Electronic Supplementary Information

A highly regioselective sp^3 C–H amination of tertiary amides based on Fe(II) complex catalysts

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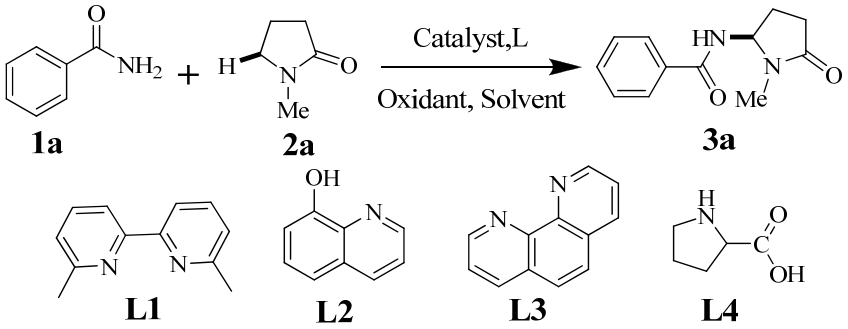
ESI 1. Instrumentation and Materials

All reactions were carried out under Nitrogen atmosphere unless otherwise noted. All solvents and reagents were commercially available and used without further purification. Melting points were determined on a hot-plate microscope apparatus and were uncorrected. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with GF-254 indicator, visualized by irradiation with UV light. MS was determined on a Micromass GCT, NMR spectra were collected on a 300-Bruker spectrometer 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR and reported as parts per million (ppm) from the internal standard TMS. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane. Abbreviations for signal couplings are: s, singlet; d, doublet; t, triplet; m, multiplet.

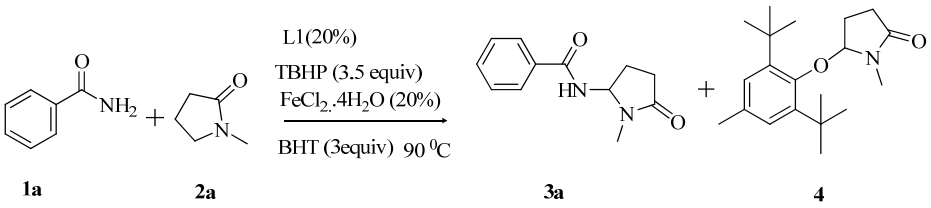
ESI 2. Optimization of the reaction condition [a]



Entry	Catalyst (10mol %)	Solvent	Ligand (20%)	Oxidant	Yield/ (%) [b]
1	CuI	n-decane	–	TBHP	<10
2	$CuSO_4$	n-decane	–	TBHP	trace
3	CuBr	n-decane	–	TBHP	trace
4	CuCl	n-decane	–	TBHP	0
5	$CuBr_2$	n-decane	–	TBHP	trace
6	$CuCl_2$	n-decane	–	TBHP	0
7	$FeCl_2.4H_2O$	n-decane	–	TBHP	64
8	$FeCl_3$	n-decane	–	TBHP	trace
9	$FeSO_4$	n-decane	–	TBHP	27
10	$Fe_2(SO_4)_3$	n-decane	–	TBHP	trace
11	$Ni(OAc)_2$	n-decane	–	TBHP	0
12	$Pb(OAc)_2$	n-decane	–	TBHP	trace
13	$FeCl_2.4H_2O$	n-decane	–	O_2	trace
14	$FeCl_2.4H_2O$	n-decane	–	PIA [b]	trace
15	$FeCl_2.4H_2O$	n-decane	–	DTBP [c]	0
16	$FeCl_2.4H_2O$	n-decane	–	H_2O_2	trace
17	$FeCl_2.4H_2O$	n-decane	–	MnO_2	trace
18	$FeCl_2.4H_2O$	DMF	–	TBHP	24
19	$FeCl_2.4H_2O$	EtOAc	–	TBHP	61
20	$FeCl_2.4H_2O$	CH_3CN	–	TBHP	52
21	$FeCl_2.4H_2O$	Toluene	–	TBHP	trace
22[e]	$FeCl_2.4H_2O$	n-decane	–	TBHP	49
23[f]	$FeCl_2.4H_2O$	n-decane	–	TBHP	68
24[g]	$FeCl_2.4H_2O$	n-decane	–	TBHP	72
25	$FeCl_2.4H_2O$	n-decane	L1	TBHP	79
26	$FeCl_2.4H_2O$	n-decane	L2	TBHP	65
27	$FeCl_2.4H_2O$	n-decane	L3	TBHP	73
28	$FeCl_2.4H_2O$	n-decane	L4	TBHP	52
29[g, h]	$FeCl_2.4H_2O$	n-decane	L1	TBHP	84
30	–	n-decane	L1	TBHP	0
31	$FeCl_2$	n-decane	L1	–	0

[a] Reaction condition: benzamide 1a (0.1 mmol), 1-methylpyrrolidin-2-one, 2a (0.3 mmol), oxidant (1.5 equiv), solvent (1.0 mL) under air; [b] the yield of 3a; [c] Iodobenzene diacetate; [d] di-tert-butylperoxide ; [e] 5 mol % $FeCl_2$ is used. [f] 15 mol % $FeCl_2$; [g] 20 mol % $FeCl_2.4H_2O$ and 3.5 equiv of TBHP are added; [h] Under nitrogen atmosphere.

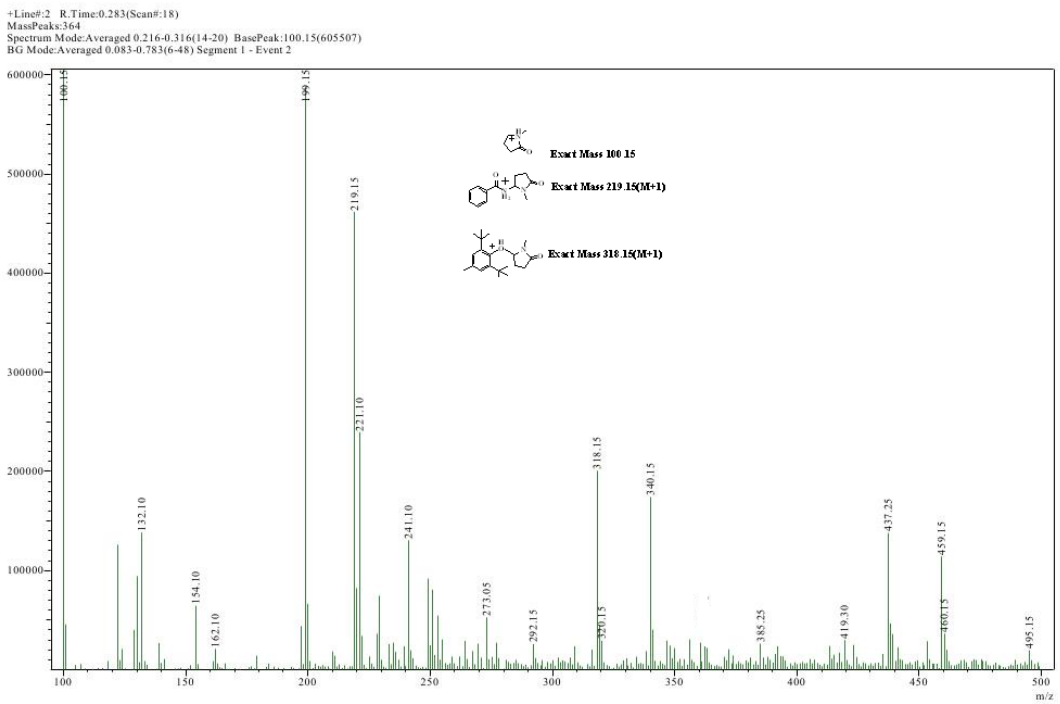
ESI 3. The study of MS (ESI) on mechanism



When 3equiv. BHT (2, 6-ditert-buthyl-p-cresol) was added to the amination reaction system of benzamide **1a** with *N*-methylpyrrolidin-2-one **2a**, we found that yield **3a** dramatically decreased, Meanwhile, 5-(2, 6-di-tert-butyl-4-methylphenoxy)-1-methylpyrrolidin-2-one **4** was checked by LUMS. It indicates that a free radical reaction would be involved.

MS (ESI, positive) for enamine intermediate **4**, found *m/z*: 318.15 (M+H), 340.15 (M+Na).

MS(ESI, positive)for product **3a**, found *m/z*: 219.15 (M+H), 241.10 (M+Na), 437.25 (2M+H), 459.15 (2M+Na).



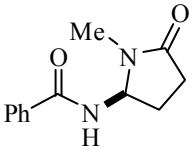
ESI 4. General procedure for amination of amide and SP^3 C–H activation reaction

A schlenk tube filled with nitrogen was placed in amide (0.10 mmol), tert-amide (0.30 mmol), $FeCl_2.4H_2O$ (0.02 mmo l), 6, 6'-dimethyl-2, 2'-bipyridine (0.02 mmol), *n*-decane (1.0 mL) and

TBHP(3.5equiv.). The resulting mixture was stirred at 90 ^{0}C until it completed. When the reaction finished, the reaction mixture was cooled to room temperature and poured into saturated $Na_2S_2O_3$ solution (3 mL), extracted with EtOAc (3×8 mL), then washed with saturated brine(3×8 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After removing the solvent in vacuo, the residue was purified by flash column chromatography on silica gel or preparative TLC on GF 254 to afford the desired product 3a.

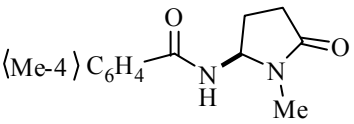
ESI 5. Characterization data of compounds

***N*-(1-methyl-5-oxopyrrolidin-2-yl)benzamide 6a**



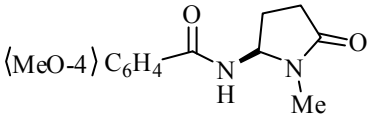
Yellow oil; Yield: 84%; ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.89-8.87 (d, *J* = 8.7 Hz, 1 H), 7.89-7.87 (d, *J* = 6.0 Hz, 1 H), 7.58-7.16 (m, 3 H), 5.64 (m, 1 H), 2.65 (s, 3 H), 2.46-1.89 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.9, 166.9, 134.2, 131.9, 128.7, 127.8, 65.6, 29.3, 27.0, 25.2; MS (ESI, negative) for $C_{12}H_{14}N_2O_2$, found *m/z*: 217.17 (M-H), 331 (M+CF_3COO).

4-methyl-*N*-(1-methyl-5-oxopyrrolidin-2-yl)benzamide 6b



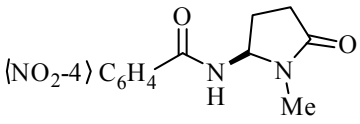
White solid; yield: 87%; mp: (108-109); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.81-8.79 (d, *J* = 9.0 Hz, 1 H), 7.81-7.78 (d, *J* = 8.7 Hz, 2 H), 7.30-7.27 (d, *J* = 8.7 Hz, 2 H), 5.66-5.60 (m, 1 H), 2.69 (s, 3 H), 2.35 (s, 3 H), 2.46-1.89 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.6, 166.4, 141.1, 133.3, 129.1, 127.5, 65.8, 29.5, 27.1, 25.0, 21.3; MS (ESI, negative) for $C_{12}H_{16}N_2O_2$, found *m/z*: 231.05 (M-H), 345.05 (M+CF_3COO).

4-methoxy-*N*-(1-methyl-5-oxopyrrolidin-2-yl)benzamide 6c



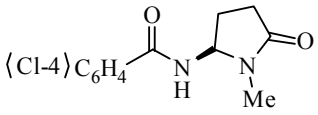
yellow oil; yield: 89%; ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.73 (d, *J* = 8.7 Hz, 1 H), 7.88-7.85 (d, *J* = 8.7 Hz, 2 H), 7.02-6.99 (d, *J* = 9.0 Hz, 2 H), 5.64-5.58 (m, 1 H), 3.81 (s, 3 H), 2.66(s, 3 H), 2.49-1.82 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO) δ (ppm) = 173.7, 166.3, 166.2, 129.7, 129.3, 114.0, 65.5, 55.7, 29.2, 26.8, 25.1; MS (ESI, negative) for $C_{12}H_{16}N_2O_3$, found *m/z*: 247.00 (M-H), 283 (M+^{35}Cl), 361 (M+CF_3COO).

_N_-(1-methyl-5-oxopyrrolidin-2-yl)-4-nitrobenzamide 6d



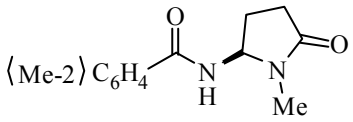
Yellow soil; yield: 63%; mp (198-199), ^{1}H NMR (300 MHz, δ_6-DMSO) δ (ppm) = 9.23-9.20 (d, *J*= 8.4 Hz, 1 H), 8.36-8.30 (m, 4 H), 5.66-5.60 (m, 1 H), 2.67 (s, 3 H), 2.51-1.86 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.9, 165.2, 149.6, 139.2, 129.3, 123.9, 65.9, 29.2, 27.1, 25.2; MS (ESI, negative) for $C_{12}H_{13}N_3O_4$, found m/z: 262.00 (M-H), 297.95 (M+^{35}Cl), 375.95 (M+CF_3COO).

4-chloro-_N_-(1-methyl-5-oxopyrrolidin-2-yl)benzamide 6e



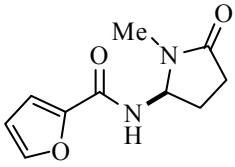
white solid; yield: 62%; mp: (113-114); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.97-8.94 (d, *J* = 8.7 Hz, 1 H), 7.92-7.89 (d, *J* = 8.7 Hz, 2 H), 7.58-7.56 (d, *J* = 8.4 Hz, 2 H), 5.62-5.59 (t, d, *J* = 3.3, 1 H), 2.65 (s, 3 H), 2.46-1.85 (m, 4 H); ^{13} C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.9, 165.7, 132.9, 129.7, 128.8, 65.7, 29.2, 27.0, 25.7; MS (ESI, negative) for $C_{12}H_{13}ClN_2O_2$, found m/z: 251.00 (M-H), 364.95 (M+CF_3COO).

2-methyl-_N_-(1-methyl-5-oxopyrrolidin-2-yl)benzamide 6f



white soil; yield: 74%; mp: (123-124); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.81-8.78 (d, *J* = 8.4 Hz, 1 H), 7.37-7.22 (m, 4 H), 5.60-5.53 (m, 1 H), 2.71 (s, 3 H), 2.50-1.84 (m, 7 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.8, 169.7, 136.8, 135.4, 130.8, 129.9, 127.4, 125.9, 65.1, 29.2, 27.1, 25.1, 19.7; MS (ESI, negative) for $C_{13}H_{16}N_2O_2$, found m/z: 231.05 (M-H), 267.00 (M+^{35}Cl), 345 (M+CF_3COO).

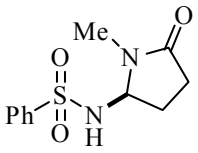
_N_-(1-methyl-5-oxopyrrolidin-2-yl)furan-2-carboxamide 6g



White solid; yield: 82%; mp: (208-209); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.88-8.85 (d, *J* = 8.7 Hz, 1 H), 7.884-7.881 (d, *J* = 1 Hz, 1 H), 7.19-7.18 (d, J = 3.6 Hz, 1 H), 6.66-6.65 (d, *J* = 3.9 Hz, 1 H), 5.64-5.59 (m, 1 H), 2.71 (s, 3 H), 2.35 (s, 3 H), 2.46-2.41 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 166.7, 152.3, 149.0, 135.5, 130.0, 123.7, 83.7, 28.8, 27.8, 26.6; MS (ESI, negative) for

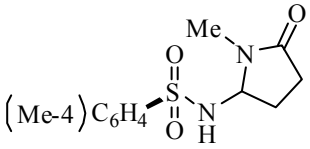
$C_{10}H_{12}N_2O_3$, found m/z: 207.00 (M-H).

***N*-(1-methyl-5-oxopyrrolidin-2-yl)benzenesulfonamide 6h**



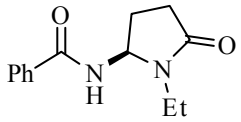
White solid; yield: 71% ; mp: (155-156); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.53-8.50 (d, *J*= 9.3 Hz, 1H), 7.85-7.61 (m, 5 H), 4.87-4.84 (t, *J* = 3.0 Hz, 1 H), 2.52 (s, 3 H), 2.51-1.90 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.4, 142.2, 132.9, 129.6, 126.6, 70.1, 29.3, 28.6, 26.7, 26.0. MS(ESI, negative) for $C_{11}H_{14}N_2O_2S$, found m/z: 253.00 (M-H), 366.95(M+CF_3COO).

4-methyl-*N*-(1-methyl-5-oxopyrrolidin-2-yl)benzenesulfonamide 6i



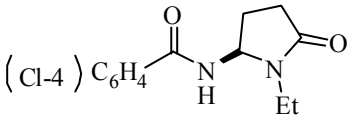
white solid; yield 69%; mp: (153-154); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.98-8.95 (d, *J* = 8.7 Hz, 1 H), 7.93-7.90 (d, *J* = 8.7 Hz, 2 H), 7.58-7.55 (d, *J* = 8.7 Hz, 2 H), 5.66-5.60 (m, 1 H), 2.69 (s, 3 H), 2.65-2.17 (m, 7 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.7, 141.8, 129.0, 126.1, 1148.1, 115.6, 67.8, 36.8, 31.1, 28.3, 22.1; MS (ESI, negative) for $C_{12}H_{16}N_2O_2S$, found m/z: 267.00 (M-H), 380.95 (M+CF_3COO).

***N*-(1-ethyl-5-oxopyrrolidin-2-yl)benzamide 6j**



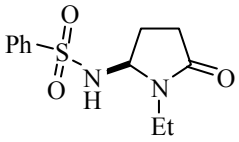
Yellow oil; yield: 60%; mp (155-156). ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.91-8.88 (d, *J* = 6.0 Hz, 1 H), 7.90-7.89 (d, *J* = 1.5 Hz, 2 H), 7.89-7.45 (m, 3 H), 5.78-5.72 (m, 1 H), 3.45-1.00 (m, 9 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.5, 166.8, 134.2, 132.0, 128.7, 127.8, 63.4, 34.5, 29.5, 27.0, 25.4, 13.2; MS (ESI, negative) for $C_{13}H_{16}N_2O_2$, found m/z: 231.05 (M-H), 267.00 (M+^{35}Cl), 345.00 (M+CF_3COO).

4-chloro-*N*-(1-ethyl-5-oxopyrrolidin-2-yl)benzamide 6k



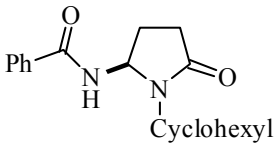
white solid; yield: 58%; mp: (113-114); ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.99-8.96 (d, *J* = 8.7 Hz, 1 H), 7.91-7.89 (d, *J* = 8.4 Hz, 2 H), 7.59-7.56 (d, *J* = 8.4 Hz, 2 H), 5.76-5.70 (m, 1 H), 3.45-1.02 (m, 9 H); ^{13}C NMR (75 MHz, δ_6-DMSO) 173.6, 163.7, 136.8, 132.8, 129.7.6, 128.8, 63.4, 34.53, 29.4, 25.4, 13.1; MS (ESI, negative) for $C_{13}H_{15}N_2O_2Cl$, found m/z: 265.00 (M-H).

***N*-(1-ethyl-5-oxopyrrolidin-2-yl)benzenesulfonamide 6l**



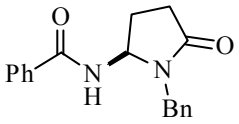
white solid; yield 56%; mp: (155-156); ^{1}H NMR (300 MHz, δ6-DMSO): δ (ppm) = 8.50-8.47 (d, *J* = 9.0 Hz, 1 H), 7.85-7.83 (d, *J* = 9.0 Hz, 2 H), 7.83-7.59 (m, 3 H), 4.99-4.92 (m, 1 H), 3.37-0.92 (m, 9 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.0, 142.5，132.9, 129.7, 126.4, 67.9, 34.0, 28.8, 26.1, 12.8; MS (ESI, negative) for $C_{12}H_{16}N_2O_2S$, found m/z: 267.00 (M-H), 380.95 (M+CF_3COO).

***N*-(1-cyclohexyl-5-oxopyrrolidin-2-yl)benzamide 6m**



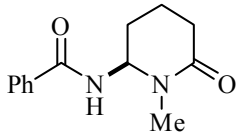
yellow oil; yield 28%; ^{1}H NMR (300 MHz, δ6-DMSO): δ (ppm) = 8.98-8.95 (d, *J* = 9.0 Hz, 1 H), 7.86-7.84 (d, *J* = 4.5 Hz, 2 H), 7.83-7.44 (m, 3 H), 5.81-5.75 (m, 1 H), 3.66-3.34 (m, 1 H), 2.36-1.00 (m, 14 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 174.3, 165.8, 147.5, 129.8, 128.8, 127.6, 65.7, 48.7, 30.4, 29.3, 29.2, 27.0, 25.2; MS (ESI, negative) for $C_{17}H_{22}N_2O_2$, found m/z: 286.17 (M-H), 321.05(M+^{35}Cl), 399.05(M+CF_3COO).

***N*-(1-benzyl-5-oxopyrrolidin-2-yl)benzamide 6n**



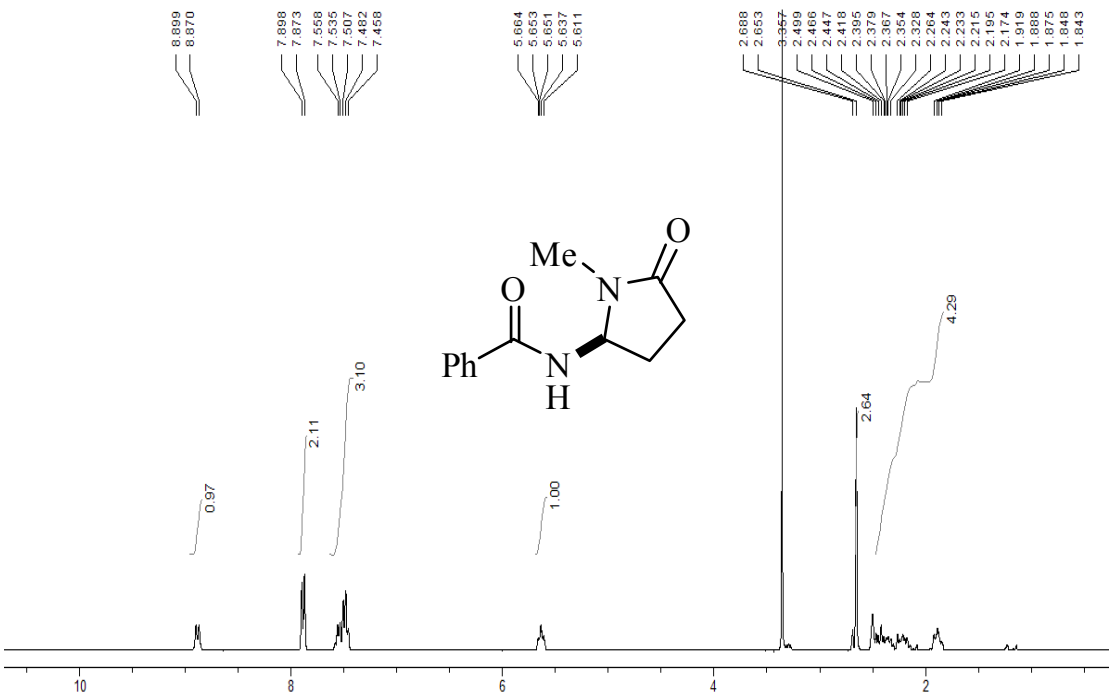
Colorless oil; yield 37%; ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.92-8.89 (d, *J* = 8.7 Hz, 1 H), 7.78-7.75 (d, *J* = 8.7 Hz, 2 H), 7.75-7.20 (m, 8 H), 5.65-5.63 (t, *J*= 4.8 Hz, 1 H), 4.60-4.55 (d, *J* = 15 Hz, 1 H), 4.08-4.03 (d, *J* = 15 Hz, 1 H), 2.50-1.99 (m, 4 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 174.3, 166.9, 137.8, 134.2, 131.9, 128.7, 128.6, 127.9, 127.7, 127.3, 63.9, 43.5, 29.2, 25.5; MS (ESI, negative) for $C_{18}H_{18}N_2O_2$, found m/z: 293.05 (M-H), 329.05(M+^{35}Cl), 407.00 (M+CF_3COO).

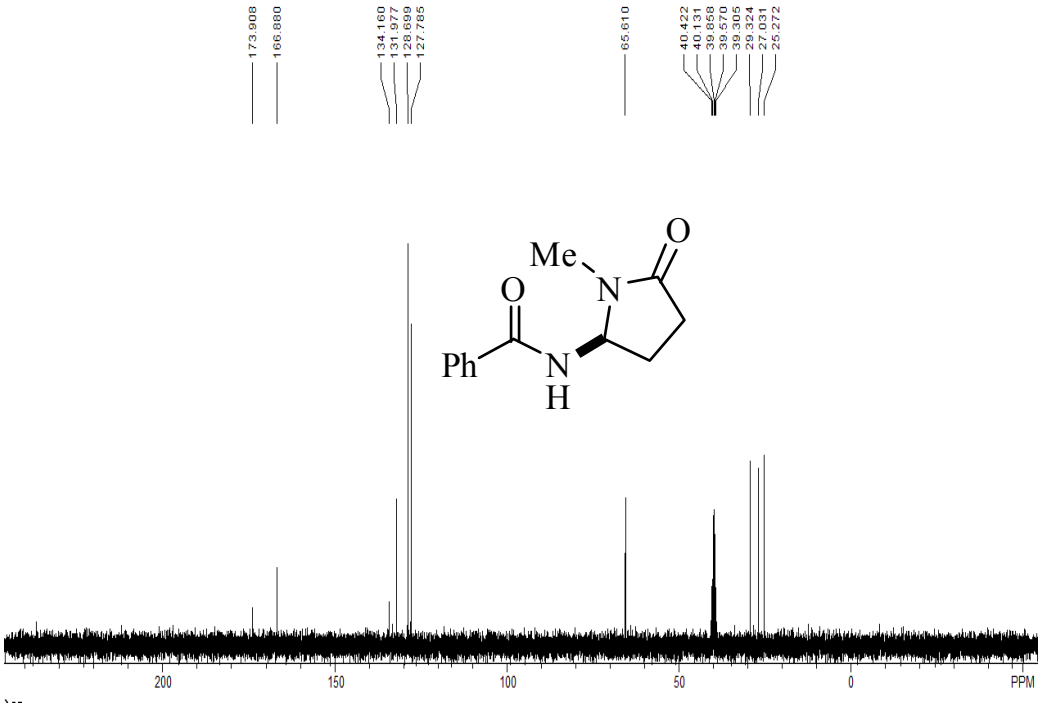
***N*-(1-methyl-6-oxopiperidin-2-yl)benzamide 6o**

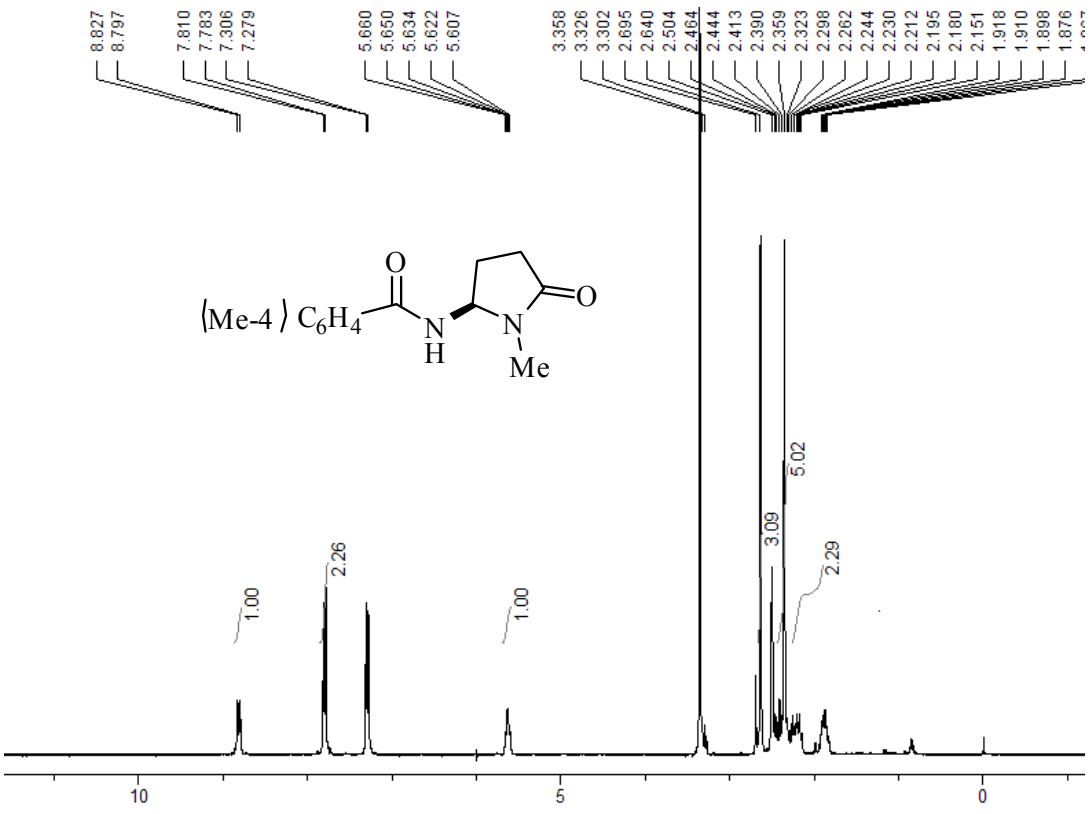


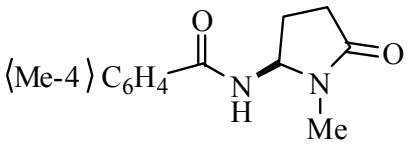
cololess oil; yield 32%; ^{1}H NMR (300 MHz, δ_6-DMSO): δ (ppm) = 8.92-8.89 (d, *J* = 8.1 Hz, 1 H), 7.91-7.88 (d, *J* = 7.5 Hz, 2 H), 7.55-7.45 (m, 3 H), 5.11-5.48 (m, 1 H), 2.70 (s, 3 H), 2.50-1.50 (m, 6 H); ^{13}C NMR (75 MHz, δ_6-DMSO): δ (ppm) = 173.9, 169.7, 131.6, 129.9, 128.7, 64.2, 32.3, 29.0, 22.1; MS (ESI, negative) for $C_{18}H_{18}N_2O_2$, found m/z: 231.05 (M-H).

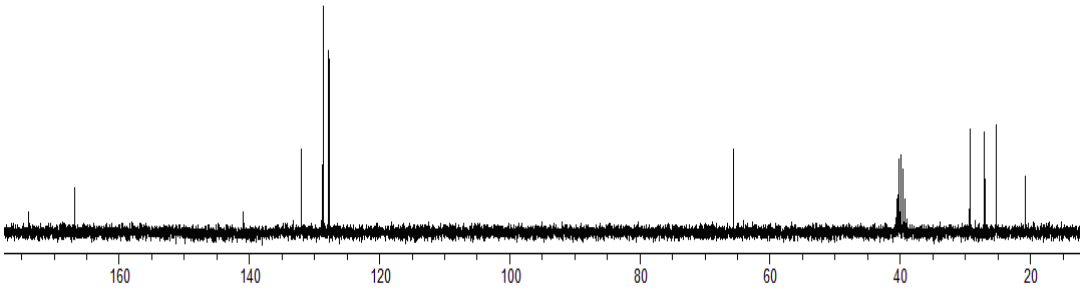
ESI 6. Copies of ^{1}H NMR, ^{13}C NMR and MS

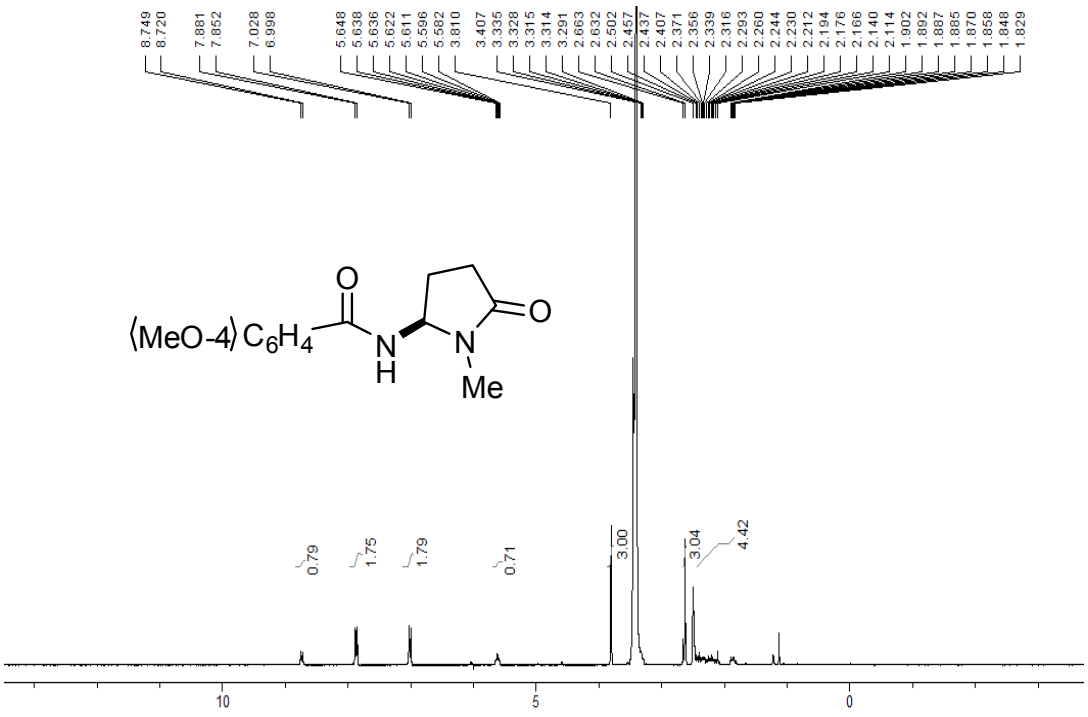


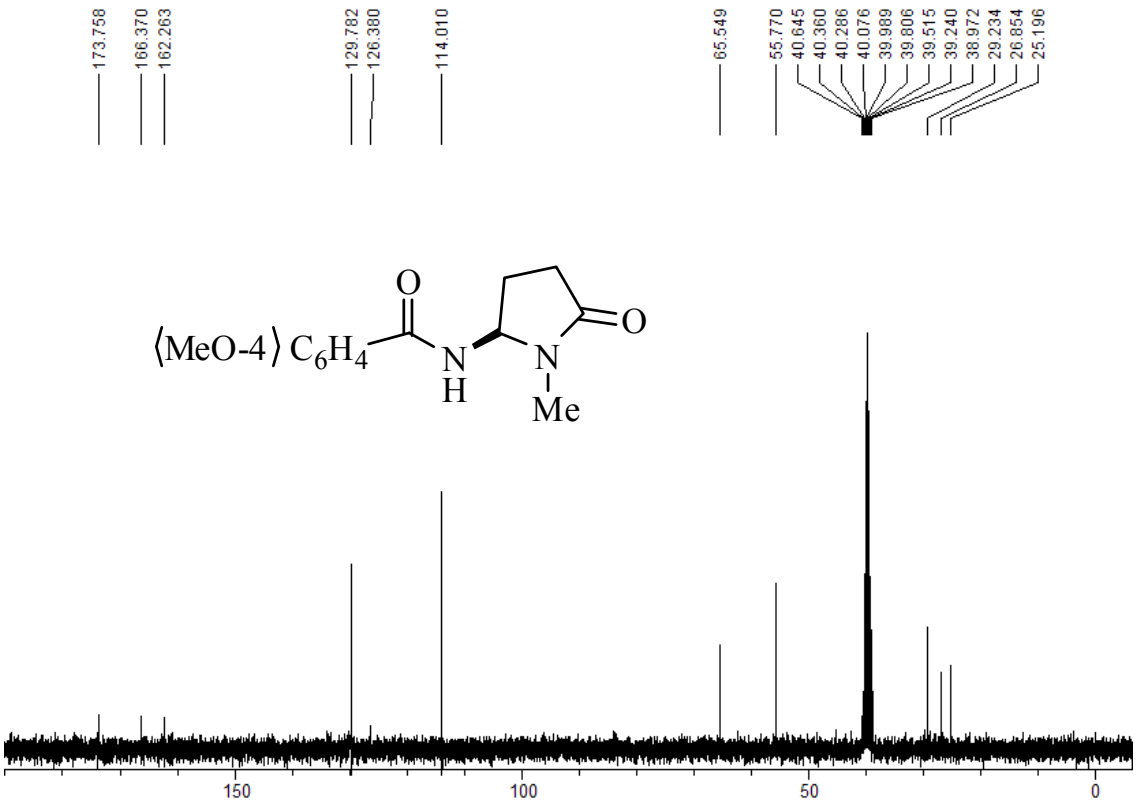


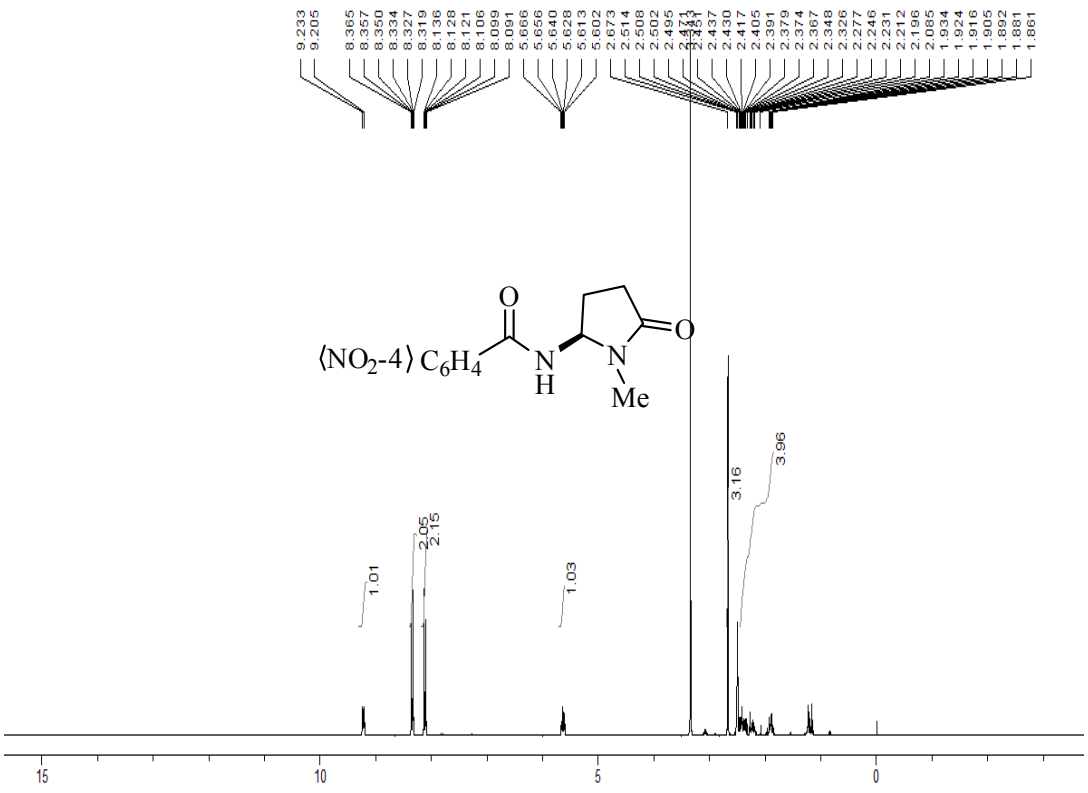


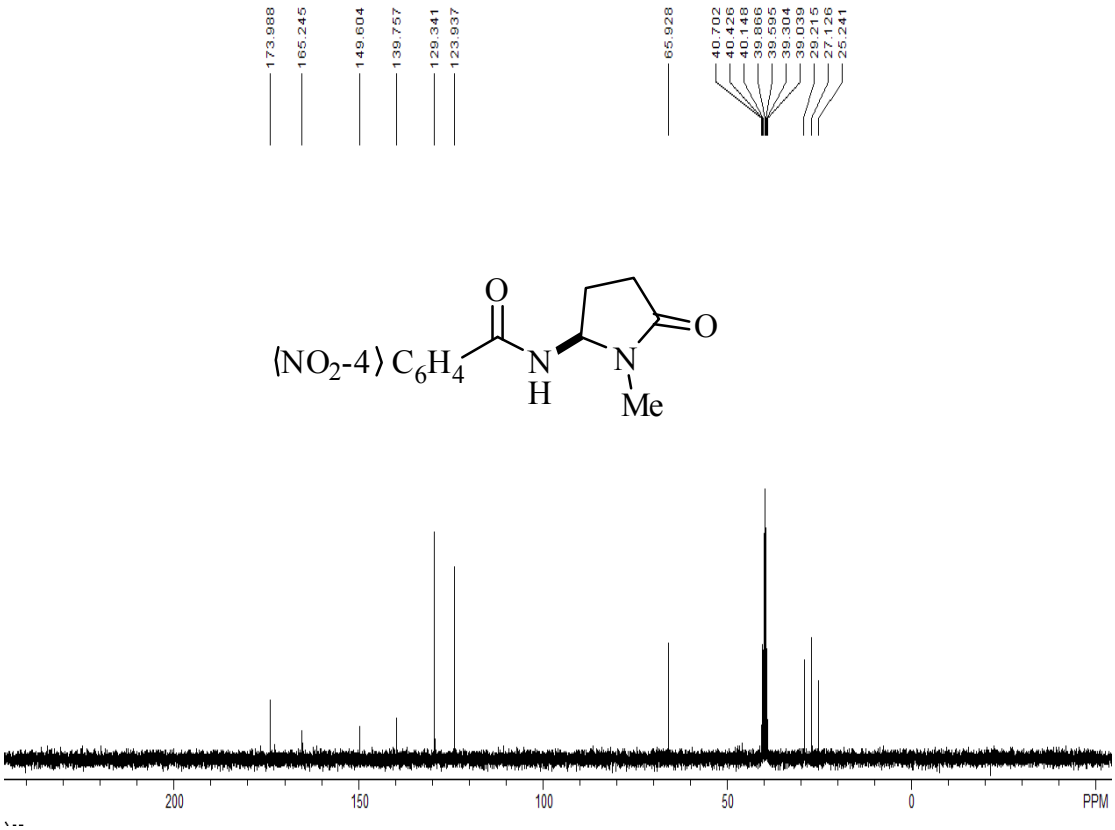


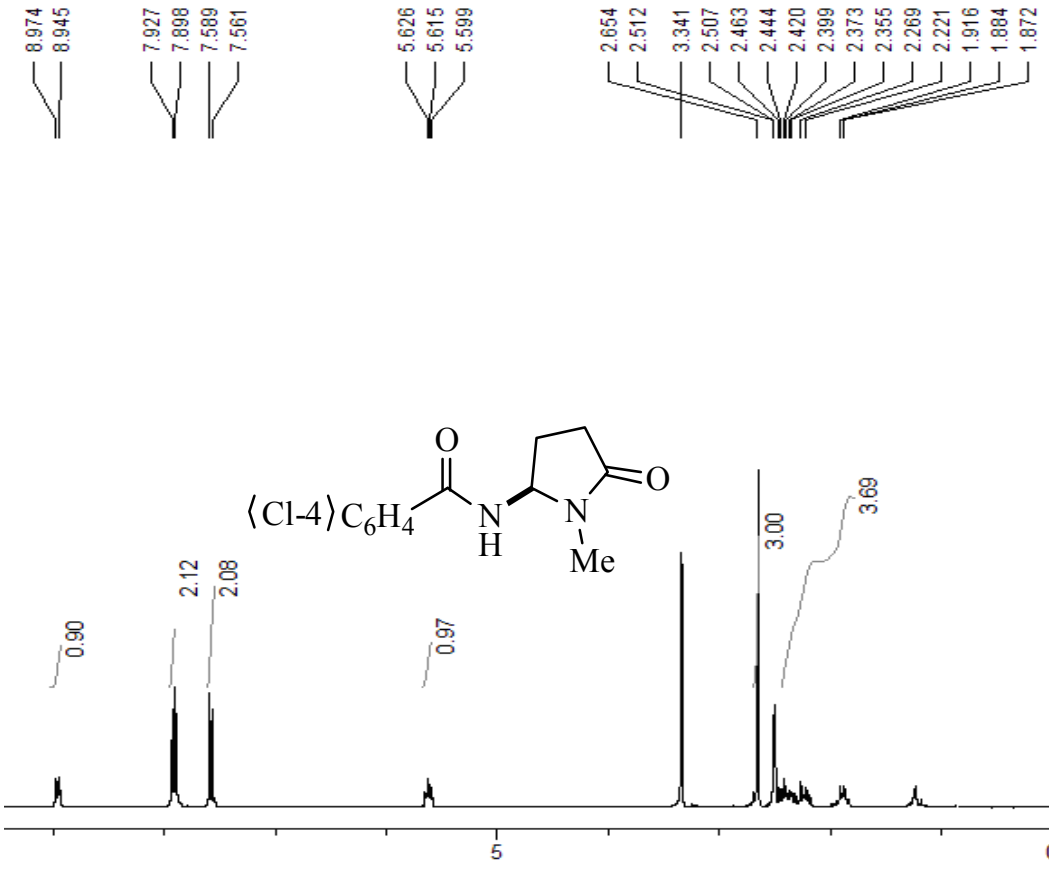


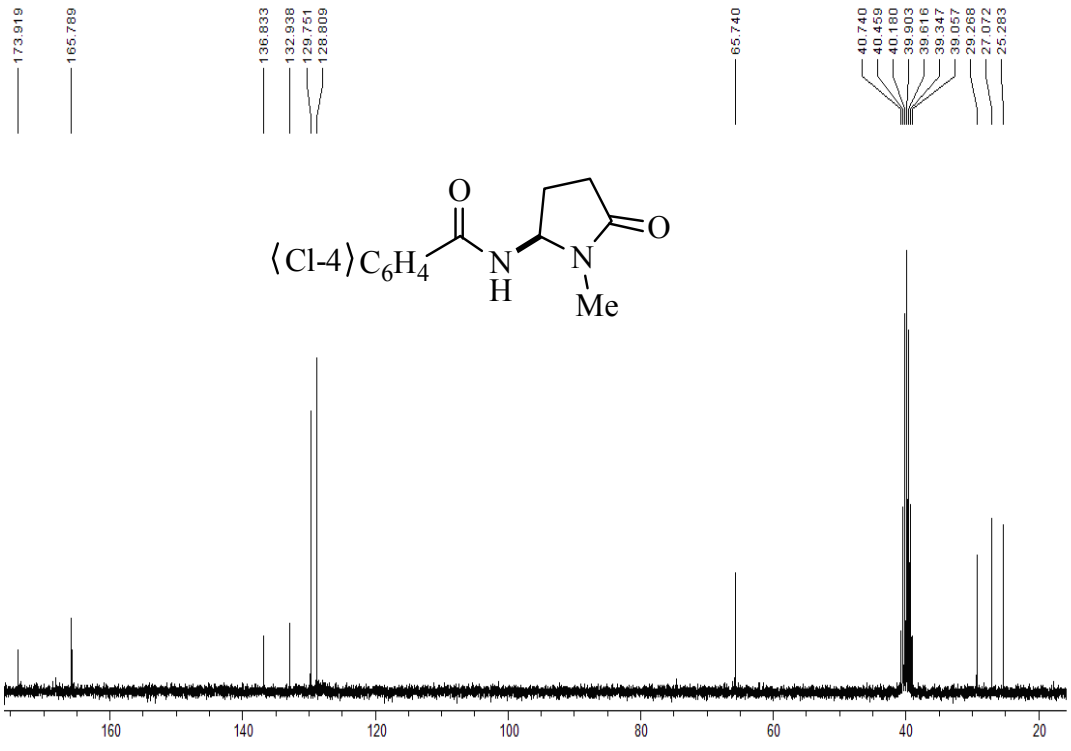


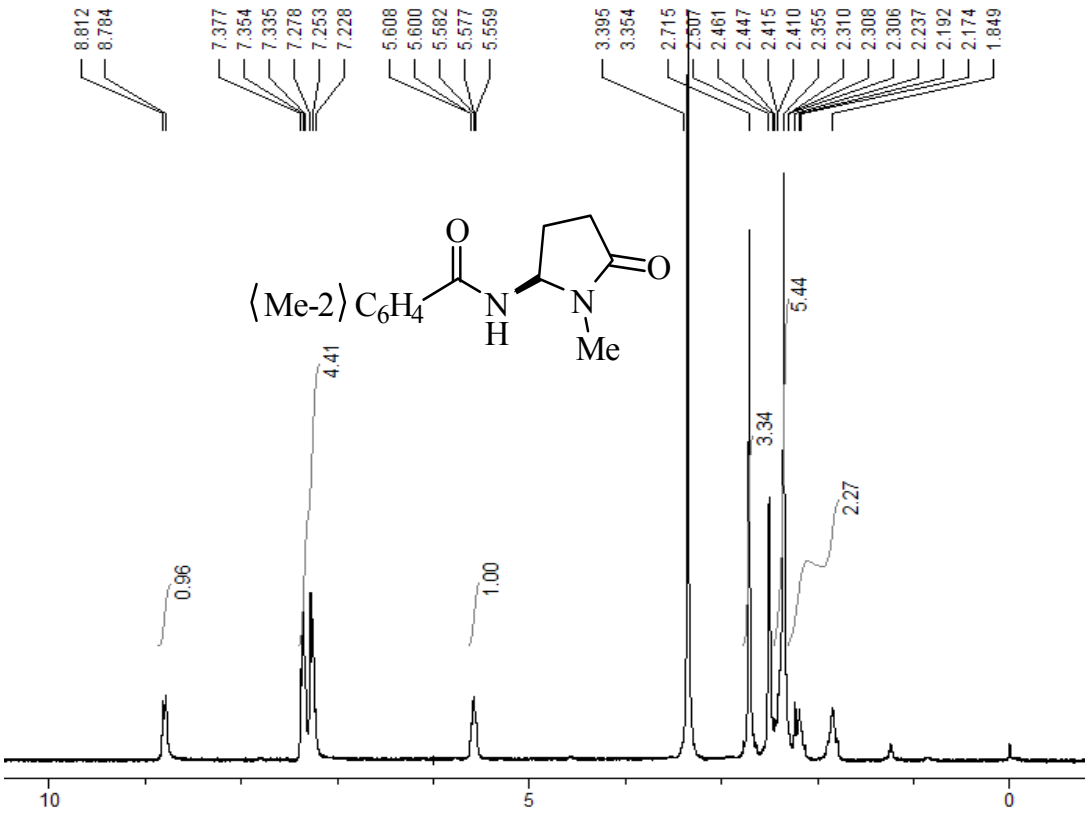


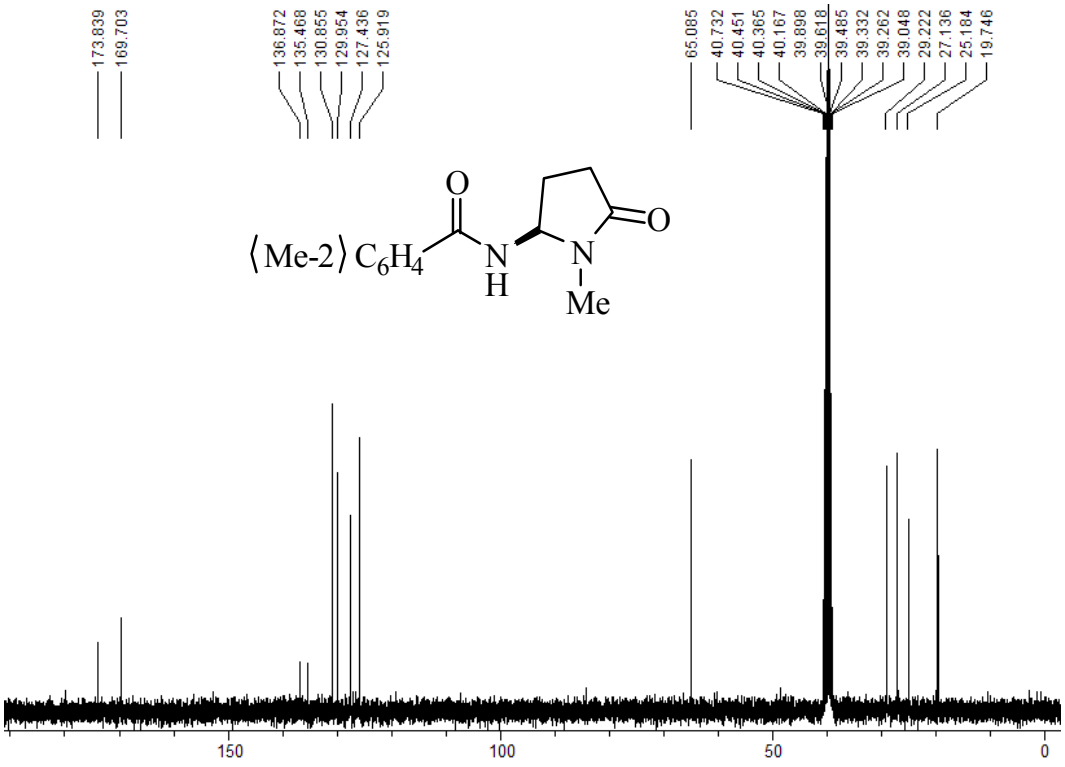


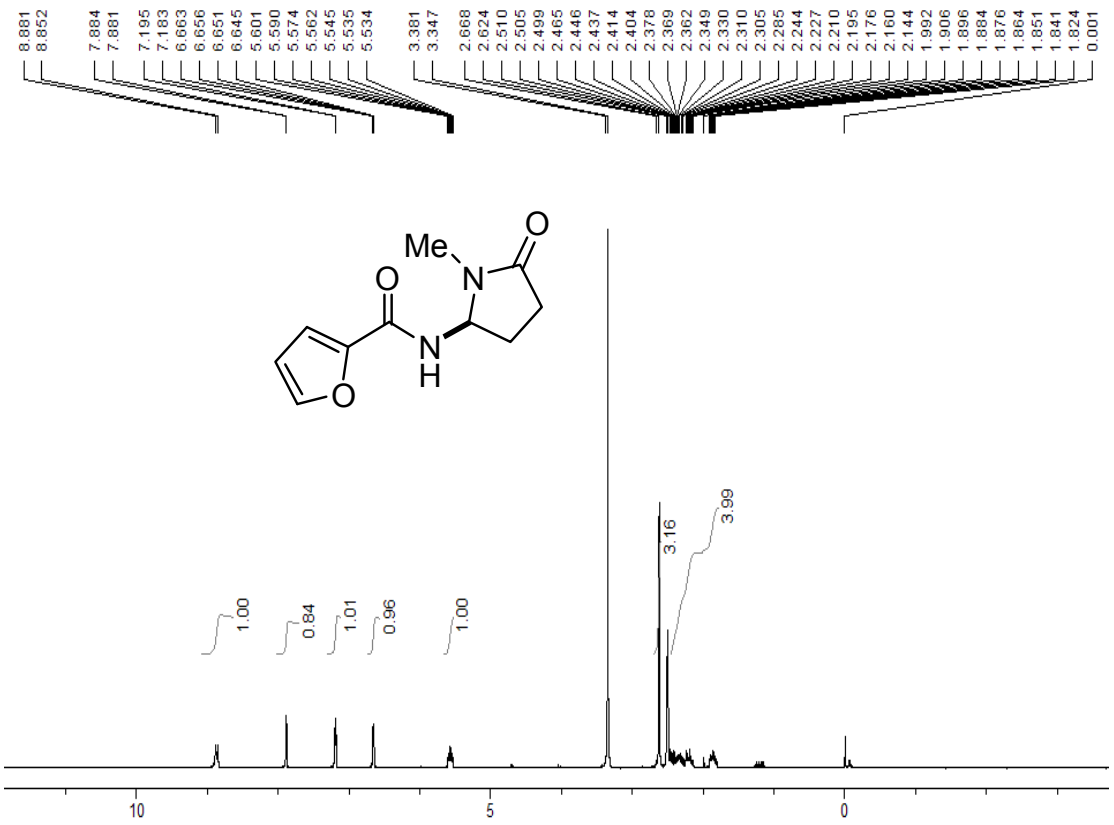


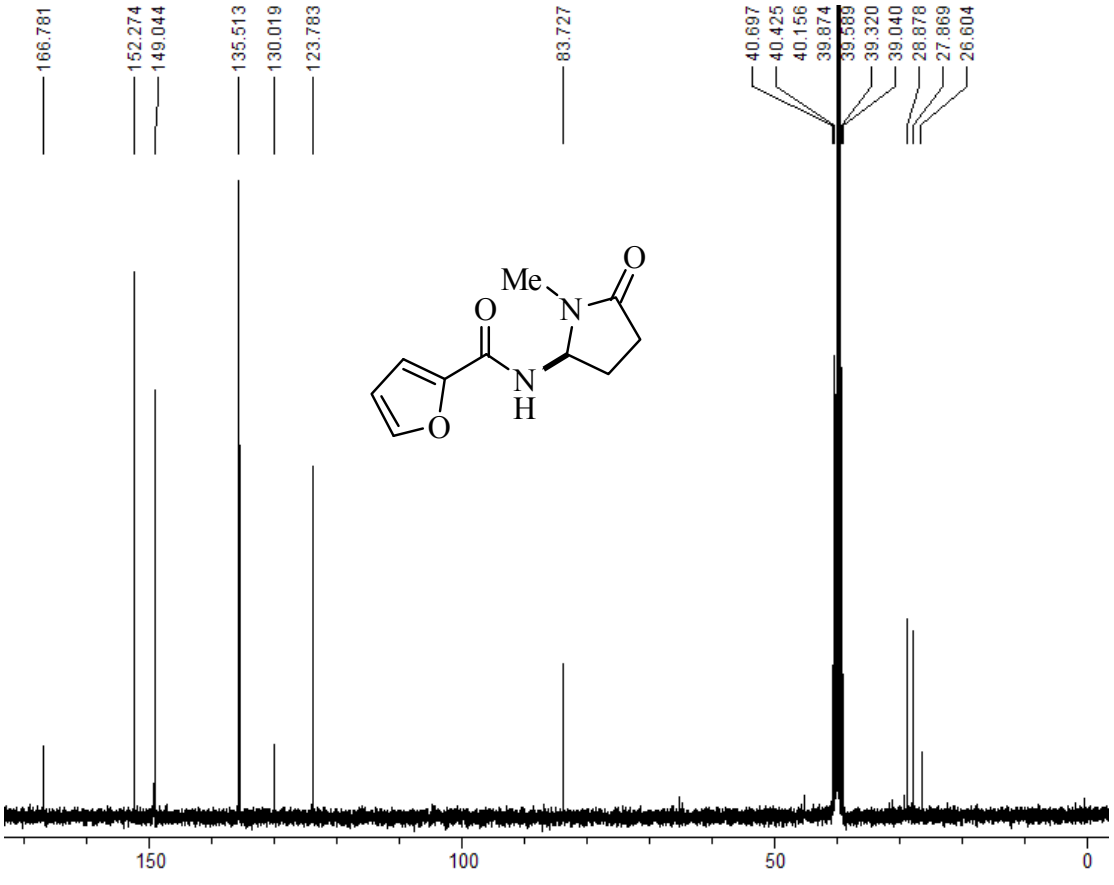


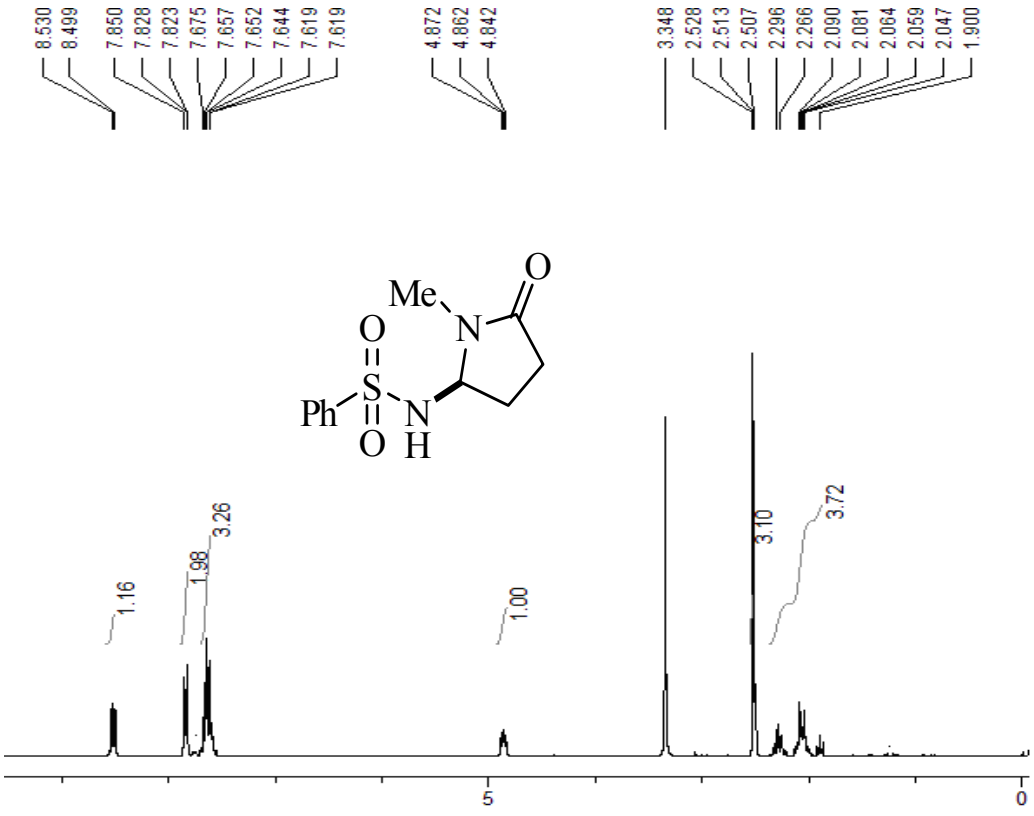


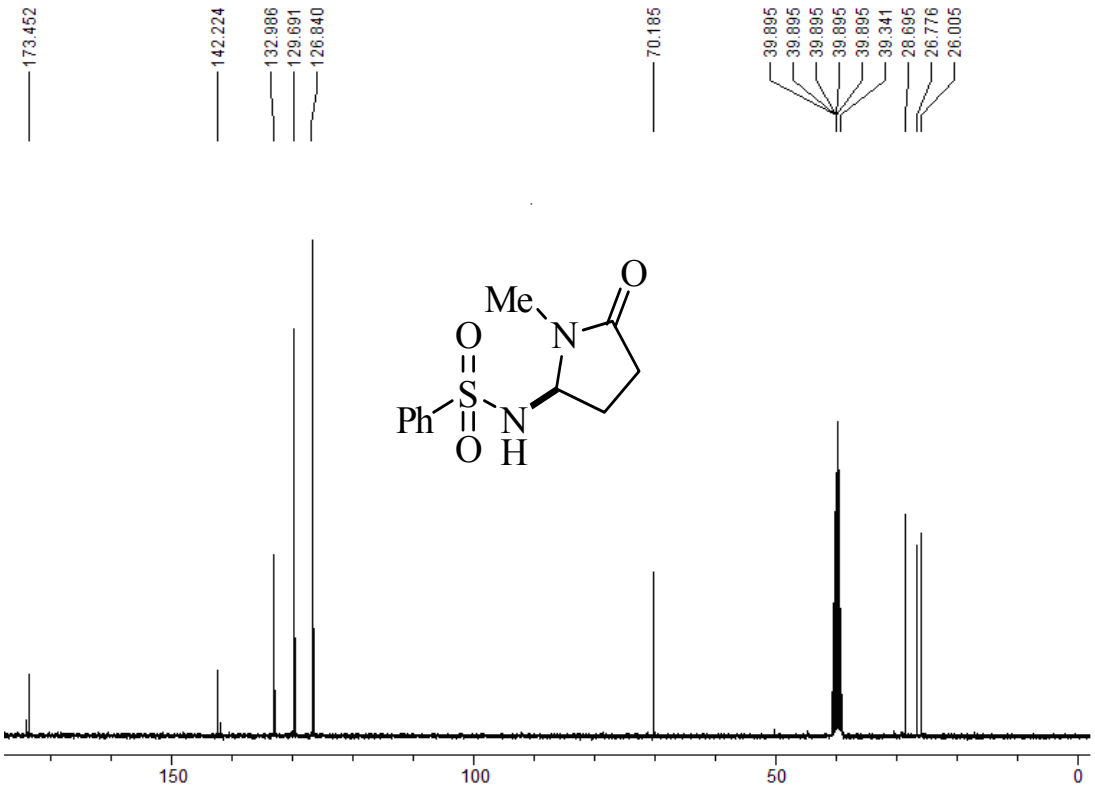


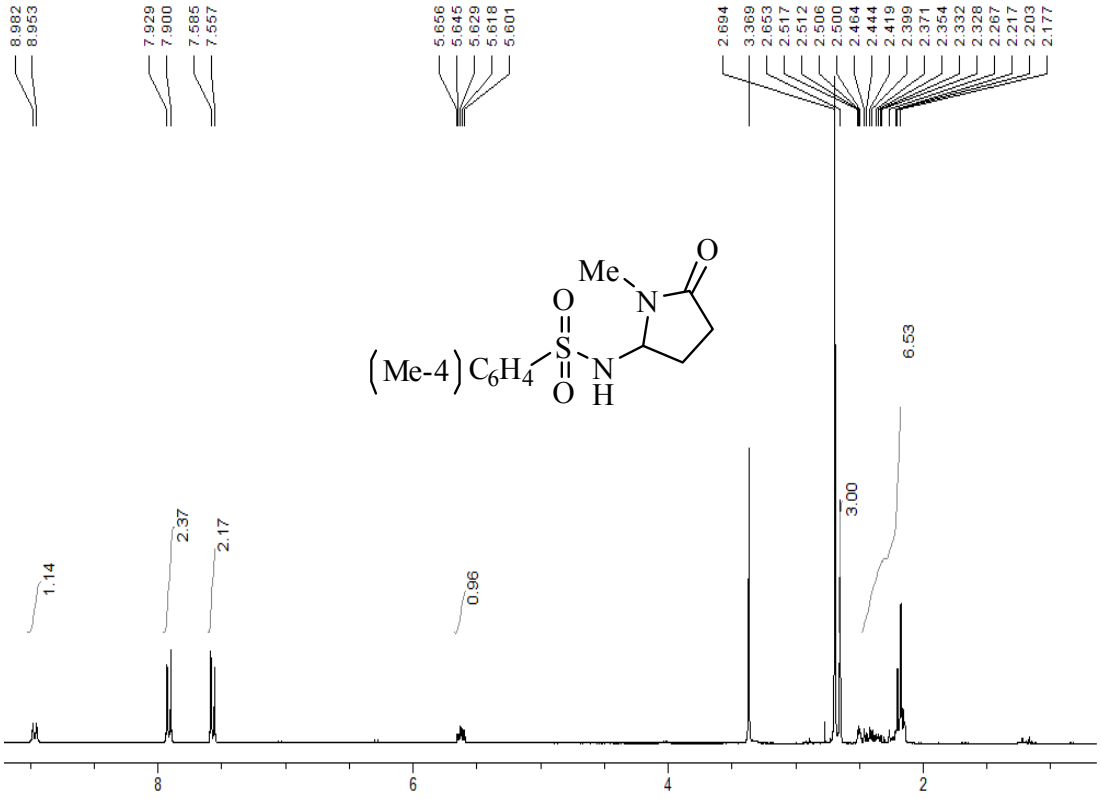


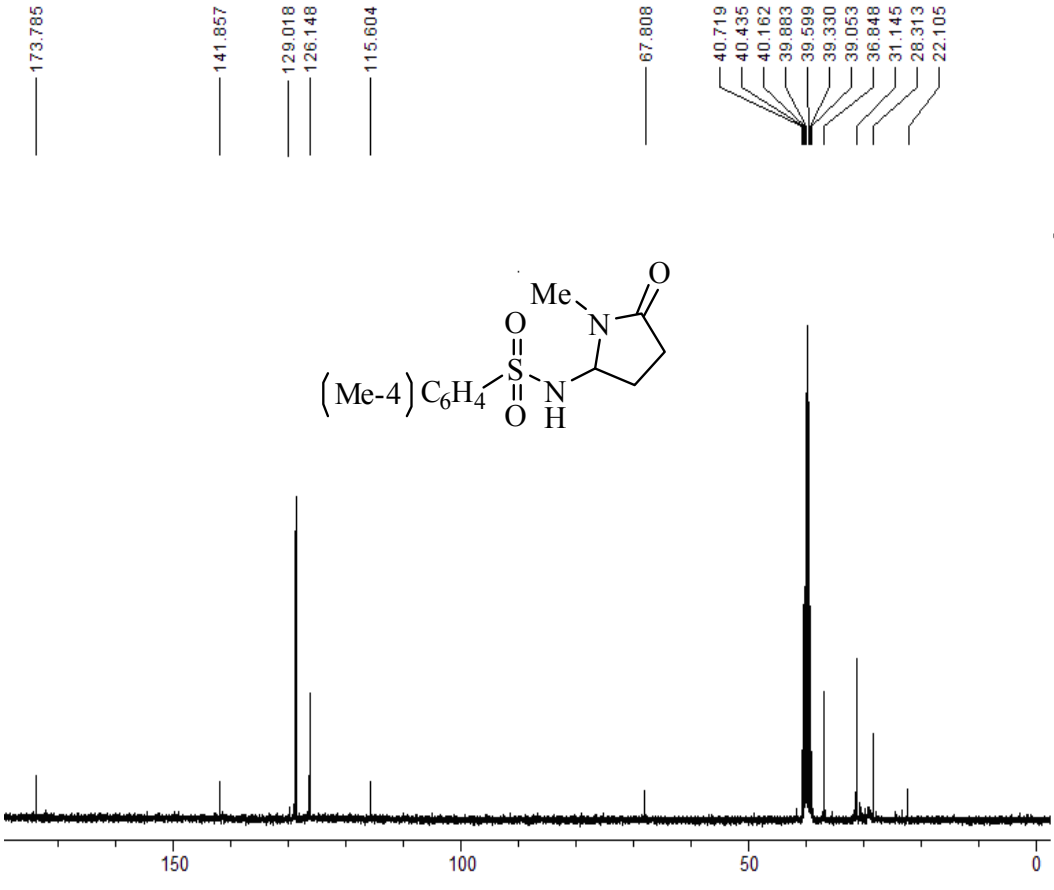


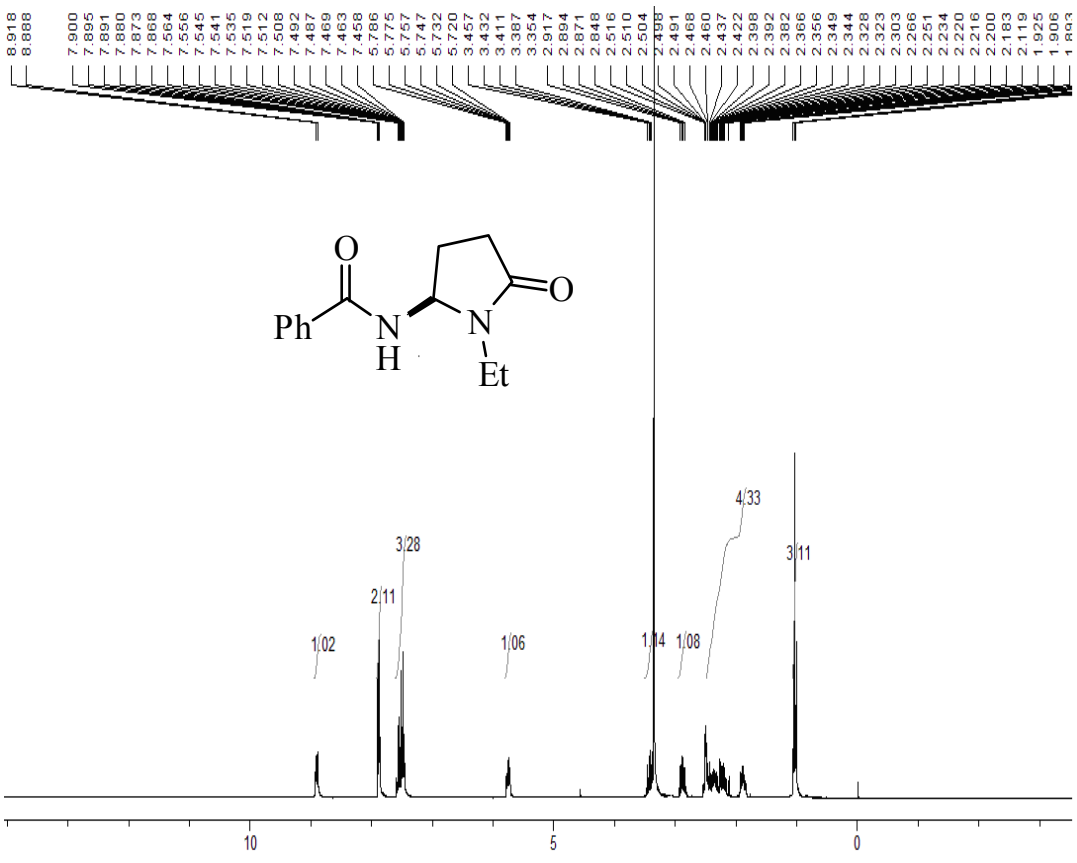


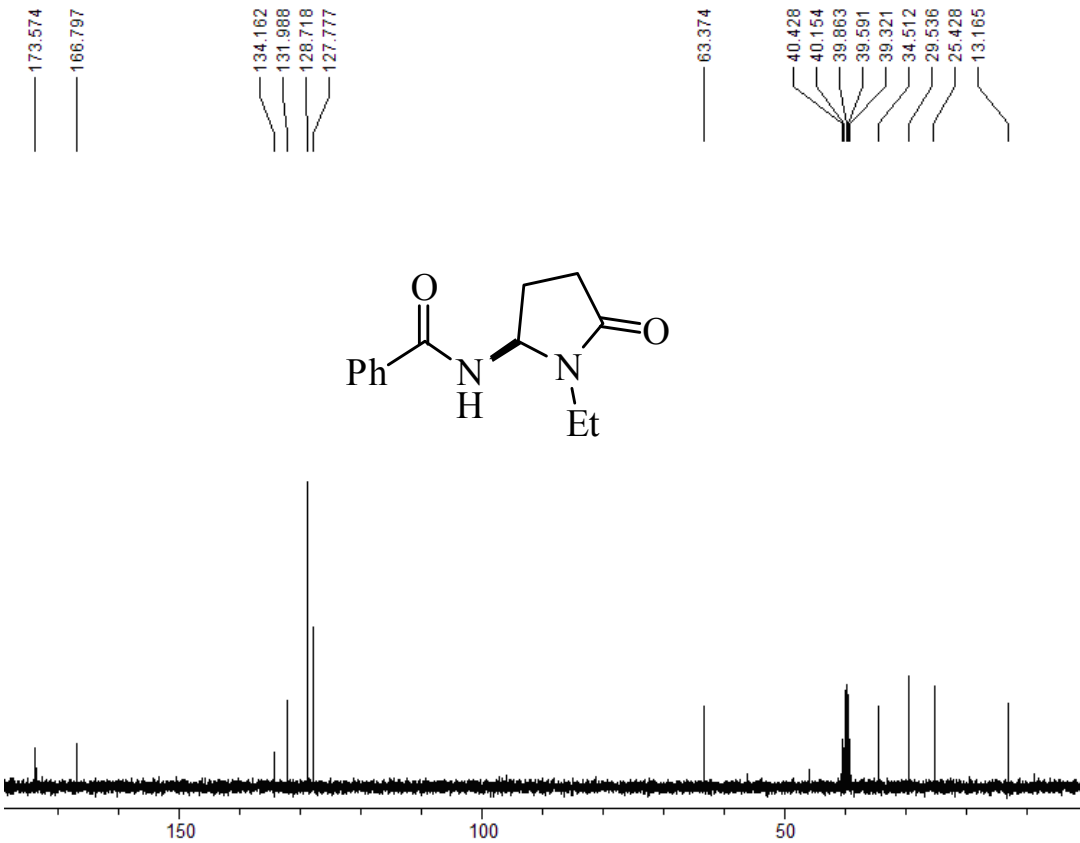


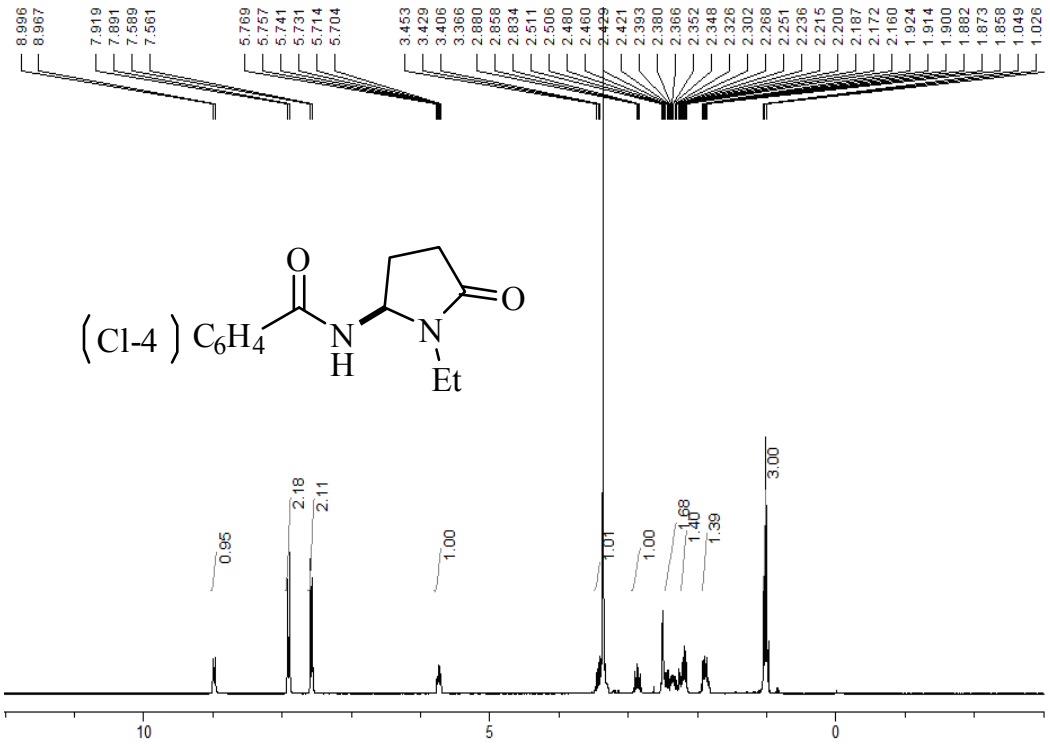


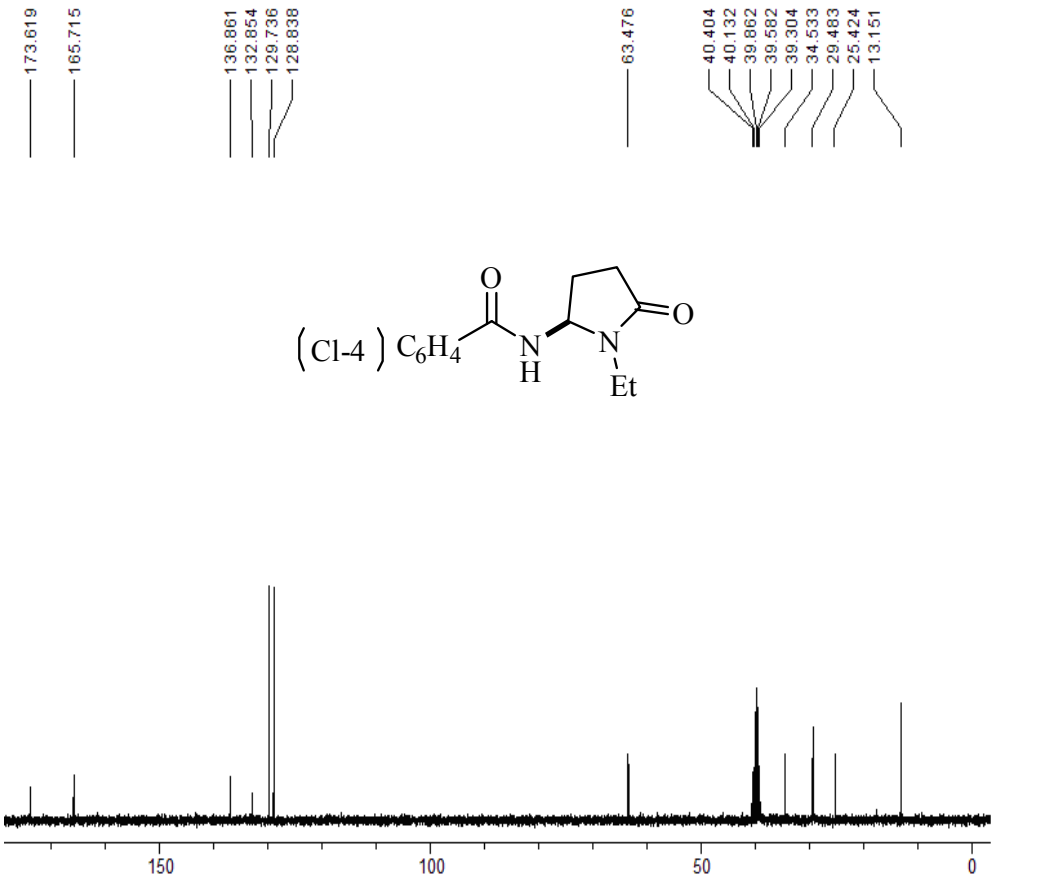


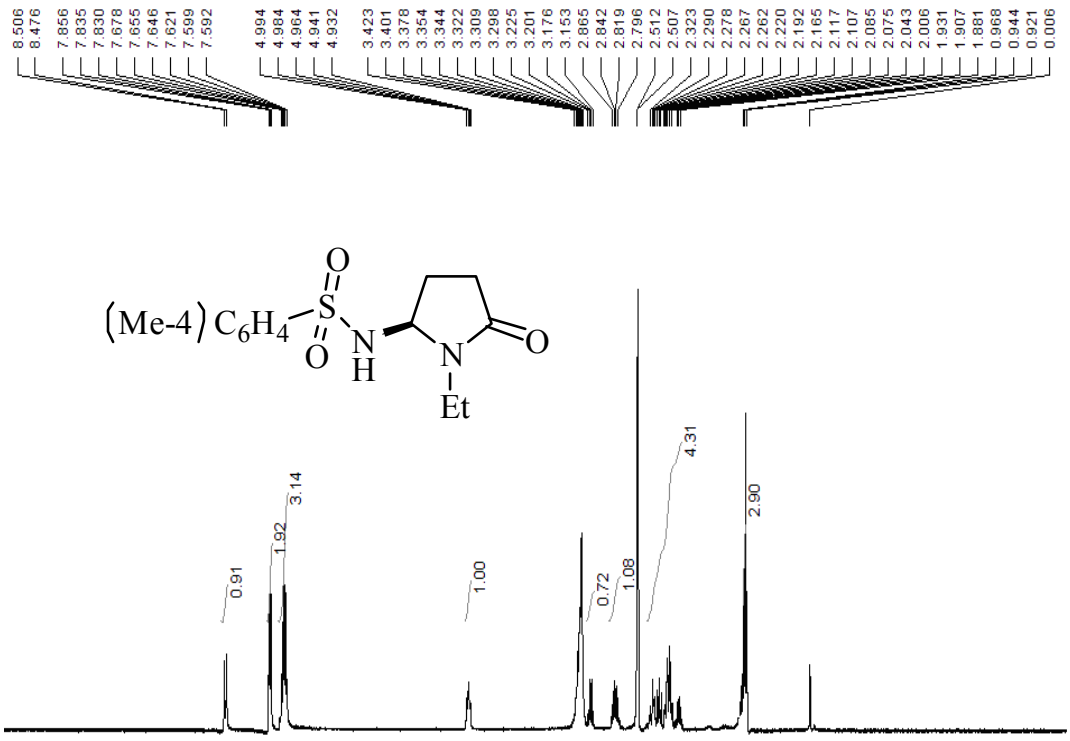


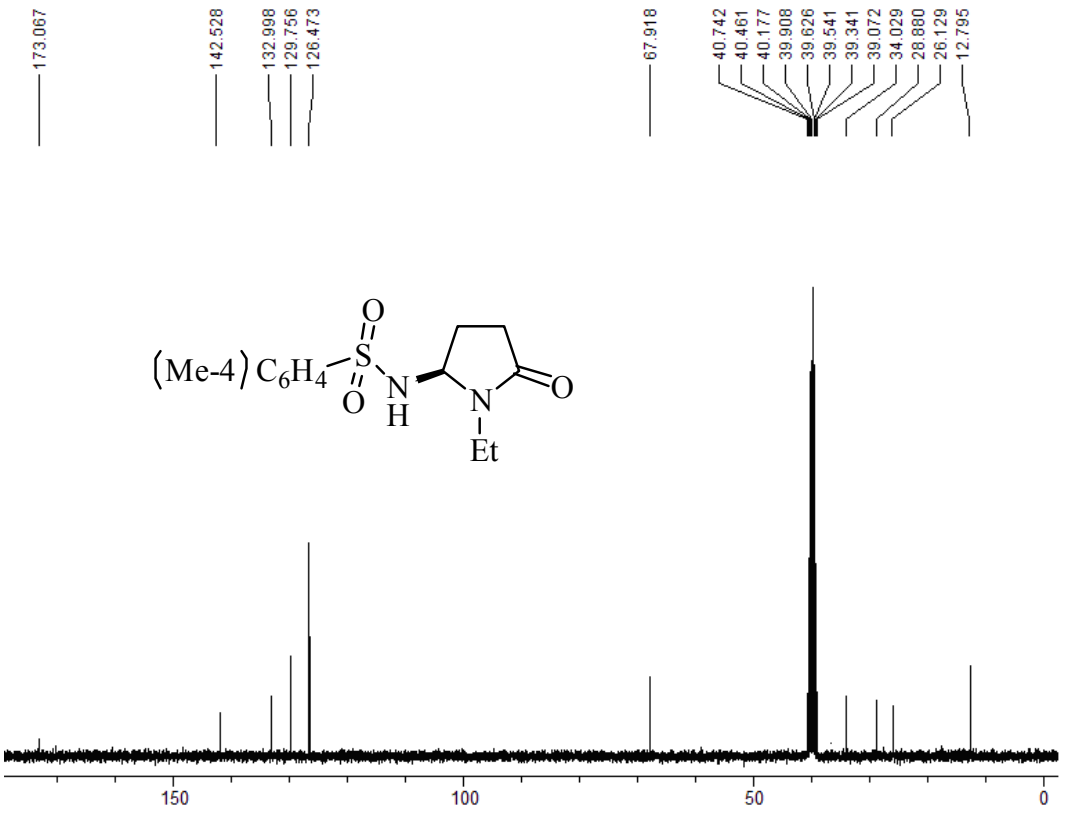


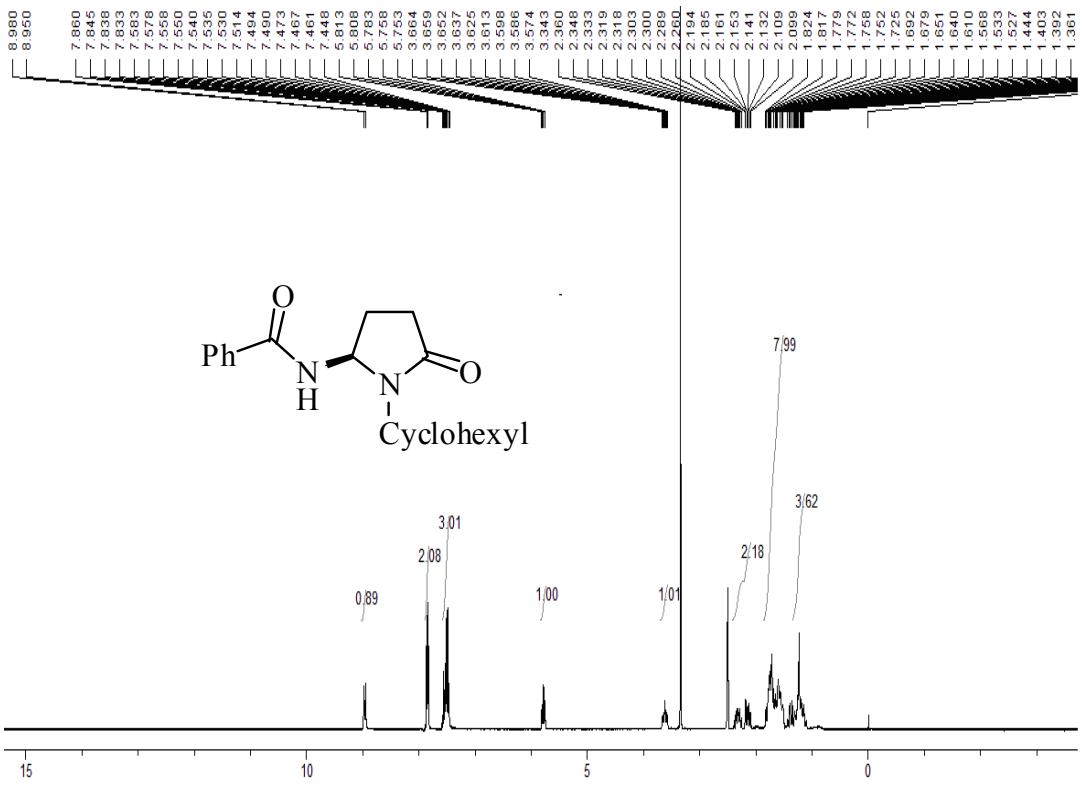


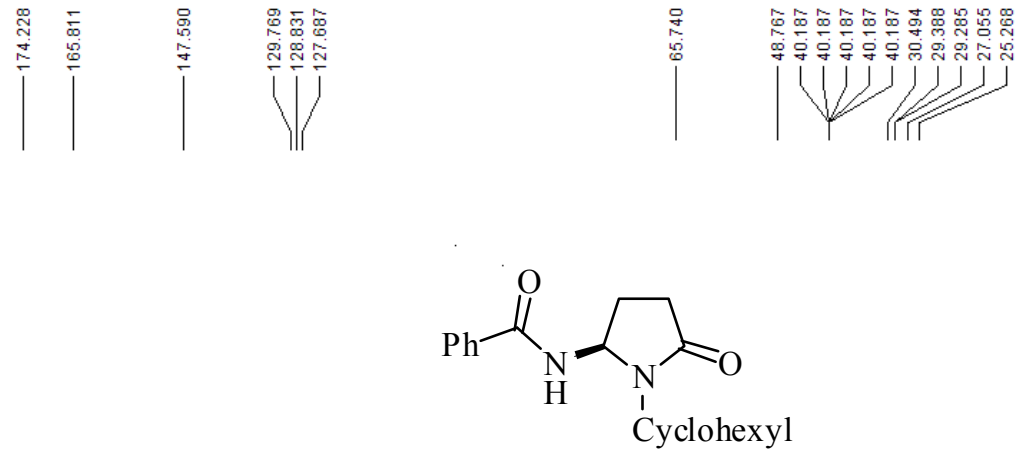


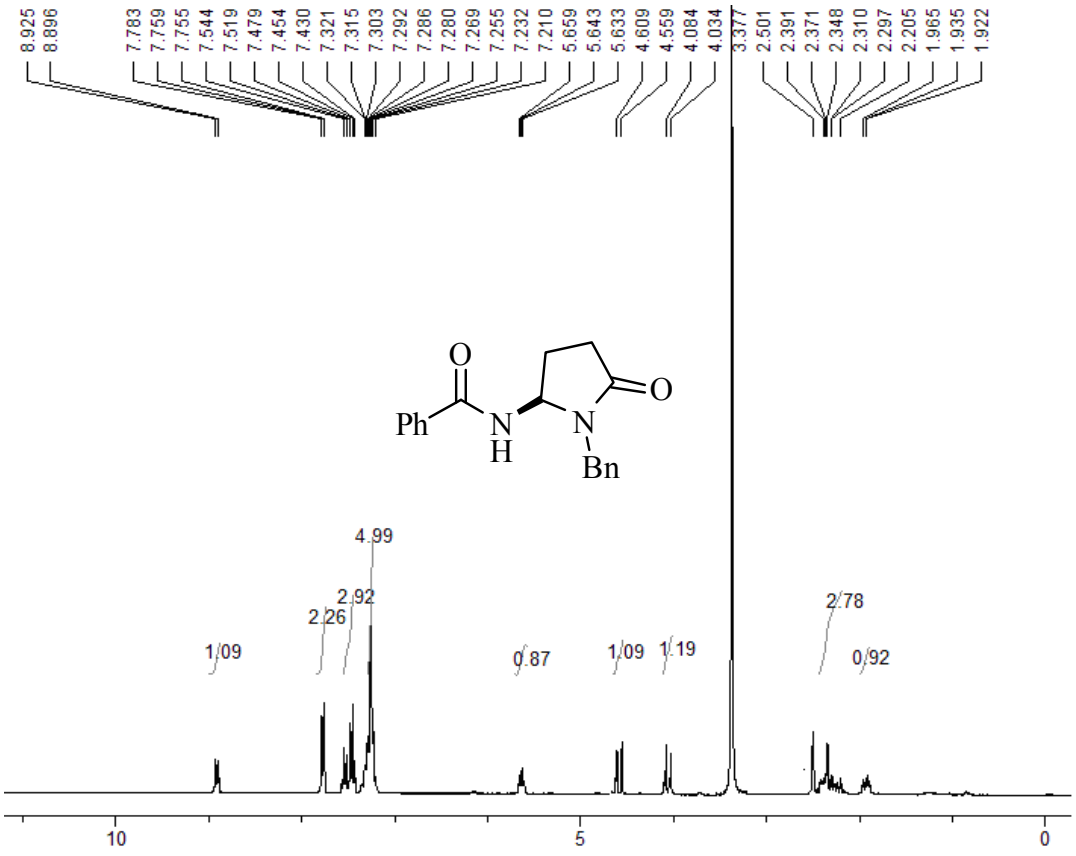


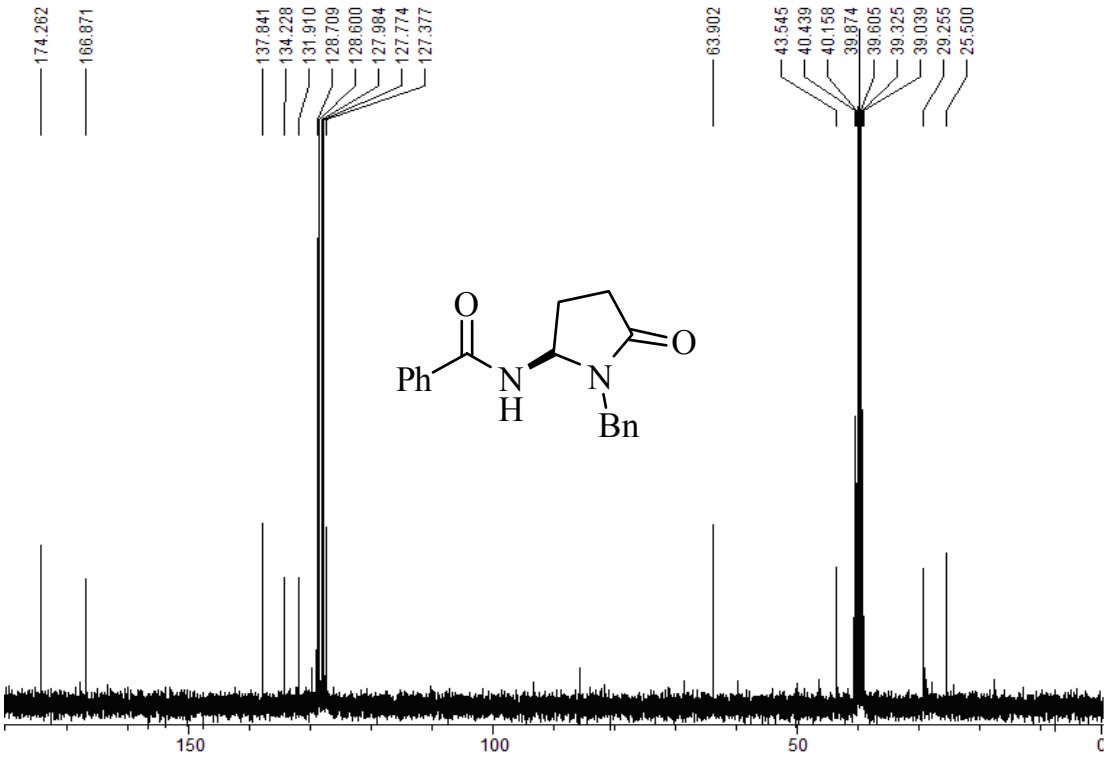


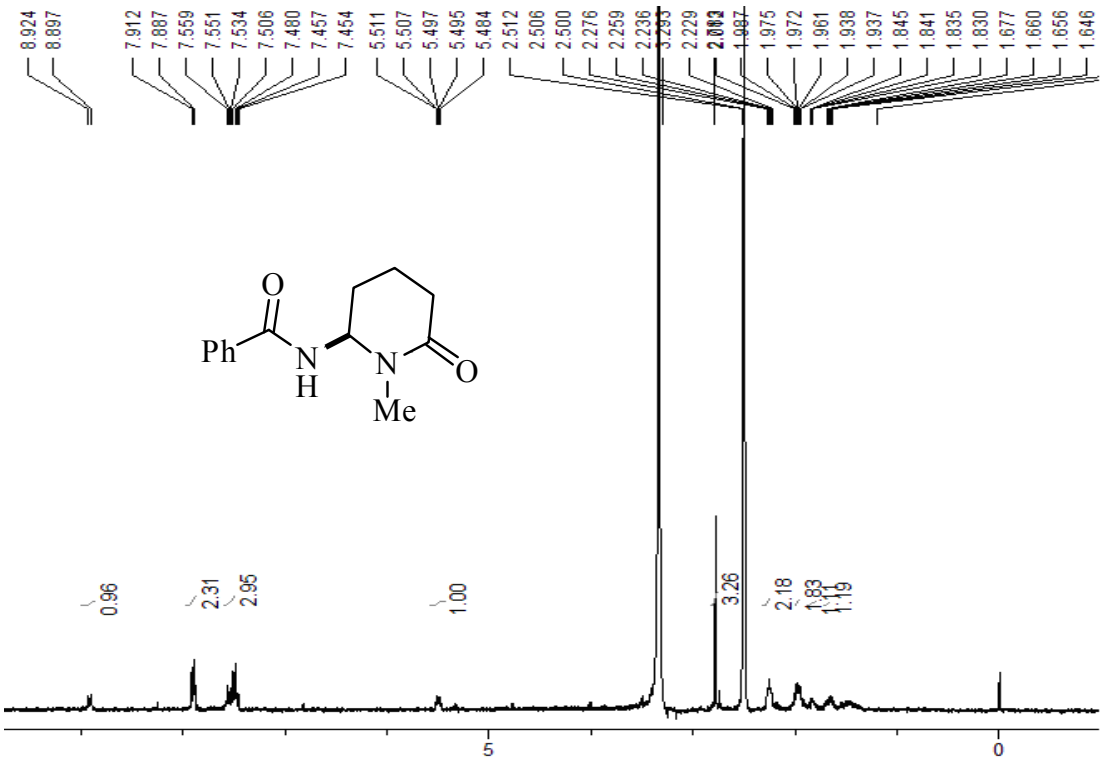


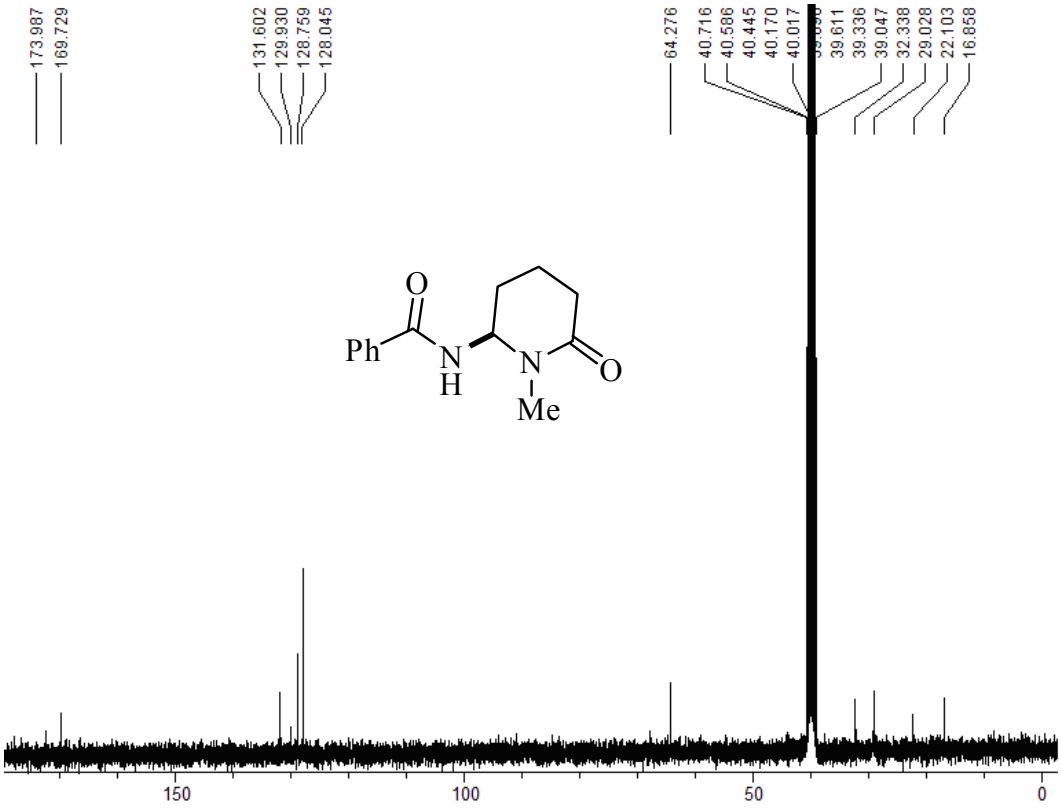


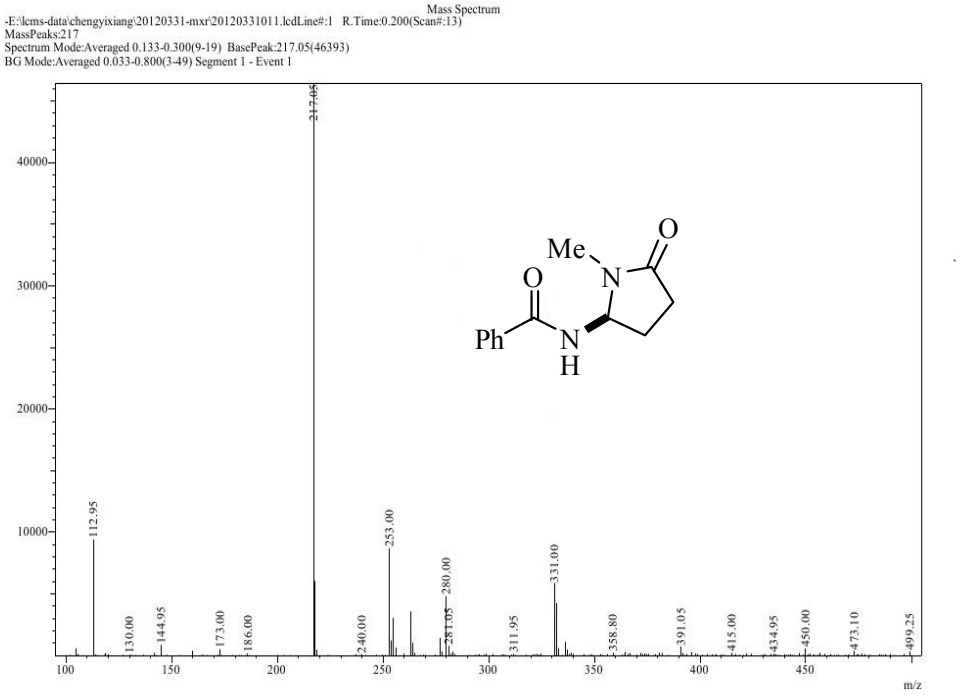


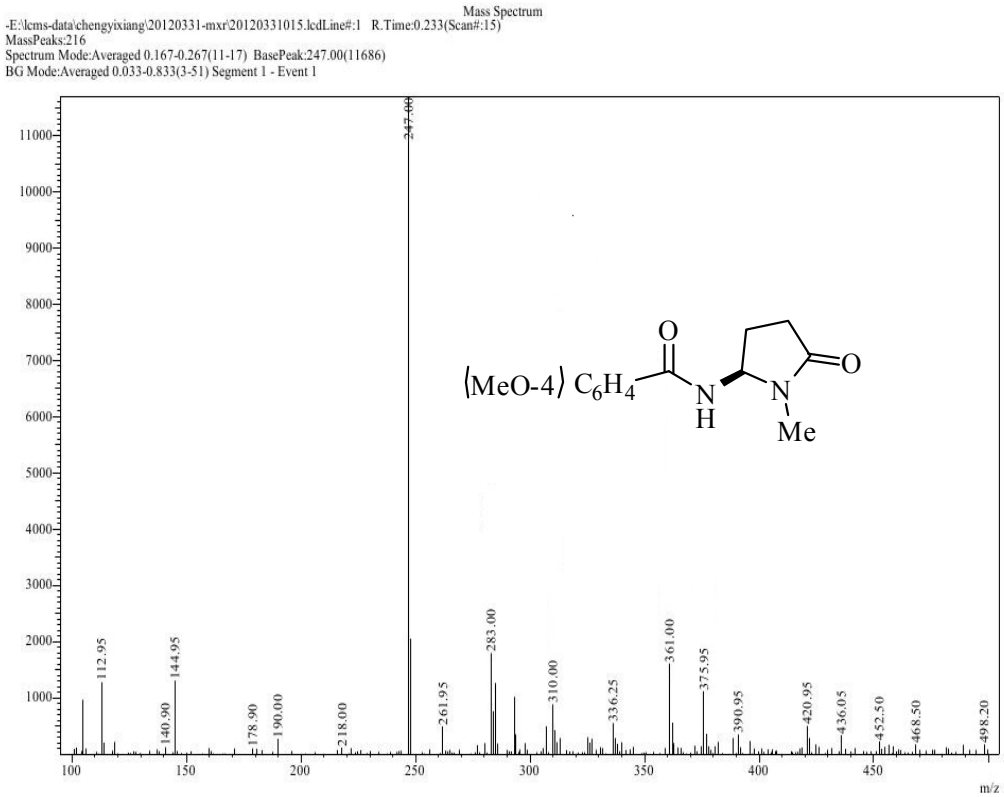


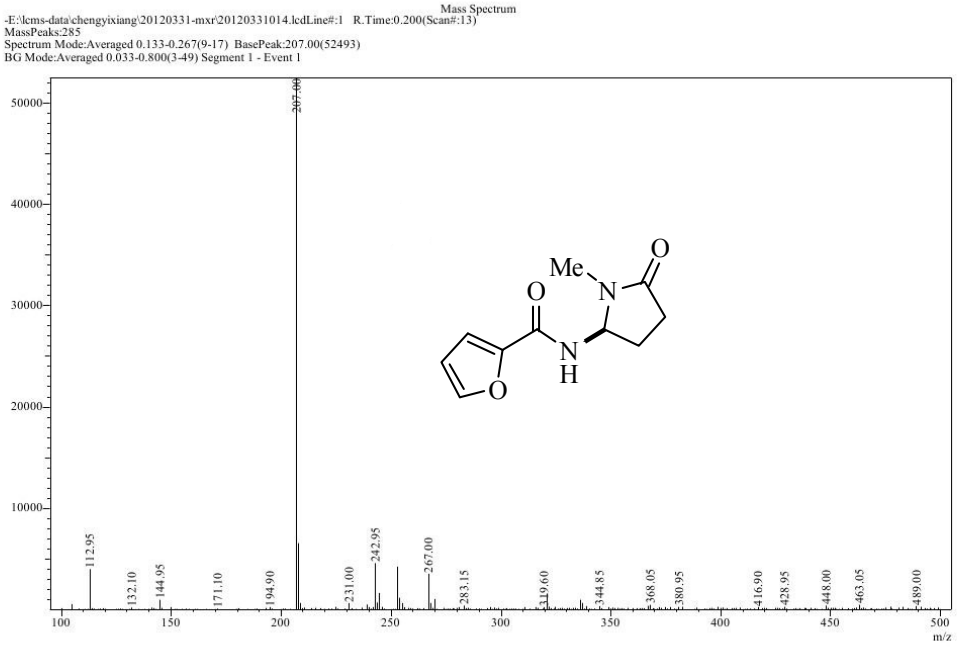


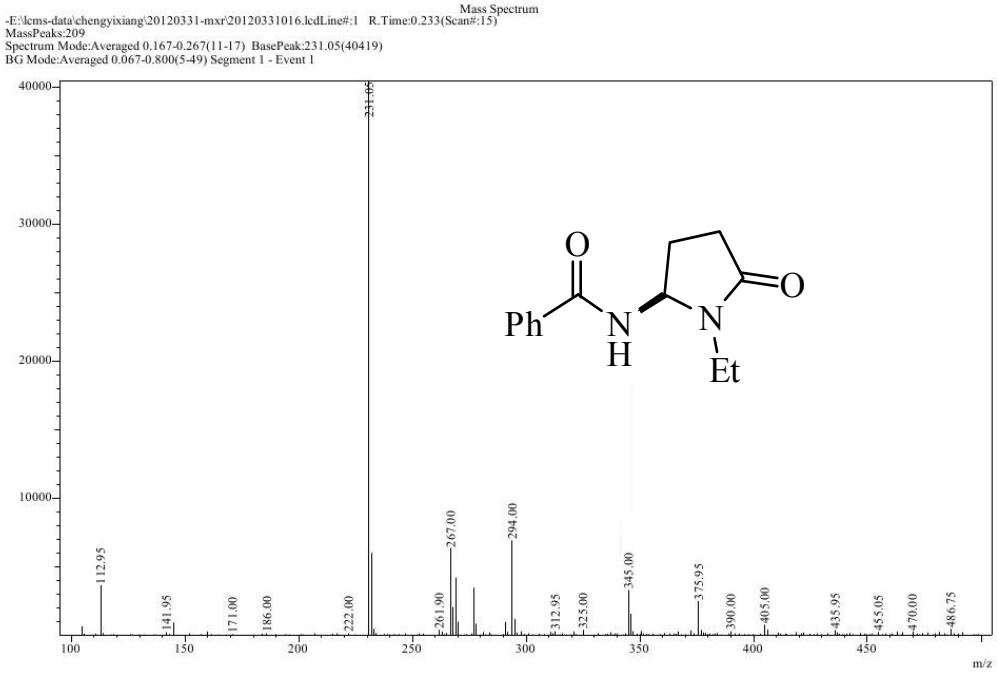


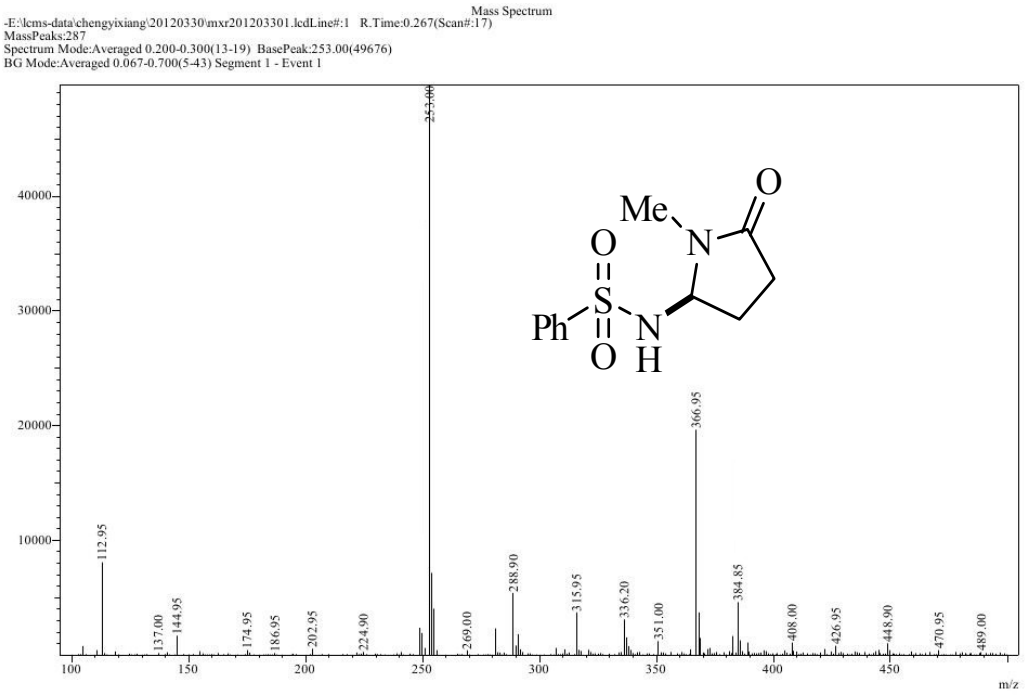








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MassPeaks:287
Spectrum Mode:Averaged 0.200-0.300(13-19) BasePeak:253.00(49676)
BG Mode:Averaged 0.067-0.700(5-43) Segment 1 - Event 1
Me
O
N
O
S
Ph
N
O
H
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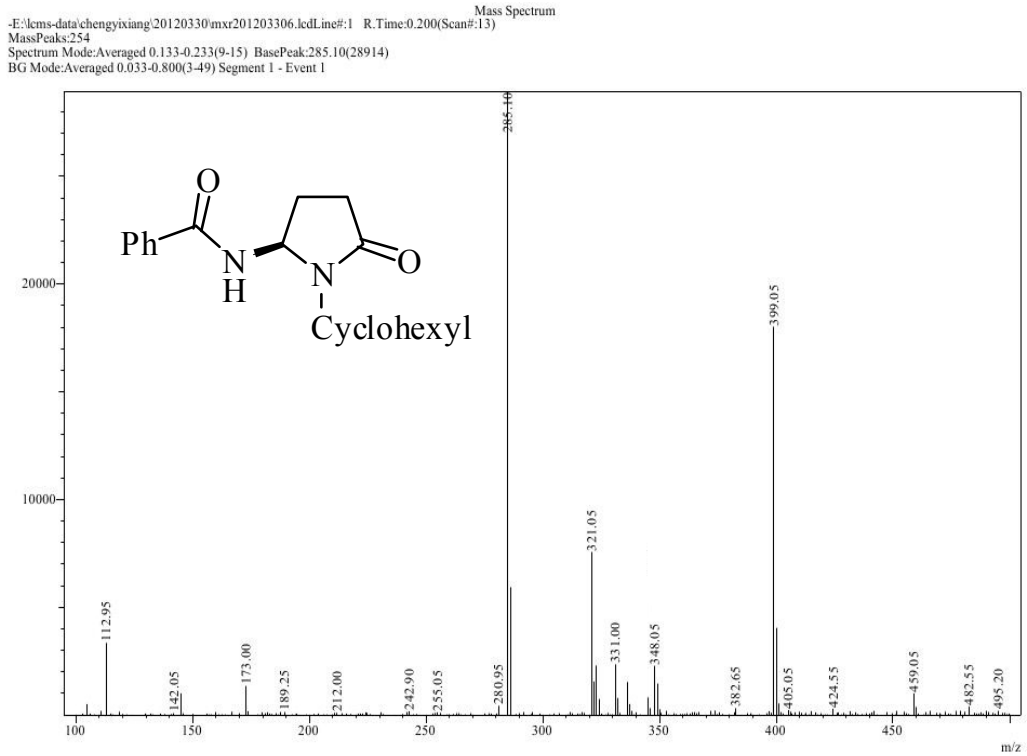
112.95
144.95
288.90
315.95
336.20
384.85
m/z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Spectrum Mode:Averaged 0.133-0.233(9-15) BasePeak:285.10(28914)
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O
Ph
N
H
N
O
Cyclohexyl
285.10
399.05
321.05
112.95
173.00
331.00
348.05
m/z