Electronic Supplementary Information

Stereodivergent Assembly of δ-Valerolactones with an Azaarene-Containing Quaternary Stereocenter Enabled by Cu/Ru Relay Catalysis

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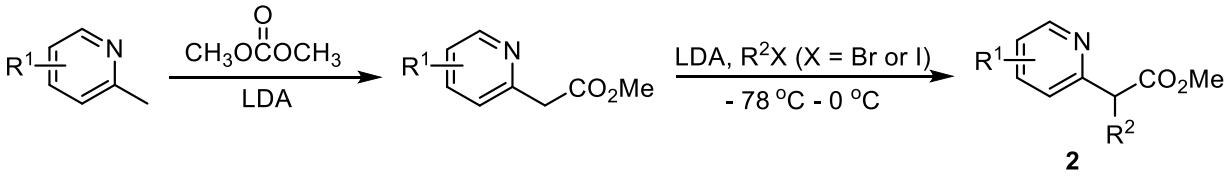
1. General remarks

^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. ^{13}C NMR spectra were recorded on a Bruker 101 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. ^{19}F NMR spectra were recorded on a Bruker 376 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal CF_3COOH signal at -76.55 ppm. The data are reported as follows: (s = single, d = double, t = triple, q = quartet, m = multiple or unresolved, brs = broad single, coupling constant(s) in Hz, integration). High resolution mass spectra (HR-MS) were recorded on a LTQ-Orbitrap Elite mass spectrometer with CH_3CN/MeOH as solvent mixture for the measurements. Commercially obtained reagents were used without further purification. Solvents were purified prior to use according to the standard methods. Unless otherwise noted, all reactions were carried out under nitrogen atmosphere. Enantiomeric ratios were determined by chiral-phase HPLC analysis in comparison with authentic racemic materials. Optical rotations were measured on a Rudolph Research Analytical Autopol VI polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. Substrates **1**[1], substrates **2a**, **2e**-**2l**, **2n**-**2o**, **2q**-**2s**[2] were prepared according to the literature procedure. Chiral ligands **L1**-**L5**[3] were prepared according to the literature procedure. The chiral Ru catalysts [Ru]-**1**~[Ru]-**3** were prepared according to the reported procedure.[4,5] The racemic products were obtained by running reactions with racemic catalysts or blending equal amount of two enantiomers. The absolute configuration of the product **3t** was assigned by crystalline structure, and those of other products were deduced on the basis of this result.

2. General procedure for the preparation of α-azaaryl acetate substrates



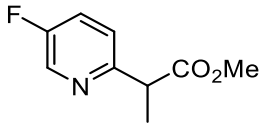
2

Take substrate **2a** as an example: Step1: To a solution of diisopropylamine (3.0 equiv) in THF (10 mL) at 0 °C was added ^{n}BuLi (2.5 M in hexanes, 3.0 equiv). The mixture was stirred at 0 °C for 30 min then cooled to -78 °C. Then, 2-methylpyridine in THF (5 mL) was added dropwise, the mixture was stirred at -78 °C for 10 min, dimethyl carbonate (1.2 equiv) was added, the mixture was stirred at -78

°C for 15 min then at 0 °C for 2 h. The mixture was quenched by adding H_2O (20 mL) and extracted with EtOAc. After removal of solvent under vacuum, the crude mixture was purified by flash column chromatography (0 to 35% EtOAc in hexanes) to give the intermediate methyl 2-(pyridin-2-yl)acetate.

Step 2: To a solution of diisopropylamine (3.0 equiv) in THF (10 mL) at 0 °C was added ^{n}BuLi (2.5 M in hexanes, 3.0 equiv). The mixture was stirred at 0 °C for 30 min then cooled to -78 °C. Thereafter, methyl 2-pyridylacetate (1.0 equiv) in THF (5 mL) was added dropwise. After the mixture being stirred at -78 °C for 30 min, methyl iodide (5.0 equiv) was added, and the mixture was stirred at -78 °C for 15 min then at r.t. for 3 h. The mixture was quenched by adding H_2O (20 mL) at 0 °C and extracted with EtOAc. After removal of solvent under vacuum, the crude mixture was purified by flash column chromatography (0 to 35% EtOAc in hexanes) to give the desired product.

Methyl 2-(5-fluoropyridin-2-yl)propanoate (2b):



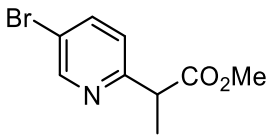
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 2.9 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.32 – 7.26 (m, 1H), 3.95 (q, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.9, 158.5 (d, *J* = 255.3 Hz), 155.7 (d, *J* = 4.3 Hz), 137.5 (d, *J* = 23.7 Hz), 123.5 (d, *J* = 18.8 Hz), 122.9 (d, *J* = 4.3 Hz), 52.2, 47.1, 17.3.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -129.49.

HRMS (ESI+) Calcd. For $C_9H_{11}FNO_2^+$ ($[M+H]^+$): 184.0768, found: 184.0768.

Methyl 2-(5-bromopyridin-2-yl)propanoate (2c):

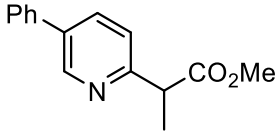


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 2.4 Hz, 1H), 7.77 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.90 (q, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 1.53 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.6, 158.3, 150.4, 139.3, 123.4, 119.1, 52.2, 47.3, 17.1.

HRMS (ESI+) Calcd. For $C_9H_{11}{}^{79}BrNO_2^+$ ($[M+H]^+$), $C_9H_{11}{}^{81}BrNO_2^+$ ($[M+H]^+$): 243.9968, 245.9947; found: 243.9965, 245.9942.

Methyl 2-(5-phenylpyridin-2-yl)propanoate (2d):

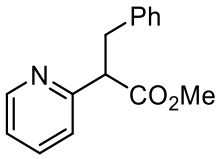


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.78 (d, *J* = 1.6 Hz, 1H), 7.84 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.49 – 7.42 (m, 2H), 7.41 – 7.33 (m, 2H), 4.01 (q, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 1.60 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.0, 158.5, 147.8, 137.5, 135.1, 135.0, 129.0, 128.0, 127.0, 121.8, 52.1, 47.5, 17.2.

HRMS (ESI+) Calcd. For $C_{15}H_{16}NO_2^+$ ([M+H]$^+$): 242.1176, found: 242.1174.

Methyl 3-phenyl-2-(pyridin-2-yl)propanoate (2m):

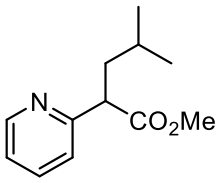


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 – 8.52 (m, 1H), 7.67 – 7.52 (m, 1H), 7.23 – 7.11 (m, 7H), 4.11 (t, *J* = 7.8 Hz, 1H), 3.64 (s, 3H), 3.46 (dd, *J* = 13.8, 8.1 Hz, 1H), 3.24 (dd, *J* = 13.8, 7.4 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8, 157.9, 149.6, 138.8, 136.6, 128.9, 128.3, 126.3, 123.0, 122.3, 55.7, 52.1, 38.2.

HRMS (ESI+) Calcd. For $C_{15}H_{16}NO_2^+$ ([M+H]$^+$): 242.1176, found: 242.1175.

Methyl 4-methyl-2-(pyridin-2-yl)pentanoate (2p):

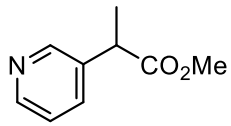


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.50 (m, 1H), 7.67 – 7.58 (m, 1H), 7.35 – 7.28 (m, 1H), 7.19 – 7.11 (m, 1H), 3.92 (t, *J* = 7.8 Hz, 1H), 3.66 (s, 3H), 2.06 – 1.96 (m, 1H), 1.84 – 1.72 (m, 1H), 1.52 – 1.39 (m, 1H), 0.98 – 0.81 (m, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.8, 158.9, 149.4, 136.6, 122.4, 122.1, 52.02, 51.95, 41.2, 25.9, 22.5, 22.3.

HRMS (ESI+) Calcd. For $C_{12}H_{18}NO_2^+$ ([M+H]$^+$): 208.1132, found: 208.1130.

Methyl 2-(pyridin-3-yl)propanoate (2t)

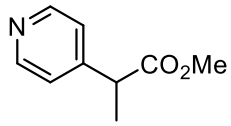


^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 – 8.37 (m, 2H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.26 (m, 1H), 3.76 (q, *J* = 6.9 Hz, 1H), 3.68 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 149.1, 148.5, 136.3, 135.3, 123.7, 52.3, 42.9, 18.4.

HRMS (ESI+) Calcd. For $C_9H_{12}NO_2^+$ ([M+H]$^+$): 166.0863, found: 166.0869.

Methyl 2-(pyridin-4-yl)propanoate (2u)



^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (s, 2H), 7.23 (s, 2H), 3.72 – 3.68 (m, 1H), 3.68 (s, 3H), 1.52 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.5, 150.0, 149.0, 122.7, 52.2, 44.8, 17.8.

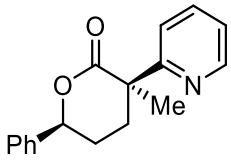
HRMS (ESI+) Calcd. For $C_9H_{12}NO_2^+$ ([M+H]$^+$): 166.0863, found: 166.0869.

3. General procedure for the stereodivergent construction of δ-valerolactones

To a clean and dried Schlenk tube was charged with $Cu(CH_3CN)_4PF_6$ (5 mol%, 3.7 mg) and (*S*,*S*$_p$)-**L5** (5.5 mol%, 6.0 mg) in glovebox, degassed THF (1 mL) was added to the tube under nitrogen atmosphere, and then the mixture was stirred at room temperature for 30 min. Then, α-azaaryl acetate **2** (0.2 mmol, 1.0 equiv), allyl alcohol **1** (0.6 mmol, 3.0 equiv), [Ru]-**1** complex (2 mol%), Cs_2CO_3 (0.3 mmol, 1.5 equiv) and THF (1 mL) were subsequently added to the tube, respectively. The mixture was stirred at room temperature for 36 h. Upon completion, the crude mixture was filtered through a short silica gel plug to remove the metal complex, and the filtrate was concentrated to dryness. The crude product was analyzed by ^{1}H NMR to determine the diastereoselectivity. Then the residue was purified by column chromatography to give the desired product **3** which was then directly analyzed by HPLC to determine the enantiomeric excess.

4. Characterization data for the products

(3*R*,6*S*)-3-methyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3a):

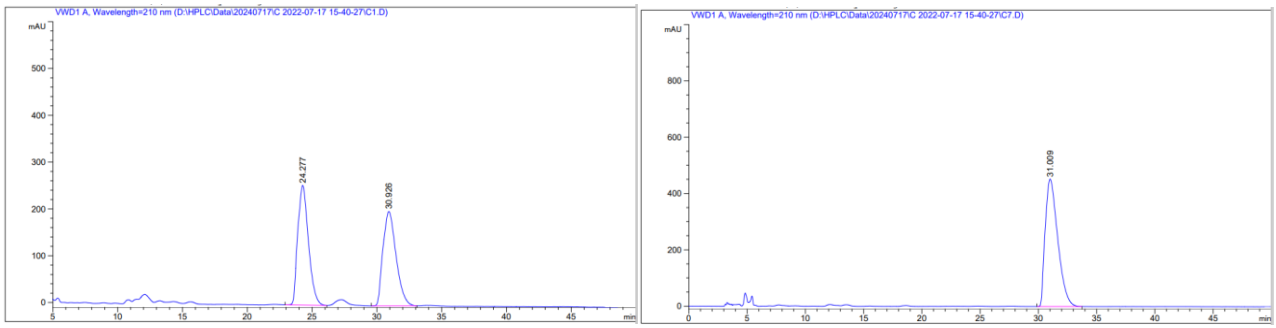


yield (42.7 mg, 80%); colorless oil; $[\alpha]^{25}_D$ = +15.1 (*c* 0.72, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 24.28 and 30.93 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 – 8.59 (m, 1H), 7.47 – 7.41 (m, 1H), 7.35 – 7.27 (m, 5H), 7.21 – 7.16 (m, 1H), 5.45 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.74 – 2.65 (m, 1H), 2.19 – 2.04 (m, 1H), 2.02 – 1.93 (m, 1H), 1.88 – 1.75 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.4, 162.3, 149.1, 140.2, 136.9, 128.5, 128.2, 125.9, 122.0, 120.8, 84.0, 50.3, 34.3, 28.7, 26.9.

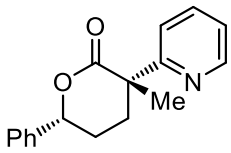
HRMS (ESI+) Calcd. For $C_{17}H_{18}NO_2^+$ ($[M+H]^+$): 268.1332, found: 268.1335



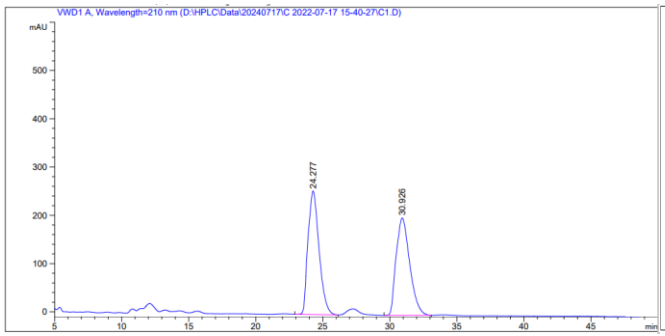
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.277	VB R	0.8287	1.46862e4	255.85551	50.9441
2	30.926	BB	0.9916	1.41419e4	201.55424	49.0559

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.009	BB	1.1219	3.38113e4	452.40396	100.0000

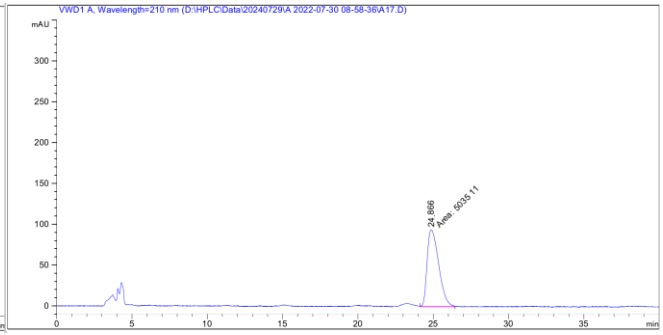
(3*S*,6*R*)-3-methyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3a):



yield (43.4 mg, 81%); colorless oil; $[\alpha]^{25}_D$ = -14.8 (*c* 1.2, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 24.28 and 30.93 min.

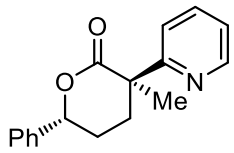


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.277	VB R	0.8287	1.46862e4	255.85551	50.9441
2	30.926	BB	0.9916	1.41419e4	201.55424	49.0559



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.866	MM	0.8896	5035.11182	94.33414	100.0000

(3*R*,6*R*)-3-methyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3a):

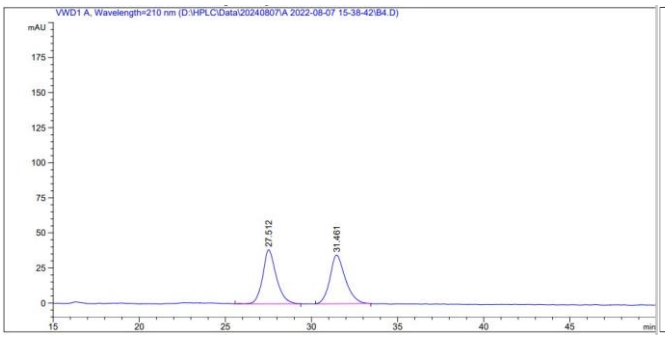


yield (34.7 mg, 65%); colorless oil; $[\alpha]^{25}_{D}$ = +8.48 (*c* 0.43, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 27.51 and 31.46 min.

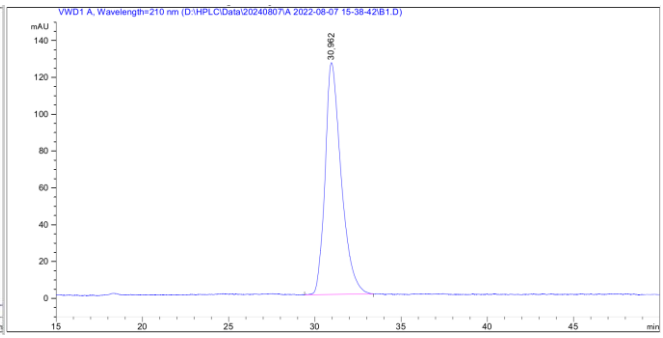
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 – 8.61 (m, 1H), 7.71 – 7.69 (m, 1H), 7.44 – 7.42 (m, 1H), 7.36 – 7.28 (m, 5H), 7.24 – 7.21 (m, 1H), 5.14 (dd, *J* = 9.9, 4.4 Hz, 1H), 2.98 – 2.91 (m, 1H), 2.26 – 2.18 (m, 1H), 2.08 – 1.91 (m, 2H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.3, 162.0, 149.4, 140.0, 137.2, 128.5, 128.1, 125.6, 122.3, 120.5, 80.0, 50.2, 31.0, 28.9, 27.0.

HRMS (ESI+) Calcd. For $C_{17}H_{18}NO_2^+$ ([M+H]$^+$): 268.1332, found: 268.1335.

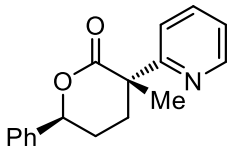


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.512	VV R	0.7869	2121.08032	38.54832	49.4255
2	31.461	BB	0.8670	2170.38965	34.73617	50.5745

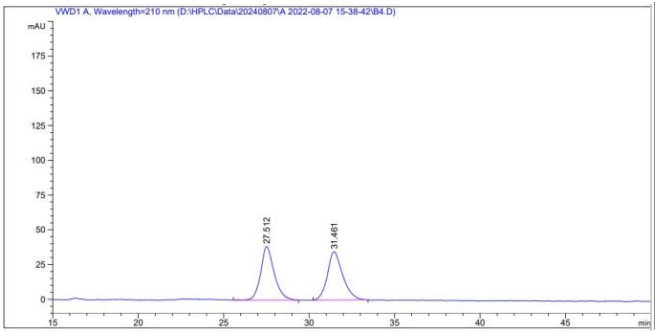


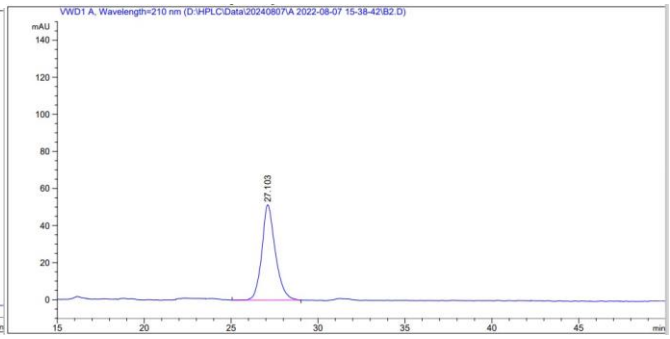
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.962	VB R	0.9445	8162.57275	125.88017	100.0000

(3*S*,6*S*)-3-methyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3a):



yield (36.3 mg, 68%); colorless oil; $[\alpha]^{25}_D$ = -8.22 (*c* 0.45, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 27.51 and 31.46 min.

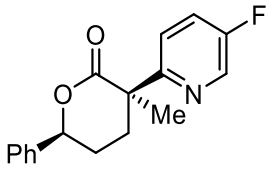




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.512	VV R	0.7869	2121.08032	38.54832	49.4255
2	31.461	BB	0.8670	2170.38965	34.73617	50.5745

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.103	VV R	0.7865	2783.78467	51.42813	100.0000

(3*R*,6*S*)-3-(5-fluoropyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3b):



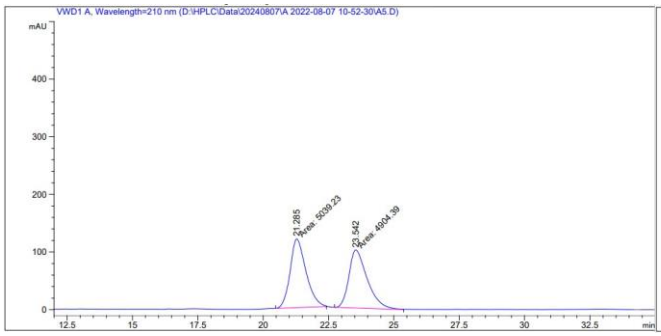
yield (41.2 mg, 72%); colorless oil; $[\alpha]^{25}_D$ = +10.6 (*c* 0.18, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 21.29 and 23.54 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.40 (m, 1H), 7.49 – 7.44 (m, 1H), 7.44 – 7.39 (m, 1H), 7.36 – 7.28 (m, 5H), 5.46 (dd, *J* = 11.6, 3.9 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.15 – 2.05 (m, 1H), 2.04 – 1.95 (m, 1H), 1.88 – 1.77 (m, 1H), 1.71 (s, 3H).

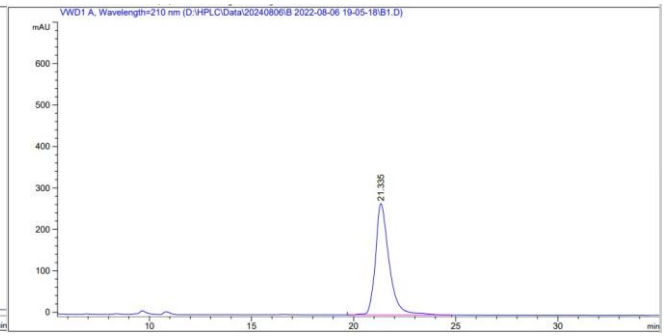
^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 158.3 (d, *J* = 255.9 Hz), 158.0 (d, *J* = 3.7 Hz), 140.0, 137.3, 137.1, 128.5 (d, *J* = 3.2 Hz), 125.8, 123.6 (d, *J* = 17.6 Hz), 121.9 (d, *J* = 6.8 Hz), 84.0, 49.7, 34.2, 28.6, 27.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -129.4.

HRMS (ESI+) Calcd. For $C_{17}H_{17}FNO_2^+$ ($[M+H]^+$): 286.1238, found: 286.1237.

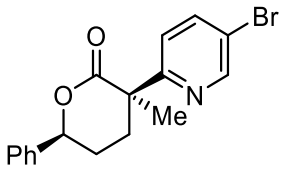


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.285	MM	0.7054	5039.23389	119.05870	50.6780
2	23.542	MM	0.8116	4904.39063	100.71267	49.3220



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.335	VB R	0.6792	1.25221e4	268.95331	100.0000

(3*R*,6*S*)-3-(5-bromopyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3c):

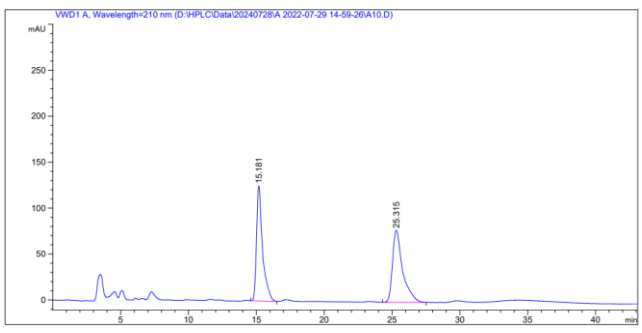


yield (45.0 mg, 65%); brown solid; m.p. 94-96 ºC; $[\alpha]^{25}_{D}$ = +8.7 (*c* 0.77, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IC, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 15.18 and 25.32 min.

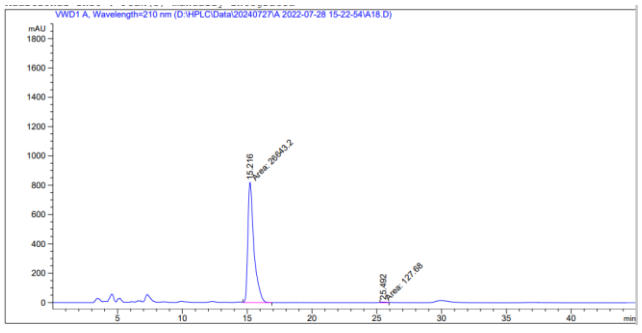
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.70 – 8.60 (m, 1H), δ 7.85 – 7.79 (m, 1H), 7.39 – 7.28 (m, 6H), 5.45 (dd, *J* = 11.5, 3.9 Hz, 1H), 2.71 – 2.64 (m, 1H), 2.14 – 2.05 (m, 1H), 2.04 – 1.95 (m, 1H), 1.89 – 1.75 (m, 1H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.0, 160.8, 150.2, 140.0, 139.5, 128.5, 128.3, 125.8, 122.3, 119.2, 84.0, 49.9, 34.1, 28.6, 27.0.

HRMS (ESI+) Calcd. For $C_{17}H_{17}{}^{79}BrNO_2^+$ ([M+H]$^+$), $C_{17}H_{17}{}^{81}BrNO_2^+$ ([M+H]$^+$): 346.0437, 348.0417; found: 346.0433, 348.0413.

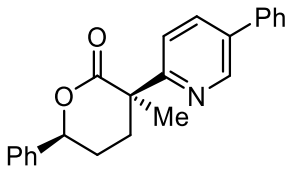


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.181	BV	0.4541	3851.52222	125.13941	48.5791
2	25.315	VB R	0.7563	4076.83081	78.44829	51.4209



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.216	FM	0.5415	2.66432e4	819.99866	99.5231
2	25.492	MF	0.5325	127.67966	3.99653	0.4769

(3*R*,6*S*)-3-methyl-6-phenyl-3-(5-phenylpyridin-2-yl)tetrahydro-2H-pyran-2-one (3d):

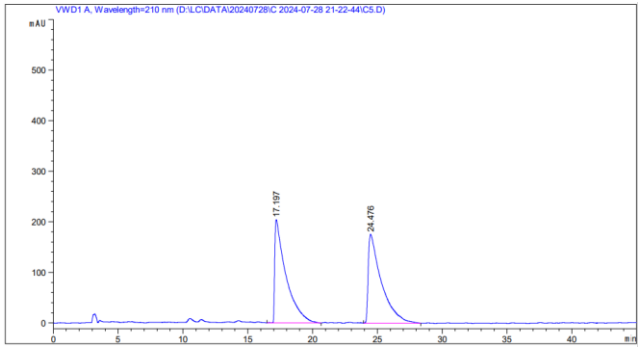


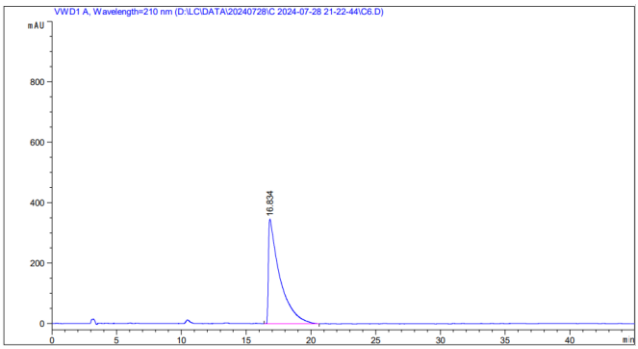
yield (46.8 mg, 68%); white solid; m.p. 140-142 °C; $[\alpha]^{25}_D$ = +23.1 (*c* 0.93, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 17.20 and 24.48 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.84 – 8.80 (m, 1H), δ 7.91 – 7.83 (m, 1H), 7.60 – 7.56 (m, 2H), 7.52 – 7.45 (m, 3H), 7.43 – 7.38 (m, 1H), 7.35 – 7.28 (m, 5H), 5.48 (dd, *J* = 11.5, 4.1 Hz, 1H), 2.77 – 2.72 (m, 1H), 2.18 – 2.11 (m, 1H), 2.04 – 1.97 (m, 1H), 1.94 – 1.84 (m, 1H), 1.77 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 161.1, 147.5, 140.2, 137.4, 135.3, 135.0, 129.1, 128.5, 128.3, 128.2, 127.1, 125.9, 120.8, 84.1, 50.1, 34.4, 28.8, 27.0.

HRMS (ESI+) Calcd. For $C_{23}H_{22}NO_2^+$ ([M+H]$^+$): 344.1645, found: 344.1645.

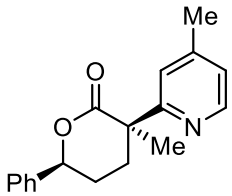




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.197	VB R	0.7848	1.22574e4	204.17654	49.8353
2	24.476	BB	0.9336	1.23384e4	175.53810	50.1647

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.834	BB	0.7791	2.11213e4	346.02222	100.0000

(3*R*,6*S*)-3-methyl-3-(4-methylpyridin-2-yl)-6-phenyltetrahydro-2H-pyran-2-one (3e):

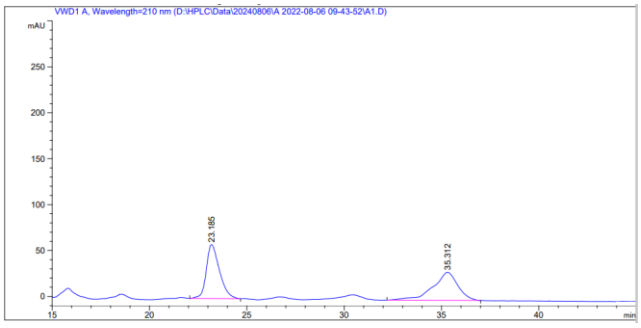


yield (35.0 mg, 62%); colorless oil; $[\alpha]^{25}_D$ = +11.9 (*c* 0.63, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 23.19 and 35.31 min.

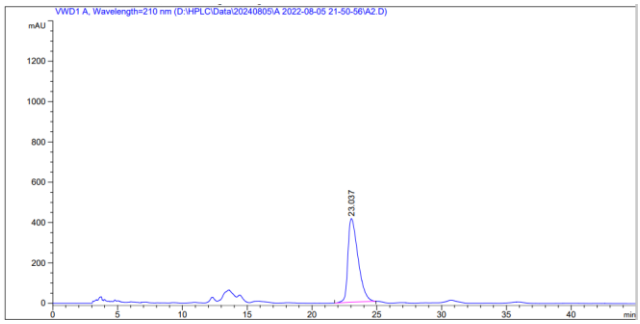
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.53 – 8.34 (m, 1H), 7.35 – 7.28 (m, 5H), 7.26 – 7.23 (m, 1H), 7.04 – 6.94 (m, 1H), 5.44 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.78 – 2.62 (m, 1H), 2.36 (s, 3H), 2.14 – 2.04 (m, 1H), 2.00 – 1.91 (m, 1H), 1.87 – 1.75 (m, 1H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.6, 161.9, 148.9, 148.1, 140.2, 128.5, 128.2, 125.9, 123.1, 121.7, 84.1, 50.1, 34.2, 28.7, 26.9, 21.2.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_2^+$ ([M+H]$^+$): 282.1489, found: 282.1489.

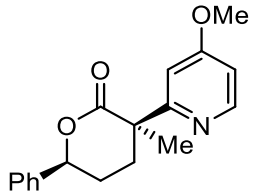


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.185	BB	0.6998	2752.68311	58.62447	50.6462
2	35.312	VB R	1.0541	2682.44043	30.44031	49.3538



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.037	BB	0.8086	2.24645e4	414.95367	100.0000

(3*R*,6*S*)-3-(4-methoxypyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3f):

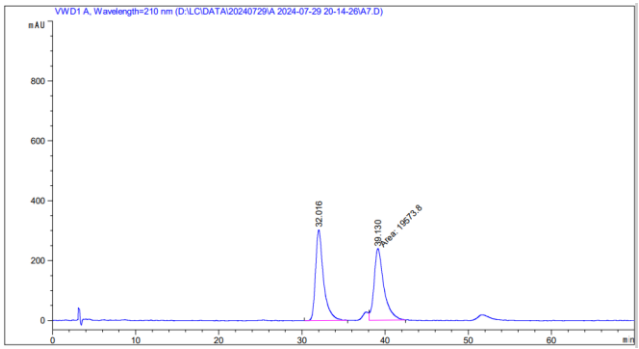


yield (38.1 mg, 64%); brown oil; $[\alpha]^{25}_D$ = +2.6 (*c* 0.58, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 32.12 and 39.13 min.

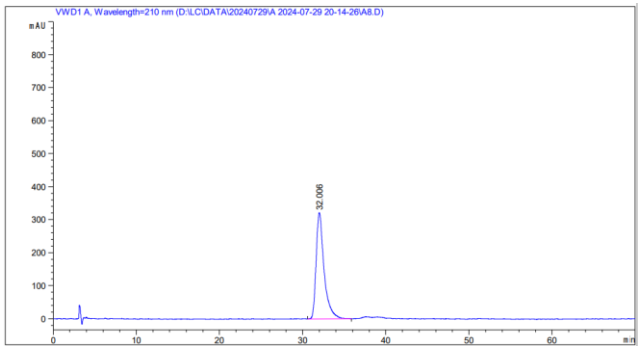
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.45 – 8.38 (m, 1H), 7.34 – 7.27 (m, 5H), 6.97 – 6.94 (m, 1H), 6.72 – 6.70 (m, 1H), 5.44 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.85 (s, 3H), 2.74 – 2.69 (m, 1H), 2.11 – 2.04 (m, 1H), 2.00 – 1.95 (m, 1H), 1.88 – 1.79 (m, 1H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 166.4, 163.8, 150.3, 140.2, 128.5, 128.2, 125.9, 108.2, 107.2, 84.1, 55.2, 50.3, 34.2, 28.7, 26.9.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_3^+$ ([M+H]$^+$): 298.1438, found: 298.1439.

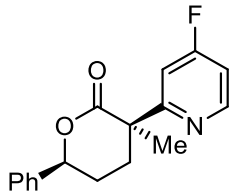


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.016	VV R	0.9720	2.01836e4	303.08310	50.7669
2	39.130	FM	1.3644	1.95738e4	239.10533	49.2331



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.006	BV R	0.9683	2.14606e4	321.98660	100.0000

(3*R*,6*S*)-3-(5-fluoropyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3g):



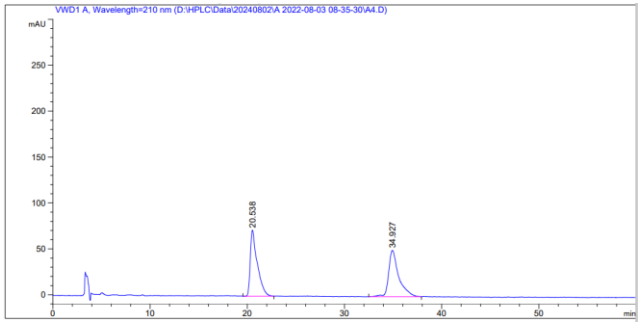
yield (37.7 mg, 66%); colorless oil; $[\alpha]^{25}_{D}$ = +38.4 (*c* 0.28, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IC, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 20.34 and 34.93 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.40 (m, 1H), 7.49 – 7.44 (m, 1H), 7.44 – 7.39 (m, 1H), 7.36 – 7.28 (m, 5H), 5.46 (dd, *J* = 11.6, 3.9 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.15 – 2.05 (m, 1H), 2.04 – 1.95 (m, 1H), 1.88 – 1.77 (m, 1H), 1.71 (s, 3H).

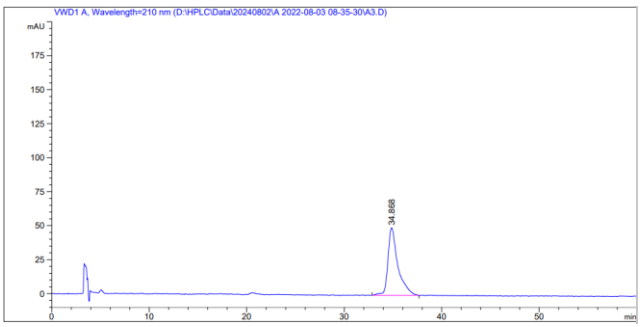
^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.9, 169.3 (d, *J* = 262.6 Hz), 165.8 (d, *J* = 6.4 Hz), 151.4 (d, *J* = 7.2 Hz), 140.0, 128.6, 128.3, 125.8, 110.2 (d, *J* = 15.9 Hz), 109.0 (d, *J* = 19.2 Hz), 84.0, 50.2, 34.17, 28.7, 26.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.2.

HRMS (ESI+) Calcd. For $C_{17}H_{17}FNO_2^+$ ($[M+H]^+$): 286.1238, found: 286.1237.

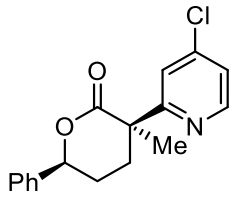


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.538	VV R	0.7013	3627.88428	72.07248	49.8950
2	34.927	VV R	1.0000	3643.14868	50.47736	50.1050



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.868	VB R	1.0230	3539.75488	49.69577	100.0000

(3*R*,6*S*)-3-(4-chloropyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3h):

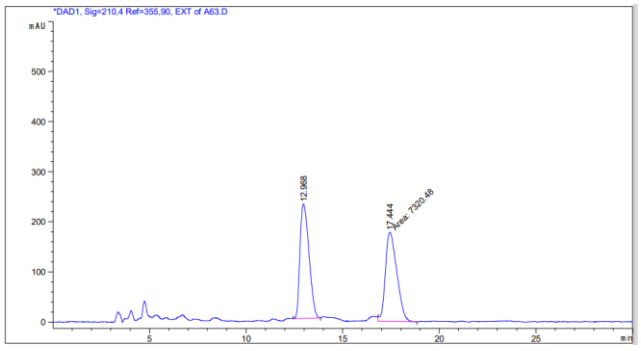


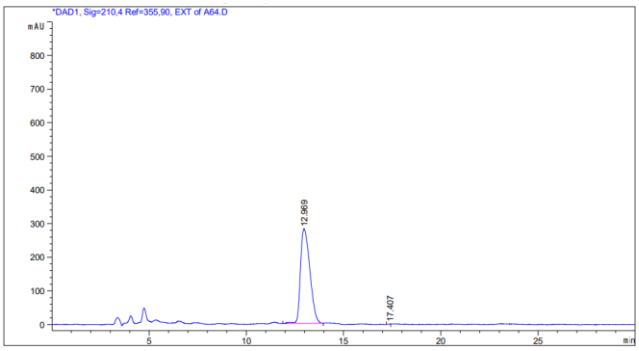
yield (4.22 mg, 70%); yellow solid; m.p. 92-94 ºC; $[\alpha]^{25}_{D}$ = +1.6 (*c* 0.81, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak ID, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 12.97 and 17.44 min.

^{1}H NMR δ 8.51 – 8.48 (m, 1H), 7.49 – 7.45 (m, 1H), 7.38 – 7.28 (m, 5H), 7.22 (dd, *J* = 5.3, 1.9 Hz, 1H), 5.46 (dd, *J* = 11.5, 4.0 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.16 – 2.06 (m, 1H), 2.04 – 1.95 (m, 1H), 1.91 – 1.80 (m, 1H), 1.72 (s, 3H).

^{13}C NMR δ 173.8, 164.1, 149.9, 145.0, 140.0, 128.5, 128.3, 125.8, 122.6, 121.4, 84.0, 50.1, 34.2, 28.6, 26.9.

HRMS (ESI+) Calcd. For $C_{17}H_{17}{}^{35}ClNO_2^+$ ([M+H]$^+$), $C_{17}H_{17}{}^{37}ClNO_2^+$ ([M+H]$^+$): 302.0942, 304.0913, found: 302.0945, 304.0910.

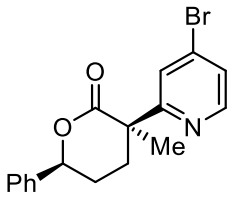




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.968	BB	0.4895	7375.33789	227.93436	50.1866
2	17.444	FM	0.6851	7320.47949	178.08029	49.8134

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.969	VV R	0.4819	9496.51660	282.28363	99.9283
2	17.407	BV	0.0905	6.81710	1.01352	0.0717

(3*R*,6*S*)-3-(4-bromopyridin-2-yl)-3-methyl-6-phenyltetrahydro-2H-pyran-2-one (3i)

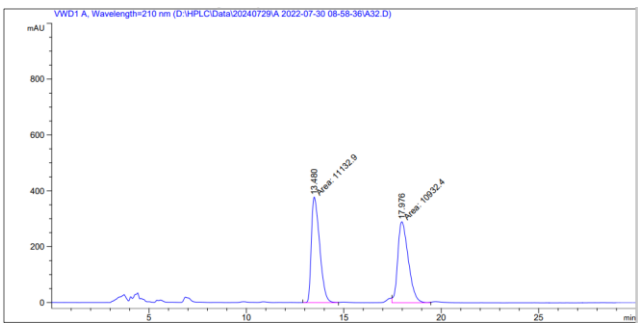


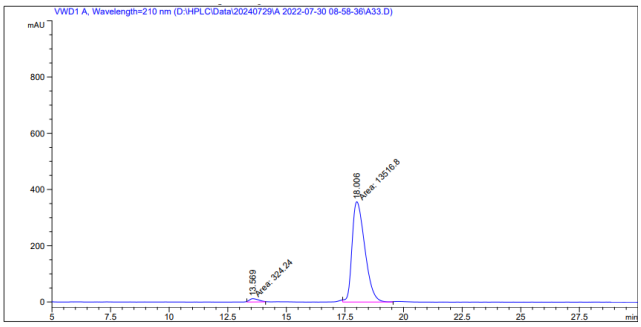
yield (49.1 mg, 71%); yellow solid; m.p. 96-98 °C; $[a]^{25}_{D}$ = +1.2 (*c* 0.69, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 95% ee (Chiralpak IE, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 13.48 and 17.98 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 – 8.37 (m, 1H), 7.66 – 7.61 (m, 1H), 7.41 – 7.29 (m, 6H), 5.46 (dd, *J* = 11.5, 4.0 Hz, 1H), 2.73 – 2.60 (m, 1H), 2.19 – 2.03 (m, 1H), 2.04 – 1.95 (m, 1H), 1.93 – 1.78 (m, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.8, 164.0, 149.7, 140.0, 133.7, 128.5, 128.3, 125.8, 125.6, 124.3, 84.0, 50.1, 34.2, 28.6, 26.9.

HRMS (ESI+) Calcd. For $C_{17}H_{17}{}^{79}BrNO_2^+$ ([M+H]$^+$), $C_{17}H_{17}{}^{81}BrNO_2^+$ ([M+H]$^+$): 346.0437, 348.0417; found: 346.0433, 348.0413.

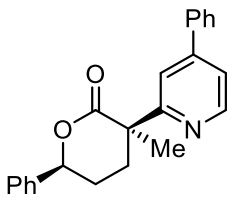




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.480	MF	0.4911	1.11329e4	377.84366	50.4544
2	17.976	FM	0.6280	1.09324e4	290.14401	49.5456

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.569	FM	0.4609	324.23984	11.72602	2.3426
2	18.006	FM	0.6317	1.35168e4	356.63818	97.6574

(3*R*,6*S*)-3-methyl-6-phenyl-3-(4-phenylpyridin-2-yl)tetrahydro-2H-pyran-2-one (3j):

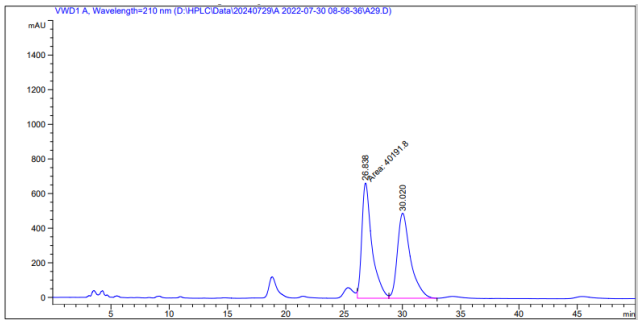


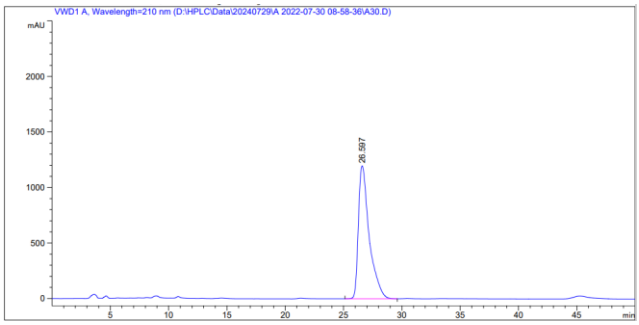
yield (50.2 mg, 73%); white solid; m.p. 106-108 ºC;l; $[a]^{25}_D$ = +21.7 (*c* 0.65, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IC, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 26.84 and 30.02 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.65 – 8.59 (m, 1H), 7.67 – 7.58 (m, 3H), 7.55 – 7.40 (m, 3H), 7.42 – 7.40 (m, 1H), 7.36 – 7.26 (m, 5H), 5.48 (dd, *J* = 11.5, 4.1 Hz, 1H), 2.78 – 2.73 (m, 1H), 2.18 – 2.09 (m, 1H), 2.04 – 1.97 (m, 1H), 1.94 – 1.86 (m, 1H), 1.78 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.8, 149.5, 149.5, 140.3, 138.2, 129.2, 129.1, 128.5, 128.2, 127.2, 125.9, 120.2, 118.9, 84.1, 50.4, 34.4, 28.7, 27.0.

HRMS (ESI+) Calcd. For $C_{23}H_{22}NO_2^+$ ([M+H]$^+$): 344.1645, found: 344.1645

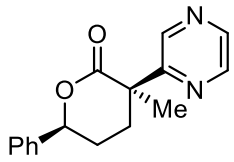




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.838	FM	1.0063	4.01918e4	665.67029	51.2856
2	30.020	VB	1.1513	3.81768e4	490.88916	48.7144

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.597	BV R	0.9450	7.70596e4	1197.09692	100.0000

(3*R*,6*S*)-3-methyl-6-phenyl-3-(pyrazin-2-yl)tetrahydro-2H-pyran-2-one (3k):

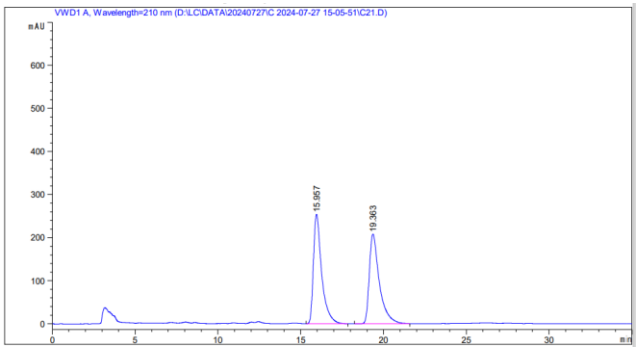


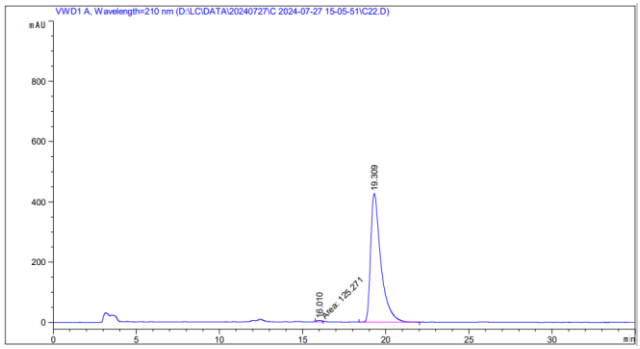
yield (30.6 mg, 57%); yellow solid; m.p. 156-158 ºC; $[\alpha]^{25}_D$ = +21.3 (*c* 0.40, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 98% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 15.96 and 19.36 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 – 8.75 (m, 1H), 8.58 – 8.49 (m, 2H), 7.39 – 7.28 (m, 5H), 5.49 (dd, *J* = 11.3, 3.9 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.20 – 2.10 (m, 1H), 2.10 – 1.99 (m, 1H), 1.87 – 1.77 (m, 1H),1.79 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.3, 158.1, 143.5, 143.2, 142.9, 139.8, 128.6, 128.4, 125.7, 83.9, 48.7, 34.2, 28.6, 26.6.

HRMS (ESI+) Calcd. For $C_{16}H_{17}N_2O_2^+$ ([M+H]$^+$): 269.1285, found: 269.1290.

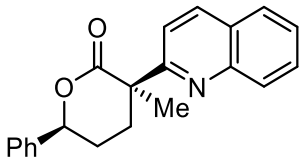




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.957	BB	0.5130	8833.43359	254.28508	50.1834
2	19.363	VB R	0.6212	8768.85352	208.10553	49.8166

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.010	MF	0.3798	125.27087	5.49687	0.6833
2	19.309	VV R	0.6322	1.82078e4	426.37717	99.3167

(3*R*,6*S*)-3-methyl-6-phenyl-3-(quinolin-2-yl)tetrahydro-2H-pyran-2-one (3l):

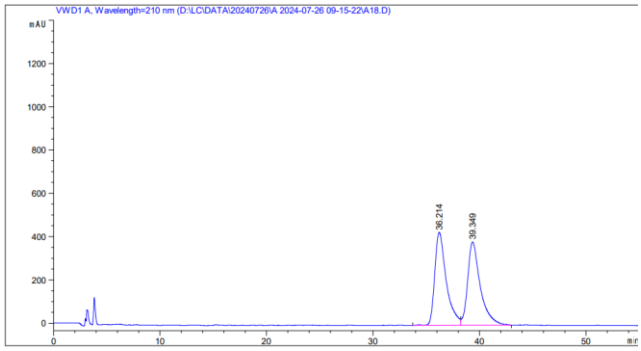


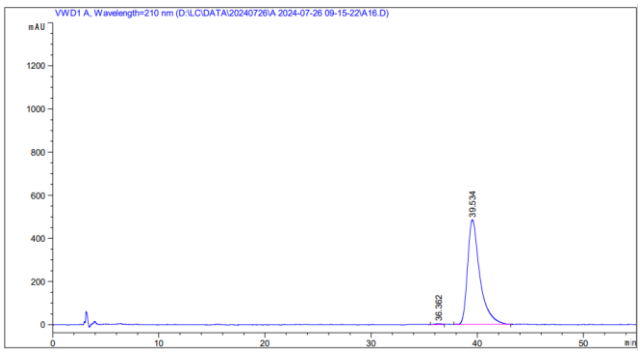
yield (42.6 mg, 67%); white solid; m.p. 126-128 °C; $[\alpha]^{25}_{D}$ = +16.8 (*c* 0.76, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 3/97, flow rate 1.0 mL/min, λ = 210 nm); t_r = 36.21 and 39.35 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.76 – 7.65 (m, 1H), 7.62 – 7.47 (m, 2H), 7.42 – 7.35 (m, 2H), 7.35 – 7.22 (m, 3H), 5.49 (dd, *J* = 11.1, 4.7 Hz, 1H), 2.93 – 2.66 (m, 1H), 2.18 (td, *J* = 13.1, 3.7 Hz, 1H), 2.04 – 1.86 (m, 2H), 1.83 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 162.1, 147.2, 140.4, 137.1, 129.6, 129.5, 128.4, 128.1, 127.4, 126.9, 126.5, 126.0, 118.2, 84.0, 50.8, 34.3, 28.8, 26.7.

HRMS (ESI+) Calcd. For $C_{21}H_{20}NO_2^+$ ([M+H]$^+$): 318.1489, found: 318.1491.

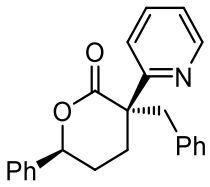




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.214	VV R	1.1110	3.22512e4	428.34756	50.5068
2	39.349	VB	1.2000	3.16040e4	384.17508	49.4932

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.362	BV	0.5186	193.76003	4.45945	0.4951
2	39.534	VV R	1.1815	3.89438e4	485.69083	99.5049

(3*S*,6*S*)-3-benzyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3m):

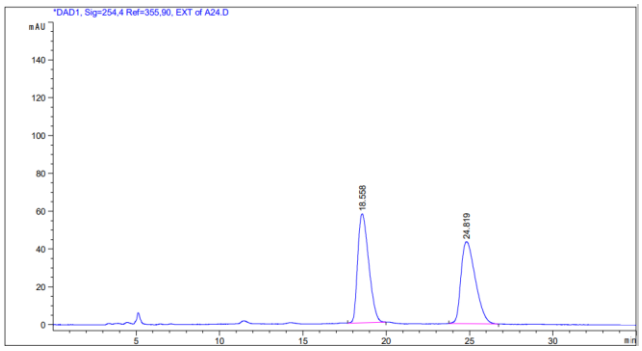


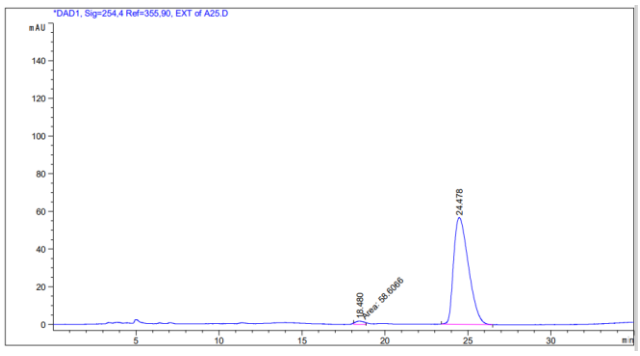
yield (56.4 mg, 82%); brown oil; $[\alpha]^{25}_{D}$ = +39.2 (*c* 0.63, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 98% ee (Chiralpak ID, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 18.56 and 24.82 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 – 8.62 (m, 1H), 7.75 – 7.71 (m, 1H), 7.62 – 7.60 (m, 1H), 7.30 – 7.24 (m, 9H), 7.20 – 7.15 (m, 2H), 5.10 (dd, *J* = 12.0, 3.8 Hz, 1H), 3.73 (d, *J* = 13.4 Hz, 1H), 3.21 (d, *J* = 13.4 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.16 – 2.08 (m, 1H), 1.93 – 1.86 (m, 1H), 1.80 – 1.69 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.9, 149.3, 140.0, 137.1, 136.9, 131.0, 128.5, 128.3, 128.2, 126.8, 125.7, 122.3, 121.9, 83.7, 55.9, 45.4, 29.4, 28.5.

HRMS (ESI+) Calcd. For $C_{23}H_{22}NO_2^+$ ([M+H]$^+$): 344.1645, found: 344.1643.

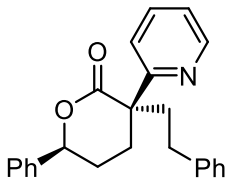




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.558	BB	0.6955	2644.19214	57.60758	50.5347
2	24.819	BB	0.8068	2588.23730	43.33372	49.4653

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.480	MM	0.5853	58.60657	1.66871	1.6410
2	24.478	BB	0.8732	3512.70020	56.66962	98.3590

(3*R*,6*S*)-3-phenethyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3n):

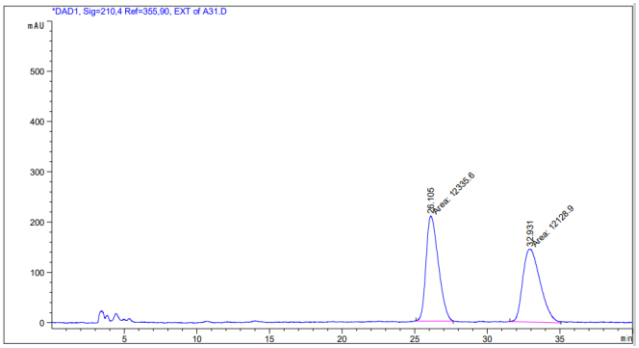


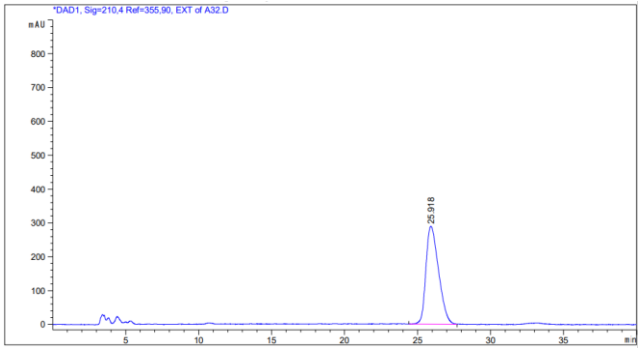
yield (53.7 mg, 75%); white solid; m.p. 150-152 ºC; $[\alpha]^{25}_{D}$ = +33.2 (*c* 0.65, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak ID, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 26.12 and 32.93 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.54 (m, 1H), 7.75 – 7.64 (m, 1H), 7.58 – 7.50 (m, 1H), 7.36 – 7.26 (m, 7H), 7.22 – 7.14 (m, 4H), 5.45 (dd, *J* = 12.0, 3.8 Hz, 1H), 2.88 – 2.72 (m, 2H), 2.70 – 2.59 (m, 1H), 2.53 – 2.41 (m, 1H), 2.38 – 2.25 (m, 2H), 2.08 – 2.01 (m, 1H), 1.91 – 1.79 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.4, 160.9, 149.1, 141.9, 140.1, 136.9, 128.53, 128.5, 128.4, 128.3, 125.9, 125.8, 122.2, 121.7, 83.92, 54.3, 42.5, 31.5, 30.6, 28.8.

HRMS (ESI+) Calcd. For $C_{24}H_{24}NO_2^+$ ([M+H]$^+$): 358.1802, found: 358.1803.

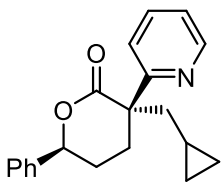




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.105	MM	0.9844	1.23356e4	208.84250	50.4225
2	32.931	MM	1.3885	1.21289e4	145.58278	49.5775

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.918	VV R	0.7167	1.73747e4	289.28229	100.0000

(3*S*,6*S*)-3-(cyclopropylmethyl)-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3o):



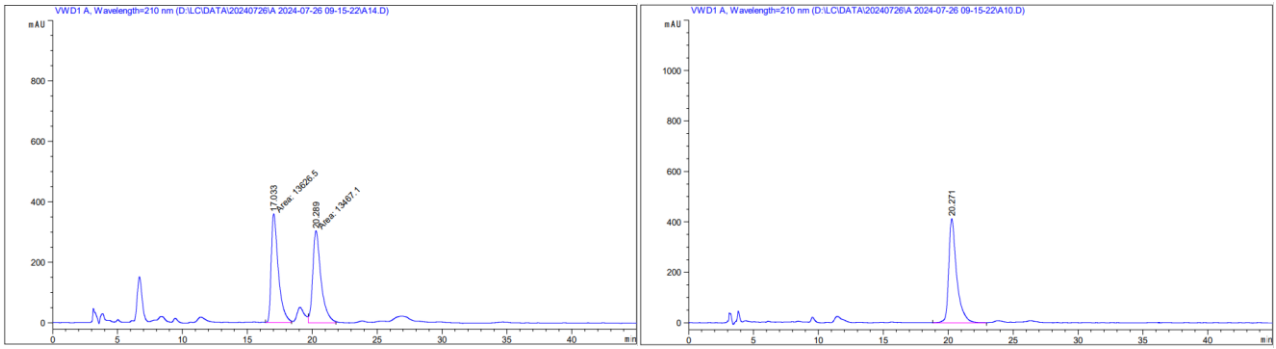
yield (44.3 mg, 72%); yellow oil; $[\alpha]^{25}_{D}$ = +56.9 (*c* 0.73, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 17.03 and 20.29 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 – 8.58 (m, 1H), 7.70 – 7.65 (m, 1H), 7.53 – 7.48 (m, 1H),

7.33 – 7.27 (m, 5H), 7.20 – 7.16 (m, 1H), 5.46 (dd, *J* = 12.1, 3.8 Hz, 1H), 2.85 – 2.80 (m, 1H), 2.57 – 2.49 (m, 1H), 2.31 (dd, *J* = 14.0, 5.6 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.88 – 1.77 (m, 2H), 0.81 – 0.77 (m, 1H), 0.53 – 0.41 (m, 2H), 0.16 – 0.05 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.8, 161.1, 149.0, 140.2, 136.8, 128.4, 128.2, 125.7, 122.0, 121.6, 83.9, 55.1, 45.0, 29.9, 28.8, 7.1, 5.7, 4.0.

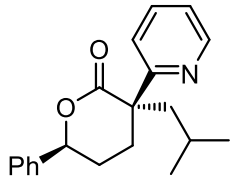
HRMS (ESI+) Calcd. For $C_{22}H_{22}NO_2^+$ ([M+H]$^+$): 308.1645, found: 308.1646.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.033	MF	0.6331	1.36265e4	358.73715	50.2942
2	20.289	MM	0.7382	1.34671e4	304.04593	49.7058

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.271	BV R	0.6259	1.75468e4	412.45255	100.0000

(3*S*,6*S*)-3-isobutyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3p):

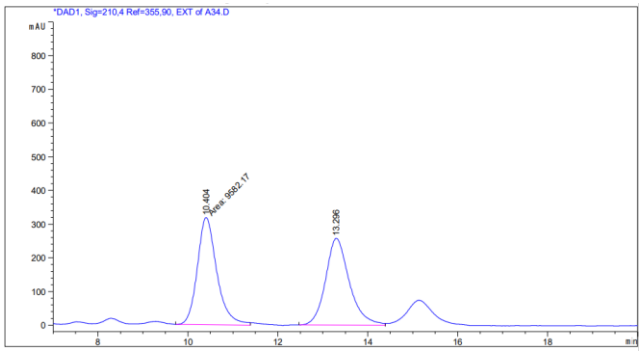


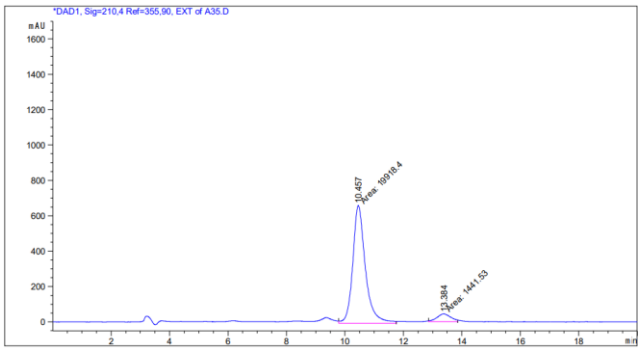
yield (40.3 mg, 65%); colorless oil; $[\alpha]^{25}_D$ = +21.9 (*c* 0.52, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 87% ee (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 10.40 and 13.30 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.51 (m, 1H), 7.74 – 7.62 (m, 1H), 7.60 – 7.52 (m, 1H), 7.36 – 7.26 (m, 4H), 7.25 – 7.22 (m, 1H), 7.20 – 7.15 (m, 1H), 5.43 (dd, *J* = 12.1, 3.7 Hz, 1H), 2.91 – 2.78 (m, 1H), 2.32 – 2.16 (m, 2H), 2.05 – 1.96 (m, 2H), 1.88 – 1.78 (m, 2H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.9, 161.3, 149.0, 140.2, 136.8, 128.5, 128.18, 125.8, 122.0, 122.0, 83.8, 54.1, 48.4, 29.4, 28.8, 25.4, 24.6, 23.5.

HRMS (ESI+) Calcd. For $C_{20}H_{24}NO_2^+$ ([M+H]$^+$): 310.1802, found: 310.1802.

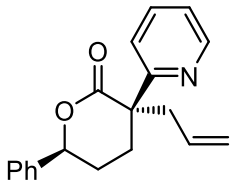




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.404	MF	0.5022	9582.17285	318.00357	50.3806
2	13.296	BV	0.5121	9437.40137	257.21472	49.6194

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.457	MM	0.4994	1.99184e4	664.75342	93.2513
2	13.384	MF	0.5494	1441.52759	43.73194	6.7487

(3*S*,6*S*)-3-allyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3q):

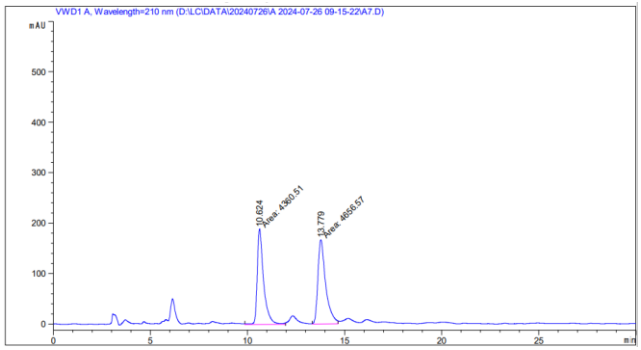


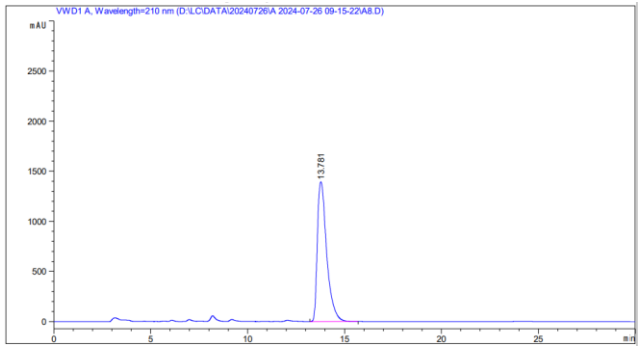
yield (48.2 mg, 82%); yellow oil; $[\alpha]^{25}_{D}$ = +45.9 (*c* 0.85, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 10.62 and 13.78 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.61 – 8.60 (m, 1H), 7.72 – 7.67 (m, 1H), 7.51 – 7.49 (m, 1H), 7.34 – 7.25 (m, 5H), 7.21 – 7.18 (m, 1H), 5.89 – 5.79 (m, 1H), 5.39 (dd, *J* = 12.0, 3.8 Hz, 1H), 5.21 – 5.15 (m, 2H), 3.04 – 2.99 (m, 1H), 2.74 – 2.63 (m, 1H), 2.32 – 2.25 (m, 1H), 2.01 – 1.95 (m, 1H), 1.87 – 1.77 (m, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.1, 161.0, 149.1, 140.0, 136.9, 133.7, 128.5, 128.2, 125.8, 122.1, 121.5, 119.5, 83.9, 54.0, 44.4, 30.1, 28.5.

HRMS (ESI+) Calcd. For $C_{19}H_{20}NO_2^+$ ([M+H]$^+$): 294.1489, found: 294.1488.

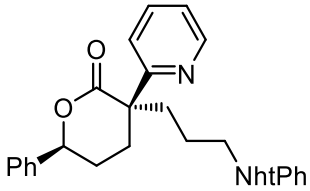




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.624	MM	0.3835	4360.51367	189.51437	48.3583
2	13.779	MM	0.4648	4656.57178	166.97227	51.6417

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.781	BB	0.5117	4.66879e4	1393.49939	100.0000

2-(3-((3*R*,6*S*)-2-oxo-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-3-yl)propyl)-1H-indene-1,3(2H)-dione (3r):

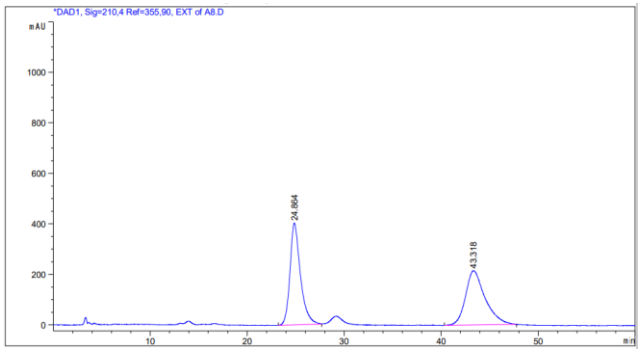


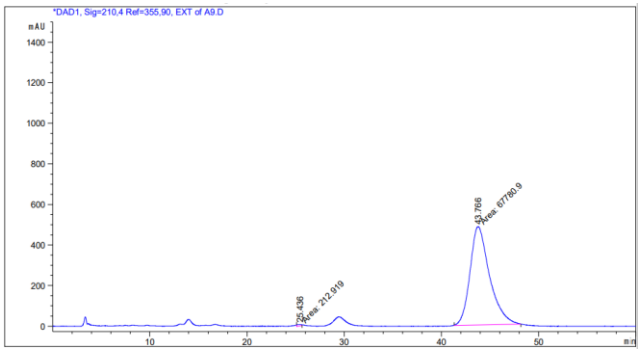
yield (70.4 mg, 80%); yellow oil; $[\alpha]^{25}_D$ = +31.5 (*c* 0.55, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, λ = 210 nm); t_r = 24.86 and 43.32 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.51 (m, 1H), 7.86 – 7.80 (m, 2H), 7.74 – 7.66 (m, 3H), 7.49 – 7.45 (m, 1H), 7.32 – 7.28 (m, 3H), 7.24 – 7.22 (m, 2H), 7.20 – 7.16 (m, 1H), 5.38 (dd, *J* = 12.0, 3.8 Hz, 1H), 3.73 – 3.65 (m, 2H), 2.84 – 2.69 (m, 1H), 2.21 – 1.72 (m, 7H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.3, 168.4, 160.5, 149.1, 140.0, 136.9, 133.9, 132.1, 128.5, 128.2, 125.8, 123.2, 122.2, 121.7, 83.8, 53.8, 38.1, 37.3, 30.4, 28.6, 24.3.

HRMS (ESI+) Calcd. For $C_{27}H_{25}N_2O_4^+$ ([M+H]$^+$): 441.1809, found: 441.1812.

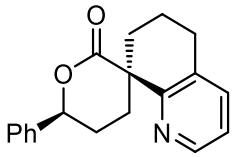




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.864	BB	0.8789	3.01612e4	403.13760	49.9521
2	43.318	VV R	1.6430	3.02190e4	215.13683	50.0479

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.436	MM	0.5713	212.91917	6.21104	0.3131
2	43.766	MM	2.3304	6.77809e4	484.76395	99.6869

(3*R*,6*S*)-6-phenyl-5,6,6',7'-tetrahydro-2H,4H,5'H-spiro[pyran-3,8'-quinolin]-2-one (3s):

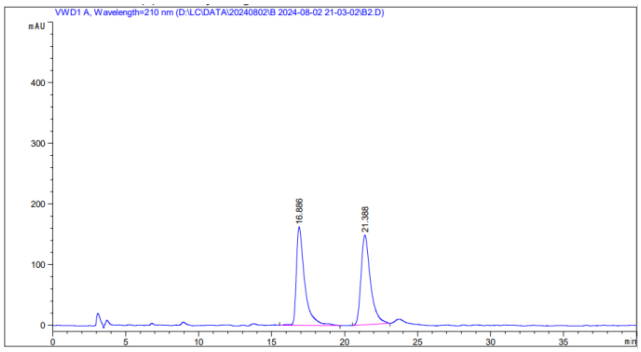


yield (45.8 mg, 78%); white solid; m.p. 166-168 °C; $[\alpha]^{25}_D$ = +28.1 (*c* 0.31, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 16.89 and 21.39 min.

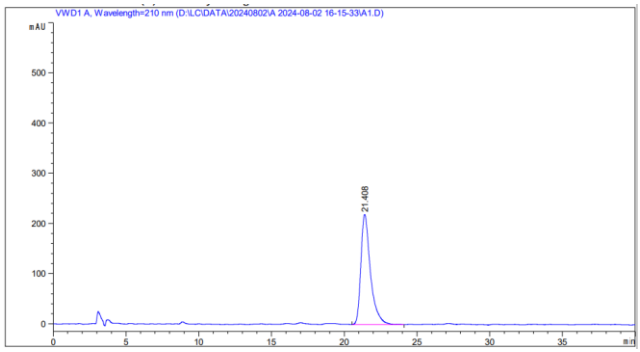
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 – 8.30 (m, 1H), 7.65 – 7.54 (m, 2H), 7.43 – 7.31 (m, 4H), 7.12 – 7.02 (m, 1H), 5.50 (dd, *J* = 9.8, 3.8 Hz, 1H), 2.98 – 2.87 (m, 1H), 2.86 – 2.76 (m, 1H), 2.64 – 2.51 (m, 2H), 2.46 – 2.37 (m, 1H), 2.12 – 1.83 (m, 5H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.0, 159.12, 146.9, 140.6, 137.2, 130.9, 128.4, 128.1, 126.4, 122.0, 82.8, 48.6, 35.5, 34.1, 28.2, 27.9, 17.9.

HRMS (ESI+) Calcd. For $C_{19}H_{20}NO_2^+$ ($[M+H]^+$): 294.1489, found: 294.1492.

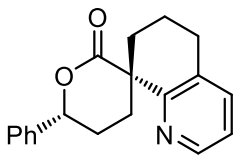


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.886	VV R	0.5777	6457.34521	162.32150	49.3704
2	21.388	BB	0.6584	6622.04834	147.71600	50.6296

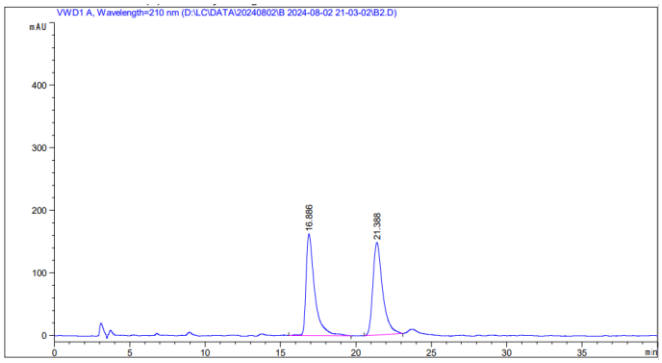


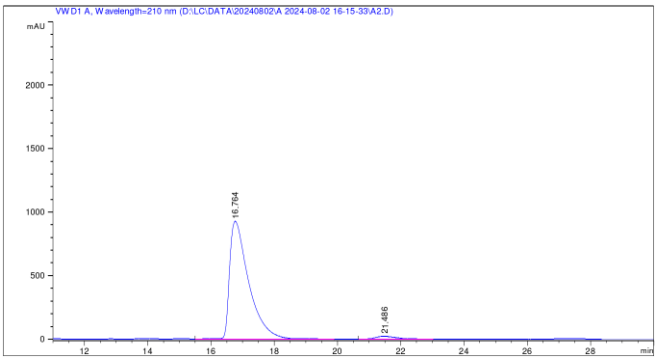
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.408	BV R	0.6820	1.00526e4	219.24490	100.0000

(3*S*,6*R*)-6-phenyl-5,6,6',7'-tetrahydro-2H,4H,5'H-spiro[pyran-3,8'-quinolin]-2-one (3s):



yield (44.6 mg, 76%); white solid; m.p. 165-167 °C; $[\alpha]^{25}_D$ = -29.5 (*c* 0.65, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 16.89 and 21.39 min.

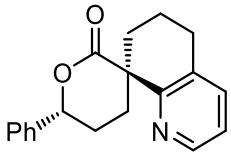




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.886	VV R	0.5777	6457.34521	162.32150	49.3704
2	21.388	BB	0.6584	6622.04834	147.71600	50.6296

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.764	VV R	0.6185	3.89453e4	926.71588	97.3902
2	21.486	BV R	0.6540	1043.62598	23.15398	2.6098

(3*R*,6*R*)-6-phenyl-5,6,6',7'-tetrahydro-2H,4H,5'H-spiro[pyran-3,8'-quinolin]-2-one (3s):

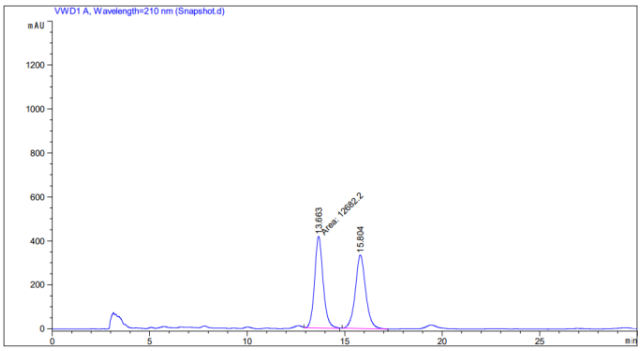


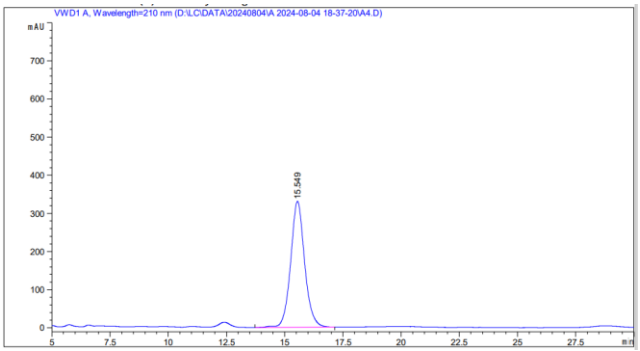
yield (40.6 mg, 69%); white solid; m.p. 166-168 °C; $[\alpha]^{25}_{D}$ = -75.0 (*c* 0.68, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 13.66 and 15.80 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.42 (m, 1H), 7.44 – 7.37 (m, 5H), 7.36 – 7.31 (m, 1H), 7.12 – 7.05 (m, 1H), 5.69 (dd, *J* = 11.0, 3.3 Hz, 1H), 2.97 – 2.86 (m, 1H), 2.81 – 2.63 (m, 2H), 2.51 – 2.42 (m, 1H), 2.22 – 2.01 (m, 5H), 1.85 – 1.75 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.6, 158.8, 147.7, 140.2, 137.2, 132.3, 128.5, 128.2, 125.8, 121.9, 82.5, 49.6, 34.2, 28.6, 28.5, 18.5.

HRMS (ESI+) Calcd. For $C_{19}H_{20}NO_2^+$ ($[M+H]^+$): 294.1489, found: 294.1492.

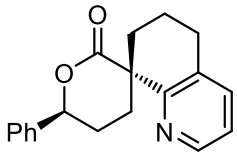




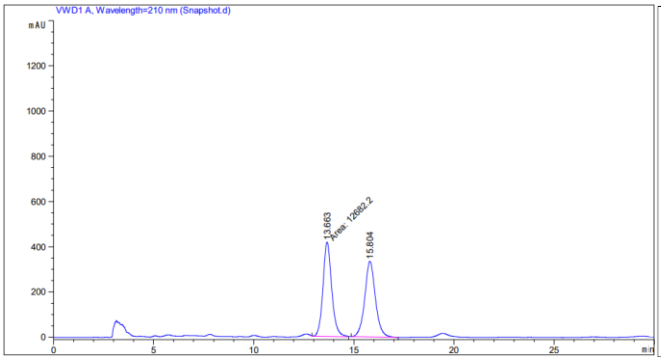
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.663	MM	0.5068	1.26822e4	417.09625	50.6373
2	15.804	BB	0.5519	1.23630e4	334.61301	49.3627

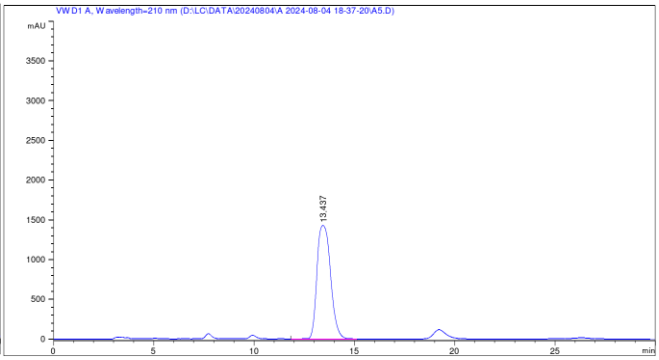
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.549	VV R	0.6264	1.38085e4	330.40942	100.0000

(3*S*,6*S*)-6-phenyl-5,6,6',7'-tetrahydro-2H,4H,5'H-spiro[pyran-3,8'-quinolin]-2-one (3s):



yield (36.5 mg, 62%); white solid; m.p. 166-168 °C; $[\alpha]^{25}_D$ = +76.1 (*c* 0.89, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 13.66 and 15.80 min.

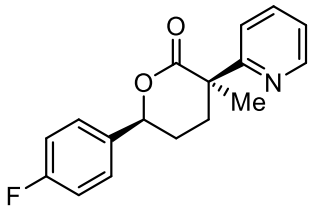




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.663	MM	0.5068	1.26822e4	417.09625	50.6373
2	15.804	BB	0.5519	1.23630e4	334.61301	49.3627

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.437	VV R	0.7451	6.71510e4	1428.17920	100.0000

(3*R*,6*S*)-6-(4-fluorophenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3t):



yield (30.2 mg, 65%); white solid; m.p. 146-148 °C; $[\alpha]^{25}_D$ = +48.2 (*c* 0.21, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 21.69 and 29.39 min.

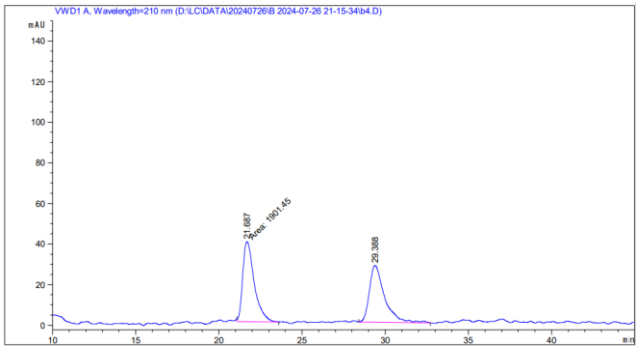
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.47 (m, 1H), 7.74 – 7.64 (m, 1H), 7.45 – 7.39 (m, 1H), 7.34 – 7.27 (m, 2H), 7.22 – 7.18 (m, 1H), 7.07 – 6.96 (m, 2H), 5.43 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.70 –

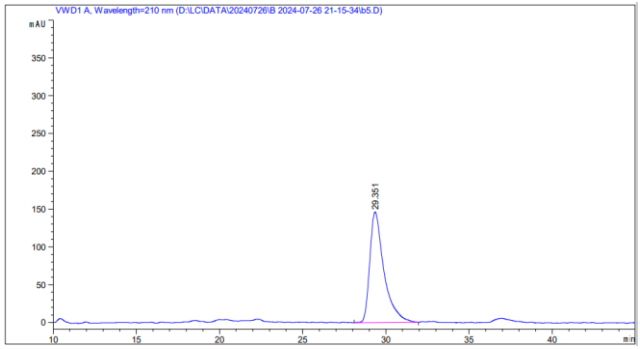
2.65 (m, 1H), 2.15 – 2.07 (m, 1H), 1.98 – 1.91 (m, 1H), 1.85 – 1.78 (m, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 162.5 (d, *J* = 247.2 Hz), 162.3, 149.1, 137.0, 136.1, 127.8 (d, *J* = 8.7 Hz), 122.1, 120.7, 115.4 (d, *J* = 21.9 Hz), 83.4, 50.2, 34.3, 28.7, 26.8.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -113.8.

HRMS (ESI+) Calcd. For $C_{17}H_{17}FNO_2^+$ ([M+H]$^+$): 286.1238, found: 286.1239.

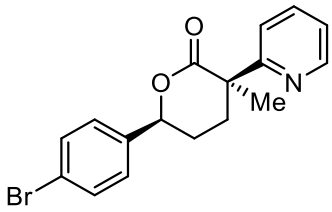




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.687	FM	0.8030	1901.45276	39.46404	51.7371
2	29.388	BV R	0.8501	1773.77051	27.93220	48.2629

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.351	BB	0.8722	8666.15527	146.18283	100.0000

(3*R*,6*S*)-6-(4-bromophenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3u):

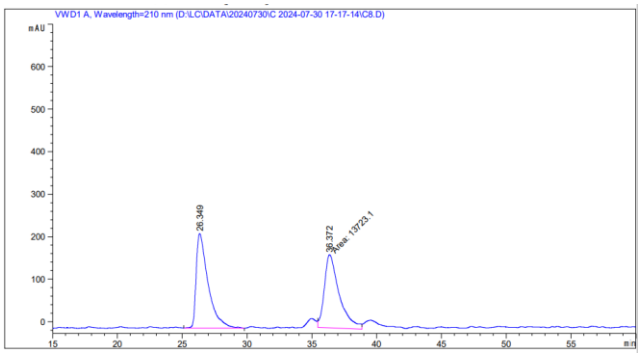


yield (46.9 mg, 68%); brown solid; m.p. 136-138 ºC; $[\alpha]^{25}_D$ = +114.6 (*c* 0.18, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 26.35 and 36.37 min.

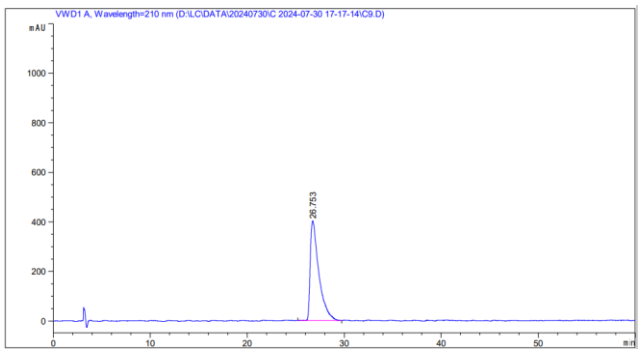
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 – 8.58 (m, 1H), 7.71 – 7.67 (m, 1H), 7.47 – 7.39 (m, 3H), 7.47 – 7.39 (m, 3H), 5.41 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.68 – 2.63 (m, 1H), 2.14 – 2.06 (m, 1H), 1.98 – 1.92 (m, 1H), 1.81 – 1.74 (m, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 162.2, 149.1, 139.3, 137.0, 131.6, 127.5, 122.1, 122.1, 120.6, 83.1, 50.2, 34.3, 28.6, 26.8.

HRMS (ESI+) Calcd. For $C_{17}H_{17}{}^{79}BrNO_2^+$ ([M+H]$^+$), $C_{17}H_{17}{}^{81}BrNO_2^+$ ([M+H]$^+$): 346.0437, 348.0417; found: 346.0433, 348.0413.

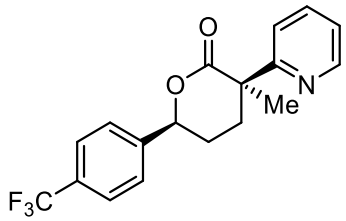


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.349	BV R	0.9137	1.41930e4	221.89450	50.8416
2	36.372	MM	1.3291	1.37231e4	172.08928	49.1584



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.753	VB R	0.8832	2.49378e4	402.38419	100.0000

(3*R*,6*S*)-3-methyl-3-(pyridin-2-yl)-6-(4-(trifluoromethyl)phenyl)tetrahydro-2H-pyran-2-one (3v):



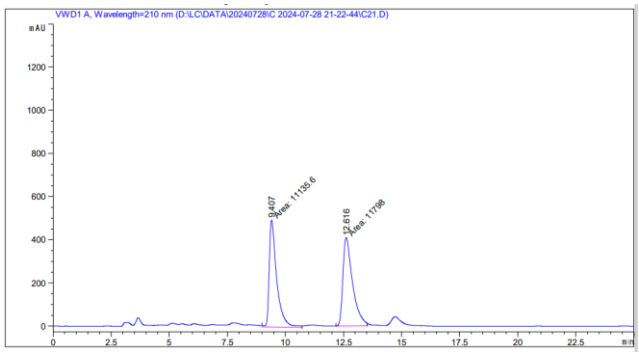
yield (36.9 mg, 55%); yellow oil; $[\alpha]^{25}_{D}$ = -13.8 (*c* 0.50, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 9.41 and 12.62 min.

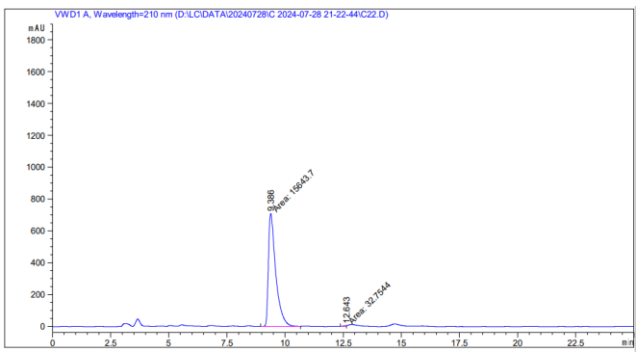
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 – 8.58 (m, 1H), 7.72 – 7.68 (m, 1H), 7.61 – 7.59 (m, 2H), 7.48 – 7.41 (m, 3H), 7.21 – 7.18 (m, 1H), 5.51 (dd, *J* = 11.7, 4.1 Hz, 1H), 2.70 – 2.65 (m, 1H), 2.17 – 2.10 (m, 1H), 2.03 – 1.97 (m, 1H), 1.83 – 1.76 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ174.0, 162.2, 149.1, 144.3, 137.0, 130.5 (q, *J* = 32.0 Hz), 126.1, 125.5 (q, *J* = 40.0 Hz), 125.3 (q, *J* = 270.0 Hz), 122.2, 120.5, 82.9, 50.2, 34.3, 28.7, 26.7.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.6.

HRMS (ESI+) Calcd. For $C_{18}H_{17}F_3NO_2^+$ ($[M+H]^+$): 336.1206, found: 336.1214.

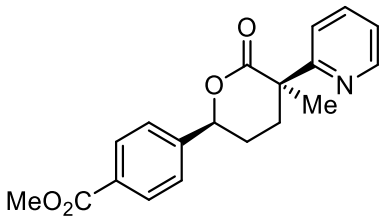




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.407	MM	0.3744	1.11356e4	495.65195	48.5559
2	12.616	MF	0.4798	1.17980e4	409.84088	51.4441

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.386	MF	0.3675	1.56437e4	709.50024	99.7911
2	12.643	MM	0.1425	32.75438	3.83133	0.2089

Methyl 4-((2*S*,5*R*)-5-methyl-6-oxo-5-(pyridin-2-yl)tetrahydro-2H-pyran-2-yl)benzoate (3w):

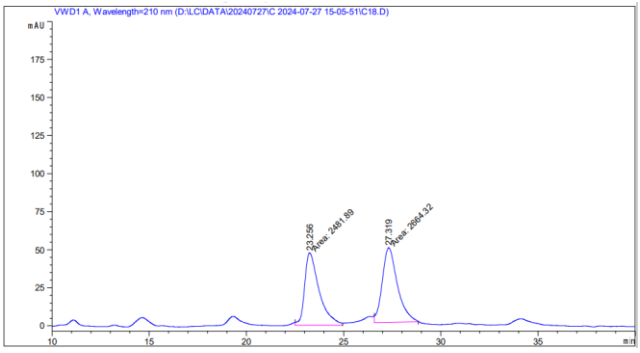


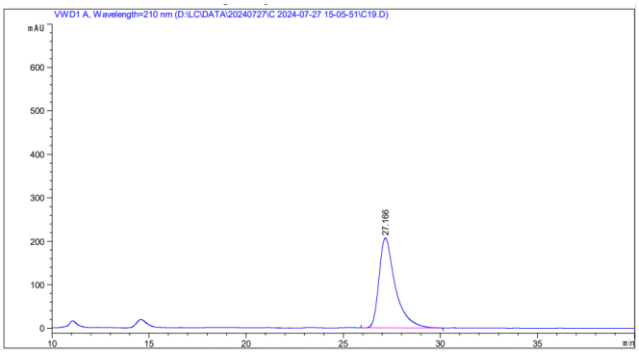
yield (39.0 mg, 60%); colorless oil; $[\alpha]^{25}_{D}$ = +29.0 (*c* 0.36, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 23.26 and 27.32 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58-8.62 (m, 1H), 8.06 – 7.96 (m, 2H), 7.68 – 7.72 (m, 1H), 7.47 – 7.38 (m, 3H), 7.25-7.16 (m, 1H), 5.51 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.91 (s, 3H), 2.65 – 2.71 (m, 1H), 2.09 – 2.17 (m, 1H), 2.04 – 1.96 (m, 1H), 1.84 – 1.75 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 166.7, 162.2, 149.1, 145.2, 137.0, 130.0, 129.9, 125.9, 122.2, 120.6, 83.2, 52.1, 50.2, 34.3, 28.7, 26.8.

HRMS (ESI+) Calcd. For $C_{19}H_{20}NO_4^+$ ([M+H]$^+$): 326.1387, found: 326.1387.

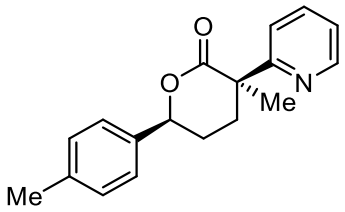




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.256	MM	0.8690	2481.89453	47.60112	48.2276
2	27.319	MM	0.9081	2664.31641	48.90176	51.7724

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.166	VB R	0.8669	1.20890e4	206.81430	100.0000

(3*R*,6*S*)-3-methyl-3-(pyridin-2-yl)-6-(p-tolyl)tetrahydro-2H-pyran-2-one (3x):

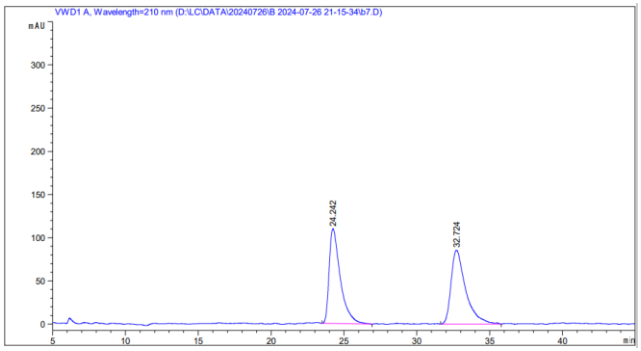


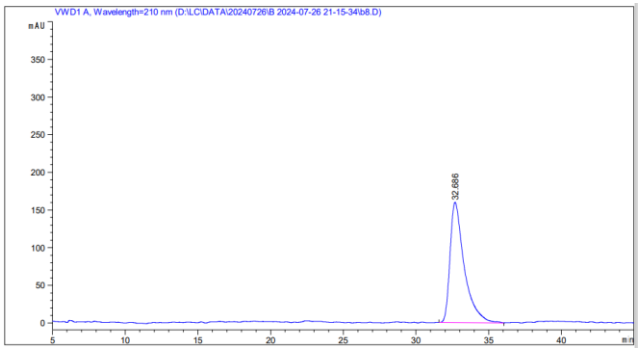
yield (41.0 mg, 73%); white solid; m.p. 90-92 ºC; $[\alpha]^{25}_{D}$ = +12.3 (*c* 0.40, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 24.24 and 32.72 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.61 – 8.59 (m, 1H), 7.70 – 7.66 (m, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.42 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.72 – 2.67 (m, 1H), 2.32 (s, 3H), 2.13 – 2.06 (m, 1H), 1.98 – 1.91 (m, 1H), 1.85 – 1.78 (m, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.3, 149.2, 138.0, 137.3, 136.9, 129.1, 125.8, 122.0, 120.9, 84.0, 50.3, 34.3, 28.6, 26.9, 21.1.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_2^+$ ([M+H]$^+$): 282.1489, found: 282.1489.

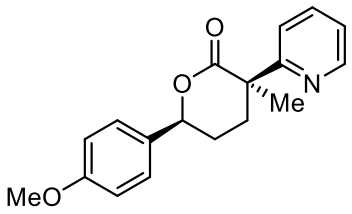




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.242	BB	0.7719	5857.54932	109.62615	49.5534
2	32.724	BV R	0.9924	5963.13281	85.53732	50.4466

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.686	BV R	0.9860	1.08512e4	159.48749	100.0000

(3*R*,6*S*)-6-(4-methoxyphenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3y):

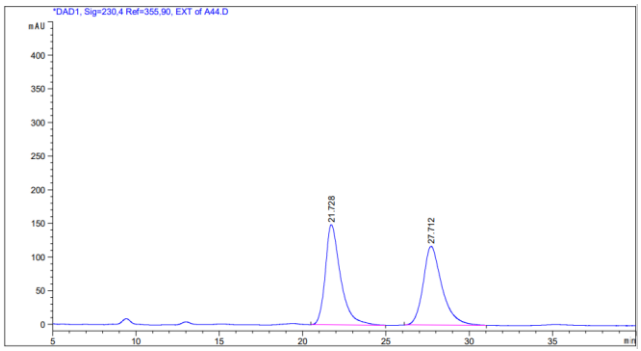


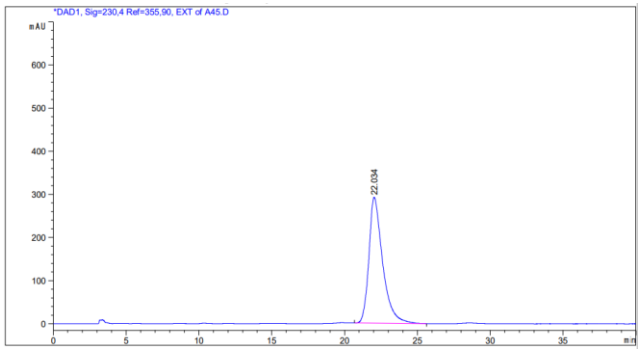
yield (39.8mg, 67%); colorless oil; $[\alpha]^{25}_D$ = +52.7 (*c* 0.42, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 230 nm); t_r = 21.73 and 27.71 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 – 8.60 (m, 1H), 7.71 – 7.67 (m, 1H), 7.44 – 7.41 (m, 1H), 7.26 – 7.18 (m, 3H), 6.87 – 6.84 (m, 2H), 5.40 (dd, *J* = 11.6, 4.1 Hz, 1H), 3.79 (s, 3H), 2.72 – 2.66 (m, 1H), 2.13 – 2.05 (m, 1H), 1.96 – 1.89 (m, 1H), 1.87 – 1.79 (m, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.3, 159.5, 149.1, 136.9, 132.3, 127.4, 122.0, 120.8, 113.8, 83.9, 55.3, 50.2, 34.4, 28.5, 26.9.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_3^+$ ([M+H]$^+$): 298.1438, found: 298.1440.

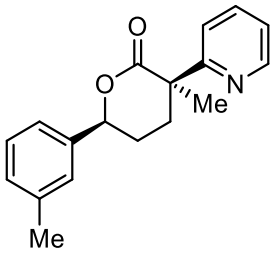




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.728	BB	0.9250	9483.09863	148.91426	50.7946
2	27.712	BB	1.0738	9186.41602	117.02611	49.2054

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.034	BB	0.9348	1.90745e4	291.74179	100.0000

(3*R*,6*S*)-3-methyl-3-(pyridine-2-yl)-6-(m-tolyl)tetrahydro-2H-pyran-2-one (3z):



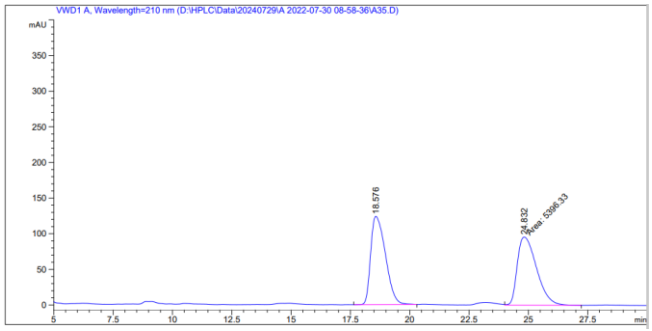
yield (34.8 mg, 62%); colorless oil; $[\alpha]^{25}_D$ = +34.2 (*c* 0.44, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: >99% ee (Chiralpak IE, *i*-propanol/hexane = 20/80, flow

rate 1.0 mL/min, λ = 210 nm); t_r = 18.58 and 24.83 min.

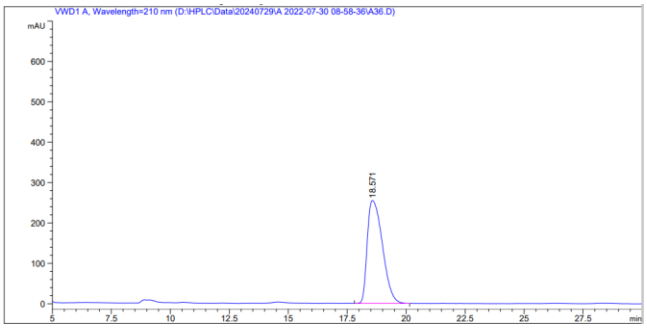
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.75 – 8.46 (m, 1H), 7.73 – 7.63 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.06 (m, 5H), 5.42 (dd, *J* = 11.6, 4.0 Hz, 1H), 2.74 – 2.65 (m, 1H), 2.33 (s, 3H), 2.15 – 2.06 (m, 1H), 2.00 – 1.93 (m, 1H), 1.85 – 1.78 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.3, 149.1, 140.2, 138.2, 136.9, 128.9, 128.4, 126.6, 122.9, 122.1, 120.9, 84.1, 50.3, 34.4, 28.7, 26.9, 21.4.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_2^+$ ([M+H]$^+$): 282.1489, found: 282.1492.

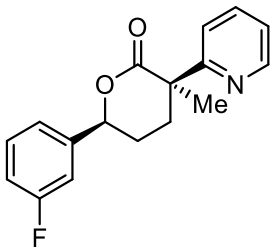


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.576	BB	0.6940	5349.43604	123.82161	49.7818
2	24.832	FM	0.9414	5396.33301	95.53723	50.2182



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.571	BB	0.7163	1.13886e4	254.86711	100.0000

(3*R*,6*S*)-6-(3-fluorophenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3A):



yield (32.5 mg, 57%); colorless oil; $[\alpha]^{25}_D$ = +3.8 (*c* 0.18, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 21.68 and 26.11 min.

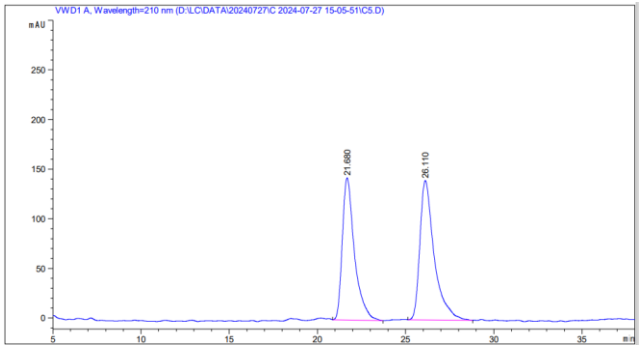
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.73 – 8.47 (m, 1H), 7.78 – 7.65 (m, 1H), 7.45 – 7.40 (m, 1H), 7.33 – 7.27 (m, 2H), 7.22 – 7.17 (m, 1H), 7.12 – 7.06 (m, 2H), 7.02 – 6.95 (m, 1H), 5.44 (dd, *J* = 11.7, 4.0 Hz, 1H), 2.74 – 2.64 (m, 1H), 2.17 – 2.07 (m, 1H), 2.02 – 1.93 (m, 1H), 1.84 – 1.75 (m, 1H), 1.73 (s, 3H).

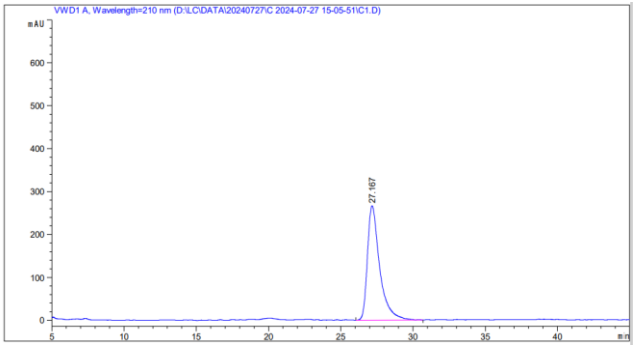
^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 162.9 (d, *J* = 246.2 Hz), 162.2, 149.1, 142.8 (d, *J* = 7.4 Hz), 137.0, 130.1, 122.2, 121.4 (d, *J* = 3.0 Hz), 120.7, 115.1 (d, *J* = 21.3 Hz), 113.0 (d, *J* = 22.8 Hz),

83.1, 50.2, 34.3, 28.6, 26.8.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -112.5.

HRMS (ESI+) Calcd. For $C_{17}H_{17}FNO_2^+$ ([M+H]$^+$): 286.1238, found: 286.1239.

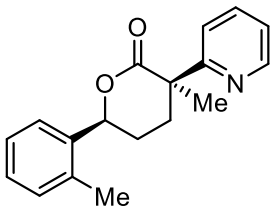




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.680	BV R	0.7132	6870.18994	143.05890	46.4764
2	26.110	BV R	0.8298	7911.91895	140.27458	53.5236

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.167	BV R	0.8763	1.57210e4	266.41232	100.0000

(3*R*,6*S*)-3-methyl-3-(pyridin-2-yl)-6-(o-tolyl)tetrahydro-2H-pyran-2-one (3B):

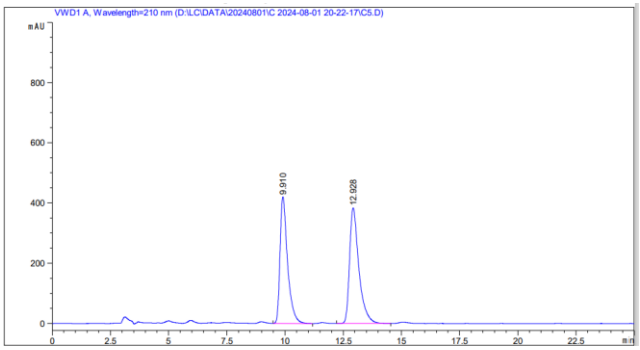


yield (34.3 mg, 61%); colorless oil; $[\alpha]^{25}_D$ = -21.6 (*c* 0.65, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 9.91 and 12.93 min.

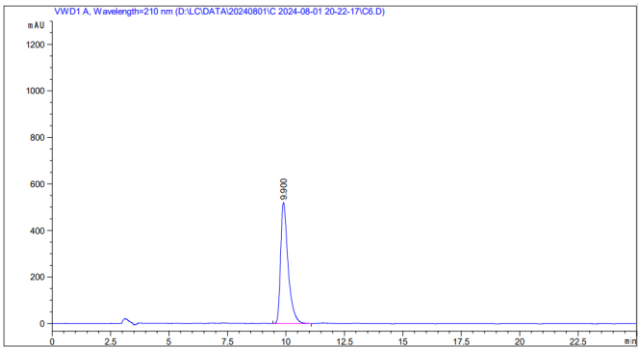
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.74 – 8.47 (m, 1H), 7.75 – 7.63 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.32 (m, 1H), 7.22 – 7.15 (m, 3H), 7.14 – 7.08 (m, 1H), 5.68 (dd, *J* = 11.7, 3.9 Hz, 1H), 2.80 – 2.65 (m, 1H), 2.33 (s, 3H), 2.19 – 2.06 (m, 1H), 1.98 – 1.87 (m, 1H), 1.85 – 1.75 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.7, 162.3, 149.2, 138.2, 136.9, 134.2, 130.4, 128.0, 126.4, 125.9, 122.1, 120.9, 81.3, 50.4, 34.6, 27.4, 27.0, 19.0.

HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_2^+$ ([M+H]$^+$): 282.1489, found: 282.1487.

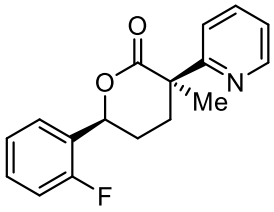


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.910	VB	0.3337	9454.76367	420.50607	47.0419
2	12.928	VB R	0.4125	1.06438e4	383.58862	52.9581



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.900	VB	0.3336	1.15536e4	519.72760	100.0000

(3*R*,6*S*)-6-(2-fluorophenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3C):



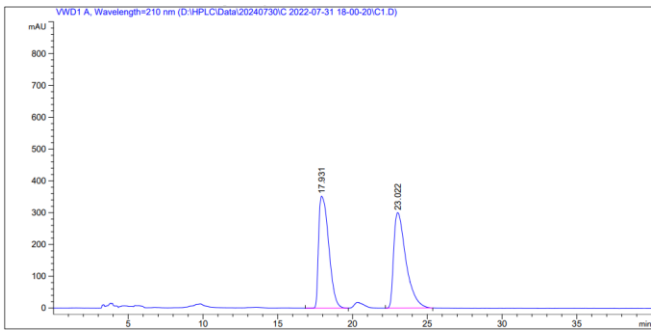
yield (36.5 mg, 64%); colorless oil; $[a]^{25}_{D}$ = -60.5 (*c* 0.51 CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 17.93 and 23.02 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 – 8.54 (m, 1H), 7.77 – 7.63 (m, 1H), 7.53 – 7.38 (m, 2H), 7.30 – 7.23 (m, 1H), 7.22 – 7.08 (m, 2H), 7.05 – 6.91 (m, 1H), 5.78 (dd, *J* = 11.6, 4.0 Hz, 1H), 2.80 – 2.53 (m, 1H), 2.13 (td, *J* = 13.5, 3.0 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.85 – 1.75 (m, 1H), 1.73 (s, 3H).

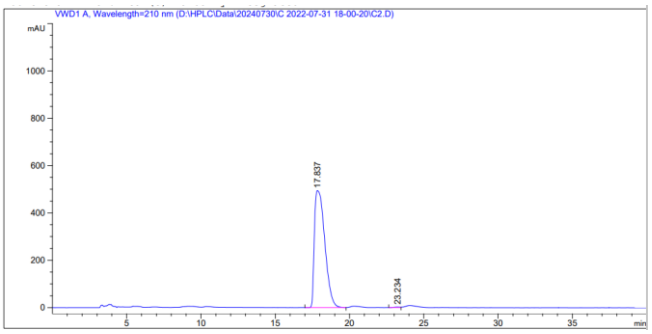
^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 162.2, 159.3 (d, *J* = 246.6 Hz), 149.1, 136.9, 129.6 (d, *J* = 8.1 Hz), 127.6, 127.5, 124.4 (d, *J* = 3.6 Hz), 122.0, 120.7, 115.3 (d, *J* = 21.4 Hz), 78.0 (d, *J* = 3.0 Hz), 50.4, 34.3, 27.5, 26.8.

^{19}F NMR (377 MHz, Chloroform-*d*) δ -119.8.

HRMS (ESI+) Calcd. For $C_{17}H_{17}FNO_2^+$ ($[M+H]^+$): 286.1238, found: 286.1239.

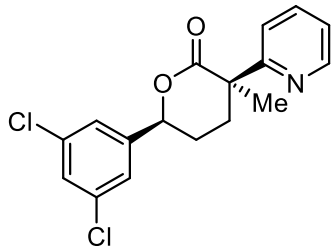


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.931	VB R	0.7477	1.65233e4	351.94574	49.1441
2	23.022	BB	0.8729	1.70988e4	300.04456	50.8559



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.837	VV R	0.7752	2.40696e4	494.23157	99.7348
2	23.234	BV	0.3677	64.00869	2.21785	0.2652

(3*R*,6*S*)-6-(3,5-dimethylphenyl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3D):

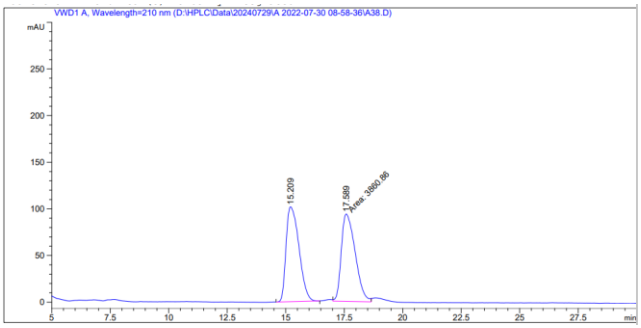


yield (44.2 mg, 66%); yellow oil; $[\alpha]^{25}_{D}$ = +33.2 (*c* 0.43 CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 15.21 and 17.59 min.

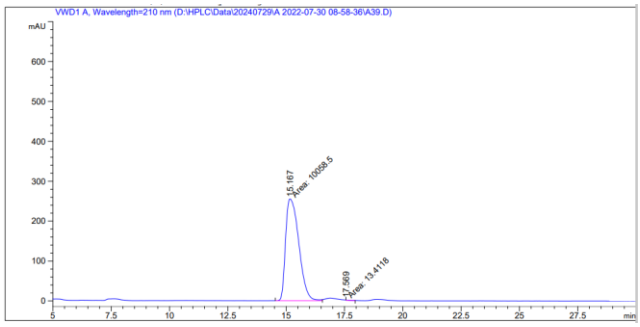
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 – 8.57 (m, 1H), 7.75 – 7.66 (m, 1H), 7.46 – 7.37 (m, 2H), 7.28 – 7.27 (m, 1H), 7.23 – 7.16 (m, 2H), 5.42 (dd, *J* = 11.6, 4.1 Hz, 1H), 2.72 – 2.61 (m, 1H), 2.17 – 2.06 (m, 1H), 2.01 – 1.94 (m, 1H), 1.85 – 1.75 (m, 1H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 162.2, 149.1, 142.3, 137.0, 134.5, 129.8, 128.3, 126.2, 124.0, 122.2, 120.6, 83.0, 50.3, 34.3, 28.6, 26.7.

HRMS (ESI+) Calcd. For $C_{17}H_{16}Cl_2NO_2^+$ ([M+H]$^+$): 336.0553, found: 336.0561.

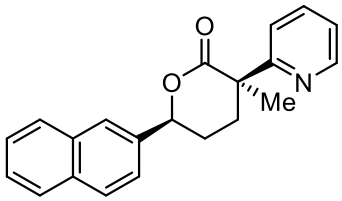


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.209	BB	0.6167	3893.21094	101.67488	50.2086
2	17.589	MF	0.6876	3860.85840	93.58244	49.7914



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.167	MF	0.6568	1.00585e4	255.24911	99.8668
2	17.569	MM	0.2605	13.41182	8.58162e-1	0.1332

(3*R*,6*S*)-3-methyl-6-(naphthalen-2-yl)-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3E):

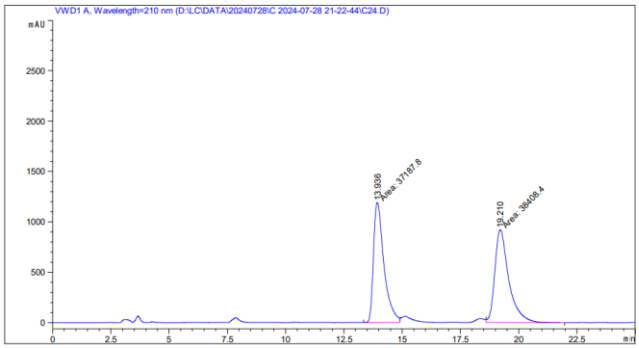


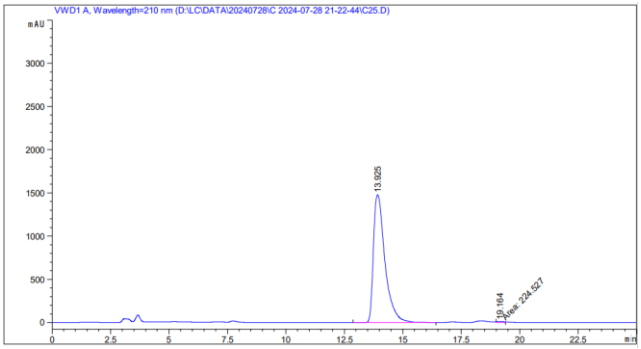
yield (51.3 mg, 81%); white solid; m.p. 150-152 °C; $[\alpha]^{25}_D$ = +146.3 (*c* 0.43 CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 13.94 and 19.21 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 – 8.60 (m, 1H), 7.84 – 7.79 (m, 4H), 7.72 – 7.68 (m, 1H), 7.49 – 7.41 (m, 4H), 7.20 – 7.15 (m, 1H), 5.63 (dd, *J* = 11.5, 4.0 Hz, 1H), 2.74 – 2.69 (m, 1H), 2.21 – 2.11 (m, 1H), 2.09 – 2.02 (m, 1H), 1.97 – 1.83 (m, 1H), 1.76 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.3, 149.1, 137.6, 136.9, 133.1, 133.0, 128.4, 128.0, 127.7, 126.3, 126.2, 124.8, 123.6, 122.1, 120.8, 84.0, 50.3, 34.4, 28.6, 26.9.

HRMS (ESI+) Calcd. For $C_{21}H_{20}NO_2^+$ ([M+H]$^+$): 318.1489, found: 318.1493.

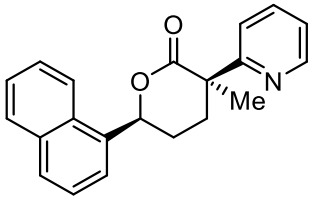




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.936	MF	0.5202	3.71878e4	1191.47681	49.1927
2	19.210	FM	0.6953	3.84084e4	920.63885	50.8073

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.925	VV R	0.5190	5.06441e4	1477.07202	99.5586
2	19.164	MF	0.3787	224.52728	9.88050	0.4414

(3*R*,6*S*)-3-methyl-6-(naphthalen-1-yl)-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3F):

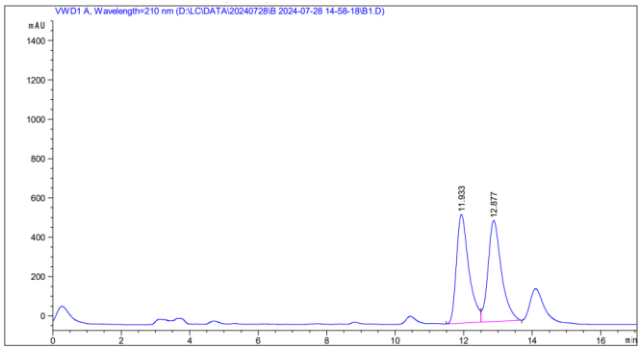


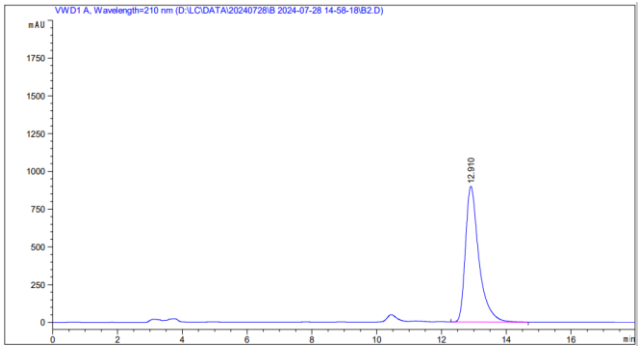
yield (45.0 mg, 71%); yellow oil; $[\alpha]^{25}_D$ = +30.0 (*c* 0.36 CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 11.93 and 12.88 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 – 8.59 (m, 1H), 8.00 – 7.93 (m, 1H), 7.89 – 7.83 (m, 1H), 7.81 – 7.77 (m, 1H), 7.75 – 7.68 (m, 1H), 7.65 – 7.60 (m, 1H), 7.52 – 7.43 (m, 4H), 7.22 – 7.16 (m, 1H), 6.24 (dd, *J* = 11.5, 3.7 Hz, 1H), 2.82 – 2.71 (m, 1H), 2.30 – 2.15 (m, 2H), 2.05 – 1.93 (m, 1H), 1.79 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.7, 162.3, 149.1, 136.9, 135.1, 133.6, 129.8, 129.0, 128.7, 126.3, 125.6, 125.4, 123.7, 122.5, 122.1, 120.8, 81.2, 50.5, 34.6, 27.9, 27.0.

HRMS (ESI+) Calcd. For $C_{21}H_{20}NO_2^+$ ([M+H]$^+$): 318.1489, found: 318.1493.

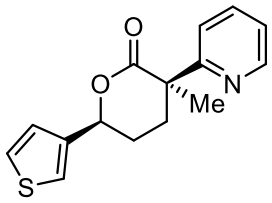




Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.933	BV	0.3767	1.39259e4	553.07965	50.0472
2	12.877	VB	0.4043	1.38997e4	513.98145	49.9528

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.910	BB	0.4283	2.57808e4	897.56140	100.0000

(3*R*,6*S*)-3-methyl-3-(pyridin-2-yl)-6-(thiophen-3-yl)tetrahydro-2H-pyran-2-one (3G):

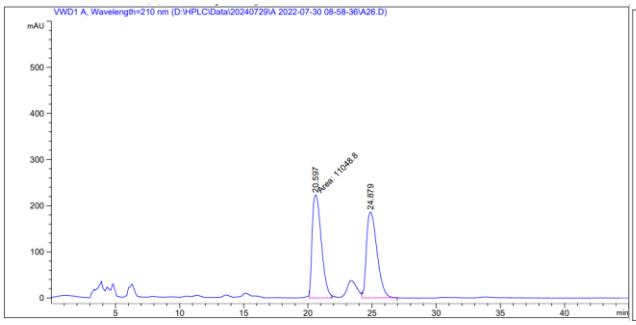


yield (28.2 mg, 70%); colorless oil; $[a]^{25}_D$ = +25.2 (*c* 0.26 CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IE, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 210 nm); t_r = 20.60 and 24.88 min.

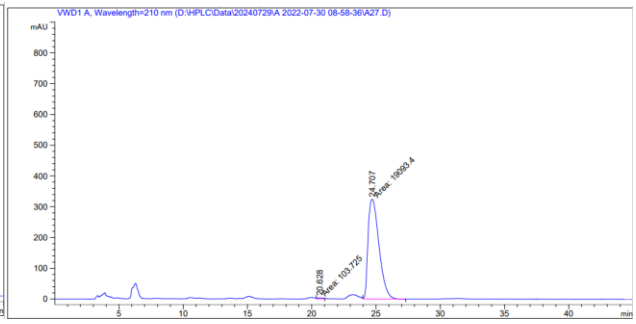
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 – 8.58 (m, 1H), 7.68 – 7.64 (m, 1H), 7.40 – 7.37 (m, 1H), 7.29 – 7.25 (m, 2H), 7.20 – 7.16 (m, 1H), 7.05 – 7.01 (m, 1H), 5.55 (dd, *J* = 11.3, 4.0 Hz, 1H), 2.74 – 2.68 (m, 1H), 2.10 – 2.01 (m, 2H), 1.93 – 1.82 (m, 1H), 1.71 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 162.1, 149.1, 141.3, 136.9, 126.3, 125.6, 122.1, 120.9, 80.0, 50.2, 34.0, 27.6, 26.9.

HRMS (ESI+) Calcd. For $C_{15}H_{16}NO_2S^+$ ([M+H]$^+$): 274.0896, found: 274.0898.

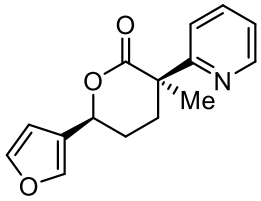


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.597	MF	0.8255	1.10488e4	223.08183	51.0341
2	24.879	VB	0.8969	1.06010e4	185.72075	48.9659



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.628	MF	0.5560	103.72456	3.10916	0.5403
2	24.707	FM	0.9813	1.90934e4	324.29114	99.4597

(3*R*,6*S*)-6-(furan-3-yl)-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3H):

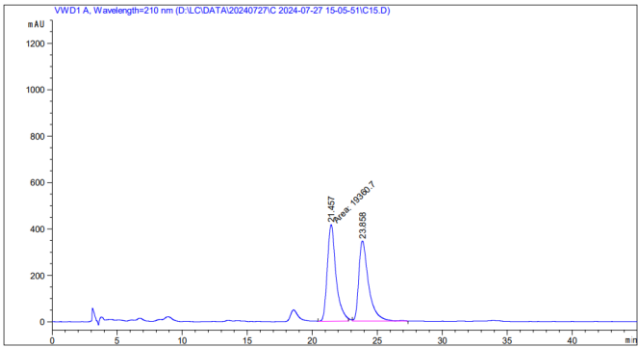


yield (33.4 mg, 65%); colorless oil; $[\alpha]^{25}_{D}$ = +53.2 (*c* 0.33, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 210 nm); t_r = 21.46 and 23.86 min.

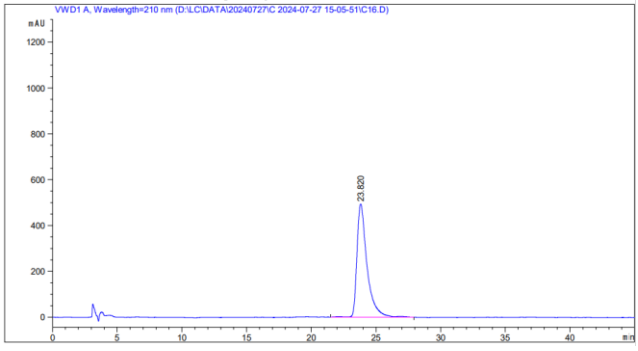
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 – 8.52 (m, 1H), 7.72 – 7.61 (m, 1H), 7.47 – 7.41 (m, 1H), 7.39 – 7.32 (m, 2H), 7.22 – 7.16 (m, 1H), 6.40 – 6.31 (m, 1H), 5.45 (dd, *J* = 11.2, 4.0 Hz, 1H), 2.76 – 2.66 (m, 1H), 2.10 – 1.94 (m, 2H), 1.91 – 1.77 (m, 1H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 162.0, 149.2, 143.4, 139.7, 136.8, 125.3, 122.1, 121.0, 108.6, 50.2, 33.9, 26.9, 26.9.

HRMS (ESI+) Calcd. For $C_{15}H_{16}NO_3^+$ ([M+H]$^+$): 258.1125, found: 258.1127.

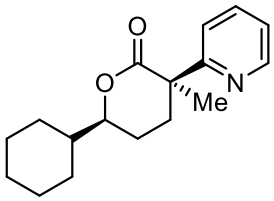


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.457	MF	0.7758	1.93607e4	415.94910	51.7635
2	23.858	VV R	0.7752	1.80415e4	345.25470	48.2365



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.820	VV R	0.7952	2.67627e4	494.07877	100.0000

(3*R*,6*S*)-6-cyclohexyl-3-methyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one (3I):

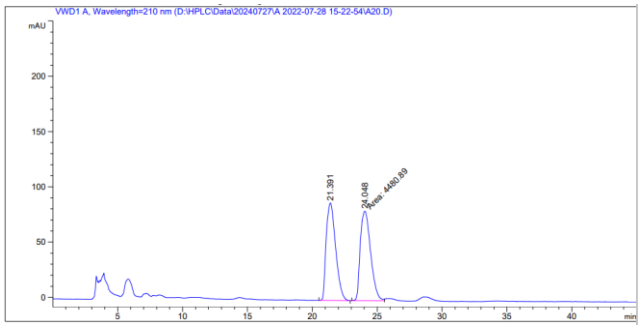


yield (32.8 mg, 60%); colorless oil; $[\alpha]^{25}_{D}$ = -50.7 (*c* 0.41, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 98% ee (Chiralpak IE, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 21.39 and 24.05 min.

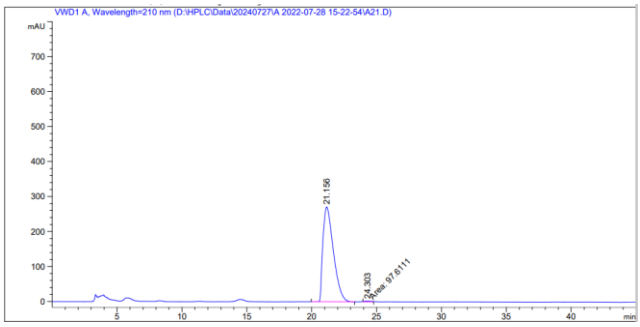
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.72 – 8.42 (m, 1H), 7.77 – 7.55 (m, 1H), 7.40 – 7.27 (m, 1H), 7.21 – 7.12 (m, 1H), 4.22 (ddd, *J* = 12.0, 5.8, 3.9 Hz, 1H), 2.73 – 2.54 (m, 1H), 1.95 – 1.81 (m, 2H), 1.67 – 1.61 (m, 6H), 1.53 – 1.43 (m, 2H), 1.29 – 0.96 (m, 7H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.0, 162.2, 149.2, 136.7, 121.9, 121.2, 87.0, 42.9, 33.8, 28.1, 27.9, 26.3, 26.0, 25.9, 22.8.

HRMS (ESI+) Calcd. For $C_{17}H_{24}NO_2^+$ ($[M+H]^+$): 274.1802, found: 274.1804.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.391	BB	0.7951	4436.43555	88.16689	49.7507
2	24.048	MF	0.9224	4480.88916	80.96325	50.2493



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.156	VB R	0.8710	1.52171e4	271.05676	99.3626
2	24.303	MF	0.6614	97.61111	2.45958	0.6374

5. Absolute configuration determination of (3*R*,6*S*)-3t

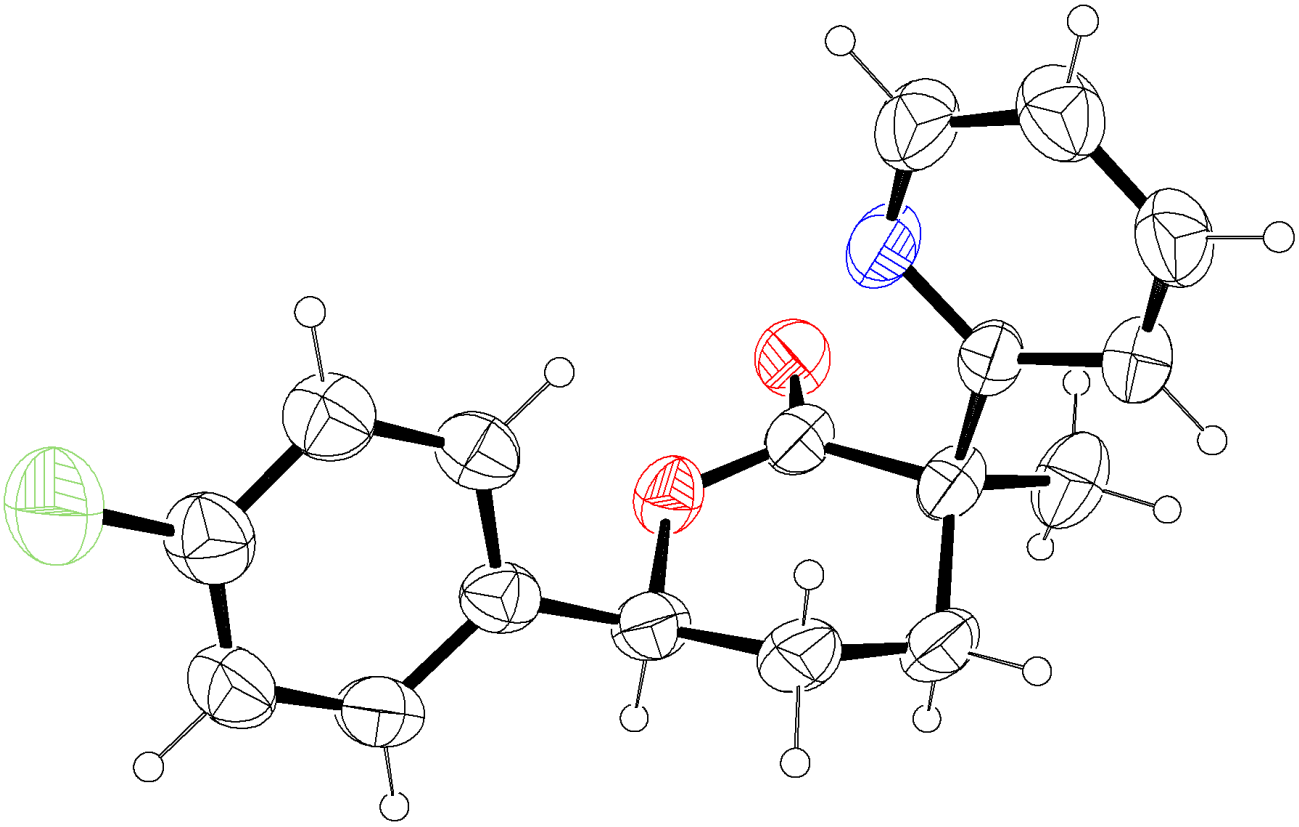
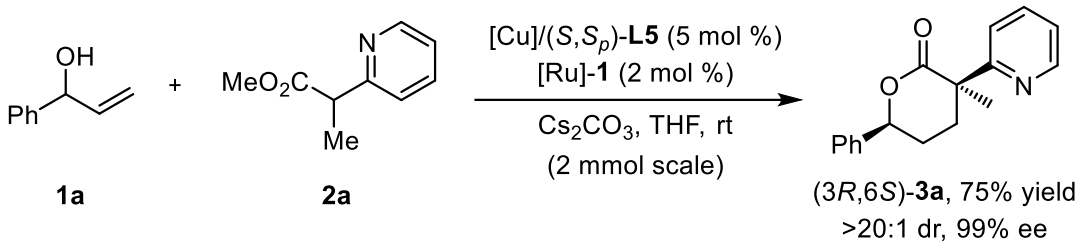


Figure S1. ORTEP representation of (3*R*,6*S*)-**3t** at 30% probability for the drawing of thermal ellipsoids.

Crystal data for (3*R*,6*S*)-**3t**: $C_{17}H_{16}FNO_2$, $M_r = 285.31$, $T = 300$ K, Monoclinic, space group P 1 21 1, $a = 6.47670(10)$ $b = 15.7755(3)$ $c = 7.4250(2)$ Å, $\beta = 100.190(2)$, $V = 746.67(3)$ Å^3, $Z = 2$, 2694 unique reflections, final $R_1 = 0.0336$ and $wR_2 = 0.0945$ for 2845 observed [$I > 2\sigma(I)$] reflections, Flack $\chi = 0.07(6)$. CCDC 2375149 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

6. Gram scale reaction and synthetic transformations

a) Scale-up experiment

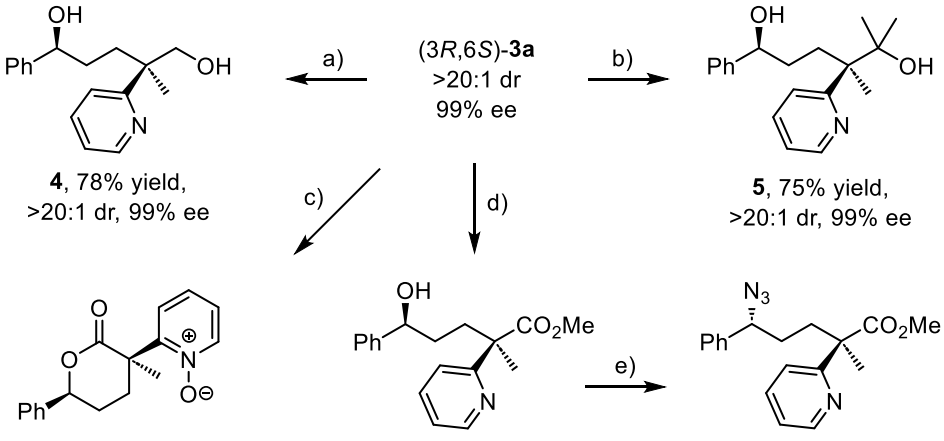


1a **2a**

(3*R*,6*S*)-**3a**, 75% yield
>20:1 dr, 99% ee

To a clean and dried Schlenk tube was charged with $Cu(CH_3CN)_4PF_6$ (5 mol%, 37 mg) and (S,S_p)-**L5** (5.5 mol%, 60 mg) in glovebox, degassed THF (5 mL) was added to the tube under nitrogen atmosphere, and then the mixture was stirred at room temperature for 30 min. Then, α-azaaryl acetate **2a** (2 mmol, 1.0 equiv), allyl alcohol **1a** (6 mmol, 3.0 equiv), [Ru]-**1** complex (2 mol%), Cs_2CO_3 (3 mmol, 1.5 equiv) and THF (15 mL) were subsequently added to the tube, respectively. The mixture was stirred at room temperature for 36 h. Upon completion, the crude mixture was filtered through a short silica gel plug to remove the metal complex, and the filtrate was concentrated to dryness. The crude product was analyzed by ^{1}H NMR to determine the diastereoselectivity. Then the residue was purified by column chromatography to give the desired product **3a**, which was then directly analyzed by HPLC to determine the enantiomeric excess.

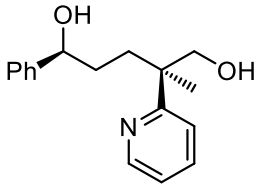
b) Synthetic transformations



Reaction conditions:
a) $LiAlH_4$, THF, 0 °C; b) MeMgBr, THF, 0 °C;
c) *m*-CPBA, DCM, 0 °C; d) MeOH, rt;
e) PPh_3, DIAD, DPPA, DCM, rt;
f) PPh_3, THF, H_2O, 70 °C

A 10 mL dried two-neck round bottom flask was charged with (3*R*,6*S*)-**3a** (26.7 mg, 0.1 mmol), then evacuated and filled with nitrogen atmosphere for three times, and 1 mL dried THF was added by syringe. $LiAlH_4$ (0.2 mmol, dissolved in THF) was added slowly at 0 °C under N_2 atmosphere, and stirred at room temperature for 30 min. After completion, the mixture was concentrated in vacuo. The ^1H NMR analysis of the crude reaction mixture showed a >20:1 diastereomer ratio of the product **4**. Finally, and the mixture was purified by column chromatography with MeOH : DCM = 20:1 to give the desired product as colorless oil.

(1*S*,4*R*)-4-methyl-1-phenyl-4-(pyridin-2-yl)pentane-1,5-diol (4):

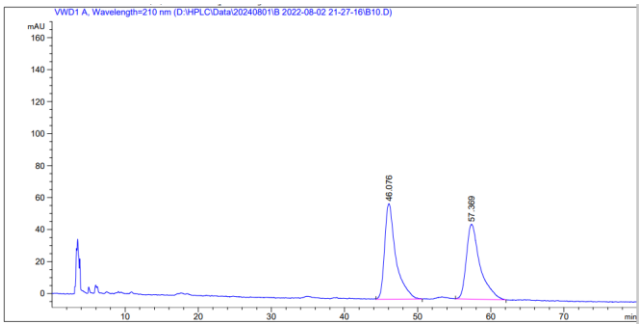


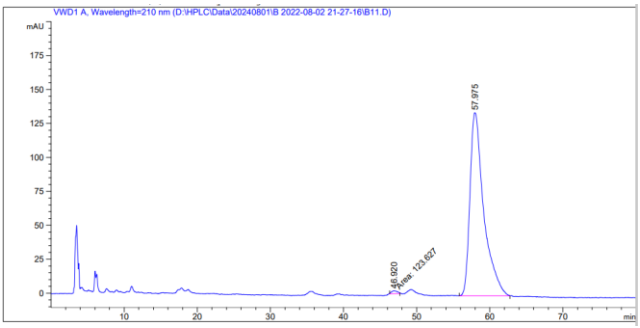
yield (21.2 mg, 78%); colorless oil; $[\alpha]^{25}_D$ = -5.7 (*c* 0.23, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak IC, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 210 nm); t_r = 46.08 and 57.37 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.46 (m, 1H), 7.66 – 7.62 (m, 1H), 7.34 – 7.27 (m, 5H), 7.22 – 7.19 (m, 1H), 7.16 – 7.12 (m, 1H), 4.61 (dd, *J* = 7.3, 5.2 Hz, 1H), 3.74 (s, 2H), 2.01 – 1.93 (m, 1H), 1.71 – 1.61(m, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.2, 148.0, 144.6, 136.9, 128.4, 127.5, 125.9, 121.4, 120.9, 74.8, 70.3, 43.8, 34.6, 33.7, 22.0.

HRMS (ESI+) Calcd. For $C_{17}H_{22}NO_2^+$ ([M+H]$^+$): 272.1645, found: 272.1646.





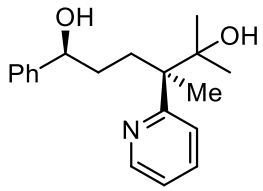
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.076	BV R	1.3622	6354.52490	59.68203	51.1244
2	57.369	BV R	1.5647	6075.02100	46.79022	48.8756

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.920	MM	0.9175	123.62688	2.24575	0.6945
2	57.975	BV R	1.8603	1.76783e4	134.86540	99.3055

A 10 mL dried two-neck round bottom flask was charged with (3*R*,6*S*)-**3a** (26.7 mg, 0.1 mmol),

then evacuated and filled with nitrogen atmosphere for three times, and 1 mL dried THF was added by syringe. CH_3MgBr (0.22 mmol) was added slowly at 0 ºC under N_2 atmosphere, and stirred at room temperature for 30 min. After completion, the mixture was concentrated in vacuo. The ^1H NMR analysis of the crude reaction mixture showed a >20:1 diastereomer ratio of the product **5**. Finally, and the mixture was purified by column chromatography with MeOH : DCM = 20:1 to give the desired product as colorless oil.

(1*S*,4*R*)-4,5-dimethyl-1-phenyl-4-(pyridin-2-yl)hexane-1,5-diol (5):

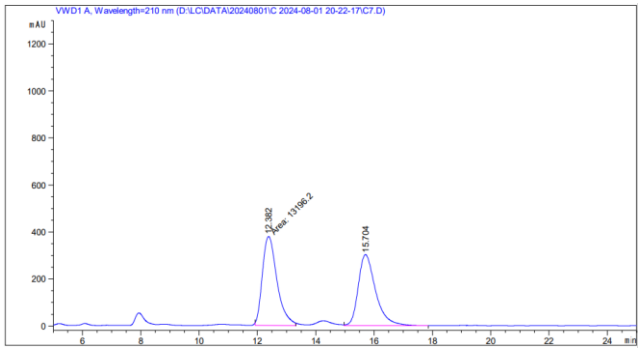


yield (22.5 mg, 75%); colorless oil; $[\alpha]^{25}_D$ = +4.8 (*c* 0.99, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 12.38 and 15.70 min.

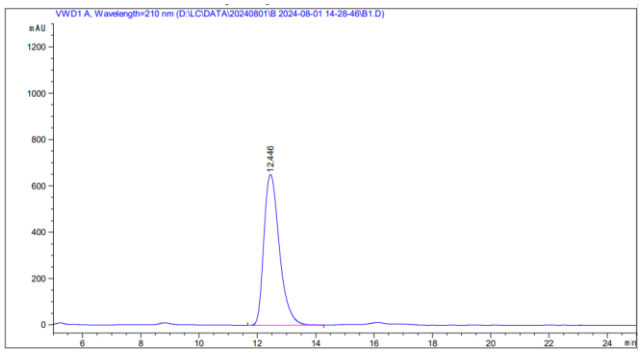
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 – 8.51 (m, 1H), 7.70 – 7.62 (m, 1H), 7.34 – 7.27 (m, 3H), 7.26 – 7.21 (m, 3H), 7.19 – 7.15 (m, 1H), 4.53 (dd, *J* = 7.2, 5.9 Hz, 1H), 2.69 – 2.58 (m, 1H), 1.65 – 1.45 (m, 4H), 1.28 (s, 3H), 1.17 (s, 3H), 1.04 – 0.93 (m, 1H), 0.85 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 148.0, 144.6, 136.7, 128.4, 127.5, 125.9, 122.0, 121.2, 75.4, 75.1, 49.2, 34.5, 31.6, 26.9, 24.9, 19.3.

HRMS (ESI+) Calcd. For $C_{19}H_{26}NO_2^+$ ([M+H]$^+$): 300.1958, found: 300.1958.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.382	FM	0.5810	1.31962e4	378.54395	51.3703
2	15.704	VB	0.6255	1.24922e4	301.84753	48.6297

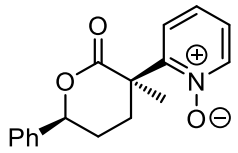


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.446	BV R	0.5741	2.39542e4	649.95844	100.0000

A 10 mL dried two-neck round bottom flask was charged with (3*R*,6*S*)-**3a** (26.7 mg, 0.1 mmol),

then 1 mL dried DCM was added by syringe. *m*-CPBA (0.2 mmol) was added slowly and stirred at room temperature for 12 h. After completion, the mixtures were concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixtures showed a >20:1 diastereomer ratio of the product **6**. Finally, the mixture was purified by column chromatography with EA to give the desired product as colorless oil.

2-((3*R*,6*S*)-3-methyl-2-oxo-6-phenyltetrahydro-2H-pyran-3-yl)pyridine 1-oxide (6):



yield (22.7 mg, 80%); colorless oil; $[\alpha]^{25}_D$ = -12.6 (*c* 0.98, CH_2Cl_2);

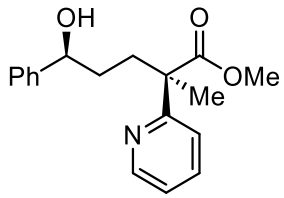
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 – 8.19 (m, 1H), 7.61 – 7.28 (m, 8H), 5.60 – 5.52 (m, 1H), 2.77 – 2.59 (m, 1H), 2.43 – 2.30 (m, 1H), 2.30 – 2.18 (m, 1H), 1.93 – 1.81 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.3, 140.0, 139.6, 128.5, 128.2, 126.2, 126.1, 124.5, 123.1, 81.3, 43.8, 32.1, 29.9, 25.8.

HRMS (ESI+) Calcd. For $C_{17}H_{17}NO_3^+$ ($[M+H]^+$): 284.1281, found: 284.1283.

A 10 mL dried two-neck round bottom flask was charged with (3*R*,6*S*)-**3a** (26.7 mg, 0.2 mmol), then evacuated and filled with nitrogen atmosphere for three times, and 1 mL dried MeOH was added by syringe. The mixture was stirred at room temperature for 12 h and monitored by TLC. After completion, the mixture was concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixture showed a >20:1 diastereomer ratio of the product **7**. Finally, and the mixture was purified by column chromatography with PE:EA = 3:1 to give the desired product as colorless oil.

Methyl (2*R*,5*S*)-5-hydroxy-2-methyl-5-phenyl-2-(pyridin-2-yl)pentanoate (7):



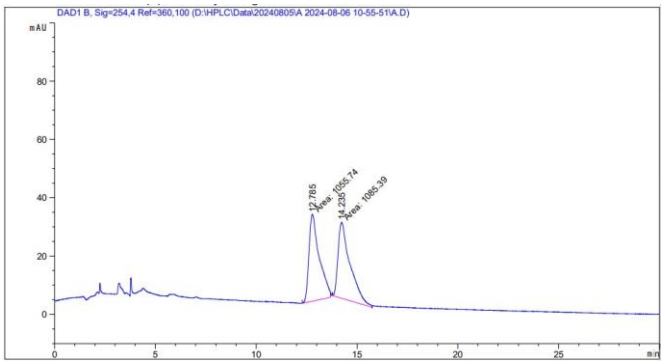
yield (53.8 mg, 90%); colorless oil; $[\alpha]^{25}_D$ = +6.6 (*c* 0.85, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AS-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm); t_r = 12.79 and 14.24 min.

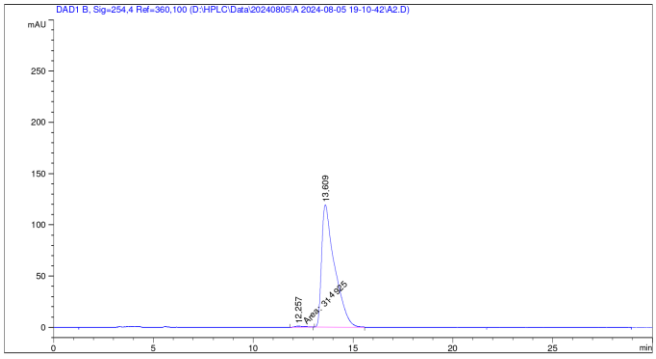
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 – 8.48 (m, 1H), 7.70 – 7.57 (m, 1H), 7.37 – 7.29 (m, 4H), 7.28 – 7.26 (m, 1H), 7.25 – 7.22 (m, 1H), 7.18 – 7.12 (m, 1H), 4.67 (t, *J* = 6.4 Hz, 1H), 3.65 (s, 3H),

2.78 (s, 1H), 2.32 – 2.22 (m, 1H), 2.15 – 2.02 (m, 1H), 1.73 – 1.67 (m, 2H), 1.56 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.0, 162.6, 148.8, 144.6, 136.6, 128.4, 127.4, 125.8, 121.8, 120.9, 52.9, 52.2, 34.3, 33.9, 22.7.

HRMS (ESI+) Calcd. For $C_{18}H_{22}NO_3^+$ ([M+H]$^+$): 300.1594, found: 300.1592.



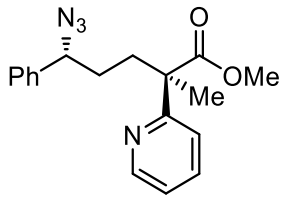


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.785	MM	0.5901	1055.74097	29.81817	49.3076
2	14.235	MM	0.6935	1085.39111	26.08564	50.6924

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.257	MM	0.4992	31.49248	1.05141	0.5806
2	13.609	BB	0.6056	5392.74170	119.25320	99.4194

A 10 mL dried two-neck round bottom flask was charged with (3*R*,6*S*)-**3a** (26.7 mg, 0.1 mmol), then THF (2 mL) under an argon atmosphere, diisopropylazodiformate (DIAD) (0.2 mmol) was added dropwise under 0 ℃ and stirred for 10 minutes. Then diphenylphosphoryl azide (DPPA) (0.2 mmol) was added dropwise under 0 ℃, and the reaction mixture was stirred at room temperature for 16 h. Then the solution was concentrated under reduced pressure. The ^{1}H NMR analysis of the crude reaction mixture showed a >20:1 diastereomer ratio of the product **8**. Finally, the crude product was purified by silica gel column chromatography to provide the product as colorless oil.

Methyl (2*R*,5*R*)-5-azido-2-methyl-5-phenyl-2-(pyridin-2-yl)pentanoate (8):



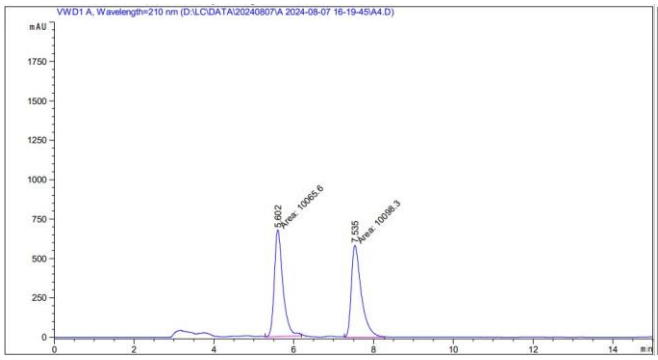
yield (23.4 mg, 72%); colorless oil; $[\alpha]^{25}_D$ = +4.8 (*c* 0.78, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 99% ee (Chiralpak AD-H, i-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 5.60 and 7.54 min.

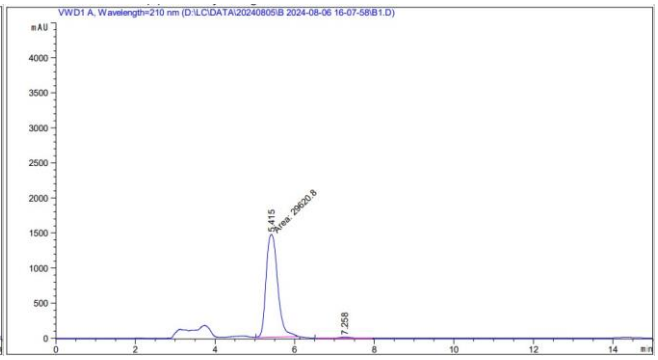
^{1}H NMR (400 MHz, Chloroform-d) δ 8.60 – 8.45 (m, 1H), 7.75 – 7.50 (m, 1H), 7.37 – 7.27 (m, 3H), 7.25 – 7.18 (m, 3H), 7.16 – 7.11 (m, 1H), 4.36 (dd, *J* = 7.8, 6.4 Hz, 1H), 3.67 (s, 3H), 2.27 – 2.17 (m,

1H), 2.04 – 1.95 (m, 1H), 1.75 – 1.64 (m, 2H), 1.58 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-d) δ 175.8, 162.3, 149.0, 139.3, 136.5, 128.8, 128.3, 126.9, 121.8, 120.4, 66.5, 52.9, 52.2, 34.9, 31.2, 22.3.

HRMS (ESI+) Calcd. For $C_{18}H_{20}N_4O_2$+ ([M+H]+): 325.1659, found: 325.1656.



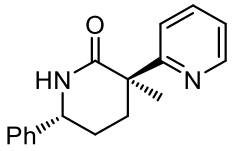


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.602	MM	0.2479	1.00656e4	676.67358	49.9188
2	7.535	MM	0.2887	1.00983e4	583.02899	50.0812

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.415	MM	0.3363	2.96208e4	1467.78027	99.2397
2	7.258	VB R	0.2673	226.92879	12.15505	0.7603

A 10 mL dried two-neck round bottom flask was charged with **8** (32.4 mg, 0.1 mmol), PPh_3 (0.20 mmol), H_2O (0.1 mL) and THF (2 mL). The mixture was stirred at 70 ºC for 12 h. After completion, the mixture was concentrated in vacuo. The ^{1}H NMR analysis of the crude reaction mixtures showed a >20:1 diastereomer ratio of the product **9**. Finally, the mixture was purified by column chromatography with EA:PE = 2:1 to give the desired product as colorless oil.

(3*R*,6*R*)-3-methyl-6-phenyl-3-(pyridin-2-yl)piperidin-2-one (9):



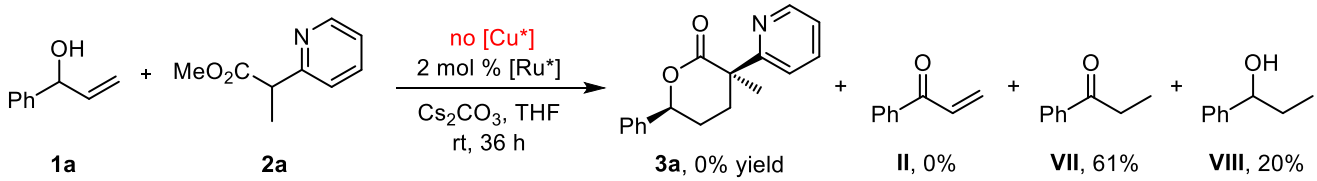
yield (22.6 mg, 85%); colorless oil; $[\alpha]^{25}_D$ = +15.2 (*c* 0.66, CH_2Cl_2);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.65 – 8.46 (m, 1H), 7.70 – 7.64 (m, 1H), 7.49 – 7.45 (m, 1H), 7.43 – 7.36 (m, 2H), 7.34 – 7.29 (m, 3H), 7.19 – 7.12 (m, 1H), 5.98 (s, 1H), 4.72 (t, *J* = 5.3 Hz, 1H), 2.52 – 2.41 (m, 1H), 2.19 – 2.04 (m, 1H), 1.95 – 1.79 (m, 2H), 1.76 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.2, 163.9, 149.1, 142.7, 136.6, 128.9, 127.9, 126.1, 121.7, 121.1, 57.5, 49.3, 33.4, 28.7, 25.0.

HRMS (ESI+) Calcd. For $C_{17}H_{18}N_2O^+$ ([M+H]$^+$): 267.1497, found: 267.1492.

7. Control Experiments



1a **2a** **3a**, 0% yield **II**, 0% **VII**, 61% **VIII**, 20%

To a clean and dried Schlenk tube was charged with allyl alcohol **1a** (0.6 mmol, 3.0 equiv), α-azaaryl acetate **2a** (0.2 mmol, 1.0 equiv), [Ru]-**1** complex (2 mol%), Cs_2CO_3 (0.3 mmol, 1.5 equiv) and THF (2 mL) were subsequently added to the tube, respectively. The mixtures were stirred at room temperature for 36 h. The crude mixture was filtered through a short silica gel plug to remove the metal complex, and the filtrate was concentrated to dryness. The crude product was analyzed by ^{1}H NMR.

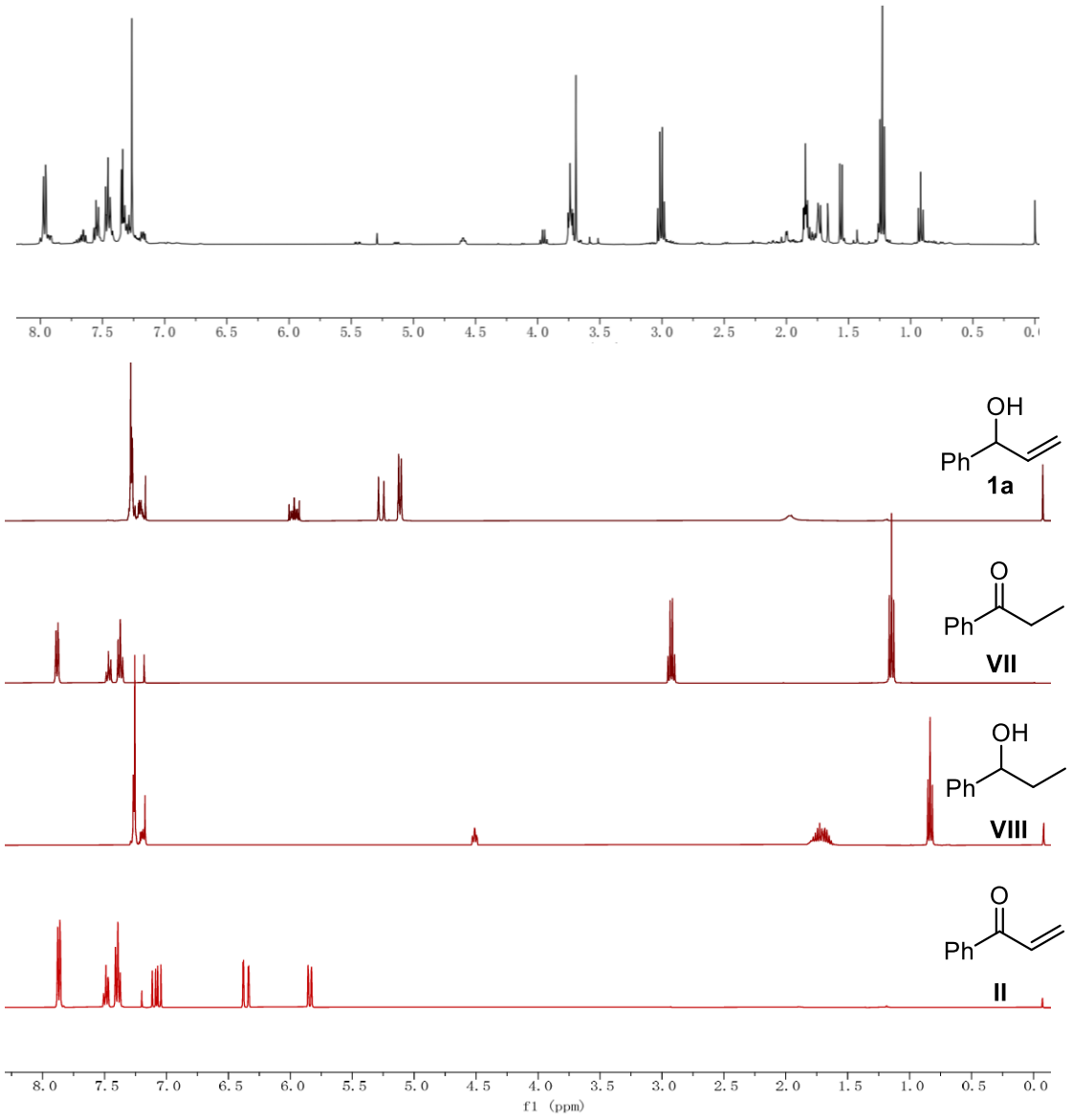
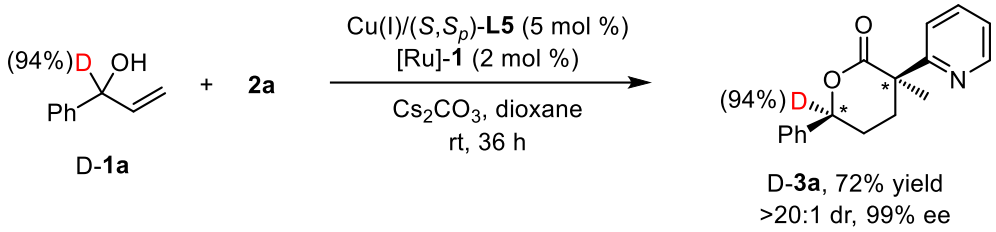
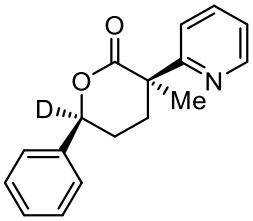


Figure S2: The crude ^{1}H NMR spectra of the reaction mixture.



To a clean and dried Schlenk tube was charged with $Cu(CH_3CN)_4PF_6$ (5 mol%, 3.7 mg) and (*S,S,S*$_p$)-**L5** (5.5 mol%, 6.0 mg) in glovebox, degassed THF (1 mL) was added to the tube under nitrogen atmosphere, and then the mixtures were stirred at room temperature for 30 min. Then, α-azaaryl acetate **2a** (0.2 mmol, 1.0 equiv), D-**1a** (0.6 mmol, 3.0 equiv), [Ru]-**1** complex (2 mol%), Cs_2CO_3 (0.3 mmol, 1.5 equiv) and THF (1 mL) were subsequently added to the tube, respectively. The mixture was stirred at room temperature for 36 h. Upon completion, the crude mixture was filtered through a short silica gel plug to remove the metal complex, and the filtrate was concentrated to dryness. The crude product was analyzed by ^{1}H NMR to determine the diastereoselectivity. Then the residue was purified by column chromatography to give the desired product D-**3a** which was then directly analyzed by HPLC to determine the enantiomeric excess.

(3*R*,6*S*)-3-methyl-6-phenyl-3-(pyridin-2-yl)tetrahydro-2H-pyran-2-one-6-d(D-**3a):**

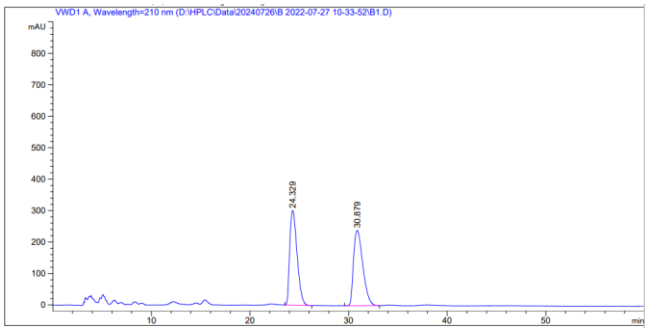


yield (38.6 mg, 72%); colorless oil; $[\alpha]^{25}_D$ = +6.6 (*c* 0.85, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: >99% ee (Chiralpak IE, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 24.33 and 30.88 min.

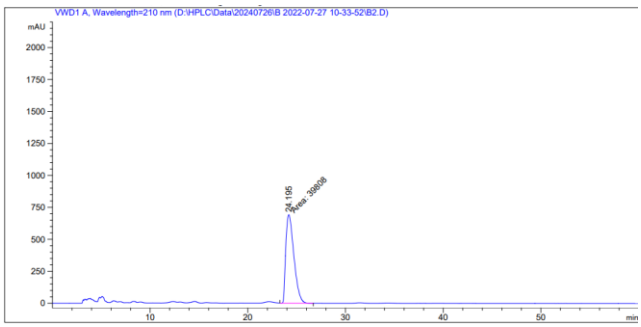
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67–8.53 (m, 1H), 7.76–7.65 (m, 1H), 7.51–7.41 (m, 1H), 7.34–7.28 (m, 5H),7.22–7.15 (m, 1H), 2.75–2.67 (m, 1H), 2.16–2.03 (m, 1H), 2.00–1.92 (m, 1H), 1.85–1.75 (m, 1H),1.73 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.5, 162.3, 149.1, 140.1, 136.9, 128.5, 128.2, 125.9, 122.0, 120.8, 83.6 (t, *J* = 25.3 Hz), 50.3, 34.3, 28.6, 26.9.

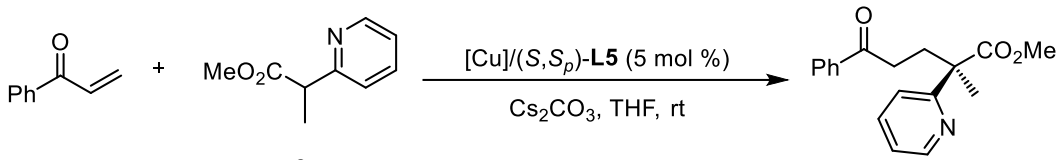
HRMS (ESI+) Calcd. For $C_{17}H_{17}DNO_2^+$ ($[M+H]^+$): 269.1395, found: 269.1397.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.329	BB	0.8236	1.56748e4	301.45047	50.0378
2	30.879	VB R	1.0037	1.56511e4	239.41792	49.9622



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.195	FM	0.9587	3.98080e4	692.06024	100.0000

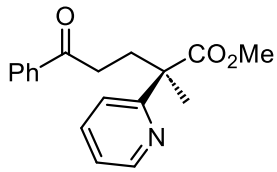


2a

12, 76% yield, 90% ee

To a clean and dried Schlenk tube was charged with $Cu(CH_3CN)_4PF_6$ (5 mol%, 3.7 mg) and (S,S_p)-**L5** (5.5 mol%, 6.0 mg) in glovebox, degassed THF (1 mL) was added to the tube under nitrogen atmosphere, and then the mixtures were stirred at room temperature for 30 min. Then, α-azaaryl acetate **2a** (0.2 mmol, 1.0 equiv), α,β-unsaturated ketone (0.24 mmol, 1.2 equiv), Cs_2CO_3 (0.3 mmol, 1.5 equiv) and THF (1 mL) were subsequently added to the tube, respectively. The mixture was stirred at room temperature for 12 h. Upon completion, the residue was purified by column chromatography to give the desired product **12** which was then directly analyzed by HPLC to determine the enantiomeric excess.

Methyl (*R*)-2-methyl-5-oxo-5-phenyl-2-(pyridin-2-yl)pentanoate (12):

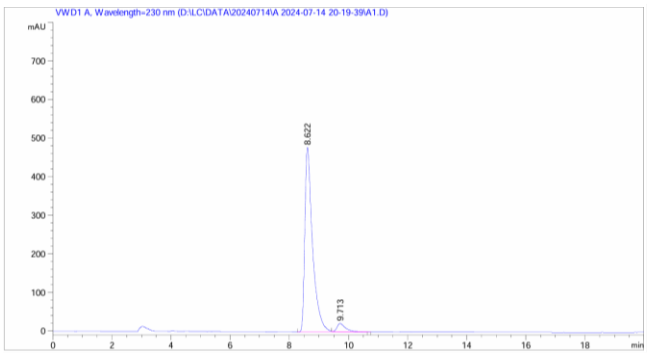


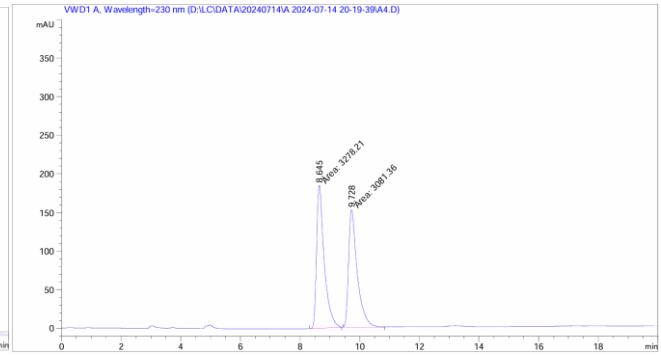
yield (45.1 mg, 76%); colorless oil; $[\alpha]^{25}_D$ = +14.2 (*c* 0.76, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (Chiralpak AD, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 8.65 and 9.73 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57–8.54 (m, 1H), 8.02–7.86 (m, 2H), 7.73–7.62 (m, 1H), 7.57–7.51 (m, 1H), 7.48–7.40 (m, 2H), 7.37–7.28 (m, 1H), 7.22–7.1 (m, 1H), 3.71 (s, 3 H), 3.10–2.81 (m, 2H), 2.65–2.35 (m, 2H), 1.66 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.8, 175.9, 162.5, 149.0, 136.8, 136.7, 133.0, 128.5, 128.1, 121.9, 120.5, 52.8, 52.2, 34.5, 32.9, 23.0.

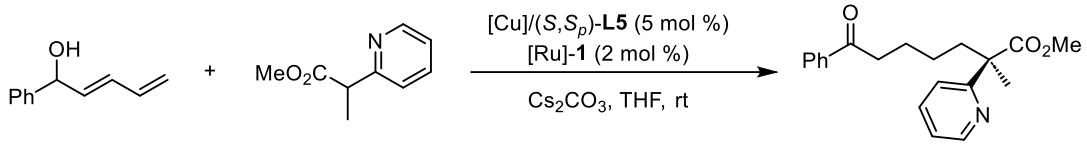
HRMS (ESI+) Calcd. For $C_{18}H_{20}NO_3^+$ ([M+H]$^+$): 298.1438, found: 298.1442.





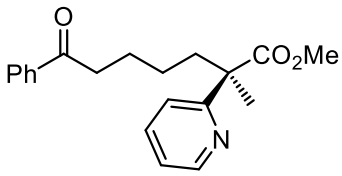
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.645	MM	0.2944	3278.21094	185.56514	51.5477
2	9.728	MM	0.3371	3081.35889	152.33296	48.4523

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.622	BV R	0.2643	8683.52832	478.13464	95.1320
2	9.713	VV E	0.2975	444.34360	21.93032	4.8680



1J **2a** **13**, 36% yield, 85% ee

Methyl (*R*)-2-methyl-7-oxo-7-phenyl-2-(pyridin-2-yl)heptanoate (13):

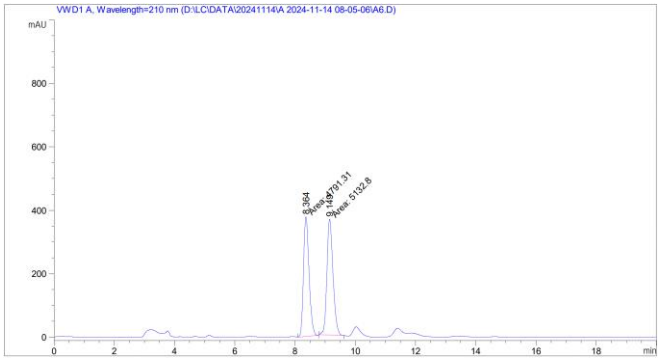


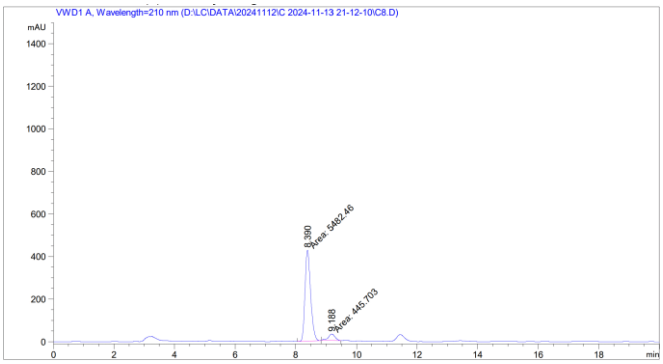
yield (23.4 mg, 36%); colorless oil; $[\alpha]^{25}_D$ = +8.6 (*c* 0.44, CH_2Cl_2); The product was analyzed by HPLC to determine the enantiomeric excess: 85% ee (Chiralpak AD, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 210 nm); t_r = 8.36 and 9.15 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58–8.51 (m, 1H), 8.02–7.89 (m, 2H), 7.68–7.59 (m, 1H), 7.58–7.50 (m, 1H), 7.49–7.40 (m, 2H), 7.27–7.22 (m, 1H), 7.17–7.09 (m, 1H), 3.67 (s, 3H), 2.99–2.91 (m, 2H), 2.27–1.98 (m, 2H), 1.87–1.67 (m, 2H), 1.58 (s, 3H), 1.36–1.23 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.2, 176.1, 163.1, 149.0, 137.0, 136.4, 132.9, 128.5, 128.0, 121.6, 120.4, 53.3, 52.1, 38.3, 38.0, 24.6, 24.4, 22.4.

HRMS (ESI+) Calcd. For $C_{20}H_{24}NO_3^+$ ([M+H]$^+$): 326.1751, found: 326.1751.





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.364	MM	0.2115	4791.31006	377.49402	48.2795
2	9.149	MM	0.2343	5132.79932	365.15616	51.7205

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.390	MM	0.2139	5482.46191	427.21664	92.4816
2	9.188	MM	0.2466	445.70309	30.12160	7.5184

8. References

[1] S. F. Musolino, O. S. Ojo, N. J. Westwood, J. E. Taylor, A. D. Smith, *Eur. Chem. J.* **2016**, *22*, 18916-18922.

[2] S.-Q. Yang, Y.-F. Wang, W.-C. Zhao, G.-Q. Lin, Z.-T. He, *J. Am. Chem. Soc.* **2021**, *143*, 7285-7291.

[3] C. J. Richards, A. W. Mulvaney, **1996**, *7*, 1419-1430.

[4] a) M. Y. Jin, Y. Zhou, D. Xiao, Y. You, Q. Zhen, G. Tao, P. Yu, X. Xing, *Angew. Chem. Int. Ed.* **2022**, *61*, e202112993; b) W. Baratta, E. Herdtweck, K. Siega, M. Toniutti, P. Rigo, *Organometallics* **2005**, *24*, 1660-1669.

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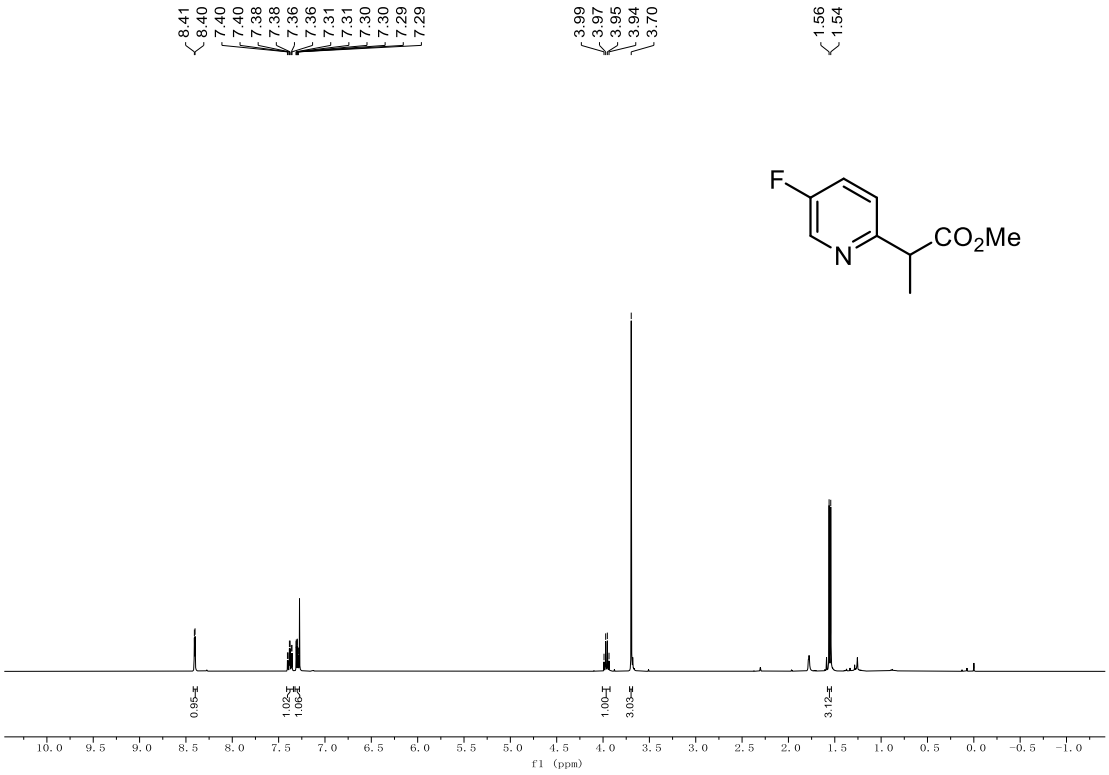
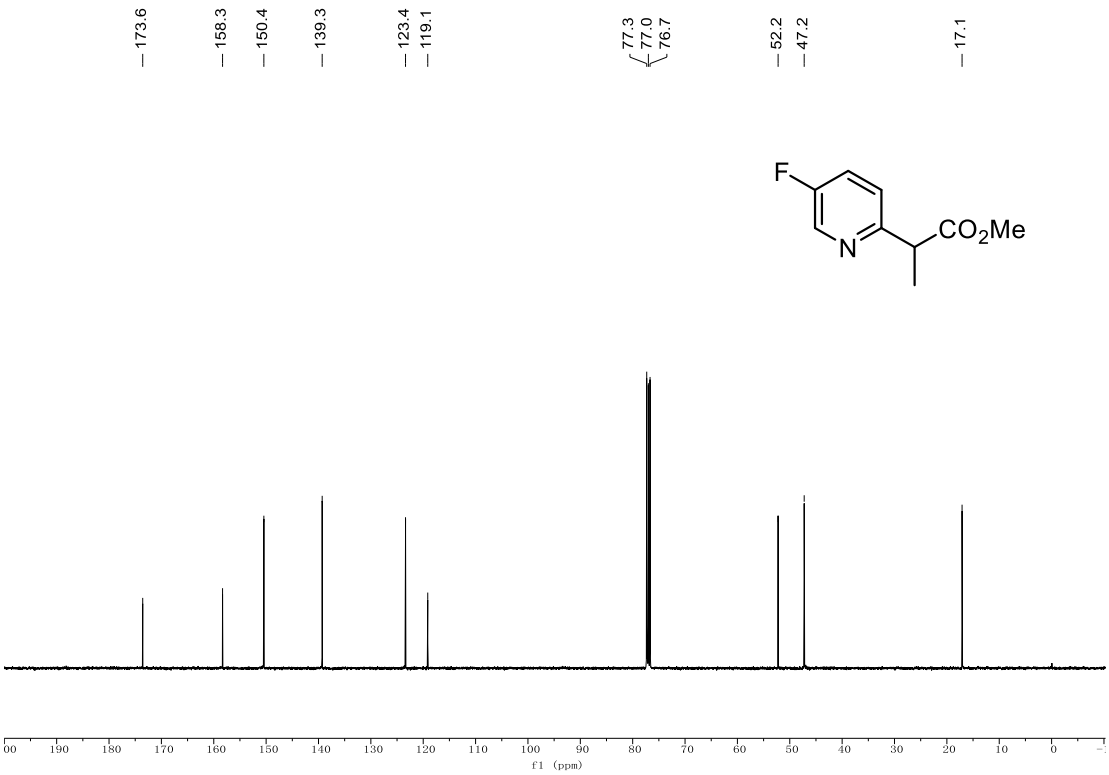
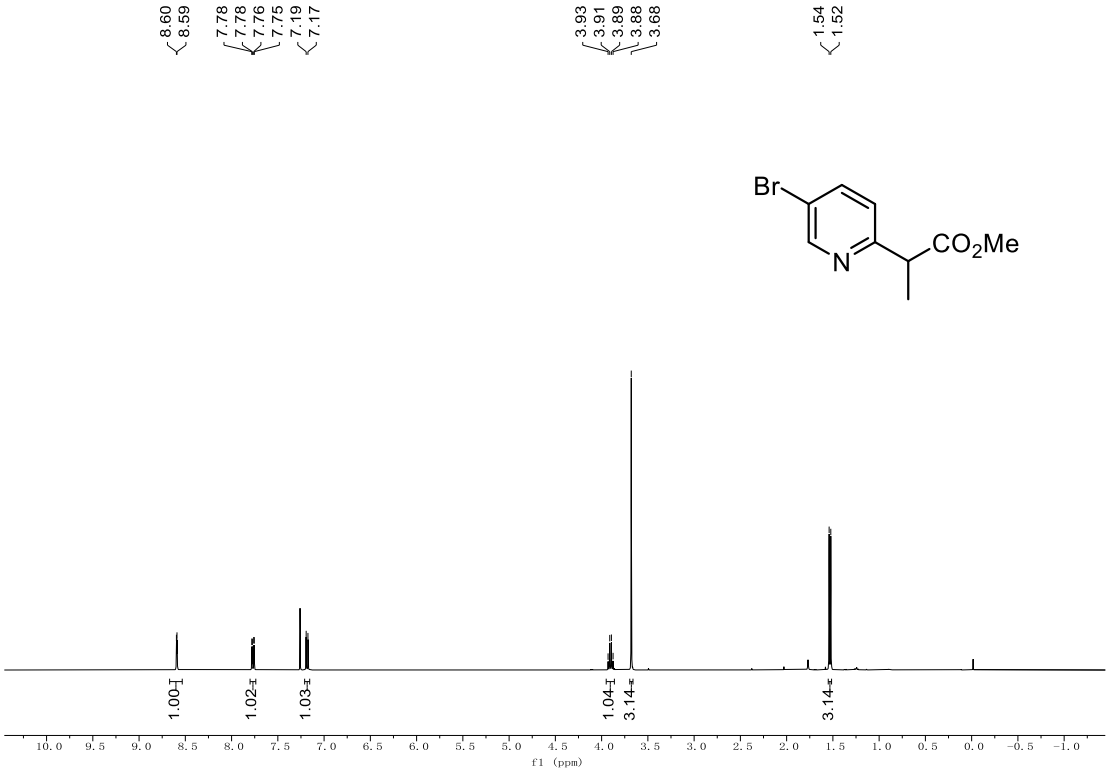
9. NMR Spectra



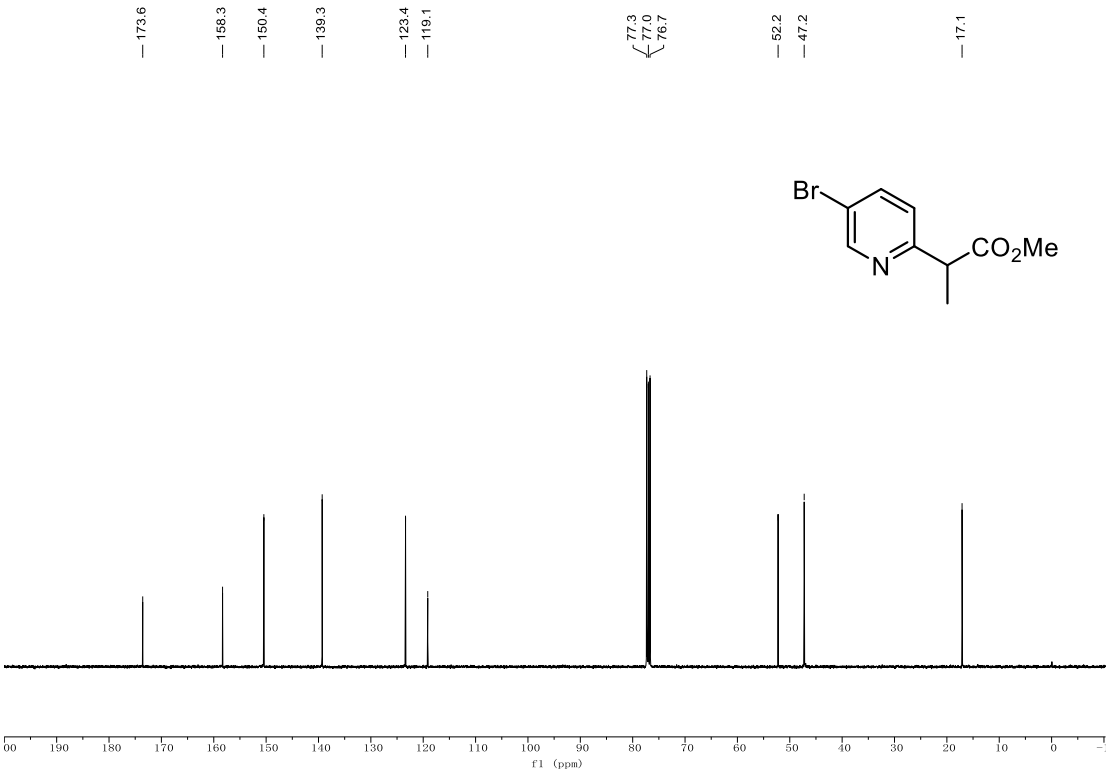
^{1}H NMR (400 MHz, $CDCl_3$) of **2b**



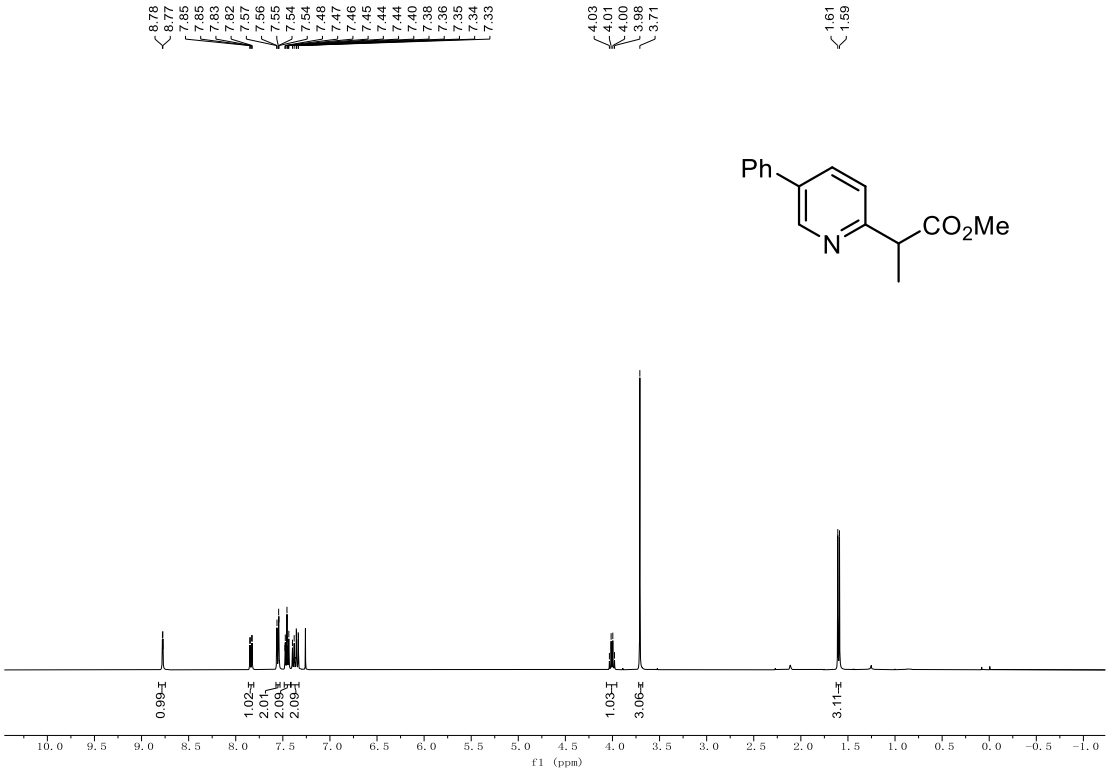
^{13}C NMR (101 MHz, $CDCl_3$) of **2b**



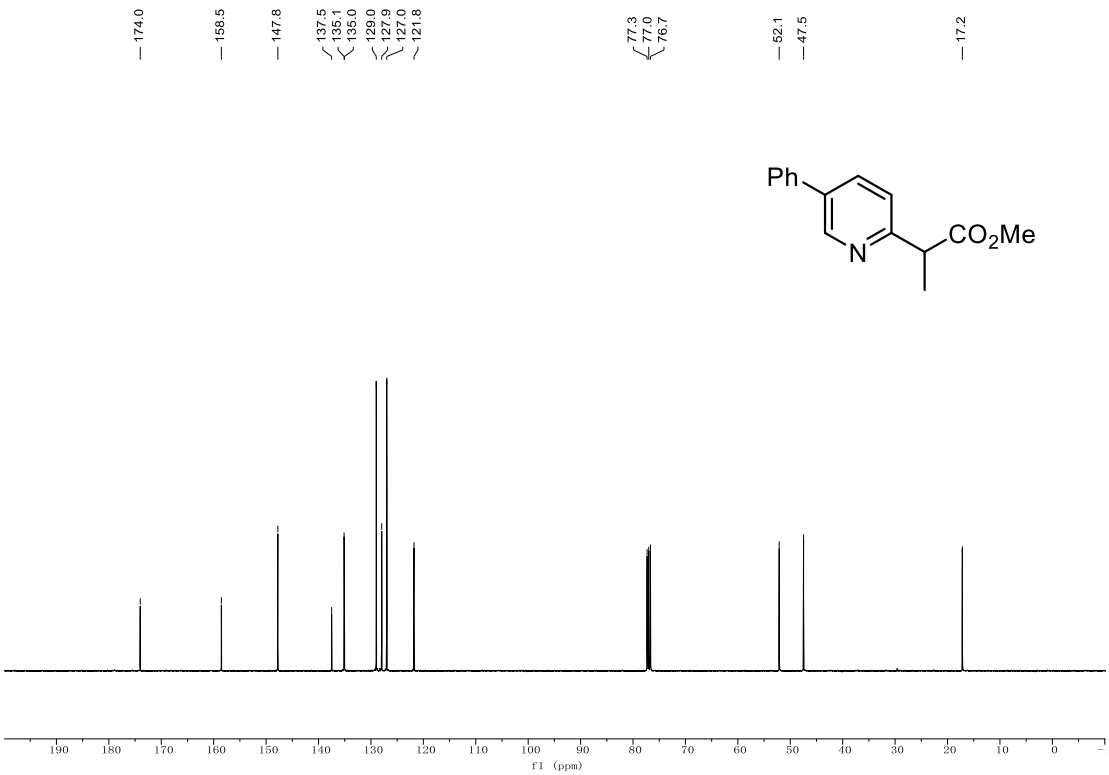
^{1}H NMR (400 MHz, $CDCl_3$) of **2c**



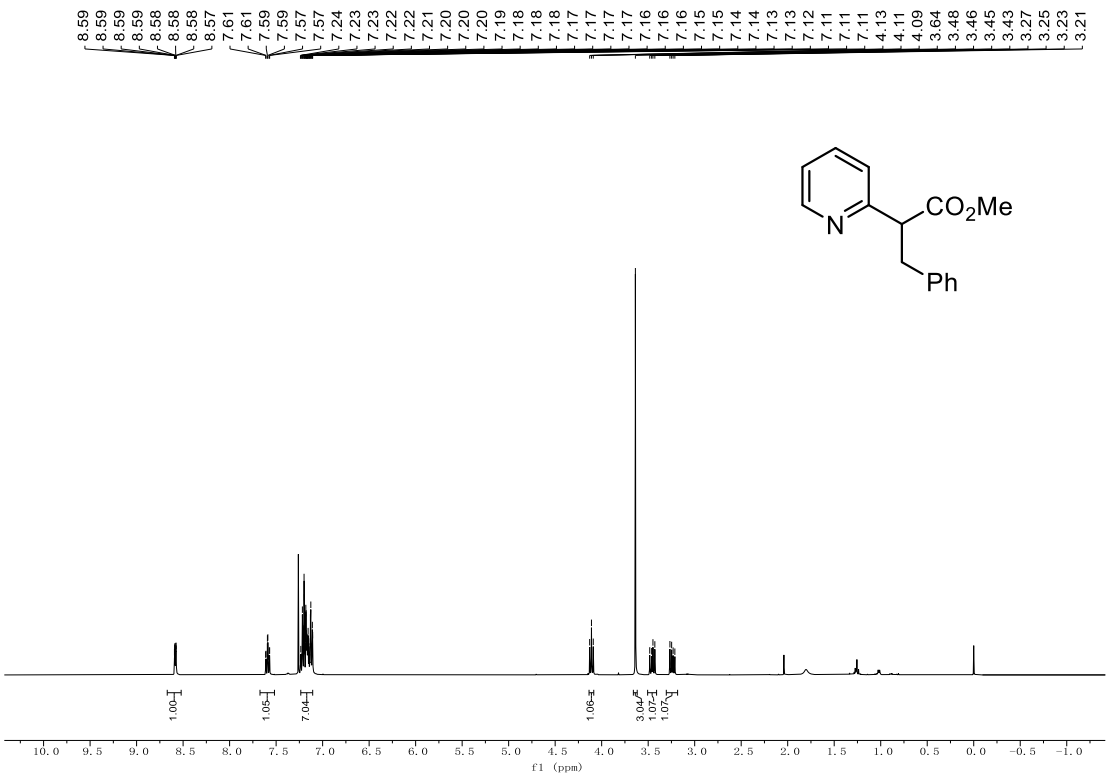
^{13}C NMR (101 MHz, $CDCl_3$) of **2c**



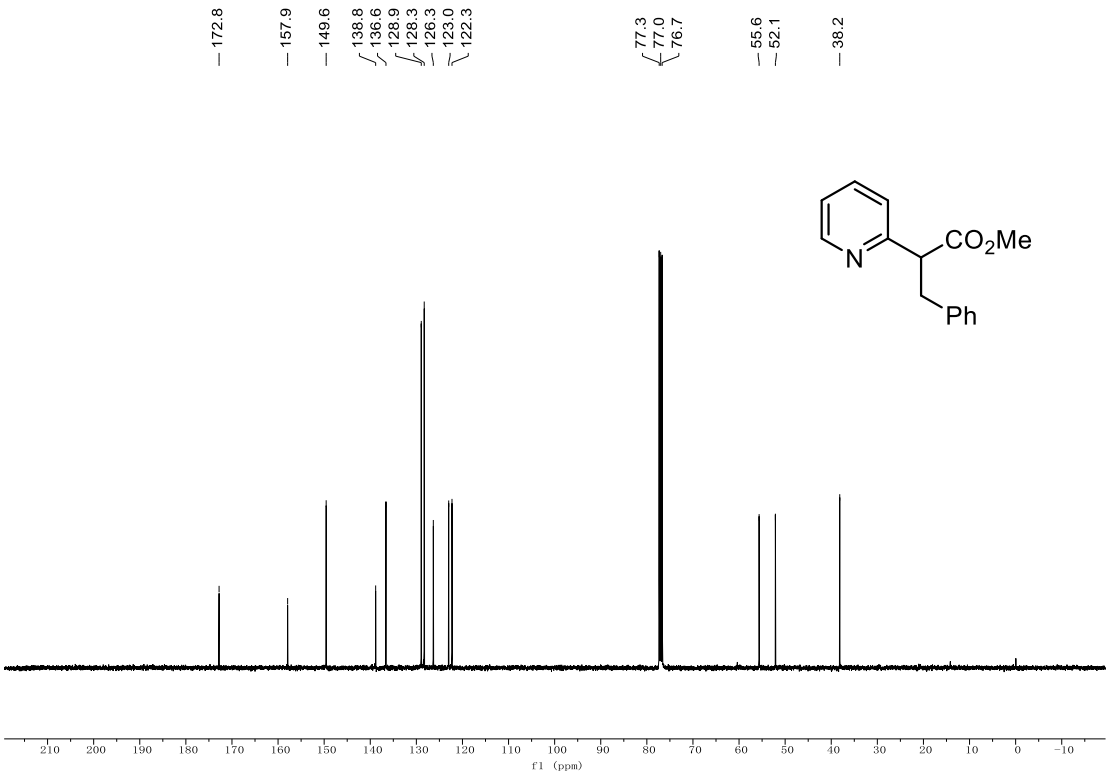
^{1}H NMR (400 MHz, $CDCl_3$) of **2d**



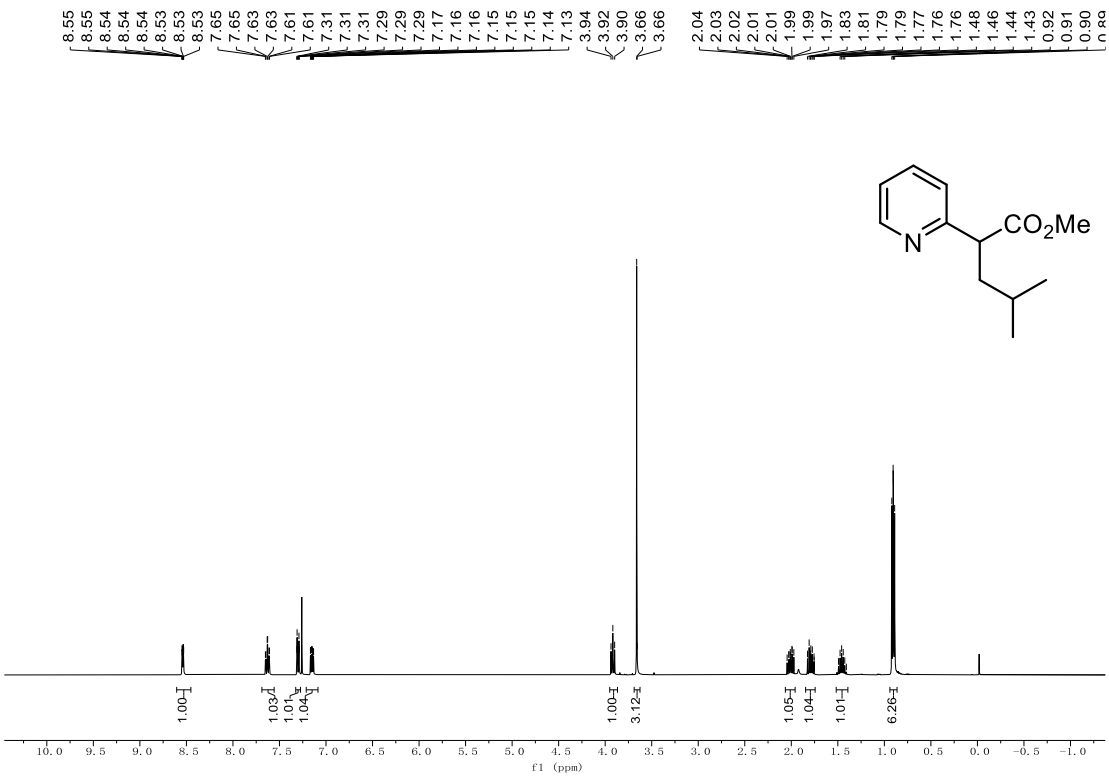
^{13}C NMR (101 MHz, $CDCl_3$) of **2d**



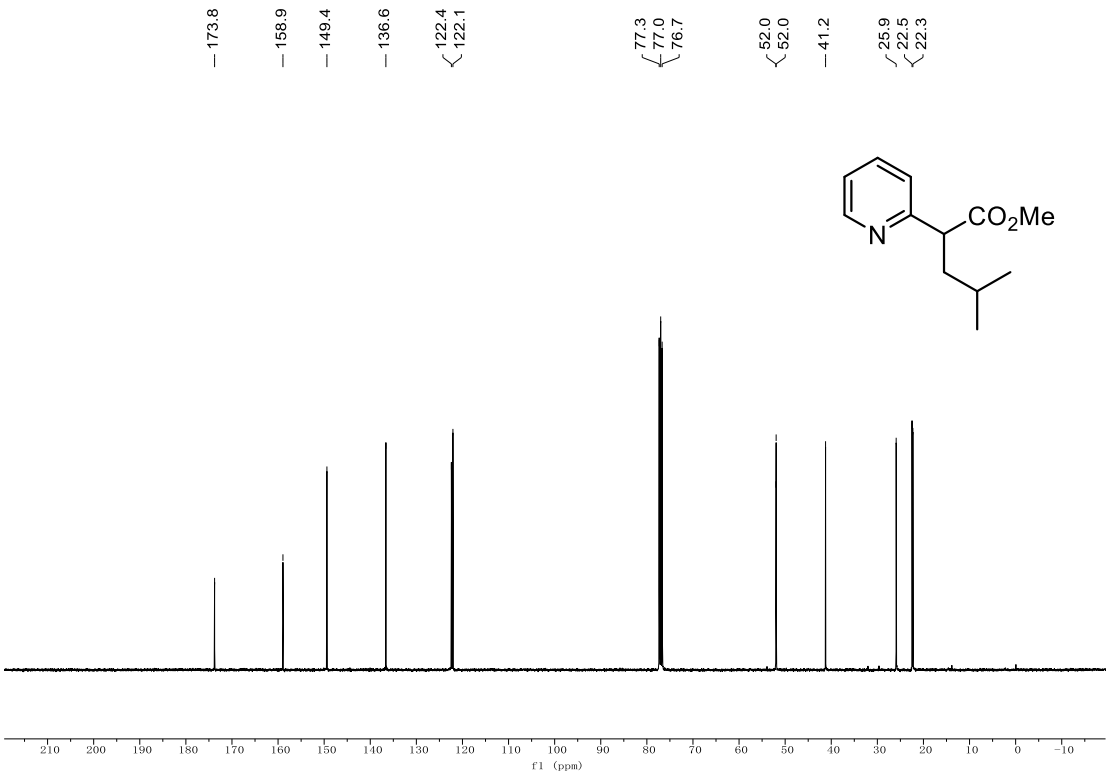
^{1}H NMR (400 MHz, $CDCl_3$) of **2m**



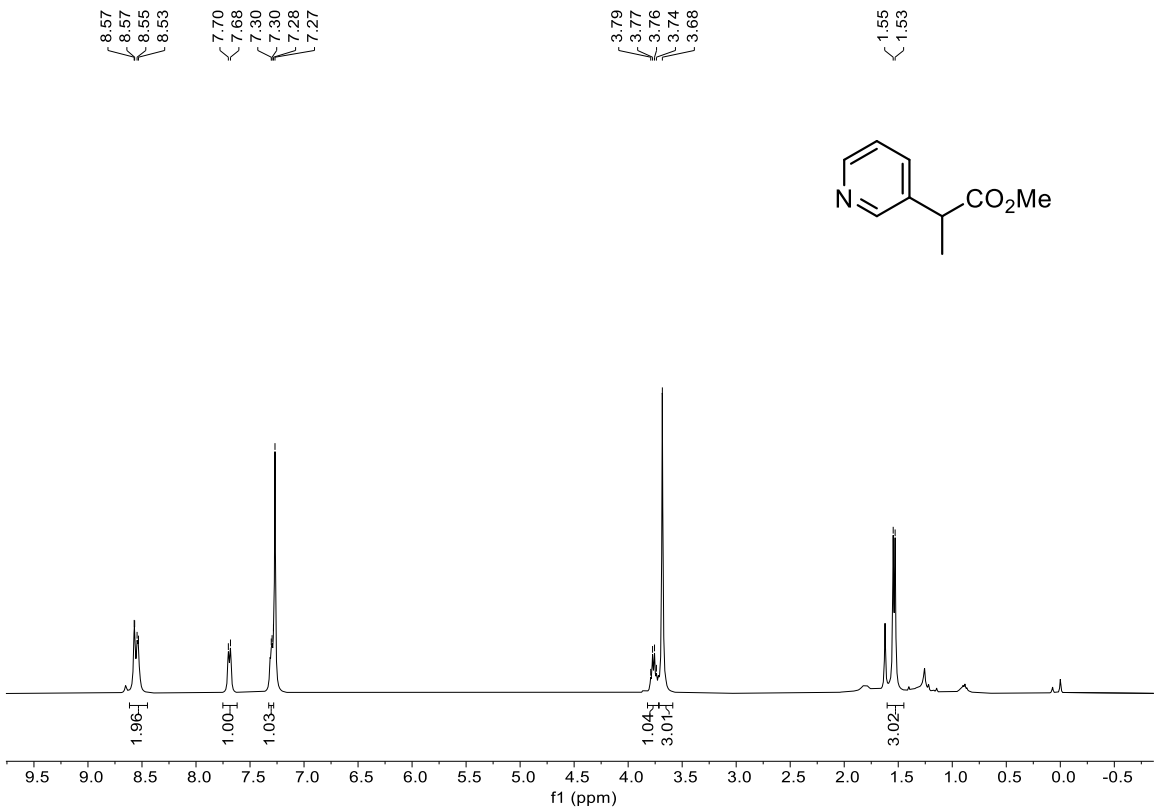
^{13}C NMR (101 MHz, $CDCl_3$) of **2m**



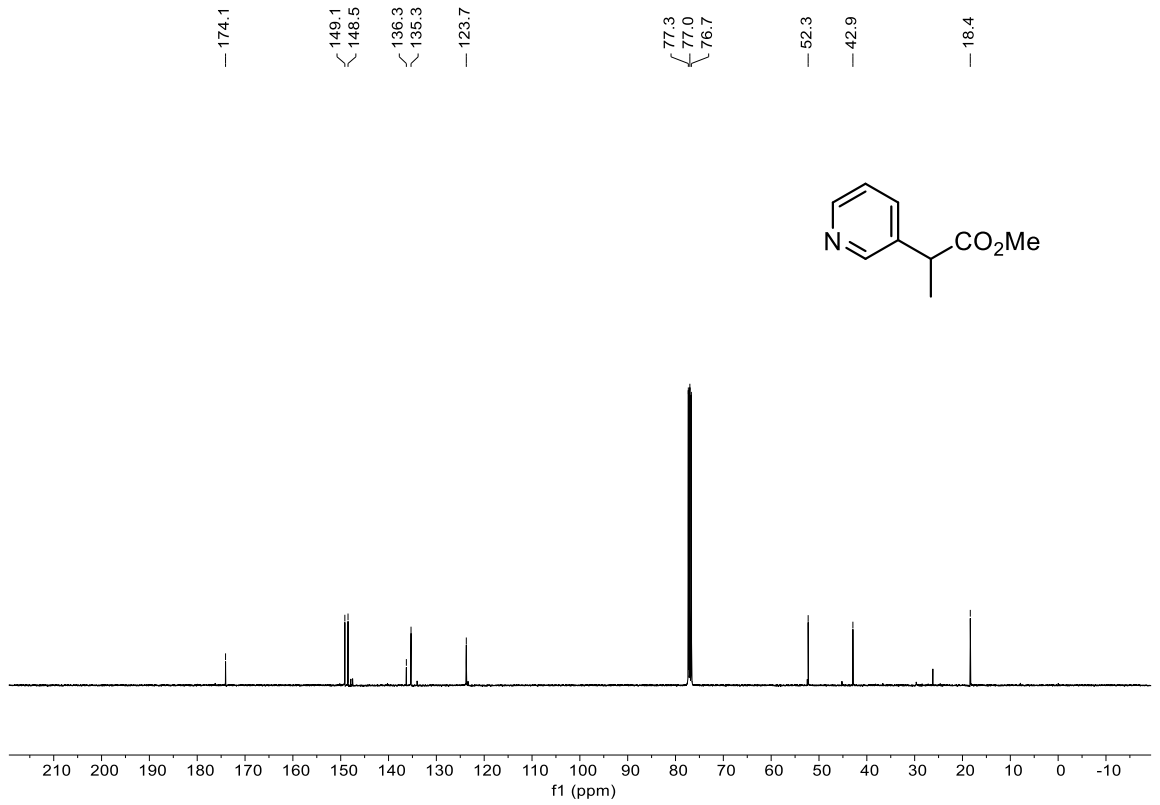
^{1}H NMR (400 MHz, $CDCl_3$) of **2p**



^{13}C NMR (101 MHz, $CDCl_3$) of **2p**



^{1}H NMR (400 MHz, $CDCl_3$) of **2t**



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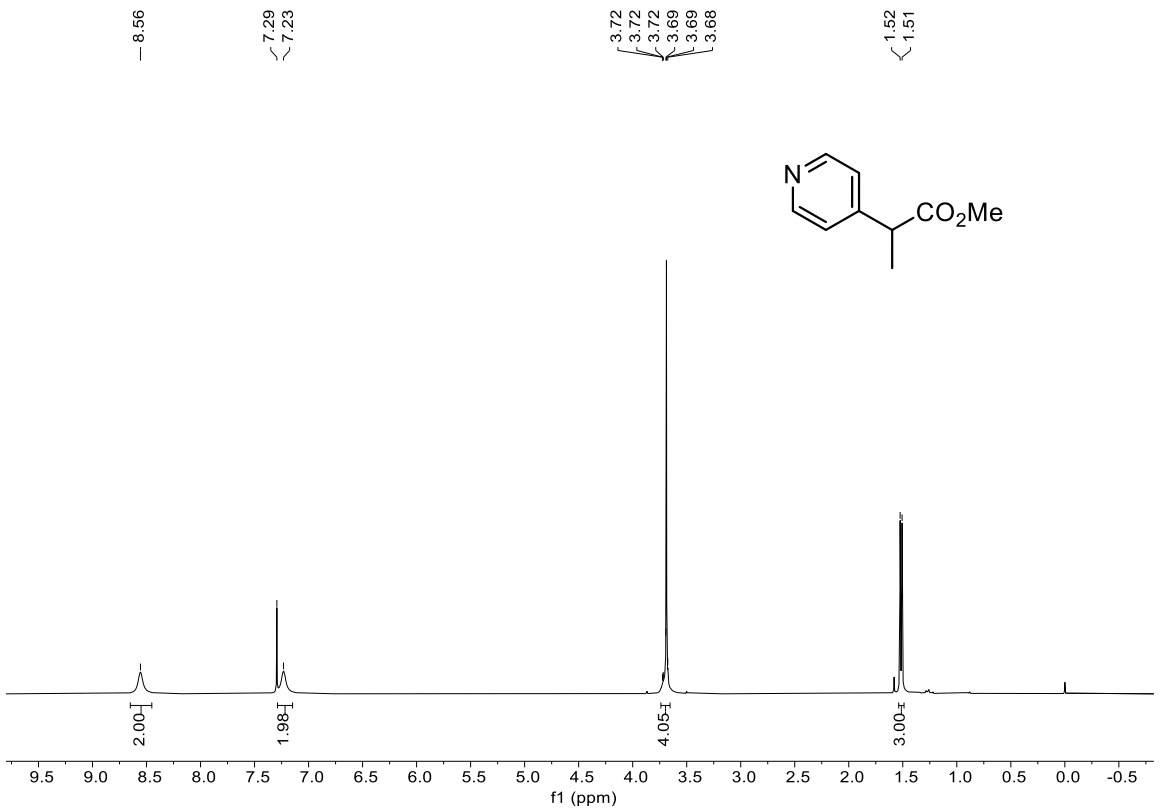

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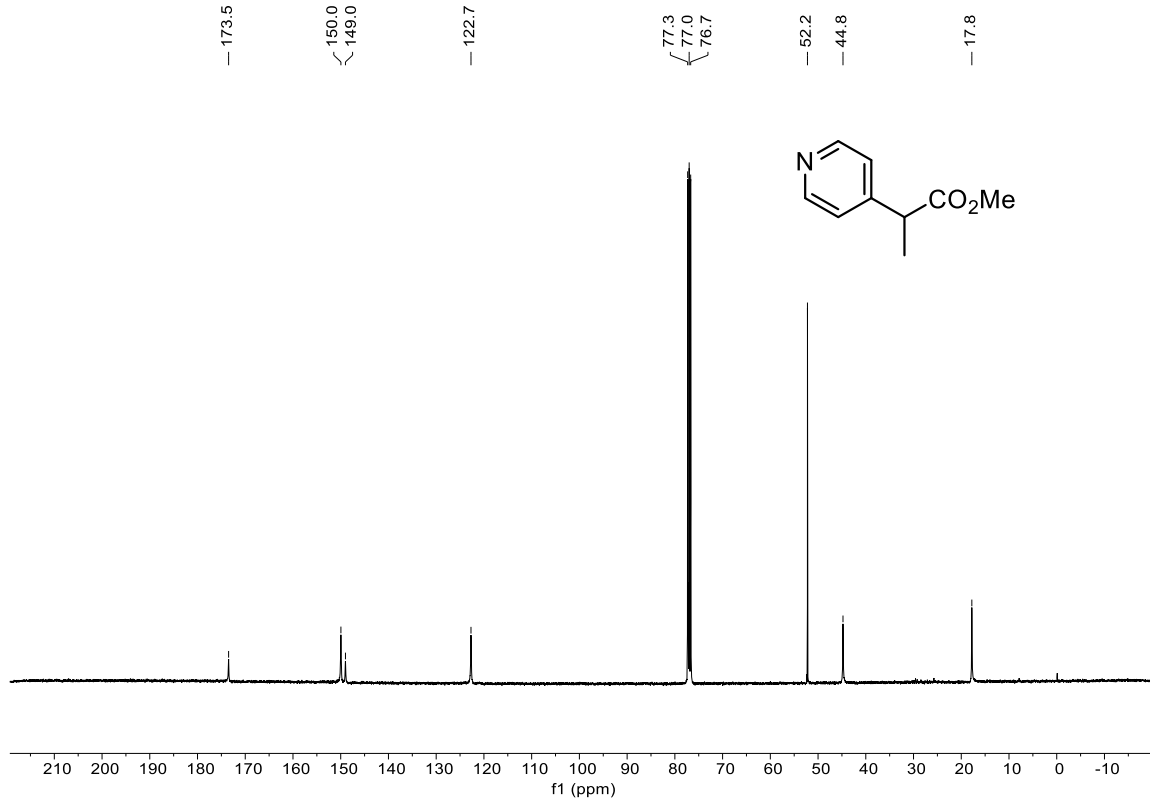

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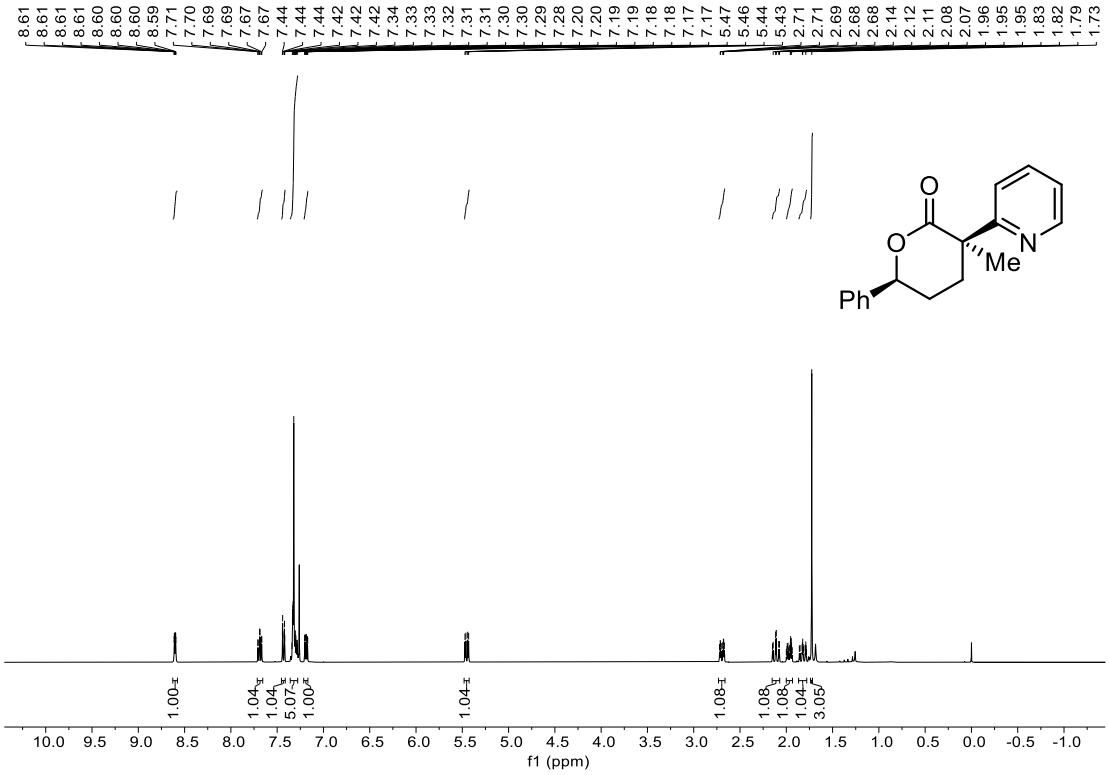
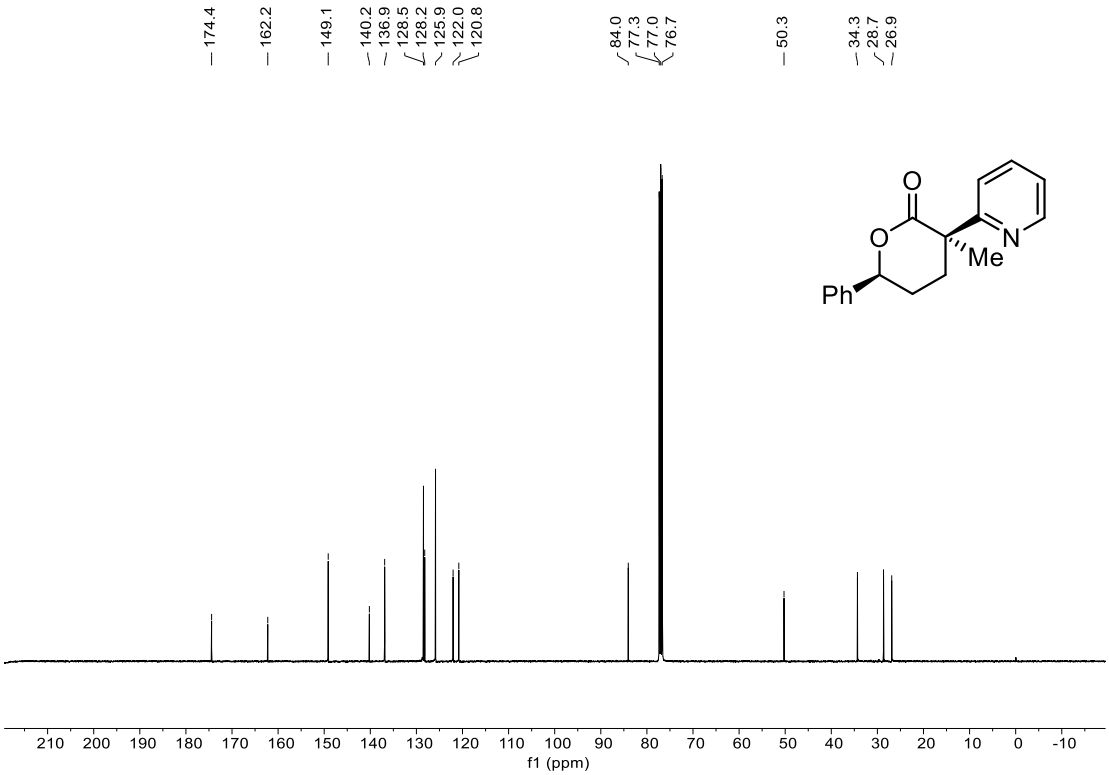
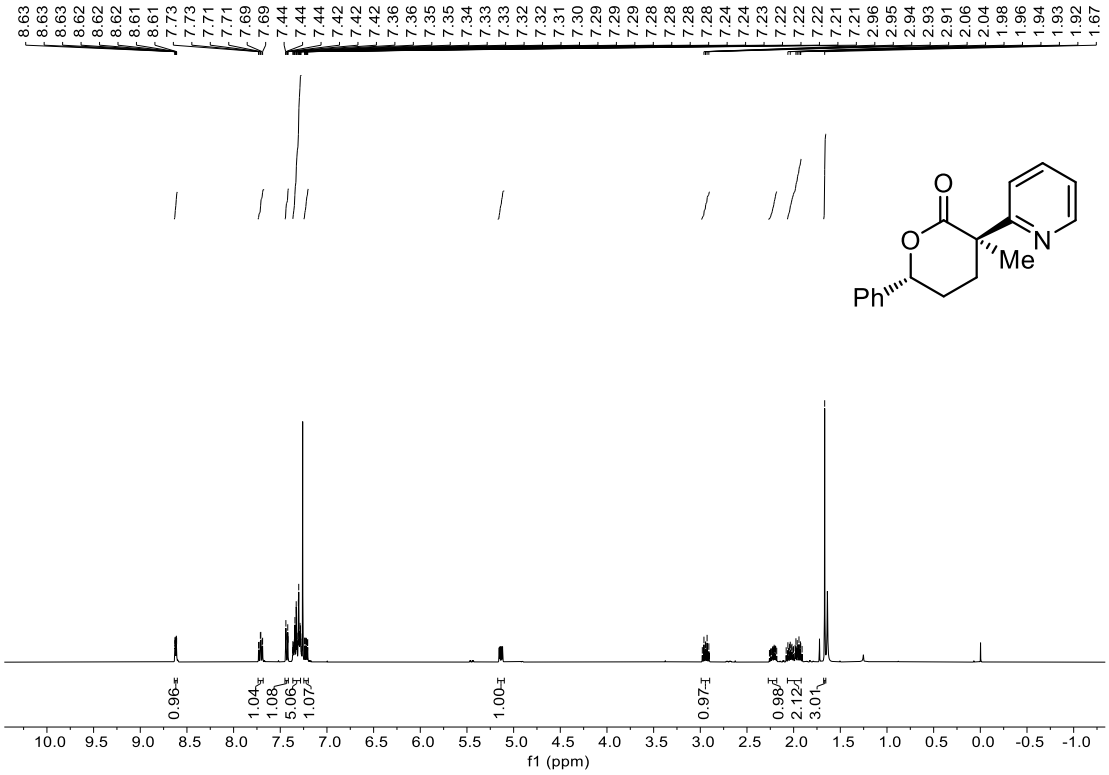


^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*,6*S*)-**3a**



^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3a**



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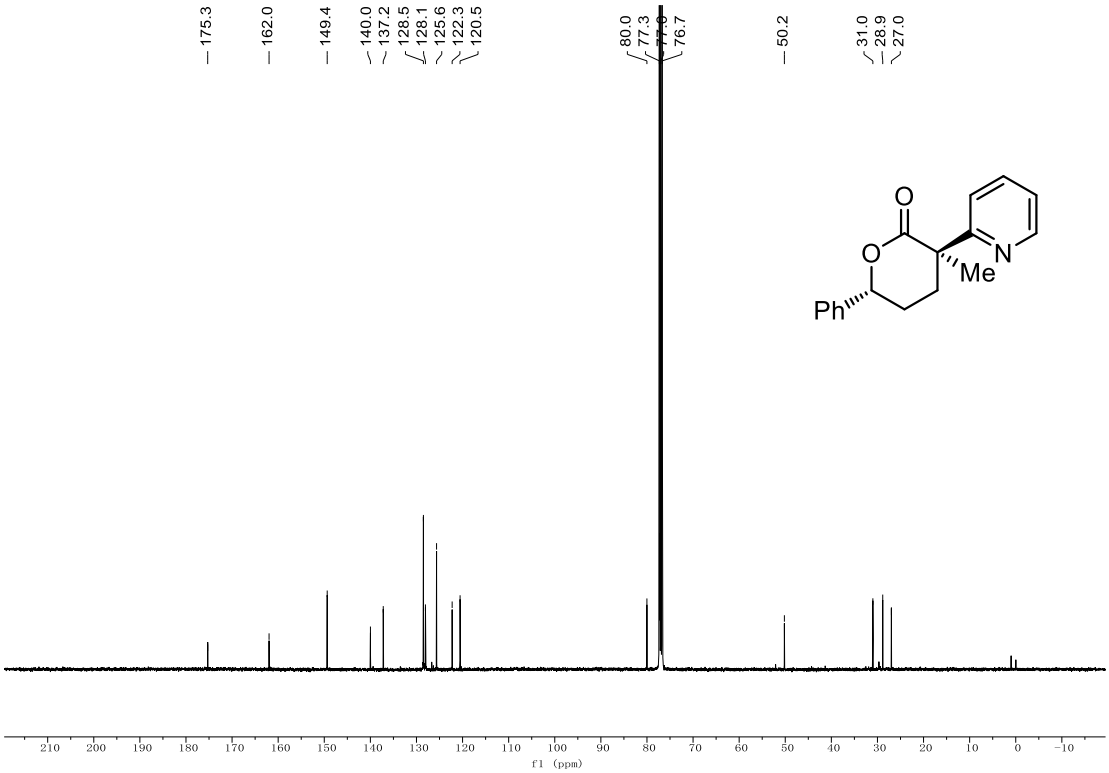
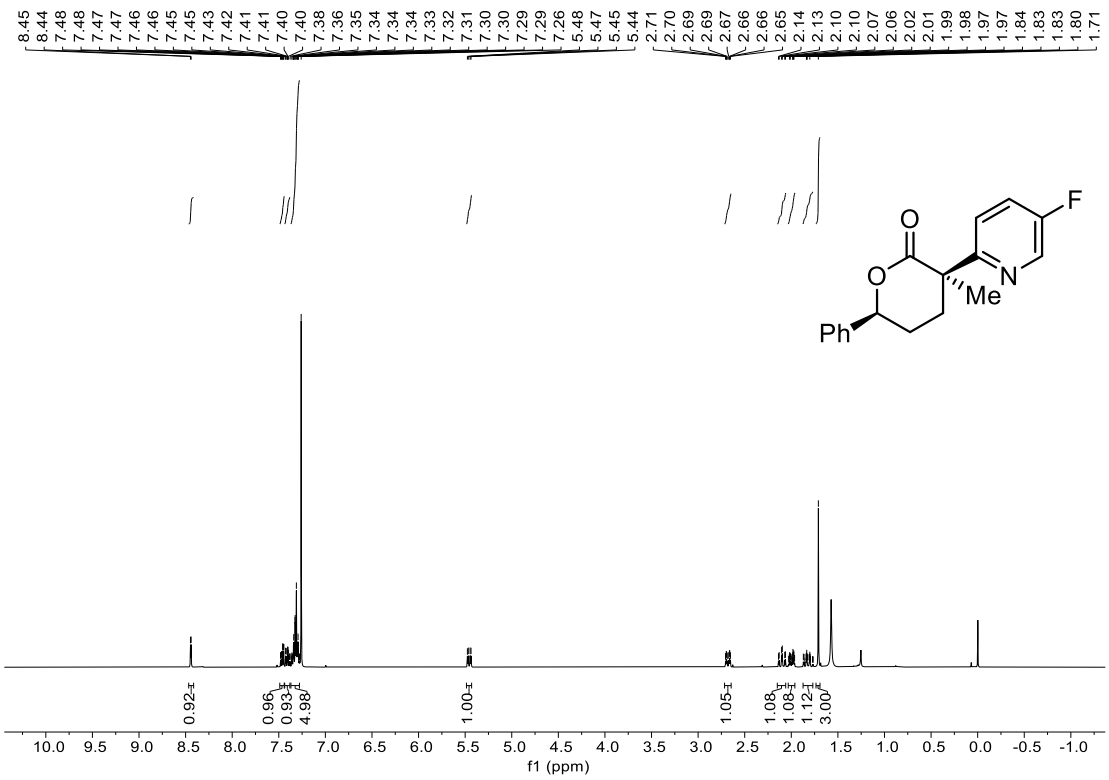
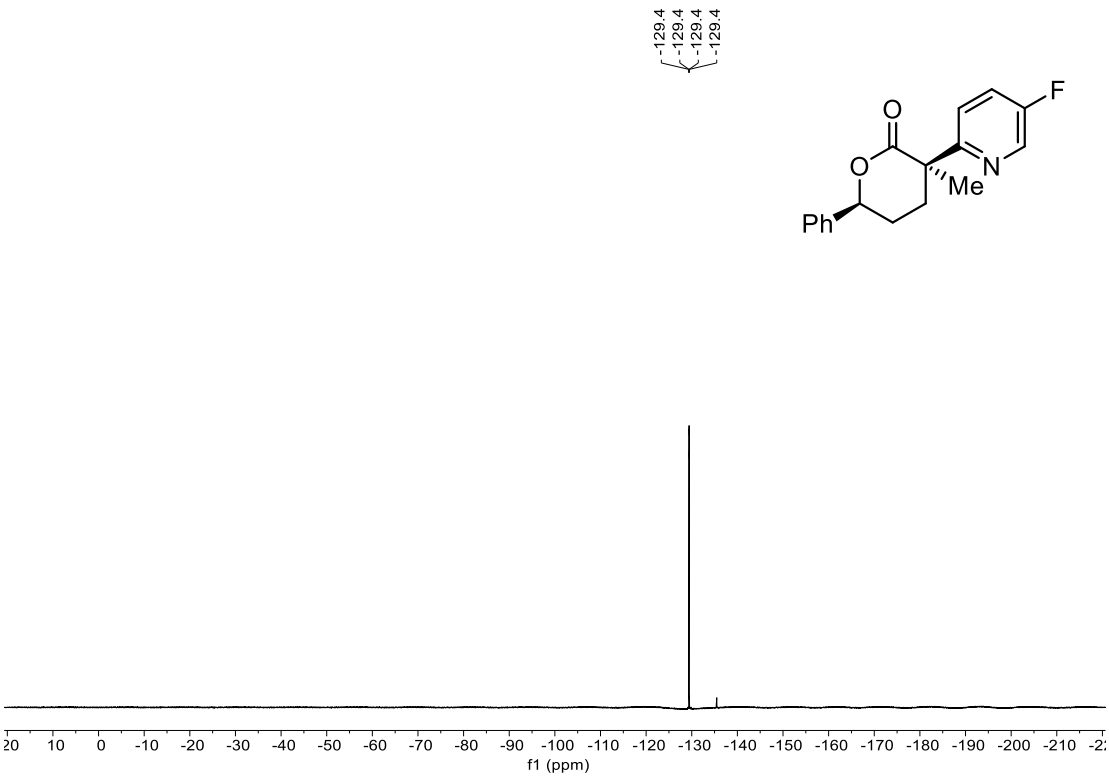


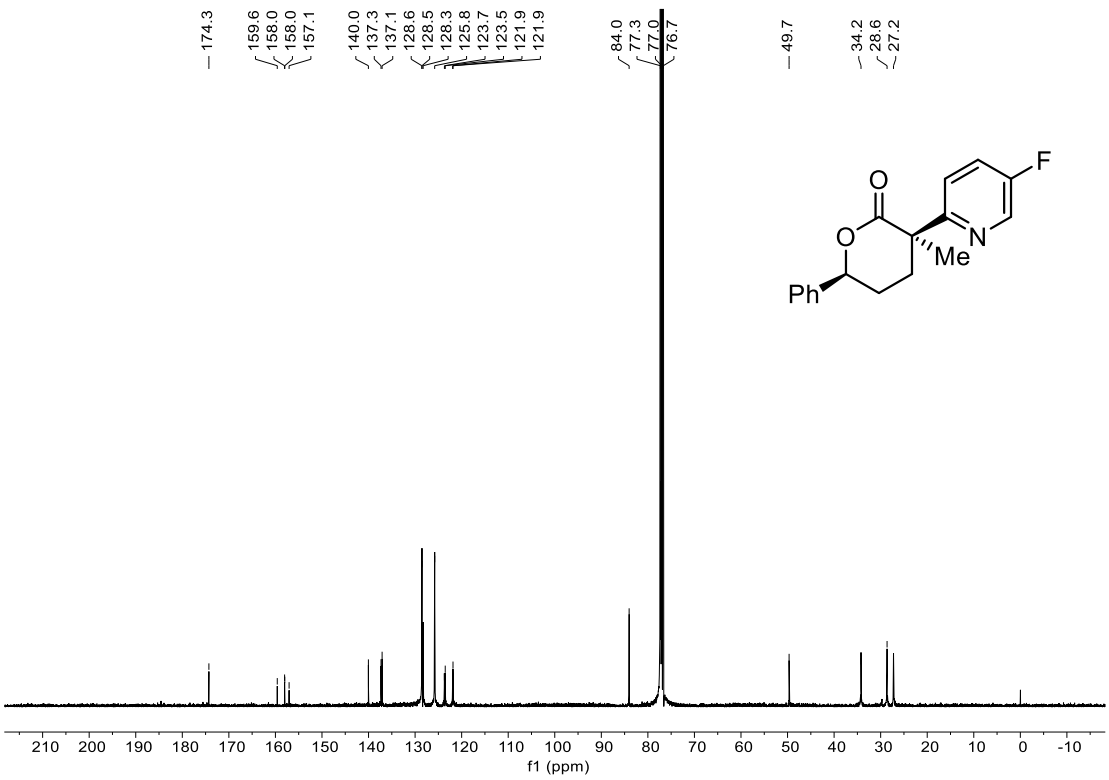
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*,6*R*)-**3a**



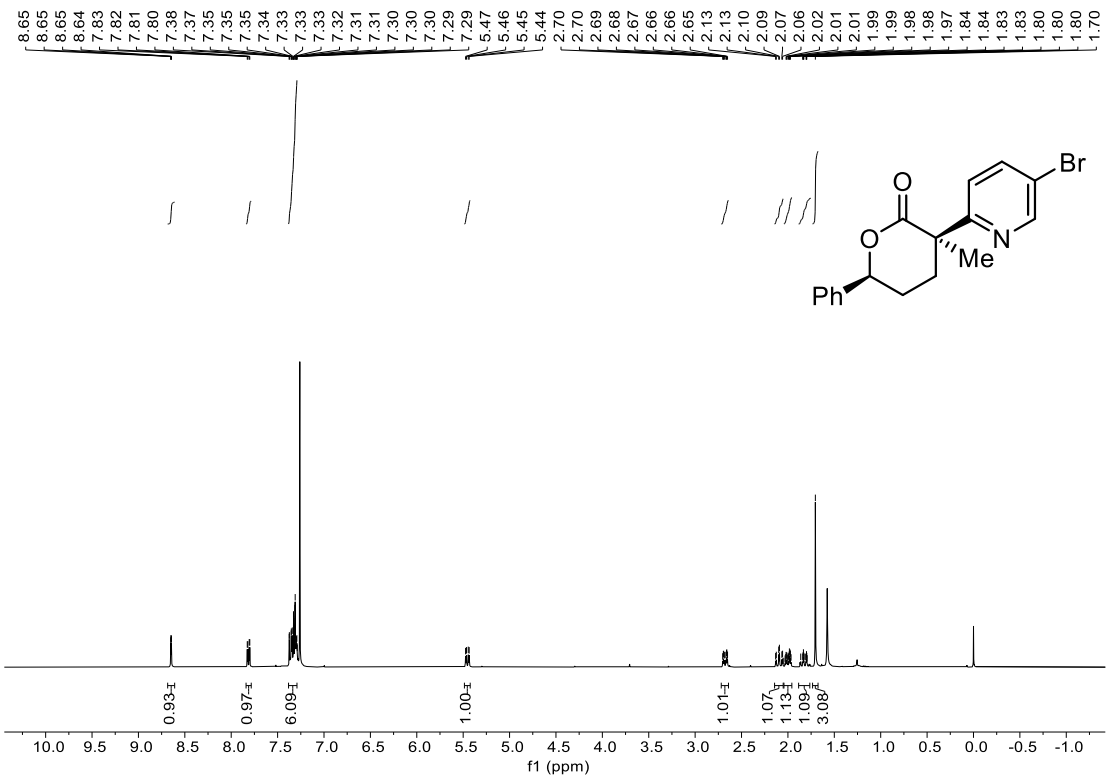
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3b**



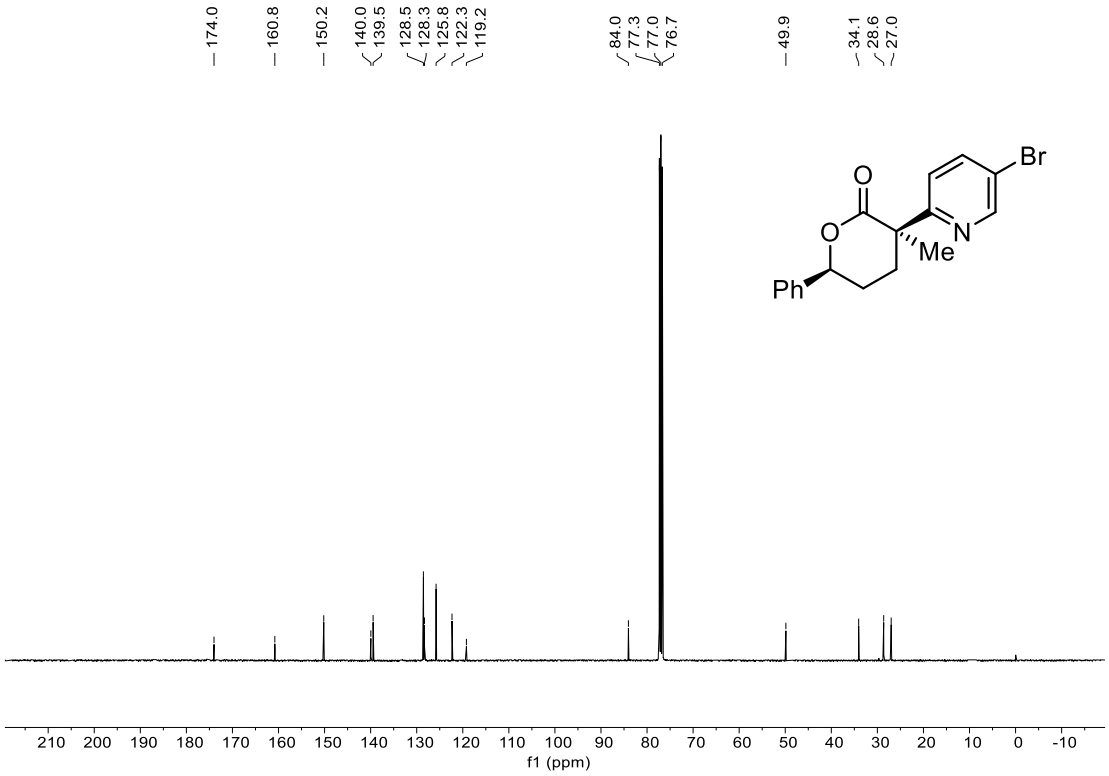
^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3b**



^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3b**



^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3c**



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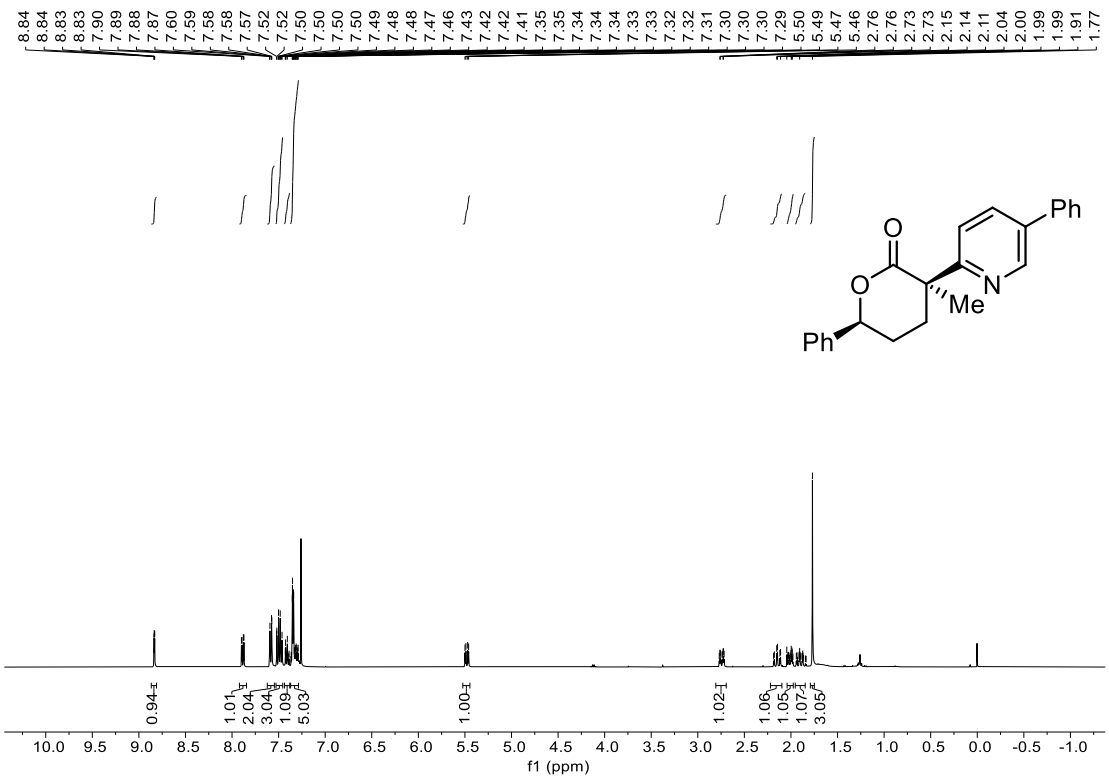

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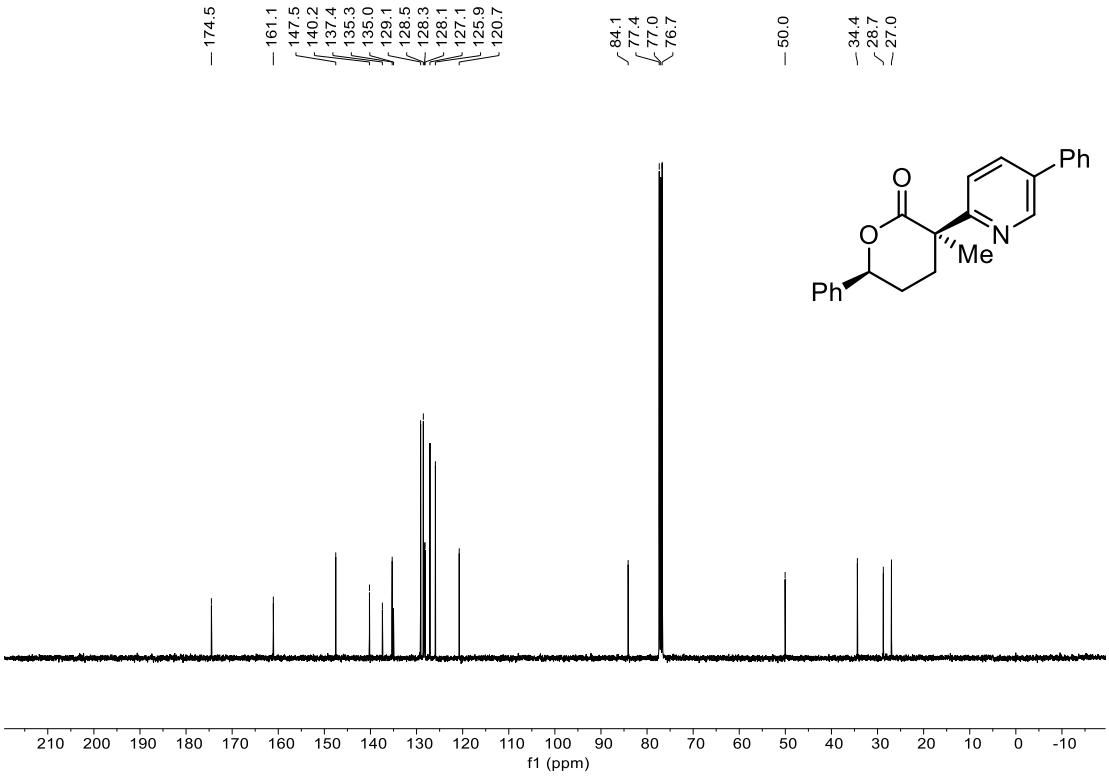
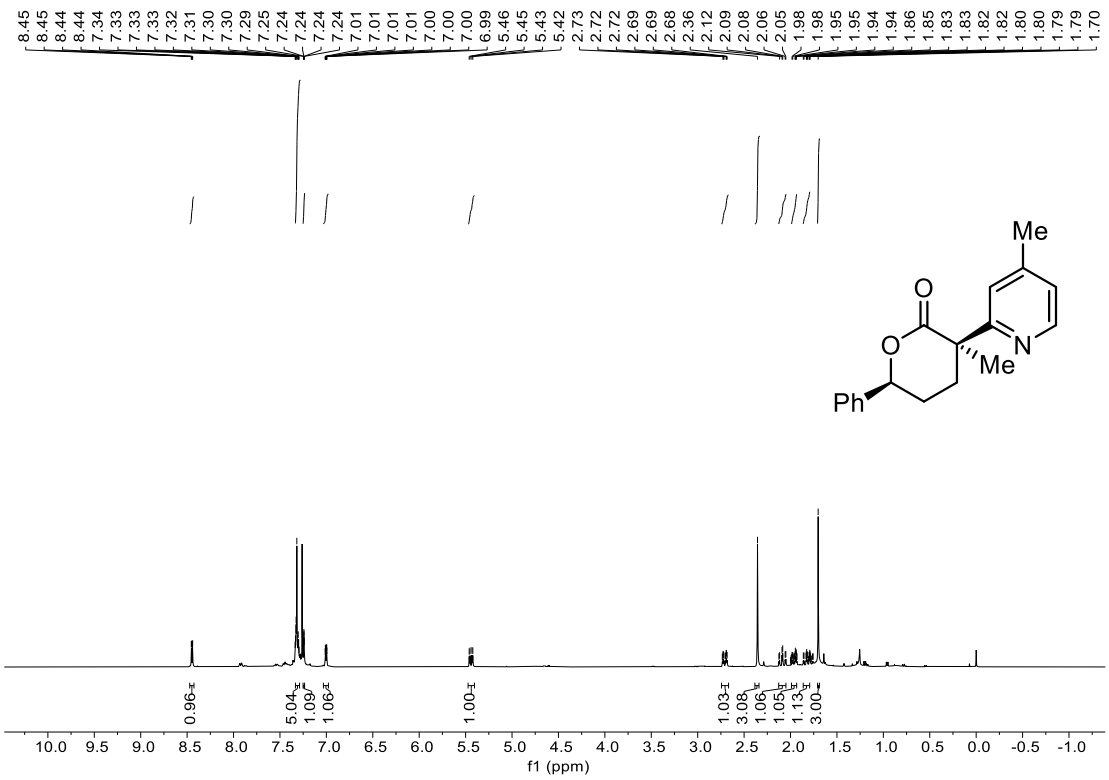
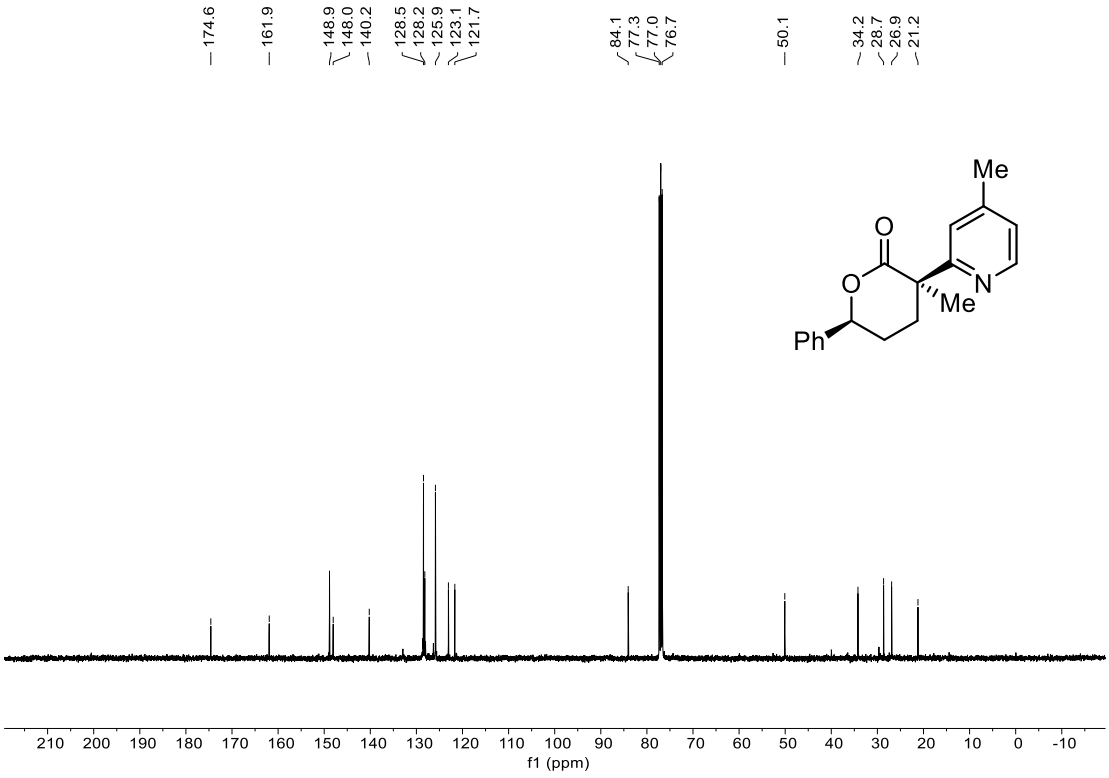


^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3d**



^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3e**



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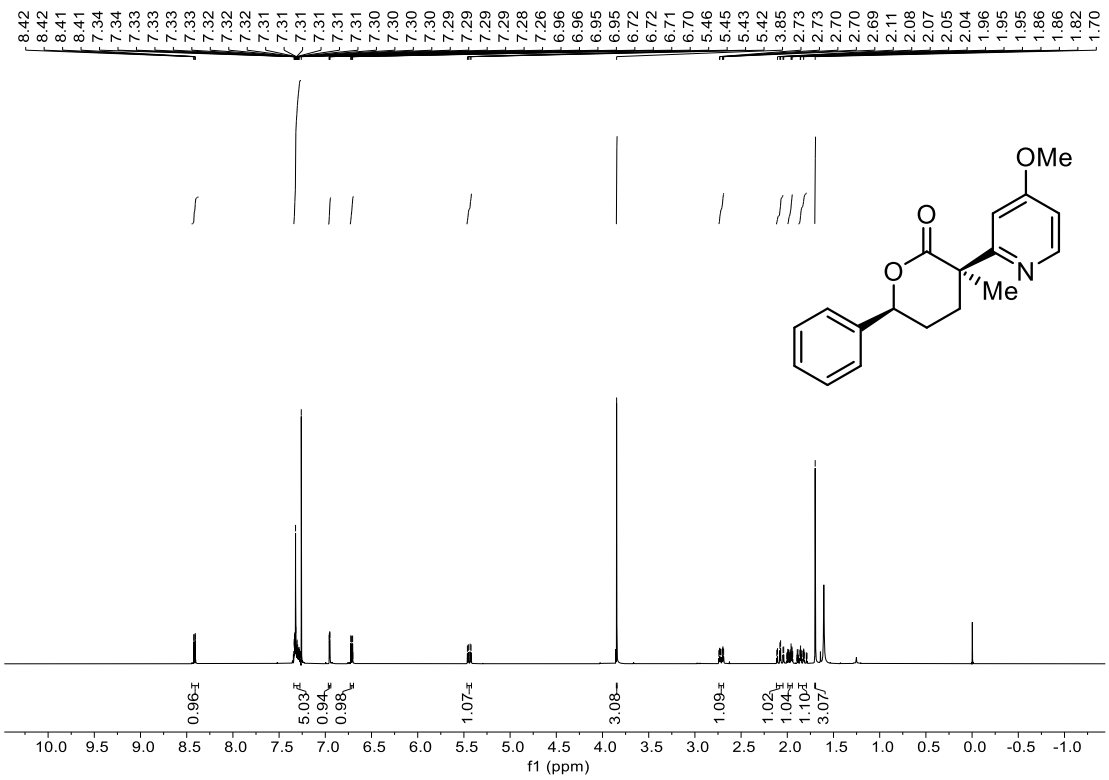
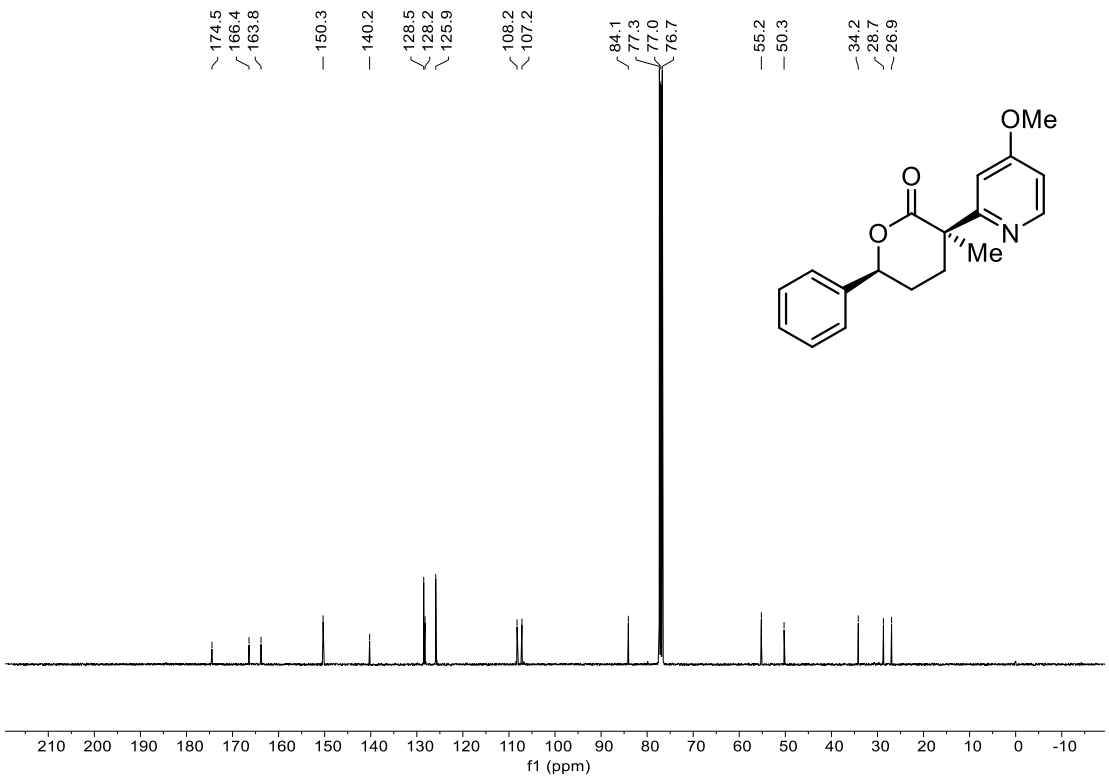


^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3f**



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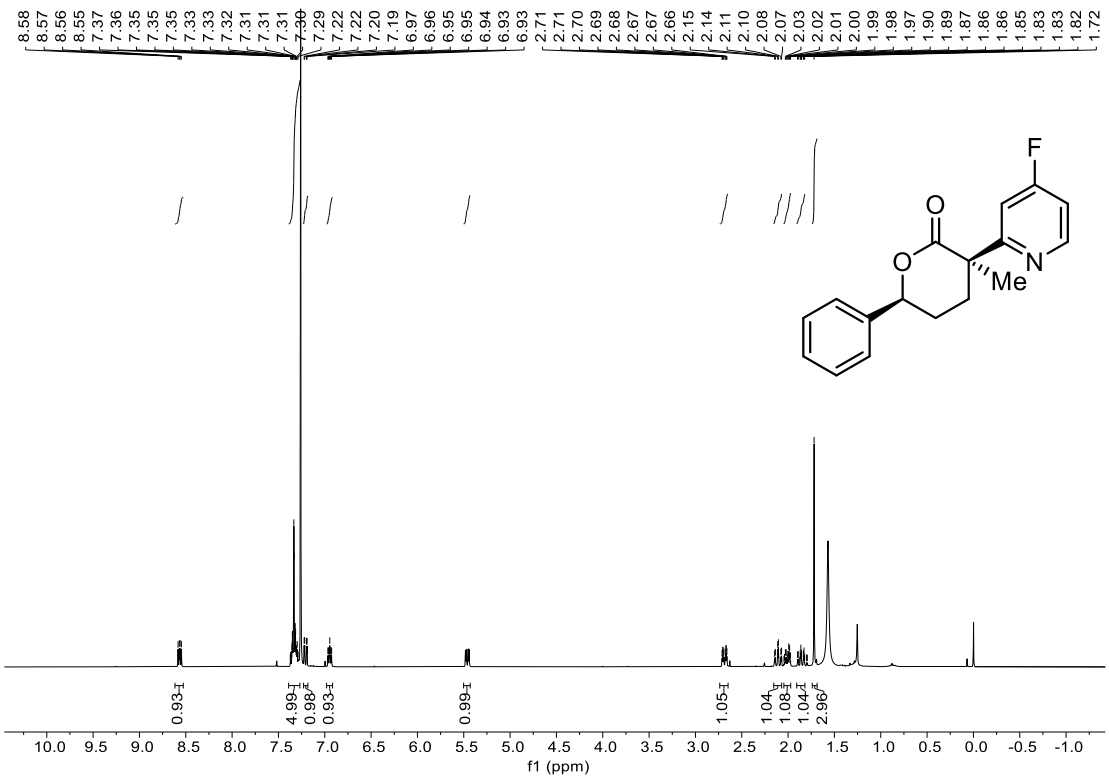
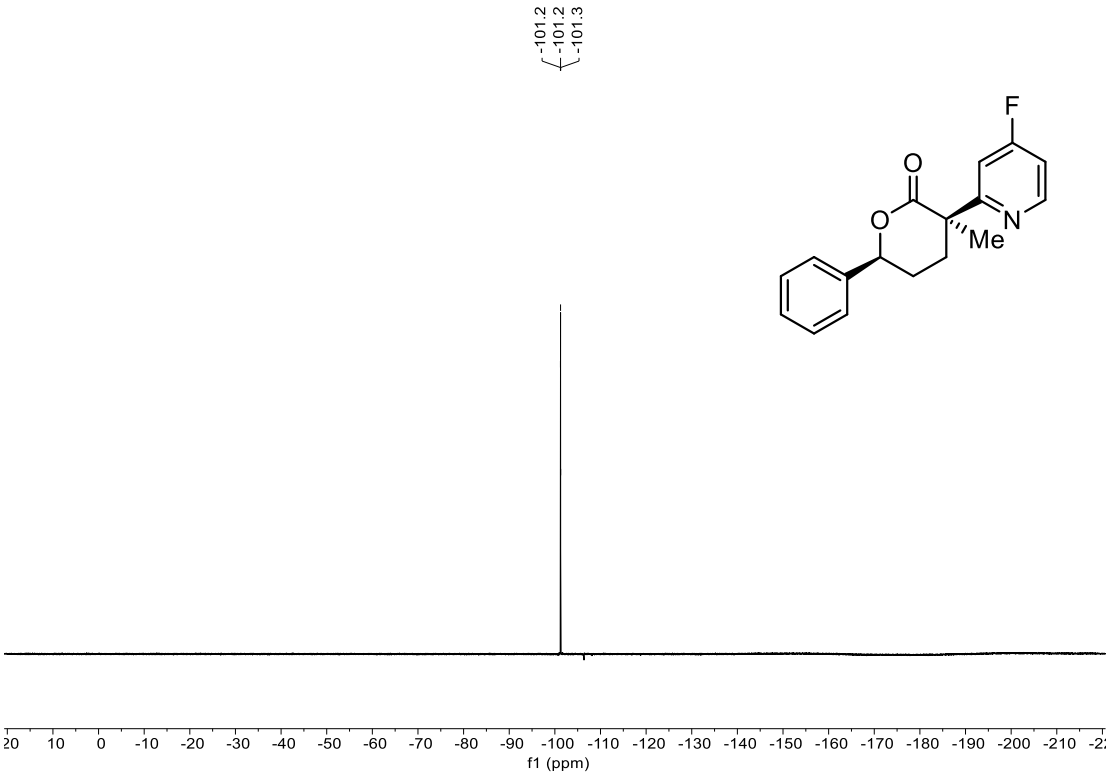
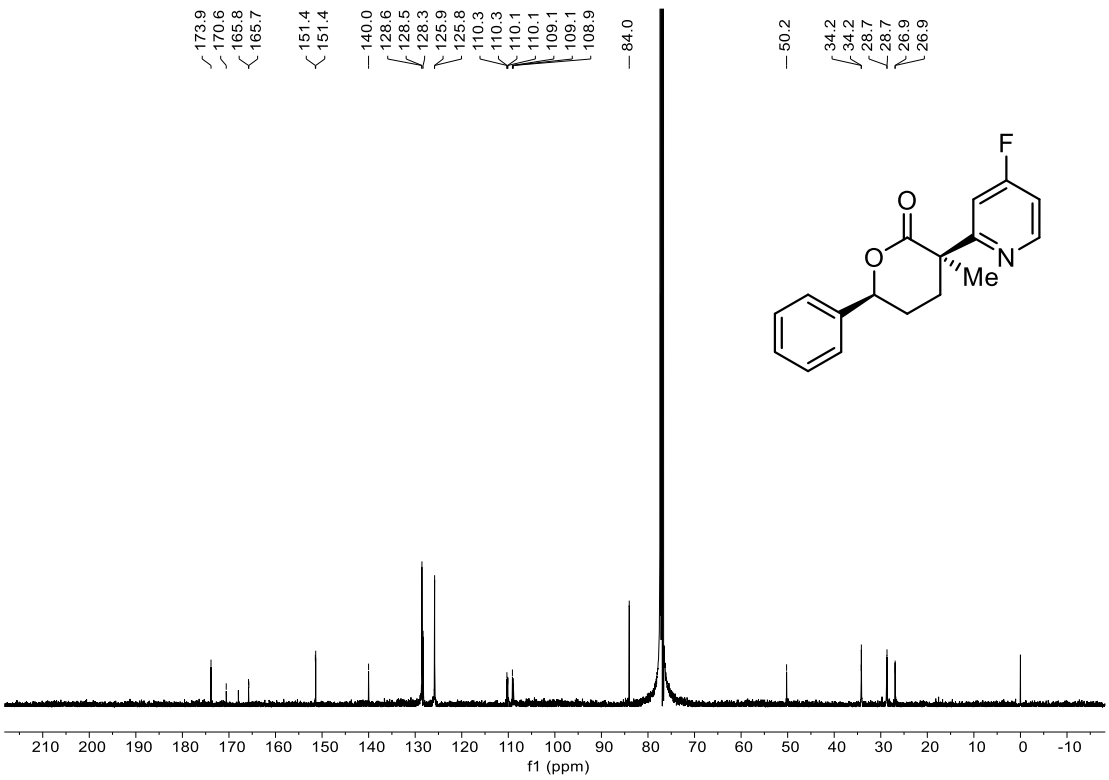


^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3g**



^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3g**



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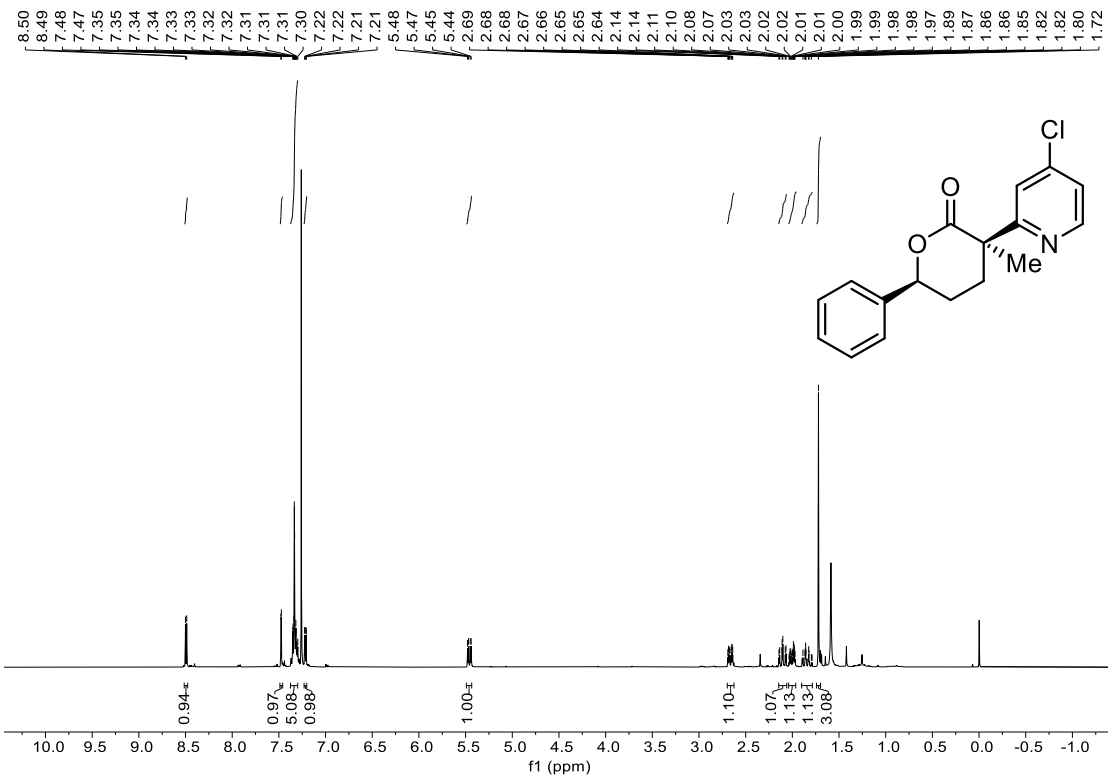
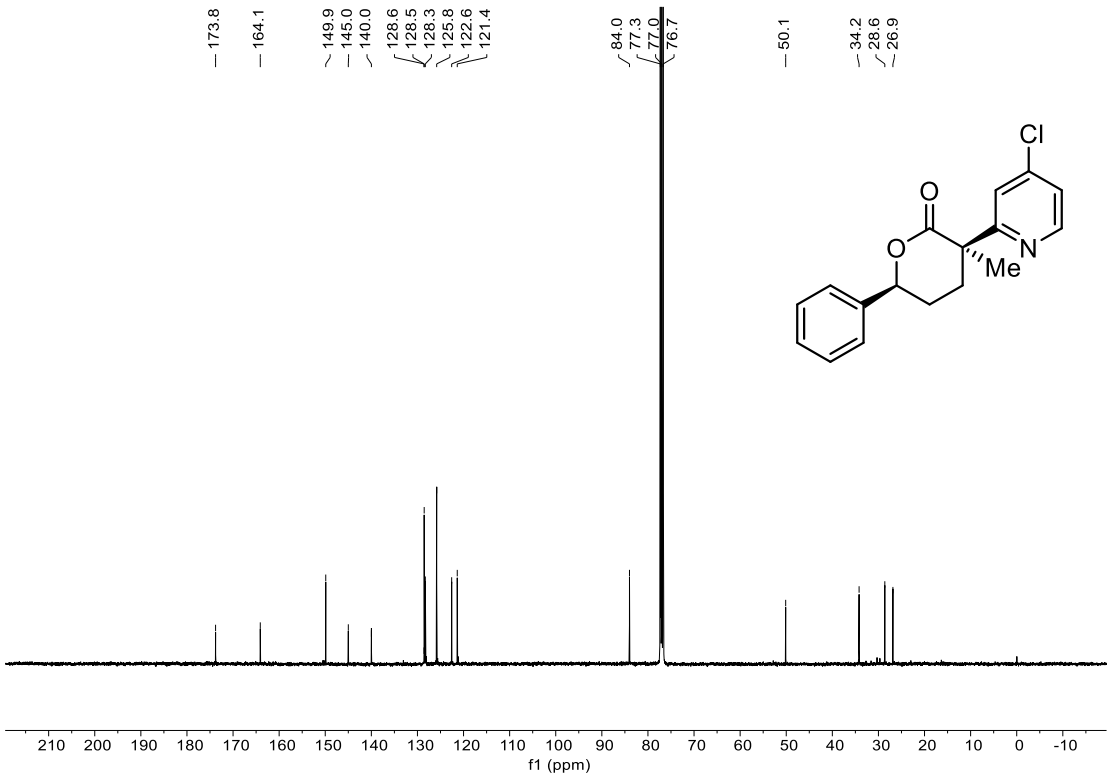
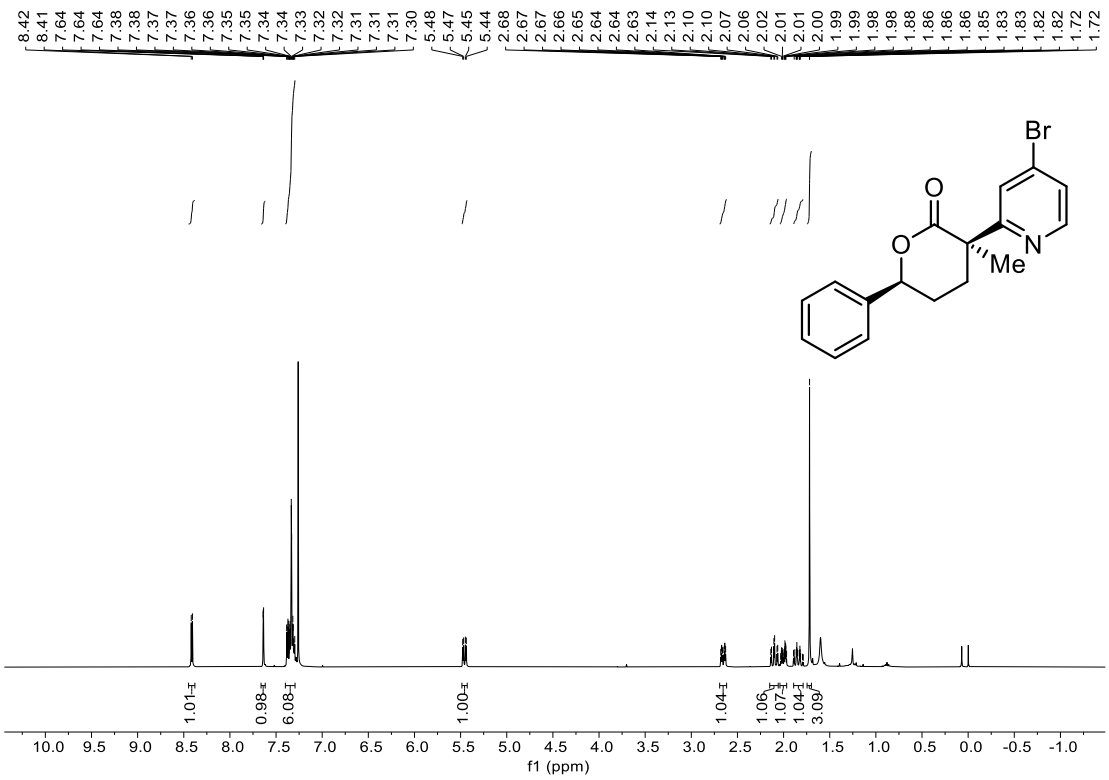


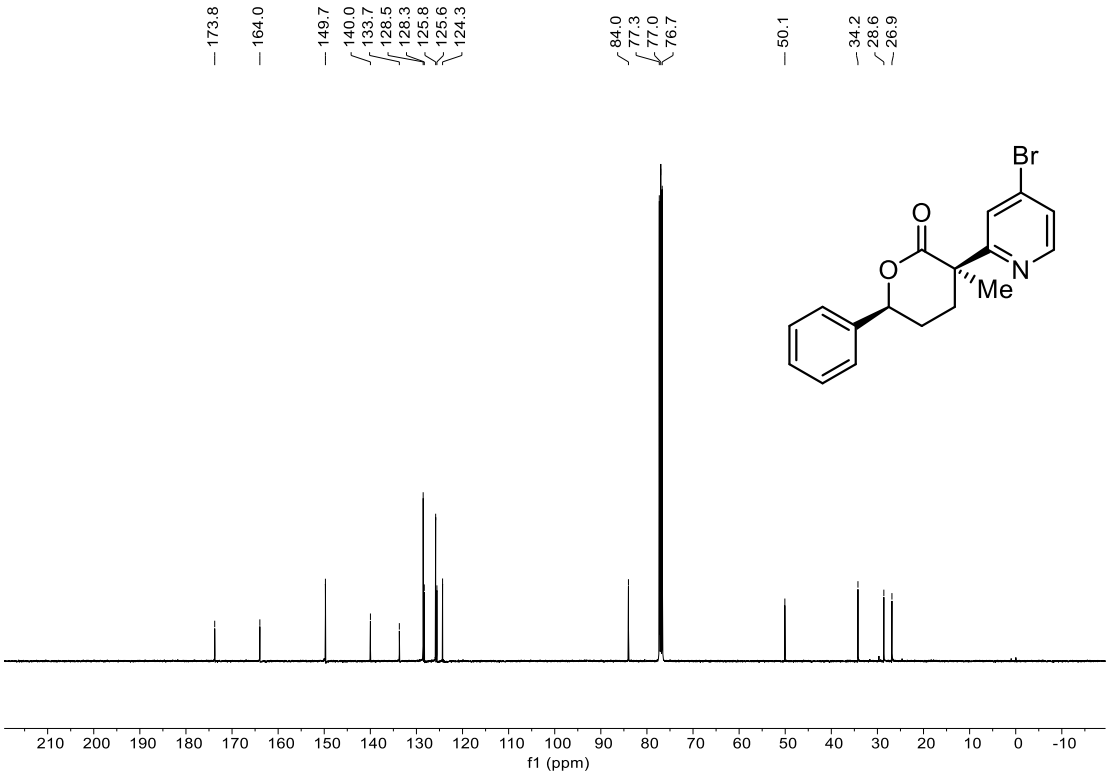
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3h**



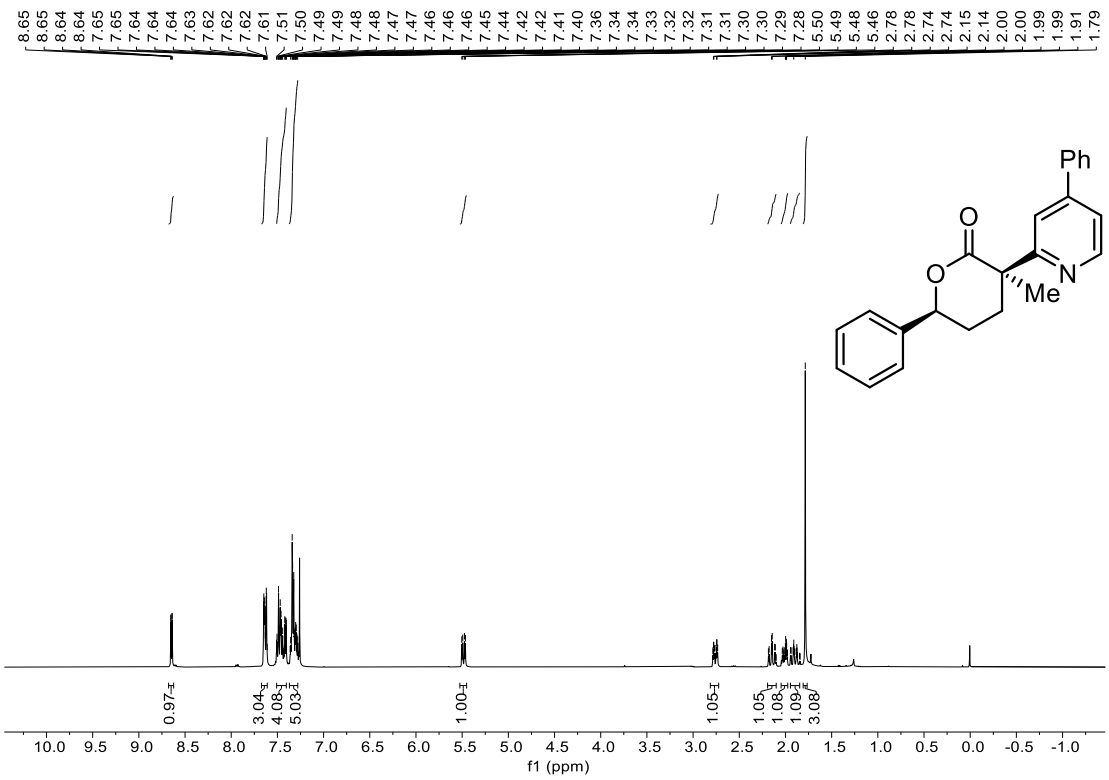
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3h**



^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3i**



^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3i**



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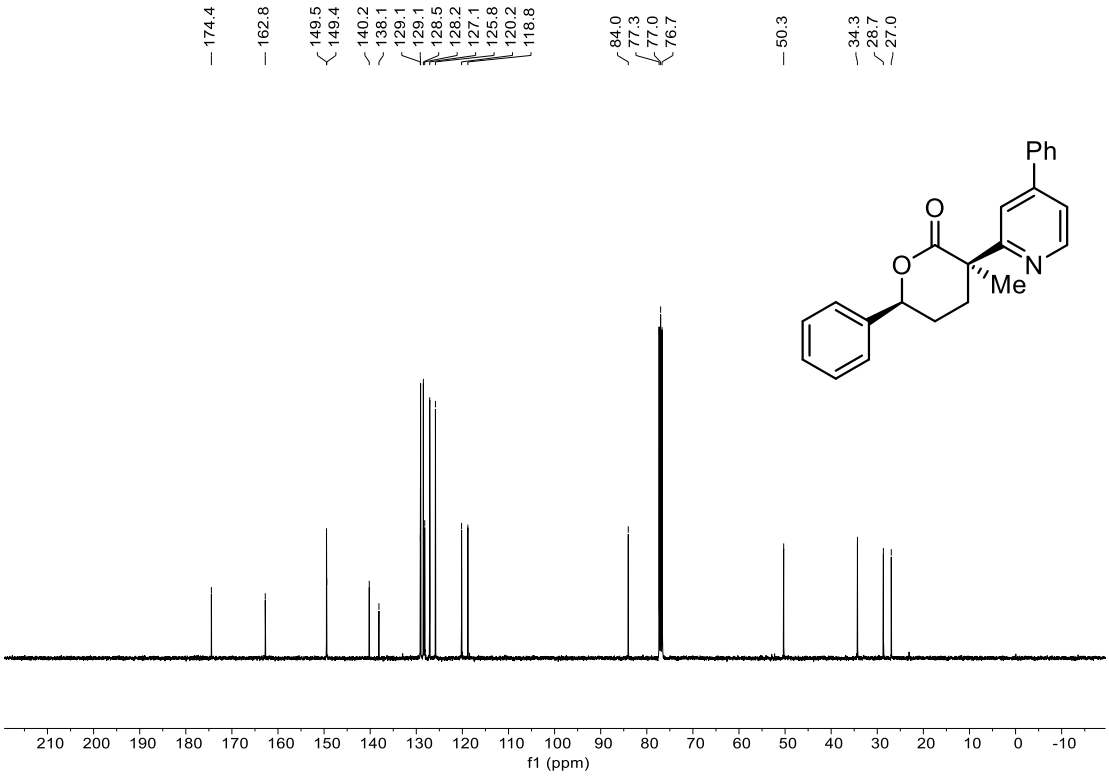
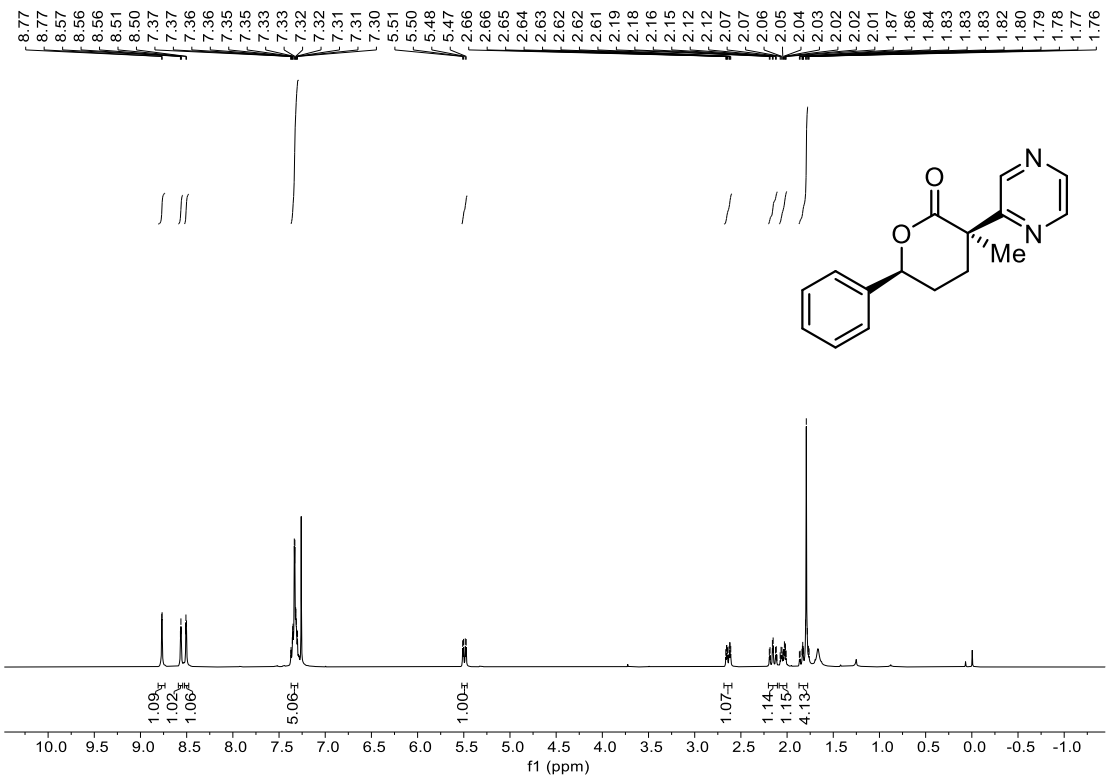
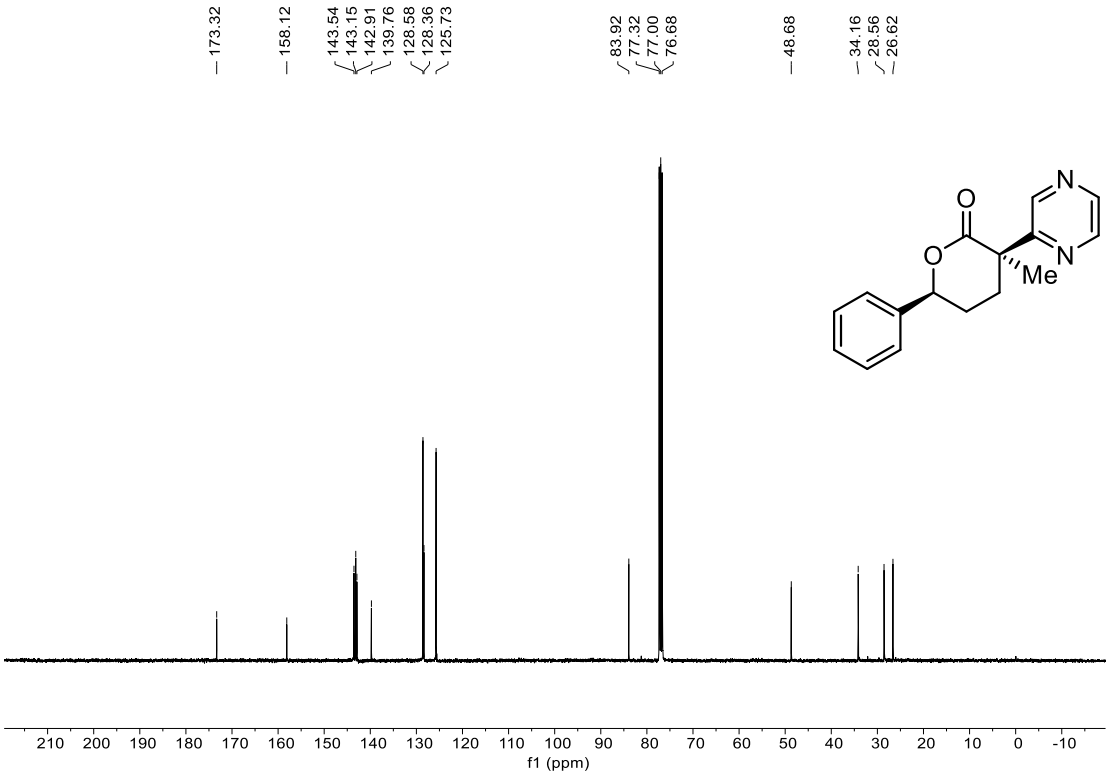


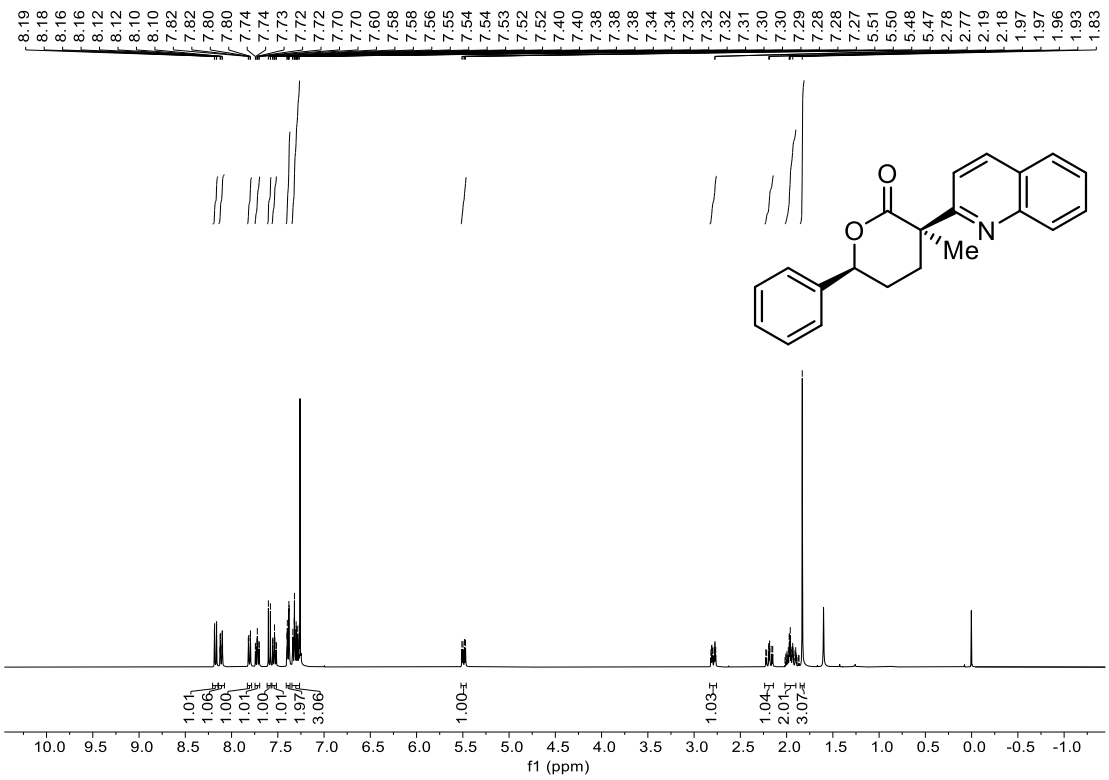
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3j**



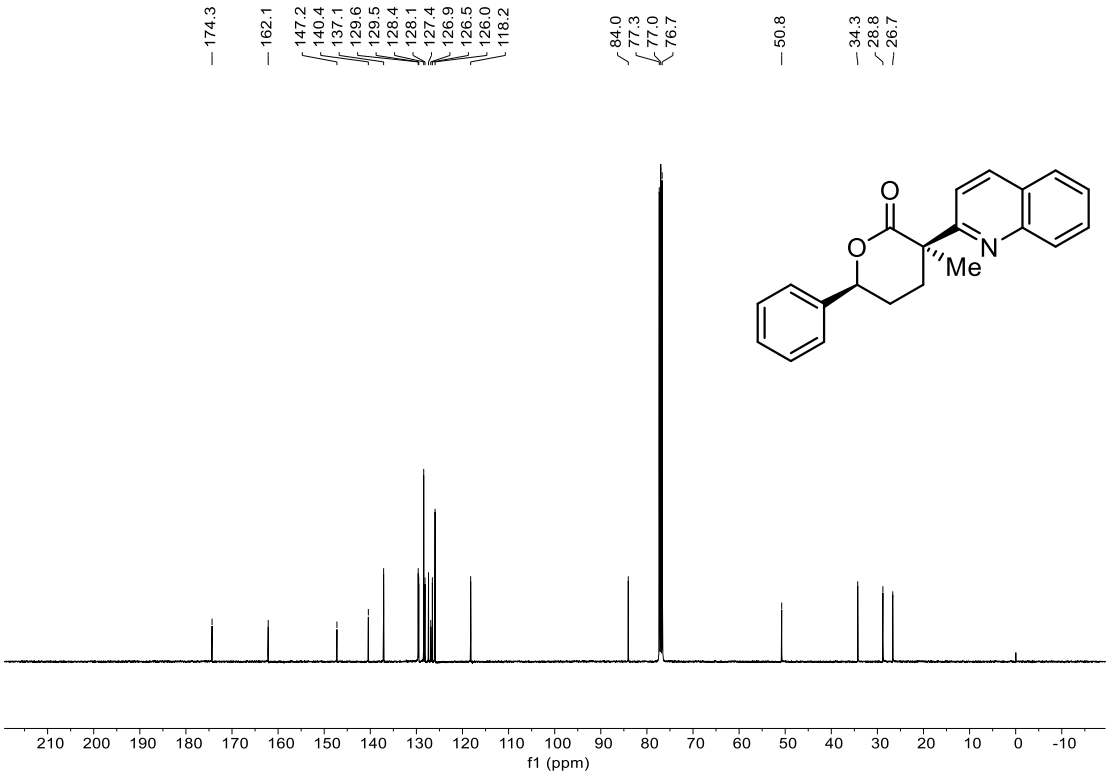
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3k**



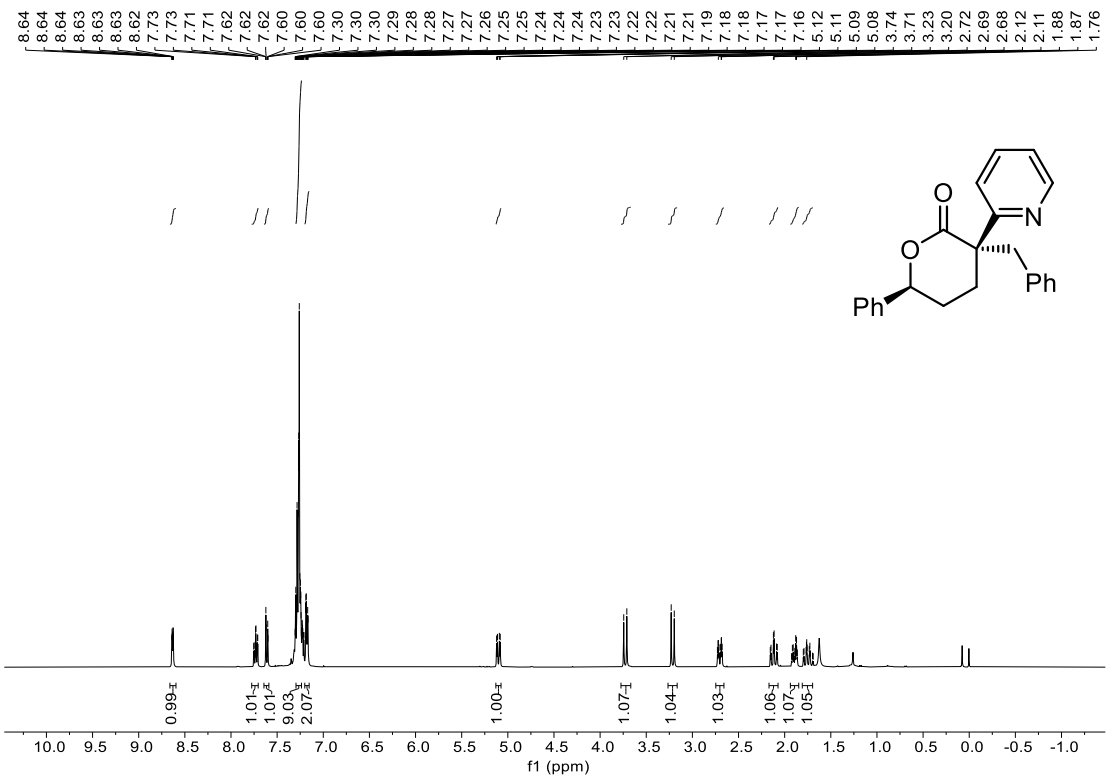
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3k**



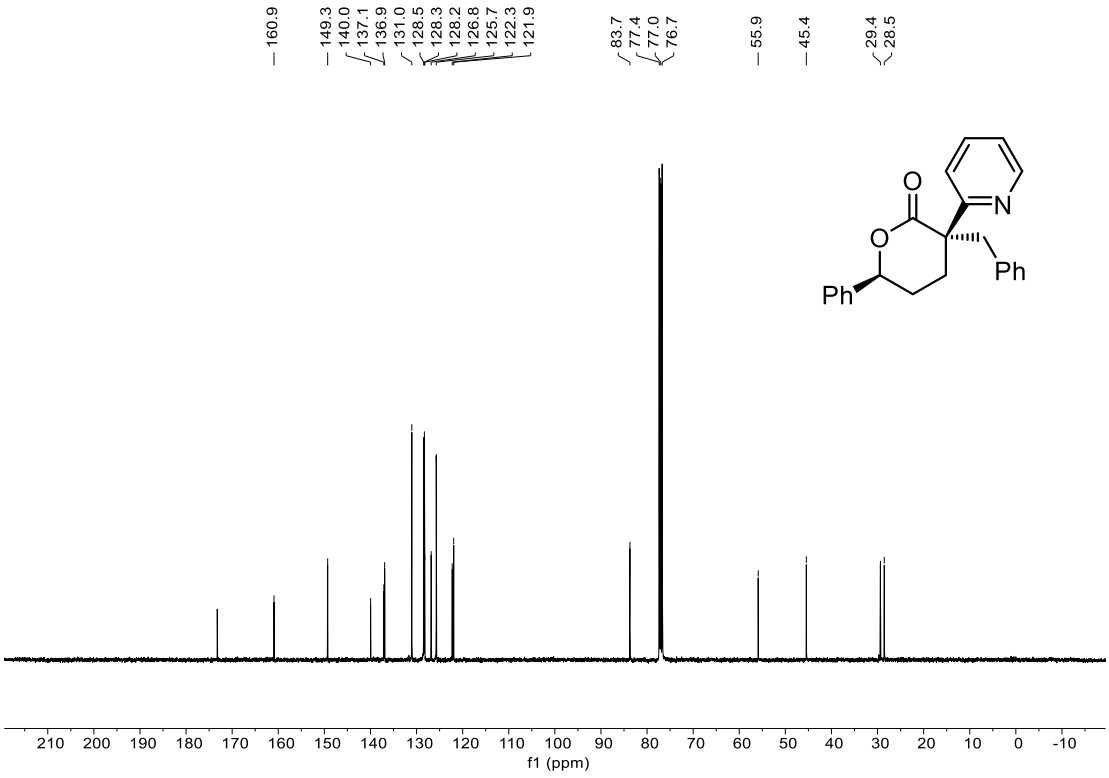
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3l**



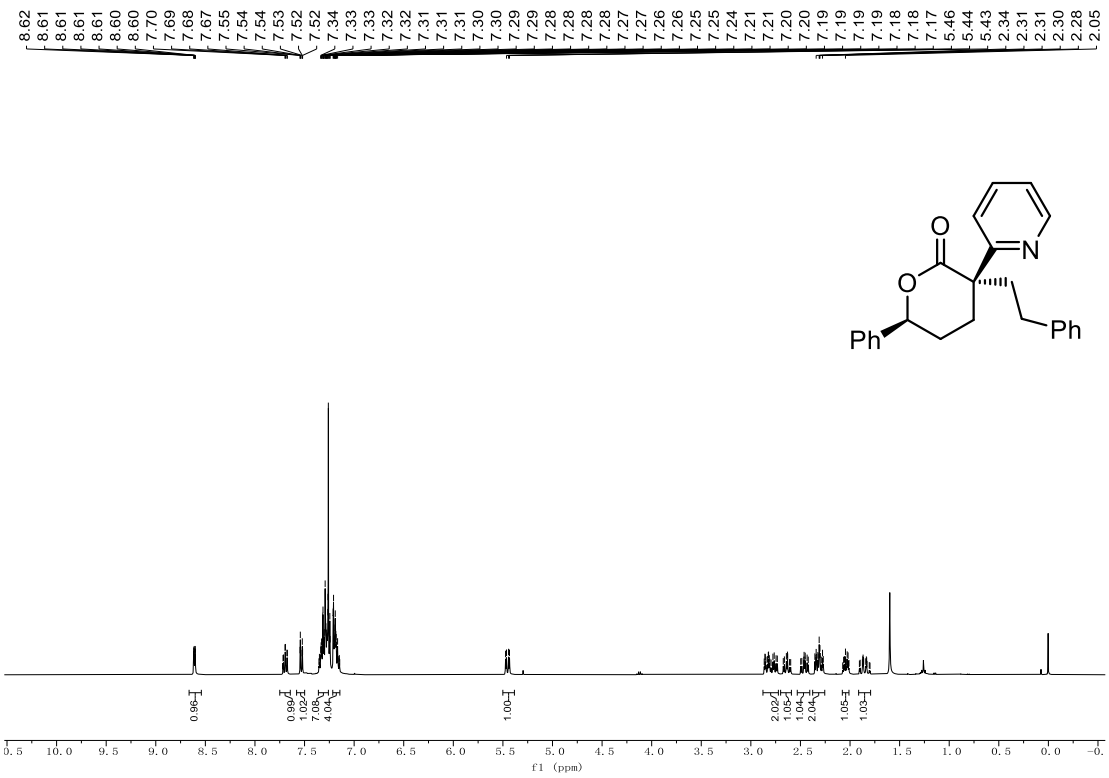
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3l**



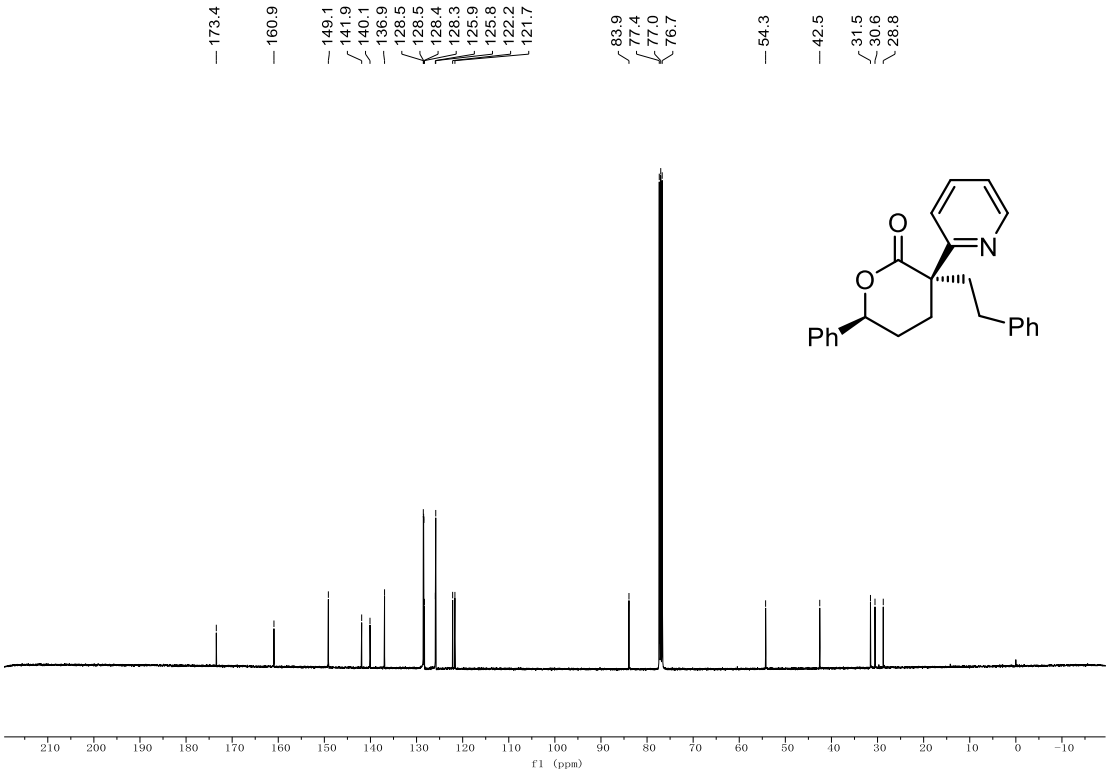
^{1}H NMR (400 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3m**



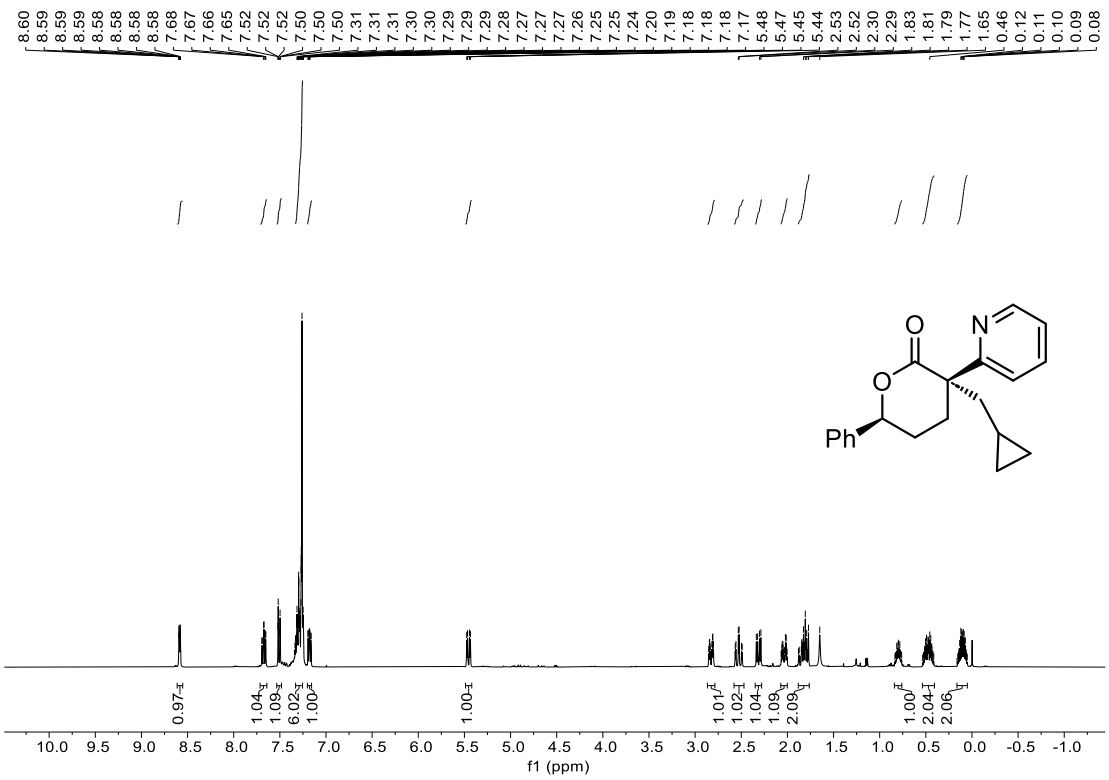
^{13}C NMR (101 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3m**



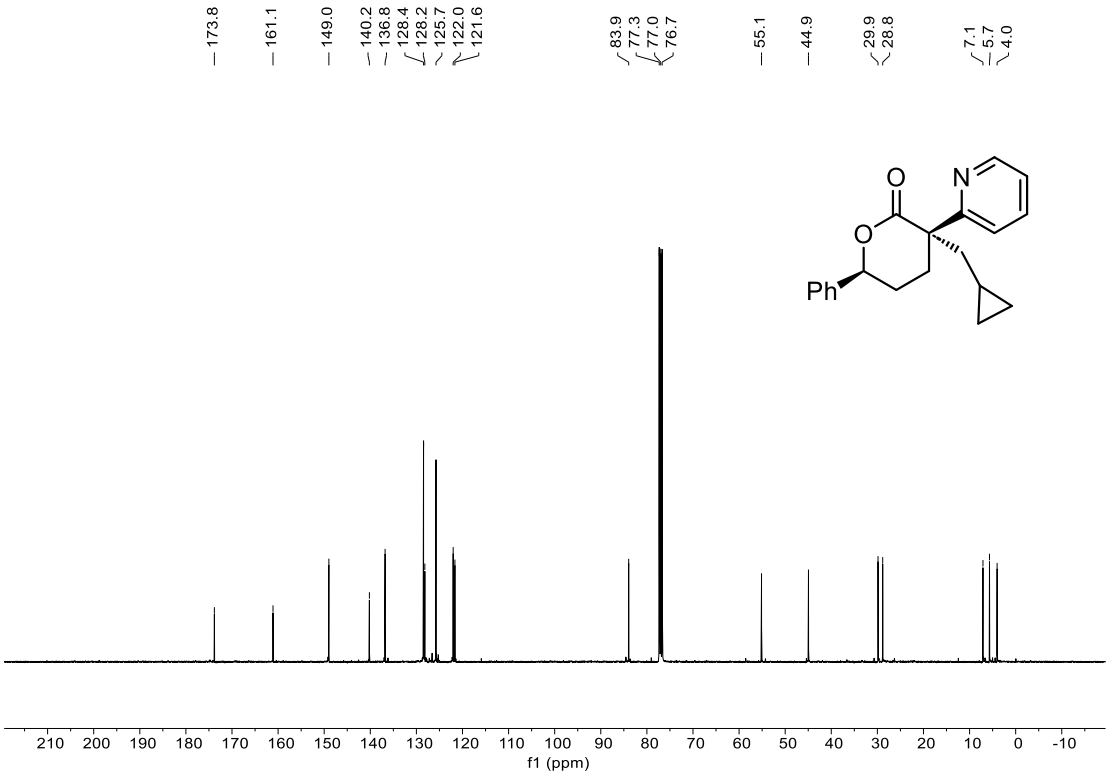
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3n**



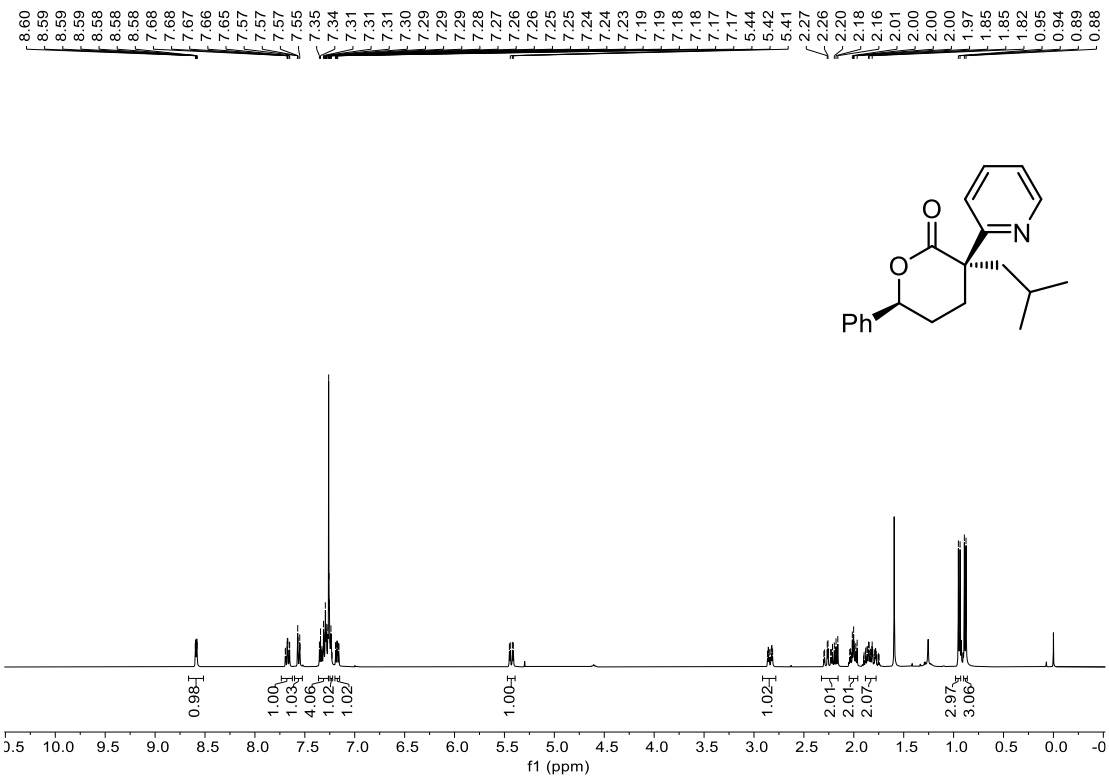
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3n**



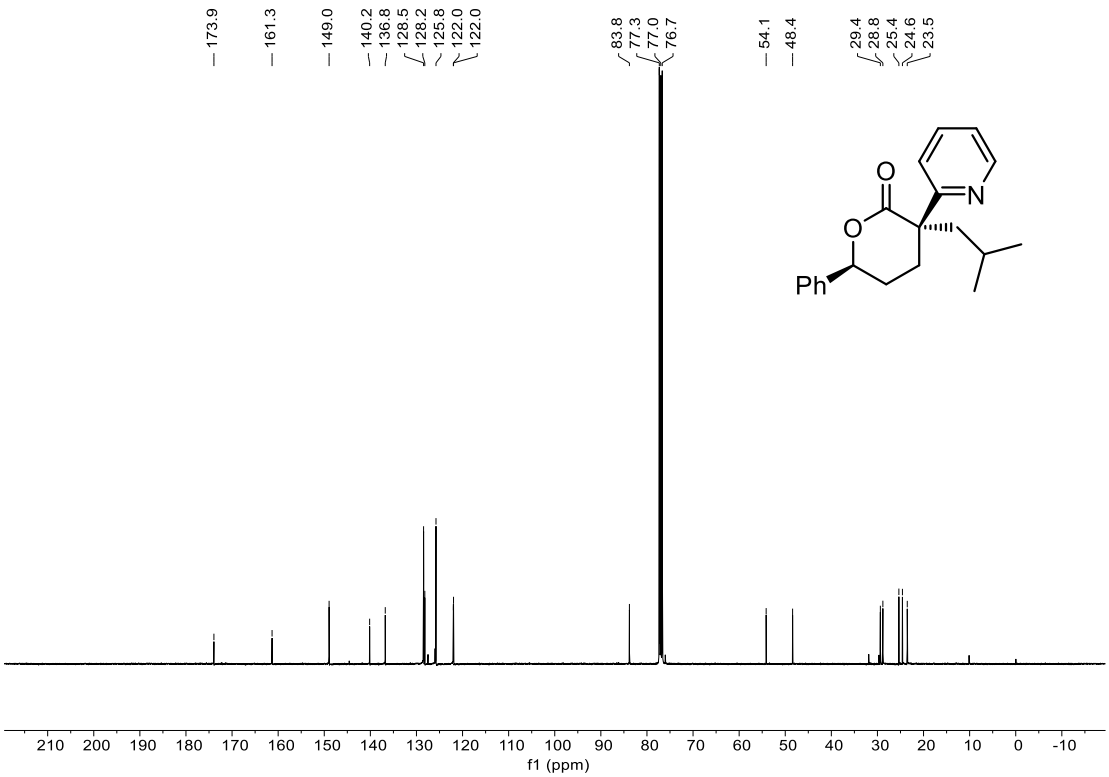
^{1}H NMR (400 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3o**



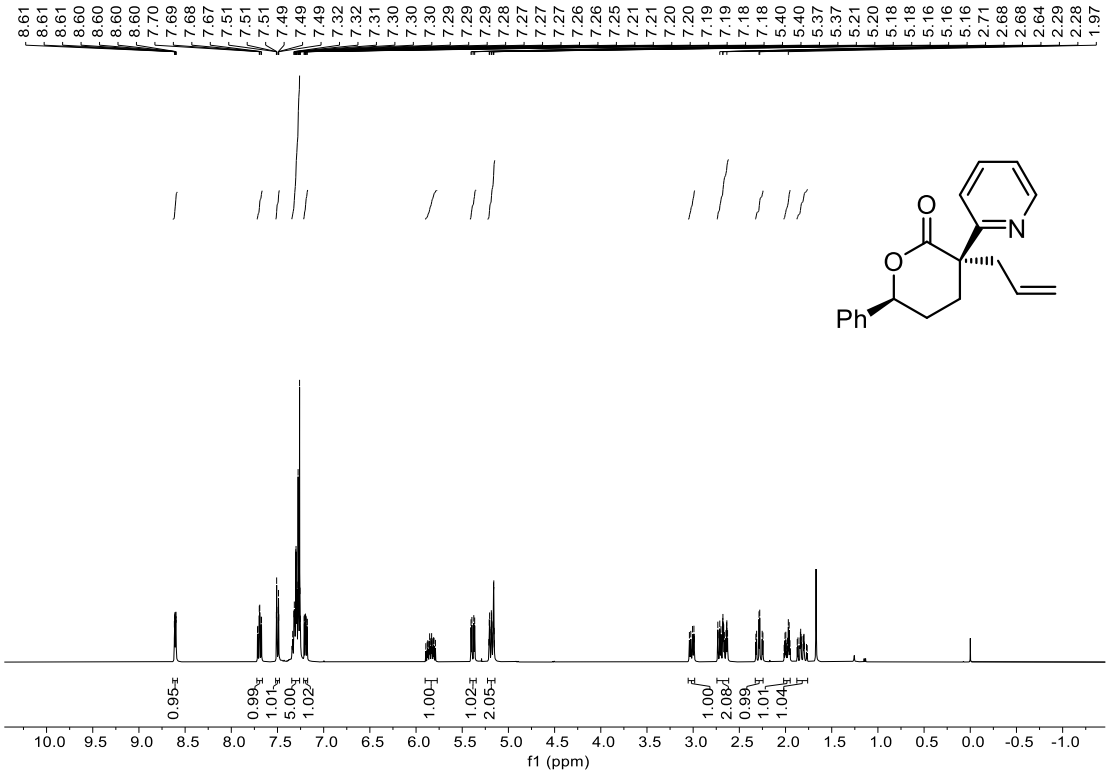
^{13}C NMR (101 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3o**



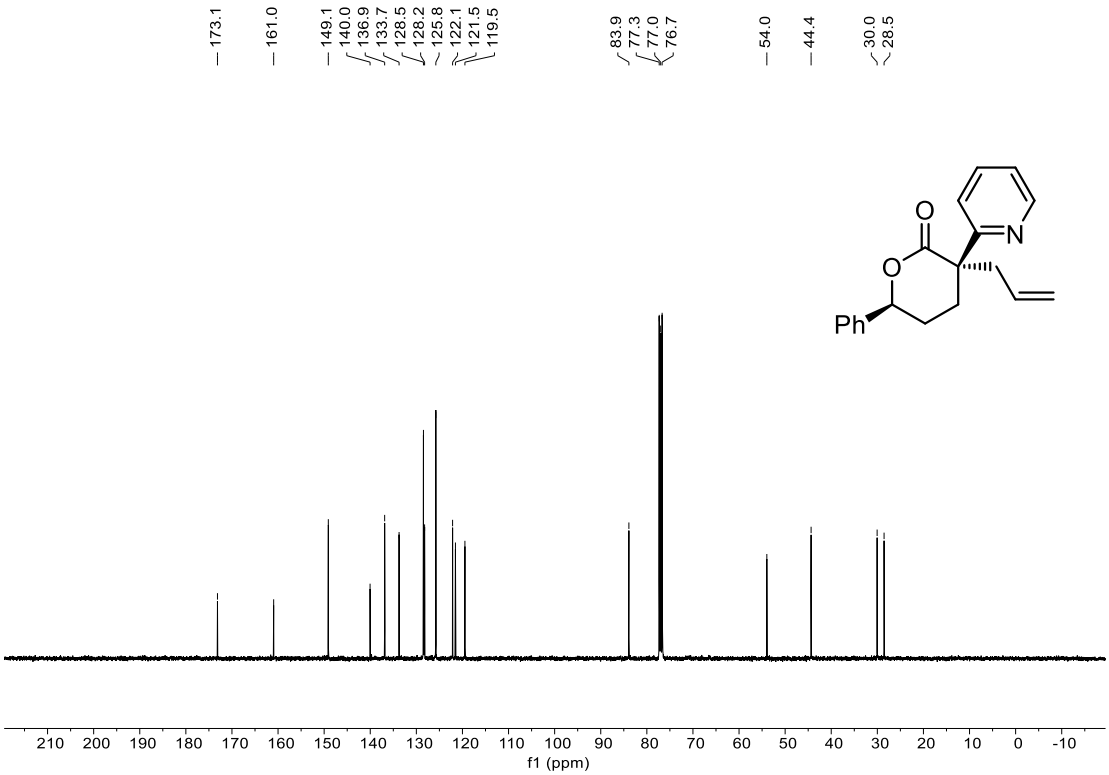
^{1}H NMR (400 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3p**



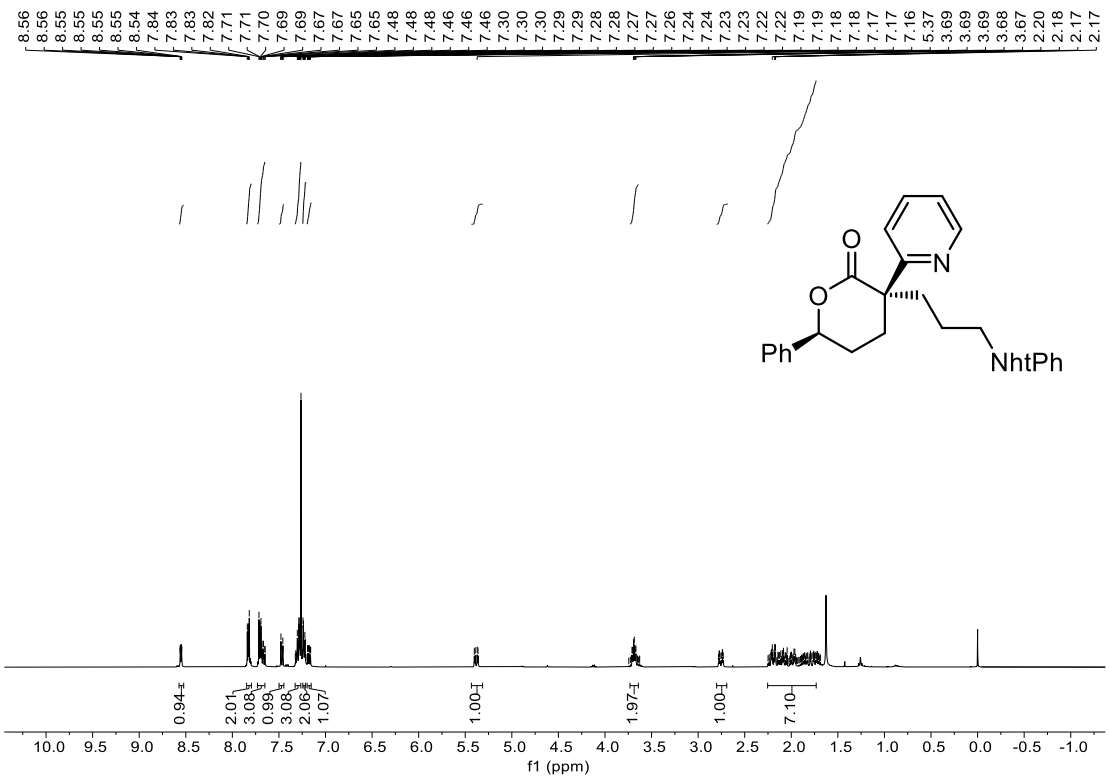
^{13}C NMR (101 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3p**



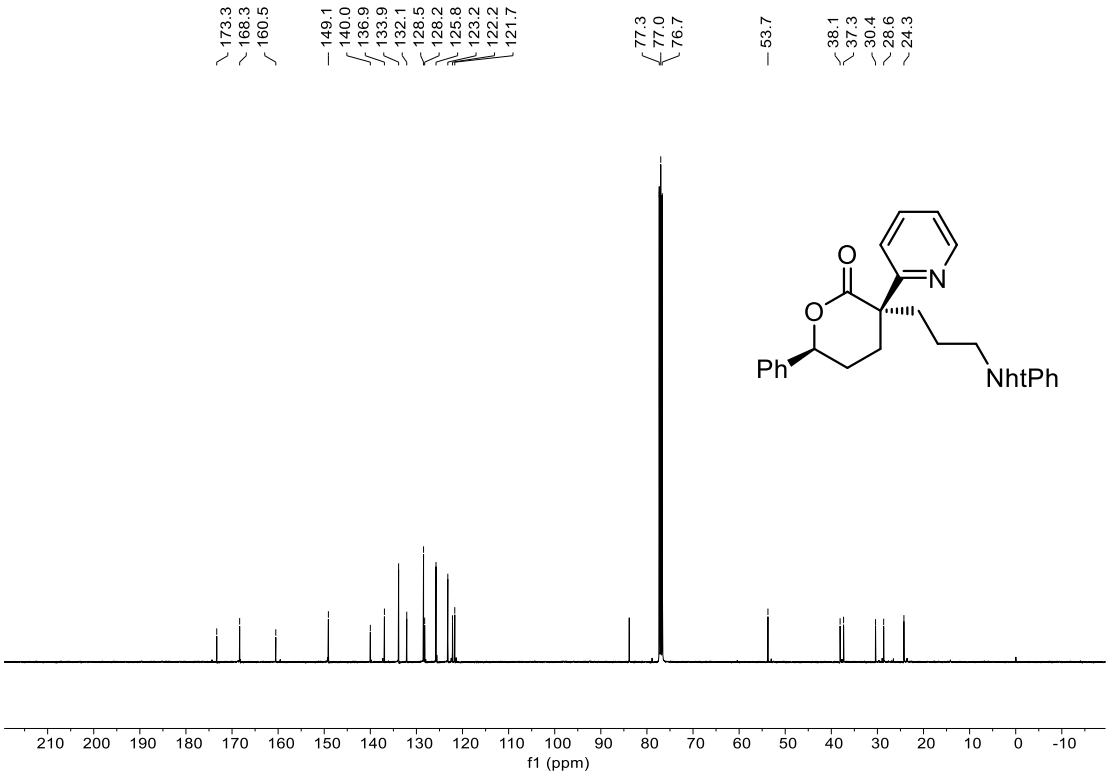
^{1}H NMR (400 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3q**



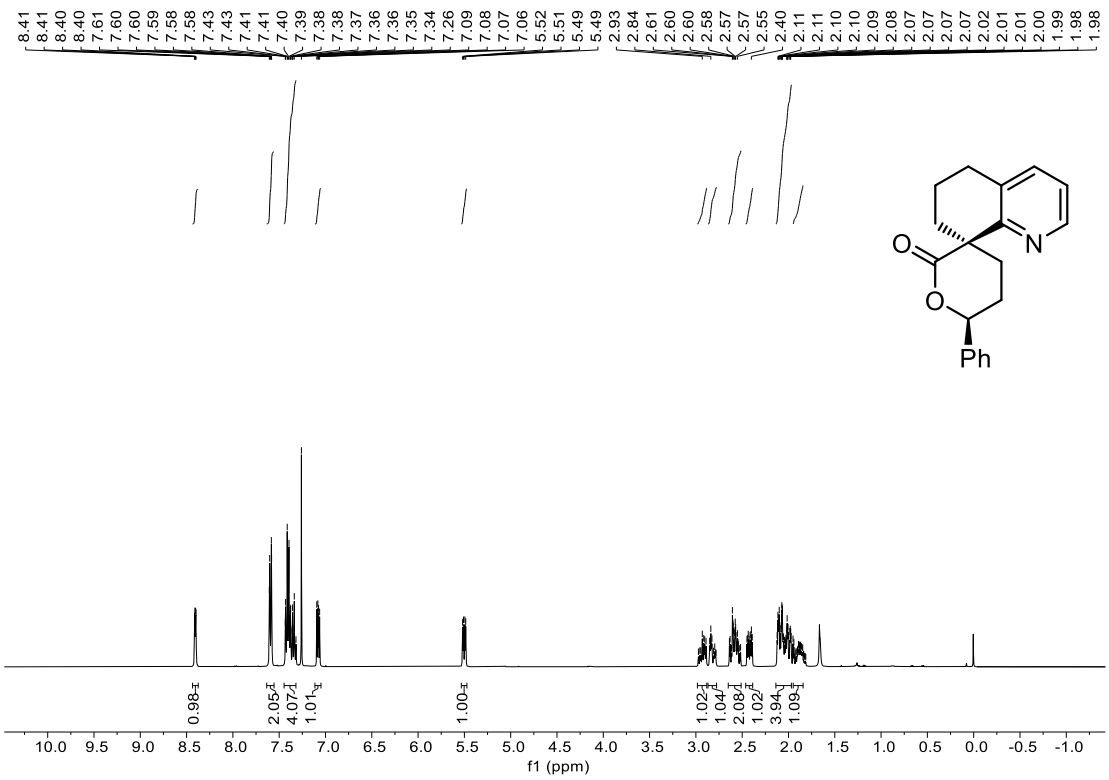
^{13}C NMR (101 MHz, $CDCl_3$) of (3*S*, 6*S*)-**3q**



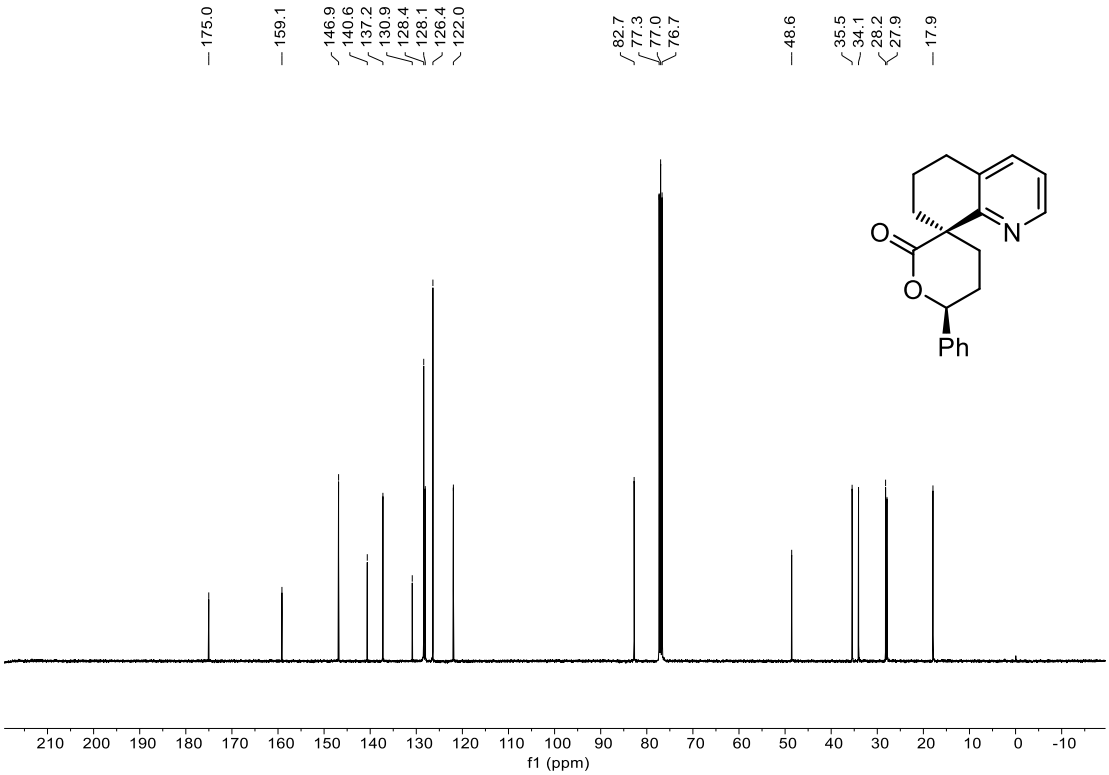
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3r**



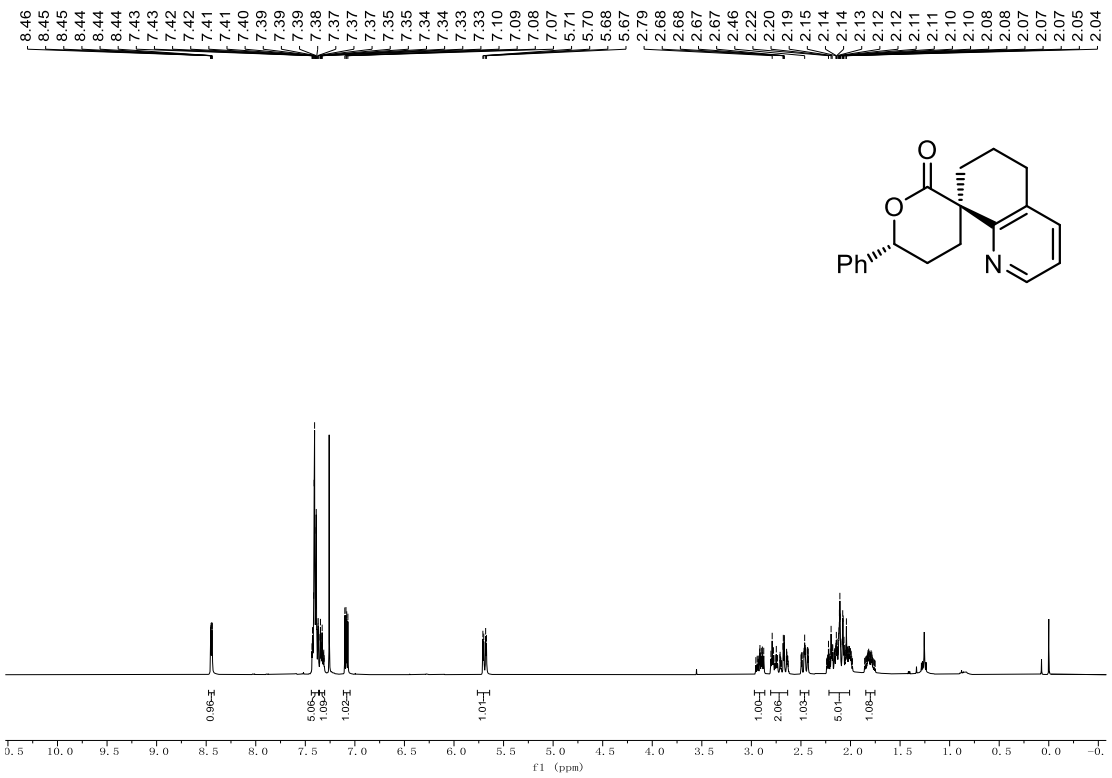
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3r**



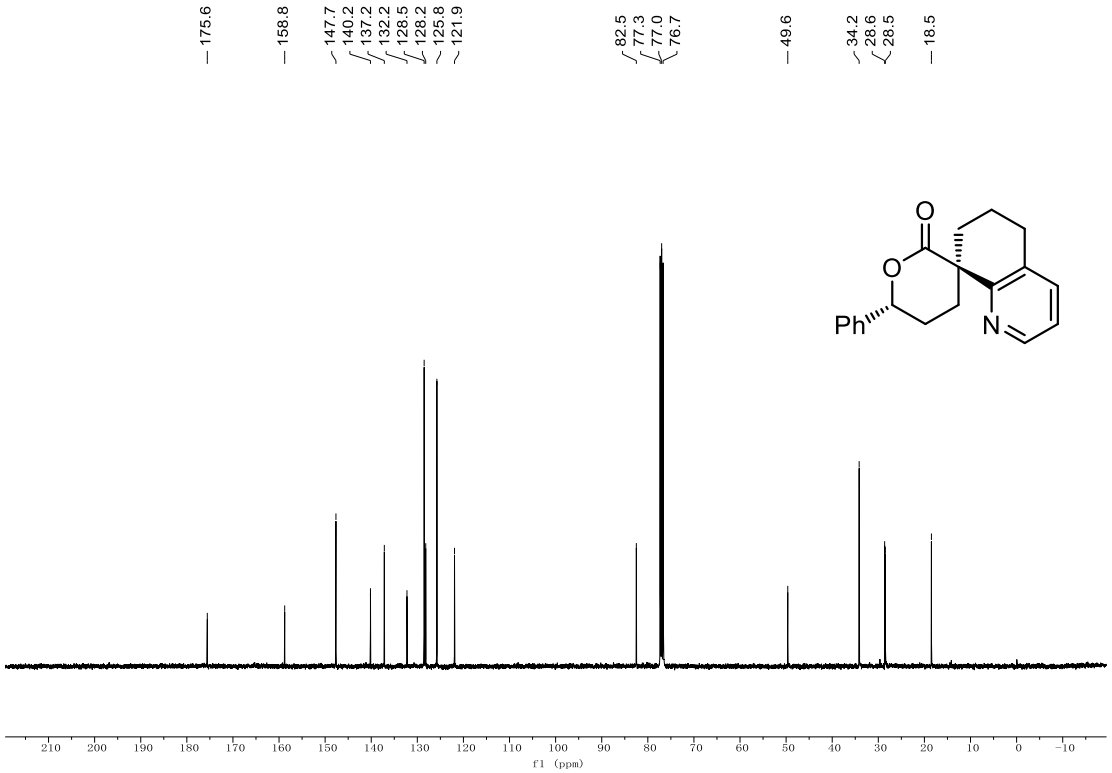
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*,6*S*)-**3s**



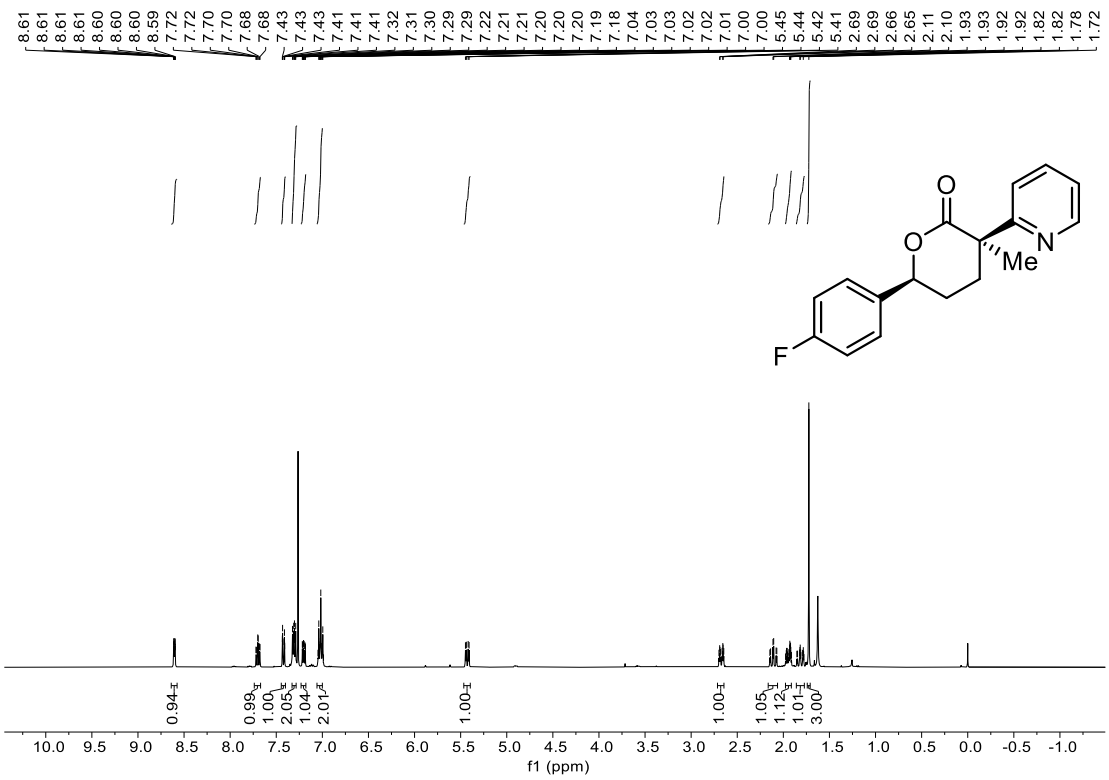
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*,6*S*)-**3s**



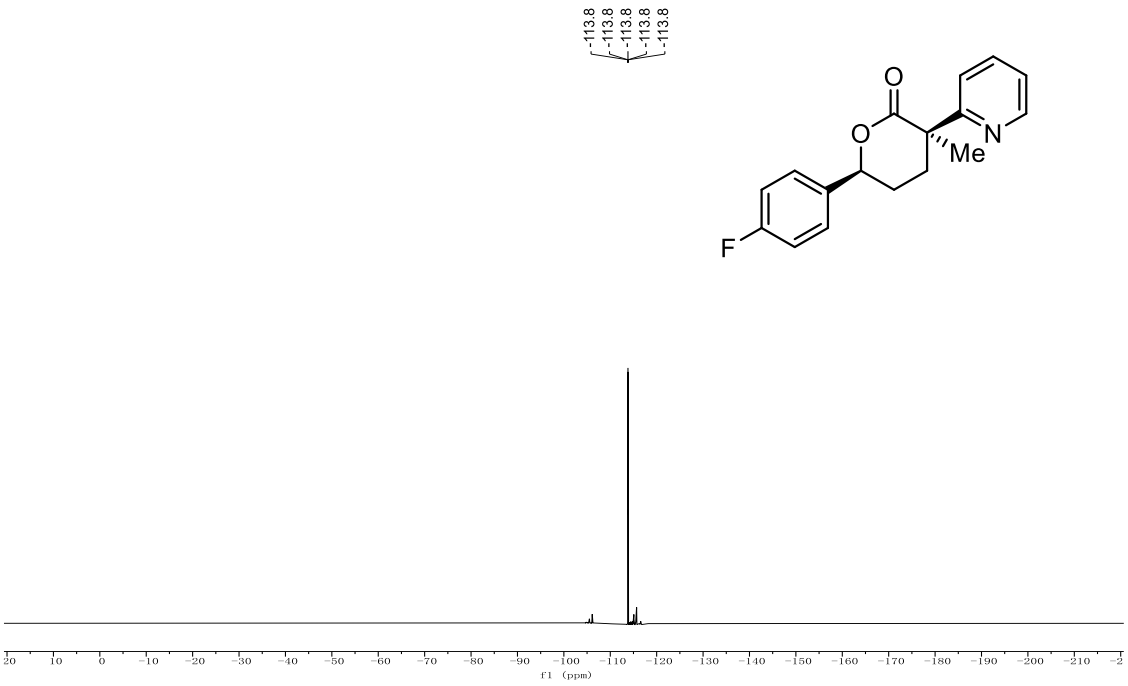
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*,6*R*)-**3s**



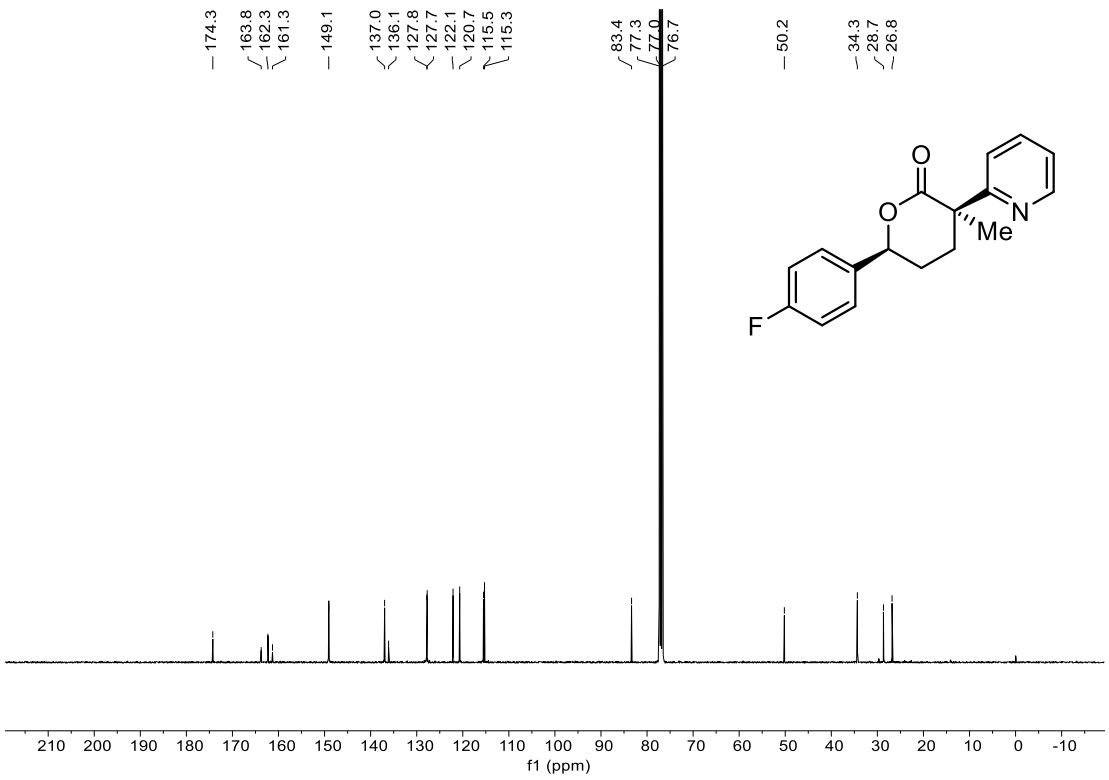
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*,6*R*)-**3s**



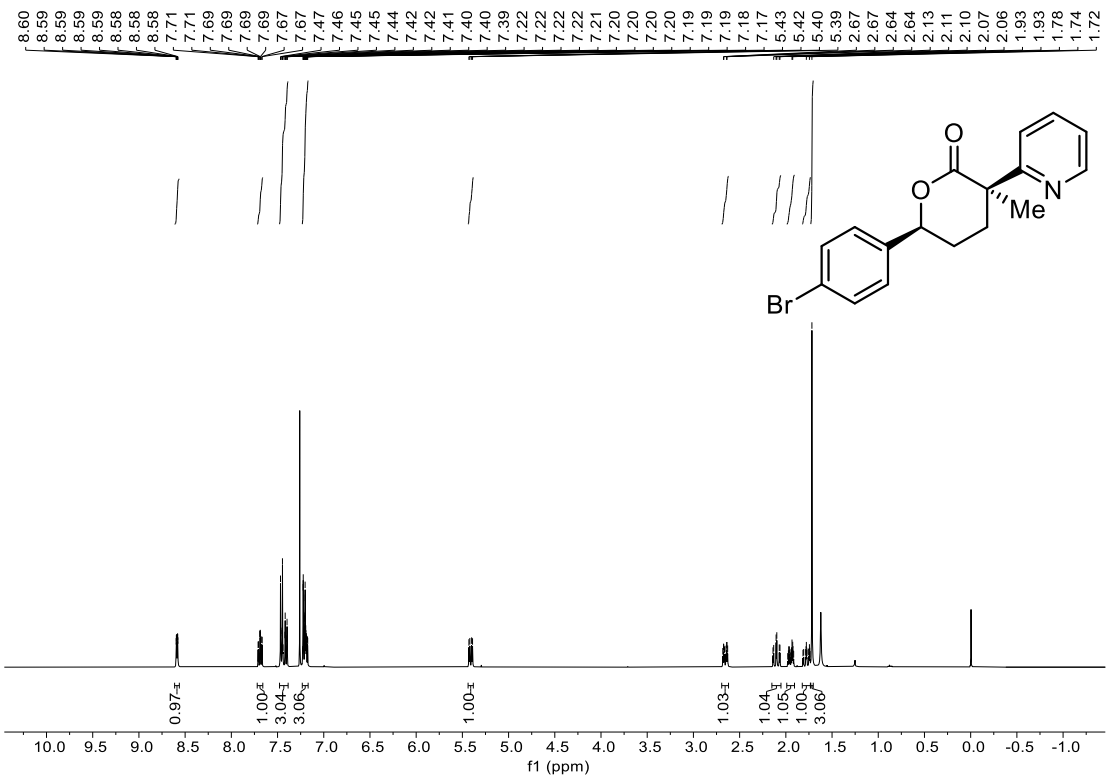
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3t**



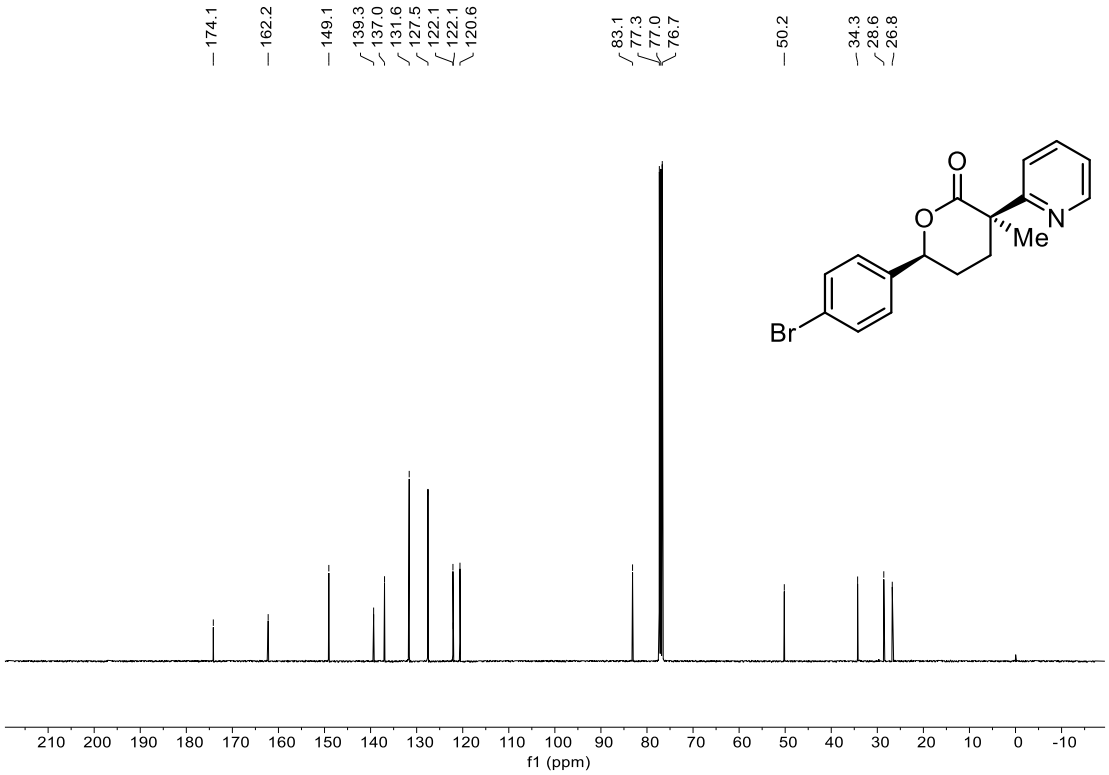
^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3t**



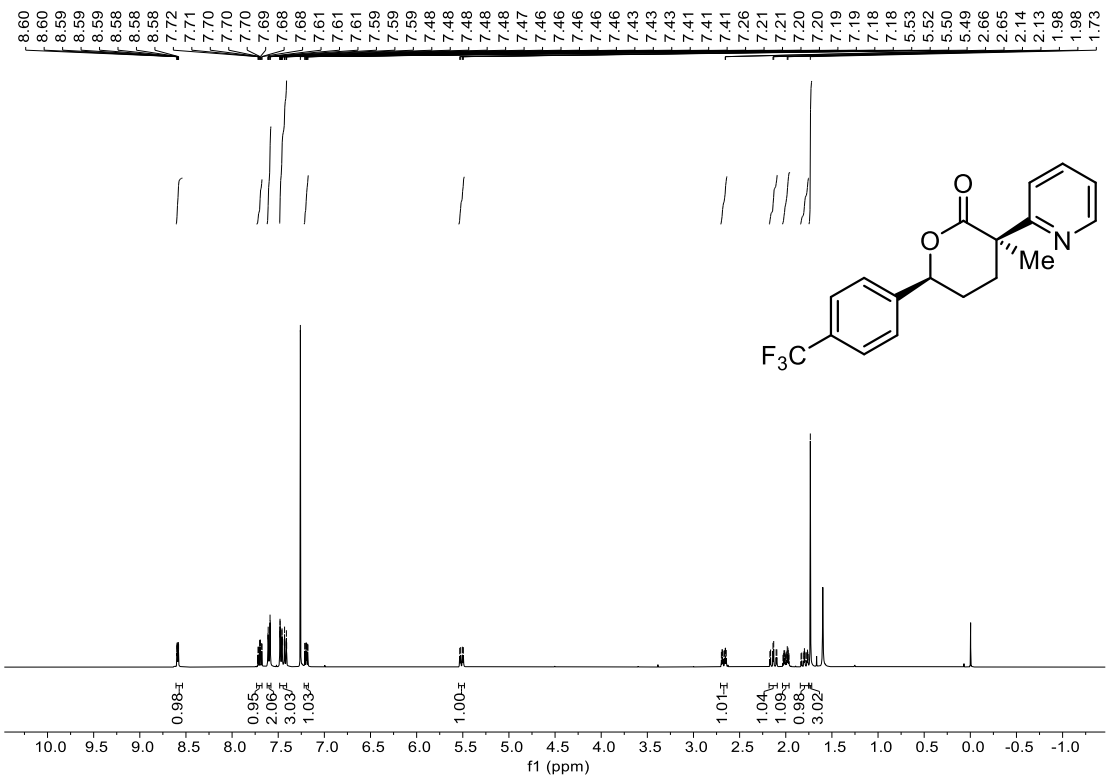
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3t**



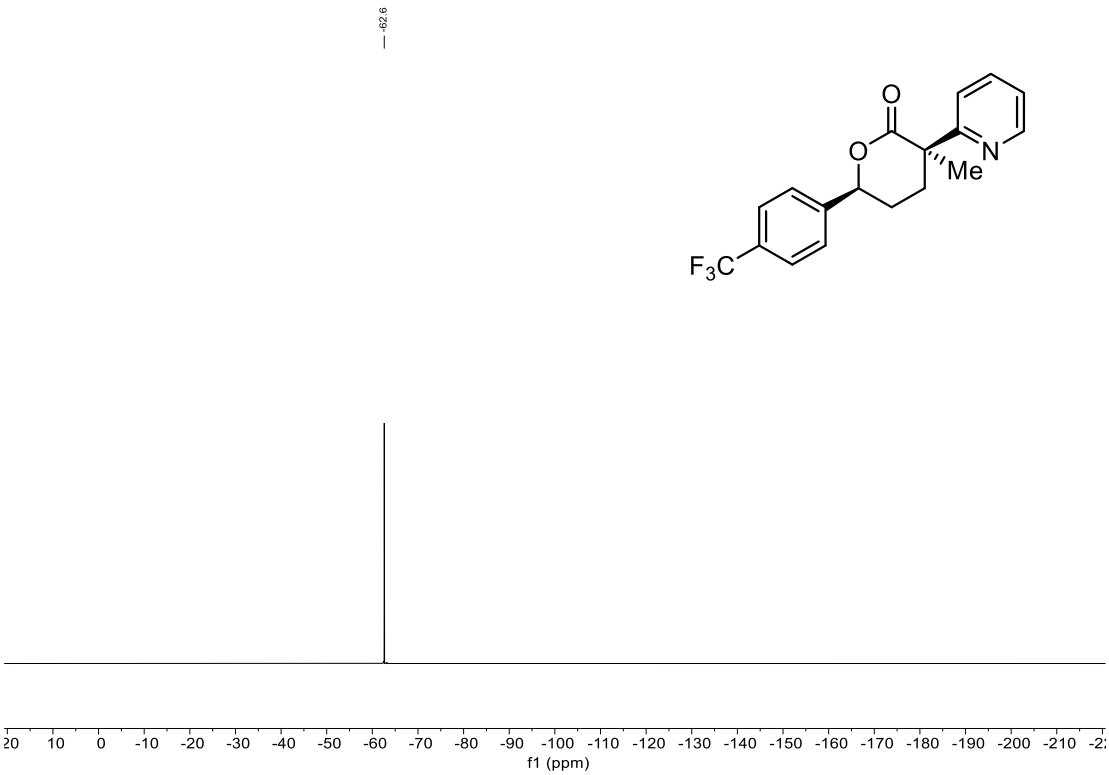
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3u**



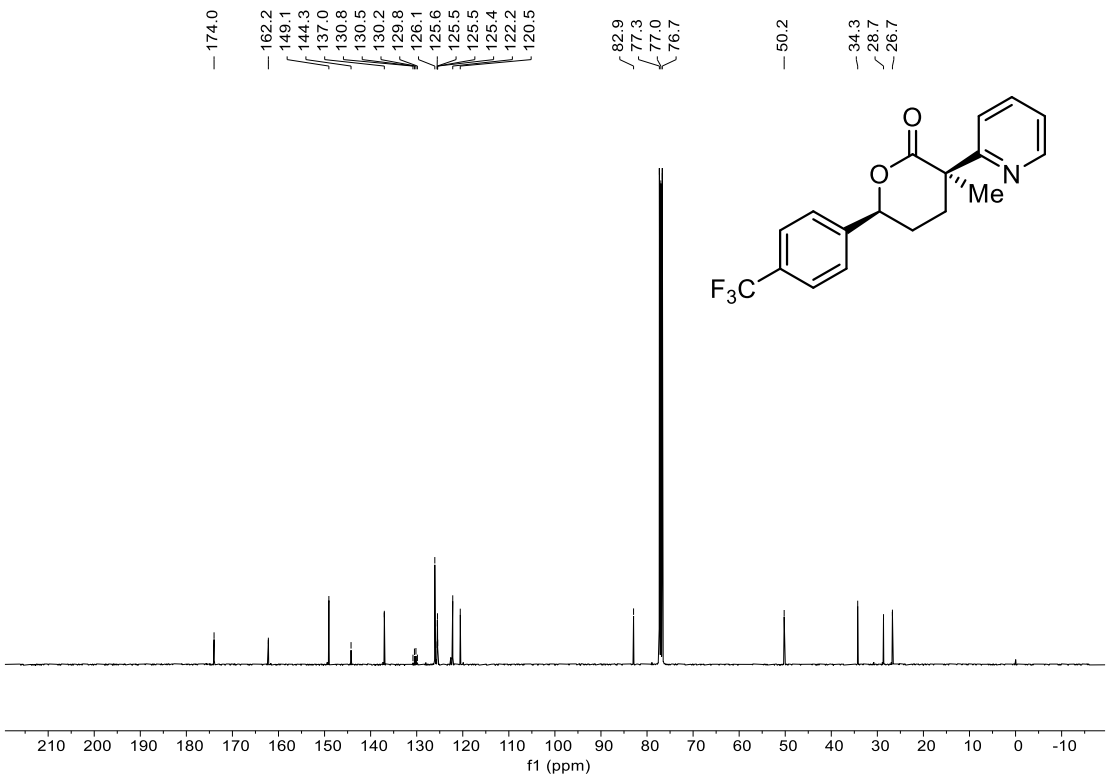
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3u**



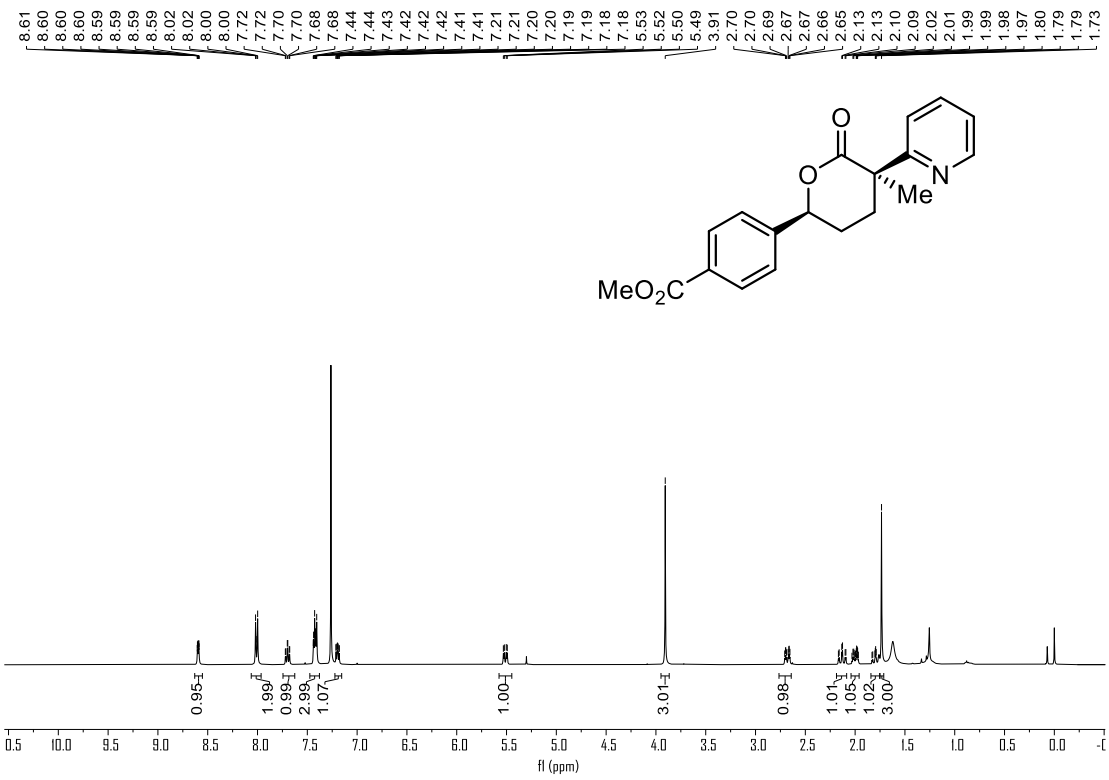
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3v**



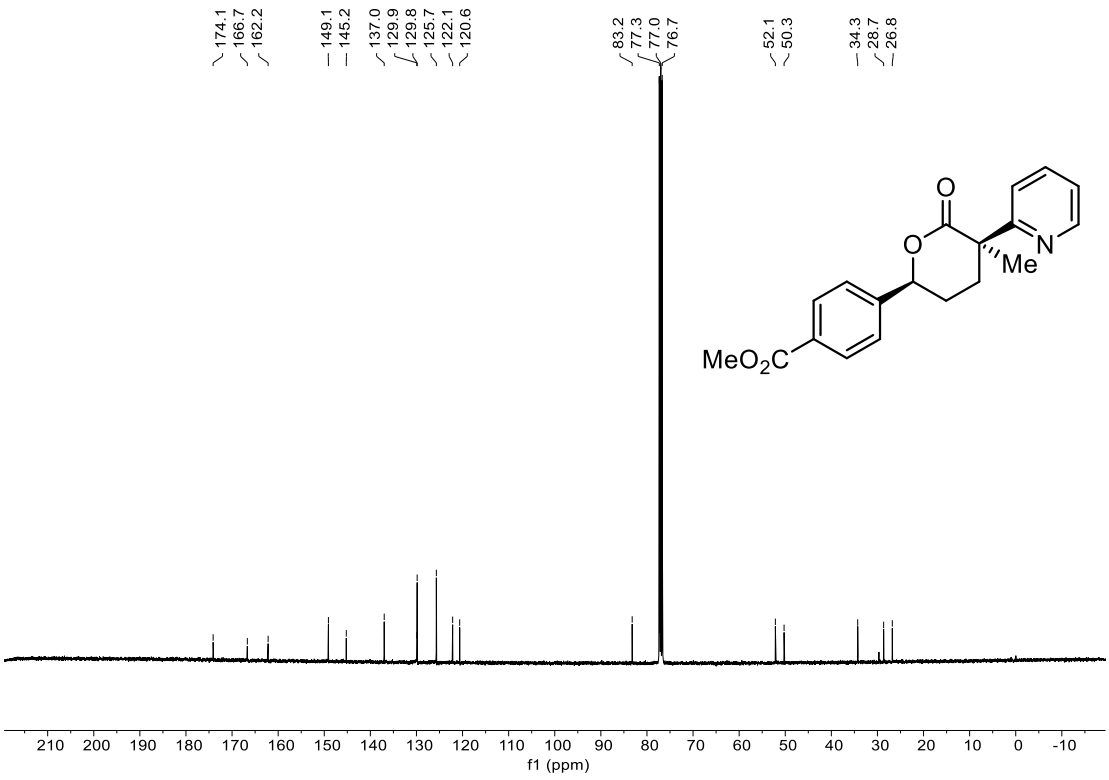
^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3v**



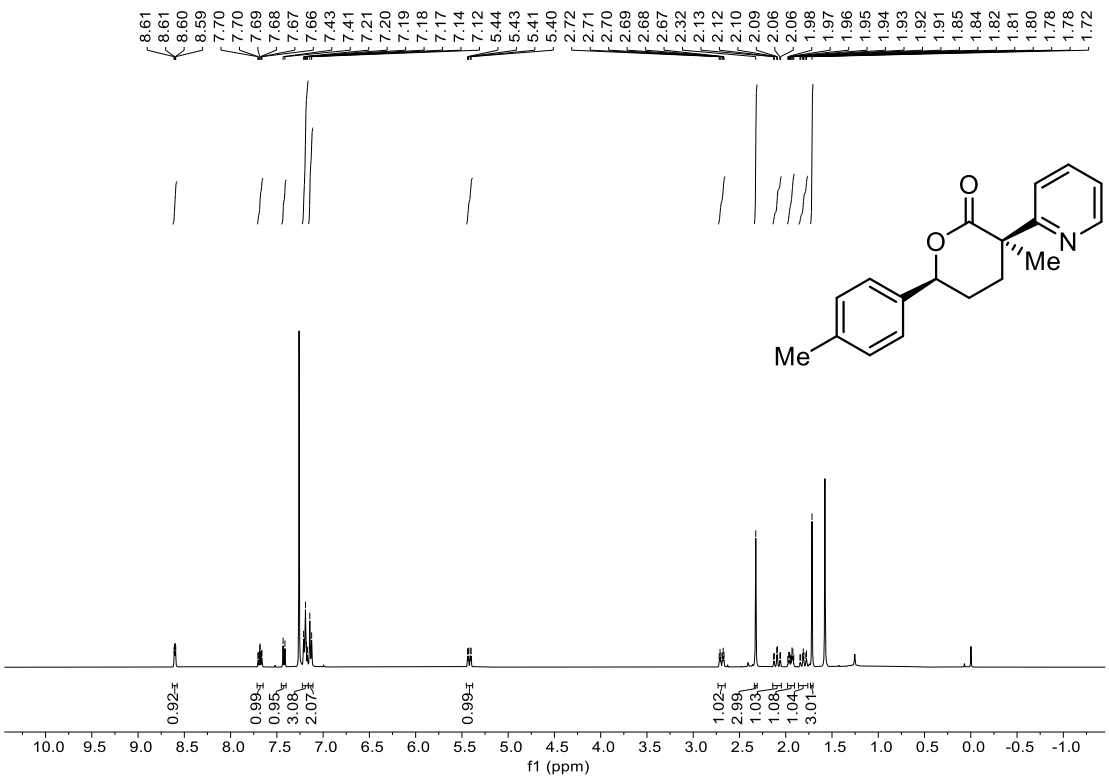
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3v**



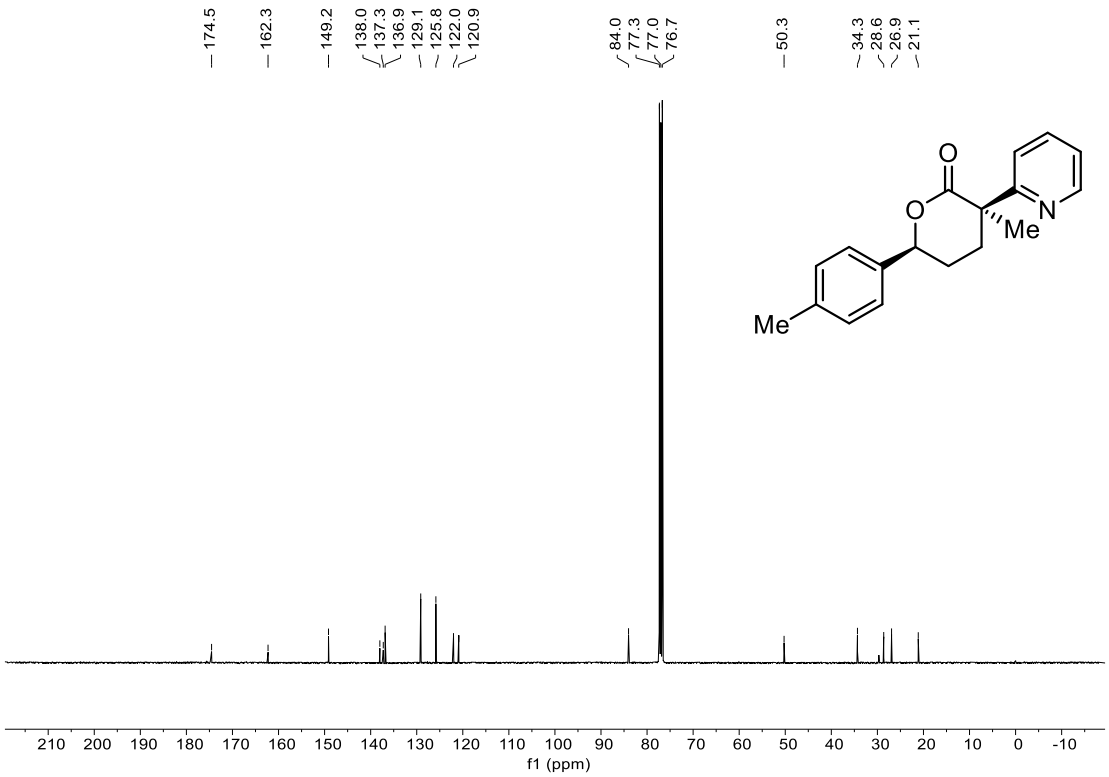
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3w**



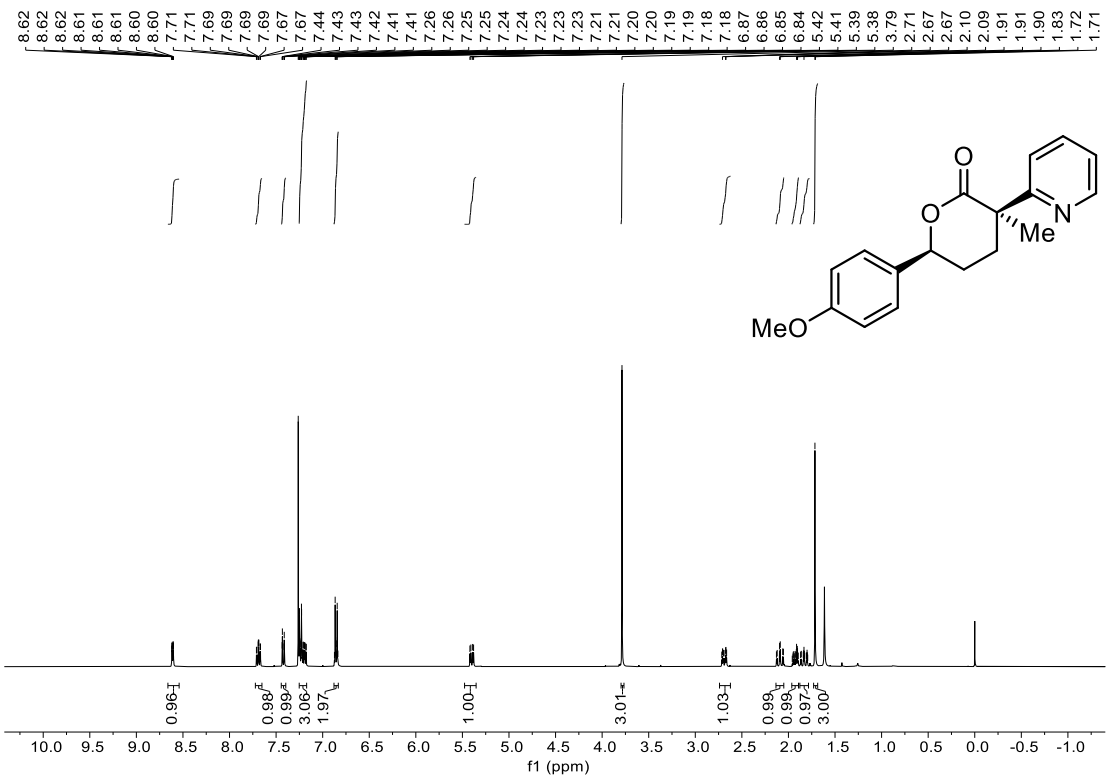
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3w**



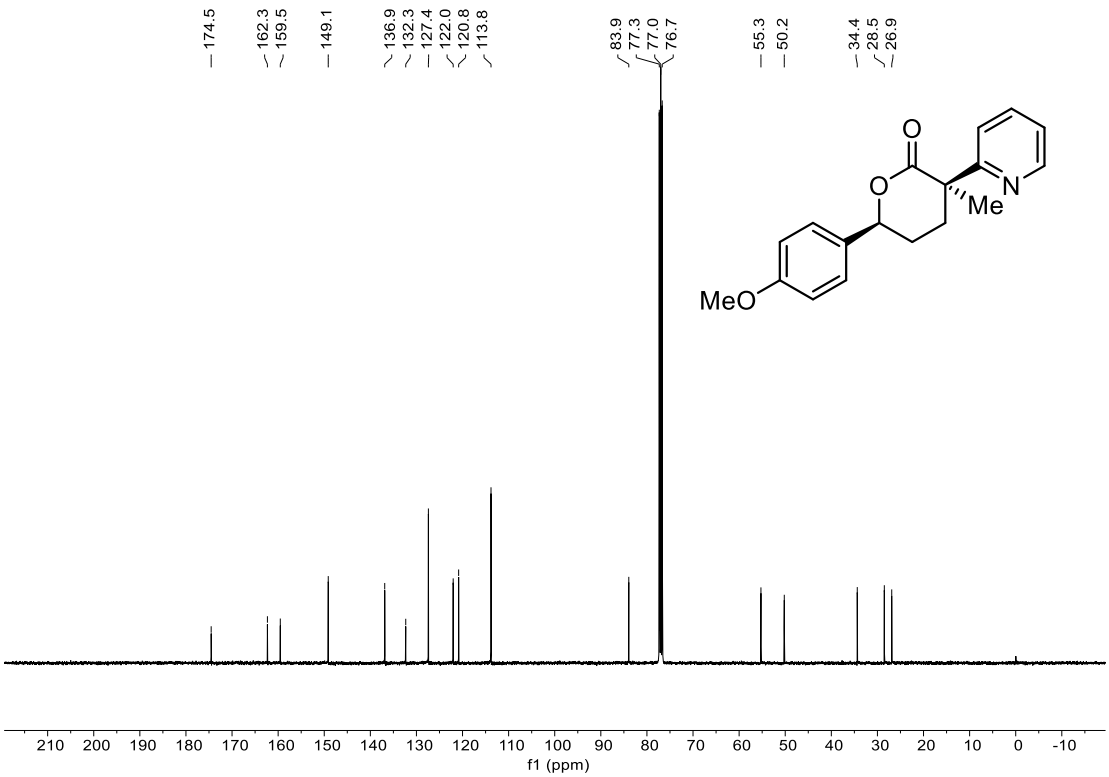
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3x**



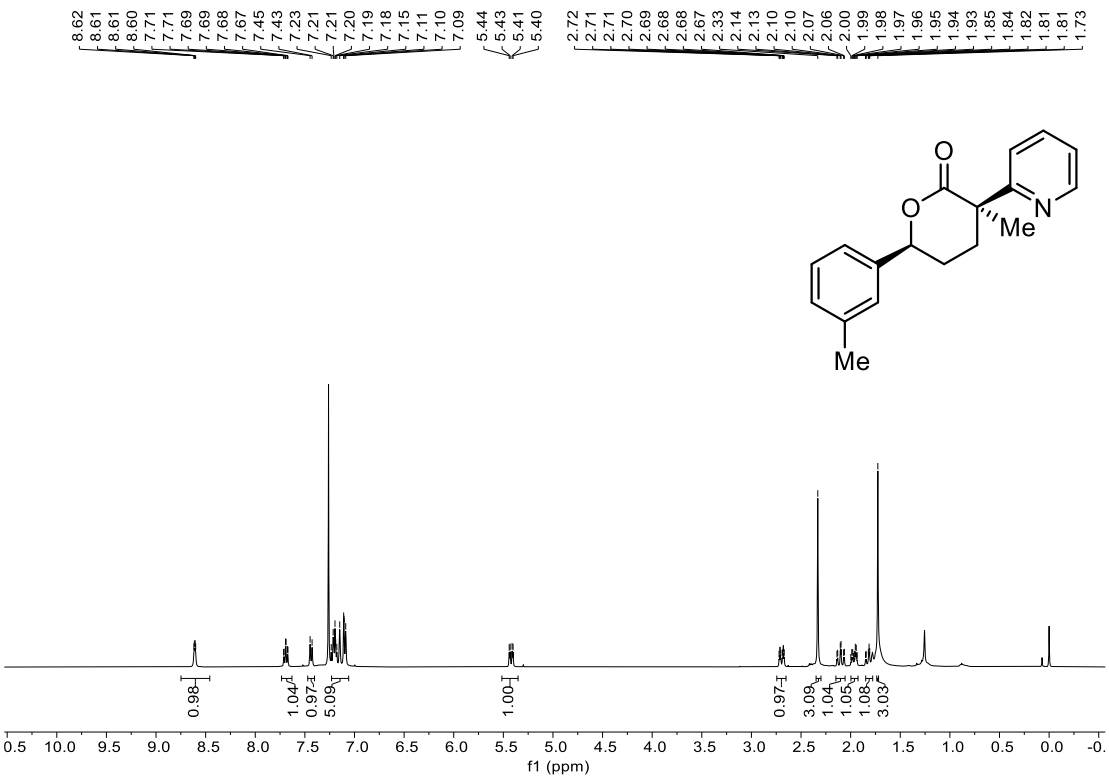
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3x**



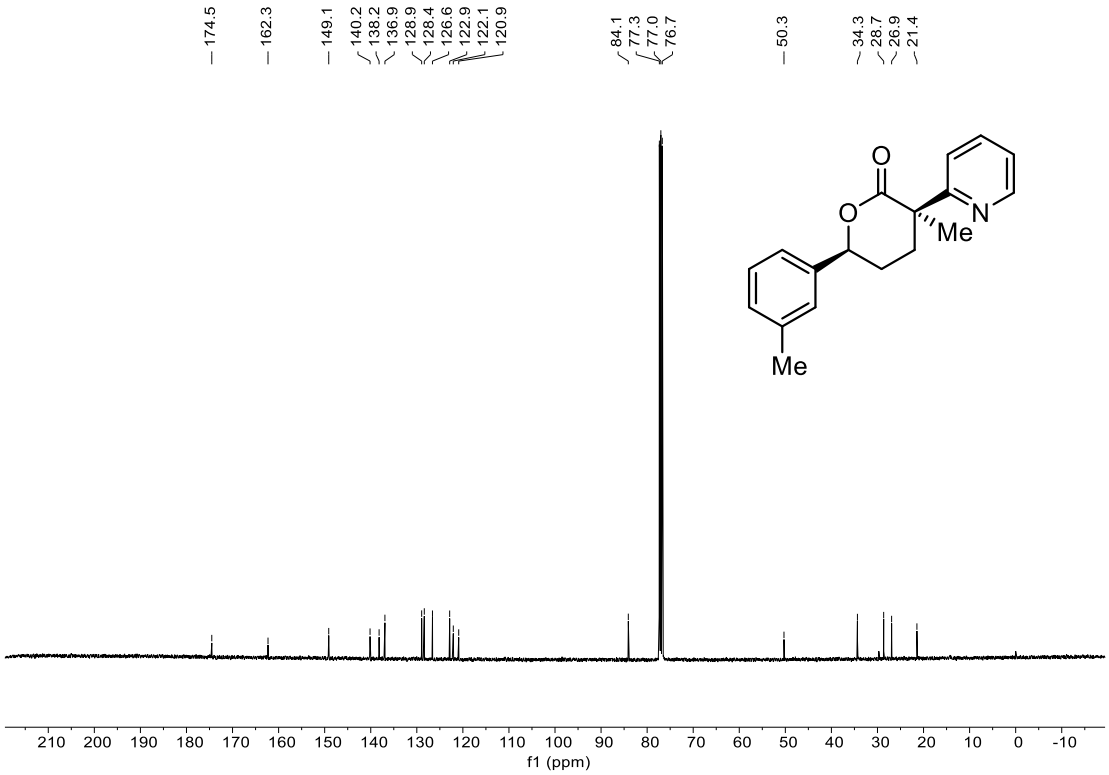
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3y**



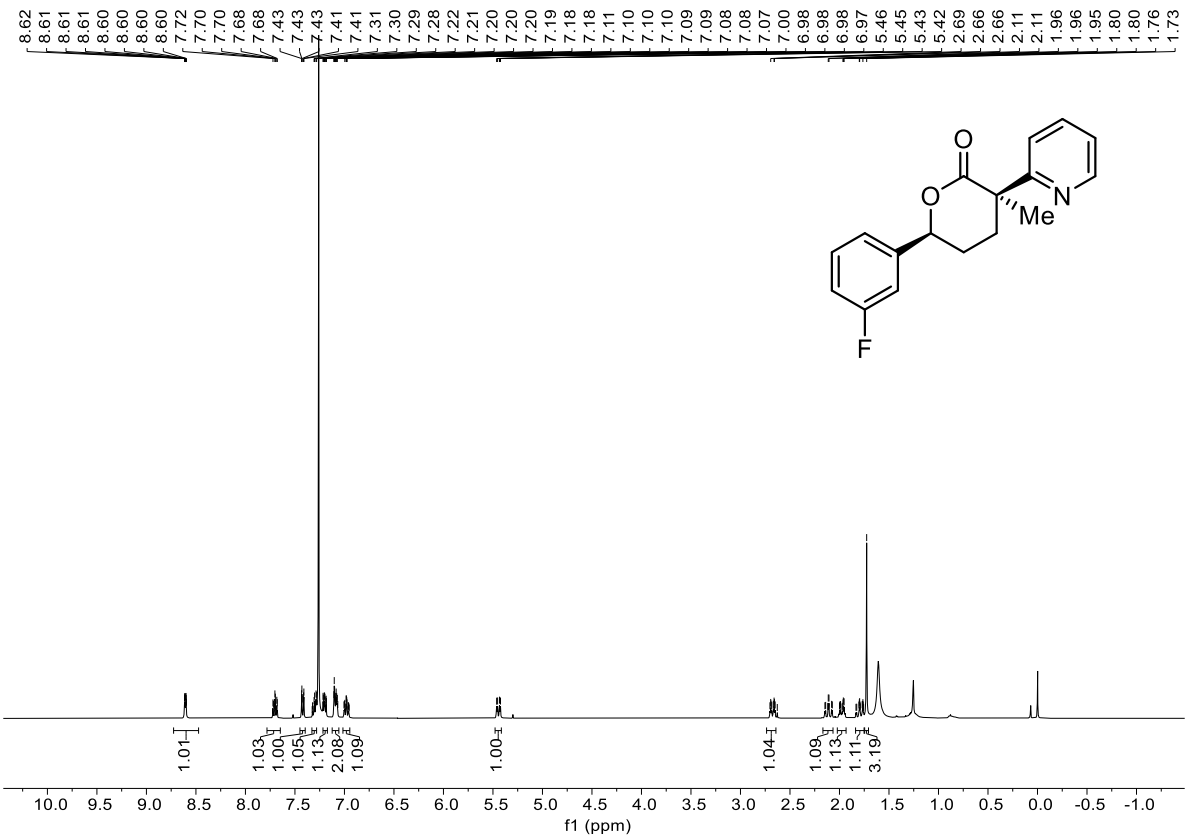
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3y**



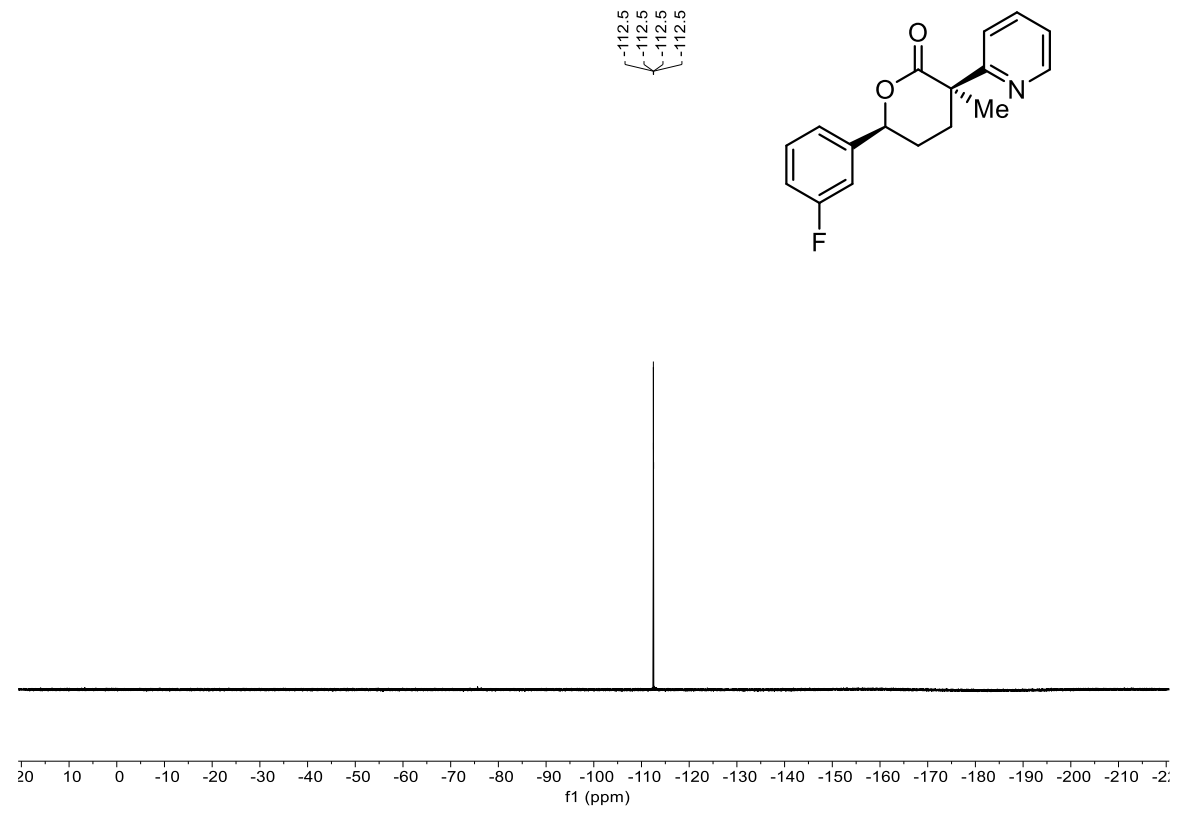
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3z**



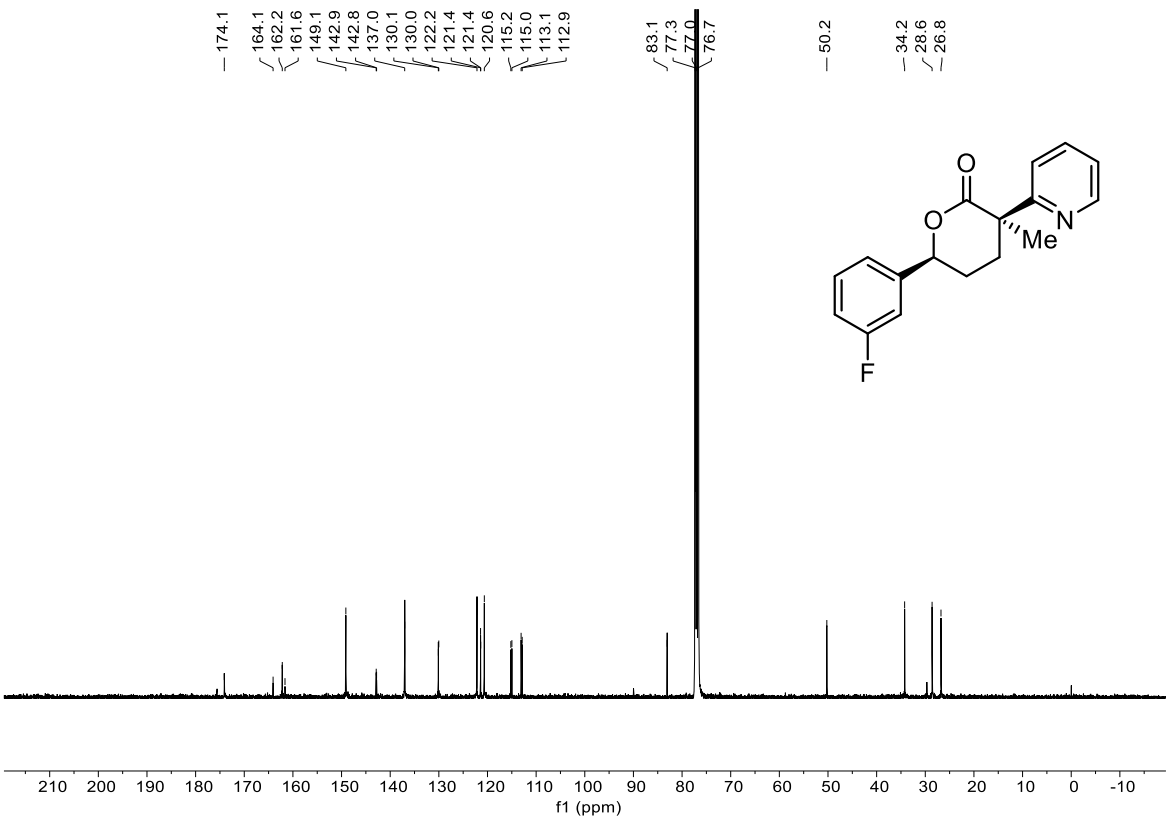
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3z**



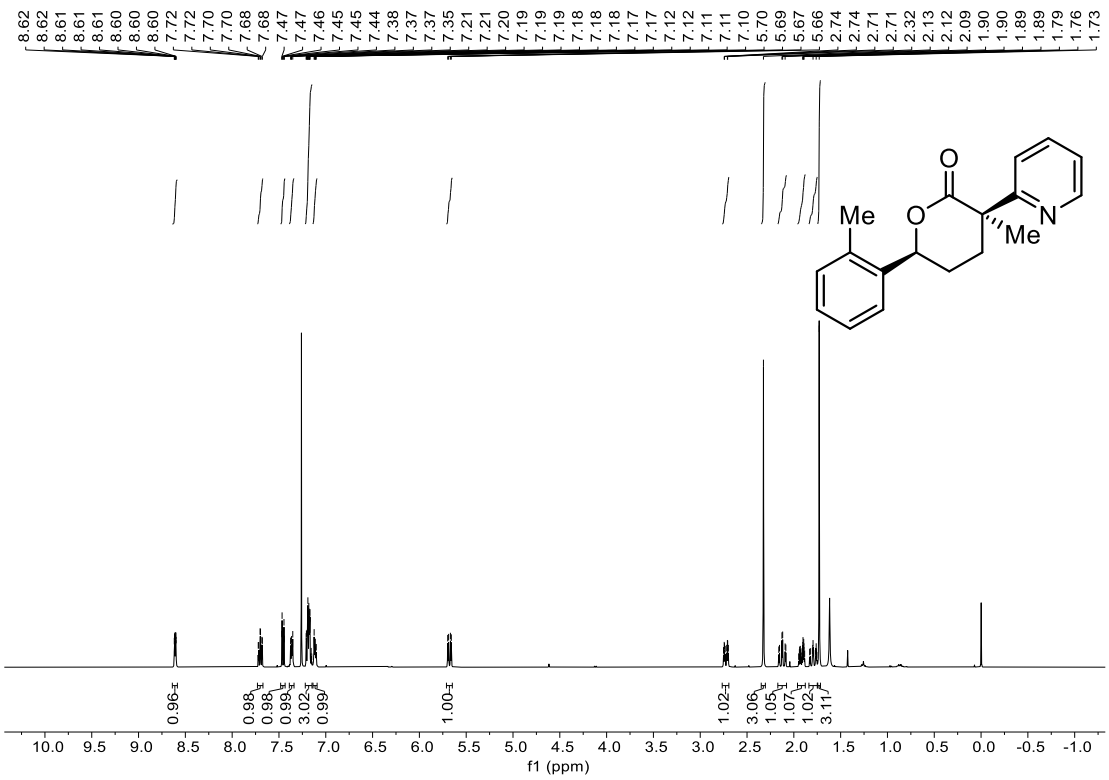
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3A**



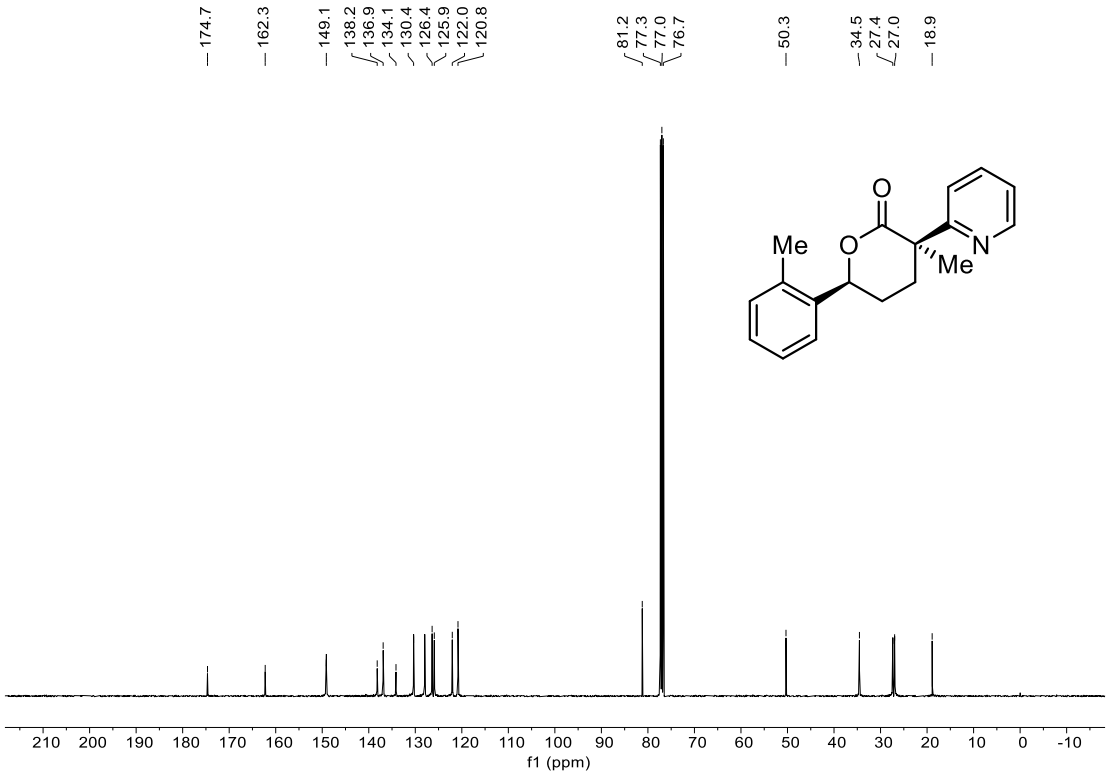
^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3A**



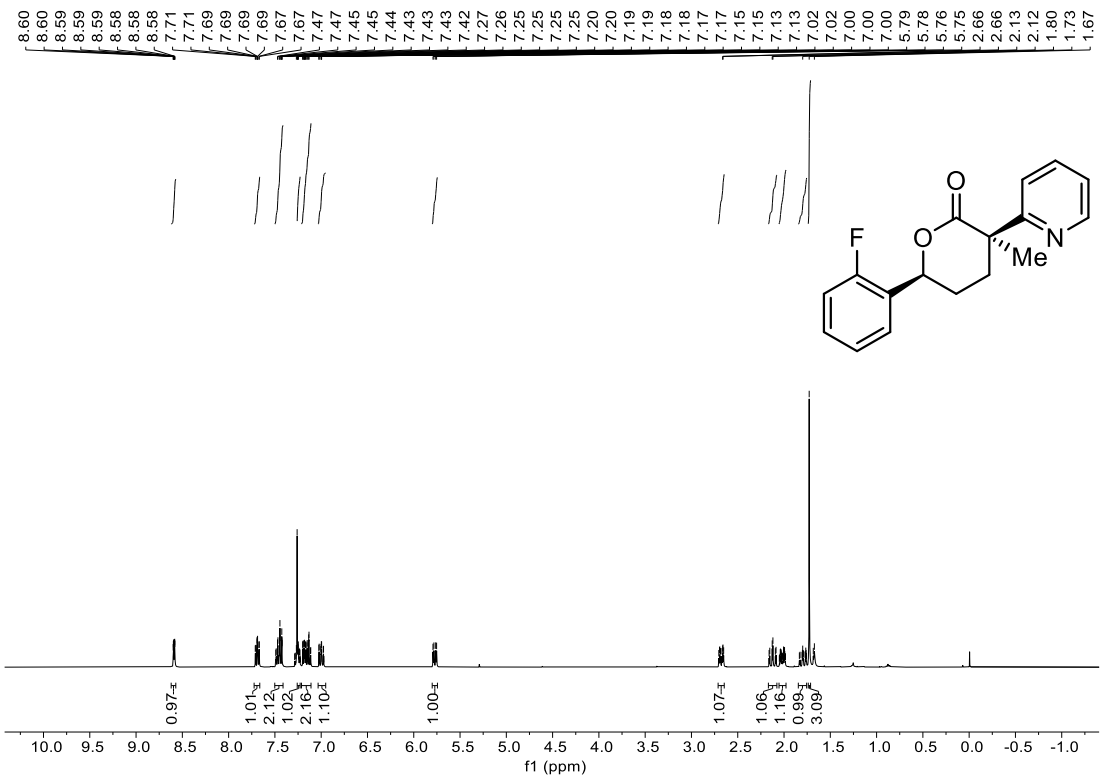
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3A**



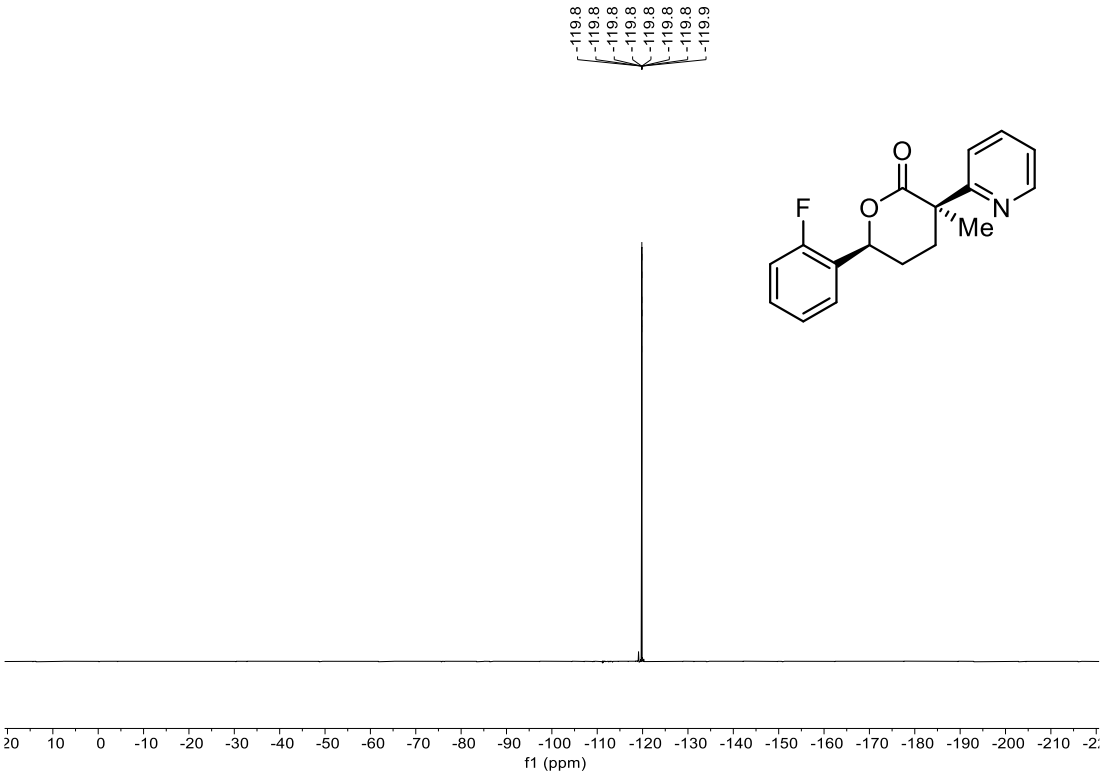
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3B**



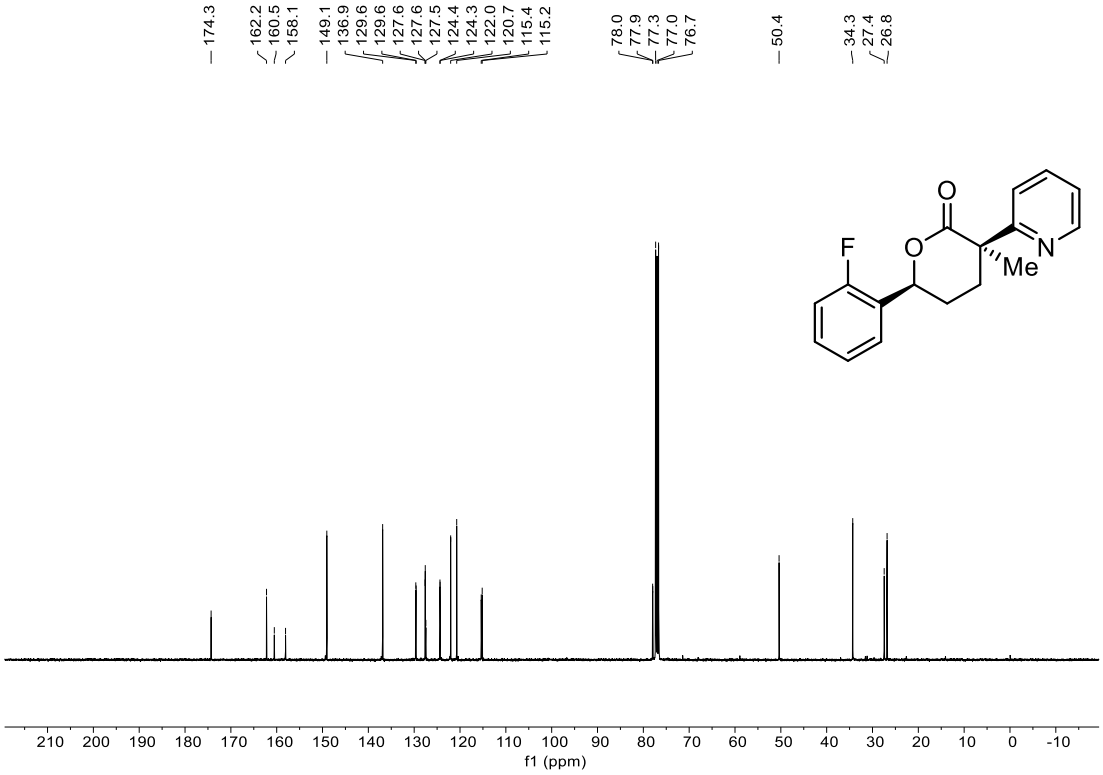
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3B**



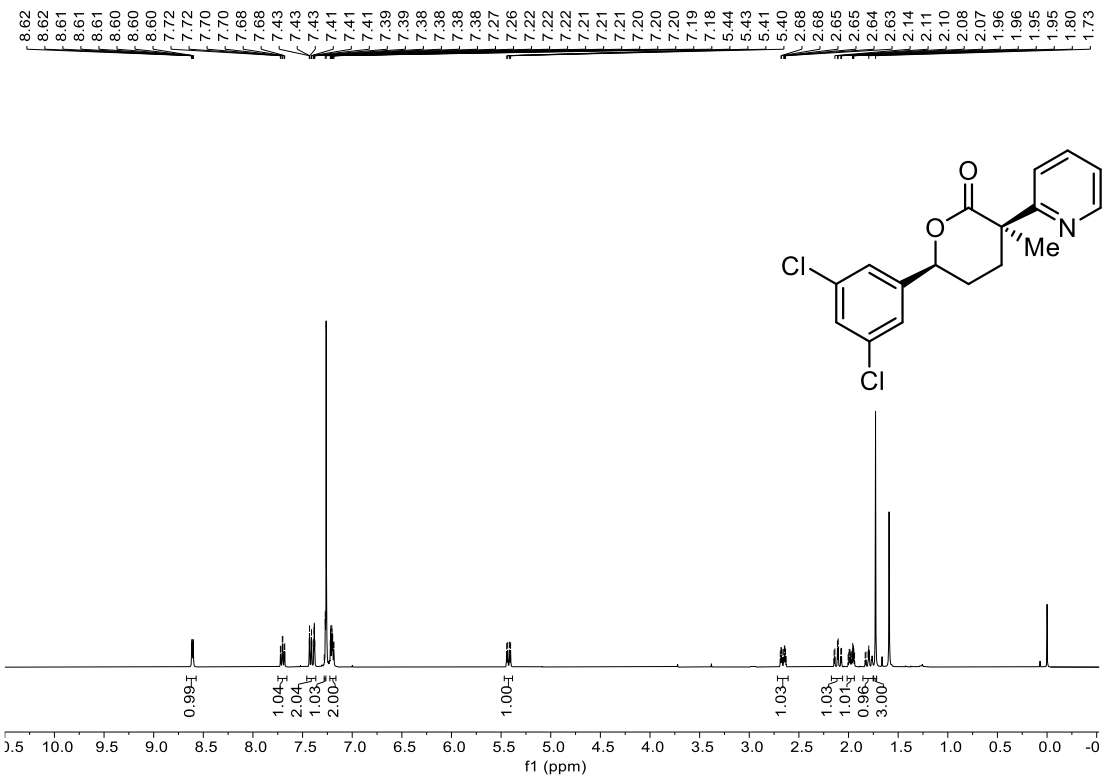
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3C**



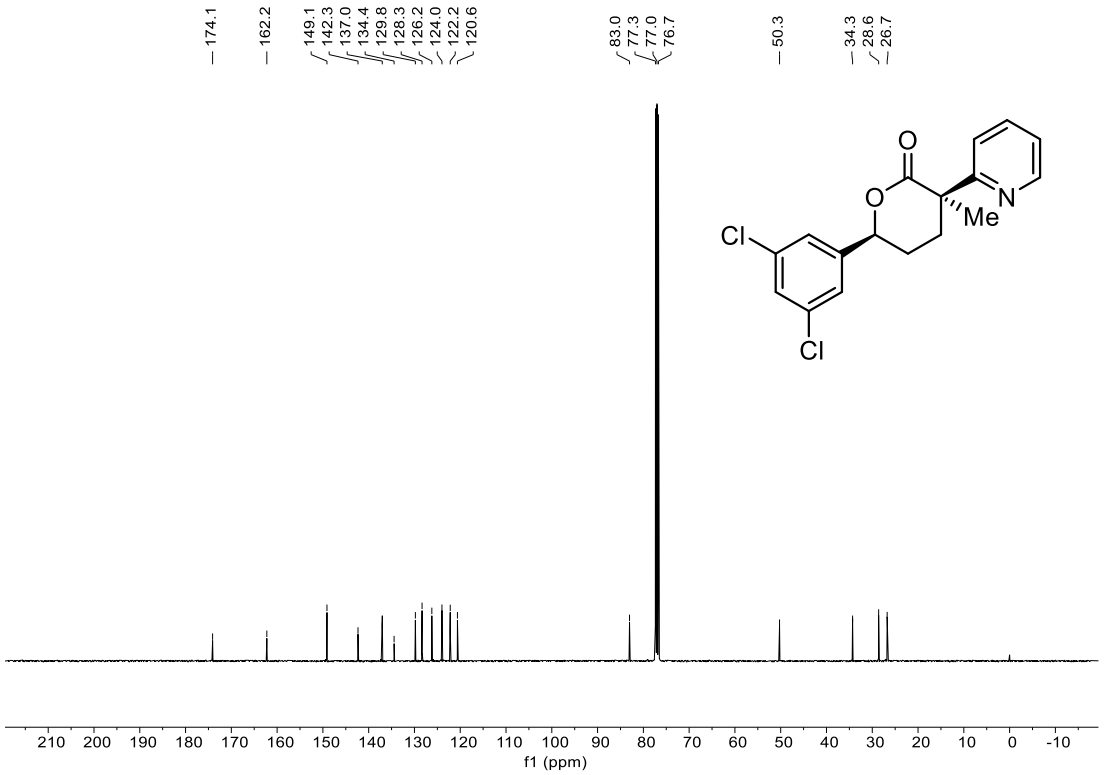
^{19}F NMR (376 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3C**



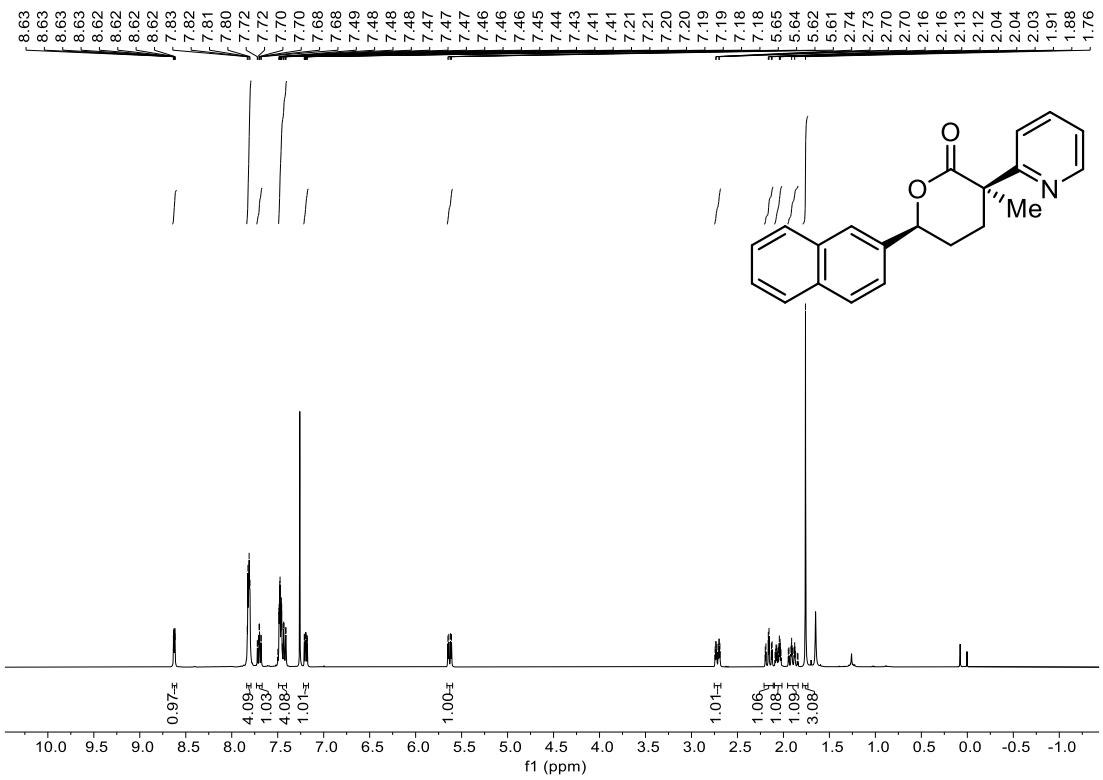
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3C**



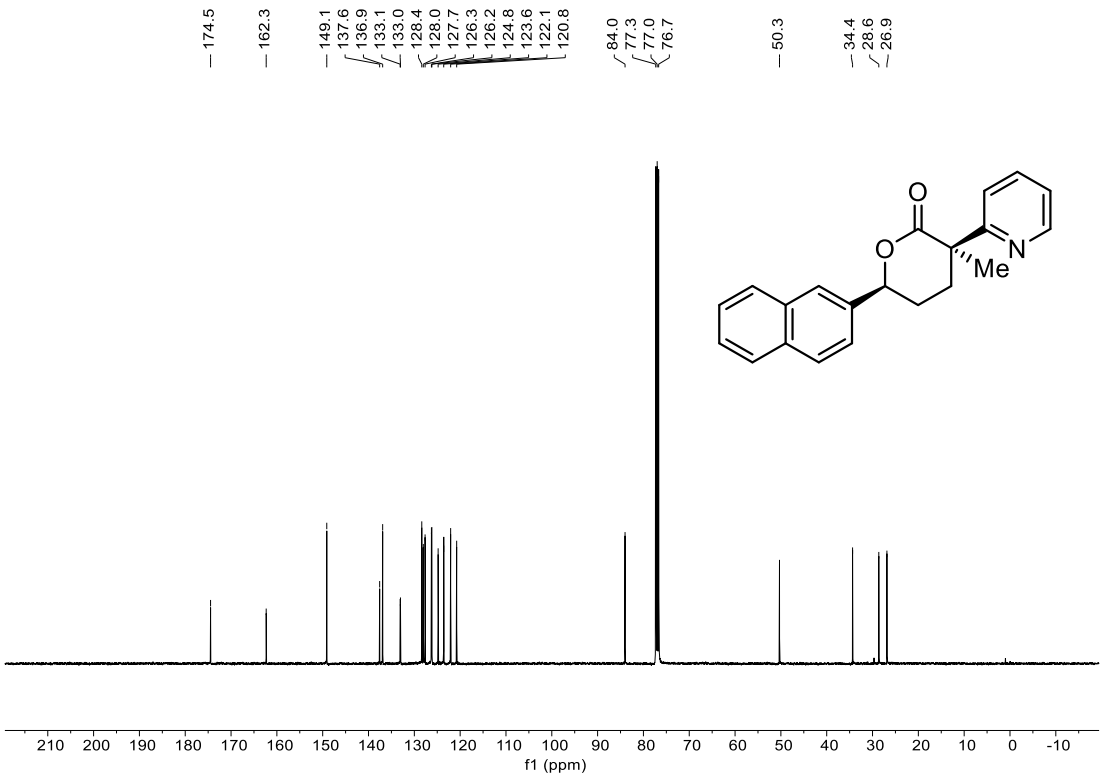
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3D**



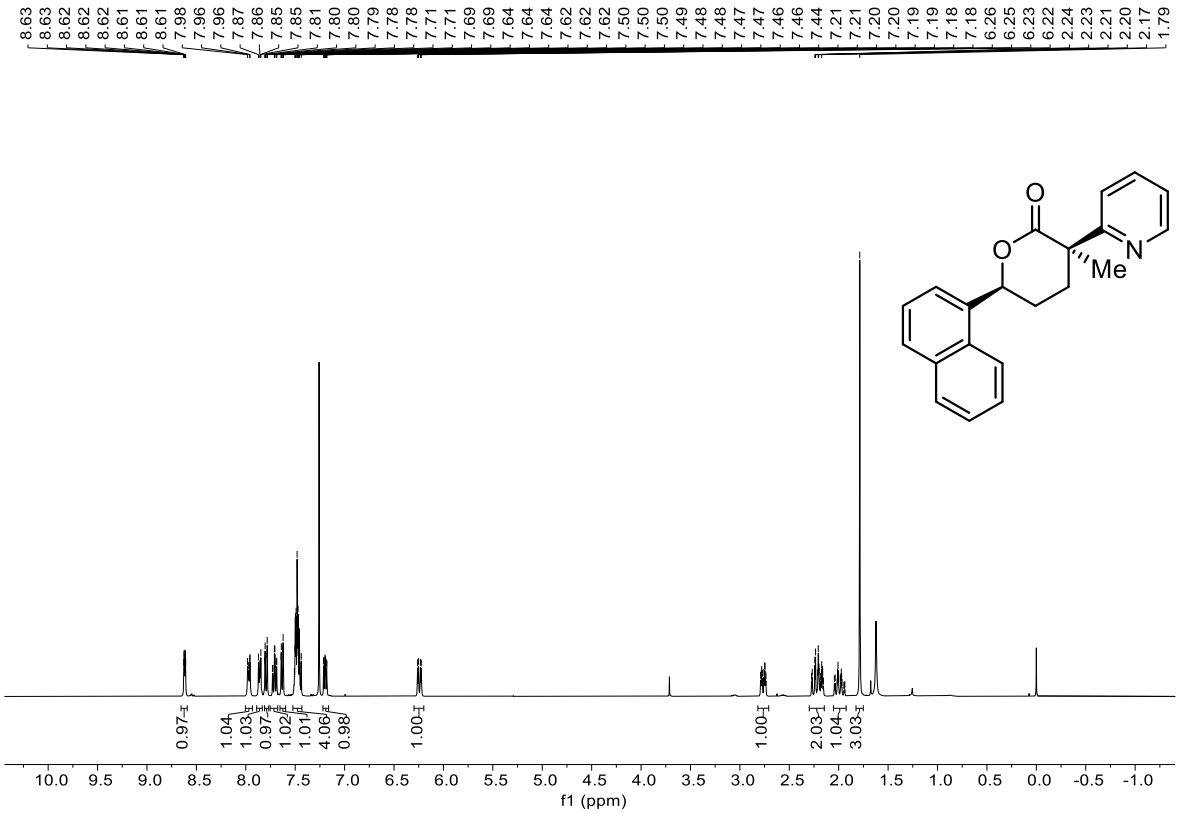
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3D**



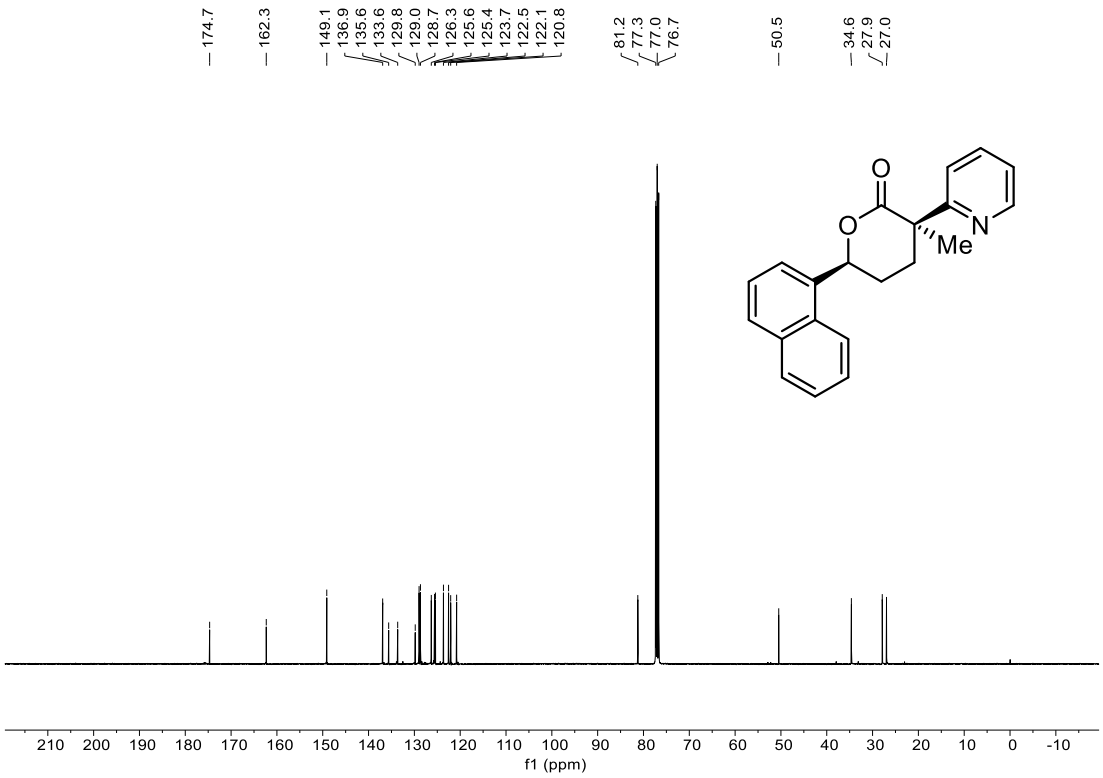
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*,6*S*)-**3E**



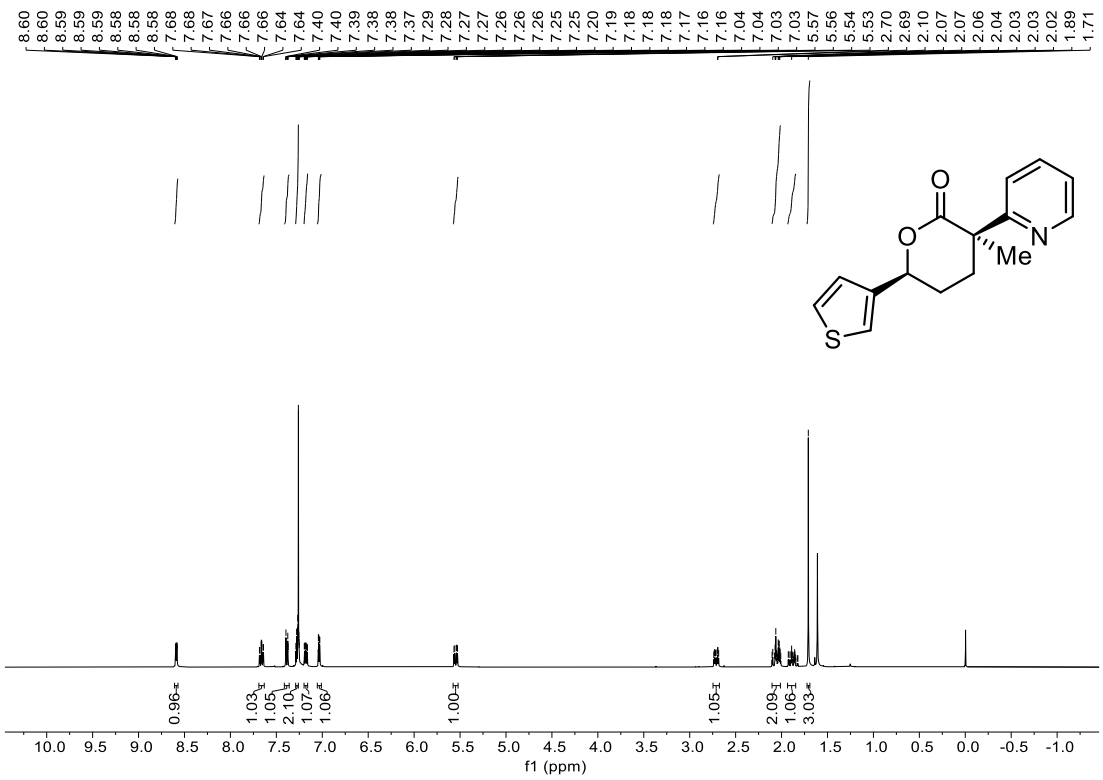
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*,6*S*)-**3E**



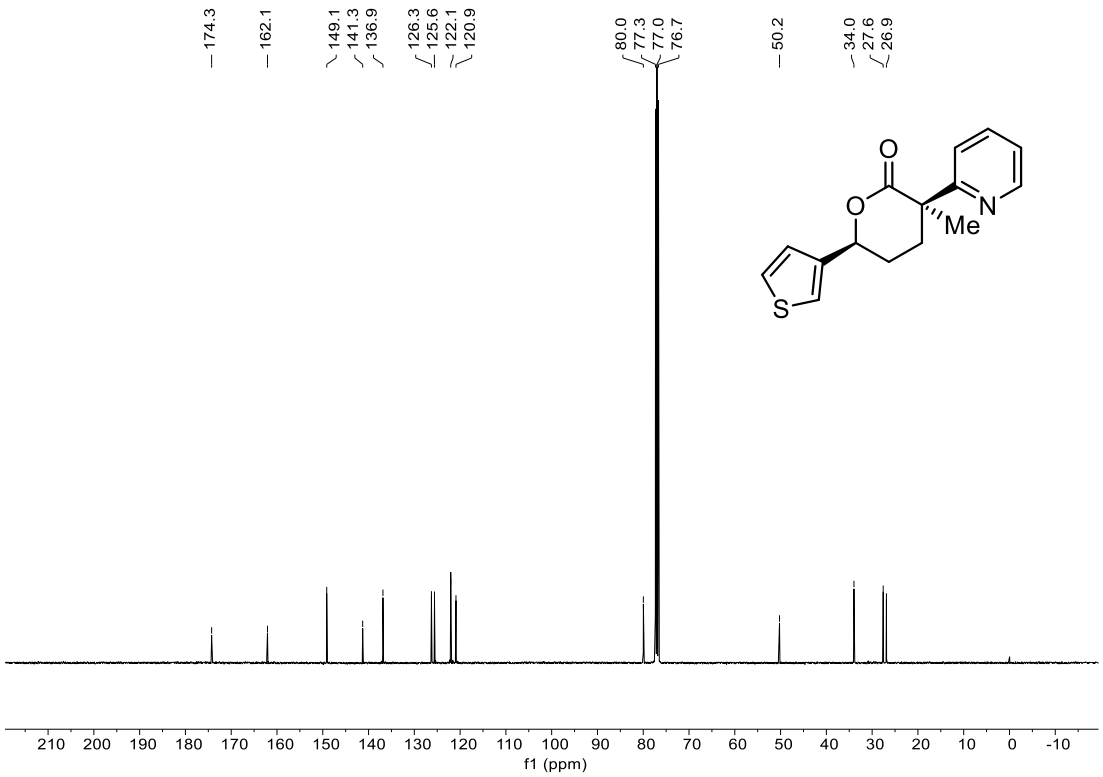
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3F**



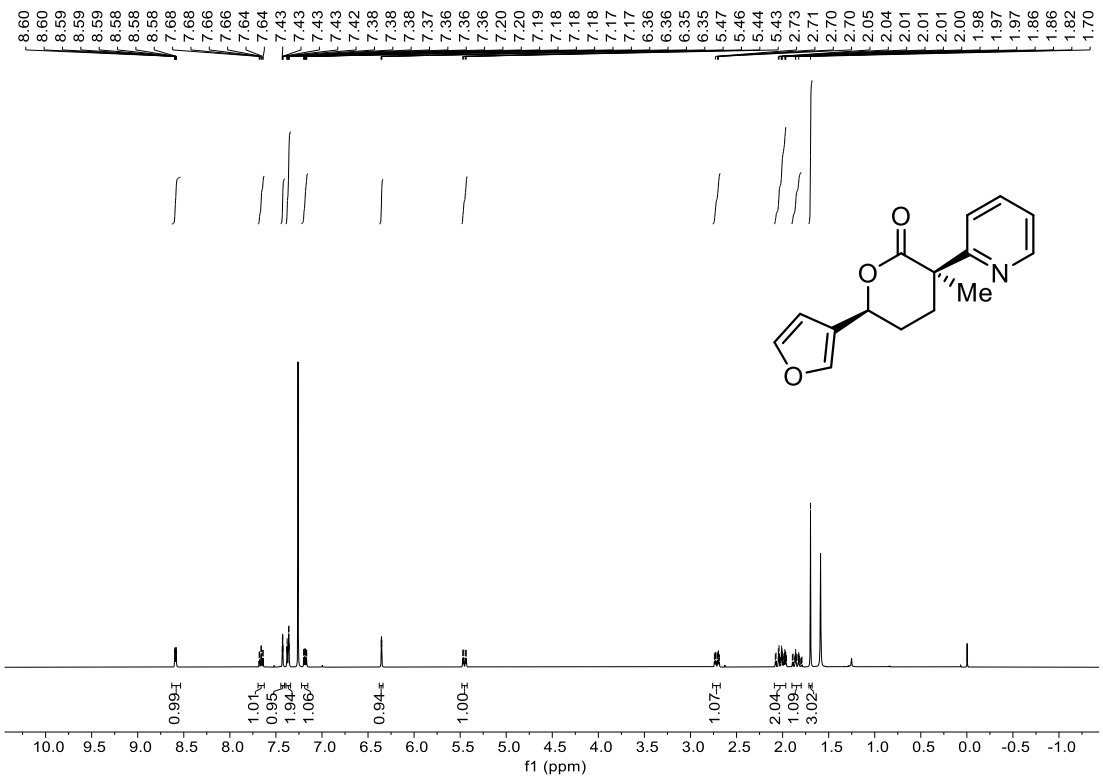
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3F**



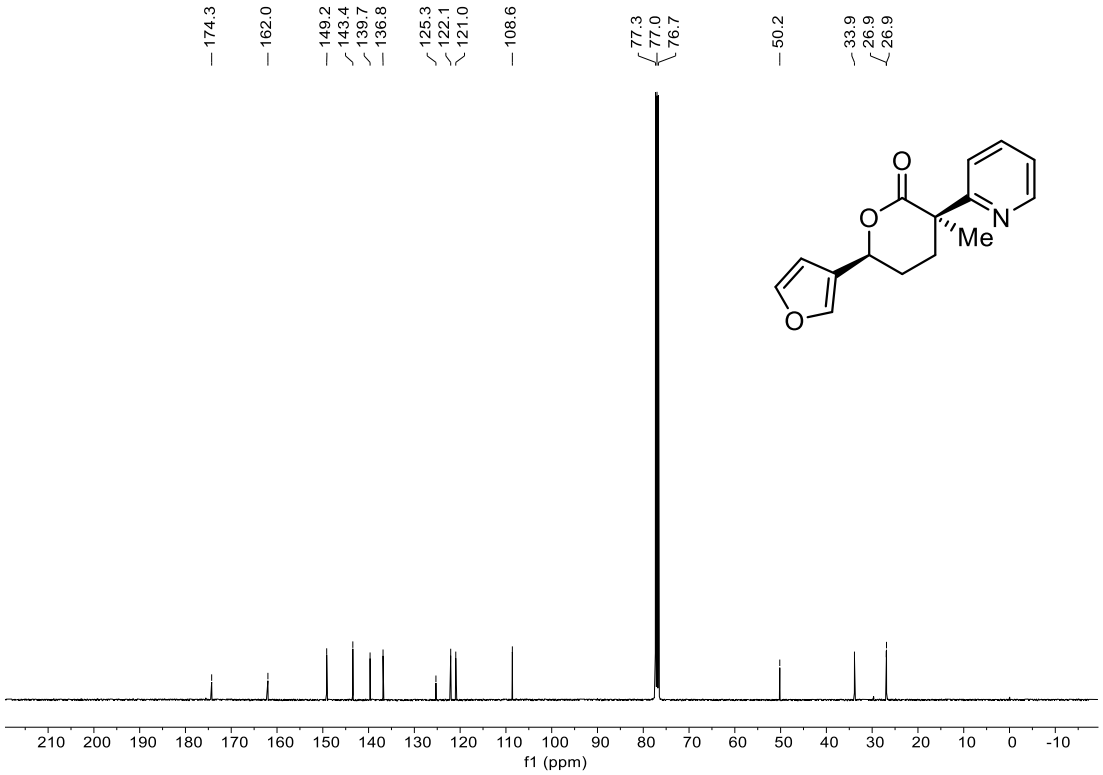
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3G**



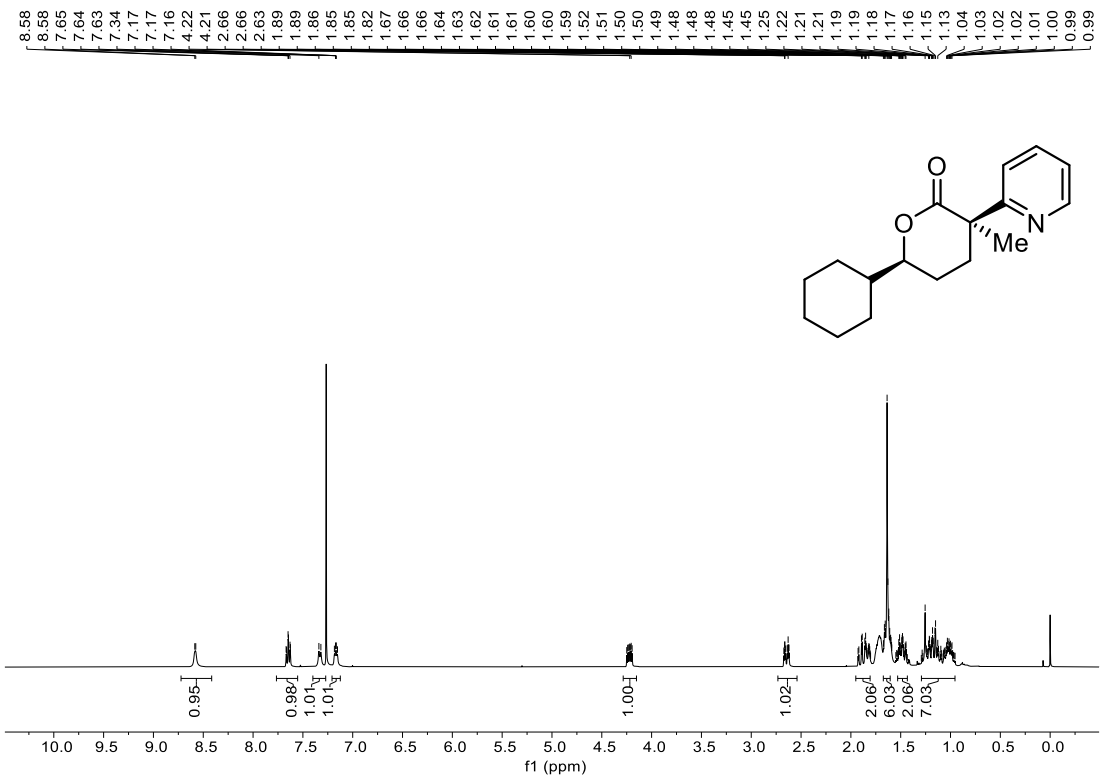
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3G**



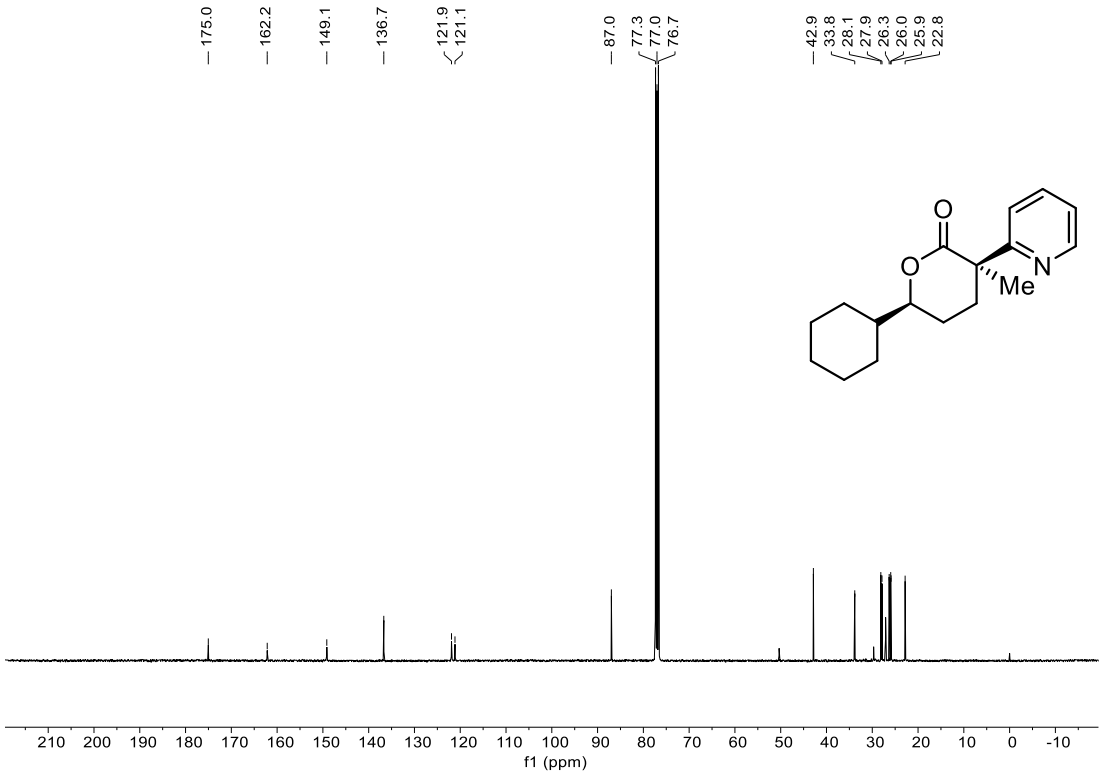
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3H**



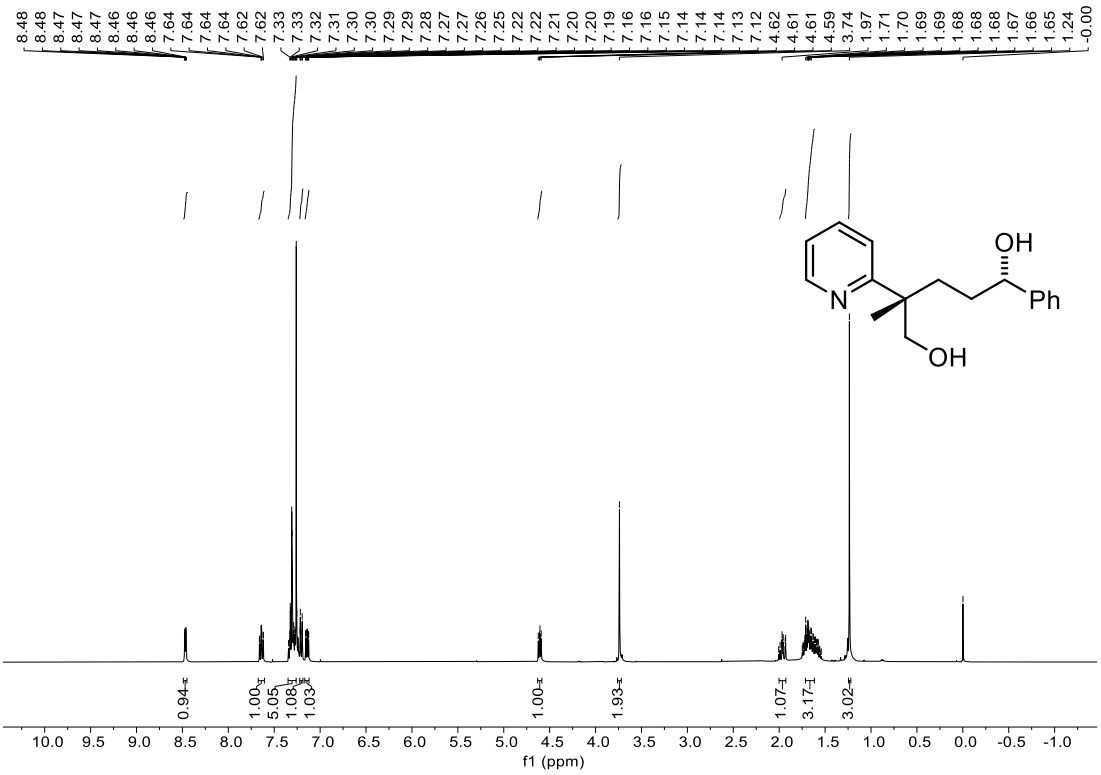
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3H**



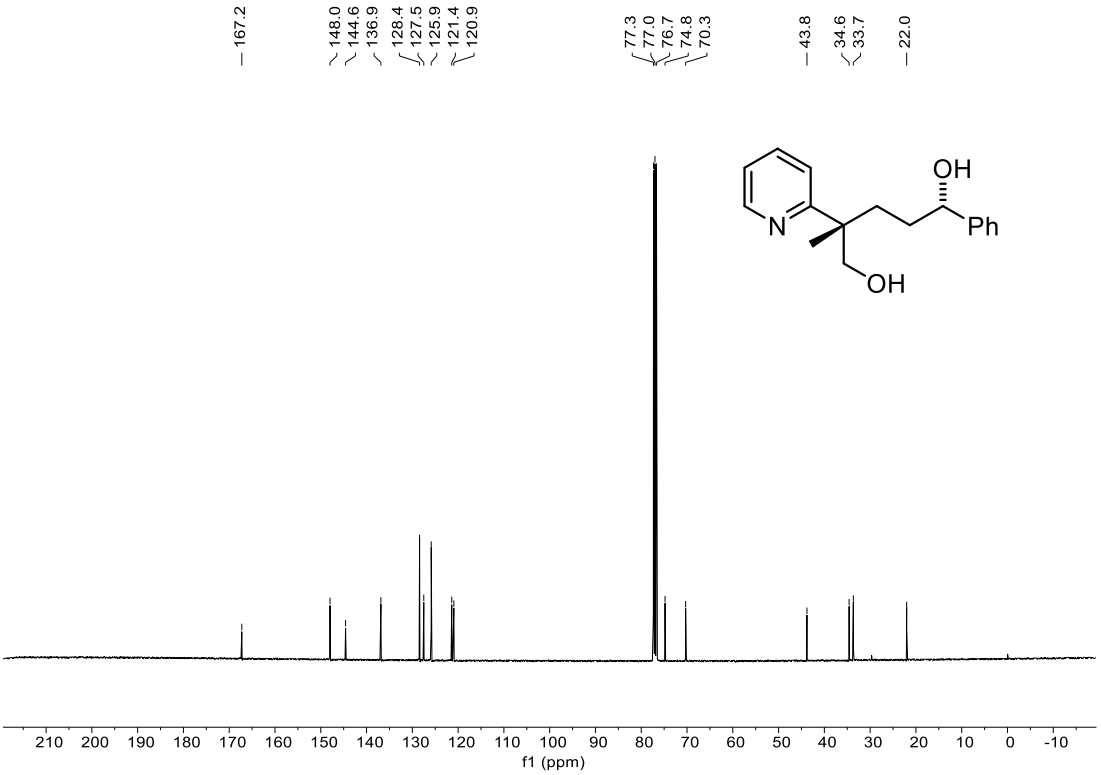
^{1}H NMR (400 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3I**



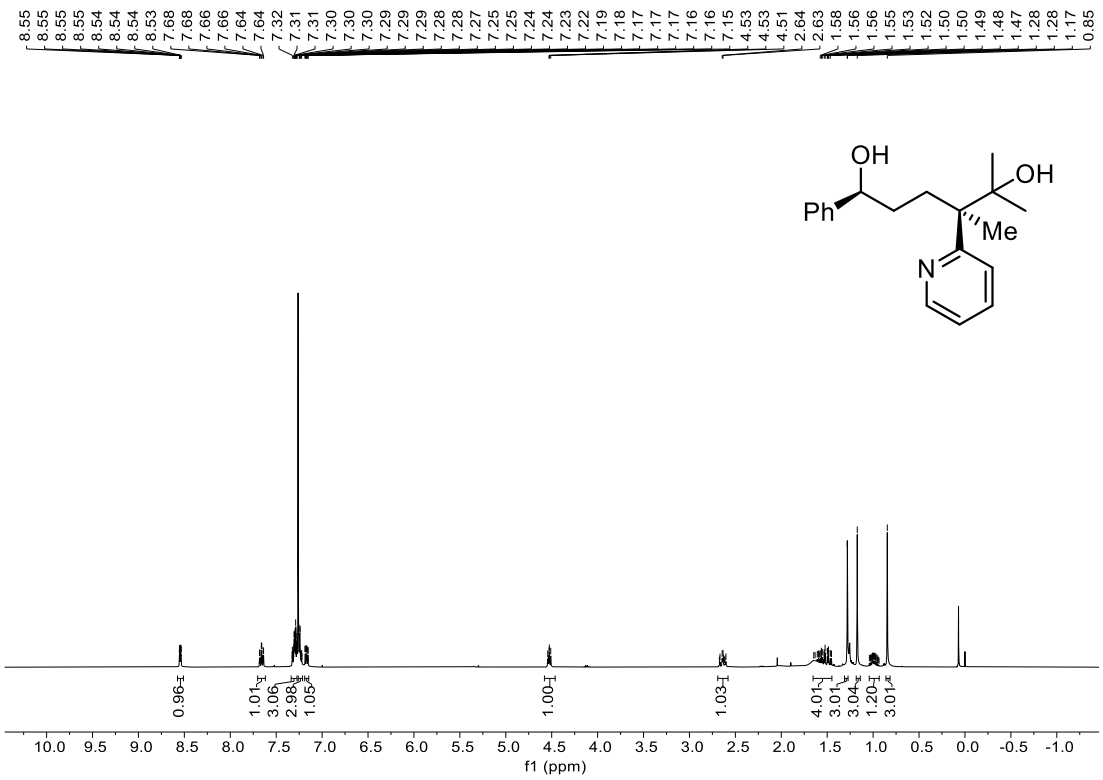
^{13}C NMR (101 MHz, $CDCl_3$) of (3*R*, 6*S*)-**3I**



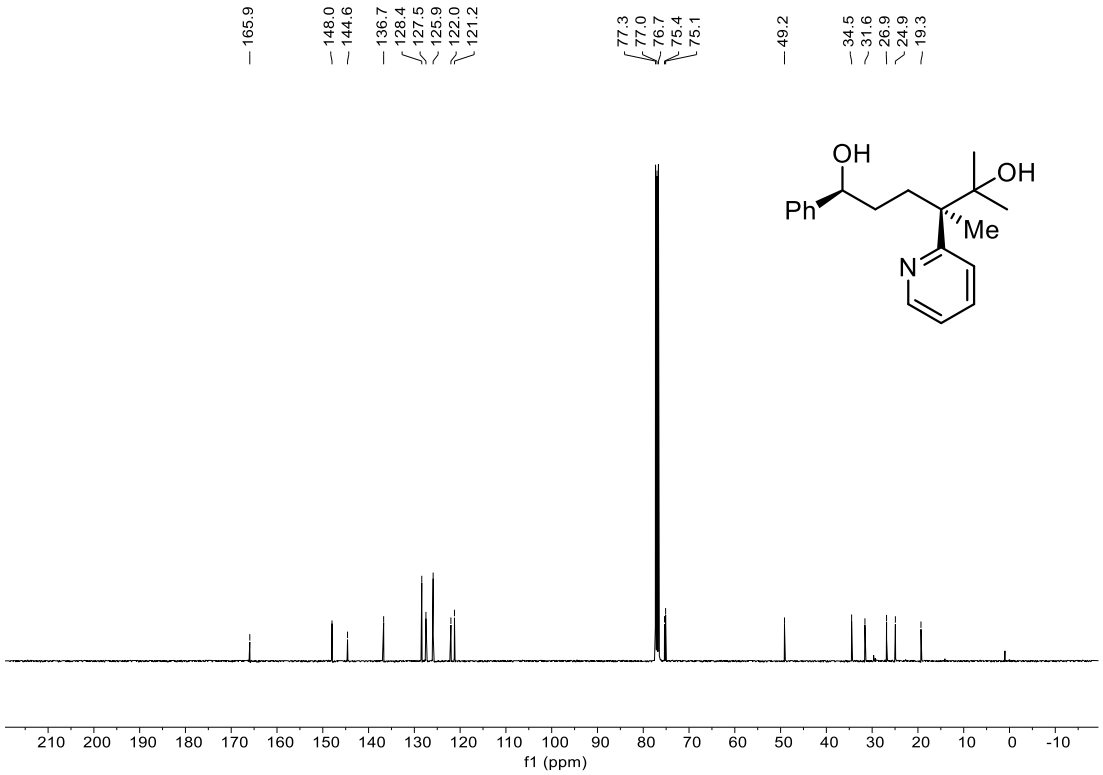
^{1}H NMR (400 MHz, $CDCl_3$) of **4**



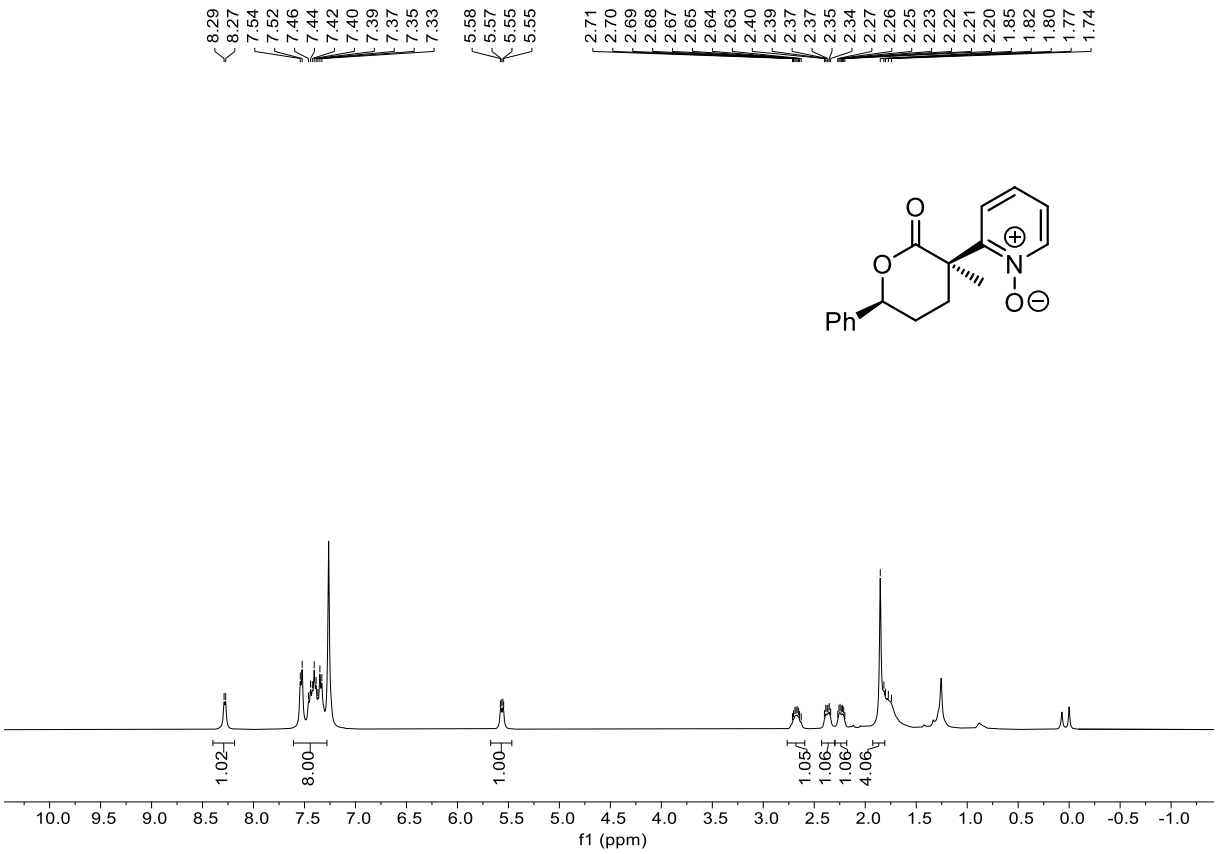
^{13}C NMR (101 MHz, $CDCl_3$) of **4**



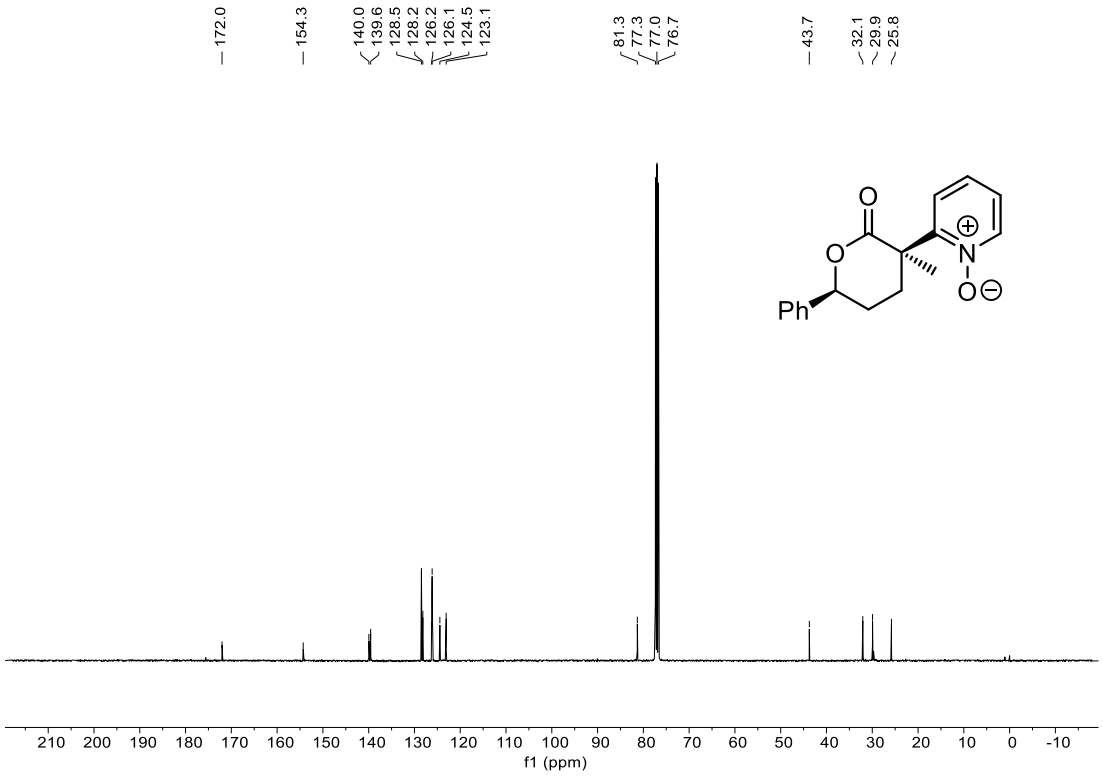
^{1}H NMR (400 MHz, $CDCl_3$) of **5**



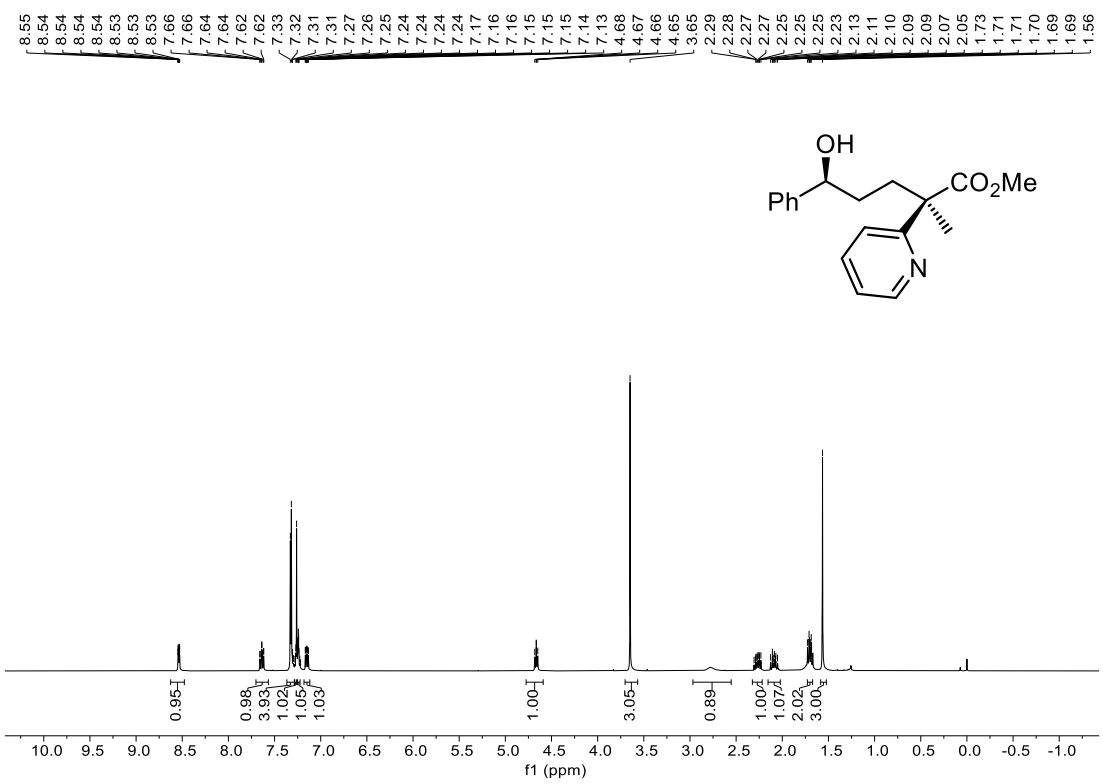
^{13}C NMR (101 MHz, $CDCl_3$) of **5**



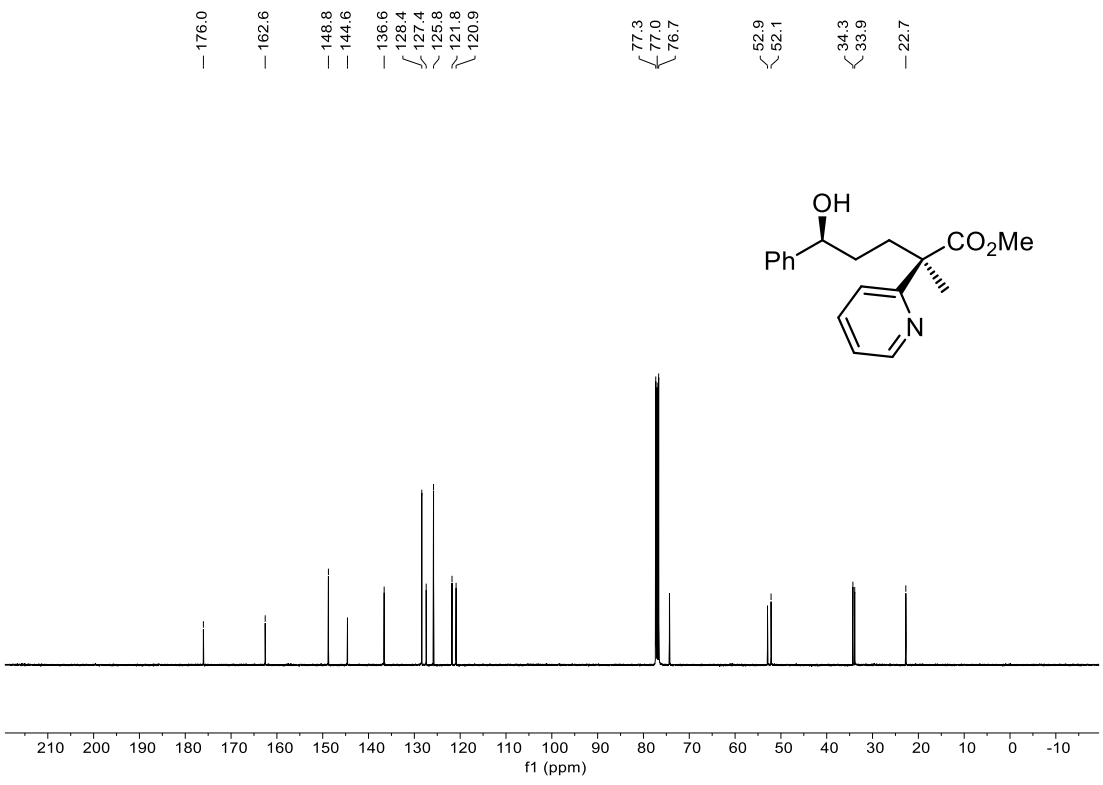
^{1}H NMR (400 MHz, $CDCl_3$) of **6**



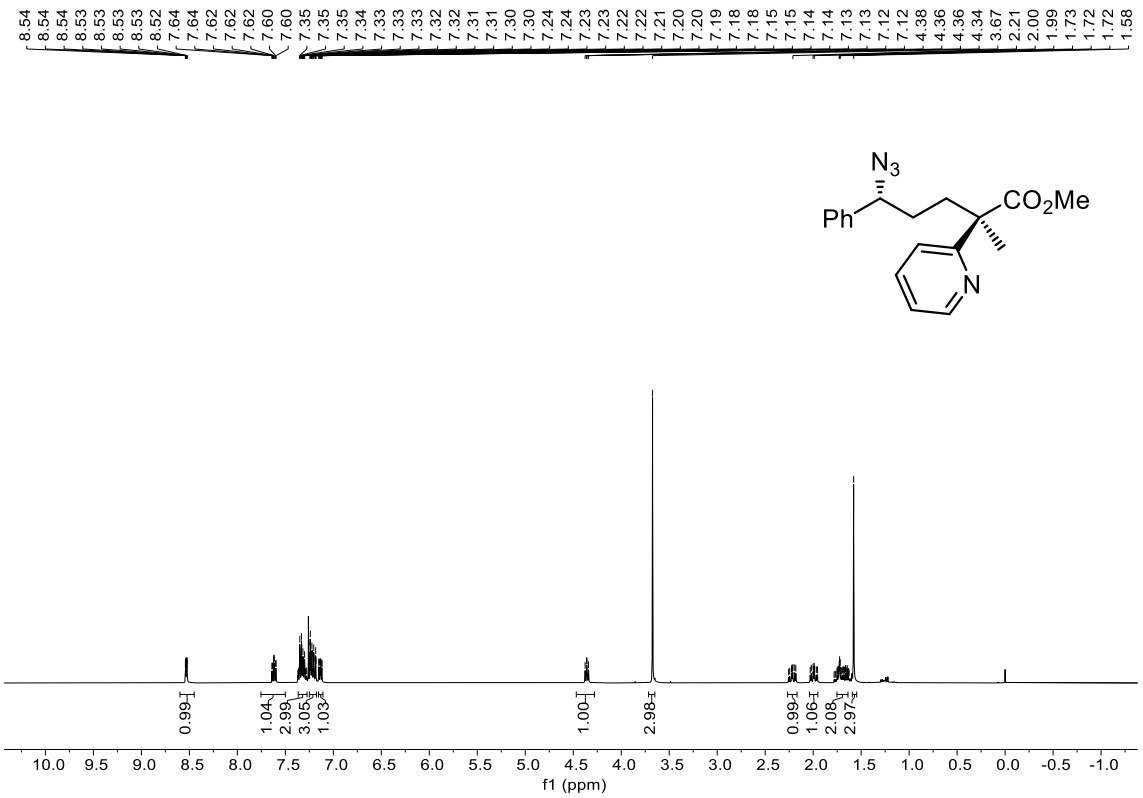
^{13}C NMR (101 MHz, $CDCl_3$) of **6**



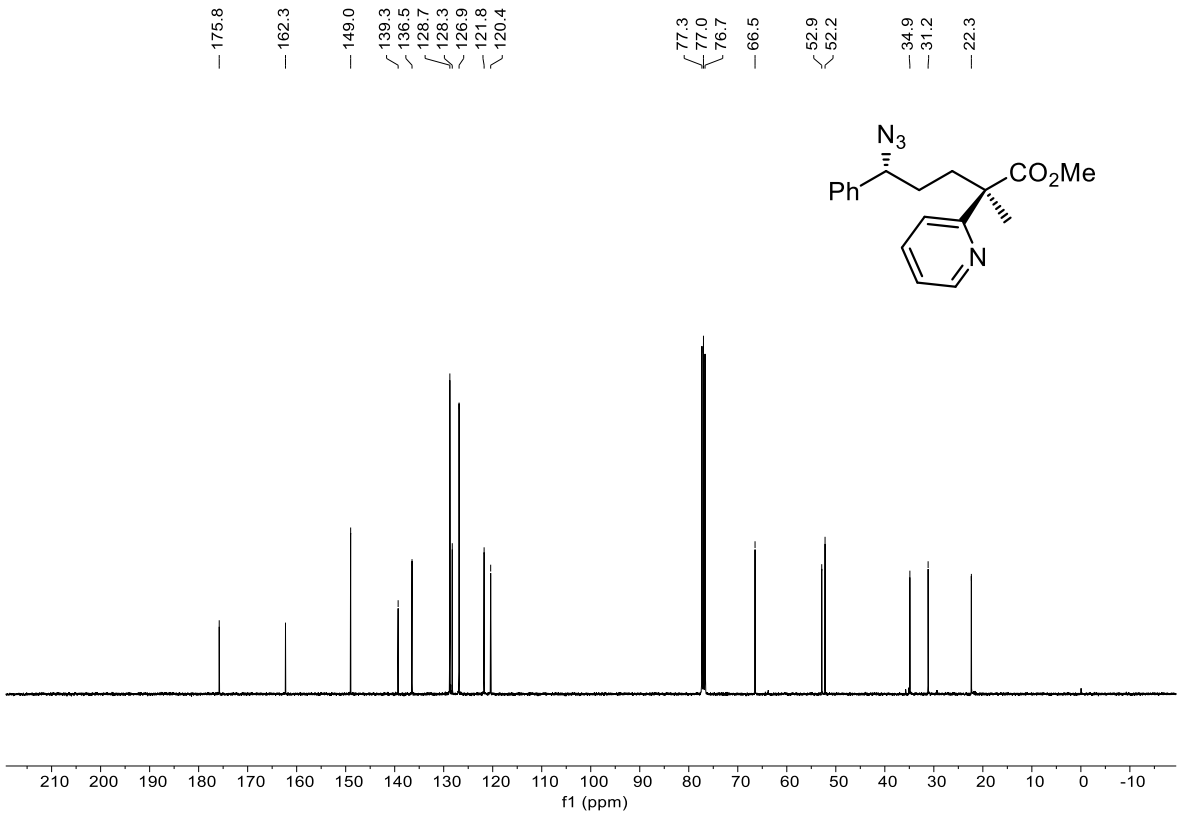
^{1}H NMR (400 MHz, $CDCl_3$) of **7**



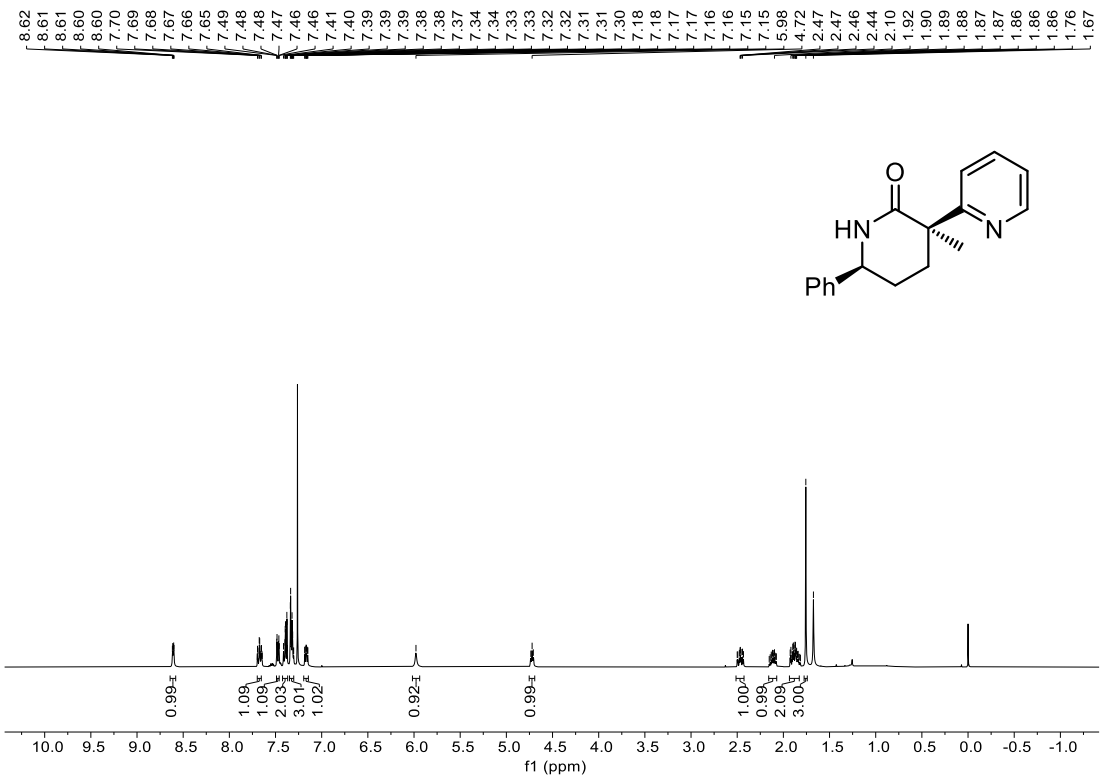
^{13}C NMR (101 MHz, $CDCl_3$) of **7**



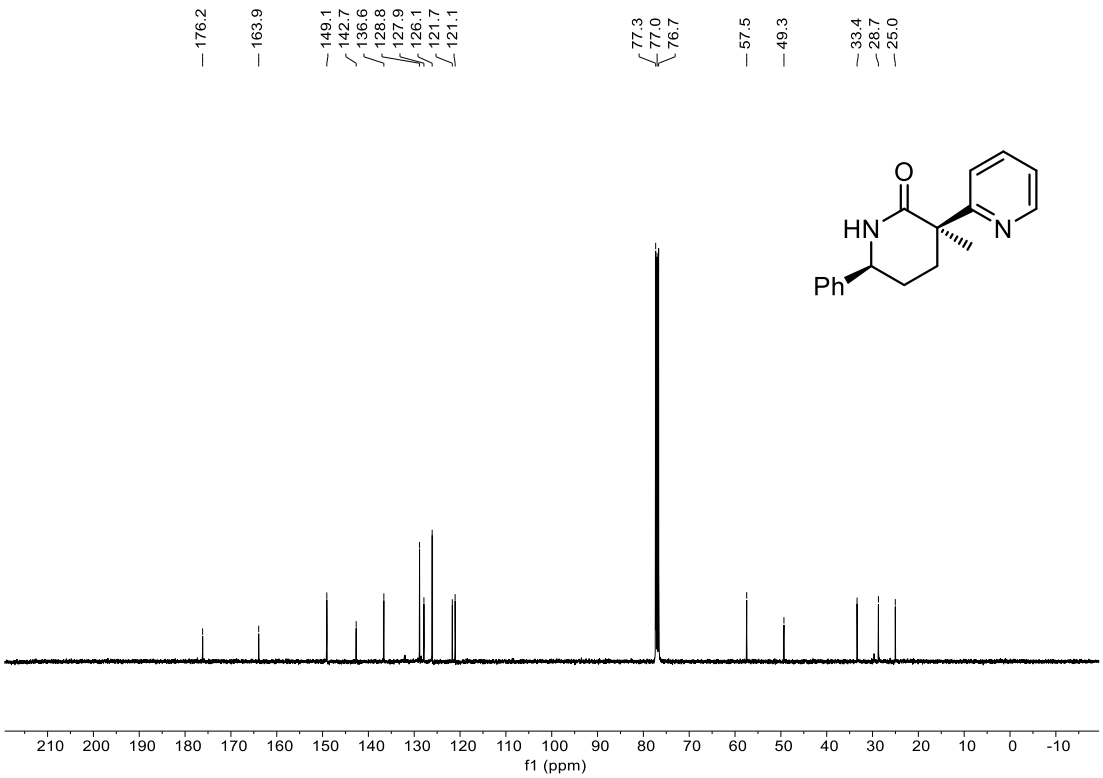
^{1}H NMR (400 MHz, $CDCl_3$) of **8**



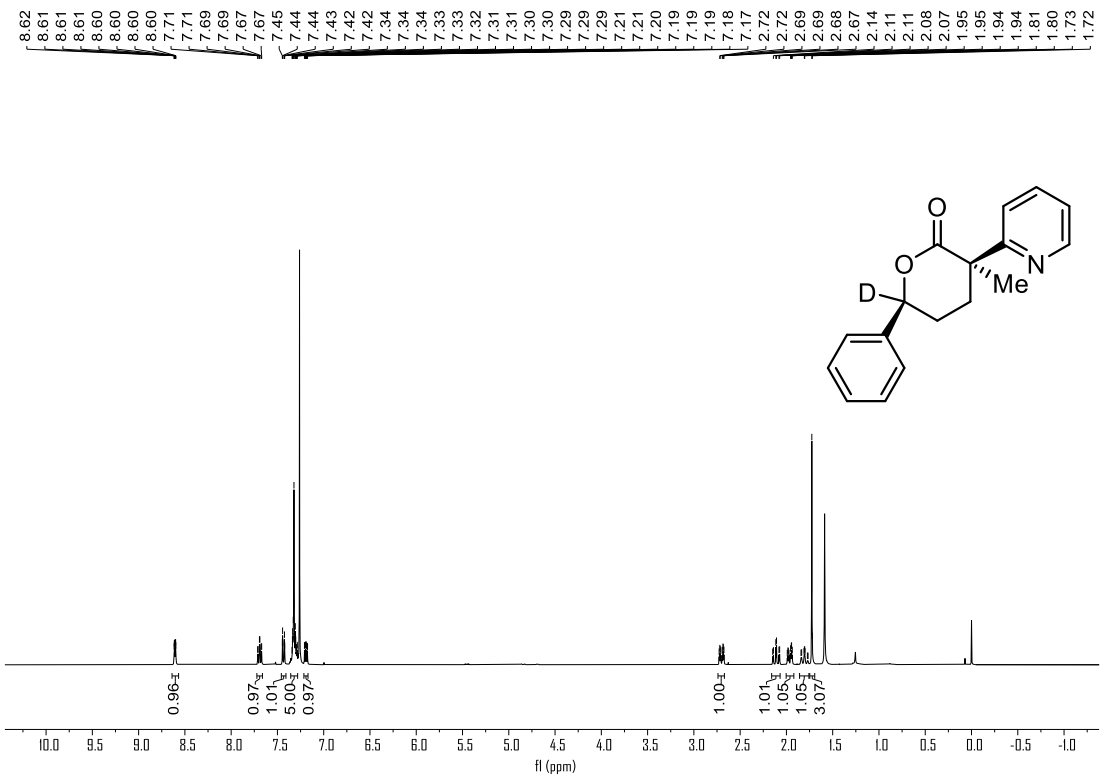
^{13}C NMR (101 MHz, $CDCl_3$) of **8**



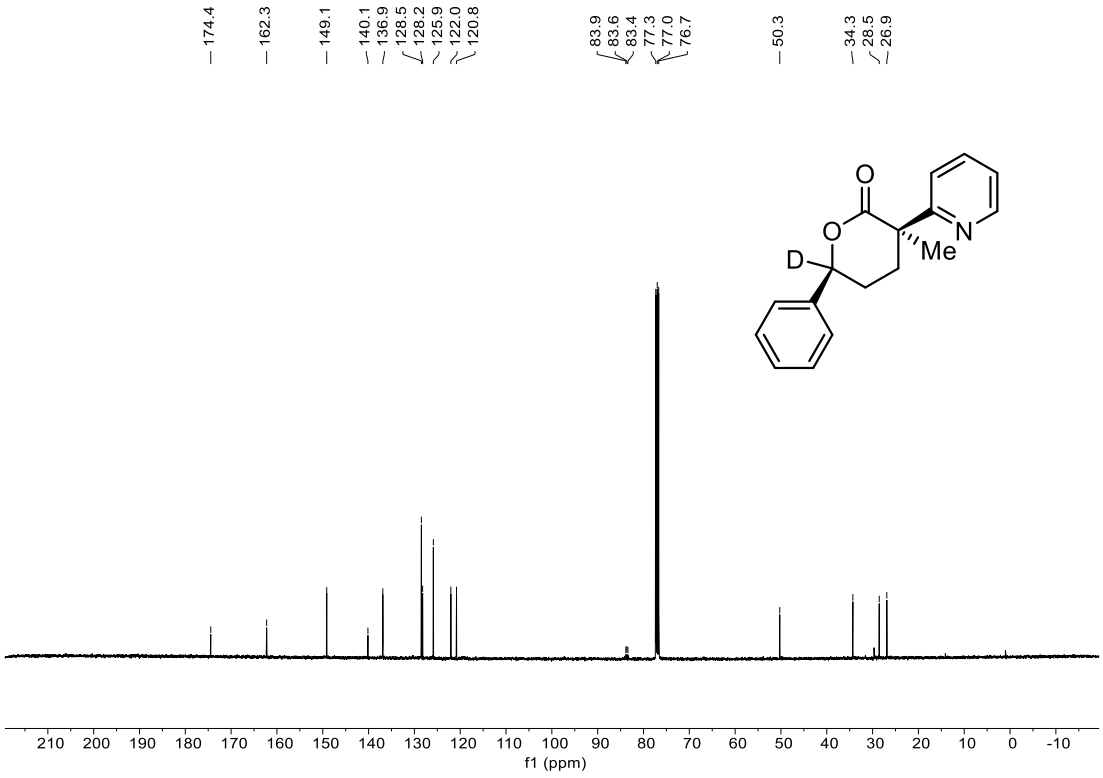
^{1}H NMR (400 MHz, $CDCl_3$) of **9**



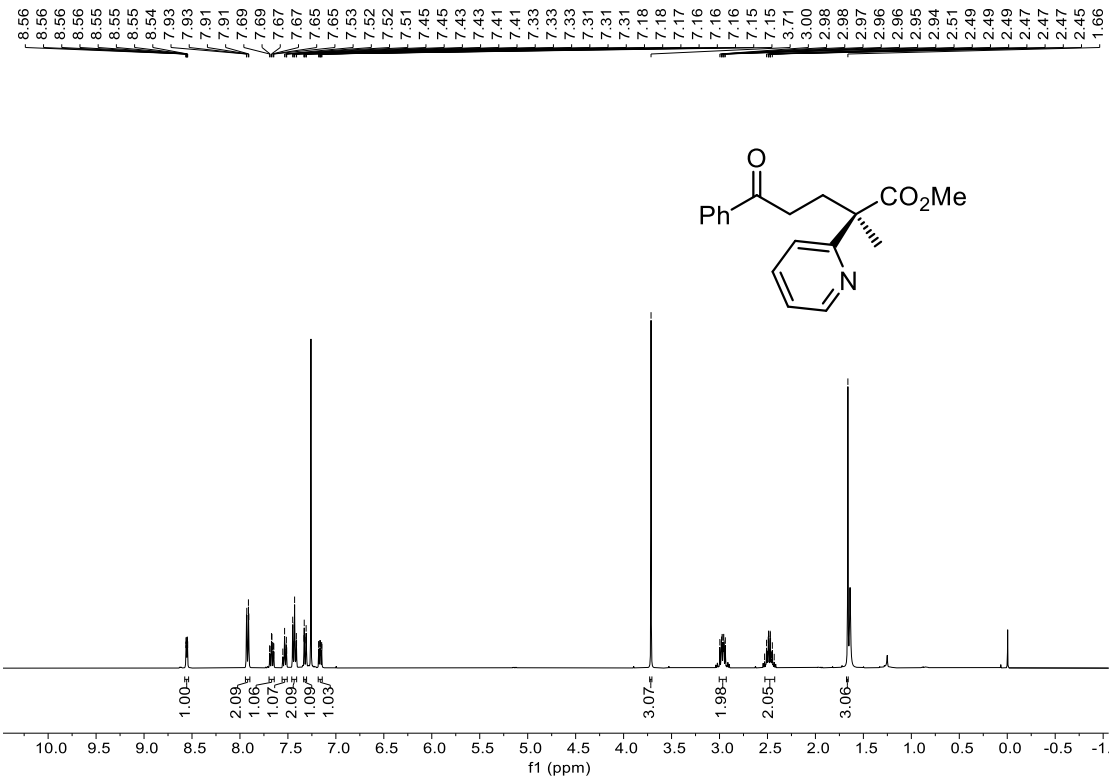
^{13}C NMR (101 MHz, $CDCl_3$) of **9**



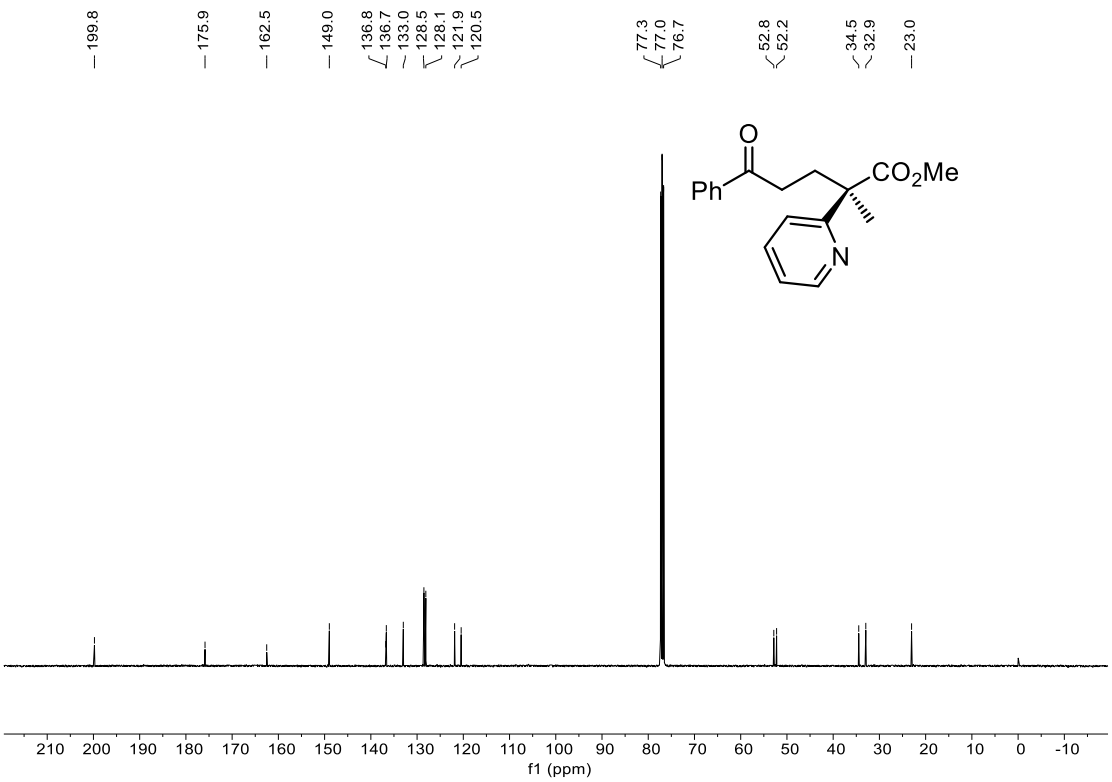
^{1}H NMR (400 MHz, $CDCl_3$) of D-**3a**



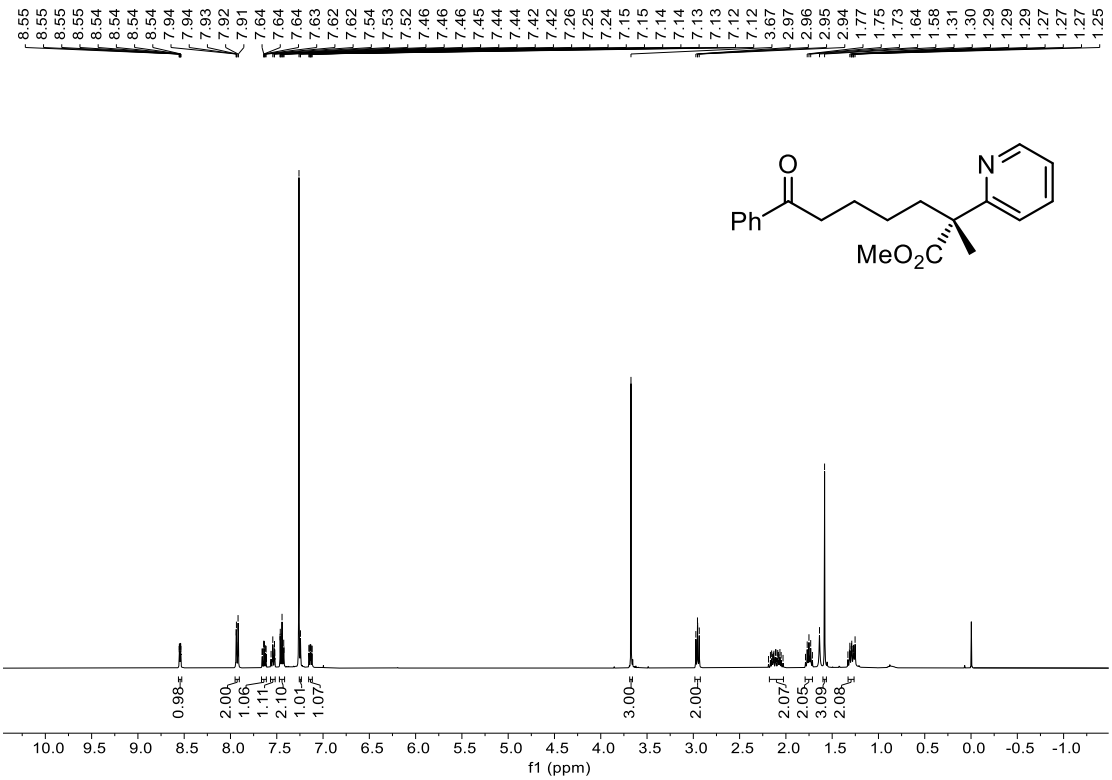
^{13}C NMR (101 MHz, $CDCl_3$) of D-**3a**



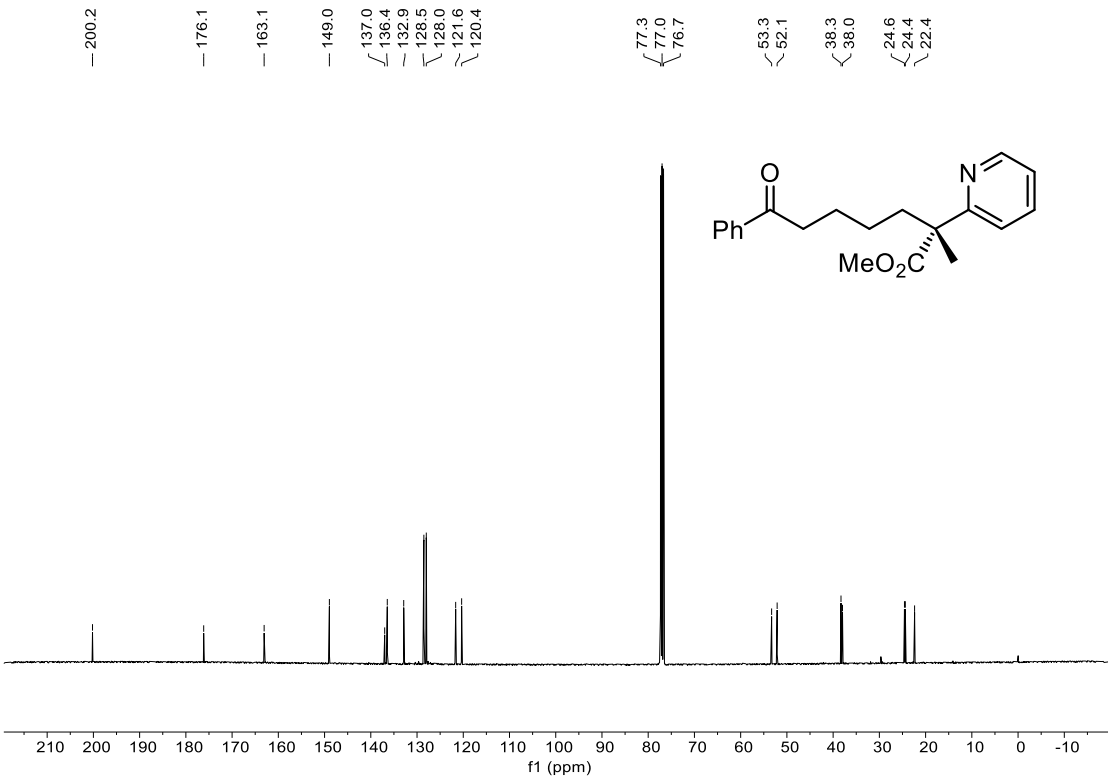
^{1}H NMR (400 MHz, $CDCl_3$) of **12**



^{13}C NMR (101 MHz, $CDCl_3$) of **12**



^{1}H NMR (400 MHz, $CDCl_3$) of **13**



^{13}C NMR (101 MHz, $CDCl_3$) of **13**