Functional-group-convergent synthesis of amides

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1. General information

Unless otherwise noted, all reactions were carried out under a carbon monoxide or nitrogen atmosphere. All reagents were from commercial sources, all solvents are extra dry solvents and used as received without further purification. Column chromatography was performed on silica gel (200-300 meshes) using the indicated solvents. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker AV400 or AV500 instruments. Chemical shifts are reported to 0.01 ppm for ^{1}H NMR to 0.1 ppm for ^{13}C NMR and ^{19}F NMR spectra. Peaks that are within 0.1 ppm for ^{13}C NMR but are still distinguishable are reported to 0.01 ppm. Reference peaks for chloroform in ^{1}H NMR and ^{13}C NMR spectra were set at 7.26 ppm and 77.0 ppm, respectively. Reference peaks for dimethyl sulfoxide in ^{1}H NMR and ^{13}C NMR spectra were set at 3.33 ppm and 40.0 ppm, respectively. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.), coupling constants (Hz), and integration.

Gas chromatography mass spectrometer (GC-MS) analyses were performed on an Thermoscientific Trace 1600 instrument with a EI detector and TG-1MS capillary column (polydimethylsiloxane with 5% phenyl groups, 30 m, 0.25 mm i.d. 0.25 μm film thickness) using argon as carrier gas. High resolution mass spectra (HRMS) were recorded on Acquity UPLC-Xevo G2 QT at the *Instrument sharing center, University of Science and Technology of China.*

Because of the high toxicity of carbon monoxide, all of the reactions should be performed in an autoclave. The laboratory should well-equipped with a CO detector and alarm system.

2. Reaction setup and reaction condition optimization

2.1 Reaction setup

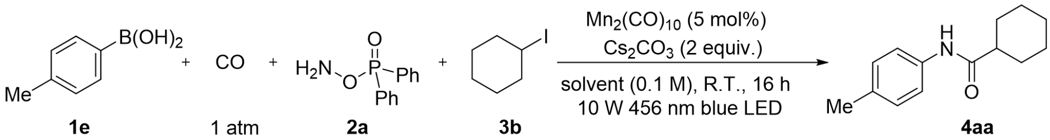
Up to 5 reactions can be performed simultaneously, one position being left empty as a temperature reference, while irradiation is partly indirect via reflection from the autoclave bottom:

Figure S1. Typical setup for the irradiation of five samples.

The top of the autoclave has a window made of quartz glass that allows radiation to reach the center. The arrangement of the reaction bottles inside the autoclave results in an even distribution of light, which is irradiated by the WattCas LED 440–445 nm for consistent reflection.

2.2 Reaction condition optimization

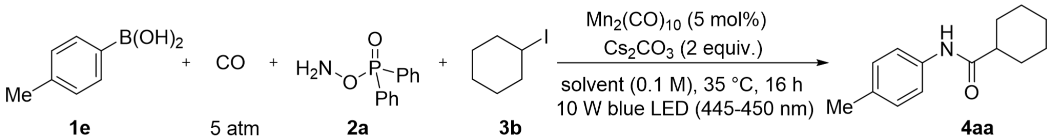
2.2.1 Initial experimental investigation under atmospheric pressure



entry	solvent	yield[a]
1	DCM	34%
2	Dioxane	40%
3	DMSO	trace
4	DMF	trace
5	CH_3CN	33%
6	2-MeTHF	55%
7	THF	44%
8	NMP	0%
9	EA	20%
10	DME	15%

Reaction conditions: boric acid **1e** (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (ballon), $Mn_2(CO)_{10}$ (5 mol%), base (2 equiv.), solvent (0.1 M), using a 10 W 456 nm blue LED as the light source, 35 ℃, 16 h. [a] Yields were determined by ^{1}H NMR analysis using dibromomethane as the internal standard.

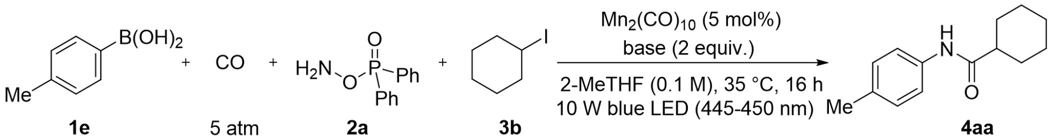
2.2.2 Evaluation of solvents



entry	solvent	yield[a]
1	2-MeTHF	88% (88%)[b]
2	THF	75%
3	CPME	54%
4	DME	37%
5	1,4-dioxane	70%

Reaction conditions, unless otherwise noted: boric acid **1e** (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (5 atm), $Mn_2(CO)_{10}$ (5 mol%), base (2 equiv.), solvent (0.1 M), using a 10 W blue LED (445-450 nm) lamp as the visible light source, 35 ℃, 16 h. [a] Yields were determined by analysis of the crude ^{1}H NMR spectra using 1,3-benzodioxole as an internal standard. [b] Isolated yields.

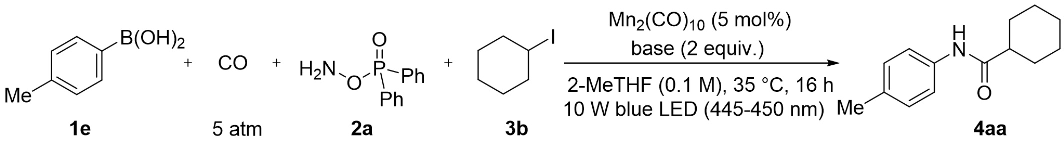
2.2.3 Bases screening

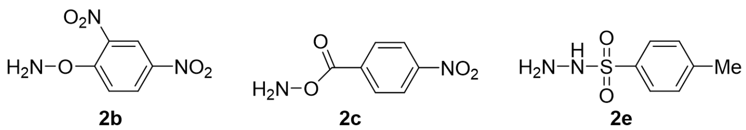


entry	base	yield[a]
1	Cs_2CO_3	88% (88%)[b]
2	K_3PO_4	45%
3	$K_3PO_4 \cdot H_2O$	65%
4	Na_2CO_3	N.D.
5	K_2CO_3	N.D.
6	$CsOH \cdot H_2O$	44%
7	CsF	N.D.
8	CsOAc	10%
9	*t*-BuONa	28%
10	LiOMe	8%

Reaction conditions, unless otherwise noted: boric acid **1e** (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (5 atm), $Mn_2(CO)_{10}$ (5 mol%), base (2 equiv.), solvent (0.1 M), using a 10 W blue LED (445-450 nm) lamp as the visible light source, 35 °C, 16 h. [a] Yields were determined by analysis of the crude ^1H NMR spectra using 1,3-benzodioxole as an internal standard. [b] Isolated yields.

2.2.3 Evaluation of aminating agents

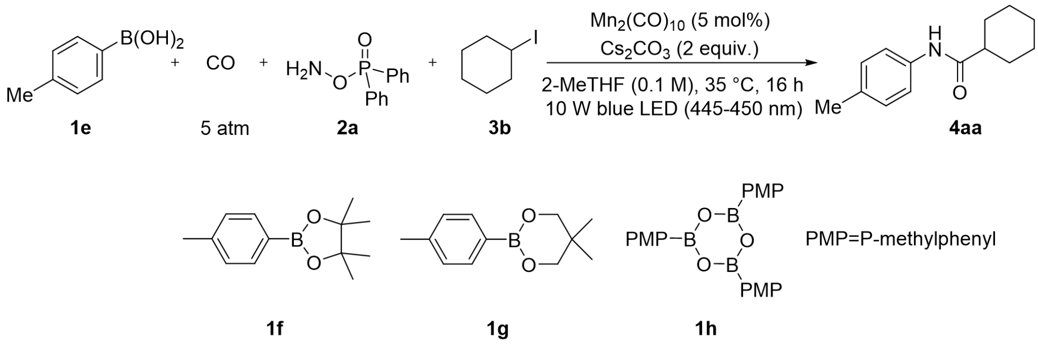




entry	aminating agents	yield[a]
1	**2a**	88%
2	**2b**	N.D.
3	**2c**	30%
4	**2e**	15%

Reaction conditions, unless otherwise noted: boric acid **1e** (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (5 atm), $Mn_2(CO)_{10}$ (5 mol%), base (2 equiv.), solvent (0.1 M), using a 10 W blue LED (445-450 nm) lamp as the visible light source, 35 °C, 16 h. Yields were determined by analysis of the crude ^1H NMR spectra using 1,3-benzodioxole as an internal standard.

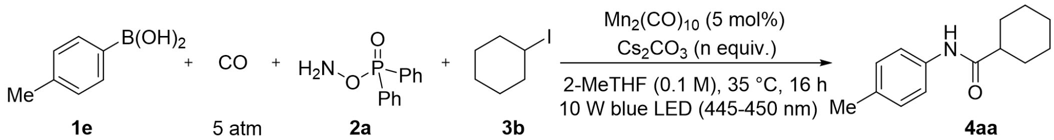
2.2.4 Evaluation of arylboronic acid and esters



entry	boronic agent	yield
1	**1e**	88%
2	**1f**	30%
3	**1g**	19%
4	**1h**[a]	78%

Reaction conditions, unless otherwise noted: boronic agent (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (5 atm), $Mn_2(CO)_{10}$ (5 mol%), base (2 equiv.), solvent (0.1 M), using a 10 W blue LED (445-450 nm) lamp as the visible light source, 35 °C, 16 h. Isolated yields. [a] *p*-tolueneboronic anhydride added 0.05 mmol.

2.2.5 Effect of base loading on the reaction

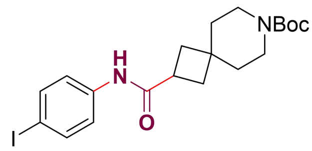


entry	equivalent of Cs_2CO_3	yield[a]
1	1	54%
2	2	88%
3	3	86%
4	4	72%
5	5	74%

Reaction conditions, unless otherwise noted: boric acid **1e** (0.2 mmol), aminating agent **2a** (0.15 mmol), iodide **3b** (0.1 mmol), CO (5 atm), $Mn_2(CO)_{10}$ (5 mol%), Cs_2CO_3 (n equiv.), solvent (0.1 M), using a 10 W blue LED (445-450 nm) lamp as the visible light source, 35 °C, 16 h. [a] Yields were determined by analysis of the crude ^1H NMR spectra using 1,3-benzodioxole as an internal standard.

3. General procedure for the FGC strategy for amide synthesis

To a 20 mL quartz tube equipped with a magnetic stir bar was added alkyl iodides (1.0 equiv., 0.2 mmol), $Mn_2(CO)_{10}$ (5 mol%, 0.01 mmol, 3.9 mg), *O*-diphenylphosphinyl hydroxylamine (DPPH) (1.5 equiv., 0.3 mmol, 70.0 mg), boronic acid (2.0 equiv., 0.4 mmol), Cs_2CO_3 (2.0 equiv., 0.4 mmol, 130.3 mg), and 2-MeTHF (0.1 M, 2 mL), which was then sealed with a rubber septum and connected to the atmosphere via a needle. The quartz tubes were arranged in a revolver-like manner, accommodating exactly 5 quartz tubes and 1 temperature reference tube (**Figure S1**), and transferred into a 500 mL mild-pressure parallel photoreactor (WP-MSAR-500PC) manufactured by WattCas Instruments. The sealed reactor was flushed with carbon monoxide (5 atm) three times, then charged with 5 atm of CO (monitored by a pressure gauge). The mixture was stirred at 700 rpm at 35 °C and irradiated with a 10 W blue LED (445–450 nm) for 16 h. Upon completion, the light was switched off, and the reaction mixture was concentrated under reduced pressure. Purification by silica gel column chromatography (PE/EA) afforded the desired amide products.



Chemical Formula: $C_{20}H_{27}IN_2O_3$
Molecular Weight: 470.35

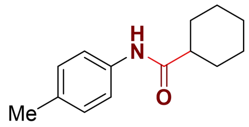
***tert*-butyl 2-((4-iodophenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (4a)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4a** (77.2 mg, 82% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.60 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.26 (br, 1H), 3.40 – 3.32 (m, 2H), 3.30 – 3.24 (m, 2H), 3.07 (p, *J* = 8.7 Hz, 1H), 2.20 – 2.11 (m, 2H), 2.09 – 2.02 (m, 2H), 1.61 – 1.50 (m, 4H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.35, 154.93, 121.45, 87.15, 79.42, 40.62, 37.98, 34.50, 34.07, 28.42.

HRMS for $C_{14}H_{19}NO$ (ESI) $[M+Na]^+$ calc.: 493.0959, found: 493.0962.



Chemical Formula: $C_{14}H_{19}NO$
Molecular Weight: 217.31

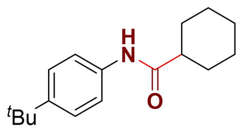
***N*-(*p*-tolyl)cyclohexanecarboxamide (4aa)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4aa** (38.3 mg, 88% yield) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.40 (d, J = 8.4 Hz, 2H), 7.27 (br, 1H), 7.10 (d, J = 8.1 Hz, 2H), 2.30 (s, 3H), 2.21 (tt, J = 11.7, 3.5 Hz, 1H), 1.96 – 1.92 (m, 2H), 1.87 – 1.77 (m, 2H), 1.72 – 1.66 (m, 1H), 1.58 – 1.48 (m, 2H), 1.33 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.31, 135.49, 133.60, 129.37, 119.82, 46.43, 29.63, 25.63, 20.80.

HRMS for $C_{14}H_{19}NO$ (ESI) $[M+H]^+$ calc.: 218.1539, found: 218.1539.



Chemical Formula: $C_{17}H_{25}NO$
Molecular Weight: 259.39

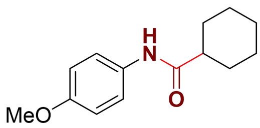
***N*-(4-(*tert*-butyl)phenyl)cyclohexanecarboxamide (4ab)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ab** (46.7 mg, 90% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.45 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.25 (br, 1H), 2.22 (tt, J = 11.9, 3.5 Hz, 1H), 1.99 – 1.90 (m, 2H), 1.87 – 1.78 (m, 2H), 1.73 – 1.67 (m, 1H), 1.59 – 1.49 (m, 2H), 1.29 (s, 9H), 1.35 – 1.20 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 174.30, 146.97, 135.44, 125.71, 119.51, 46.45, 34.30, 31.32, 29.64, 25.64.

HRMS for $C_{17}H_{25}NO$ (ESI) $[M+Na]^+$ calc.: 282.1828, found: 282.1827.



Chemical Formula: $C_{14}H_{19}NO_2$
Molecular Weight: 233.31

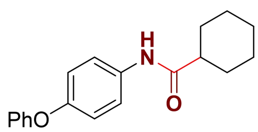
_N_-(4-methoxyphenyl)cyclohexanecarboxamide (4ac)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ac** (42.9 mg, 92% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.41 (d, *J* = 9.0 Hz, 1H), 7.07 (br, 1H), 6.85 (d, *J* = 8.9 Hz, 1H), 3.78 (s, 3H), 2.20 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.97 – 1.94 (m, 2H), 1.85 – 1.81 (m, 2H), 1.72 – 1.68 (m, 1H), 1.58 – 1.50 (m, 2H), 1.36 – 1.21 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 174.16, 156.24, 131.17, 121.62, 114.08, 55.47, 46.37, 29.69, 25.68.

HRMS for $C_{14}H_{19}NO_2$ (ESI) $[M+H]^+$ calc.: 234.1489, found: 234.1485.



Chemical Formula: $C_{19}H_{21}NO_2$
Molecular Weight: 295.38

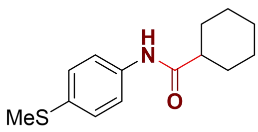
_N_-(4-phenoxyphenyl)cyclohexanecarboxamide (4ad)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ad** (47.3 mg, 80% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.49 (d, *J* = 8.6 Hz, 2H), 7.39 (br, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 7.8 Hz, 1H), 7.00 – 6.93 (m, 4H), 2.23 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.01 – 1.89 (m, 2H), 1.88 – 1.77 (m, 2H), 1.74 – 1.66 (m, 1H), 1.59 – 1.49 (m, 2H), 1.34 – 1.23 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 174.42, 157.57, 153.15, 133.62, 129.66, 122.94, 121.52, 119.61, 118.26, 46.36, 29.62, 25.62.

HRMS for $C_{19}H_{21}NO_2$ (ESI) $[M+Na]^+$ calc.: 318.1464, found: 318.1469.



Chemical Formula: $C_{14}H_{19}NOS$
Molecular Weight: 249.37

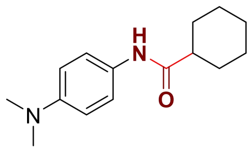
N-(4-(methylthio)phenyl)cyclohexanecarboxamide (4ae)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ae** (27.4 mg, 55% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.46 (d, J = 8.4 Hz, 2H), 7.24 – 7.17 (m, 3H), 2.45 (s, 3H), 2.21 (tt, J = 11.7, 3.5 Hz, 1H), 1.96 – 1.93 (m, 2H), 1.88 – 1.78 (m, 2H), 1.74 – 1.67 (m, 1H), 1.57 – 1.49 (m, 2H), 1.36 – 1.27 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.29, 135.77, 133.24, 128.09, 120.38, 46.50, 29.64, 25.64, 16.79.

HRMS for $C_{14}H_{19}NOS$ (ESI) $[M+Na]^+$ calc.: 272.1080, found: 272.1080.



Chemical Formula: $C_{15}H_{22}N_2O$
Molecular Weight: 246.35

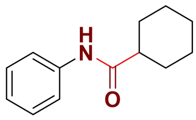
N-(4-(dimethylamino)phenyl)cyclohexanecarboxamide (4af)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4af** (19.7 mg, 40% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.36 (d, J = 9.0 Hz, 2H), 7.19 (br, 1H), 6.69 (d, J = 9.0 Hz, 2H), 2.90 (s, 6H), 2.19 (tt, J = 11.8, 3.5 Hz, 1H), 1.97 – 1.90 (m, 2H), 1.85 – 1.78 (m, 2H), 1.72 – 1.65 (m, 1H), 1.58 – 1.48 (m, 2H), 1.34 – 1.24 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.18, 147.69, 128.39, 121.70, 113.31, 46.32, 41.14, 29.76, 25.75.

HRMS for $C_{15}H_{22}N_2O$ (ESI) $[M+Na]^+$ calc.: 269.1624, found: 269.1633.



Chemical Formula: $C_{13}H_{17}NO$
Molecular Weight: 203.29

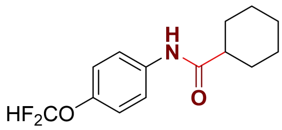
***N*-phenylcyclohexanecarboxamide (4ag)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ag** (33.4 mg, 82% yield) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.53 (d, *J* = 8.0 Hz, 2H), 7.43 (br, 1H), 7.33 – 7.25 (m, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 2.23 (tt, *J* = 11.8, 3.6 Hz, 1H), 1.97 – 1.92 (m, 1H), 1.86 – 1.77 (m, 1H), 1.71 – 1.68 (m, 1H), 1.59 – 1.49 (m, 2H), 1.36 – 1.20 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 174.52, 138.10, 128.88, 124.01, 119.79, 46.45, 29.61, 25.61.

HRMS for $C_{13}H_{17}NO$ (ESI) $[M+H]^+$ calc.: 204.1383, found: 204.1385.



Chemical Formula: $C_{14}H_{17}F_2NO_2$
Molecular Weight: 269.29

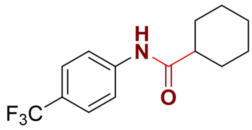
***N*-(4-(difluoromethoxy)phenyl)cyclohexanecarboxamide (4ah)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ah** (29.1 mg, 54% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.52 (d, *J* = 8.6 Hz, 2H), 7.22 (brf, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.45 (t, *J* = 74.0 Hz, 1H), 2.22 (tt, *J* = 12.0, 3.5 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.88 – 1.79 (m, 2H), 1.74 – 1.67 (m, 1H), 1.59 – 1.49 (m, 2H), 1.36 – 1.25 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.33, 147.11, 135.54, 121.11, 120.40, 115.97 (t, $J_{C\text{–}F}$ = 259.9 Hz), 46.45, 29.62, 25.62.

HRMS for $C_{14}H_{17}F_2NO_2$ (ESI) $[M+H]^+$ calc.: 270.1300, found: 270.1309.



Chemical Formula: $C_{14}H_{16}F_3NO$
Molecular Weight: 271.28

***N*-(4-(trifluoromethyl)phenyl)cyclohexanecarboxamide (4ai)**

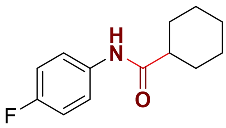
The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ai** (26.5 mg, 49% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.66 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.45 (br, 1H), 2.25 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.99 – 1.91 (m, 2H), 1.88 – 1.80 (m, 2H), 1.73 – 1.68 (m, 1H), 1.60 – 1.48 (m, 2H), 1.33 – 1.25 (m, 3H).

^{19}F NMR (471 MHz, $CDCl_3$): δ/ppm = –62.08.

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.75, 141.11, 126.19 (q, $J_{C–F}$ = 3.8 Hz), δ 125.78 (q, $J_{C–F}$ = 24.8 Hz), 124.05 (q, $J_{C–F}$ = 271.4 Hz), 119.26, 46.54, 29.55, 25.54.

HRMS for $C_{14}H_{16}F_3NO$ (ESI) $[M+H]^+$ calc.: 272.1257, found: 272.1264.



Chemical Formula: $C_{13}H_{16}FNO$
Molecular Weight: 221.28

***N*-(4-fluorophenyl)cyclohexanecarboxamide (4aj)**

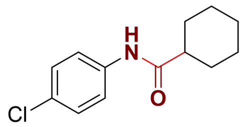
The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4aj** (30.1 mg, 68% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.59 – 7.40 (m, 3H), 6.98 (m, 2H), 2.22 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.96 – 1.90 (m, 2H), 1.87 – 1.76 (m, 2H), 1.72 – 1.66 (m, 1H), 1.58 – 1.48 (m, 2H), 1.35 – 1.21 (m, 3H).

^{19}F NMR (471 MHz, $CDCl_3$): δ/ppm = -118.34.

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.57, 159.16 (d, $J_{C–F}$ = 243.3 Hz), 134.06 (d, $J_{C–F}$ = 2.9 Hz), 121.65 (d, $J_{C–F}$ = 7.8 Hz), 115.45 (d, $J_{C–F}$ = 22.3 Hz), 46.28, 29.58, 25.58.

HRMS for $C_{13}H_{16}FNO$ (ESI) $[M+H]^+$ calc.: 222.1289, found: 222.1296.



Chemical Formula: $C_{13}H_{16}ClNO$
Molecular Weight: 237.73

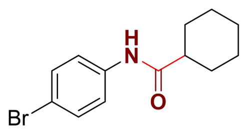
***N*-(4-chlorophenyl)cyclohexanecarboxamide (4ak)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ak** (30.9 mg, 65% yield) as white solid.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ/ppm = 7.48 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 5.9 Hz, 2H), 7.19 (br, 1H), 2.23 (tt, *J* = 11.7, 3.6 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.90 – 1.80 (m, 2H), 1.76 – 1.67 (m, 1H), 1.59 – 1.48 (m, 2H), 1.37 – 1.27 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.38, 136.61, 128.99, 128.93, 120.96, 46.50, 29.60, 25.60.

HRMS for $C_{13}H_{16}ClNO$ (ESI) $[M+H]^+$ calc.: 238.0993, found: 238.1002.



Chemical Formula: $C_{13}H_{16}BrNO$
Molecular Weight: 282.18

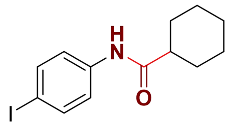
***N*-(4-bromophenyl)cyclohexanecarboxamide (4al)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4al** (40.1 mg, 71% yield) as white solid.

^{1}**H NMR** (400 MHz, $CDCl_3$): δ/ppm = 7.50 – 7.35 (m, 4H), 7.30 (br, 1H), 2.22 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.00 – 1.89 (m, 2H), 1.88 – 1.77 (m, 2H), 1.75 – 1.63 (m, 1H), 1.59 – 1.46 (m, 2H), 1.37 – 1.24 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.45, 137.12, 131.85, 121.29, 116.55, 46.48, 29.57, 25.58.

HRMS for $C_{13}H_{16}BrNO$ (ESI) $[M+H]^+$ calc.: 282.0488, found: 282.0488.



Chemical Formula: $C_{13}H_{16}INO$
Molecular Weight: 329.18

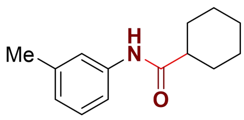
***N*-(4-iodophenyl)cyclohexanecarboxamide (4am)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4am** (54.0 mg, 82% yield) as white solid.

^{1}**H NMR** (500 MHz, $CDCl_3$): δ/ppm = 7.60 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.19 (br, 1H), 2.21 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.99 – 1.90 (m, 2H), 1.87 – 1.77 (m, 2H), 1.74 – 1.66 (m, 1H), 1.57 – 1.47 (m, 2H), 1.36 – 1.25 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.40, 137.82, 121.54, 46.54, 29.56, 25.58.

HRMS for $C_{13}H_{16}INO$ (ESI) $[M+H]^+$ calc.: 330.0349, found: 330.0358.



Chemical Formula: $C_{14}H_{19}NO$
Molecular Weight: 217.31

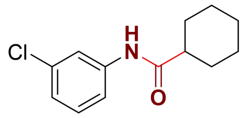
***N*-(m-tolyl)cyclohexanecarboxamide (4an)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4an** (30.4 mg, 70% yield) as white solid.

^{1}**H NMR** (500 MHz, $CDCl_3$): δ/ppm = 7.42 (s, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 7.22 (br, 1H), 7.21 – 7.15 (m, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 2.32 (s, 3H), 2.22 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.98 – 1.90 (m, 2H), 1.88 – 1.78 (m, 2H), 1.73 – 1.66 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.22 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.35, 138.85, 138.00, 128.72, 124.83, 120.42, 116.77, 46.53, 29.65, 25.66, 25.64, 21.43.

HRMS for $C_{14}H_{19}NO$ (ESI) $[M+H]^+$ calc.: 218.1539, found: 218.1545.



Chemical Formula: $C_{13}H_{16}ClNO$
Molecular Weight: 237.73

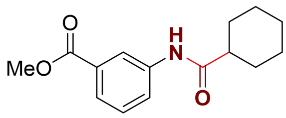
***N*-(3-chlorophenyl)cyclohexanecarboxamide (4ao)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ao** (28.6 mg, 60% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.67 (s, 1H), 7.38 – 7.33 (m, 1H), 7.28 (s, 1H), 7.21 (t, *J* = 8.1 Hz, 1H), 7.10 – 7.03 (m, 1H), 2.22 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.98 – 1.90 (m, 2H), 1.88 – 1.78 (m, 2H), 1.73 – 1.66 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.50, 139.16, 134.58, 129.90, 124.08, 119.81, 117.60, 46.48, 29.56, 25.56.

HRMS for $C_{13}H_{16}ClNO$ (ESI) $[M+H]^+$ calc.: 238.0993, found: 238.1009.



Chemical Formula: $C_{15}H_{19}NO_3$
Molecular Weight: 261.32

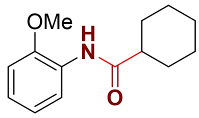
methyl 3-(cyclohexanecarboxamido)benzoate (4ap)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ap** (26.2 mg, 50% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.05 (s, 1H), 7.91 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.47 (br, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 3.89 (s, 3H), 2.25 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.89 – 1.79 (m, 2H), 1.73 – 1.66 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.64, 166.75, 138.29, 130.73, 129.09, 125.07, 124.28, 120.56, 52.20, 46.42, 29.57, 25.58.

HRMS for $C_{15}H_{19}NO_3$ (ESI) $[M+Na]^+$ calc.: 284.1257, found: 284.1265.



Chemical Formula: $C_{14}H_{19}NO_2$
Molecular Weight: 233.31

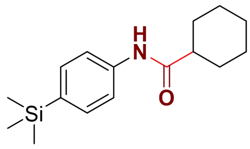
***N*-(2-methoxyphenyl)cyclohexanecarboxamide (4aq)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4aq** (23.8 mg, 51% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.41 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.82 (br, 1H), 7.02 (td, *J* = 7.8, 1.7 Hz, 1H), 6.95 (td, *J* = 7.8, 1.4 Hz, 1H), 6.87 (dd, *J* = 8.1, 1.4 Hz, 1H), 3.89 (s, 3H), 2.27 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.01 – 1.94 (m, 2H), 1.89 – 1.79 (m, 2H), 1.74 – 1.68 (m, 1H), 1.62 – 1.48 (m, 2H), 1.37 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.18, 147.71, 127.84, 123.30, 121.09, 119.65, 109.75, 55.65, 46.75, 29.68, 25.70, 25.68.

HRMS for $C_{14}H_{19}NO_2$ (ESI) $[M+Na]^+$ calc.: 256.1308, found: 256.1299.



Chemical Formula: $C_{16}H_{25}NOSi$
Molecular Weight: 275.47

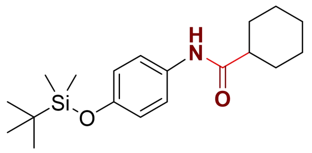
***N*-(4-(trimethylsilyl)phenyl)cyclohexanecarboxamide (4ar)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4ar** (24.3 mg, 44% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.52 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.22 (br, 1H), 2.22 (tt, *J* = 11.7, 3.3 Hz, 1H), 1.98 – 1.92 (m, 2H), 1.85 – 1.79 (m, 2H), 1.73 – 1.67 (m, 1H), 1.60 – 1.48 (m, 2H), 1.34 – 1.24 (m, 3H), 0.24 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.35, 138.59, 135.72, 134.07, 118.94, 46.57, 29.64, 25.64, –1.11.

HRMS for $C_{16}H_{25}NOSi$ (ESI) $[M+H]^+$ calc.: 276.1778, found: 276.1780.



Chemical Formula: $C_{19}H_{31}NO_2Si$
Molecular Weight: 333.55

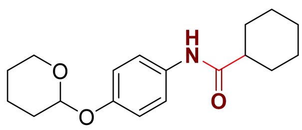
***N*-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)cyclohexanecarboxamide (4as)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4as** (50.7 mg, 76% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.36 (d, *J* = 8.9 Hz, 2H), 7.17 (br, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 2.20 (tt, *J* = 11.7, 3.6 Hz, 1H), 1.96 – 1.91 (m, 2H), 1.85 – 1.80 (m, 2H), 1.73 – 1.65 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.23 (m, 3H), 0.97 (s, 9H), 0.17 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.13, 152.11, 131.74, 121.35, 120.26, 46.39, 29.67, 25.67, 25.66, 18.17, -4.50.

HRMS for $C_{19}H_{31}NO_2Si$ (ESI) $[M+H]^+$ calc.: 334.2197, found: 334.2206.



Chemical Formula: $C_{18}H_{25}NO_3$
Molecular Weight: 303.40

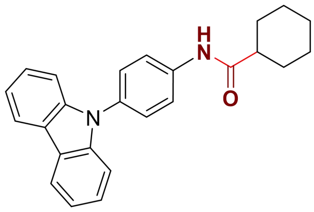
***N*-(4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)cyclohexanecarboxamide (4at)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4at** (48.0 mg, 79% yield) as white solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ/ppm = 9.65 (br, 1H), 7.49 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 5.36 (t, *J* = 3.5 Hz, 1H), 3.76 (dt, *J* = 11.5, 4.5 Hz, 1H), 3.52 (dt, *J* =F 11.5, 4.5 Hz, 1H), 2.28 (tt, *J* = 11.8, 3.4 Hz, 1H), 1.90 – 1.82 (m, 1H), 1.81 – 1.68 (m, 6H), 1.66 – 1.47 (m, 4H), 1.45 – 1.35 (m, 2H), 1.31 – 1.12 (m, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ/ppm = 173.85, 152.10, 133.61, 120.34, 116.60, 96.12, 61.50, 44.80, 29.95, 29.21, 25.45, 25.30, 24.76, 18.72.

HRMS for $C_{19}H_{31}NO_2Si$ (ESI) $[M+Na]^+$ calc.: 326.1727, found: 326.1733.



Chemical Formula: $C_{25}H_{24}N_2O$
Molecular Weight: 368.48

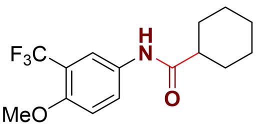
methyl 3-(cyclohexanecarboxamido)benzoate (4au)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4au** (48.0 mg, 60% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.14 (d, *J* = 7.8 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.34 (m, 5H), 7.28 (t, *J* = 7.5 Hz, 2H), 2.31 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.08 – 1.97 (m, 2H), 1.93 – 1.84 (m, 2H), 1.78 – 1.71 (m, 1H), 1.68 – 1.56 (m, 2H), 1.42 – 1.27 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 140.96, 137.25, 133.34, 127.75, 125.90, 123.23, 121.01, 120.25, 119.83, 109.64, 46.57, 29.68, 25.64.

HRMS for $C_{25}H_{24}N_2O$ (ESI) $[M+H]^+$ calc.: 369.1961, found: 369.1973.



Chemical Formula: $C_{15}H_{18}F_3NO_2$
Molecular Weight: 301.31

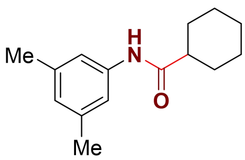
***N*-(4-methoxy-3-(trifluoromethyl)phenyl)cyclohexanecarboxamide (4av)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 20:1) to afford product **4av** (35.6 mg, 59% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.75 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.62 (d, *J* = 2.7 Hz, 1H), 7.26 (br, 1H), 6.94 (d, *J* = 9.0 Hz, 1H), 3.87 (s, 3H), 2.22 (tt, *J* = 11.7, 3.5 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.87 – 1.79 (m, 2H), 1.73 – 1.66 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.24 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.51, 153.93, 130.64, 125.13, δ 123.25 (q, $J_{C–F}$ = 272.5 Hz), 119.34 (q, $J_{C–F}$ = 5.4 Hz), 118.75 (q, $J_{C–F}$ = 31.0 Hz), 112.52, 56.20, 46.26, 29.61, 25.60.

HRMS for $C_{15}H_{18}F_3NO_2$ (ESI) $[M+H]^+$ calc.: 302.1362, found: 302.1369.



Chemical Formula: $C_{15}H_{21}NO$
Molecular Weight: 231.34

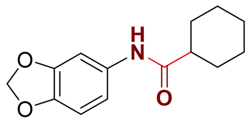
N-(3,5-dimethylphenyl)cyclohexanecarboxamide (4aw)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **4aw** (37.9 mg, 82% yield) as white solid.

^{1}**H NMR** (500 MHz, $CDCl_3$): δ/ppm = 7.17 (s, 3H), 6.73 (br, 1H), 2.28 (s, 6H), 2.20 (tt, J = 11.7, 3.4 Hz, 1H), 2.00 – 1.90 (m, 2H), 1.88 – 1.78 (m, 2H), 1.73 – 1.66 (m, 1H), 1.58 – 1.49 (m, 2H), 1.36 – 1.24 (m, 3H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.33, 138.61, 137.92, 125.74, 117.45, 46.53, 29.64, 25.66, 25.63, 21.31.

HRMS for $C_{15}H_{21}NO$ (ESI) $[M+H]^+$ calc.: 232.1696, found: 232.1704.



Chemical Formula: $C_{14}H_{17}NO_3$
Molecular Weight: 247.29

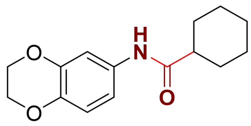
N-(benzo[*d*][1,3]dioxol-5-yl)cyclohexanecarboxamide (4ax)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 20:1) to afford product **4ax** (36.5 mg, 73% yield) as white solid.

^{1}**H NMR** (500 MHz, $CDCl_3$): δ/ppm = 7.38 (br, 1H), 7.23 (d, J = 2.1 Hz, 1H), 6.79 (dd, J = 8.4, 2.1 Hz, 1H), 6.70 (d, J = 8.3 Hz, 1H), 5.91 (s, 2H), 2.19 (tt, J = 11.8, 3.5 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.84 – 1.78 (m, 2H), 1.71 – 1.65 (m, 1H), 1.56 – 1.46 (m, 2H), 1.33 – 1.20 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.38, 147.65, 143.99, 132.31, 112.99, 107.90, 102.84, 101.13, 46.28, 29.59, 25.60.

HRMS for $C_{14}H_{17}NO_3$ (ESI) $[M+Na]^+$ calc.: 270.1101, found: 270.1113.



Chemical Formula: $C_{15}H_{19}NO_3$
Molecular Weight: 261.32

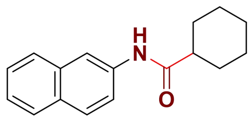
***N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)cyclohexanecarboxamide (4ay)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 20:1) to afford product **4ay** (41.9 mg, 80% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.26 (br, 1H), 7.16 (d, *J* = 2.6 Hz, 1H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 4.24 – 4.18 (m, 4H), 2.18 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.84 – 1.77 (m, 2H), 1.70 – 1.63 (m, 1H), 1.55 – 1.45 (m, 2H), 1.33 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.25, 143.34, 140.13, 131.78, 117.00, 113.44, 109.68, 64.35, 64.21, 46.30, 29.59, 25.61.

HRMS for $C_{15}H_{19}NO_3$ (ESI) $[M+Na]^+$ calc.: 284.1257, found: 284.1262.



Chemical Formula: $C_{17}H_{19}NO$
Molecular Weight: 253.35

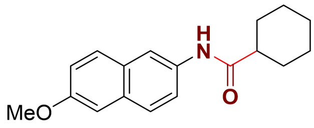
***N*-(naphthalen-2-yl)cyclohexanecarboxamide (4az)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4az** (35.5 mg, 70% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.24 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 3H), 7.50 – 7.28 (m, 4H), 2.29 (tt, *J* = 11.6, 3.5 Hz, 1H), 2.00 – 1.90 (m, 2H), 1.88 – 1.80 (m, 2H), 1.78 – 1.68 (m, 1H), 1.58 – 1.49 (m, 2H), 1.42 – 1.19 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.58, 135.46, 133.86, 130.51, 128.66, 127.61, 127.48, 126.44, 124.87, 119.81, 116.48, 46.61, 29.69, 25.65.

HRMS for $C_{17}H_{19}NO$ (ESI) $[M+Na]^+$ calc.: 276.1359, found: 276.1360.



Chemical Formula: $C_{18}H_{21}NO_2$
Molecular Weight: 283.37

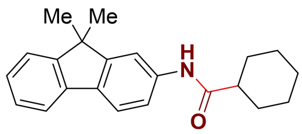
***N*-(6-methoxynaphthalen-2-yl)cyclohexanecarboxamide (4ba)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4ba** (43.7 mg, 77% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.14 (s, 1H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.43 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.32 (br, 1H), 7.12 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.08 (d, *J* = 2.6 Hz, 1H), 3.90 (s, 3H), 2.27 (tt, *J* = 11.7, 3.6 Hz, 1H), 2.04 – 1.94 (m, 2H), 1.91 – 1.80 (m, 2H), 1.74 – 1.70 (m, 1H), 1.62 – 1.54 (m, 2H), 1.39 – 1.26 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 157.02, 133.61, 131.55, 129.12, 129.07, 127.34, 120.40, 119.22, 116.84, 105.61, 55.26, 46.56, 29.70, 25.67.

HRMS for $C_{18}H_{21}NO_2$ (ESI) $[M+H]^+$ calc.: 284.1645, found: 284.1654.



Chemical Formula: $C_{22}H_{25}NO$
Molecular Weight: 319.45

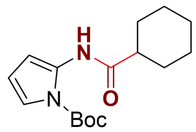
***N*-(9,9-dimethyl-9*H*-fluoren-2-yl)cyclohexanecarboxamide (4bb)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **4bb** (56.2 mg, 88% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.84 (d, *J* = 2.0 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.42 (br, 1H), 7.36 – 7.26 (m, 4H), 2.26 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.04 – 1.95 (m, 2H), 1.89 – 1.82 (m, 2H), 1.74 – 1.68 (m, 1H), 1.63 – 1.54 (m, 2H), 1.47 (s, 6H), 1.38 – 1.25 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 170.92, 162.27, 135.28, 133.91, 133.81, 129.41, 119.82, 119.30, 115.09, 103.56, 67.97, 37.34, 28.71, 25.58, 25.14, 20.80.

HRMS for $C_{22}H_{25}NO$ (ESI) $[M+H]^+$ calc.: 320.2009, found: 320.2011.



Chemical Formula: $C_{16}H_{24}N_2O_3$
Molecular Weight: 292.38

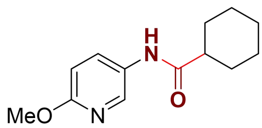
tert-butyl 2-(cyclohexanecarboxamido)-1_H_-pyrrole-1-carboxylate (4bc)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bc** (24.6 mg, 42% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 10.07 (br, 1H), 6.81 (dd, *J* = 3.7, 1.8 Hz, 1H), 6.68 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.11 (t, *J* = 3.6 Hz, 1H), 2.27 (tt, *J* = 11.9, 3.6 Hz, 1H), 2.01 – 1.94 (m, 2H), 1.86 – 1.79 (m, 2H), 1.72 – 1.66 (m, 1H), 1.61 (s, 9H), 1.56 – 1.45 (m, 2H), 1.35 – 1.23 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.33, 151.00, 130.77, 113.87, 110.89, 99.70, 84.92, 46.03, 29.55, 28.00, 25.72, 25.69.

HRMS for $C_{16}H_{24}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 315.1679, found: 315.1693.



Chemical Formula: $C_{13}H_{18}N_2O_2$
Molecular Weight: 234.30

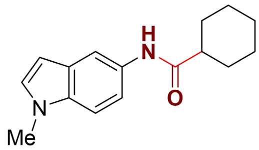
***N*-(6-methoxypyridin-3-yl)cyclohexanecarboxamide (4bd)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bd** (36.6 mg, 78% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.14 (d, *J* = 2.7 Hz, 1H), 7.93 (dd, *J* = 8.9, 2.7 Hz, 1H), 7.40 (br, 1H), 6.70 (d, *J* = 8.9 Hz, 1H), 3.89 (s, 3H), 2.23 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.98 – 1.89 (m, 2H), 1.86 – 1.76 (m, 2H), 1.74 – 1.65 (m, 1H), 1.57 – 1.47 (m, 2H), 1.34 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.78, 160.81, 138.31, 132.45, 128.78, 110.47, 53.59, 46.09, 29.59, 25.58.

HRMS for $C_{13}H_{18}N_2O_2$ (ESI) $[M+Na]^+$ calc.: 257.1260, found: 257.1266.



Chemical Formula: $C_{16}H_{20}N_2O$
Molecular Weight: 256.35

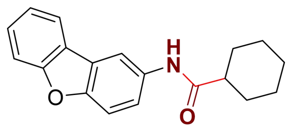
***N*-(1-methyl-1*H*-indol-5-yl)cyclohexanecarboxamide (4be)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4be** (30.8 mg, 60% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.82 (d, *J* = 2.0 Hz, 1H), 7.35 (br, 1H), 7.28 – 7.19 (m, 2H), 7.01 (d, *J* = 3.0 Hz, 1H), 6.40 (d, *J* = 3.0 Hz, 1H), 3.74 (s, 3H), 2.23 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.01 – 1.93 (m, 2H), 1.87 – 1.80 (m, 2H), 1.73 – 1.67 (m, 1H), 1.61 – 1.51 (m, 2H), 1.35 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.30, 134.04, 130.28, 129.50, 128.40, 115.80, 112.58, 109.13, 100.88, 46.39, 32.86, 29.71, 25.69.

HRMS for $C_{16}H_{20}N_2O$ (ESI) $[M+Na]^+$ calc.: 279.1468, found: 279.1476.



Chemical Formula: $C_{19}H_{19}NO_2$
Molecular Weight: 293.37

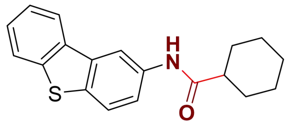
***N*-(dibenzo[*b,d*]furan-2-yl)cyclohexanecarboxamide (4bf)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bf** (30.5 mg, 52% yield) as white solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ/ppm = 9.97 (br, 1H), 8.47 (d, *J* = 2.1 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 2.37 (tt, *J* = 11.6, 3.5 Hz, 1H), 1.88 – 1.73 (m, 4H), 1.70 – 1.63 (m, 1H), 1.51 – 1.40 (m, 2H), 1.33 – 1.19 (m, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ/ppm = 174.19, 155.93, 151.40, 135.10, 127.56, 123.71, 123.37, 123.00, 120.97, 119.76, 111.67, 111.51, 111.33, 44.82, 29.19, 25.43, 25.26.

HRMS for $C_{19}H_{19}NO_2$ (ESI) $[M+H]^+$ calc.: 294.1489, found: 294.1496.



Chemical Formula: $C_{19}H_{19}NOS$
Molecular Weight: 309.43

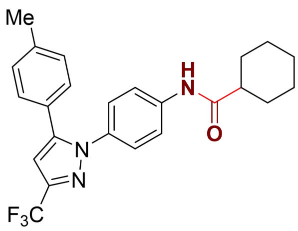
***N*-(dibenzo[*b,d*]thiophen-2-yl)cyclohexanecarboxamide (4bg)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bg** (38.9 mg, 63% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.57 (d, *J* = 2.2 Hz, 1H), 8.14 – 8.06 (m, 1H), 7.86 – 7.78 (m, 1H), 7.76 – 7.71 (m, 1H), 7.47 (br, 1H), 7.46 – 7.38 (m, 3H), 2.29 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.04 – 1.96 (m, 2H), 1.93 – 1.81 (m, 2H), 1.76 – 1.69 (m, 1H), 1.66 – 1.55 (m, 2H), 1.39 – 1.24 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.59, 140.10, 136.15, 135.33, 135.14, 134.67, 126.83, 124.29, 122.88, 122.77, 121.82, 119.36, 112.85, 46.57, 29.69, 25.65.

HRMS for $C_{19}H_{19}NOS$ (ESI) $[M+H]^+$ calc.: 310.1260, found: 310.1266.



Chemical Formula: $C_{24}H_{24}F_3N_3O$
Molecular Weight: 427.47

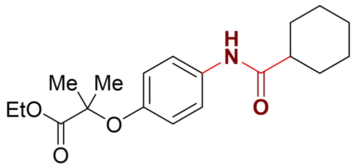
***N*-(4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)phenyl)cyclohexanecarboxamide (4bh)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bh** (53.1 mg, 62% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.52 (d, *J* = 8.8 Hz, 2H), 7.37 (br, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.14 – 7.06 (m, 4H), 6.70 (s, 1H), 2.34 (s, 3H), 2.22 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.98 – 1.90 (m, 2H), 1.86 – 1.80 (m, 2H), 1.72 – 1.67 (m, 1H), 1.58 – 1.47 (m, 2H), 1.36 – 1.25 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.62, 144.78, δ 142.93 (q, J_{C-F} = 38.0 Hz), 139.10, 138.20, 134.80, 129.40, 128.58, 126.02, 125.99, δ 121.28 (q, J_{C-F} = 268.9 Hz), 105.12 (d, *J* = 2.3 Hz), 46.44, 29.53, 25.56, 25.54, 21.23.

HRMS for $C_{24}H_{24}F_3N_3O$ (ESI) $[M+H]^+$ calc.: 428.1944, found:428.1948.



Chemical Formula: $C_{19}H_{27}NO_4$
Molecular Weight: 333.43

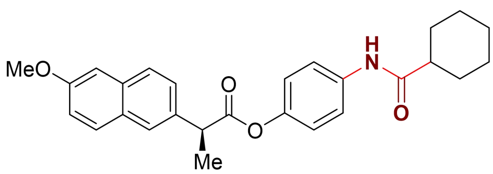
ethyl 2-(4-(cyclohexanecarboxamido)phenoxy)-2-methylpropanoate (4bi)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 20:1) to afford product **4bi** (56.1 mg, 84% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.38 (d, *J* = 9.0 Hz, 2H), 7.22 (br, 1H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.19 (tt, J = 11.8, 3.5 Hz, 1H), 1.96 – 1.89 (m, 2H), 1.85 – 1.77 (m, 2H), 1.71 – 1.66 (m, 1H), 1.55 – 1.46 (m, 2H), 1.32 – 1.22 (m, 3H), 1.26 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.24, 151.63, 132.77,120.86, 120.13, 79.42, 61.41, 46.38, 29.63, 25.63, 25.25, 14.06.

HRMS for $C_{24}H_{24}F_3N_3O$ (ESI) $[M+Na]^+$ calc.: 356.1832, found: 356.1834.



Chemical Formula: $C_{27}H_{29}NO_4$
Molecular Weight: 431.53

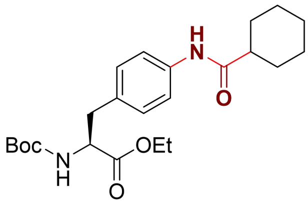
4-(cyclohexanecarboxamido)phenyl (*S*)-2-(6-methoxynaphthalen-2-yl)propanoate (4bj)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bj** (50.1 mg, 58% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.80 – 7.72 (m, 3H), 7.49 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.45 (d, *J* = 9.0 Hz, 2H), 7.34 (br, 1H), 7.19 – 7.11 (m, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 4.08 (q, *J* = 7.1 Hz, 1H), 3.92 (s, 3H), 2.17 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.94 – 1.87 (m, 2H), 1.85 – 1.77 (m, 2H), 1.71 – 1.66 (m, 1H), 1.68 (d, *J* = 7.1 Hz, 3H), 1.55 – 1.46 (m, 2H), 1.32 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.34, 173.40, 157.69, 146.69, 135.75, 135.03, 133.77, 129.28, 128.93, 127.35, 126.09, 126.04, 121.68, 120.55, 119.08, 105.55, 55.29, 46.34, 45.47, 29.54, 25.58, 18.48.

HRMS for $C_{27}H_{29}NO_4$ (ESI) $[M+Na]^+$ calc.: 454.1989, found: 454.1992.



Chemical Formula: $C_{23}H_{34}N_2O_5$
Molecular Weight: 418.53

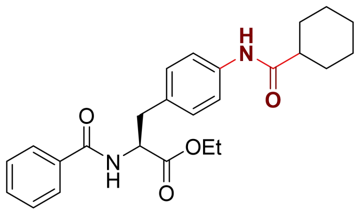
ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(cyclohexanecarboxamido)phenyl)-propanoate (4bk)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bk** (54.5 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.45 (d, *J* = 8.1 Hz, 2H), 7.17 (br, 1H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.98 – 4.92 (m, 1H), 4.55 – 4.47 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.10 – 2.99 (m, 2H), 2.21 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.98 – 1.92 (m, 2H), 1.88 – 1.80 (m, 2H), 1.72 – 1.67 (m, 1H), 1.59 – 1.48 (m, 2H), 1.42 (s, 1H), 1.37 – 1.27 (m, 3H), 1.24 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.28, 171.77, 155.09, 137.02, 131.69, 129.86, 119.74, 79.85, 61.35, 54.43, 46.52, 37.62, 29.63, 28.28, 25.64, 14.14.

HRMS for $C_{23}H_{34}N_2O_5$ (ESI) $[M+Na]^+$ calc.: 441.2360, found: 441.2366.



Chemical Formula: $C_{25}H_{30}N_2O_4$
Molecular Weight: 422.53

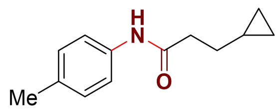
ethyl (*S*)-2-benzamido-3-(4-(cyclohexanecarboxamido)phenyl)propanoate (4bl)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 5:1:1) to afford product **4bl** (43.9 mg, 52% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.73 (d, *J* = 7.2 Hz, 2H), 7.54 – 7.38 (m, 5H), 7.31 (br, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.63 (d, *J* = 7.5 Hz, 1H), 5.03 (dt, *J* = 7.6, 5.5 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.30 – 3.09 (m, 1H), 2.21 (tt, *J* = 11.7, 3.6 Hz, 1H), 1.97 – 1.89 (m, 2H), 1.85 – 1.77 (m, 2H), 1.72 – 1.66 (m, 1H), 1.58 – 1.48 (m, 2H), 1.33 – 1.22 (m, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.38, 171.49, 166.84, 137.22, 133.86, 131.76, 131.42, 129.89, 128.61, 126.96, 119.75, 61.69, 53.55, 46.47, 37.26, 29.61, 29.59, 25.61, 14.16.

HRMS for $C_{25}H_{30}N_2O_4$ (ESI) $[M+Na]^+$ calc.: 445.2098, found: 445.2100.



Chemical Formula: $C_{13}H_{17}NO$
Molecular Weight: 203.29

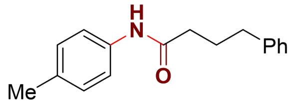
3-cyclopropyl-*N*-(*p*-tolyl)propanamide (5aa)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5aa** (26.4 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.39 (d, *J* = 8.5 Hz, 2H), 7.20 (br, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 2.43 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 1.63 (q, *J* = 7.3 Hz, 2H), 0.80 – 0.70(m, 1H), 0.49 – 0.41 (m, 2H), 0.13 – 0.06 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.18, 135.33, 133.78, 129.44, 119.86, 37.88, 30.68, 20.83, 10.55, 4.48.

HRMS for $C_{13}H_{17}NO$ (ESI) $[M+H]^+$ calc.: 204.1383, found: 204.1386.



Chemical Formula: $C_{17}H_{19}NO$
Molecular Weight: 253.35

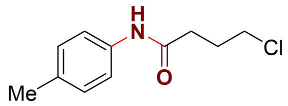
3-cyclopropyl-*N*-(*p*-tolyl)propanamide (5ab)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ab** (29.9 mg, 59% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.37 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.08 (br, 1H), 2.71 (t, J = 7.5 Hz, 2H), 2.36 – 2.32 (m, 2H), 2.31 (s, 3H), 2.07 (p, J = 7.5 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 170.80, 141.36, 135.26, 133.83, 129.45, 128.51, 128.42, 126.01, 119.87, 36.70, 35.04, 26.86, 20.82.

HRMS for $C_{17}H_{19}NO$ (ESI) $[M+H]^+$ calc.: 254.1539, found:254.1542.



Chemical Formula: $C_{11}H_{14}ClNO$
Molecular Weight: 211.69

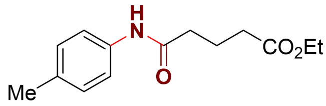
3-cyclopropyl-*N*-(*p*-tolyl)propanamide (5ac)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ac** (22.9 mg, 54% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.38 (d, J = 8.0 Hz, 2H), 7.30 (br, 1H), 7.12 (d, J = 8.1 Hz, 2H), 3.65 (t, J = 6.1 Hz, 2H), 2.54 (t, J = 7.1 Hz, 2H), 2.31 (s, 3H), 2.20 (p, J = 7.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.84, 135.06, 134.04, 129.47, 119.94, 77.00, 44.48, 34.04, 27.91, 20.83.

HRMS for $C_{11}H_{14}NO$ (ESI) $[M+H]^+$ calc.: 212.0837, found: 212.0842.



Chemical Formula: $C_{14}H_{19}NO_3$
Molecular Weight: 249.31

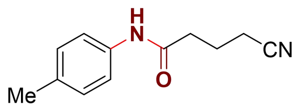
3-cyclopropyl-*N*-(*p*-tolyl)propanamide (5ad)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ad** (31.4 mg, 63% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.42 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.46 – 2.38 (m, 4H), 2.30 (s, 3H), 2.08 – 2.00 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.44, 170.40, 135.33, 133.86, 129.48, 119.87, 60.55, 36.42, 33.24, 20.88, 14.25.

HRMS for $C_{14}H_{19}NO_3$ (ESI) $[M+Na]^+$ calc.: 272.1257, found: 272.1267.



Chemical Formula: $C_{12}H_{14}N_2O$
Molecular Weight: 202.26

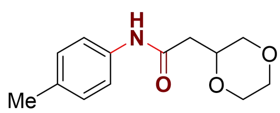
4-cyano-*N*-(*p*-tolyl)butanamide (5ae)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ae** (20.6 mg, 51% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.43 (br, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 2.56 – 2.50 (m, 4H), 2.31 (s, 3H), 2.07 (p, *J* = 6.9 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.04, 134.95, 134.18, 129.49, 119.98, 119.35, 77.00, 34.86, 20.87, 20.83, 16.56.

HRMS for $C_{12}H_{14}N_2O$ (ESI) $[M+H]^+$ calc.: 203.1179, found: 203.1185.



Chemical Formula: $C_{13}H_{17}NO_3$
Molecular Weight: 235.28

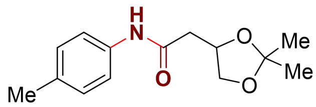
2-(1,4-dioxan-2-yl)-*N*-(*p*-tolyl)acetamide (5af)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5af** (27.3 mg, 58% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.08 (br, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 4.09 – 4.00 (m, 1H), 3.89 – 3.73 (m, 4H), 3.68 – 3.59 (m, 1H), 3.41 – 3.34 (m, 1H), 2.47 (dd, *J* = 15.3, 8.7 Hz, 1H), 2.38 (dd, *J* = 15.3, 3.3 Hz, 1H), 2.31 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 168.01, 135.25, 133.86, 129.42, 119.93, 72.39, 70.33, 66.88, 66.25, 39.74, 20.84.

HRMS for $C_{13}H_{17}NO_3$ (ESI) $[M+Na]^+$ calc.: 258.1101, found: 258.1104.



Chemical Formula: $C_{14}H_{19}NO_3$
Molecular Weight: 249.31

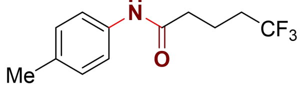
2-(2,2-dimethyl-1,3-dioxolan-4-yl)-*N*-(*p*-tolyl)acetamide (5ag)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ag** (31.9 mg, 64% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.01 (br, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 4.54 – 4.46 (m, 1H), 4.17 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.68 (dd, *J* = 8.4, 6.9 Hz, 1H), 2.69 – 2.59 (m, 2H), 2.31 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 168.04, 135.17, 133.90, 129.42, 119.93, 109.57, 72.39, 68.98, 41.32, 26.92, 25.52, 20.82.

HRMS for C_{14}H19NO_3 (ESI) $[M+Na]^+$ calc.: 272.1257, found: 272.1268.



Chemical Formula: $C_{12}H_{14}F_3NO$
Molecular Weight: 245.25

5,5,5-trifluoro-*N*-(*p*-tolyl)pentanamide (5ah)

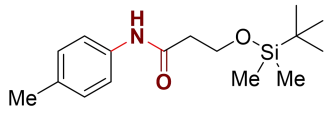
The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ah** (26.9 mg, 55% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.36 (d, J = 8.5 Hz, 2H), 7.31 (br, 1H), 7.11 (d, J = 8.1 Hz, 2H), 2.42 (t, J = 7.3 Hz, 2H), 2.31 (s, 3H), 2.25 – 2.15 (m, 2H), 2.02 – 1.94 (m, 2H).

^{19}F NMR (471 MHz, $CDCl_3$): δ/ppm = -66.02 (t, J = 10.9 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.73, 135.01, 134.23, 129.54, 127.02 (q, J_{C-F} = 276.4 Hz), 120.09, 35.59, 32.88 (q, J_{C-F} = 28.7 Hz), 20.87, 17.86 (q, J_{C-F} = 3.2 Hz).

HRMS for $C_{12}H_{14}F_3NO$ (ESI) $[M+H]^+$ calc.: 246.1100, found: 246.1111.



Chemical Formula: $C_{16}H_{27}NO_2Si$
Molecular Weight: 293.48

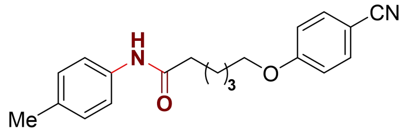
3-((*tert*-butyldimethylsilyl)oxy)-*N*-(*p*-tolyl)propanamide (5ai)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ai** (32.9 mg, 56% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.45 (br, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 3.96 (t, J = 5.5 Hz, 2H), 2.57 (t, J = 5.5 Hz, 2H), 2.31 (s, 3H), 0.94 (s, 9H), 0.13 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 170.12, 133.51, 129.42, 119.76, 59.58, 40.39, 25.83, 20.82, 18.13, -5.48.

HRMS for $C_{16}H_{17}NO_2Si$ (ESI) $[M+Na]^+$ calc.: 316.1703, found: 316.1706.



Chemical Formula: $C_{20}H_{22}N_2O_2$
Molecular Weight: 322.41

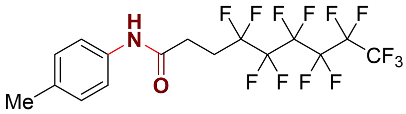
6-(4-cyanophenoxy)-*N*-(*p*-tolyl)hexanamide (5aj)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5aj** (50.9 mg, 79% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.55 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.32 (br, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 3.99 (t, J = 6.4 Hz, 2H), 2.37 (t, J = 7.4 Hz, 2H), 2.30 (s, 3H), 1.88 – 1.76 (m, 4H), 1.59 – 1.50 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.34, 154.69, 153.55, 138.78, 137.39, 135.19, 126.92, 126.71, 122.52, 120.26, 119.53, 118.43, 114.39, 46.96, 46.61, 29.68, 27.07, 25.66.

HRMS for $C_{20}H_{22}N_2O_2$ (ESI) $[M+Na]^+$ calc.: 345.1573, found: 345.1579.



Chemical Formula: $C_{16}H_{12}F_{13}NO$
Molecular Weight: 481.26

4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-*N*-(*p*-tolyl)nonanamide (5ak)

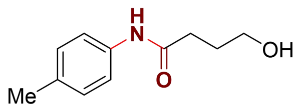
The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 25:1) to afford product **5ak** (51.9 mg, 54% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.35 (d, J = 8.4 Hz, 2H), 7.31 (br, 1H), 7.12 (d, J = 8.1 Hz, 2H), 2.69 – 2.51 (m, 4H), 2.31 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm -80.81 (t, J = 9.9 Hz), -114.38 – -114.58 (m), -121.80 – -121.99 (m), -122.88 (dt, J = 10.0, 5.7 Hz), -123.49 (dp, J = 11.6, 4.5, 3.9 Hz), -126.04 – -126.24 (m).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm =168.04, 134.62 (d, $J_{C–F}$ = 34.5 Hz), 129.54, 120.26, 118.72 – 117.57 (m), 116.09 (td, $J_{C–F}$ = 33.2, 17.0 Hz), 111.38 – 110.06 (m), 109.28 – 107.81 (m), 107.25 – 106.02 (m), 27.92 (t, $J_{C–F}$ = 3.7 Hz), 26.65 (t, $J_{C–F}$ = 21.9 Hz), 20.80.

HRMS for $C_{16}H_{12}F_{13}NO$ (ESI) $[M+H]^+$ calc.: 482.0784, found: 482.0794.



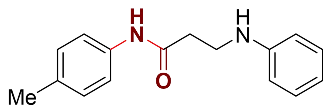
4-hydroxy-*N*-(*p*-tolyl)butanamide (5al)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (DCM/MeOH = 100:1) to afford product **5al** (17.1 mg, 44% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.60 (br, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.75 (t, *J* = 5.7 Hz, 2H), 2.68 (br, 1H), 2.52 (t, *J* = 6.8 Hz, 2H), 2.30 (s, 3H), 1.96 (p, *J* = 6.2 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.60, 135.19, 134.01, 129.46, 120.05, 62.24, 34.76, 27.92, 20.83.

HRMS for $C_{11}H_{15}NO_2$ (ESI) $[M+Na]^+$ calc.: 216.0995, found: 216.0996.



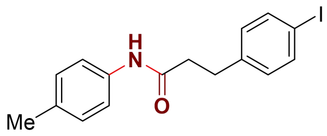
3-(phenylamino)-*N*-(*p*-tolyl)propenamide (5am)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5am** (32.1 mg, 63% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.72 (br, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.23 – 7.18 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 2H), 3.53 (t, *J* = 6.0 Hz, 2H), 2.63 (t, *J* = 6.0 Hz, 2H), 2.31 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.84, 147.33, 135.03, 134.03, 129.44, 129.37, 120.03, 118.30, 113.57, 40.22, 36.41, 20.83.

HRMS for $C_{16}H_{18}N_2O$ (ESI) $[M+Na]^+$ calc.: 277.1311, found: 277.1313.



Chemical Formula: $C_{16}H_{16}INO$
Molecular Weight: 365.21

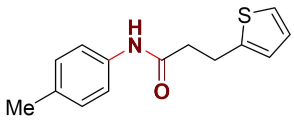
3-(4-iodophenyl)-*N*-(*p*-tolyl)propenamide (5an)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5an** (38.0 mg, 52% yield) as white solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ/ppm = 9.81 (br, 1H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.10 – 7.05 (m, 4H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.6 Hz, 2H), 2.23 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ/ppm = 170.34, 141.55, 137.47, 137.14, 132.36, 131.29, 129.52, 119.52, 92.03, 38.01, 30.73, 20.91.

HRMS for $C_{16}H_{16}INO$ (ESI) $[M+H]^+$ calc.: 366.0349, found: 366.0350.



Chemical Formula: $C_{14}H_{15}NOS$
Molecular Weight: 245.34

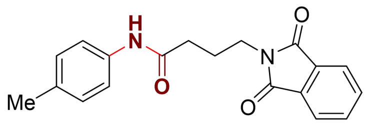
3-(thiophen-2-yl)-*N*-(*p*-tolyl)propanamide (5ao)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ao** (27.5 mg, 56% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.33 (d, *J* = 8.4 Hz, 2H), 7.16 (br, 1H), 7.14 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 6.92 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.87 – 6.83 (m, 1H), 3.26 (t, *J* = 7.4 Hz, 2H), 2.69 (t, *J* = 7.4 Hz, 2H), 2.30 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.67, 143.16, 135.04, 134.00, 129.43, 126.95, 124.95, 123.62, 120.03, 39.52, 25.69, 20.84.

HRMS for $C_{14}H_{15}NOS$ (ESI) $[M+Na]^+$ calc.: 268.0767, found: 268.0777.



Chemical Formula: $C_{19}H_{18}N_2O_3$
Molecular Weight: 322.36

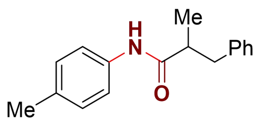
4-(1,3-dioxoisoindolin-2-yl)-*N*-(*p*-tolyl)butanamide (5ap)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ap** (28.4 mg, 44% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.04 (br, 1H), 7.84 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 3.84 – 3.77 (m, 2H), 2.35 (t, *J* = 6.8 Hz, 2H), 2.30 (s, 3H), 2.11 (p, *J* = 6.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 168.92, 135.47, 134.13, 133.65, 131.87, 129.36, 123.35, 119.72, 37.07, 34.85, 25.31, 20.84.

HRMS for $C_{19}H_{18}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 345.1210, found: 345.1219.



Chemical Formula: $C_{17}H_{19}NO$
Molecular Weight: 253.35

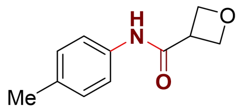
2-methyl-3-phenyl-*N*-(*p*-tolyl)propanamide (5aq)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ap** (41.0 mg, 81% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.30 – 7.19 (m, 7H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.93 (br, 1H), 3.03 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.76 (dd, *J* = 13.5, 6.3 Hz, 1H), 2.63 – 2.53 (m, 1H), 2.29 (s, 3H), 1.27 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.76, 139.68, 135.03, 133.82, 129.31, 128.93, 128.49, 126.38, 120.11, 44.72, 40.57, 20.81, 17.72.

HRMS for $C_{17}H_{19}NO$ (ESI) $[M+H]^+$ calc.: 254.1539, found: 254.1540.



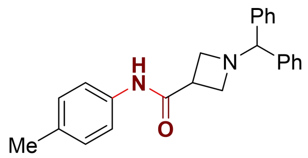
_N_-(_p_-tolyl)oxetane-3-carboxamide (5ar)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ar** (24.9 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.53 (br, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 4.95 (t, J = 6.3 Hz, 2H), 4.83 (dd, J = 8.4, 6.0 Hz, 2H), 3.89 – 3.80 (m, 1H), 2.31 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.49, 134.83, 134.41, 129.52, 120.14, 73.27, 41.08, 20.84.

HRMS for $C_{11}H_{13}NO_2$ (ESI) $[M+Na]^+$ calc.: 214.0838, found: 214.0835.



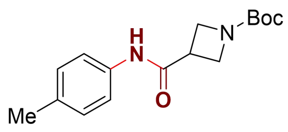
1-benzhydryl-_N_-(_p_-tolyl)azetidine-3-carboxamide (5as)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5as** (50.0 mg, 70% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 8.63 (br, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.44 – 7.40 (m, 4H), 7.30 (t, J = 7.6 Hz, 4H), 7.24 – 7.19 (m, 2H), 7.16 (d, J = 8.2 Hz, 2H), 4.47 (s, 1H), 3.42 (d, J = 6.3 Hz, 4H), 3.19 – 3.12 (m, 1H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.56, 141.11, 135.51, 133.77, 129.51, 128.60, 127.36, 127.32, 119.71, 77.31, 56.45, 37.07, 20.84.

HRMS for $C_{24}H_{24}N_2O$ (ESI) $[M+Na]^+$ calc.: 379.1781, found: 379.1784.



Chemical Formula: $C_{16}H_{22}N_2O_3$
Molecular Weight: 290.36

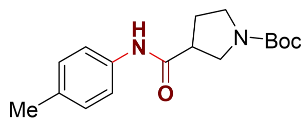
***tert*-butyl 3-(*p*-tolylcarbamoyl)azetidine-1-carboxylate (5at)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5at** (34.9 mg, 60% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.69 (br, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.23 – 4.15 (m, 2H), 4.06 (t, *J* = 8.5 Hz, 2H), 3.32 (tt, *J* = 8.7, 6.0 Hz, 1H), 2.30 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 169.80, 156.24, 134.96, 134.28, 129.49, 120.07, 79.89, 51.72, 34.16, 28.33, 20.83.

HRMS for $C_{16}H_{22}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 313.1523, found: 313.1527.



Chemical Formula: $C_{17}H_{24}N_2O_3$
Molecular Weight: 304.39

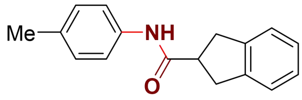
***tert*-butyl 3-(*p*-tolylcarbamoyl)pyrrolidine-1-carboxylate (5au)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5au** (43.2 mg, 71% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.73 (br, 1H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.22 – 4.14 (m, 2H), 4.06 (t, *J* = 8.5 Hz, 2H), 3.36 – 3.28 (m, 1H), 2.30 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.88, 156.25, 134.99, 134.24, 129.46, 120.08, 79.90, 51.82, 34.09, 28.32, 20.82.

HRMS for $C_{17}H_{24}N_2O_3$ (ESI) $[M+H]^+$ calc.: 305.1860, found: 305.1867.



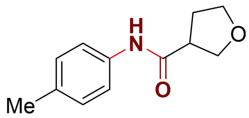
***tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (5av)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 15:1:1) to afford product **5av** (30.2 mg, 60% yield) as white solid.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ/ppm = 9.94 (br, 1H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.21 – 7.16 (m, 2H), 7.14 – 7.04 (m, 4H), 3.40 – 3.33 (m, 1H), , 3.15 – 3.08 (m, 4H), 2.22 (s, 3H).

^{13}C NMR (126 MHz, DMSO-*d*$_6$): δ/ppm = 173.32, 142.36, 137.32, 132.41, 129.53, 126.84, 124.64, 119.66, 45.46, 36.86, 20.91.

HRMS for $C_{17}H_{17}NO$ (ESI) $[M+H]^+$ calc.: 252.1383, found: 252.1392.



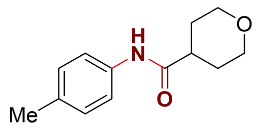
***N*-(*p*-tolyl)tetrahydrofuran-3-carboxamide (5aw)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5av** (30.8 mg, 75% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.53 (br, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 4.06 – 3.98 (m, 2H), 3.99 – 3.92 (m, 1H), 3.87 – 3.82 (m, 1H), 3.06 – 3.00 (m, 1H), 2.31 (s, 3H), 2.30 – 2.21 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.85, 135.13, 134.05, 129.46, 119.95, 70.96, 68.16, 46.49, 30.58, 20.83.

HRMS for $C_{12}H_{15}NO_2$ (ESI) $[M+Na]^+$ calc.: 228.0995, found: 228.1009.



Chemical Formula: $C_{13}H_{17}NO_2$
Molecular Weight: 219.28

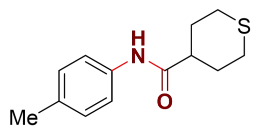
N-(p-tolyl)tetrahydro-2H-pyran-4-carboxamide (5ax)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ax** (33.3 mg, 76% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = 7.60 (br, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 4.07 – 3.98 (m, 2H), 3.44 – 3.34 (m, 2H), 2.47 (tt, J = 11.5, 3.9 Hz, 1H), 2.29 (s, 3H), 1.94 – 1.85 (m, 2H), 1.83 – 1.72 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ/ppm = 135.14, 134.05, 129.49, 119.93, 77.00, 67.17, 43.19, 29.23, 20.83.

HRMS for $C_{13}H_{17}NO_2$ (ESI) $[M+H]^+$ calc.: 220.1332, found: 220.1339.



Chemical Formula: $C_{13}H_{17}NOS$
Molecular Weight: 235.35

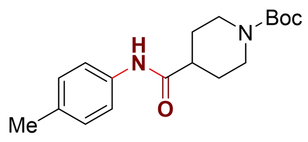
N-(p-tolyl)tetrahydro-2H-thiopyran-4-carboxamide (5ay)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ay** (43.7 mg, 93% yield) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.38 (d, J = 8.4 Hz, 2H), 7.28 (br, 1H), 7.11 (d, J = 8.1 Hz, 2H), 2.79 – 2.62 (m, 4H), 2.30 (s, 3H), 2.29 – 2.16 (m, 3H), 2.02 – 1.89 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.84, 135.10, 134.03, 129.45, 119.97, 77.00, 45.91, 30.46, 27.84, 20.82.

HRMS for $C_{13}H_{17}NOS$ (ESI) $[M+Na]^+$ calc.: 258.0923, found: 258.0935.



Chemical Formula: $C_{18}H_{26}N_2O_3$
Molecular Weight: 318.42

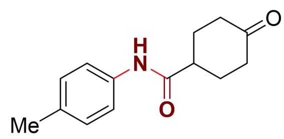
***tert*-butyl 4-(*p*-tolylcarbamoyl)piperidine-1-carboxylate (5az)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5az** (43.3 mg, 68% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.44 (br, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.27 – 4.08 (m, 2H), 2.82 – 2.68 (m, 2H), 2.39 – 2.33 (m, 1H), 2.30 (s, 3H), 1.92 – 1.83 (m, 2H), 1.78 – 1.68 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.61, 154.67, 135.15, 133.99, 129.44, 119.97, 79.72, 77.00, 44.16, 28.57, 28.39, 20.81.

HRMS for $C_{18}H_{26}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 341.1836, found: 341.1838.



Chemical Formula: $C_{14}H_{17}NO_2$
Molecular Weight: 231.30

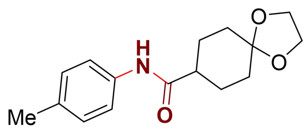
4-oxo-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (5ba)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5ba** (28.3 mg, 61% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.44 – 7.36 (m, 3H), 7.12 (d, *J* = 8.0 Hz, 2H), 2.67 (tt, *J* = 10.4, 3.8 Hz, 1H), 2.61 – 2.53 (m, 2H), 2.41 – 2.32 (m, 2H), 2.31 (s, 3H), 2.27 – 2.20 (m, 2H), 2.16 – 2.05 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 209.92, 172.15, 134.99, 134.24, 129.51, 120.01, 43.58, 39.79, 29.20, 20.83.

HRMS for $C_{14}H_{17}NO_2$ (ESI) $[M+Na]^+$ calc.: 254.1151, found: 254.1155.



Chemical Formula: $C_{16}H_{21}NO_3$
Molecular Weight: 275.35

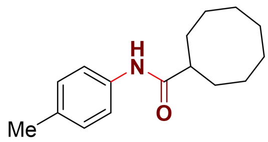
_N_-(_p_-tolyl)-1,4-dioxaspiro[4.5]decane-8-carboxamide (5bb)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5bb** (43.0 mg, 78% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.39 (d, J = 8.1 Hz, 2H), 7.35 (br, 1H), 7.09 (d, J = 8.1 Hz, 2H), 3.97 – 3.90 (m, 4H), 2.29 (s, 3H), 2.99 – 2.22 (m, 1H), 2.00 – 1.93 (m, 2H), 1.92 – 1.81 (m, 4H), 1.61 – 1.53 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.29, 135.32, 133.74, 129.38, 119.92, 107.87, 64.32, 64.28, 44.87, 33.99, 27.10, 20.80.

HRMS for $C_{16}H_{21}NO_3$ (ESI) $[M+Na]^+$ calc.: 298.1414, found: 298.1412.



Chemical Formula: $C_{16}H_{23}NO$
Molecular Weight: 245.37

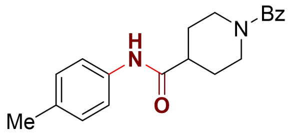
_N_-(_p_-tolyl)cyclooctanecarboxamide (5bc)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5bc** (30.9 mg, 63% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.39 (d, J = 8.4 Hz, 2H), 7.14 – 7.08 (m, 3H), 2.40 (tt, J = 9.4, 3.8 Hz, 1H), 2.30 (s, 3H), 1.97 – 1.89 (m, 2H), 1.84 – 1.75 (m, 4H), 1.72 – 1.39 (m, 10H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 175.70, 135.56, 133.58, 129.40, 119.78, 46.77, 29.73, 26.64, 26.17, 25.43, 20.82.

HRMS for $C_{16}H_{23}NO$ (ESI) $[M+H]^+$ calc.: 246.1852, found: 246.1855.



Chemical Formula: $C_{20}H_{22}N_2O_2$
Molecular Weight: 322.41

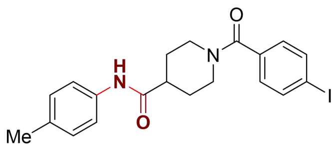
1-benzoyl-*N*-(*p*-tolyl)piperidine-4-carboxamide (5bd)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 15:1) to afford product **5bd** (42.0 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.93 (br, 1H), 7.44 – 7.33 (m, 7H), 7.09 (d, *J* = 7.8 Hz, 2H), 4.81 – 4.58 (m, 1H), 3.90 – 3.70 (m, 1H), 3.05 – 2.74 (m, 2H), 2.54 – 2.42 (m, 1H), 2.29 (s, 3H), 2.00 – 1.70 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.38, 135.91, 135.41, 133.95, 129.78, 129.45, 128.60, 126.79, 120.06, 43.81, 20.88.

HRMS for $C_{20}H_{22}N_2O_2$ (ESI) $[M+Na]^+$ calc.: 345.1573, found: 345.1578.



Chemical Formula: $C_{20}H_{21}IN_2O_2$
Molecular Weight: 448.30

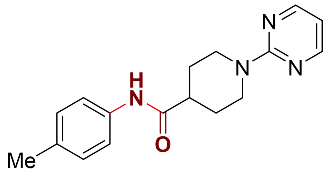
1-(4-iodobenzoyl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (5be)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5be** (57.4 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.49 (br, 1H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.16 – 7.07 (m, 4H), 4.79 – 4.55 (m, 1H), 3.87 – 3.71 (m, 1H), 3.09 – 2.80 (m, 2H), 2.48 (tt, *J* = 11.1, 3.9 Hz, 1H), 2.31 (s, 3H), 2.03 – 1.72 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.97, 169.53, 137.70, 135.22, 135.10, 134.11, 129.47, 128.56, 119.97, 95.88, 43.83, 28.65, 20.83.

HRMS for $C_{20}H_{21}IN_2O_2$ (ESI) $[M+Na]^+$ calc.: 471.0540, found: 471.0553.



Chemical Formula: $C_{17}H_{20}N_4O$
Molecular Weight: 296.37

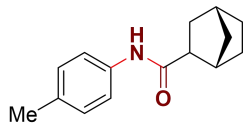
1-(pyrimidin-2-yl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (5bf)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bf** (41.5 mg, 70% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.30 (d, *J* = 4.7 Hz, 2H), 7.42 (br, 1H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.47 (t, *J* = 4.7 Hz, 1H), 4.86 – 4.78 (m, 2H), 2.93 (t, *J* = 11.9 Hz, 2H), 2.53 – 2.45 (m, 1H), 2.29 (s, 3H), 2.03 – 1.91 (m, 2H), 1.86 – 1.76 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.75, 161.34, 157.68, 135.20, 133.96, 129.43, 120.00, 109.71, 44.58, 43.32, 28.49, 20.80.

HRMS for $C_{17}H_{20}N_4O$ (ESI) $[M+H]^+$ calc.: 297.1710, found: 297.1714.



Chemical Formula: $C_{15}H_{19}NO$
Molecular Weight: 229.32

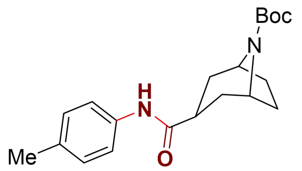
(1*S*,4*R*)-*N*-(*p*-tolyl)bicyclo[2.2.1]heptane-2-carboxamide (5bg)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bg** (42.2 mg, 92% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.28 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 2.50 – 2.46 (m, 1H), 2.34 – 2.31 (m, 1H), 2.29 (s, 3H), 2.24 (dd, *J* = 9.0, 5.2 Hz, 1H), 2.00 – 1.94 (m, 1H), 1.67 – 1.62 (m, 1H), 1.59 – 1.53 (m, 2H), 1.47 (ddd, *J* = 11.6, 9.0, 2.1 Hz, 1H), 1.29 – 1.15 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.92, 135.69, 133.41, 129.34, 119.68, 48.93, 41.65, 36.41, 35.89, 34.18, 29.74, 28.61, 20.79.

HRMS for $C_{15}H_{19}NO$ (ESI) $[M+H]^+$ calc.: 230.1539, found: 230.1543.



Chemical Formula: $C_{20}H_{28}N_2O_3$
Molecular Weight: 344.46

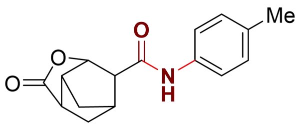
***tert*-butyl (1*R*,3s,5*S*)-3-(*p*-tolylcarbamoyl)-8-azabicyclo[3.2.1]octane-8-carboxyl-ate (5bh)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bh** (44.8 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.37 (d, *J* = 8.0 Hz, 2H), 7.27 (br, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 4.33 – 4.26 (m, 2H), 2.82 – 2.72 (m, 1H), 2.29 (s, 3H), 2.06 – 1.92 (m, 4H), 1.78 – 1.71 (m, 2H), 1.69 – 1.62 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.36, 153.26, 135.24, 133.91, 129.43, 119.92, 79.50, 53.25, 52.55, 37.45, 33.86, 33.45, 28.49, 28.32, 27.61, 20.80.

HRMS for $C_{20}H_{28}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 367.1992, found: 367.1998.



Chemical Formula: $C_{16}H_{17}NO_3$
Molecular Weight: 271.32

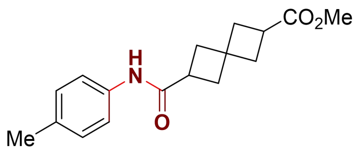
2-oxo-*N*-(*p*-tolyl)hexahydro-2*H*-3,5-methanocyclopenta[b]furan-6-carboxamide (5bi)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bi** (27.2 mg, 65% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.85 (br, 1H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 5.18 (d, *J* = 5.0 Hz, 1H), 3.26 (t, *J* = 5.0 Hz, 1H), 2.76 – 2.69 (m, 1H), 2.62 (dd, *J* = 11.3, 4.7 Hz, 1H), 2.50 (d, *J* = 2.1 Hz, 1H), 2.30 (s, 3H), 2.27 (dd, *J* = 11.4, 2.0 Hz, 1H), 2.12 – 2.04 (m, 1H), 1.82 – 1.72 (m, 1H), 1.65 – 1.58 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 181.40, 169.61, 135.20, 134.06, 129.46, 119.85, 82.80, 55.36, 46.01, 41.77, 38.81, 35.53, 35.07, 20.83.

HRMS for $C_{16}H_{17}NO_3$ (ESI) $[M+H]^+$ calc.: 272.1281, found: 272.1288.



Chemical Formula: $C_{17}H_{21}NO_3$
Molecular Weight: 287.36

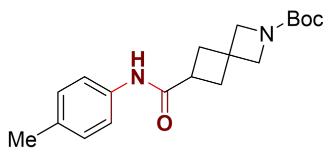
methyl 6-(*p*-tolylcarbamoyl)spiro[3.3]heptane-2-carboxylate (5bj)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bj** (42.5 mg, 74% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.13 – 7.07 (m, 3H), 3.66 (s, 3H), 3.05 – 2.93 (m, 2H), 2.46 – 2.39 (m, 1H), 2.29 (s, 3H), 2.38 – 2.17 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 175.77, 172.59, 135.38, 133.70, 129.42, 119.69, 51.66, 37.95, 37.78, 37.35, 37.22, 36.29, 35.42, 32.69, 20.80.

HRMS for $C_{17}H_{21}NO_3$ (ESI) $[M+Na]^+$ calc.: 310.1414, found: 310.1427.



Chemical Formula: $C_{19}H_{26}N_2O_3$
Molecular Weight: 330.43

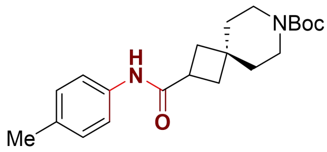
***tert*-butyl 6-(*p*-tolylcarbamoyl)-2-azaspiro[3.3]heptane-2-carboxylate (5bk)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bk** (52.8 mg, 80% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.34 (br, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 3.93 (s, 2H), 3.89 (s, 2H), 2.95 (p, *J* = 8.1 Hz, 1H), 2.58 – 2.48 (m, 2H), 2.42 – 2.34 (m, 2H), 2.30 (s, 3H), 1.42 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 172.23, 156.18, 135.28, 133.85, 129.43, 119.77, 79.39, 61.32, 35.78, 35.24, 34.28, 28.35, 20.82.

HRMS for $C_{19}H_{26}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 353.1836, found: 353.1839.



Chemical Formula: $C_{21}H_{30}N_2O_3$
Molecular Weight: 358.48

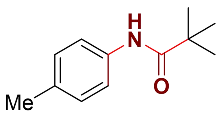
***tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (5bl)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bl** (62.4 mg, 87% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.44 (br, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 3.34 (t, *J* = 5.6 Hz, 2H), 3.26 (t, *J* = 5.6 Hz, 2H), 3.12 – 3.02 (m, 1H), 2.29 (s, 3H), 2.17 – 2.09 (m, 2H), 2.07 – 1.99 (m, 2H), 1.58 – 1.42 (m, 4H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.22, 154.92, 135.49, 133.64, 129.37, 119.70, 79.33, 37.96, 36.30, 34.51, 34.37, 33.99, 28.40, 20.78.

HRMS for $C_{21}H_{30}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 381.2149, found: 381.2155.



Chemical Formula: $C_{12}H_{17}NO$
Molecular Weight: 191.2740

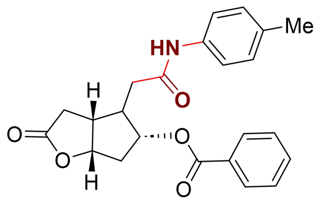
***N*-(*p*-tolyl)pivalamide (5bm)**

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 20:1) to afford product **5bm** (16.1 mg, 42% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.26 (s, 1H), 7.12 (d, *J* = 8.2 Hz, 2H), 2.31 (s, 3H), 1.31 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 176.43, 135.39, 133.77, 129.41, 119.97, 39.49, 27.62, 20.82.

HRMS for $C_{12}H_{17}NO$ (ESI) $[M+H]^+$ calc.: 192.1383, found: 192.1389.



Chemical Formula: $C_{23}H_{23}NO_5$
Molecular Weight: 393.44

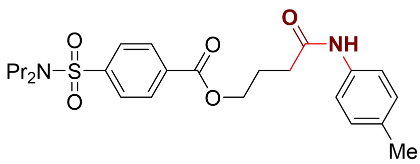
(3a*R*,5*R*,6a*S*)-2-oxo-4-(2-oxo-2-(p-tolylamino)ethyl)hexahydro-2*H*-cyclopenta[b]furan-5-yl benzoate (5bn)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bn** (36.2 mg, 46% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.11 (br, 1H), 7.99 (d, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.38 (m, 4H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.33 – 5.26 (m, 1H), 5.08 – 5.02 (m, 1H), 2.97 – 2.85 (m, 2H), 2.64 – 2.42 (m, 5H), 2.39 – 2.34 (m, 1H), 2.30 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 176.65, 168.25, 166.67, 135.06, 134.18, 133.54, 129.74, 129.46, 129.14, 128.52, 120.05, 83.60, 79.31, 48.94, 42.84, 39.42, 37.63, 35.70, 20.83.

HRMS for $C_{23}H_{23}NO_5$ (ESI) $[M+Na]^+$ calc.: 416.1468, found: 416.1477.



Chemical Formula: $C_{24}H_{32}N_2O_5S$
Molecular Weight: 460.59

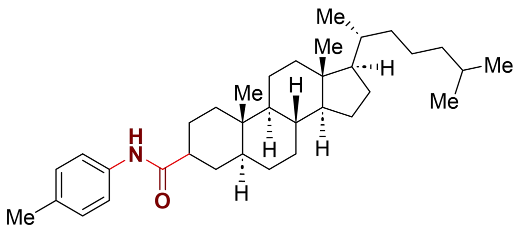
4-oxo-4-(*p*-tolylamino)butyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (5bo)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bn** (56.2 mg, 61% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.11 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.36 (br, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 4.46 (t, *J* = 6.2 Hz, 2H), 3.15 – 3.02 (m, 4H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 2.27 – 2.19 (m, 2H), 1.58 – 1.48 (m, 4H), 0.86 (t, *J* = 7.4 Hz, 6H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 169.89, 165.36, 144.26, 135.20, 134.00, 133.29, 130.23, 129.47, 126.94, 119.79, 64.91, 49.89, 34.05, 24.61, 21.90, 20.82, 11.13.

HRMS for $C_{24}H_{32}NO_5S$ (ESI) $[M+Na]^+$ calc.: 483.1924, found: 483.1931.



Chemical Formula: $C_{35}H_{55}NO$
Molecular Weight: 505.83

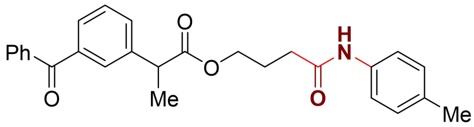
2.84:1 mixture of diastereoisomers) of (5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-di-methyl-17-((*R*)-6-methylheptan-2-yl)-*N*-(*p*-tolyl)hexadecahydro-1*H*-cyclopenta-[a]phenanthrene-3-carboxamide (5bp)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bp** (85.0 mg, 84% yield) as white solid.

^{1}**H NMR** (500 MHz, $CDCl_3$): δ/ppm = δ 7.44 – 7.38 (m, 2H), 7.31 – 7.26 (m, 1H), 7.14 – 7.08 (m, 2H), 2.66 – 2.60 (m, 1H), 2.34 – 2.28 (m, 3H), 2.00 – 1.91 (m, 2H), 1.85 – 1.74 (m, 2H), 1.68 – 0.85 (m, 35H), 0.84 – 0.79 (m, 3H), 0.74 – 0.67 (m, 1H), 0.65 (s, 0.78H), 0.63 (s, 2.22H).

^{13}**C NMR** (126 MHz, $CDCl_3$): δ/ppm = 174.25, 173.74, 135.66, 133.57, 129.44, 119.83, 119.79, 56.57, 56.44, 56.33, 56.19, 54.12, 42.56, 41.94, 40.59, 40.05, 39.97, 39.54, 37.87, 36.18, 35.92, 35.84, 35.81, 35.44, 34.83, 32.07, 31.90, 31.74, 30.71, 28.82, 28.75, 28.27, 28.04, 25.25, 24.21, 24.18, 23.87, 23.59, 22.87, 22.60, 21.00, 20.87, 20.74, 18.71, 18.68, 12.08, 11.66.

HRMS for $C_{35}H_{55}NO$ (ESI) $[M+H]^+$ calc.: 506.4356, found: 506.4348.



Chemical Formula: $C_{27}H_{27}NO_4$
Molecular Weight: 429.52

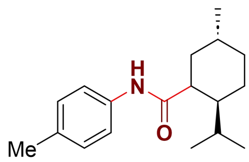
4-oxo-4-(*p*-tolylamino)butyl 2-(3-benzoylphenyl)propanoate (5bq)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bq** (38.7 mg, 45% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.07 (br, 1H), 7.90 (d, *J* = 1.9 Hz, 1H), 7.86 – 7.78 (m, 2H), 7.66 – 7.57 (m, 2H), 7.57 – 7.46 (m, 5H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 4.25 (ddd, *J* = 11.6, 7.2, 4.7 Hz, 1H), 4.13 (ddd, *J* = 11.6, 6.5, 4.7 Hz, 1H), 3.84 (q, *J* = 7.2 Hz, 1H), 2.35 – 2.31 (m, 2H), 2.31 (s, 3H), 2.07 – 1.99 (m, 2H), 1.57 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 197.41, 170.13, 141.29, 137.09, 135.75, 133.51, 132.96, 131.61, 130.28, 129.36, 129.11, 128.94, 128.43, 128.40, 119.82, 64.15, 45.55, 33.48, 31.57, 24.40, 20.84, 17.89, 14.10.

HRMS for $C_{27}H_{27}NO_4$ (ESI) $[M+Na]^+$ calc.: 452.1832, found: 452.1842.



Chemical Formula: $C_{18}H_{27}NO$
Molecular Weight: 273.42

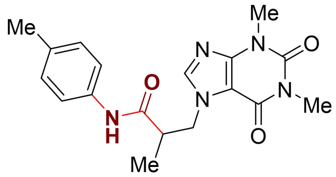
2-isopropyl-5-methyl-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (5br)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5br** (37.2 mg, 68% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.41 (d, *J* = 8.3 Hz, 2H), 7.19 (br, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 2.30 (s, 3H), 2.13 (td, *J* = 11.4, 3.5 Hz, 1H), 1.93 – 1.86 (m, 1H), 1.85 – 1.78 (m, 1H), 1.77 – 1.68 (m, 2H), 1.65 – 1.57 (m, 1H), 1.44 – 1.35 (m, 1H), 1.35 – 1.26 (m, 1H), 1.11 – 0.92 (m, 2H), 1.92 – 0.88 (m, 6H), 0.82 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 174.11, 135.41, 133.72, 129.40, 119.87, 50.73, 44.54, 39.39, 34.50, 32.29, 28.74, 23.91, 22.30, 21.37, 20.82, 16.25.

HRMS for $C_{18}H_{27}NO$ (ESI) $[M+H]^+$ calc.: 274.2165, found: 274.2180.



Chemical Formula: $C_{18}H_{21}N_5O_3$
Molecular Weight: 355.40

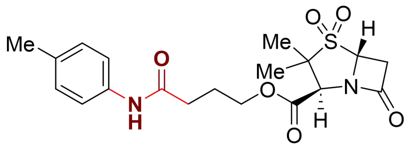
3-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7*H*-purin-7-yl)-2-methyl-*N*-(*p*-tolyl) propanamide (5bs)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bs** (50.5 mg, 71% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.15 (br, 1H), 7.62 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.60 (dd, *J* = 13.5, 7.2 Hz, 1H), 4.22 (dd, *J* = 13.5, 6.2 Hz, 1H), 3.56 (s, 3H), 3.35 (s, 3H), 3.13 – 3.02 (m, 1H), 2.29 (s, 3H), 1.30 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.10, 155.39, 151.41, 149.29, 142.17, 135.16, 134.09, 129.42, 119.78, 106.50, 50.60, 43.29, 29.87, 27.99, 20.82, 15.13.

HRMS for $C_{18}H_{21}N_5O_3$ (ESI) $[M+Na]^+$ calc.: 378.1537, found: 378.1544.



Chemical Formula: $C_{19}H_{24}N_2O_6S$
Molecular Weight: 408.47

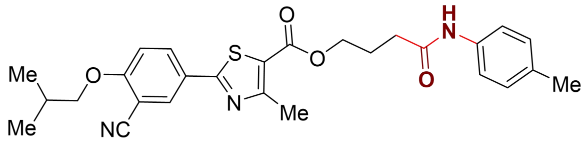
4-oxo-4-(*p*-tolylamino)butyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptane-2-carboxylate 4,4-dioxide (5bt)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bt** (35.2 mg, 43% yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.54 (br, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.58 (dd, *J* = 4.4, 2.0 Hz, 1H), 4.36 (s, 1H), 4.35 – 4.23 (m, 2H), 3.46 – 3.32 (m, 2H), 2.47 – 2.39 (m, 2H), 2.30 (s, 3H), 2.17 – 2.06 (m, 2H), 1.58 (s, 3H), 1.42 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 171.10, 169.58, 166.81, 135.21, 134.03, 129.51, 119.78, 65.53, 63.25, 62.91, 61.18, 38.27, 33.37, 24.12, 20.81, 20.12, 18.62.

HRMS for $C_{18}H_{21}N_5O_3$ (ESI) $[M+Na]^+$ calc.: 431.1247, found: 431.1240.



Chemical Formula: $C_{27}H_{29}N_3O_4S$
Molecular Weight: 491.61

4-oxo-4-(*p*-tolylamino)butyl
2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxyl-ate (5bu)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford product **5bu** (58.0 mg, 59% yield) as white solid.

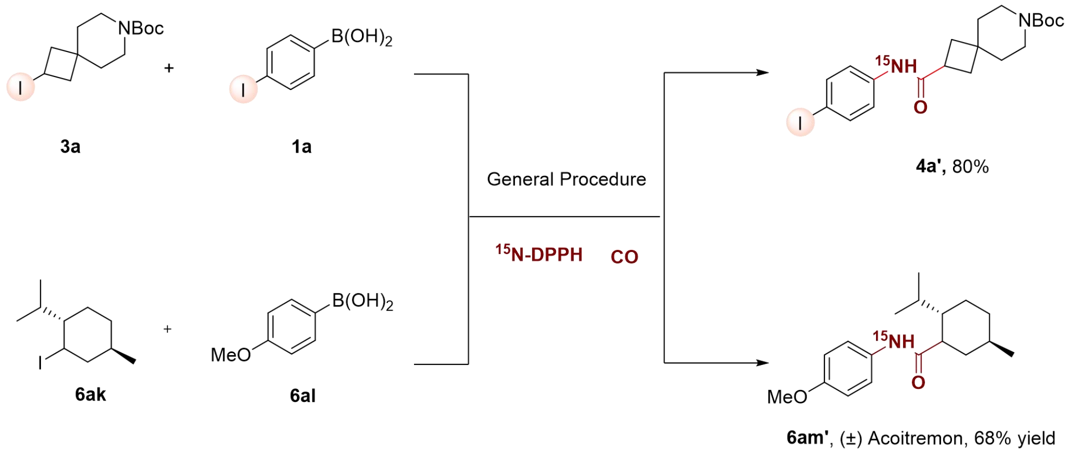
^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 8.07 (d, *J* = 2.4 Hz, 1H), 7.96 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.58 (br, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 1H), 4.38 (t, *J* = 6.1 Hz, 2H), 3.88 (d, *J* = 6.5 Hz, 2H), 2.73 (s, 3H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.27 (s, 3H), 2.22 – 2.13 (m, 3H), 1.08 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.97, 167.21, 162.42, 162.01, 161.39, 135.38, 133.75, 132.52, 131.91, 129.39, 125.79, 121.30, 119.73, 115.36, 112.50, 102.73, 75.64, 64.58, 33.96, 28.09, 24.56, 20.78, 18.98, 17.44.

HRMS for $C_{27}H_{29}N_3O_4S$ (ESI) $[M+Na]^+$ calc.: 514.1771, found: 514.1760.

4. ^{15}N labeling experiment

4.1 Synthesis and characterization of ^{15}N-Enriched 4a’ and 6am’



Moreover, the strategy enables the direct incorporation of isotopically labeled nitrogen, facilitating the efficient synthesis of ^{15}N-labeled amides from ^{15}N-enriched DPPH (**2a’**). The reaction was conducted according to the general procedure on a 0.20 mmol scale and stirred for 16 h under the standard conditions. Upon completion, the reaction mixture was concentrated under reduced pressure, and the resulting crude residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford **4a’** (79.1 mg, 80% yield) and **6am’** (39.6 mg, 68% yield), both isolated as white solids.

HRMS for **4a’** $C_{20}H_{27}IN_2O_3$ (ESI) $[M+Na]^+$ calc.: 494.0929, found: 494.0936.

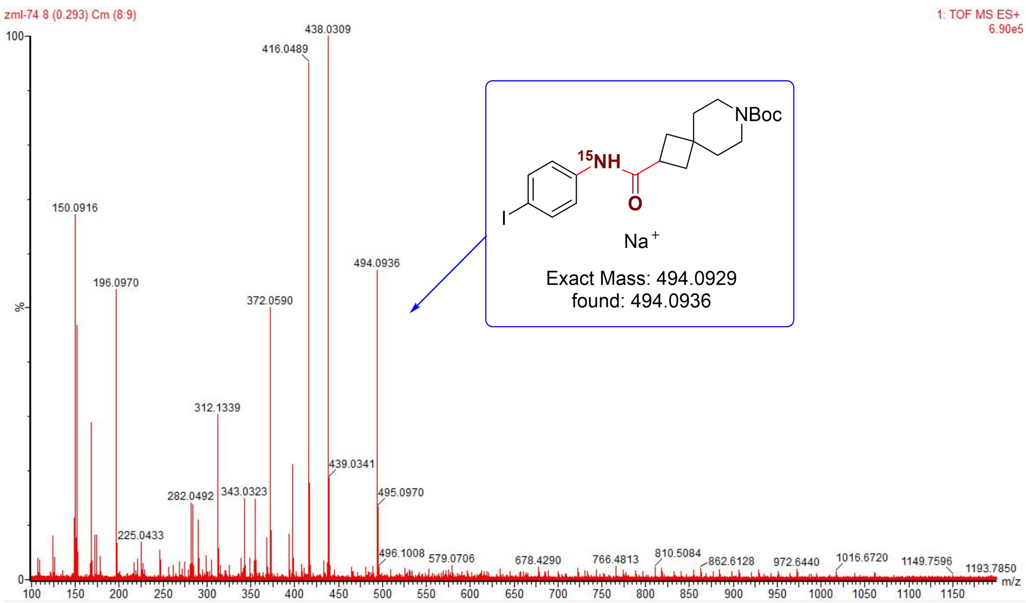


Figure S2 HRMS for compound **4a’**

HRMS for **6am'** $C_{18}H_{27}{}^{15}NO_2$ (ESI) $[M+H]^+$ calc.: 291.2085, found: 291.2090.

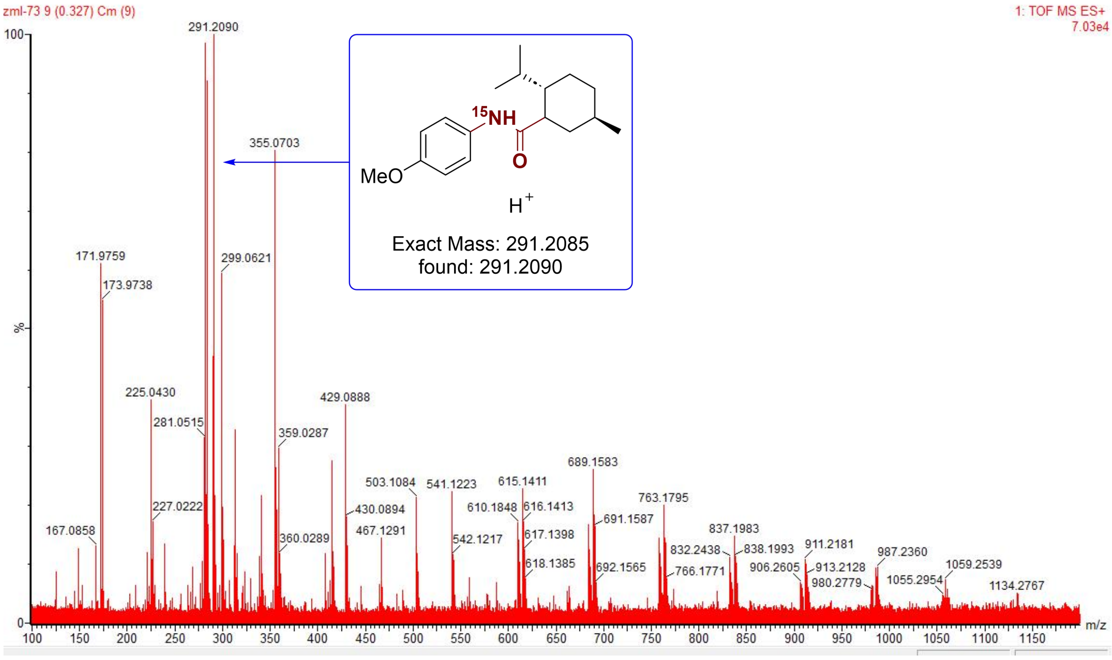
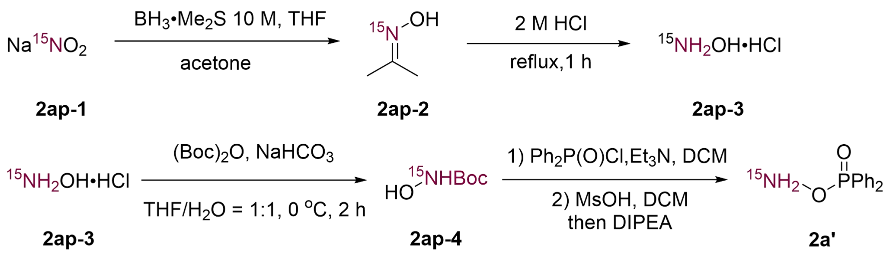


Figure S3 HRMS for compound **6am'**

A sample of ^{15}N-DPPH was synthesized from $Na^{15}NO_2$.



4.2 Preparation of ^{15}N-enriched DPPH(2a')

4.2.1 Preparation of ^{15}N-enriched hydroxylamine hydrochloride

Following a reported procedure[1-2], a dry 100 mL Schlenk flask was charged with ^{15}N-enriched sodium nitrite ($Na^{15}NO_2$, 1.25 g, 99% atom). Under a nitrogen atmosphere, 25 mL THF was added, followed by the dropwise addition of borane–dimethyl sulfide complex (10 M, 3.90 mL). The reaction mixture was stirred at room temperature overnight and then cooled to –5 °C. To the cooled mixture, 7.4 mL of water was added over 15 min, followed by 7.4 mL of 6 M hydrochloric acid over 20 min. After stirring for an additional 20 min, 1.85 mL of acetone was added. After 15 min, 8 mL of 6 M sodium hydroxide solution was added to the aqueous phase, and solid NaCl was added to saturation. The organic and aqueous phases were separated, and the aqueous phase was extracted with diethyl ether twice (25 mL each time). The combined organic phase was dried over anhydrous sodium sulfate and concentrated to afford ^{15}N-enriched acetone oxime **2ap-2** (0.9 g, 68%) as a white solid.

In a 50 mL flask, 0.9 g **2ap-2** was mixed with 30 mL of 2 M HCl. The mixture was gently refluxed for 6 h, followed by distillation at atmospheric pressure. When acetone was no longer detected in the distillate, the distillation was continued under reduced pressure until the volume was concentrated to approximately 1 mL. The concentrated solution was cooled in an ice-salt mixture, and colorless crystals of hydroxylamine hydrochloride precipitated immediately. The crystals were lyophilized to give dry crystalline, which was further purified by recrystallization from anhydrous ethanol to afford the final product **2ap-3** $^{15}NH_2OH \cdot HCl$ (0.53 g, 60% yield).

4.2.2 Synthesis of *tert*-butyl *N*-hydroxycarbamate (2ap-4)

According to the literature procedure[3-4], to a 1:1 tetrahydrofuran–water mixed solution (16 mL) of **2ap-3** (0.5 g, 7.2 mmol) and di-*tert*-butyl dicarbonate (1.57 g, 7.2 mmol) at 0 °C was added sodium bicarbonate (1.21 g, 14.4 mmol). The mixture was stirred at 0 °C for 4 hours.

The reaction mixture was then diluted with EtOAc (10 mL), and the organic phase was separated. The aqueous phase was extracted once more with EtOAc (25 mL). The combined organic phases were washed successively with saturated aqueous sodium bicarbonate solution (10 mL), water (20 mL), and saturated aqueous NaCl solution (10 mL), then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to afford **2ap-4** (0.86 g, 90%) as a white solid.

4.2.3 Synthesis of ^{15}N-enriched DPPH(2a')

According to the literature procedure[5], a dry 50 mL Schlenk flask was charged with *tert*-butyl *N*-hydroxycarbamate (0.9 g, 6.76 mmol, 1.1 equiv.) under nitrogen atmosphere, followed by the addition of DCM (6.4 mL) in one portion. The mixture was cooled to −5 °C to −15 °C until the solid was completely dissolved.

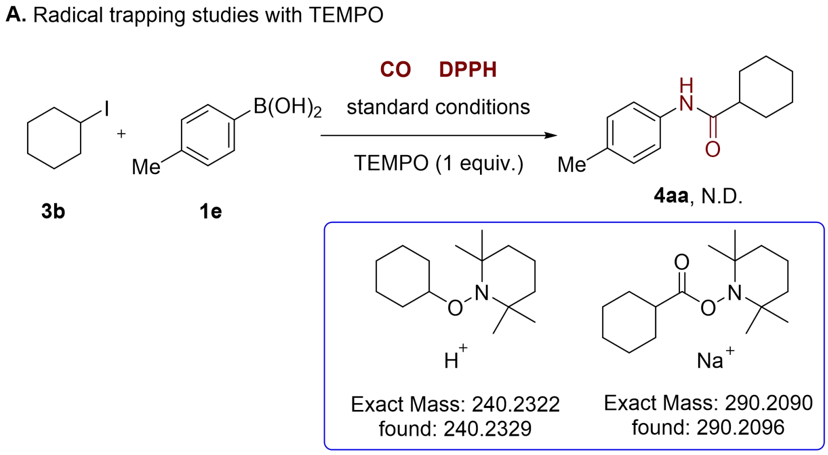
Triethylamine (1.2 mL, 8.54 mmol, 1.25 equiv.) was added dropwise over 10 min. Then a solution of diphenylphosphinyl chloride (1.30 mL, 1.61 g, 6.14 mmol, 1.0 equiv.) in DCM (1.6 mL) was added dropwise, while maintaining the internal temperature below 0 °C. After completion of the reaction as confirmed by TLC, the organic phase was warmed to above 10 °C using a warm water bath. A 5% aqueous citric acid solution (3.2 mL) was added via dropping funnel over 5 min. After stirring for 15 min, the mixture was transferred to a separatory funnel, and the aqueous layer was discarded. The organic phase was concentrated on a rotary evaporator. n-Hexane (4.0 mL) was added to the suspension, and the mixture was concentrated again to approximately 3–4 mL. Another portion of n-hexane (4.0 mL) was added, and the mixture was concentrated to a total volume of about 3–4 mL. The resulting suspension was stirred at room temperature for 12 h. The solid was collected by filtration through a fritted Büchner funnel and washed with a 4:1 mixture of n- hexane/DCM (8.0 mL). The solid was dried at room temperature under vacuum to afford *tert*-butyl (diphenylphosphoryl)oxycarbamate (1.95 g, 5.83 mmol, 95% yield) as a white solid.

A dry 50 mL Schlenk flask was charged with *tert*-butyl (diphenylphosphoryl)-oxycarbamate (1.95 g, 5.83 mmol, 1.0 equiv.) and suspended in DCM 4.0 mL. The system was cooled to −5 °C using a cryostat. Methanesulfonic acid (1.1 mL, 1.68 g, 17.5 mmol, 3.0 equiv.) was added dropwise via dropping funnel over 15 min. The reaction mixture was stirred at −5 °C for 2 h. After completion was confirmed by TLC, DCM (4.0 mL) was added, and the bath temperature was adjusted to 0 °C. A solution of *N,N*-diisopropylethylamine (2.1 mL, 11.7 mmol, 2.0 equiv.) in DCM (6.0 mL) was added dropwise while maintaining the internal temperature between 0 °C and 5 °C. After quenching, the suspension was allowed to warm naturally to 15 °C and filtered through a fritted Büchner funnel.

The filter cake was washed by resuspension in DCM (3 × 4.0 mL). The final product was dried under vacuum at room temperature to afford **2a’** (0.48 g 35%) as a white solid.

5. Mechanistic studies

5.1 Radical trapping experiments



To a 20 mL quartz tube equipped with a magnetic stir bar was added alkyl iodide **3b** (0.2 mmol, 42 mg), $Mn_2(CO)_{10}$ (5 mol%, 3.9 mg), DPPH (1.5 equiv., 70.0 mg), boronic acid (2.0 equiv., 0.4 mmol, 54.4 mg), Cs_2CO_3 (2.0 equiv., 130.3 mg), TEMPO (1.0 equiv., 0.2 mmol, 31.3 mg) and 2-MeTHF (0.1 M, 2 mL), which was then sealed with a rubber septum and connected to the atmosphere via a needle. The quartz tubes were arranged in a revolver-like manner, accommodating exactly 5 quartz tubes and 1 temperature reference tube (**Figure S1**), and transferred into a 500 mL mild-pressure parallel photoreactor (WP-MSAR-500PC) manufactured by WattCas Instruments. The sealed reactor was flushed with carbon monoxide (5 atm) three times, then charged with 5 atm of CO (monitored by a pressure gauge). The mixture was stirred at 700 rpm at 35 °C and irradiated with a 10 W blue LED (445–450 nm) for 0.3 h. Upon completion, the light was turned off, and the system was cooled to room temperature. And a proper amount of solvent was taken for HRMS analysis. In addition, a TEMPO-trapped manganese radical species (**I**) was detected, consistent with photoinduced homolytic cleavage of the Mn–Mn bond in $Mn_2(CO)_{10}$ to generate manganese-centered radicals. **HRMS** m/z (ESI) calcd for Int **I** $C_{14}H_{18}MnNO_6$ $[M+H]^+$ 352.0587, found: 352.0594.

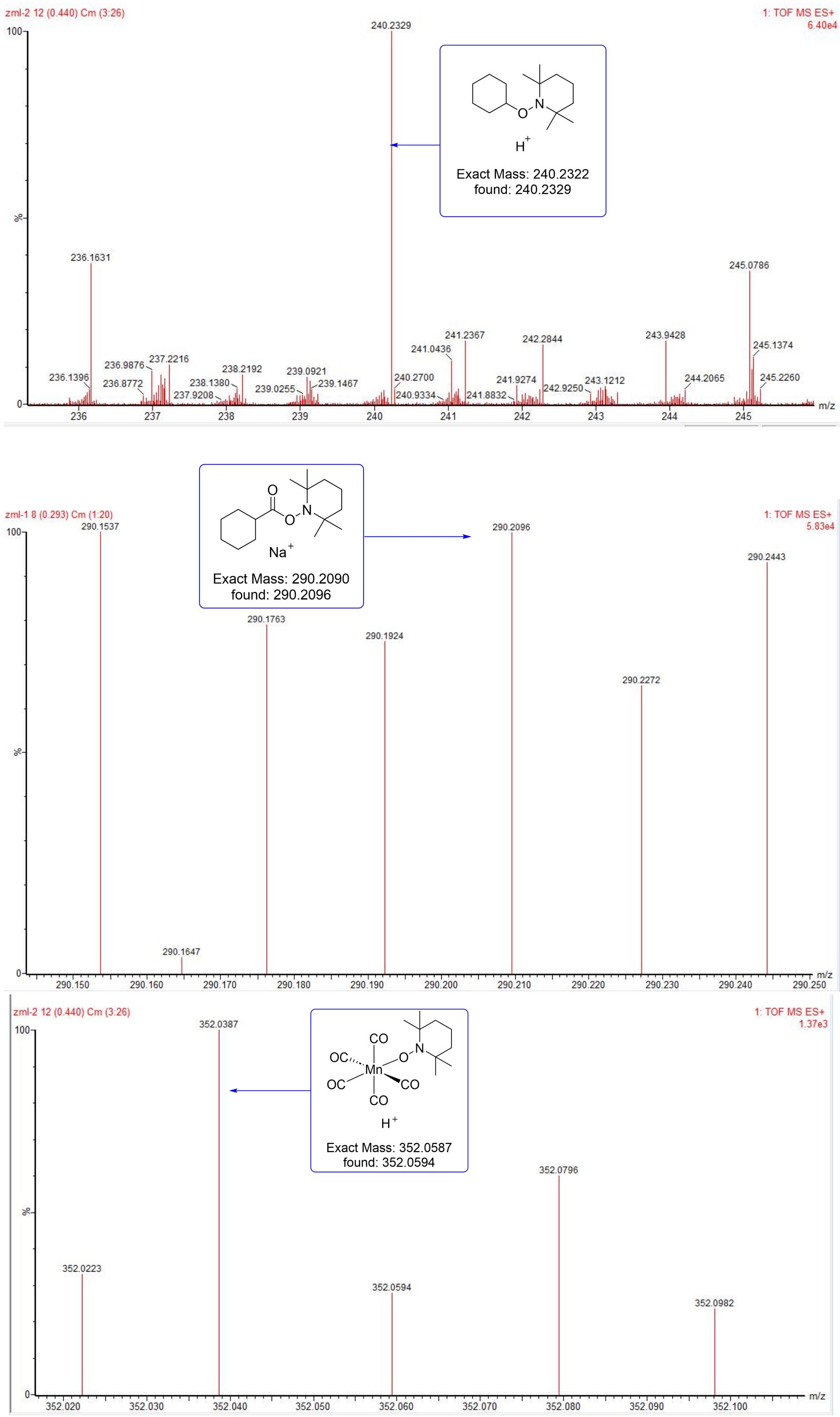
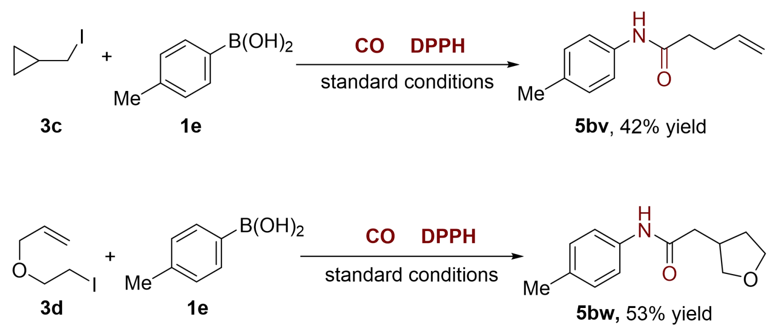


Figure S4 HRMS for radical trapping with TEMPO

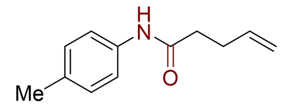
5.2 Radical clock experiments

B. Radical clock experiments



N-(*p*-tolyl)pent-4-enamide (5av)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 10:1) to afford product **5bv** (15.9 mg, 42% yield) as white solid.



Chemical Formula: $C_{12}H_{15}NO$
Molecular Weight: 189.26

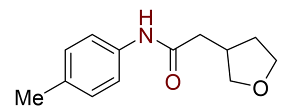
^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.22 (s, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 5.93 – 5.76 (m, 1H), 5.16 – 5.00 (m, 2H), 2.55 – 2.44 (m, 4H), 2.31 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 170.36, 136.90, 135.23, 133.87, 129.45, 119.89, 115.89, 36.77, 29.47, 20.83.

HRMS for $C_{13}H_{17}NO_2$ (ESI) $[M+H]^+$ calc.: 190.1226, found: 190.1236.

2-(tetrahydrofuran-3-yl)-*N*-(*p*-tolyl)acetamide (5aw)

The reaction was carried out according to the general procedure on 0.20-mmol scale (16 h). The residue was purified by flash column chromatography (PE/EA = 10:1) to afford product **5bw** (23.2 mg, 53% yield) as white solid.



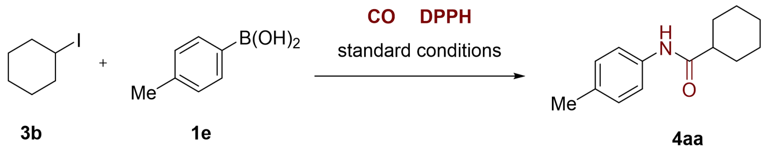
Chemical Formula: $C_{13}H_{17}NO_2$
Molecular Weight: 219.28

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.26 (br, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 3.95 (dd, *J* = 8.7, 6.8 Hz, 1H), 3.89 (td, *J* = 8.3, 5.2 Hz, 1H), 3.81 – 3.74 (m, 1H), 3.53 – 3.48 (m, 1H), 2.82 – 2.72 (m, 1H), 2.43 (d, *J* = 7.4 Hz, 2H), 2.31 (s, 3H), 2.20 – 2.13 (m, 1H), 1.66 – 1.58 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 169.71, 135.08, 134.04, 129.48, 119.90, 72.89, 67.63, 41.08, 35.87, 31.98, 20.83.

HRMS for $C_{13}H_{17}NO_2$ (ESI) $[M+H]^+$ calc.: 220.1332, found: 220.1324.

5.3 HRMS analysis for monitoring intermediates



Procedure for HRMS analysis: To a 20 mL quartz tube equipped with a magnetic stir bar was added alkyl iodide **3b** (0.2 mmol, 42 mg), $Mn_2(CO)_{10}$ (5 mol%, 3.9 mg), DPPH (1.5 equiv., 70.0 mg), boronic acid (2.0 equiv., 0.4 mmol, 54.4 mg), Cs_2CO_3 (2.0 equiv., 130.3 mg) and 2-MeTHF (0.1 M, 2 mL), which was then sealed with a rubber septum and connected to the atmosphere via a needle. The quartz tubes were arranged in a revolver-like manner, accommodating exactly 5 quartz tubes and 1 temperature reference tube (Figure S1), and transferred into a 500 mL mild-pressure parallel photoreactor (WP-MSAR-500PC) manufactured by WattCas Instruments. The sealed reactor was flushed with carbon monoxide (5 atm) three times, then charged with 5 atm of CO (monitored by a pressure gauge). The mixture was stirred at 700 rpm at 35 °C and irradiated with a 10 W blue LED (445–450 nm) for 0.3 h. Upon completion, the light was turned off, and the system was cooled to room temperature. And a proper amount of solvent was taken for HRMS analysis. Based on that, Int **A** ,Int **B**, Int **C** and Int **D** was successfully confirmed:

HRMS m/z (ESI) calcd. for Int **A** C_5IMnO_5 $[M+Na]^+$ 344.8063, found: 344.8064;

HRMS m/z (ESI) calcd. for Int **B** $C_{12}H_7MnO_5$ $[M+Na]^+$ 308.9566, found: 308.9565;

HRMS m/z (ESI) calcd. for Int **C** $C_{23}H_{18}MnNO_6P$ $[M+H]^+$ 491.0325, found: 491.0327;

HRMS m/z (ESI) calcd for Int **D** $C_{11}H_8MnNO_4$ $[M+Na]^+$ 295.9726, found: 295.9718.

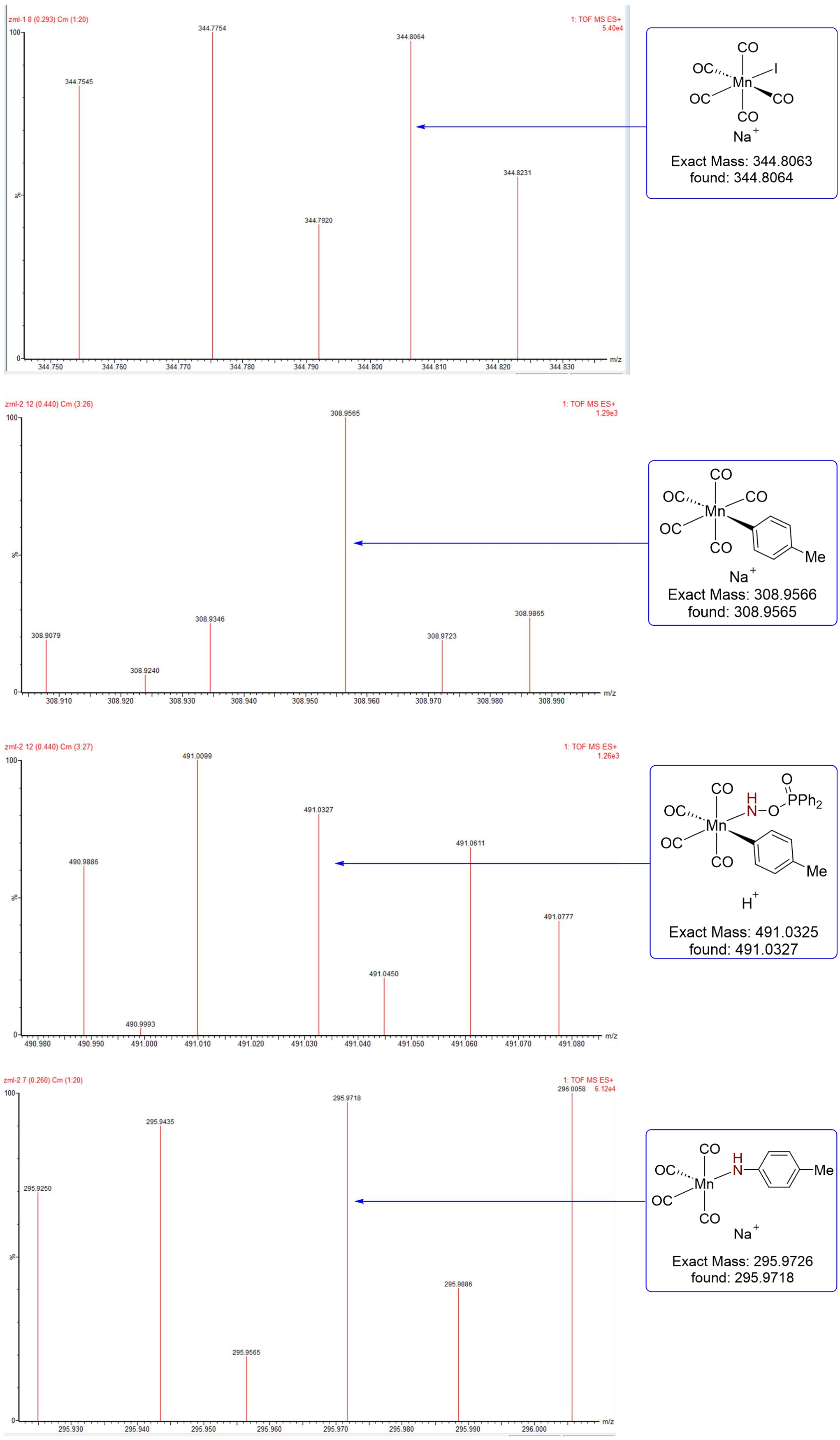
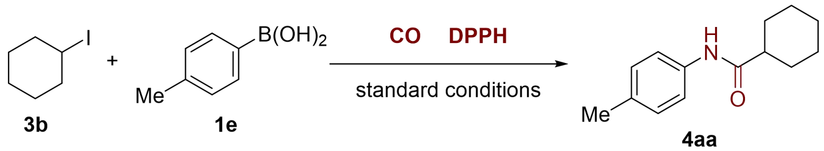


Figure S5 HRMS analysis for monitoring intermediates

5.4 Light on/off experiments



To a 20 mL quartz tube equipped with a magnetic stir bar were added alkyl iodide **3b** (0.2 mmol, 42 mg), $Mn_2(CO)_{10}$ (5 mol%, 3.9 mg), DPPH (1.5 equiv., 70.0 mg), boronic acid **1e** (2.0 equiv., 0.4 mmol, 54.4 mg), Cs_2CO_3 (2.0 equiv., 130.3 mg) and 2-MeTHF (0.1 M, 2 mL). The tube was sealed with a rubber septum, connected to the atmosphere via a needle, flushed with carbon monoxide (5 atm) three times, and then charged with 5 atm of CO. The mixture was stirred at 700 rpm and irradiated with a 10 W blue LED (445–450 nm) at 35 °C. A light-dark cycling procedure was then performed: irradiation with blue LED for 2 h at room temperature followed by 2 h in darkness, and this cycle was repeated over a total reaction time of 16 h.

Three parallel experiments were conducted under these standard conditions, and product yields were monitored by ^{1}H NMR at 2 intervals using 1,3-benzodioxole (0.1 mmol) as an internal standard. The average yield of the three parallel runs is reported.

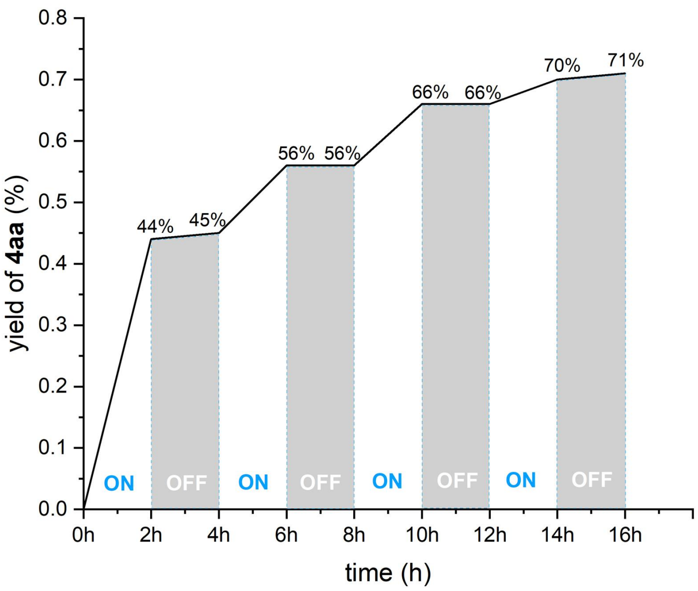
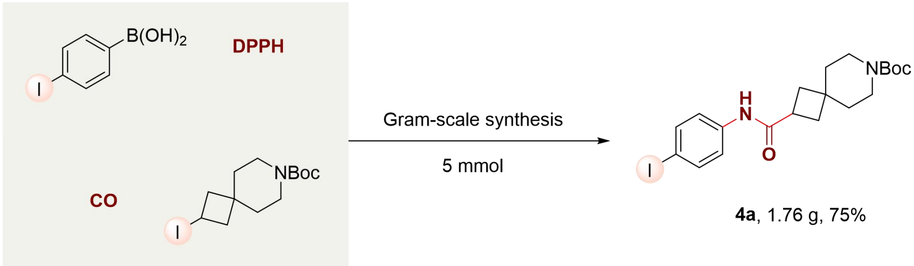


Figure S6 Light on/off experiments

6. Experimental procedures and characterization data for derivatization

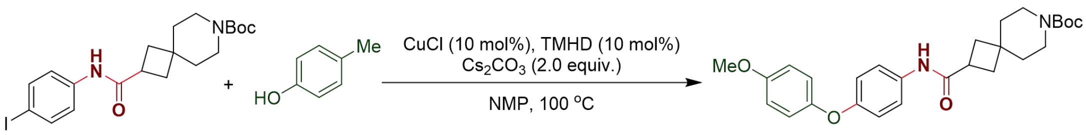
6.1 Gram-scale synthesis



4a, 1.76 g, 75%

To two quartz tubes equipped with a magnetic stir bar were added alkyl iodide **1a** (1.0 equiv., 5 mmol, 1.76 g), $Mn_2(CO)_{10}$ (10 mol%, 195 mg), *O*-diphenylphosphinyl hydroxylamine (DPPH) (1.5 equiv., 7.5 mmol, 1.75 g), boronic acid **3a** (2.0 equiv., 10 mmol, 2.48 g), Cs_2CO_3 (2.0 equiv., 10 mmol, 3.26 g), and 2-MeTHF (20 mL). Tube was sealed with a rubber septum and connected to the atmosphere via a needle. The quartz tubes were arranged in a revolver-like manner, accommodating exactly 5 quartz tubes and 1 temperature reference tube, and transferred into a 500 mL mild-pressure parallel photoreactor (WP-MSAR-500PC) manufactured by WattCas Instruments. The sealed reactor was flushed with carbon monoxide (5 atm) three times, then charged with 5 atm of CO (monitored by a pressure gauge). The mixture was stirred at 700 rpm at 35 °C and irradiated with blue LED (445–450 nm) for 16 h. Upon completion, the light was turned off, and the system was cooled to room temperature. The resulting solutions were combined, concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (PE/EA/DCM = 10:1:1) to afford product **4a** (1.76 g, 75% yield) as a white solid.

6.2 Experimental procedures for Ullmann-type C–O coupling

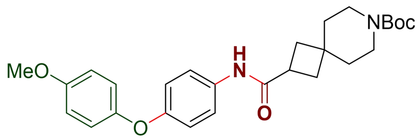


4a **6a** **6aa**

***tert*-butyl 2-((4-(4-methoxyphenoxy)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (6aa)**

Following a reported procedure[6], to a flame-dried Schlenk tube were added aryl iodide **4a** (0.2 mmol, 1.0 equiv., 94.1 mg), *p*-cresol (2.0 equiv., 43.2 mg), Cs_2CO_3 (2.0 equiv., 130.3 mg), CuCl (10 mol%, 2.0 mg), 2,2,6,6-tetramethylheptane-3,5-dione (TMHD) (10 mol%, 3.7 mg), and anhydrous *N*-methylpyrrolidone 1.0 mL under nitrogen atmosphere. The mixture was degassed by bubbling dry nitrogen for 5 minutes, then the tube was sealed and heated to 100 °C in a preheated oil bath. The reaction mixture was stirred vigorously at this temperature under nitrogen protection until complete consumption of the starting material aryl iodide **4a**, monitored by thin-layer chromatography (TLC). After cooling to ambient temperature naturally, the reaction mixture was transferred into a separatory funnel and partitioned between EtOAc (15 mL) and deionized water (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated aqueous NaCl solution (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to remove volatile solvents.

The crude residue was purified by flash column chromatography on silica gel, eluting with PE/EA (4:1, v/v). The fractions containing the desired product were collected and evaporated under reduced pressure to afford the target product **6aa** as a white solid (58.7 mg, 63% yield).



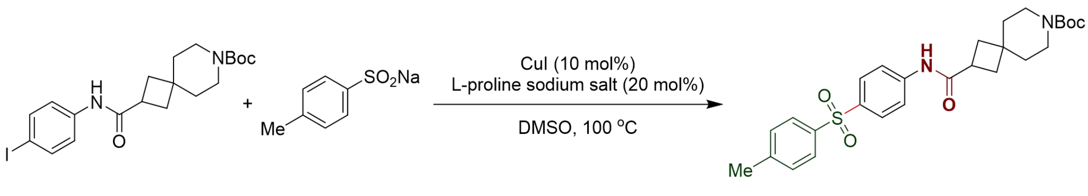
Chemical Formula: $C_{27}H_{34}N_2O_5$
Molecular Weight: 466.58

^{1}H NMR (500 MHz, $CDCl_3$): δ/ppm = δ 7.81 (br, 1H), 7.44 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.88 – 6.80 (m, 4H), 3.76 (s, 3H), 3.37 – 3.29 (m, 2H), 3.27 – 3.22 (m, 2H), 3.07 (p, *J* = 8.6 Hz, 1H), 2.18 – 2.08 (m, 2H), 2.04 – 1.96 (m, 2H), 1.59 – 1.50 (m, 4H), 1.43 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ/ppm = 173.34, 155.60, 154.87, 154.47, 150.39, 133.02, 121.40, 120.17, 118.09, 114.72, 79.34, 55.52, 40.92, 40.16, 37.89, 36.20, 34.43, 34.13, 33.92, 33.90, 28.33.

HRMS for $C_{27}H_{34}N_2O_5$ (ESI) $[M+Na]^+$ calc.: 489.2360, found: 489.2370.

6.3 Experimental procedures for copper-catalysed C–S coupling



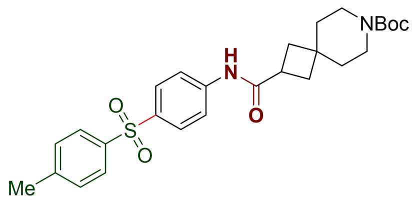
4a **6b** **6ab**, 87%

***tert*-butyl**

2-((4-tosylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxyl-ate(6ab)

Following the general protocol described in the reported literature[7], to a flame- dried sealed tube were added aryl iodide **4a** (0.2 mmol, 1.0 equiv., 94.1 mg), sodium methanesulfinate (1.2 equiv., 24.7 mg), CuI (10 mol%, 3.8 mg), *L*- proline sodium salt (20 mol%, 5.6 mg), and anhydrous DMSO 1.0 mL under nitrogen atmosphere. The tube was sealed and heated to 100 °C with stirring under nitrogen for **24 hours** (reaction progress monitored by TLC). After cooling to ambient temperature, the mixture was partitioned between EtOAc (15 mL) and water (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure.

The crude residue was purified by flash column chromatography on silica gel, eluting with PE/EA (4:1, v/v) to afford the desired product **6ab** as a solid (86.7 mg, 87% yield).



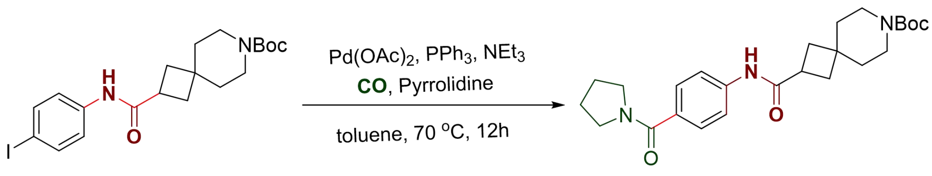
Chemical Formula: $C_{27}H_{34}N_2O_5S$
Molecular Weight: 498.64

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 8.20 (br, 1H), 7.80 (dd, *J* = 9.0, 2.1 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 3.37 – 3.19 (m, 4H), 3.11 (p, *J* = 8.6 Hz, 1H), 2.37 (s, 3H), 2.13 – 2.05 (m, 2H), 2.03 – 1.95 (m, 2H), 1.54 – 1.46 (m, 4H), 1.43 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 174.06, 154.92, 144.14, 142.92, 138.67, 135.68, 129.89, 128.62, 127.30, 119.41, 79.46, 40.53, 37.88, 36.07, 34.31, 33.95, 28.37, 21.49.

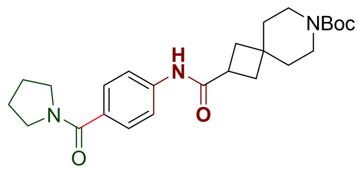
HRMS for $C_{27}H_{34}N_2O_5$ (ESI) $[M+H]^+$ calc.: 521.2081, found: 521.2091.

6.4 Experimental procedures for palladium-catalysed carbonylative amidation



***tert*-butyl 2-((4-(pyrrolidine-1-carbonyl)phenyl)carbamoyl)-7-azaspiro[3.5]-nonane-7-carboxylate (6ac)**

Following the general procedure of reported literature[8], to a seal tube were added aryl iodide **4a** (0.2 mmol, 1.0 equiv., 94.1 mg), pyrrolidine (1.5 equiv., 25 uL), $Pd(OAc)_2$(5 mol%, 2.3 mg), PPh_3(10 mol%, 5.3 mg), and triethylamine (2.0 equiv., 56 uL). The tube was flushed with carbon monoxide 5 atm, then sealed tightly and heated to 70 °C with stirring for 12 h. After cooling to room temperature, the reaction mixture was partitioned between EtOAc (15 mL) and water (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel, eluting with PE/EA (4:1, v/v) to afford the desired product **6ac** as a white solid (68.9 mg, 78%).



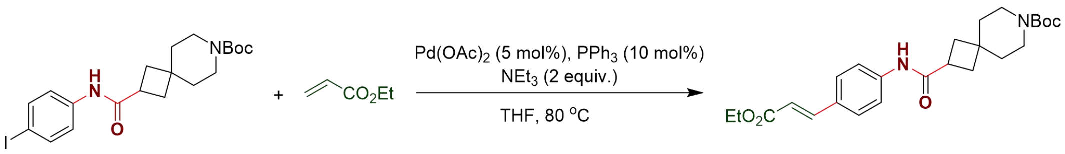
Chemical Formula: $C_{25}H_{35}N_3O_4$
Molecular Weight: 441.57

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm =8.82 (br, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 3.58 (t, J = 6.8 Hz, 2H), 3.41 (t, J = 6.5 Hz, 2H), 3.31 – 3.26 (m, 2H), 3.25 – 3.20 (m, 2H), 3.10 (p, J = 8.6 Hz, 1H), 2.12 – 2.04 (m, 2H), 1.97 – 1.88 (m, 4H), 1.86 – 1.80 (m, 2H), 1.53 – 1.46 (m, 4H), 1.41 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 174.04, 169.44, 154.86, 140.32, 131.54, 127.88, 118.97, 79.28, 49.67, 46.29, 40.66, 39.98, 37.87, 36.21, 34.32, 34.10, 33.85, 28.33, 26.30, 24.31.

HRMS for $C_{27}H_{34}N_2O_5$ (ESI) $[M+Na]^+$ calc.: 464.2520, found: 464.2519.

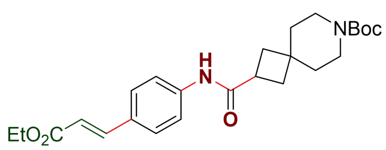
6.5 Experimental procedures for Heck reaction



4a **6d** **6ad**, 72%

***tert*-butyl (*E*)-2-((4-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)carbamoyl)-7-azaspiro-[3.5]nonane-7-carboxylate(6ad)**

According to the general method reported in the literature[9], A mixture of aryl iodide **4a** (0.2 mmol, 1.0 equiv., 94.1 mg), olefin (0.4 mmol, 43.5 uL), $Pd(OAc)_2$ (5 mol%, 2.3 mg), PPh_3 (10 mol%, 5.3 mg), NEt_3 (2 equiv., 56 uL), and THF (2 mL) in a Schlenk flask was stirred under air atmosphere at 80 °C for the desired time until complete consumption of starting material as monitored by TLC. After the mixture was poured into ether, then washed with water, extracted with EtOAc, dried by anhydrous Na_2SO_4, then filtered and evaporated under vacuum, the residue was purified by flash column chromatography (PE/EA = 10:1) to afford the corresponding coupling product **6ad** (63.8 mg, 72% yield).



Chemical Formula: $C_{25}H_{34}N_2O_5$
Molecular Weight: 442.56

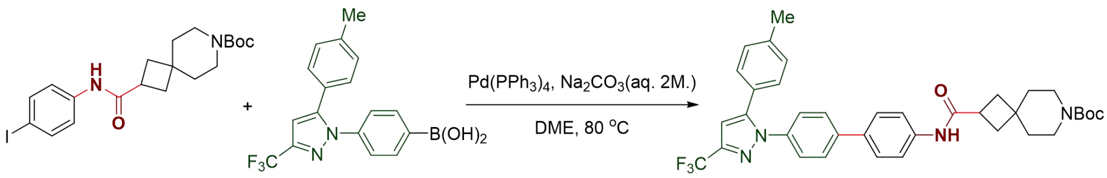
^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.79 (br, 1H), 7.64 – 7,61 (m, 1H), 7.58 (d, J = 8.9 Hz, 2H), 7.45 (d, J = 7.5 Hz, 2H), 6.34 (dd, J = 15.9, 1.2 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 3.39 – 3.30 (m, 2H), 3.29 – 3.22 (m, 2H), 3.11 (p, J = 8.6 Hz, 1H), 2.19 –

2.11 (m, 2H), 2.09 – 2.00 (m, 2H), 1.60 – 1.50 (m, 4H), 1.43 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 173.57, 167.18, 154.92, 143.89, 140.02, 129.94, 128.89, 119.51, 116.86, 79.43, 60.42, 40.62, 40.13, 37.91, 36.62, 34.44, 34.00, 28.37, 14.26.

HRMS for $C_{25}H_{34}N_2O_5$ (ESI) $[M+Na]^+$ calc.: 465.2360, found: 465.2365.

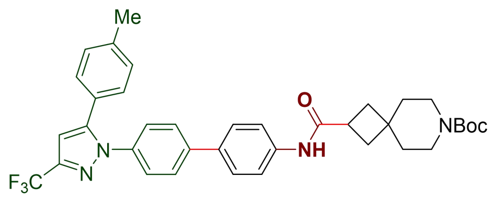
6.6 Experimental procedures for Pd-catalyzed Suzuki-Miyaura coupling



4a **1i** **6ae**, 75% yield

***tert*-butyl 2-((4'-(5-(p-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (6ae)**

Following the general experimental procedure reported previously [10], to a schlenk tube were added aryl iodide **4a** (0.2 mmol, 1.0 equiv., 94.1 mg), arylboronic acid (1.5 equiv., 103.9 mg), $Pd(PPh_3)_4$ (5 mol%, 11.6 mg), and anhydrous DME (2 mL). The mixture was degassed with nitrogen for 5 min, then 2 M aqueous sodium carbonate (1 mL) was added, and the tube was sealed. The reaction was heated to 80 °C with stirring under nitrogen atmosphere until complete. After cooling to room temperature, the reaction mixture was partitioned between EtOAc (15 mL) and water (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel, eluting with PE/EA (4:1, v/v) to afford the desired product **6ae** as a white solid (75% yield).



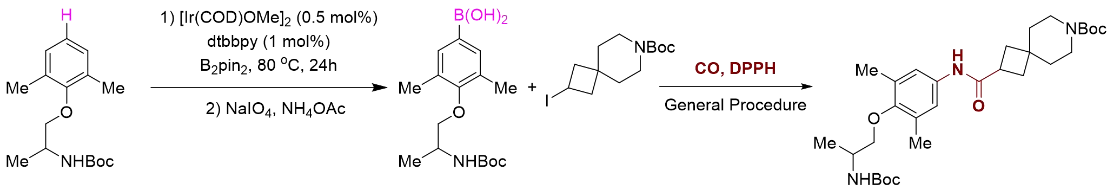
Chemical Formula: $C_{37}H_{39}F_3N_4O_3$
Molecular Weight: 644.74

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.72 (br, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.54 – 7.47 (m, 4H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.19 – 7.09 (m, 4H), 6.73 (s, 1H), 3.41 – 3.33 (m, 2H), 3.32 – 3.25 (m, 2H), 3.12 (p, *J* = 8.5 Hz, 1H), 2.34 (s, 3H), 2.20 – 2.13 (m, 2H), 2.05 (t, *J* = 10.5 Hz, 2H), 1.63 – 1.53 (m, 4H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 173.52, 154.92, 144.73, δ 142.07 (q, $J_{C–F}$ = 38.3 Hz), 140.35, 139.09, 138.09, 137.95, 135.17, 129.39, 128.60, 127.42, 127.15, 126.11, 125.56, δ 121.6 (q, $J_{C–F}$ = 269.0 Hz), 119.91, 105.34, 79.40, 37.96, 34.46, 34.39, 33.99, 28.38, 21.22.

HRMS for $C_{37}H_{39}F_3N_4O_3$ (ESI) $[M+Na]^+$ calc.: 667.2866, found: 667.2874.

6.7 Experimental procedures for selective C-H bond borylation and amidation



***tert*-Butyl**

(1-(2,6-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)-propan-2-yl)carbamate (6af).

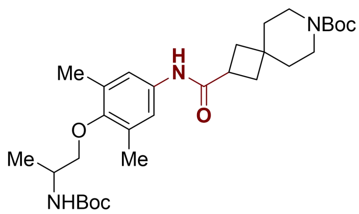
According to the literature[11-12], to a 25 mL of stirred Schlenk tube were added N Boc-Mexiletine (559 mg, 2 mmol), B_2pin_2 (315 mg, 1.24 mmol), $[Ir(COD)OMe]_2$ (6.63 mg, 0.01 mmol), 4,4'-Bis(*t*-butyl)-2,2'-bipyridine (5.36 mg, 0.02 mmol) and dry THF (10 mL) under nitrogen. The tube was screw capped and heated to 80 °C (oil bath). After stirring for 24 h, the reaction was cooled to room temperature. The reaction mixture was then diluted with EtOAc (100 mL), filtered through a pad of

Celite and concentrated. The residue was purified with silica gel chromatography (DCM/ EA = 10:1) to give aryl boronate ester **6af** (535 mg, 66% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.48 (s, 2H), 4.88 (br, 1H), 3.99 (br, 1H), 3.79 (br, 1H), 3.69 (dd, J = 9.0, 3.5 Hz, 1H), 2.26 (s, 6H), 1.46 (s, 9 H), 1.37 (d, J = 6.8 Hz, 3 H), 1.33 (s, 12 H).

(4-(2-((*tert*-butoxycarbonyl)amino)propoxy)-3,5-dimethylphenyl)boronic acid (6af-1).

To a 25 mL of Schlenk tube were added **6af** (365 mg, 0.90 mmol), NH_4OAc (416 mg, 5.4 mmol), $NaIO_4$ (1.16 g, 5.4 mmol), acetone (10 mL) and H_2O (5 mL) under argon. The reaction mixture was stirred at room temperature for 48 h. The reaction mixture was filtered with a pad of Cellit, and the filtrate was concentrated under reduced pressure. The residue was then extracted with EtOAc (3 x 10.0 mL, 1.0 mmol scale) and brine, and the combined organic layer was concentrated under reduced pressure and high vacuum to obtain the corresponding boronic acid **6af-1** (300 mg, 82% yield) as a white solid, which was used without purification.



Chemical Formula: $C_{30}H_{47}N_3O_6$
Molecular Weight: 545.72

***tert*-butyl 2-((4-(2-((*tert*-butoxycarbonyl)amino)propoxy)-3,5-dimethylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate(6af-2).**

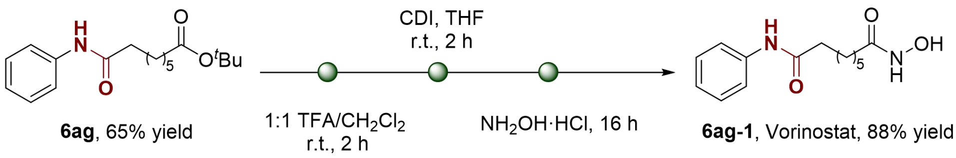
The reaction was carried out according to the general procedure on 0.2 mmol scale. The product **6af-2** (74.2 mg, 64% yield) as white solid was purified with silica gel chromatography (Hexane/ EtOAc/DCM = 10:1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.21 (br, 1H), 7.16 (s, 2H), 4.88 (br, 1H), 4.01 – 3.89 (m, 1H), 3.77 – 3.68 (m, 1H), 3.61 (dd, J = 9.0, 3.5 Hz, 1H), 3.39 – 3.31 (m, 2H), 3.29 – 3.22 (m, 2H), 3.05 (p, J = 8.5 Hz, 1H), 2.21 (s, 6H), 2.16 – 2.10 (m, 2H), 2.07 – 2.00 (m, 2H), 1.60 – 1.52 (m, 4H), 1.44 (s, 9H), 1.44 (s, 9H), 1.34 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 173.23, 155.32, 154.92, 151.47, 133.65, 131.31, 120.23, 79.35, 74.23, 46.62, 40.72, 40.04, 37.92, 36.37, 34.51, 34.32, 34.00, 28.40, 28.36, 17.81, 16.21.

HRMS for $C_{30}H_{47}N_3O_6$ (ESI) $[M+Na]^+$: calc.: 568.3357, found: 568.3350.

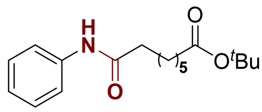
6.8 Experimental procedures for synthesis of bioactive and drug molecules.



6.8.1 synthesis of vorinostat

***tert*-butyl 8-oxo-8-(phenylamino)octanoate(6ag)**

The reaction was carried out according to the general procedure on 0.4 mmol scale. The product **6ag** (79.4 mg, 65% yield) as white solid was purified with silica gel chromatography (Hexane/ EtOAc/DCM = 20:1:1).



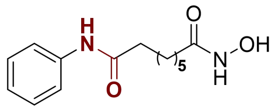
^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.60 (br, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 2.32 (t, *J* = 7.5 Hz, 2H), 2.20 (t, *J* = 7.5 Hz, 2H), 1.71 (p, *J* = 7.5 Hz, 2H), 1.57 (p, *J* = 7.5 Hz, 2H), 1.43 (s, 9H), 1.39 – 1.27 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 173.30, 171.49,138.03, 128.86, 124.04, 119.77, 80.05, 37.49, 35.40, 28.72, 28.60, 28.05, 25.36, 24.78.

HRMS for $C_{18}H_{27}NO_3$ (ESI) $[M+Na]^+$ calc.: 328.1883, found: 328.1887

***N*^{1}-hydroxy-*N*^{8}-phenyloctanediamide(6ag-1)**

Modified slightly from the reported literature procedure[13], *tert*-butyl 8-oxo-8-(phenylamino)octanoate (**6ag**) (0.4 mmol) was dissolved in 1:1 trifluoroacetic acid/DCM (1 mL) and the reaction mixture was stirred at room temperature for 2 h. The solvent was concentrated under reduced pressure to afford the desired carboxylic acid product. A mixture of obtained carboxylic acid (0.2 mmol), CDI (1.5 equiv.), and THF (1 mL) in a Schlenk flask was stirred under air atmosphere at room temperature for one hour, followed by the addition of hydroxylamine hydrochloride and continued reaction for 16 hours. The product **6ag-1** (46.5 mg, 88% yield) as colorless oil was purified with silica gel chromatography (DCM/MeOH = 30:1).



Chemical Formula: $C_{14}H_{20}N_2O_3$
Molecular Weight: 264.33

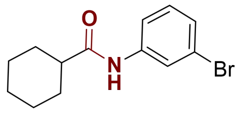
^{1}H NMR (500 MHz, DMSO-d_6) δ/ppm = 10.32 (br, 1H), 9.83 (br, 1H), 8.64 (br, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.9 Hz, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.95 (t, *J* = 7.4 Hz, 2H), 1.58 (p, *J* = 7.2 Hz, 2H), 1.50 (p, *J* = 7.3 Hz, 2H), 1.35 – 1.26 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ/ppm = 171.74, 169.62, 139.86, 129.16, 123.43, 119.52, 36.88, 32.76, 28.94, 25.56.

HRMS for $C_{14}H_{20}N_2O_3$ (ESI) $[M+Na]^+$ calc.: 287.1366, found: 287.1364.

6.8.2 synthesis of type I CDK8 inhibitor

***tert*-butyl 8-oxo-8-(phenylamino)octanoate(6ah)**



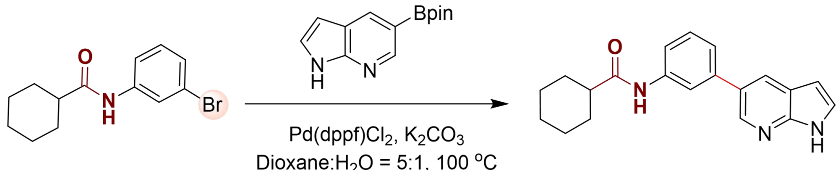
Chemical Formula: $C_{13}H_{16}BrNO$
Molecular Weight: 282.18

The reaction was carried out according to the general procedure on 0.4 mmol scale. The product **6ah** (83.5 mg, 74% yield) as white solid was purified with silica gel chromatography (Hexane/ EtOAc/DCM = 20:1:3).

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 7.81 (s, 1H), 7.61 (br, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.13 (t, J = 8.0 Hz, 1H), 2.23 (tt, J = 11.8, 3.6 Hz, 1H), 1.98 – 1.88 (m, 2H), 1.85 – 1.77 (m, 2H), 1.72 – 1.66 (m, 1H), 1.58 – 1.48 (m, 2H), 1.33 – 1.22 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 174.79, 139.36, 130.14, 126.96, 122.77, 122.49, 118.26, 46.35, 29.53, 25.54, 25.52.

HRMS for $C_{13}H_{16}BrNO$ (ESI) $[M+H]^+$ calc.: 282.0488, found: 282.0454.

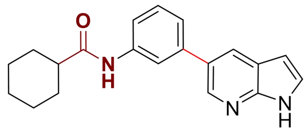


6ah, 74% yield **6ah-1**, type I CDK8 inhibitor, 86% yield

_N_-(3-(1_H_-pyrrolo[2,3-b]pyridin-5-yl)phenyl)cyclohexanecarboxamide (6ah-1)

A modified version of the reported procedure was employed[14], to a dry tube were added aryl bromide **6ah** (0.2 mmol, 1.0 equiv.), 7-azaindolyl boronate pinacol ester (0.24 mmol, 1.2 equiv.), ($Pd(dppf)Cl_2$, 5 mol%), and potassium carbonate (K_2CO_3, 2.0 equiv.). Anhydrous 1,4-dioxane and water (5:1, 2 mL) were added, and the mixture was degassed with nitrogen for 5 min. The tube was sealed tightly and heated to 100 °C with stirring under nitrogen atmosphere until the reaction was complete (monitored by TLC).

After cooling to room temperature, the reaction mixture was partitioned between EtOAc (15 mL) and water (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel, eluting with PE/EA (4:1, v/v) to afford the desired product **6ah-1** (type I CDK8 inhibitor) as a white solid (86% yield).



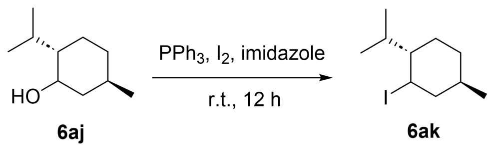
Chemical Formula: $C_{20}H_{21}N_3O$
Molecular Weight: 319.41

^{1}**H NMR** (500 MHz, DMSO-d_6) δ/ppm = 11.68 (br, 1H), 9.84 (br, 1H), 8.44 (d, J = 1.8 Hz, 1H), 8.15 – 8.07 (m, 1H), 7.97 (s, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.39 – 7.28 (m, 2H), 6.49 (s, 1H), 2.33 (tt, J = 11.7, 3.5 Hz, 1H), 1.85 – 1.78 (m, 2H), 1.77 – 1.70 (m, 2H), 1.65 – 1.58 (m, 1H), 1.48 – 1.37 (m, 2H), 1.30 – 1.18 (m, 3H).

^{13}**C NMR** (126 MHz, DMSO-d_6) δ/ppm = 175.00, 148.62, 141.87, 140.64, 140.06, 129.81, 128.74, 127.53, 126.50, 121.98, 120.21, 118.05, 118.03, 100.71, 45.49, 29.69, 25.94, 25.78..

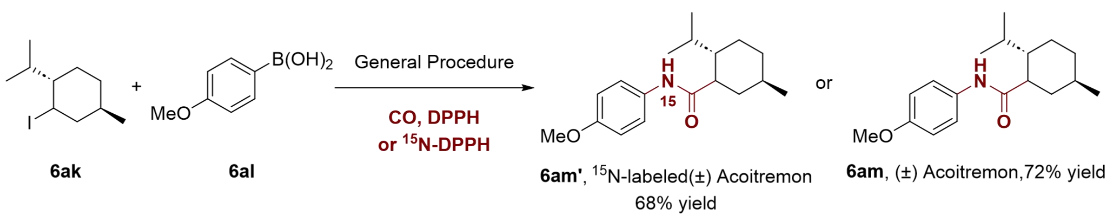
HRMS for $C_{20}H_{21}N_3O$ (ESI) $[M+H]^+$ calc.: 320.1757, found: 320.1762.

6.8.2 synthesis of type I CDK8 inhibitor

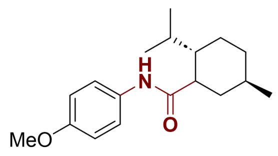


(1*S*,4*R*)-2-iodo-1-isopropyl-4-methylcyclohexane(6ak)

A round-bottom flask equipped with a stirring bar was charged with (878 uL, 5 mmol, 1 equiv.), Ph_3P (1.6 g, 6.0 mmol, 1.2 equiv.) and imidazole (0.41 g, 6.0 mmol, 1.2 equiv.). The flask was evacuated and refilled with Ar. CH_2Cl_2 (0.1 M) was added and the reaction was cooled to 0 °C with an ice-water bath. I_2 (1.5 g, 6.0 mmol, 1.2 equiv.) was added portion wise and then the cooling bath was removed. The reaction was stirred for 16 h at room temperature and then diluted with H_2O (40 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 60 mL). The crude residue was purified by flash column chromatography on silica gel, eluting with petroleum ether to afford the desired product **6aj** as a yellow oil (1.04 g, 78% yield).



***tert*-butyl 8-oxo-8-(phenylamino)octanoate(6am)**



Chemical Formula: $C_{18}H_{27}NO_2$
Molecular Weight: 289.42

The reaction was conducted according to the general procedure on a 0.20 mmol scale and stirred for 16 h under the standard conditions. Upon completion, the reaction mixture was concentrated under reduced pressure, and the resulting crude residue was purified by flash column chromatography (PE/EA/DCM = 10:1:1) to afford **6am** (41.7 mg, 72% yield) and **6am'** (39.6 mg, 68% yield), both isolated as white solids.

^{1}H NMR (500 MHz, $CDCl_3$) δ/ppm = 6.79 (d, *J* = 8.9 Hz, 2H), 6.59 (d, *J* = 8.9 Hz, 2H), 3.75 (s, 3H), 3.24 (dd, *J* = 11.9, 3.5 Hz, 1H), 2.84 (dd, *J* = 11.9, 7.7 Hz, 1H), 2.02 (td, *J* = 6.9, 2.7 Hz, 1H), 1.90 – 1.83 (m, 1H), 1.78 – 1.73 (m, 1H), 1.71 – 1.66 (m, 1H), 1.60 – 1.50 (m, 1H), 1.42 – 1.32 (m, 1H), 1.13 – 1.00 (m, 2H), 0.94 – 0.90 (m, 6H), 0.92 – 0.83 (m, 1H), 0.80 (d, *J* = 6.9 Hz, 3H).

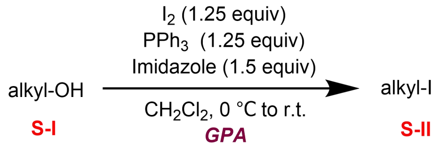
^{13}C NMR (126 MHz, $CDCl_3$) δ/ppm = 151.81, 143.09, 114.89, 113.89, 55.82, 48.00, 45.38, 40.26, 38.86, 35.16, 32.64, 26.68, 24.24, 22.69, 21.55, 15.52.

HRMS for $C_{18}H_{27}NO_2$ (ESI) $[M+Na]^+$ calc.: 312.19344, found: 312.1935.

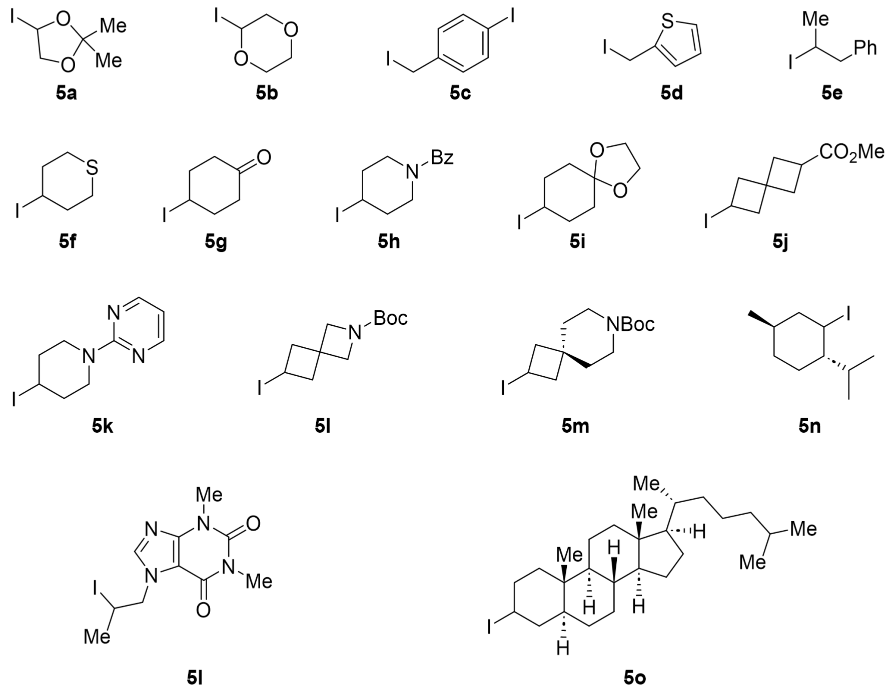
HRMS for $C_{18}H_{27}{}^{15}NO_2$ (ESI) $[M+H]^+$ calc.: 291.2085, found: 291.2090.

7. General procedure for substrate synthesis

7.1 General procedure A for the synthesis of alkyl halides.

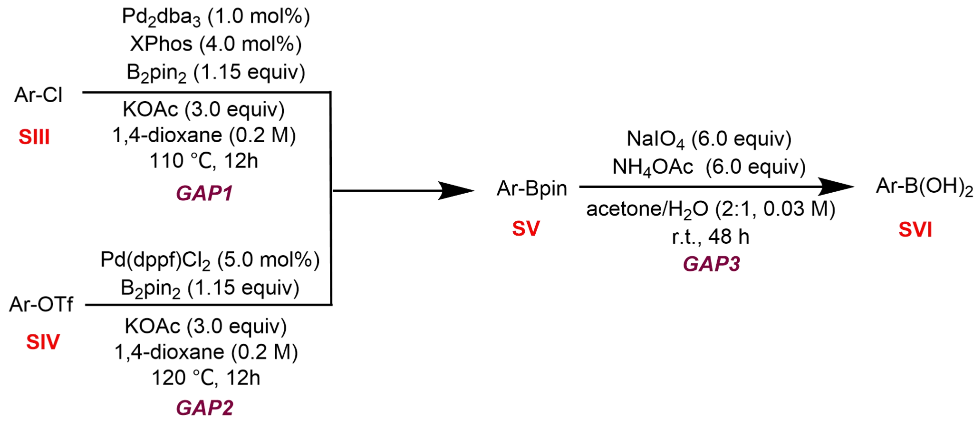


GPA*:* Add I_2 (10 mmol, 1.25 equiv.) in three portions to a mixture of alcohols (8.0 mmol, 1.0 equiv.), PPh_3 (10 mmol, 1.25 equiv.) and imidazole (12 mmol, 1.5 equiv.) in 40 mL anhydrous CH_2Cl_2, at 0 ˚C. Stir the reaction mixture at 0 ˚C for about 2 h before allowing warm to room temperature. After stir at room temperature for 4 –16 h, the mixture was quenched with 5% $Na_2S_2O_3$ aqueous solution 20 ml and extracted with CH_2Cl_2 (50 mL x 3). The organic phase was collected, dried over Na_2SO_4, and concentrated in vacuo. Further purification was performed by silica gel column chromatography using PE/EA solution as eluent.



5a-5o were prepared following the literature procedures.[16-17]

7.2 General procedure B for the synthesis of alkyl halides.



General procedure 1: borylation of chloride-containing drugs and natural products

GAP1: An oven-dried tube with a screw cap, containing a stirring bar, was introduced into the nitrogen-filled glovebox. Subsequently added $Pd_2(dba)_3$ (1.0 mol%), XPhos (4.0 mol%), B_2pin_2 (1.15 equiv.), KOAc (3.0 equiv.), dry 1,4-dioxane (0.2 M) and **SIII** (1.0 equiv.) into the tube. The tube was taken out of the glovebox and immediately placed in a pre-heated 110 ˚C aluminum heating block for 12 hours under stirring. The reaction was cooled to room temperature and extracted with DI water and EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure, and the crude residue was purified by flash column chromatography (height of packing silica gel: 8.0–10.0 cm, dry loading, gradient elution) to obtain the desired product.

General procedure 2: borylation of trifluoromethylsulfonate-containing drugs and natural products

GAP2: An oven-dried tube with a screw cap, containing a stirring bar, was introduced into the nitrogen-filled glovebox. Subsequently added $Pd(dppf)Cl_2$ (5.0 mol%), B_2pin_2 (2.0 equiv.), KOAc (3.0 equiv.), dry 1,4-dioxane (0.2 M) and **SIV** (1.0 equiv.) into the tube. The tube was taken out of the glovebox and immediately placed in a pre-heated 120 ˚C aluminum heating block for 12 hours under stirring. The reaction was cooled to room temperature and filtered through a Celite pad, which was washed with EtOAc. The filtrate was concentrated under reduced pressure, and the crude residue was purified by flash column chromatography (height of packing silica gel: 8.0 – 10.0 cm, dry loading, gradient elution) to obtain the desired product.

General procedure 3: hydrolysis of boronic esters

GAP3: Compound **SV** (1.0 equiv.), $NaIO_4$ (6.0 equiv.), NH_4OAc (6.0 equiv.) and acetone/H_2O (2:1, 0.03 M) were subsequently added into a round-bottom flask containing a stirring bar. The reaction mixture was stirred at room temperature for 48 hours. The reaction mixture was filtered with a pad of Cellit, and the filtrate was concentrated under reduced pressure. The residue was then extracted with EtOAc (3 x 50 mL, 5.0 mmol scale) and brine, and the combined organic layer was concentrated under reduced pressure and high vacuum to obtain the corresponding boronic acid, which was used without purification.

Common arylboronic acids were purchased from Leyan, and complex arylboronic acids were synthesized according to the general procedure described above and literature reports.[18-20]

8. Supplementary references

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9. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra

Figure S7. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-iodophenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**4a**)

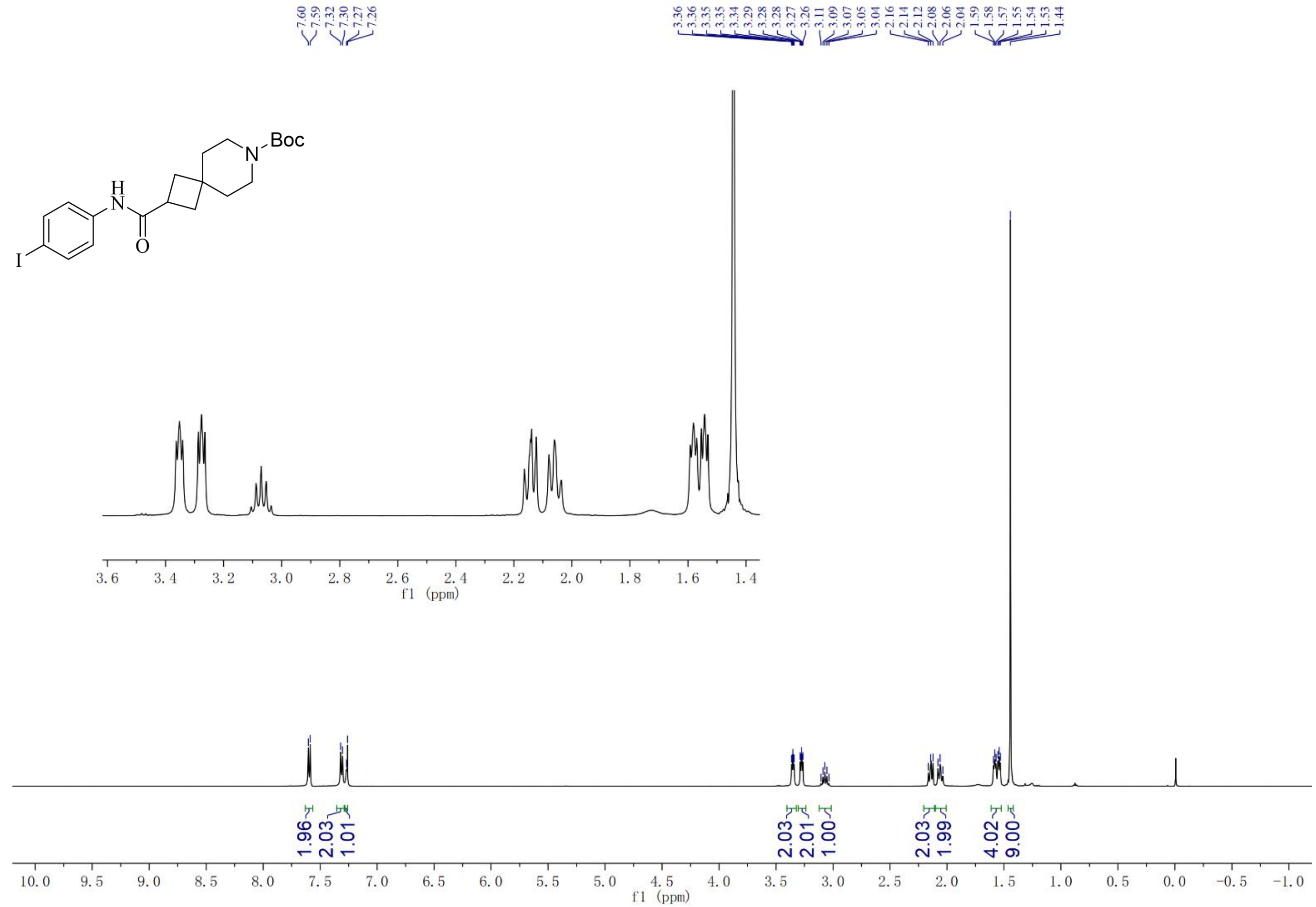


Figure S8. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-iodophenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**4a**)

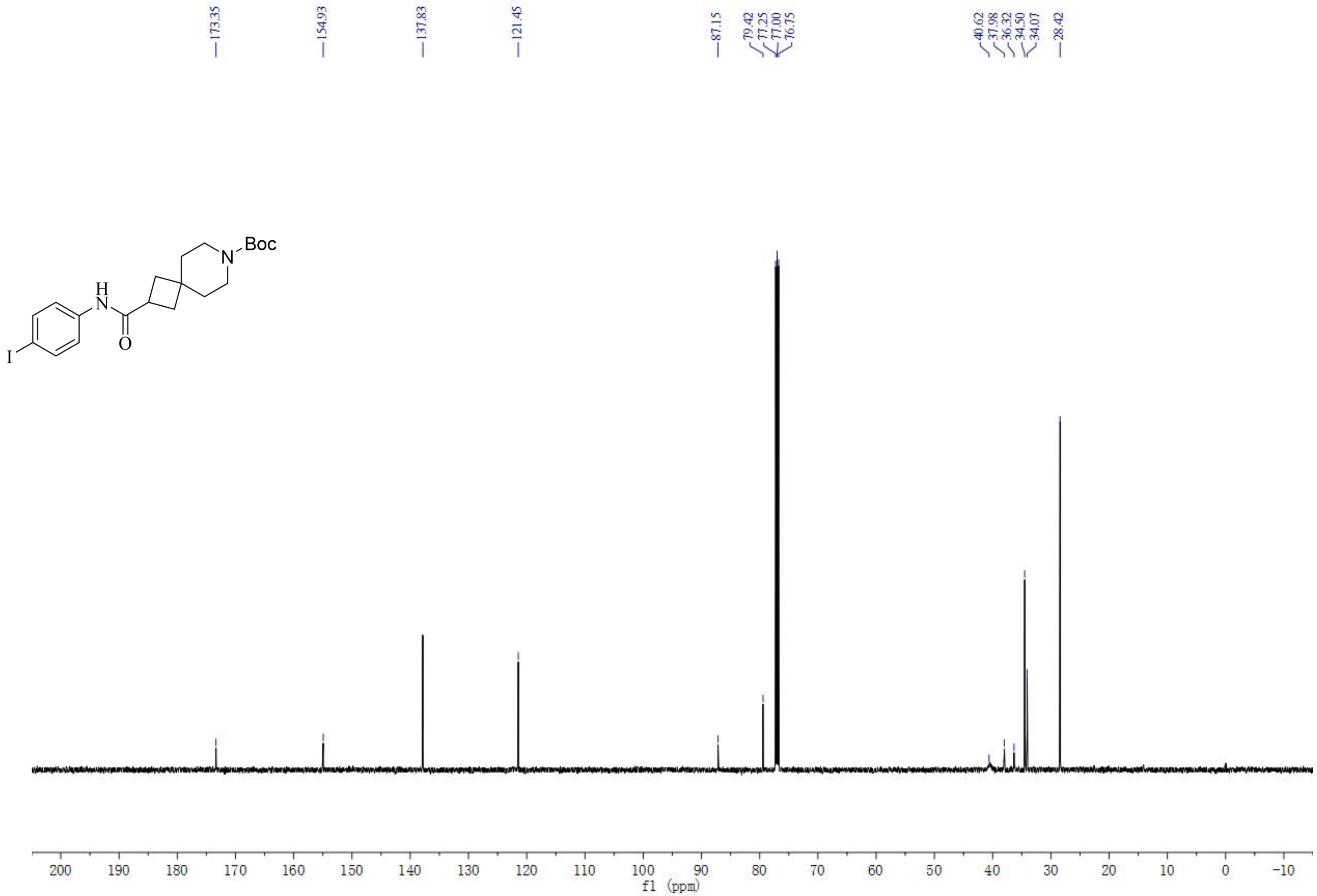


Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of *N*-(*p*-tolyl)cyclohexanecarboxamide (**4aa**)

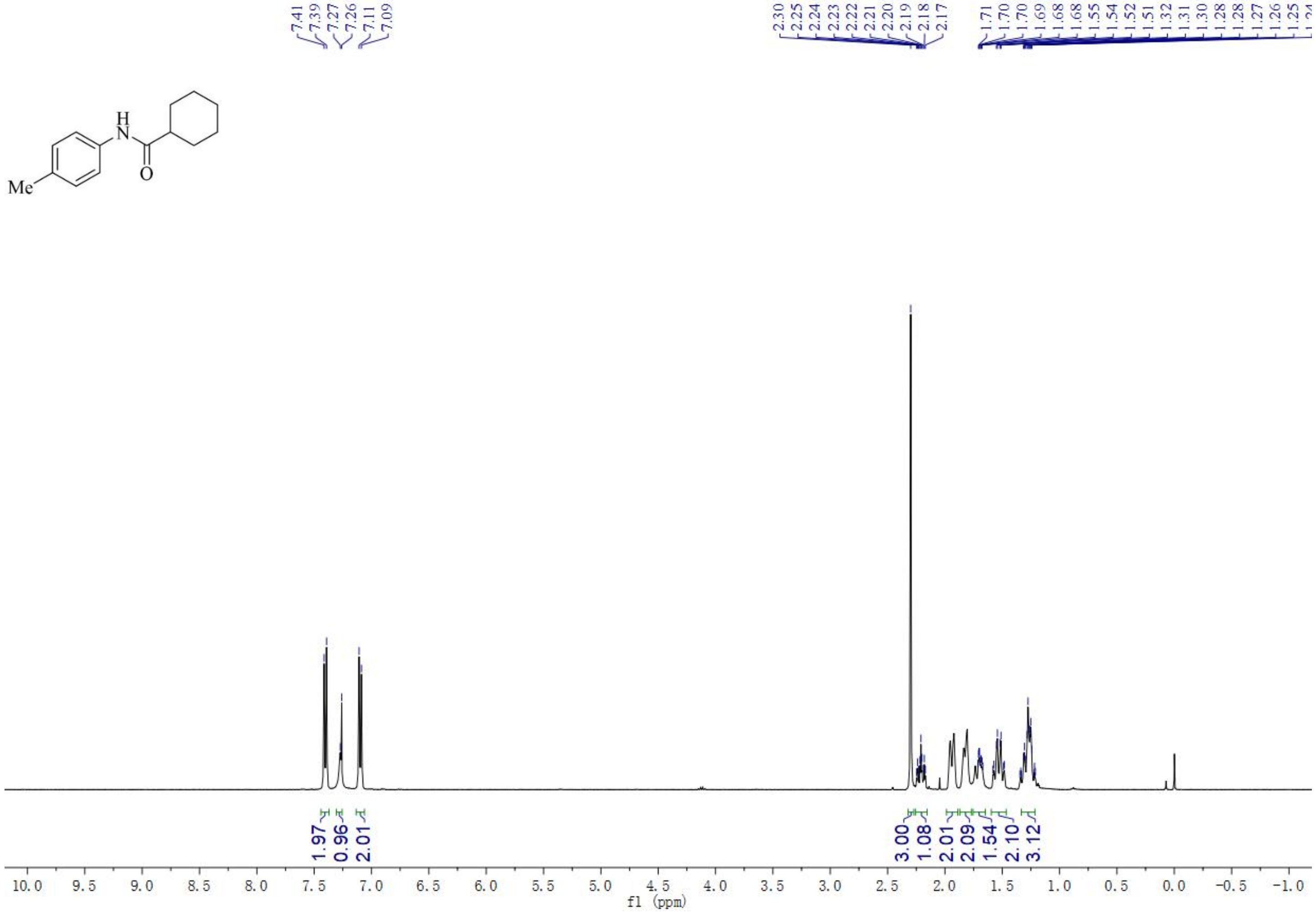


Figure S10. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)cyclohexanecarboxamide (**4aa**)

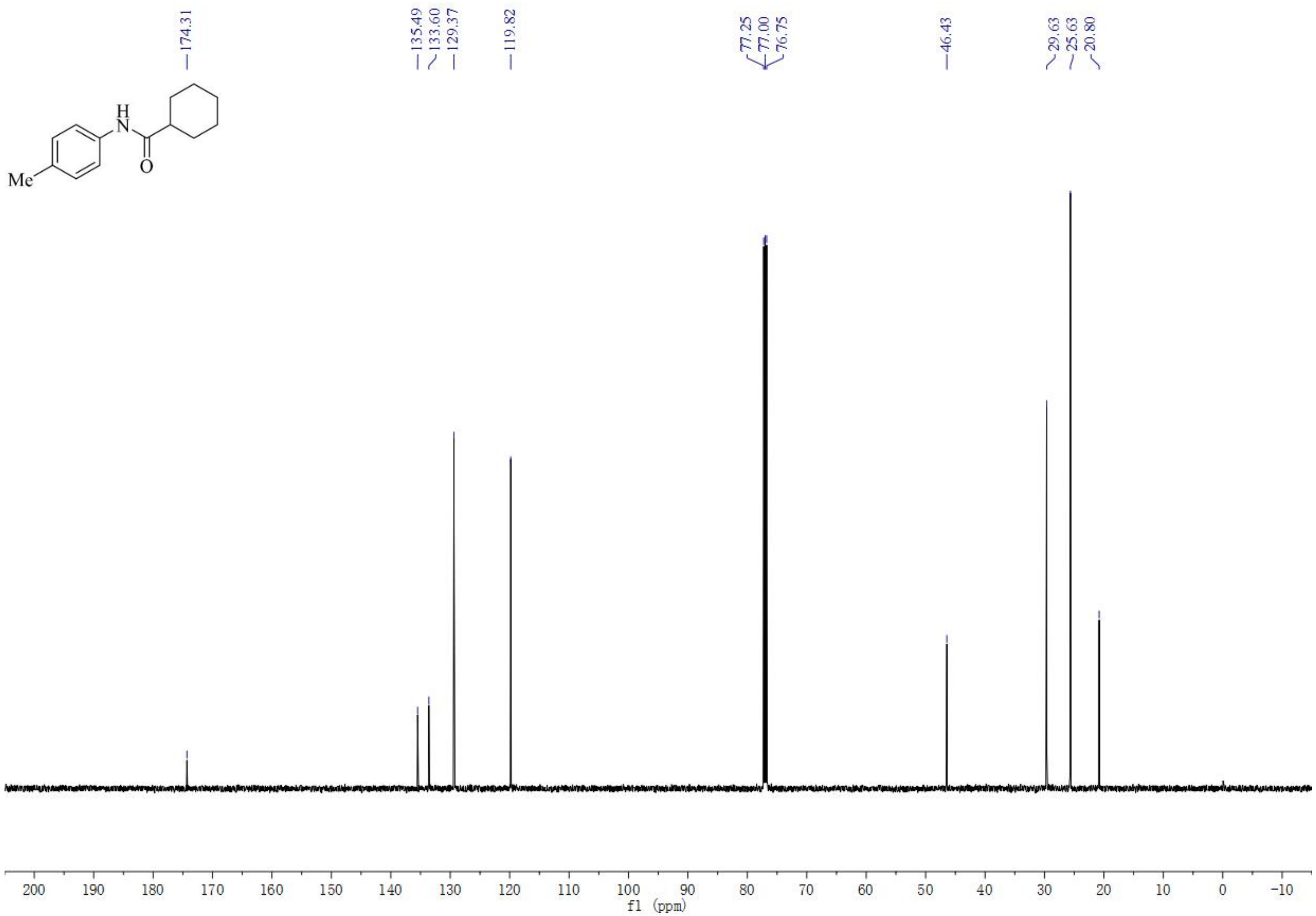


Figure S11. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(*tert*-butyl)phenyl)cyclohexanecarboxamide (**4ab**)

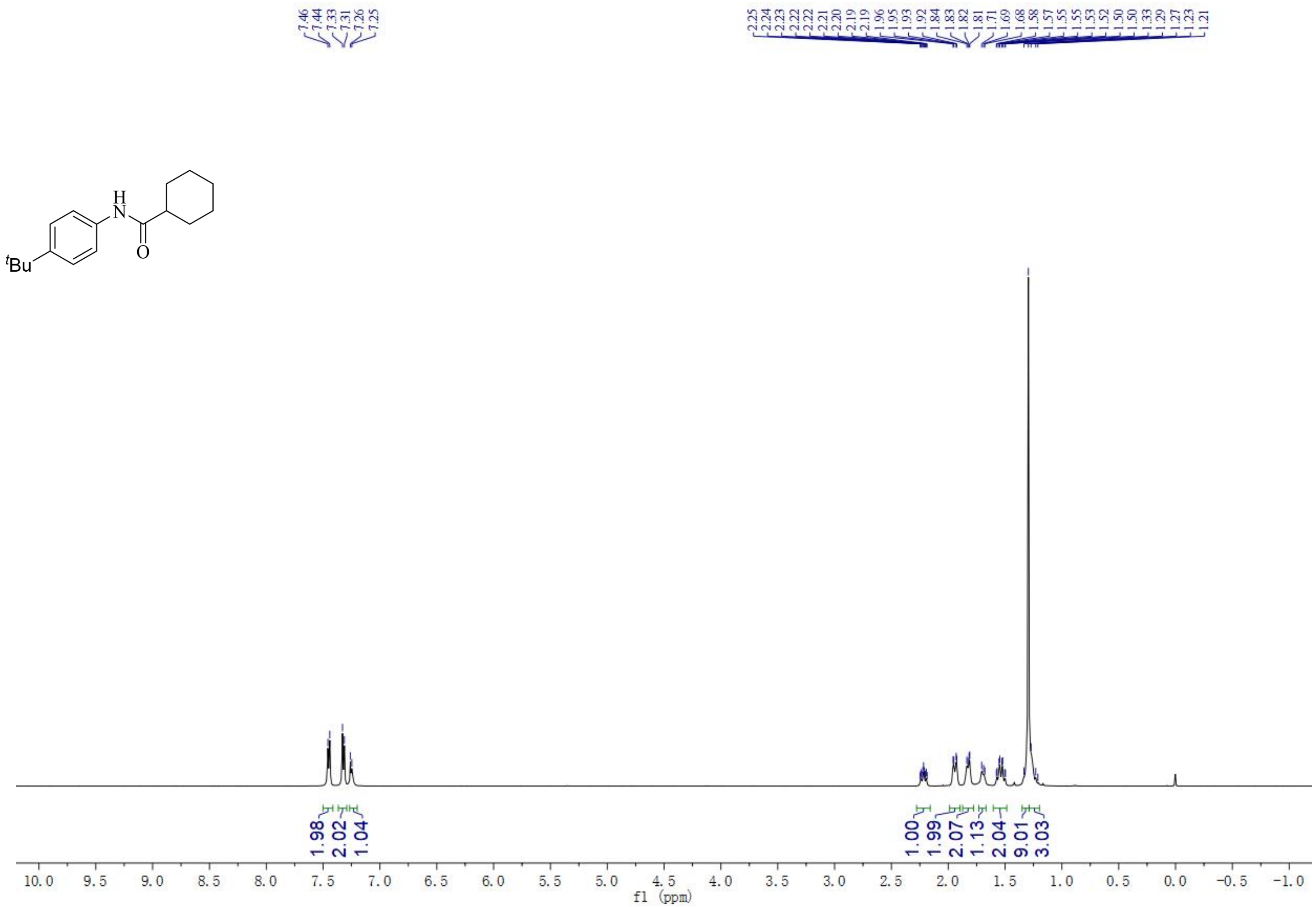


Figure S12. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *N*-(4-(*tert*-butyl)phenyl)cyclohexanecarboxamide (**4ab**)

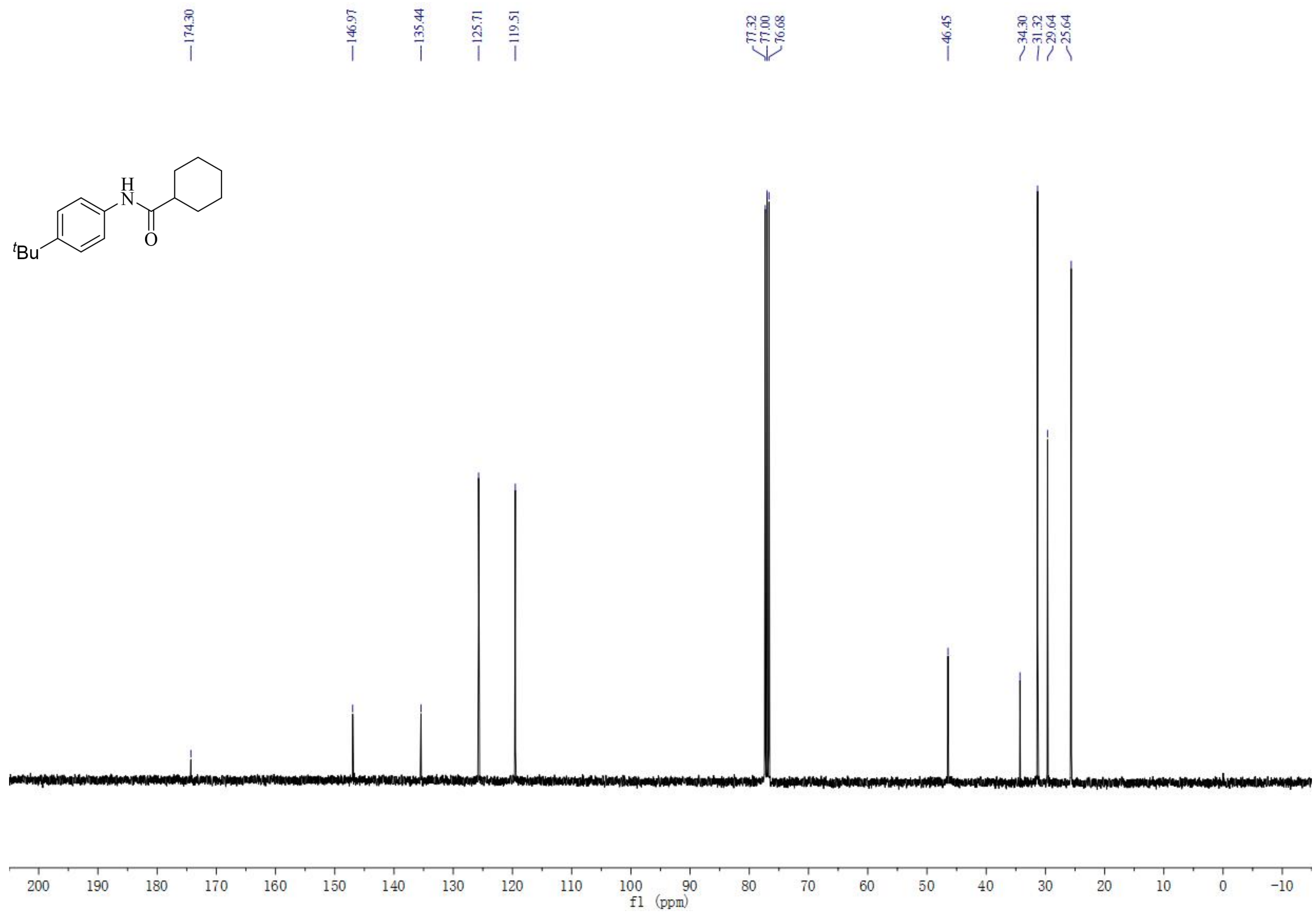


Figure S13. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-methoxyphenyl)cyclohexanecarboxamide (**4ac**)

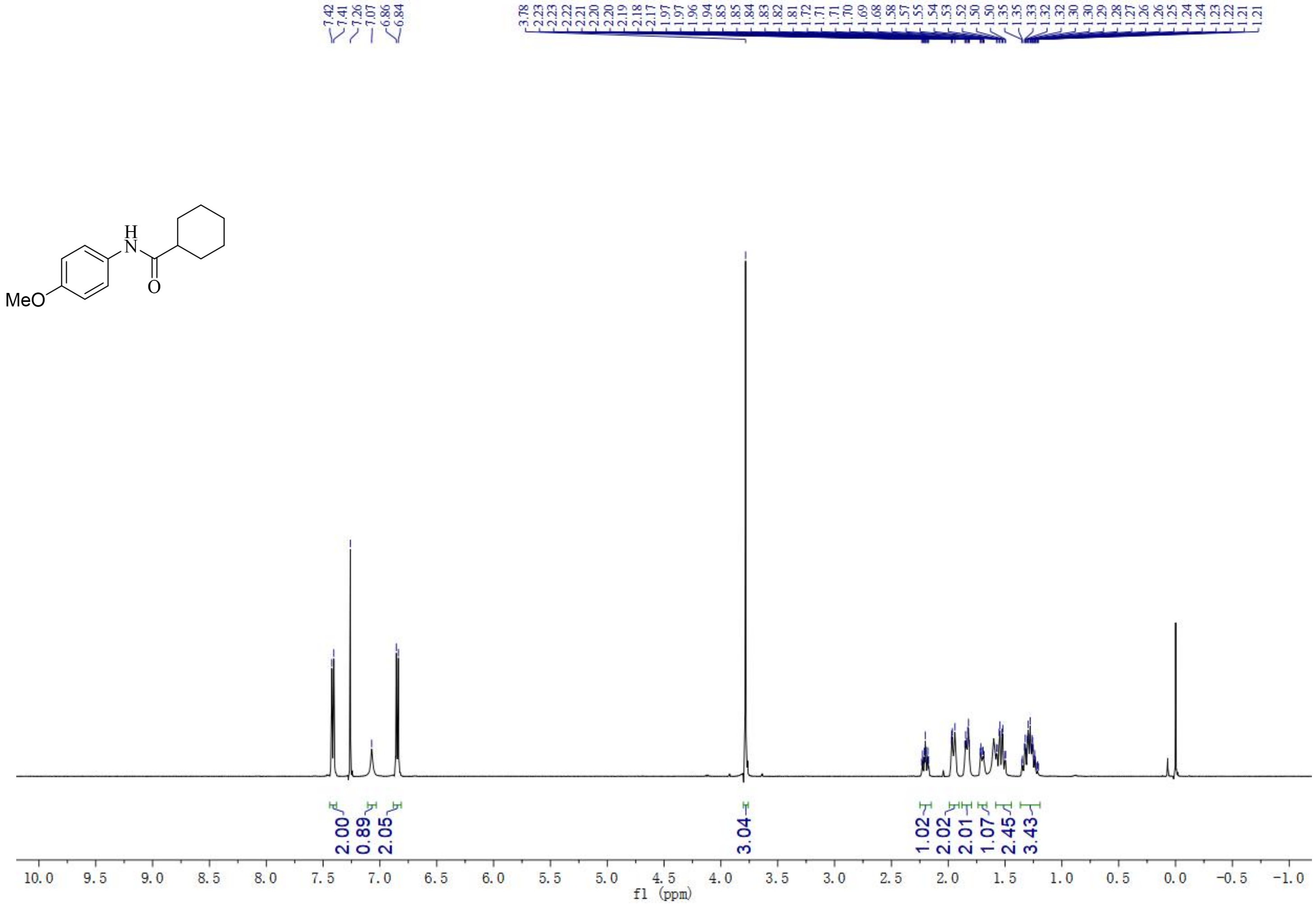


Figure S14. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *N*-(4-methoxyphenyl)cyclohexanecarboxamide (**4ac**)

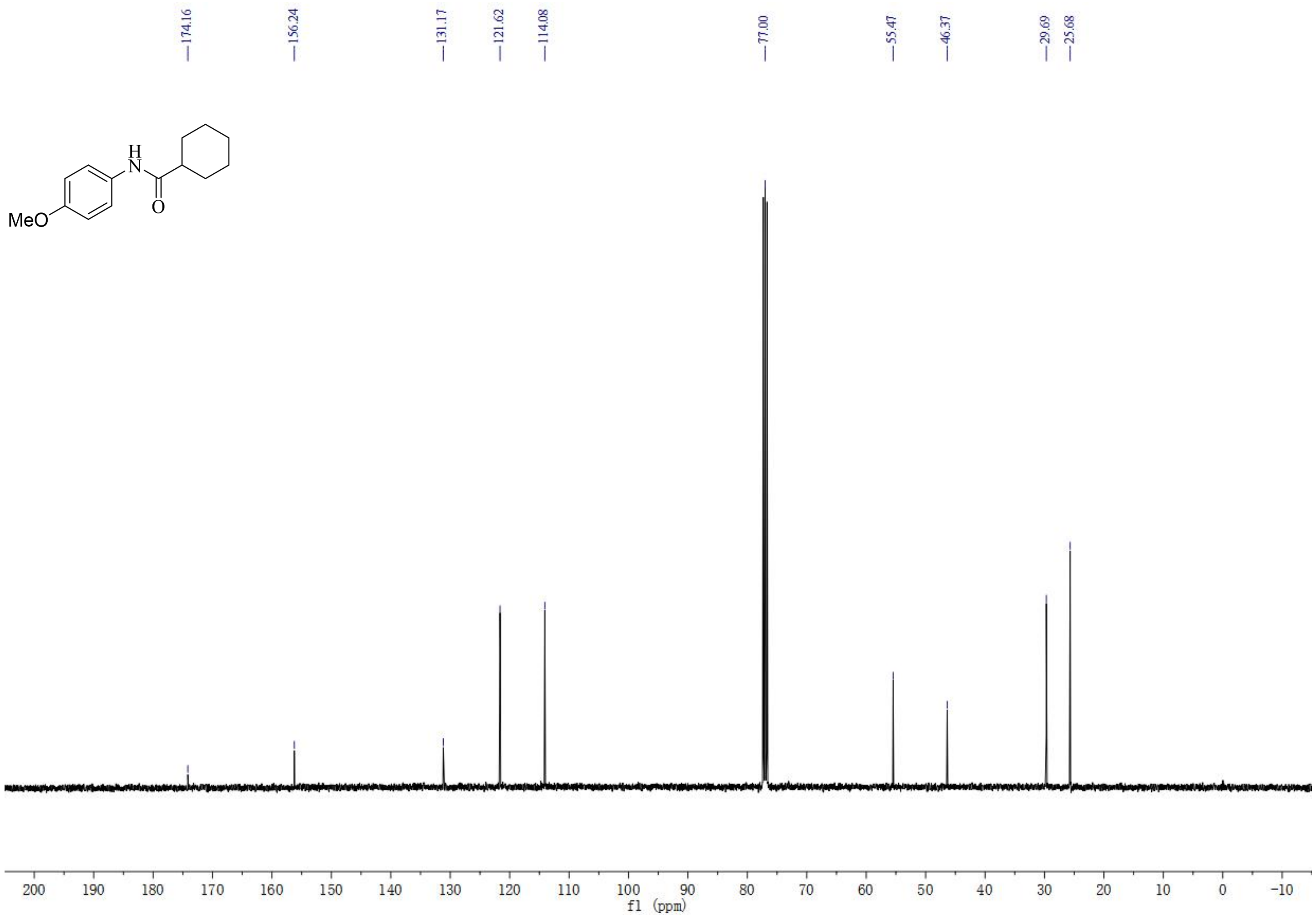


Figure S15. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-phenoxyphenyl)cyclohexanecarboxamide (**4ad**)

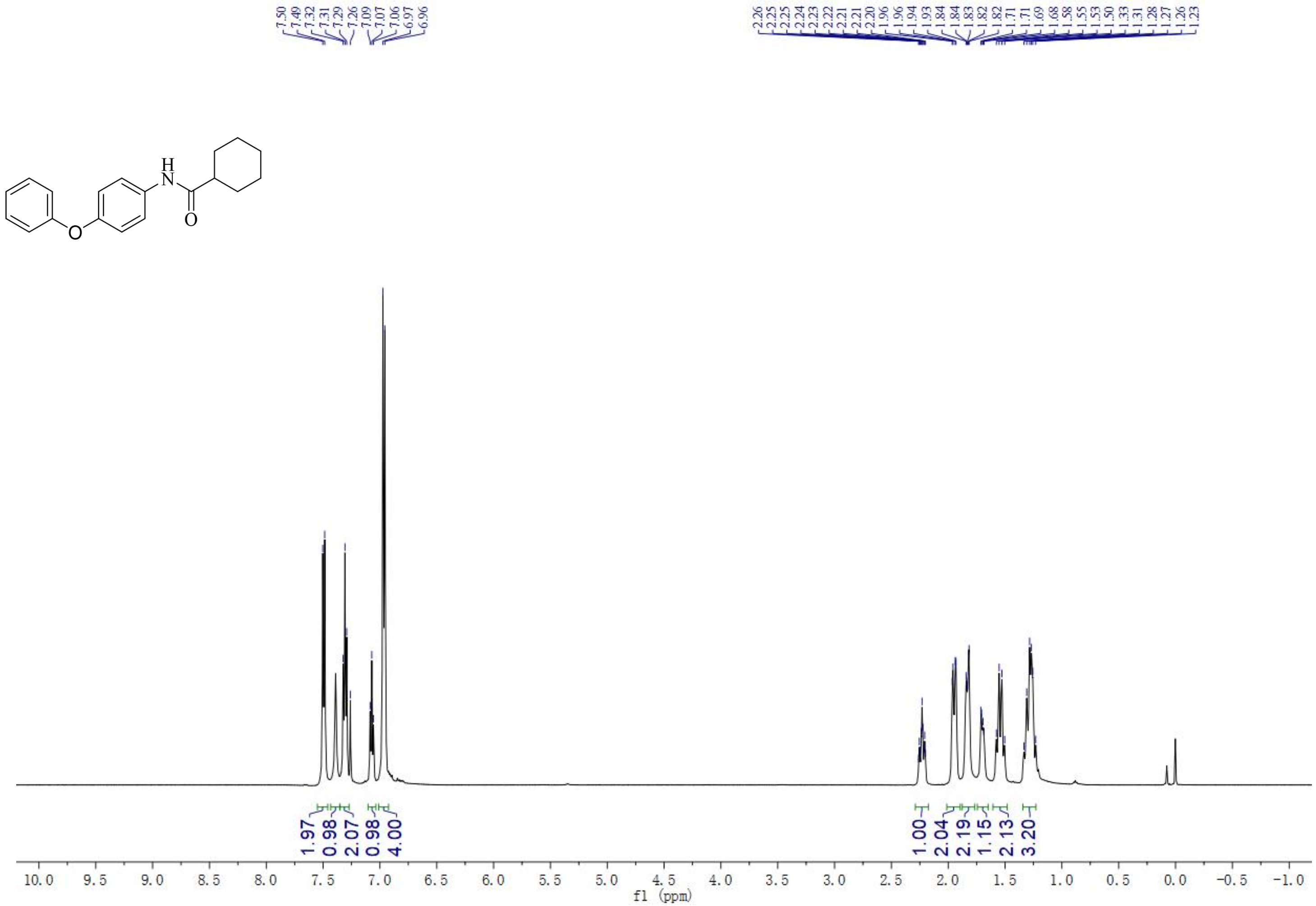


Figure S16. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-phenoxyphenyl)cyclohexanecarboxamide (**4ad**)

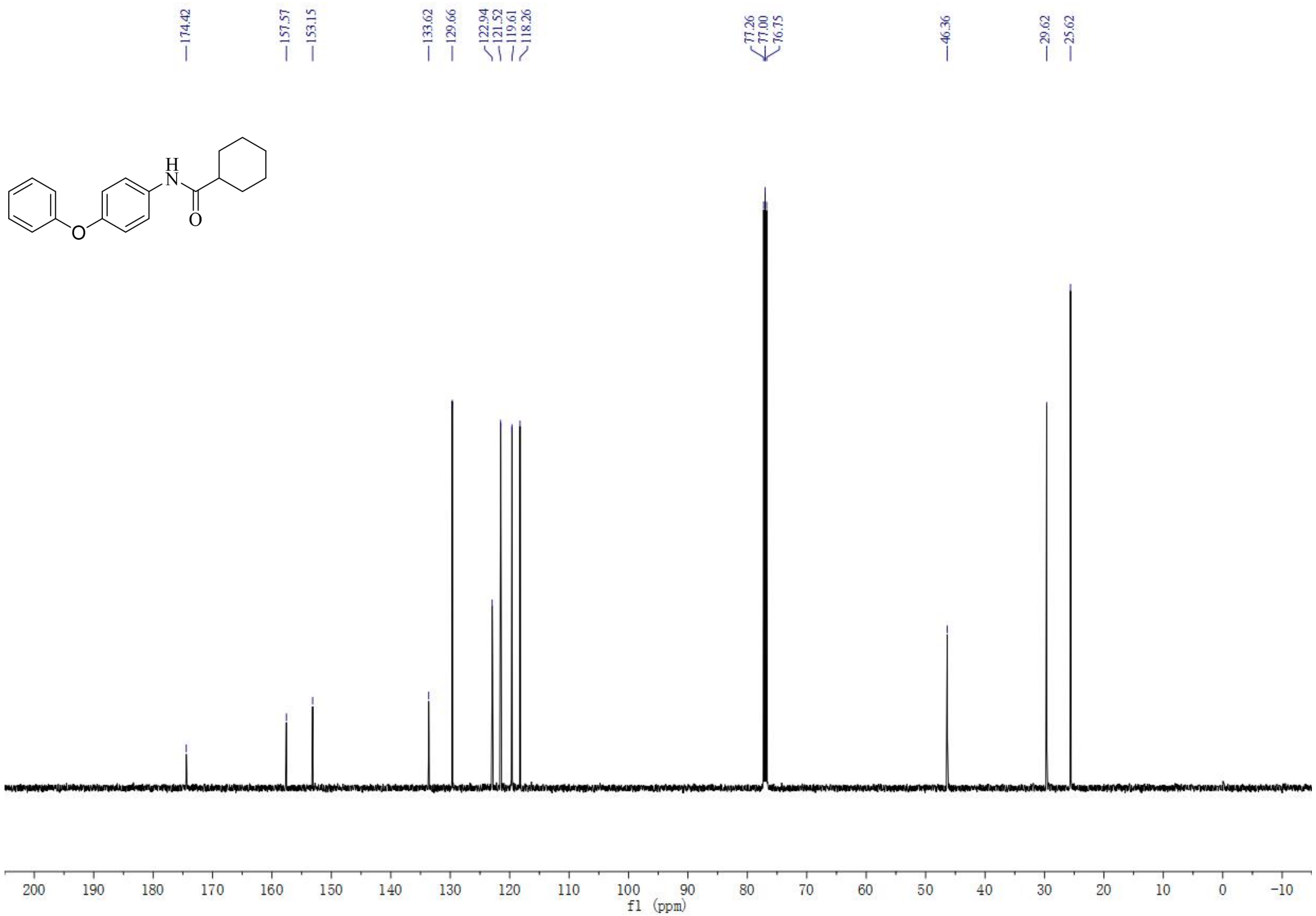


Figure S17. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(methylthio)phenyl)cyclohexanecarboxamide (**4ae**)

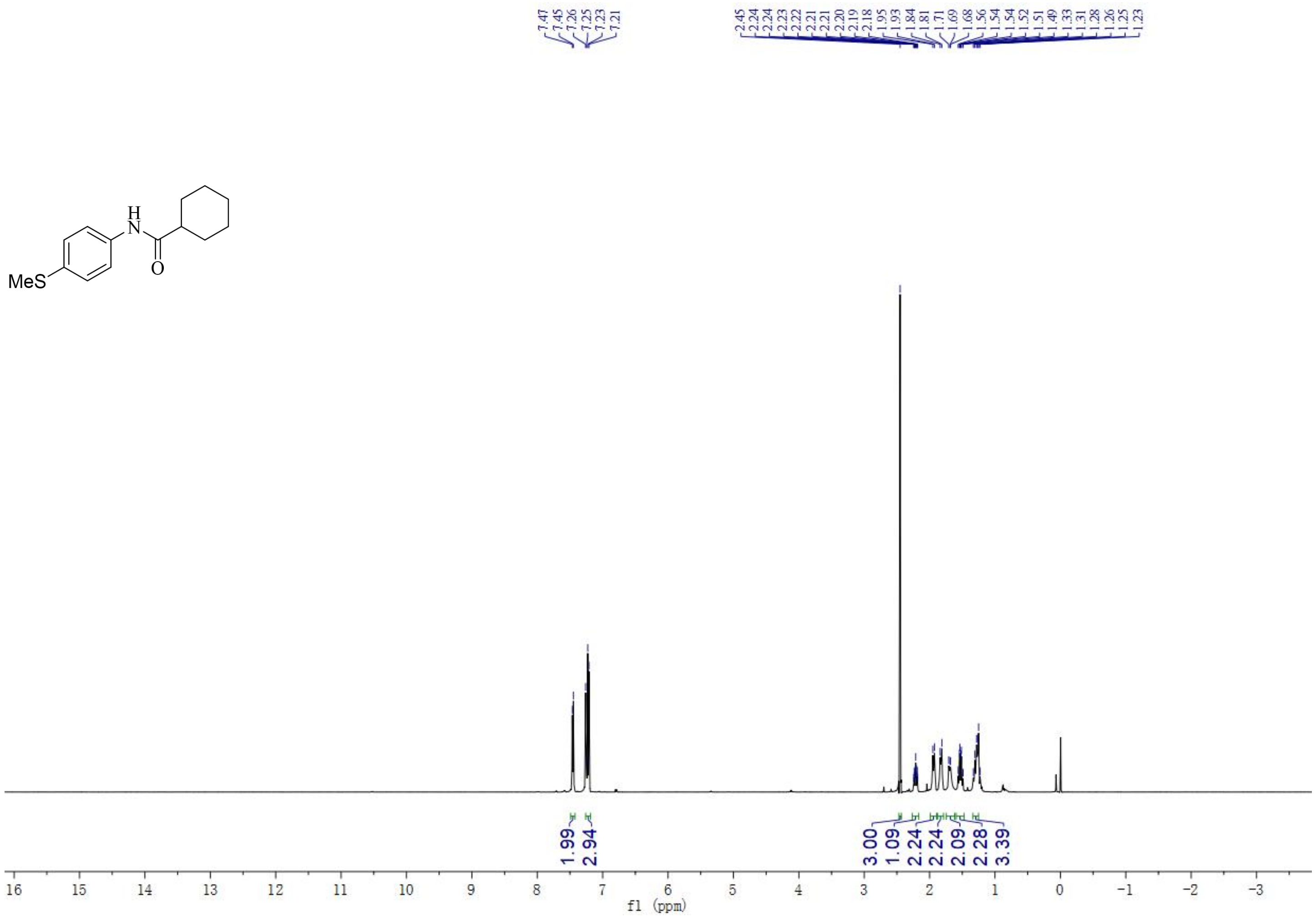


Figure S18. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(methylthio)phenyl)cyclohexanecarboxamide (**4ae**)

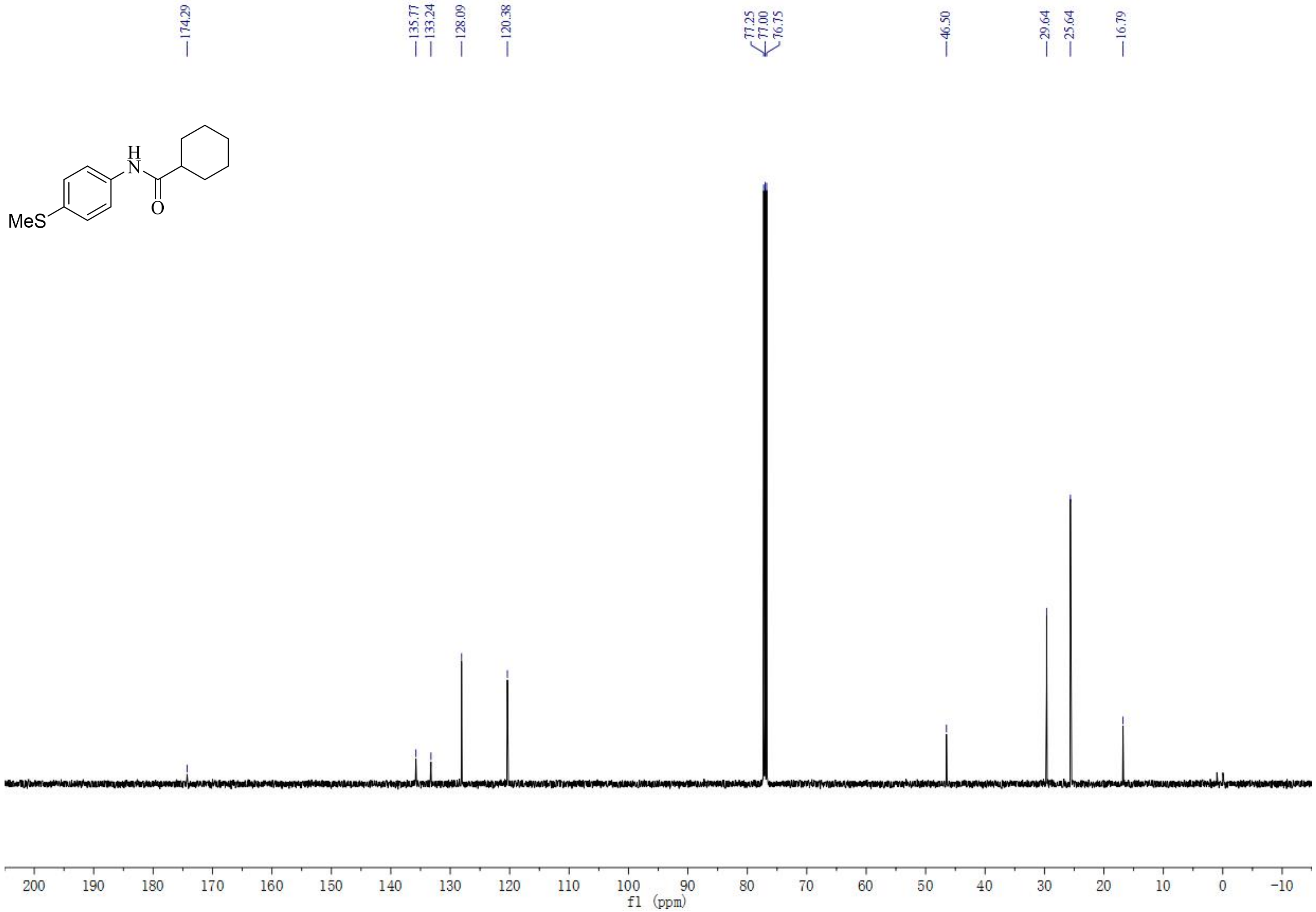
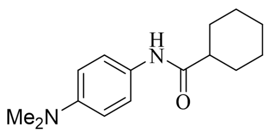


Figure S19. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(dimethylamino)phenyl)cyclohexanecarboxamide (**4af**)



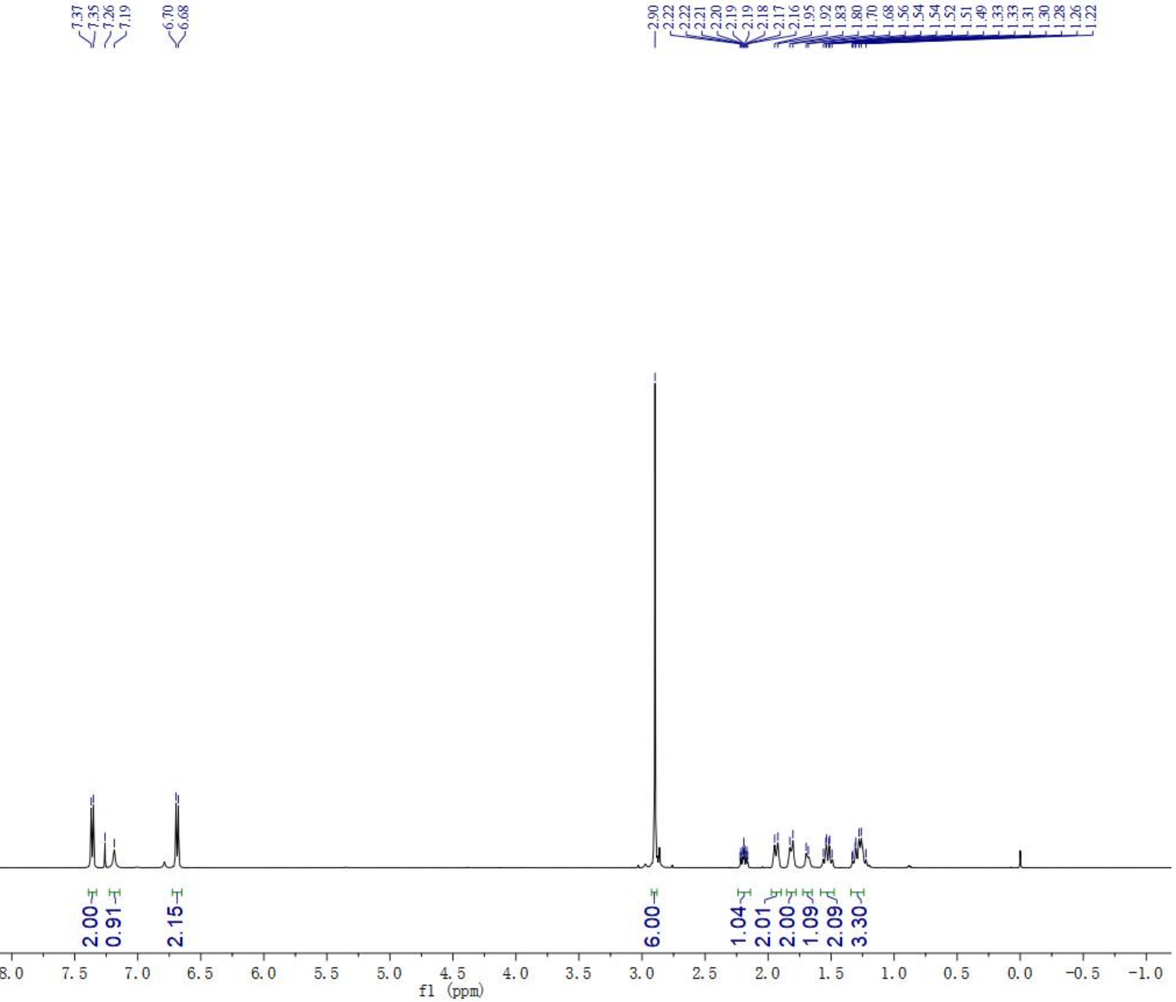


Figure S20. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(dimethylamino)phenyl)cyclohexanecarboxamide (**4af**)

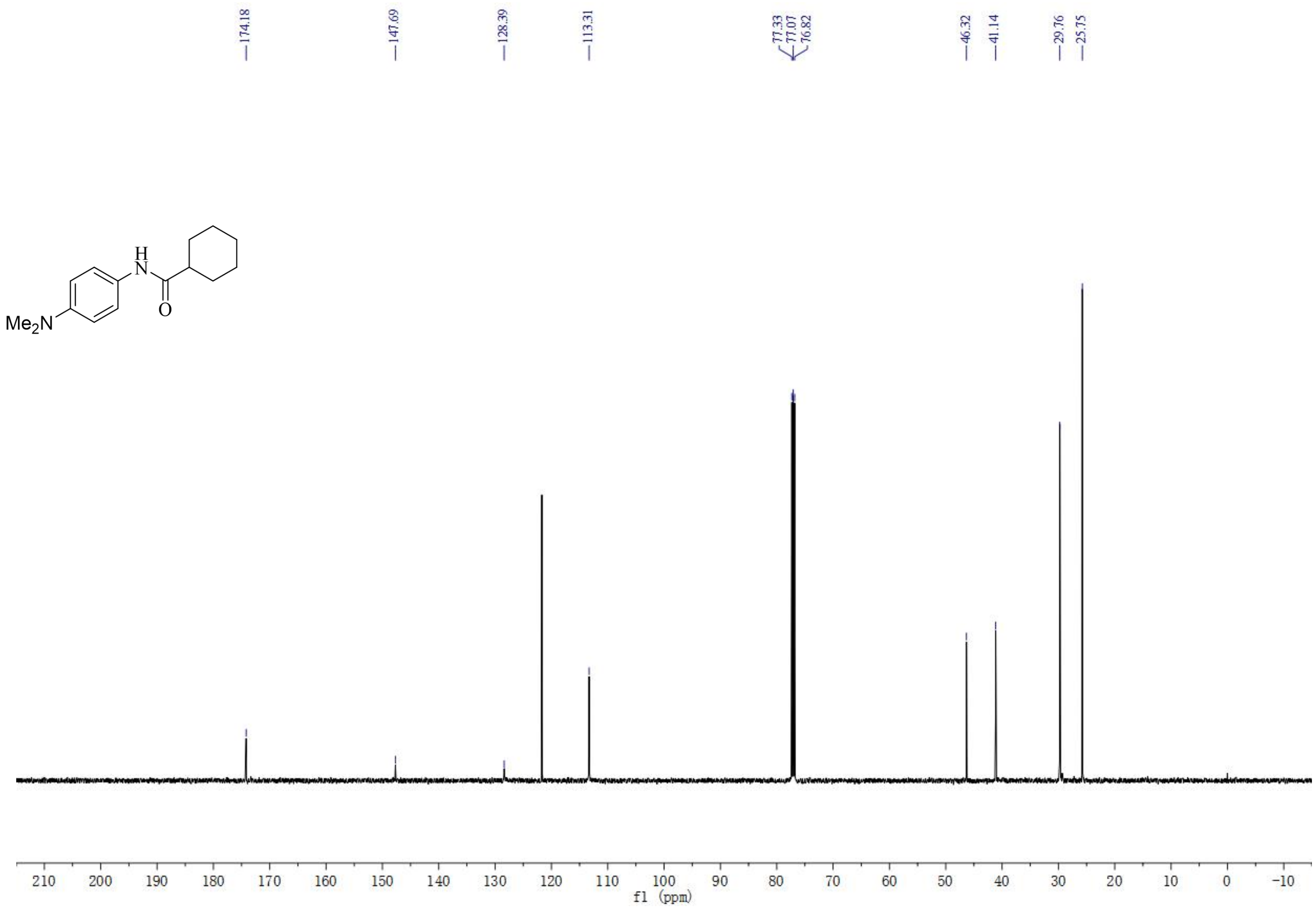


Figure S21. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) of *N*-phenylcyclohexanecarboxamide (**4ag**)

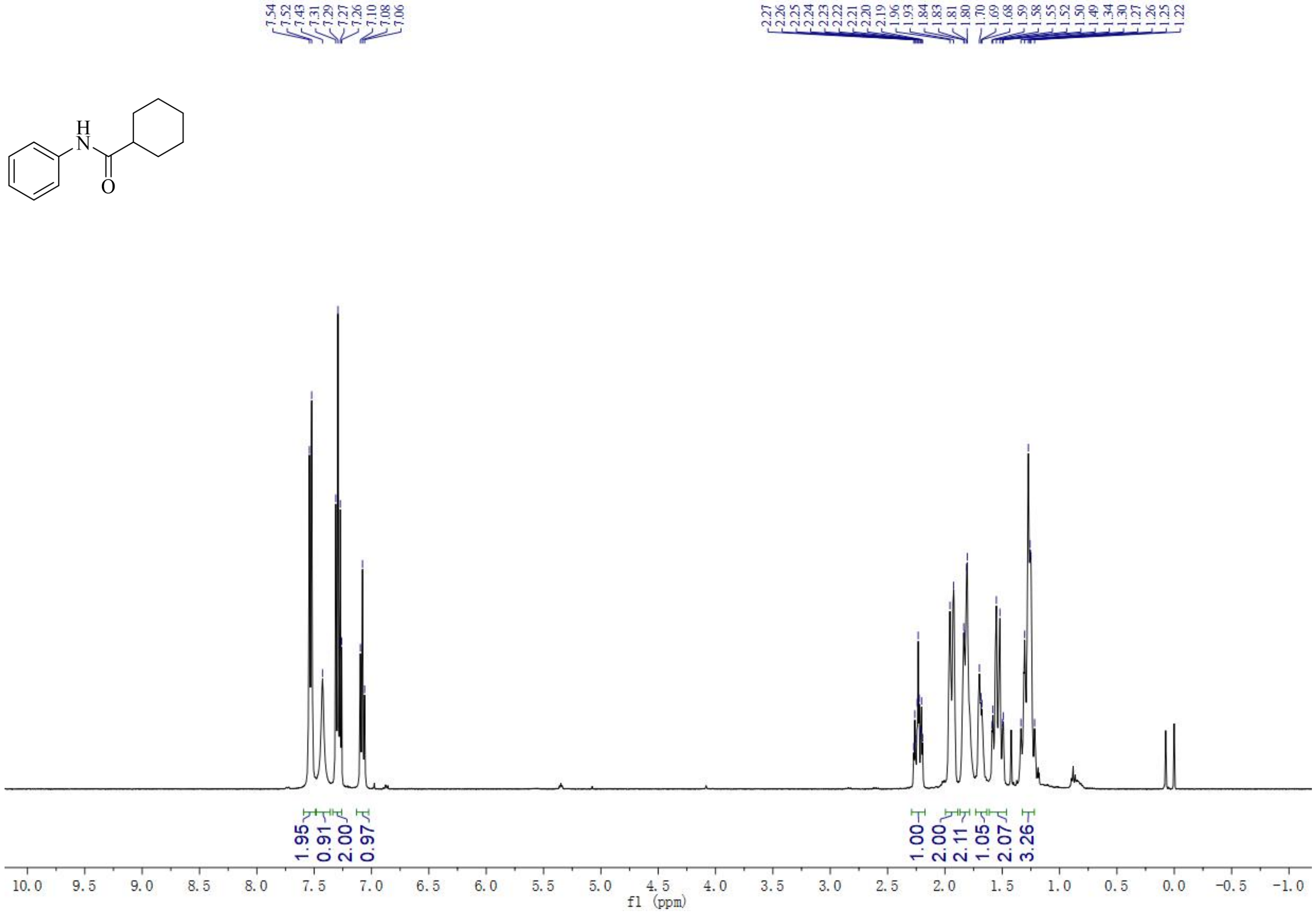


Figure S22. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *N*-phenylcyclohexanecarboxamide (**4ag**)

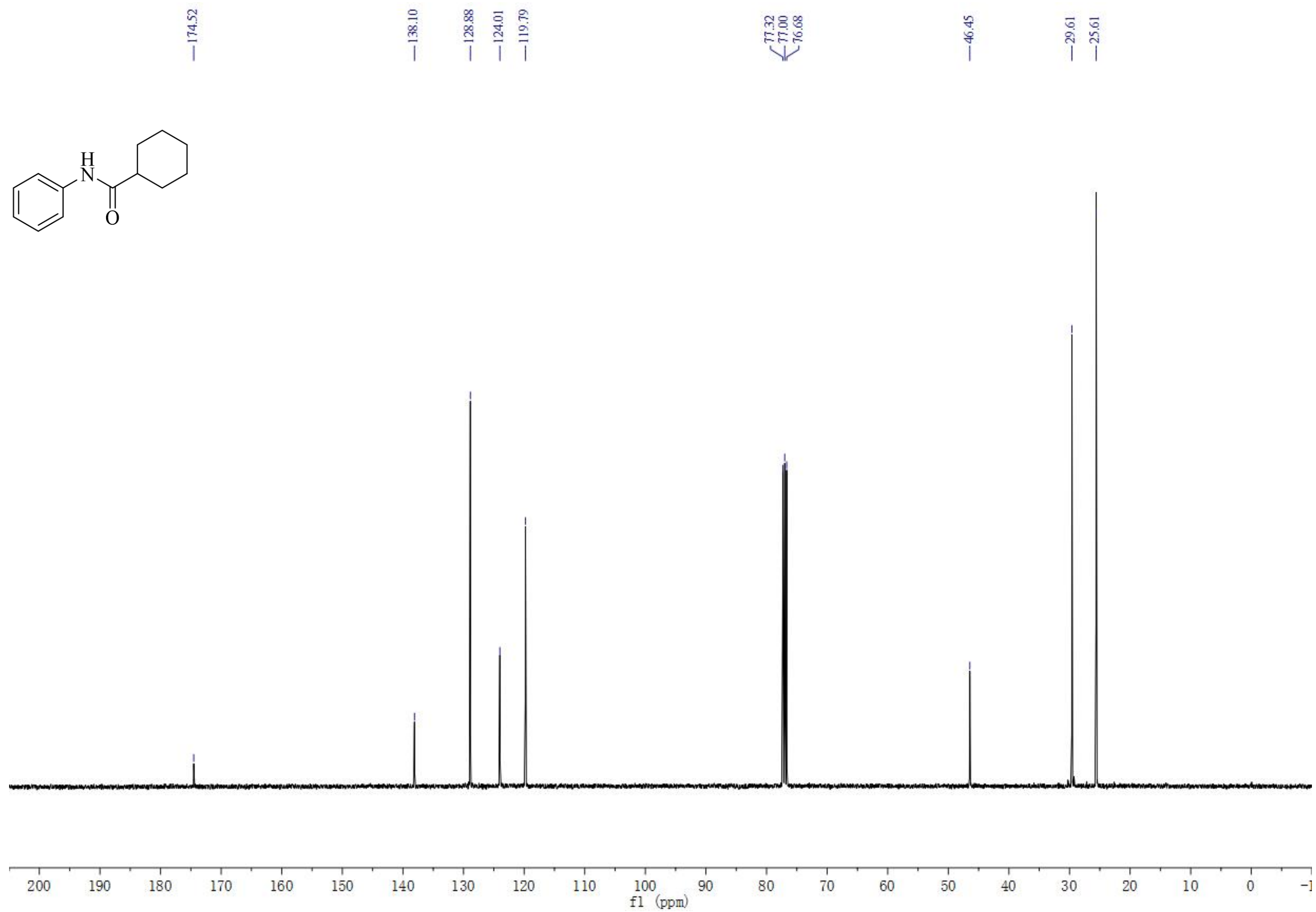


Figure S23. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(difluoromethoxy)phenyl)cyclohexanecarboxamide (**4ah**)

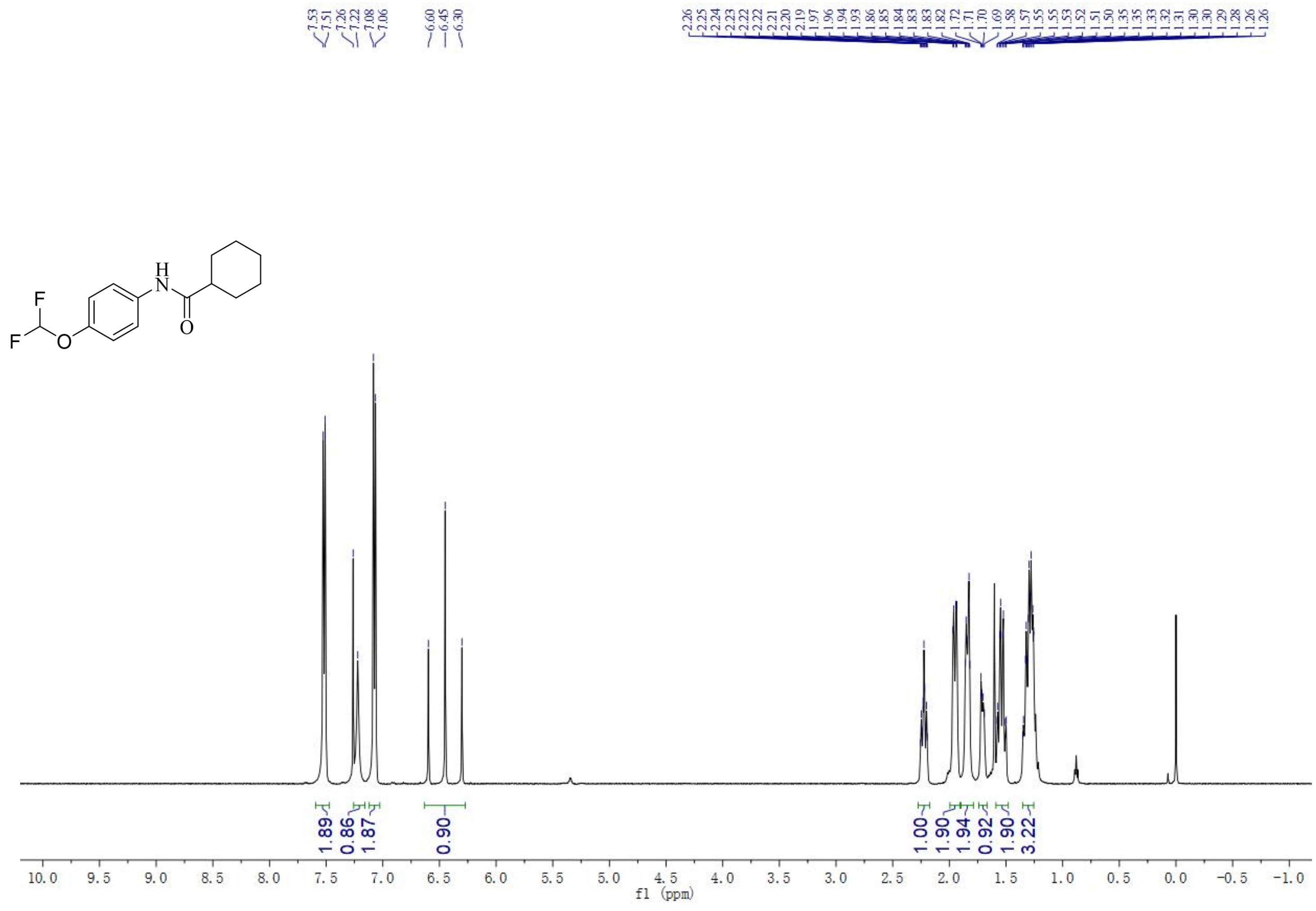


Figure S24. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(difluoromethoxy)phenyl)cyclohexanecarboxamide (**4ah**)

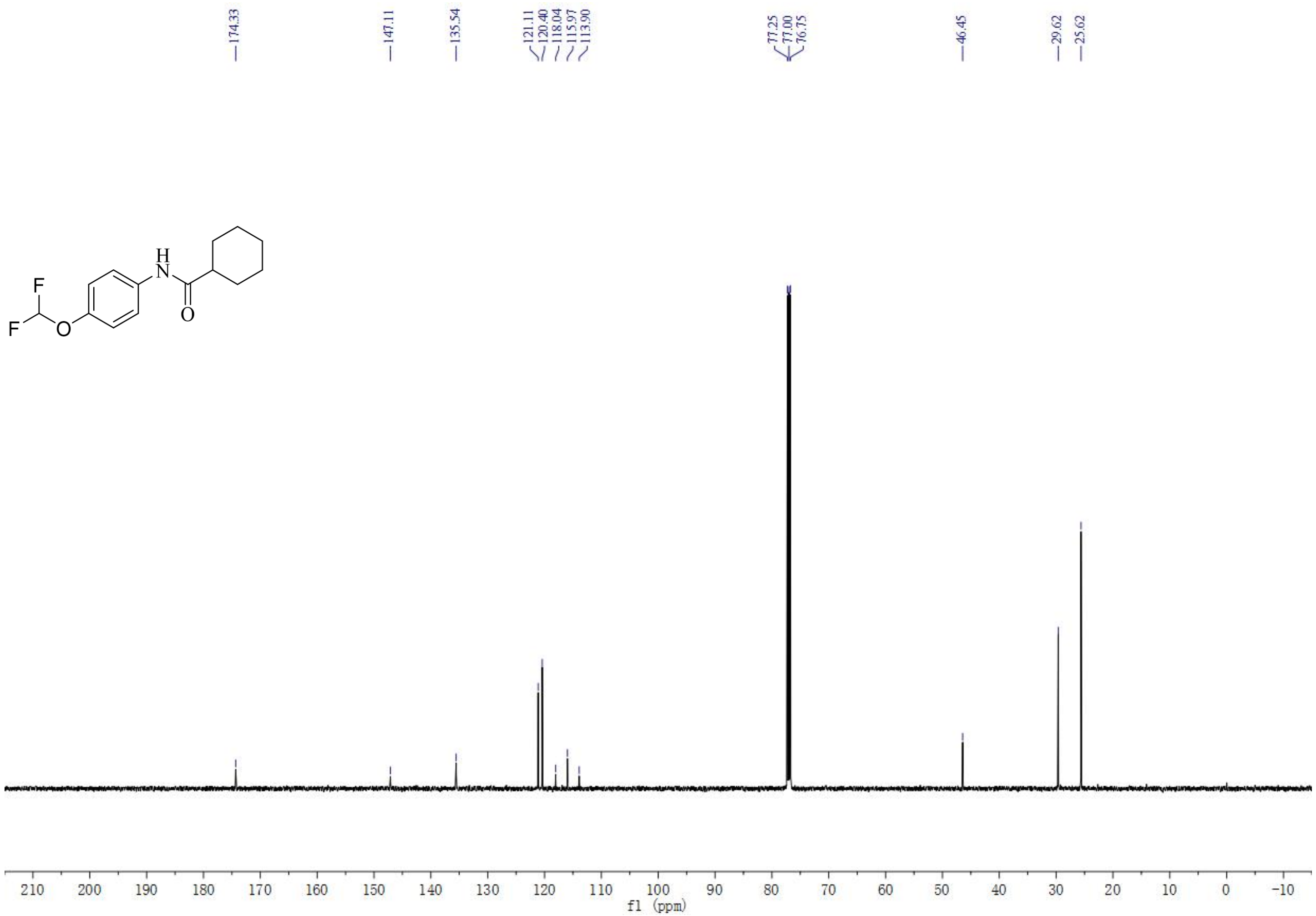


Figure S25. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of *N*-(4-(trifluoromethyl)phenyl)cyclohexanecarboxamide**(4ai)**.

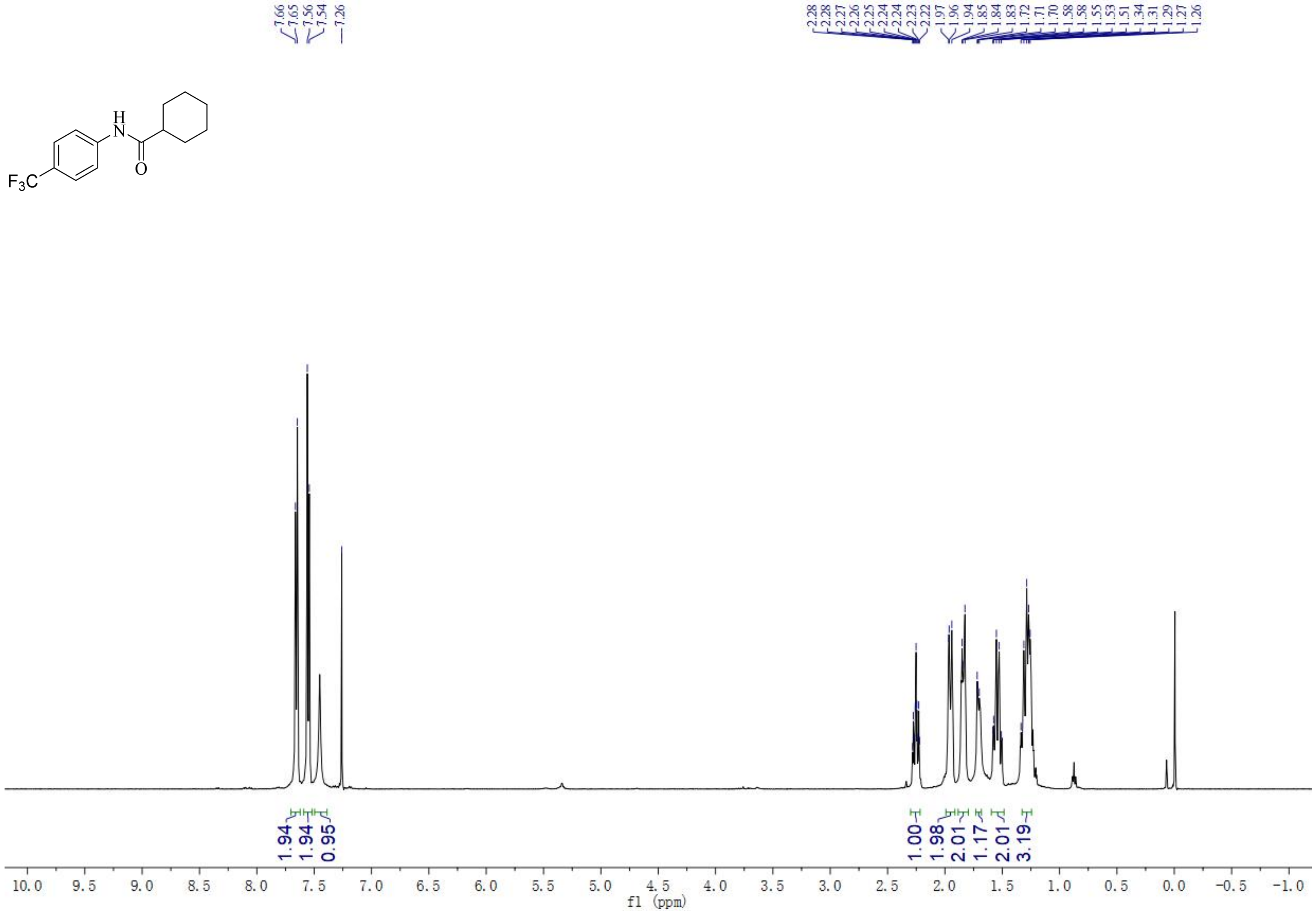


Figure S26.[19]F NMR (471 MHz, $CDCl_3$, 298K) of *N*-(4-(trifluoromethyl)phenyl)cyclohexanecarboxamide**(4ai)**.

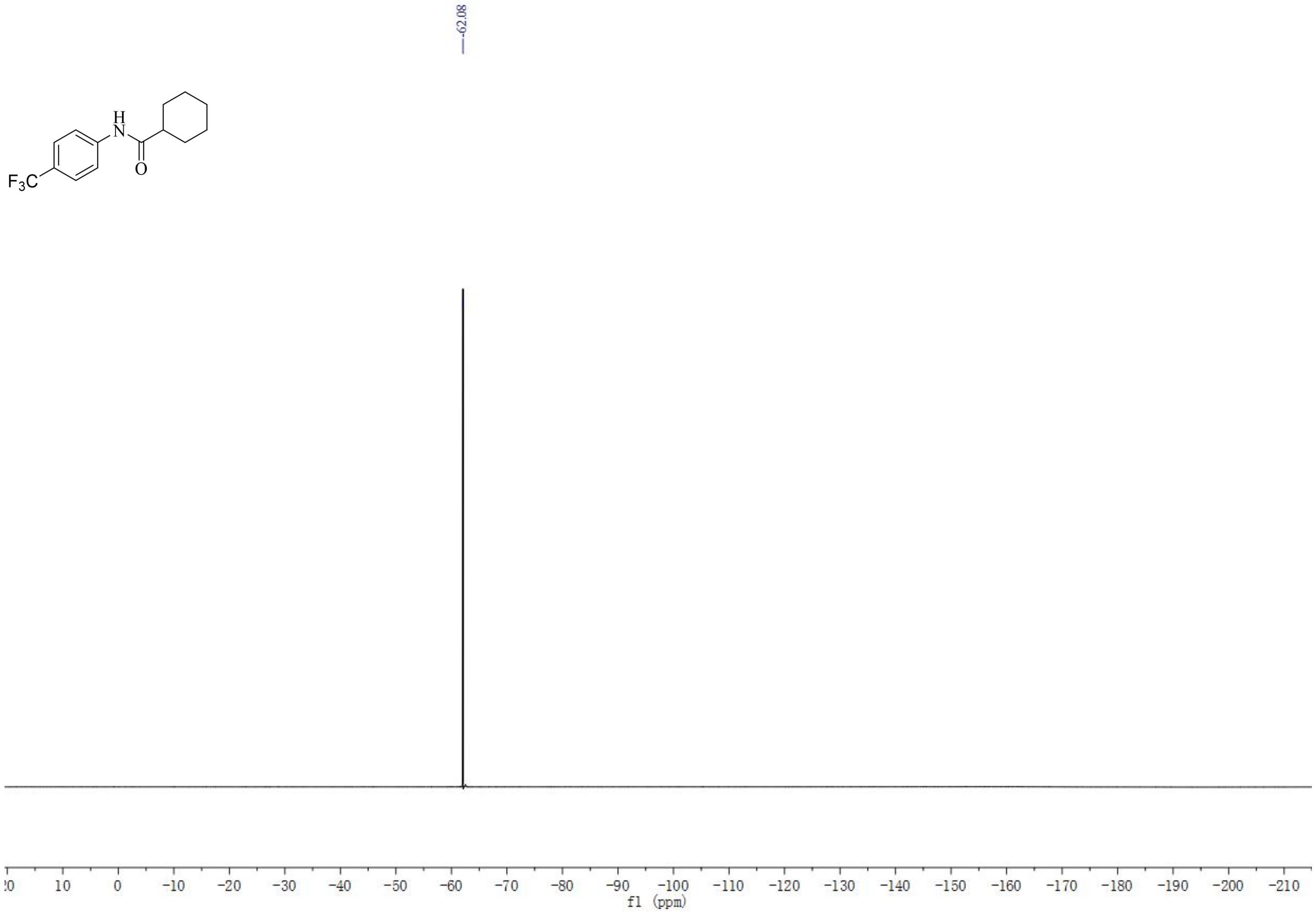


Figure S27. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(trifluoromethyl)phenyl)cyclohexanecarboxamide**(4ai)**.

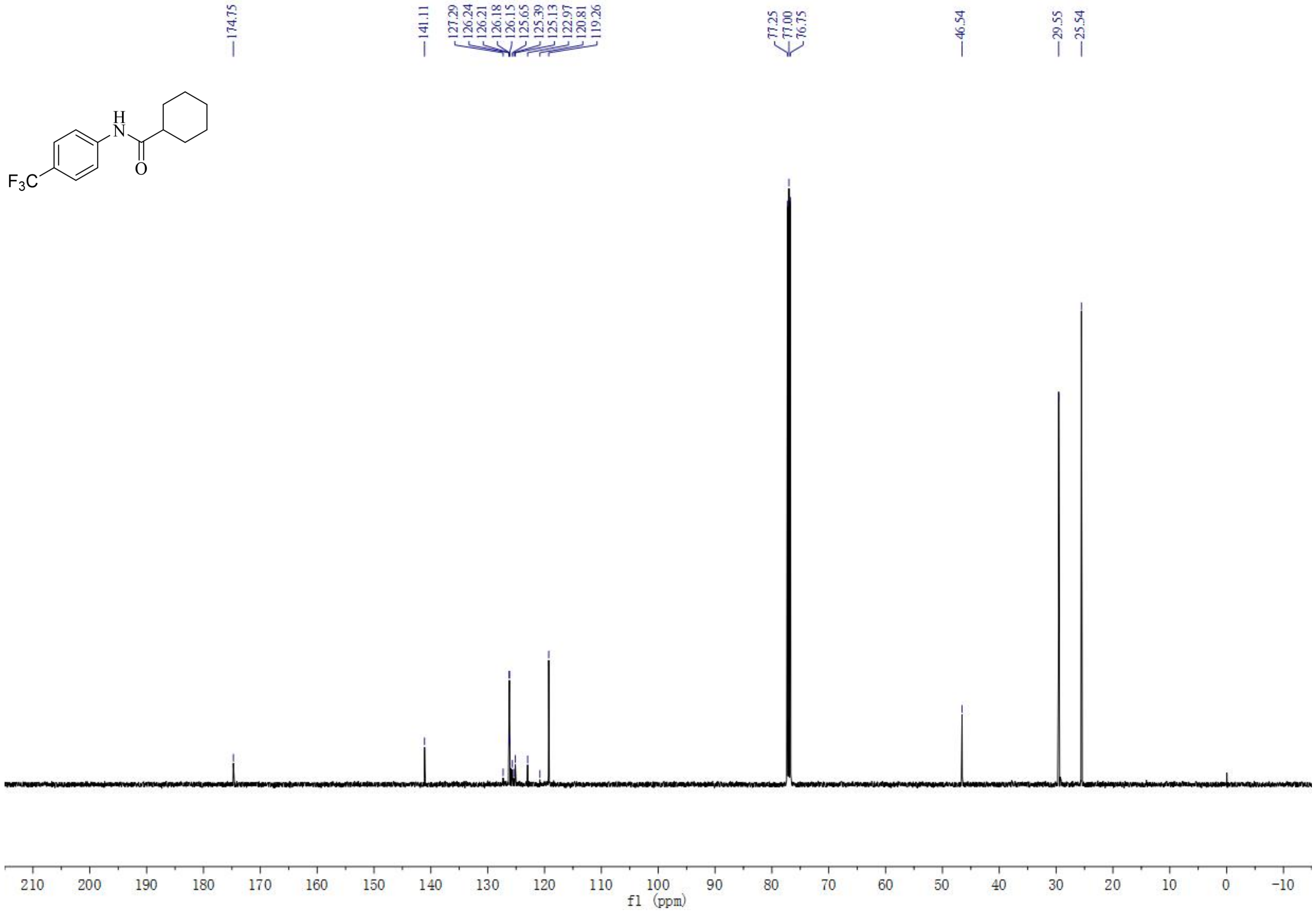


Figure S28. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-fluorophenyl)cyclohexanecarboxamide (**4aj**)

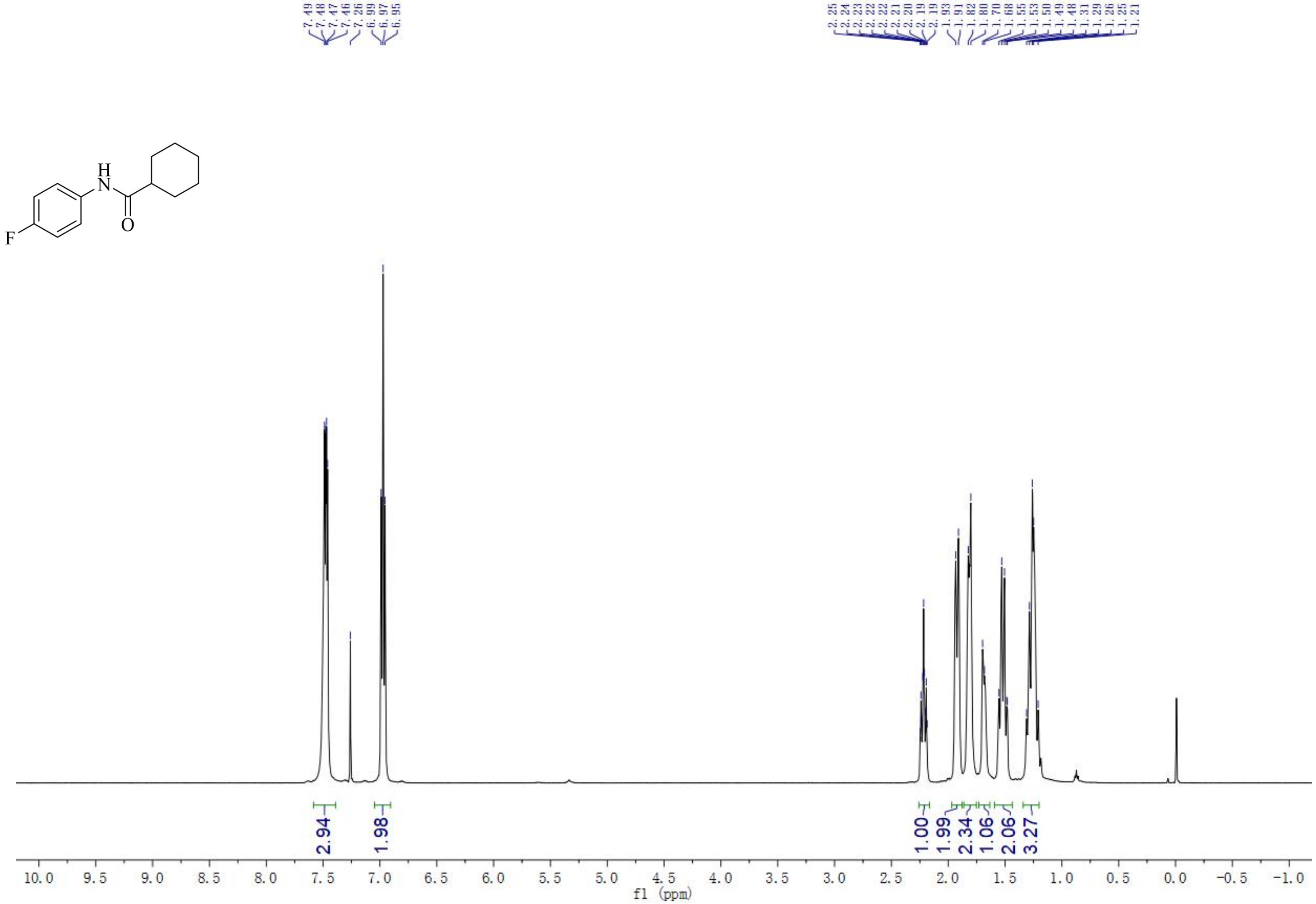


Figure S29. ^{19}F NMR (471 MHz, $CDCl_3$, 298K) of *N*-(4-fluorophenyl)cyclohexanecarboxamide (**4aj**)

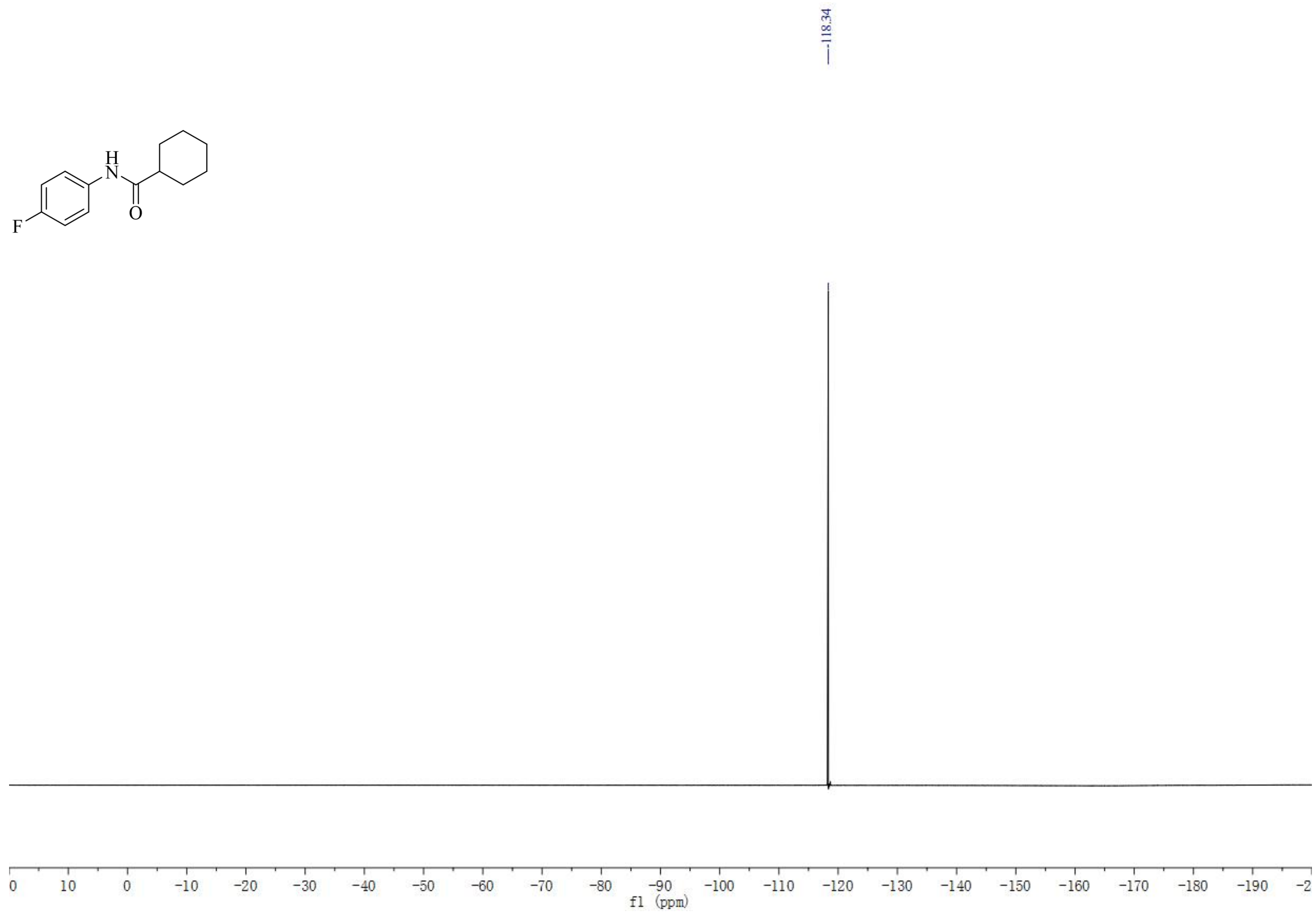


Figure S30. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-fluorophenyl)cyclohexanecarboxamide (**4aj**)

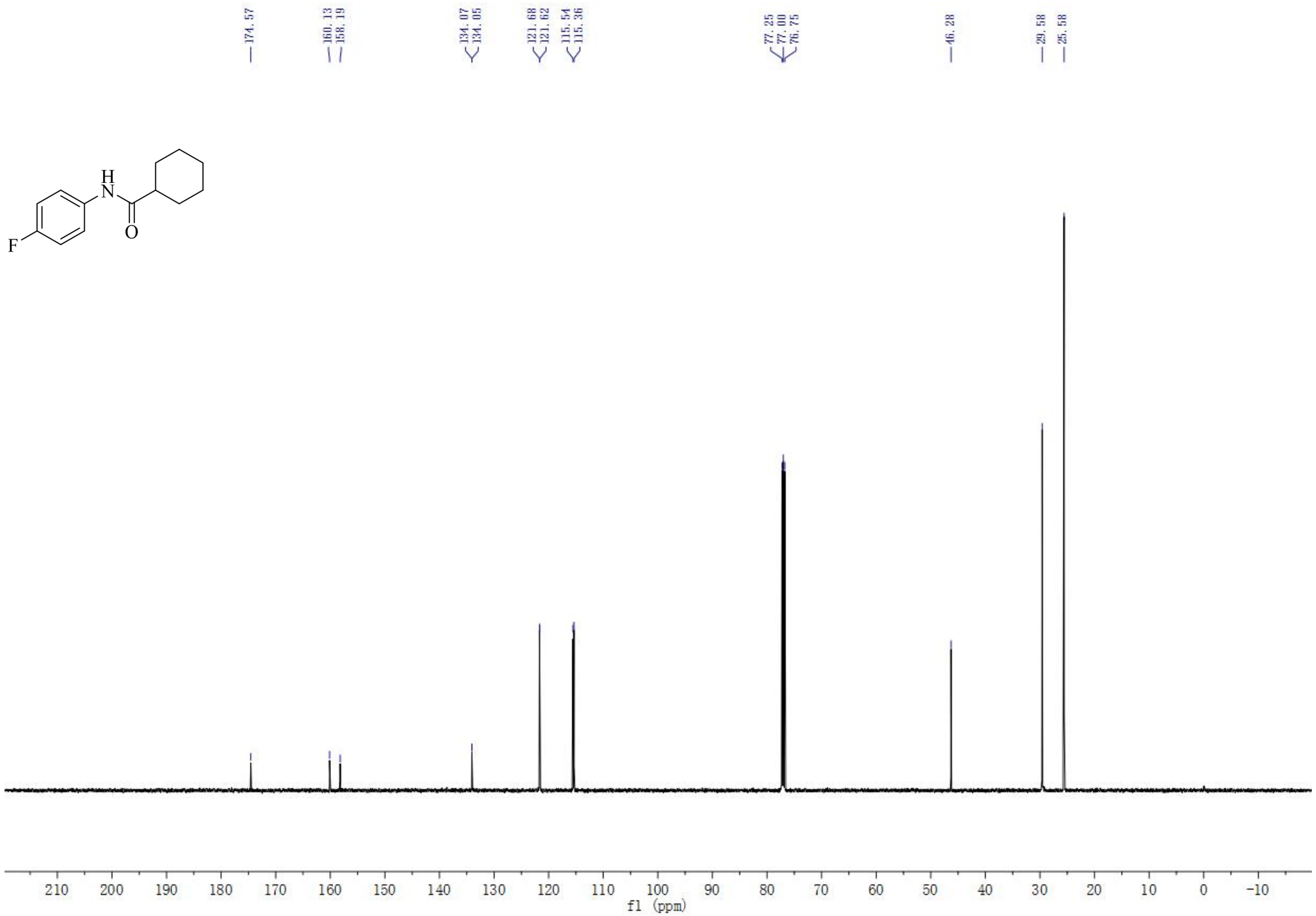


Figure S31. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) of *N*-(4-chlorophenyl)cyclohexanecarboxamide (**4ak**)

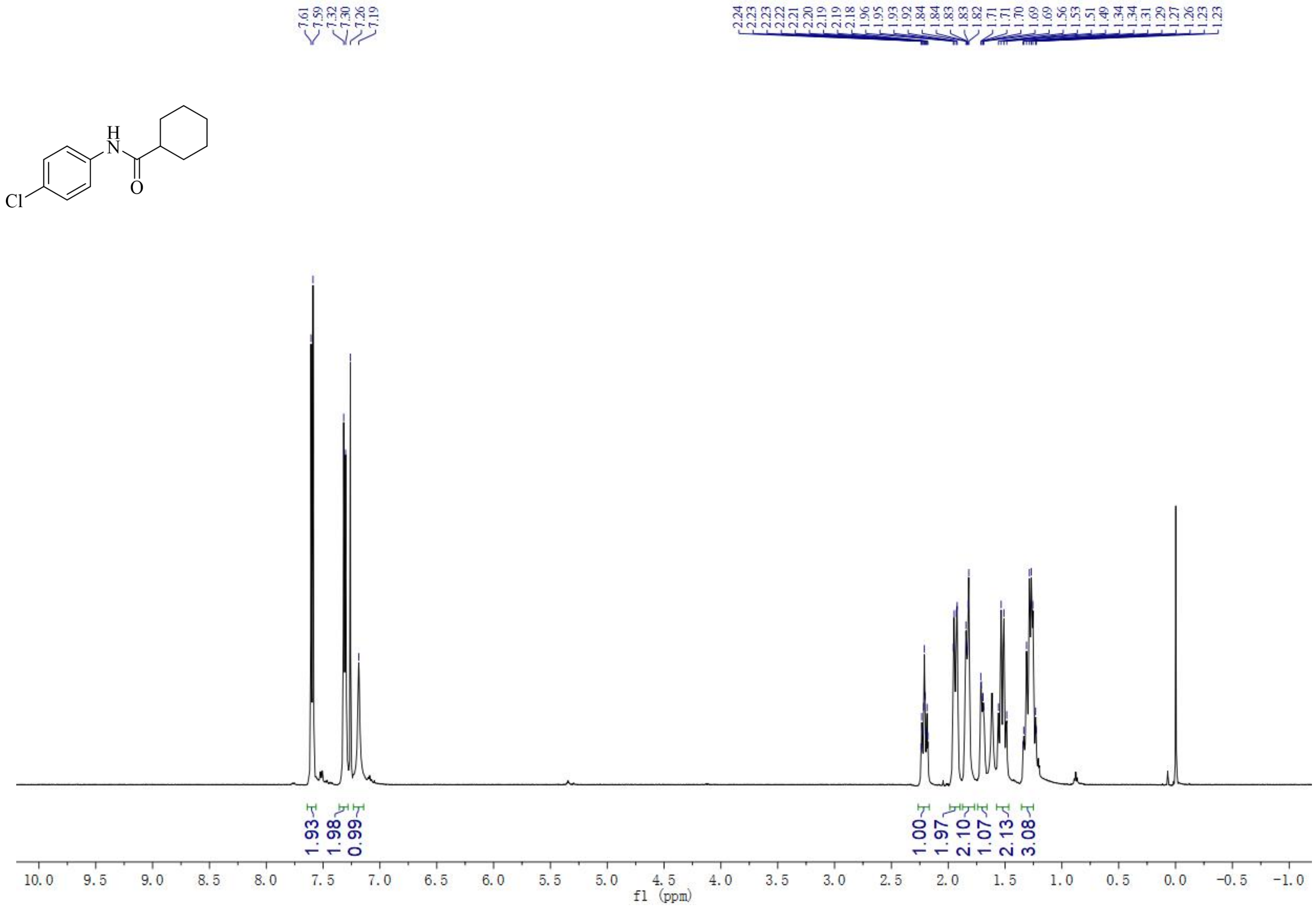


Figure S32. [13]C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-chlorophenyl)cyclohexanecarboxamide (**4ak**)

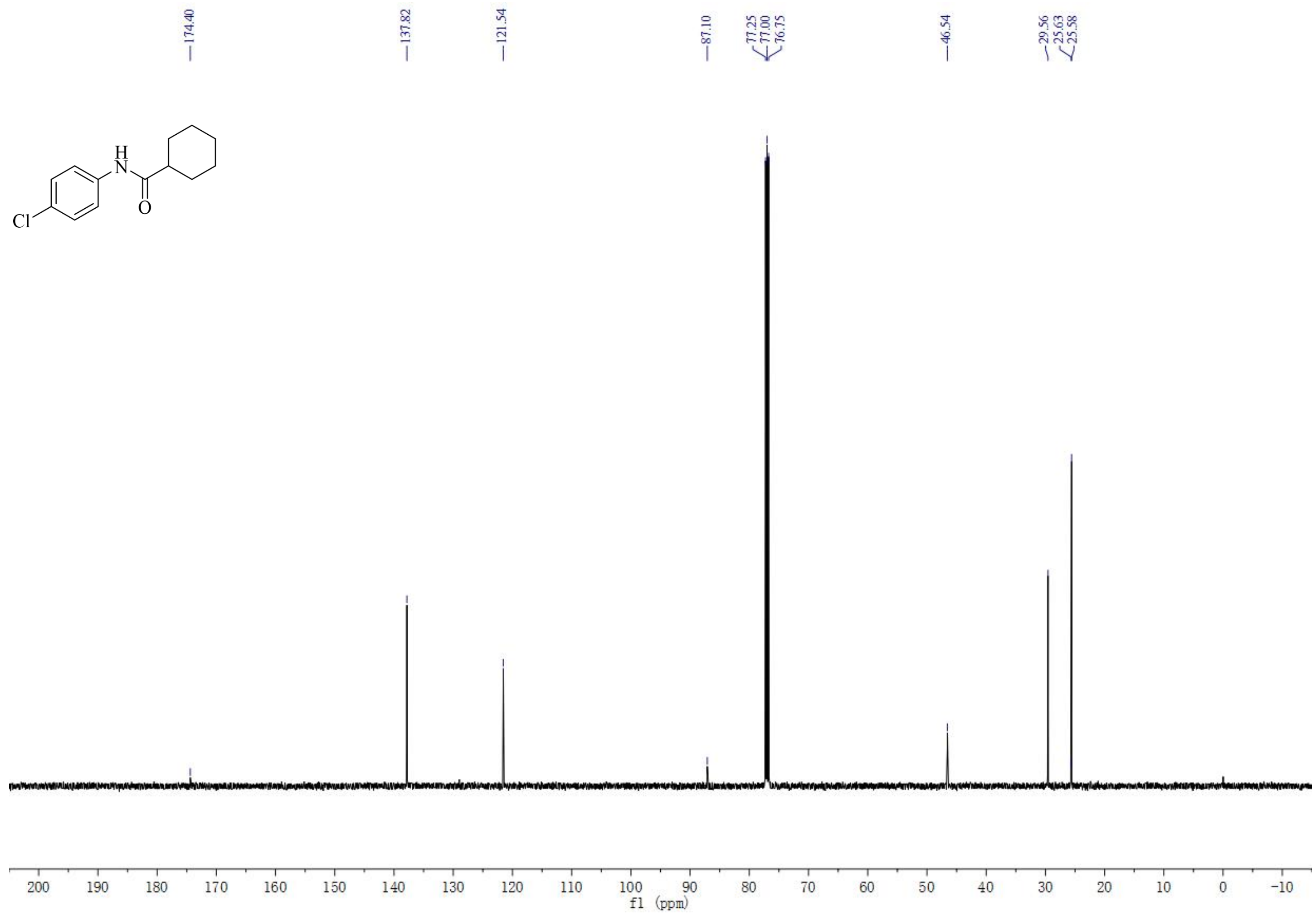


Figure S33. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) of *N*-(4-bromophenyl)cyclohexanecarboxamide (**4al**)

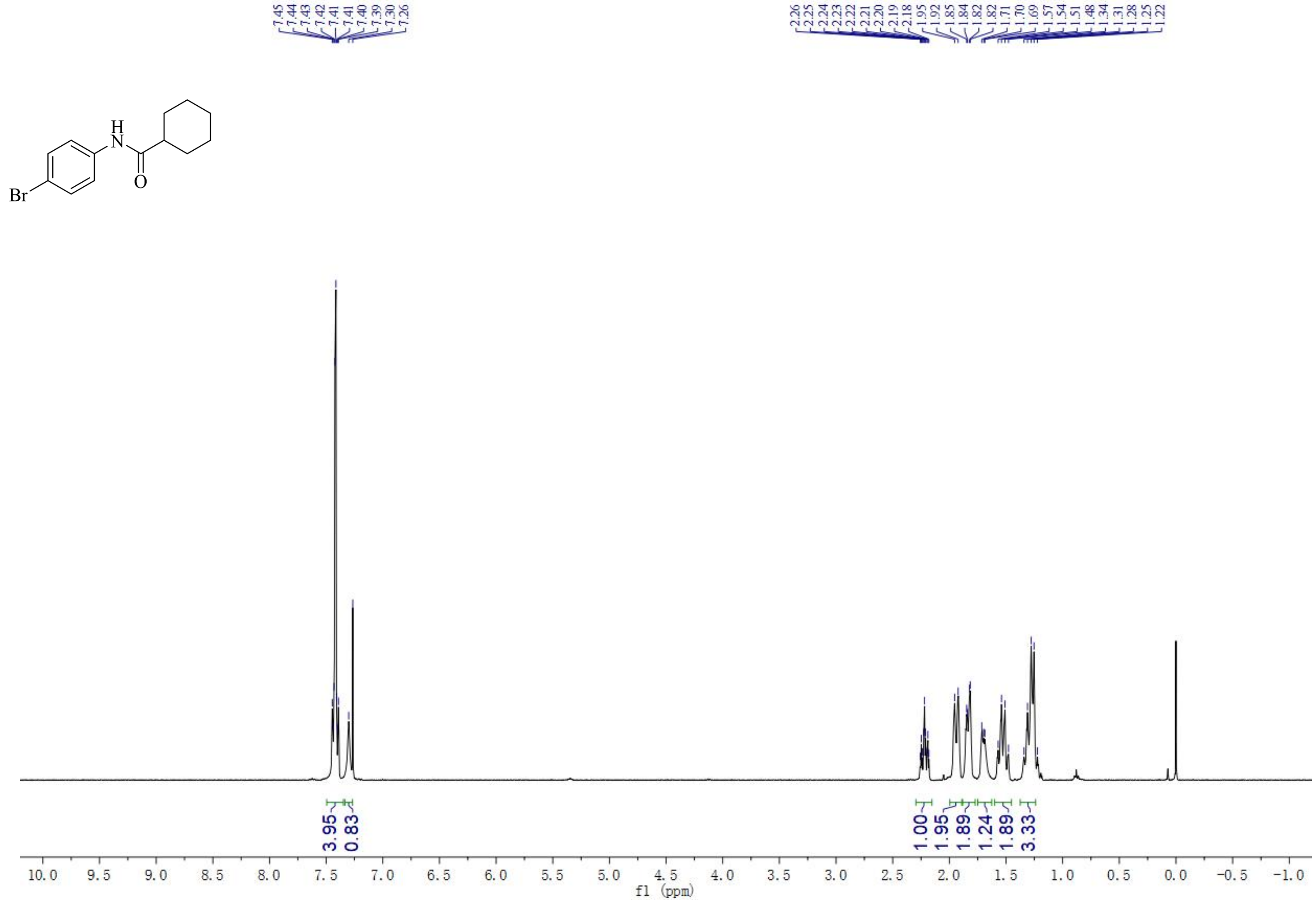


Figure S34. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-bromophenyl)cyclohexanecarboxamide (**4al**)

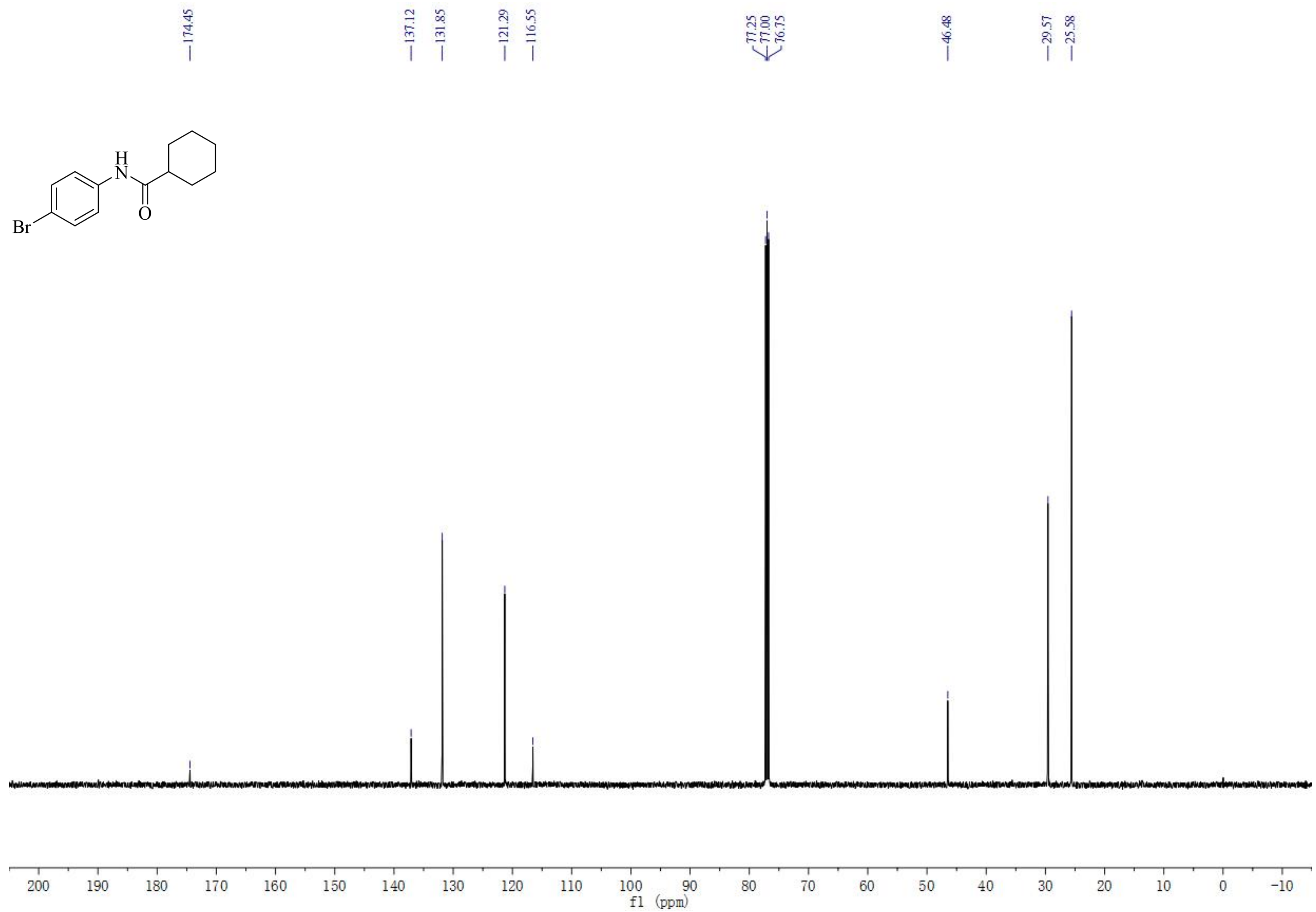


Figure S35. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-iodophenyl)cyclohexanecarboxamide (**4am**)

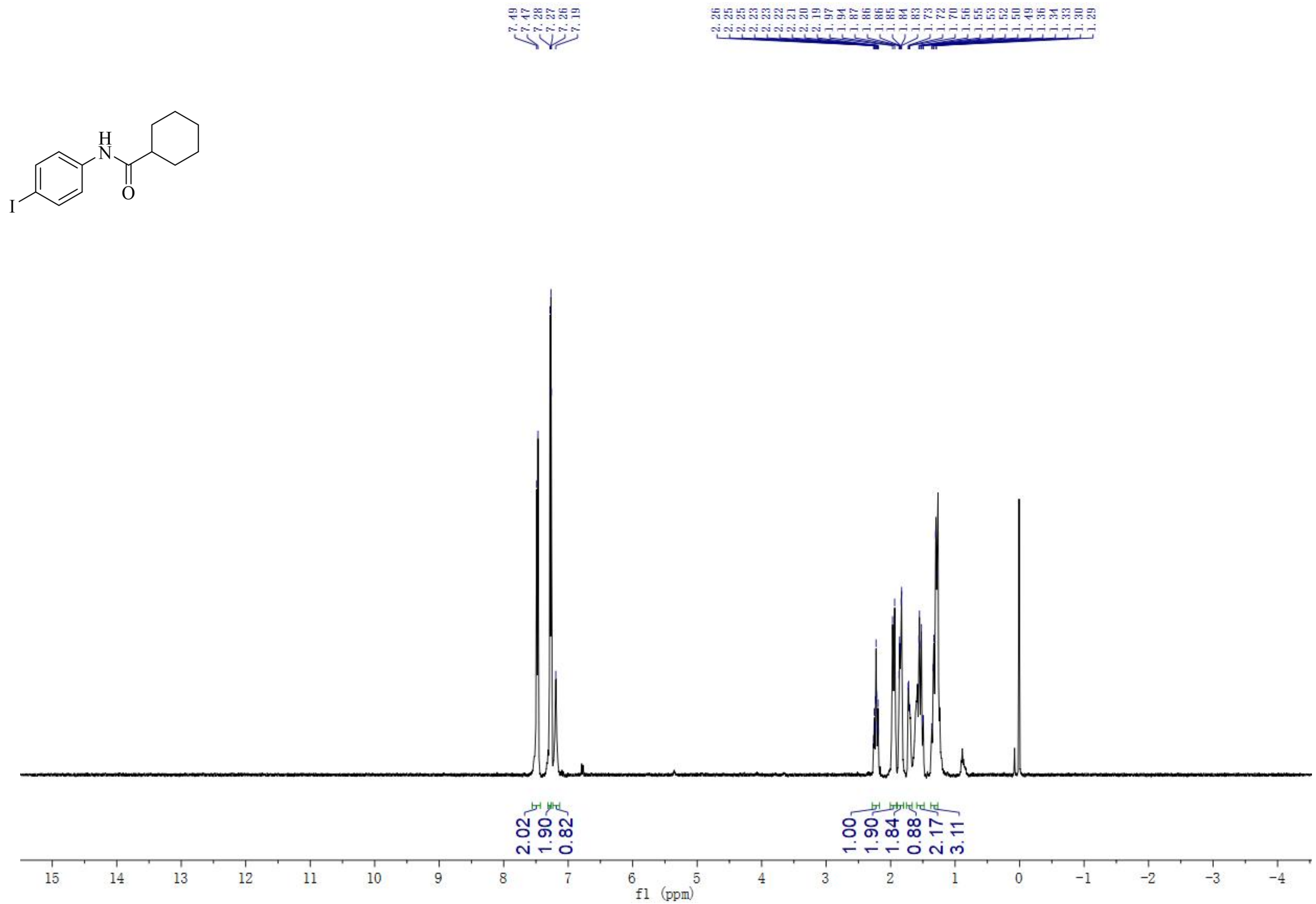


Figure S36. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-iodophenyl)cyclohexanecarboxamide (**4am**)

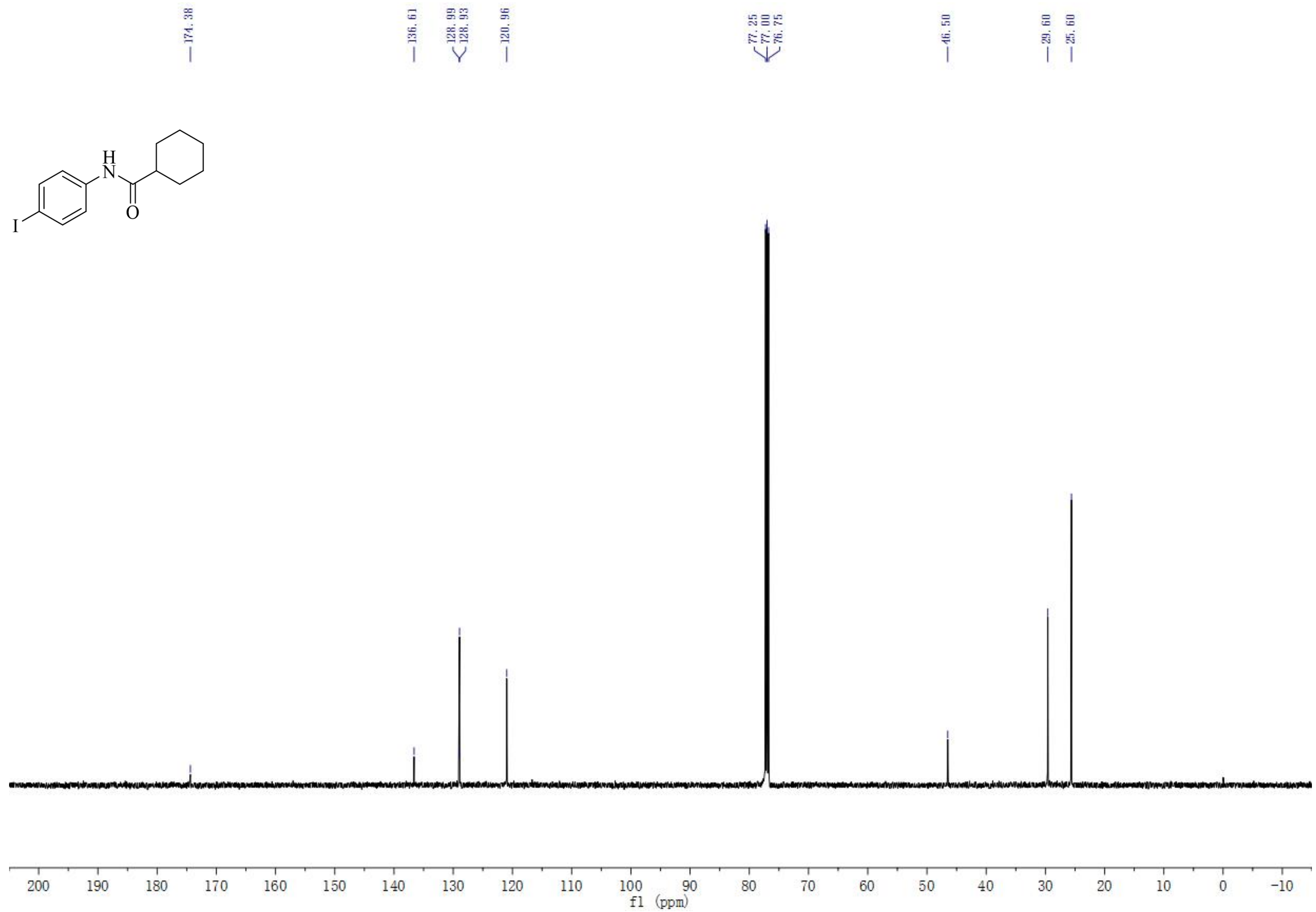


Figure S37. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(m-tolyl)cyclohexanecarboxamide (**4an**)

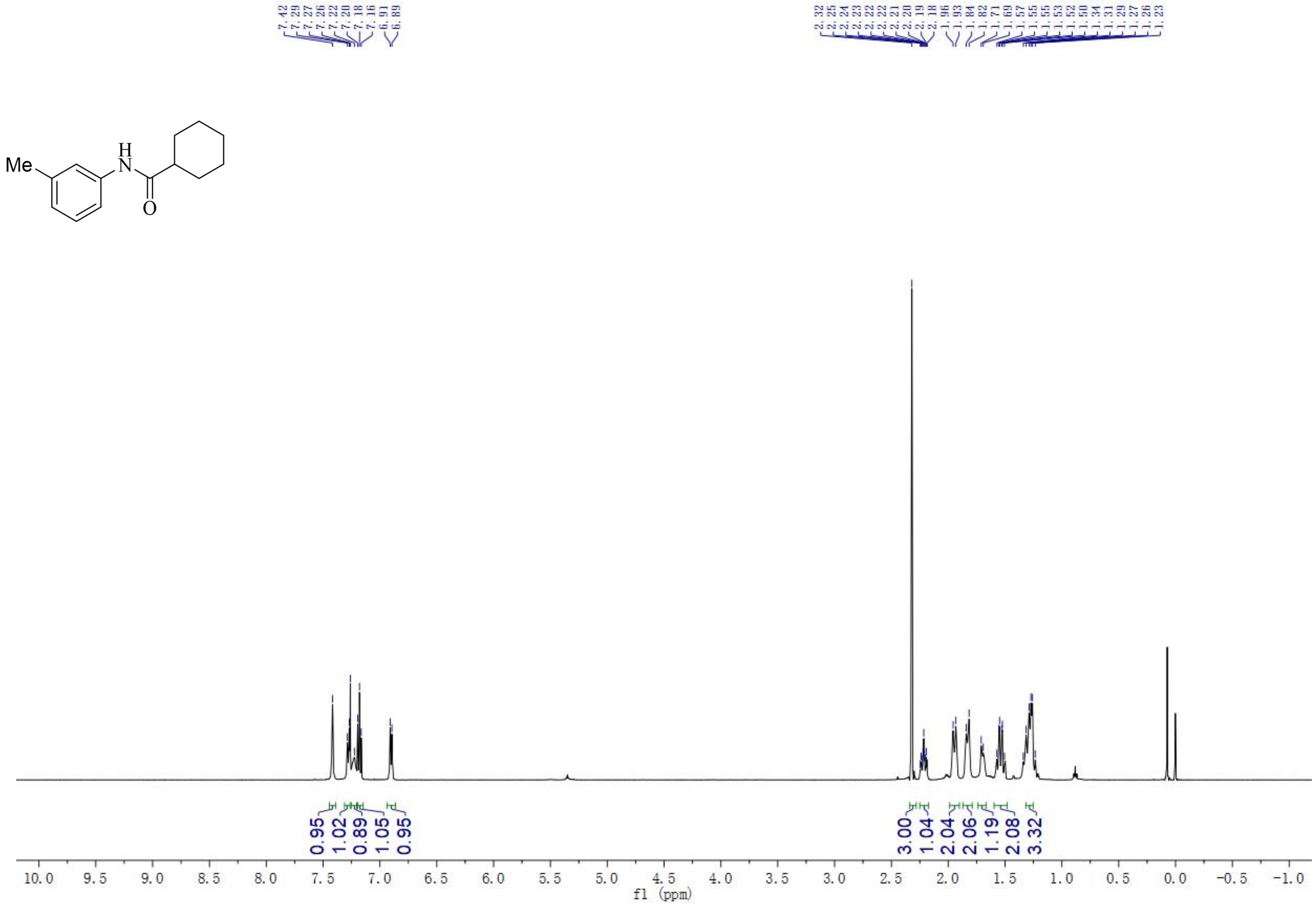


Figure S38. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(m-tolyl)cyclohexanecarboxamide (**4an**)

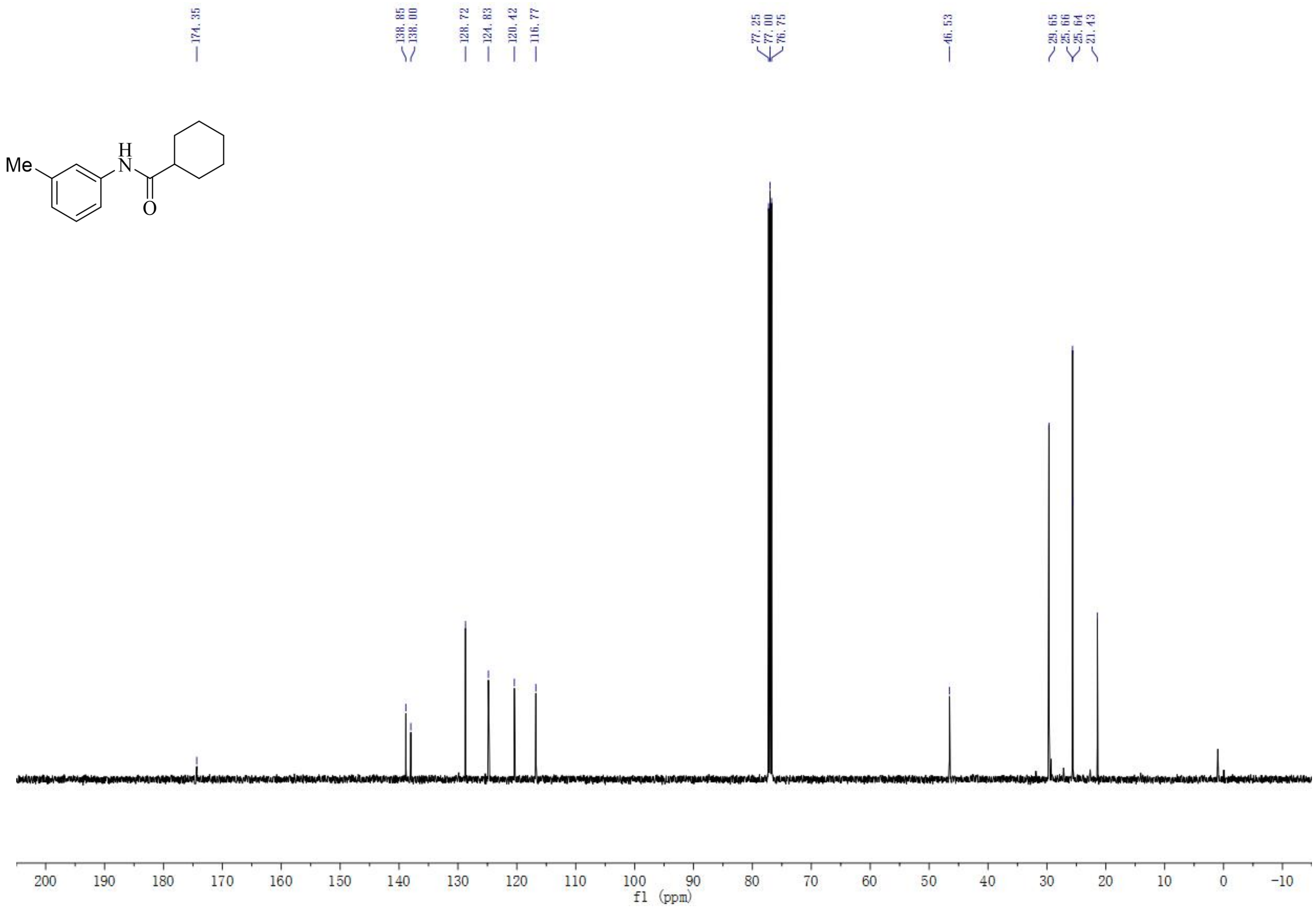
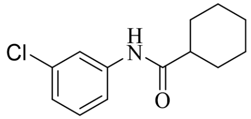


Figure S39. [1]H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(3-chlorophenyl)cyclohexanecarboxamide (**4ao**)



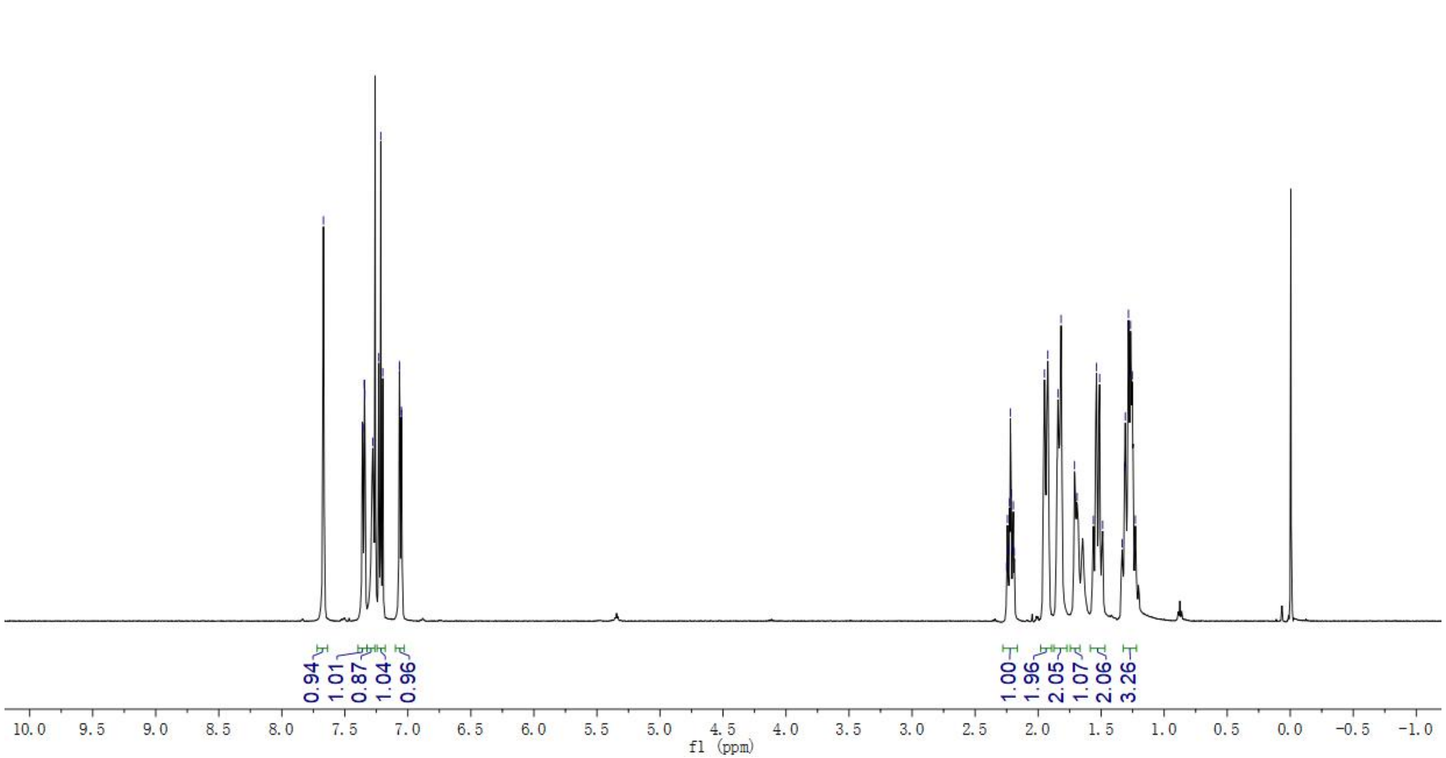


Figure S40. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(3-chlorophenyl)cyclohexanecarboxamide (**4ao**)

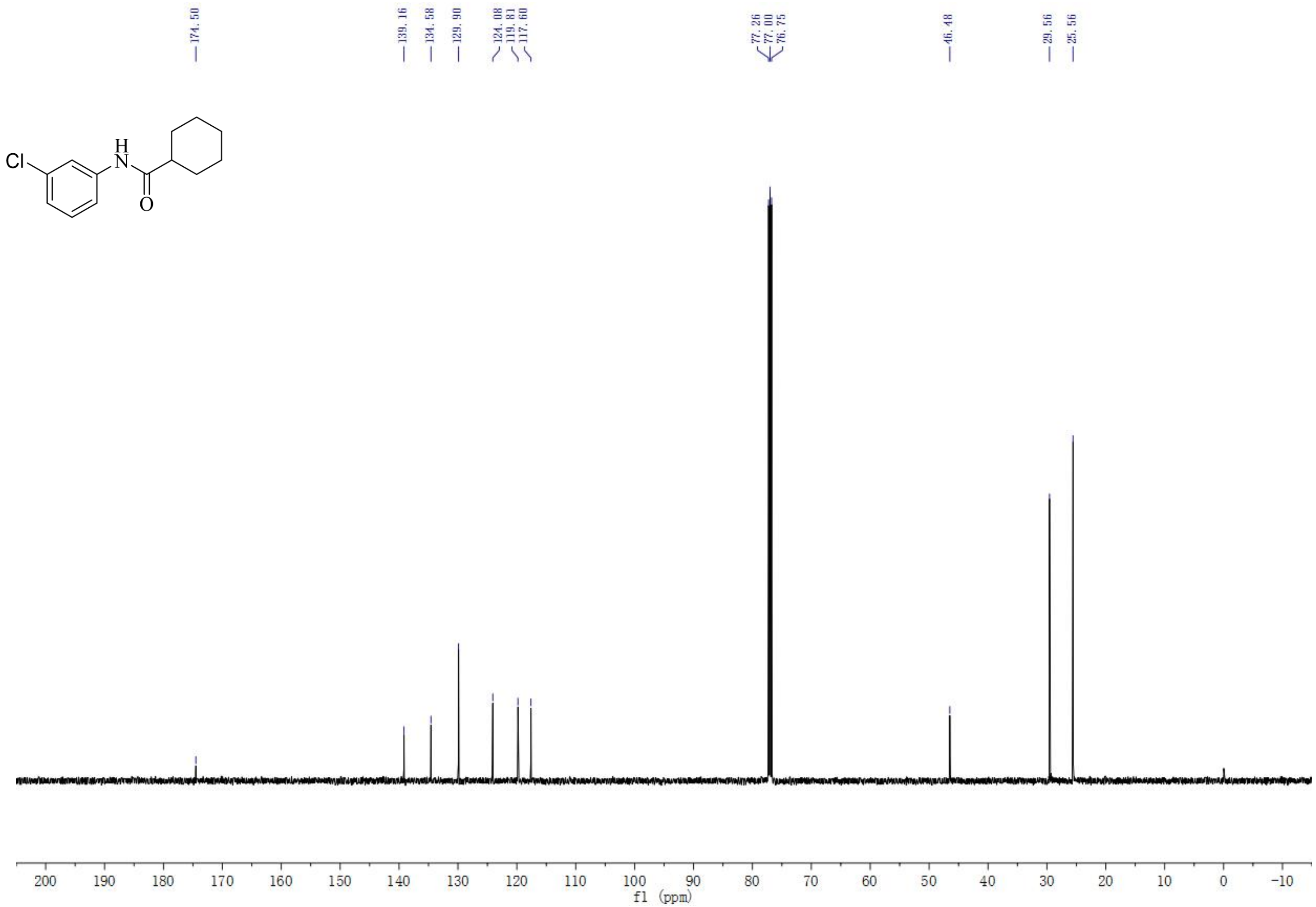


Figure S41. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of methyl 3-(cyclohexanecarboxamido)benzoate (**4ap**)

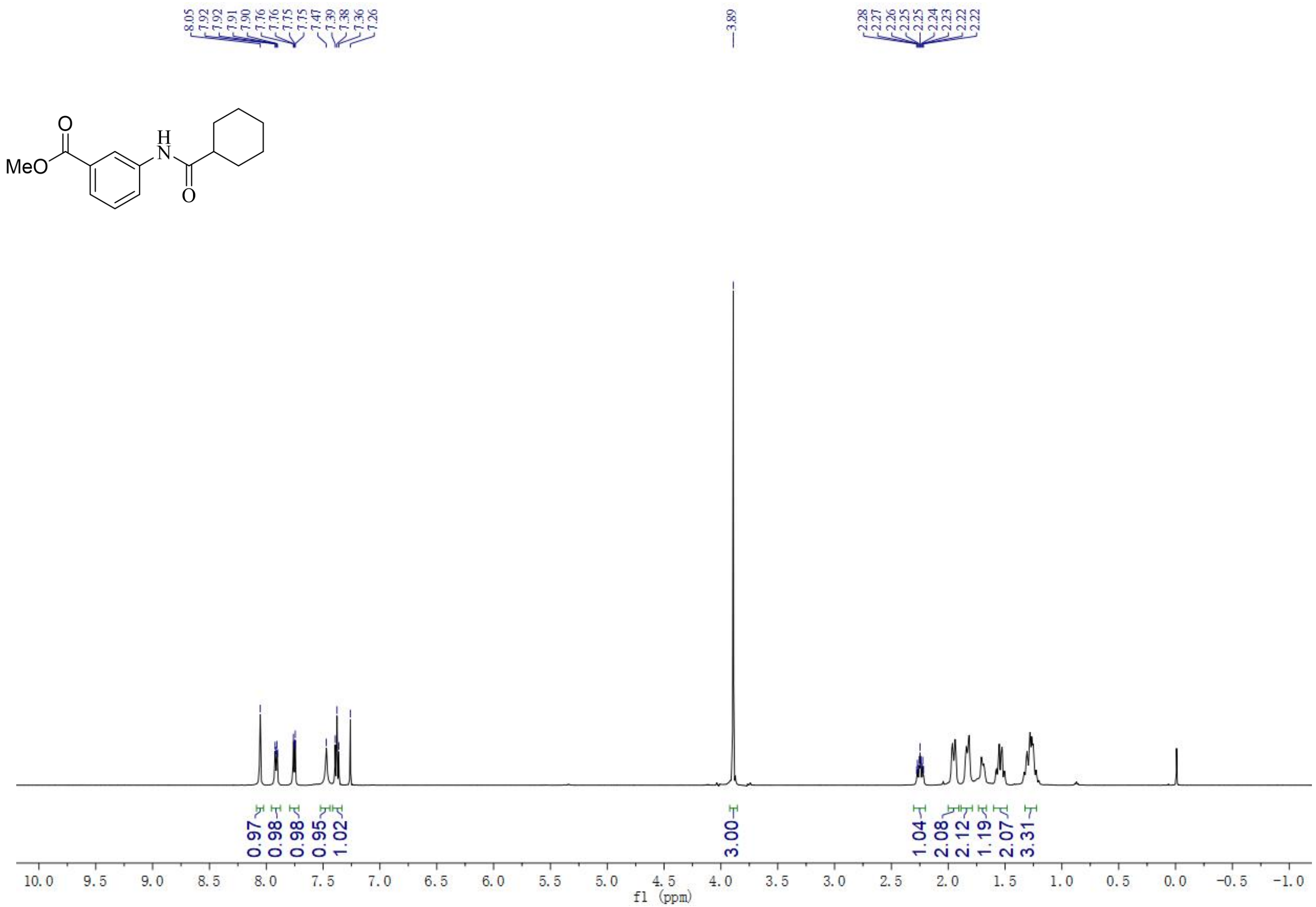


Figure S42. [13]C NMR (126 MHz, $CDCl_3$, 298K) of methyl 3-(cyclohexanecarboxamido)benzoate (**4ap**)

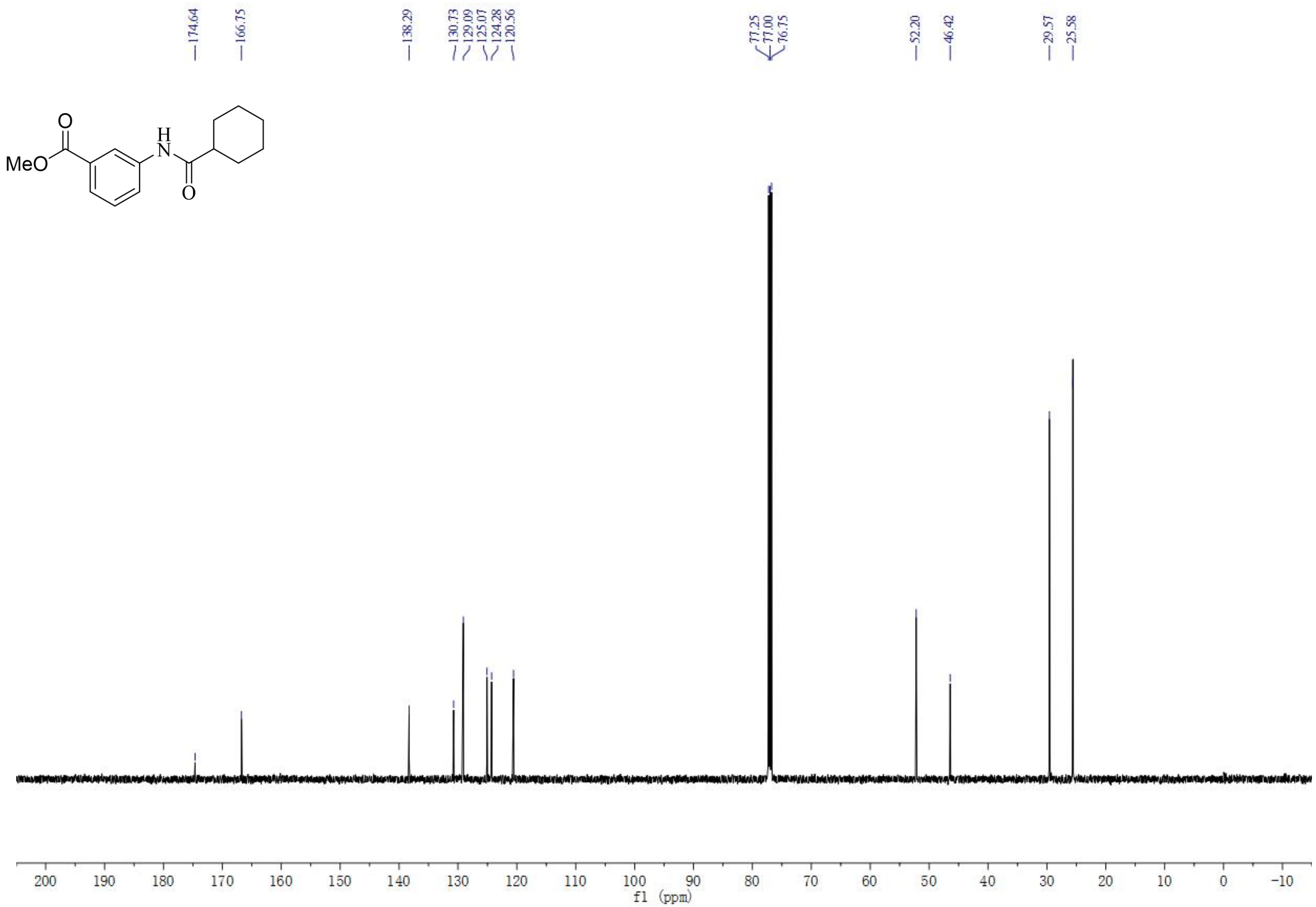


Figure S43. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(2-methoxyphenyl)cyclohexanecarboxamide (**4aq**)

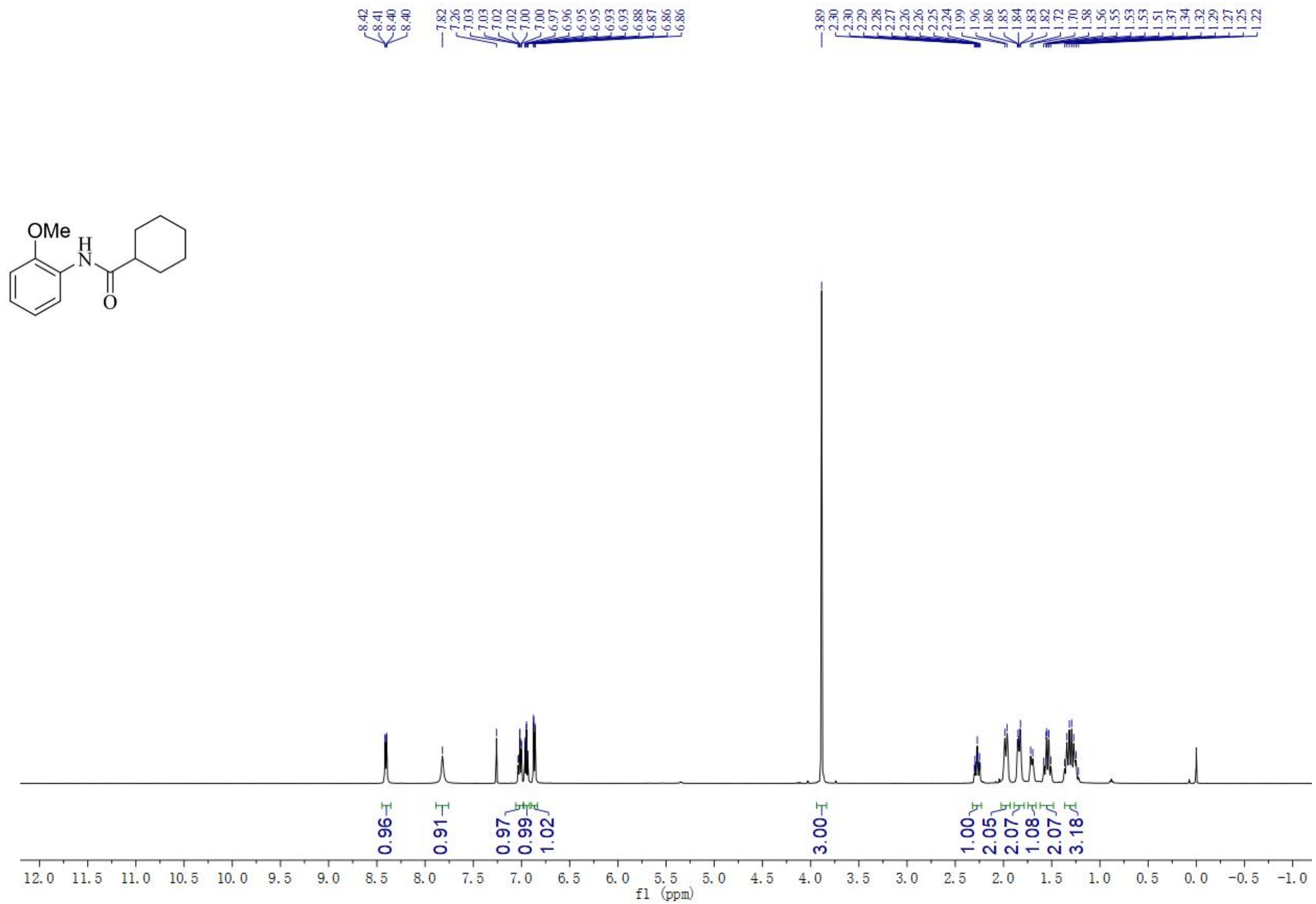


Figure S44. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(2-methoxyphenyl)cyclohexanecarboxamide (**4aq**)

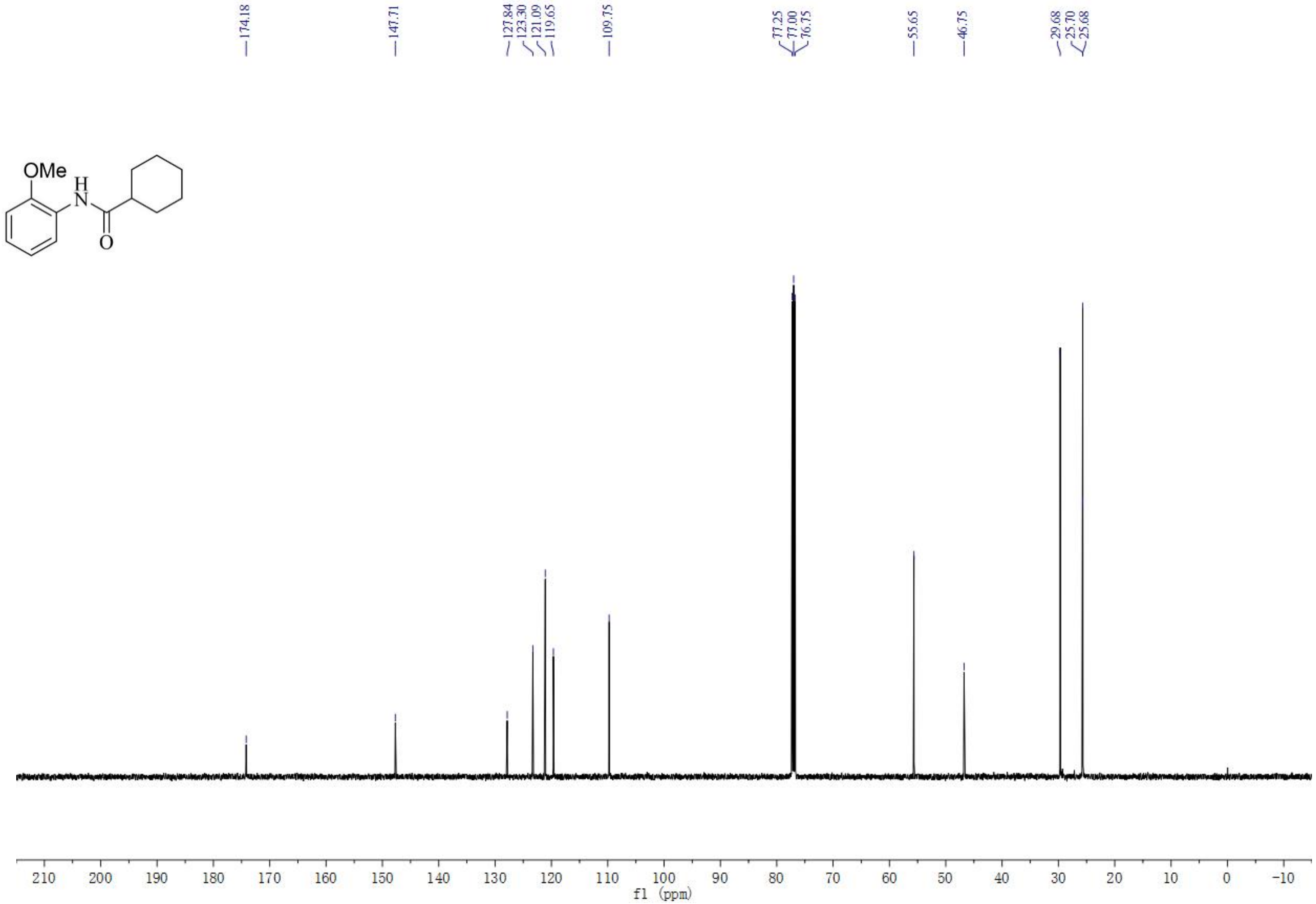
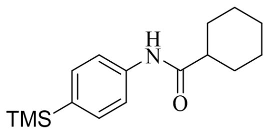


Figure S45. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(trimethylsilyl)phenyl)cyclohexanecarboxamide **(4ar)**



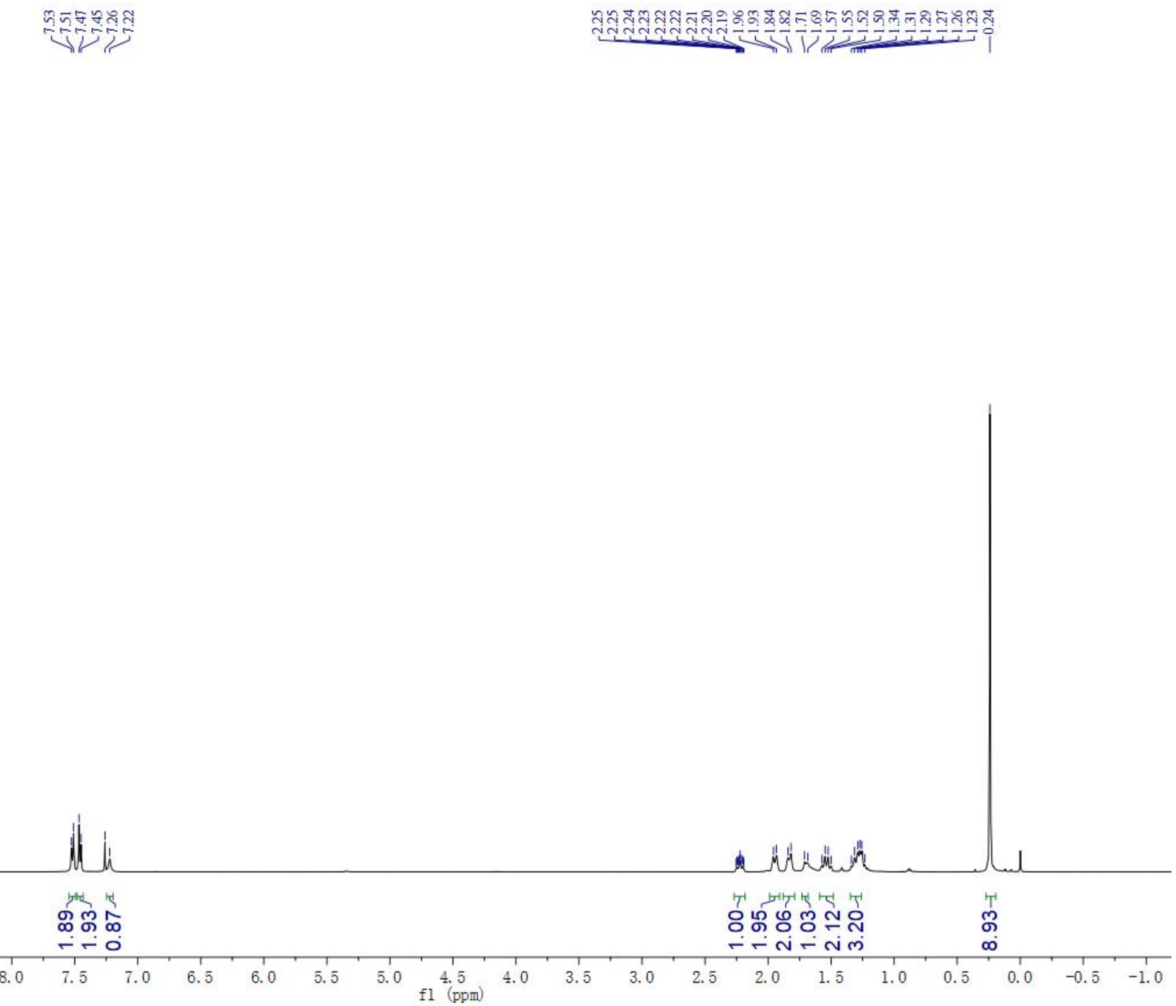


Figure S46. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(trimethylsilyl)phenyl)cyclohexanecarboxamide (**4ar**)

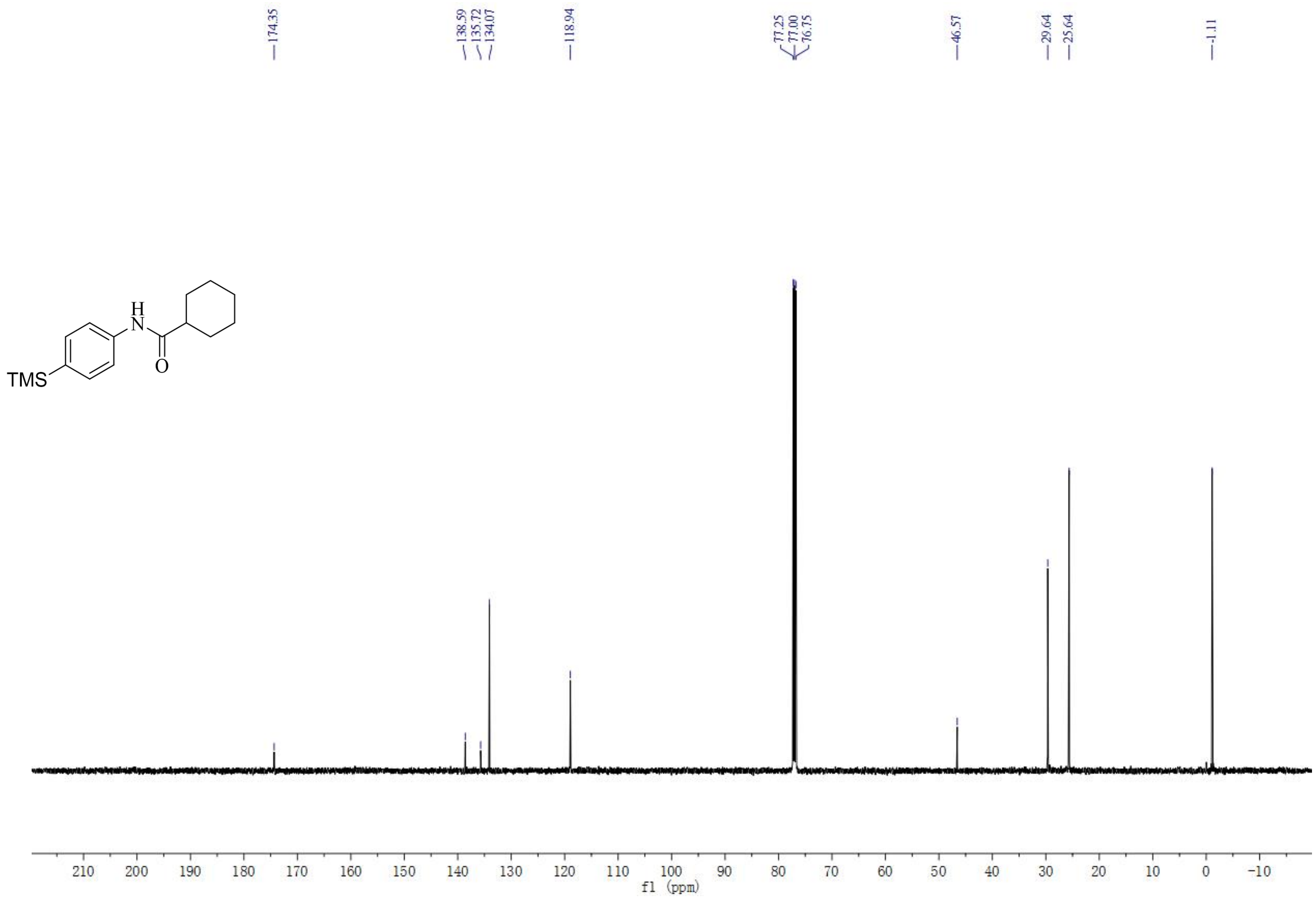


Figure S47. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)cyclohexanecarboxamide (**4as**)

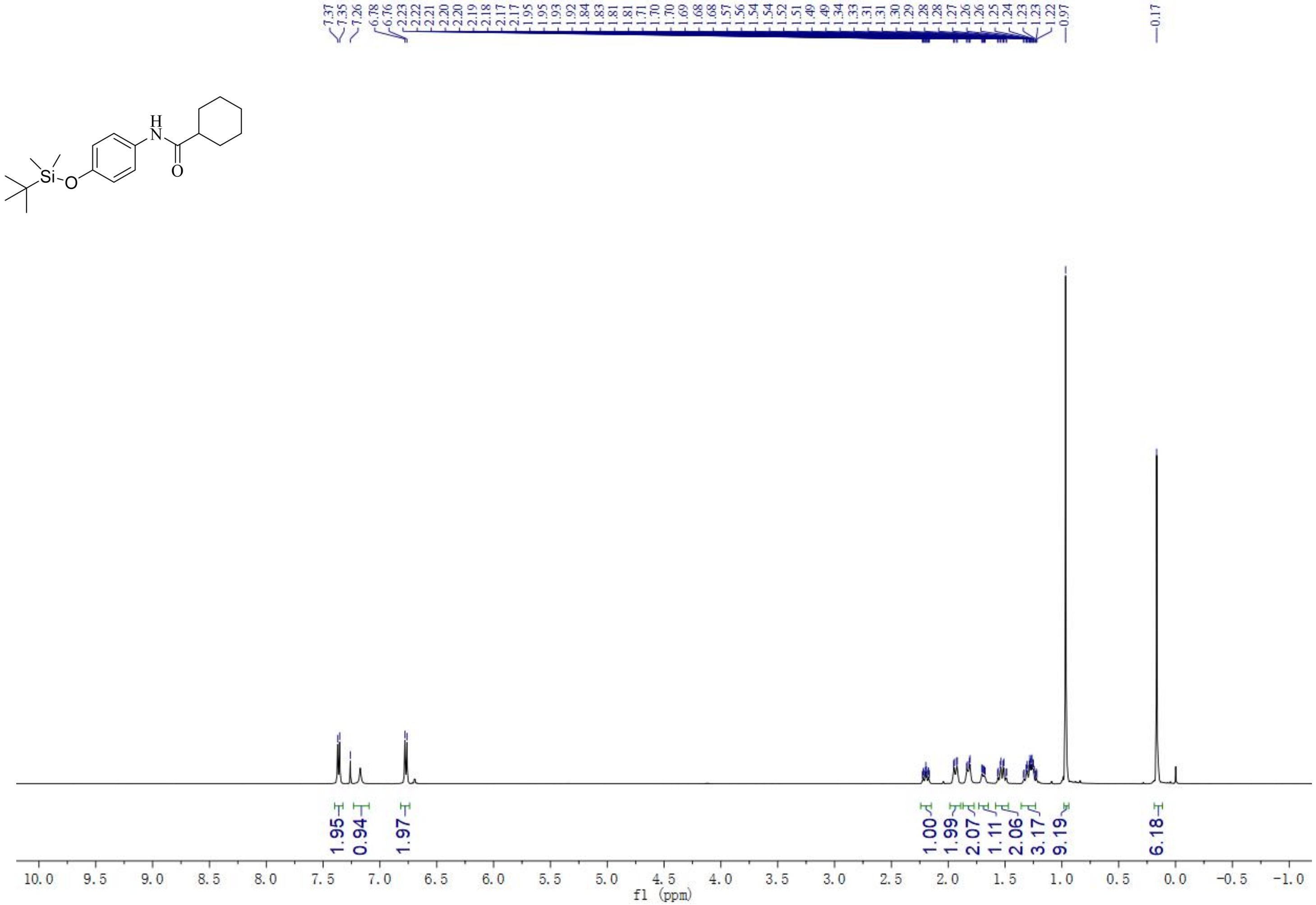


Figure S48. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)cyclohexanecarboxamide (**4as**)

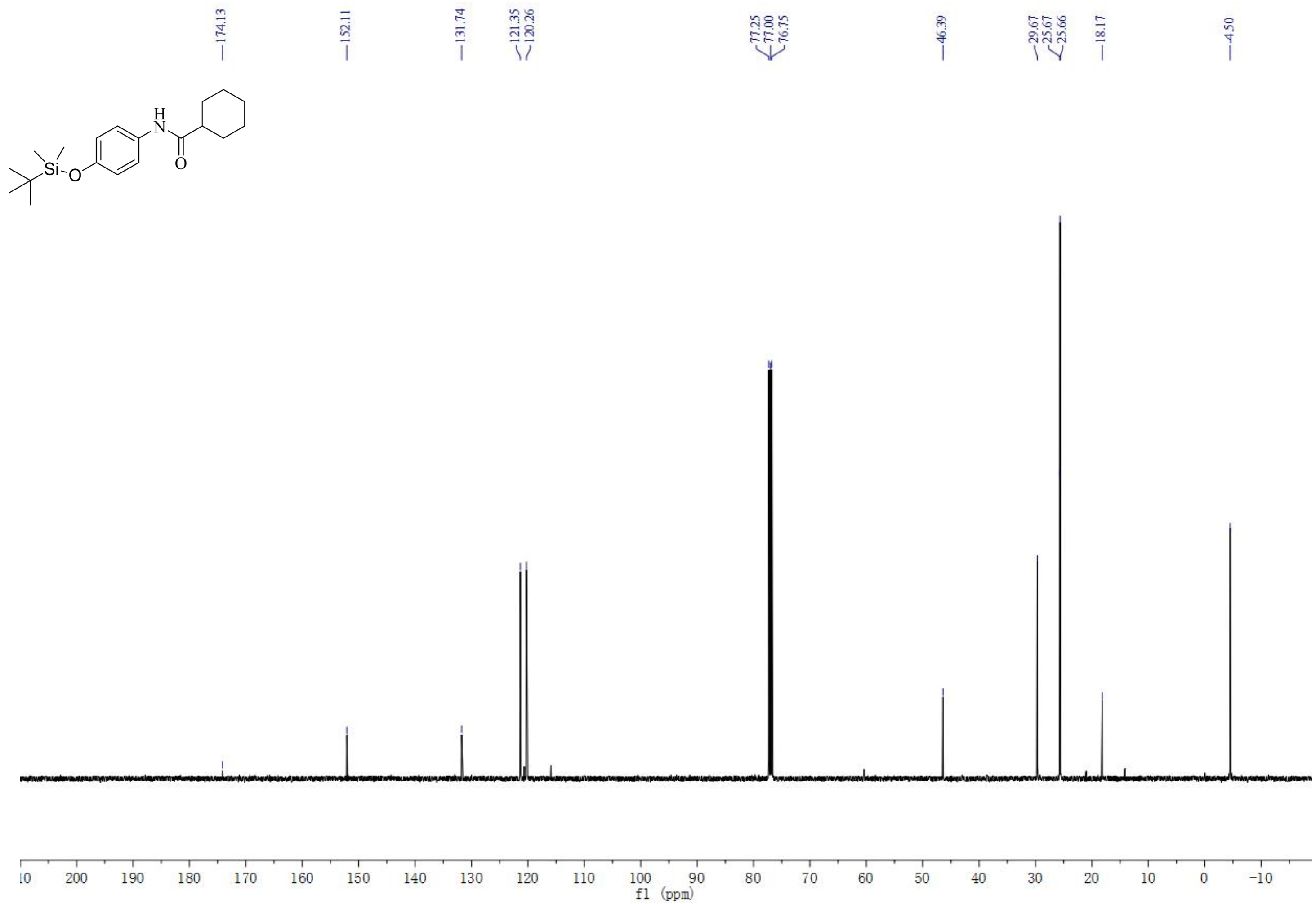
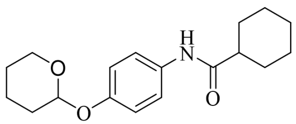


Figure S49. ^{1}H NMR (500 MHz, DMSO-d_6, 298K) of *N*-(4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)cyclohexanecarboxamide (**4at**)



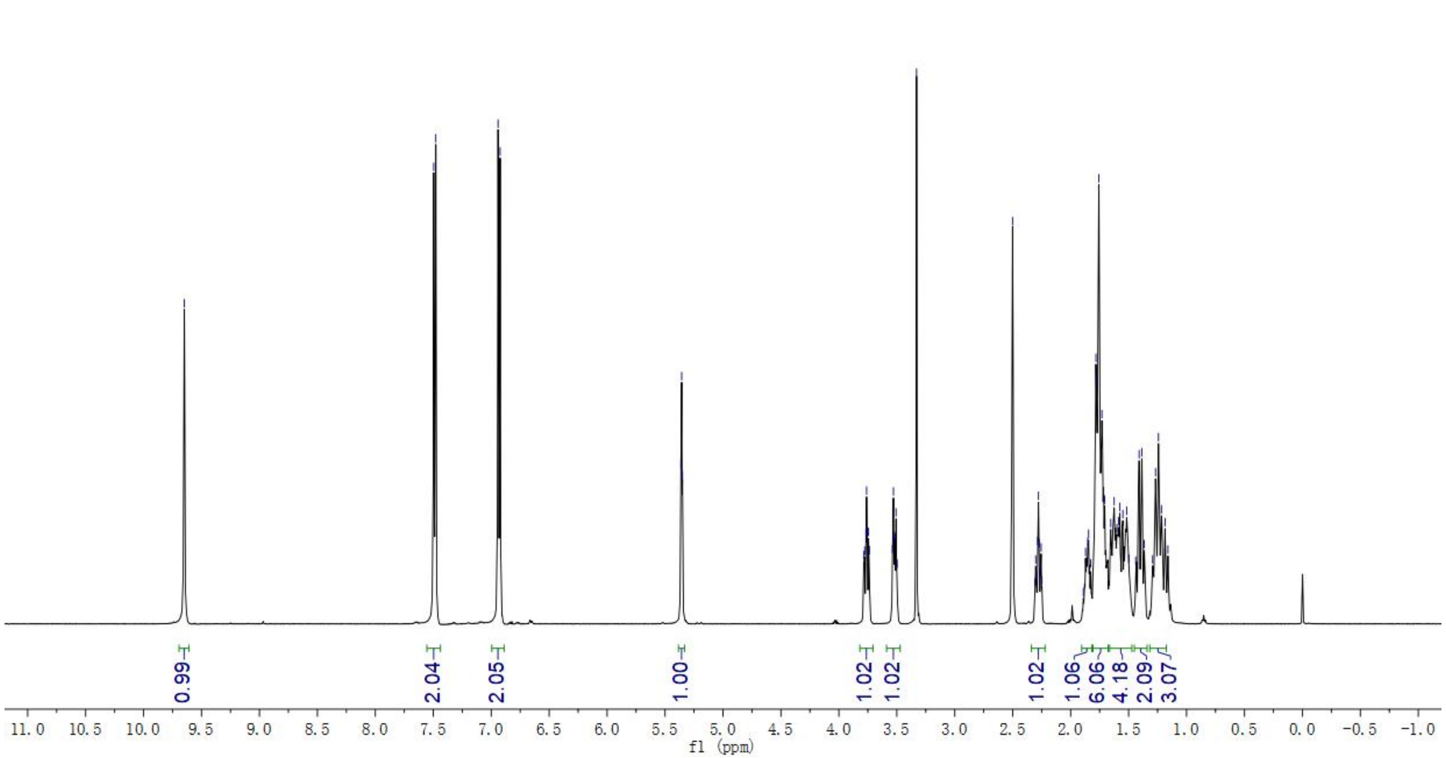


Figure S50. ^{13}C NMR (126 MHz, DMSO-d_6, 298K) of *N*-(4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)cyclohexanecarboxamide (**4at**)

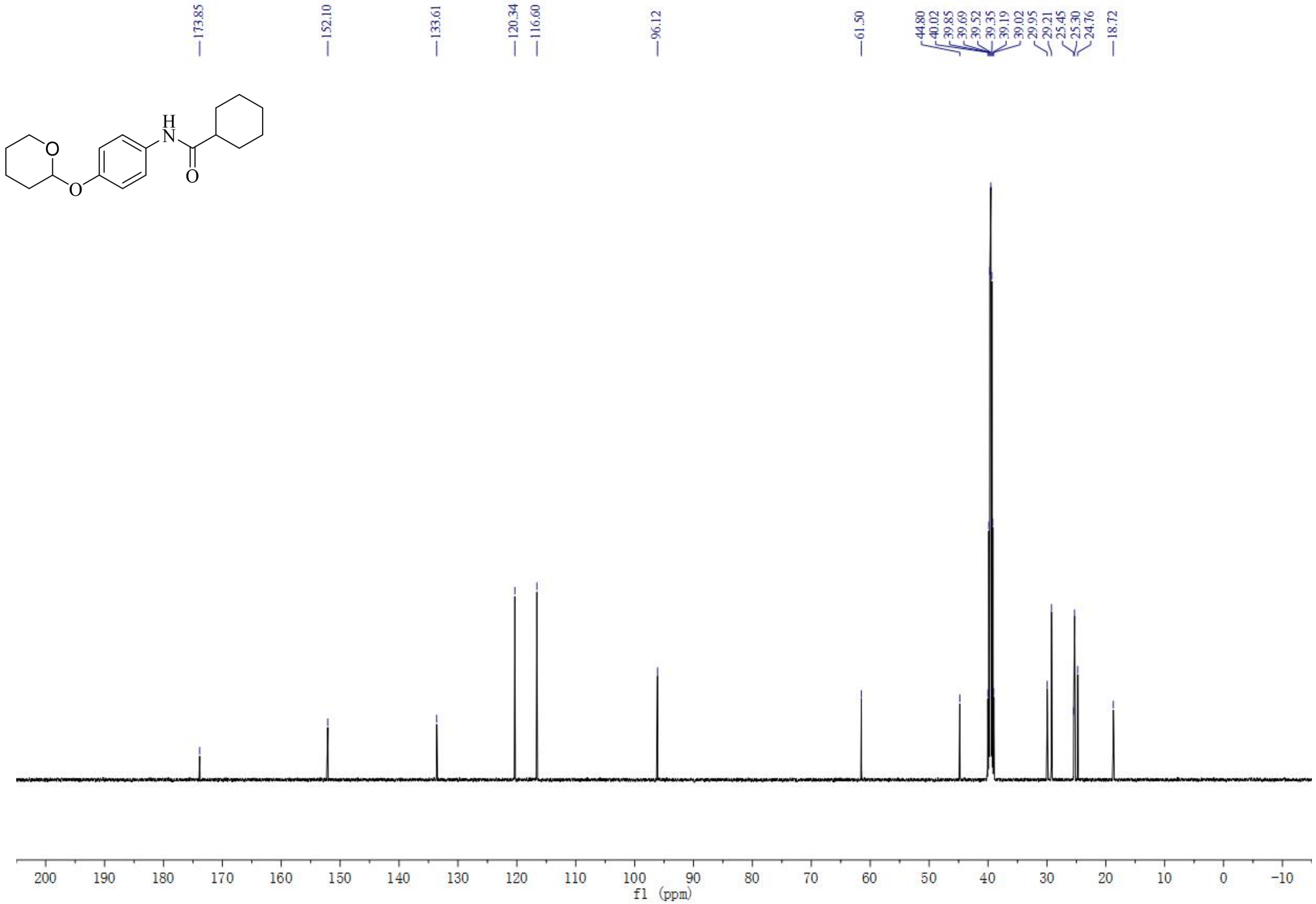


Figure S51. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(9H-carbazol-9-yl)phenyl)cyclohexanecarboxamide (**4au**)

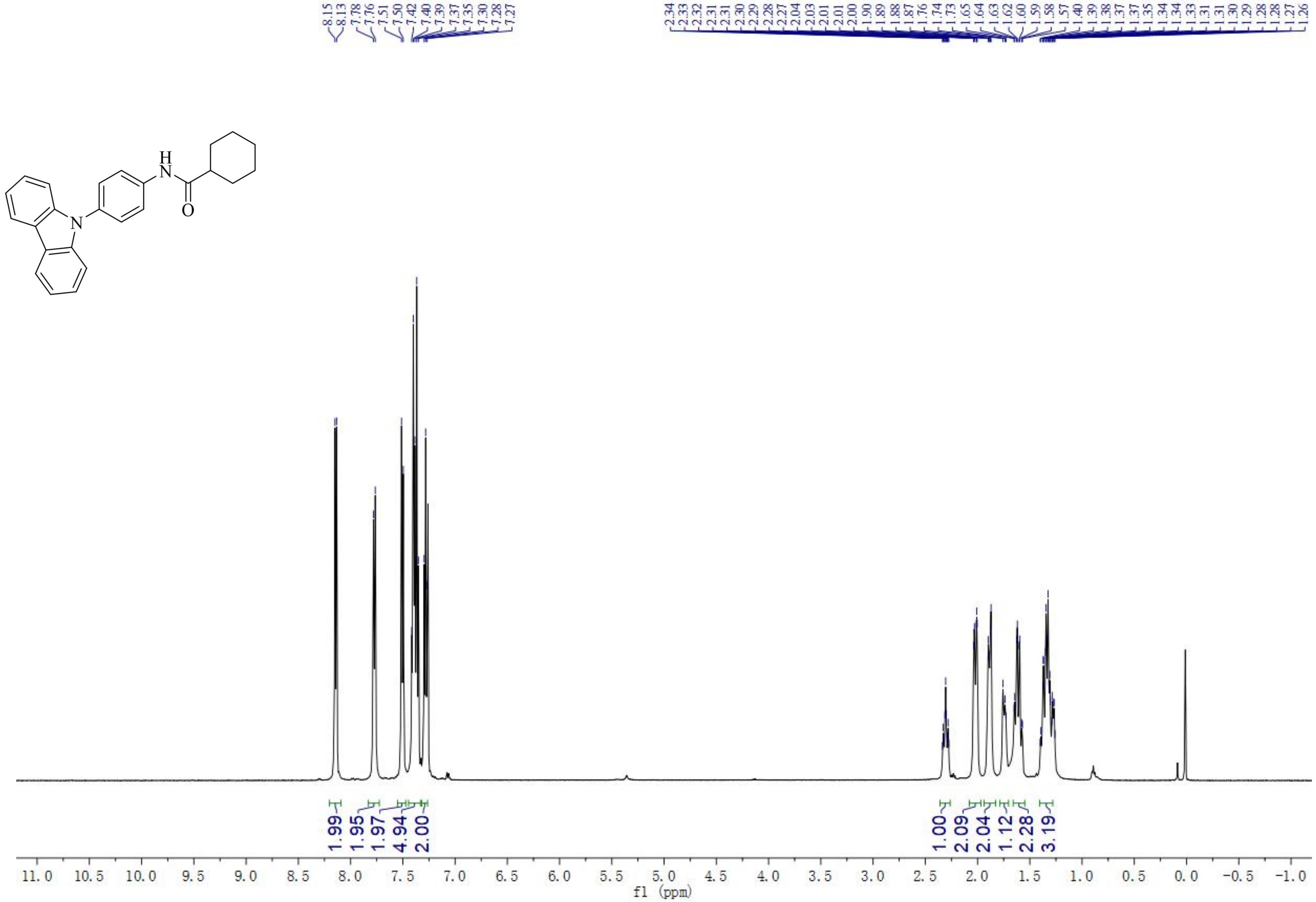


Figure S52. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(4-(9H-carbazol-9-yl)phenyl)cyclohexanecarboxamide (**4au**)

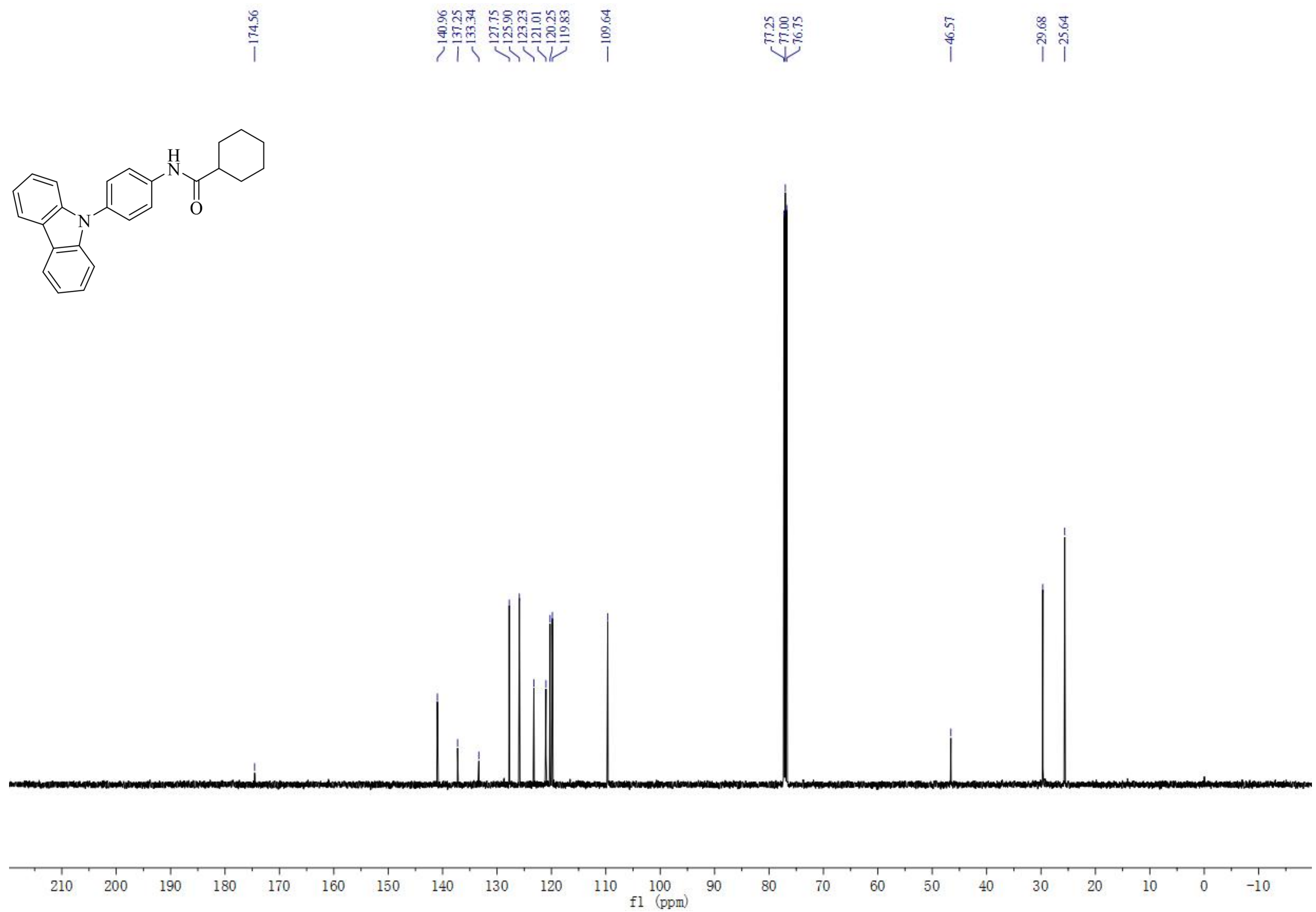


Figure S53. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of methyl 3-(cyclohexanecarboxamido)benzoate (**4av**)

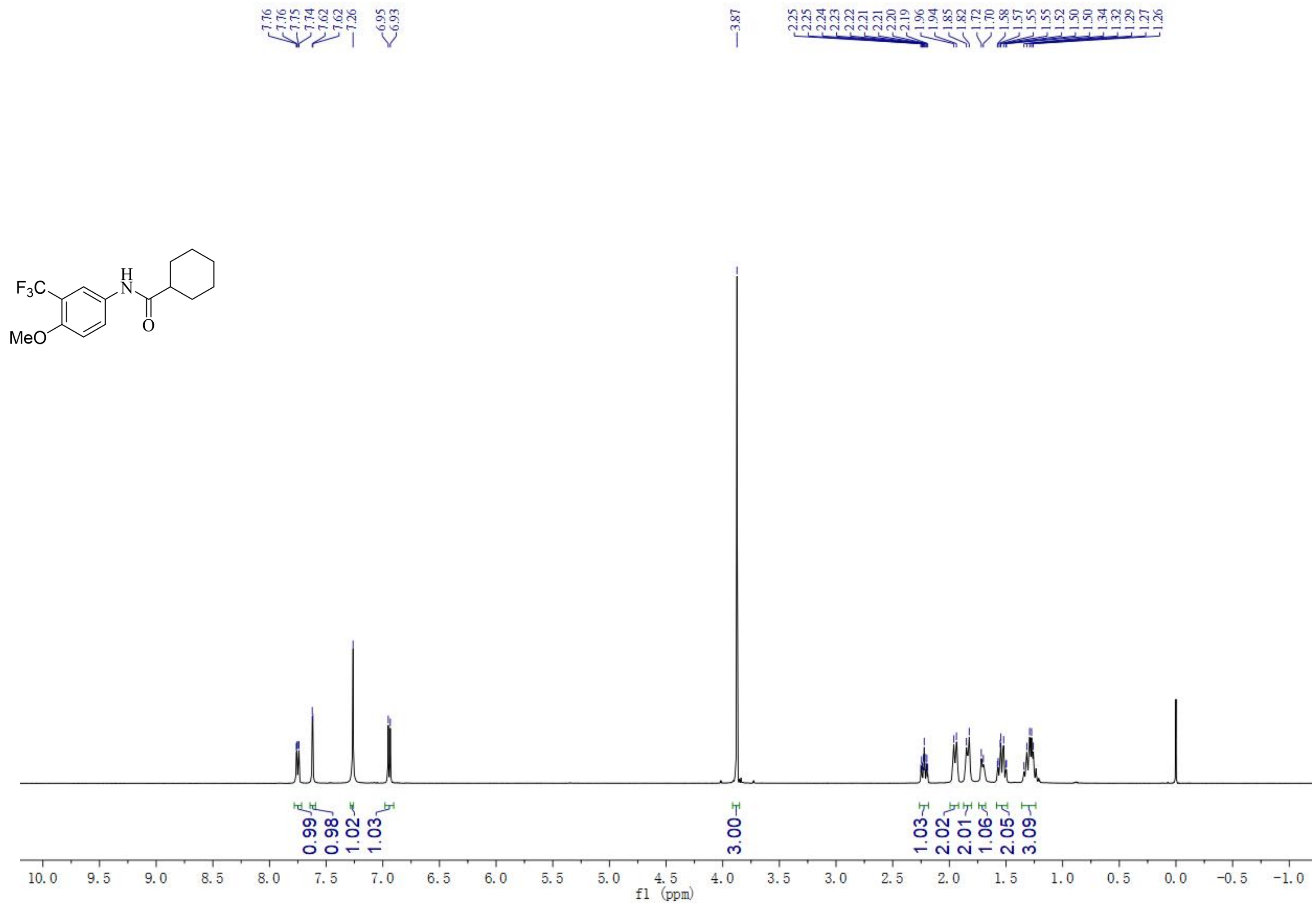


Figure S54. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of methyl 3-(cyclohexanecarboxamido)benzoate (**4av**)

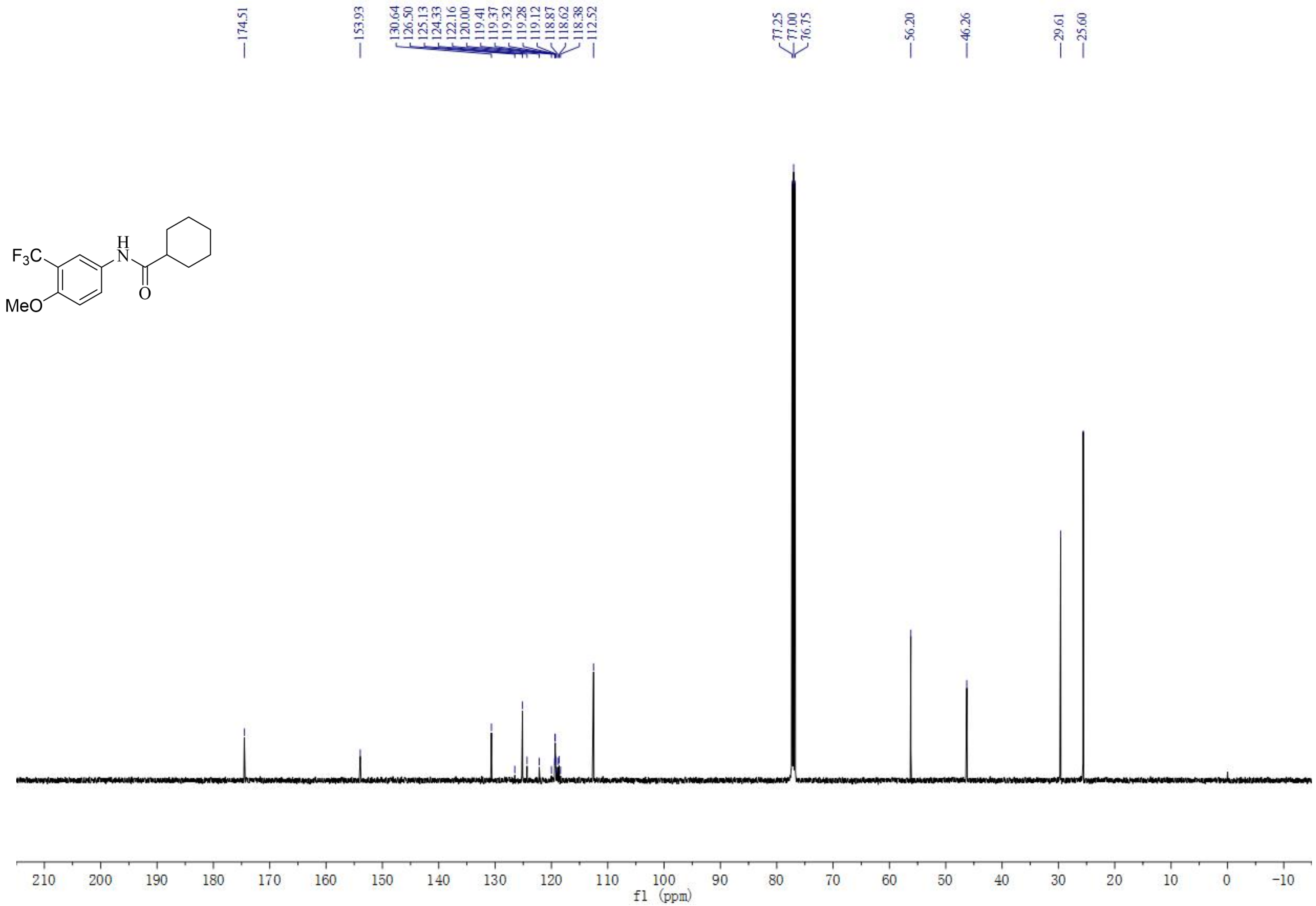
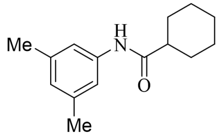


Figure S55. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(3,5-dimethylphenyl)cyclohexanecarboxamide (**4aw**)



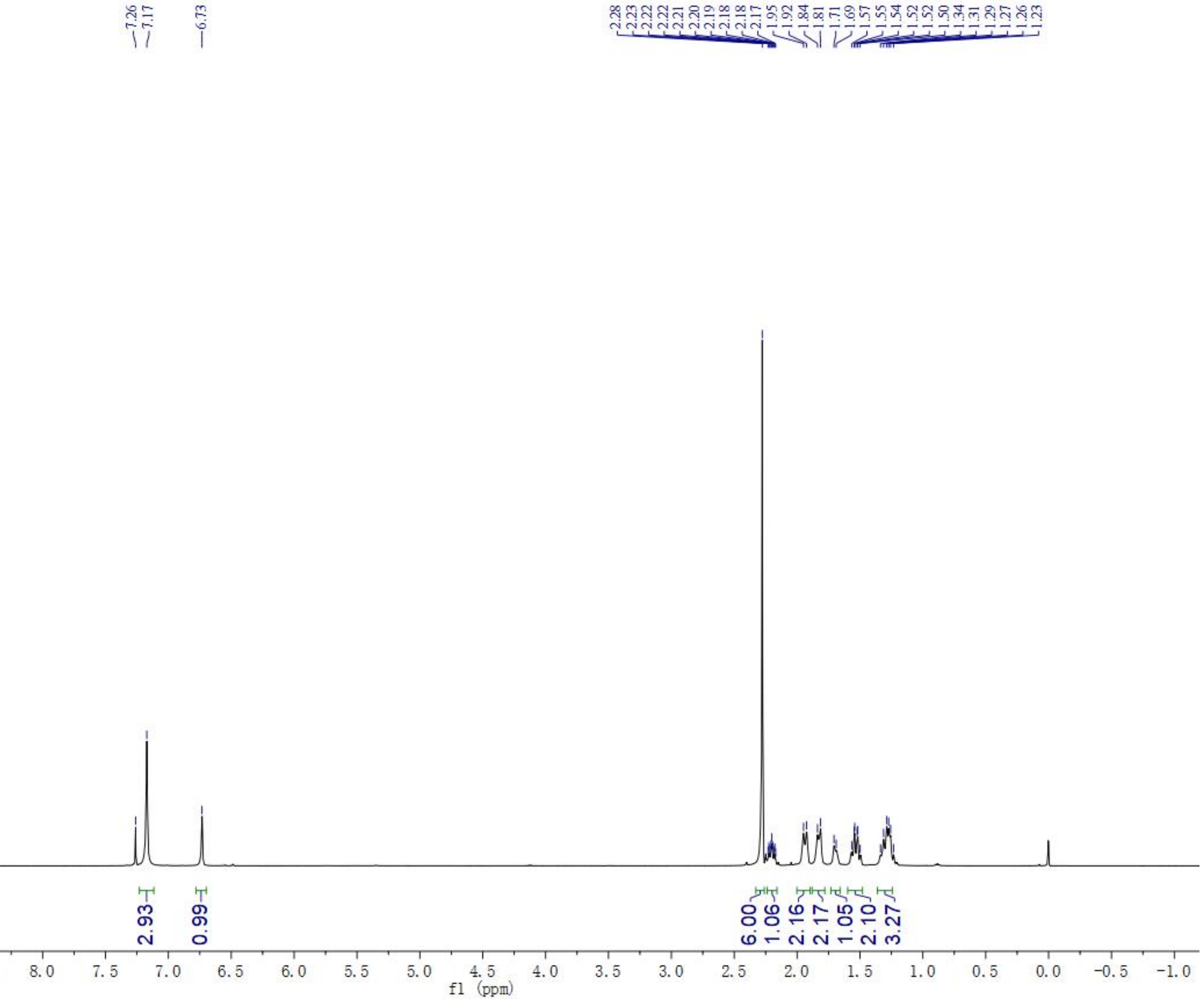


Figure S56. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(3,5-dimethylphenyl)cyclohexanecarboxamide (**4aw**)

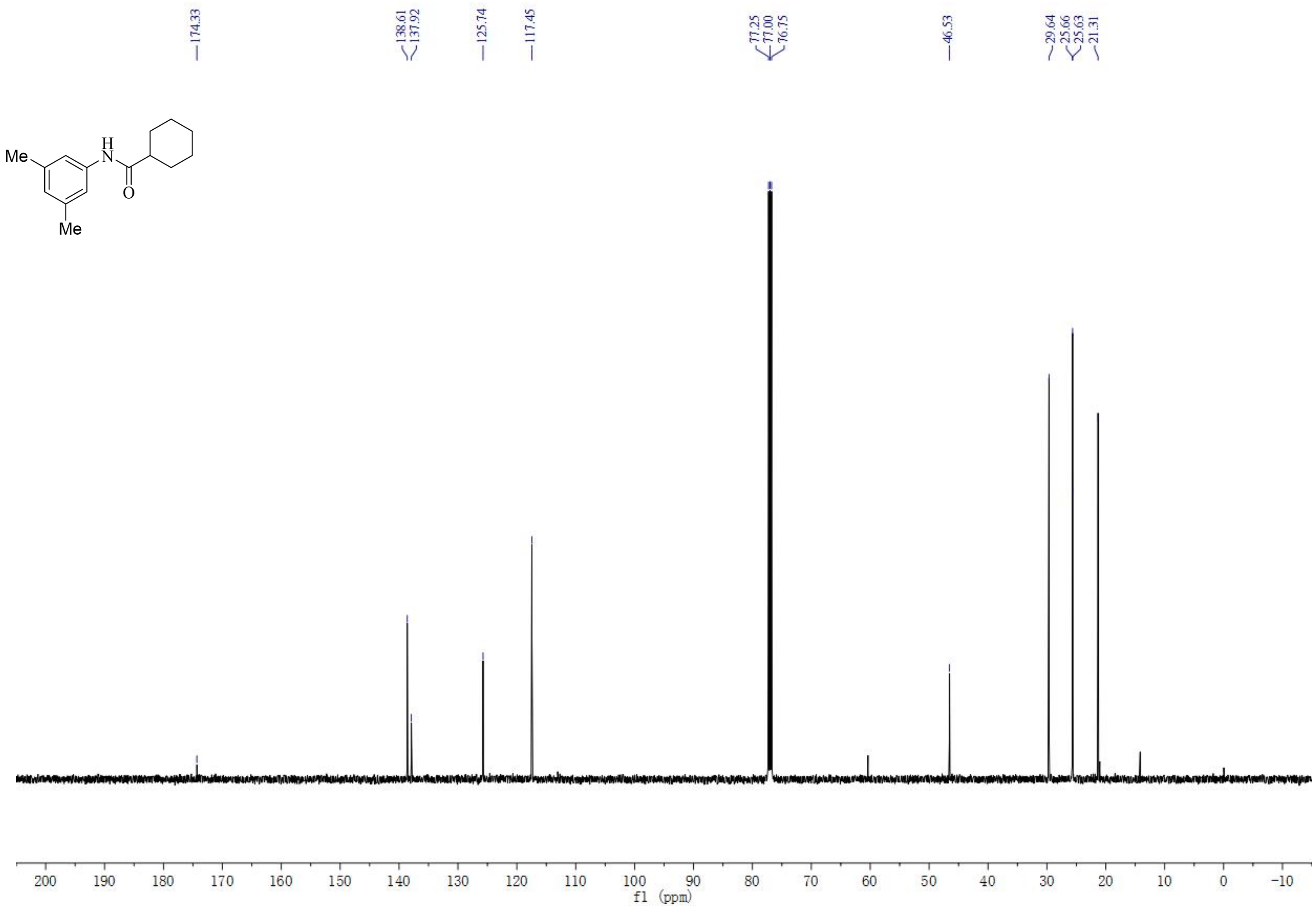
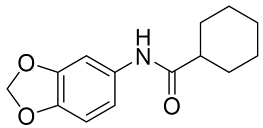


Figure S57. ¹H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(benzo[*d*][1,3]dioxol-5-yl)cyclohexanecarboxamide (**4ax**)



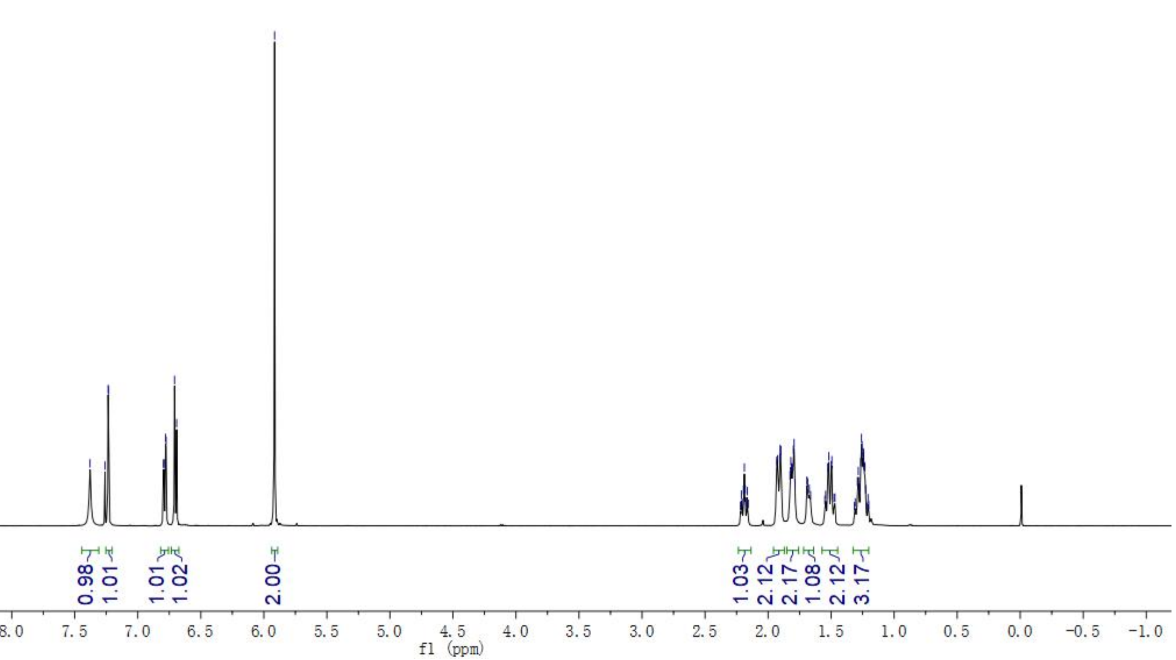


Figure S58. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(benzo[*d*][1,3]dioxol-5-yl)cyclohexanecarboxamide (**4ax**)

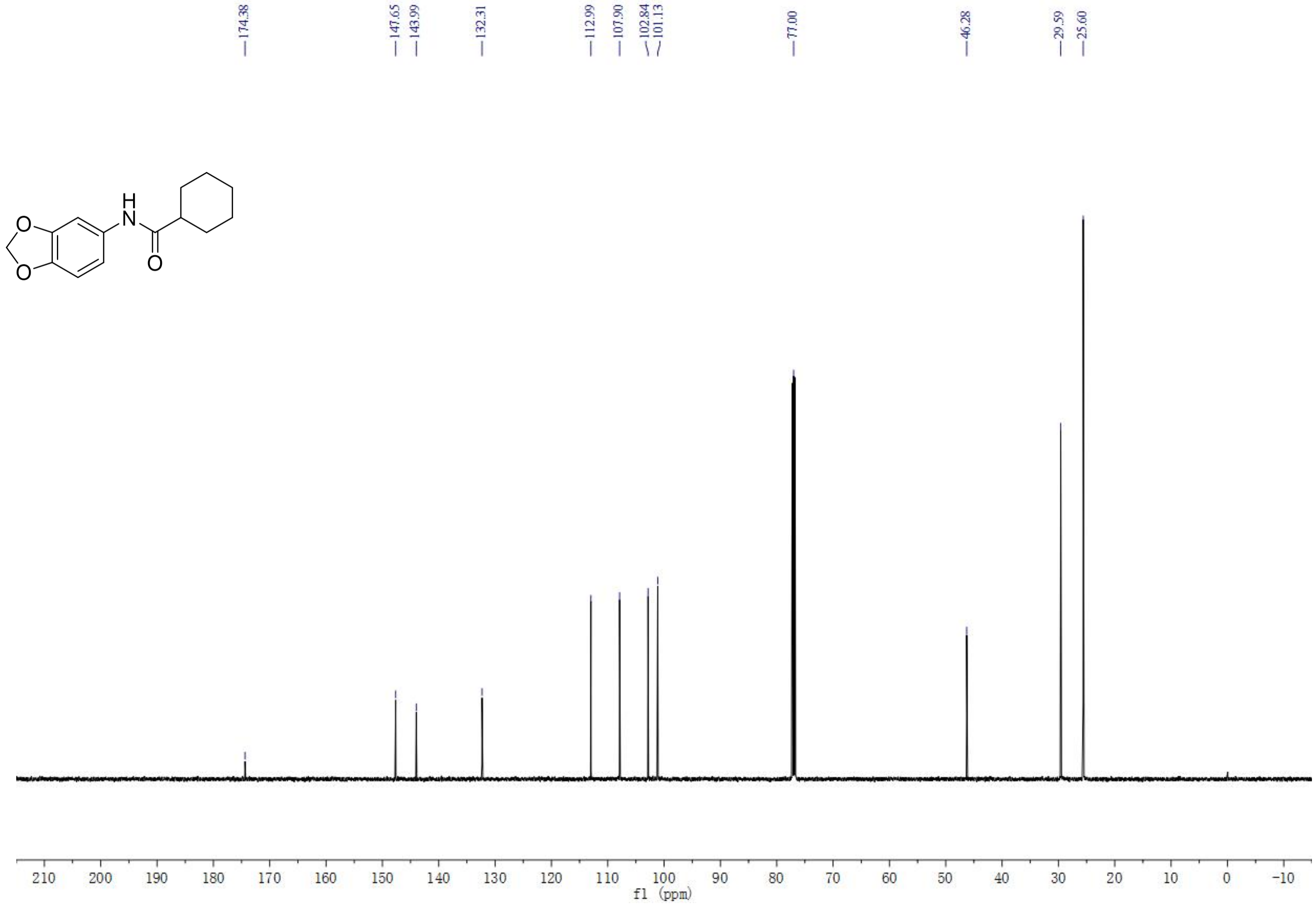


Figure S59. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)cyclohexanecarboxamide (**4ay**)

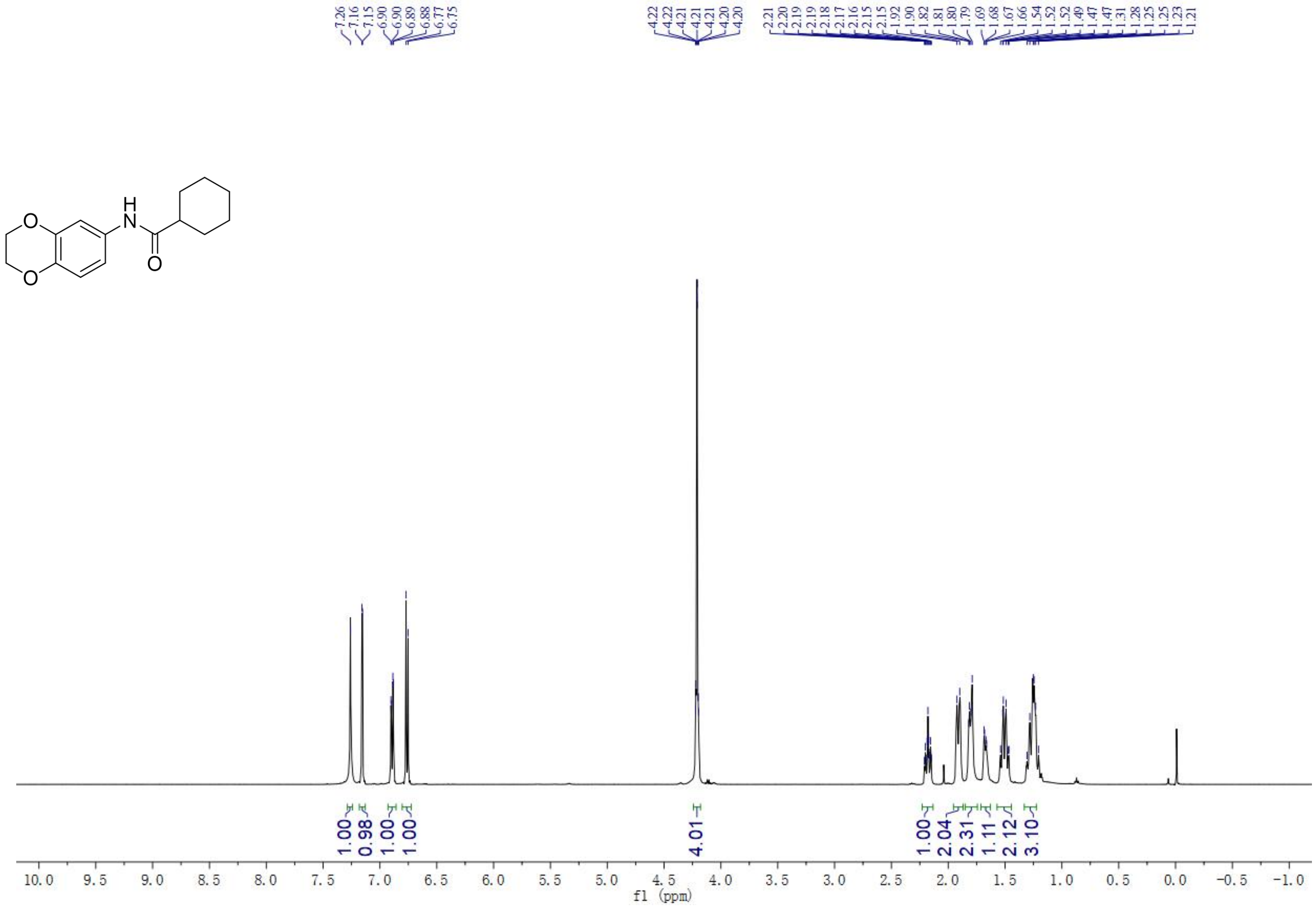


Figure S60. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)cyclohexanecarboxamide (**4ay**)

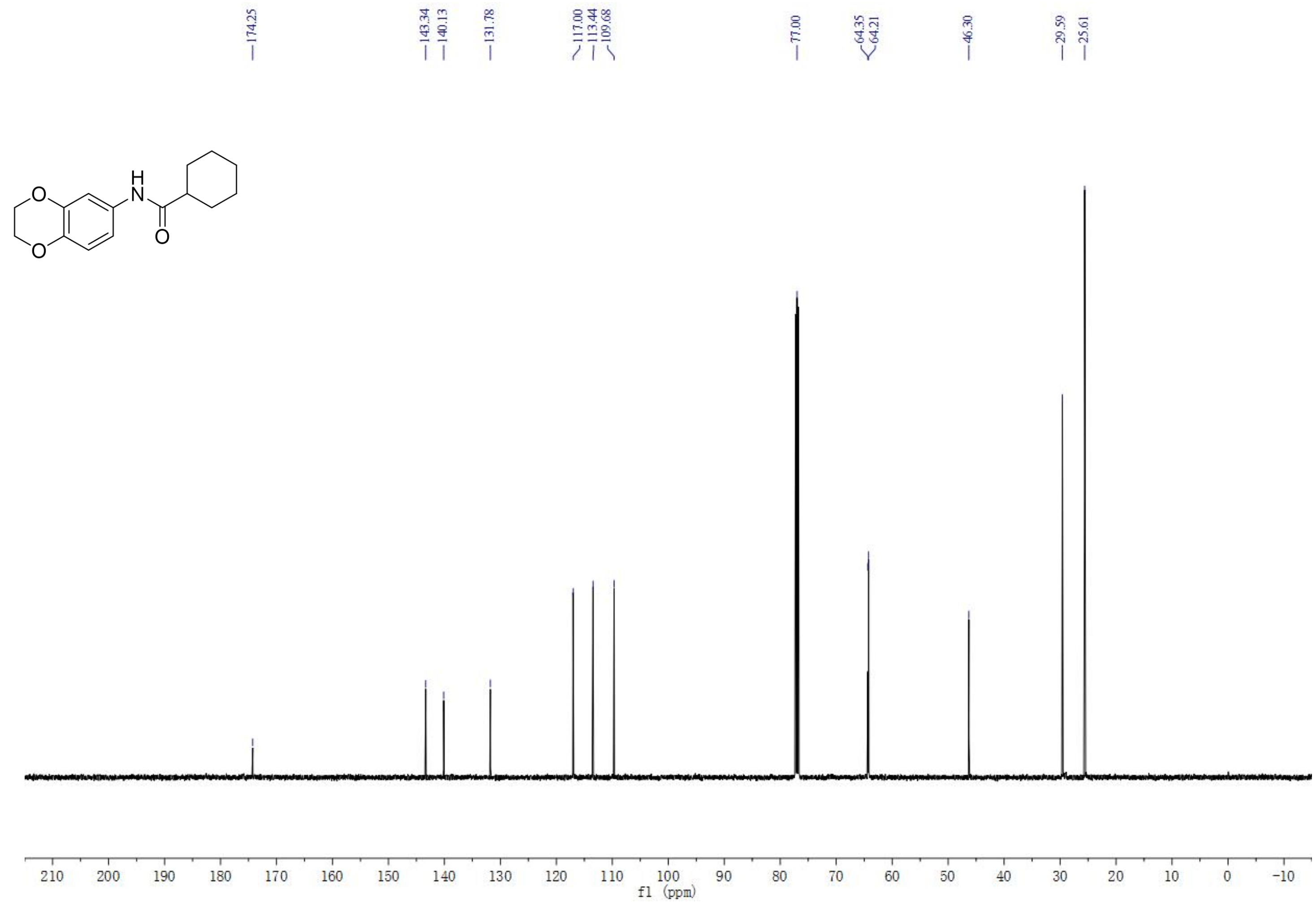


Figure S61. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) of *N*-(naphthalen-2-yl)cyclohexanecarboxamide (**4az**)

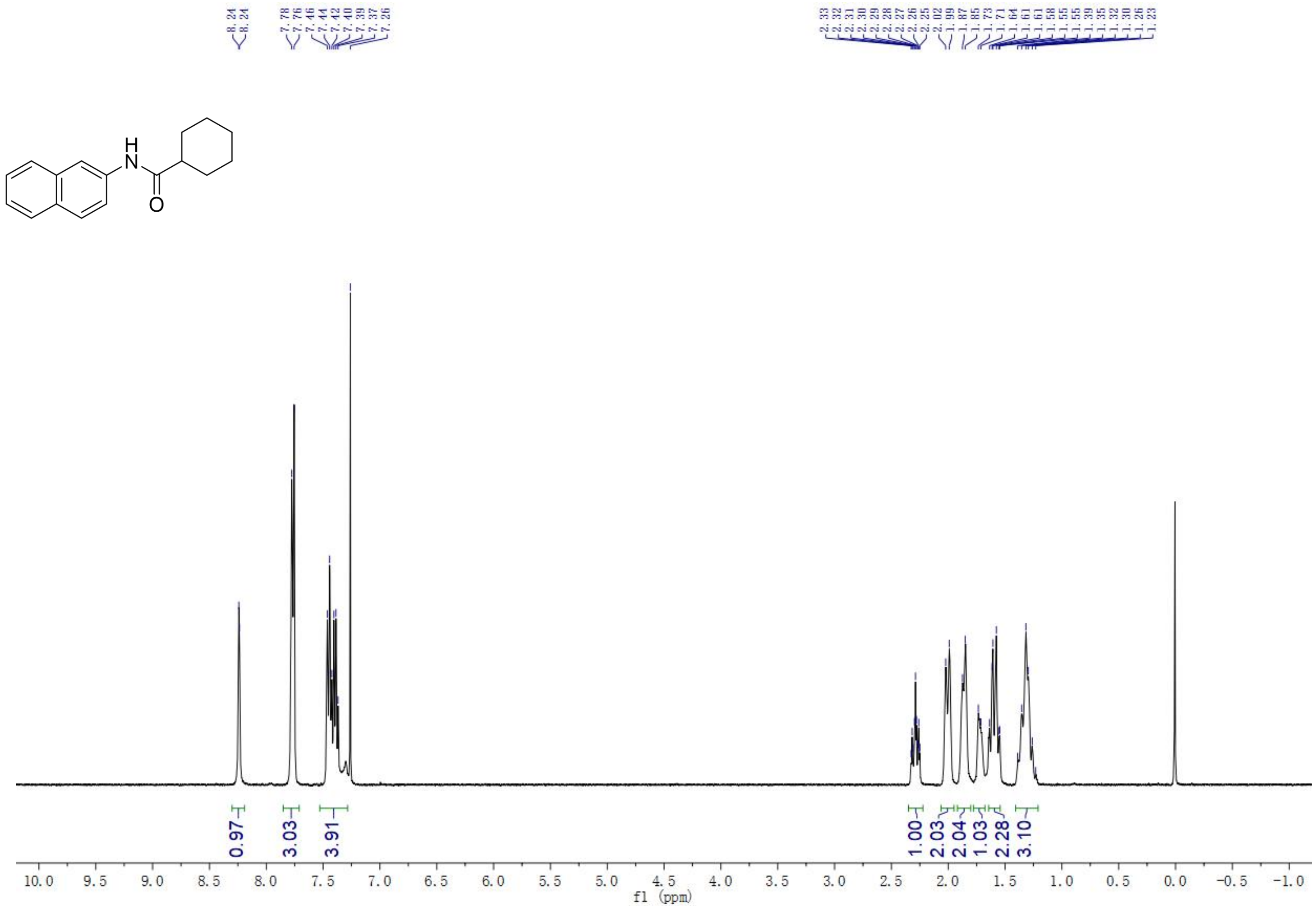


Figure S62. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(naphthalen-2-yl)cyclohexanecarboxamide (**4az**)

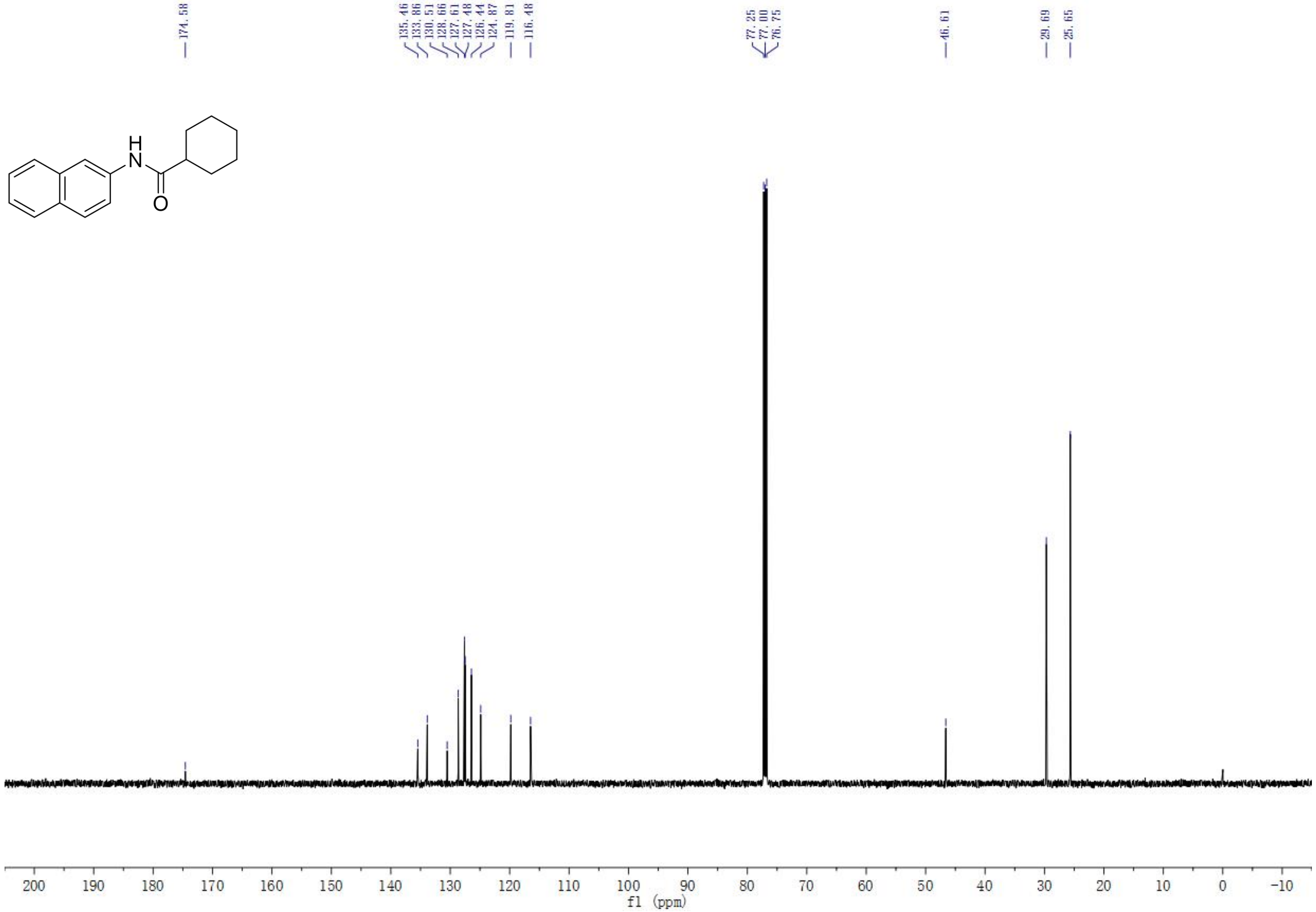


Figure S63. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(6-methoxynaphthalen-2-yl)cyclohexanecarboxamide (**4ba**)

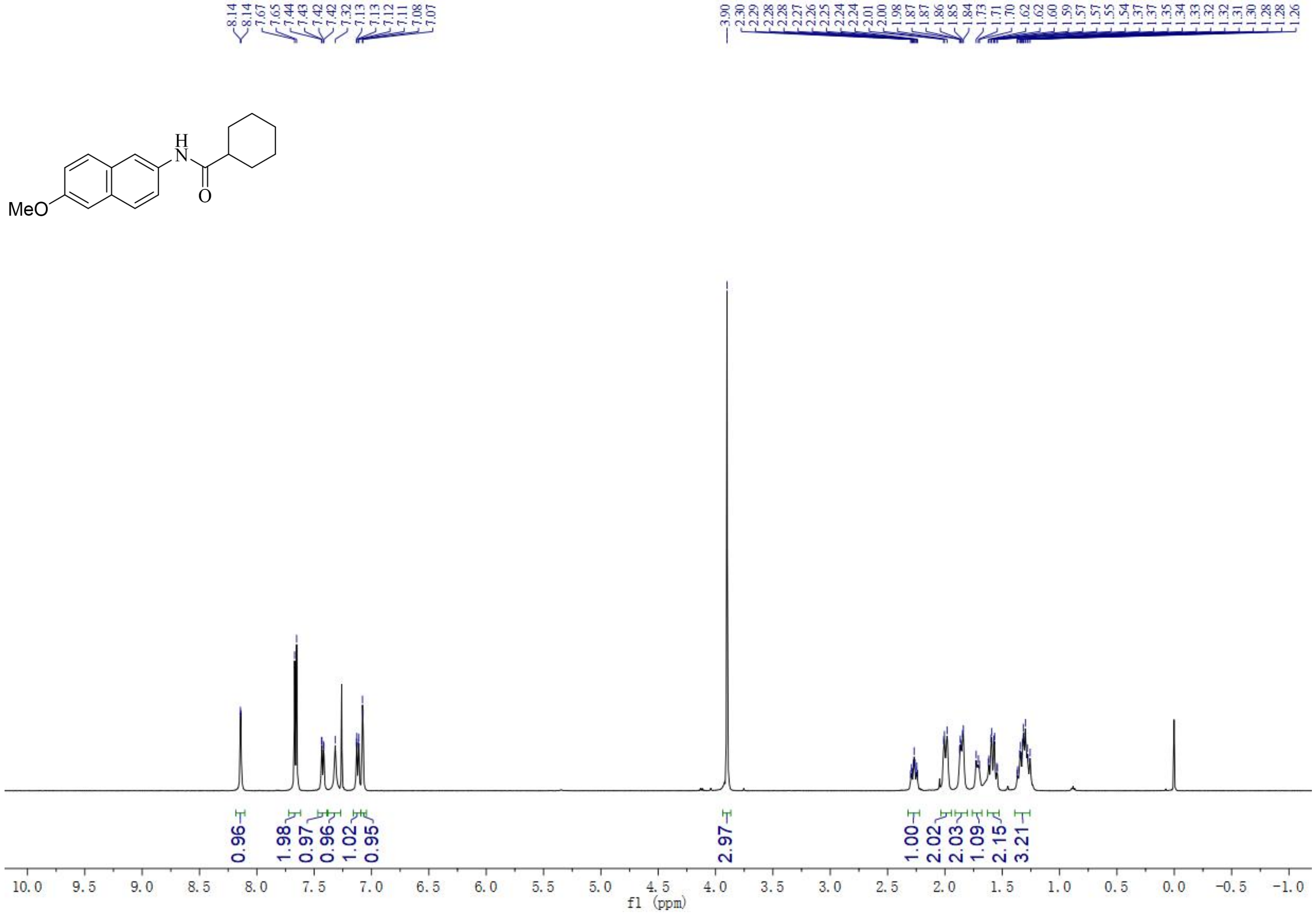


Figure S64. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *N*-(6-methoxynaphthalen-2-yl)cyclohexanecarboxamide (**4ba**)

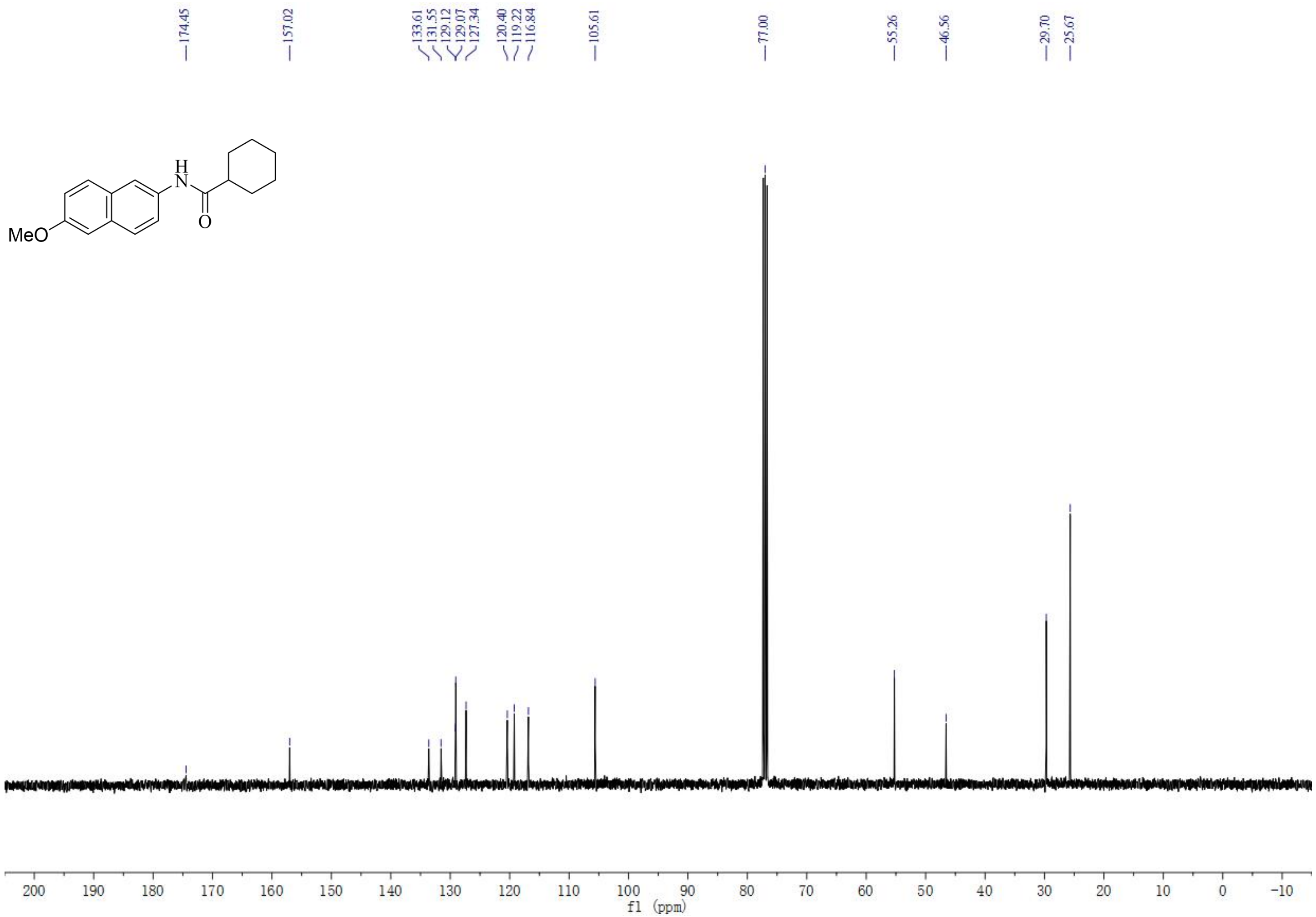


Figure S65. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(9,9-dimethyl-9*H*-fluoren-2-yl)cyclohexanecarboxamide (**4bb**)

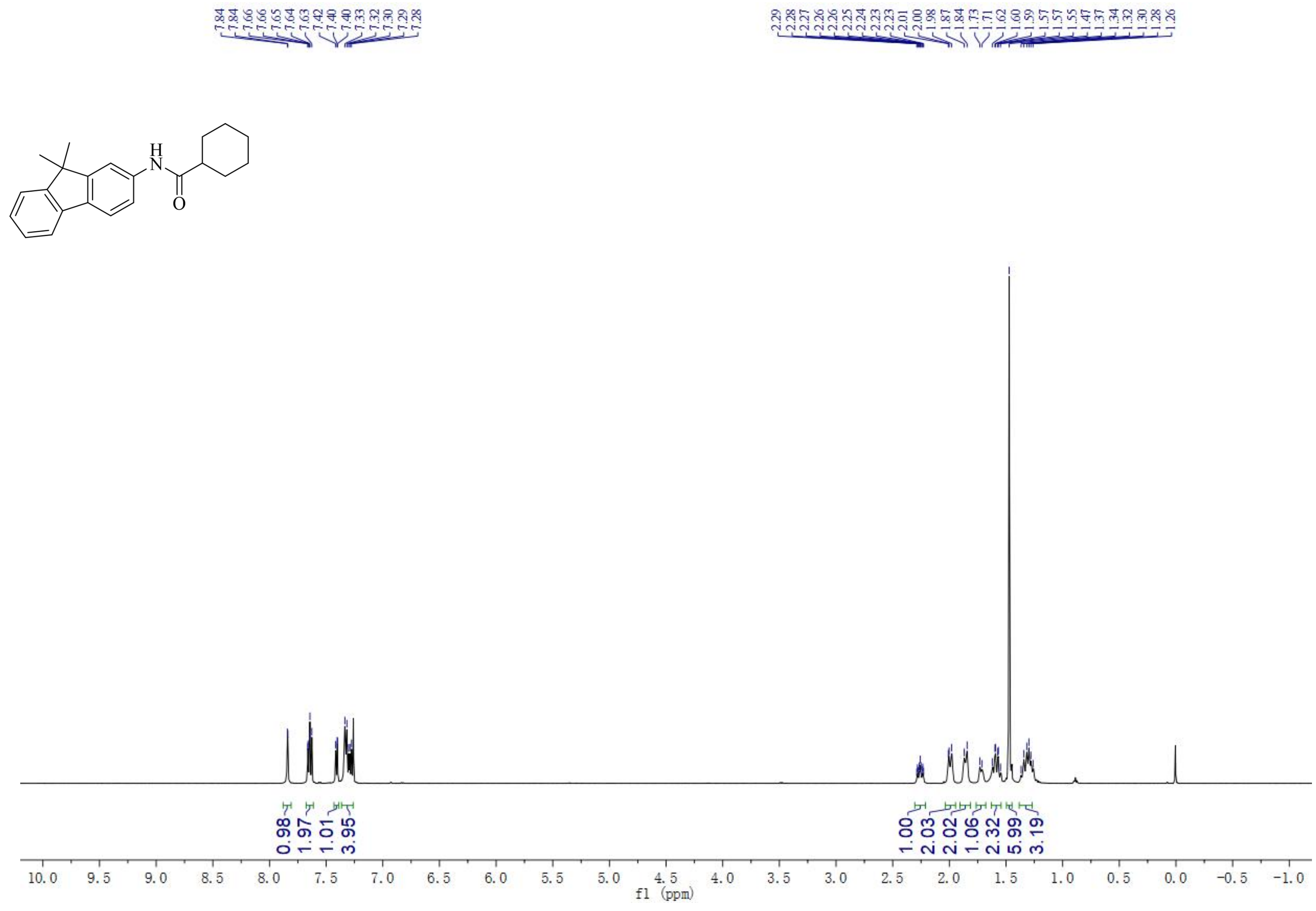


Figure S66. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(9,9-dimethyl-9*H*-fluoren-2-yl)cyclohexanecarboxamide (**4bb**)

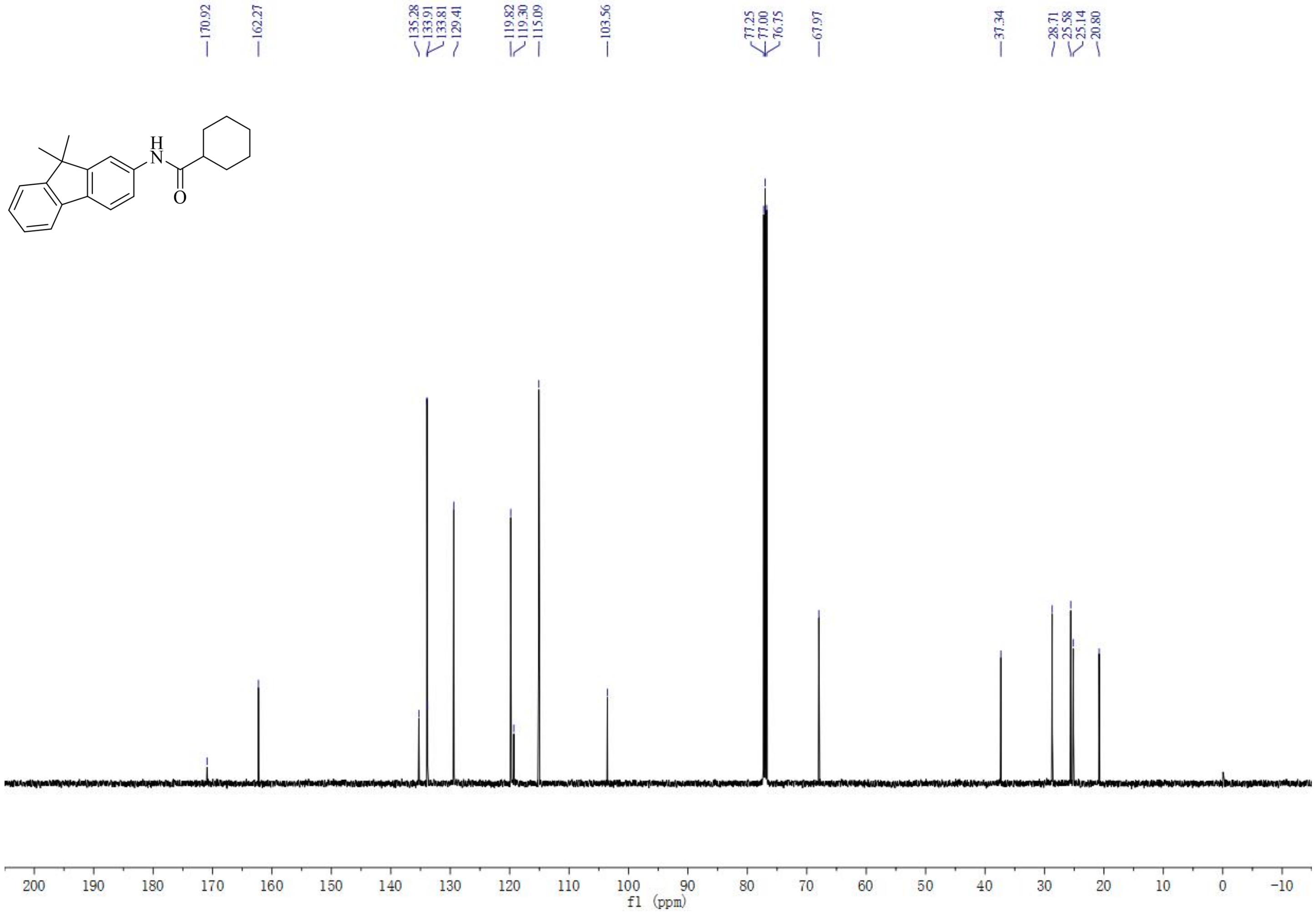


Figure S67. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-(cyclohexanecarboxamido)-1*H*-pyrrole-1-carboxylate (**4bc**)

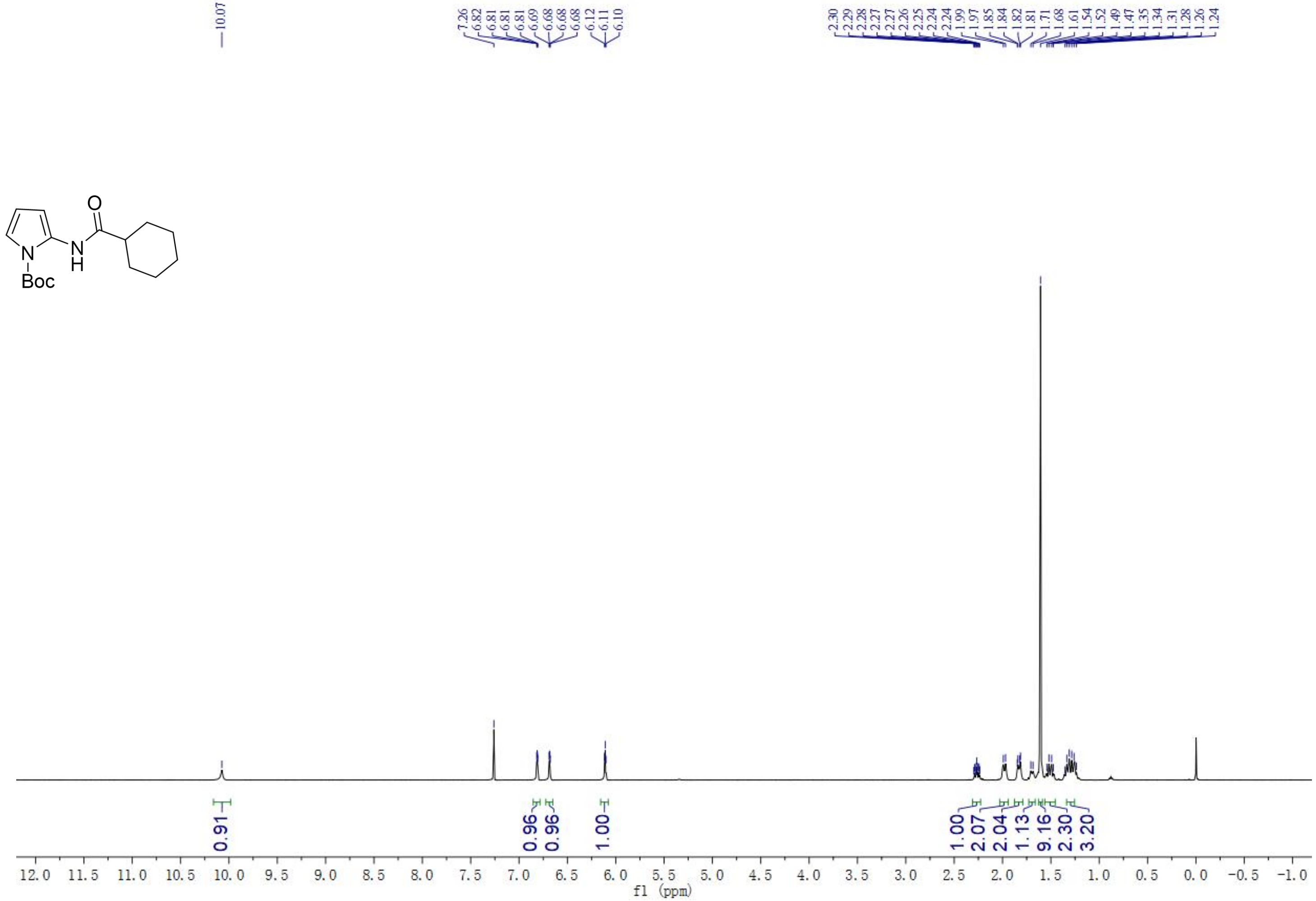


Figure S68. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-(cyclohexanecarboxamido)-1*H*-pyrrole-1-carboxylate (**4bc**)

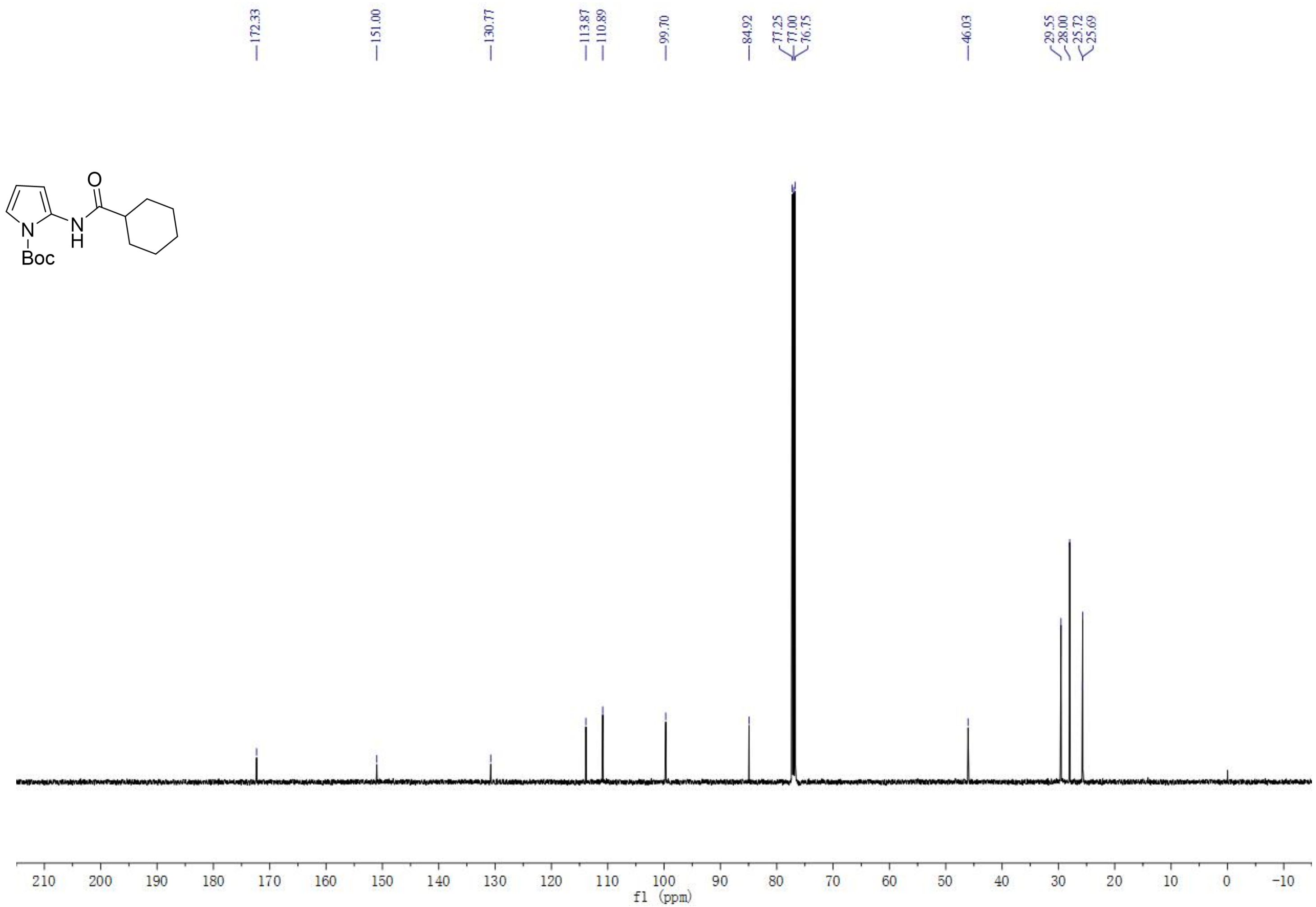
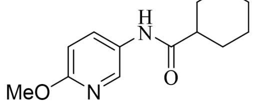


Figure S69. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(6-methoxypyridin-3-yl)cyclohexanecarboxamide (**4bd**)



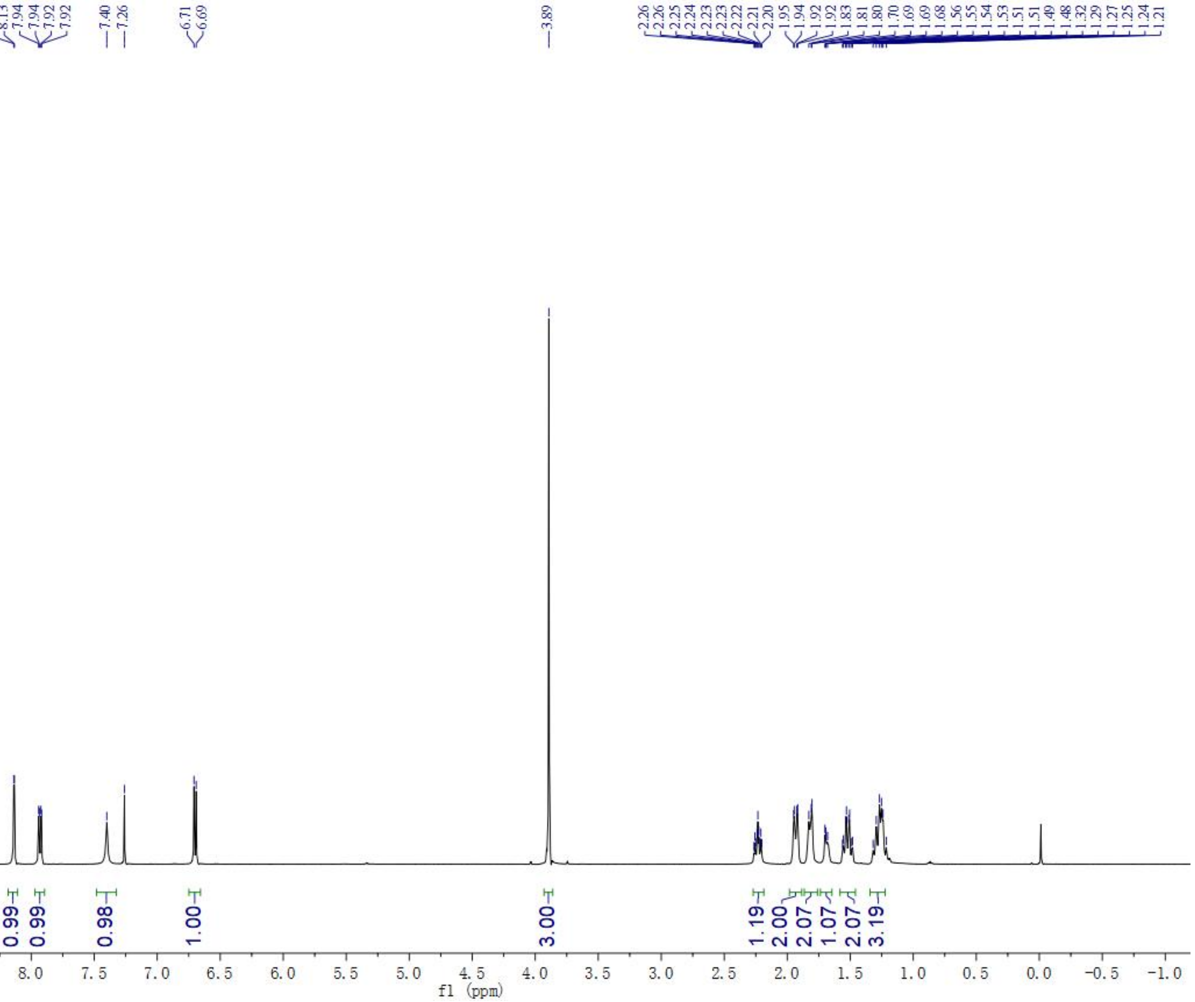


Figure S70. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(6-methoxypyridin-3-yl)cyclohexanecarboxamide (**4bd**)

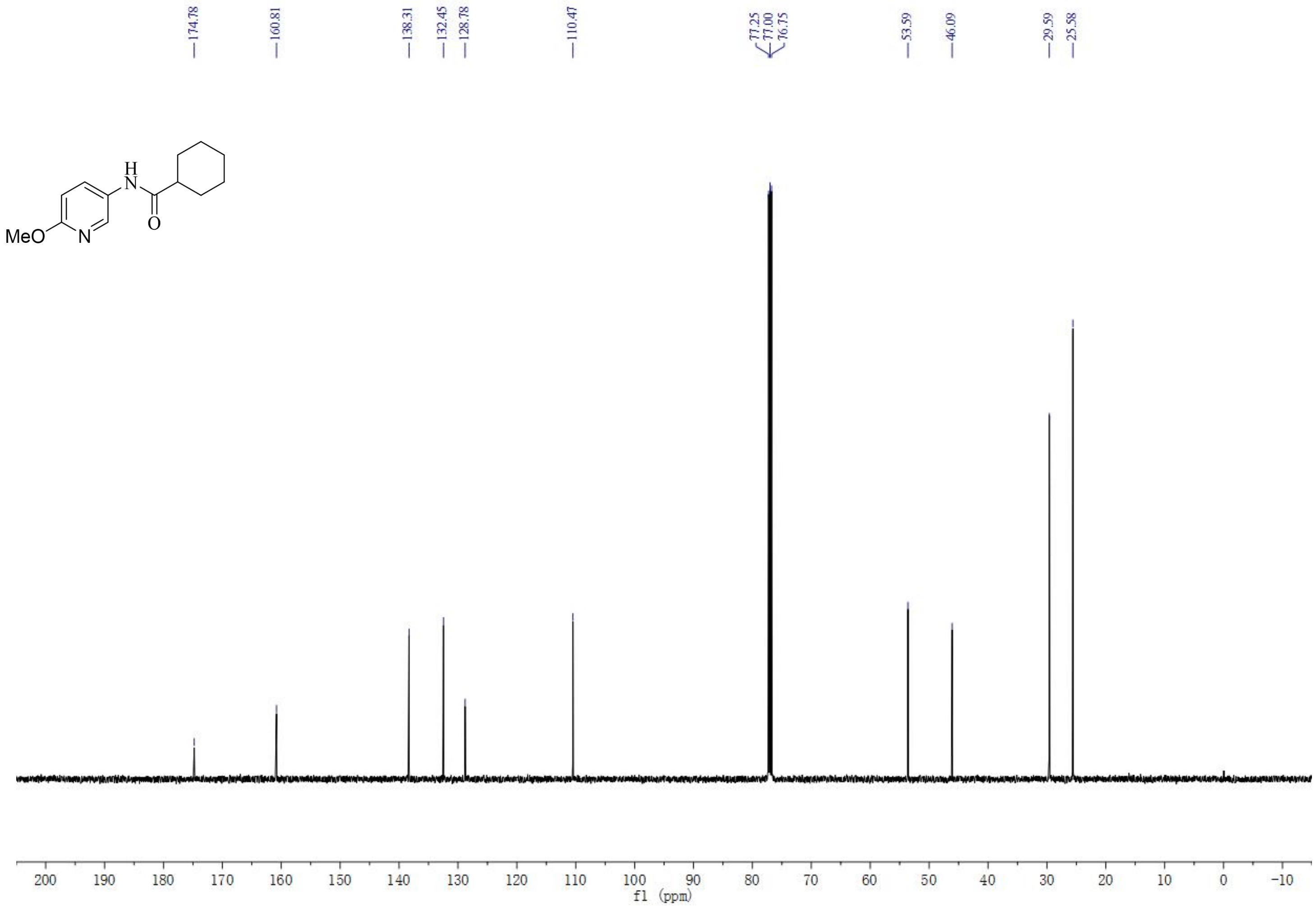


Figure S71. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(1-methyl-1*H*-indol-5-yl)cyclohexanecarboxamide (**4be**)

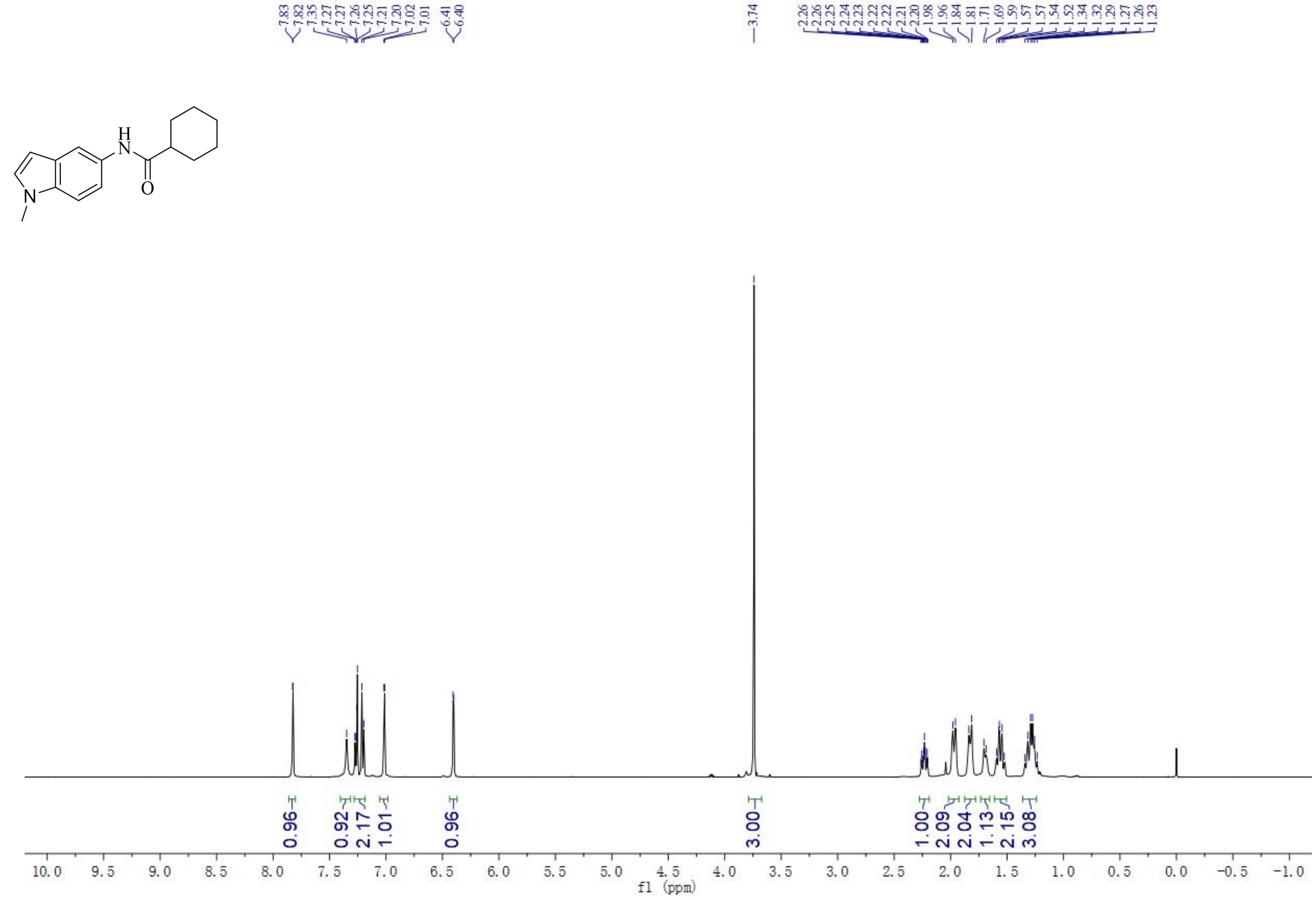


Figure S72. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(1-methyl-1*H*-indol-5-yl)cyclohexanecarboxamide (**4be**)

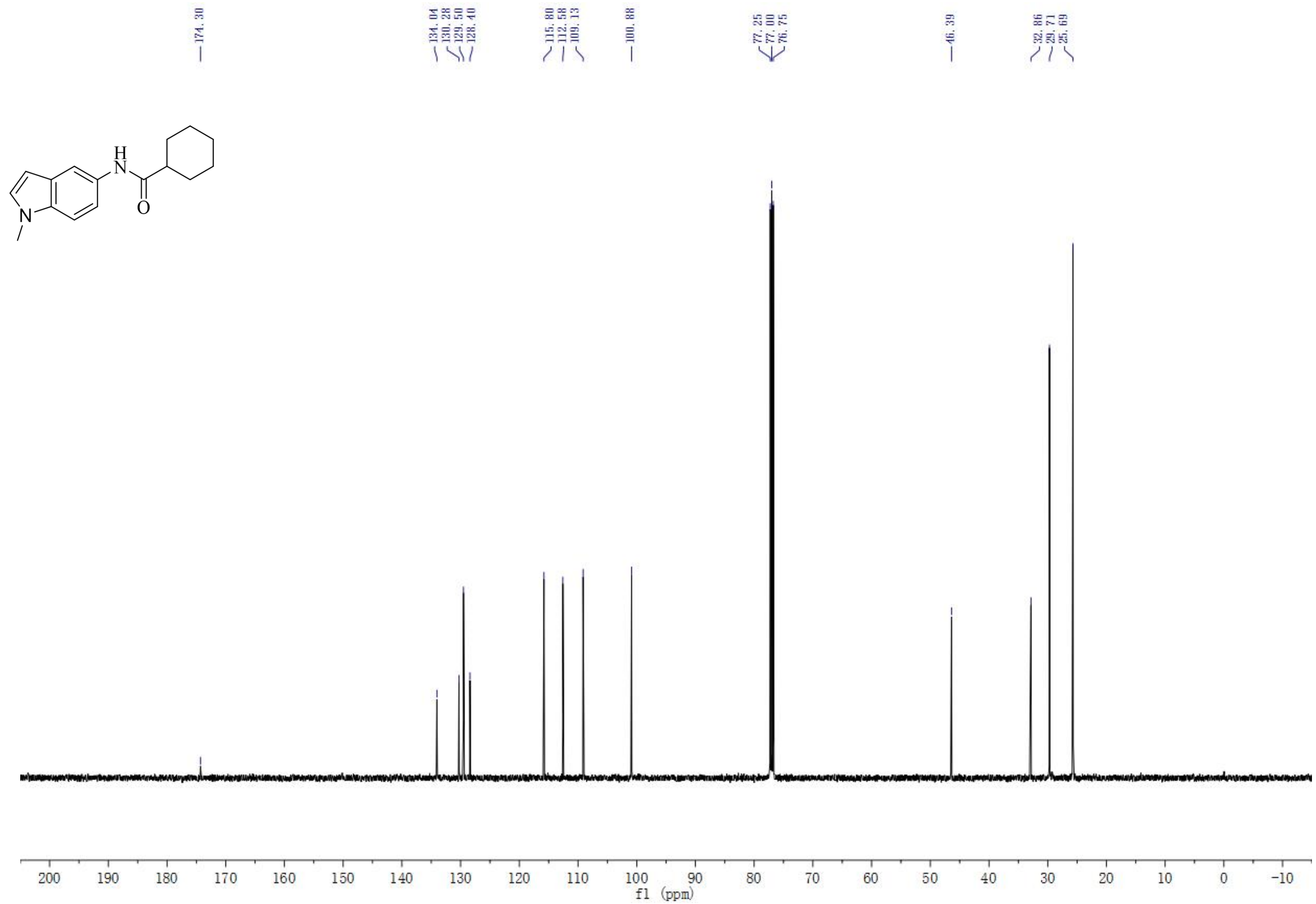


Figure S73. ¹H NMR (500 MHz, DMSO-d_6, 298K) of *N*-(dibenzo[*b,d*]furan-2-yl)cyclohexanecarboxamide (**4bf**)

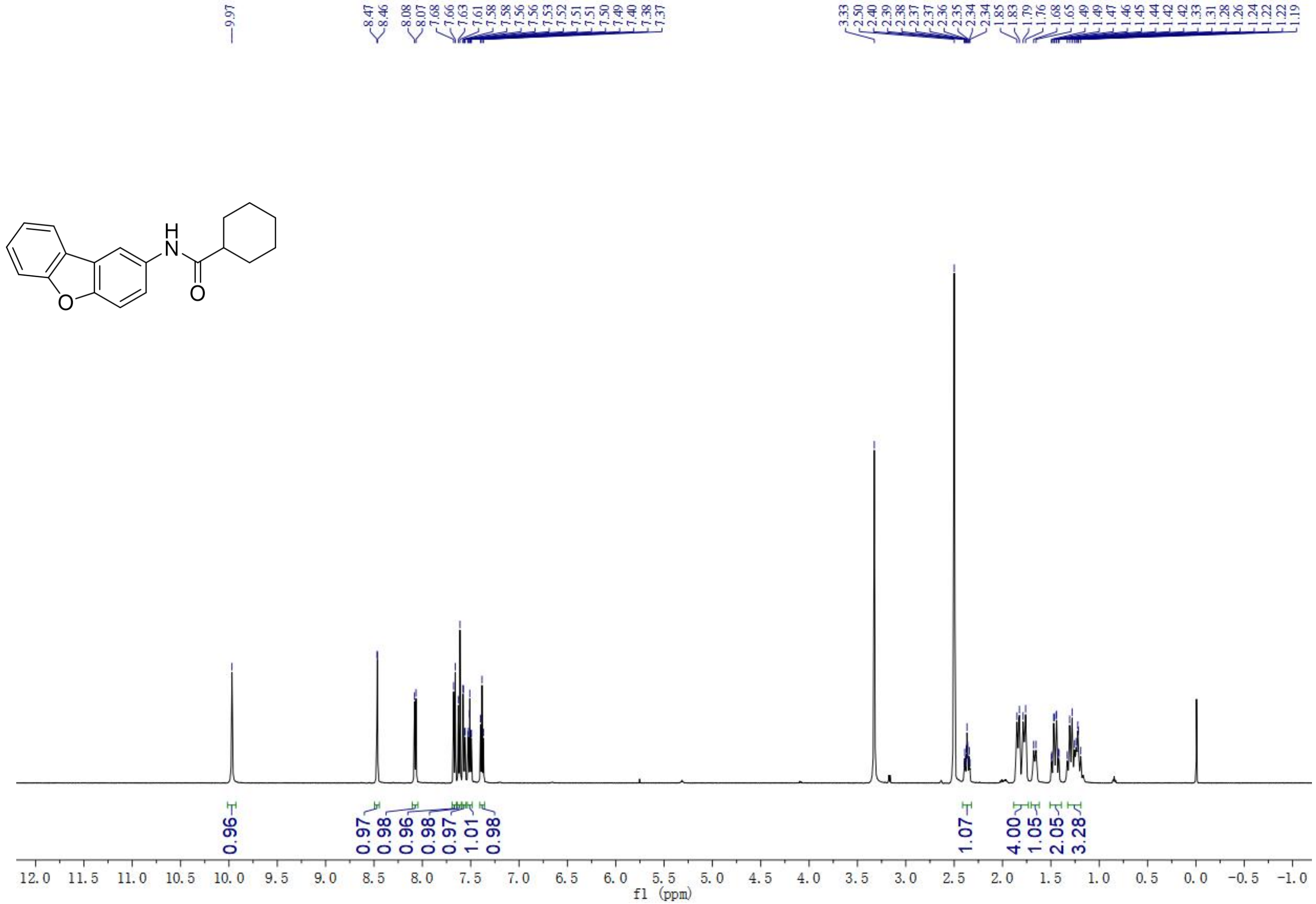


Figure S74. ^{13}C NMR (126 MHz, DMSO-d_6, 298K) of *N*-(dibenzo[*b,d*]furan-2-yl)cyclohexanecarboxamide (**4bf**)

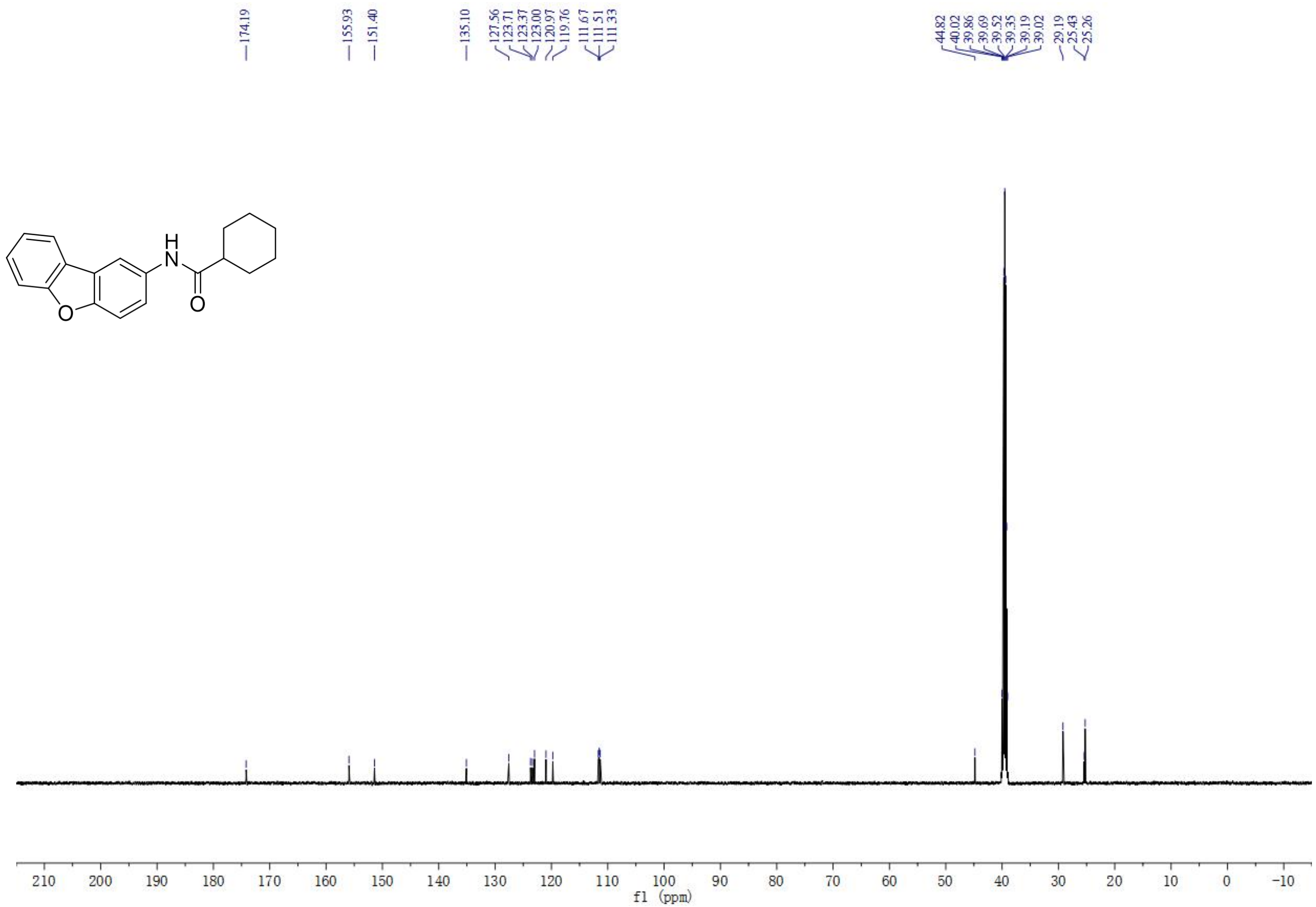


Figure S75. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(dibenzo[*b,d*]thiophen-2-yl)cyclohexanecarboxamide (**4bg**)

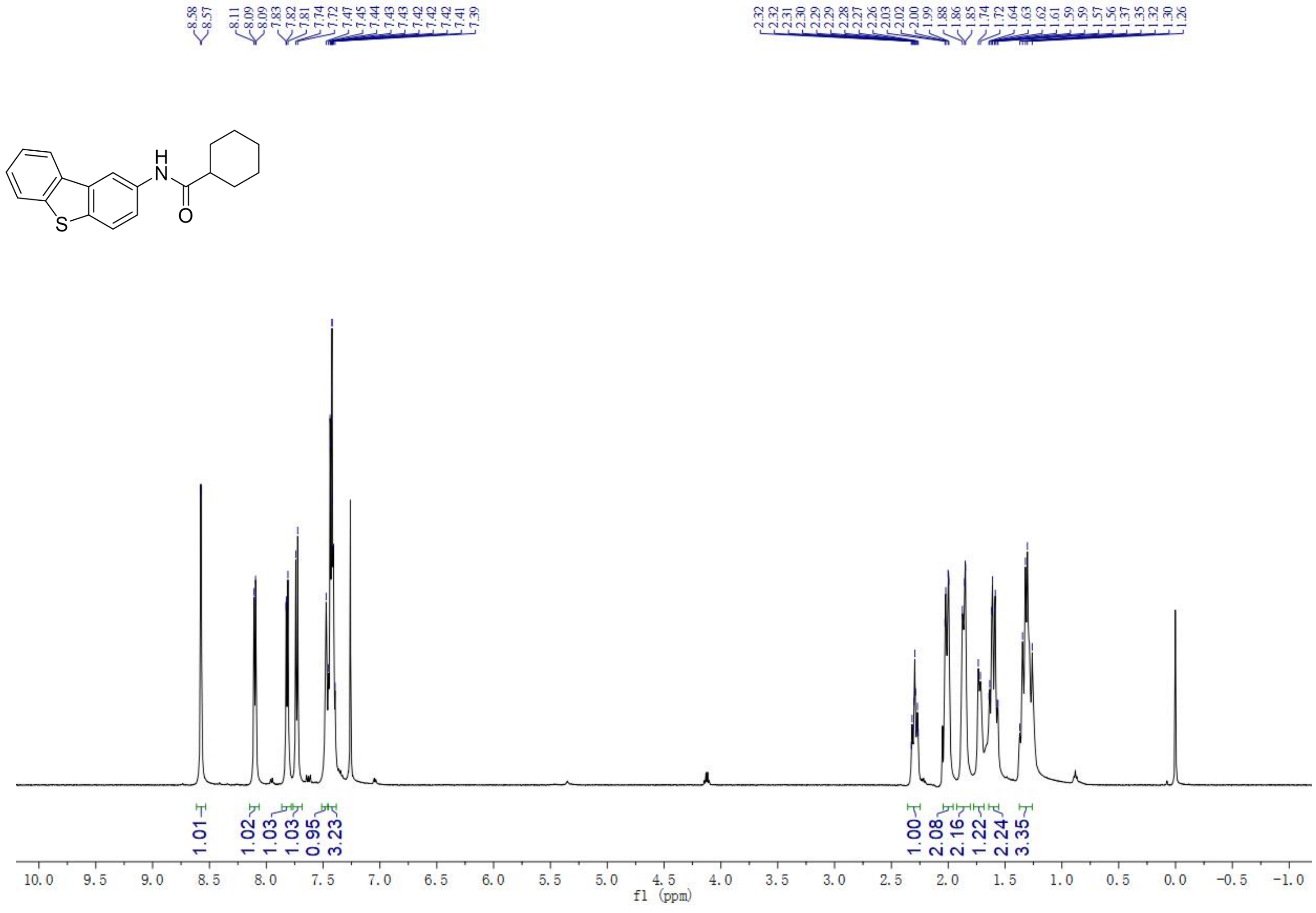


Figure S76. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(dibenzo[*b,d*]thiophen-2-yl)cyclohexanecarboxamide (**4bg**)

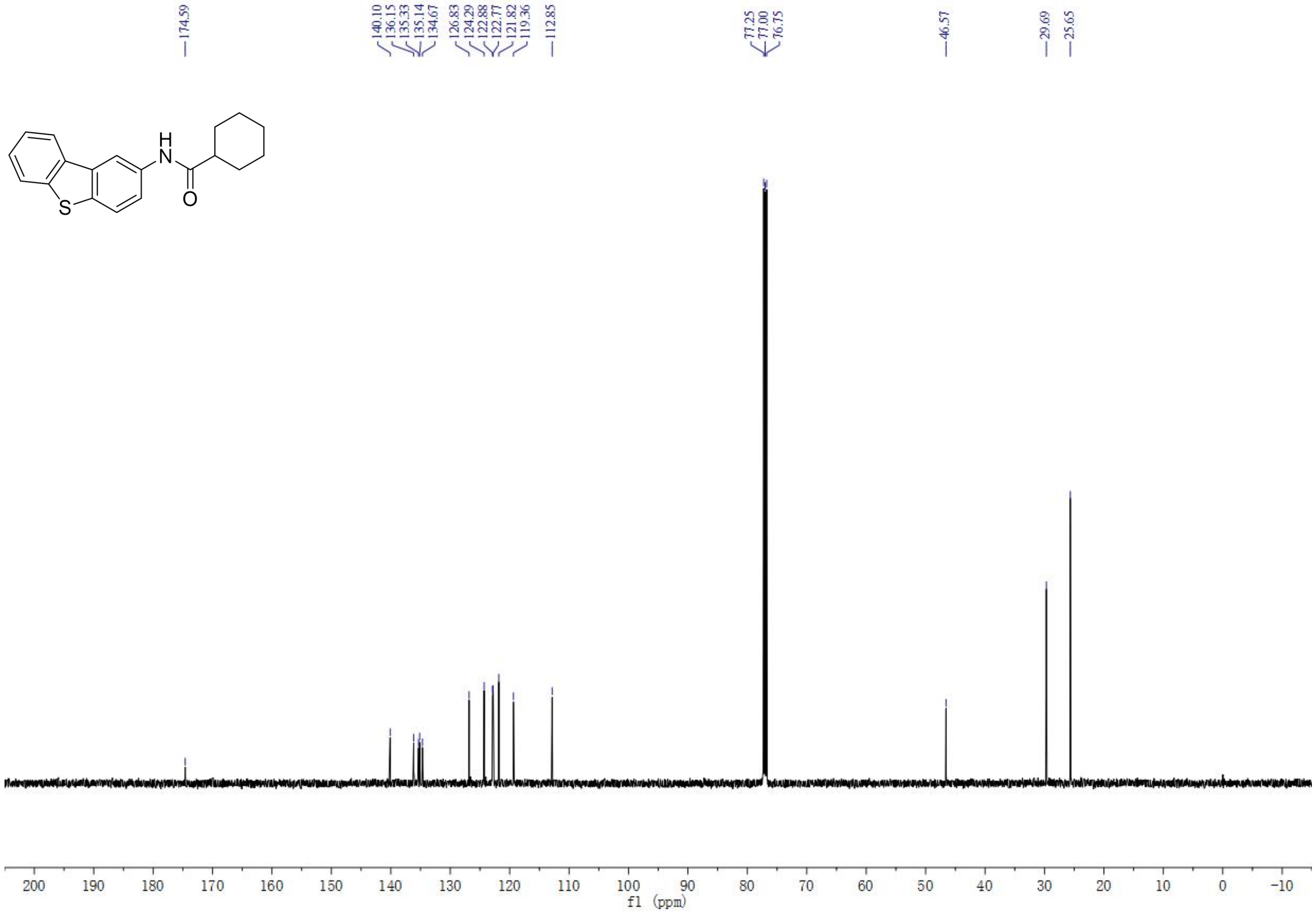


Figure S77. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)phenyl)cyclohexanecarboxamide (**4bh**)

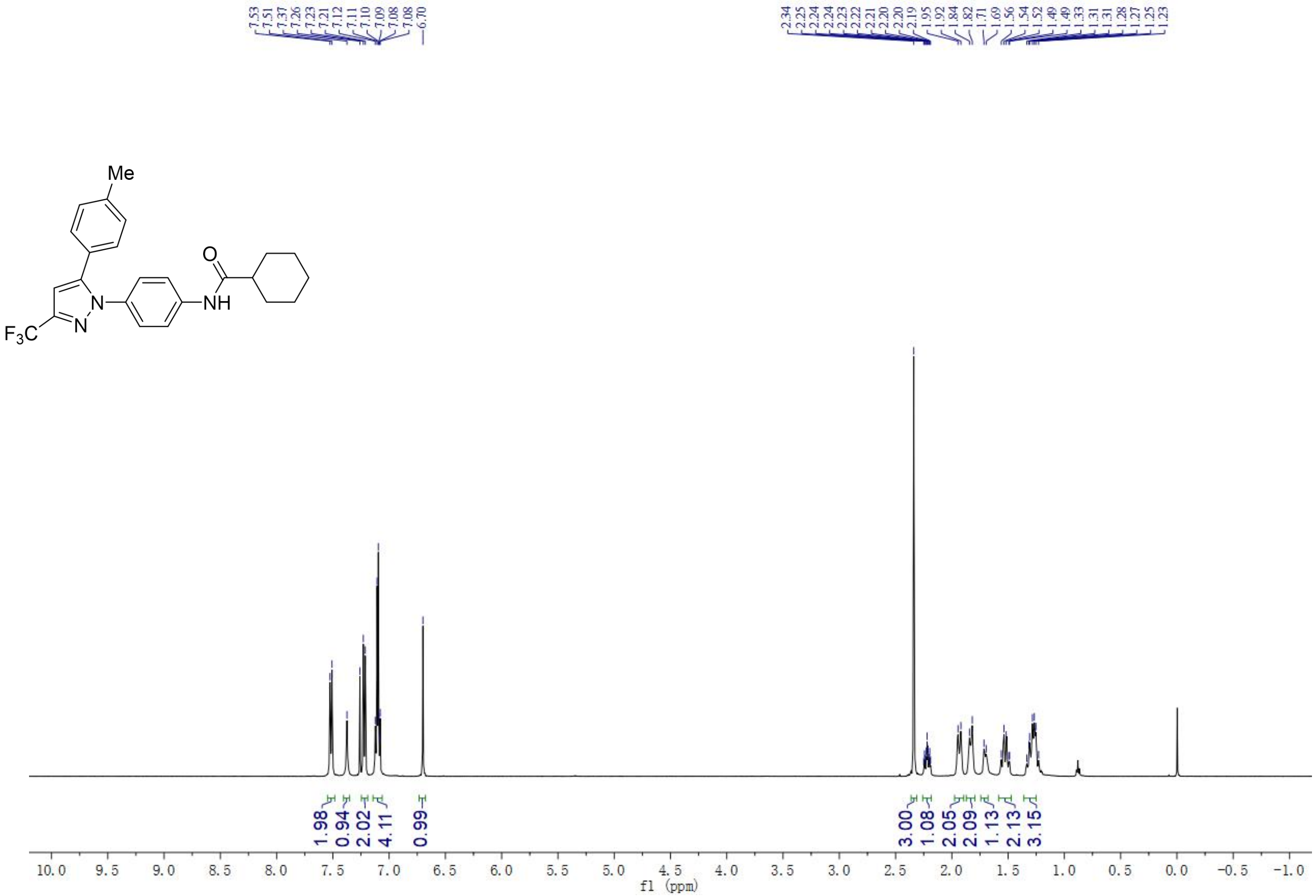


Figure S78. ^{13}C NMR (126 MHz, CDCl$_3$, 298K) of *N*-(4-(5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)phenyl)cyclohexanecarboxamide (**4bh**)

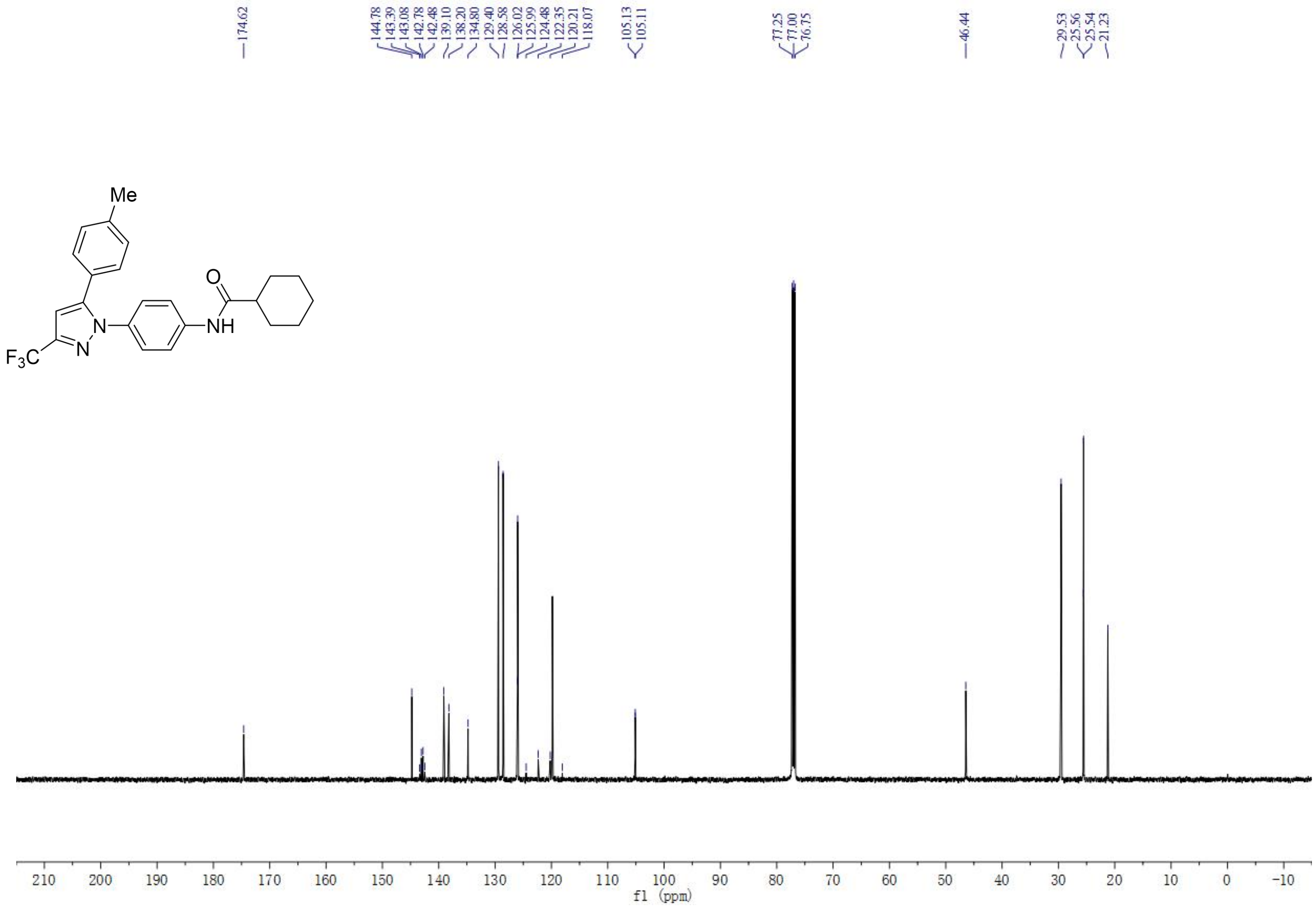


Figure S79. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of ethyl 2-(4-(cyclohexanecarboxamido)phenoxy)-2-methylpropanoate **(4bi)**

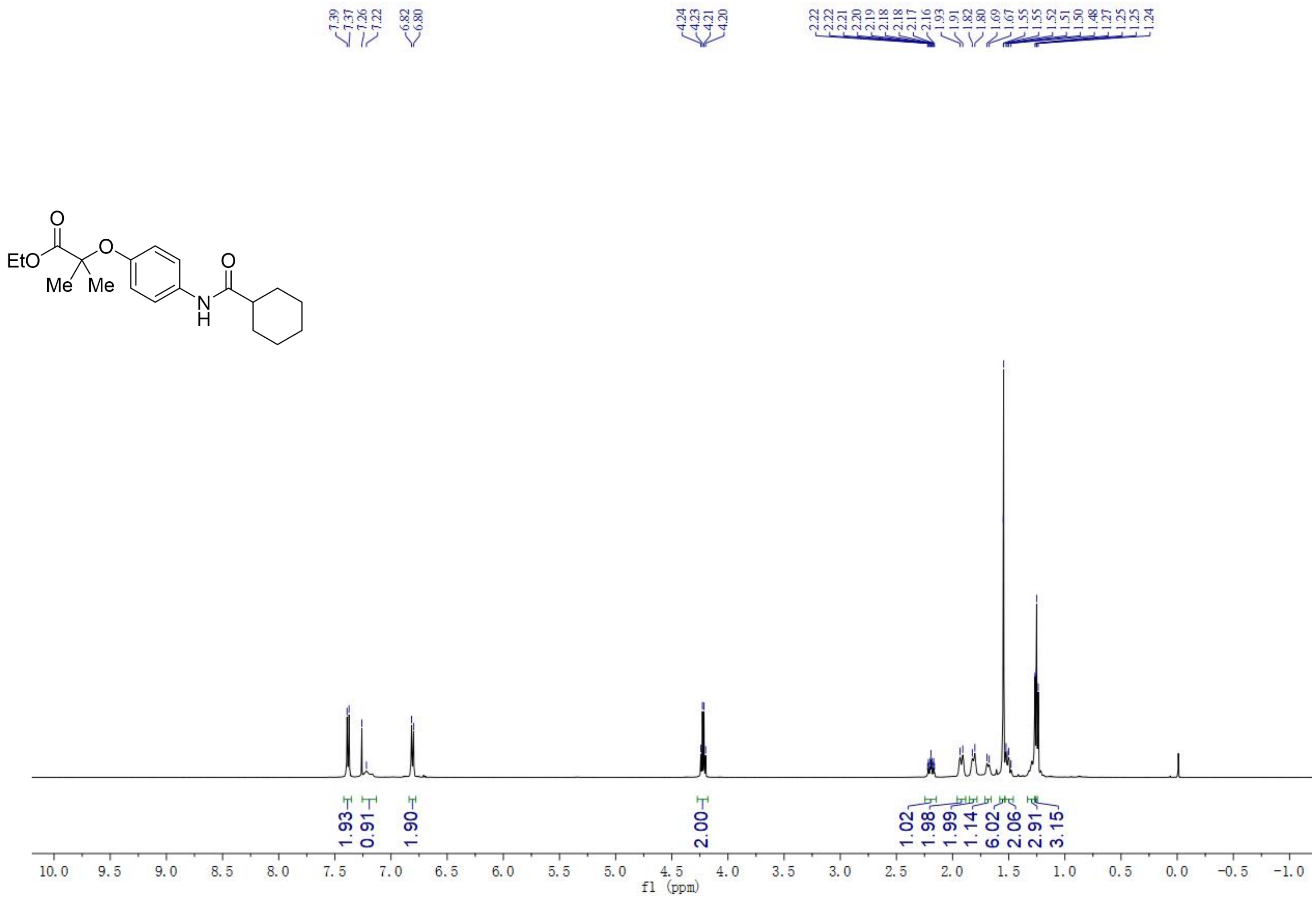


Figure S80. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of ethyl 2-(4-(cyclohexanecarboxamido)phenoxy)-2-methylpropanoate **(4bi)**

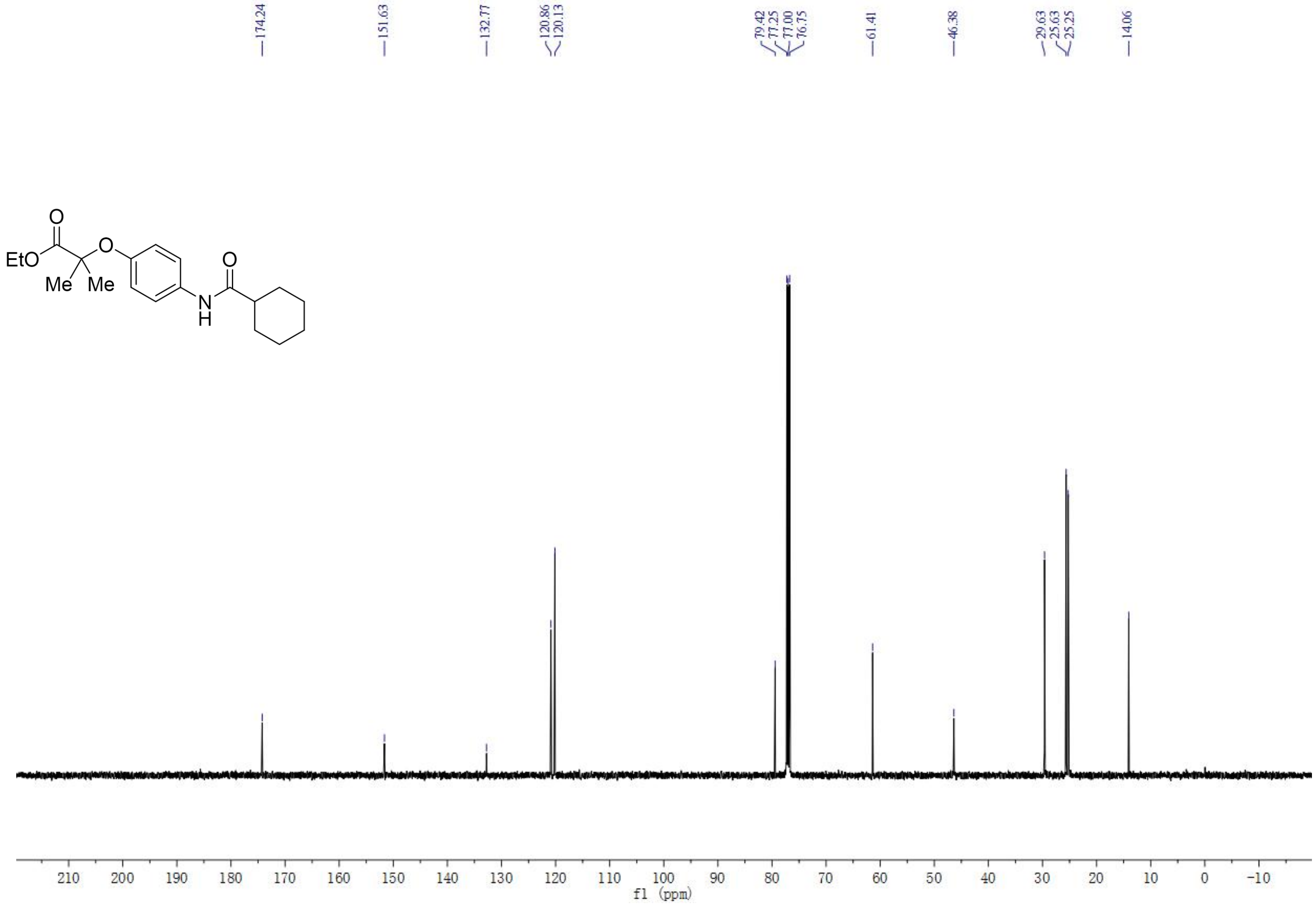


Figure S81. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-(cyclohexanecarboxamido)phenyl (*R*)-2-(6-methoxynaphthalen-2-yl)propanoate (**4bj**)

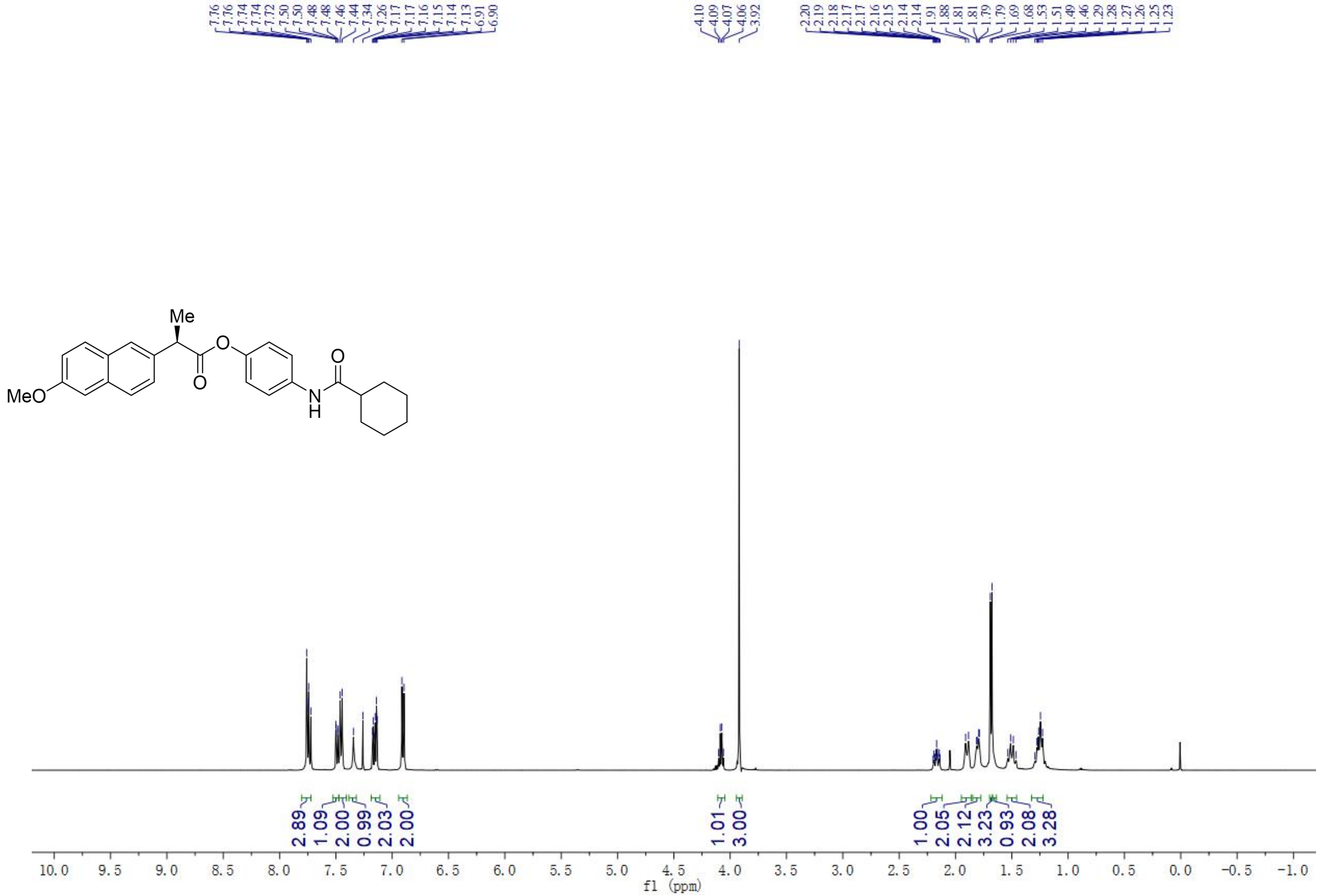


Figure S82. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-(cyclohexanecarboxamido)phenyl (*R*)-2-(6-methoxynaphthalen-2-yl)propanoate (**4bj**)

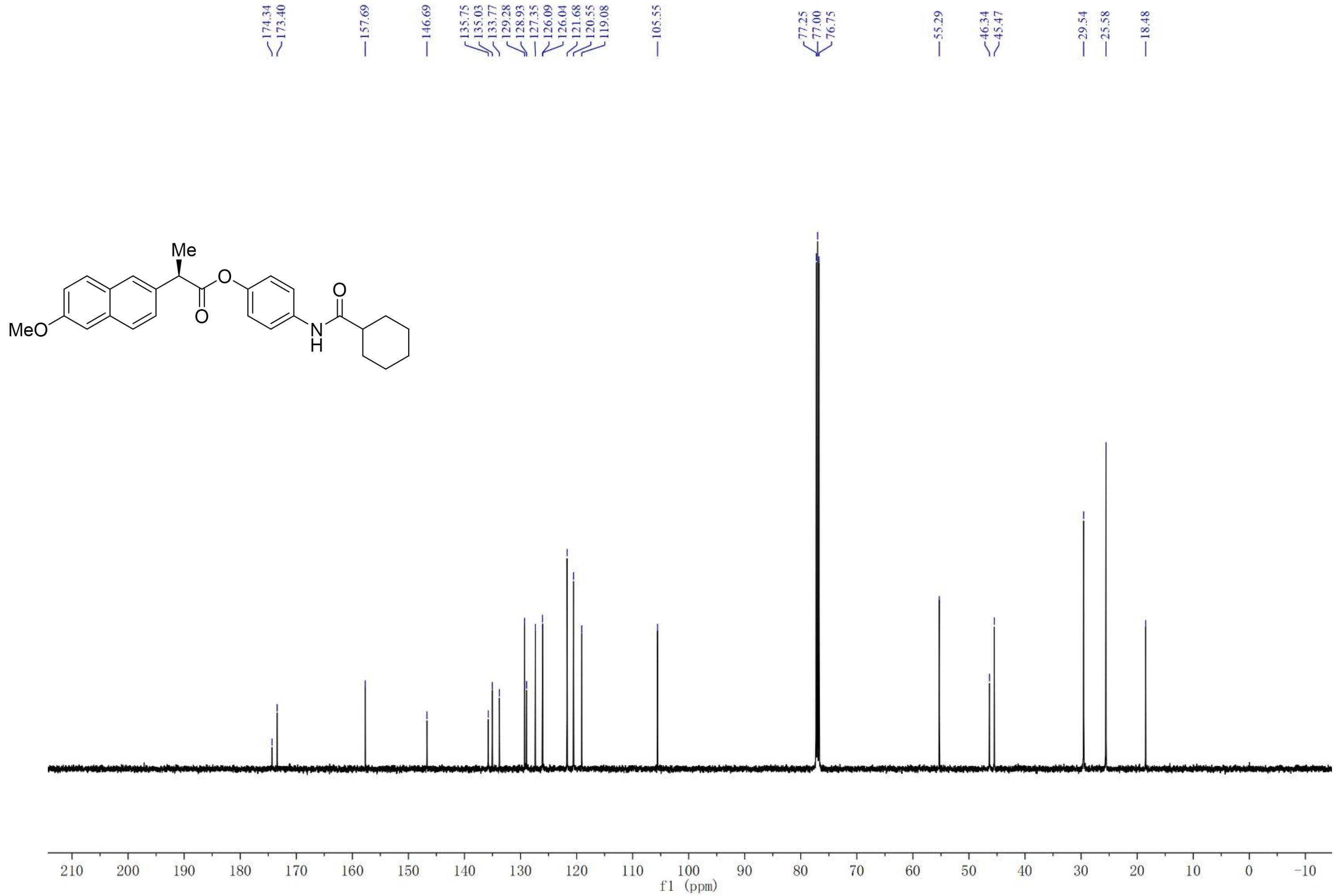


Figure S83. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(cyclohexanecarboxamido)phenyl)propanoate (**4bk**)

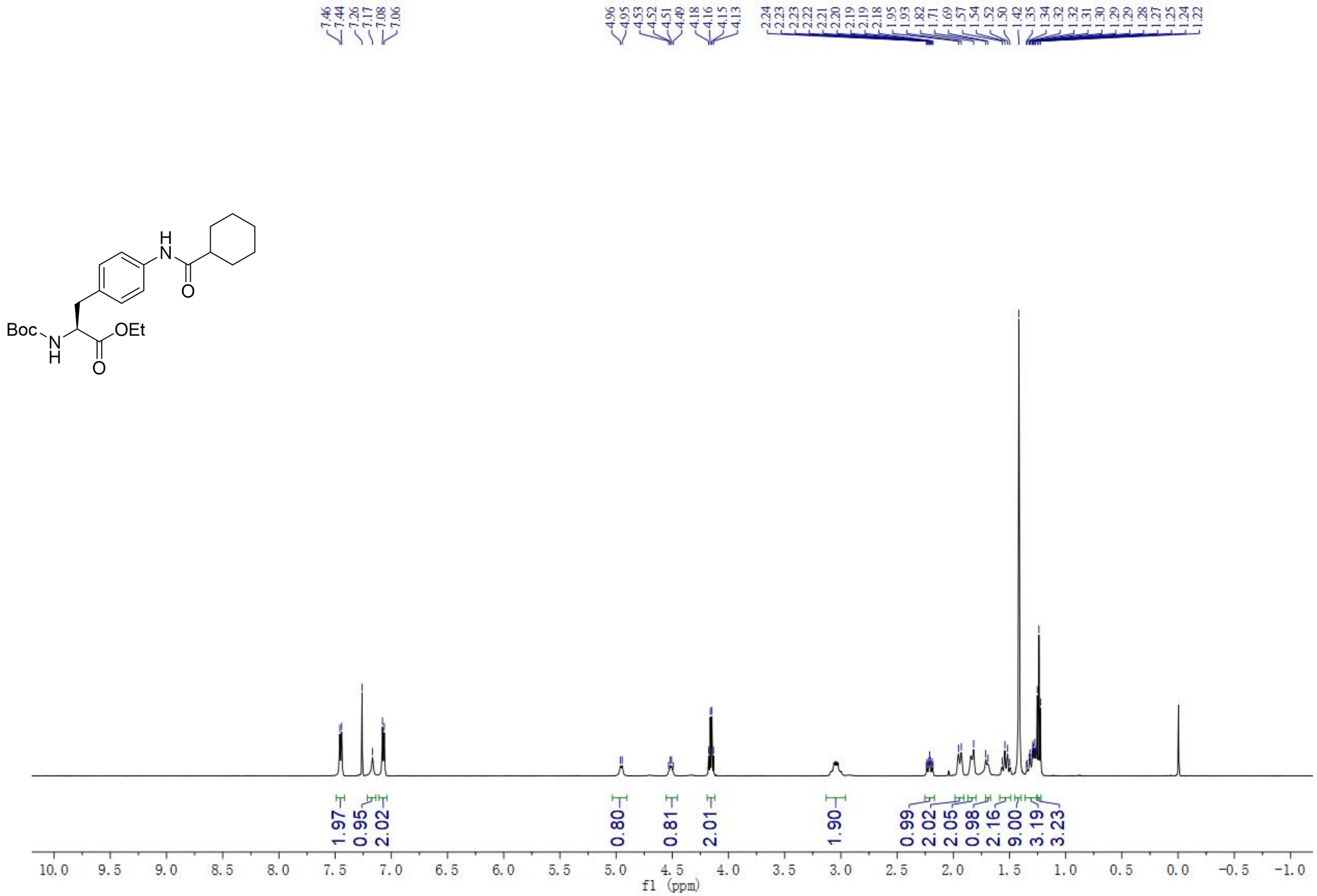


Figure S84. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(cyclohexanecarboxamido)phenyl)propanate (**4bk**)

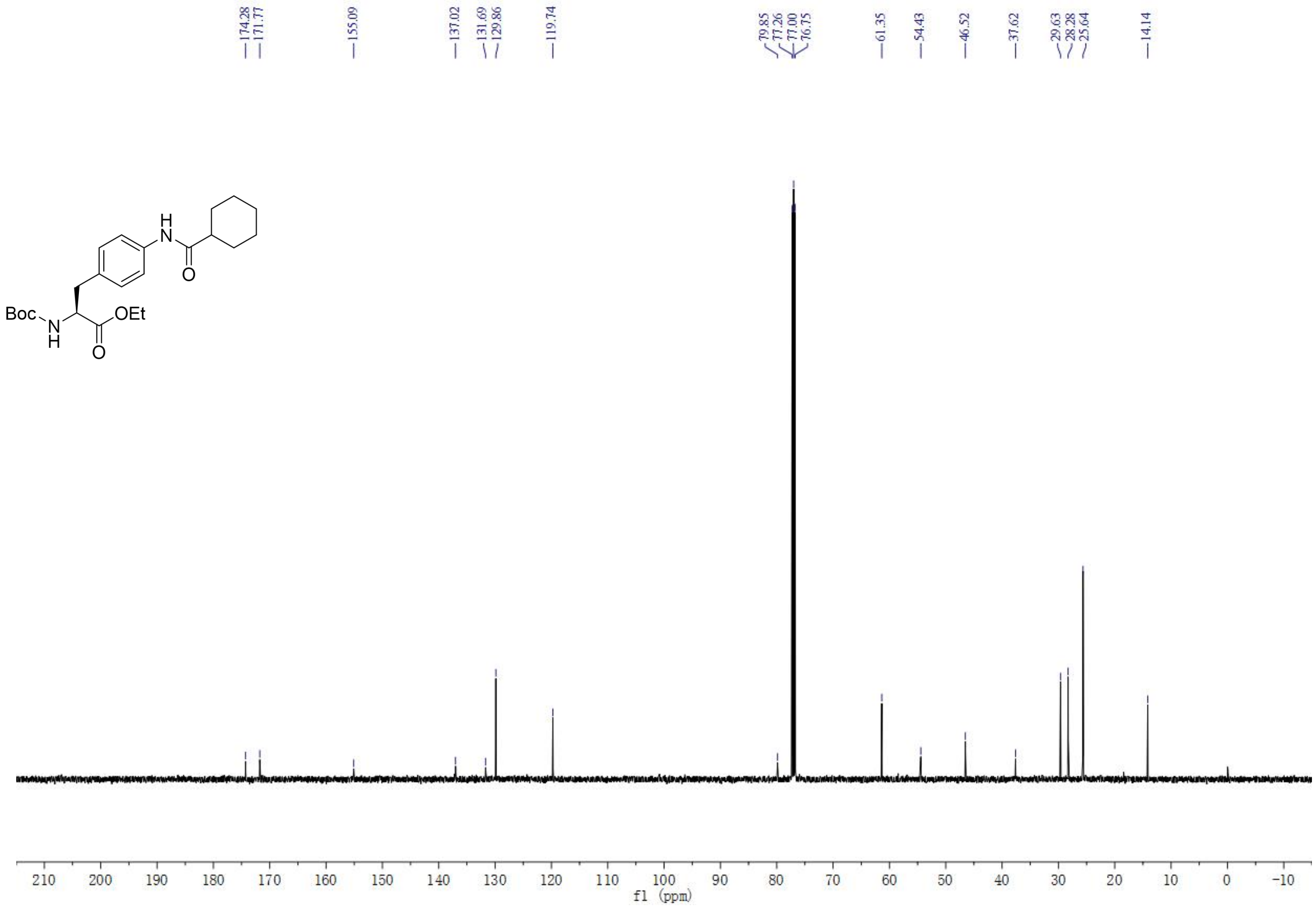


Figure S85. ^{1}H NMR (500 MHz, CDCl$_3$, 298K) of ethyl (*S*)-2-benzamido-3-(4-(cyclohexanecarboxamido)phenyl)propanoate (**4bl**)

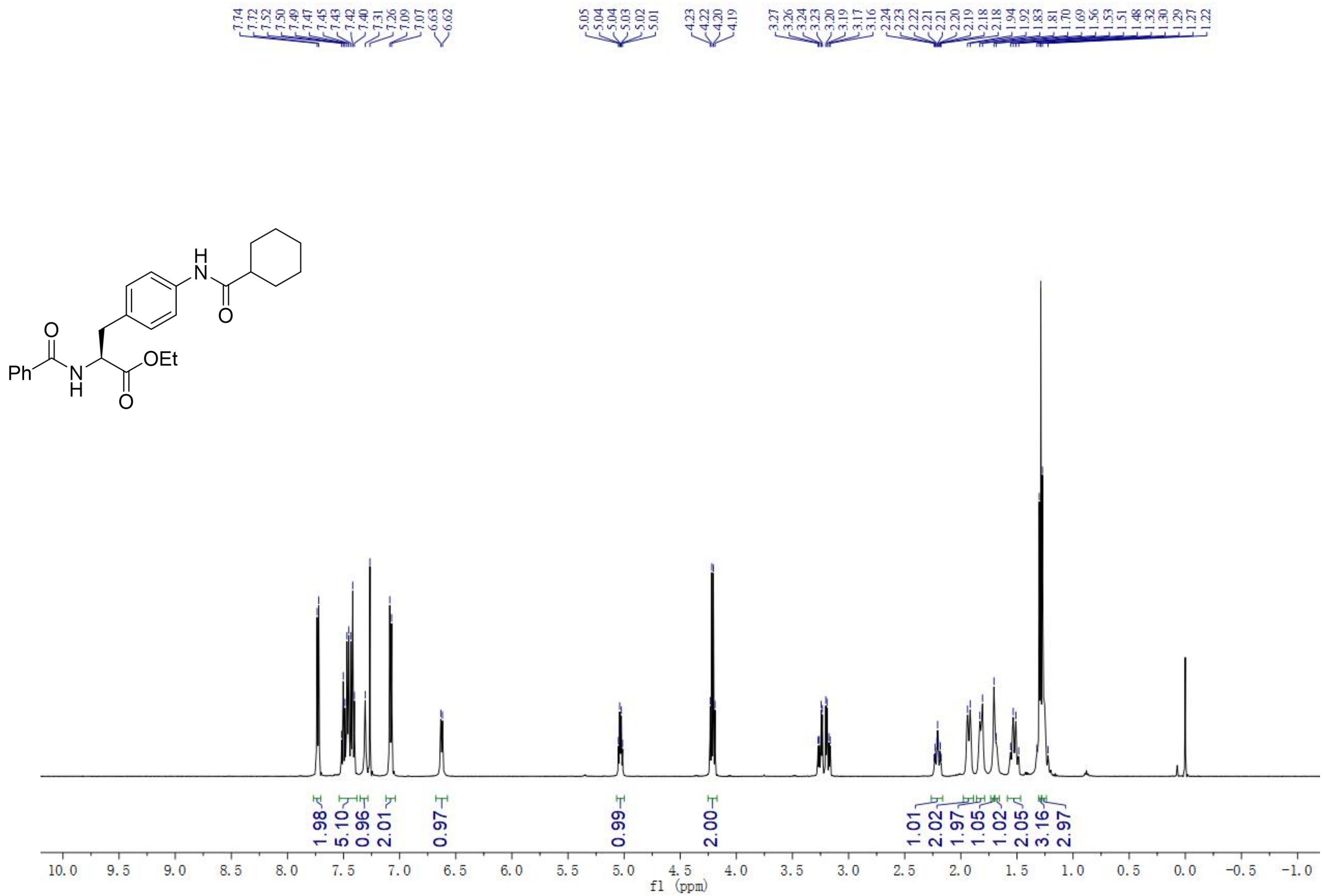


Figure S86. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of ethyl (*S*)-2-benzamido-3-(4-(cyclohexanecarboxamido)phenyl)propanoate (**4bl**)

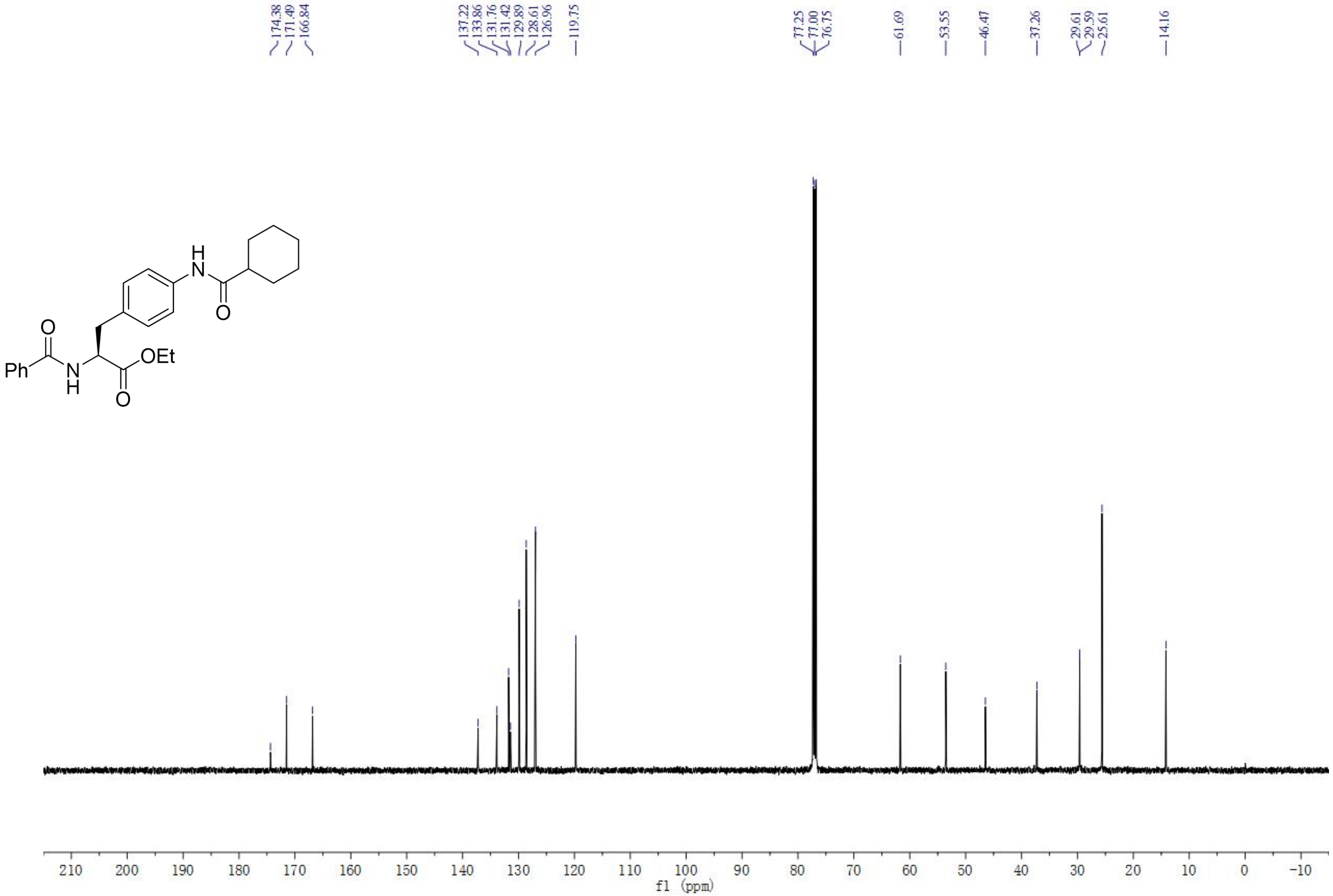
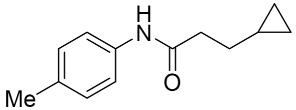


Figure S87. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 3-cyclopropyl-*N*-(*p*-tolyl)propanamide (**5aa**)



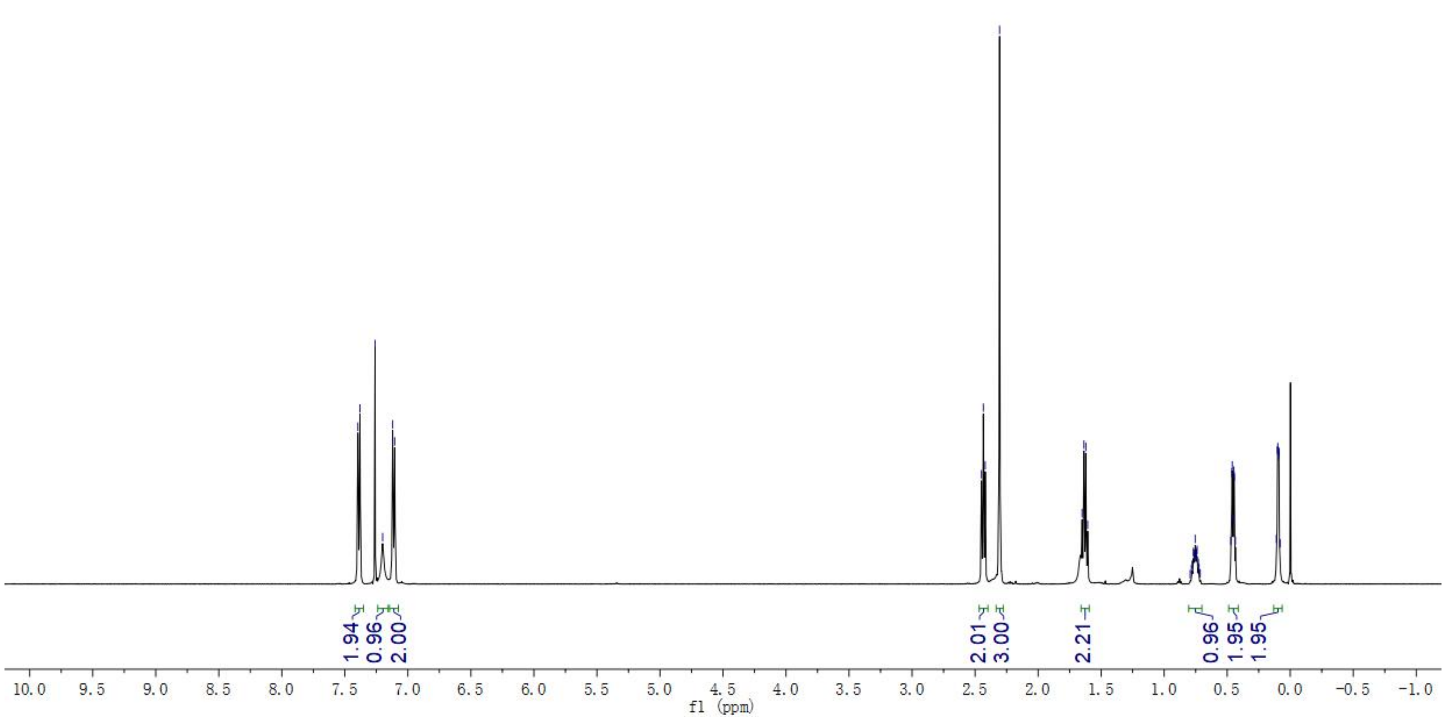


Figure S88. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 3-cyclopropyl-*N*-(*p*-tolyl)propanamide (**5aa**)

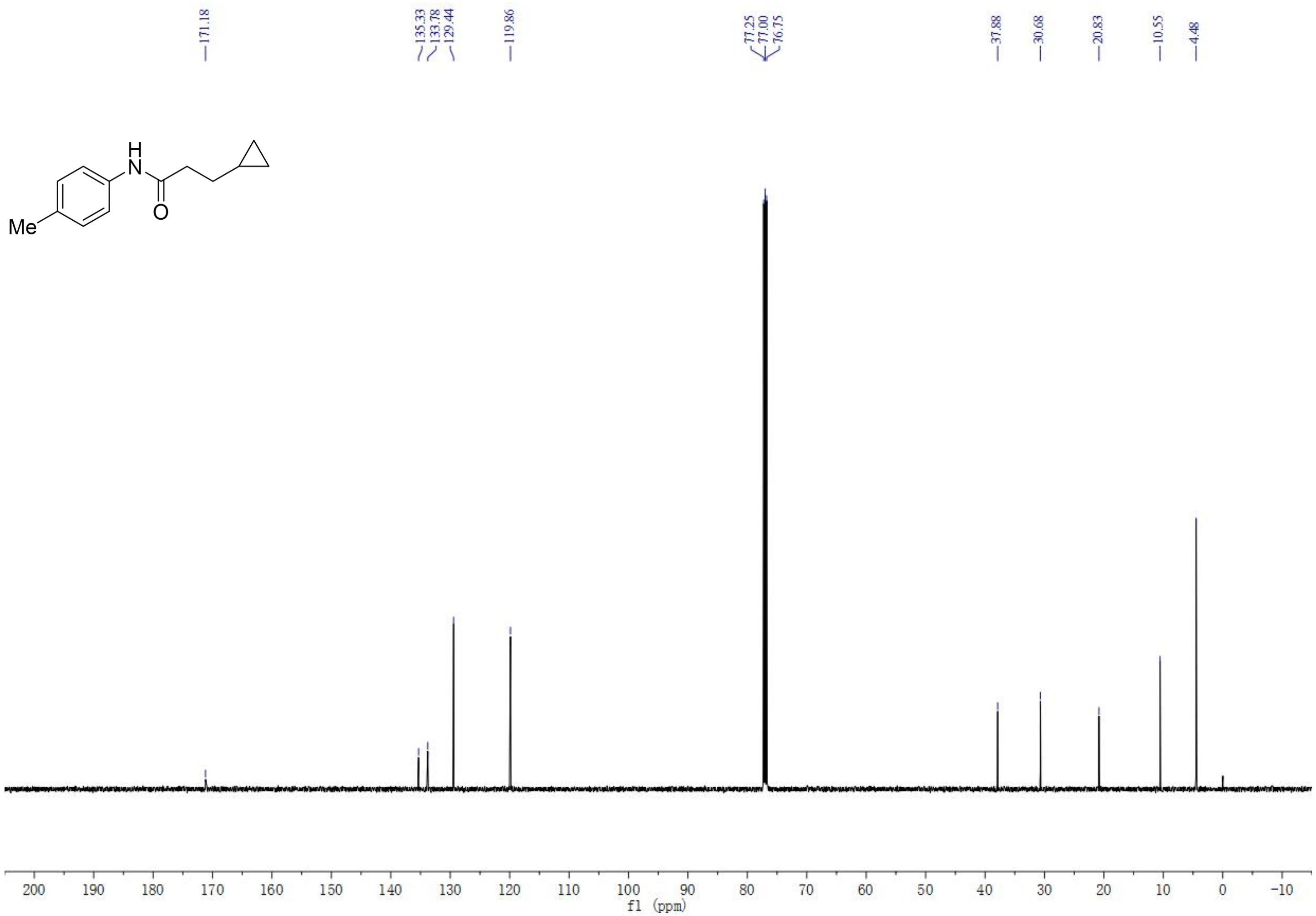


Figure S89. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-phenyl-*N*-(*p*-tolyl)butanamide (**5ab**)

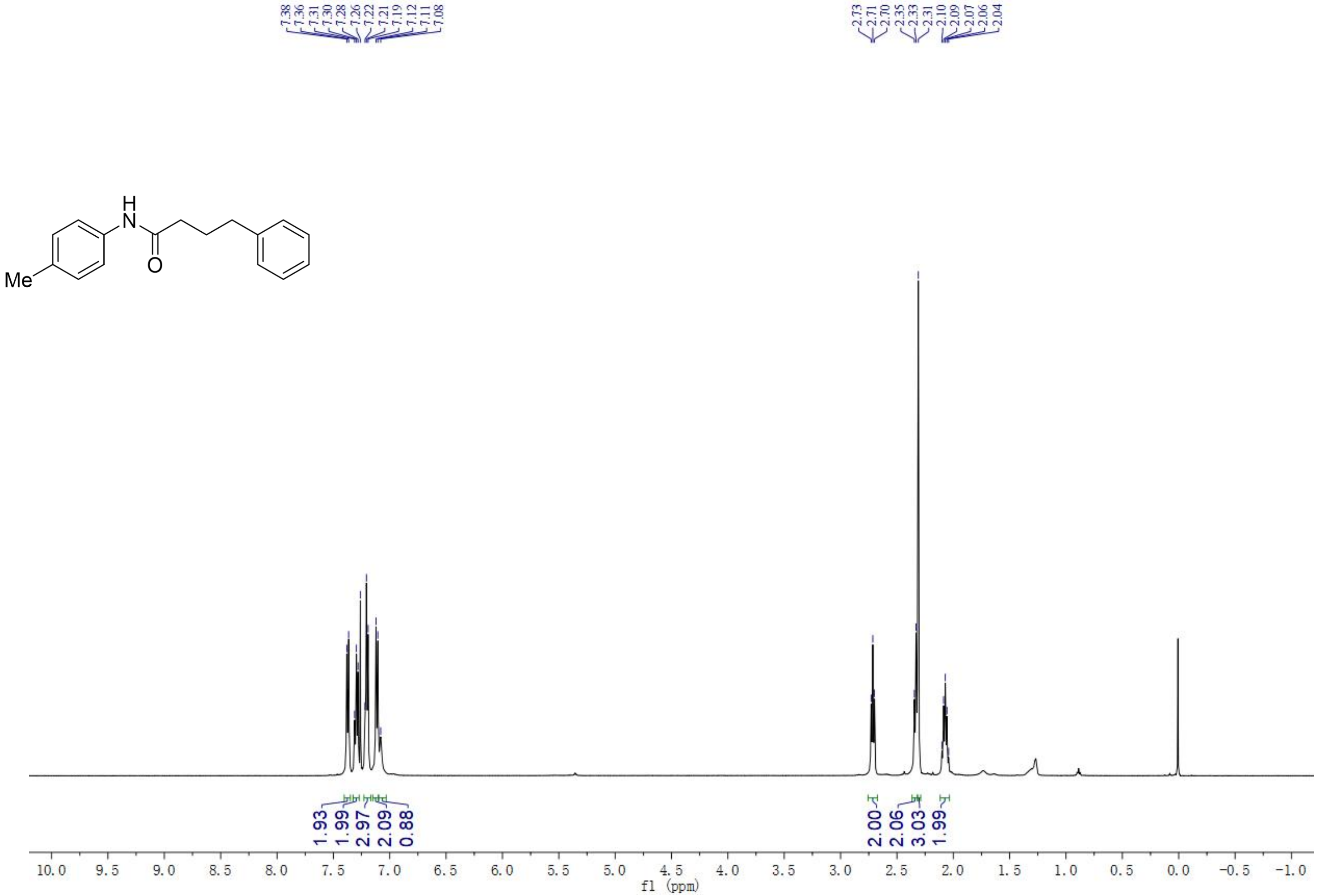


Figure S90. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-phenyl-*N*-(*p*-tolyl)butanamide (**5ab**)

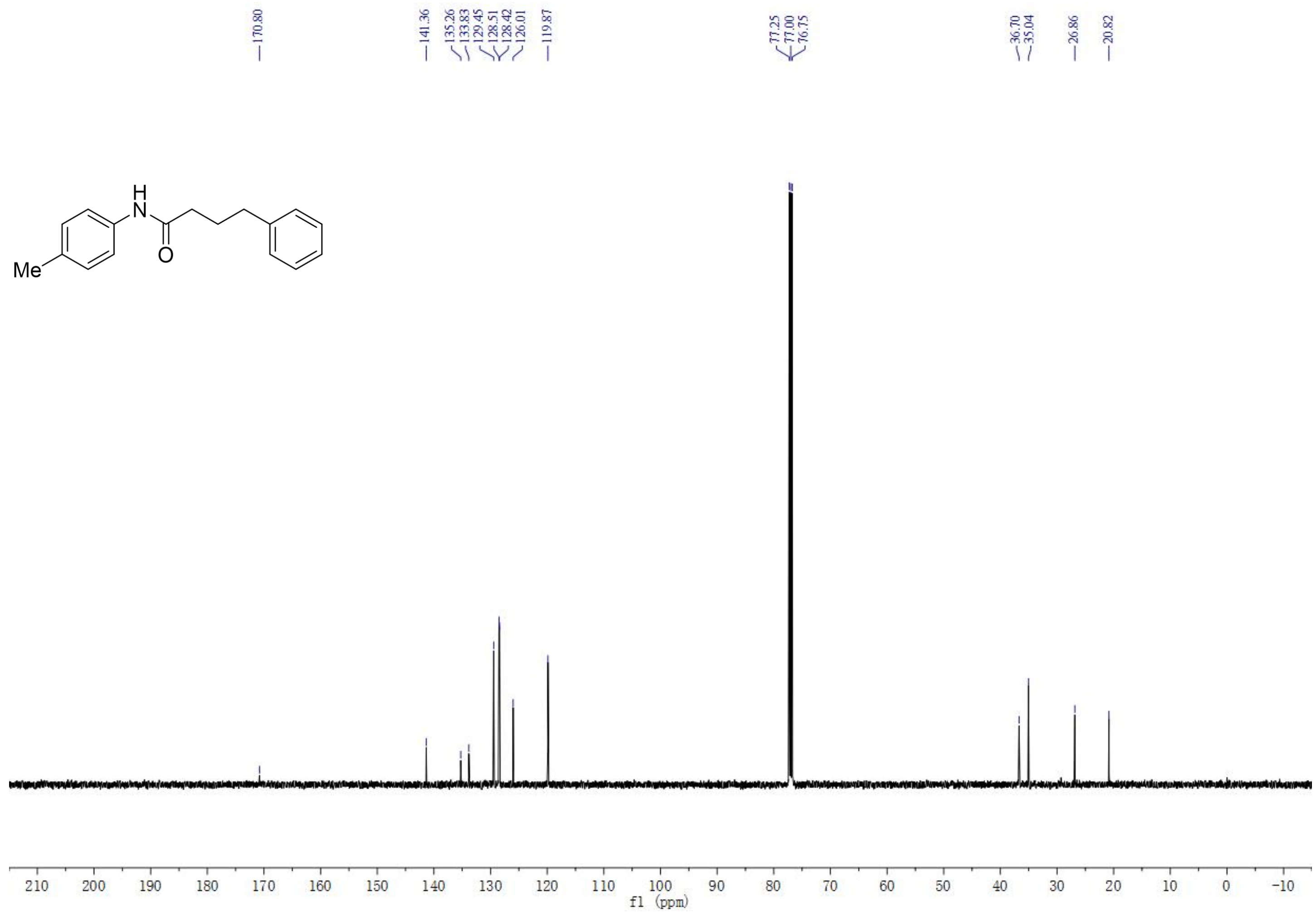


Figure S91. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-chloro-*N*-(*p*-tolyl)butanamide (**5ac**)

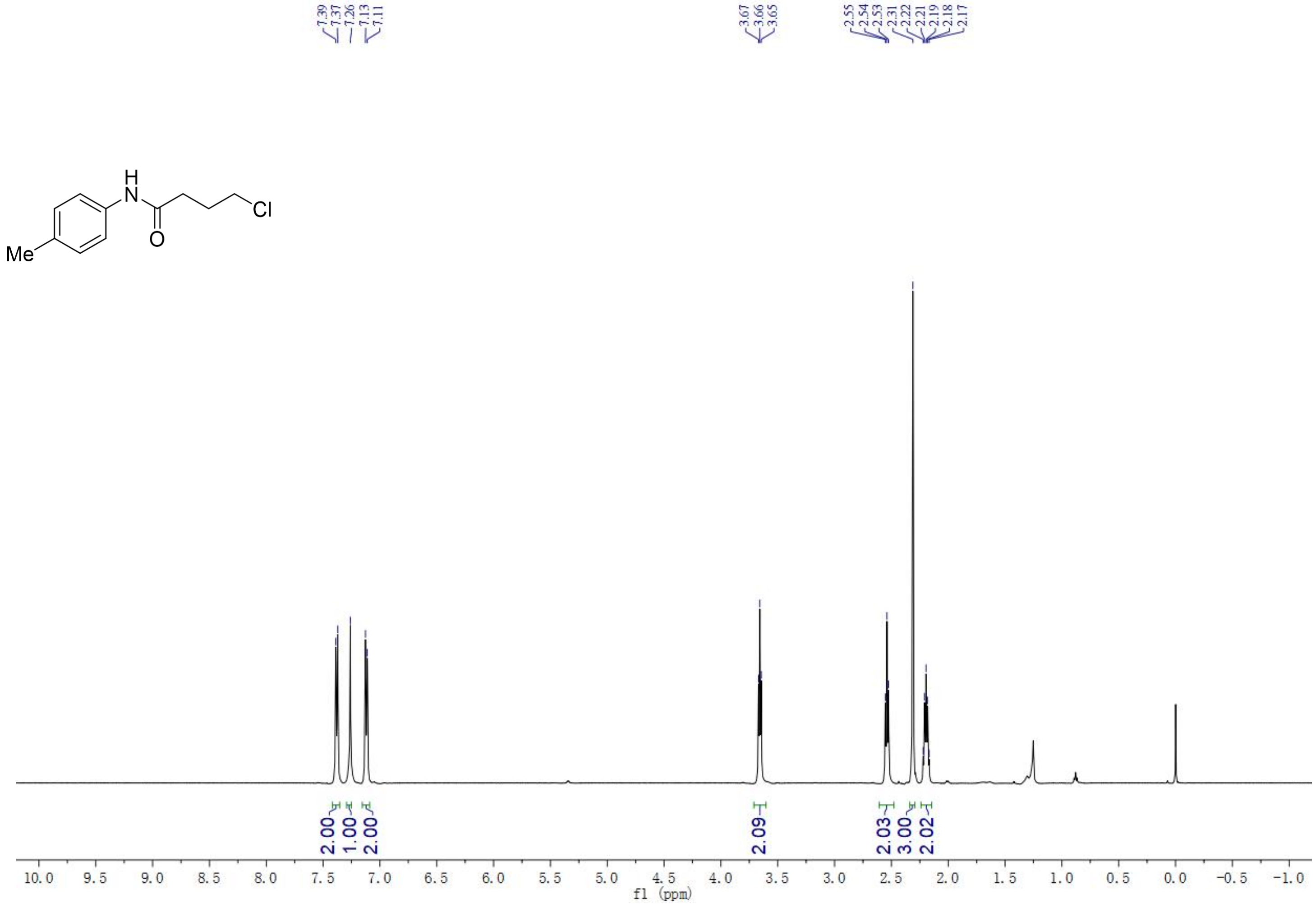


Figure S92. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-chloro-*N*-(*p*-tolyl)butanamide (**5ac**)

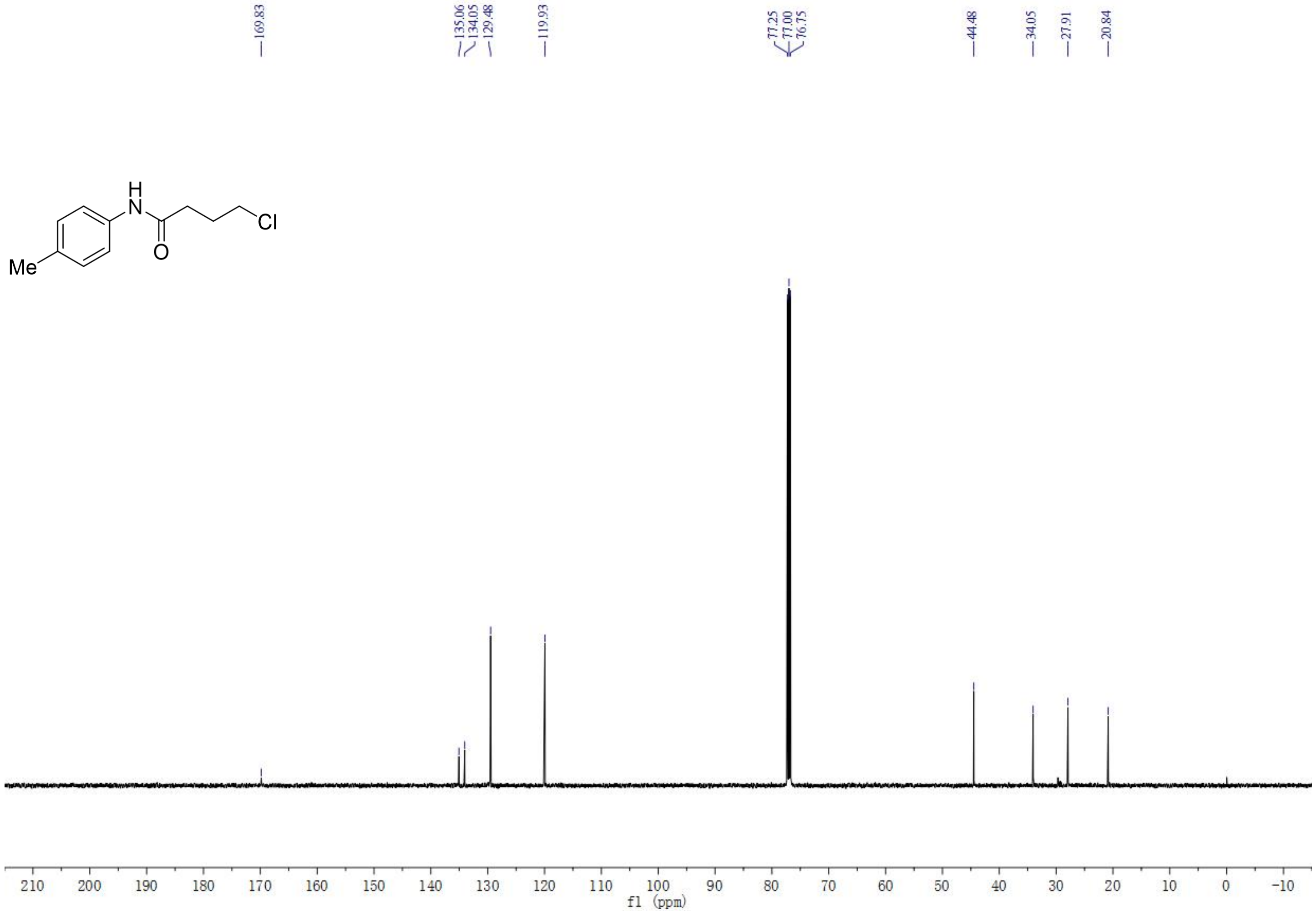


Figure S93. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 5-oxo-5-(*p*-tolylamino)pentanoate (**5ad**)

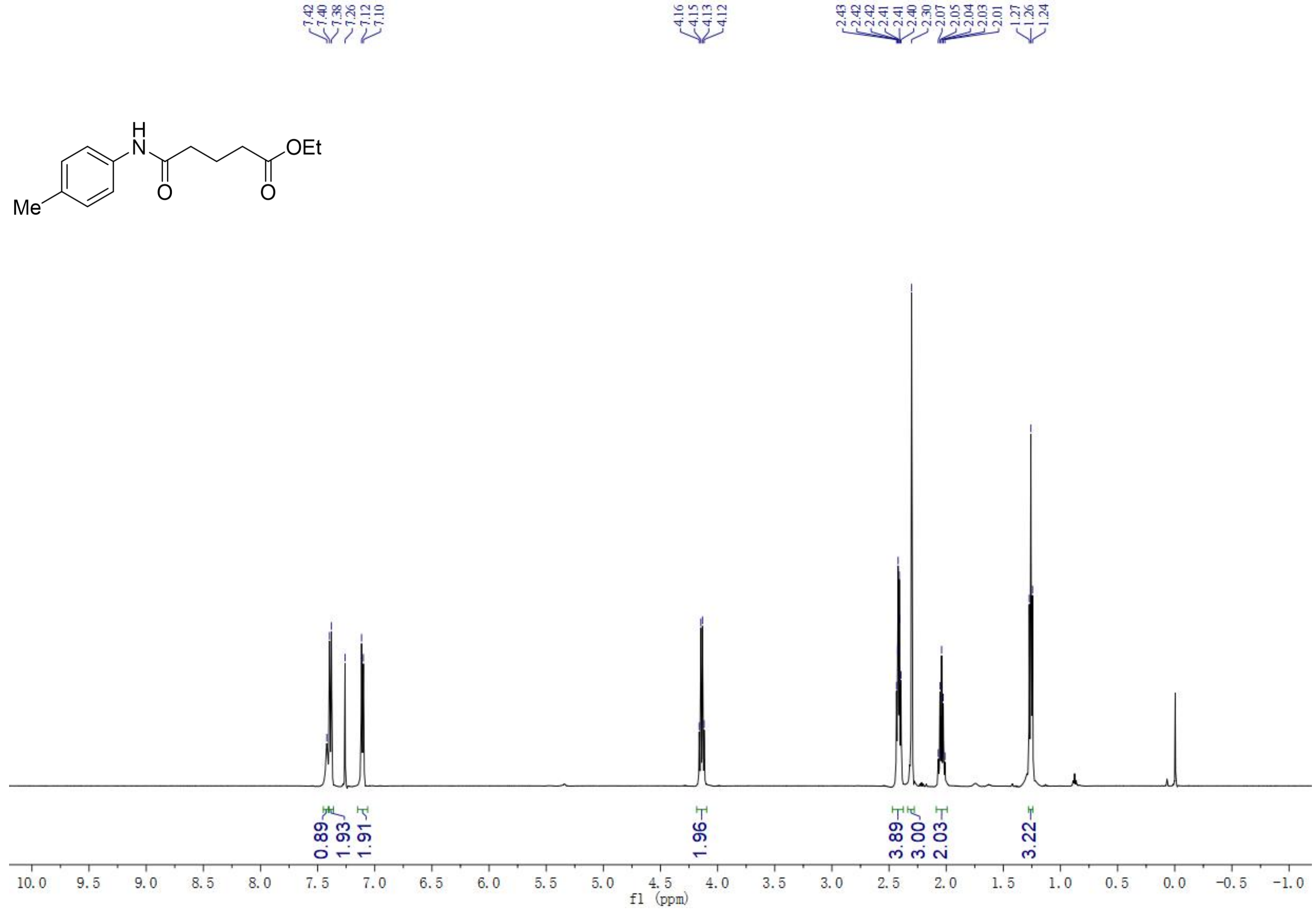


Figure S94. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of ethyl 5-oxo-5-(*p*-tolylamino)pentanoate (**5ad**)

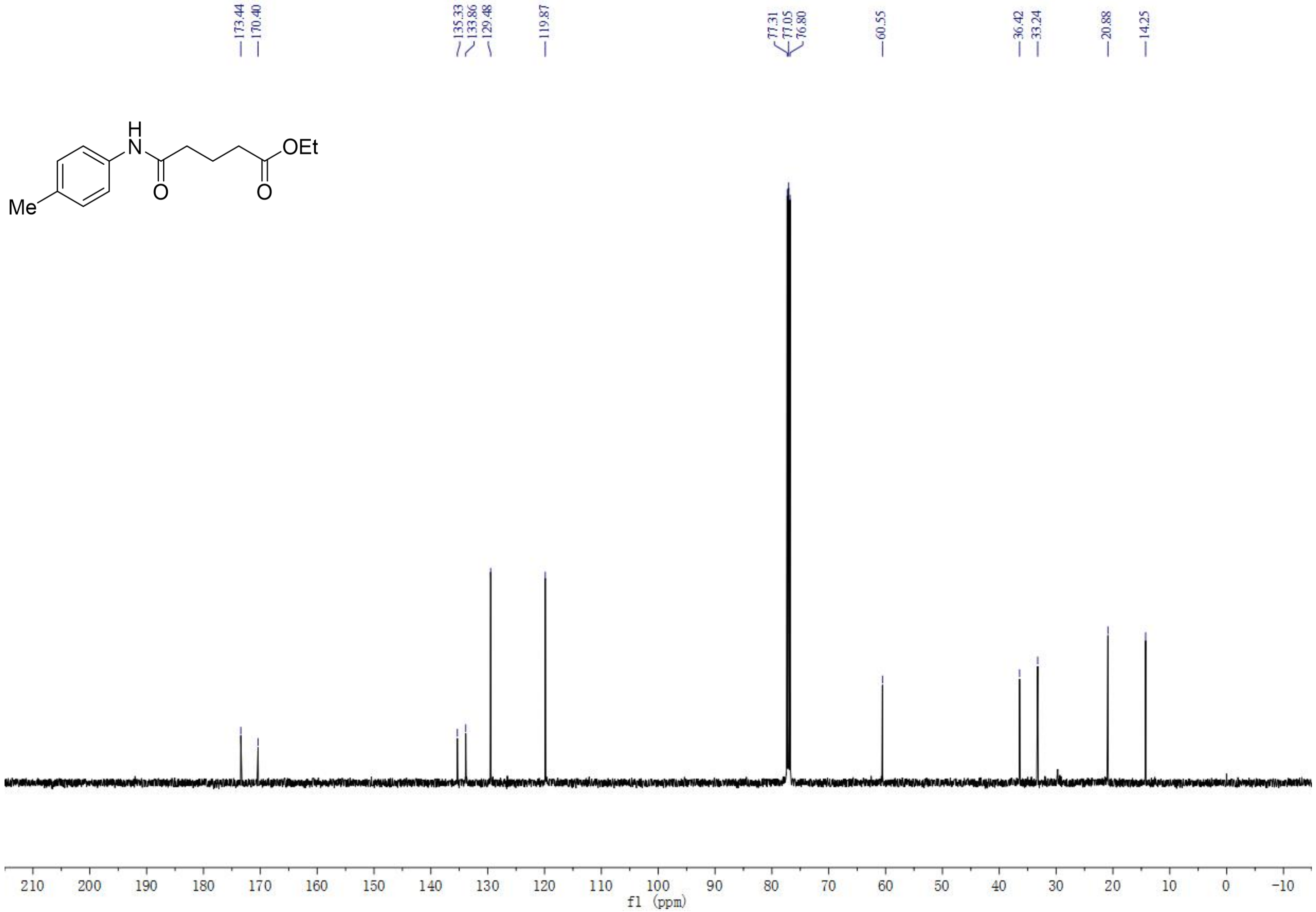


Figure S95. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-cyano-*N*-(*p*-tolyl)butanamide (**5ae**)

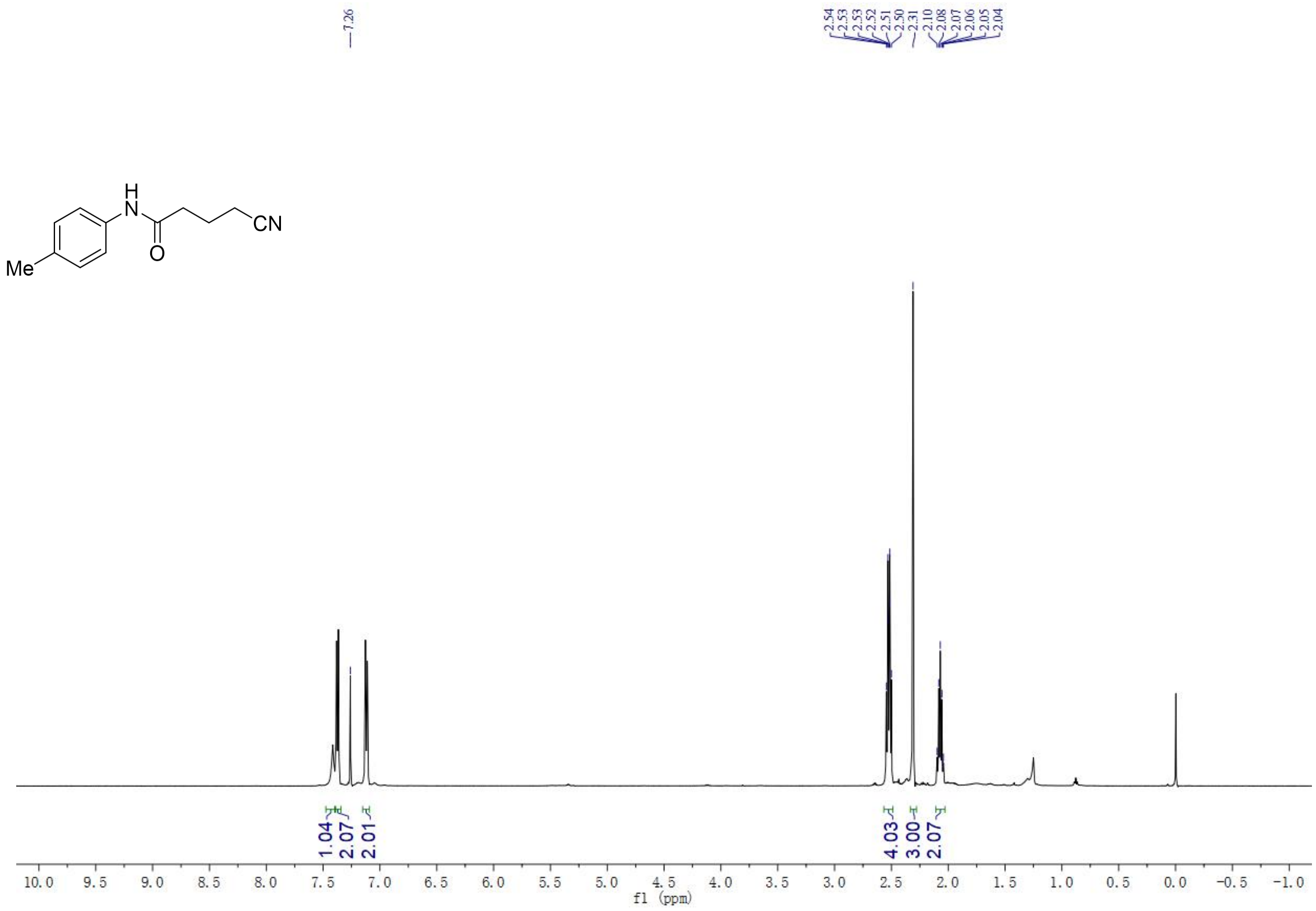


Figure S96. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-cyano-*N*-(*p*-tolyl)butanamide (**5ae**)

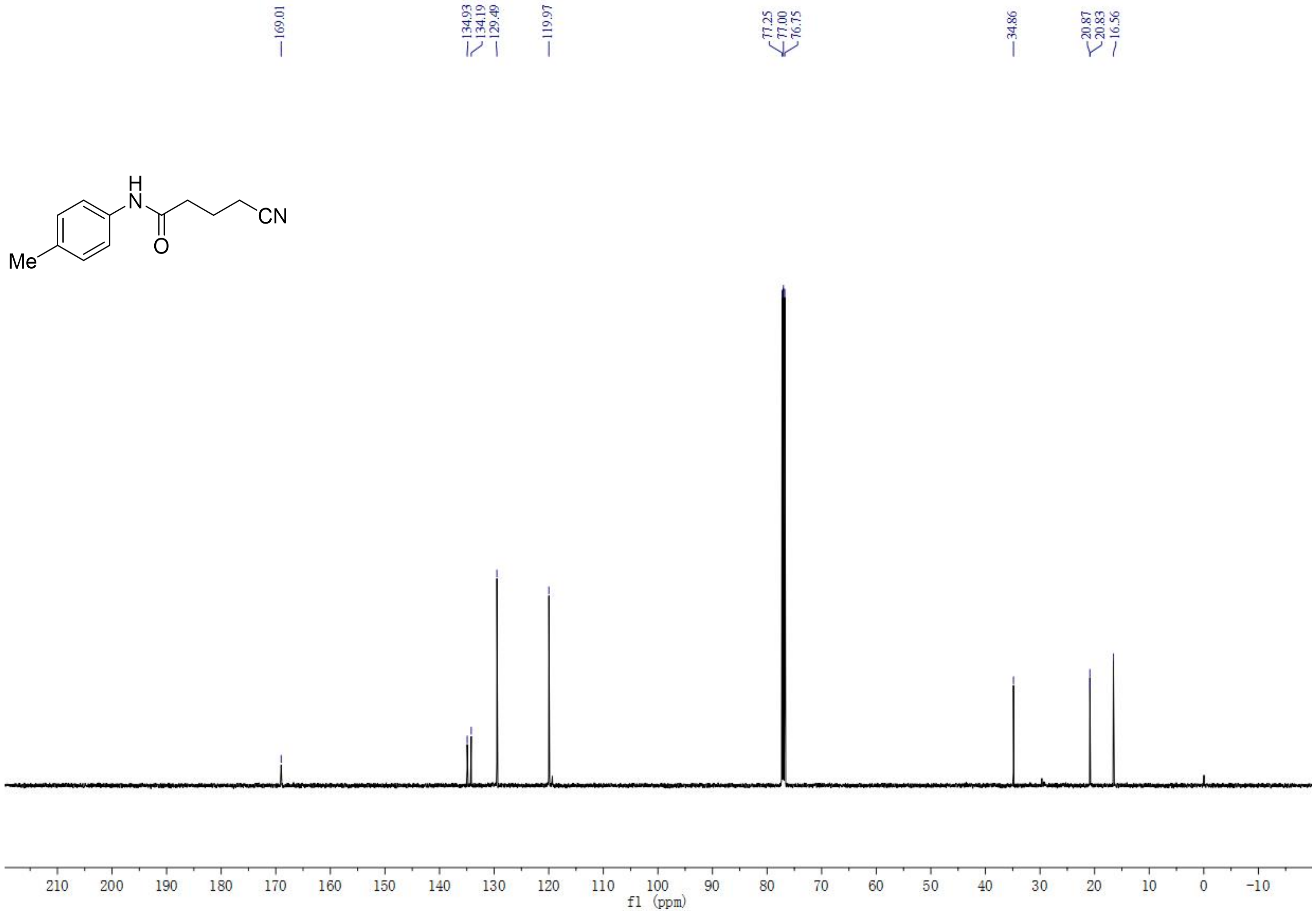


Figure S97. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-(1,4-dioxan-2-yl)-*N*-(*p*-tolyl)acetamide (**5af**)

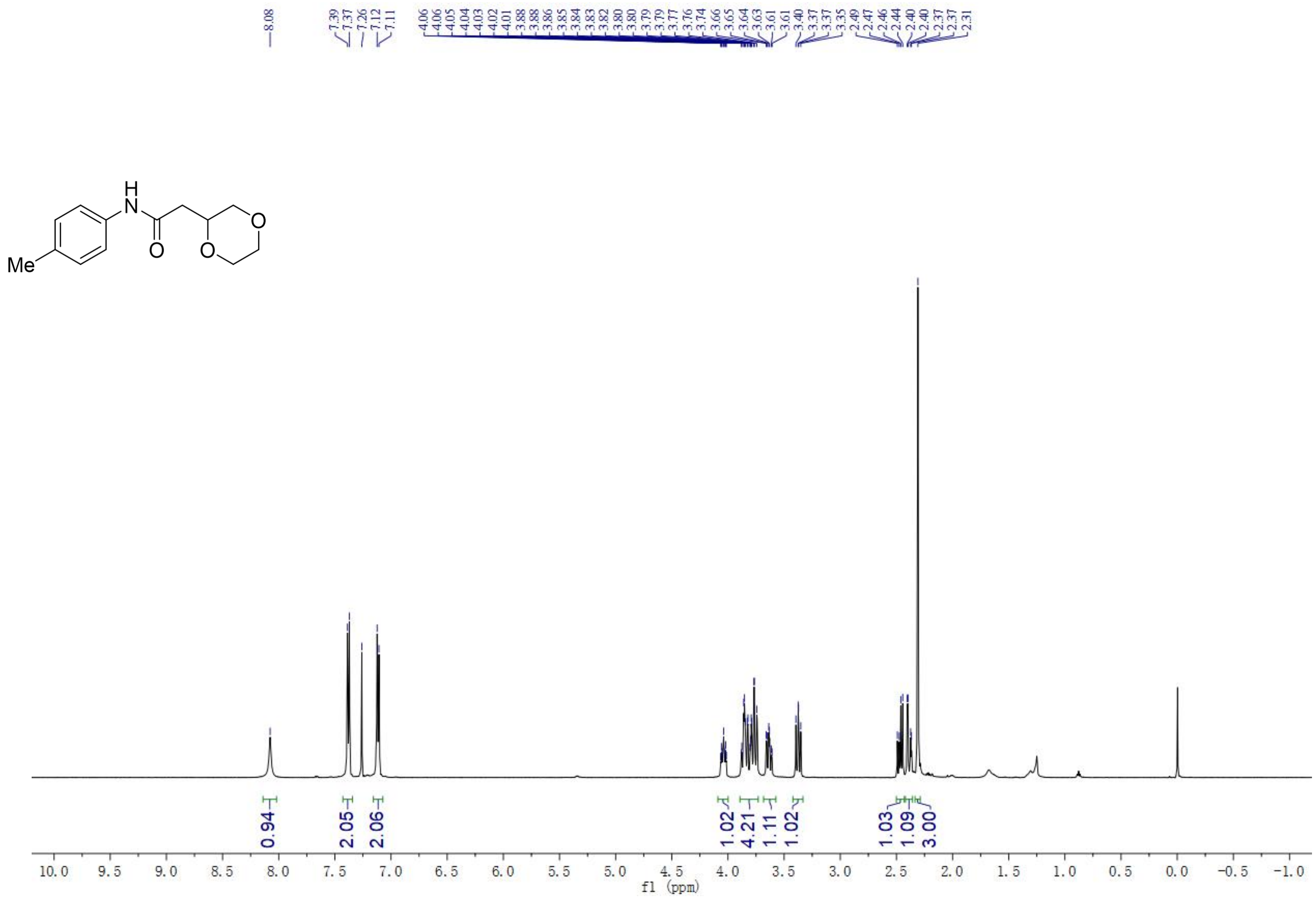


Figure S98. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of 2-(1,4-dioxan-2-yl)-*N*-(*p*-tolyl)acetamide (**5af**)

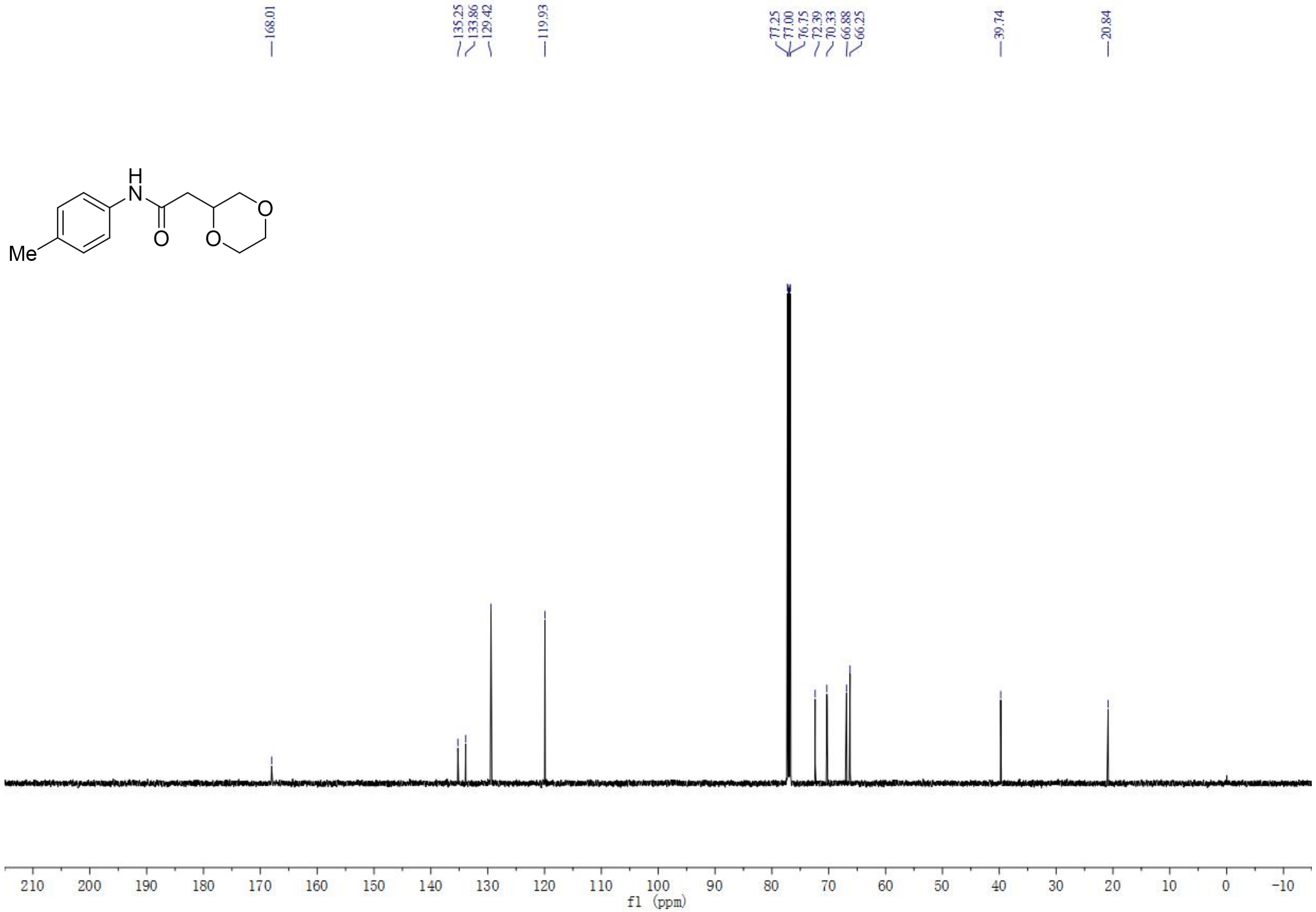
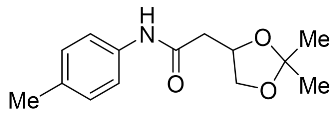


Figure S99. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-(2,2-dimethyl-1,3-dioxolan-4-yl)-*N*-(*p*-tolyl)acetamide (**5ag**)



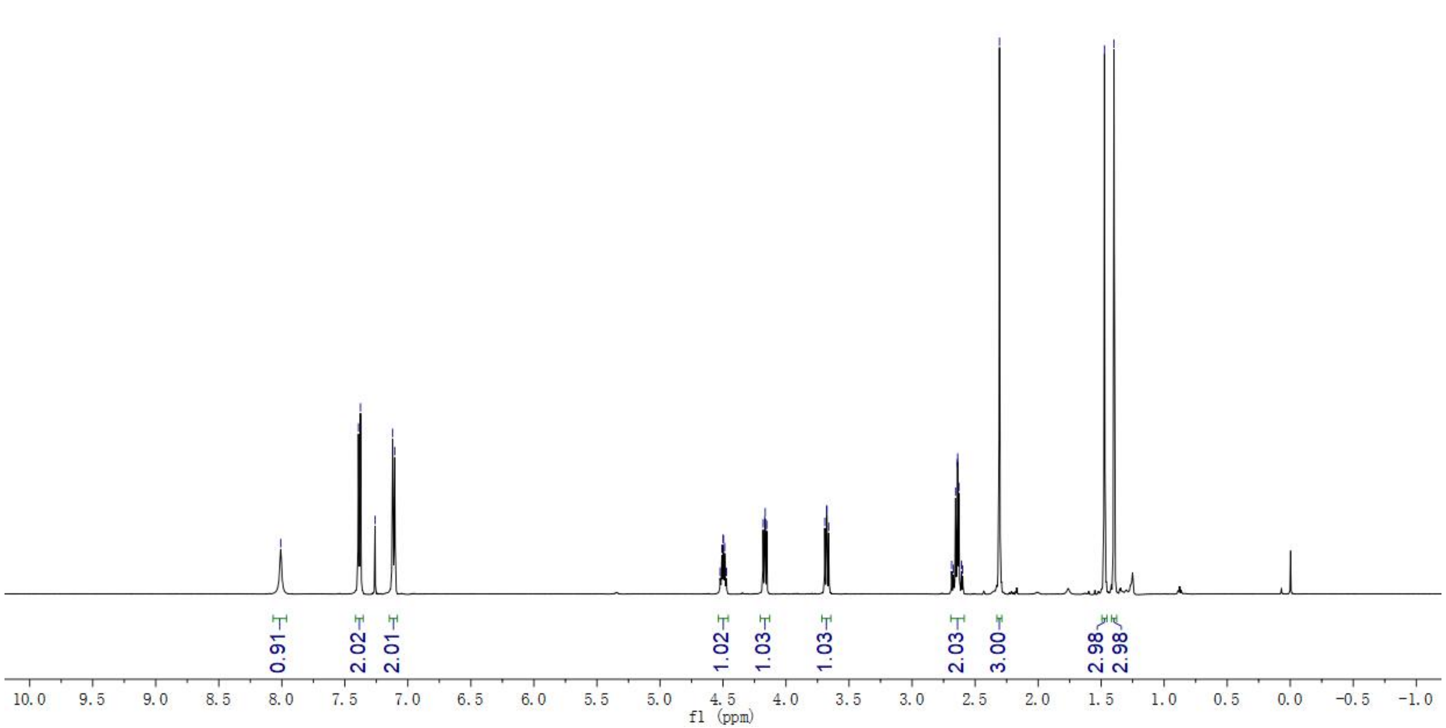


Figure S100. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of 2-(2,2-dimethyl-1,3-dioxolan-4-yl)-*N*-(*p*-tolyl)acetamide (**5ag**)

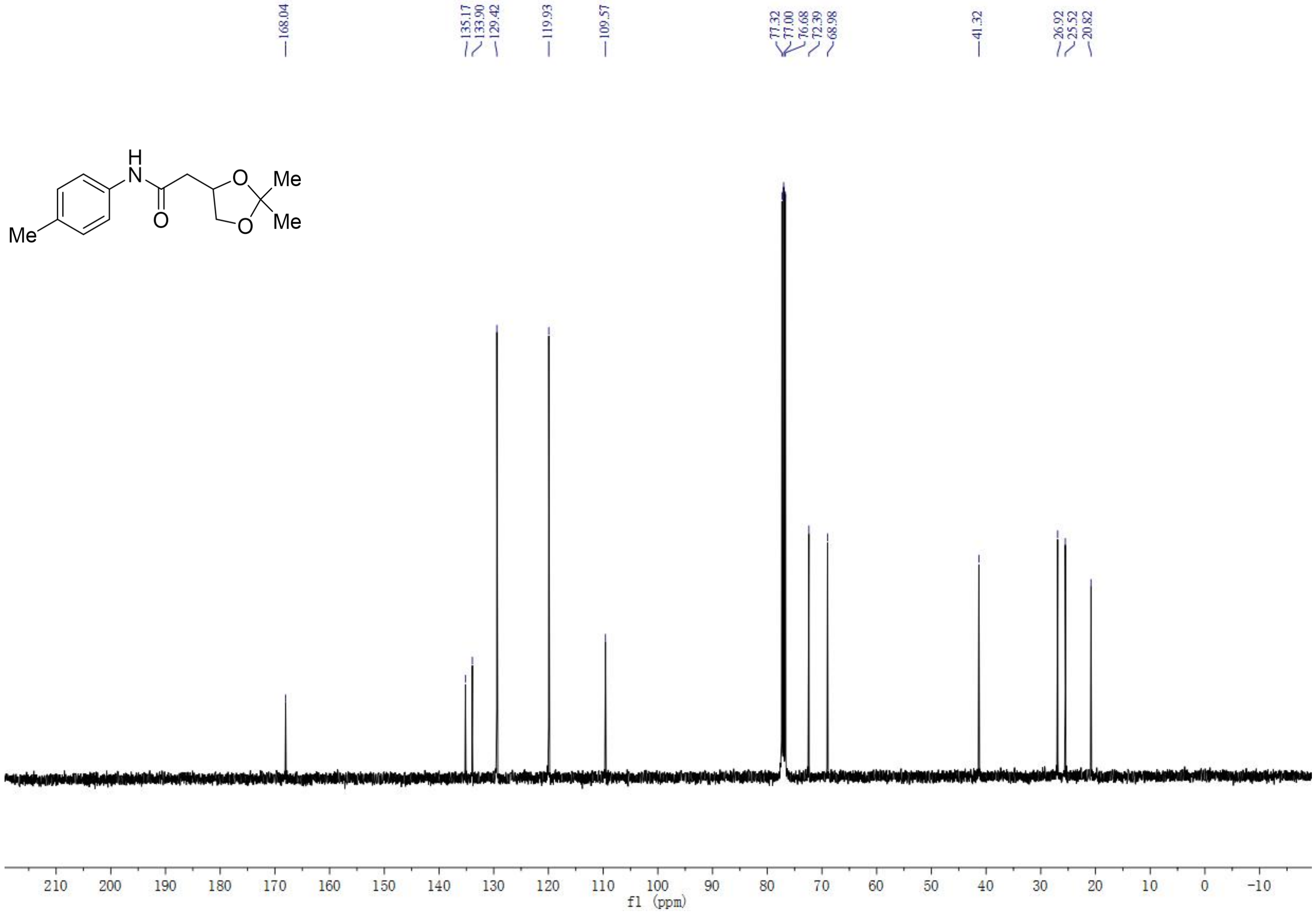


Figure S101. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 5,5,5-trifluoro-*N*-(*p*-tolyl)pentanamide (**5ah**)

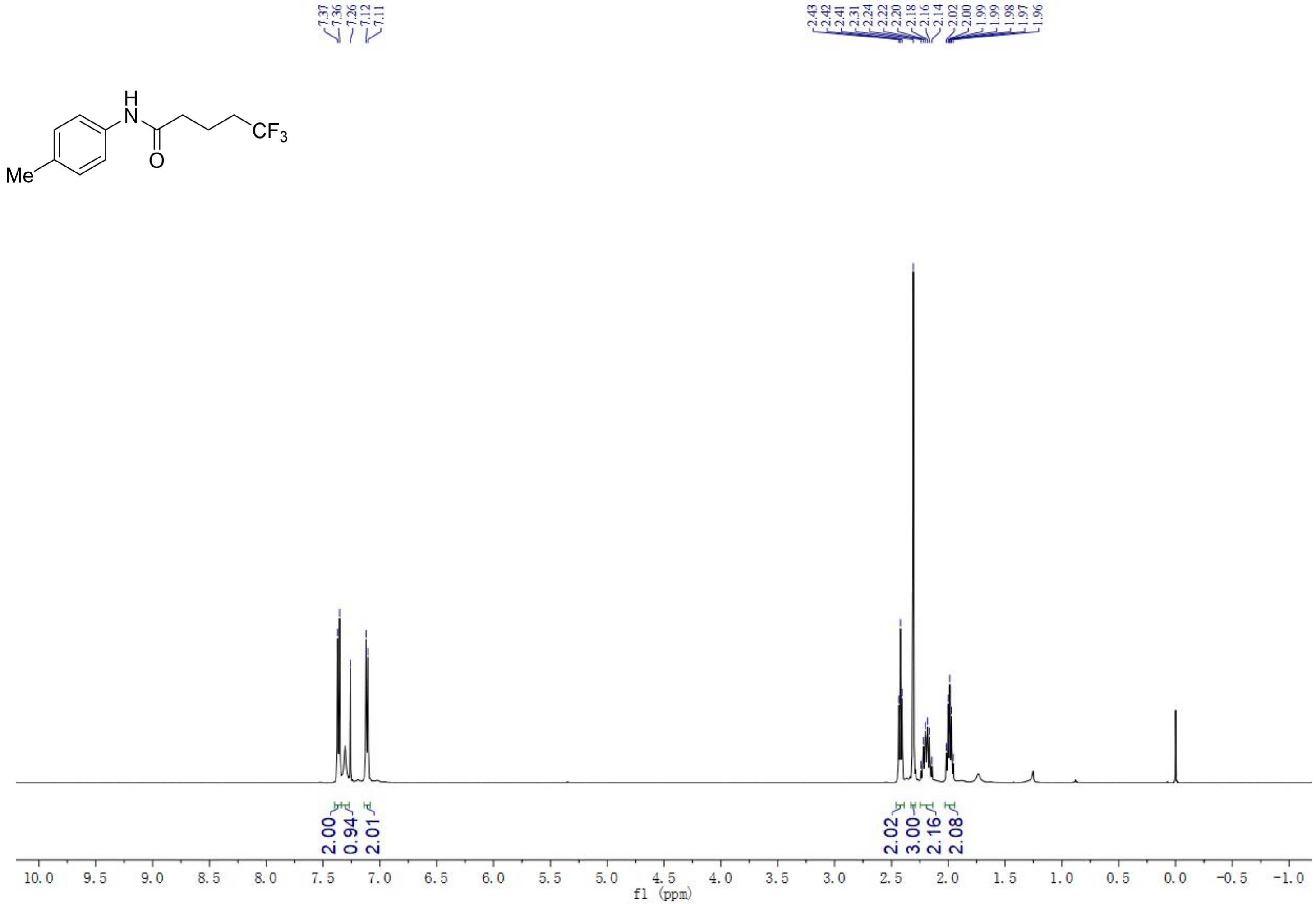


Figure S102. ^{19}F NMR (471 MHz, $CDCl_3$, 298K) of 5,5,5-trifluoro-*N*-(*p*-tolyl)pentanamide (**5ah**)

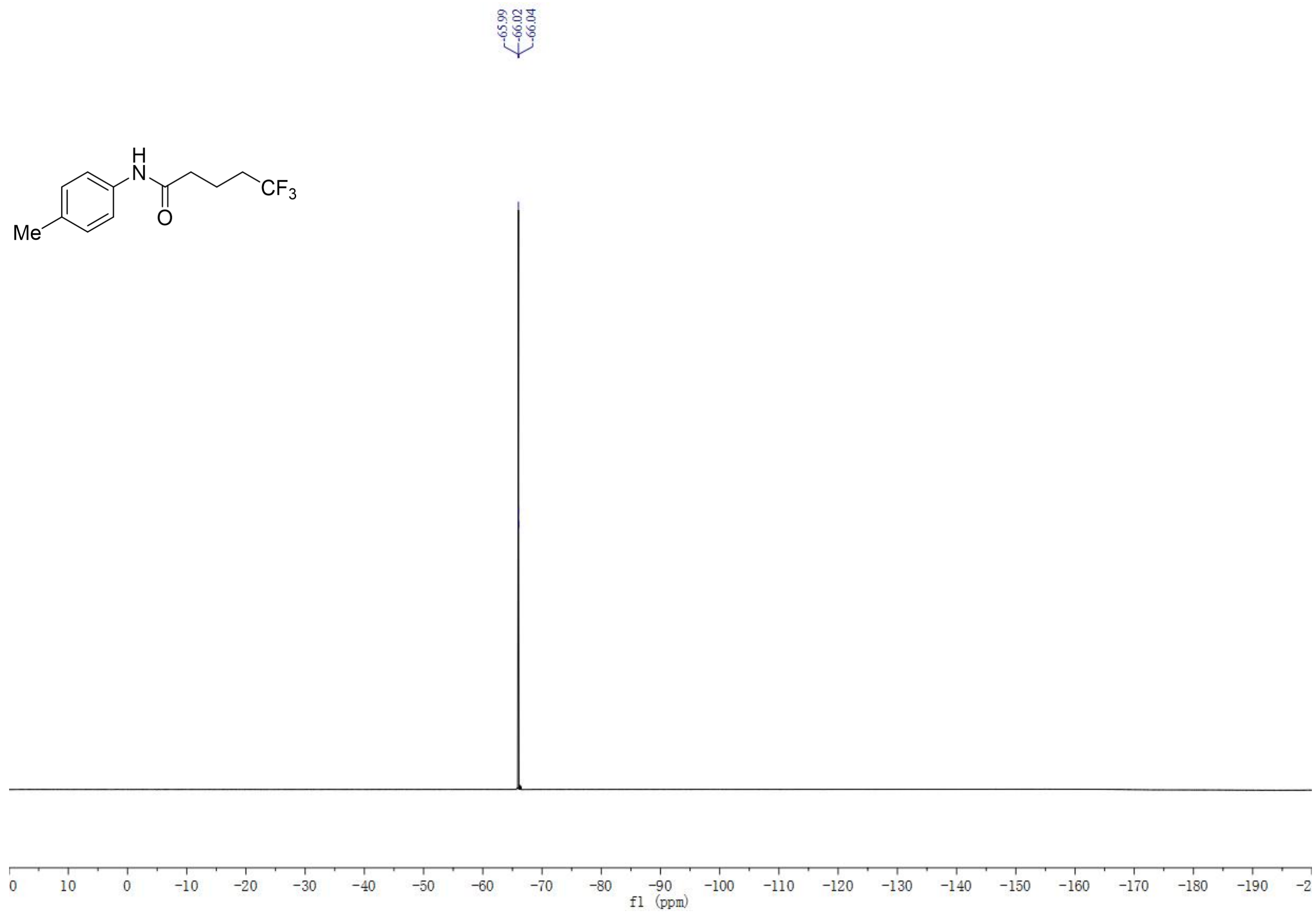


Figure S103. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 5,5,5-trifluoro-*N*-(*p*-tolyl)pentanamide (**5ah**)

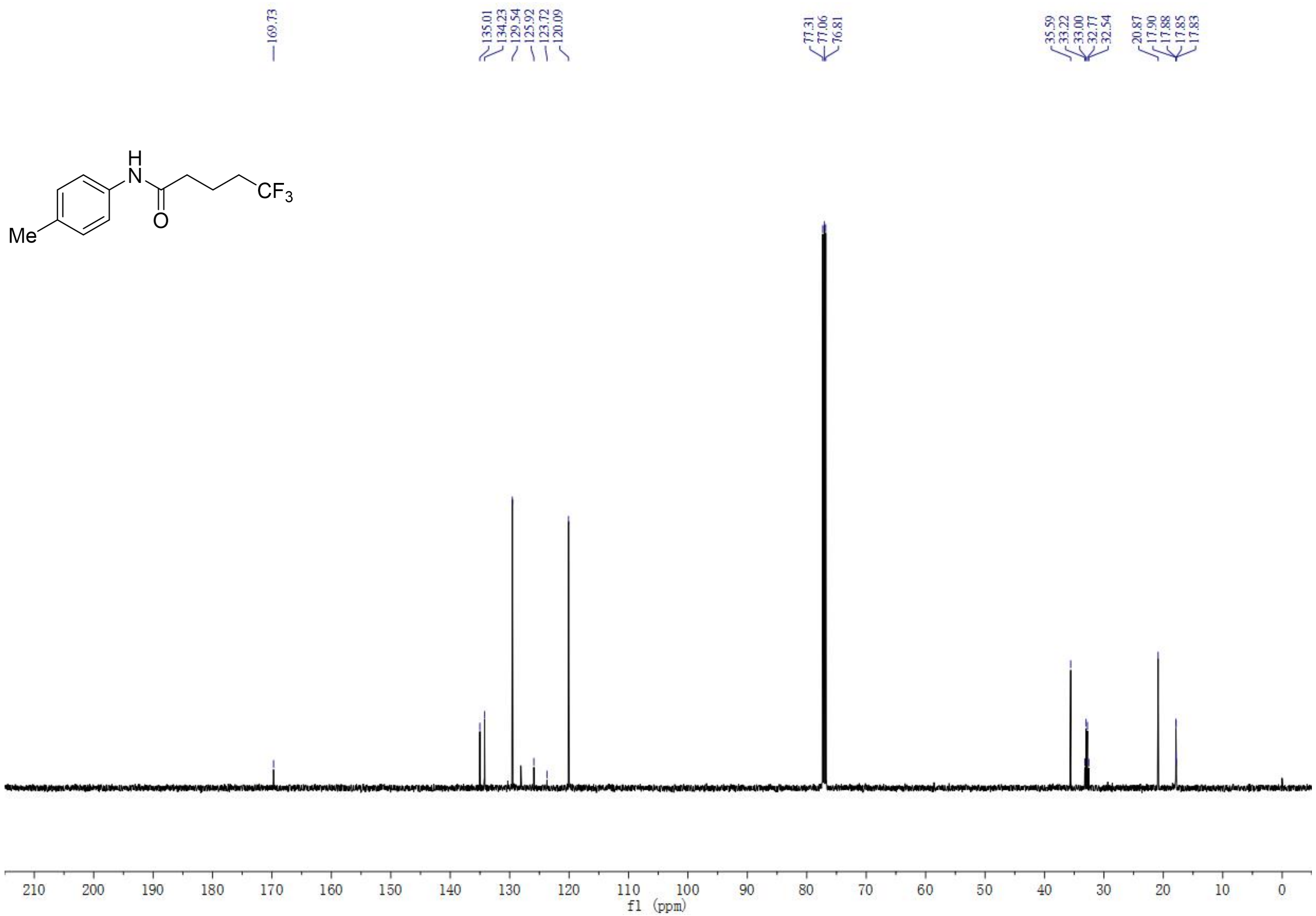


Figure S104. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 3-((*tert*-butyldimethylsilyl)oxy)-N-(p-tolyl)propanamide (**5ai**)

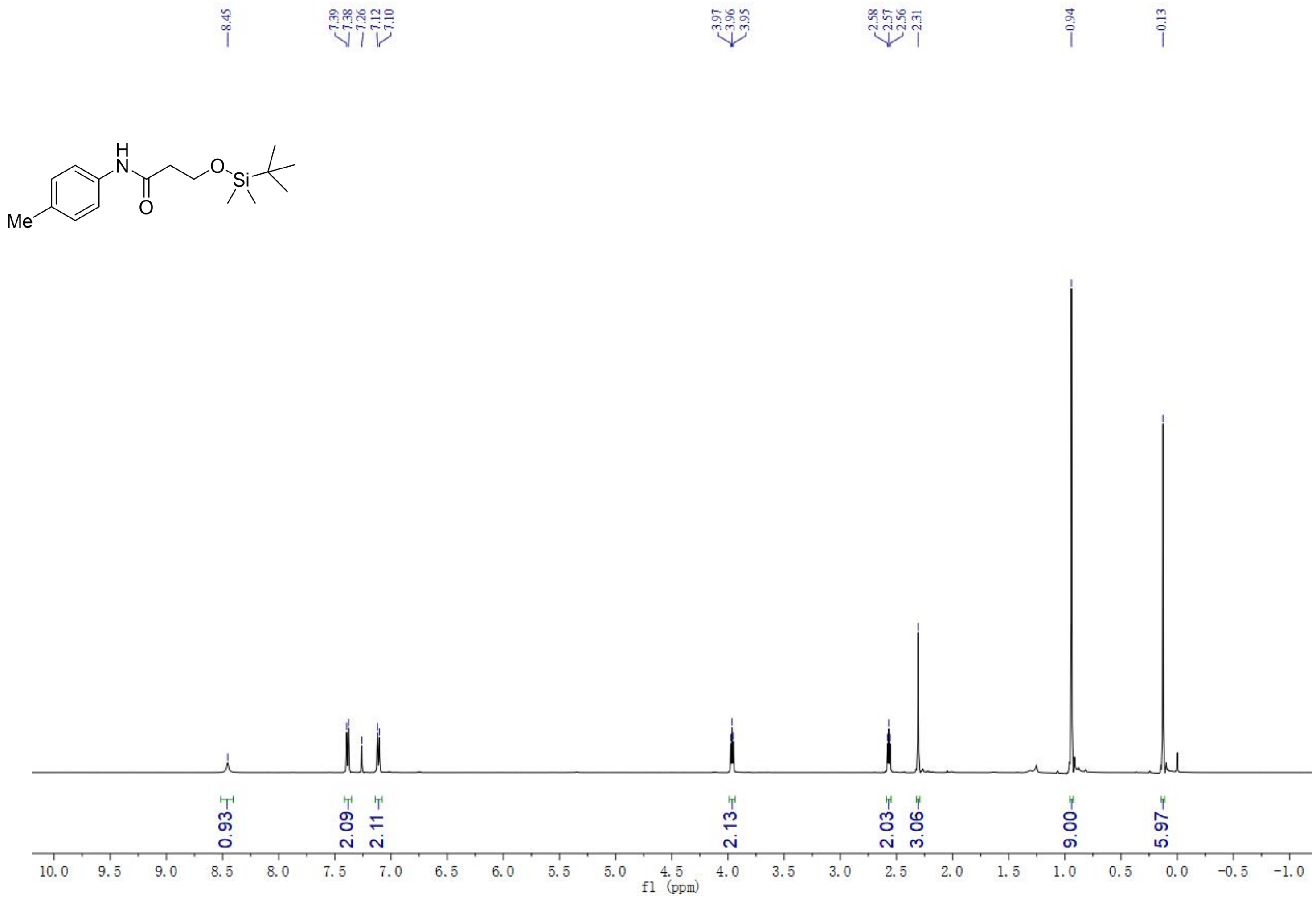


Figure S105. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 3-((*tert*-butyldimethylsilyl)oxy)-N-(p-tolyl)propanamide (**5ai**)

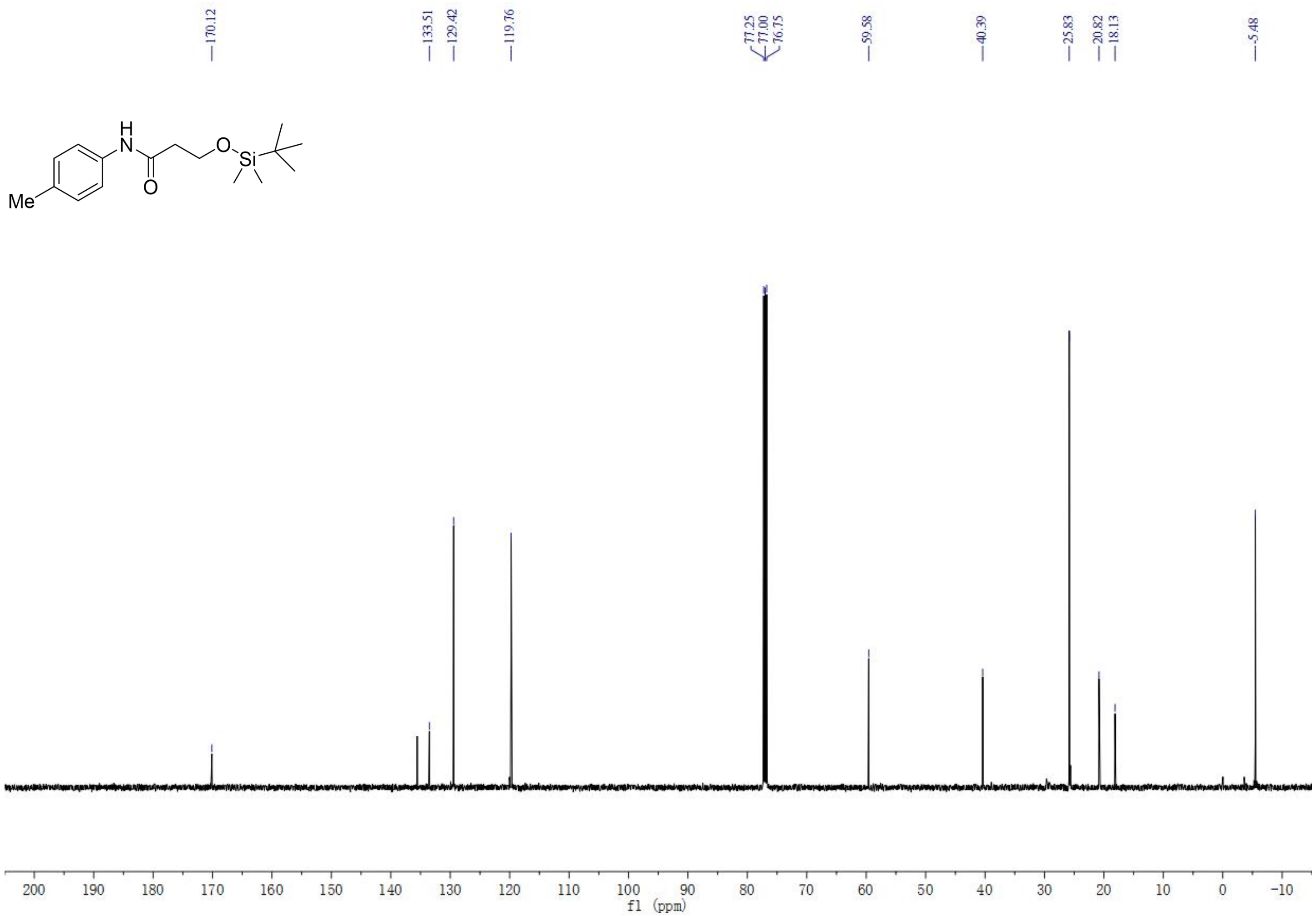


Figure S106. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 6-(4-cyanophenoxy)-*N*-(*p*-tolyl)hexanamide (**5aj**)

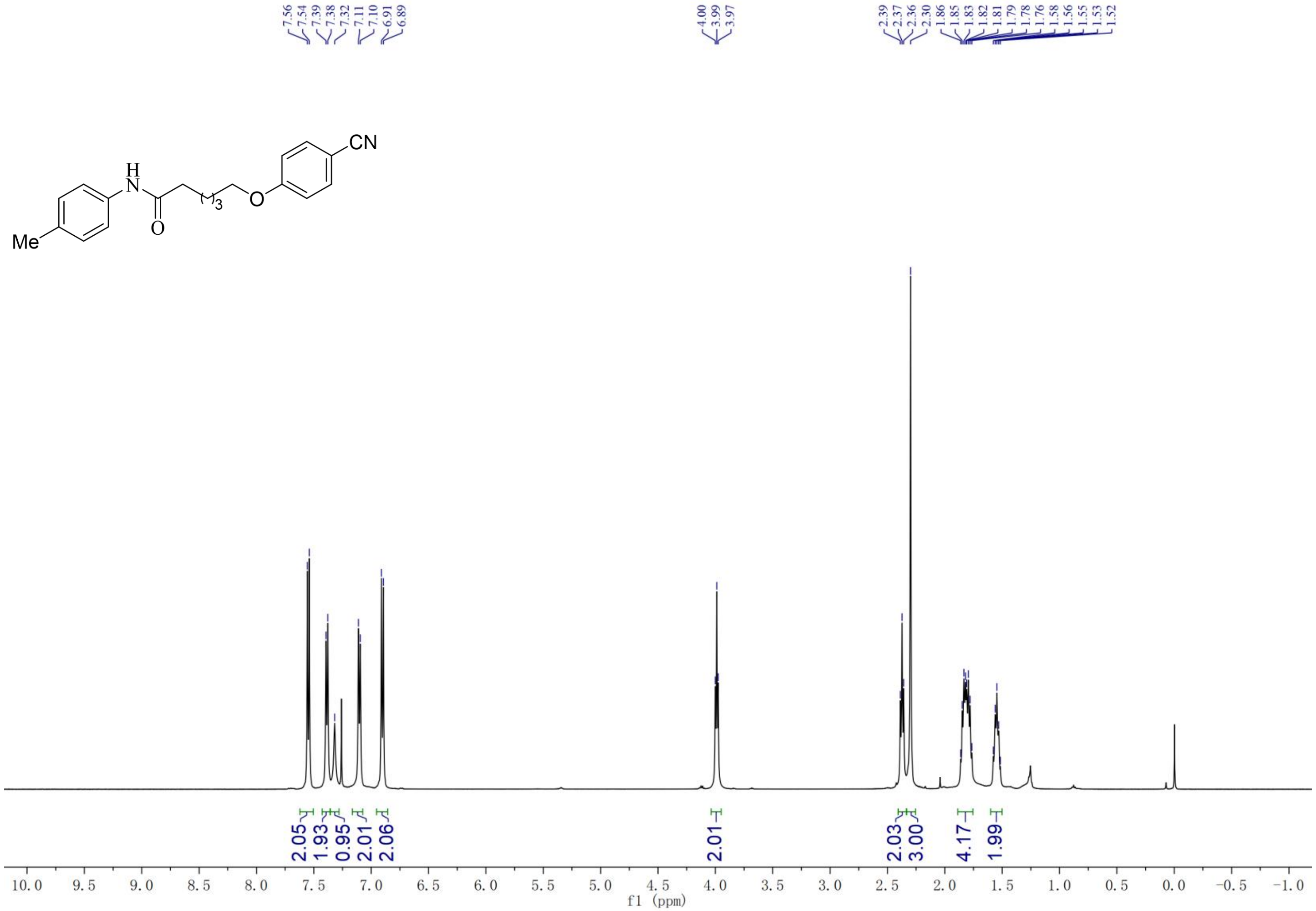


Figure S107. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 6-(4-cyanophenoxy)-*N*-(*p*-tolyl)hexanamide (**5aj**)

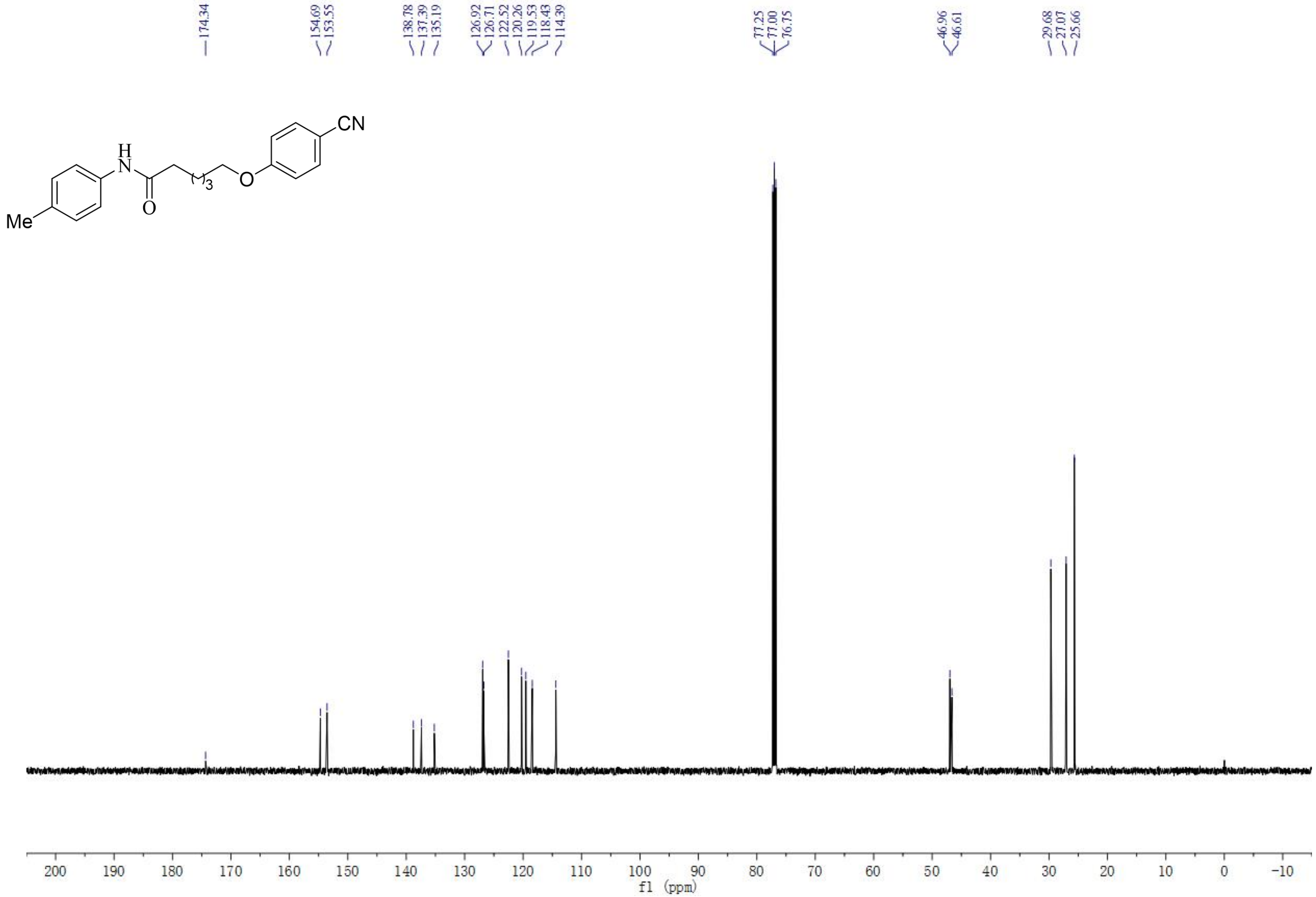


Figure S108. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-*N*-(*p*-tolyl)nonanamide (**5ak**)

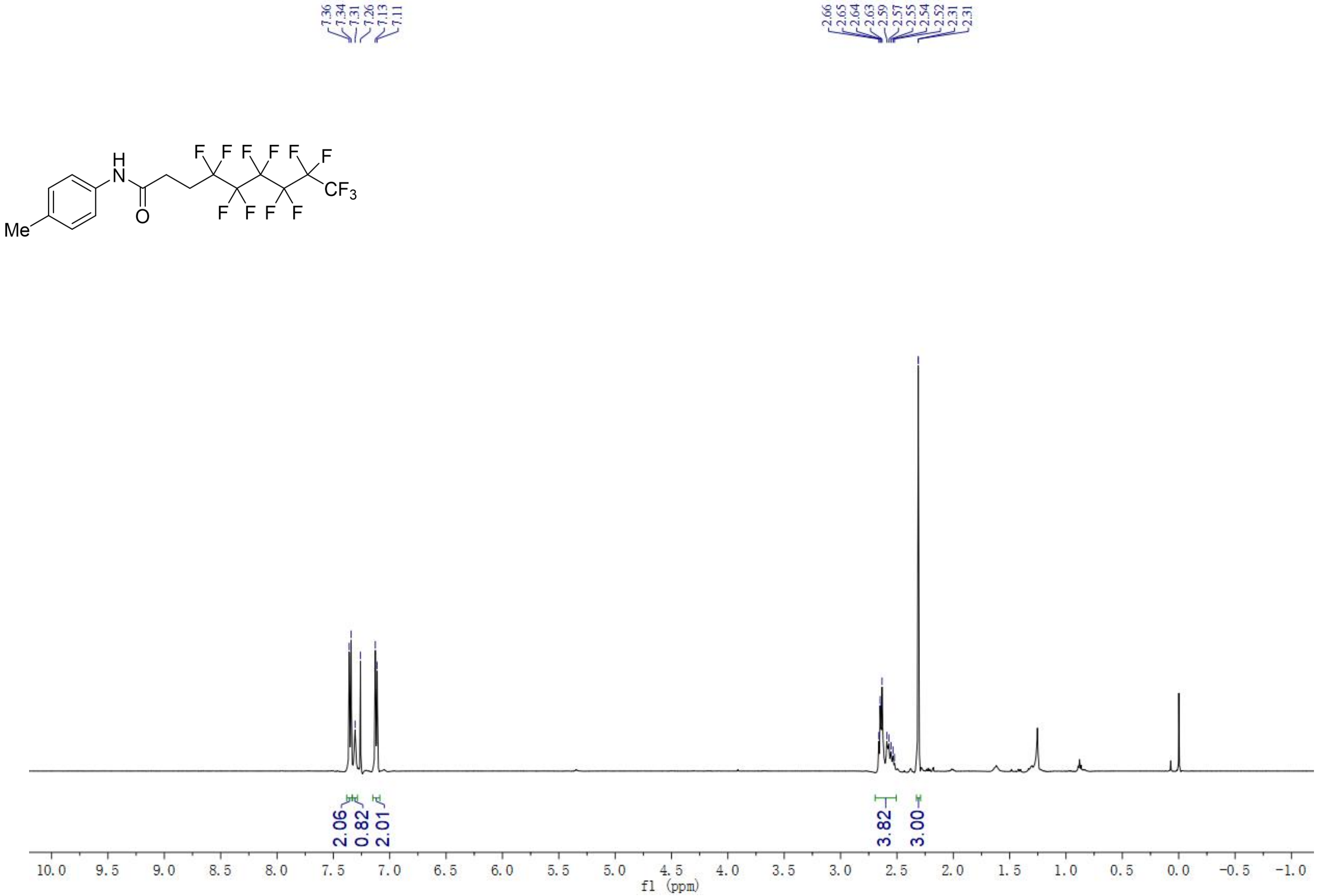


Figure S109. ^{19}F NMR (376 MHz, $CDCl_3$, 298K) of 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-*N*-(*p*-tolyl)nonanamide (**5ak**)

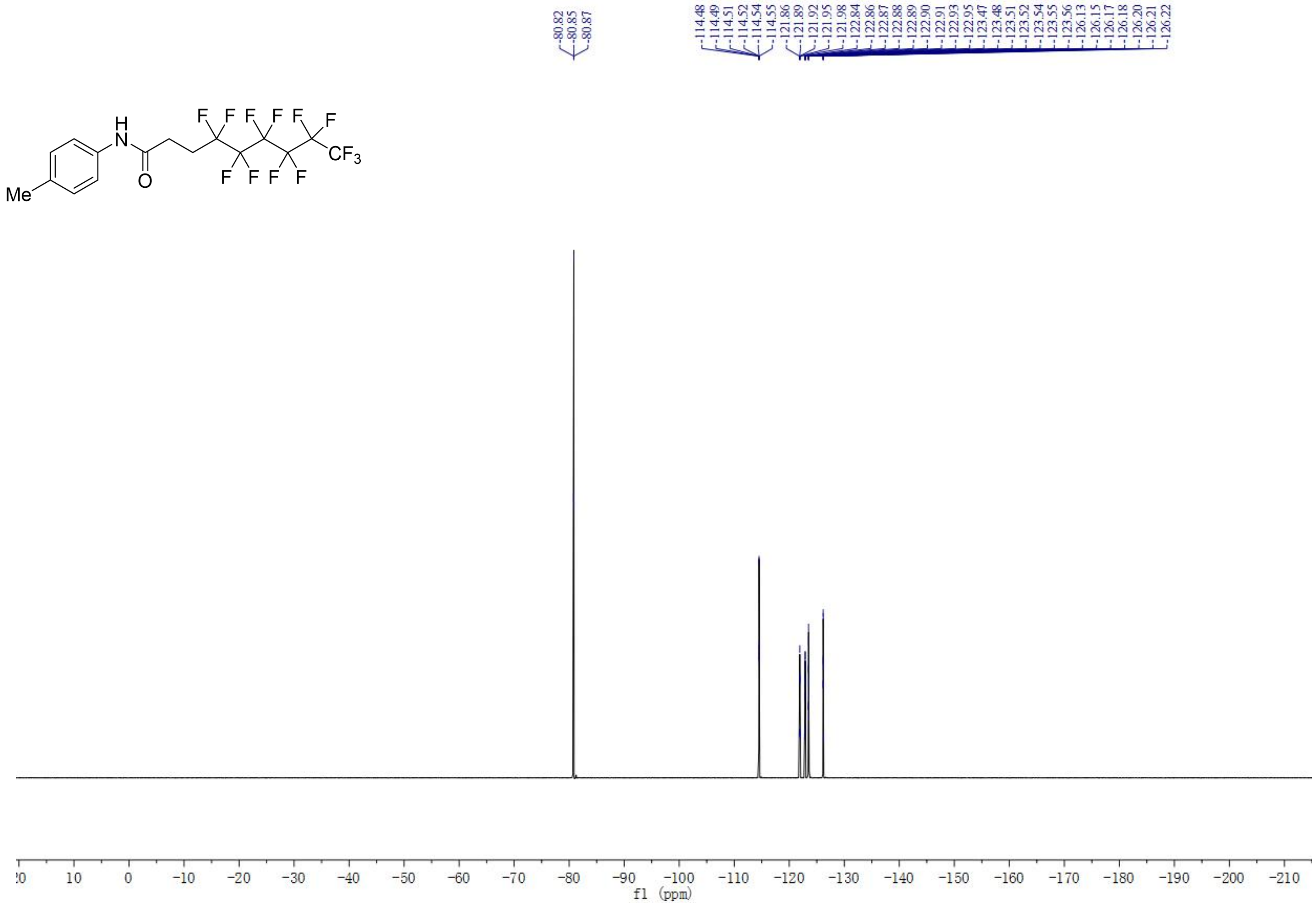


Figure S110. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-*N*-(*p*-tolyl)nonanamide (**5ak**)

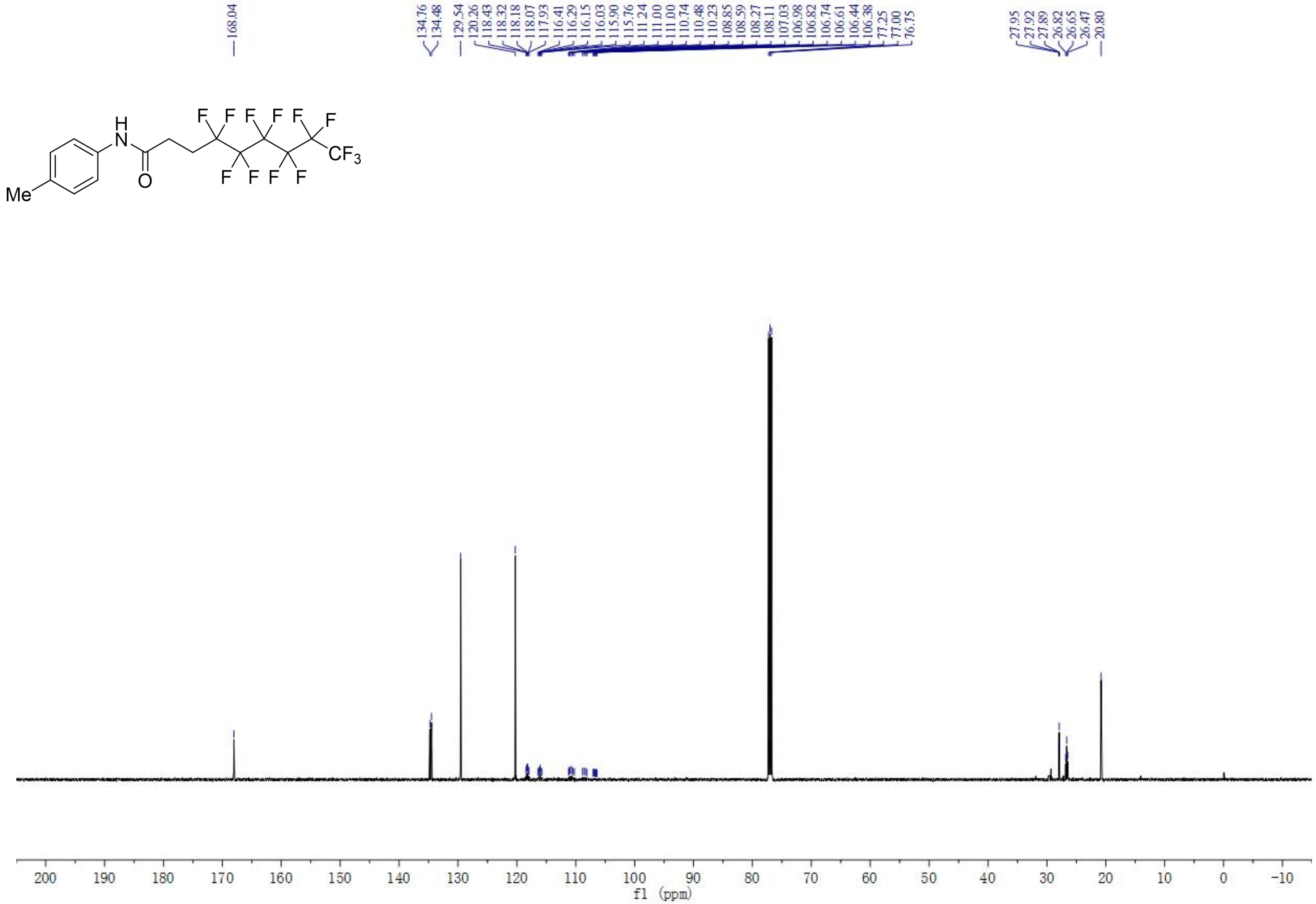


Figure S111. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-hydroxy-*N*-(*p*-tolyl)butanamide (**5al**)

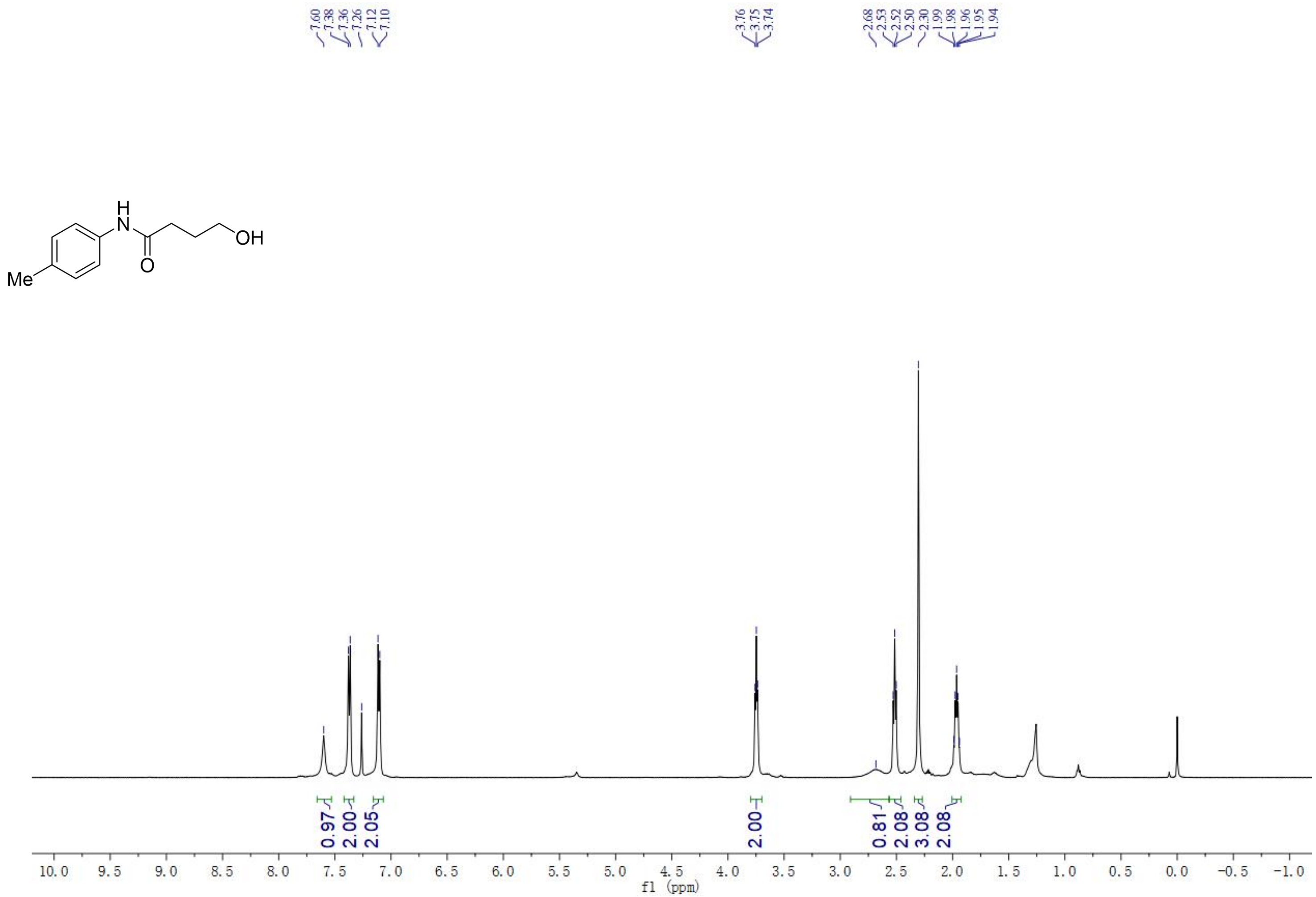


Figure S112. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-hydroxy-*N*-(*p*-tolyl)butanamide (**5al**)

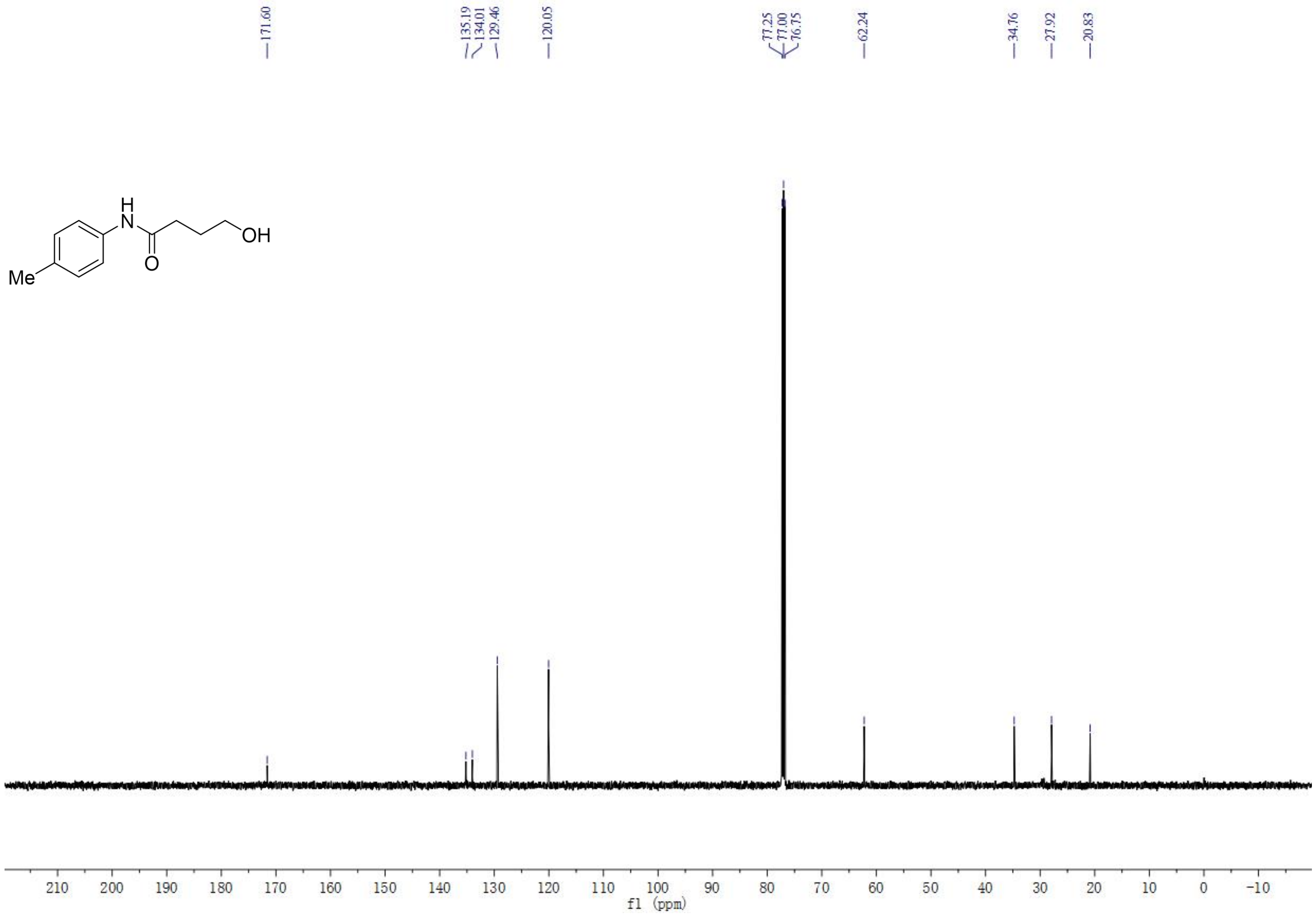
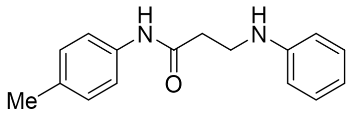


Figure S113. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 3-(phenylamino)-*N*-(*p*-tolyl)propanamide (**5am**)



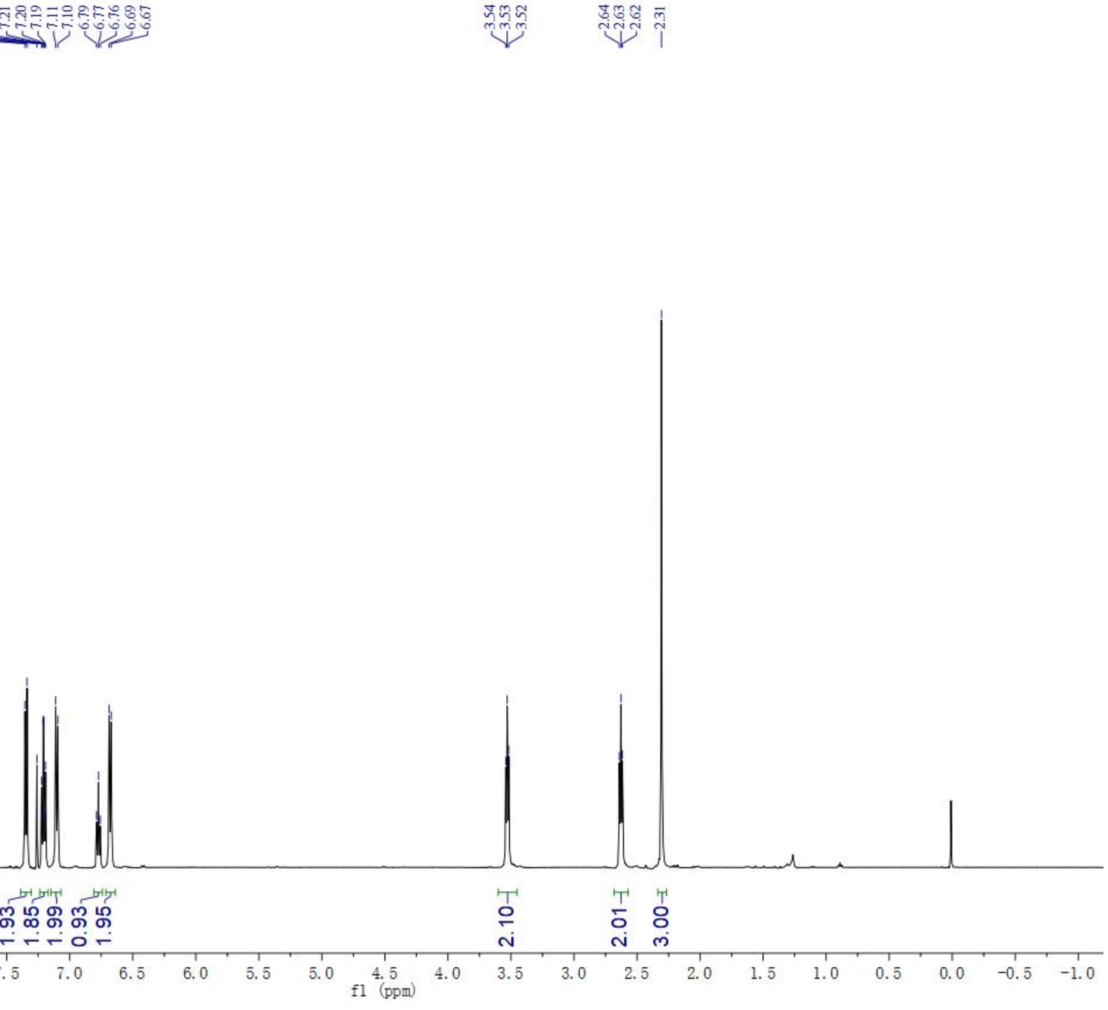


Figure S114. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 3-(phenylamino)-*N*-(*p*-tolyl)propanamide (**5am**)

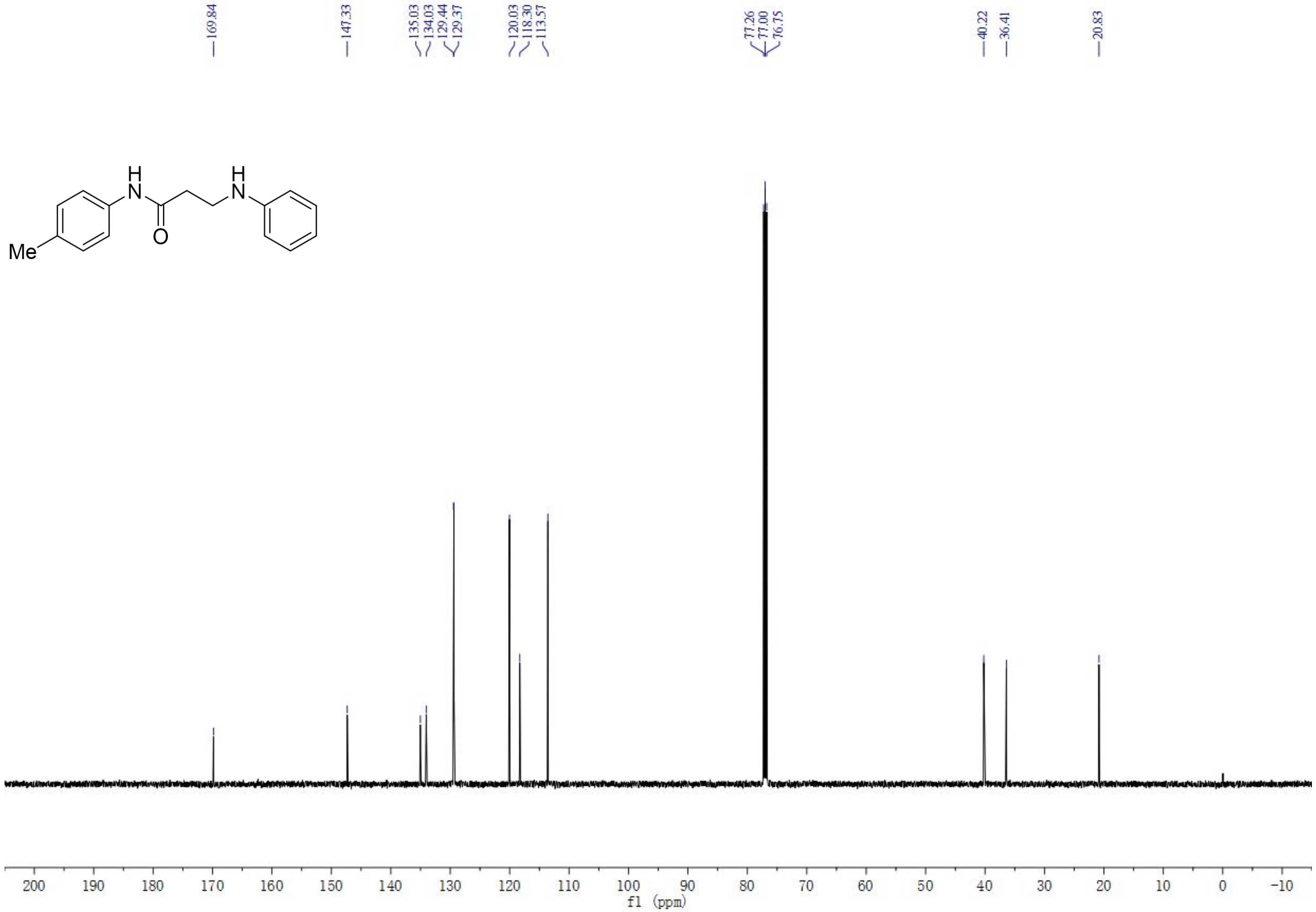


Figure S115. ^{1}H NMR (500 MHz, DMSO-d_6, 298 K) of 3-(4-iodophenyl)-*N*-(*p*-tolyl)propanamide **(5an).**

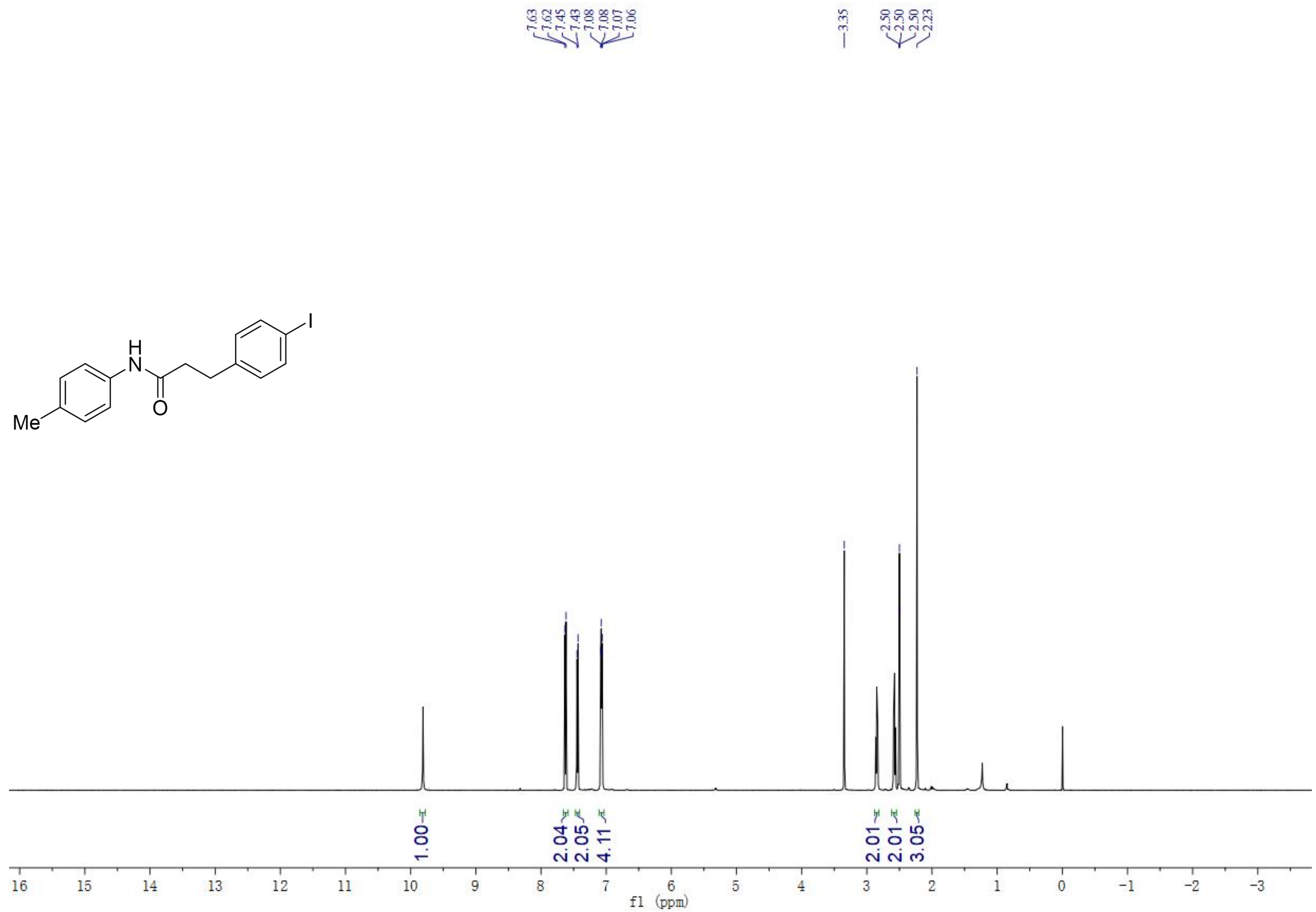


Figure S116. ^{13}C NMR (126 MHz, DMSO-d_6, 298 K) of 3-(4-iodophenyl)-*N*-(*p*-tolyl)propenamide **(5an).**

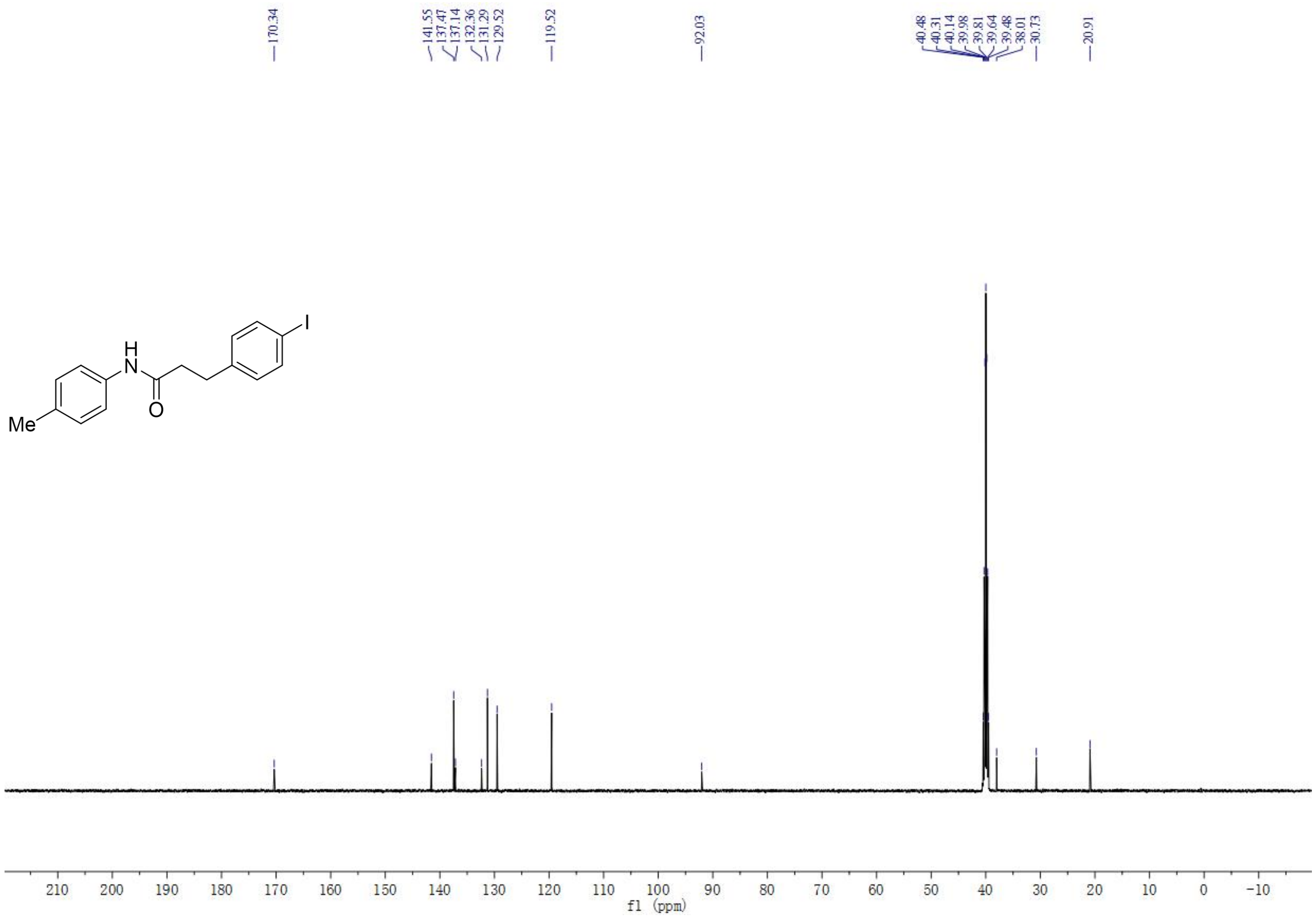


Figure S117. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 3-(thiophen-2-yl)-*N*-(*p*-tolyl)propanamide (**5ao**)

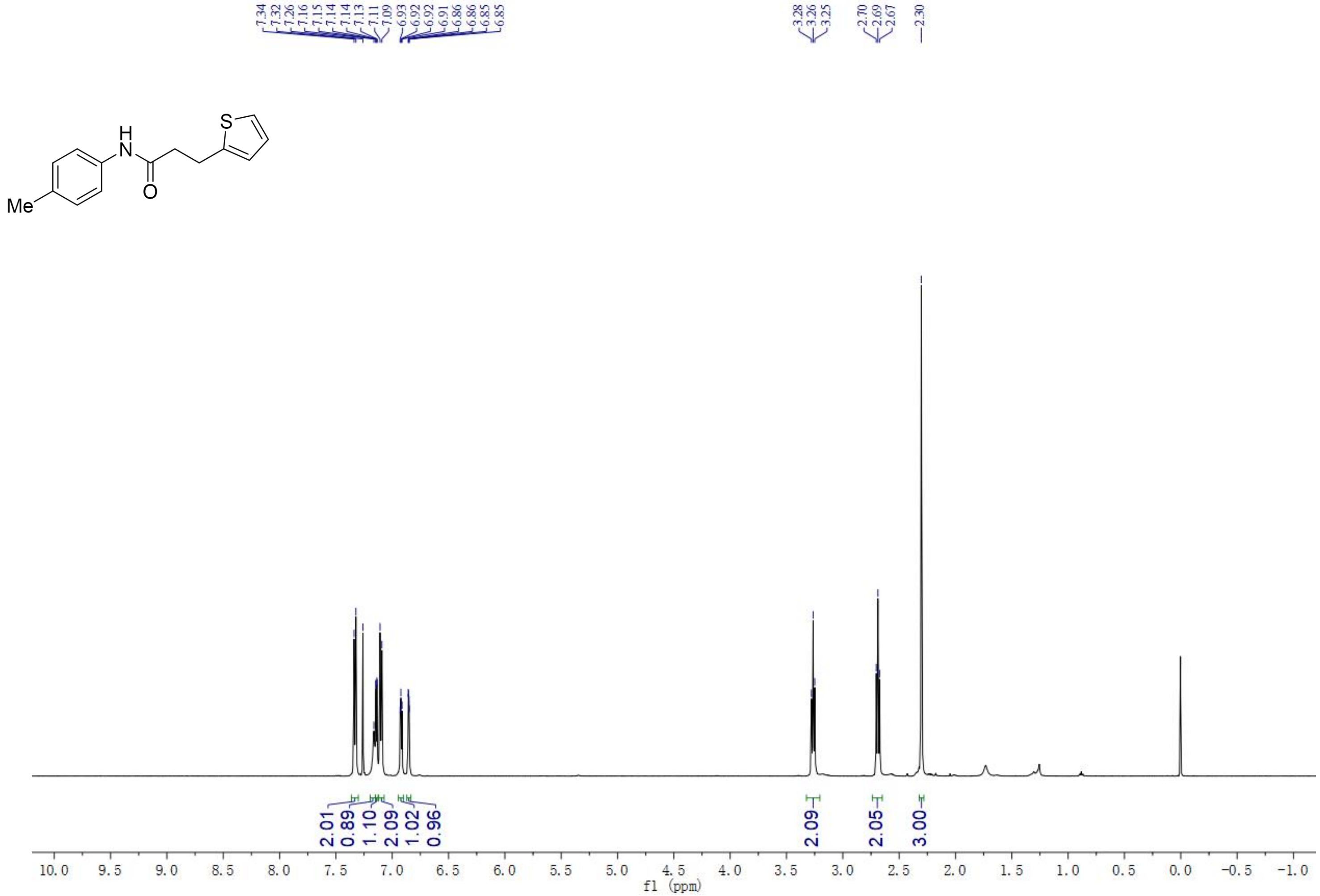


Figure S118. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 3-(thiophen-2-yl)-*N*-(*p*-tolyl)propanamide (**5ao**)

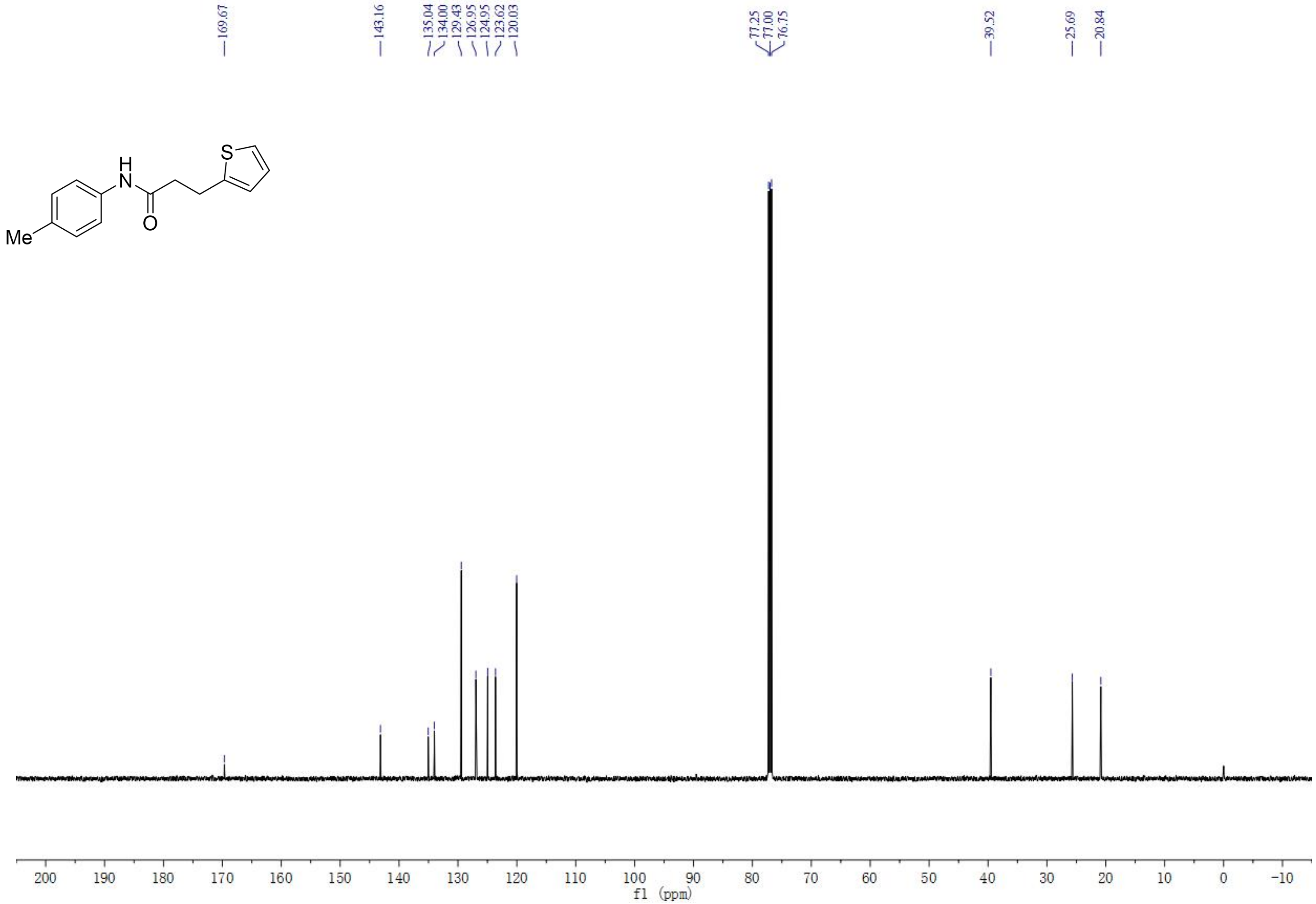


Figure S119. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-(1,3-dioxoisoindolin-2-yl)-*N*-(*p*-tolyl)butanamide (**5ap**)

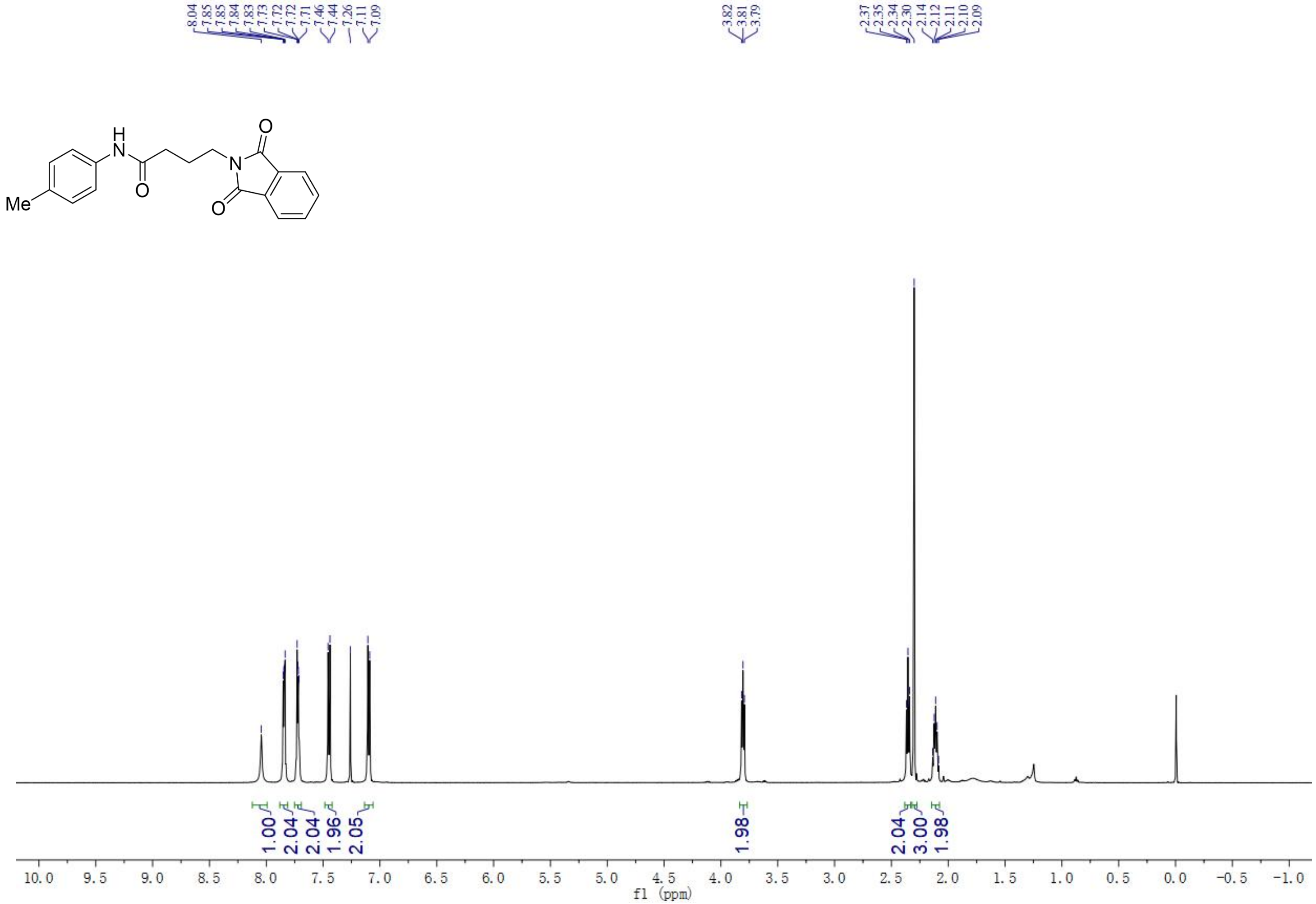


Figure S120. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-(1,3-dioxoisoindolin-2-yl)-*N*-(*p*-tolyl)butanamide (**5ap**)

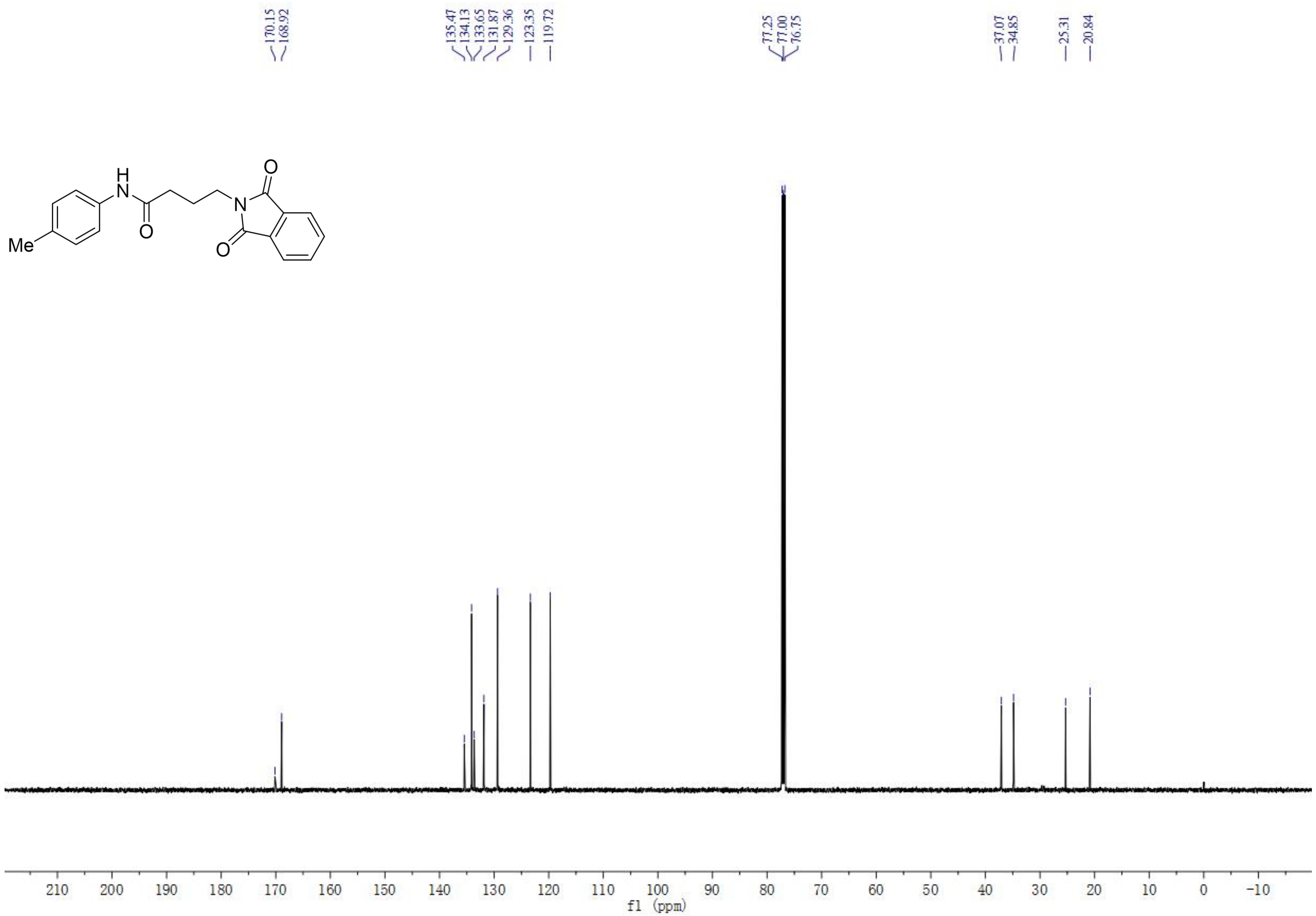


Figure S121. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-methyl-3-phenyl-*N*-(*p*-tolyl)propanamide (**5aq**)

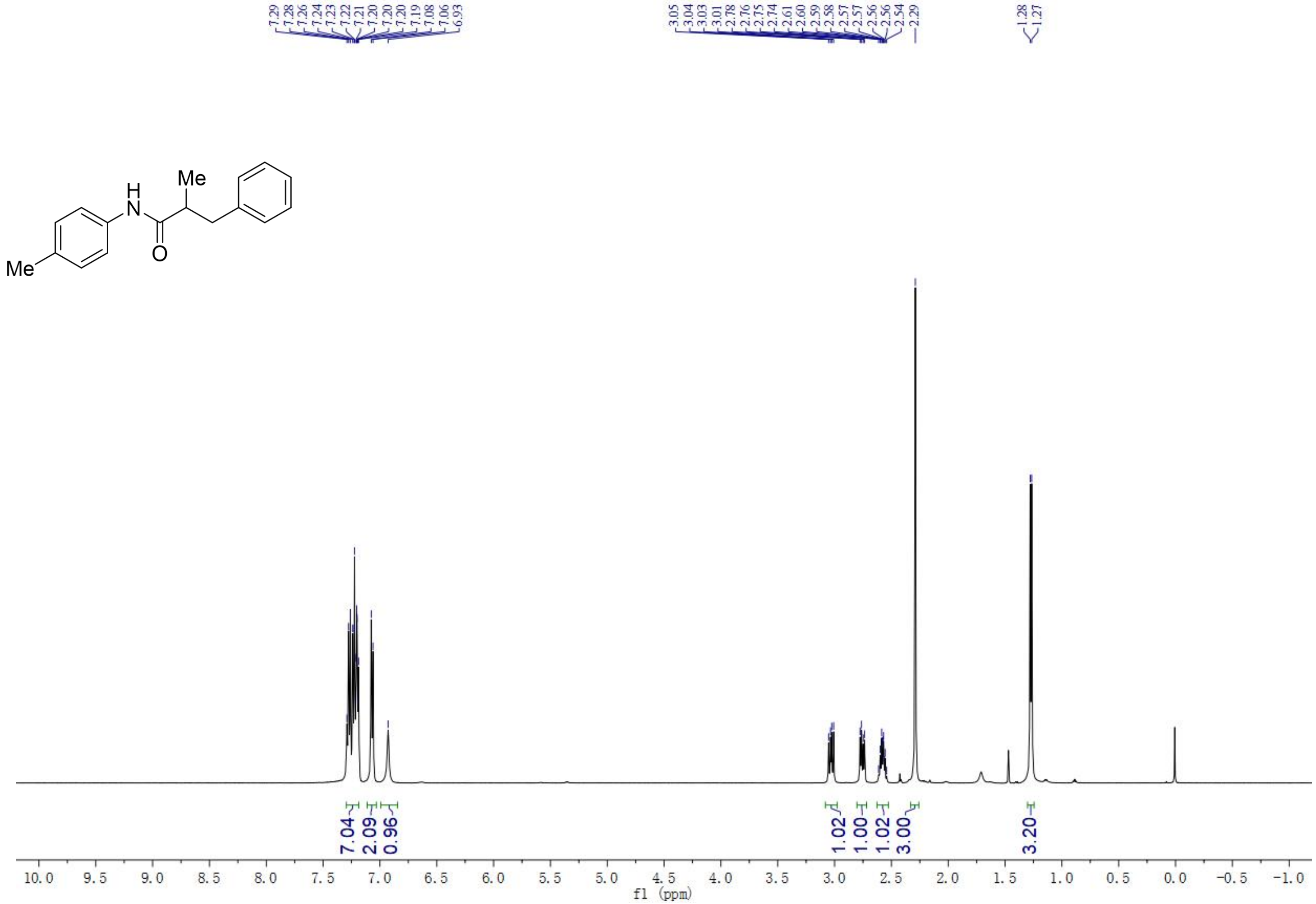


Figure S122. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 2-methyl-3-phenyl-*N*-(*p*-tolyl)propanamide (**5aq**)

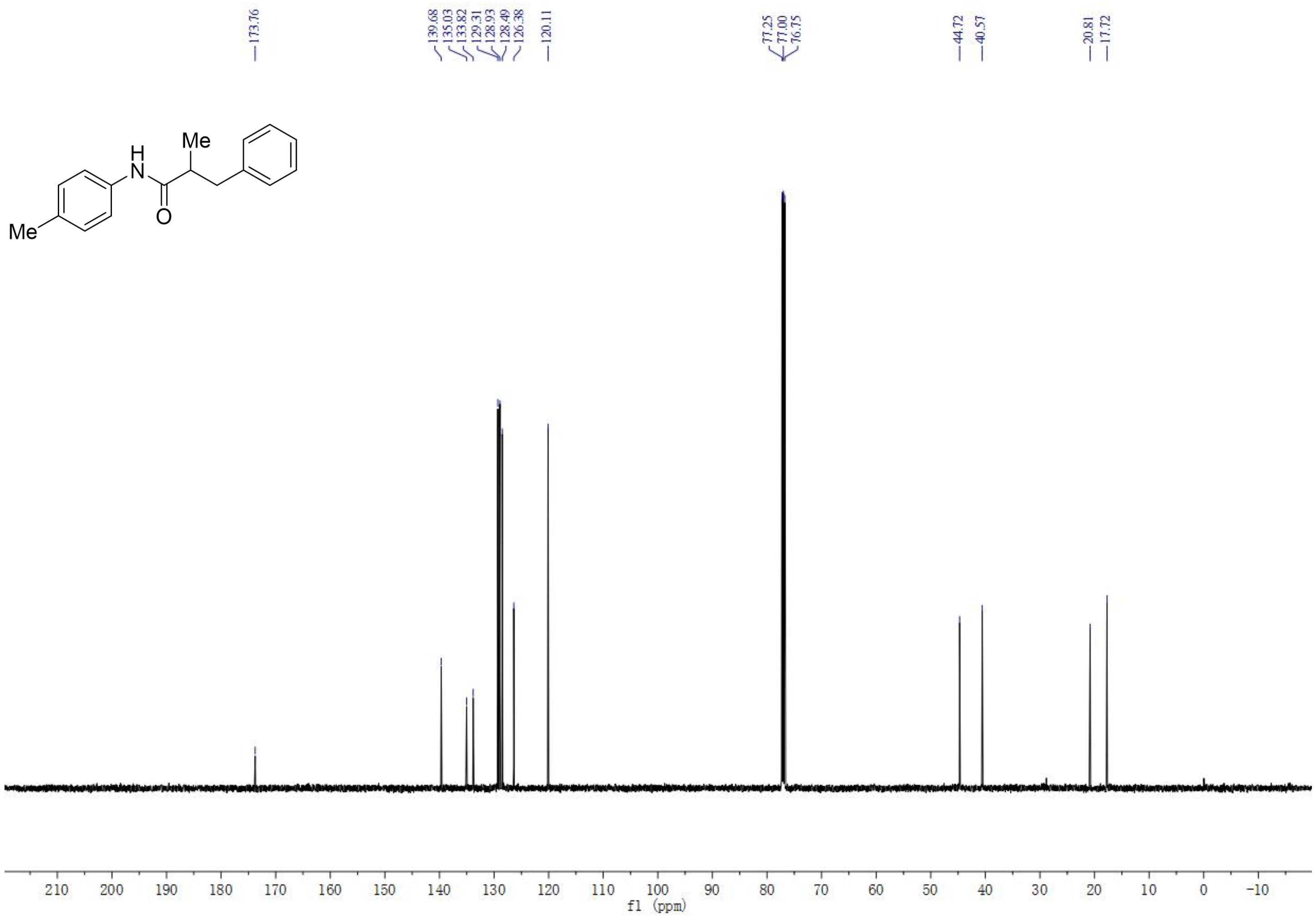


Figure S123. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)oxetane-3-carboxamide (**5ar**)

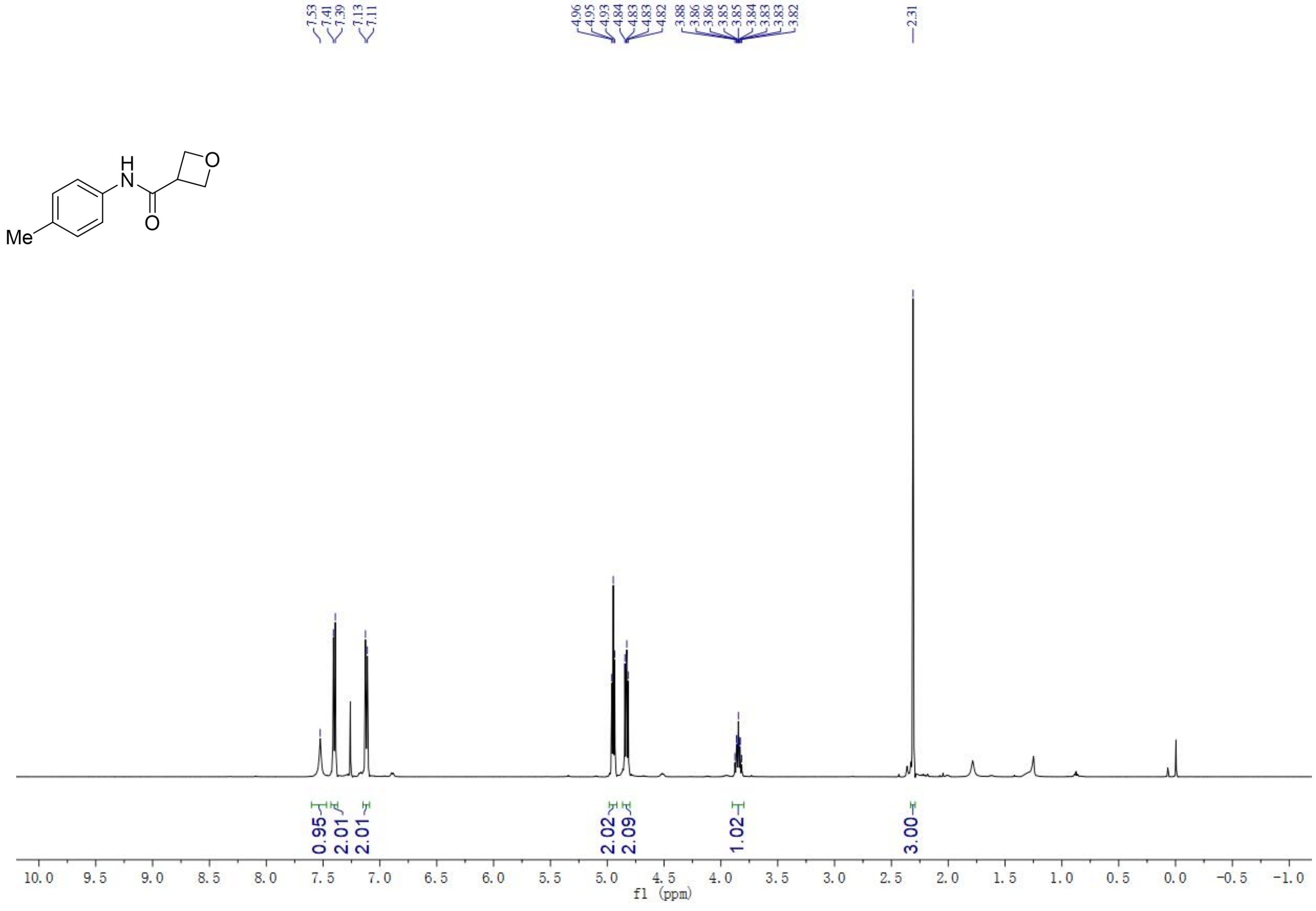


Figure S124. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)oxetane-3-carboxamide (**5ar**)

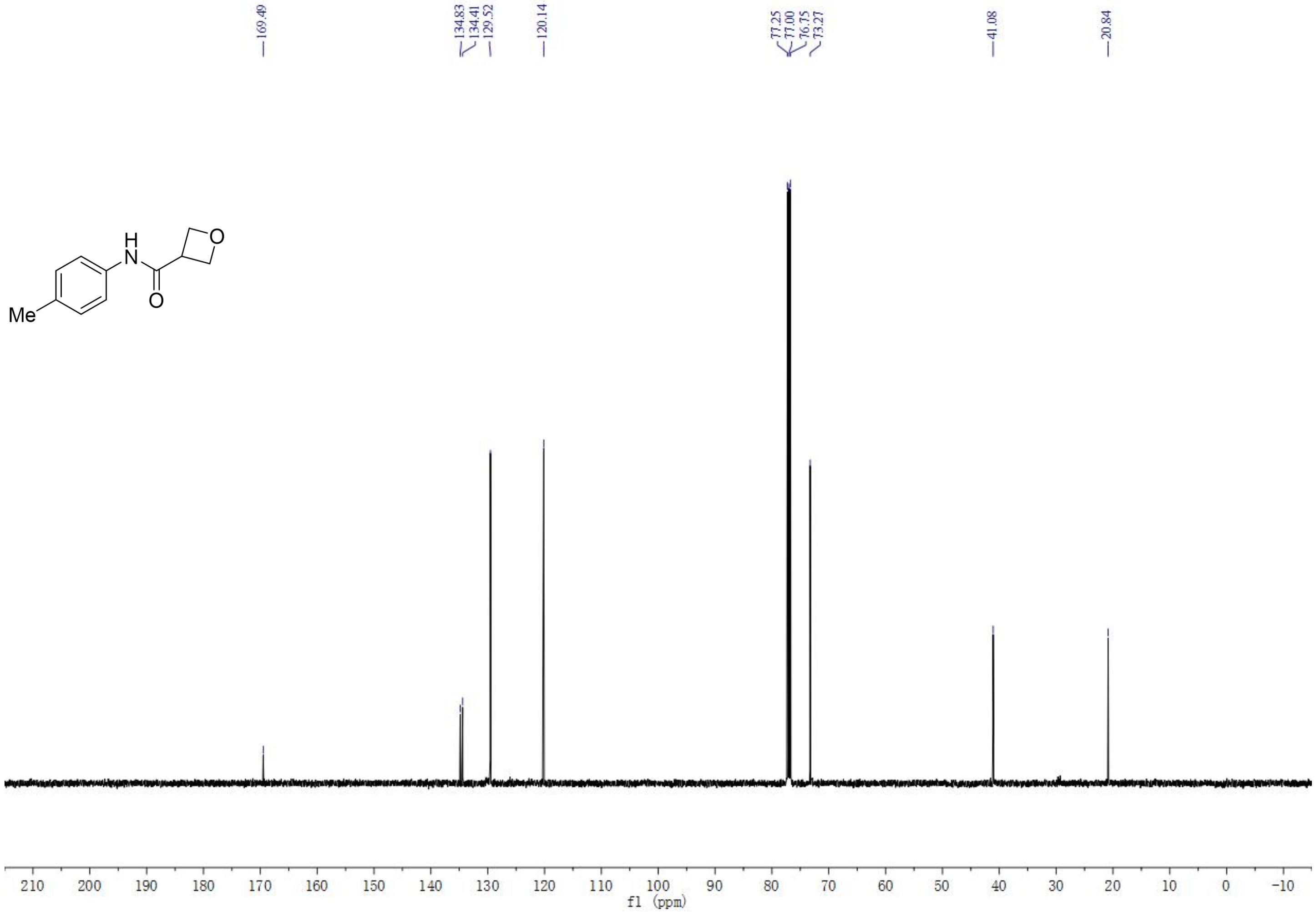


Figure S125. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 1-benzhydryl-*N*-(*p*-tolyl)azetidine-3-carboxamide (**5as**)

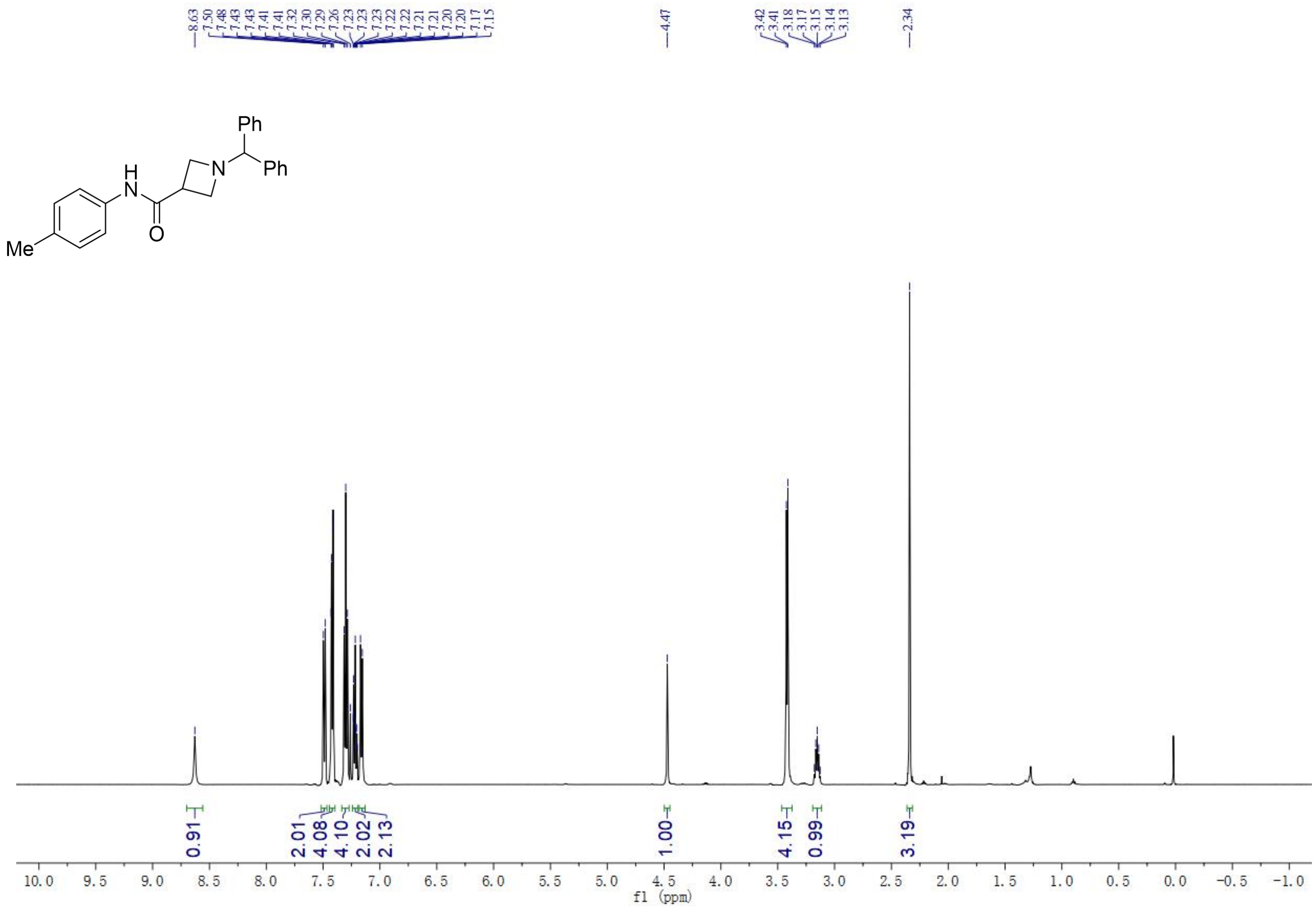


Figure S126. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 1-benzhydryl-*N*-(*p*-tolyl)azetidine-3-carboxamide (**5as**)

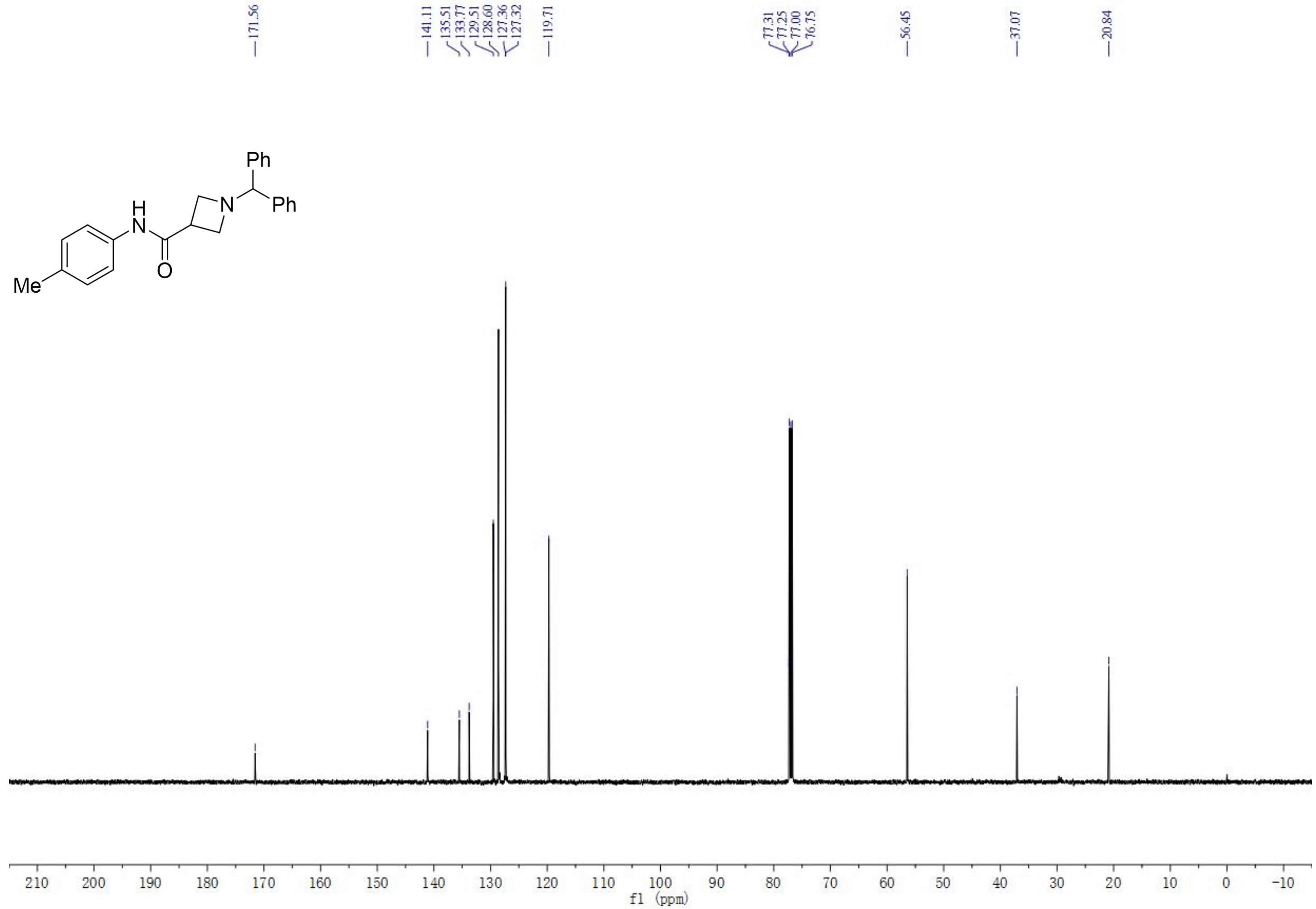


Figure S127. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 3-(*p*-tolylcarbamoyl)azetidine-1-carboxylate (**5at**)

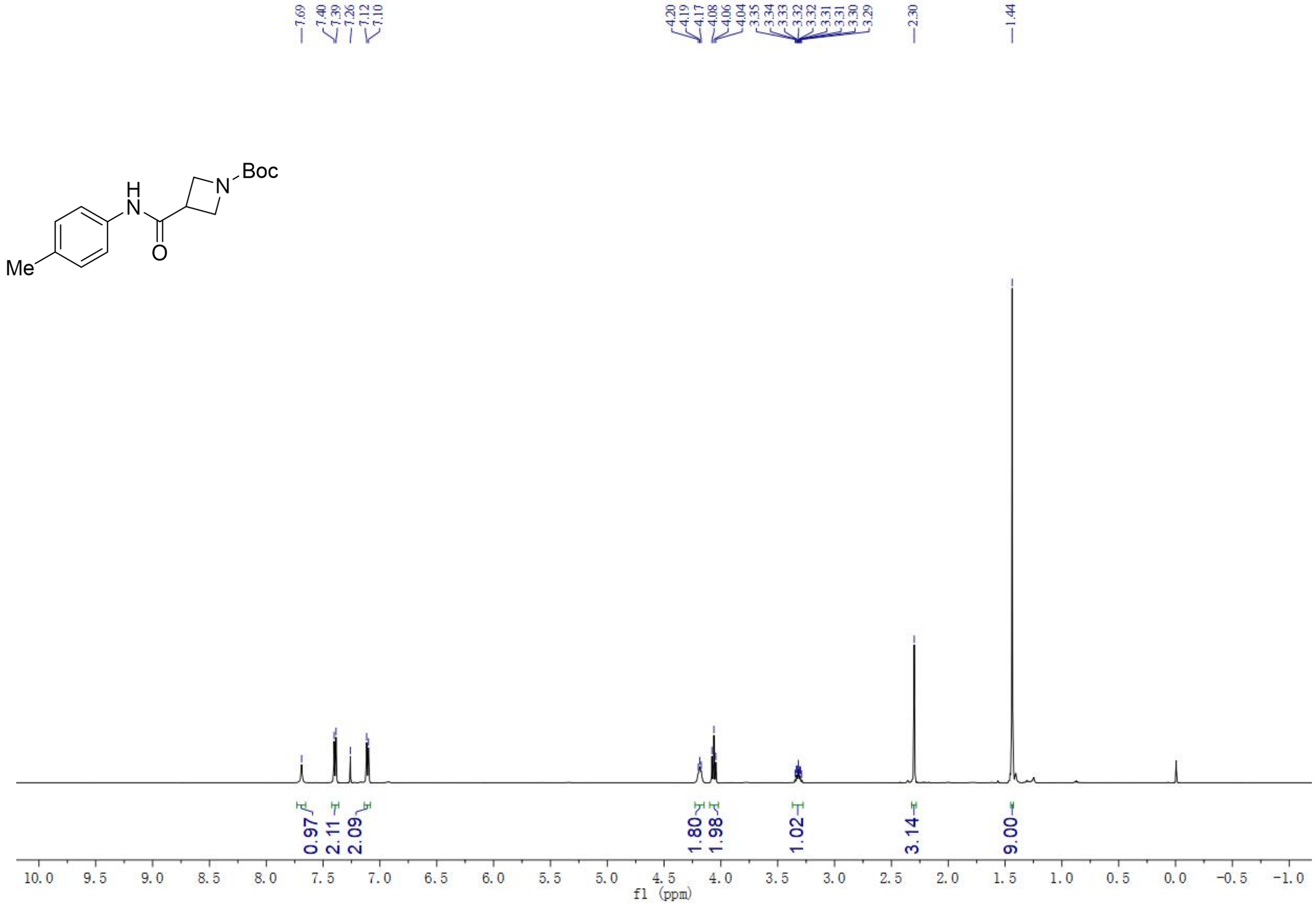


Figure S128. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *tert*-butyl 3-(*p*-tolylcarbamoyl)azetidine-1-carboxylate (**5at**)

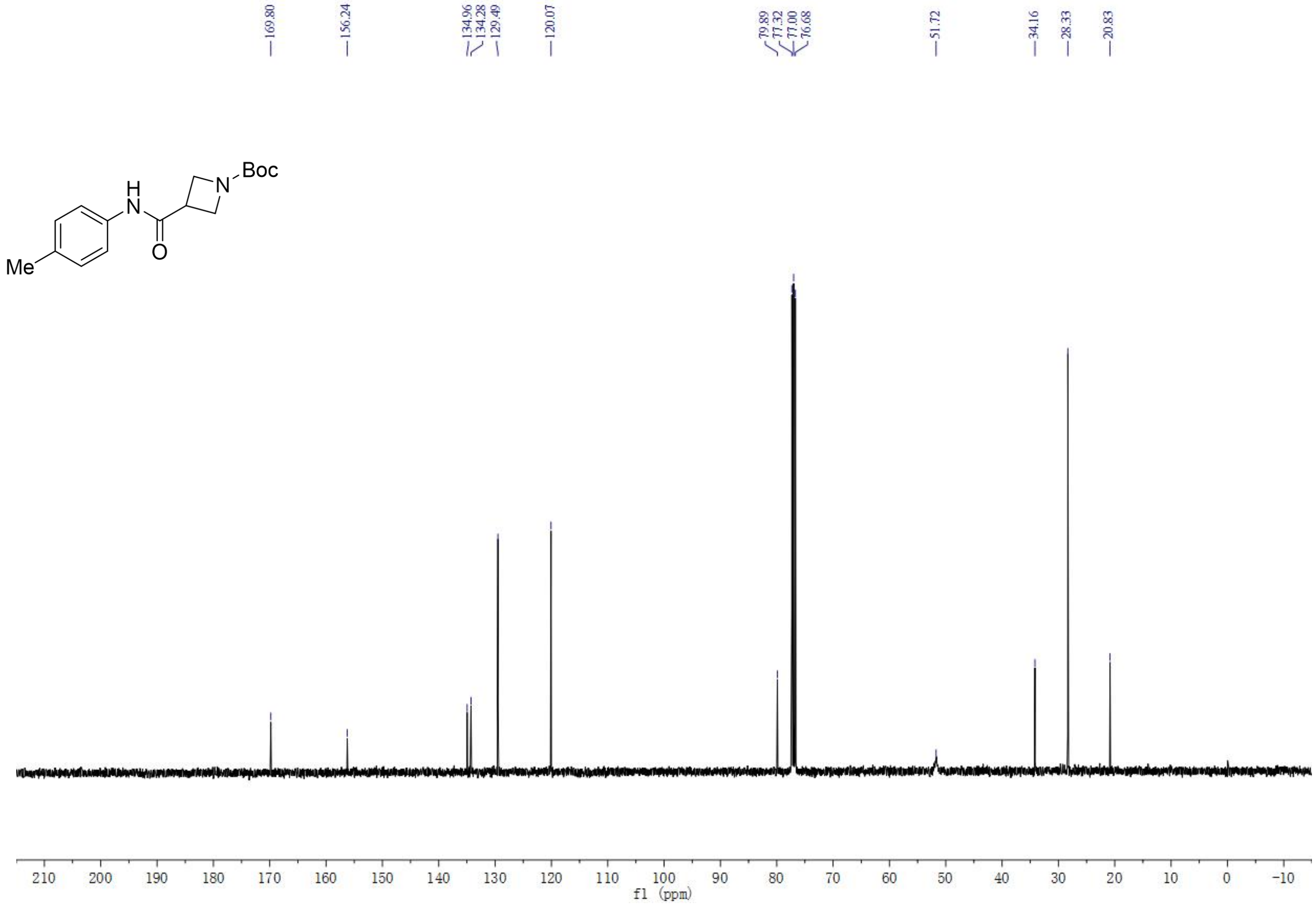


Figure S129. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 3-(*p*-tolylcarbamoyl)pyrrolidine-1-carboxylate (**5au**)

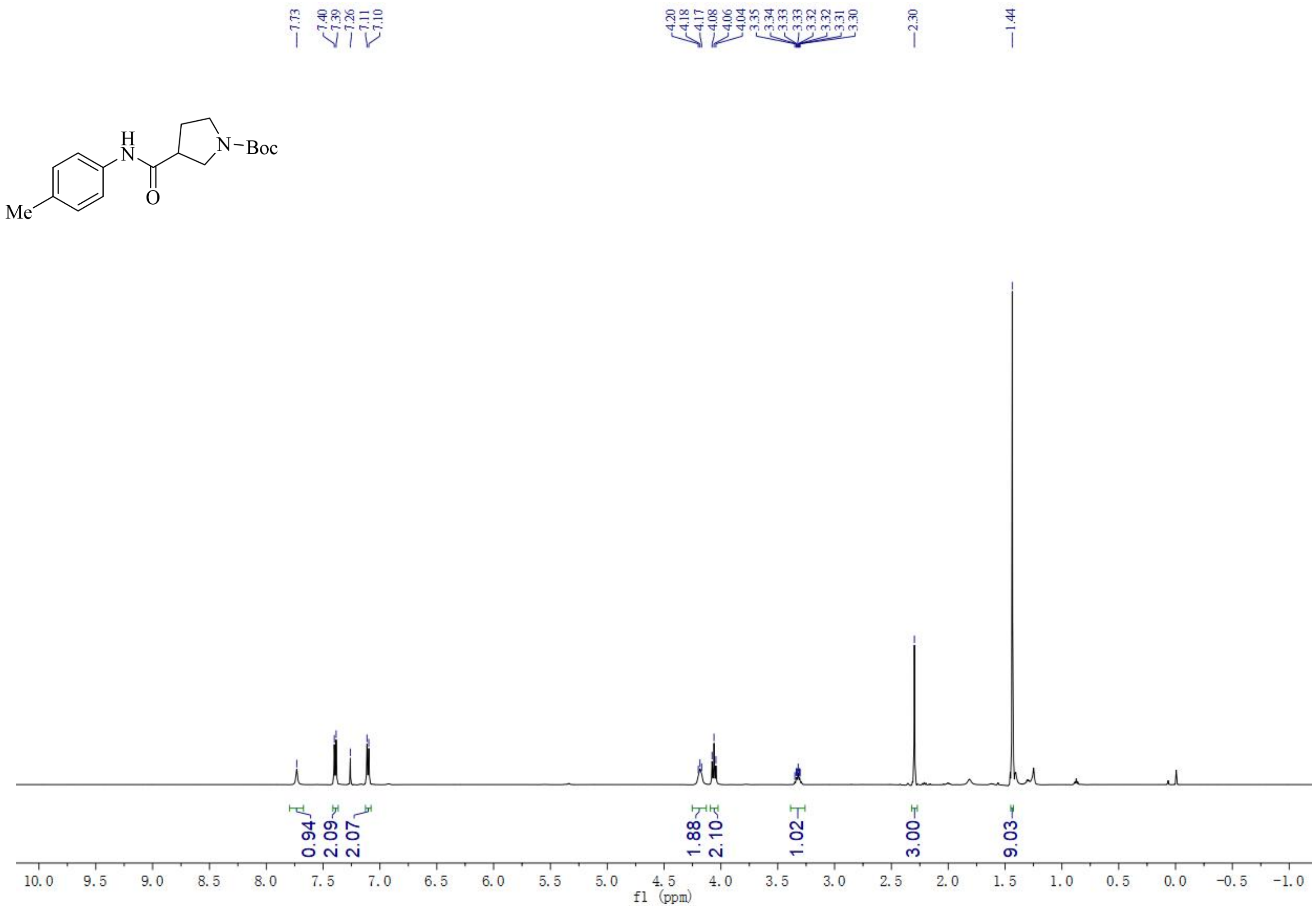


Figure S130. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 3-(*p*-tolylcarbamoyl)pyrrolidine-1-carboxylate (**5au**)

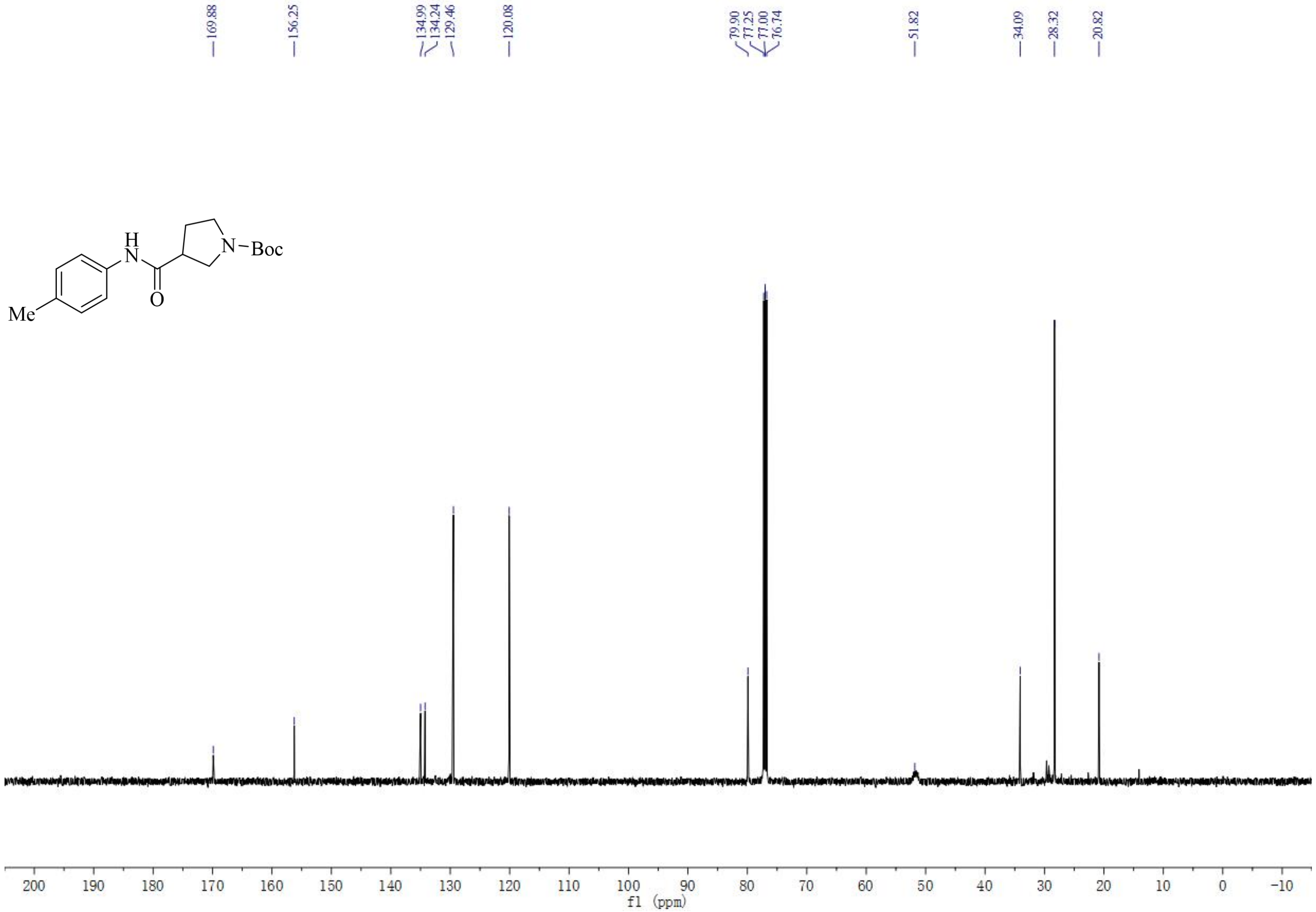


Figure S131. ^{1}H NMR (500 MHz, DMSO-d_6, 298K) of *tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**5av**)

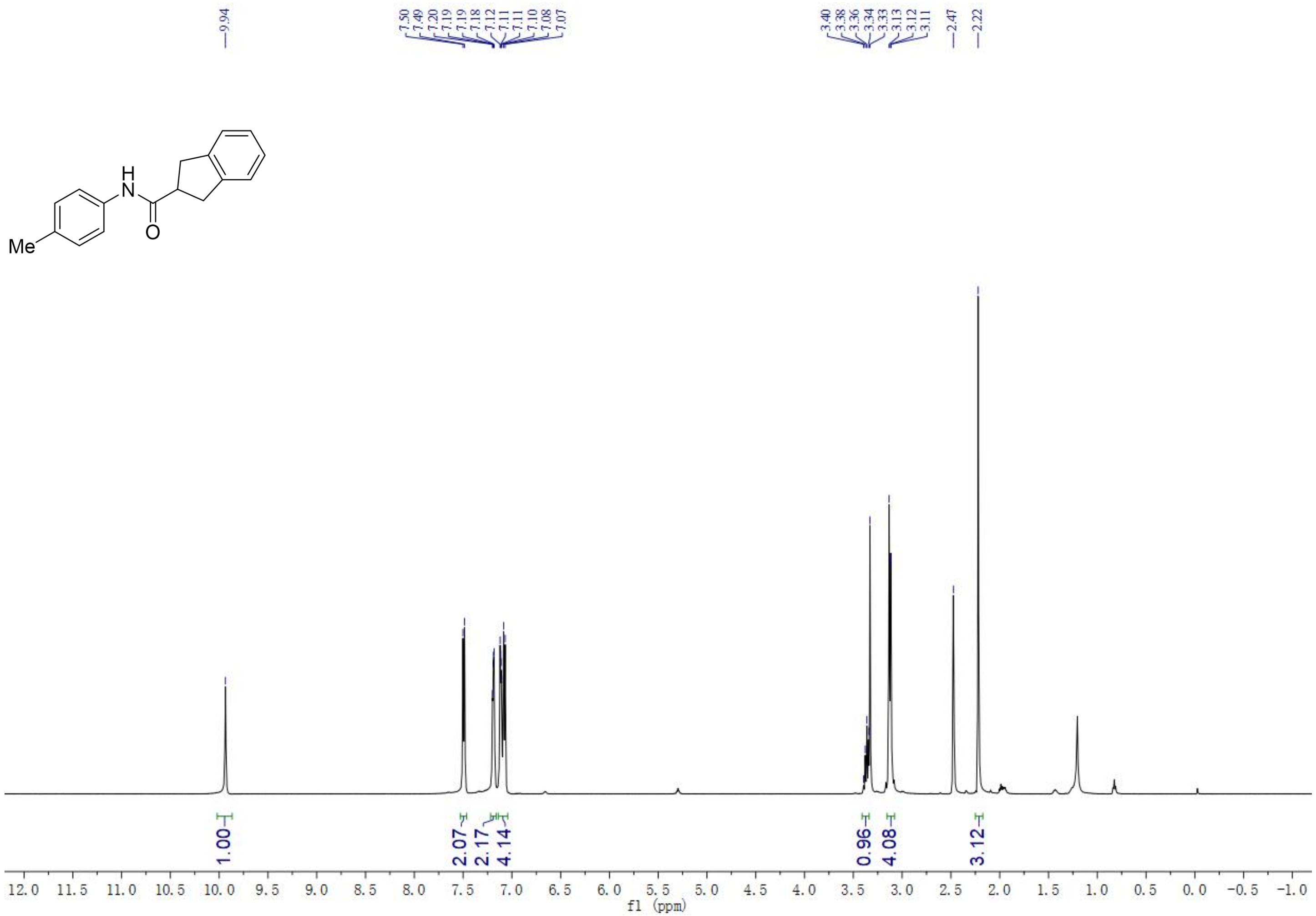


Figure S132. ^{13}C NMR (126 MHz, DMSO-d_6, 298K) of *tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**5av**)

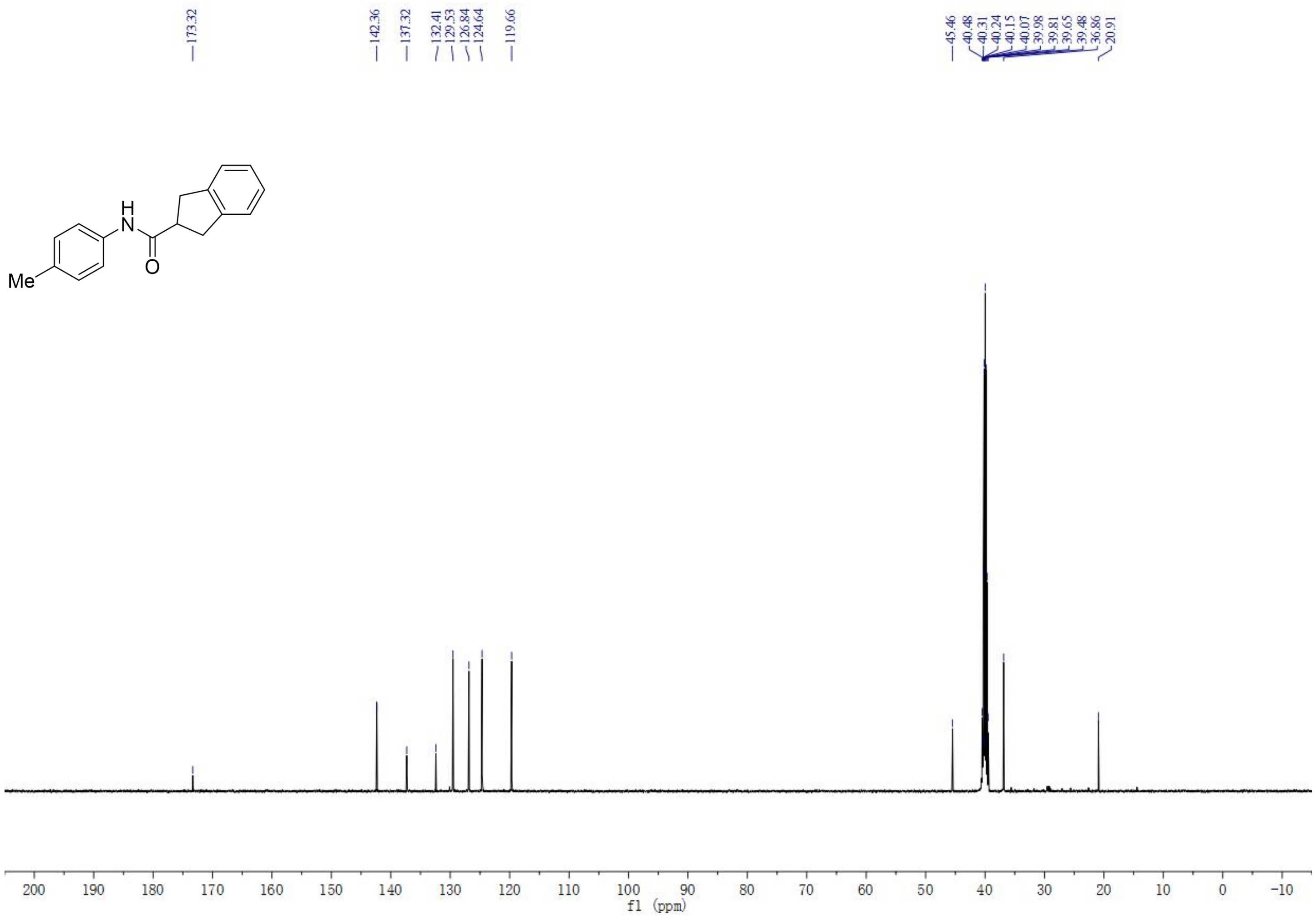


Figure S133. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydrofuran-3-carboxamide (**5aw**)

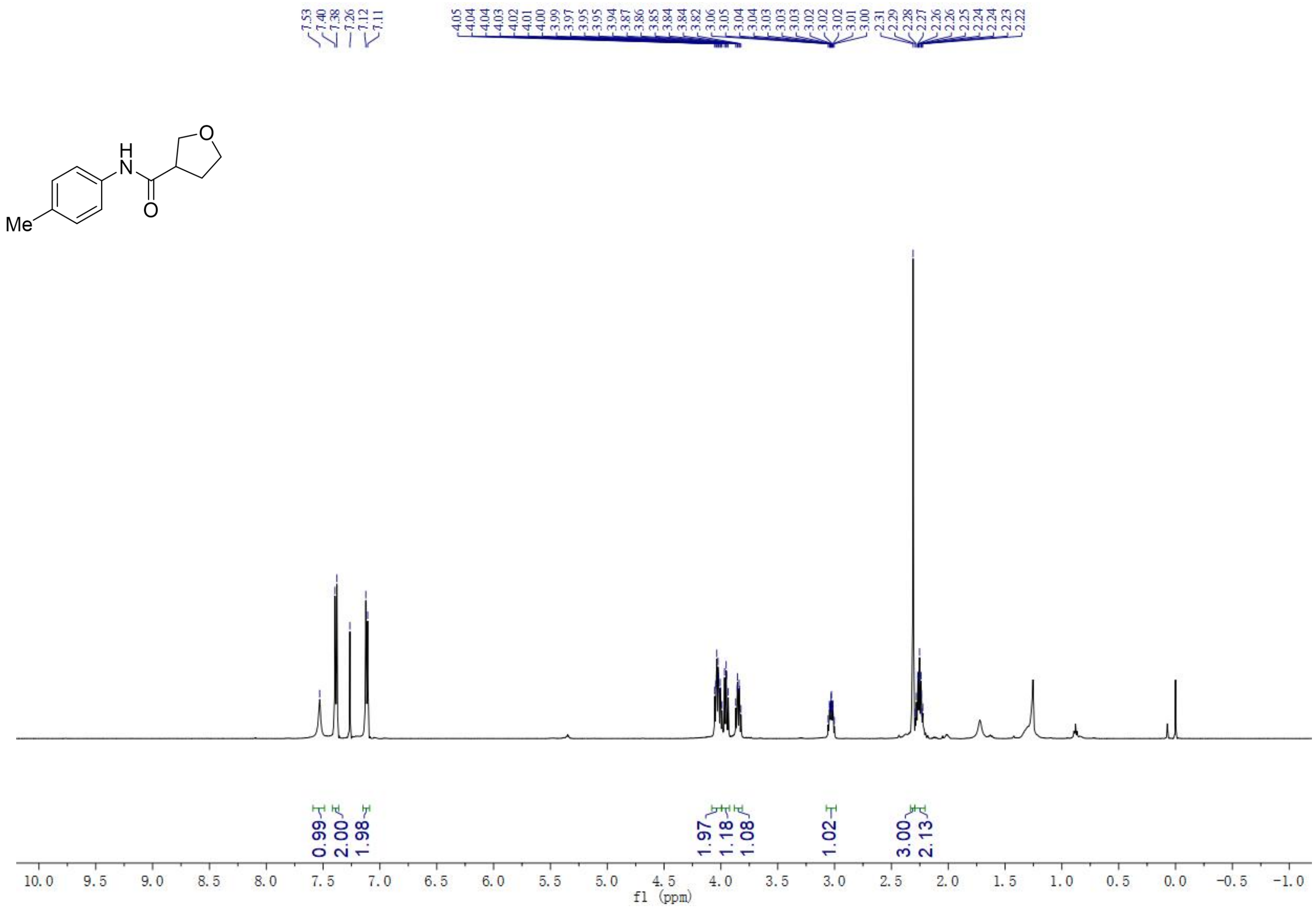


Figure S134. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydrofuran-3-carboxamide (**5aw**)

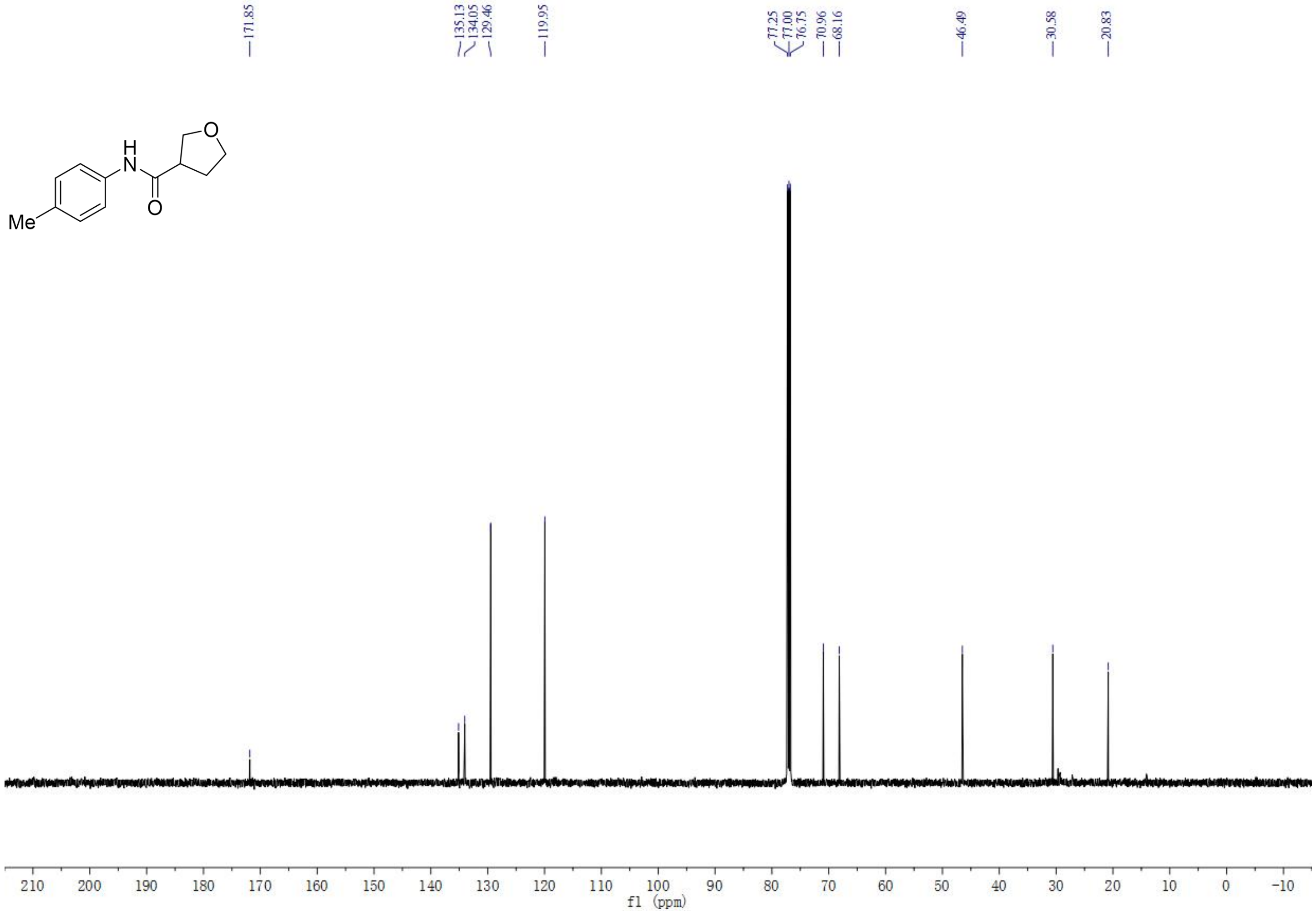


Figure S135. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydro-2*H*-pyran-4-carboxamide (**5ax**)

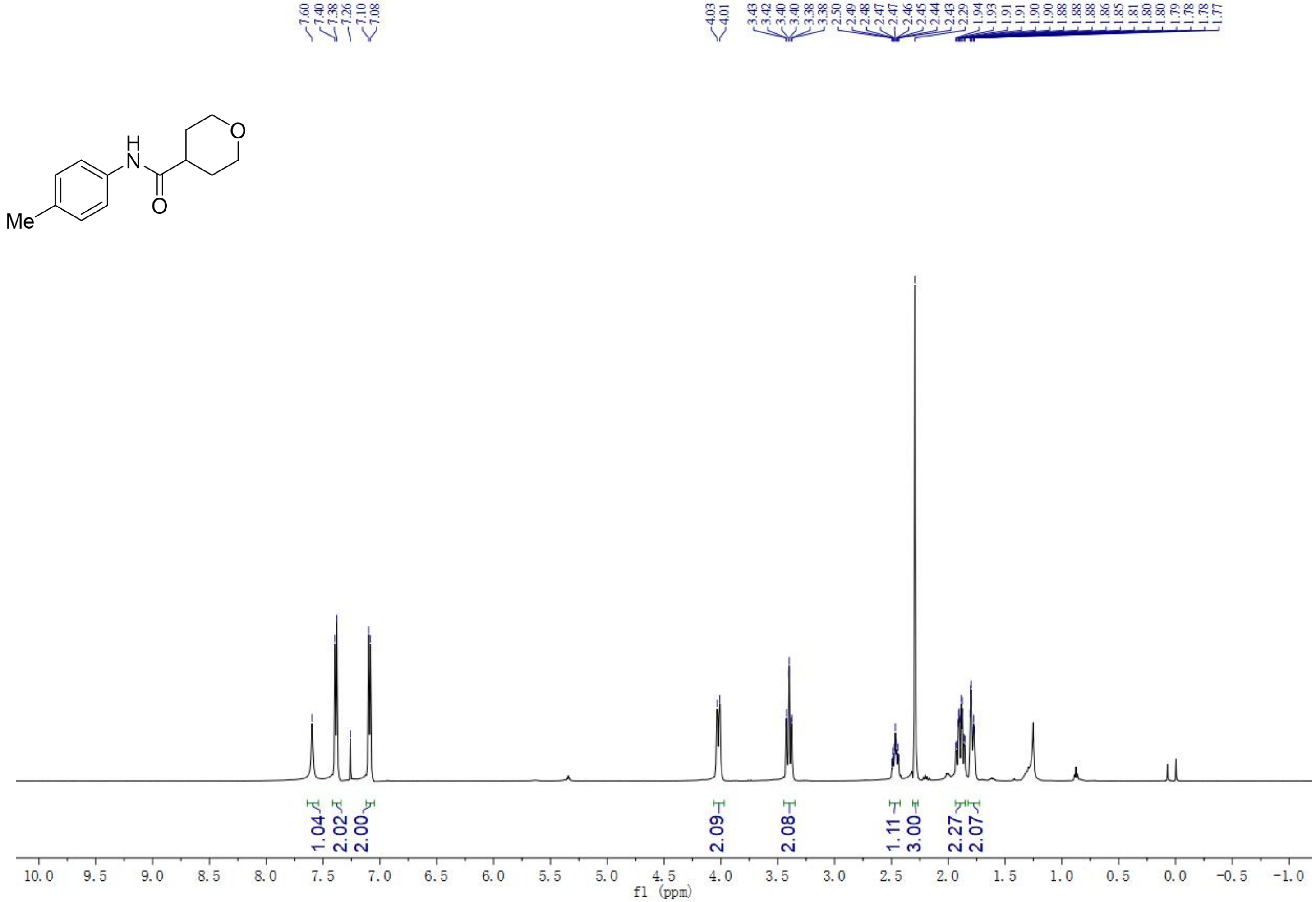
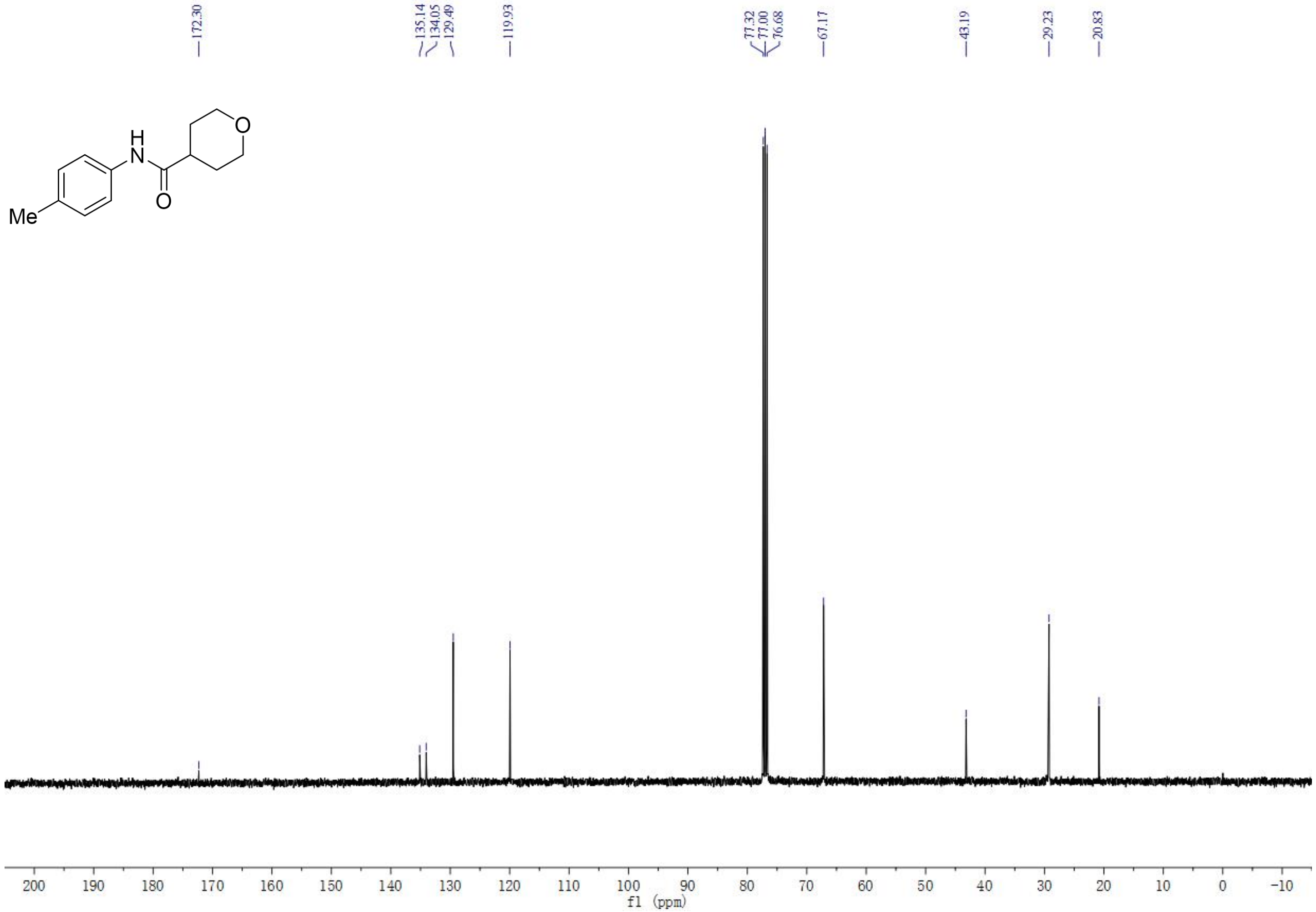
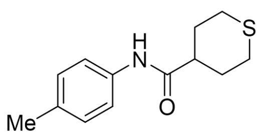


Figure S136. ^{13}C NMR (101 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydro-2*H*-pyran-4-carboxamide (**5ax**)



igure S137. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydro-2*H*-thiopyran-4-carboxamide (**5ay**)



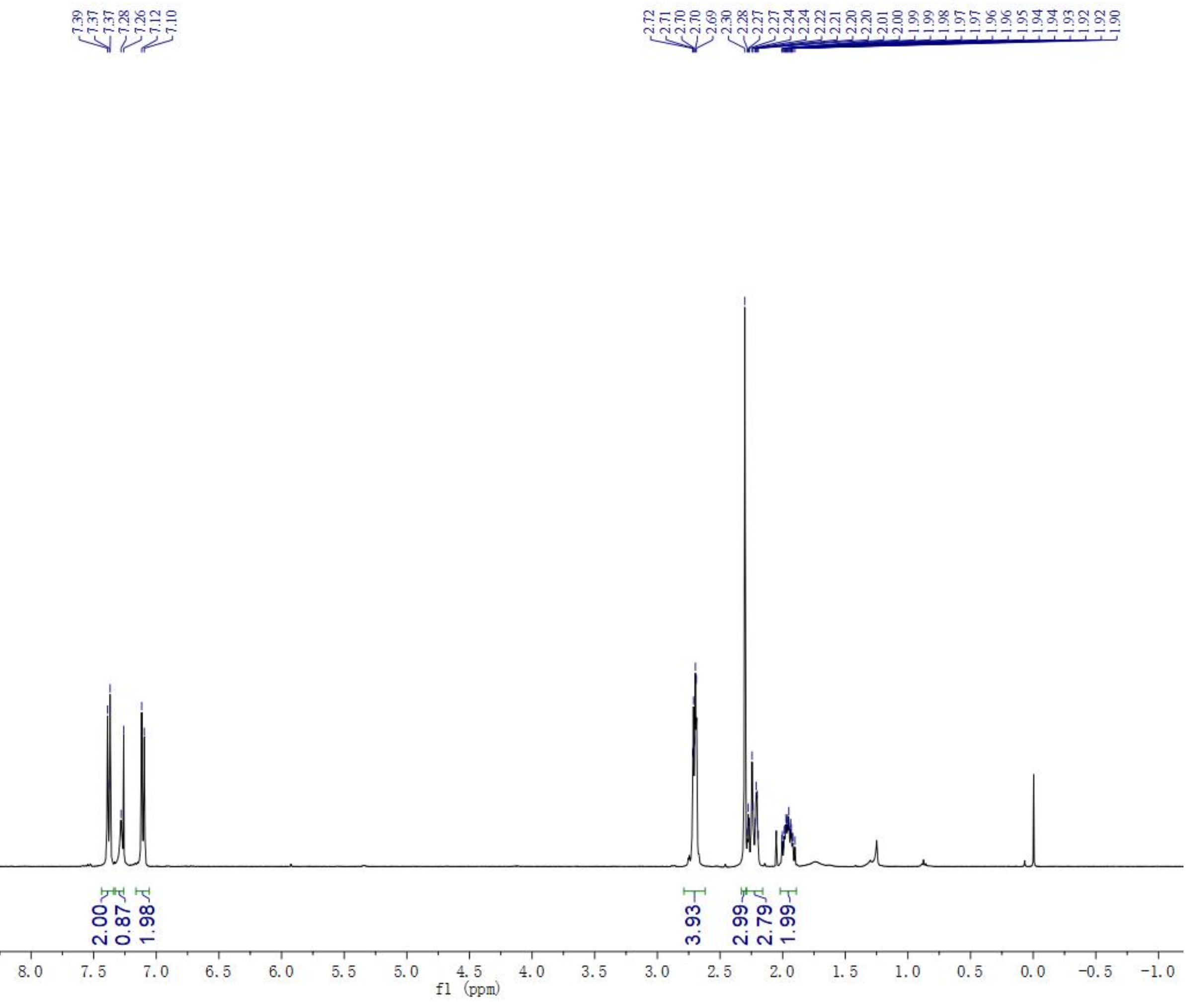


Figure S138. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)tetrahydro-2*H*-thiopyran-4-carboxamide (**5ay**)

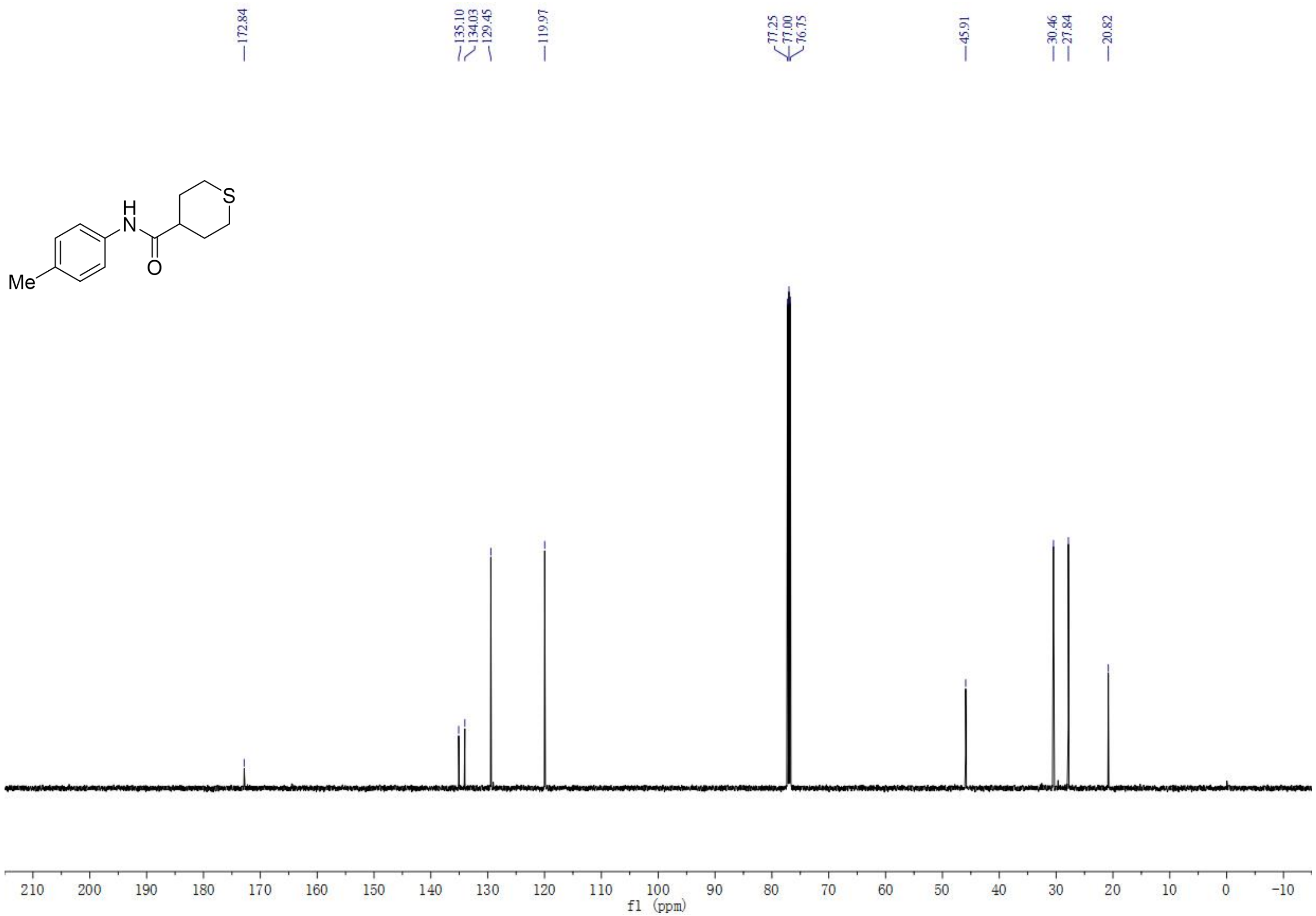


Figure S139. [1]H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 4-(*p*-tolylcarbamoyl)piperidine-1-carboxylate (**5az**)

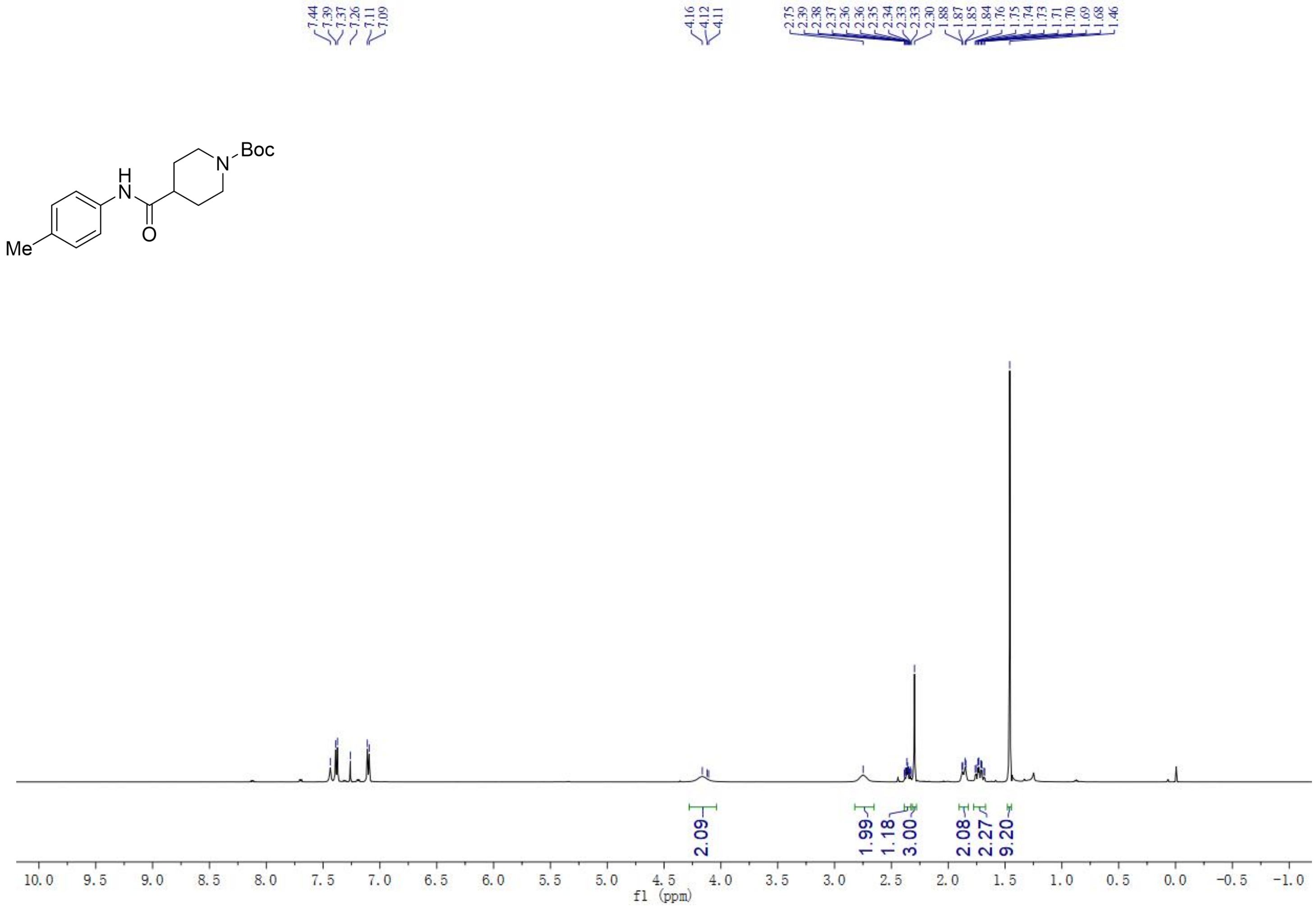


Figure S140. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 4-(*p*-tolylcarbamoyl)piperidine-1-carboxylate (**5az**)

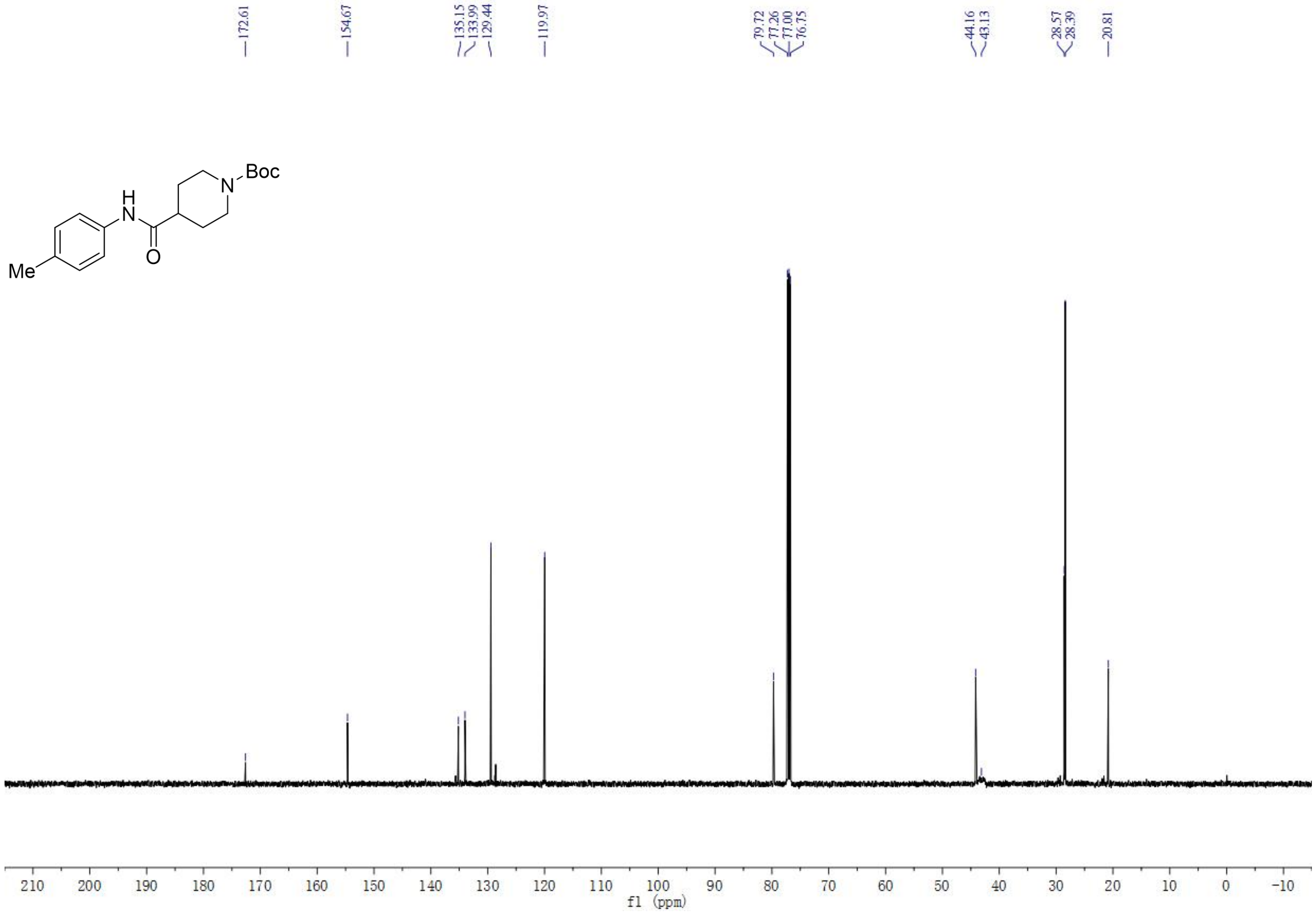


Figure S141. ¹H NMR (500 MHz, $CDCl_3$, 298K) of 4-oxo-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (**5ba**)

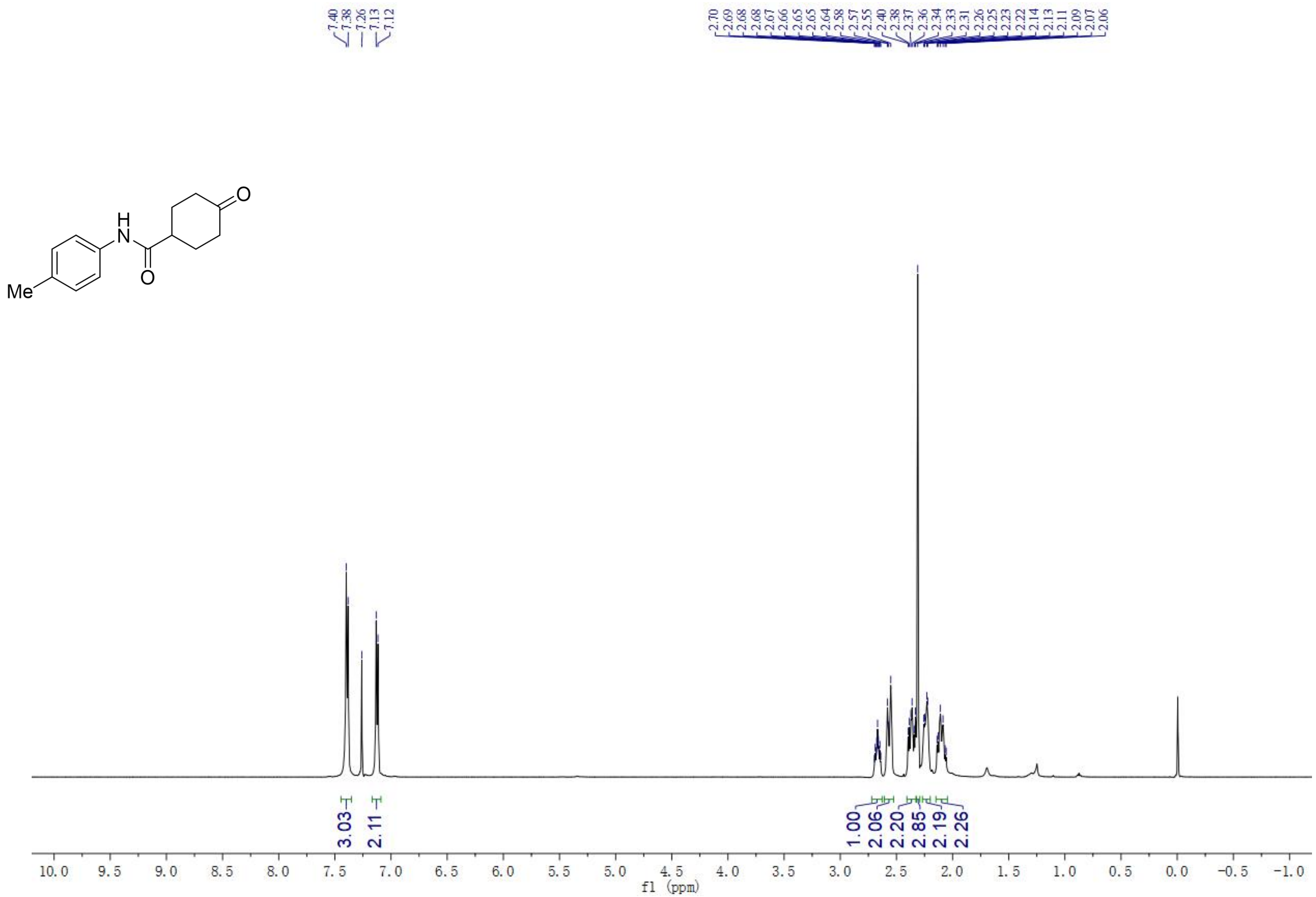


Figure S142. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-oxo-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (**5ba**)

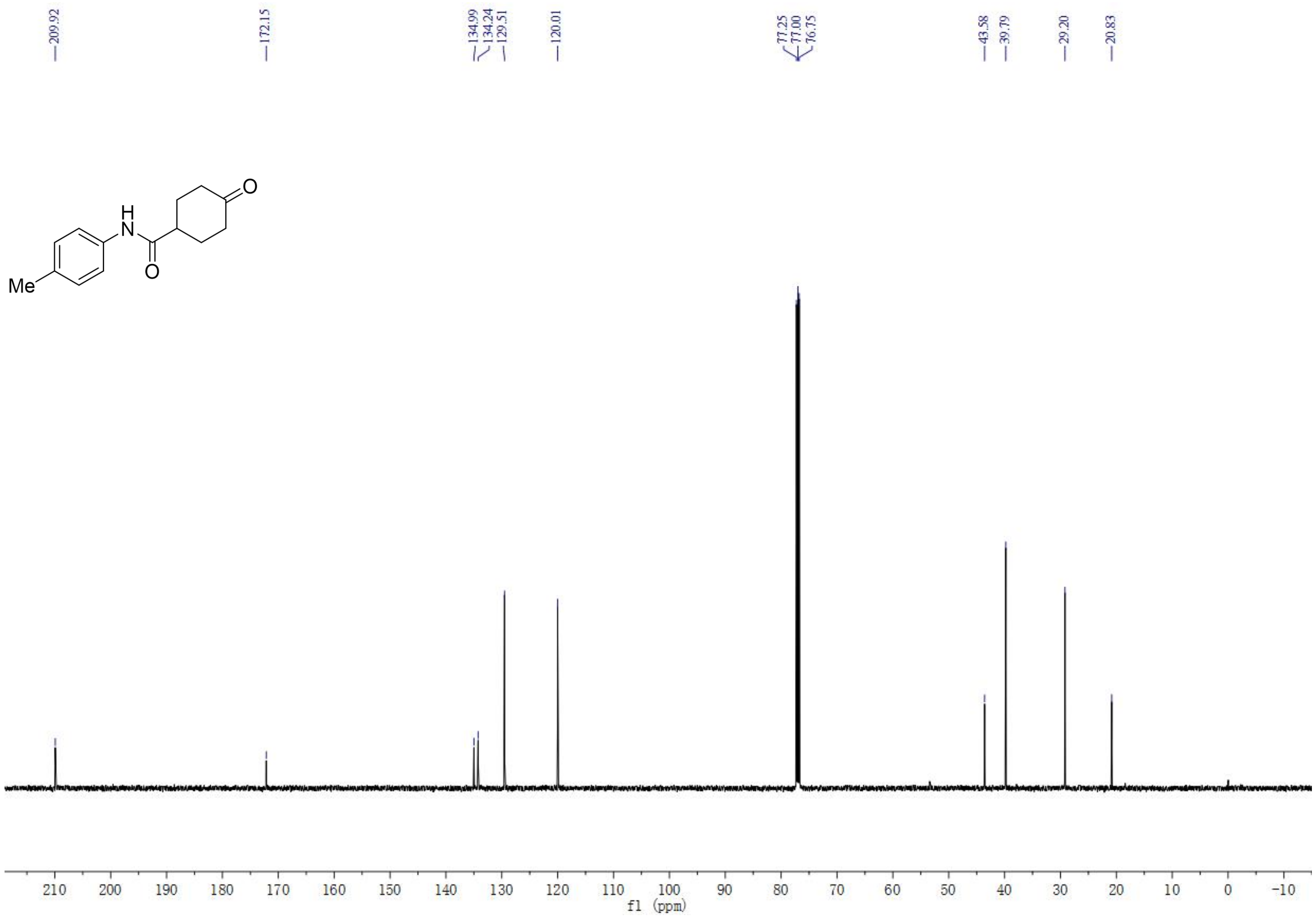


Figure S143. ^1H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)-1,4-dioxaspiro[4.5]decane-8-carboxamide (**5bb**)

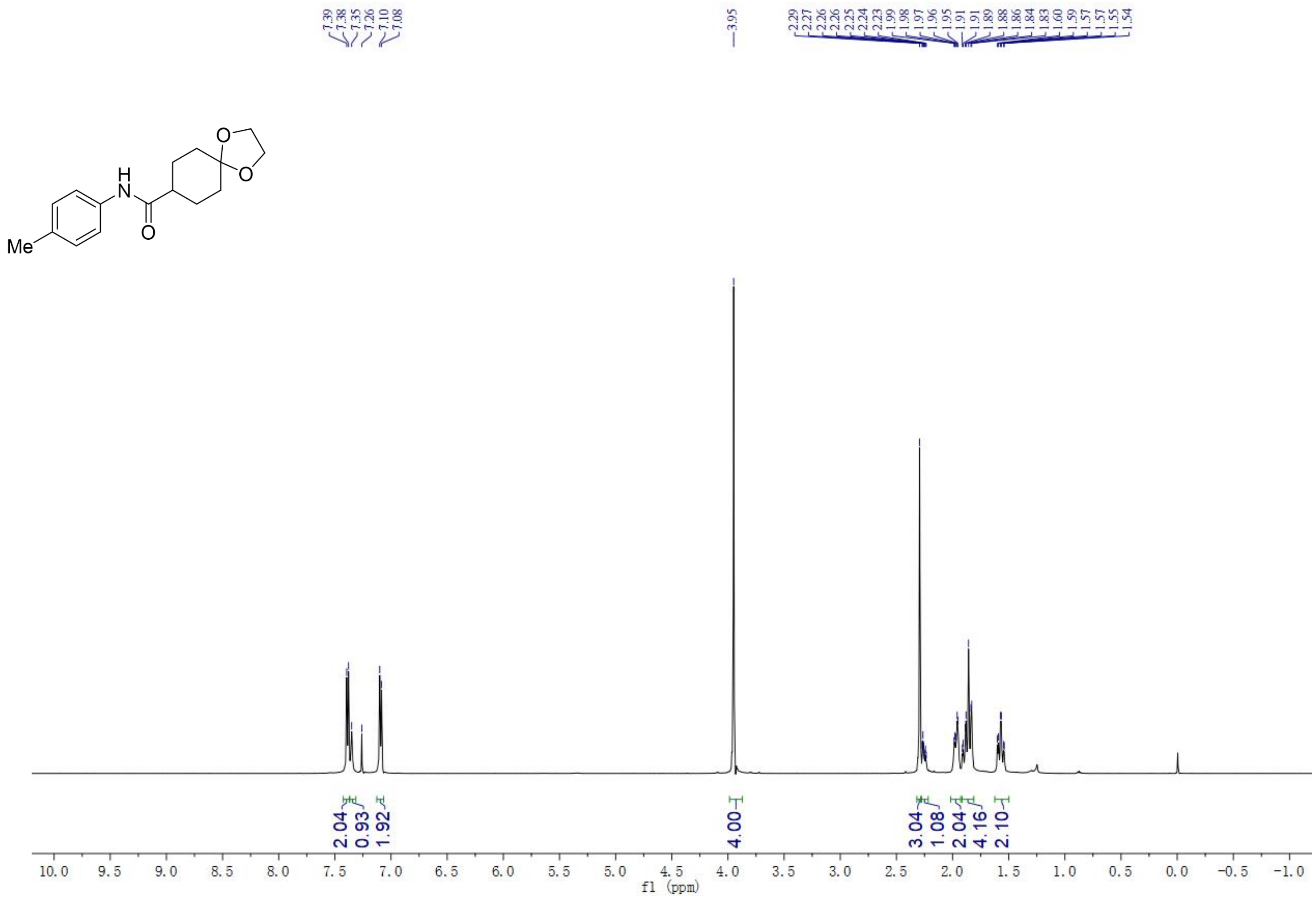


Figure S144. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)-1,4-dioxaspiro[4.5]decane-8-carboxamide (**5bb**)

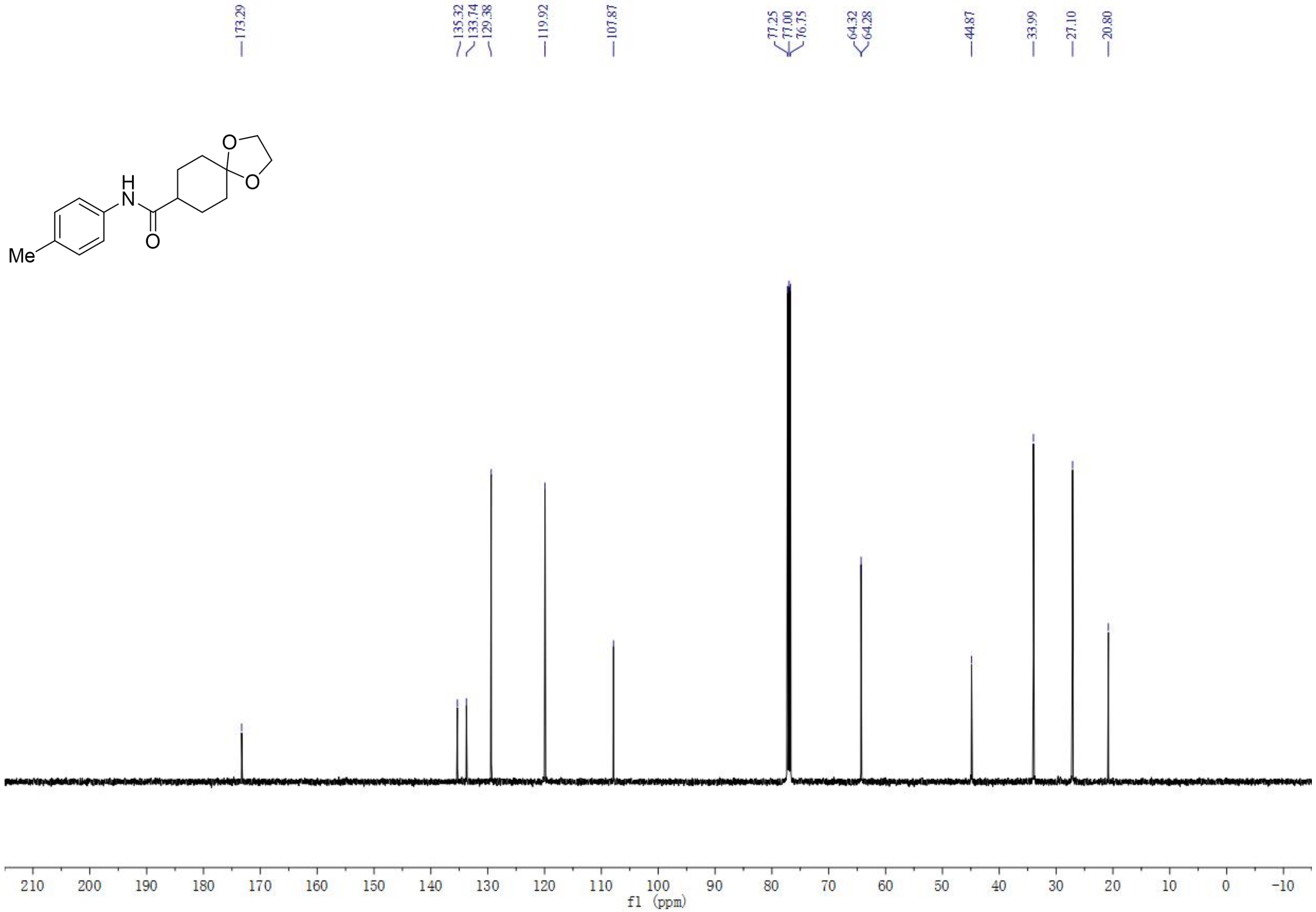
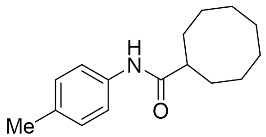


Figure S145. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)cyclooctanecarboxamide (**5bc**)



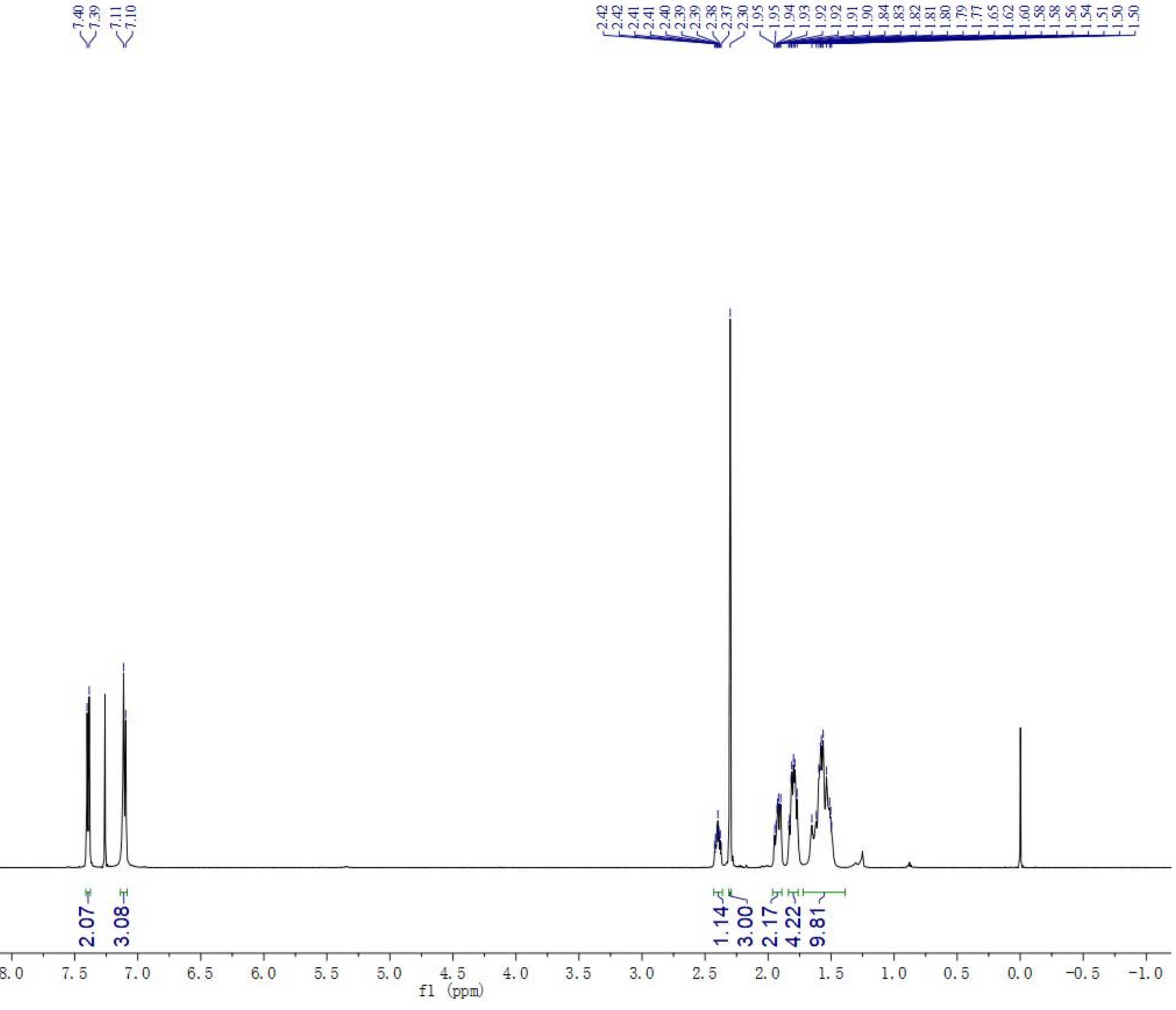


Figure S146. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)cyclooctanecarboxamide (**5bc**)

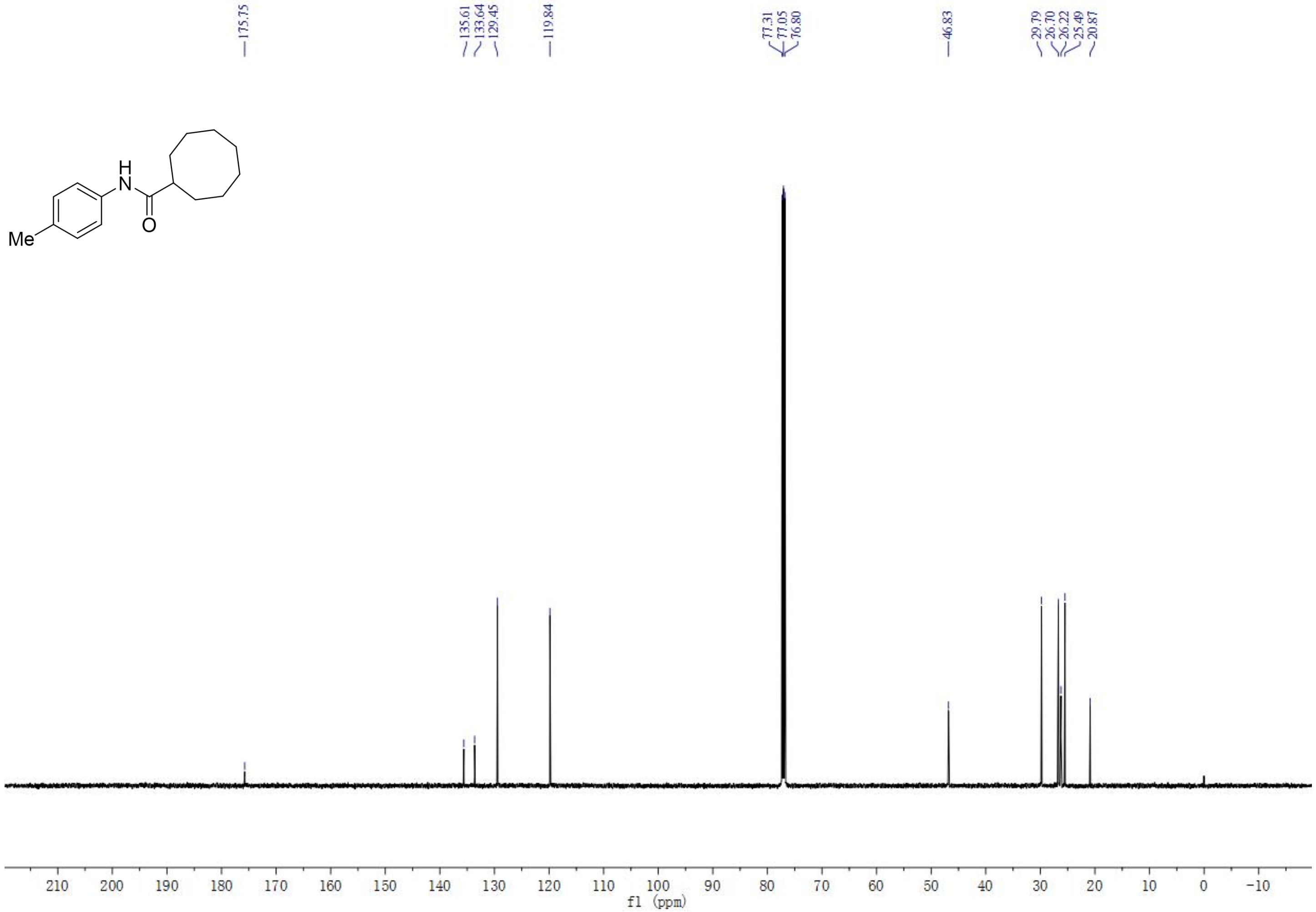


Figure S147. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 1-benzoyl-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5bd**)

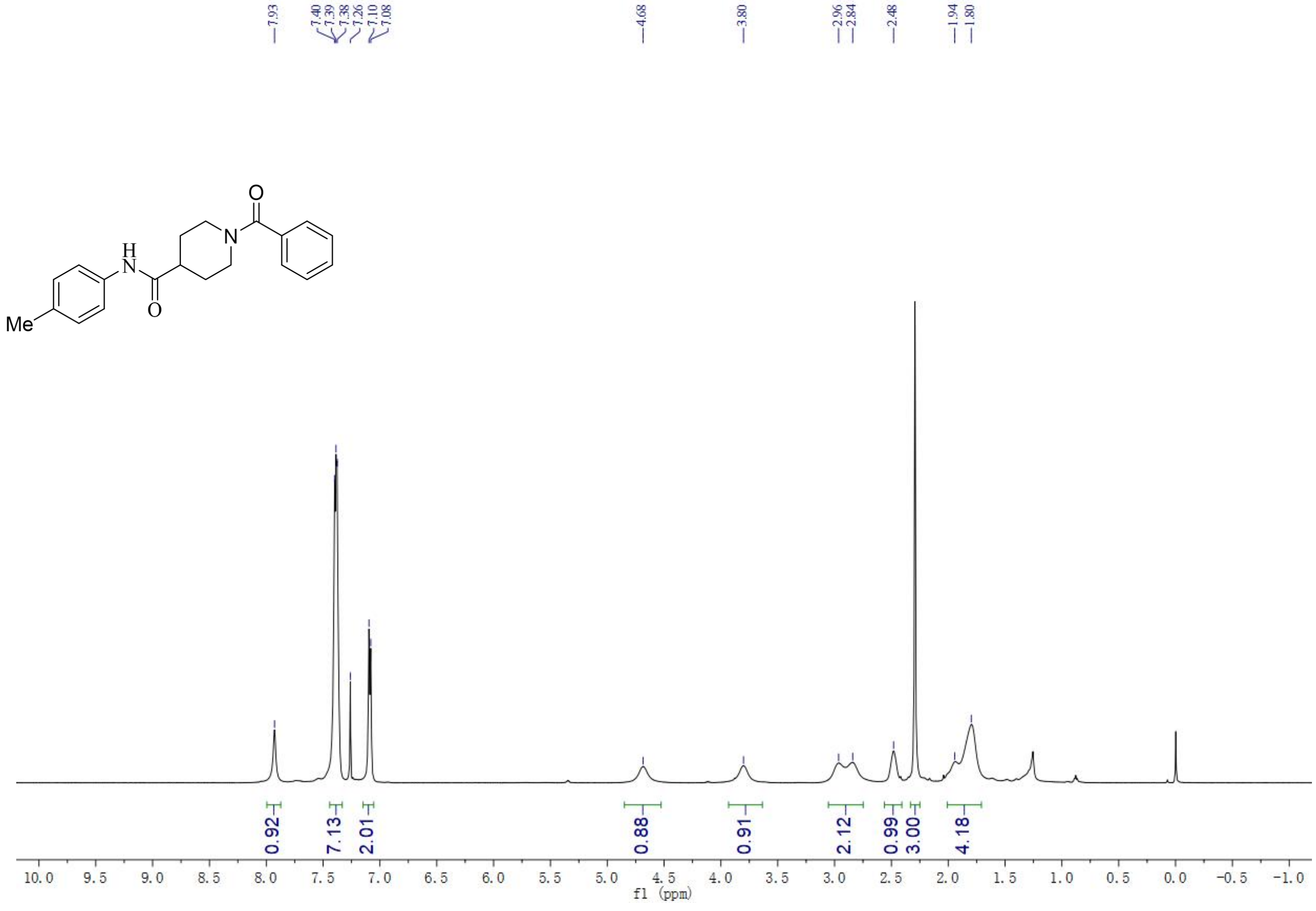


Figure S148. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 1-benzoyl-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5bd**)

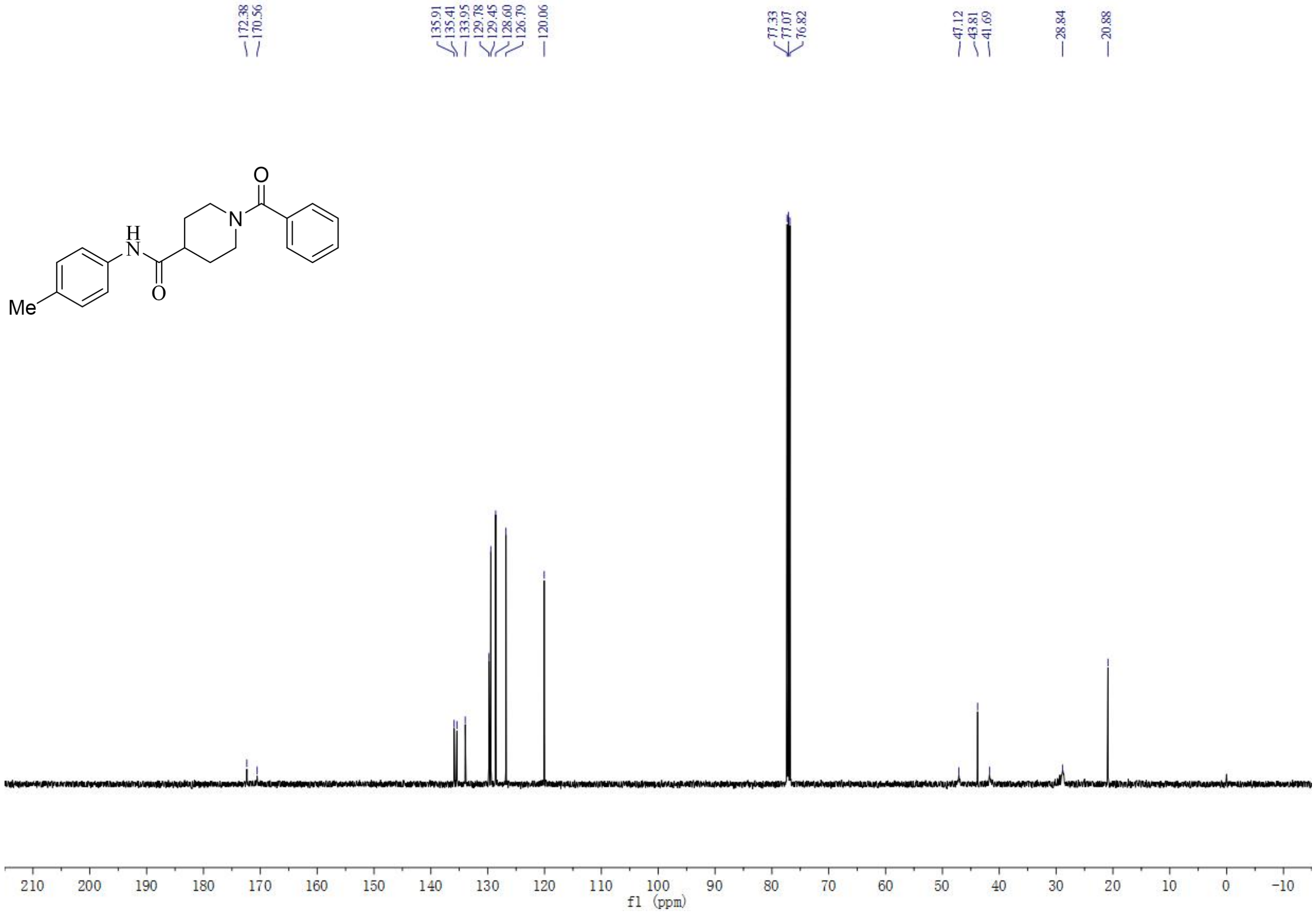


Figure S149. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of 1-(4-iodobenzoyl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5be**)

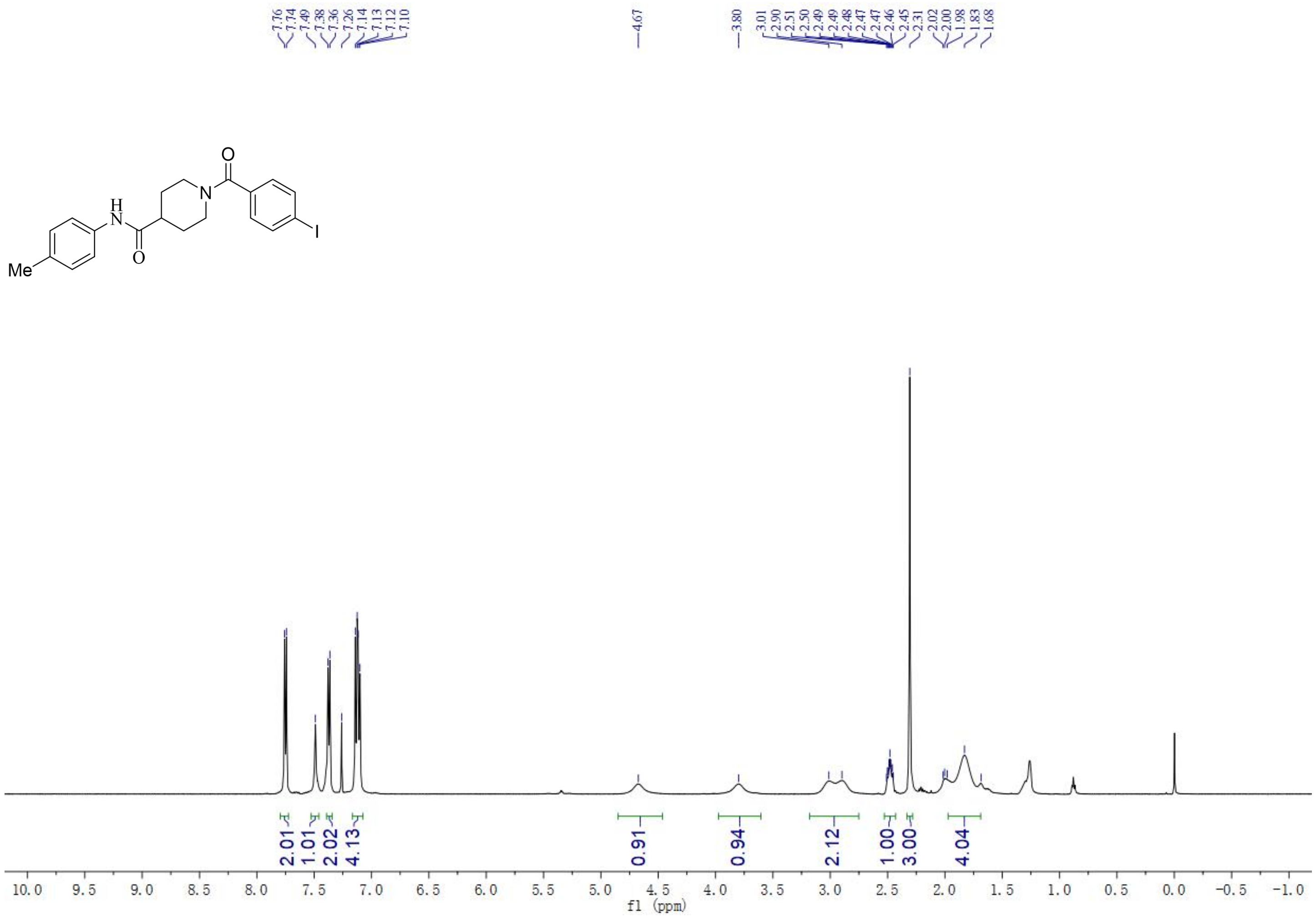


Figure S150. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 1-(4-iodobenzoyl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5be**)

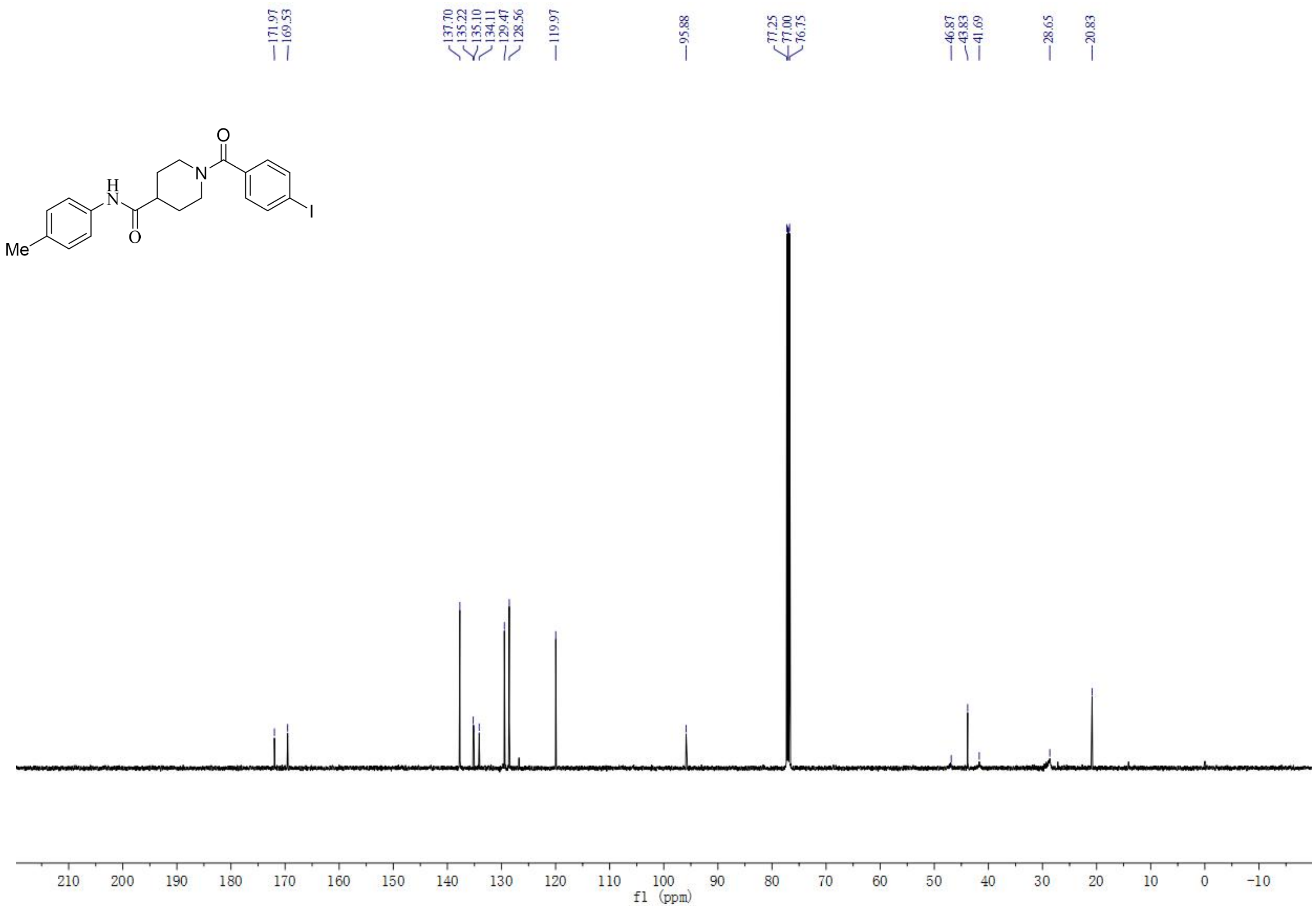
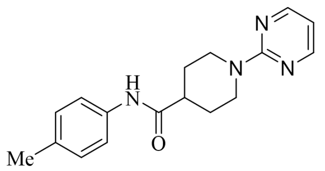


Figure S151. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 1-(pyrimidin-2-yl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5bf**)



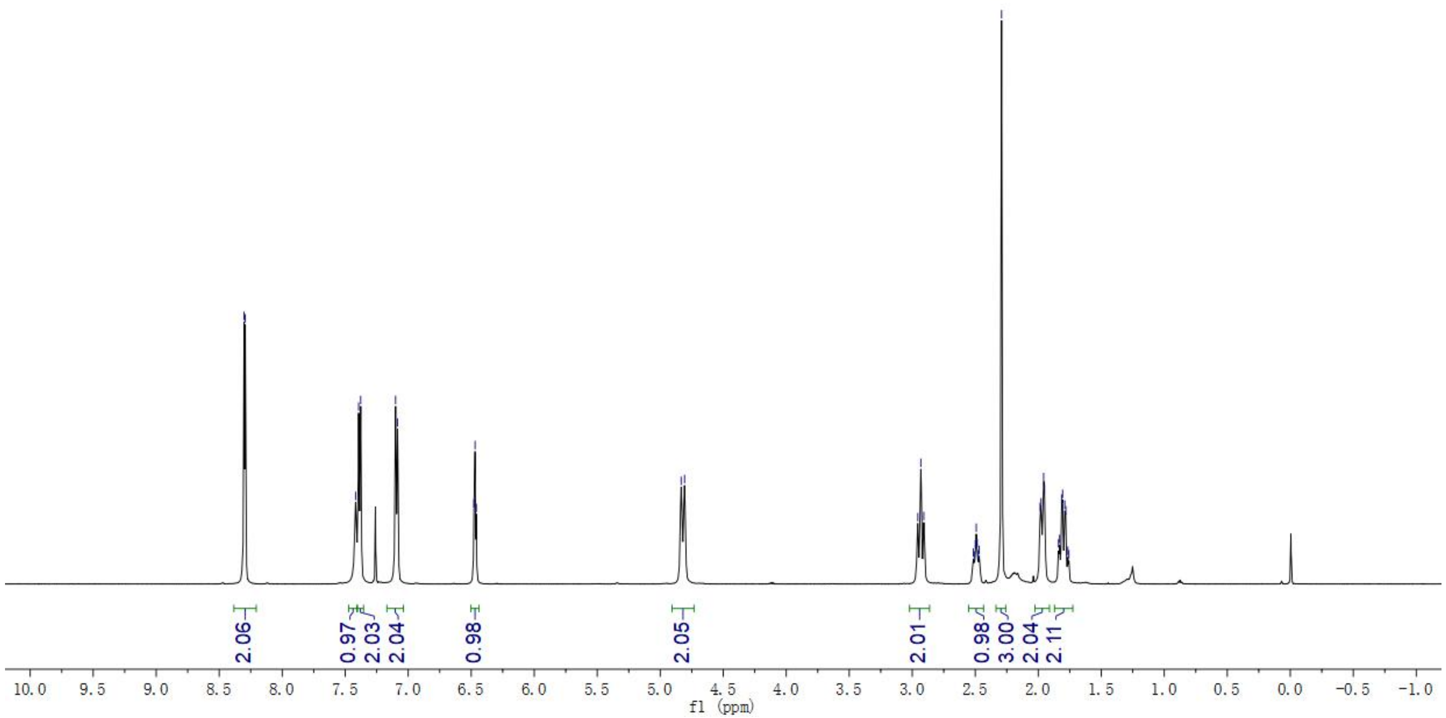


Figure S152. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 1-(pyrimidin-2-yl)-*N*-(*p*-tolyl)piperidine-4-carboxamide (**5bf**)

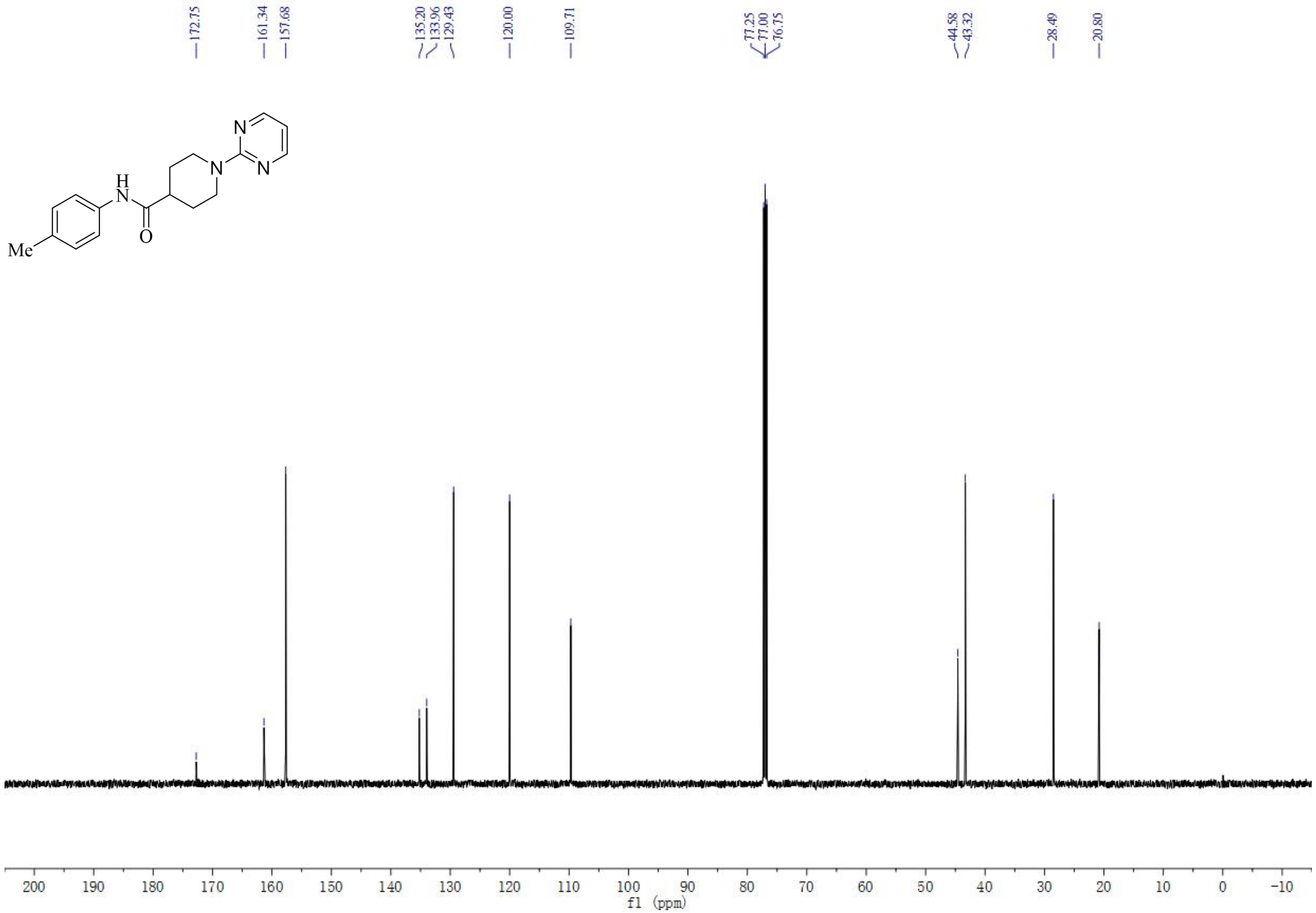
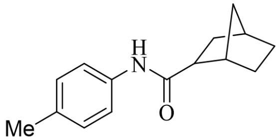


Figure S153. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of (1*S*,4*R*)-*N*-(*p*-tolyl)bicyclo[2.2.1]heptane-2-carboxamide (**5bg**)



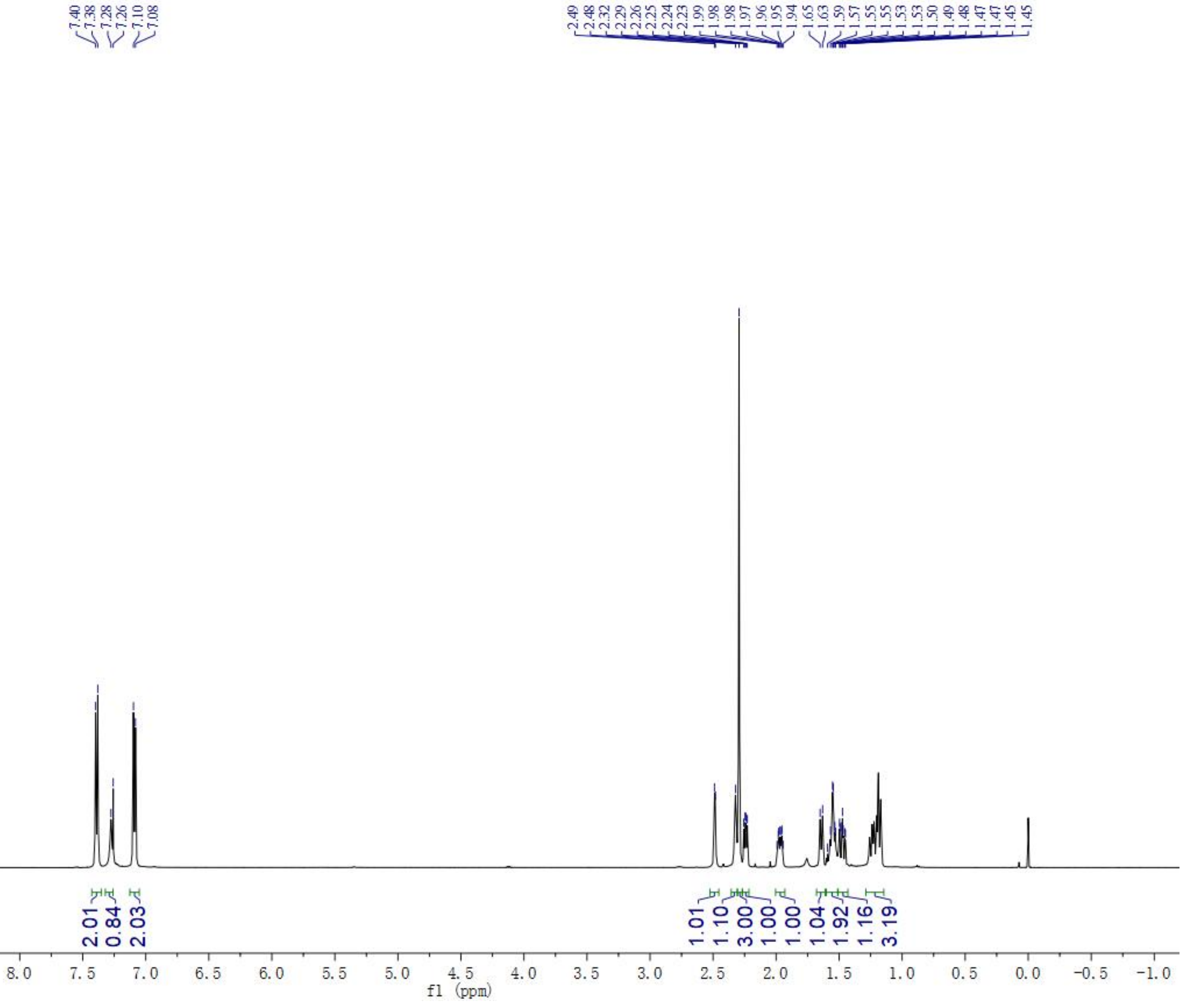


Figure S154. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of (1*S*,4*R*)-*N*-(*p*-tolyl)bicyclo[2.2.1]heptane-2-carboxamide (**5bg**)

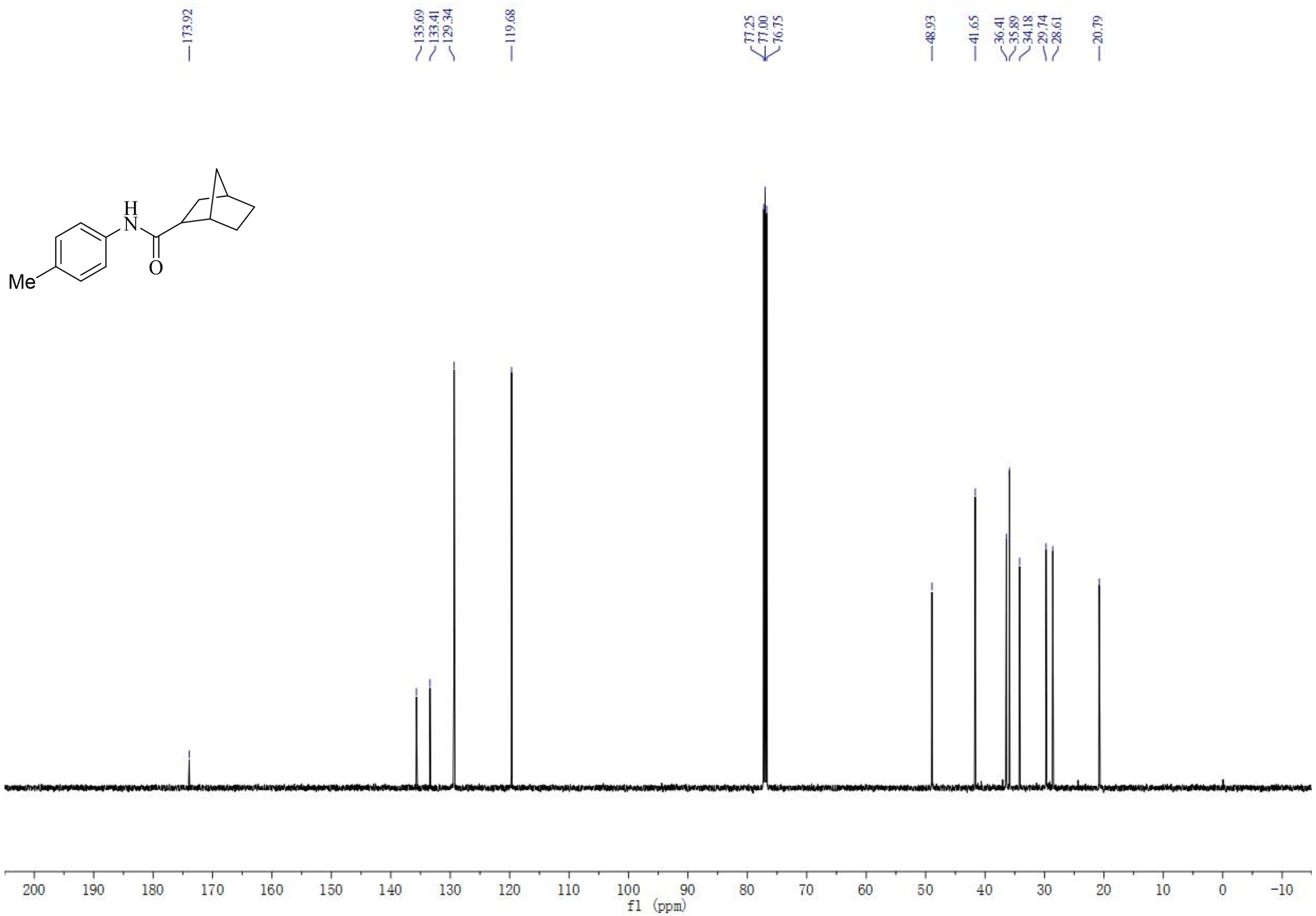


Figure S155. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl (1*R*,3s,5*S*)-3-(*p*-tolylcarbamoyl)-8-azabicyclo[3.2.1]octane-8-carboxylate (**5bh**)

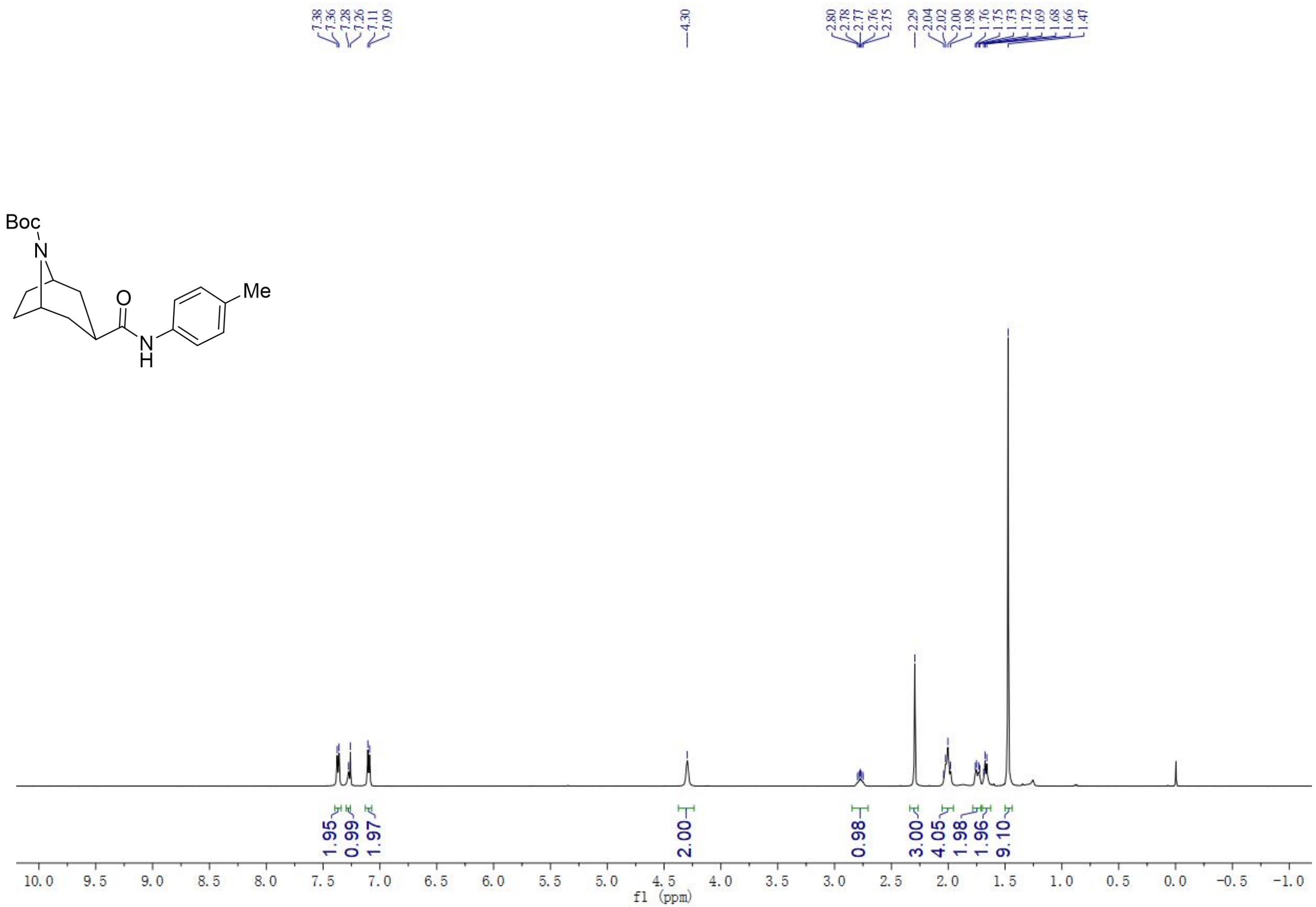


Figure S156. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl (1*R*,3s,5*S*)-3-(*p*-tolylcarbamoyl)-8-azabicyclo[3.2.1]octane-8-carboxylate (**5bh**)

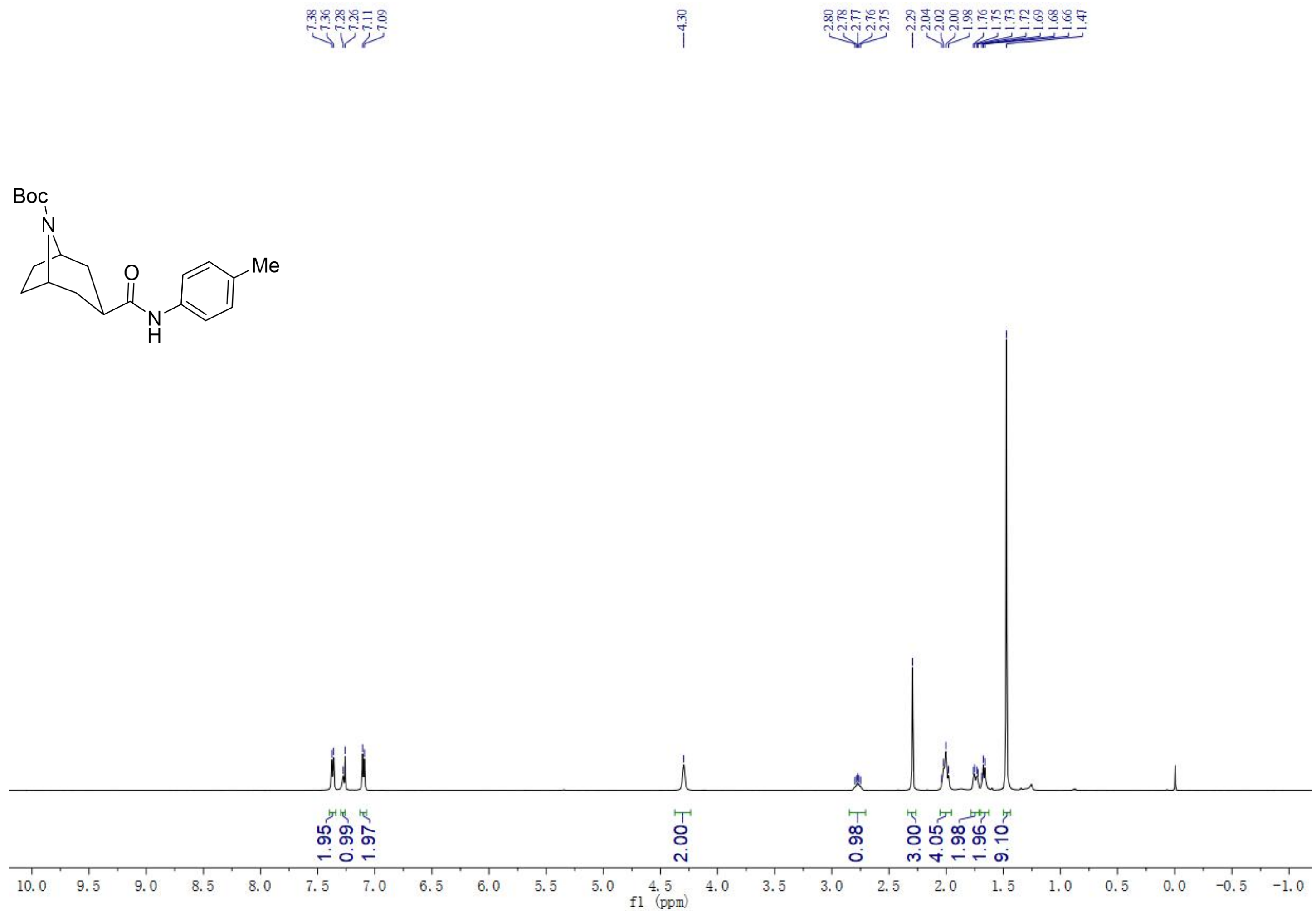


Figure S157. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-oxo-*N*-(*p*-tolyl)hexahydro-2*H*-3,5-methanocyclopenta[b]furan-6-carboxamide (**5bi**)

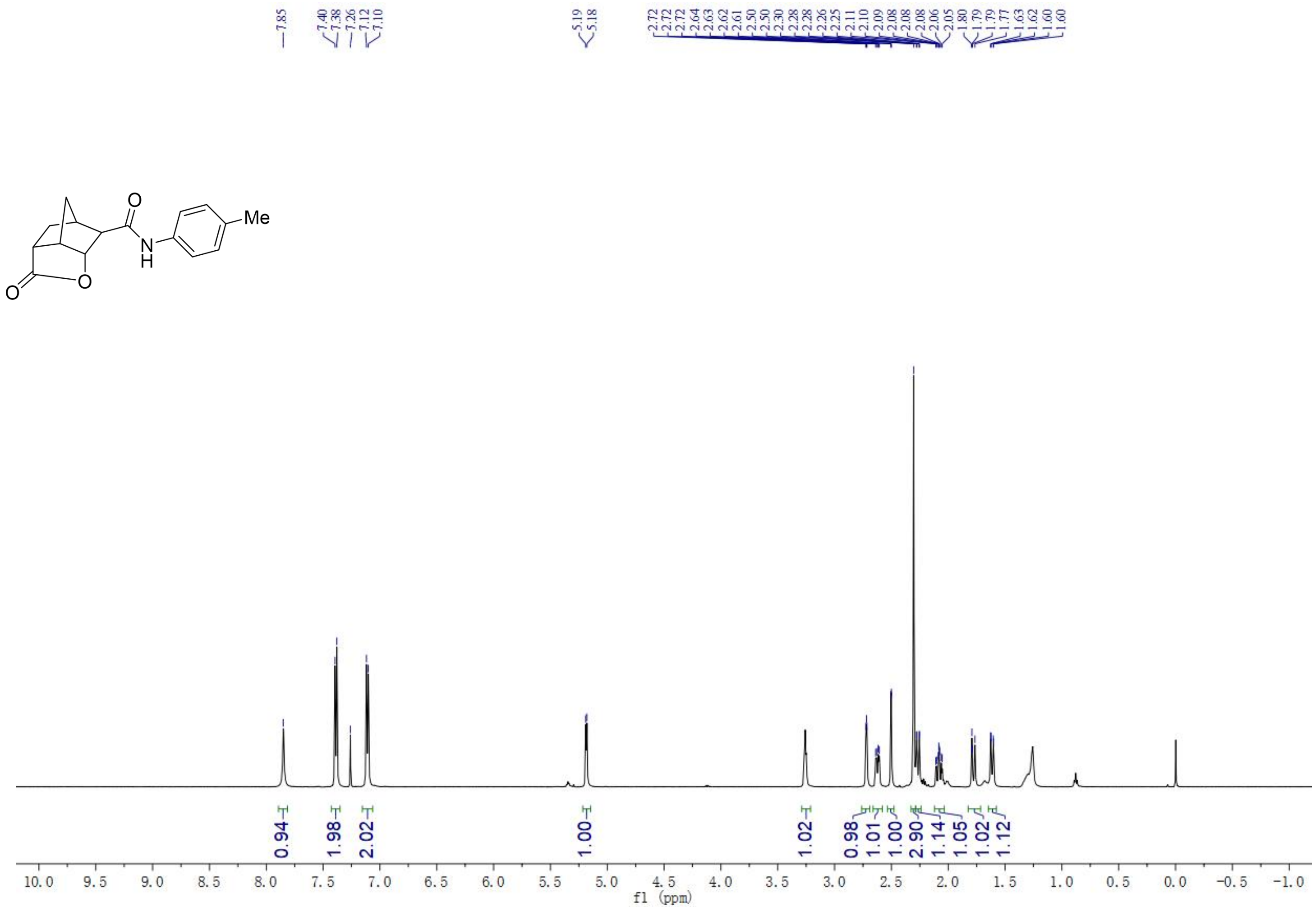


Figure S158. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 2-oxo-*N*-(*p*-tolyl)hexahydro-2*H*-3,5-methanocyclopenta[b]furan-6-carboxamide (**5bi**)

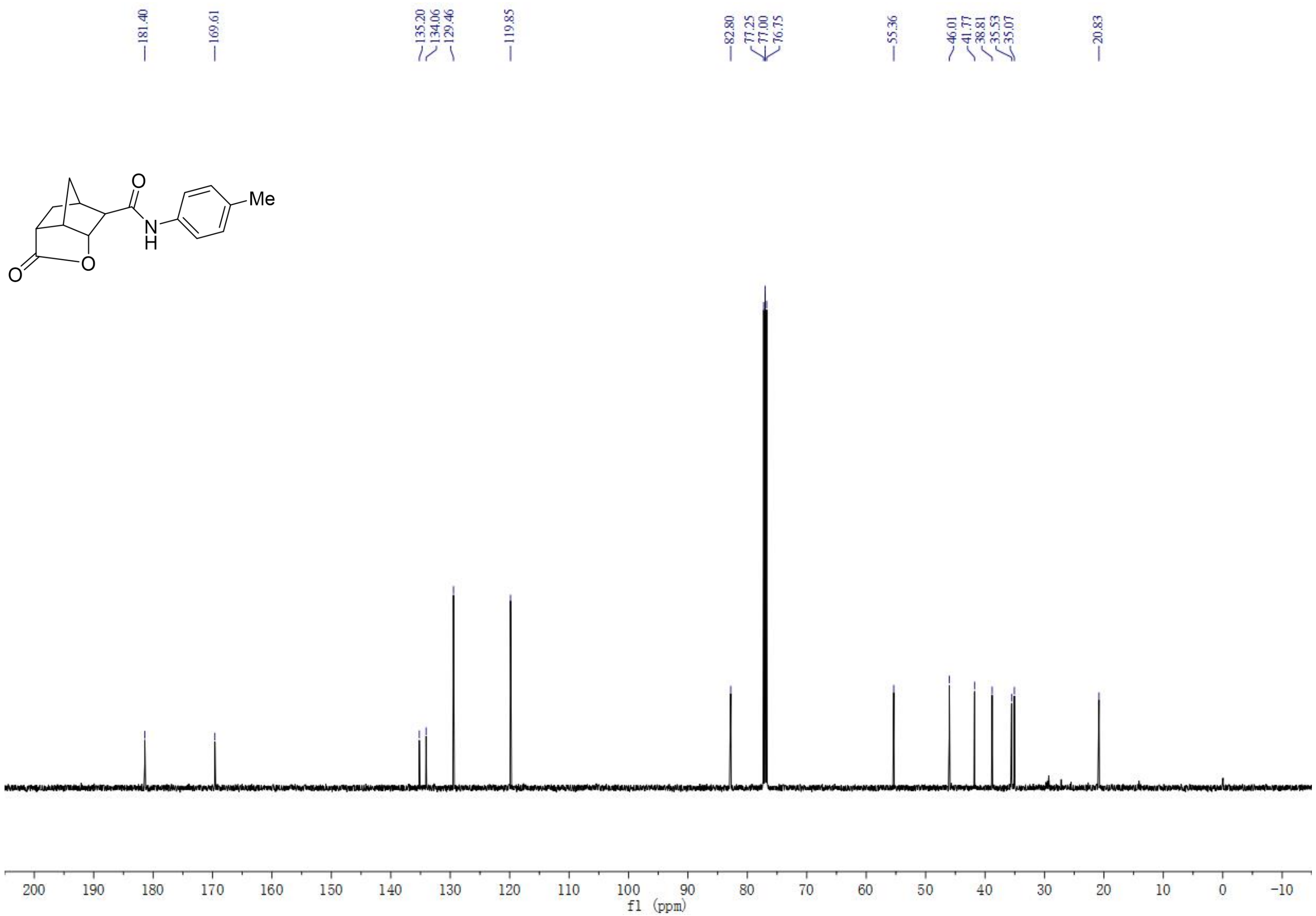


Figure S159. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of methyl 6-(*p*-tolylcarbamoyl)spiro[3.3]heptane-2-carboxylate (**5bj**)

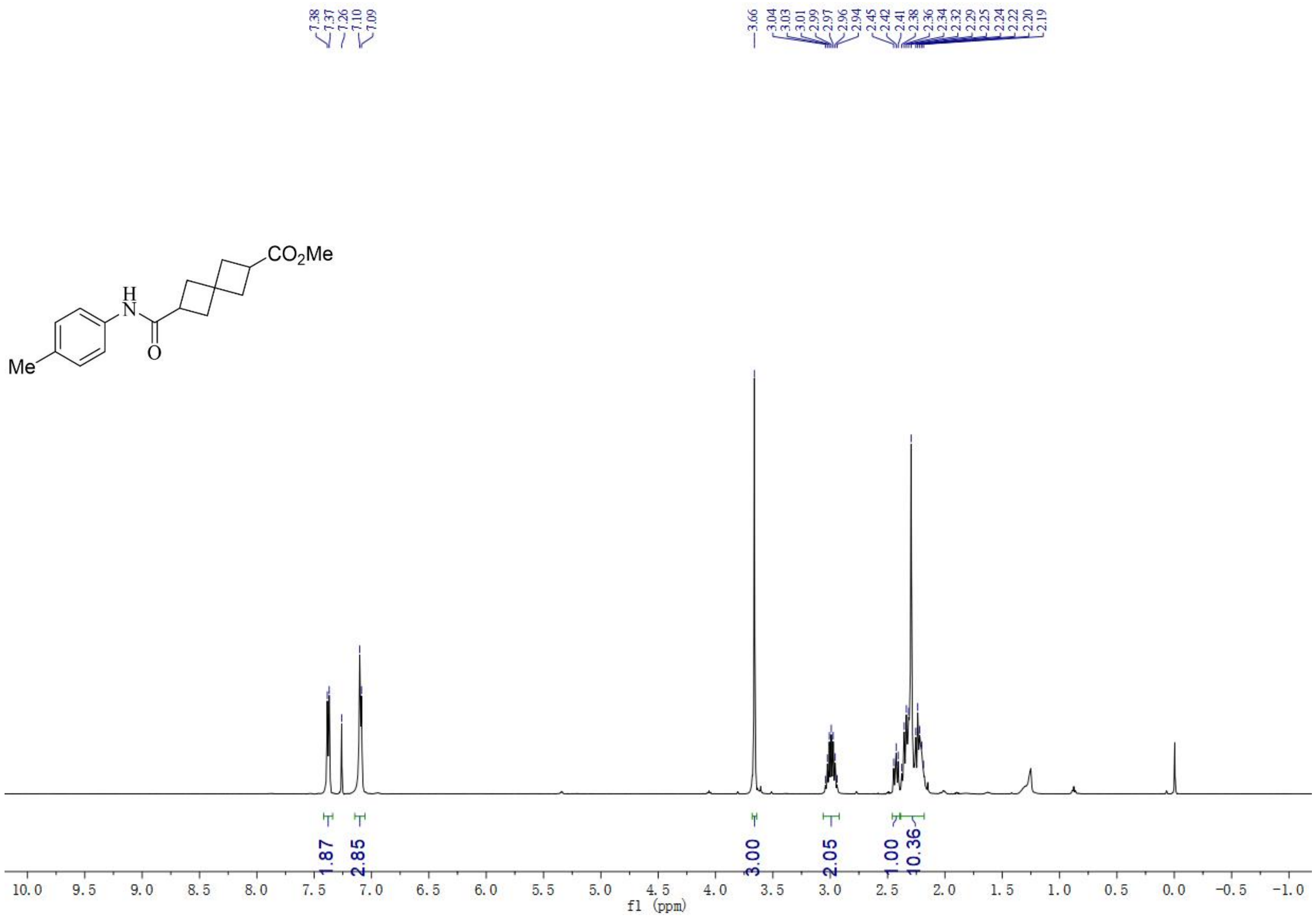


Figure S160. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of methyl 6-(*p*-tolylcarbamoyl)spiro[3.3]heptane-2-carboxylate (**5bj**)

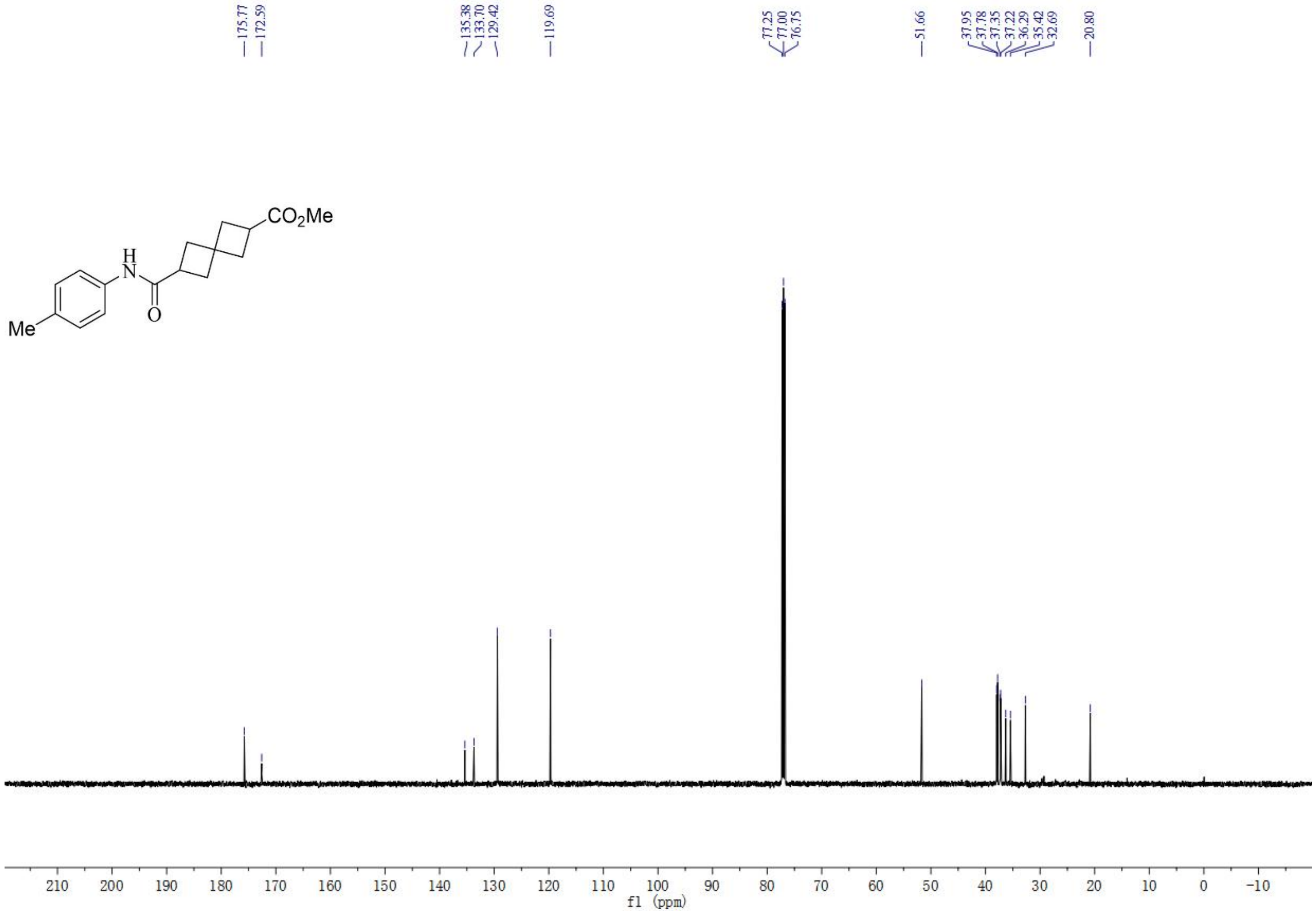


Figure S161. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 6-(*p*-tolylcarbamoyl)-2-azaspiro[3.3]heptane-2-carboxylate (**5bk**)

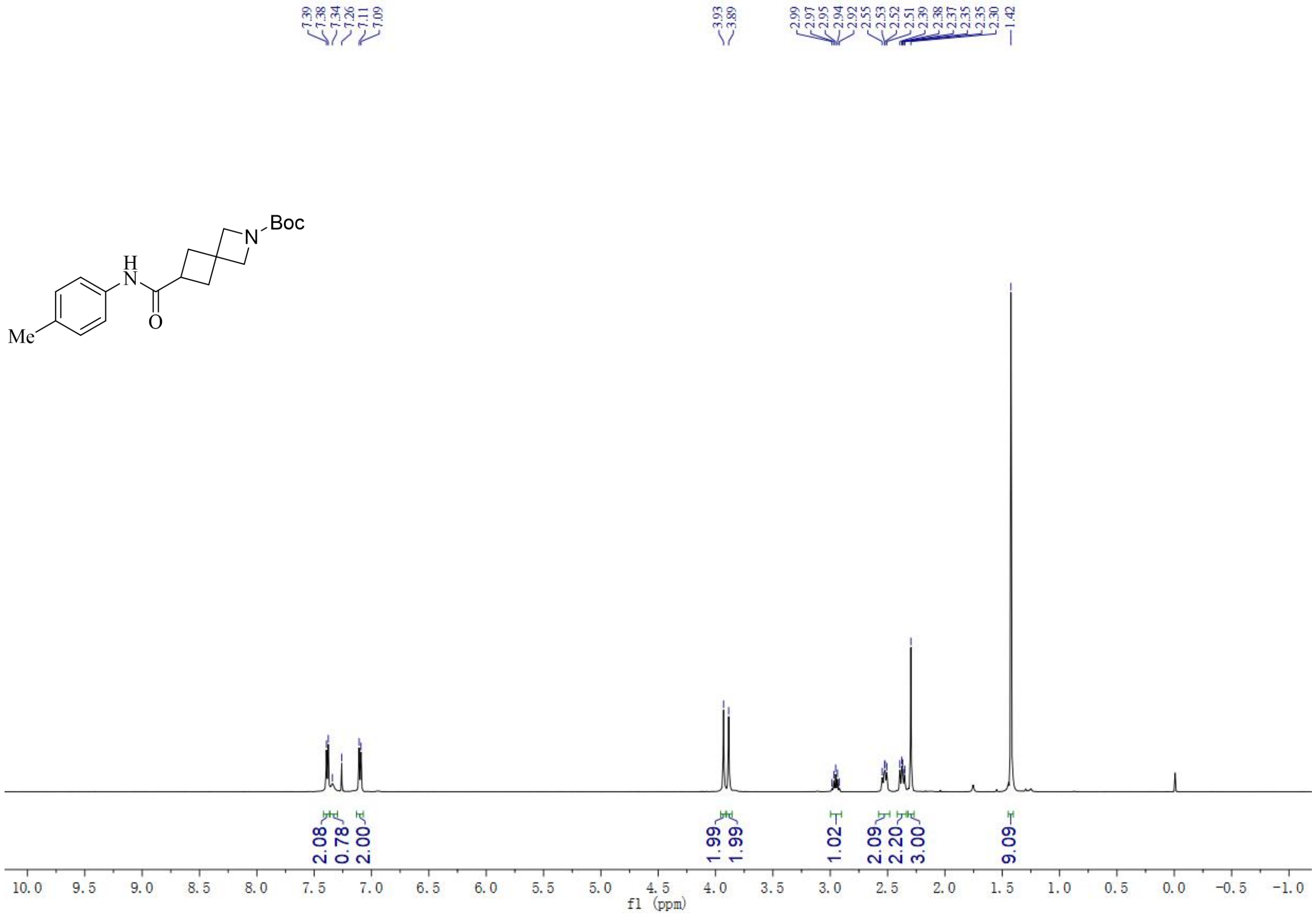


Figure S162. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 6-(*p*-tolylcarbamoyl)-2-azaspiro[3.3]heptane-2-carboxylate (**5bk**)

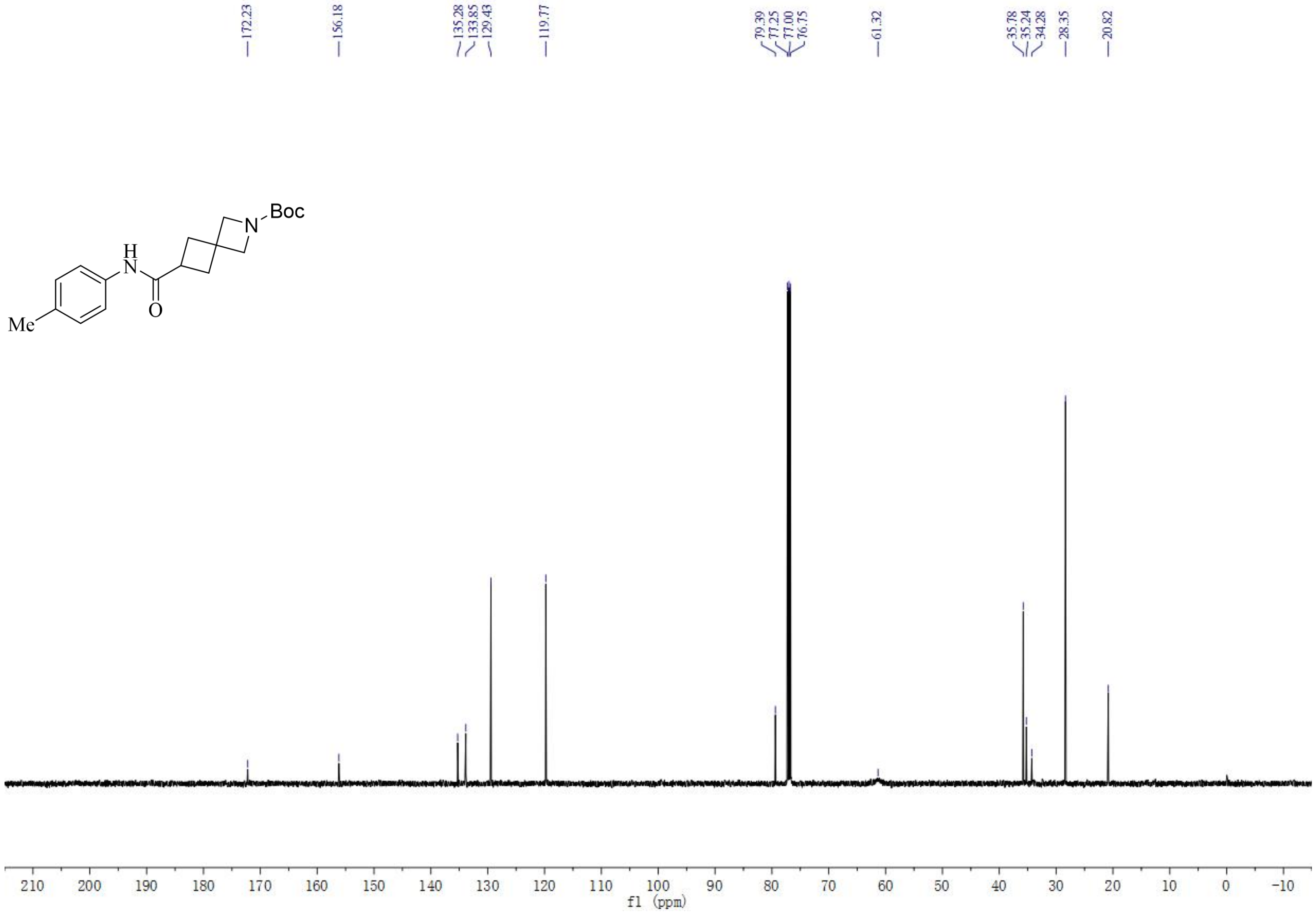


Figure S163. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**5bl**)

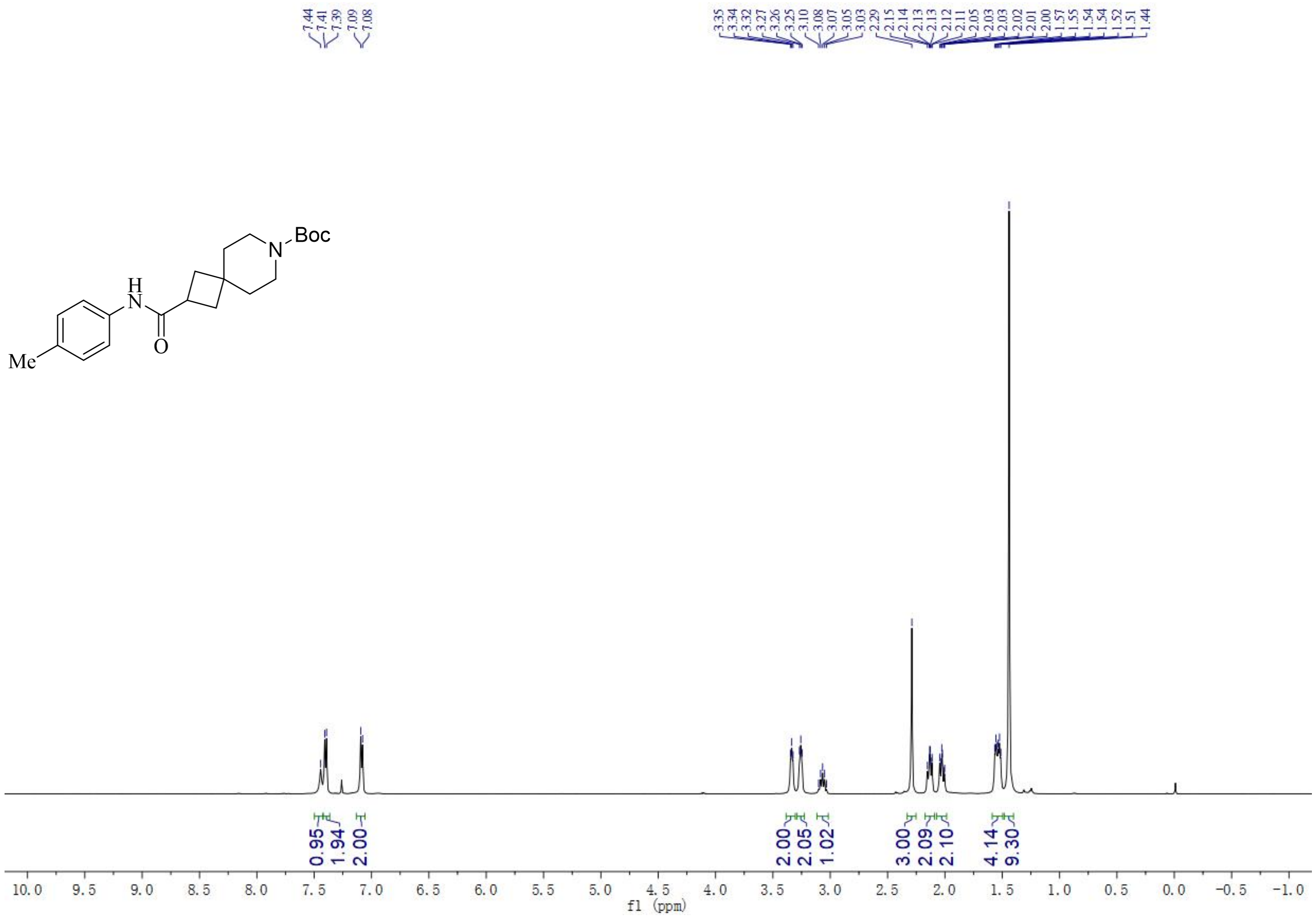


Figure S164. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-(*p*-tolylcarbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**5bl**)

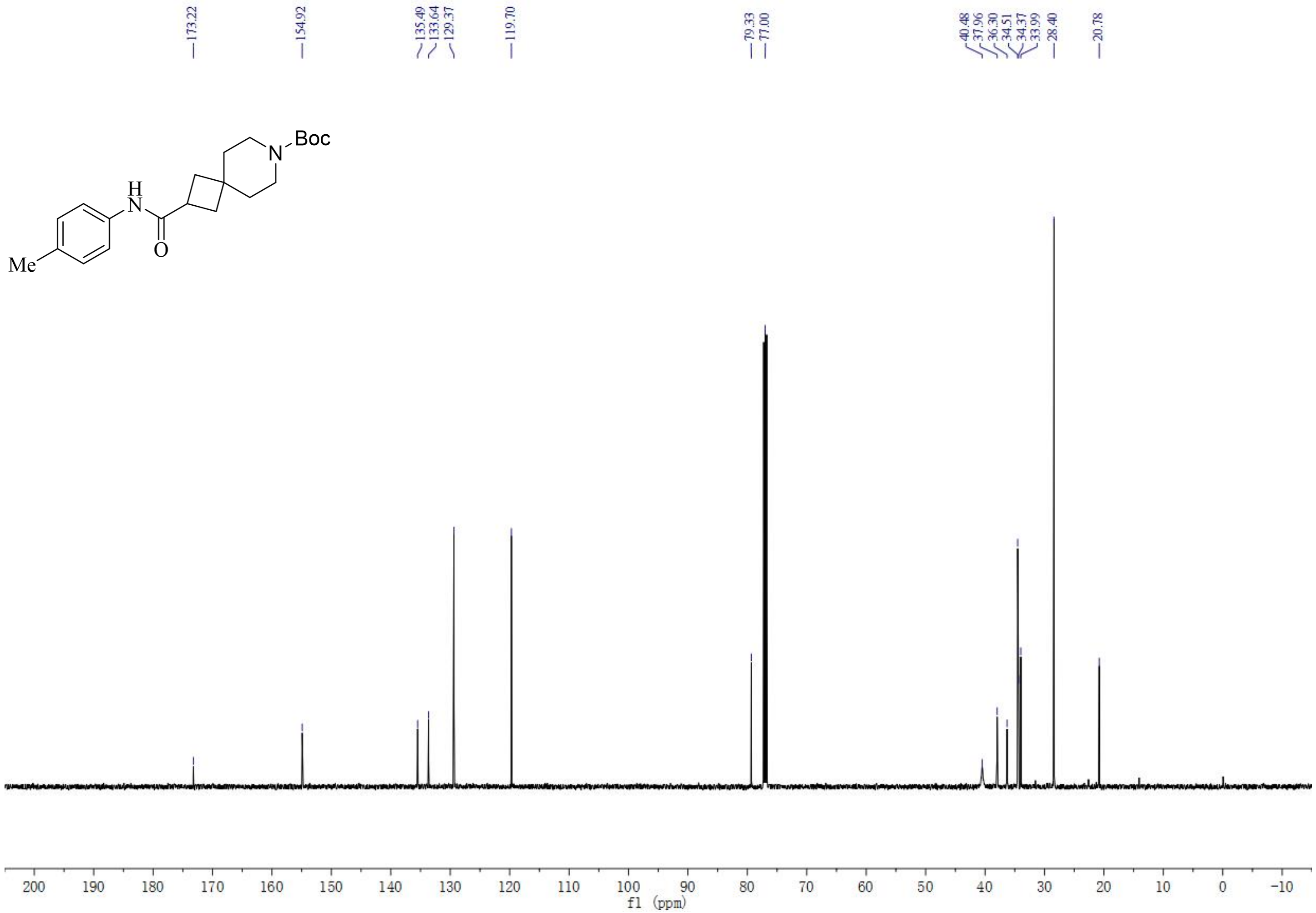


Figure S165. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)pivalamide (**5bm**)

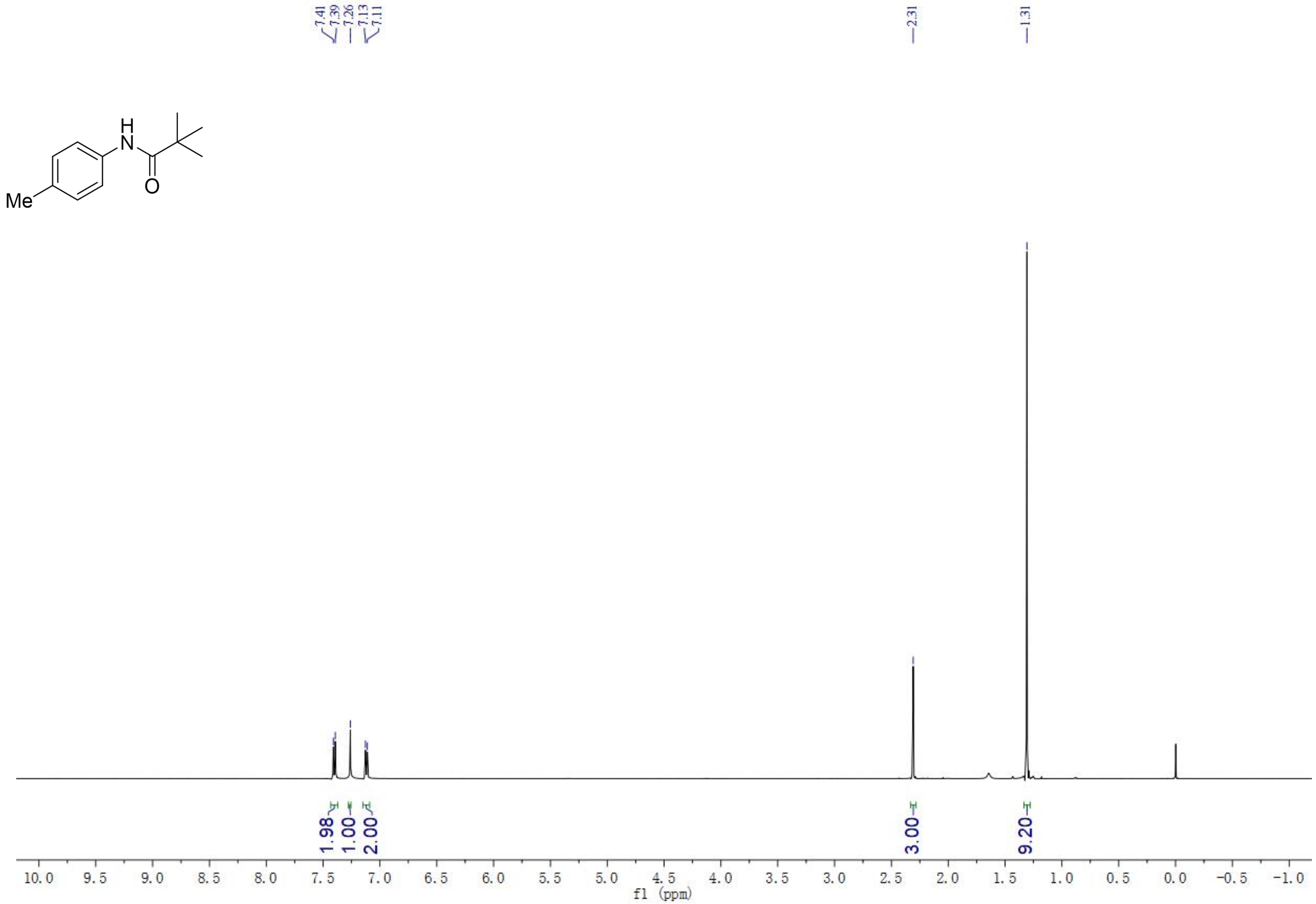


Figure S166. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)pivalamide (**5bm**)

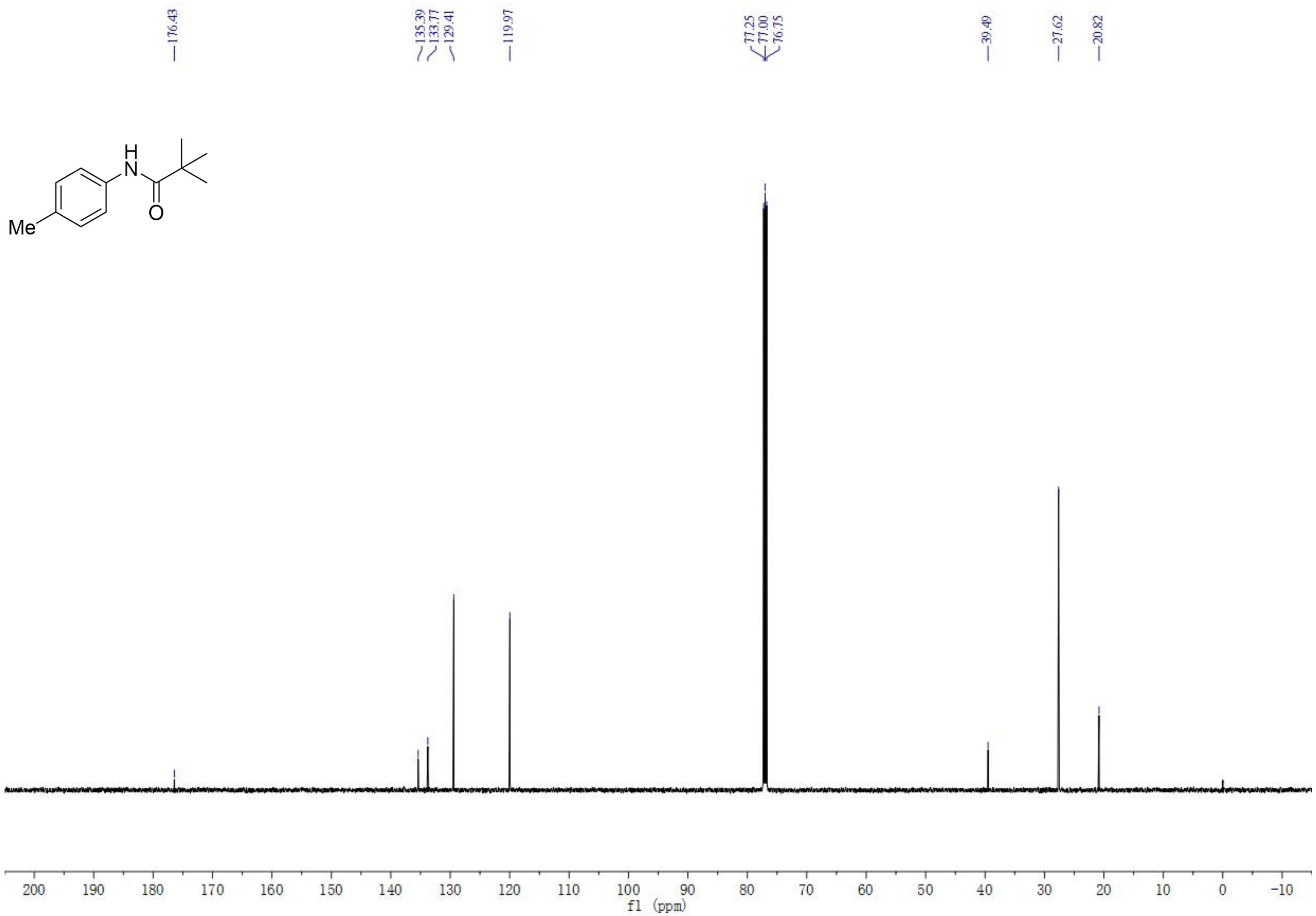


Figure S167. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of (3a*R*,5*R*,6a*S*)-2-oxo-4-(2-oxo-2-(p-tolylamino)ethyl)hexahydro-2*H*-cyclopenta[b]furan-5-yl benzoate (**5bn**)

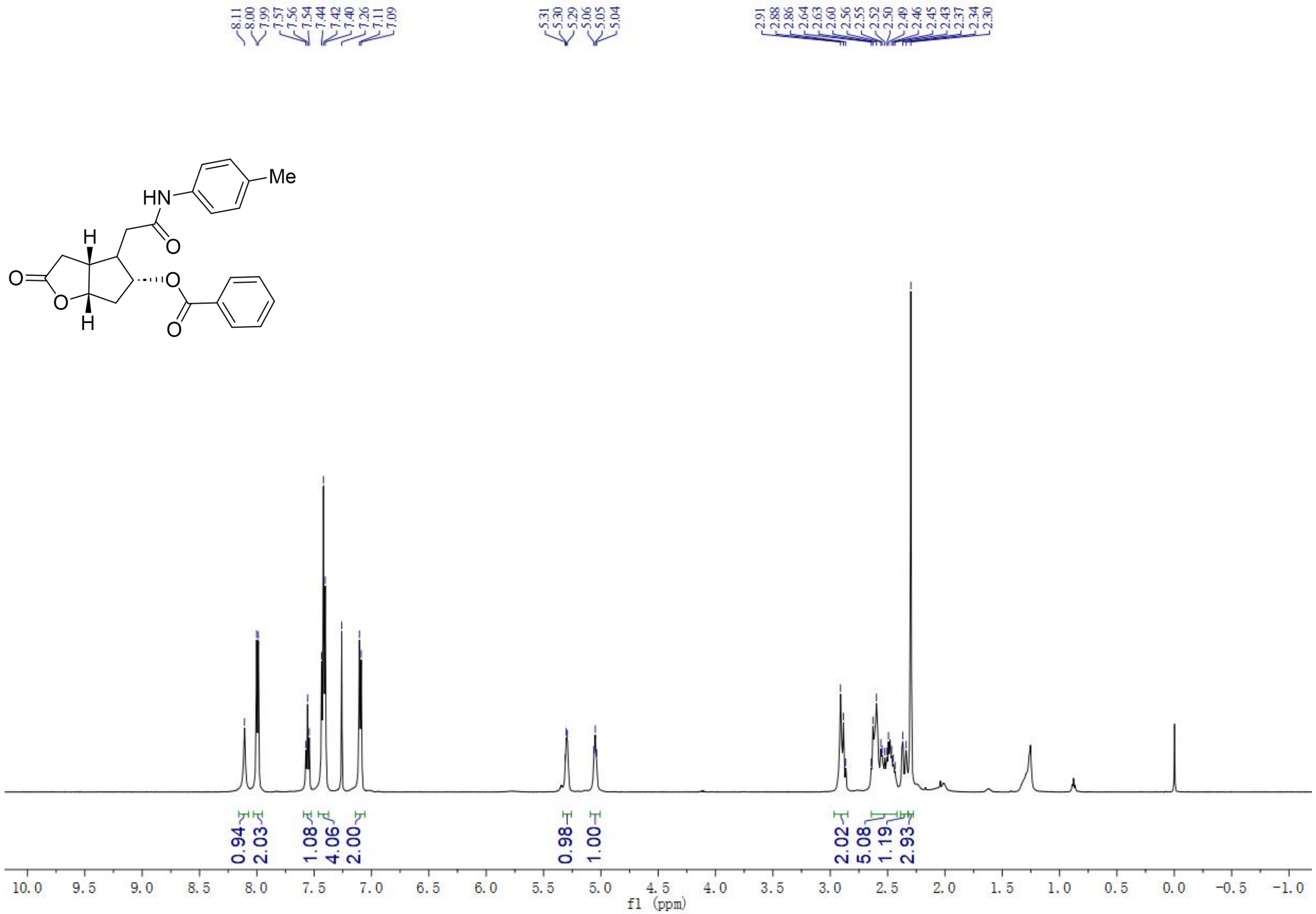


Figure S168. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of (3a*R*,5*R*,6a*S*)-2-oxo-4-(2-oxo-2-(p-tolylamino)ethyl)hexahydro-2*H*-cyclopenta[b]furan-5-yl benzoate (**5bn**)

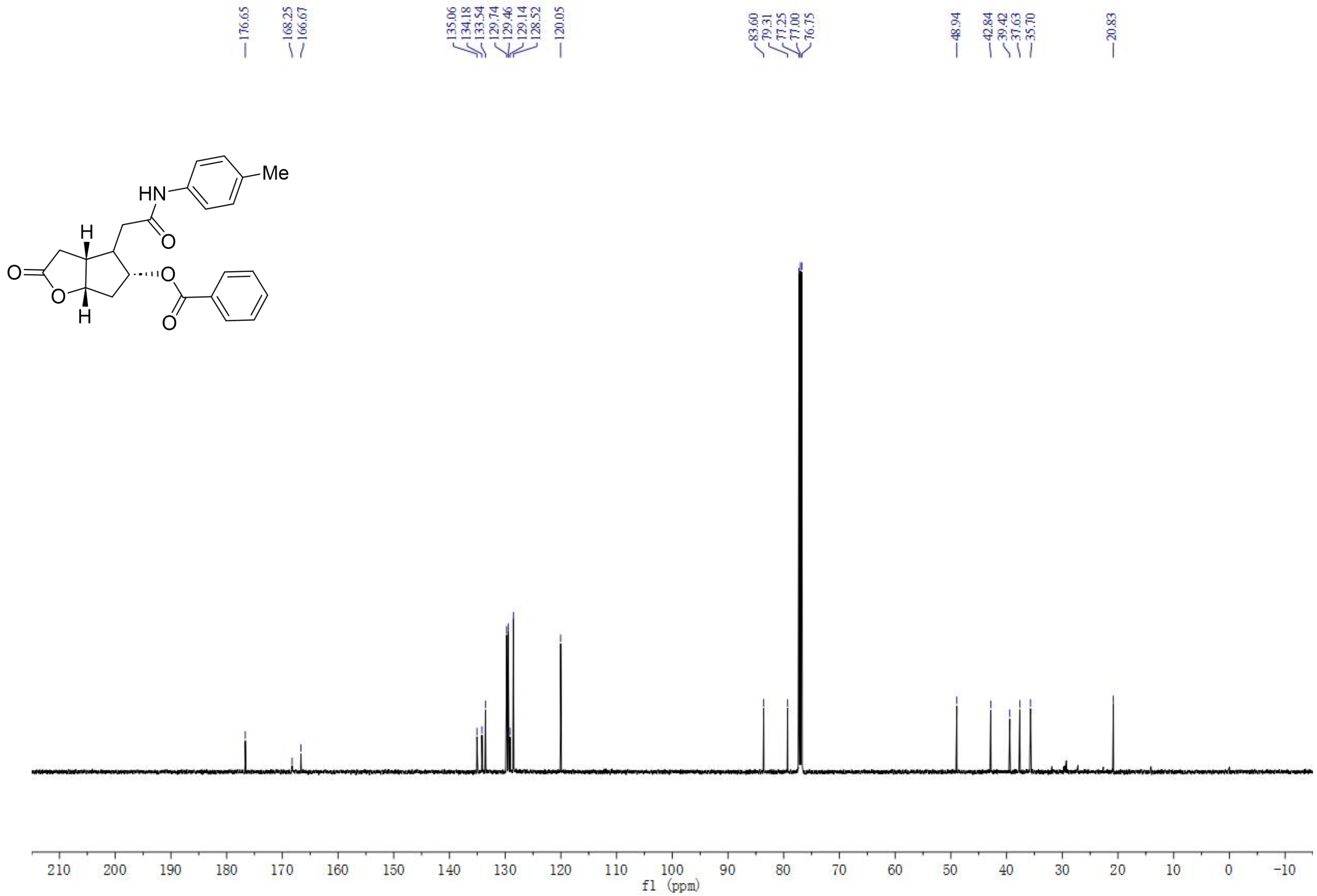
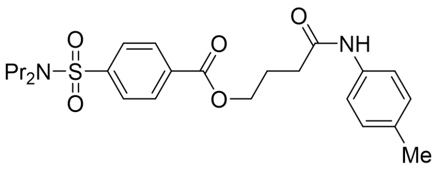


Figure S169. [1]H NMR (500 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (**5bo**)



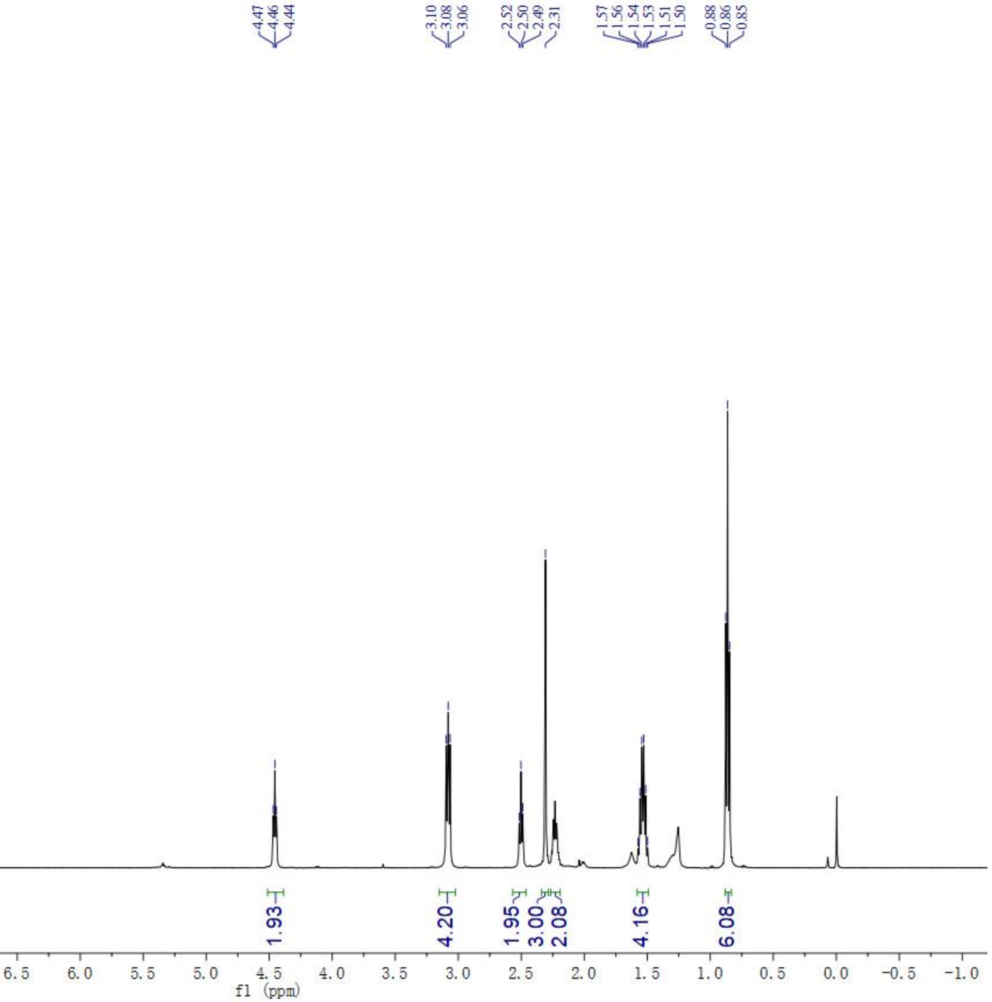


Figure S170. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (**5bo**)

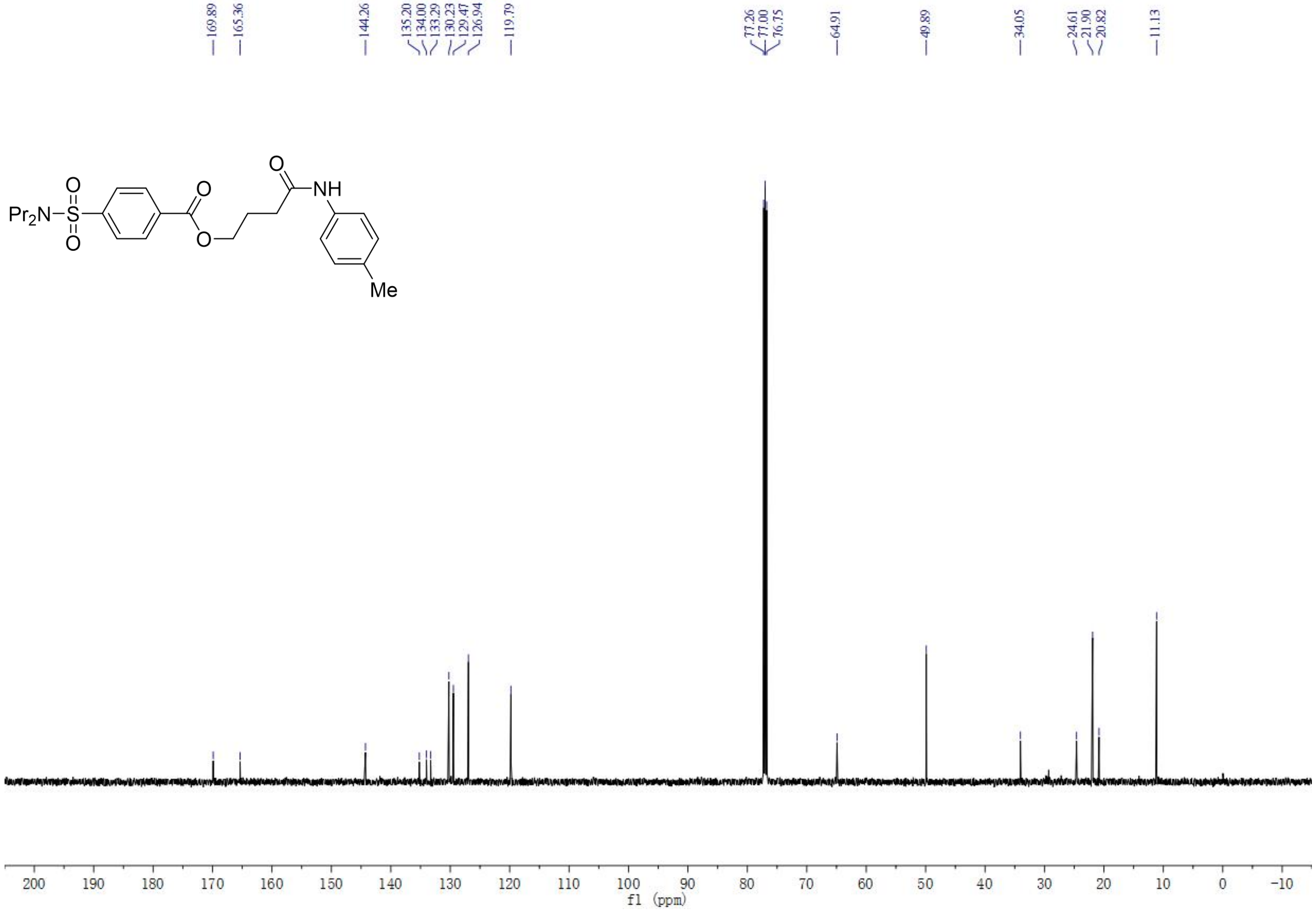


Figure S171. ^{1}H NMR (500 MHz, $CDCl_3$, 298K, 2.84:1 mixture of diastereoisomers) of (5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-*N*-(*p*-tolyl)hexadecahydro-1*H*-cyclopenta[a]phenanthrene-3-carboxamide (**5bp**)

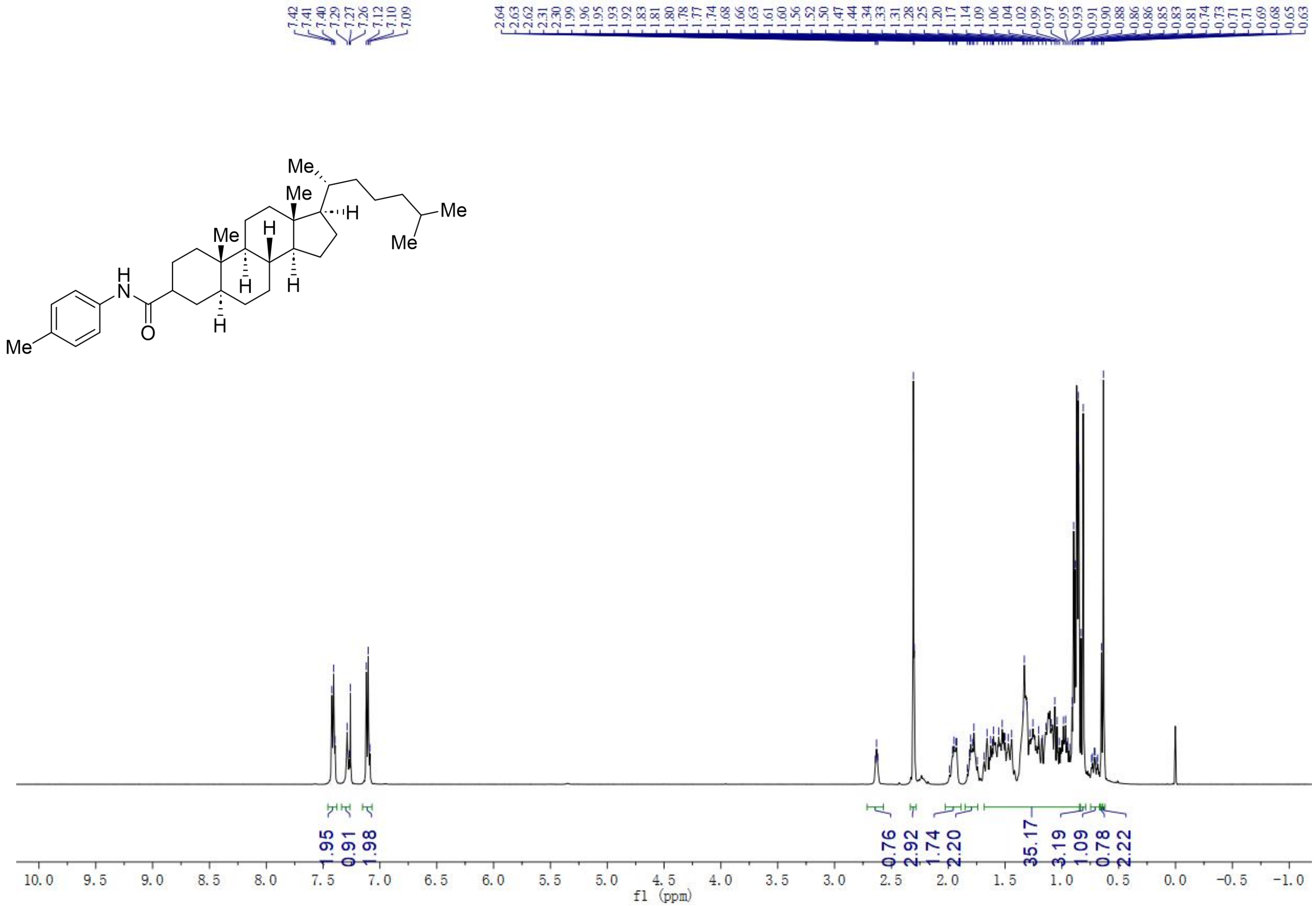


Figure S172. ^{13}C NMR (126 MHz, $CDCl_3$, 298K, 2.84:1 mixture of diastereoisomers) of (5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-*N*-(*p*-tolyl)hexadecahydro-1*H*-cyclopenta[a]phenanthrene-3-carboxamide (**5bp**)

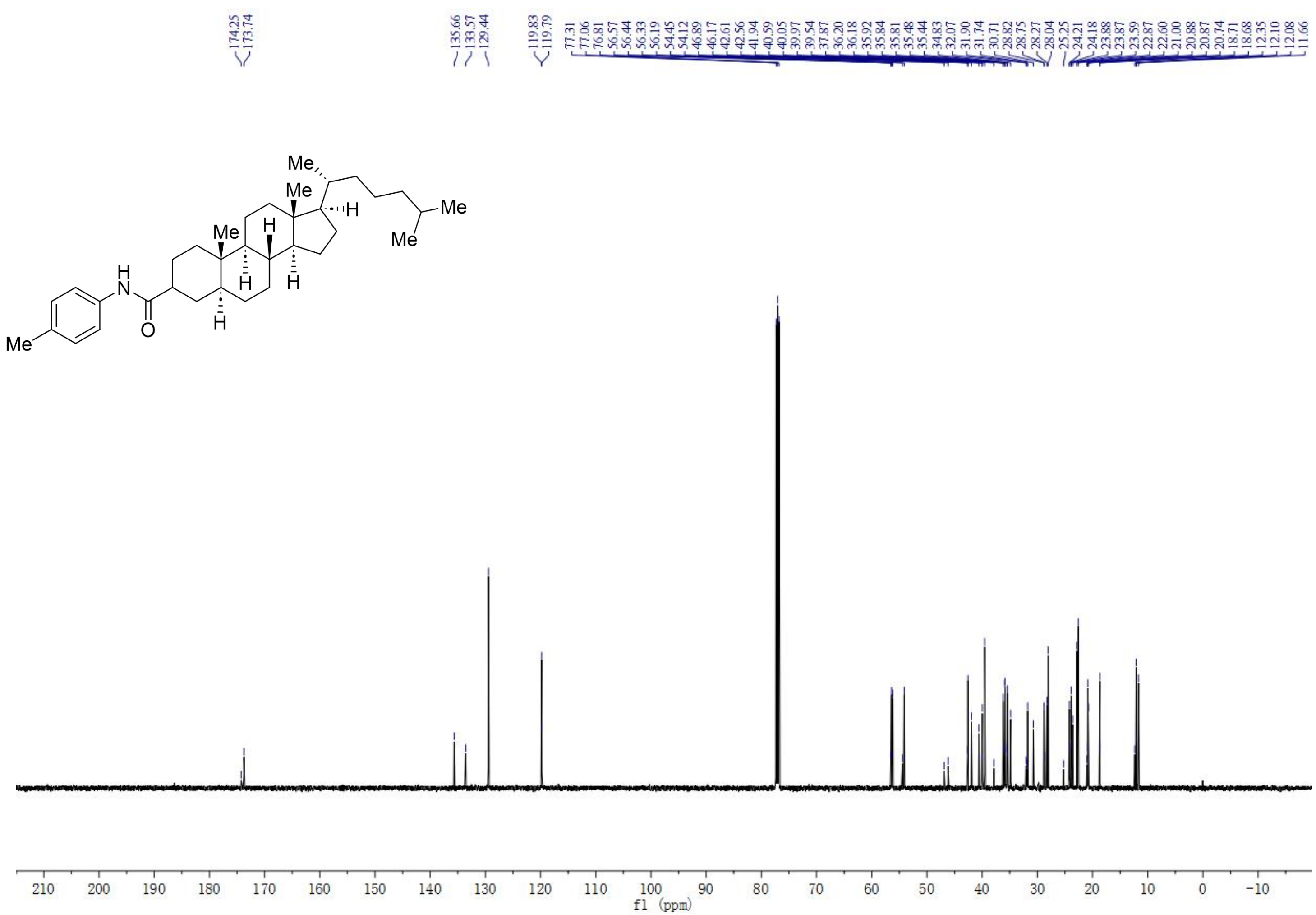


Figure S173. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of 4-oxo-4-(*p*-tolylamino)butyl 2-(3-benzoylphenyl)propanoate **(5bq)**

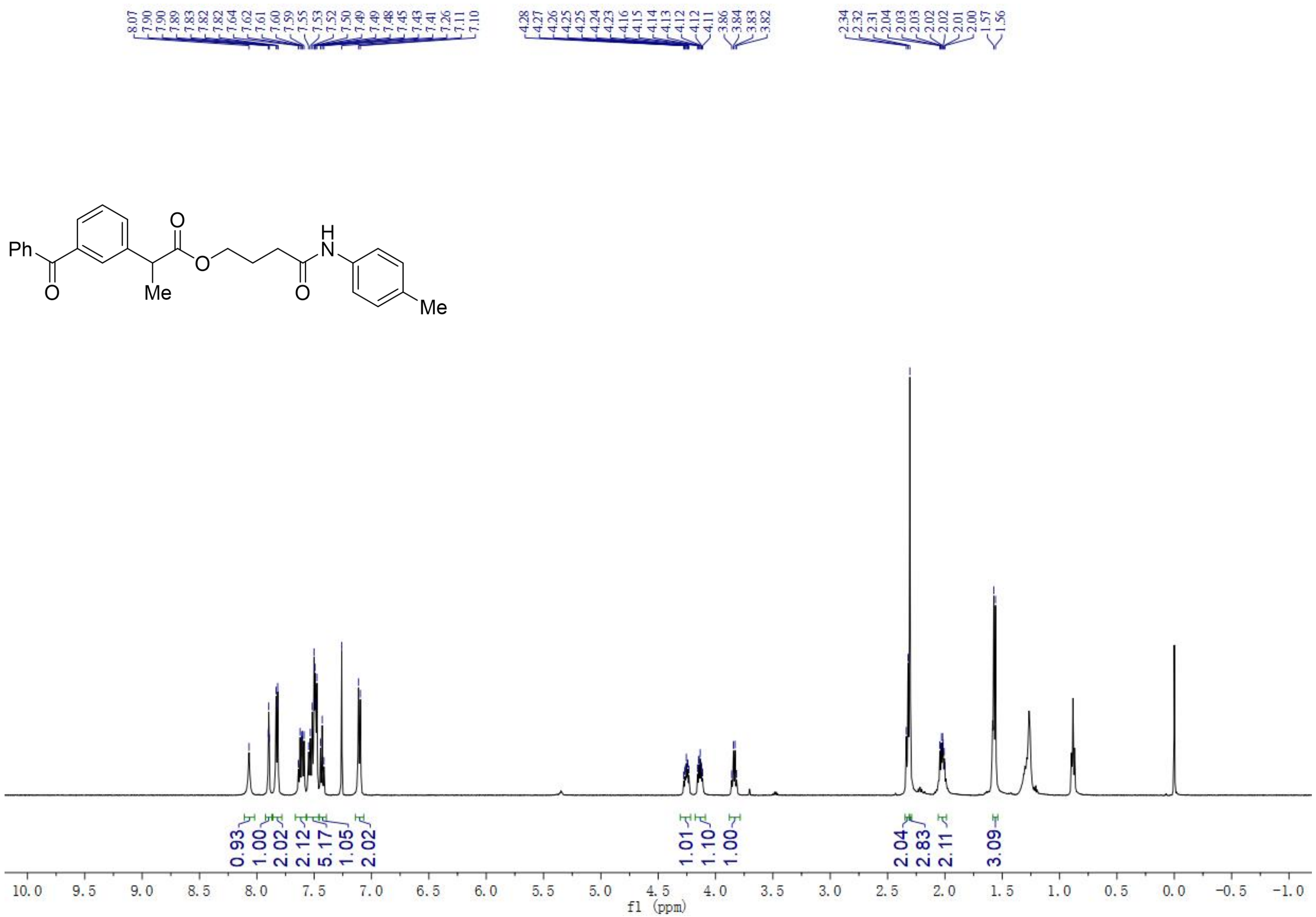


Figure S174. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl 2-(3-benzoylphenyl)propanoate **(5bq)**

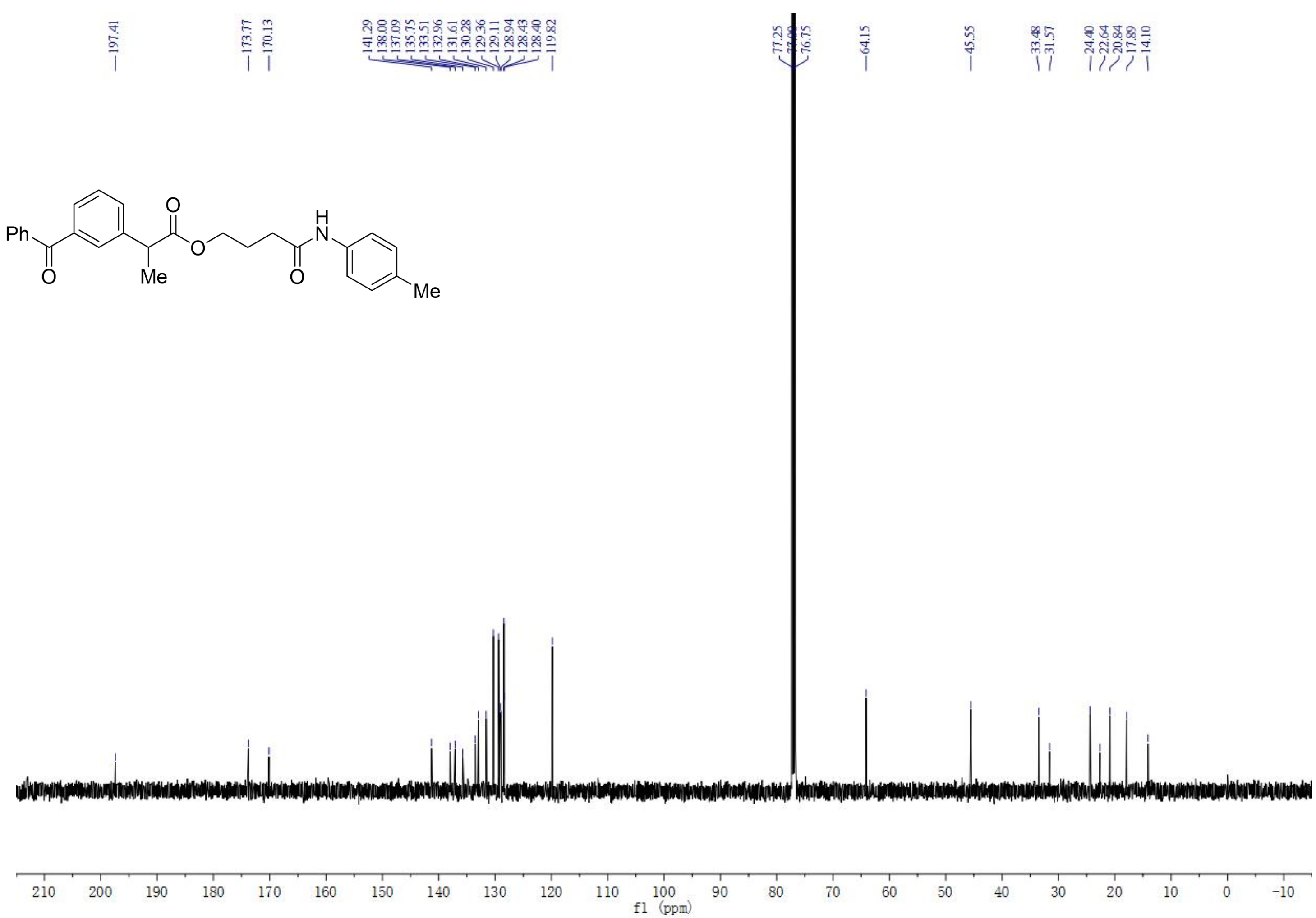


Figure S175. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-isopropyl-5-methyl-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (**5br**)

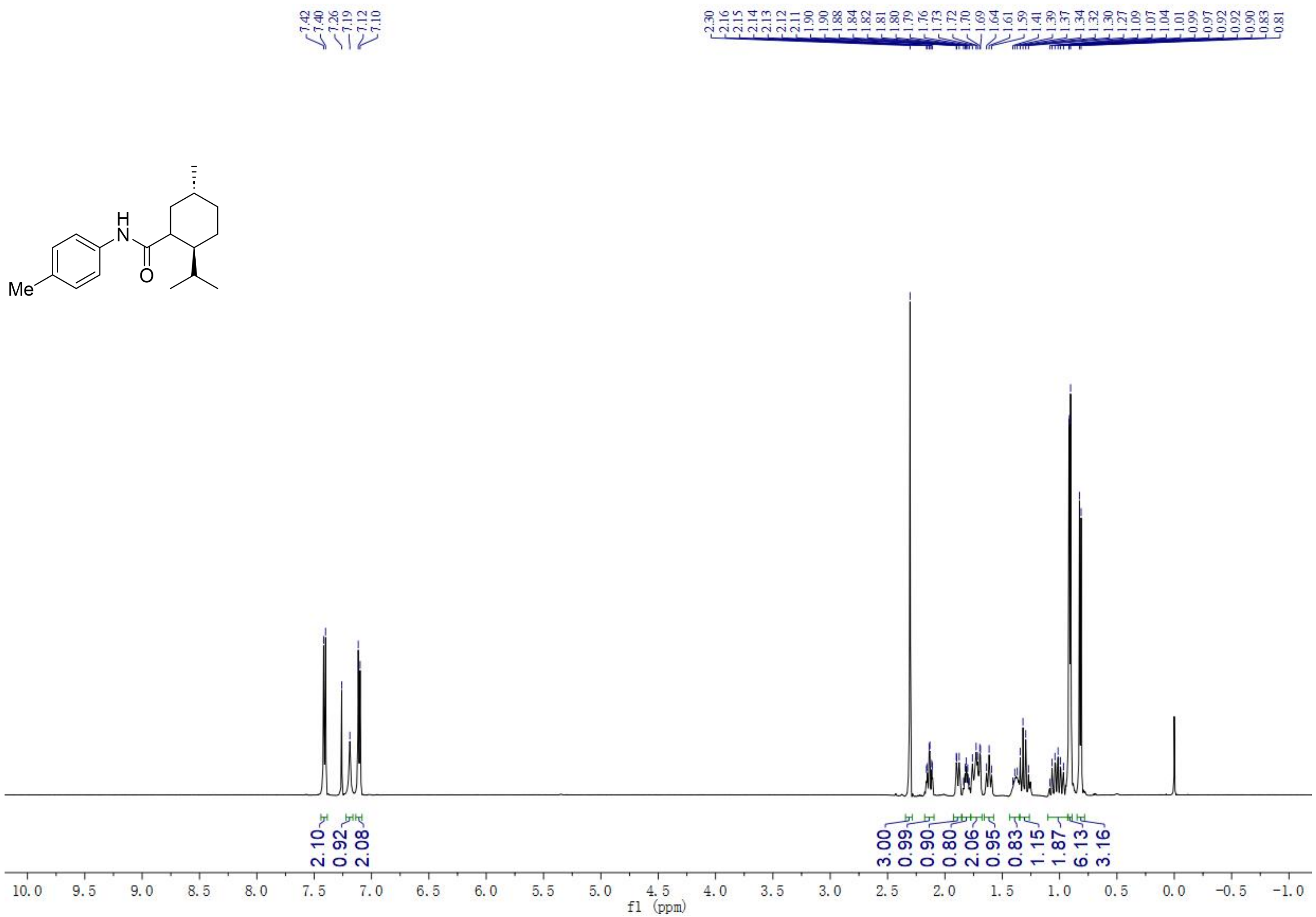


Figure S176. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 2-isopropyl-5-methyl-*N*-(*p*-tolyl)cyclohexane-1-carboxamide (**5br**)

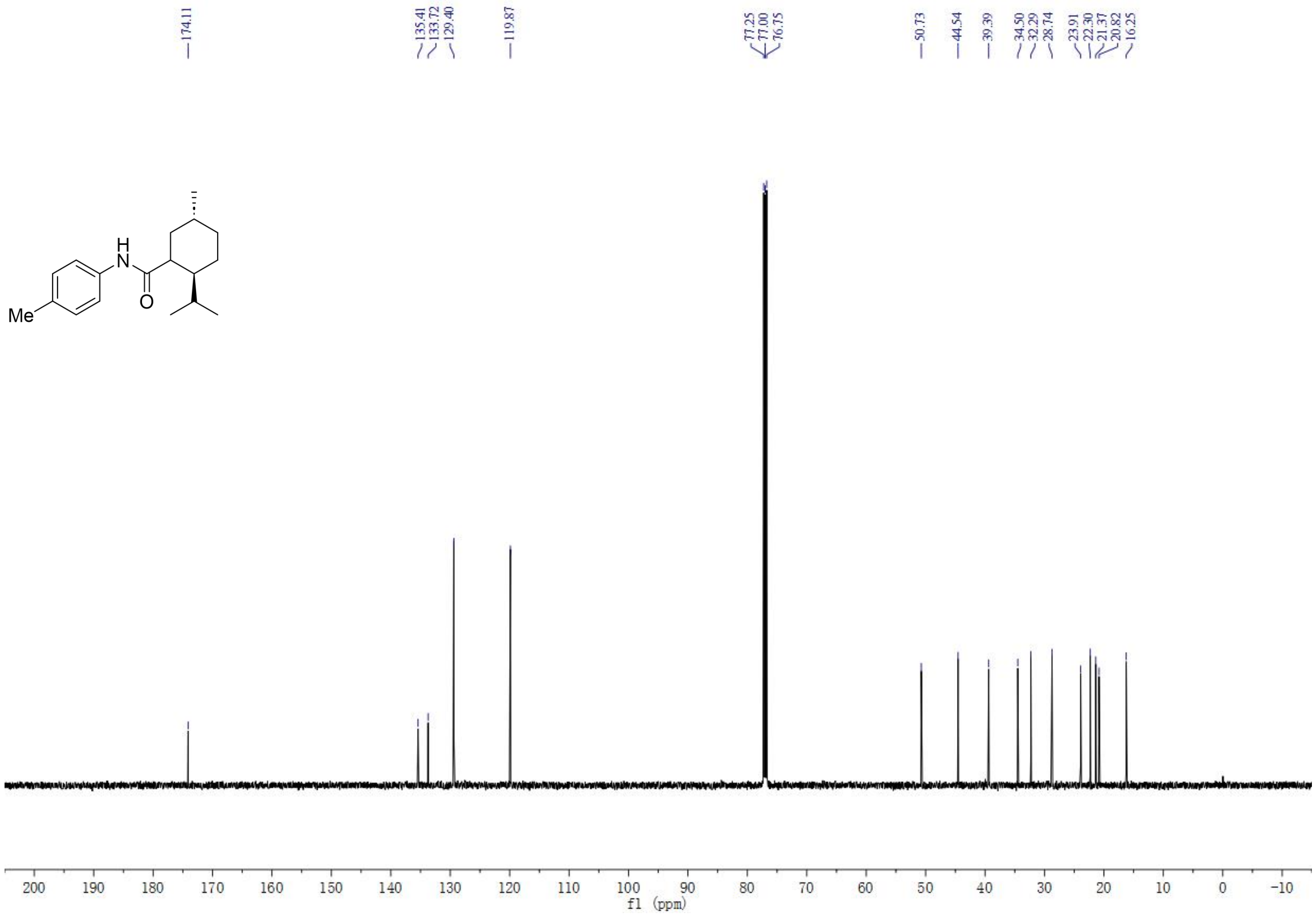

174.11
135.41
133.72
129.40
119.87
77.25
77.00
76.75
50.73
44.54
39.39
34.50
32.29
28.74
23.91
22.30
21.37
20.82
16.25
H
N
O
Me
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Figure S177. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of
3-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7*H*-purin-7-yl)-2-methyl-*N*-(*p*-tolyl)propanamide (**5bs**)

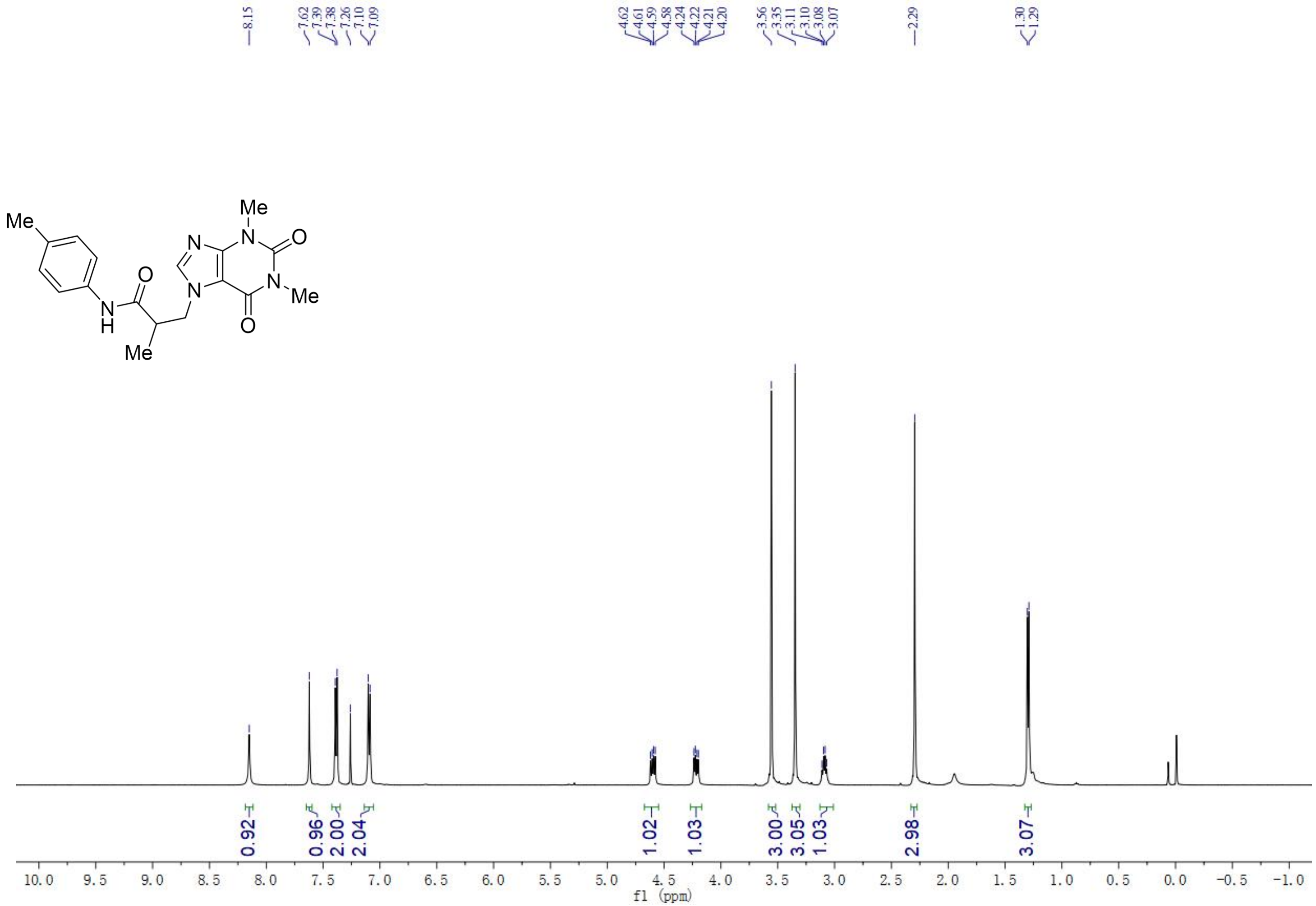


Figure S178. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 3-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7*H*-purin-7-yl)-2-methyl-*N*-(*p*-tolyl)propanamide (**5bs**)

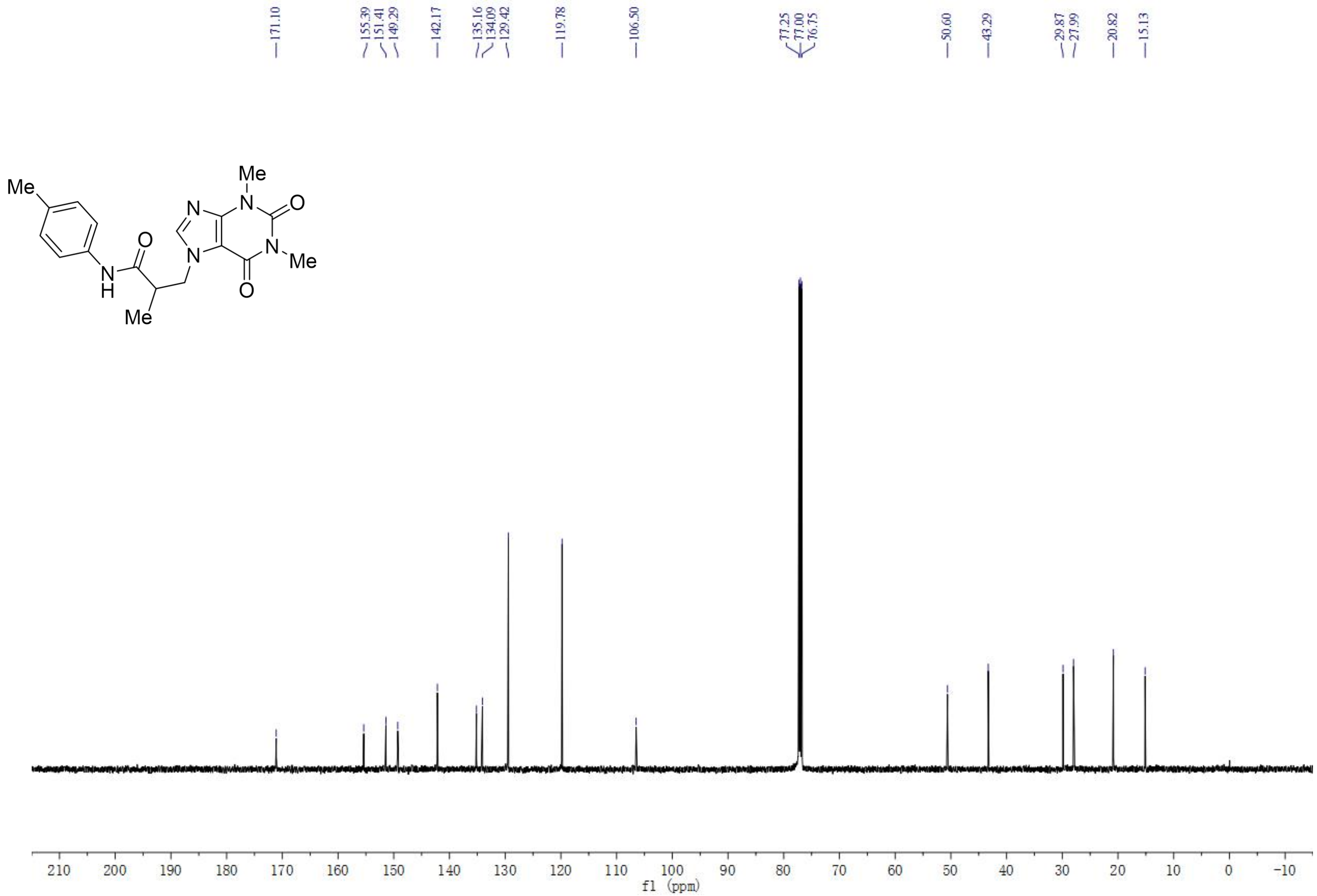


Figure S179. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (**5bt**)

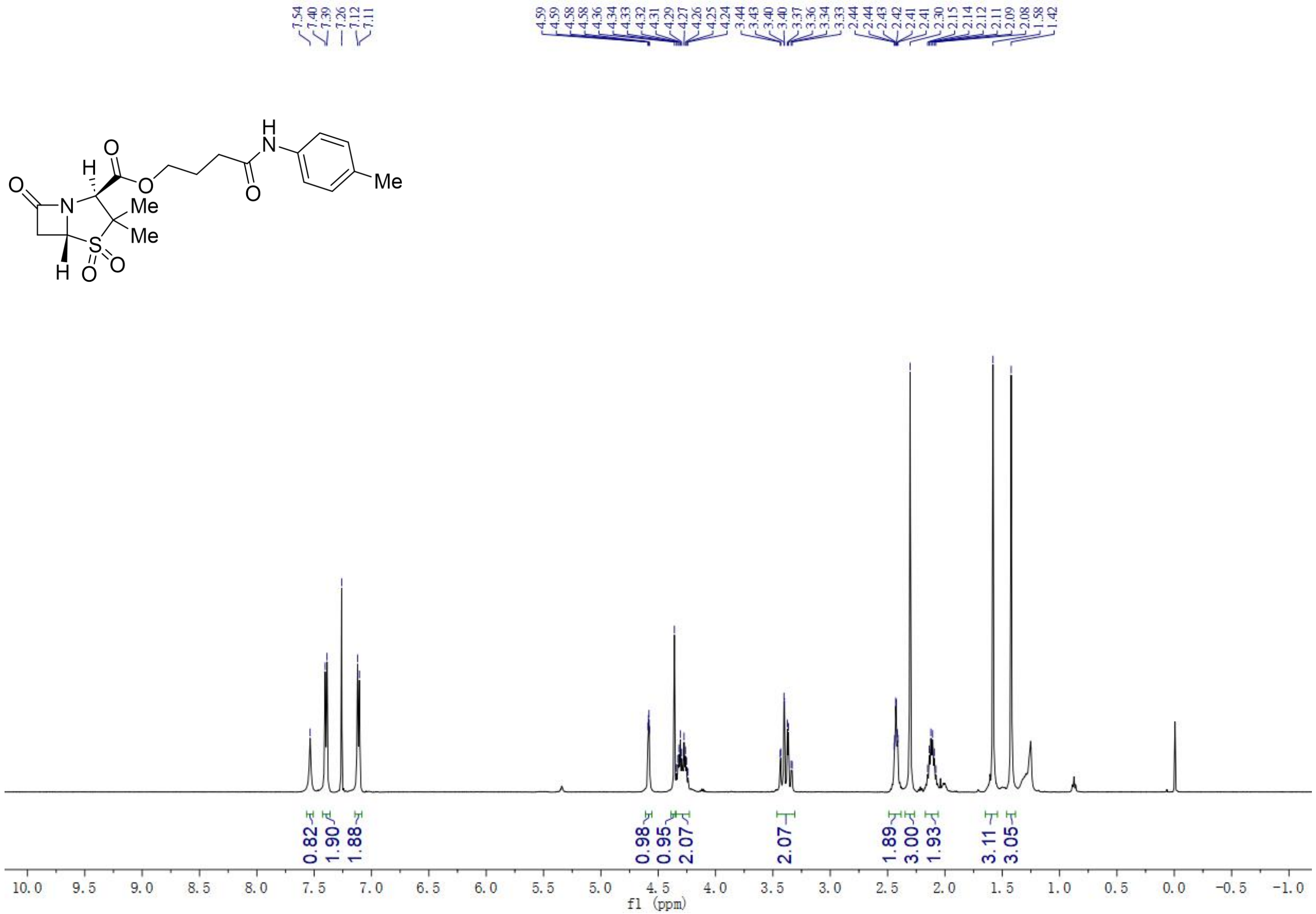


Figure S180. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (**5bt**)

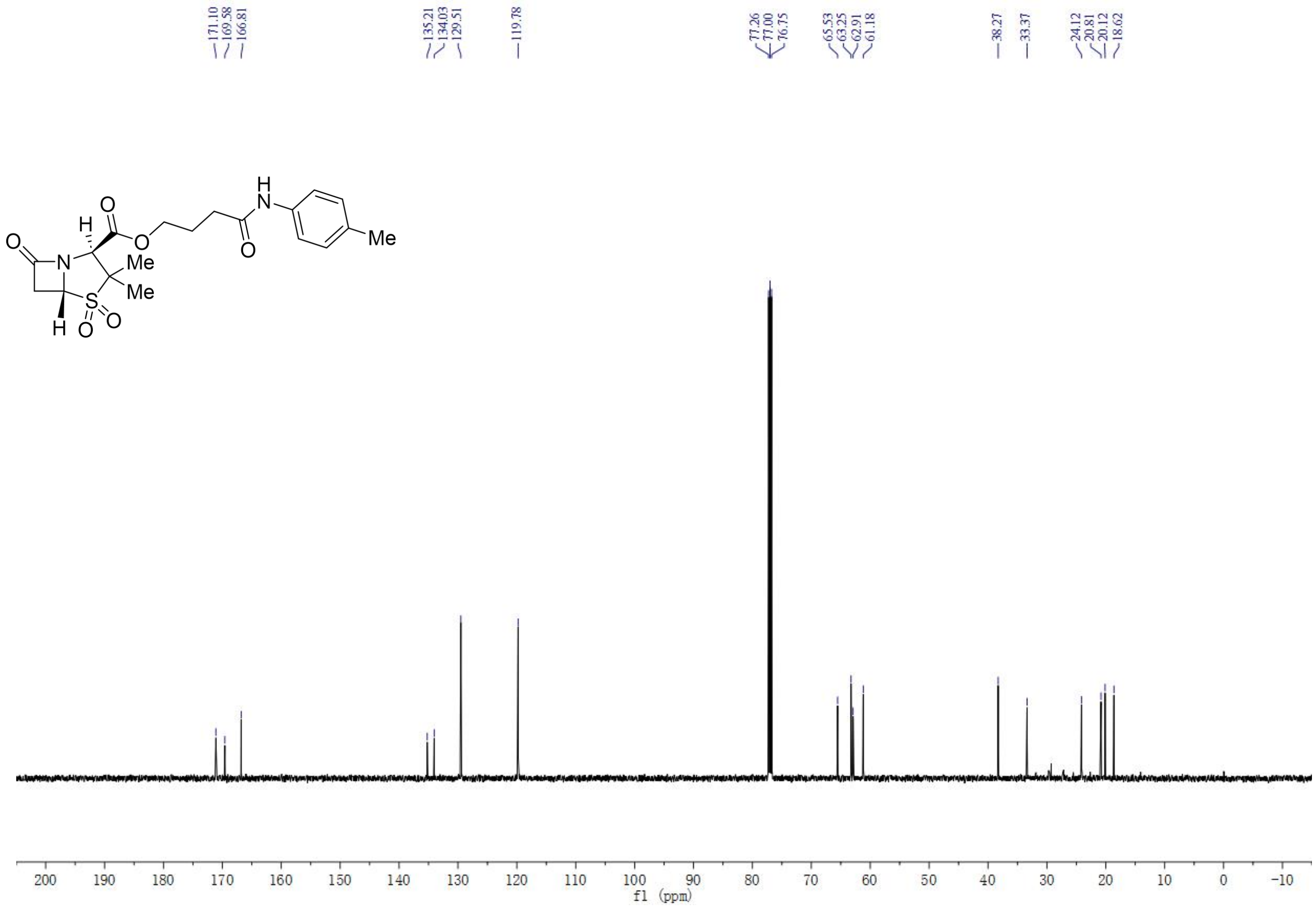


Figure S181. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (**5bu**)

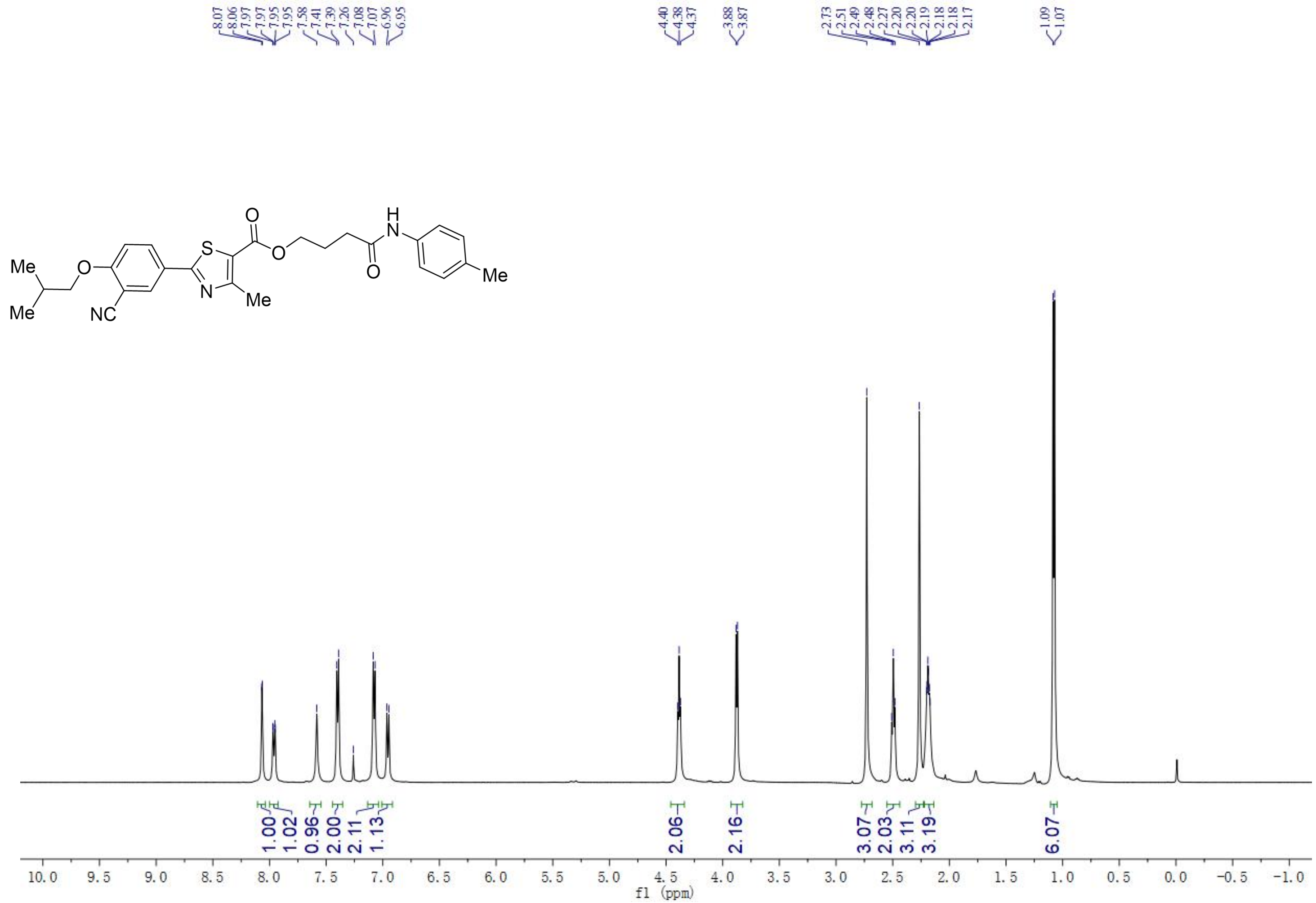


Figure S182. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 4-oxo-4-(*p*-tolylamino)butyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (**5bu**)

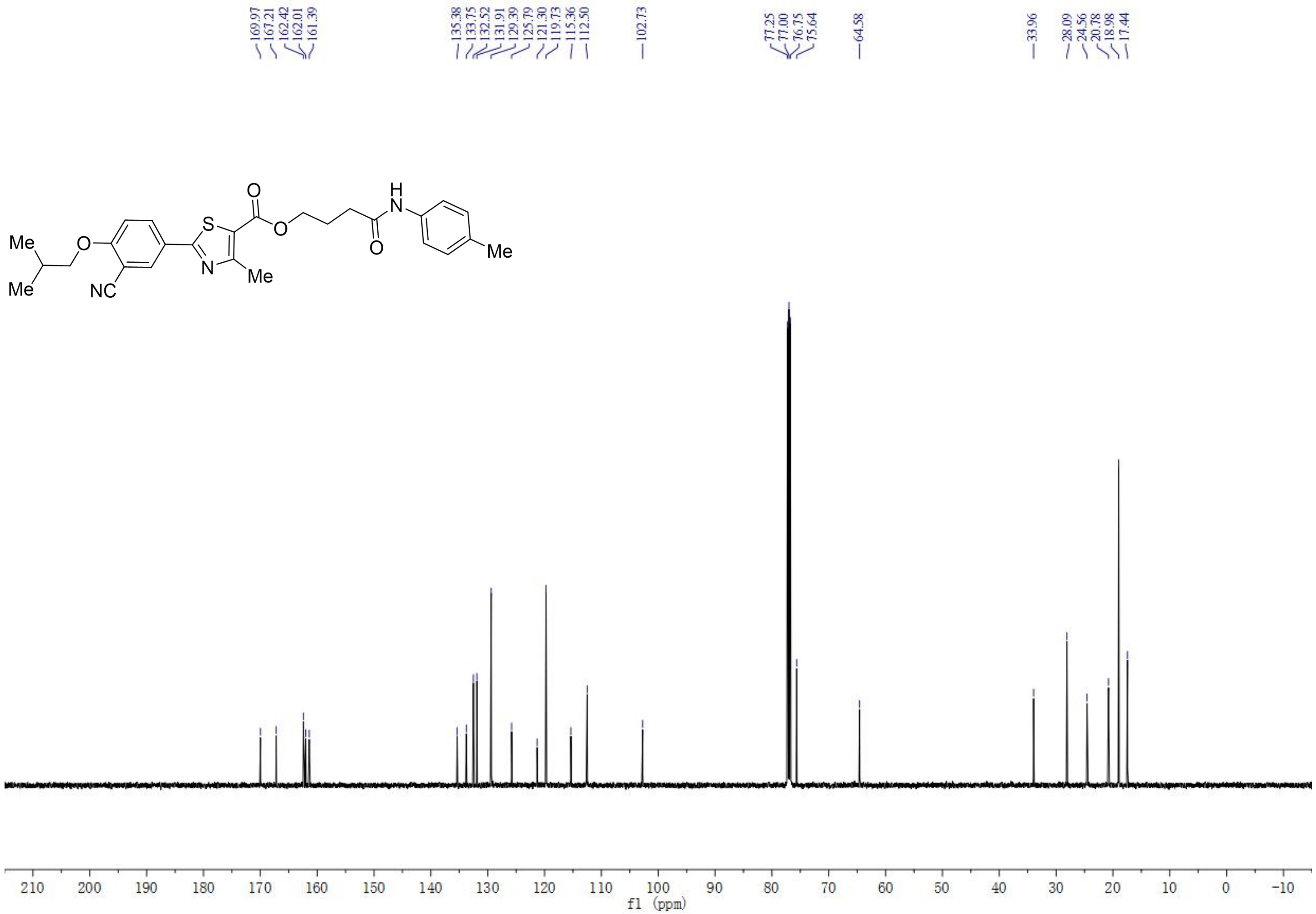


Figure S183. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)pent-4-enamide (**5av**)

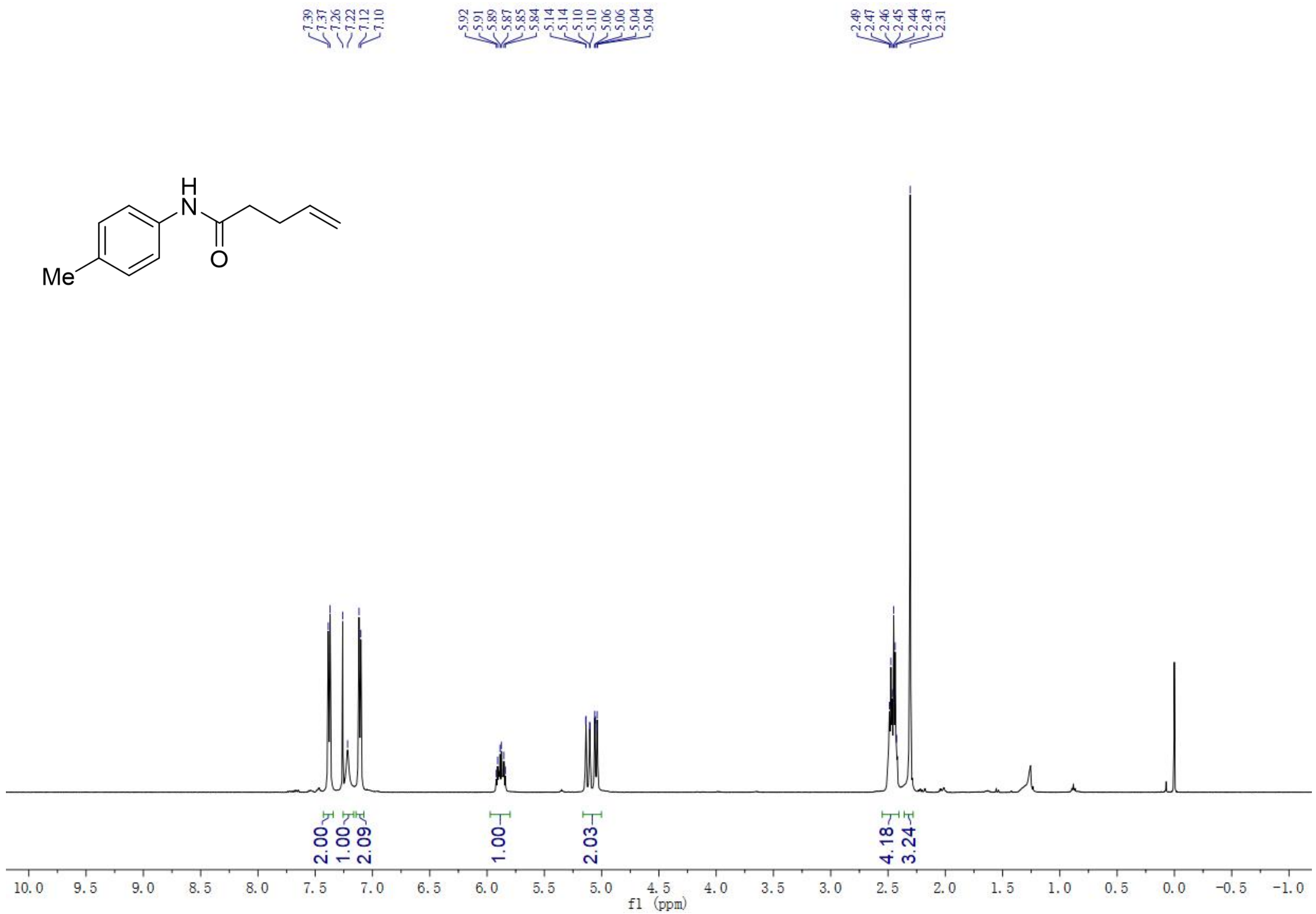


Figure S184. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *N*-(*p*-tolyl)pent-4-enamide (**5av**)

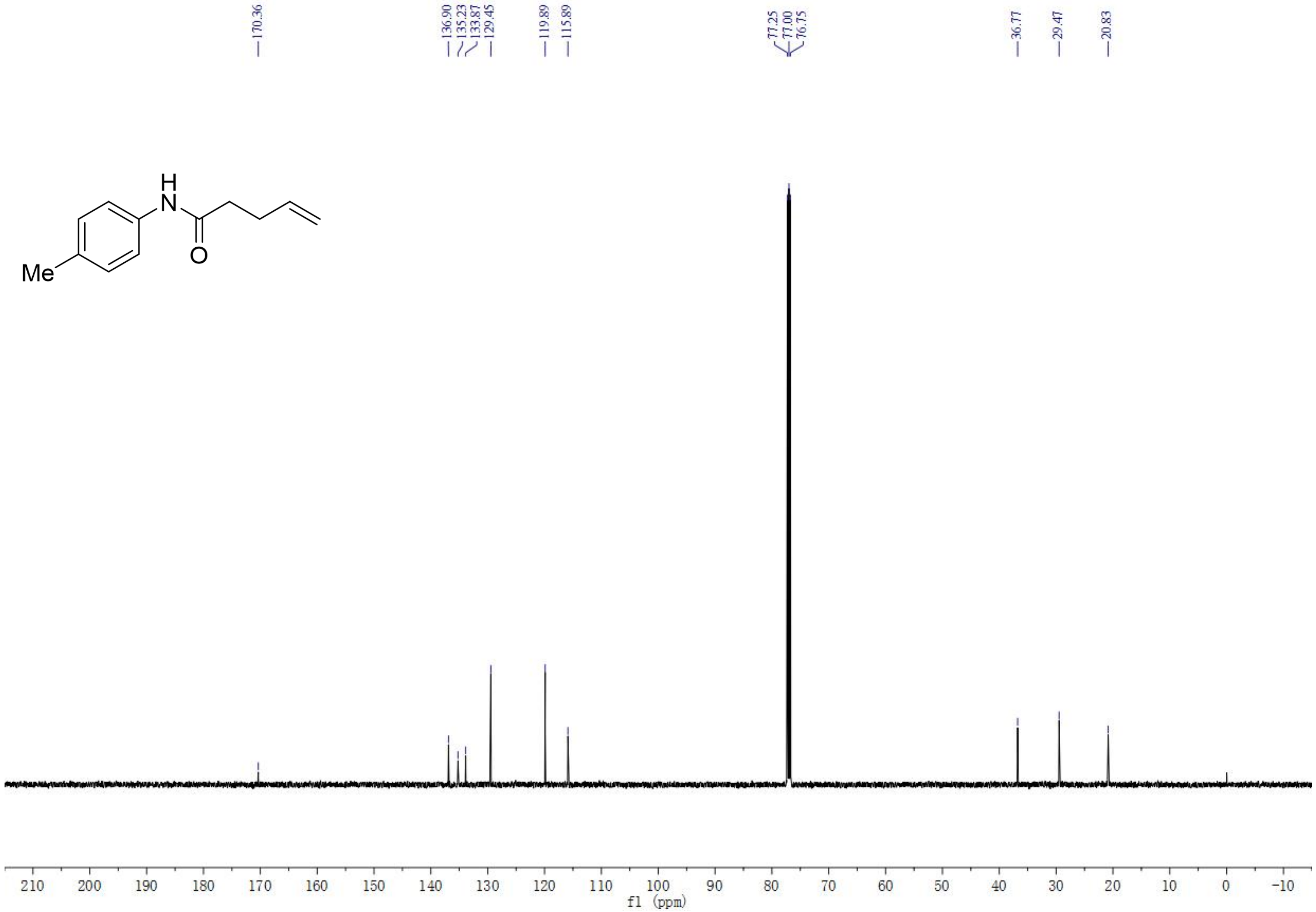
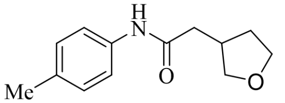


Figure S185. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 2-(tetrahydrofuran-3-yl)-*N*-(*p*-tolyl)acetamide (**5aw**)



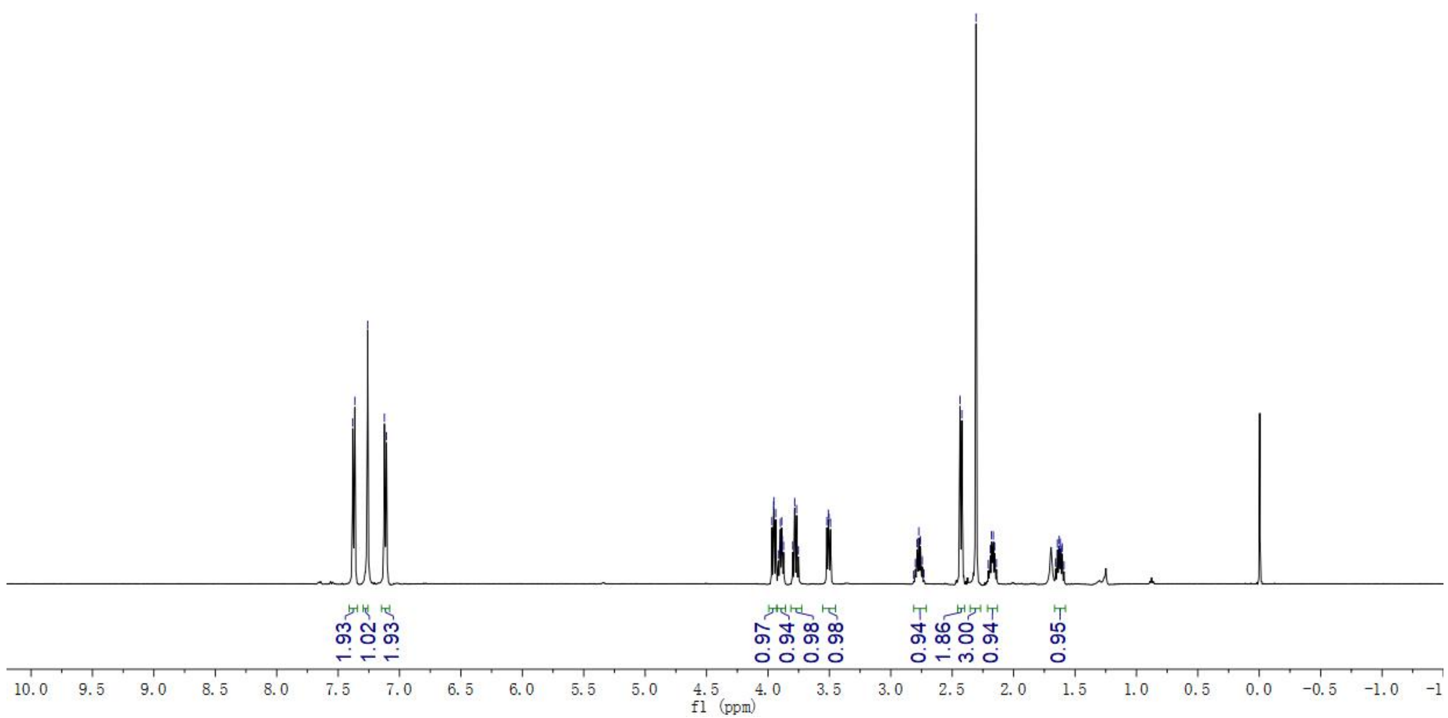


Figure S186. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of 2-(tetrahydrofuran-3-yl)-*N*-(*p*-tolyl)acetamide (**5aw**)

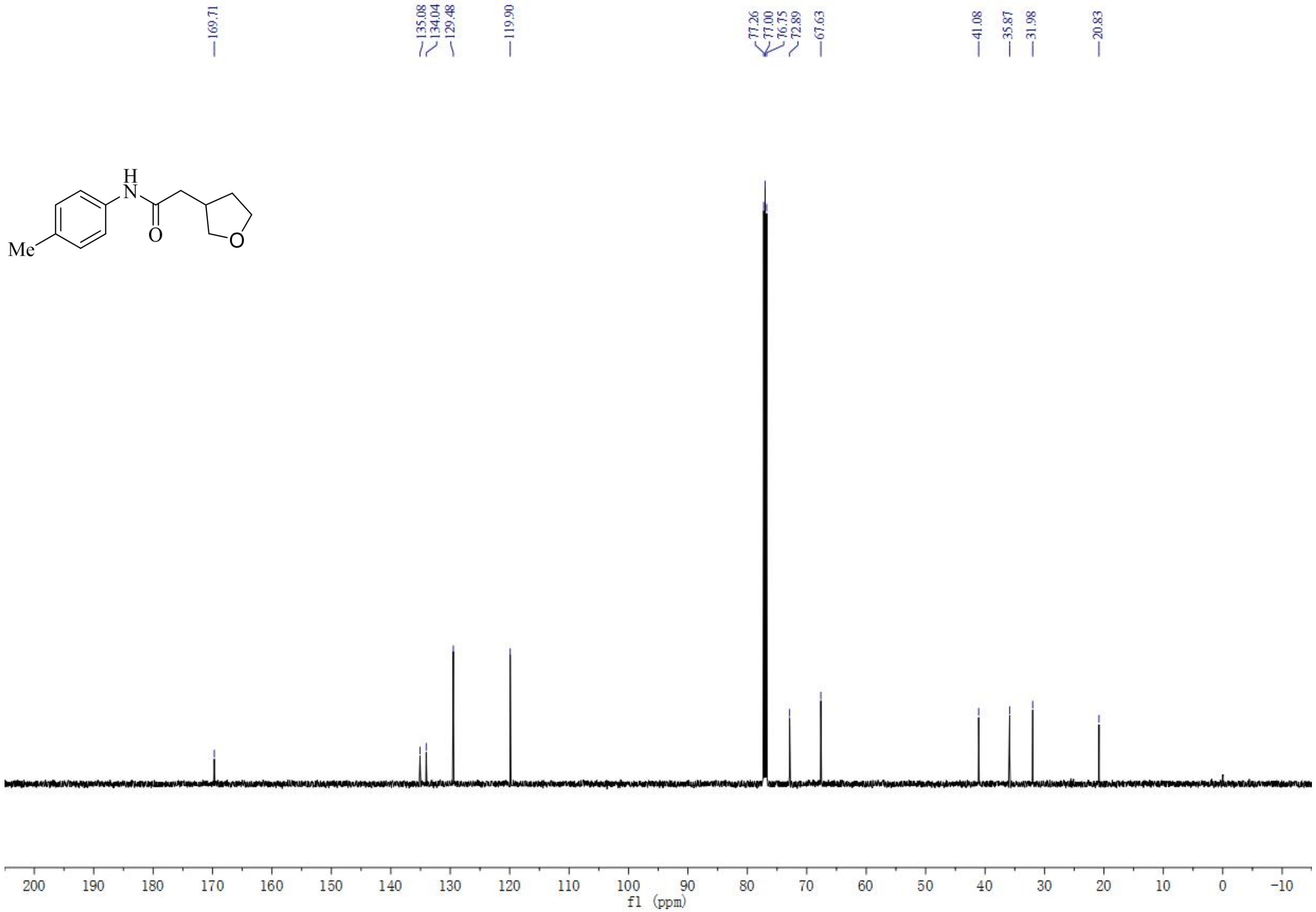


Figure S187. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-(4-methoxyphenoxy)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6aa**)

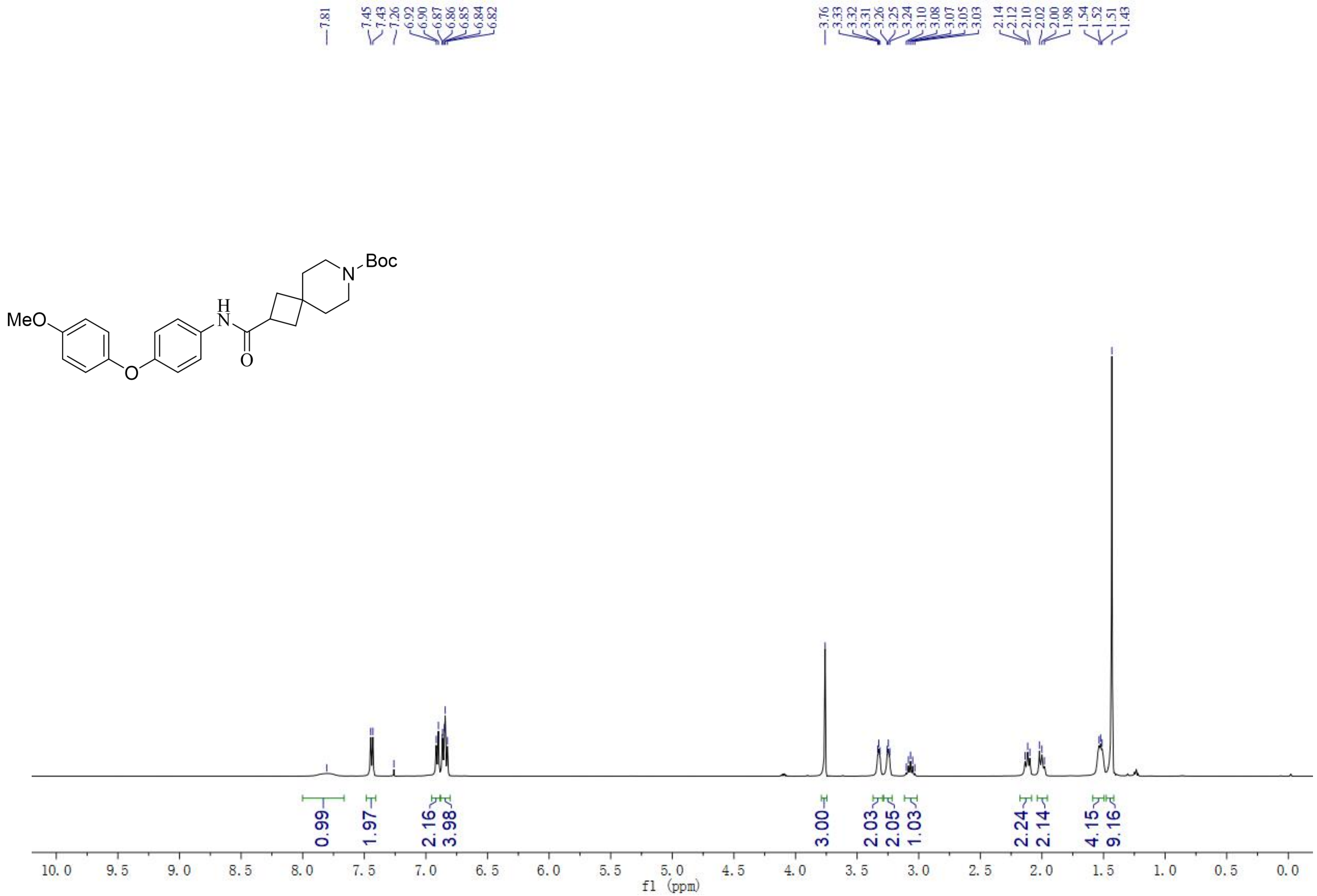


Figure S188. ^{13}C NMR (126 MHz, CDCl$_3$, 298K) of *tert*-butyl 2-((4-(4-methoxyphenoxy)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6aa**)

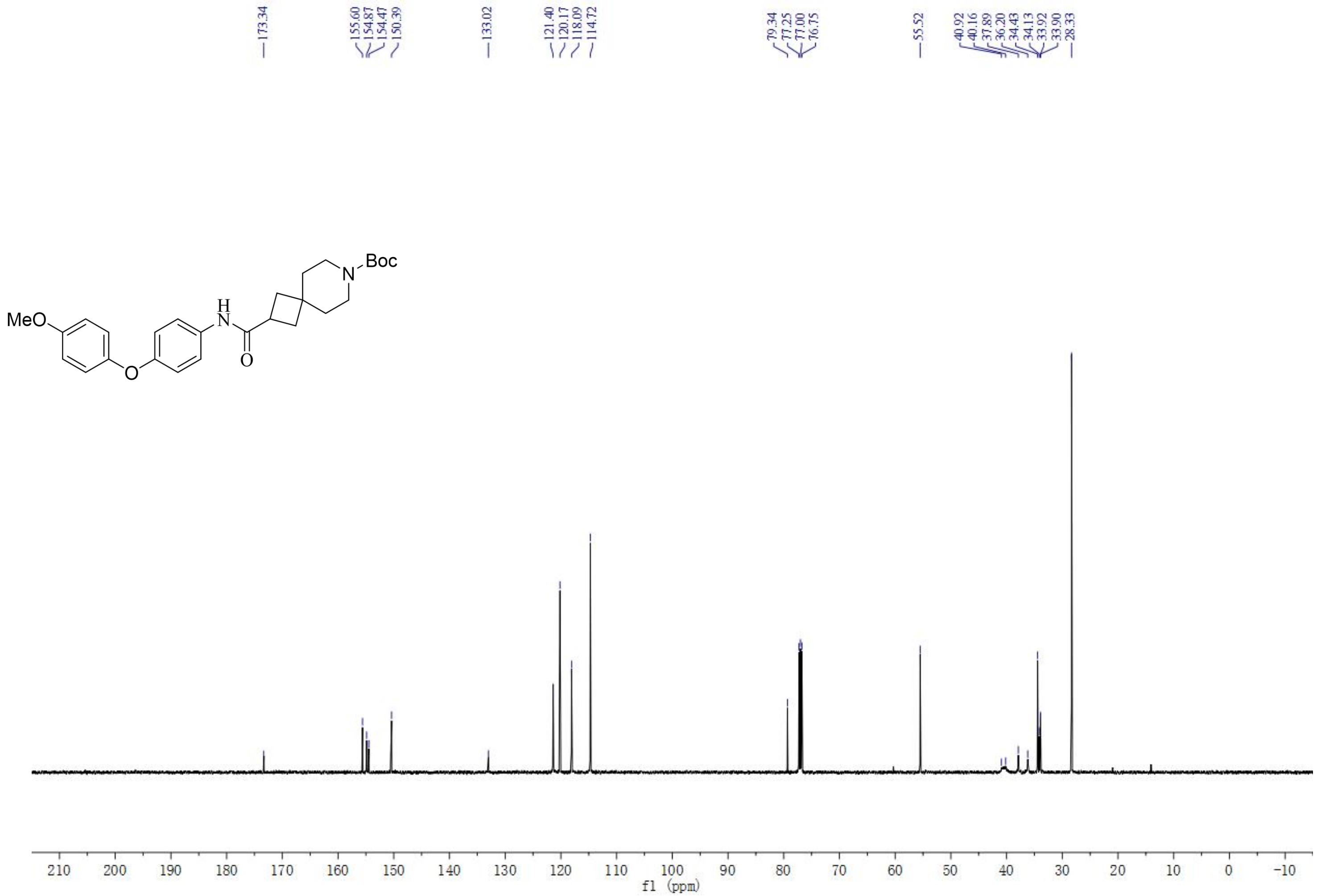


Figure S189. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of *tert*-butyl 2-((4-tosylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6ab)**.

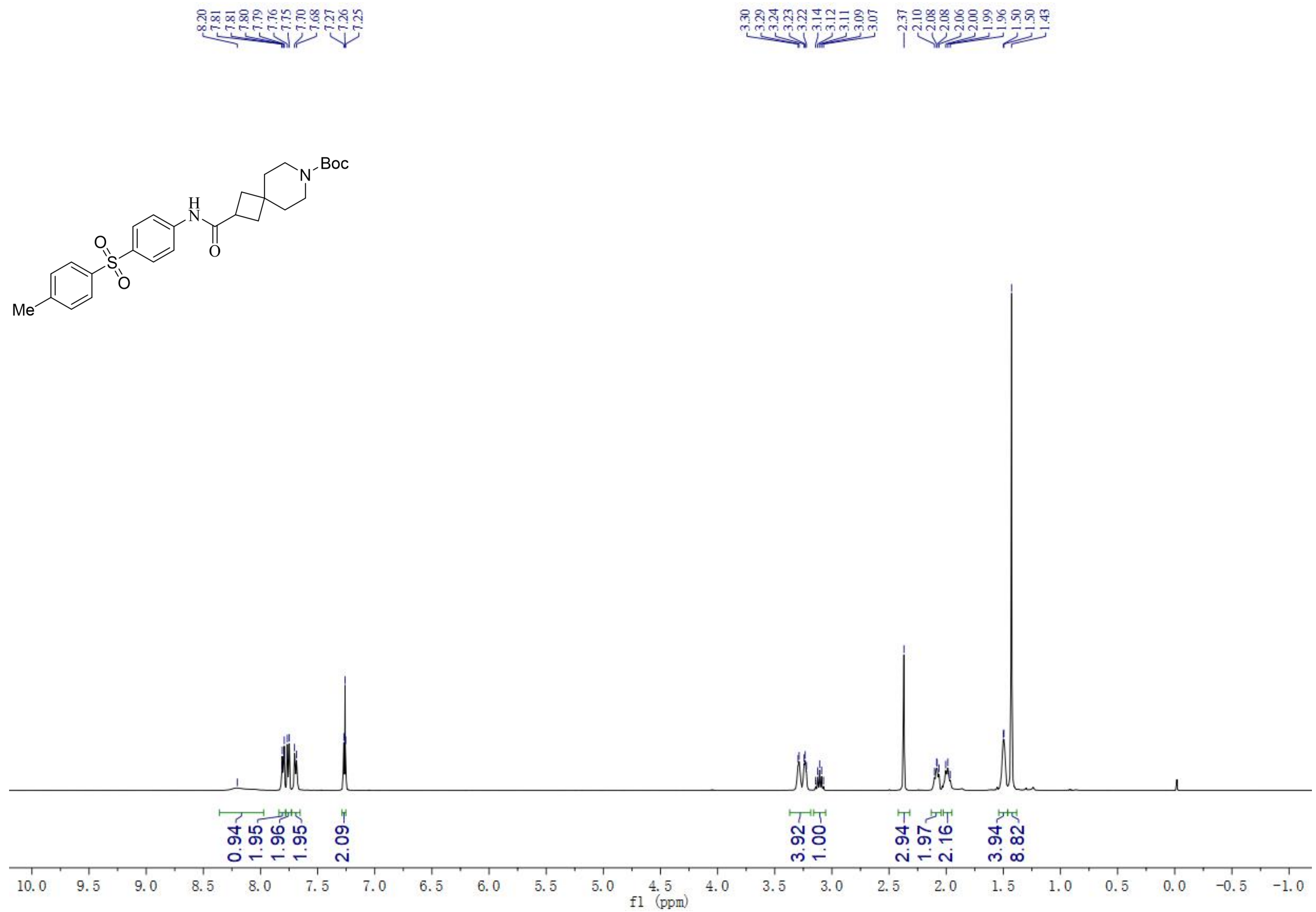


Figure S190. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-tosylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6ab)**.

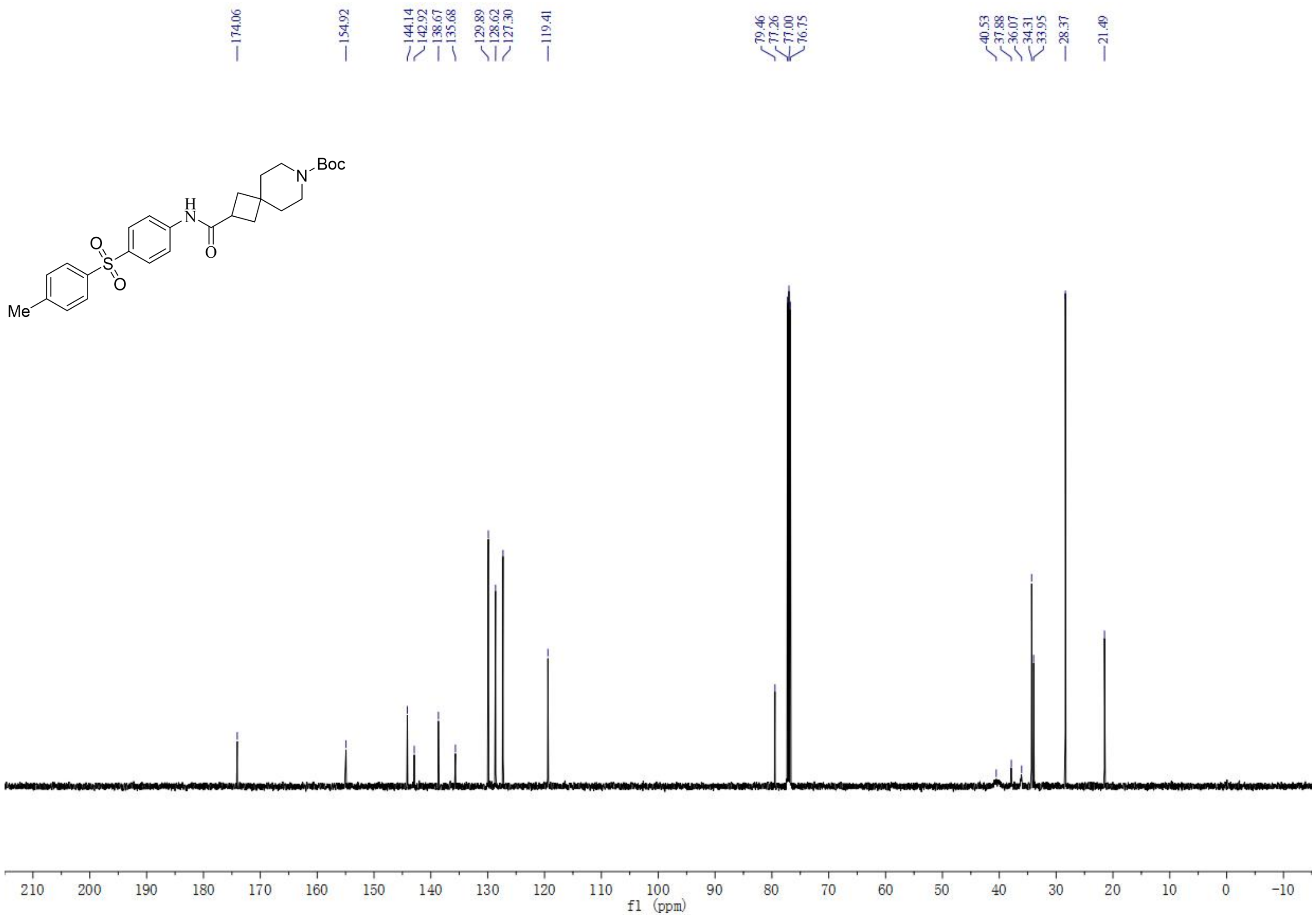


Figure S191. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-(pyrrolidine-1-carbonyl)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6ac**)

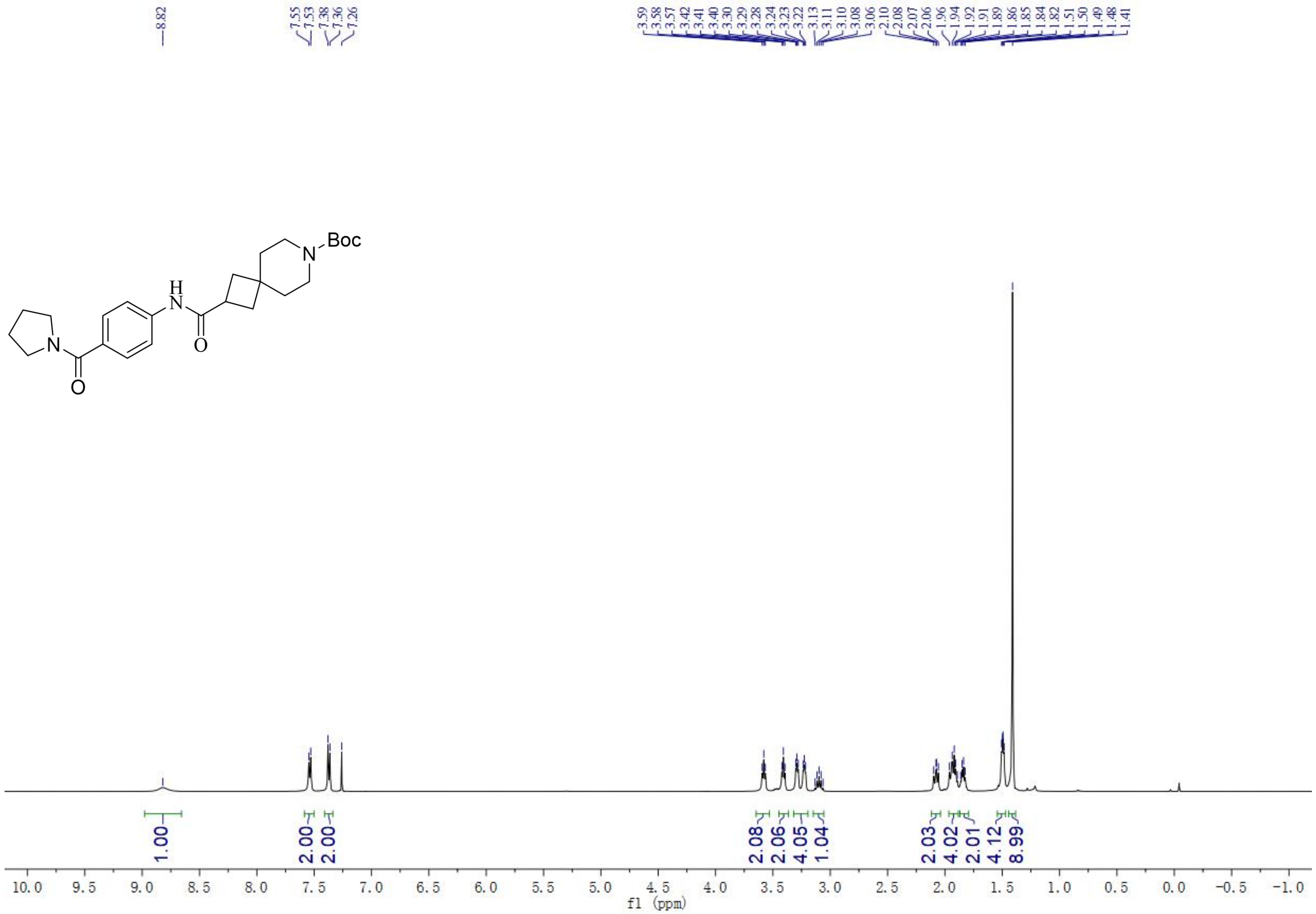


Figure S192. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of -butyl 2-((4-(pyrrolidine-1-carbonyl)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6ac**)

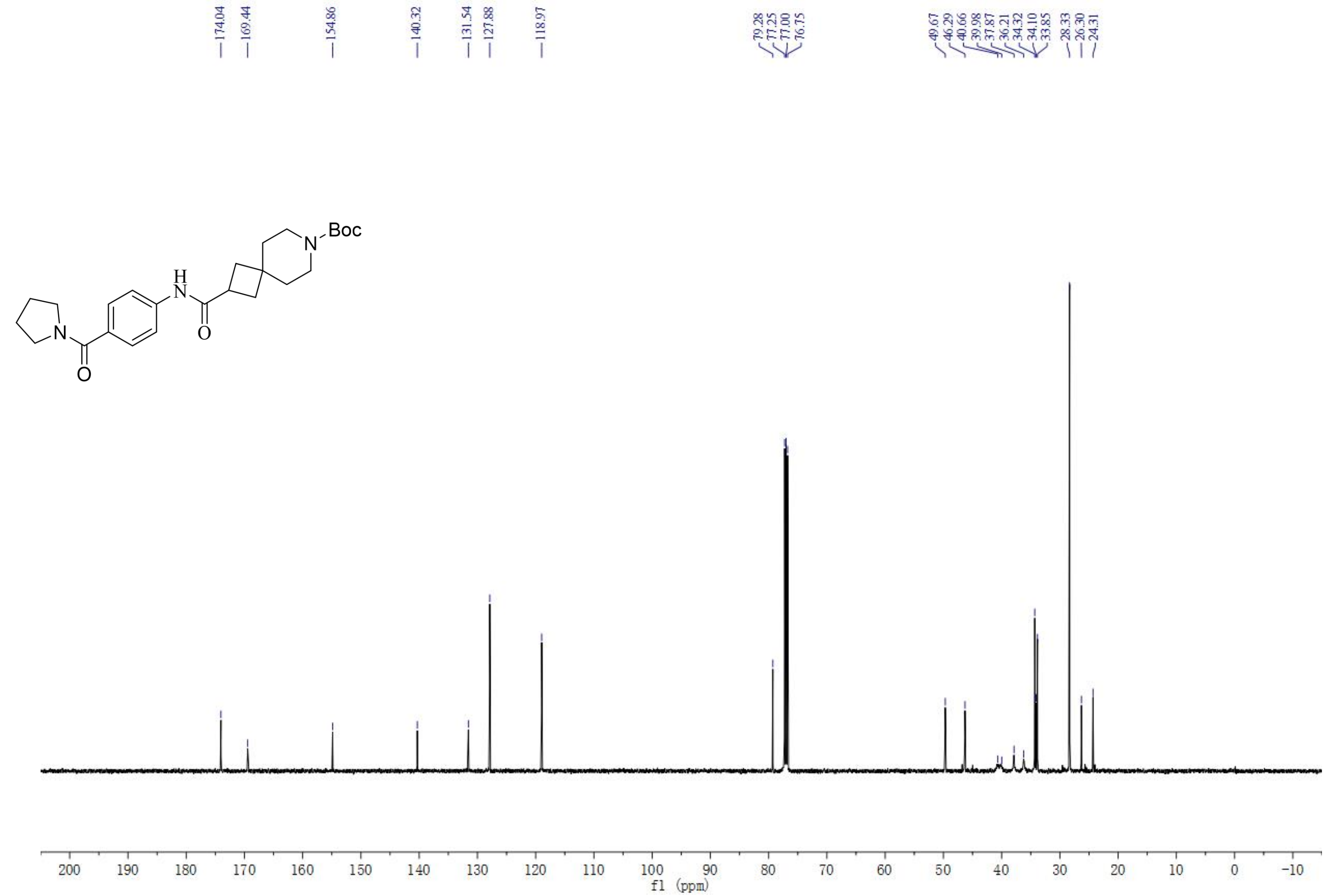


Figure S193. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of *tert*-butyl (*E*)-2-((4-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6ad).**

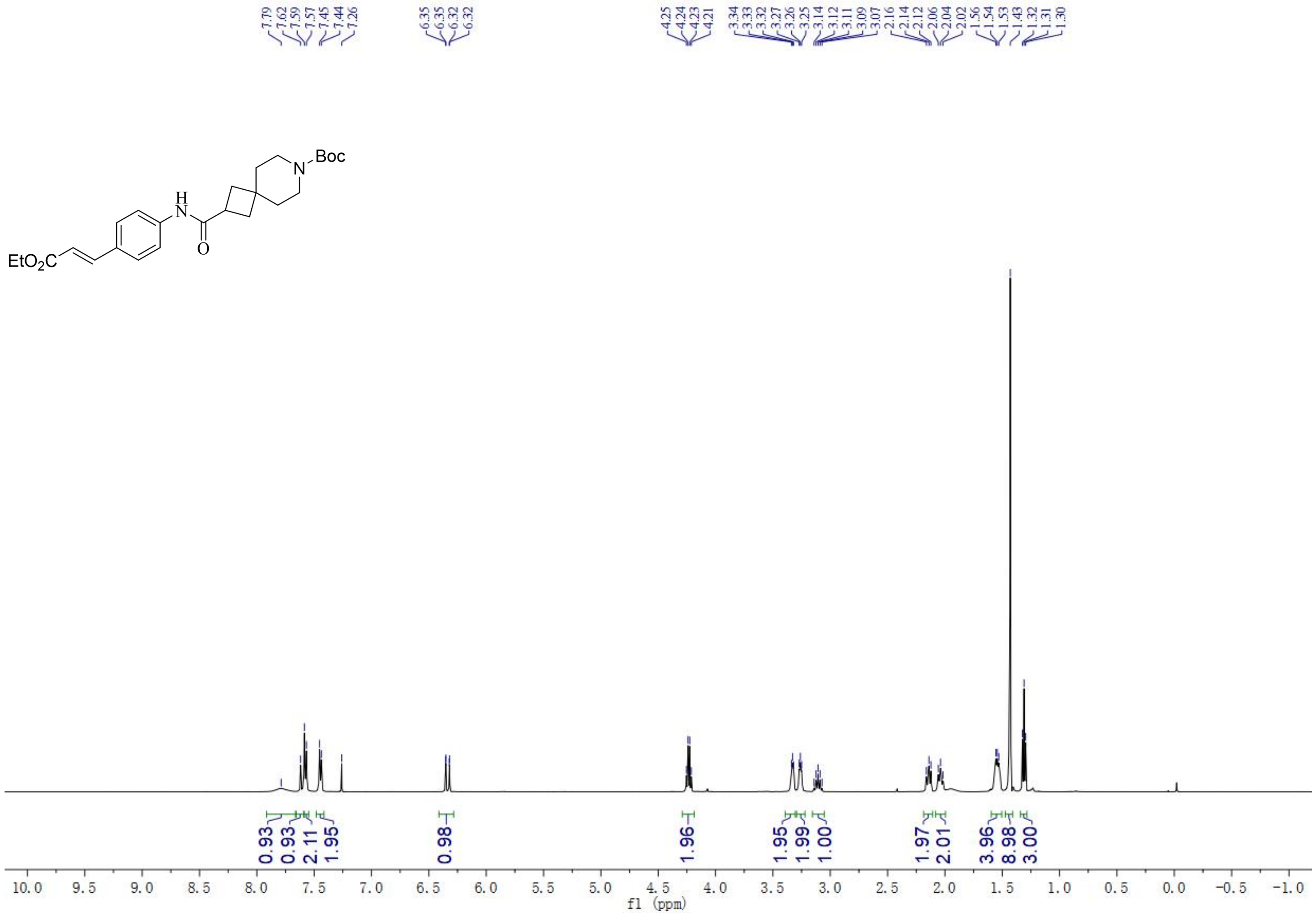


Figure S194. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl (*E*)-2-((4-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6ad).**

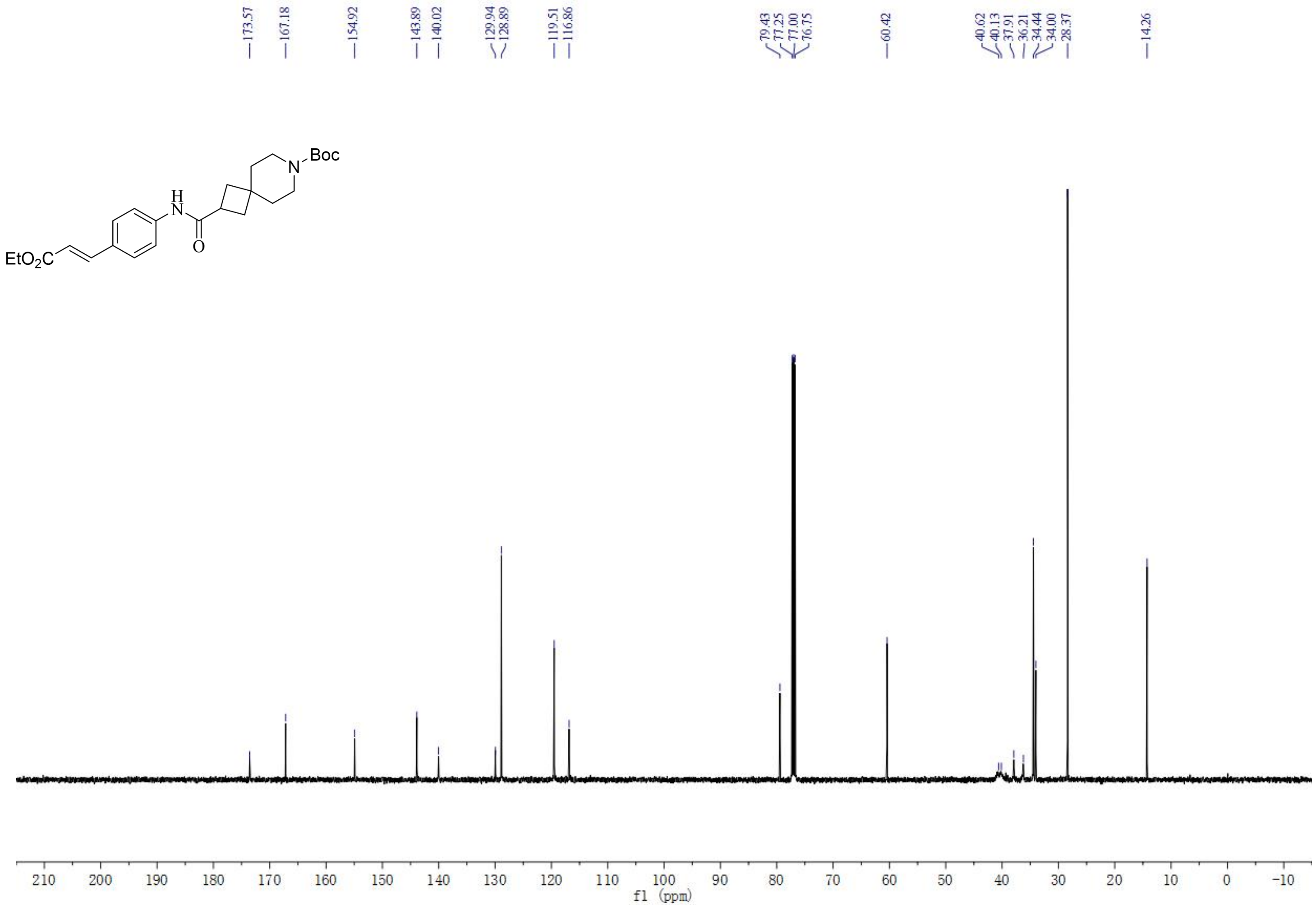


Figure S195. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4'-(5-(p-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6ae**)

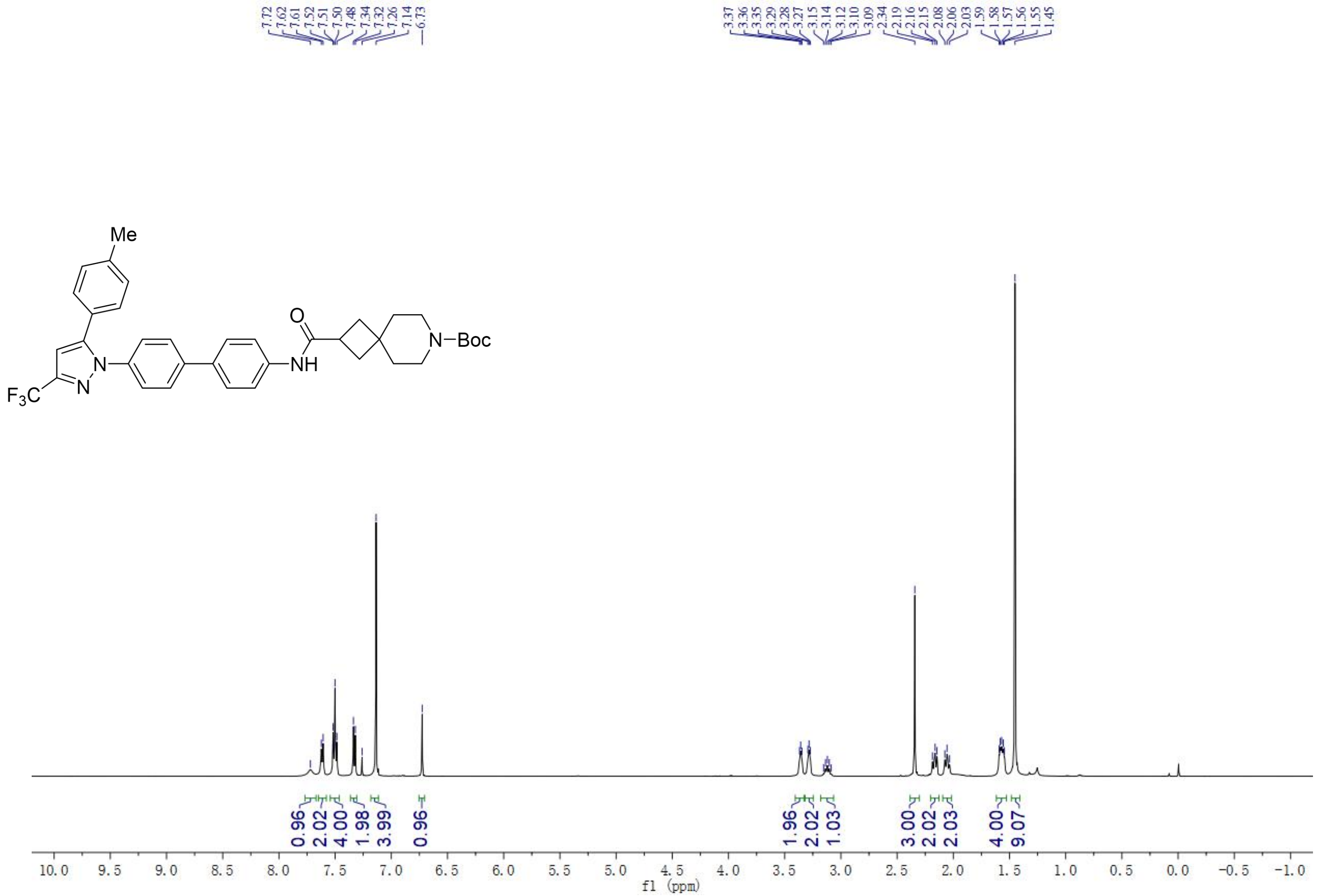


Figure S196. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4'-(5-(p-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate (**6ae**)

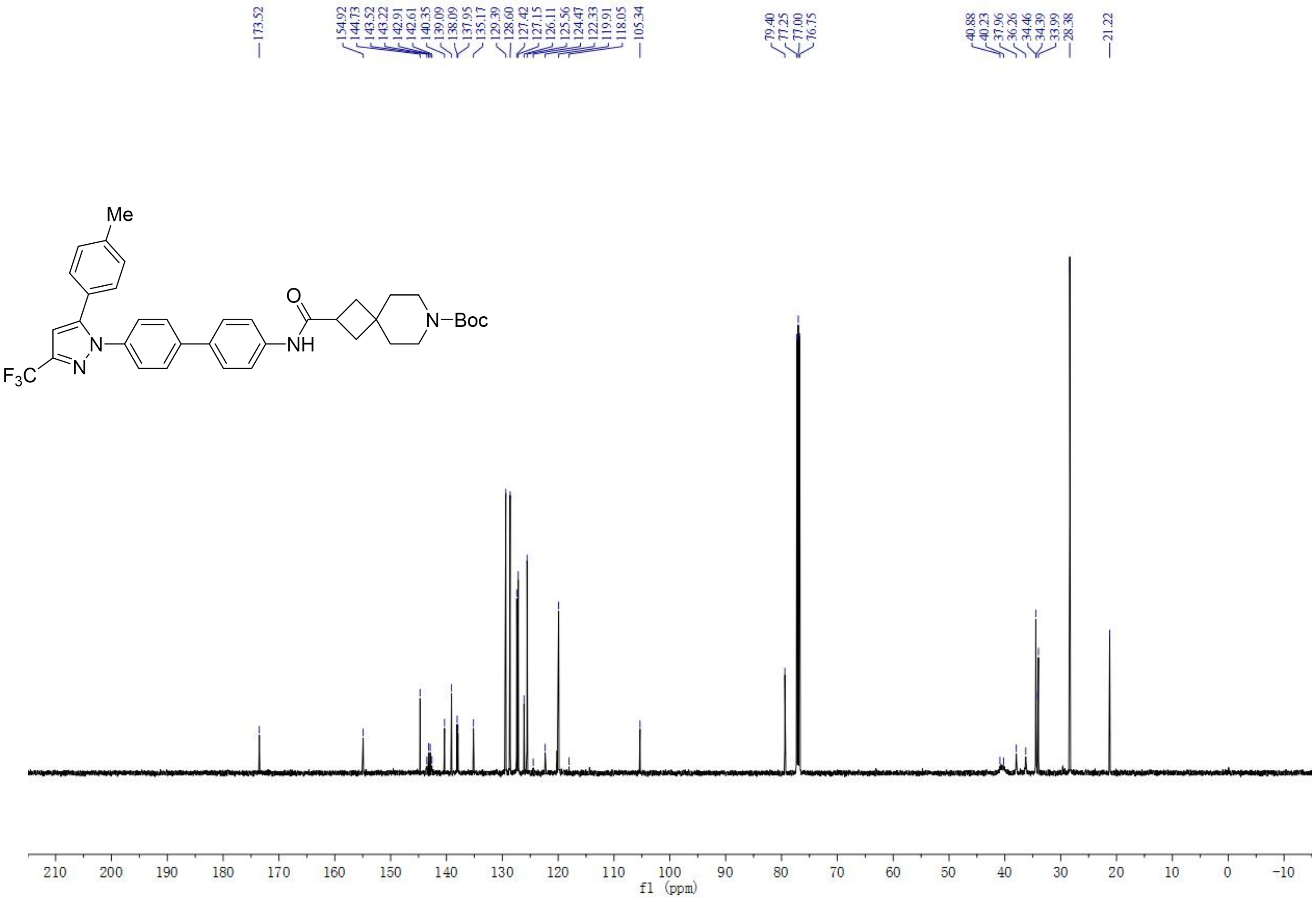
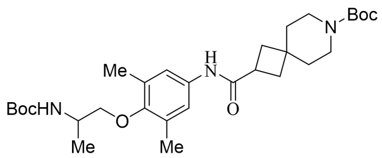


Figure S197. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of *tert*-butyl 2-((4-(2-((*tert*-butoxycarbonyl)amino)propoxy)-3,5-dimethylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6af-2)**.



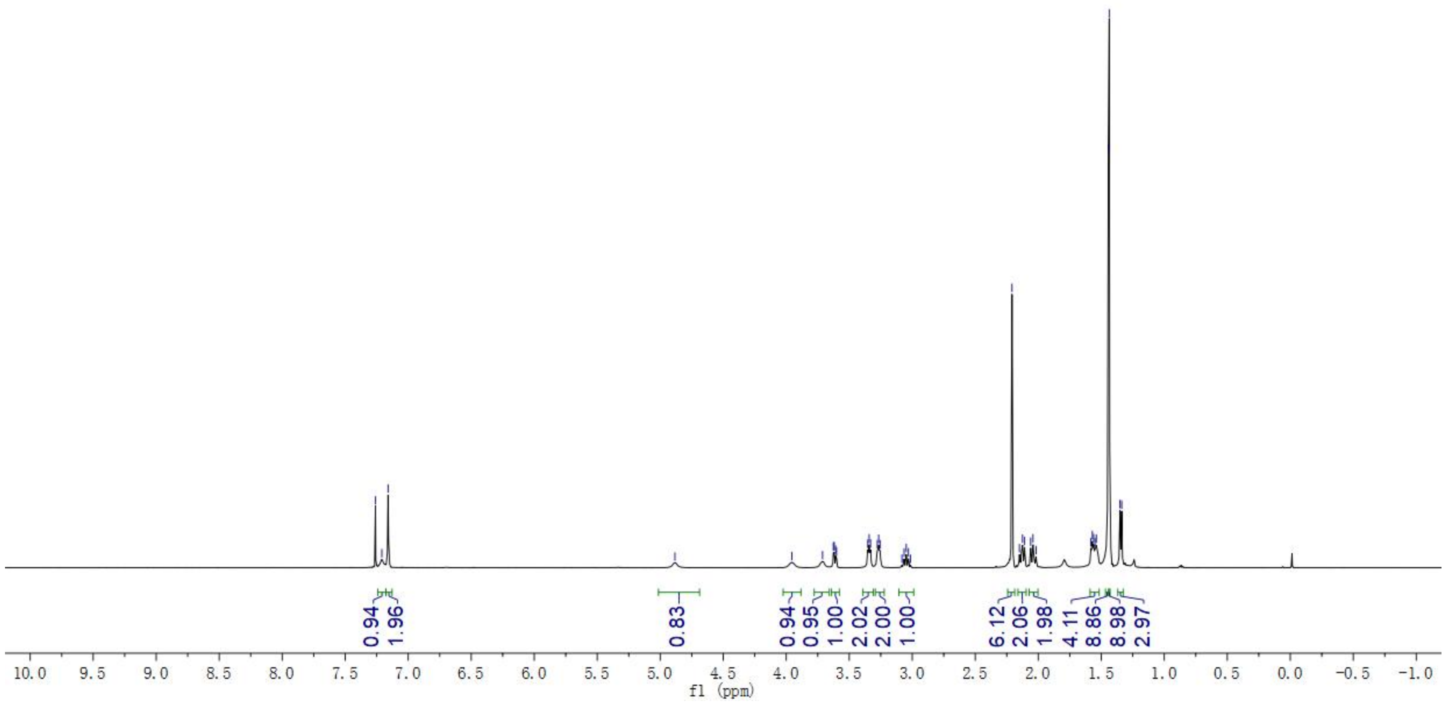


Figure S198. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 2-((4-(2-((*tert*-butoxycarbonyl)amino)propoxy)-3,5-dimethylphenyl)carbamoyl)-7-azaspiro[3.5]nonane-7-carboxylate**(6af-2).**

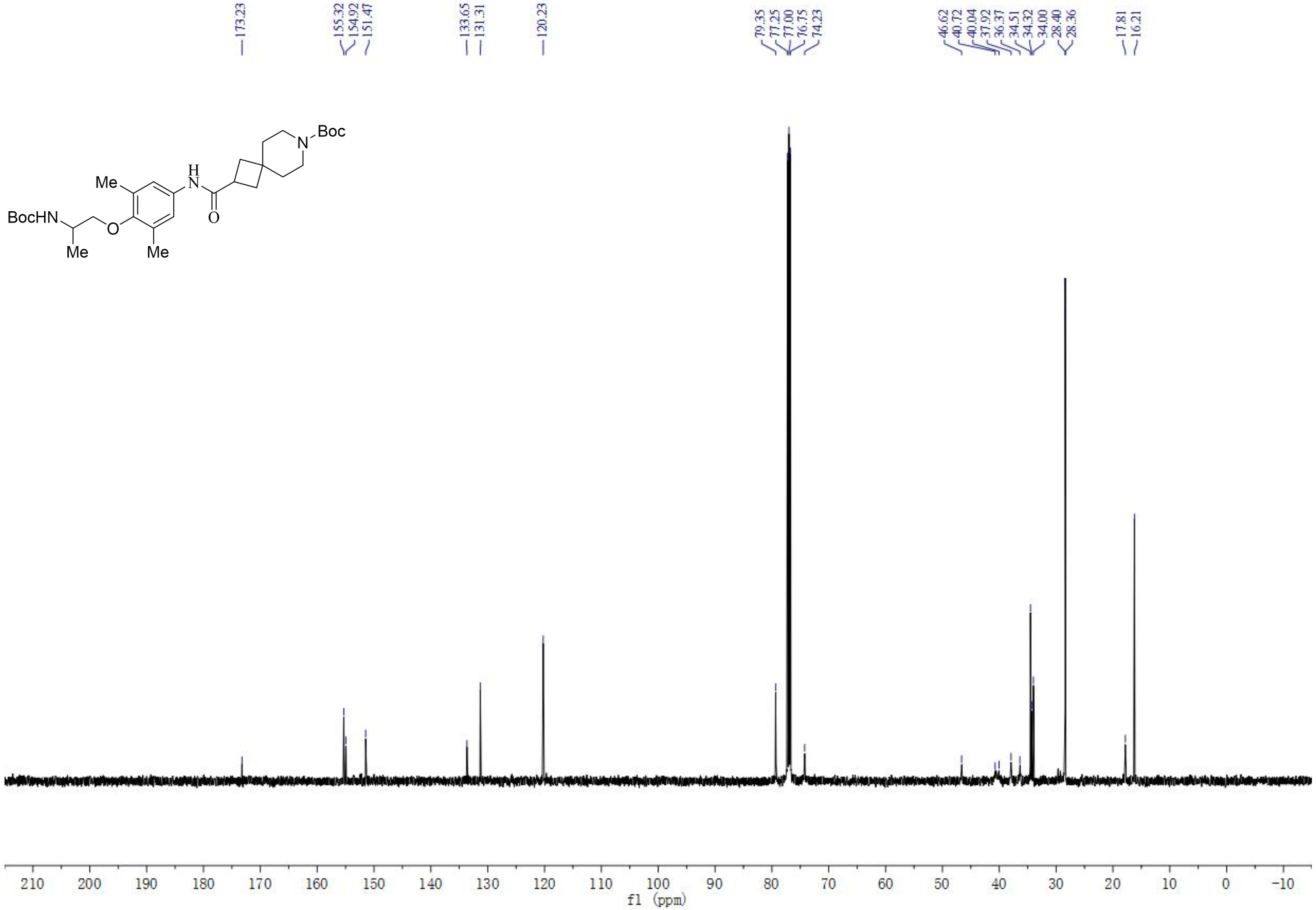


Figure S199. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) of *tert*-butyl 8-oxo-8-(phenylamino)octanoate**(6ag)**

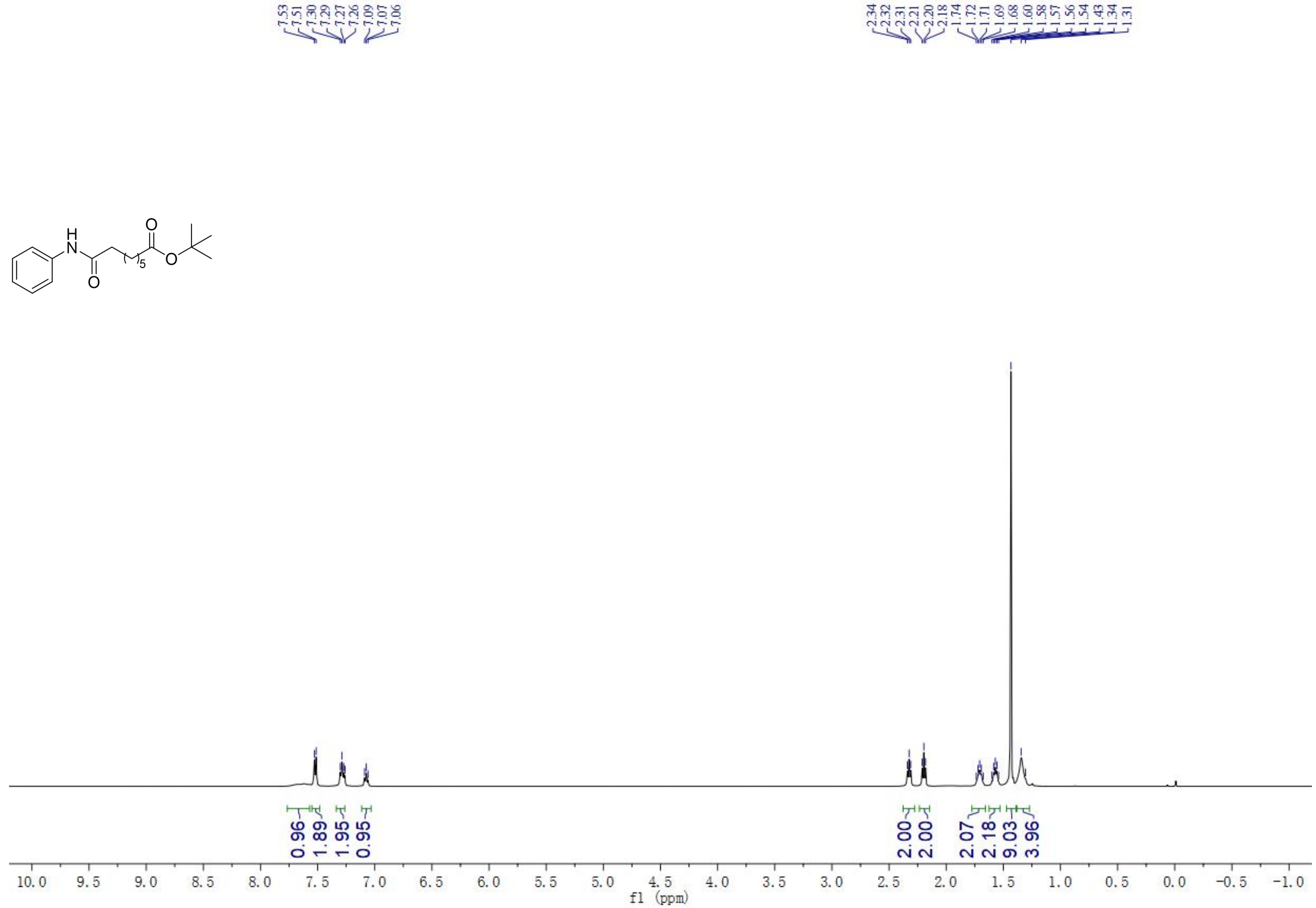
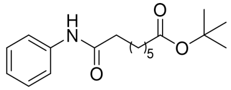


Figure S200. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of *tert*-butyl 8-oxo-8-(phenylamino)octanoate**(6ag)**



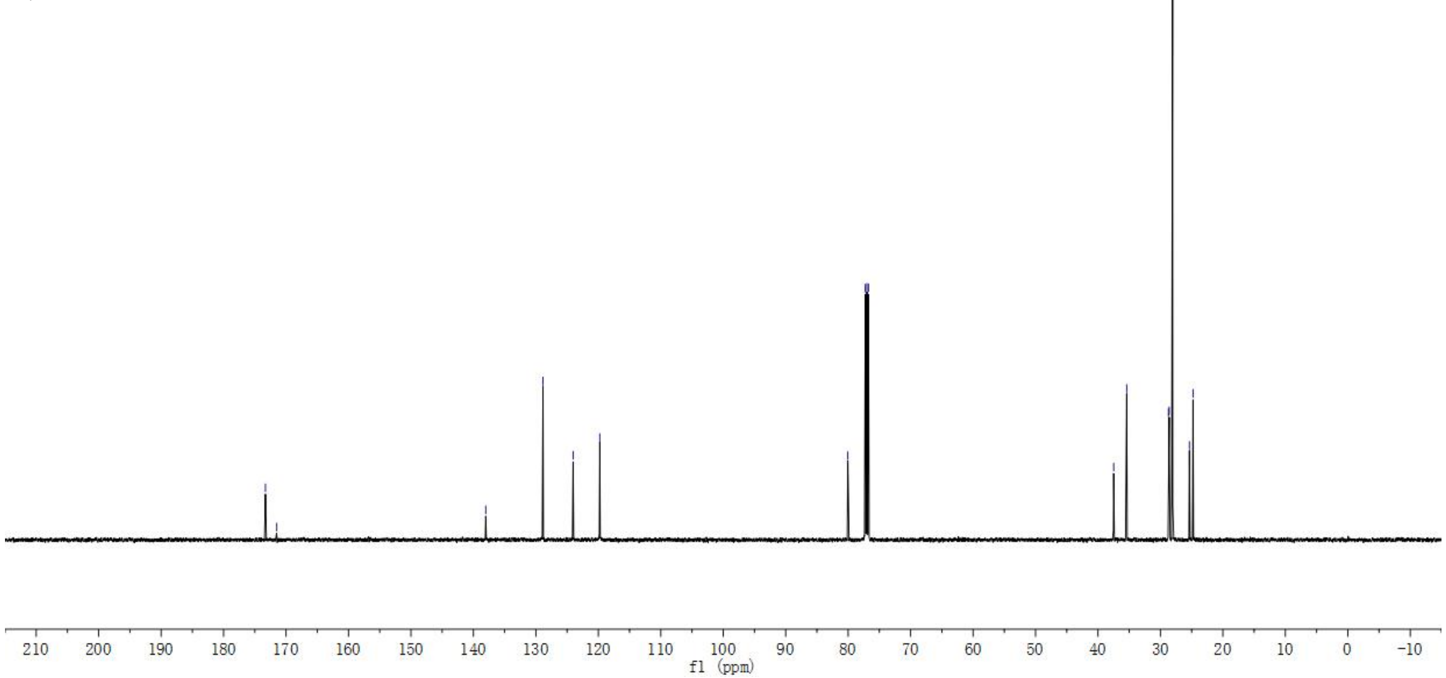
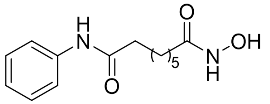


Figure S201. [1]H NMR (500 MHz, DMSO-d_6, 298 K) of N^1-hydroxy-N^8-phenyloctanediamide**(6ag-1)**



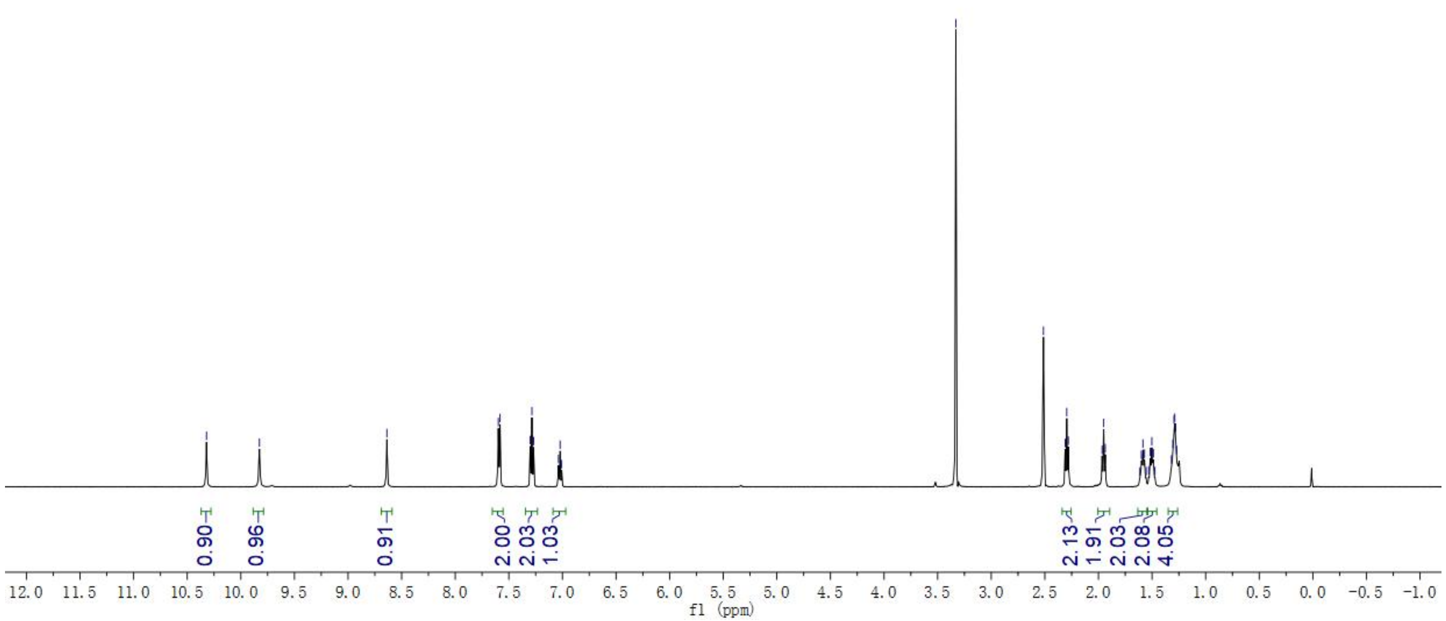


Figure S202. ^{13}C NMR (126 MHz, DMSO-d_6, 298K) of N^1-hydroxy-N^8-phenyloctanediamide**(6ag-1)**

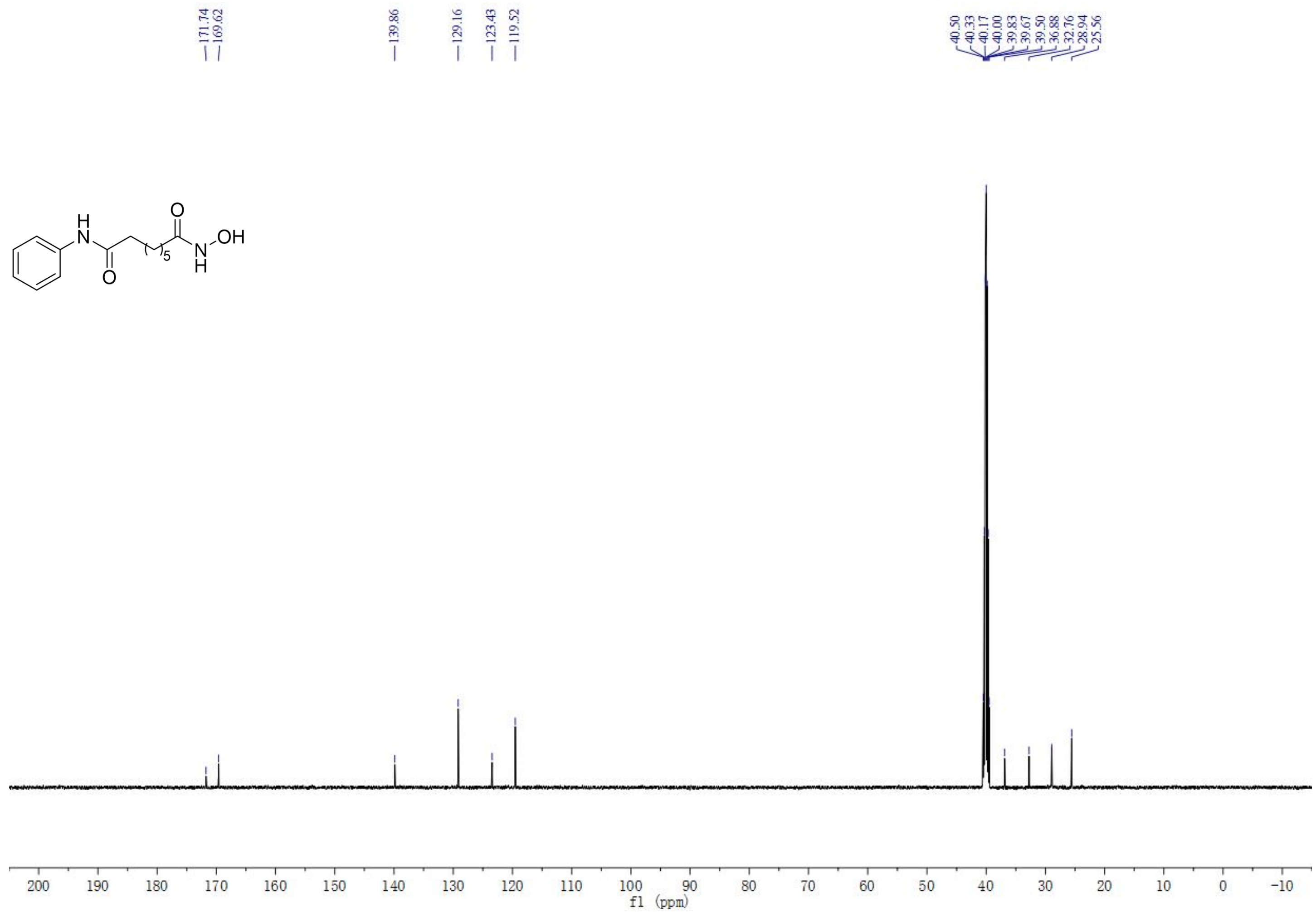


Figure S203. ^{1}H NMR (500 MHz, $CDCl_3$, 298K) of 3-bromo-*N*-cyclohexylbenzamide (**6ah**)

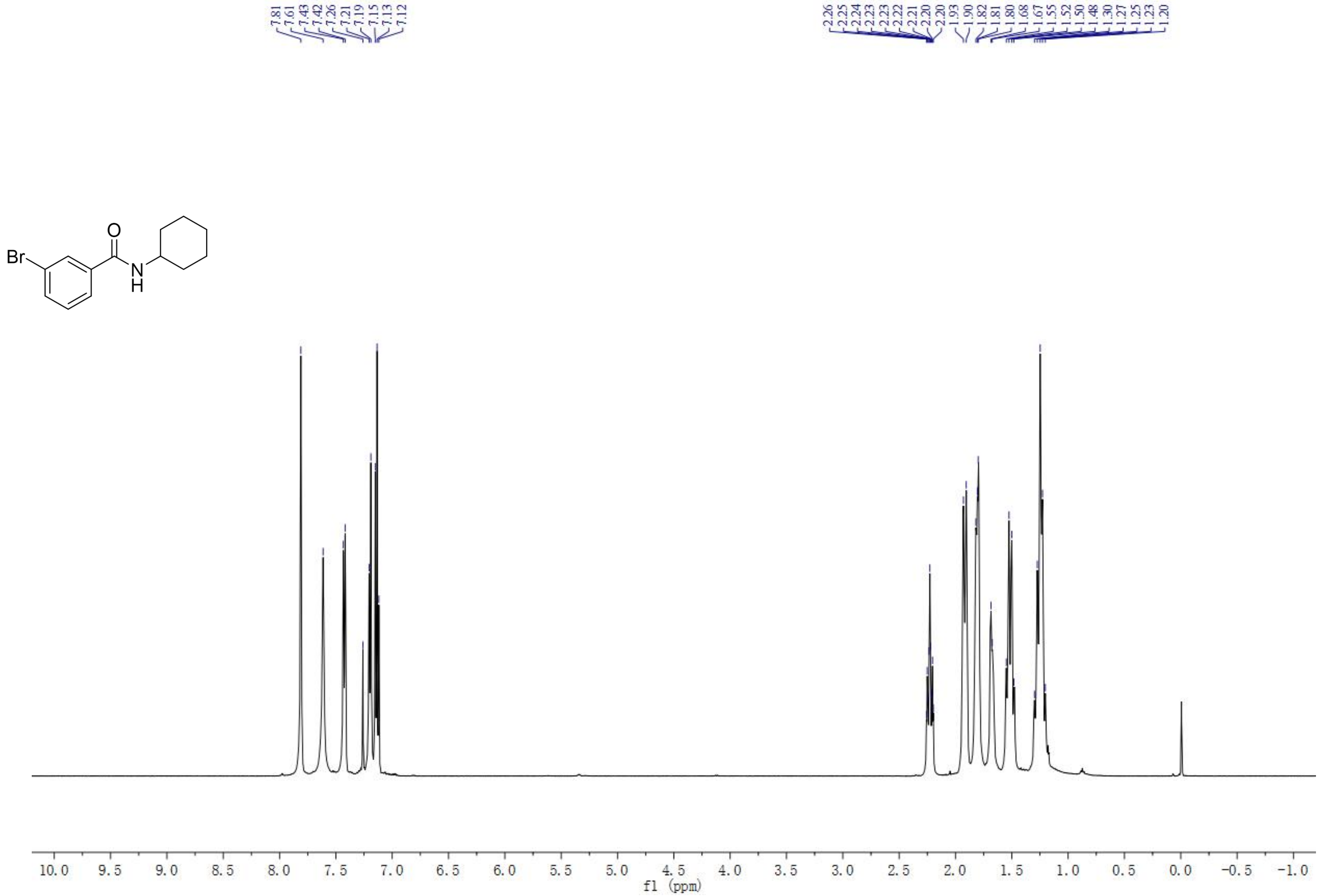


Figure S204 ^13^C NMR (126 MHz, $CDCl_3$, 298K) of 3-bromo-*N*-cyclohexylbenzamide (**6ah**)

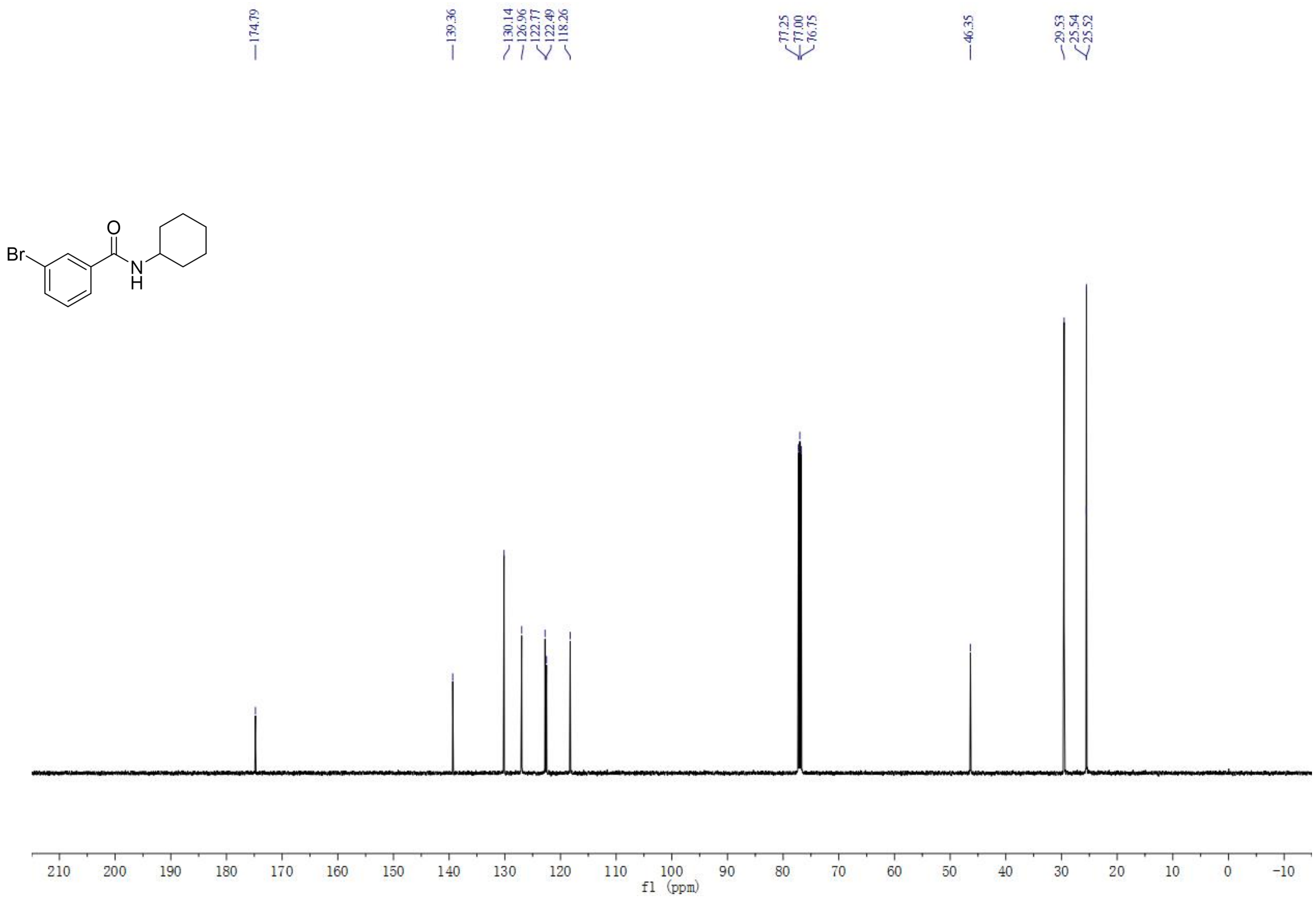


Figure S205. ^{1}H NMR (500 MHz, DMSO-d_6, 298K) of *N*-(3-(1*H*-pyrrolo[2,3-b]pyridin-5-yl)phenyl)cyclohexanecarboxamide (**6ah-1**)

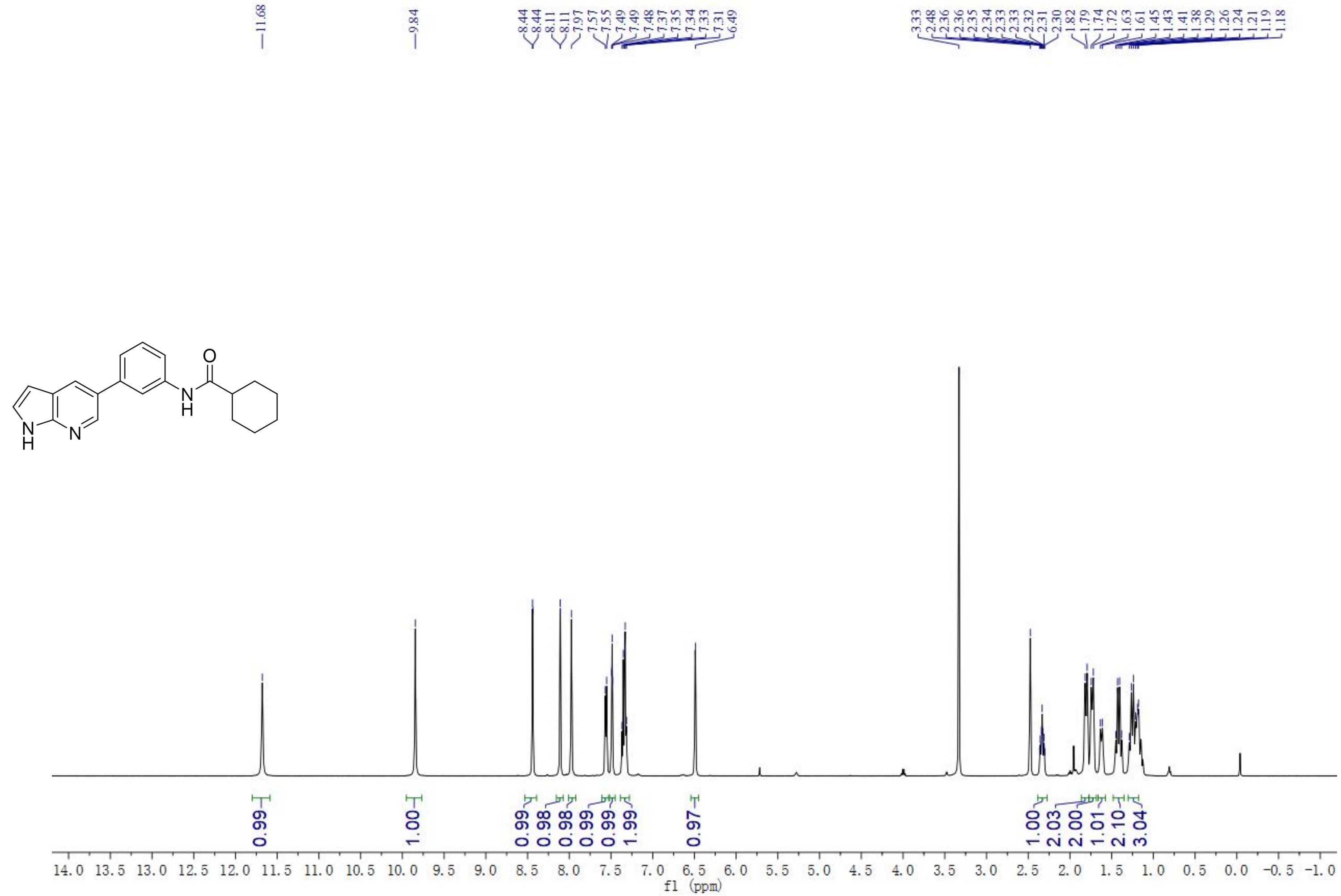


Figure S206. ^{13}C NMR (126 MHz, DMSO-d_6, 298K) of *N*-(3-(1*H*-pyrrolo[2,3-b]pyridin-5-yl)phenyl)cyclohexanecarboxamide (**6ah-1**)

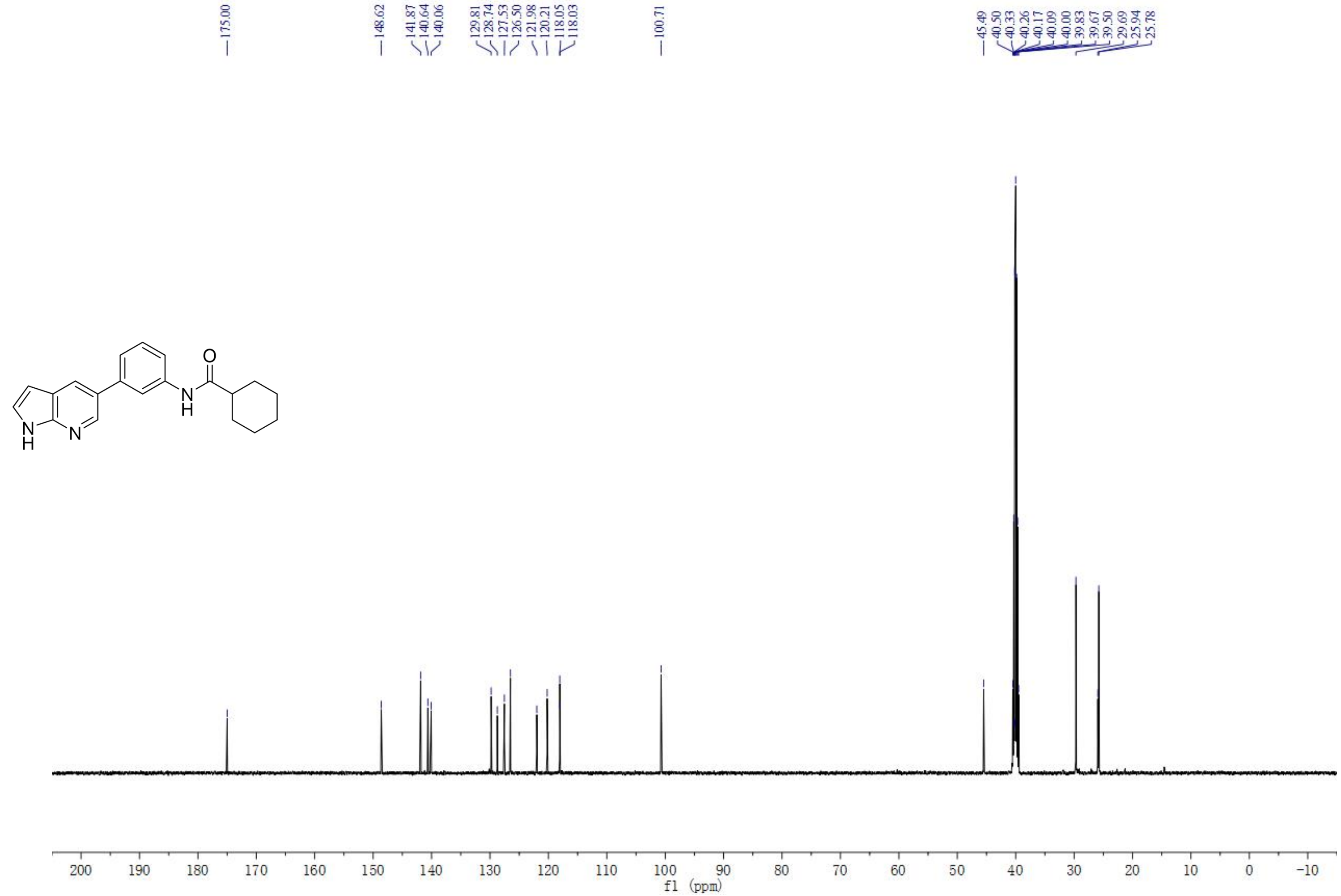


Figure S207. ¹H NMR (500 MHz, $CDCl_3$, 298K) of (2*S*,5*R*)-2-isopropyl-*N*-(4-methoxyphenyl)-5-methylcyclohexane-1-carboxamide (**6am**)

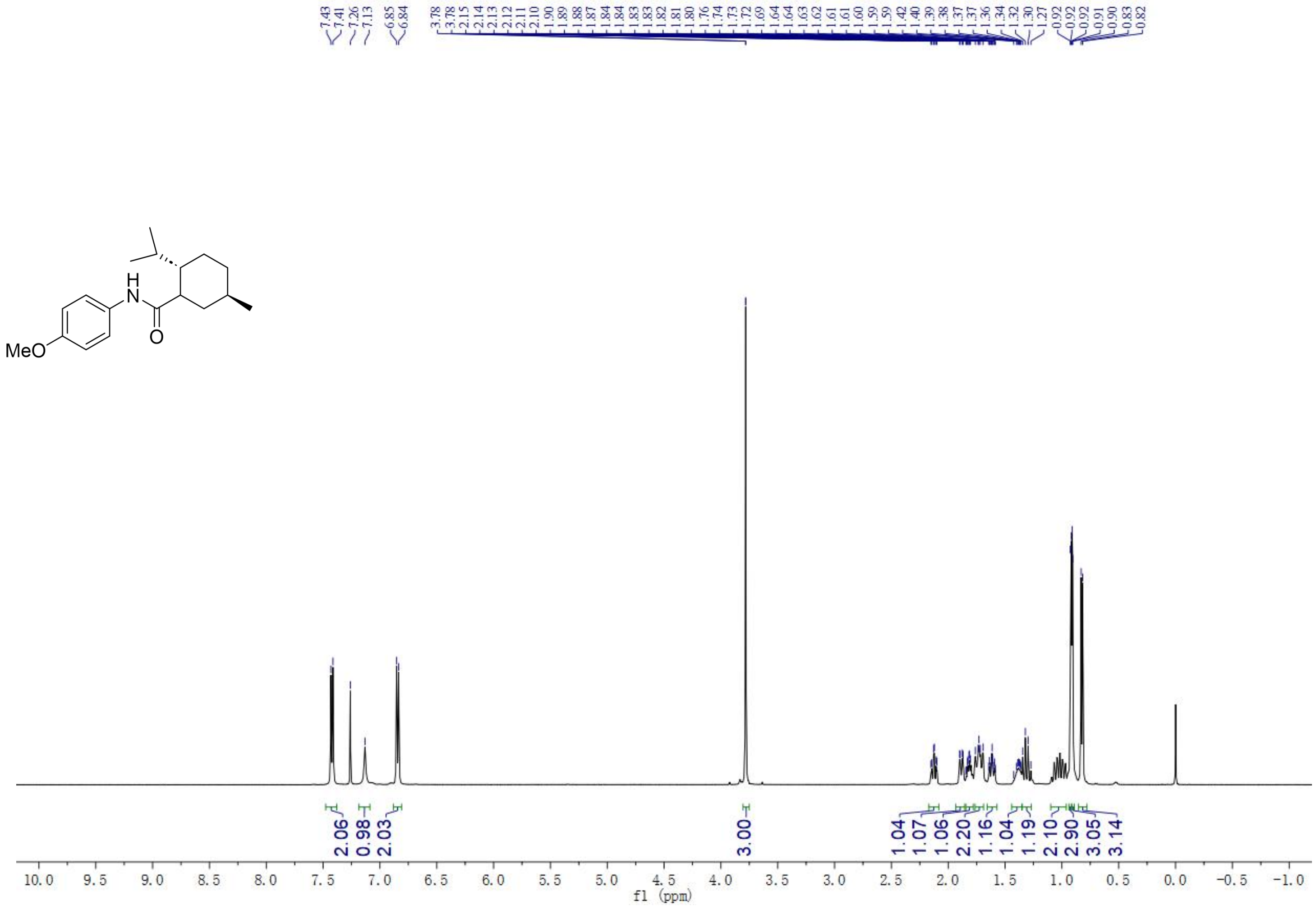


Figure S208. ^{13}C NMR (126 MHz, $CDCl_3$, 298K) of (2*S*,5*R*)-2-isopropyl-*N*-(4-methoxyphenyl)-5-methylcyclohexane-1-carboxamide (**6am**)