Direct Synthesis of Chiral NH Lactams via Ru-catalyzed Asymmetric Reductive Amination/Cyclization Cascade of Keto-Acids/Esters

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Supporting Information

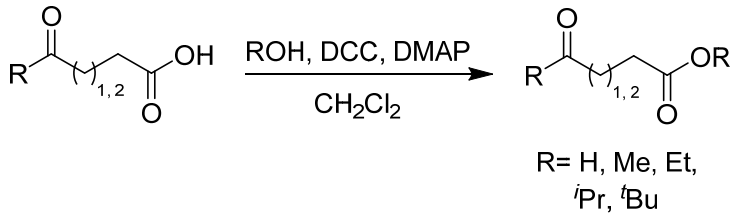
Contents

Ⅰ. General Information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon in a glovebox or using standard Schlenk techniques. Solvents were dried with standard procedures and degassed with N_2. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for ^{1}H NMR, 101 MHz for ^{13}C NMR or a Bruker DPX 500 spectrometer at 500 MHz for ^{1}H NMR, 126 MHz for ^{13}C NMR in $CDCl_3$ or CD_3OD with tetramethylsilane (TMS) as internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Chemical shifts were reported relative to TMS (0.00 ppm) for ^{1}H NMR and relative to $CDCl_3$ (77.00 ppm) or CD_3OD (49.00 ppm) for ^{13}C NMR. GC analysis was carried out on Angilent 1200 Series instrument using achiral capillary columns. Substrates **1ae, 3a**, **5g, 5j** and **3i** were purchased from commercial suppliers and used without further purification. High resolution mass spectra (HRMS) were obtained on Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer. PE refers to petroleum ether, EA refers to ethyl acetate, TFE refers to 2,2,2-trifluoroethanol, and MTBE refers to methyl *tert*-butyl ether.

Ⅱ. General Procedures for the Synthesis of Substrates

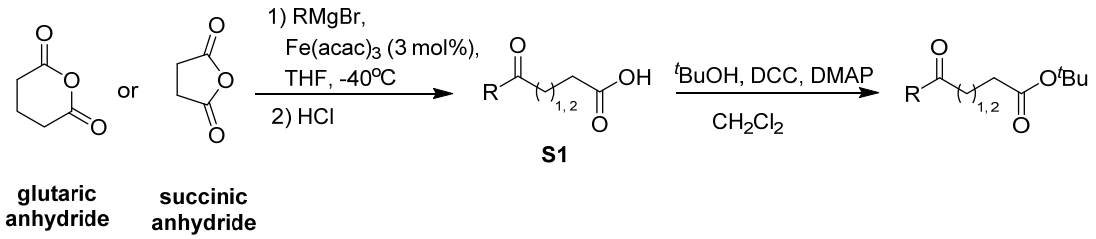
2.1 General Procedure A:



The keto-acid (20 mmol) was dissolved in 20 mL DCM, followed by successively addition of the corresponding alcohol (60 mmol) and DMAP (4-Dimethylaminopyridine, 1.95 g, 16 mmol). DCC (N,N'-Dicyclohexylcarbodiimide, 22 mmol) was then added at 0 ^{o}C. The resulting mixture was stirred at room

temperature for 24 h. Upon completion, the reaction mixture was filtered over a small silica gel column. The filtrate was collected and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=5-10%) to afford the corresponding ester (68-96% yield).

2.2 General Procedure B:



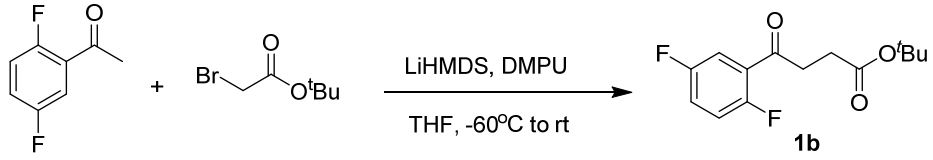
General procedure B was implemented following a reported method with modification.[1]

Under Argon, succinic anhydride (20.0 mmol) or glutaric anhydride (20.0 mmol), $Fe(acac)_3$ (212 mg, 0.6 mmol) were dissolved in 24 mL of THF. The mixture was cooled to -40 ℃. A solution of the corresponding Grignard reagent (20 mmol) in THF was added dropwise over 40 minutes. The resulting mixture was then warmed to room temperature and stirred overnight. Upon completion, the reaction was quenched by slowly addition of 80 mL HCl_{aq} solution (2 M) and the organic layer was extracted with Et_2O (3×40 mL). The combined organic layer was washed with 1 M $NaOH_{aq}$ solution (3×30 mL). The organic layer was discarded and the combined aqueous phases were acidified with 2 M HCl_{aq} solution until the PH value was *ca*. 1. The mixture was then extracted with Et_2O (3×40 mL), and the combined organic layer was dried over anhydrous $NaSO_4$. The solvent was removed under reduced pressure, and the resulting crude keto-acid **S1** was directly used in the next step without further purification.

The keto-acid **S1** obtained from the last step was dissolved in 20 mL DCM, followed by successively addition of *tert*-butyl alcohol (3 equiv) and DMAP (4-Dimethylaminopyridine, 0.8 equiv). DCC (N,N'-Dicyclohexylcarbodiimide, 1.1 euiqv) was then added at 0 °C. The resulting mixture was warmed to room

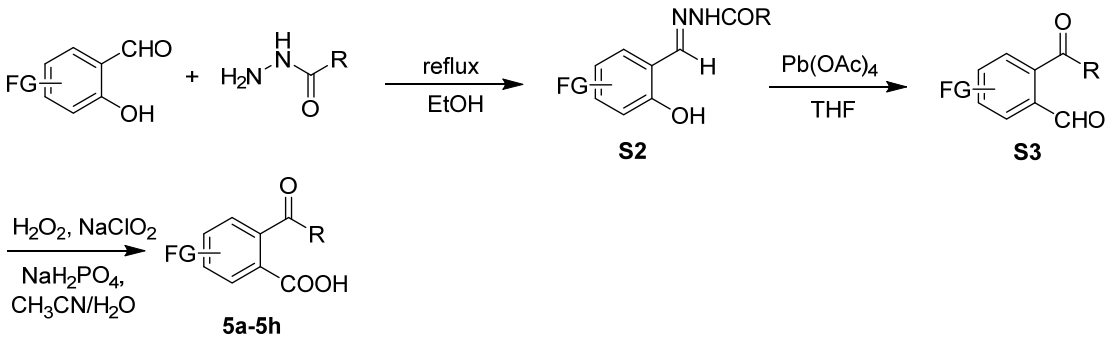
temperature and stirred for 24 h. Upon completion, the reaction mixture was filtered over celite, and the organic layer was collected and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=5-10%) to afford the corresponding easter (10-78% yields overall two steps).

2.3 General Procedure C:



1-(2,5-difluorophenyl)ethan-1-one (4.68 g, 30 mmol) was dissolved in 75 mL THF and 23 mL DMPU (N, N′-Dimethylpropyleneurea), LiHMDS (1.3M in THF, 23.1 mL, 30 mmol) was then added dropwise at -60 ℃. After stirring for 10 min, *tert*-butyl 2-bromoacetate (8.78 g, 45 mmol) was added quickly at the same temperature, and the resulting mixture was continuously stirred for another 10 min. The reaction was warmed to room temperature and stirred for 4 h before quenching with saturated aqueous NH_4Cl. The mixture was diluted with water, then extracted with MTBE (3×100 mL). The combined organic layer was dried over anhydrous $NaSO_4$. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=2%) to afford **1b** (2.84 g, 32% yield).

2.4 General Procedure D:



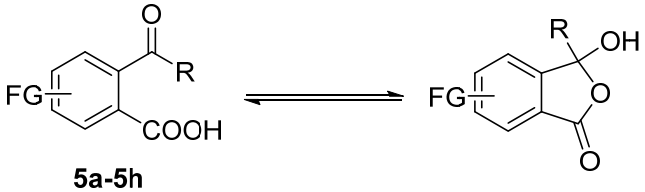
General procedure D was implemented following reported methods with modification.[2][3]

Acethydrazide (10 mmol) was added to a solution of the salicylaldehyde derivative (10 mmol) in EtOH (50 mL). The reaction was heated to reflux for 12 h. Upon completion, the mixture was cooled to room temperature, concentrated and washed with PE. The crude **S2** was directly used in the next step without purification.

Hydrazide **S2** (20 mmol) was dissolved in 100 mL THF, and $Pb(OAc)_4$ (9.76 g, 22 mmol) was added in portions while stirring. The reaction was stirred at room temperature for 2 h. The resulting solid was filtered through a short column of celite, and the filtrate was collected and evaporated under reduced pressure. The residue was dissolved in 300 mL of EA and washed with water (2x50 mL). The combined organic phases were successively washed with saturated aqueous $NaHCO_3$ and brine. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=10%) to afford **S3**.

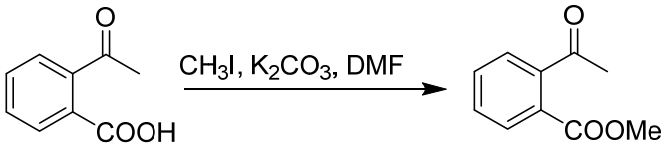
NaH_2PO_4 (480 mg, 3.09 mmol), H_2O_2 (30% in H_2O, 2.2 mL) and $NaClO_2$ (3.24 g, 36 mmol) were successively added to a solution of **S3** (9 mmol) in MeCN (90 mL) and water (7.5 mL) at 0 ℃. The mixture was vigorously stirred at 0 ℃ for 1 h and then diluted with EA (120 mL) and water (75 mL). The organic layer was separated, and the aqueous layer was extracted by EA (3×50 mL). The combined organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered and evaporated. The resulting acid is generally pure enough to use without further purification unless other notification (33-47% overall yield).

Notification： Dependent on the substituent on the benzene ring, free acid **5** may exist in equilibrium with its intramolecular cyclization hemiketal at rt.[4]



5a-5h

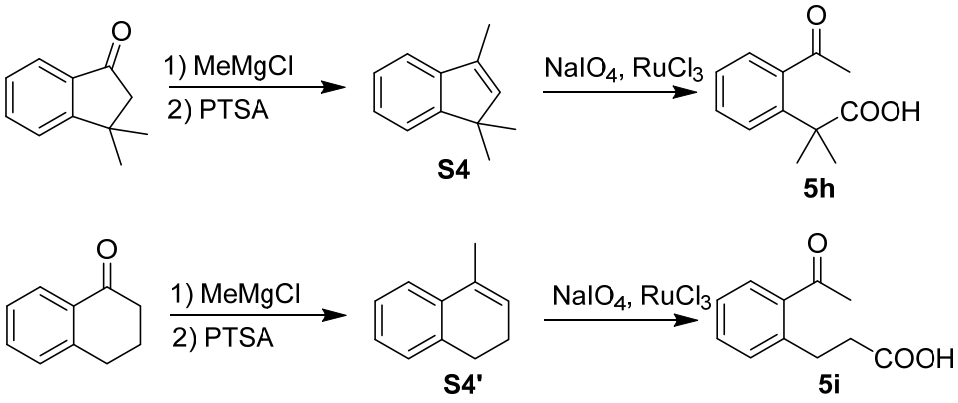
Synthesis of **5ab**.



5a **5ab**

2-Propionylbenzoic acid (**5a**, 1.0g, 6 mmol), K_2CO_3 (1.3g, 9 mmol) were dissolved in 5 mL DMF. CH_3I (2.6g, 18mmol) in 4 mL DMF was added over 10 min and then stirred for 3 h at room temperature. Upon completion, DMF was removed under vacuum. The residue was dissolved in DCM (60 mL), and washed with water for 3 times (3x10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=10%) to afford **5 ba** in 92% yield.

2.5 General Procedure E:



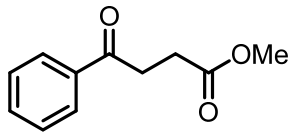
General procedure E was implemented following a reported method with modification.[5]

Benzo-fused ketone (20 mmol) was dissolved in 40 mL THF, followed by slow addition of 10 mL MeMgCl (3M in THF) at 0 ℃. The reaction was warmed to room temperature and stirred for 2 h. The reaction was quenched by saturated aqueous NH_4Cl, diluted with water, and then extracted with EA (3×50 mL). The combined organic layers were dried over anhydrous $NaSO_4$, filtrated and evaporated under reduced pressure. The residue was dissolved in 50 mL MeOH, followed by slow addition of PTSA (*p*-toluenesulfonic acid, 1 mmol). The resulting mixture was heated

to reflux for 3 h. The reaction was then cooled to room temperature, and the solvent was removed under vacuum. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=10%) to afford **S4** or **S4'**.

S4 or **S4'** (16.8 mmol) and $NaIO_4$ (84 mmol) were dissolved in 100 mL mixed solvent (CCl_4/MeCN/H_2O = 3/3/4 and stirred at rt for 15 min. $RuCl_3$ (0.42 mmol x 2) was then added every 30 min. Upon completion, the reaction mixture was filtered through a short column of celite. The filtrate was washed with 1 M $NaOH_{aq}$ solution (3×50 mL). The organic layer was discarded and the combined aqueous basic phase was acidified with 12 M HCl_{aq} solution until the PH value reached *ca.* 1. The mixture was then extracted with EA (3×40 mL), and the combined organic layers were dried over anhydrous $NaSO_4$, filtered and evaporated under reduced pressure. The resulting acid **5h** (42% yield) or **5i** (34% yield) was pure enough to use and analyze.

2.6 Characterization data of substrates

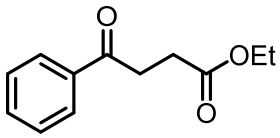


1aa

Chemical Formula: $C_{11}H_{12}O_3$
Exact Mass: 192.0786

Methyl 4-oxo-4-phenylbutanoate (1aa)

Followed by **General procedure A**. Light yellow oil, 3.68 g, 96% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 3.71 (s, 3H), 3.33 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 198.0, 173.3, 136.4, 133.2, 128.6, 128.0, 51.8, 33.3, 27.9. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{13}O_3^+$ 193.0859; Found 193.0860.

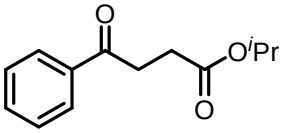


1ab

Chemical Formula: $C_{12}H_{14}O_3$
Exact Mass: 206.0943

Ethyl 4-oxo-4-phenylbutanoate (1ab)

Followed by **General procedure A**. Light yellow oil, 3.91g, 95% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.99 (d, *J* = 8.5 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.32 (t, *J* = 6.6 Hz, 2H), 2.76 (t, *J* = 6.7 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.1, 172.9, 136.5, 133.2, 128.6, 128.0, 60.6, 33.4, 28.3, 14.2. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}O_3^+$ 207.1016; Found 207.1016.

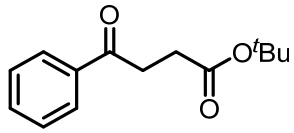


1ac

Chemical Formula: $C_{13}H_{16}O_3$
Exact Mass: 220.1099

***Iso*propyl 4-oxo-4-phenylbutanoate (1ac)**

Followed by **General procedure A**. Light yellow oil, 3.96 g, 90% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), δ 5.10 – 4.96 (hept, *J* = 6.2 Hz, 1H), 3.31 (t, *J* = 6.6 Hz, 2H), 2.73 (t, *J* = 6.5 Hz, 2H), 1.25 (d, *J* = 6.2 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 197.0, 172.1, 136.3, 132.9, 128.3, 127.7, 67.6, 33.1, 28.3, 21.5. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{17}O_3^+$ 221.1172; Found 221.1173.

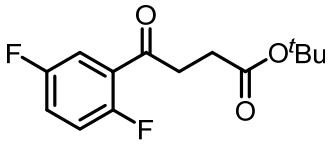


1ad

Chemical Formula: $C_{14}H_{18}O_3$
Exact Mass: 234.1256

***Tert*-butyl 4-oxo-4-phenylbutanoate (1ad)**

Followed by **General procedure A**. Light yellow oil, 3.98 g, 82% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.47 (d, J = 7.8 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.68 (t, J = 6.7 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.3, 172.1, 136.7, 133.1, 128.5, 128.0, 80.5, 33.4, 29.4, 28.0. HRMS (ESI), m/z: $[M+H]^+$, Calcd for $C_{14}H_{19}O_3^+$ 235.1329; Found: 235.1327.

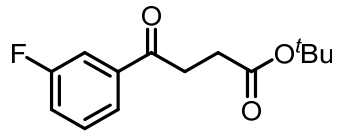


1b

Chemical Formula: $C_{14}H_{16}F_2O_3$
Exact Mass: 270.1068

***Tert*-butyl 4-(2,5-difluorophenyl)-4-oxobutanoate (1b)**

Followed by **General procedure C**. Light yellow oil, 2.56 g, 32% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61-7.51 (m, 1H), 7.25-7.18 (m, 1H), 7.17-7.08 (m, 1H), 3.22-3.26(m, 2H), 2.67 (t, J = 6.4 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) δ 195.3 (d, J_{CF} = 4.6 Hz), 171.7, 158.5 (dd, J_{CF} = 244.6, 2.1 Hz), 158.0 (dd, J_{CF} = 250.7, 2.1 Hz), 126.2 (dd, J_{CF} = 15.9, 6.3 Hz), 121.2 (dd, J_{CF} = 24.6, 9.4 Hz), 118.1 (dd, J_{CF} = 27.2, 7.9 Hz), 116.4 (dd, J_{CF} = 25.1, 3.3 Hz), 80.5, 38.2 (d, J_{CF} = 8.7 Hz), 29.26 (d, J_{CF} = 2.2 Hz), 27.93. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{16}F_2NaO_3^+$ 293.0960; Found 293.0961.

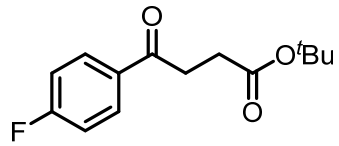


1c

Chemical Formula: $C_{14}H_{17}FO_3$
Exact Mass: 252.1162

***Tert*-butyl 4-(3-fluorophenyl)-4-oxobutanoate (1c)**

Followed by **General procedure A**. Light yellow oil, 3.42 g, 68% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.73 (m, 1H), 7.66 (m, 1H), 7.45 m, 1H), 7.26 (m, 1H), 3.23 (t, J = 6.6 Hz, 2H), 2.69 (t, J = 6.6 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 197.0 (d, J_{CF} = 2.1 Hz), 171.9, 162.8 (d, J_{CF} = 247.8 Hz), 138.7 (d, J_{CF} = 6.2 Hz), 130.2 (d, J_{CF} = 7.6 Hz), 123.7 (d, J_{CF} = 3.1 Hz), 120.0 (d, J_{CF} = 21.5 Hz), 114.7 (d, J_{CF} = 22.2 Hz), 80.6, 33.5, 29.2, 28.0. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}FNaO_3^+$ 275.1054; Found 275.1053.

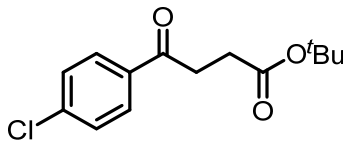


1d

Chemical Formula: $C_{14}H_{17}FO_3$
Exact Mass: 252.1162

***Tert*-butyl 4-(4-fluorophenyl)-4-oxobutanoate (1d)**

Followed by **General procedure B**. White solid, 806 mg, 16% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-7.96 (m, 2H), 7.18-7.08 (m, 2H), 3.23 (t, J = 6.6 Hz, 2H), 2.68 (t, J = 6.6 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 196.7, 172.0, 165.7 (d, J_{CF} = 254.6 Hz), 133.1 (d, J_{CF} = 3.1 Hz), 130.6 (d, J_{CF} = 9.3 Hz), 115.6 (d, J_{CF} = 21.9 Hz), 80.6, 33.3, 29.4, 28.0. HRMS (ESI) m/z: $[M+Na]^+$, Calcd for $C_{14}H_{17}FNaO_3^+$ 275.1054; Found 275.1054.

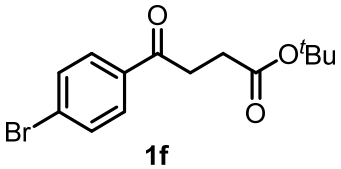


1e

Chemical Formula: $C_{14}H_{17}ClO_3$
Exact Mass: 268.0866

***Tert*-butyl 4-(4-chlorophenyl)-4-oxobutanoate (1e)**

Followed by **General procedure A**. Yellowish solid, 4.28 g, 80% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.87 (m, 2H), 7.47-7.37 (m, 2H), 3.22 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 1.45 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-d) δ 197.1, 171.9, 139.5, 135.0, 129.4, 128.8, 80.6, 33.4, 29.3, 28.0. HRMS (ESI) m/z: $[M+Na]^+$, Calcd for $C_{14}H_{17}ClNaO_3^+$ 291.0758; Found: 291.0760.

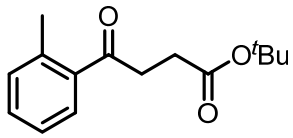


1f

Chemical Formula: $C_{14}H_{17}BrO_3$
Exact Mass: 312.0361

***Tert*-butyl 4-(4-bromophenyl)-4-oxobutanoate (1f)**

Followed by **General procedure A**. Yellowish solid, 1.50 g, 24% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.81 (m, 2H), 7.63-7.56 (m, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.68 (t, *J* = 6.6 Hz, 2H), 1.45 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-d) δ 197.3, 171.9, 135.3, 131.8, 129.5, 128.2, 80.6, 33.3, 29.2, 28.0. HRMS (ESI) m/z: ($[M+Na]^+$) Calcd for $C_{14}H_{17}BrNaO_3^+$ 335.0253; Found 335.0255.

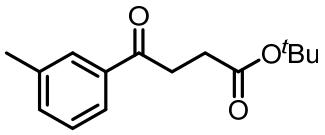


1g

Chemical Formula: $C_{15}H_{20}O_3$
Exact Mass: 248.1412

***Tert*-butyl 4-oxo-4-(o-tolyl)butanoate (1g)**

Followed by **General procedure B**. Light yellow oil, 1.19 g, 24% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.66 (m, 1H), 7.40-7.31 (m, 1H), 7.30-7.19 (m, 2H), 3.15 (t, *J* = 6.6 Hz, 2H), 2.65 (t, *J* = 6.6 Hz, 2H), 2.48 (s, 3H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 202.2, 172.0, 137.9, 137.7, 131.8, 131.1, 128.3, 125.6, 80.4, 36.2, 29.6, 28.0, 21.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}NaO_3^+$ 271.1305; Found 271.1305.

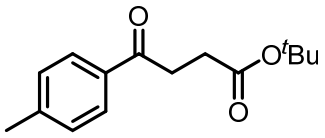


1h

Chemical Formula: $C_{15}H_{20}O_3$
Exact Mass: 248.1412

***Tert*-butyl 4-oxo-4-(m-tolyl)butanoate (1h)**

Followed by **General procedure B**. Light yellow oil, 3.87 g, 78% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.73 (m, 2H), 7.40-7.29 (m, 2H), 3.24 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 3H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.4, 172.1, 138.3, 136.7, 133.8, 128.5, 128.4, 125.2, 80.5, 33.5, 29.4, 28.0, 21.3. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}NaO_3^+$ 271.1305; 271.1305.

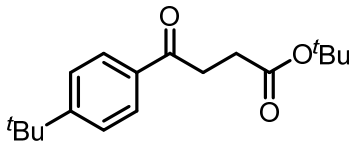


1i

Chemical Formula: $C_{15}H_{20}O_3$
Exact Mass: 248.1412

***Tert*-butyl 4-oxo-4-(p-tolyl)butanoate (1i)**

Followed by **General procedure B**.Yellowish solid, 2.78 g, 56% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 3.23 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 3H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 197.9, 172.2, 143.8, 134.2, 129.2, 128.1, 80.5, 33.3, 29.4, 28.0, 21.6. HRMS (ESI) m/z: 271.1304 $[M+Na]^+$ Calcd for $C_{15}H_{20}NaO_3^+$ 271.1305; Found 271.1305.

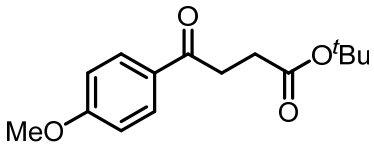


1j

Chemical Formula: $C_{18}H_{26}O_3$
Exact Mass: 290.1882

***Tert*-butyl 4-(4-(tert-butyl)phenyl)-4-oxobutanoate (1j)**

Followed by **General procedure B**. Light yellow oil, 2.32 g, 40% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.90 (m, 2H), 7.50-7.44 (m, 2H), 3.24 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H), 1.45 (s, 9H), 1.34 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 197.9, 172.2, 156.7, 134.1, 127.9, 125.4, 80.4, 35.0, 33.3, 31.0, 29.5, 28.0. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{18}H_{26}NaO_3^+$ 313.1774; Found 313.1775.

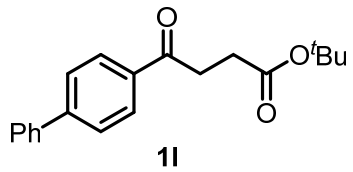


1k

Chemical Formula: $C_{15}H_{20}O_4$
Exact Mass: 264.1362

***Tert*-butyl 4-(4-methoxyphenyl)-4-oxobutanoate (1k)**

Followed by **General procedure B**. Yellowish solid, 1.74 g, 33% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.92 (m, 2), 6.98-6.89 (m, 2H), 3.87 (s, 3H), 3.21 (t, *J* = 6.7 Hz, 2H), 2.67 (t, *J* = 6.7 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 196.8, 172.3, 163.4, 130.2, 129.8, 113.6, 80.5, 55.4, 33.0, 29.5, 28.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{21}O_4^+$: 265.1434; Found 265.1433.

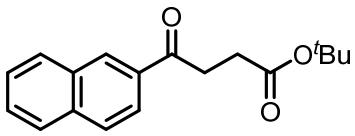


1l

Chemical Formula: $C_{20}H_{22}O_3$
Exact Mass: 310.1569

***Tert*-butyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (1l)**

Followed by **General procedure A**. White solid, 1.05 g, 17% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.10-8.02 (m, 2H), 7.72-7.58 (m, 4H), 7.51-7.37 (m, 3H), 3.29 (t, *J* = 6.7 Hz, 2H), 2.71 (t, *J* = 6.7 Hz, 2H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 197.9, 172.2, 145.7, 139.8, 135.4, 128.9, 128.6, 128.2, 127.2, 127.2, 80.6, 33.5, 29.5, 28.1. RMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{22}NaO_3^+$ 333.1461; Found 303.1452.

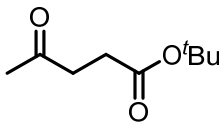


1m

Chemical Formula: $C_{18}H_{20}O_3$
Exact Mass: 284.1412

***Tert*-butyl 4-(naphthalen-2-yl)-4-oxobutanoate (1m)**

Followed by **General procedure B**. Yellow solid, 568 mg, 10% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.50 (s, 1H), 8.07-8.00 (m, 1H), 7.98-7.91 (m, 1H), 7.91-7.82 (m, 2H), 7.63-7.49 (m, 2H), 3.39 (t, *J* = 6.7 Hz, 2H), 2.74 (t, *J* = 6.7 Hz, 2H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.2, 172.2, 135.5, 134.0, 132.4, 129.6, 129.5, 128.4, 127.7, 126.7, 123.7, 80.6, 33.5, 29.5, 28.0. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{20}NaO_3^+$ 307.1305; Found 307.1307.

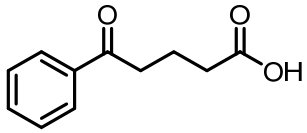


1n

Chemical Formula: $C_9H_{16}O_3$
Exact Mass: 172.1099

***Tert*-butyl 4-oxopentanoate (1n)**

Followed by **General procedure A**. Colorless oil, 2.13 g, 62% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.70 (t, *J* = 6.6 Hz, 2H), 2.49 (t, *J* = 6.5 Hz, 2H), 2.19 (s, 3H), 1.44 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 206.71, 171.81, 80.35, 37.90, 29.71, 29.03. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_9H_{16}NO_3Na^+$ 195.0992; Found 195.0994.

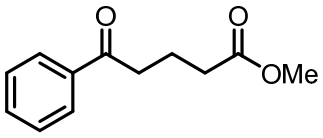


3aa

Chemical Formula: $C_{11}H_{12}O_3$
Exact Mass: 192.0786

5-oxo-5-phenylpentanoic acid (3aa)

Commercially available and used as received. White solid.

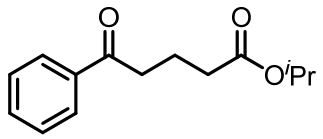


3ab

Chemical Formula: $C_{12}H_{14}O_3$
Exact Mass: 206.0943

Methyl 5-oxo-5-phenylpentanoate (3ab)

Followed by **General procedure A**. Colorless oil, 3.71 g, 90% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.97 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 3.68 (s, 3H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.16-1.98 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 199.3, 173.6, 136.7, 133.0, 128.5, 127.9, 51.5, 37.4, 33.0, 19.2. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}O_3^+$ 207.1016; Found 207.1016.



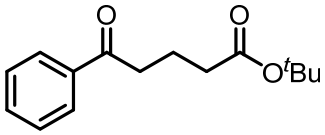
3ac

Chemical Formula: $C_{14}H_{18}O_3$
Exact Mass: 234.1256

Isopropyl 5-oxo-5-phenylpentanoate (3ac)

Followed by **General procedure A**. Colorless oil, 4.21 g, 90% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether

1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.96 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 5.14-4.91 (hept, *J* = 5.0 Hz, 1H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.40 (t, *J* = 7.2 Hz, 2H), 2.13 – 1.97 (m, 2H), 1.23 (d, *J* = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 199.2, 172.5, 136.6, 132.8, 128.4, 127.8, 67.4, 37.2, 33.5, 21.6, 19.3. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{14}H_{19}O_3^+$ 235.1329; Found 235.1329.

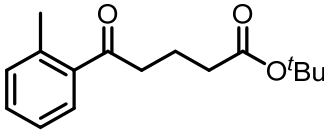


3a

Chemical Formula: $C_{15}H_{20}O_3$
Exact Mass: 248.1412

***Tert*-butyl 5-oxo-5-phenylpentanoate (3a)**

Followed by **General procedure A**. Colorless oil, 3.52 g, 71% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.01-7.92 (m, 2H), 7.59-7.41 (m, 3H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 2.08-1.98 (m, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 199.2, 172.3, 136.7, 132.8, 128.4, 127.8, 80.0, 37.3, 34.4, 27.9, 19.4. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{20}NaO_3^+$ 271.1305; Found 271.1305.



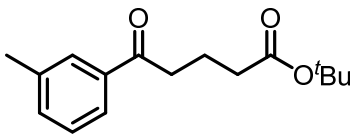
3b

Chemical Formula: $C_{16}H_{22}O_3$
Exact Mass: 262.1569

***Tert*-butyl 5-oxo-5-(o-tolyl)pentanoate (3b)**

Followed by **General procedure B**. Colorless oil, 3.20 g, 61% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.40-7.32

(m, 1H), 7.27-7.20 (m, 2H), 2.95 (t, J = 7.2 Hz, 2H), 2.49 (s, 3H), 2.32 (t, J = 7.2 Hz, 2H), 2.06-1.95 (m, 2H), 1.44 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 203.6, 172.5, 137.9, 131.8, 131.1, 128.3, 125.6, 80.2, 40.3, 34.6, 28.0, 21.2, 19.7. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}NaO_3^+$ 285.1461; Found 285.1462.

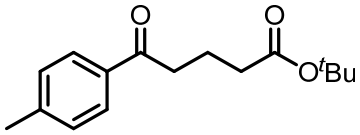


3c

Chemical Formula: $C_{16}H_{22}O_3$
Exact Mass: 262.1569

***Tert*-butyl 5-oxo-5-(m-tolyl)pentanoate (3c)**

Followed by **General procedure B**. Pale yellow oil, 2.36 g, 45% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.79-7.73 (m, 2H), 7.40-7.31 (m, 2H), 3.02 (t, J = 7.2 Hz, 2H), 2.41 (s, 3H), 2.34 (t, J = 7.2 Hz, 2H), 2.07-1.98 (m, 2H), 1.45 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 199.7, 172.6, 138.3, 136.8, 133.7, 128.5, 128.4, 125.2, 80.2, 37.5, 34.6, 28.0, 21.3, 19.6. HRMS (ESI), m/z: $[M+Na]^+$ Calcd for $C_{16}H_{22}NaO_3^+$ 285.1461; Found 285.1463.



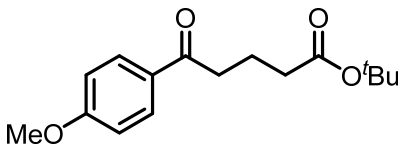
3d

Chemical Formula: $C_{16}H_{22}O_3$
Exact Mass: 262.1569

***Tert*-butyl 5-oxo-5-(p-tolyl)pentanoate (3d)**

Followed by **General procedure B**. White solid, 3.25 g, 62% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.86 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 3.00 (t, J = 7.2 Hz, 2H), 2.41 (s, 3H), 2.34 (t, J = 7.2 Hz, 2H), 2.08 – 1.97 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 199.3, 172.7, 143.8,

134.4, 129.3, 128.2, 80.3, 37.4, {^{1}H}34.8, 28.1, 21.7, 19.8. HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{16}H_{22}NaO_3^+$ 285.1461; Found 285.1462.

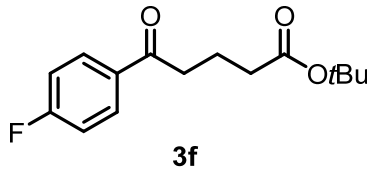


3e

Chemical Formula: $C_{16}H_{22}O_4$
Exact Mass: 278.1518

***Tert*-butyl 5-(4-methoxyphenyl)-5-oxopentanoate (3e)**

Followed by **General procedure B**. White solid, 3.28 g, 59% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.94 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 3.86 (s, 3H), 2.98 (t, J = 7.3 Hz, 2H), 2.33 (t, J = 7.2 Hz, 2H), 2.00 (q, J = 7.3 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.1, 172.5, 163.3, 130.2, 129.8, 113.6, 80.1, 55.3, 37.0, 34.6, 28.0, 19.8. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{23}O_4^+$ 279.1591; Found 279.1592.



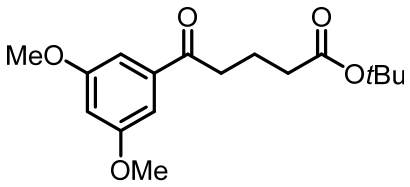
3f

Chemical Formula: $C_{15}H_{19}FO_3$
Exact Mass: 266.1318

***Tert*-butyl 5-(4-fluorophenyl)-5-oxopentanoate (3f)**

Followed by **General procedure A**. White solid, 3.19 g, 60% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.07 – 7.88 (m, 2H), 7.20 – 7.07 (m, 2H), 3.01 (t, J = 7.2 Hz, 2H), 2.34 (t, J = 7.2 Hz, 2H), 2.12 – 1.95 (m, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 198.0, 172.5, 165.7 (d, J_{CF} = 254.5 Hz), 133.3 (d, J_{CF} = 3.0 Hz), 130.6 (d, J_{CF} = 9.3 Hz), 115.6 (d, J_{CF} = 21.8 Hz), 80.3, 37.4, 34.6, 28.1, 19.6. HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{15}H_{19}FNaO_3^+$ 289.1210;

Found 289.1211.

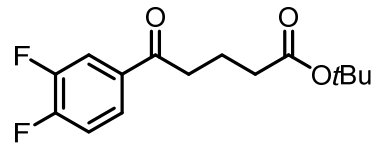


3g

Chemical Formula: $C_{17}H_{24}O_5$
Exact Mass: 308.1624

***Tert*-butyl 5-(3,5-dimethoxyphenyl)-5-oxopentanoate (3g)**

Followed by **General procedure B**. Light yellow oil, 3.02 g, 49% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.10 (d, J = 2.3 Hz, 2H), 6.64 (t, J = 2.3 Hz, 1H), 3.83 (s, 6H), 2.99 (t, J = 7.2 Hz, 2H), 2.33 (t, J = 7.2 Hz, 2H), 2.08 – 1.94 (m, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 199.3, 172.6, 160.8, 138.8, 105.8, 105.3, 80.3, 55.6, 37.6, 34.6, 28.1, 19.7. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{17}H_{25}O_5^+$ 309.1697; Found 309.1697.



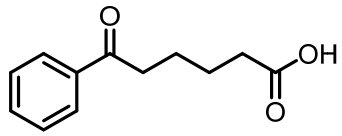
3h

Chemical Formula: $C_{15}H_{18}F_2O_3$
Exact Mass: 284.1224

***Tert*-butyl 5-(3,4-difluorophenyl)-5-oxopentanoate (3h)**

Followed by **General procedure B**. White solid, 2.50 g, 44% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:19-1:9). ^{1}H NMR (600 MHz, Chloroform-d) δ 7.83 – 7.78 (m, 1H), 7.77 – 7.73 (m, 1H), 7.27 – 7.21 (m, 1H), 2.99 (t, J = 7.2 Hz, 2H), 2.34 (t, J = 7.1 Hz, 2H), 2.02 (p, J = 7.2 Hz, 2H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) δ 197.0, 172.5, 153.6 (dd, J_{CF} = 256.7, 12.8 Hz), 150.4 (dd, J_{CF} = 250.7, 12.8 Hz), 133.9 (t, J_{CF} = 3.8 Hz), 125.0 (dd, J_{CF} = 7.4, 3.6 Hz), 117.5 (d, J_{CF} = 17.8 Hz), 117.3 (dd, J_{CF} = 18.0, 1.4 Hz), 80.4, 37.4, 34.4, 28.1, 19.5. HRMS (ESI) m/z $[M+Na]^+$ Calcd for

$C_{15}H_{18}F_2NaO_3^+$ 307.1116; Found 307.1122.

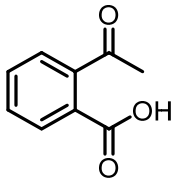


3i

Chemical Formula: $C_{12}H_{14}O_3$
Exact Mass: 206.0943

6-oxo-6-phenylhexanoic acid (3i)

Commercially available and used as received. White solid.

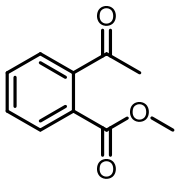


5aa

Chemical Formula: $C_9H_8O_3$
Exact Mass: 164.0473

2-acetylbenzoic acid (5aa)

Commercially available and used as received. White solid.

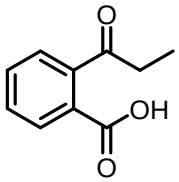


5ab

Chemical Formula: $C_{10}H_{10}O_3$
Exact Mass: 178.0630

Methyl 2-acetylbenzoate (5ab)

Colorless oil, 982 mg, 92% yield, obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 1:9). 1H NMR (400 MHz, Chloroform-d) δ 7.85 (d, J = 8.0 Hz, 1H), 7.60 – 7.48 (m, 2H), 7.43 (d, J = 7.6 Hz, 1H), 3.90 (s, 3H), 2.55 (s, 3H). HRMS (ESI), m/z 179.0703 ($[M+H]^+$), Calcd for $C_{10}H_{11}O_3^+$: 179.0703. The ^{1}H NMR data is consistent with that reported.[6]

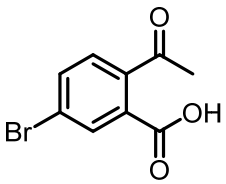


5b

Chemical Formula: $C_{10}H_{10}O_3$
Exact Mass: 178.0630

2-propionylbenzoic acid (5b)

Followed by **General procedure D**, recrystallized from EA/Hex. White solid, 673 mg, 42% yield. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.2 Hz, 1H), 7.71 (t, *J* = 7.1 Hz, 1H), 7.63 – 7.50 (m, 2H), 2.19 (d, *J* = 54.7 Hz, 2H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 168.6, 148.5, 134.6, 130.6, 126.9, 125.5, 122.3, 108.0, 32.0, 7.7. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}O_3^+$ 179.0703; Found 179.0703.

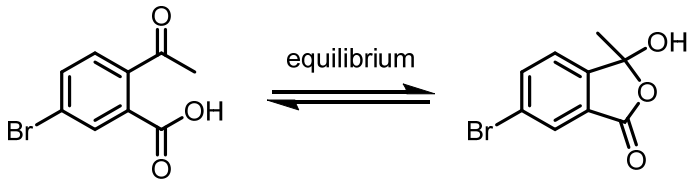


5c

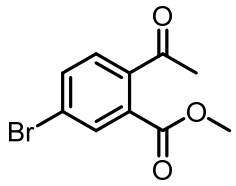
Chemical Formula: $C_9H_7BrO_3$
Exact Mass: 241.9579

2-acetyl-5-bromobenzoic acid (5c)

Followed by **General procedure D**. Yellow solid, 2.27 g, 47% yield. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_8BrO_3^+$ 242.9651; Found 242.9652. The NMR of **5c** is messy, possibly due to a fast equilibrium between **5c** and **5c'** at rt. Therefore, its structure was determined by converting it to the corresponding methyl ester **5cb**. However, the catalytic reaction was performed with **5c**.



5c **5c'**

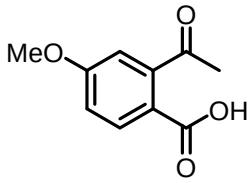


5cb

Chemical Formula: $C_{10}H_9BrO_3$
Exact Mass: 255.9735

methyl 2-acetyl-5-bromobenzoate (5cb)

^{1}H NMR (400 MHz, Chloroform-d) δ 7.97 (d, J = 1.9 Hz, 1H), 7.70 (dd, J = 8.2, 1.9 Hz, 1H), 7.32 (d, J = 8.2 Hz, 1H), 3.91 (s, 3H), 2.53 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 201.47, 166.21, 140.94, 134.86, 132.61, 130.81, 128.16, 124.39, 52.85, 29.73. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{10}BrO_3^+$: 256.9808; Found 256.9801.

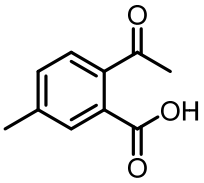


5d

Chemical Formula: $C_{10}H_{10}O_4$
Exact Mass: 194.0579

2-acetyl-4-methoxybenzoic acid (5d)

Followed by **General procedure D**, recrystallized from EA/Hex. White solid, 699 mg, 40% yield. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 8.4 Hz, 1H), 7.07 – 6.91 (m, 2H), 3.91 (s, 3H), 1.86 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 168.3，165.2, 152.6, 127.1, 118.2, 117.7, 106.0, 105.0, 55.9, 26.0. HRMS (ESI), m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}O_4^+$ 195.0652; Found 195.0654.

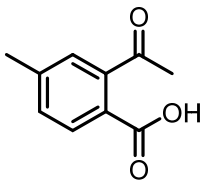


5e

Chemical Formula: $C_{10}H_{10}O_3$
Exact Mass: 178.0630

2-acetyl-5-methylbenzoic acid (5e)

Followed by **General procedure D**. White solid, 561 mg, 35% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.65 (s, 1H), 7.56 – 7.38 (m, 2H), 4.68 (s, 1H), 2.47 (s, 3H), 2.01 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, Methanol-d_4) δ 170.7, 149.4, 142.1, 136.9, 127.8, 125.9, 123.1, 108.0, 26.4, 21.2. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}O_3^+$ 179.0703; Found 179.0704.

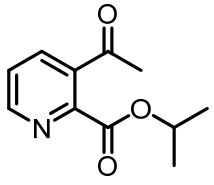


5f

Chemical Formula: $C_{10}H_{10}O_3$
Exact Mass: 178.0630

2-acetyl-4-methylbenzoic acid (5f)

Followed by **General procedure D**. White solid, 529 mg, 33% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.69 (s, 1H), 7.35 (d, *J* = 7.7 Hz, 2H), 4.41 (br, 1H), 2.49 (s, 3H), 1.87 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 168.7, 150.2, 146.1, 131.5, 125.3, 123.5, 122.4, 105.7, 26.0, 22.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}O_3^+$ 179.0703; Found 179.0702.

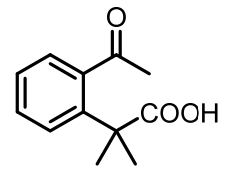


5g

Chemical Formula: $C_{11}H_{13}NO_3$
Exact Mass: 207.0895

Isopropyl 3-acetylpicolinate (5g)

Brown liquid. Commercially available and used as received.

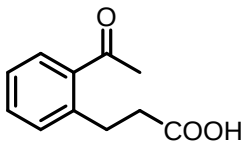


5h

Chemical Formula: $C_{12}H_{14}O_3$
Exact Mass: 206.0943

2-(2-acetylphenyl)-2-methylpropanoic acid (5h)

Followed by **General procedure E**. Yellow solid, 1.73 g, 42% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.52 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.44 (m, 2H), 7.32 – 7.15 (m, 1H), 5.19 (br, 1H), 2.36 (s, 3H), 1.59 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-d) δ 180.8, 143.6, 137.1, 130.7, 127.4, 126.5, 126.1, 45.5, 29.8, 28.7. HRMS (ESI) m/z：[M+H]$^+$ Calcd for $C_{12}H_{15}O_3^+$ 207.1016; Found 207.1017.

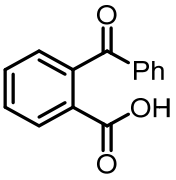


5i

Chemical Formula: $C_{11}H_{12}O_3$
Exact Mass: 192.0786

3-(2-acetylphenyl)propanoic acid (5i)

Followed by **General procedure E**. White solid, 1.31 g, 34% yield. ^{1}H NMR (400 MHz, Methanol-d4) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.39 – 7.27 (m, 2H), 3.10 (t, J = 7.7 Hz, 2H), 2.65 – 2.52 (m, 5H). ^{13}C{^{1}H} NMR (101 MHz, Methanol-d4) δ 204.2, 176.7, 142.1, 139.0, 132.9, 132.4, 130.8, 127.6, 36.7, 30.4, 29.7. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{11}H_{13}O_3^+$ 193.0859; Found 193.0860.



5j

Chemical Formula: $C_{14}H_{10}O_3$
Exact Mass: 226.0630

2-benzoylbenzoic acid (5j)

Commercially available and used as received.

Ⅲ. Ru-catalyzed Asymmetric Reductive Amination/Cyclization Cascade of Keto-Acids/Esters

3.1. Synthesis of $Ru(OAc)_2$(L2)[7][8]

(*R*)-DTBM-C3*-TunePhos (**L2**, 59 mg, 0.05 mmol) and $[RuCl_2(benzene)]_2$ (12.5 mg, 0.025 mmol) were placed in a Schlenk tube, followed by addition of *N*,*N*-Dimethylformamide (2 mL). The resulting solution was stirred at 100℃ for 1 h. The reaction was cooled to room temperature, then a solution of NaOAc (1 mmol) in methanol (3 mL, degassed) was added in one portion. The reaction was stirred for 20 minutes followed by adding water (degassed, 8 mL). After vigorously stirring for 5 minutes, the precipitated yellow solids were filtered, washed with water for three times, and then dried under vacuum to give a lightly yellow solid which was used directly as catalyst. Other $Ru(OAc)_2$ complexes were prepared accordingly.

3.2. General Procedure F: In a glovebox, $Ru(OAc)_2$(**L2**) (2.8 mg, 0.002 mmol), substrate (0.2 mmol), ammonium salt (30.8 mg, 0.4 mmol) and TFE (0.4 ml) were successively added to a 5 mL vial equipped with a magnetic stirring bar. The mixture was then transferred to a stain-less autoclave and purged by three cycles of pressurization/venting with H_2. The required H_2 pressure (50 atm) was then installed and the autoclave was placed in an oil bath preheated to 90 ℃. The autoclave was

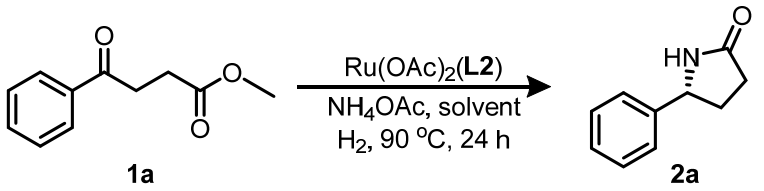
cooled down to room temperature after 24 h and the pressure was slowly released in the hood. The reaction was quenched by H_2O (1 mL) and extracted with ethyl ether (1 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane = 30%) to afford desired products.

3.3 General Procedure G (Scale-up reactions):

In a glovebox, $Ru(OAc)_2$(**L2**) (11.2 mg, 0.008 mmol), substrate (4 mmol), ammonium salt (616 mg, 8 mmol) and TFE (8 ml) were successively added to a 20 mL vial equipped with a magnetic stirring bar. The mixture was then transferred to a stain-less autoclave and purged by three cycles of pressurization/venting with H_2. The required H_2 pressure (50 atm) was then installed and the autoclave was placed in an oil bath preheated to 90 ℃. The autoclave was cooled down to room temperature after 24 h and the pressure was slowly released in the hood. The reaction was quenched by H_2O (10 mL) and extracted with ethyl ether (10 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane = 30%) to afford desired products.

3.4 Details of condition optimization

Table S1. Evaluation of the solvents

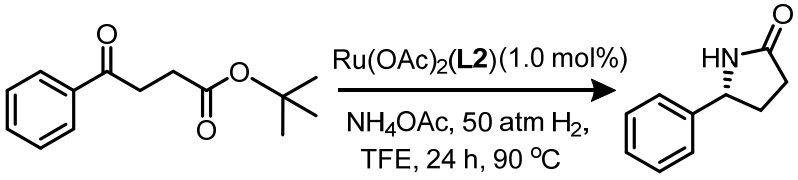


1a **2a**

Entry[a]	Solvent	conversion (%)[b]	ee (%)[c]
1	MeOH	Messy	20
2	EtOH	Messy	48
3	^{i}PrOH	Messy	--
4	TFE	> 99	77
5	HFIP	> 99	57
6	DCM	low	--
7	toluene	low	--
8	THF	low	--

[a] Reaction conditions: **1a** (0.2 mmol), NH_4OAc (0.4 mmol), [Ru] (1 mol%), solvent (0.4 mL),H_2 (50 bar), 90 °C, 24 h. TFE = trifluoroethanol. [b] Determined by ^1H NMR analysis. [c] The ee values were determined by HPLC using chiral columns.

Table S2. Evaluation of the equivalent of ammonium salts

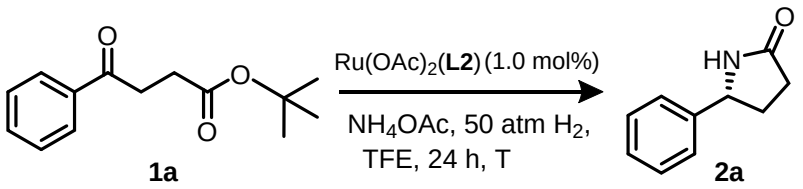


1a **2a**

entry[a]	NH_4OAc	conversion (%)[b]	ee (%)[c]
1	1.2 equiv	>99	92
2	1.6 equiv	>99	93
3	2.0 equiv	>99	94
4	2.6 equiv	>99	94

[a] Reaction conditions: **1a** (0.2 mmol), NH_4OAc, [Ru] (1 mol%), TFE (0.4 mL), H_2 (50 bar), 90 °C, 24 h. [b] Determined by ^1H NMR analysis. [c] The ee values were determined by HPLC using chiral columns.

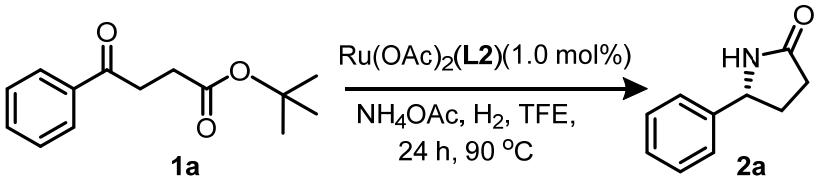
Table S3. Evaluation of reaction temperature



entry[a]	T (^{o}C)	conversion (%)[b]	ee (%)[c]
1	80	92	93
2	90	>99	94
3	100	>99	90

[a] Reaction conditions: **1a** (0.2 mmol), NH_4OAc (0.4 mmol), [Ru] (1 mol%), TFE (0.4 mL), H_2 (50 bar), 24 h. [b] Determined by ^1H NMR analysis. [c] The ee values were determined by HPLC using chiral columns.

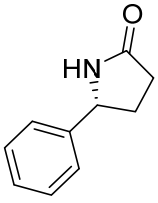
Table S4. Evaluation of hydrogen pressure



entry[a]	P (atm)	conversion (%)[b]	ee (%)[c]
1	40	>99	91
3	50	>99	94
3	60	>99	93

[a] Reaction conditions: **1a** (0.2 mmol), NH_4OAc (0.4 mmol), [Ru] (1 mol%), TFE (0.4 mL), H_2 (50 bar), 90 ^{o}C, 24 h. [b] Determined by ^1H NMR analysis. [c] The ee values were determined by HPLC using chiral columns.

3.5 Characterization data of Chiral NH Lactams

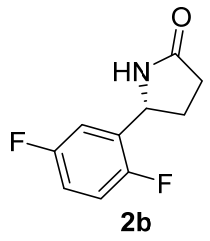


2a

Chemical Formula: $C_{10}H_{11}NO$
Exact Mass: 161.0841

(*R*)-5-phenylpyrrolidin-2-one (2a)

White solid, 30.9 mg, 96% yield, 94% ee, $[\alpha]^{25}_{D}$ = 40.9 (c=0.6, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.39 – 7.34 (m, 2H), 7.32 – 7.28 (m, 3H), 6.43 (br, 1H), 4.75 (t, *J* = 7.1 Hz, 1H), 2.61 – 2.53 (m, 1H), 2.50 – 2.36 (m, 2H), 2.02 – 1.93 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) δ 178.5, 142.5, 128.9, 127.9, 125.6, 58.1, 31.3, 30.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}NO^+$ 162.0913; Found 162.0913. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow = 0.8 mL/min; Retention time: 12.7 min (minor), 13.9 min (major). The absolute configuration of **2a** was determined by comparison of its optical rotation with that reported.[9] The absolute configuration of **2b**-**2n** was determined by comparing with **2a**.



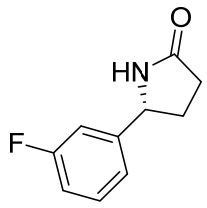
2b

Chemical Formula: $C_{10}H_9F_2NO$
Exact Mass: 197.0652

(*R*)-5-(2,5-difluorophenyl)pyrrolidin-2-one (2b)

White solid, 31.9 mg, 81% yield, 87% ee, on 0.2 mmol scale; 323mg, 82% yield, 87% ee, on 2.0 mmol scale(68% yield, > 99% ee after recrystallization from EtOH), $[\alpha]^{25}_{D}$ = 40.2 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.10 – 7.00 (m, 2H), 7.00 – 6.91 (m, 1H), 6.03 (s, 1H), 5.04 (t, *J* = 6.9 Hz, 1H), 2.71 – 2.63 (m, 1H), 2.52 – 2.38 (m, 2H), 2.06 – 1.96 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 178.7, 159.0 (dd, J_{CF} = 243.6, 2.3 Hz), 155.9 (dd, J_{CF} = 242.4, 2.6 Hz), 131.4 (dd, J_{CF} = 15.7, 6.8 Hz), 116.8 (dd, J_{CF} = 24.3, 8.6 Hz),

115.5 (dd, J_{CF} = 24.2, 8.6 Hz), 113.0 (dd, J_{CF} = 25.2, 4.6 Hz), 51.6 (d, J_{CF} = 3.5 Hz), 29.7, 29.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{10}F_2NO^+$: 198.0725; Found 198.0726. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 12.4 min (major), 14.2 min (minor).

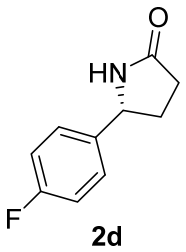


2c

Chemical Formula: $C_{10}H_{10}FNO$
Exact Mass: 179.0746

(*R*)-5-(3-fluorophenyl)pyrrolidin-2-one (2c)

White solid, 31.2 mg, 87% yield, 91% ee, $[\alpha]^{26}_D$ = 46.8 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.29 (m, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.04 – 6.96 (m, 2H), 6.02 (br, 1H), 4.76 (t, *J* = 7.1 Hz, 1H), 2.65 – 2.55 (m, 1H), 2.54 – 2.37 (m, 2H), 2.04 – 1.88 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 178.3, 163.2 (d, *J* = 247.2 Hz), 145.2 (d, *J* = 6.6 Hz), 130.6 (d, *J* = 8.3 Hz), 121.2 (d, *J* = 2.9 Hz), 114.9 (d, *J* = 21.1 Hz), 112.6 (d, *J* = 22.0 Hz), 57.5 (d, *J* = 1.9 Hz), 31.3, 30.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}FNO^+$ 180.0819; Found 180.0819. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 11.6 min (minor), 12.6 min (major).

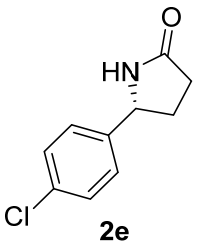


2d

Chemical Formula: $C_{10}H_{10}FNO$
Exact Mass: 179.0746

(*R*)-5-(4-fluorophenyl)pyrrolidin-2-one (2d)

White solid, 34.0 mg, 95% yield, 90% ee, $[\alpha]^{26}_{D}$ = 52.5 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.24 (m, 2H), 7.10 – 7.01 (m, 2H), 6.69 (br, 1H), 4.75 (t, *J* = 7.1 Hz, 1H), 2.60-2.51 (m, 1H), 2.50 – 2.35 (m, 2H), 1.97-1.88 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 178.6, 162.3 (d, J_{CF} = 246.3 Hz), 138.2 (d, J_{CF} = 3.2 Hz), 127.3 (d, J_{CF} = 8.2 Hz), 115.7 (d, J_{CF} = 21.6 Hz), 57.5, 31.4, 30.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}FNO^+$ 180.0819; Found 180.0820. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 13.0 min (minor), 13.7 min (major).



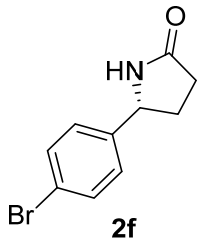
2e

Chemical Formula: $C_{10}H_{10}ClNO$
Exact Mass: 195.0451

(*R*)-5-(4-chlorophenyl)pyrrolidin-2-one (2e)

White solid, 35.9 mg, 92% yield, 85% ee, $[\alpha]^{25}_{D}$ = 47.7 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 2H), 7.26 – 7.20 (m, 2H), 6.11 (s, 1H), 4.74 (t, *J* = 7.1 Hz, 1H), 2.64 – 2.52 (m, 1H), 2.52 – 2.36 (m, 2H),

2.00 – 1.86 (m, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 178.3, 141.0, 133.7, 129.1, 127.0, 57.4, 31.4, 30.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}ClNO^+$ 196.0524; Found 196.0525. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 14.1 min (major), 15.3 min (minor).

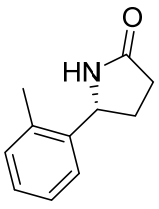


2f

Chemical Formula: $C_{10}H_{10}BrNO$
Exact Mass: 238.9946

(*R*)-5-(4-bromophenyl)pyrrolidin-2-one (2f)

White solid, 44.5 mg, 93% yield, 86% ee, $[\alpha]^{25}_D$ = 28.0 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.47 (t, *J* = 6.4 Hz, 1H), 2.71 – 2.62 (m, 3H), 2.19 – 2.07 (m, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 176.5, 138.4, 131.9, 126.9, 122.4, 80.4, 30.9, 28.8. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}BrNO^+$ 240.0019; Found 240.0019. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 14.8 min (major), 16.3 min (minor).

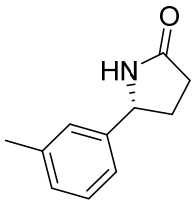


2g

Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

(*R*)-5-(o-tolyl)pyrrolidin-2-one (2g)

White solid, 17.9 mg, 51% yield, 90% ee, $[\alpha]^{26}_{D}$ = 121.2 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.31 (m, 1H), 7.26 – 7.15 (m, 3H), 5.78 (s, 1H), 5.00 (t, *J* = 6.4 Hz, 1H), 2.70 – 2.58 (m, 1H), 2.53 – 2.38 (m, 2H), 2.35 (s, 3H), 1.94 – 1.84 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 178.4, 140.4, 134.4, 130.8, 127.5, 126.6, 124.0, 54.4 29.8, 29.6, 19.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO^+$ 176.1070; Found 176.1071. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 11.5 min (minor), 13.2 min (major).

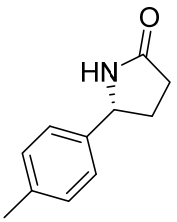


2h

Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

(*R*)-5-(m-tolyl)pyrrolidin-2-one (2h)

White solid, 27.0 mg, 77% yield, 91% ee, $[\alpha]^{24}_{D}$ = 30.1 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 – 7.25 (m, 1H), 7.10 (q, *J* = 7.9 Hz, 3H), 6.02 (s, 1H), 4.72 (t, *J* = 7.1 Hz, 1H), 2.59-2.53 (m, 1H), 2.52 – 2.38 (m, 2H), 2.36 (s, 3H), 2.01 – 1.94 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 178.4, 142.4, 138.7, 128.8, 128.7, 126.3, 122.7, 58.0, 31.4, 30.2, 21.4. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO^+$ 176.1070; Found 176.1071. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.7 min (minor), 12.1 min (major).

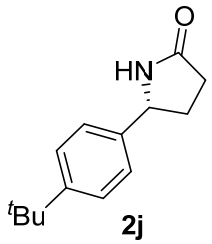


2i

Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

(*R*)-5-(p-tolyl)pyrrolidin-2-one (2i)

White solid, 30.5 mg, 87% yield, 90% ee, $[\alpha]^{25}_{D}$ = 36.6 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.18 (br, 4H), 5.84 (s, 1H), 4.72 (t, *J* = 7.2 Hz, 1H), 2.57-2.54 (m, 1H), 2.51 – 2.38 (m, 2H), 2.35 (s, 3H), 2.01 – 1.92 (m, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-*d*) δ 178.2, 139.4, 137.8, 129.6, 125.6, 57.8, 31.5, 30.3, 21.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO^+$ 176.1070; Found 176.1070. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 13.0 min (minor), 13.7 min (major).



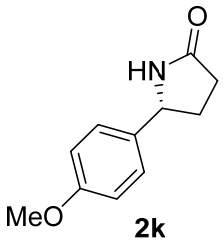
2j

Chemical Formula: $C_{14}H_{19}NO$
Exact Mass: 217.1467

(*R*)-5-(4-(tert-butyl)phenyl)pyrrolidin-2-one (2j)

White solid, 40.8 mg, 94% yield, 95% ee, $[\alpha]^{25}_{D}$ = 25.4 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 5.08 (br, 1H)，4.73 (t, J = 7.2 Hz, 1H), 2.61 – 2.37 (m, 3H), 2.05 – 1.94 (m, 1H), 1.32 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 178.2, 151.1, 139.3,

125.8, 125.4, 57.8, 34.6, 31.4, 31.3, 30.3. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{20}NO^+$ 218.1539; Found 218.1514. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.9 min (minor), 12.1 min (major).

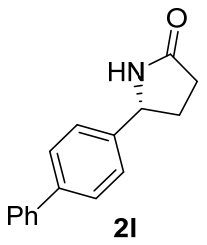


2k

Chemical Formula: $C_{11}H_{13}NO_2$
Exact Mass: 191.0946

(*R*)-5-(4-methoxyphenyl)pyrrolidin-2-one (2k)

White solid, 36.3 mg, 95% yield, 85% ee, $[\alpha]^{25}_D$ = 19.7 (c=0.93, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.18 (m, 2H), 6.93 – 6.86 (m, 2H), 6.30 (s, 1H), 4.70 (t, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 2.58 – 2.34 (m, 3H), 2.00 – 1.90 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 178.4, 159.3, 134.4, 126.9, 114.2, 57.6, 55.3, 31.5, 30.4. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO_2^+$ 192.1019; Found 192.1020. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 18.6 min (minor), 19.8 min (major).

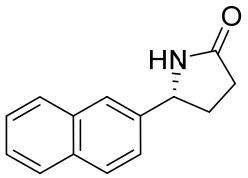


2l

Chemical Formula: $C_{16}H_{15}NO$
Exact Mass: 237.1154

(*R*)-5-([1,1'-biphenyl]-4-yl)pyrrolidin-2-one (2l)

White solid, 43.16 mg, 91% yield, 89% ee, $[\alpha]^{24}_{D}$ = 6.2 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.55 (m, 4H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.37 (dd, *J* = 7.8, 2.4 Hz, 3H), 5.89 (s, 1H), 4.81 (t, *J* = 7.1 Hz, 1H), 2.70 – 2.40 (m, 3H), 2.09 – 1.97 (m, 1H). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}NO^+$ 238.1226; Found 238.1226. $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 178.3, 141.4, 141.1, 140.5, 128.8, 127.7, 127.5, 127.1, 126.1, 57.8, 31.5, 30.2. HPLC: Chiracel IE Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 85/15; flow = 0.8 mL/min; Retention time: 30.2 min (major), 32.9 min (minor).

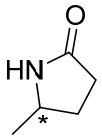


2m

Chemical Formula: $C_{14}H_{13}NO$
Exact Mass: 211.0997

(*R*)-5-(naphthalen-2-yl)pyrrolidin-2-one (2m)

White solid, 32.9 mg, 78% yield, 92% ee, $[\alpha]^{27}_{D}$ = 17.2 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.91 – 7.80 (m, 3H), 7.73 (s, 1H), 7.55 – 7.46 (m, 2H), 7.40 (d, *J* = 8.5 Hz, 1H), 6.23 (s, 1H), 4.91 (t, *J* = 7.1 Hz, 1H), 2.69 – 2.60 (m, 1H), 2.58 – 2.41 (m, 2H), 2.12 – 2.02 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 178.4, 139.7, 133.2, 133.0, 129.0, 127.8, 127.7, 126.5, 126.2, 124.3, 123.6, 58.1, 31.2, 30.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{14}NO^+$ 212.1070; Found 212.1070. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 14.4 min (minor), 15.6 min (major).

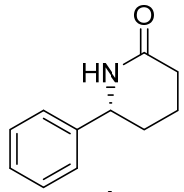


2n

Chemical Formula: C_5H_9NO
Exact Mass: 99.0684

5-methylpyrrolidin-2-one (2n)

Light yellow oil, 8.1 mg, 41% yield, 50% ee, $[\alpha]^{22}_D$ = 21.0 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.50 (s, 1H), 3.79 (h, *J* = 6.4 Hz, 1H), 2.42 – 2.21 (m, 3H), 1.71 – 1.60 (m, 1H), 1.23 (d, *J* = 6.3 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 178.30, 50.04, 30.53, 29.13, 22.16. Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 9.3 min (major), 10.4 min (minor). The NMR data is consistent with that reported. [10]



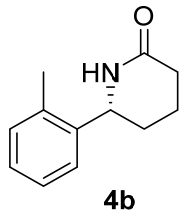
4a

Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

(*R*)-6-phenylpiperidin-2-one (4a)

White solid, 32.9 mg, 94% yield, 94% ee, on 0.2 mmol scale; 595 mg, 85% yield, 91% ee, on 4.0 mmol scale, $[\alpha]^{25}_D$ = 61.7 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (m *J* = 7.8, 6.5, 1.2 Hz, 2H), 7.33 – 7.25 (m, 3H), 6.01 (s, 1H), 4.60 – 4.49 (m, 1H), 2.53 – 2.36 (m, 2H), 2.17 – 2.06 (m, 1H), 1.96 – 1.86 (m, 1H), 1.86 – 1.73 (m, 1H), 1.73 – 1.62 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 172.3, 142.5, 128.8, 127.9, 126.0, 57.7, 32.1, 31.2, 19.6. HRMS (ESI)

m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO^+$ 176.1070; Found 176.1070. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 18.9 min (major), 22.0 min (minor). The absolute configuration of **4a** was identified by comparison of its physical and spectroscopic data with the ones reported in the literature.[9] The absolute configuration of **4b**-**4h** was determined by comparing with **4a**.

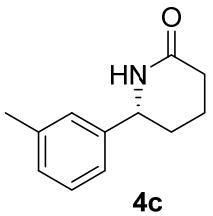


4b

Chemical Formula: $C_{12}H_{15}NO$
Exact Mass: 189.1154

(*R*)-6-(o-tolyl)piperidin-2-one (4b)

White solid, 34.4 mg, 91% yield, 91% ee, $[\alpha]^{25}_D$ = 44.4 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 7.6 Hz, 1H), 7.26-7.23 (m, 1H), 7.21-7.19 (m, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 5.80 (s, 1H), 4.80 (dd, *J* = 8.9, 4.8 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.35 (s, 3H), 2.17 – 2.07 (m, 1H), 1.97 – 1.88 (m, 1H), 1.84-1.77 (m, 1H), 1.64-1.58 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 172.5, 140.3, 134.4, 130.8, 127.6, 126.6, 125.6, 54.0, 31.4, 30.0, 19.6, 18.9. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NO^+$ 190.1226; Found 190.1227. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.7 min (major), 21.9 min (minor).

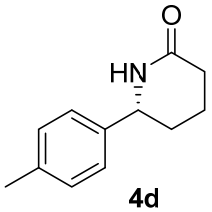


4c

Chemical Formula: $C_{12}H_{15}NO$
Exact Mass: 189.1154

(*R*)-6-(m-tolyl)piperidin-2-one (4c)

White solid, 35.2 mg, 93% yield, 91% ee, $[\alpha]^{25}_{D}$ = 37.6 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 – 7.23 (m, 1H), 7.13 – 7.06 (m, 3H), 5.87 (s, 1H), 4.51 (dd, *J* = 9.3, 4.6 Hz, 1H), 2.51-2.40 (m, 2H), 2.36 (s, 3H), 2.14 – 2.06 (m, 1H), 1.95-1.89 (m, 1H), 1.83 – 1.74 (m, 1H), 1.71 – 1.63 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 172.3, 142.5, 138.6, 128.7, 128.7, 126.7, 123.1, 57.8, 32.2, 31.3, 21.4, 19.7. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NO^+$ 190.1226; Found 190.1228. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 16.2 min (minor), 17.7 min (major).

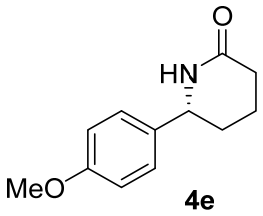


4d

Chemical Formula: $C_{12}H_{15}NO$
Exact Mass: 189.1154

(*R*)-6-(p-tolyl)piperidin-2-one (4d)

White solid, 35.9 mg, 95% yield, 90% ee, $[\alpha]^{25}_{D}$ = 35.0 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.18 (br, 4H), 5.85 (s, 1H), 4.51 (dd, *J* = 9.4, 4.6 Hz, 1H), 2.51-2.39 (m, 2H), 2.35 (s, 3H), 2.13 – 2.06 (m, 1H), 1.94-1.90 (m, 1H), 1.83-1.76 (m, 1H), 1.68 – 1.61 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 172.3, 139.5, 137.7, 129.5, 126.0, 57.6, 32.2, 31.3, 21.0, 19.8. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NO^+$ 190.1226; Found 190.1228. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 16.7 min (major), 21.6 min (minor).

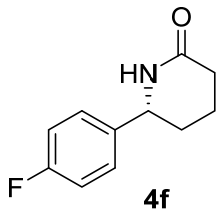


4e

Chemical Formula: $C_{12}H_{15}NO_2$
Exact Mass: 205.1103

(*R*)-6-(4-methoxyphenyl)piperidin-2-one.

White solid, 35.3 mg, 86% yield, 90% ee, $[\alpha]^{25}_D$ = 39.6 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.80 (s, 1H), 4.49 (dd, *J* = 9.3, 4.4 Hz, 1H), 3.81 (s, 3H), 2.51-2.39 (m, 2H), 2.10-2.05 (m, 1H), 1.83-1.75 (m, 1H), 1.83 – 1.75 (m, 1H), 1.68 – 1.61 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 172.3, 159.3, 134.5, 127.3, 114.2, 57.4, 55.3, 32.3, 31.2, 19.8. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{12}H_{16}NO_2^+$ 206.1176; Found 206.1177. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 25.6 min (major), 29.6 min (minor).



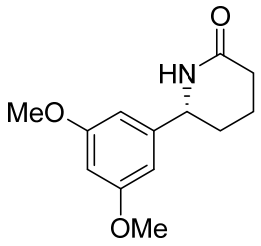
4f

Chemical Formula: $C_{11}H_{12}FNO$
Exact Mass: 193.0903

(*R*)-6-(4-fluorophenyl)piperidin-2-one (4f)

White solid, 34.9 mg, 91% yield, 90% ee, $[\alpha]^{25}_D$ = 50.5 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.27 (m, 2H), 7.06 (t, *J* = 8.4 Hz, 2H), 5.91 (s, 1H), 4.58 – 4.50 (m, 1H), 2.53 – 2.38 (m, 2H), 2.14 – 2.06 (m, 1H), 1.96 – 1.88 (m, 1H), 1.85 – 1.76 (m, 1H), 1.69 – 1.60 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 172.3, 162.3 (d, J_{CF} = 246.4 Hz), 138.3 (d, J_{CF} = 3.2 Hz), 127.7 (d,

J_{CF} = 8.2 Hz), 115.7 (d, J_{CF} = 21.6 Hz), 57.2, 32.3, 31.2, 19.6. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{13}FNO^+$ 194.0976; Found 194.0978. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 17.1 min (major), 22.6 min (minor).

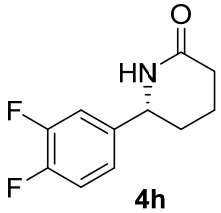


4g

Chemical Formula: $C_{13}H_{17}NO_3$
Exact Mass: 235.1208

(*R*)-6-(3,5-dimethoxyphenyl)piperidin-2-one (4g)

White solid, 42.8 mg, 91% yield, 92% ee, $[\alpha]^{25}_D$ = 36.1 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 6.46 – 6.41 (m, 2H), 6.39 (t, J = 2.3 Hz, 1H), 5.89 (s, 1H), 4.48 (dd, J = 9.2, 4.6 Hz, 1H), 3.79 (s, 6H), 2.54 – 2.37 (m, 2H), 2.15 – 2.05 (m, 1H), 1.98 – 1.88 (m, 1H), 1.86 – 1.75 (m, 1H), 1.71 – 1.62 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 172.3, 161.2, 145.0, 104.0, 99.6, 57.9, 55.4, 32.0, 31.3, 19.8. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{18}NO_3^+$ 236.1281; Found 236.1282. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 85/5; flow = 0.8 mL/min; Retention time: 22.9 min (minor), 27.0 min (major).

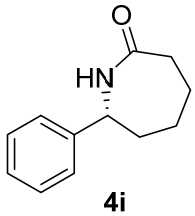


4h

Chemical Formula: $C_{11}H_{11}F_2NO$
Exact Mass: 211.0809

(*R*)-6-(3,4-difluorophenyl)piperidin-2-one (4h)

White solid, 37.6 mg, 89% yield, 91% ee, $[\alpha]^{25}_{D}$ = 43.2 (c=1.0, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.21 – 7.07 (m, 2H), 7.07 – 6.98 (m, 1H), 6.23 (s, 1H), 4.54 (dd, J = 9.0, 4.7 Hz, 1H), 2.53 – 2.35 (m, 2H), 2.16 – 2.06 (m, 1H), 1.96 – 1.85 (m, 1H), 1.85 – 1.73 (m, 1H), 1.70 – 1.58 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 172.33, 150.5 (dd, J_{CF} = 250.5, 13.1 Hz), 149.8 (dd, J_{CF} = 249.5, 13.1 Hz), 139.61 (dd, J_{CF} = 15.4, 18.4 Hz), 121.98 (dd, J_{CF} = 6.4, 3.6 Hz), 117.62 (d, J_{CF} = 17.4 Hz), 115.16 (d, J_{CF} = 18.1 Hz), 56.75 (d, J_{CF} = 1.4 Hz), 32.04, 31.19, 19.36. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{12}F_2NO^+$ 212.0881; Found 212.0884. HPLC: Chiracel ODH Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 19.9 min (major), 24.9 min (minor).



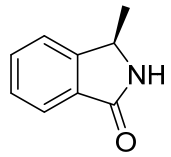
4i

Chemical Formula: $C_{12}H_{15}NO$
Exact Mass: 189.1154

7-phenylazepan-2-one (4i)

White solid, 15.9 mg, 42% yield, 90% ee, $[\alpha]^{25}_{D}$ = 25.7 (c=0.7, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-d) δ 7.37 (t, *J* = 7.5 Hz, 2H), 7.32 (t, J = 7.3 Hz, 3H), 5.68 (s, 1H), 4.46 (q, J = 10.0, 3.9 Hz, 1H), 2.65 – 2.52 (m, 2H), 2.08 (dd, J = 11.1, 3.8 Hz, 1H), 2.02 – 1.97 (m, 1H), 1.97 – 1.88 (m, 2H), 1.72 – 1.61 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 177.2, 142.4, 129.1, 128.1, 126.2, 58.7, 37.1, 37.1, 29.9, 23.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NO^+$ 190.1226; Found 190.1226. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 12.6 min (major),

14.0 min (minor). The absolute configuration of **4a** was identified by comparison of its physical and spectroscopic data with the one reported in the literature.[1]

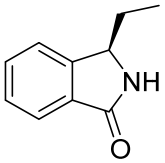


6a

Chemical Formula: C_9H_9NO
Exact Mass: 147.0684

(*R*)-3-methylisoindolin-1-one (6a)

White solid, 26.8 mg, 91% yield, 97% ee, $[\alpha]^{26}_D$ = 14.5 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 (br, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5, 1.2 Hz, 1H), 7.50 – 7.41 (m, 2H), 4.72 (q, *J* = 6.7 Hz, 1H), 1.52 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 171.1, 148.9, 131.8, 131.6, 128.0, 123.6, 122.2, 52.6, 20.2. HPLC: Chiracel OD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 9.6 min (minor), 10.4 min (major). The absolute configuration of **6a** was identified by comparison of its physical and spectroscopic data with the one reported in the literature.[11] The absolute configuration of **6c**-**6i** was determined by comparing with **4a**.



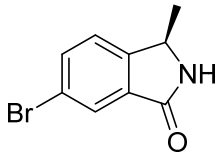
6b

Chemical Formula: $C_{10}H_{11}NO$
Exact Mass: 161.0841

(*R*)-3-ethylisoindolin-1-one (6b)

White solid, 29.6 mg, 92% yield, 96% ee, $[\alpha]^{25}_D$ = 42.2 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.64 – 7.53

(m, 2H), 7.51 – 7.38 (m, 2H), 4.61 (q, *J* = 6.4, 4.4 Hz 1H), 2.10 – 1.97 (m, 1H), 1.79 – 1.66 (m, 1H), 0.97 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 171.3, 147.4, 132.1, 131.7, 128.0, 123.7, 122.4, 58.0, 27.3, 9.5. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}NO^+$ 162.0913; Found 162.0914. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.4 min (major), 11.3 min (minor). The absolute configuration of **6b** was identified by comparison of its physical and spectroscopic data with the one reported in the literature.[11]

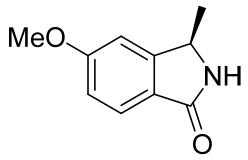


6c

Chemical Formula: C_9H_8BrNO
Exact Mass: 224.9789

(*R*)-6-bromo-3-methylisoindolin-1-one (6c)

White solid, 42.7 mg, 95% yield, 97% ee, on 0.2 mmol scale; 864 mg, 95% yield, 96% ee, on 4.0 mmol scale, $[\alpha]^{26}_{D}$ = 20.1 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-d) δ 7.97 (s, 1H), 7.82 (s, 1H), 7.69 (dd, J = 8.0, 1.8 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 4.68 (q, J = 6.8 Hz, 1H), 1.51 (d, J = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, Chloroform-d) δ 169.5, 147.5, 134.8, 133.7, 126.9, 123.9, 122.1, 52.4, 20.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_9BrNO^+$ 225.9862; Found 225.9863. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 10.5 min (major), 11.7 min (minor).

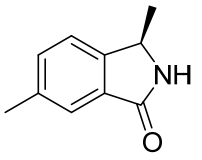


6d

Chemical Formula: $C_{10}H_{11}NO_2$
Exact Mass: 177.0790

(*R*)-5-methoxy-3-methylisoindolin-1-one (6d)

White solid, 29.4 mg, 83% yield, 96% ee, $[\alpha]^{25}_D$ = 50.5 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.70 (br, 1H), 6.98 (m, 1H), 6.90 (d, *J* = 2.1 Hz, 1H), 4.65 (q, *J* = 6.7 Hz, 1H), 3.88 (s, 3H), 1.50 (d, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 170.9, 163.0, 151.3, 125.0, 124.2, 114.5, 107.0, 55.6, 52.3, 20.4. HRMS (ESI) m/z: 178.0862 $[M+H]^+$ Calcd for $C_{10}H_{12}NO_2^+$ 178.0863; Found 225.9863. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 17.8 min (minor), 21.4 min (major).



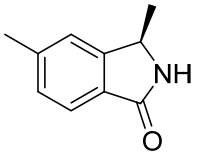
6e

Chemical Formula: $C_{10}H_{11}NO$
Exact Mass: 161.0841

(*R*)-3,6-dimethylisoindolin-1-one (6e)

White solid, 29.6 mg, 92% yield, 92% ee, $[\alpha]^{25}_D$ = 18.3 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.65 (s, 1H), 7.49 (s, 1H), 7.38 (d, J = 8.5 Hz, 1H), 7.31 (d, J = 7.7 Hz, 1H), 4.67 (q, J = 6.7 Hz, 1H), 2.45 (s, 3H), 1.49 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 171.1, 146.2, 138.0, 132.8, 131.7, 123.9, 121.9, 52.4, 21.3, 20.4. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}NO^+$ 162.0913; Found 162.0915. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention

time: 9.9 min (major), 10.9 min (minor).

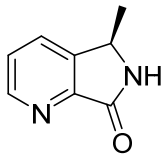


6f

Chemical Formula: $C_{10}H_{11}NO$
Exact Mass: 161.0841

(*R*)-3,5-dimethylisoindolin-1-one (6f)

White solid, 29.6mg, 92% yield, 96% ee, $[\alpha]^{25.5}_{D}$ = 42.6 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.38 (br, 1H), 7.27 (d, *J* = 7.7 Hz, 1H), 7.23 (s, 1H), 4.65 (q, *J* = 6.7 Hz, 1H), 2.47 (s, 3H), 1.49 (d, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 171.0, 149.3, 142.5, 129.1, 123.5, 122.7, 52.3, 21.9, 20.3. HRMS (ESI) m/z $[M+H]^+$ Calcd for $C_{10}H_{12}NO^+$ 162.0913; Found 162.0915. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 13.2 min (minor), 14.4 min (major).



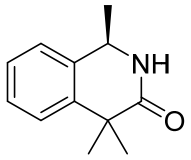
6g

Chemical Formula: $C_8H_8N_2O$
Exact Mass: 148.0637

(*R*)-5-methyl-5,6-dihydro-7H-pyrrolo[3,4-b]pyridin-7-one (6g)

Obtained from the corresponding isopropyl ester **5g**. White solid, 24.0 mg, 81% yield, 91% ee, $[\alpha]^{25}_{D}$ = 18.6 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.84 – 8.77 (m, 1H), 8.24 (d, J = 58.8 Hz, 1H), 7.86 – 7.79 (m, 1H), 7.47 (dd, J = 7.7, 4.8 Hz, 1H), 4.76 (q, J = 6.8 Hz, 1H), 1.56 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 168.9, 150.9, 149.9, 142.3, 130.6, 125.5,

50.6, 19.9. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_8H_9N_2O^+$ 149.0709; Found 149.0710. HPLC: Chiracel OJ-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 21.2 min (minor), 23.3 min (major).

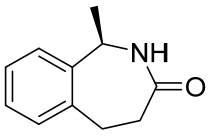


6h

Chemical Formula: $C_{12}H_{15}NO$
Exact Mass: 189.1154

(*R*)-1,4,4-trimethyl-1,4-dihydroisoquinolin-3(2H)-one (6h)

White solid, 34.0 mg, 90% yield, 94% ee, $[\alpha]^{25}_D$ = 17.6 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (600 MHz, Chloroform-d) δ 7.38 (d, J = 7.8 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.17 (d, J = 7.6 Hz, 1H), 6.66 (s, 1H), 4.73 (q, J = 6.1 Hz, 1H), 1.59 (s, 3H), 1.56 (d, J = 6.7 Hz, 3H), 1.54 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-d) δ 176.4, 140.7, 134.3, 127.7, 126.4, 125.7, 125.0, 50.1, 41.3, 28.7, 27.2, 25.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NO^+$ 190.1226; Found 190.1228. HPLC: Chiracel IE Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 16.7 min (minor), 17.6 min (major).



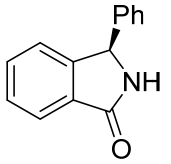
6i

Chemical Formula: $C_{11}H_{13}NO$
Exact Mass: 175.0997

(*R*)-1-methyl-1,2,4,5-tetrahydro-3H-benzo[c]azepin-3-one (6i)

White solid, 18.2 mg, 52% yield, 90% ee, $[\alpha]^{25}_D$ = - 41.5 (c=0.4, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum

ether 3:7). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.30 – 7.21 (m, 4H), 5.83 (s, 1H), 4.99 – 4.82 (m, 1H), 3.36 – 3.20 (m, 1H), 3.00 – 2.79 (m, 2H), 2.64 – 2.48 (m, 1H), 1.64 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 173.5, 140.3, 139.9, 129.0, 128.2, 126.8, 123.9, 47.7, 35.4, 28.3, 19.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{14}NO^+$ 176.1070; Found 176.1071. HPLC: Chiracel IA Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 20.4 min (minor), 23.5 min (major). The absolute configuration of **6i** was identified by comparison of the physical and spectroscopic data with the similar ones reported in the literature.[12]



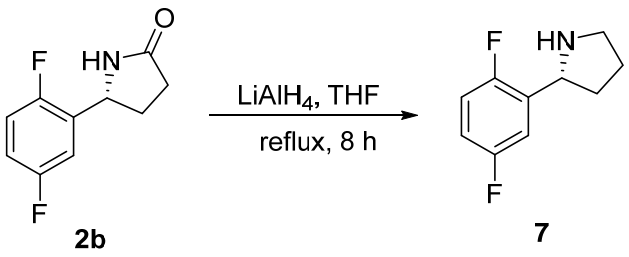
6j

Chemical Formula: $C_{14}H_{11}NO$
Exact Mass: 209.0841

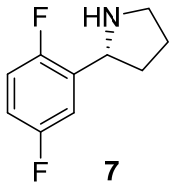
(*R*)-3-phenylisoindolin-1-one (6j)

White solid, 22.2 mg, 53% yield, 88% ee, $[\alpha]^{25}_{D}$ = -65.9 (c=0.5, $CHCl_3$), obtained by the purification with flash column chromatography on silica gel (EtOAc/petroleum ether 3:7). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 1H), 7.71 (d, *J* = 7.2 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.39 – 7.34 (m, 2H), 7.33 – 7.27 (m, 4H), 5.73 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 169.76, 148.23, 139.71, 131.93, 131.43, 128.86, 128.20, 127.97, 126.63, 123.57, 122.96, 59.58. HPLC: Chiracel AD-3 Column (250 mm); detected at 210 nm; n-hexane / i-propanol = 90/10; flow = 0.8 mL/min; Retention time: 13.0 min (major), 21.9 min (minor). The NMR data is consistent with that reported. [13] The absolute configuration of **6j** was identified by comparison of the physical and spectroscopic data with the similar ones reported in the literature.[14]

3.6 Reduction of 2b



A suspension of $LiAlH_4$ in 5 mL THF was heated to reflux. **2b** (97 mg, 0.5 mmol, >99% ee) in 1 mL THF was added slowly. The resulting mixture was continued to stir for 8 hours under reflux. The reaction was cooled to 0 °C and quenched by successive addition of H_2O, NaOH (15%, aq.), and H_2O (19 μL /19μL /57 μL, 1 : 1 : 3). The solid was filterted and washed with CH_2Cl_2. The filtrate was dried over anhydrous Na_2SO_4, and then concentrated under vacuum. The residue was purified with column chromatography on silica gel (eluent: DCM/MeOH/Et_2NH = 97:2:1) to afford **7** as yellow oil.



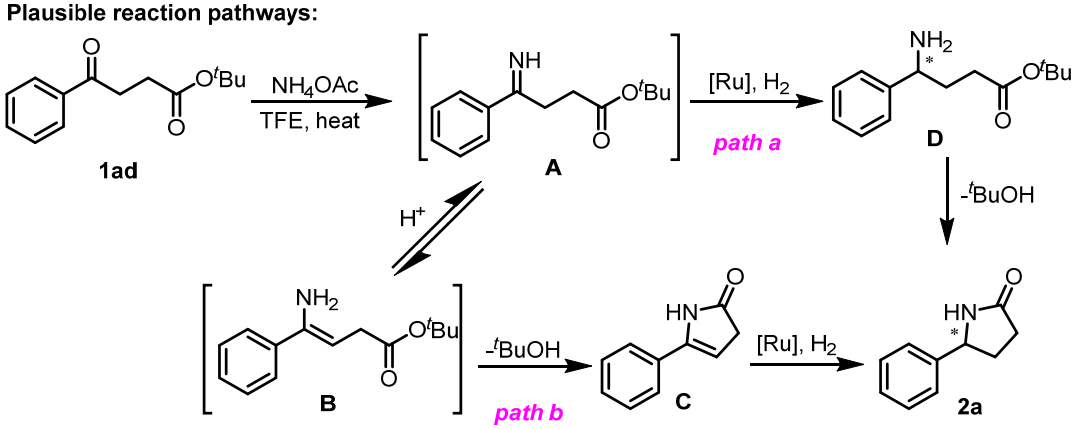
Chemical Formula: $C_{10}H_{11}F_2N$
Exact Mass: 183.0860

(R)-2-(2,5-difluorophenyl)pyrrolidine (7)

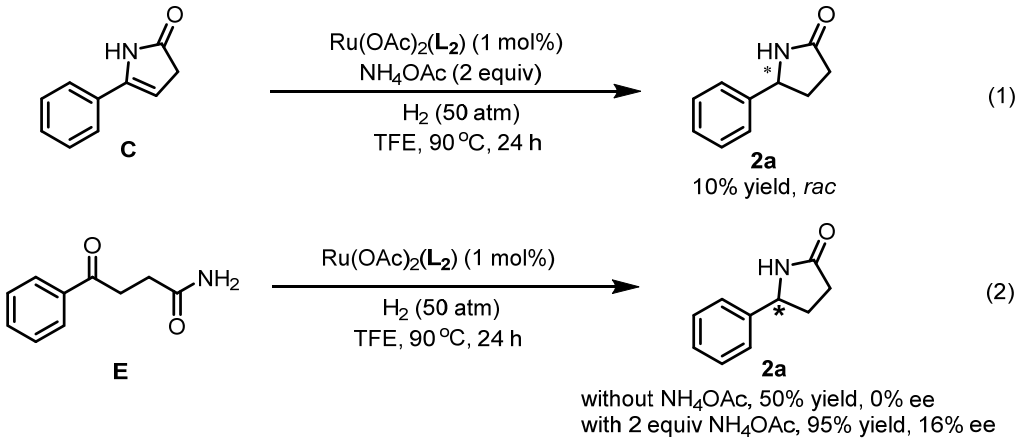
Yellow oil. 77.8 mg, 85% yield, $[\alpha]^{25}_D$ = 37.8 (c=0.1, $CHCl_3$). ^{1}H NMR (600 MHz, Chloroform-d) δ 7.26 – 7.22 (m, 1H), 6.96 – 6.92 (m, 1H), 6.88 – 6.83 (m, 1H), 4.40 (t, J = 7.6 Hz, 1H), 3.22 – 3.14 (m, 1H), 3.10 – 3.01 (m, 1H), 2.29 – 2.23 (m, 1H), 2.08 (br, 1H), 1.94 – 1.80 (m, 2H), 1.66 – 1.59 (m, 1H). The ^{1}H NMR data is consistent with that reported, $[\alpha]^{20}_D$ = 38.4 (c= 0.1, $CHCl_3$).[15]

Ⅳ. Control Experiments

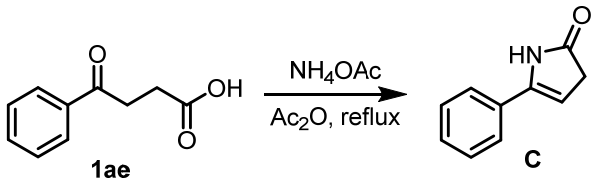
Plausible reaction pathways:



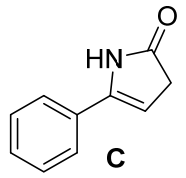
Control experiments:



Independent synthesis of **C**[16]



4-Oxo-4-phenylbutanoic acid **1ae** (1.41 g, 7.9 mmol) and NH_4OAc (1.53 g, 19.8 mmol) were dissolved in 20 mL of acetic anhydride. The resulting mixture was heated to 100℃ for 3 h and then cooled to room temperature. The reaction was slowly quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with water, and extracted with EA (3×30 mL). The combined organic layers were dried over anhydrous $NaSO_4$, filtered and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (eluent: EA/Hexane=5%) to afford **C** (0.89 g, 70% yield).



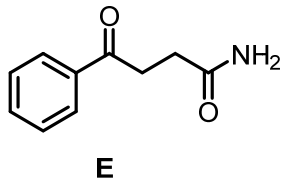
C

Chemical Formula: $C_{10}H_9NO$
Exact Mass: 159.0684

5-phenyl-1,3-dihydro-2H-pyrrol-2-one

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (dd, *J* = 7.7, 2.0 Hz, 2H), 7.40 – 7.31 (m, 3H), 5.73 (t, *J* = 2.8 Hz, 1H), 3.33 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 175.64, 153.47, 129.26, 128.39, 128.12, 124.39, 97.67, 34.30.

(4-Oxo-4-phenylbutanamide) E is synthesized according to a reported literature.[17]



E

Chemical Formula: $C_{10}H_{11}NO_2$
Exact Mass: 177.0790

4-Oxo-4-phenylbutanamide (E)

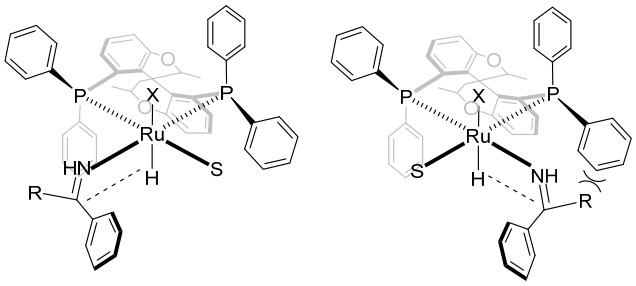
Pale solid. ^{1}H NMR (400 MHz, Methanol-d4) δ 8.03 – 7.97 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 3.34 (t, *J* = 6.7 Hz, 2H), 2.63 (t, *J* = 6.7 Hz, 2H).

Following **General Procedure F**, product **2a** was obtained in 10% yield as a racemic form from compound **C** (eq 1).

Following **General Procedure F**, in the absence of NH_4OAc, product **2a** was obtained in 50% yield as a racemic form from compound **E** (eq 2).

Following **General Procedure F**, in the prsence of 2 equiv of NH_4OAc, product **2a** was obtained in 95% yield and 16% ee from compound **E** (eq2).

Ⅴ. Plausible enantioinduction models



(*R*)-product favored　　(*S*)-product disfavored

We tentatively propose enantioinduction models for this reaction, which are depicted as above. We speculate the ester group in the substrate will not coordinate to the Ru center otherwise it will form a seven- or eight-membered ring transition state which is energetically unfavorable. The steric repulsion between the tethered ester moiety and the phenyl group on P atom results in the energy difference between two transition states, which is consistent with the fact that the enantioselectivity of **2a** is increasing along with the bulkiness of ester moiety increasing. Therefore, the *R*-configuration product is dominated.

Ⅵ. References

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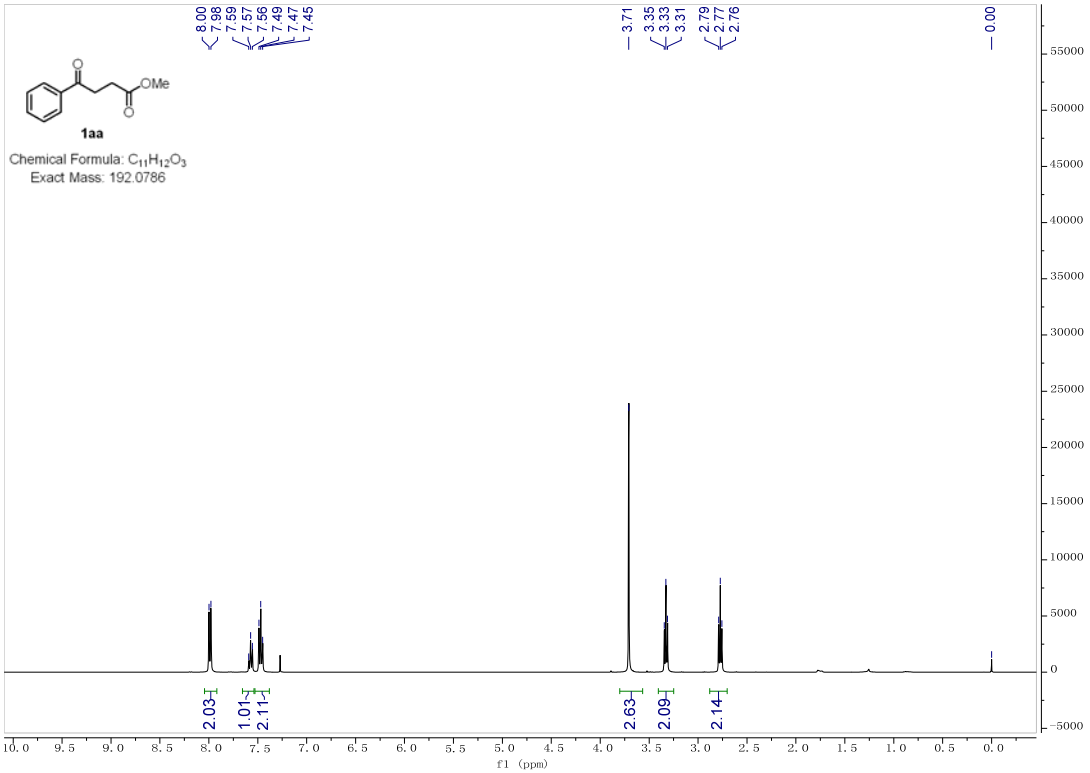
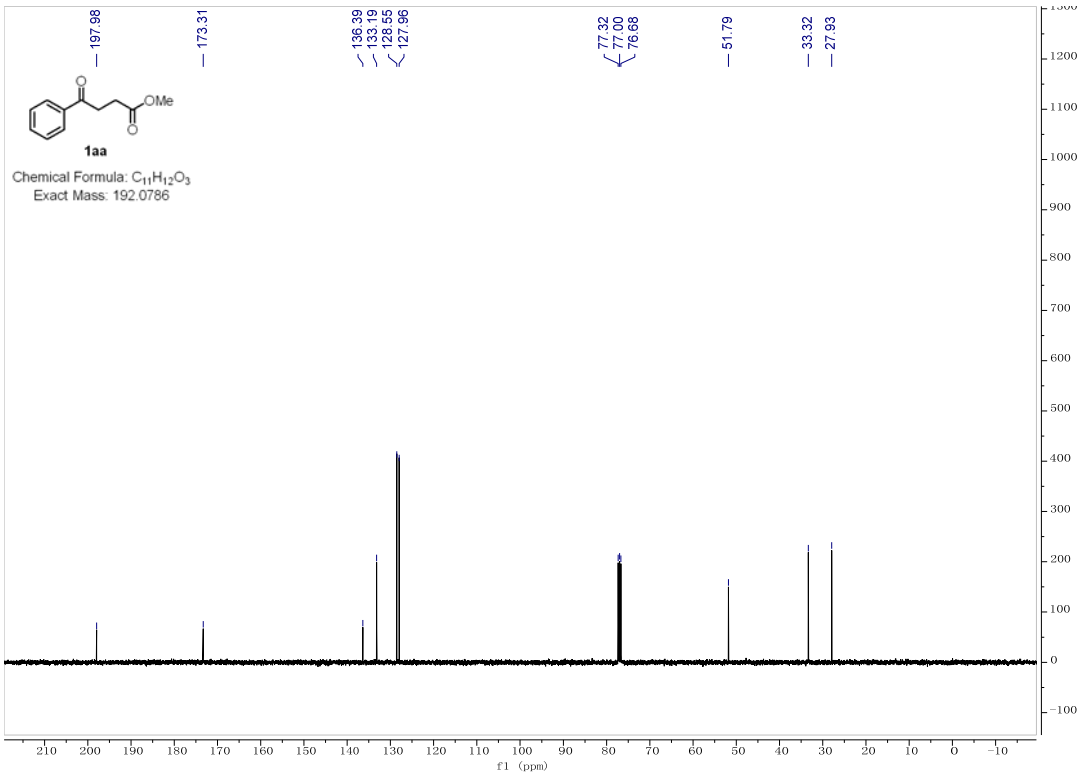
Ⅶ. NMR Spectra

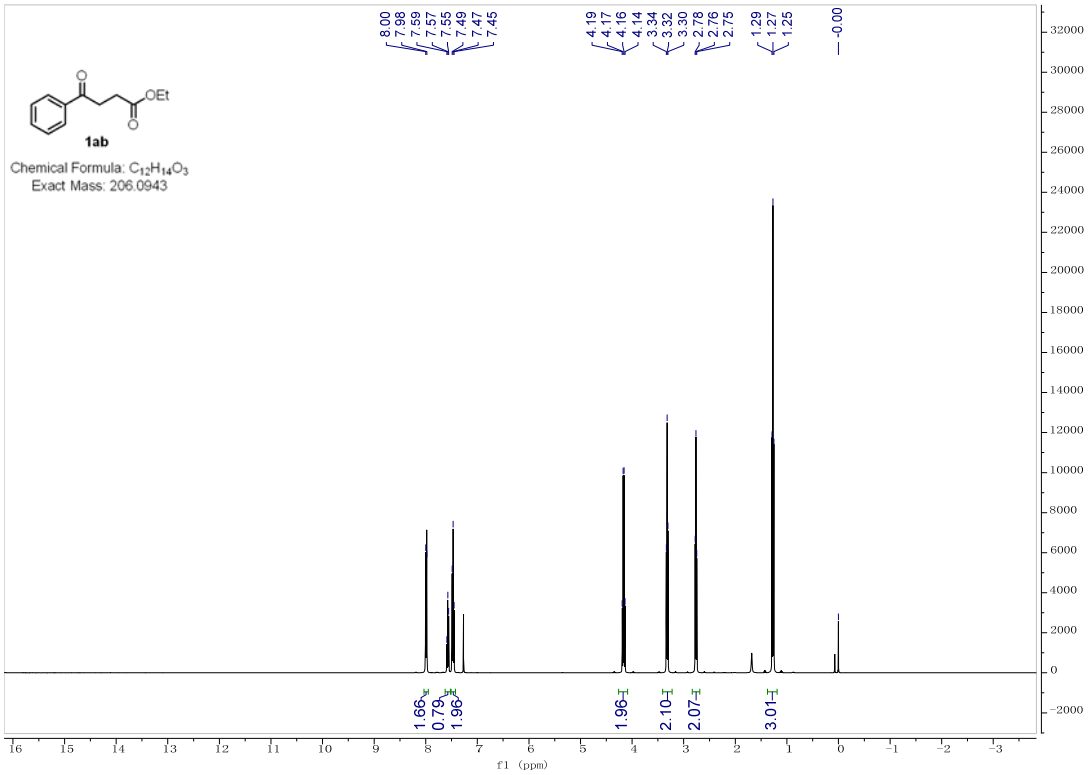
^{1}H NMR (400 MHz, Chloroform-d) of compound **1aa**



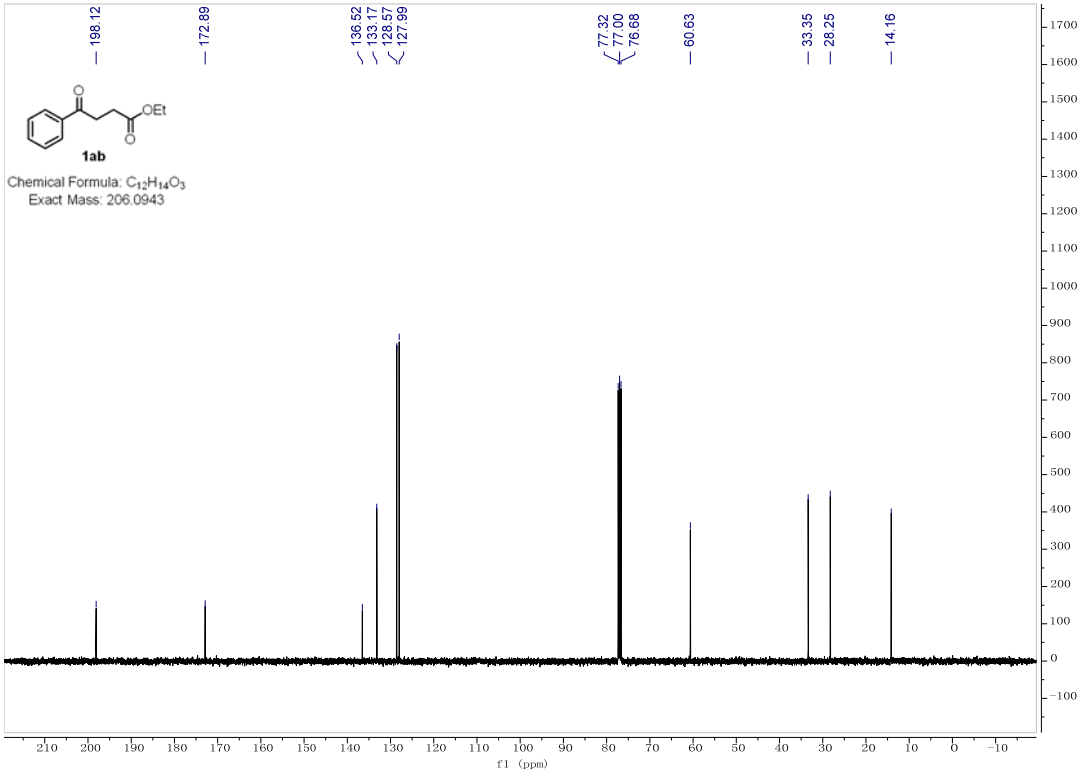
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1aa**



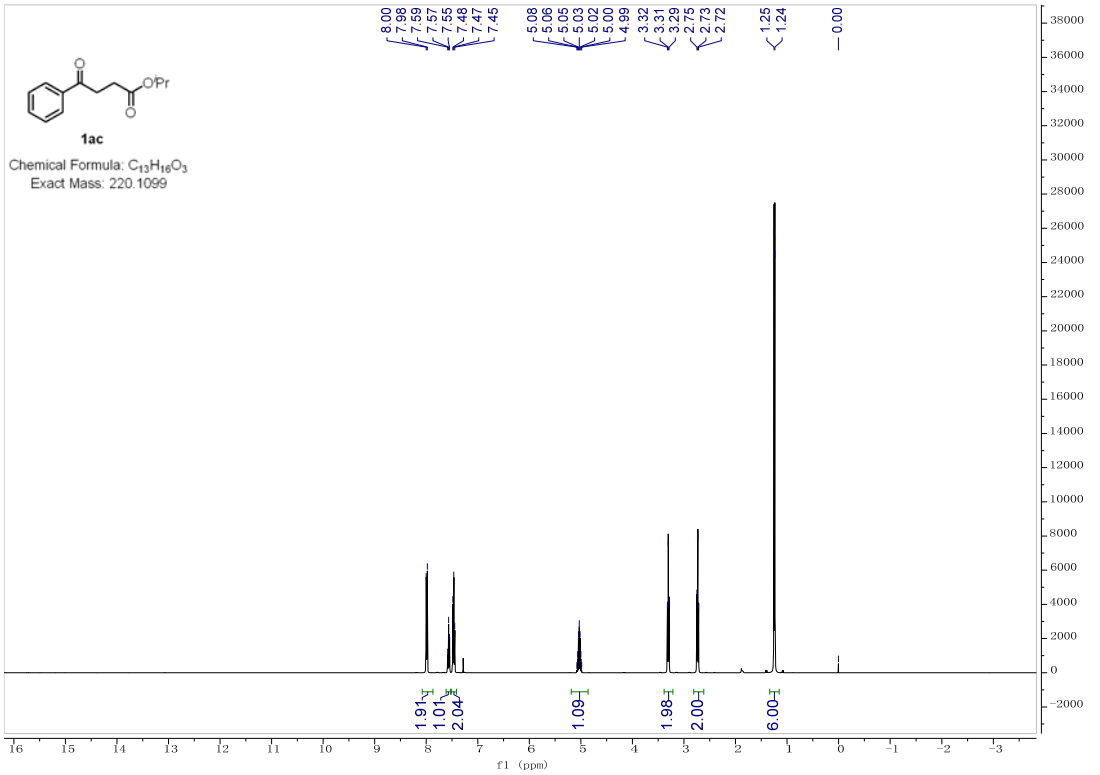
^{1}H NMR (400 MHz, Chloroform-d) of compound **1ab**



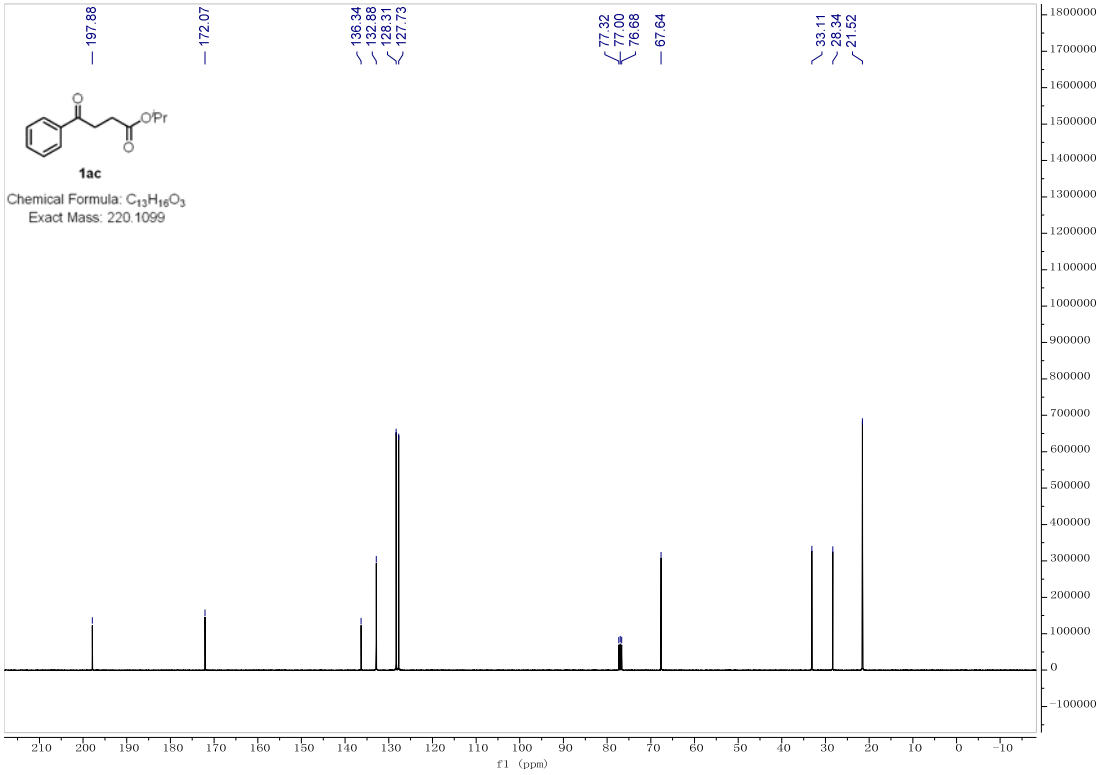
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1ab**



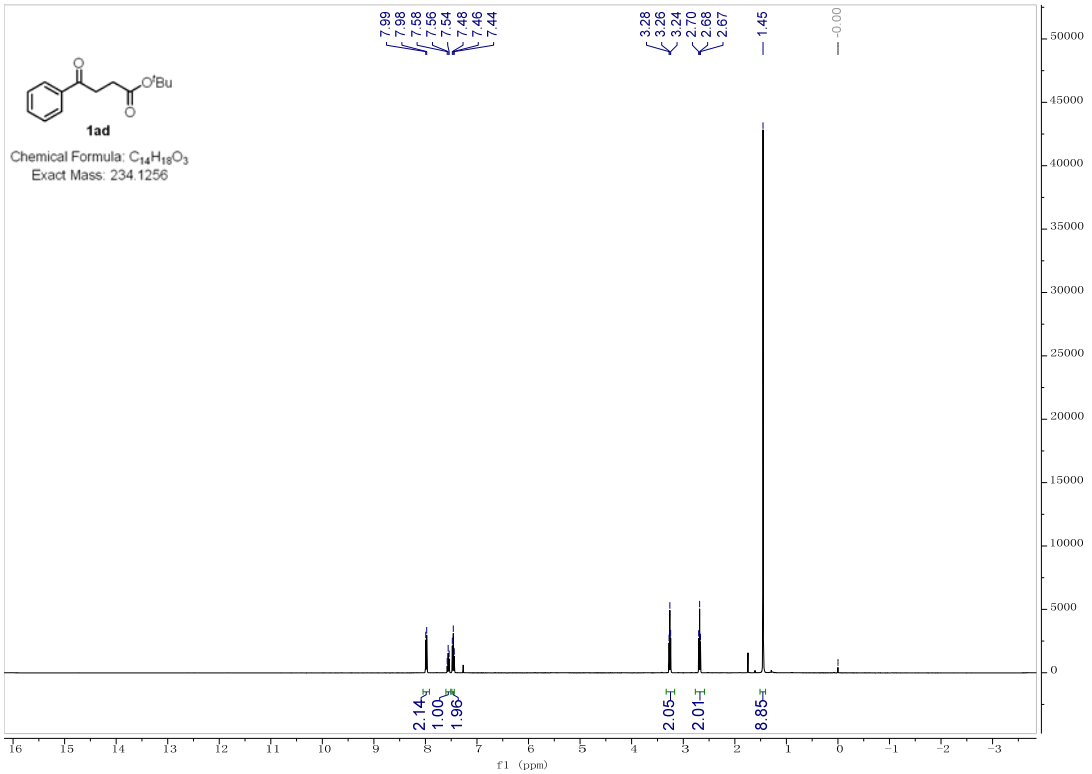
^{1}H NMR (400 MHz, Chloroform-d) of compound **1ac**



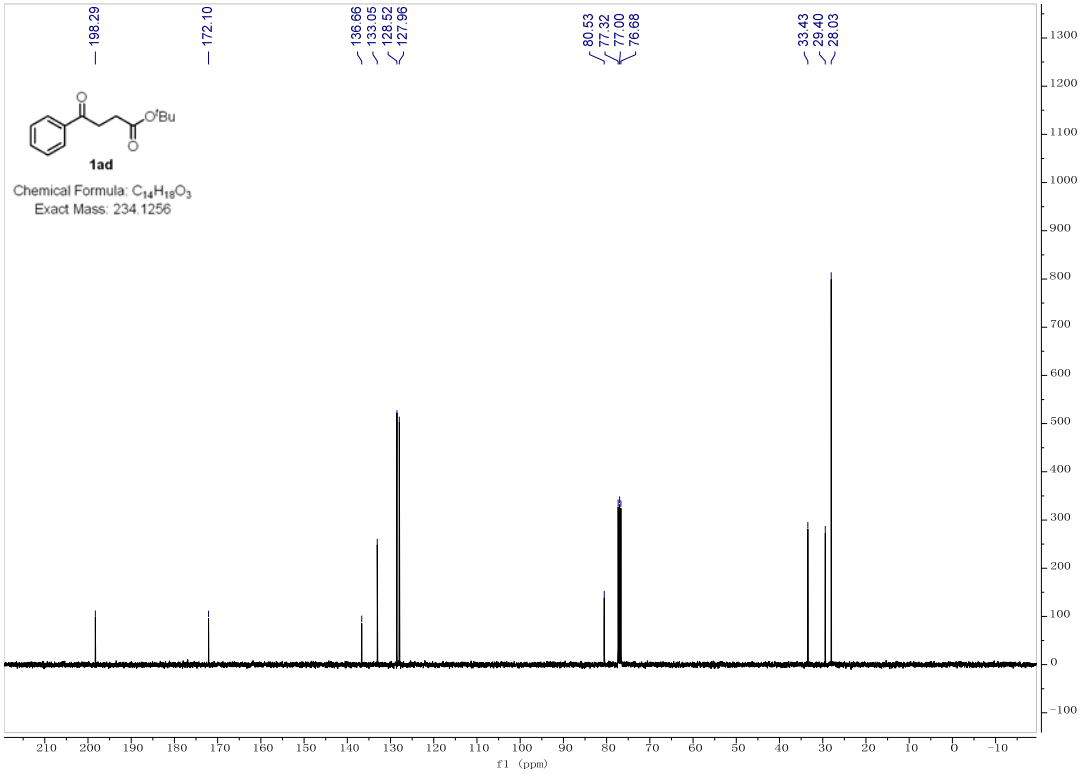
^{13}C{^{1}H} NMR (101MHz, Chloroform-d) of compound **1ac**



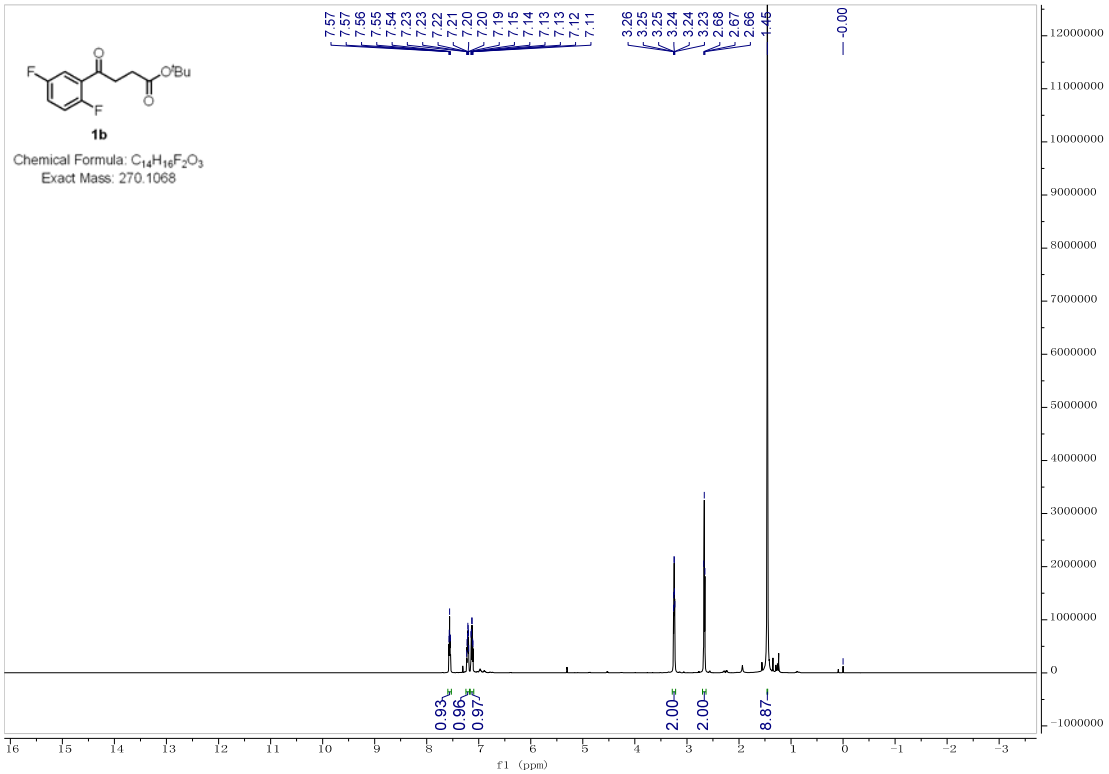
^{1}H NMR (400 MHz, Chloroform-d) of compound **1ad**



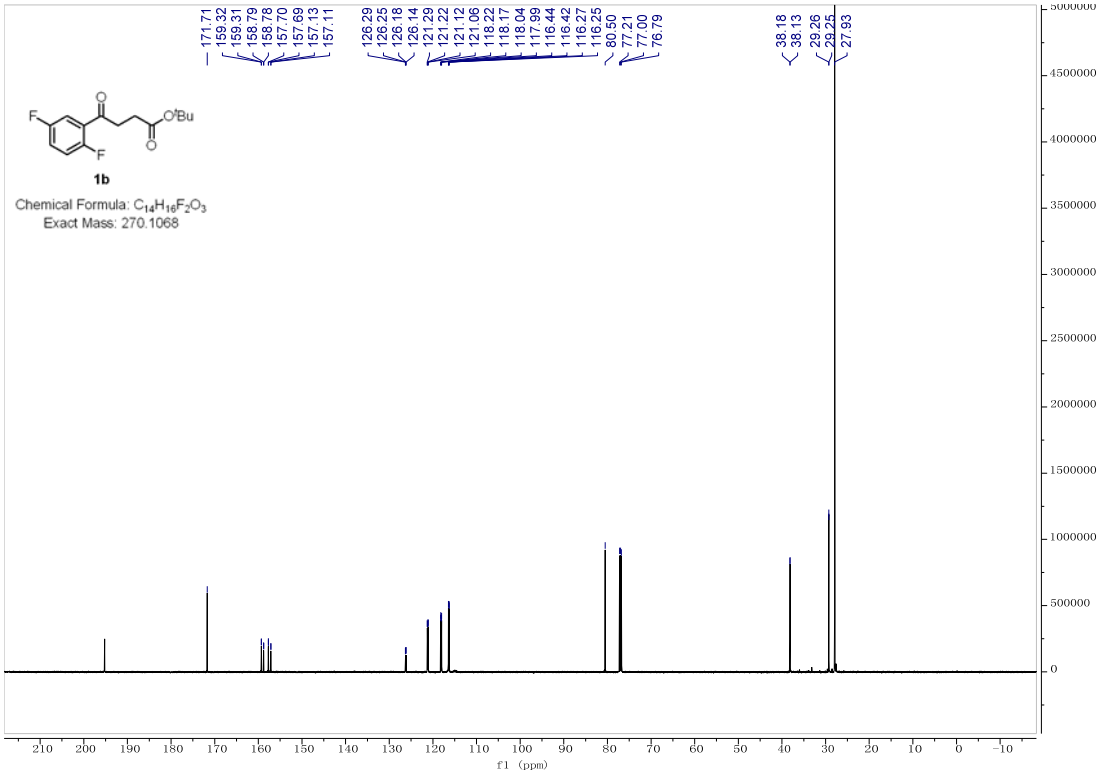
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1ad**



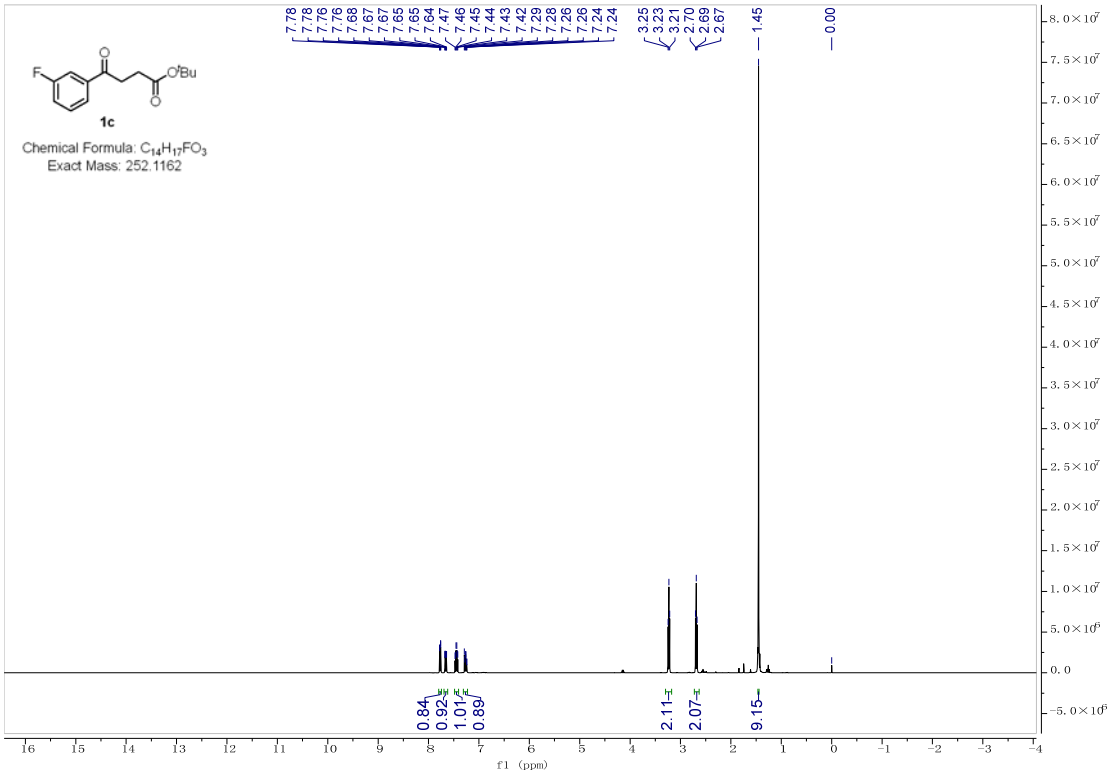
^{1}H NMR (600 MHz, Chloroform-d) of compound **1b**



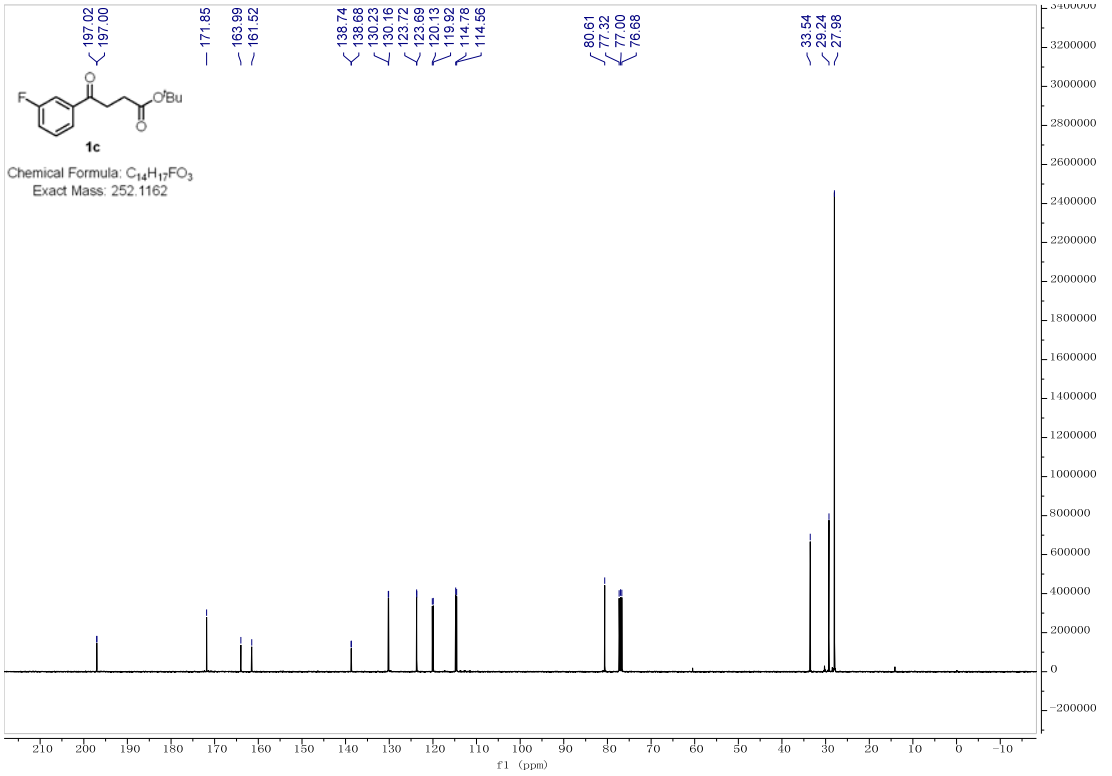
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **1b**



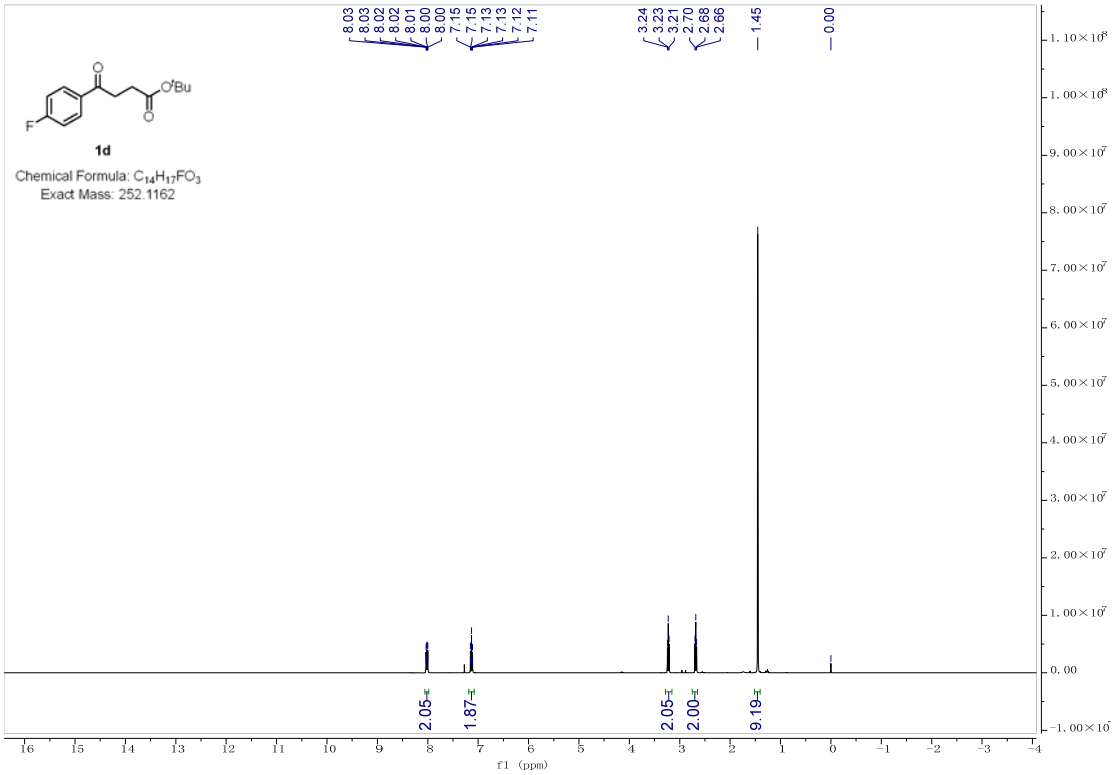
^{1}H NMR (400 MHz, Chloroform-d) of compound **1c**



^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1c**



^{1}H NMR (400 MHz, Chloroform-d) of compound **1d**



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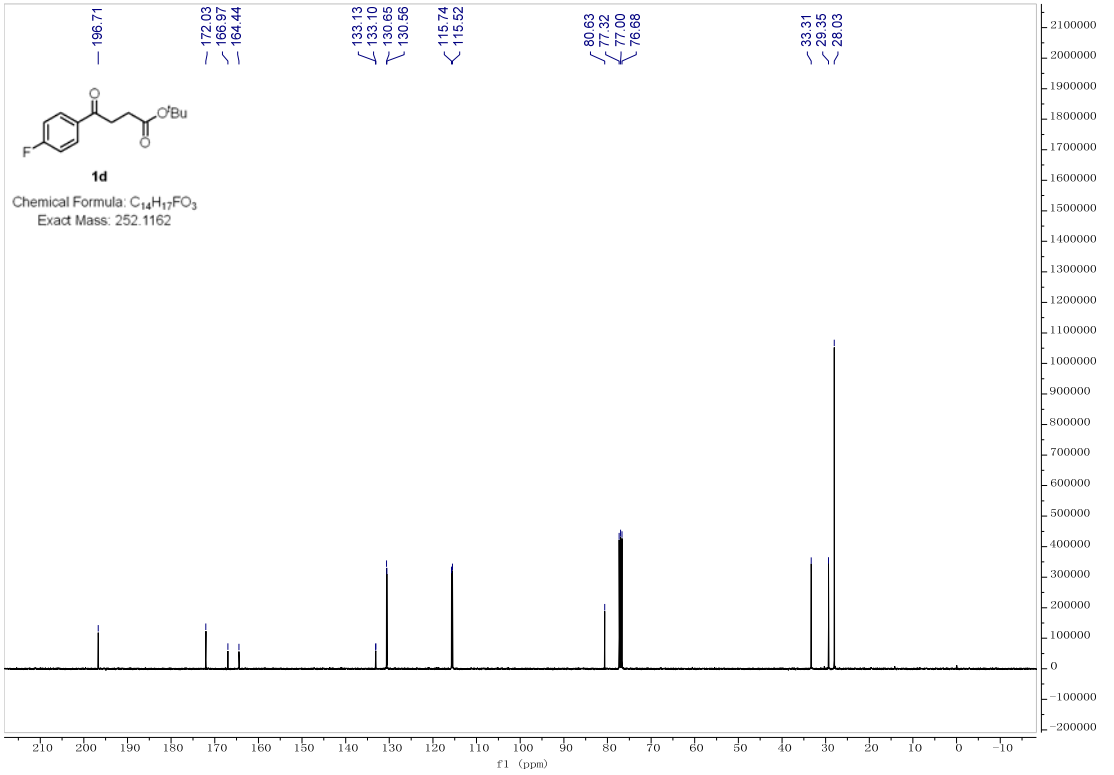
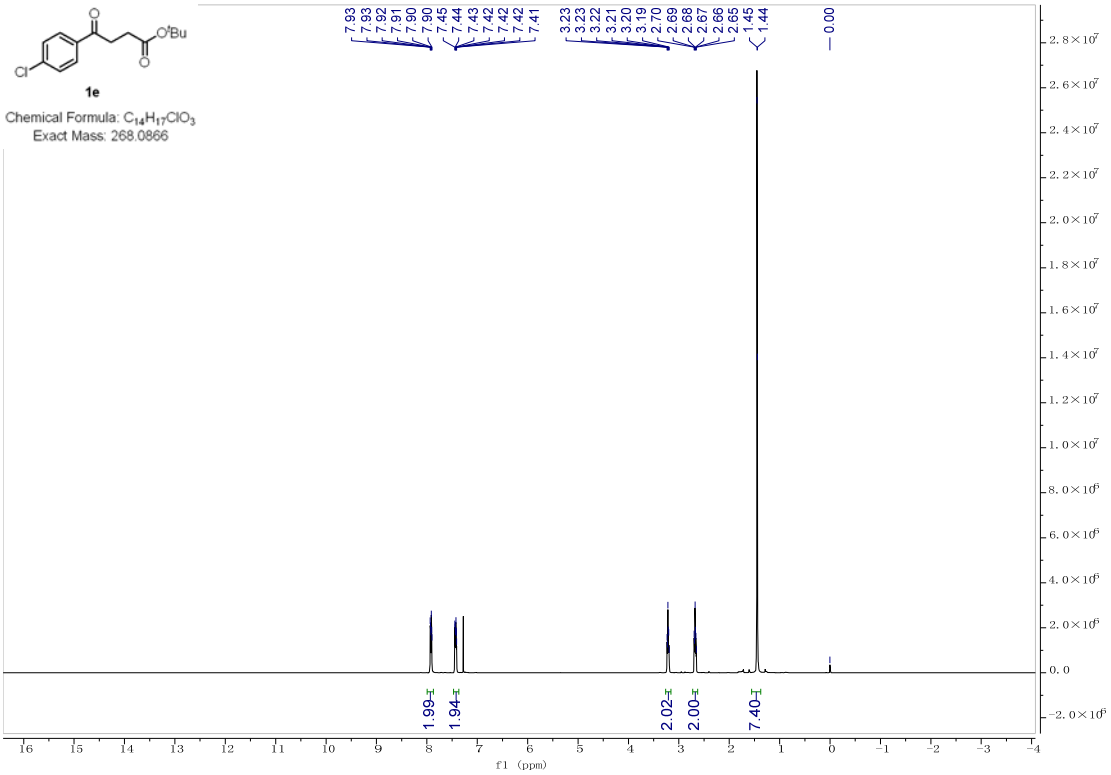


^{1}H NMR (400 MHz, Chloroform-d) of compound **1e**



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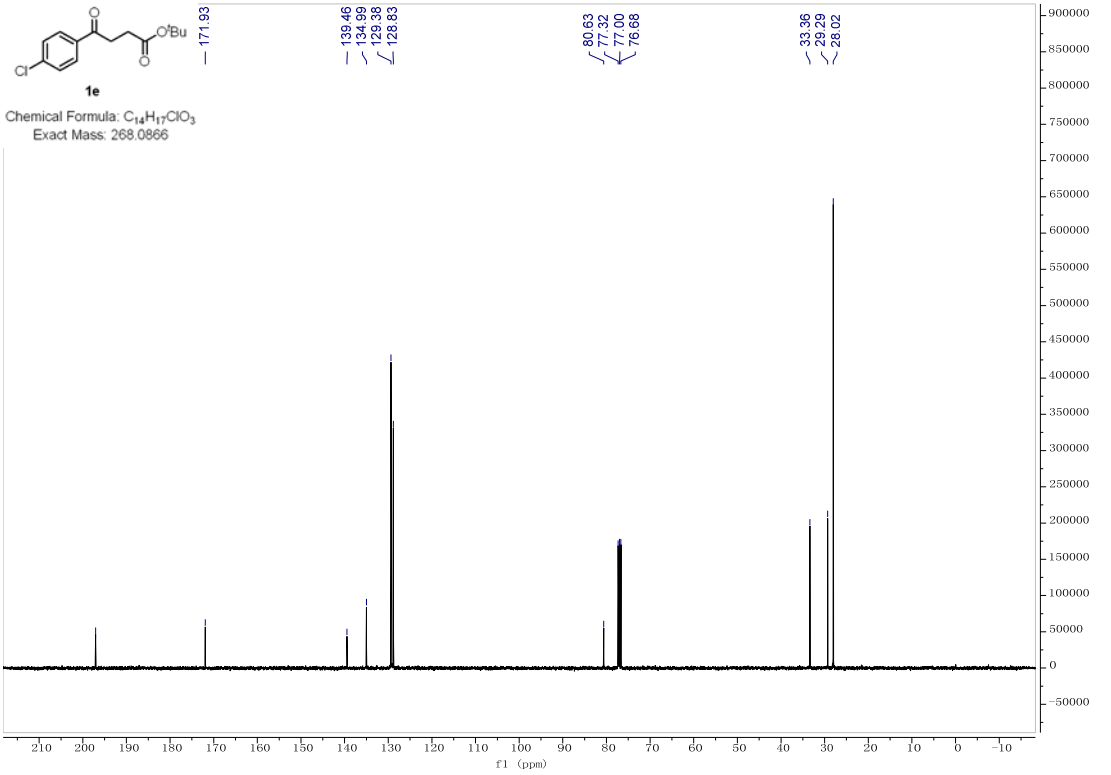
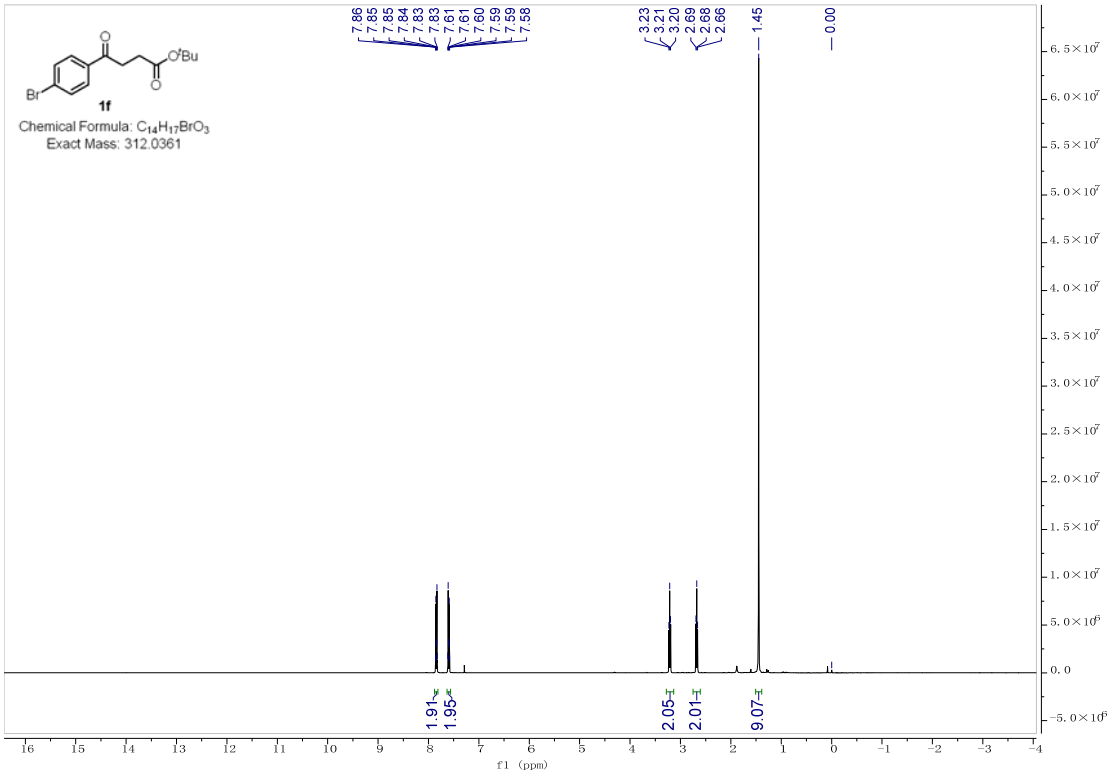
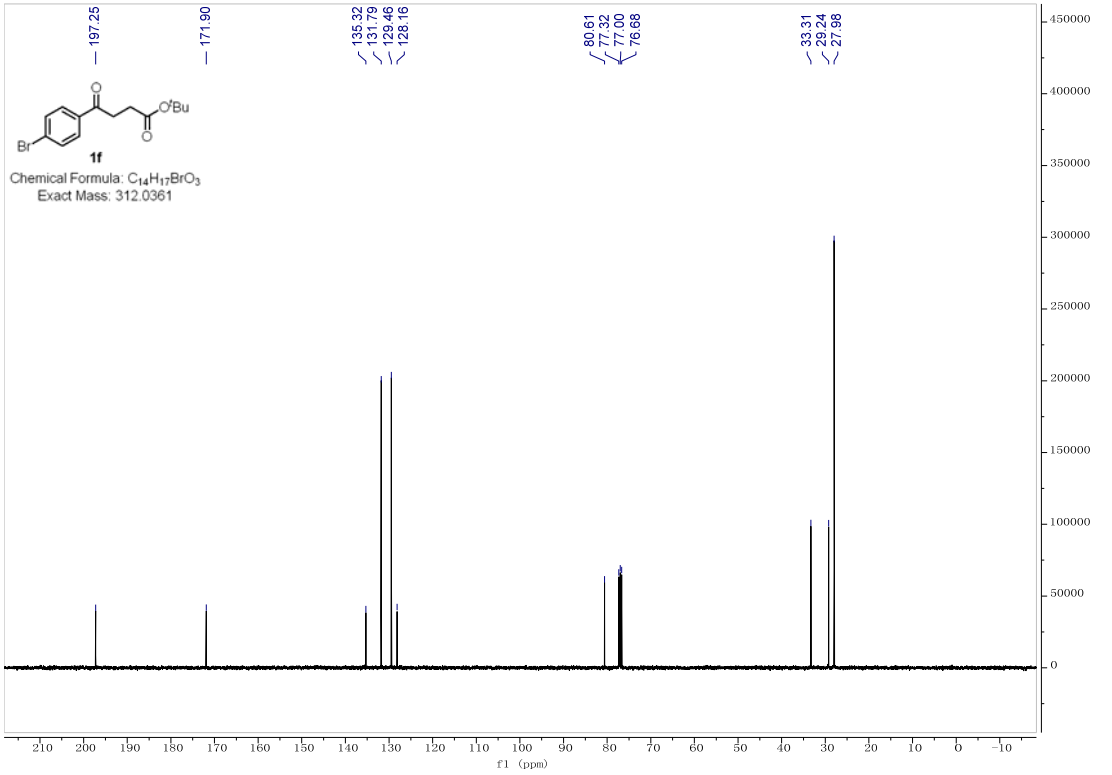


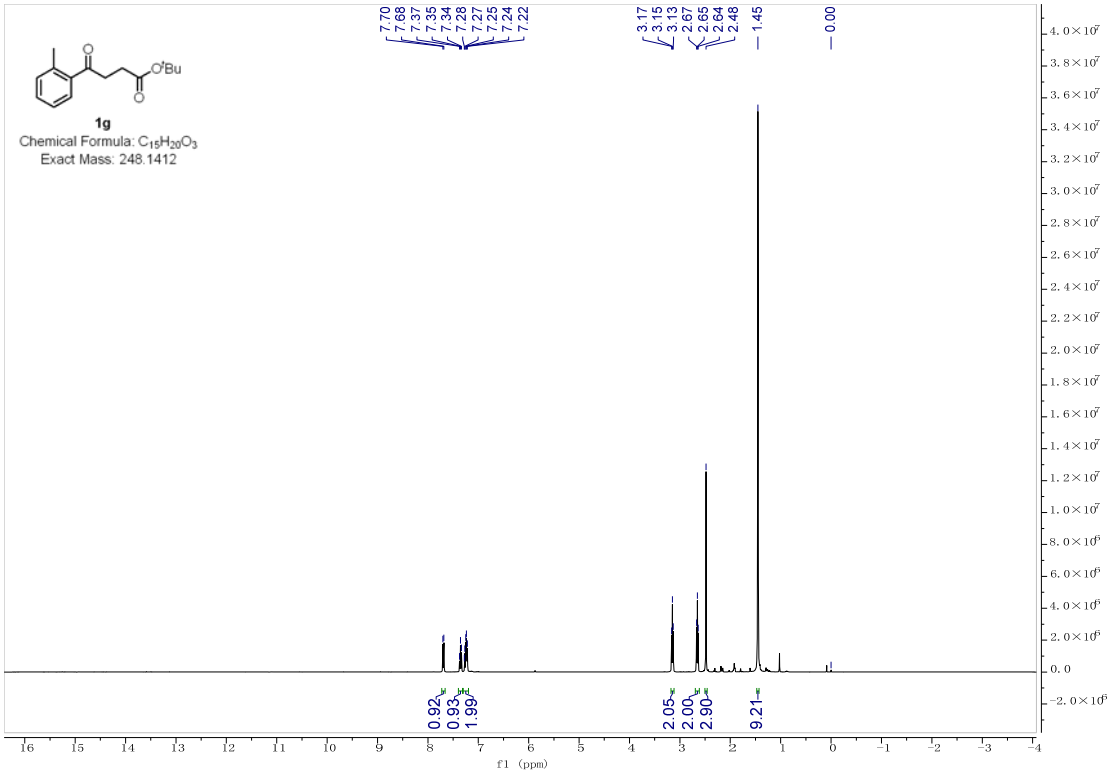
^{1}H NMR (400 MHz, Chloroform-d) of compound **1f**



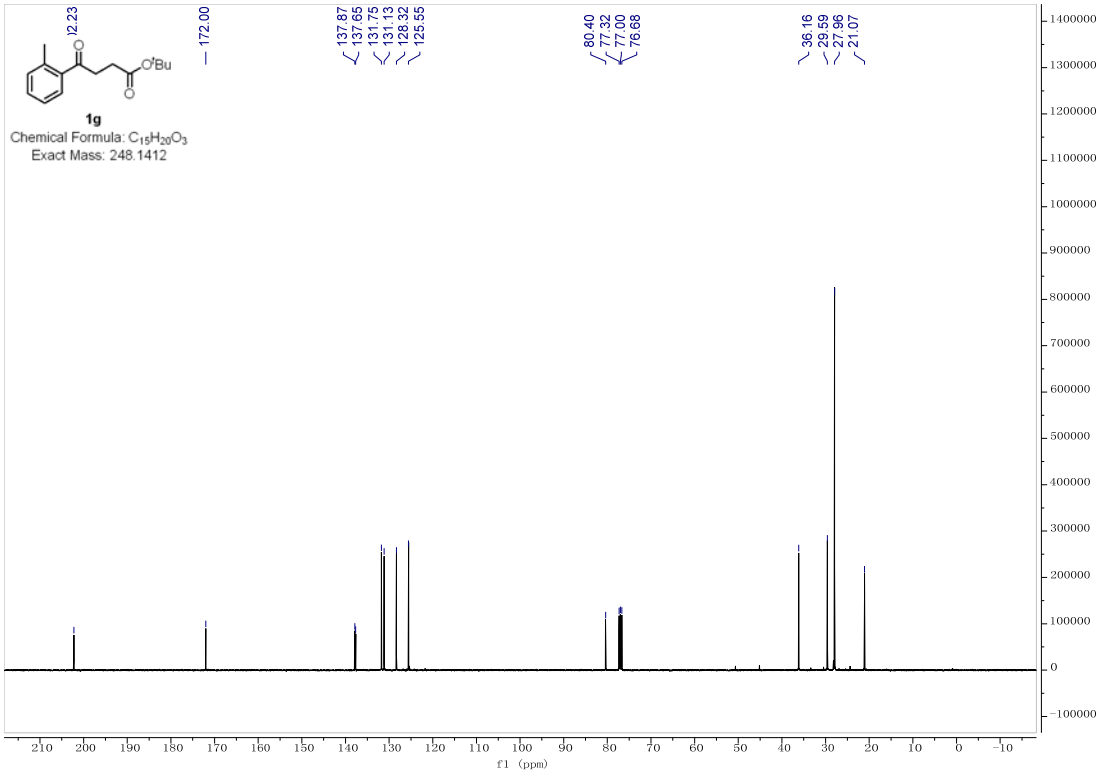
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1f**



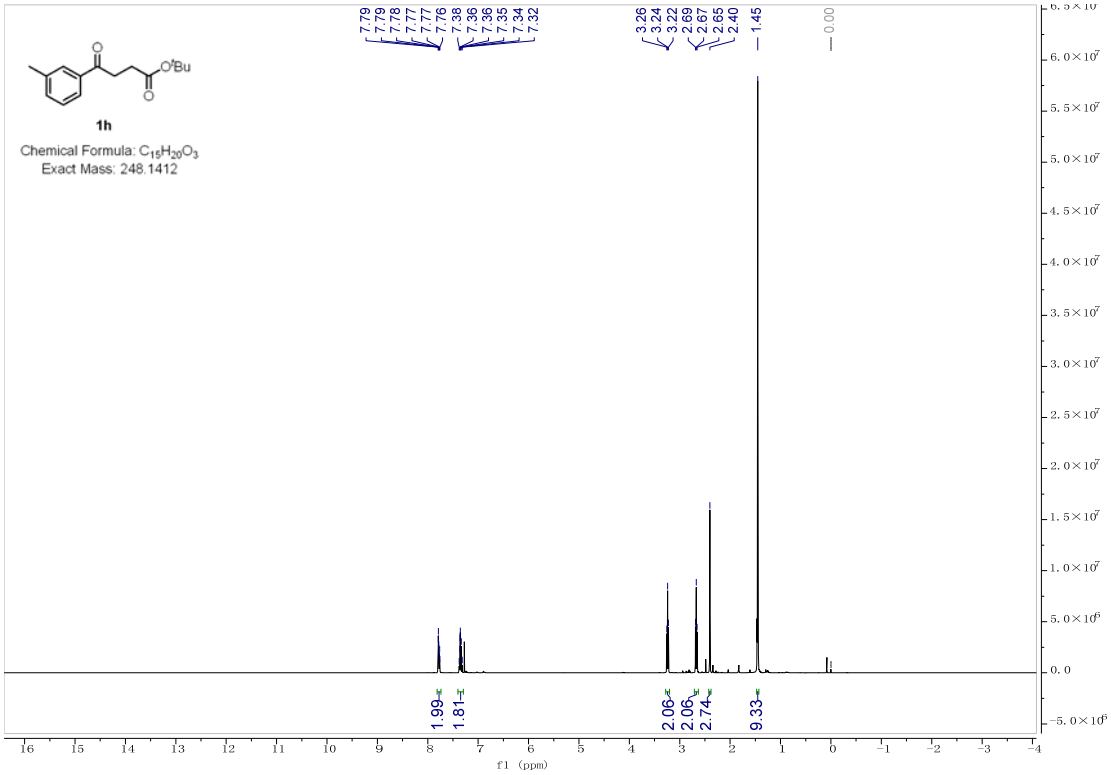
^{1}H NMR (400 MHz, Chloroform-d) of compound **1g**



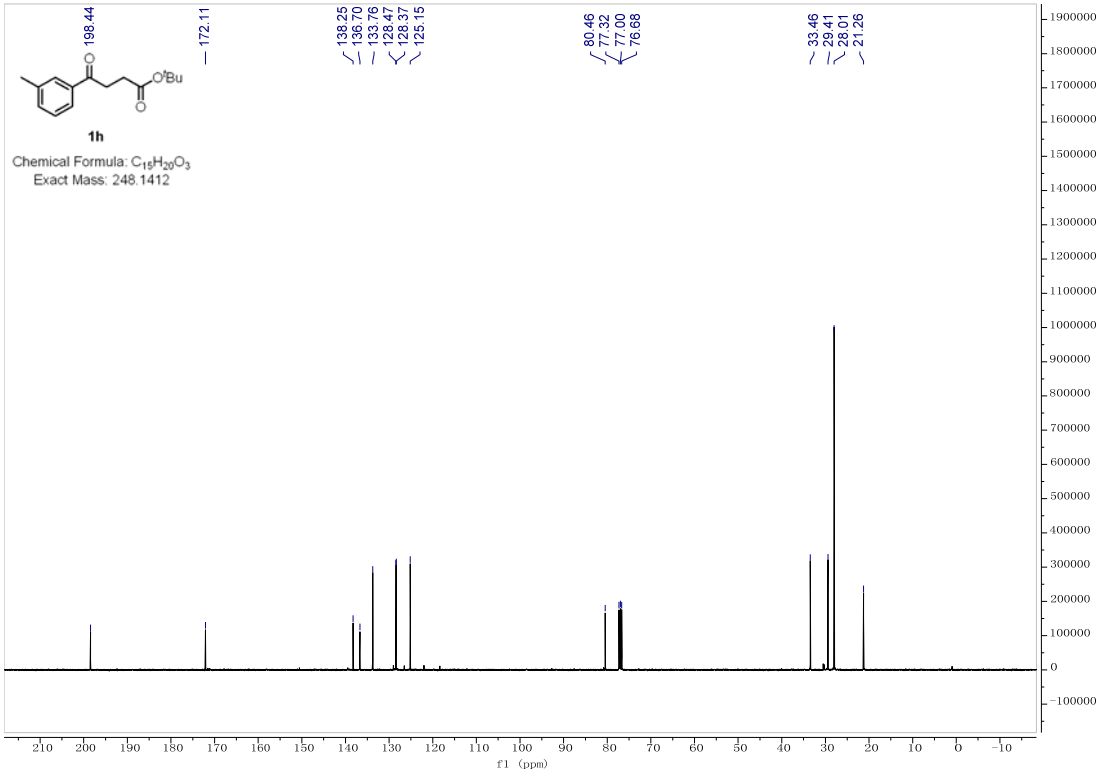
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1g**



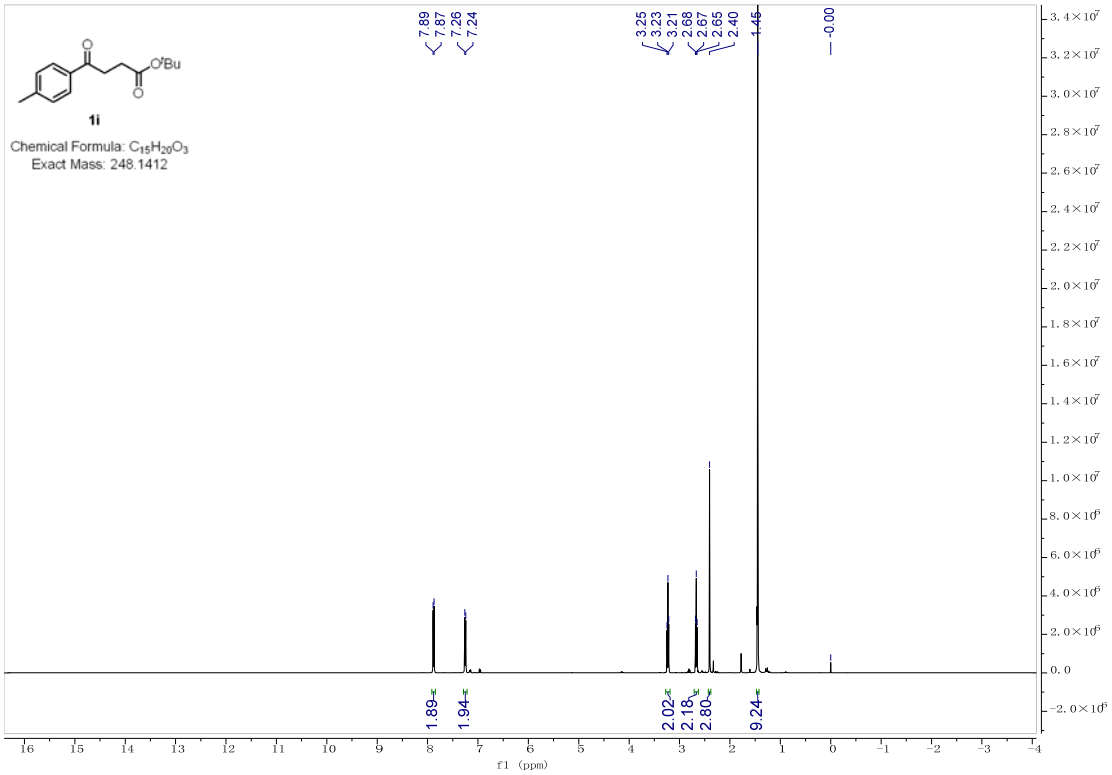
^{1}H NMR (400 MHz, Chloroform-d) of compound **1h**



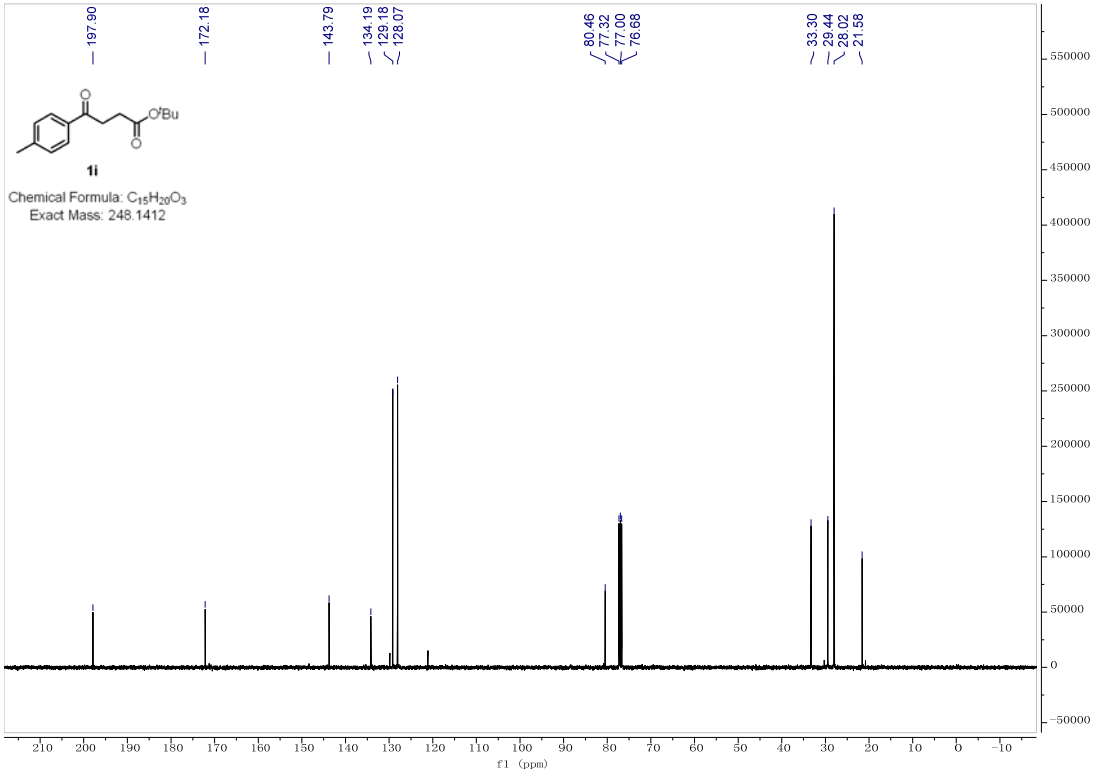
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1h**



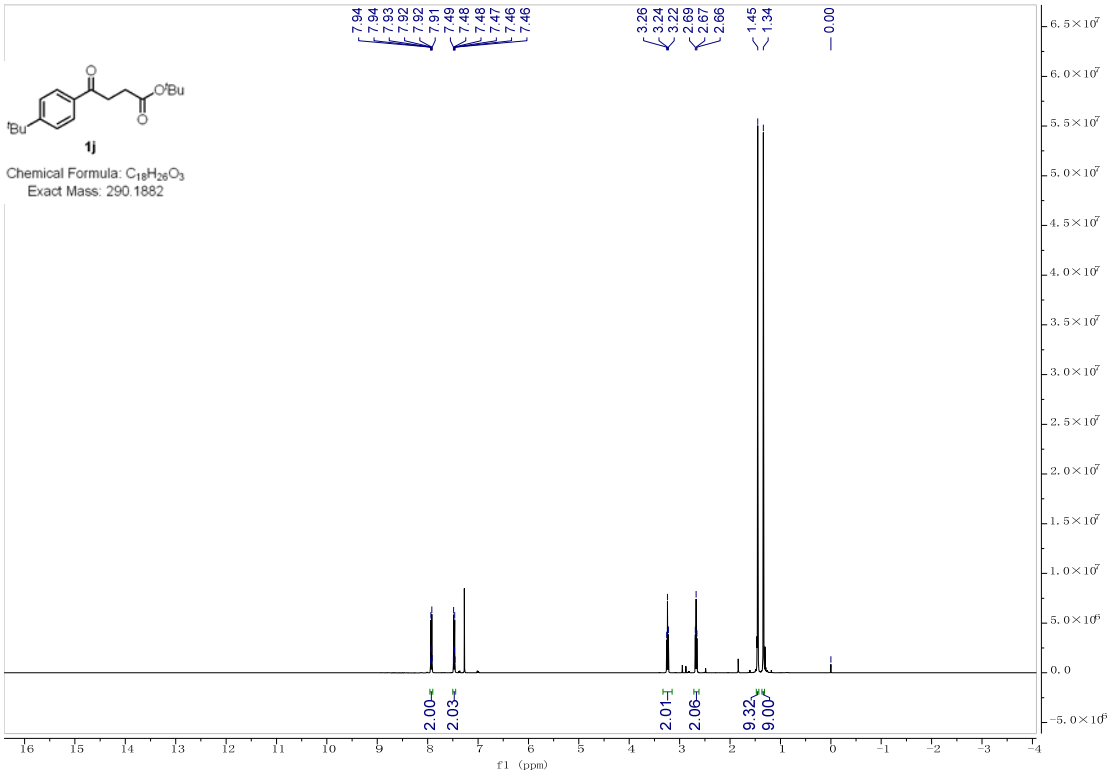
^{1}H NMR (400 MHz, Chloroform-d) of compound **1i**



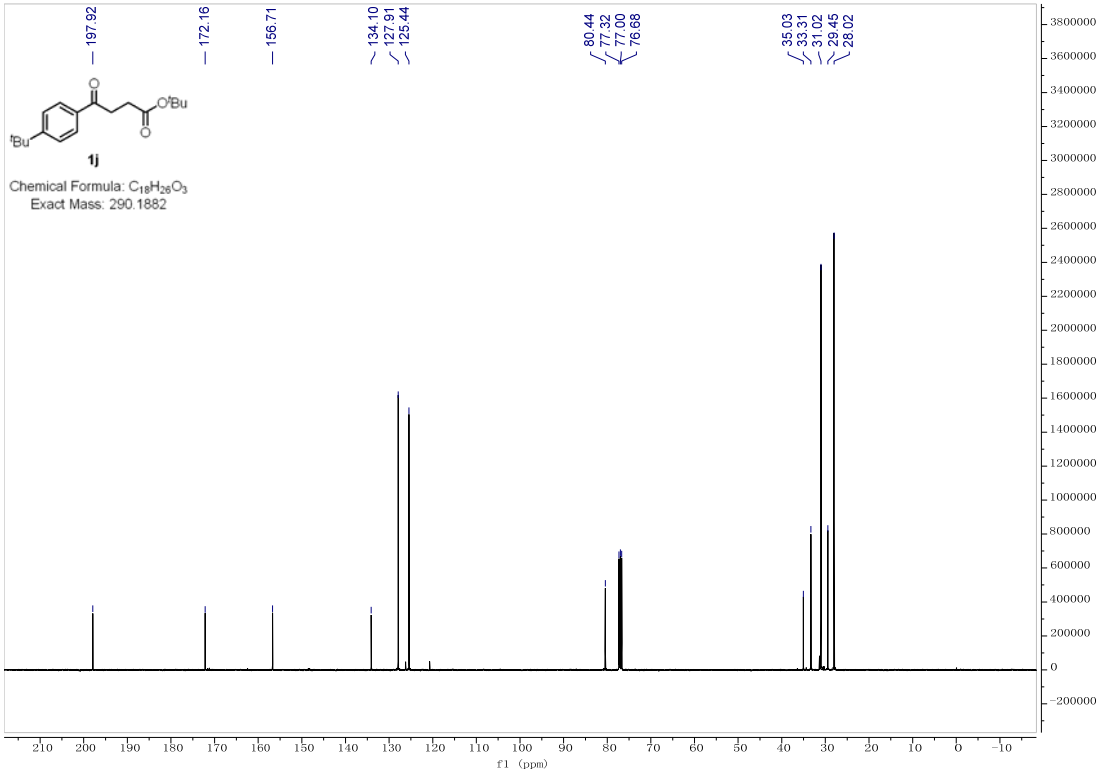
^{1}H{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1h**



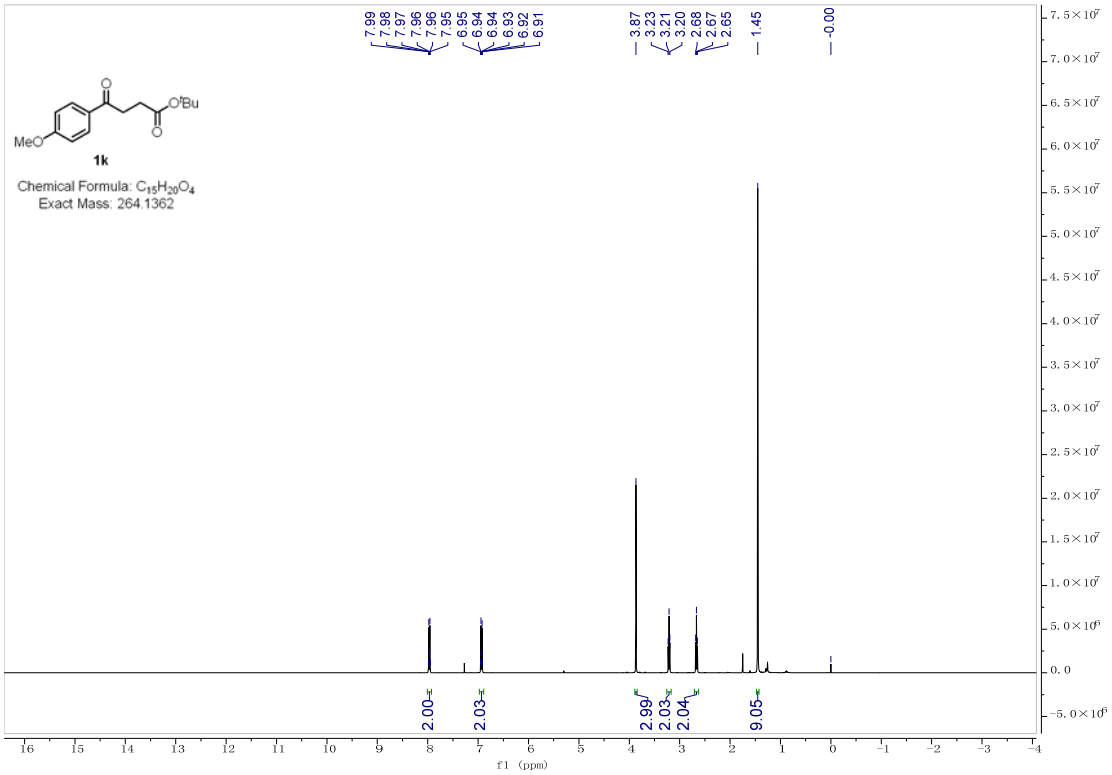
^{1}H NMR (400 MHz, Chloroform-d) of compound **1j**



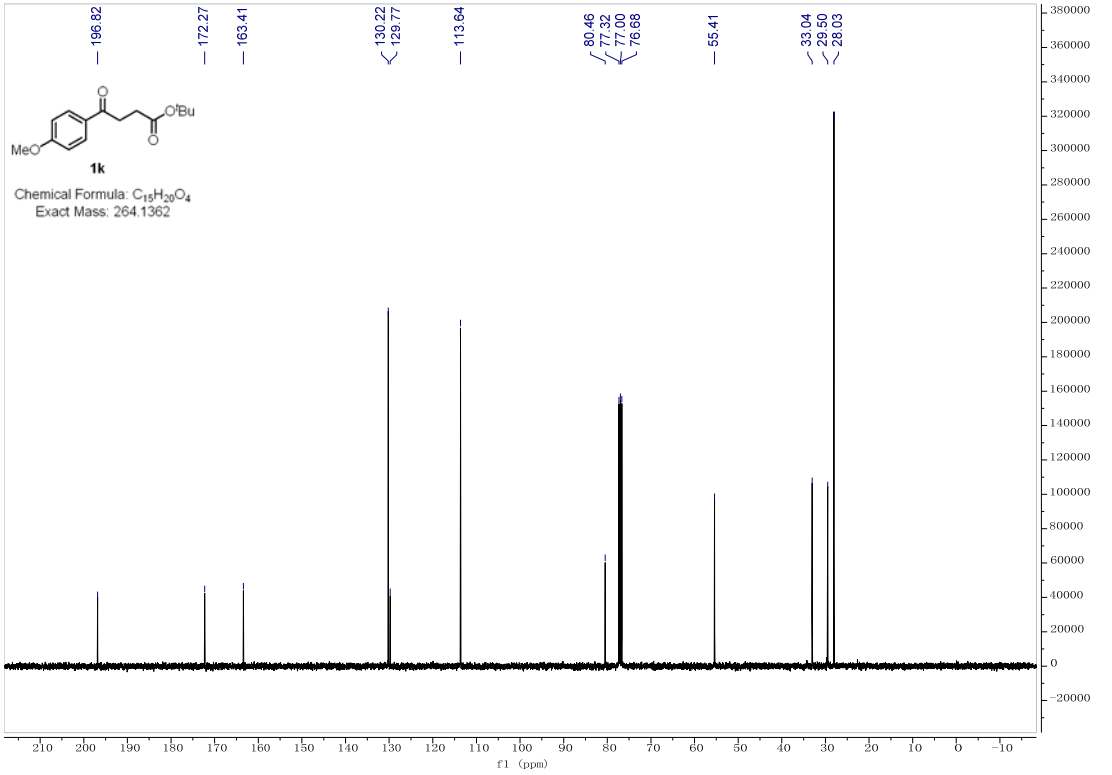
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1j**



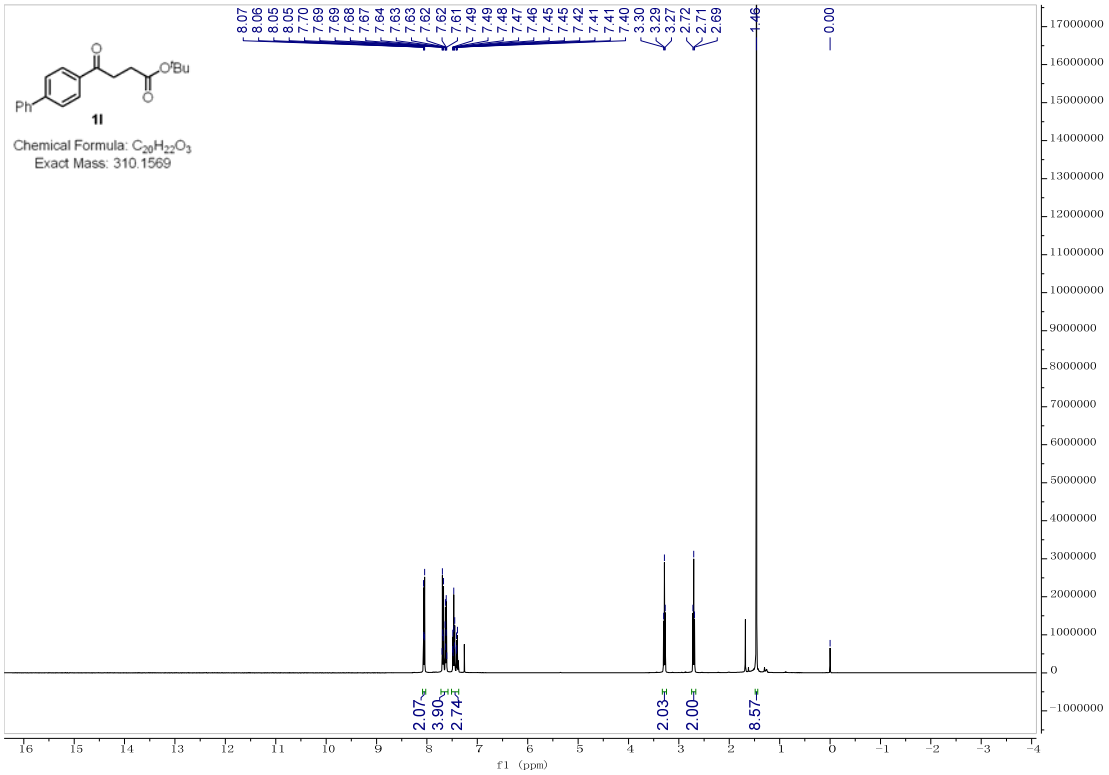
^{1}H NMR (400 MHz, Chloroform-d) of compound **1k**



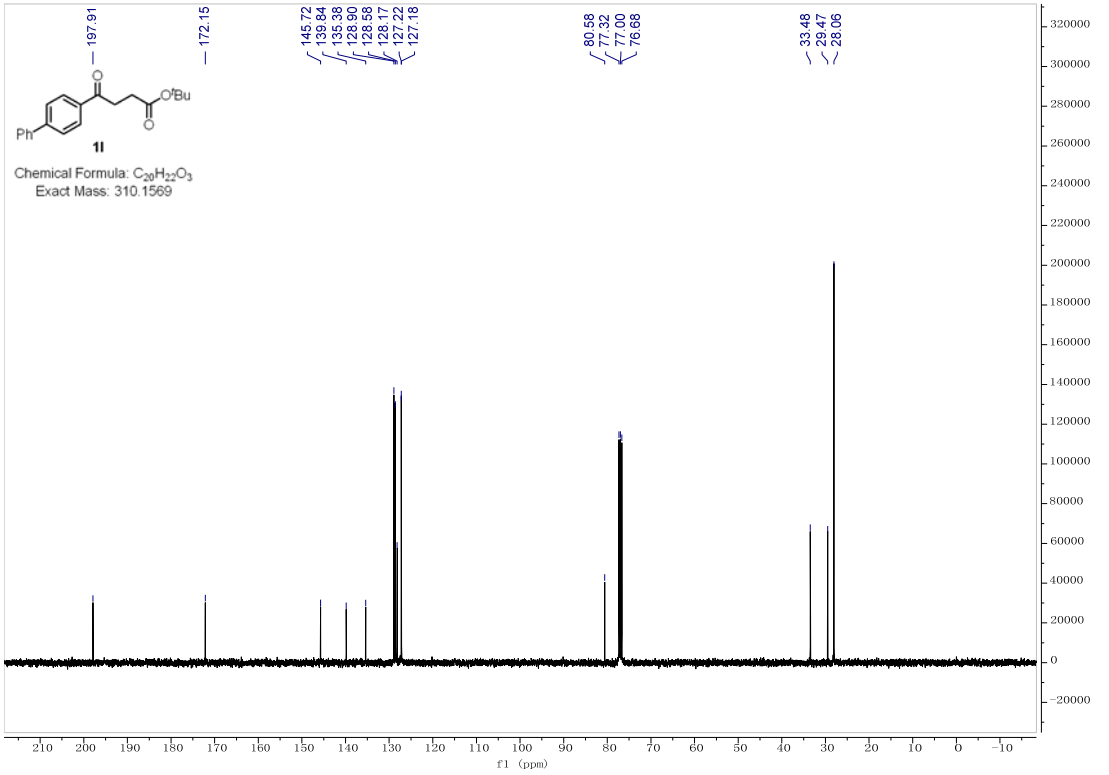
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1k**



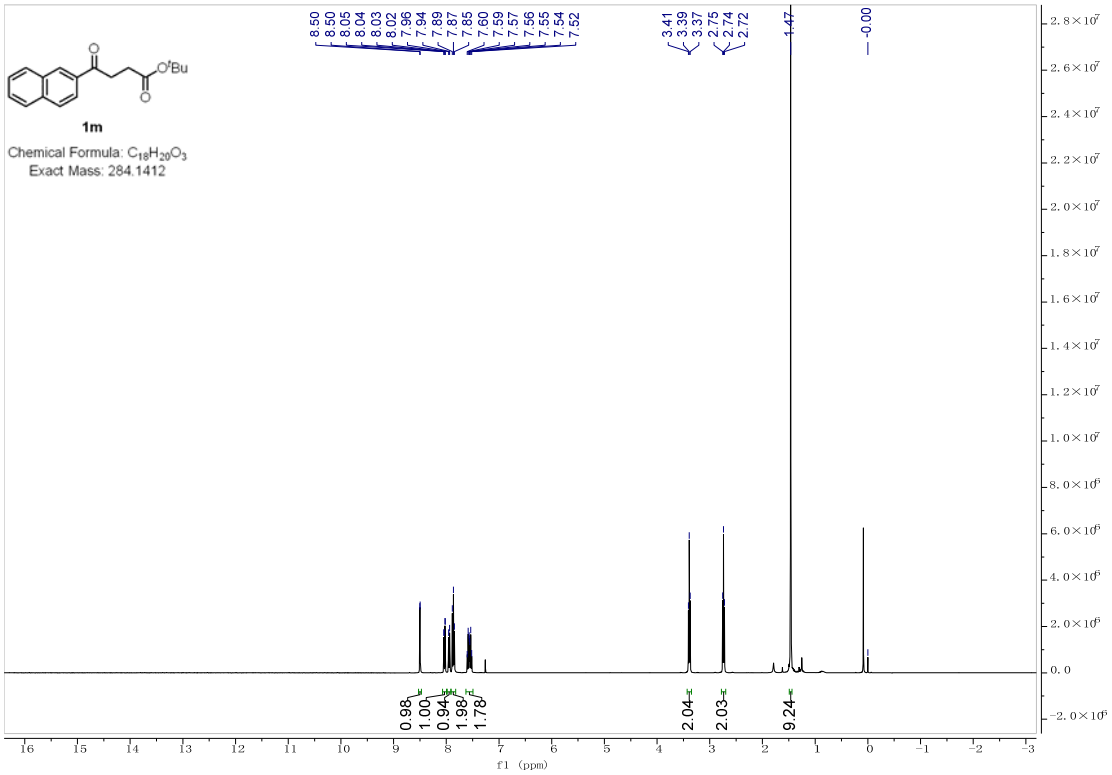
^{1}H NMR (400 MHz, Chloroform-d) of compound **1l**



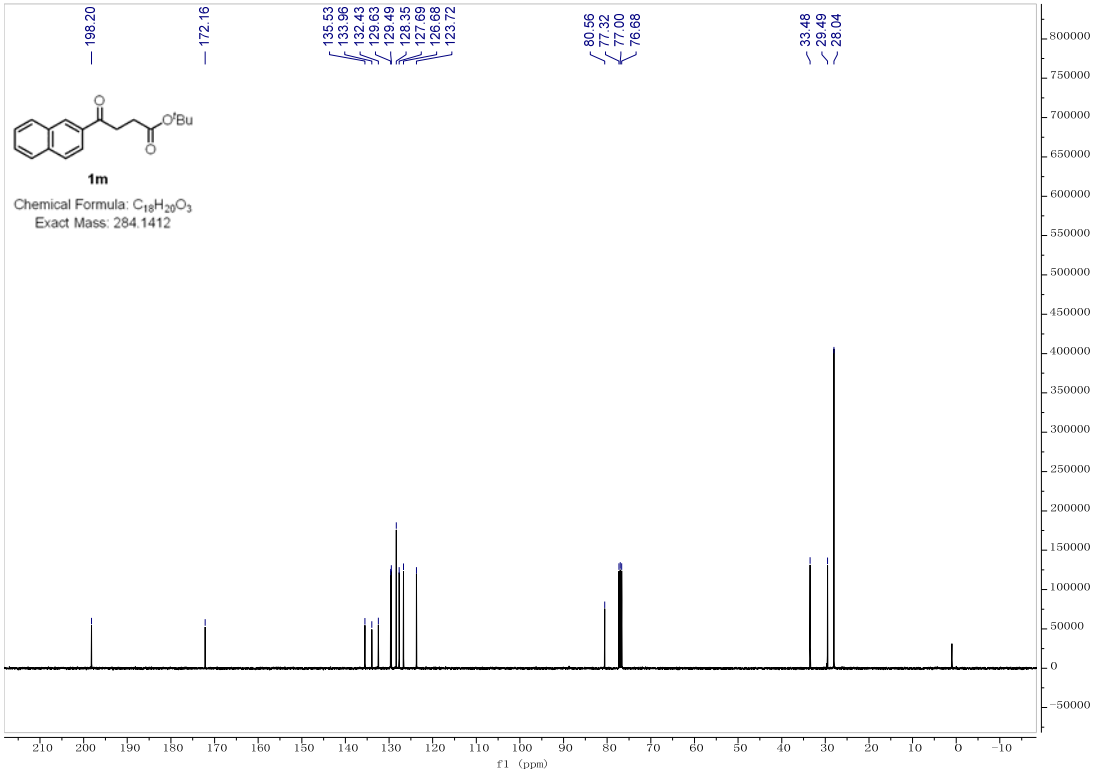
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1l**



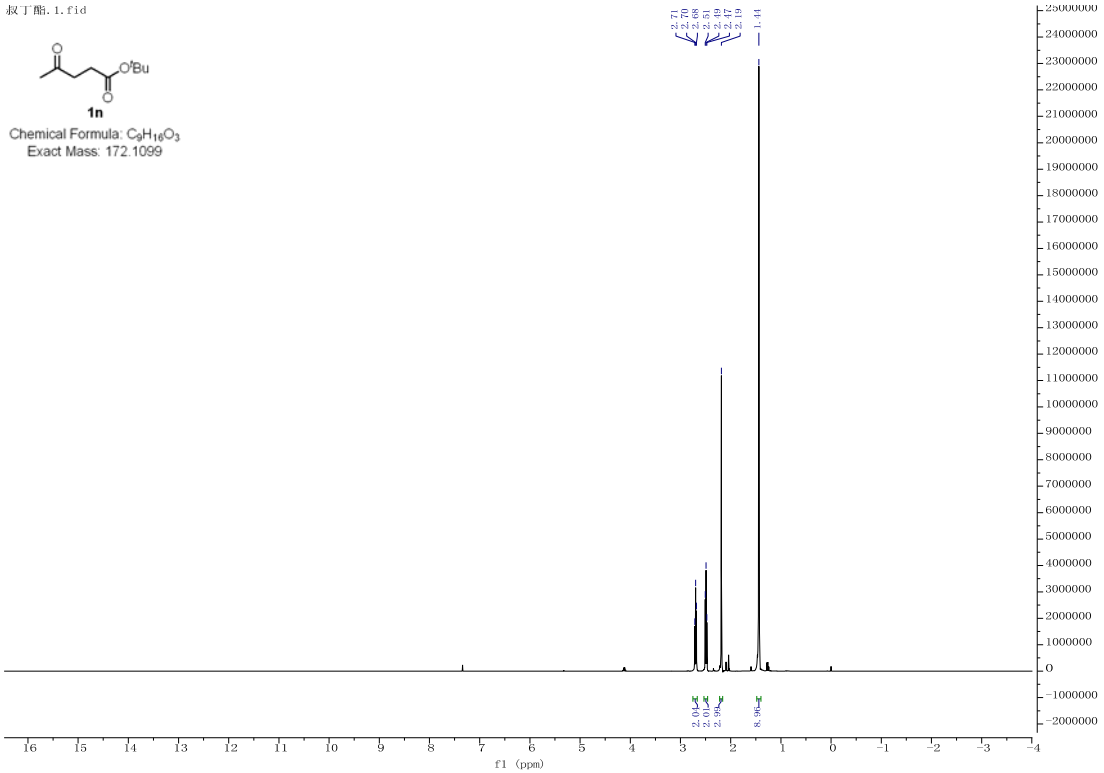
^{1}H NMR (400 MHz, Chloroform-d) of compound **1m**



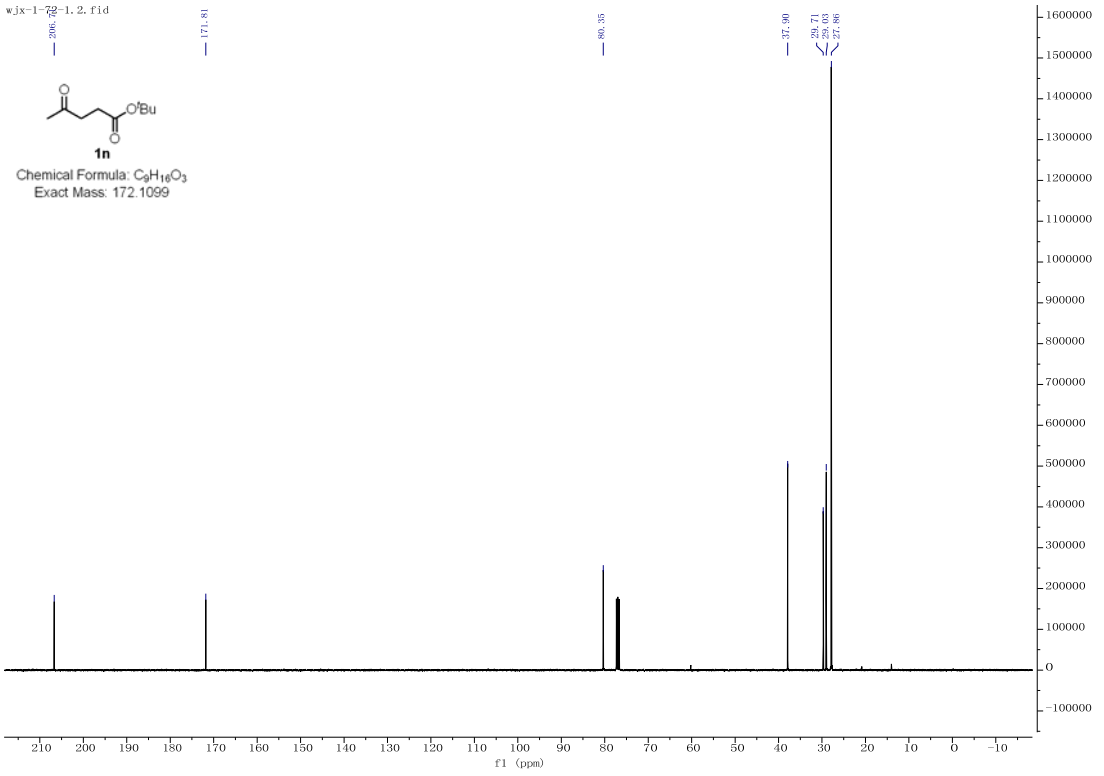
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1m**



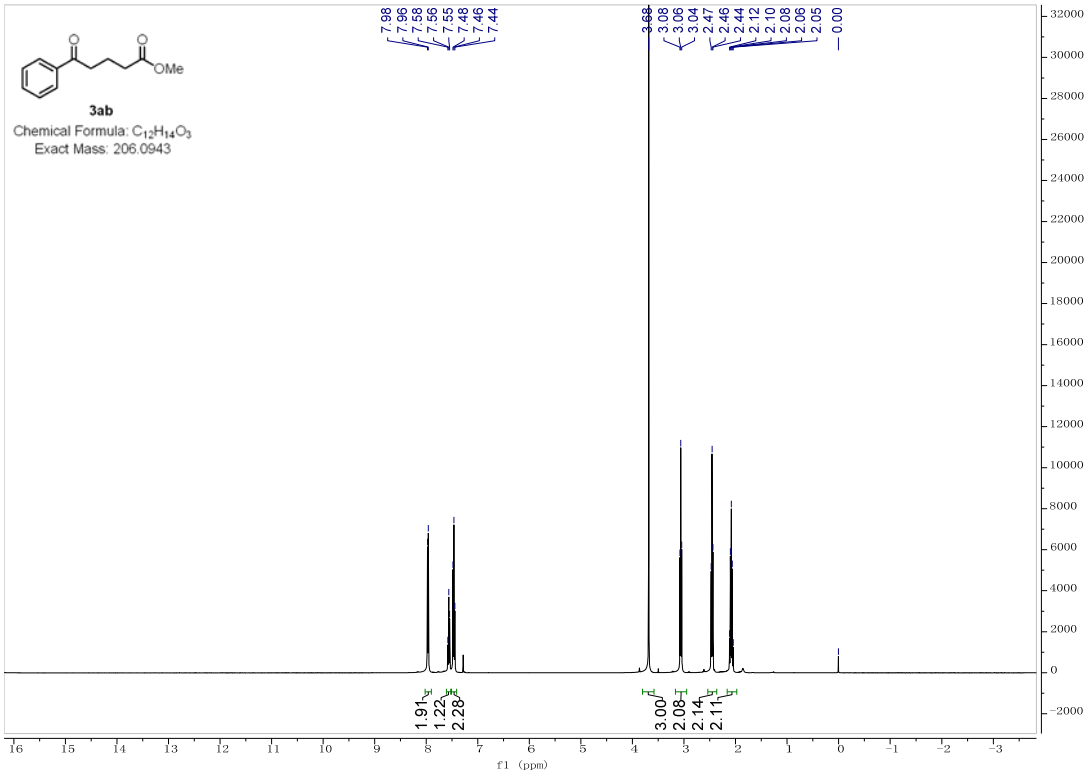
^{1}H NMR (400 MHz, Chloroform-d) of compound **1n**



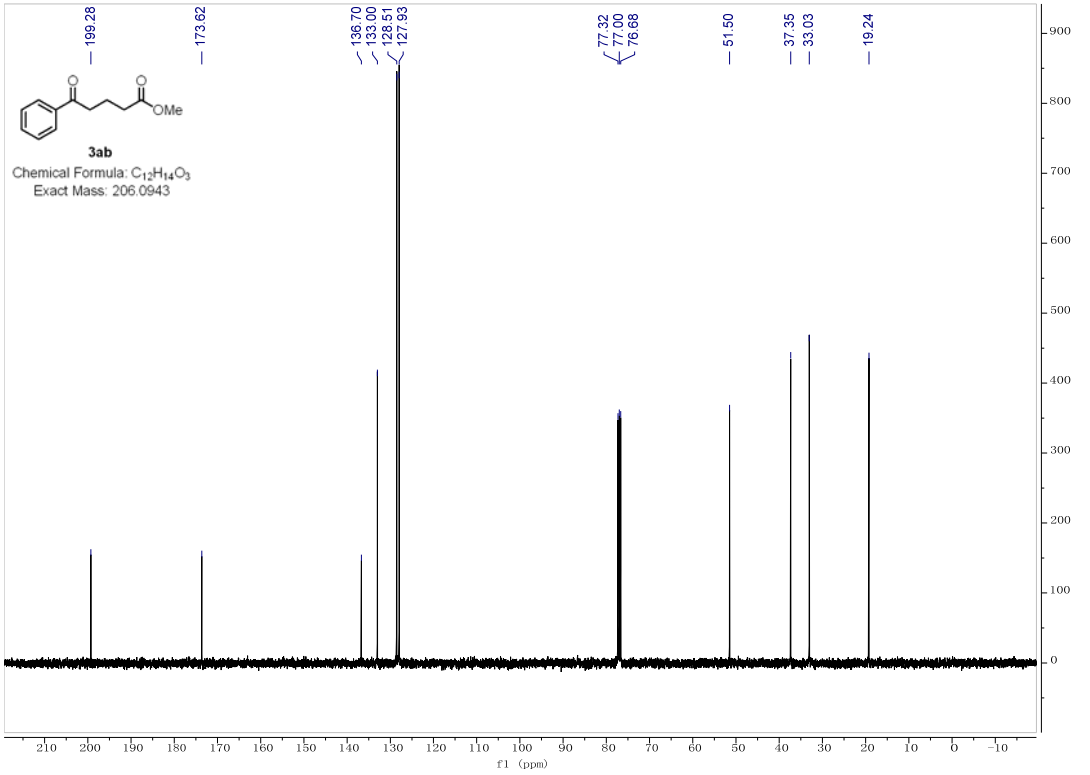
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **1m**



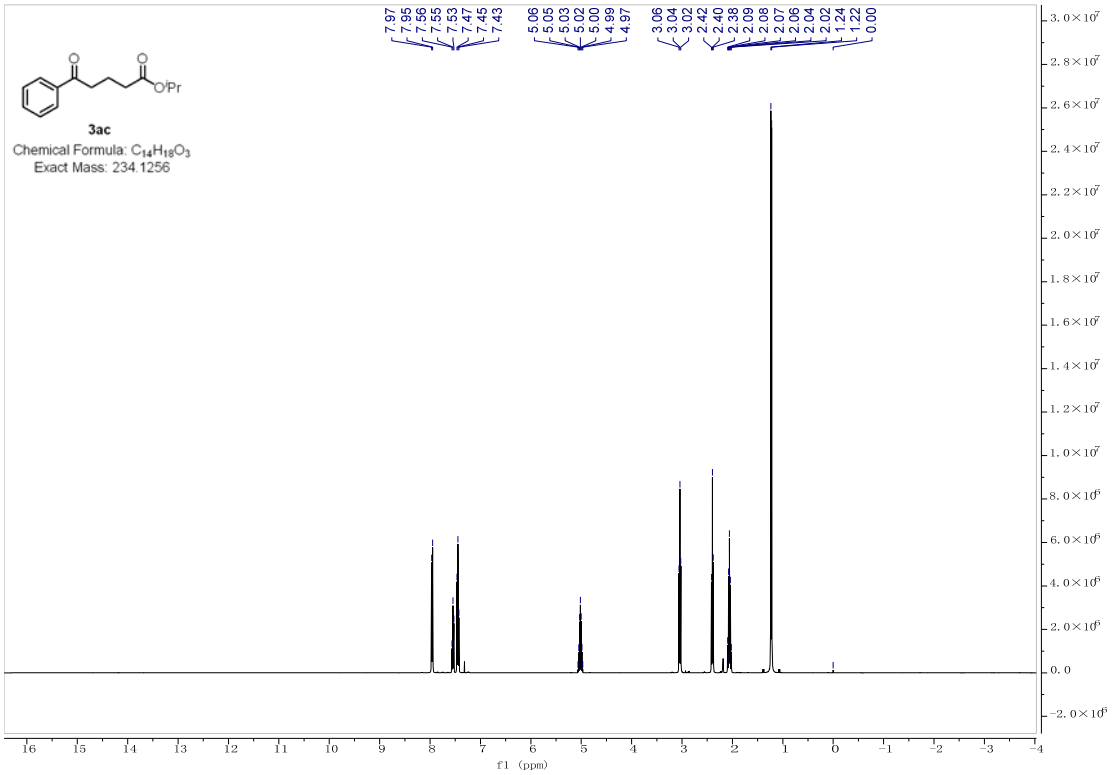
^{1}H NMR (400 MHz, Chloroform-d) of compound **3ab**



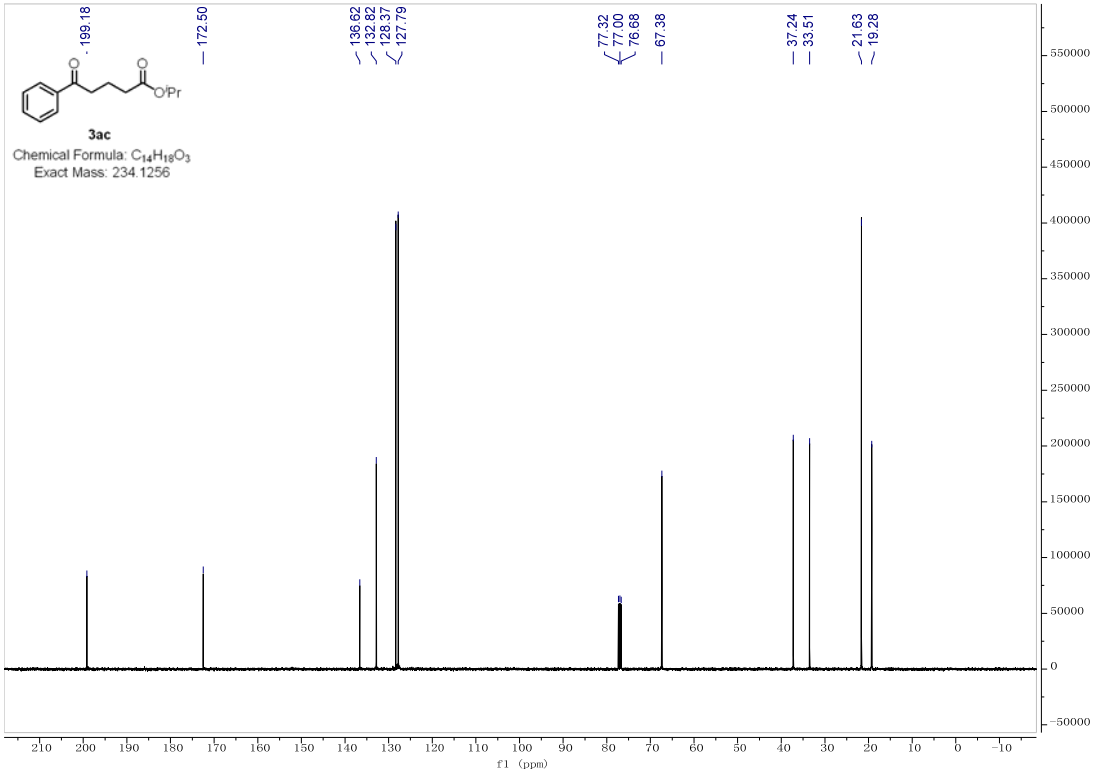
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3ab**



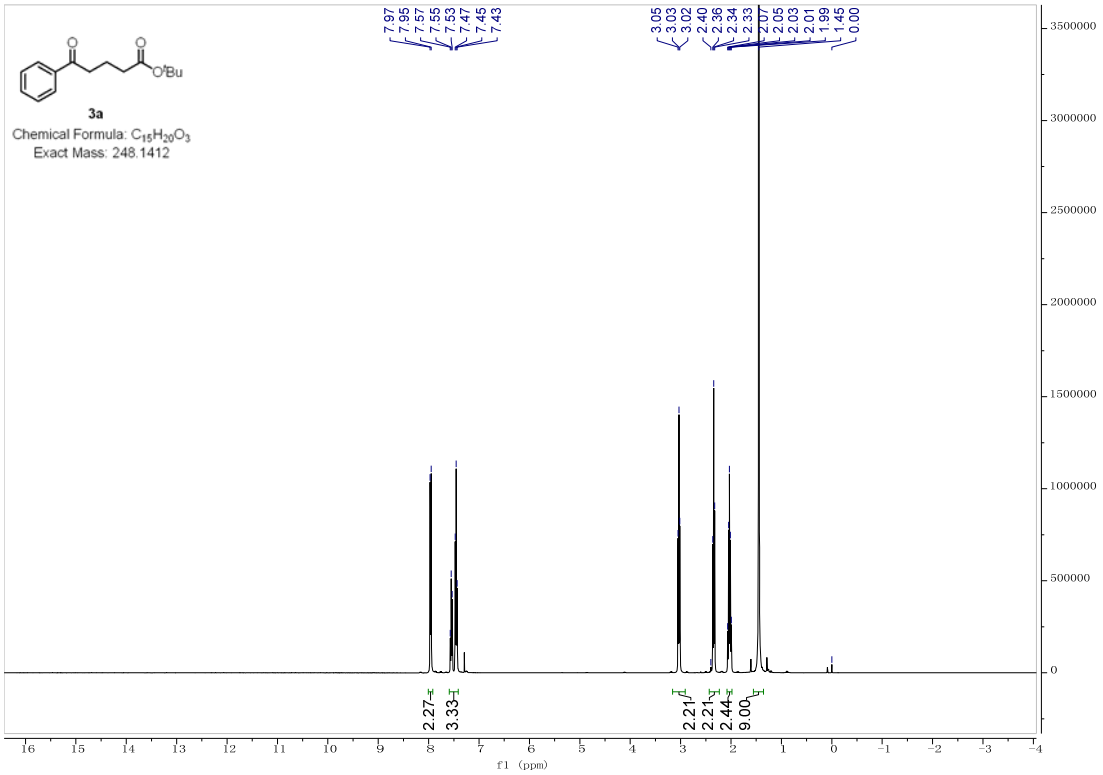
^{1}H NMR (400 MHz, Chloroform-d) of compound **3ac**



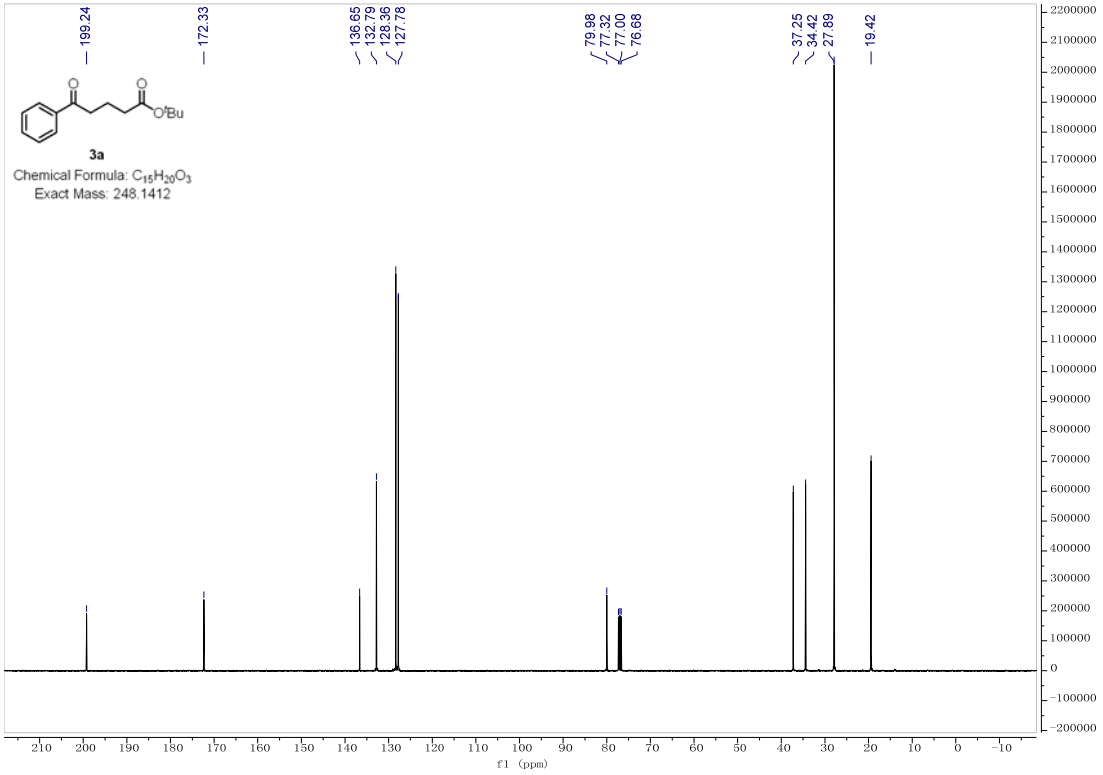
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3ac**



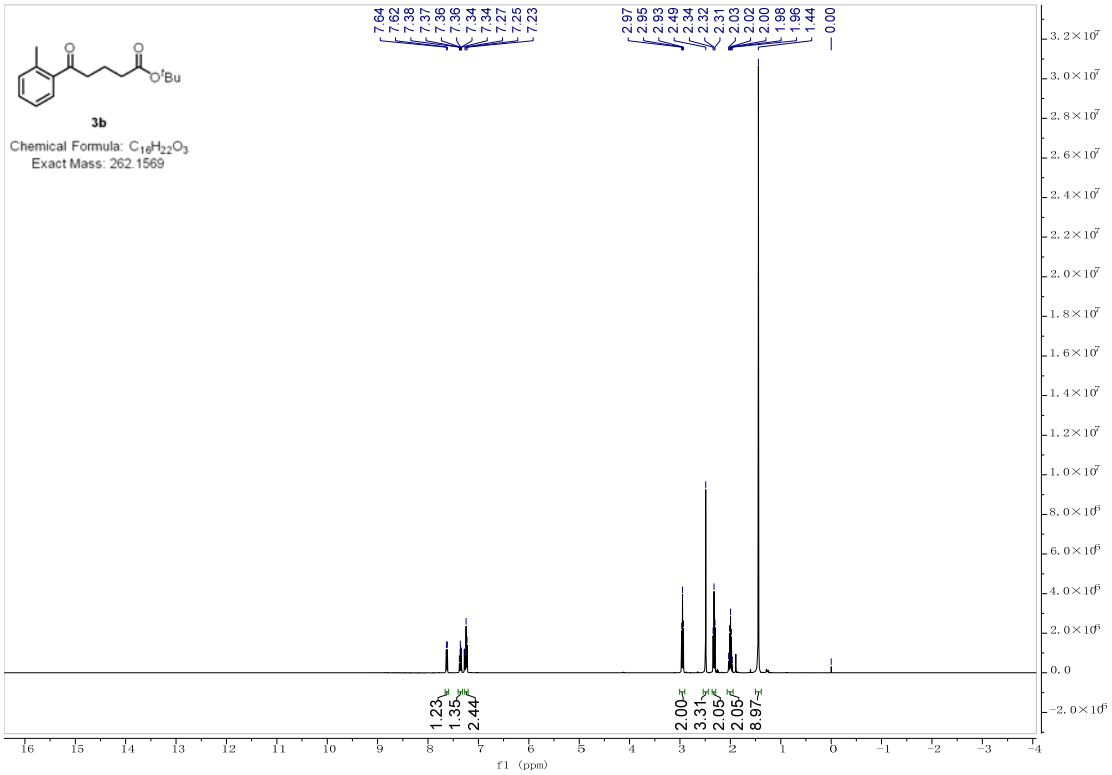
^{1}H NMR (400 MHz, Chloroform-d) of compound **3a**



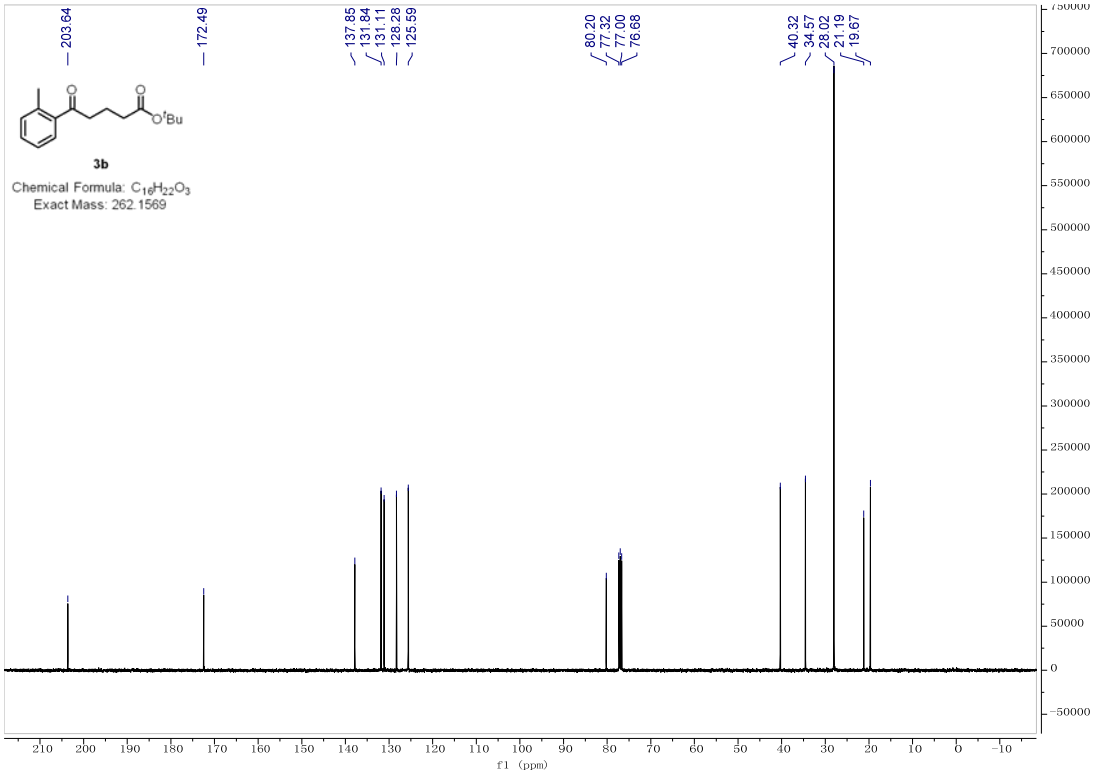
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3a**



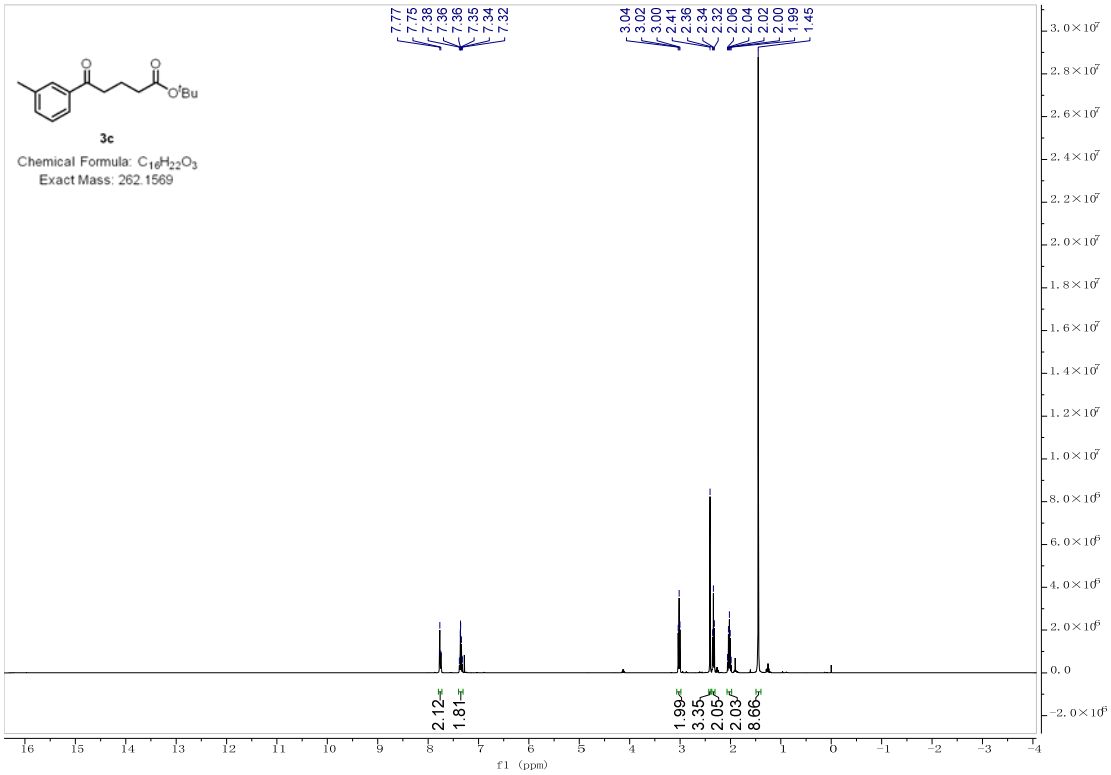
^{1}H NMR (400 MHz, Chloroform-d) of compound **3b**



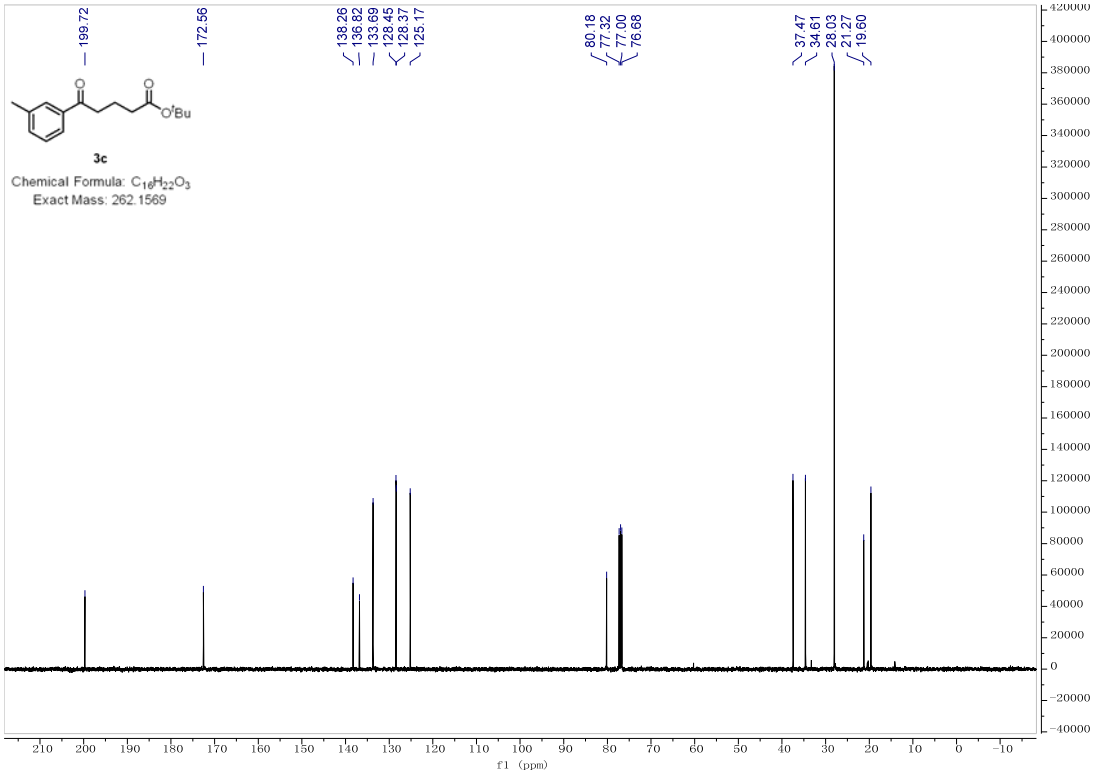
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3b**



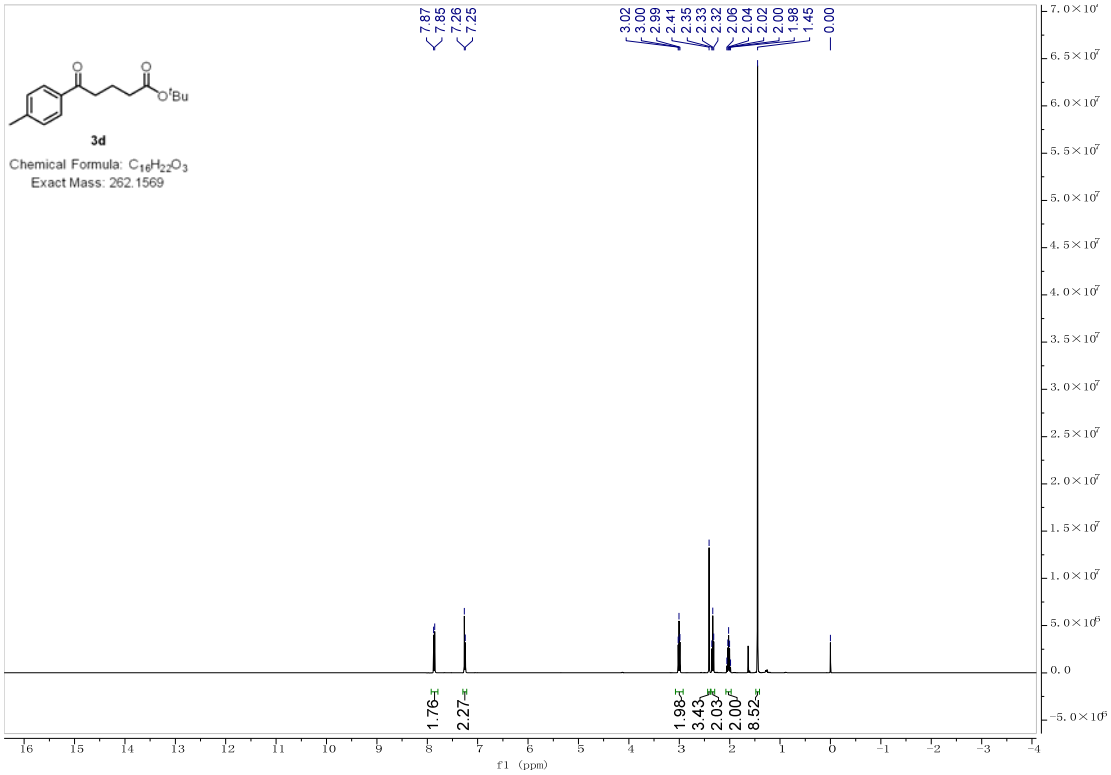
^{1}H NMR (400 MHz, Chloroform-d) of compound **3c**



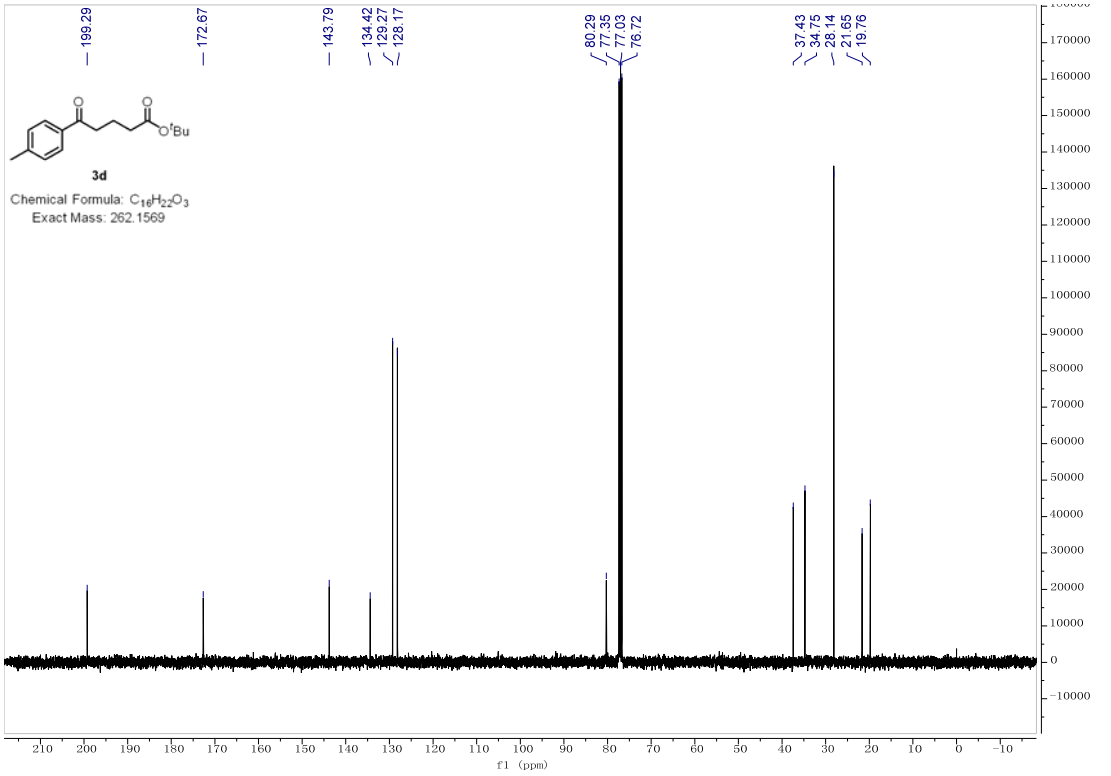
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3c**



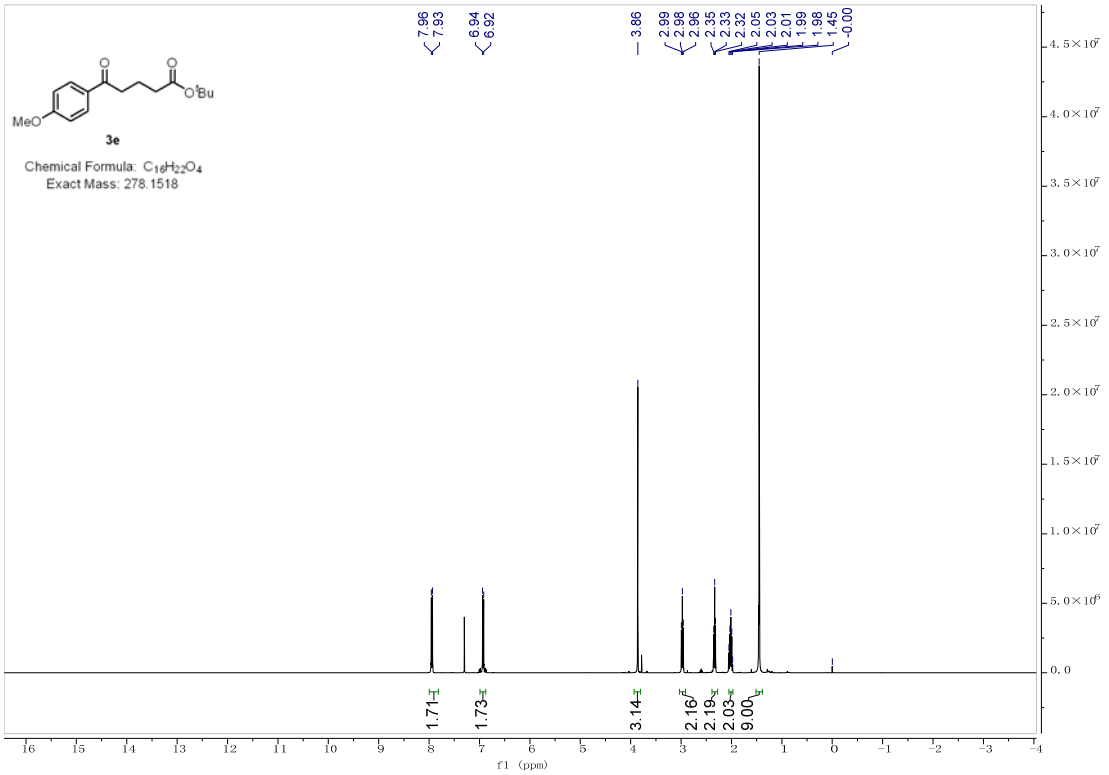
^{1}H NMR (400 MHz, Chloroform-d) of compound **3d**



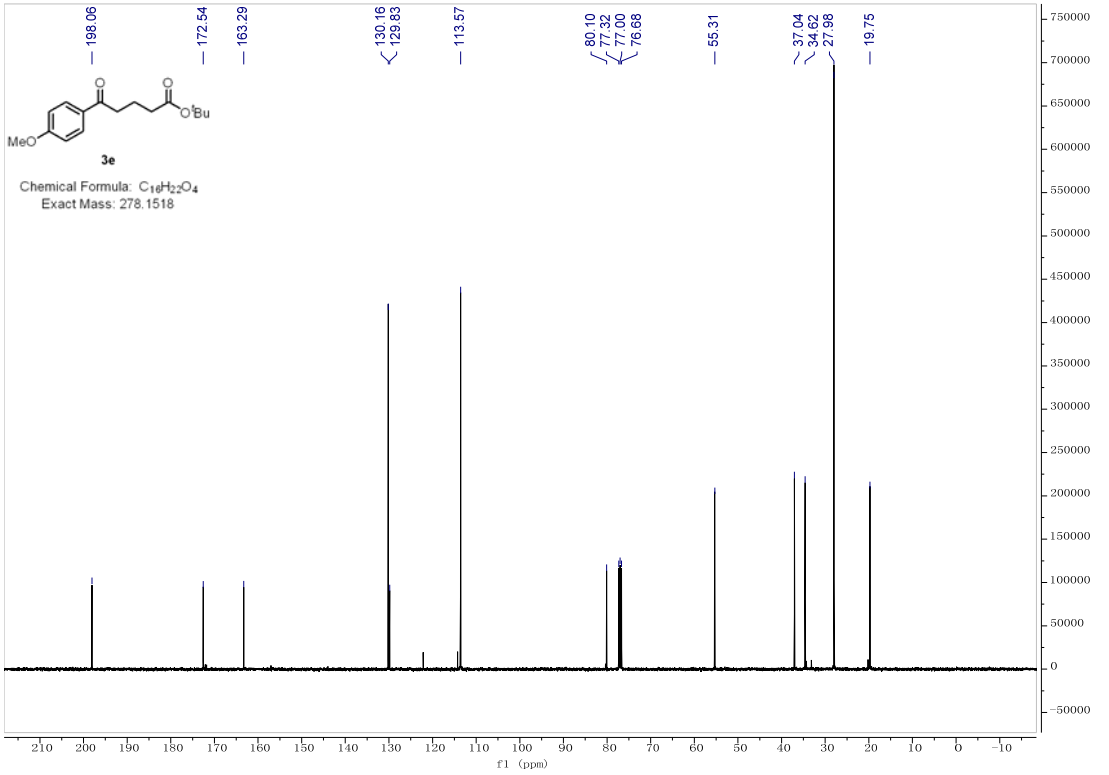
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3d**



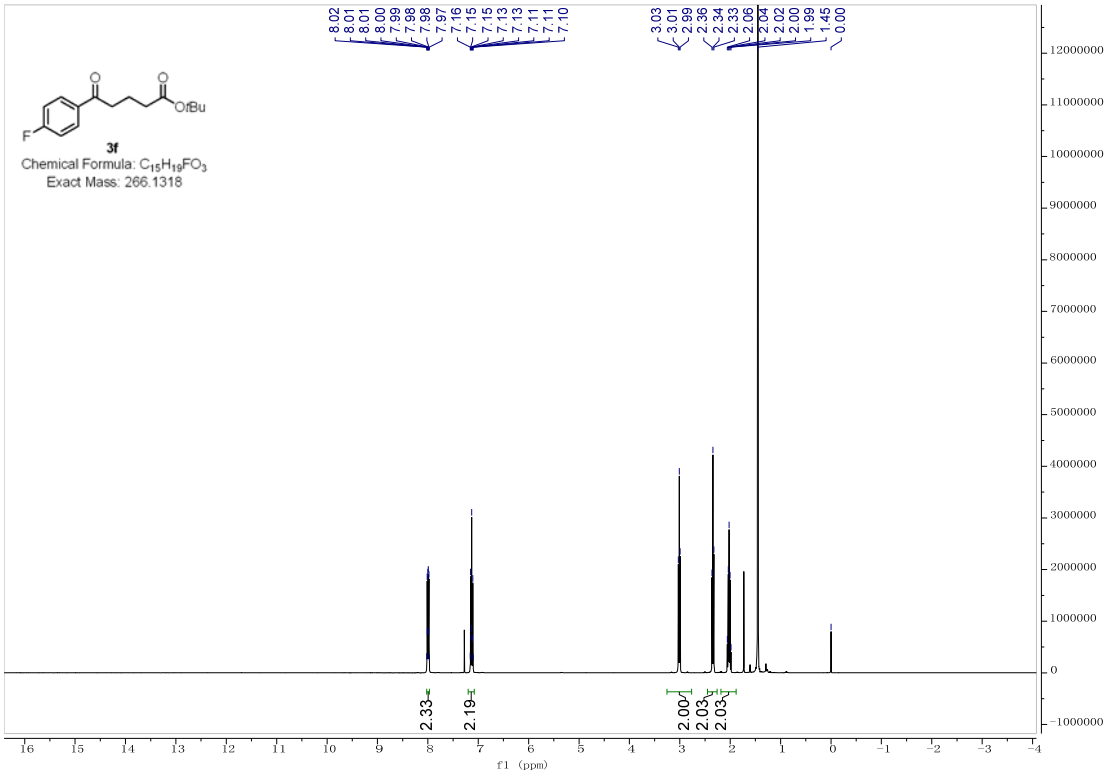
^{1}H NMR (400 MHz, Chloroform-d) of compound **3e**



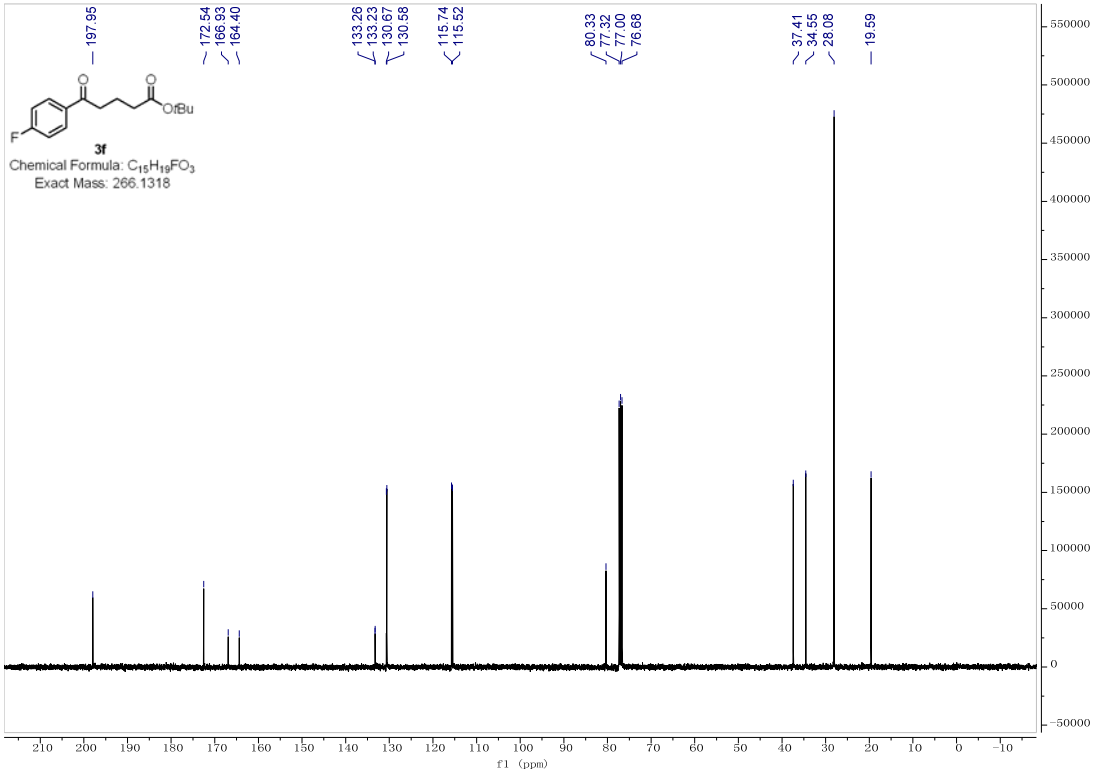
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3e**



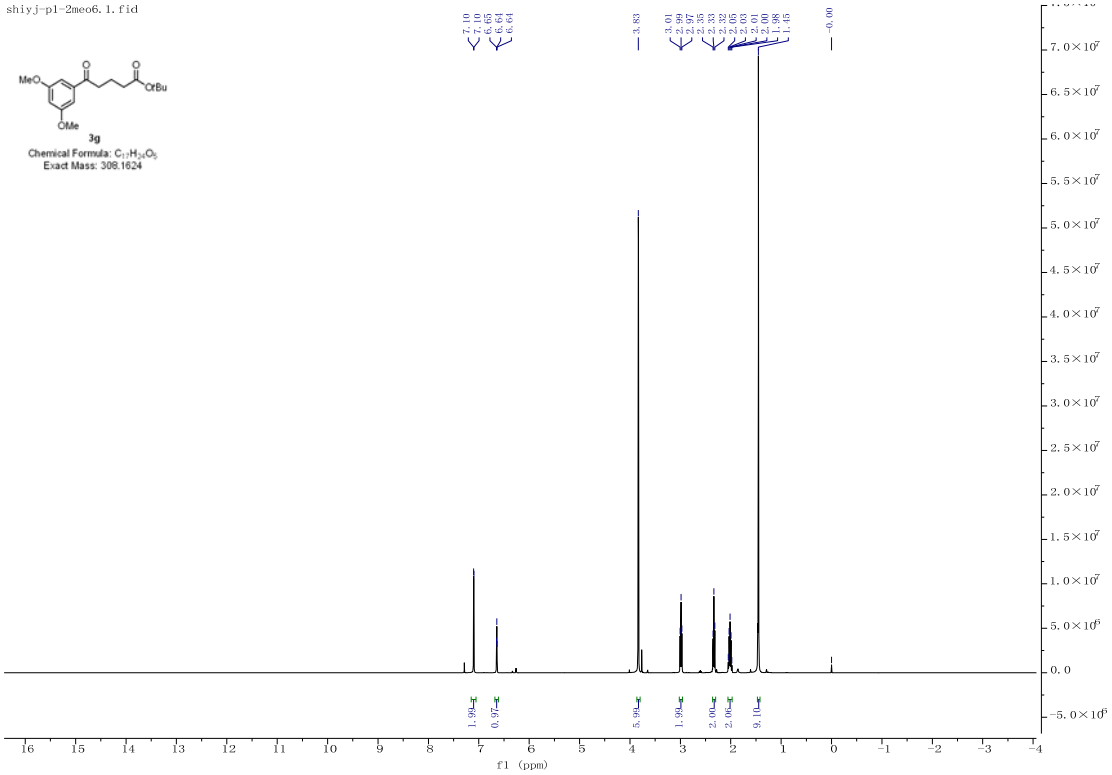
^{1}H NMR (400 MHz, Chloroform-d) of compound **3f**



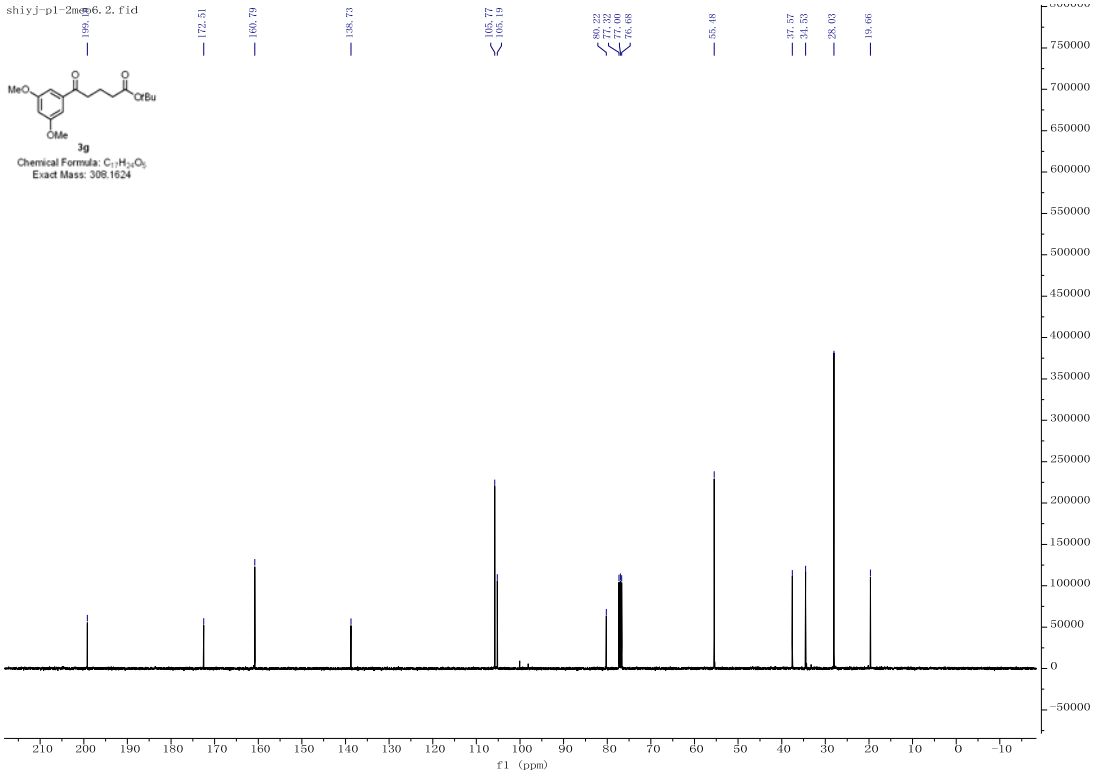
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3f**



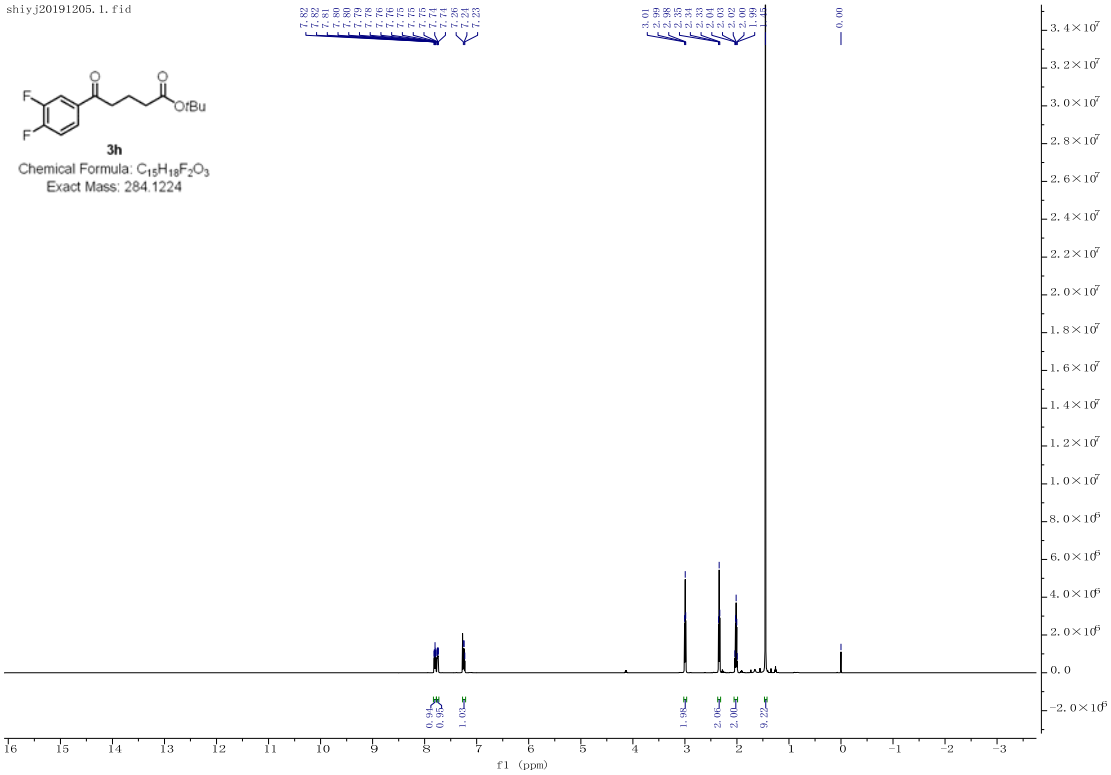
^{1}H NMR (400 MHz, Chloroform-d) of compound **3g**



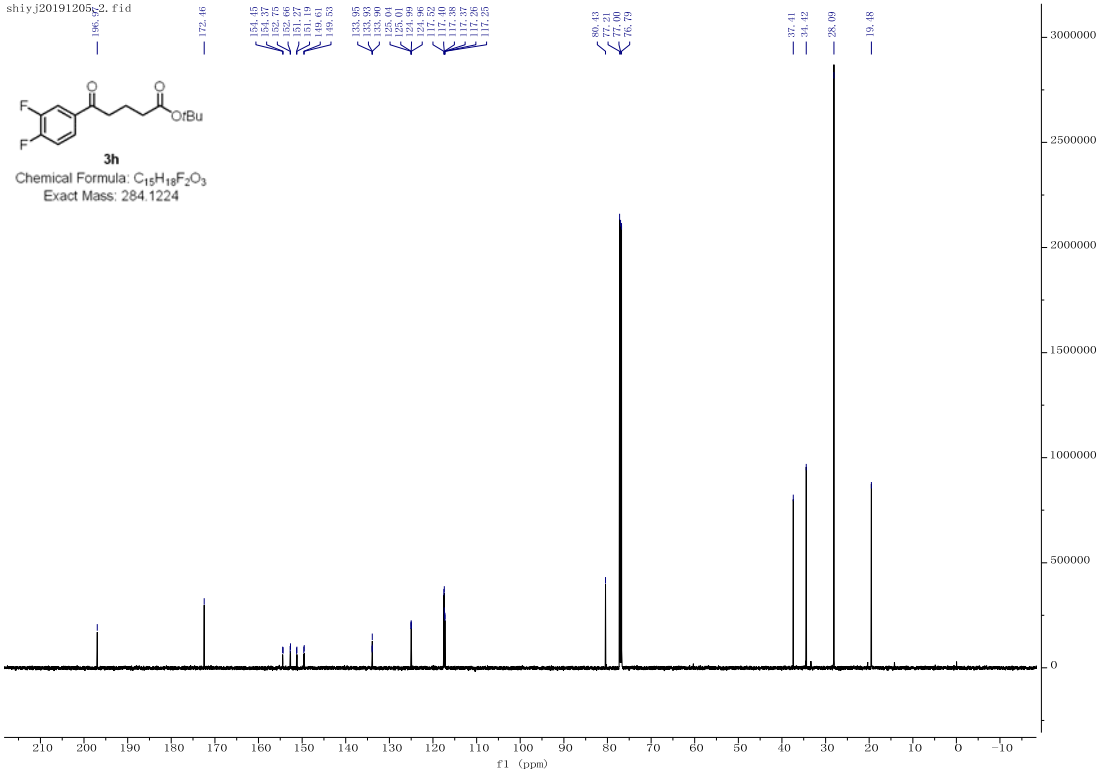
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **3g**



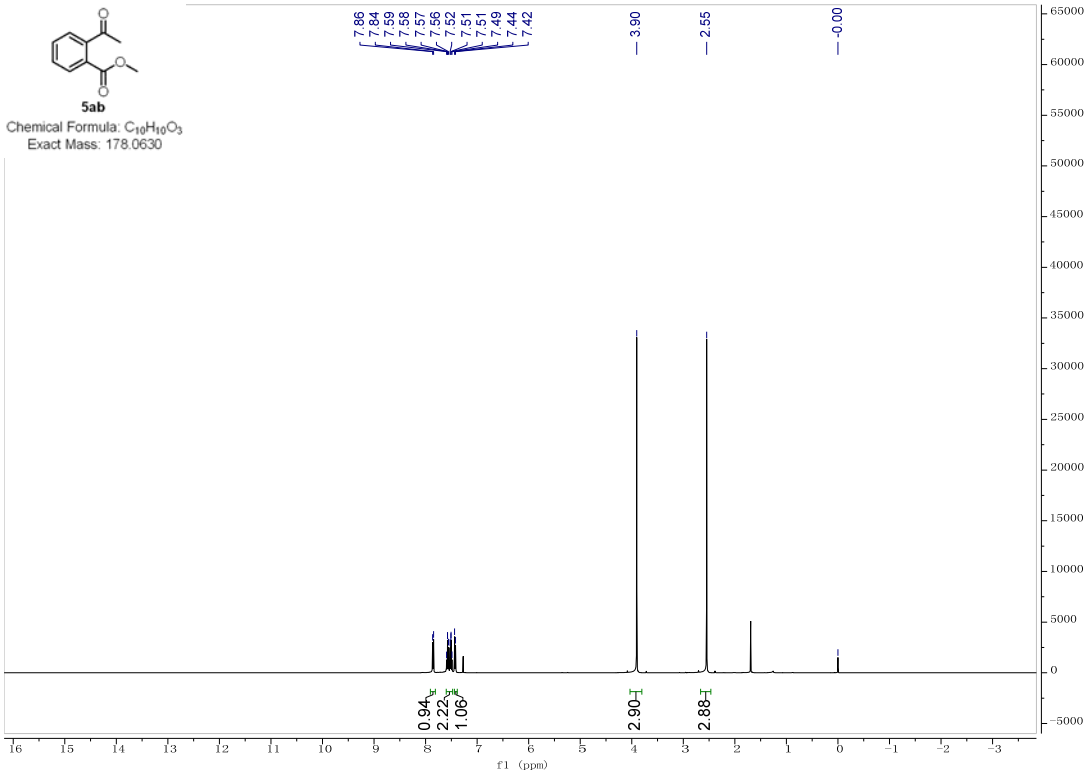
^{1}H NMR (600 MHz, Chloroform-d) of compound **3h**



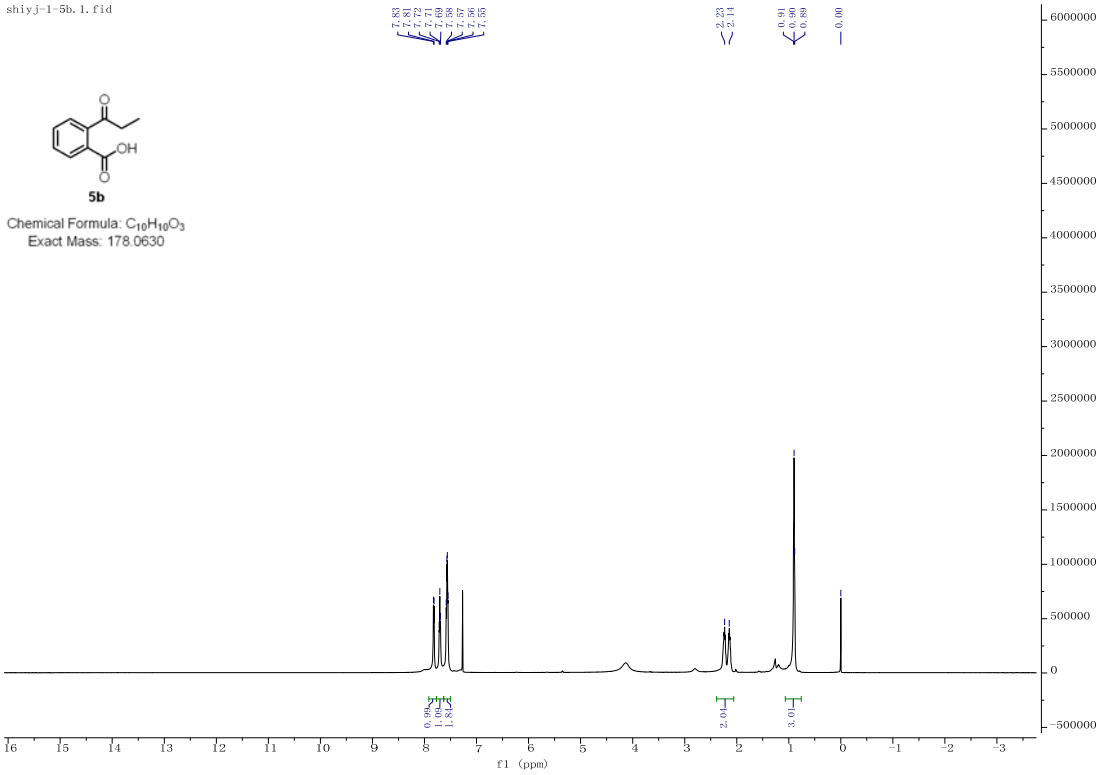
^{13}C NMR (151 MHz, Chloroform-d) of compound **3h**



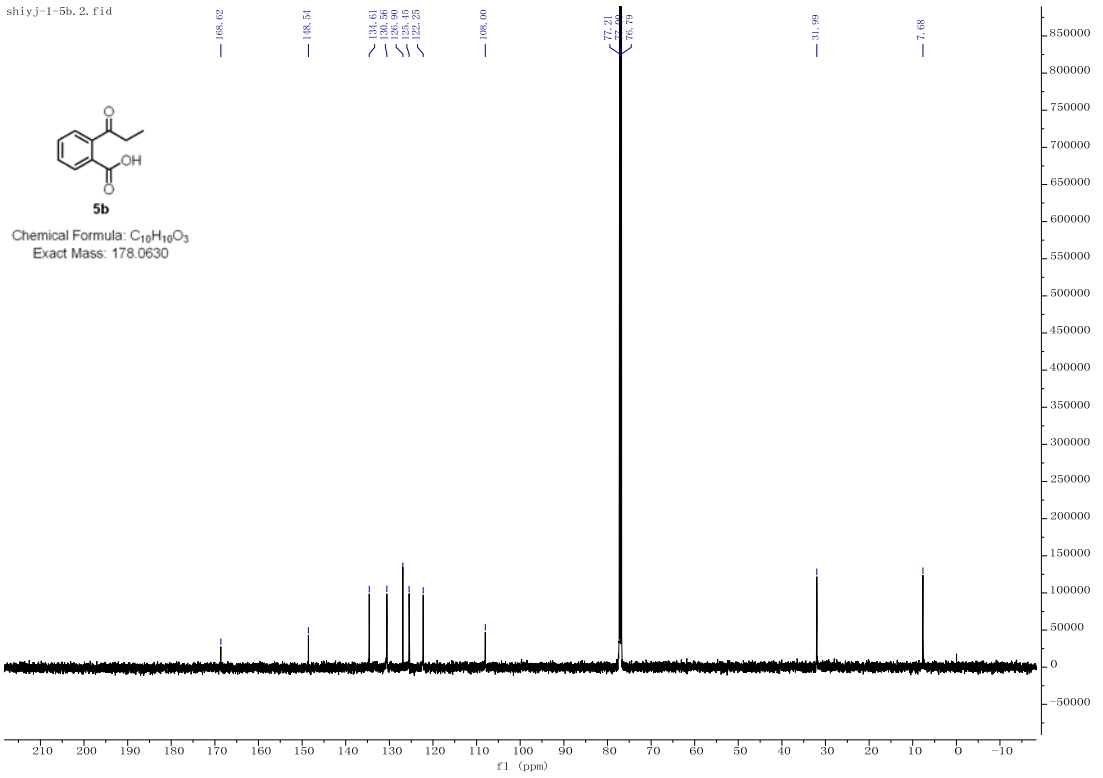
^{1}H NMR (400 MHz, Chloroform-d) of compound **5ab**



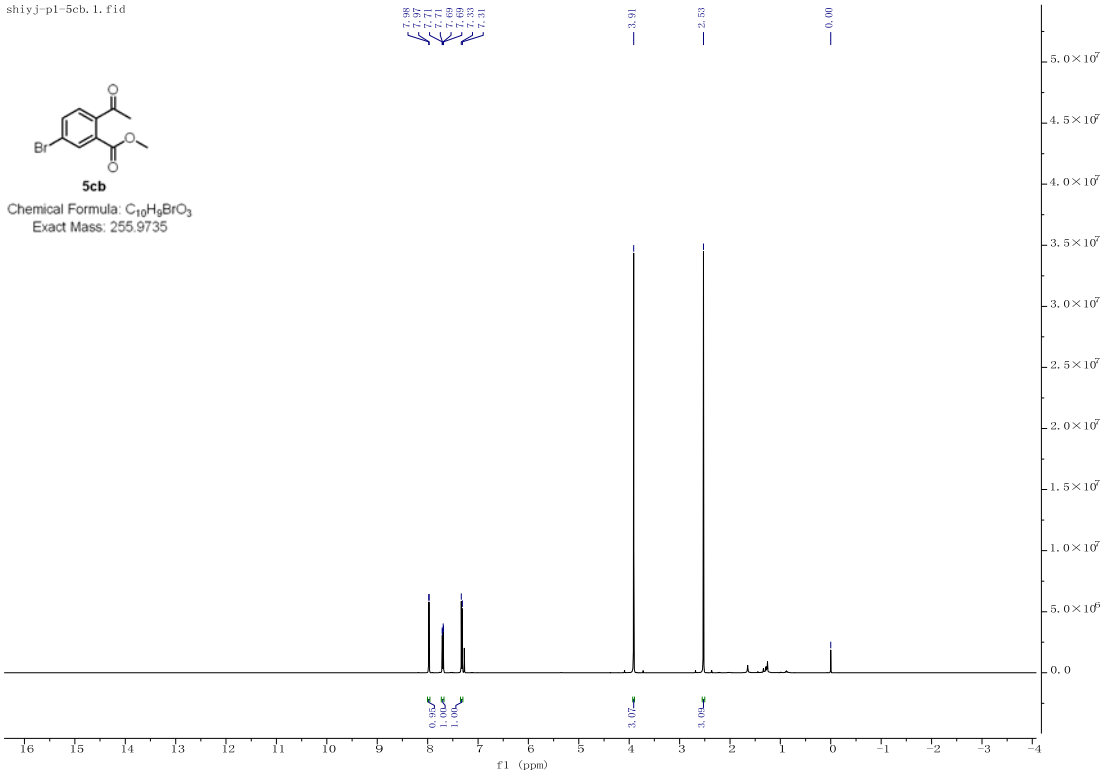
^{1}H NMR (600 MHz, Chloroform-d) of compound **5b**



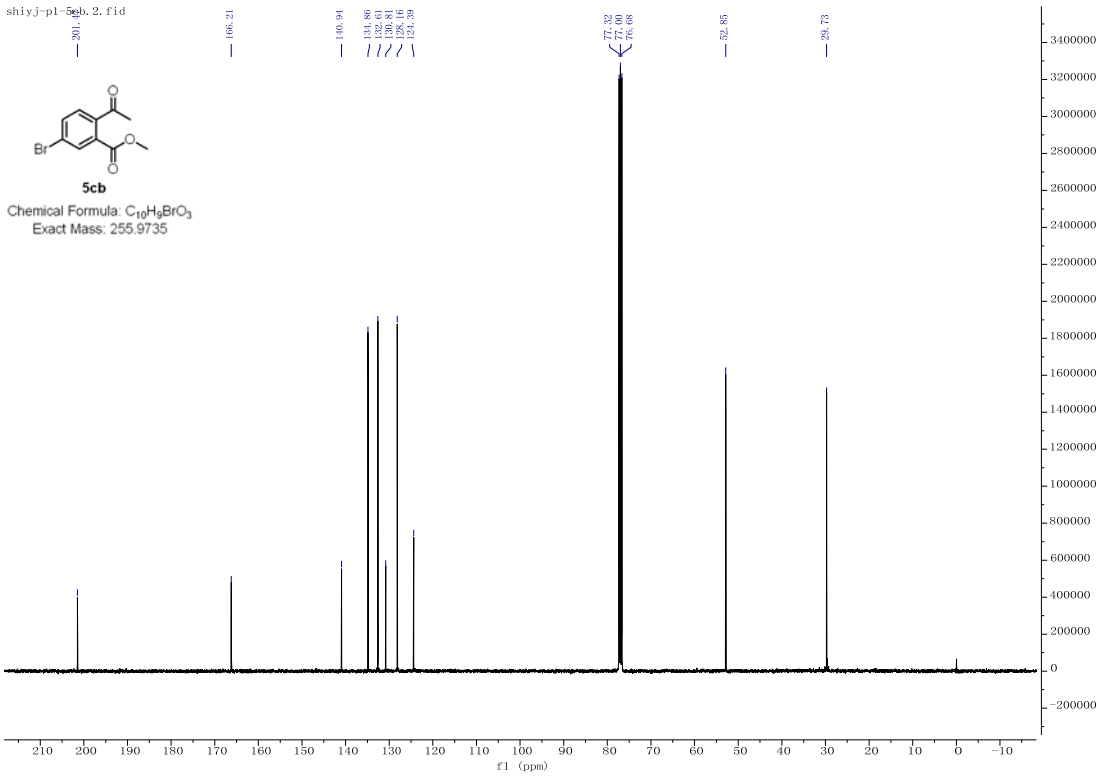
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **5b**



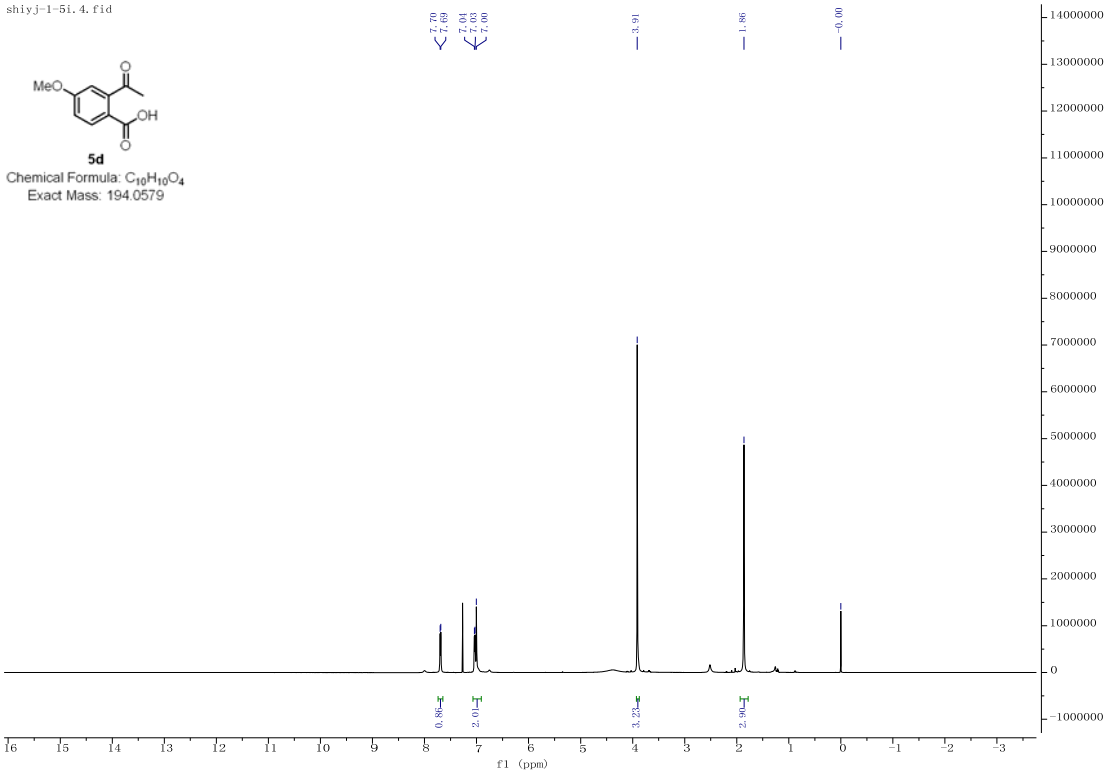
^{1}H NMR (400 MHz, Chloroform-d) of compound **5cb**



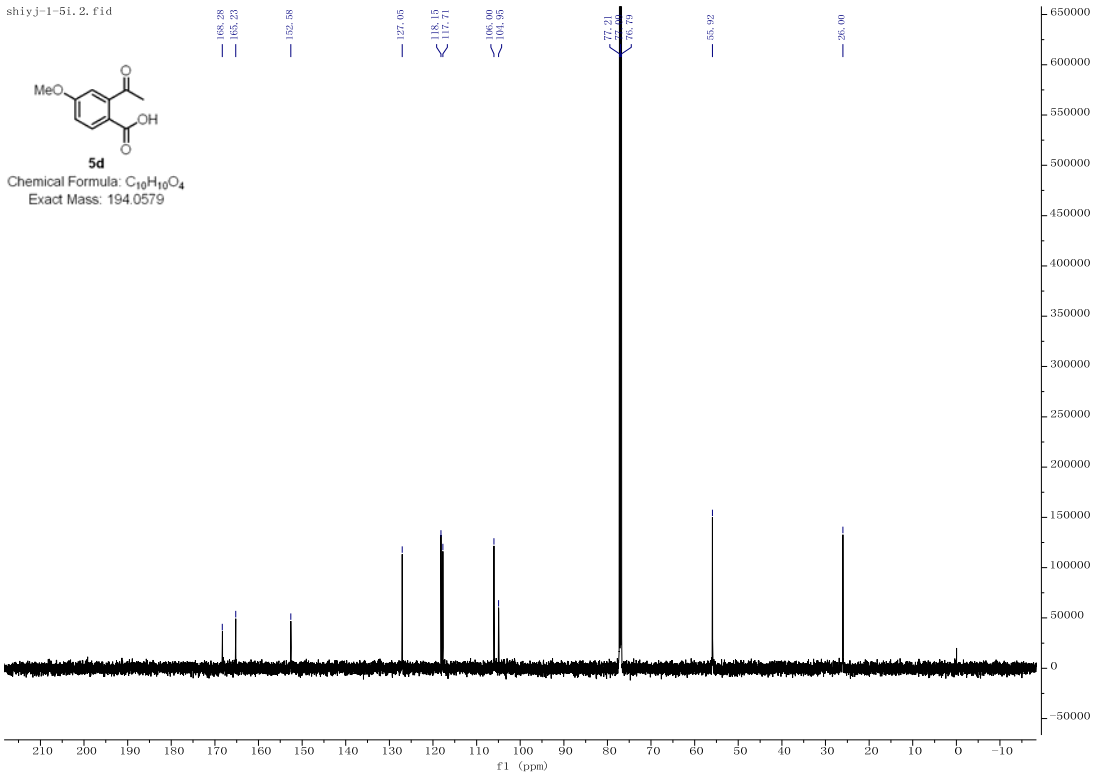
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **5cb**



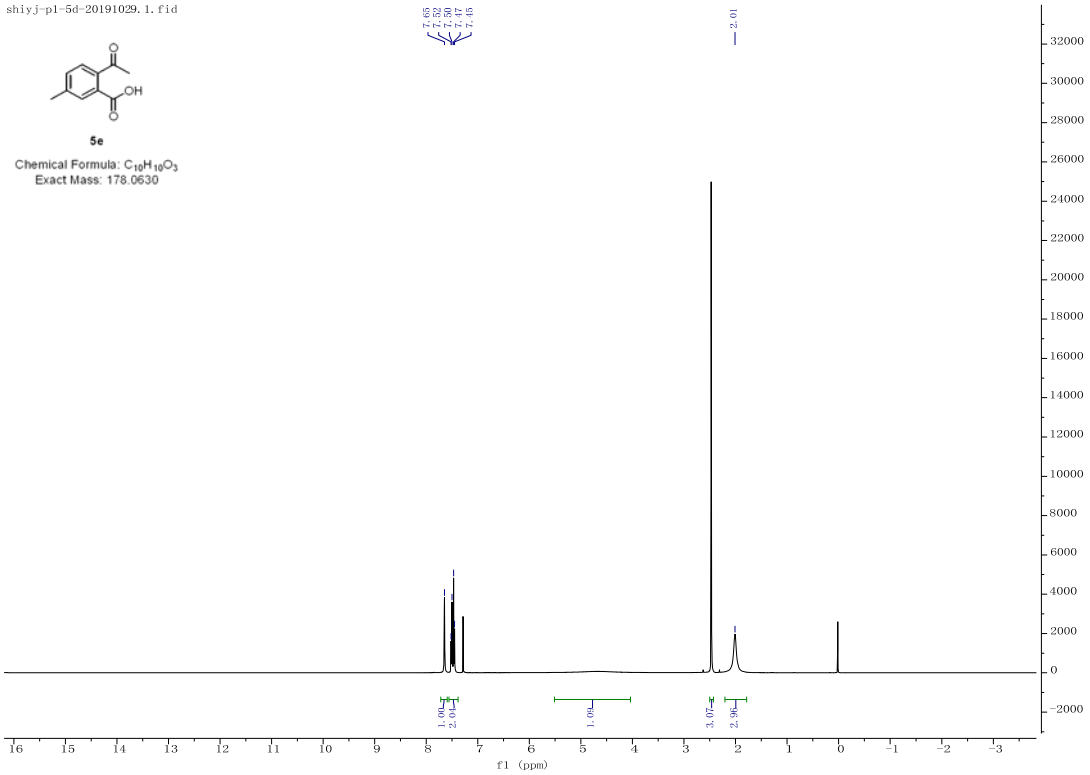
^{1}H NMR (600 MHz, Chloroform-d) of compound **5d**



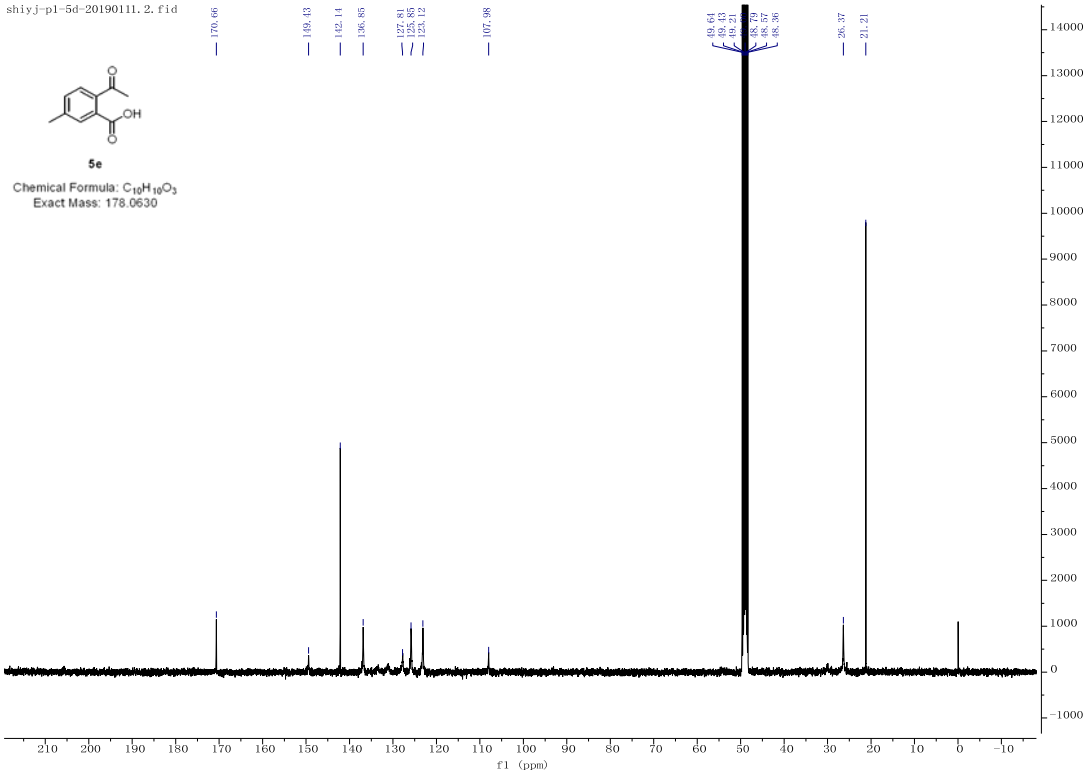
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **5d**



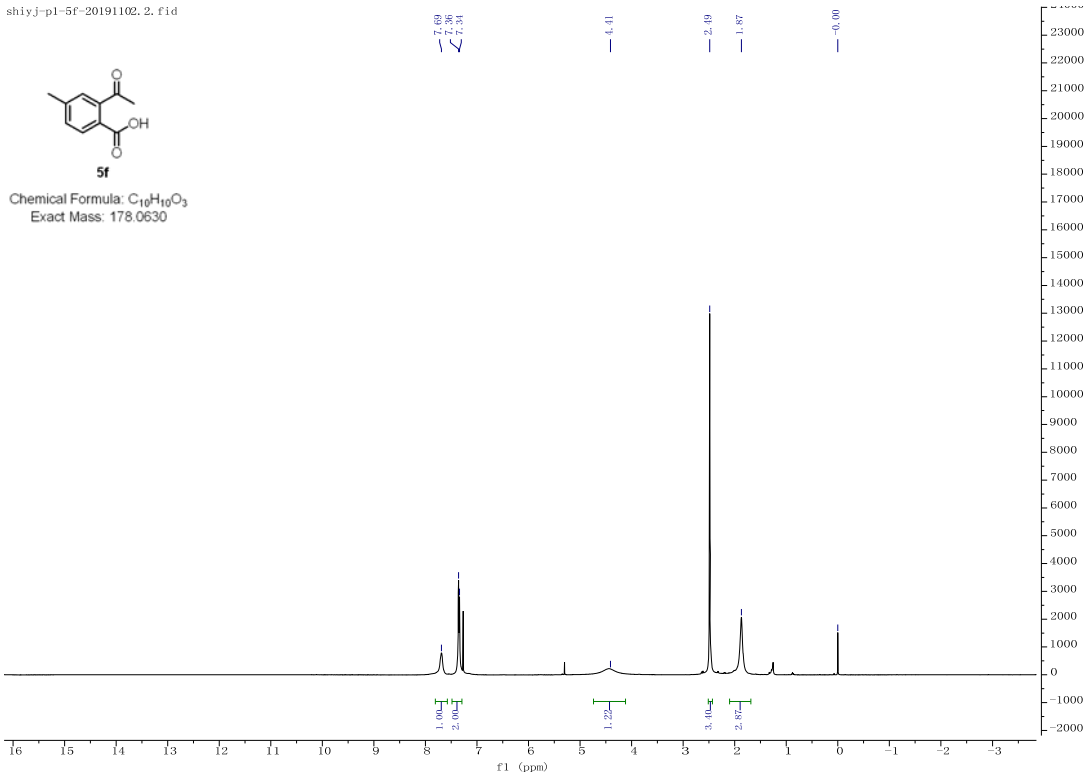
^{1}H NMR (600 MHz, Methanol-d4) of compound **5e**



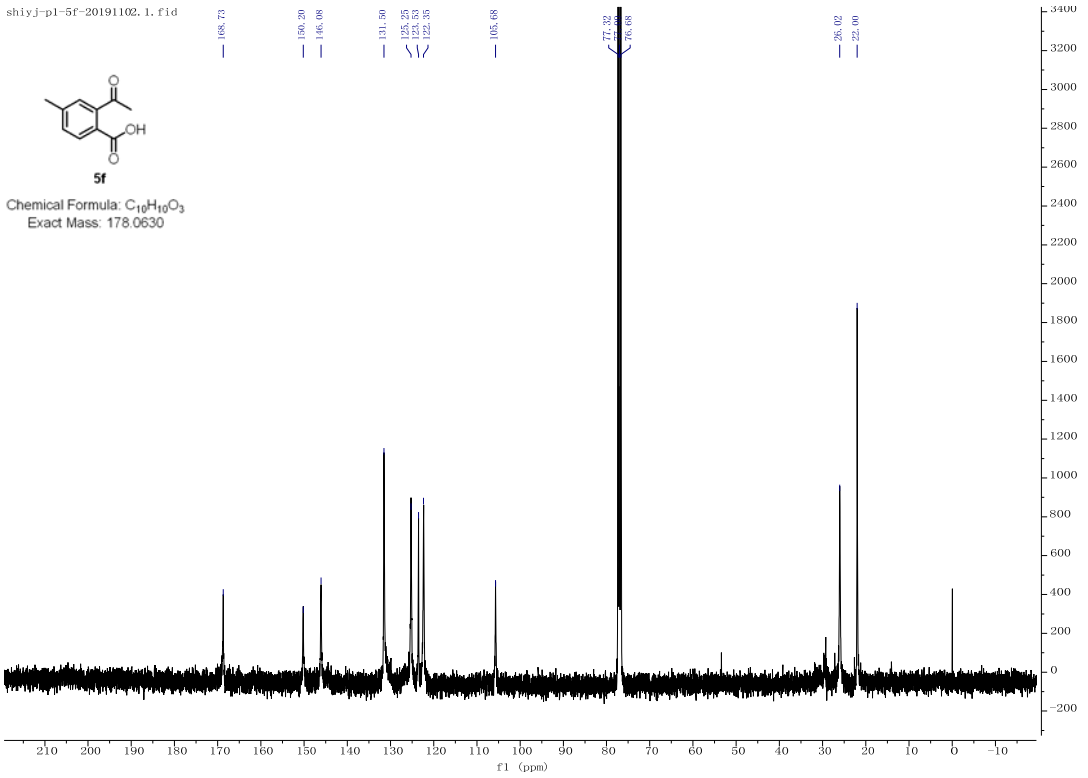
^{13}C{^{1}H} NMR (101 MHz, Methanol-d4) of compound **5e**



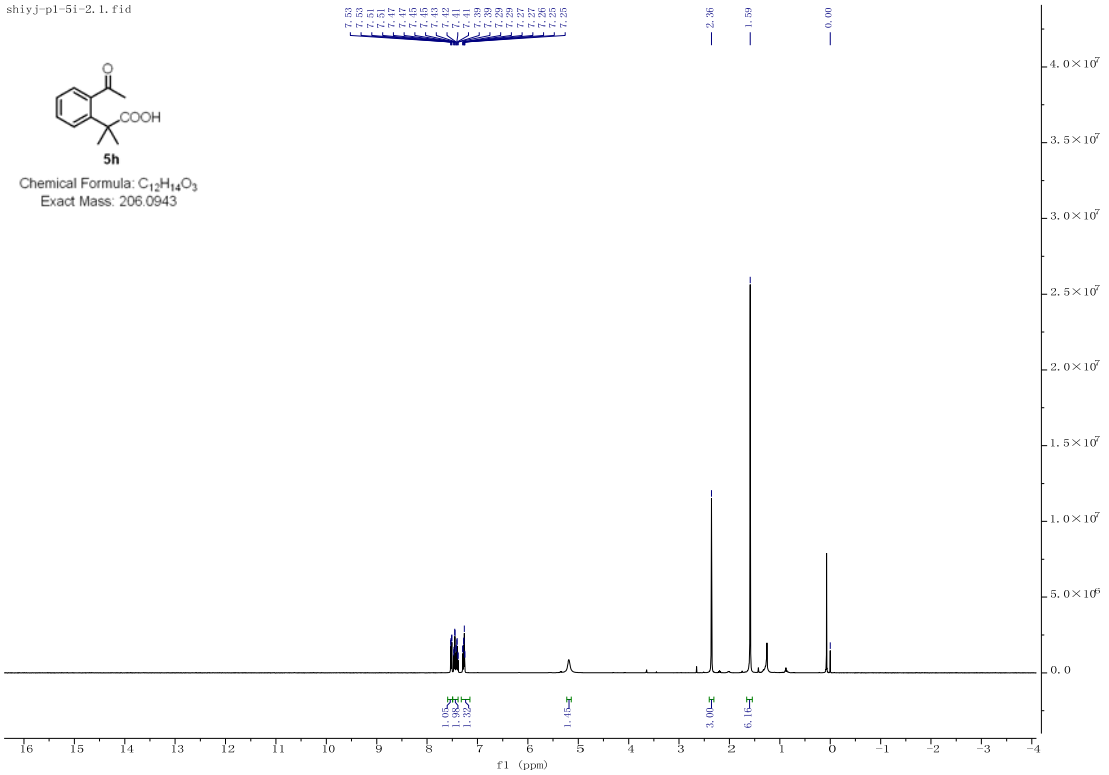
^{1}H NMR (400 MHz, Chloroform-d) of compound **5f**



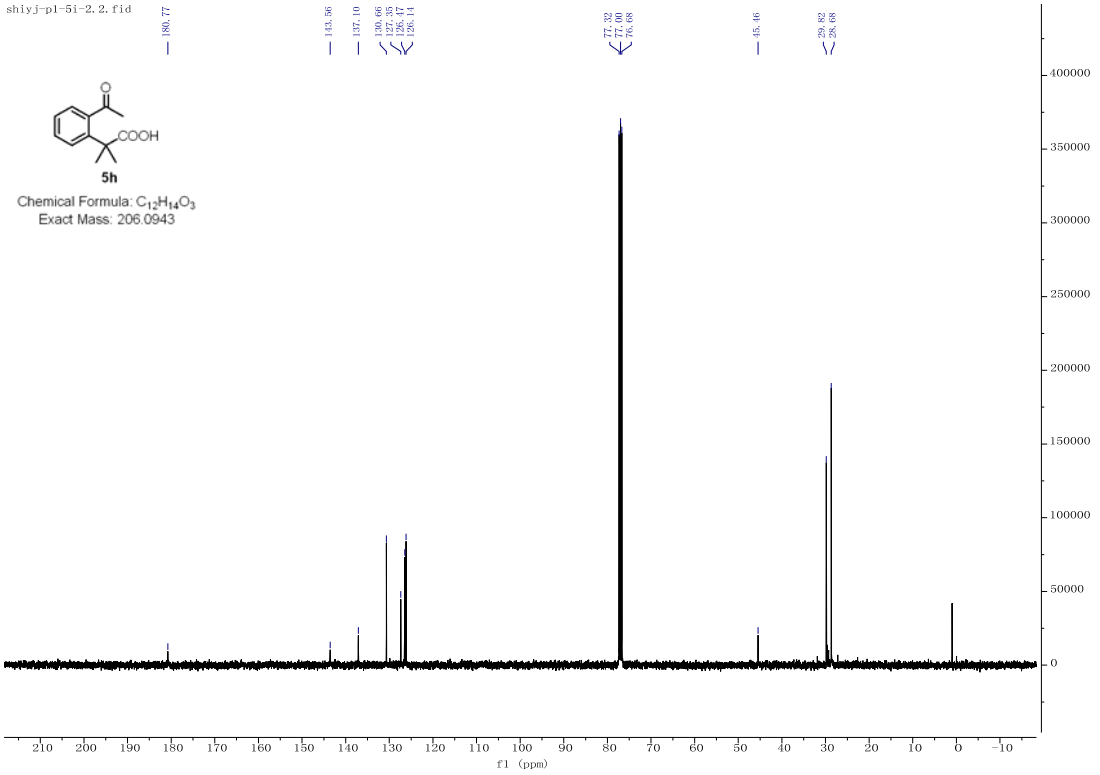
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **5b**



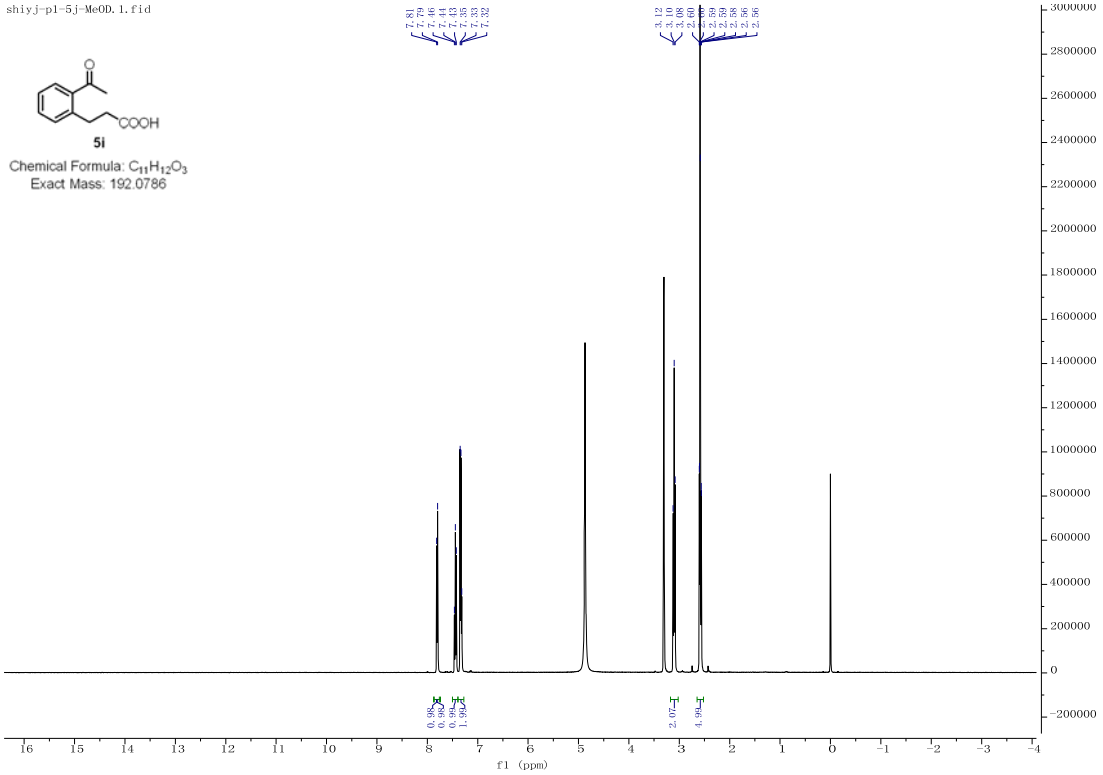
^{1}H NMR (600 MHz, Chloroform-d) of compound **5h**



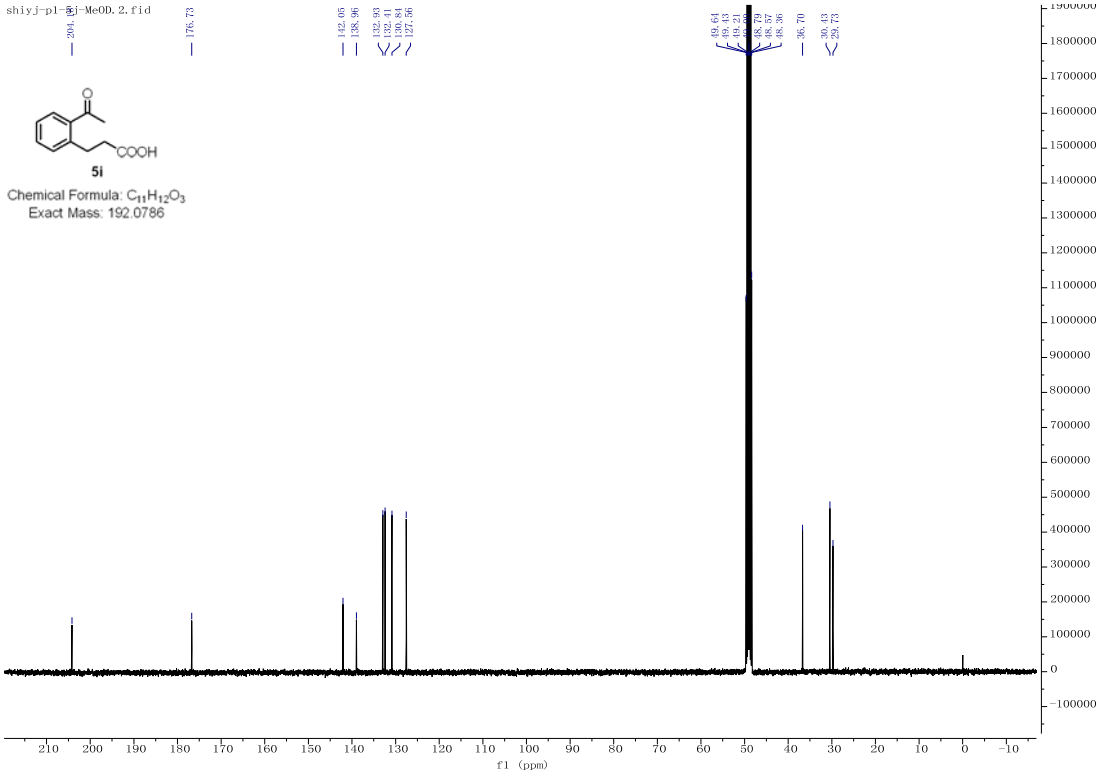
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **5b**



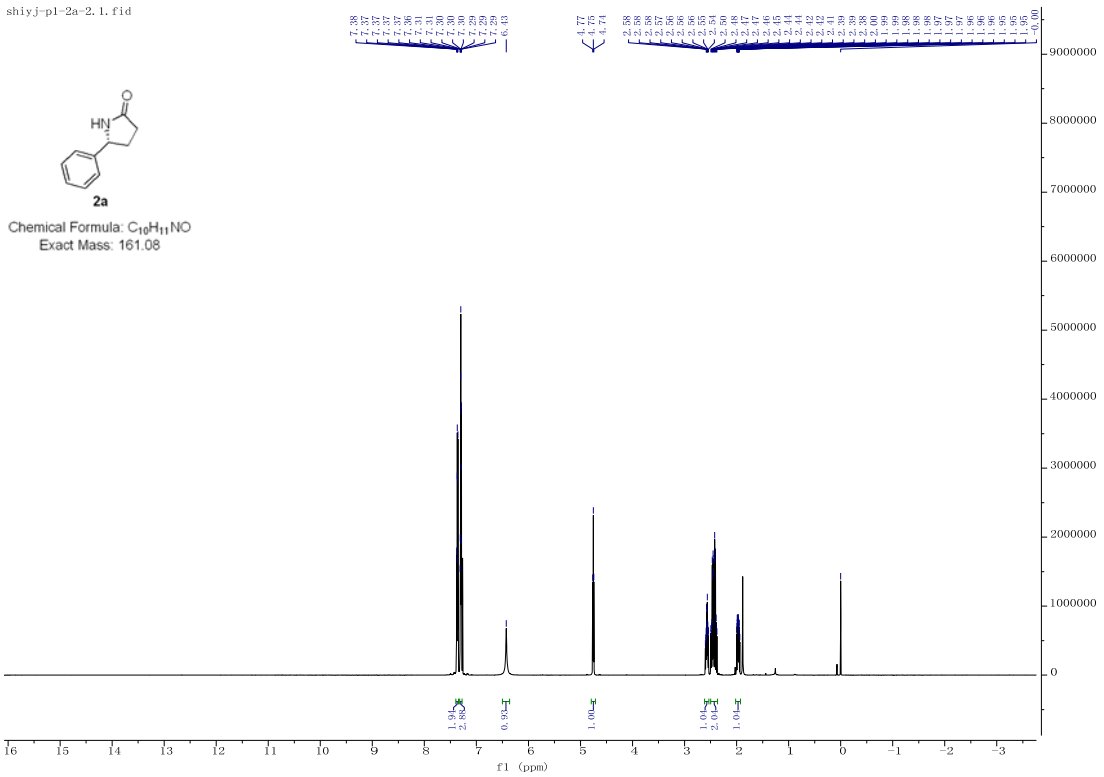
^{1}H NMR (400 MHz, Methanol-d4) of compound **5i**



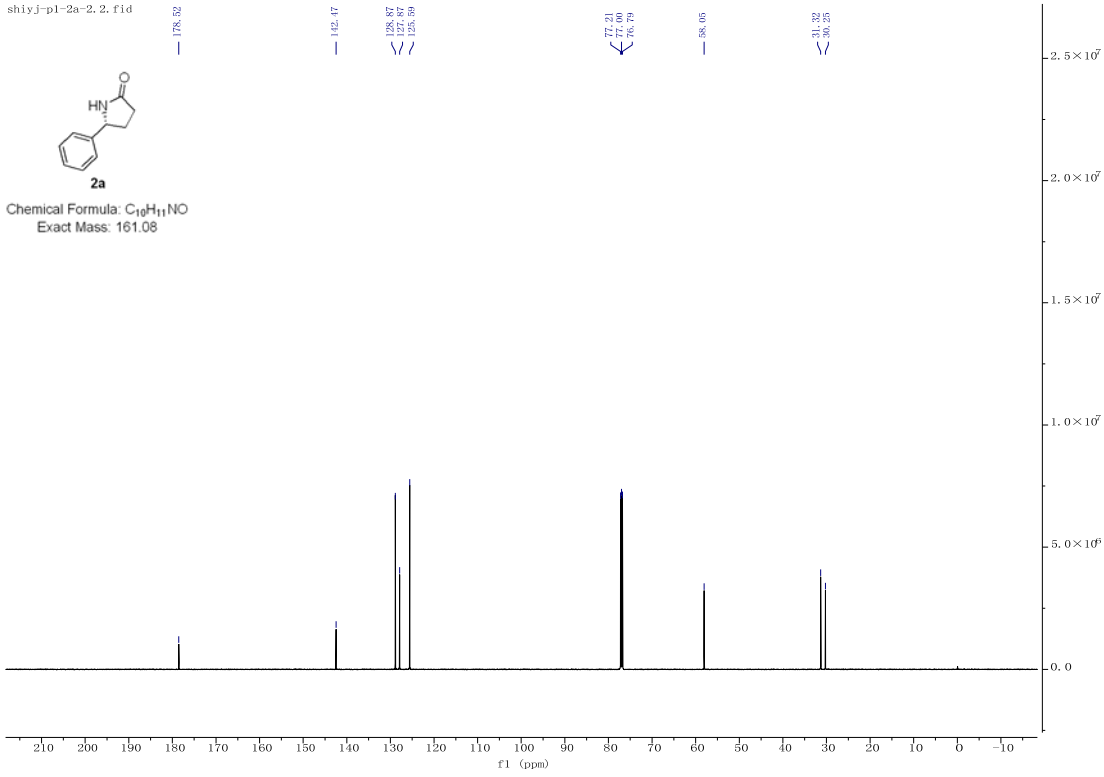
^{13}C{^{1}H} NMR (101 MHz, Methanol-d4) of compound **5i**



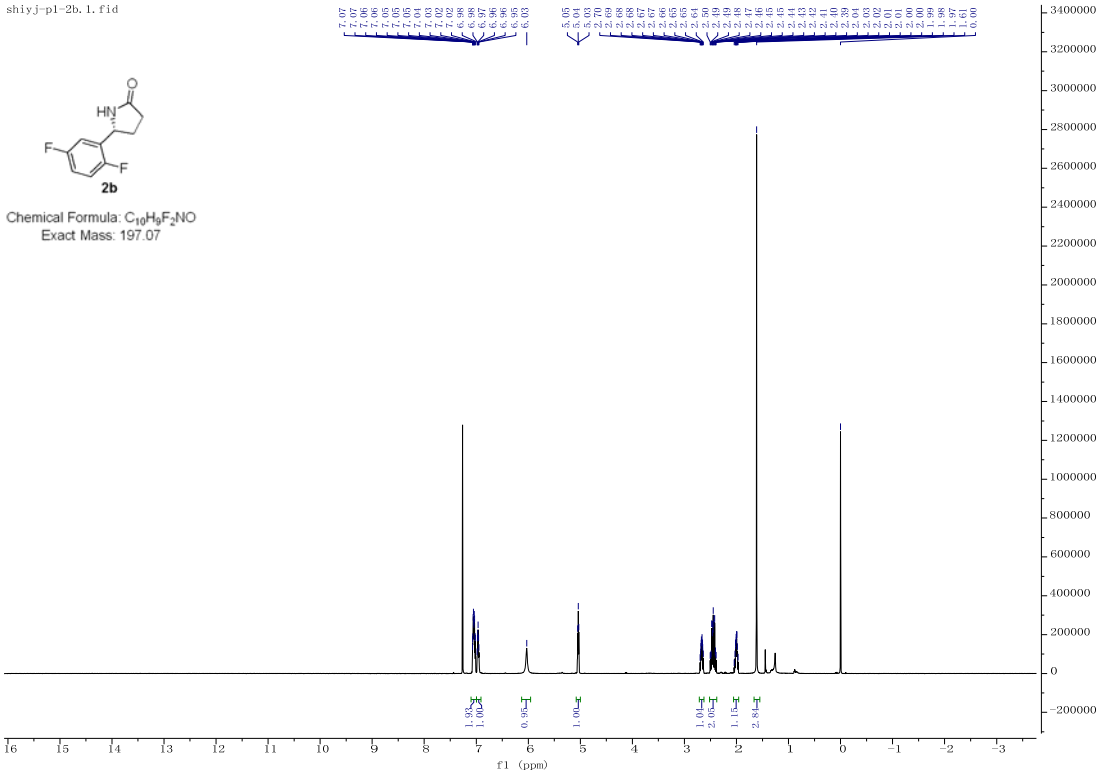
^{1}H NMR (600 MHz, Chloroform-d) of compound **2a**



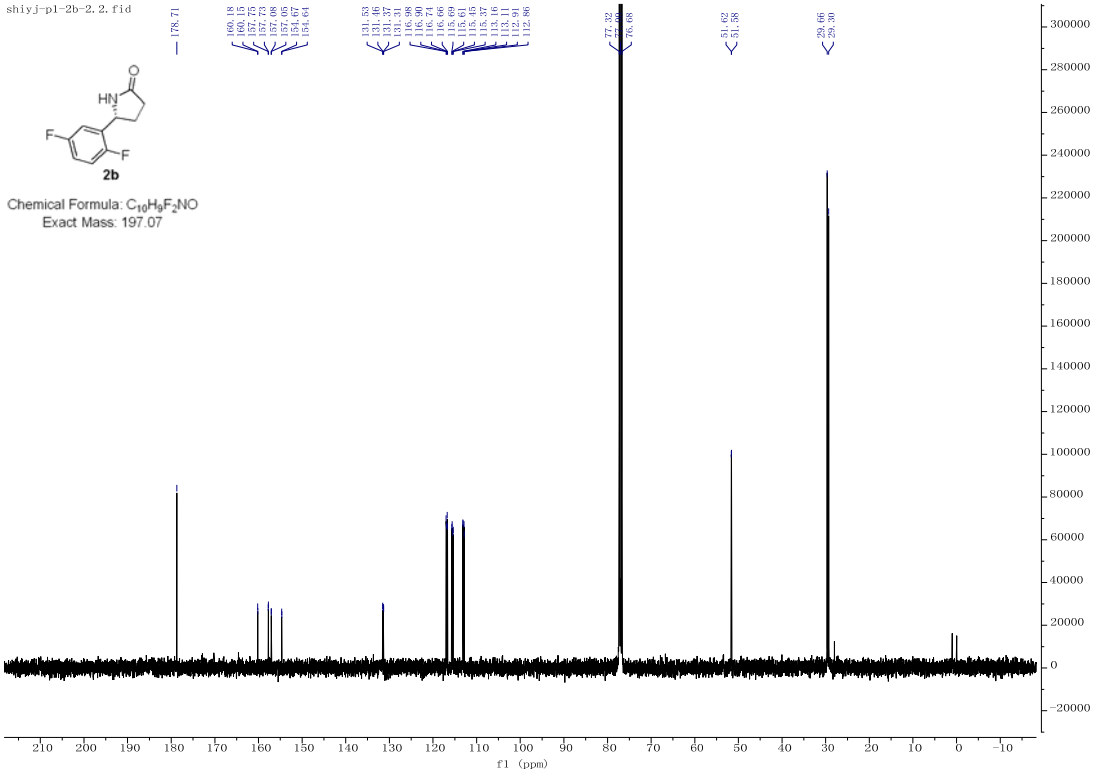
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2a**



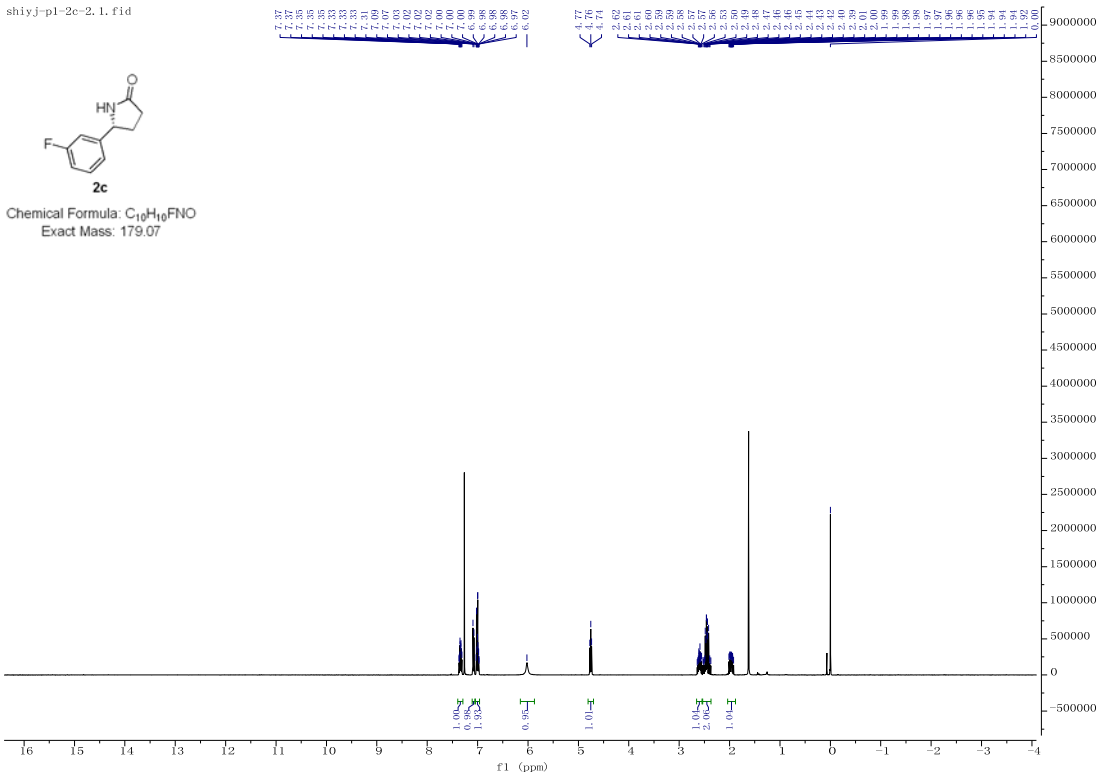
^{1}H NMR (600 MHz, Chloroform-d) of compound **2b**



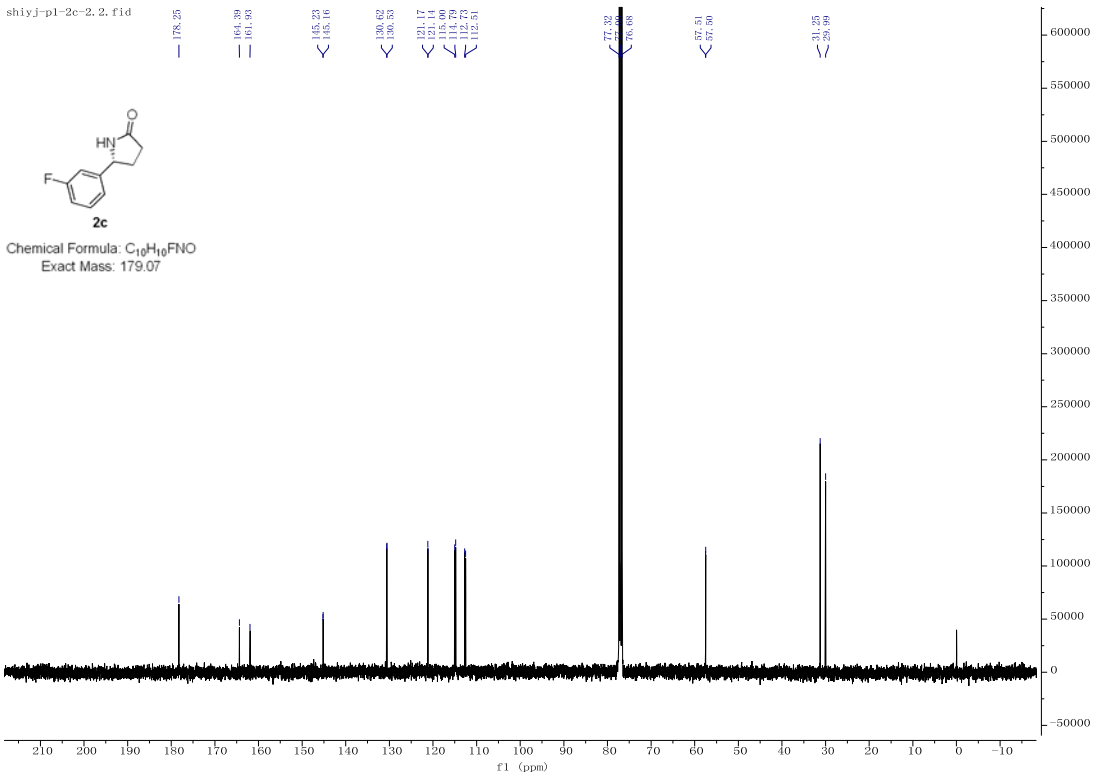
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2b**



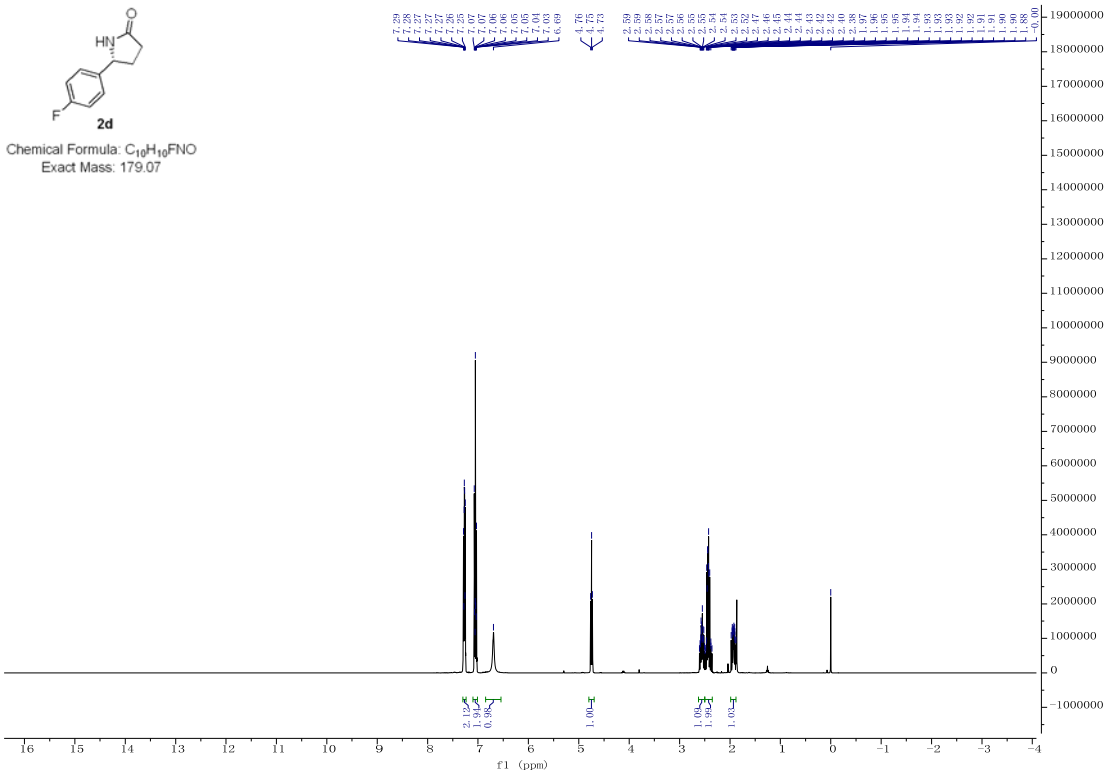
^{1}H NMR (400 MHz, Chloroform-d) of compound **2c**



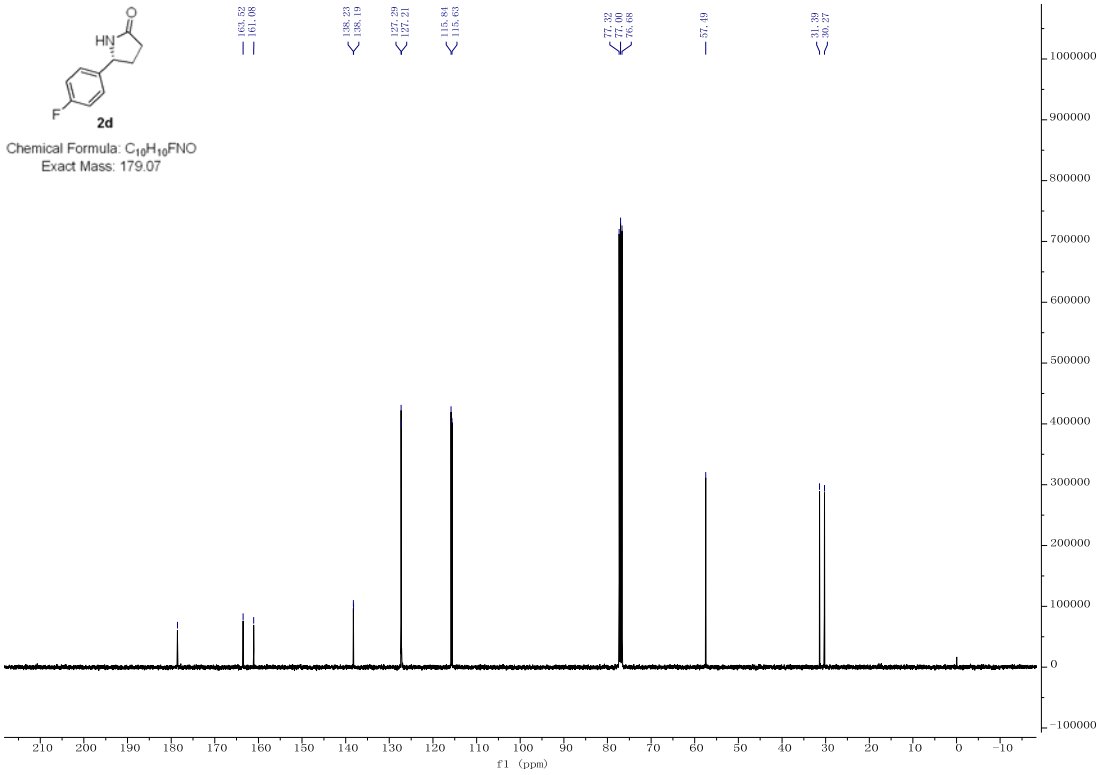
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2c**



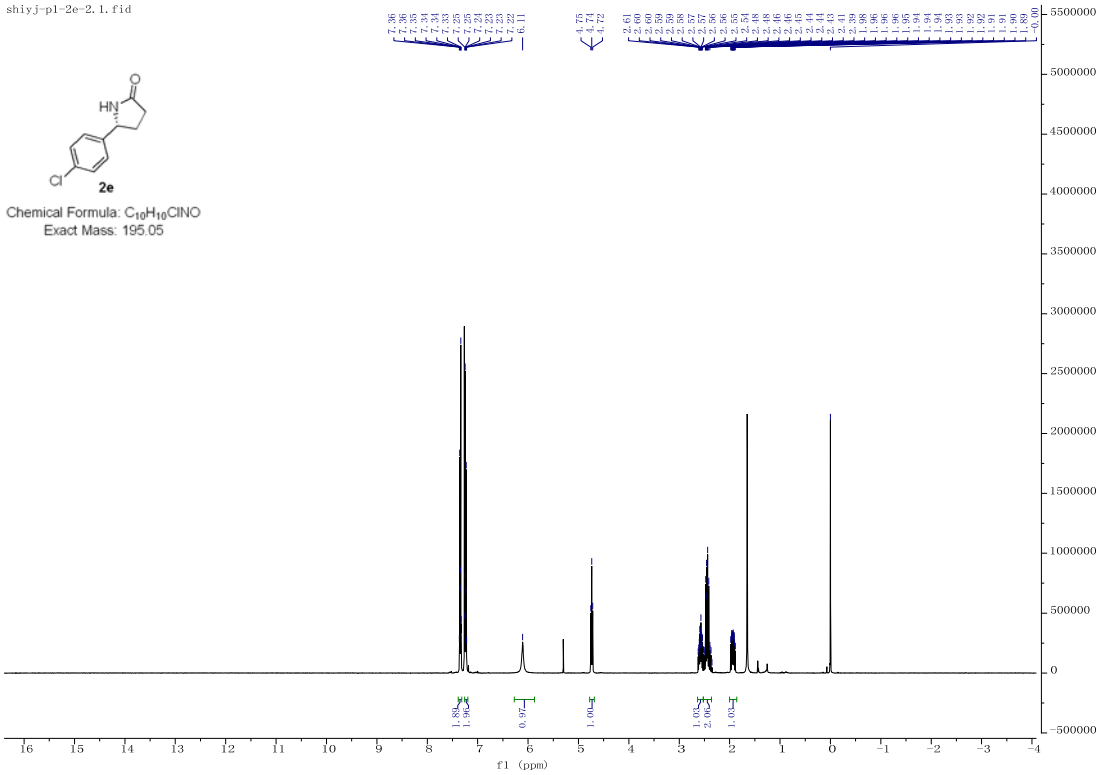
^{1}H NMR (400 MHz, Chloroform-d) of compound **2d**



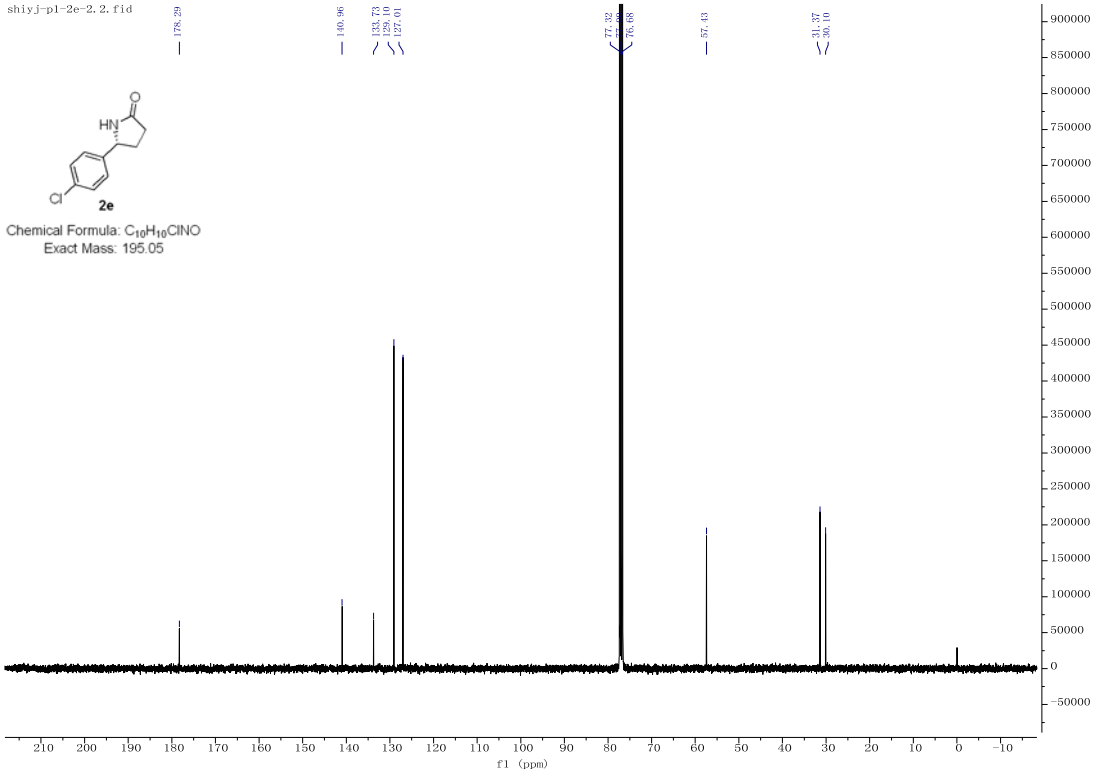
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2d**



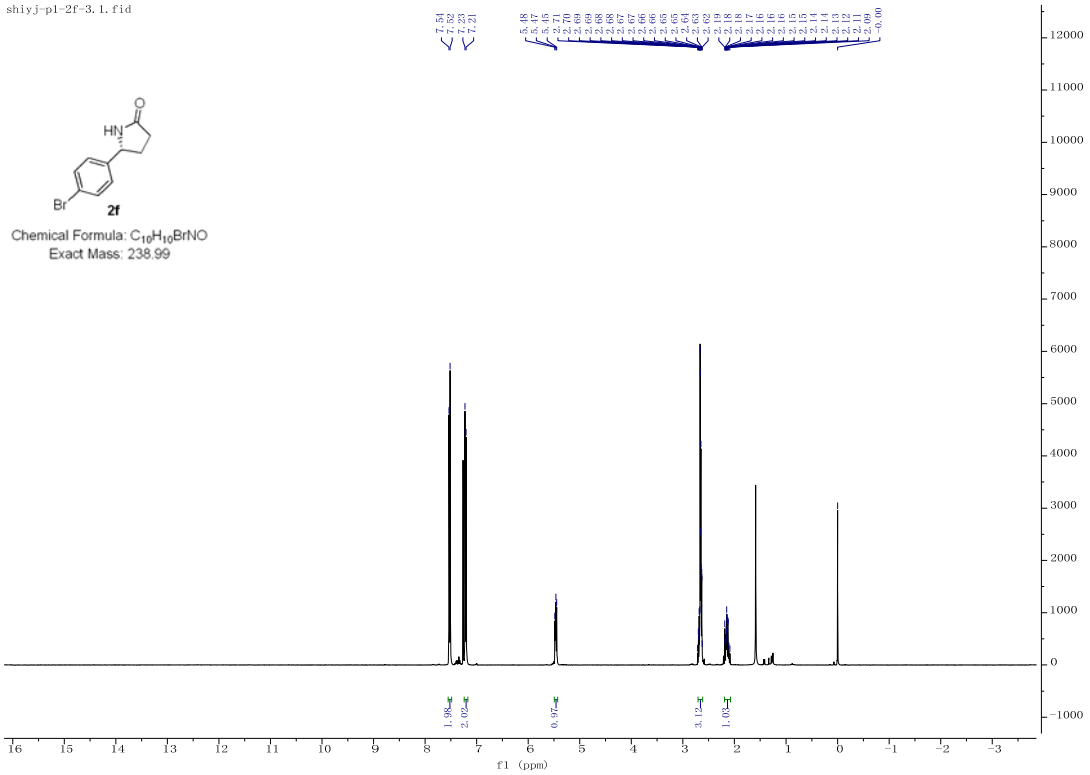
^{1}H NMR (400 MHz, Chloroform-d) of compound **2e**



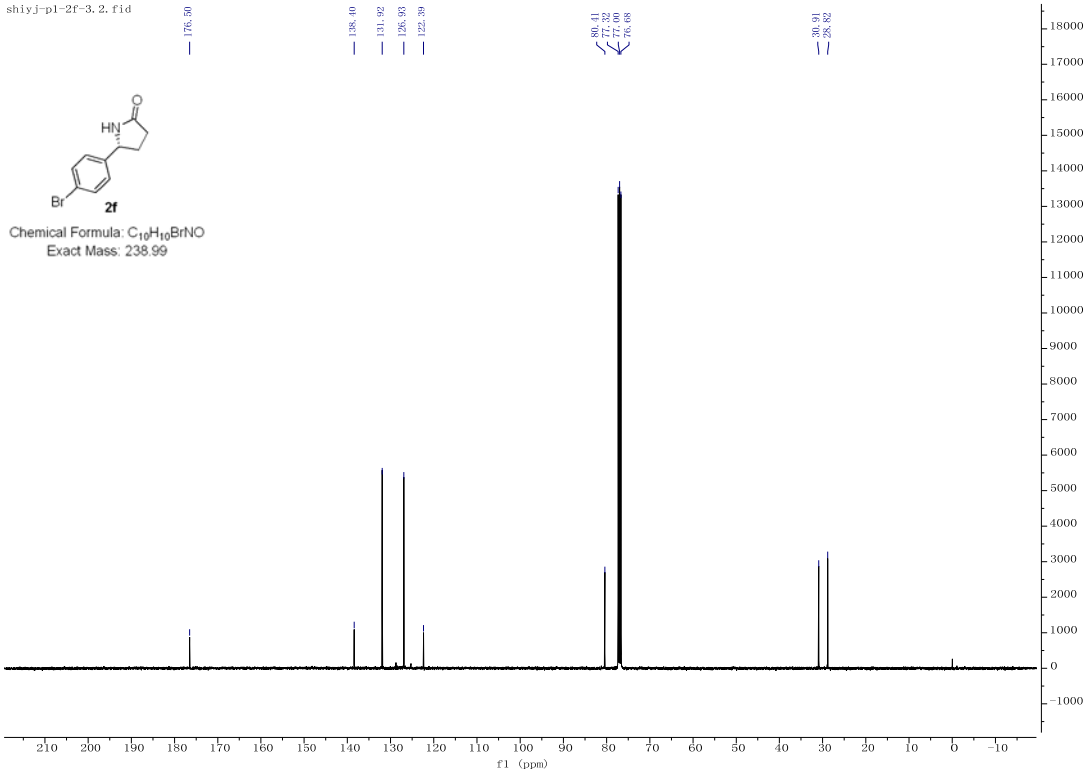
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2e**



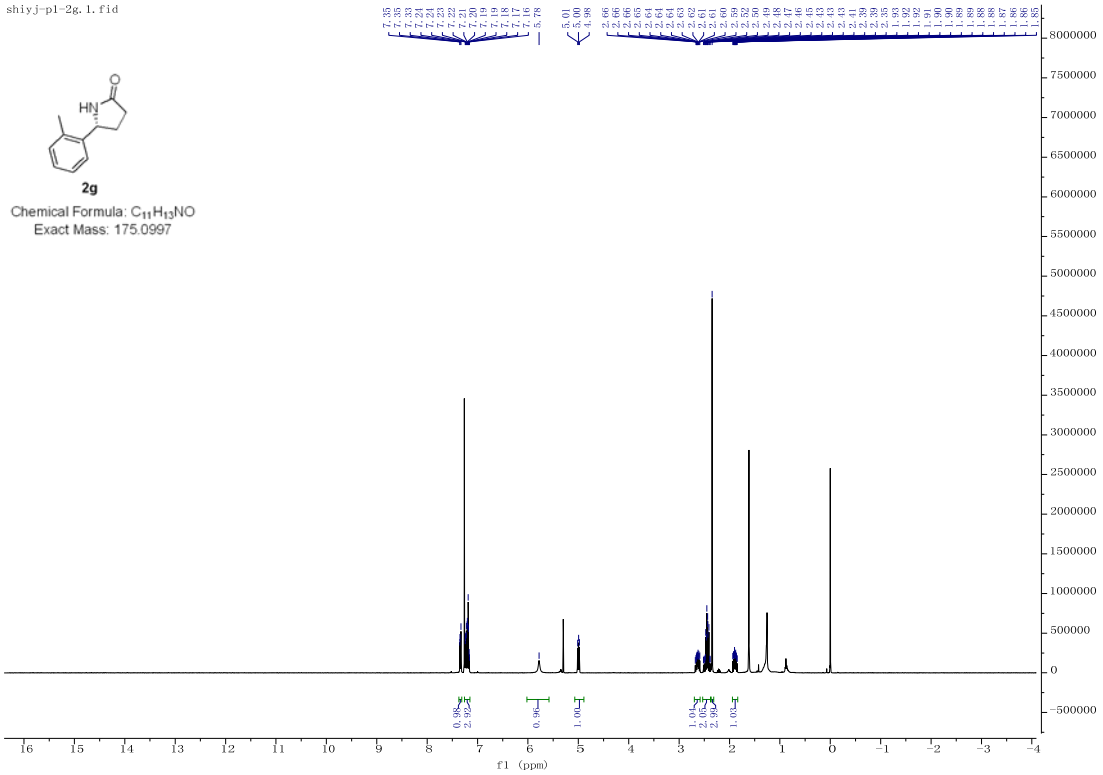
^{1}H NMR (400 MHz, Chloroform-d) of compound **2f**



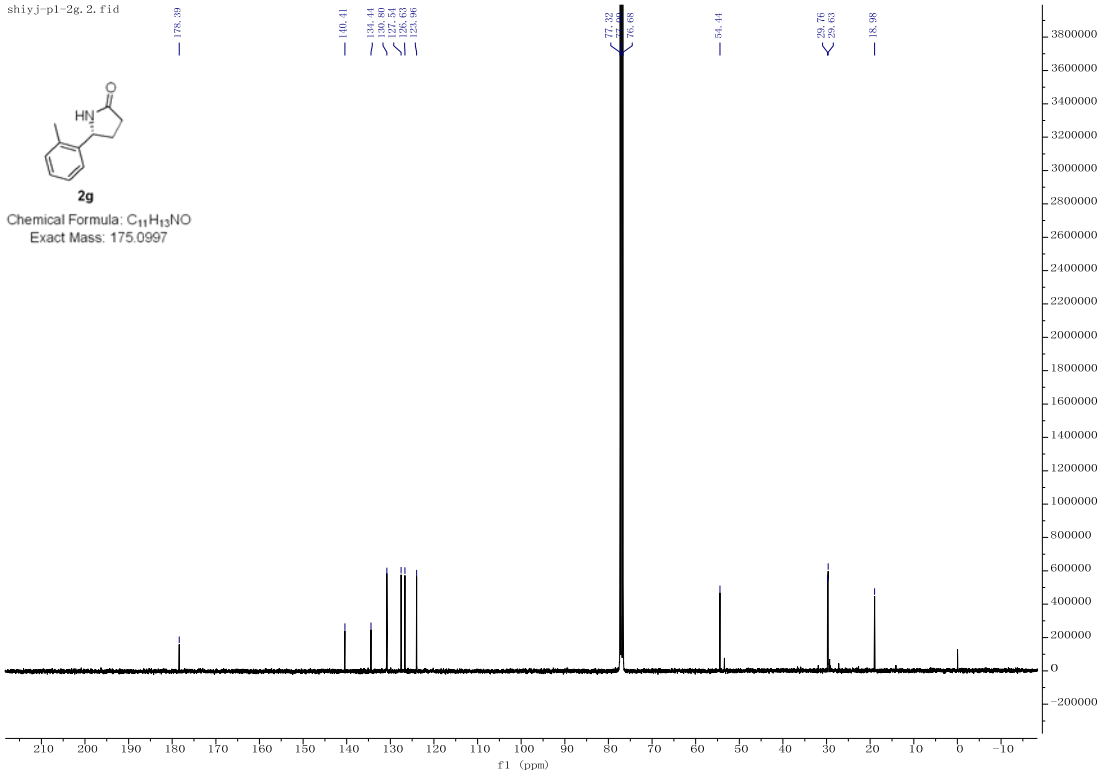
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2f**



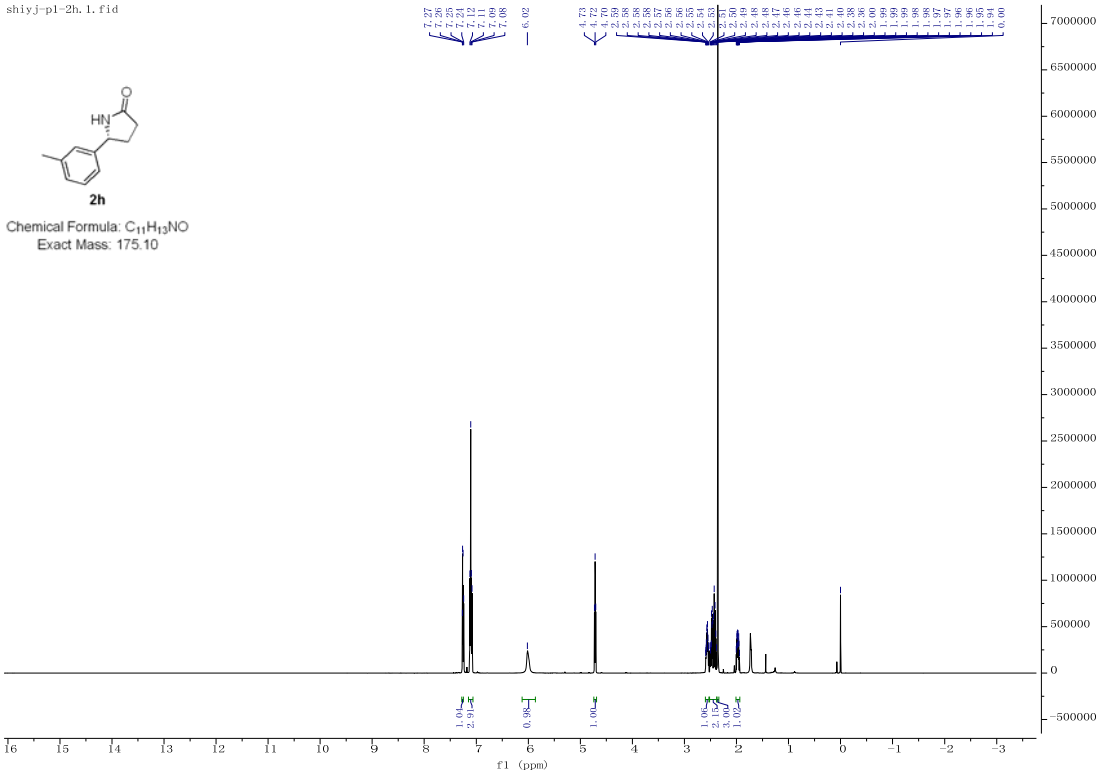
^{1}H NMR (400 MHz, Chloroform-d) of compound **2g**



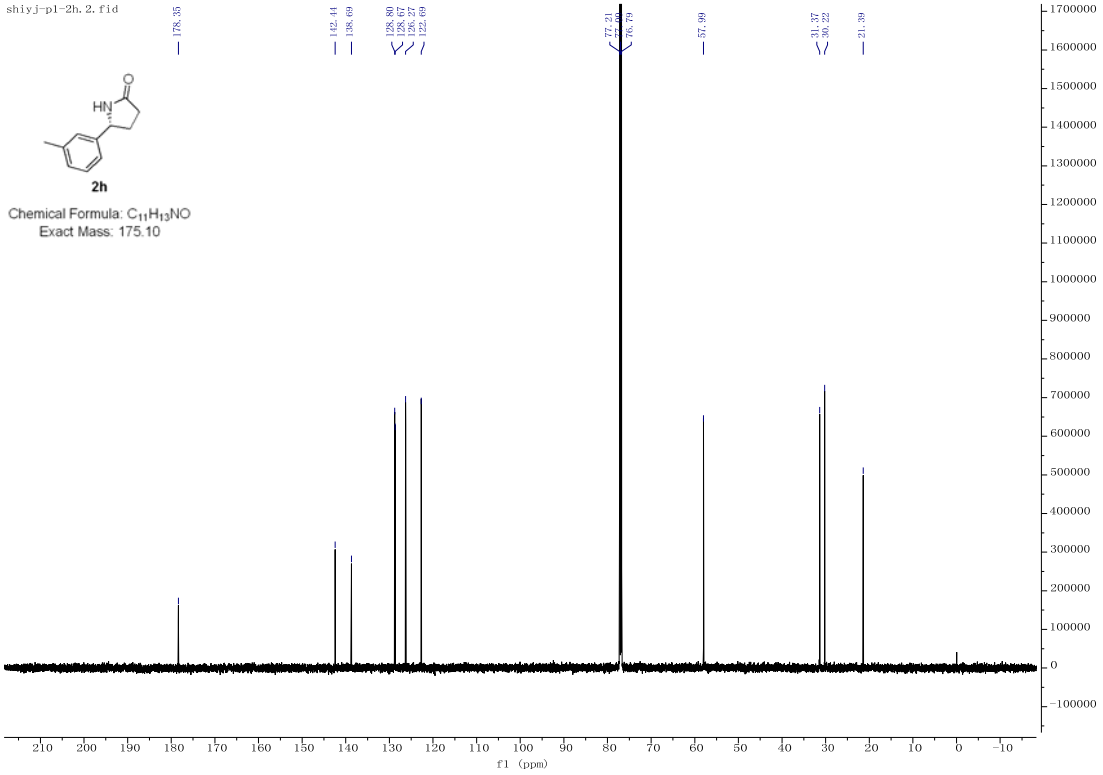
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2g**



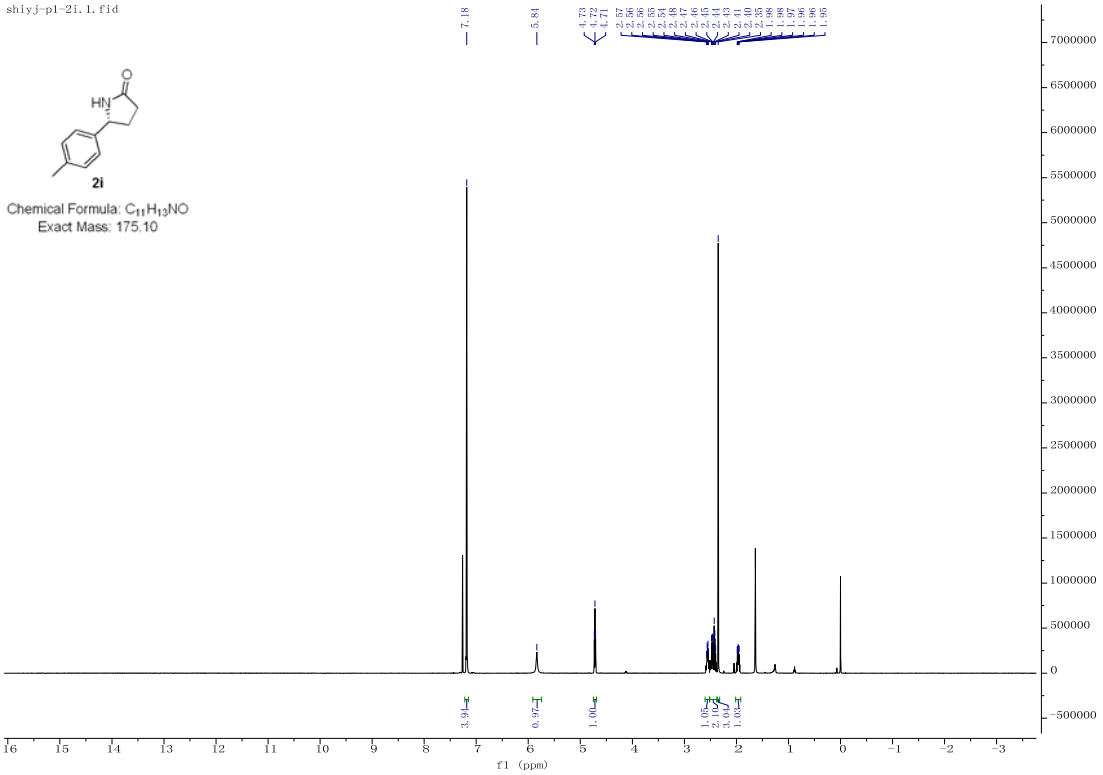
^{1}H NMR (600 MHz, Chloroform-d) of compound **2h**



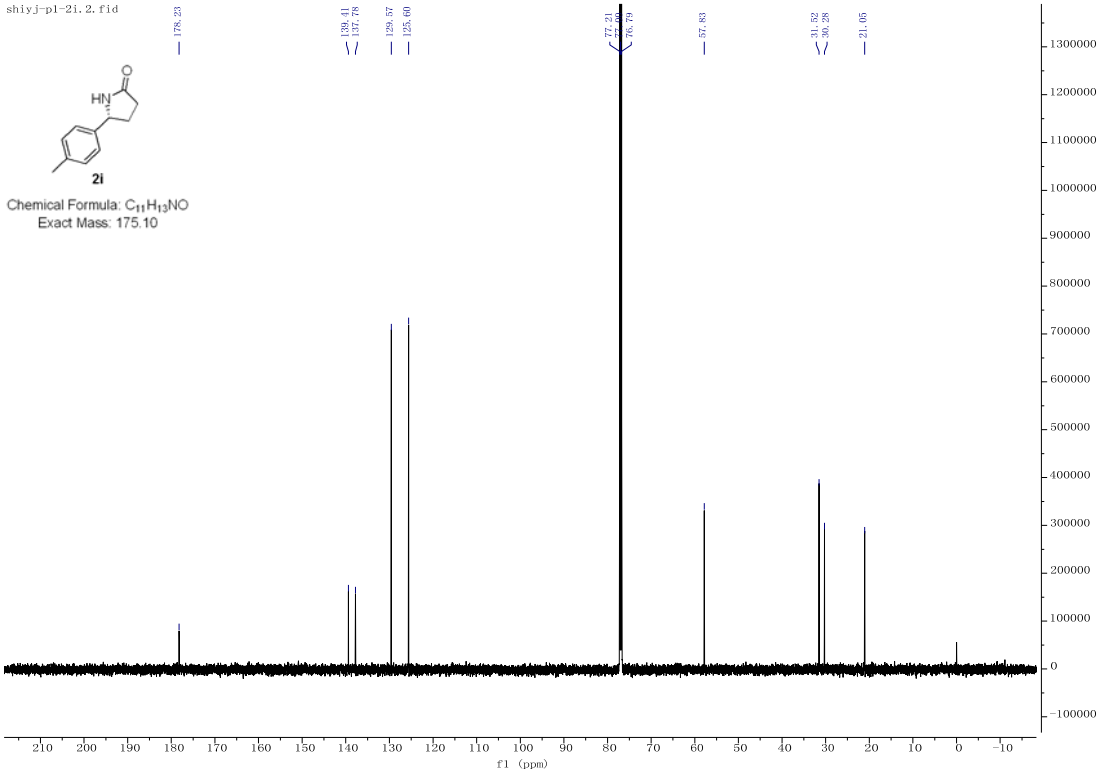
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2h**



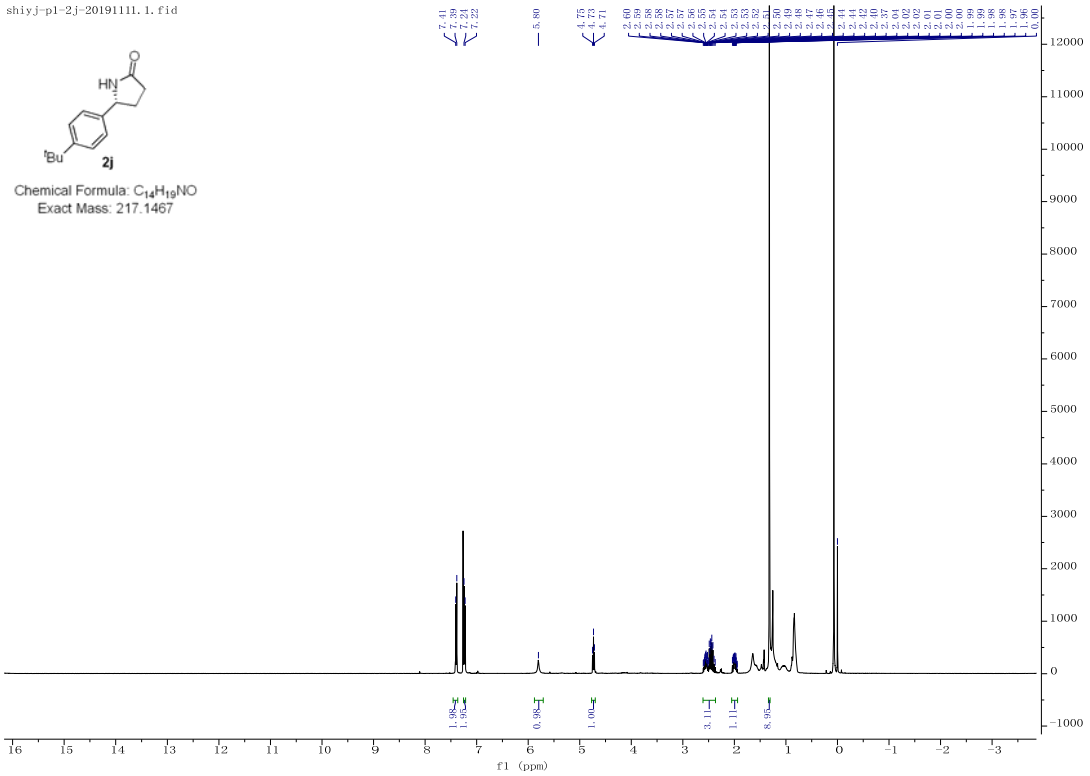
^{1}H NMR (600 MHz, Chloroform-d) of compound **2i**



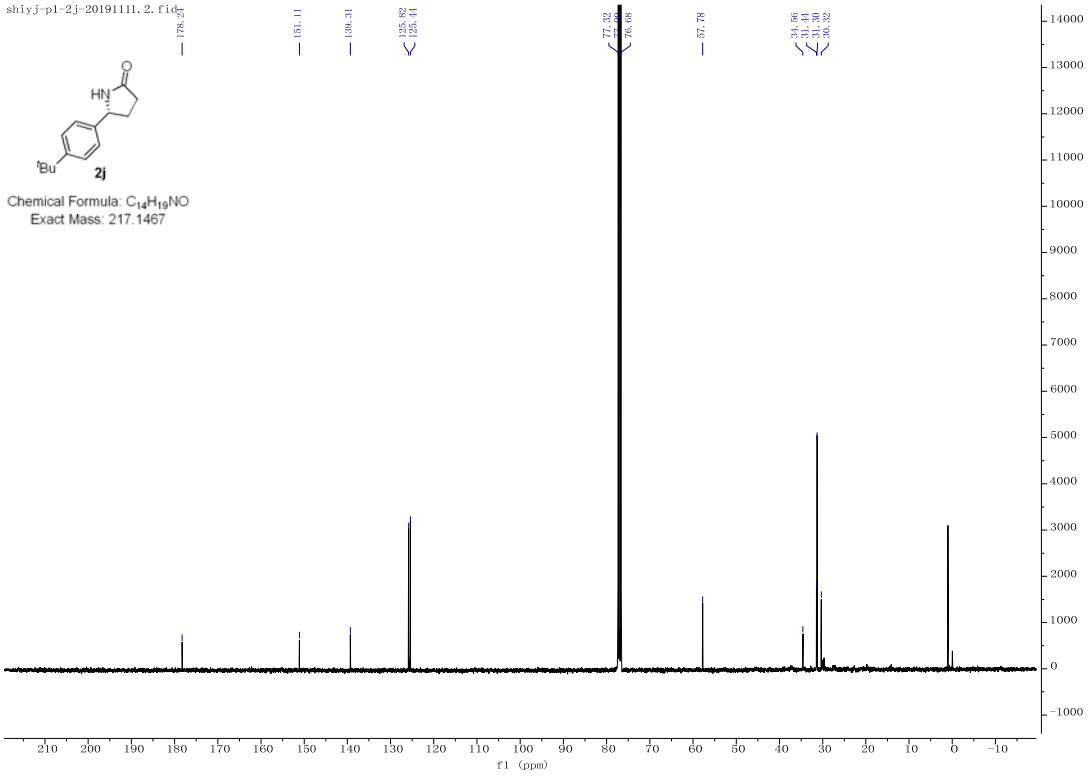
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2i**



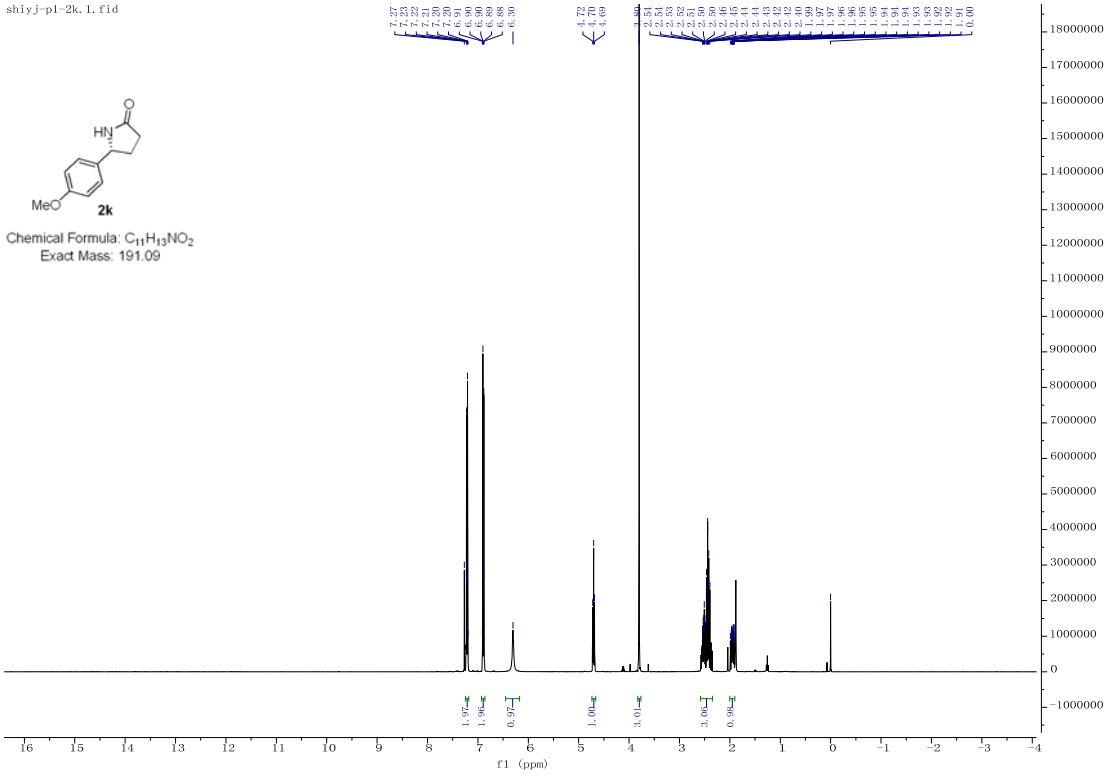
^{1}H NMR (400 MHz, Chloroform-d) of compound **2j**



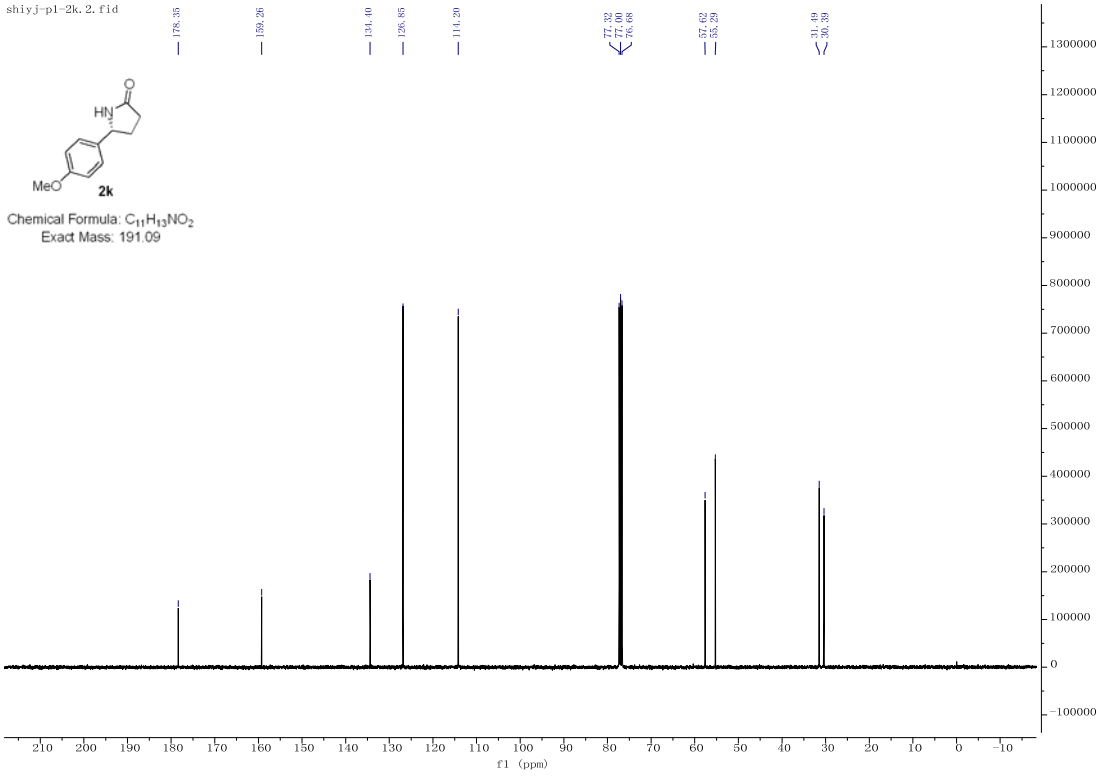
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2j**



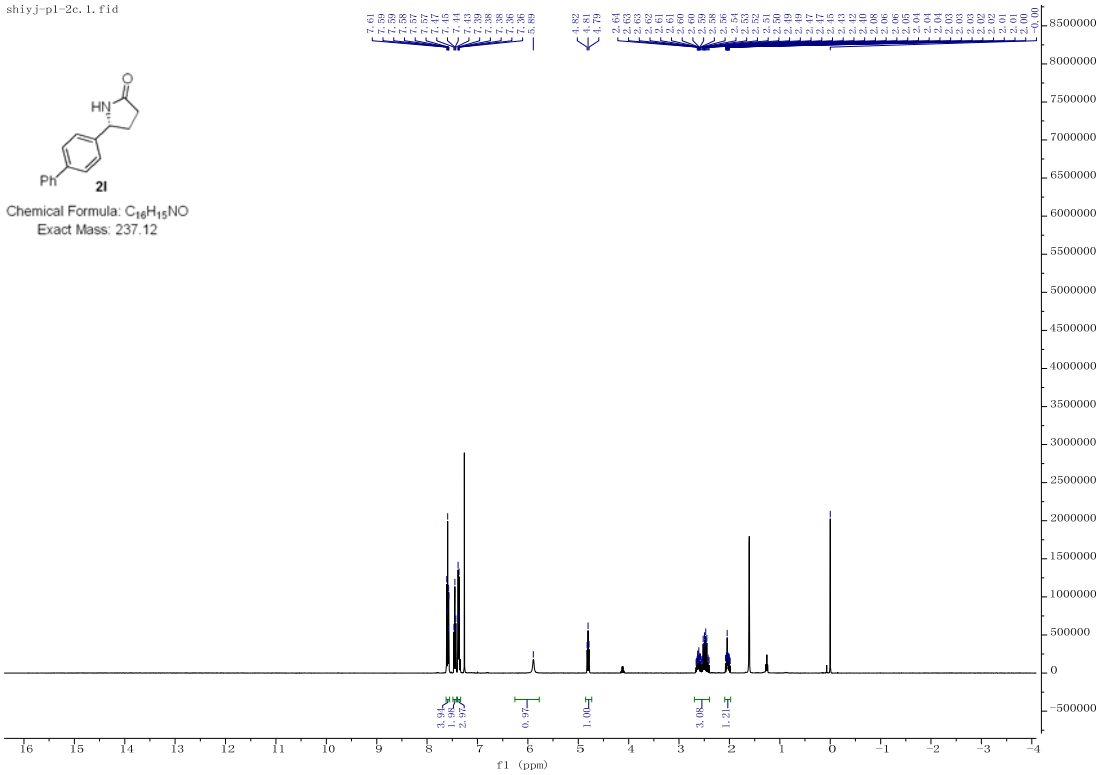
^{1}H NMR (400 MHz, Chloroform-d) of compound **2k**



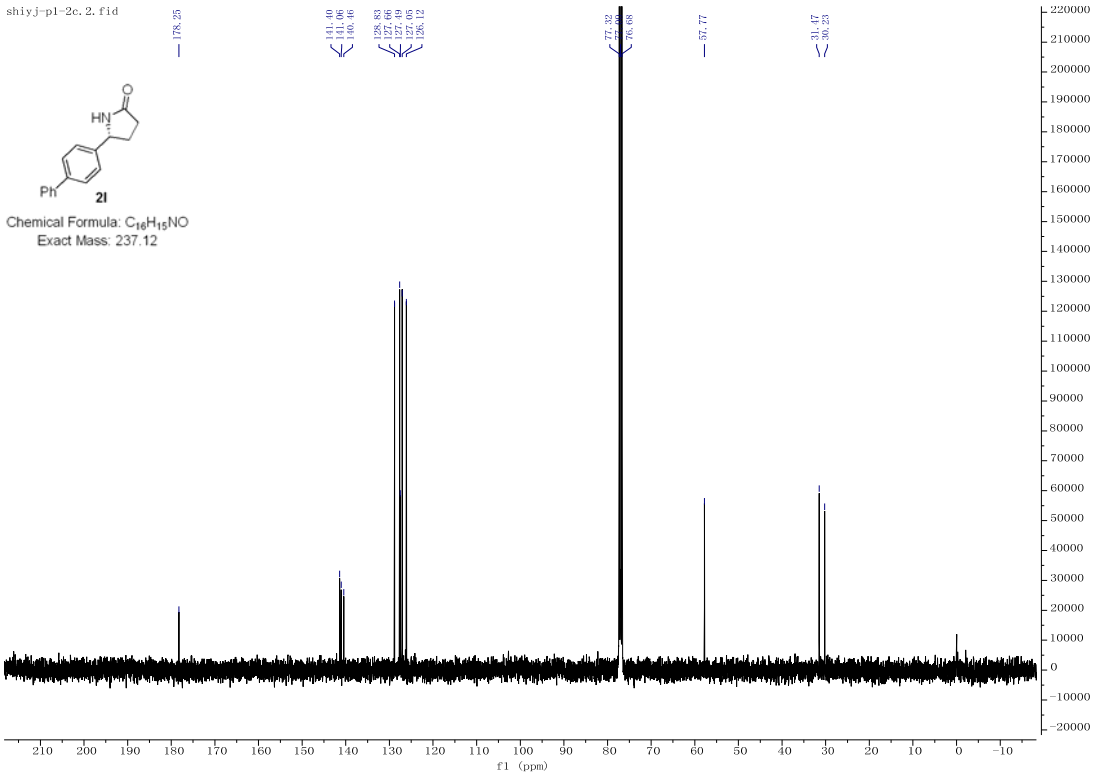
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2k**



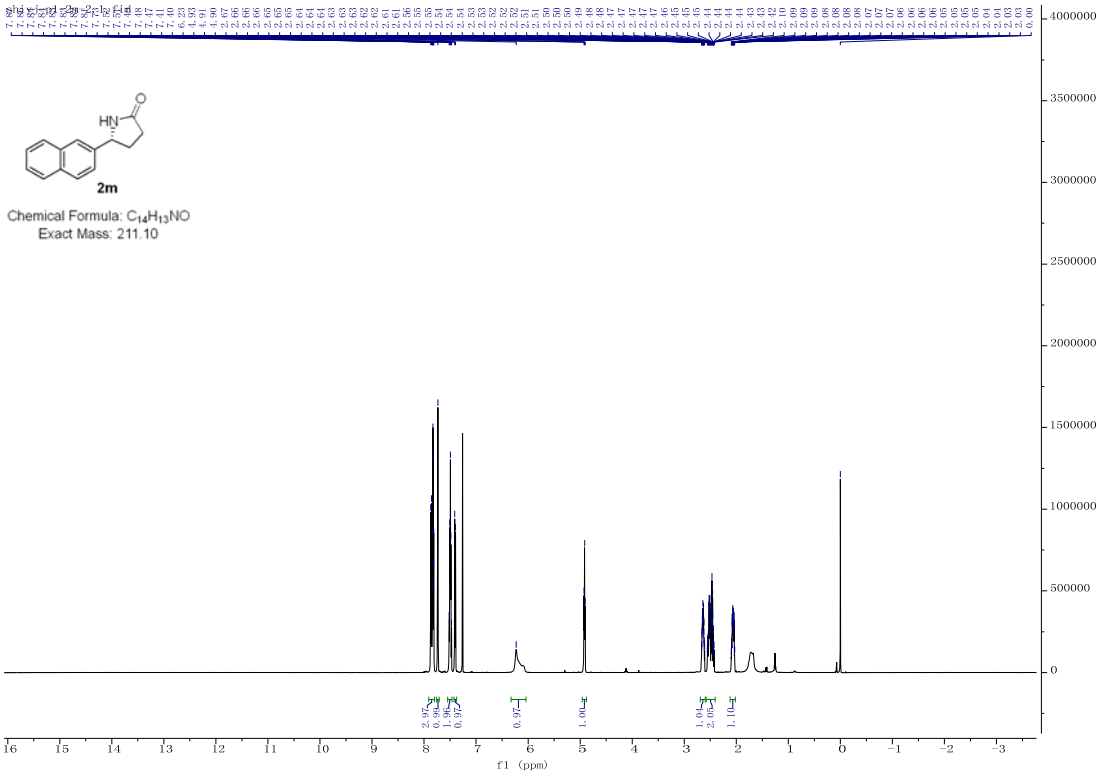
^{1}H NMR (400 MHz, Chloroform-d) of compound **2l**



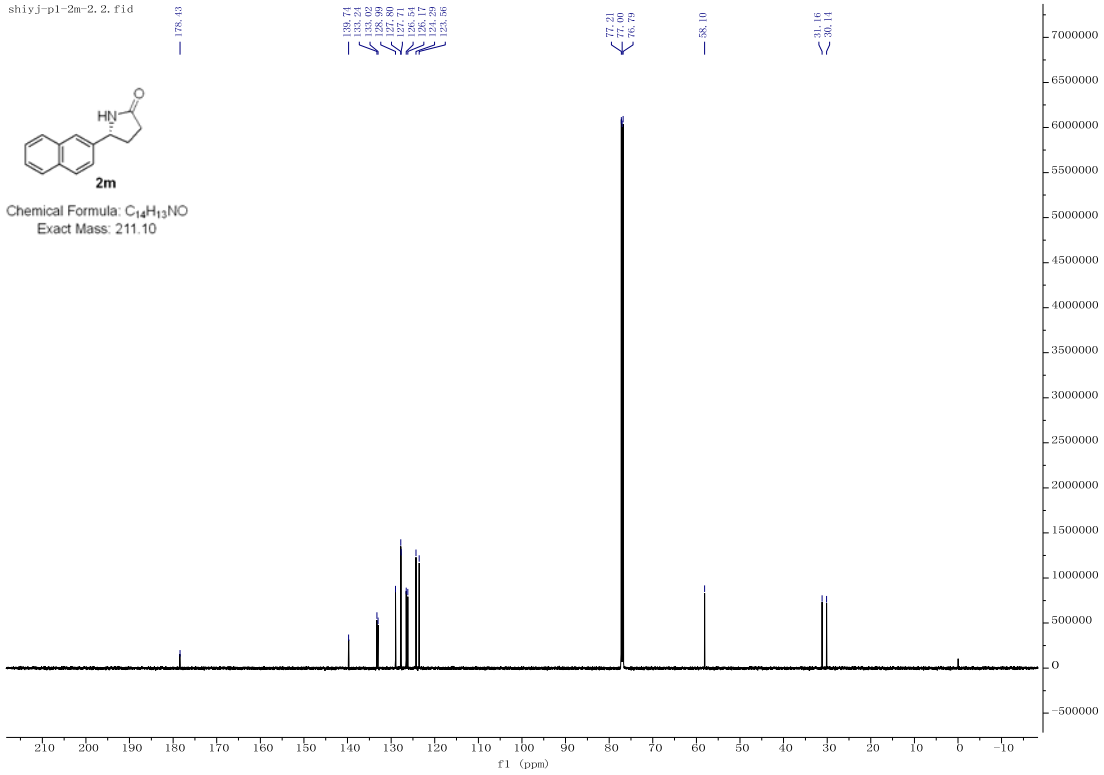
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **2e**



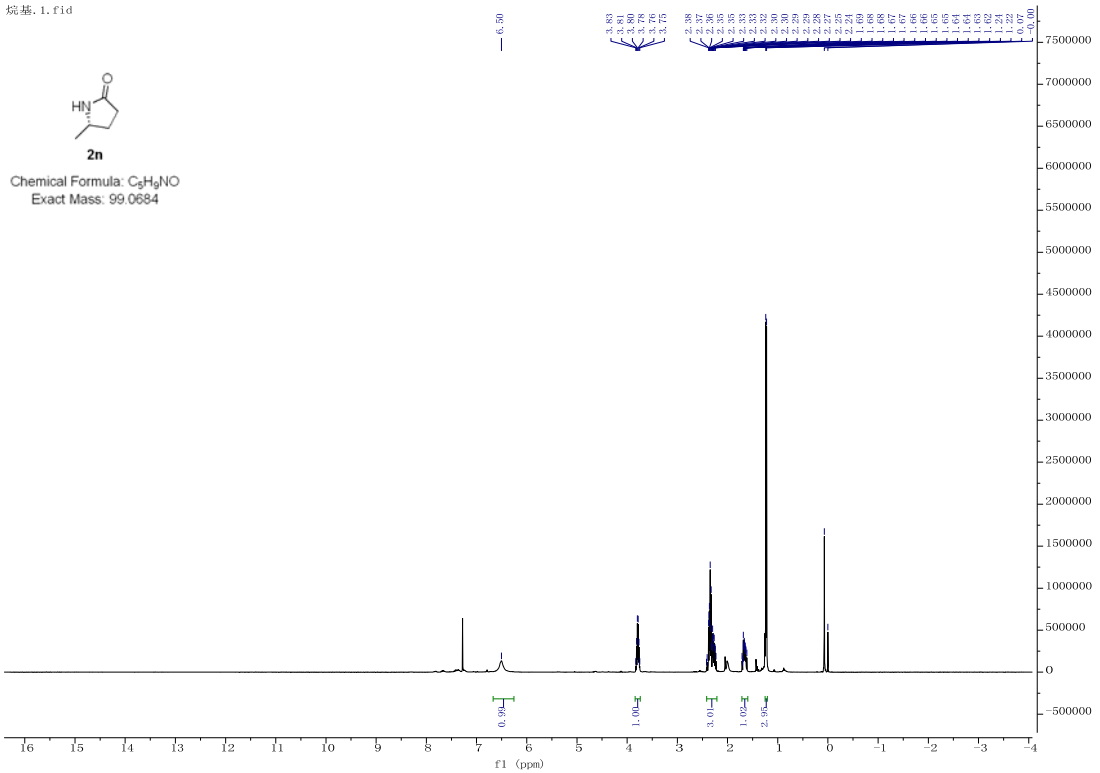
^{1}H NMR (600 MHz, Chloroform-d) of compound **2m**



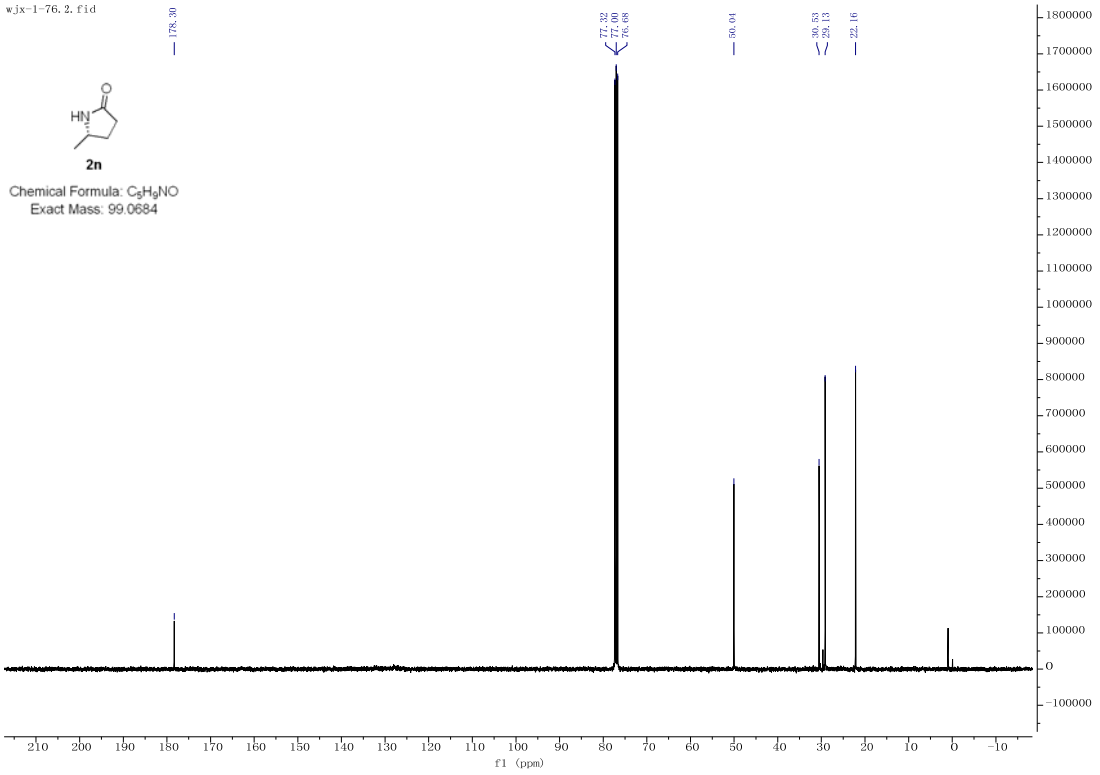
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **2m**



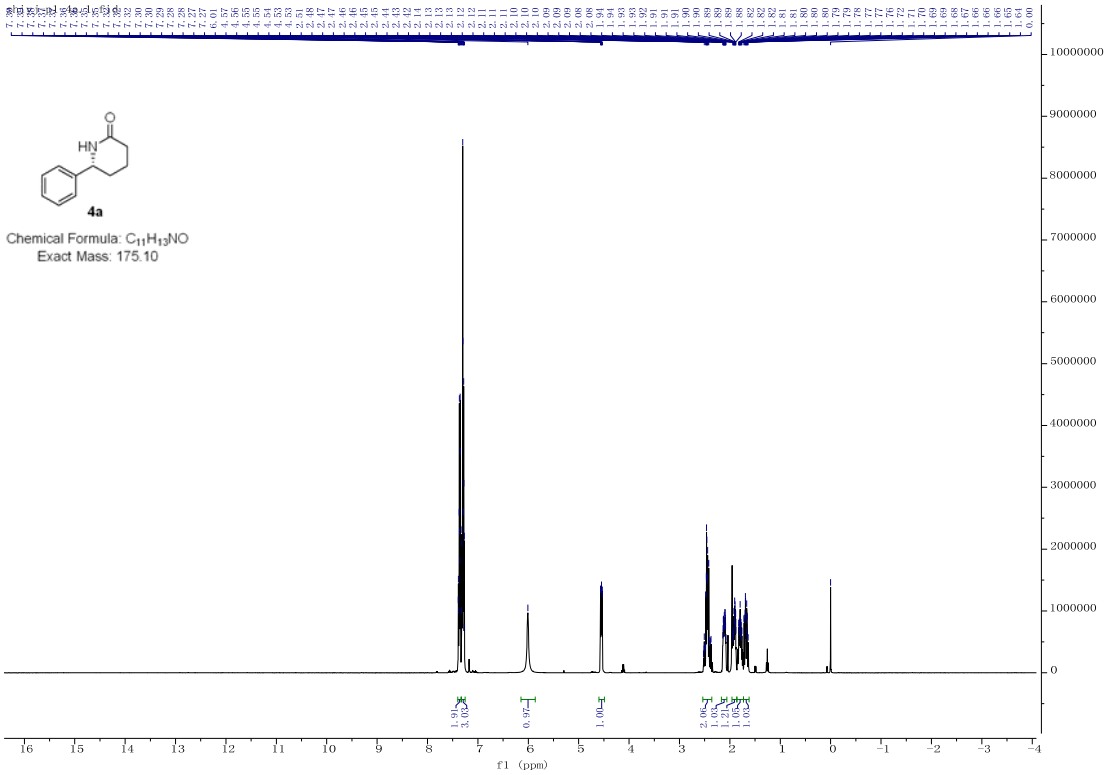
^{1}H NMR (400 MHz, Chloroform-d) of compound **2n**



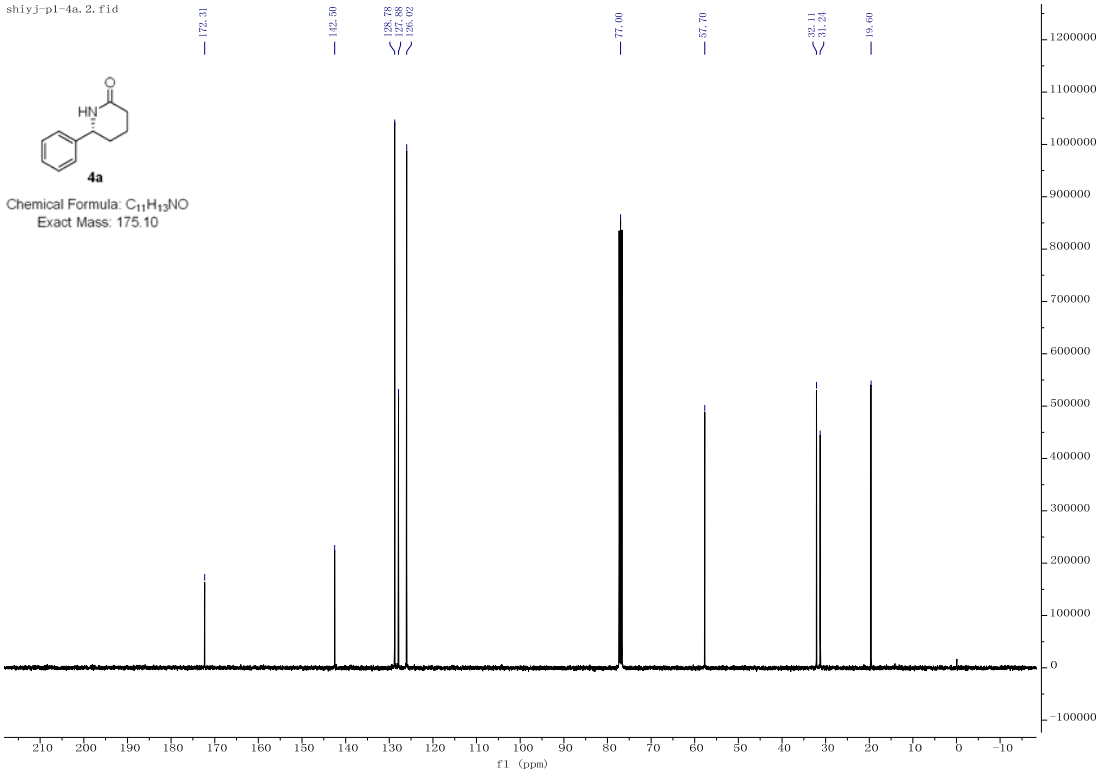
^{13}C{^{1}H} NMR (400 MHz, Chloroform-d) of compound **2n**



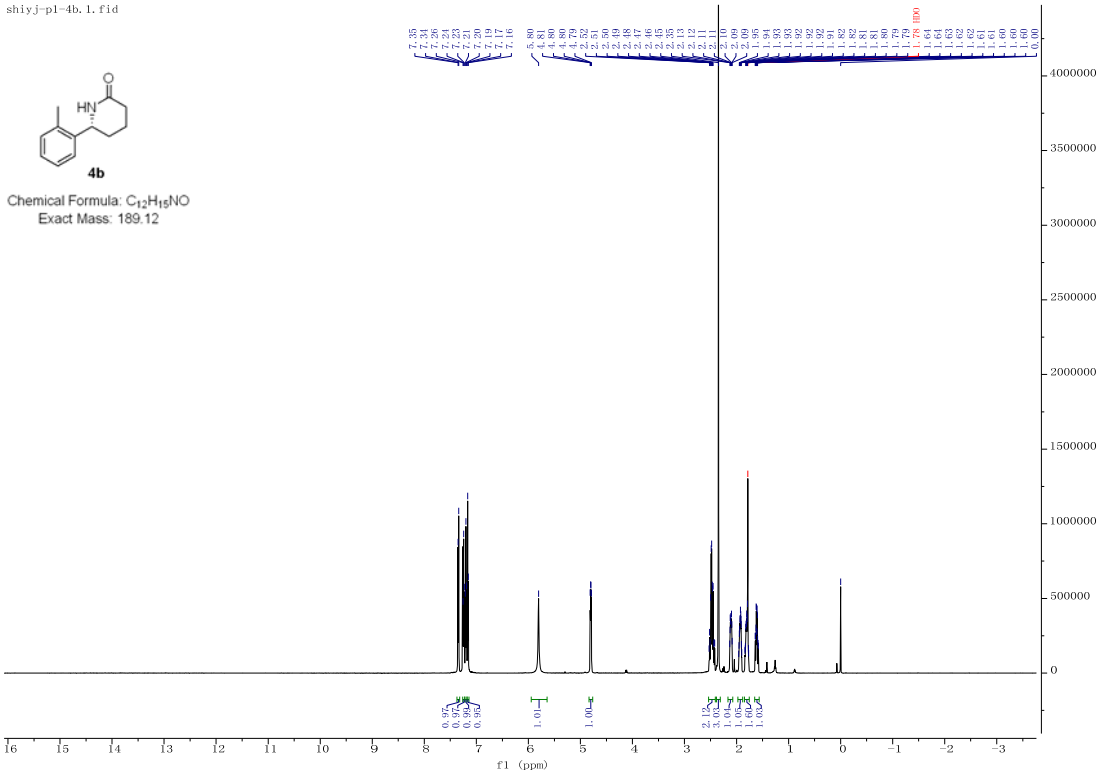
^{1}H NMR (400 MHz, Chloroform-d) of compound **4a**



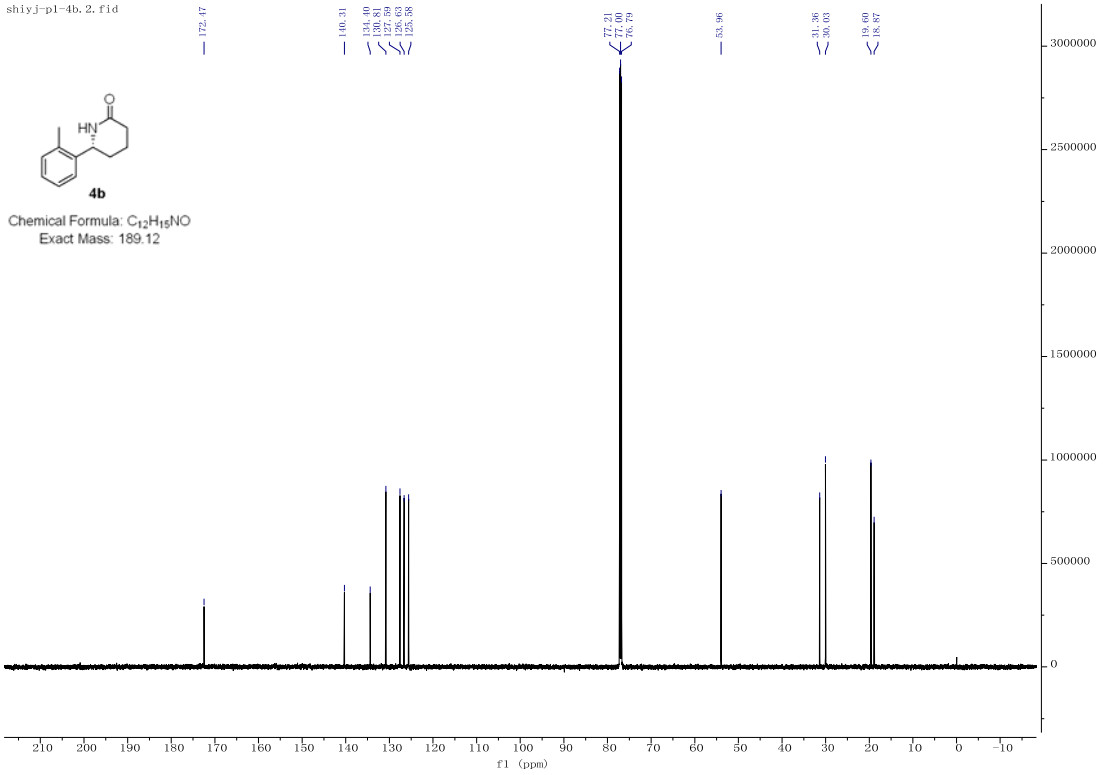
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **4a**



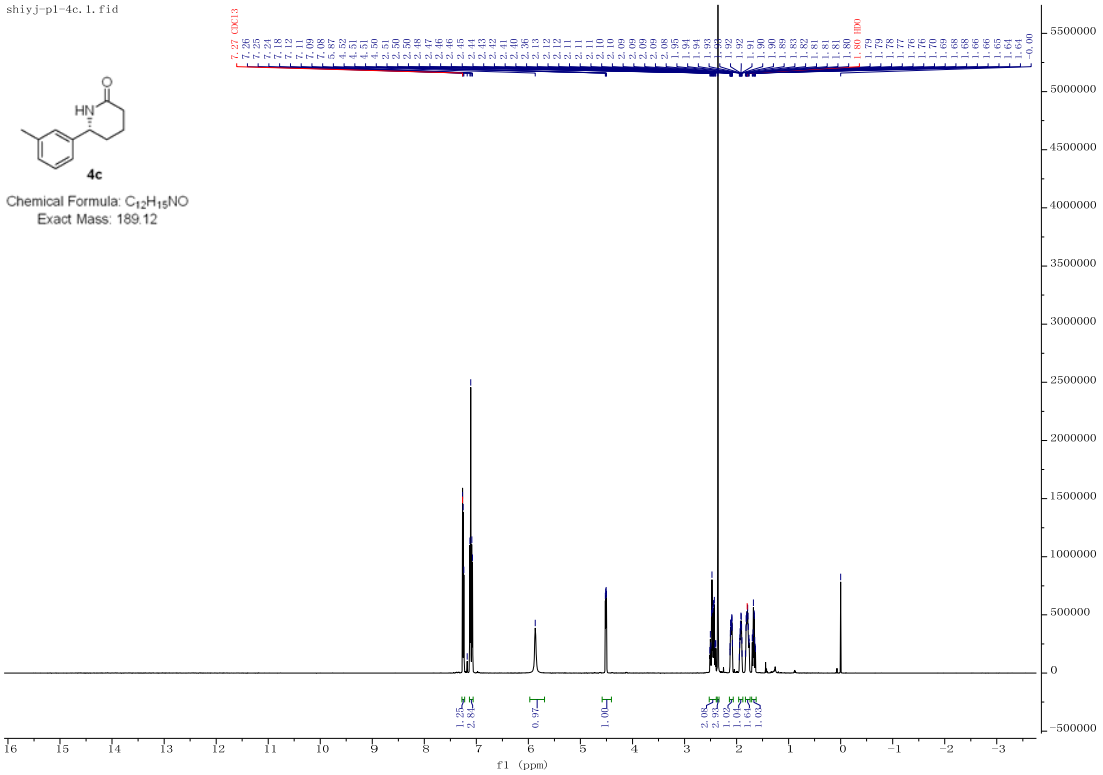
^{1}H NMR (600 MHz, Chloroform-d) of compound **4b**



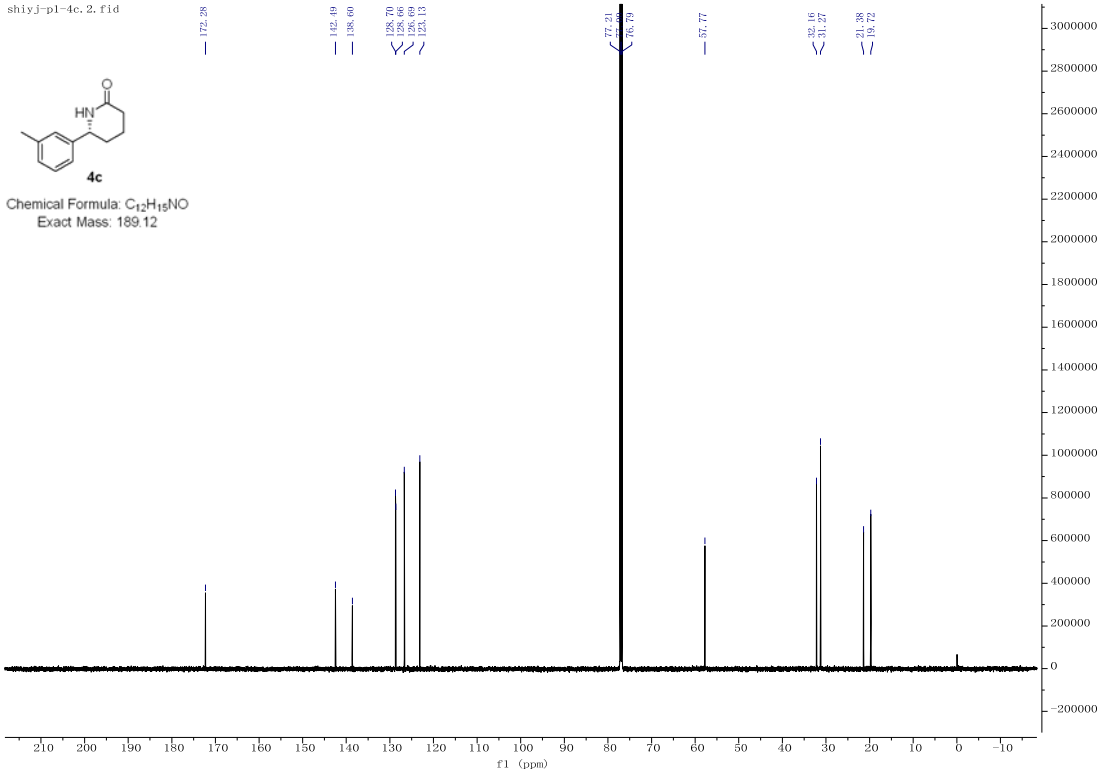
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **4b**



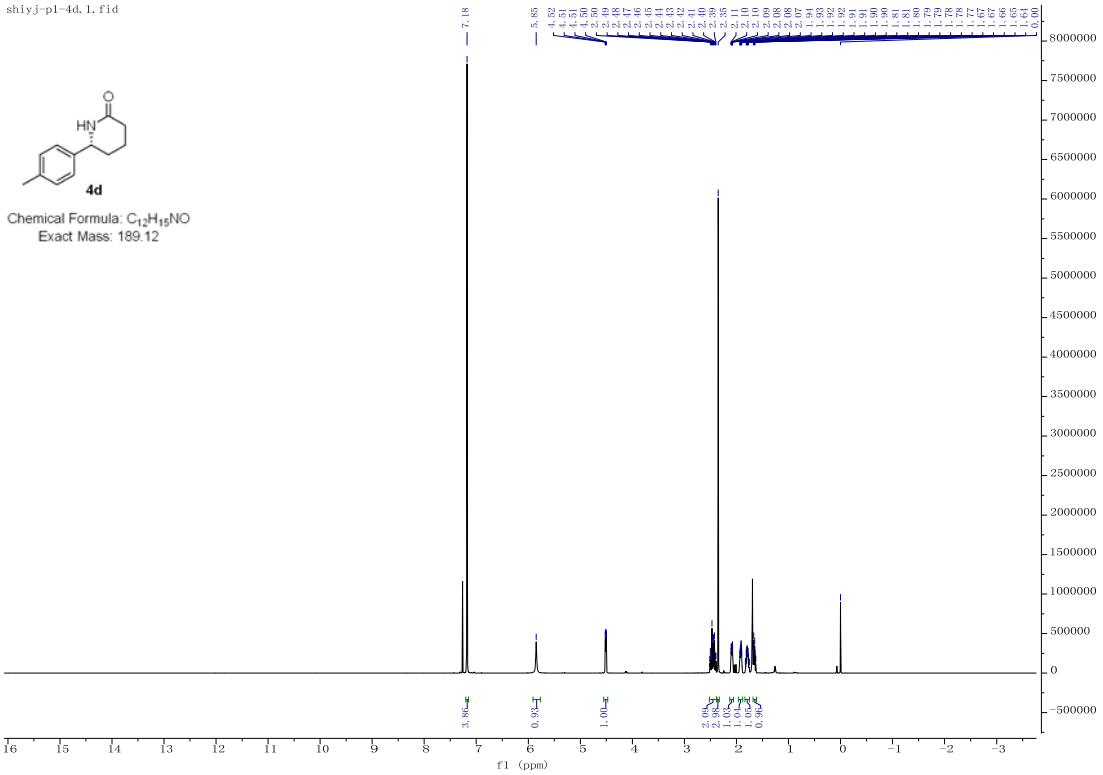
^{1}H NMR (600 MHz, Chloroform-d) of compound **4c**



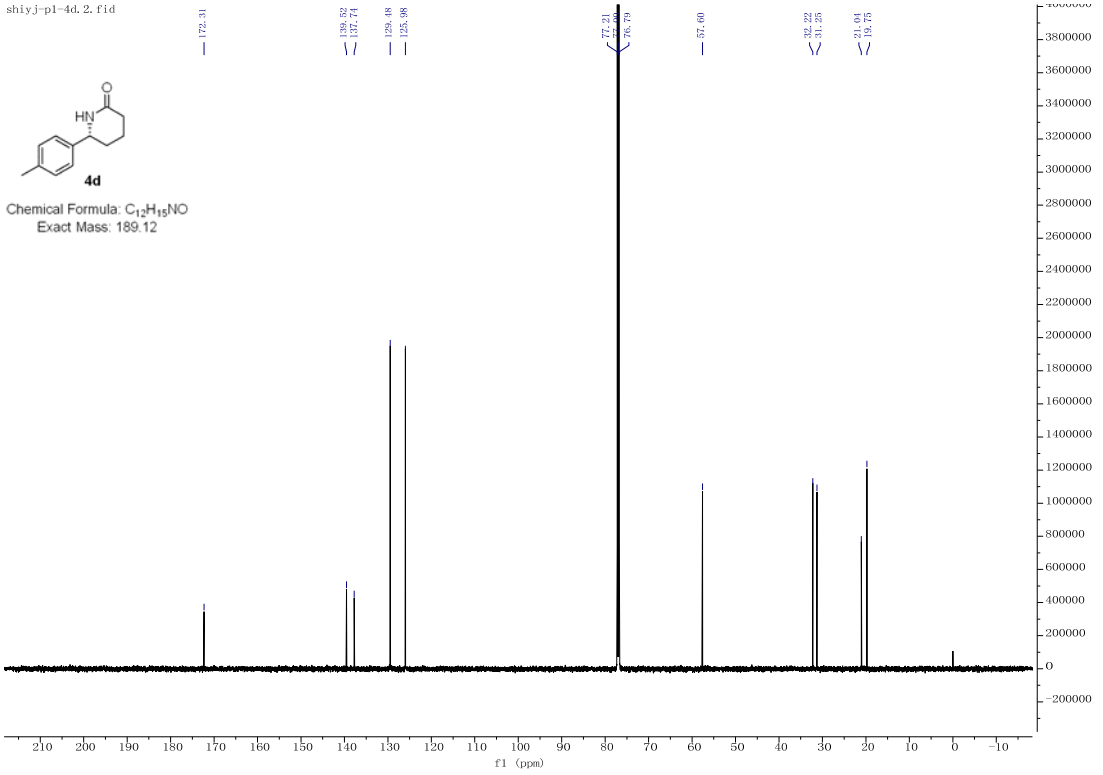
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **4c**



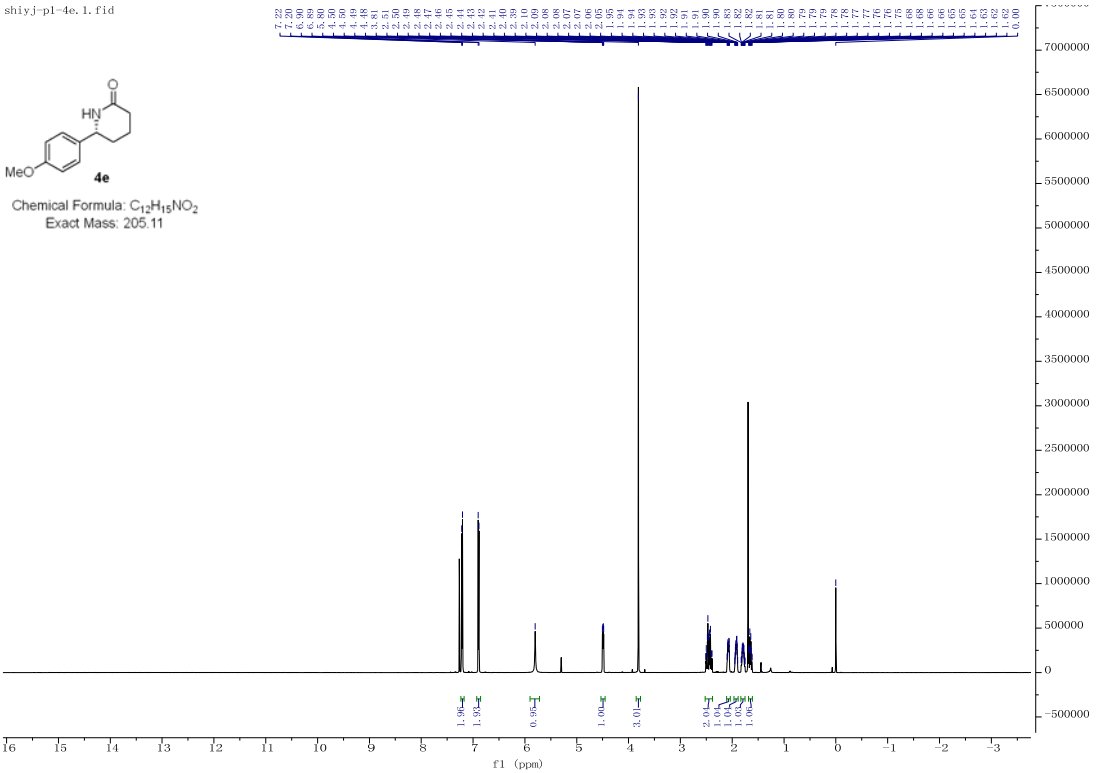
^{1}H NMR (600 MHz, Chloroform-d) of compound **4d**



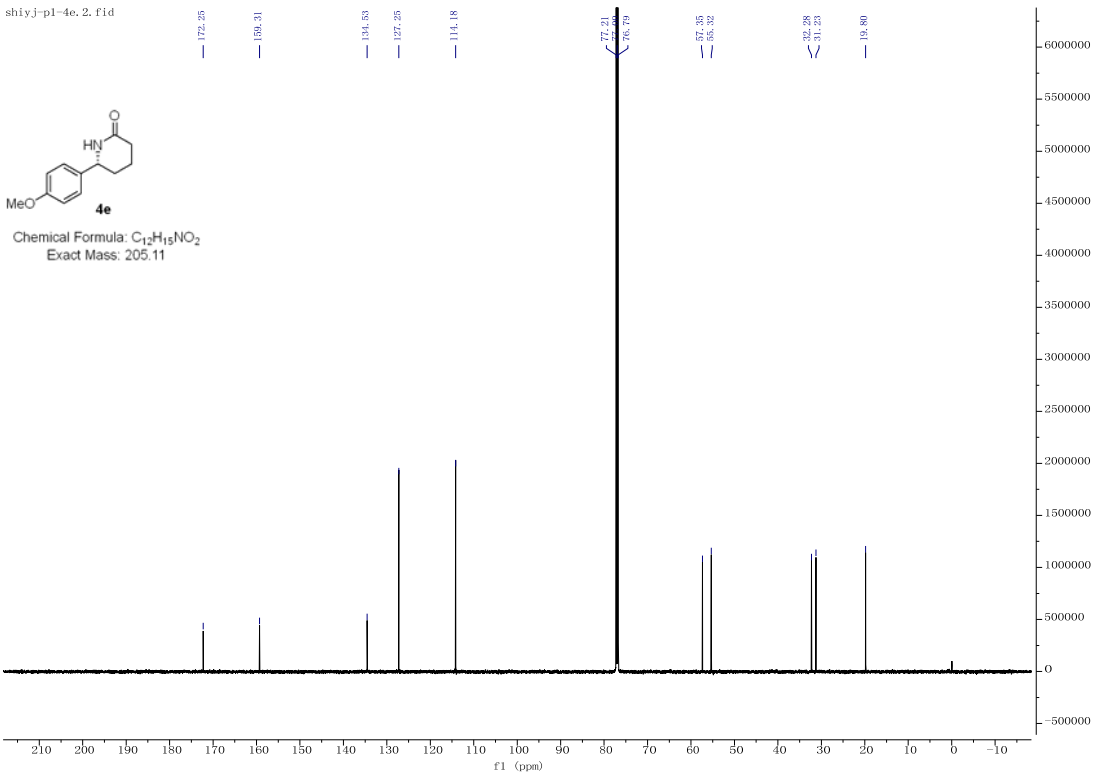
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **4d**



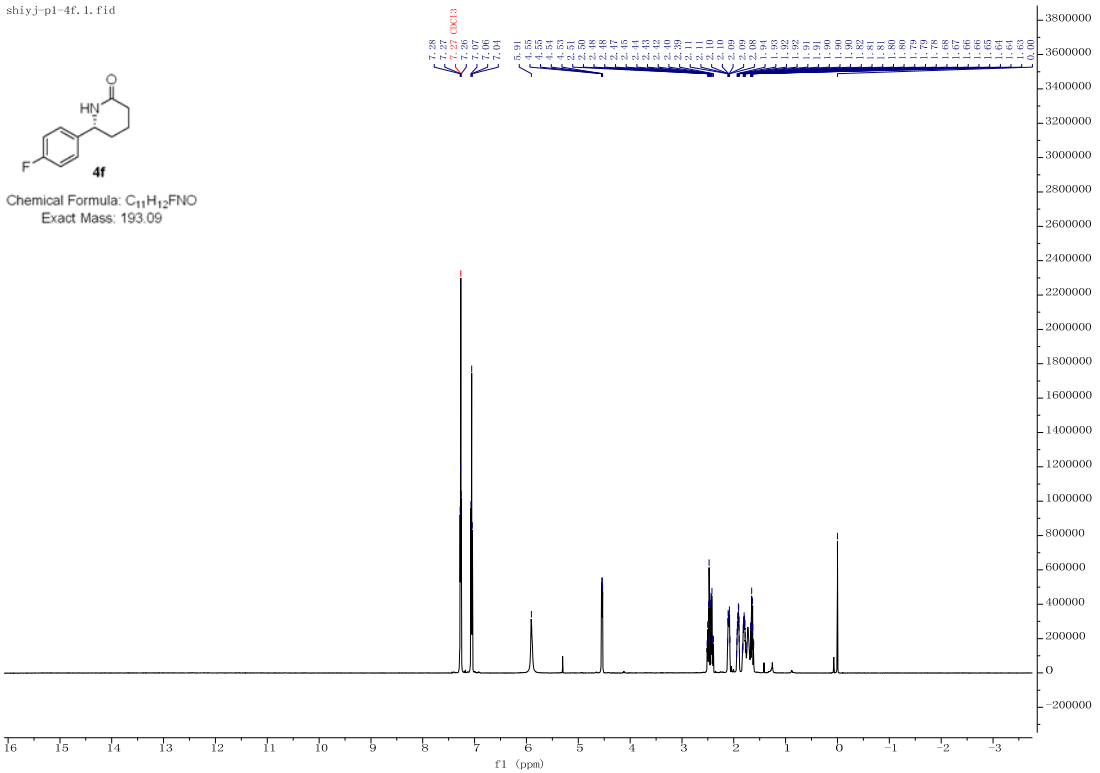
^{1}H NMR (600 MHz, Chloroform-d) of compound **4e**



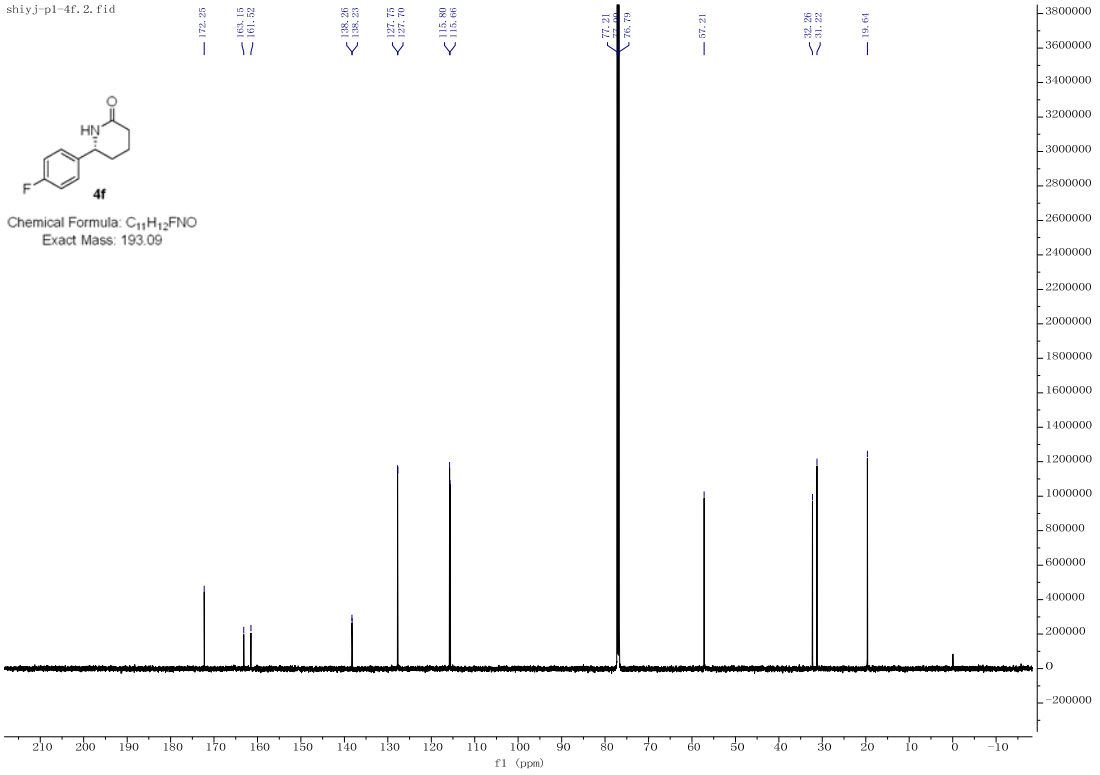
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **4e**



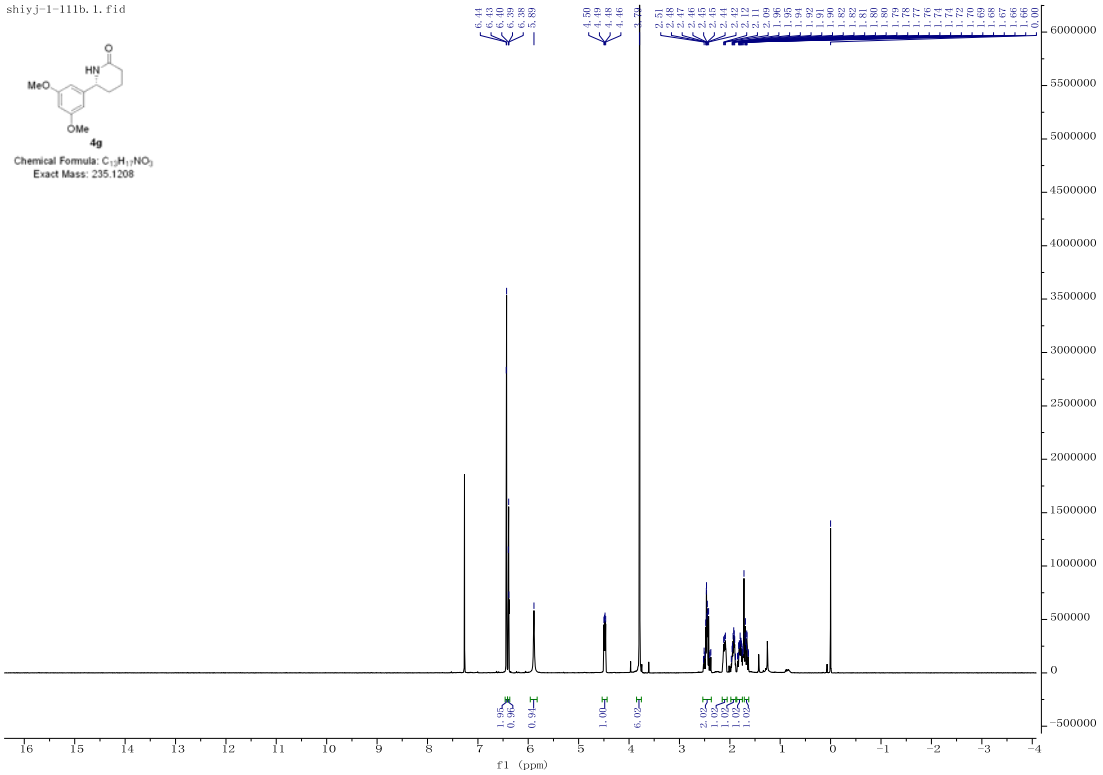
^{1}H NMR (600 MHz, Chloroform-d) of compound **4f**



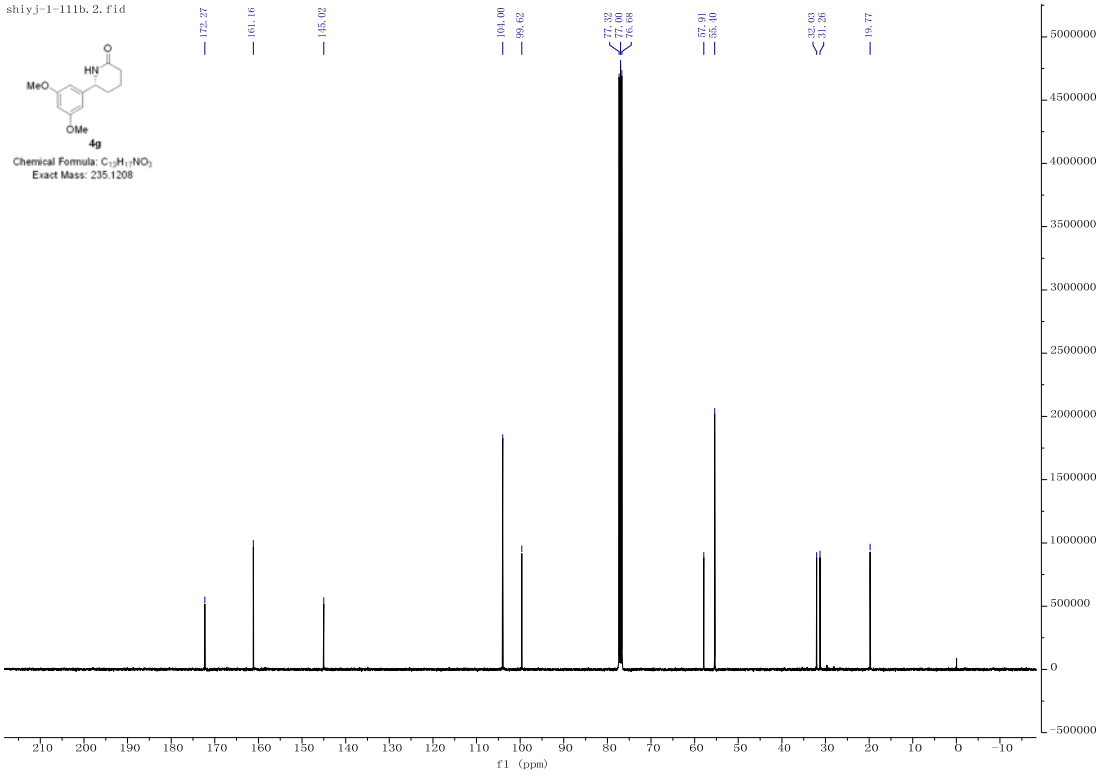
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **4f**



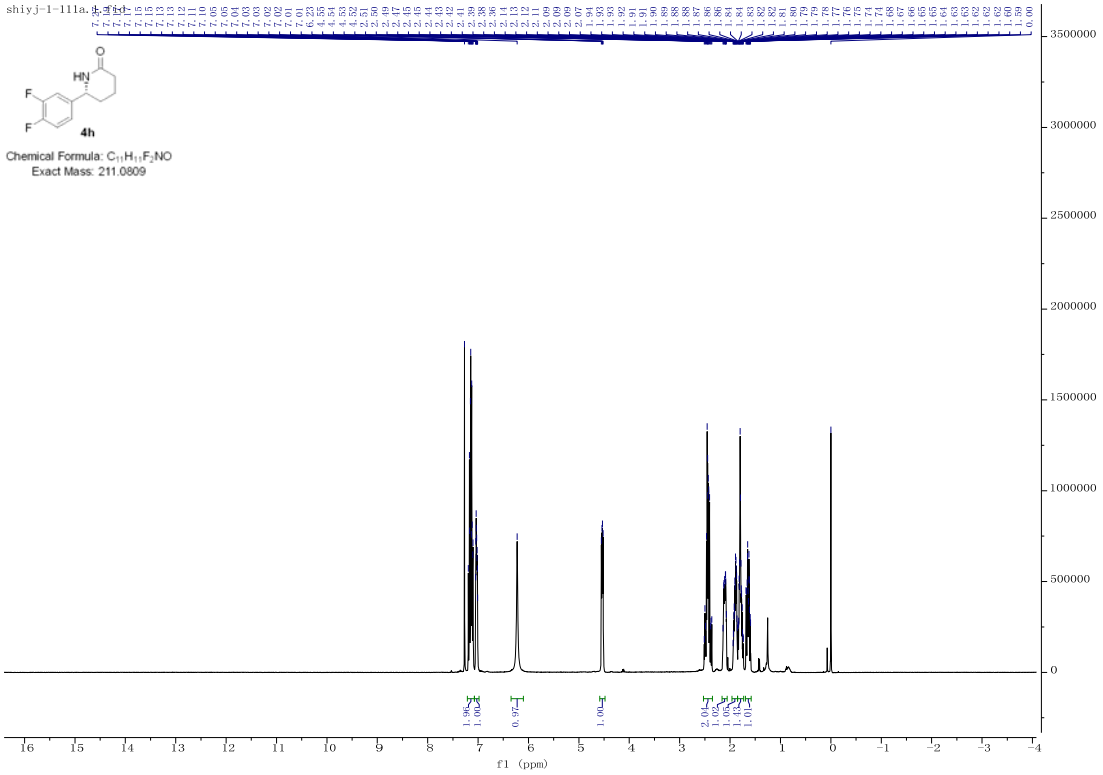
^{1}H NMR (400 MHz, Chloroform-d) of compound **4g**



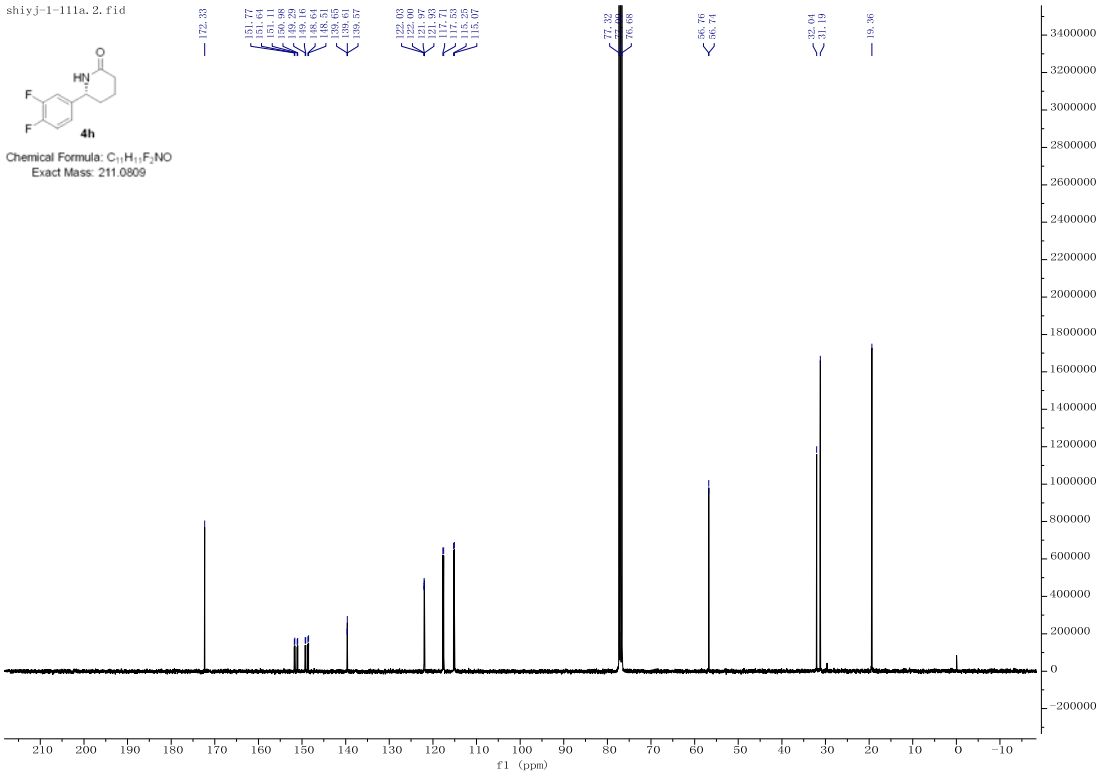
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **4g**



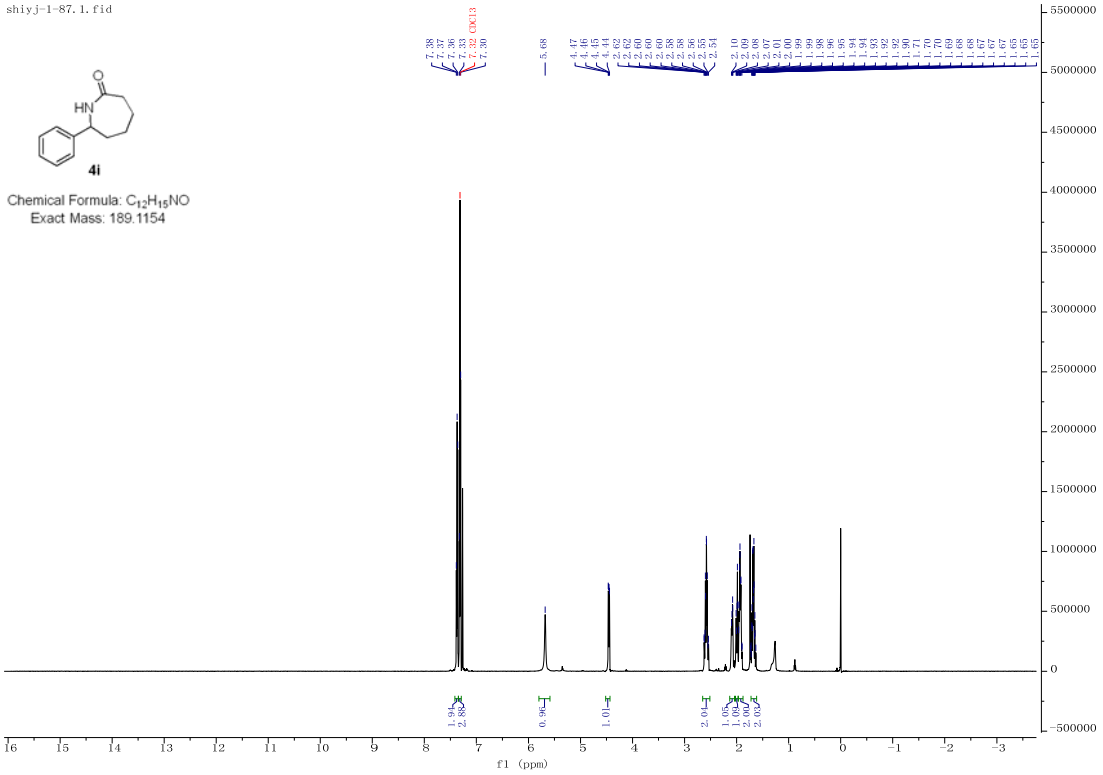
^{1}H NMR (400 MHz, Chloroform-d) of compound **4h**



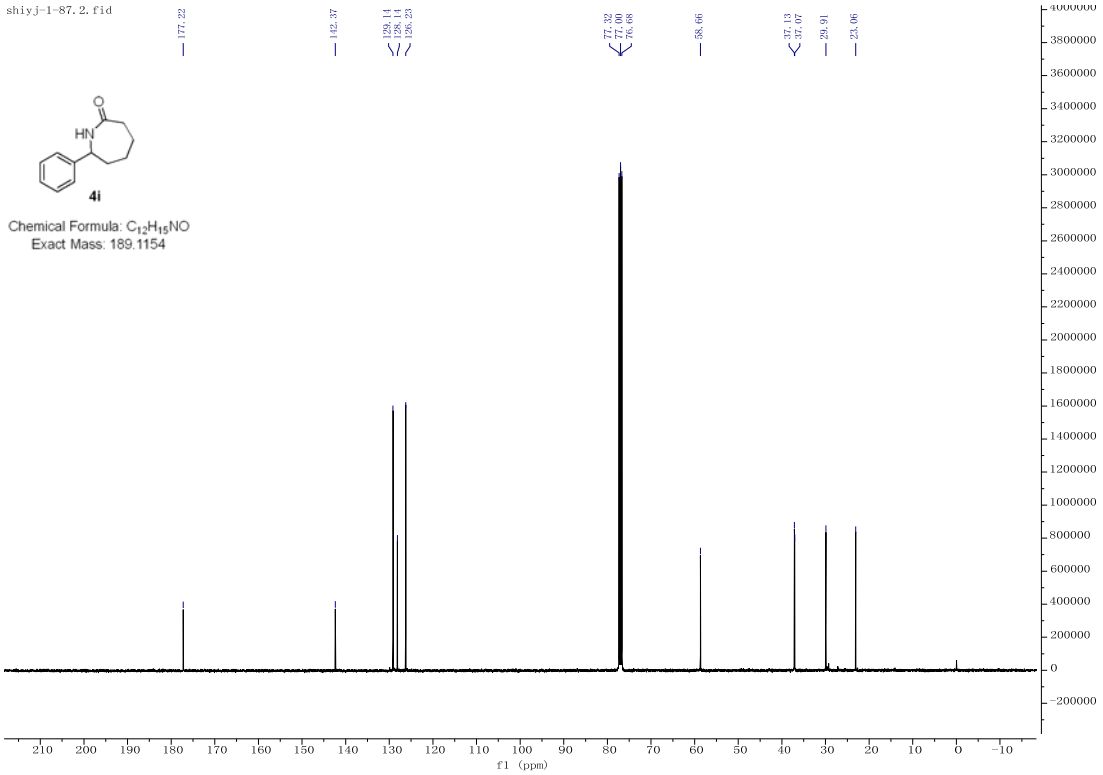
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **4f**



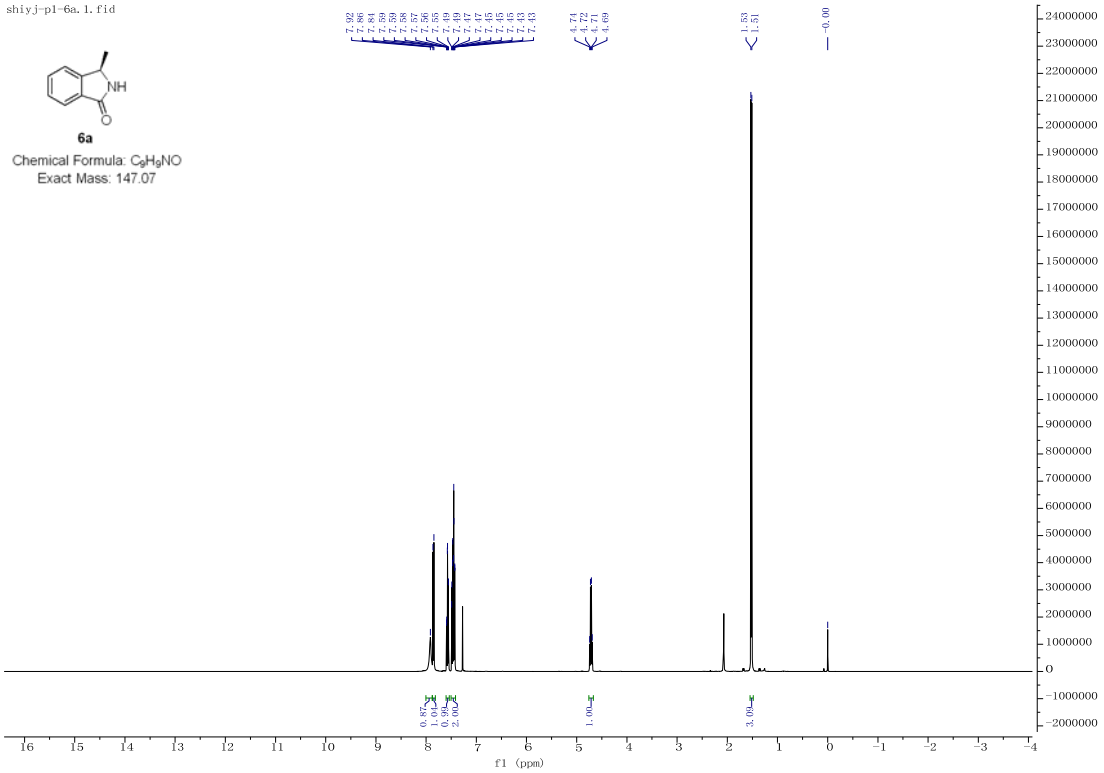
^{1}H NMR (600 MHz, Chloroform-d) of compound **4i**



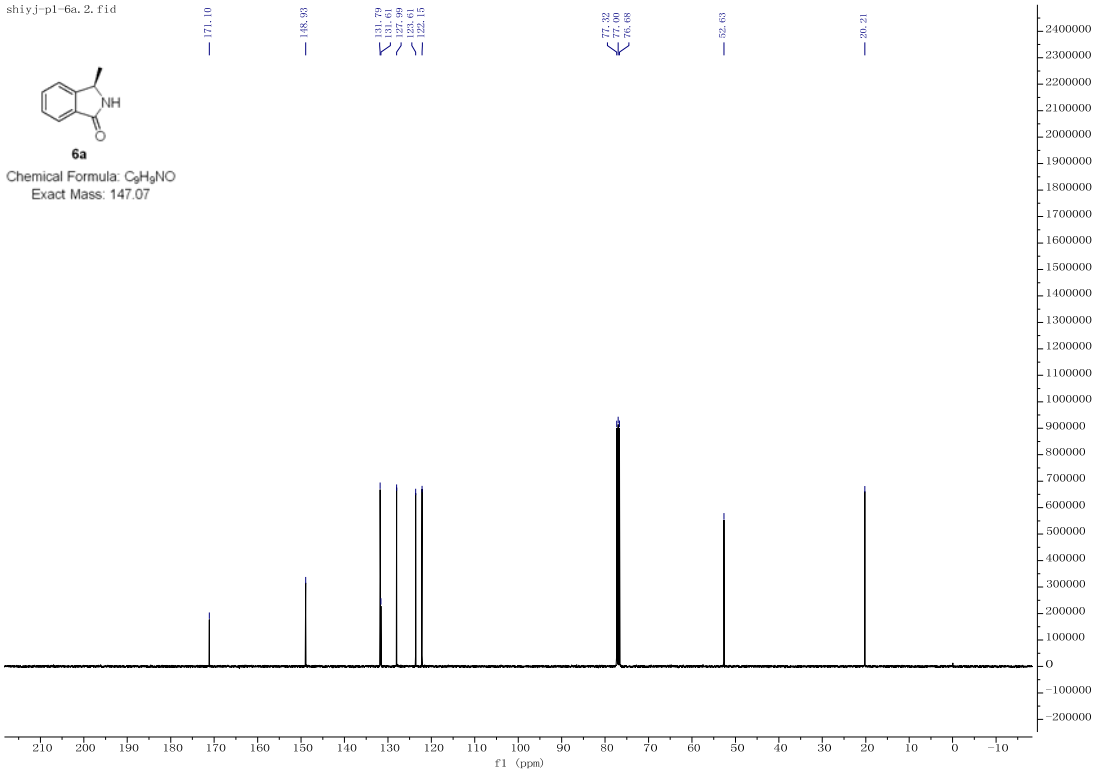
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **4i**



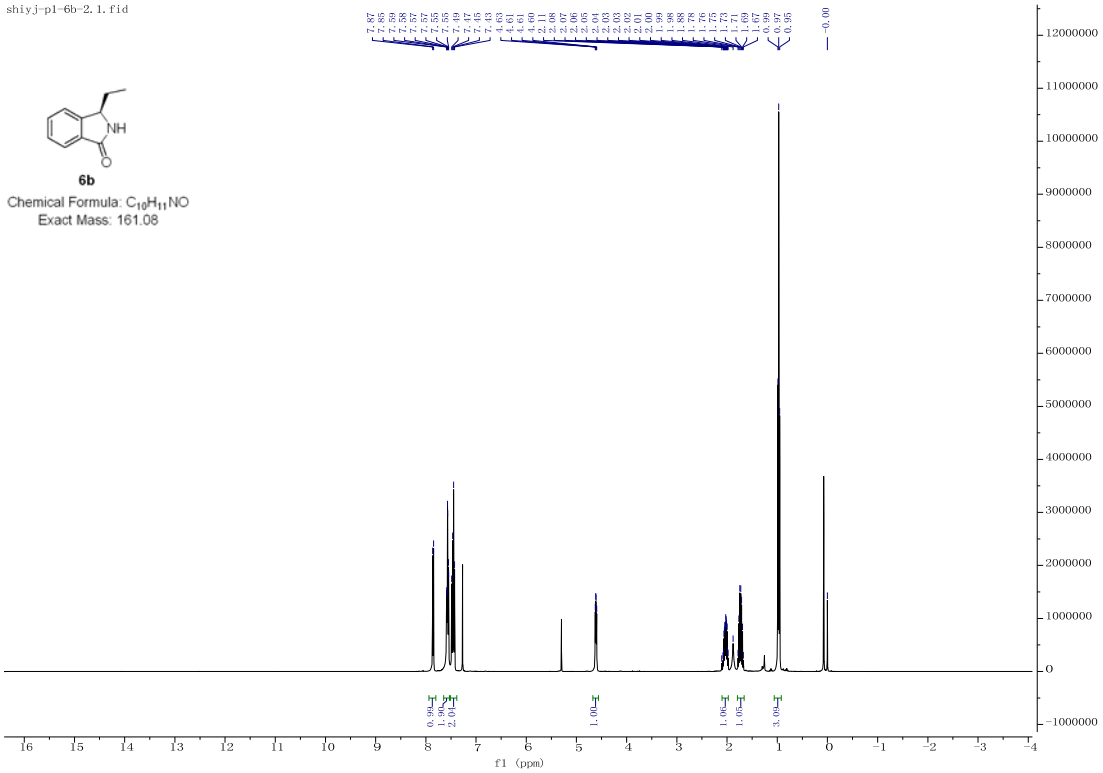
^{1}H NMR (400 MHz, Chloroform-d) of compound **6a**



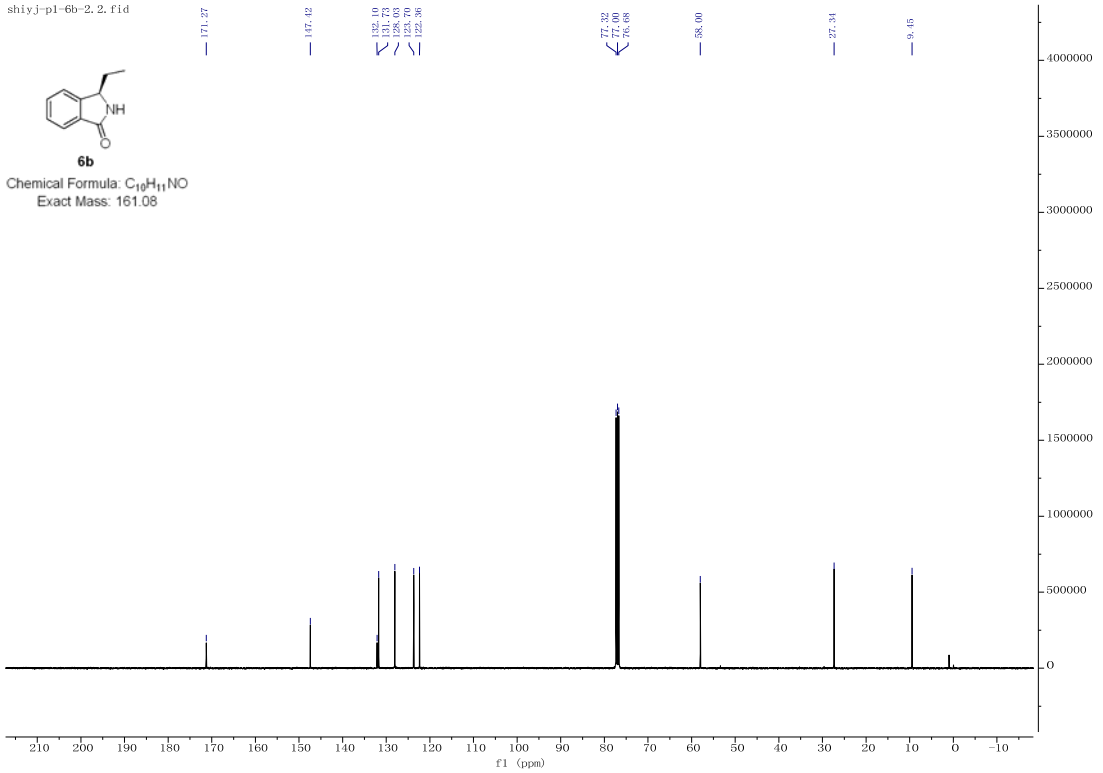
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6a**



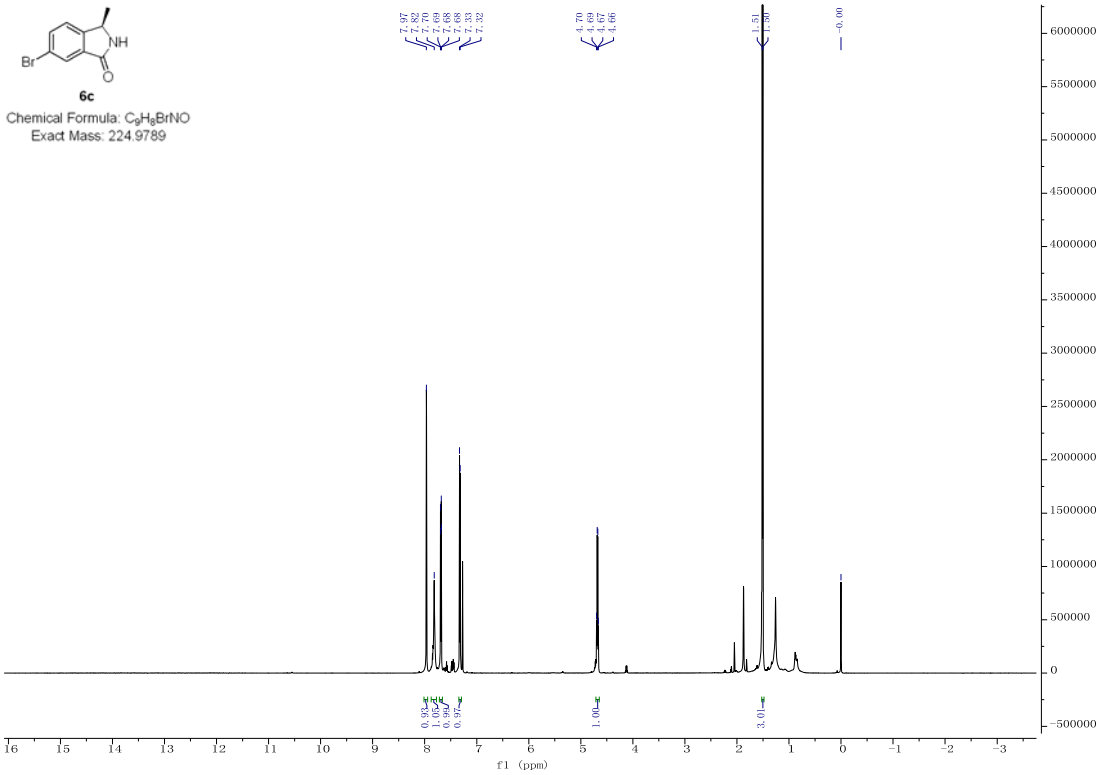
^{1}H NMR (400 MHz, Chloroform-d) of compound **6b**



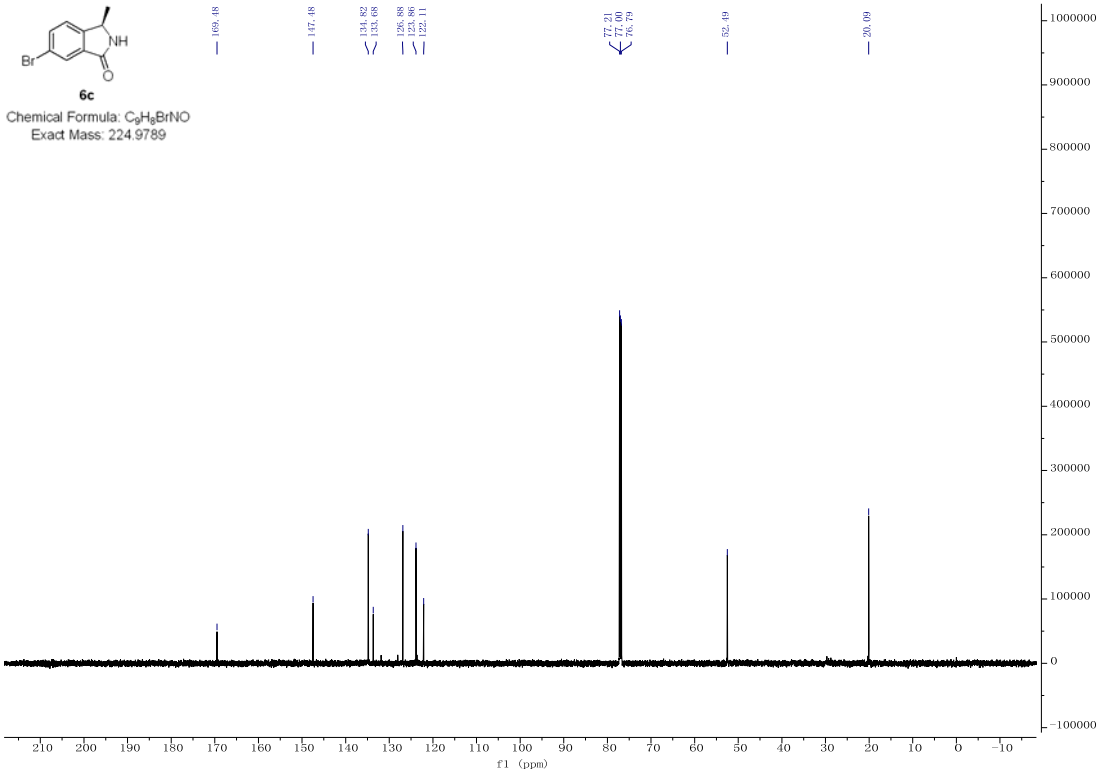
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6b**



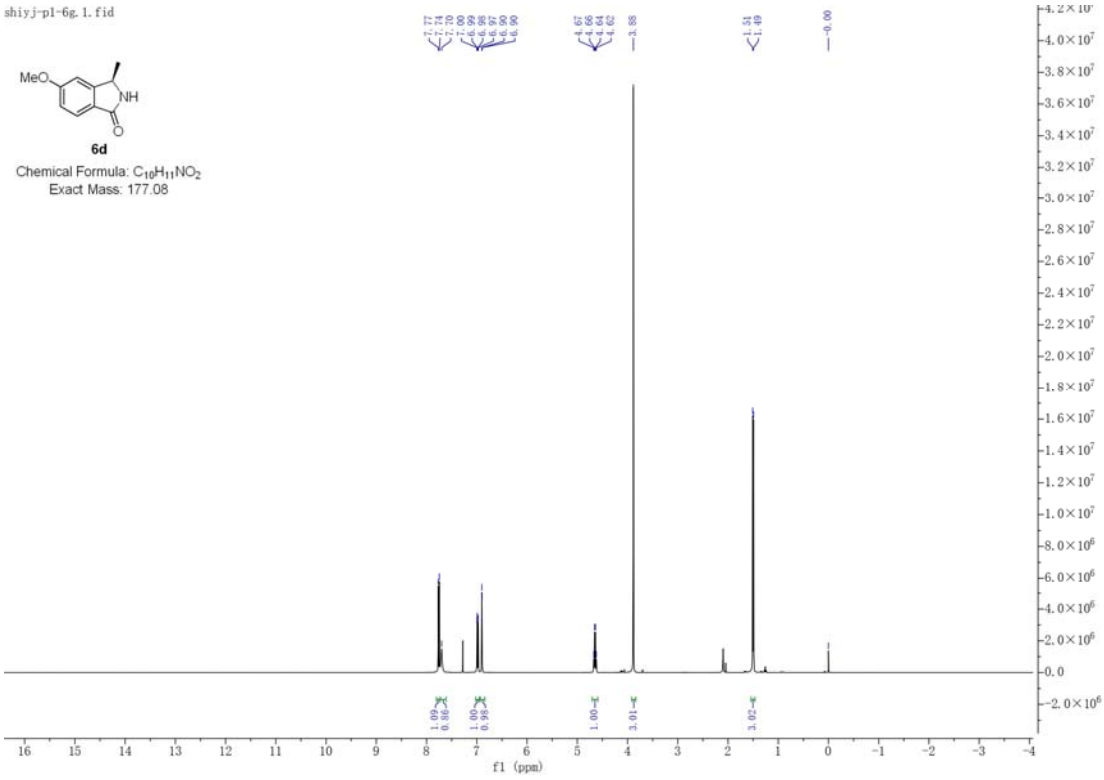
^{1}H NMR (600 MHz, Chloroform-d) of compound **6c**



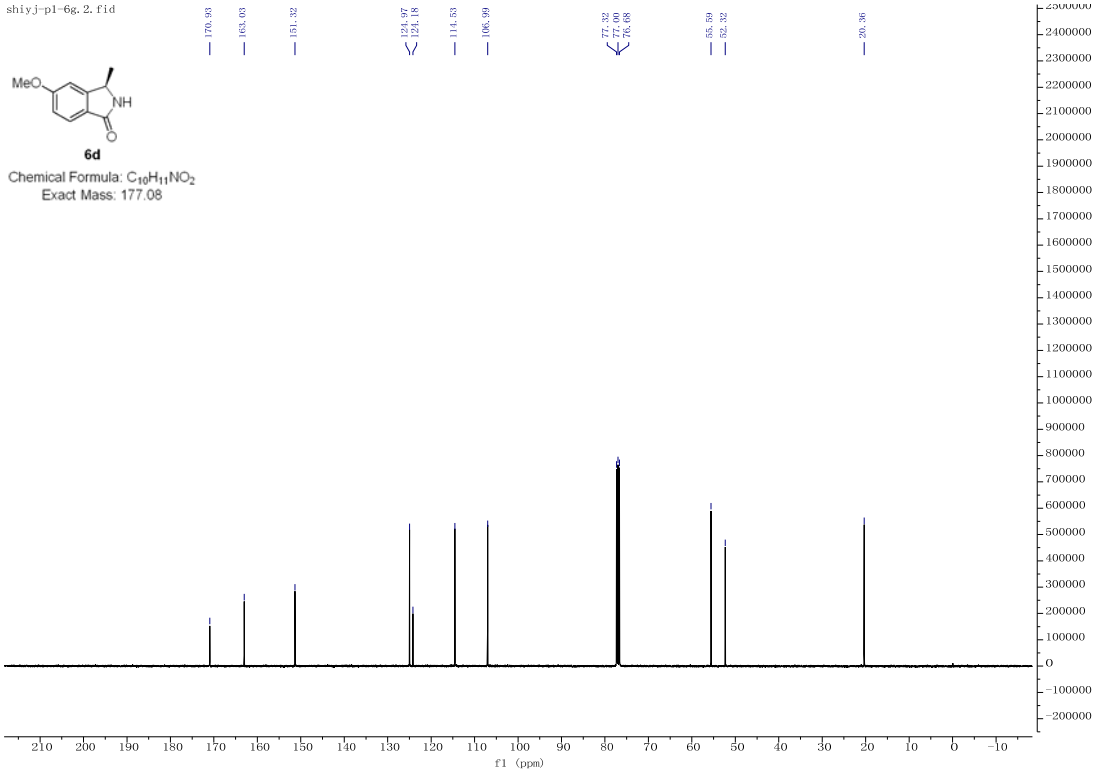
^{13}C{^{1}H} NMR (151 MHz, Chloroform-d) of compound **6c**



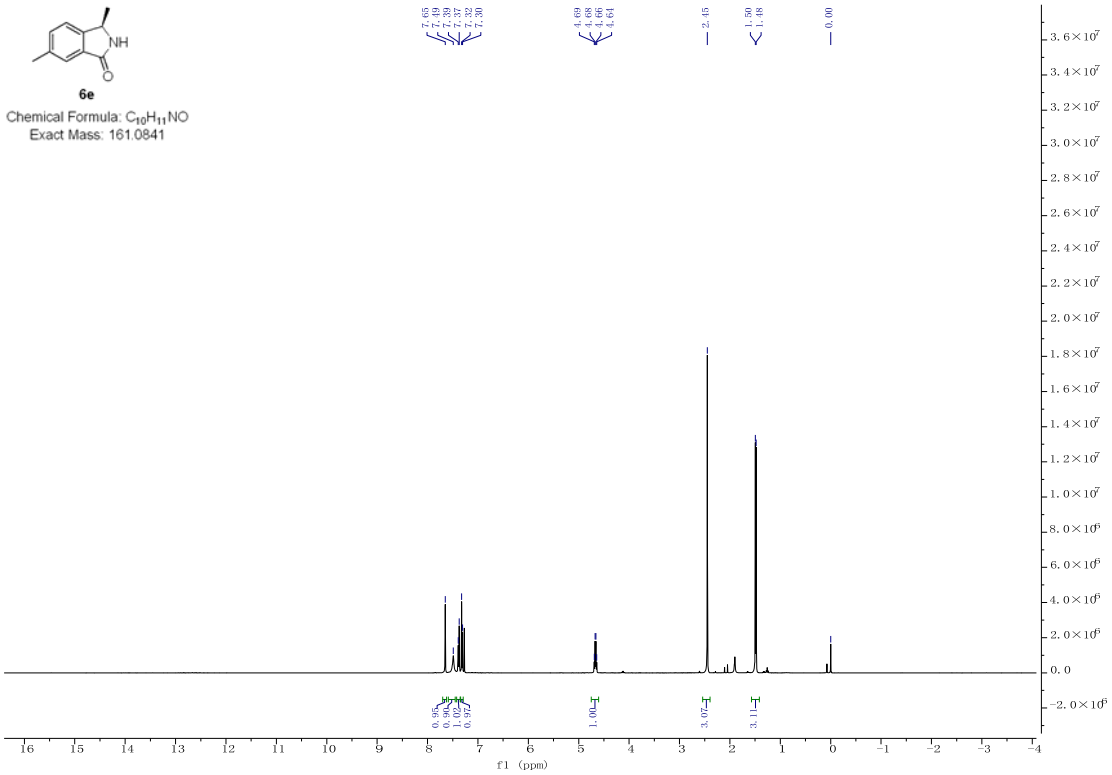
^{1}H NMR (400 MHz, Chloroform-d) of compound **6d**



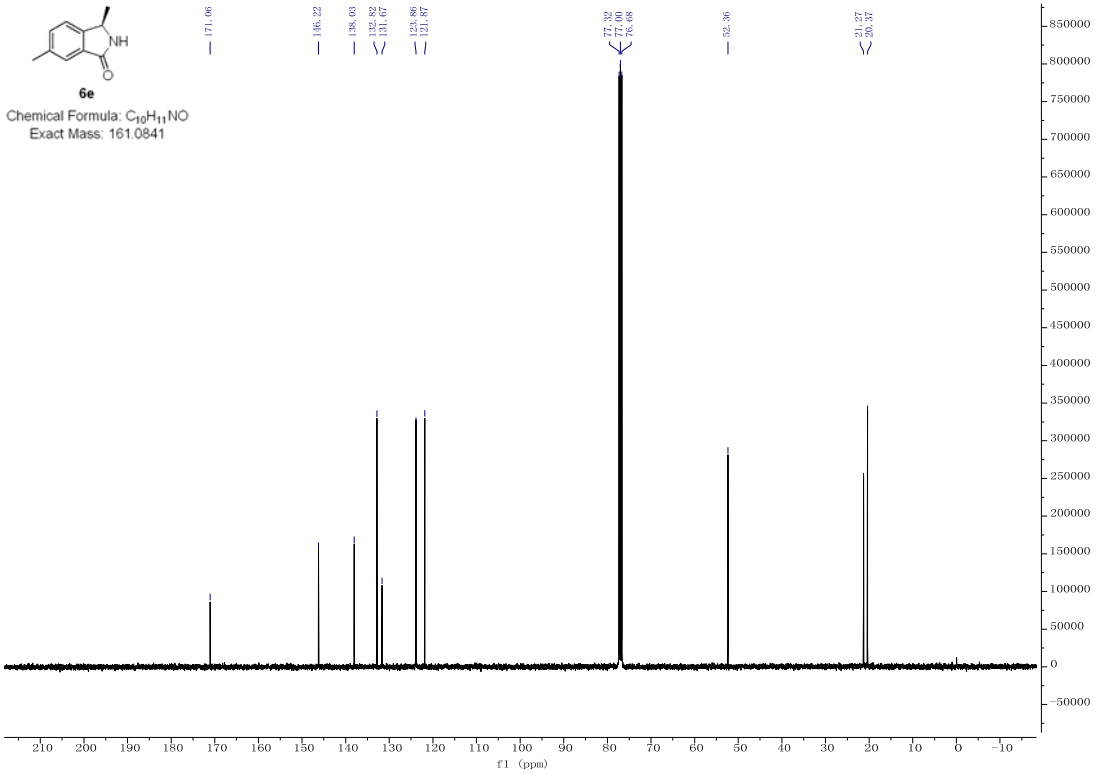
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6d**



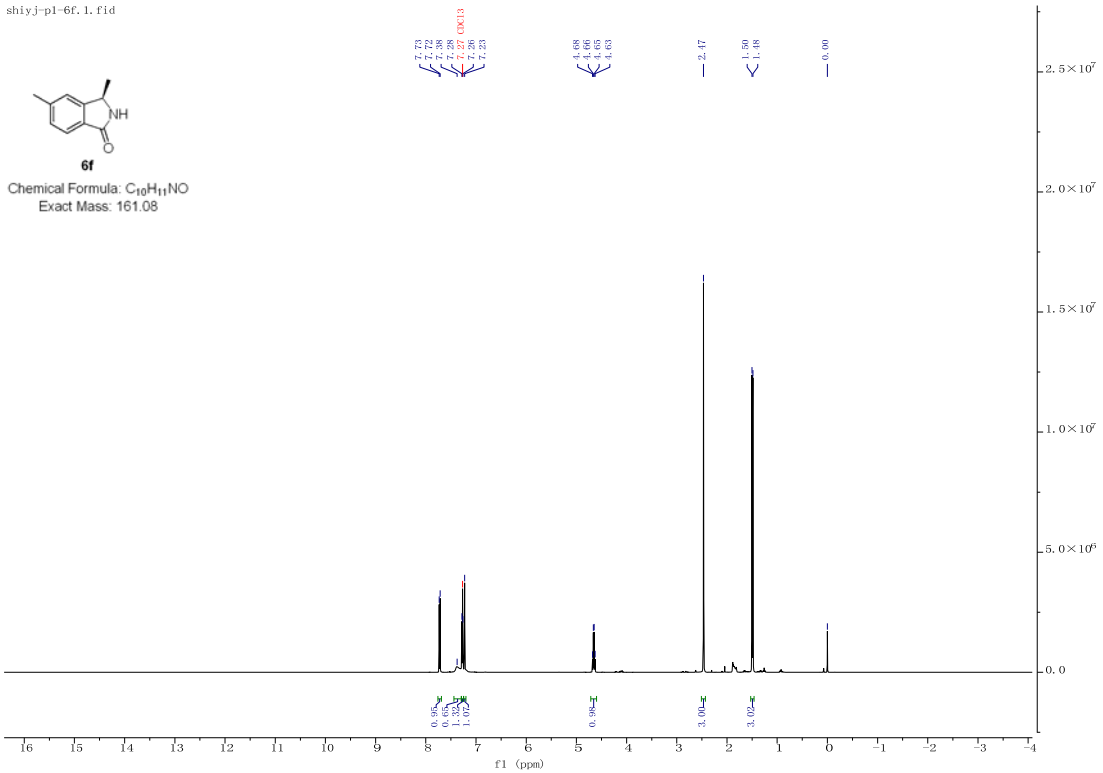
^{1}H NMR (400 MHz, Chloroform-d) of compound **6e**



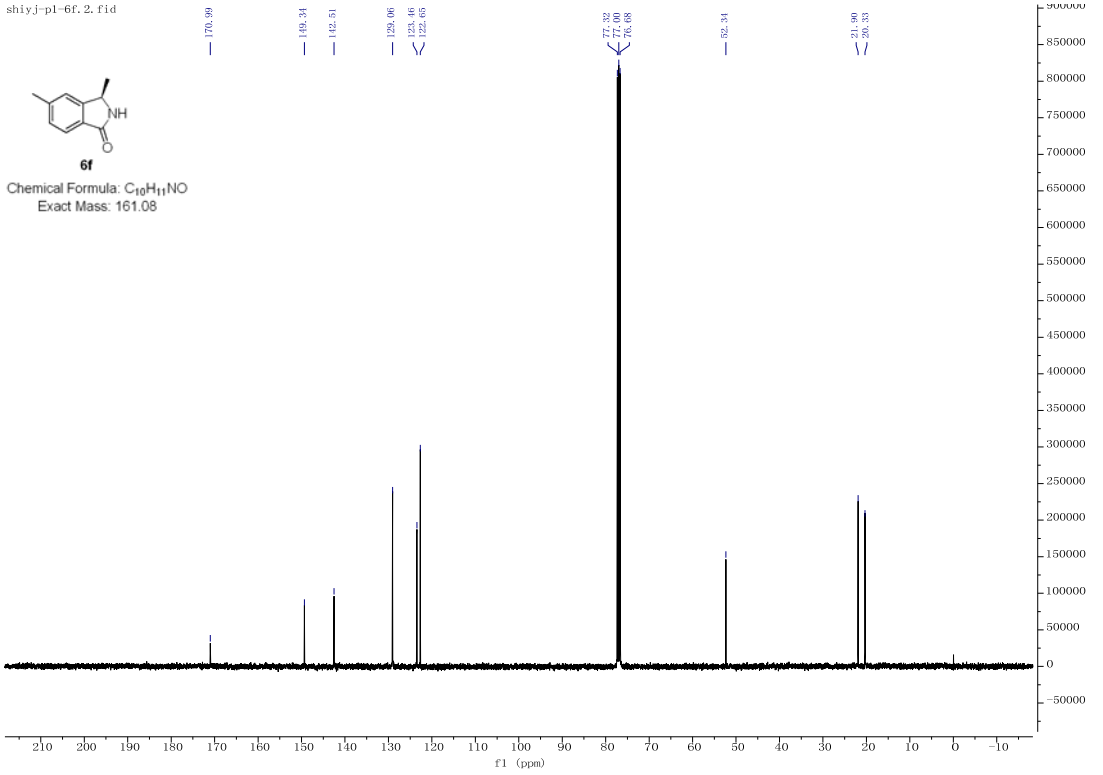
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6e**



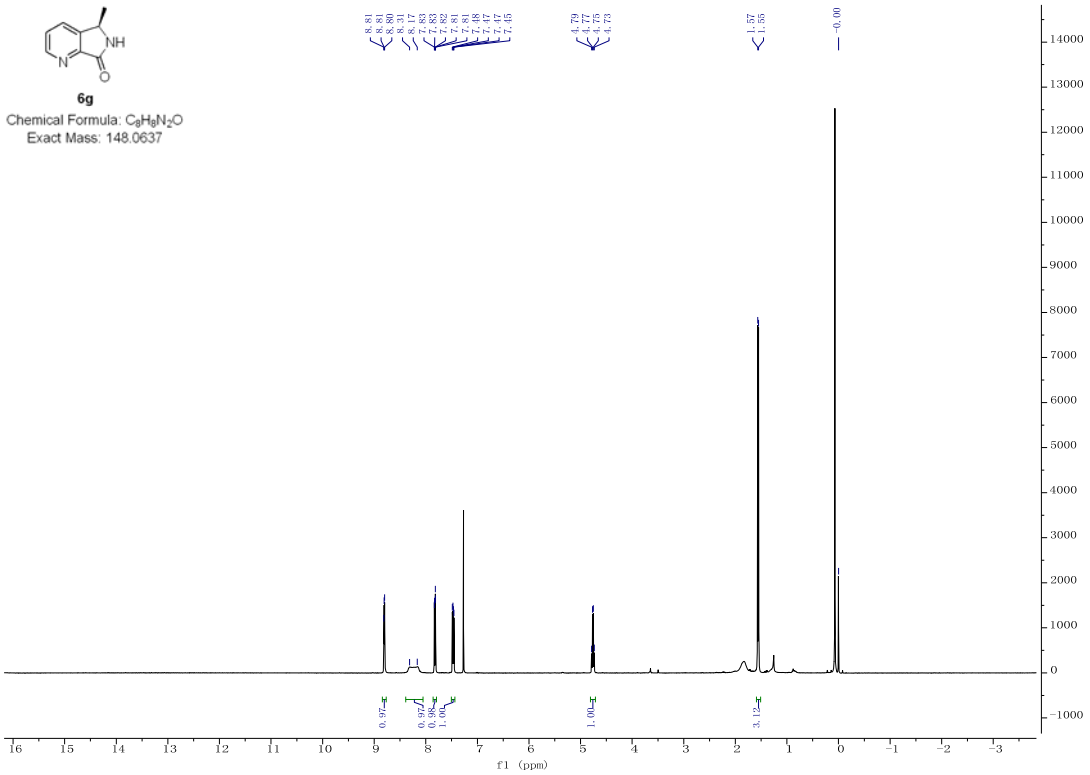
^{1}H NMR (400 MHz, Chloroform-d) of compound **6f**



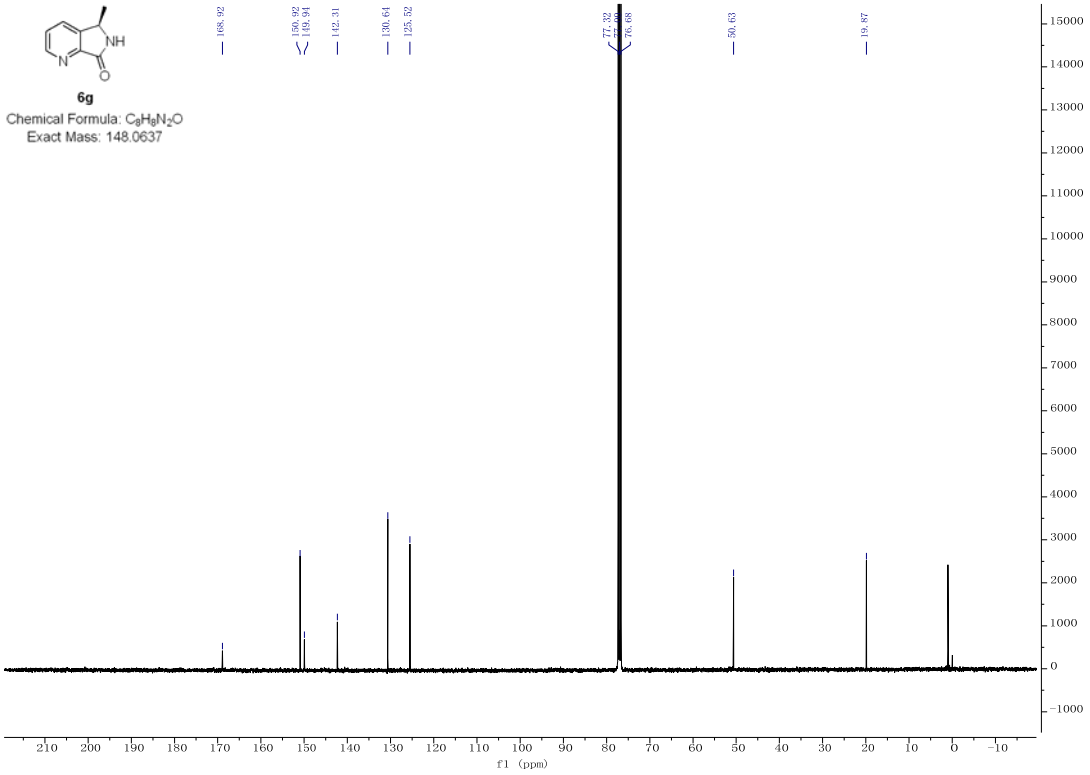
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6f**



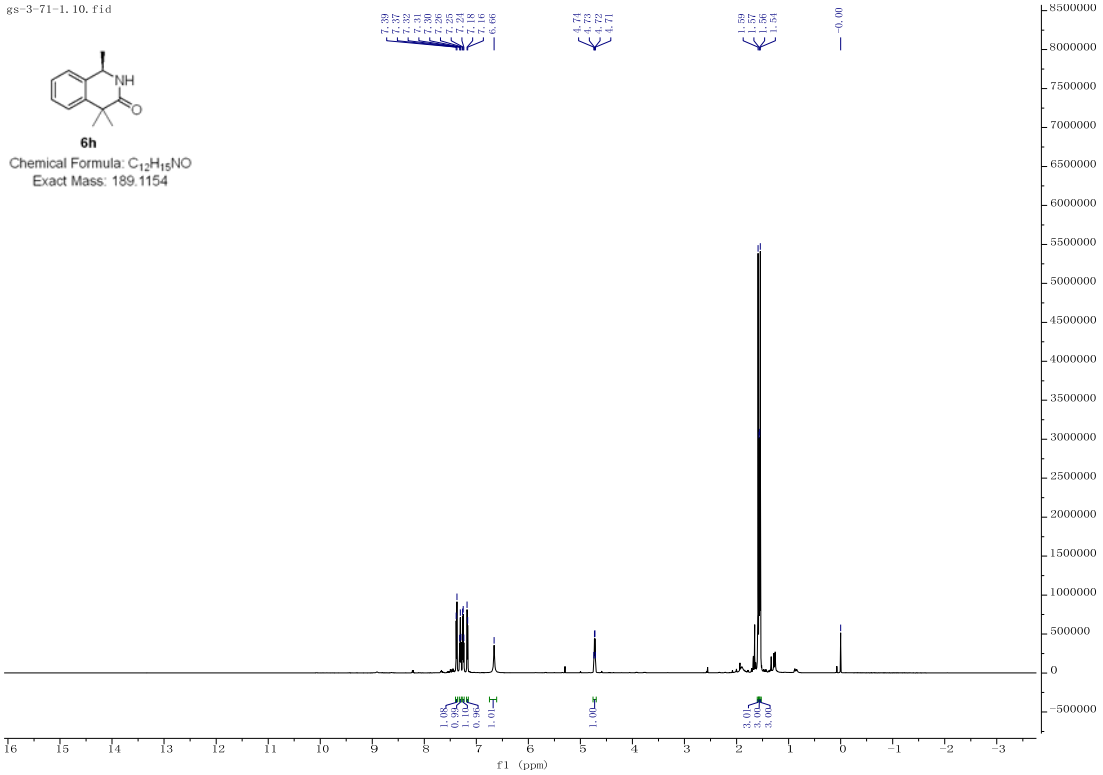
^{1}H NMR (400 MHz, Chloroform-d) of compound **6g**



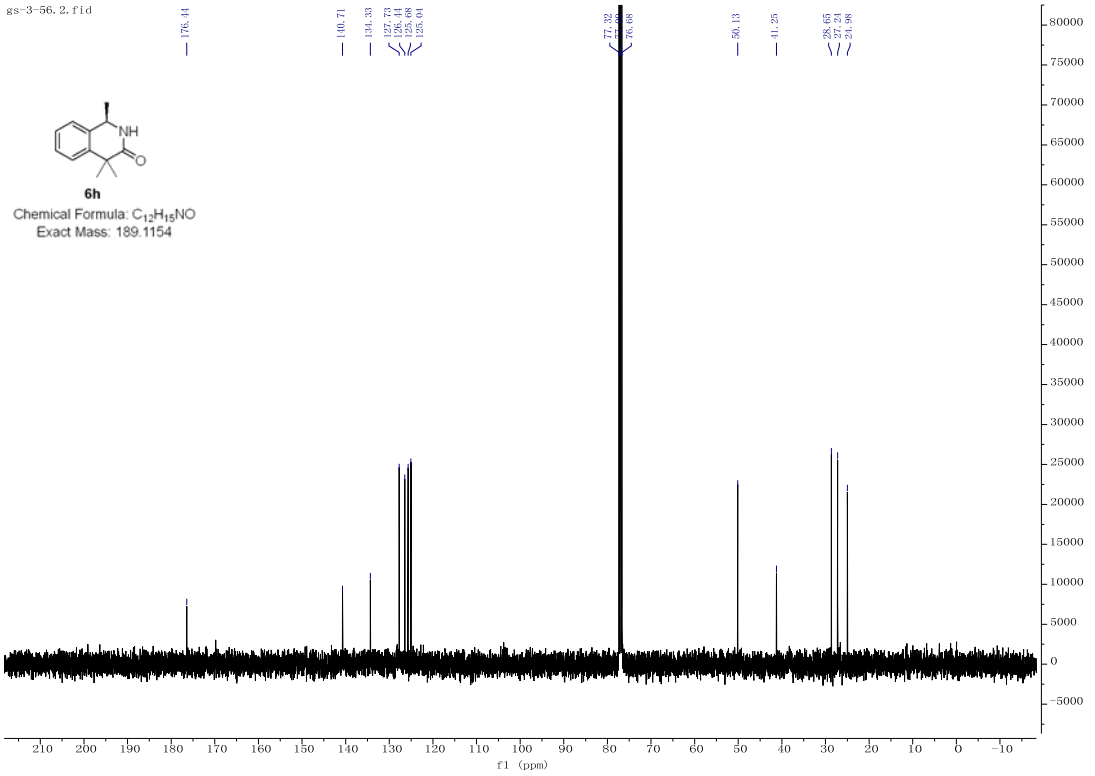
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6g**



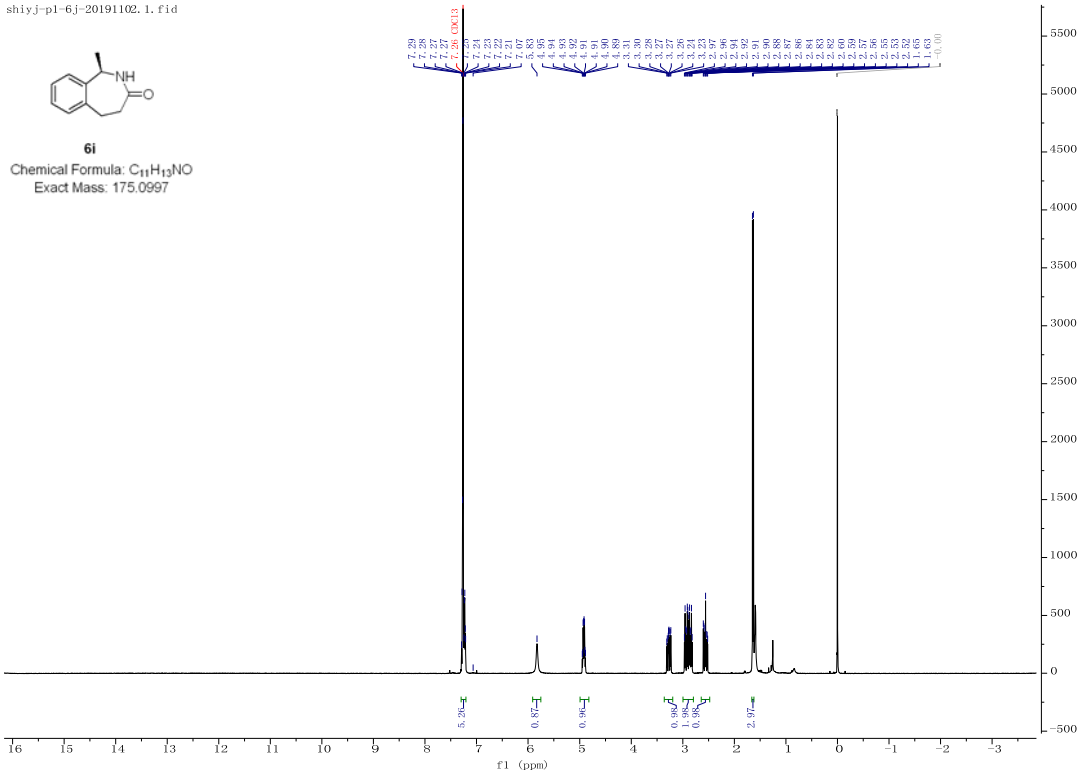
^{1}H NMR (600 MHz, Chloroform-d) of compound **6h**



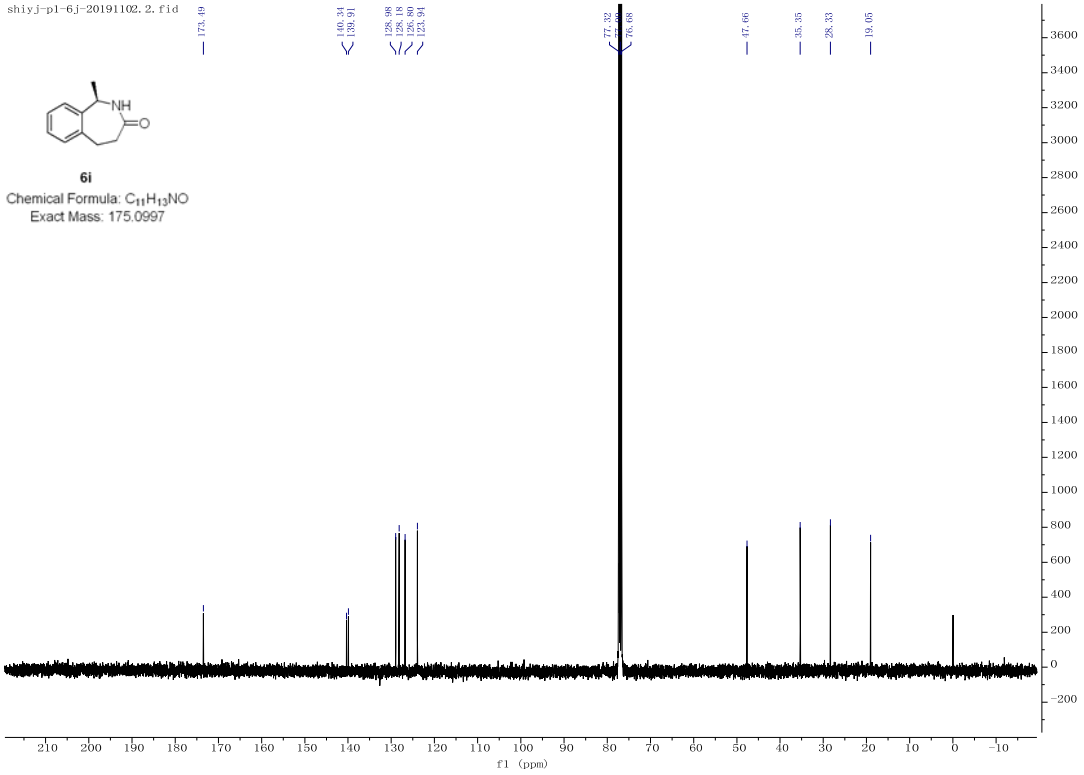
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6h**



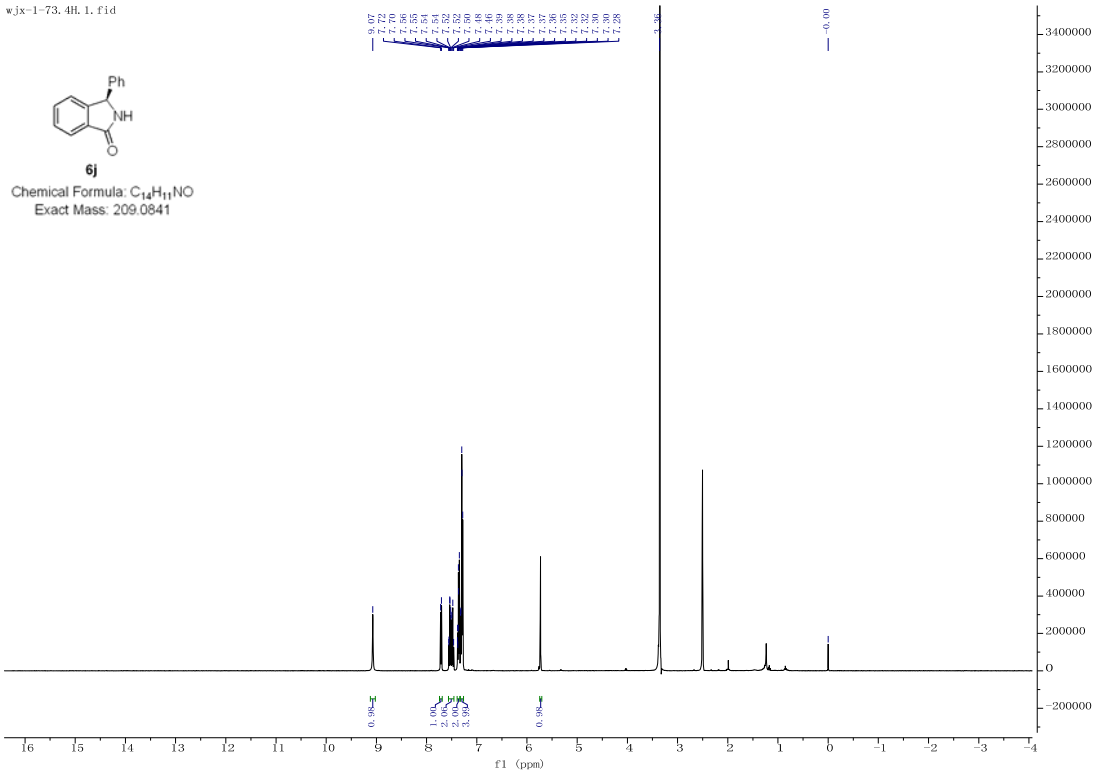
^{1}H NMR (400 MHz, Chloroform-d) of compound **6i**



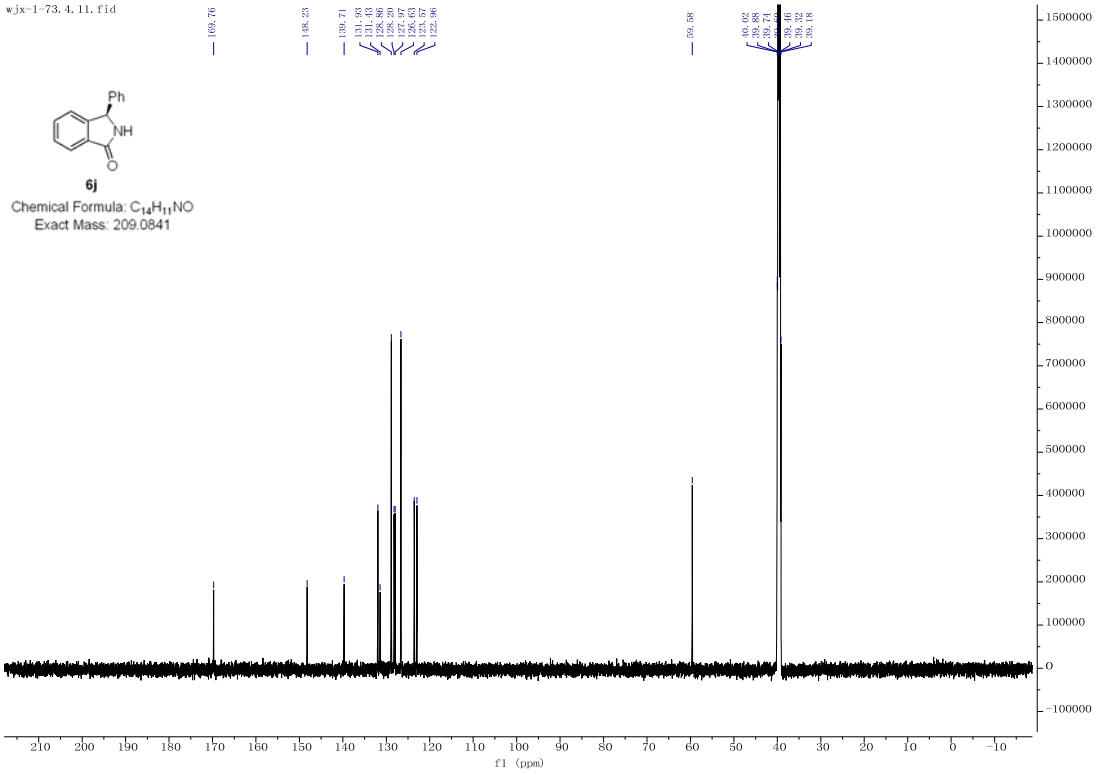
^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **6i**



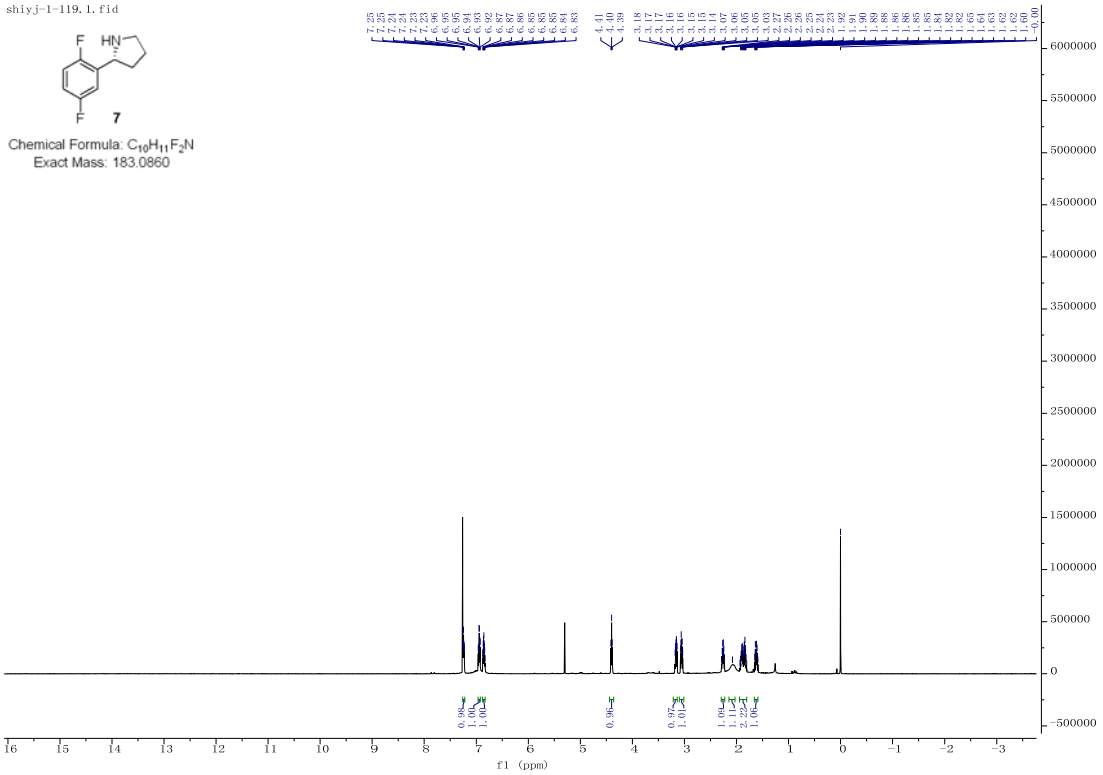
^{1}H NMR (400 MHz, DMSO-d$_6$) of compound **6j**



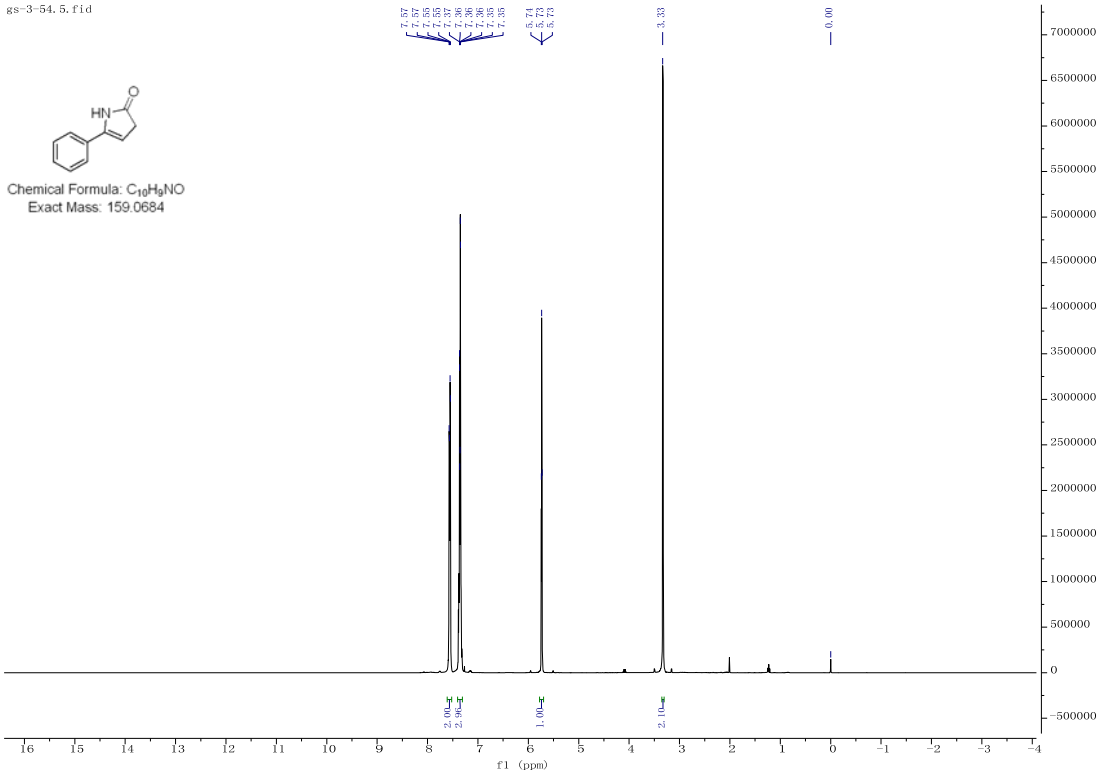
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$) of compound **6j**



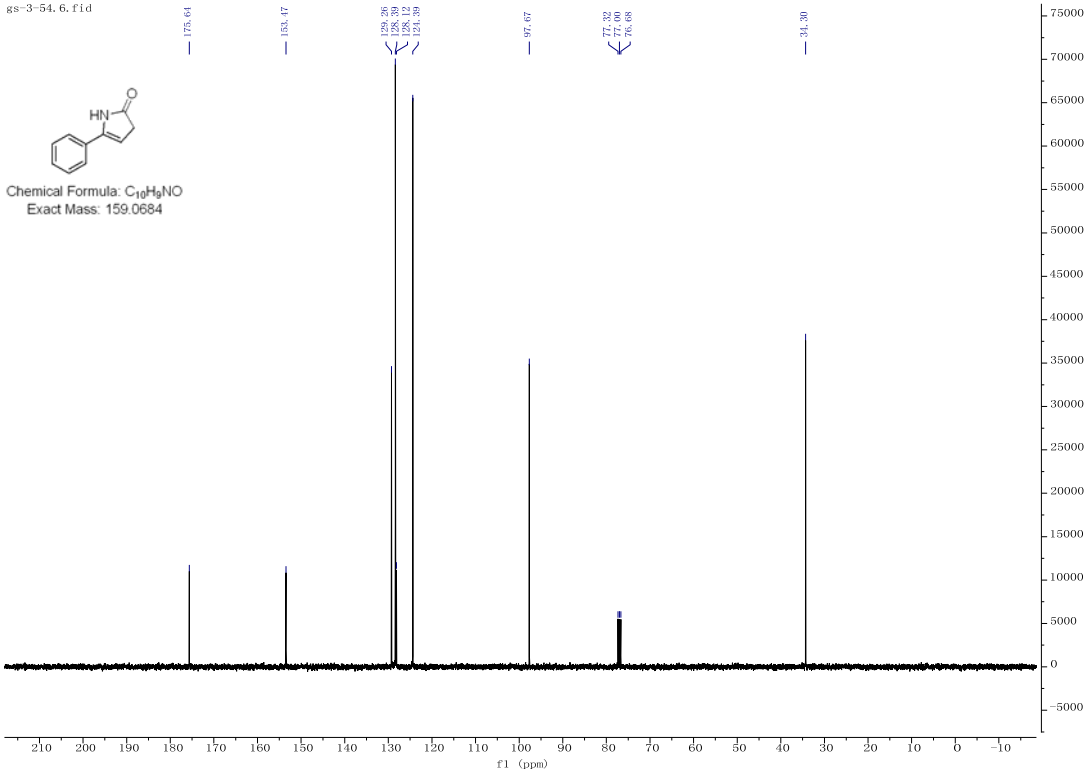
^{1}H NMR (600 MHz, Chloroform-d) of compound **7**



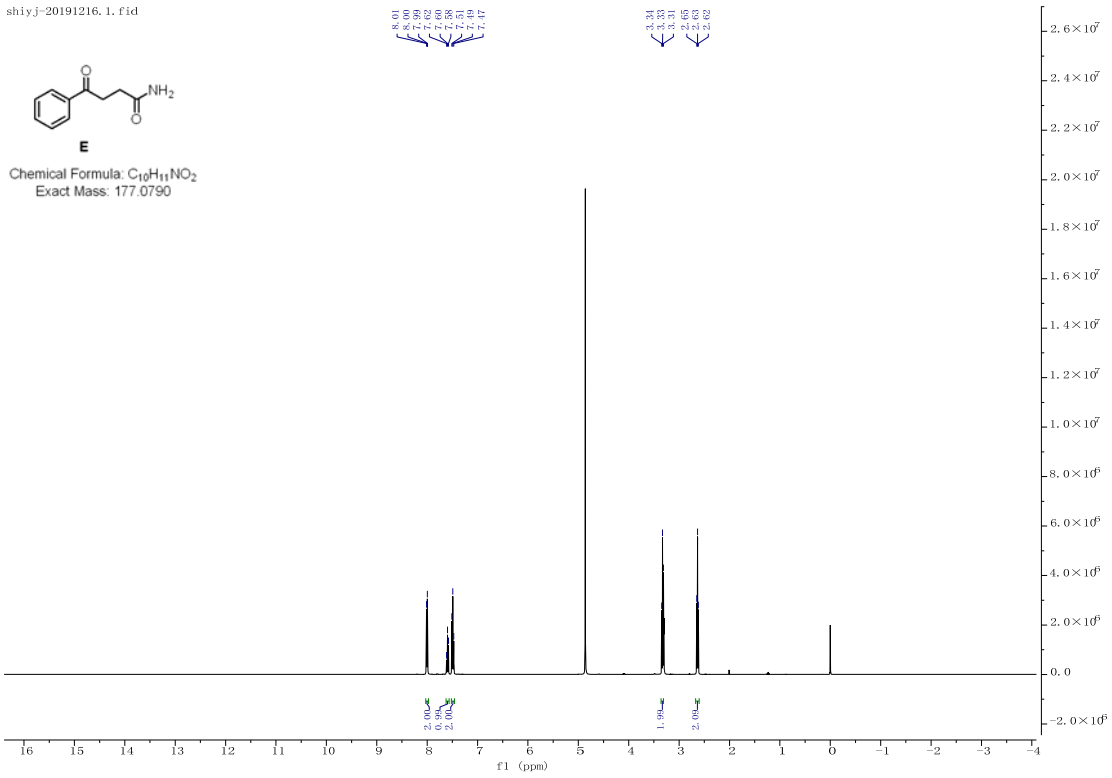
^{1}H NMR (400 MHz, Chloroform-d) of compound **C**



^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) of compound **C**

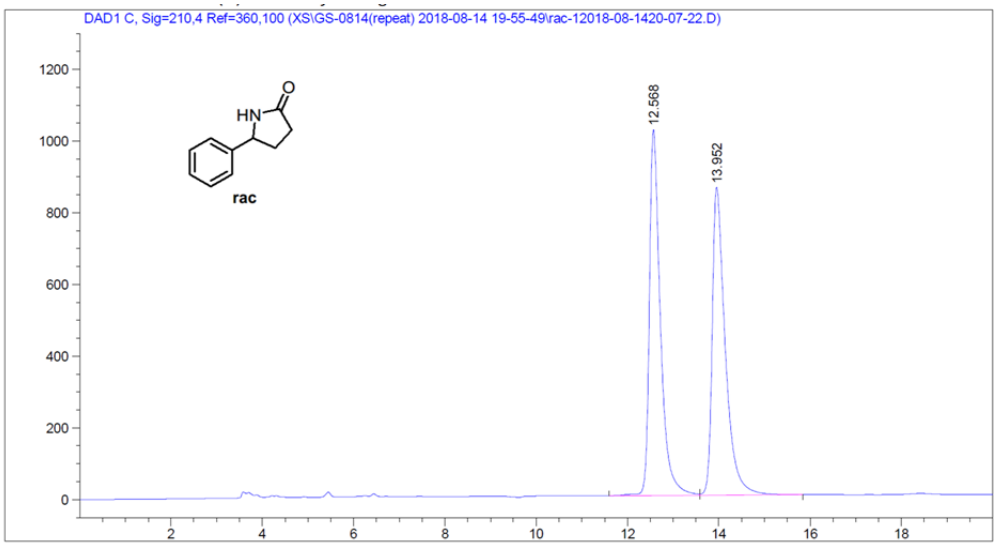


^{1}H NMR (400 MHz, Methanol-d) of compound **E**



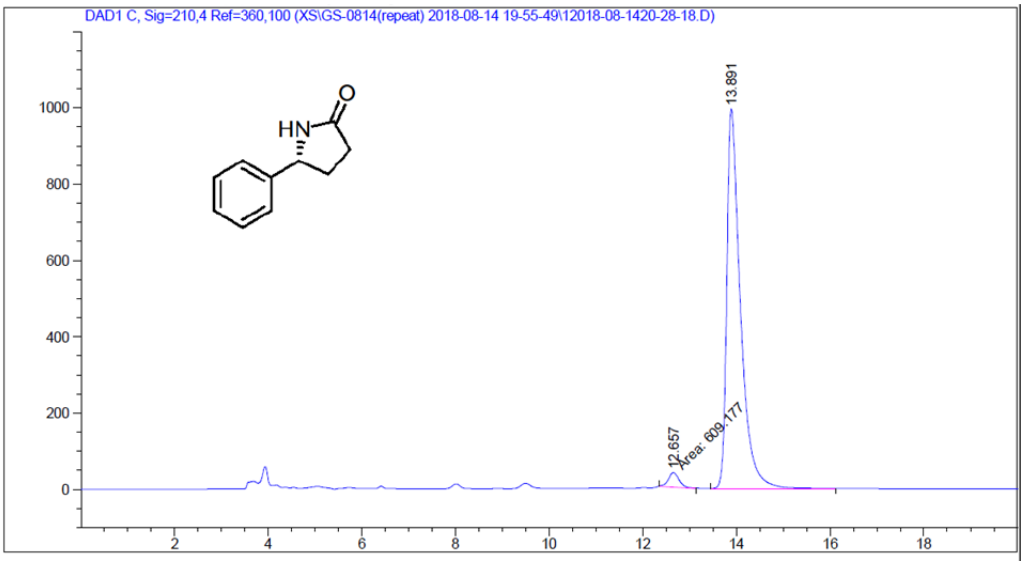
Ⅷ. HPLC Spectra

(*R*)-5-phenylpyrrolidin-2-one (2a)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

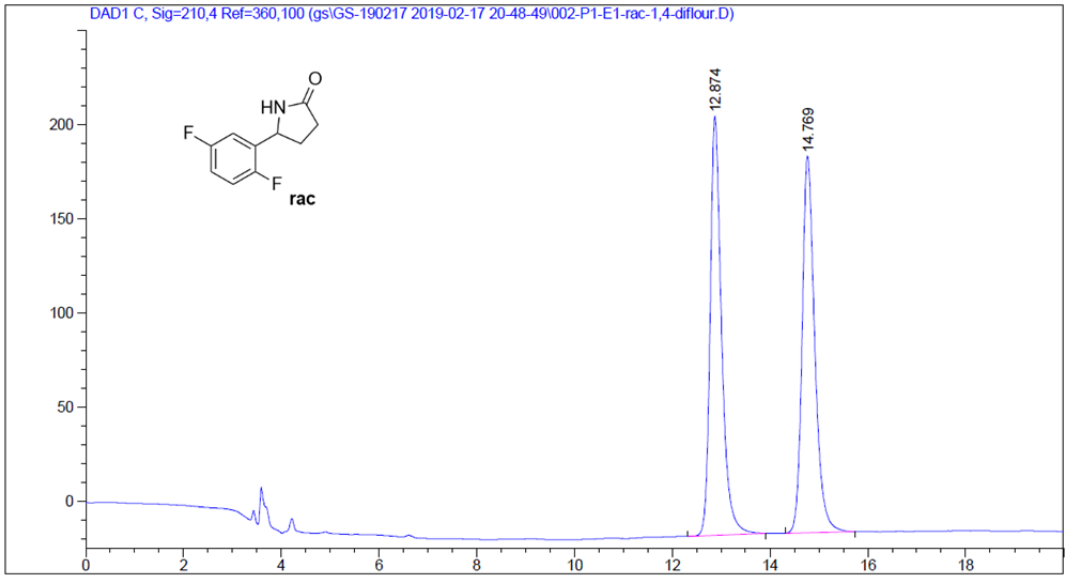
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.568	BV	0.2474	1.70773e4	1019.60889	50.0872
2	13.952	VB	0.2913	1.70178e4	858.22931	49.9128



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

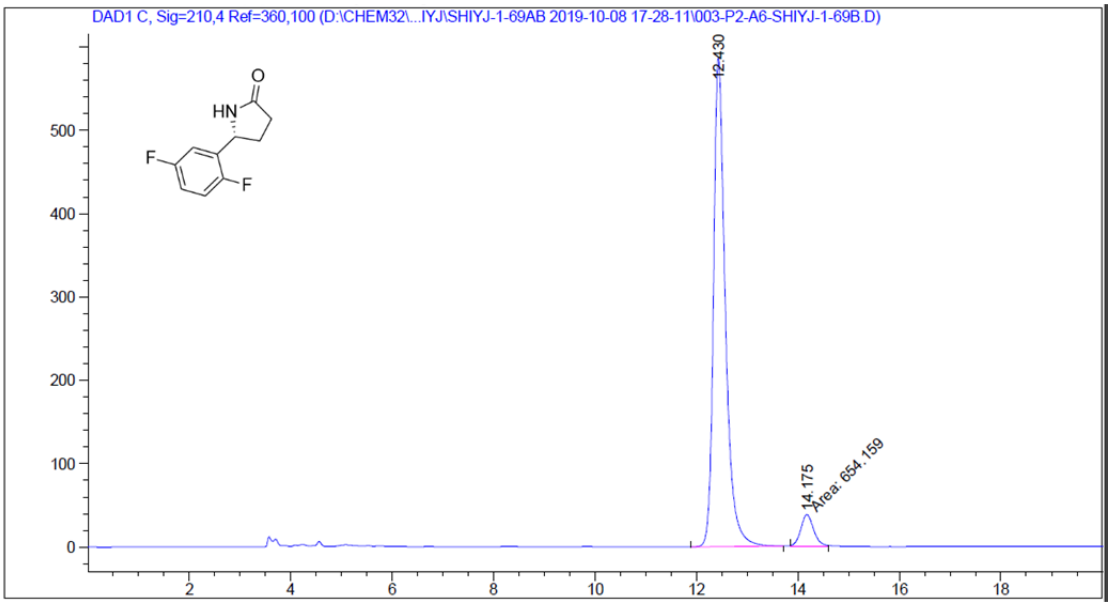
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.657	MM	0.2659	609.17657	38.18148	2.9473
2	13.891	BB	0.2952	2.00597e4	994.82056	97.0527

(*R*)-5-(2,5-difluorophenyl)pyrrolidin-2-one (2b)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

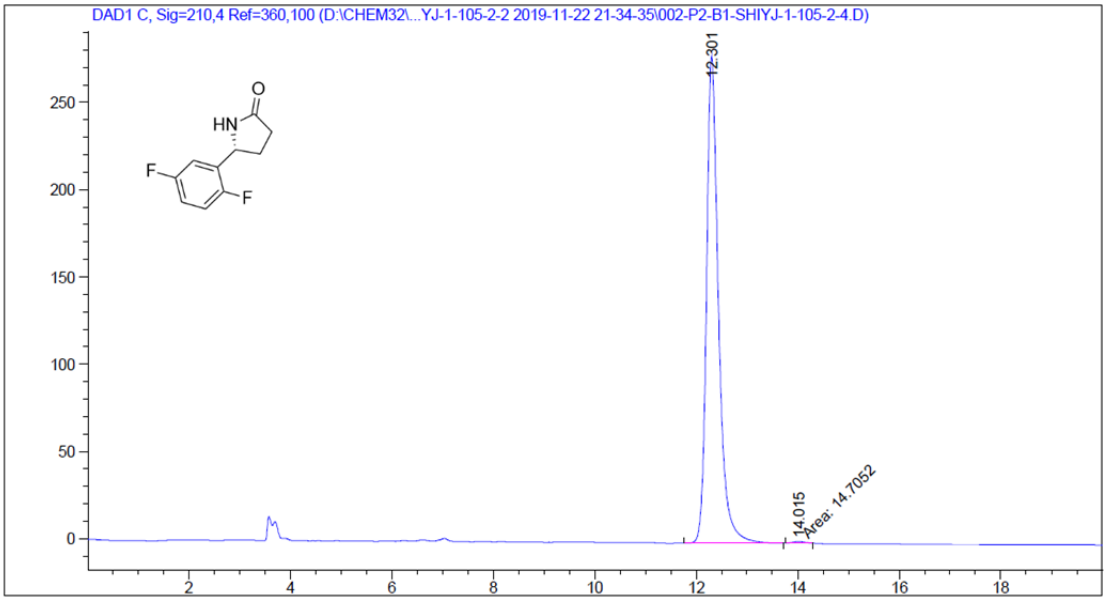
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.874	BB	0.2429	3599.99316	222.31839	50.0929
2	14.769	BB	0.2693	3586.63940	199.96323	49.9071



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.430	BB	0.2408	9486.34668	586.05933	93.5491
2	14.175	MM	0.2894	654.15881	37.67200	6.4509

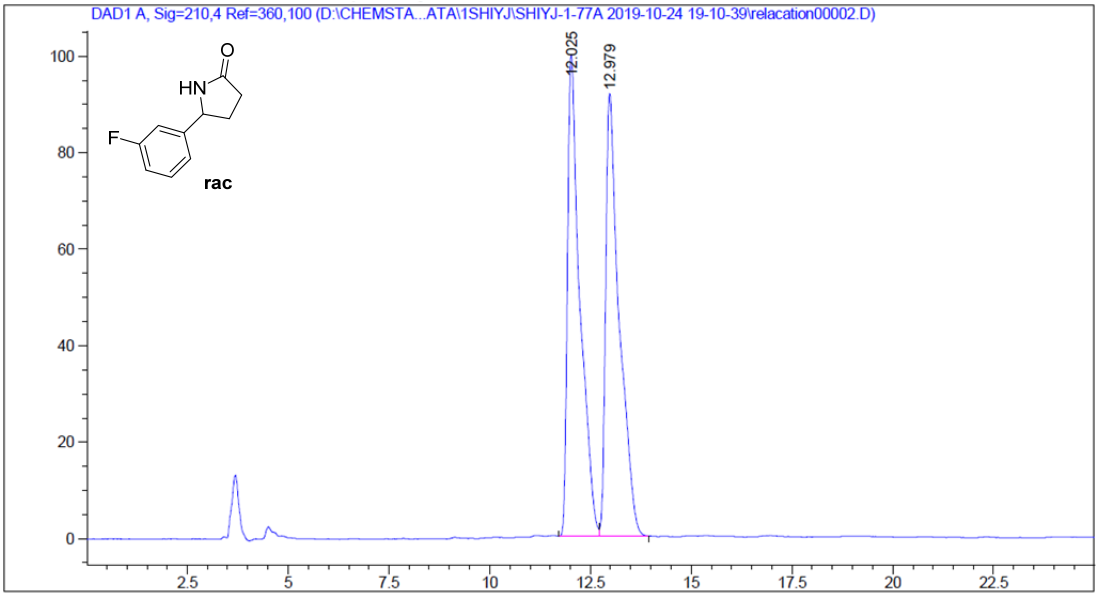
2b (>99% ee after once recrystallization)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

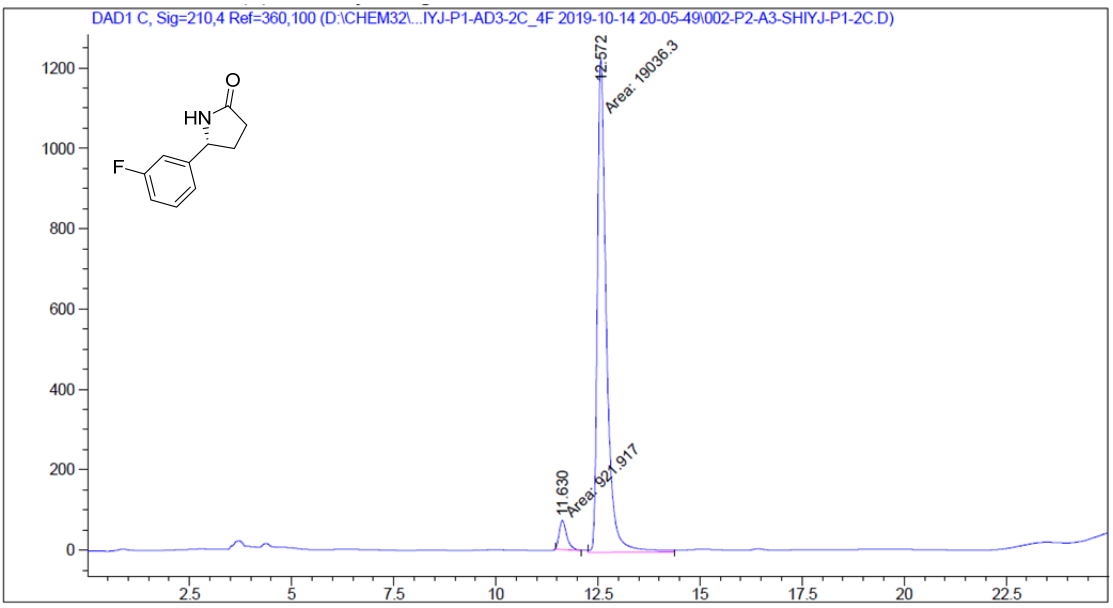
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.301	BB	0.2453	4574.27344	279.02209	99.6796
2	14.015	MM	0.2808	14.70524	8.72711e-1	0.3204

(R)-5-(3-fluorophenyl)pyrrolidin-2-one (2c)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

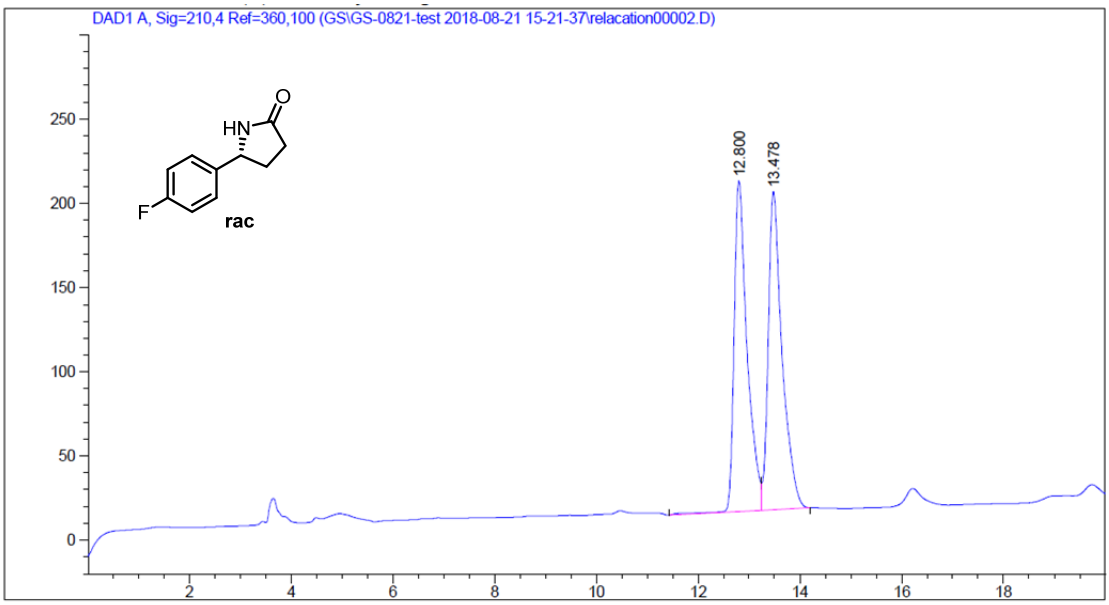
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.025	BV	0.3024	2140.34473	99.73316	49.8146
2	12.979	VB	0.3321	2156.27271	91.76775	50.1854



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

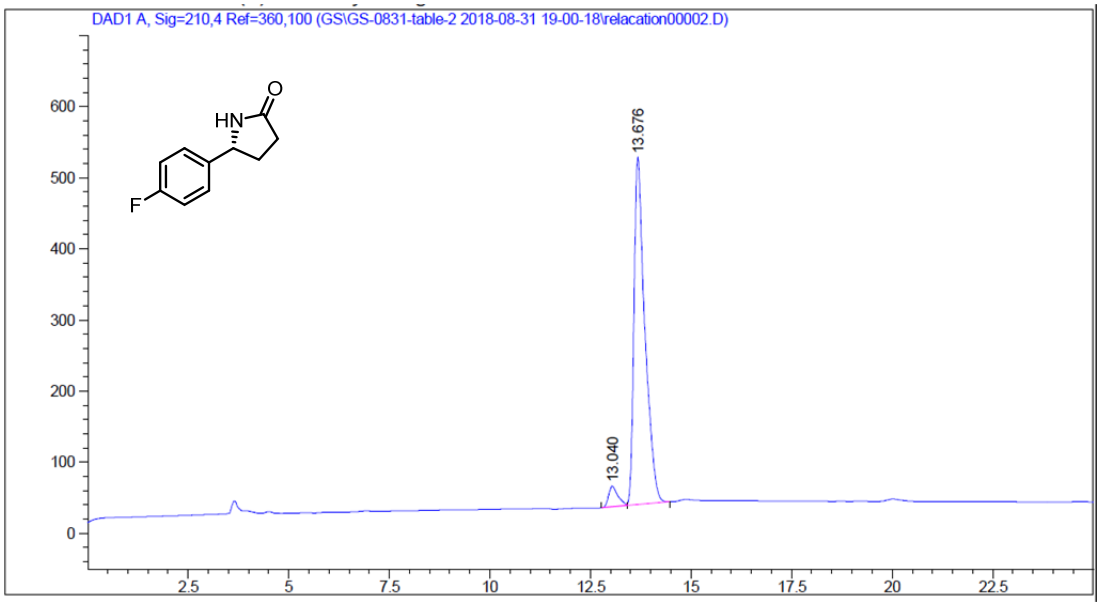
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.630	MM	0.2140	921.91663	71.80766	4.6192
2	12.572	MM	0.2586	1.90363e4	1226.66406	95.3808

(*R*)-5-(4-fluorophenyl)pyrrolidin-2-one (2d)



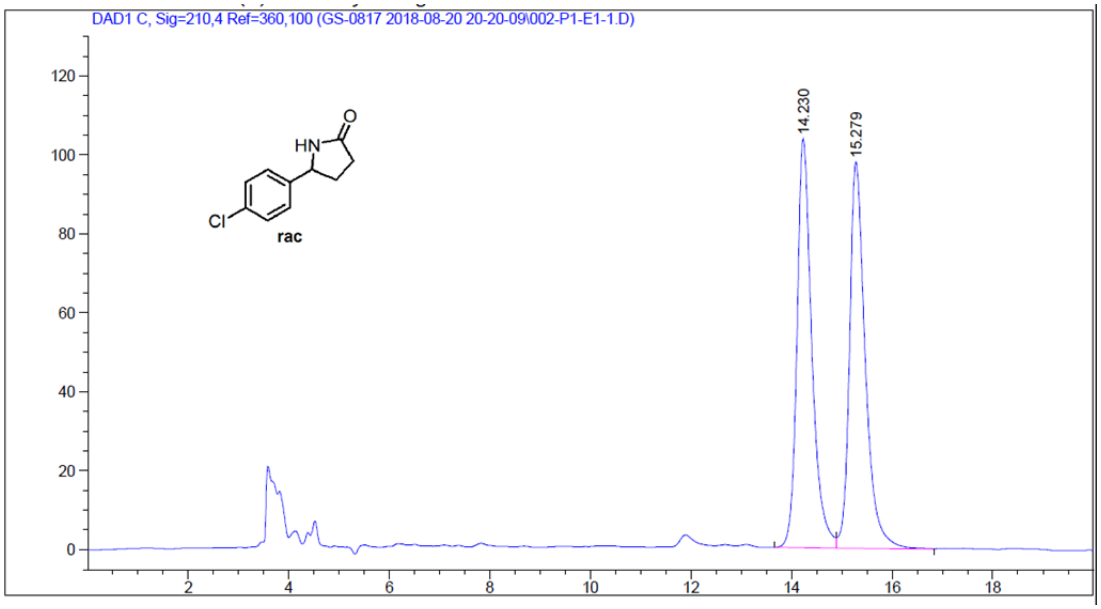
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.800	BV	0.2597	3499.40088	196.59767	49.4219
2	13.478	VB	0.2769	3581.26416	189.15977	50.5781



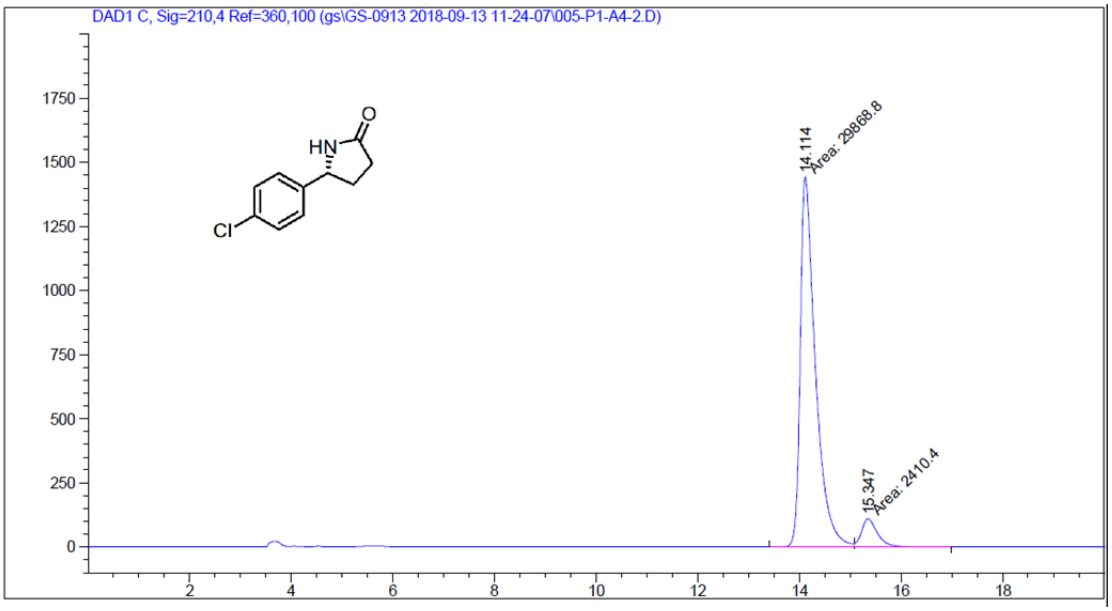
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.040	BV E	0.2376	465.29779	28.94249	4.7873
2	13.676	VB R	0.2751	9254.19727	488.33295	95.2127

(*R*)-5-(4-chlorophenyl)pyrrolidin-2-one (2e)



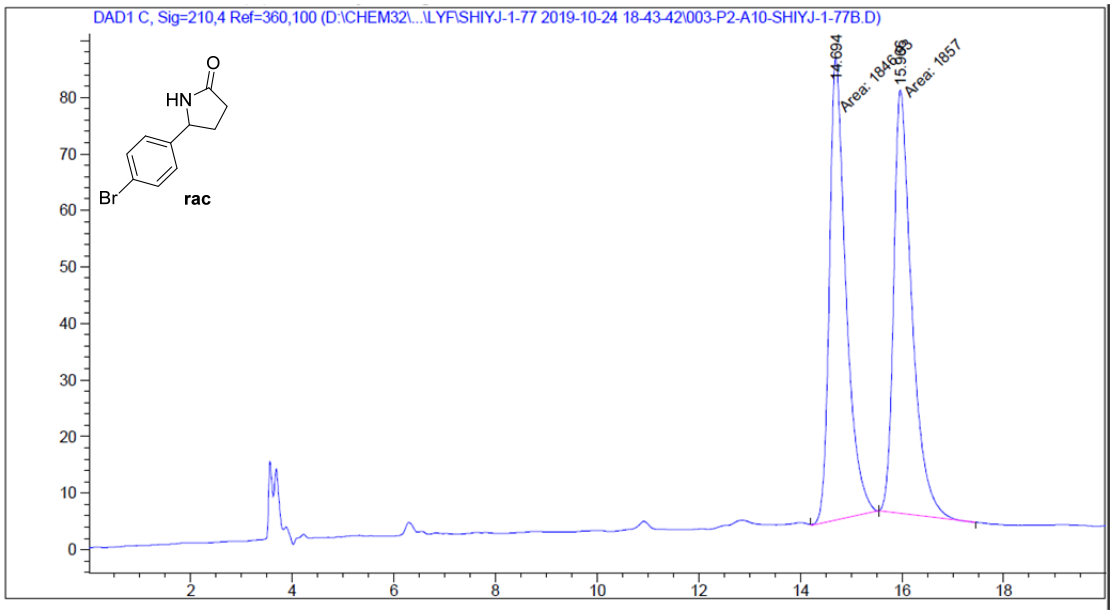
Signal 1: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.230	BV	0.3052	2123.73120	103.58163	49.9986
2	15.279	VB	0.3232	2123.84644	97.86845	50.0014



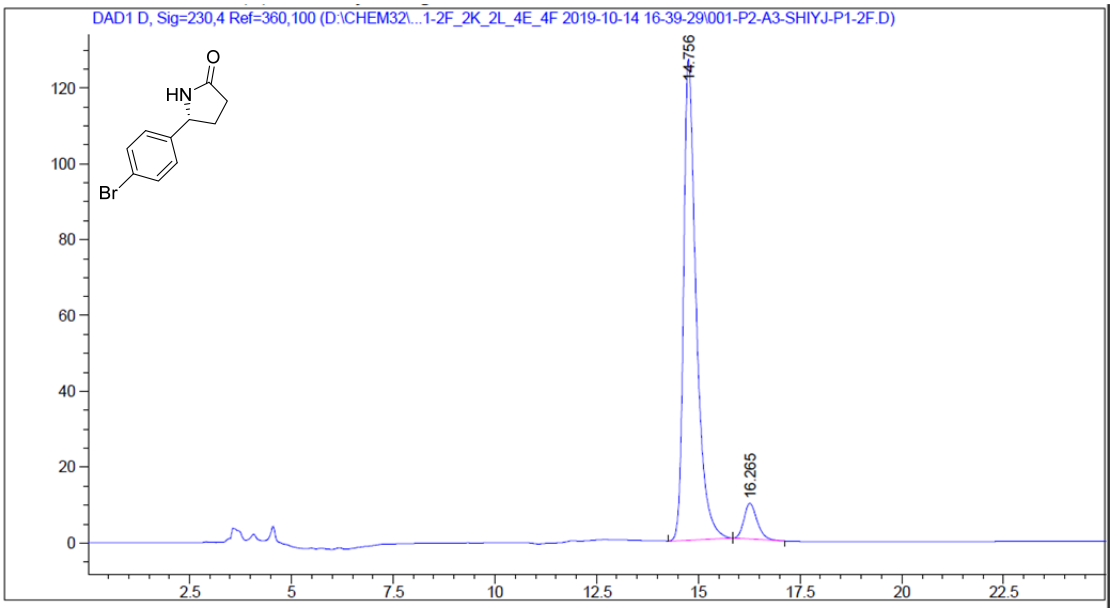
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.114	MF	0.3450	2.98688e4	1442.94885	92.5327
2	15.347	FM	0.3650	2410.39648	110.05206	7.4673

(*R*)-5-(4-bromophenyl)pyrrolidin-2-one (2f)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

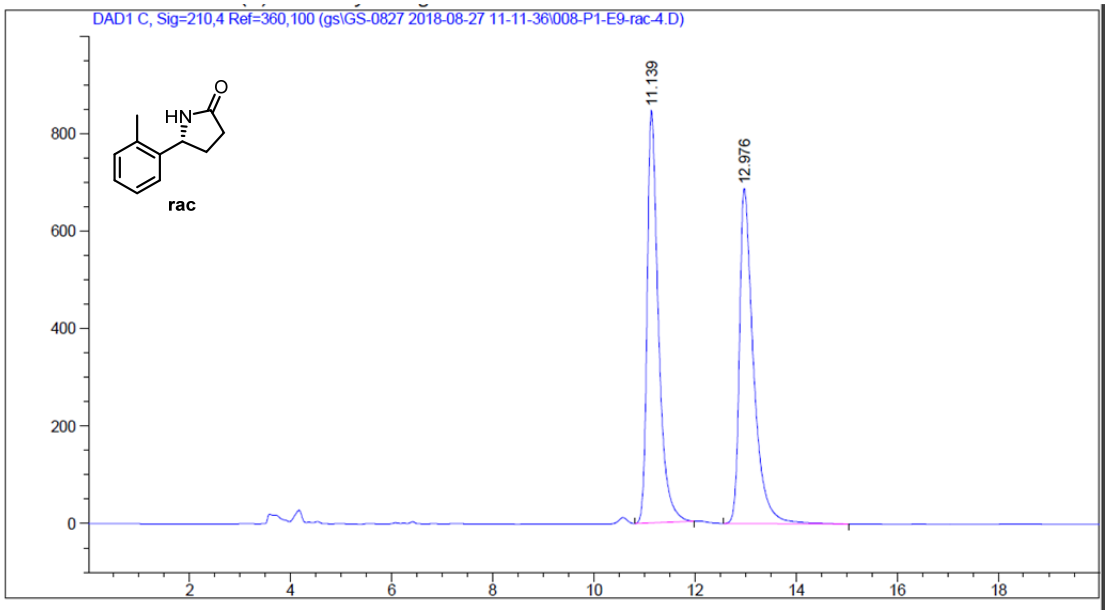
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.694	MM	0.3771	1846.93323	81.61962	49.8641
2	15.966	MM	0.4132	1856.99963	74.90785	50.1359



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

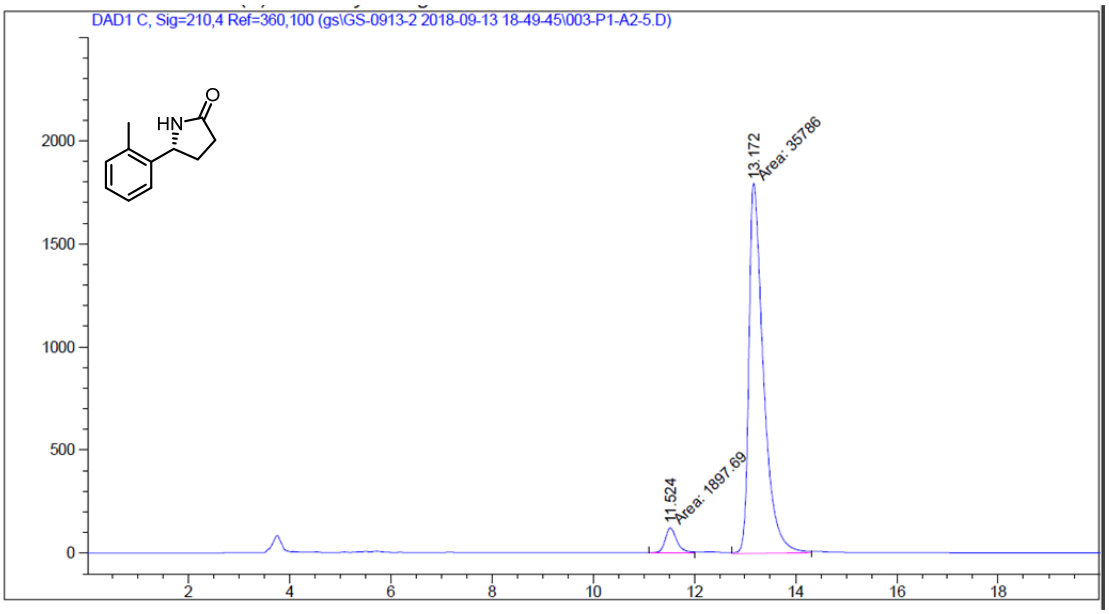
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.756	BB	0.3191	2728.09985	126.76987	92.7789
2	16.265	BB	0.3419	212.33244	9.46004	7.2211

(*R*)-5-(o-tolyl)pyrrolidin-2-one (2g)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

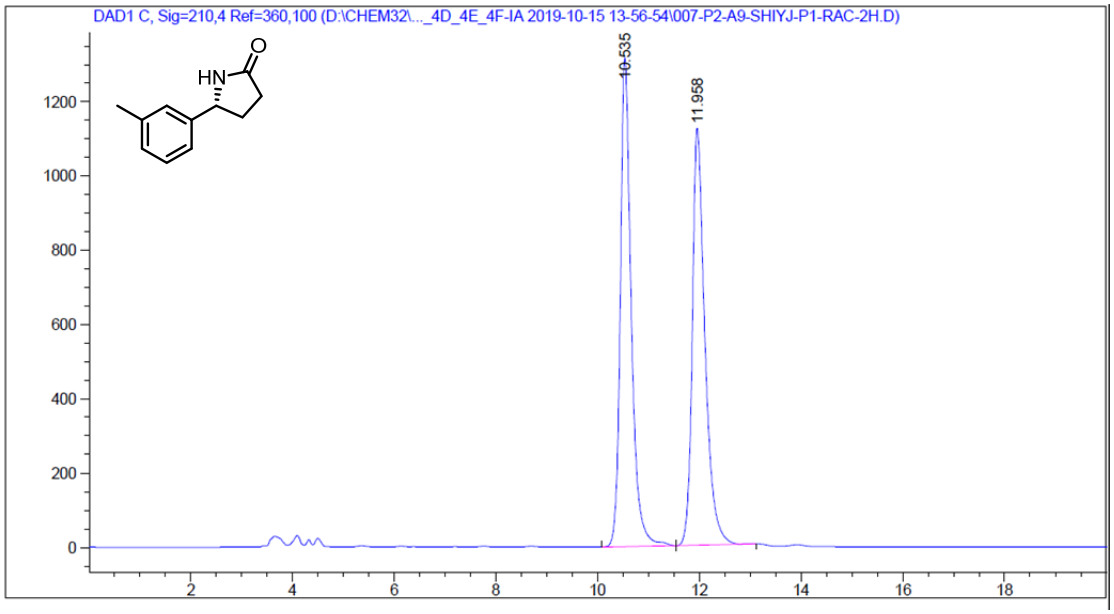
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.139	BB	0.2304	1.30964e4	846.84076	49.7416
2	12.976	BB	0.2825	1.32324e4	687.70020	50.2584



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

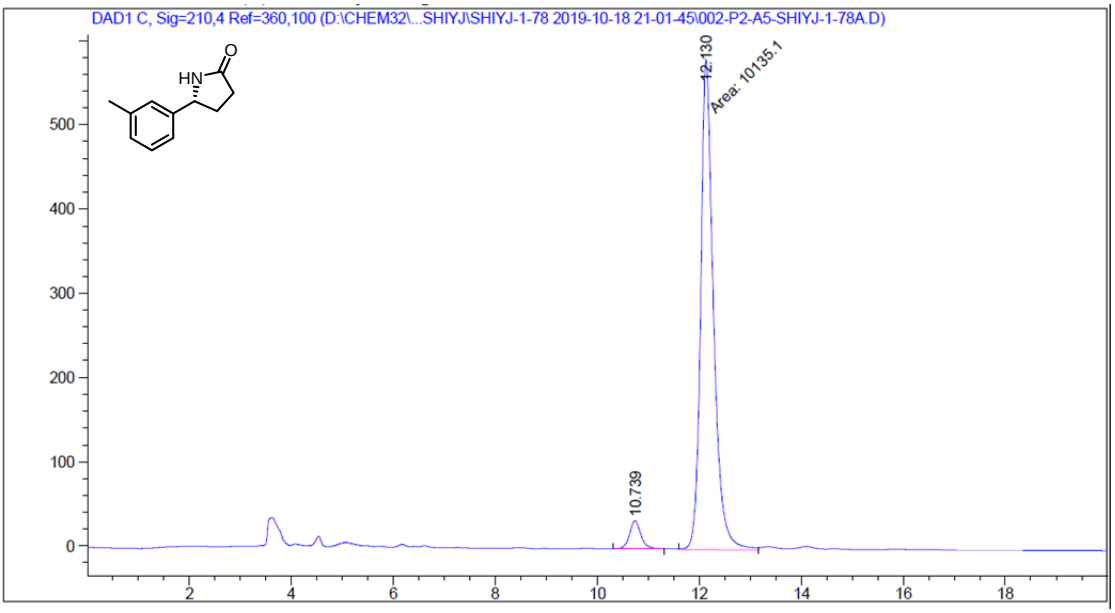
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.524	MM	0.2636	1897.69067	119.97943	5.0358
2	13.172	MM	0.3321	3.57860e4	1795.76685	94.9642

(*R*)-5-(m-tolyl)pyrrolidin-2-one (2h)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

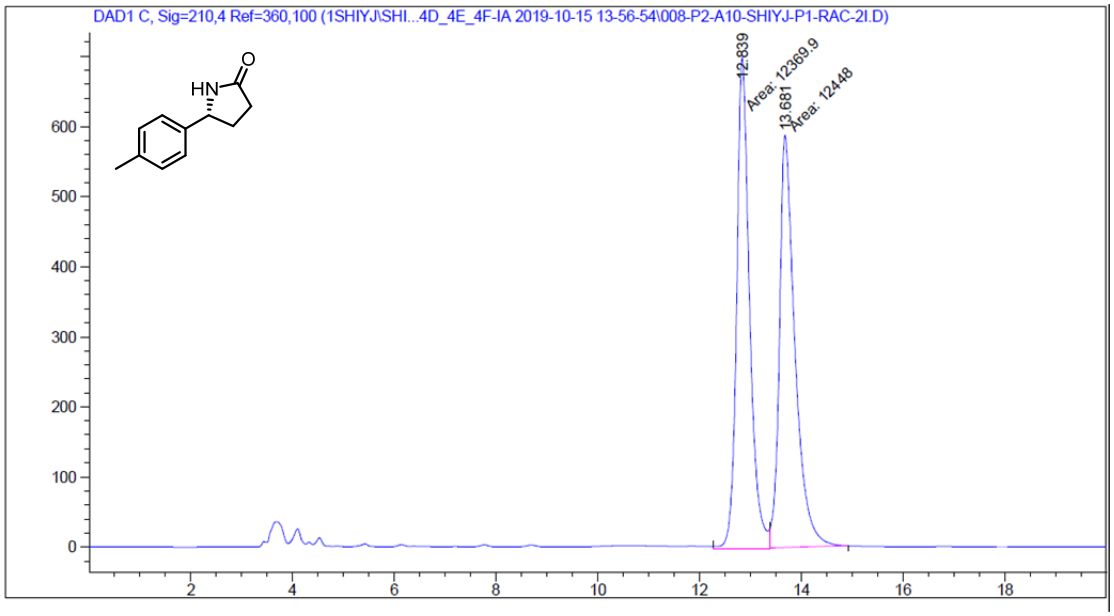
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.535	BB	0.2214	1.95954e4	1318.33472	50.3705
2	11.958	BV R	0.2522	1.93072e4	1124.34644	49.6295



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

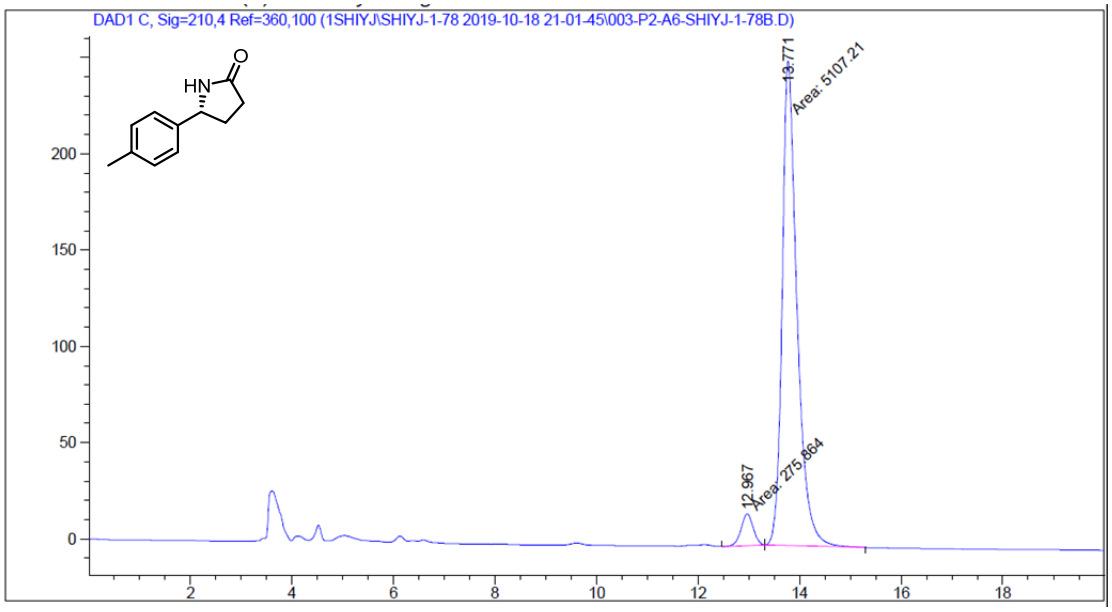
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.739	BB	0.2279	498.71146	33.06837	4.6899
2	12.130	MM	0.2903	1.01351e4	581.79559	95.3101

(*R*)-5-(p-tolyl)pyrrolidin-2-one (2i)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

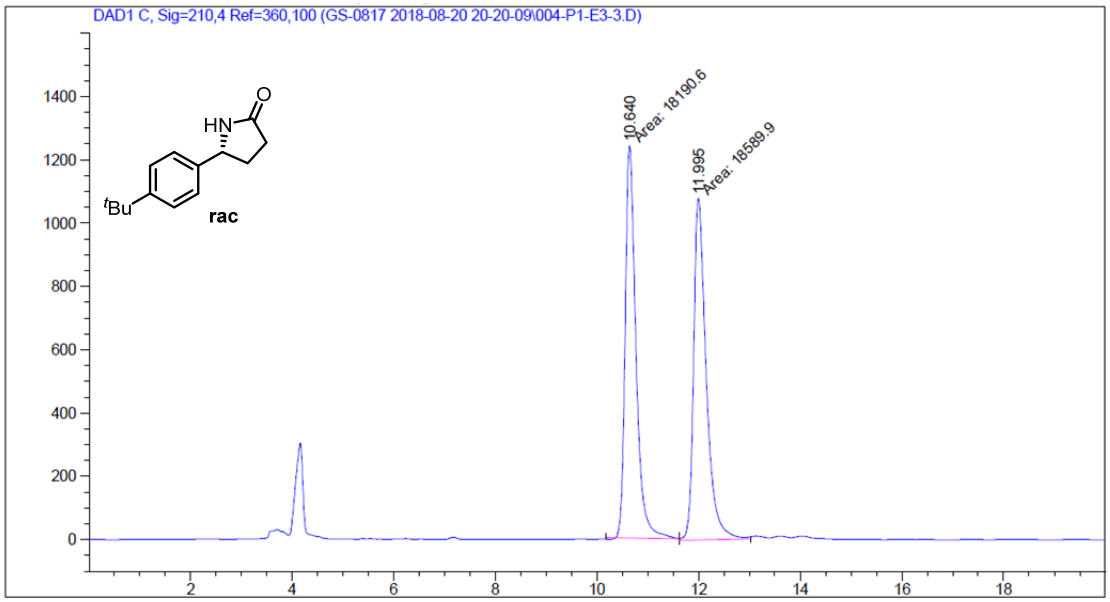
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.839	MM	0.2945	1.23699e4	700.01471	49.8425
2	13.681	MM	0.3526	1.24480e4	588.45490	50.1575



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

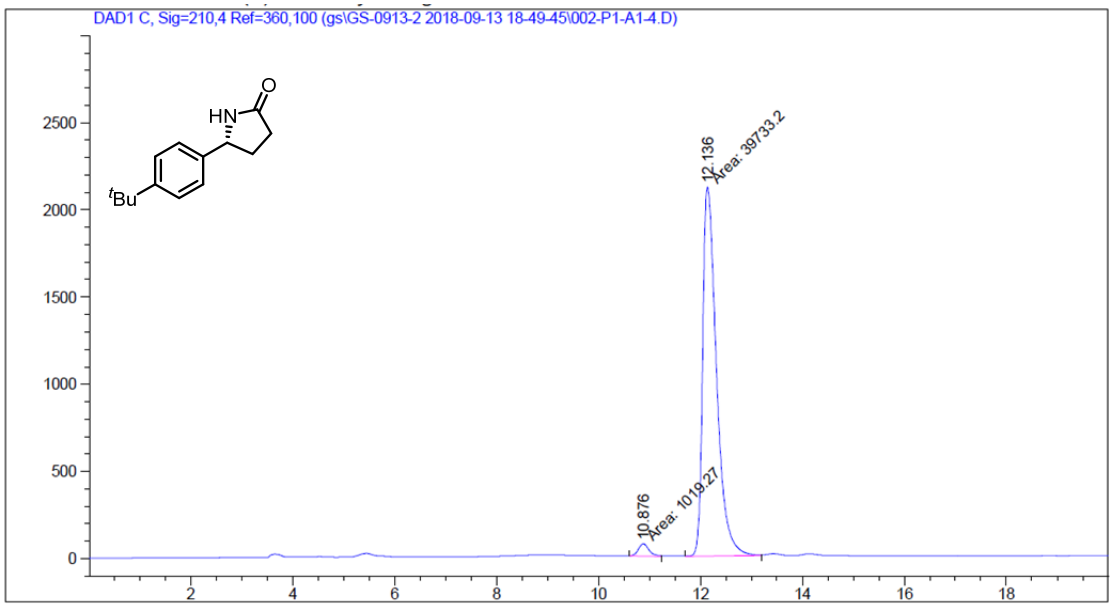
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.967	MM	0.2783	275.86435	16.51952	5.1247
2	13.771	MM	0.3383	5107.21143	251.59737	94.8753

(*R*)-5-(4-(tert-butyl)phenyl)pyrrolidin-2-one (2j)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

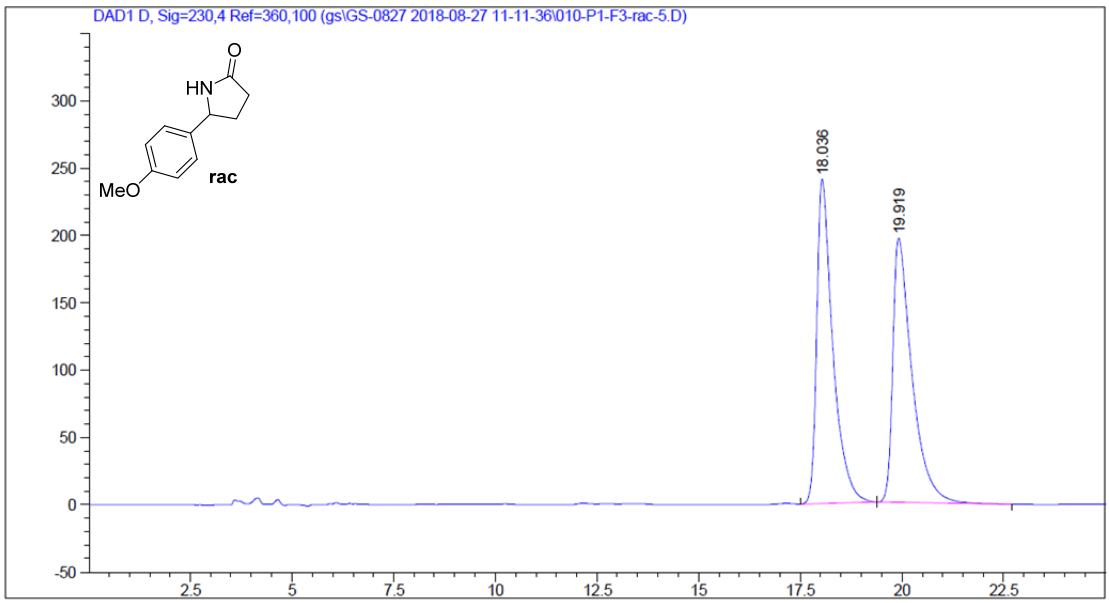
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.640	MM	0.2444	1.81906e4	1240.58313	49.4572
2	11.995	MM	0.2868	1.85899e4	1080.48474	50.5428



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

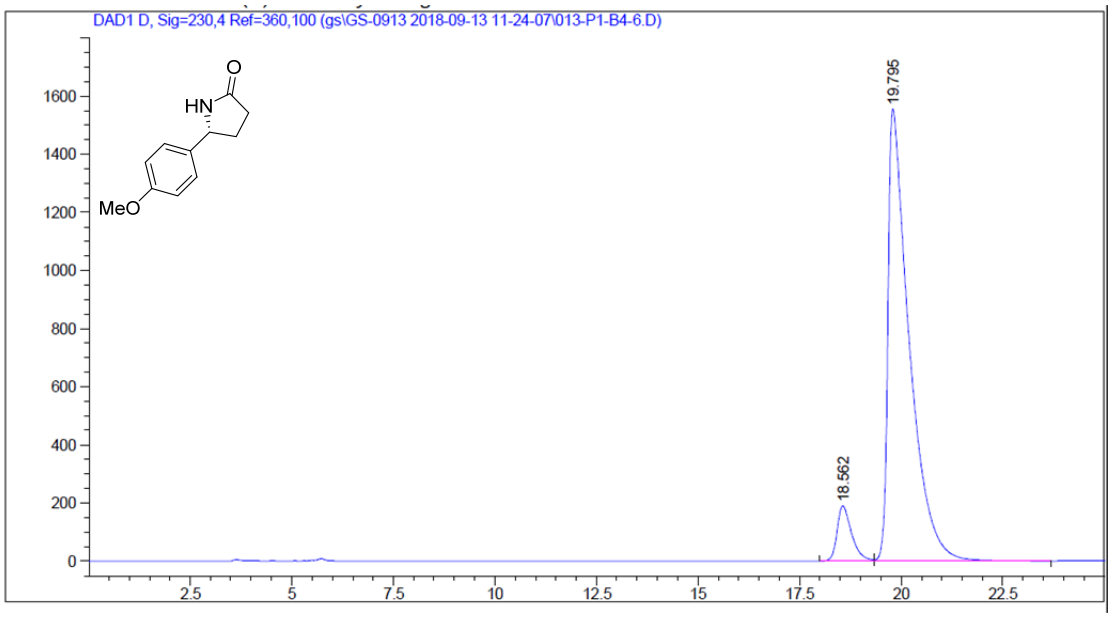
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.876	MM	0.2386	1019.26520	71.19077	2.5011
2	12.136	MM	0.3125	3.97332e4	2118.87866	97.4989

(*R*)-5-(4-methoxyphenyl)pyrrolidin-2-one (2k)



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

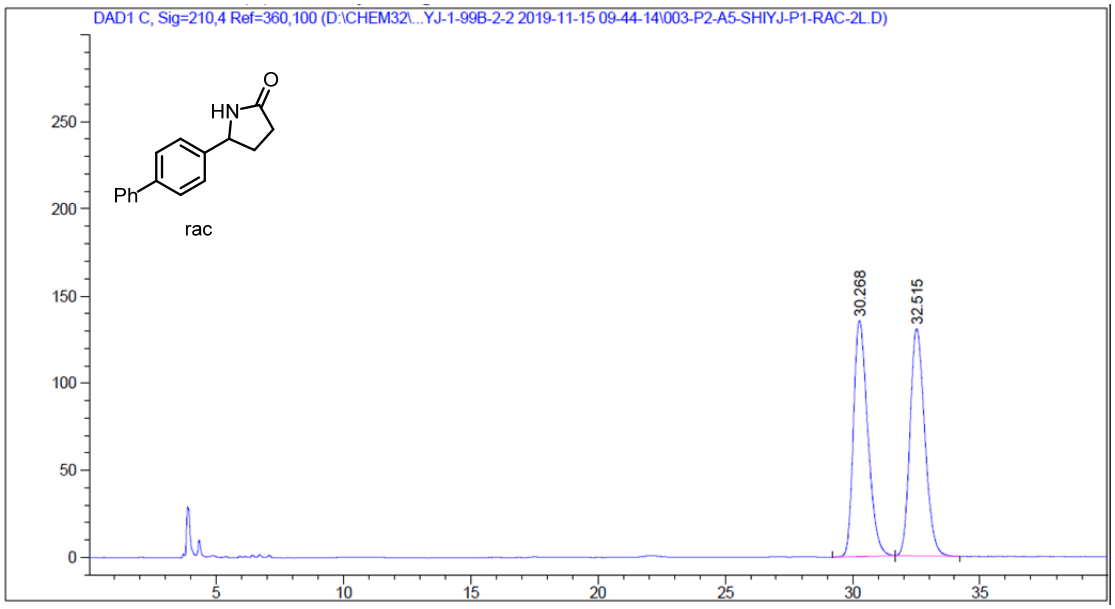
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.036	BB	0.4047	6621.26074	240.88106	50.6862
2	19.919	BB	0.4787	6441.96826	196.40167	49.3138



Signal 1: DAD1 D, Sig=230,4 Ref=360,100

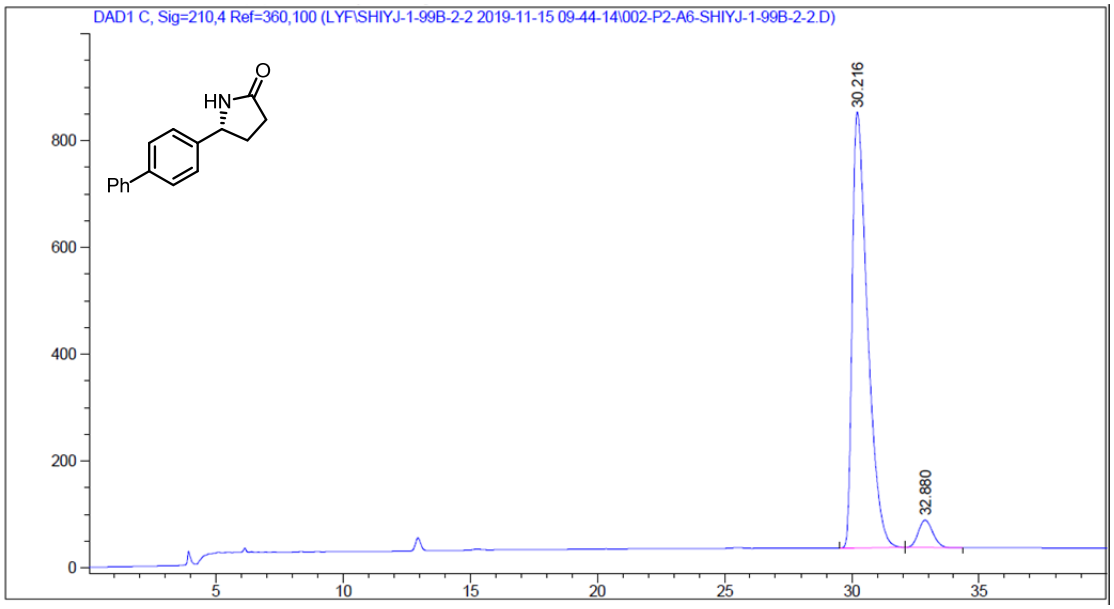
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.562	BV	0.3726	4732.84326	190.01025	7.7400
2	19.795	VB	0.5133	5.64150e4	1555.04822	92.2600

(*R*)-5-([1,1'-biphenyl]-4-yl)pyrrolidin-2-one (2l)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

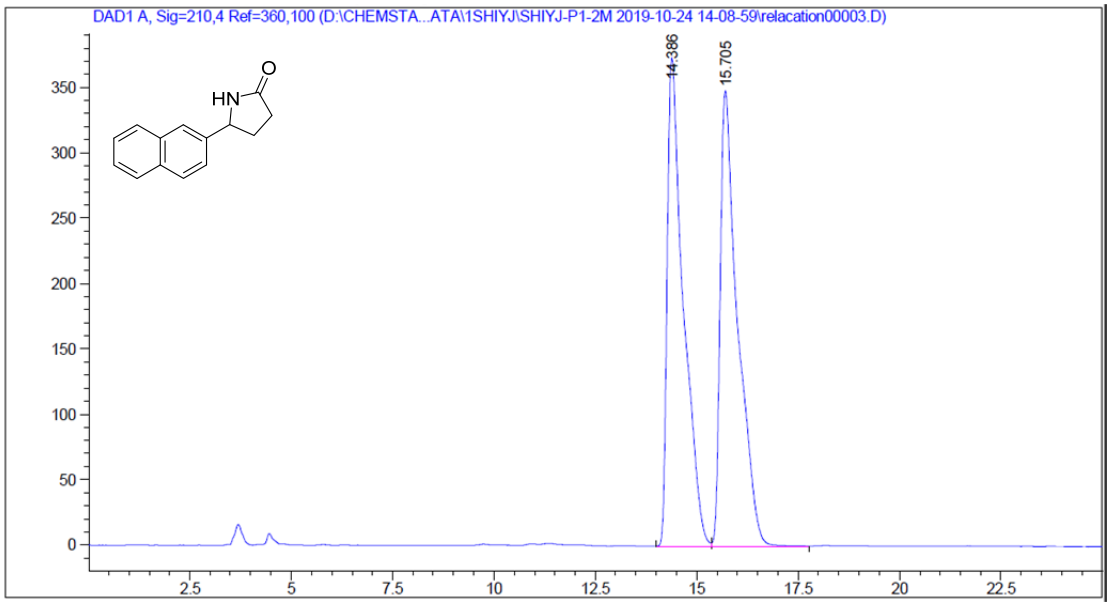
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.268	BB	0.5991	5283.77686	135.45219	50.0193
2	32.515	BB	0.6276	5279.69141	130.60262	49.9807



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

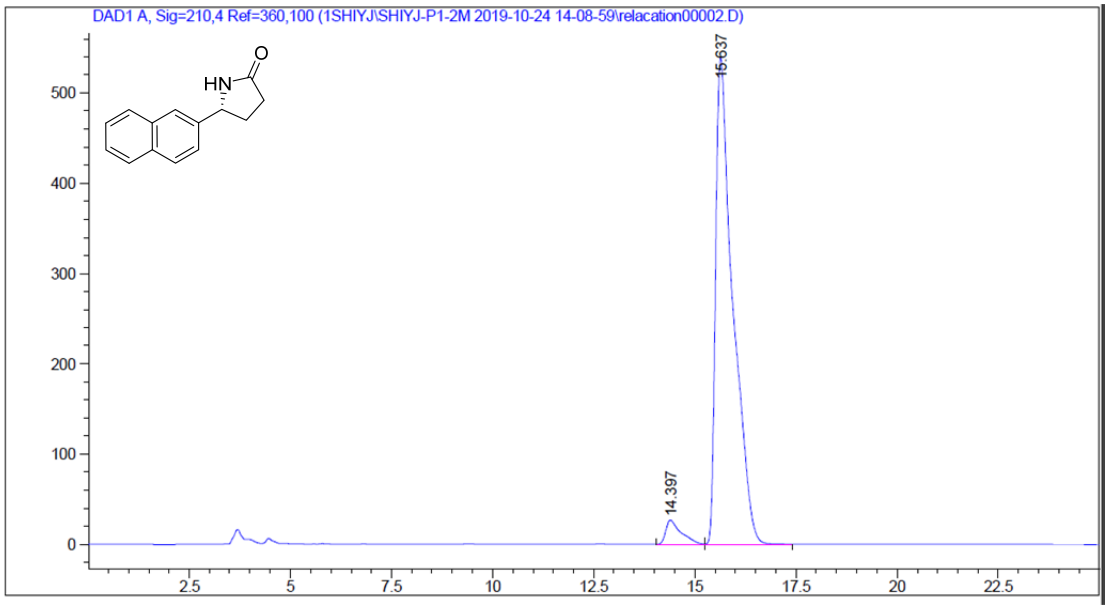
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.216	BB	0.6258	3.40084e4	816.71210	94.3567
2	32.880	BB	0.6153	2033.96411	51.44038	5.6433

(*R*)-5-(naphthalen-2-yl)pyrrolidin-2-one (2m)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

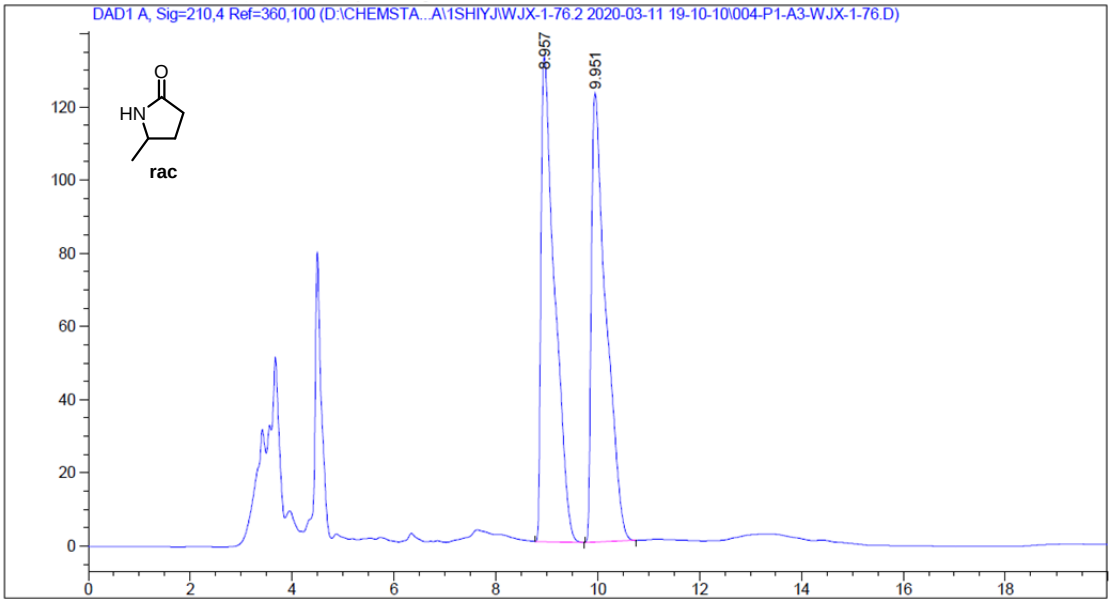
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.386	BV	0.3957	1.03527e4	373.15173	49.8295
2	15.705	VB	0.4231	1.04236e4	348.33176	50.1705



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

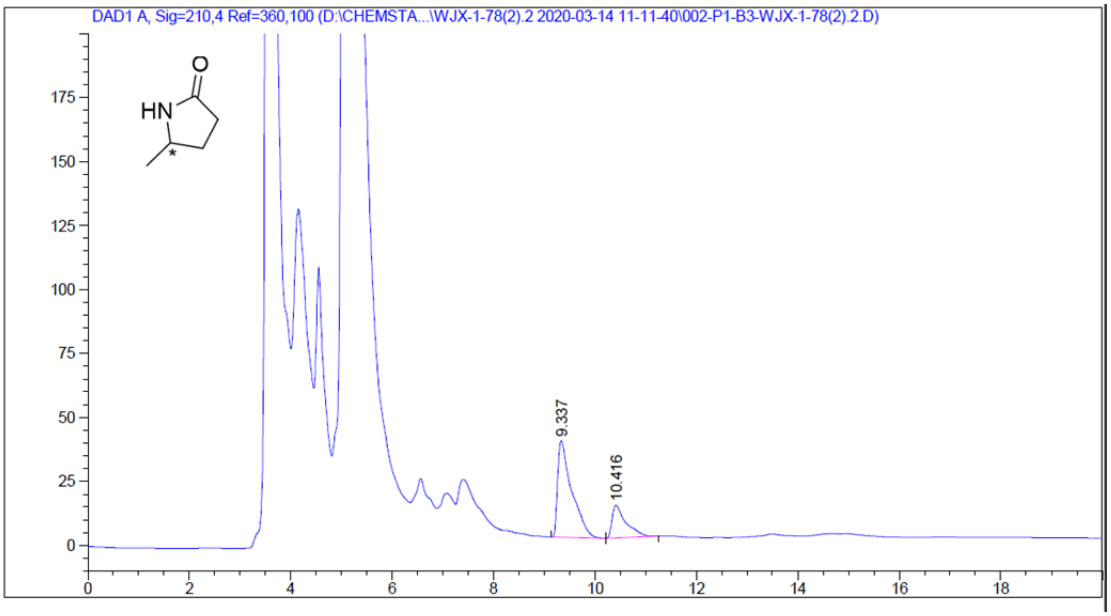
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.397	BV	0.3703	701.85541	26.73432	4.2162
2	15.637	VB	0.4210	1.59449e4	539.23969	95.7838

(*S*)-5-methylpyrrolidin-2-one (2n)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

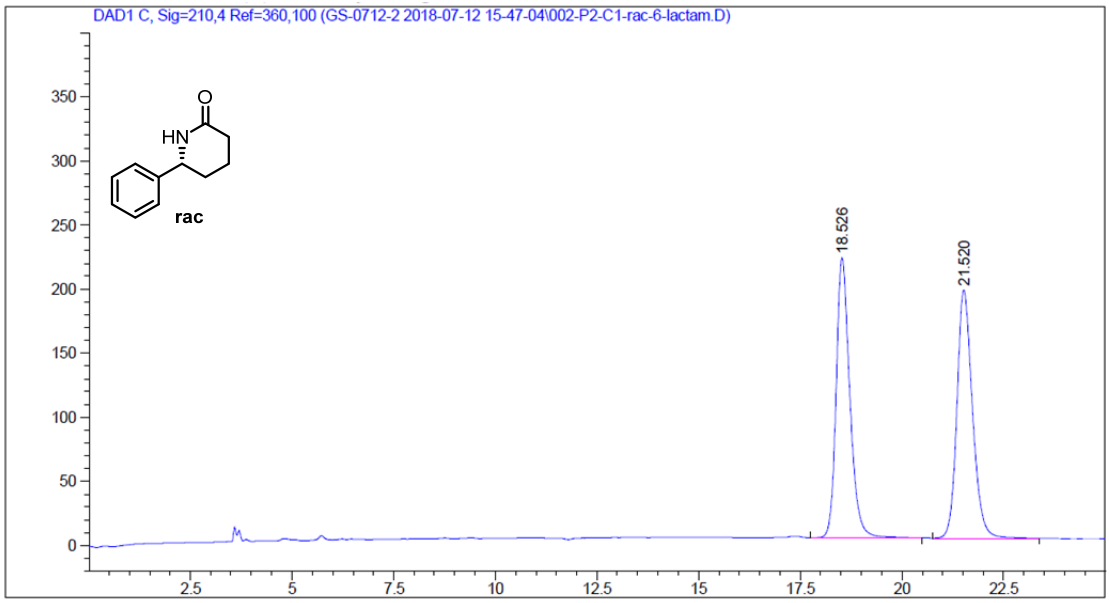
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.957	BB	0.2616	2451.93970	132.68640	50.0335
2	9.951	BB	0.2828	2448.65820	122.69194	49.9665



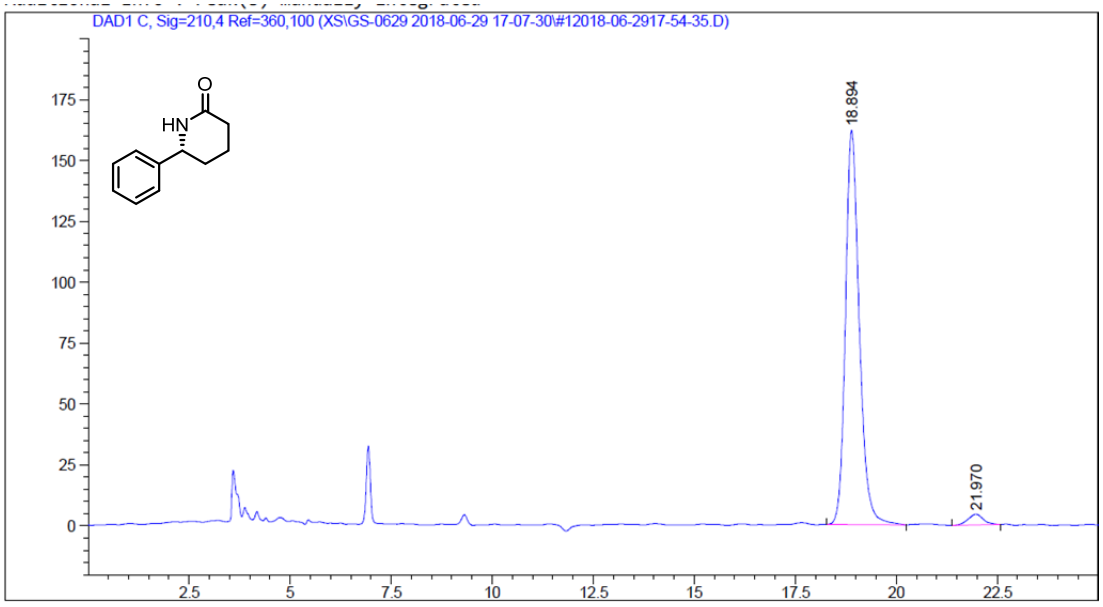
Signal 1: DAD1 A, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.337	BB	0.2714	728.90601	37.72571	74.9325
2	10.416	BB	0.2701	243.84419	12.80784	25.0675

(*R*)-6-phenylpiperidin-2-one (4a)



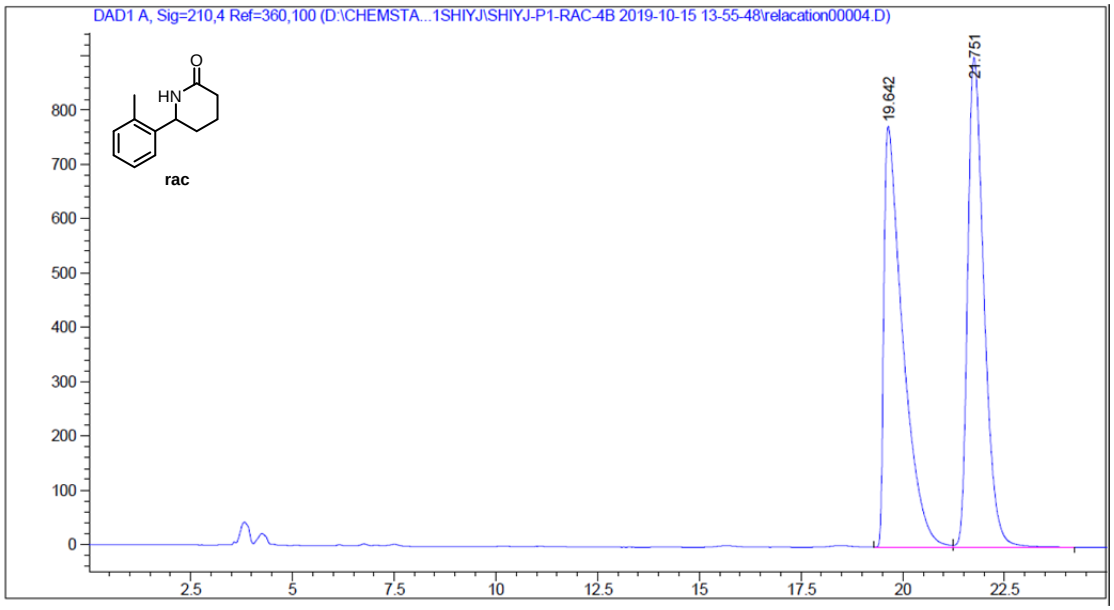
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.526	BB	0.3530	5114.17578	218.53065	49.8092
2	21.520	BB	0.4046	5153.36084	193.55563	50.1908



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

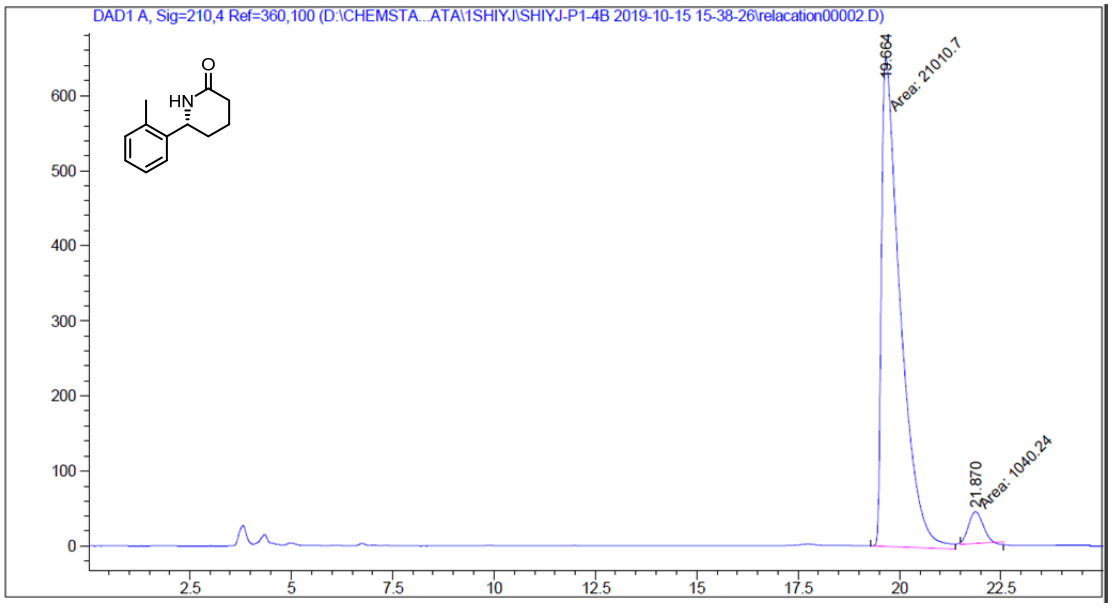
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.894	BB	0.3612	3844.08057	161.79329	97.0720
2	21.970	BB	0.3924	115.94972	4.35778	2.9280

(*R*)-6-(o-tolyl)piperidin-2-one (4b)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

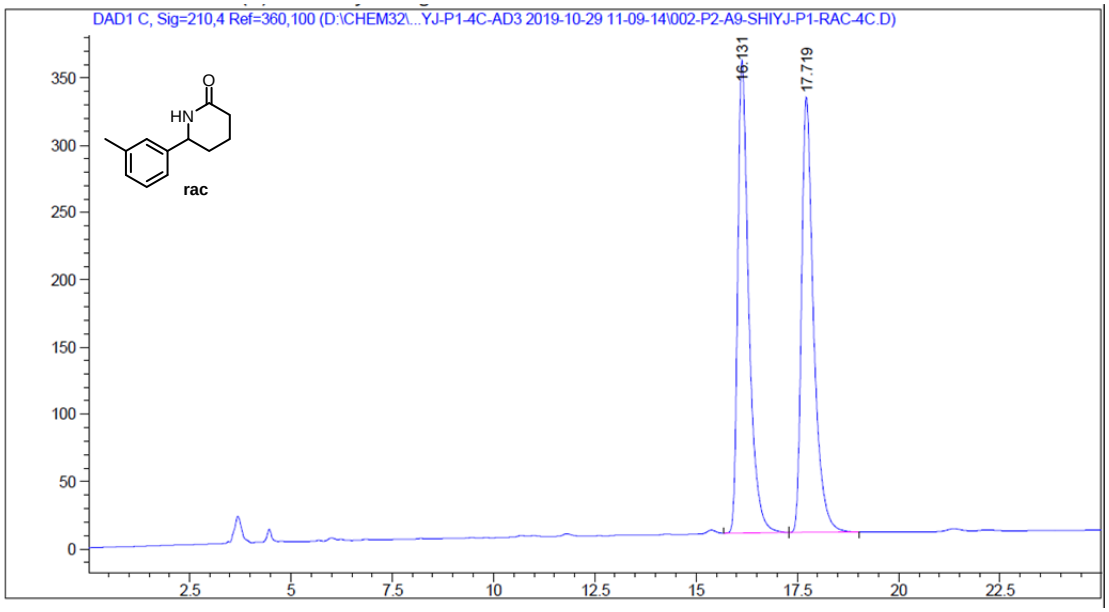
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.642	BV	0.4641	2.49833e4	775.02325	49.8840
2	21.751	VB	0.4247	2.50995e4	901.76825	50.1160



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

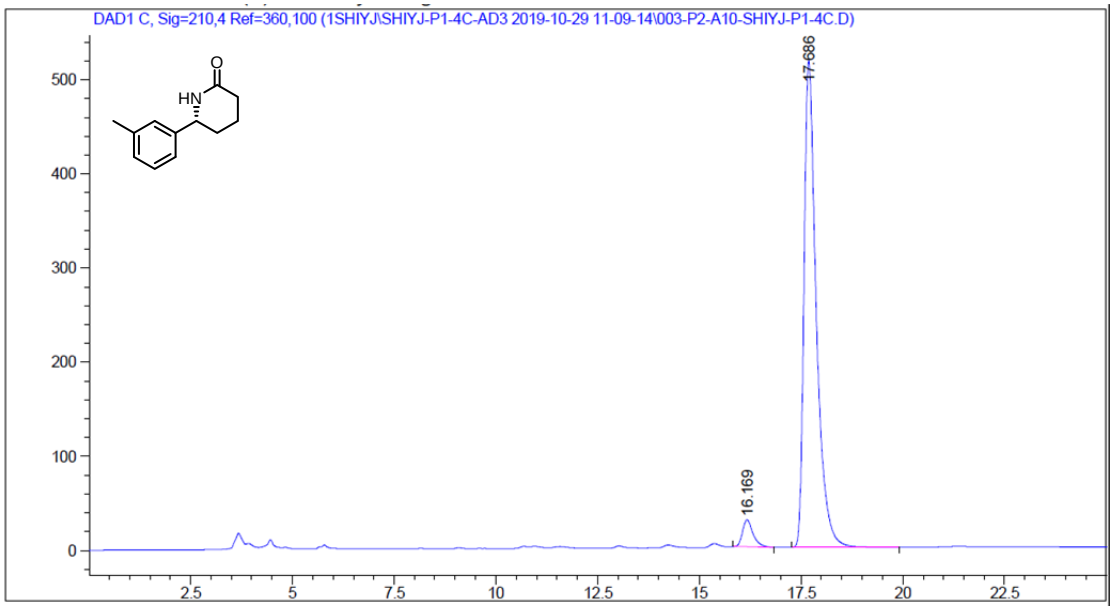
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.664	MM	0.5376	2.10107e4	651.40686	95.2826
2	21.870	MM	0.4118	1040.24426	42.09724	4.7174

(*R*)-6-(m-tolyl)piperidin-2-one (4c)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

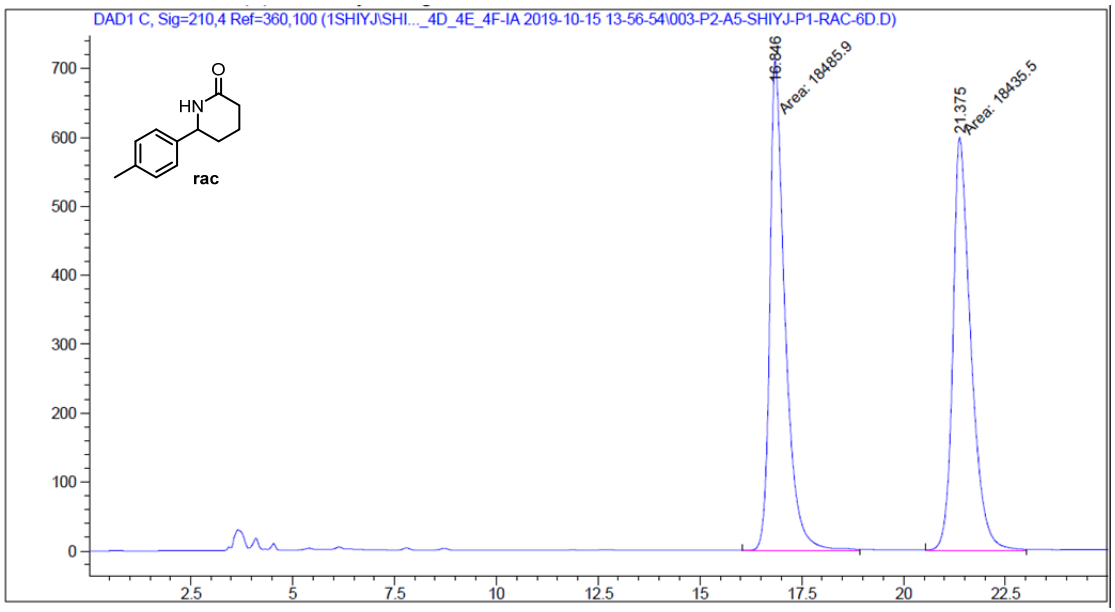
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.131	BB	0.2829	6653.85791	351.36380	49.8965
2	17.719	BB	0.3089	6681.46289	323.54901	50.1035



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

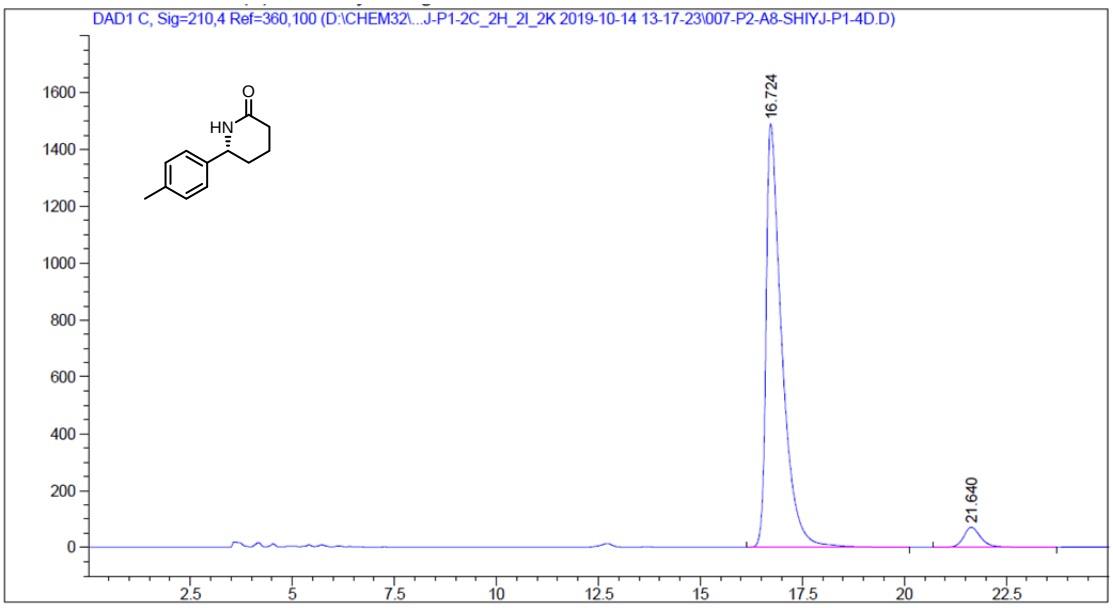
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.169	BB	0.2683	513.10370	28.73791	4.5220
2	17.686	BB	0.3122	1.08338e4	517.59314	95.4780

(*R*)-6-(p-tolyl)piperidin-2-one (4d)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

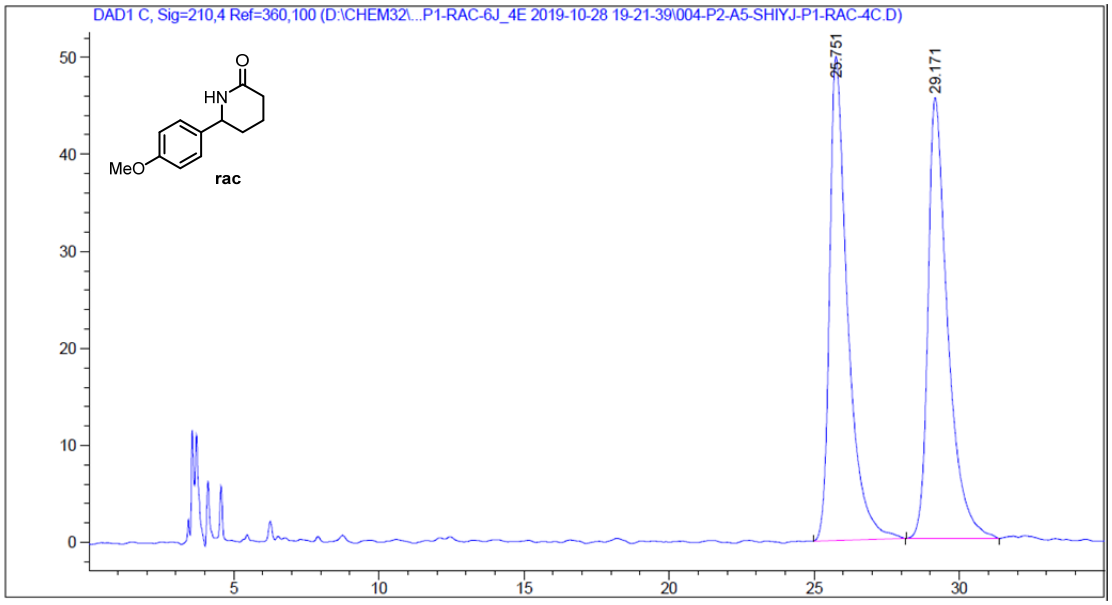
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.846	MM	0.4335	1.84859e4	710.69879	50.0682
2	21.375	MM	0.5131	1.84355e4	598.77026	49.9318



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

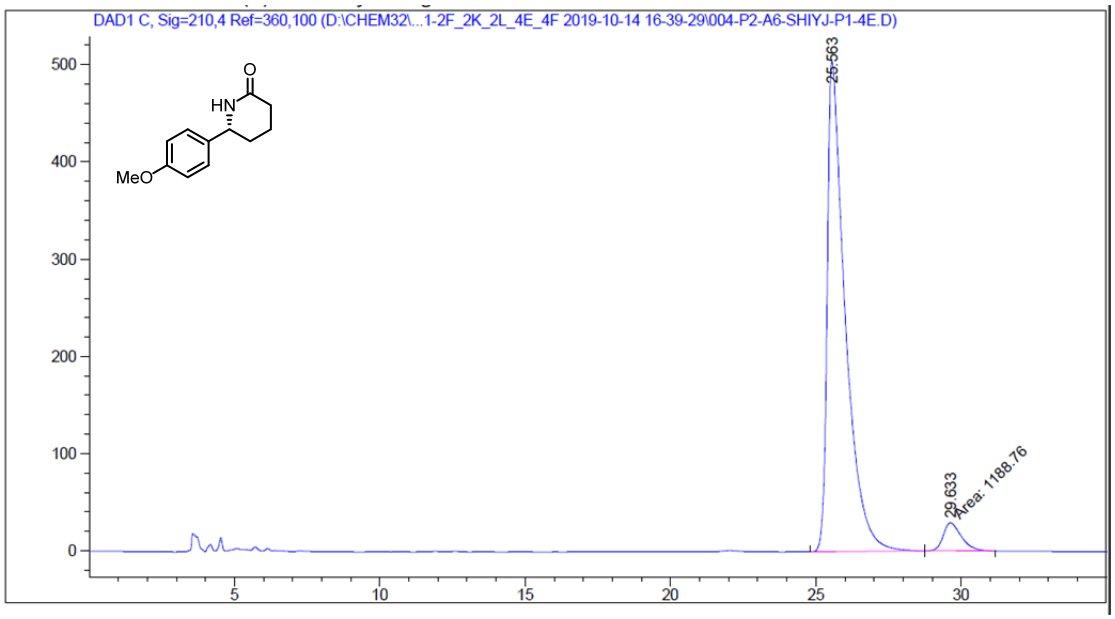
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.724	BB	0.3882	3.98682e4	1489.70557	94.9630
2	21.640	BB	0.4473	2114.67627	71.03542	5.0370

(*R*)-6-(4-methoxyphenyl)piperidin-2-one (4e)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

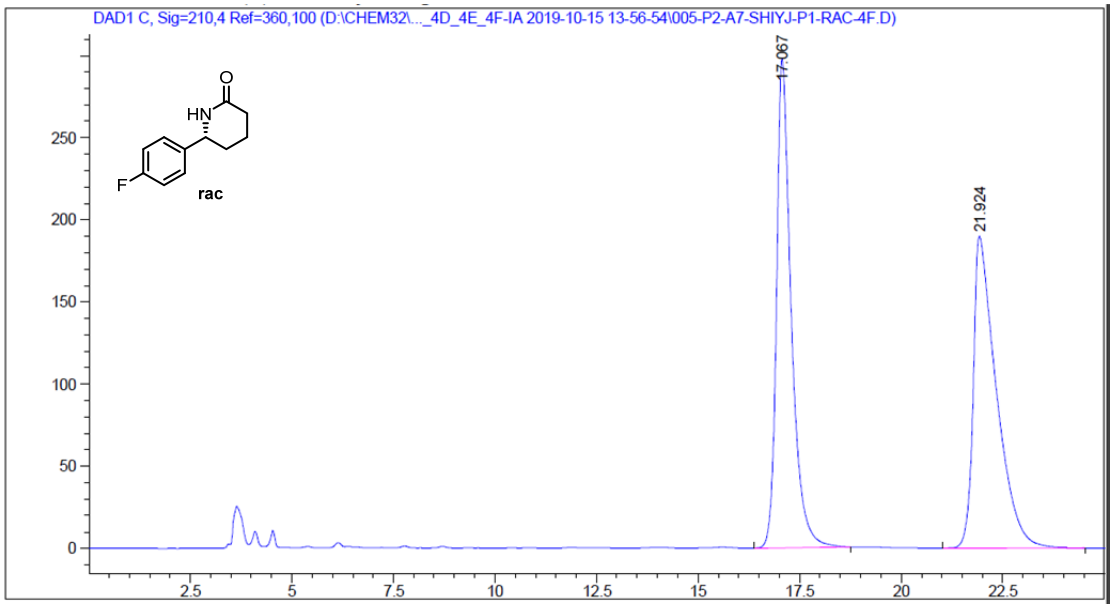
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.751	BB	0.6318	2152.04419	49.83823	50.0838
2	29.171	BB	0.6873	2144.84131	45.38601	49.9162



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

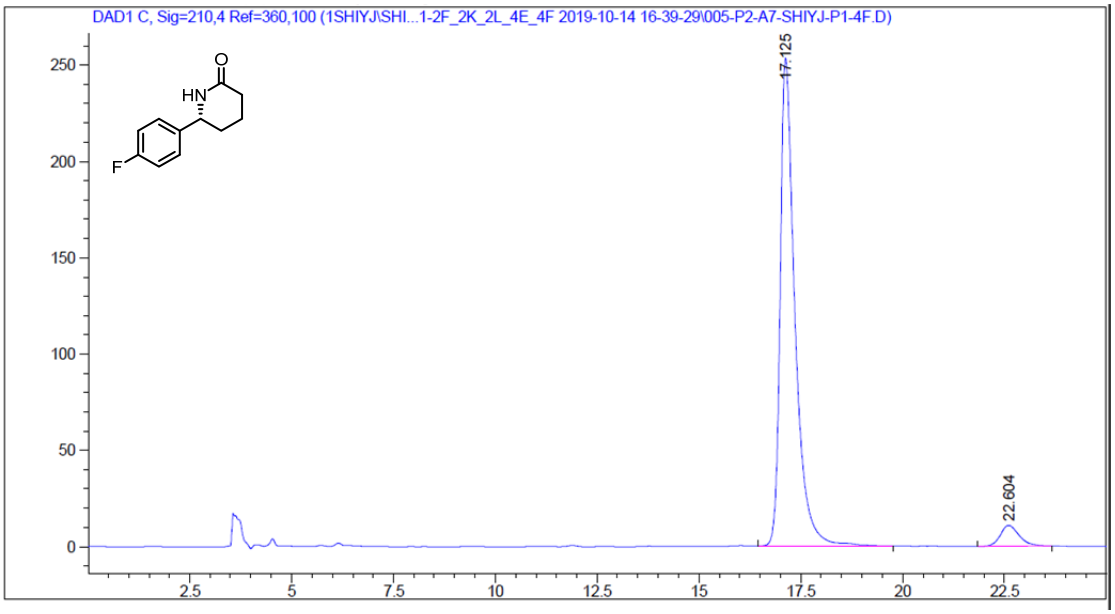
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.563	BB	0.6189	2.16337e4	503.90970	94.7913
2	29.633	MM	0.6981	1188.76343	28.37964	5.2087

(*R*)-6-(4-fluorophenyl)piperidin-2-one (4f)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

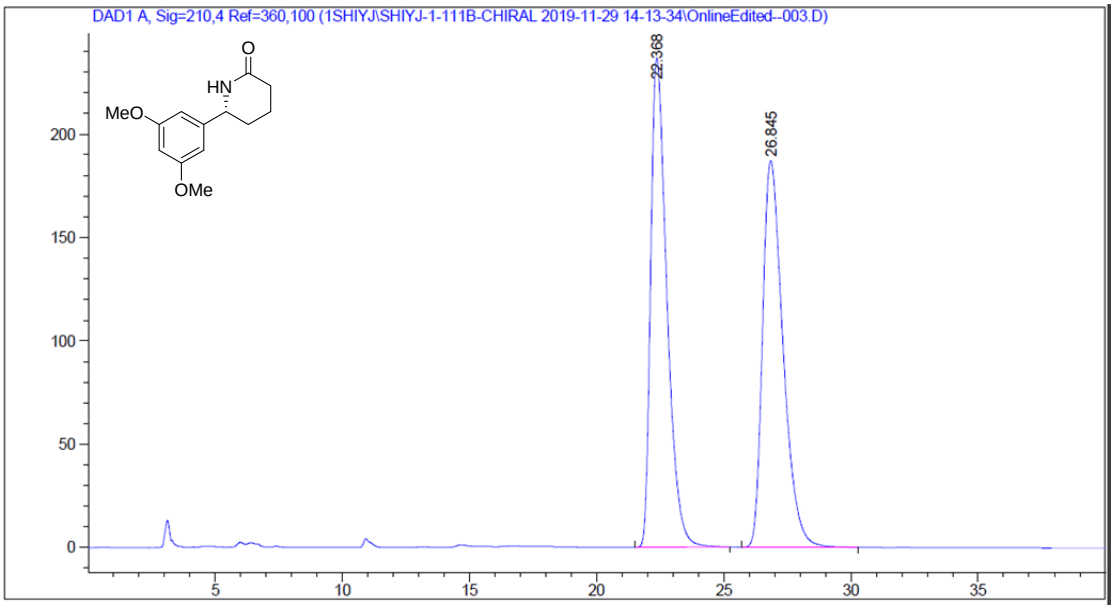
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.067	BB	0.3668	7467.58936	297.54294	49.8623
2	21.924	BB	0.5674	7508.82813	189.86357	50.1377



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

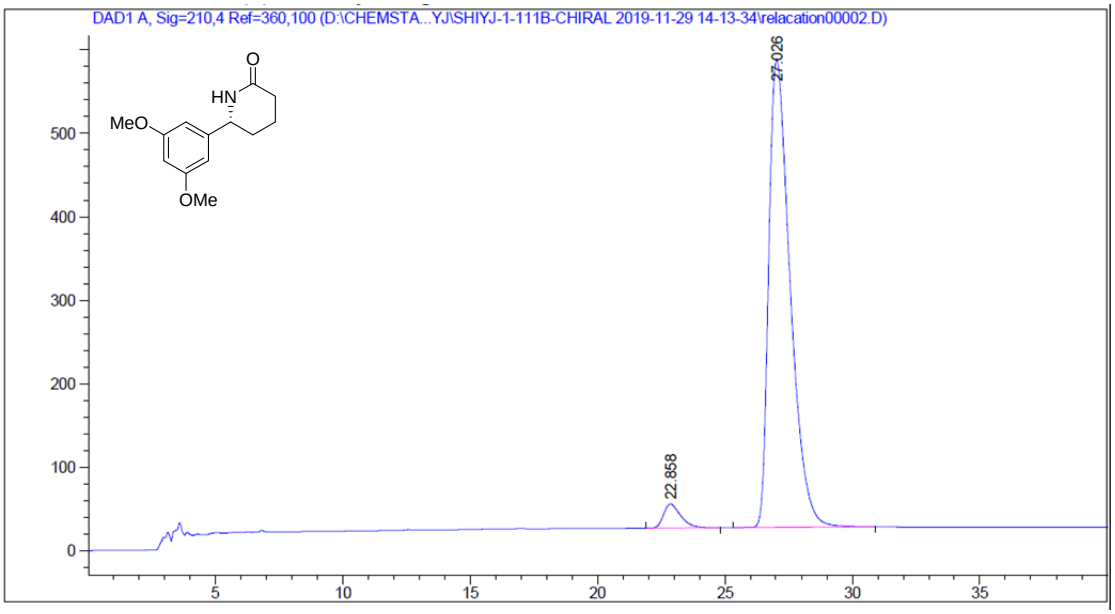
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.125	BB	0.3696	6373.56836	253.23863	94.8080
2	22.604	BB	0.4803	349.03955	10.87801	5.1920

(*R*)-6-(3,5-dimethoxyphenyl)piperidin-2-one (4g)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

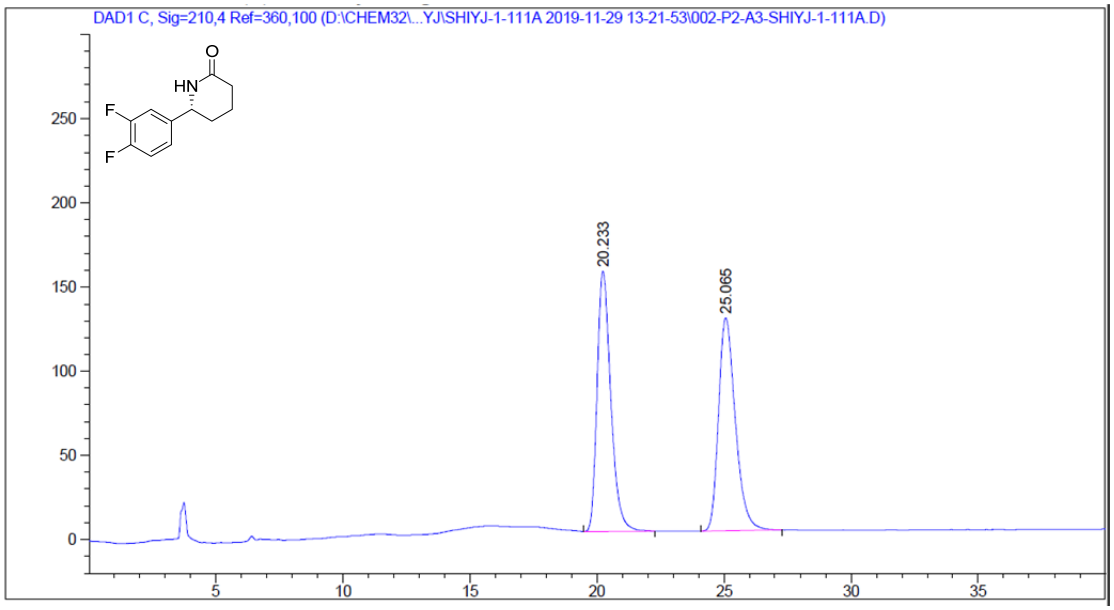
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.368	BB	0.6718	1.04699e4	236.82520	50.0295
2	26.845	BB	0.8544	1.04575e4	187.00970	49.9705



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

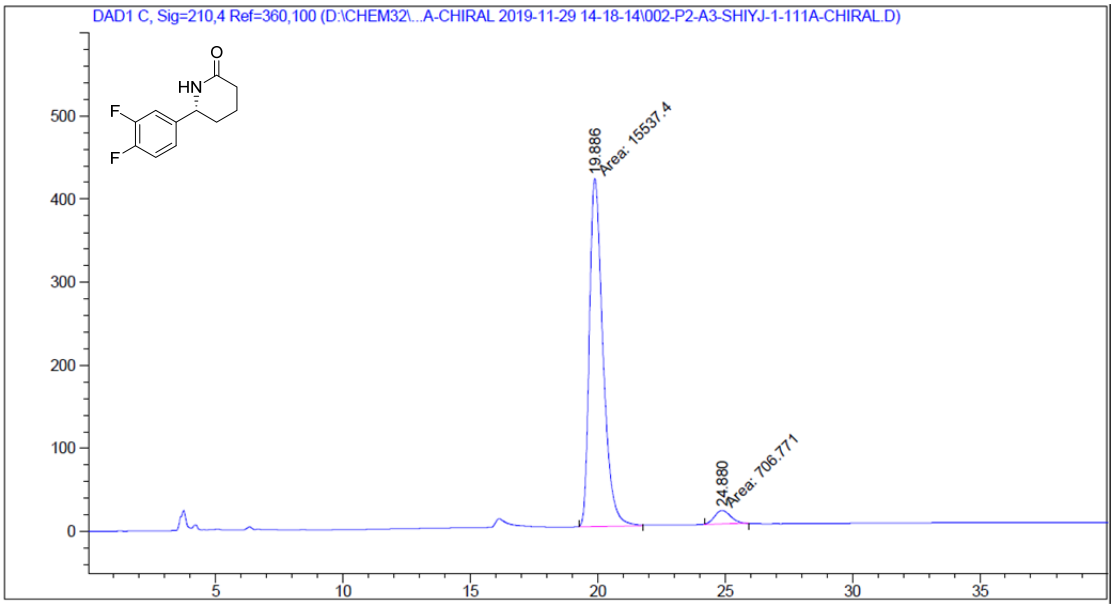
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.858	BB	0.7025	1348.48657	28.78746	3.9727
2	27.026	BB	0.8916	3.25957e4	559.56018	96.0273

(*R*)-6-(3,4-difluorophenyl)piperidin-2-one (4h)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

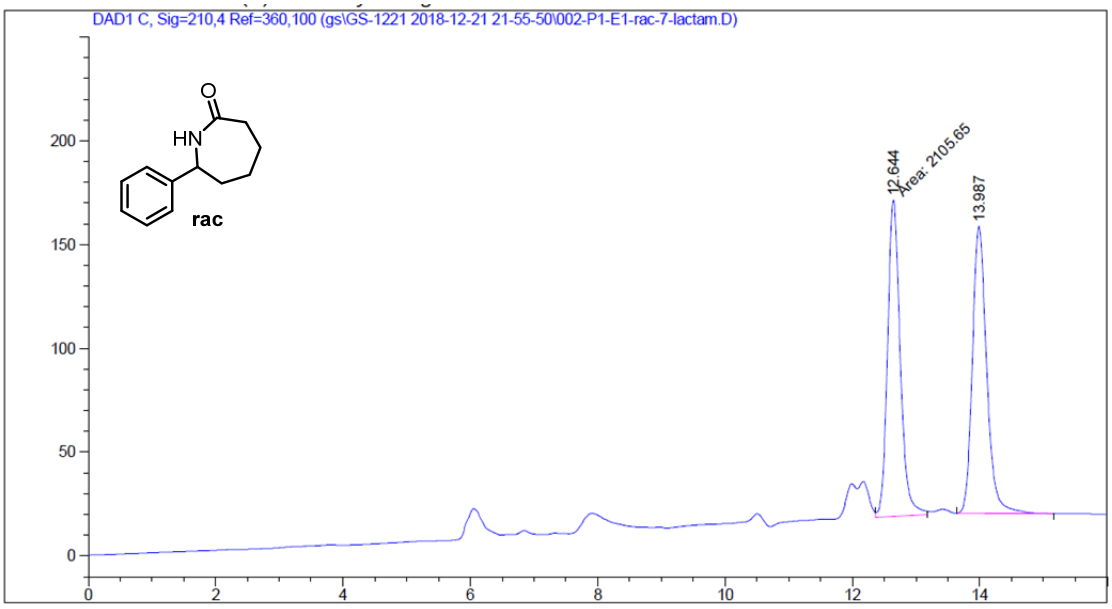
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.233	BB	0.5766	5785.74268	154.60043	49.8239
2	25.065	BB	0.7091	5826.65234	126.56580	50.1761



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

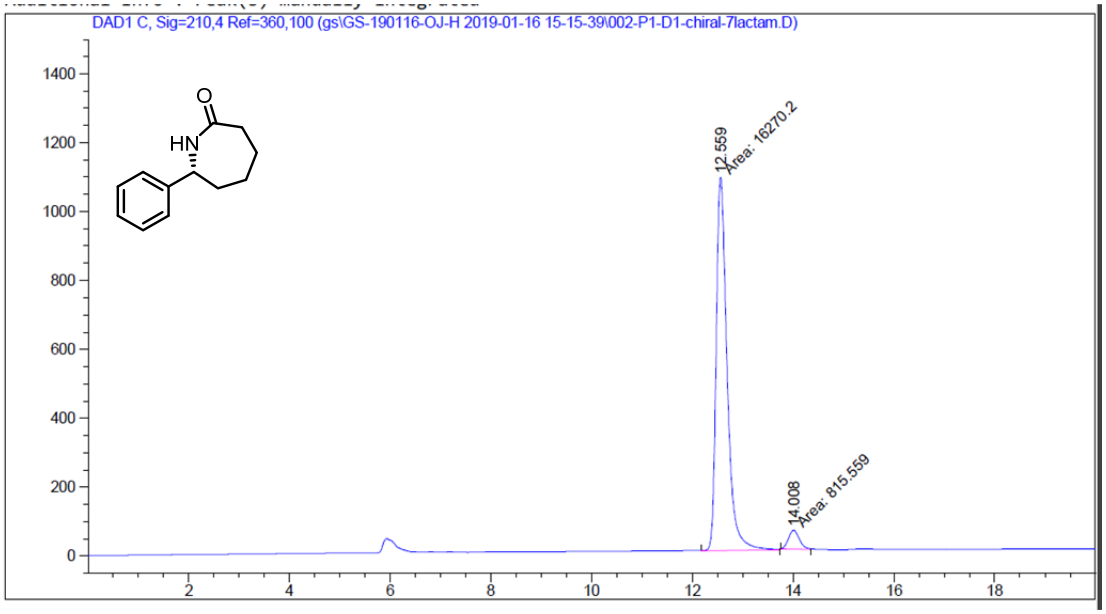
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.886	MM	0.6184	1.55374e4	418.77347	95.6491
2	24.880	MM	0.7236	706.77112	16.27941	4.3509

7-phenylazepan-2-one (4i)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

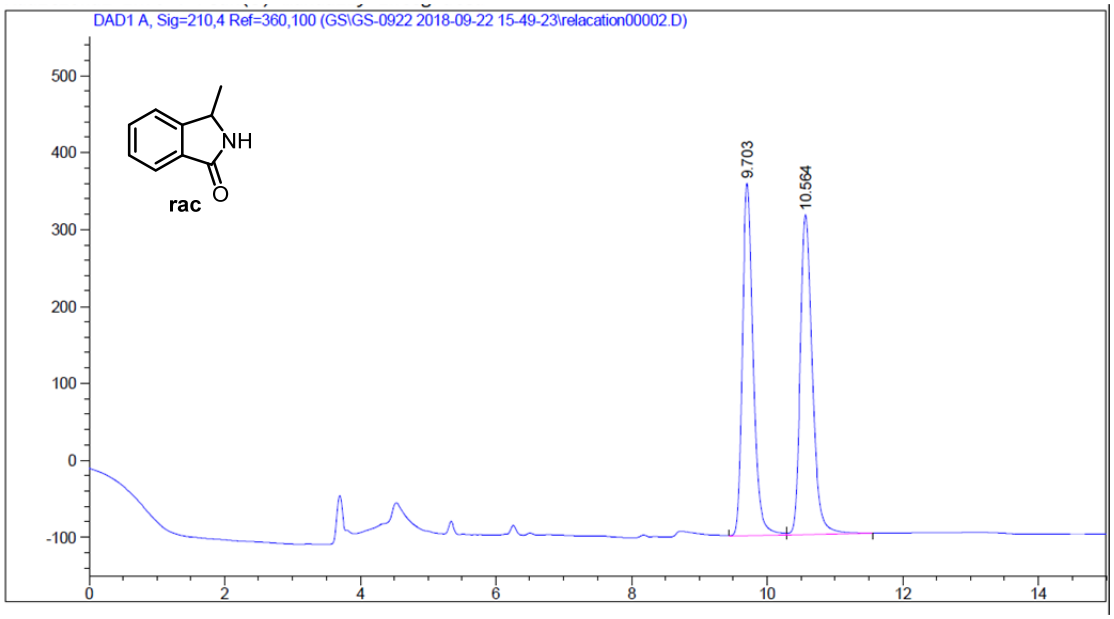
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.644	MF	0.2302	2105.64551	152.42691	49.3473
2	13.987	BB	0.2381	2161.34644	138.47665	50.6527



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

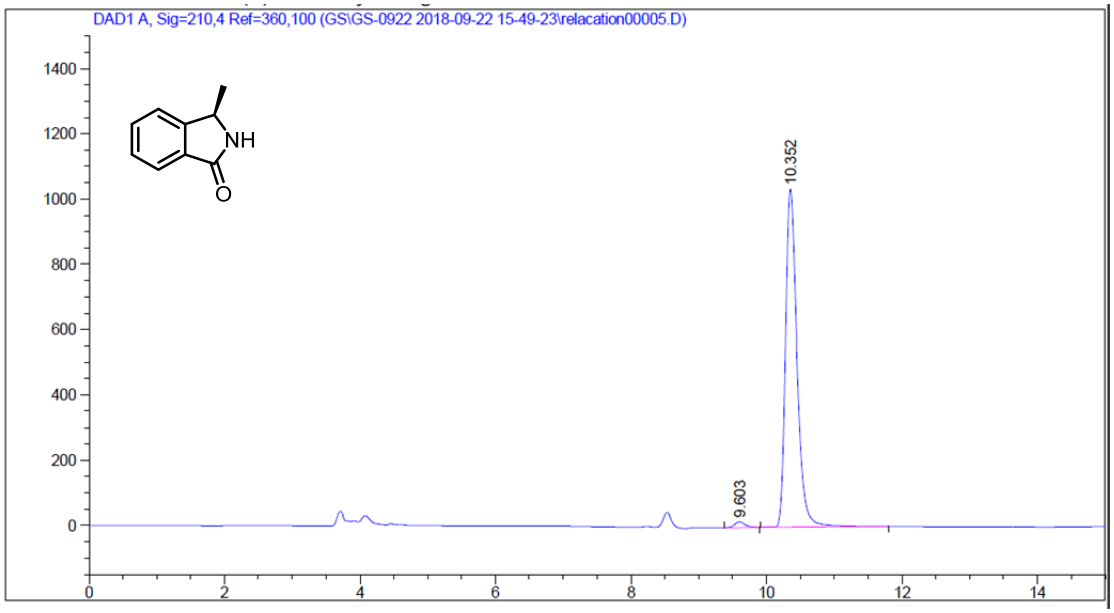
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.559	MM	0.2500	1.62702e4	1084.63574	95.2267
2	14.008	MM	0.2495	815.55859	54.47503	4.7733

(*R*)-3-methylisoindolin-1-one (6a)



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

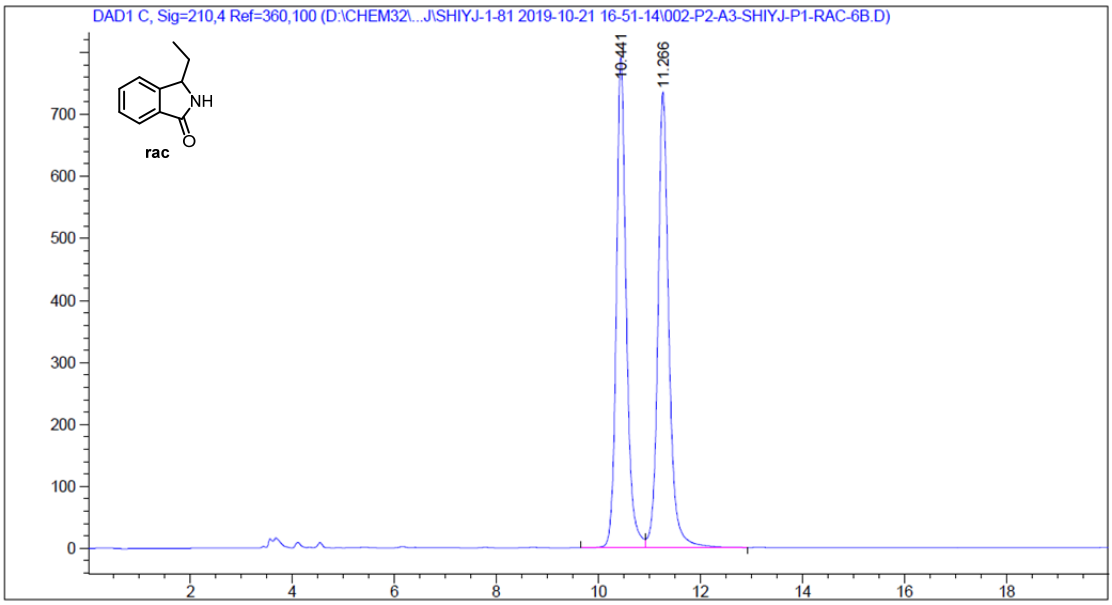
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.703	VV	0.1691	5070.63623	458.29245	49.6472
2	10.564	VB	0.1903	5142.70947	415.69778	50.3528
Totals :				1.02133e4	873.99023	



Signal 1: DAD1 A, Sig=210,4 Ref=360,100

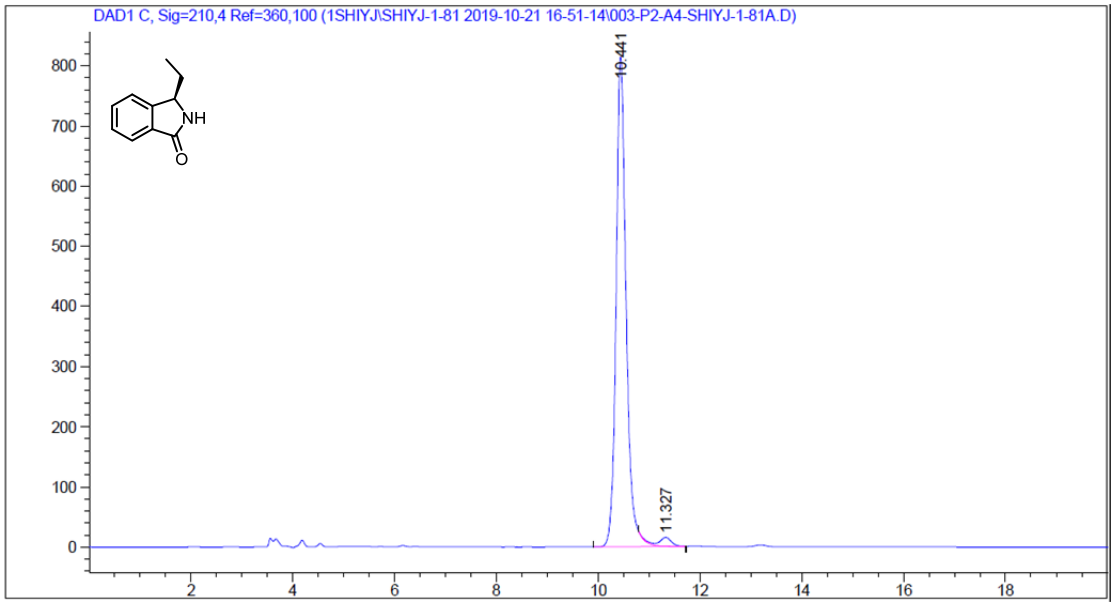
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.603	BB	0.1590	182.44847	17.59014	1.4867
2	10.352	BB	0.1781	1.20895e4	1036.08948	98.5133
Totals :				1.22720e4	1053.67962	

(*R*)-3-ethylisoindolin-1-one (6b)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

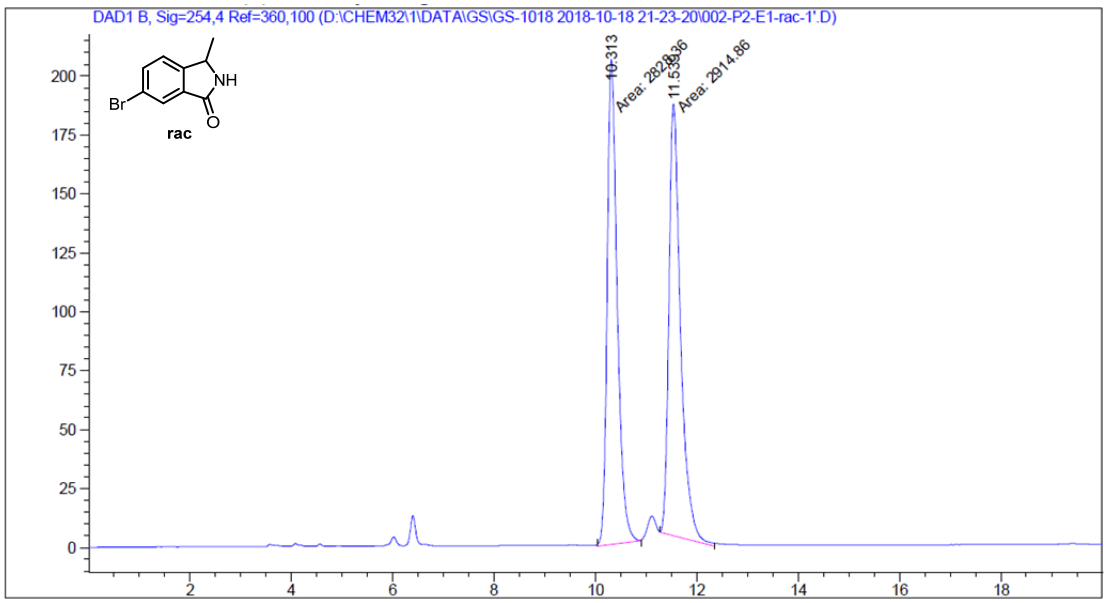
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.441	BV	0.2016	1.06822e4	790.89142	49.3118
2	11.266	VB	0.2224	1.09804e4	734.57422	50.6882



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

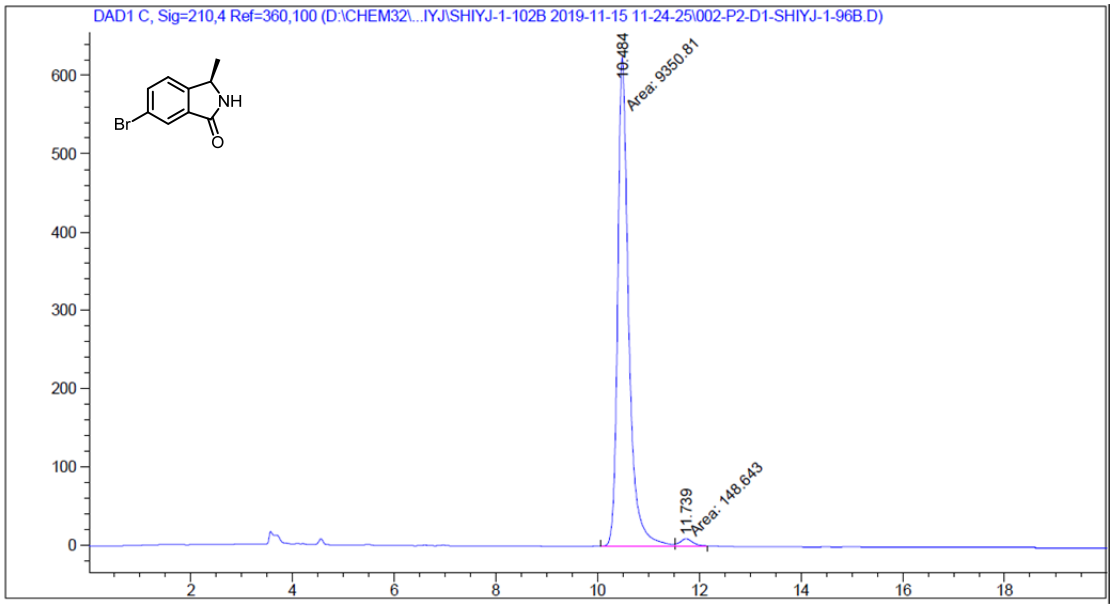
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.441	BV R	0.2056	1.11385e4	814.33008	97.7905
2	11.327	VB E	0.2501	251.66557	14.67115	2.2095

(*R*)-6-bromo-3-methylisoindolin-1-one (6c)



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

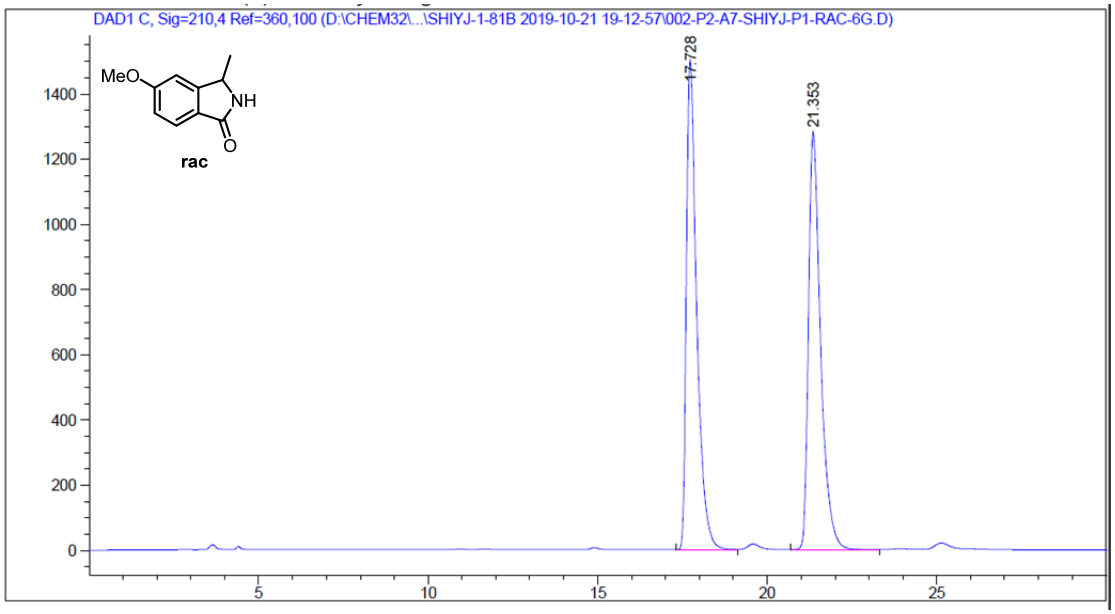
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.313	MM	0.2288	2828.36035	206.06406	49.2469
2	11.539	MM	0.2652	2914.86426	183.19814	50.7531



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

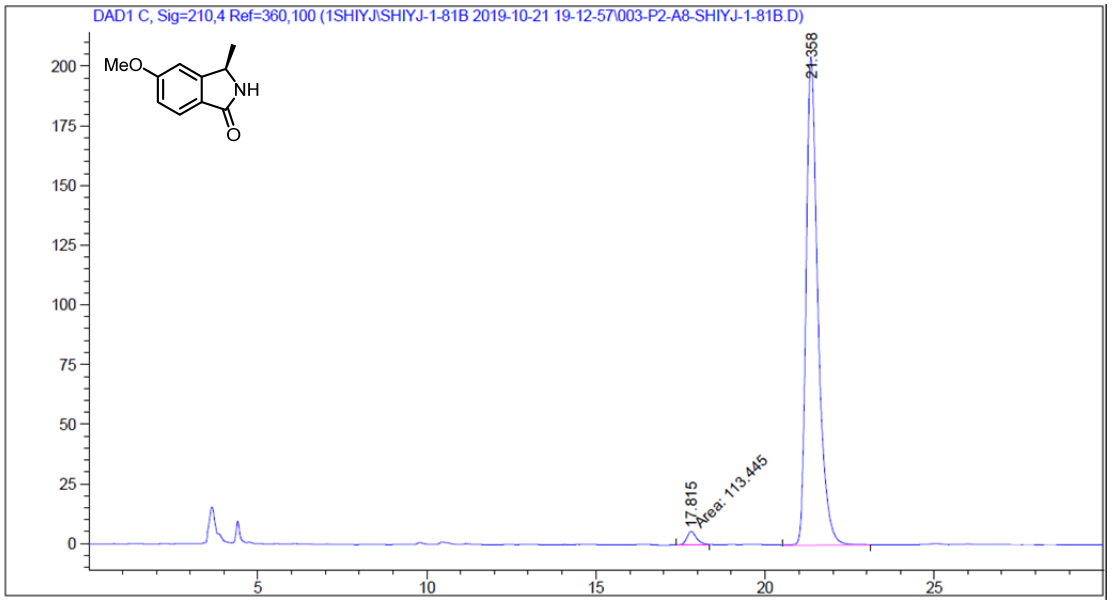
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.484	MM	0.2496	9350.80762	624.34955	98.4352
2	11.739	MM	0.2774	148.64319	8.93089	1.5648

(*R*)-5-methoxy-3-methylisoindolin-1-one (6d)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

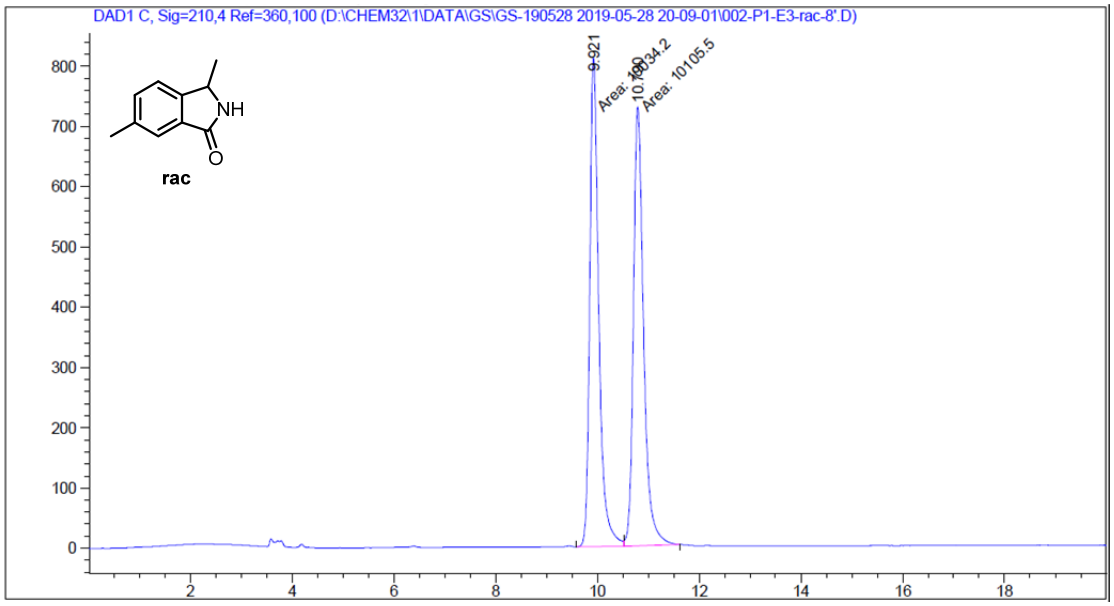
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.728	BB	0.3161	3.16365e4	1499.80432	49.9351
2	21.353	BB	0.3728	3.17188e4	1281.40247	50.0649



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

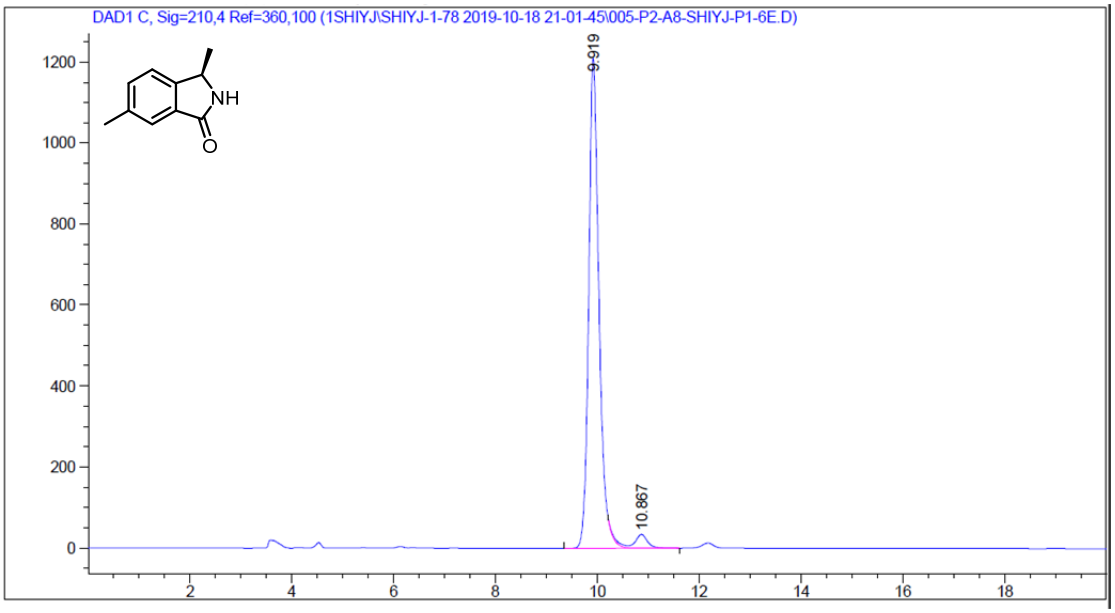
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.815	MM	0.3356	113.44519	5.63420	2.2347
2	21.358	BB	0.3631	4963.10889	204.51950	97.7653

(*R*)-3,6-dimethylisoindolin-1-one (6e)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

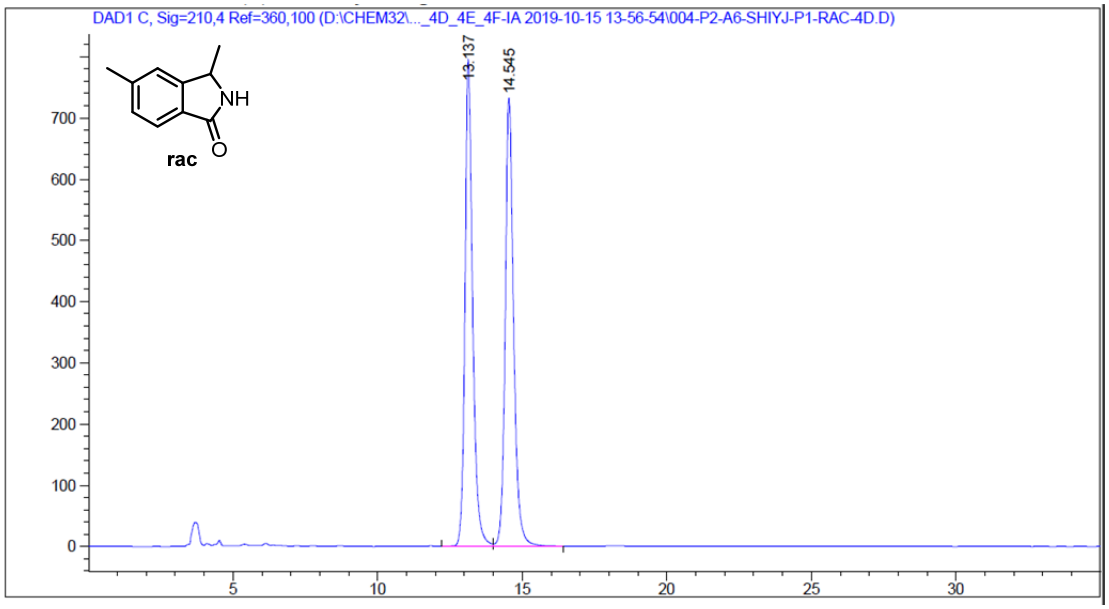
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.921	MM	0.2061	1.00342e4	811.38324	49.8232
2	10.790	MM	0.2312	1.01055e4	728.55713	50.1768



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

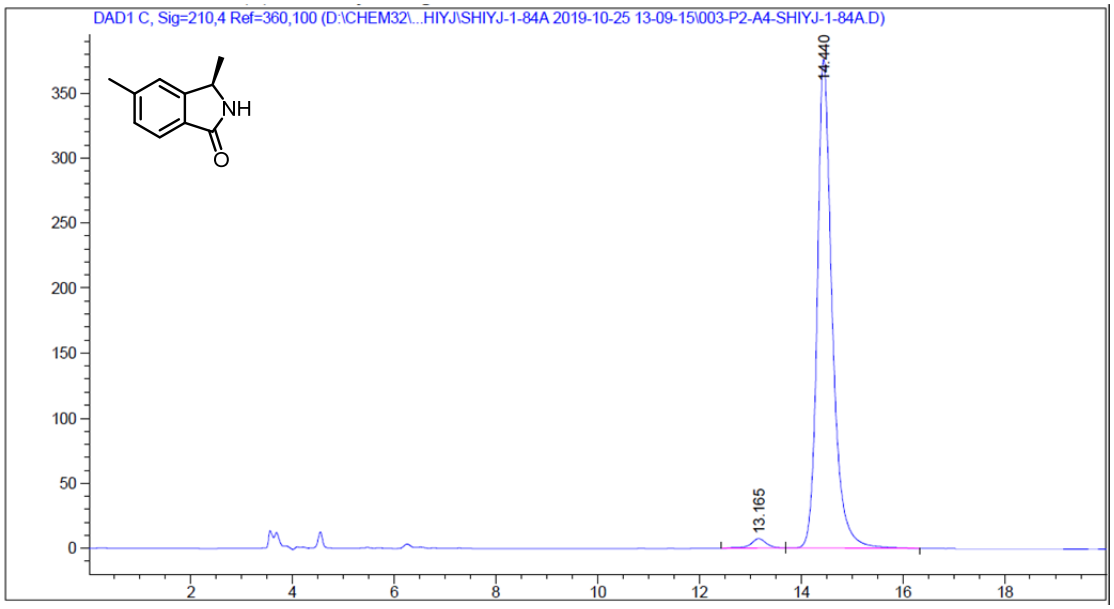
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.919	BV R	0.2124	1.70444e4	1209.87122	96.1716
2	10.867	VB E	0.2814	678.50201	34.50324	3.8284

(*R*)-3,5-dimethylisoindolin-1-one (6f)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

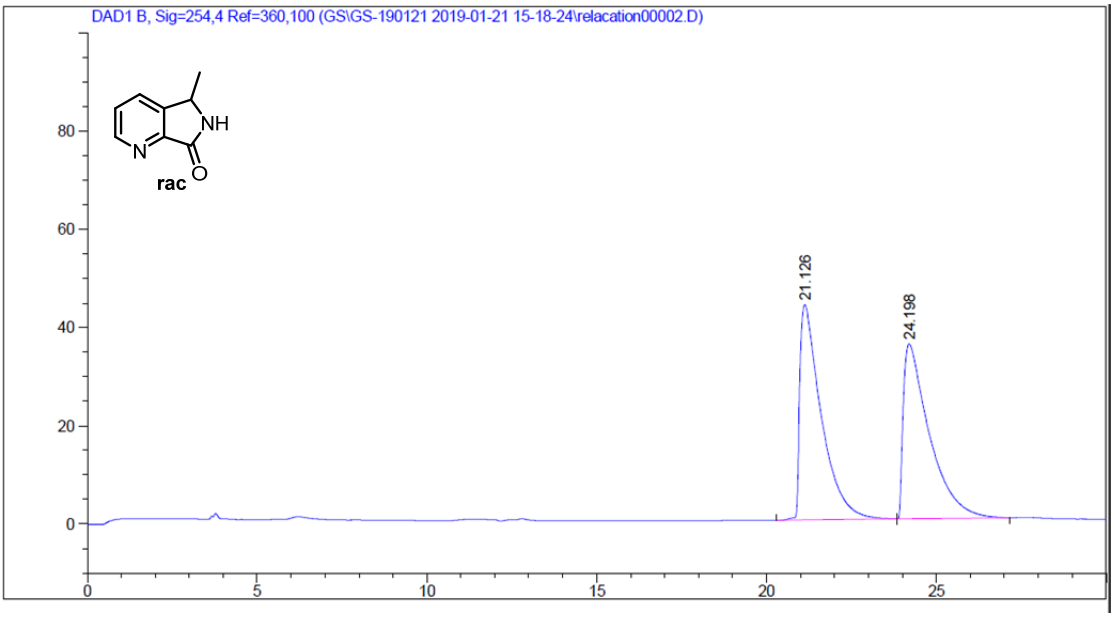
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.137	BV	0.2730	1.46834e4	796.67596	49.8430
2	14.545	VB	0.2992	1.47759e4	732.86377	50.1570



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

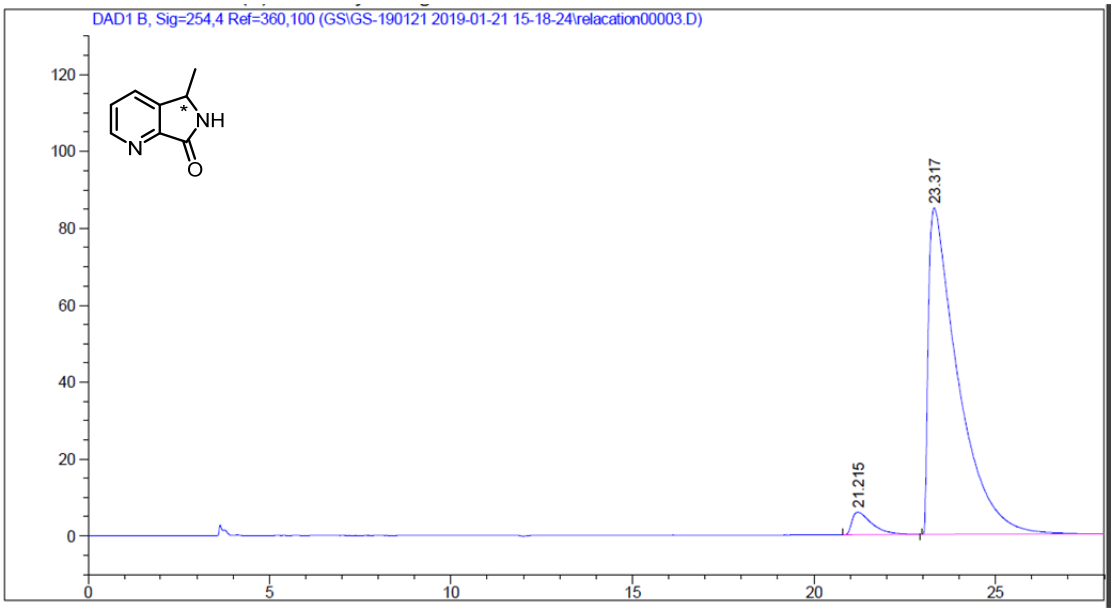
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.165	BB	0.3179	159.08031	7.31106	2.0285
2	14.440	BB	0.3024	7683.27051	376.04767	97.9715

(*R*)-5-methyl-5,6-dihydro-7H-pyrrolo[3,4-b]pyridin-7-one (6g)



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

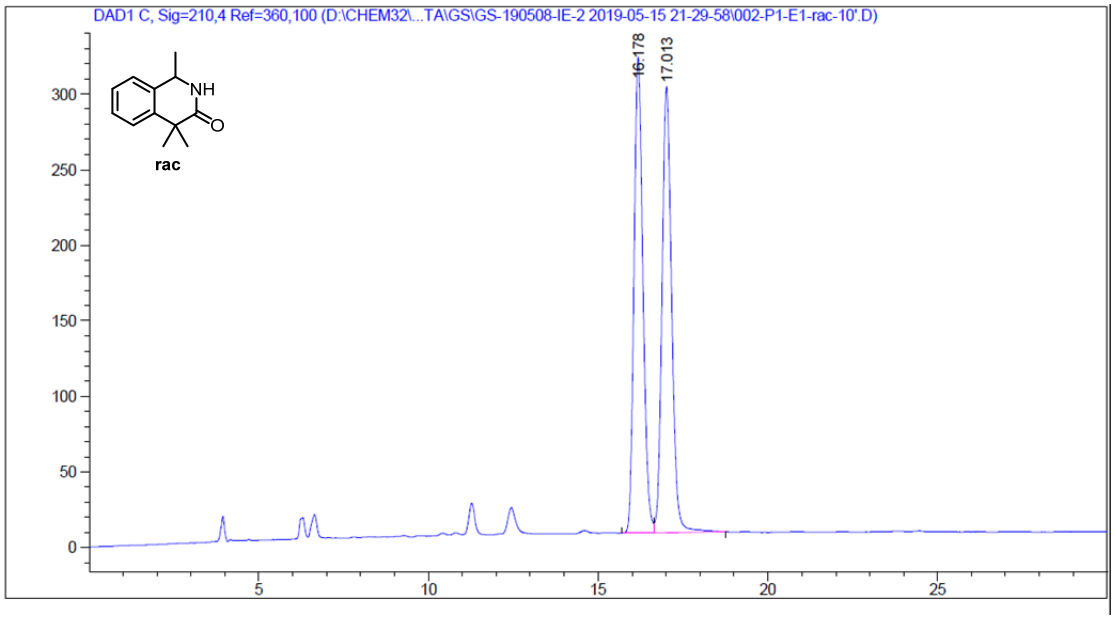
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.126	BB	0.6227	1927.79968	43.86827	50.4012
2	24.198	BB	0.7549	1897.10742	35.64874	49.5988
Totals :				3824.90710	79.51701	



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

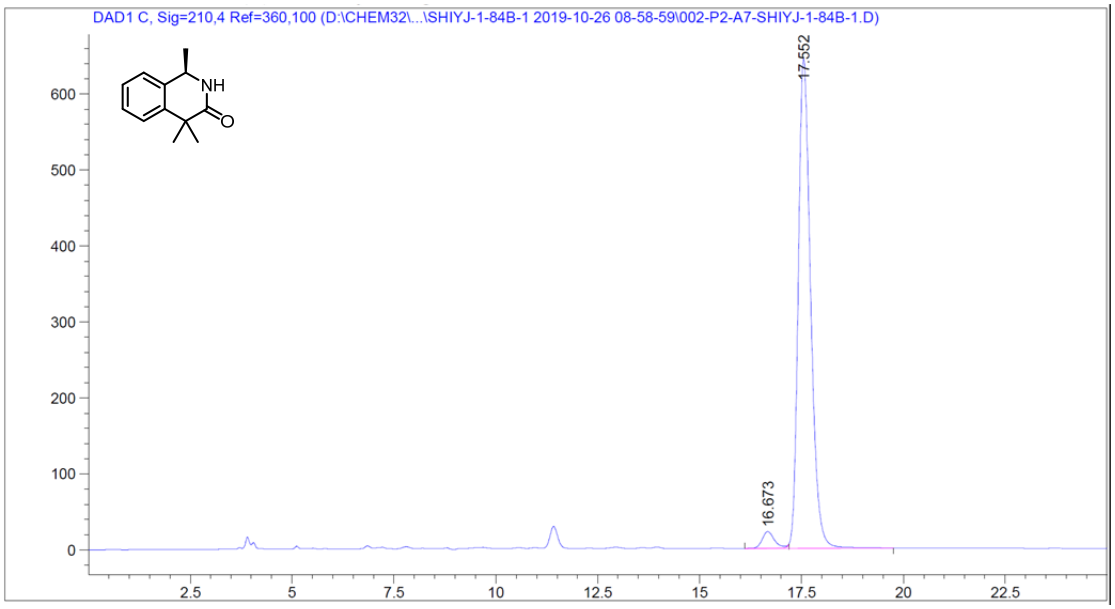
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.215	BB	0.5431	224.54185	5.88495	4.4507
2	23.317	BB	0.8003	4820.53076	84.91447	95.5493
Totals :				5045.07262	90.79942	

(*R*)-5-methyl-5,6-dihydro-7H-pyrrolo[3,4-b]pyridin-7-one (6g)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

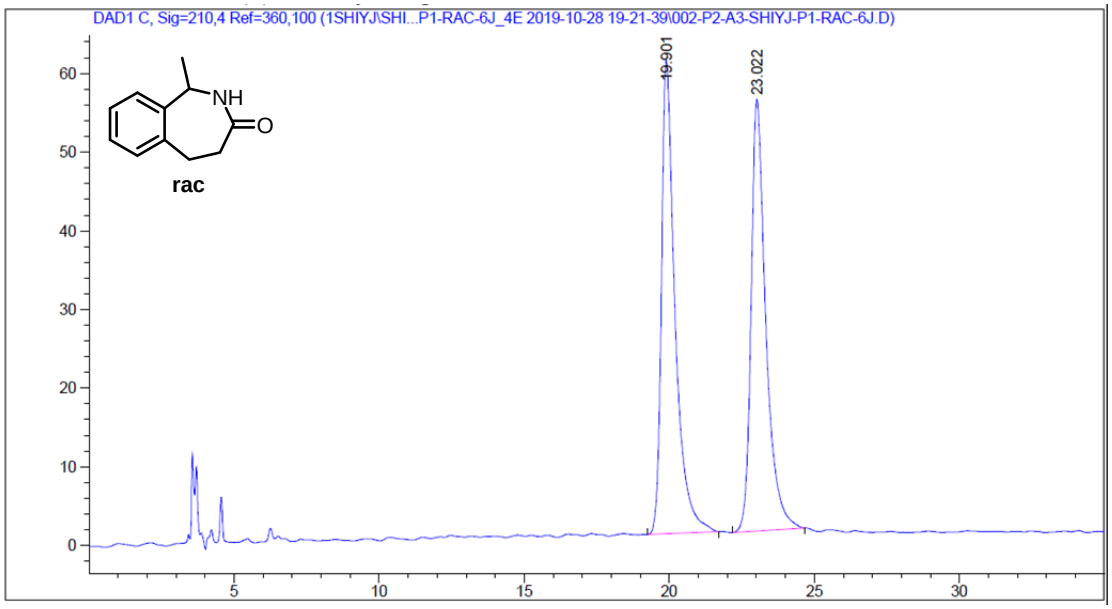
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.178	BV	0.2854	5756.21289	314.72772	49.7236
2	17.013	VB	0.3022	5820.21680	294.94183	50.2764



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

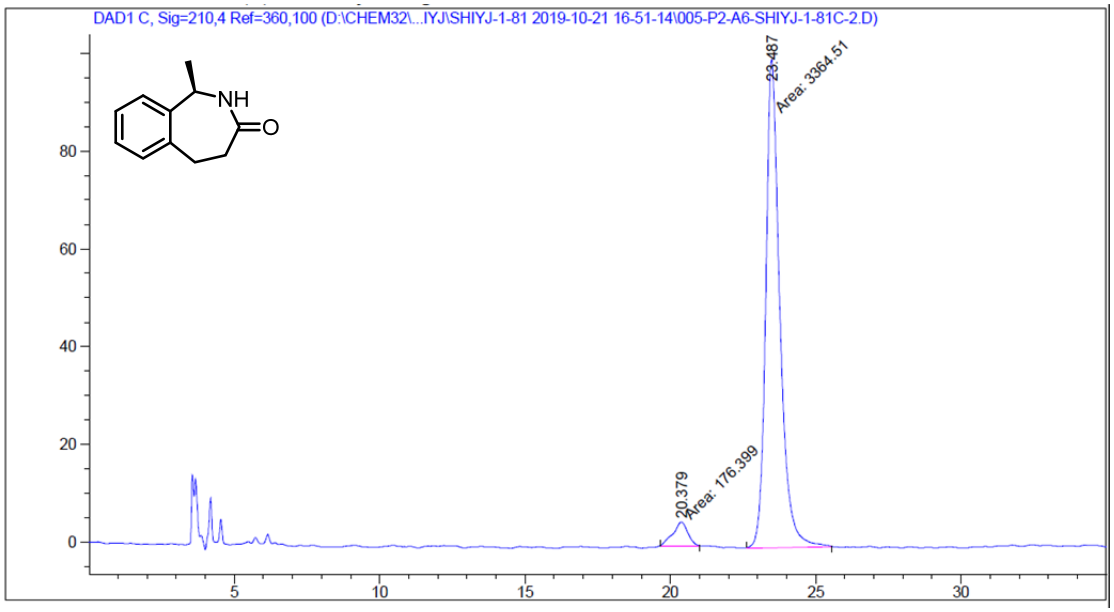
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.673	BV E	0.3154	455.74448	22.02495	3.2492
2	17.552	VB R	0.3238	1.35704e4	644.06665	96.7508

(*R*)-1-methyl-1,2,4,5-tetrahydro-3H-benzo[c]azepin-3-one (6i)



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

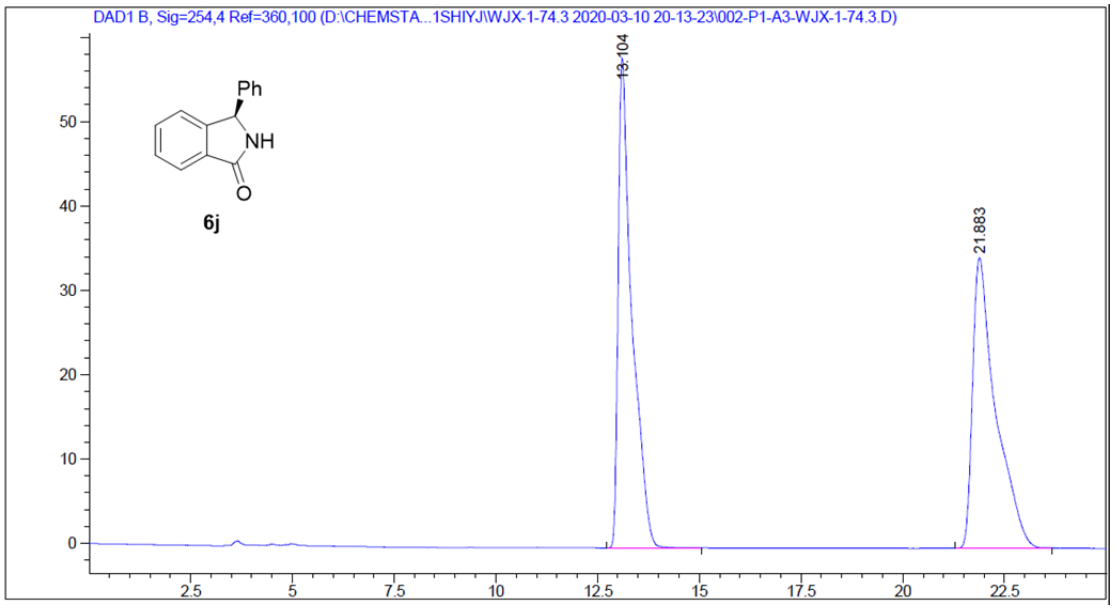
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.901	BB	0.4738	1962.32983	60.27996	50.3247
2	23.022	BB	0.5219	1937.00854	54.86320	49.6753



Signal 1: DAD1 C, Sig=210,4 Ref=360,100

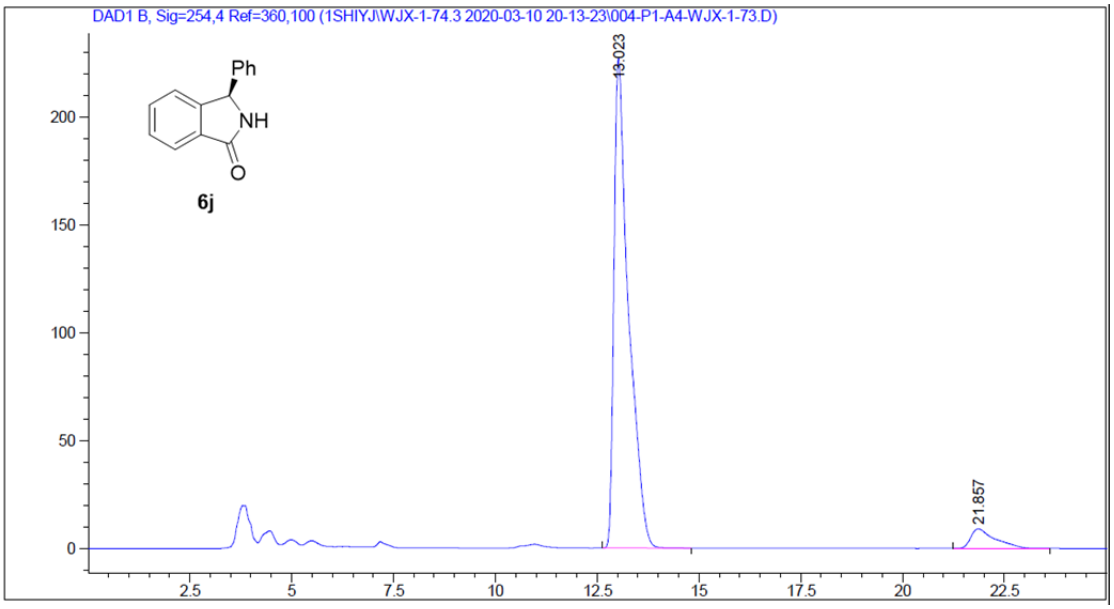
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.379	MM	0.6003	176.39909	4.89720	4.9817
2	23.487	MM	0.5607	3364.51318	100.01168	95.0183

(*R*)-3-phenylisoindolin-1-one (6j)



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.104	BB	0.3289	1368.53577	58.08244	50.1045
2	21.883	BB	0.5574	1362.82471	34.45839	49.8955
Totals :				2731.36047	92.54082	



Signal 1: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.023	BB	0.3543	5653.96777	227.23563	93.7530
2	21.857	BB	0.5816	376.73703	9.12721	6.2470