Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting information

Ethanol-assisted mechanochemical asymmetric cross-dehydrogenative coupling reaction with recoverable chiral amine/NaCl for accessing chiral *α*-alkyl *α*-glycine derivatives

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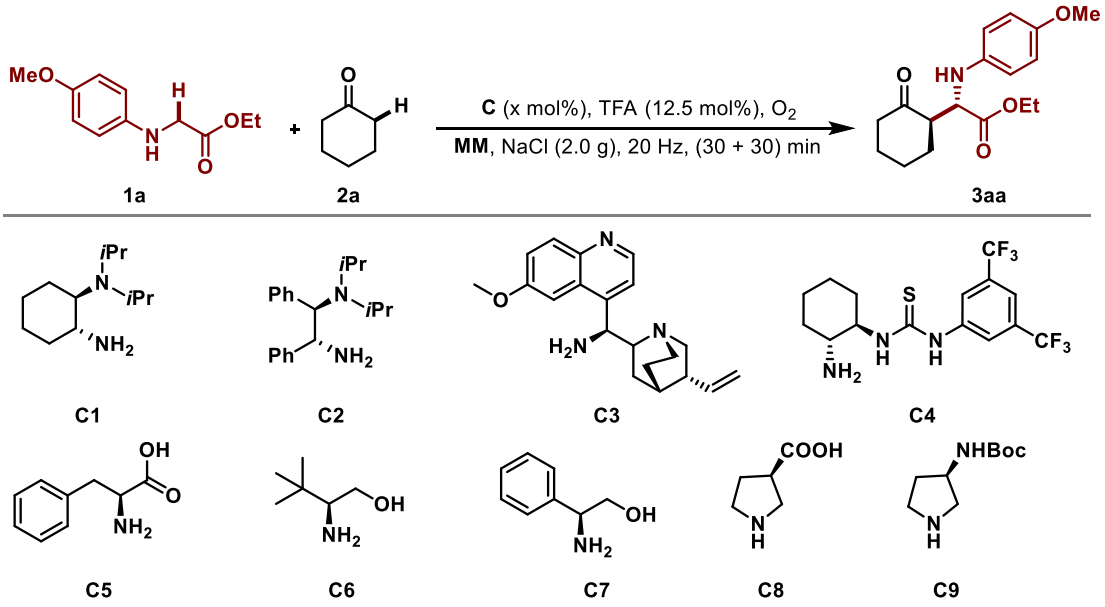
1. General information

All of the ball milling reactions were conducted in a Mixer mill (MM 400 RetschGmbh, Hann, Germany) with 25 mL stainless-steel vessels (equipped with gas inlet and outlet valve) with stainless-steel balls, if not mentioned otherwise. Reactions were monitored by Thin Layer Chromatography (TLC) using UV light (254 nm) for detection. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker 400, 500 or 600 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in parts per million (ppm). The following abbreviations were used to explain multiplicities: s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet and the coupling constants (*J*) were reported in Hertz unit (Hz). Melting points were measured using an SRS OptiMelt MPA100 apparatus and were uncorrected. High Resolution Mass Spectrometry (HRMS) and Electrospray Ionization-Mass Spectrometry (ESI-MS) were recorded on an Agilent 6210 LC/TOFMS or Agilent 6550 QTOFMS. High Performance Liquid Chromatography (HPLC) were performed on SHIMADZU LC-20AT apparatus, using Daicel Chiralpak AD-H chiral column, eluted with a mixture of hexane and isopropyl alcohol. Optical Rotations were measured with Rudolph Autopol V polarimeter. X-ray crystallographic experiments were performed by the Crystallography Service of the Department of Chemistry, Zhejiang University. The synthesis of *N*-arylglycine esters/amide substrates was meticulously carried out under solvent-free ball-milling conditions, in accordance with our recent publication[1].

2. Reaction optimization & typical procedures

2.1 Optimization of the reaction conditions

Table S1. Screening of ligands[a]

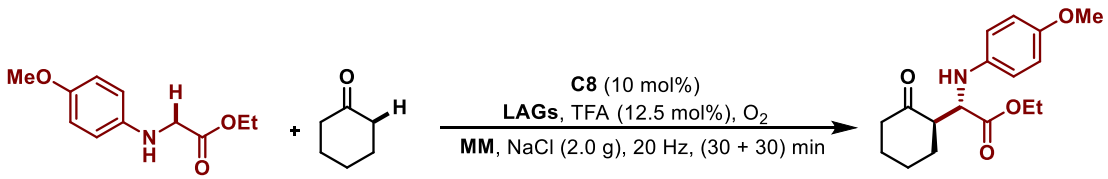


entry	catalyst (mol%)	yield (%)[b]	*ee* (%)[b]	*dr*[b]
1	**C1** (20)	39	<5	96: 4
2	**C2** (20)	35	<5	84: 16
3	**C3** (20)	31	<5	50: 50

4	**C4** (20)	39	43	82: 18
5	**C5** (20)	35	16	60: 40
6	**C6** (20)	30	13	50: 50
7	**C7** (20)	33	10	55: 45
8	**C8** (20)	37	58	88: 12
9	**C9** (20)	42	<5	50: 50
10	**C8** (15)	47	55	85: 15
11	**C8** (10)	46	58	87: 13
12	**C8** (5)	43	52	75: 25
13[c]	**C8** (10)	51	59	88: 12
14[d]	**C8** (10)	42	55	85: 15
15[e]	**C8** (10)	35	52	81: 19

[a] Reaction conditions: **1a** (0.2 mmol), TFA (12.5 mol%), NaCl (2.0 g) were pre-milled at 20 Hz for 30 min under oxygen conditions, using two stainless-steel balls (d_{MB} = 1.2 cm) in a 25 mL stainless vial, then **2a** (5 equiv.), **C** (x mol%) were added and milled for another 30 min. [b] Yields were those of the isolated products, *ee* values were determined by HPLC, *dr* values were determined by ^{1}H NMR. [c] **2a** (4 equiv.) was used. [d] **2a** (3.5 equiv.) was used. [e] **2a** (3 equiv.) was used.

Table S2. Screening of LAGs[a]

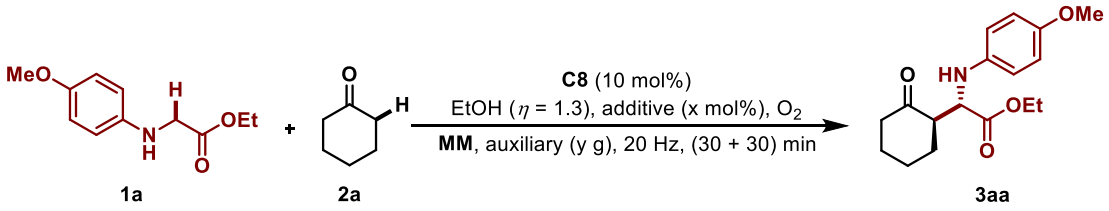


entry	LAGs (η)	yield (%)[b]	*ee* (%)[b]	*dr*[b]
1	TFA (1.5)	21	<5	20: 80
2	DMAE (1.5)	56	79	77: 23
3	MeOH (1.5)	53	73	80: 20
4	EtOH (1.5)	62	85	98: 2
5	*i*-PrOH (1.5)	58	83	98: 2
6	*t*-BuOH (1.5)	57	82	95 :5
7	BnOH (1.5)	45	74	68: 32
8	HFIP (1.5)	39	75	78: 22
9	H_2O (1.5)	42	9	56: 14
10	MeCN (1.5)	52	57	83: 17
11	EtOAc (1.5)	40	<5	50: 50
12	DMF (1.5)	25	54	50: 50

13	DMSO (1.5)	29	53	85: 15
14	NMP (1.5)	20	41	70: 30
15	Acetone (1.5)	49	37	60: 40
16	Et_2O (1.5)	32	5	55: 45
17	DBE (1.5)	22	14	50: 50
18	THF (1.5)	27	18	64: 36
19	1,4-Dioxane (1.5)	23	13	50: 50
20	DCM (1.5)	38	<5	55: 45
21	Cyclohexane (1.5)	35	5	50: 50
22	*n*-Hexane (1.5)	37	<5	43: 57
23	Toluene (1.5)	24	5	50: 50
24	EtOH (1.3)	71	89	98: 2
25	EtOH (1.1)	63	80	95: 5
26	EtOH (1.7)	61	87	96: 4

[a] Reaction conditions: **1a** (0.2 mmol), TFA (12.5 mol%), NaCl (2.0 g) were pre-milled at 20 Hz for 30 min under oxygen conditions, using two stainless-steel balls (d_{MB} = 1.2 cm) in a 25 mL stainless vial, then **2a** (4 equiv.), **C8** (10 mol%) and LAGs (η) [η = V (liquid; μL)/m (reagents; mg)] were added and milled for another 30 min. [b] Yields were those of the isolated products, *ee* values were determined by HPLC, *dr* values were determined by ^{1}H NMR. TFA = Trifluoroacetic acid; DMAE = Dimethylaminoethanol; HFIP = Hexafluoroisopropanol; DMF = *N*,*N*-Dimethylformamide; DMSO = Dimethyl sulfoxide; NMP = *N*-Methylpyrrolidone; DBE=Dibutyl ether; THF = Tetrahydrofuran; DCM = Dichloromethane.

Table S3. Screening of the additives and auxiliaries[a]

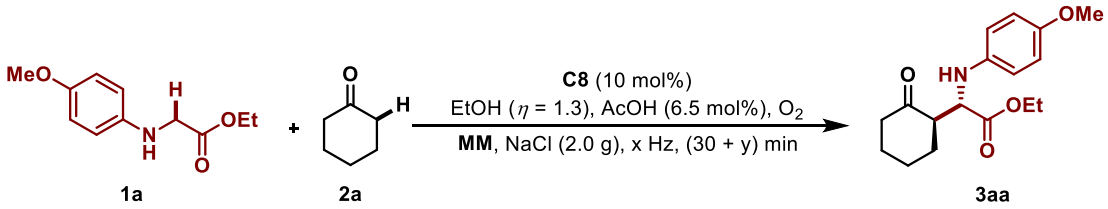


entry	additive (mol%)	auxiliary (g)	yield (%)[b]	*ee* (%)[b]	*dr*[b]
1	TFA (12.5)	NaCl (2.0)	71	89	98: 2
2	$MeSO_3H$ (12.5)	NaCl (2.0)	n.r.	–	–
3	TfOH (12.5)	NaCl (2.0)	48	80	94: 6
4	AcOH (12.5)	NaCl (2.0)	66	90	97: 3
5	AcOH (9.5)	NaCl (2.0)	69	89	97: 3
6	AcOH (6.5)	NaCl (2.0)	75	91	98: 2
7	AcOH (6.5)	Silica gel (2.0)	53	51	65: 35
8	AcOH (6.5)	Neutral Al_2O_3 (2.0)	n.r.	–	–

9	AcOH (6.5)	Na_2SO_4 (2.0)	72	85	90: 10
10	AcOH (6.5)	NaCl (1.0)	65	90	97: 3
11	AcOH (6.5)	NaCl (3.0)	66	89	97: 3

[a] Reaction conditions: **1a** (0.2 mmol), additive, and grinding auxiliary were pre-milled at 20 Hz for 30 min under oxygen conditions, using two stainless-steel balls (d_{MB} = 1.2 cm) in a 25 mL stainless vial, then **2a** (4 equiv.), **C8** (10 mol%) and EtOH (η = 1.3) were added and milled for another 30 min. [b] Yields were those of the isolated products, *ee* values were determined by HPLC, *dr* values were determined by ^{1}H NMR. n.r. = no reaction.

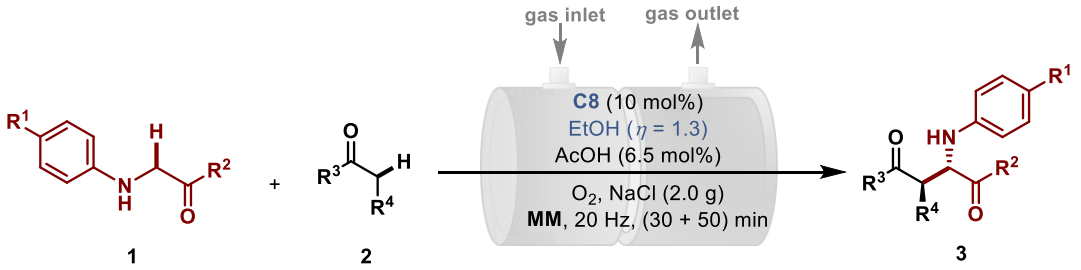
Table S4. Screening of the mechanical parameters[a]



entry	Frequency (Hz)	balls (n×mm)	time (min+min)	yield (%)[b]	*ee* (%)[b]	*dr*[b]
1	25	2×12	30+30	82	82	88: 12
2	15	2×12	30+30	54	78	76: 24
3	20	2×12	30+30	75	91	98: 2
4	20	2×12	30+40	78	93	99: 1
5	20	2×12	30+50	80	95	>99: 1
6	20	2×12	30+60	83	89	97: 3
7	20	2×14	30+50	78	85	97: 3
8	20	2×10	30+50	76	90	99: 1

[a] Reaction conditions: **1a** (0.2 mmol), AcOH (6.5 mol%), NaCl (2.0 g) were pre-milled at x Hz for 30 min under oxygen conditions, using two stainless-steel balls in a 25 mL stainless vial, then **2a** (4 equiv.), **C8** (10 mol%) and EtOH (η = 1.3) were added and milled for another y min. [b] Yields were those of the isolated products, *ee* values were determined by HPLC, *dr* values were determined by ^{1}H NMR.

2.2 Typical procedures for LAG induced asymmetric CDC reaction



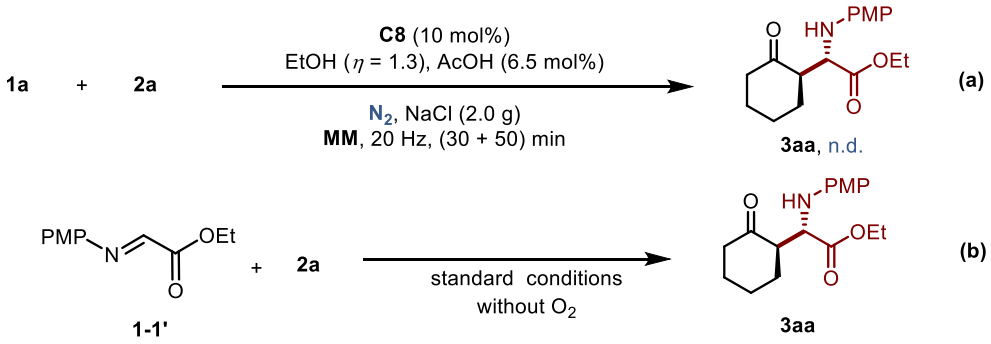
Typical procedure: a mixture of **1** (0.2 mmol), AcOH (6.5 mol%) and NaCl (2.0 g) were placed in a stainless-steel vessel (25 mL, equipped with gas inlet and outlet valve) with two stainless-steel balls (d_{MB} = 1.2 cm), and oxygen was filled in through the gas inlet valve. Then, the ball milling vessel was placed in

the mixer mill and pre-milled at 20 Hz for 30 min. After that, **2** (0.8 mmol, 4.0 equiv.), **C8** (0.02 mmol, 0.1 equiv.) and EtOH (η = 1.3) were added and oxygen was also filled in through the gas inlet valve. The mixtures were milled at 20 Hz for another 2×25 min, then the contents were scratched off the vessel and purified directly by column chromatography on silica gel using petroleum ether/EtOAc as eluent to give the desired products **3**.

The preparation procedure for **3ac**, **3ah**, **3aj**, **3ak** and **3am**, using the LAG method follows the typical procedure. After the ball-milling, the contents were rinsed with petroleum ether/EtOAc (10:1), the filtrate was concentrated and dried under vacuum to give the pure products.

3. Mechanism study

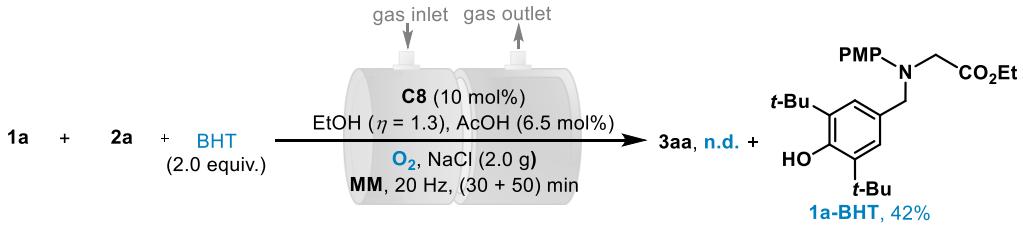
3.1 Control experiments



entry	variation from "standard conditions[a] (without O_2)"	yield (%)[b]	*ee* (%)[b]
1	--	85	82
2	without EtOH	78	70
3	without AcOH	86	90
4	without AcOH and EtOH	82	91

Reaction conditions: (a) **1a** (0.2 mmol), AcOH (6.5 mol%) and NaCl (2.0 g) were placed in a stainless-steel vessel (25 mL, equipped with gas inlet and outlet valve) with two stainless-steel balls (d_{MB} = 1.2 cm) under nitrogen atmospheres in a mixer mill and pre-milled at 20 Hz for 30 min. Then, **2a** (4.0 equiv.), **C8** (10 mol%) and EtOH (η = 1.3) were added under nitrogen atmospheres and the mixtures were milled for another 2×25 min under nitrogen atmospheres. (b) **1-1'** (0.2 mmol), AcOH (6.5 mol%) and NaCl (2.0 g) was placed in a stainless-steel vessel (25 mL) with two stainless-steel balls (d_{MB} = 1.2 cm). Then, the ball milling vessel was placed in the mixer mill and pre-milled at 20 Hz for 30 min. After that, **2a** (4.0 equiv.), **C8** (10 mol%) and EtOH (η = 1.3) were added. The mixtures were milled at 20 Hz for another 2×25 min.

3.2 Radical trapping experiments



Reaction conditions: **1a** (0.2 mmol), AcOH (6.5 mol%), BHT (2.0 equiv.) and NaCl (2.0 g) were placed in a stainless-steel vessel (25 mL, equipped with gas inlet and outlet valve) with two stainless-steel balls (d_{MB} = 1.2 cm), and oxygen was filled in through the gas inlet valve. Then, the ball milling vessel was placed in the mixer mill and pre-milled at 20 Hz for 30 min. After that, **2a** (4.0 equiv.), **C8** (10 mol%) and EtOH (η = 1.3) were added and oxygen was also filled in through the gas inlet valve. The mixtures were milled at 20 Hz for another 2×25 min.

3.3 Linear effect experiments

The reactions were conducted following the typical procedure (see section 2.2).

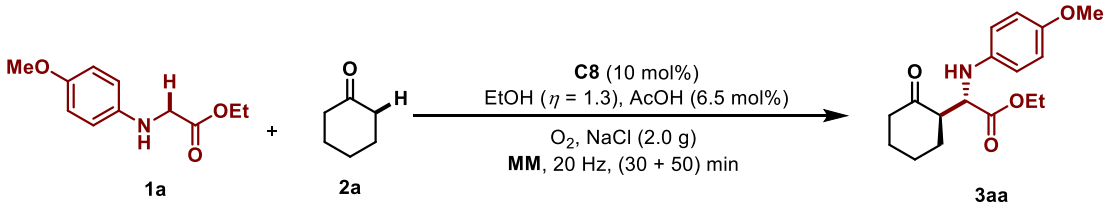


Table S5. Relationship between the *ee* values of **C8** and **3aa.**

ee % (**C8**)	0	5	15	25	30	40	50	60	75	85	99
ee % (**3aa**)	0	3	15	27	33	46	57	65	77	82	95

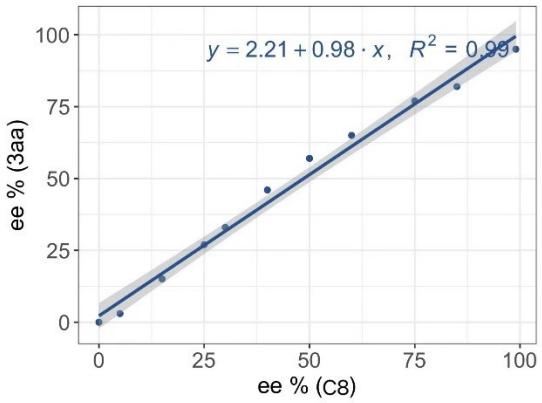
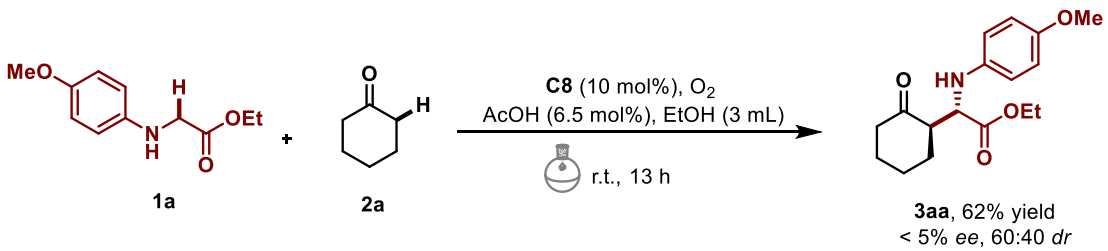


Figure S1. Relationship between the *ee* values of **C8** and **3aa**.

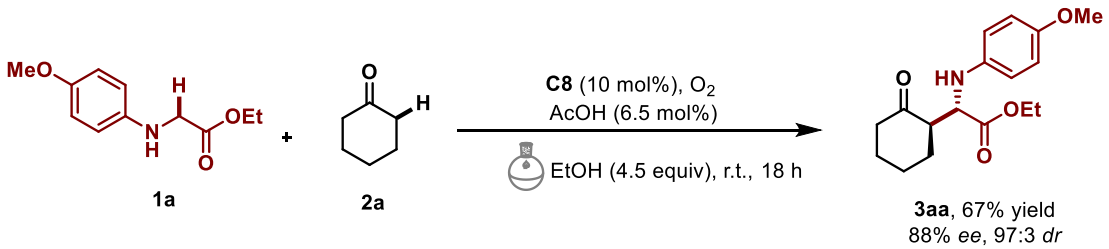
3.4 Comparative experiments

Comparative experiments under solution-based conditions.



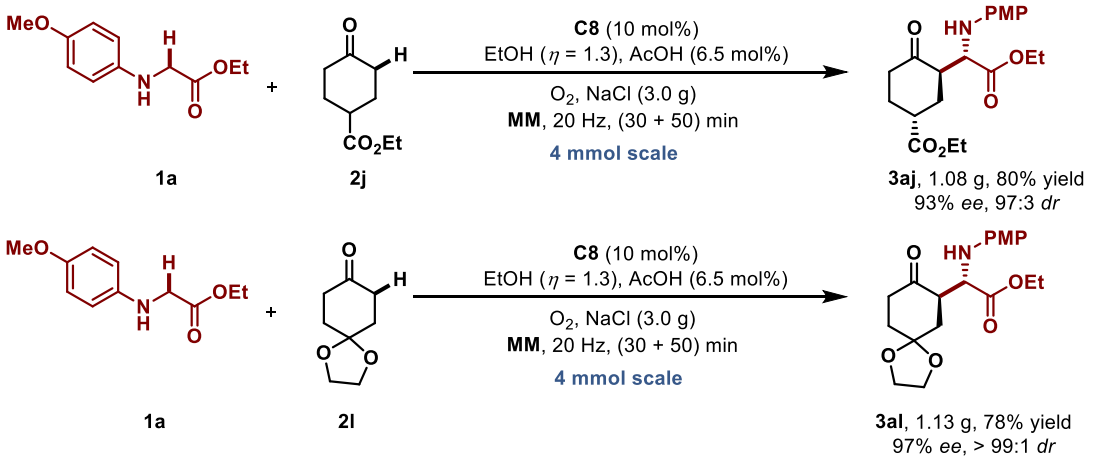
Reaction of **1a** and **2a** under solution-based conditions. Reaction conditions: **1a** (0.2 mmol) and AcOH (6.5 mol%) were placed in a flask (10 mL) with EtOH (3 mL) under oxygen atmosphere pre-stirred at rt for 6 h, then **2a** (0.8 mmol, 4.0 equiv.) and **C8** (10 mol%) were added, and the mixtures were stirring for 7 h.

Comparative experiments under neat-stirring conditions.



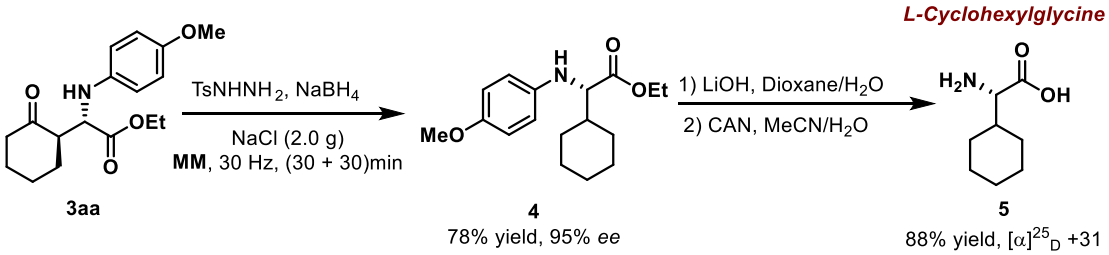
Reaction of **1a** and **2a** under neat stirring conditions. Reaction conditions: **1a** (0.2 mmol) and AcOH (6.5 mol%) were placed in a flask (10 mL) with EtOH (η = 1.3, 4.5 equiv.) under oxygen atmosphere pre-stirred at rt for 6 h, then **2a** (0.8 mmol, 4.0 equiv.) and **C8** (10 mol%) were added, and the mixtures were stirring for 12 h.

3.5 Gram-scale reactions



A mixture of **1a** (4 mmol), AcOH (6.5 mol%) and NaCl (3.0 g) were placed in a stainless-steel vessel (50 mL, equipped with gas inlet and outlet valve) with two stainless-steel balls (d_{MB} = 1.2 cm), and oxygen was filled in through the gas inlet valve. Then, the ball milling vessel was placed in the mixer mill and pre-milled at 20 Hz for 30 min. After that, **2j** (4.0 equiv.) or **2k** (4.0 equiv.), **C8** (10 mmol%) and EtOH (η = 1.3) were added and oxygen was also filled in through the gas inlet valve. The mixtures were milled at 20 Hz for another 2×25 min. *After the ball-milling, the contents were rinsed with petroleum ether/EtOAc (10:1), the filtrate was concentrated and dried under vacuum to give **3aj** (1.08 g) or **3al** (1.13 g).*

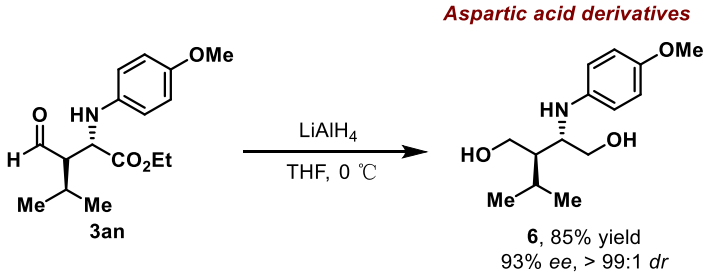
3.6 Synthetic applications



Step1: A mixture of **3aa** (500 mg, 1.637 mmol), tosylhydrazine (427 mg, 1.4 equiv.) and NaCl (2.0 g) were placed in a stainless-steel vessel (25 mL) with two stainless-steel balls (d_{MB} = 1.2 cm). Then, the ball milling vessel was placed in the mixer mill and milled at 30 Hz for 30 min. After that, $NaBH_4$ (620 mg)

were added and the mixtures were milled at 30 Hz for 30 min, then the contents were scratched off the vessel, then brine was added and the mixture was extracted with EtOAc. The combined organic layers were dried and concentrated, and the residue was purified by flash column chromatography to afford ethyl (*R*)-*N*-(*p*-methoxyphenyl)-cyclohexylglycinate **4** in 78% yield with 95% *ee*.

Step2: To a solution of **4** (291 mg, 1.0 mmol) in dioxane/water (14 mL, 1:1) was added LiOH (280 mg) and the mixture was stirred at room temperature for 14 h. Then, the mixture was acidified with 1 N HCl and extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. Purification of the residue by flash column chromatography afforded known *N*-PMP-protected cyclohexylglycine. The solution of ceric ammonium nitrate (CAN, 1.1 g, 2 mmol, 2.5 equiv.) distilled water (8.0 mL) was added slowly to the stirred solution of *N*-PMP-protected cyclohexylglycine (200 mg, 0.81 mmol) in MeCN/H_2O (3/1, 16.0 mL) at 0 °C. The reaction mixture was further stirred at 0℃ for about 1 h, till the reaction completed as monitored by TLC. The reaction was then quenched by adding the saturated Na_2SO_4 solution and extracted with EtOAc. The combined organic layer was extracted with 0.1 M HCl. The combine aqueous layer was neutralized by $NaHCO_3$ (pH = 7) and extracted with EtOAc. The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure, product **5** (138.2 mg, 88% yield) was afforded without further purification.



A solution of **3an** (118 mg, 0.4 mmol) in THF (20 mL) was cooled to 0 °C and $LiAH_4$ (10 mL, 1 M solution in THF) was added. After stirring for 30 min, the ice-bath was removed and the mixture was stirred for 1.5 h at room temperature. The mixture was quenched by careful addition of aqueous NH_4Cl solution, followed by 3 M HCl, and then extracted with EtOAc. The combined organic layers were dried, filtered, and concentrated. Purification of the residue by flash column chromatography afforded (2*R*,3*S*)-2-isopropyl-3-((4-methoxyphenyl)amino)butane-1,4-diol **6** (86 mg, 85% yield, 93% *ee*, >99:1 *dr*) as pale yellow oil.

3.7 Recycling of grinding auxiliary (NaCl) and C8

After the reaction was completed (see section 2.2), the mixtures were dissolved in EtOAc, then filtered to give the recovered NaCl as offwhite solid, which can be directly used for the next reaction after drying under reduced pressure. *No additional acetic acid or **C8** was required when using the recovered NaCl for a fresh reaction, which implies the chiral catalyst can be simultaneously recovered with NaCl, and its inherent acidity was enough to promote the aerobic oxidation of glycinate*.

For the synthesis of **3aa**, NaCl along with **C8** can be recycled and reused for at least 5 times and its recovery yields (mass of recovered solid g/2.0 g) were ranging from 96% to 99%. The average consumption of NaCl for single reaction is 16 mg. (*Fresh NaCl was added to keep its mass at 2.0 g for each reaction.*)

Table S6. Recycling and recovery of NaCl and **C8**.

Recovery of NaCl and **C8** (g)	*ee* (%)	Yield (%)	*dr* (n:1)

Run 1	1.98	93	78	99
Run 2	1.97	92	77	99
Run 3	1.95	92	79	99
Run 4	1.94	91	77	99
Run 5	1.92	91	76	98

3.8. Green chemistry metrics evaluation

The green chemistry metrics including Effective Mass Yield (EMY), Atom Economy (AE), Atom Efficiency (AEF), Reaction Mass Efficiency (RME), Optimum Efficiency (OE), Process Mass Intensity (PMI), Mass Intensity (MI), Mass Productivity (MP), *E*-factor, and Solvent Intensity (SI), were calculated according to the reported method. [1] EcoScale was also calculated according to the reported method.[2]

Based on the mechanochemical LAG method, the green chemistry metrics were calculated as follows （all the calculations are made on the basis that NaCl and **C8** can be recovered for five times）:

$$\text{E factor} = \frac{\sum m\,(\text{reactants}) + \sum m\,(\text{reagents}) + \sum m\,(\text{solvent}) + \sum m\,(\text{additives}) - \sum m\,(\text{products})}{\sum m\,(\text{products})}$$

$$= \frac{39.04 + 78.52 + 0.23 + 44.90 + 0.525 + 16 - 46.03}{46.03} = 2.89$$

$$\text{RME} = \frac{\sum m\,(\text{products})}{\sum m\,(\text{reactants})} \times 100\% = \frac{46.03}{39.04 + 78.52} \times 100\% = 39.15\%$$

$$\text{EMY} = \frac{\sum m\,(\text{products})}{\sum m\,(\text{toxic reagents})} \times 100\% = \frac{46.03}{39.04 + 78.52 + 0.23 + 44.90 + 0.525 + 16} \times 100\% = 25.68\%$$

$$\text{AE} = \frac{\sum \text{MW}\,(\text{products})}{\sum \text{MW}\,(\text{reactants})} \times 100\% = \frac{291.35}{195.22 + 98.15 \times 4} = 49.56\%$$

$$\text{AEF} = \text{AE} \times Yield\% = 49.56\% \times 79\% = 39.15\%$$

$$\text{OE} = \frac{\text{RME}}{\text{AE}} \times 100\% = \frac{39.15}{49.56} = 80.00\%$$

$$\text{PMI} = \frac{\sum m\,(\text{reactants}) + \sum m\,(\text{reagents}) + \sum m\,(\text{solvents}) + \sum m\,(\text{additives})}{\sum m\,(\text{products})}$$

$$= \frac{39.04 + 78.52 + 0.23 + 44.90 + 0.525 + 16}{46.03} = 3.89$$

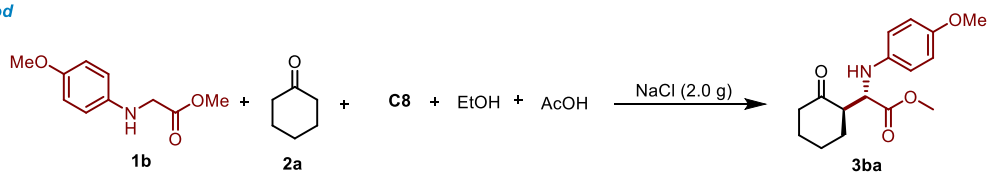
$$\text{MI} = \frac{\sum m\,(\text{reactants}) + \sum m\,(\text{reagents}) + \sum m\,(\text{solvents (except water)}) + \sum m\,(\text{additives})}{\sum m\,(\text{products})}$$

$$= \frac{39.04 + 78.52 + 0.23 + 44.90 + 0.525 + 16}{46.03} = 3.89$$

$$MP = \frac{1}{MI} \times 100\% = \frac{1}{3.89} = 25.69\%$$

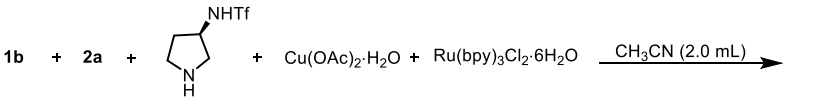
$$SI = \frac{\sum m\ (\text{solvents}\ \ (\text{except water})\ )}{\sum m\ (\text{products})} = \frac{44.90}{46.03} = 0.98$$

LAG method



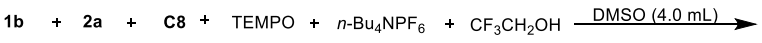
MW	195.22	98.15	115.13	46.07	60.05		291.35
n/mmol	0.20	0.80	0.01		0.013		96% *ee*
m/mg	39.04	78.52	1.15	44.90	1.05	2000	46.03 mg, 79% yield

Zhang's method



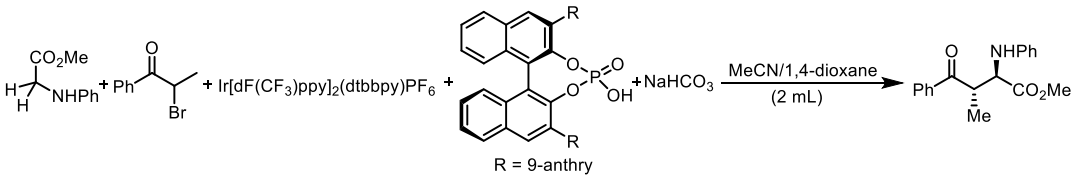
MW	195.22	98.15	218.19	199.65	623.10	41.052	291.35
n/mmol	0.10	0.50	0.02	0.01	0.005		96% *ee*
m/mg	19.52	49.08	4.36	1.99	3.12	1572	22.73 mg, 78% yield

Mei's method



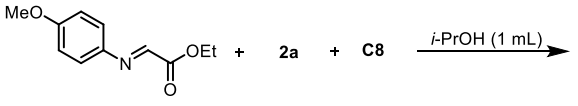
MW	195.22	98.15	115.13	156.25	387.43	100.04	78.13	291.35
n/mmol	0.20	1.00	0.04	0.04	0.40	0.20		89% *ee*
m/mg	39.04	98.15	4.61	6.25	154.97	20.00	4400	34.96 mg, 60% yield

Wang's method



MW	165.19	213.07	1121.91	700.73	84.01		297.35
n/mmol	0.20	0.60	0.004	0.02	0.22		97% *ee*
m/mg	41.85	127.84	4.49	14.01	18.48	1819	51.14 mg, 86% yield

Tanaka's method



MW	207.22	98.15	115.13	60.10	305.37
n/mmol	0.50	5.00	0.05		96% *ee*
m/mg	103.61	490.75	5.76	785	146.58 mg, 96% yield

Table S7. Comparison of green chemistry metrics.

Entry		LAG method	Zhang's work	Mei's work	Wang's work	Tanaka's work
Product	Yield (%)	79	78	60	86	96

	ee (%)	96	96	89	97	96
	dr	>99:1	97:3	>99:1	>20:1	>99:1
Effective Mass Yield	EMY (%)	25.68	1.39	0.74	2.52	10.58
Atom Economy	AE (%)	49.56	42.47	42.47	36.97	25.69
Atom Efficiency	AEF (%)	39.15	33.13	25.48	31.79	24.66
Reaction Mass Efficiency	RME (%)	39.15	33.13	25.48	30.14	24.66
Optimum Efficiency	OE (%)	79.00	78.01	60.00	81.53	96.00
Process Mass Intensity	PMI	3.89	71.74	135.10	39.61	9.45
Mass Intensity	MI	3.55	69.16	135.10	39.61	9.45
Mass Productivity	MP (%)	25.69	1.45	0.74	2.52	10.58
E-Factor	*E*-Factor	2.89	70.74	134.10	38.61	8.45
Solvent Intensity	SI	0.98	69.16	125.86	35.57	5.36
Reaction Time	h	1.33	>3	8	24	12

Table S8. Calculation of eco-scale score of LAG method for the preparation of **3ba**.

<table>
<tr><th colspan="3">Parameters</th><th>Penalty points (LAG method)</th></tr>
<tr><td colspan="3">1. Yield (100-x)/2
Mechanochemical synthesis: 79%</td><td>10.5</td></tr>
<tr><td colspan="3">2. Price of reaction components (to obtain 10 mmol of end product)</td><td rowspan="8"></td></tr>
<tr><td>Reaction components to get 10 mmol of product</td><td>Price/g or mL</td><td>Price to get 10 mmol of product</td></tr>
<tr><td>a. 1c (2.471 g)</td><td></td><td></td></tr>
<tr><td>b. 2a (5.215 mL)</td><td>0.08</td><td>0.42</td></tr>
<tr><td>c. C8 (0.0146 g)</td><td>112.70</td><td>1.646</td></tr>
<tr><td>d. EtOH (3.6 mL)</td><td>0.063</td><td>0.23</td></tr>
<tr><td>e. AcOH (0.0126 mL)</td><td>0.020</td><td>0.00026</td></tr>
<tr><td>f. NaCl (25.32 g)</td><td>0.012</td><td>0.304</td></tr>
<tr><td colspan="3">total price (Mechanochemical synthesis) = $2.596
Expensive (> $10 and <$50)</td><td>0</td></tr>
<tr><td colspan="3">3. Safety
EtOH (F, highly flammable)</td><td>5</td></tr>
<tr><td colspan="3">4. Technical setup
Mechanochemical synthesis:
Unconventional activation technique (mechanial activation)</td><td>2</td></tr>
<tr><td colspan="3">5. Temperature/Time
Mechanochemical synthesis: Room temperature, <24 h</td><td>1</td></tr>
<tr><td colspan="3">6. Workup and purification
Mechanochemical synthesis: Classical chromatography</td><td>0</td></tr>
</table>

Total	**19.5**
Eco-scale score	**81.5**

Table S9. Calculation of eco-scale score of Zhang's method for the preparation of **3ba**.

Parameters			**Penalty points (Zhang's method)**
1. Yield (100-x)/2 Synthesis: 78%			**11**
2. Price of reaction components (to obtain 10 mmol of end product)			
Reaction components to get 10 mmol of product	**Price/g or mL**	**Price to get 10 mmol of product**	
a. **1c** (2.502 g)			
b. **2a** (6.601 mL)	101.44	253.80	
c. $C_5H_9F_3N_2O_2S$ (0.559 g)	0.08	0.53	
d. $Cu(OAc)_2·H_2O$ (0.255 g)	0.039	0.01	
e. $Ru(bpy)_3Cl_2·6H_2O$ (0.400 g)	18.80	7.52	
f. MeCN (256.6 mL)	0.0083	2.14	
total price (Mechanochemical synthesis) = \$264 **Very expensive (> \$50)**			**5**
3. Safety a. $Cu(OAc)_2·H_2O$ (N, dangerous for environment) b. MeCN (T, toxic) c. MeCN (F+, extremely flammable)			**5** **5** **10**
4. Technical setup Photocatalytic synthesis: Unconventional activation technique (photochemical activation)			**2**
5. Temperature/Time Photocatalytic synthesis: Room temperature, <24 h			**1**
6. Workup and purification Photocatalytic synthesis: Classical chromatography			**0**
Total			**39**
Eco-scale score			**61**

Table S10. Calculation of eco-scale score of Mei's method for the preparation of **3ba**.

Parameters			**Penalty points (Mei's method)**
1. Yield (100-x)/2 Synthesis: 60%			**20**
2. Price of reaction components (to obtain 10 mmol of end product)			
Reaction components	**Price/g or mL**	**Price to get 10**	

to get 10 mmol of product		**mmol of product**	
a. **1c** (3.254 g)			
b. **2a** (8.583 mL)	0.08	0.68	
c. **L8** (0.384 g)	112.70	43.27	
d. TEMPO (0.521 g)	3.0596	1.59	
e. *n*-Bu_4NPF_6 (12.915 g)	0.667	8.62	
f. CF_3CH_2OH (1.667 g)	4.1722	6.95	
g. DMSO (333.4 mL)	0.0092	3.06	
total price (Mechanochemical synthesis) = \$64.17 Very expensive (> \$50)			**5**
3. Safety			
a. CF_3CH_2OH (T, toxic)			**5**
b. CF_3CH_2OH (F, highly flammable)			**5**
c. DMSO (T, toxic)			**5**
d. DMSO (F+, extremely flammable)			**10**
4. Technical setup Electrochemical synthesis: Unconventional activation technique (electrical activation)			**2**
5. Temperature/Time Electrochemical synthesis: Room temperature, <24 h			**1**
6. Workup and purification Electrochemical synthesis: Classical chromatography			**0**
Total			**53**
Eco-scale score			**47**

Table S11. Calculation of eco-scale score of Wang's method.

Parameters			**Penalty points (Wang's method)**
1. Yield (100-x)/2 Synthesis: 86%			**7**
2. Price of reaction components (to obtain 10 mmol of end product)			
Reaction components to get 10 mmol of product	**Price/g or mL**	**Price to get 10 mmol of product**	
a. $C_9H_{11}NO_2$ (2.433 g)	0.4033	0.98	
b. C_9H_9Br (7.4333 g)			
c. $Ir[dF(CF_3)ppy]_2$ (dtb bpy)PF_6 (0.261 g)	237.65	62.03	
d. Ligand (0.815 g)	624.30	508.80	
e. $NaHCO_3$ (1.074 g)	0.0042	0.0045	
f. MeCN (58.14 mL)	0.0083	0.48	
g. 1,4-dioxane (58.14 mL)	0.0078	0.45	

total price (Mechanochemical synthesis) = $686.47 Very expensive (> $50)	**5**
3. Safety a. MeCN (T, toxic) b. MeCN (F+, extremely flammable) c. 1,4-dioxane (F, highly flammable)	 **5** **10** **5**
4. Technical setup Photocatalytic synthesis: Unconventional activation technique (photochemical activation)	 **2**
5. Temperature/Time Photocatalytic synthesis: Room temperature, <24 h	 **1**
6. Workup and purification Photocatalytic synthesis: Classical chromatography	 **0**
Total	**35**
Eco-scale score	**65**

Table S12. Calculation of eco-scale score of Tanaka's method.

Parameters			**Penalty points (Tanaka's method)**
1. Yield (100-x)/2 Synthesis: 96%			 **2**
2. Price of reaction components (to obtain 10 mmol of end product)			
Reaction components to get 10 mmol of product	**Price/g or mL**	**Price to get 10 mmol of product**	
a. $C_{11}H_{13}NO_3$ (2.158 g)			
b. **2a** (10.73 mL)	0.08	0.86	
c. **C8** (0.112 g)	112.70	12.62	
d. *i*-PrOH (3 mL)	0.005	0.10	
total price (Mechanochemical synthesis) = $13.58 Expensive (> $10 and <$50)			**3**
3.Safety *i*-PrOH (F, highly flammable)			 **5**
4. Technical setup: Solution synthesis: Common setup			 **0**
5. Temperature/Time Solution synthesis: Room temperature, <24 h			 **1**
6. Workup and purification Solution synthesis: Classical chromatography			 **0**
Total			**11**
Eco-scale score			**89**

3.9 Crystal data for 3ha.

Single crystal of minor diastereomers of **3ha** suitable for X-ray analysis was obtained by slow evaporation of 0.01 M solution in 7:3 mixture of petroleum ether/ ethyl acetate at room temperature. A suitable crystal was selected on a Bruker APEX-II CCD diffractometer. The crystal was kept at 296.15 K during data collection. Using Olex2,[3] the structure was solved with the SHELXT[4] structure solution program using Intrinsic Phasing and refined with the SHELXT refinement package using Least Squares minimisation.

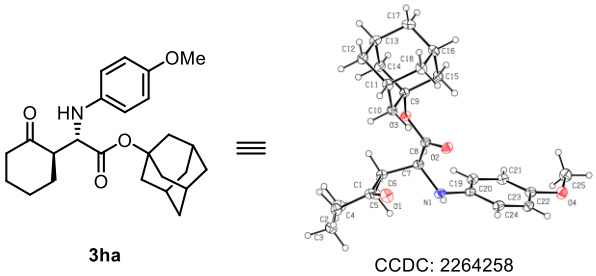


Table S13. Crystal data and structure refinement for compound **3ha**.

Identification code	cu_230519_CH_3ka_0m
Empirical formula	$C_{25}H_{33}NO_4$
Formula weight	411.52
Temperature/K	170.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.82470(10)
b/Å	15.1975(3)
c/Å	20.6745(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2144.33(7)
Z	4
ρ_{calc}g/cm^3	1.275
μ/mm^{-1}	0.682
F(000)	888.0
Crystal size/mm^3	0.48 × 0.26 × 0.2
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.218 to 149.136
Index ranges	-8 ≤ h ≤ 7, -19 ≤ k ≤ 19, -25 ≤ l ≤ 25
Reflections collected	22064
Independent reflections	4363 [R_{int} = 0.0621, R_{sigma} = 0.0384]
Data/restraints/parameters	4363/1/275
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0407, wR_2 = 0.1041

Final R indexes [all data]	R_1 = 0.0464, wR_2 = 0.1077
Largest diff. peak/hole / e Å^{-3}	0.25/-0.21
Flack parameter	-0.12(12)

Table S14. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for cu_230519_CH_3ka_0m. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	x	y	z	U(eq)
O1	6185(3)	3537.6(14)	5434.7(11)	41.4(5)
O2	6052(3)	5381.0(13)	4782.1(8)	34.3(4)
O3	4854(2)	5660.5(11)	5785.7(8)	27.8(3)
O4	-764(3)	5649.6(14)	2380.5(9)	38.0(4)
N1	3115(3)	4213.0(14)	4516.1(10)	30.2(4)
C1	4722(3)	3389.9(16)	5744.8(12)	27.6(5)
C2	4586(4)	2621.7(18)	6204.1(13)	35.7(6)
C3	2669(4)	2112.7(17)	6138.7(14)	35.8(5)
C4	922(4)	2738.8(18)	6187.8(14)	37.3(6)
C5	1036(4)	3439.4(17)	5660.5(14)	35.1(5)
C6	2933(3)	3984.6(14)	5701.9(11)	25.7(4)
C7	3101(3)	4649.9(15)	5144.8(11)	26.4(4)
C8	4873(3)	5262.9(15)	5203.8(11)	26.6(4)
C9	6514(3)	6206.5(15)	6002.7(11)	24.2(4)
C10	8341(3)	5636.7(15)	6070.8(11)	27.5(5)
C11	9989(4)	6202.0(17)	6366.5(12)	30.4(5)
C12	9347(4)	6533.4(19)	7034.4(12)	35.1(5)
C13	7510(4)	7102.6(18)	6959.8(12)	34.1(5)
C14	5858(4)	6540.2(17)	6664.5(11)	29.4(5)
C15	6903(4)	6987.6(15)	5552.6(12)	27.7(5)
C16	8560(4)	7546.2(16)	5848.3(13)	32.0(5)
C17	7949(4)	7882.2(17)	6513.9(14)	36.9(6)
C18	10407(4)	6979.1(17)	5915.5(13)	33.2(5)
C19	2094(3)	4598.6(15)	3997.2(12)	27.5(4)
C20	205(4)	4932.4(16)	4061.6(12)	30.0(5)
C21	-804(3)	5283.5(17)	3536.0(12)	29.8(5)
C22	76(4)	5298.3(16)	2931.0(12)	29.5(5)
C23	1936(4)	4940.2(17)	2852.0(12)	32.3(5)
C24	2929(4)	4603.7(16)	3380.0(12)	31.0(5)
C25	-2535(4)	6115(2)	2461.8(15)	42.3(6)

Table S15. Anisotropic Displacement Parameters ($Å^2×10^3$) for cu_230519_CH_3ka_0m. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	23.6(9)	47.8(11)	52.7(11)	6.9(9)	5.8(8)	5.3(8)
O2	32.7(9)	39.4(9)	30.8(8)	-4.9(7)	7.4(7)	-3.2(8)
O3	24.8(8)	31.8(8)	26.8(7)	-4.8(6)	3.4(6)	-3.6(7)
O4	36.8(10)	44.4(10)	32.9(8)	0.7(8)	-3.0(8)	11.3(8)
N1	28.0(10)	31.6(9)	31.0(10)	-7.7(8)	-2.7(8)	6.3(8)
C1	20.8(11)	31.1(11)	30.8(10)	-4.3(9)	-2.5(9)	0.5(9)
C2	31.1(13)	36.9(13)	38.9(13)	3.4(10)	-1.2(10)	4.9(10)
C3	37.0(14)	29.6(11)	40.8(13)	0.3(10)	2.8(11)	0.7(10)
C4	27.3(12)	34.4(13)	50.1(15)	-3.5(11)	7.0(11)	-3.6(10)
C5	20.6(11)	30.4(12)	54.4(15)	-1.7(11)	0.0(10)	-0.1(9)
C6	19.7(10)	26.4(10)	31.1(10)	-5.1(8)	3.2(8)	-1.0(8)
C7	21.5(10)	27.9(10)	29.7(11)	-4.2(9)	0.1(8)	4.0(9)
C8	26.0(11)	26.2(10)	27.5(10)	-3.3(8)	0.0(9)	2.9(9)
C9	21.6(10)	25.9(10)	25.2(10)	-3.0(8)	1.3(8)	-0.1(8)
C10	27.9(11)	23.9(10)	30.8(10)	1.0(8)	1.9(9)	2.5(9)
C11	22.9(11)	33.4(12)	34.8(12)	2.2(9)	-1.7(10)	5.0(10)
C12	32.8(13)	42.0(13)	30.5(12)	-0.1(10)	-7.6(10)	0.9(11)
C13	30.9(13)	39.0(13)	32.3(12)	-9.2(10)	-1.2(10)	2.4(10)
C14	24.3(10)	35.9(12)	28.1(10)	-4.5(9)	1.8(9)	1.1(9)
C15	25.2(11)	26.6(10)	31.1(11)	2.6(8)	-2.2(9)	0.6(9)
C16	30.6(12)	25.2(10)	40.3(13)	4.0(9)	-3.0(10)	-2.5(9)
C17	32.3(13)	28.4(12)	50.1(15)	-9.1(10)	-7.4(12)	2.8(10)
C18	22.7(12)	35.6(12)	41.4(13)	2.6(10)	1.2(10)	-2.5(9)
C19	24.8(10)	25.2(10)	32.5(11)	-6.8(8)	-2.6(9)	-3.6(9)
C20	24.6(11)	34.8(11)	30.7(11)	-2.6(9)	1.2(9)	-1.9(9)
C21	20.0(10)	33.8(12)	35.6(12)	-5.3(9)	-0.1(9)	1.2(9)
C22	25.8(11)	30.7(11)	31.9(11)	-3.5(9)	-3.9(9)	0.0(9)
C23	31.0(13)	36.7(12)	29.2(11)	-6.1(9)	2.8(10)	3.5(10)
C24	24.3(10)	33.7(11)	35.1(12)	-7.5(9)	-0.2(9)	3.0(10)
C25	36.9(14)	46.3(15)	43.7(14)	1.8(12)	-4.0(11)	11.1(11)

Table S16. Bond Lengths for cu_230519_CH_3ka_0m.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.207(3)	C9	C14	1.526(3)
O2	C8	1.200(3)	C9	C15	1.531(3)
O3	C8	1.346(3)	C10	C11	1.541(3)

Table S16 continued. Bond Lengths for cu_230519_CH_3ka_0m.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O3	C9	1.474(3)	C9	C14	1.526(3)
O4	C22	1.382(3)	C9	C15	1.531(3)
O4	C25	1.411(3)	C10	C11	1.541(3)
N1	C7	1.460(3)	C11	C12	1.534(3)
N1	C19	1.407(3)	C11	C18	1.531(3)
C1	C2	1.508(3)	C12	C13	1.531(4)
C1	C6	1.521(3)	C13	C14	1.541(3)
C2	C3	1.526(4)	C13	C17	1.531(4)
C3	C4	1.529(4)	C15	C16	1.541(3)
C4	C5	1.526(4)	C16	C17	1.526(4)
C5	C6	1.539(3)	C16	C18	1.533(3)
C6	C7	1.537(3)	C19	C20	1.392(3)
C6	C7	1.537(3)	C19	C24	1.398(3)

Table S17. Bond Angles for cu_230519_CH_3ka_0m.

Atom	Atom	Atom	Length/Å	Atom	Atom	Atom	Length/Å
C8	O3	C9	121.16(18)	C9	C10	C11	108.48(18)
C22	O4	C25	116.8(2)	C12	C11	C10	109.4(2)
C19	N1	C7	119.10(19)	C18	C11	C10	108.92(19)
O1	C1	C2	122.0(2)	C18	C11	C12	110.4(2)
O1	C1	C6	121.5(2)	C13	C12	C11	109.2(2)
C2	C1	C6	116.6(2)	C12	C13	C14	109.0(2)
C1	C2	C3	112.9(2)	C17	C13	C12	109.7(2)
C2	C3	C4	110.3(2)	C17	C13	C14	109.5(2)
C5	C4	C3	110.3(2)	C9	C14	C13	108.97(19)
C4	C5	C6	112.3(2)	C9	C15	C16	108.27(19)
C1	C6	C5	111.00(18)	C17	C16	C15	110.0(2)
C1	C6	C7	112.01(19)	C17	C16	C18	109.3(2)
C7	C6	C5	112.0(2)	C18	C16	C15	109.3(2)
N1	C7	C6	111.62(19)	C16	C17	C13	109.7(2)
N1	C7	C8	110.04(19)	C11	C18	C16	109.6(2)
C8	C7	C6	113.55(18)	C20	C19	N1	122.5(2)
O2	C8	O3	126.0(2)	C20	C19	C24	117.6(2)
O2	C8	C7	124.2(2)	C24	C19	N1	119.8(2)
O3	C8	C7	109.68(19)	C19	C20	C21	121.5(2)
O3	C9	C10	109.69(17)	C22	C21	C20	119.7(2)
O3	C9	C14	103.57(17)	O4	C22	C21	124.7(2)
O3	C9	C15	112.63(18)	O4	C22	C23	115.7(2)
C10	C9	C14	110.22(19)	C21	C22	C23	119.6(2)
C10	C9	C15	110.75(18)	C24	C23	C22	119.9(2)
C14	C9	C15	109.75(19)	C23	C24	C19	121.5(2)

Table S18. Torsion Angles for cu_230519_CH_3ka_0m.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
O1	C1	C2	C3	-134.7(3)	C9	C15	C16	C17	-60.2(2)
O1	C1	C6	C5	136.6(3)	C9	C15	C16	C18	59.8(3)
O1	C1	C6	C7	10.6(3)	C10	C9	C14	C13	60.8(3)
O3	C9	C10	C11	-174.07(17)	C10	C9	C15	C16	-60.6(2)
O3	C9	C14	C13	178.12(19)	C10	C11	C12	C13	-61.0(3)
O3	C9	C15	C16	176.10(18)	C10	C11	C18	C16	61.1(3)
O4	C22	C23	C24	177.5(2)	C11	C12	C13	C14	60.7(3)
N1	C7	C8	O2	2.2(3)	C11	C12	C13	C17	-59.2(3)
N1	C7	C8	O3	-179.75(19)	C12	C11	C18	C16	-59.0(3)
N1	C19	C20	C21	-177.7(2)	C12	C13	C14	C9	-60.3(3)
N1	C19	C24	C23	177.0(2)	C12	C13	C17	C16	60.5(3)
C1	C2	C3	C4	-52.4(3)	C14	C9	C10	C11	-60.6(2)
C1	C6	C7	N1	65.2(2)	C14	C9	C15	C16	61.3(2)
C1	C6	C7	C8	-59.9(2)	C14	C13	C17	C16	-59.1(3)
C2	C1	C6	C5	-44.7(3)	C15	C9	C10	C11	61.0(2)
C2	C1	C6	C7	-170.7(2)	C15	C9	C14	C13	-61.4(2)
C2	C3	C4	C5	58.9(3)	C15	C16	C17	C13	59.7(3)
C3	C4	C5	C6	-58.9(3)	C15	C16	C18	C11	-61.0(3)
C4	C5	C6	C1	50.4(3)	C17	C13	C14	C9	59.8(3)
C4	C5	C6	C7	176.4(2)	C17	C16	C18	C11	59.4(3)
C5	C6	C7	N1	-60.3(2)	C18	C11	C12	C13	58.8(3)
C5	C6	C7	C8	174.62(19)	C18	C16	C17	C13	-60.3(3)
C6	C1	C2	C3	46.6(3)	C19	N1	C7	C6	140.8(2)
C6	C7	C8	O2	128.1(2)	C19	N1	C7	C8	-92.2(2)
C6	C7	C8	O3	-53.8(2)	C19	C20	C21	C22	0.5(4)
C7	N1	C19	C20	-45.3(3)	C20	C19	C24	C23	1.0(4)
C7	N1	C19	C24	138.9(2)	C20	C21	C22	O4	-178.3(2)
C8	O3	C9	C10	-63.9(3)	C20	C21	C22	C23	1.8(4)
C8	O3	C9	C14	178.4(2)	C21	C22	C23	C24	-2.5(4)
C8	O3	C9	C15	59.9(3)	C22	C23	C24	C19	1.1(4)
C9	O3	C8	O2	-9.3(4)	C24	C19	C20	C21	-1.8(3)
C9	O3	C8	C7	172.71(18)	C25	O4	C22	C21	7.8(4)
C9	C10	C11	C12	60.4(2)	C25	O4	C22	C23	-172.2(2)
C9	C10	C11	C18	-60.3(2)					

Table S19. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for cu_230519_CH_3ka_0m.

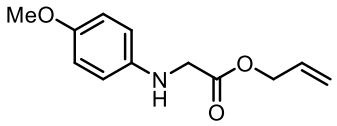
Atom	x	y	z	U(eq)
H2A	4708	2840.48	6653.34	43
H2B	5695.23	2217.11	6121.83	43

Table S19 continued. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for cu_230519_CH_3ka_0m.

Atom	x	y	z	U(eq)
H3A	2584.32	1663.94	6484.7	43
H3B	2638.27	1805.63	5716.52	43
H4A	-311.54	2402.14	6141.7	45
H4B	918.4	3025.03	6617.9	45
H5A	-105.11	3837.82	5699.76	42
H5B	967.41	3150.87	5231.78	42
H6	2873.24	4329.79	6113.14	31
H7	1902.77	5027.83	5159.69	32
H10A	8748.83	5412.86	5641.73	33
H10B	8062.66	5126.7	6354.16	33
H11	11200.43	5837.14	6412.86	36
H12A	9062.99	6027.18	7320.93	42
H12B	10411.96	6883.59	7232.78	42
H13	7091.7	7325.15	7393.57	41
H14A	5563.09	6036.11	6951.71	35
H14B	4653.96	6898.23	6618.65	35
H15A	5701.06	7346.87	5506.15	33
H15B	7292.67	6774.01	5118.93	33
H16	8842.81	8057.72	5558.66	38
H17A	6769.35	8257	6472.85	44
H17B	9015.22	8243.24	6701.12	44
H18A	10811.41	6758.5	5485.19	40
H18B	11490.61	7338.19	6093.57	40
H20	-410.3	4920.56	4473.72	36
H21	-2089.05	5511.87	3591.44	36
H23	2524.33	4926.79	2435.66	39
H24	4208.01	4370.63	3321.8	37
H25A	-2917.09	6383.82	2049.66	63
H25B	-2354.72	6576.61	2787.65	63
H25C	-3563.17	5709.27	2604.47	63
H1	4320(40)	4090(30)	4400(18)	51

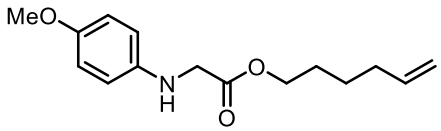
4. Characterization data

For substrates 1:



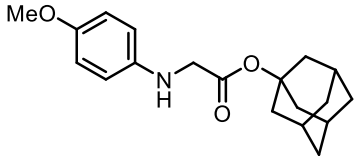
Allyl (4-methoxyphenyl)glycinate (**1e**)[5]

Yellow oil (375.7 mg, 85% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.79 (d, *J* = 8.9 Hz, 2H), 6.59 (d, *J* = 8.9 Hz, 2H), 6.01–5.83 (m, 1H), 5.35–5.24 (m, 2H), 4.67–4.66 (m, 2H), 3.90 (s, 2H), 3.74 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 171.06, 152.61, 141.10, 131.58, 118.74, 114.83, 114.35, 65.68, 55.63, 46.69.



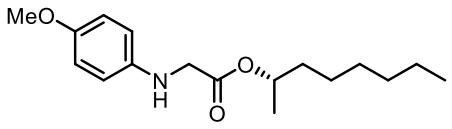
Hex-5-en-1-yl (4-methoxyphenyl)glycinate (**1f**)

Colorless oil (432.3 mg, 82% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.79 (d, *J* = 9.0 Hz, 2H), 6.58 (d, *J* = 8.9 Hz, 2H), 5.83–5.72 (m, 1H), 5.04–4.95 (m, 2H), 4.17 (t, *J* = 6.6 Hz, 2H), 3.86 (s, 2H), 3.74 (s, 3H), 2.10–2.04 (m, 2H), 1.70–1.62 (m, 2H), 1.44 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 171.44, 152.59, 141.23, 138.15, 114.86, 114.32, 65.06, 55.67, 46.75, 33.15, 27.94, 25.01. **HRMS (ESI)** *m/z*: calcd for $C_{15}H_{22}NO_3$ $[M+H]^+$ 264.1594, found 264.1593.



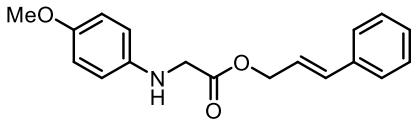
(1S,3S)-Adamantan-1-yl (4-methoxyphenyl)glycinate (**1h**)

White solid (460 mg, 73% yield). m.p. = 86-87 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.78 (d, *J* = 8.9 Hz, 2H), 6.58 (d, *J* = 8.9 Hz, 2H), 3.75 (d, *J* = 5.5 Hz, 5H), 2.14 (m, 9H), 1.66 (d, *J* = 3.1 Hz, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 170.15, 152.50, 141.38, 114.85, 114.39, 81.89, 55.72, 47.56, 41.30, 36.05, 30.81. **HRMS (ESI)** *m/z*: calcd for $C_{19}H_{26}NO_3$ $[M+H]^+$ 316.1907, found 316.1906.



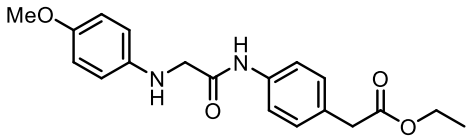
(S)-octan-2-yl (4-methoxyphenyl)glycinate (**1i**)

Colorless oil (439.5 mg, 75% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.78 (d, *J* = 8.9 Hz, 2H), 6.58 (d, *J* = 8.9 Hz, 2H), 4.99 (m, 1H), 3.83 (s, 2H), 3.73 (s, 3H), 1.64–1.44 (m, 2H), 1.31–1.21 (m, 11H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 171.02, 152.55, 141.32, 114.83, 114.31, 72.22, 55.66, 46.99, 35.83, 31.65, 29.02, 25.23, 22.51, 19.91, 14.00. **HRMS (ESI)** *m/z*: calcd for $C_{17}H_{28}NO_3$ $[M+H]^+$ 294.2063, found 294.2051.



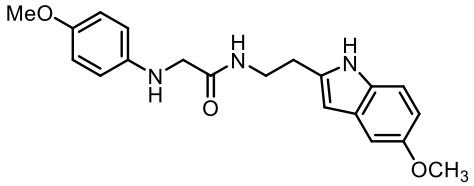
Cinnamyl (4-methoxyphenyl)glycinate (**1n**)[6]

Colorless oil (469.3 mg, 79% yield). **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.39–7.35 (m, 2H), 7.34–7.30 (m, 2H), 7.28–7.24 (m, 1H), 6.81–6.73 (m, 2H), 6.69–6.56 (m, 3H), 6.26 (m, 1H), 4.82 (m, 2H), 3.92 (s, 2H), 3.73 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 171.21, 152.72, 141.06, 135.96, 134.76, 128.59, 128.18, 126.61, 122.45, 114.89, 114.50, 65.69, 55.67, 46.88.



Ethyl 2-(4-(2-((4-methoxyphenyl)amino)acetamido)phenyl)acetate (**1r**)

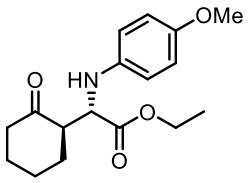
White Solid (266.7 mg, 78% yield). m.p. = 80-81 ˚C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.72 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 4.14 (t, *J* = 7.1 Hz, 2H), 3.82 (s, 2H), 3.74 (s, 3H), 3.56 (s, 2H), 1.23 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 171.56, 169.13, 153.48, 140.88, 136.28, 130.16, 129.78, 119.87, 114.98, 114.74, 60.84, 55.65, 50.59, 40.77, 14.11. **HRMS (ESI)** *m/z*: calcd for $C_{19}H_{23}N_2O_4$ $[M+H]^+$ 343.1652, found 343.1645.



N-(2-(5-methoxy-1H-indol-2-yl)ethyl)-2-((4-methoxyphenyl)amino)acetamide (**1t**)

White Solid (254.2 mg, 72% yield). m.p. = 116-117 ˚C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.09 (s, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 7.00 (d, *J* = 2.5 Hz, 1H), 6.93 (t, *J* = 6.0 Hz, 1H), 6.84 (m, 1H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.71 (d, *J* = 2.4 Hz, 1H), 6.47 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H), 3.74 (s, 3H), 3.66 (s, 2H), 3.59 (m, 2H), 2.93–2.84 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 170.81, 153.80, 152.85, 141.13, 131.46, 127.50, 122.98, 114.79, 114.17, 112.05, 111.93, 100.35, 55.85, 55.66, 49.40, 39.00, 25.21. **HRMS (ESI)** *m/z*: calcd for $C_{20}H_{24}N_3O_3$ $[M+H]^+$ 354.1812, found 354.1804.

For products:

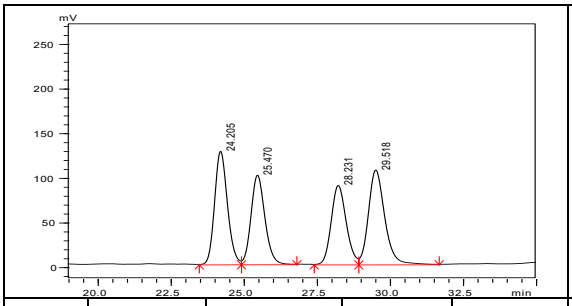


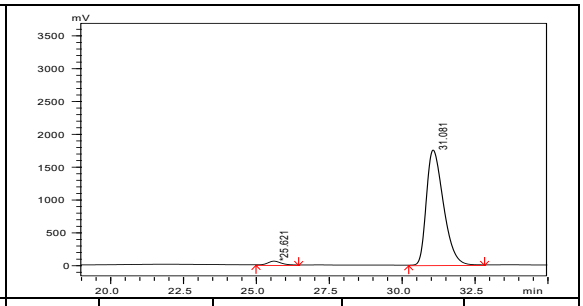
Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3aa**)[7]

Yellow oil (49 mg, 80% yield); > 99:1 *dr*. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 4.18–4.10 (m, 2H), 3.98 (d, *J* = 4.1 Hz, 1H), 3.73 (s, 3H), 3.14–3.05 (m, 1H), 2.50–2.37 (m, 1H), 2.36–2.27 (m, 1H), 2.17–2.08 (m, 1H), 2.06–2.01 (m, 1H), 1.97–1.87 (m, 2H), 1.77–1.62 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.03, 173.08, 152.74,

142.13, 115.60, 114.74, 61.19, 59.07, 55.68, 53.57, 41.80, 30.52, 26.83, 24.53, 14.09.

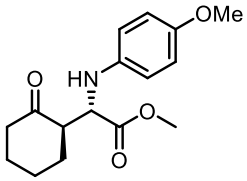
Optical Rotation: $[\alpha]^{25}_{D}$ = 29 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.6:2.4 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 214 nm, retention time: t_{major} = 31.1 min, t_{minor} = 25.6 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	24.205	3846963	126553	27.057
2	25.470	3275560	99700	23.038
3	28.231	3159949	88154	22.225
4	29.518	3935492	105945	27.680
Total		14217964	420352	100.000

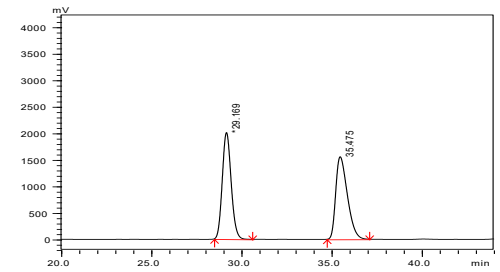
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	25.621	1715454	56826	2.356
2	31.081	71096735	1750742	97.644
Total		72812190	1807568	100.000

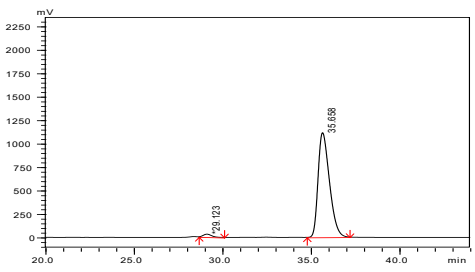


Methyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ba**)[7]

Pale yellow oil (46 mg, 79% yield); > 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 8.8 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 3.99 (d, *J* = 3.9 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.16–3.08 (m, 1H), 2.45–2.39 (m, 1H), 2.37–2.28 (m, 1H), 2.11–2.02 (m, 2H), 1.97–1.83 (m, 2H), 1.78–1.61 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.10, 173.64, 152.74, 142.02, 115.44, 114.77, 58.87, 55.67, 53.65, 52.27, 41.83, 30.56, 26.84, 24.57.

Optical Rotation: $[\alpha]^{25}_{D}$ = 24.3 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.2:1.8 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 214 nm, retention time: t_{major} = 35.7 min, t_{minor} = 29.1 min.

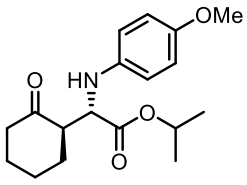




Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)

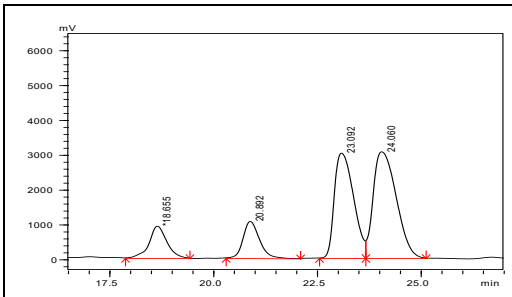
1	29.169	68858297	2006741	49.731	1	29.123	907934	30034	1.795
2	35.475	69603611	1554593	50.269	2	35.658	49673100	1114778	98.205
Total		138461909	3561334	100.000	Total		50581034	1144812	100.000

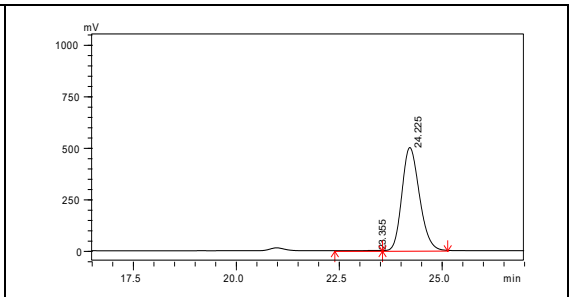


Isopropyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ca**)[7]

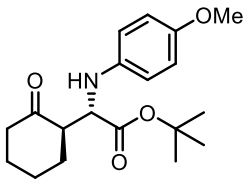
Yellow oil (48.5 mg, 76% yield); > 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 5.06–4.92 (m, 1H), 3.96 (d, *J* = 4.2 Hz, 1H), 3.73 (s, 3H), 3.10–3.04 (m, 1H), 2.46–2.26 (m, 2H), 2.14–2.00 (m, 2H), 1.98–1.84 (m, 2H), 1.78–1.62 (m, 2H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.13 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.86, 172.49, 152.72, 142.20, 115.68, 114.68, 68.74, 59.18, 55.67, 53.52, 41.73, 30.45, 26.83, 24.47, 21.62.

Optical Rotation: $[\alpha]^{25}_D$ = 18.9 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 99.9:0.1 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 24.2 min, t_{minor} = 21.0 min.





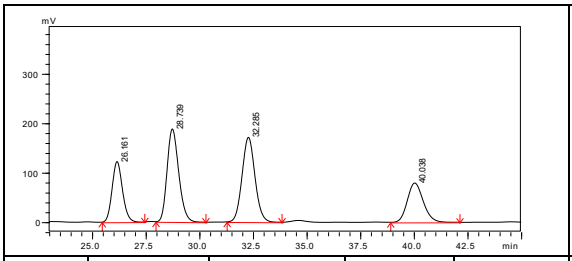
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	18.655	26909593	913510	10.173					
2	20.892	28183015	1049268	10.655					
3	23.092	104514440	3016069	39.511	1	23.355	1161	661	0.008
4	24.060	104909784	2978521	39.661	2	24.225	14731263	499373	99.992
Total		264516831	7957368	100.000	Total		14732424	500034	100.000

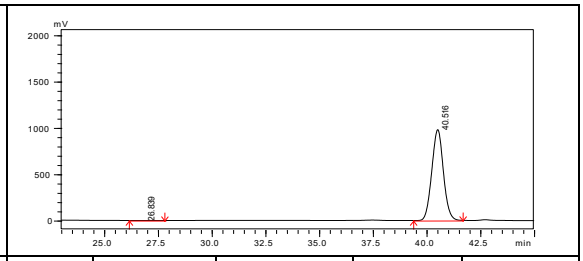


Tert-butyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3da**)[7]

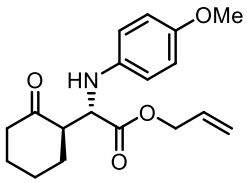
White solid (52 mg, 79% yield); > 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 3.92 (d, *J* = 4.3 Hz, 1H), 3.73 (s, 3H), 3.07–2.97 (m, 1H), 2.51–2.38 (m, 1H), 2.36–2.24 (m, 1H), 2.15–1.97(m, 2H), 1.96–1.83 (m, 2H), 1.78–1.63 (m, 2H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.84, 172.00, 152.59, 142.32, 115.46, 114.67, 81.54, 59.47, 55.67, 53.45, 41.68, 30.32, 27.88, 26.78, 24.41.

Optical Rotation: $[\alpha]^{25}_D$ = 26 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 99.9:0.1 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.5 mL/min, λ = 214 nm, retention time: t_{major} = 26.8 min, t_{minor} = 40.5 min.





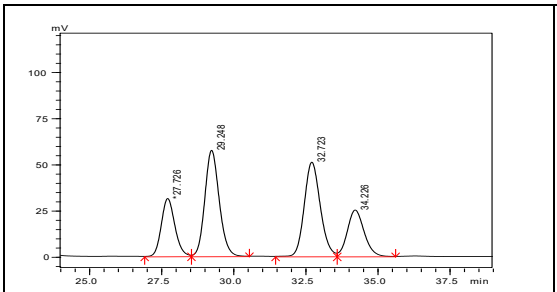
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	26.161	4111310	122213	18.325	1	26.839	11483	207	0.031
2	28.739	7073238	187502	31.527					
3	32.285	7153016	171055	31.883					
4	40.038	4097981	79348	18.266	2	40.516	36719794	979707	99.969
Total		22435545	560118	100.000	Total		36731276	979914	100.000

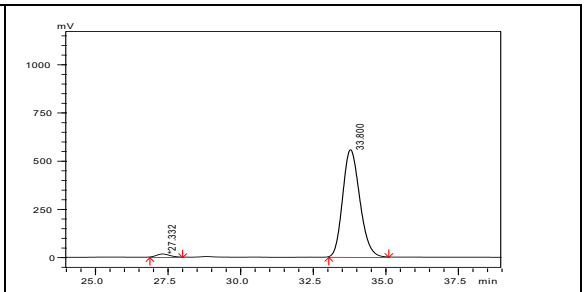


Allyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ea**)[7]

Yellow oil (49.5 mg, 78% yield); > 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 2H), 5.95–5.75 (m, 1H), 5.31–5.14 (m, 2H), 4.58 (d, *J* = 5.5 Hz, 2H), 4.01 (d, *J* = 3.7 Hz, 1H), 3.73 (s, 3H), 3.17–3.10 (m, 1H), 2.47–2.40 (m, 1H), 2.37–2.27 (m, 1H), 2.15–2.02 (m, 2H), 1.98–1.87 (m, 2H), 1.80–1.59 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.02, 172.79, 152.78, 142.06, 131.77, 118.27, 115.55, 114.77, 65.75, 59.04, 55.69, 53.59, 41.81, 30.55, 26.83, 24.56.

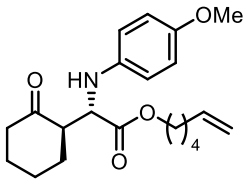
Optical Rotation: $[\alpha]^{25}_D$ = 22.4 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.0:2.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 33.8 min, t_{minor} = 27.3 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.726	1017998	31284	17.020	1	27.332	475533	15719	2.046
2	29.248	1988601	57327	33.247					
3	32.723	1963296	50967	32.824					
4	34.226	1011427	25075	16.910	2	33.800	22760879	555126	97.954

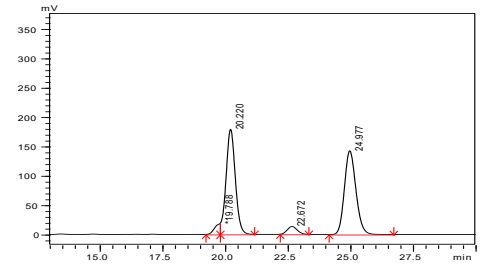
Total		5981322	164653	100.000	Total		23236412	570846	100.000

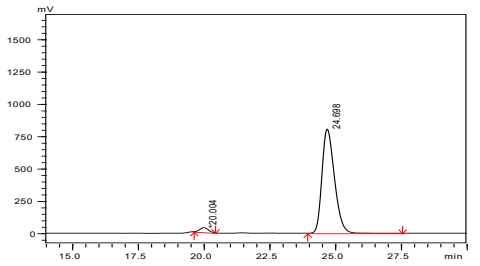


Allyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3fa**)[8]

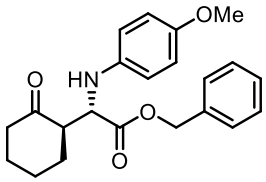
Yellow oil (53.2 mg, 74% yield); > 99:1 *dr.* **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.77 (d, *J* = 9.1 Hz, 2H), 6.73 (d, *J* = 9.1 Hz, 2H), 5.81–5.70 (m, 1H), 5.03–4.92 (m, 2H), 4.22 (d, *J* = 5.2 Hz, 1H), 4.15–4.04 (m, 2H), 3.74 (s, 3H), 2.90–2.76 (m, 1H), 2.51–2.41 (m, 1H), 2.37–2.27 (m, 1H), 2.26–2.16 (m, 1H), 2.12–1.93 (m, 4H), 1.86–1.76 (m, 1H), 1.74–1.64 (m, 2H), 1.64–1.53 (m, 2H), 1.42–1.32 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.05, 173.48, 153.11, 140.93, 138.28, 116.12, 114.79, 114.74, 65.04, 58.18, 55.66, 53.54, 41.83, 33.16, 29.66, 27.91, 26.85, 25.07, 24.78.

Optical Rotation: $[\alpha]^{25}_D$ = 16.4 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.1:2.9 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 24.7 min, t_{minor} = 20.0 min.





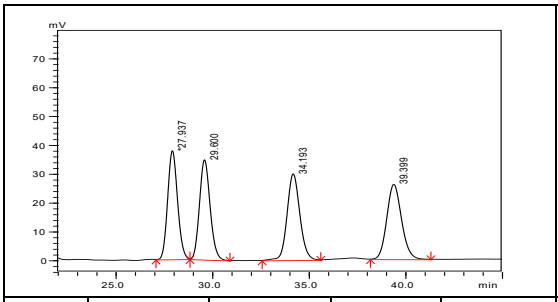
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	19.788	266759	18072	2.718					
2	20.220	4633894	178889	47.222	1	20.004	787344	35499	2.886
3	22.672	366568	13279	3.736					
4	24.977	4545856	142445	46.324	2	24.698	26492828	804783	97.114
Total		9813077	352684	100.000	Total		27280172	840282	100.000

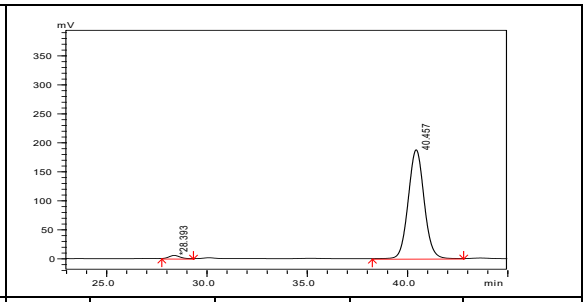


Benzyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ga**)[7]

Yellow oil (58 mg, 79% yield); > 99:1 *dr.* **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.40–7.29 (m, 3H), 7.25–7.20 (m, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.62 (d, *J* = 8.9 Hz, 2H), 5.20–5.08 (m, 2H), 4.06 (d, *J* = 4.0 Hz, 1H), 3.74 (s, 3H), 3.16–3.07 (m, 1H), 2.46–2.37 (m, 1H), 2.35–2.25 (m, 1H), 2.12–1.99 (m, 2H), 1.95–1.85 (m, 2H), 1.74–1.60 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.02, 172.96, 152.83, 142.03, 135.58, 128.44, 128.14, 128.01, 115.67, 114.78, 66.88, 59.05, 55.71, 53.52, 41.78, 30.51, 26.82, 24.51.

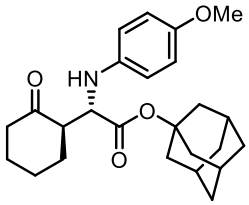
Optical Rotation: $[\alpha]^{25}_D$ = 25.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.2:1.8 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 214 nm, retention time: t_{major} = 40.5 min, t_{minor} = 28.3 min.





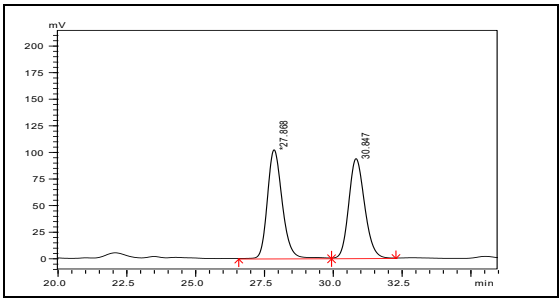
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.937	1365916	29874	25.349
2	29.600	1318026	34574	24.460
3	34.193	1335804	37580	24.790
4	39.399	1368799	25930	25.402
Total		5388545	127957	100.000

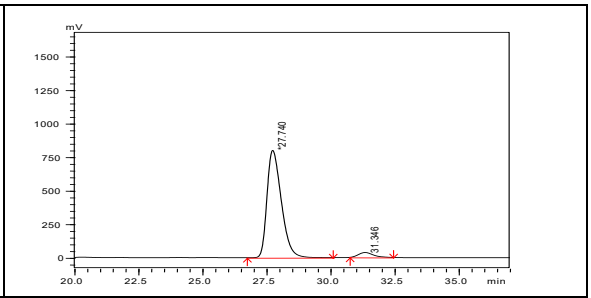
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	28.393	193017	5334	1.839
2	40.457	10302721	187576	98.161
Total		10495738	192910	100.000



(1S,3R)-Adamantan-1-yl (2S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)aceta-te (**3ha**)[8]
White solid (60.9 mg, 74% yield); > 99:1 *dr.* m.p. = 122-123 ˚C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 8.8 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 3.93 (d, *J* = 4.4 Hz, 1H), 3.73 (s, 3H), 3.07–2.96 (m, 1H), 2.47–2.39 (m, 1H), 2.35–2.24 (m, 1H), 2.14–1.99 (m, 11H), 1.96–1.85 (m, 2H), 1.74–1.59 (m, 8H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.83, 171.65, 152.63, 142.24, 115.57, 114.67, 81.61, 59.52, 55.67, 53.43, 41.69, 41.15, 36.04, 30.73, 30.26, 26.76, 24.40.

Optical Rotation: $[\alpha]^{25}_D$ = 8.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.5:4.5 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 27.7 min, t_{minor} = 31.3 min.

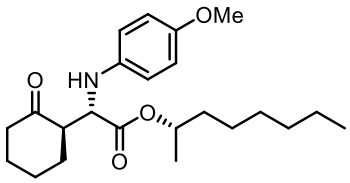




Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.868	3809801	102097	50.484
2	30.847	3736737	93521	49.516

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.740	31078933	799028	95.476
2	31.346	1472565	36418	4.524

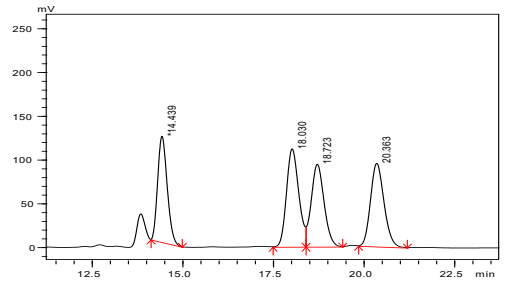
Total		7546538	195617	100.000	Total		32551498	835446	100.000

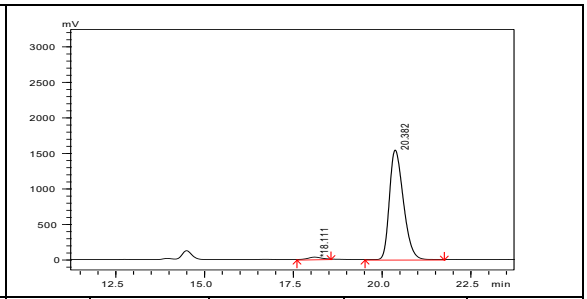


(S)-Octan-2-yl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ia**)

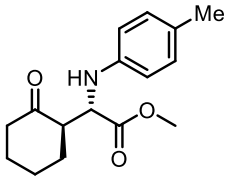
Yellow oil (60 mg, 77% yield); 98:2 *dr.* **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.74 (d, *J* = 8.8 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 4.95–4.78 (m, 1H), 3.94 (d, *J* = 4.3 Hz, 1H), 3.72 (s, 3H), 3.18–3.00 (m, 1H), 2.49–2.37 (m, 1H), 2.35–2.26 (m, 1H), 2.14–2.00 (m, 2H), 1.99–1.88 (m, 2H), 1.79–1.65 (m, 2H), 1.51–1.35 (m, 2H), 1.27–1.06(m, 11H), 0.85 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.80, 172.72, 152.79, 142.32, 115.63, 114.71, 72.19, 59.32, 55.65, 53.57, 41.75, 35.76, 31.66, 30.61, 29.00, 26.91, 25.05, 24.51, 22.49, 19.80, 13.98. **HRMS (ESI)** *m/z*: calcd for $C_{23}H_{36}NO_4$ $[M+H]^+$ 390.2644, found 390.2645.

Optical Rotation: $[\alpha]^{25}_D$ = 17.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.2:1.8 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 20.4 min, t_{minor} = 18.1 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	14.439	2671214	125882	26.912					
2	18.030	2619223	111720	26.388					
3	18.723	2325365	94107	23.428	1	18.111	747959	30617	1.751
4	20.363	2309897	93008	23.272	2	20.382	41960894	1540734	98.249
Total		9925701	424717	100.000	Total		42708853	1571352	100.000

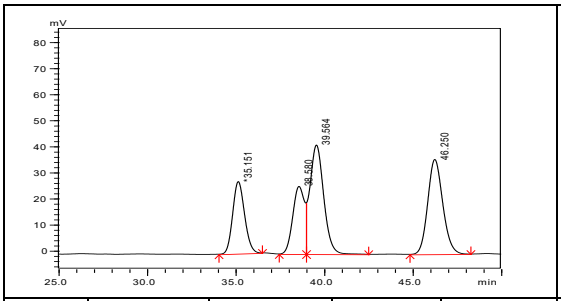


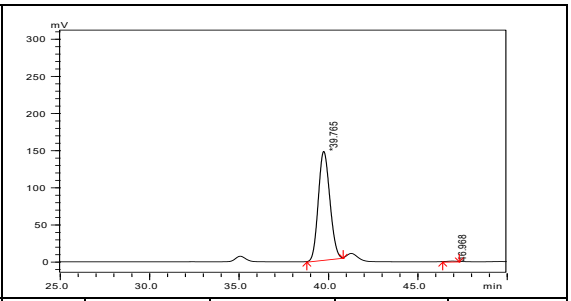
Methyl (S)-2-((R)-2-oxocyclohexyl)-2-(p-tolylamino)acetate (**3ja**)

Yellow oil (38.2 mg, 71% yield); > 99:1 *dr.* **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.98 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 8.4 Hz, 2H), 4.09 (d, *J* = 3.8 Hz, 1H), 3.69 (s, 3H), 3.19–3.12 (m, 1H), 2.47–2.38 (m, 1H), 2.36–2.31 (m, 1H), 2.23 (s, 3H), 2.14–2.08 (m, 1H), 2.06–2.03 (m, 1H), 1.95–1.85 (m, 2H), 1.76–1.63 (m, 2H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 211.12, 173.48, 145.50, 129.79, 127.73, 113.95, 57.89, 53.67, 52.32, 41.84, 30.50, 26.84, 24.59, 20.36. **HRMS (ESI)** *m/z*: calcd for $C_{16}H_{22}NO_3$ $[M+H]^+$ 276.1594, found

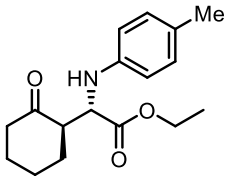
276.1585.

Optical Rotation: $[\alpha]^{25}_{D}$ = 14.7 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 99.7:0.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 98/2, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 39.8 min, t_{minor} = 47.0 min.





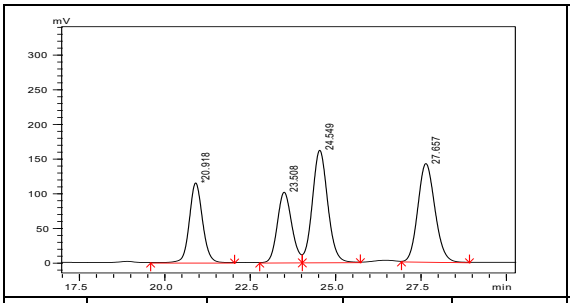
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	35.151	1288456	27617	19.212	1	39.765	6524173	145824	99.761
2	38.580	1247975	25987	18.609	2	46.968	15605	462	0.239
3	39.564	2025035	41009	30.195					
4	46.250	2145008	36342	31.984					
Total		6706474	130955	100.000	Total		6539778	146286	100.000

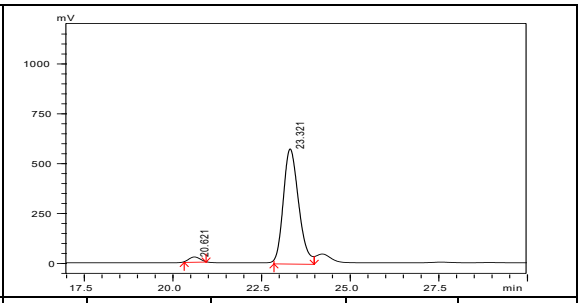


Ethyl (S)-2-((R)-2-oxocyclohexyl)-2-(p-tolylamino)acetate (**3ka**)[7]

Yellow oil (39 mg, 66% yield); 98:2 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.97 (d, *J* = 7.8 Hz, 2H), 6.57 (d, *J* = 7.8 Hz, 2H), 4.23–4.05 (m, 3H), 3.21–3.05 (m, 1H), 2.48–2.37 (m, 1H), 2.32 (m, 1H), 2.22 (s, 3H), 2.16–2.00 (m, 2H), 1.97–1.81 (m, 2H), 1.80–1.61 (m, 2H), 1.25–1.17 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.03, 172.90, 145.66, 129.71, 127.56, 113.97, 61.21, 57.95, 53.58, 41.78, 30.41, 26.79, 24.51, 20.34, 14.09.

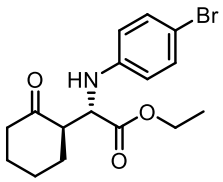
Optical Rotation: $[\alpha]^{25}_{D}$ = 18.0 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.3:2.7 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 96/4, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 20.6 min, t_{minor} = 23.3 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	20.918	3058164	114757	19.186	1	20.621	479084	23542	2.712
2	23.508	2952149	101188	18.521	2	23.321	17185657	574309	97.288

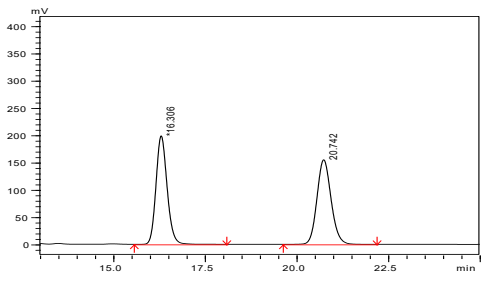
3	24.549	5036013	161456	31.594					
4	27.657	4893371	141462	30.699					
Total		15939697	518863	100.000	Total		17664742	597851	100.000

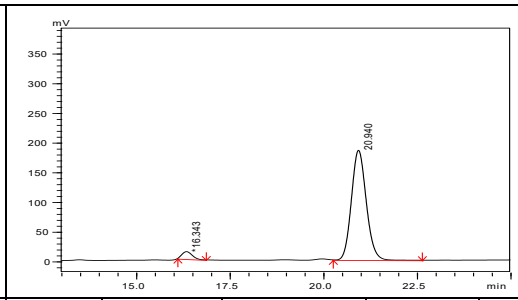


Ethyl (S)-2-((4-bromophenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3la**)[7]

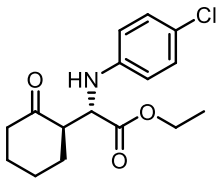
Yellow oil (41.1 mg, 58% yield); 80:20 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 4.23 (d, *J* = 5.0 Hz, 1H), 4.13 (m, 2H), 3.19–2.77 (m, 1H), 2.52–2.36 (m, 1H), 2.36–2.04 (m, 3H), 1.95 (m, 1H), 1.89–1.54 (m, 3H), 1.26–1.22 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 209.90, 172.72, 145.97, 131.92, 115.63, 110.22, 61.33, 56.56, 53.35, 41.77, 29.77, 26.80, 24.77, 14.08.

Optical Rotation: $[\alpha]^{25}_D$ = 30.0 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.6:4.4 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 20.9 min, t_{minor} = 16.3 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	16.306	4187100	198750	50.252	1	16.343	229834	12381	4.347
2	20.742	4145163	155010	49.748	2	20.940	5057564	184743	95.653
Total		8332263	353760	100.000	Total		5287398	197125	100.000

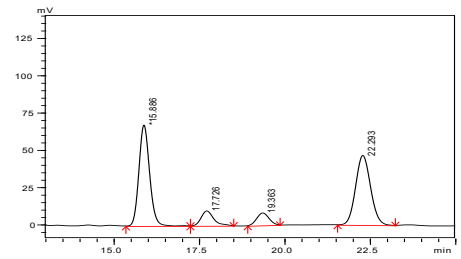


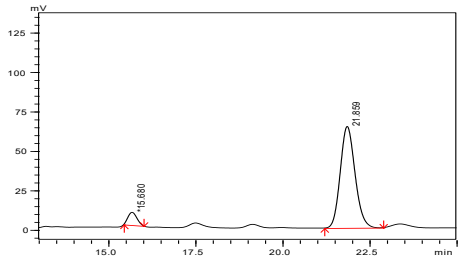
Ethyl (S)-2-((4-chlorophenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ma**)[7]

Yellow oil (37.2 mg, 60% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.66 (d, *J* = 8.8 Hz, 2H), 4.24 (d, *J* = 4.9 Hz, 1H), 4.19–4.11 (m, 2H), 2.91–2.74 (m, 1H), 2.53–2.41 (m, 1H), 2.36–2.26 (m, 1H), 2.23–2.15 (m, 1H), 2.12–2.04 (m, 1H), 2.00–1.91 (m, 1H), 1.86–1.76 (m, 1H), 1.73–1.61 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 209.92, 172.85, 145.60, 129.12, 123.27, 115.30, 61.39, 56.80, 53.45, 41.85, 29.80, 26.85, 24.84, 14.15.

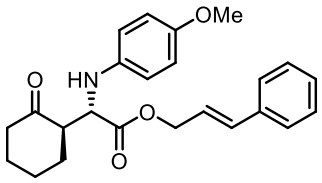
Optical Rotation: $[\alpha]^{25}_D$ = 42.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 93.0:7.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention

time: t_{major} = 21.9 min, t_{minor} = 15.7 min.





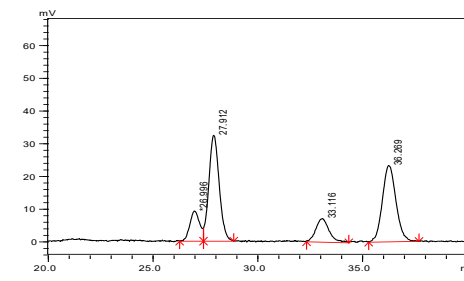
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	15.886	1460095	67557	43.814	1	15.680	141608	8053	6.968
2	17.726	250532	9907	7.518					
3	19.363	205141	8267	6.156					
4	22.293	1416725	46567	42.512	2	21.859	1890559	64275	93.032
Total		3332493	132298	100.000	Total		2032167	72327	100.000

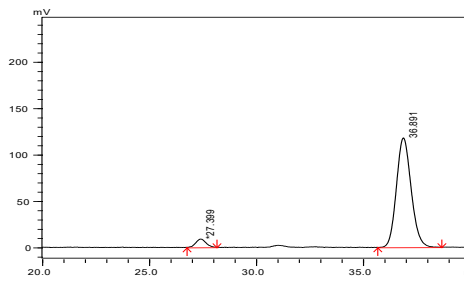


Cinnamyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3na**)

Brown oil (52 mg, 69% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38–7.31 (m, 4H), 7.30–7.26 (m, 1H), 6.79 (d, *J* = 8.9 Hz, 2H), 6.68 (d, *J* = 8.9 Hz, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.28–6.16 (m, 1H), 4.77 (m, 2H), 4.06 (d, *J* = 4.1 Hz, 1H), 3.75 (s, 3H), 3.23–3.13 (m, 1H), 2.51–2.42 (m, 1H), 2.40–2.32 (m, 1H), 2.20–2.04 (m, 2H), 2.03–1.91 (m, 2H), 1.82–1.65 (m, 2H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.07, 172.91, 152.78, 142.06, 133.88, 128.53, 127.98, 126.56, 122.75, 115.59, 114.78, 65.58, 59.07, 55.65, 53.58, 41.83, 30.59, 26.85, 24.54. **HRMS (ESI)** *m/z*: calcd for $C_{24}H_{28}NO_4$ $[M+H]^+$ 394.2013, found 394.2005.

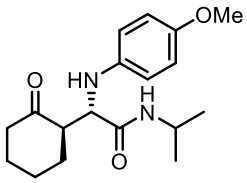
Optical Rotation: $[\alpha]^{25}_D$ = 22.3 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.1:4.9 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 36.9 min, t_{minor} = 27.4 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	26.996	302564	9361	11.308	1	27.399	286522	8841	4.854
2	27.912	1035880	31539	38.716					
3	33.116	300989	7082	11.249					

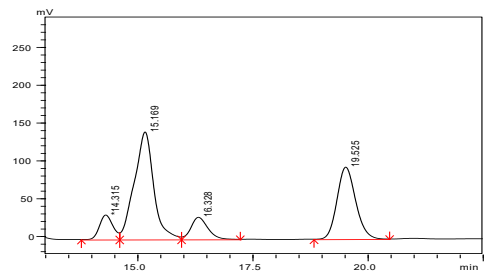
4	36.269	1036173	23235	38.727	2	36.891	5616542	117881	95.146
Total		2675606	71218	100.000	Total		5903064	126722	100.000

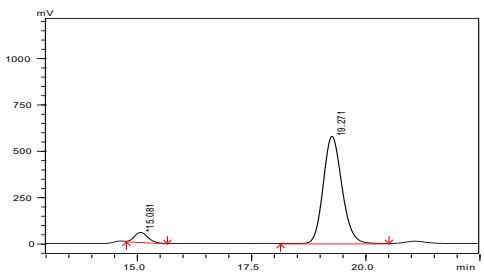


(S)-*N*-isopropyl-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3oa**)

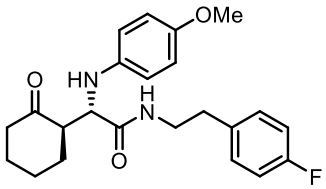
White solid (44.9 mg, 70% yield); 95:5 *dr*. m.p. = 118-120 ˚C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.84 (dd, *J* = 12.7, 8.5 Hz, 1H), 6.76 (d, *J* = 8.9 Hz, 2H), 6.55 (d, *J* = 8.9 Hz, 2H), 4.09–3.97 (m, 1H), 3.92 (d, *J* = 3.0 Hz, 1H), 3.73 (s, 3H), 3.36–3.20 (m, 1H), 2.38 (m, 2H), 2.10–2.01 (m, 2H), 1.90–1.82 (m, 1H), 1.71–1.50 (m, 3H), 1.13 (d, *J* = 6.6 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.61, 170.97, 152.53, 141.14, 114.98, 114.46, 58.92, 55.68, 53.22, 42.34, 41.22, 31.08, 27.62, 24.91, 22.57, 22.55. **HRMS (ESI)** *m/z*: calcd for $C_{18}H_{26}N_2NaO_3$ $[M+Na]^+$ 341.1836, found 314.1835.

Optical Rotation: $[\alpha]^{25}_D$ = 36.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.3:4.7 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 19.3 min, t_{minor} = 15.1 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	14.315	672392	32522	10.110					
2	15.169	2681236	117944	40.314	1	15.081	805876	52062	4.692
3	16.328	623874	27008	9.380					
4	19.525	2673381	95141	40.196	2	19.271	16369050	577166	95.308
Total		6650883	272615	100.000	Total		17174926	629228	100.000

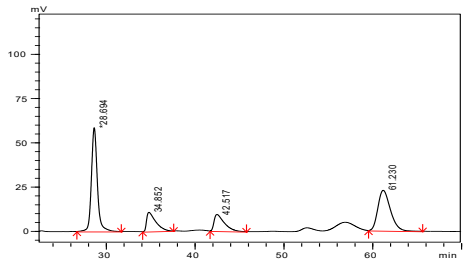


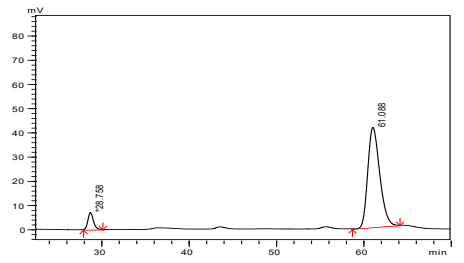
(S)-*N*-(4-fluorophenethyl)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3pa**)

White solid (55 mg, 69% yield); >99:1 *dr*. m.p. = 146-147 ˚C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.09 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.07–6.97 (m, 1H), 6.93 (t, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.50 (d, *J* = 8.9 Hz, 2H), 3.87 (d, *J* = 2.9 Hz, 1H), 3.74 (s, 3H), 3.47 (q, *J* = 6.7 Hz, 2H), 3.38–3.26 (m, 1H), 2.74 (t, *J* = 6.9 Hz, 2H), 2.45–2.31 (m, 2H), 2.11–1.97 (m, 2H), 1.90–1.81 (m, 1H), 1.72–1.52 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.42, 172.10, 161.52 (d, J_1 = 243 Hz, Cq), 152.70, 140.92, 134.47 (d, J_4 = 3 Hz,

Cq), 134.44, 130.21 (d, J_3 = 7 Hz, CH), 130.13, 115.22 (d, J_2 = 21 Hz, CH), 115.03, 114.40, 59.28, 55.69, 53.13, 42.34, 40.51, 34.87, 31.28, 27.59, 24.90. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -116.85. **HRMS (ESI)** *m/z*: calcd for $C_{23}H_{27}FN_2NaO_3$ $[M+Na]^+$ 421.1903, found 421.1912.

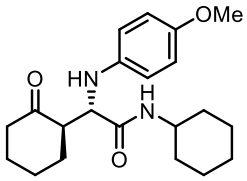
Optical Rotation: $[\alpha]^{25}_D$ = 42 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.0:5.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 61.1 min, t_{minor} = 28.8 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	28.694	2234997	55243	37.527
2	34.852	767908	10827	12.894
3	42.517	741143	9354	12.444
4	61.230	2211722	22806	37.136
Total		5955770	98229	100.000

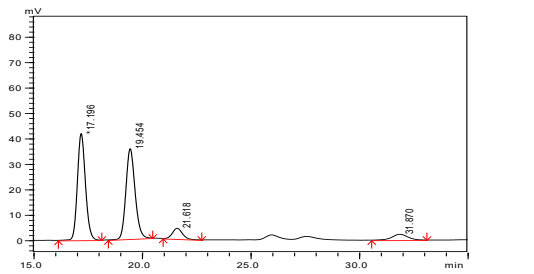
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	28.758	205079	7050	4.993
2	61.088	3902270	41180	95.007
Total		4107350	48230	100.000

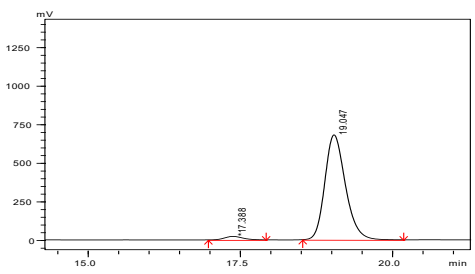


(S)-*N*-cyclohexyl-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3qa**)

Yellow oil (53.8 mg, 75% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.89 (s, 1H), 6.77 (d, *J* = 8.3 Hz, 2H), 6.58 (d, *J* = 8.3 Hz, 2H), 3.97 (s, 1H), 3.74 (s, 4H), 3.30 (m, 1H), 2.39 (m, 2H), 2.13–2.04 (m, 2H), 1.89–1.55 (m, 9H), 1.39–1.27 (m, 2H), 1.24–1.07 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.68, 170.71, 152.67, 141.01, 115.04, 114.62, 58.92, 55.74, 53.25, 47.98, 42.37, 32.83, 30.98, 27.66, 26.51, 25.49, 24.94, 24.65. **HRMS (ESI)** *m/z*: calcd for $C_{21}H_{30}N_2NaO_3$ $[M+Na]^+$ 381.2149, found 381.2142.

Optical Rotation: $[\alpha]^{25}_D$ = 22.9 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.2:2.8 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 19.0 min, t_{minor} = 17.4 min.

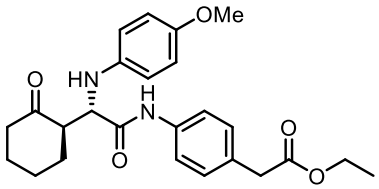




Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)

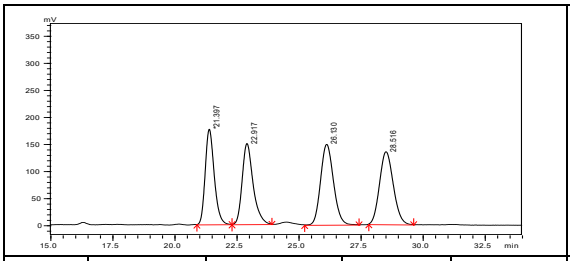
1	17.196	1078515	41896	45.667	1	17.388	460063	22238	2.802
2	19.454	1039284	35459	44.006	2	19.047	15956562	679586	97.198
3	21.618	130158	4175	5.511					
4	31.870	113733	2270	4.816					
Total		2361690	83800	100.000	Total		16416625	701824	100.000

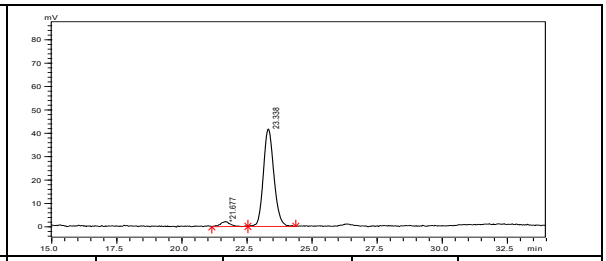


Ethyl 2-(4-((S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamido)phenyl)-acetate (**3ra**)

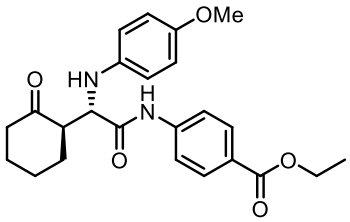
Brown oil (61.3 mg, 70% yield); 96:4 dr. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.36–7.27 (m, 4H), 6.77 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 8.9 Hz, 2H), 4.20–4.09 (m, 3H), 3.74 (s, 3H), 3.63–3.59 (m, 2H), 2.83–2.58 (m, 1H), 2.42–2.17 (m, 1H), 2.16–1.91 (m, 3H), 1.75–1.46 (m, 4H), 1.28–1.25 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.48, 175.06, 171.40, 152.31, 141.67, 133.91, 133.60, 130.01, 127.51, 114.88, 114.04, 90.08, 61.01, 57.91, 55.74, 46.97, 40.89, 33.51, 24.70, 23.24, 22.17, 14.12. **HRMS (ESI)** *m/z*: calcd for $C_{25}H_{31}N_2O_5$ $[M+H]^+$ 439.2233, found 439.2231.

Optical Rotation: $[\alpha]^{25}_D$ = 15.4 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.5:3.5 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 95/5, flow rate = 0.7 mL/min, λ = 240 nm, retention time: t_{major} = 21.7 min, t_{minor} = 23.4 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	21.397	4442924	175831	22.775	1	21.677	42227	1976	3.523
2	22.917	4562205	149089	23.386	2	23.338	1156504	41481	96.477
3	26.130	5338881	148492	27.368					
4	28.516	5164019	134127	26.471					
Total		19508028	607539	100.000	Total		1198731	43457	100.000

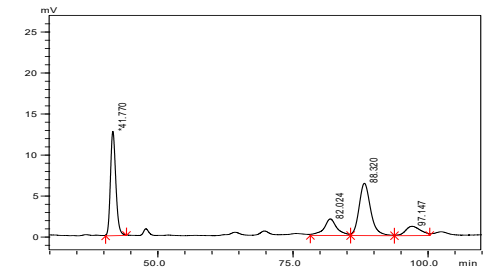


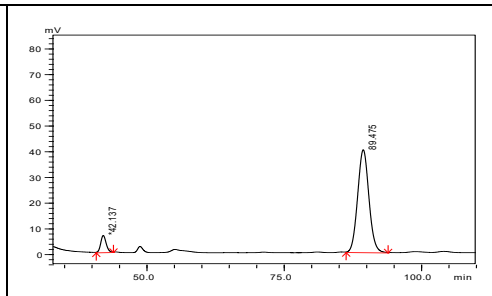
Ethyl 4-((S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamido)benzoate (**3sa**)

Brown oil (57.7 mg, 68% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 9.1 Hz, 2H), 6.62 (d, *J* = 8.9 Hz, 2H), 4.64 (d, *J* = 5.9 Hz, 1H),

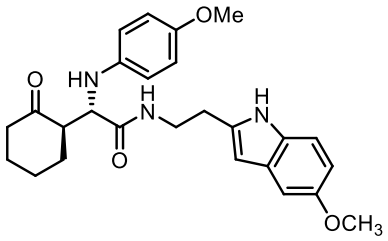
4.40–4.33 (m, 2H), 3.73 (s, 3H), 2.83–2.62 (m, 1H), 2.17–2.08 (m, 1H), 1.78–1.60 (m, 2H), 1.59–1.41 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.28–1.12 (m, 1H), 1.12–0.96 (m, 1H), 0.96–0.73 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.67, 174.86, 166.03, 152.41, 141.38, 139.32, 130.68, 130.28, 126.62, 118.85, 114.90, 114.09, 90.26, 61.16, 57.92, 55.72, 47.15, 42.26, 33.32, 24.76, 23.19, 21.96, 14.26. **HRMS (ESI)** *m/z*: calcd for $C_{24}H_{29}N_2O_5$ $[M+H]^+$ 425.2076, found 425.2056.

Optical Rotation: $[\alpha]^{25}_D$ = 16.3 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 94.0:6.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 240 nm, retention time: t_{major} = 89.4 min, t_{minor} = 42.1 min.





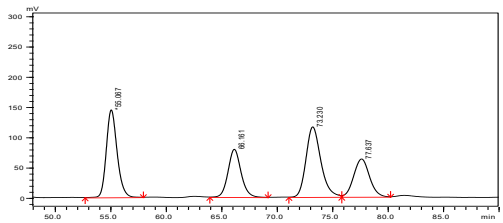
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	41.770	873039	12681	38.624	1	42.137	357382	6507	5.949
2	82.024	258042	1839	11.416					
3	88.320	877316	6217	38.813	2	89.475	5649770	39827	94.051
4	97.147	251969	1068	11.147					
Total		2260365	21807	100.000	Total		6007152	46334	100.000

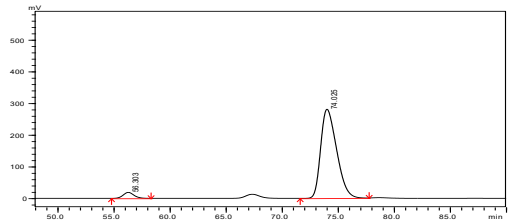


(S)-*N*-(2-(5-methoxy-1H-indol-2-yl)ethyl)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclo-hexyl)acetamide (**3ta**)

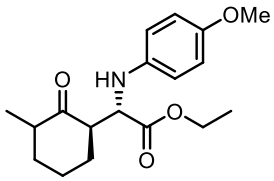
Brown oil (67.4mg, 75% yield);85:15 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.05 (s, 1H), 7.22 (d, *J* = 8.8 Hz, 1H), 7.09 (t, *J* = 5.8 Hz, 1H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.84 (m, 1H), 6.72 (d, *J* = 8.9 Hz, 2H), 6.47 (d, *J* = 8.9 Hz, 2H), 3.89 (d, *J* = 3.2 Hz, 1H), 3.85 (s, 3H), 3.73 (s, 3H), 3.56 (m, 2H), 3.36–3.06 (m, 1H), 2.89 (t, *J* = 6.8 Hz, 2H), 2.51–2.24 (m, 2H), 2.09–1.96 (m, 2H), 1.88–1.78 (m, 1H), 1.73–1.48 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 213.46, 172.15, 153.89, 152.47, 141.10, 131.40, 127.61, 122.97, 114.96, 114.34, 112.39, 112.20, 111.85, 100.35, 59.16, 55.87, 55.69, 53.08, 42.29, 39.40, 31.21, 27.50, 25.18, 24.86. **HRMS (ESI)** *m/z*: calcd for $C_{26}H_{32}N_3O_4$ $[M+H]^+$ 450.2393, found 450.2380.

Optical Rotation: $[\alpha]^{25}_D$ = 63.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.7:4.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 98/2, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 74 min, t_{minor} = 56.3 min.





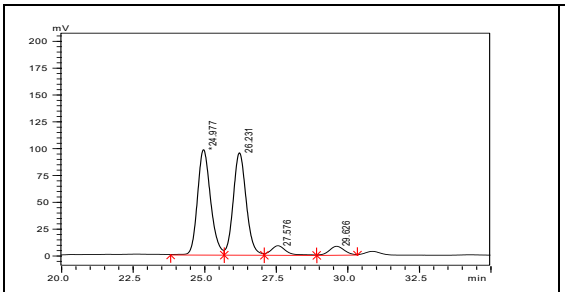
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	55.067	9755168	144597	31.148	1	56.303	1244005	18722	4.303
2	66.161	5841788	76480	18.653					
3	73.230	9857390	112482	31.475	2	74.025	27669404	280501	95.697
4	77.637	5864184	61254	18.724					
Total		31318529	394813	100.000	Total		28913409	299222	100.000

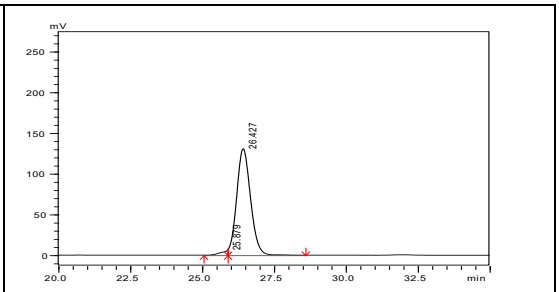


Ethyl (2S)-2-((4-methoxyphenyl)amino)-2-((1R)-3-methyl-2-oxocyclohexyl)acetate (**3ab**)

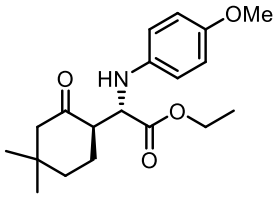
Yellow oil (42.2 mg, 66% yield); 97:3 *dr*. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 6.71 (d, *J* = 9.0 Hz, 2H), 6.61 (d, *J* = 9.0 Hz, 2H), 5.48 (d, *J* = 10.1 Hz, 1H), 4.34–4.24 (m, 1H), 3.96 (q, *J* = 7.1 Hz, 2H), 3.63 (s, 3H), 2.81–2.66 (m, 2H), 2.07–1.92 (m, 2H), 1.82–1.73 (m, 2H), 1.67–1.58 (m, 1H), 1.49–1.40 (m, 1H), 1.07 (t, *J* = 7.1 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 212.85, 172.89, 151.38, 141.86, 114.52, 114.06, 60.13, 56.07, 55.27, 51.91, 42.62, 34.55, 28.59, 19.70, 15.24, 14.00. **HRMS (ESI)** *m/z*: calcd for $C_{18}H_{25}NNaO_4$ [M+Na]$^+$ 342.1681, found 342.1670.

Optical Rotation: $[\alpha]^{25}_D$ = 23.9 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.9:2.1 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 240 nm, retention time: t_{major} = 26.4 min, t_{minor} = 25.9 min.





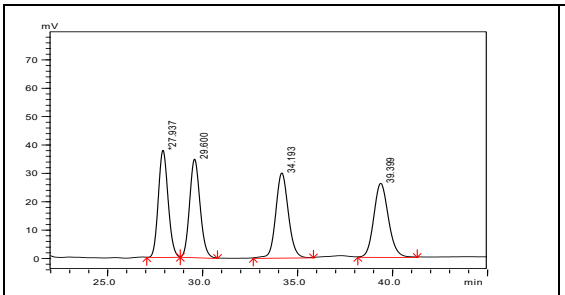
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	24.977	2793962	93977	46.357	1	25.879	92878	5818	2.075
2	26.231	2739353	91913	45.451	2	26.427	4383119	130595	97.925
3	27.576	227473	7670	3.774					
4	29.626	266269	7816	4.418					
Total		6027057	201377	100.000	Total		4475997	136413	100.000

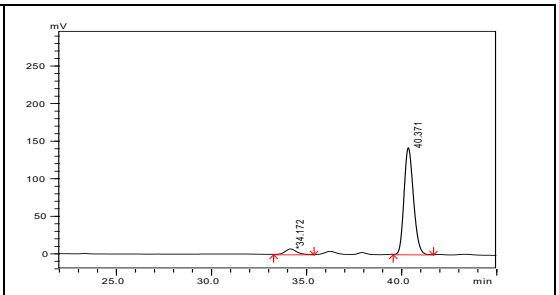


Ethyl (S)-2-((R)-4,4-dimethyl-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ac**)

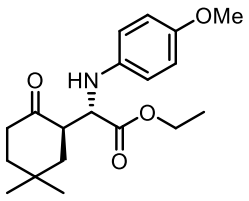
Yellow oil (51.3 mg, 77% yield); >99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 8.9 Hz, 2H), 6.65 (d, *J* = 8.9 Hz, 2H), 4.18–4.10 (m, 2H), 3.97 (d, *J* = 4.0 Hz, 1H), 3.73 (s, 3H), 3.09–2.95 (m, 1H), 2.26–2.19 (m, 1H), 2.16–2.00 (m, 3H), 1.76–1.62 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 3H), 0.87 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.02, 173.11, 152.84, 142.18, 115.83, 114.75, 61.20, 58.97, 55.69, 54.66, 52.44, 37.47, 36.25, 31.41, 26.16, 25.35, 14.09. **HRMS (ESI)** *m/z*: calcd for $C_{19}H_{27}NNaO_4$ $[M+Na]^+$ 356.1838, found 356.1827.

Optical Rotation: $[\alpha]^{25}_D$ = 16.8 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.0:4.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 40.4 min, t_{minor} = 34.2 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.937	1335804	37580	24.824					
2	29.600	1316936	34566	24.474					
3	34.193	1359528	29841	25.265	1	34.172	201896	6151	3.976
4	39.399	1368799	25930	25.437	2	40.371	4875395	141926	96.024
Total		5381067	127917	100.000	Total		5077291	148077	100.000

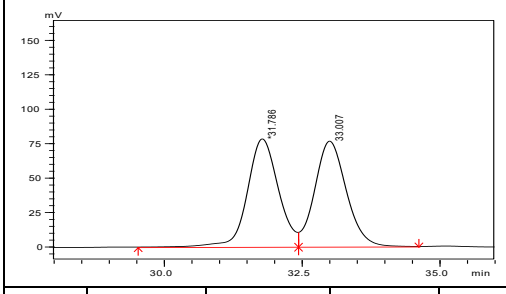


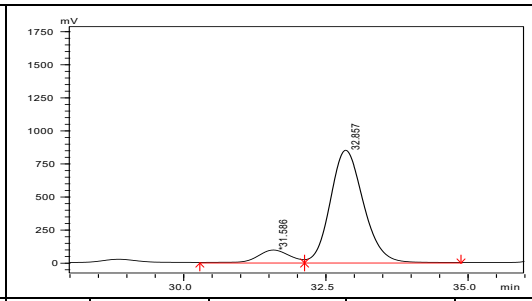
Ethyl (S)-2-((R)-5,5-dimethyl-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ad**)[7]

Yellow oil (50.7 mg, 76% yield); 95:5 *dr*. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 9.0 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 4.17–4.10 (m, 2H), 3.86 (d, *J* = 3.4 Hz, 1H), 3.73 (s, 3H), 3.33–3.21(m, 1H), 2.51–2.44 (m, 1H), 2.31–2.25 (m, 1H), 1.93 (t, *J* = 13.2 Hz, 1H), 1.78–1.73 (m, 1H), 1.71–1.62 (m, 2H), 1.24 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 4H), 1.04 (s, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 211.46, 173.12, 152.79, 142.36, 115.72, 114.74, 61.16, 59.42, 55.66, 49.55, 42.88, 38.80, 37.99, 31.48, 30.63, 24.55, 14.06.

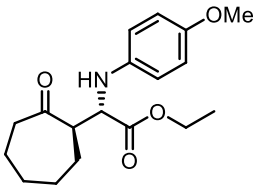
Optical Rotation: $[\alpha]^{25}_D$ = 14.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 94.8:5.2 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, retention

time: t_{major} = 22.7 min, t_{minor} = 17.9 min.





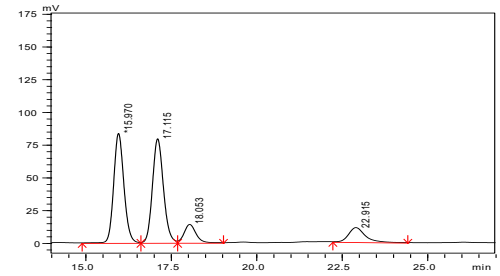
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	31.786	3048777	78276	50.013	1	31.586	3503601	93847	9.285
2	33.007	3047239	76567	49.987	2	32.857	34230219	848048	90.715
Total		6096016	154843	100.000	Total		37733820	941895	100.000

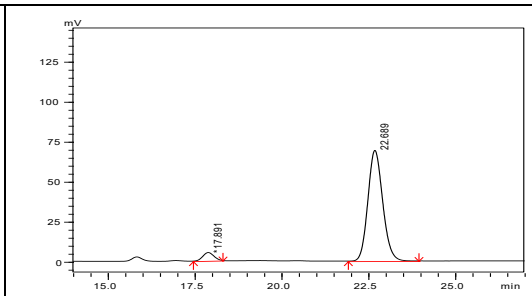


Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocycloheptyl)acetate (**3ae**)[7]

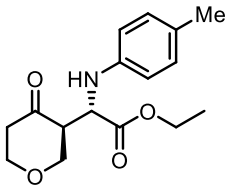
Yellow oil (48 mg, 75% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.77 (d, *J* = 8.9 Hz, 2H), 6.67 (d, *J* = 8.9 Hz, 2H), 4.31 (d, *J* = 4.9 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 3.07–2.98 (m, 1H), 2.61–2.47 (m, 2H), 2.03–1.84 (m, 4H), 1.60–1.49 (m, 2H), 1.43–1.32 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 214.19, 172.55, 152.73, 140.91, 115.23, 114.85, 61.29, 60.69, 55.70, 54.34, 43.88, 29.90, 29.01, 27.16, 24.22, 14.15.

Optical Rotation: $[\alpha]^{25}_D$ = 15.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 94.8:5.2 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 22.7 min, t_{minor} = 17.9 min.





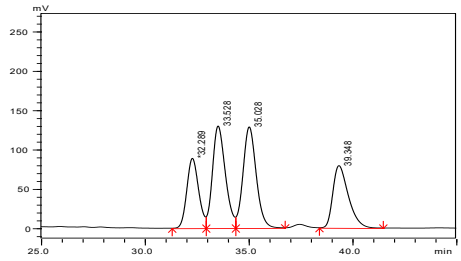
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	15.970	1731385	83534	41.341					
2	17.115	1769265	79423	42.245					
3	18.053	329642	13978	7.871	1	17.891	111584	5139	5.164
4	22.915	357791	11004	8.543	2	22.689	2049045	69129	94.836
Total		4188084	187938	100.000	Total		2160629	74268	100.000

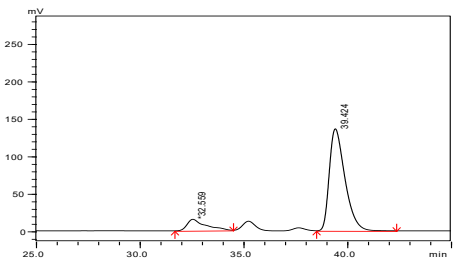


Ethyl (S)-2-((S)-4-oxotetrahydro-2H-pyran-3-yl)-2-(p-tolylamino)acetate (**3kf**)

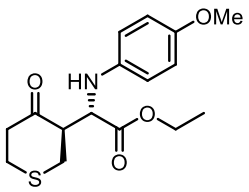
Yellow oil (42 mg, 72% yield); 85:15 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.98 (d, *J* = 8.4 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 4.26–4.08 (m, 5H), 3.97 (t, *J* = 5.9 Hz, 1H), 3.93–3.82 (m, 1H), 3.84–3.72 (m, 1H), 3.32–2.88 (m, 1H), 2.65–2.54 (m, 1H), 2.53–2.43 (m, 2H), [2.23, 2.04] (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 206.21, 171.97, 144.86, 129.77, 128.21, 114.19, 69.94, 67.75, 61.52, 55.32, 53.77, 42.81, 42.02, 20.33, 14.05. **HRMS (ESI)** *m/z*: calcd for $C_{16}H_{21}NNaO_4$ $[M+Na]^+$ 314.1368, found 314.1353.

Optical Rotation: $[\alpha]^{25}_D$ = 8.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 93.3:7.7 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 96/4, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 39.4 min, t_{minor} = 32.6 min.





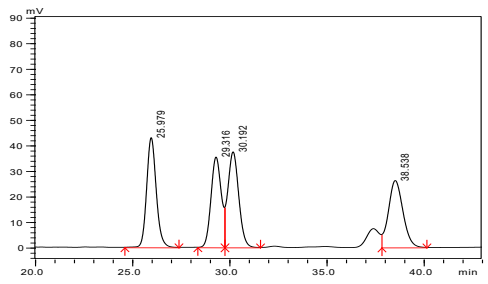
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	32.289	3489720	88601	18.529	1	32.559	509141	15123	6.697
2	33.528	5593590	129593	29.700					
3	35.028	5675774	128370	30.137					
4	39.348	4074303	78963	21.633	2	39.424	7093033	135971	93.303
Total		18833387	425527	100.000	Total		7602174	151094	100.000

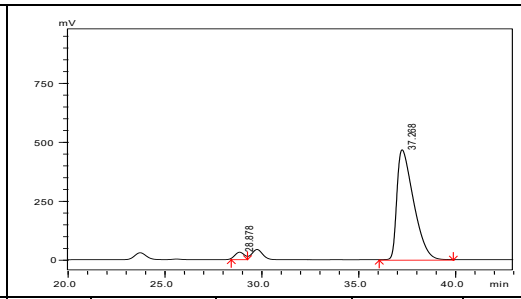


Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-4-oxotetrahydro-2H-thiopyran-3-yl)acetate (**3ag**)[7]

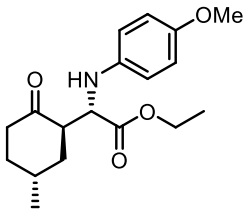
Yellow oil (49.2mg, 76% yield); 95:5 *dr*. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 6.71 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 5.17 (d, *J* = 10.0 Hz, 1H), 4.52–4.35 (m, 1H), 4.09–4.03 (m, 2H), 3.64 (s, 3H), 3.26–3.16 (m, 1H), 3.09–3.01 (m, 1H), 2.99–2.88 (m, 3H), 2.71–2.58 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 207.42, 171.93, 151.59, 141.83, 114.49, 114.34, 60.50, 56.64, 55.26, 54.50, 43.25, 31.32, 29.18, 14.03.

Optical Rotation: $[\alpha]^{25}_D$ = 32.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.7:3.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 37.3 min, t_{minor} = 28.9 min.





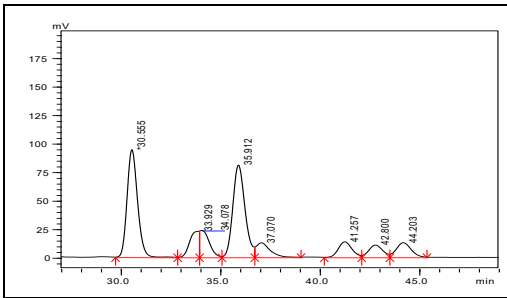
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	25.979	1464355	42912	26.461					
2	29.316	1289711	35313	23.306	1	28.878	957661	29339	3.329
3	30.192	1464988	37351	26.473					
4	38.538	1314855	27447	23.760	2	37.268	27811493	465943	96.671
Total		5533909	143022	100.000	Total		28769154	495282	100.000

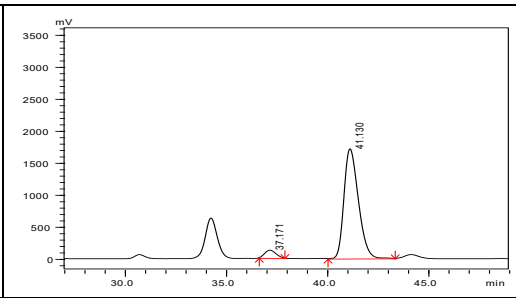


Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((1R,5R)-5-methyl-2-oxocyclohexyl)acetate (**3ah**)[7]

Yellow oil (50.5 mg, 79% yield); 80:20 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.73 (d, *J* = 8.9 Hz, 2H), 6.60 (d, *J* = 8.9 Hz, 2H), 4.16–4.07 (m, 3H), 3.69 (s, 3H), 3.20–2.94 (m, 1H), 2.42–2.31 (m, 2H), 2.26–2.09 (m, 1H), 2.06–1.90 (m, 2H), 1.79–1.48 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 211.17, 172.65, 152.74, 141.23, 115.35, 114.57, 61.00, 58.80, 55.43, 50.23, 37.58, 36.13, 33.16, 26.66, 19.27, 13.99.

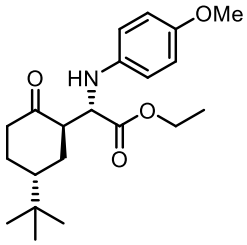
Optical Rotation: $[\alpha]^{25}_D$ = 23.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.6:4.4 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, retention time: t_{major} = 41.1 min, t_{minor} = 37.2 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	30.555	3429179	94170	31.856					
2	33.929	718696	22789	6.676					
3	34.078	797666	23474	7.410					
4	35.912	3413487	80732	31.710					
5	37.070	604612	12602	5.617	1	37.171	3920731	111616	4.437

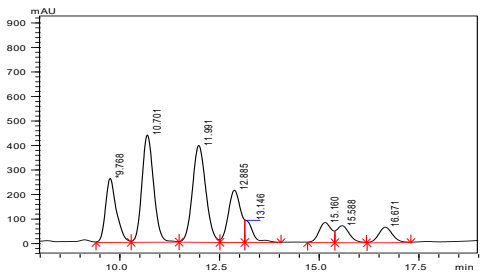
6	41.257	634184	13496	5.891	2	41.130	84444729	1713470	95.563
7	42.800	518317	10633	4.815					
8	44.203	648479	12665	6.024					
Total		10764620	270560	100.000	Total		88365460	1825086	100.000

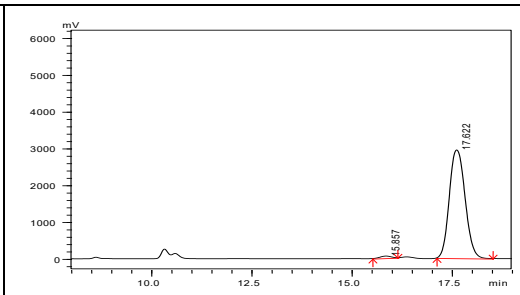


Ethyl (S)-2-((1R,5R)-5-(tert-butyl)-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ai**)[7]

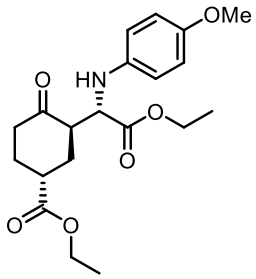
Yellow oil (52 mg, 72% yield); 98:2 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.74 (d, *J* = 8.9 Hz, 2H), 6.62 (d, *J* = 8.9 Hz, 2H), 4.32 (d, *J* = 9.2 Hz, 1H), 4.19–4.10 (m, 2H), 3.72 (s, 3H), 2.85–2.66 (m, 1H), 2.46–2.32 (m, 2H), 2.08–1.97 (m, 2H), 1.78–1.62 (m, 2H), 1.55–1.44 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 4H), 0.92 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 210.35, 173.03, 151.72, 142.78, 114.90, 114.43, 60.56, 57.09, 55.69, 52.11, 46.01, 41.08, 32.63, 30.98, 27.85, 27.59, 14.55.

Optical Rotation: $[\alpha]^{25}_D$ = 26.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.7:1.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 17.6 min, t_{minor} = 15.9 min.





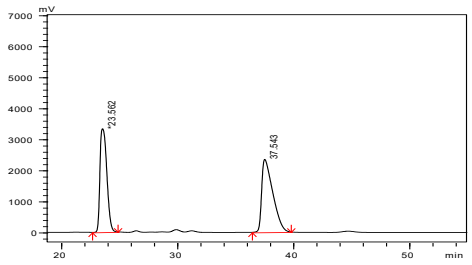
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	9.768	4836354	258659	14.620					
2	10.701	8820779	435507	26.665					
3	11.991	9103491	392540	27.520					
4	12.885	4495806	210943	13.591					
5	13.146	1233104	90993	3.728					
6	15.160	1702352	79772	5.146					
7	15.588	1471966	67255	4.450	1	15.857	1024175	55899	1.259
8	16.671	1416189	61151	4.281	2	17.622	80332209	2940636	98.741
Total		33080042	1596820	100.000	Total		81356384	2996535	100.000

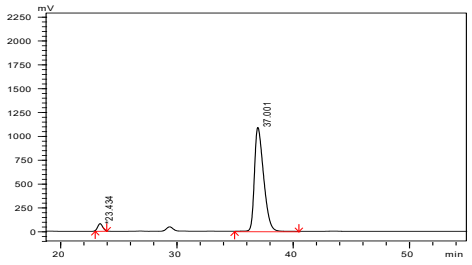


Ethyl (1R,3R)-3-((S)-2-ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)-4-oxocyclohexan-e-1-carboxylate (**3aj**)[7]

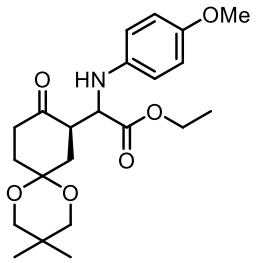
Yellow oil (62.6 mg, 83% yield); 97:3 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.78 (d, *J* = 8.9 Hz, 2H), 6.66 (d, *J* = 8.9 Hz, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.21–4.14 (m, 2H), 3.96 (d, *J* = 4.3 Hz, 1H), 3.76 (s, 3H), 3.45–3.30 (m, 1H), 3.02–2.90 (m, 1H), 2.60–2.32 (m, 4H), 2.28–2.19 (m, 1H), 2.01–1.95 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 4H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 210.12, 173.99, 172.67, 152.94, 142.05, 115.75, 114.79, 61.30, 60.95, 59.13, 55.70, 50.20, 38.48, 38.20, 31.05, 27.61, 14.25, 14.10.

Optical Rotation: $[\alpha]^{25}_D$ = 29.2 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.5:3.5 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 37.0 min, t_{minor} = 23.4 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	23.562	136890929	3331390	49.090	1	23.434	2140847	74778	3.492
2	37.543	141965903	2284773	50.910	2	37.001	59160419	1088375	96.508
Total		278856831	5616163	100.000	Total		61301265	1163153	100.000

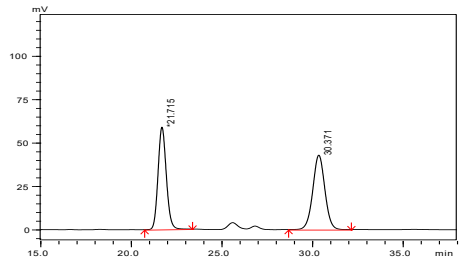


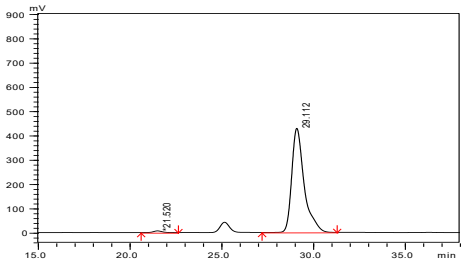
Ethyl 2-((R)-3,3-dimethyl-9-oxo-1,5-dioxaspiro[5.5]undecan-8-yl)-2-((4-methoxyphenyl)a-mino)acetate (**3ak**)[7]

Yellow oil (63 mg, 78% yield); 97:3 *dr*. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.76 (d, *J* = 8.8 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 4.25–4.07 (m, 3H), 3.94 (d, *J* = 3.4 Hz, 1H), 3.73 (s, 3H), 3.57 (s, 2H), 3.55 (d, *J* = 5.1 Hz, 2H), 3.40–3.32 (m, 1H), 2.60–2.50 (m, 3H), 2.36–2.29 (m, 1H), 2.07 (t, *J* = 13.3 Hz, 1H), 1.80–1.72 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.04 (s, 3H), 0.98 (s, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 209.91,

172.69, 152.97, 142.13, 115.89, 114.81, 96.60, 70.74, 70.47, 61.30, 59.02, 55.71, 48.82, 36.85, 35.42, 30.51, 30.24, 22.64, 22.52, 14.10.

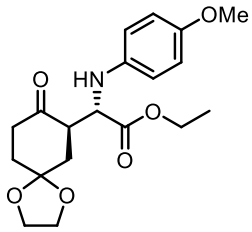
Optical Rotation: $[\alpha]^{25}_{D}$ = 20.8 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 98.9:1.1 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 29.1 min, t_{minor} = 21.5 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	21.715	1868303	58941	49.522
2	30.371	1904339	42274	50.478
Total		3772642	101215	100.000

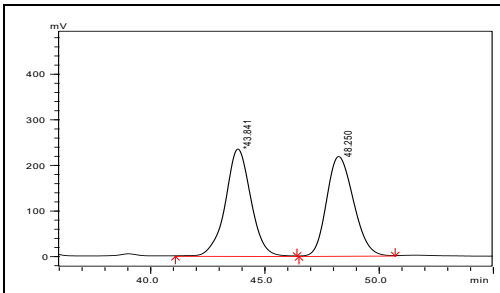
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	21.520	225377	6923	1.106
2	29.112	20156943	428309	98.894
Total		20382320	435232	100.000

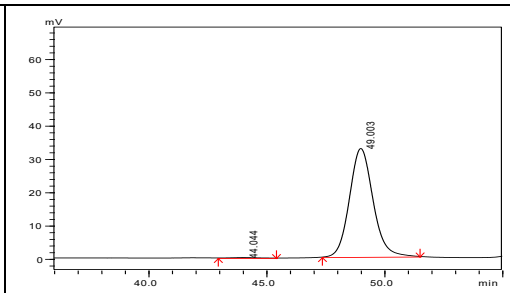


Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-8-oxo-1,4-dioxaspiro[4.5]decan-7-yl)acetate (**3al**)[7]

Yellow oil (59.5mg, 82% yield); >99:1 dr. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 8.9 Hz, 2H), 6.62 (d, *J* = 8.9 Hz, 2H), 4.37–4.09 (m, 3H), 4.09–4.00 (m, 4H), 3.91 (d, *J* = 3.6 Hz, 1H), 3.73 (s, 3H), 3.53–3.42 (m, 1H), 2.72–2.62 (m, 1H), 2.45–2.36 (m, 1H), 2.29 (t, *J* = 13.1 Hz, 1H), 2.14–2.07 (m, 1H), 2.05–1.93 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 209.58, 172.65, 152.89, 142.10, 115.83, 114.72, 107.47, 64.81, 64.65, 61.29, 58.98, 55.65, 50.00, 37.96, 37.59, 33.81, 14.08.

Optical Rotation: $[\alpha]^{25}_{D}$ = 22.0 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 99.7:0.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 49.0 min, t_{minor} = 44.0 min.

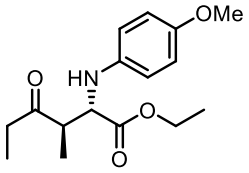




Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	43.841	17987636	234192	50.400
2	48.250	17702408	217515	49.600

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	44.044	7170	128	0.317
2	49.003	2256971	32519	99.683

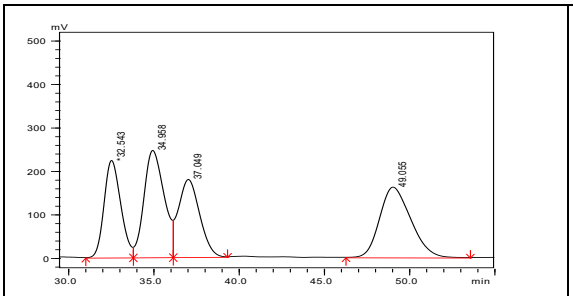
Total		35690044	451707	100.000	Total		2264141	32646	100.000

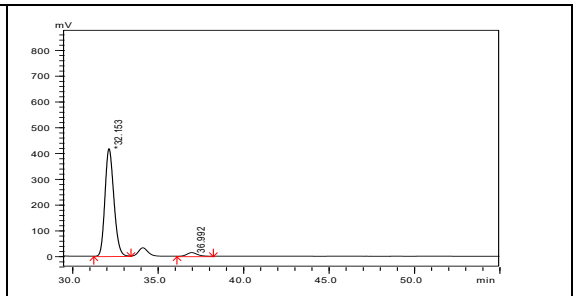


Ethyl (2S,3R)-2-((4-methoxyphenyl)amino)-3-methyl-4-oxohexanoate (**3am**)[7]

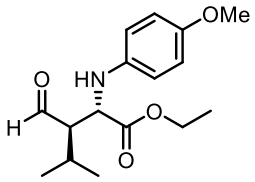
Yellow oil (37 mg, 63% yield); 99:1 *dr*. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 9.0 Hz, 2H), 6.64 (d, *J* = 9.0 Hz, 2H), 4.19 (d, *J* = 7.0 Hz, 1H), 4.16–4.10 (m, 2H), 3.73 (s, 3H), 3.08–2.98 (m, 1H), 2.58–2.49 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 212.20, 172.76, 153.05, 140.80, 115.81, 114.79, 61.16, 60.78, 55.64, 48.36, 34.94, 14.12, 13.36, 7.50.

Optical Rotation: $[\alpha]^{25}_D$ = -19.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.5:3.5 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 96/4, flow rate = 1.0 mL/min, λ = 240 nm, retention time: t_{major} = 32.2 min, t_{minor} = 37.0 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	32.543	15123649	223170	21.235	1	32.153	15097968	416546	96.450
2	34.958	20192530	245644	28.352					
3	37.049	15524631	178304	21.798	2	36.992	555761	13746	3.550
4	49.055	20379392	161616	28.615					
Total		71220201	808733	100.000	Total		15653728	430292	100.000

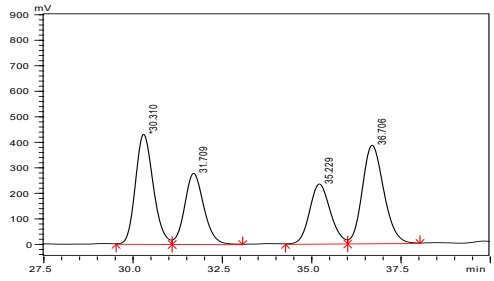


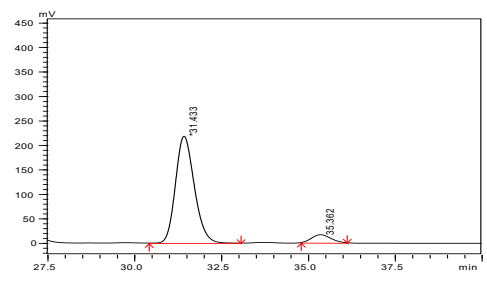
Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)-4-methylpentanoate (**3an**)[7]

Yellow oil (38.7 mg, 66% yield); 90:10 *dr*. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 9.74 (d, *J* = 3.5 Hz, 1H), 6.76 (d, *J* = 8.9 Hz, 2H), 6.66 (d, *J* = 8.9 Hz, 2H), 4.35 (d, *J* = 7.7 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 2.61–2.53 (m, 1H), 2.16–2.05 (m, 1H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 203.20, 172.81, 153.26, 140.46, 115.86, 114.77, 61.30, 59.58, 57.24, 55.59, 27.51, 21.20, 19.12, 14.08.

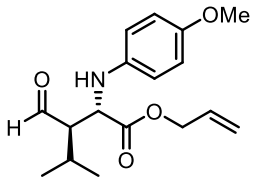
Optical Rotation: $[\alpha]^{25}_D$ = -17.8 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:**

96.4:3.6 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 88/12, flow rate = 0.5 mL/min, λ = 240 nm, retention time: t_{major} = 31.4 min, t_{minor} = 35.4 min.





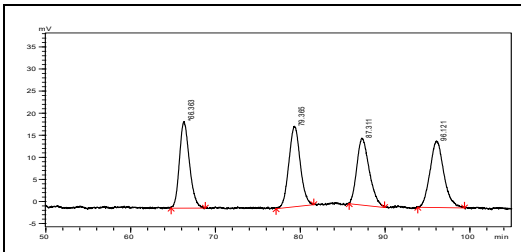
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	30.310	14305758	422877	29.542					
2	31.709	9734467	271744	20.102	1	31.433	8218583	218268	96.388
3	35.229	9849046	233238	20.339	2	35.362	307995	16204	3.612
4	36.706	14535711	381538	30.017					
Total		48424982	1309397	100.000	Total		8526578	234472	100.000

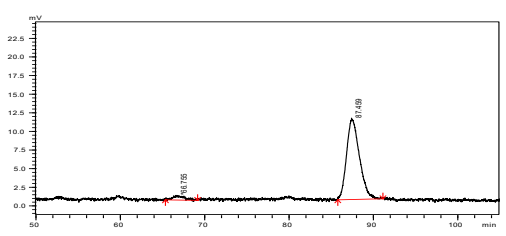


Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)octanoate (**3en**)[7]

Yellow oil (43.3 mg, 71% yield); 99:1 *dr*. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.66 (d, *J* = 3.9 Hz, 1H), 6.73 (d, *J* = 9.0 Hz, 2H), 6.68 (d, *J* = 9.0 Hz, 2H), 5.83 (m, 1H), 5.66 (d, *J* = 10.7 Hz, 1H), 5.24 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.17 (dd, *J* = 10.5, 1.6 Hz, 1H), 4.56 (d, *J* = 5.3 Hz, 2H), 4.53–4.47 (m, 1H), 3.64 (s, 3H), 2.50–2.44 (m, 1H), 2.02–1.88 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 203.74, 172.27, 151.87, 141.20, 132.19, 117.85, 114.62, 114.48, 64.83, 58.60, 56.02, 55.23, 26.87, 20.97, 18.42.

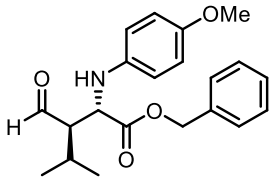
Optical Rotation: $[\alpha]^{25}_D$ = -26.5 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.1:3.9 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 98/2, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 87.5 min, t_{minor} = 66.8 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	66.363	1584624	19538	24.426	1	66.755	46786	583	3.958
2	79.365	1685158	18159	25.975					
3	87.311	1533840	15090	23.643	2	87.459	1135291	10879	96.042

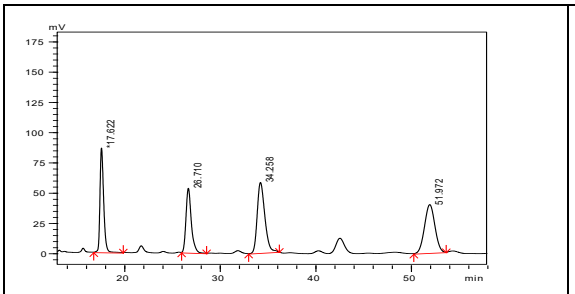
4	96.121	1683905	15029	25.956					
Total		6487528	67816	100.000	Total		1182078	11463	100.000

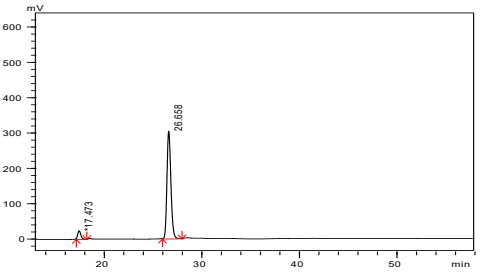


Benzyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)-4-methylpentanoate (**3gn**)[7]

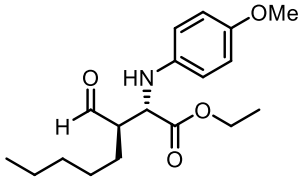
Yellow oil (48 mg, 68% yield); 92:8 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.72 (d, *J* = 3.4 Hz, 1H), 7.37–7.28 (m, 3H), 7.26–7.14 (m, 2H), 6.76 (d, *J* = 8.9 Hz, 2H), 6.66 (d, *J* = 8.9 Hz, 2H), 5.13 (d, *J* = 1.1 Hz, 2H), 4.43 (d, *J* = 7.9 Hz, 1H), 3.74 (s, 3H), 2.68–2.57 (m, 1H), 2.09–1.98 (m, 1H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 203.09, 172.66, 153.22, 140.30, 135.11, 128.42, 128.27, 128.13, 115.85, 114.72, 66.95, 59.41, 57.16, 55.52, 27.46, 21.12, 18.98.

Optical Rotation: $[\alpha]^{25}_D$ = -11.3 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 96.7:3.3 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 26.7 min, t_{minor} = 17.5 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)	Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	17.622	2143617	84667	20.954	1	17.473	291905	23351	3.332
2	26.710	2042773	53207	19.968	2	26.658	8469989	303636	96.668
3	34.258	3051029	57401	29.824					
4	51.972	2992729	39849	29.254					
Total		10230149	235124	100.000	Total		8761893	326988	100.000

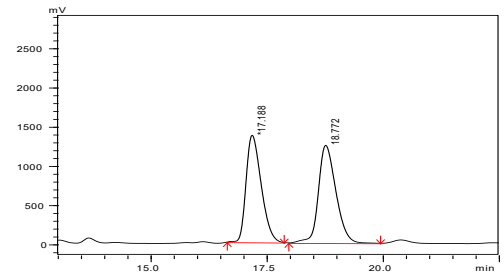


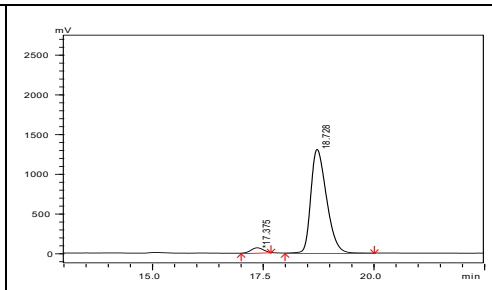
Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)octanoate (**3ao**)[7]

Yellow oil (43.7 mg, 68% yield); 92:8 *dr*. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.65 (d, *J* = 2.5 Hz, 1H), 6.77 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 8.9 Hz, 2H), 4.26 (d, *J* = 6.5 Hz, 1H), 4.21–4.12 (m, 2H), 3.73 (s, 3H), 2.87–2.64 (m, 1H), 1.78–1.67 (m, 1H), 1.60–1.51 (m, 1H), 1.37–1.26 (m, 6H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.89–0.84 (m, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 202.34, 172.27, 153.20, 140.39, 115.72, 114.88, 61.53, 58.14, 55.68, 53.97, 31.68, 26.99, 25.69, 22.36, 14.18, 13.96.

Optical Rotation: $[\alpha]^{25}_D$ = -22.6 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:**

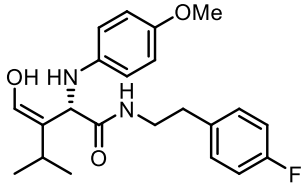
96.6:3.4 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 0.7 mL/min, λ = 254 nm, retention time: t_{major} = 17.4 min, t_{minor} = 18.3 min.





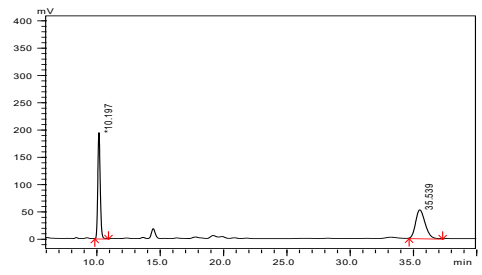
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	17.188	30944242	1363793	49.740
2	18.772	31267358	1230548	50.260
Total		62211600	2594341	100.000

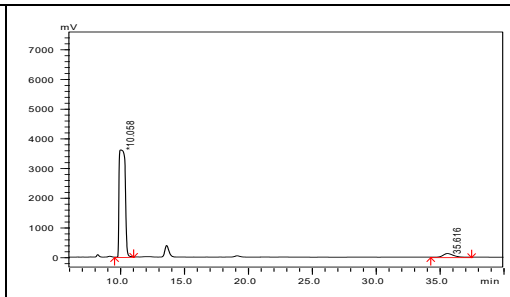
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	17.375	1142500	61585	3.449
2	18.728	31984718	1303755	96.551
Total		33127217	1365339	100.000



(S,Z)-*N*-(4-fluorophenethyl)-3-(hydroxymethylene)-2-((4-methoxyphenyl)amino)-4-methyl-pentanamide (**3pn**)

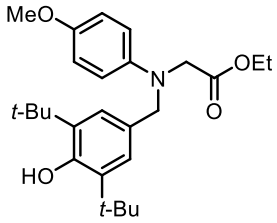
Yellow oil (47.9 mg, 62% yield); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.23–7.03 (m, 1H), 7.03–6.86 (m, 5H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.51 (d, *J* = 8.9 Hz, 2H), 5.84 (s, 1H), 5.07 (s, 1H), 3.75 (s, 3H), 3.72 (s, 1H), 3.31–3.19 (m, 1H), 3.01–2.77 (m, 2H), 2.75–2.67 (m, 1H), 2.60–2.48 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 169.99, 167.85, 161.52 (d, J_1 = 243 Hz, Cq), 153.30, 139.14, 134.74, 134.71 (d, J_4 = 3 Hz, Cq), 130.27 (d, J_3 = 7 Hz, CH), 130.19, 120.58, 115.52, 115.20 (d, J_2 = 21 Hz, CH), 115.00, 72.93, 55.64, 41.40, 34.08, 27.03, 22.27, 20.08. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -116.58. **HRMS (ESI)** *m/z*: calcd for $C_{22}H_{26}{}^{19}FN_2O_4$ $[M+H]^+$ 369.1973, found 369.1981. **Optical Rotation:** $[\alpha]^{25}_D$ = -19.4 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 95.0:5.0 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 90/10, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_{major} = 10.1 min, t_{minor} = 35.5 min.





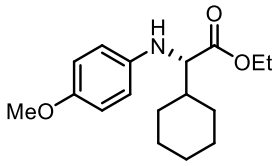
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	10.197	2573929	193933	49.092
2	35.539	2669143	52080	50.908
Total		5243072	246013	100.000

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	10.058	118459950	3602324	94.978
2	35.616	6263026	119553	5.022
Total		124722977	3721877	100.000



Ethyl *N*-(3,5-di-tert-butyl-4-hydroxybenzyl)-*N*-(4-methoxyphenyl)glycinate (**1a-BHT**)[9]

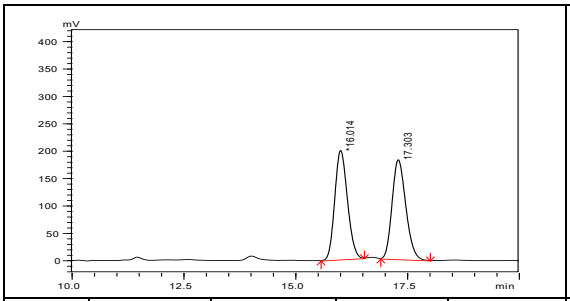
Colorless oil; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.07 (s, 2H), 6.81 (d, *J* = 9.1 Hz, 2H), 6.73 (d, *J* = 9.2 Hz, 2H), 5.14 (s, 1H), 4.47 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 2H), 3.75 (s, 3H), 1.41 (s, 18H), 1.23 (s, 3H).

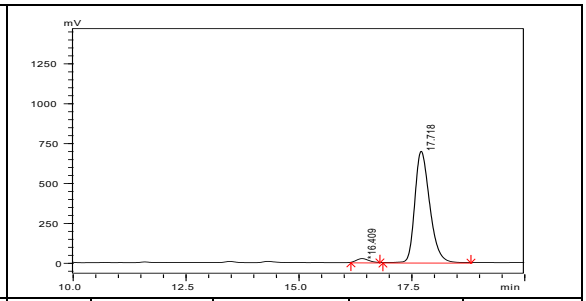


Ethyl (S)-2-cyclohexyl-2-((4-methoxyphenyl)amino)acetate (**4**)[10]

Colorless oil (371 mg, 78% yield). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 6.66 (d, *J* = 9.0 Hz, 2H), 6.52 (d, *J* = 8.9 Hz, 2H), 4.04 (m, 2H), 3.63 (m, 1H), 3.60 (s, 3H), 1.83 (m, 1H), 1.73–1.51 (m, 5H), 1.12–1.11 (m, 8H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 173.68, 151.07, 142.25, 114.49, 113.62, 62.16, 59.93, 55.26, 40.22, 29.15, 29.13, 25.86, 25.64, 14.24.

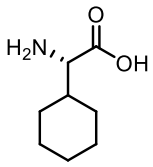
Optical Rotation: $[\alpha]^{25}_D$ = 26.8 (c = 1.0, CH_2Cl_2). The *ee* value was determined by **HPLC analysis:** 97.4:2.6 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 88/12, flow rate = 1.0 mL/min, λ = 214 nm, retention time: t_{major} = 17.7 min, t_{minor} = 16.4 min.





Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	16.014	3908795	198740	50.261
2	17.303	3868228	181463	49.739
Total		7777023	380203	100.000

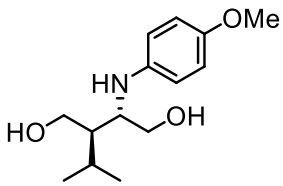
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	16.409	420509	23480	2.574
2	17.718	15918243	696906	97.426
Total		16338751	720386	100.000



(S)-2-amino-2-cyclohexylacetic acid (**5**)[11]

White powder (138 mg, 88% yield). **^{1}H NMR** (600 MHz, Methanol-d_4) δ 3.75 (m, 1H), 1.93–1.86 (m, 1H), 1.81–1.75 (m, 3H), 1.65 (m, 2H), 1.27 (m, 3H), 1.18–1.08 (m, 2H). **^{13}C NMR** (150 MHz, Methanol-d_4) δ 171.18, 58.88, 40.24, 29.54, 29.28, 27.05, 26.97, 26.77.

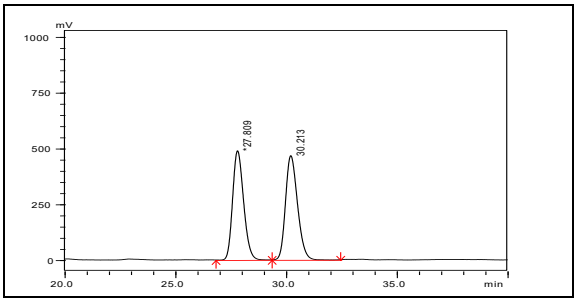
Optical Rotation: $[\alpha]^{25}_D$ = 31 (c = 1.0, MeOH).

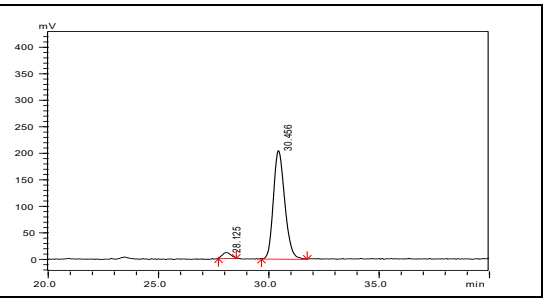


(2R,3S)-2-Isopropyl-3-((4-methoxyphenyl)amino)butane-1,4-diol (**6**)[12]

Yellow oil (86 mg, 85% yiled); > 99:1 dr. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 6.75 (d, *J* = 8.9 Hz, 2H), 6.68 (d, *J* = 8.9 Hz, 2H), 3.83–3.80 (m, 1H), 3.78–3.75 (m, 1H), 3.73 (s, 3H), 3.69 (m, 1H), 3.59 (m, 1H), 3.52 (m, 1H), 1.86 (m, 1H), 1.58 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, Chloroform-*d*) δ 152.66, 141.69, 141.67, 116.21, 114.87, 62.47, 61.47, 58.60, 55.66, 47.55, 27.38, 21.20, 18.925.

Optical Rotation: $[\alpha]^{25}_D$ = 26.3 (c = 1.0, MeOH). The *ee* value was determined by **HPLC analysis:** 96.4:3.6 *er*, Chiralcel AD-H colum, hexane/*i*-PrOH = 93/7, flow rate = 0.5 mL/min, λ = 254 nm, retention time: t_{major} = 30.5 min, t_{minor} = 28.1 min.



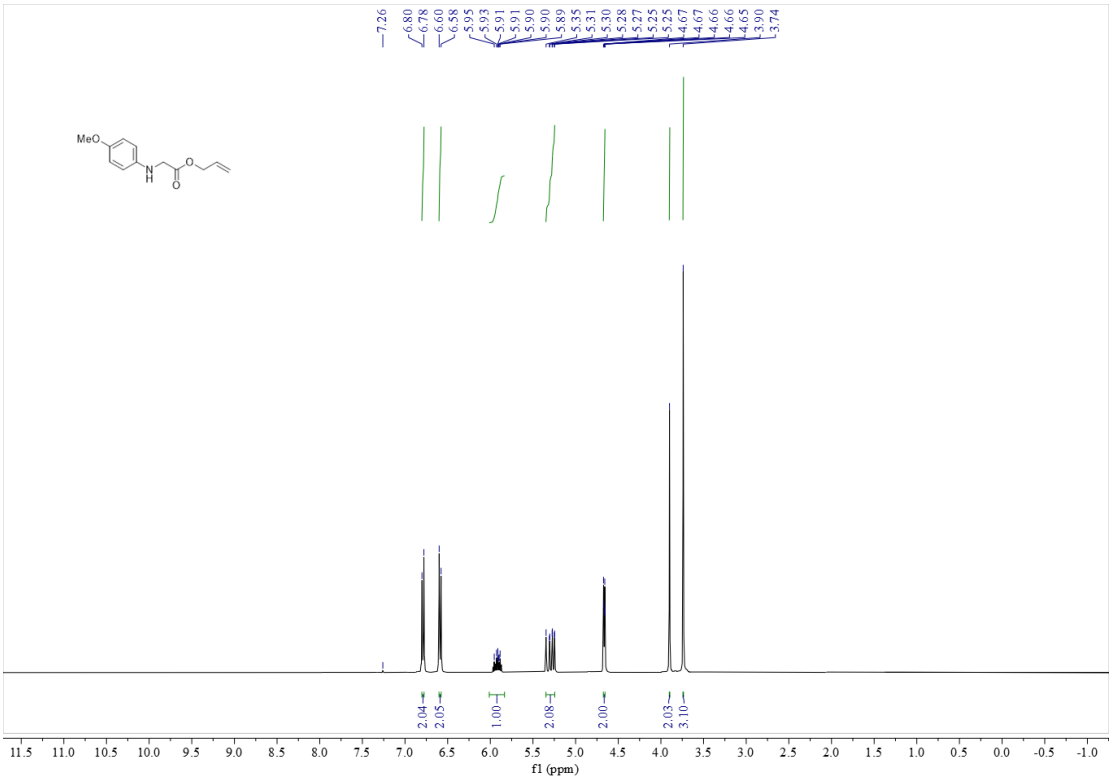


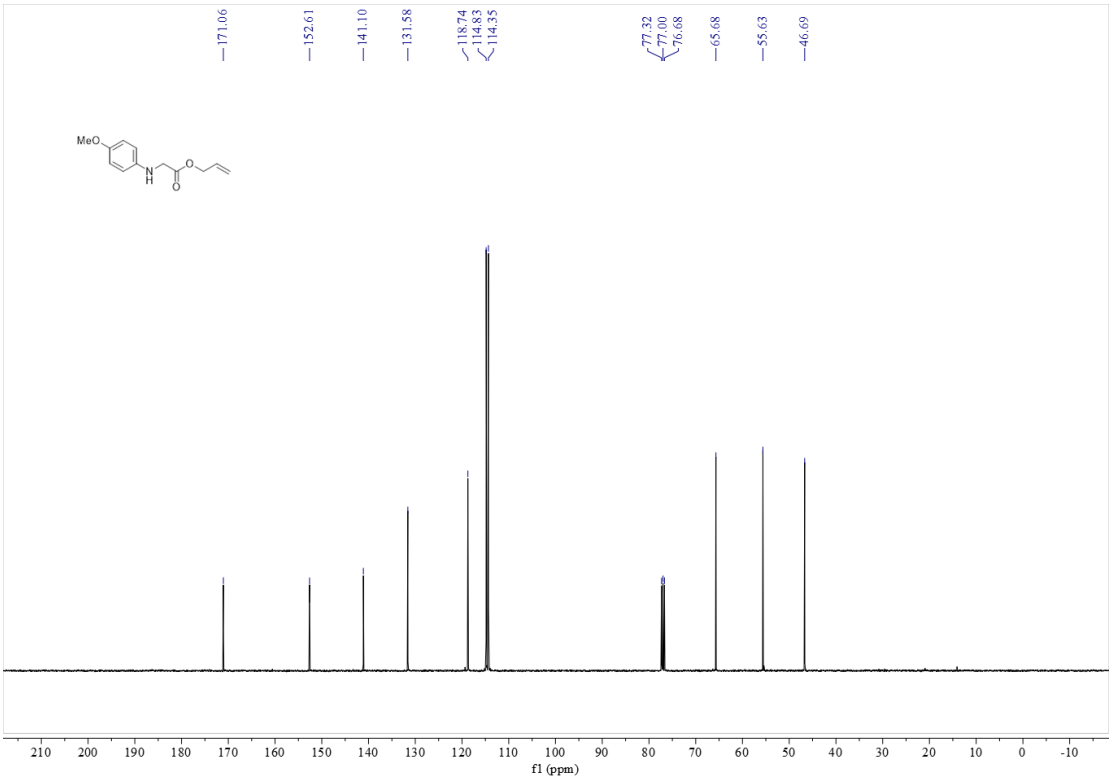
Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	27.809	16788171	488795	49.039
2	30.213	17446327	466302	50.961
Total		34234498	955097	100.000

Peak	RetTime (min)	Area (mV*s)	Height (mV)	Conc. (%)
1	28.125	268128	10169	3.557
2	30.456	7269158	203683	96.443
Total		7537287	213852	100.000

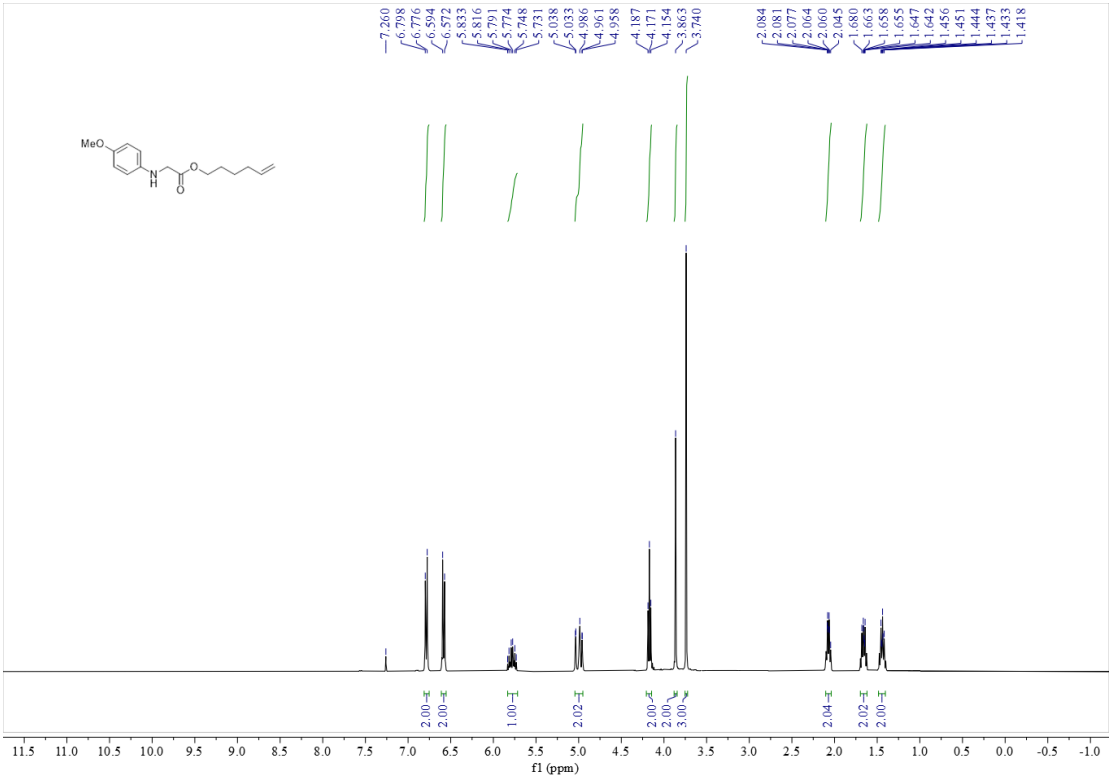
5. NMR spectra

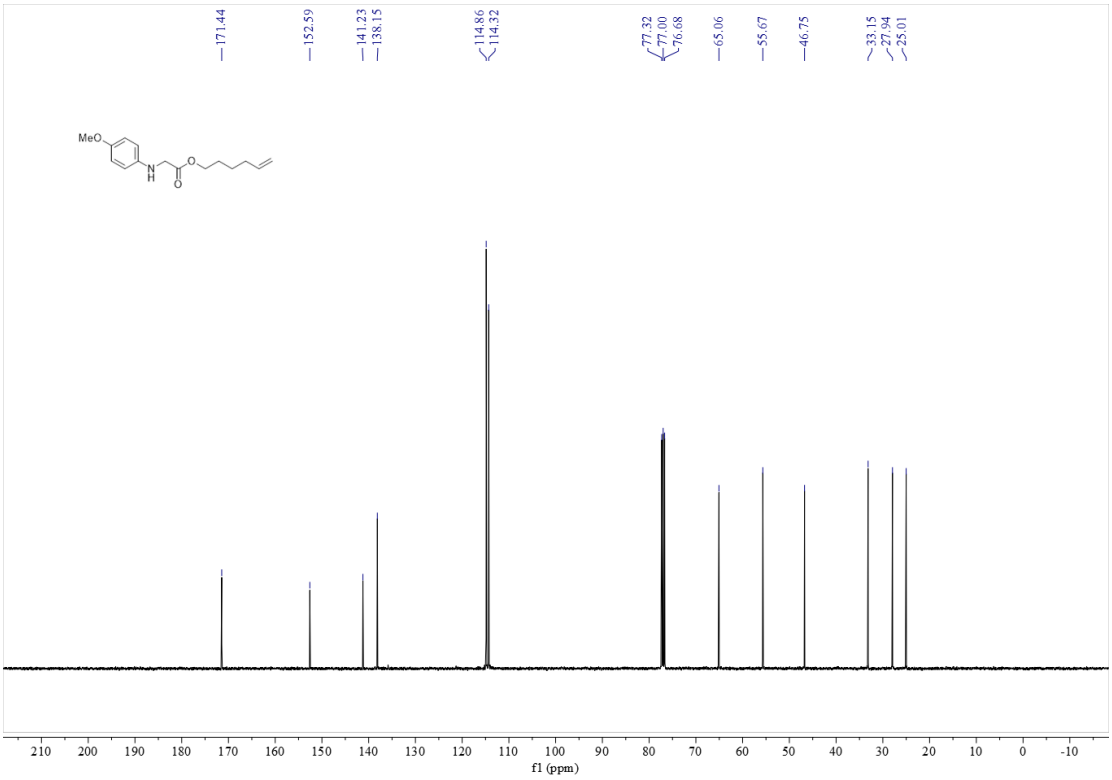
Allyl (4-methoxyphenyl)glycinate (**1e**)



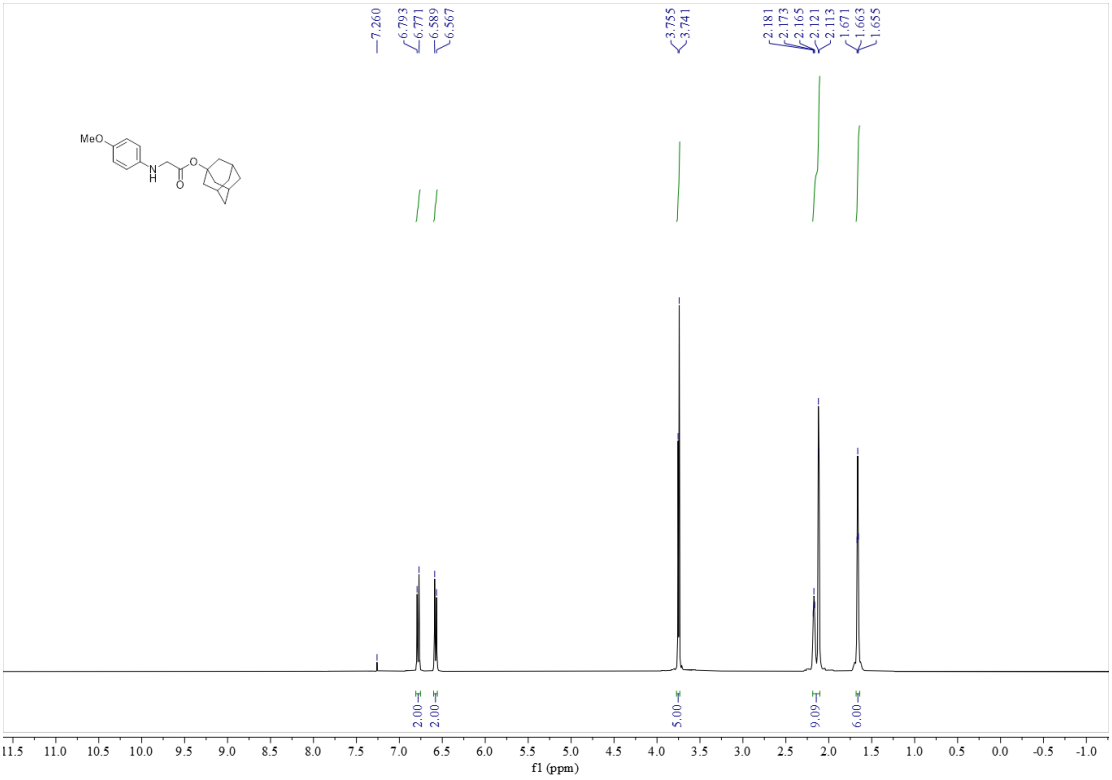


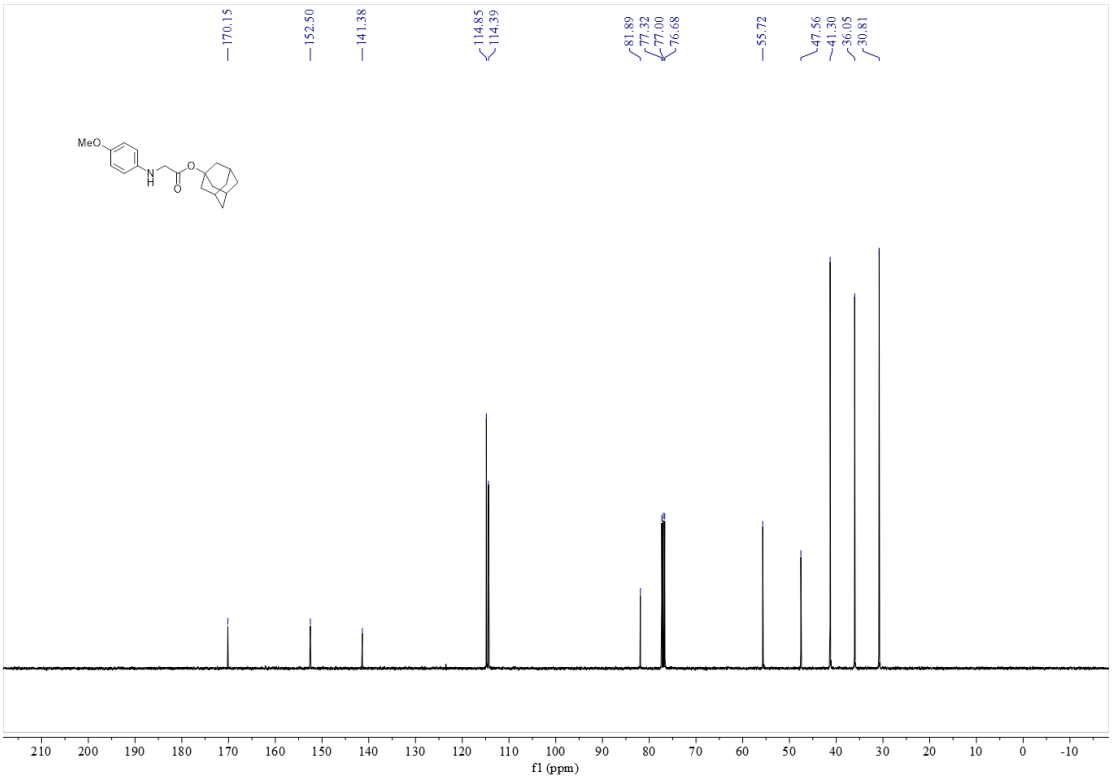
Hex-5-en-1-yl (4-methoxyphenyl)glycinate (**1f**)



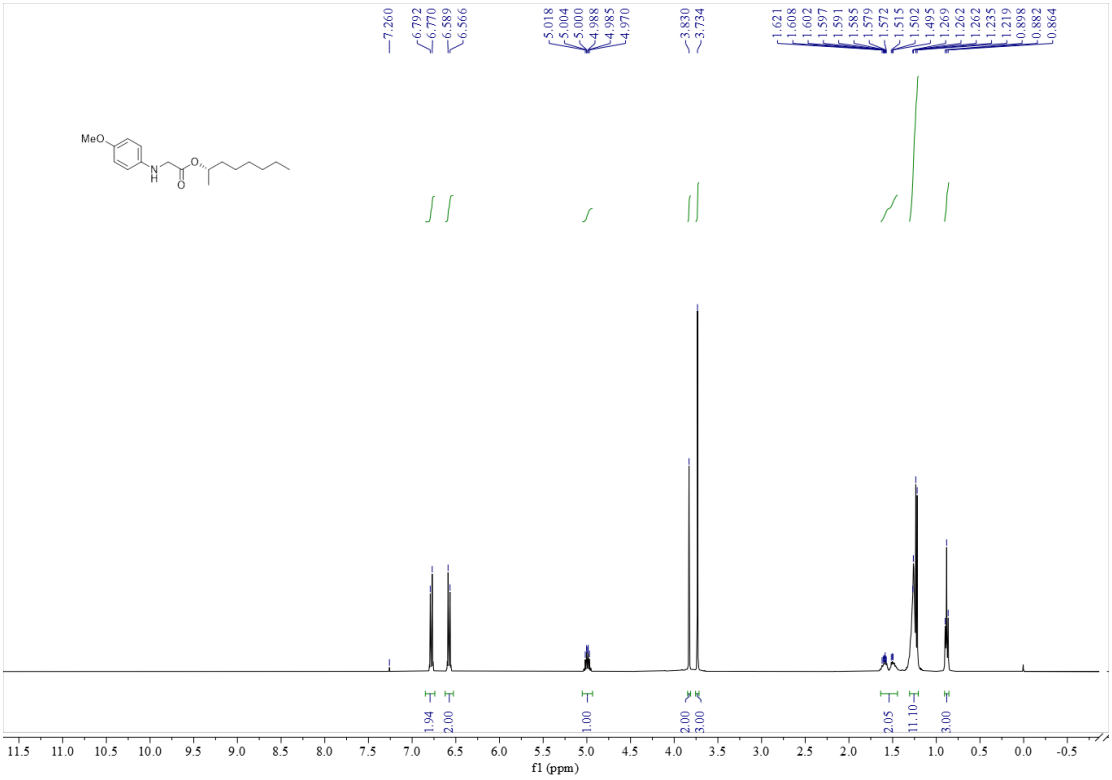


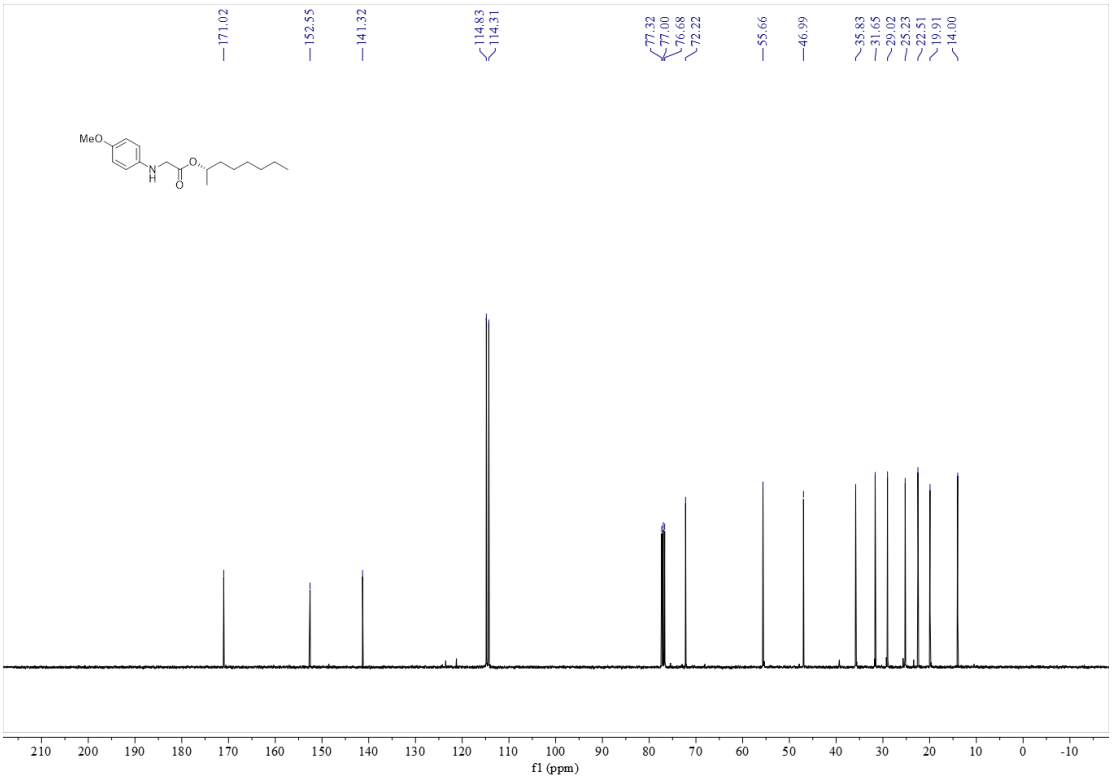
(1S,3S)-Adamantan-1-yl (4-methoxyphenyl)glycinate (**1h**)



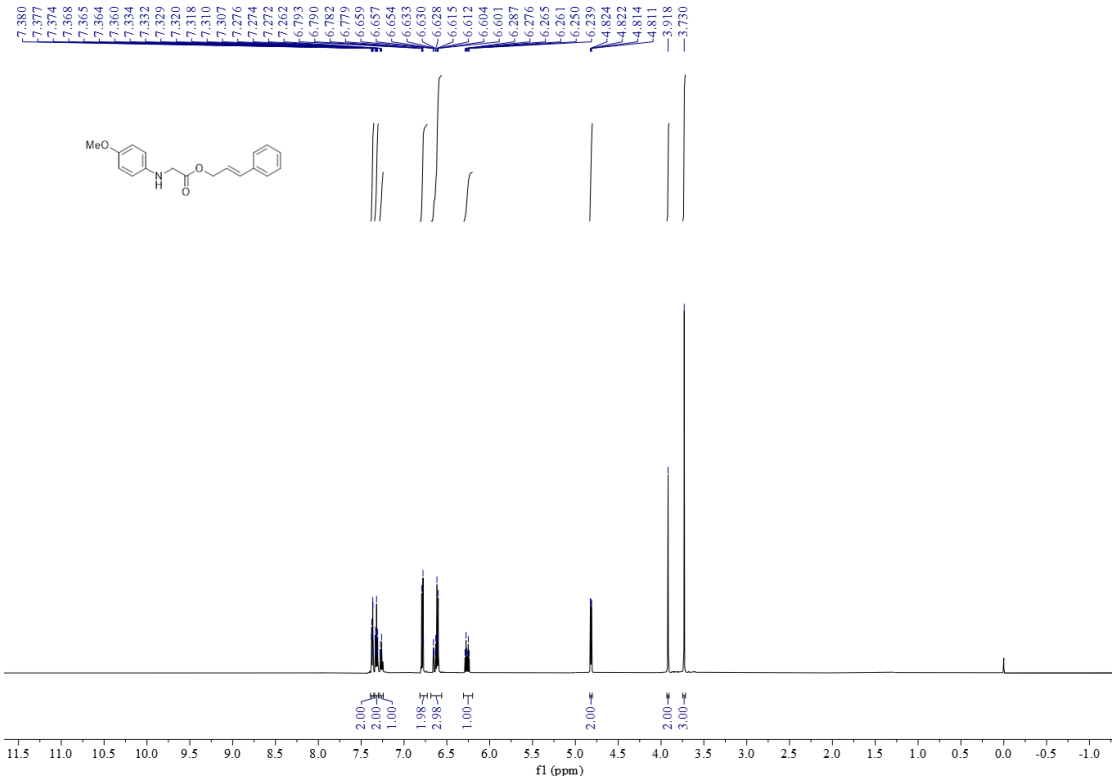


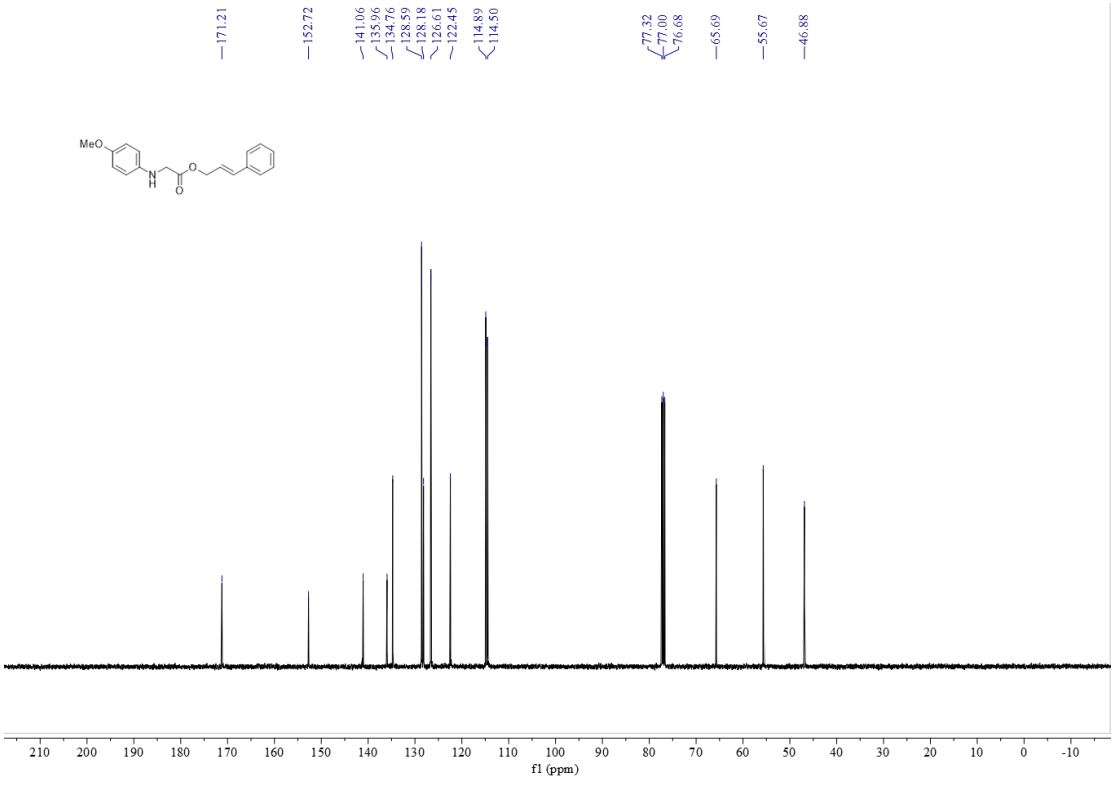
(S)-octan-2-yl (4-methoxyphenyl)glycinate (**1i**)



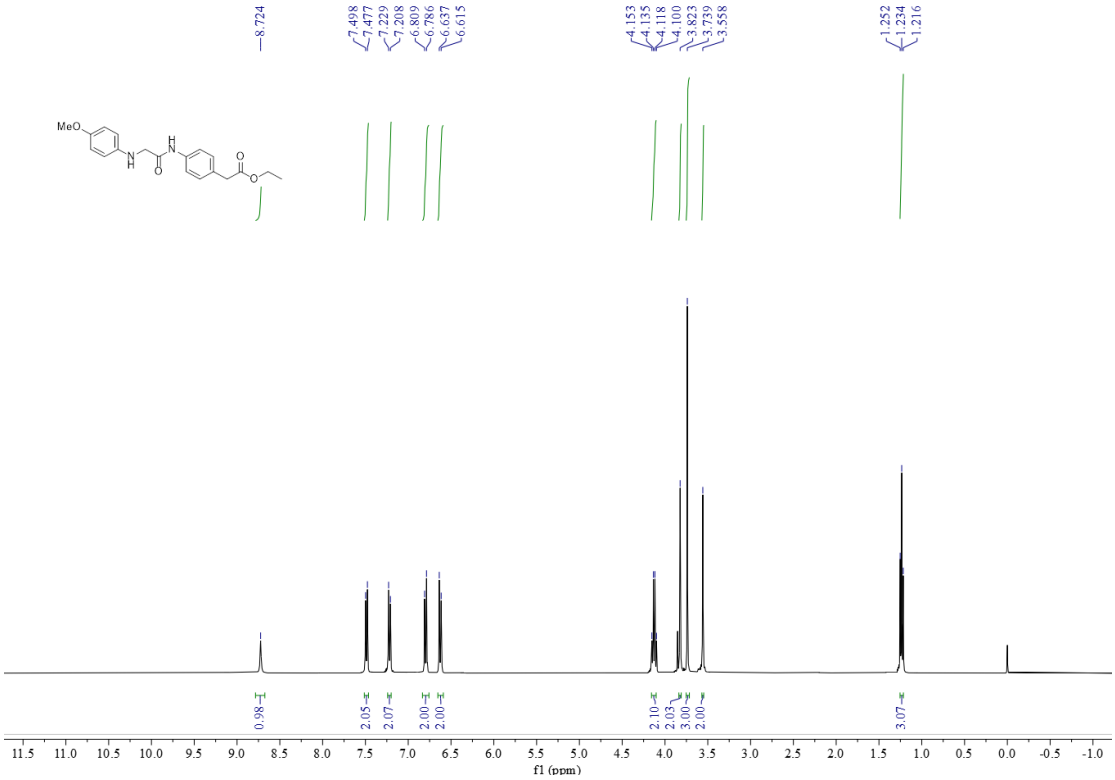


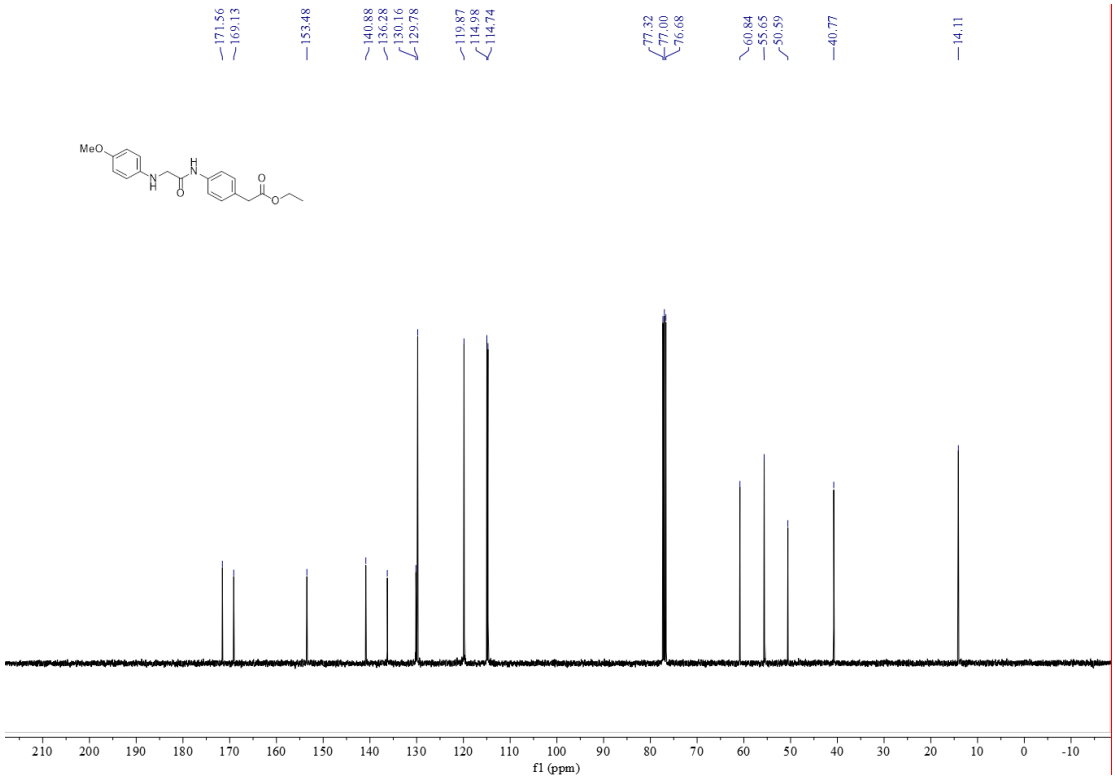
Cinnamyl (4-methoxyphenyl)glycinate (**1n**)



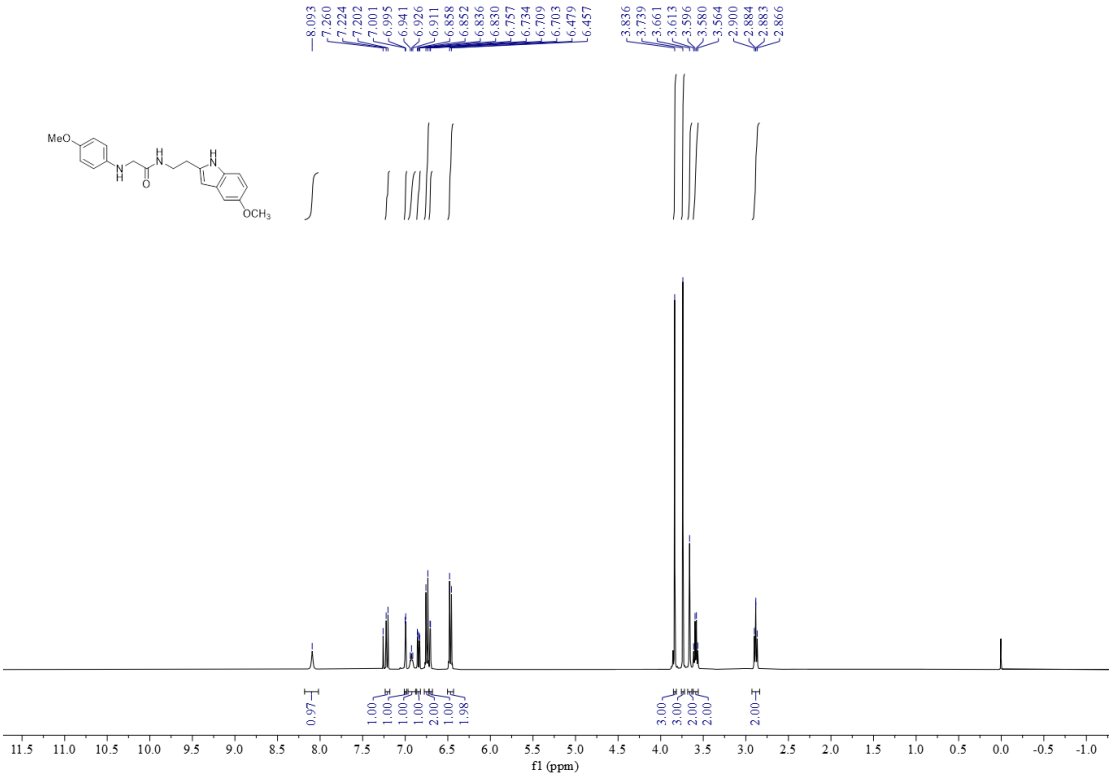


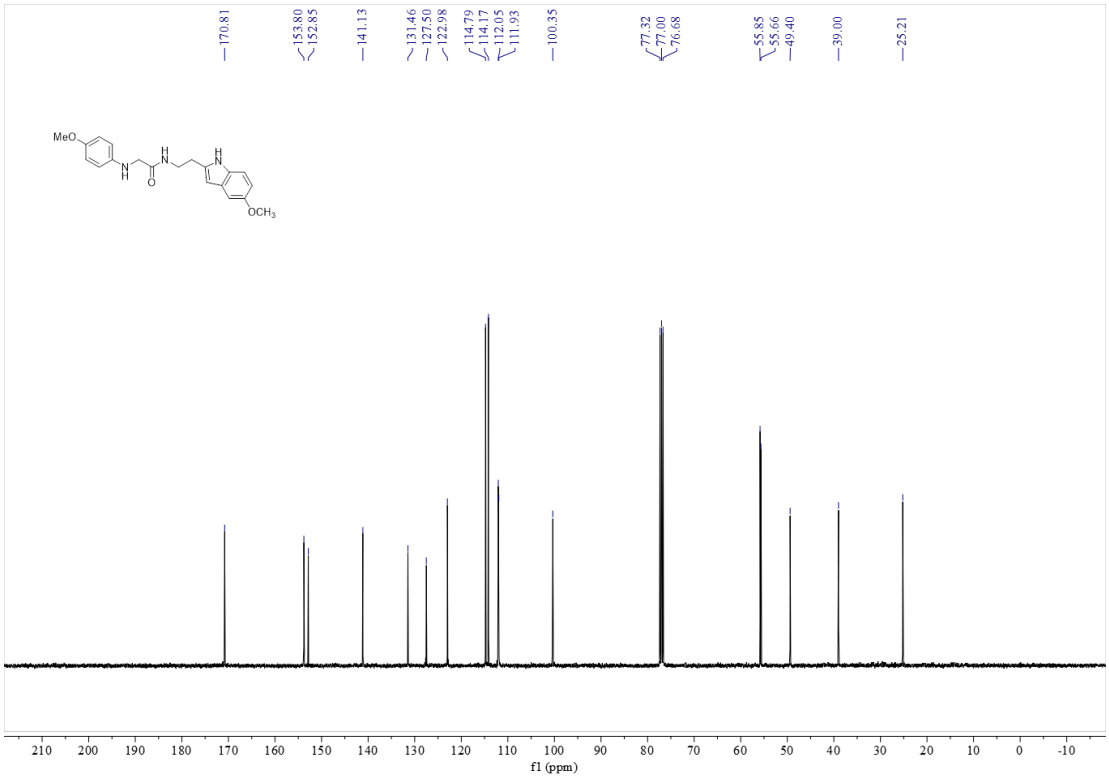
Ethyl 2-(4-(2-((4-methoxyphenyl)amino)acetamido)phenyl)acetate (**1r**)



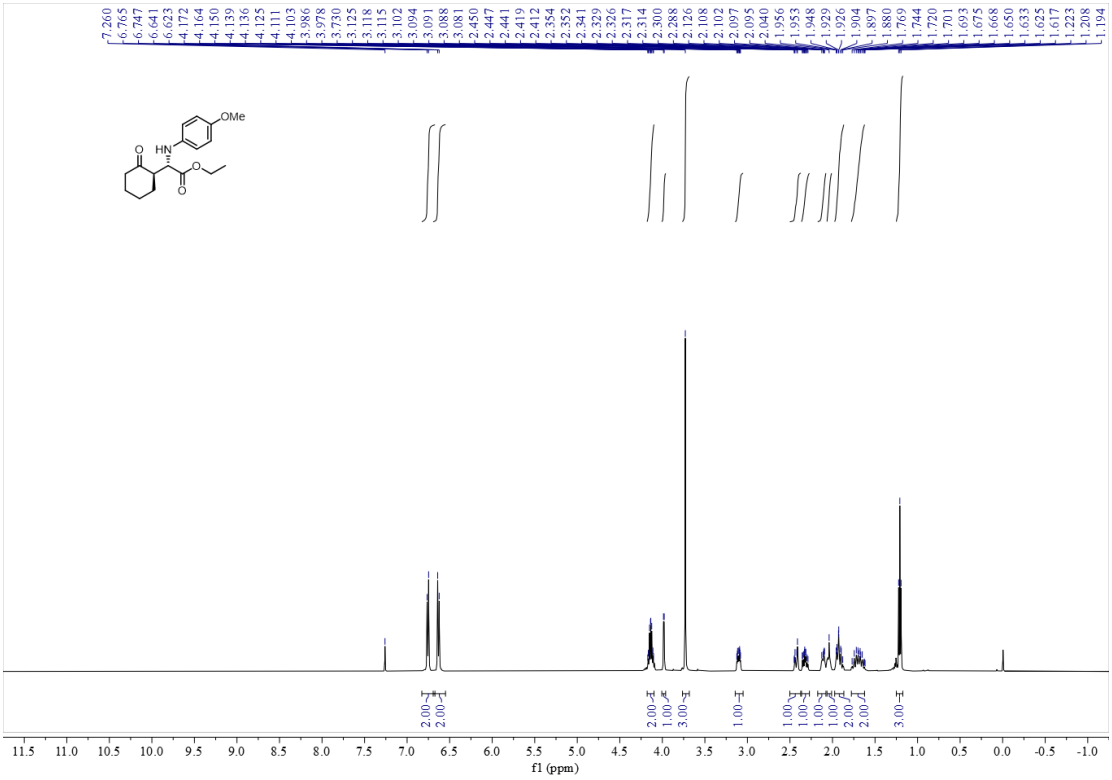


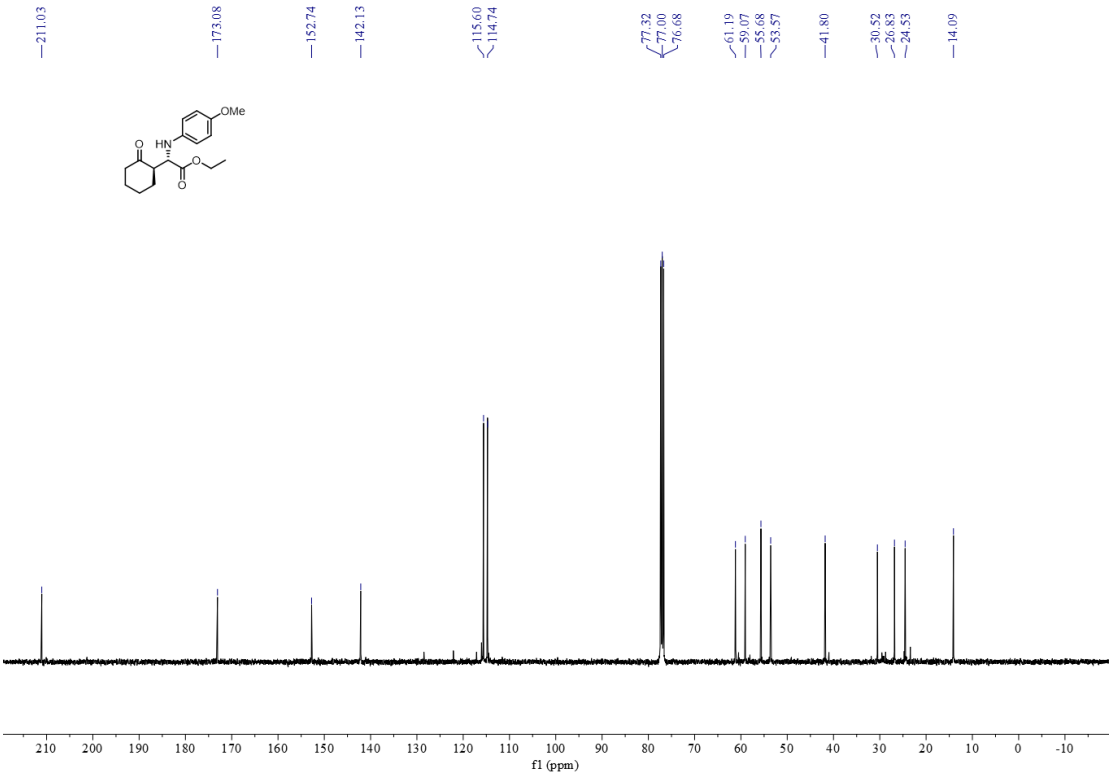
N-(2-(5-methoxy-1H-indol-2-yl)ethyl)-2-((4-methoxyphenyl)amino)acetamide (**1t**)



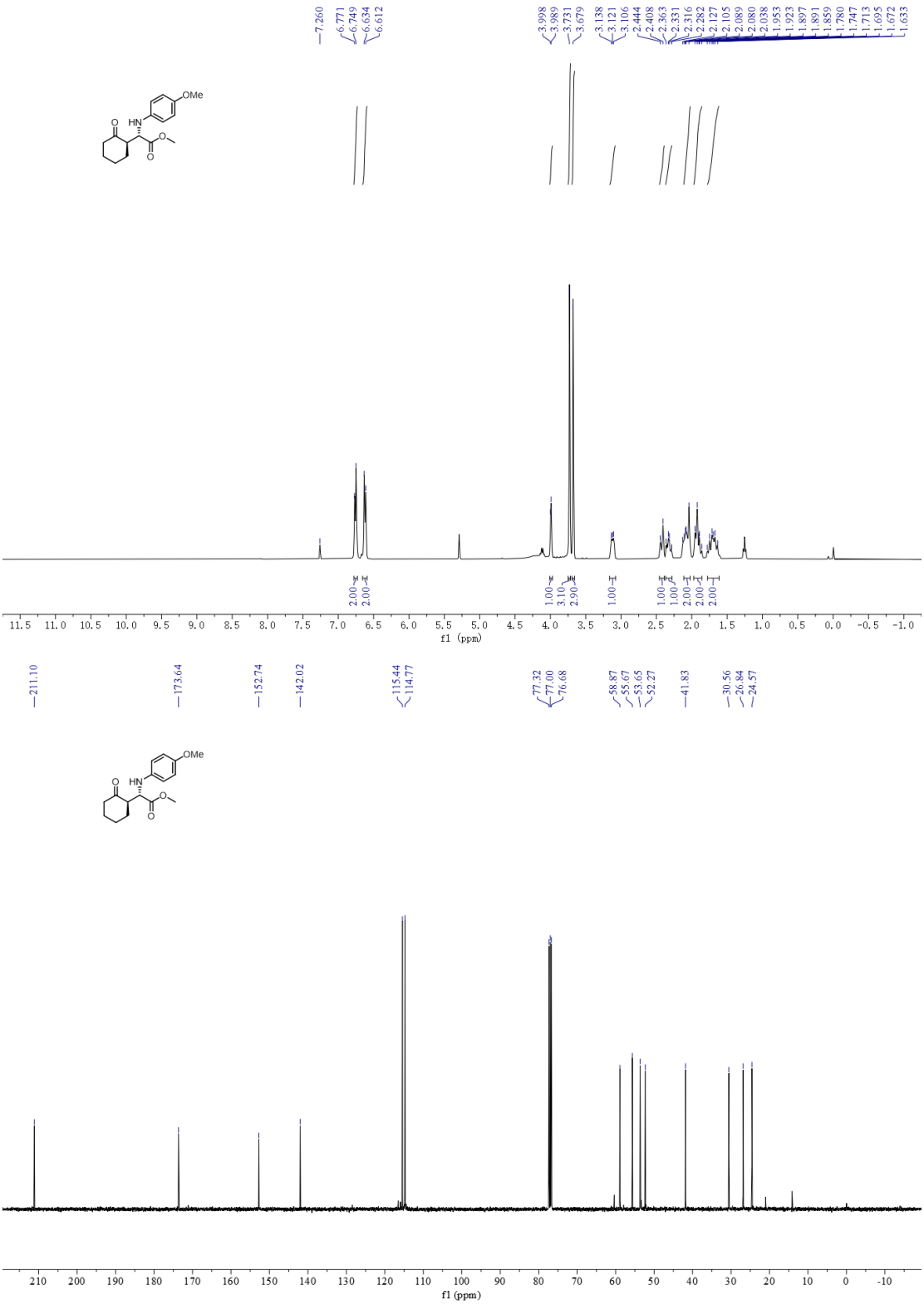


Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3aa**)

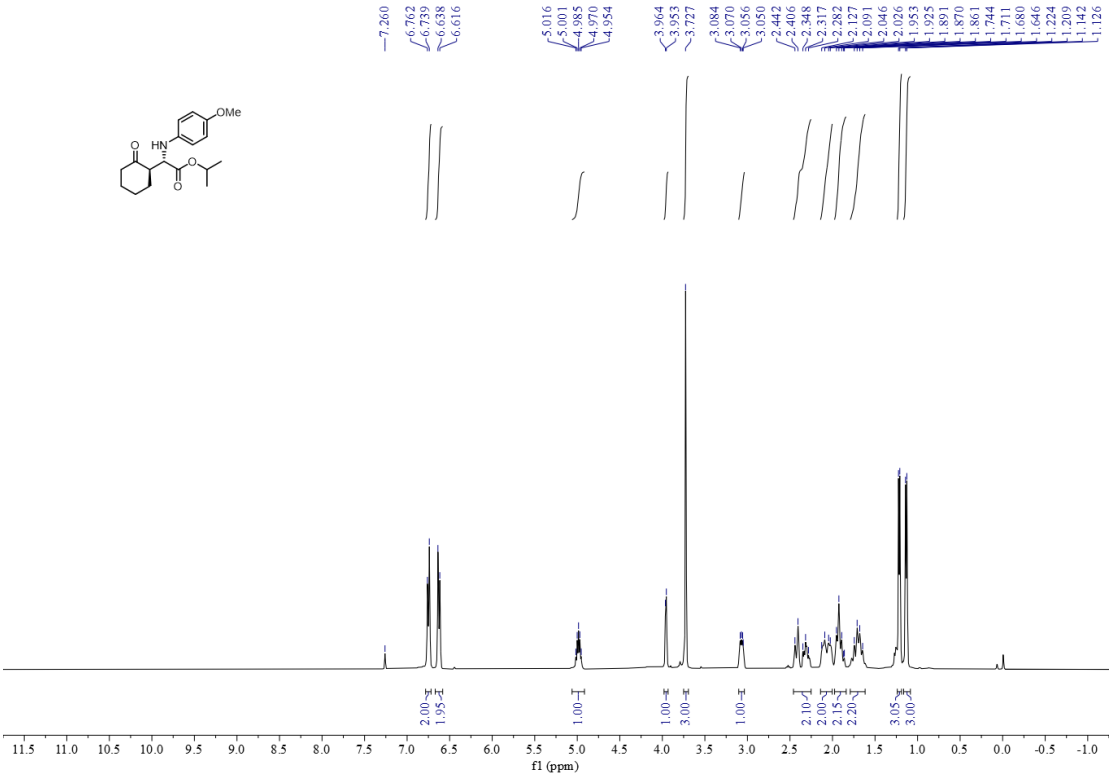


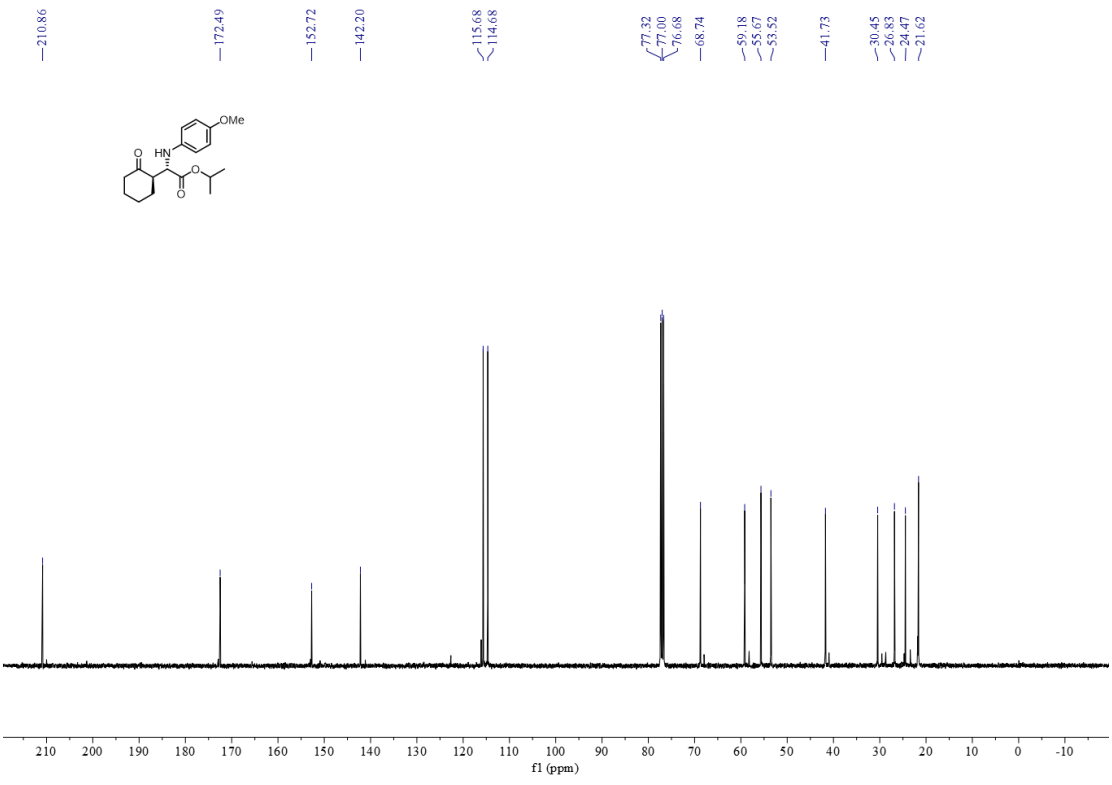


Methyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ba**)

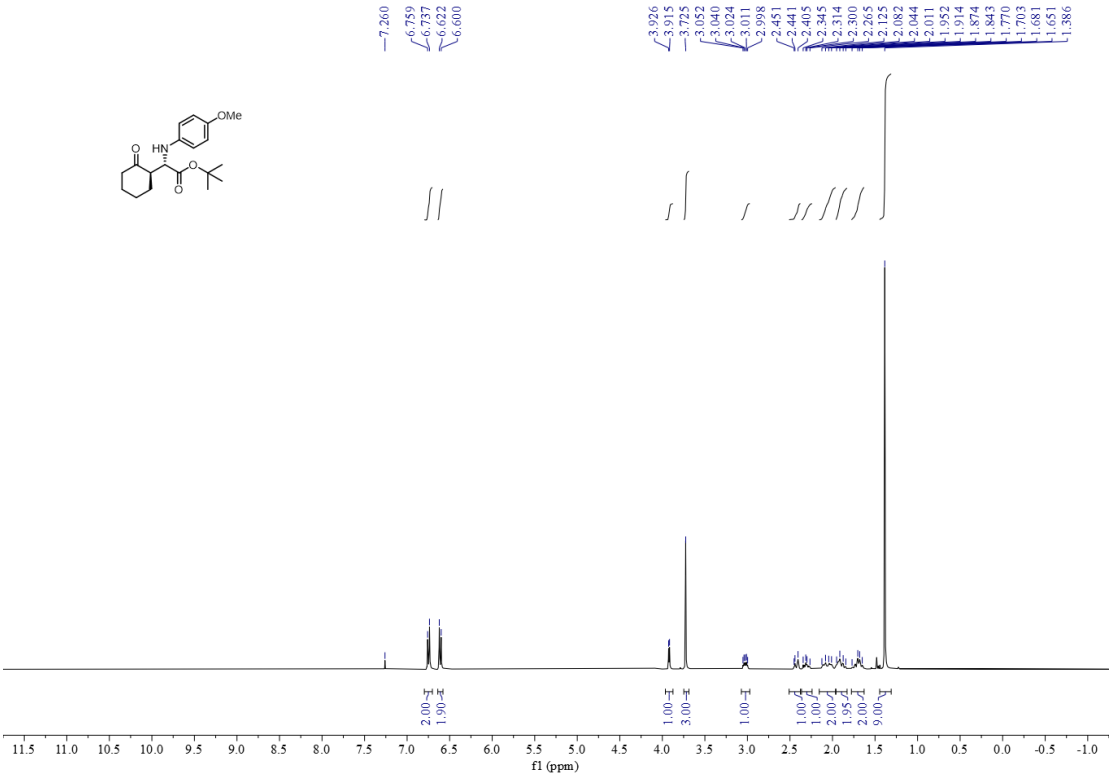


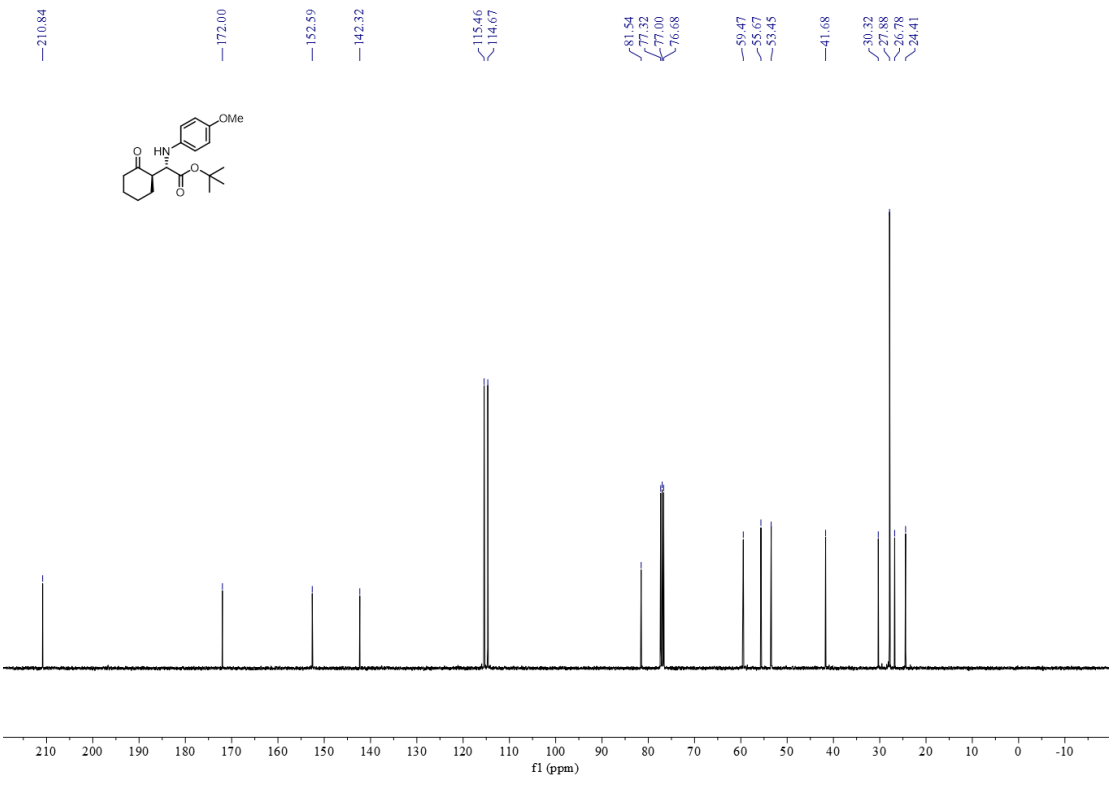
Isopropyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ca**)



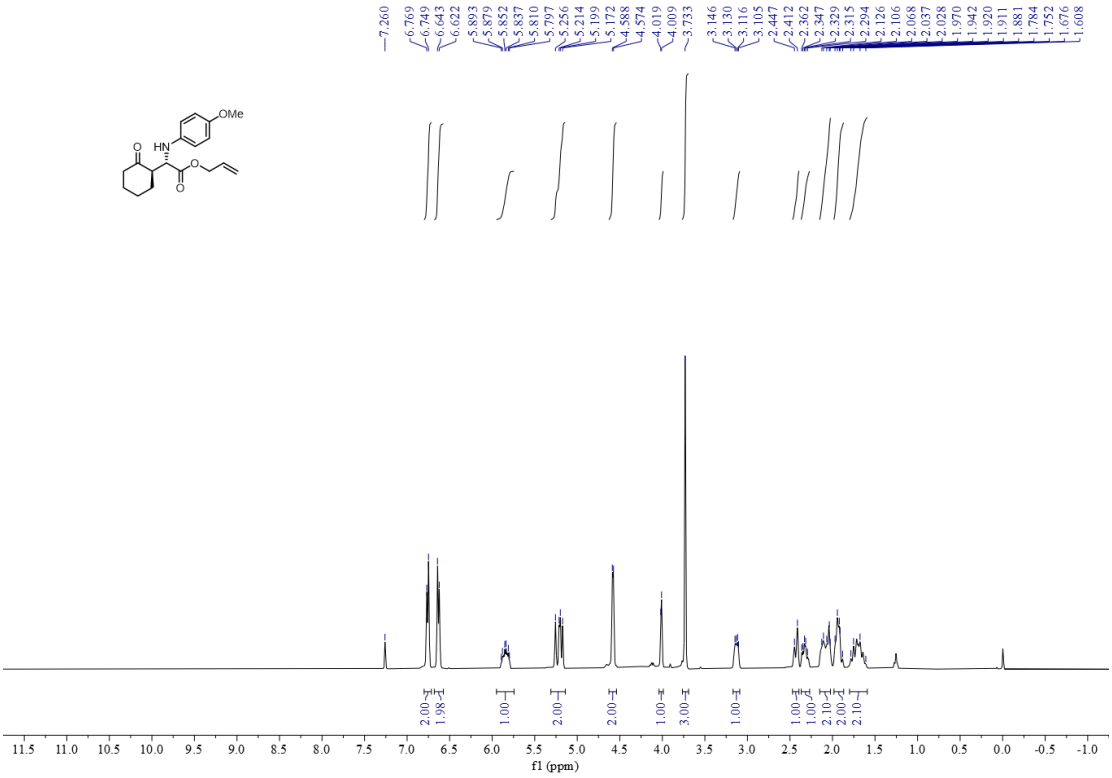


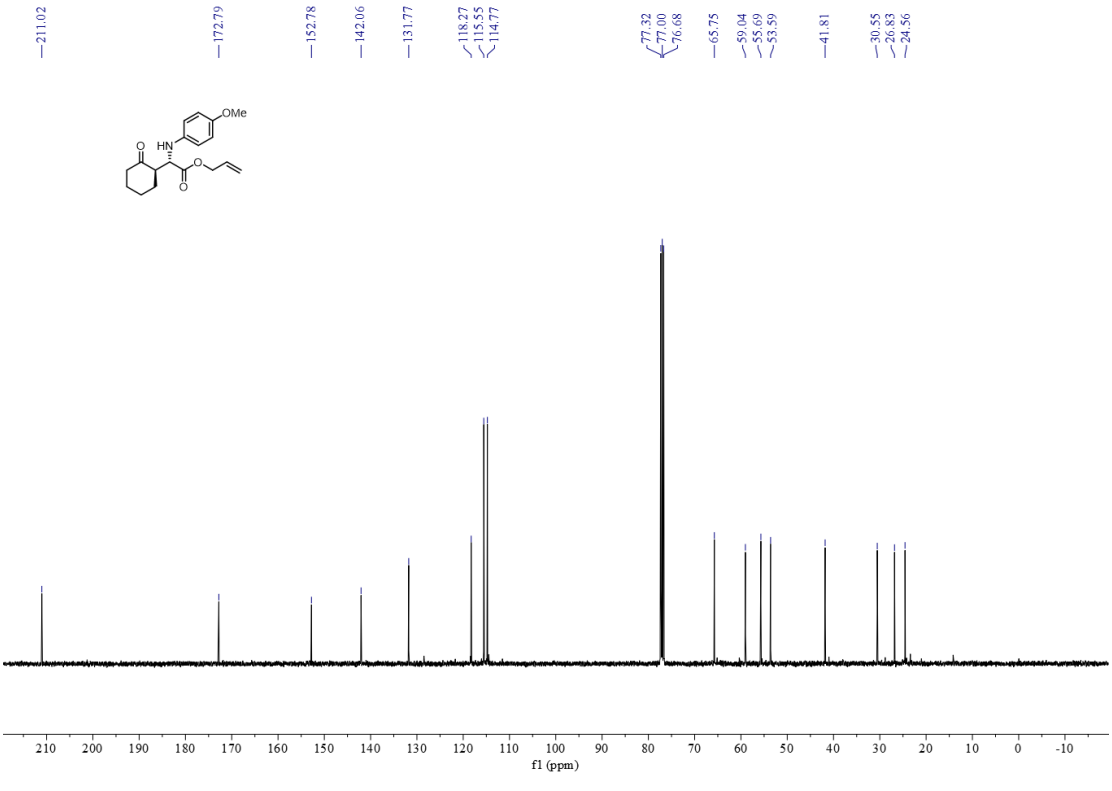
Tert-butyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3da**)



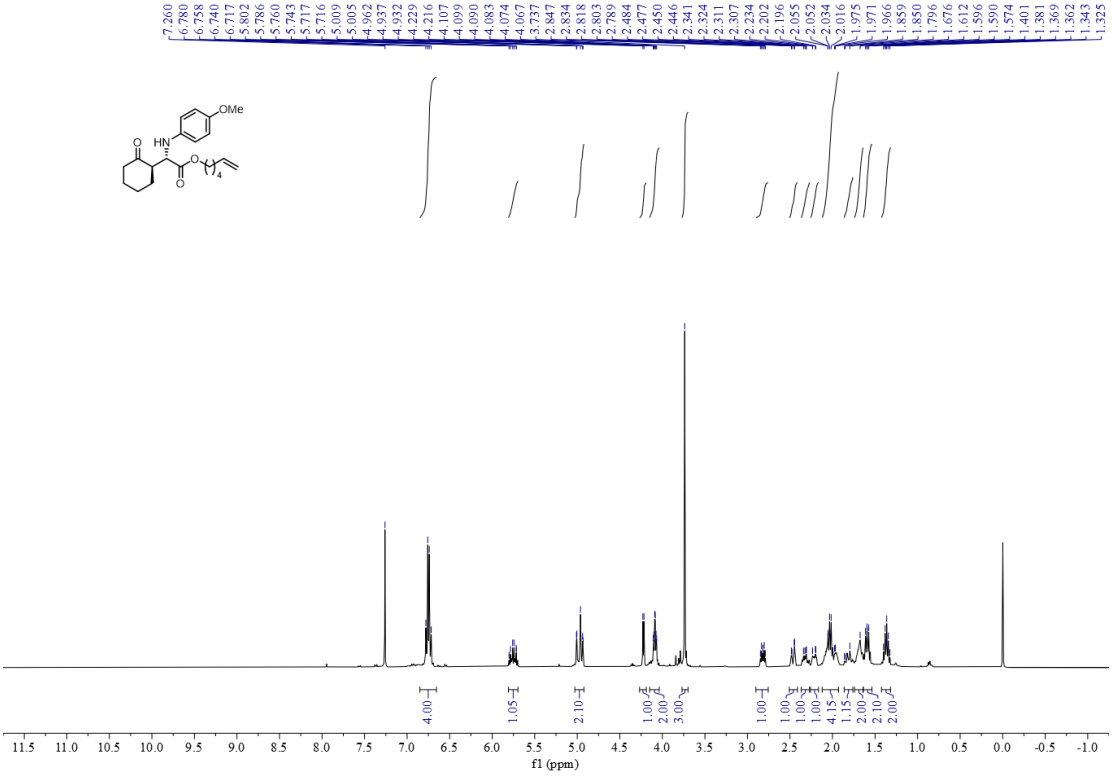


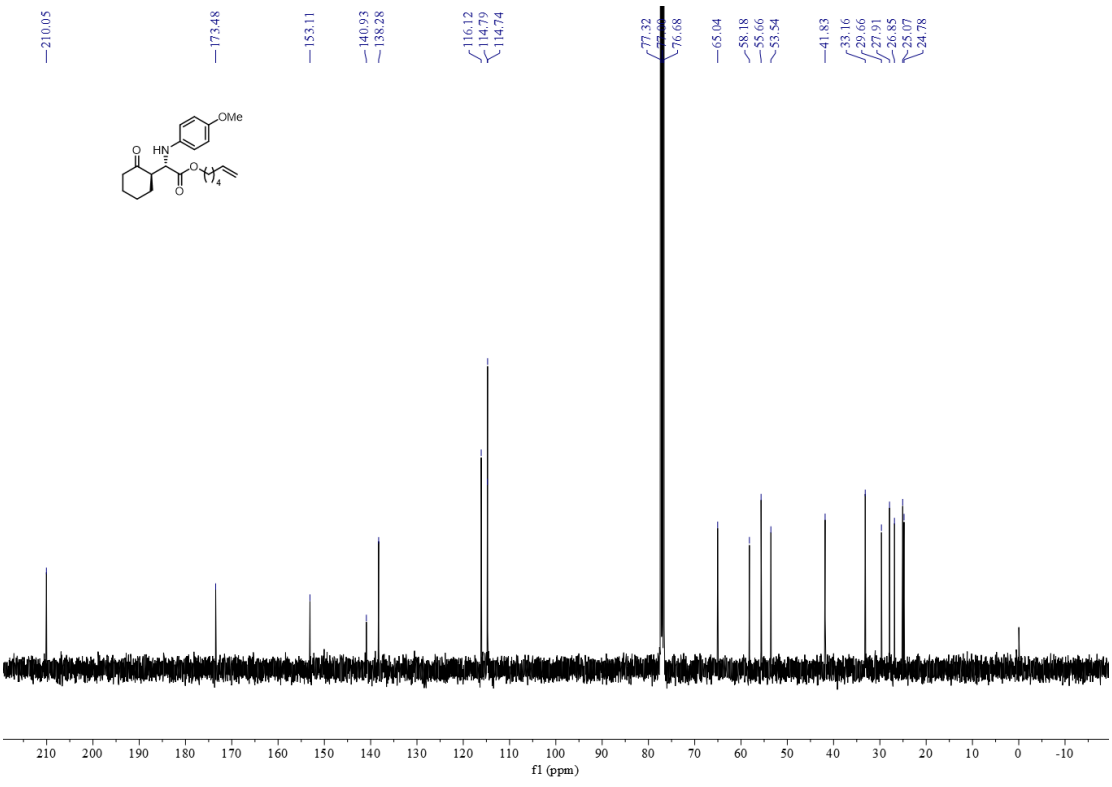
Allyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ea**)



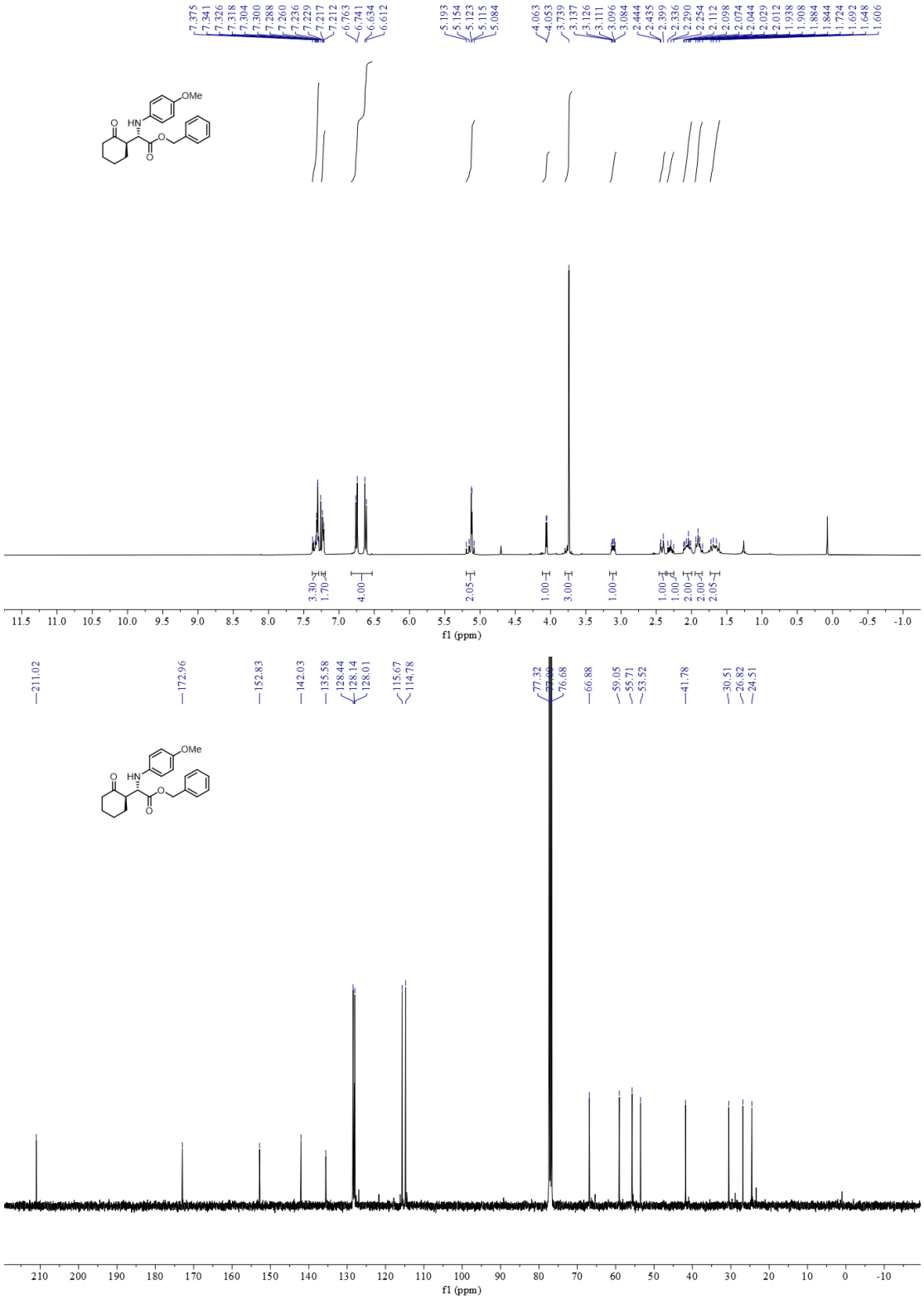


Allyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3fa**)

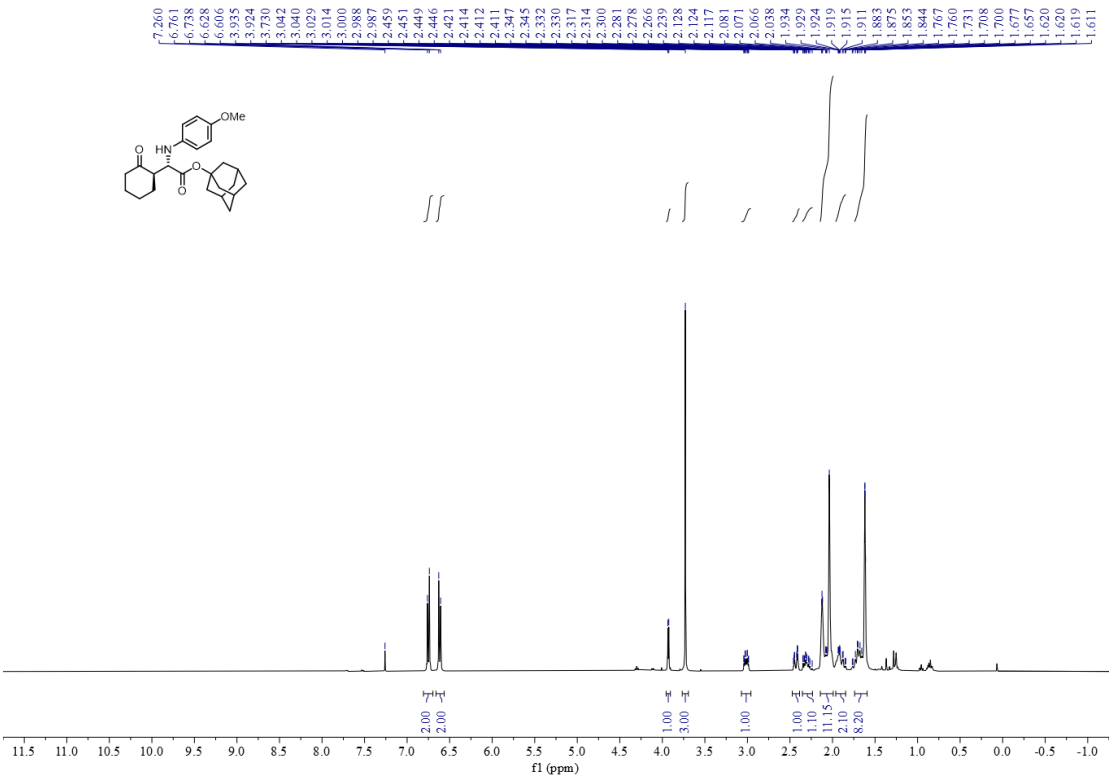


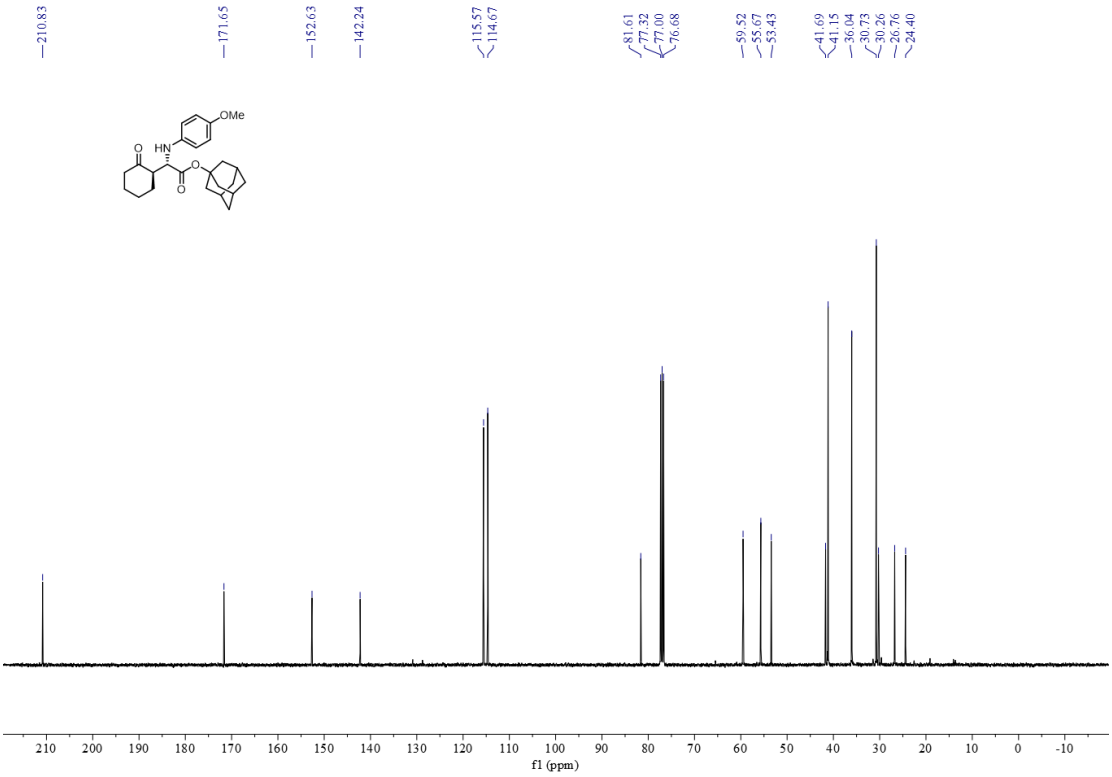


Benzyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ga**)

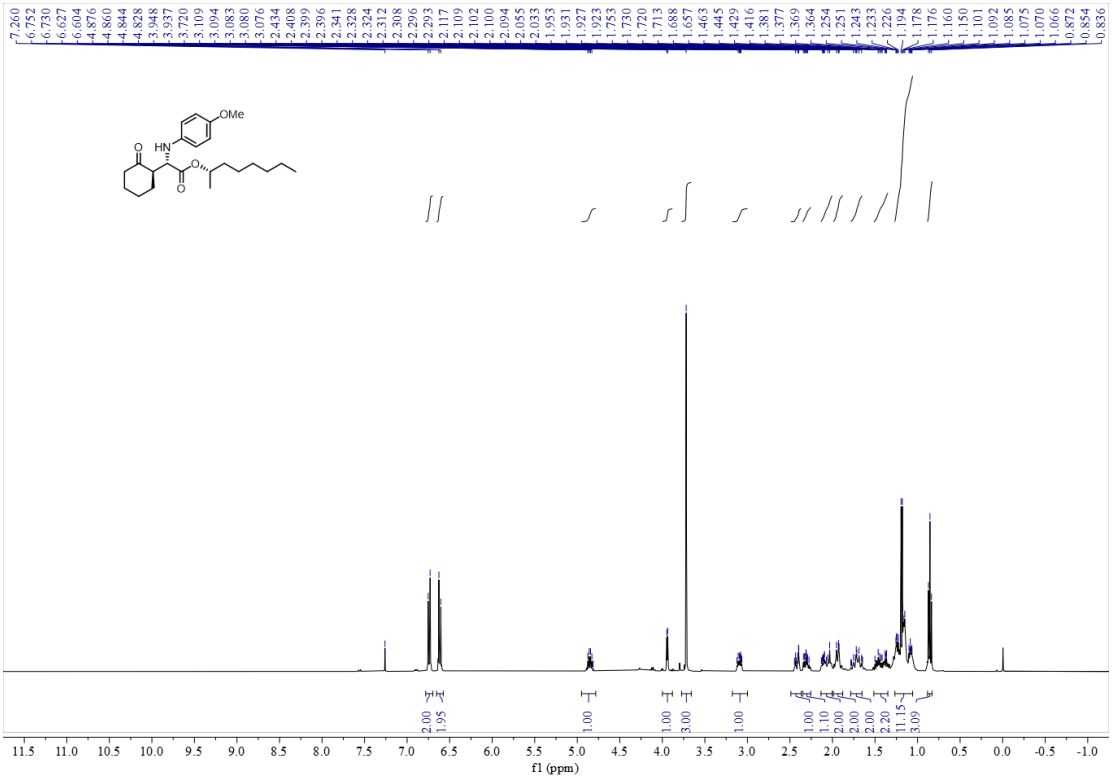


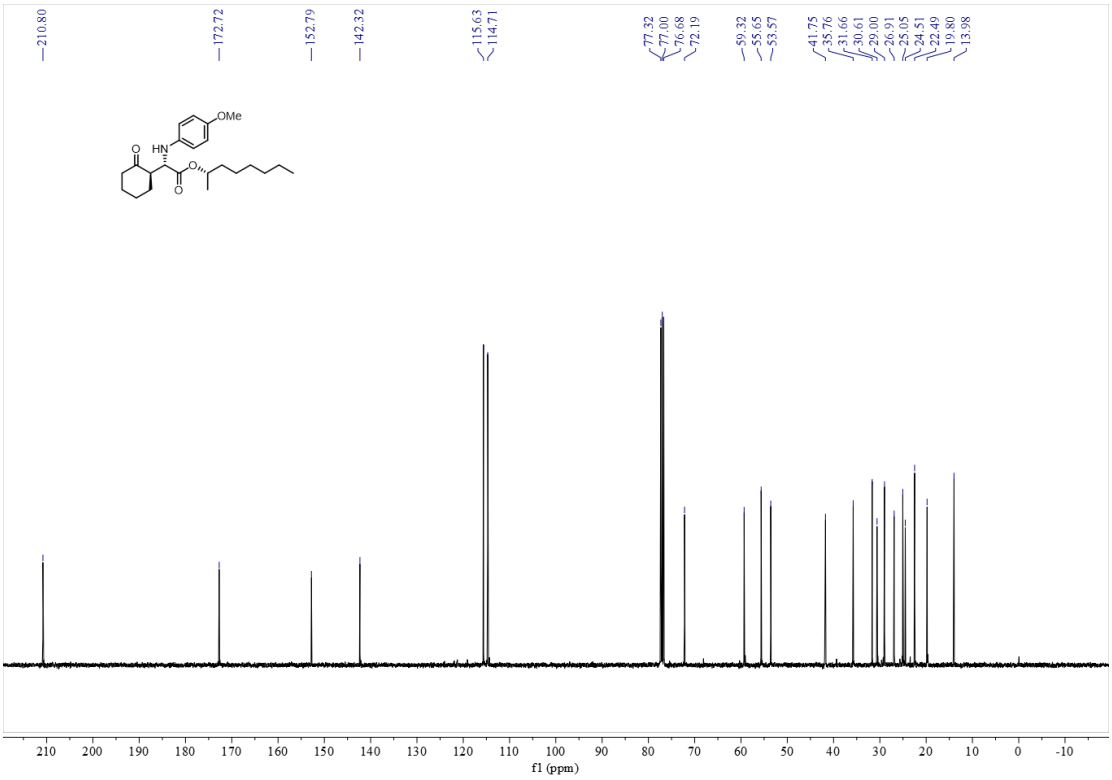
(1S,3R)-Adamantan-1-yl (2S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)aceta-te (**3ha**)



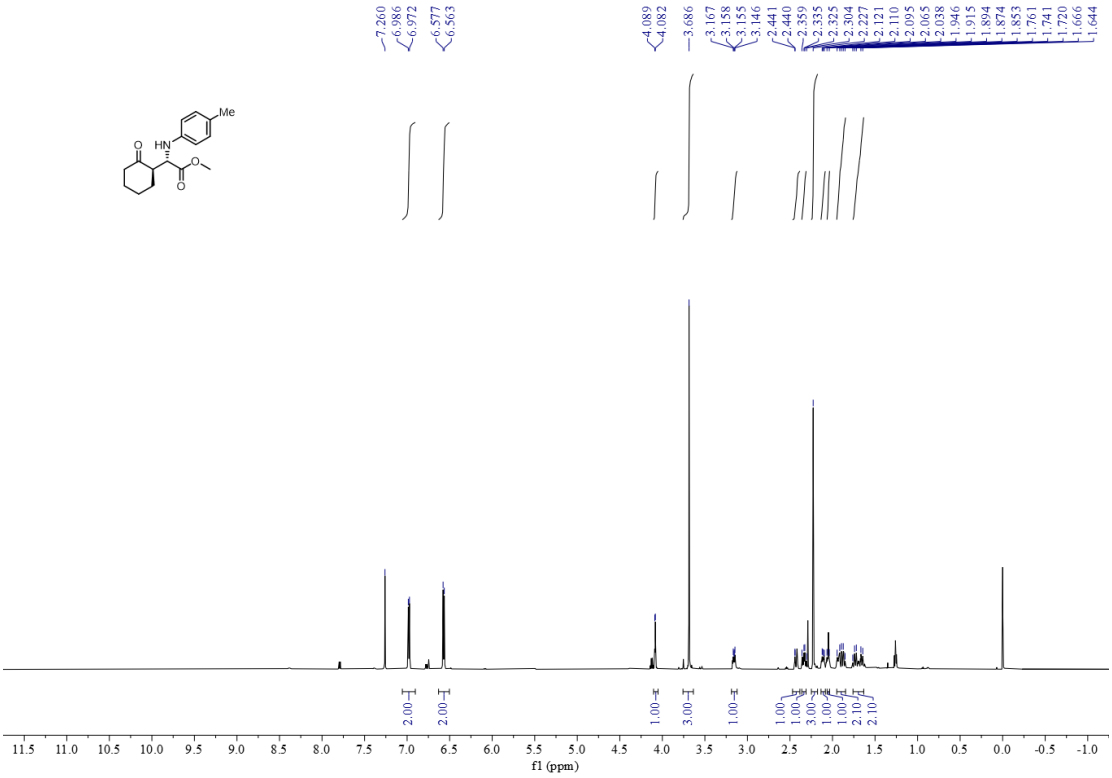


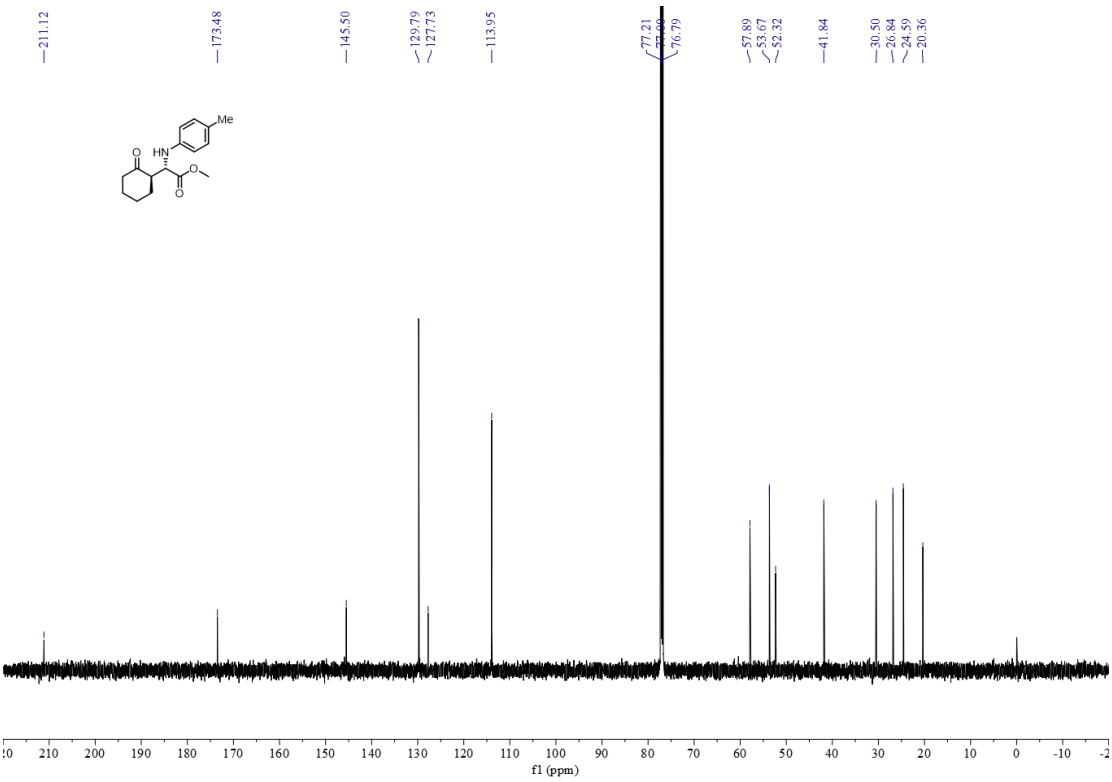
(S)-Octan-2-yl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ia**)



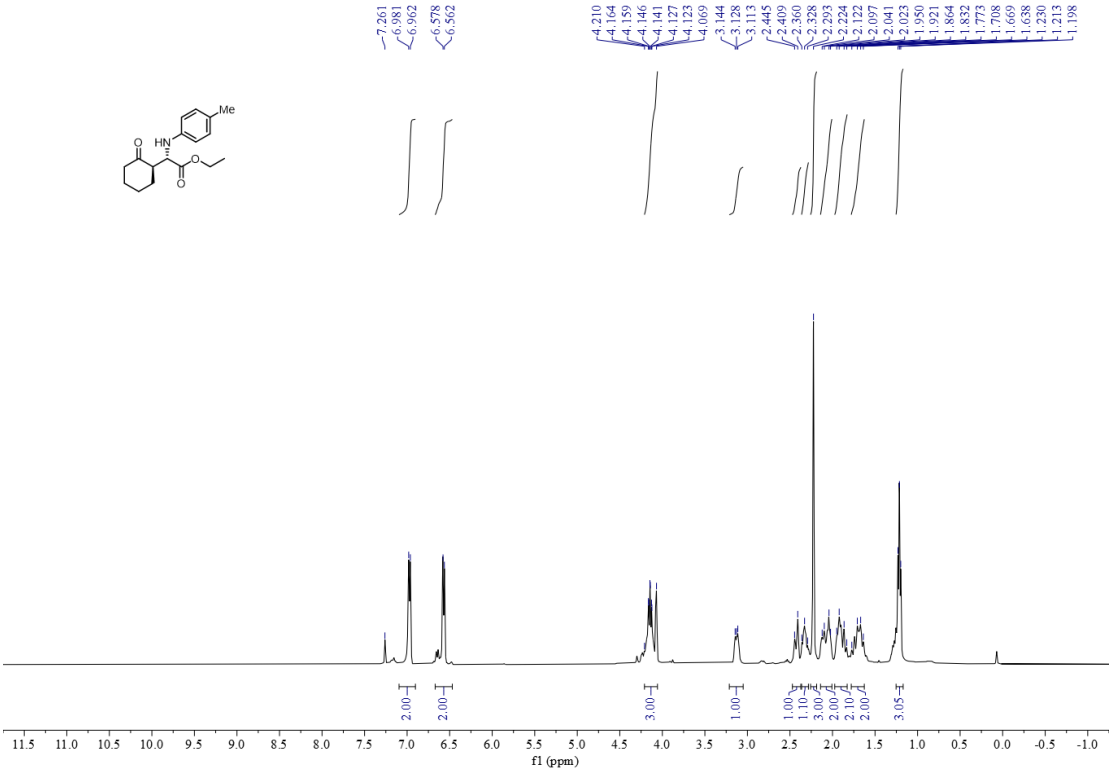


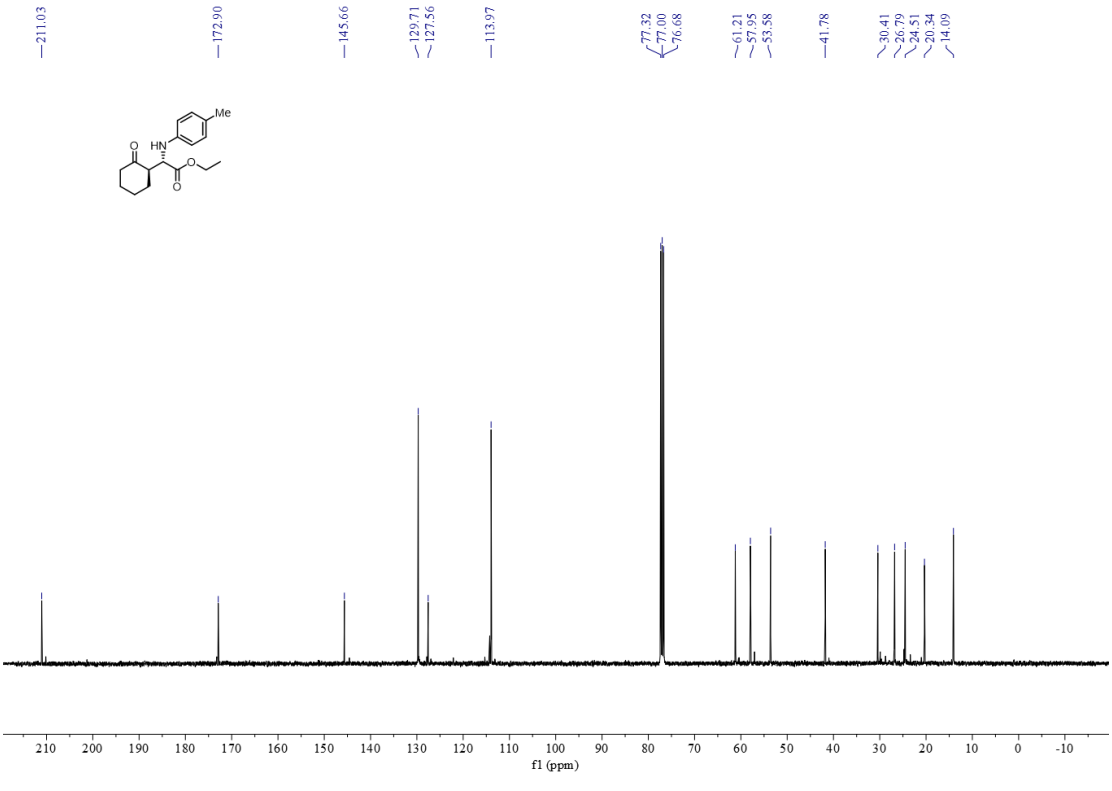
Methyl (S)-2-((R)-2-oxocyclohexyl)-2-(p-tolylamino)acetate (**3ja**)



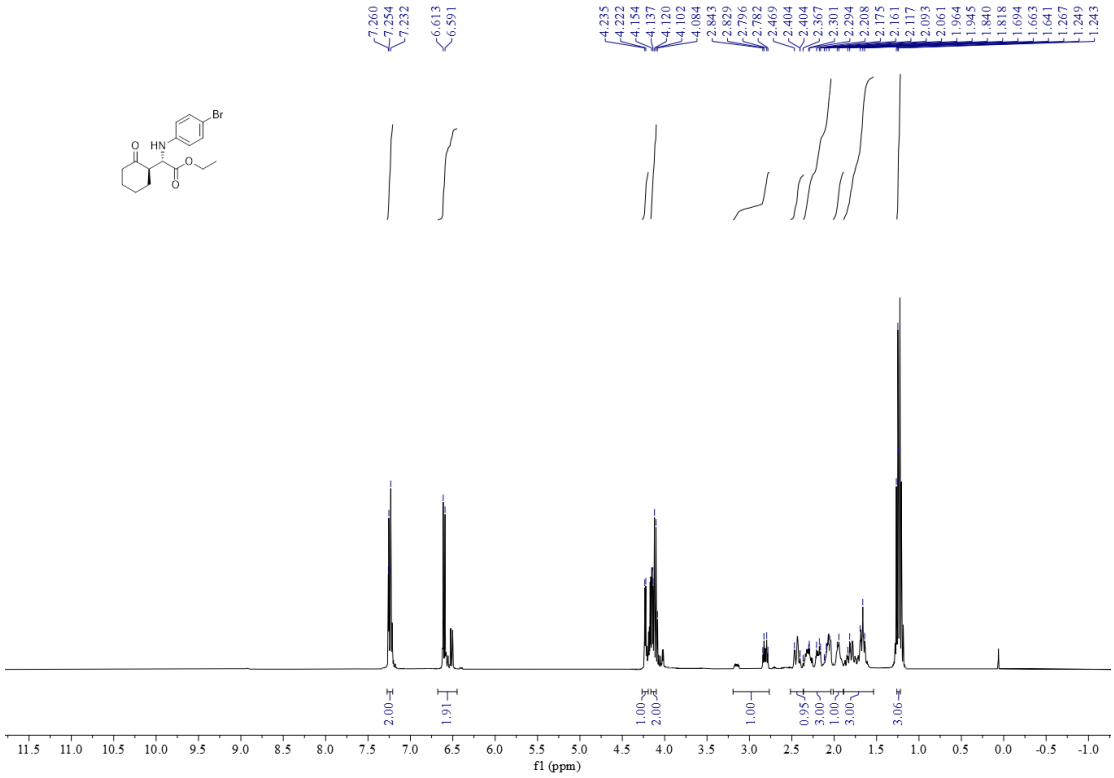


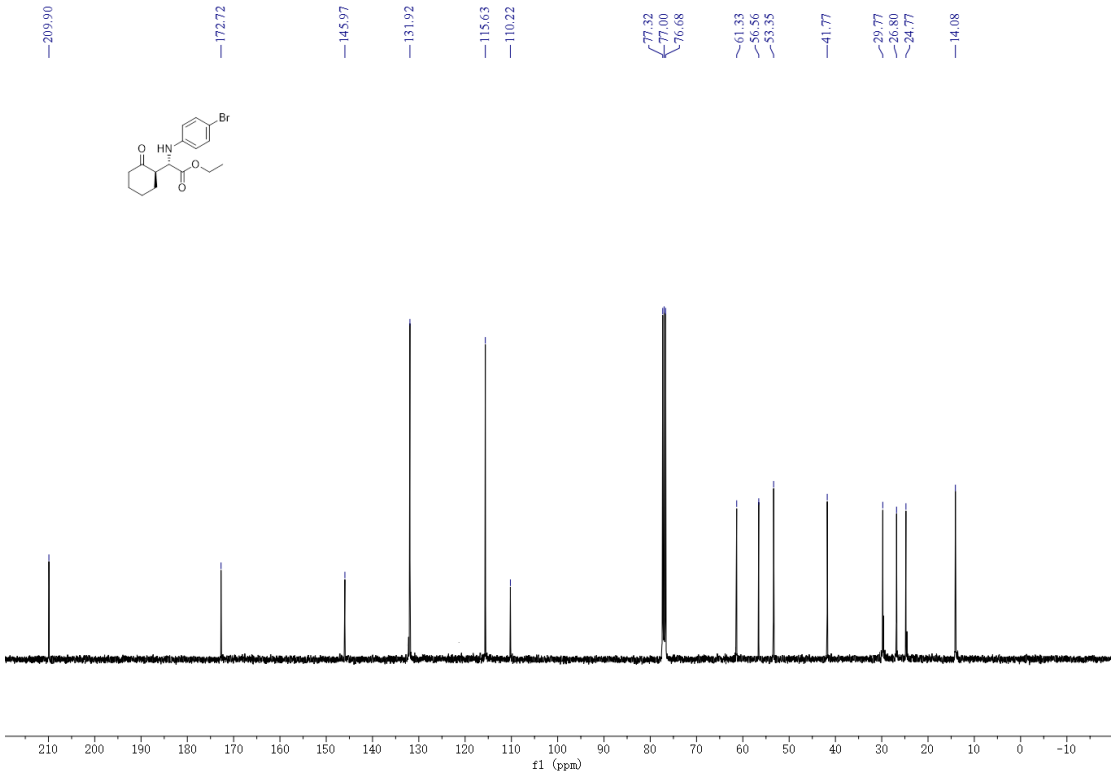
Ethyl (S)-2-((R)-2-oxocyclohexyl)-2-(p-tolylamino)acetate (**3ka**)



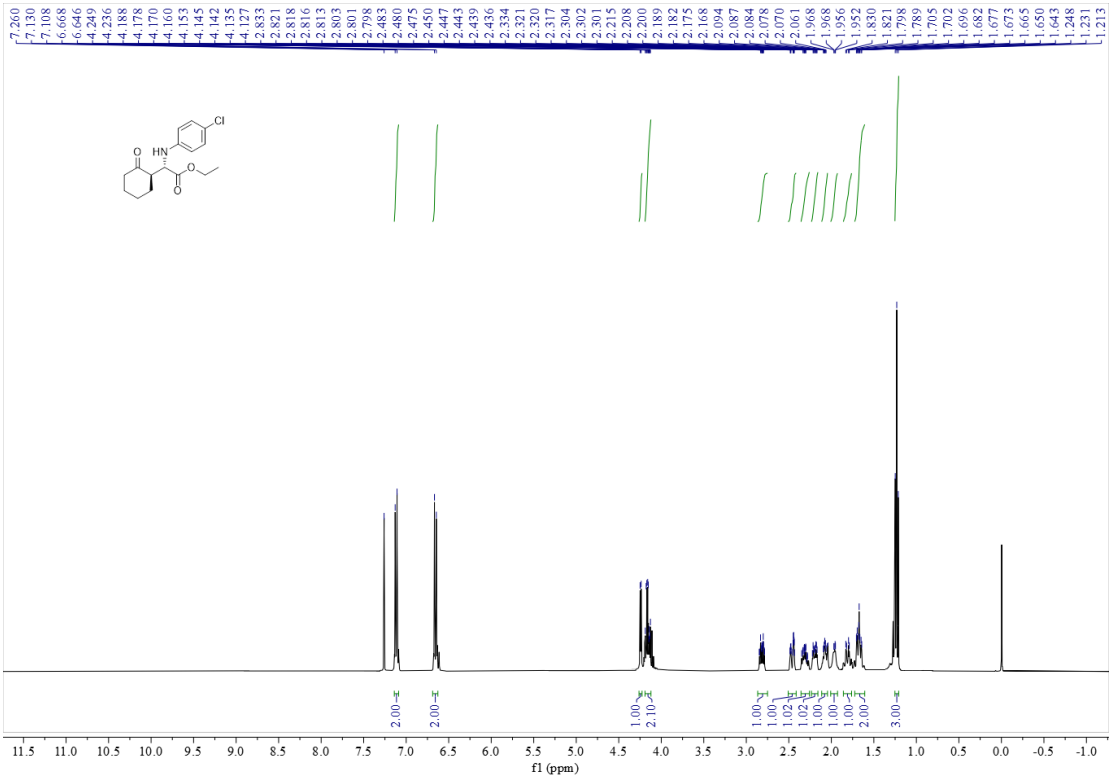


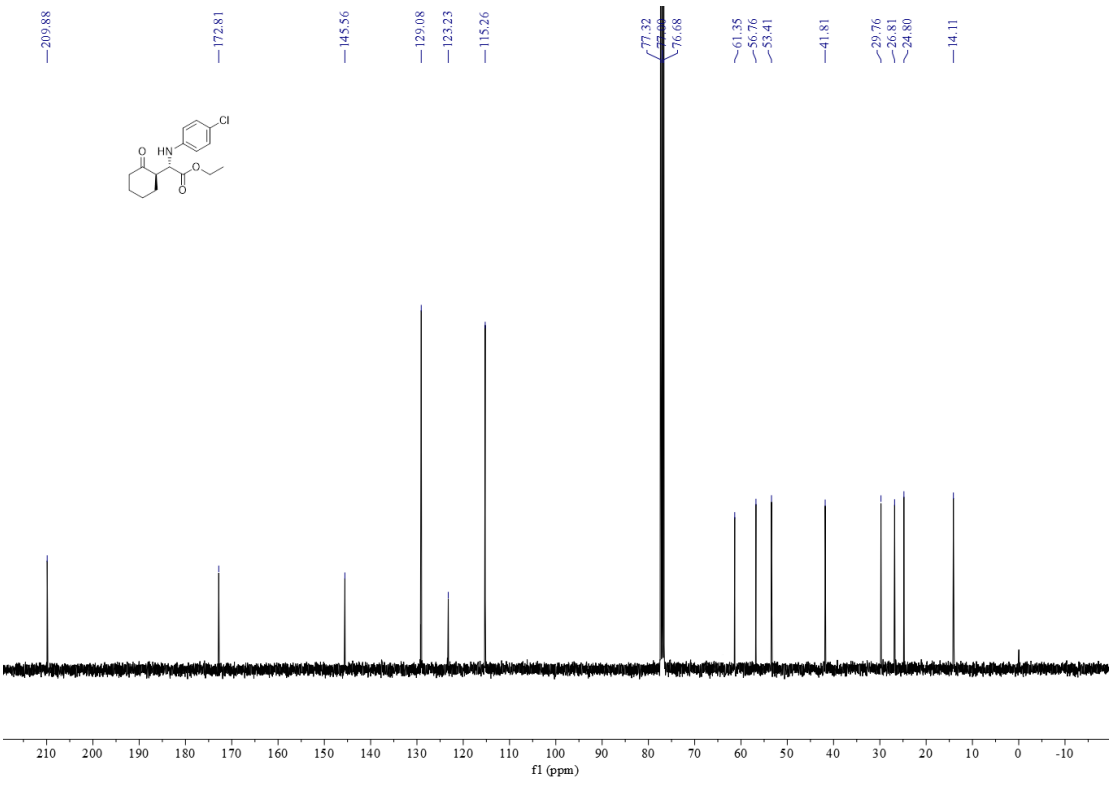
Ethyl (S)-2-((4-bromophenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3la**)



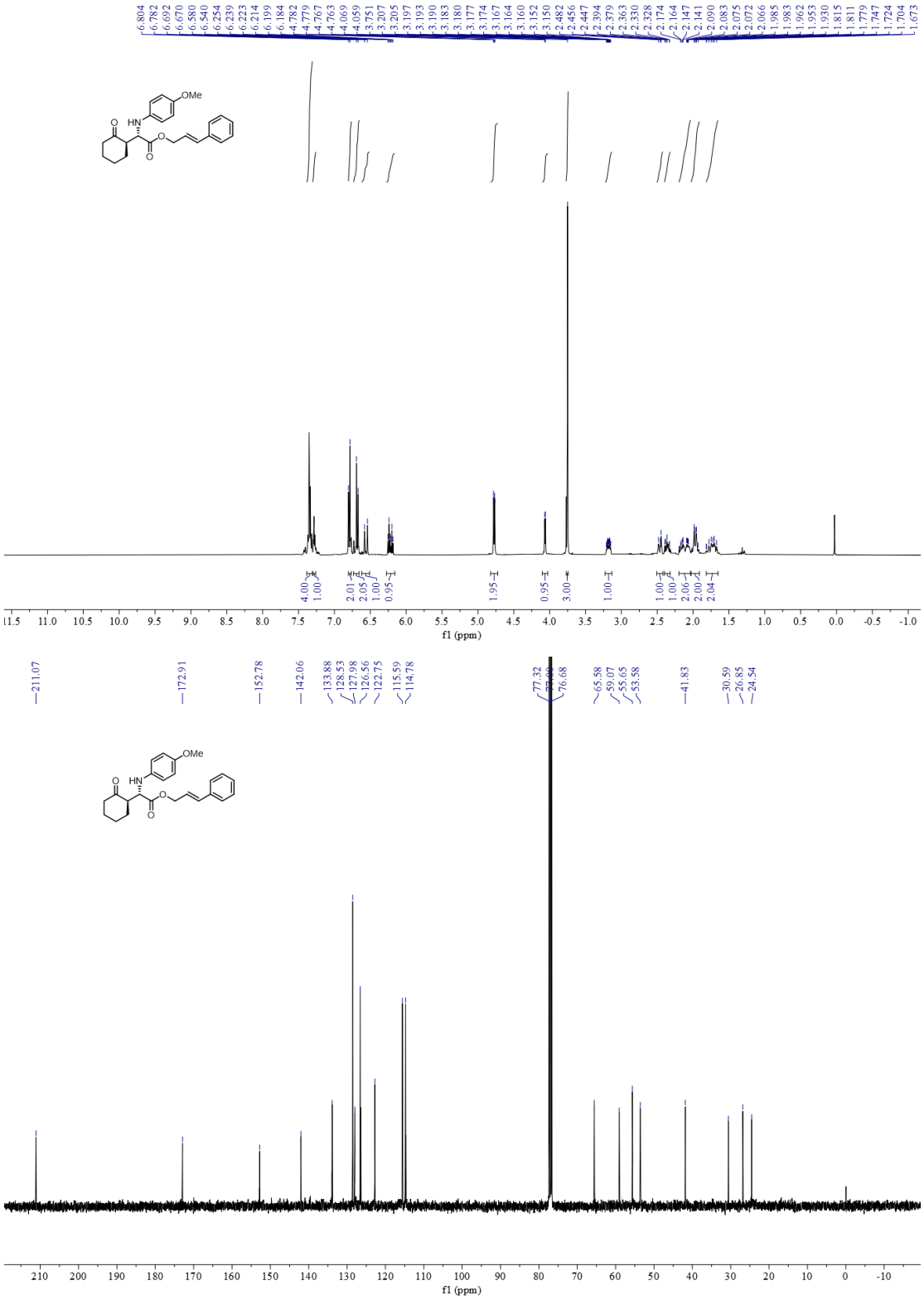


Ethyl (S)-2-((4-chlorophenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3ma**)

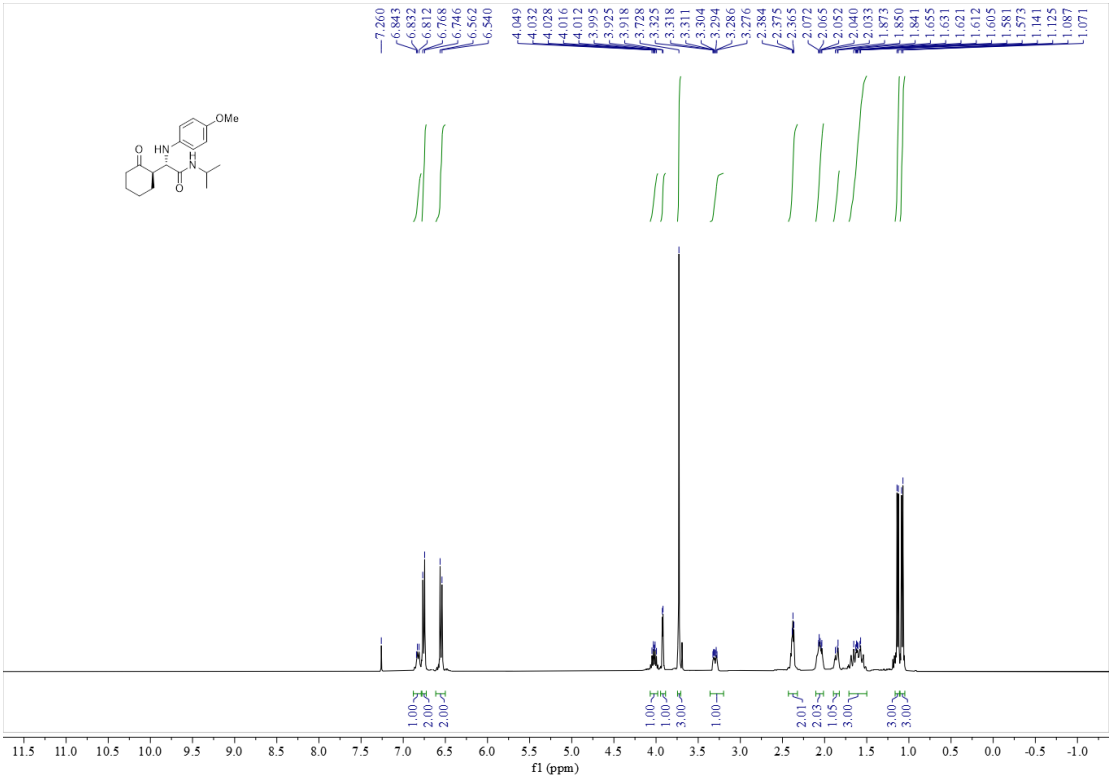


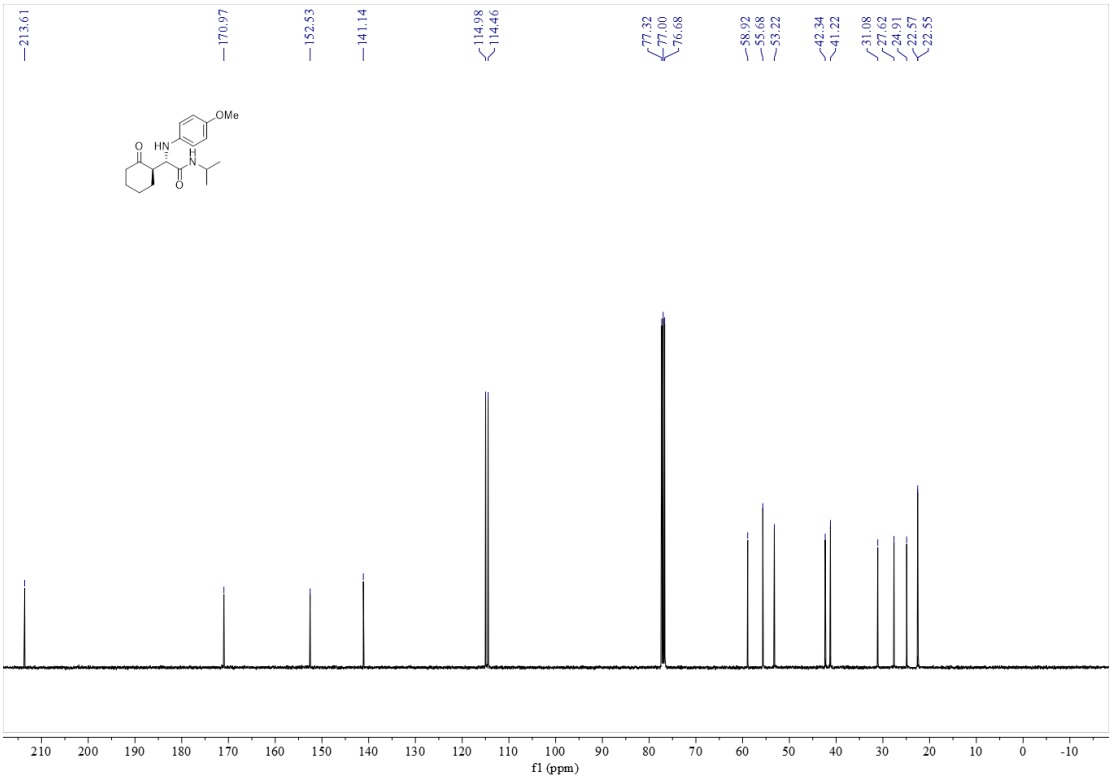


Cinnamyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetate (**3na**)

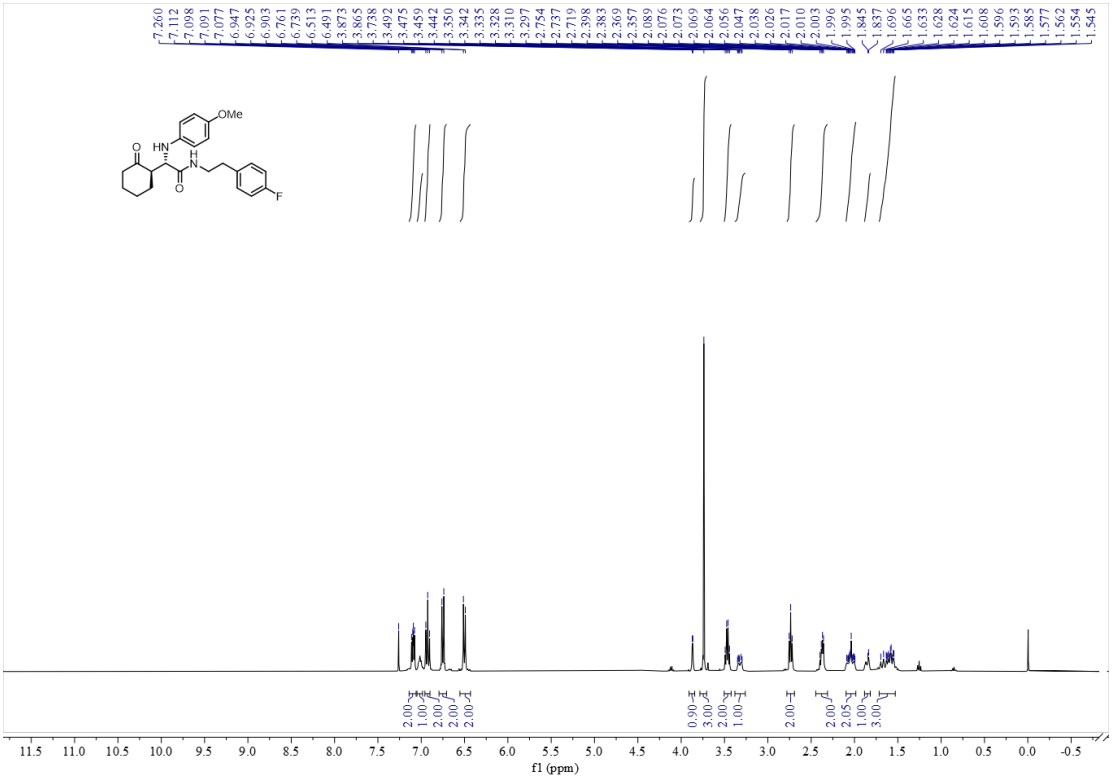


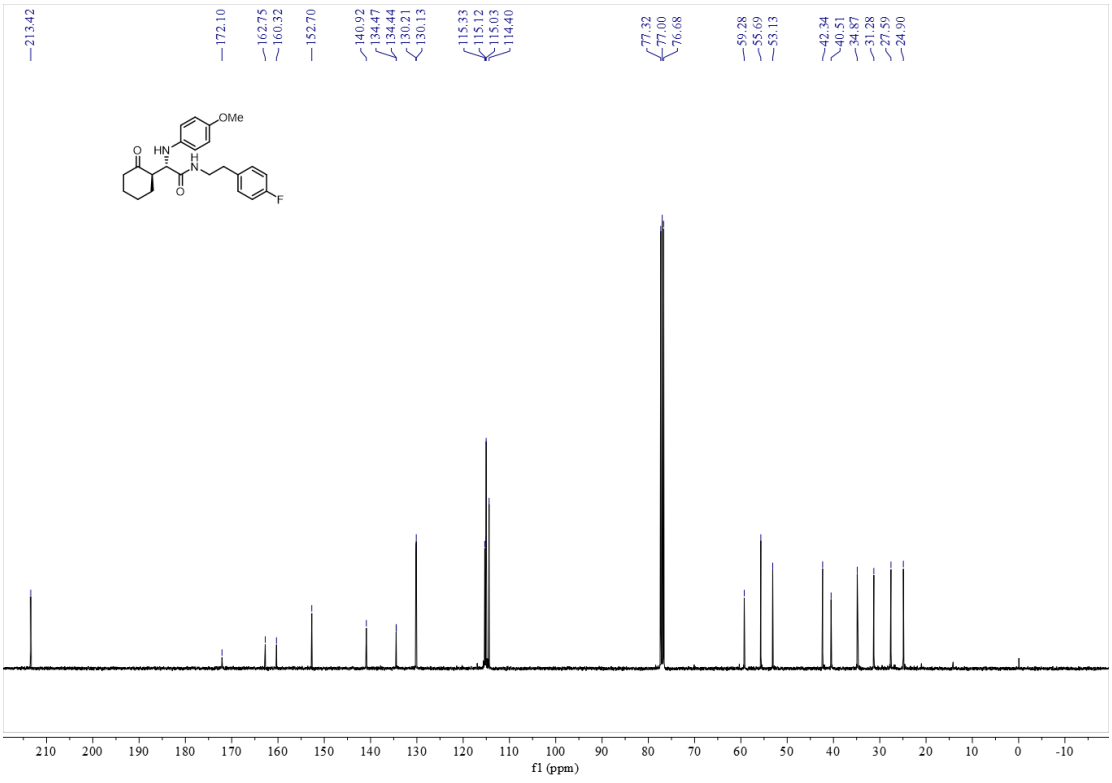
(S)-*N*-isopropyl-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3oa**)

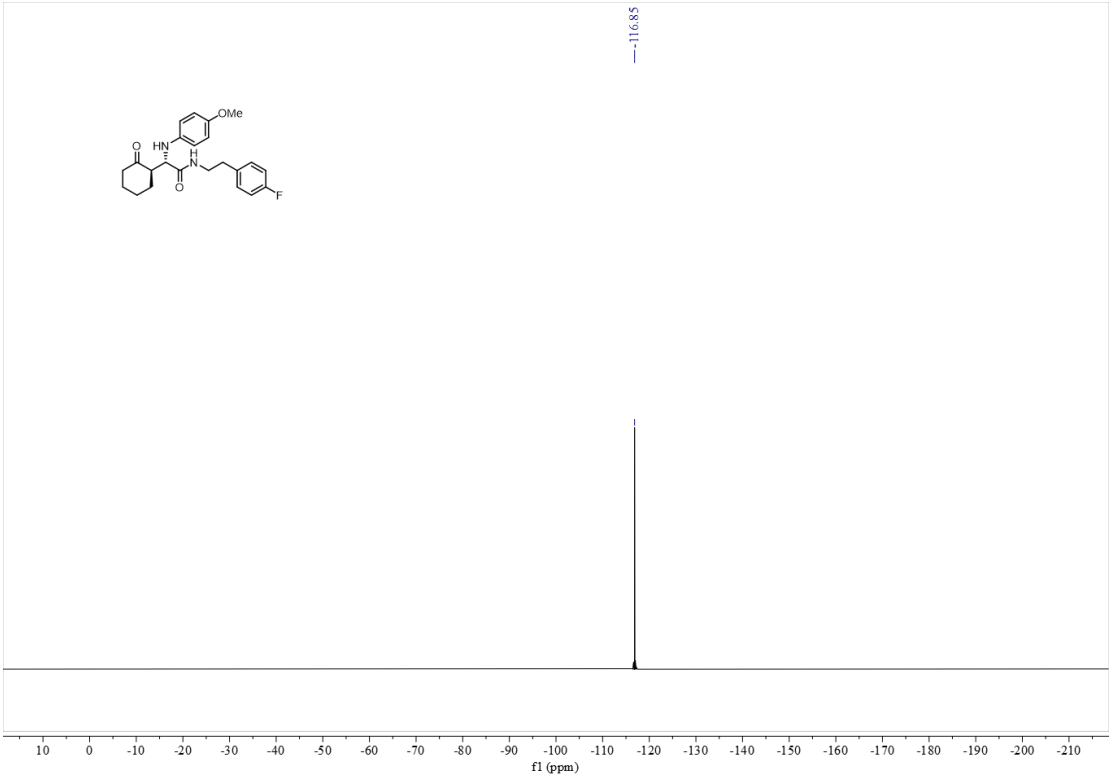




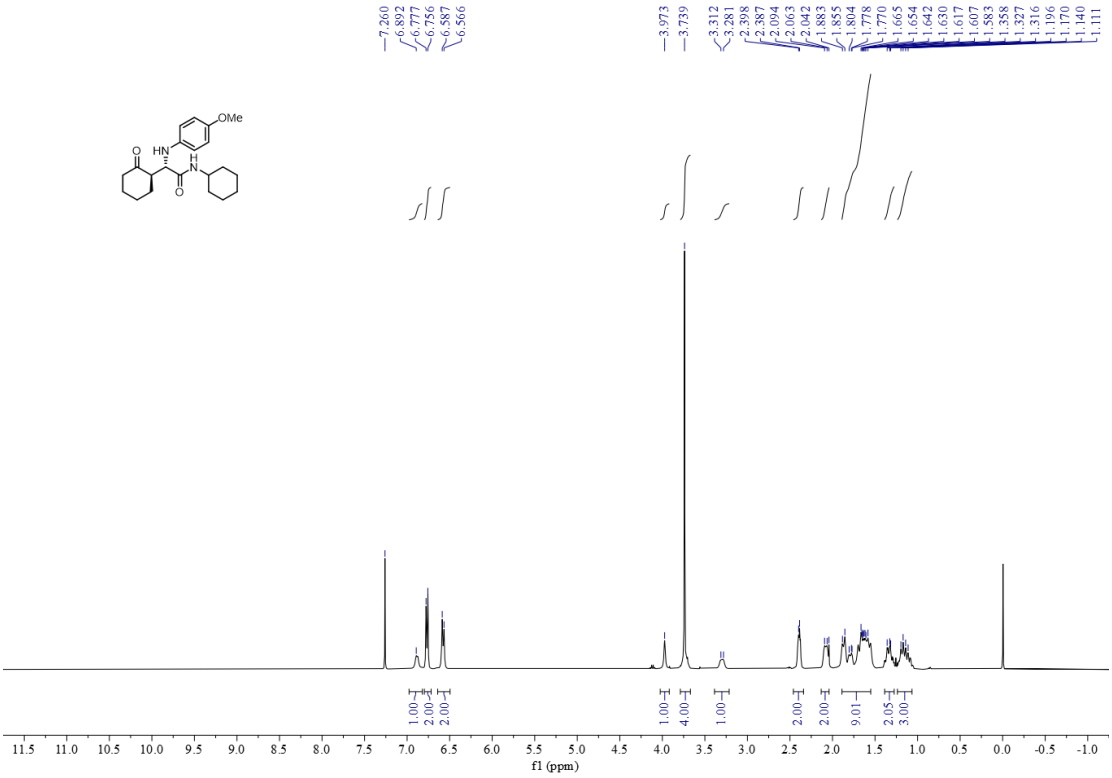
(S)-*N*-(4-fluorophenethyl)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3pa**)

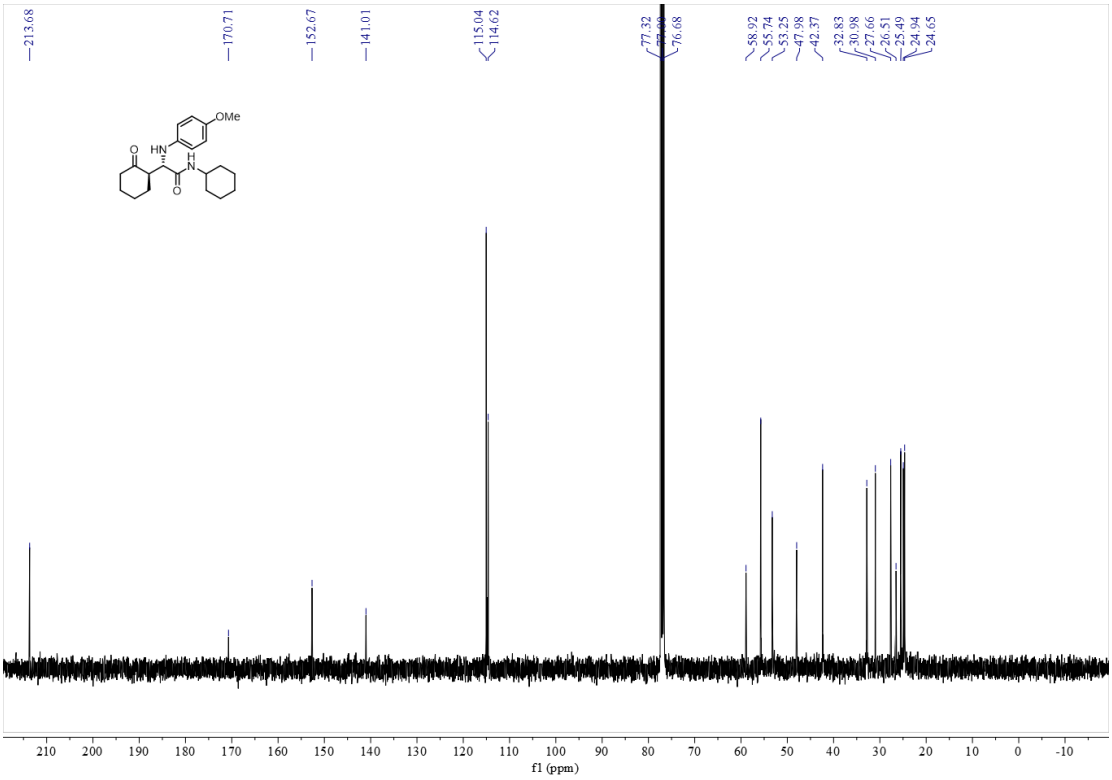




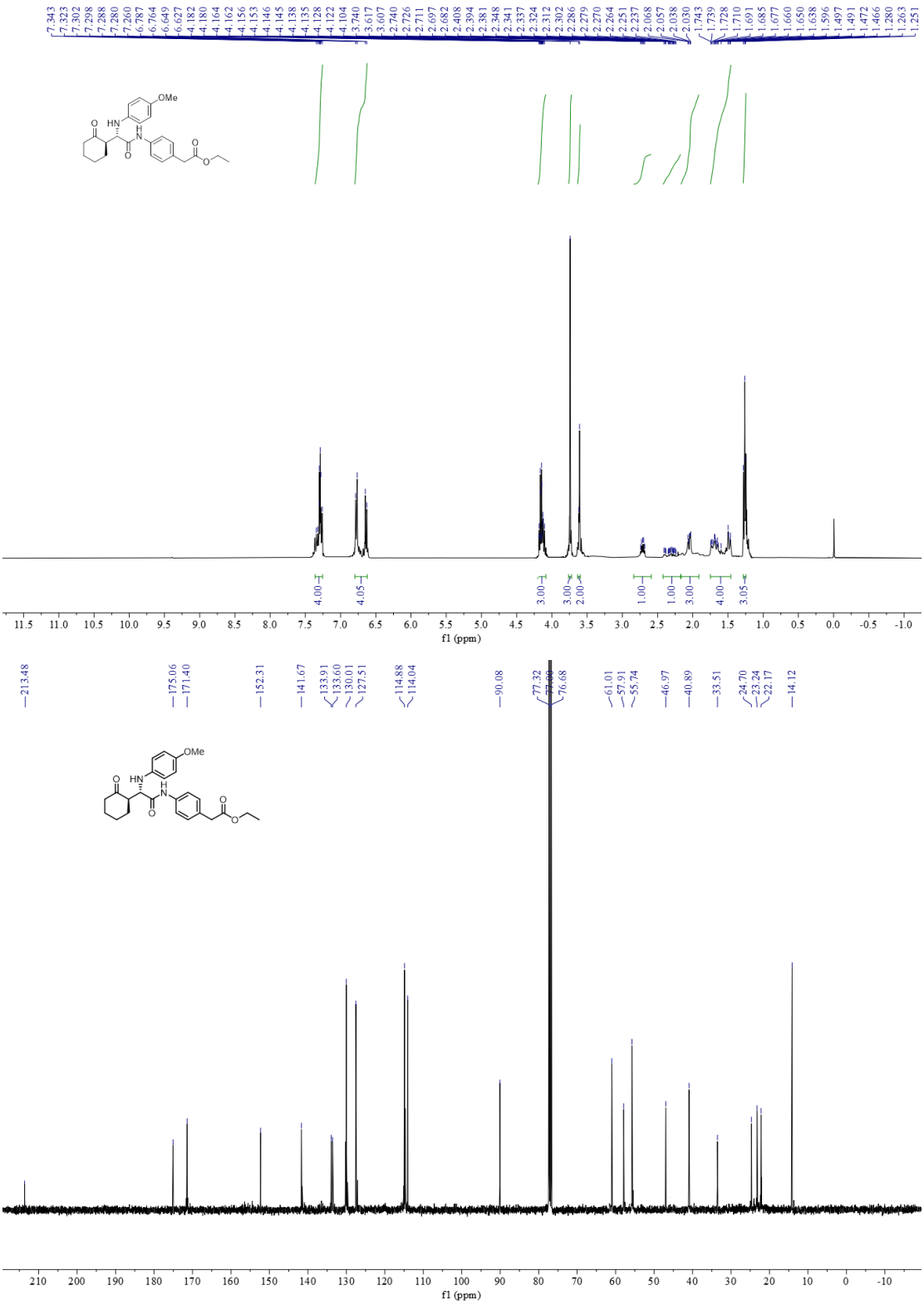

-116.85
OMe
HN
O
H
N
O
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

(S)-*N*-cyclohexyl-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamide (**3qa**)

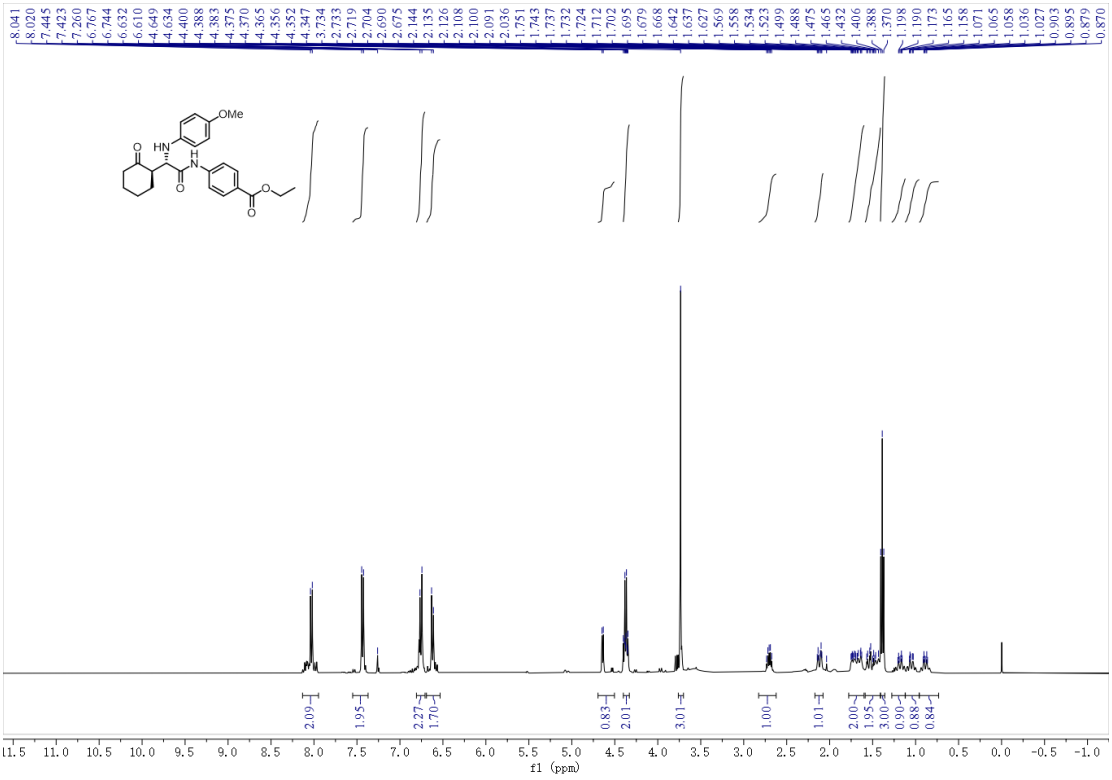


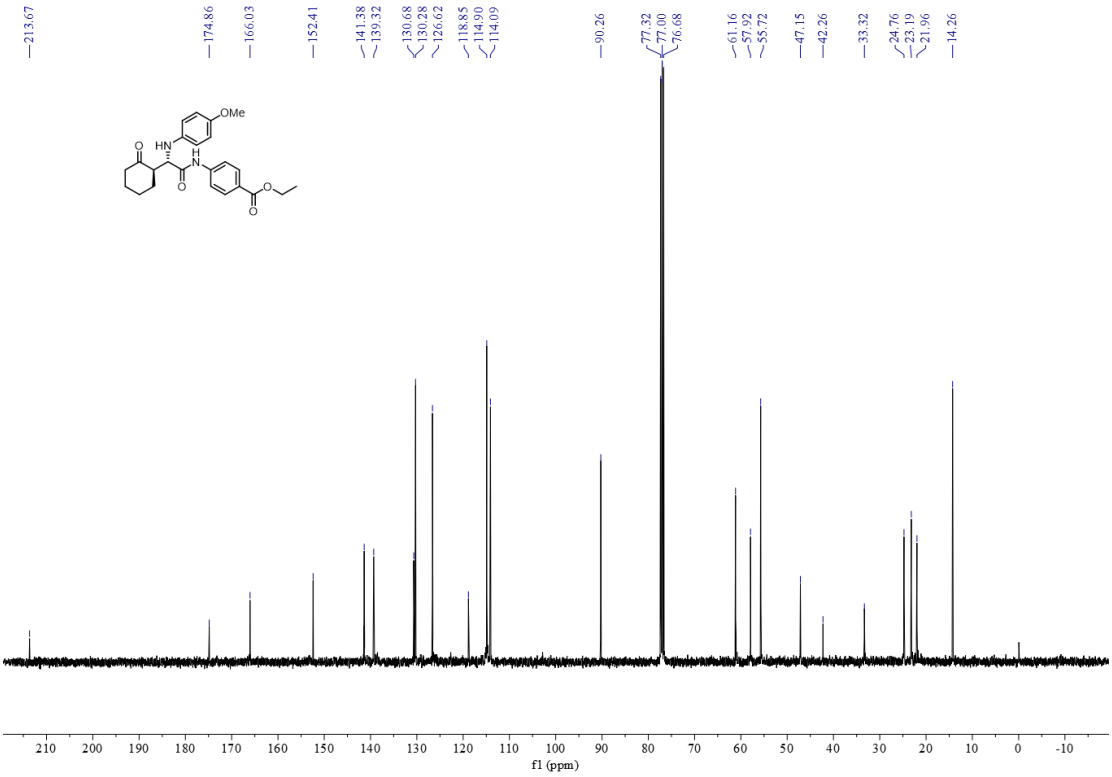


Ethyl 2-(4-((S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamido)phenyl)ac-etate (**3ra**)

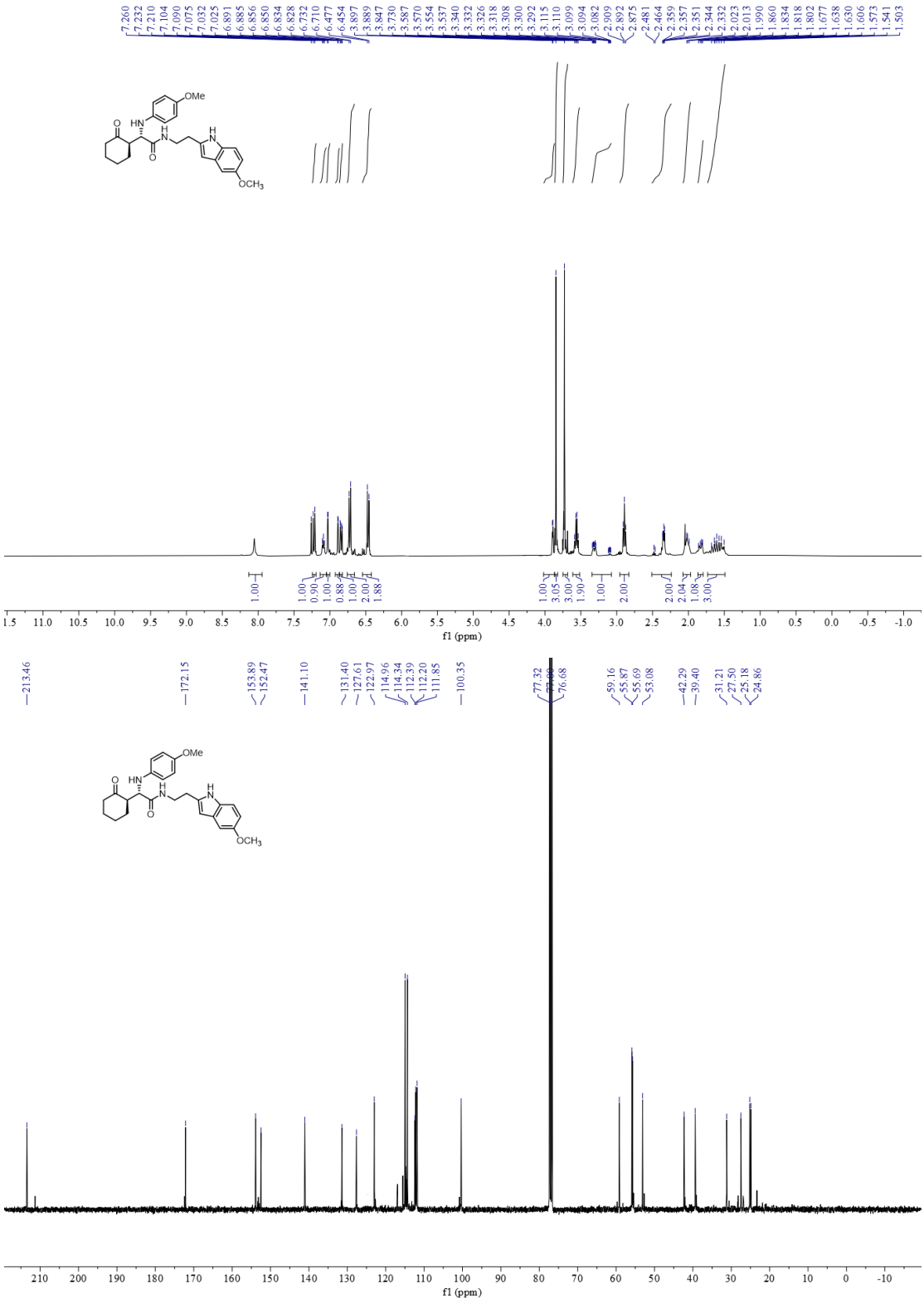


Ethyl 4-((S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclohexyl)acetamido)benzoate (**3sa**)

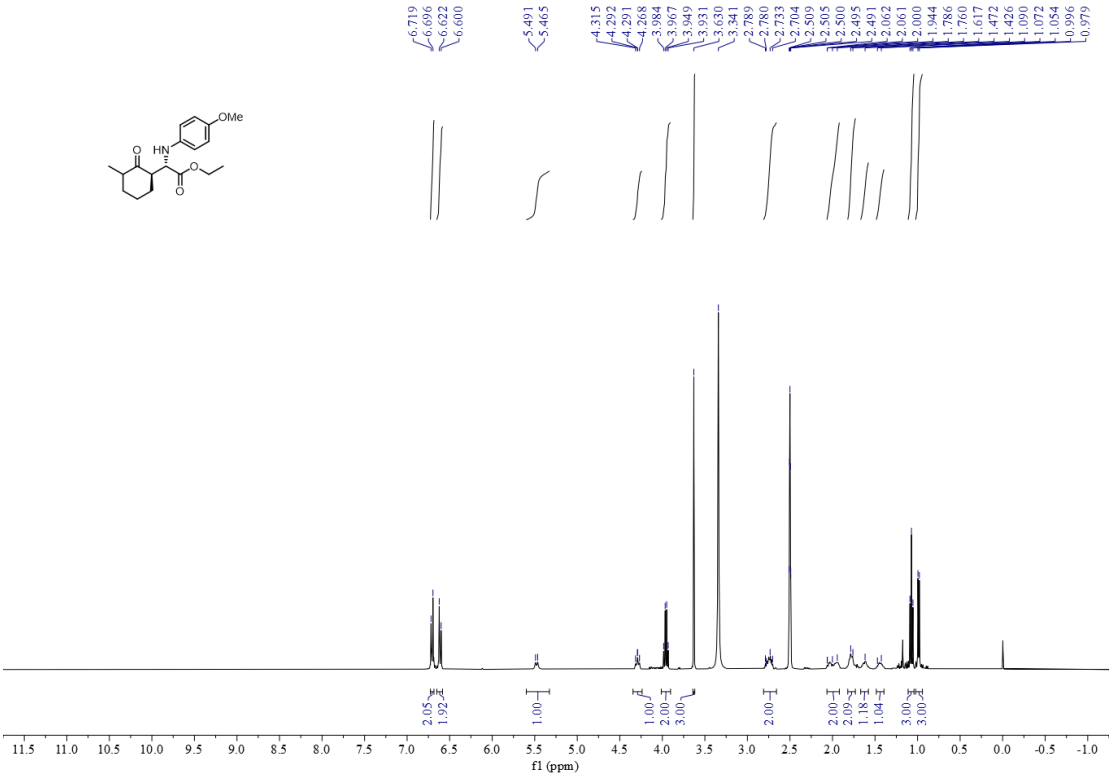


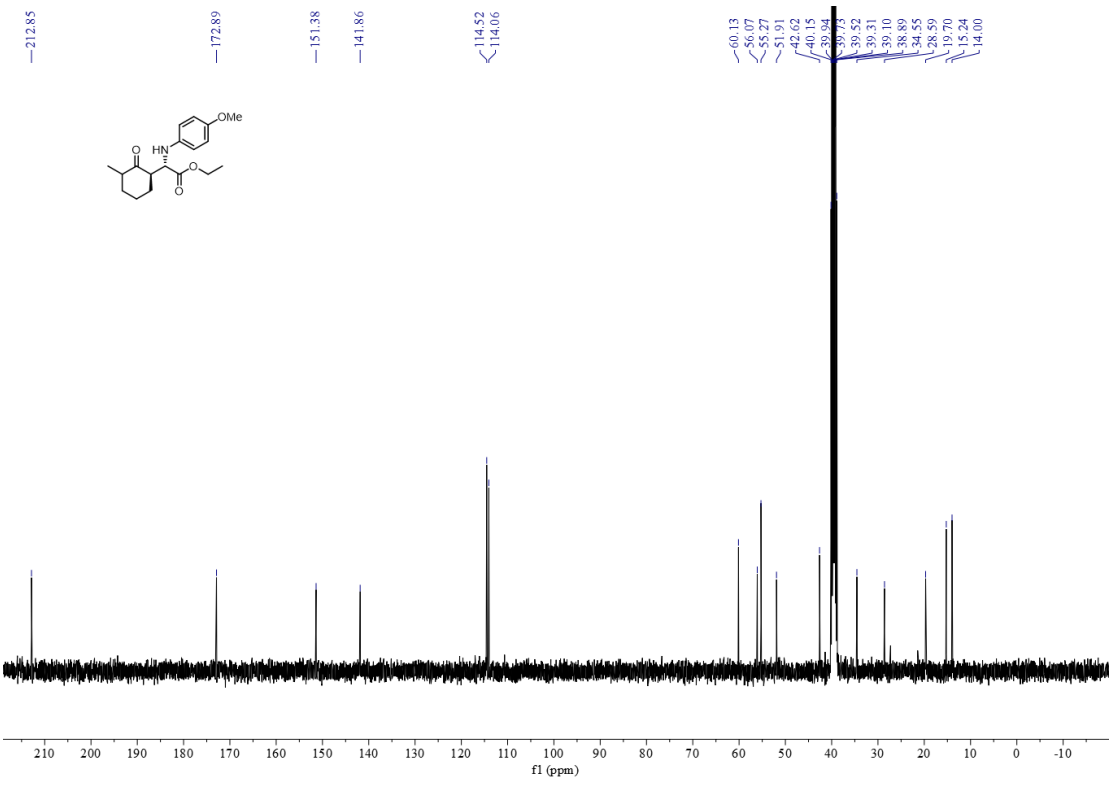


(S)-*N*-(2-(5-methoxy-1H-indol-2-yl)ethyl)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocyclo-hexyl)acetamide (**3ta**)

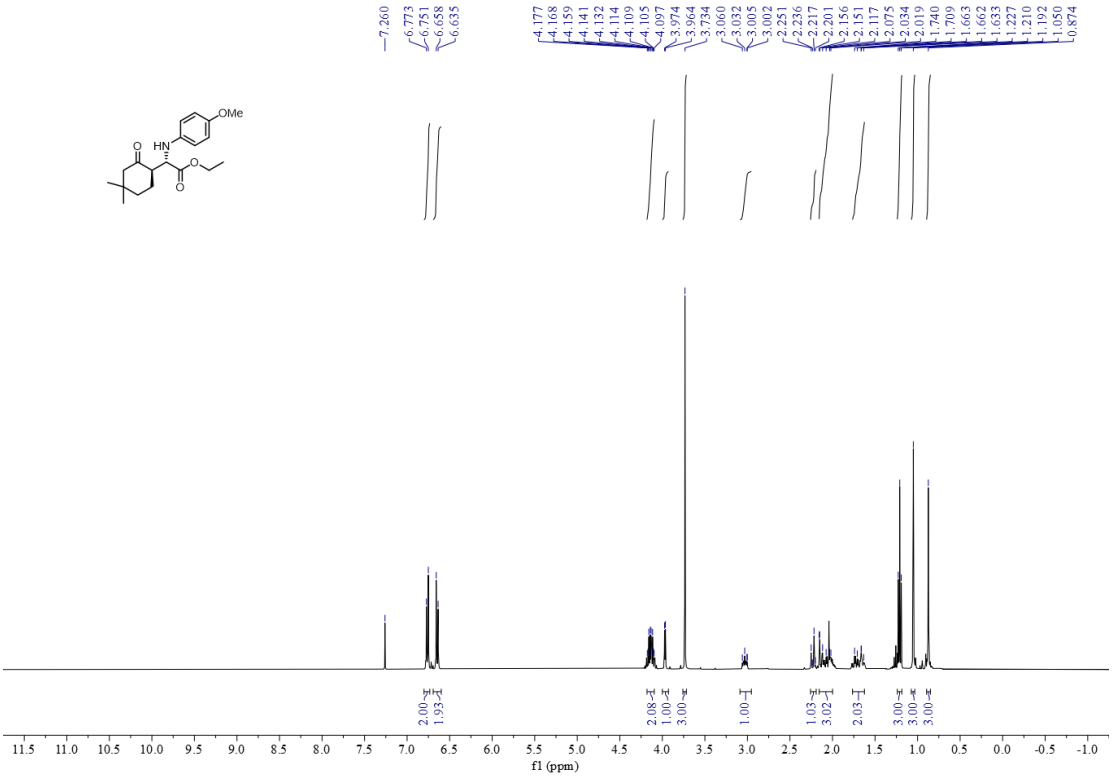


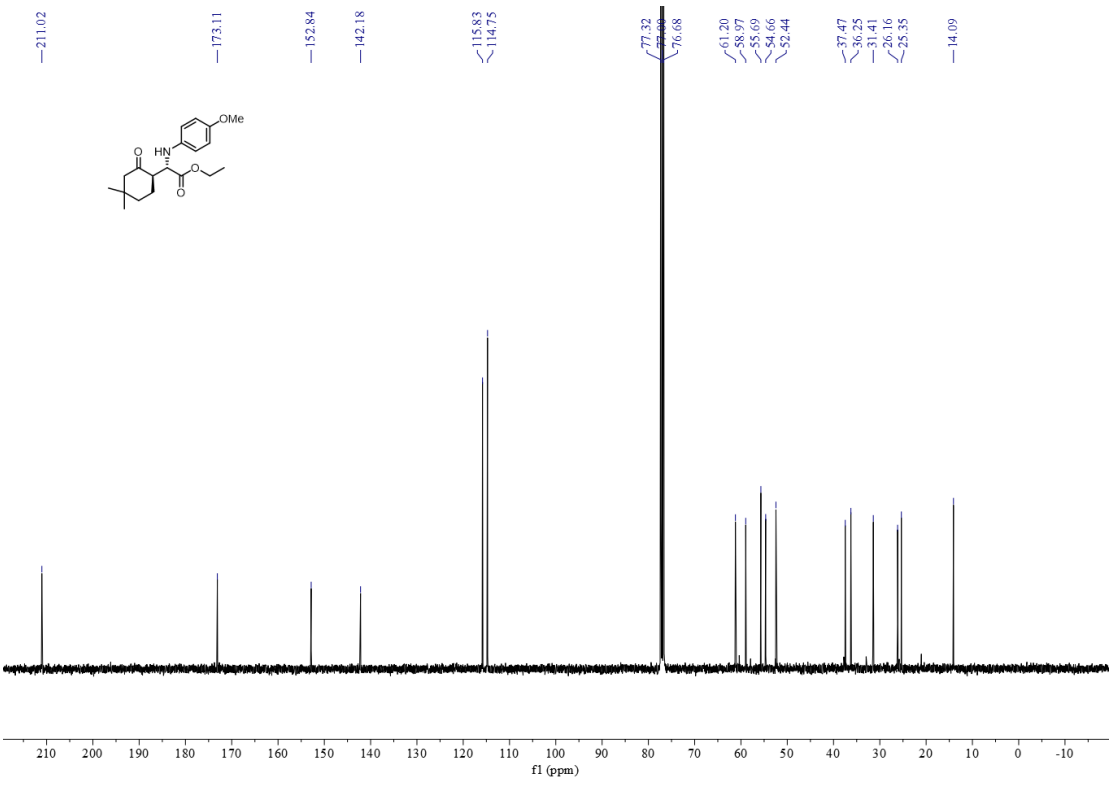
Ethyl (2S)-2-((4-methoxyphenyl)amino)-2-((1R)-3-methyl-2-oxocyclohexyl)acetate (**3ab**)



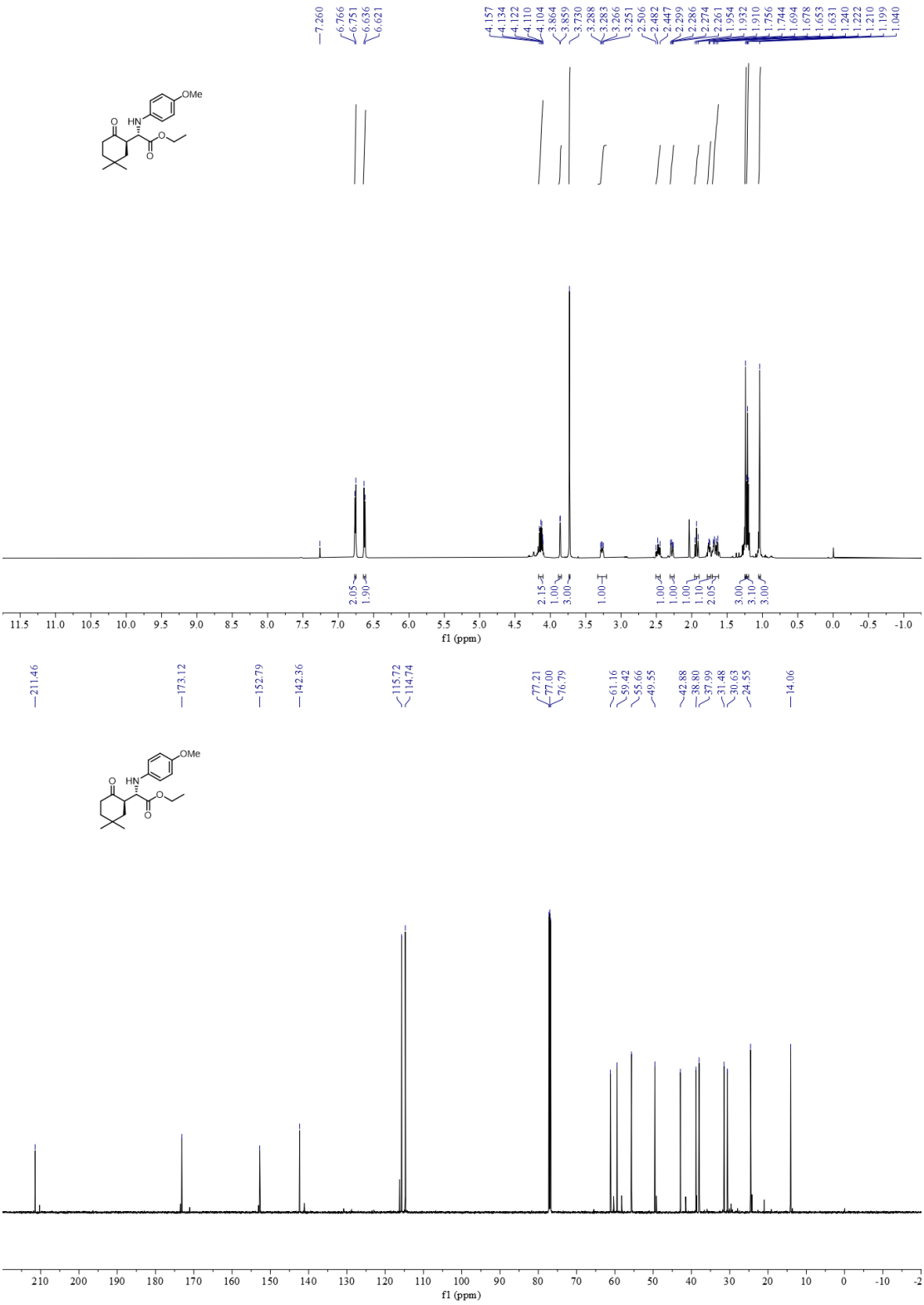


Ethyl (S)-2-((R)-4,4-dimethyl-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ac**)

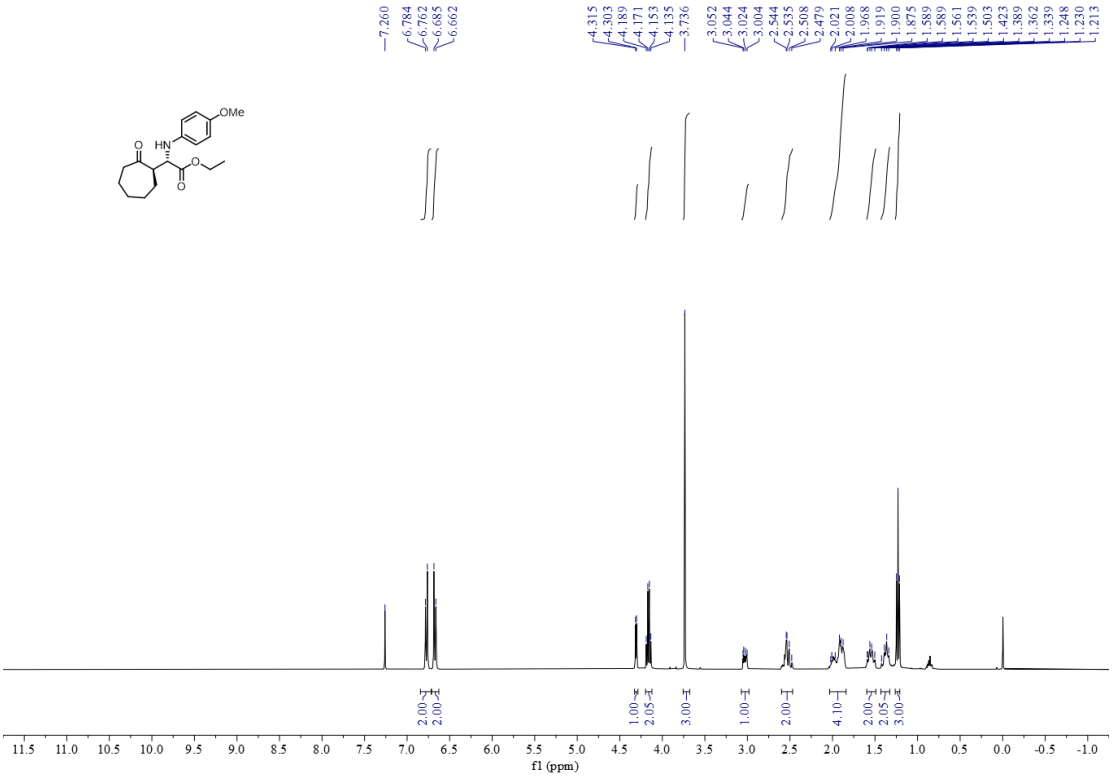


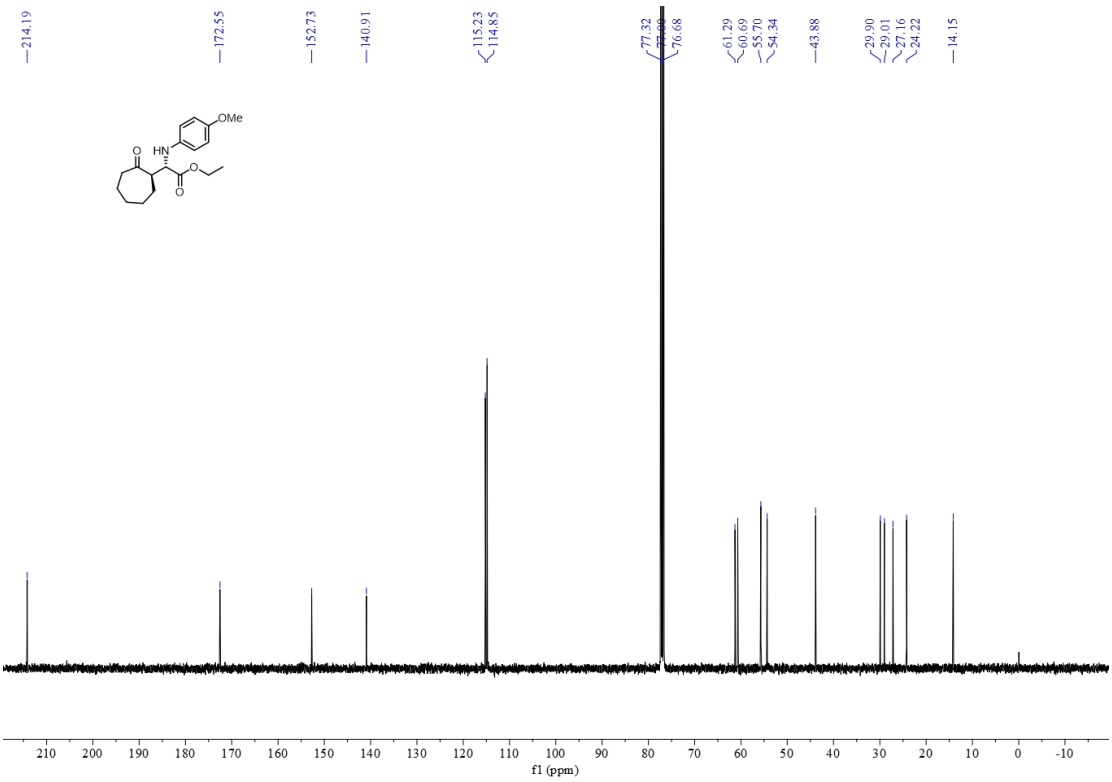


Ethyl (S)-2-((R)-5,5-dimethyl-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ad**)

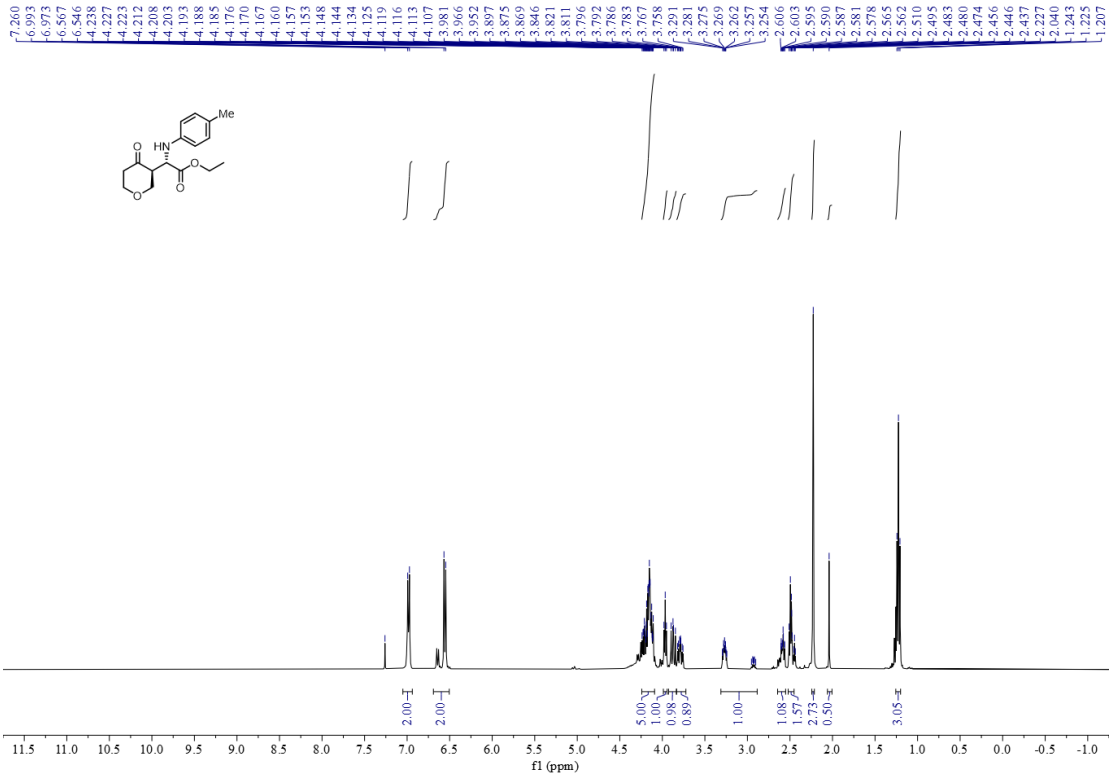


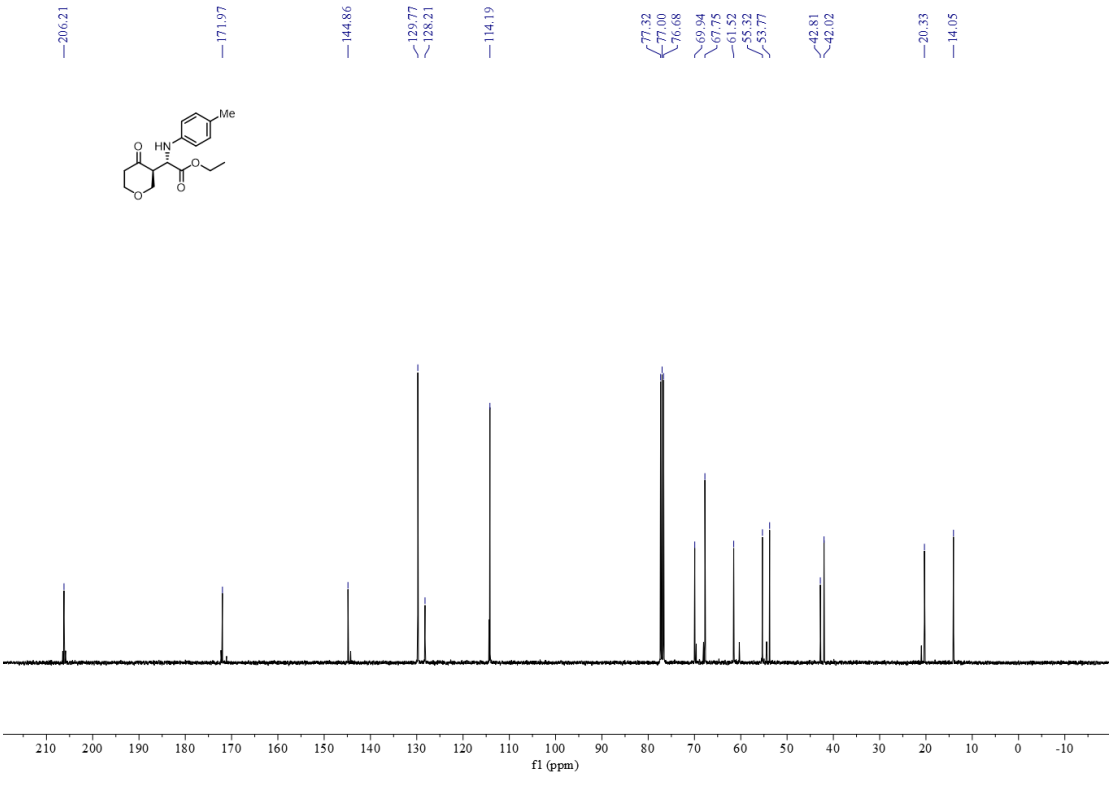
Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-2-oxocycloheptyl)acetate (**3ae**)



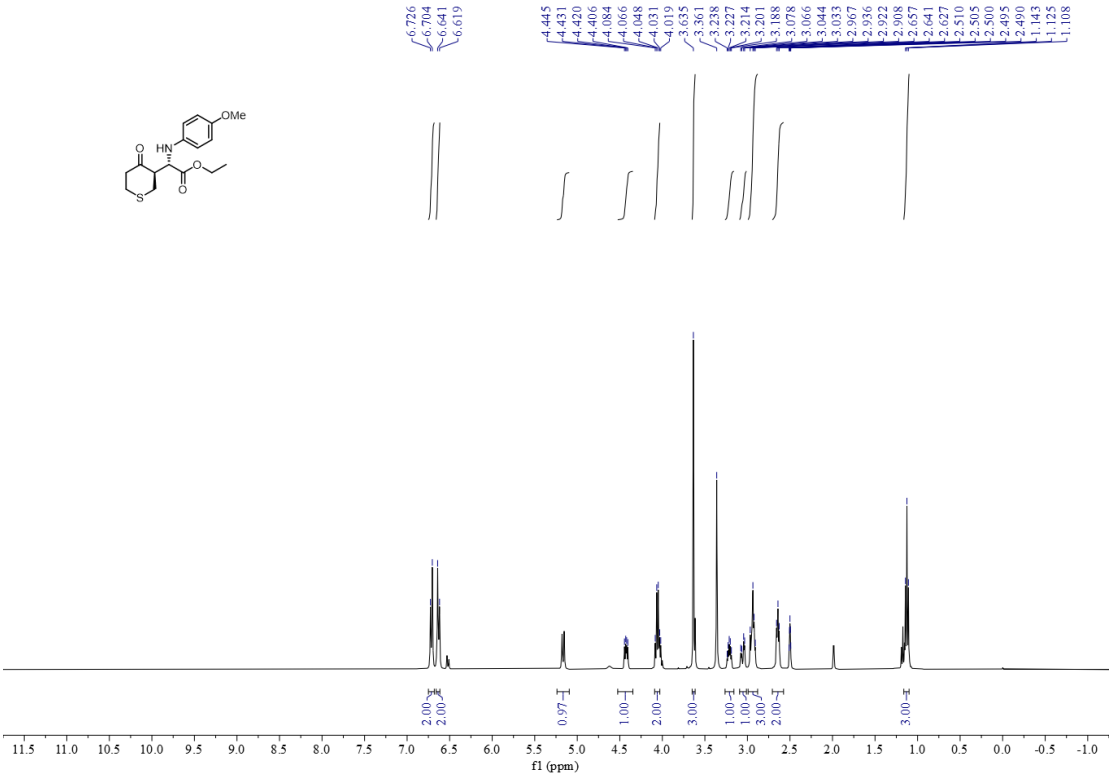


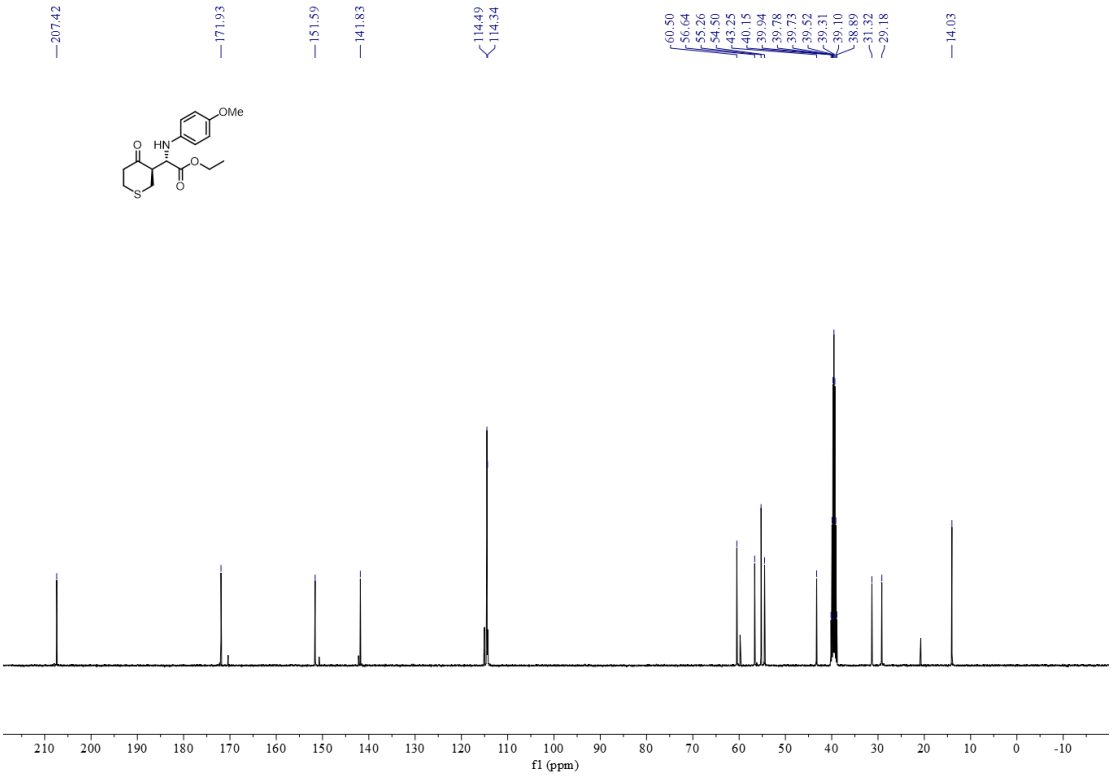
Ethyl (S)-2-((S)-4-oxotetrahydro-2H-pyran-3-yl)-2-(p-tolylamino)acetate (**3kf**)



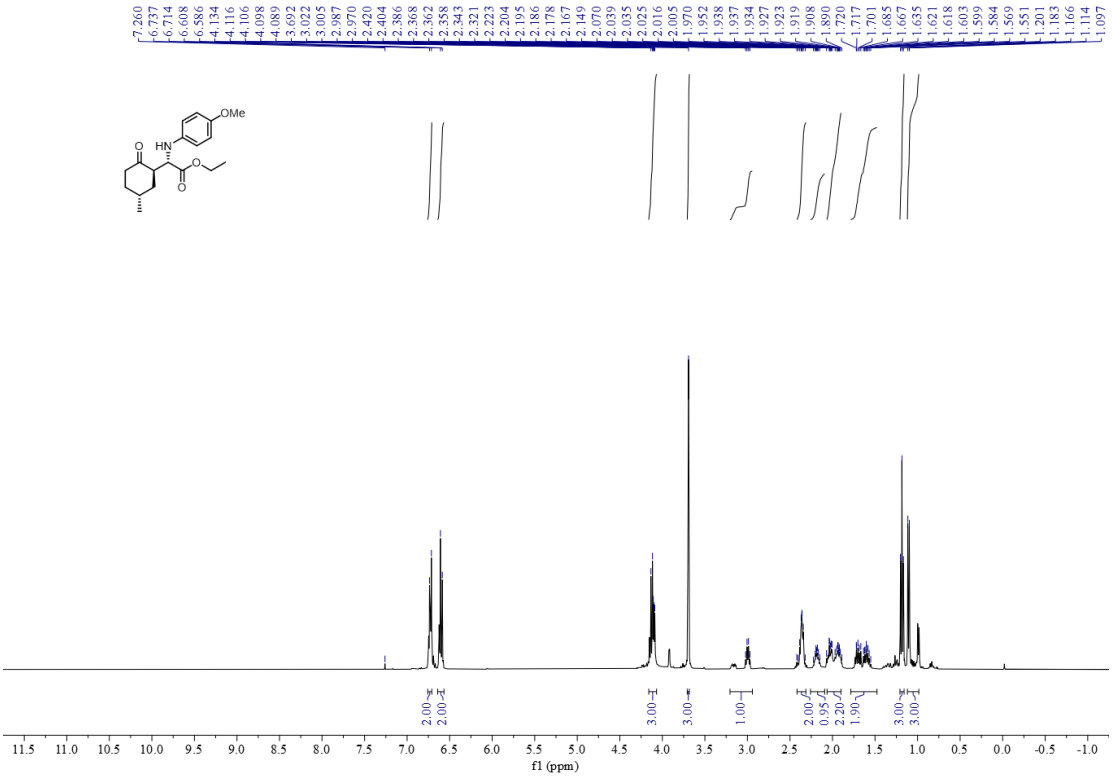


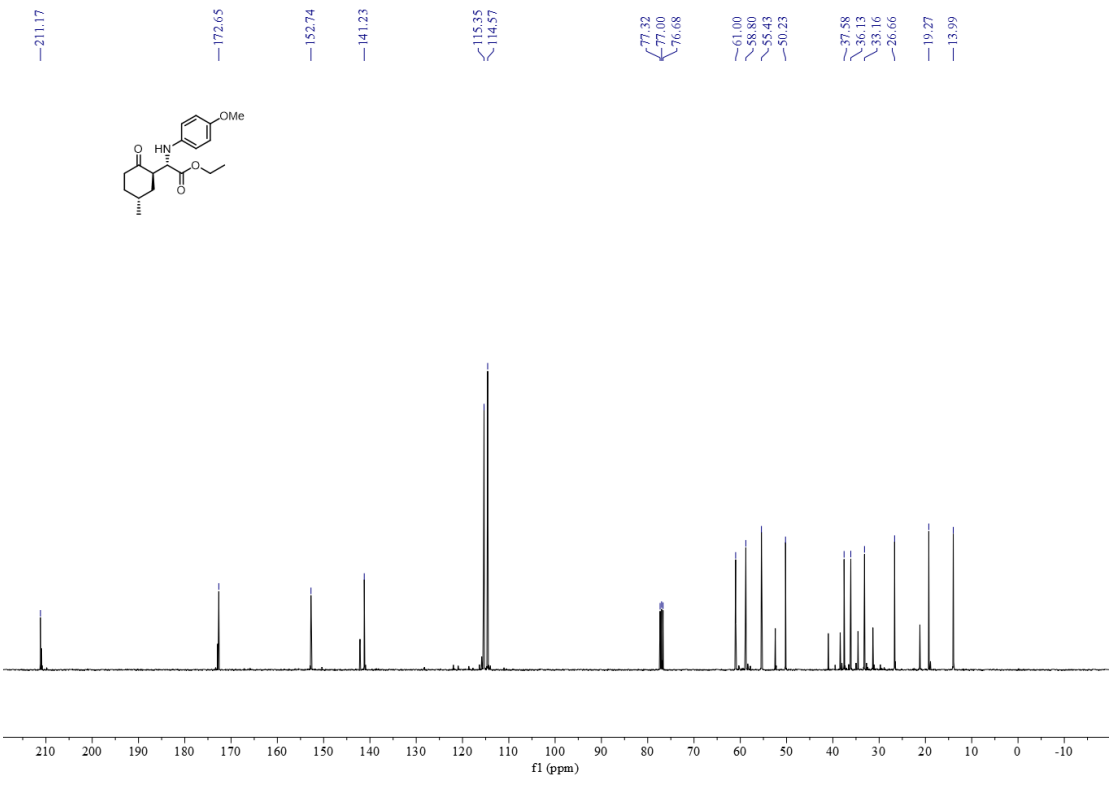
Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-4-oxotetrahydro-2H-thiopyran-3-yl)acetate (**3ag**)



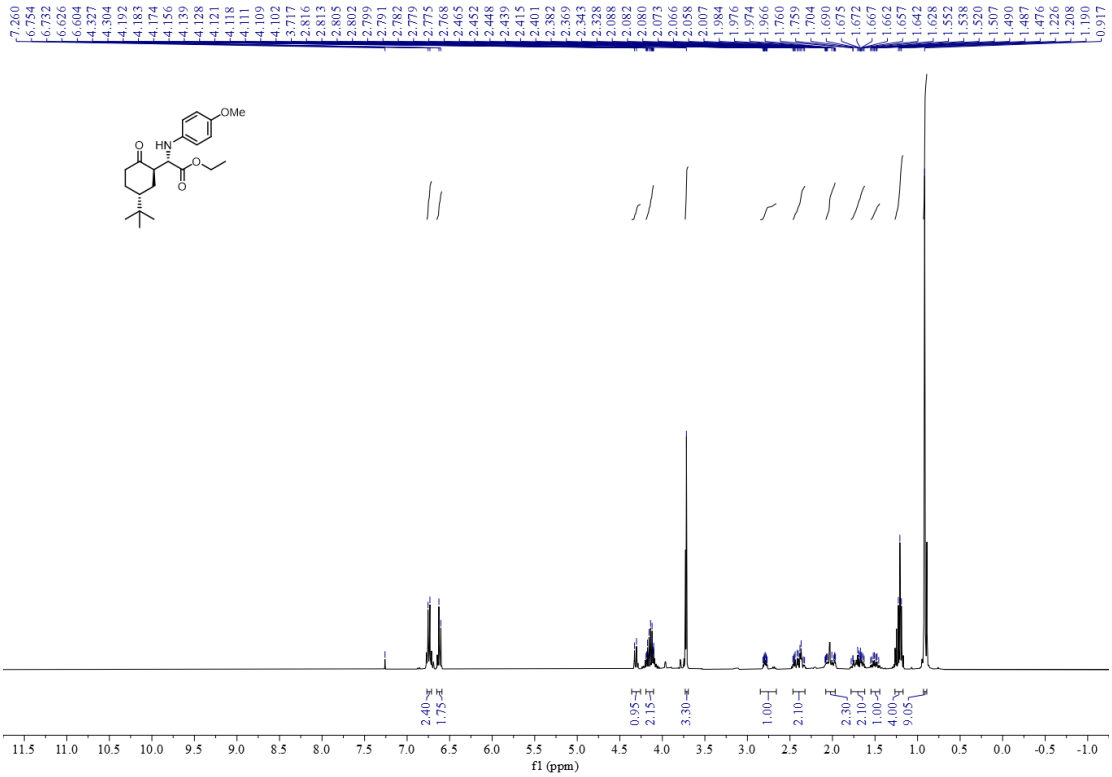


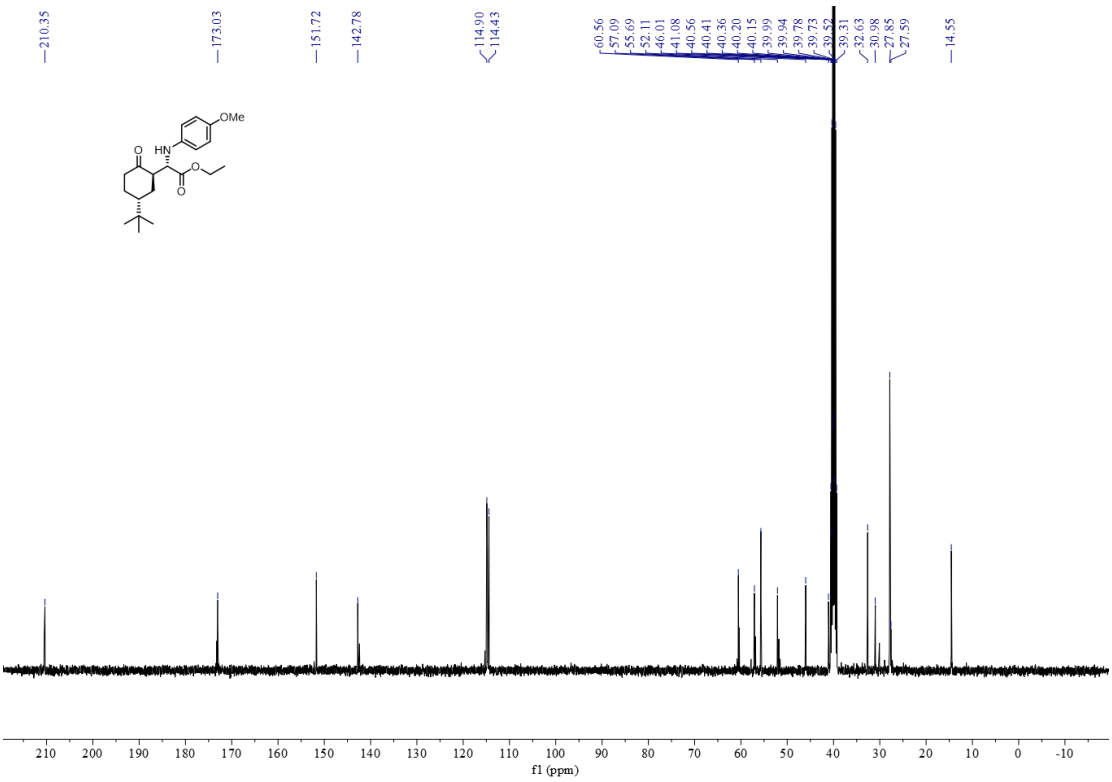
Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((1R,5R)-5-methyl-2-oxocyclohexyl)acetate (**3ah**)



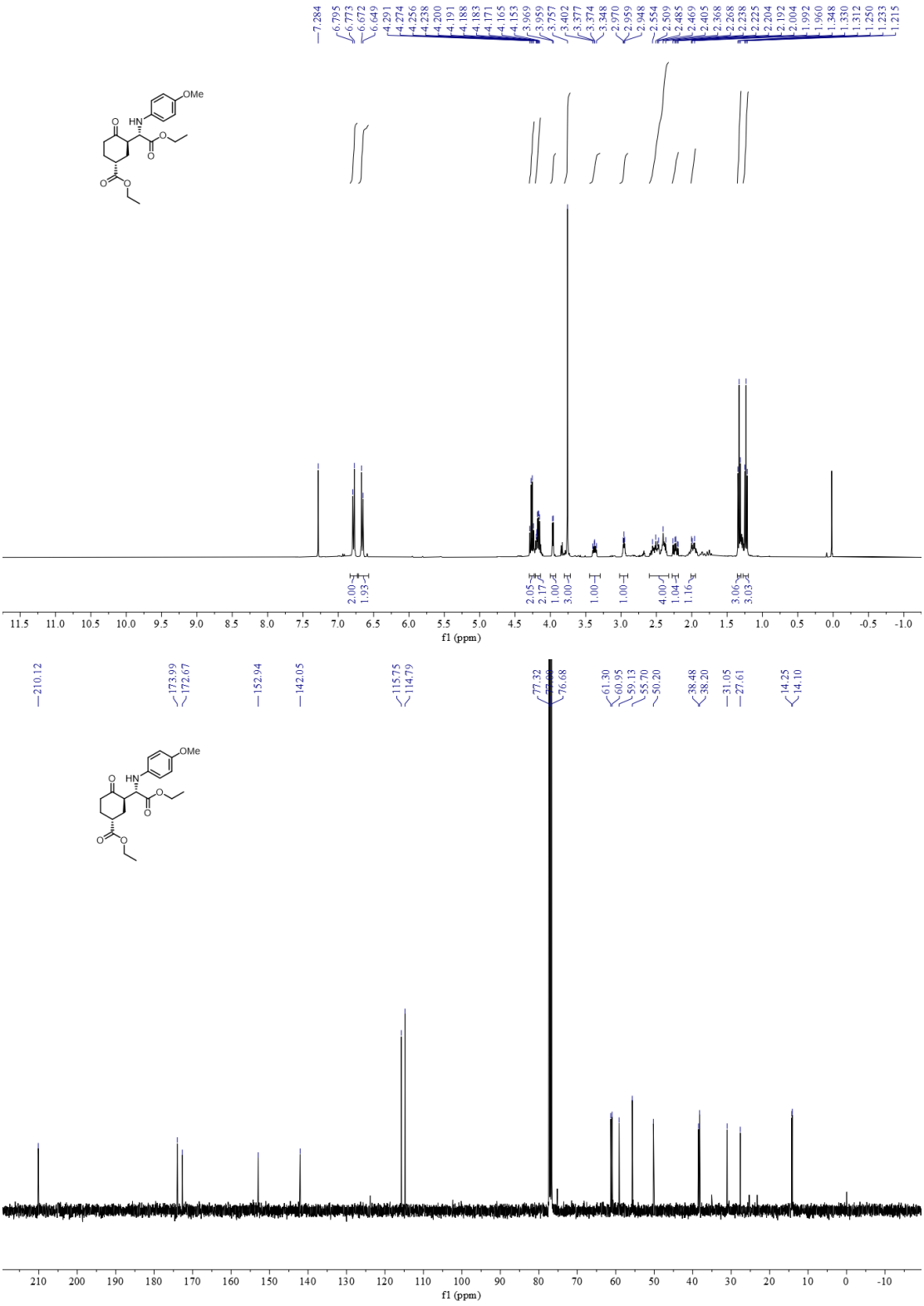


Ethyl (S)-2-((1R,5R)-5-(tert-butyl)-2-oxocyclohexyl)-2-((4-methoxyphenyl)amino)acetate (**3ai**)

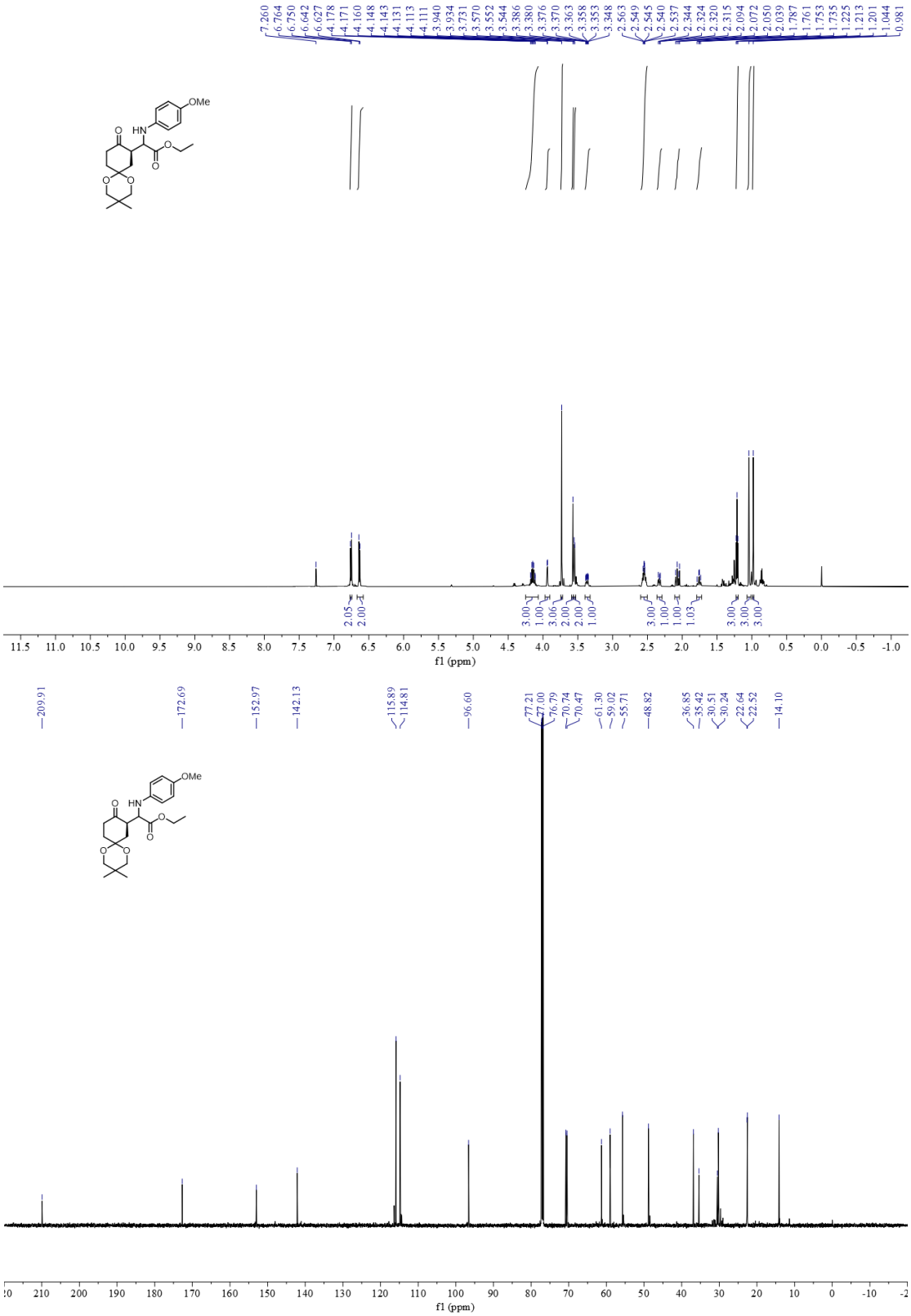




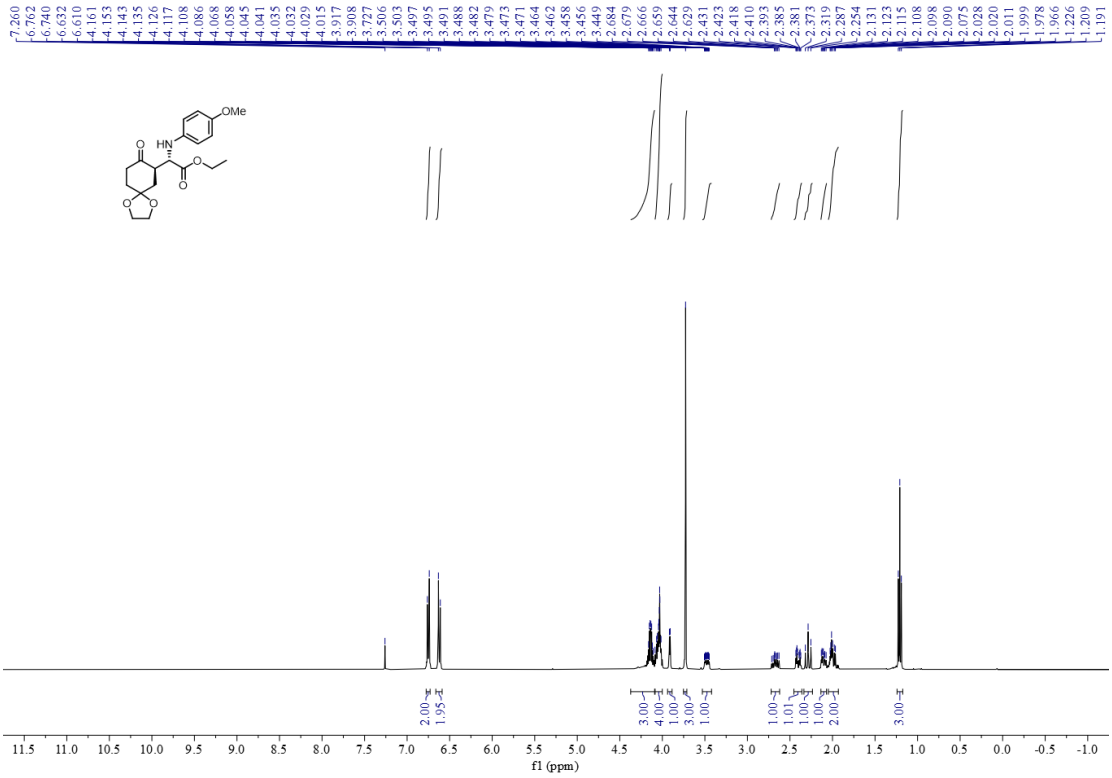
Ethyl (1R,3R)-3-((S)-2-ethoxy-1-((4-methoxyphenyl)amino)-2-oxoethyl)-4-oxocyclohexan-e-1-carbox-ylate (**3aj**)

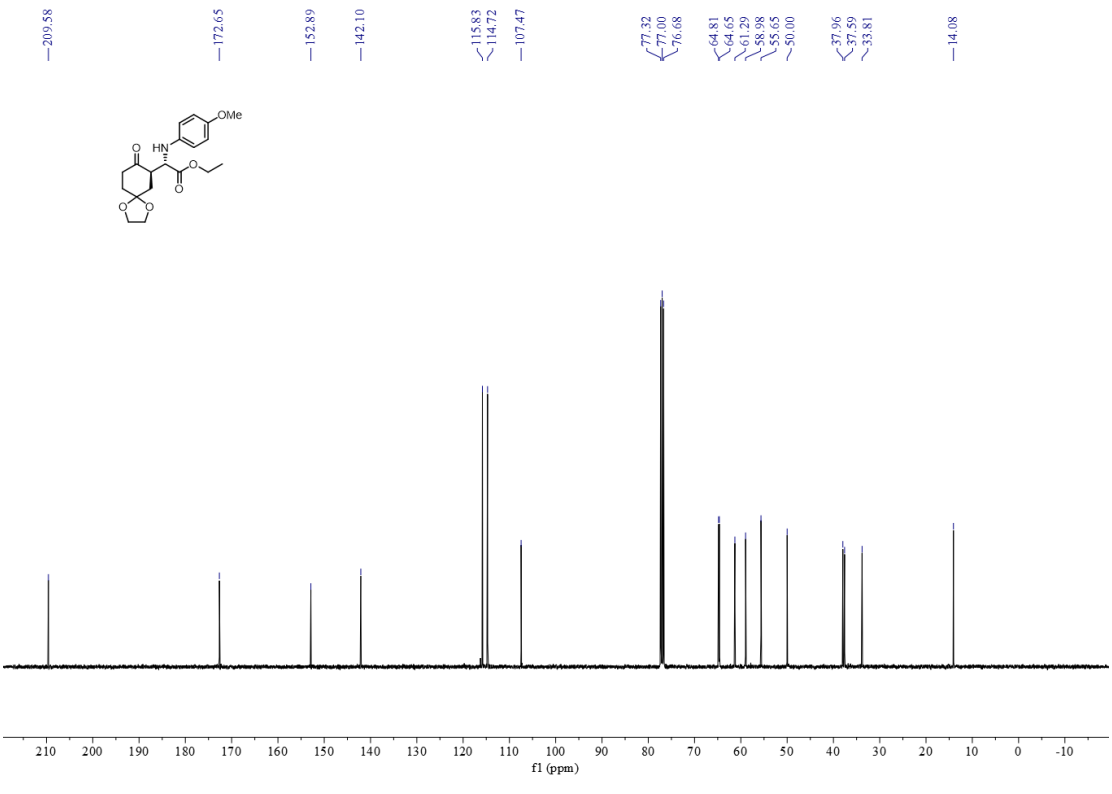


Ethyl 2-((R)-3,3-dimethyl-9-oxo-1,5-dioxaspiro[5.5]undecan-8-yl)-2-((4-methoxyphenyl)a-mino)acetate (**3ak**)

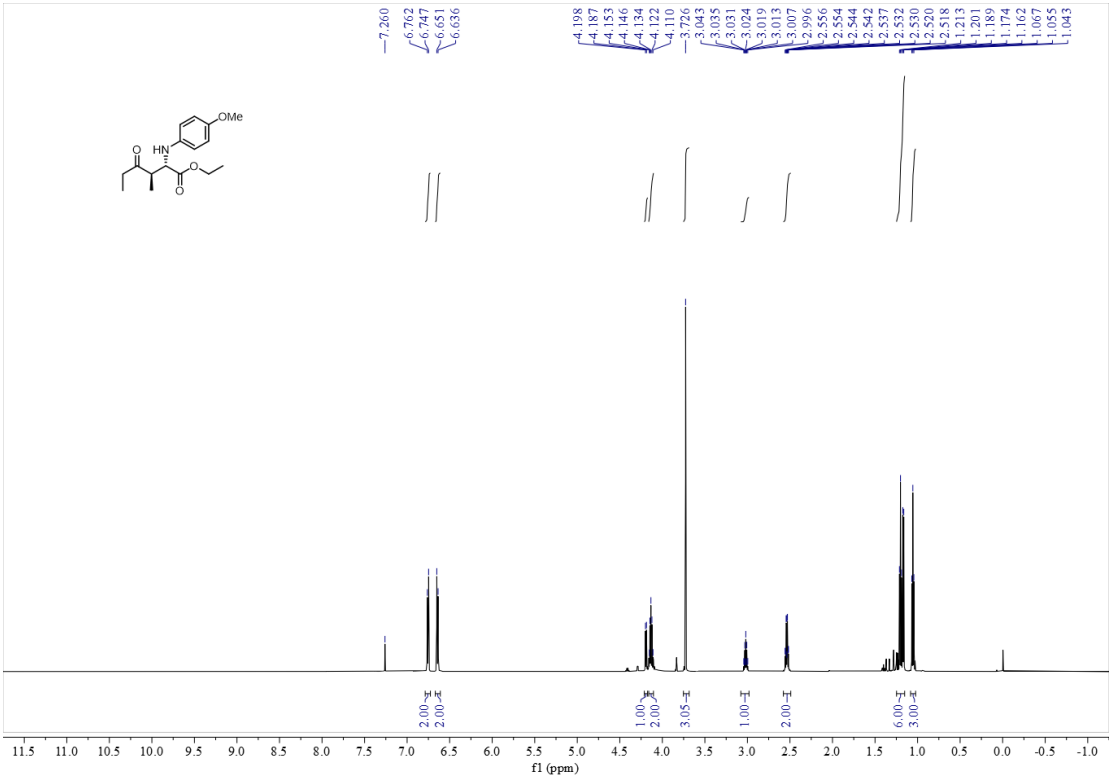


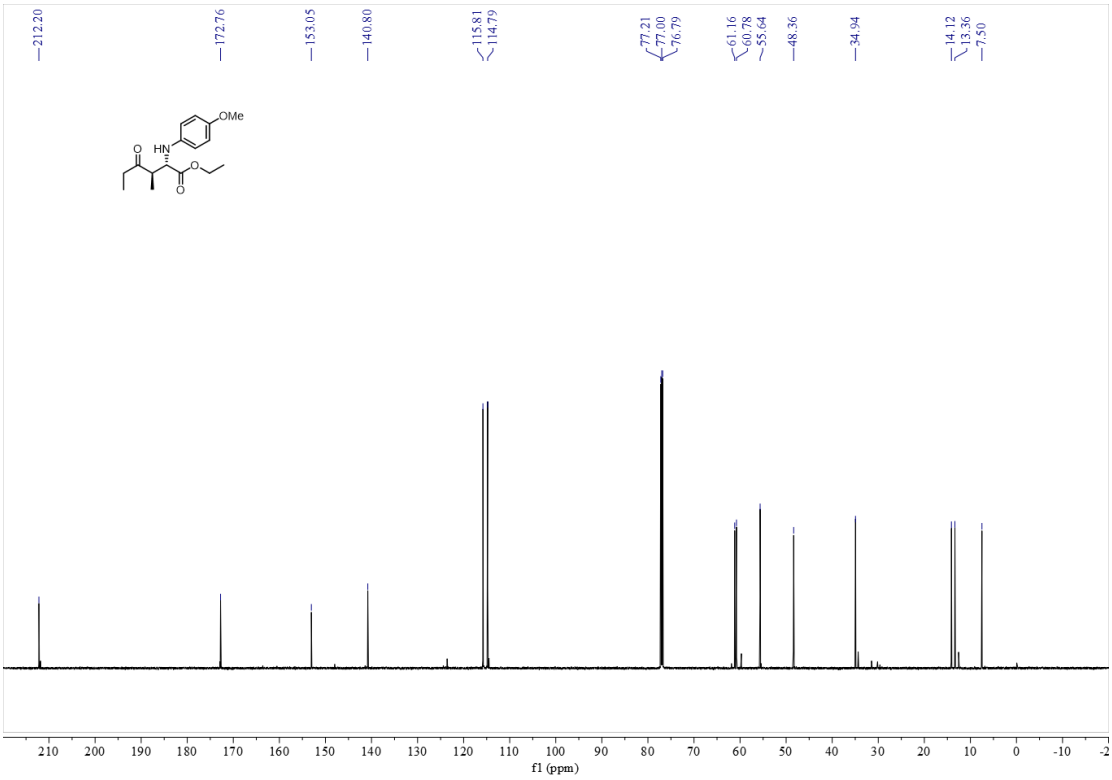
Ethyl (S)-2-((4-methoxyphenyl)amino)-2-((R)-8-oxo-1,4-dioxaspiro[4.5]decan-7-yl)acetate (**3al**)



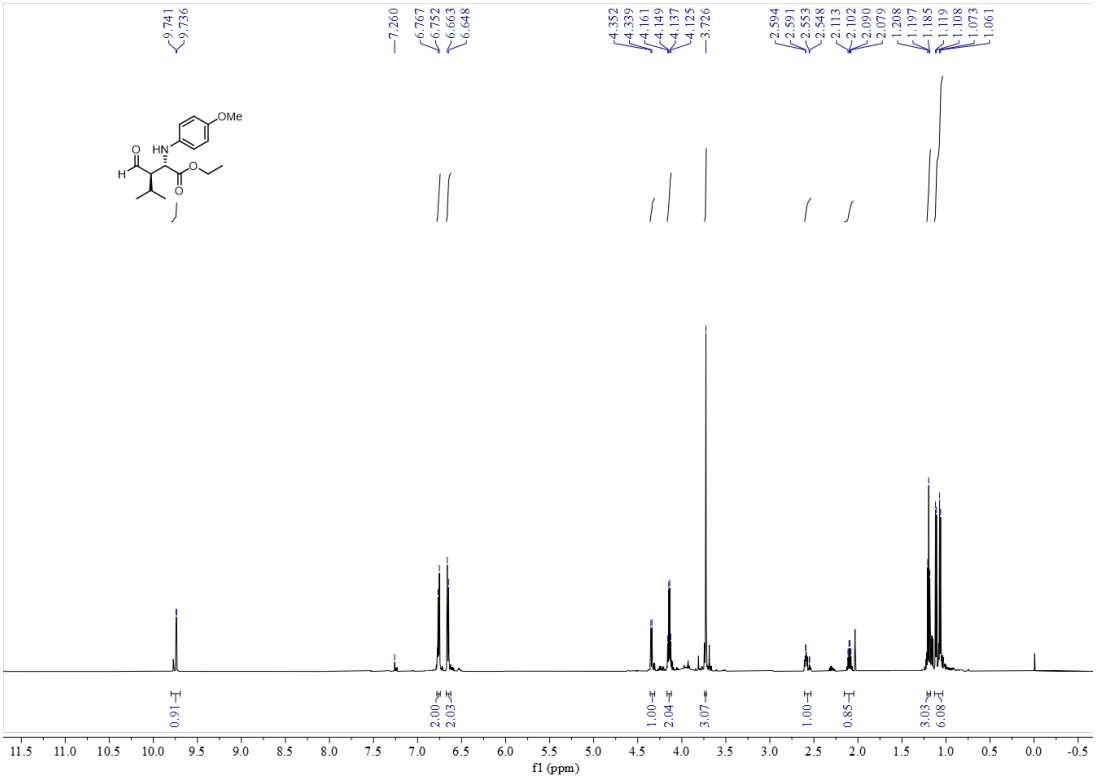


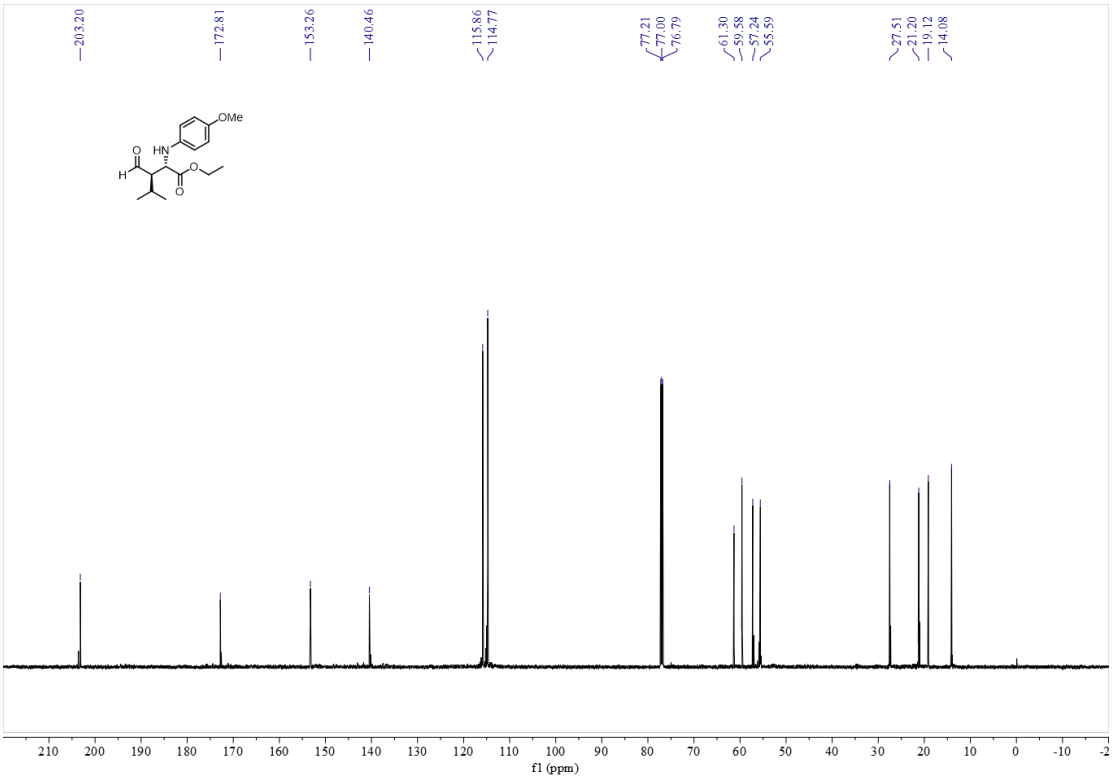
Ethyl (2S,3R)-2-((4-methoxyphenyl)amino)-3-methyl-4-oxohexanoate (**3am**)



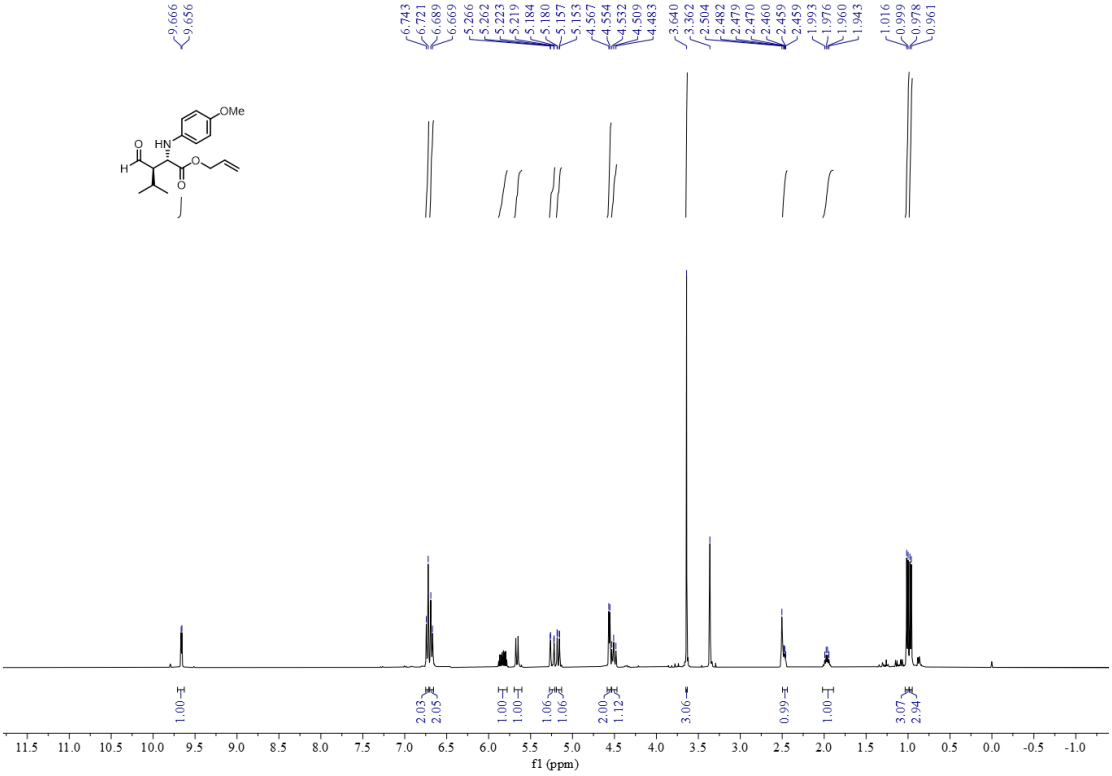


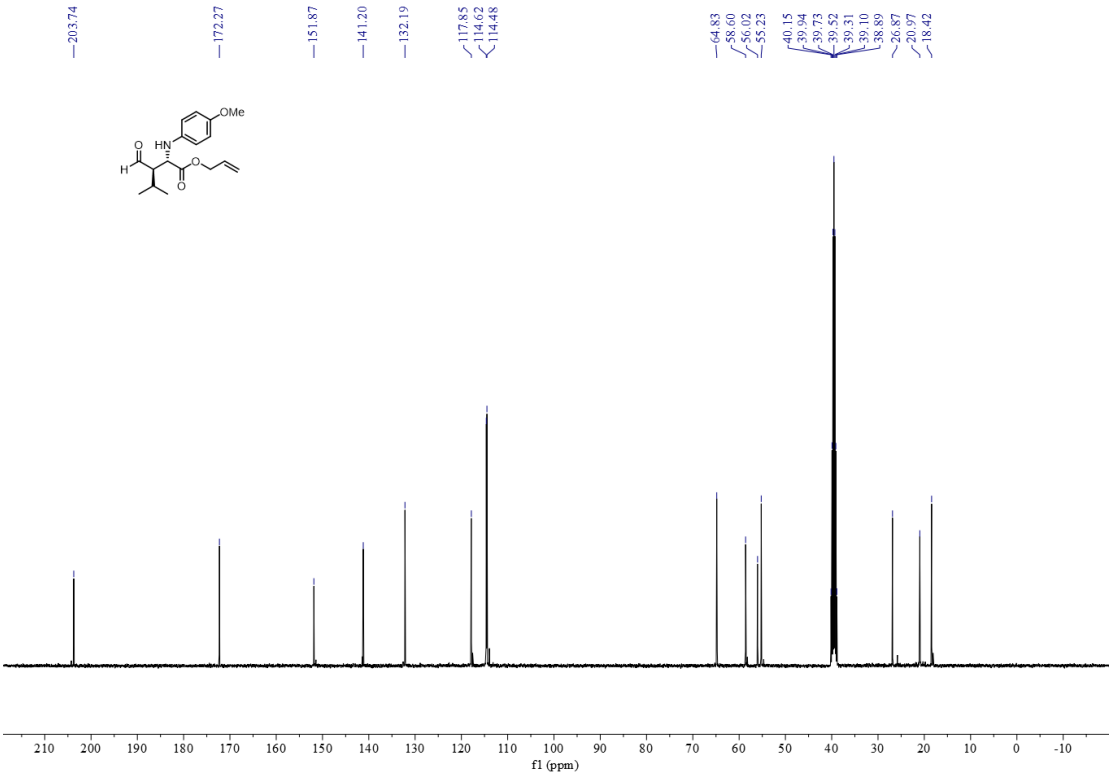
Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)-4-methylpentanoate (**3an**)



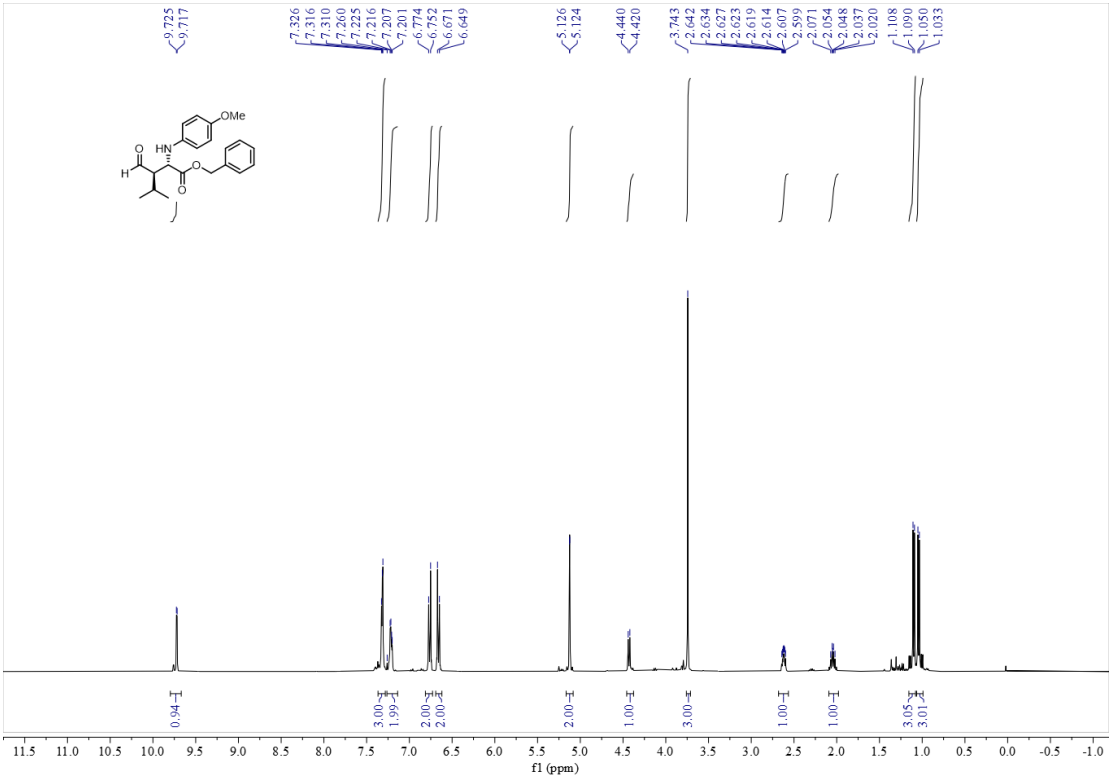


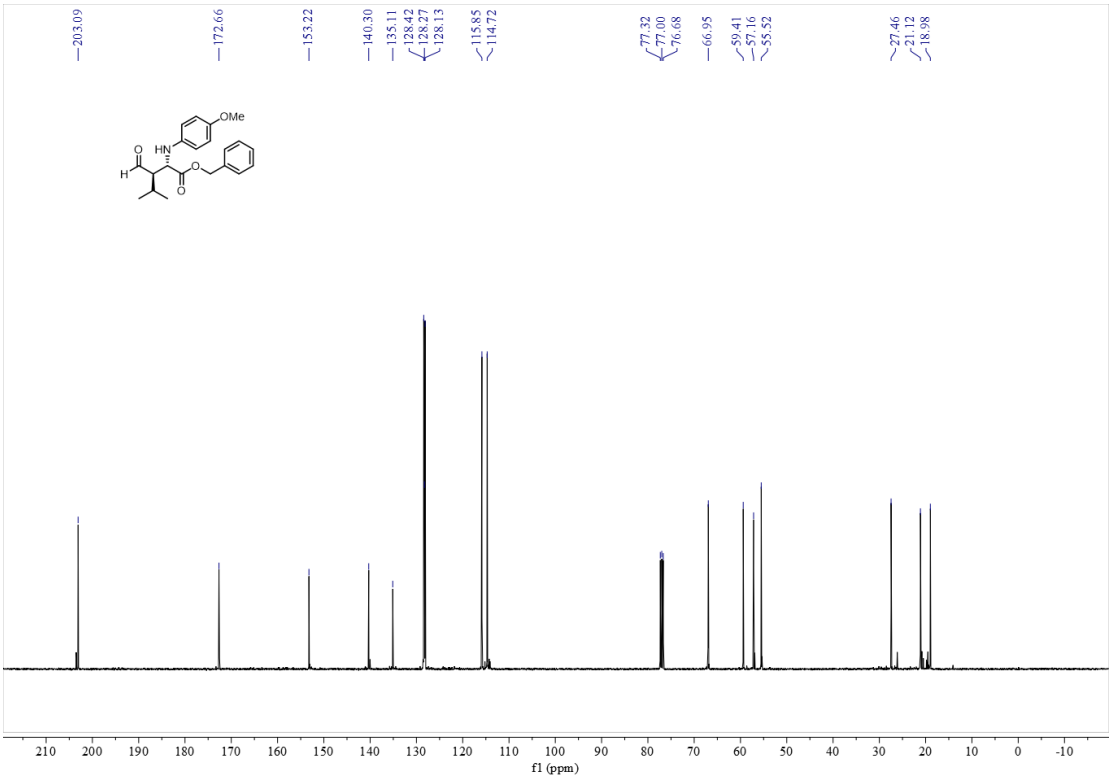
Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)octanoate (**3en**)



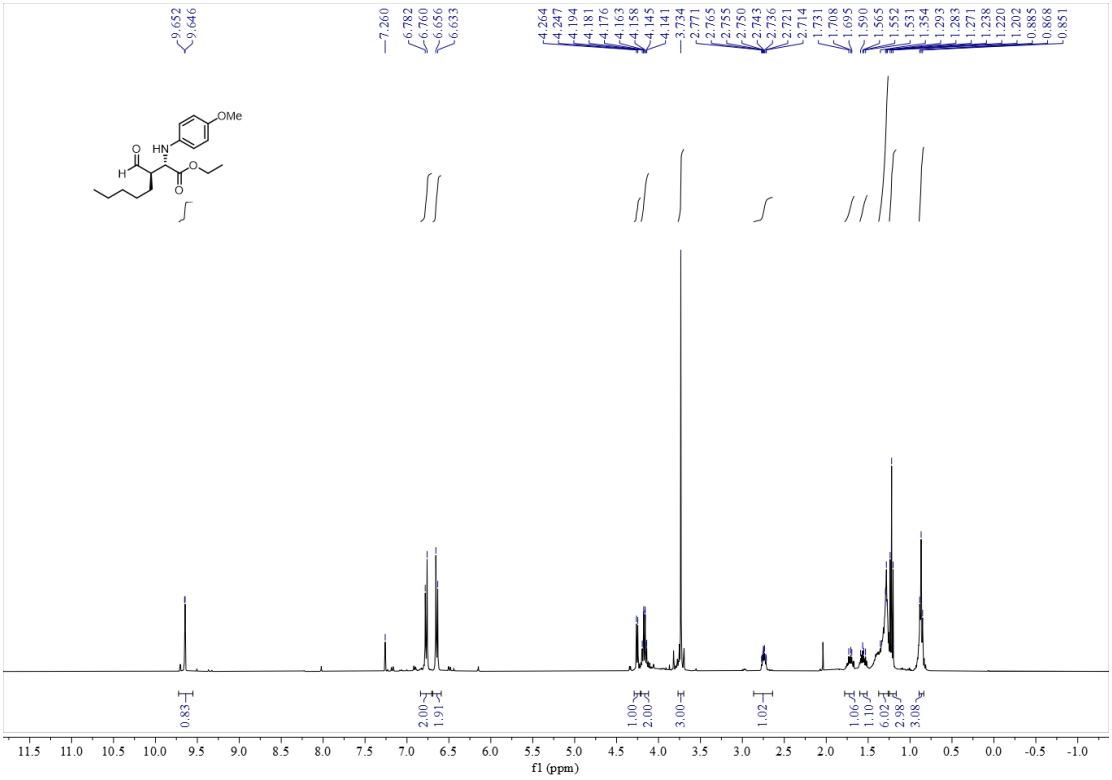


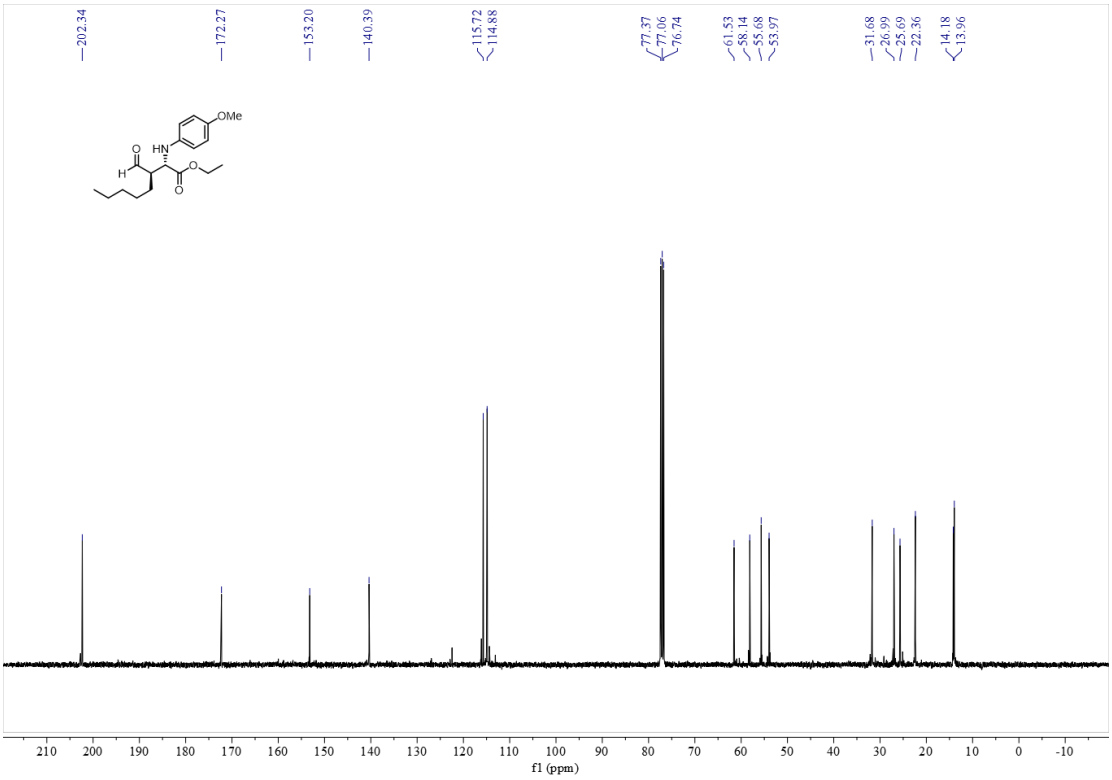
Benzyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)-4-methylpentanoate (**3gn**)



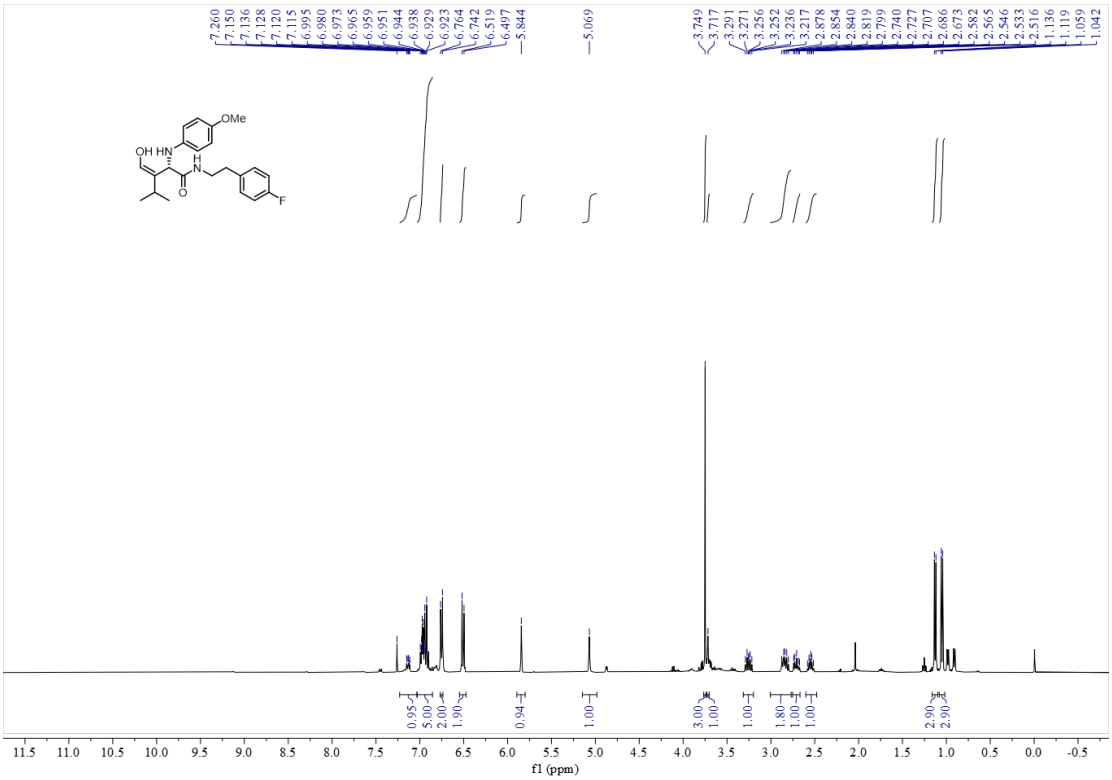


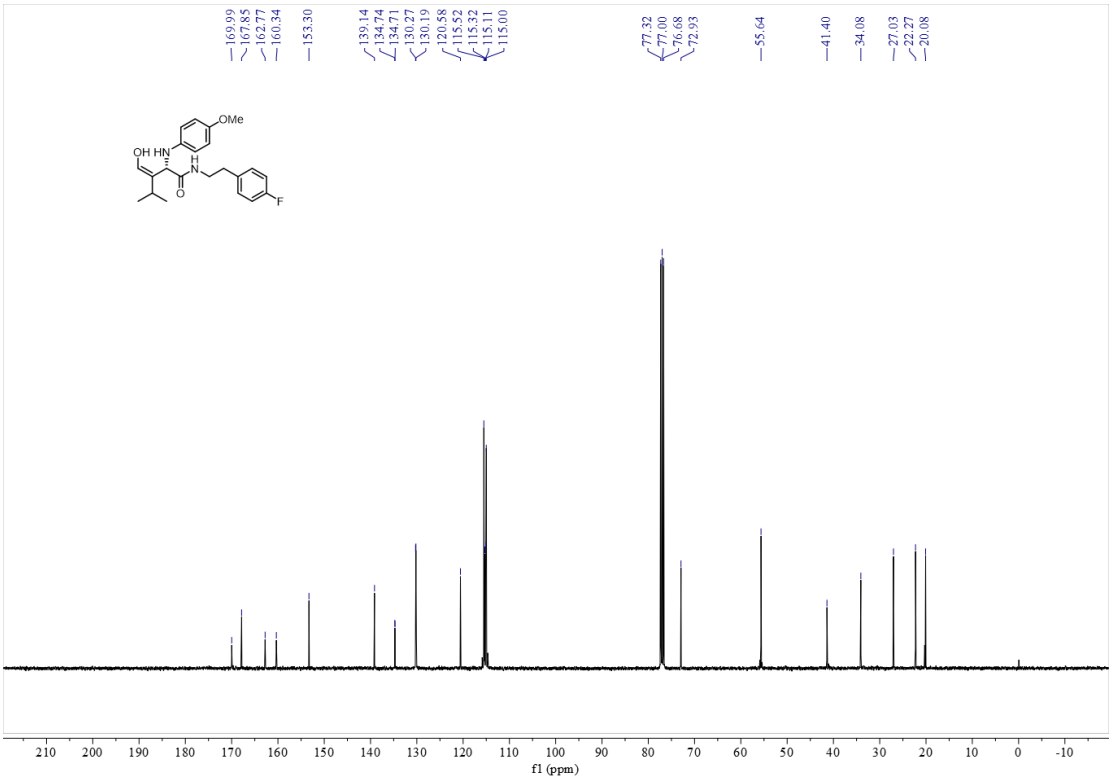
Ethyl (2S,3R)-3-formyl-2-((4-methoxyphenyl)amino)octanoate (**3ao**)

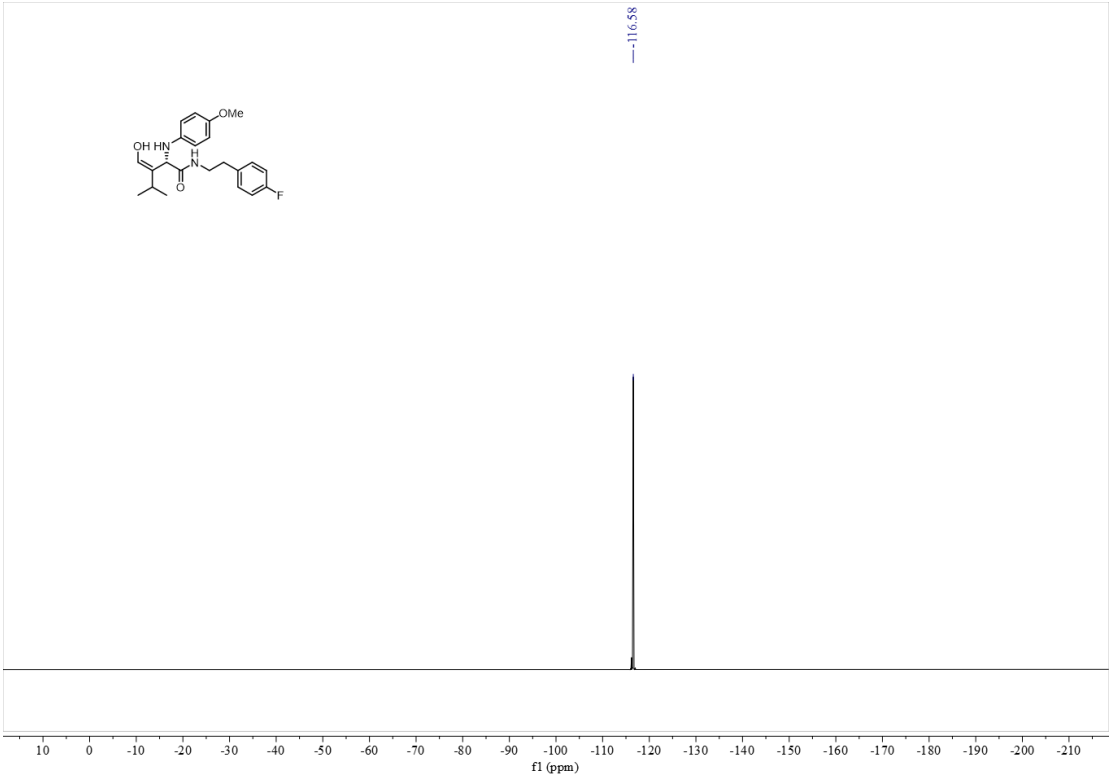




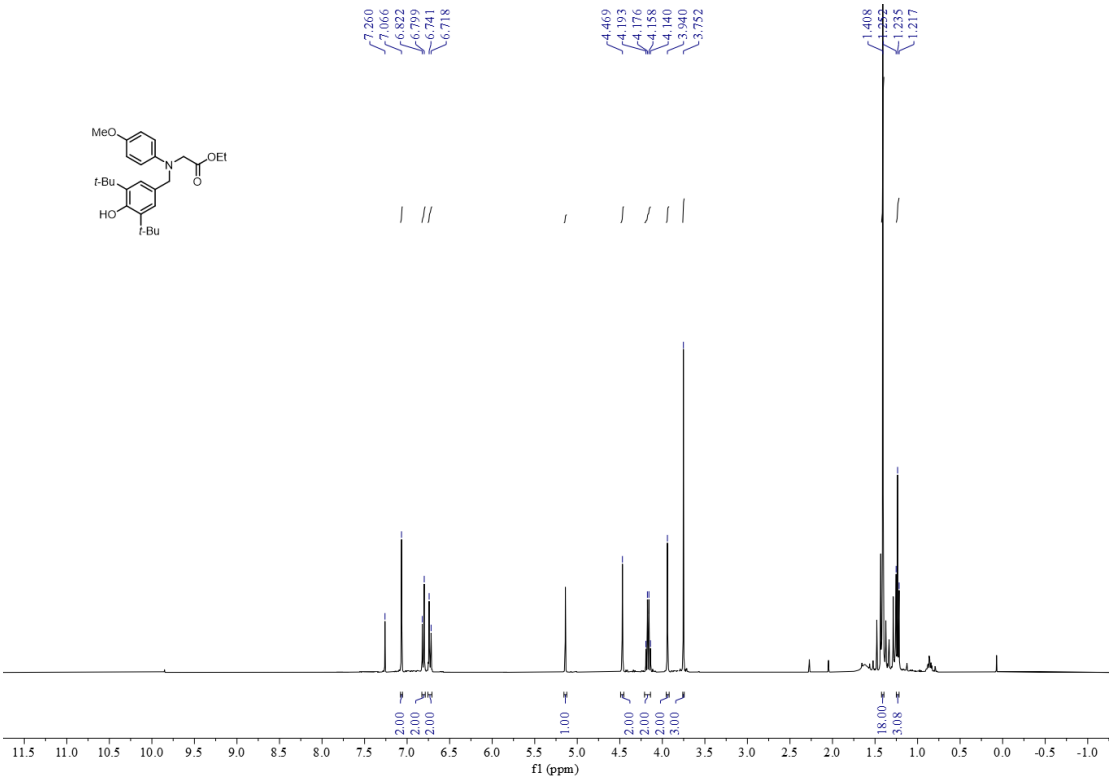
(S,Z)-*N*-(4-fluorophenethyl)-3-(hydroxymethylene)-2-((4-methoxyphenyl)amino)-4-methylpentanamide (**3pn**)



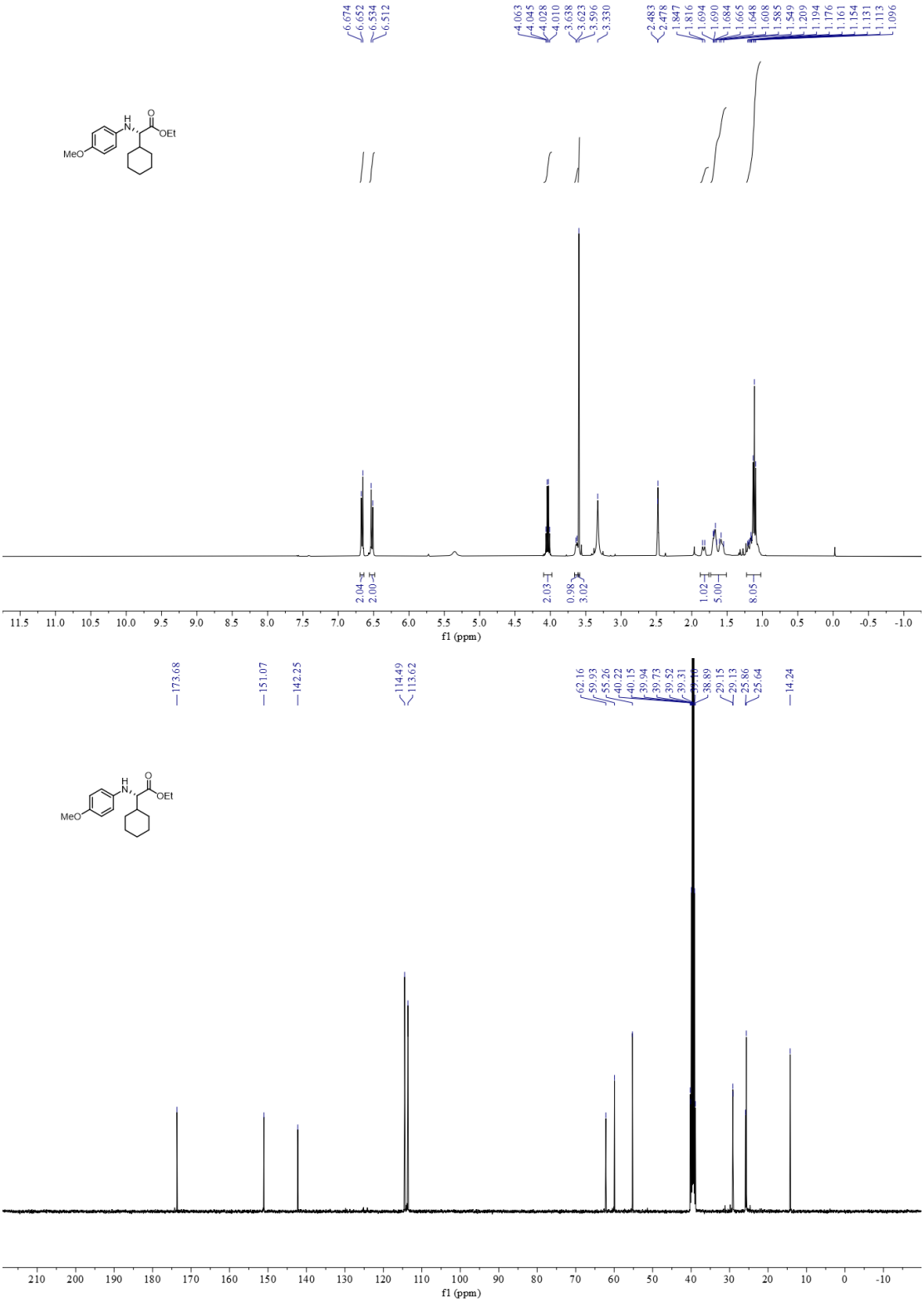



-116.58
OMe
OH HN
H
N
O
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

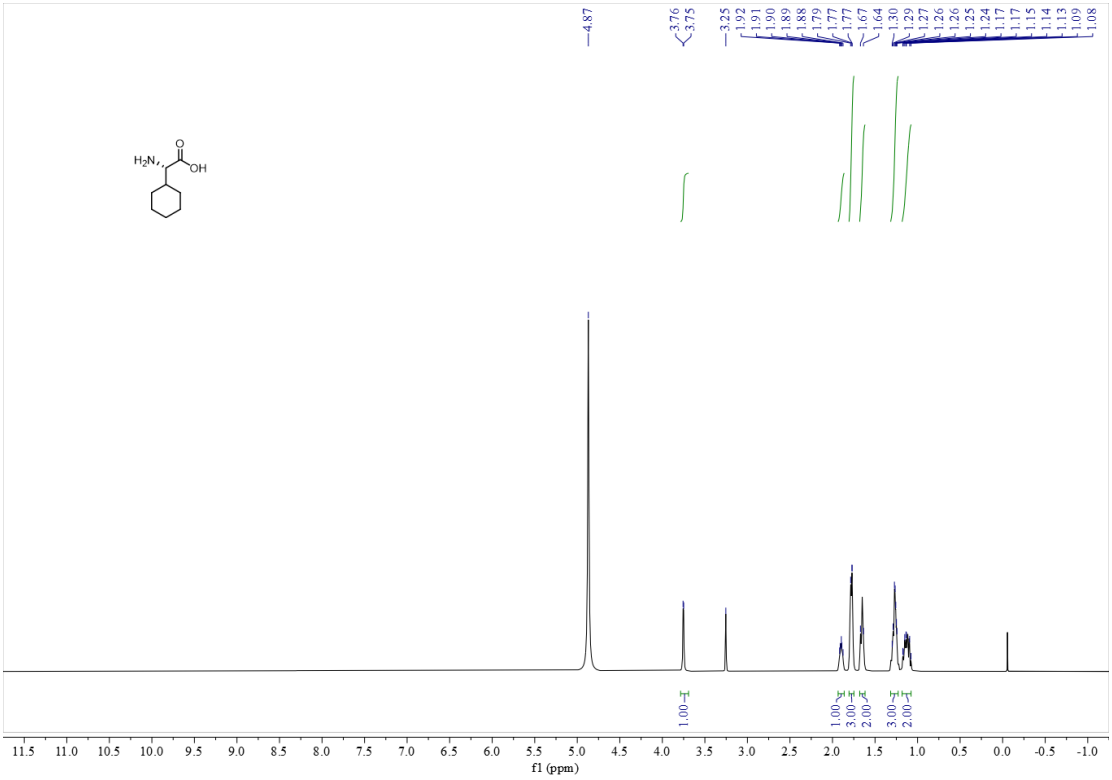
Ethyl *N*-(3,5-di-tert-butyl-4-hydroxybenzyl)-N-(4-methoxyphenyl)glycinate (**1a-BHT**)

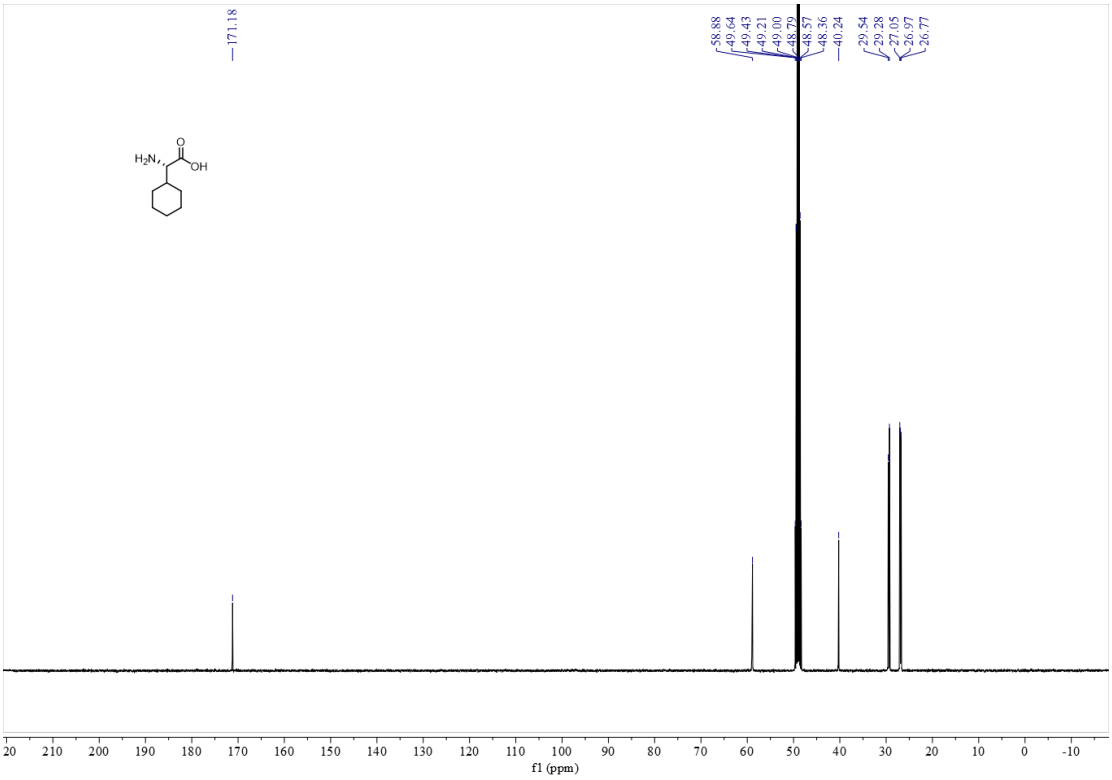


Ethyl (S)-2-cyclohexyl-2-((4-methoxyphenyl)amino)acetate (**4**)

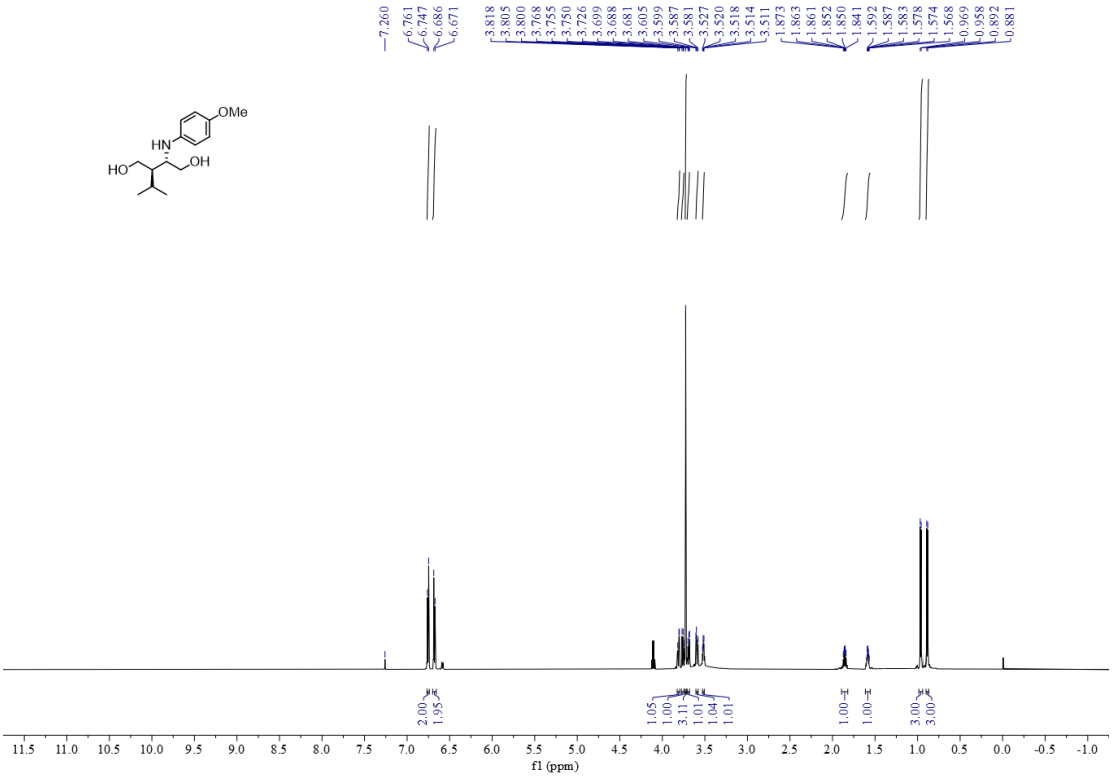


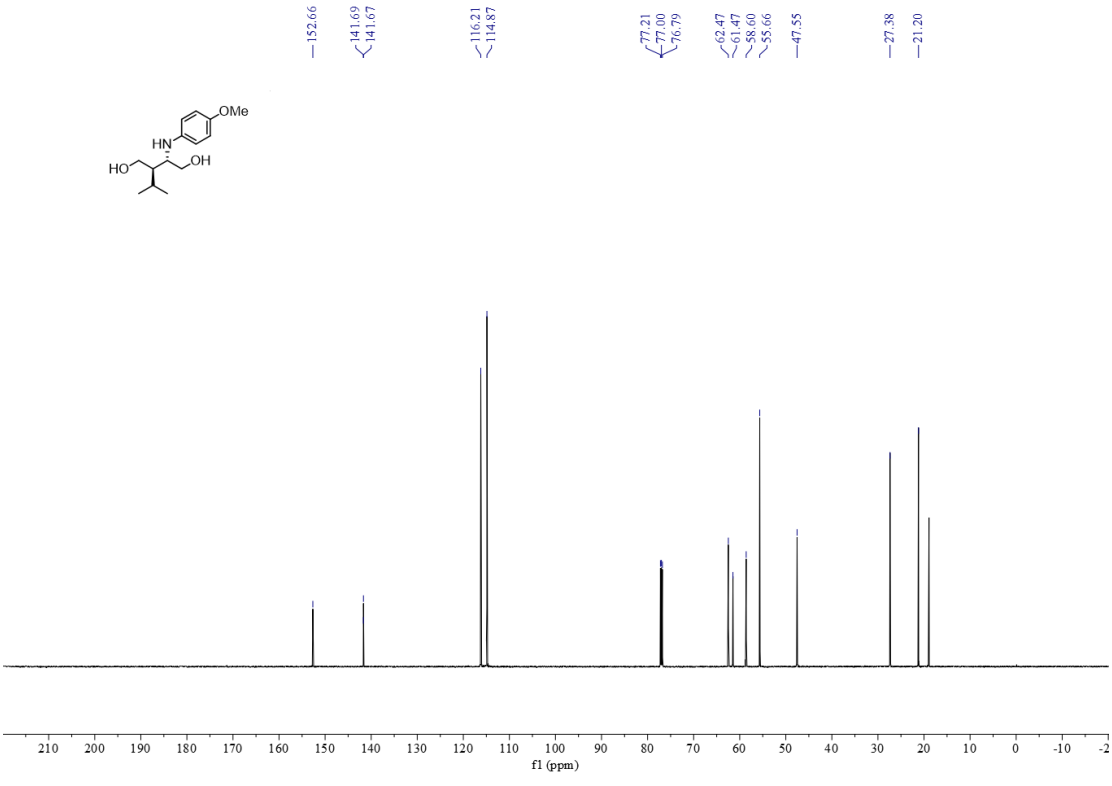
(S)-2-amino-2-cyclohexylacetic acid (**5**)





(2R,3S)-2-Isopropyl-3-((4-methoxyphenyl)amino)butane-1,4-diol (**6**)





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