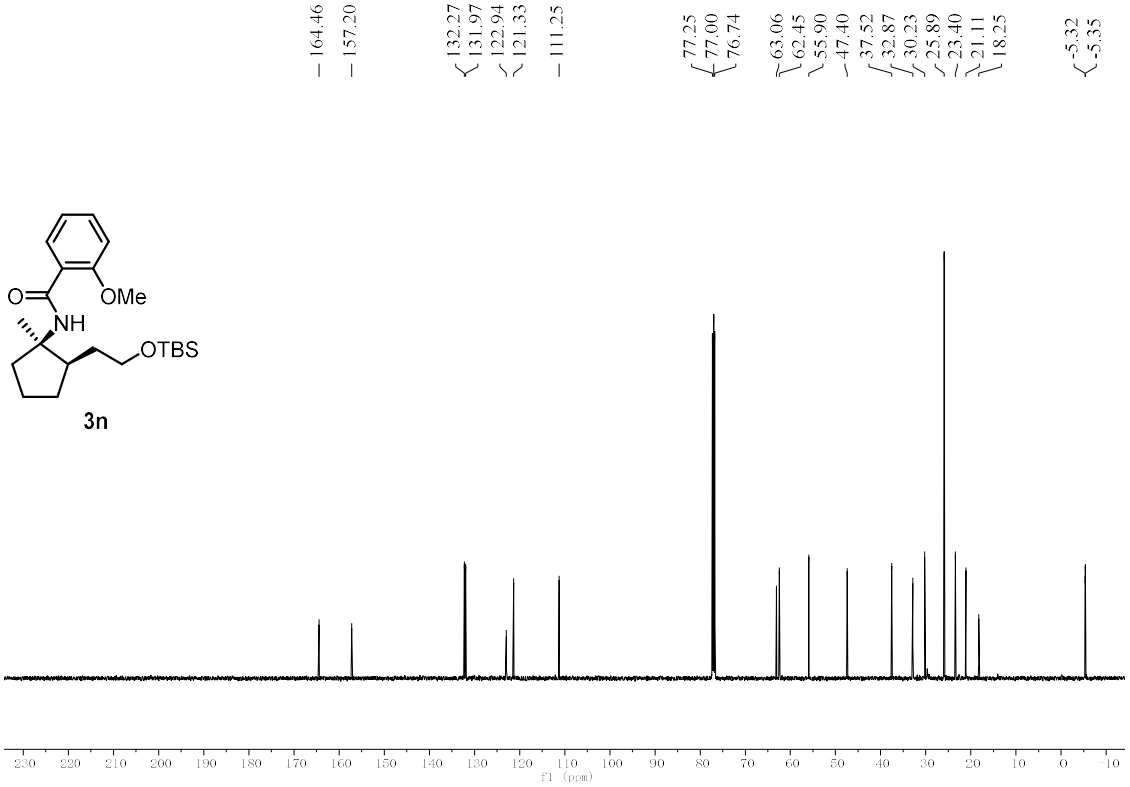


3m

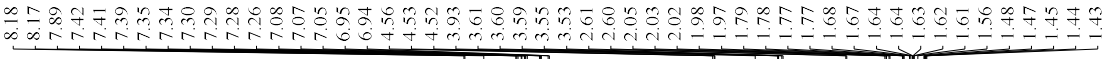
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

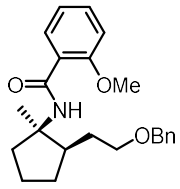


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



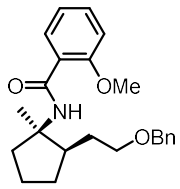
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





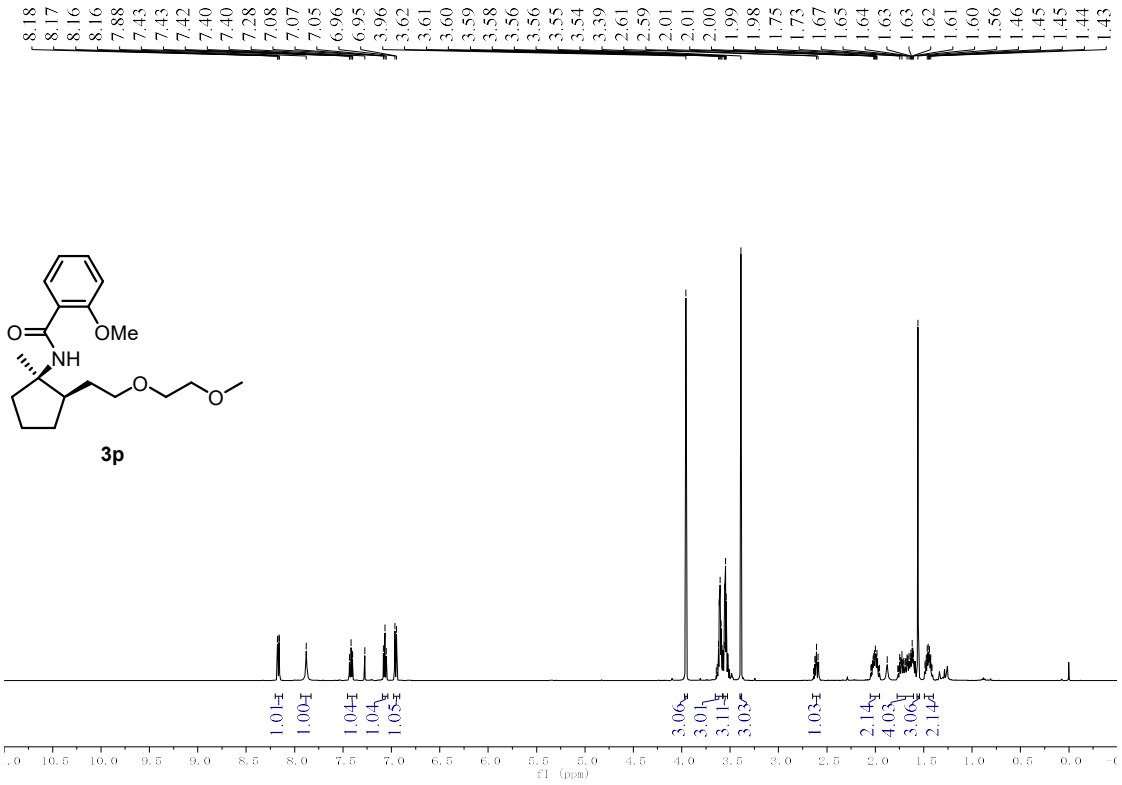
3o

^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

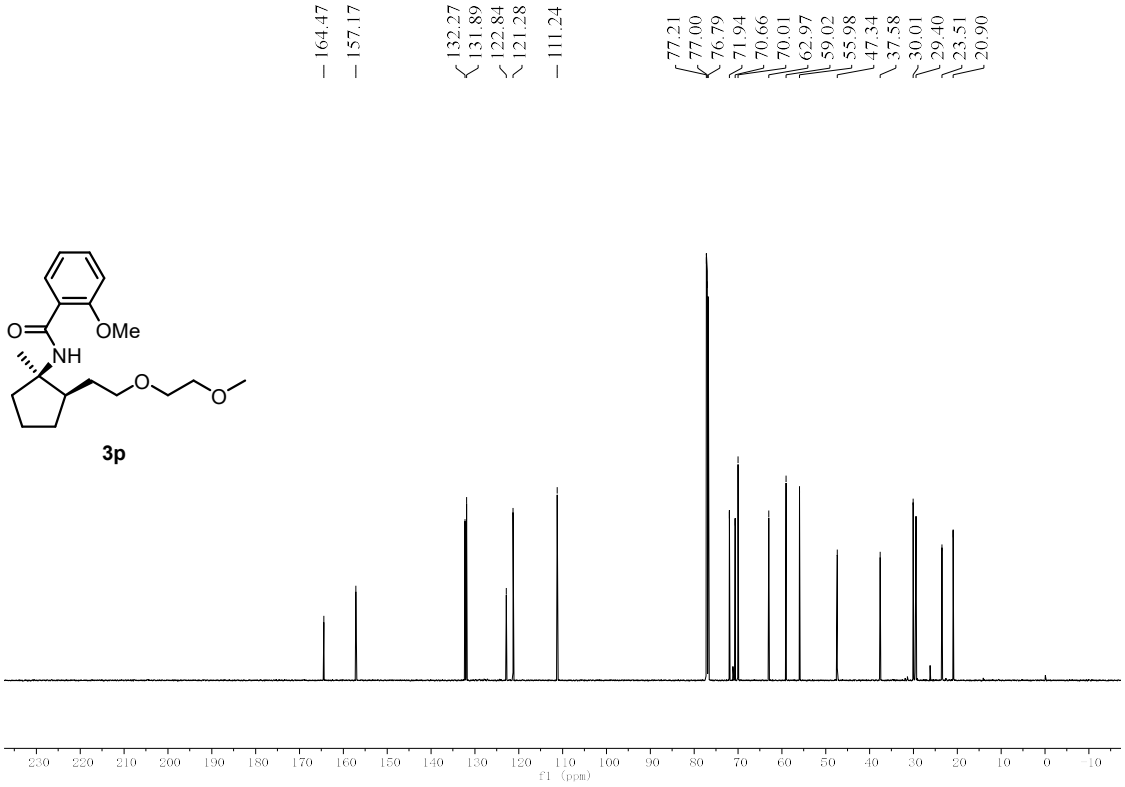


3o

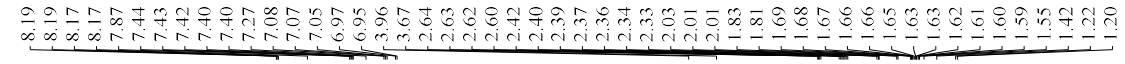
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

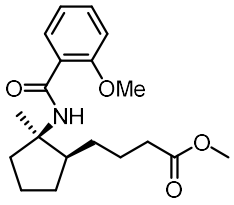


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



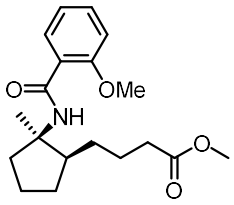
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):





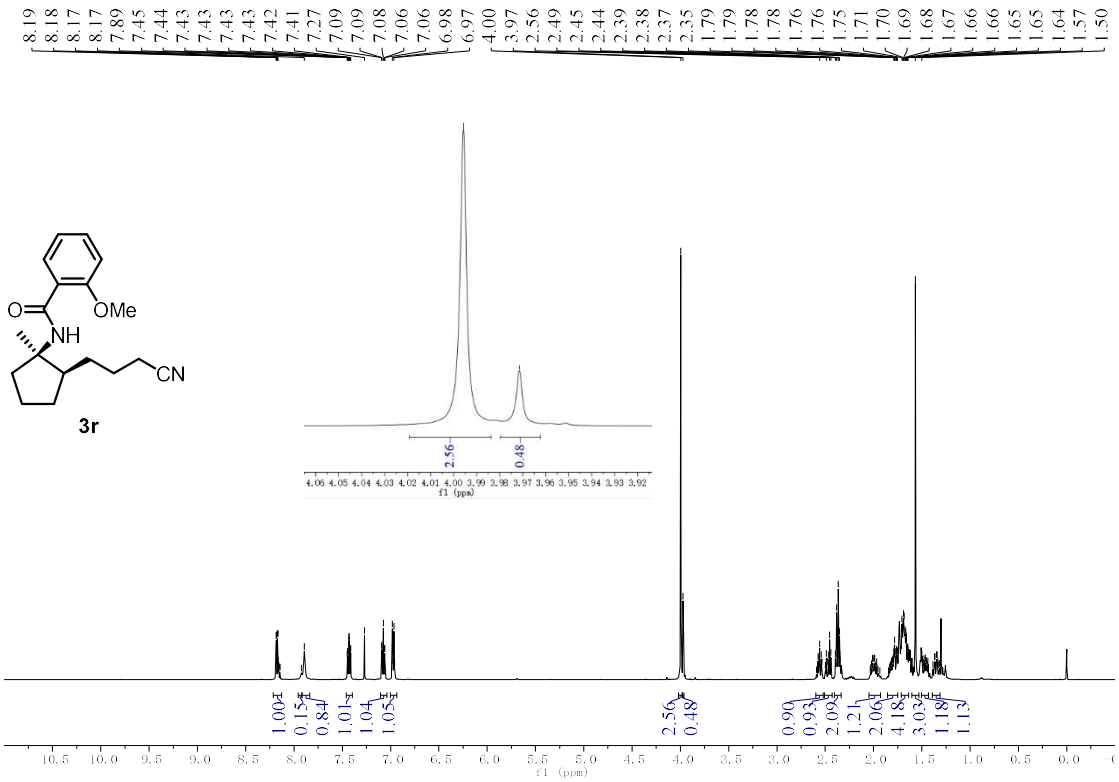
3q

^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

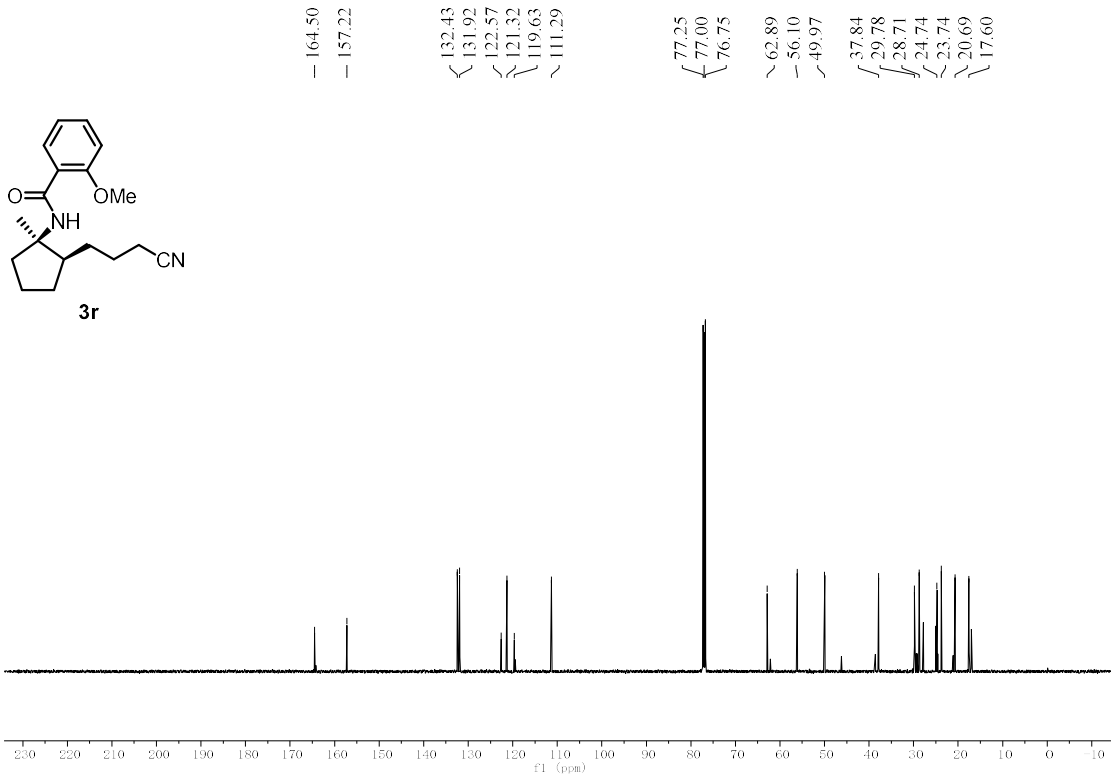


3q

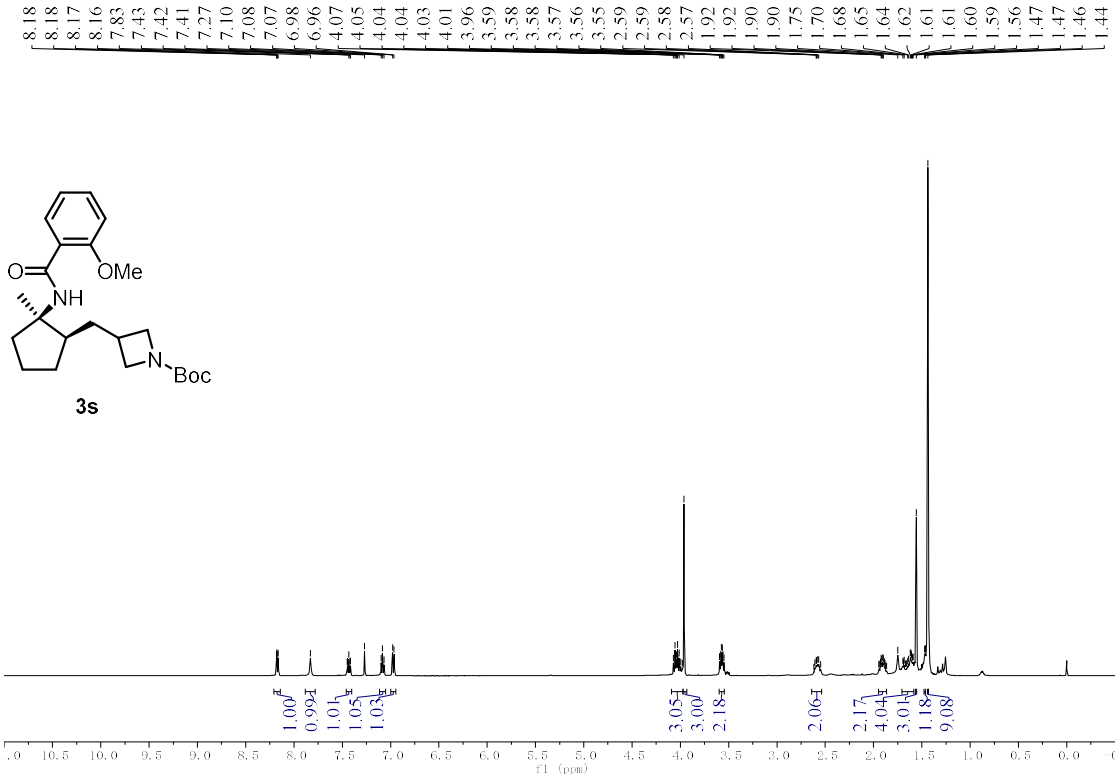
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



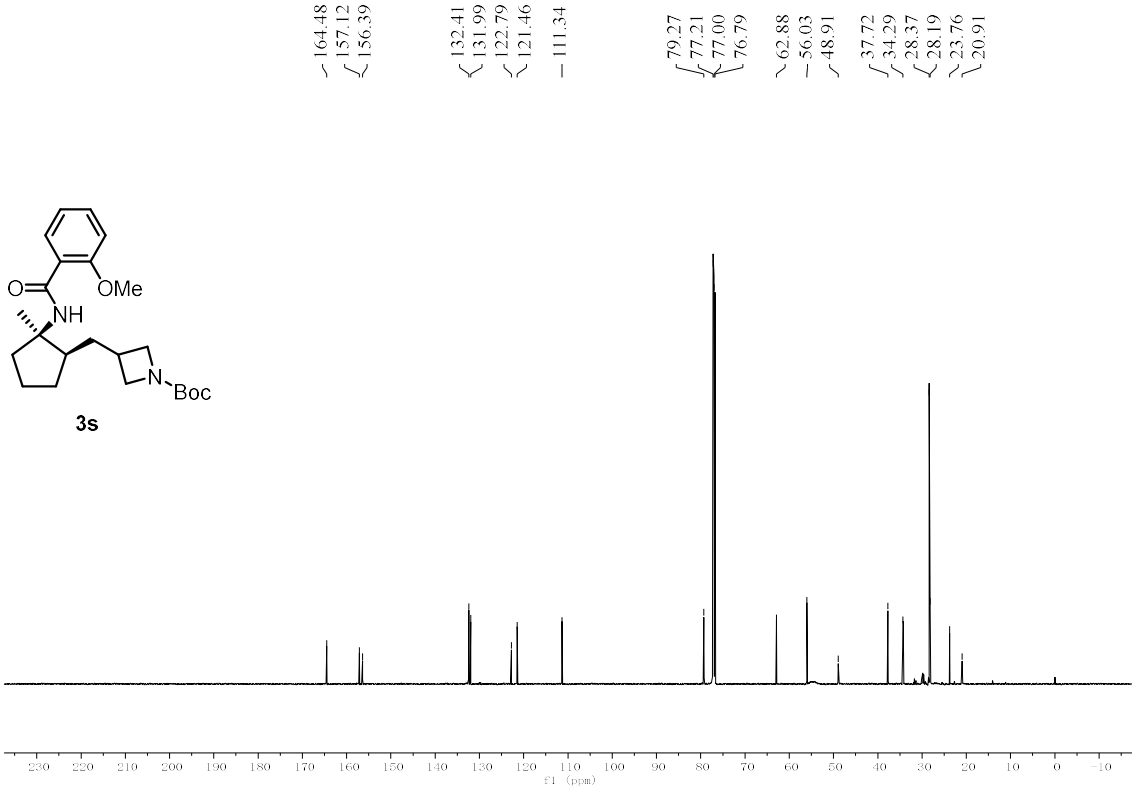
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



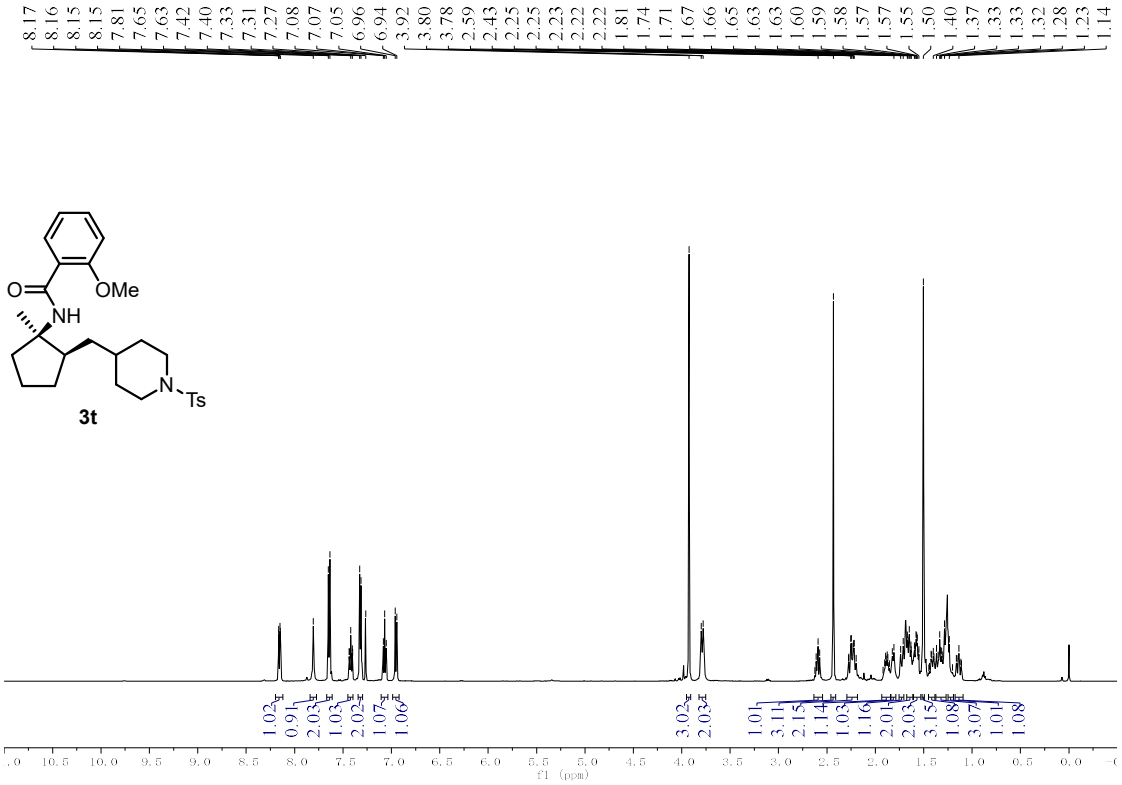
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



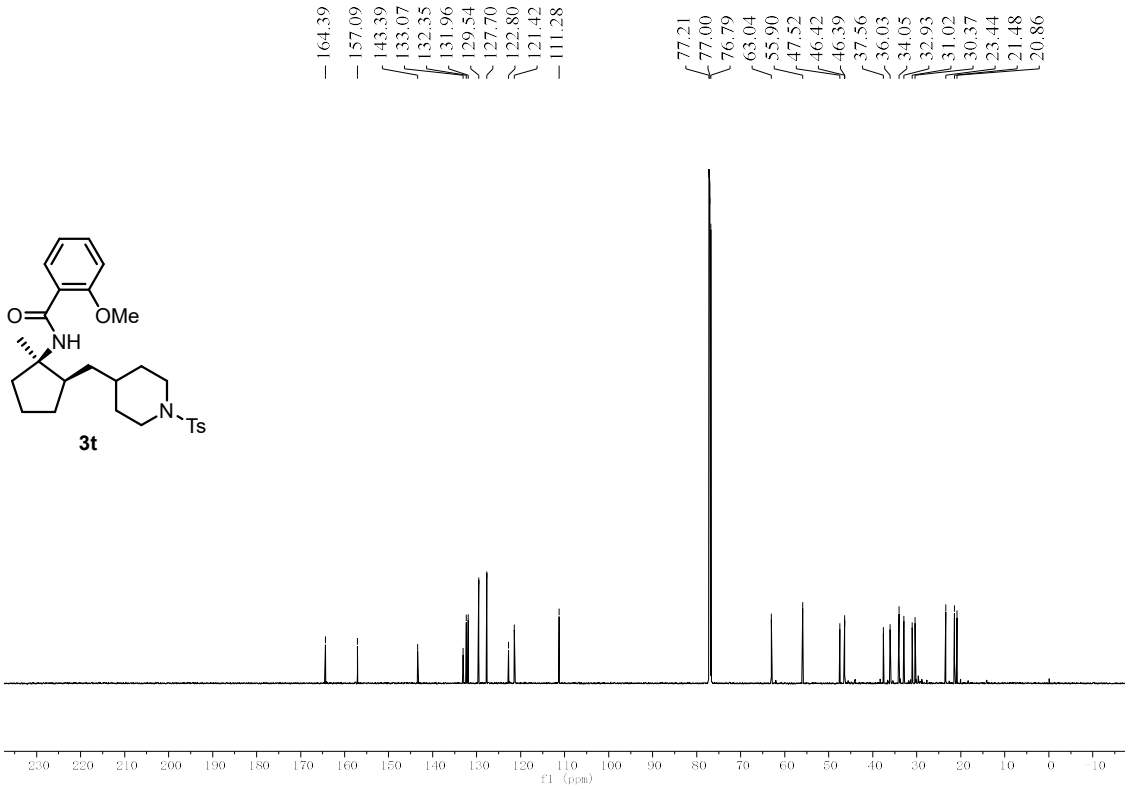
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



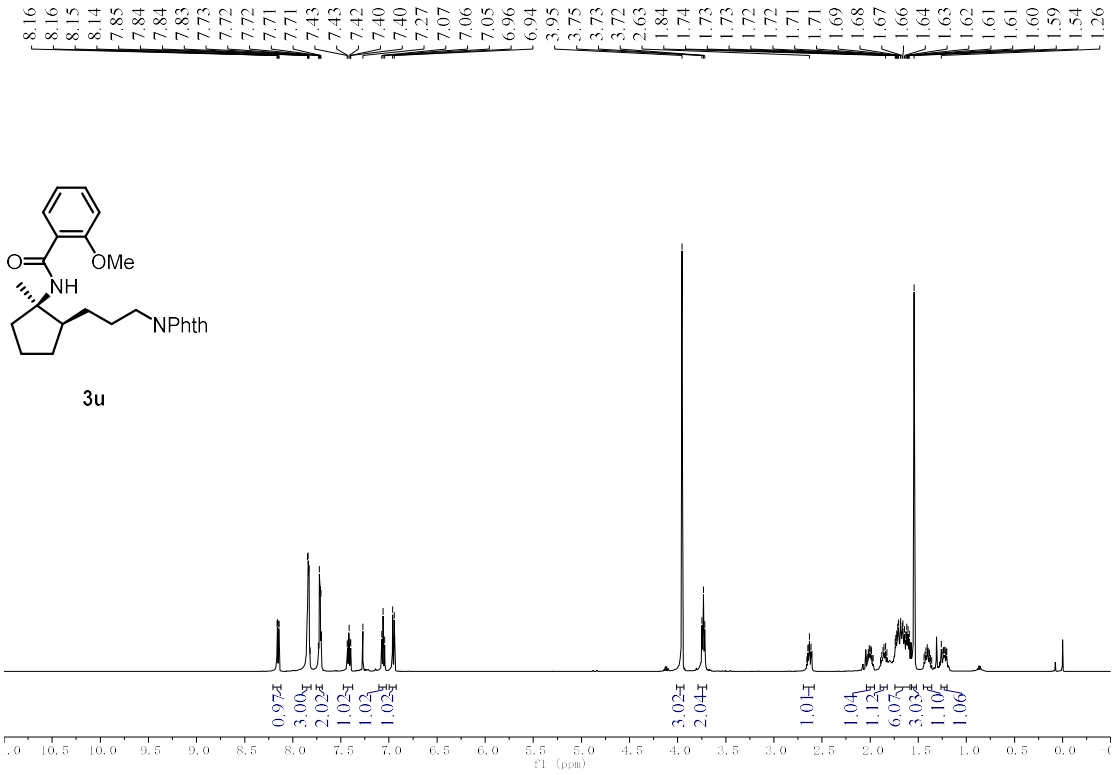
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



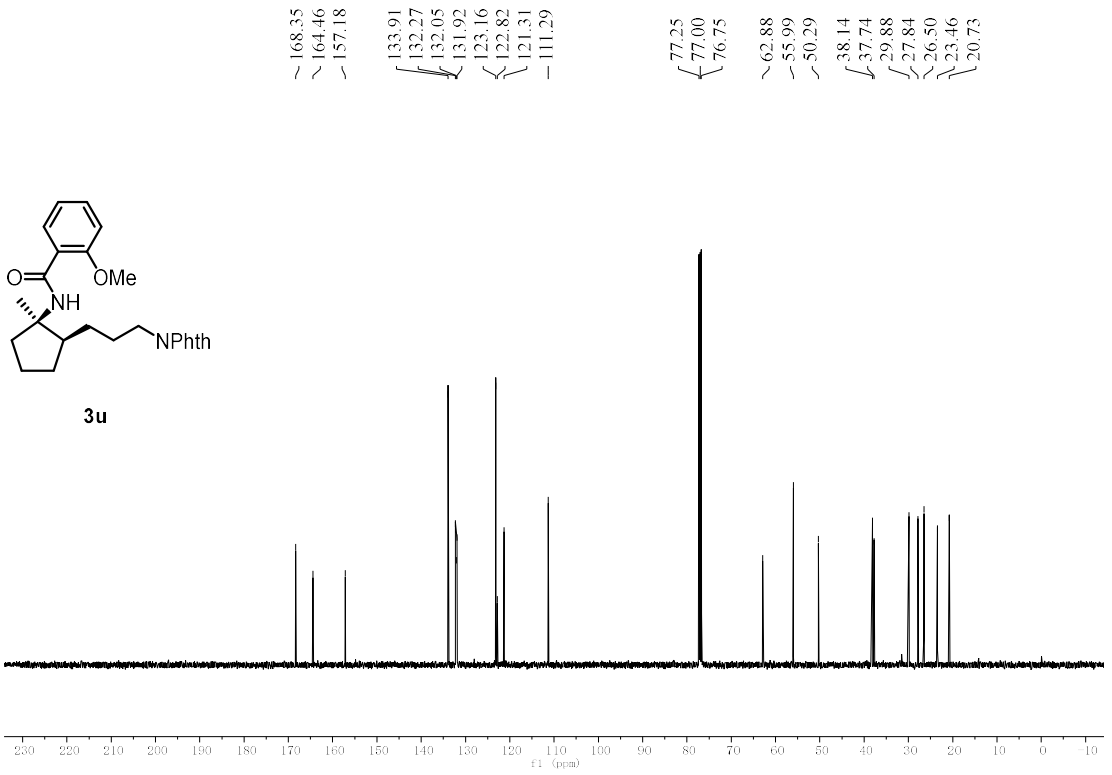
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



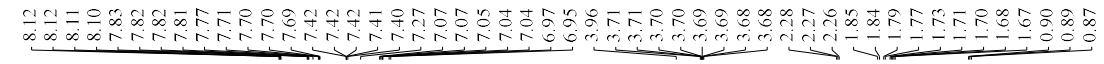
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

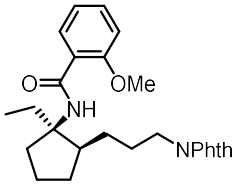


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



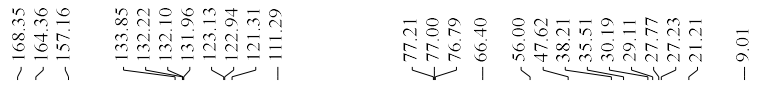
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

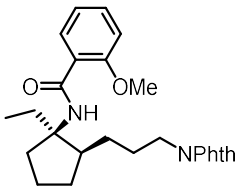




3v

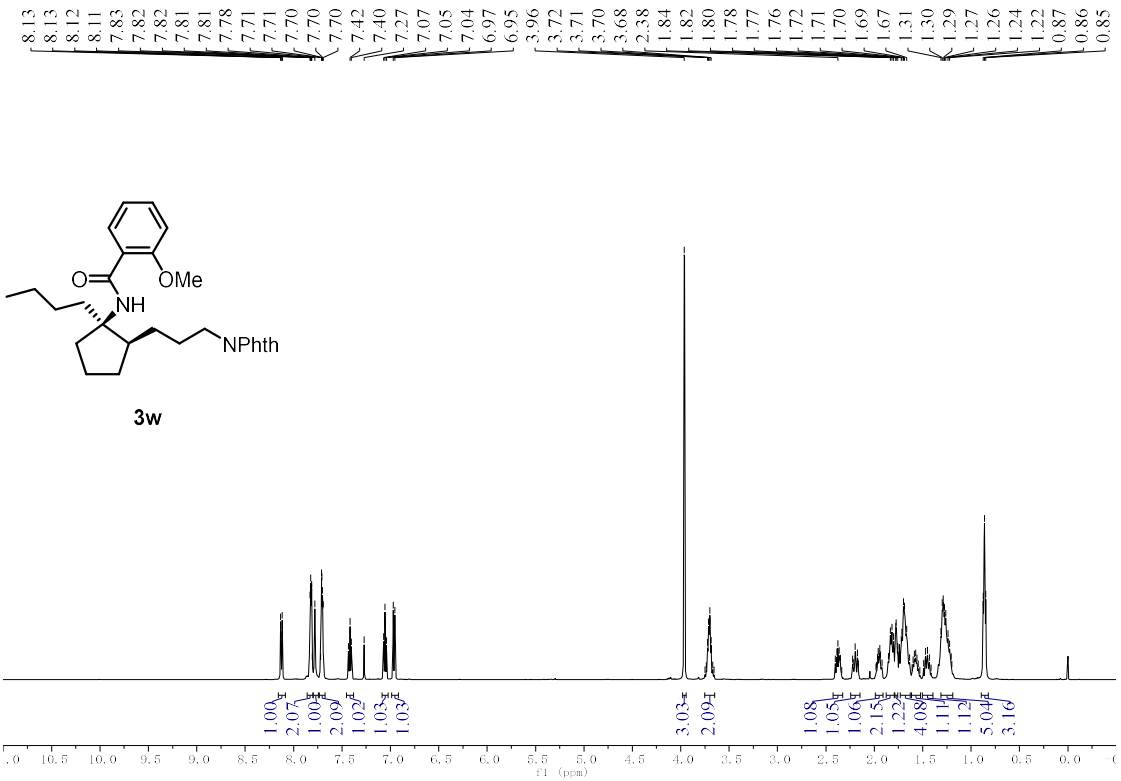
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



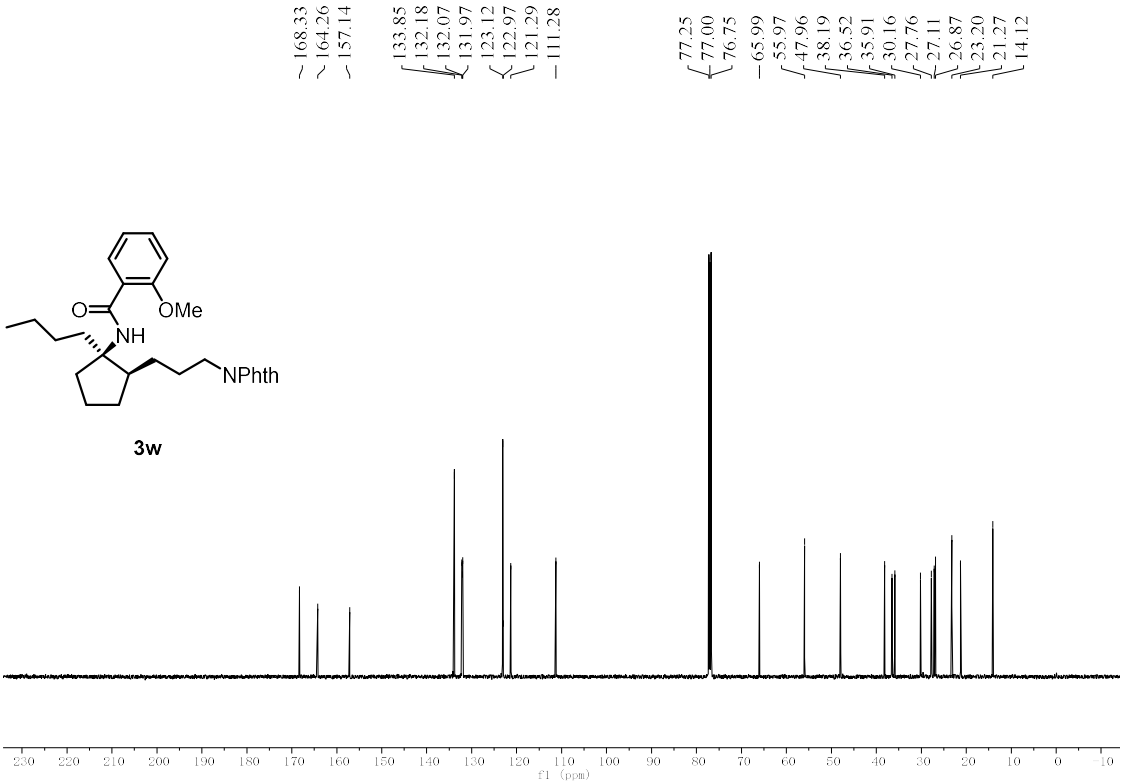


3v

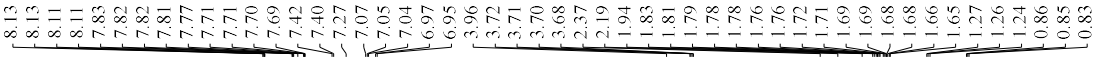
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

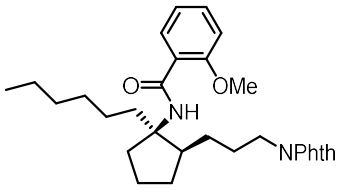


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

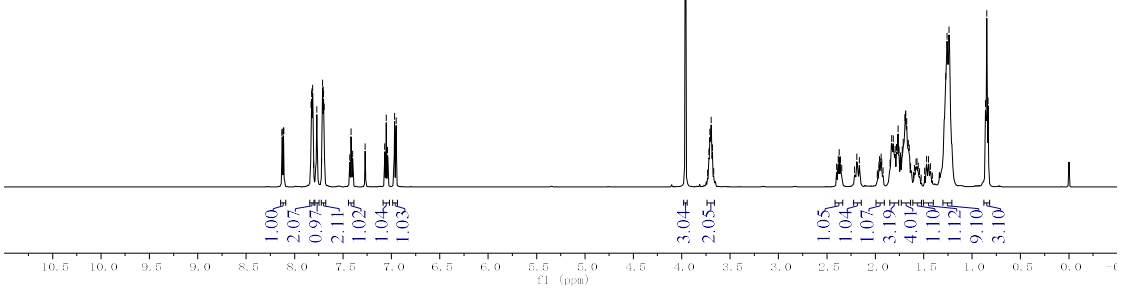


^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

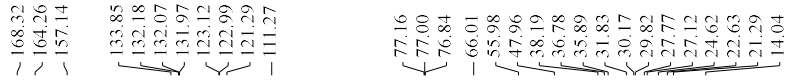


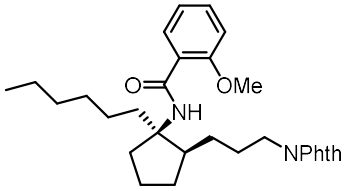


3x



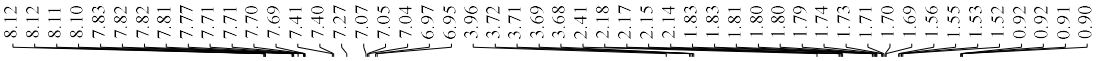
^{13}C NMR spectrum (201 MHz, in $CDCl_3$):

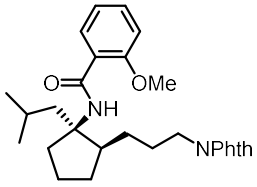




3x

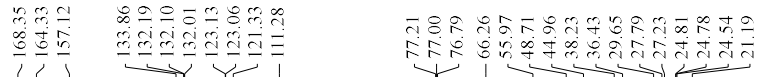
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

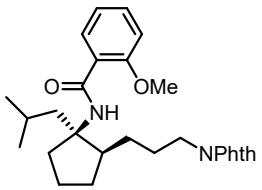




3y

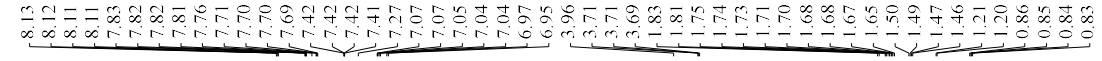
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

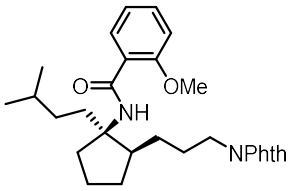




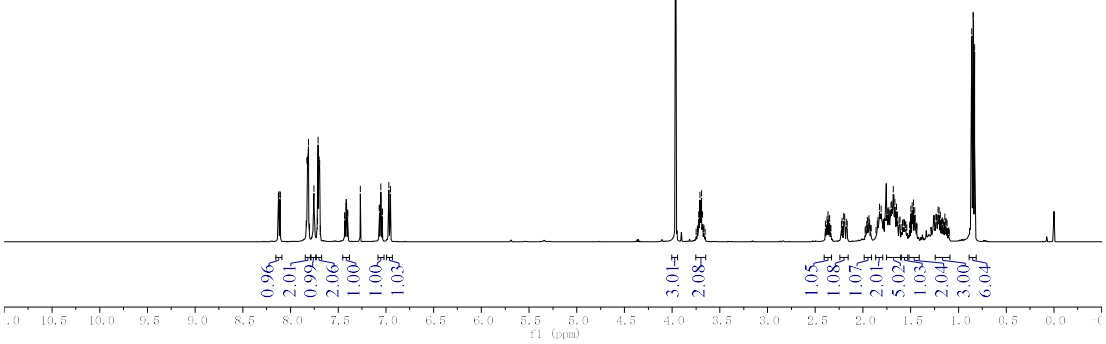
3y

^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

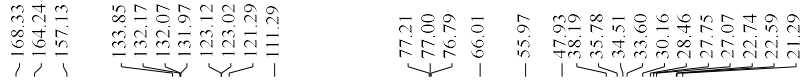


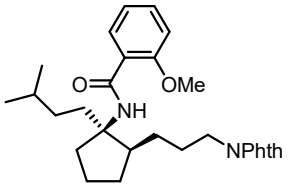


3z



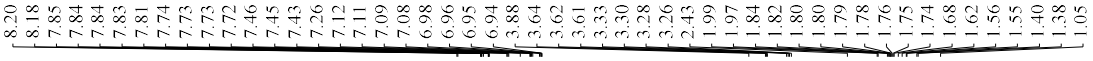
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

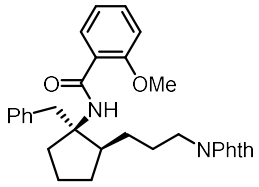




3z

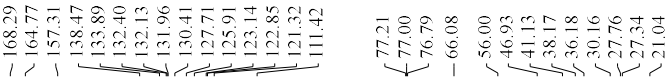
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

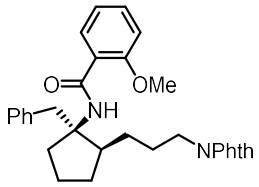




3aa

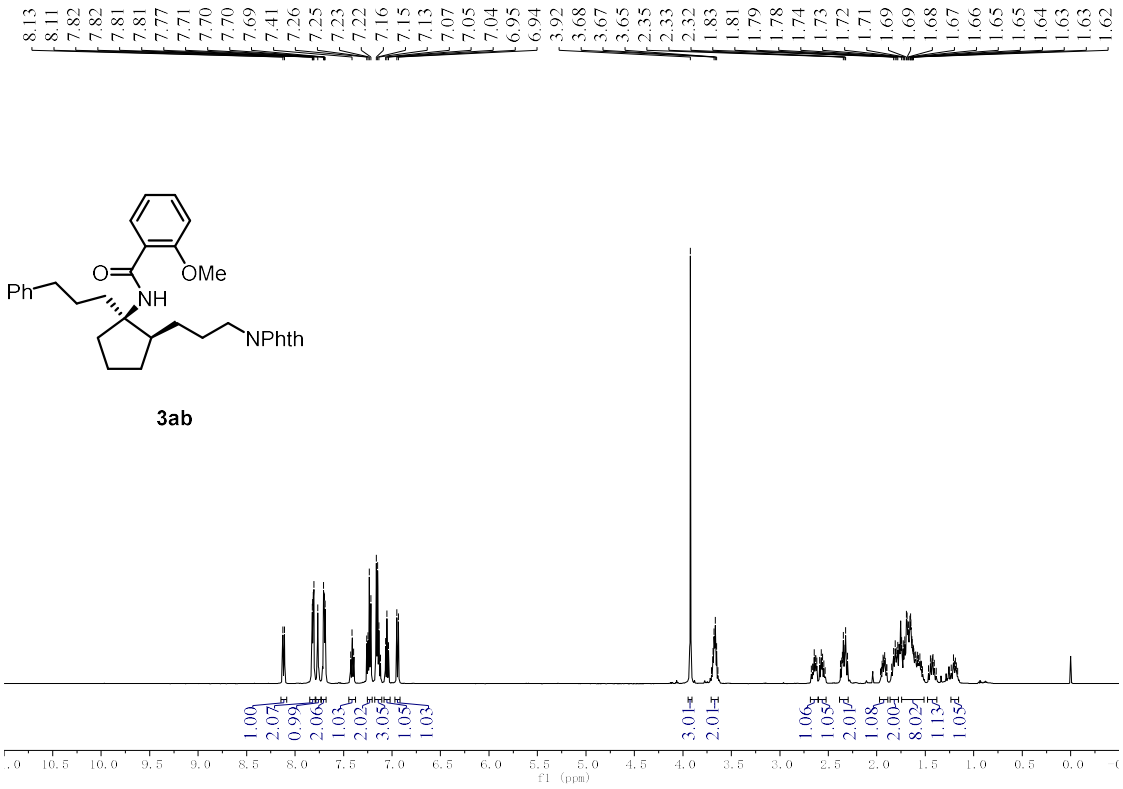
^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



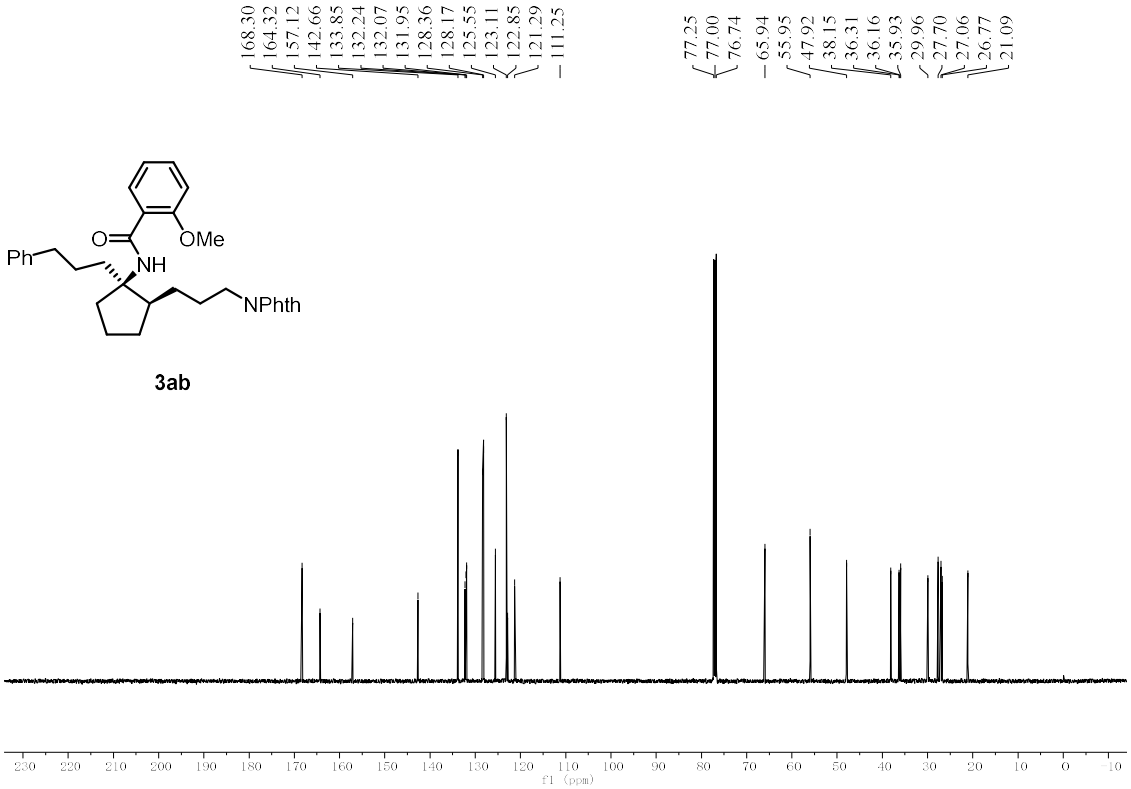


3aa

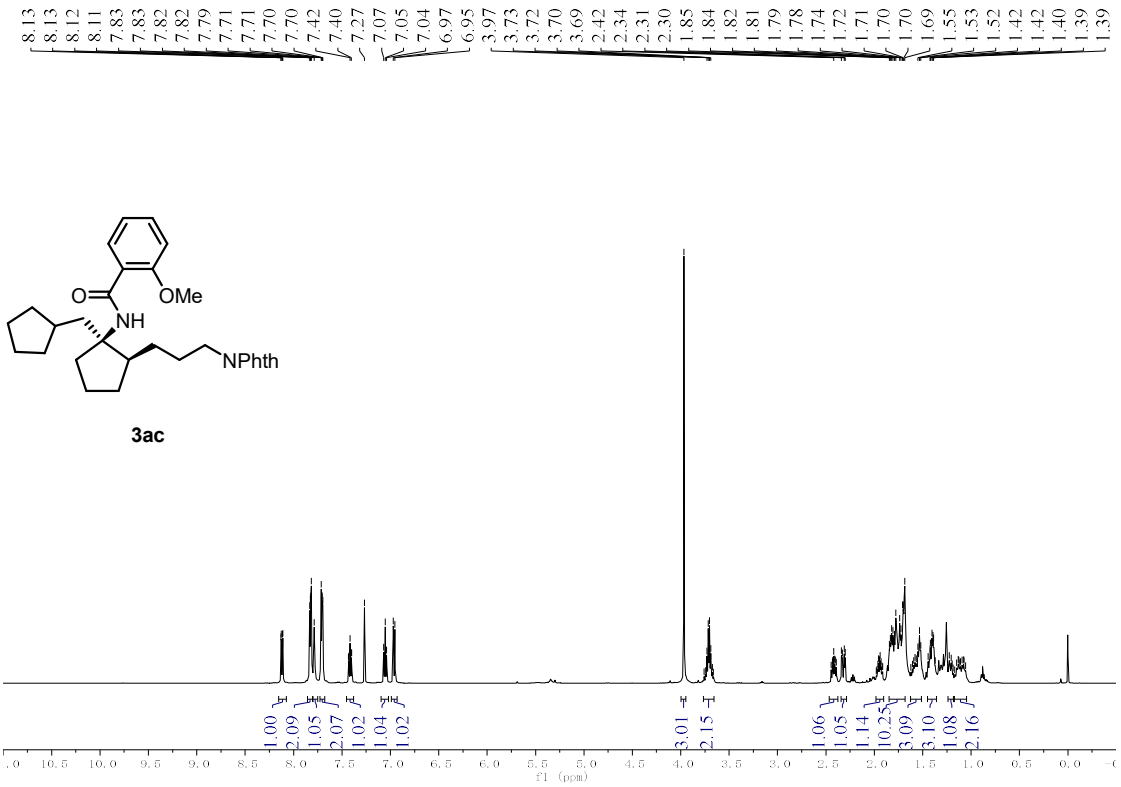
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



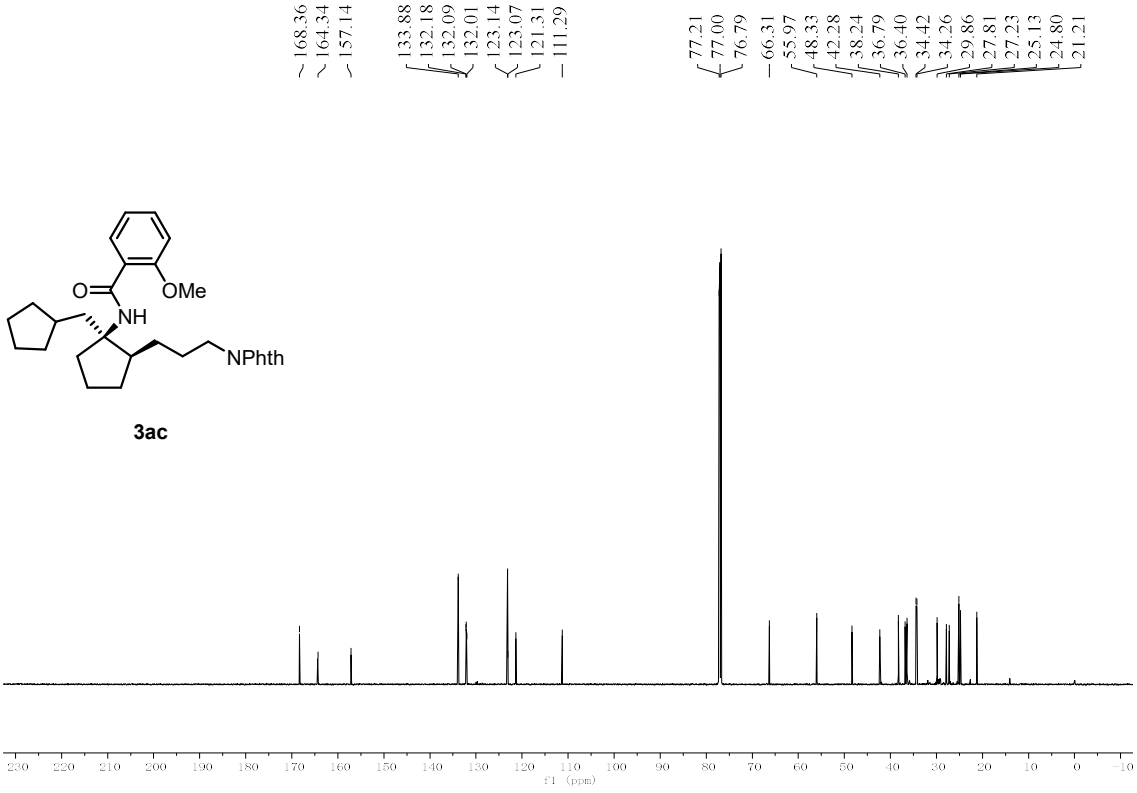
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



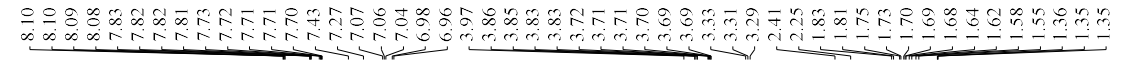
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

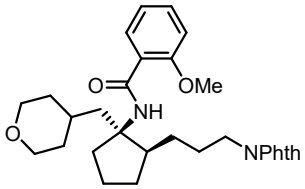


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):



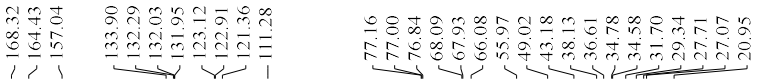
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

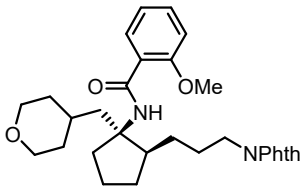




3ad

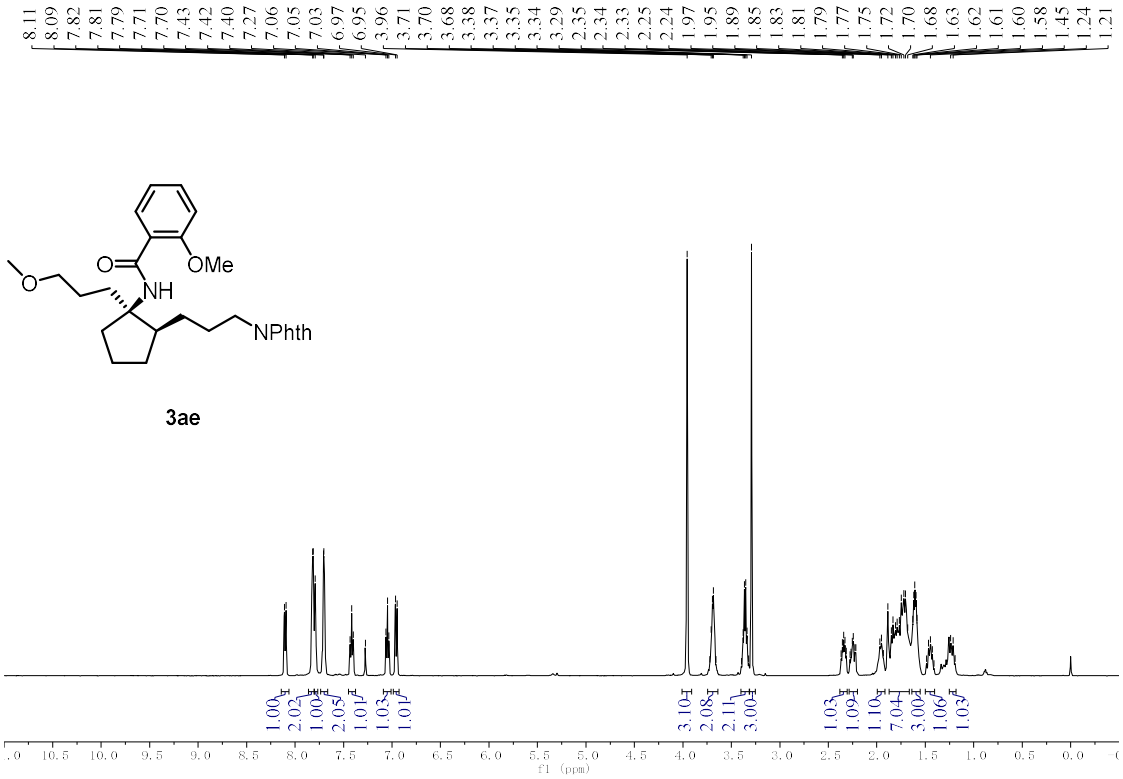
^{13}C NMR spectrum (201 MHz, in $CDCl_3$):



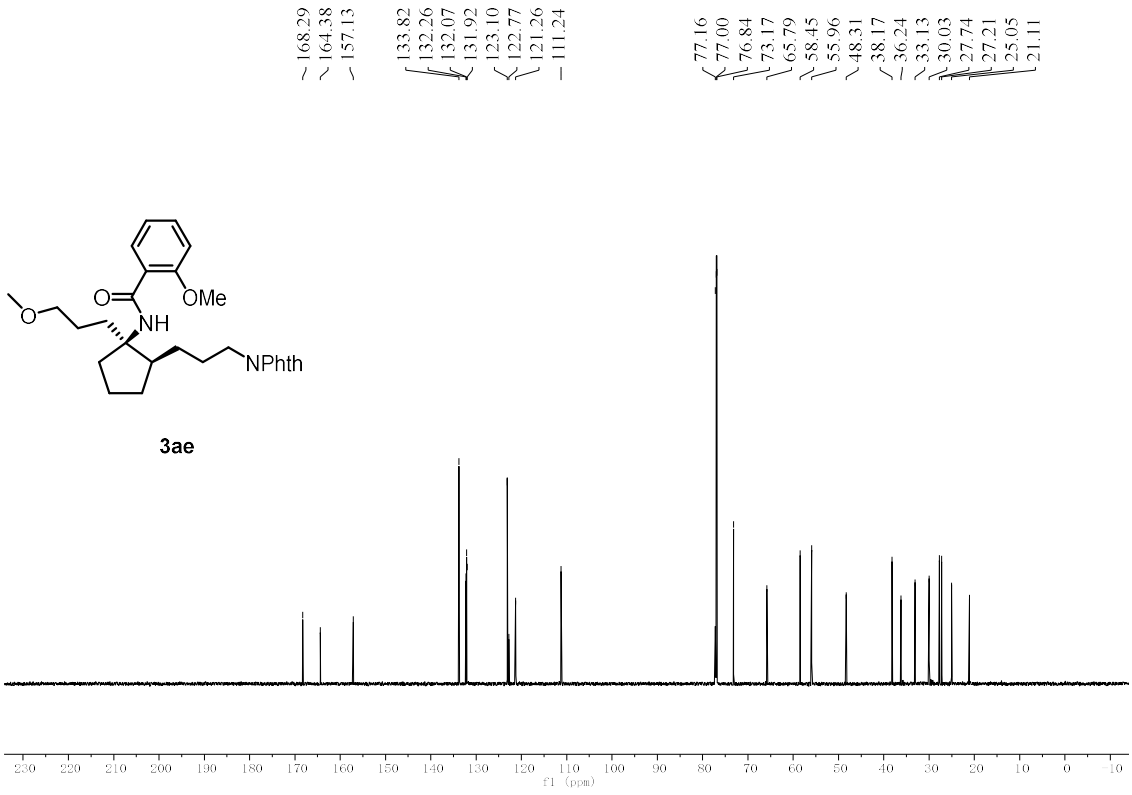


3ad

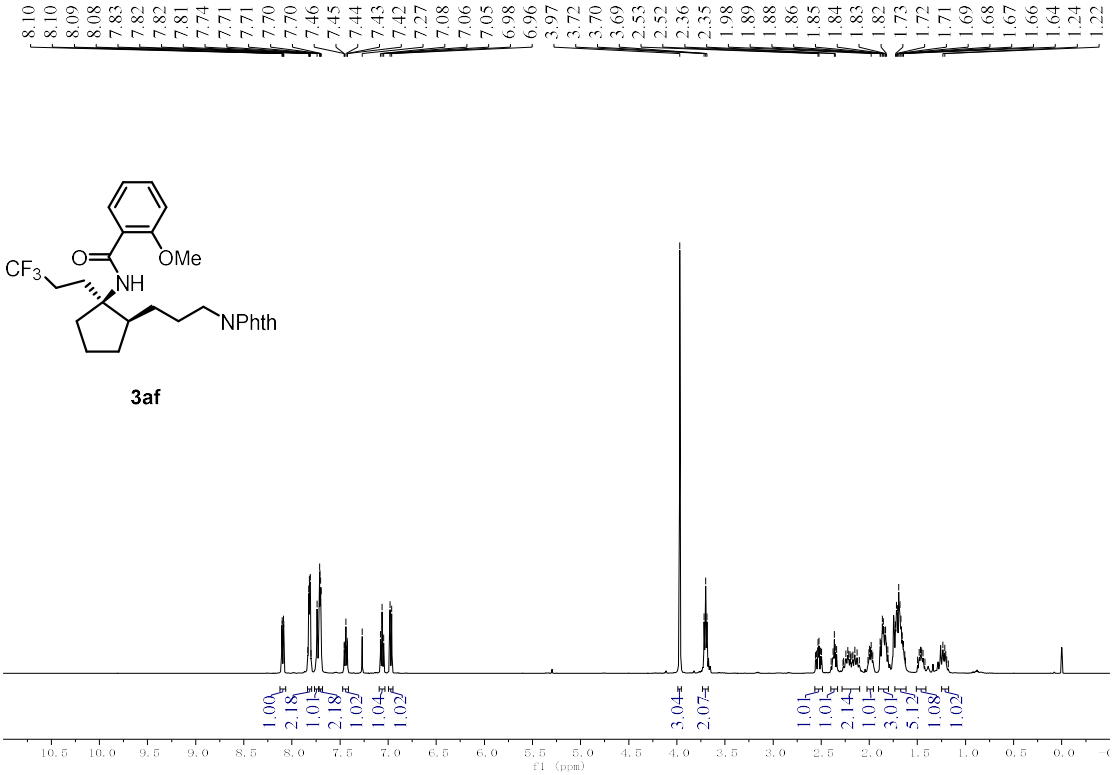
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



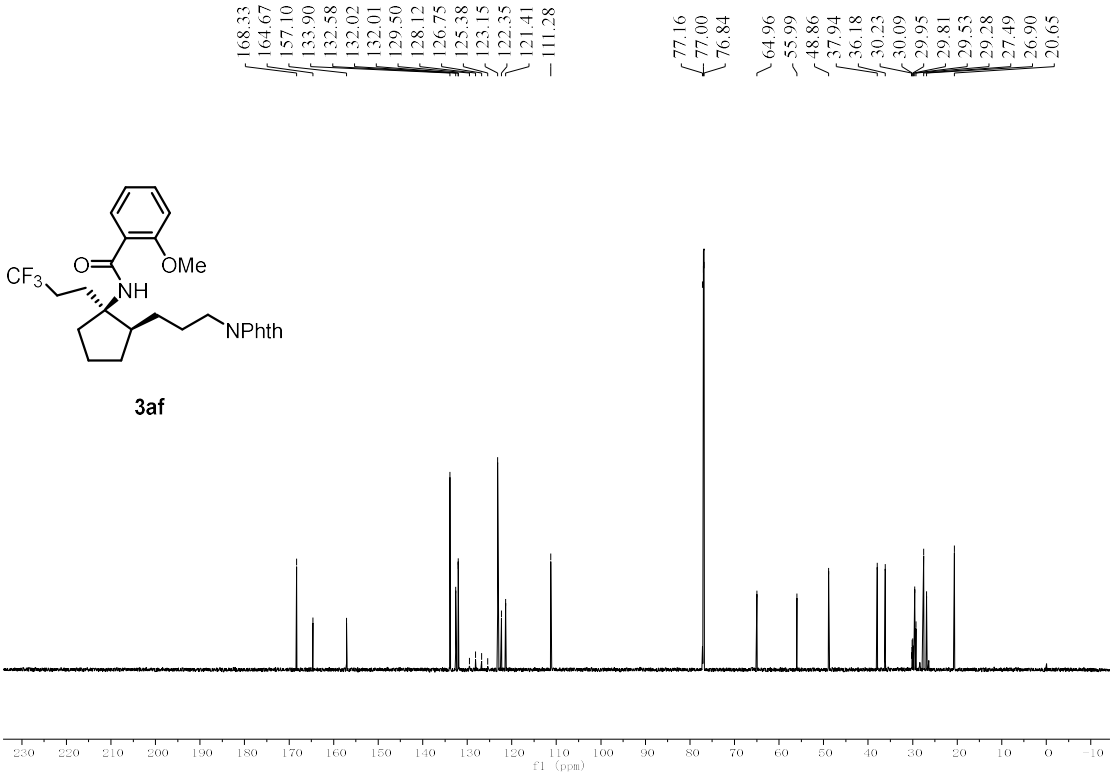
^{13}C NMR spectrum (201 MHz, in $CDCl_3$):



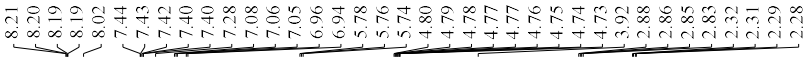
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

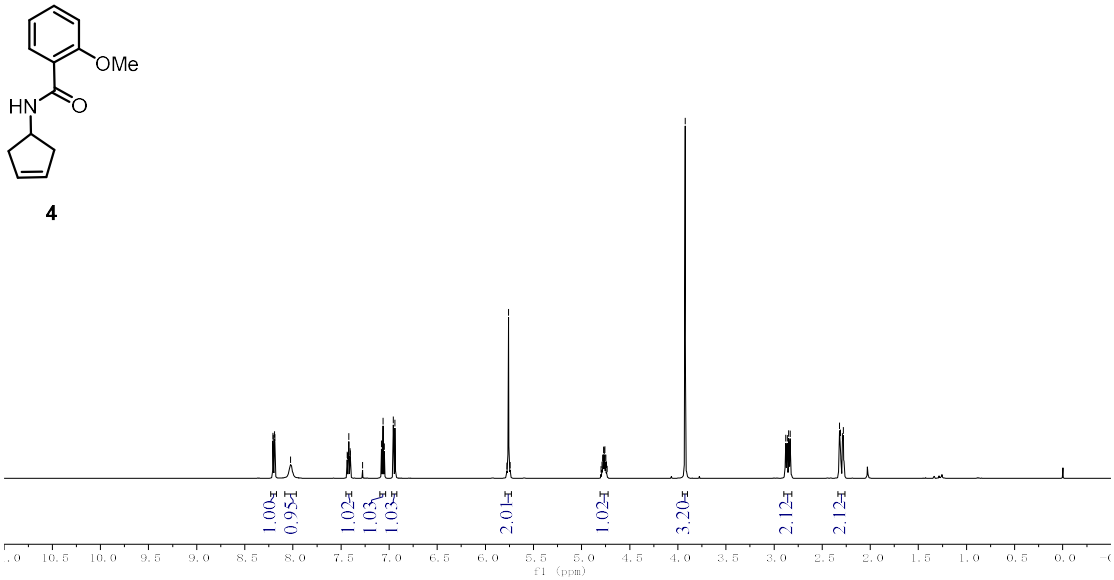


^{13}C NMR spectrum (201 MHz, in $CDCl_3$):

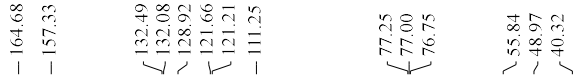


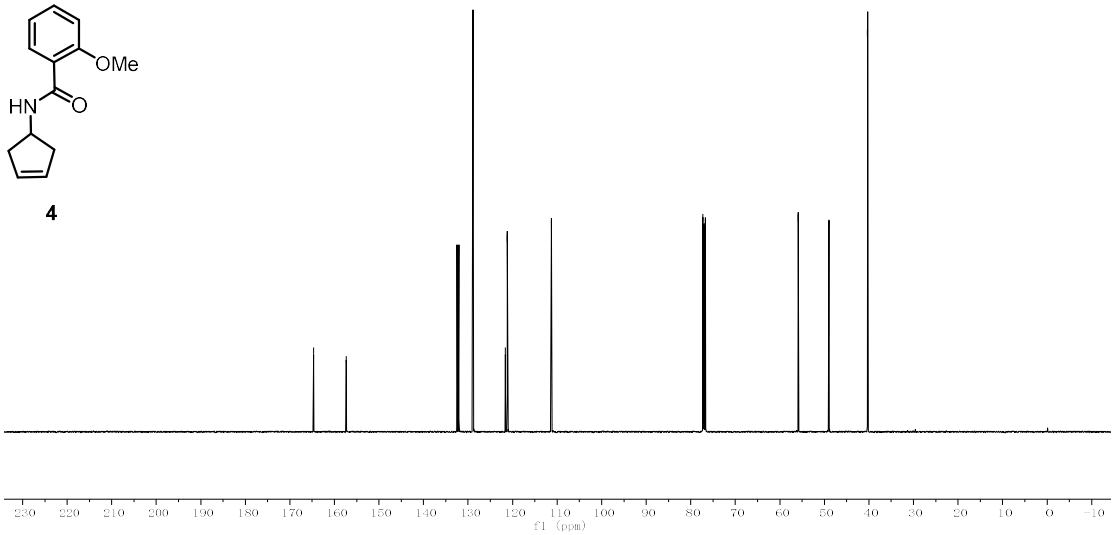
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



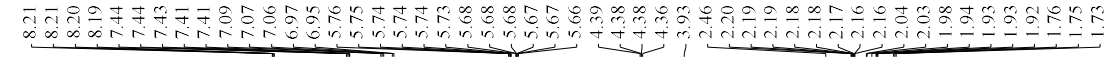


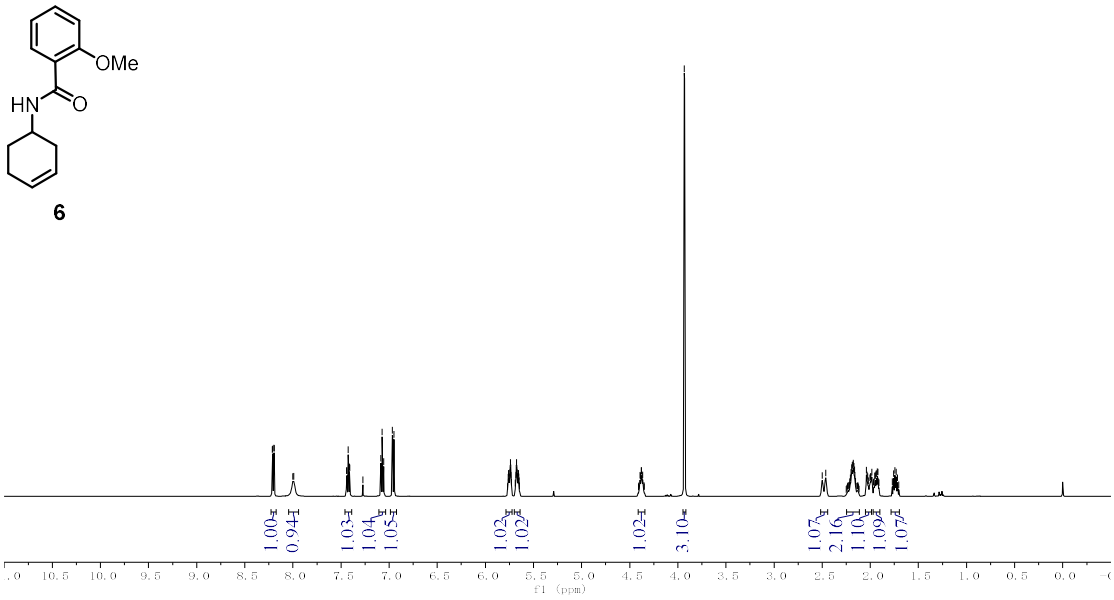
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



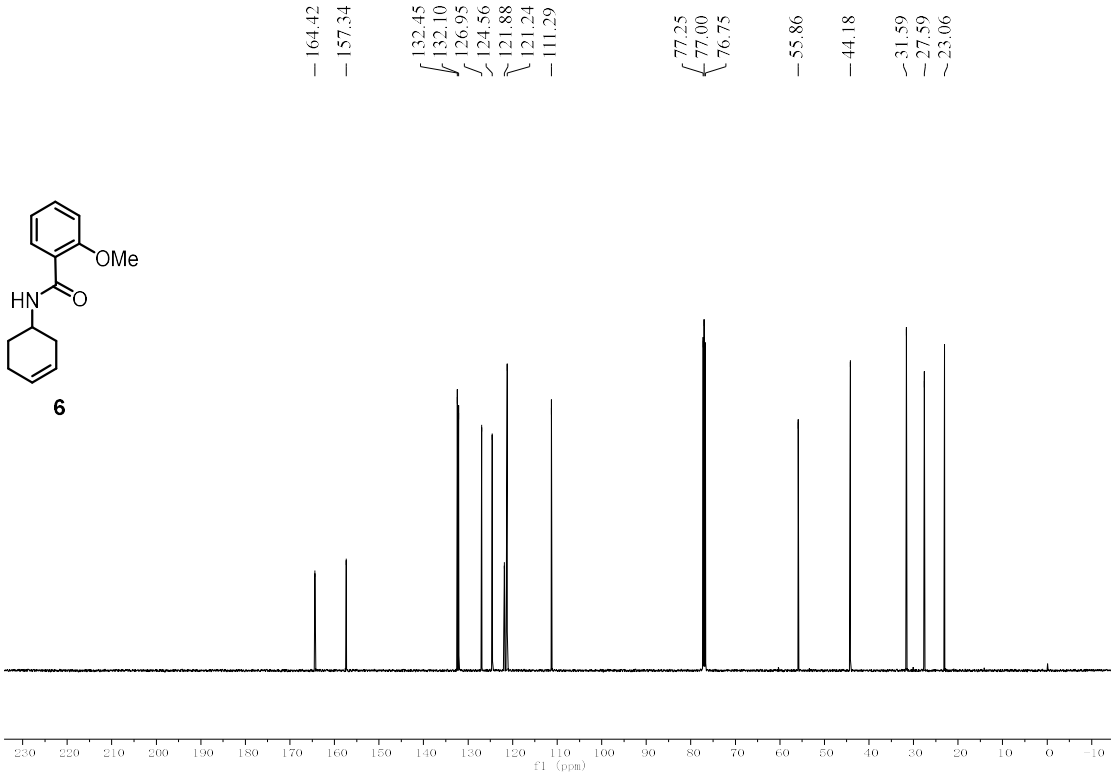


^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

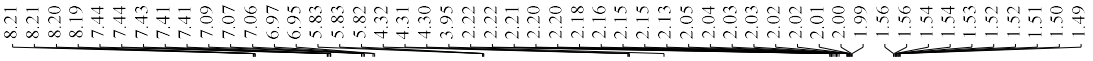


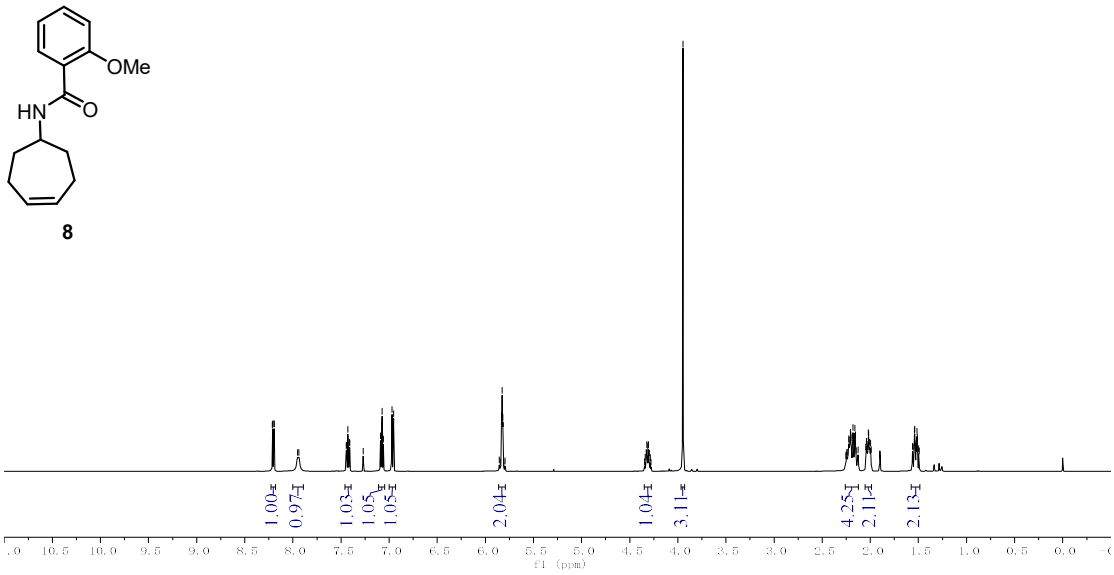


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

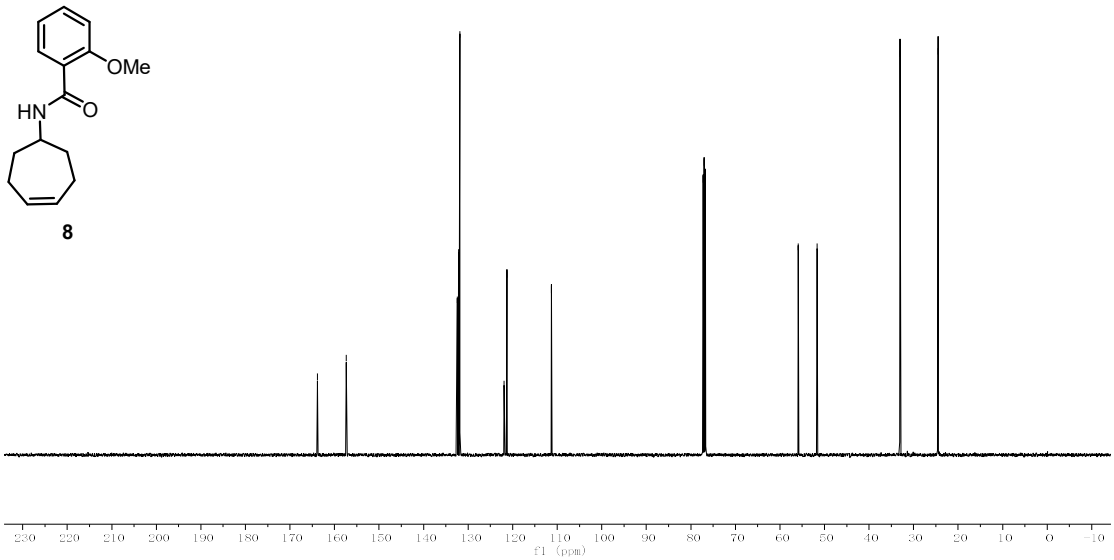


^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

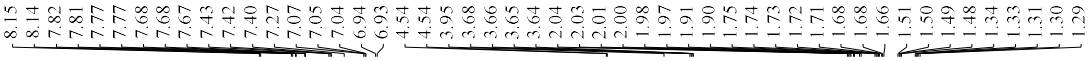


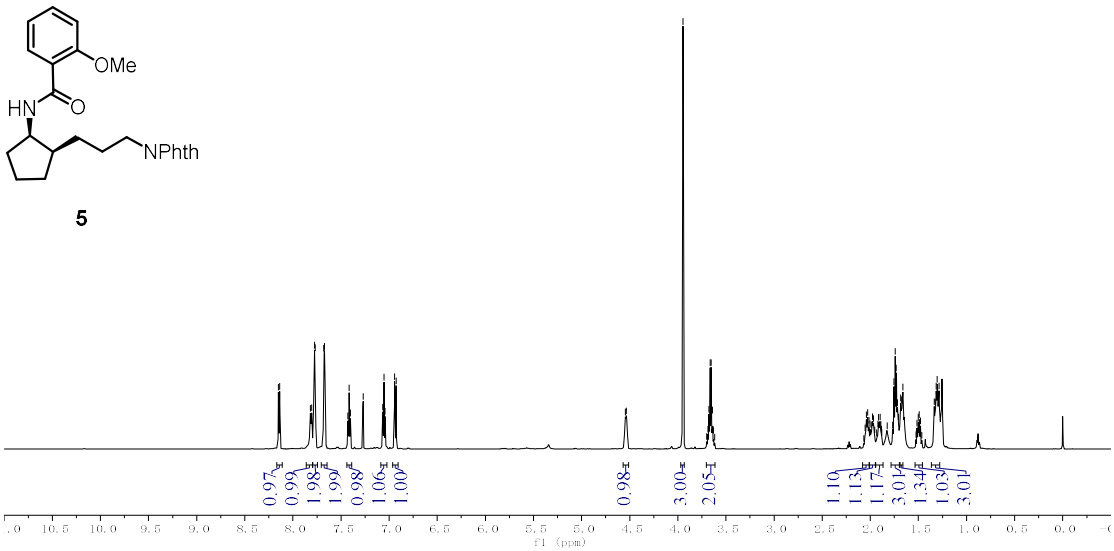


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

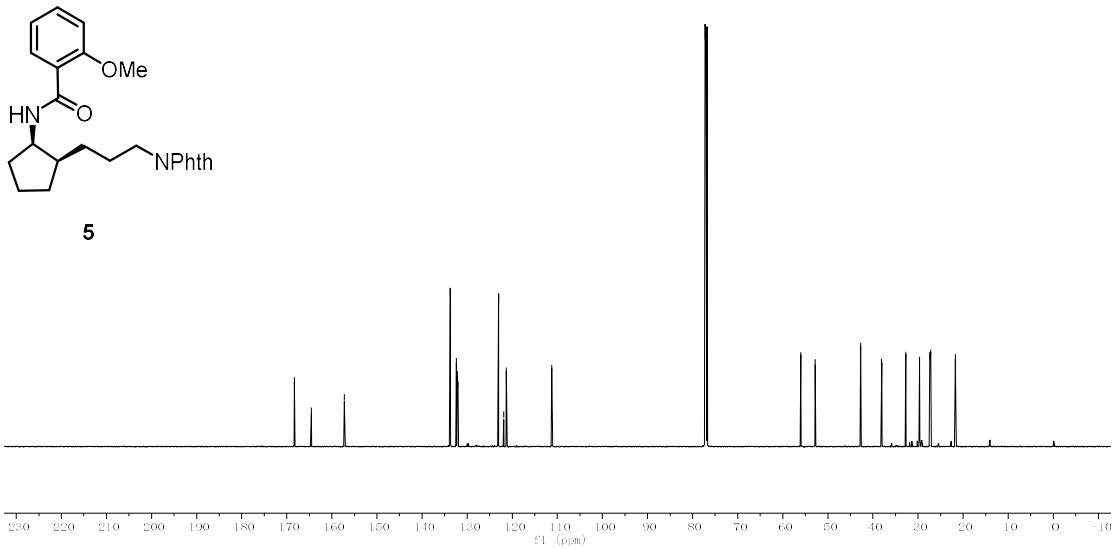


^{1}H NMR spectrum (600 MHz, in $CDCl_3$):

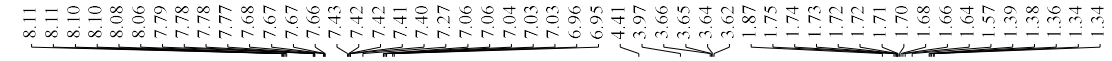


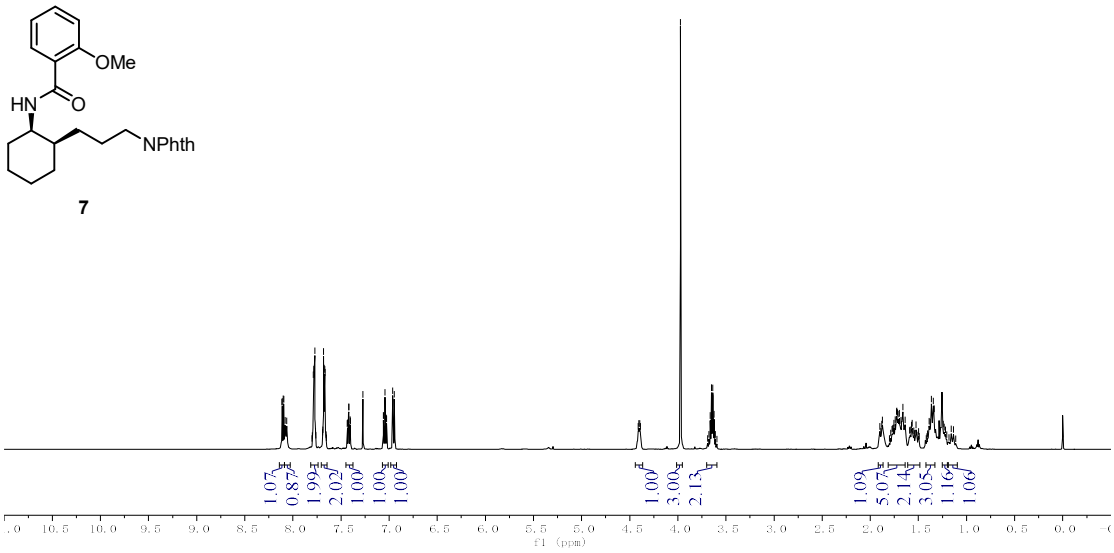


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

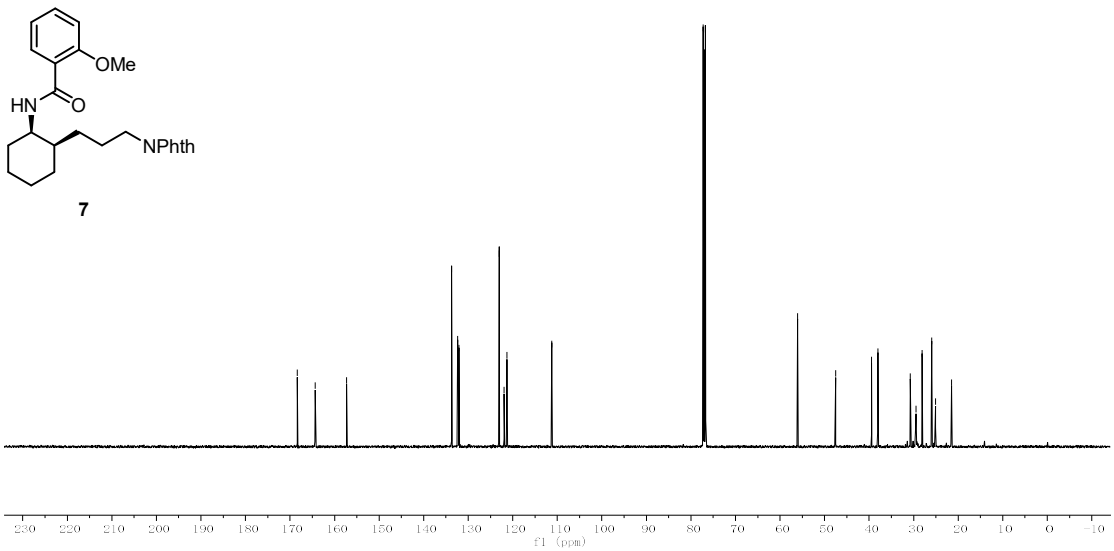


^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

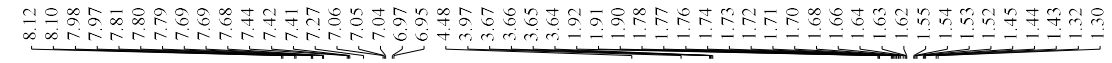


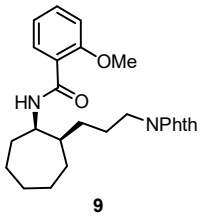


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



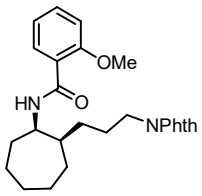
^{1}H NMR spectrum (600 MHz, in $CDCl_3$):





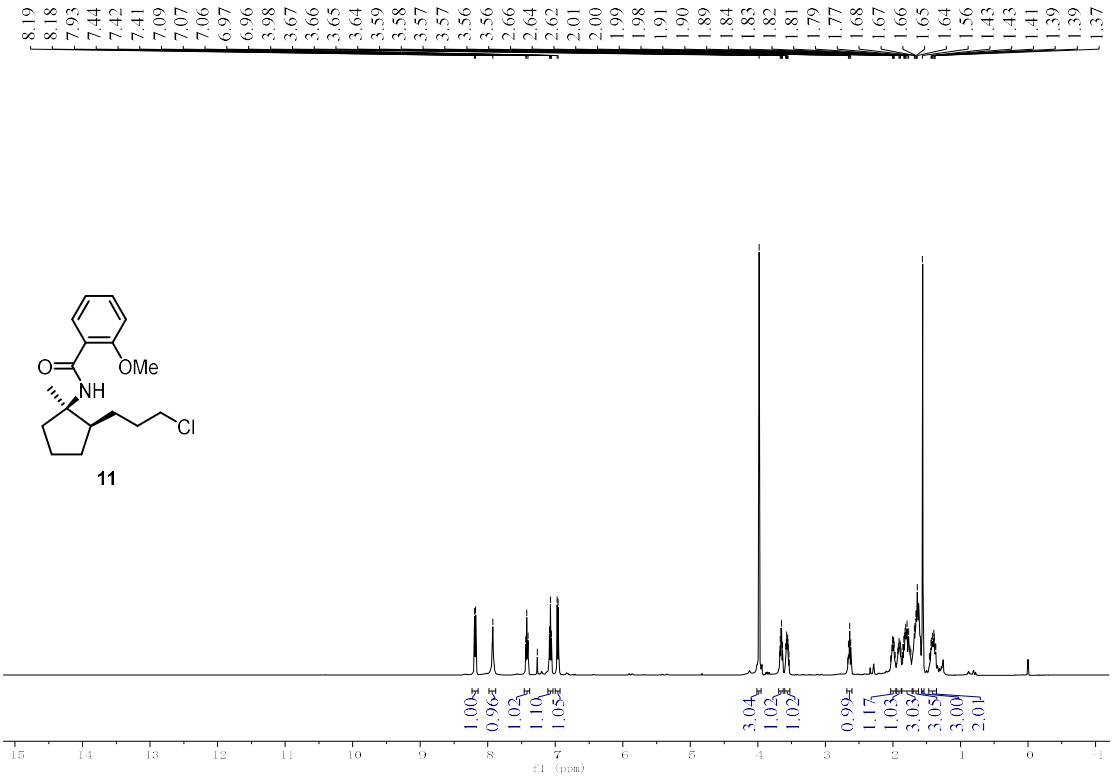
9

^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

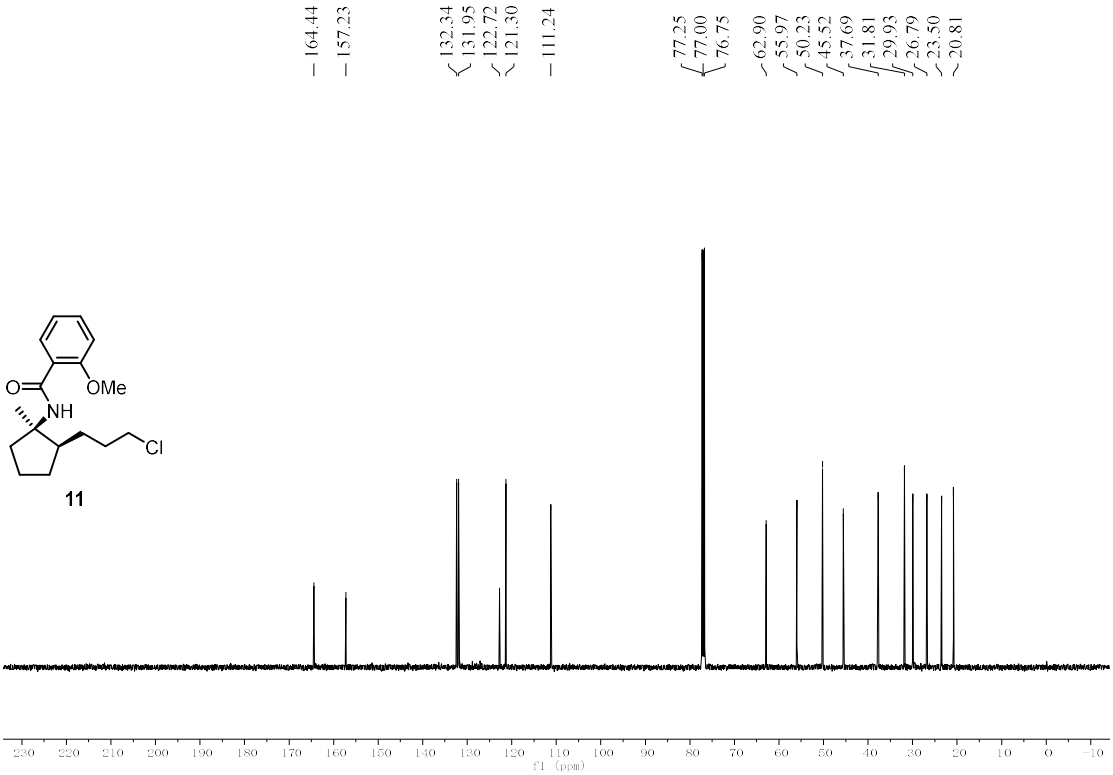


9

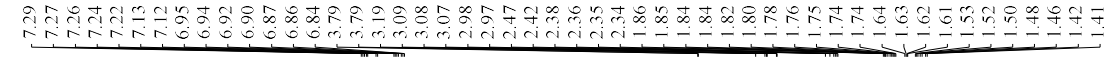
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

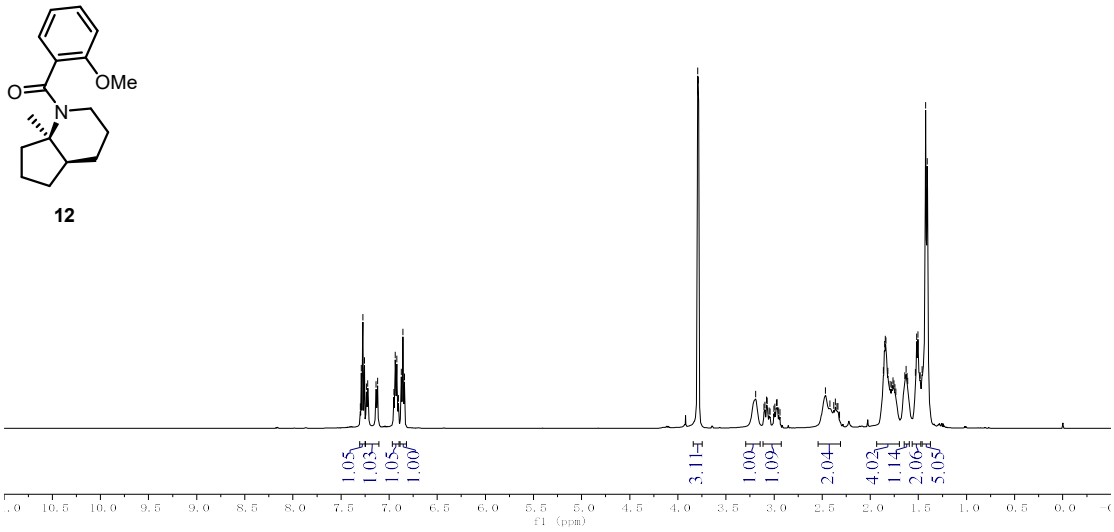


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):

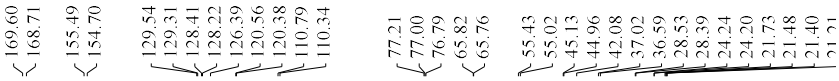


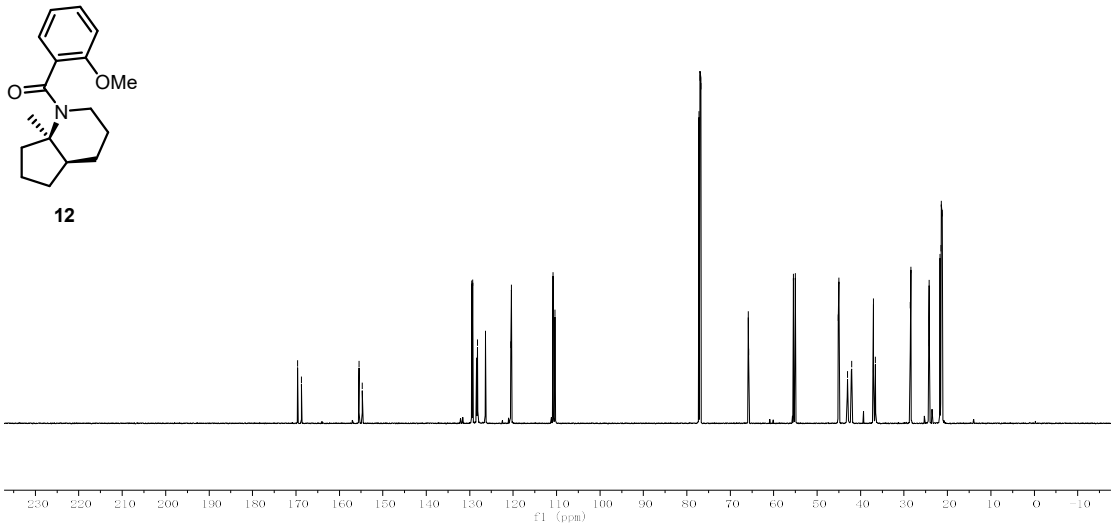
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



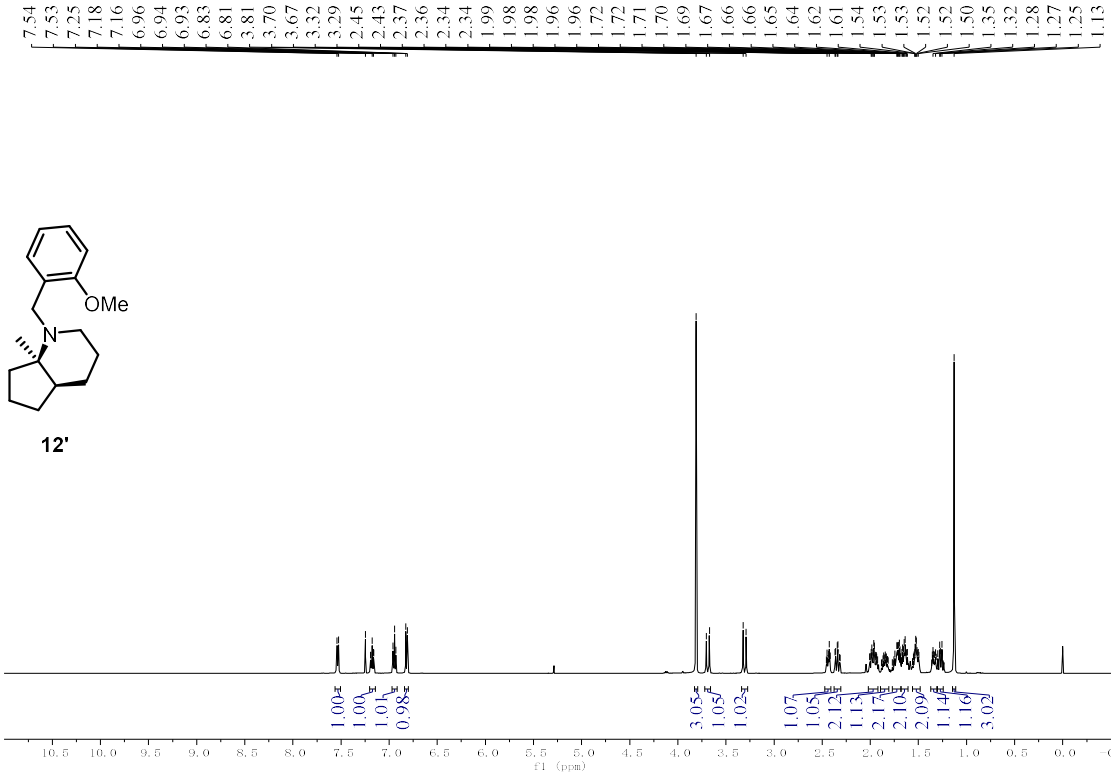


^{13}C NMR spectrum (151 MHz, in $CDCl_3$):

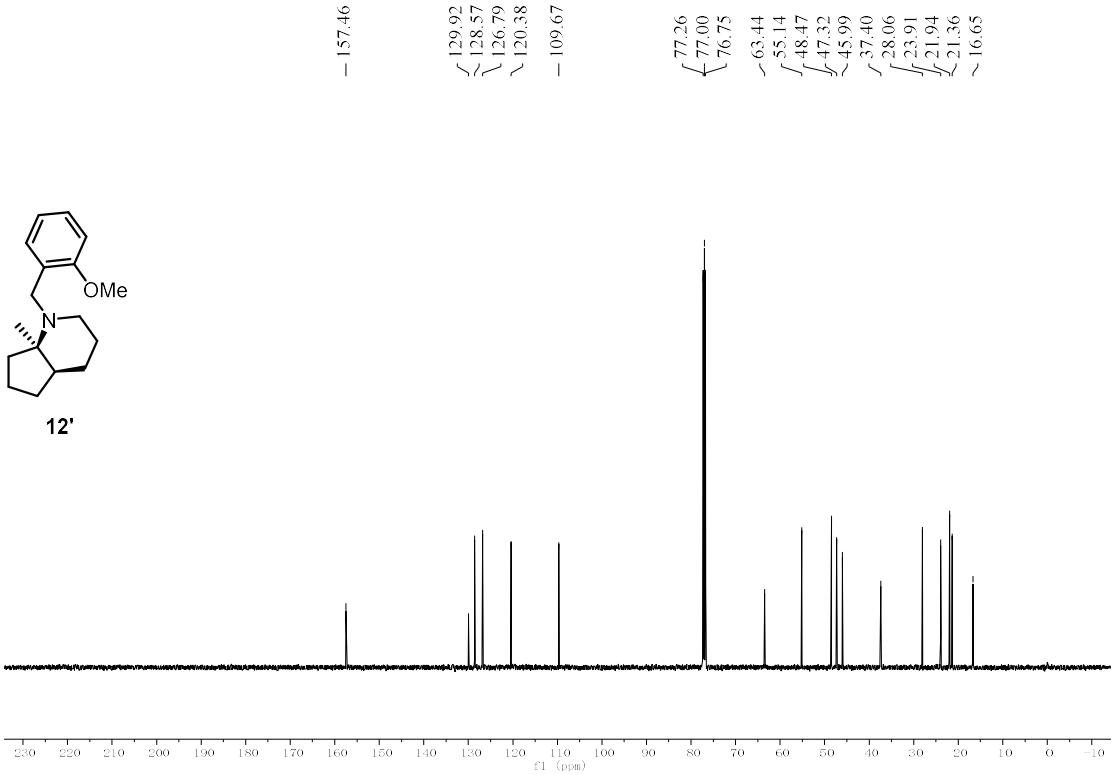




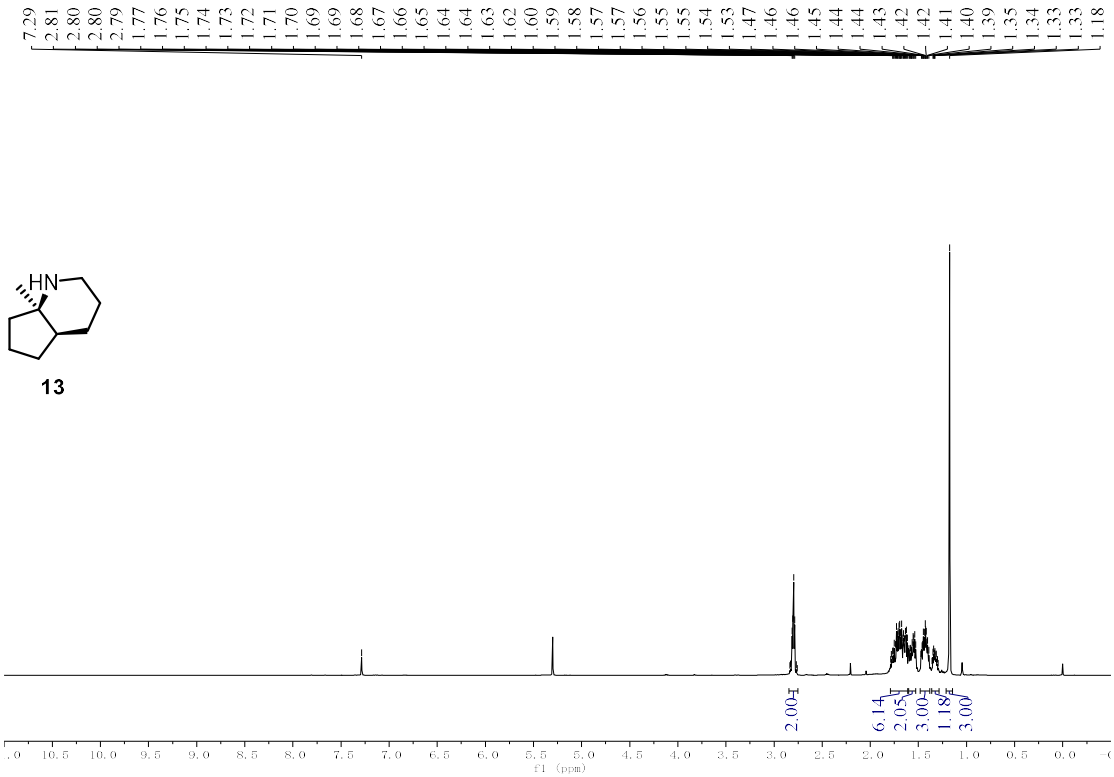
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



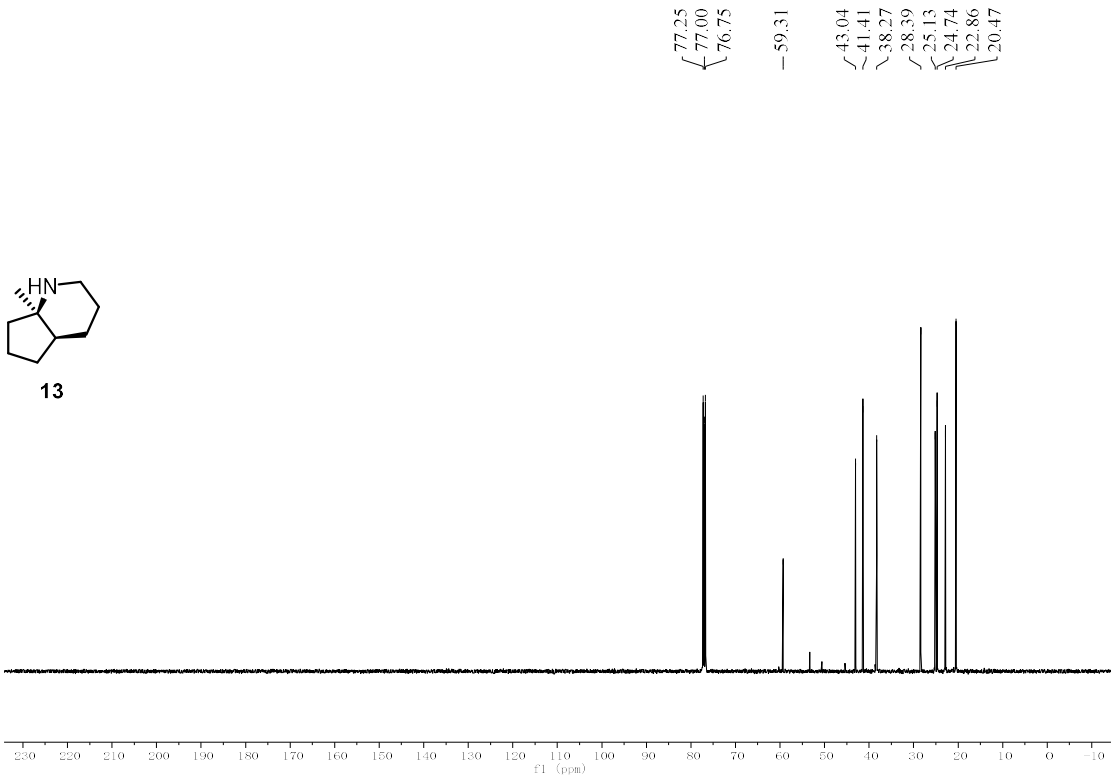
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



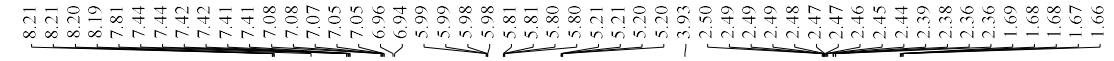
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):

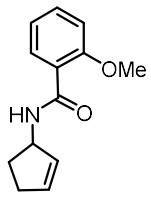


^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



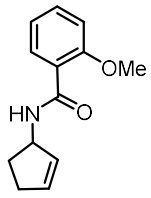
^{1}H NMR spectrum (500 MHz, in $CDCl_3$):



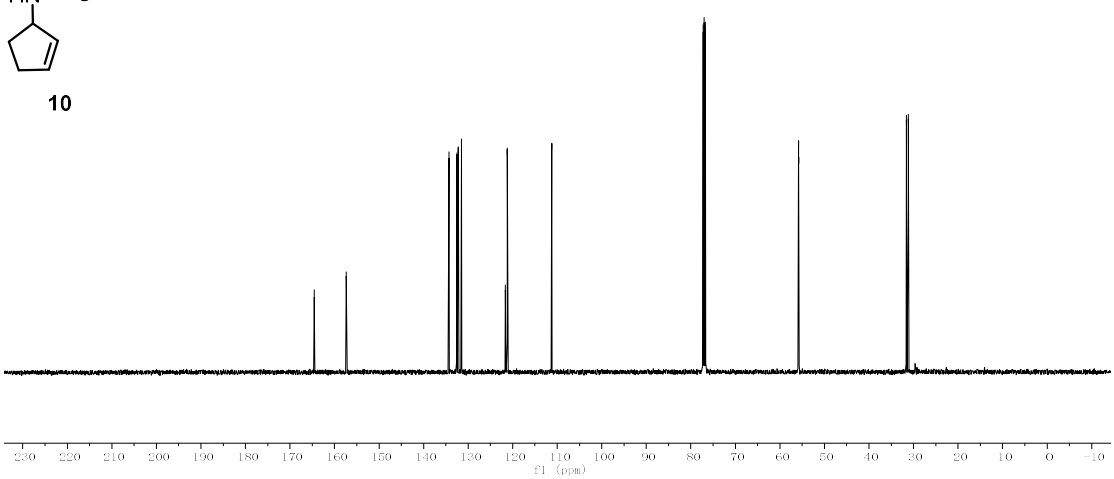


10

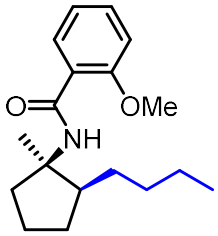
^{13}C NMR spectrum (126 MHz, in $CDCl_3$):



10

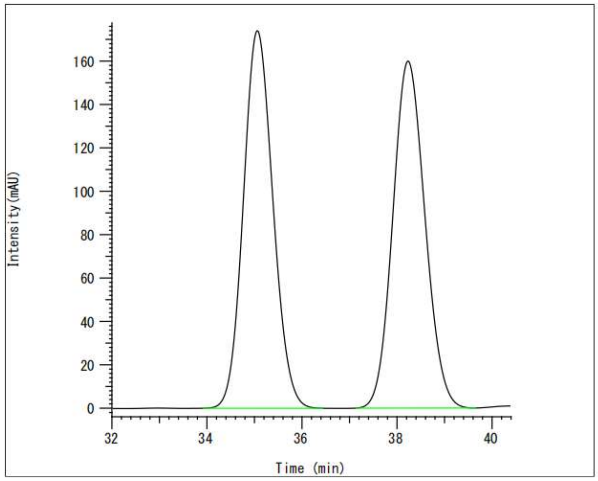


HPLC Spectra



3a

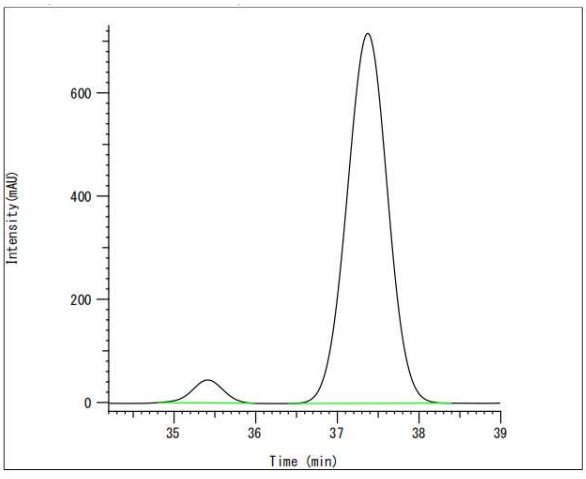
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:3 LLD-C-29-5 (230nm) Repeat:1

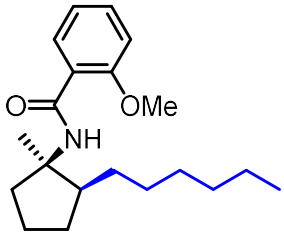
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	35.060	7527353	49.996	174036	52.110
2	Peak 2	38.230	7528411	50.004	159944	47.890
			15055764	100.000	333980	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



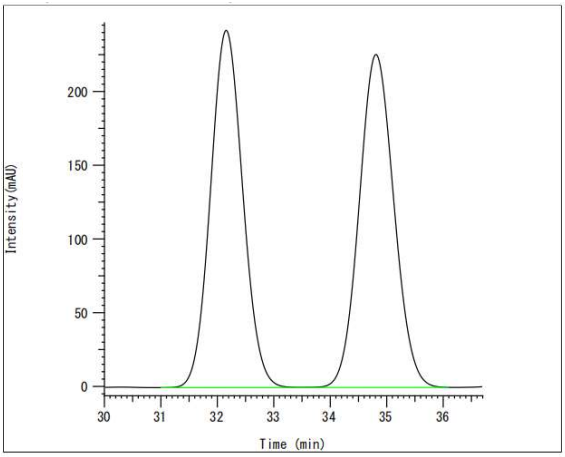
1410 UV Detector Ch1 SampleID:1 LLD-C-29-6 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	35.413	1200099	4.577	44530	5.848
2	Peak 2	37.373	25021838	95.423	716924	94.152
			26221937	100.000	761453	100.000



3b

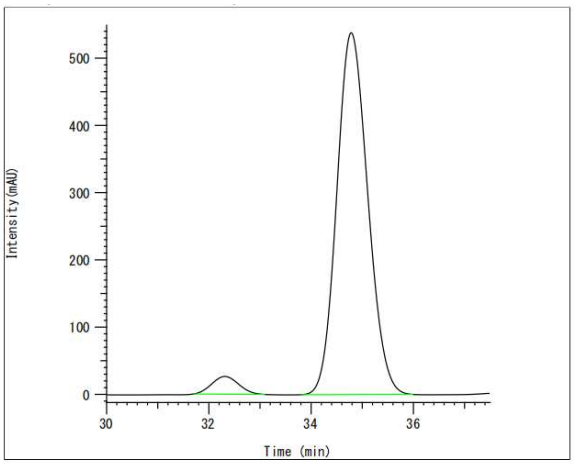
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-27-3 (230nm) Repeat:1

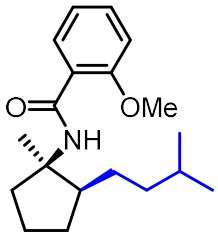
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	32.157	9611777	49.882	242177	51.753
2	Peak 2	34.810	9657170	50.118	225772	48.247
			19268947	100.000	467949	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



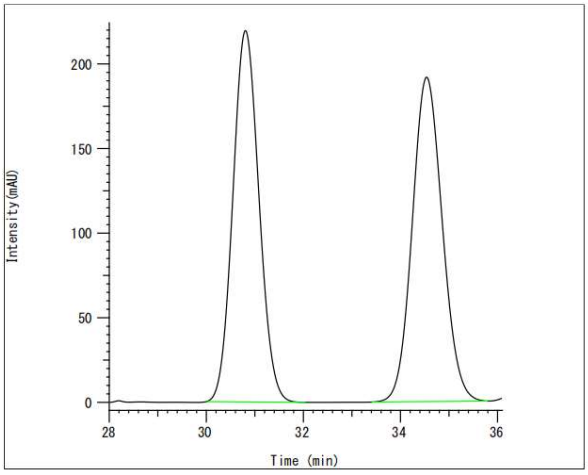
1410 UV Detector Ch1 SampleID:1 LLD-C-27-4 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	32.313	965911	4.086	26374	4.672
2	Peak 2	34.783	22675117	95.914	538074	95.328
			23641028	100.000	564447	100.000



3c

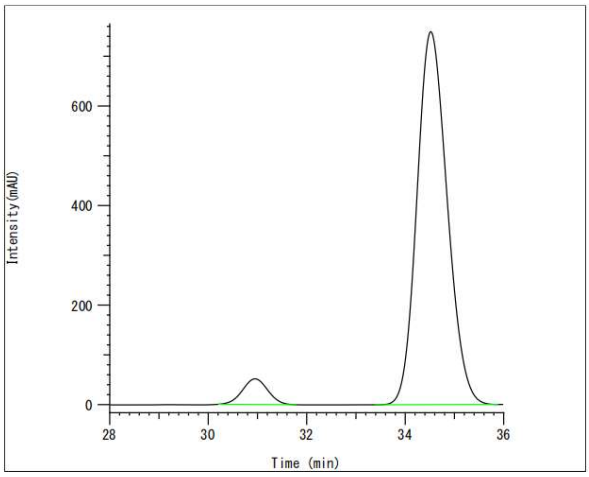
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:2 LLD-C-29-3 (230nm) Repeat:1

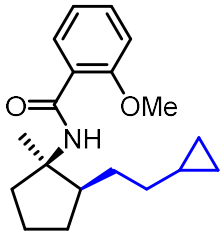
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	30.807	8200852	49.840	219429	53.374
2	Peak 2	34.540	8253572	50.160	191685	46.626
			16454424	100.000	411113	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



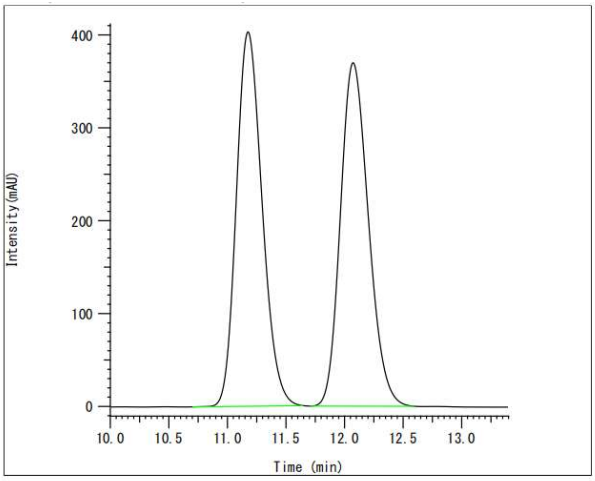
1410 UV Detector Ch1 SampleID:1 LLD-C-29-4 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	30.950	1853146	5.473	51630	6.446
2	Peak 2	34.520	32003731	94.527	749389	93.554
			33856876	100.000	801019	100.000



3d

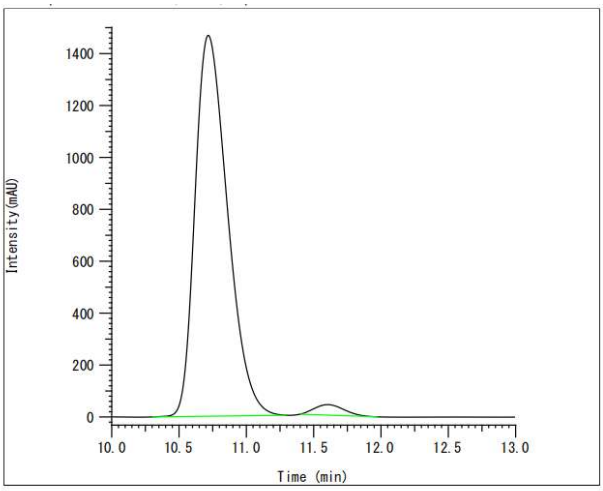
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-33-1 (230nm) Repeat:1

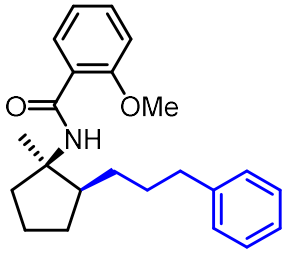
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	11.177	6158035	50.041	403071	52.157
2	Peak 2	12.073	6147952	49.959	369739	47.843
			12305987	100.000	772810	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



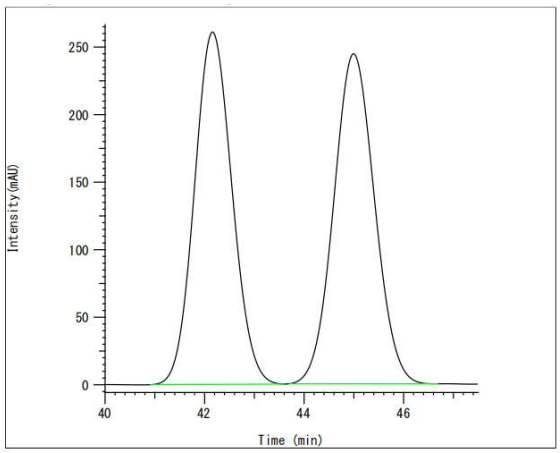
1410 UV Detector Ch1 SampleID:1 LLD-C-33-2 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	10.717	24599108	97.553	1467680	97.330
2	Peak 2	11.603	617168	2.447	40261	2.670
			25216276	100.000	1507940	100.000



3e

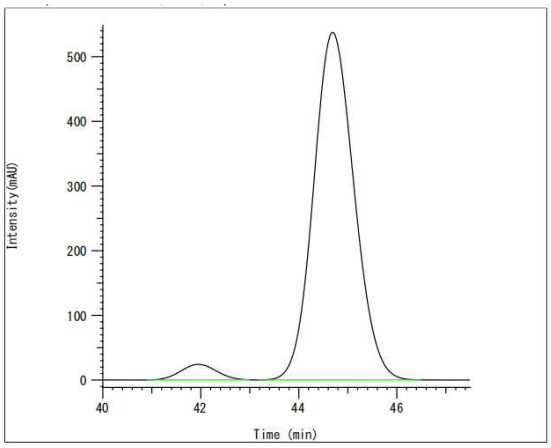
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-22-5 (230nm) Repeat:1

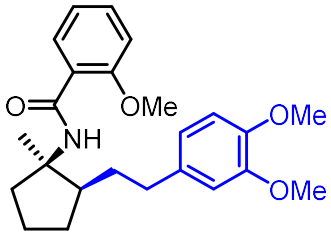
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	42.160	13727637	49.597	260818	51.639
2	Peak 2	44.993	13950757	50.403	244258	48.361
			27678394	100.000	505075	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



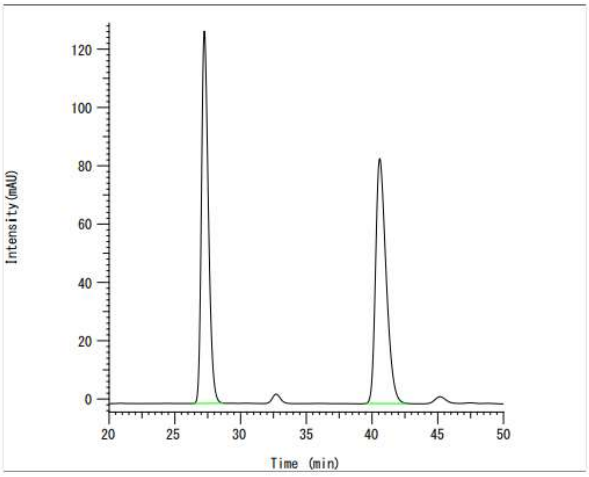
1410 UV Detector Ch1 SampleID:1 LLD-C-22-6 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	41.950	1226415	3.807	24052	4.285
2	Peak 2	44.690	30984776	96.193	537272	95.715
			32211190	100.000	561324	100.000



3f

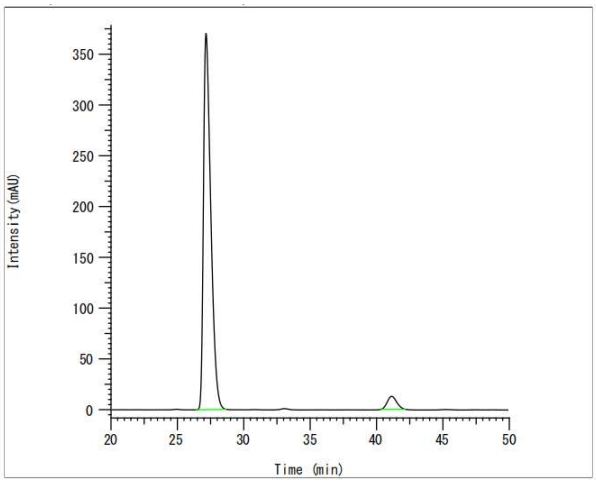
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-23-1 (250nm) Repeat:1

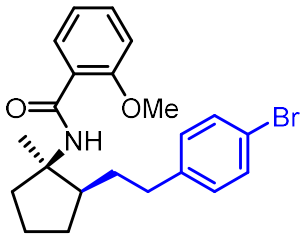
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	27.243	4674742	49.860	127734	60.322
2	Peak 2	40.587	4700914	50.140	84019	39.678
			9375657	100.000	211753	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



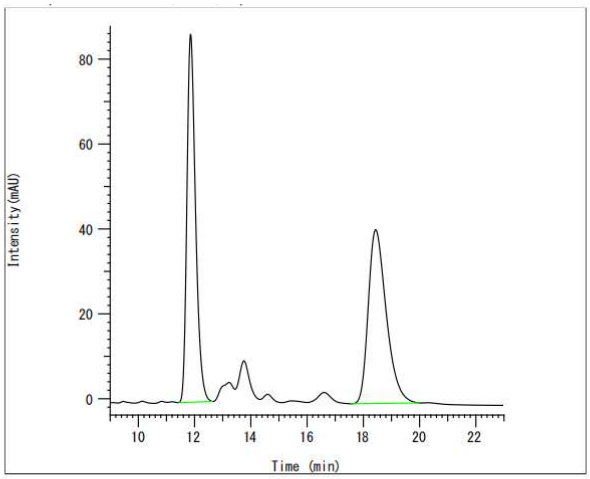
1410 UV Detector Ch1 SampleID:2 LLD-C-23-2 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	27.157	14205891	95.687	370568	96.639
2	Peak 2	41.137	640334	4.313	12887	3.361
			14846225	100.000	383455	100.000



3g

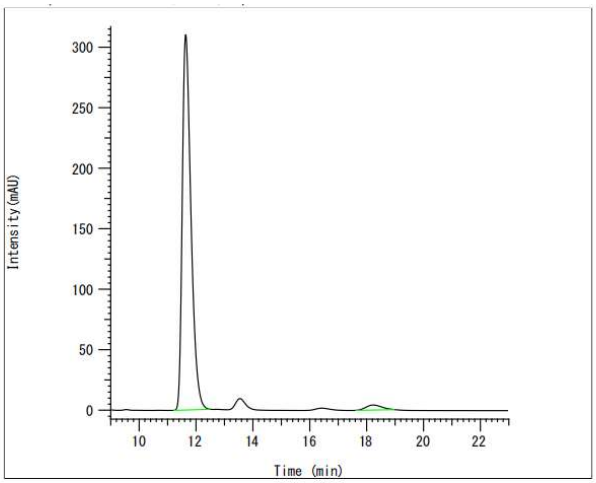
HPLC for analysis of the racemates: 1410 UV Detector, IJ column, EtOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-33-7 (250nm) Repeat:1

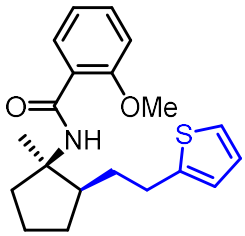
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	11.860	1848077	50.373	86703	67.922
2	Peak 2	18.437	1820736	49.627	40948	32.078
			3668813	100.000	127651	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IJ column, EtOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



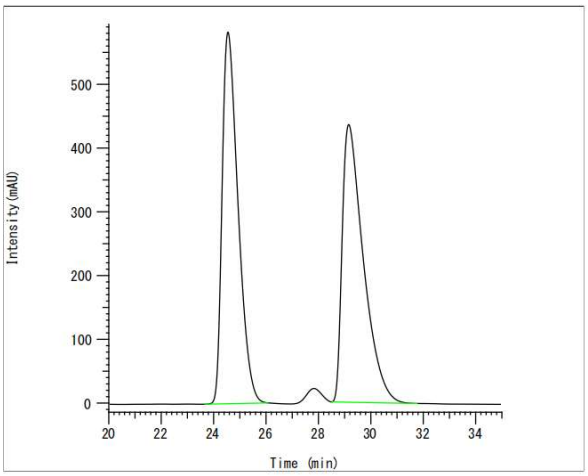
1410 UV Detector Ch1 SampleID:1 LLD-C-33-8 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	11.637	6585139	97.596	310405	98.675
2	Peak 2	18.237	162226	2.404	4167	1.325
			6747365	100.000	314572	100.000



3h

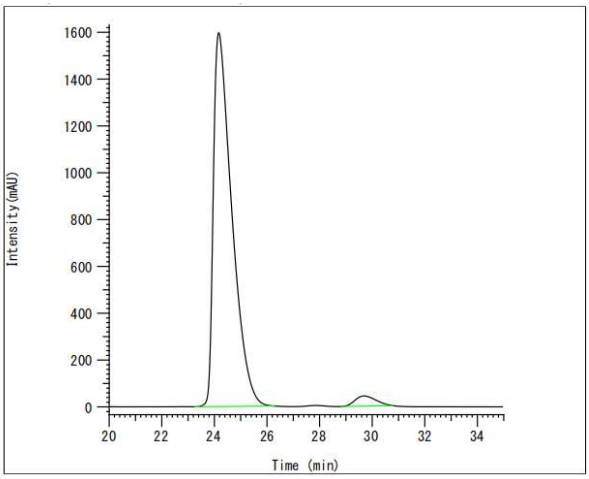
HPLC for analysis of the racemates: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:2 LLD-C-23-5 (230nm) Repeat:1

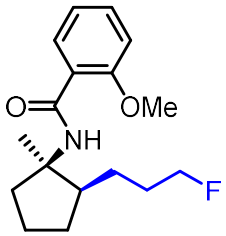
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	24.547	24649100	50.202	582955	57.235
2	Peak 2	29.157	24451211	49.798	435577	42.765
			49100311	100.000	1018532	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



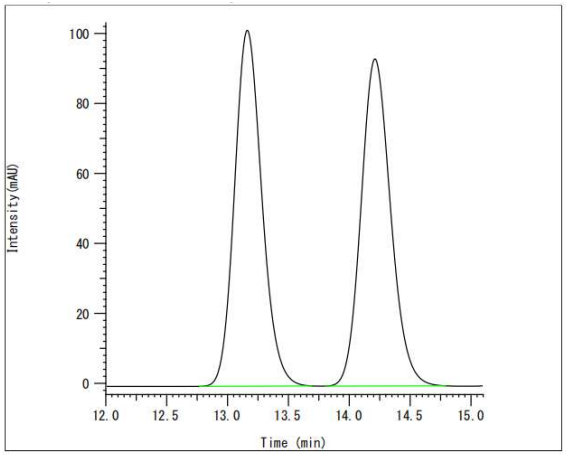
1410 UV Detector Ch1 SampleID:2 LLD-C-23-6 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	24.167	77821859	96.976	1596926	97.339
2	Peak 2	29.690	2426840	3.024	43656	2.661
			80248700	100.000	1640582	100.000



3i

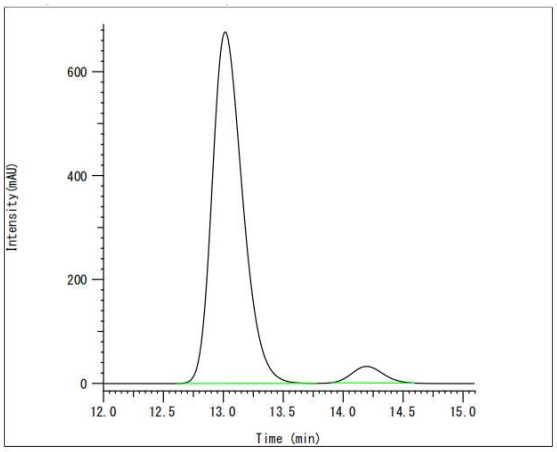
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-29-1 (250nm) Repeat:1

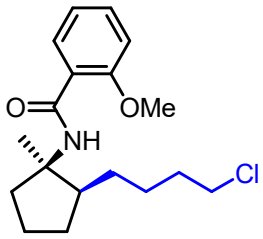
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.163	1591870	50.137	101709	52.105
2	Peak 2	14.210	1583145	49.863	93492	47.895
			3175015	100.000	195201	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



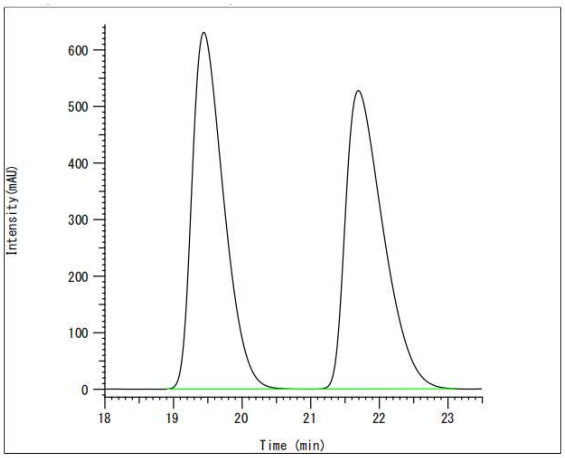
1410 UV Detector Ch1 SampleID:1 LLD-C-29-2 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.017	11965874	95.441	676577	95.528
2	Peak 2	14.197	571612	4.559	31670	4.472
			12537486	100.000	708247	100.000



3j

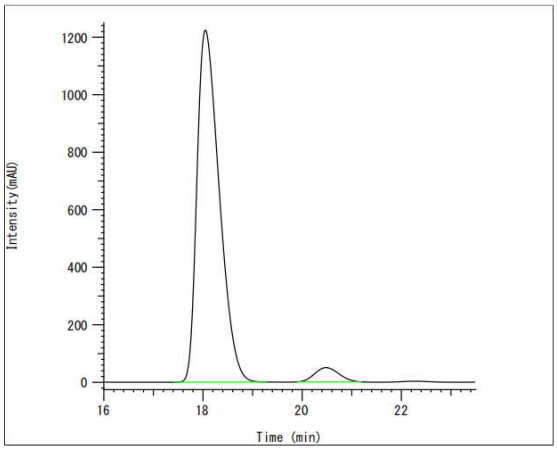
HPLC for analysis of the racemates: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-22-3 (230nm) Repeat:1

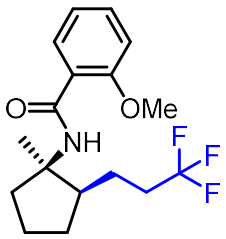
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	19.440	20170569	50.055	630781	54.453
2	Peak 2	21.693	20125950	49.945	527616	45.547
			40296519	100.000	1158397	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



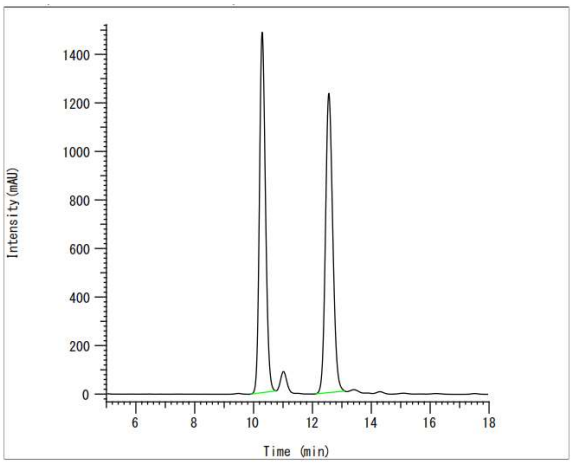
1410 UV Detector Ch1 SampleID:1 LLD-C-22-4 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	18.047	38151178	95.764	1224110	96.097
2	Peak 2	20.480	1687715	4.236	49720	3.903
			39838893	100.000	1273830	100.000



3k

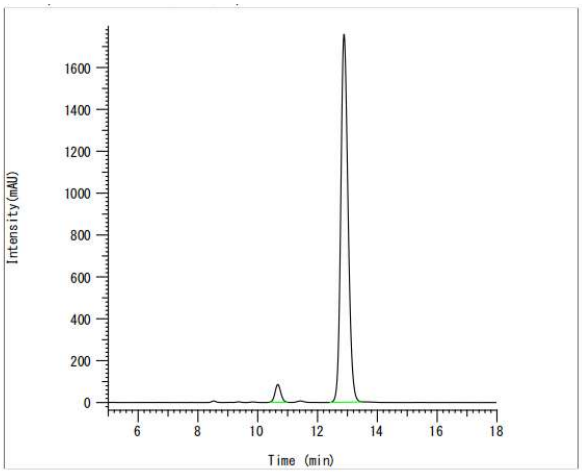
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-22-7 (230nm) Repeat:1

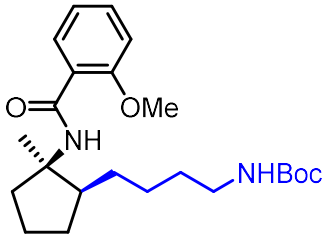
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	10.293	21176712	49.945	1485268	54.617
2	Peak 2	12.557	21223022	50.055	1234155	45.383
			42399734	100.000	2719422	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



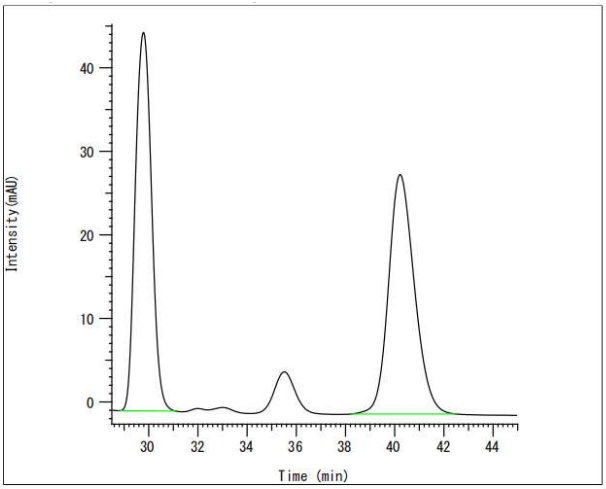
1410 UV Detector Ch1 SampleID:1 LLD-C-22-8 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	10.670	1142594	3.735	84908	4.607
2	Peak 2	12.887	29446550	96.265	1758282	95.393
			30589144	100.000	1843190	100.000



3l

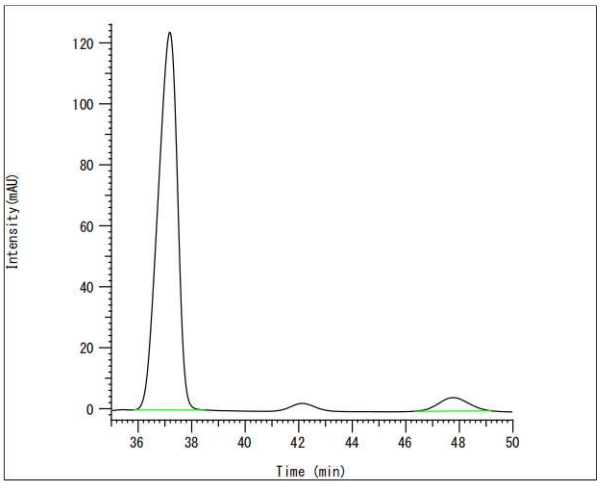
HPLC for analysis of the racemates: 1410 UV Detector, OJ-H column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-33-13 (250nm) Repeat:1

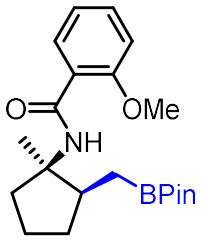
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	29.787	2076145	49.791	45295	61.244
2	Peak 2	40.220	2093613	50.209	28663	38.756
			4169758	100.000	73958	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OJ-H column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



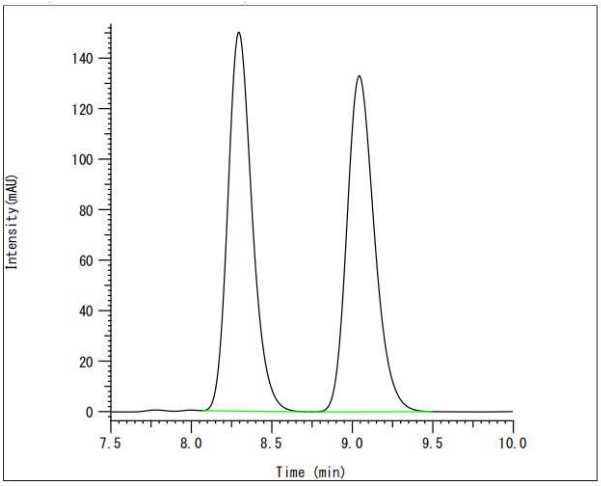
1410 UV Detector Ch1 SampleID:1 LLD-C-33-14 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	37.183	6231344	94.745	123917	96.563
2	Peak 2	47.747	345635	5.255	4411	3.437
			6576978	100.000	128328	100.000



3m

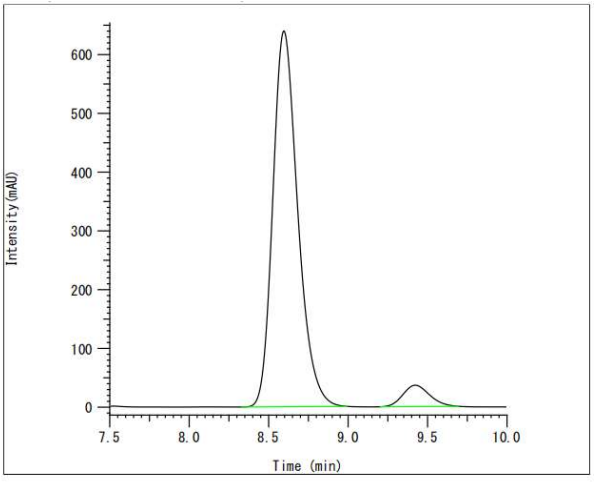
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:2 LLD-C-29-7 (250nm) Repeat:1

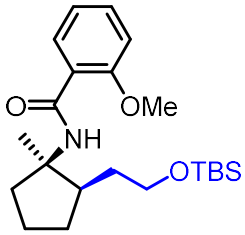
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	8.297	1574630	49.837	150063	52.996
2	Peak 2	9.043	1584935	50.163	133095	47.004
			3159565	100.000	283157	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



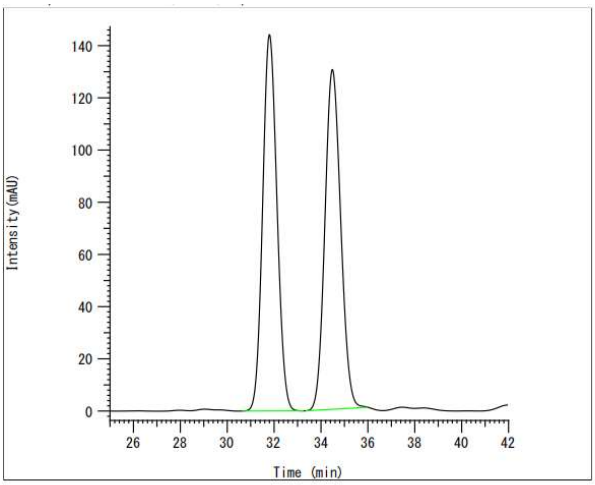
1410 UV Detector Ch1 SampleID:1 LLD-C-29-8 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	8.597	6981036	94.264	639641	94.623
2	Peak 2	9.423	424809	5.736	36351	5.377
			7405846	100.000	675992	100.000



3n

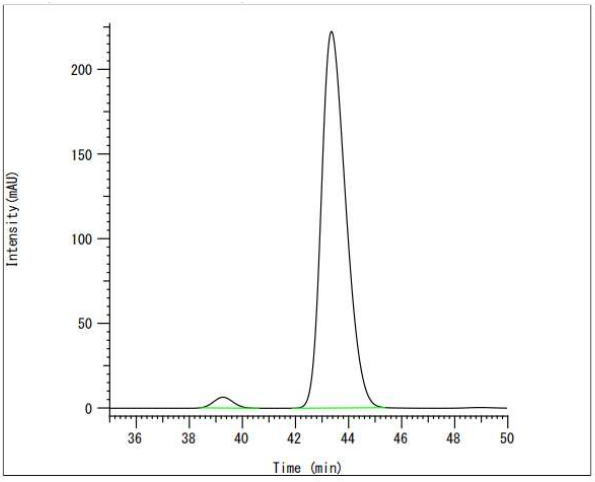
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 3 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-33-5 (230nm) Repeat:1

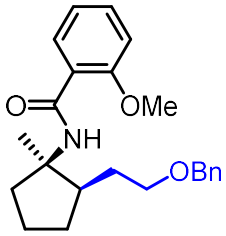
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	31.800	6112574	49.985	144226	52.556
2	Peak 2	34.487	6116139	50.015	130197	47.444
			12228712	100.000	274422	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 3 : 93, 0.8 mL/min, 250nm.



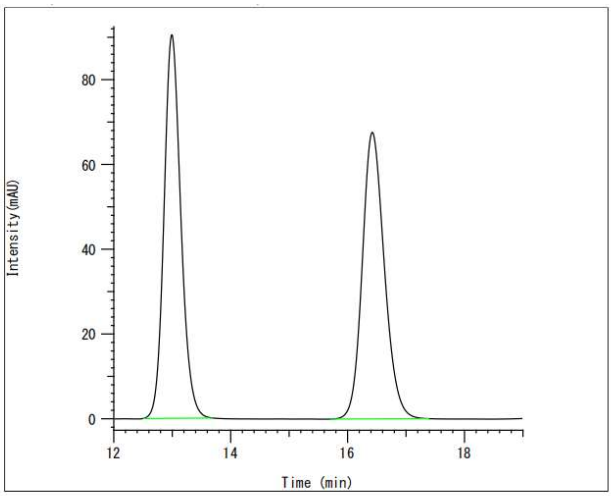
1410 UV Detector Ch1 SampleID:1 LLD-C-33-6 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	39.267	324549	2.237	6363	2.782
2	Peak 2	43.353	14184222	97.763	222375	97.218
			14508771	100.000	228738	100.000



3o

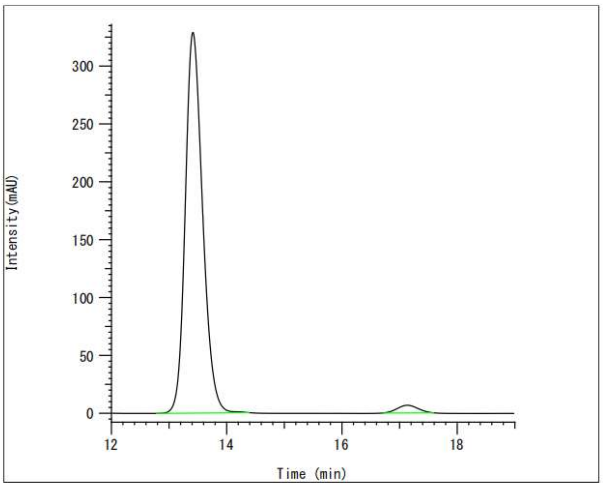
HPLC for analysis of the racemates: 1410 UV Detector, OJ-H column, EtOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:2 LLD-C-33-15 (250nm) Repeat:1

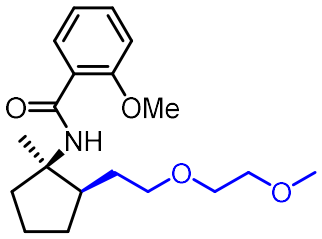
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	12.993	1810284	50.470	90488	57.237
2	Peak 2	16.423	1776581	49.530	67604	42.763
			3586865	100.000	158092	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OJ-H column, EtOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



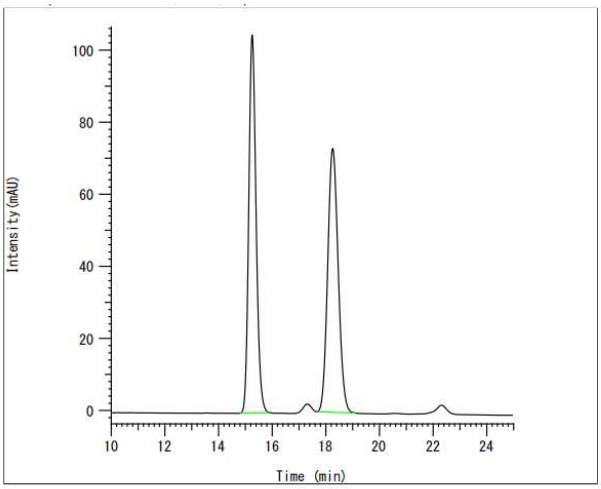
1410 UV Detector Ch1 SampleID:1 LLD-C-33-16 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.413	6877183	97.637	329011	98.023
2	Peak 2	17.137	166441	2.363	6635	1.977
			7043624	100.000	335646	100.000



3p

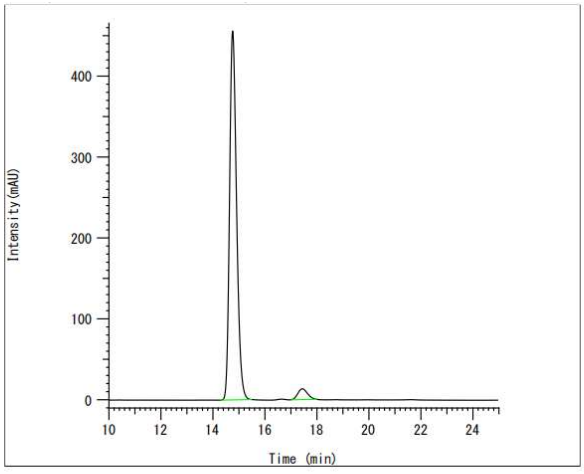
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-33-9 (250nm) Repeat:1

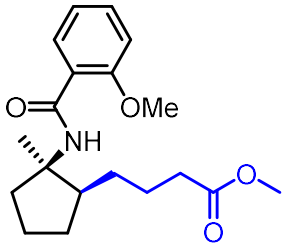
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	15.253	1983190	49.952	104946	58.890
2	Peak 2	18.257	1987001	50.048	73262	41.110
			3970191	100.000	178208	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



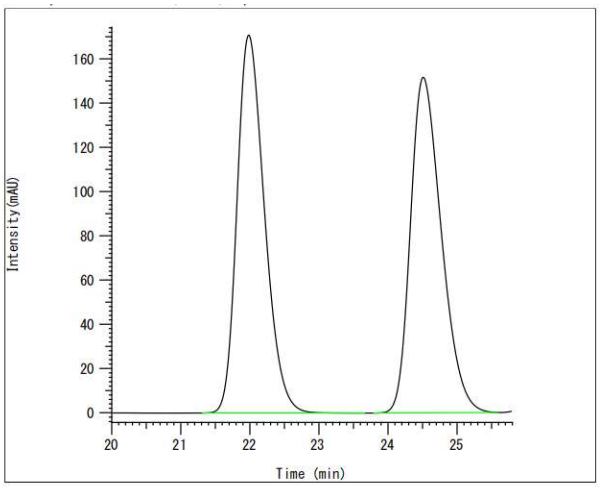
1410 UV Detector Ch1 SampleID:1 LLD-C-33-10 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	14.757	8493310	96.072	456116	97.149
2	Peak 2	17.437	347278	3.928	13384	2.851
			8840588	100.000	469499	100.000



3q

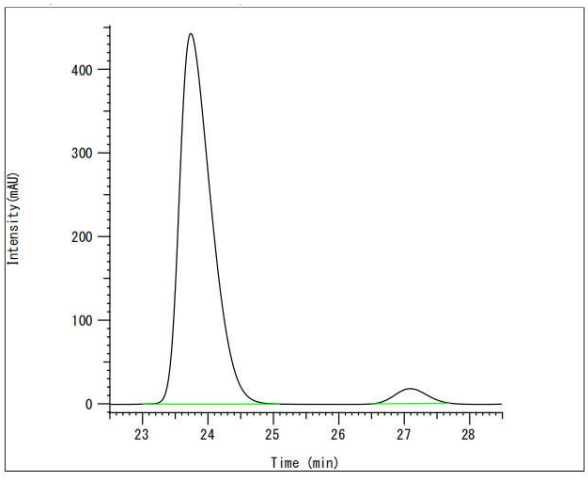
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 2 : 98, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-24-3 (250nm) Repeat:1

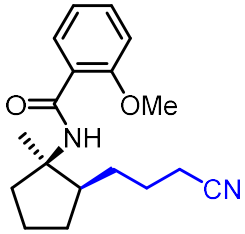
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	21.983	4726307	50.066	170875	52.974
2	Peak 2	24.510	4713847	49.934	151688	47.026
			9440154	100.000	322563	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 2 : 98, 0.8 mL/min, 250nm.



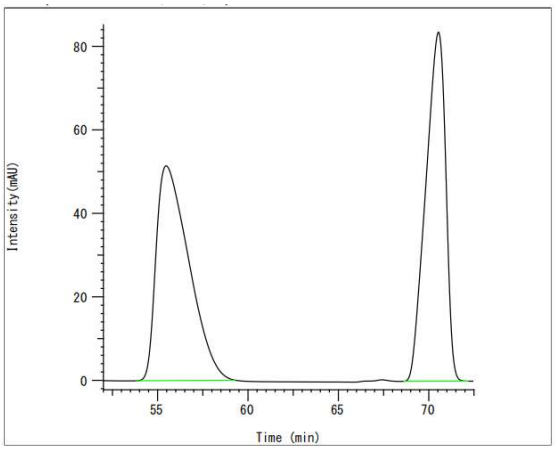
1410 UV Detector Ch1 SampleID:1 LLD-C-24-4 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	23.740	14876964	96.129	443107	96.149
2	Peak 2	27.090	599149	3.871	17748	3.851
			15476113	100.000	460855	100.000



3r

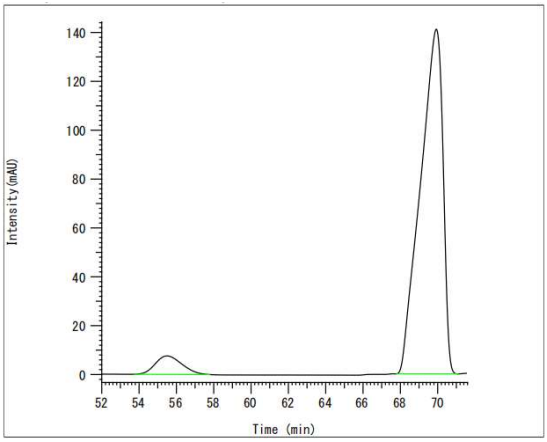
HPLC for analysis of the racemates: 1410 UV Detector, AD-H column, EtOH : hexane = 2 : 98, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-22-1 (250nm) Repeat:1

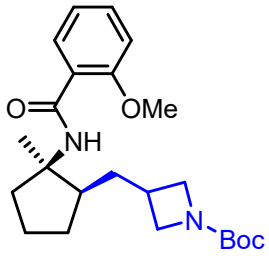
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	55.470	6467108	50.239	51455	38.096
2	Peak 2	70.537	6405493	49.761	83611	61.904
			12872601	100.000	135065	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, AD-H column, EtOH : hexane = 2 : 98, 0.8 mL/min, 250nm.



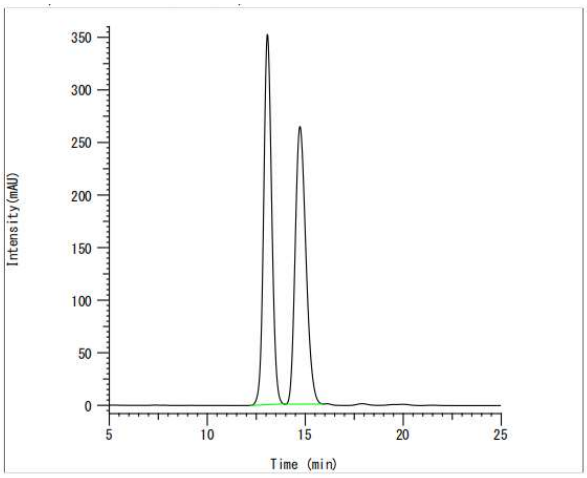
1410 UV Detector Ch1 SampleID:2 LLD-C-22-2 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	55.507	753134	5.996	7571	5.093
2	Peak 2	69.927	11807590	94.004	141096	94.907
			12560724	100.000	148667	100.000



3s

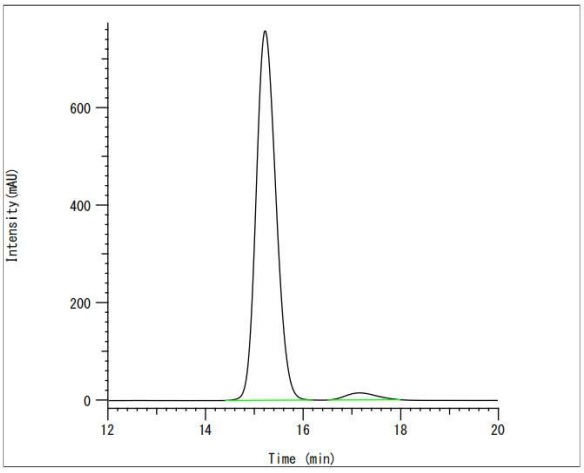
HPLC for analysis of the racemates: 1410 UV Detector, IH column, i-PrOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-24-7 (230nm) Repeat:1

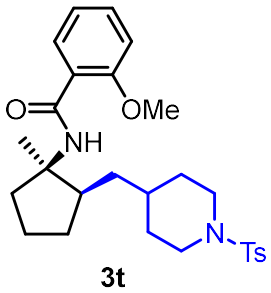
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.070	10069842	50.077	352299	57.147
2	Peak 2	14.730	10038798	49.923	264175	42.853
			20108640	100.000	616475	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IH column, i-PrOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



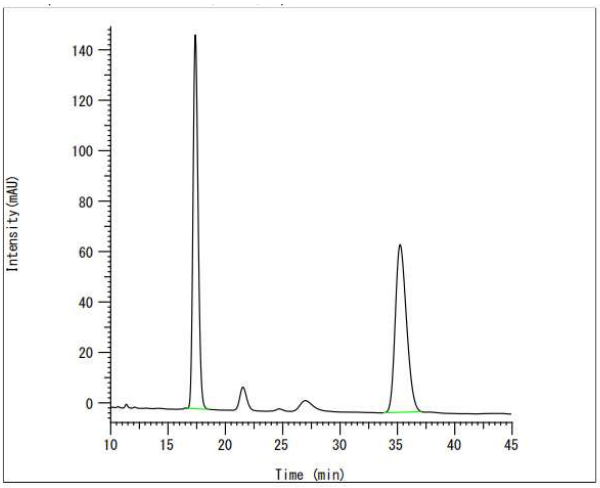
1410 UV Detector Ch1 SampleID:1 LLD-C-Boc (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	15.220	21381460	97.144	757934	98.139
2	Peak 2	17.157	628551	2.856	14372	1.861
			22010011	100.000	772306	100.000



3t

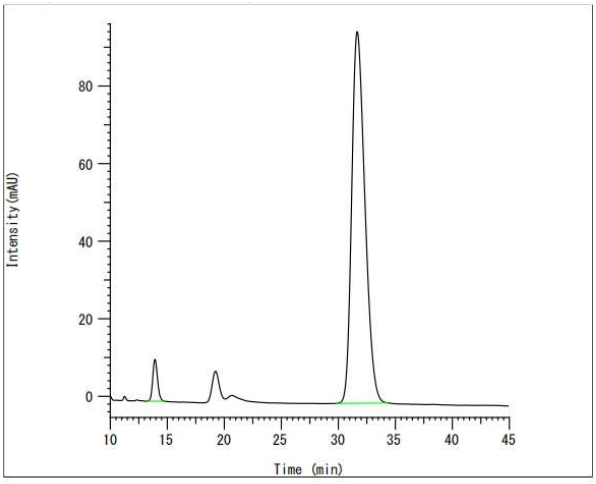
HPLC for analysis of the racemates: 1410 UV Detector, AD-H column, EtOH : hexane = 20 : 80, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-29-9-EtOH (250nm) Repeat:1

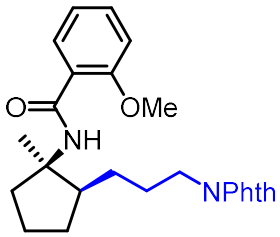
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	17.380	4542944	50.099	148290	69.033
2	Peak 2	35.237	4525072	49.901	66522	30.967
			9068016	100.000	214811	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, AD-H column, EtOH : hexane = 20 : 80, 0.8 mL/min, 250nm.



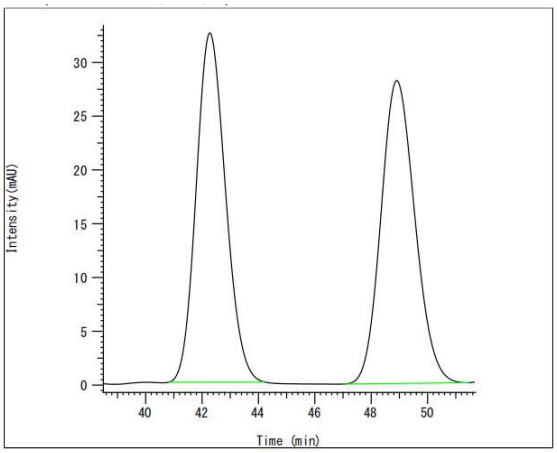
1410 UV Detector Ch1 SampleID:1 LLD-C-29-10 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.920	316488	3.929	10803	10.131
2	Peak 2	31.653	7737914	96.071	95833	89.869
			8054402	100.000	106637	100.000



3u

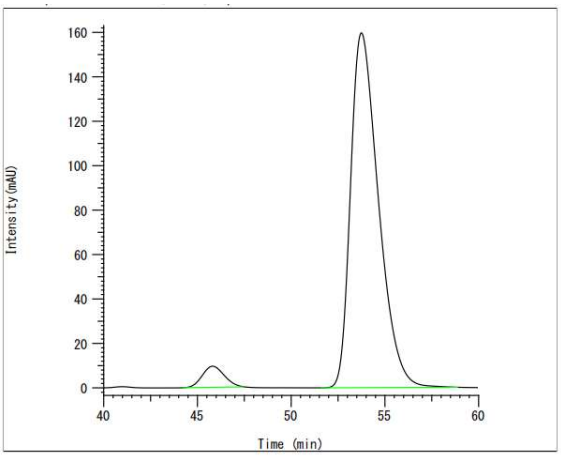
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 25 : 75, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-B-61-3 (250nm) Repeat:1

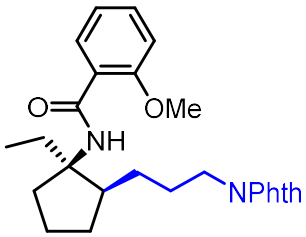
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	42.277	2345442	49.872	32465	53.551
2	Peak 2	48.903	2357444	50.128	28159	46.449
			4702887	100.000	60624	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 25 : 75, 0.8 mL/min, 250nm.



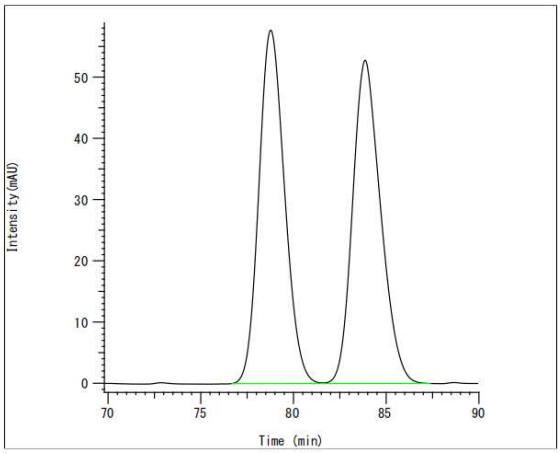
1410 UV Detector Ch1 SampleID:1 LLD-C-18-7 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	45.800	773659	4.479	9494	5.611
2	Peak 2	53.747	16499805	95.521	159694	94.389
			17273463	100.000	169188	100.000



3v

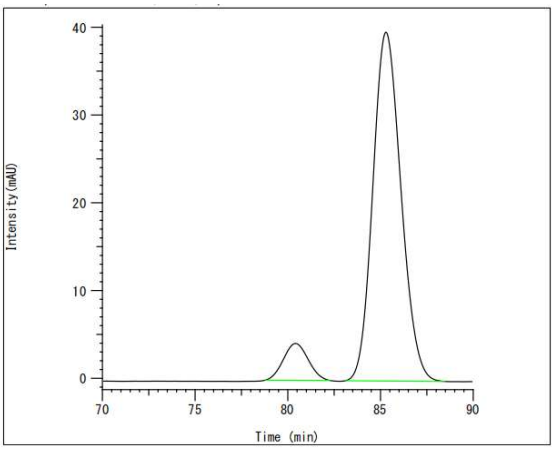
HPLC for analysis of the racemates: 1410 UV Detector, IC column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-B-144-1-IC-7%EtOH (250nm) Repeat:1

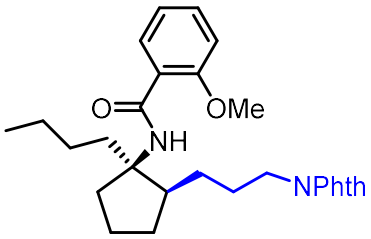
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	78.773	5564727	50.062	57718	52.224
2	Peak 2	83.863	5550869	49.938	52802	47.776
			11115596	100.000	110519	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



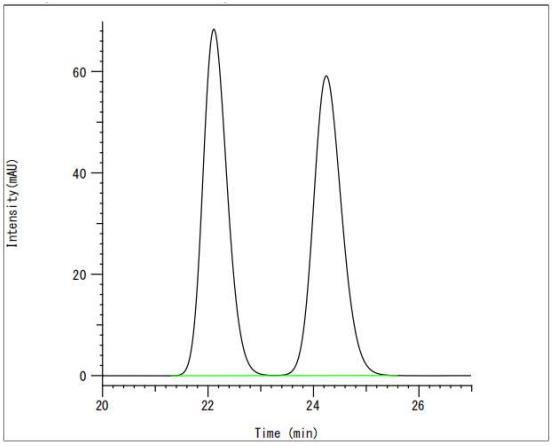
1410 UV Detector Ch1 SampleID:3 LLD-C-4-5 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	80.403	390243	8.516	4199	9.556
2	Peak 2	85.293	4192041	91.484	39744	90.444
			4582284	100.000	43943	100.000



3w

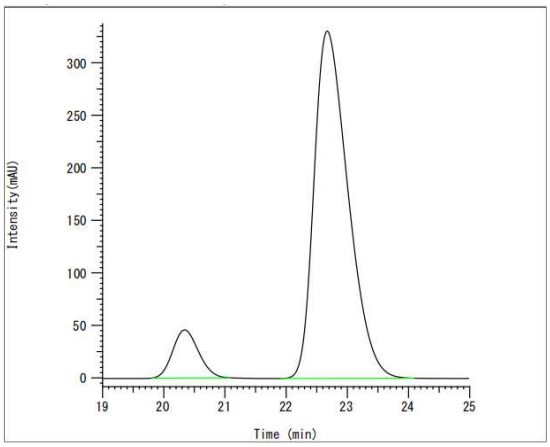
HPLC for analysis of the racemates: 1410 UV Detector, AD-H column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-20-5 (250nm) Repeat:1

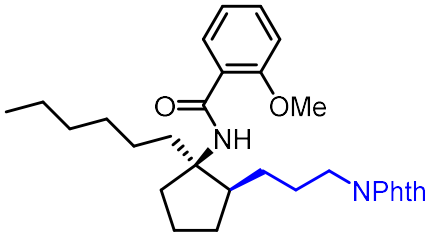
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	22.110	2222905	49.922	68373	53.620
2	Peak 2	24.243	2229895	50.078	59141	46.380
			4452801	100.000	127514	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, AD-H column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



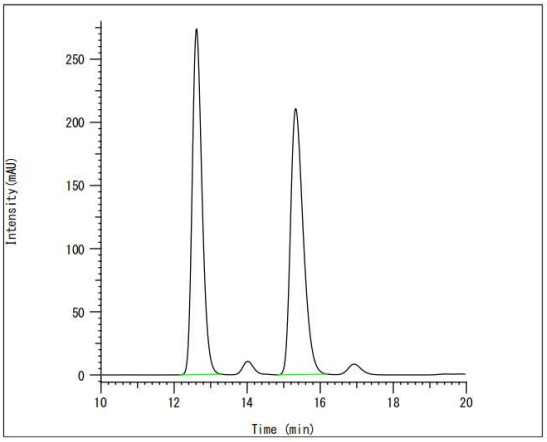
1410 UV Detector Ch1 SampleID:1 LLD-C-20-6 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	20.340	1344799	9.548	45779	12.163
2	Peak 2	22.673	12739369	90.452	330602	87.837
			14084168	100.000	376381	100.000



3x

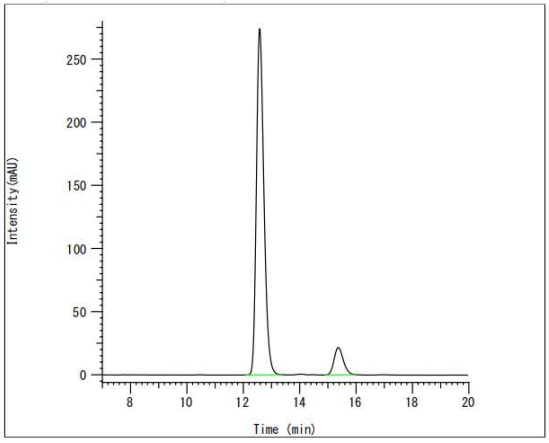
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:3 LLD-C-14-5 (250nm) Repeat:1

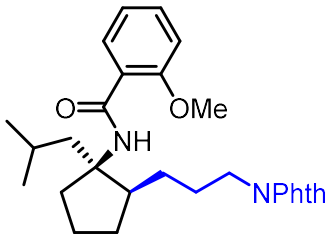
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	12.613	5115756	50.008	273863	56.527
2	Peak 2	15.330	5114193	49.992	210620	43.473
			10229949	100.000	484483	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



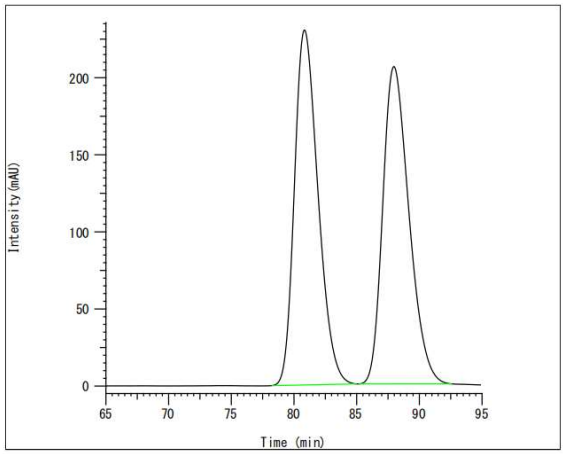
1410 UV Detector Ch1 SampleID:1 LLD-C-14-6 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	12.580	5073065	91.132	274236	92.685
2	Peak 2	15.370	493686	8.868	21643	7.315
			5566751	100.000	295879	100.000



3y

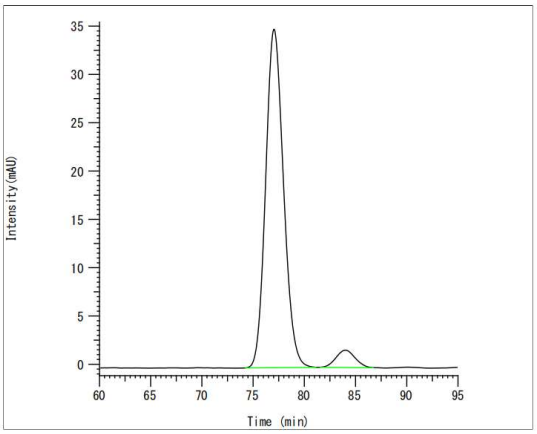
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:2 LLD-B-144-2 (230nm) Repeat:1

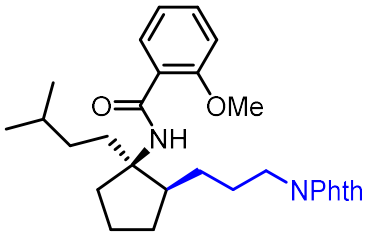
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	80.837	30127467	50.165	230231	52.796
2	Peak 2	87.967	29929519	49.835	205844	47.204
			60056986	100.000	436075	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



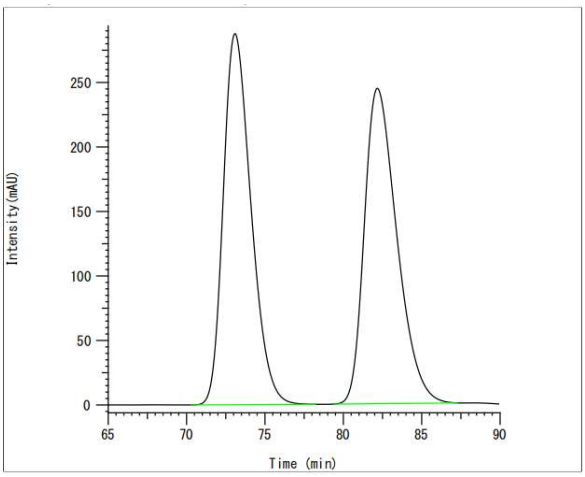
1410 UV Detector Ch1 SampleID:3 LLD-C-4-6 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	77.037	4246545	94.795	35037	95.137
2	Peak 2	84.023	233180	5.205	1791	4.863
			4479725	100.000	36828	100.000



3z

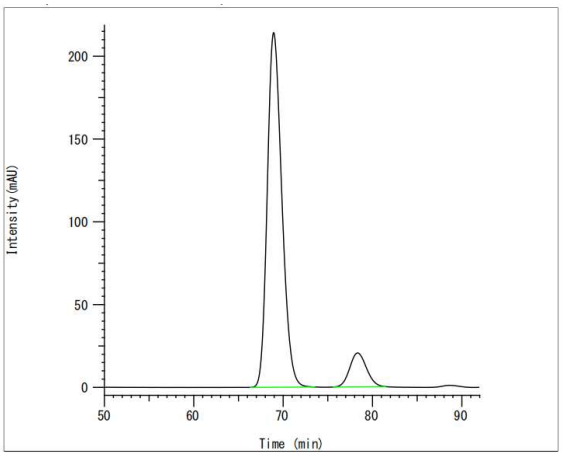
HPLC for analysis of the racemates: 1410 UV Detector, IC column, i-PrOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:3 LLD-B-144-3 (230nm) Repeat:1

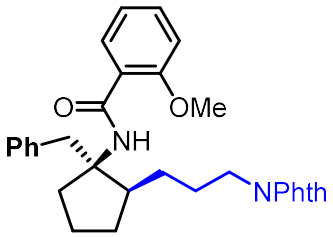
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	73.087	35385335	50.107	287647	54.059
2	Peak 2	82.170	35233951	49.893	244453	45.941
			70619286	100.000	532100	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, i-PrOH : hexane = 10 : 90, 0.8 mL/min, 250nm.



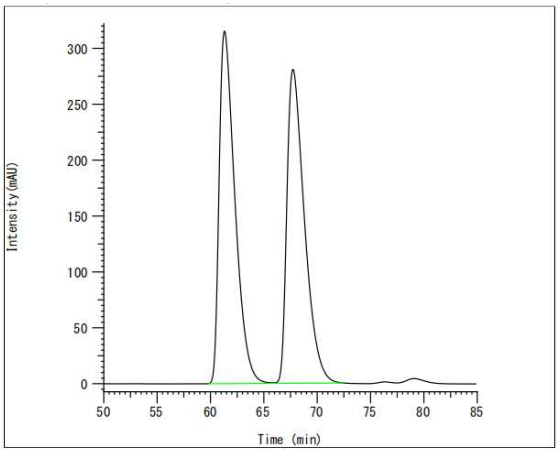
1410 UV Detector Ch1 SampleID:4 LLD-C-4-7 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	68.937	24226899	90.032	214217	91.266
2	Peak 2	78.327	2682256	9.968	20501	8.734
			26909154	100.000	234718	100.000



3aa

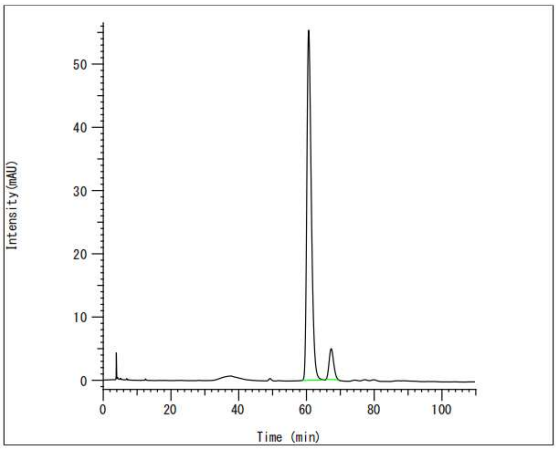
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-14-3 (230nm) Repeat:1

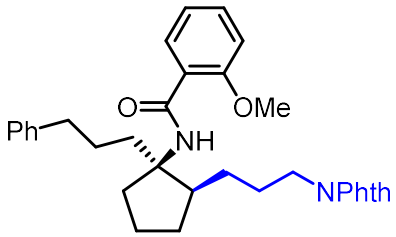
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	61.313	32414450	50.250	315416	52.894
2	Peak 2	67.727	32092340	49.750	280902	47.106
			64506790	100.000	596318	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



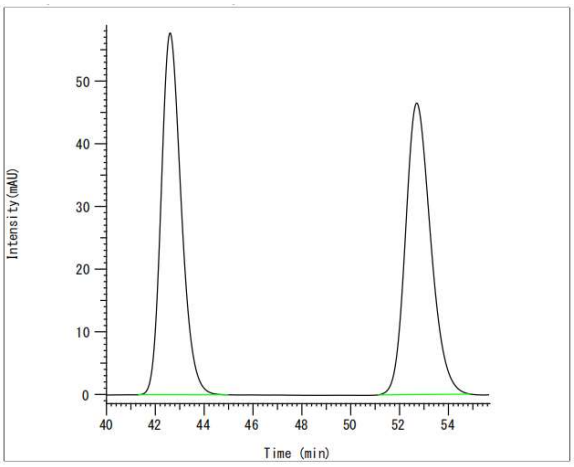
1410 UV Detector Ch1 SampleID:2 LLD-C-14-4 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	60.657	5111855	91.787	55385	91.905
2	Peak 2	67.290	457432	8.213	4878	8.095
			5569286	100.000	60263	100.000



3ab

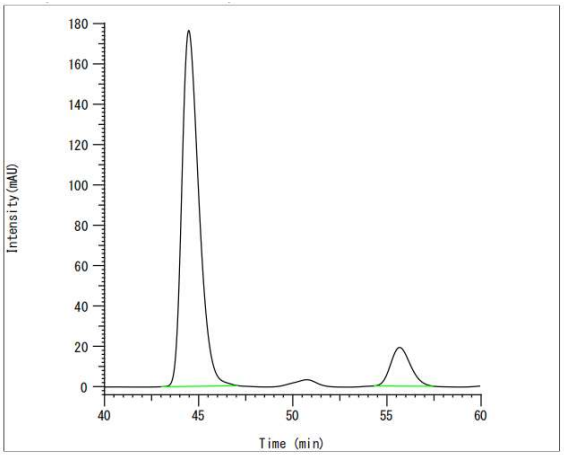
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 4 : 96, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-11-7 (250nm) Repeat:1

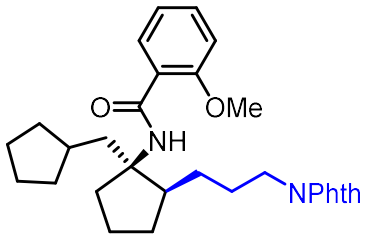
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	42.607	3288442	49.681	57724	55.378
2	Peak 2	52.703	3330703	50.319	46511	44.622
			6619145	100.000	104235	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 4 : 96, 0.8 mL/min, 250nm.



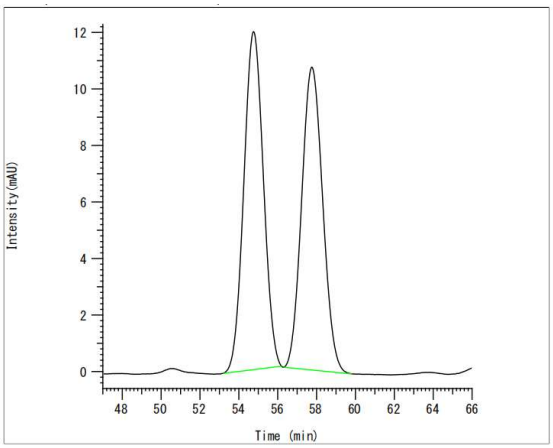
1410 UV Detector Ch1 SampleID:1 LLD-C-11-8 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	44.473	11094172	88.755	176459	90.204
2	Peak 2	55.670	1405659	11.245	19164	9.796
			12499831	100.000	195623	100.000



3ac

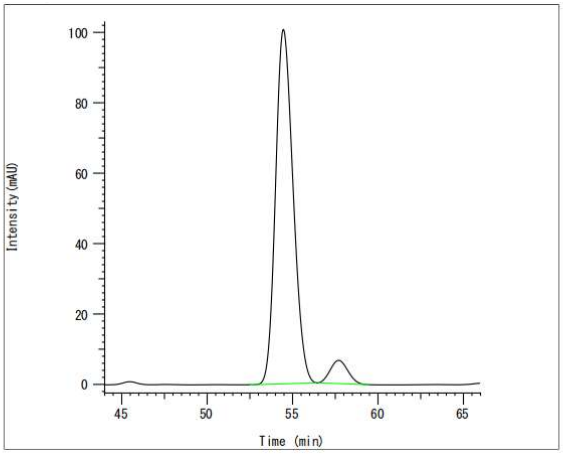
HPLC for analysis of the racemates: 1410 UV Detector, IC column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-4-9 (250nm) Repeat:1

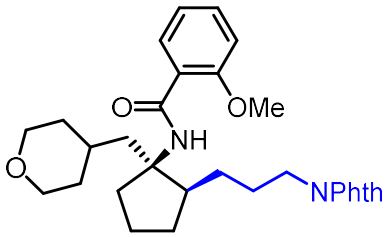
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	54.760	835123	50.884	11960	52.736
2	Peak 2	57.757	806106	49.116	10719	47.264
			1641229	100.000	22679	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



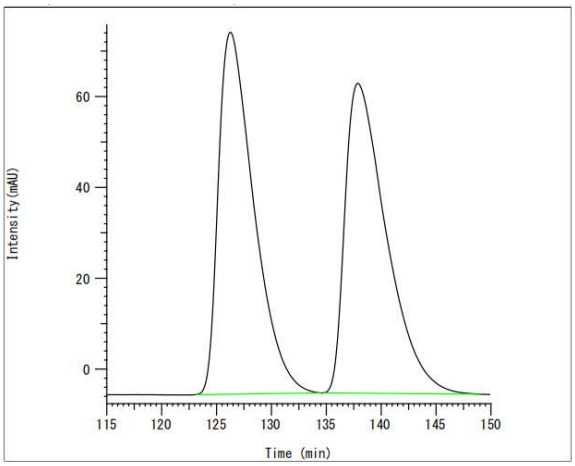
1410 UV Detector Ch1 SampleID:3 LLD-C-4-8 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	54.460	7192820	93.819	100671	93.857
2	Peak 2	57.697	473908	6.181	6590	6.143
			7666728	100.000	107261	100.000



3ad

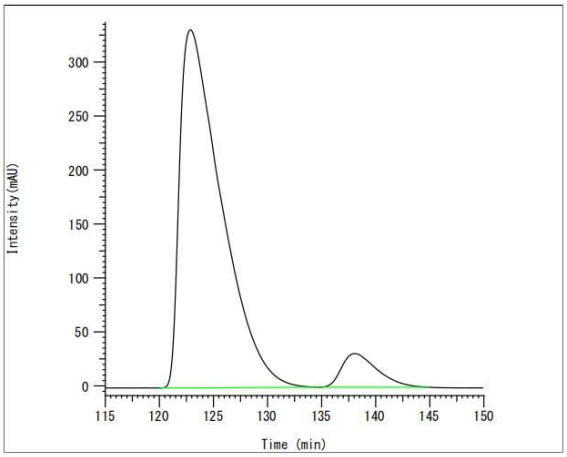
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-14-1 (230nm) Repeat:1

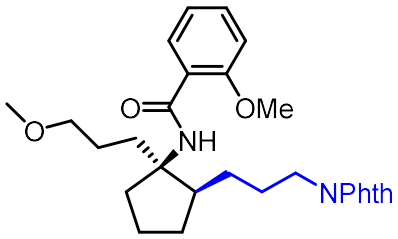
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	126.260	17884750	50.095	79666	53.873
2	Peak 2	137.873	17817110	49.905	68211	46.127
			35701859	100.000	147877	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, i-PrOH : hexane = 5 : 95, 0.8 mL/min, 250nm.



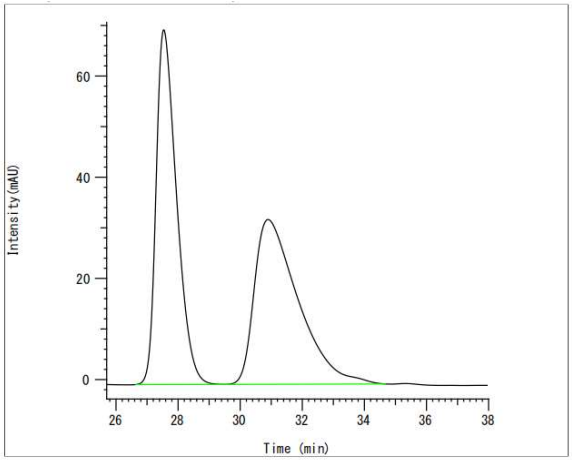
1410 UV Detector Ch1 SampleID:1 LLD-C-14-2 (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	122.860	88691057	92.574	331517	91.403
2	Peak 2	138.047	7114196	7.426	31181	8.597
			95805252	100.000	362698	100.000



3ae

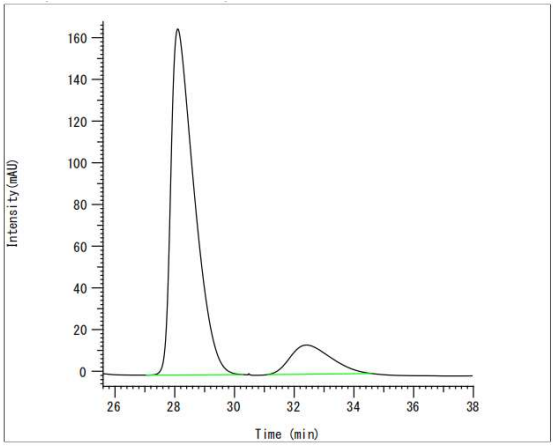
HPLC for analysis of the racemates: 1410 UV Detector, IA column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-11-3 (250nm) Repeat:1

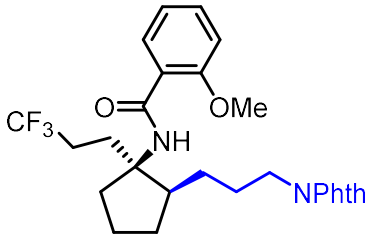
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	27.537	3211706	50.125	70110	68.279
2	Peak 2	30.900	3195687	49.875	32572	31.721
			6407394	100.000	102683	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IA column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



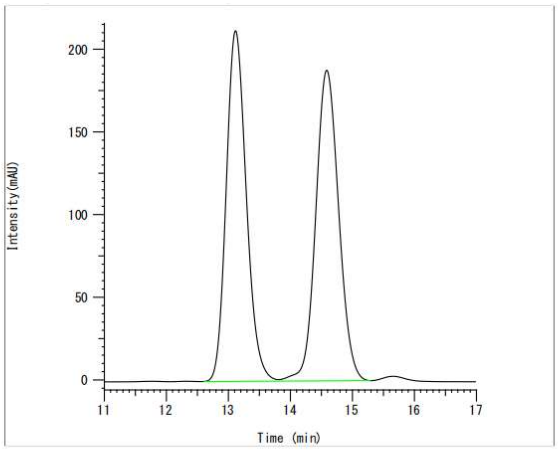
1410 UV Detector Ch1 SampleID:1 LLD-C-11-4 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	28.100	8988422	87.108	165987	92.220
2	Peak 2	32.413	1330309	12.892	14003	7.780
			10318731	100.000	179990	100.000



3af

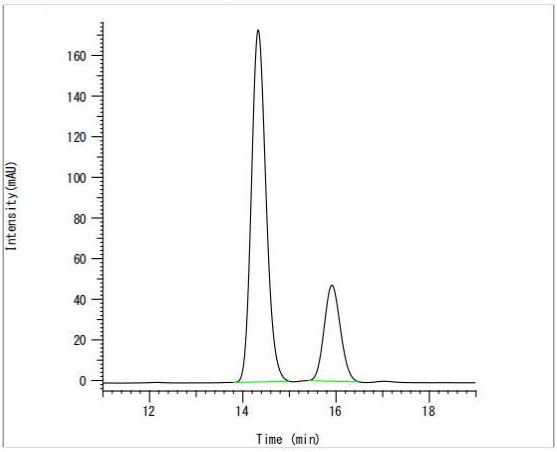
HPLC for analysis of the racemates: 1410 UV Detector, AS-H column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-11-5 (250nm) Repeat:1

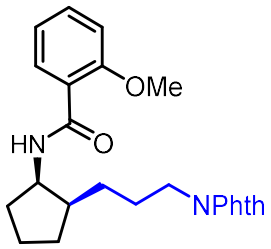
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	13.113	4762391	49.660	212049	53.024
2	Peak 2	14.587	4827631	50.340	187862	46.976
			9590022	100.000	399911	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, AS-H column, EtOH : hexane = 7 : 93, 0.8 mL/min, 250nm.



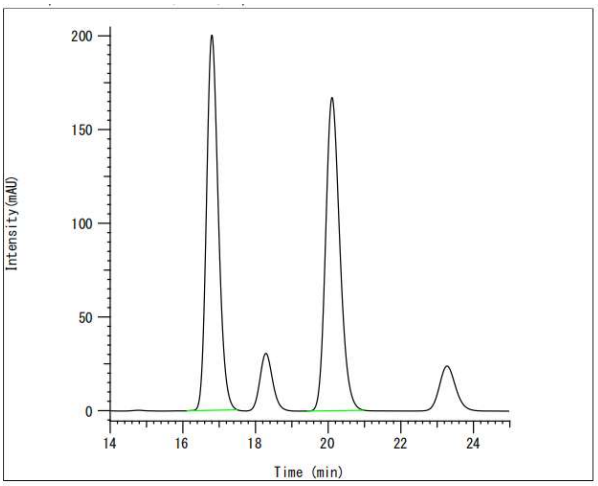
1410 UV Detector Ch1 SampleID:1 LLD-C-11-6 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	14.330	3775027	76.742	173312	78.572
2	Peak 2	15.910	1144107	23.258	47264	21.428
			4919134	100.000	220576	100.000



5

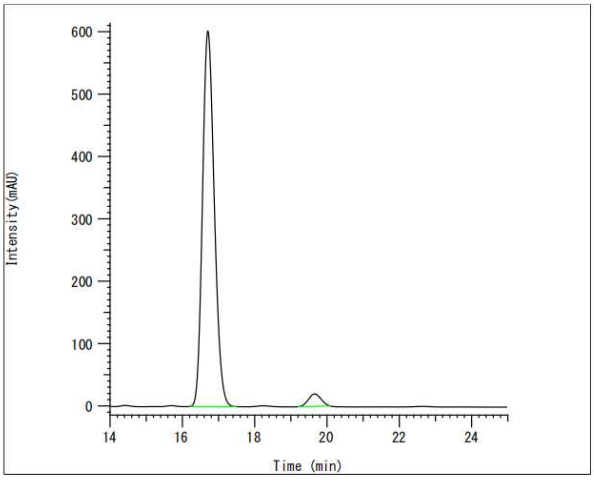
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-41-1 (250nm) Repeat:1

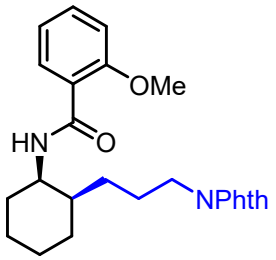
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	16.800	4524567	49.911	200273	54.507
2	Peak 2	20.107	4540640	50.089	167153	45.493
			9065206	100.000	367426	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



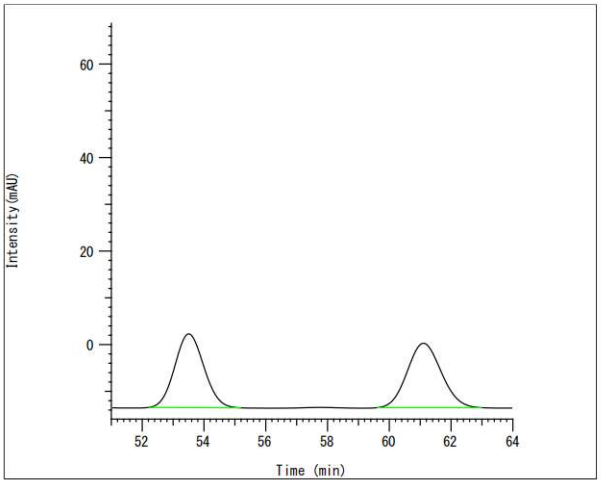
1410 UV Detector Ch1 SampleID:1 LLD-C-41-2 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	16.707	13640492	96.582	602228	96.812
2	Peak 2	19.660	482793	3.418	19832	3.188
			14123285	100.000	622060	100.000



7

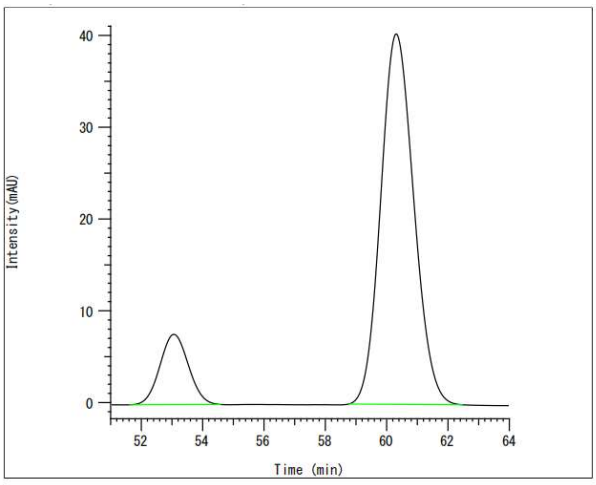
HPLC for analysis of the racemates: 1410 UV Detector, IC column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-41-4 (250nm) Repeat:1

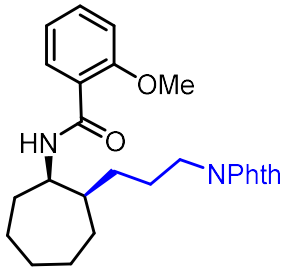
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	53.507	1035113	49.470	15761	53.359
2	Peak 2	61.103	1057300	50.530	13777	46.641
			2092412	100.000	29537	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IC column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



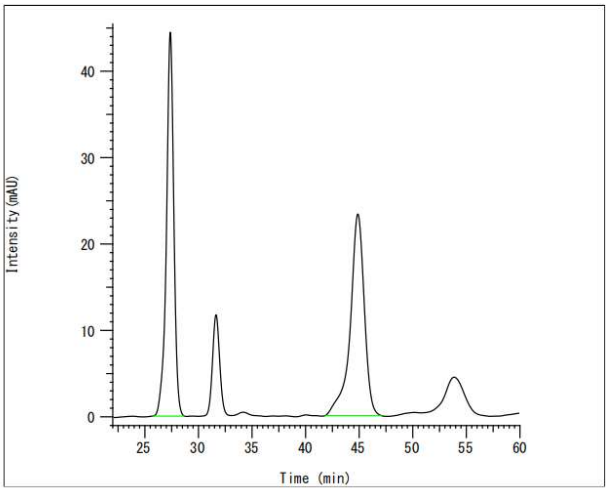
1410 UV Detector Ch1 SampleID:5 LLD-C-60-5 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	53.060	495037	14.076	7659	15.951
2	Peak 2	60.313	3021925	85.924	40356	84.049
			3516961	100.000	48015	100.000



9

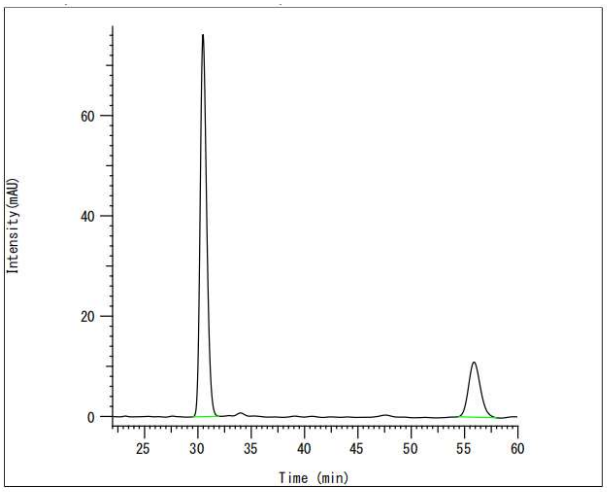
HPLC for analysis of the racemates: 1410 UV Detector, OD-H column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



1410 UV Detector Ch2 SampleID:1 LLD-C-47-1 (250nm) Repeat:1

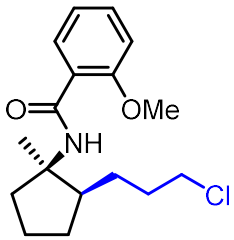
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	27.370	2124169	49.880	44452	65.569
2	Peak 2	44.873	2134396	50.120	23342	34.431
			4258565	100.000	67794	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OD-H column, EtOH : hexane = 15 : 85, 0.8 mL/min, 250nm.



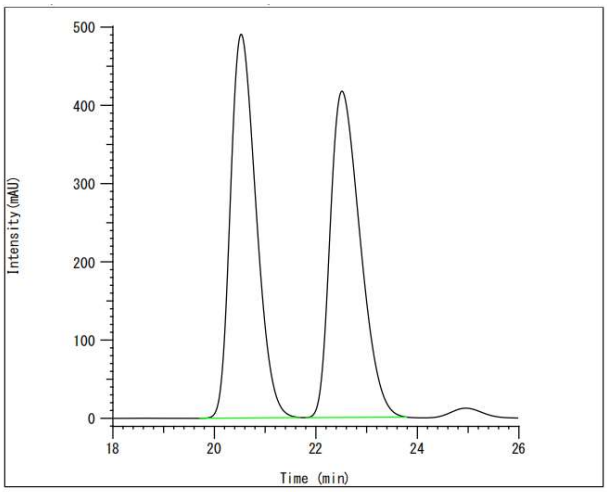
1410 UV Detector Ch2 SampleID:6 LLD-C-57-6 (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	30.480	3228995	79.133	76211	87.403
2	Peak 2	55.887	851470	20.867	10984	12.597
			4080465	100.000	87195	100.000



11

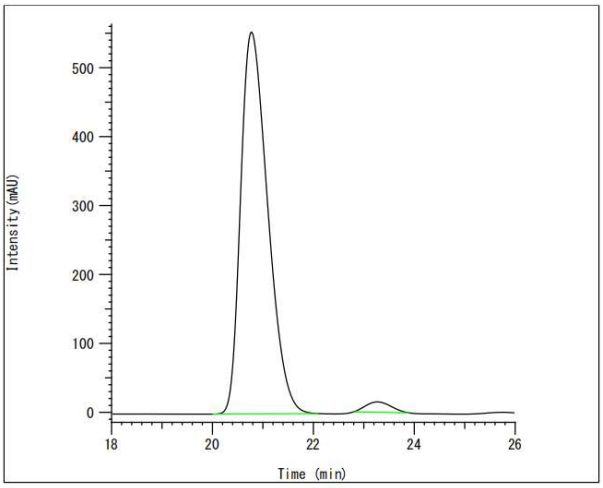
HPLC for analysis of the racemates: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-C-Cl-XIAO (230nm) Repeat:1

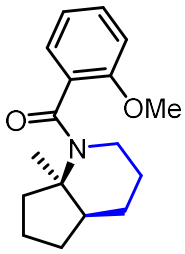
No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	20.527	17239612	50.186	490507	54.043
2	Peak 2	22.513	17111871	49.814	417112	45.957
			34351483	100.000	907618	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, OD-H column, i-PrOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



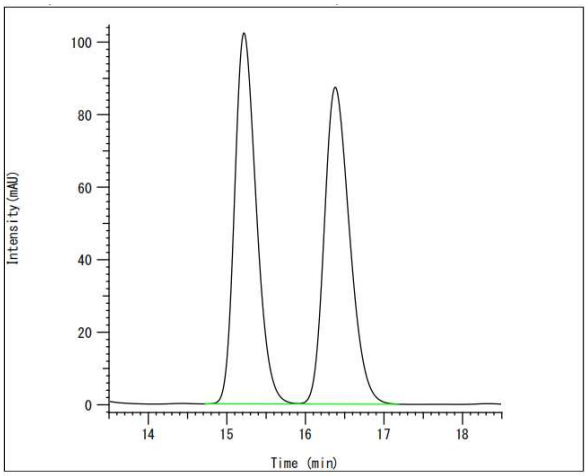
1410 UV Detector Ch1 SampleID:1 Cl (230nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	20.773	20647580	97.514	553938	97.351
2	Peak 2	23.267	526435	2.486	15076	2.649
			21174015	100.000	569014	100.000



12

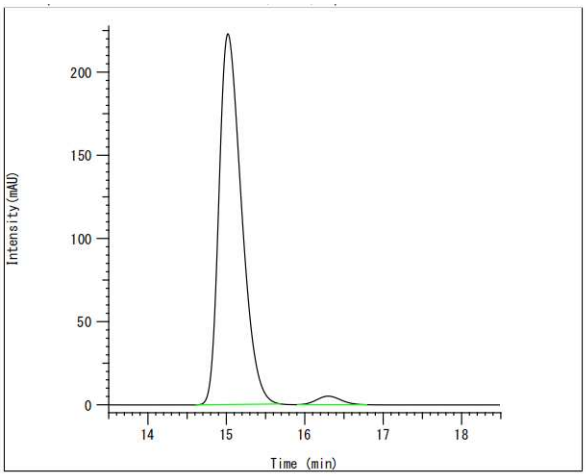
HPLC for analysis of the racemates: 1410 UV Detector, IBN-5 column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-5&6-XX-IBN5-3%EtOH (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	15.217	1963136	50.046	102303	53.934
2	Peak 2	16.380	1959511	49.954	87378	46.066
			3922647	100.000	189682	100.000

HPLC for analysis of the enantioenriched material: 1410 UV Detector, IBN-5 column, EtOH : hexane = 3 : 97, 0.8 mL/min, 250nm.



1410 UV Detector Ch1 SampleID:1 LLD-5&6-SX-IBN5-3%EtOH (250nm) Repeat:1

No.	Compounds	RT	Area	Area%	Height	Height%
1	Peak 1	15.020	4442154	97.576	222881	97.755
2	Peak 2	16.297	110354	2.424	5120	2.245
			4552508	100.000	228001	100.000