Electronic Supplementary Information

Photoredox organocatalytic α-amino C(sp^3)-H Functionalization for the synthesis of 5-membered heterocyclic γ-amino acid derivatives

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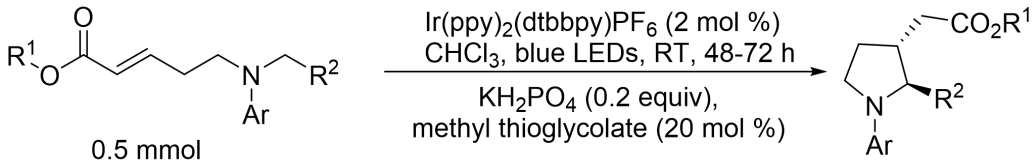
1. General information

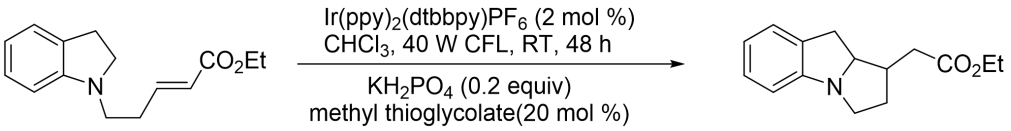
All reactions were carried out under argon atmosphere unless otherwise noted. Dry acetonitrile and dichloromethane was distilled from CaH_2. Dry tetrahydrofuran was distilled from Na. Other dry solvents were purchased from Sigma & Aldrich. Thin layer chromatography (TLC) was performed on silica coated glass plates (GF 254) with detection by UV (λ = 254 and 366 nm). Flash chromatography was performed on silica (200-300 mesh) with the indicated eluent mixtures. ^{1}H NMR, ^{13}C NMR spectra and ^{19}F NMR spectra were recorded on Bruker AVANCE 400 spectrometer. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane. Abbreviations for signal couplings are: s, singlet; d, doublet; t, triplet; m, multiplet. The relative configuration of product **2a** were determined by two-dimensional NMR spectra (COSY, HSQC, HMBC, NOESY). High resolution mass spectra were obtained using an Agilent 6210 Series TOF LC-MS equipped with electrospray ionization (ESI) probe operating in positive ion mode. Melting points (m.p.) were determined with a digital electrothermal apparatus without further correction.

2. General procedure and characterization of products



A 10 mL Schlenk-tube equipped with magnetic stirring bar was charged with substrate **1a-1u** (0.5 mmol), $Ir(ppy)_2(dtbbpy)PF_6$ (2 mol %), methyl thioglycolate (20 mol %), KH_2PO_4 (0.2 equiv), $CHCl_3$ (5 mL), the resulting mixture was evacuated and backfilled with argon by "pump-freeze-thaw" cycles (3 times). The tube was irradiated by a 5 W cyclized blue LED strip at room temperature for 48-72 hours (monitored by TLC). After complete， the reaction mixture was transferred to separating funnel, and 20 mL saturated brine was added and extracted with Et_2O (3× 5 mL). The combined organic layers was dried over Na_2SO_4 and purified by flash column chromatography using PE/EA as eluent to get single isomer or isomeric mixture. The dr value of crude mixture was determined by ^{1}H NMR.

Procedure for gram-scale experiments:

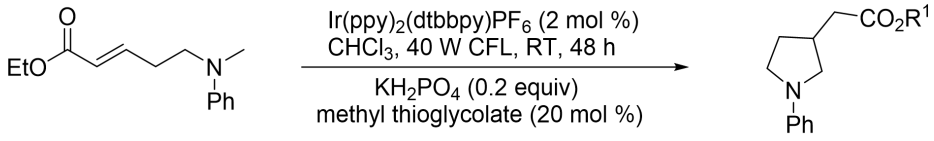


1.5 g, 6.1 mmol

1q

65% yield, 0.97 g

2q



1.7 g, 7.3 mmol

1p

71% yield, 1.2 g

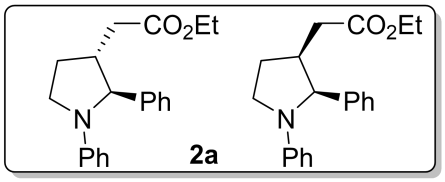
2p

A 100 mL Schlenk-tube equipped with magnetic stirring bar was charged with **1q** (6.1 mmol, 1.5 g) or **1p** (7.3 mmol, 1.7 g), $Ir(ppy)_2(dtbbpy)PF_6$ (2 mol %), methyl thioglycolate (20 mol %), KH_2PO_4 (0.2 equiv), $CHCl_3$ (50 mL), the resulting mixture was evacuated and backfilled with argon by "pump-freeze-thaw" cycles (3 times). The tube was irradiated by two 40 W CFL at room temperature for 48 hours (monitored by TLC). The solid was filter out and the solvent was evaporated in vacuum. The crude product was purified by flash column chromatography using petrol ether/ethyl acetate as eluent to get **2q (**0.97 g, 65% yield) or **2p** (1.2 g, 71% yield).

Characterization Data of Products

The following characterization of coumpound **2** are almost *trans*-isomers obtained by flash coclumn chromatography. We afforded the NMR and HRMS datas of *cis* and *trans*-**2a** as an example. It's important to note that some desired products were isomeric mixture which couldn't be separated during the purification process, so we just gave the characterization data of mixture targets.

ethyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2a)**

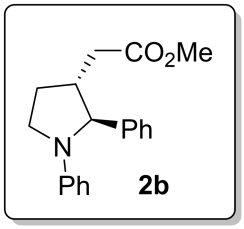


2a

Total yield of trans and cis isomers: 72%, 48 h, dr = 7:1 (the isomers were separated during the purification process). *trans*-**2a:** clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 4H), 7.23 – 7.19 (m, 1H), 7.15 – 7.10 (m, 2H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 2H), 4.46 (d, *J* = 2.6 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.71 (td, *J* = 8.8, 3.4 Hz, 1H), 3.58 – 3.50 (m, 1H), 2.67 – 2.60 (m, 1H), 2.56 (dd, *J* = 15.6, 8.0 Hz, 1H), 2.38 (dd, *J* = 15.6, 6.5 Hz, 1H), 2.31 – 2.21 (m, 1H), 1.78 – 1.70 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 146.9, 143.2, 129.0, 128.6, 126.9, 126.1, 116.0, 112.5, 68.1, 60.6, 47.6, 45.1, 38.0, 28.4, 14.3. HRMS (ESI) m/z calcd for $C_{20}H_{24}NO_2$ $[M+H]^+$: 310.1802, found 310.1802. *cis*-**2a:** clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 7.17 – 7.09 (m, 4H), 6.61 (t, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 2H), 4.79 (d, *J* = 8.1 Hz, 1H), 4.18 – 4.05 (m, 2H), 3.73 (t, *J* = 8.5 Hz, 1H), 3.49 – 3.42 (m, 1H), 2.94 (hept, *J* = 6.9 Hz, 1H), 2.18 (dt, *J* = 12.2, 6.1 Hz, 1H), 2.05 (dd, *J* = 16.5, 7.2 Hz, 1H), 1.95 – 1.83 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 146.7,

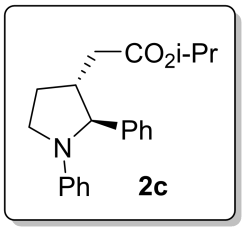
140.9, 129.0, 128.5, 127.3, 127.3, 115.9, 112.0, 65.3, 60.4, 47.8, 40.0, 35.6, 28.8, 14.3. HRMS (ESI) m/z calcd for C20H24NO2 $[M+H]^+$: 310.1802, found 310.1801.

(trans)-methyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2b**)



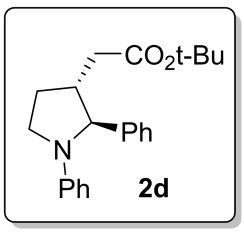
Total yield of trans and cis isomers: 65%, 48 h, dr =7:1. *trans*-**2b:** clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.18 (m, 4H), 7.17 – 7.12 (m, 1H), 7.09 – 7.02 (m, 2H), 6.56 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 2H), 4.38 (d, *J* = 2.5 Hz, 1H), 3.61 (s, 4H), 3.51 – 3.43 (m, 1H), 2.60 – 2.47 (m, 2H), 2.33 (dd, *J* = 15.3, 6.2 Hz, 1H), 2.24 – 2.14 (m, 1H), 1.70 – 1.62 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 145.8, 142.0, 127.9, 127.5, 125.9, 125.0, 114.9, 111.4, 67.0, 50.6, 46.5, 44.0, 36.6, 27.3. HRMS (ESI) m/z calcd for $C_{19}H_{22}NO_2$ $[M+H]^+$: 296.1645, found 296.1650.

isopropyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2c**)



Total yield of trans and cis isomers: 76%, 48 h, dr = 5:1. *trans*-**2c:** clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 4H), 7.24 – 7.19 (m, 1H), 7.16 – 7.11 (m, 2H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 7.9 Hz, 2H), 5.04 (hept, *J* = 6.09 Hz, 1H), 4.46 (d, *J* = 2.7 Hz, 1H), 3.71 (td, *J* = 8.7, 3.3 Hz, 1H), 3.59 – 3.49 (m, 1H), 2.66 – 2.59 (m, 1H), 2.54 (dd, *J* = 15.7, 8.1 Hz, 1H), 2.35 (dd, *J* = 15.7, 6.7 Hz, 1H), 2.29 – 2.21 (m, 1H), 1.77 – 1.68 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 146.9, 143.2, 129.0, 128.6, 126.9, 126.1, 115.9, 112.4, 68.1, 68.0, 47.5, 45.1, 38.3, 28.3, 21.9, 21.9. HRMS (ESI) m/z calcd for $C_{21}H_{26}NO_2$ $[M+H]^+$: 324.1958, found 324.1960.

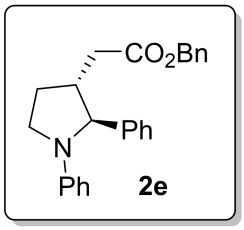
tert-butyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2d**)



Total yield of trans and cis isomers: 82%, 48 h, dr =5:1. *trans*-**2d:** clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.18 (m, 4H), 7.16 – 7.11 (m, 1H), 7.08 – 7.03 (m, 2H), 6.55 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 2H), 4.37 (d, *J* = 2.7 Hz, 1H), 3.63 (td, *J* = 8.7, 3.3 Hz, 1H), 3.49 – 3.42 (m, 1H), 2.56 – 2.48 (m, 1H), 2.41 (dd, *J* = 15.6, 8.0 Hz, 1H), 2.26 – 2.14 (m, 2H), 1.69 – 1.61 (m, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 145.9, 142.2, 127.9, 127.5, 125.8, 125.1, 114.8, 111.3, 79.6,

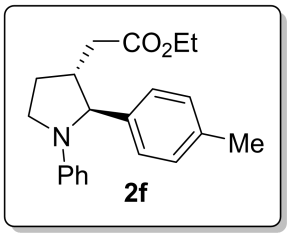
67.0, 46.5, 44.2, 38.1, 27.2, 27.1. HRMS (ESI) m/z calcd for $C_{22}H_{28}NO_2$ $[M+H]^+$: 338.2115, found 338.2115.

benzyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2e**)



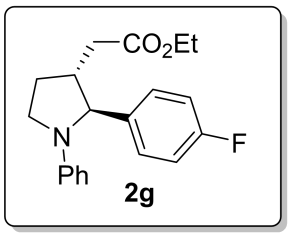
Total yield of trans and cis isomers: 66%, 48 h, dr =6:1. *trans*-**2e**: clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 5H), 7.29 – 7.24 (m, 2H), 7.22 – 7.19 (m, 3H), 7.15 – 7.10 (m, 2H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.45 (d, *J* = 7.8 Hz, 2H), 5.13 (s, 2H), 4.45 (d, *J* = 2.1 Hz, 1H), 3.74 – 3.67 (m, 1H), 3.57 – 3.49 (m, 1H), 2.65 – 2.57 (m, 2H), 2.49 – 2.40 (m, 1H), 2.31 – 2.19 (m, 1H), 1.76 – 1.68 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 146.9, 143.1, 135.8, 129.0, 128.6, 128.5, 128.4, 128.4, 126.9, 126.1, 116.0, 112.4, 68.0, 66.5, 47.5, 45.1, 37.98, 28.3. HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_2$ $[M+H]^+$: 372.1958, found 372.1954.

ethyl 2-(1-phenyl-2-(p-tolyl)pyrrolidin-3-yl)acetate (**2f**)



Total yield of trans and cis isomers: 79%, 48 h, dr =4:1. *trans*-**2f**: clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 – 7.08 (m, 6H), 6.65 – 6.59 (m, 1H), 6.49 – 6.44 (m, 2H), 4.42 (d, *J* = 2.4 Hz, 1H), 4.18 – 4.11 (m, 2H), 3.73 – 3.67 (m, 1H), 3.57 – 3.49 (m, 1H), 2.64 – 2.52 (m, 2H), 2.37 (dd, *J* = 15.2, 6.3 Hz, 1H), 2.31 (s, 3H), 2.29 – 2.20 (m, 1H), 1.76 – 1.68 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 147.0, 140.1, 136.4, 129.2, 129.0, 126.0, 115.8, 112.4, 68.0, 60.5, 47.5, 45.2, 38.0, 28.3, 21.1, 14.3. HRMS (ESI) m/z calcd for $C_{21}H_{26}NO_2$ $[M+H]^+$: 324.1958, found 324.1961.

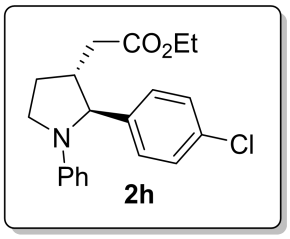
ethyl 2-(2-(4-fluorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2g**)



Total yield of trans and cis isomers: 65%, 48 h, dr =4:1. *trans*-**2g:** yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.21 (m, 2H), 7.17 – 7.10 (m, 2H), 6.97 (t, *J* = 8.7 Hz, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.45 (d, *J* = 7.9 Hz, 2H), 4.44 (d, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.71 (td, *J* = 8.7, 3.3 Hz, 1H), 3.57 – 3.48 (m, 1H), 2.63 – 2.50 (m, 2H), 2.38 (dd, *J* = 15.3, 5.7 Hz, 1H), 2.29 – 2.19 (m, 1H), 1.77 – 1.70

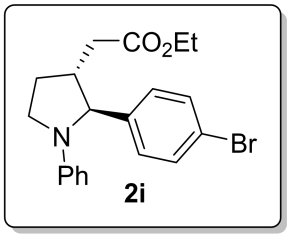
(m, 1H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 161.9 (d, J = 244.6 Hz), 146.8, 138.8 (d, J = 2.9 Hz), 129.0, 127.6 (d, J = 7.9 Hz), 116.2, 115.4 (d, J = 21.4 Hz), 112.5, 67.5, 60.6, 47.5, 45.1, 37.8, 28.3, 14.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.21. HRMS (ESI) m/z calcd for $C_{20}H_{23}FNO_2$ $[M+H]^+$: 328.1707, found 328.1707.

ethyl 2-(2-(4-chlorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2h**)



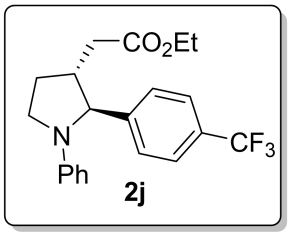
Total yield of trans and cis isomers: 65%, 48 h, dr =5:1. *trans*-**2h**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.20 (m, 5H), 7.17 – 7.10 (m, 2H), 6.65 (t, J = 7.5 Hz, 1H), 6.44 (d, J = 8.0 Hz, 2H), 4.44 (s, 1H), 4.18 – 4.11 (m, 2H), 3.70 (td, J = 8.3, 2.1 Hz, 1H), 3.57 – 3.48 (m, 1H), 2.63 – 2.49 (m, 2H), 2.38 (dd, J = 14.2, 5.8 Hz, 1H), 2.28 – 2.17 (m, 1H), 1.79 – 1.69 (m, 1H), 1.28 – 1.23 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 146.7, 141.8, 132. 6, 129.1, 128.7, 127. 6, 116.3, 112.5, 67.5, 60.6, 47.5, 45.0, 37.8, 28.3, 14.3. HRMS (ESI) m/z calcd for $C_{20}H_{23}ClNO_2$ $[M+H]^+$: 344.1412, found 344.1412.

ethyl 2-(2-(4-bromophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2i**)



Total yield of trans and cis isomers: 66%, 48 h, dr =4:1. *trans*-**2i**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (d, J = 8.3 Hz, 2H), 7.20 – 7.10 (m, 4H), 6.65 (t, J = 7.3 Hz, 1H), 6.44 (d, J = 8.1 Hz, 2H), 4.42 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.70 (td, J = 8.7, 3.1 Hz, 1H), 3.56 – 3.48 (m, 1H), 2.62 – 2.49 (m, 2H), 2.38 (dd, J = 15.2, 5.5 Hz, 1H), 2.27 – 2.17 (m, 1H), 1.77 – 1.69 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 146.7, 142.3, 131.7, 129.1, 128.0, 120.7, 116.3, 112.5, 67.6, 60.6, 47.5, 45.0, 37.8, 28.3, 14.3. HRMS (ESI) m/z calcd for $C_{20}H_{23}BrNO_2$ $[M+H]^+$: 388.0907, found 388.0908.

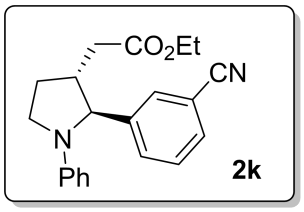
ethyl 2-(1-phenyl-2-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)acetate (**2j**)



Total yield of trans and cis isomers: 66%, 72 h, dr =4:1. *trans*-**2j**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.1 Hz, 2H), 7.15 (dd, J = 8.6, 7.3 Hz, 2H), 6.67

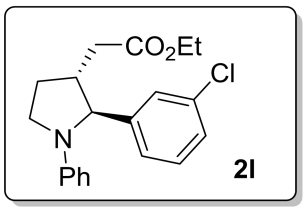
(t, *J* = 7.3 Hz, 1H), 6.44 (d, *J* = 7.9 Hz, 2H), 4.53 (d, *J* = 1.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.78 – 3.70 (m, 1H), 3.60 – 3.51 (m, 1H), 2.66 – 2.52 (m, 2H), 2.41 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.30 – 2.17 (m, 1H), 1.81 – 1.70 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4 , 147.5 , 146.6 , 129.1 , 126.5 , 125.6 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 270.1 Hz), 117.1 (q, *J* = 10.6 Hz), 116.4 , 112.4 , 67.7 , 60.7 , 47.5 , 44.9 , 37.9 , 28.3 , 14.2. HRMS (ESI) m/z calcd for $C_{21}H_{23}F_3NO_2$ $[M+H]^+$: 378.1675, found 378.1679.

ethyl 2-(2-(3-cyanophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2k**)



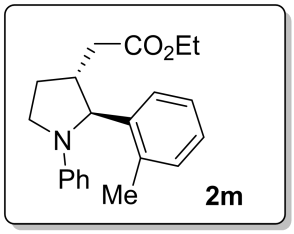
Total yield of trans and cis isomers: 48%, 72 h, dr =4:1. *trans*-**2k**: clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.18 – 7.14 (m, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.43 (d, *J* = 7.9 Hz, 2H), 4.51 (d, *J* = 1.6 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.77 – 3.72 (m, 1H), 3.58 – 3.50 (m, 1H), 2.64 – 2.50 (m, 2H), 2.41 (dd, *J* = 15.7, 5.2 Hz, 1H), 2.25 – 2.18 (m, 1H), 1.81 – 1.73 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 146.4, 145.1, 130.8, 130.8, 129.8, 129.4, 129.2, 119.0, 116.7, 112.5, 112.1, 67.5, 60.8, 47.5, 44.8, 37.8, 28.2, 14.2. HRMS (ESI) m/z calcd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$: 335.1754, found 335.1752.

ethyl 2-(2-(3-chlorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2l**)



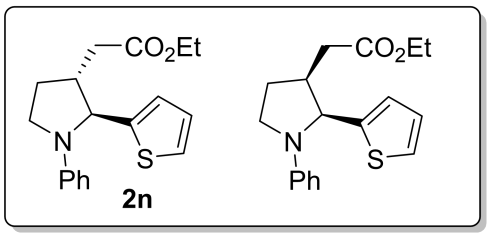
Total yield of trans and cis isomers: 54%, 72 h, dr = 3.8:1. *trans*-**2l**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.11 (m, 7H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 7.9 Hz, 2H), 4.43 (d, *J* = 2.4 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.72 (td, *J* = 8.7, 3.1 Hz, 1H), 3.57 – 3.48 (m, 1H), 2.64 – 2.49 (m, 2H), 2.39 (dd, *J* = 15.8, 6.2 Hz, 1H), 2.30 – 2.18 (m, 1H), 1.79 – 1.69 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 146.7, 145.7, 134.5, 129.9, 129.1, 127.2, 126.2, 124.3, 116.3, 112.5, 67. 8, 60.7, 47.5, 45.0, 38.0, 28.3, 14.3. HRMS (ESI) m/z calcd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$: 335.1754, found 335.1752.

ethyl 2-(1-phenyl-2-(o-tolyl)pyrrolidin-3-yl)acetate (**2m**)



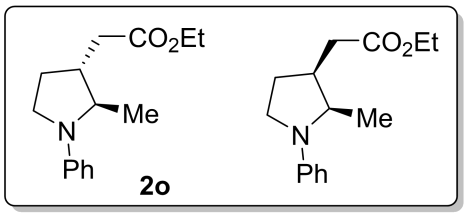
Total yield of trans and cis isomers: 68%, 48 h, dr = 5:1. *trans*-**2m**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 – 7.17 (m, 1H), 7.15 – 7.10 (m, 3H), 7.09 – 7.04 (m, 1H), 7.02 – 6.99 (m, 1H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 2H), 4.57 (s, 1H), 4.15 – 4.06 (m, 2H), 3.70 (td, *J* = 8.9, 2.3 Hz, 1H), 3.57 (td, *J* = 9.5, 6.9 Hz, 1H), 2.62 – 2.53 (m, 2H), 2.47 – 2.39 (m, 4H), 2.32 – 2.21 (m, 1H), 1.86 – 1.79 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 146.5, 140.6, 134.6, 130.8, 129.1, 126.9, 126.2, 125.7, 115.9, 112.1, 65.8, 60.6, 46.9, 43.3, 38.4, 27.7, 19.5, 14.2. HRMS (ESI) m/z calcd for $C_{21}H_{26}NO_2$ $[M+H]^+$: 324.1958, found 324.1958.

ethyl 2-(1-phenyl-2-(thiophen-2-yl)pyrrolidin-3-yl)acetate (**2n**)



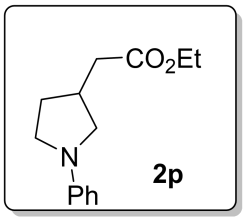
Total yield of trans and cis isomers: 54%, 48 h, dr =2:1(the isomers couldn't be separated during the purification process). *trans*-**2n**: brown oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 – 7.11 (m, 3H), 6.98 – 6.85 (m, 2H), 6.71 – 6.63 (m, 1H), 6.60 – 6.54 (m, 2H), 5.15 – 4.68 (m, 1H), 4.19 – 4.10 (m, 2H), 3.72 – 3.62 (m, 1H), 3.51 – 3.31 (m, 1H), 2.92 – 2.68 (m, 1H), 2.59 – 2.34 (m, 2H), 2.22 – 1.73 (m, 2H), 1.30 – 1.22 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 172.3, 148.5, 146.9, 146.8, 146.1, 129.0, 129.0, 126.9, 126.9, 124.5, 124.4, 123.8, 123.4, 116.5, 116.4, 112.6, 112.0, 64.4, 61.4, 60.6, 60.5, 47.3, 47.2, 45.4, 40.0, 37.7, 35.2, 28.7, 28.6, 14.3, 14.3. HRMS (ESI) m/z calcd for $C_{18}H_{22}NO_2S$ $[M+H]^+$: 316.1366, found 316.1369.

ethyl 2-(2-methyl-1-phenylpyrrolidin-3-yl)acetate (**2o**)



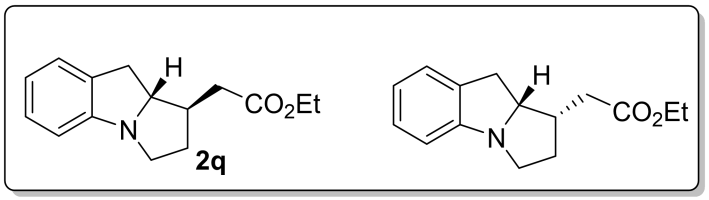
Total yield of trans and cis isomers: 54%, 50 h, dr =3:1(the isomers couldn't be separated during the purification process). *trans*-**2o:** yellow oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.21 (dd, *J* = 8.7, 7.2 Hz, 2H), 6.64 (q, *J* = 6.8, 6.3 Hz, 1H), 6.56 (d, *J* = 8.5 Hz, 2H), 4.15 (dq, *J* = 16.0, 7.1 Hz, 2H), 4.04 – 3.93 (m, 0H), 3.59 (dd, *J* = 6.2, 1.8 Hz, 1H), 3.45 – 3.14 (m, 2H), 2.70 – 2.03 (m, 4H), 1.88 – 1.66 (m, 1H), 1.30 – 1.20 (m, 5H), 1.02 (d, *J* = 6.4 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 172.5, 147.0, 146.7, 129.3, 129.2, 115.4, 115.2, 112.0, 111.3, 60.5, 60.5, 59.1, 55.1, 46.5, 46.3, 42.1, 38.6, 38.4, 34.9, 28.7, 28.4, 18.8, 14.3, 14.3, 13.3. HRMS (ESI) m/z calcd for $C_{15}H_{22}NO_2$ $[M+H]^+$: 248.1645, found 248.1646.

ethyl 2-(1-phenylpyrrolidin-3-yl)acetate (**2p**)



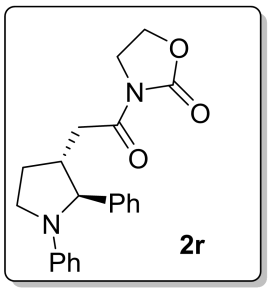
Yield: 68%, 48 h, clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.18 (m, 2H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.52 (dd, *J* = 9.2, 7.3 Hz, 1H), 3.42 – 3.25 (m, 2H), 2.98 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.79 – 2.65 (m, 1H), 2.46 (d, *J* = 7.4 Hz, 2H), 2.27 – 2.15 (m, 1H), 1.77 – 1.64 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 147.7, 129.2, 115.7, 111.6, 60.5, 53.1, 47.1, 38.4, 35.1, 31.4, 14.3. HRMS (ESI) m/z calcd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1489, found 234.1489.

ethyl 2-(2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]indol-1-yl)acetate (**2q**)



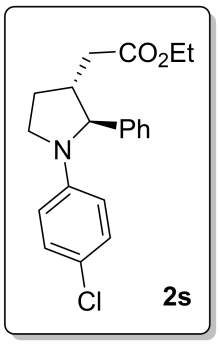
Total yield of trans and cis isomers: 74%, 48 h, dr =1.5:1(the isomers couldn't be separated during the purification process), *trans*-**2q**: brown oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 – 6.97 (m, 2H), 6.78 – 6.67 (m, 1H), 6.60 – 6.52 (m, 1H), 4.16 – 4.08 (m, 2H), 3.61 – 2.90 (m, 5H), 2.61 – 2.43 (m, 1H), 2.34 – 2.20 (m, 1H), 2.16 – 1.79 (m, 2H), 1.71 – 1.56 (m, 1H), 1.29 – 1.15 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 172.4, 154.6, 154.6, 130.3, 129.2, 127.7, 127.7, 124.9, 124.1, 119.5, 119.4, 110.6, 110.0, 70.2, 67.1, 60.5, 60.4, 51.9, 50.7, 40.1, 37.7, 36.8, 33.7, 32.8, 32.6, 31.7, 30.1, 14.3, 14.2. HRMS (ESI) m/z calcd for $C_{15}H_{20}NO_2$ $[M+H]^+$: 246.1489, found 246.1486.

3-(2-(1,2-diphenylpyrrolidin-3-yl)acetyl)oxazolidin-2-one (**2r**)



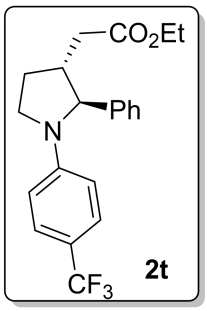
Total yield of trans and cis isomers: 54%, 48 h, dr =4:1. *trans*-**2r**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.26 (m, 4H), 7.24 – 7.18 (m, 1H), 7.16 – 7.09 (m, 2H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 7.9 Hz, 2H), 4.53 (d, *J* = 2.4 Hz, 1H), 4.36 (t, *J* = 8.1 Hz, 2H), 3.99 (t, *J* = 8.1 Hz, 2H), 3.71 (td, *J* = 8.8, 3.0 Hz, 1H), 3.64 – 3.53 (m, 1H), 3.16 (dd, *J* = 17.7, 8.2 Hz, 1H), 3.03 (dd, *J* = 17.7, 6.2 Hz, 1H), 2.77 – 2.67 (m, 1H), 2.35 – 2.23 (m, 1H), 1.83 – 1.71 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 153.5, 146.9, 143.3, 129.0, 128.5, 126.9, 126.2, 115.9, 112.4, 68.0, 62.1, 47.4, 44.3, 42.5, 39.1, 28.2. HRMS (ESI) m/z calcd for $C_{21}H_{22}N_2NaO_3$ $[M+Na]^+$: 373.1523, found 373.1526.

ethyl 2-1-(4-chlorophenyl)-2-phenylpyrrolidin-3-yl)acetate (**2s**)



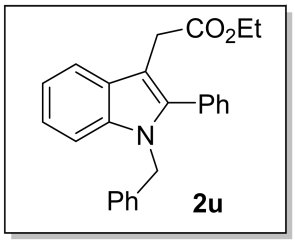
Total yield of trans and cis isomers: 54%, 48 h, dr =6.7:1. *trans*-**2s**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.36 (d, *J* = 8.9 Hz, 2H), 4.41 (d, *J* = 2.8 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.69 (td, *J* = 8.7, 3.7 Hz, 1H), 3.55 – 3.47 (m, 1H), 2.66 – 2.51 (m, 2H), 2.39 (dd, *J* = 15.6, 6.7 Hz, 1H), 2.32 – 2.22 (m, 1H), 1.79 – 1.70 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 145.4, 142.6, 128.7, 128.6, 127.1, 126.0, 120.8, 113.5, 68.2, 60.6, 47.8, 45.2, 37.9, 28.4, 14.3. HRMS (ESI) m/z calcd for $C_{20}H_{23}ClNO_2$ $[M+H]^+$: 344.1412, found 344.1414.

ethyl 2-(2-phenyl-1-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)acetate (**2t**)



Total yield of trans and cis isomers: 46%, 48 h, dr =5.2:1. *trans*-**2t**: yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 4H), 7.26 – 7.21 (m, 3H), 6.47 (d, *J* = 8.7 Hz, 2H), 4.51 (d, *J* = 2.8 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.74 (td, *J* = 8.9, 3.6 Hz, 1H), 3.63 – 3.55 (m, 1H), 2.71 – 2.62 (m, 1H), 2.56 (dd, *J* = 15.9, 8.0 Hz, 1H), 2.41 (dd, *J* = 15.9, 6.8 Hz, 1H), 2.35 – 2.25 (m, 1H), 1.83 – 1.72 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.3 , 149.0 , 142.0 , 128.7 , 127.2 , 126.2 (q, *J* = 3.8 Hz), 125.9, 125.1 (q, *J* = 268.5), 117.5 (q, *J* = 32.4 Hz), 111.9 , 68.1 , 60.7 , 47.7 , 45.1 , 37.8 , 28.2 , 14.2 . HRMS (ESI) m/z calcd for $C_{21}H_{23}F_3NO_2$ $[M+H]^+$: 378.1675, found 378.1675.

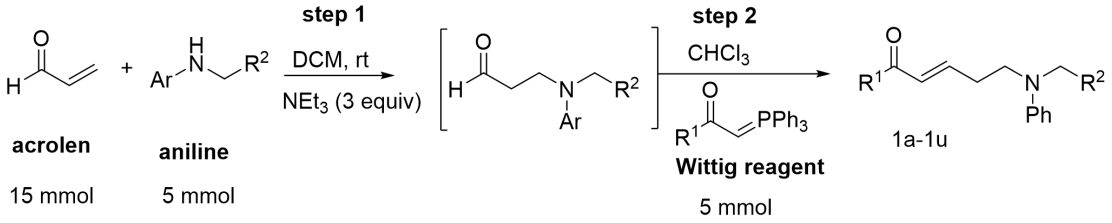
ethyl 2-(1-benzyl-2-phenyl-1H-indol-3-yl)acetate (**2u**)



Yield: 51%, 48 h, clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.67 (m, 1H), 7.42 – 7.35 (m, 5H), 7.31 – 7.07 (m, 6H), 6.94 (d, *J* = 6.6 Hz, 2H), 5.22 (s, 2H), 4.13 (q, *J* = 7.1 Hz, 6H), 3.68 (s, 2H), 1.23

(t, J = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 139.6, 138.2, 136.8, 131.2, 130.7, 128.7, 128.5, 128.0, 127.1, 126.1, 122.3, 120.0, 119.3, 110.5, 106.6, 60.7, 47.8, 31.3, 14.3. HRMS (ESI) m/z calcd for $C_{25}H_{24}NO_2$ $[M+H]^+$: 370.1802, found 370.1804.

3. Synthetic procedures for substrates 1

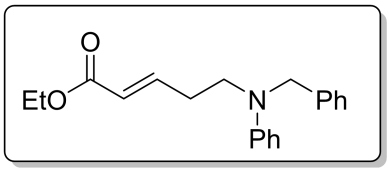


Step 1. The corresponding *N*-substituted aniline (5 mmol), acrolein (15 mmol), NEt_3 (15 mmol) were added to 20 mL CH_2Cl_2. The resulting mixture was stirred at room temperature for 12 h. Then the reaction mixture was concentrated in vacuo to remove excess acrolen and NEt_3. The resulting residue was used in the next step without any further purification.

Step 2. The residue obtained from former step was dissolved in 20 mL $CHCl_3$, the Wittig reagent (5 mmol) was added. Then the mixture was stirred at room temperature for 12 h. Then the solvent was removed via vacuo concentration. The mixture was subjected to flash chromatography on silica gel to give the desired product.

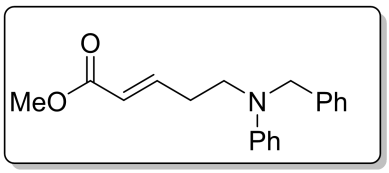
Characterization data of substrates

ethyl (*E*)-5-(benzyl(phenyl)amino)pent-2-enoate **(1a)**



Oil; 74% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.26 (m, 2H), 7.26 – 7.15 (m, 5H), 7.02 – 6.87 (m, 1H), 6.76 – 6.62 (m, 3H), 5.86 (d, J = 15.7 Hz, 1H), 4.52 (s, 2H), 4.18 (q, J = 6.8 Hz, 2H), 3.52 (t, J = 6.8 Hz, 2H), 2.58 – 2.47 (m, 2H), 1.27 (t, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 148.0, 145.6, 138.6, 129.3, 128.6, 126.9, 126.6, 123.1, 116.8, 112.5, 60.3, 54.7, 49.8, 30.1, 14.3.

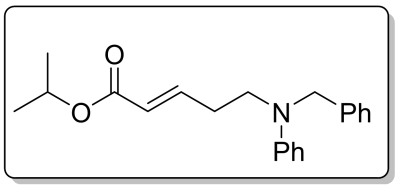
methyl (*E*)-5-(benzyl(phenyl)amino)pent-2-enoate (**1b)**



Oil; 78% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.10 (m, 7H), 6.94 (dt, J = 15.6, 7.2 Hz, 1H), 6.72 – 6.60 (m, 3H), 5.85 (dt, J = 15.6, 1.4 Hz, 1H), 4.49 (s, 2H), 3.68 (s, 3H), 3.53 – 3.44 (m, 2H), 2.56 – 2.44 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 148.2, 146.2, 138.7, 129.5,

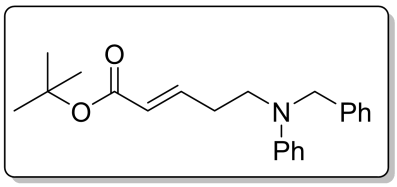
128.7, 127.0, 126.7, 122.8, 116.9, 112.6, 54.8, 51.6, 49.9, 30.3.

isopropyl (*E*)-5-(benzyl(phenyl)amino)pent-2-enoate (**1c**)



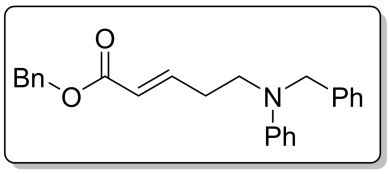
Oil; 68% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.16 (m, 7H), 7.00 – 6.85 (m, 1H), 6.76 – 6.64 (m, 3H), 5.84 (d, *J* = 15.7 Hz, 1H), 5.06 (hept, *J* = 6.3 Hz, 1H), 4.52 (s, 2H), 3.57 – 3.46 (m, 2H), 2.60 – 2.46 (m, 2H), 1.25 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 148.1, 145.3, 138.7, 129.4, 128.7, 127.0, 126.6, 123.6, 116.8, 112.5, 67.6, 54.7, 49.8, 30.1, 21.9.

tert-butyl (*E*)-5-(benzyl(phenyl)amino)pent-2-enoate (**1d**)



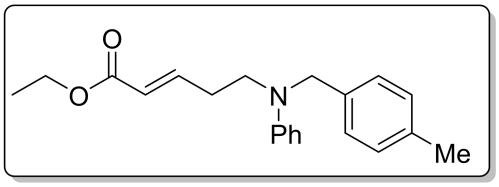
Oil; 71% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.18 (m, 7H), 6.89 – 6.79 (m, 1H), 6.72 – 6.67 (m, 3H), 5.79 (d, *J* = 15.6 Hz, 1H), 4.52 (s, 2H), 3.54 – 3.49 (m, 2H), 2.55 – 2.46 (m, 2H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 148.1, 144.4, 138.7, 129.4, 128.6, 127.0, 126.6, 124.8, 116.7, 112.5, 80.3, 54.6, 49.9, 29.9, 28.2.

benzyl (*E*)-5-(benzyl(phenyl)amino)pent-2-enoate (**1e**)



Oil; 71% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.13 (m, 12H), 7.08 – 6.91 (m, 1H), 6.73 – 6.64 (m, 3H), 5.95 – 5.86 (m, 1H), 5.16 (s, 2H), 4.50 (s, 2H), 3.55 – 3.46 (m, 2H), 2.58 – 2.47 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 148.1, 146.5, 138.4, 136.1, 129.4, 128.7, 128.6, 128.3, 127.0, 126.7, 122.8, 116.9, 112.6, 66.2, 54.7, 49.8, 30.2.

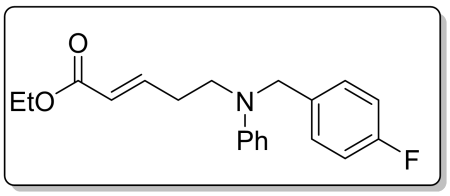
ethyl (*E*)-5-((4-methylbenzyl)(phenyl)amino)pent-2-enoate (**1f**)



Oil; 77% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.16 (m, 2H), 7.11 (s, 4H), 6.94 (dt, *J* = 14.8, 7.2 Hz, 1H), 6.74 – 6.64 (m, 3H), 5.86 (d, *J* = 15.7 Hz, 1H), 4.49 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.55 – 3.46 (m, 2H), 2.57 – 2.48 (m, 2H), 2.32 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR

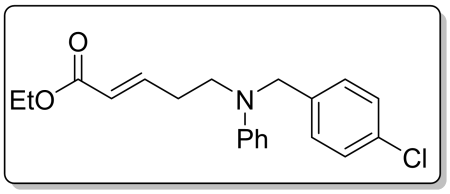
(101 MHz, $CDCl_3$) δ 166.3, 148.1, 145.7, 136.5, 135.5, 129.3, 129.3, 126.6, 123.1, 116.7, 112.5, 60.3, 54.4, 49.7, 30.1, 21.1, 14.3.

ethyl (*E*)-5-((4-fluorobenzyl)(phenyl)amino)pent-2-enoate (**1g**)



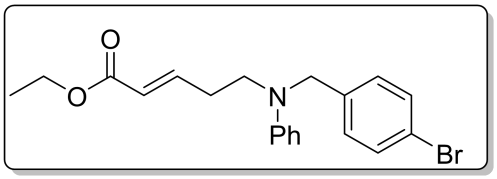
Oil; 62% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.14 (m, 4H), 7.04 – 6.88 (m, 3H), 6.76 – 6.65 (m, 3H), 5.86 (dt, *J* = 15.6, 1.4 Hz, 1H), 4.49 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.52 (t, *J* = 6.0 Hz 2H), 2.53 (q, *J* = 7.0 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 161.9 (d, *J* = 244.8 Hz), 147.9, 145.5, 134.1, 129.4, 128.1 (d, *J* = 8.0 Hz), 123.2, 117.0, 115.4 (d, *J* = 21.4 Hz), 112.6, 60.3, 54.2, 49.8, 30.0, 14.3.

ethyl (*E*)-5-((4-chlorobenzyl)(phenyl)amino)pent-2-enoate (**1h**)



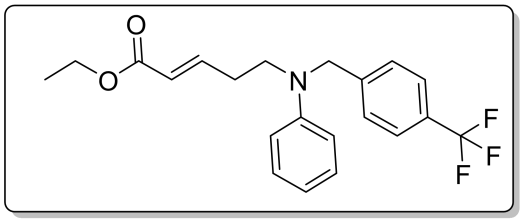
Oil; 73% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.10 (m, 6H), 6.99 – 6.88 (m, 1H), 6.75 – 6.62 (m, 3H), 5.86 (d, *J* = 15.7 Hz, 1H), 4.48 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.55 – 3.48 (m, 2H), 2.57 – 2.48 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 147.7, 145.4, 137.1, 132.6, 129.4, 128.7, 128.0, 123.2, 117.1, 112.6, 60.3, 54.3, 50.0, 30.1, 14.3.

ethyl (*E*)-5-((4-bromobenzyl)(phenyl)amino)pent-2-enoate (**1i**)



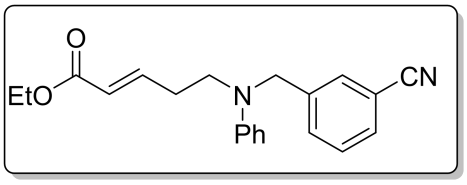
Oil; 81% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.23 – 7.15 (m, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.98 – 6.88 (m, 1H), 6.74 – 6.62 (m, 3H), 5.86 (d, *J* = 15.7 Hz, 1H), 4.45 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.54 – 3.47 (m, 2H), 2.57 – 2.47 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 147.7, 145.4, 137.7, 131.6, 129.4, 128.3, 123.2, 120.6, 117.1, 112.6, 60.3, 54.3, 49.9, 30.1, 14.3.

ethyl (*E*)-5-(phenyl(4-(trifluoromethyl)benzyl)amino)pent-2-enoate (**1j**)



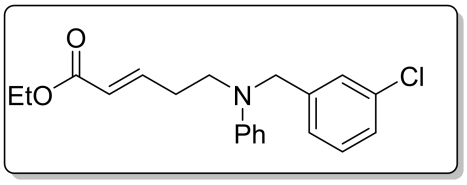
Oil; 75% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.0 Hz,2H), 7.24 – 7.17 (m, 2H), 6.95 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.76 – 6.71 (m, 1H), 6.67 (d, *J* = 8.8 Hz, 2H), 5.88 (dt, *J* = 15.6, 1.4 Hz, 1H), 4.57 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.59 – 3.51 (m, 2H), 2.60 – 2.52 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 147.7, 145.3, 143.0, 129.5, 126.8, 125.6 (q, *J* = 3.7Hz), 124.2 (q, *J* = 270.1 Hz), 123.3, 117.3, 112.6, 60.4, 54.6, 50.2, 30.1, 14.3.

ethyl (E)-5-((3-cyanobenzyl)(phenyl)amino)pent-2-enoate (**1k**)



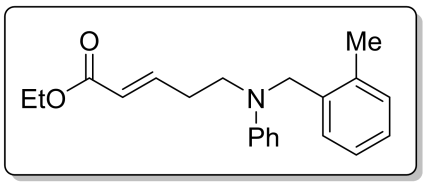
Oil; 67% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.49 (m, 2H), 7.48 – 7.38 (m, 2H), 7.24 – 7.18 (m, 2H), 6.94 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 5.88 (dt, *J* = 15.6, 1.3 Hz, 1H), 4.54 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.55 (t, *J* = 7.4 Hz 2H), 2.60 – 2.51 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 147.4, 145.2, 140.5, 131.1, 130.8, 130.1, 129.5, 129.5, 123.4, 118.8, 117.6, 112.8, 60.4, 54.4, 50.3, 30.1, 14.3.

ethyl (*E*)-5-((3-chlorobenzyl)(phenyl)amino)pent-2-enoate (**1l**)



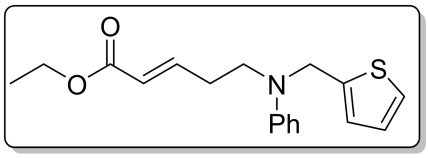
Oil; 76% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.17 (m, 5H), 7.11 – 7.07 (m, 1H), 6.94 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.76 – 6.64 (m, 3H), 5.87 (dt, *J* = 15.7, 1.4 Hz, 1H), 4.48 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.53 (t, 2H), 2.59 – 2.48 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 147.7, 145.4, 141.0, 134.6, 129.9, 129.4, 127.2, 126.6, 124.7, 123.2, 117.2, 112.6, 60.3, 54.5, 50.0, 30.0, 14.3.

ethyl (*E*)-5-((2-methylbenzyl)(phenyl)amino)pent-2-enoate (**1m**)



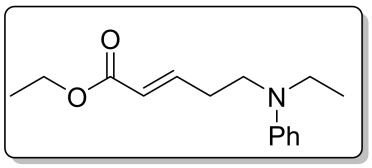
Oil; 71% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.08 (m, 6H), 6.95 (dt, *J* = 15.5, 7.2 Hz, 1H), 6.73 – 6.61 (m, 3H), 5.87 (dt, *J* = 15.6, 1.4 Hz, 1H), 4.43 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.55 – 3.49 (m, 2H), 2.59 – 2.51 (m, 2H), 2.30 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 148.0, 145.6, 135.7, 135.5, 130.3, 129.3, 126.8, 126.2, 126.1, 123.1,116.6, 112.2, 60.3, 52.7, 49.6, 30.1, 18.9, 14.3.

ethyl (*E*)-5-(phenyl(thiophen-2-ylmethyl)amino)pent-2-enoate (**1n**)



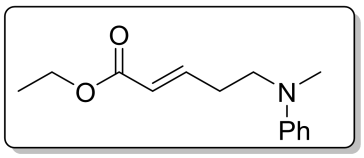
Oil; 59% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.20 (m, 2H), 7.16 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.99 – 6.89 (m, 3H), 6.81 – 6.72 (m, 3H), 5.87 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.65 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.53 – 3.46 (m, 2H), 2.54 – 2.47 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 147.6, 145.6, 142.4, 129.4, 126.8, 124.8, 124.4, 123.1, 117.5, 113.3, 60.3, 50.4, 49.5, 30.1, 14.3.

ethyl (*E*)-5-(ethyl(phenyl)amino)pent-2-enoate (**1o**)



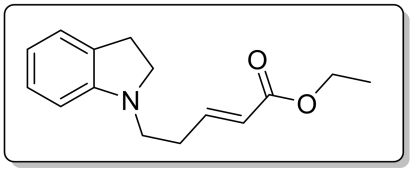
Oil; 83% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.18 (m, 2H), 6.97 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.70 – 6.64 (m, 3H), 5.88 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.40 (t, 2H), 3.35 (q, *J* = 7.1 Hz, 2H), 2.48 (qd, *J* = 7.3, 1.5 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 147.4, 146.0, 129.4, 123.0, 116.1, 112.2, 60.3, 49.2, 45.2, 30.5, 14.3, 12.4.

ethyl (*E*)-5-(methyl(phenyl)amino)pent-2-enoate (**1p**)



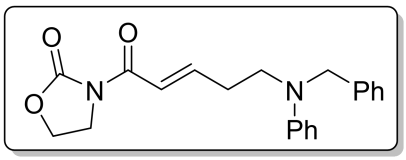
Oil; 86% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 – 7.19 (m, 2H), 6.96 (dt, *J* = 15.6, 7.3 Hz, 1H), 6.74 – 6.66 (m, 3H), 5.87 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.49 – 3.40 (m, 2H), 2.92 (s, 3H), 2.50 – 2.42 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 148.6, 145.9, 129.3, 123.0, 116.6, 112.4, 60.2, 51.5, 38.5, 29.5, 14.3.

ethyl (*E*)-5-(indolin-1-yl)pent-2-enoate (**1q**)



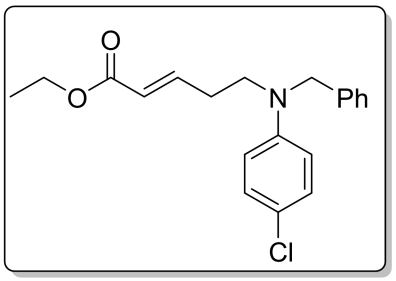
Oil; 69% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 6.97 (m, 3H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 1H), 5.92 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.35 (t, *J* = 8.3 Hz, 2H), 3.21 (t, *J* = 8.3 Hz, 2H), 3.00 – 2.92 (m, 2H), 2.50 (qd, *J* = 7.2, 1.5 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 152.0, 146.3, 130.0, 127.3, 124.5, 122.8, 117.8, 107.0, 60.3, 53.0, 47.9, 30.1, 28.6, 14.3.

(*E*)-3-(5-(benzyl(phenyl)amino)pent-2-enoyl)oxazolidin-2-one (**1r**)



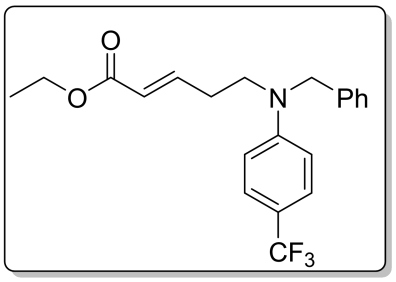
Oil; 75% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.26 (m, 3H), 7.25 – 7.10 (m, 6H), 6.77 – 6.66 (m, 3H), 4.55 (s, 2H), 4.40 (t, *J* = 8.0Hz, 2H), 4.04 (t, *J* = 8.0 Hz, 2H), 3.57 (t, *J* = 7.4Hz, 2H), 2.69 – 2.58 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 153.5, 147.8, 138.5, 129.3, 128.6, 126.9, 126.7, 121.6, 116.9, 112.6, 62.1, 54.7, 49.9, 42.7, 30.6.

ethyl (*E*)-5-(benzyl(4-chlorophenyl)amino)pent-2-enoate (**1s**)



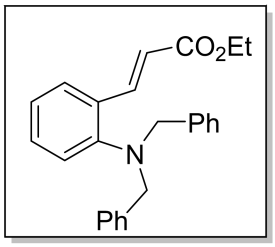
Oil; 74% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.09 (m, 7H), 6.93 (dt, *J* = 15.6, 7.1 Hz, 1H), 6.63 – 6.56 (m, 2H), 5.86 (dt, *J* = 15.7, 1.4 Hz, 1H), 4.50 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.55 – 3.47 (m, 2H), 2.55 – 2.47 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 146.5, 145.2, 137.9, 129.1, 128.7, 127.1, 126.5, 123.3, 121.7, 113.7, 60.3, 54.9, 50.1, 30.0, 14.2.

ethyl (*E*)-5-(benzyl(4-(trifluoromethyl)phenyl)amino)pent-2-enoate (**1t**)



Oil; 83% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 8.7 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.27 – 7.22 (m, 1H), 7.20 – 7.14 (m, 2H), 6.94 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.69 (d, *J* = 8.8 Hz, 2H), 5.88 (dt, *J* = 15.6, 1.4 Hz, 1H), 4.58 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.59 (t, *J* = 7.4 Hz, 2H), 2.59 – 2.52 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 150.2, 144.8, 137.4, 128.8, 127.3, 126.7 (q, *J* = 3.7 Hz), 126.4, 125.0 (q, *J* = 271.1 Hz), 123.6, 118.2 (q, *J* = 32.7 Hz), 111.4, 60.4, 54.5, 49.9, 30.0, 14.2.

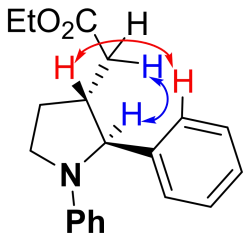
ethyl (*E*)-3-(2-(dibenzylamino)phenyl)acrylate (**1u**)



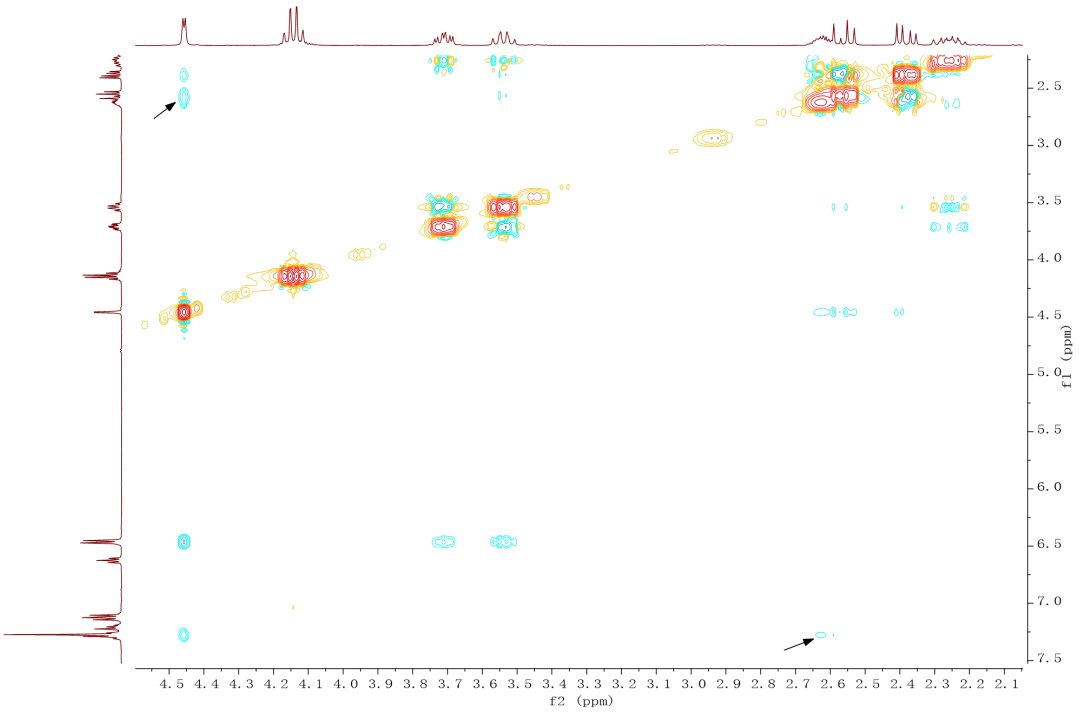
Oil; 60% yield for two steps. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 16.1 Hz, 1H), 7.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.29 – 7.19 (m, 12H), 7.06 – 7.00 (m, 1H), 6.94 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.41 (d, *J* = 16.1 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.13 (s, 4H), 1.35 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 150.8, 142.3, 137.7, 130.3, 130.0, 128.8, 128.7, 128.3, 128.2, 127.8, 127.1, 123.3, 122.4, 118.1, 60.4, 57.6, 14.4.

4. Determination of the relative configuration of 2a

NOE

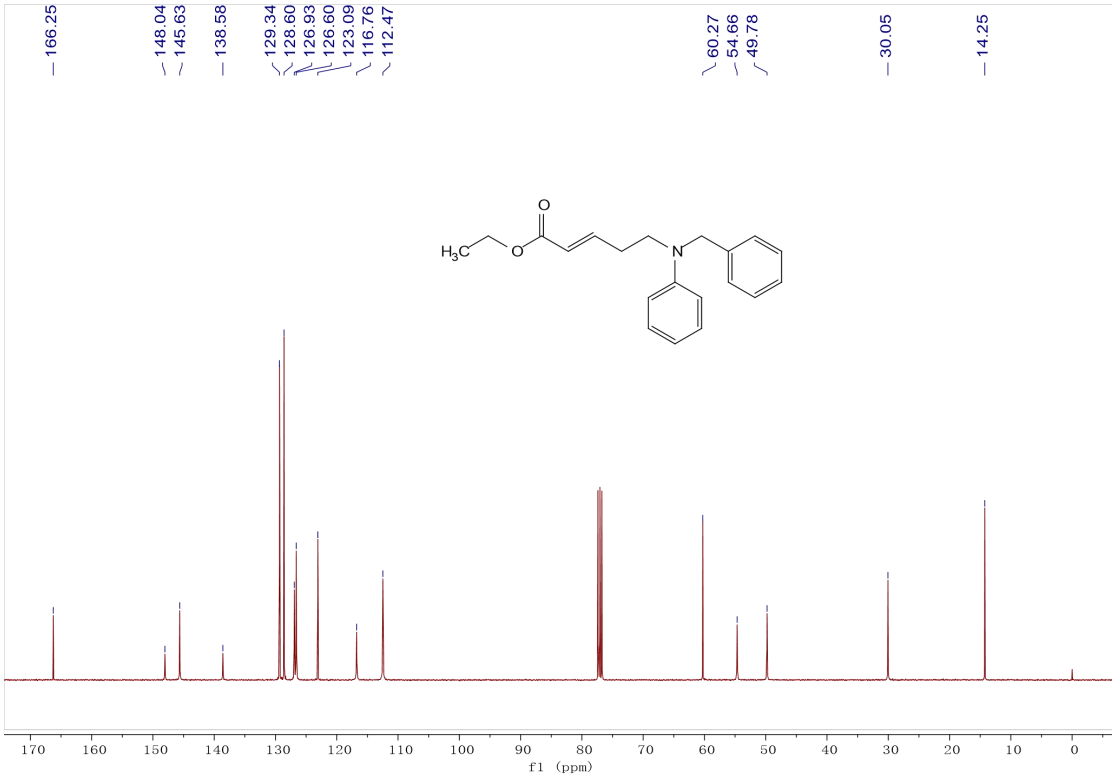


2a

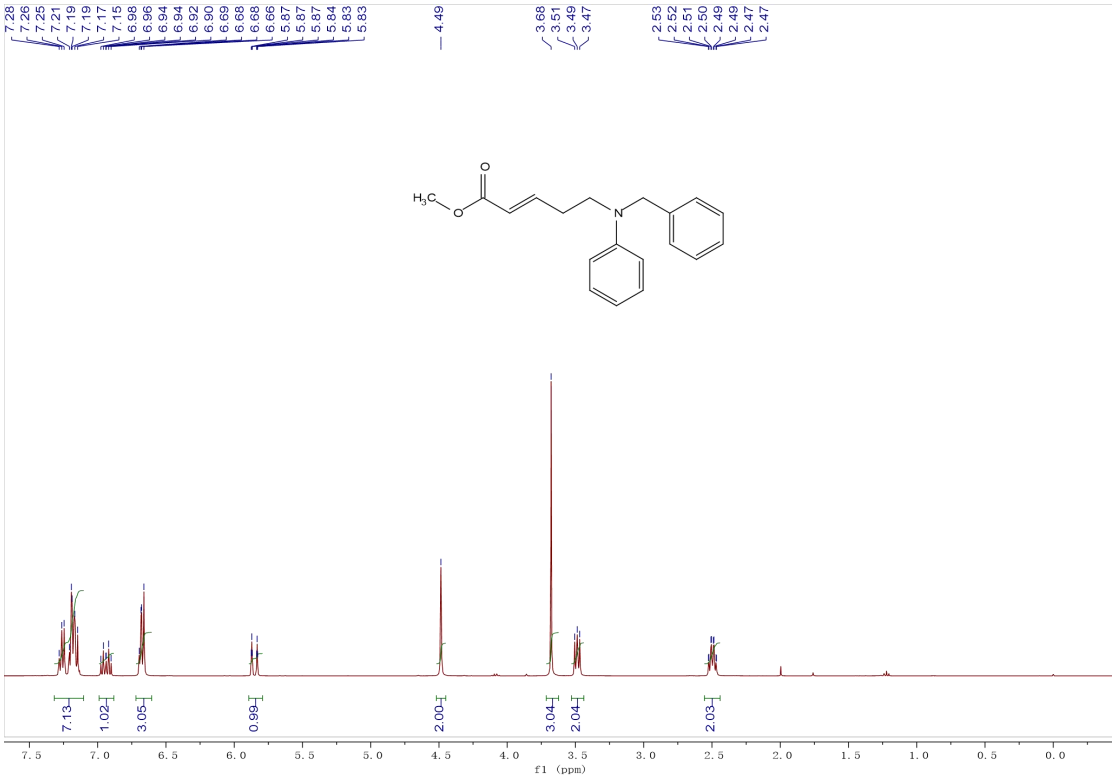


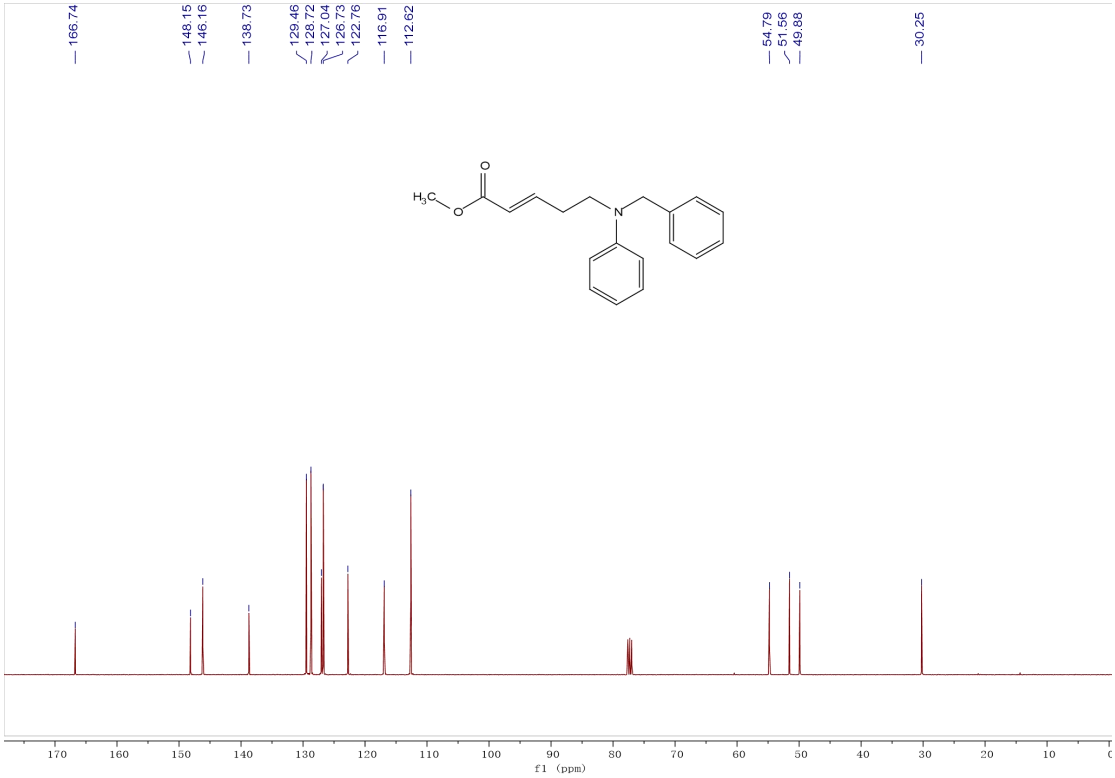
5. NMR Spectra

ethyl (E)-5-(benzyl(phenyl)amino)pent-2-enoate (**1a)**

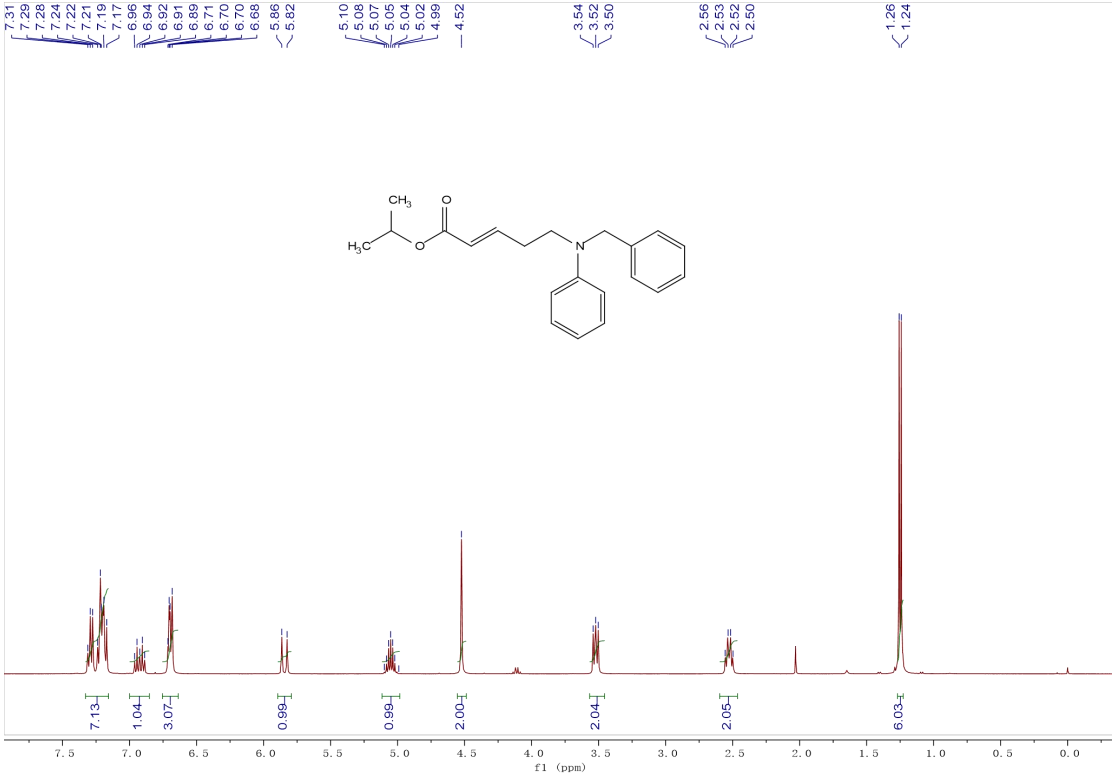


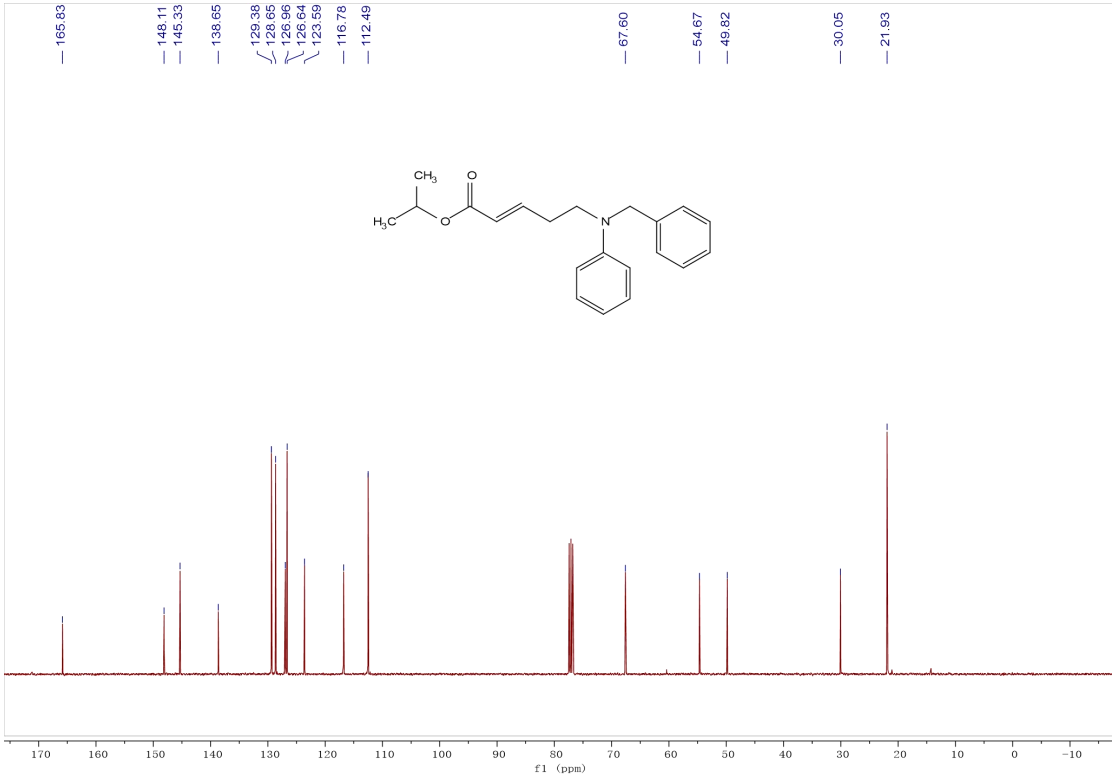
methyl (E)-5-(benzyl(phenyl)amino)pent-2-enoate (**1b**)



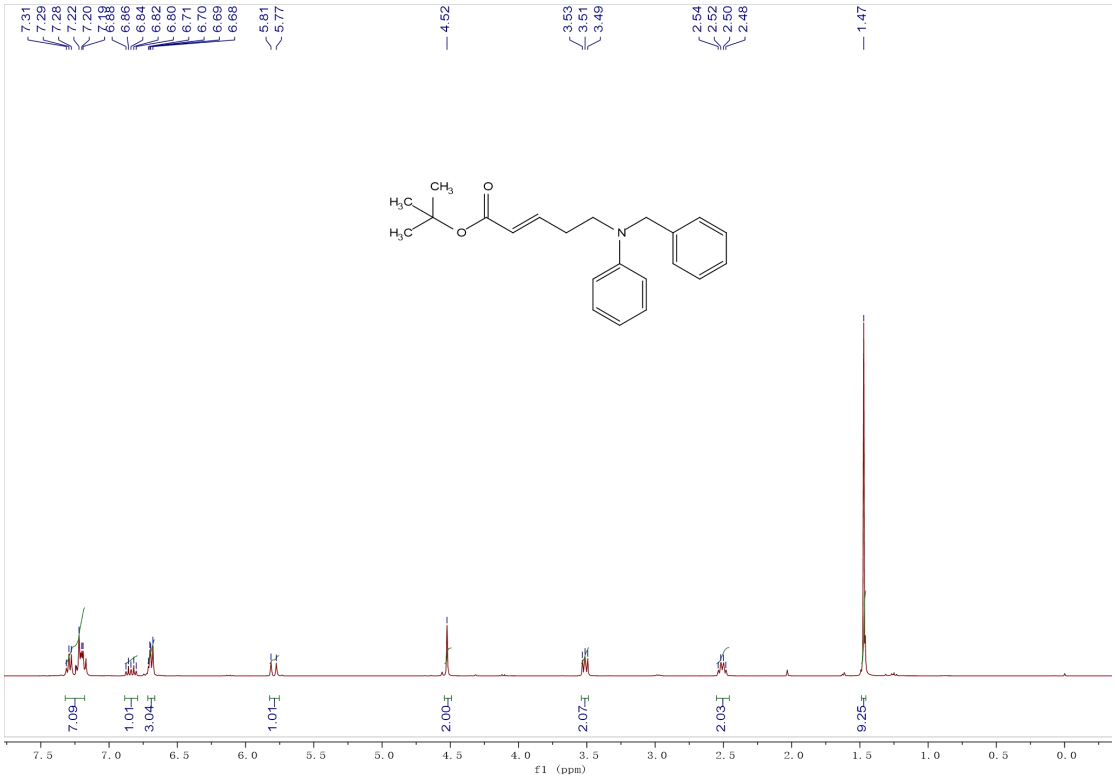


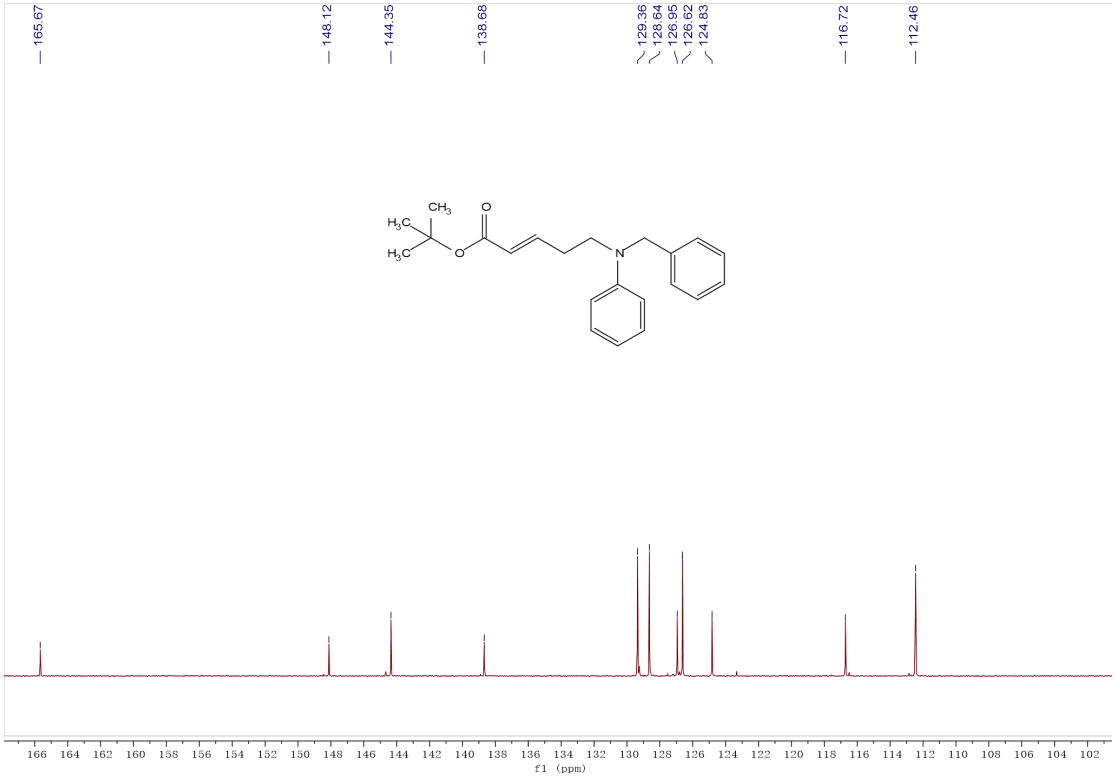
isopropyl (E)-5-(benzyl(phenyl)amino)pent-2-enoate (**1c**)



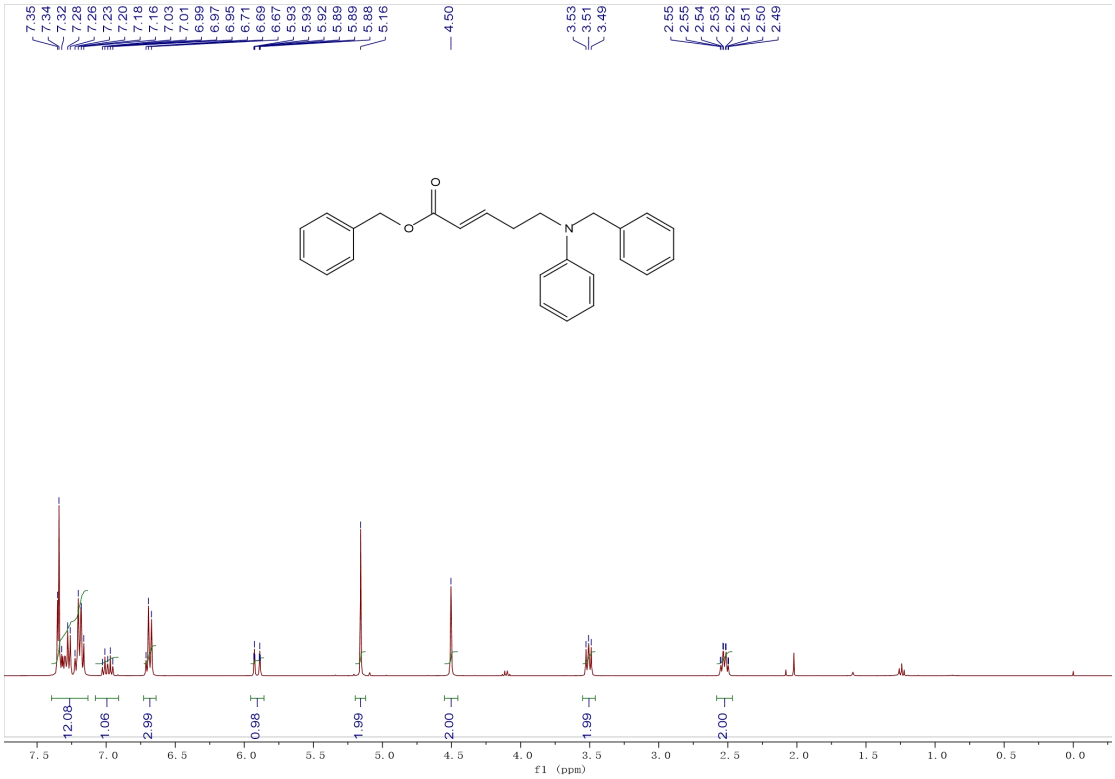


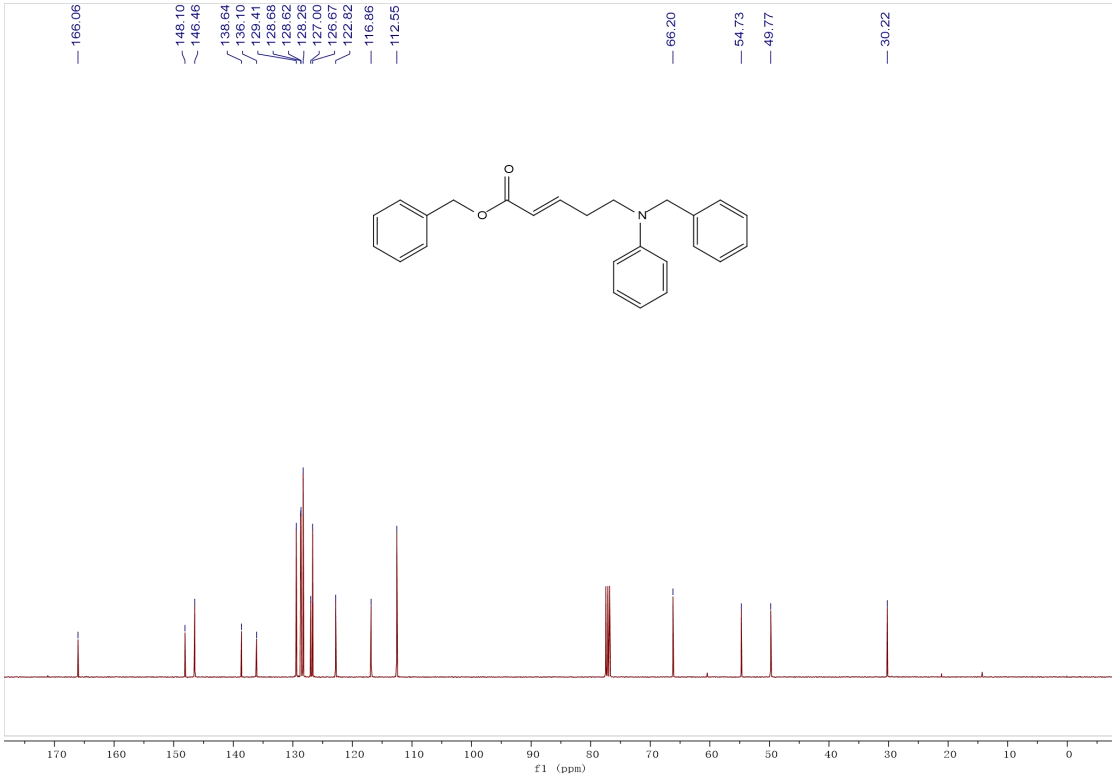
tert-butyl (E)-5-(benzyl(phenyl)amino)pent-2-enoate (**1d**)



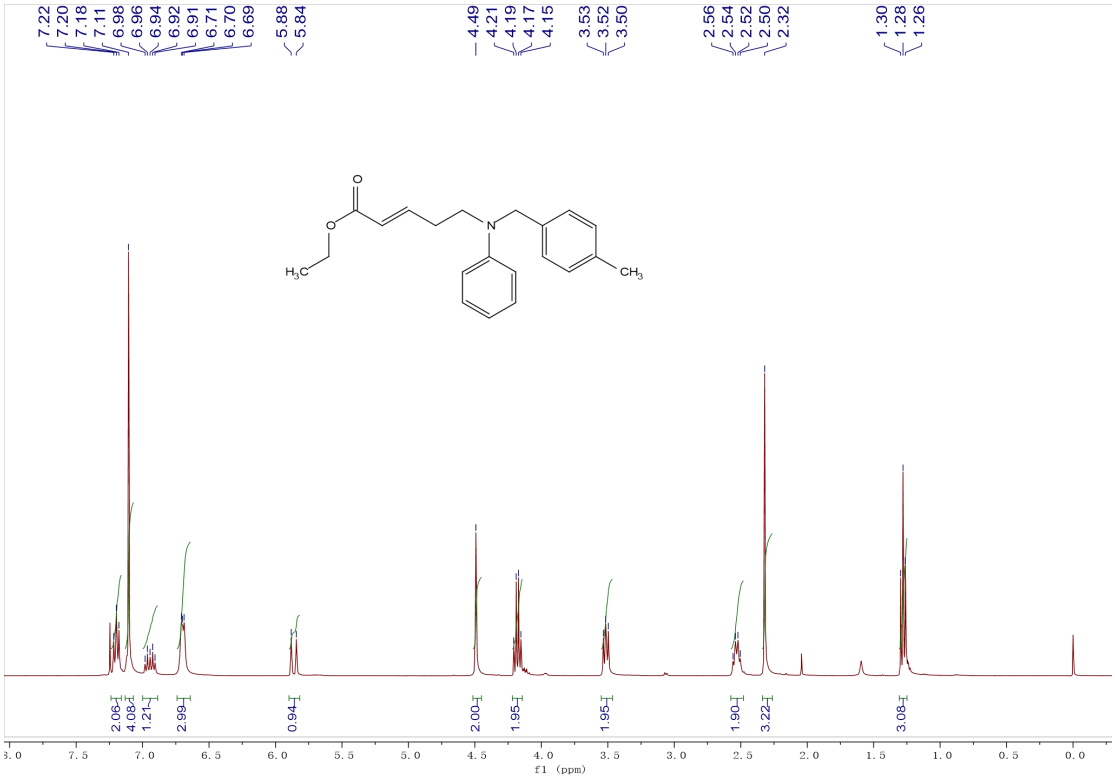


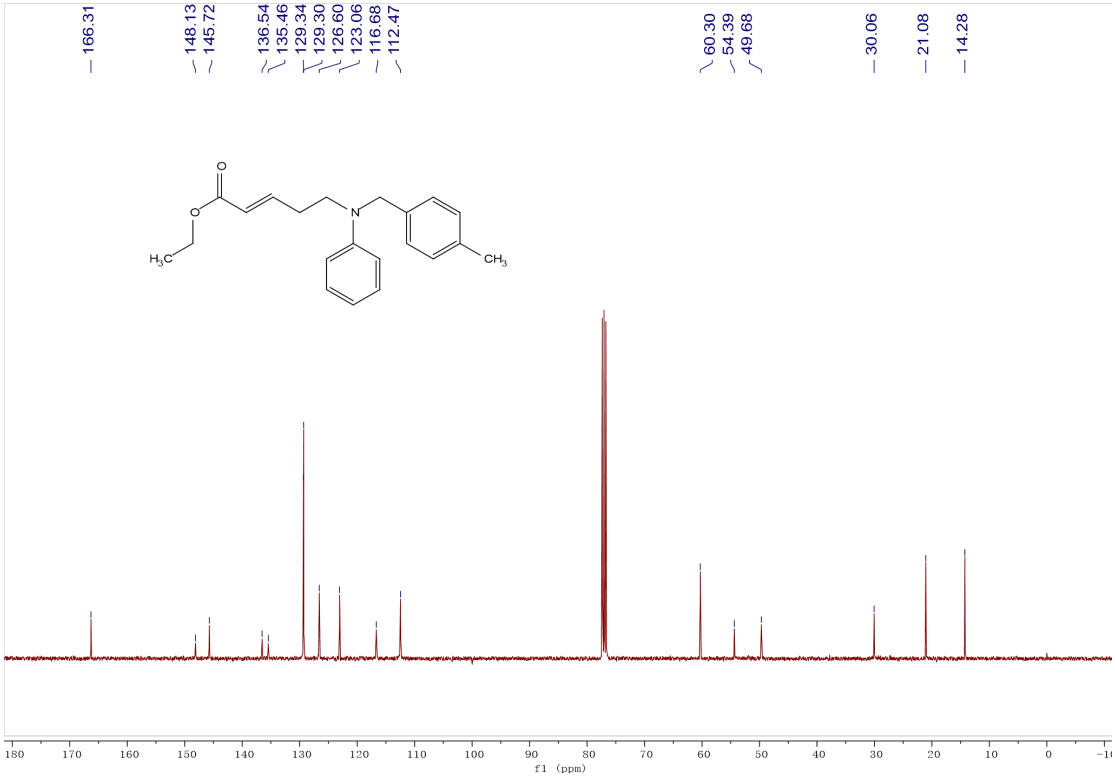
benzyl (E)-5-(benzyl(phenyl)amino)pent-2-enoate (**1e**)



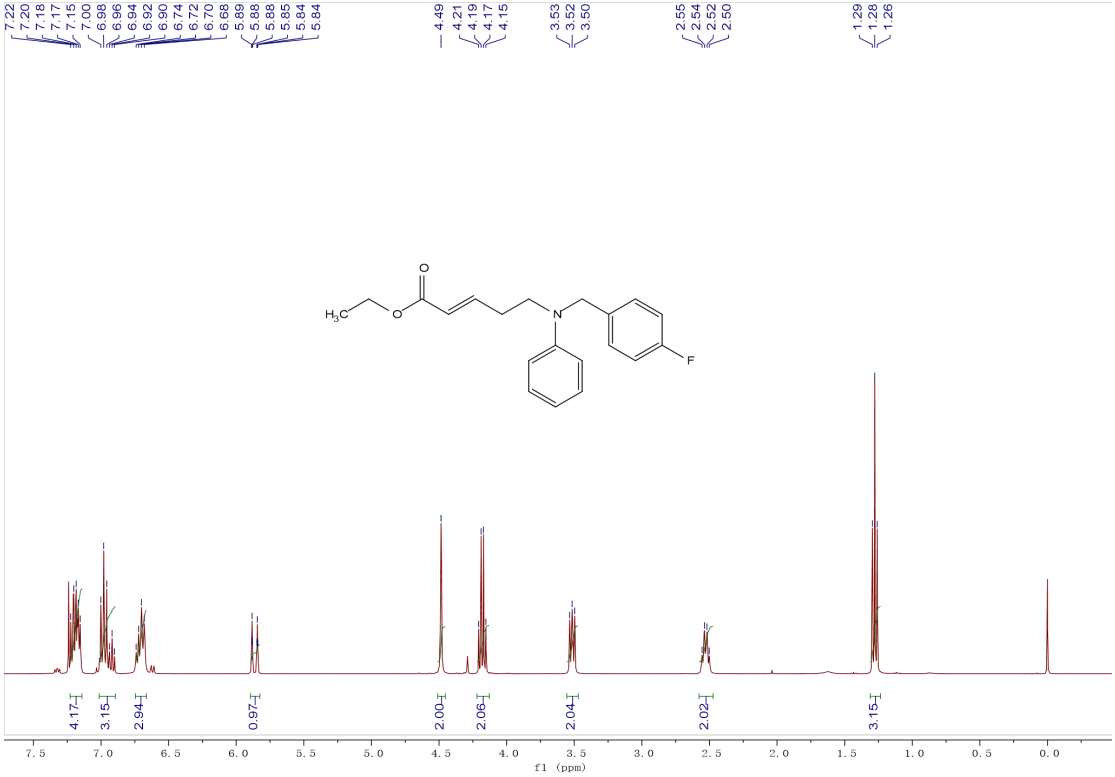


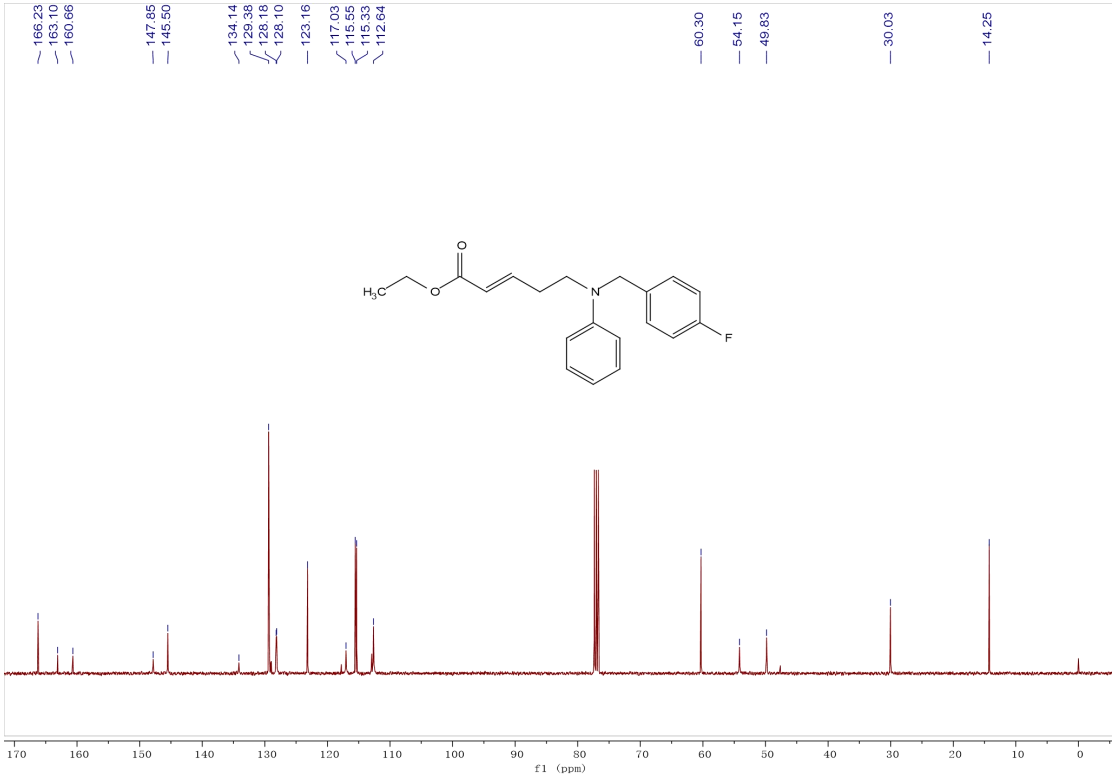
ethyl (E)-5-((4-methylbenzyl)(phenyl)amino)pent-2-enoate (**1f**)



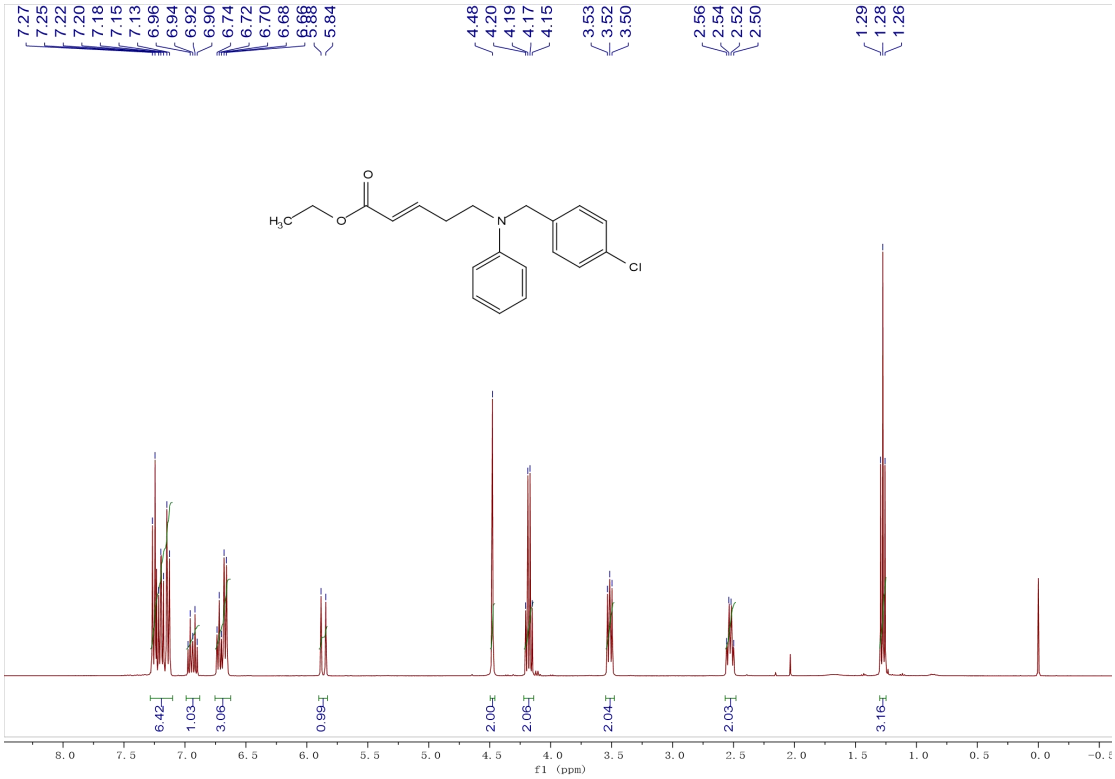


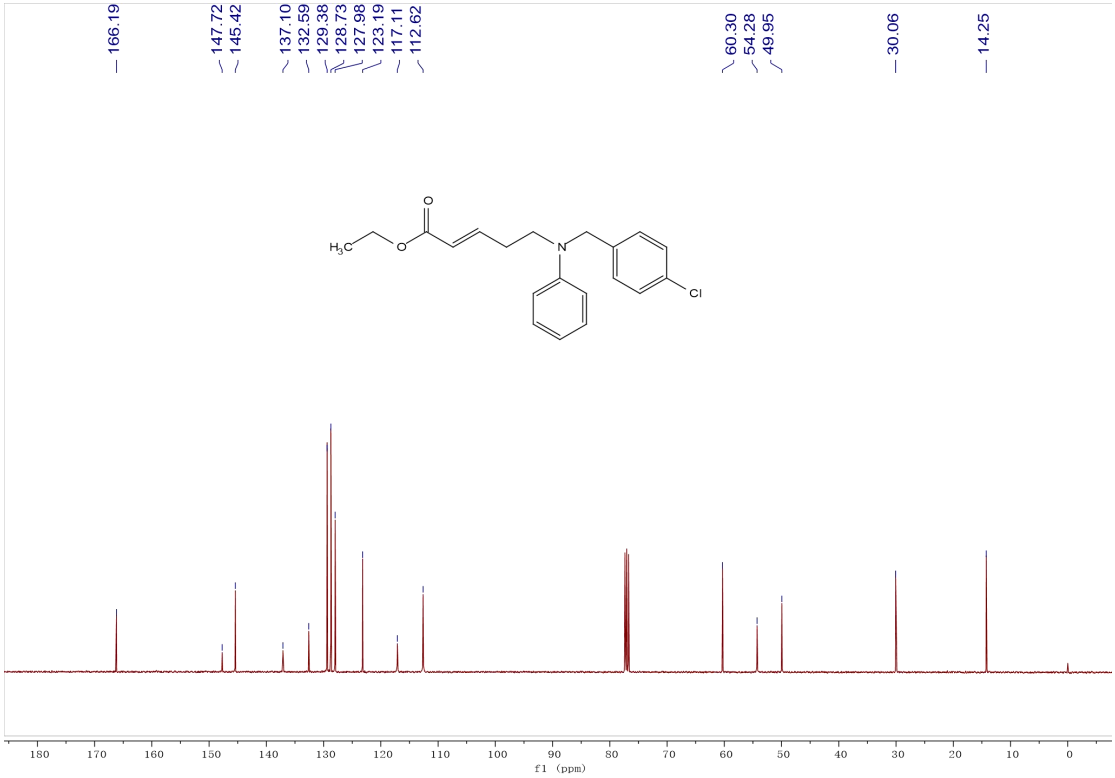
ethyl (E)-5-((4-fluorobenzyl)(phenyl)amino)pent-2-enoate (**1g**)



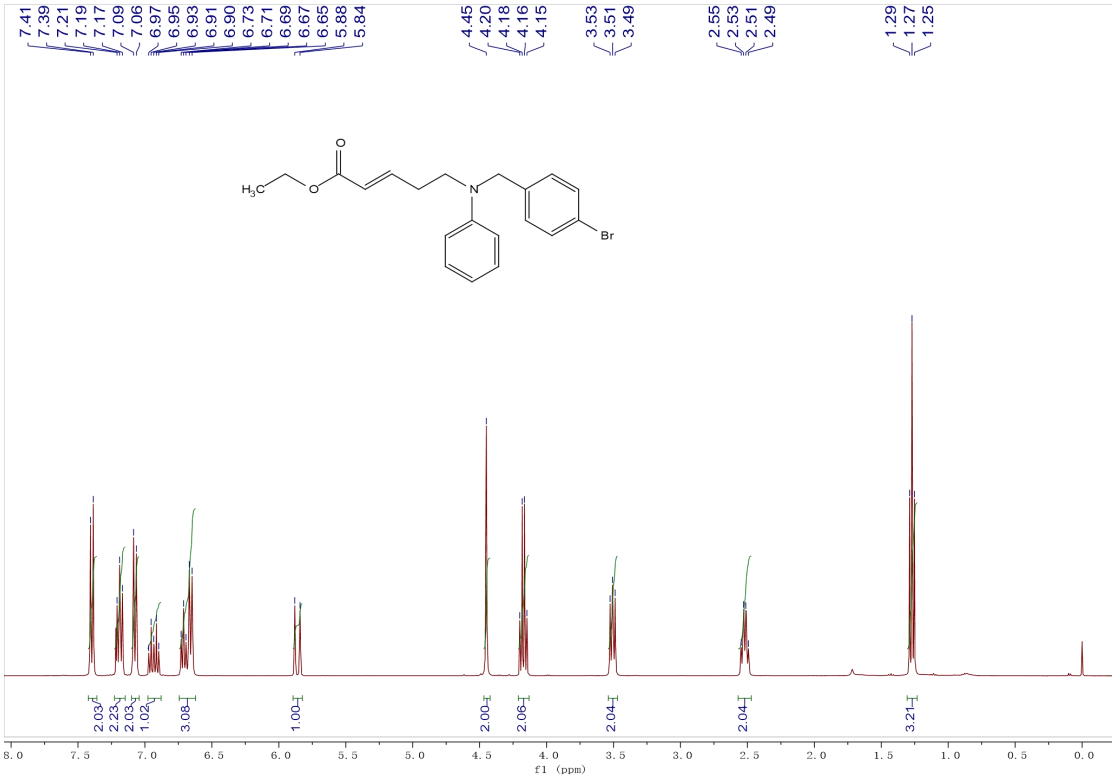


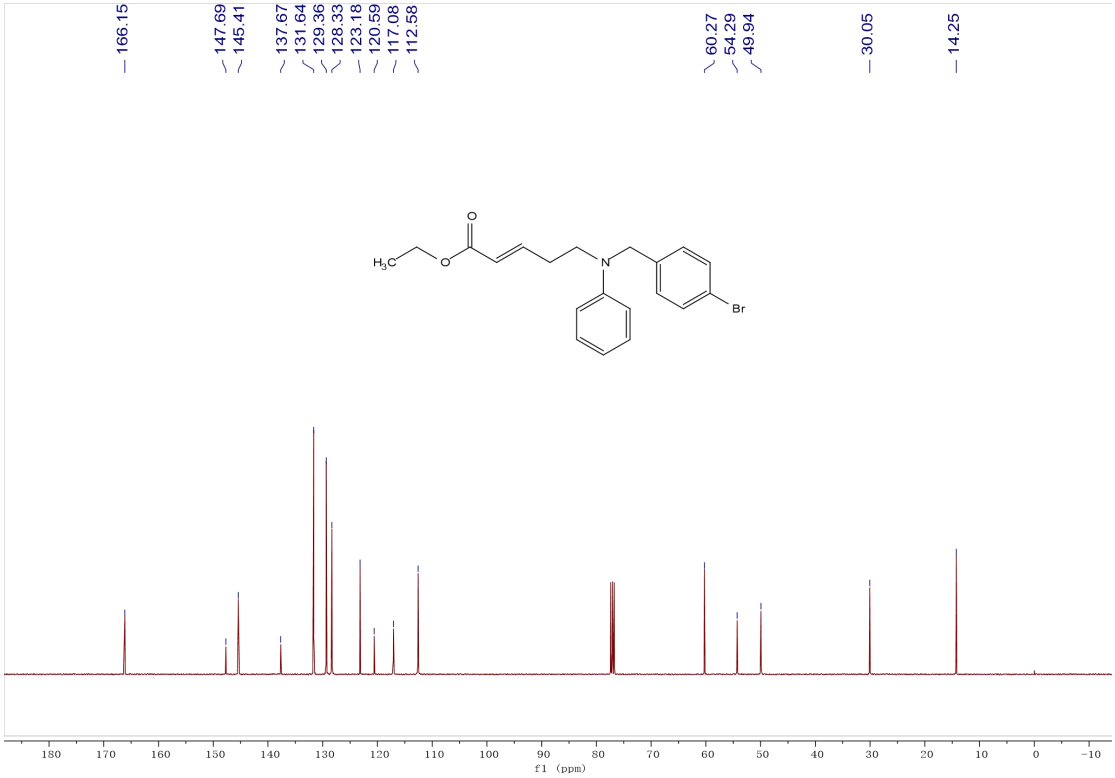
ethyl (E)-5-((4-chlorobenzyl)(phenyl)amino)pent-2-enoate (**1h**)



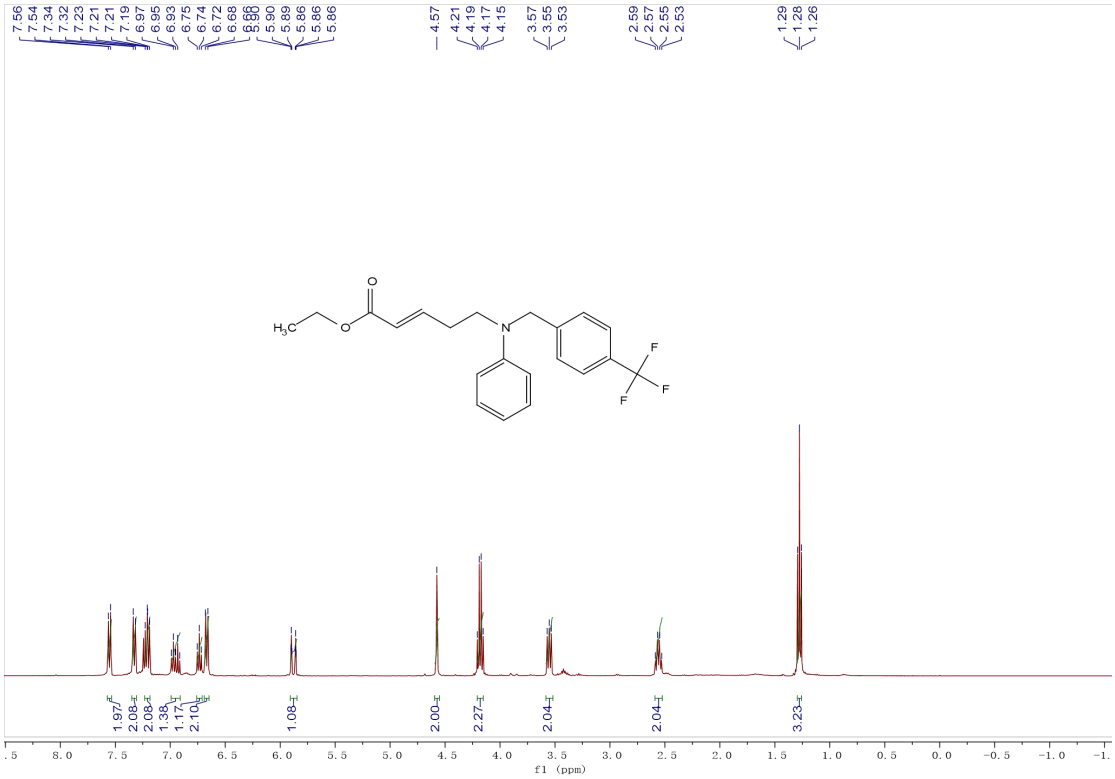


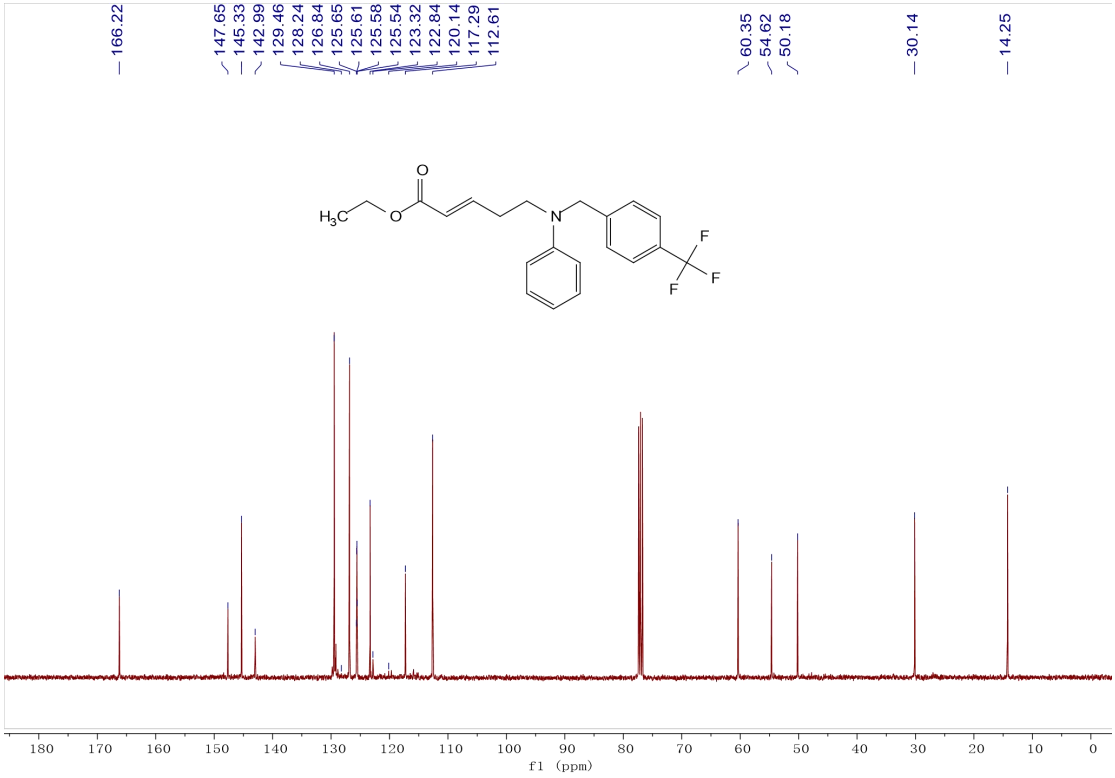
ethyl (E)-5-((4-bromobenzyl)(phenyl)amino)pent-2-enoate (**1i**)



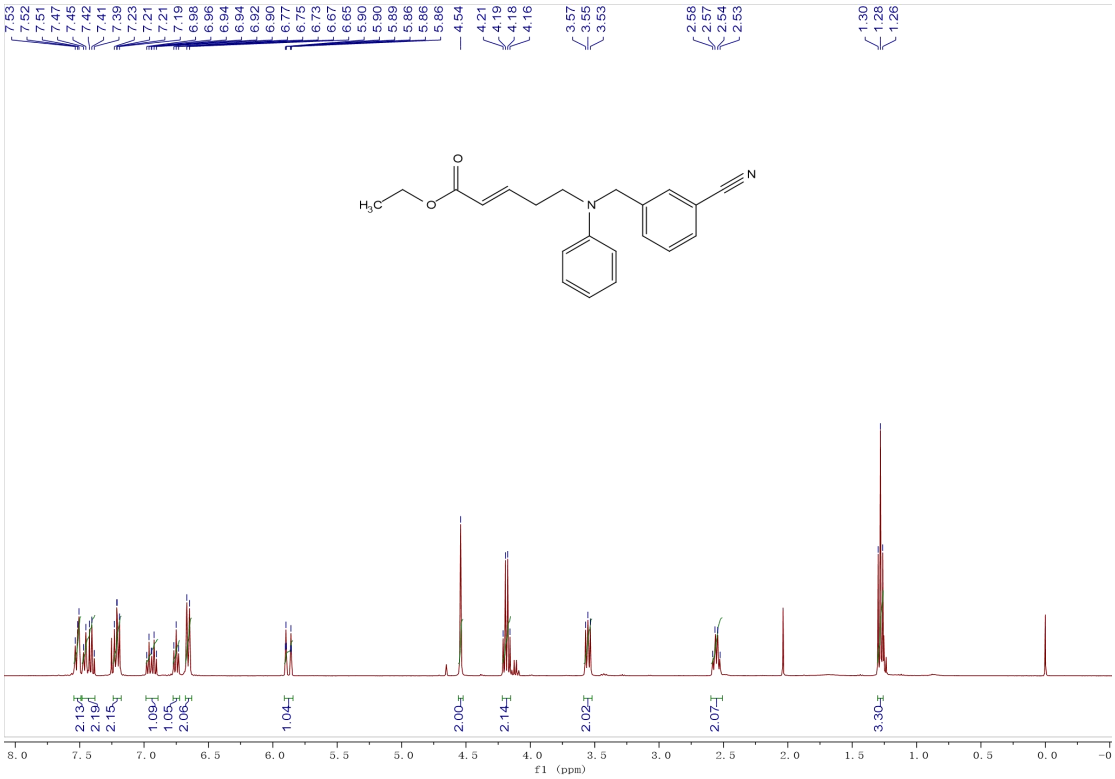


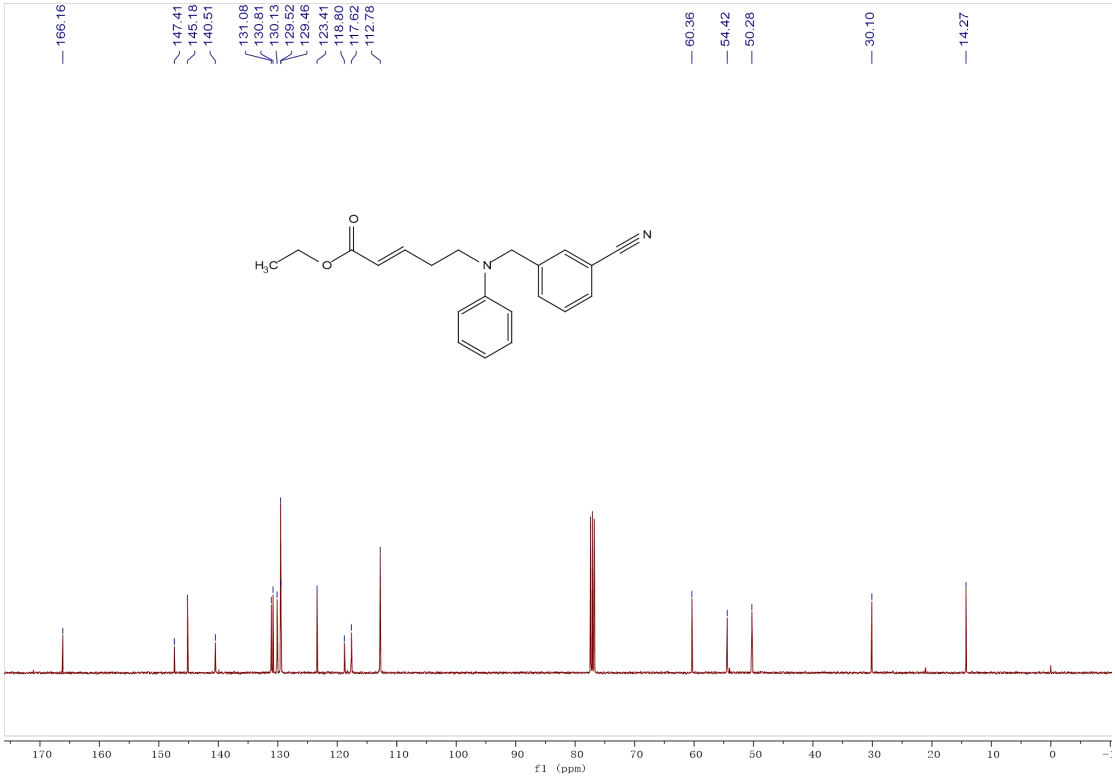
ethyl (E)-5-(phenyl(4-(trifluoromethyl)benzyl)amino)pent-2-enoate (**1j**)



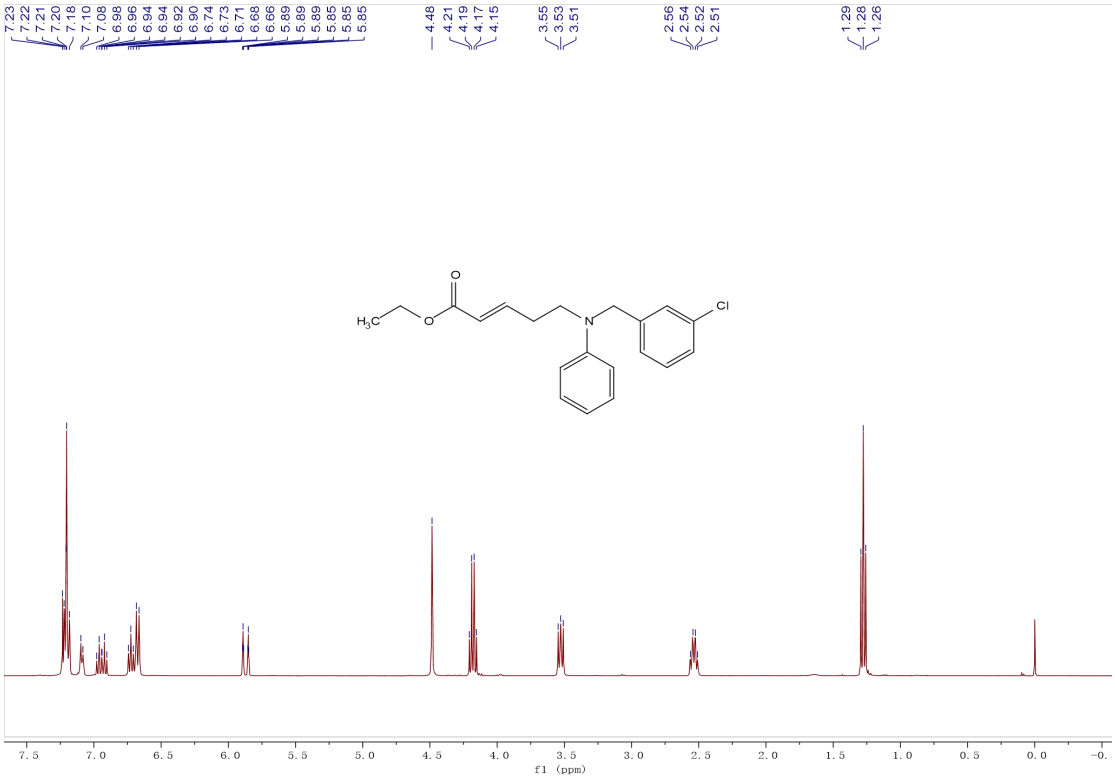


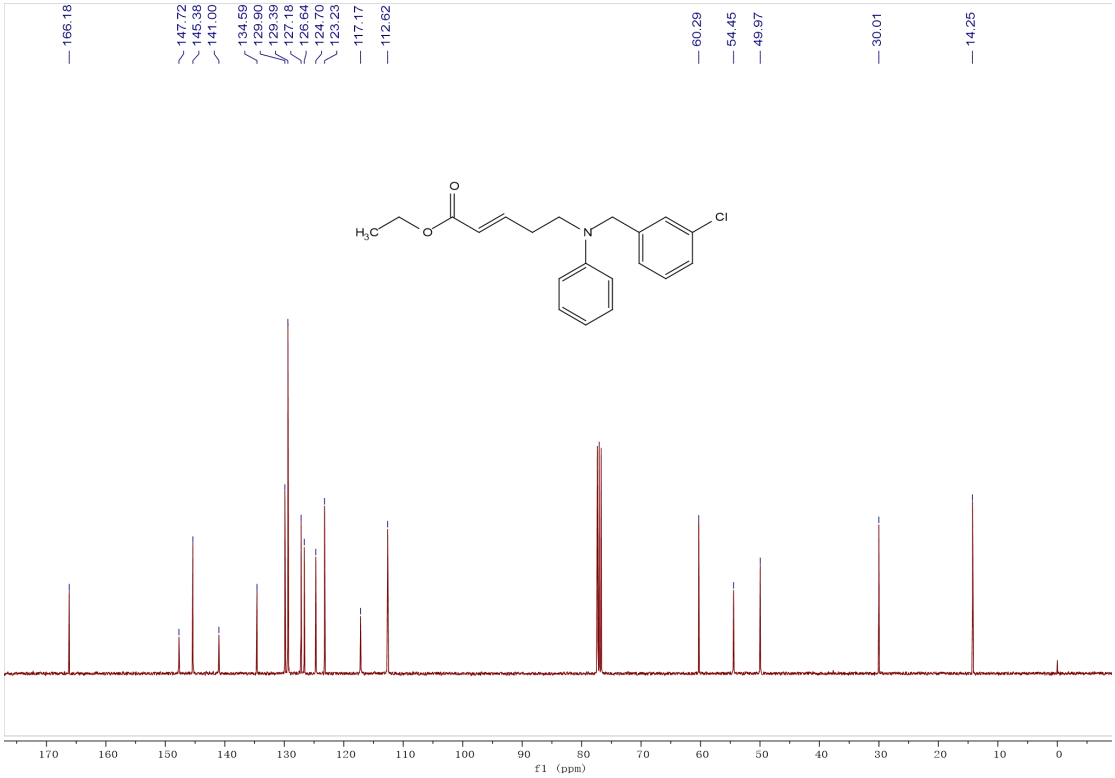
ethyl (E)-5-((3-cyanobenzyl)(phenyl)amino)pent-2-enoate (**1k**)



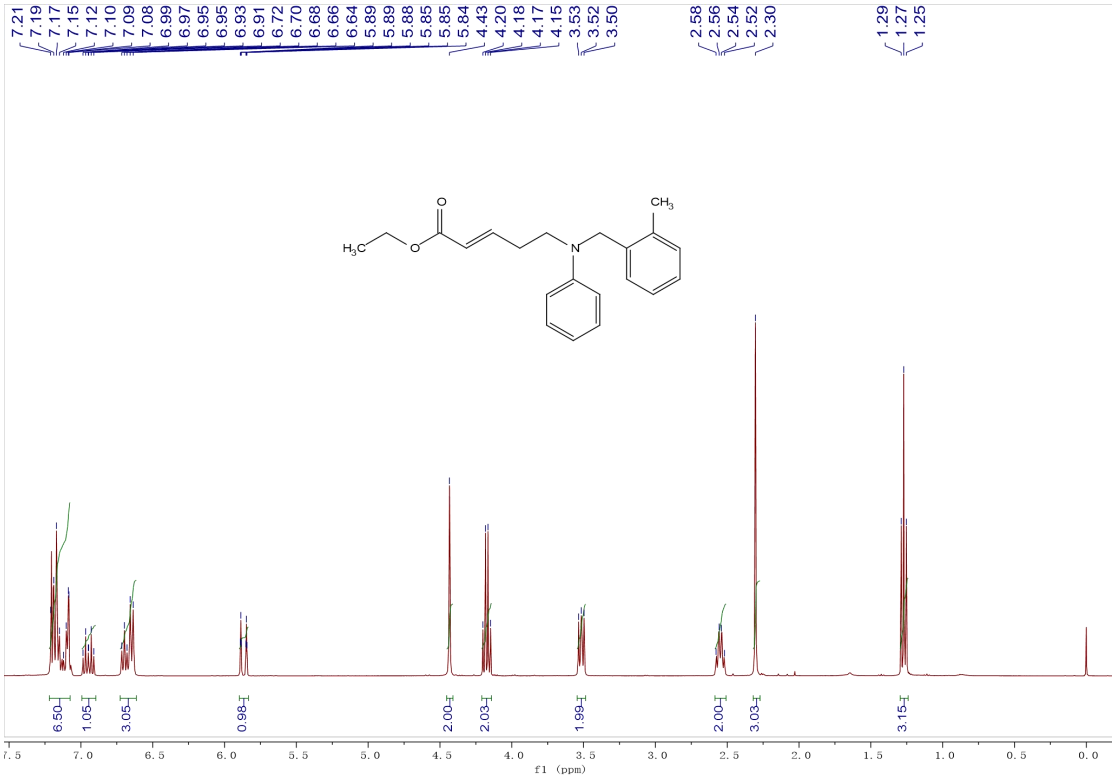


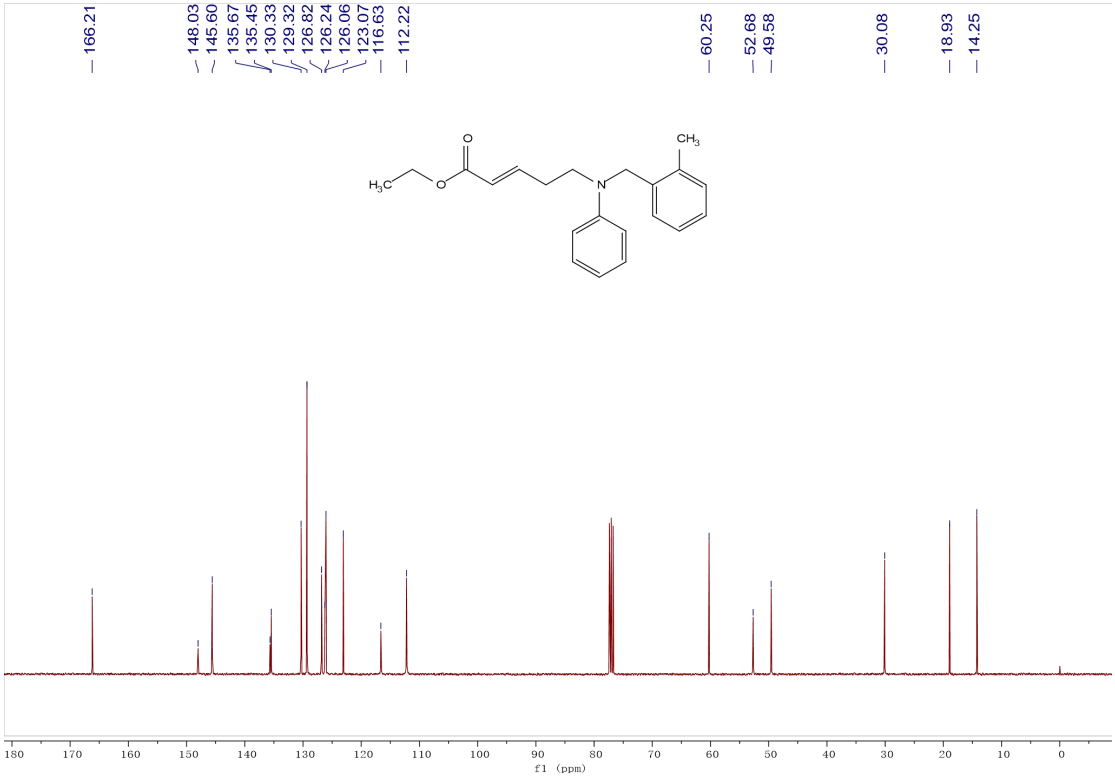
ethyl (E)-5-((3-chlorobenzyl)(phenyl)amino)pent-2-enoate (**1l**)



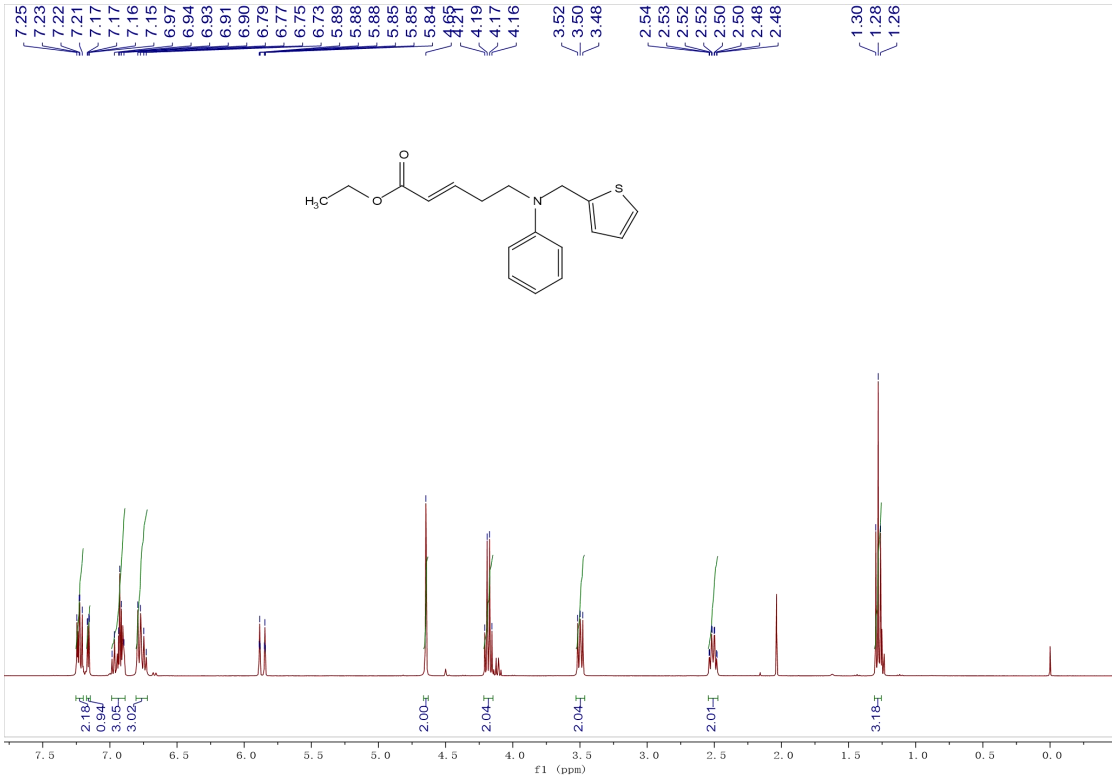


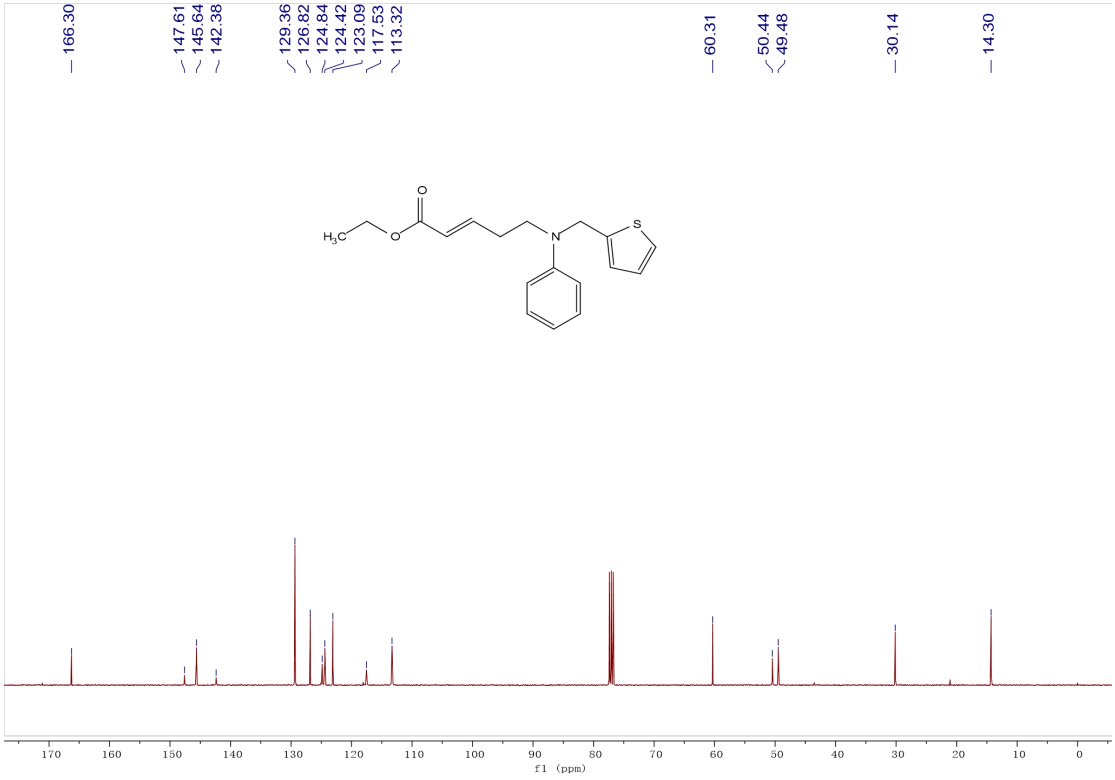
ethyl (E)-5-((2-methylbenzyl)(phenyl)amino)pent-2-enoate (**1m**)



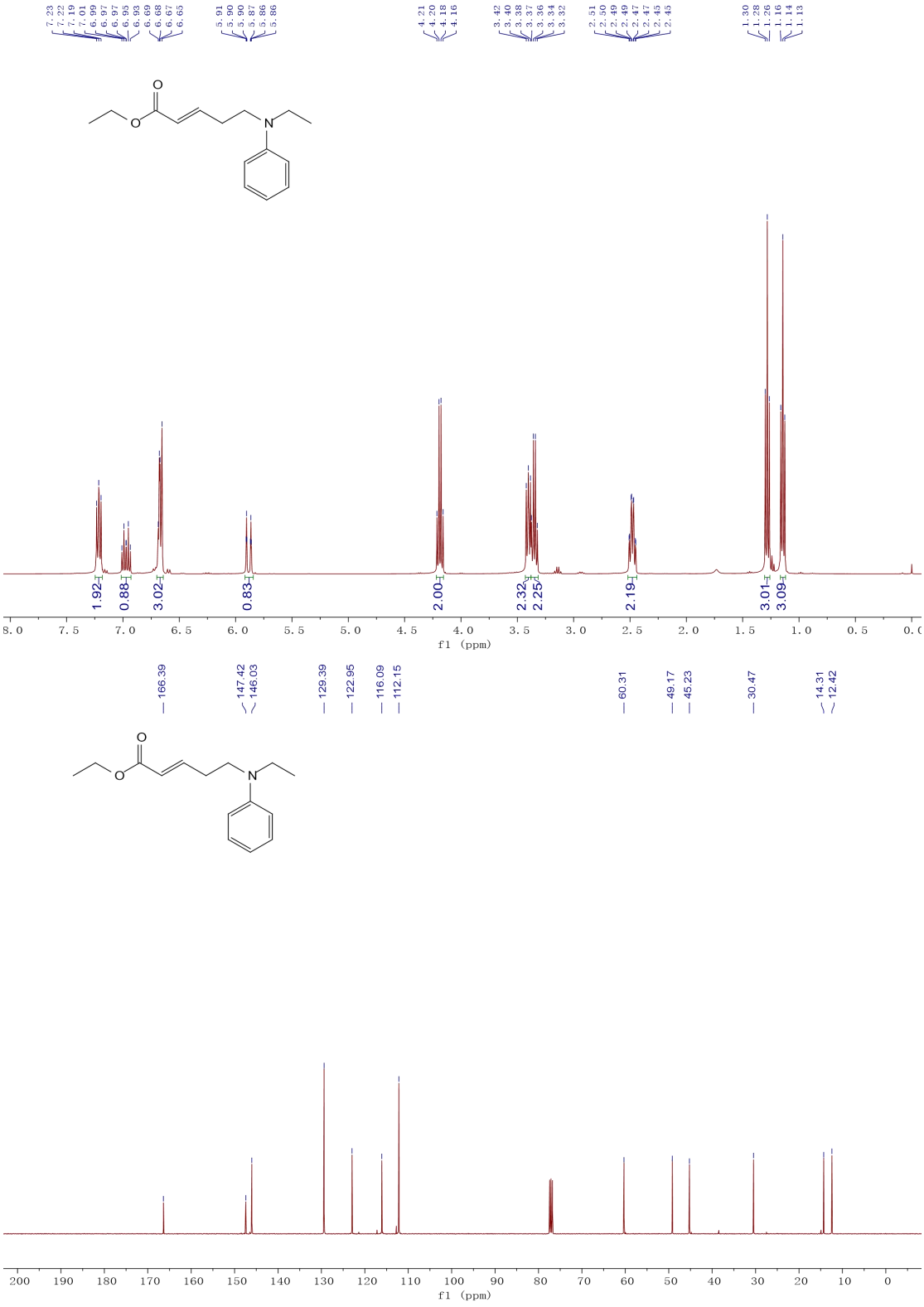


ethyl (*E*)-5-(phenyl(thiophen-2-ylmethyl)amino)pent-2-enoate (**1n**)

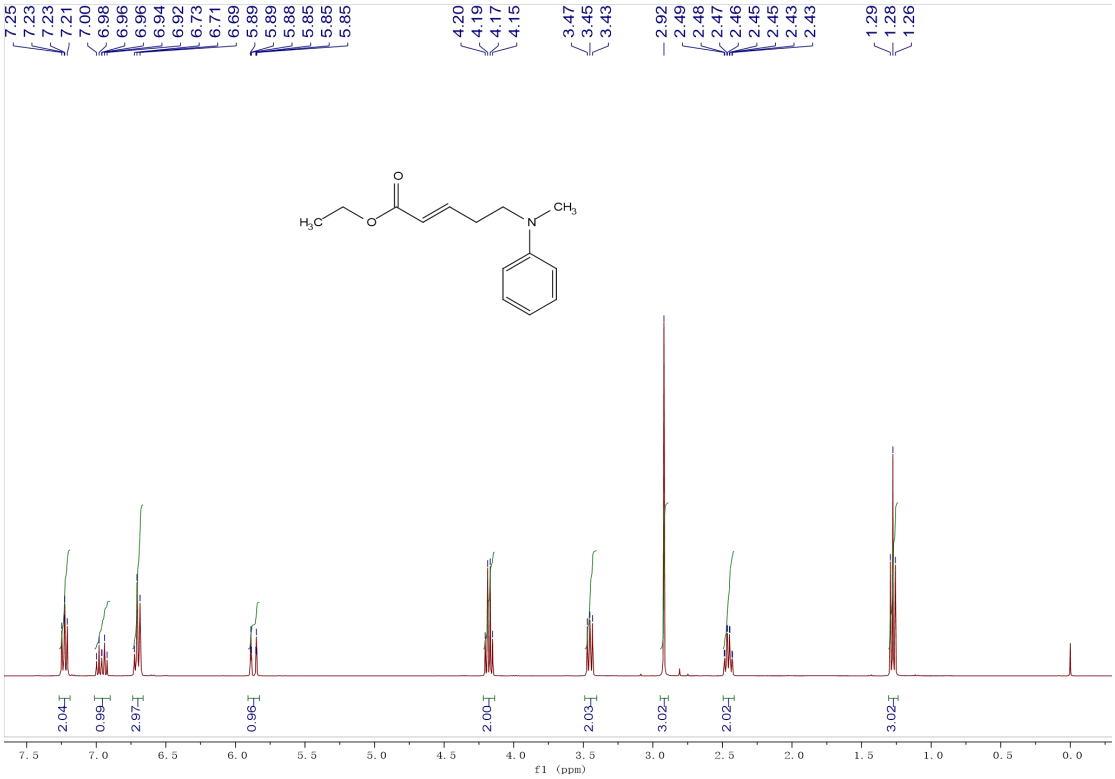


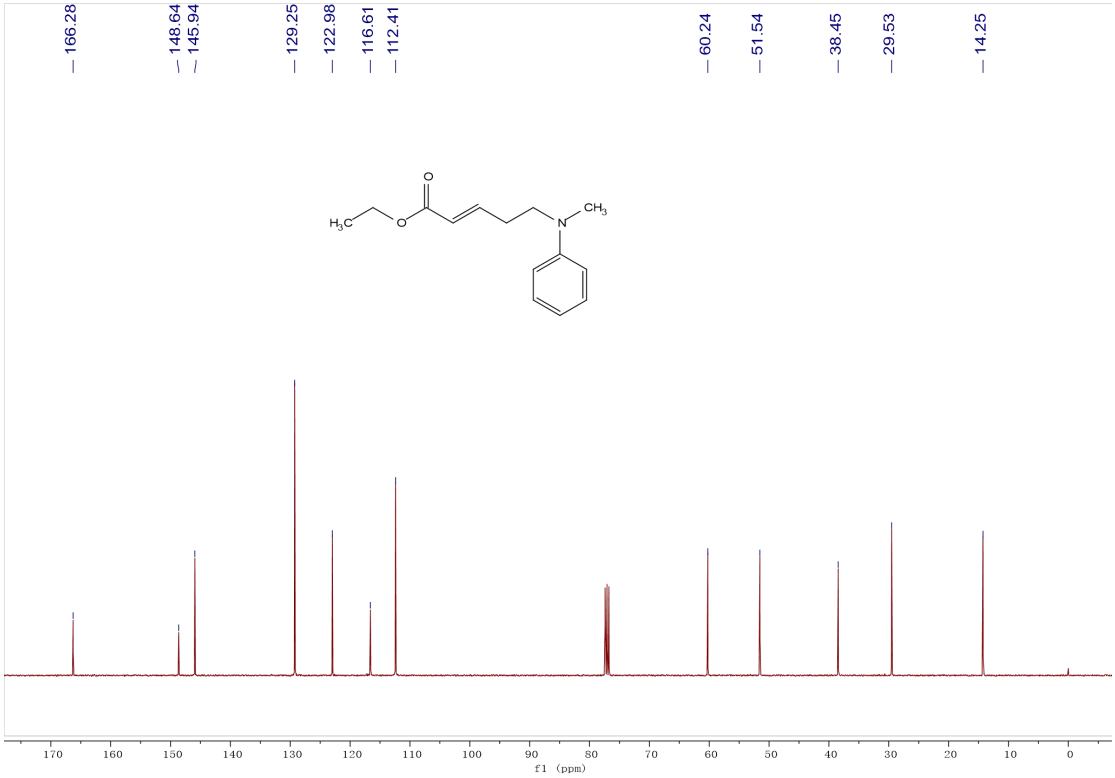


ethyl (E)-5-(ethyl(phenyl)amino)pent-2-enoate (**1o**)

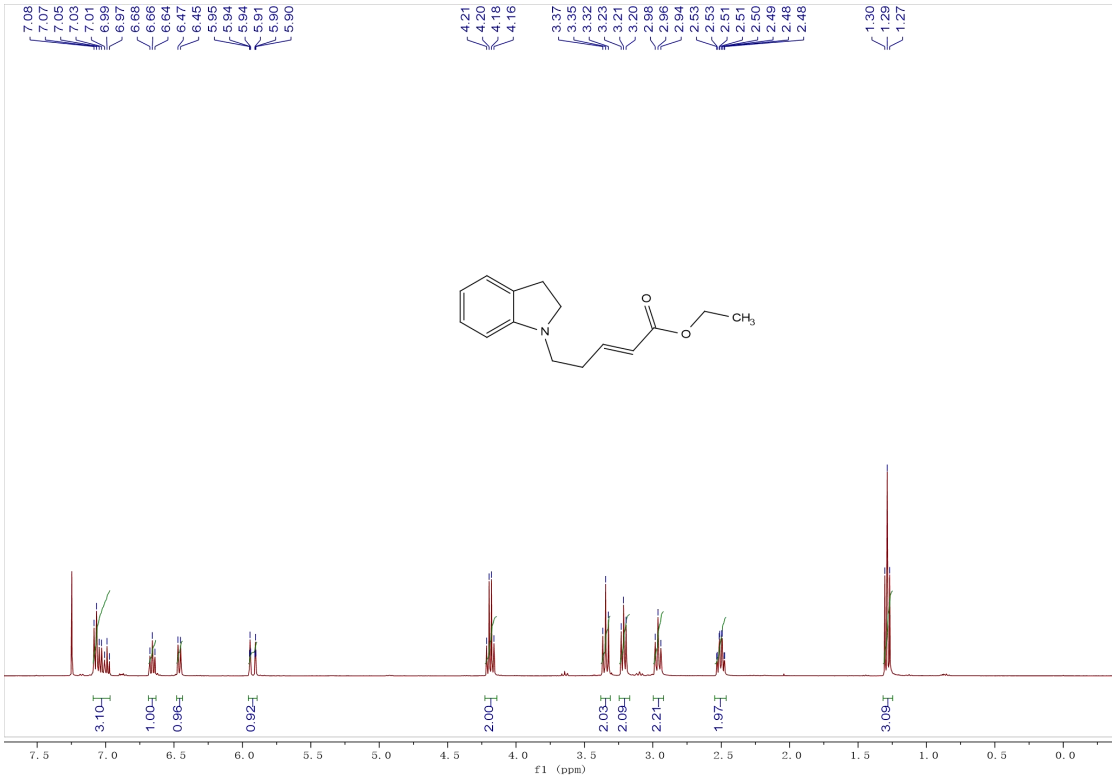


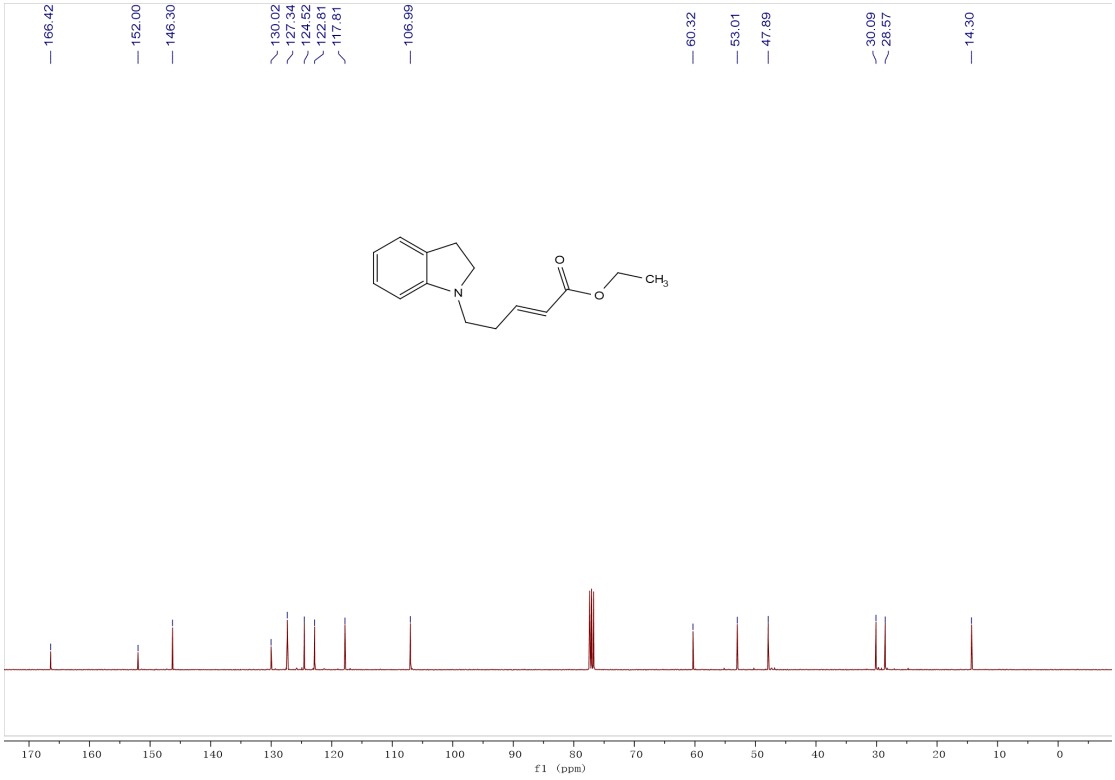
ethyl (E)-5-(methyl(phenyl)amino)pent-2-enoate (**1p**)



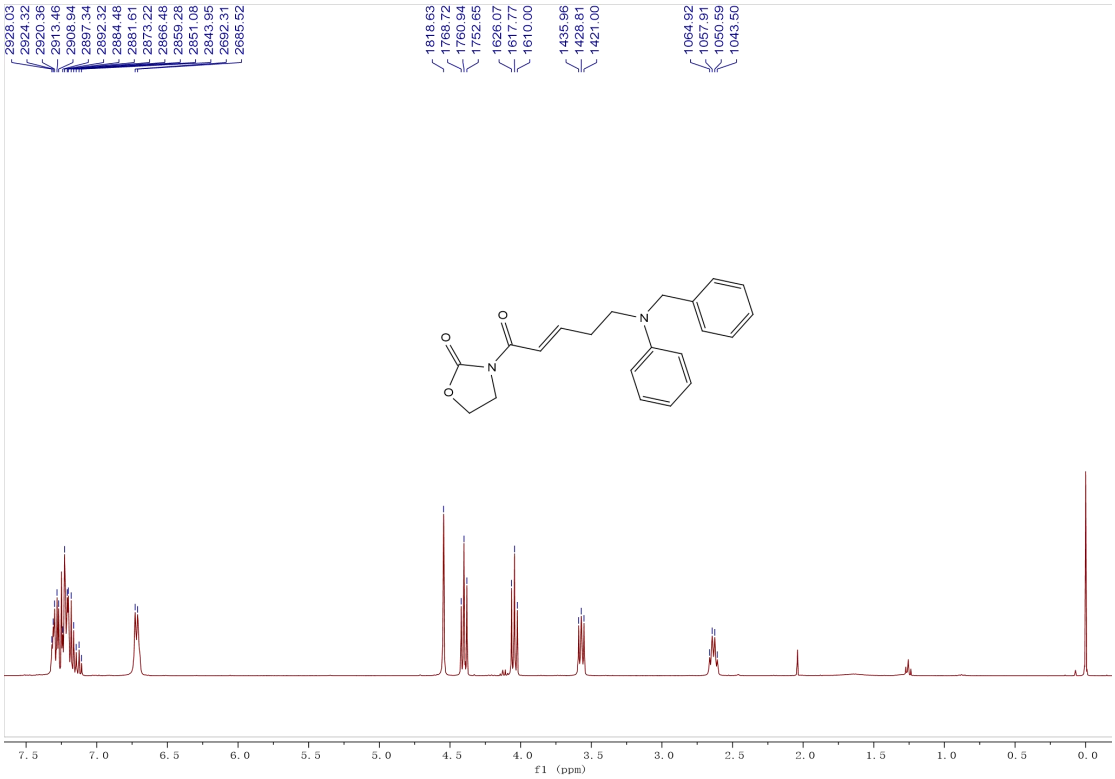


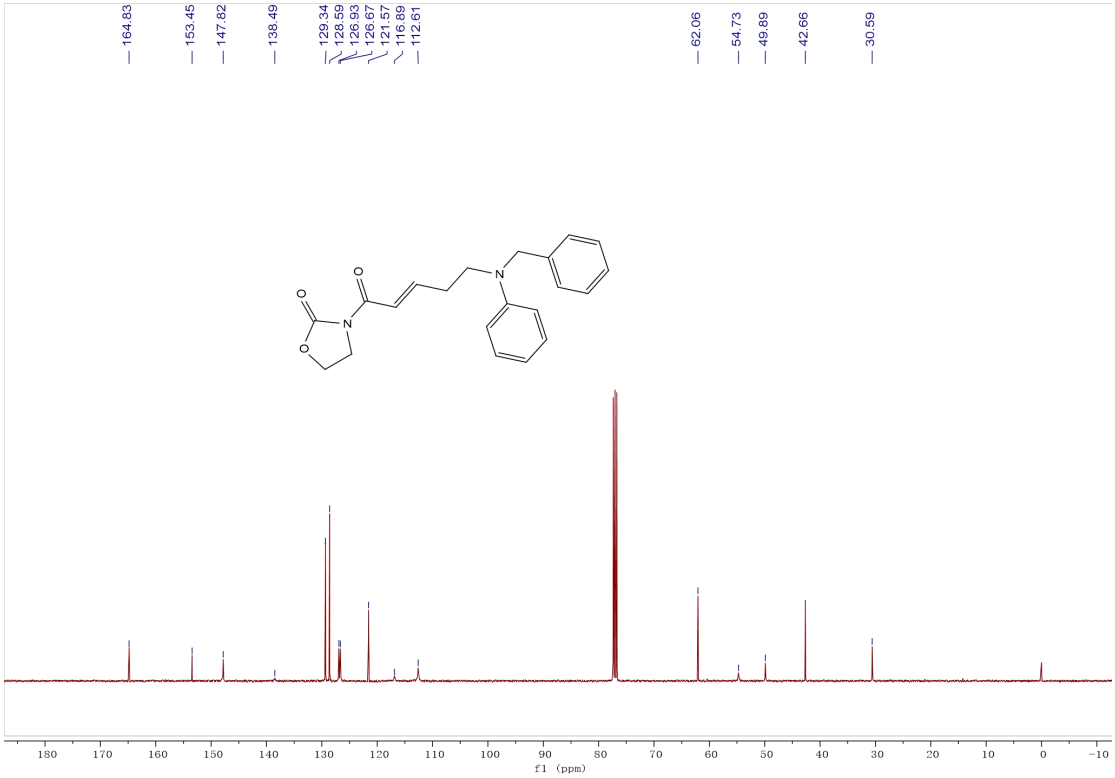
ethyl (E)-5-(indolin-1-yl)pent-2-enoate (**1q**)



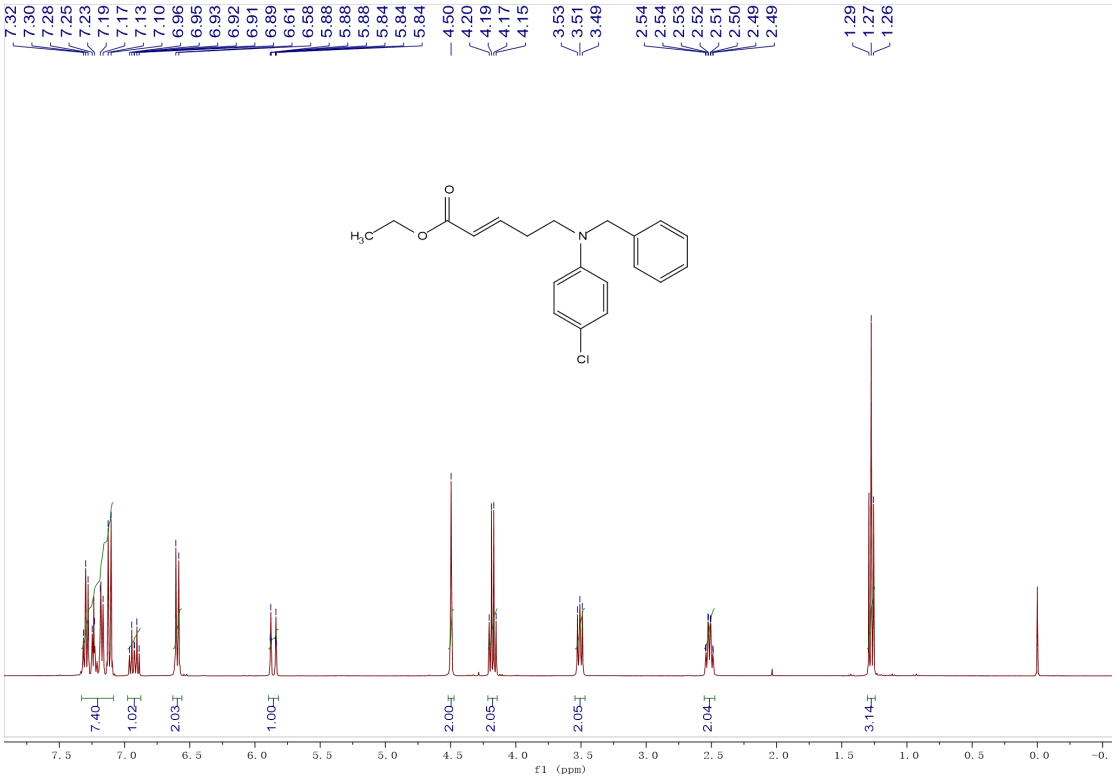


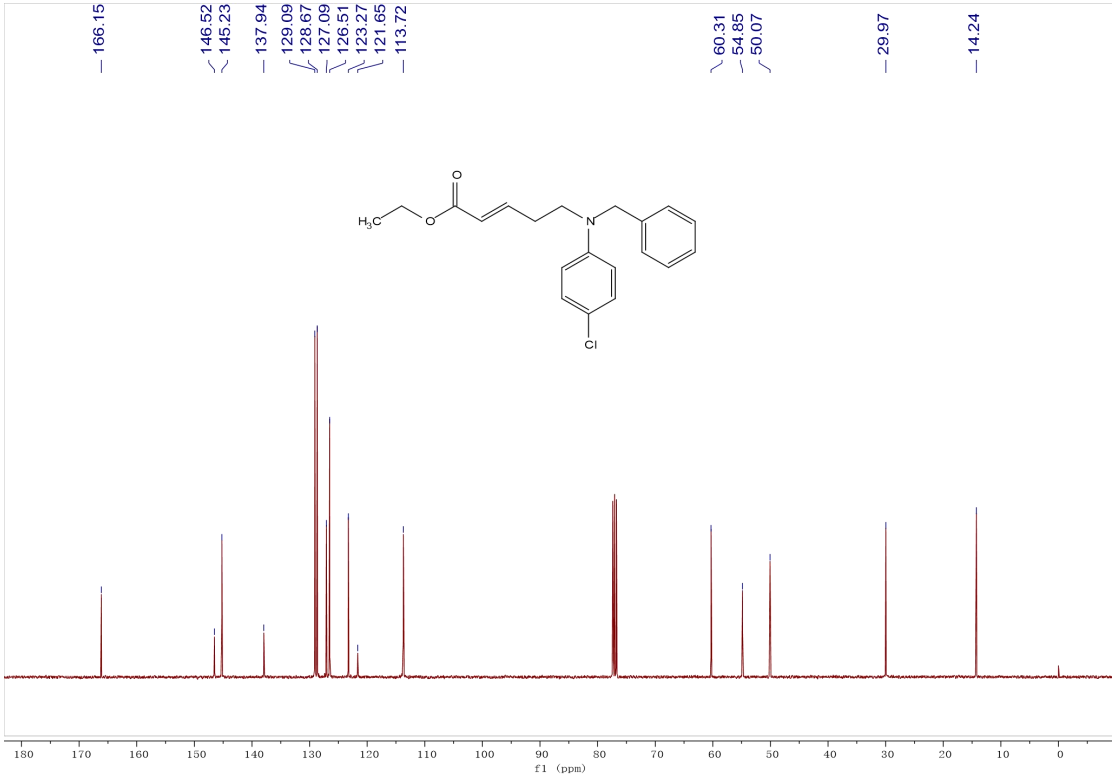
(E)-3-(5-(benzyl(phenyl)amino)pent-2-enoyl)oxazolidin-2-one (**1r**)



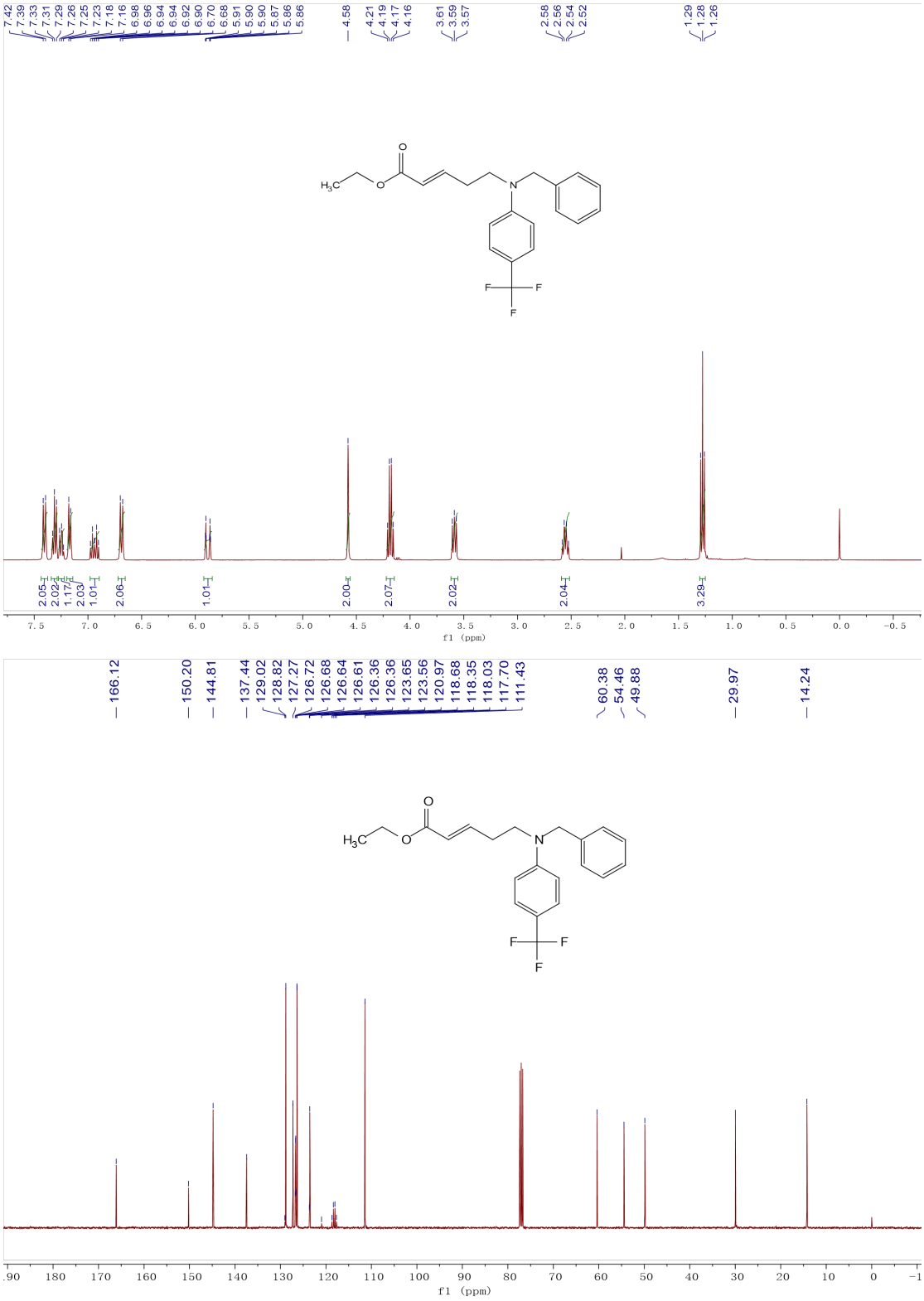


ethyl (E)-5-(benzyl(4-chlorophenyl)amino)pent-2-enoate (**1s**)

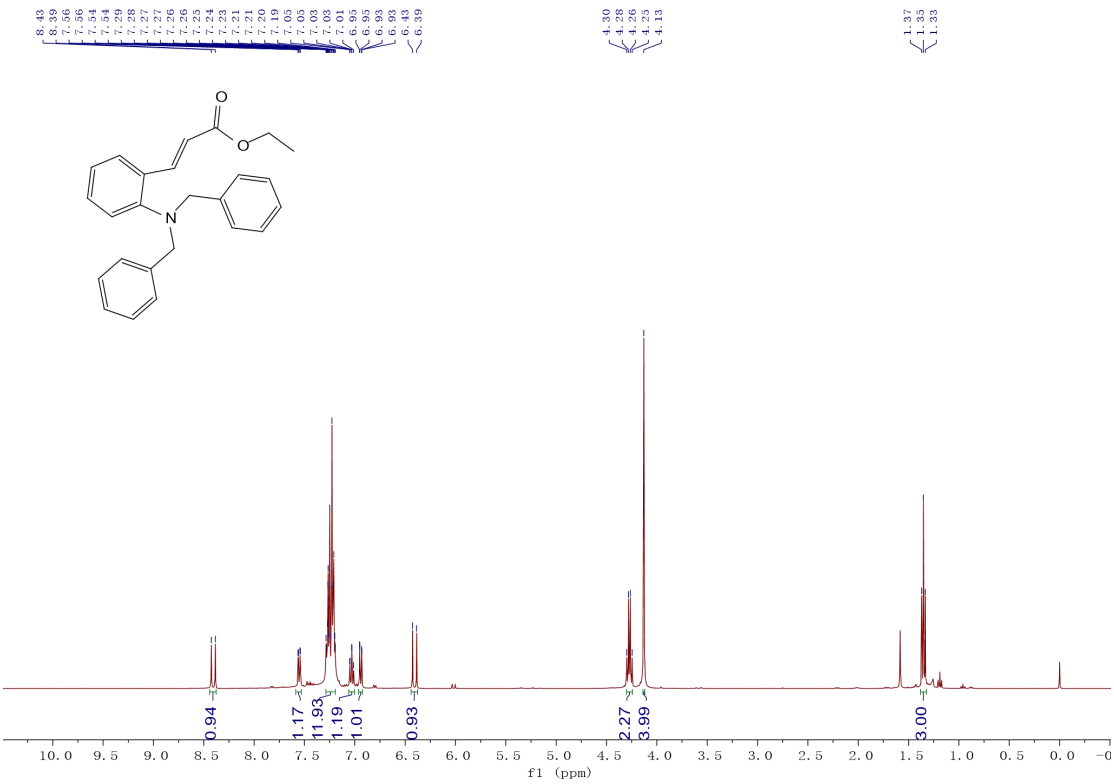


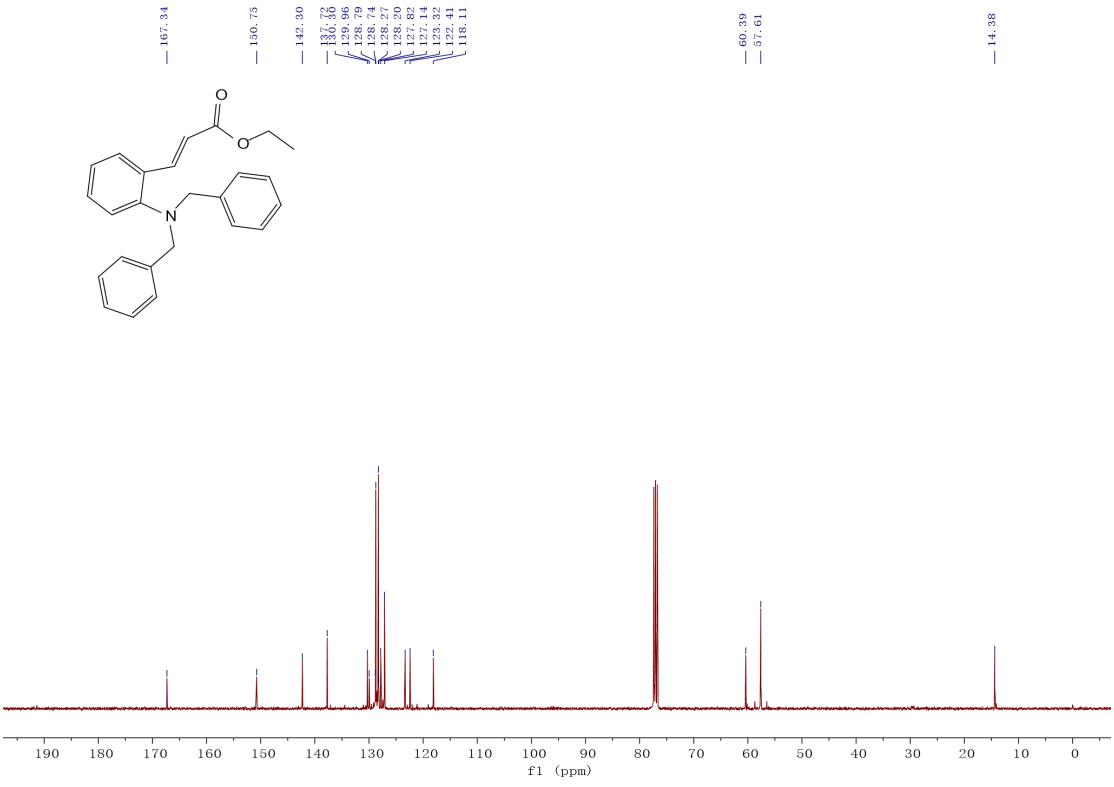


ethyl (E)-5-(benzyl(4-(trifluoromethyl)phenyl)amino)pent-2-enoate (**1t**)



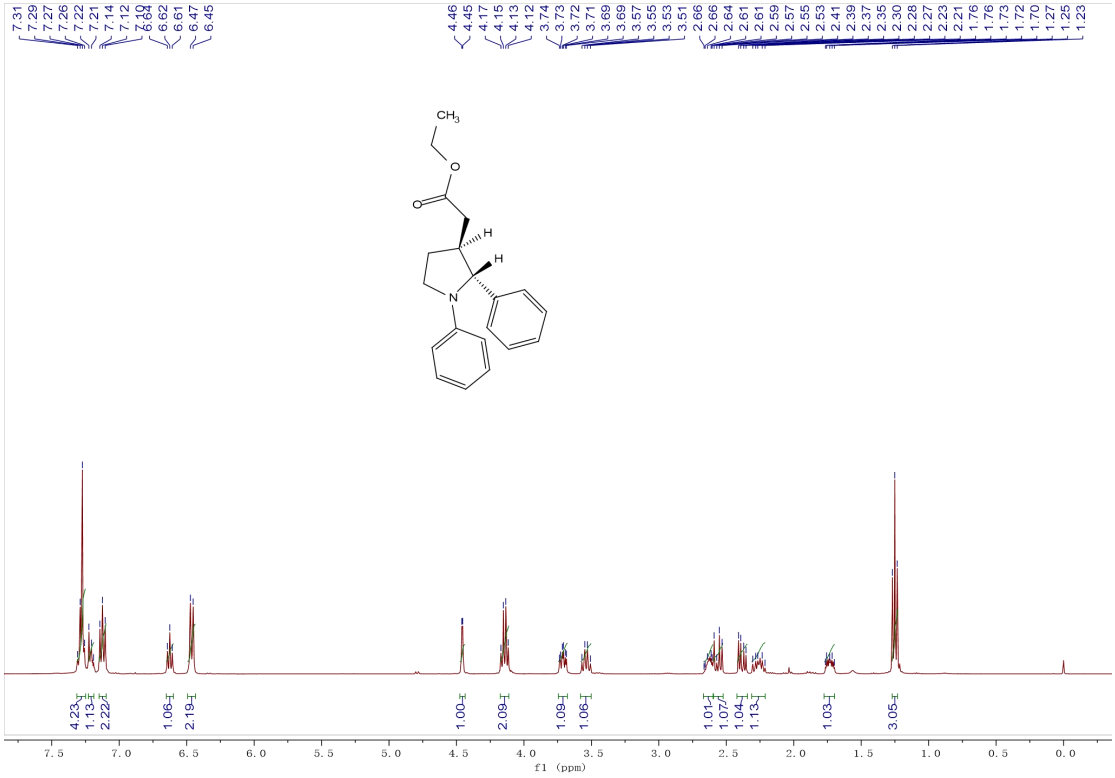
ethyl (E)-3-(2-(dibenzylamino)phenyl)acrylate (**1u**)

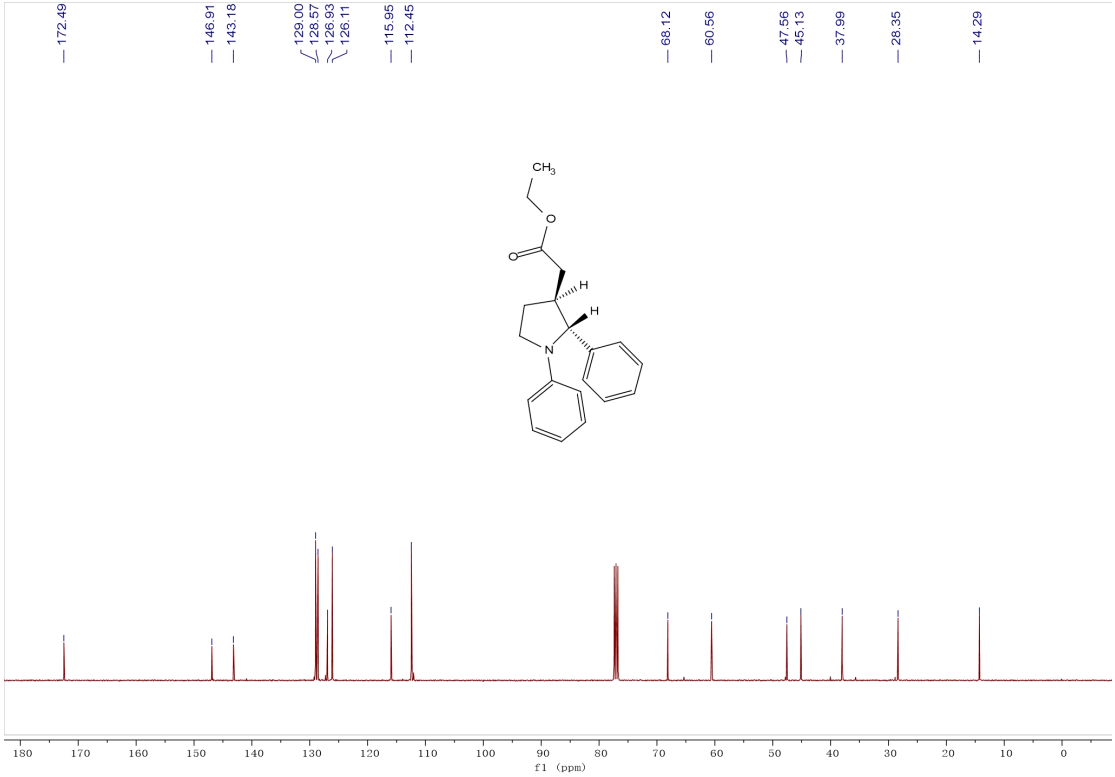

8.43
8.39
7.56
7.56
7.54
7.54
7.29
7.28
7.27
7.27
7.26
7.26
7.25
7.24
7.23
7.21
7.21
7.20
7.19
7.05
7.05
7.03
7.03
7.01
6.95
6.95
6.93
6.93
6.43
6.39
4.30
4.28
4.26
4.25
4.13
1.37
1.35
1.33
O
O
N
0.94
1.17
11.93
1.19
1.01
0.93
2.27
3.99
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

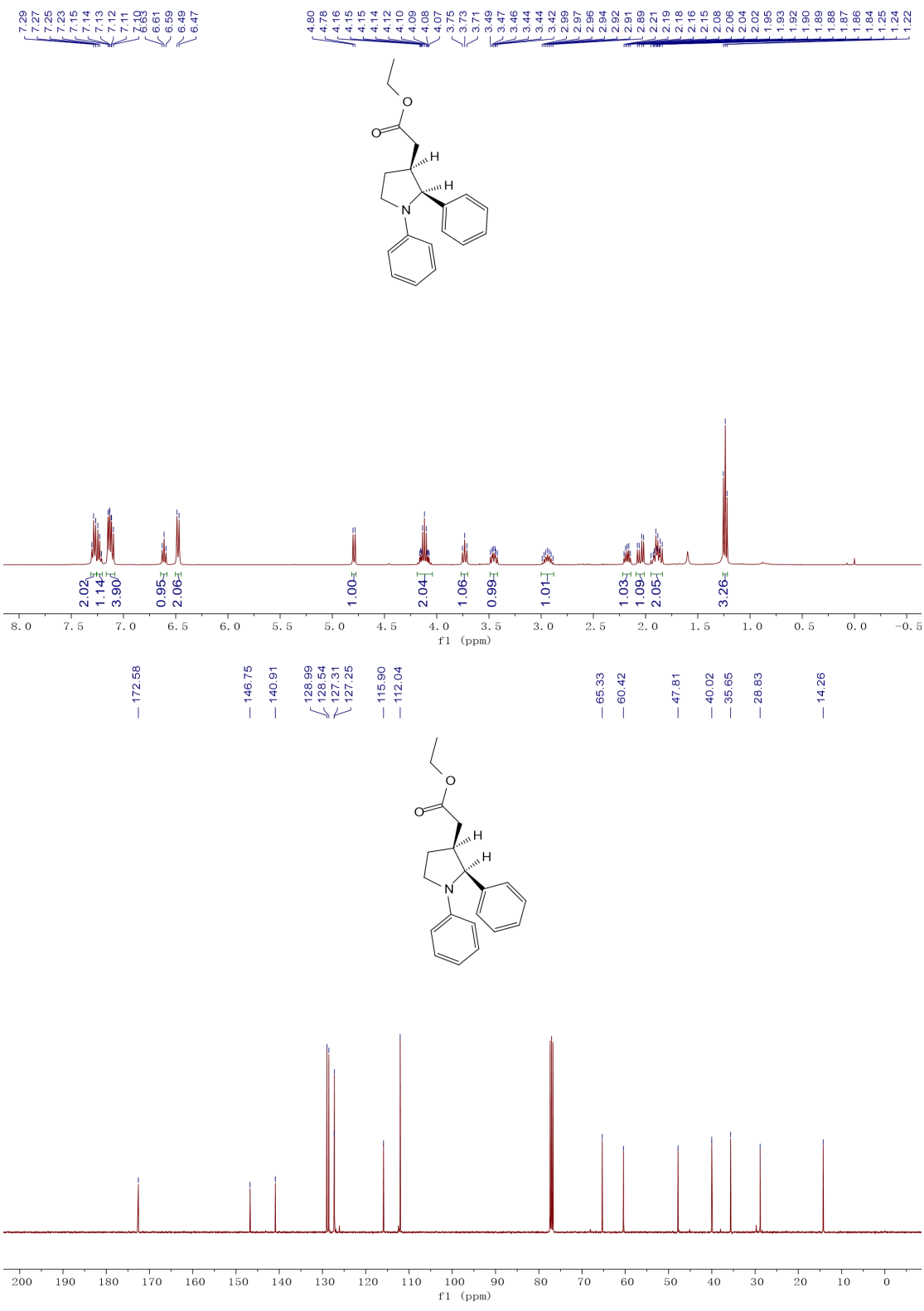

167.34
150.75
142.30
137.72
130.36
129.96
128.79
128.74
128.27
128.20
127.82
127.14
123.32
122.41
118.11
60.39
57.61
14.38
O
O
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

NMR-Spectra of Products

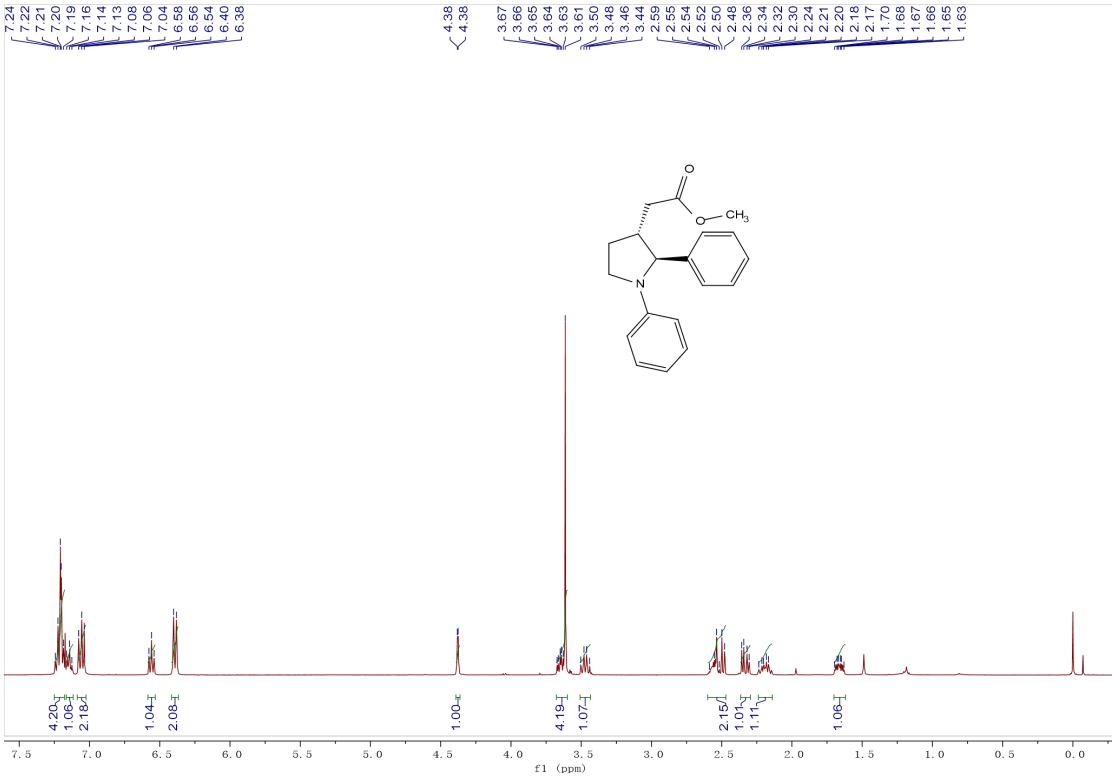
ethyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2a**)

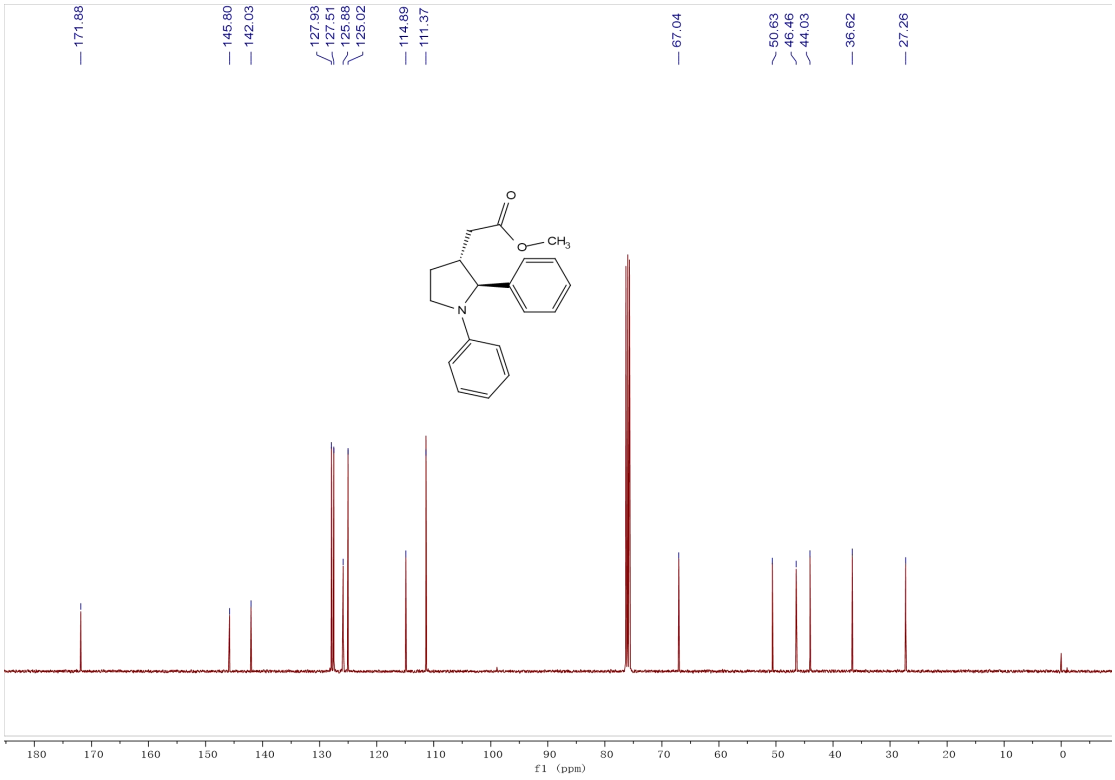




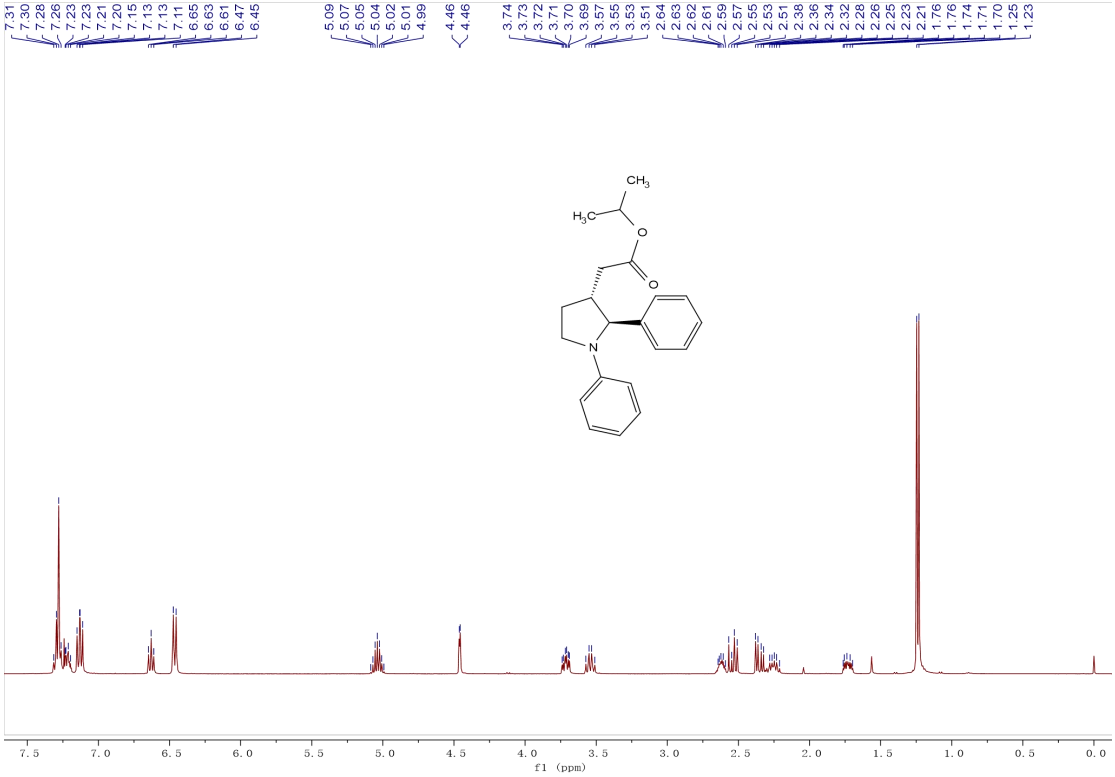


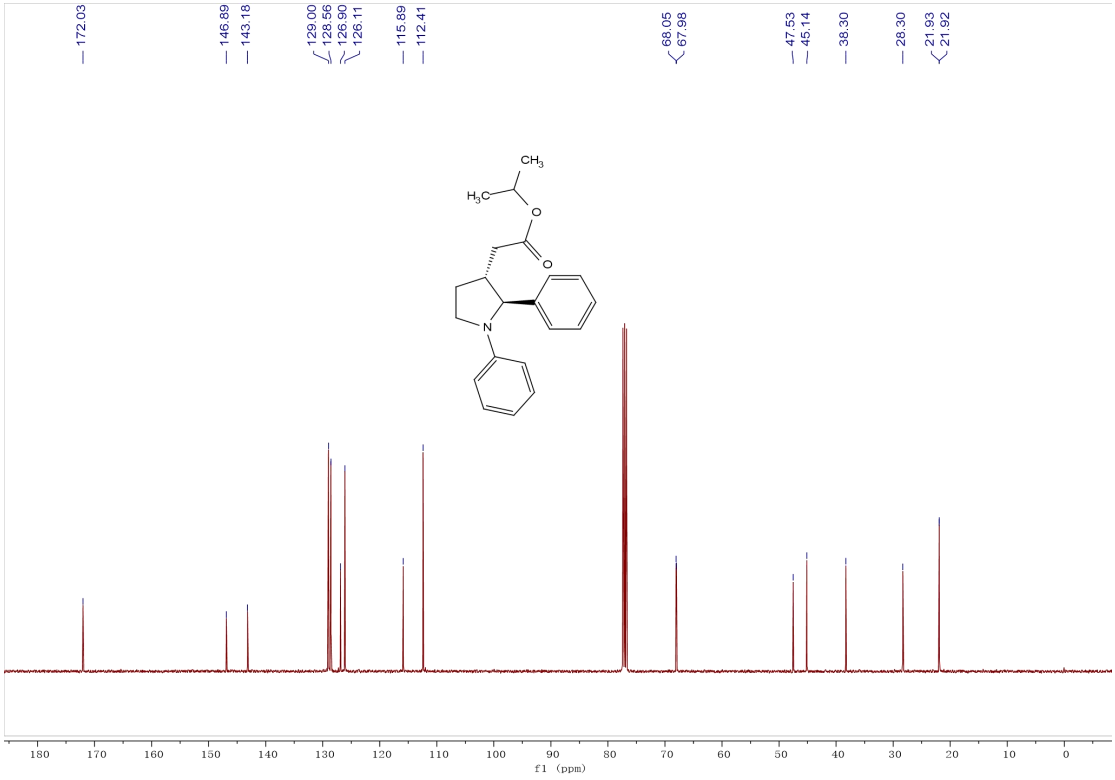
(trans)-methyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2b**)


7.24
7.22
7.21
7.20
7.19
7.16
7.14
7.13
7.08
7.06
7.04
6.58
6.56
6.54
6.40
6.38
4.38
4.38
3.67
3.66
3.65
3.64
3.63
3.61
3.50
3.48
3.46
3.44
2.59
2.55
2.54
2.52
2.50
2.48
2.36
2.34
2.32
2.30
2.24
2.21
2.20
2.18
2.17
1.70
1.68
1.67
1.66
1.65
1.63
O
O
CH3
N
4.20
1.06
2.18
1.04
2.08
1.00
4.19
1.07
2.15
1.01
1.11
1.06
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

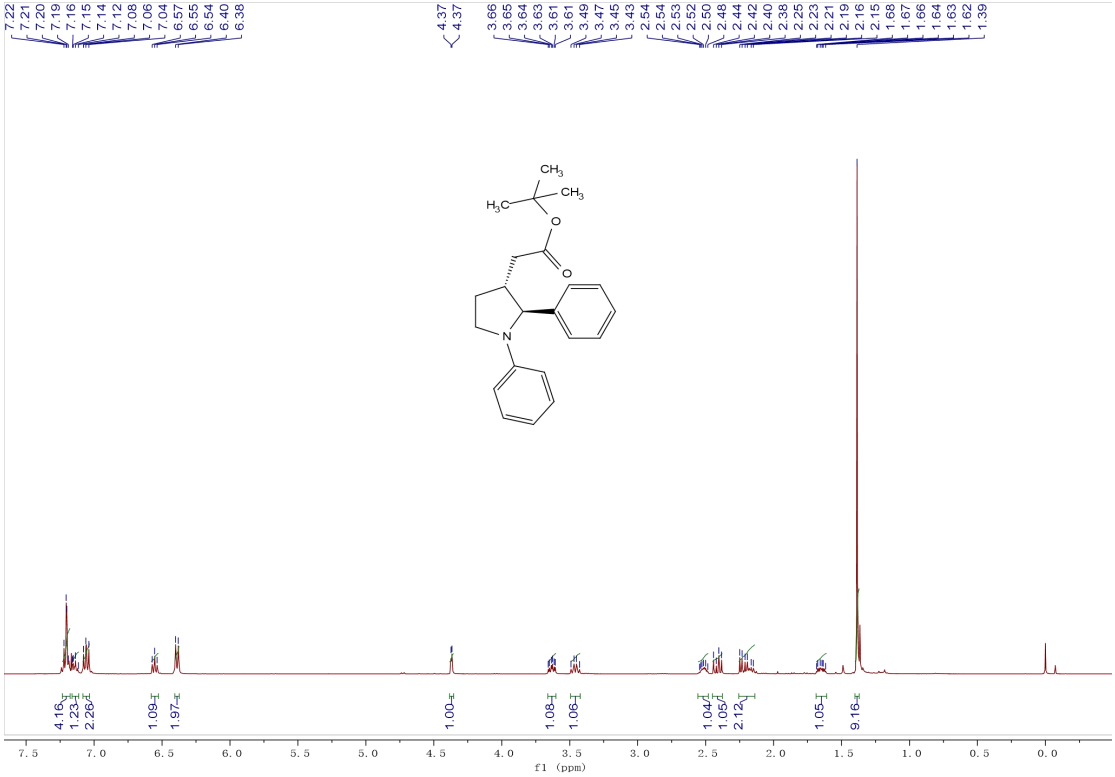

171.88
145.80
142.03
127.93
127.51
125.88
125.02
114.89
111.37
67.04
50.63
46.46
44.03
36.62
27.26
O
O
CH3
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

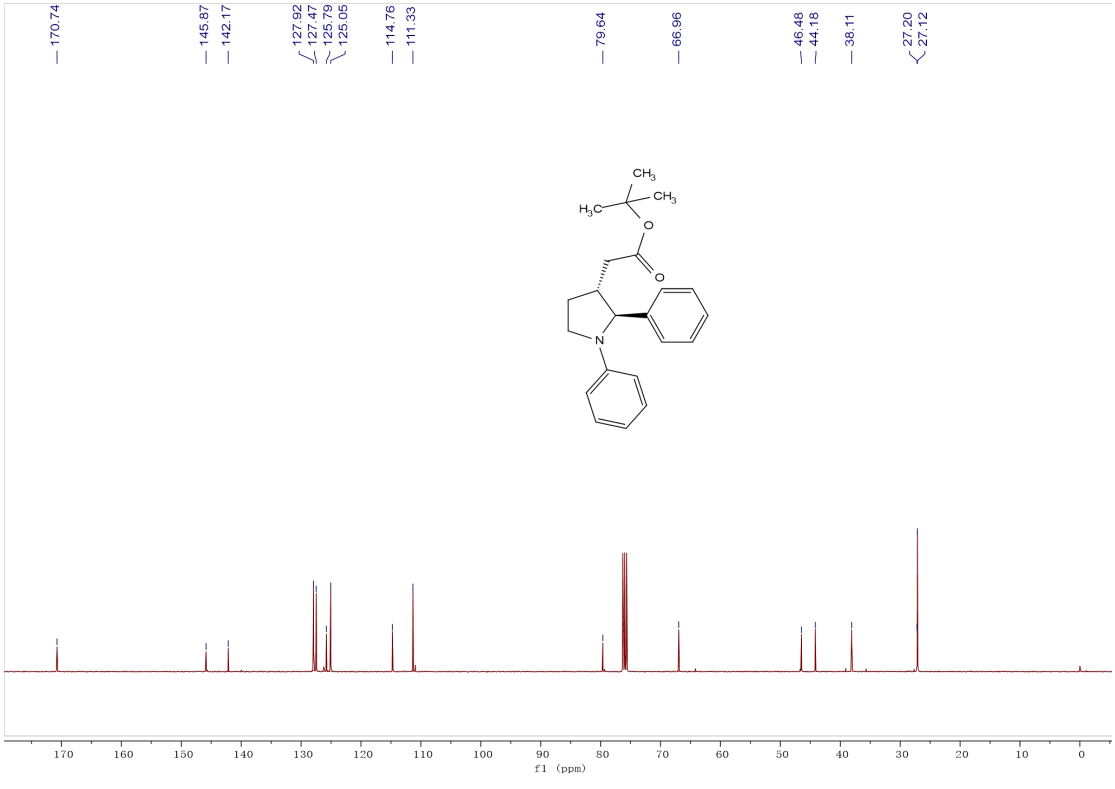
isopropyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2c**)



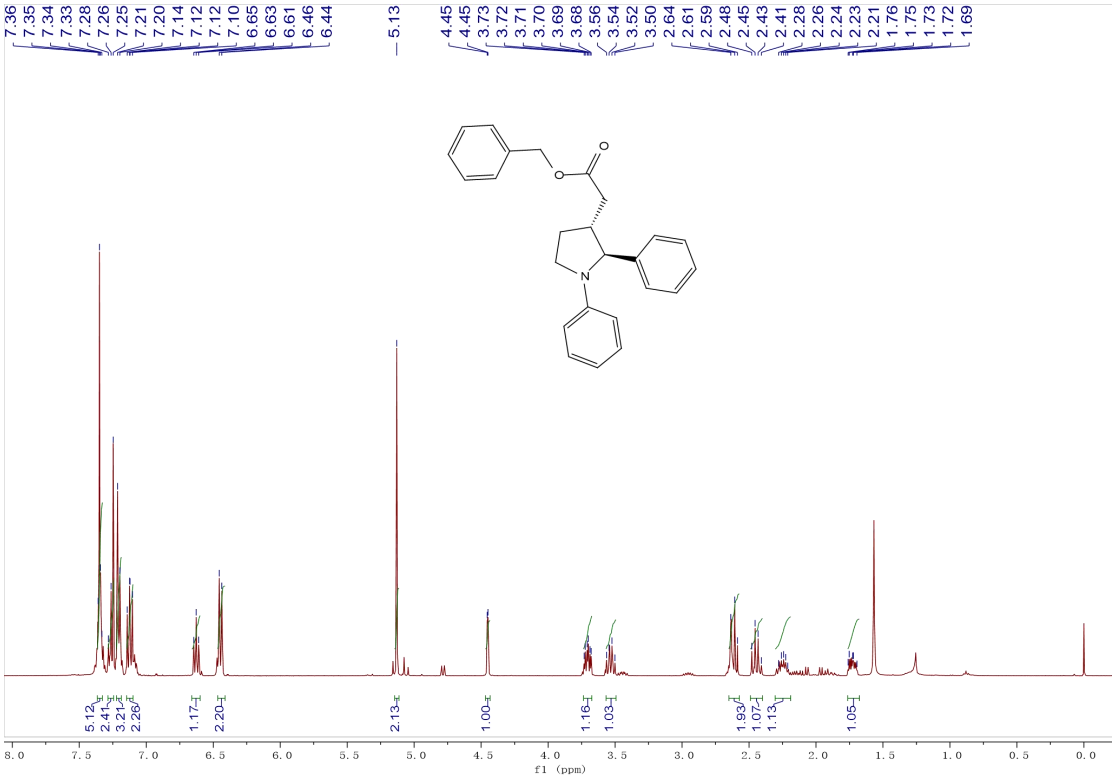


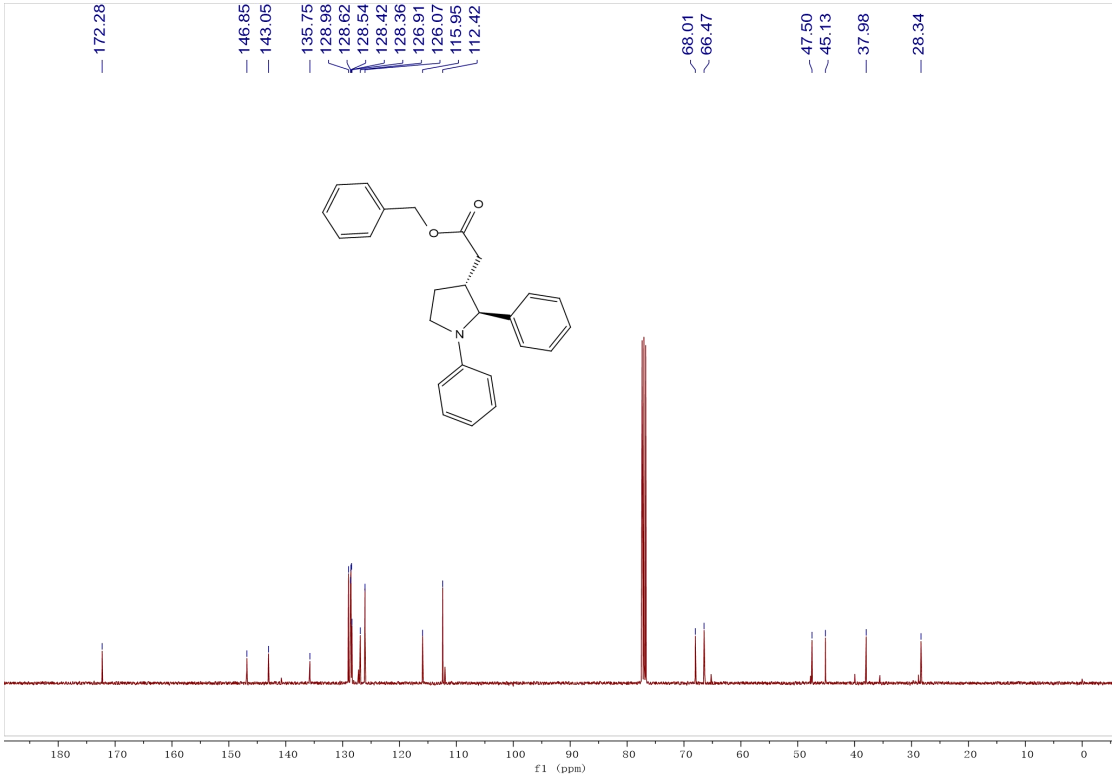
tert-butyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2d**)



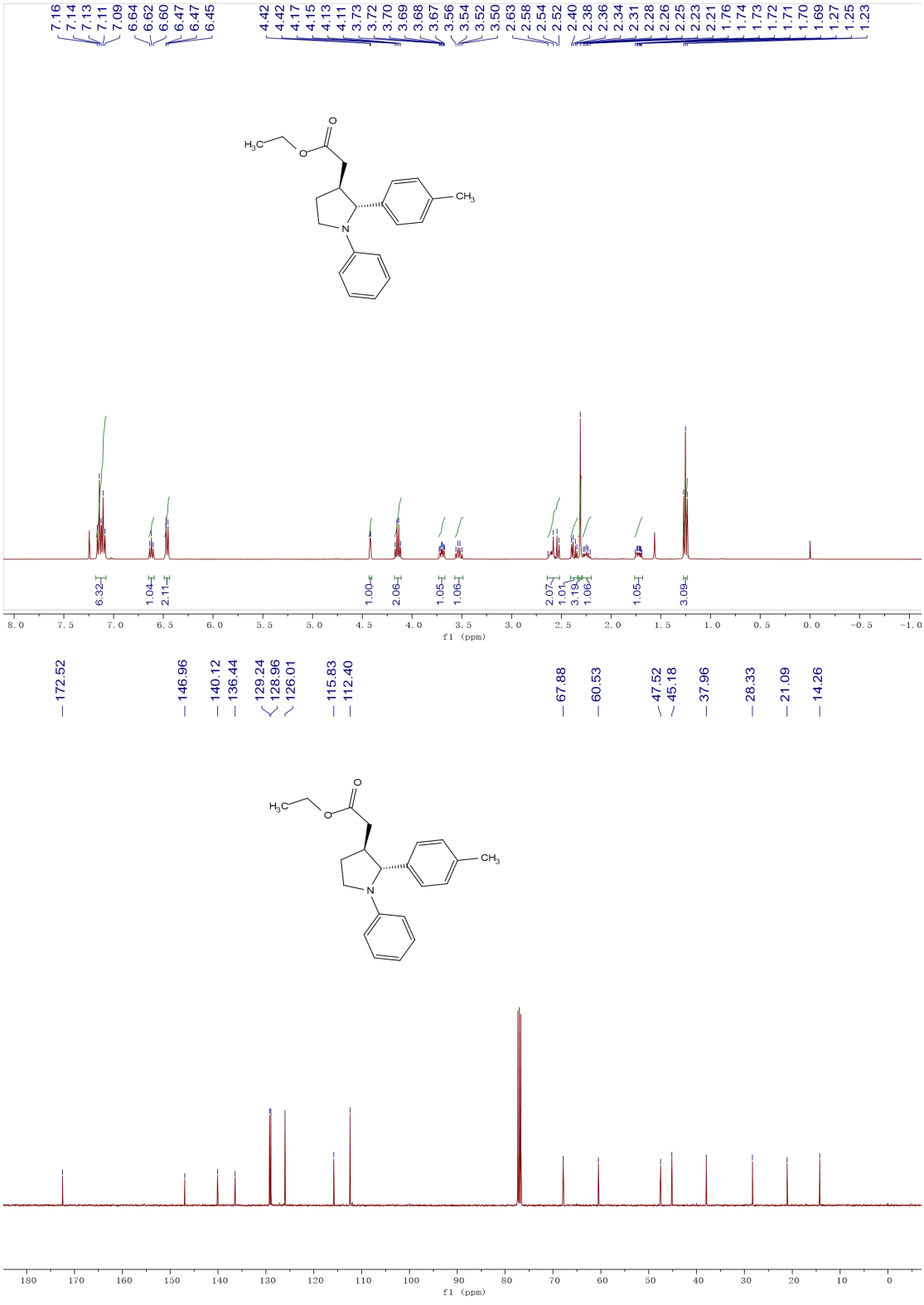


benzyl 2-(1,2-diphenylpyrrolidin-3-yl)acetate (**2e**)

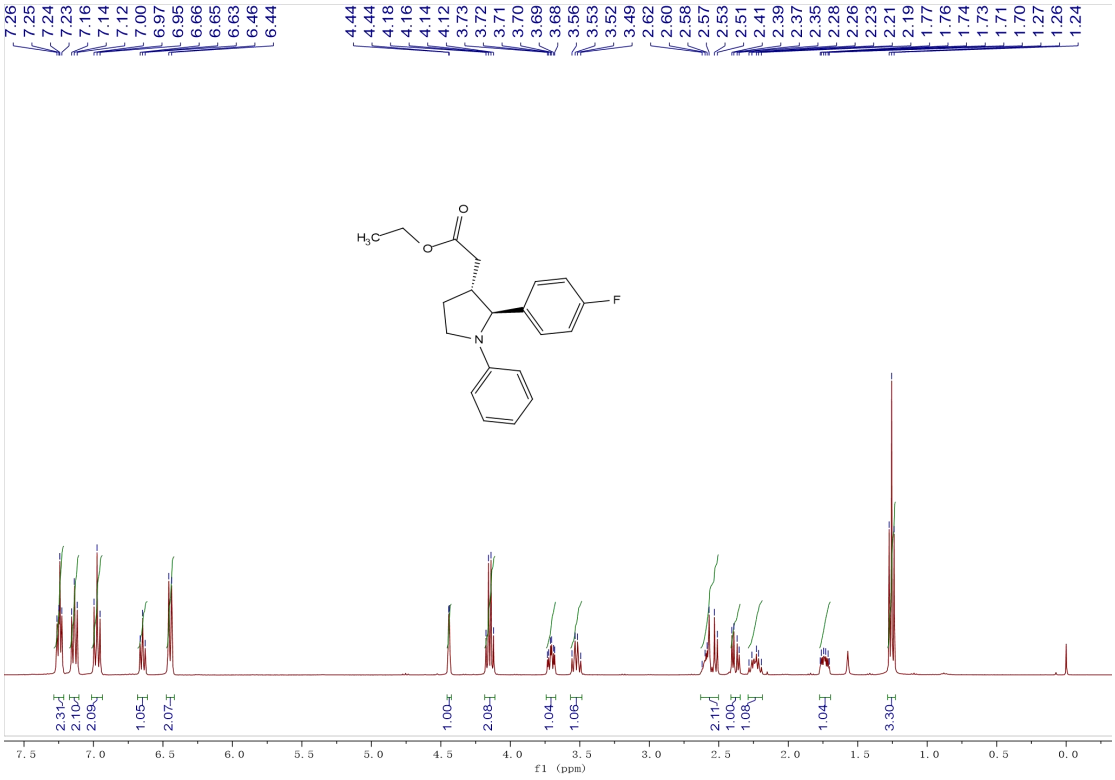


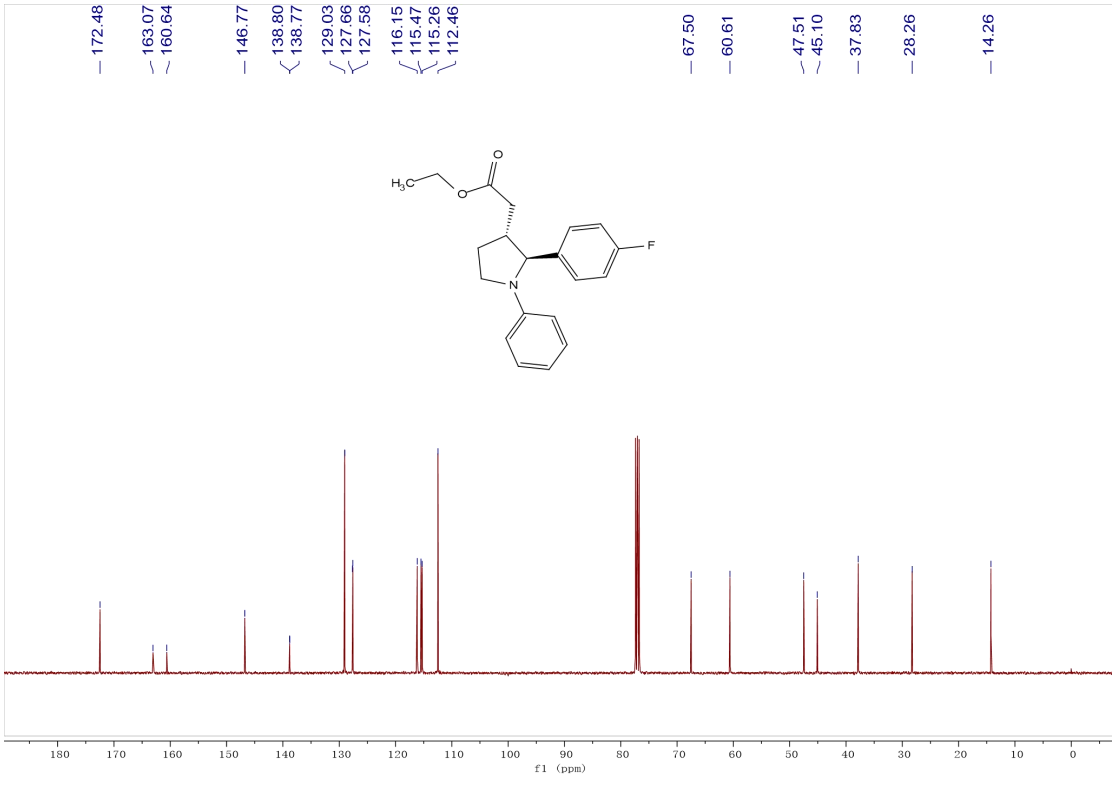


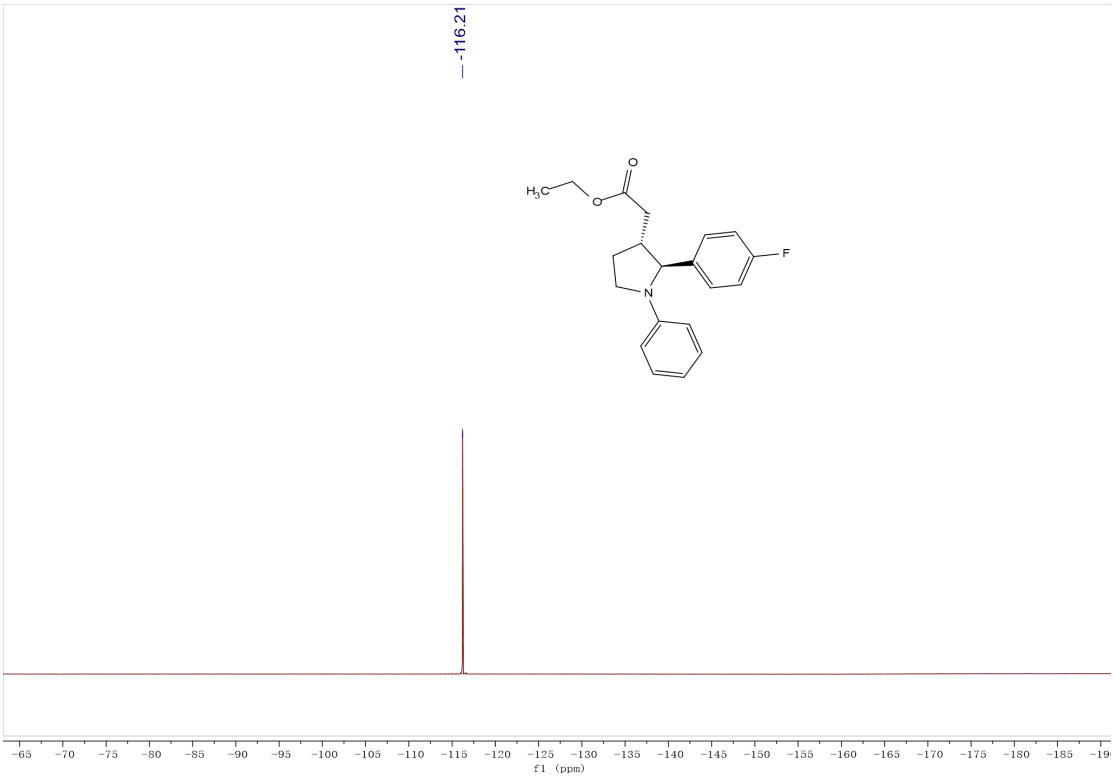
ethyl 2-(1-phenyl-2-(p-tolyl)pyrrolidin-3-yl)acetate (**2f**)



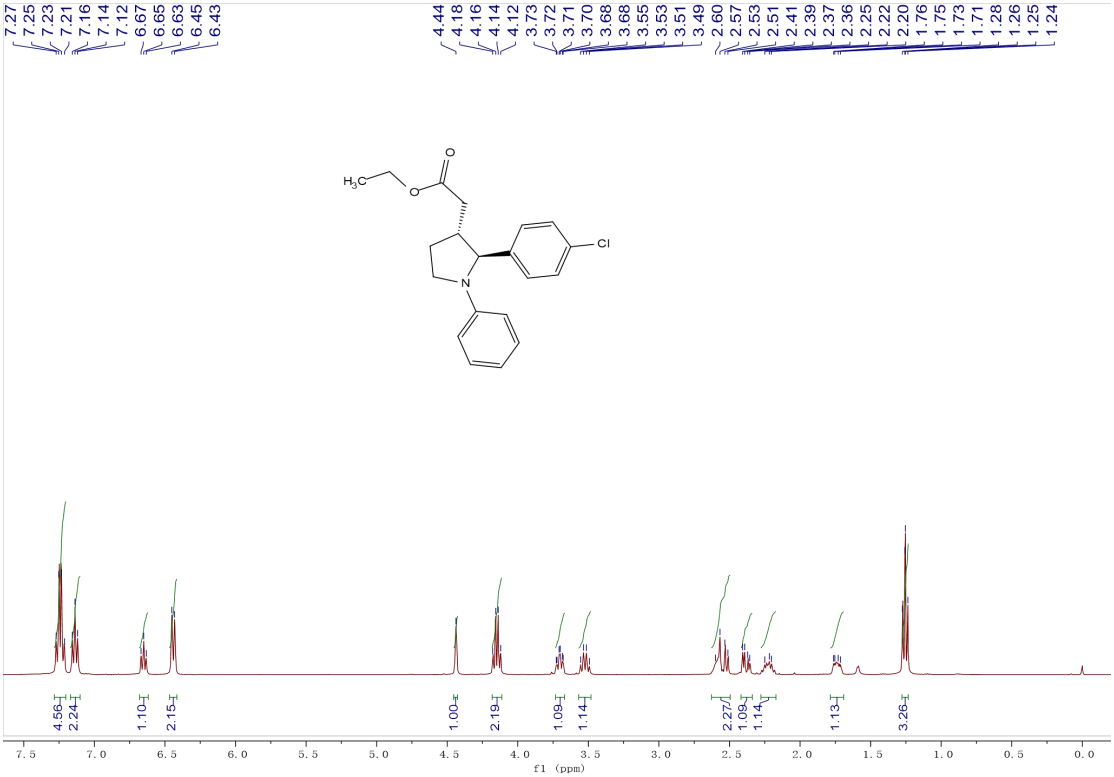
ethyl 2-(2-(4-fluorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2g**)

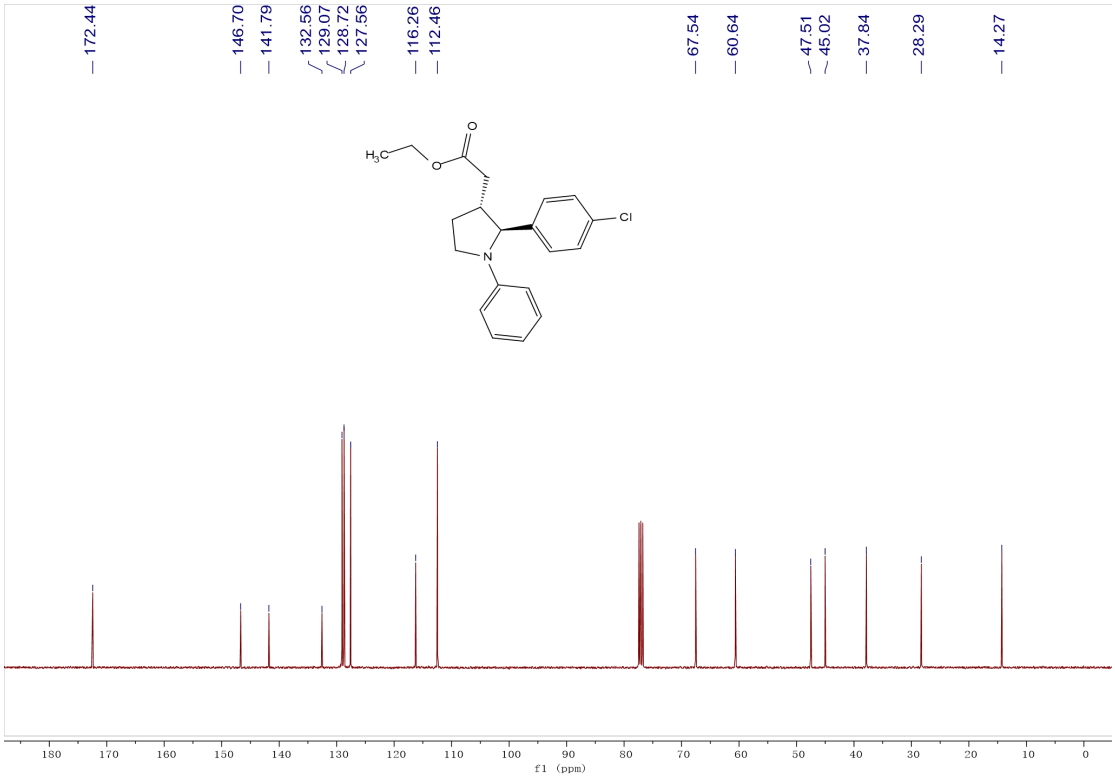

7.26 7.25 7.24 7.23 7.16 7.14 7.12 7.00 6.97 6.95 6.66 6.65 6.63 6.46 6.44
4.44 4.44 4.18 4.16 4.14 4.12 3.73 3.72 3.71 3.70 3.69 3.68 3.56 3.53 3.52 3.49
2.62 2.60 2.58 2.57 2.53 2.51 2.41 2.39 2.37 2.35 2.28 2.26 2.23 2.21 2.19 1.77 1.76 1.74 1.73 1.71 1.70 1.27 1.26 1.24
O
H3C
O
F
N
2.31 2.10 2.09 1.05 2.07 1.00 2.08 1.04 1.06 2.11 1.00 1.08 1.04 3.30
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


172.48 163.07 160.64 146.77 138.80 138.77 129.03 127.66 127.58 116.15 115.47 115.26 112.46
67.50 60.61 47.51 45.10 37.83 28.26 14.26
O
H3C
O
F
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

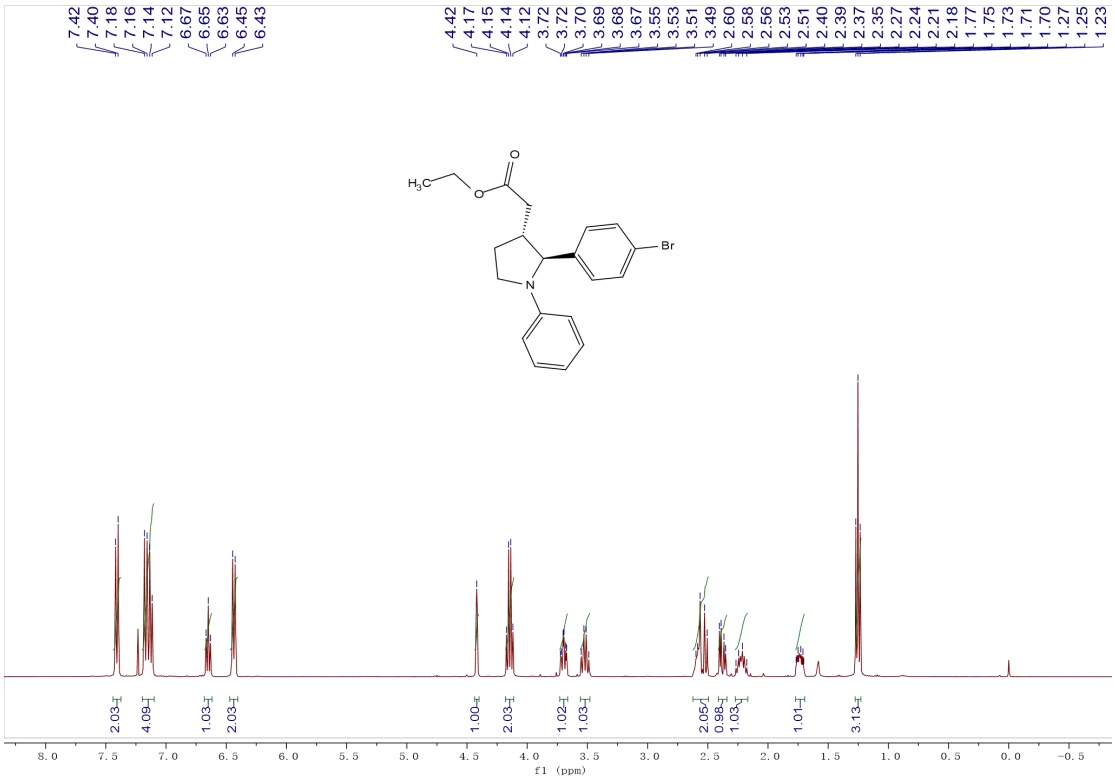


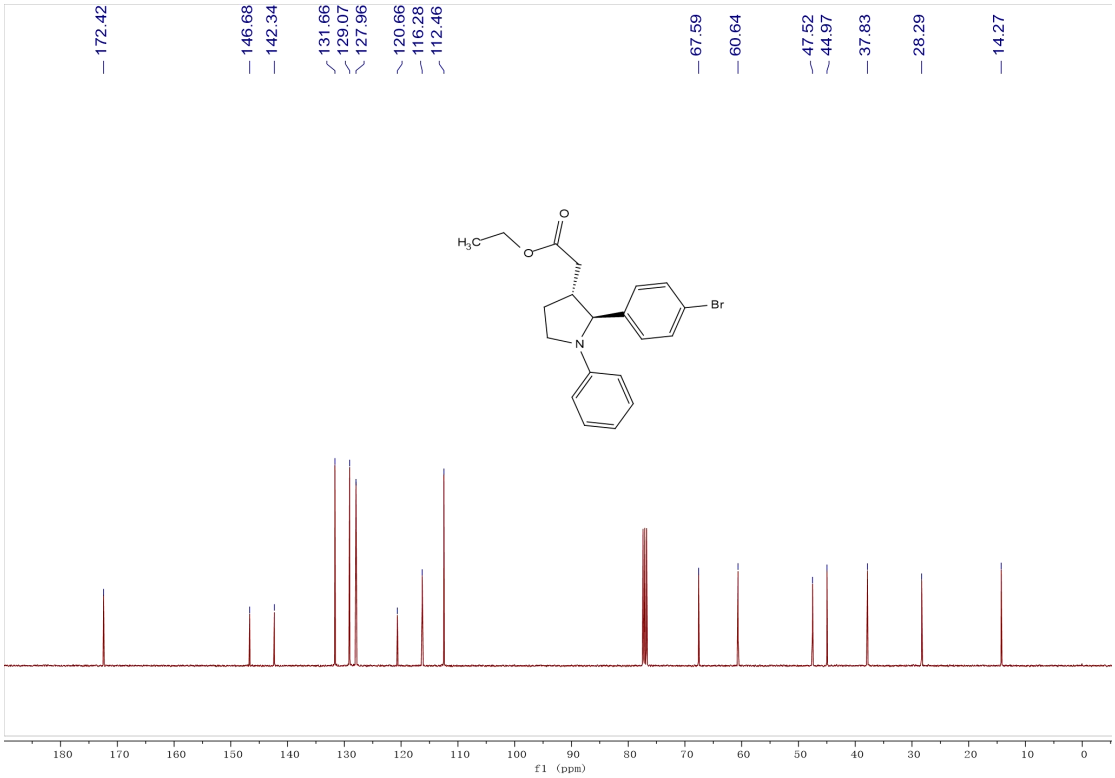
ethyl 2-(2-(4-chlorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2h**)



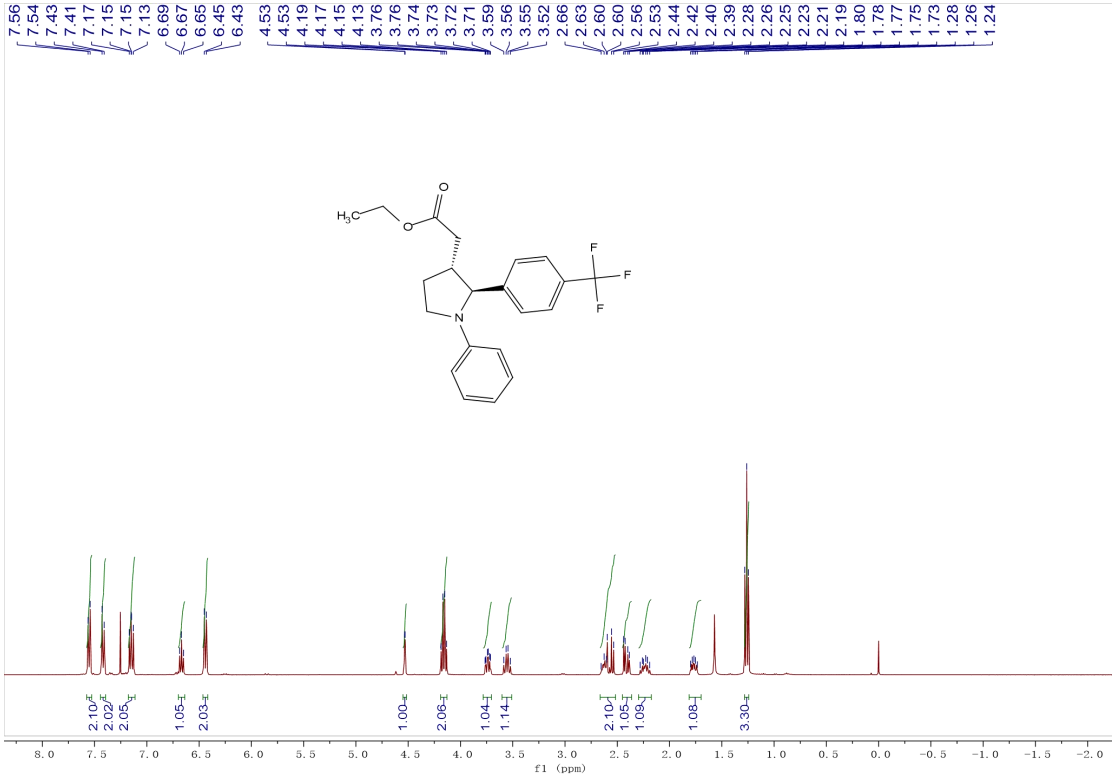


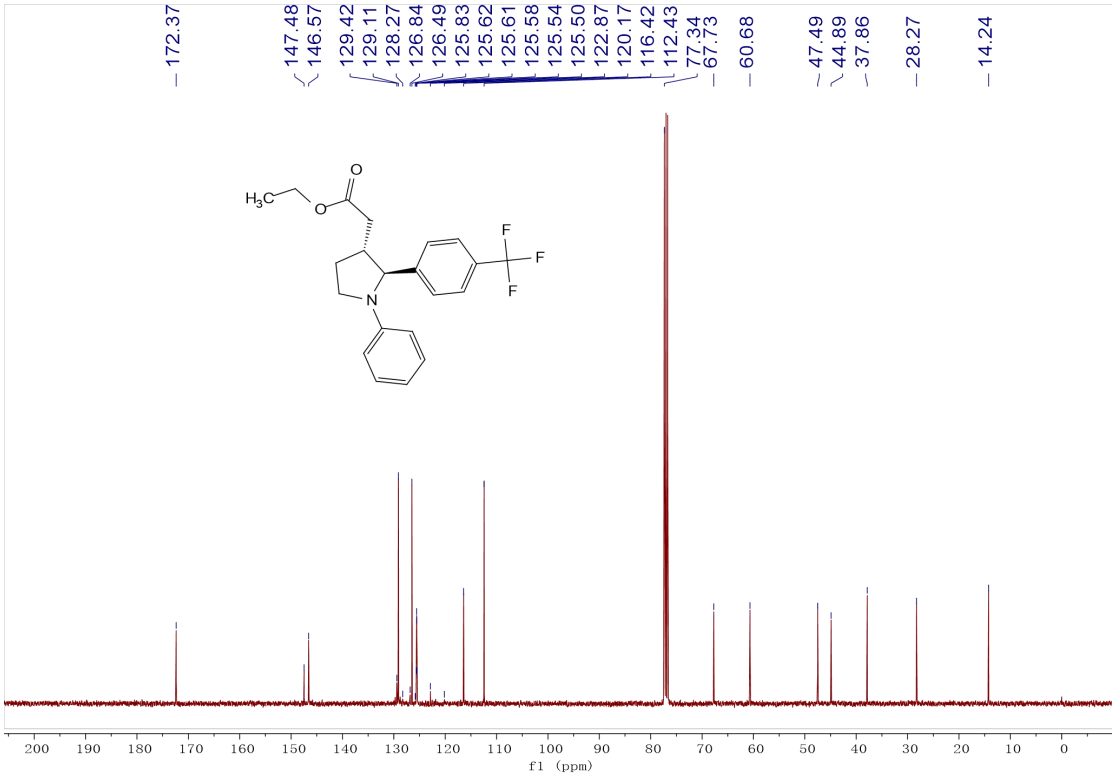
ethyl 2-(2-(4-bromophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2i**)



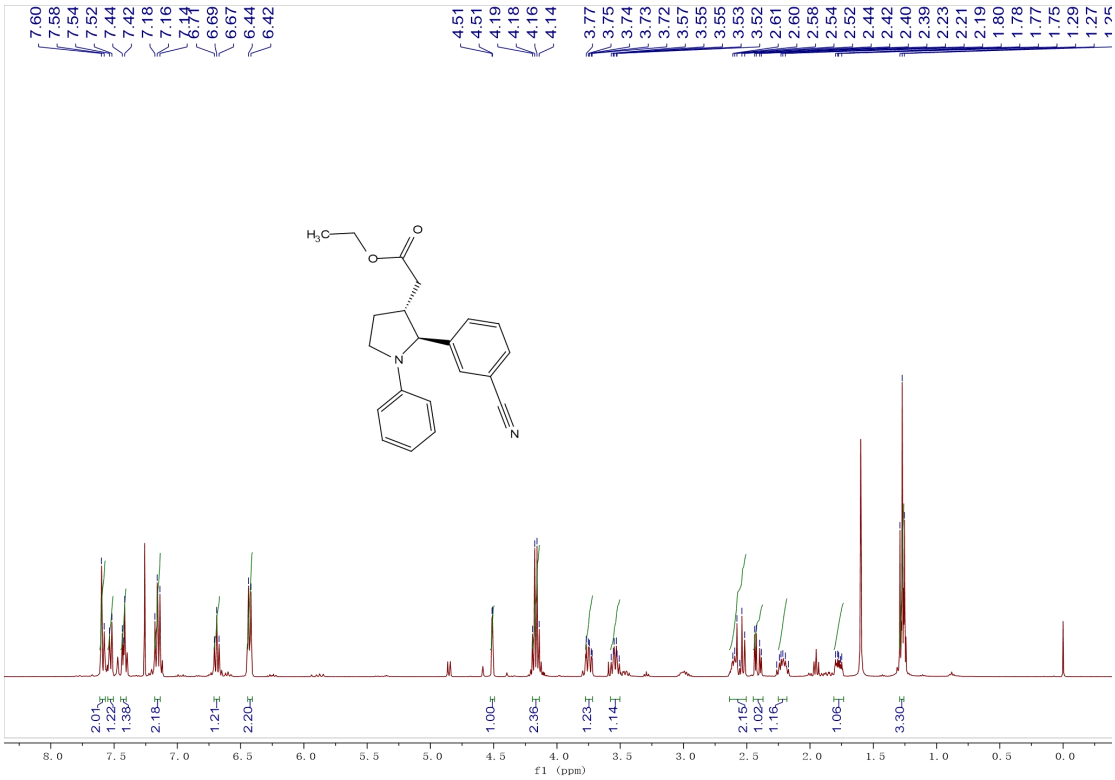


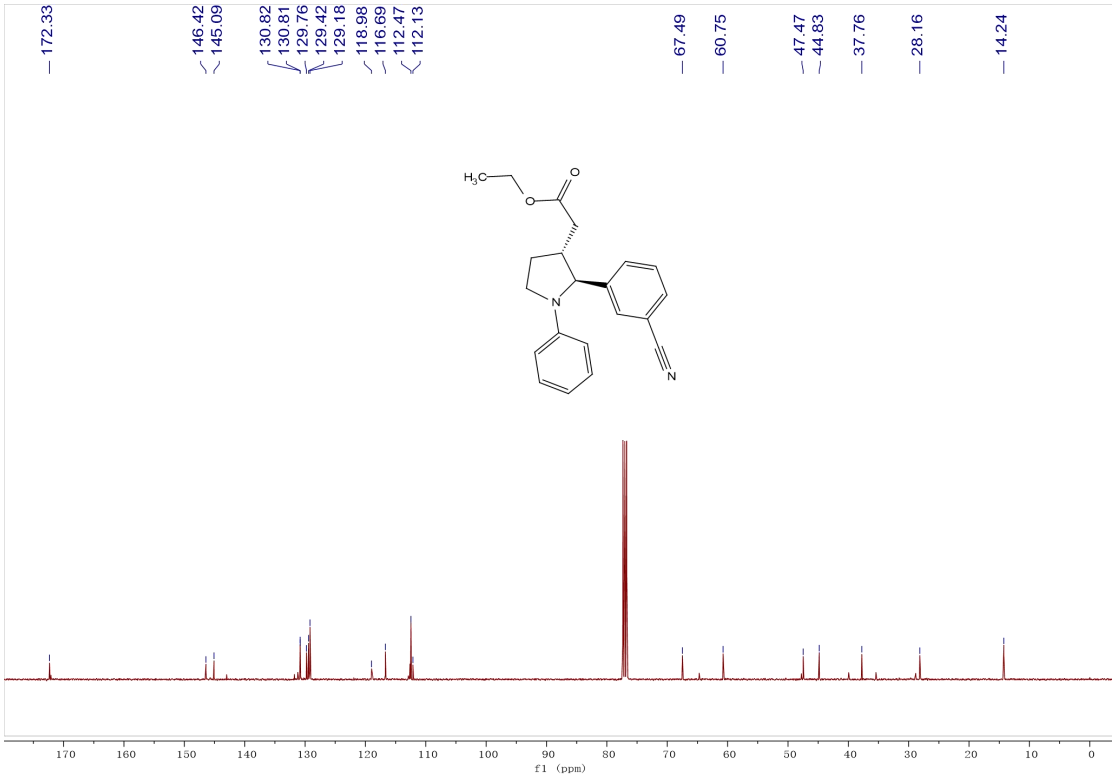
ethyl 2-(1-phenyl-2-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)acetate (**2j**)



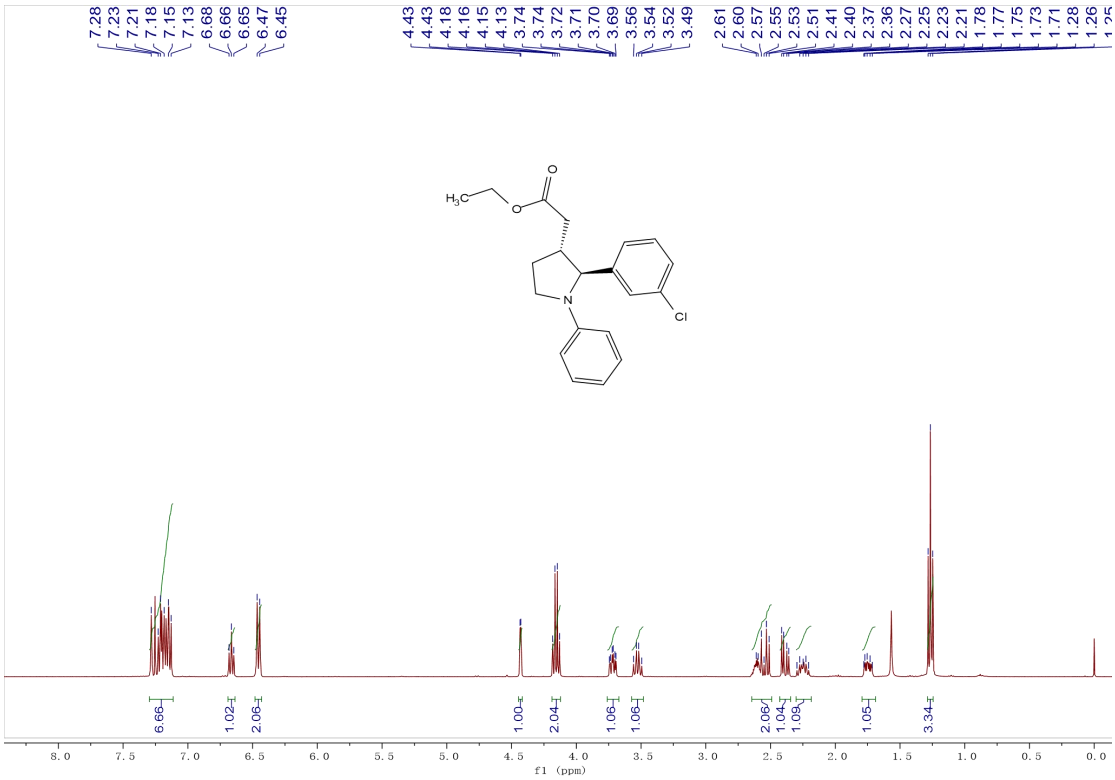


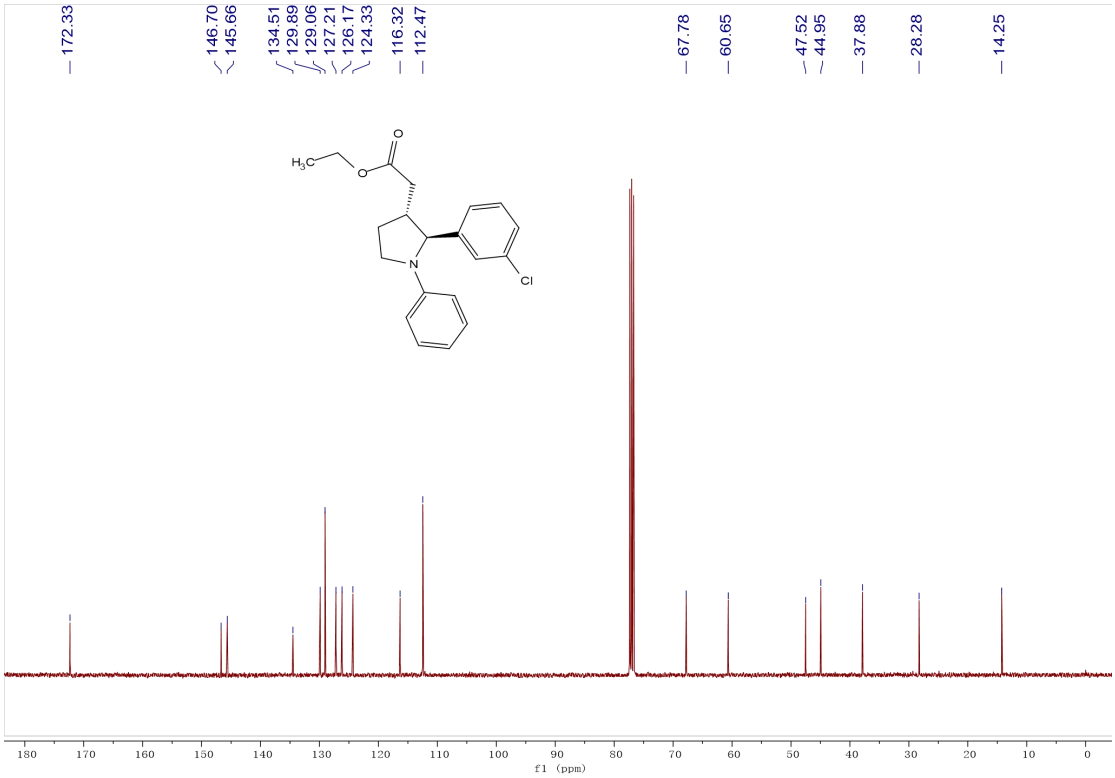
ethyl 2-(2-(3-cyanophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2k**)



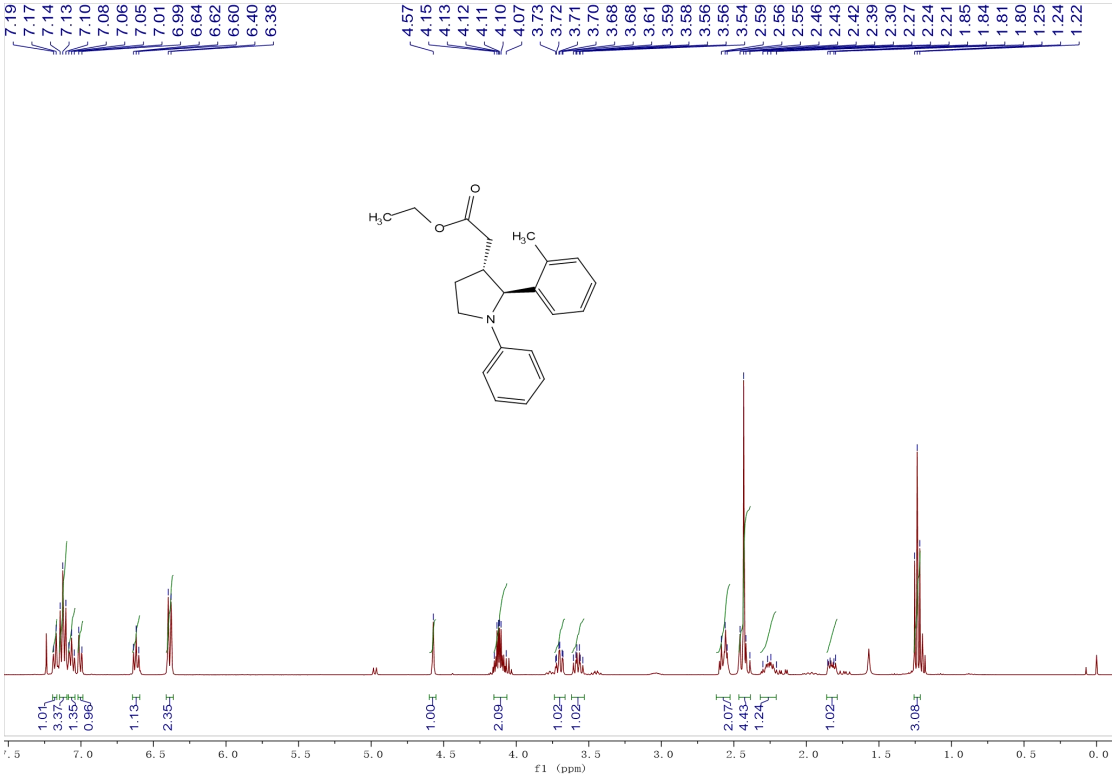


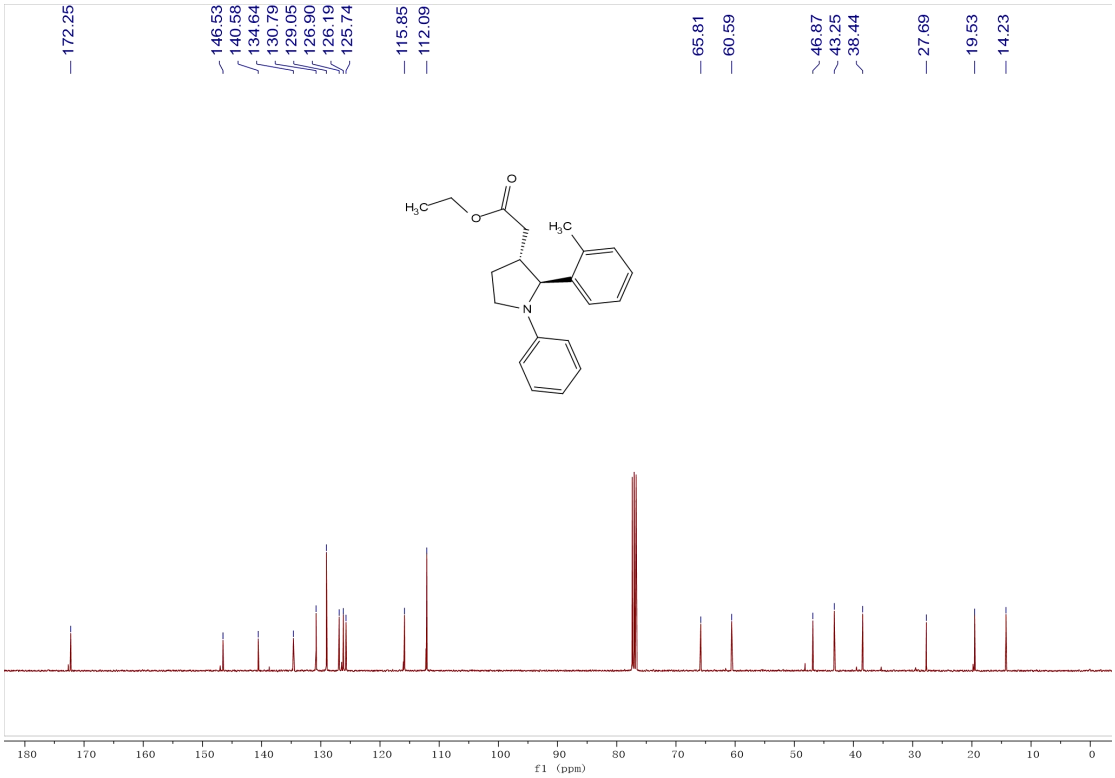
ethyl 2-(2-(3-chlorophenyl)-1-phenylpyrrolidin-3-yl)acetate (**2l**)



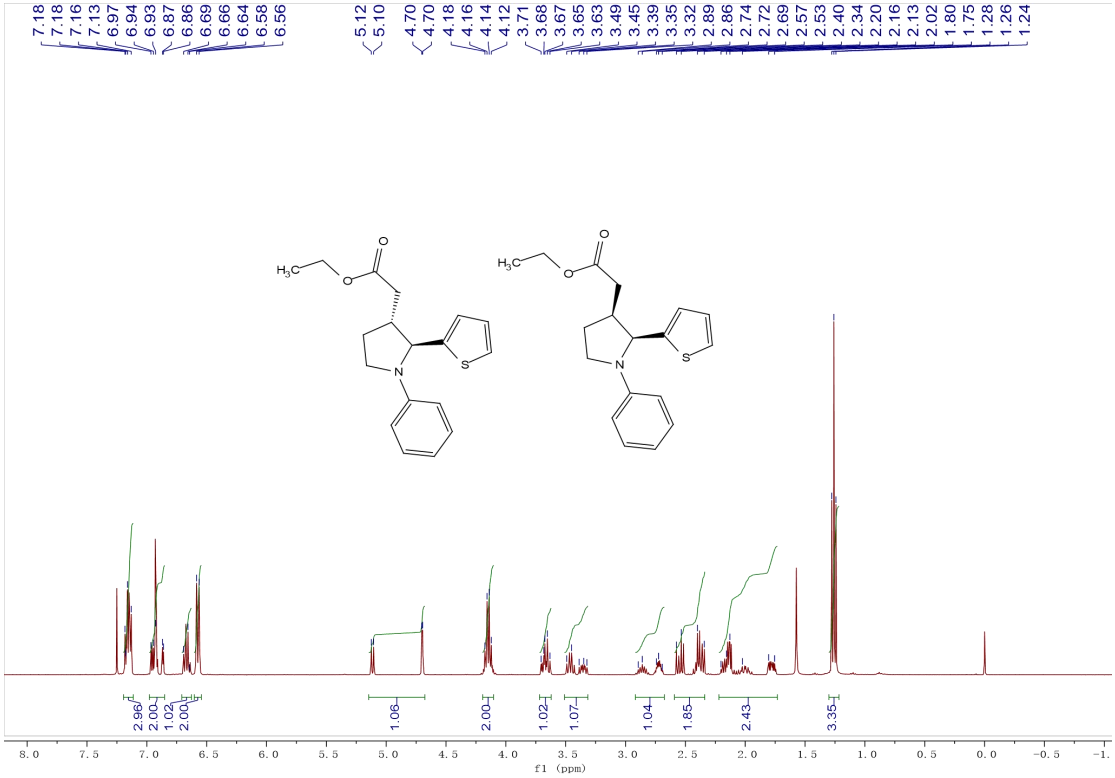


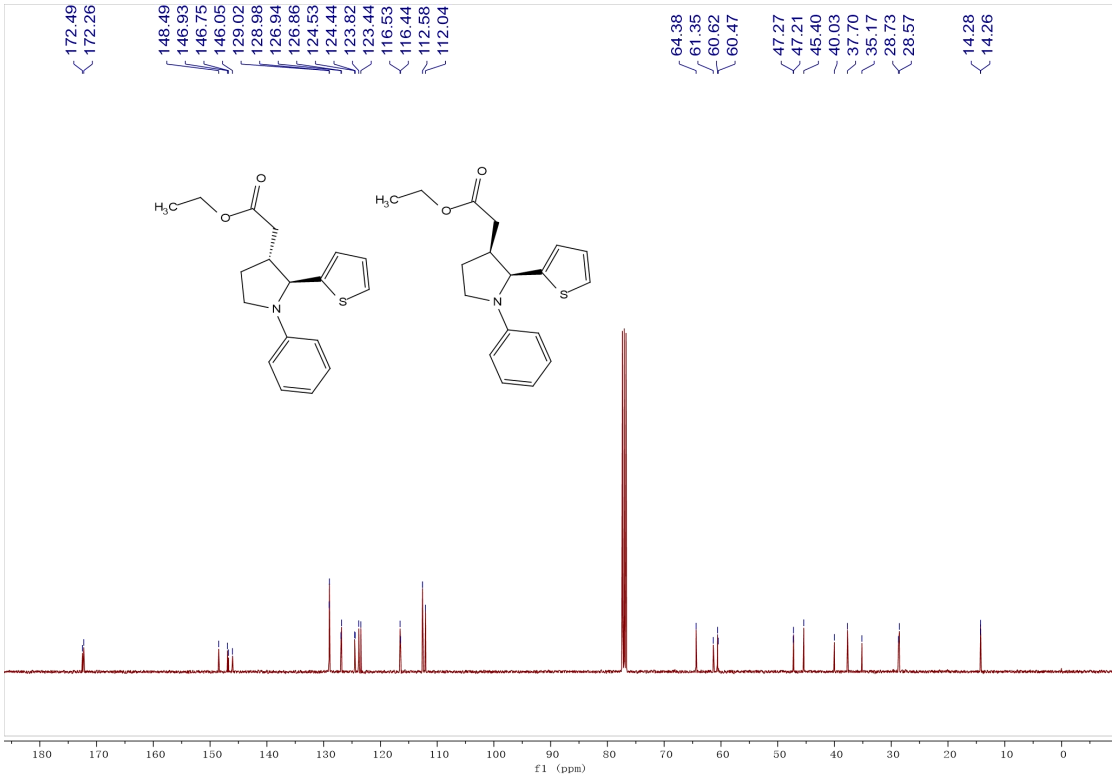
ethyl 2-(1-phenyl-2-(o-tolyl)pyrrolidin-3-yl)acetate (**2m**)



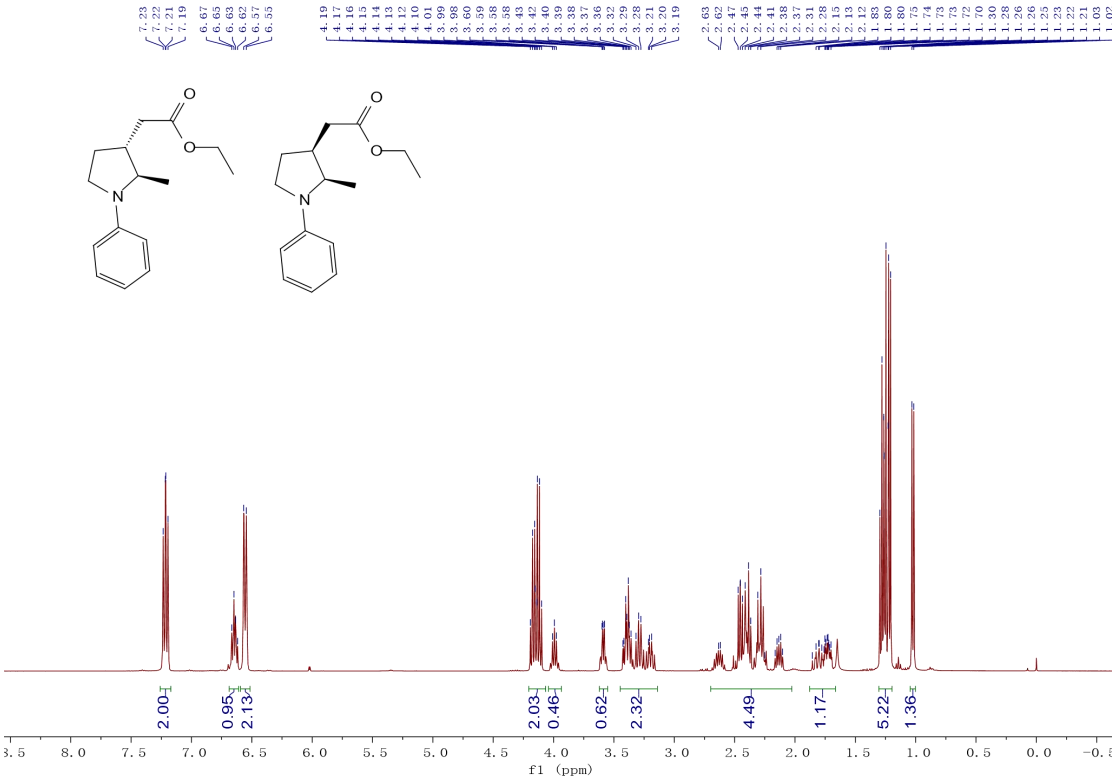


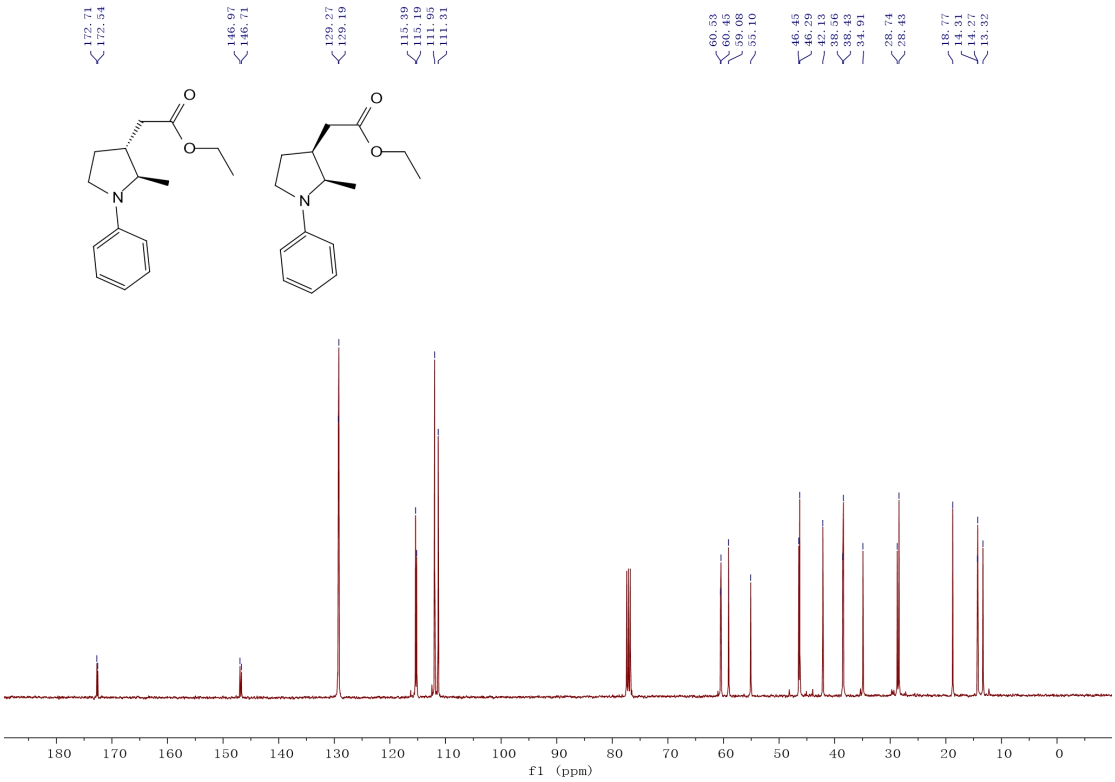
ethyl 2-(1-phenyl-2-(thiophen-2-yl)pyrrolidin-3-yl)acetate (**2n**)



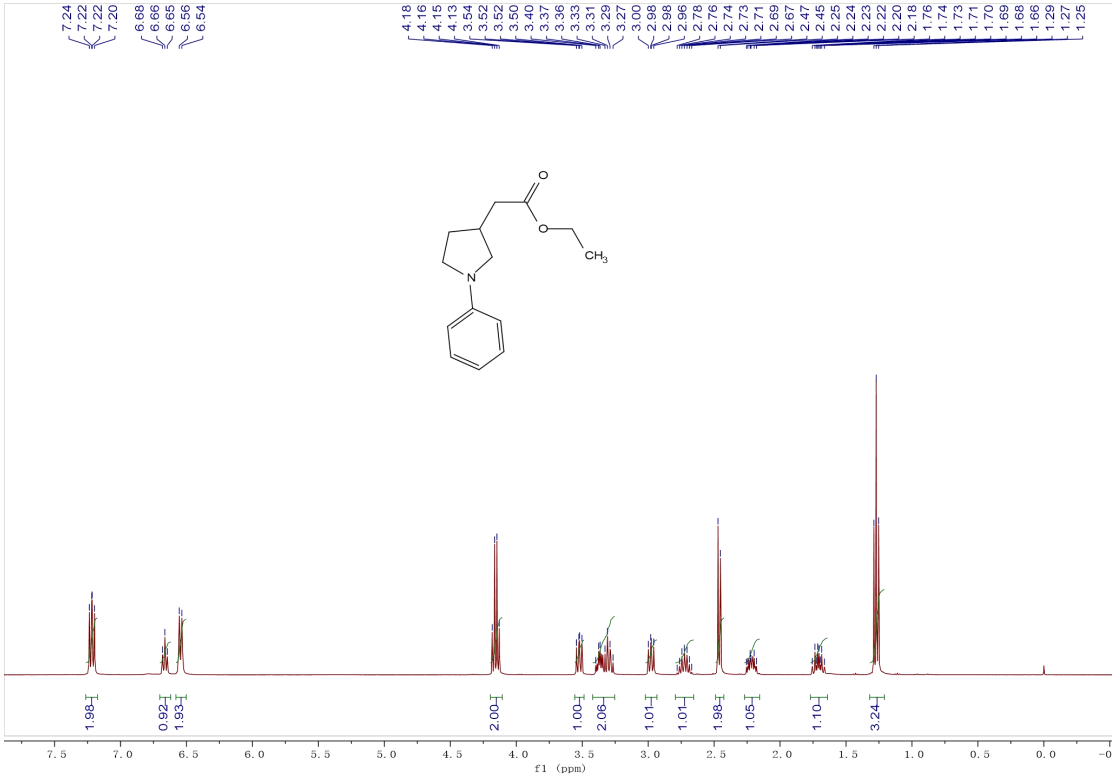


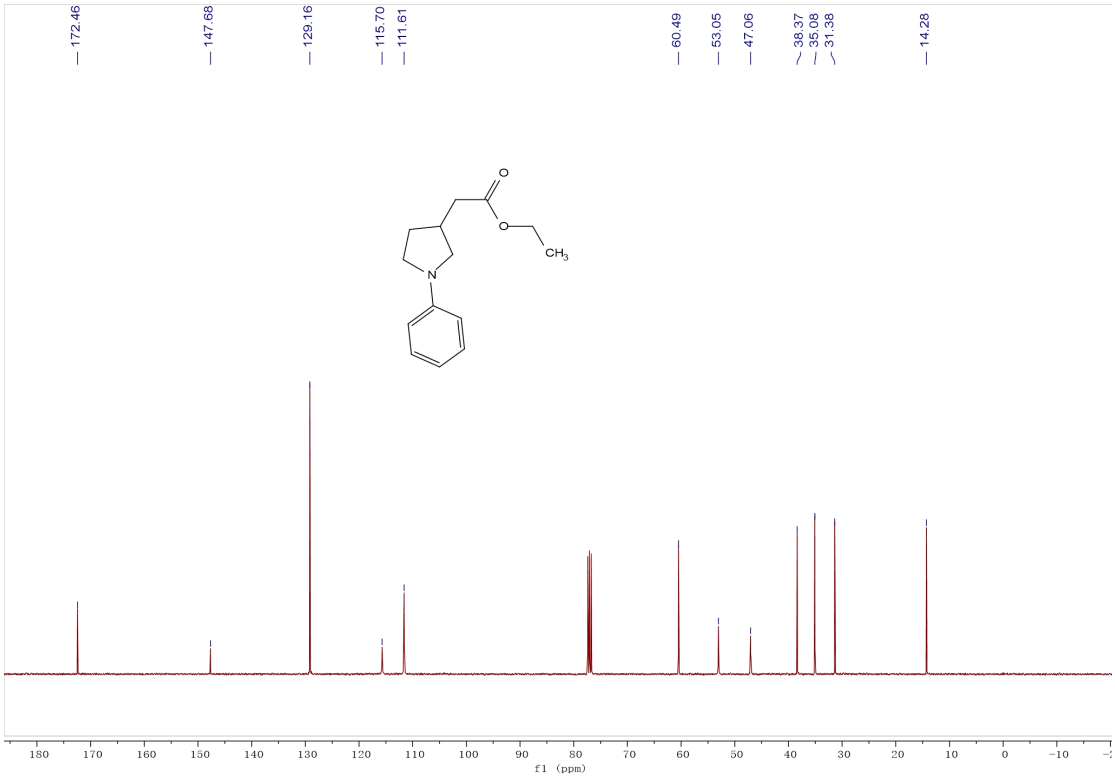
ethyl 2-(2-methyl-1-phenylpyrrolidin-3-yl)acetate (**2o**)



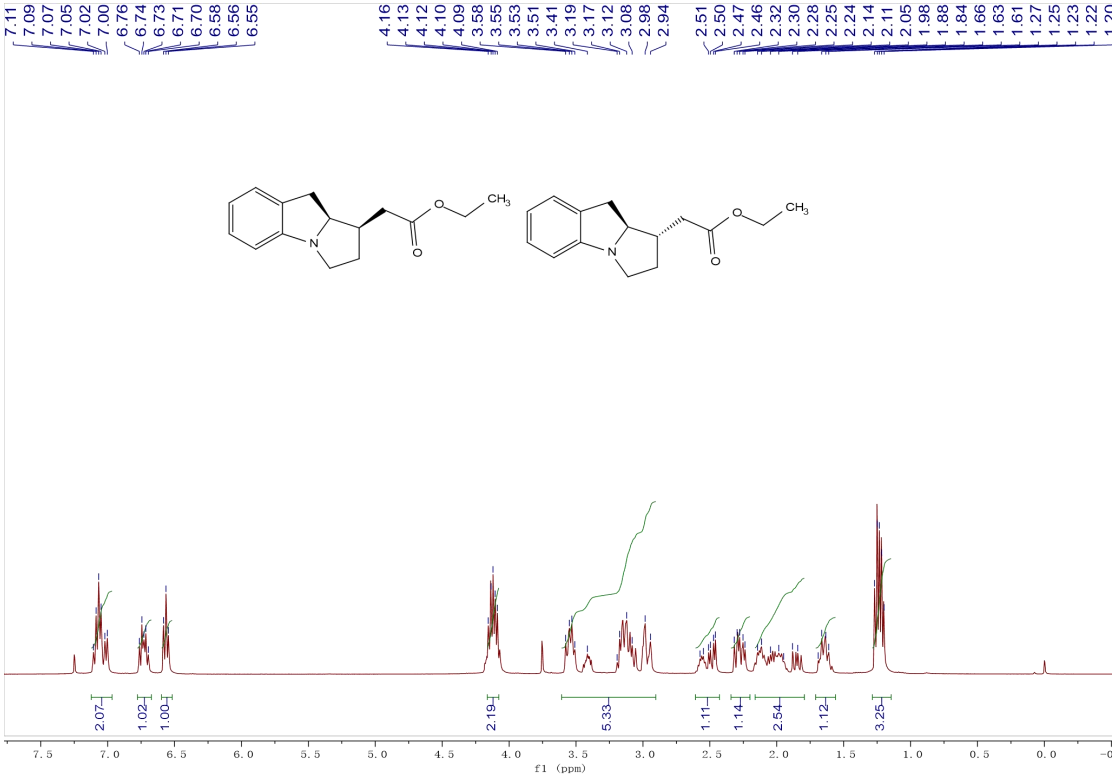


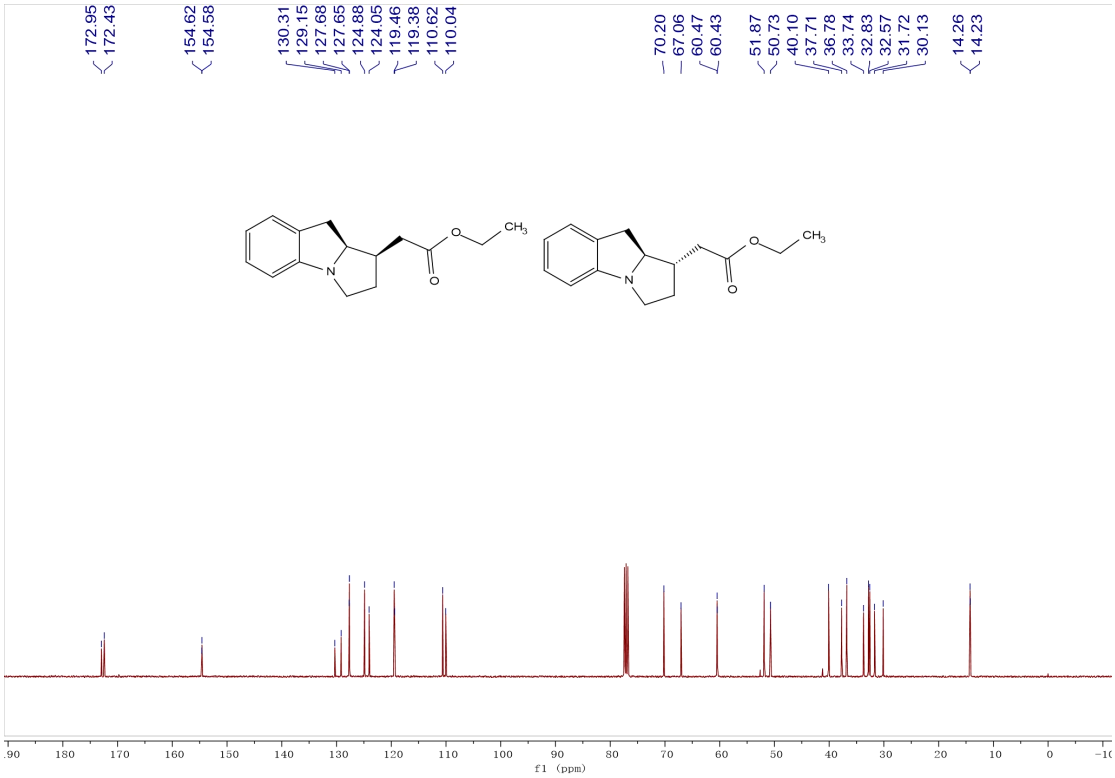
ethyl 2-(1-phenylpyrrolidin-3-yl)acetate (**2p**)



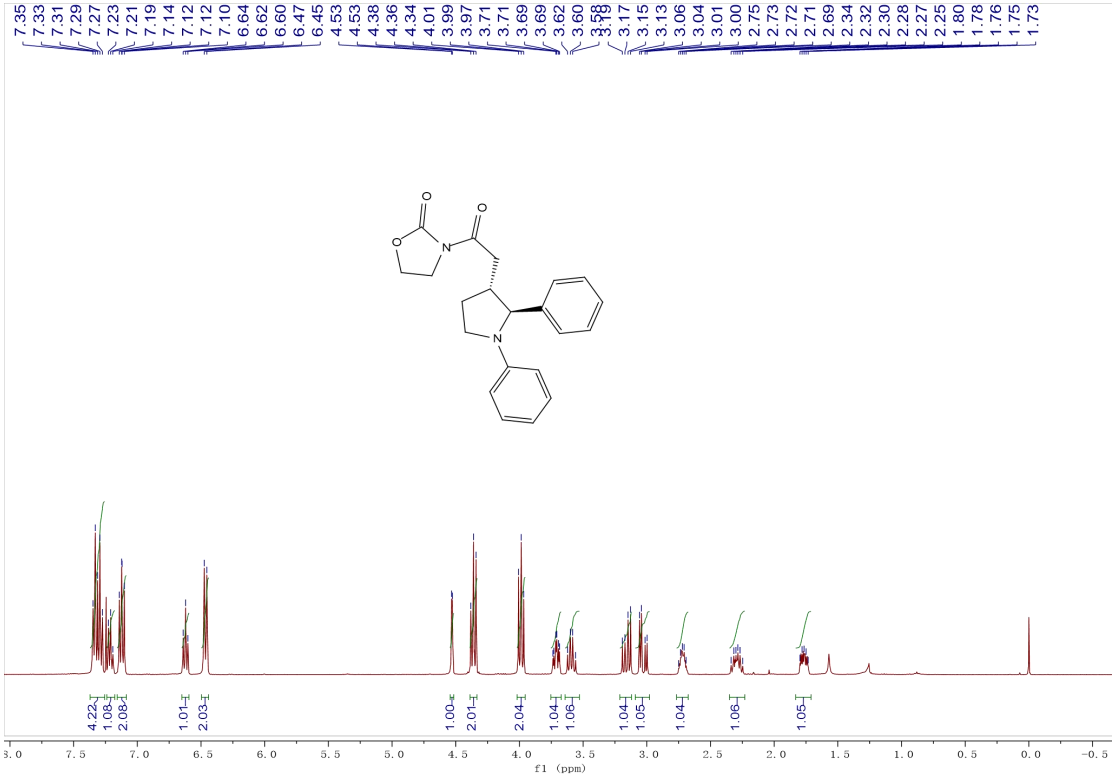


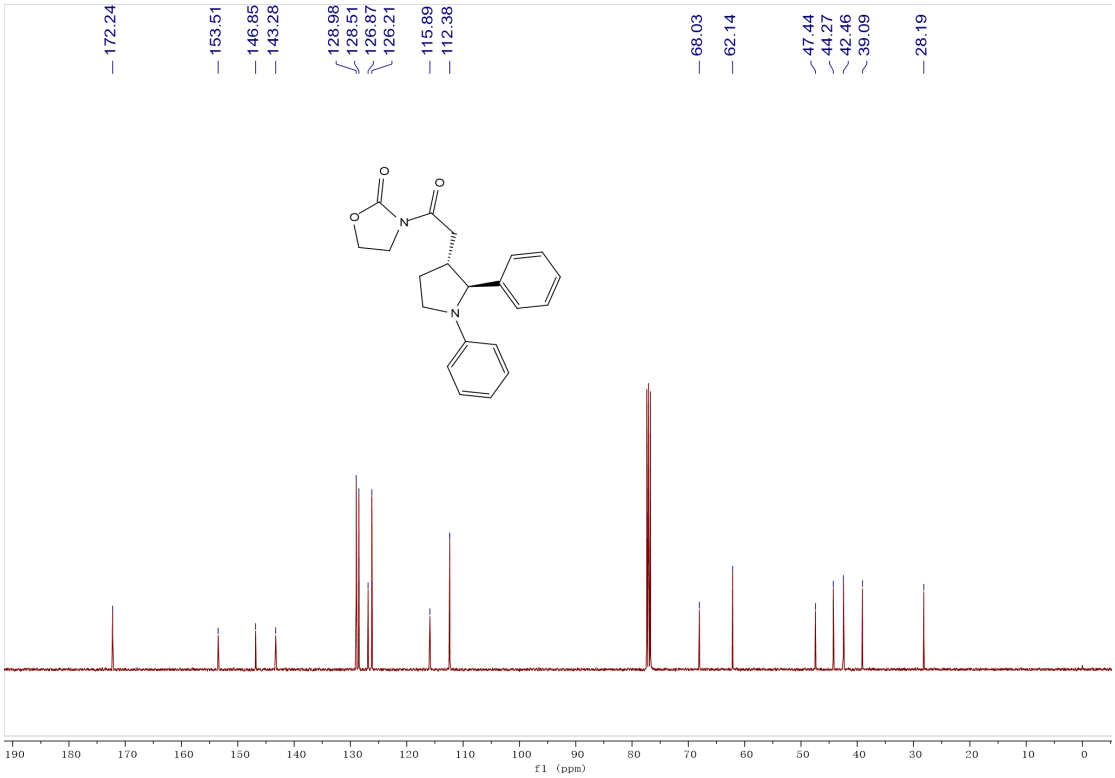
ethyl 2-(2,3,9,9a-tetrahydro-1H-pyrrolo[1,2-a]indol-1-yl)acetate (**2q**)



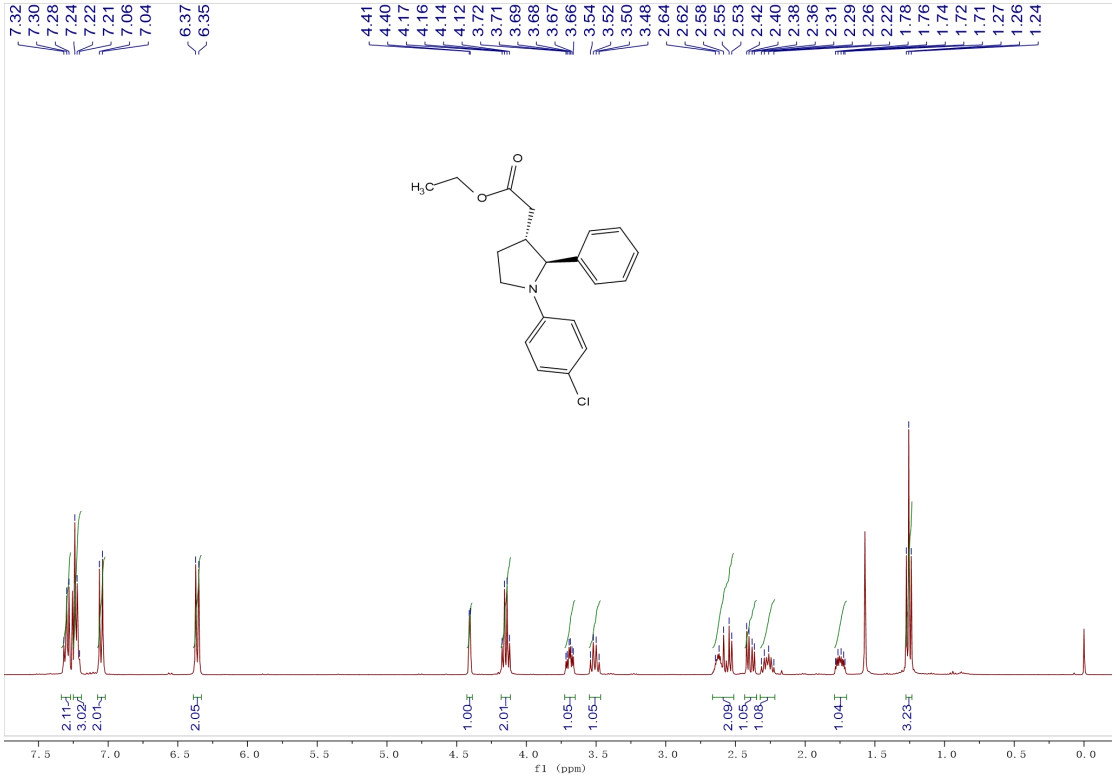


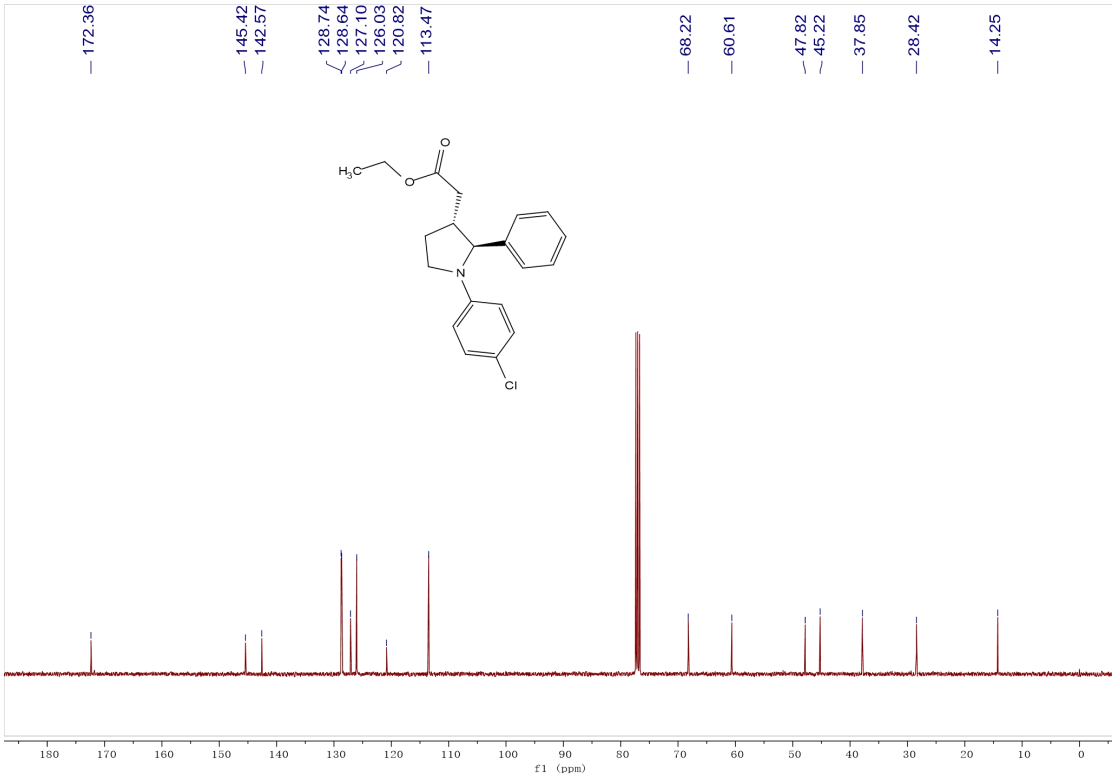
3-(2-(1,2-diphenylpyrrolidin-3-yl)acetyl)oxazolidin-2-one (**2r**)



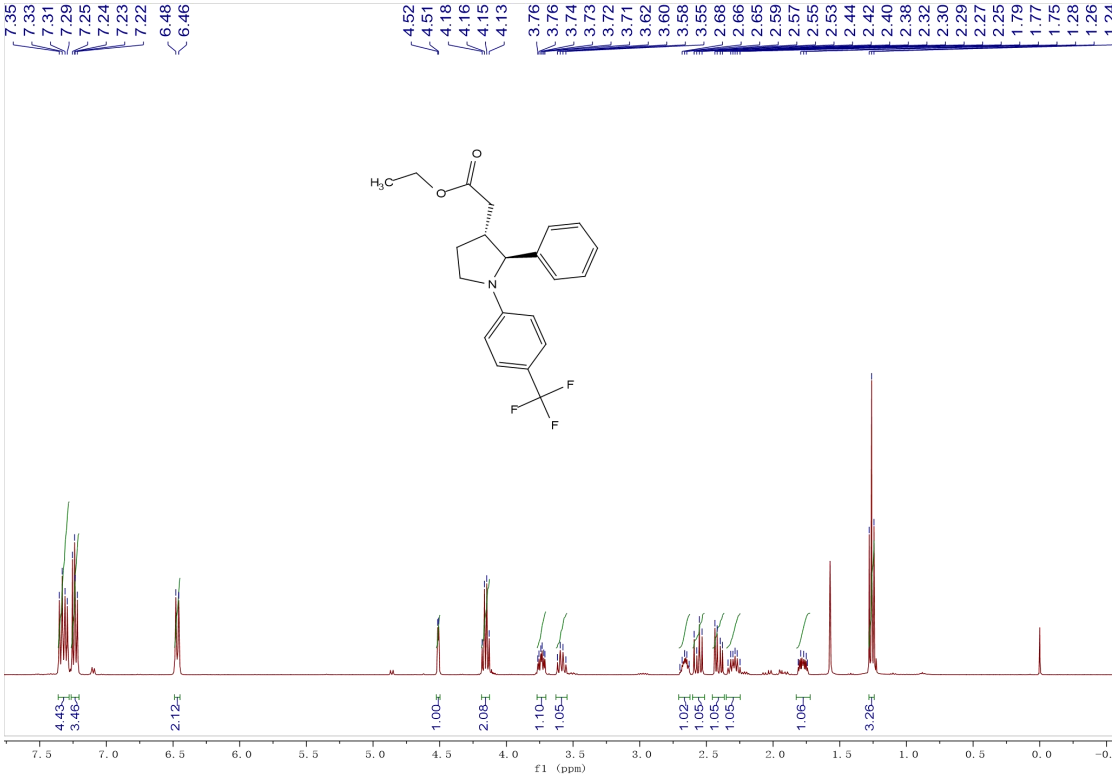


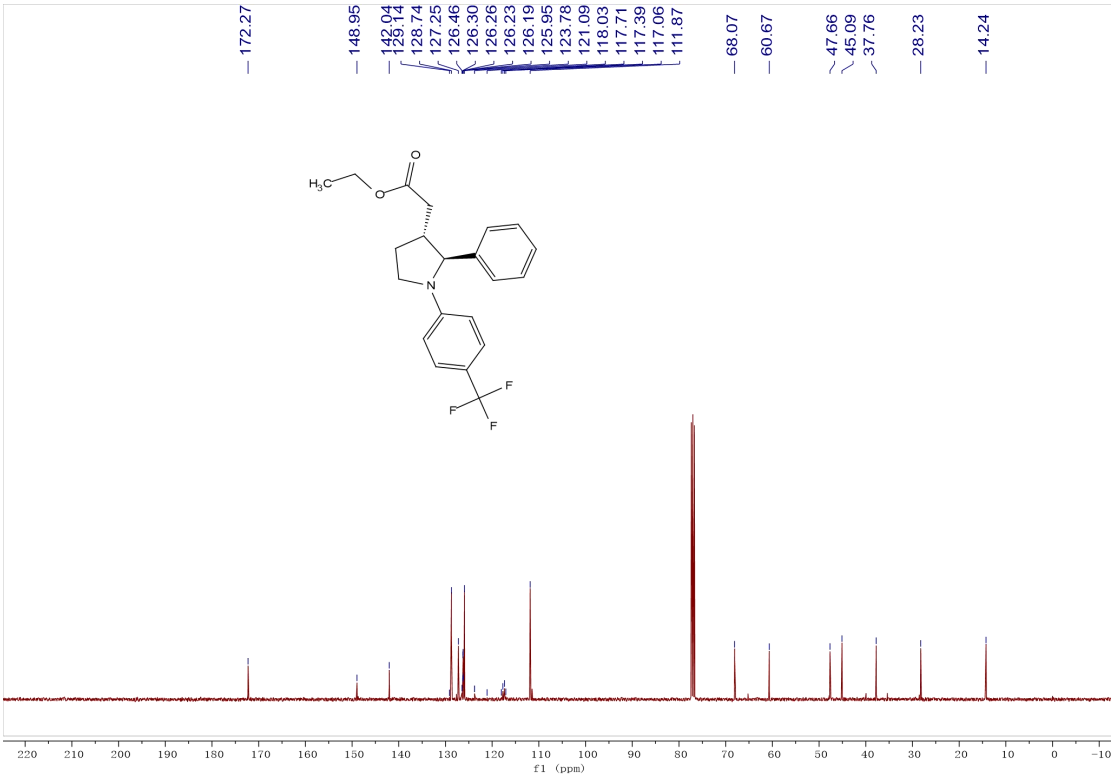
ethyl 2-1-(4-chlorophenyl)-2-phenylpyrrolidin-3-yl)acetate (**2s**)



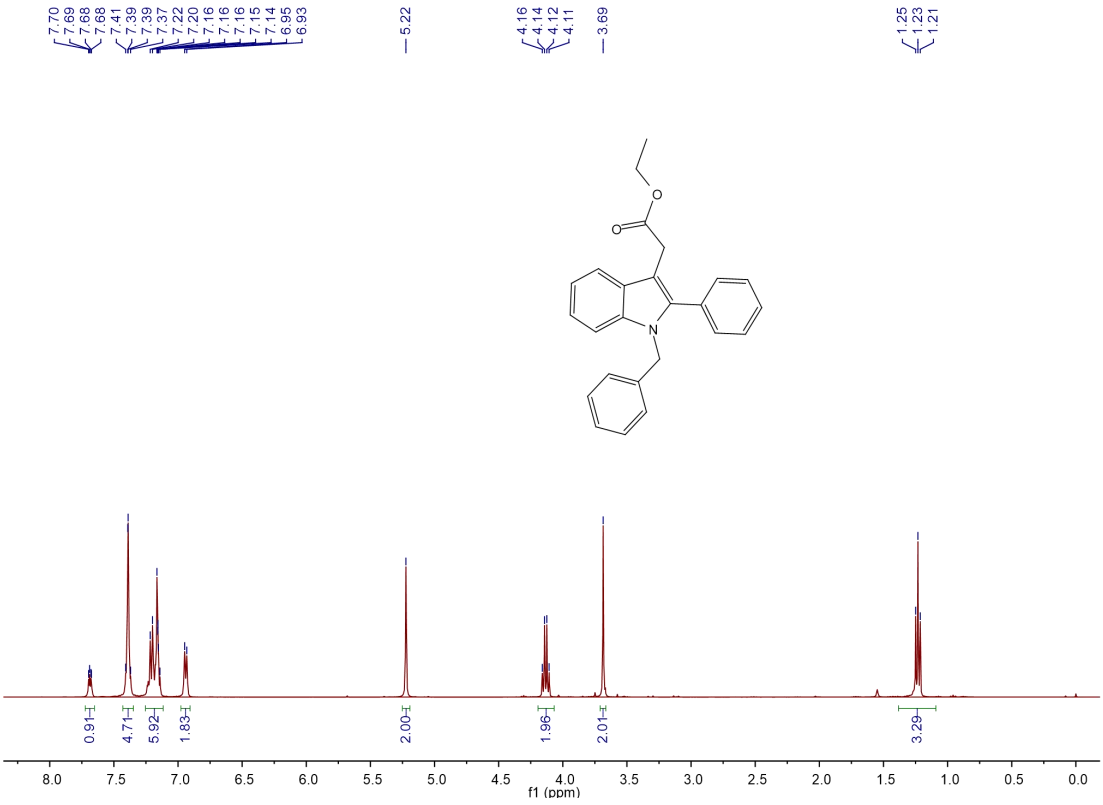


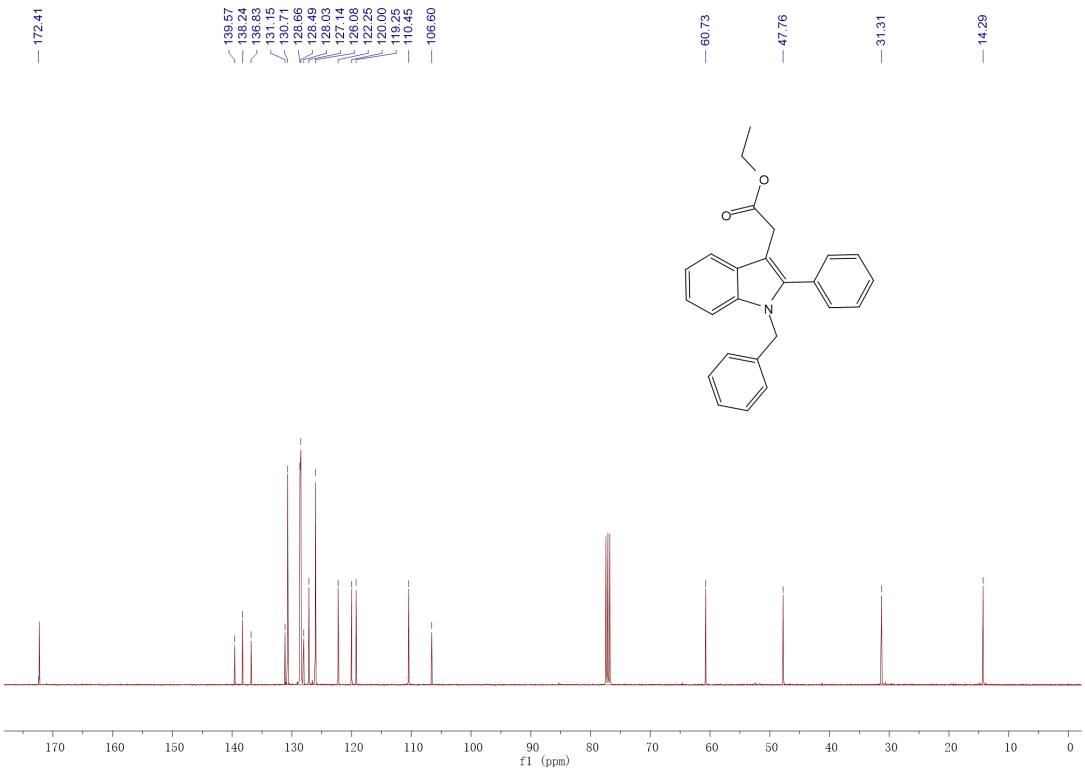
ethyl 2-(2-phenyl-1-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)acetate (**2t**)





ethyl 2-(1-benzyl-2-phenyl-1H-indol-3-yl)acetate (**2u**)

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f1 (ppm)