Supporting Information

Practical conversion of *gem*-difluorocyclopropenes for the chemodivergent assembly of fluorinated heterocyclic frameworks

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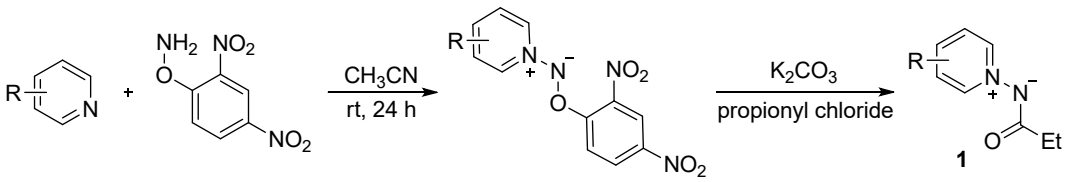
I. General

NMR spectra were recorded on JEOL 400 NMR (^{1}H 400 MHz; ^{13}C 100 MHz) in either $CDCl_3$ or DMSO-d_6. Abbreviations for data quoted are s, singlet; brs, broad singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; d_6-DMSO: δ_H = 2.50 ppm, δ_C = 39.52 ppm). Mass spectra and high-resolution mass spectra were measured on an agilent TOF-G6230B mass spectrometer and Thermo-DFS mass spectrometer. Thin-layer chromatographies were done on pre-coated silica gel 60 F254 plates (Merck). Silica gel 60H (200-300 mesh) and preparative TLC (200x200 mm, 0.2-0.25 mm in thickness) manufactured by Qingdao Haiyang Chemical Group Co. (China) were used for general chromatography. Other chemicals were purchased from commercial suppliers and were dried and purified when necessary. *gem*-Difluorocyclopropenes[1-4] were prepared according to published procedures. No attempts were made to optimize yields for substrate synthesis. Diastereomeric ratio (dr) was measured by ^{1}H and ^{19}F NMR and indicated in ^{1}H NMR; PE: petrol ether; EA: ethyl acetate; DCM: dichloromethane; MeOH: methanol.

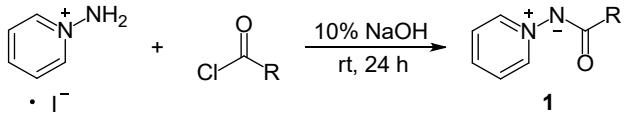
II. Experimental Information and Characterization Data

General procedure for the synthesis of 1-aminopyridinium ylides:



Method A[5-10]: To a solution of pyridine, quinoline or isoquinoline derivative (6.0 mmol, 1 equiv) in acetonitrile (25 mL) was added *O*-(2,4-dinitrophenyl) hydroxylamine (6.6 mmol, 1.1 equiv). The reaction flask was sealed with rubber plug, and the reaction mixture was stirred for 24 h at room temperature, then upon filtering off the solvent. The orange solid product was obtained, which was carried out to the next step without further purification. The orange precipitate was dissolved in THF/

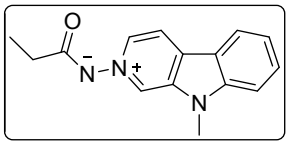
H_2O (30 mL, 1/1, v/v), K_2CO_3 (21.0 mmol, 3.5 equiv) was added at room temperature, followed by the slow addition of propionyl chloride (12.0 mmol, 2 equiv). The reaction was monitored by TLC after 12 h, then the mixture was diluted with 20 mL of H_2O and extracted with DCM (10 x 3 mL). The combined organic phases were dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by column chromatography on silica gel (DCM/CH_3OH = 20/1, v/v) to afford the corresponding product **1**.



Method B[5-10]: In a 100 mL round bottom flask equipped with magnetic stir bar, *N*-aminopyridinium iodide (10 mmol, 1 equiv) was dissolved in aqueous NaOH (30 mL, 10% w/w) at 0 °C. The corresponding acyl chloride (20 mmol, 2 equiv) was added dropwise in 10 minutes and the resulting solution was allowed to warm to room temperature and stirred for 24 h. After completion, the suspension was extracted with DCM (100 x 3 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Purification was performed by column chromatography on silica gel to yield the desired imidoylides **1**.

The 1-aminopyridinium ylides derivatives **1a**-**z**, **1aa**-**ai** were known compounds and all characteristic data were in agreement with that reported.

(9-methyl-9*H*-pyrido[3,4-*b*]indol-2-ium-2-yl)(propionyl)amide (1aj)



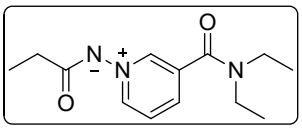
This compound was synthesized following Method A using 9-methyl-9*H*-β-carboline (0.91 g, 5 mmol) in 75% (1.11 g) yield as a light yellow oil, R_f = 0.2 (DCM/MeOH = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.08-9.01 (m, 1H), 8.26-8.21 (m, 1H), 8.17-8.01 (m, 2H), 7.75-7.63 (m, 1H), 7.53-7.43 (m, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 3.86 (s, 3H), 2.42 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 144.0, 136.4, 132.8, 130.6, 128.6, 127.1, 122.5, 121.5, 119.9, 116.0, 110.0, 30.0, 29.8, 11.2.

HRMS (ESI) calculated for $C_{15}H_{16}N_3O$ ($[M+H]^+$): 254.1288; found: 254.1283.

(3-(diethylcarbamoyl)pyridin-1-ium-1-yl)(propionyl)amide (1ak)



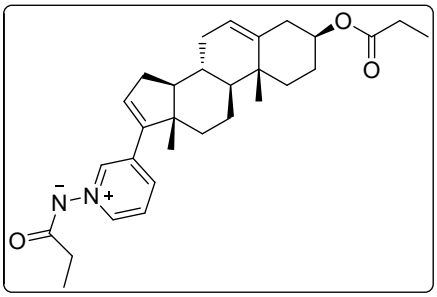
This compound was synthesized following Method A using Nikethamide (0.89 g, 5 mmol) in 89% (1.11 g) yield as light yellow oil, R_f = 0.2 (DCM/MeOH = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.61 (d, *J* = 6.3 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.69 (dd, *J* = 7.7, 6.5 Hz, 1H), 3.69-3.47 (m, 2H), 3.45-3.29 (m, 2H), 2.34 (q, *J* = 7.6 Hz, 2H), 1.36-1.11 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.5, 164.7, 142.6, 141.8, 135.5, 135.1, 126.1, 43.8, 40.1, 29.7, 14.3, 12.8, 10.9.

HRMS (ESI) calculated for $C_{13}H_{20}N_3O_2$ ($[M+H]^+$): 250.1550; found: 250.1552.

(3-((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-3-(propionyloxy)-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pyridin-1-ium-1-yl)(propionyl)amide (1al)



This compound was synthesized following Method A using Abiraterone (1.75 g, 5 mmol) in 80% (1.91 g) yield as light yellow oil, R_f = 0.2 (DCM/MeOH = 20/1).

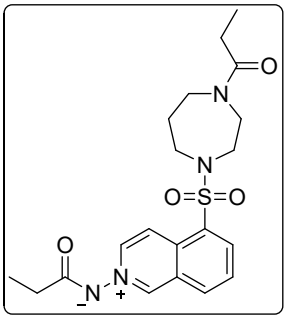
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.47 (d, *J* = 6.2 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.53 (dd, *J* = 8.0, 6.3 Hz, 1H), 6.20 (dd, *J* = 3.1, 1.7 Hz, 1H), 5.41 (d, *J* = 5.1 Hz, 1H), 4.62 (tt, *J* = 10.2, 4.3 Hz, 1H), 2.39-2.26 (m, 8H), 2.14-1.99 (m, 3H), 1.91-

1.84 (m, 2H), 1.78-1.44 (m, 7H), 1.24 (t, *J* = 7.6 Hz, 3H), 1.14 (t, *J* = 7.6 Hz, 3H), 1.08 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3, 174.1, 148.8, 141.0, 140.7, 140.2, 136.4, 134.5, 133.9, 125.3, 122.1, 73.6, 57.5, 50.1, 47.6, 38.2, 37.0, 36.8, 35.0, 32.1, 31.5, 30.4, 29.8, 28.0, 27.8, 20.8, 19.3, 16.7, 11.1, 9.3.

HRMS (ESI) calculated for $C_{30}H_{41}N_2O_3$ ($[M+H]^+$): 477.3112; found: 477.3117.

propionyl(5-((4-propionyl-1,4-diazepan-1-yl)sulfonyl)isoquinolin-2-ium-2-yl) amide (isomer) (1am)



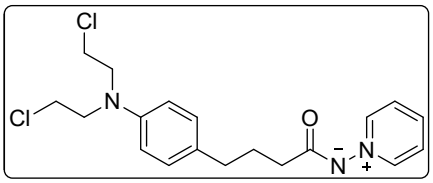
This compound was synthesized following Method A using Fasudil Monohydrochloride Salt (1.64 g, 5 mmol) in 60% (2.51 g) yield as light yellow oil, R_f = 0.2 (DCM/MeOH = 20/1). A pair of inseparable keto-enol tautomerism isomers has been observed in NMR spectra.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.09-10.06 (m, 1H), 8.81-8.67 (m, 1H), 8.47-8.32 (m, 2H), 8.24 (d, *J* = 8.3 Hz, 1H), 7.85 (t, *J* = 7.9 Hz, 1H), 3.78-3.73 (m, 1H), 3.68 (q, *J* = 5.3, 2H), 3.62 (t, *J* = 6.4 Hz, 1H), 3.51-3.46 (m, 1H), 3.44 (t, *J* = 5.4 Hz, 2H), 3.36 (t, *J* = 6.1 Hz, 1H), 2.40 (q, *J* = 7.6 Hz, 2H), 2.31 (q, *J* = 7.3 Hz, 2H), 2.09-1.93 (m, 2H), 1.27 (t, *J* = 7.5 Hz, 3H), 1.17-1.12 (m, 3H).

^{13}C NMR (400 MHz, $CDCl_3$): δ 178.77, 178.73, 173.5, 173.3, 145.00, 144.98, 137.7, 137.6, 135.5, 135.4, 134.4, 134.3, 133.48, 133.47, 129.5, 129.40, 129.35, 128.88, 128.86, 121.5, 121.4, 50.4, 49.7, 49.3, 48.7, 47.8, 47.1, 46.7, 44.7, 30.17, 30.15, 29.3, 27.8, 26.5, 26.1, 10.9, 9.42, 9.36.

HRMS (ESI) calculated for $C_{20}H_{27}N_4O_4S$ ($[M+H]^+$): 419.1746; found: 419.1750.

(4-(4-(bis(2-chloroethyl)amino)phenyl)butanoyl)(pyridin-1-ium-1-yl)amide (1an)



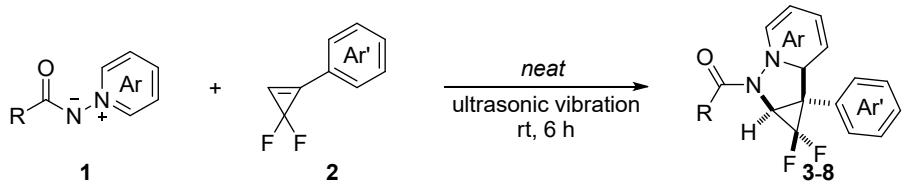
This compound was synthesized following Method B in 45% (0.86 g) yield as light yellow oil, R_f = 0.2 (DCM/MeOH = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79-8.46 (m, 2H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 7.1 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.62 (d, *J* = 8.5 Hz, 2H), 3.69 (t, *J* = 7.0 Hz, 4H), 3.61 (t, *J* = 6.4 Hz, 4H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.01 (p, *J* = 7.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.3, 144.2, 143.4, 137.2, 131.9, 129.9, 126.1, 112.2, 53.8, 40.7, 36.2, 34.8, 28.7.

HRMS (ESI) calculated for $C_{19}H_{24}Cl_2N_3O$ ($[M+H]^+$): 380.1291; found: 380.1296.

General procedure for the [3+2] cycloaddition of 1-amino ylides with *gem*-difluorocyclopropene:

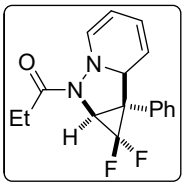


In a 10 mL Schlenk tube was added 1-amino ylides **1** (0.2 mmol, 1 equiv) and *gem*-difluorocyclopropene **2** (0.2 mmol, 1 equiv), the resulted mixture was sonicated in neat at room temperature using a ultrasonic cleaner (40 kHz) for 6 h without exclusion of air or moisture. Afterwards, the resulted mixture was diluted with EA and purified by preparative TLC to afford the corresponding pyrazolo[1,5-*a*]pyridine derivatives **3-8**.

Characterization of pyrazolo[1,5-*a*]pyridine products:

(The ratio of dr and rr isomers was determined by ^{1}H NMR and ^{19}F NMR and indicated in ^{1}H NMR and ^{19}F NMR.)

1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3aa)



This compound was obtained in 78% yield (47.1 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

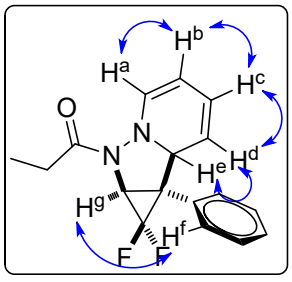
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.27 (m, 5H), 6.08 (d, *J* = 7.8 Hz, 1H), 5.74 (dd, *J* = 9.9, 5.4 Hz, 1H), 5.17-5.05 (m, 2H), 4.45 (d, *J* = 4.8 Hz, 1H), 3.75 (d, *J* = 7.1 Hz, 1H), 2.58-2.45 (m, 2H), 1.16 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 136.0, 130.0, 129.9, 128.7, 128.6, 123.3, 117.4, 112.0 (dd, *J* = 296.2, 291.8 Hz), 103.9, 60.9 (dd, *J* = 5.4, 1.3 Hz), 53.6 (dd, *J* = 11.6, 4.8 Hz), 46.0 (t, *J* = 12.9 Hz), 27.2, 8.9.

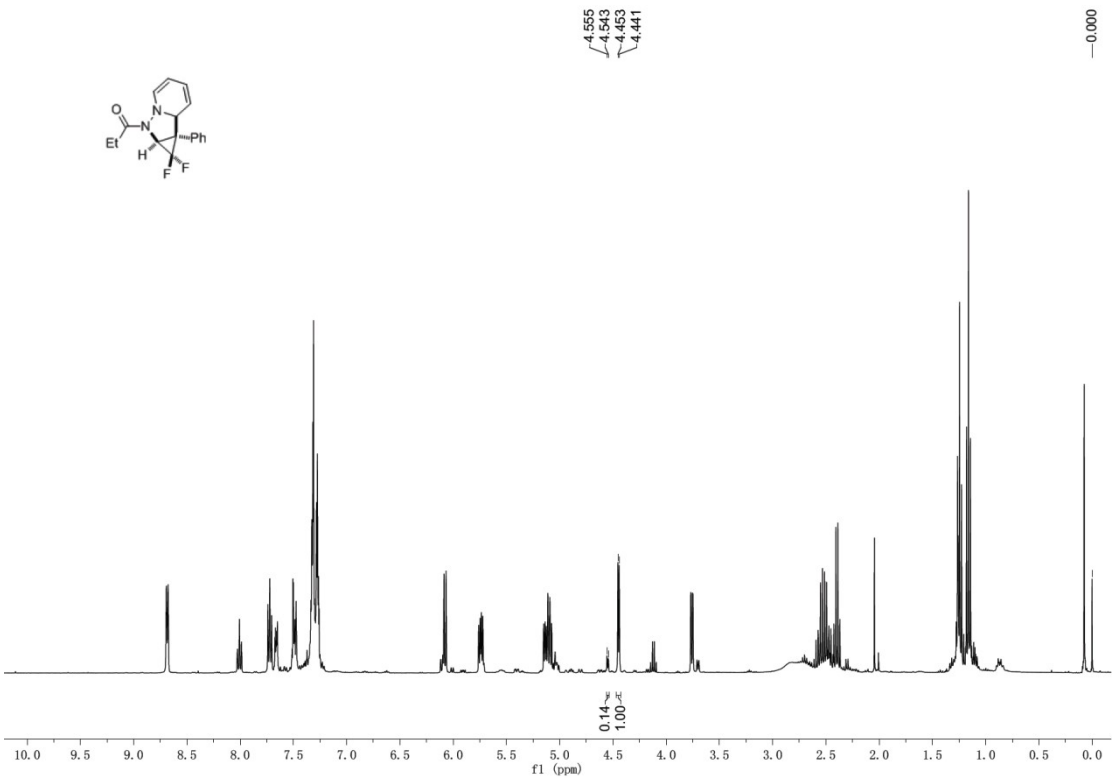
^{19}F NMR (376 MHz, $CDCl_3$): δ -120.99 (dd, *J* = 150.8, 6.9 Hz), -148.73 (d, *J* = 151.1 Hz).

HRMS (ESI) calculated for $C_{17}H_{17}F_2N_2O$ ($[M+H]^+$): 303.1304; found: 303.1297.

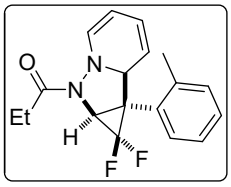
^{1}H-^{1}H NOESY of **3aa**:



Crude ^{1}H-NMR spectrum of 3aa:



1-(1,1-difluoro-7b-(*o*-tolyl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridine-2-yl)propan-1-one (3ab)



This compound was obtained in 66% yield (41.7 mg, dr = 6:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.19 (m, 3H), 7.14-7.09 (m, 1H), 6.06 (dt, *J* = 7.7, 0.9 Hz, 1H), 5.68 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.17-5.12 (m, 1H), 5.04-4.99 (m, 1H), 4.46 (d, *J* = 5.1 Hz, 1H), 3.80 (dd, *J* = 7.0, 1.7 Hz, 1H), 2.58-2.48 (m, 2H), 2.29 (s, 3H), 1.17 (t, *J* = 7.5 Hz, 3H).

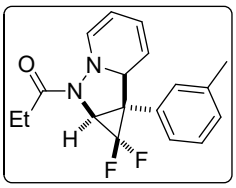
^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 138.0, 136.2, 130.0, 129.09, 129.06, 128.9, 126.1, 123.6, 116.7, 112.1 (dd, *J* = 297.5, 289.8 Hz), 103.9, 60.7 (dd, *J* = 4.9, 1.3 Hz), 52.9 (dd, *J* = 11.4, 5.5 Hz), 45.0 (dd, *J* = 13.4, 12.0 Hz), 27.2, 19.6, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -122.39 (dd, *J* = 151.2, 10.6 Hz), -149.77 (d, *J* =

152.2 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1454.

1-(1,1-difluoro-7b-(m-tolyl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)propan-1-one (3ac)



This compound was obtained in 68% yield (43.0 mg, dr = 6:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

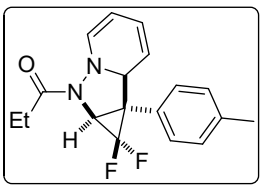
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.18 (m, 1H), 7.13-7.07 (m, 3H), 6.07 (d, *J* = 7.7 Hz, 1H), 5.75 (dd, *J* = 10.0, 5.6 Hz, 1H), 5.14 (dd, *J* = 9.8, 5.1 Hz, 1H), 5.11-5.06 (m, 1H), 4.43 (d, *J* = 5.0 Hz, 1H), 3.74 (d, *J* = 7.1 Hz, 1H), 2.61-2.47 (m, 2H), 2.33 (s, 3H), 1.16 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 138.2, 136.0, 130.57, 130.55, 129.4, 128.4, 126.9, 123.2, 117.4, 112.1 (dd, *J* = 296.1, 291.6 Hz), 103.8, 60.9 (dd, *J* = 5.5, 1.5 Hz), 53.5 (dd, *J* = 11.4, 5.1 Hz), 45.9 (t, *J* = 12.8 Hz), 27.2, 21.5, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.04 (dd, *J* = 150.2, 10.3 Hz), -148.74 (d, *J* = 149.7 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 37.1455.

1-(1,1-difluoro-7b-(p-tolyl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)propan-1-one (3ad)



This compound was obtained in 70% yield (44.2 mg, dr = 7:1, in 0.2 mmol scale) as light yellow oil, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer

were presented.

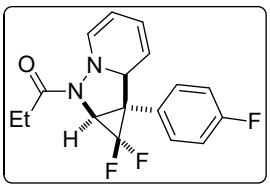
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16-7.11 (m, 4H), 6.07 (d, *J* = 7.7 Hz, 1H), 5.76 (dd, *J* = 9.9, 5.6 Hz, 1H), 5.16-5.11 (m, 1H), 5.11-5.07 (m, 1H), 4.42 (d, *J* = 5.1 Hz, 1H), 3.72 (dd, *J* = 7.2, 1.2 Hz, 1H), 2.58-2.46 (m, 2H), 2.34 (s, 3H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 138.5, 136.0, 129.82, 129.80, 129.3, 123.2, 117.5, 112.1 (dd, *J* = 295.8, 291.6 Hz), 103.8, 60.9 (dd, *J* = 5.5, 1.4 Hz), 53.3 (dd, *J* = 11.4, 5.0 Hz), 46.0 (dd, *J* = 13.1, 12.4 Hz), 27.2, 21.4, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.06 (dd, *J* = 150.8, 10.3 Hz), -148.79 (d, *J* = 151.4 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1454.

1-(1,1-difluoro-7b-(4-fluorophenyl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ae)



This compound was obtained in 61% yield (39.0 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

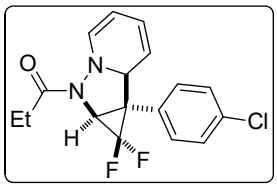
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.23 (m, 2H), 7.02-6.97 (m, 2H), 6.09-6.05 (m, 1H), 5.76 (dd, *J* = 9.4, 5.6 Hz, 1H), 5.14-5.07 (m, 2H), 4.41 (d, *J* = 5.2 Hz, 1H), 3.71 (d, *J* = 7.2 Hz, 1H), 2.55-2.44 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 162.8 (d, *J* = 246.7 Hz), 136.0, 131.7 (dd, *J* = 8.3, 1.8 Hz), 123.4, 117.3, 115.8, 115.5, 112.0 (dd, *J* = 296.0, 291.7 Hz), 103.9, 60.8 (d, *J* = 5.5 Hz), 52.8 (dd, *J* = 11.7, 5.1 Hz), 46.2 (t, *J* = 12.8 Hz), 27.2, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -112.55, -120.89 (dd, *J* = 151.6, 9.3 Hz), -148.76 (d, *J* = 151.0 Hz).

HRMS (ESI) calculated for $C_{17}H_{16}F_3N_2O$ ($[M+H]^+$): 321.1210; found: 321.1204.

1-(7b-(4-chlorophenyl)-1,1-difluoro-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3af)



This compound was obtained in 70% yield (47.1 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

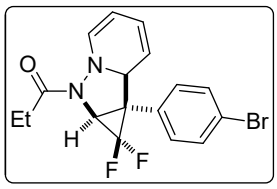
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.08 (d, *J* = 7.5 Hz, 1H), 5.78 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.15-5.08 (m, 2H), 4.43 (d, *J* = 5.0 Hz, 1H), 3.72 (d, *J* = 7.1 Hz, 1H), 2.57-2.46 (m, 2H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 136.0, 134.6, 131.32, 131.30, 128.9, 123.6, 117.2, 111.8 (dd, *J* = 296.3, 291.7 Hz), 103.9, 60.8 (dd, *J* = 5.4, 1.2 Hz), 52.9 (dd, *J* = 12.0, 5.0 Hz), 46.1 (t, *J* = 12.8 Hz), 27.2, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.82 (dd, *J* = 152.0, 9.8 Hz), -148.70 (d, *J* = 152.0 Hz).

HRMS (ESI) calculated for $C_{17}H_{16}ClF_2N_2O$ ($[M+H]^+$): 337.0914; found: 337.0909.

1-(7b-(4-bromophenyl)-1,1-difluoro-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ag)



This compound was obtained in 71% yield (53.9 mg, dr = 7:1, in 0.2 mmol scale) as light yellow oil, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.09-6.04 (m, 1H), 5.78 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.16-5.08 (m, 2H), 4.43 (d, *J* = 5.0

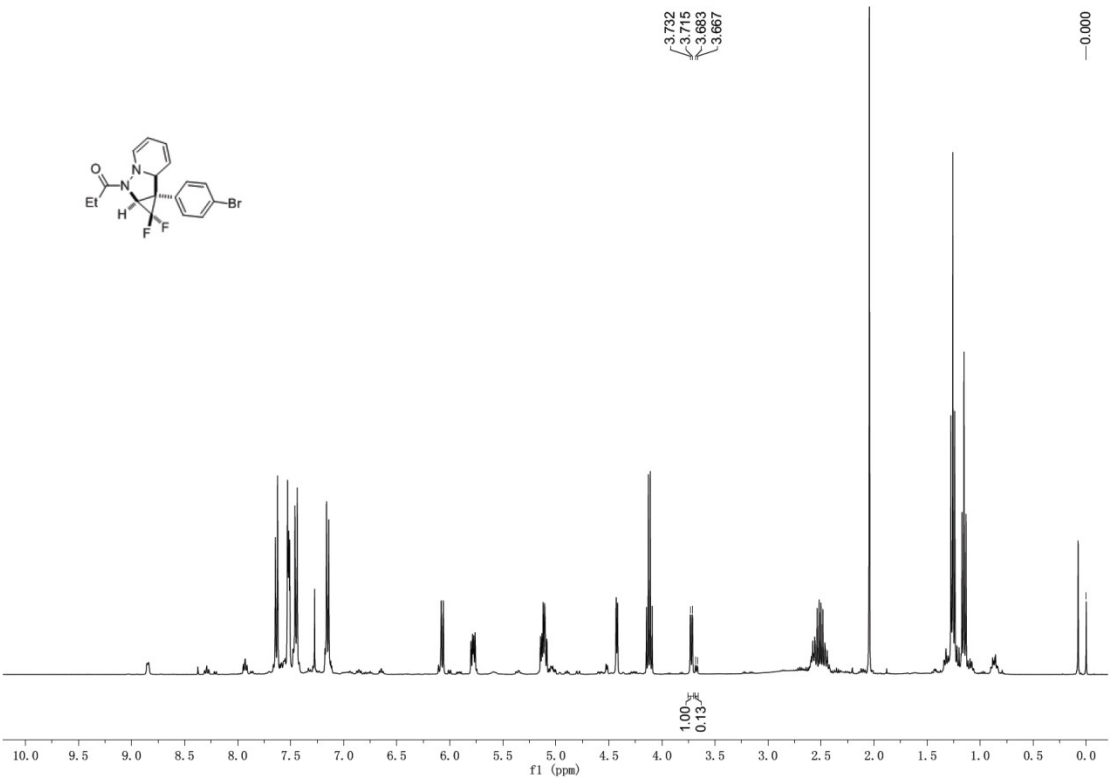
Hz, 1H), 3.72 (dd, *J* = 7.3, 1.1 Hz, 1H), 2.56-2.45 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 136.0, 131.8, 131.61, 131.59, 123.6, 122.8, 117.1, 111.8 (dd, *J* = 296.4, 291.5 Hz), 103.9, 60.8 (dd, *J* = 5.7, 1.3 Hz), 53.0 (dd, *J* = 11.8, 4.8 Hz), 46.0 (t, *J* = 12.7 Hz), 27.2, 8.8.

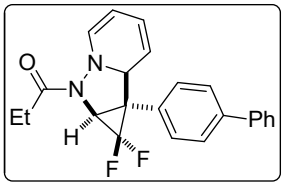
^{19}F NMR (376 MHz, $CDCl_3$): δ -120.78 (dd, *J* = 150.6, 10.3 Hz), -148.68 (d, *J* = 151.8 Hz)

HRMS (ESI) calculated for $C_{17}H_{16}BrF_2N_2O$ ([M+H]$^+$): 381.0409; found: 381.0403.

Crude ^{1}H-NMR spectrum of 3ag:



1-(7b-([1,1'-biphenyl]-4-yl)-1,1-difluoro-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ah)



This compound was obtained in 66% yield (49.9 mg, dr = 7:1, in 0.2 mmol scale) as light yellow oil, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

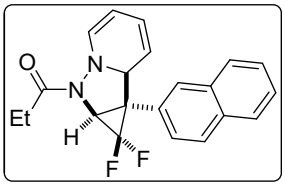
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.53 (m, 5H), 7.45-7.41 (m, 2H), 7.35-7.33 (m, 2H), 6.09 (dt, *J* = 7.7, 0.9 Hz, 1H), 5.78 (dd, *J* = 9.9, 5.7 Hz, 1H), 5.21-5.15 (m, 1H), 5.14-5.09 (m, 1H), 4.48 (d, *J* = 5.1 Hz, 1H), 3.78 (dd, *J* = 7.2, 1.2 Hz, 1H), 2.58-2.46 (m, 2H), 1.17 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 141.4, 140.4, 136.0, 130.37, 130.35, 128.9, 127.7, 127.23, 127.15, 123.4, 117.4, 112.1 (dd, *J* = 296.3, 291.8 Hz), 103.8, 61.0 (dd, *J* = 5.4, 1.8 Hz), 53.3 (dd, *J* = 11.6, 5.0 Hz), 46.1 (t, *J* = 12.7 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.83 (dd, *J* = 150.1, 10.5 Hz), -148.59 (d, *J* = 150.1 Hz)

HRMS (ESI) calculated for $C_{23}H_{21}F_2N_2O$ ($[M+H]^+$): 379.1617; found: 379.1612.

1-(1,1-difluoro-7b-(naphthalen-2-yl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ai)



This compound was obtained in 68% yield (47.8 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

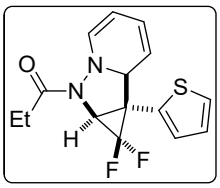
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75-7.67 (m, 5H), 7.42-7.38 (m, 2H), 7.30-7.25 (m, 1H), 6.04 (d, *J* = 7.6 Hz, 1H), 5.58 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.08-5.00 (m, 2H), 4.44 (d, *J* = 5.0 Hz, 1H), 3.77 (d, *J* = 7.3 Hz, 1H), 2.53-2.40 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 136.0, 133.2, 133.1, 129.3, 128.3, 128.0, 127.8, 127.23, 127.21, 126.7, 126.6, 123.4, 117.3, 112.2 (dd, *J* = 296.1, 291.8 Hz), 103.8, 61.0 (dd, *J* = 5.4, 1.4 Hz), 53.6 (dd, *J* = 11.5, 4.9 Hz), 46.1 (t, *J* = 12.3 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.72 (dd, *J* = 150.5, 7.2 Hz), -148.40 (d, *J* = 151.6 Hz).

HRMS (ESI) calculated for $C_{21}H_{19}F_2N_2O$ ([M+H] $^+$): 353.1460; found: 353.1453.

1-(1,1-difluoro-7b-(thiophen-2-yl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3aj)



This compound was obtained in 79% yield (48.5 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

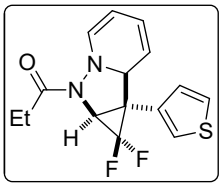
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.27 (m, 1H), 7.00-6.95 (m, 2H), 6.06 (dt, *J* = 7.7, 1.0 Hz, 1H), 5.87 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.31-5.24 (m, 1H), 5.15-5.09 (m, 1H), 4.38 (d, *J* = 5.2 Hz, 1H), 3.81 (dd, *J* = 7.0, 1.2 Hz, 1H), 2.56-2.46 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 135.9, 129.81, 129.80, 127.0, 126.8, 124.0, 116.8, 111.7 (dd, *J* = 296.7, 291.5 Hz), 104.1, 60.9 (dd, *J* = 5.4, 1.6 Hz), 48.4 (dd, *J* = 12.8, 5.4 Hz), 47.3 (dd, *J* = 13.2, 11.8 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.28 (dd, *J* = 148.9, 9.0 Hz), -148.35 (d, *J* = 149.0 Hz).

HRMS (ESI) calculated for $C_{15}H_{15}F_2N_2O$ ([M+H] $^+$): 309.0868; found: 309.0863.

1-(1,1-difluoro-7b-(thiophen-3-yl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ak)



This compound was obtained in 65% yield (40.1 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

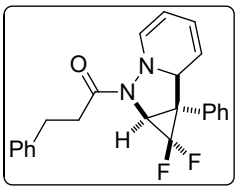
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.26 (m, 1H), 7.25-7.23 (m, 1H), 6.98 (dd, *J* = 8.8, 1.2 Hz, 1H), 6.07 (d, *J* = 7.7 Hz, 1H), 5.85-5.80 (m, 1H), 5.19-5.11 (m, 2H), 4.39 (d, *J* = 5.1 Hz, 1H), 3.68 (dd, 1H), 2.54-2.45 (m, 2H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 136.2, 129.00, 128.98, 126.1, 125.8, 123.5, 117.4, 112.0 (dd, *J* = 295.7, 292.7 Hz), 103.7, 60.7 (dd, *J* = 5.6, 1.6 Hz), 48.9 (dd, *J* = 11.9, 5.1 Hz), 46.3 (dd, *J* = 13.2, 12.3 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.83 (dd, *J* = 150.5, 9.2 Hz), -148.80 (d, *J* = 150.3 Hz).

HRMS (ESI) calculated for $C_{15}H_{15}F_2N_2O$ ($[M+H]^+$): 309.0868; found: 309.0861.

1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)-3-phenylpropan-1-one (3ba)



This compound was obtained in 72% yield (54.4 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

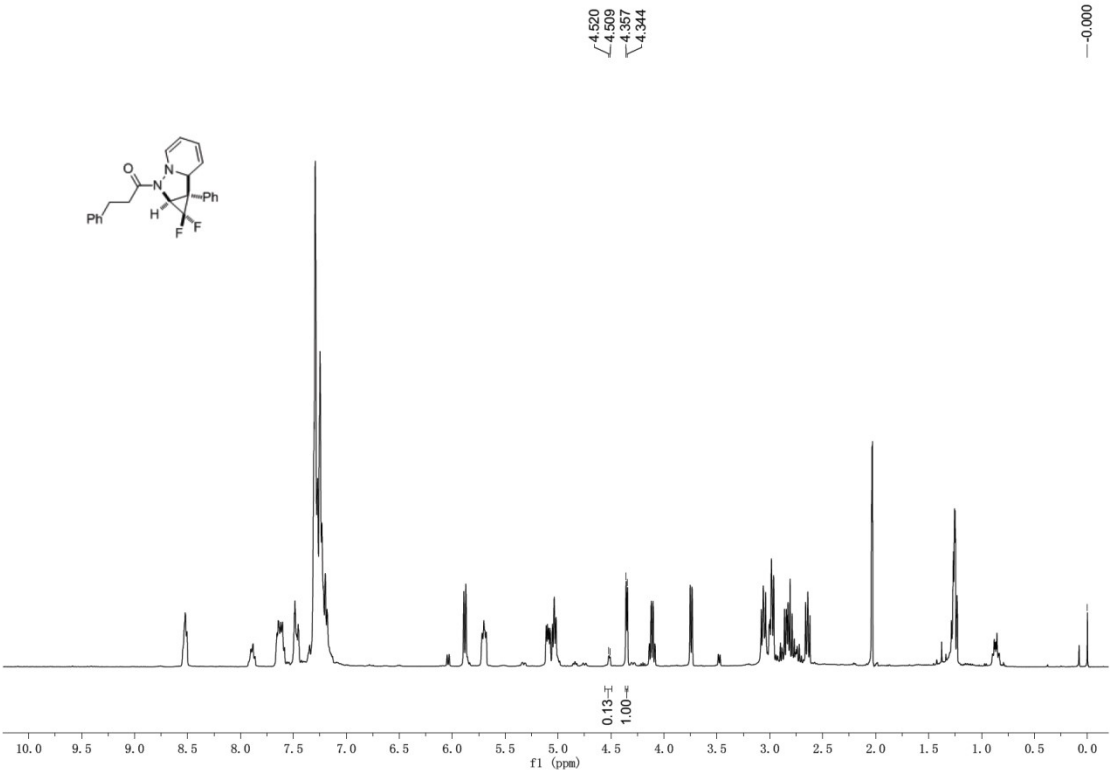
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.23 (m, 5H), 7.21-7.16 (m, 5H), 5.81 (d, *J* = 7.6 Hz, 1H), 5.66-5.60 (m, 1H), 5.05-4.99 (m, 1H), 4.98-4.94 (m, 1H), 4.28 (d, *J* = 4.3 Hz, 1H), 3.67 (d, *J* = 6.9 Hz, 1H), 2.94-2.88 (m, 2H), 2.82-2.68 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 141.0, 135.8, 129.89, 129.88, 128.64, 128.59, 128.58, 128.55, 126.3, 123.2, 117.3, 111.9 (dd, *J* = 296.5, 291.7 Hz), 104.0, 60.9 (dd, *J* = 5.5, 1.0 Hz), 53.5 (dd, *J* = 11.6, 5.1 Hz), 45.9 (t, *J* = 12.9 Hz), 35.4, 30.7.

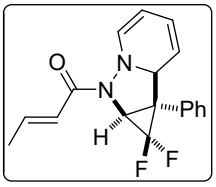
^{19}F NMR (376 MHz, $CDCl_3$): δ -120.93 (dd, *J* = 150.6, 6.8 Hz), -148.38 (d, *J* = 150.1 Hz).

HRMS (ESI) calculated for $C_{23}H_{21}F_2N_2O$ ($[M+H]^+$): 379.1617; found: 379.1612.

Crude ^{1}H-NMR spectrum of 3ba:



(*E*)-1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)but-2-en-1-one (3ca)



This compound was obtained in 57% yield (35.8 mg, dr = 10:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

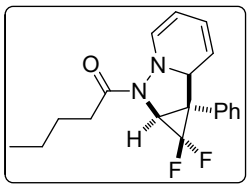
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.28 (m, 5H), 7.15-7.05 (m, 1H), 6.55-6.48 (m, 1H), 6.08 (d, *J* = 7.6 Hz, 1H), 5.77-5.72 (m, 1H), 5.15-5.07 (m, 2H), 4.47 (d, *J* = 5.0 Hz, 1H), 3.82 (d, *J* = 7.0 Hz, 1H), 1.92 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 144.9, 136.2, 129.91, 129.89, 128.6, 128.5, 123.2, 120.9, 117.3, 112.1 (dd, *J* = 296.7, 291.6 Hz), 103.9, 60.9 (dd, *J* = 5.4, 1.4 Hz), 53.3 (dd, *J* = 11.5, 5.1 Hz), 45.9 (dd, *J* = 13.3, 12.6 Hz), 18.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.90 (dd, *J* = 151.0, 10.7 Hz), -148.64 (d, *J* = 149.5 Hz).

HRMS (ESI) calculated for $C_{18}H_{17}F_2N_2O$ ([M+H] $^+$): 315.1304; found: 315.1298.

1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)pentan-1-one (3da)



This compound was obtained in 82% yield (54.1 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

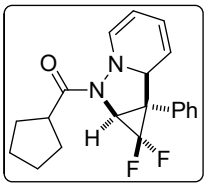
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.26 (m, 5H), 6.07 (d, *J* = 7.7 Hz, 1H), 5.74 (dd, *J* = 10.0, 5.4 Hz, 1H), 5.17-5.06 (m, 2H), 4.44 (d, *J* = 5.0 Hz, 1H), 3.75 (d, *J* = 7.2 Hz, 1H), 2.58-2.43 (m, 2H), 1.68-1.58 (m, 2H), 1.41-1.34 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2, 136.1, 129.92, 129.90, 128.62, 128.55, 123.3, 117.4, 112.1 (dd, *J* = 296.3, 291.7 Hz), 103.8, 60.9 (dd, *J* = 5.4, 1.4 Hz), 53.5 (dd, *J* = 11.5, 5.0 Hz), 45.9 (t, *J* = 13.2 Hz), 33.4, 26.7, 22.5, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.97 (dd, *J* = 150.8, 9.3 Hz), -148.58 (d, *J* = 151.5 Hz)

HRMS (ESI) calculated for $C_{19}H_{21}F_2N_2O$ ([M+H] $^+$): 331.1617; found: 331.1610.

cyclopentyl(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)methanone (3ea)



This compound was obtained in 71% yield (48.5 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

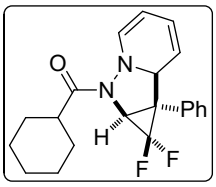
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.26 (m, 5H), 6.12-6.08 (m, 1H), 5.74 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.17-5.06 (m, 2H), 4.43 (d, *J* = 5.0 Hz, 1H), 3.75 (d, *J* = 6.5 Hz, 1H), 3.29-3.06 (m, 1H), 1.92-1.87 (m, 2H), 1.77-1.52 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4, 136.5, 129.94, 129.92, 128.6, 128.5, 123.3, 117.3, 112.1 (dd, *J* = 296.2, 291.5 Hz), 103.8, 61.0 (dd, *J* = 5.4, 1.4 Hz), 53.5 (dd, *J* = 11.5, 5.1 Hz), 46.2 (t, *J* = 12.8 Hz), 42.2, 30.0, 29.8, 26.3, 26.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.73 (dd, *J* = 150.7, 9.3 Hz), -148.93 (d, *J* = 150.8 Hz).

HRMS (ESI) calculated for $C_{20}H_{21}F_2N_2O$ ($[M+H]^+$): 343.1617; found: 343.1611.

cyclohexyl(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)methanone (3fa)



This compound was obtained in 75% yield (53.4 mg, dr = 10:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

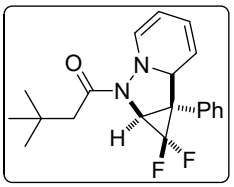
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.27 (m, 5H), 6.09 (dt, *J* = 7.7, 1.0 Hz, 1H), 5.74 (dd, *J* = 9.8, 5.7 Hz, 1H), 5.17-5.12 (m, 1H), 5.12-5.08 (m, 1H), 4.44 (d, *J* = 5.1 Hz, 1H), 3.75 (dd, *J* = 7.3, 1.4 Hz, 1H), 2.87-2.69 (m, 1H), 1.81-1.57 (m, 6H), 1.43-1.26 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9, 136.4, 129.90, 129.88, 128.6, 128.5, 123.2, 117.4, 111.9 (dd, *J* = 296.2, 291.6 Hz), 103.9, 61.1 (dd, *J* = 5.4, 1.5 Hz), 53.3 (dd, *J* = 11.5, 5.1 Hz), 46.1 (dd, *J* = 13.1, 12.4 Hz), 41.3, 29.0, 28.6, 25.8, 25.7, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.12 (dd, *J* = 150.5, 9.3 Hz), -149.21 (d, *J* = 150.0 Hz)

HRMS (ESI) calculated for $C_{21}H_{23}F_2N_2O$ ($[M+H]^+$): 357.1773; found: 357.1765.

1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)-3,3-dimethylbutan-1-one (3ga)



This compound was obtained in 66% yield (45.5 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.6. NMR spectra of the major isomer were presented.

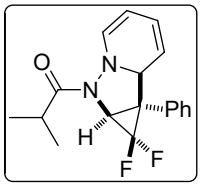
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.18 (m, 5H), 6.01 (d, *J* = 7.7 Hz, 1H), 5.66 (dd, *J* = 9.9, 5.4 Hz, 1H), 5.10-4.97 (m, 2H), 4.35 (d, *J* = 5.0 Hz, 1H), 3.69 (d, *J* = 7.1 Hz, 1H), 2.47 (d, *J* = 14.3 Hz, 1H), 2.27 (d, *J* = 14.1 Hz, 1H), 1.01 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 136.3, 129.92, 129.90, 128.6, 128.5, 123.3, 117.4, 112.1 (dd, *J* = 296.8, 291.6 Hz), 104.1, 60.9 (d, *J* = 5.5 Hz), 53.3 (dd, *J* = 11.5, 5.4 Hz), 45.8 (t, *J* = 13.2 Hz), 45.0, 31.4, 29.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.81 (dd, *J* = 150.9, 7.7 Hz), -147.89 (d, *J* = 150.9 Hz).

HRMS (ESI) calculated for $C_{20}H_{23}F_2N_2O$ ($[M+H]^+$): 345.1773; found: 345.1768.

1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)-2-methylpropan-1-one (3ha)



This compound was obtained in 53% yield (33.3 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.31 (m, 3H), 7.29-7.26 (m, 2H), 6.10 (d, *J* = 7.5 Hz, 1H), 5.75 (dd, *J* = 9.8, 5.5 Hz, 1H), 5.18-5.08 (m, 2H), 4.46 (d, *J* = 5.1 Hz, 1H), 3.76 (d, *J* = 7.3 Hz, 1H), 3.12-2.99 (m, 1H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* =

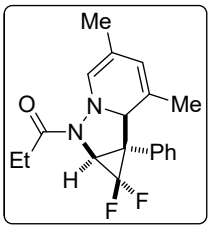
6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 180.0, 136.3, 129.93, 129.91, 128.63, 128.56, 123.3, 117.4, 112.0 (dd, *J* = 296.0, 291.7 Hz), 104.0, 61.0 (dd, *J* = 5.4, 1.5 Hz), 53.4 (dd, *J* = 11.5, 5.0 Hz), 46.1 (dd, *J* = 13.0, 12.3 Hz), 31.7, 19.1, 18.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.02 (dd, *J* = 151.0, 9.3 Hz), -149.29 (d, *J* = 149.3 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1460.

1-(1,1-difluoro-5,7-dimethyl-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ia)



This compound was obtained in 60% yield (39.6 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

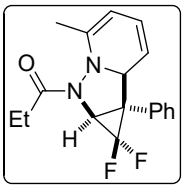
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.25 (m, 5H), 5.74 (s, 1H), 5.47 (s, 1H), 4.13 (s, 1H), 3.68 (dd, *J* = 7.4, 1.1 Hz, 1H), 2.56-2.41 (m, 2H), 1.66 (s, 3H), 1.42 (s, 3H), 1.14 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 130.60, 130.58, 128.7, 128.5, 128.3, 127.4, 124.3, 113.3, 112.1 (dd, *J* = 295.3, 292.8 Hz), 66.0 (dd, *J* = 5.4, 1.6 Hz), 52.3 (dd, *J* = 11.9, 4.7 Hz), 47.4 (t, *J* = 12.9 Hz), 27.3, 21.1, 17.6, 9.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -119.93 (dd, *J* = 150.6, 9.1 Hz), -148.17 (d, *J* = 151.1 Hz).

HRMS (ESI) calculated for $C_{19}H_{21}F_2N_2O$ ($[M+H]^+$): 331.1617; found: 331.1618.

1-(1,1-difluoro-4-methyl-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ja)



This compound was obtained in 58% yield (36.6 mg, dr = 4:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

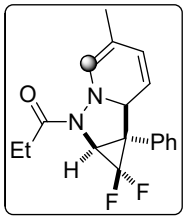
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.29 (m, 3H), 7.24-7.20 (m, 2H), 5.71-5.67 (m, 1H), 5.13 (dd, *J* = 9.8, 5.2 Hz, 1H), 4.99-4.96 (m, 1H), 4.38 (d, *J* = 5.2 Hz, 1H), 3.70 (dd, *J* = 7.3, 1.6 Hz, 1H), 2.63-2.52 (m, 2H), 1.94 (s, 3H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 142.6, 129.93, 129.91, 128.6, 128.5, 124.5, 115.7, 112.3 (dd, *J* = 298.4, 293.2 Hz), 102.6, 62.7 (dd, *J* = 5.8, 1.5 Hz), 54.0 (dd, *J* = 11.5, 4.6 Hz), 45.8 (t, *J* = 12.7 Hz), 27.1, 18.5, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -119.73 (dd, *J* = 150.6, 9.2 Hz), -147.94 (d, *J* = 151.9 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1460.

1-(1,1-difluoro-5-methyl-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ka)



This compound was obtained in 62% yield (39.2 mg, dr = 8:1, rr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

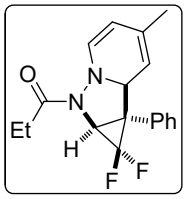
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.34 (m, 2H), 7.31-7.29 (m, 3H), 6.01 (d, *J* = 7.7 Hz, 1H), 5.59 (d, *J* = 5.1 Hz, 1H), 5.14 (dd, *J* = 7.6, 5.9 Hz, 1H), 4.23 (s, 1H), 3.68 (dd, *J* = 7.4, 1.4 Hz, 1H), 2.57-2.47 (m, 2H), 1.40 (s, 3H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 133.4, 130.73, 130.71, 128.6, 128.3, 127.0, 120.1, 112.2 (dd, *J* = 294.2, 293.4 Hz), 104.3, 66.1 (dd, *J* = 5.7, 1.4 Hz), 52.8 (dd, *J* = 11.7, 4.7 Hz), 47.3 (t, *J* = 12.7 Hz), 27.2, 21.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -119.62 (dd, *J* = 151.1, 9.3 Hz), -148.13 (d, *J* = 151.6 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1459.

1-(1,1-difluoro-6-methyl-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3la)



This compound was obtained in 82% yield (51.8 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

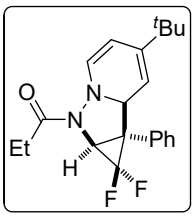
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.29 (m, 3H), 7.26-7.24 (m, 2H), 6.05 (d, *J* = 7.7 Hz, 1H), 4.98 (dd, *J* = 7.7, 1.8 Hz, 1H), 4.83-4.79 (m, 1H), 4.38 (dd, *J* = 5.1, 1.3 Hz, 1H), 3.76 (dd, *J* = 7.2, 1.6 Hz, 1H), 2.57-2.46 (m, 2H), 1.48 (s, 3H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 135.6, 131.8, 129.88, 129.86, 128.5, 128.4, 112.4, 112.0 (dd, *J* = 295.7, 293.8 Hz), 107.9, 61.5 (dd, *J* = 5.4, 1.4 Hz), 53.4 (dd, *J* = 11.5, 4.6 Hz), 46.2 (dd, *J* = 13.2, 12.5 Hz), 27.2, 20.8, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.24 (dd, *J* = 151.1, 10.7 Hz), -148.72 (d, *J* = 151.1 Hz).

HRMS (ESI) calculated for $C_{18}H_{19}F_2N_2O$ ($[M+H]^+$): 317.1460; found: 317.1460.

1-(1,1-difluoro-6-methyl-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3ma)



This compound was obtained in 75% yield (53.7 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

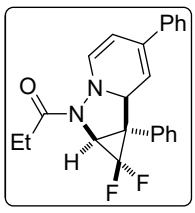
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.23 (m, 5H), 6.06 (dd, *J* = 8.0, 0.9 Hz, 1H), 5.18 (dd, *J* = 8.0, 2.2 Hz, 1H), 4.90-4.86 (m, 1H), 4.37 (d, *J* = 5.3 Hz, 1H), 3.78 (dd, *J* = 7.2, 1.5 Hz, 1H), 2.59-2.46 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H), 0.72 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 143.7, 135.7, 129.85, 129.84, 128.4, 128.3, 112.1 (dd, *J* = 296.3, 291.4 Hz), 109.1, 105.3, 61.2 (dd, *J* = 5.2, 1.4 Hz), 53.5 (dd, *J* = 11.7, 4.8 Hz), 45.6 (t, *J* = 12.9 Hz), 33.6, 28.1, 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.41 (dd, *J* = 150.8, 10.0 Hz), -148.65 (d, *J* = 151.8 Hz).

HRMS (ESI) calculated for $C_{21}H_{25}F_2N_2O$ ($[M+H]^+$): 359.1930; found: 359.1928.

1-(1,1-difluoro-6,7b-diphenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)propan-1-one (3na)



This compound was obtained in 65% yield (49.1 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

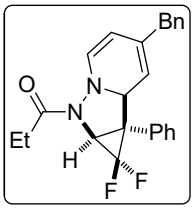
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 5H), 7.22-7.19 (m, 3H), 6.87 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.21 (d, *J* = 7.8 Hz, 1H), 5.42 (dd, *J* = 7.9, 1.9 Hz, 1H), 5.24-5.20 (m, 1H), 4.58 (d, *J* = 5.3 Hz, 1H), 3.83 (d, *J* = 7.0 Hz, 1H), 2.60-2.46 (m, 2H), 1.18 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 138.9, 136.7, 135.6, 129.82, 129.80, 128.7, 128.6, 128.5, 128.0, 125.6, 113.5, 112.0 (dd, *J* = 297.6, 293.4 Hz), 106.0, 61.3 (dd, *J* = 5.5, 1.4 Hz), 53.7 (dd, *J* = 11.7, 5.0 Hz), 46.0 (dd, *J* = 13.1, 12.5 Hz), 27.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.17 (dd, *J* = 151.4, 9.3 Hz), -148.35 (d, *J* = 151.3 Hz).

HRMS (ESI) calculated for $C_{23}H_{21}F_2N_2O$ ($[M+H]^+$): 379.1617; found: 379.1617.

1-(6-benzyl-1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3oa)



This compound was obtained in 65% yield (50.9 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

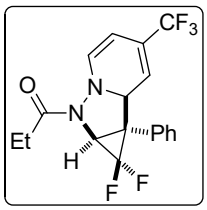
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.33 (m, 3H), 7.23 (t, *J* = 7.1 Hz, 2H), 7.15-7.12 (m, 3H), 6.59-6.54 (m, 2H), 6.04 (d, *J* = 7.8 Hz, 1H), 4.92 (dd, *J* = 7.8, 1.9 Hz, 1H), 4.85 (d, *J* = 5.1 Hz, 1H), 4.39 (d, *J* = 5.2 Hz, 1H), 3.79 (d, *J* = 7.0 Hz, 1H), 3.18-3.04 (m, 2H), 2.56-2.44 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 137.8, 136.2, 135.1, 129.85, 129.84, 129.1, 128.7, 128.5, 128.4, 126.4, 113.3, 112.1 (dd, *J* = 297.4, 295.4 Hz), 106.6, 61.3 (d, *J* = 4.7 Hz), 53.4 (dd, *J* = 11.4, 5.1 Hz), 45.8 (t, *J* = 12.9 Hz), 41.0, 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.60 (dd, *J* = 150.9, 9.3 Hz), -148.75 (d, *J* = 149.9 Hz).

HRMS (ESI) calculated for $C_{24}H_{23}F_2N_2O$ ($[M+H]^+$): 393.1773; found: 393.1778.

1-(1,1-difluoro-7b-phenyl-6-(trifluoromethyl)-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)propan-1-one (3pa)



This compound was obtained in 85% yield (62.9 mg, dr = 5:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

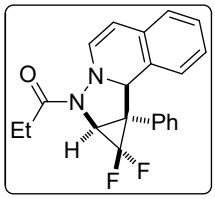
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.32 (m, 3H), 7.27-7.24 (m, 2H), 6.26 (d, *J* = 8.0 Hz, 1H), 5.56-5.51 (m, 1H), 5.20 (dd, *J* = 7.9, 1.9 Hz, 1H), 4.57-4.53 (m, 1H), 3.79 (dd, *J* = 7.1, 1.0 Hz, 1H), 2.54-2.46 (m, 2H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 137.9, 129.62, 129.60, 129.3, 128.9, 127.1 (q, *J* = 33.3 Hz), 122.0 (q, *J* = 271.8 Hz), 117.8 (q, *J* = 5.9 Hz), 111.8 (dd, *J* = 297.5, 294.0 Hz), 98.5 (q, *J* = 2.1 Hz), 59.9 (dd, *J* = 5.9, 1.4 Hz), 53.6 (dd, *J* = 11.4, 5.8 Hz), 46.0 (dd, *J* = 13.5, 12.2 Hz), 27.2, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -69.68 (s), -121.26 (dd, *J* = 152.2, 9.3 Hz), -147.94 (d, *J* = 152.0 Hz).

HRMS (ESI) calculated for $C_{18}H_{16}F_5N_2O$ ($[M+H]^+$): 371.1178; found: 371.1178.

1-(9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4]pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4aa)



This compound was obtained in 81% yield (57.1 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

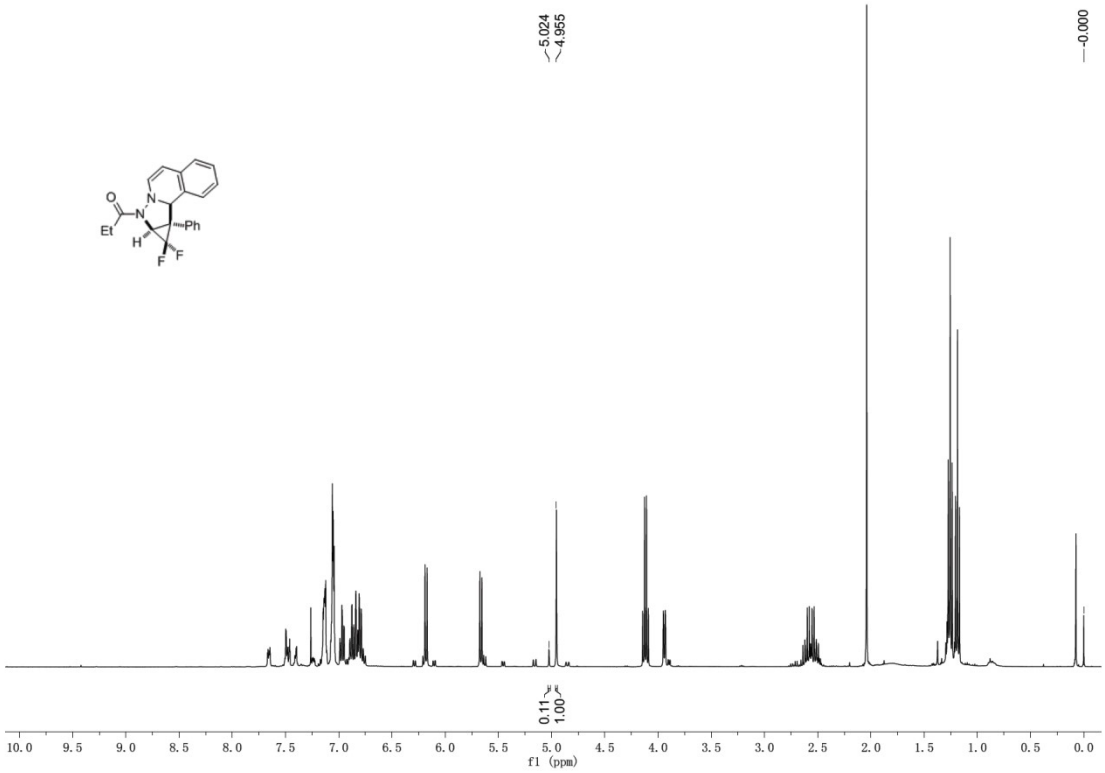
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15-7.11 (m, 2H), 7.07-7.03 (m, 3H), 7.00-6.94 (m, 1H), 6.88-6.78 (m, 3H), 6.18 (d, *J* = 7.8 Hz, 1H), 5.66 (d, *J* = 7.8 Hz, 1H), 4.95 (s, 1H), 3.94 (d, *J* = 7.0 Hz, 1H), 2.64-2.49 (m, 2H), 1.18 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 136.1, 130.03, 130.01, 129.95, 128.6, 128.2, 128.1, 126.9, 126.5, 125.0, 112.3 (dd, *J* = 298.0, 293.3 Hz), 108.3, 65.2 (dd, *J* = 5.5, 1.4 Hz), 53.8 (dd, *J* = 11.4, 5.6 Hz), 47.1 (dd, *J* = 13.2, 12.4 Hz), 27.3, 9.0.

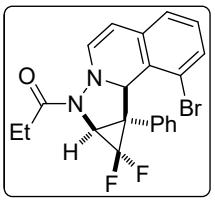
^{19}F NMR (376 MHz, $CDCl_3$): δ -121.58 (dd, *J* = 150.1, 9.3 Hz), -147.72 (d, *J* = 151.0 Hz).

HRMS (ESI) calculated for $C_{21}H_{19}F_2N_2O$ ($[M+H]^+$): 353.1460; found: 353.1463.

Crude ^{1}H-NMR spectrum of 4aa:



1-(1-bromo-9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4ba)



This compound was obtained in 91% yield (78.3 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.33 (m, 2H), 7.09-7.05 (m, 4H), 6.86 (t, *J* = 7.8

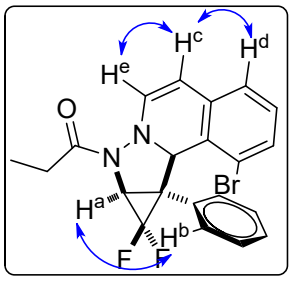
Hz, 1H), 6.77 (d, *J* = 7.4 Hz, 1H), 6.23 (d, *J* = 7.6 Hz, 1H), 5.64 (d, *J* = 7.7 Hz, 1H), 5.16 (s, 1H), 3.86 (d, *J* = 7.1 Hz, 1H), 2.62-2.50 (m, 2H), 1.19 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 137.1, 132.8, 130.4, 130.04, 130.02, 129.99, 128.5, 127.9, 127.0, 124.2, 123.4, 112.2 (dd, *J* = 298.7, 293.5 Hz), 107.8, 64.5 (dd, *J* = 5.8, 1.4 Hz), 53.1 (dd, *J* = 11.5, 6.1 Hz), 47.3 (dd, *J* = 13.8, 12.4 Hz), 27.2, 8.9.

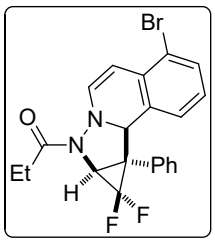
^{19}F NMR (376 MHz, $CDCl_3$): δ -121.03 (dd, *J* = 149.0, 8.8 Hz), -148.75 (d, *J* = 149.9 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}BrF_2N_2O$ ($[M+H]^+$): 431.0566; found: 431.0565.

^{1}H-^{1}H NOESY of **4ba**:



1-(4-bromo-9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4ca)



This compound was obtained in 85% yield (73.1 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

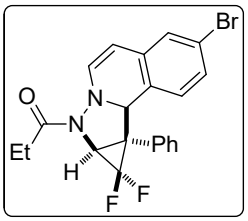
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13-7.08 (m, 1H), 7.06-7.00 (m, 5H), 6.72-6.62 (m, 2H), 6.20 (d, *J* = 8.0 Hz, 1H), 5.95 (d, *J* = 8.0 Hz, 1H), 4.82 (s, 1H), 3.85 (dd, *J* = 7.0, 1.4 Hz, 1H), 2.52-2.40 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 137.9, 132.6, 129.95, 129.93, 129.7, 128.9, 128.5, 128.2, 127.3, 120.5, 112.1 (dd, *J* = 297.8, 293.6 Hz), 106.8, 64.9 (dd, *J* = 5.7, 1.4 Hz), 53.9 (dd, *J* = 11.2, 5.8 Hz), 47.0 (dd, *J* = 13.5, 12.4 Hz), 27.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.64 (dd, *J* = 150.2, 6.7 Hz), -147.57 (d, *J* = 151.6 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}BrF_2N_2O$ ($[M+H]^+$): 431.0566; found: 431.0567.

1-(3-bromo-9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4da)



This compound was obtained in 90% yield (77.4 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

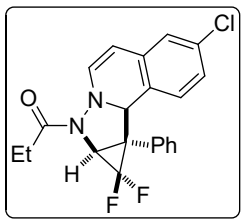
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14-7.08 (m, 1H), 7.05-6.99 (m, 5H), 6.72-6.62 (m, 2H), 6.20 (d, *J* = 8.0 Hz, 1H), 5.95 (d, *J* = 8.0 Hz, 1H), 4.82 (s, 1H), 3.85 (d, *J* = 7.0 Hz, 1H), 2.52-2.39 (m, 2H), 1.11 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 137.9, 132.6, 129.96, 129.95, 129.7, 128.9, 128.6, 128.2, 127.3, 120.6, 112.1 (dd, *J* = 296.3, 292.0 Hz), 106.8, 64.9 (dd, *J* = 5.8, 1.3 Hz), 53.9 (dd, *J* = 11.3, 5.9 Hz), 47.0 (dd, *J* = 13.5, 12.4 Hz), 27.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.67 (dd, *J* = 150.0, 9.1 Hz), -147.62 (d, *J* = 151.8 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}BrF_2N_2O$ ($[M+H]^+$): 431.0566; found: 431.0566.

1-(3-chloro-9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4ea)



This compound was obtained in 85% yield (65.6 mg, dr = 8:1, in 0.2 mmol scale) as

light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

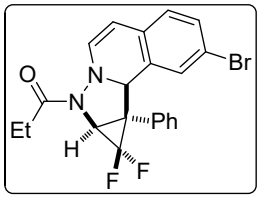
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05-7.01 (m, 5H), 6.94-6.90 (m, 1H), 6.89-6.86 (m, 1H), 6.62 (d, *J* = 8.1 Hz, 1H), 6.15 (d, *J* = 7.7 Hz, 1H), 5.51 (d, *J* = 7.8 Hz, 1H), 4.83 (s, 1H), 3.85 (d, *J* = 7.0 Hz, 1H), 2.53-2.41 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 137.4, 132.0, 129.91, 129.90, 129.6, 129.1, 128.6, 128.4, 127.8, 125.8, 122.4, 112.1 (dd, *J* = 297.8, 293.8 Hz), 106.9, 64.6 (dd, *J* = 5.6, 1.3 Hz), 53.7 (dd, *J* = 11.2, 5.8 Hz), 47.1 (dd, *J* = 13.4, 12.4 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.68 (dd, *J* = 149.8, 9.2 Hz), -147.63 (d, *J* = 150.5 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}ClF_2N_2O$ ($[M+H]^+$): 387.1067; found: 387.1071.

1-(2-bromo-9,9-difluoro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4fa)



This compound was obtained in 87% yield (74.8 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

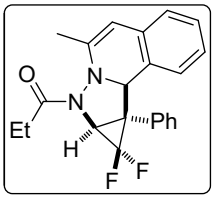
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05-7.00 (m, 5H), 6.76 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.72 (d, *J* = 2.0 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 6.16 (d, *J* = 7.8 Hz, 1H), 5.52 (d, *J* = 7.8 Hz, 1H), 4.85 (s, 1H), 3.86 (d, *J* = 7.0 Hz, 1H), 2.54-2.42 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 137.3, 134.3, 131.7, 129.91, 129.89, 129.3, 128.6, 128.4, 126.2, 125.3, 124.8, 112.1 (dd, *J* = 297.8, 293.5 Hz), 107.0, 64.6 (dd, *J* = 5.5, 1.4 Hz), 53.8 (dd, *J* = 11.3, 5.7 Hz), 47.1 (dd, *J* = 13.6, 12.3 Hz), 27.2, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.69 (dd, *J* = 146.9, 7.9 Hz), -147.62 (d, *J* = 150.9 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}BrF_2N_2O$ ([M+H]$^+$): 431.0566; found: 431.0568.

1-(9,9-difluoro-6-methyl-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4ga)



This compound was obtained in 75% yield (54.9 mg, dr = 10:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

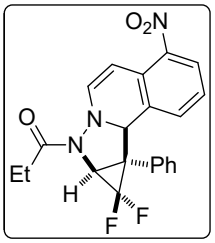
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07-7.03 (m, 2H), 6.99-6.96 (m, 3H), 6.66-6.59 (m, 2H), 6.53 (s, 1H), 6.08 (d, *J* = 7.9 Hz, 1H), 5.54 (d, *J* = 7.8 Hz, 1H), 4.85 (s, 1H), 3.85 (d, *J* = 7.0 Hz, 1H), 2.54-2.40 (m, 2H), 2.03 (s, 3H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 138.3, 136.0, 130.02, 130.01, 129.7, 128.2, 128.1, 128.0, 127.2, 125.7, 124.0, 112.3 (dd, *J* = 297.8, 293.2 Hz), 108.4, 65.2 (dd, *J* = 5.3, 1.4 Hz), 53.7 (dd, *J* = 11.4, 5.4 Hz), 47.2 (dd, *J* = 13.3, 12.4 Hz), 27.3, 21.1, 9.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.62 (dd, *J* = 149.4, 9.2 Hz), -147.17 (d, *J* = 149.7 Hz).

HRMS (ESI) calculated for $C_{22}H_{21}F_2N_2O$ ([M+H]$^+$): 367.1617; found: 367.1614.

1-(9,9-difluoro-4-nitro-9a-phenyl-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (4ha)



This compound was obtained in 85% yield (67.7 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

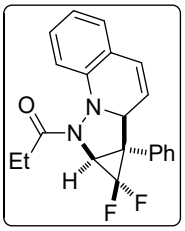
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.2 Hz, 1H), 7.18-7.14 (m, 2H), 7.12-7.08 (m, 4H), 6.99 (t, *J* = 7.9 Hz, 1H), 6.49-6.40 (m, 2H), 5.01 (s, 1H), 3.97 (d, *J* = 7.6 Hz, 1H), 2.60-2.50 (m, 2H), 1.19 (t, *J* = 7.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 144.5, 140.6, 133.1, 129.9, 129.8, 129.7, 128.9, 128.5, 126.2, 125.3, 125.2, 112.0 (dd, *J* = 297.9, 294.0 Hz), 102.3, 64.4 (dd, *J* = 5.8, 1.4 Hz), 54.0 (dd, *J* = 11.1, 6.2 Hz), 46.8 (dd, *J* = 13.7, 12.3 Hz), 27.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.80 (dd, *J* = 150.3, 10.1 Hz), -147.41 (d, *J* = 151.5 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}F_2N_3O_3$ ($[M+H]^+$): 398.1311; found: 398.1314.

1-(7,7-difluoro-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5aa)



This compound was obtained in 86% yield (60.5 mg, dr = 7:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

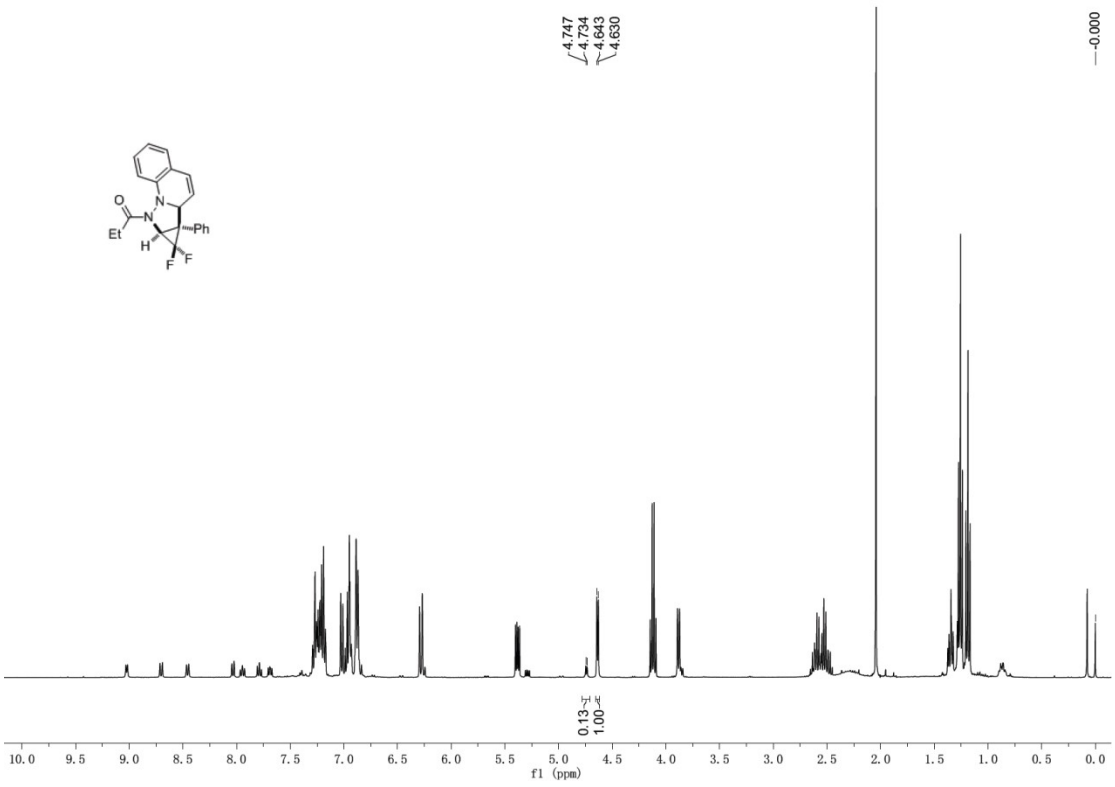
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.18 (m, 4H), 7.03-6.94 (m, 3H), 6.88 (d, *J* = 6.9 Hz, 2H), 6.28 (d, *J* = 9.8 Hz, 1H), 5.38 (dd, *J* = 9.9, 5.3 Hz, 1H), 4.64 (d, *J* = 5.3 Hz, 1H), 3.88 (d, *J* = 7.3 Hz, 1H), 2.62-2.46 (m, 2H), 1.18 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 142.4, 130.0, 129.72, 129.70, 128.6, 128.5, 127.4, 127.3, 122.8, 119.5, 113.7, 112.3 (dd, *J* = 298.9, 293.2 Hz), 62.5 (dd, *J* = 5.7, 1.4 Hz), 52.8 (dd, *J* = 11.3, 5.7 Hz), 47.8 (dd, *J* = 13.6, 12.3 Hz), 26.8, 8.9.

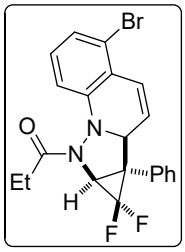
^{19}F NMR (376 MHz, $CDCl_3$): δ -121.28 (dd, *J* = 150.8, 10.3 Hz), -147.53 (d, *J* = 151.3 Hz).

HRMS (ESI) calculated for $C_{21}H_{19}F_2N_2O$ ($[M+H]^+$): 353.1460; found: 353.1458.

Crude ^{1}H-NMR spectrum of 5aa:



1-(4-bromo-7,7-difluoro-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5ba)



This compound was obtained in 91% yield (78.3 mg, dr = 6:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.09 (m, 4H), 7.02 (t, *J* = 8.1 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.81 (d, *J* = 6.4 Hz, 2H), 6.63 (d, *J* = 10.3 Hz, 1H), 5.39 (dd, *J* = 10.2, 5.3 Hz, 1H), 4.56 (dd, *J* = 5.3, 1.3 Hz, 1H), 3.80 (d, *J* = 8.3 Hz, 1H), 2.50-2.34 (m, 2H), 1.10 (t, *J* = 7.4 Hz, 3H).

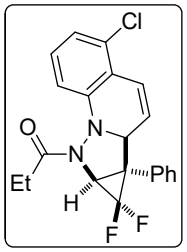
^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 144.0, 130.4, 129.63, 129.61, 128.77, 128.75, 126.9, 126.0, 122.7, 121.8, 121.1, 112.9, 112.1 (dd, *J* = 298.9, 293.4 Hz), 62.2 (dd, *J*

= 5.8, 1.4 Hz), 52.8 (dd, *J* = 11.3, 6.0 Hz), 47.9 (dd, *J* = 13.8, 12.4 Hz), 26.8, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.45 (dd, *J* = 150.8, 10.4 Hz), -147.33 (d, *J* = 150.8 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}BrF_2N_2O$ ($[M+H]^+$): 431.0566; found: 431.0567.

1-(4-chloro-7,7-difluoro-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5ca)



This compound was obtained in 78% yield (60.2 mg, dr = 6:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

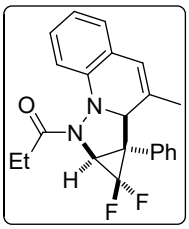
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.13 (m, 3H), 7.09 (t, *J* = 8.1 Hz, 1H), 6.94-6.91 (m, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.84-6.80 (m, 2H), 6.65 (d, *J* = 10.3 Hz, 1H), 5.40 (dd, *J* = 10.2, 5.3 Hz, 1H), 4.59-4.56 (m, 1H), 3.80 (d, *J* = 7.3 Hz, 1H), 2.52-2.36 (m, 2H), 1.10 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 143.9, 132.2, 130.0, 129.62, 129.61, 128.8, 128.7, 123.6, 123.3, 120.9, 120.4, 112.2, 112.2 (dd, *J* = 297.4, 291.8 Hz), 62.2 (d, *J* = 5.8, 1.4 Hz), 52.8 (dd, *J* = 11.3, 5.9 Hz), 47.8 (dd, *J* = 13.9, 12.2 Hz), 26.8, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.46 (dd, *J* = 151.3, 8.0 Hz), -147.37 (d, *J* = 151.3 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}ClF_2N_2O$ ($[M+H]^+$): 387.1071; found: 387.1072.

1-(7,7-difluoro-6-methyl-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5da)



This compound was obtained in 85% yield (62.4 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

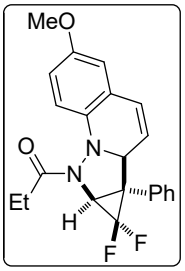
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18-7.12 (m, 2H), 7.10-7.04 (m, 2H), 6.92 (dd, *J* = 15.0, 7.6 Hz, 2H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 7.4 Hz, 2H), 6.02 (s, 1H), 4.32 (s, 1H), 3.72 (d, *J* = 7.5 Hz, 1H), 2.55-2.41 (m, 2H), 1.48 (s, 3H), 1.11 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 141.1, 130.4, 130.3, 129.0, 128.6, 128.5, 128.3, 126.5, 124.1, 123.5, 123.1, 113.6, 112.5 (dd, *J* = 298.3, 294.3 Hz), 67.4 (dd, *J* = 5.7, 1.4 Hz), 48.8 (t, *J* = 13.0 Hz), 26.8, 21.1, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.03 (dd, *J* = 151.9, 9.1 Hz), -146.97 (d, *J* = 151.0 Hz).

HRMS (ESI) calculated for $C_{22}H_{21}F_2N_2O$ ($[M+H]^+$): 367.1617; found: 367.1618.

1-(7,7-difluoro-3-methoxy-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5ea)



This compound was obtained in 89% yield (68.0 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.3. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17-7.10 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.81-6.77 (m, 2H), 6.74 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.43 (d, *J* = 2.8 Hz, 1H), 6.14 (d, *J* = 9.9

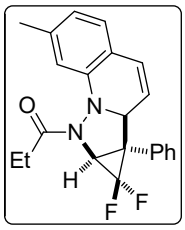
Hz, 1H), 5.34 (dd, *J* = 9.9, 5.4 Hz, 1H), 4.51 (dd, *J* = 5.4, 0.9 Hz, 1H), 3.79 (dd, *J* = 7.4, 1.0 Hz, 1H), 3.70 (s, 3H), 2.56-2.38 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 155.5, 136.0, 129.69, 129.67, 128.6, 128.5, 127.3, 124.0, 120.6, 115.0, 114.6, 113.1, 112.2 (dd, *J* = 298.8, 293.1 Hz), 62.7 (dd, *J* = 5.6, 1.3 Hz), 55.6, 52.6 (dd, *J* = 11.5, 5.6 Hz), 47.8 (t, *J* = 12.8 Hz), 26.9, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.38 (dd, *J* = 150.4, 10.3 Hz), -147.57 (d, *J* = 149.4 Hz).

HRMS (ESI) calculated for $C_{22}H_{21}F_2N_2O_2$ ($[M+H]^+$): 383.1566; found: 383.1564.

1-(7,7-difluoro-2-methyl-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5fa)



This compound was obtained in 85% yield (62.2 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15-7.08 (m, 3H), 6.82-6.77 (m, 2H), 6.76-6.72 (m, 2H), 6.71-6.66 (m, 1H), 6.16 (d, *J* = 9.9 Hz, 1H), 5.23 (dd, *J* = 9.9, 5.3 Hz, 1H), 4.53 (d, *J* = 5.3 Hz, 1H), 3.81-3.78 (m, 1H), 2.55-2.40 (m, 2H), 2.28 (s, 3H), 1.11 (t, *J* = 7.5 Hz, 3H).

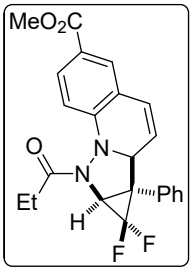
^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9, 142.2, 140.3, 129.8, 129.7, 128.53, 128.45, 127.4, 127.1, 123.5, 120.3, 118.3, 114.4, 112.3 (dd, *J* = 298.8, 293.1 Hz), 62.6 (dd, *J* = 5.6, 1.4 Hz), 52.8 (dd, *J* = 11.4, 5.5 Hz), 47.8 (dd, *J* = 13.5, 12.4 Hz), 26.8, 21.9, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.17 (dd, *J* = 151.2, 9.1 Hz), -147.59 (d, *J* = 151.4 Hz).

HRMS (ESI) calculated for $C_{22}H_{21}F_2N_2O$ ($[M+H]^+$): 367.1617; found: 367.1618.

methyl-7,7-difluoro-6b-phenyl-8-propionyl-6a,6b,7a,8-tetrahydro-7*H*-cyclopropa

[3,4]pyrazolo[1,5-*a*]quinoline-3-carboxylate (5ga)



This compound was obtained in 68% yield (55.8 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.2. NMR spectra of the major isomer were presented.

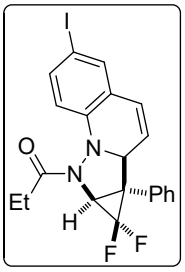
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.16-7.13 (m, 2H), 7.08-7.05 (m, 3H), 7.01-6.97 (m, 1H), 6.92 (t, *J* = 7.7 Hz, 1H), 6.31 (d, *J* = 8.3 Hz, 1H), 4.96 (s, 1H), 3.98-3.91 (m, 1H), 3.83 (s, 3H), 3.04-2.23 (m, 2H), 1.19 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 167.1, 138.2, 132.2, 131.02, 131.01, 130.0, 129.9, 128.5, 128.3, 125.7, 124.9, 112.1 (dd, *J* = 297.7, 293.6 Hz), 105.7, 65.0 (dd, *J* = 5.6, 1.4 Hz), 53.9 (dd, *J* = 11.2, 5.7 Hz), 52.2, 46.8 (dd, *J* = 13.4, 12.3 Hz), 27.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.80 (dd, *J* = 149.5, 6.8 Hz), -147.74 (d, *J* = 149.7 Hz).

HRMS (ESI) calculated for $C_{23}H_{21}F_2N_2O_3$ ($[M+H]^+$): 411.1515; found: 411.1517.

1-(7,7-difluoro-3-iodo-6b-phenyl-6a,6b,7,7a-tetrahydro-8*H*-cyclopropa[3,4] pyrazolo[1,5-*a*]quinolin-8-yl)propan-1-one (5ha)



This compound was obtained in 84% yield (80.3 mg, dr = 9:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

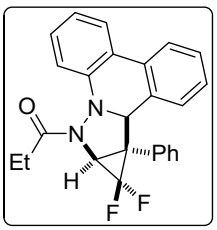
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.17-7.06 (m, 5H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.56 (t, *J* = 7.7 Hz, 1H), 6.24 (d, *J* = 8.0 Hz, 1H), 5.90 (d, *J* = 8.0 Hz, 1H), 4.84 (s, 1H), 3.93 (dd, *J* = 7.0, 1.4 Hz, 1H), 2.78-2.27 (m, 2H), 1.18 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 139.3, 138.3, 132.8, 129.99, 129.97, 128.6, 128.34, 128.29, 128.23, 127.7, 112.1 (dd, *J* = 297.7, 293.8 Hz), 111.8, 96.5, 65.2 (dd, *J* = 5.7, 1.3 Hz), 53.9 (dd, *J* = 11.4, 5.8 Hz), 47.0 (dd, *J* = 13.6, 12.4 Hz), 27.3, 9.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.64 (dd, *J* = 150.4, 7.7 Hz), -147.56 (d, *J* = 151.3 Hz).

HRMS (ESI) calculated for $C_{21}H_{18}F_2IN_2O$ ($[M+H]^+$): 479.0427; found: 479.0430.

1-(11,11-difluoro-11a-phenyl-10a,11,11a,11b-tetrahydro-10*H*-cyclopropa[3,4] pyrazolo[1,5-*f*]phenanthridin-10-yl)propan-1-one (6)



This compound was obtained in 47% yield (37.8 mg, dr = 11:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.5. NMR spectra of the major isomer were presented.

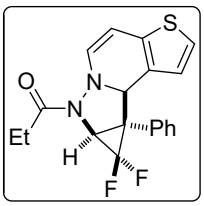
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.41-7.34 (m, 1H), 7.28-7.20 (m, 1H), 7.20-7.12 (m, 2H), 7.12-7.05 (m, 2H), 6.99-6.95 (m, 1H), 6.95-6.89 (m, 2H), 6.62-6.58 (m, 2H), 5.07 (s, 1H), 4.02 (d, *J* = 7.3 Hz, 1H), 2.88-2.46 (m, 2H), 1.22 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 143.1, 130.3, 129.80, 129.78, 129.76, 129.1, 128.5, 128.13, 128.11, 127.74, 127.69, 123.9, 123.7, 123.5, 122.3, 115.9, 112.7 (dd, *J* = 298.4, 291.4 Hz), 66.9 (dd, *J* = 5.8, 1.4 Hz), 53.3 (dd, *J* = 11.2, 6.1 Hz), 48.4 (dd, *J* = 13.8, 12.9 Hz), 27.0, 9.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.23 (dd, *J* = 150.2, 7.7 Hz), -146.52 (d, *J* = 147.9 Hz).

HRMS (ESI) calculated for $C_{25}H_{21}F_2N_2O$ ([M+H]$^+$): 403.1617; found: 403.1620.

1-(8,8-difluoro-8a-phenyl-7a,8,8a,8b-tetrahydro-7*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]thieno[3,2-c]pyridin-7-yl)propan-1-one (7)



This compound was obtained in 70% yield (56.3 mg, dr = 8:1, in 0.2 mmol scale) as light yellow solid, Eluent: PE/EA = 5/1. R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.16 (m, 2H), 7.16-7.12 (m, 3H), 6.94 (d, *J* = 5.0 Hz, 1H), 6.61 (d, *J* = 5.0 Hz, 1H), 6.14 (d, *J* = 7.8 Hz, 1H), 5.75 (d, *J* = 7.8 Hz, 1H), 5.21 (s, 1H), 3.90 (d, *J* = 7.0 Hz, 1H), 2.64-2.49 (m, 2H), 1.19 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 134.0, 132.6, 130.30, 130.28, 128.4, 128.2, 125.9, 125.6, 124.0, 112.0 (dd, *J* = 297.1, 294.5 Hz), 103.0, 63.7 (dd, *J* = 6.0, 1.4 Hz), 53.5 (dd, *J* = 11.3, 5.2 Hz), 47.8 (dd, *J* = 13.3, 12.2 Hz), 27.2, 8.9.

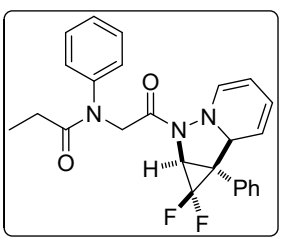
^{19}F NMR (376 MHz, $CDCl_3$): δ -120.78 (dd, *J* = 152.5, 7.3 Hz), -148.18 (d, *J* = 152.2 Hz).

HRMS (ESI) calculated for $C_{19}H_{17}F_2N_2OS$ ([M+H]$^+$): 359.1024; found: 359.1021.

III. Synthesis applications

Late-stage modification of drug or drug intermediate:

***N*-(2-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclo propa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)-2-oxoethyl)-*N*-phenylpropionamide (8a)**



This compound was obtained in 61% yield (53.0 mg, dr > 20:1, in 0.2 mmol scale) as light yellow solid, m.p.: 120-122 °C, Eluent: PE/EA = 5/1, R_f = 0.3. NMR spectra of the major isomer were presented.

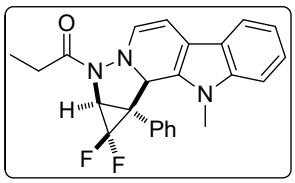
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (m, 4H), 7.37-7.29 (m, 4H), 7.26 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.27 (d, *J* = 8.1 Hz, 1H), 5.73 (dd, *J* = 9.9, 5.7 Hz, 1H), 5.16-5.09 (m, 2H), 4.84 (d, *J* = 17.0 Hz, 1H), 4.42 (d, *J* = 5.0 Hz, 1H), 4.26 (d, *J* = 17.0 Hz, 1H), 3.81 (d, *J* = 6.9 Hz, 1H), 2.18 (q, *J* = 7.4 Hz, 2H), 1.08 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 170.9, 143.4, 135.6, 129.90, 129.88, 129.78, 128.7, 128.6, 128.4, 128.2, 123.3, 117.4, 111.8 (dd, *J* = 298.1, 293.3 Hz), 104.5, 60.9 (dd, *J* = 5.3, 1.4 Hz), 53.2 (dd, *J* = 11.5, 5.2 Hz), 51.9, 45.9 (t, *J* = 13.0 Hz), 27.5, 9.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.07 (dd, *J* = 151.3, 6.8 Hz), -148.05 (d, *J* = 151.4 Hz).

HRMS (ESI) calculated for $C_{25}H_{24}F_2N_3O_2$ ($[M+H]^+$): 436.1832; found: 436.1823.

1-(1,1-difluoro-10-methyl-10c-phenyl-1a,10,10b,10c-tetrahydrocyclopropa[3',4'] pyrazolo[1',5':1,2]pyrido[3,4-*b*]indol-2(1*H*)-yl)propan-1-one (8b)



This compound was obtained in 50% yield (40.5 mg, dr = 10:1, in 0.2 mmol scale) as as light yellow solid, Eluent: PE/EA = 5/1, R_f = 0.6. NMR spectra of the major isomer were presented.

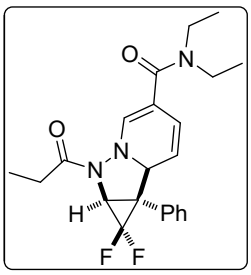
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 6.7, 1.5 Hz, 1H), 7.19 (d, *J* = 6.9 Hz, 2H), 7.11-7.05 (m, 2H), 7.04-6.96 (m, 4H), 6.07-6.05 (m, 2H), 5.30 (s, 1H), 3.90 (dd, *J* = 7.3, 1.1 Hz, 1H), 3.41 (s, 3H), 2.72-2.54 (m, 2H), 1.20 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 137.5, 129.78, 129.76, 129.3, 128.6, 128.2, 126.8, 123.3, 122.1, 120.1, 118.5, 112.2 (dd, *J* = 295.2, 294.0 Hz), 109.1, 108.5, 101.0, 62.1 (dd, *J* = 6.3, 1.6 Hz), 52.6 (dd, *J* = 11.6, 4.3 Hz), 49.2 (dd, *J* = 12.9, 12.2 Hz), 30.0, 27.3, 9.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.35 (dd, *J* = 152.6, 7.3 Hz), -147.93 (d, *J* = 151.9 Hz).

HRMS (ESI) calculated for $C_{24}H_{22}F_2N_3O$ ($[M+H]^+$): 406.1726; found: 406.1716.

***N*,*N*-diethyl-1,1-difluoro-7b-phenyl-2-propionyl-1a,2,7a,7b-tetrahydro-1*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridine-5-carboxamide (8c)**



This compound was obtained in 55% yield (44.1 mg, dr = 5:1, in 0.2 mmol scale) as as light yellow solid, Eluent: PE/EA = 5/1, R_f = 0.4. NMR spectra of the major isomer were presented.

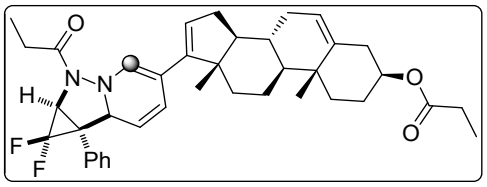
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.32 (m, 3H), 7.27-7.22 (m, 2H), 6.56 (s, 1H), 5.81 (d, *J* = 10.0 Hz, 1H), 5.19 (dd, *J* = 10.4, 4.6 Hz, 1H), 4.52 (d, *J* = 5.0 Hz, 1H), 3.83 (d, *J* = 6.9 Hz, 1H), 3.27 (q, *J* = 7.0 Hz, 4H), 2.60-2.49 (m, 2H), 1.16 (t, *J* = 7.5 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 168.2, 138.1, 129.69, 129.67, 128.9, 128.8, 123.0, 116.4, 113.1, 111.9 (dd, *J* = 298.4, 293.6 Hz), 60.5 (dd, *J* = 5.8, 1.4 Hz), 53.6 (dd, *J* = 11.2, 5.8 Hz), 45.8 (dd, *J* = 13.8, 12.1 Hz), 41.2, 21.1, 13.6, 8.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.60 (dd, *J* = 151.5, 6.8 Hz), -148.10 (d, *J* = 151.4 Hz).

HRMS (ESI) calculated for $C_{22}H_{26}F_2N_3O_2$ ($[M+H]^+$): 402.1988; found: 402.1987.

(3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-17-(1,1-difluoro-7b-phenyl-2-propionyl-1a,2,7a,7b-tetrahydro-1*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-5-yl)-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15-dodecahydro-1*H*-cyclopenta[*a*] phenanthren-3-yl propionate (8d)



This compound was obtained in 64% yield (80.5 mg, dr = 9:1, rr = 13:1, in 0.2 mmol scale) as as light yellow solid, Eluent: PE/EA = 5/1, R_f = 0.4. NMR spectra of the major isomer were presented.

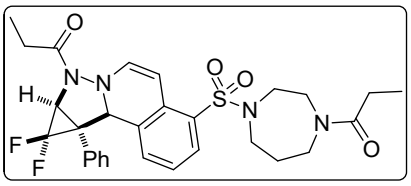
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.15 (m, 3H), 7.15-7.11 (m, 2H), 6.09 (d, *J* = 7.5 Hz, 1H), 5.88 (d, *J* = 6.3 Hz, 1H), 5.69 (s, 1H), 5.34 (d, *J* = 4.8 Hz, 1H), 5.18 (dd, *J* = 7.5, 6.3 Hz, 1H), 4.64 (s, 1H), 4.62-4.54 (m, 1H), 3.71 (d, *J* = 7.2 Hz, 1H), 2.57-2.43 (m, 2H), 2.30-2.24 (m, 5H), 2.20-2.11 (m, 1H), 1.97-1.71 (m, 6H), 1.60-1.47 (m, 5H), 1.37-1.28 (m, 2H), 1.16-1.04 (m, 6H), 0.94 (s, 3H), 0.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 174.1, 151.4, 140.2, 134.8, 131.6, 129.8, 128.2, 127.7, 127.3, 124.1, 122.3, 117.9, 112.5 (t, *J* = 294.4), 104.6, 73.7, 62.8 (d, *J* = 5.8 Hz), 56.9, 53.2 (dd, *J* = 11.8, 4.6 Hz), 50.1, 47.6 (t, *J* = 12.8 Hz), 46.3, 38.2, 36.9, 36.7, 34.0, 31.6, 31.3, 30.1, 28.0, 27.8, 27.2, 20.7, 19.3, 16.3, 9.3, 8.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -119.30 (dd, *J* = 150.6, 7.6 Hz), -149.11 (d, *J* = 150.2 Hz).

HRMS (ESI) calculated for $C_{25}H_{24}F_2N_3O_2$ ($[M+H]^+$): 629.3550; found: 629.3546.

1-(9,9-difluoro-9a-phenyl-4-((4-propionyl-1,4-diazepan-1-yl)sulfonyl)-8a,9,9a,9b-tetrahydro-8*H*-cyclopropa[3,4]pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (8e)



This compound was obtained in 78% yield (88.9 mg, dr = 7:1, in 0.2 mmol scale) as as light yellow solid, Eluent: DCM/MeOH = 30/1, R_f = 0.3. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.15-7.11 (m, 2H), 7.11-7.04 (m, 4H), 7.03-6.98 (m, 1H), 6.45-6.40 (m, 1H), 6.39-6.35 (m, 1H), 4.96 (s,

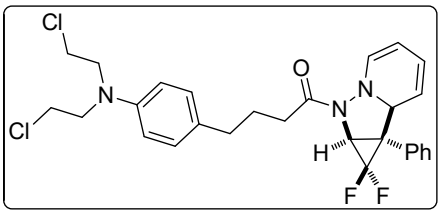
1H), 3.96 (d, *J* = 6.7 Hz, 1H), 3.70-3.49 (m, 4H), 3.28-3.10 (m, 4H), 2.60-2.48 (m, 2H), 2.40-2.25 (m, 2H), 1.99-1.84 (m, 2H), 1.22-1.11 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): Two groups of peaks were observed owing to the keto-enol tautomerism. δ 176.43, 176.39, 173.5, 173.1, 139.1, 139.0, 132.9, 132.8, 132.7, 129.83, 129.78, 129.65, 129.50, 129.47, 129.1, 128.6, 128.5, 128.33, 128.28, 125.8, 111.9 (dd, *J* = 298.0, 293.6 Hz), 103.94, 103.88, 64.6 (d, *J* = 5.1 Hz), 53.9 (dd, *J* = 11.1, 5.8 Hz), 49.9, 49.6, 49.1, 48.1, 47.9, 46.7, 46.5, 44.5, 28.8, 27.5, 27.2, 26.4, 26.0, 9.5, 9.3, 8.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.83 (dd, *J* = 151.0, 8.9 Hz), -147.42 (d, *J* = 149.5 Hz).

HRMS (ESI) calculated for $C_{29}H_{33}F_2N_4O_3S$ ($[M+H]^+$): 571.2186; found: 571.2187.

4-(4-(bis(2-chloroethyl)amino)phenyl)-1-(1,1-difluoro-7b-phenyl-1,1a,7a,7b-tetrahydro-2*H*-cyclopropa[3,4]pyrazolo[1,5-*a*]pyridin-2-yl)butan-1-one (8f)



This compound was obtained in 70% yield (73.1 mg, dr = 7:1, in 0.2 mmol scale) as as light yellow solid, Eluent: PE/EA = 5/1, R_f = 0.4. NMR spectra of the major isomer were presented.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.30 (m, 3H), 7.28-7.26 (m, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.62 (d, *J* = 8.7 Hz, 2H), 6.03 (d, *J* = 7.7 Hz, 1H), 5.77-5.68 (m, 1H), 5.13-5.05 (m, 2H), 4.43 (d, *J* = 5.1 Hz, 1H), 3.76 (d, *J* = 7.1 Hz, 1H), 3.70-3.67 (m, 4H), 3.64-3.61 (m, 4H), 2.63-2.53 (m, 3H), 2.51-2.40 (m, 1H), 2.00-1.85 (m, 2H).

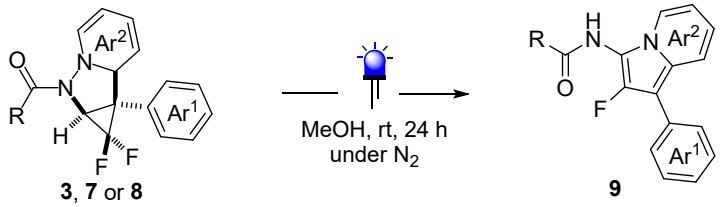
^{13}C NMR (100 MHz, $CDCl_3$): δ 175.8, 144.3, 136.0, 130.9, 129.91, 129.89, 129.80, 128.64, 128.55, 123.2, 117.3, 112.2, 112.1 (dd, *J* = 297.7, 293.3 Hz), 103.9, 60.9 (dd, *J* = 5.4, 1.6 Hz), 53.7, 53.5 (dd, *J* = 11.5, 4.9 Hz), 45.9 (t, *J* = 12.9 Hz), 40.6, 34.0, 33.0, 26.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -120.89 (dd, *J* = 150.4, 7.0 Hz), -148.39 (d, *J* =

150.7 Hz).

HRMS (ESI) calculated for $C_{28}H_{30}Cl_2F_2N_3O_2$ ($[M+H]^+$): 532.1729; found: 532.1730.

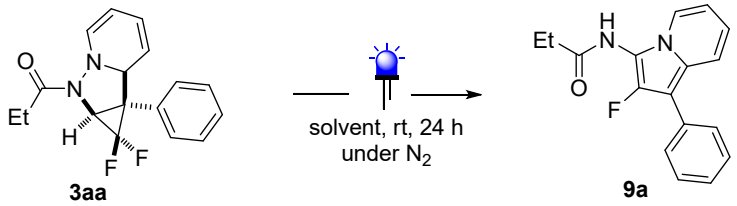
Photo-mediated ring-opening/rearrangement of product 3-5, 7 and 8:



3, **7** or **8** **9**

In a 10 mL Schlenk tube with a magnetic stirring bar was added with 1,2-dihydropyridine derivatives (0.2 mmol) in MeOH (1.0 mL) under the N_2 atmosphere. Then, the tube was placed at a reaction bath equipped with Kessil PR 450 nm blue LEDs (24W, 1 cm distance) and allowed to stir at room temperature for 24 h. Afterwards, the resulted mixture was purified by preparative TLC to afford the corresponding *N*-(2-fluoro-1-phenylindolizin-3-yl)propionamide derivatives **9a-9n**.

Table S1. Comparison of different solvents for the photo-induced rearrangement.

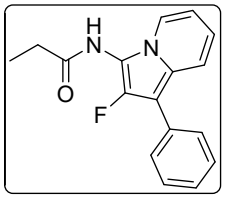


3aa **9a**

Entry	Solvent	Yield (%)
1	MeOH	81
2	EtOH	72
3	2-Me THF	55
4	GVL	60

Characterization of fluorinated indolizine products:

***N*-(2-fluoro-1-phenylindolizin-3-yl)propionamide (9a)**



This compound was obtained in 81% yield (45.7 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 152-153 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

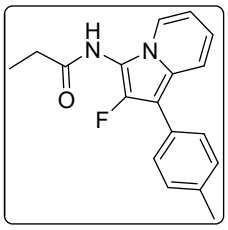
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.84 (s, 1H), 7.86 (d, *J* = 7.1 Hz, 1H), 7.67 (dt, *J* = 8.8, 1.0 Hz), 7.54 (d, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.30-7.24 (m, 1H), 6.97-6.92 (m, 1H), 6.77 (td, *J* = 7.8, 1.2 Hz, 1H), 2.46 (q, *J* = 7.6 Hz, 2H), 1.15 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.0, 145.4 (d, *J* = 244.6 Hz), 131.7, 129.0, 127.8, 126.0, 122.9 (d, *J* = 5.8 Hz), 122.5, 119.7, 116.7 (d, *J* = 4.5 Hz), 111.2, 104.1 (d, *J* = 25.4 Hz), 98.4 (d, *J* = 10.6 Hz), 28.2, 9.6.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -163.79.

HRMS (ESI) calculated for $C_{17}H_{16}FN_2O$ ($[M+H]^+$): 283.1247; found: 283.1234.

***N*-(2-fluoro-1-(*p*-tolyl)indolizin-3-yl)propionamide (9b)**



This compound was obtained in 60% yield (35.6 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 151-152 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

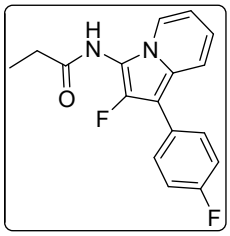
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.81 (s, 1H), 7.83 (dt, *J* = 7.0, 1.1 Hz, 1H), 7.64 (dt, *J* = 9.0, 1.2 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.95-6.89 (m, 1H), 6.75 (td, *J* = 6.8, 1.3 Hz, 1H), 2.50-2.45 (m, 2H), 2.35 (s, 3H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.0, 145.3 (d, *J* = 245.8 Hz), 135.1, 129.6, 128.7 (d, *J* = 2.8 Hz), 127.7, 122.8 (d, *J* = 5.8 Hz), 122.4, 119.4, 116.8 (d, *J* = 4.6 Hz), 111.1, 104.0 (d, *J* = 25.5 Hz), 98.5 (d, *J* = 10.6 Hz), 28.2, 20.8, 9.6.

^{19}F NMR (376 MHz, DMSO-d_6): δ -163.86.

HRMS (ESI) calculated for $C_{18}H_{18}FN_2O$ ([M+H]$^+$): 297.1398; found: 297.1395.

***N*-(2-fluoro-1-(4-fluorophenyl)indolizin-3-yl)propionamide (9c)**



This compound was obtained in 68% yield (40.8 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 143-145 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

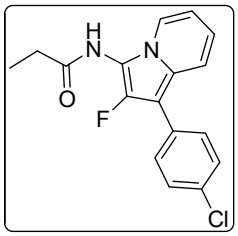
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.83 (s, 1H), 7.86 (d, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 7.57 (dd, *J* = 8.5, 5.6 Hz, 2H), 7.32 (t, *J* = 8.9 Hz, 2H), 6.99-6.92 (m, 1H), 6.77 (td, *J* = 6.8, 1.2 Hz, 1H), 2.47 (q, *J* = 7.6 Hz, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 160.6 (d, *J* = 243.0 Hz), 145.3 (d, *J* = 245.7 Hz), 129.7 (dd, *J* = 7.9, 1.8 Hz), 128.1 (t, *J* = 3.1 Hz), 122.9 (d, *J* = 5.6 Hz), 122.5, 119.7, 116.6 (d, *J* = 4.6 Hz), 116.0, 115.8, 111.2 (d, *J* = 2.1 Hz), 104.1 (d, *J* = 25.4 Hz), 97.5 (d, *J* = 10.6 Hz), 28.2, 9.6.

^{19}F NMR (376 MHz, DMSO-d_6): δ -116.21, -164.13.

HRMS (ESI) calculated for $C_{17}H_{15}F_2N_2O$ ([M+H]$^+$): 301.1147; found: 301.1141.

***N*-(1-(4-chlorophenyl)-2-fluoroindolizin-3-yl)propionamide (9d)**



This compound was obtained in 72% yield (45.5 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 165-167 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

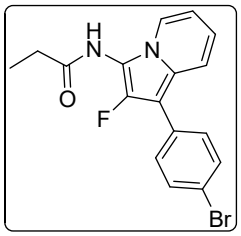
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.84 (s, 1H), 7.87 (dt, *J* = 7.1, 1.2 Hz, 1H), 7.68 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.55-7.51 (m, 2H), 7.01-6.95 (m, 1H), 6.79 (td, *J* = 6.8, 1.2 Hz, 1H), 2.47 (q, *J* = 7.6 Hz, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 145.3 (d, *J* = 246.3 Hz), 130.6 (d, *J* = 2.8 Hz), 130.3, 129.3 (d, *J* = 2.0 Hz), 129.0, 123.0 (d, *J* = 5.6 Hz), 122.6, 120.1, 116.6 (d, *J* = 4.4 Hz), 111.4, 104.3 (d, *J* = 25.5 Hz), 97.2 (d, *J* = 10.3 Hz), 28.2, 9.5.

^{19}F NMR (376 MHz, DMSO-d_6): δ -163.60.

HRMS (ESI) calculated for $C_{17}H_{15}ClFN_2O$ ([M+H]$^+$): 317.0852; found: 317.0846.

***N*-(1-(4-bromophenyl)-2-fluoroindolizin-3-yl)propionamide (9e)**



This compound was obtained in 82% yield (59.0 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 185-188 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

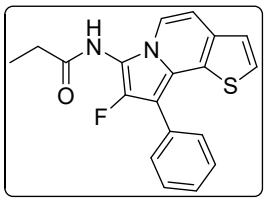
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.85 (s, 1H), 7.88 (d, *J* = 7.0 Hz, 1H), 7.70-7.64 (m, 3H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.02-6.95 (m, 1H), 6.83-6.76 (m, 1H), 2.47 (q, *J* = 7.5 Hz, 2H), 1.15 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.0, 145.3 (d, *J* = 246.5 Hz), 131.9, 131.0 (d, *J* = 2.2 Hz), 129.6, 123.0 (d, *J* = 5.7 Hz), 122.7, 120.1, 118.7, 116.6 (d, *J* = 4.6 Hz), 111.4, 104.4 (d, *J* = 25.3 Hz), 97.2 (d, *J* = 10.0 Hz), 28.2, 9.5.

^{19}F NMR (376 MHz, DMSO-d_6): δ -163.54.

HRMS (ESI) calculated for $C_{17}H_{15}BrFN_2O$ ([M+H]$^+$): 361.0347; found: 361.0339.

***N*-(8-fluoro-9-phenylthieno[3,2-*g*]indolizin-7-yl)propionamide (9f)**



This compound was obtained in 53% yield (35.8 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 142-143 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.85 (s, 1H), 7.81 (d, *J* = 7.3 Hz, 1H), 7.61-7.54

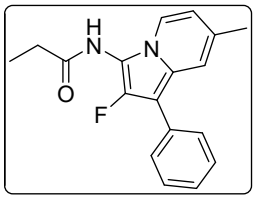
(m, 3H), 7.54-7.49 (m, 2H), 7.45-7.39 (m, 1H), 7.38 (d, *J* = 5.2 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 2.51-2.48 (m, 2H), 1.17 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.2, 145.0 (d, *J* = 244.1 Hz), 132.5, 130.7 (d, *J* = 2.1 Hz), 130.0, 128.7, 127.4, 127.1 (d, *J* = 3.9 Hz), 124.4, 124.2, 120.1, 118.3 (d, *J* = 5.8 Hz), 107.1 (d, *J* = 1.8 Hz), 104.6 (d, *J* = 24.8 Hz), 99.9 (d, *J* = 13.4 Hz), 28.2, 9.5.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -165.45.

HRMS (ESI) calculated for $C_{19}H_{16}FN_2OS$ ([M+H]$^+$): 339.0962; found: 339.0959.

***N*-(2-fluoro-7-methyl-1-phenylindolizin-3-yl)propionamide (9g)**



This compound was obtained in 51% yield (30.3 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 158-160 ºC, Eluent: PE/EA = 2/1. R_f = 0.4.

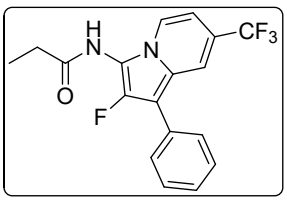
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.76 (s, 1H), 7.76 (d, *J* = 7.1 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 2H), 7.49-7.44 (m, 3H), 7.29-7.25 (m, 1H), 6.62 (dd, *J* = 7.1, 1.7 Hz, 1H), 2.46 (q, *J* = 7.6 Hz, 2H), 2.30 (s, 3H), 1.13 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.1, 145.4 (d, *J* = 245.7 Hz), 132.0 (d, *J* = 2.3 Hz), 129.8, 129.0, 127.7 (d, *J* = 1.8 Hz), 125.7, 123.1 (d, *J* = 5.7 Hz), 122.2 (d, *J* = 1.0 Hz), 114.7 (d, *J* = 3.7 Hz), 113.7 (d, *J* = 2.1 Hz), 103.4 (d, *J* = 25.5 Hz), 97.2 (d, *J* = 10.4 Hz), 28.2, 20.9, 9.6.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -164.07.

HRMS (ESI) calculated for $C_{18}H_{18}FN_2O$ ([M+H]$^+$): 297.1398; found: 297.1390.

***N*-(2-fluoro-1-phenyl-7-(trifluoromethyl)indolizin-3-yl)propionamide (9h)**



This compound was obtained in 58% yield (40.6 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 153-156 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

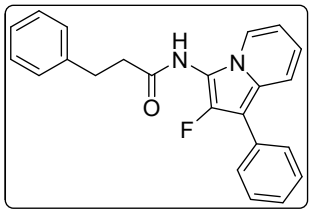
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.09 (s, 1H), 8.08 (d, *J* = 7.3 Hz, 1H), 7.91 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.41-7.35 (m, 1H), 6.99 (dd, *J* = 7.4, 1.9 Hz, 1H), 2.56-2.51 (m, 2H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 173.9, 145.6 (d, *J* = 248.4 Hz), 130.3 (d, *J* = 2.8 Hz), 129.3, 128.3, 127.0, 124.1 (q, *J* = 270.9 Hz), 123.9, 120.3 (d, *J* = 5.9 Hz), 119.1 (q, *J* = 33.5 Hz), 115.1 (t, *J* = 5.1 Hz), 107.1 (d, *J* = 25.3 Hz), 106.3, 103.0 (d, *J* = 10.8 Hz), 28.2, 9.4.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -61.44, -160.73.

HRMS (ESI) calculated for $C_{18}H_{15}F_4N_2O$ ($[M+H]^+$): 351.1116; found: 351.1109.

***N*-(2-fluoro-1-phenylindolizin-3-yl)-3-phenylpropanamide (9i)**



This compound was obtained in 71% yield (50.8 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 140-141 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

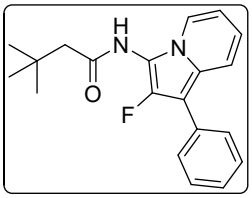
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.88 (s, 1H), 7.66 (dt, *J* = 9.0, 1.2 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.50-7.44 (m, 3H), 7.37-7.29 (m, 5H), 7.28-7.25 (m, 1H), 6.96-6.89 (m, 1H), 6.69 (td, *J* = 6.8, 1.2 Hz, 1H), 2.99 (t, *J* = 7.6 Hz, 2H), 2.79 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 172.5, 145.4 (d, *J* = 246.2 Hz), 140.9, 131.7 (d, *J* = 2.4 Hz), 129.0, 128.53, 128.46, 127.8, 126.2, 126.0, 123.0 (d, *J* = 5.8 Hz), 122.3, 119.7, 116.7 (d, *J* = 4.7 Hz), 111.1, 103.8 (d, *J* = 25.5 Hz), 98.5 (d, *J* = 10.4 Hz), 36.6, 30.9.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -163.72.

HRMS (ESI) calculated for $C_{23}H_{20}FN_2O$ ($[M+H]^+$): 359.1555; found: 359.1560.

***N*-(2-fluoro-1-phenylindolizin-3-yl)-3,3-dimethylbutanamide (9j)**



This compound was obtained in 76% yield (49.2 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 153-155 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

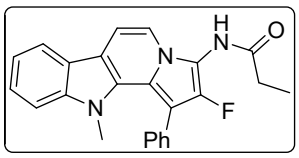
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.80 (s, 1H), 7.81 (dt, *J* = 7.0, 1.1 Hz, 1H), 7.68 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.33-7.26 (m, 1H), 6.99-6.92 (m, 1H), 6.80 (td, *J* = 6.8, 1.2 Hz, 1H), 2.32 (s, 2H), 1.09 (s, 9H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 171.8, 145.3 (d, *J* = 246.6 Hz), 131.7 (d, *J* = 2.5 Hz), 129.0, 127.8, 126.0, 122.9 (d, *J* = 5.6 Hz), 122.2, 119.6, 116.8 (d, *J* = 4.5 Hz), 111.4, 104.3 (d, *J* = 25.6 Hz), 98.6 (d, *J* = 10.2 Hz), 48.4, 30.7, 29.7.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -163.44.

HRMS (ESI) calculated for $C_{20}H_{22}FN_2O$ ($[M+H]^+$): 325.1711; found: 325.1705.

***N*-(2-fluoro-11-methyl-1-phenyl-11H-indolizino[8,7-*b*]indol-3-yl)propionamide (9k)**



This compound was obtained in 80% yield (61.6 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 192-193 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

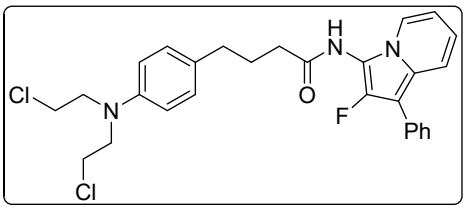
^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.88 (s, 1H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 7.1 Hz, 1H), 7.54-7.48 (m, 5H), 7.47-7.41 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 3.18 (s, 3H), 2.61-2.52 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 174.1, 145.1 (d, *J* = 241.9 Hz), 140.7, 133.4 (d, *J* = 1.5 Hz), 131.2 (d, *J* = 3.4 Hz), 130.7, 128.9, 127.5, 124.0, 123.1, 120.2, 119.0, 115.8, 114.5 (d, *J* = 5.0 Hz), 112.3, 110.5, 105.2 (d, *J* = 24.4 Hz), 104.7, 100.2 (d, *J* = 13.7 Hz), 34.7, 28.3, 9.6.

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -165.25.

HRMS (ESI) calculated for $C_{24}H_{21}FN_3O$ ([M+H]$^+$): 386.1664; found: 386.1660.

4-(4-(bis(2-chloroethyl)amino)phenyl)-*N*-(2-fluoro-1-phenylindolizin-3-yl) butanamide (9l)



This compound was obtained in 63% yield (64.4 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 156-157 °C, Eluent: PE/EA = 2/1. R_f = 0.4.

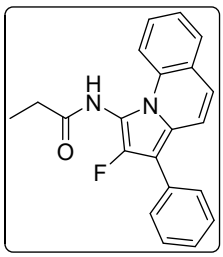
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.84 (s, 1H), 7.82 (d, *J* = 7.0 Hz, 1H), 7.67 (d, *J* = 9.1 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.98-6.90 (m, 1H), 6.77 (td, *J* = 6.8, 1.0 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 2H), 3.73-3.70 (m, 8H), 2.57 (t, *J* = 7.4 Hz, 2H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.91 (p, *J* = 7.2 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 173.1, 145.3 (d, *J* = 246.0 Hz), 144.5, 131.7 (d, *J* = 2.9 Hz), 129.7, 129.4, 129.0, 127.8 (d, *J* = 1.8 Hz), 125.9, 122.9 (d, *J* = 6.0 Hz), 122.4, 119.6, 116.7 (d, *J* = 4.5 Hz), 112.0, 111.2 (d, *J* = 1.8 Hz), 104.1 (d, *J* = 25.4 Hz), 98.5 (d, *J* = 10.6 Hz), 52.3, 41.2, 34.5, 33.6, 27.1.

^{19}F NMR (376 MHz, DMSO-d_6): δ -163.62.

HRMS (ESI) calculated for $C_{28}H_{29}Cl_2FN_3O$ ([M+H]$^+$): 512.1667; found: 512.1663.

***N*-(2-fluoro-3-phenylpyrrolo[1,2-*a*]quinolin-1-yl)propionamide (9m)**



This compound was obtained in 42% yield (27.9 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 208-209 °C, Eluent: PE/EA = 2/1. R_f = 0.5.

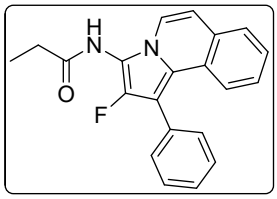
^{1}H NMR (400 MHz, DMSO-d_6): δ 10.16 (s, 1H), 8.52 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.62-7.49 (m, 6H), 7.45-7.28 (m, 3H), 2.56 (q, *J* = 7.6 Hz, 2H), 1.19 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.4, 145.9 (d, *J* = 243.5 Hz), 133.5, 130.8 (d, *J* = 2.8 Hz), 129.0, 128.8, 128.6 (d, *J* = 1.0 Hz), 128.1, 126.7, 124.3 (d, *J* = 1.3 Hz), 124.1, 121.9 (d, *J* = 5.4 Hz), 121.0, 116.4 (d, *J* = 3.8 Hz), 115.3, 108.7 (d, *J* = 25.9 Hz), 102.8 (d, *J* = 10.8 Hz), 28.5, 9.4.

^{19}F NMR (376 MHz, DMSO-d_6): δ -163.75.

HRMS (ESI) calculated for $C_{21}H_{18}FN_2O$ ($[M+H]^+$): 333.1403; found: 333.1393.

***N*-(2-fluoro-1-phenylpyrrolo[2,1-*a*]isoquinolin-3-yl)propionamide (9n)**



This compound was obtained in 55% yield (36.5 mg, in 0.2 mmol scale) as light yellow solid, m.p.: 168-169 °C, Eluent: PE/EA = 2/1. R_f = 0.5.

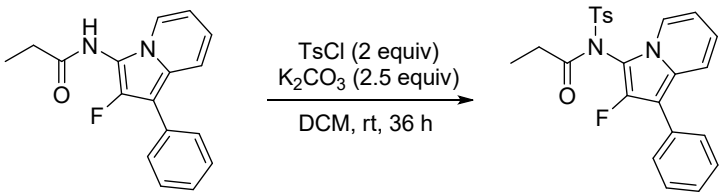
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.81 (s, 1H), 7.77 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.59-7.44 (m, 5H), 7.41-7.32 (m, 1H), 7.29-7.21 (m, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 2.53-2.46 (m, 2H), 1.17 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 174.2, 144.6 (d, *J* = 242.7 Hz), 132.1 (d, *J* = 1.7 Hz), 130.5, 129.0, 127.7, 127.5, 127.3, 127.0, 126.0, 125.1 (d, *J* = 3.6 Hz), 121.4, 121.1, 117.9 (d, *J* = 4.7 Hz), 110.6 (d, *J* = 1.9 Hz), 105.3 (d, *J* = 24.4 Hz), 104.2 (d, *J* = 13.5 Hz), 28.2, 9.5.

^{19}F NMR (376 MHz, DMSO-d_6): δ -166.06.

HRMS (ESI) calculated for $C_{21}H_{18}FN_2O$ ($[M+H]^+$): 333.1403; found: 333.1396.

Derivatizations of product 9:



9a **10**

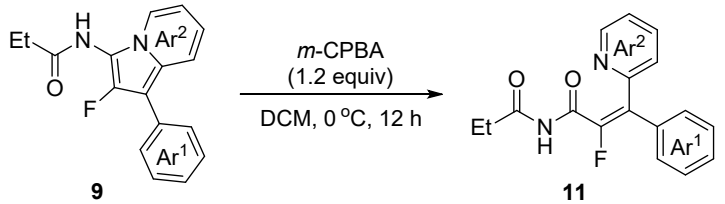
To a solution of indoleazines **9a** (0.2 mmol, 1.0 equiv) in DCM (1 mL) was added 4-methylbenzenesulfonyl chloride (0.4 mmol, 2.0 equiv) and K_2CO_3 (0.5 mmol, 2.5 equiv), the mixture was allowed to stir at room temperature for 36 h. Afterwards, the reaction mixture was concentrated and purified by preparative TLC (Eluent: PE/EA =8/1, R_f = 0.6) to afford the desired product **10** in 32% (27.9 mg) isolated yield as a reddish brown solid, m.p.: 147-148 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-7.96 (m,3H), 7.74 (d, *J* = 9.1 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.40-7.28 (m, 1H), 7.08-6.96 (m, 1H), 6.83 (td, *J* = 6.9, 1.2 Hz, 1H), 2.46 (s, 3H), 2.31-2.15 (m, 1H), 2.08-1.81 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 147.9 (d, *J* = 252.8 Hz), 145.5, 135.7, 131.3 (d, *J* = 2.8 Hz), 129.6, 129.4 (d, *J* = 1.3 Hz), 129.0, 128.5 (d, *J* = 1.8 Hz), 126.9 (d, *J* = 5.8 Hz), 126.7, 121.7, 121.4, 117.9 (d, *J* = 5.0 Hz), 113.0 (d, *J* = 2.6 Hz), 101.4 (d, *J* = 25.9 Hz), 100.9 (d, *J* = 10.1 Hz), 28.5, 21.9, 8.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ -158.50.

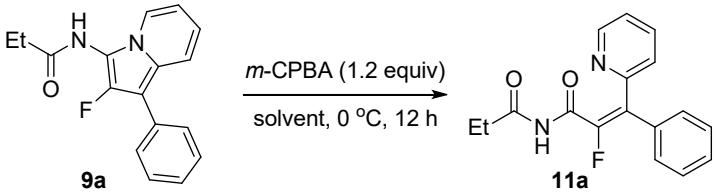
HRMS (ESI) calculated for $C_{24}H_{22}FN_2O_3S$ ($[M+H]^+$): 437.1330; found: 437.1223.



9 **11**

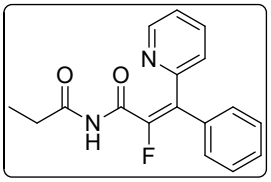
To a solution of indoleazines **9** (0.2 mmol, 1.0 equiv) in DCM (1 mL) was added *m*-CPBA (0.24 mmol, 1.2 equiv), the mixture was allowed to stir at 0 °C for 12 h. Afterwards, the reaction mixture was concentrated and purified by preparative TLC to afford the corresponding Chalcone derivatives **11a-11e**.

Table S2. Comparison of different solvents for the oxidation of compound **9a**.



Entry	Solvent	Yield (%)
1	DCM	52
2	EtOH	61
3	2-Me THF	69
4	GVL	50

(*E*)-2-fluoro-3-phenyl-*N*-propionyl-3-(pyridin-2-yl)acrylamide (11a)



This compound was obtained in 52% yield (15.5 mg, in 0.1 mmol scale) as light yellow solid, m.p.: 110-112 °C, Eluent: PE/EA = 2/1. R_f = 0.3.

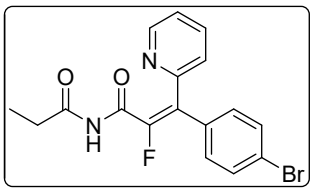
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (s, 1H), 8.88-8.54 (m, 1H), 7.78-7.67 (m, 1H), 7.40-7.34 (m, 3H), 7.34-7.30 (m, 3H), 7.21 (d, *J* = 7.9 Hz, 1H), 2.77 (q, *J* = 7.3 Hz, 1H), 1.10 (t, *J* = 7.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 158.6 (d, *J* = 31.1 Hz), 155.1 (d, *J* = 8.3 Hz), 149.4, 146.8 (d, *J* = 268.7 Hz), 136.8, 134.6, 132.2 (d, *J* = 12.9 Hz), 129.83, 129.78, 129.5, 128.6, 123.4, 31.5, 8.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -122.24.

HRMS (ESI) calculated for $C_{17}H_{16}FN_2O_2$ ($[M+H]^+$): 299.1191; found: 299.1191.

(*E*)-3-(4-bromophenyl)-2-fluoro-*N*-propionyl-3-(pyridin-2-yl)acrylamide (11b)



This compound was obtained in 53% yield (19.9 mg, in 0.1 mmol scale) as light yellow solid, m.p.: 95-97 °C, Eluent: PE/EA = 2/1. R_f = 0.3.

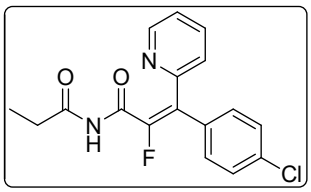
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.25 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 1H), 7.74 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.34 (dd, *J* = 7.6, 4.9 Hz, 1H), 7.20 (t, *J* = 7.3 Hz, 3H), 2.76 (q, *J* = 7.3 Hz, 2H), 1.10 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7, 158.3 (d, *J* = 32.3 Hz), 154.6 (d, *J* = 8.3 Hz), 149.6, 147.0 (d, *J* = 270.6 Hz), 136.9, 133.5, 131.9, 131.4, 131.3, 125.1 (d, *J* = 3.8 Hz), 124.1 (d, *J* = 1.8 Hz), 123.6, 31.5, 8.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.05.

HRMS (ESI) calculated for $C_{17}H_{15}BrFN_2O_2$ ([M+H]$^+$): 377.0296; found: 377.0310.

(*E*)-3-(4-chlorophenyl)-2-fluoro-*N*-propionyl-3-(pyridin-2-yl)acrylamide (11c)



This compound was obtained in 59% yield (19.6 mg, in 0.1 mmol scale) as light yellow solid, m.p.: 101-103 °C, Eluent: PE/EA = 2/1. R_f = 0.3.

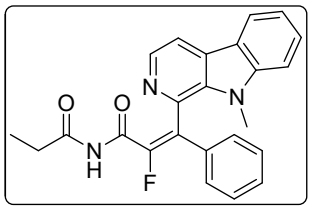
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.26 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 1H), 7.74 (td, *J* = 7.7, 1.8 Hz, 1H), 7.37-7.31 (m, 3H), 7.25 (d, *J* = 8.9 Hz, 3H), 7.21 (d, *J* = 7.8 Hz, 1H), 2.76 (q, *J* = 7.3 Hz, 2H), 1.10 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.8, 158.4 (d, *J* = 32.4 Hz), 154.7 (d, *J* = 8.5 Hz), 149.6, 147.0 (d, *J* = 270.4 Hz), 136.9, 135.7, 133.0, 131.2, 131.1, 128.9, 125.0 (d, *J* = 3.6 Hz), 123.6, 31.5, 8.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.32.

HRMS (ESI) calculated for $C_{17}H_{15}ClFN_2O_2$ ([M+H]$^+$): 333.0801; found: 333.0800.

(*E*)-2-fluoro-3-(9-methyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-3-phenyl-*N*-propionylacrylamide (11d)



This compound was obtained in 43% yield (17.2. mg, in 0.1 mmol scale) as light yellow solid, m.p.: 119-121 °C, Eluent: PE/EA = 2/1. R_f = 0.3.

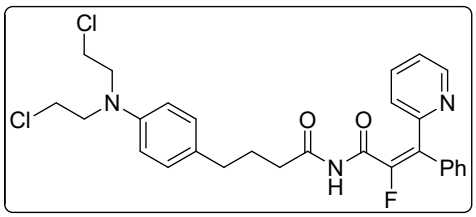
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.52 (d, *J* = 5.2 Hz, 1H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.05 (d, *J* = 5.2 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.44-7.37 (m, 3H), 7.35-7.27 (m, 4H), 3.79 (s, 3H), 2.62 (q, *J* = 6.7 Hz,2H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 158.3 (d, *J* = 31.7 Hz), 147.2 (d, *J* = 274.5 Hz), 142.3, 138.5, 138.0 (d, *J* = 9.6 Hz), 135.6 (d, *J* = 2.7 Hz), 134.7 (d, *J* = 2.9 Hz), 130.1, 129.99, 129.96, 129.89, 128.9, 128.8, 121.8, 121.2, 120.1, 115.0, 109.6, 31.4, 31.3, 7.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -122.69.

HRMS (ESI) calculated for $C_{24}H_{21}FN_3O_2$ ($[M+H]^+$): 402.1613; found: 402.1609.

(*E*)-4-(4-(bis(2-chloroethyl)amino)phenyl)-*N*-(2-fluoro-3-phenyl-3-(pyridin-2-yl)acryloyl)butanamide (11e)



This compound was obtained in 53% yield (19.0 mg, in 0.1 mmol scale) as light yellow solid, m.p.: 107-109 °C, Eluent: PE/EA = 2/1. R_f = 0.3.

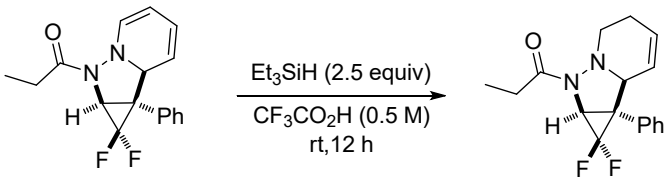
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 8.68-8.64 (m, 1H), 7.74 (td, *J* = 7.7, 1.6 Hz, 1H), 7.43-7.36 (m, 3H), 7.34-7.29 (m, 2H), 7.21 (d, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.60 (d, *J* = 8.6 Hz, 2H), 3.73-3.66 (m, 4H), 3.65-3.58 (m, 4H), 2.77 (t, *J* = 7.3 Hz, 2H), 2.58-2.50 (m, 2H), 1.90 (p, *J* = 7.3 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 158.5 (d, *J* = 32.3 Hz), 155.1 (d, *J* = 8.3 Hz), 149.4, 146.8 (d, *J* = 268.0 Hz), 144.4, 136.9, 134.6, 130.9 (d, *J* = 0.8 Hz), 129.83, 129.81, 129.79, 129.6, 128.7, 125.2 (d, *J* = 3.7 Hz), 123.4, 112.2 (d, *J* = 1.6 Hz), 53.7, 40.6, 37.2, 33.9, 25.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ -121.45.

HRMS (ESI) calculated for $C_{28}H_{29}Cl_2FN_3O_2$ ($[M+H]^+$): 528.1616; found: 528.1630.

1-(1,1-difluoro-7b-phenyl-1,1a,4,5,7a,7b-hexahydro-2*H*-cyclopropa[3,4]pyrazolo [1,5-*a*]pyridin-2-yl)propan-1-one (12)



3aa **12**

The mixture of **3aa** (0.2 mmol, 60.4 mg), Et_3SiH (0.5 mmol, 2.5 equiv) in CF_3CO_2H (0.4 mL) was stirred at room temperature for 12 h without exclusion of air or moisture. Afterwards, the reaction was quenched with H_2O and extracted with EA. The combined organic layers were washed with water and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulted mixture was purified by preparative TLC (Eluent: PE/EA = 5/1, R_f = 0.2) to afford the desired product **12** in 80% (24.3 mg, dr = 7:1) as light yellow solid.

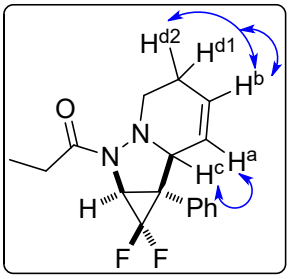
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.30 (m, 3H), 7.28-7.24 (m, 2H), 5.73-5.64 (m, 1H), 5.22 (dt, *J* = 10.1, 3.4 Hz, 1H), 4.28 (dt, *J* = 4.2, 2.7 Hz, 1H), 4.22 (dd, *J* = 7.0, 1.2 Hz, 1H), 3.07-3.02 (m, 2H), 2.67 (dq, *J* = 15.2, 7.5 Hz, 1H), 2.49-2.41 (m, 1H), 2.39-2.31 (m, 1H), 2.12-2.03 (m, 1H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 129.83, 129.81, 128.9, 128.3, 126.7, 122.9, 112.0 (dd, *J* = 298.0, 290.1 Hz), 63.2 (dd, *J* = 4.5, 1.4 Hz), 49.7 (dd, *J* = 11.2, 6.6 Hz), 48.8, 47.2 (dd, *J* = 13.6, 12.2 Hz), 27.0, 25.2, 9.2.

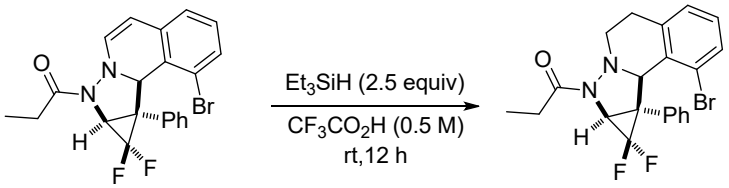
^{19}F NMR (376 MHz, $CDCl_3$): δ -126.17 (dd, *J* = 148.4, 7.7 Hz), -148.88 (d, *J* = 147.4 Hz).

HRMS (ESI) calculated for $C_{24}H_{22}F_2N_3O$ ($[M+H]^+$): 305.1460; found: 305.1456.

^{1}H-^{1}H NOESY of **12**:



1-(1-bromo-9,9-difluoro-9a-phenyl-5,6,8a,9,9a,9b-hexahydro-8*H*-cyclopropa[3,4] pyrazolo[5,1-*a*]isoquinolin-8-yl)propan-1-one (13)



4ba **13**

The mixture of **4ba** (0.1 mmol, 43 mg), Et_3SiH (0.25 mmol, 2.5 equiv) in CF_3CO_2H (0.2 mL) was stirred at room temperature for 12 h without exclusion of air or moisture. Afterwards, the reaction was quenched with H_2O and extracted with EA. The combined organic layers were washed with water and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulted mixture was purified by preparative TLC (Eluent: PE/EA = 5/1, R_f = 0.2) to afford the desired product **13** in 88% (38.0 mg, dr = 7:1) as light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.36 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.13-7.09 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 4.17 (d, *J* = 7.4 Hz, 1H), 3.57 (td, *J* = 12.1, 4.2 Hz, 1H), 3.33-3.25 (m, 1H), 3.20-3.10 (m, 1H), 2.95 (dd, *J* = 16.9, 2.9 Hz, 1H), 2.70 (dq, *J* = 15.1, 7.5 Hz, 1H), 2.50 (dq, *J* = 15.3, 7.5 Hz, 1H), 1.19 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.5, 135.2, 130.95, 130.93, 130.6, 130.2, 129.0, 128.0, 127.9, 127.2, 123.6, 112.4 (dd, *J* = 298.4, 291.8 Hz), 67.4 (dd, *J* = 6.0, 1.7 Hz), 50.4 (dd, *J* = 11.4, 6.1 Hz), 48.8, 48.7 (dd, *J* = 14.1, 12.2 Hz), 28.9, 27.2, 9.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ -122.36 (dd, *J* = 148.0, 7.0 Hz), -148.54 (d, *J* = 147.5 Hz).

HRMS (ESI) calculated for $C_{21}H_{19}BrF_2N_2O$ ([M+H]$^+$): 433.0722; found: 433.0720.

Scale-up synthesis of 3aa：

The mixture of propionyl(pyridin-1-ium-1-yl)amide **1a** (5 mmol, 1 equiv), *gem*-difluorocyclopropene **2a** (5 mmol, 1 equiv) was sonicated for 6 h without exclusion of air or moisture. Afterwards, the spectral pure 1, 2-dihydropyridine derivatives **3aa** could be obtained directly via filtration without further purification in 70% yield (1.06 g).

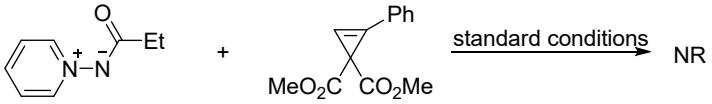
Scale-up synthesis of 4ba：

The mixture of (8-bromoisoquinolin-2-ium-2-yl)(propionyl)amide **1r** (1 mmol, 1 equiv), *gem*-difluorocyclopropene **2a** (1 mmol, 1 equiv) was sonicated for 6 h without exclusion of air or moisture. Afterwards, the spectral pure 1, 2-dihydropyridine derivatives **3ab** could be obtained directly via filtration without further purification in 95% yield (0.41 g).

Scale-up synthesis of 9a：

In a 25 mL Schlenk tube with a magnetic stirring bar was added 1,2-dihydropyridine derivative **3aa** (1 mmol) and MeOH (10 mL) under an atmosphere of N_2. Then, the tube was placed at a reaction bath equipped with Kessil PR 450 nm blue LEDs (24W, 1 cm distance) and allowed to stir at room temperature for 24 h. Afterwards, the resulted mixture was purified by preparative TLC to afford the corresponding *N*-(2-fluoro-1-phenylindolizin-3-yl)propionamide derivatives **9a** in 64% yield (0.18 g).

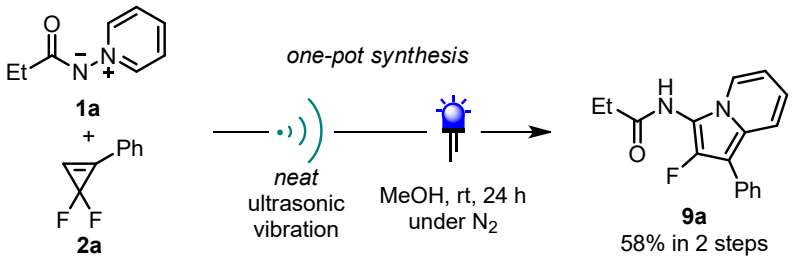
Control experiment with nonfluorinated cyclopropene substrate:



The mixture of propionyl(pyridin-1-ium-1-yl)amide **1a** (0.2 mmol, 1 equiv), dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (0.2 mmol, 1 equiv) was sonicated for 6 h without exclusion of air or moisture. Afterwards, the reaction mixture was diluted

with EA and monitored by TLC/^{1}H-NMR analysis. The result revealed that no reaction occurred while the raw materials were recovered.

One-pot synthesis of 9a:



In a 10 mL Schlenk tube with a magnetic stirring bar was added propionyl(pyridin-1-ium-1-yl)amide **1a** (0.2 mmol, 1 equiv) and *gem*-difluorocyclopropene **2a** (0.2 mmol, 1 equiv). The resulted mixture was sonicated for 6 h without exclusion of air or moisture (Fig. S1a and S1b). Afterwards, the reaction was quenched by adding MeOH (1.0 mL) under an atmosphere of N_2, and the tube was placed at a reaction bath equipped with Kessil PR 450 nm blue LEDs (24W, 1 cm distance) and allowed to stir at room temperature for 24 h (Fig. S1c and S1d). Finally, the resulted mixture was purified by preparative TLC to afford the corresponding *N*-(2-fluoro-3-phenyl-3-(pyridin-2-yl)cycloprop-1-en-1-yl)propionamide **9a** in 58% isolated yield as light yellow solid.

Fig. S1. One-pot synthesis of **9a** via cascade 1,3-dipolar cycloaddition/photo-mediated ring-opening rearrangement.

IV. X-Ray Crystallographic Data

Compound 3aa (CCDC 2279973):

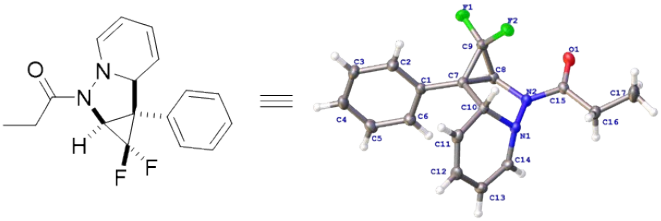


Table S3. Crystal data and structure refinement for 3aa.

Identification code	3aa
Empirical formula	$C_{17}H_{16}F_2N_2O$
Formula weight	302.32
Temperature/K	294.60(10)
Crystal system	orthorhombic
Space group	Fdd2
a/Å	37.7194(4)
b/Å	16.9142(2)
c/Å	9.49011(12)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	6054.64(13)
Z	16
ρ_{calc}g/cm^3	1.327
μ/mm^{-1}	0.842
F(000)	2528.0
Crystal size/mm^3	0.13 × 0.11 × 0.09
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.378 to 151.012
Index ranges	-46 ≤ h ≤ 35, -20 ≤ k ≤ 20, -11 ≤ l ≤ 11
Reflections collected	10107
Independent reflections	2875 [R_{int} = 0.0253, R_{sigma} = 0.0226]
Data/restraints/parameters	2875/1/200
Goodness-of-fit on F^2	1.051
Final R indexes [I>=2σ (I)]	R_1 = 0.0323, wR_2 = 0.0859
Final R indexes [all data]	R_1 = 0.0335, wR_2 = 0.0871

Largest diff. peak/hole / e Å^{-3}	0.14/-0.18
Flack parameter	-0.02(7)

Compound 4ba (CCDC 2279970):

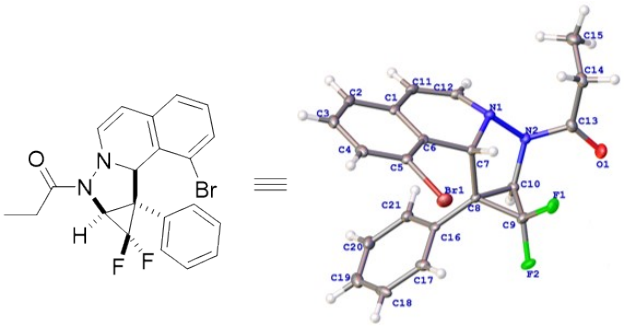


Table S4. Crystal data and structure refinement for 4ba.

Identification code	4ba
Empirical formula	$C_{21}H_{17}BrF_2N_2O$
Formula weight	431.27
Temperature/K	220.03(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.5594(7)
b/Å	19.9216(15)
c/Å	10.3113(8)
α/°	90
β/°	110.294(9)
γ/°	90
Volume/Å^3	1841.8(3)
Z	4
ρ_{calc}g/cm^3	1.555
μ/mm^{-1}	2.265
F(000)	872.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.09 to 49.994
Index ranges	-11 ≤ h ≤ 8, -23 ≤ k ≤ 22, -12 ≤ l ≤ 11
Reflections collected	8451
Independent reflections	3249 [R_{int} = 0.0368, R_{sigma} = 0.0500]

Data/restraints/parameters	3249/0/245
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0372, wR_2 = 0.0795
Final R indexes [all data]	R_1 = 0.0546, wR_2 = 0.0874
Largest diff. peak/hole / e $Å^{-3}$	0.62/-0.59

Compound 10 (CCDC 2279972):

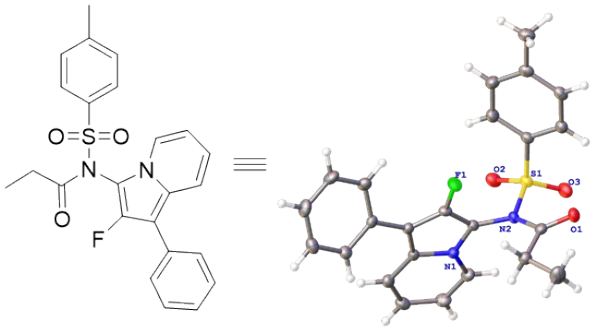


Table S5. Crystal data and structure refinement for 10.

Identification code	10
Empirical formula	$C_{24}H_{21}FN_2O_3S$
Formula weight	436.49
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.0253(12)
b/Å	19.0234(19)
c/Å	11.0800(13)
α/°	90
β/°	117.375(15)
γ/°	90
Volume/$Å^3$	2063.7(5)
Z	4
ρ_{calc}g/cm^3	1.405
μ/mm^{-1}	0.196
F(000)	912.0
Crystal size/mm^3	0.15 × 0.12 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.16 to 49.994

Index ranges	$-12 \le h \le 13$, $-21 \le k \le 22$, $-13 \le l \le 10$
Reflections collected	11871
Independent reflections	3564 [R_{int} = 0.0391, R_{sigma} = 0.0427]
Data/restraints/parameters	3564/0/282
Goodness-of-fit on F^2	1.073
Final R indexes [I>=2σ (I)]	R_1 = 0.0422, wR_2 = 0.0986
Final R indexes [all data]	R_1 = 0.0518, wR_2 = 0.1036
Largest diff. peak/hole / e $Å^{-3}$	0.31/-0.44

Compound 11a (CCDC 2279971):

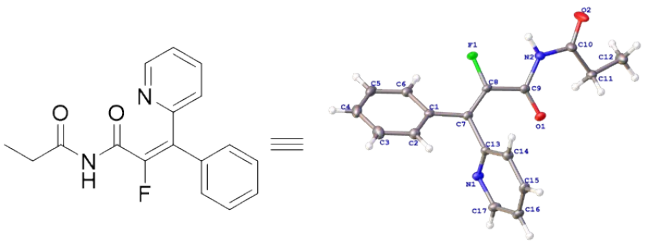


Table S6. Crystal data and structure refinement for 11a.

Identification code	11a
Empirical formula	$C_{17}H_{15}FN_2O_2$
Formula weight	298.31
Temperature/K	149.99(10)
Crystal system	triclinic
Space group	P-1
a/Å	8.8203(5)
b/Å	9.1068(6)
c/Å	10.6468(6)
α/°	67.050(6)
β/°	88.220(4)
γ/°	71.172(5)
Volume/$Å^3$	740.95(9)
Z	2
ρ_{calc}g/cm^3	1.337
μ/mm^{-1}	0.807
F(000)	312.0
Crystal size/mm^3	0.14 × 0.13 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.074 to 147.556

Index ranges	$-9 \le h \le 10$, $-7 \le k \le 11$, $-13 \le l \le 13$
Reflections collected	4658
Independent reflections	2887 [R_{int} = 0.0341, R_{sigma} = 0.0311]
Data/restraints/parameters	2887/0/205
Goodness-of-fit on F^2	1.082
Final R indexes [I>=2σ (I)]	R_1 = 0.0581, wR_2 = 0.1552
Final R indexes [all data]	R_1 = 0.0611, wR_2 = 0.1585
Largest diff. peak/hole / e $Å^{-3}$	0.39/-0.37

V. References

[1] T. Nihei, T. Hoshino and T. Konno, *Org. Biomol. Chem.*, 2015, **13**, 3721.

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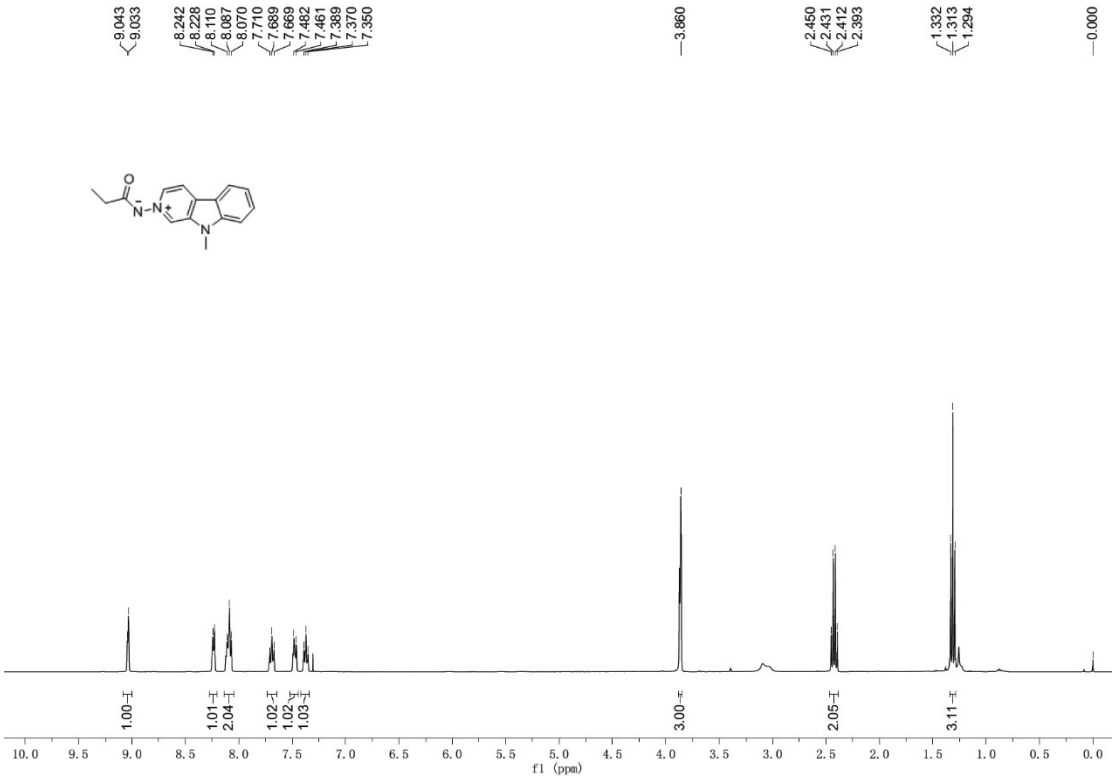
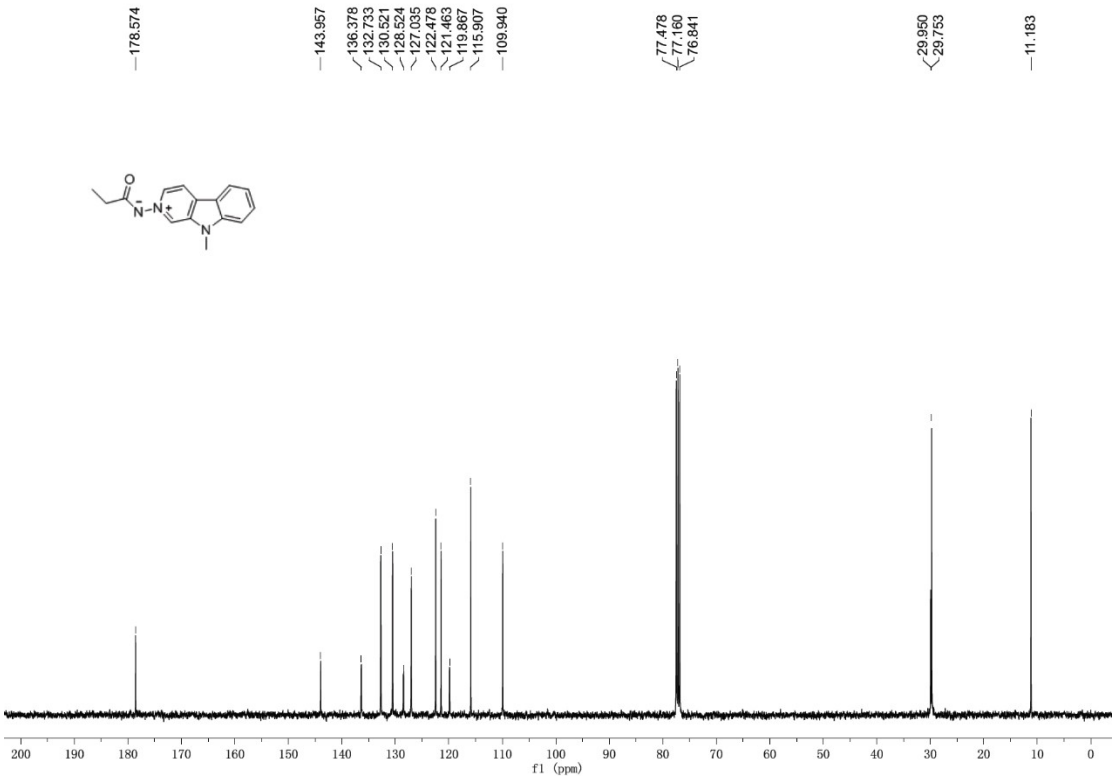
VI. Copies of NMR Spectra

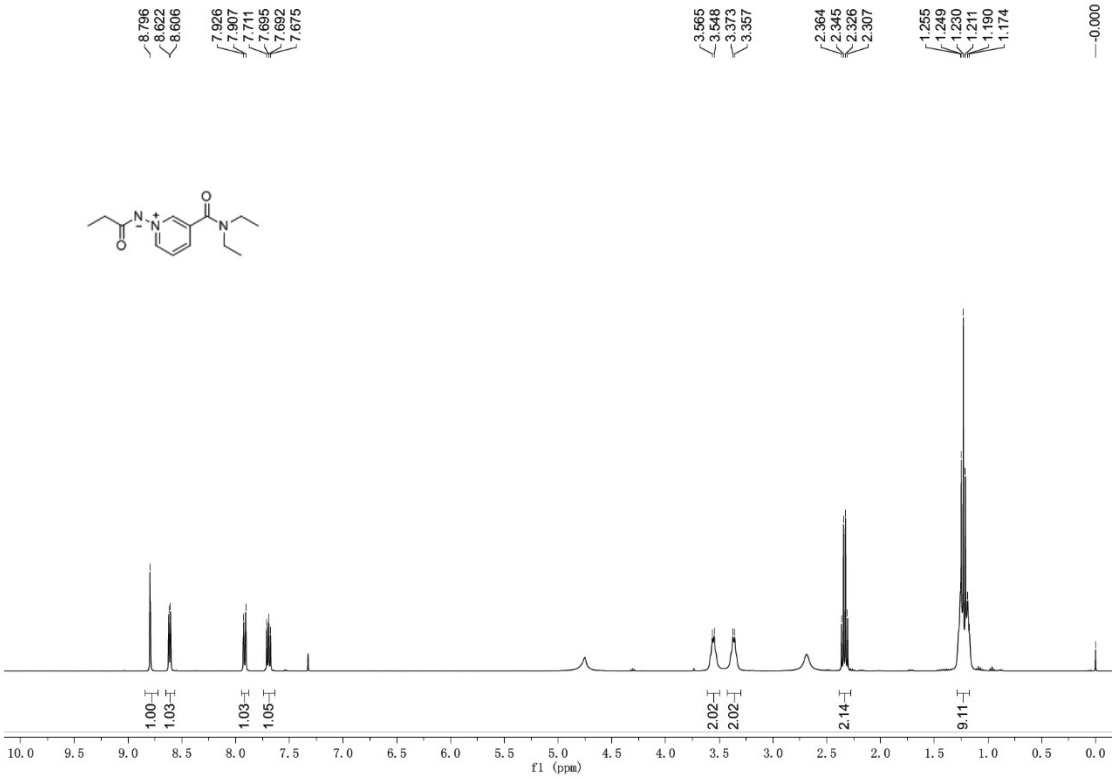
1aj-^{1}H NMR (400 MHz, $CDCl_3$)



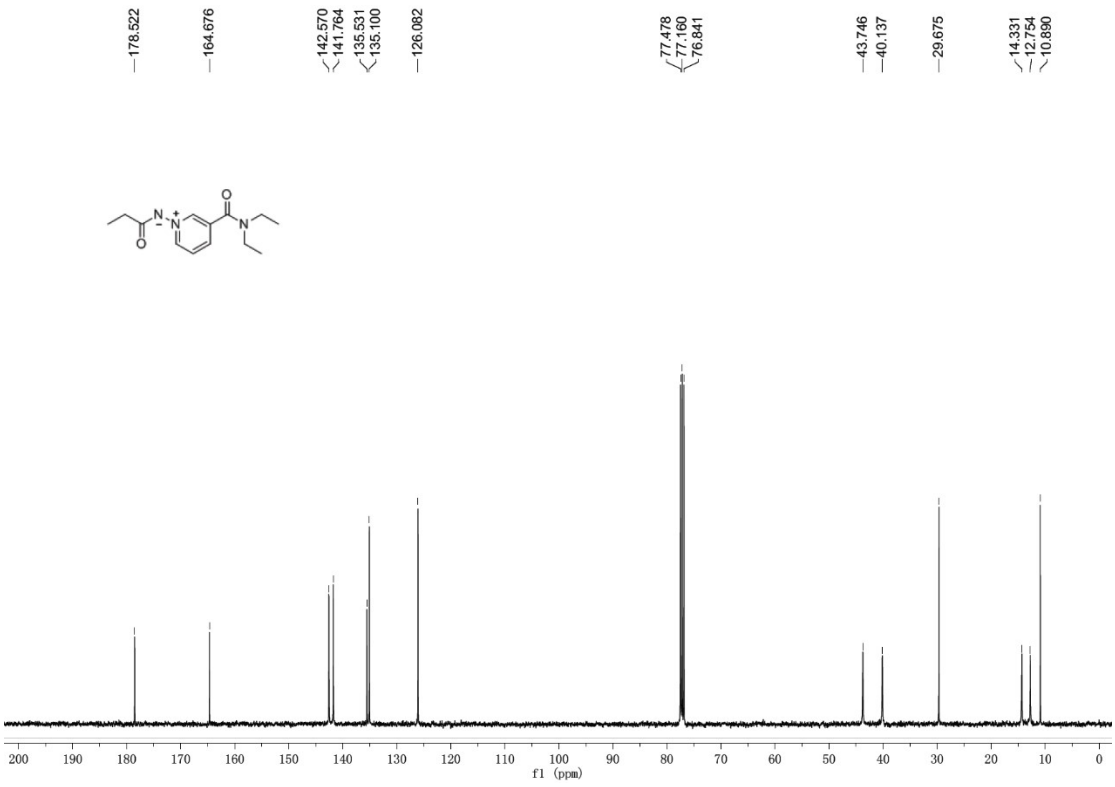
1aj-^{13}C NMR (100 MHz, $CDCl_3$)



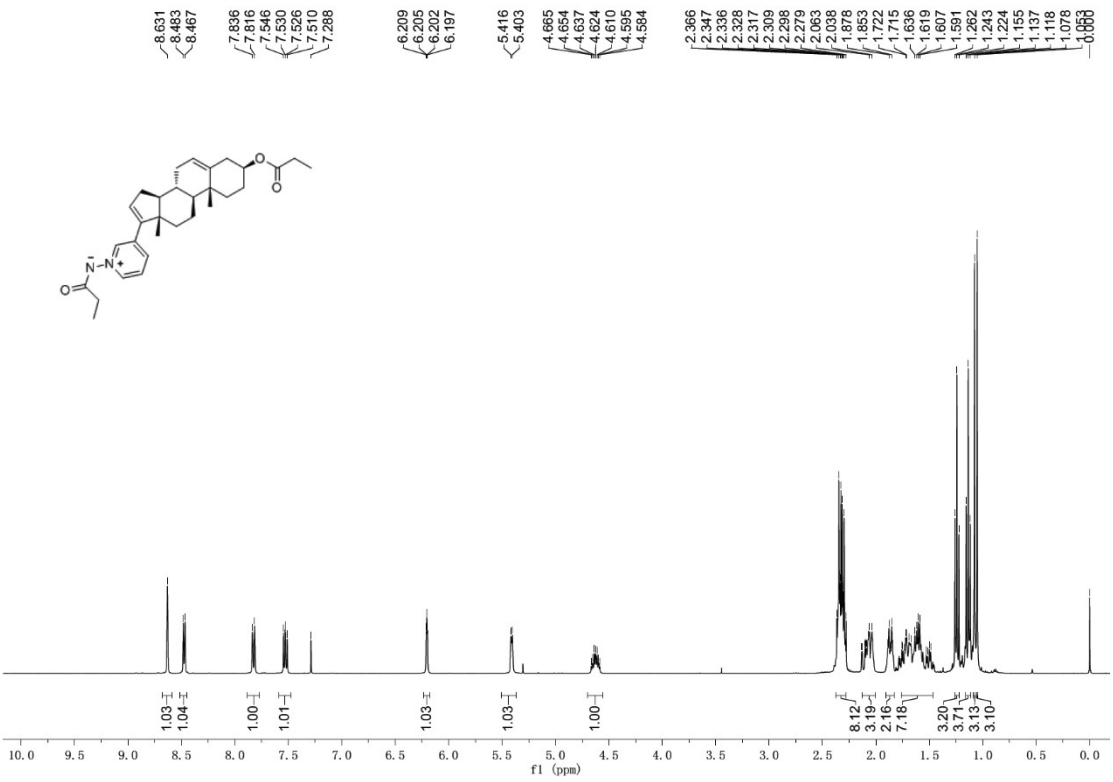
1ak-^{1}H NMR (400 MHz, $CDCl_3$)



1ak-^{13}C NMR (100 MHz, $CDCl_3$)



1al-^{1}H NMR (400 MHz, $CDCl_3$)



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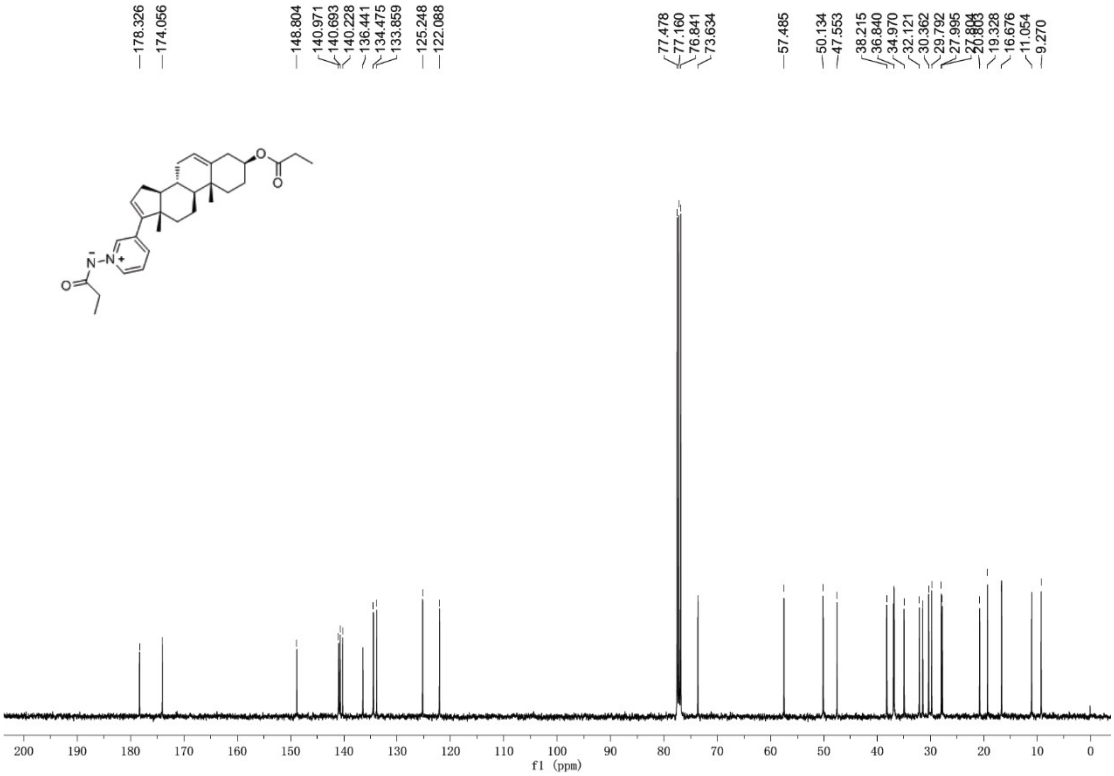
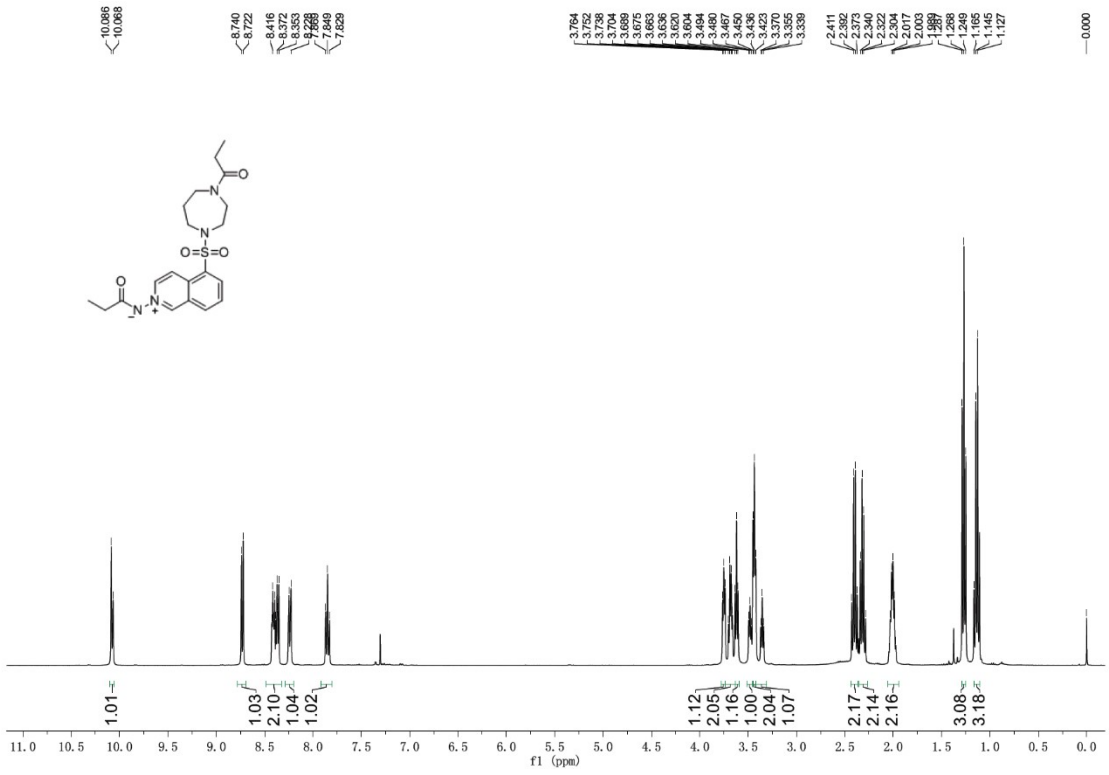
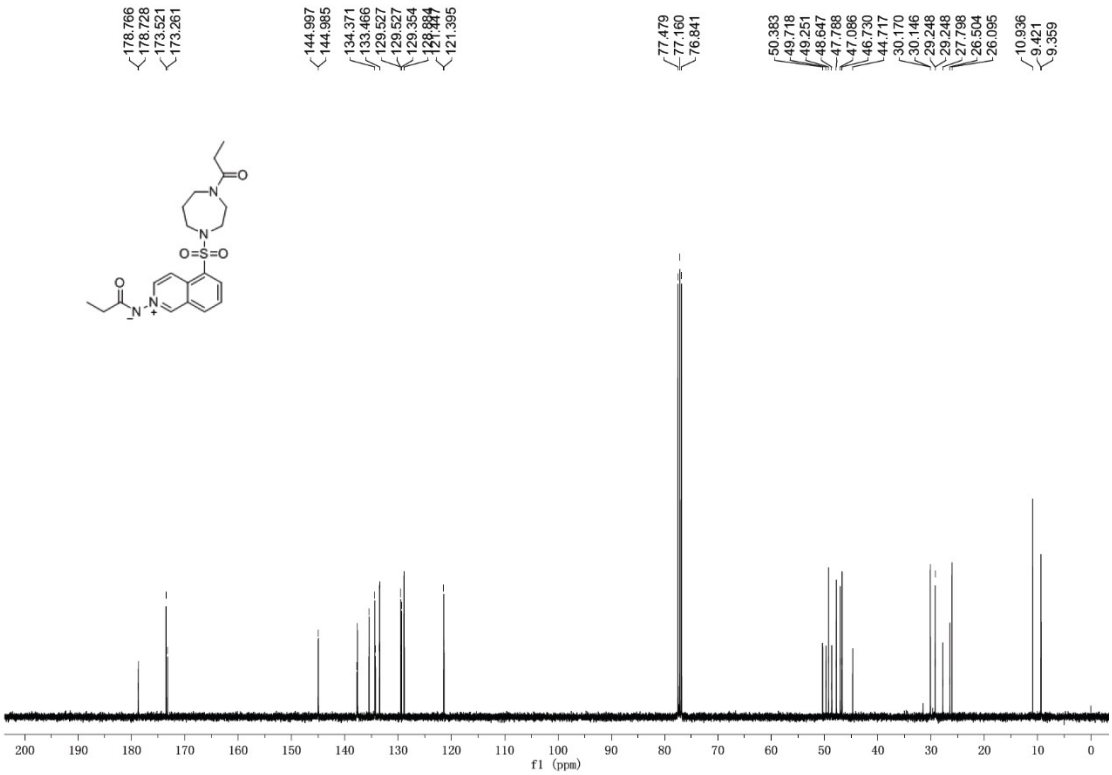


1am-^{1}H NMR (400 MHz, $CDCl_3$)



1am-^{13}C NMR (100 MHz, $CDCl_3$)



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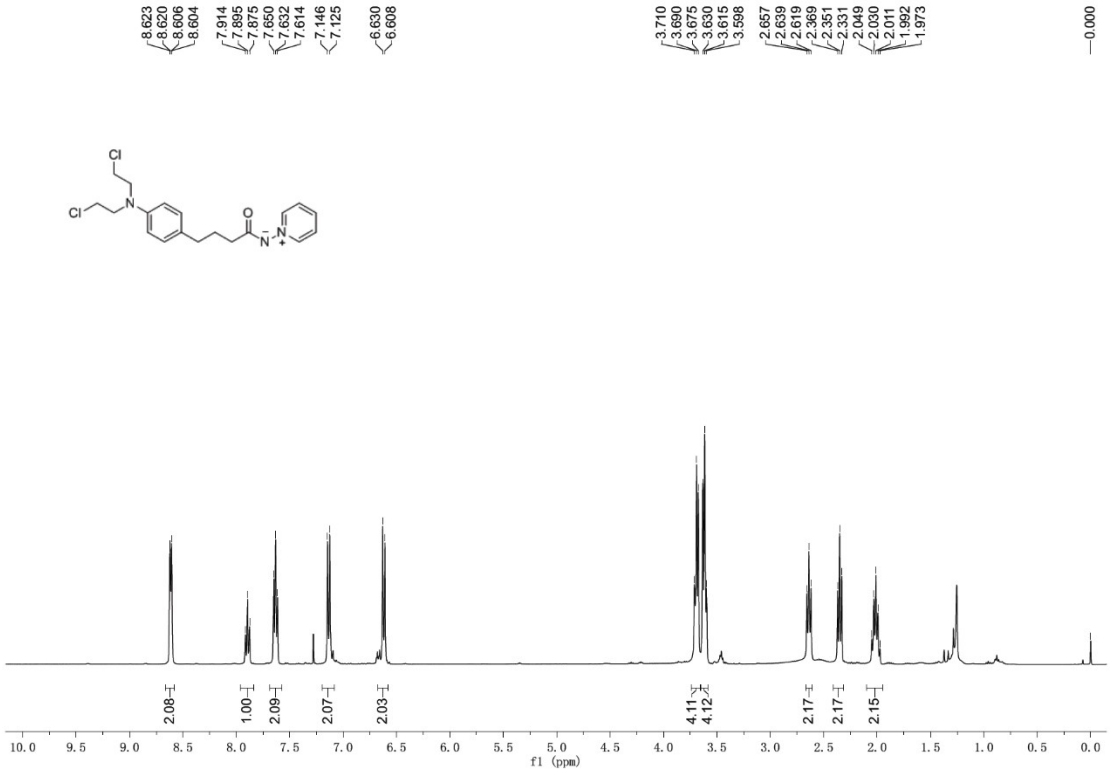

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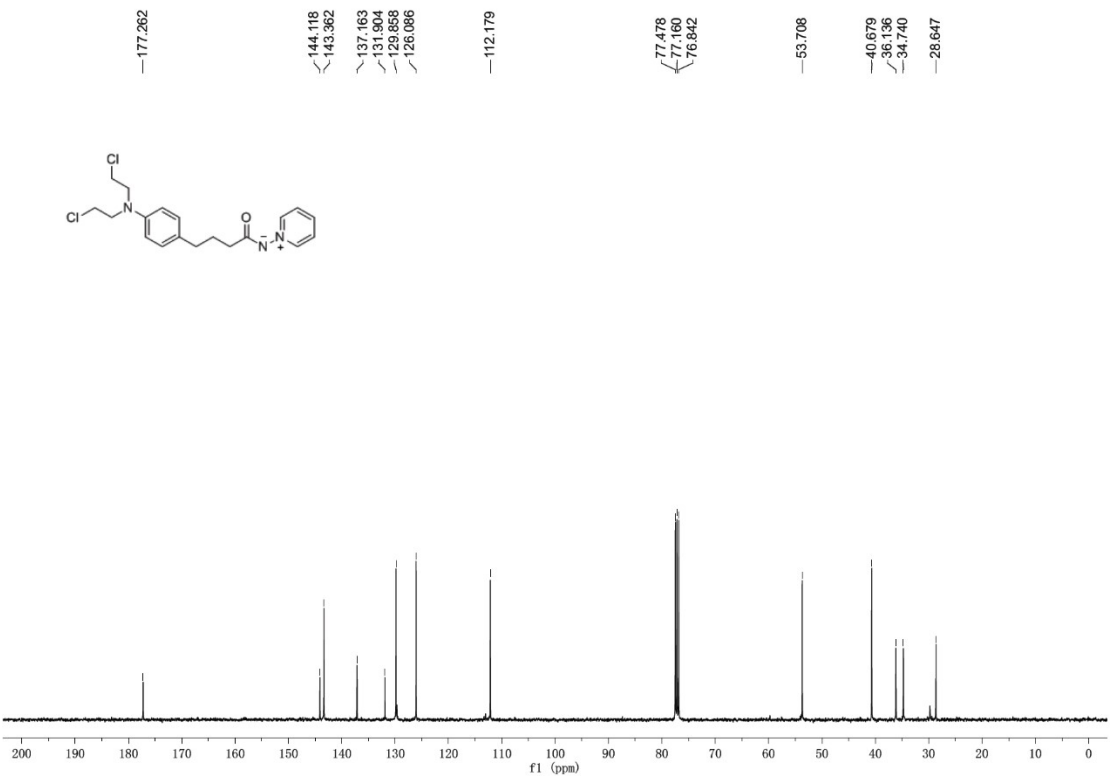
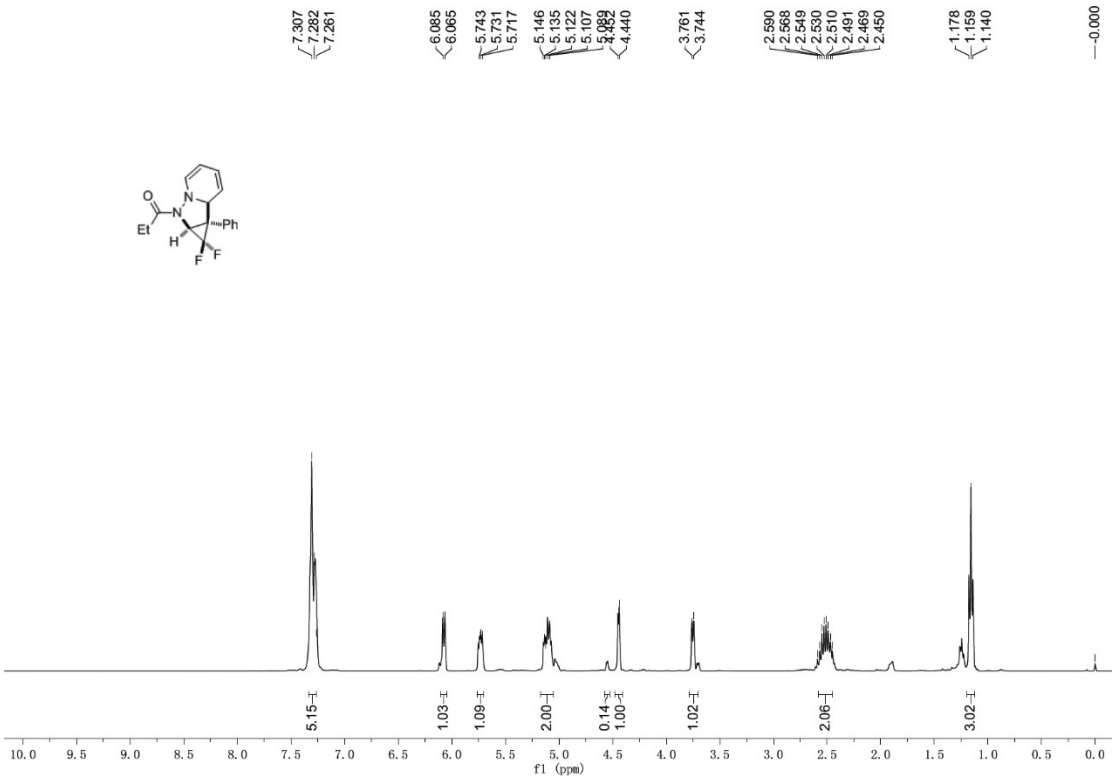
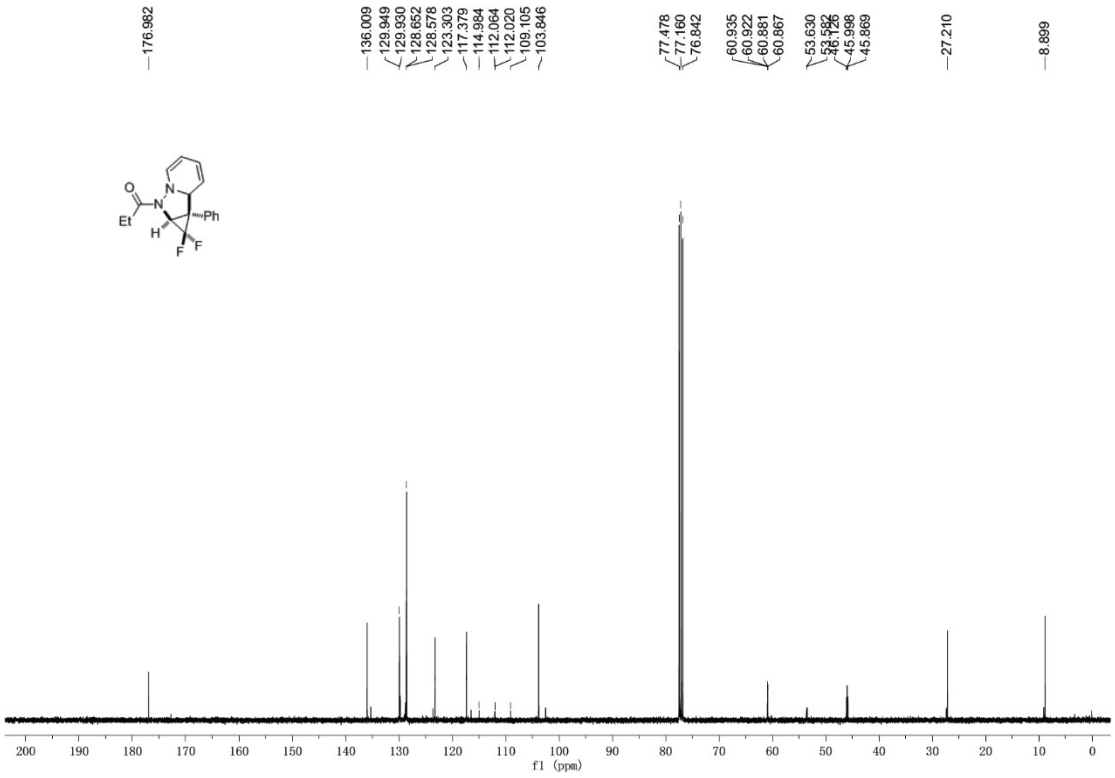


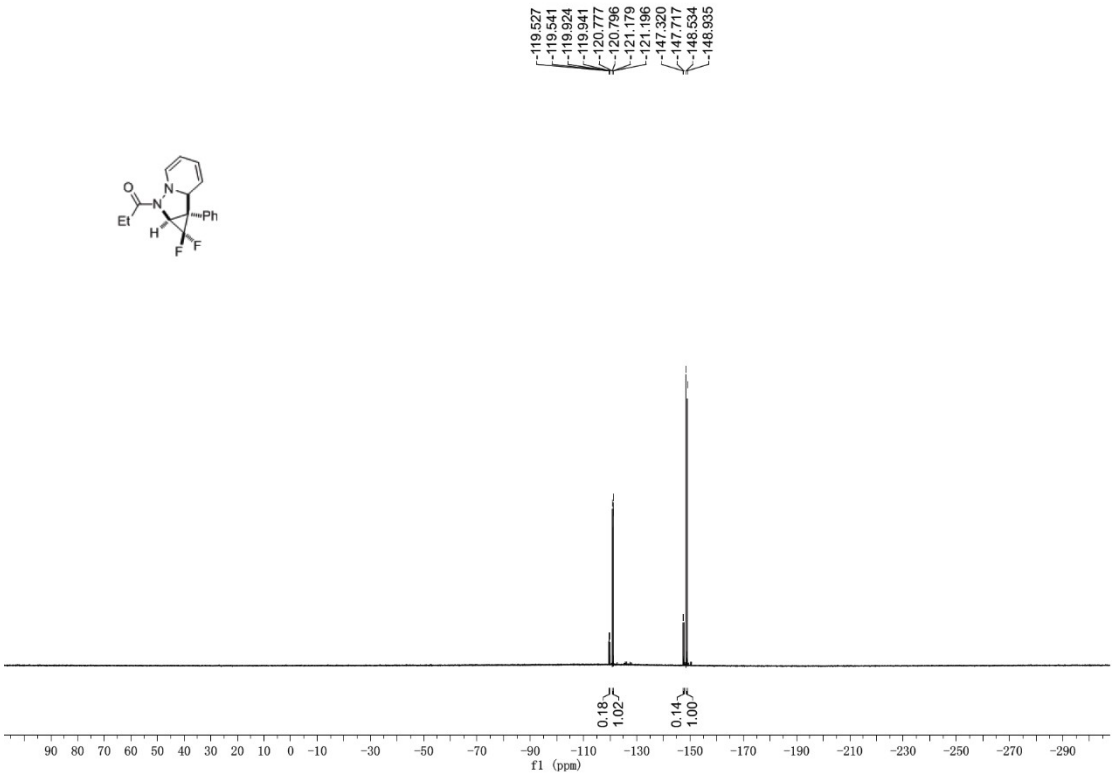
3aa-^{1}H NMR (400 MHz, $CDCl_3$)



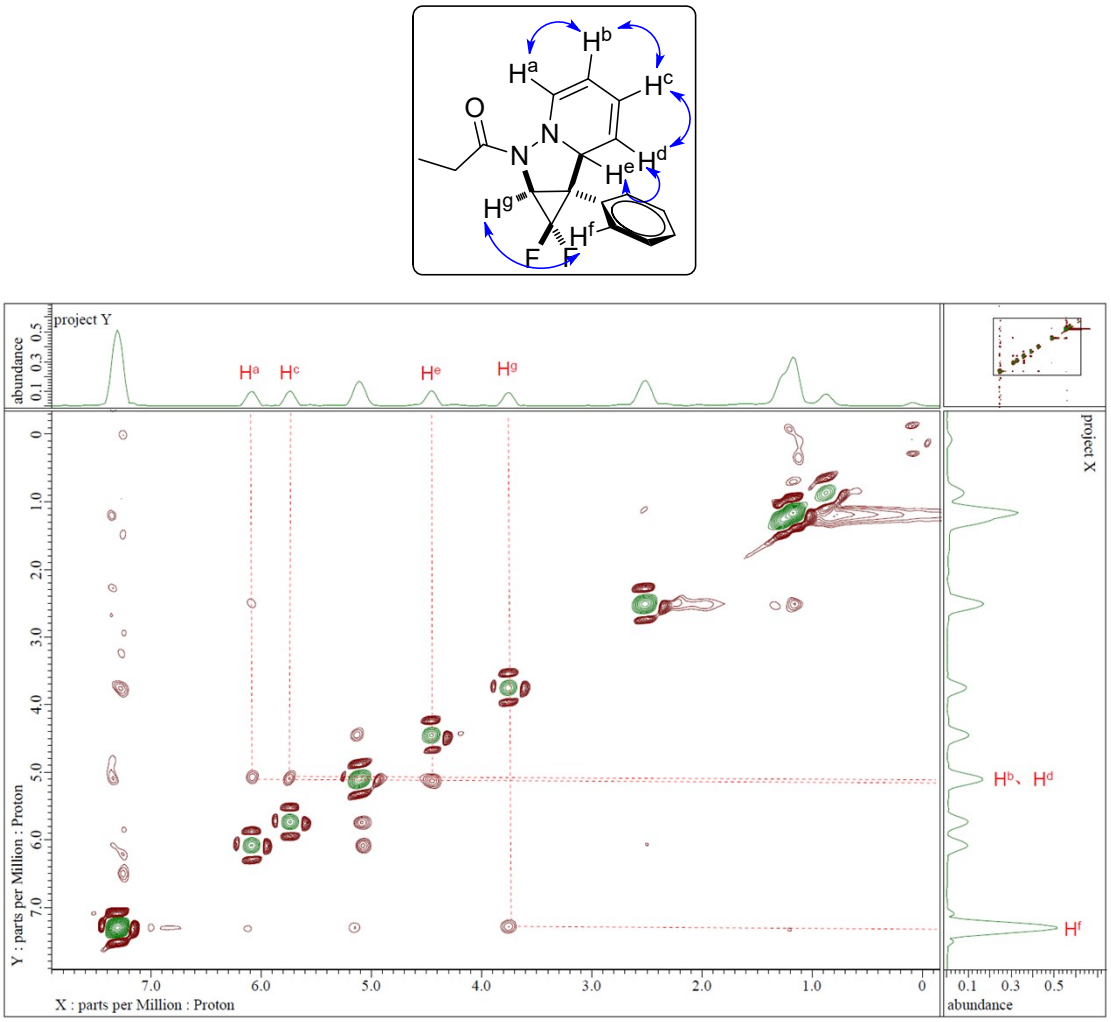
3aa-^{13}C NMR (100 MHz, $CDCl_3$)



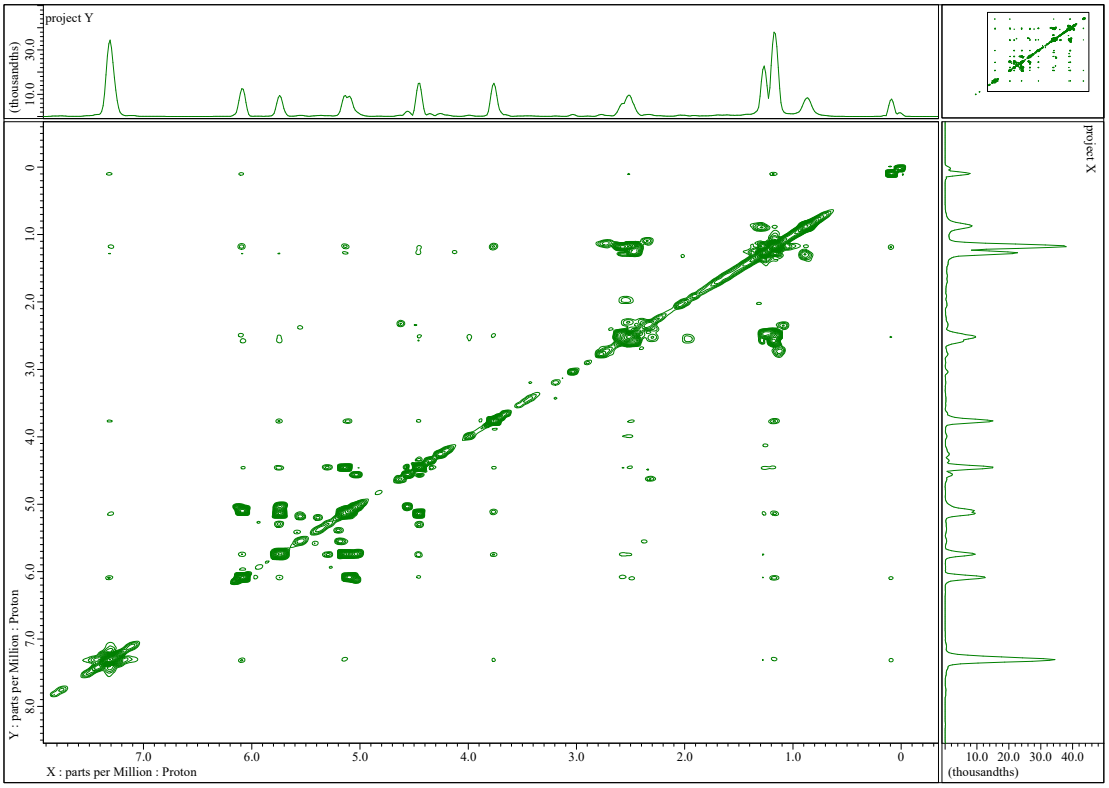
3aa-^{19}F NMR (376 MHz, $CDCl_3$)



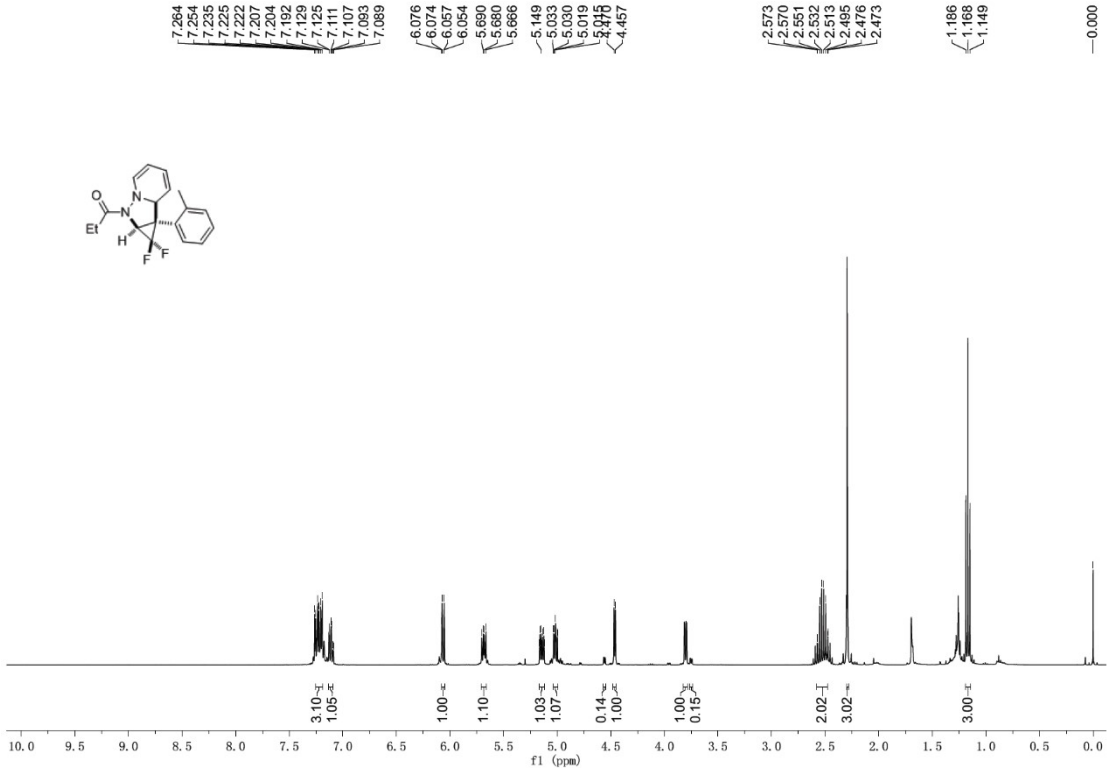
3aa-^{1}H-^{1}H NOESY (400 MHz, $CDCl_3$)



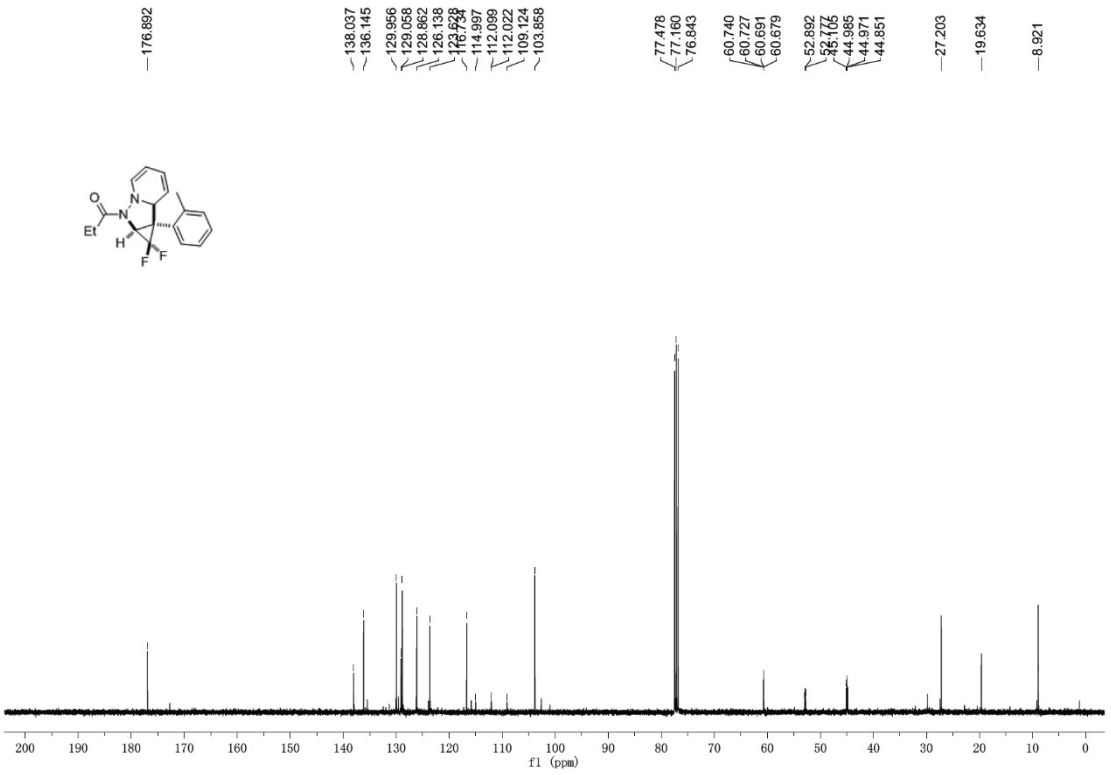
3aa-^{1}H-^{1}H COSY (400 MHz, $CDCl_3$)



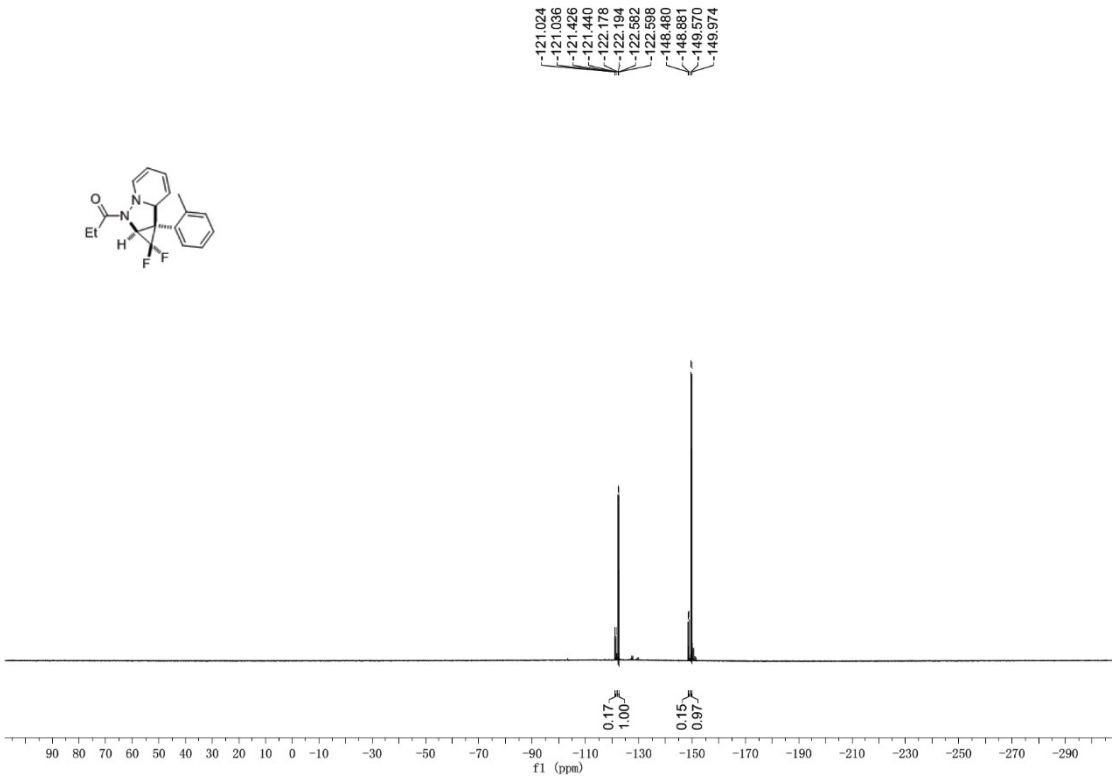
3ab-^{1}H NMR (400 MHz, $CDCl_3$)



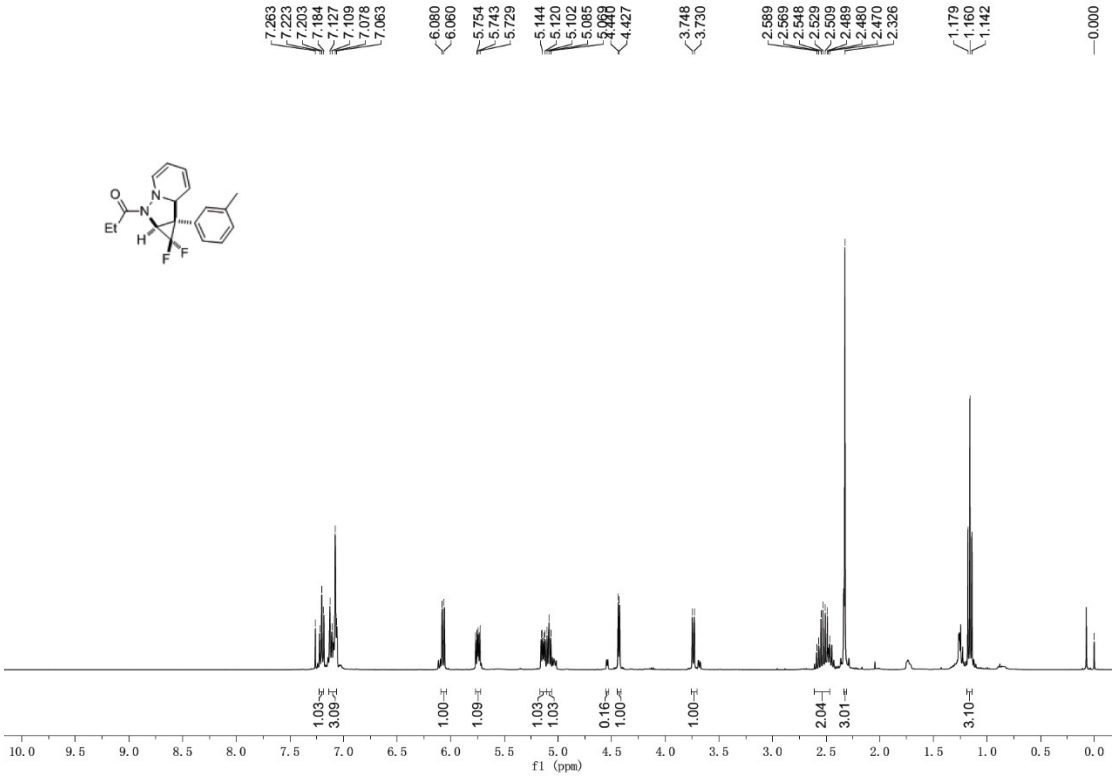
3ab-^{13}C NMR (100 MHz, $CDCl_3$)



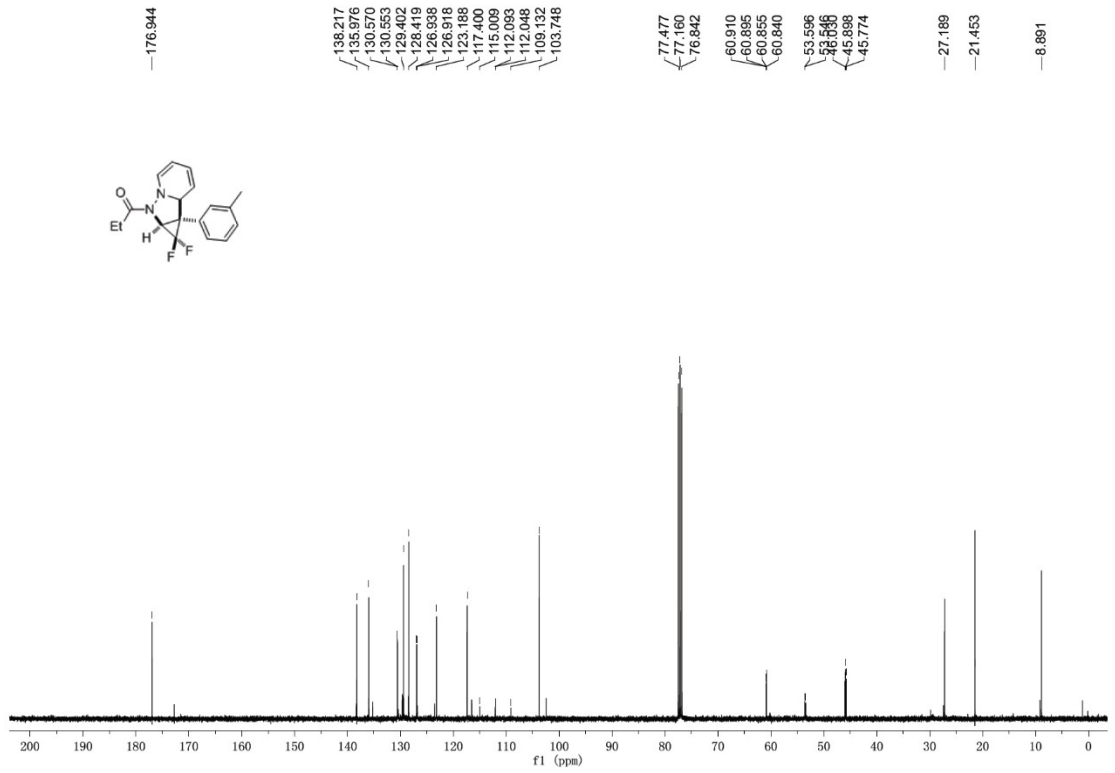
3ab-^{19}F NMR (376 MHz, $CDCl_3$)



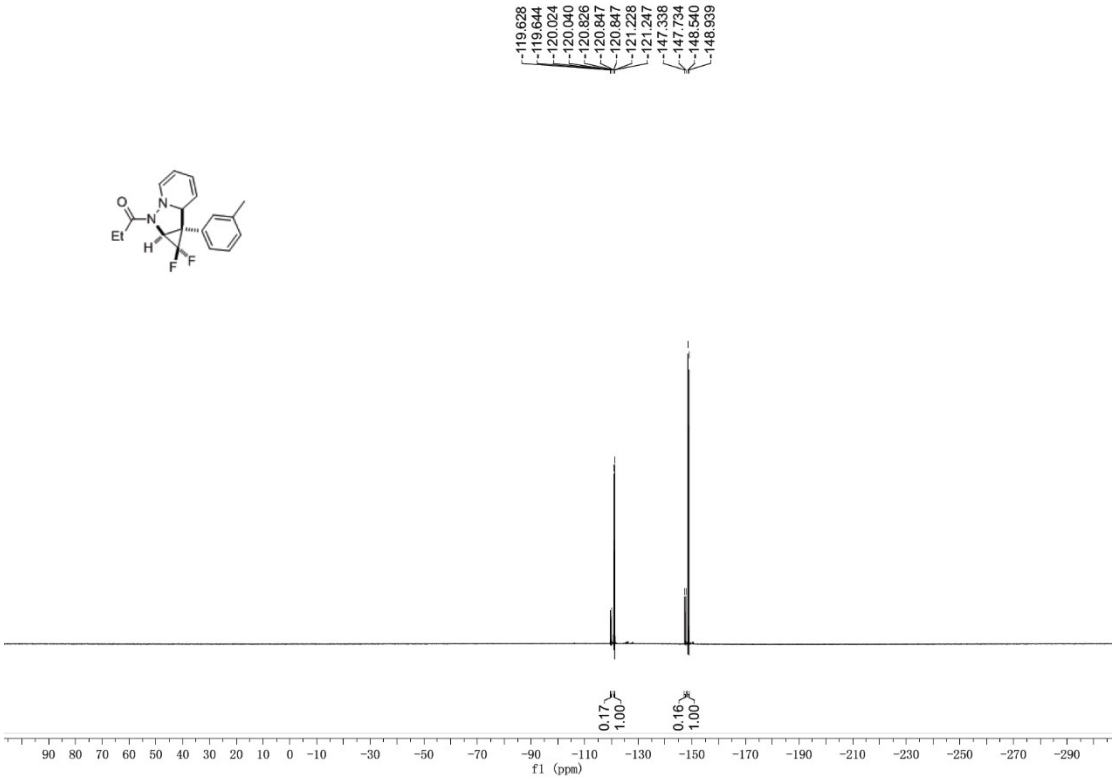
3ac-^{1}H NMR (400 MHz, $CDCl_3$)



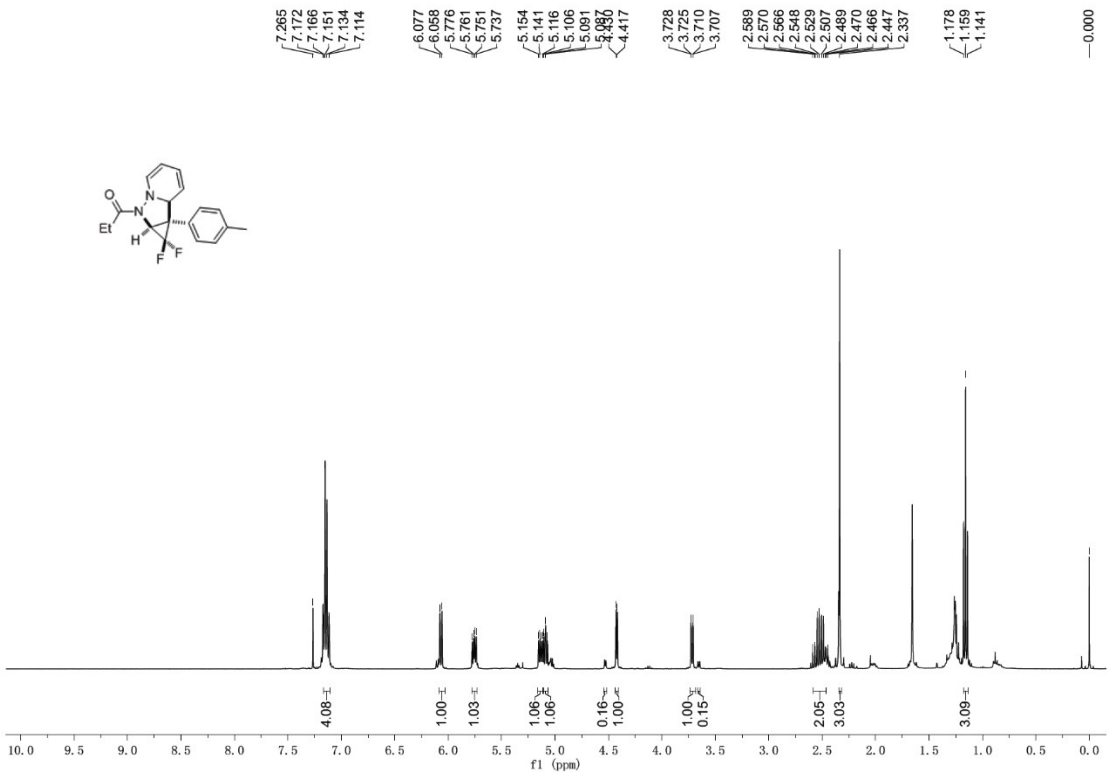
3ac-^{13}C NMR (100 MHz, $CDCl_3$)



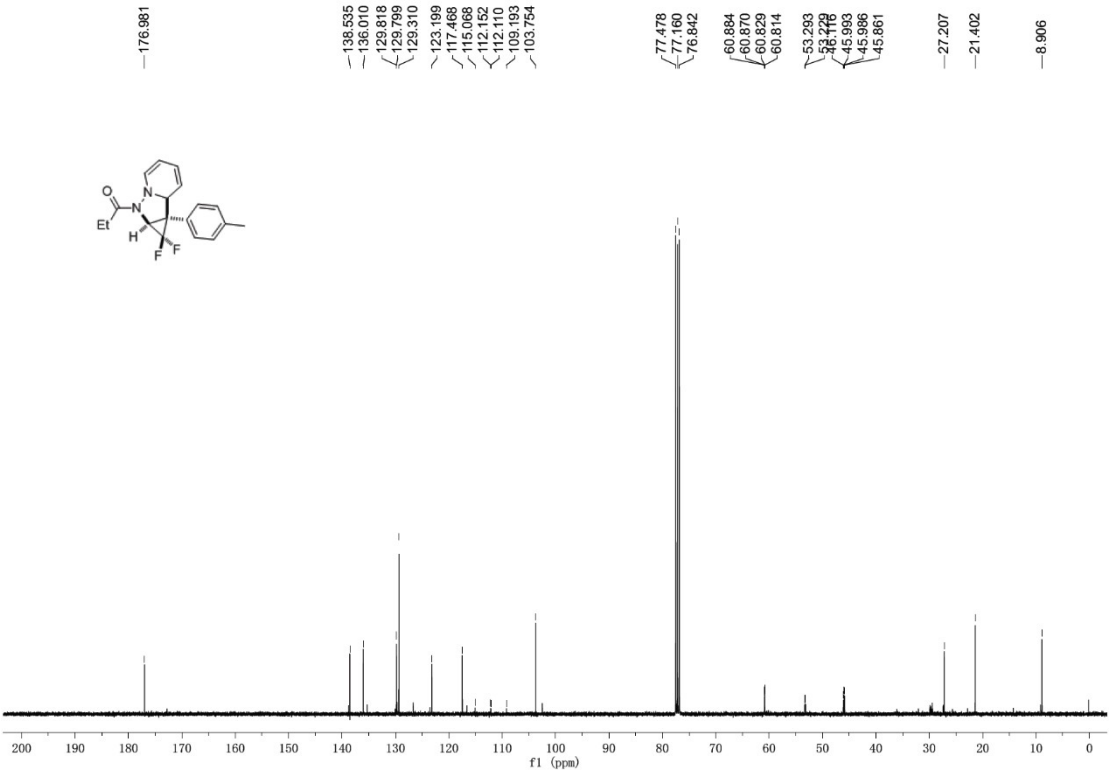
3ac-^{19}F NMR (376 MHz, $CDCl_3$)



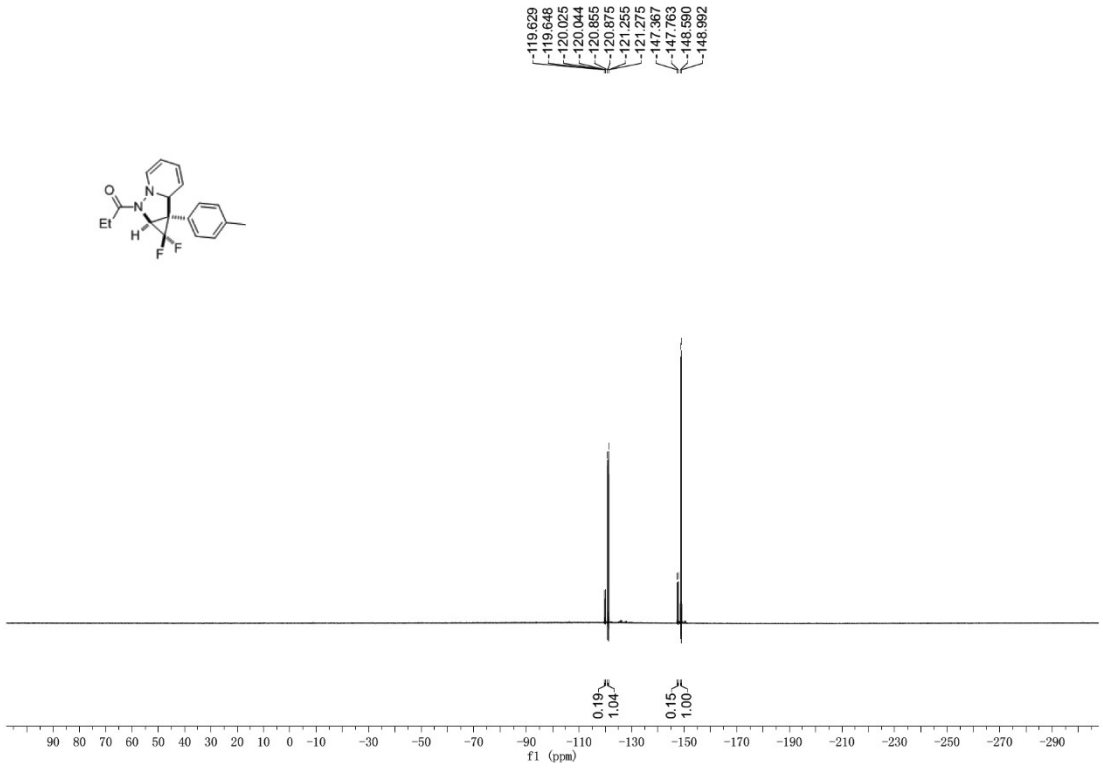
3ad-^{1}H NMR (400 MHz, $CDCl_3$)



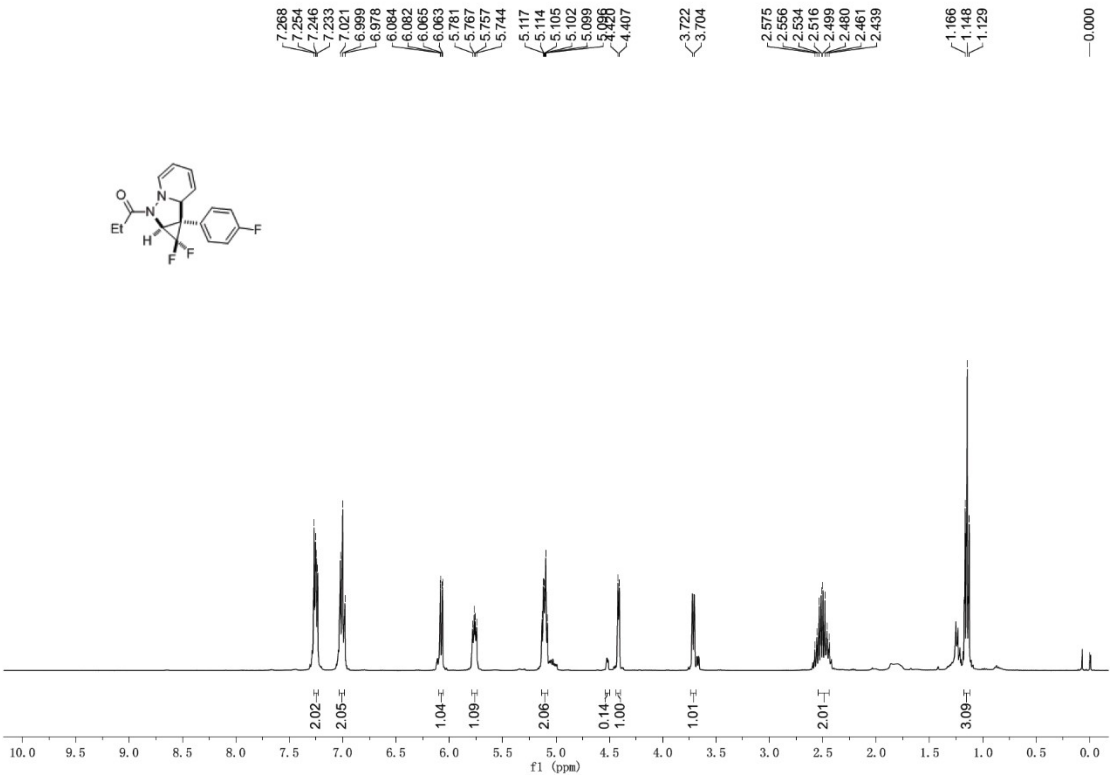
3ad-^{13}C NMR (100 MHz, $CDCl_3$)



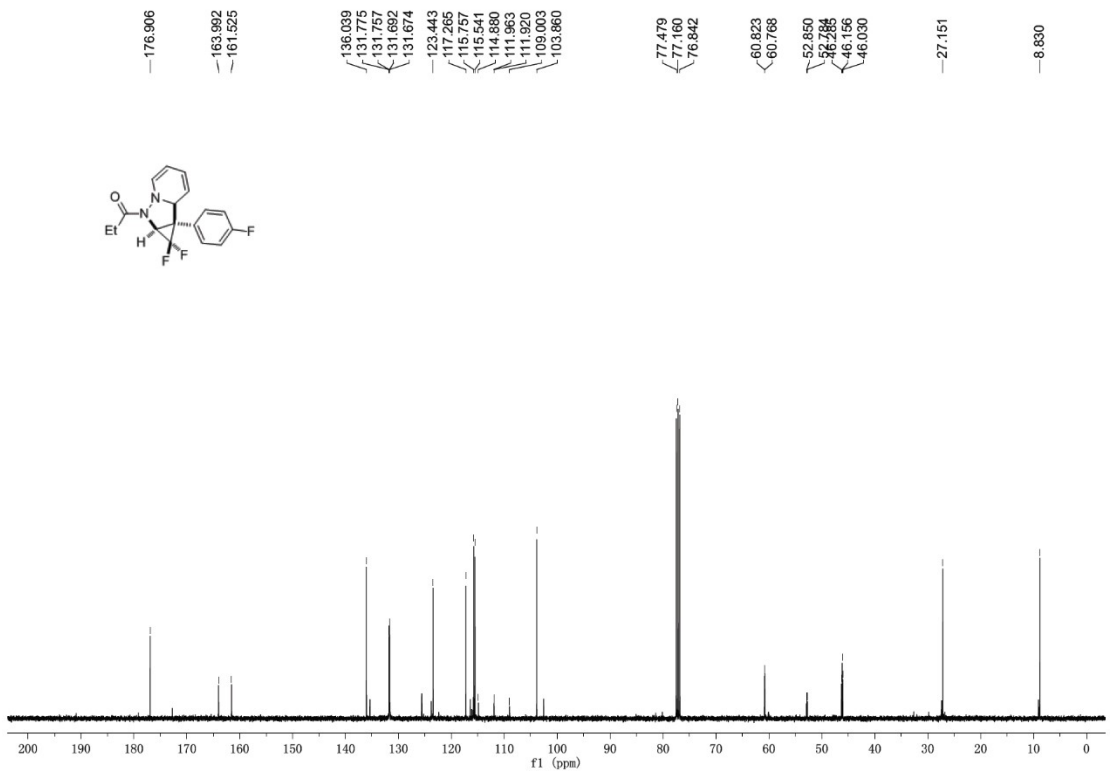
3ad-^{19}F NMR (376 MHz, $CDCl_3$)



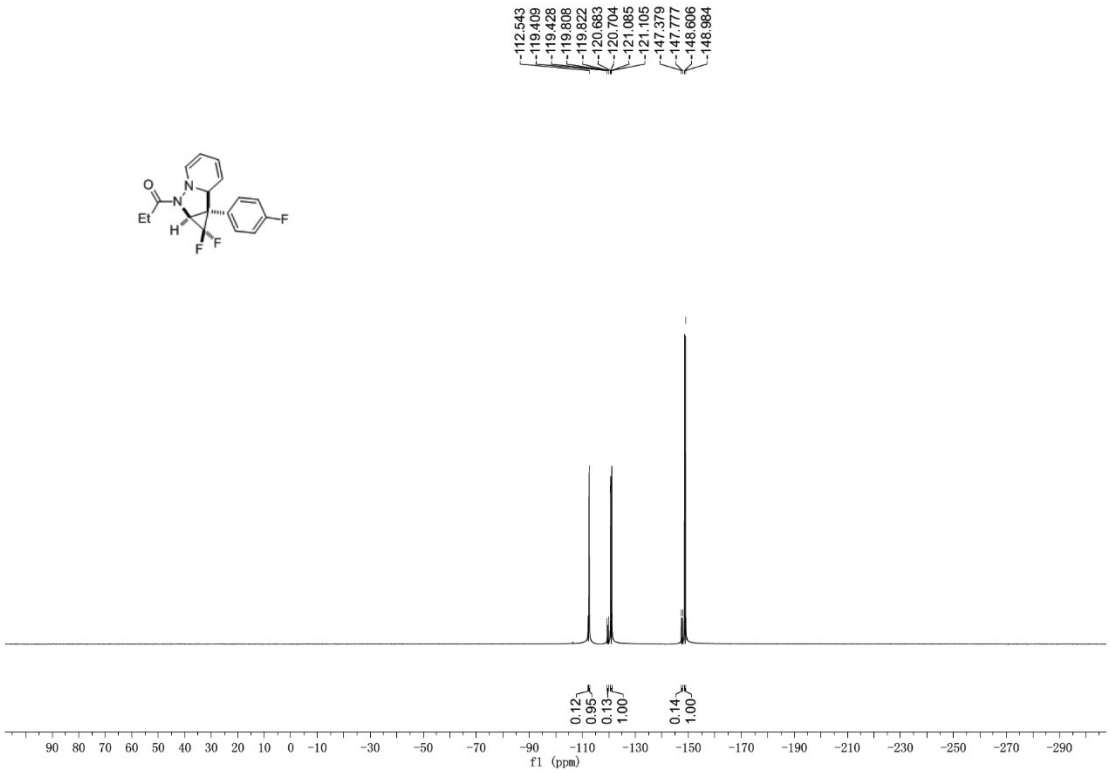
3ae-^{1}H NMR (400 MHz, $CDCl_3$)



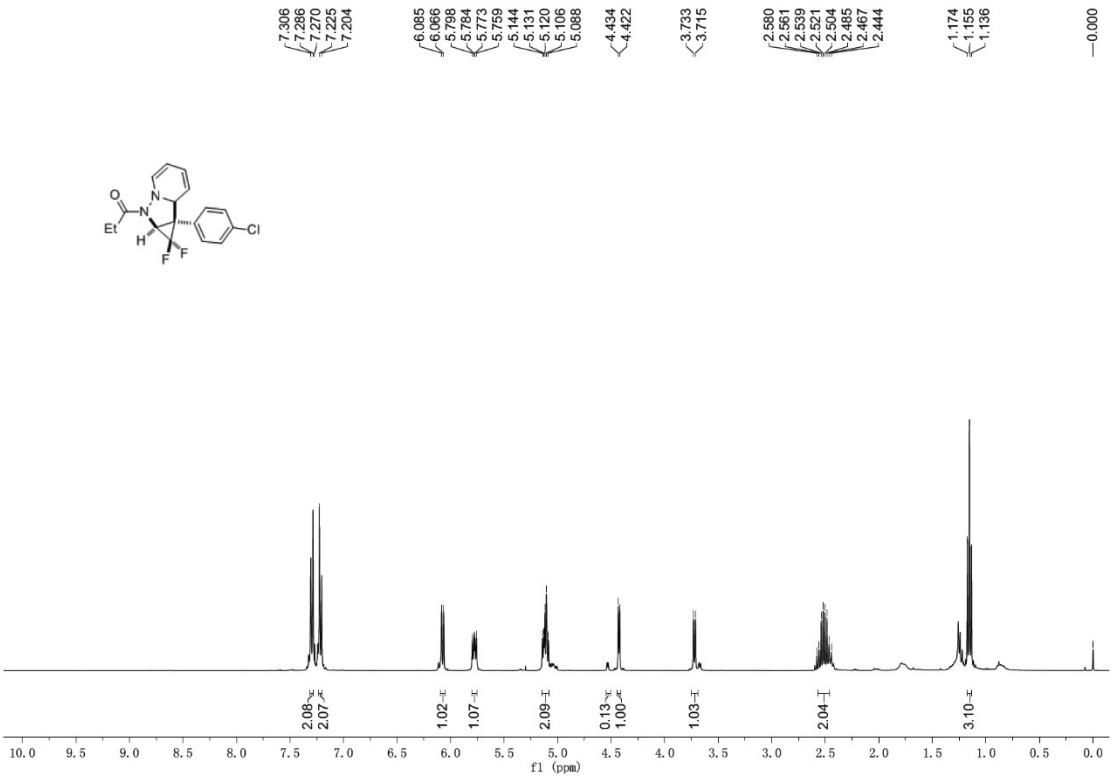
3ae-^{13}C NMR (100 MHz, $CDCl_3$)



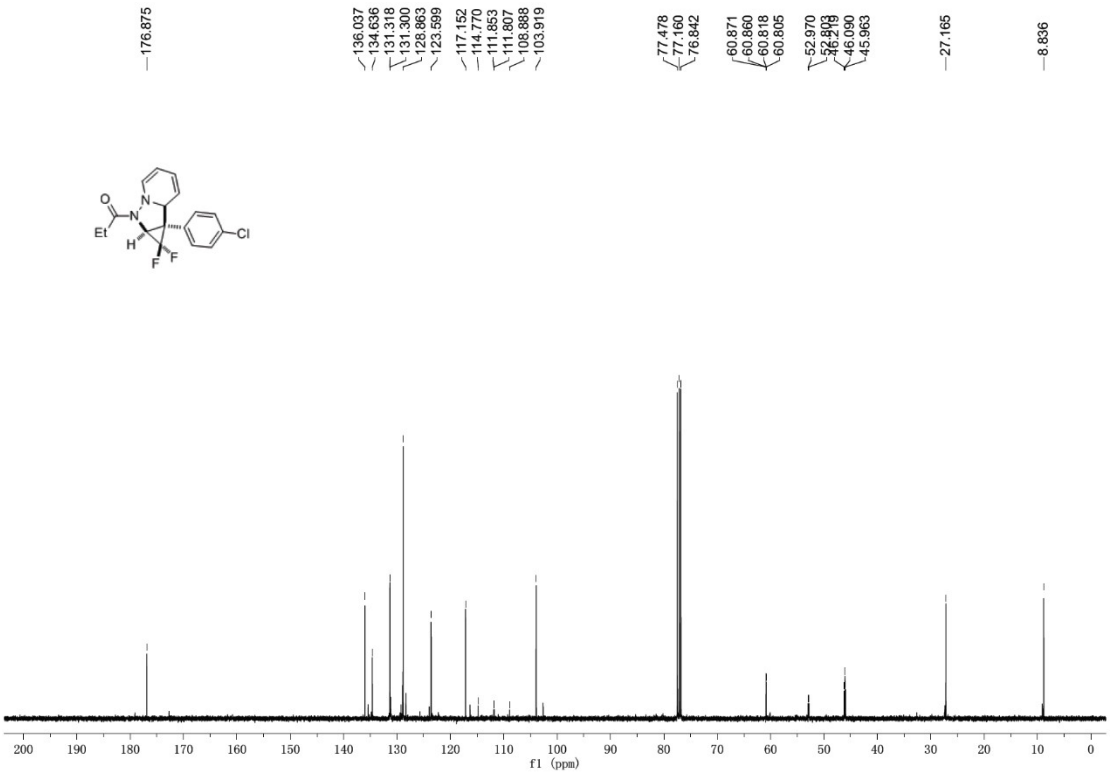
3ae-^{19}F NMR (376 MHz, $CDCl_3$)



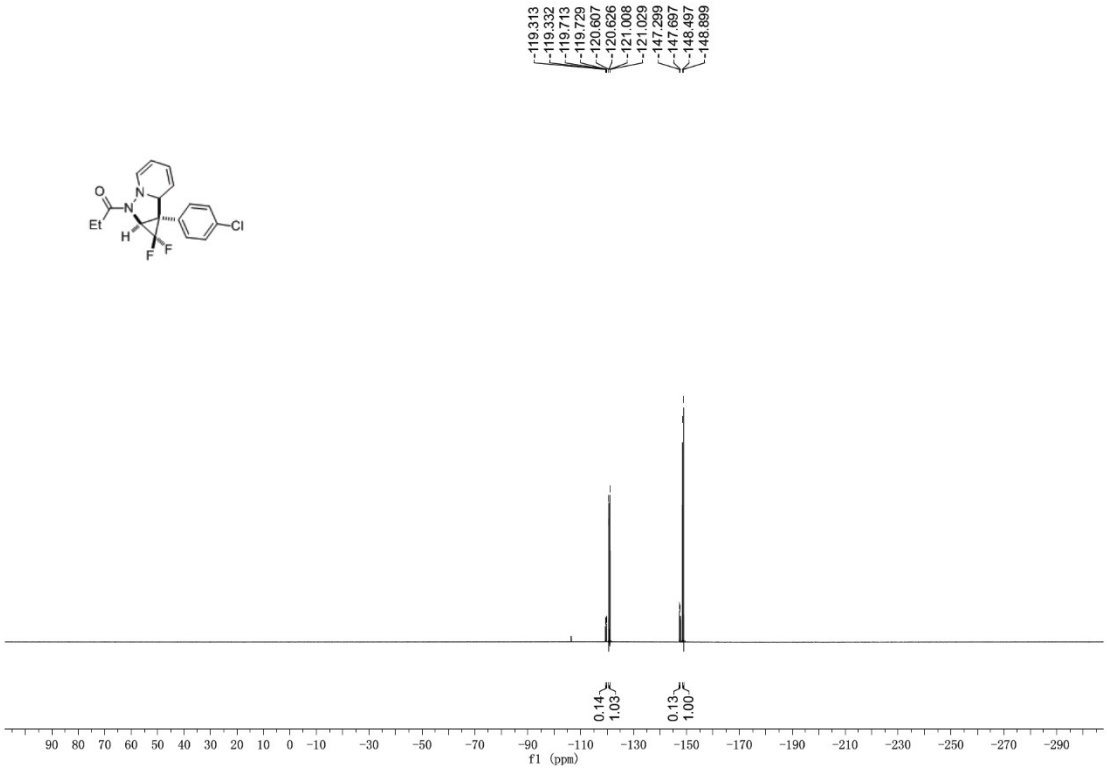
3af-^{1}H NMR (400 MHz, $CDCl_3$)



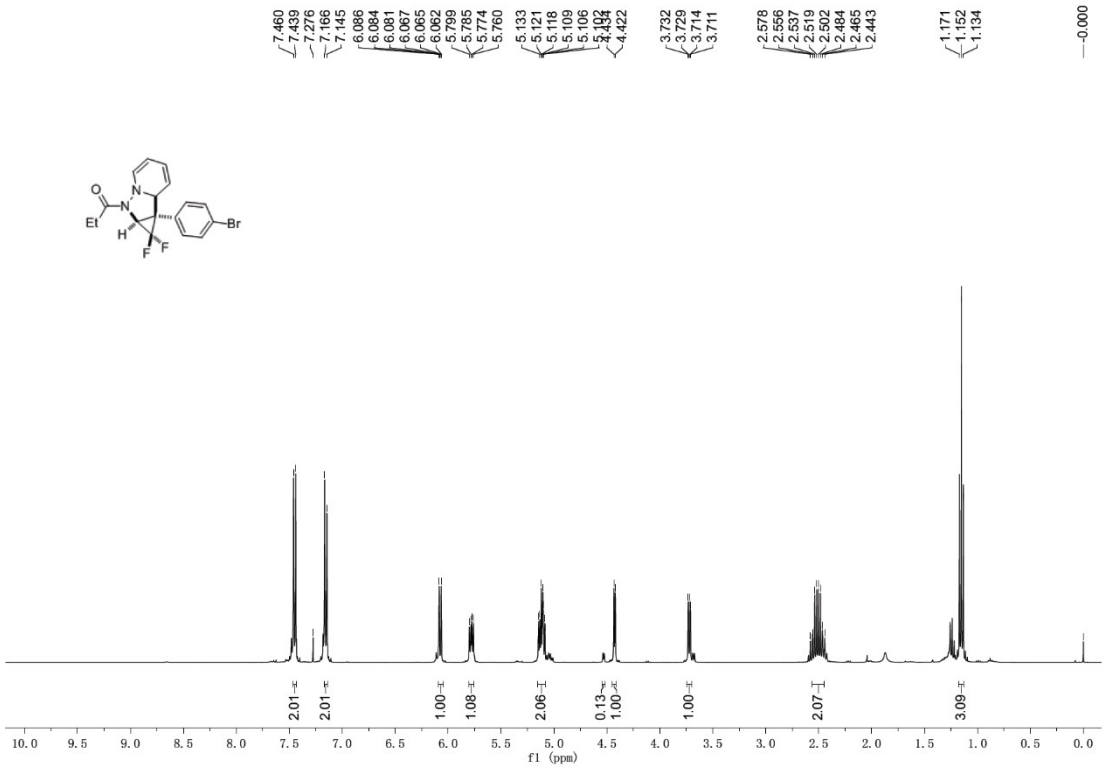
3af-^{13}C NMR (100 MHz, $CDCl_3$)



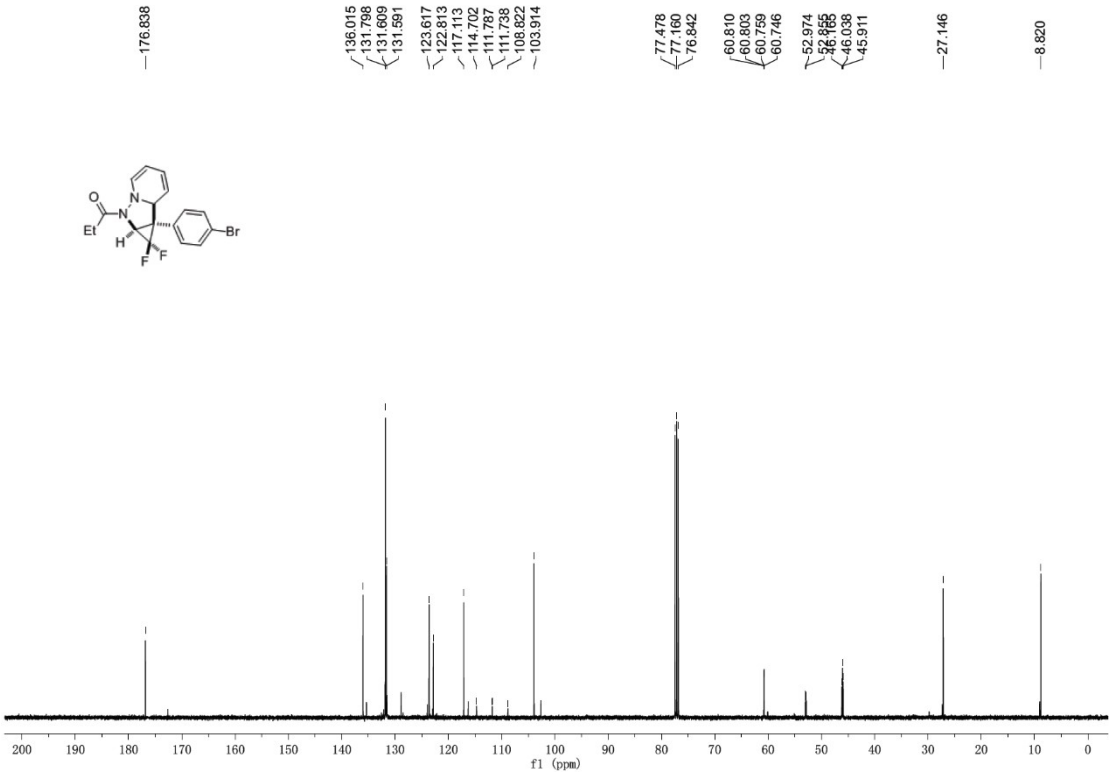
3af-^{19}F NMR (376 MHz, $CDCl_3$)



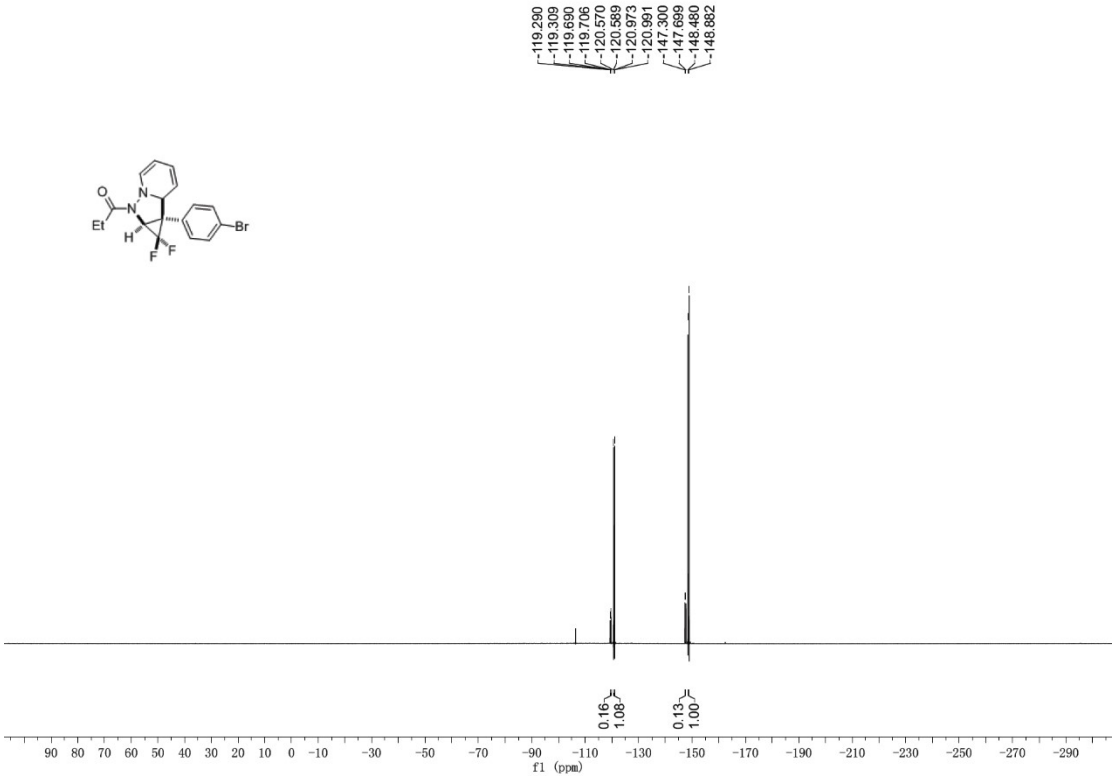
3ag-^{1}H NMR (400 MHz, $CDCl_3$)



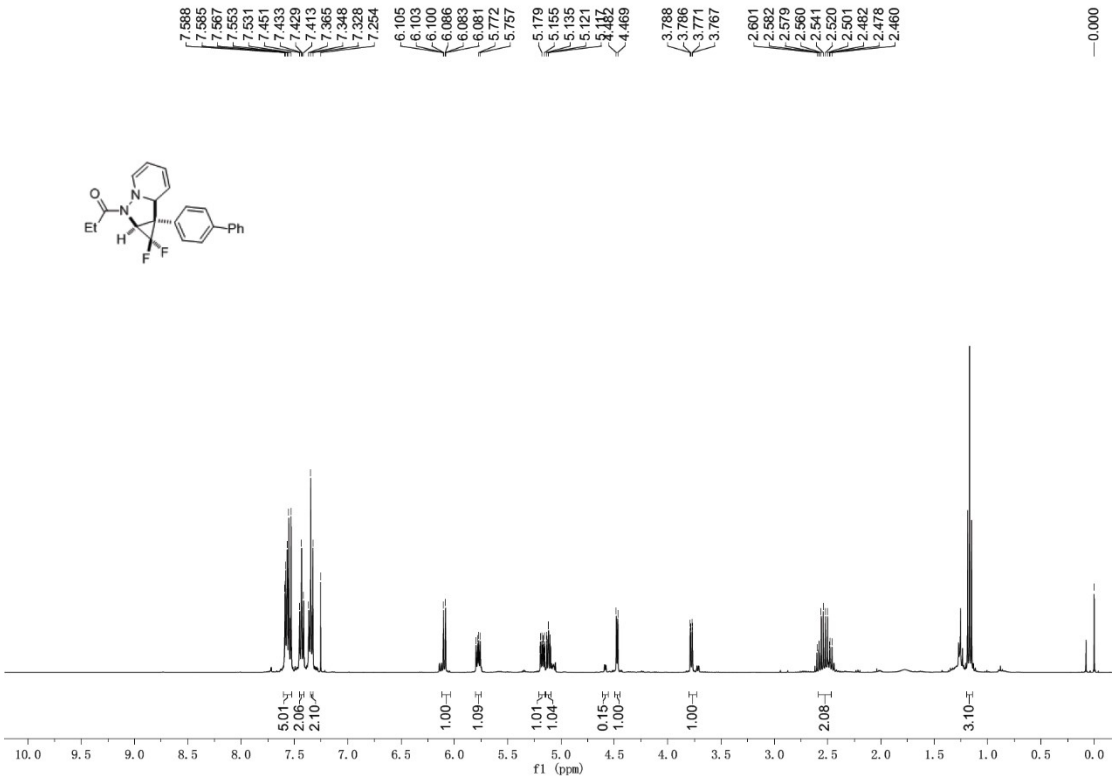
3ag-^{13}C NMR (100 MHz, $CDCl_3$)



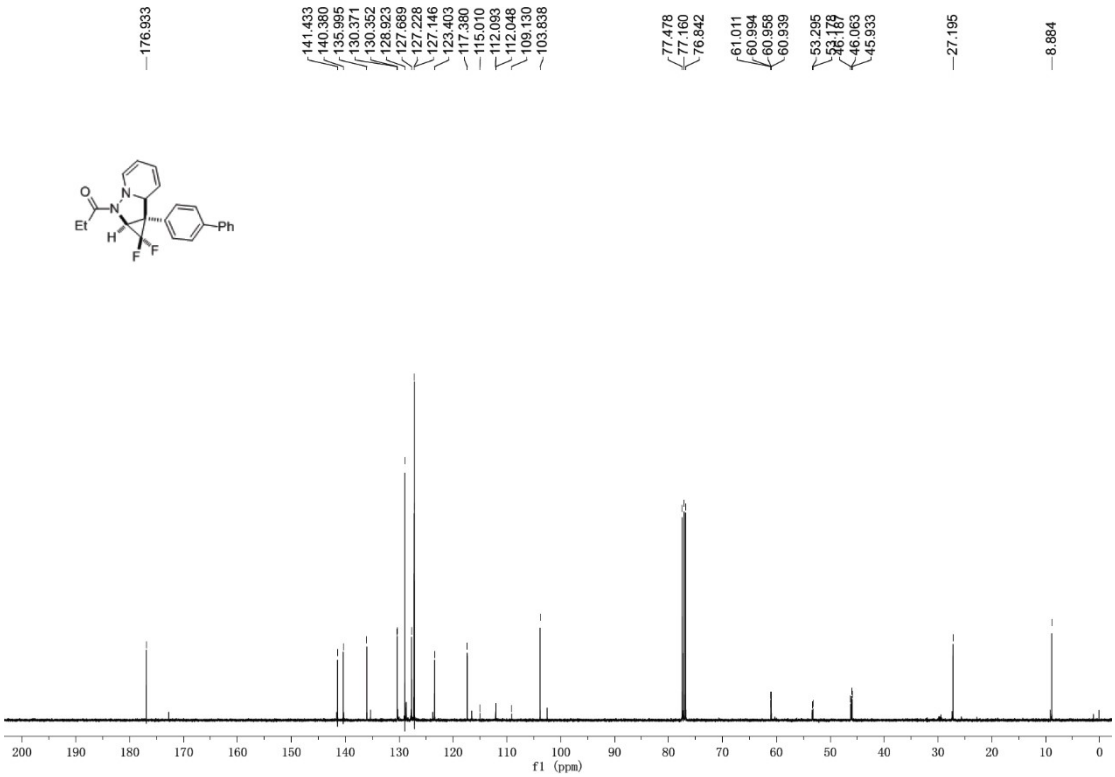
3ag-^{19}F NMR (376 MHz, $CDCl_3$)



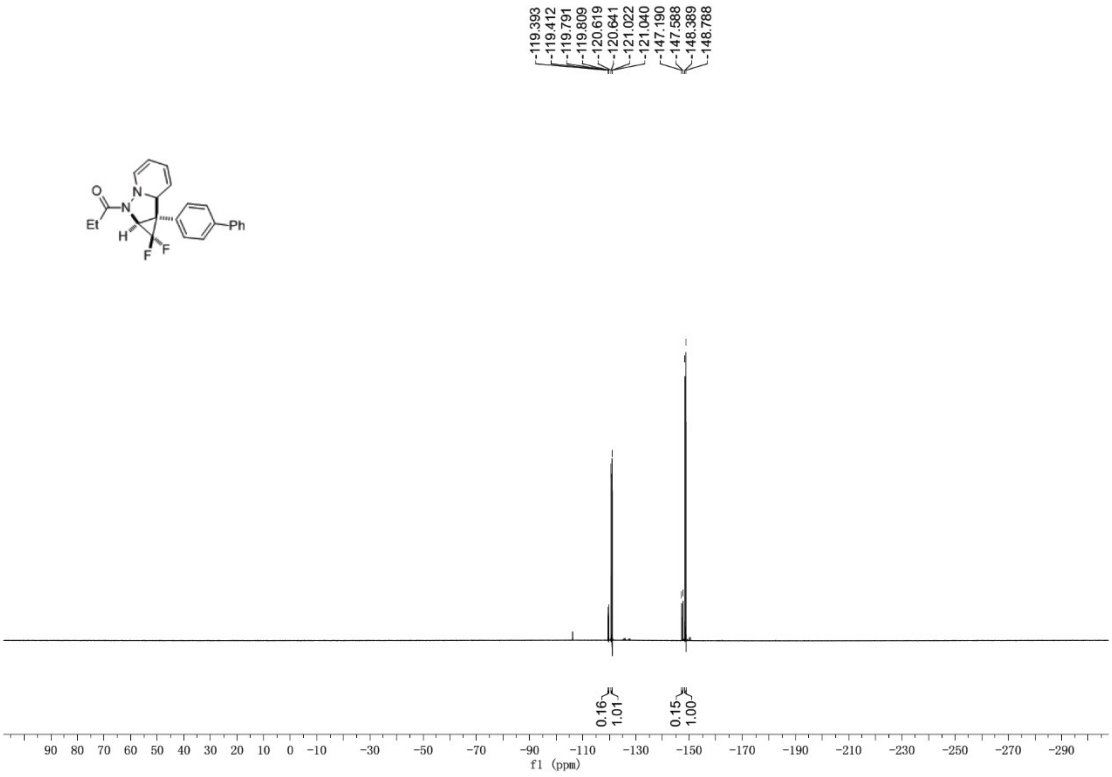
3ah-^{1}H NMR (400 MHz, $CDCl_3$)



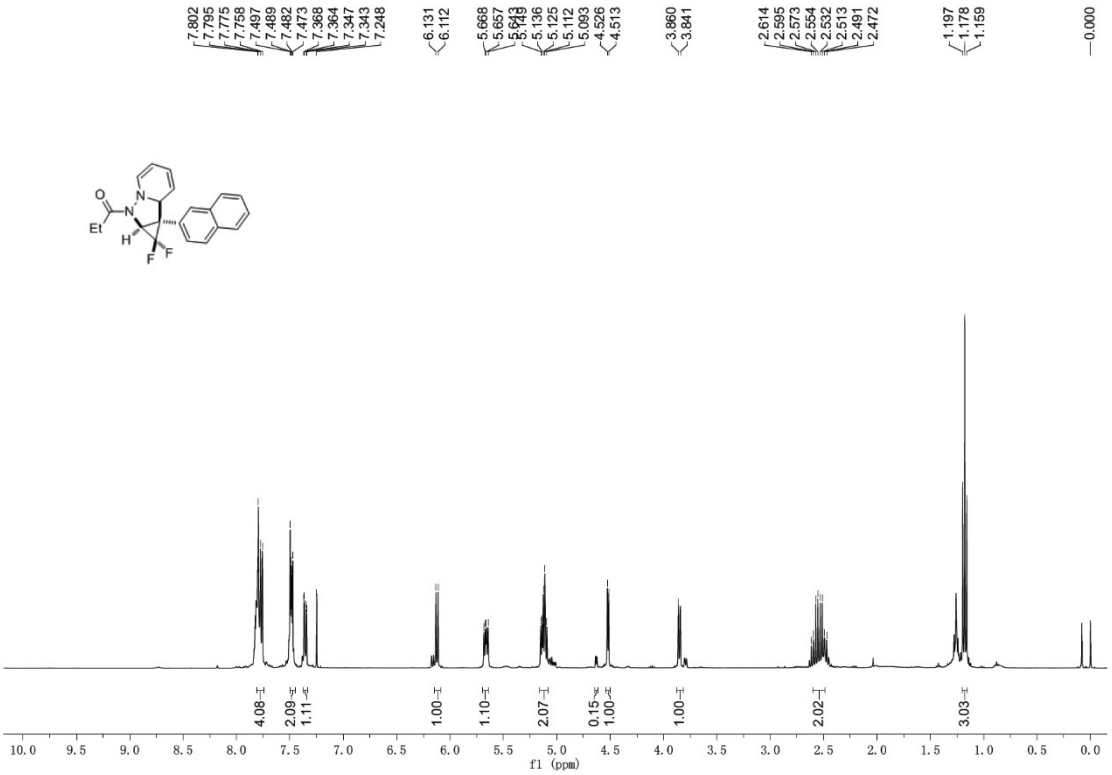
3ah-^{13}C NMR (100 MHz, $CDCl_3$)



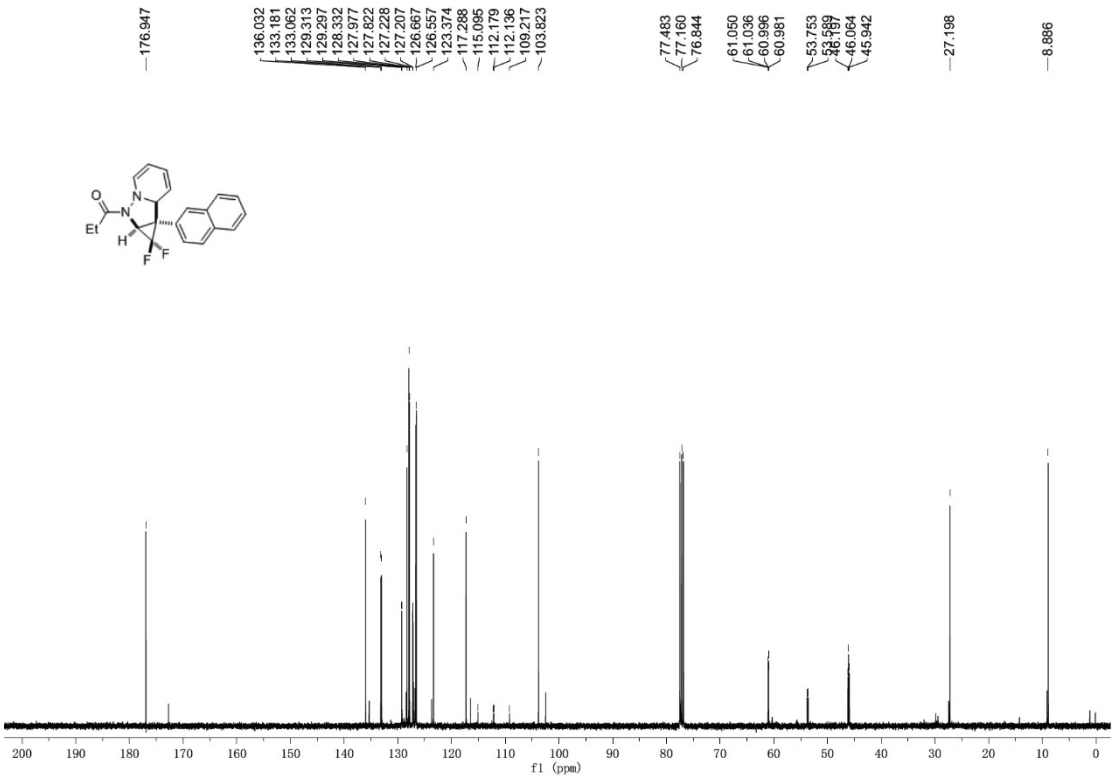
3ah-^{19}F NMR (376 MHz, $CDCl_3$)



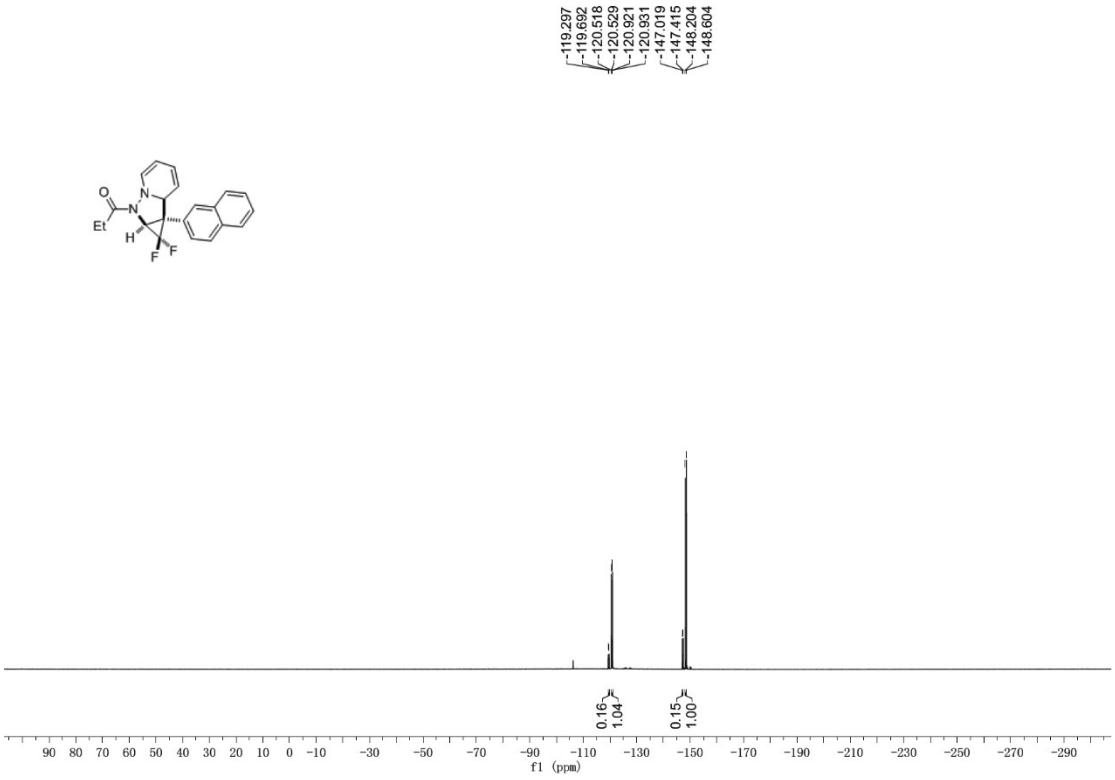
3ai-^{1}H NMR (400 MHz, $CDCl_3$)



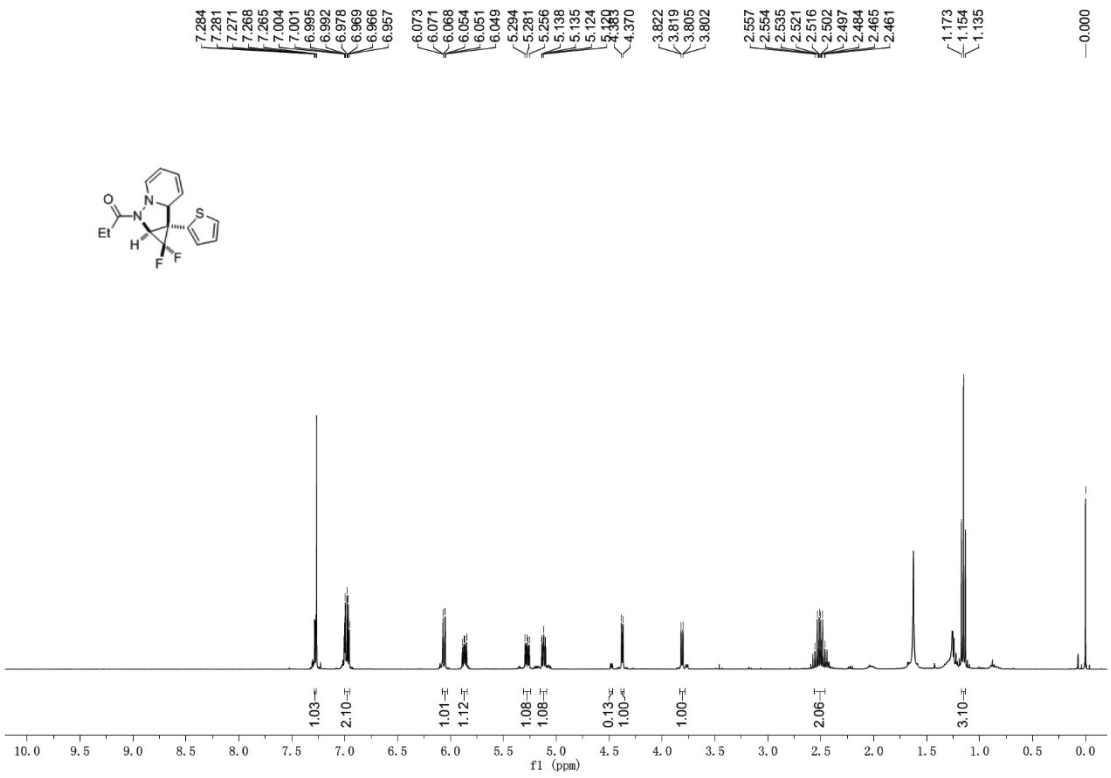
3ai-^{13}C NMR (100 MHz, $CDCl_3$)



3ai-^{19}F NMR (376 MHz, $CDCl_3$)



3aj-^{1}H NMR (400 MHz, $CDCl_3$)



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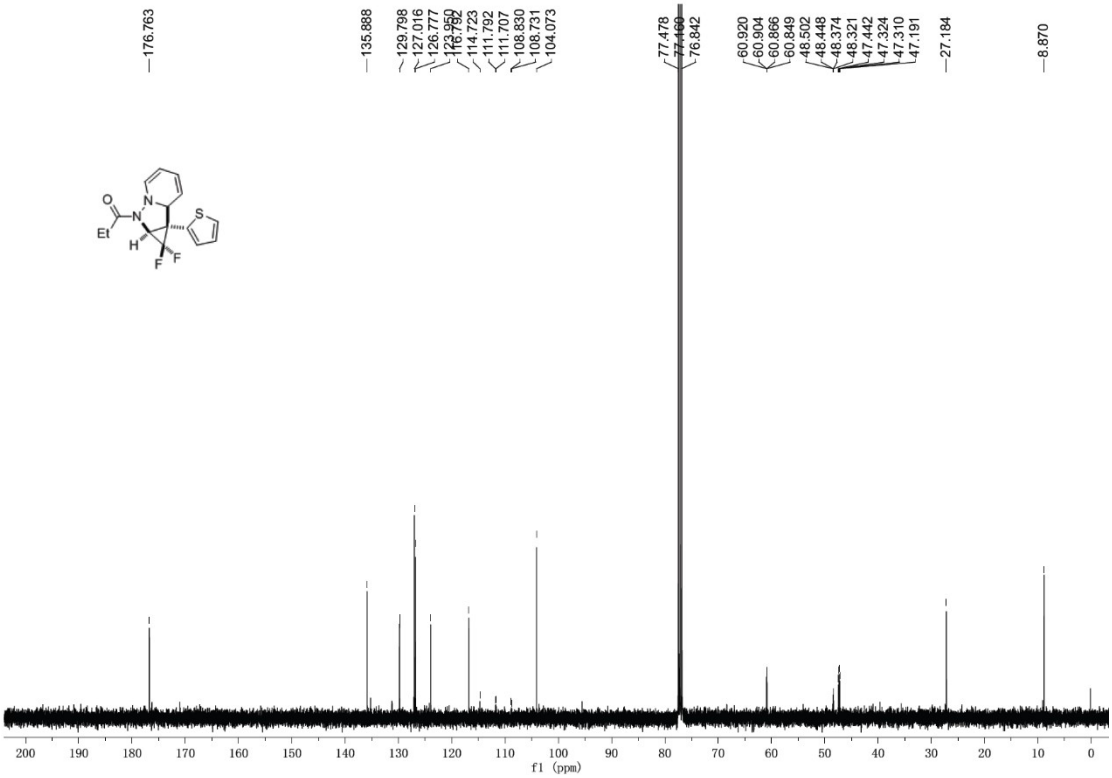
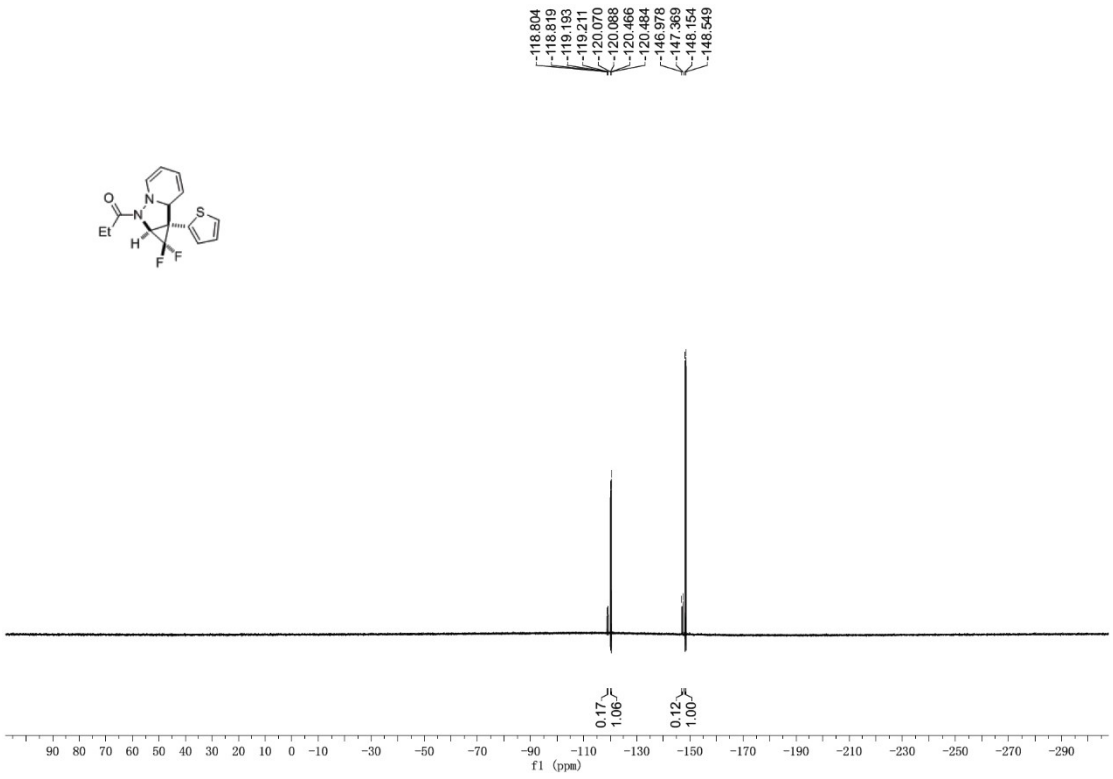
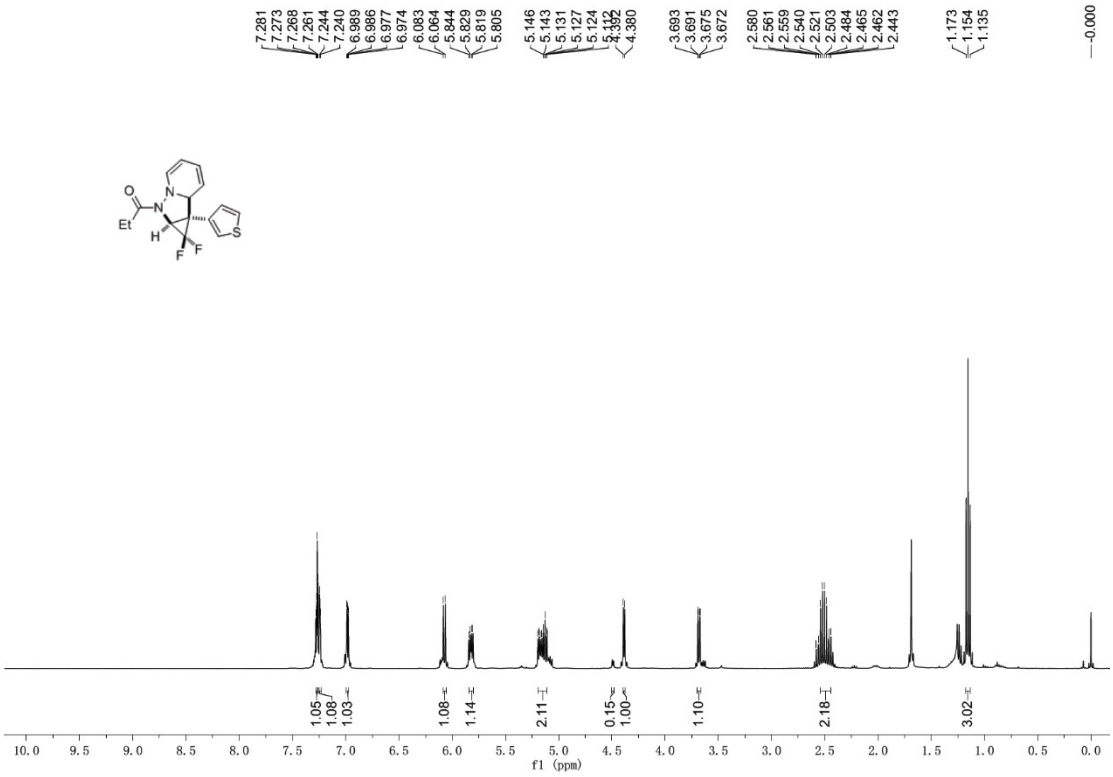


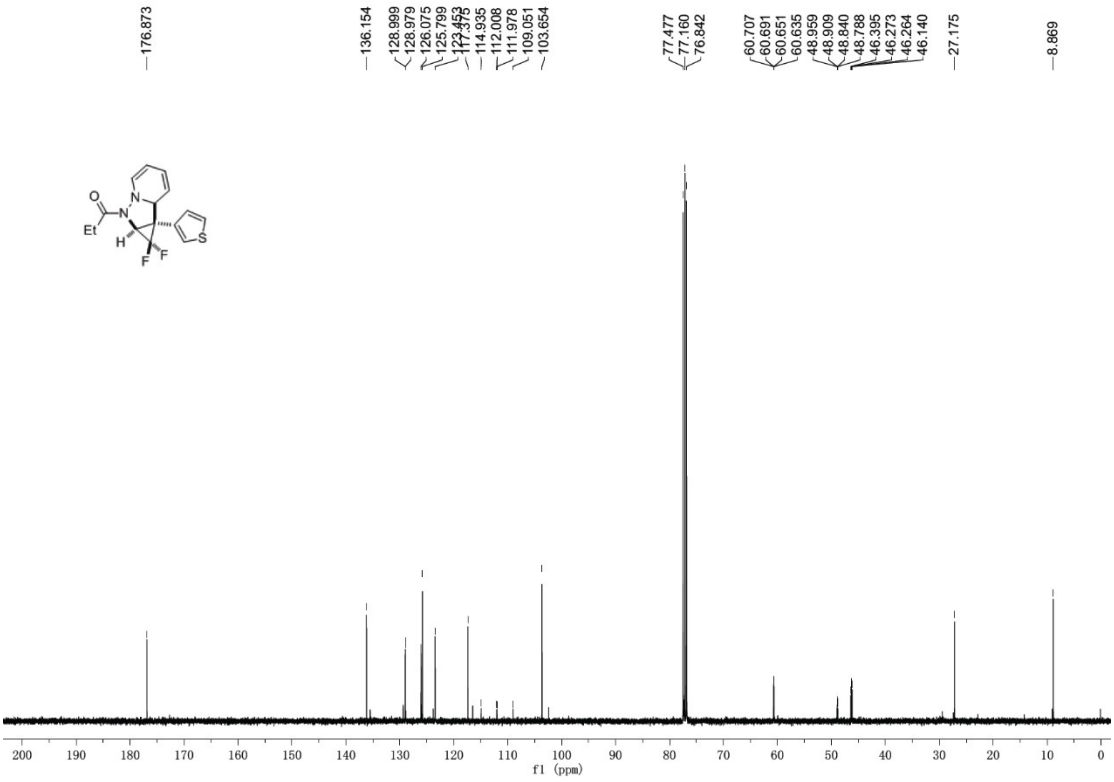
3aj-^{19}F NMR (376 MHz, $CDCl_3$)



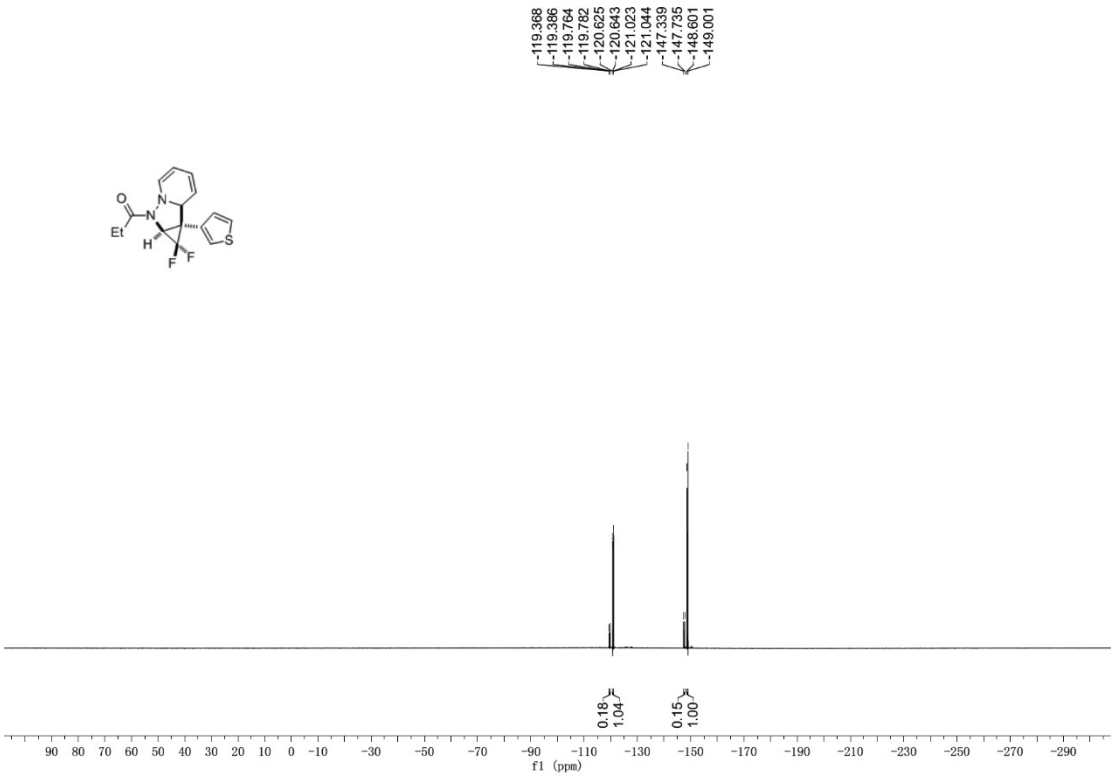
3ak-^{1}H NMR (400 MHz, $CDCl_3$)



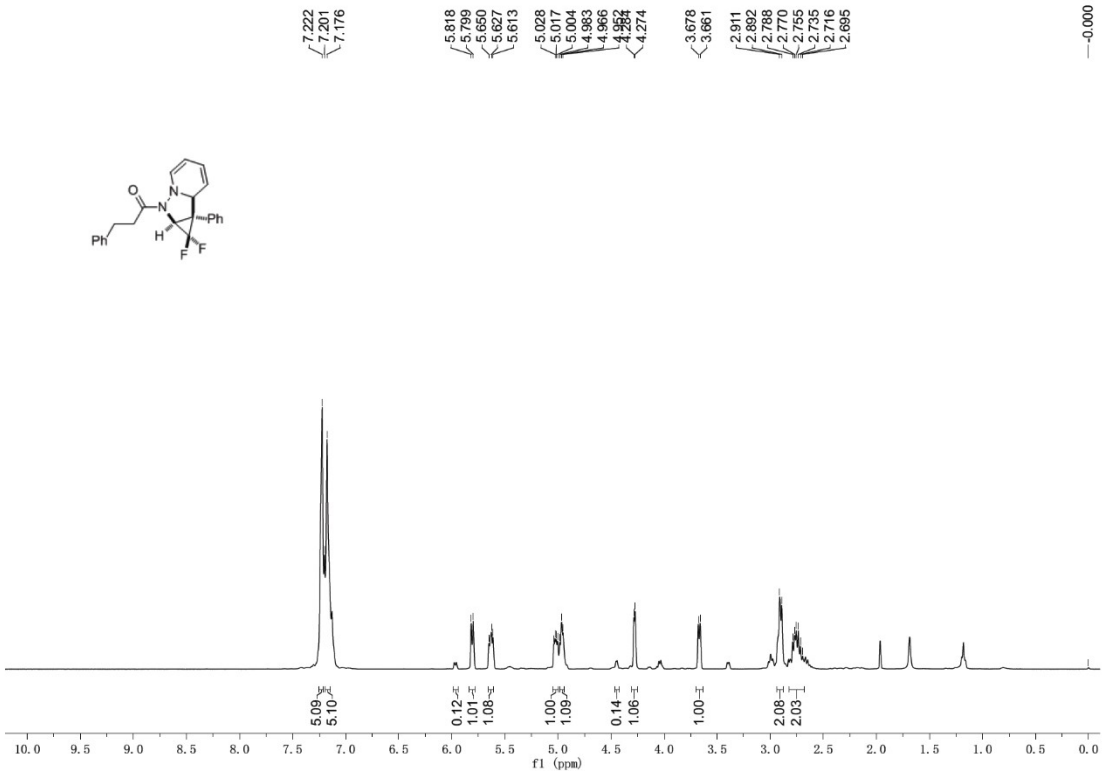
3ak-^{13}C NMR (100 MHz, $CDCl_3$)



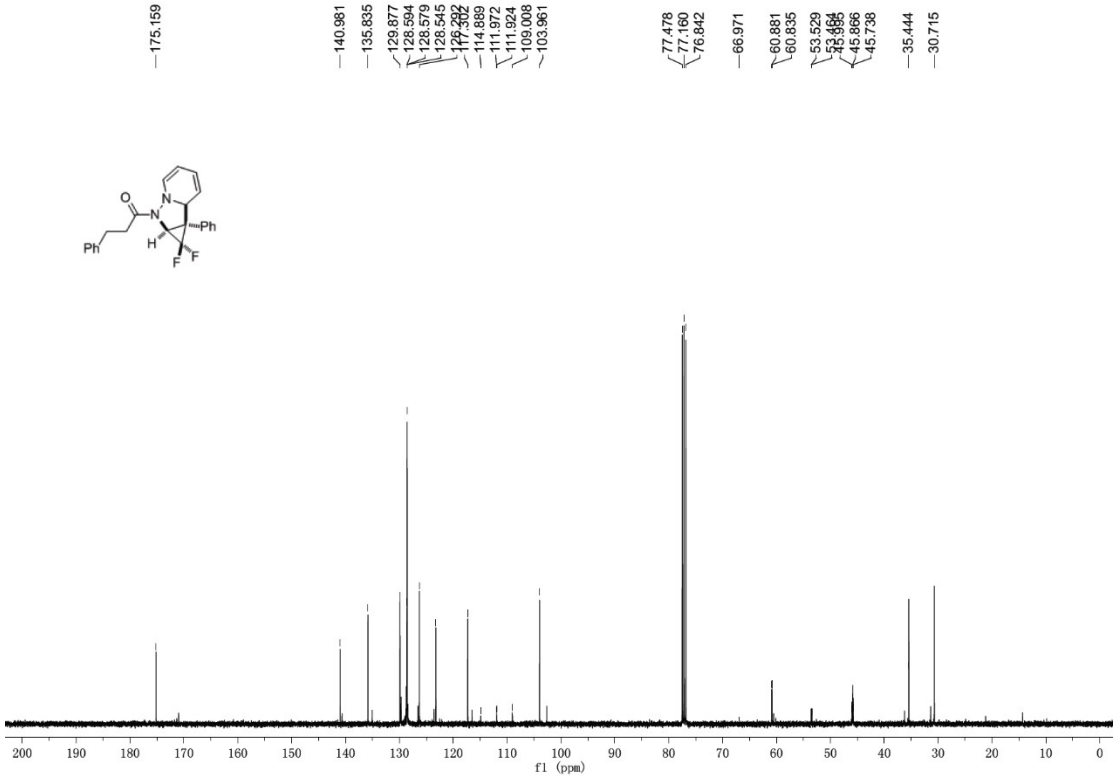
3ak-^{19}F NMR (376 MHz, $CDCl_3$)



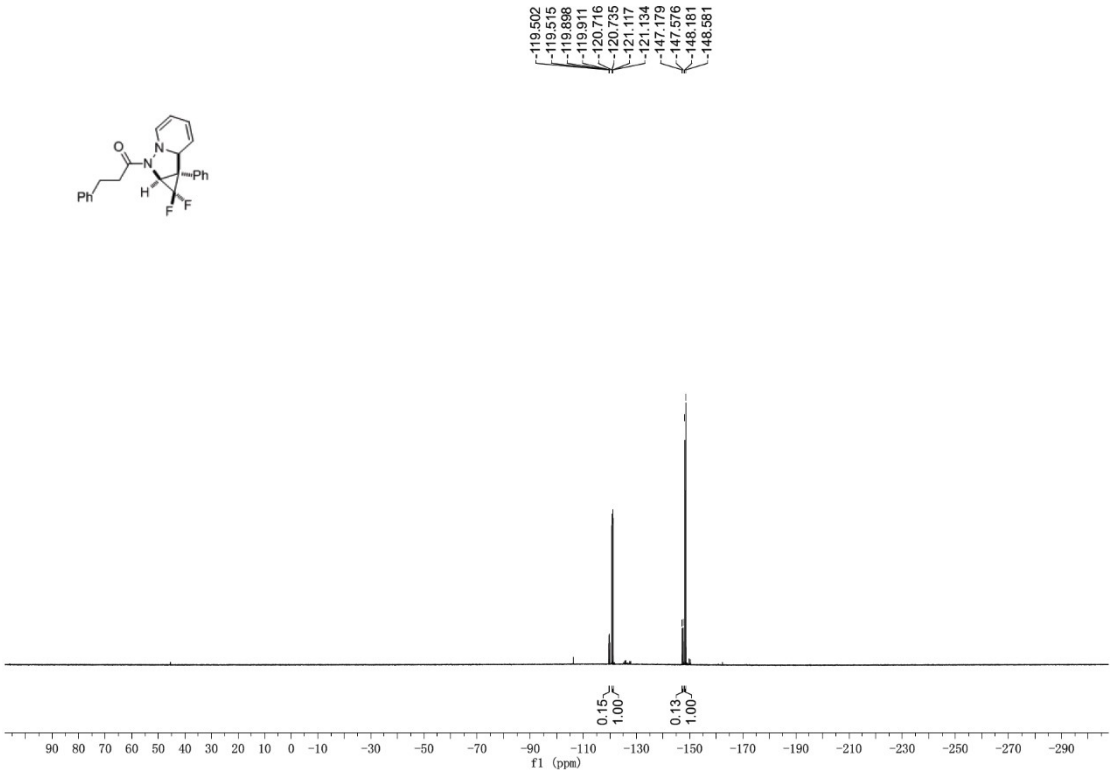
3ba-^{1}H NMR (400 MHz, $CDCl_3$)



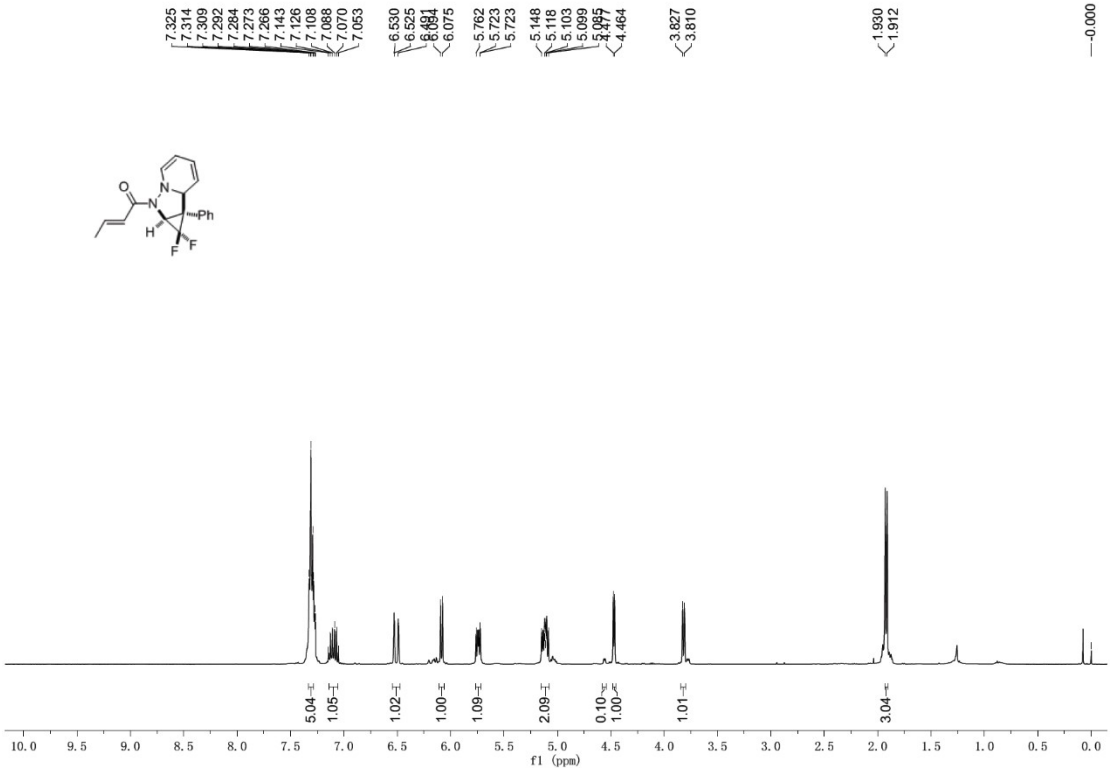
3ba-^{13}C NMR (100 MHz, $CDCl_3$)



3ba-^{19}F NMR (376 MHz, $CDCl_3$)



3ca-^{1}H NMR (400 MHz, $CDCl_3$)



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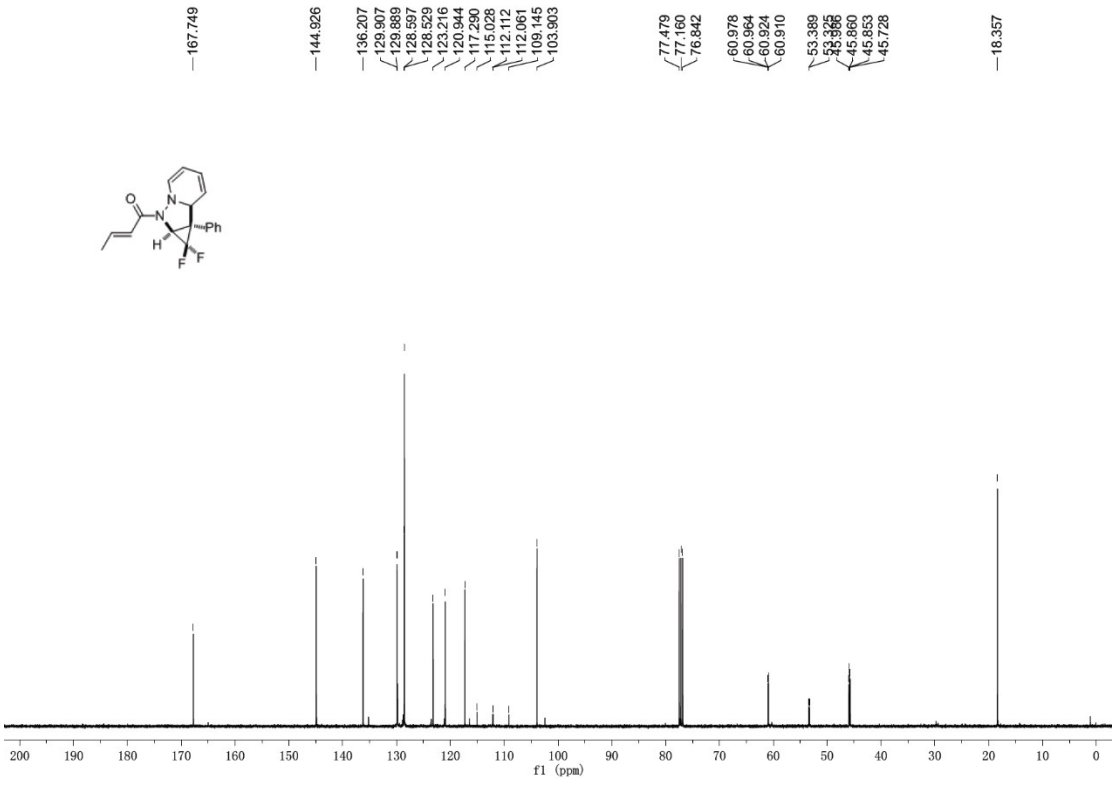
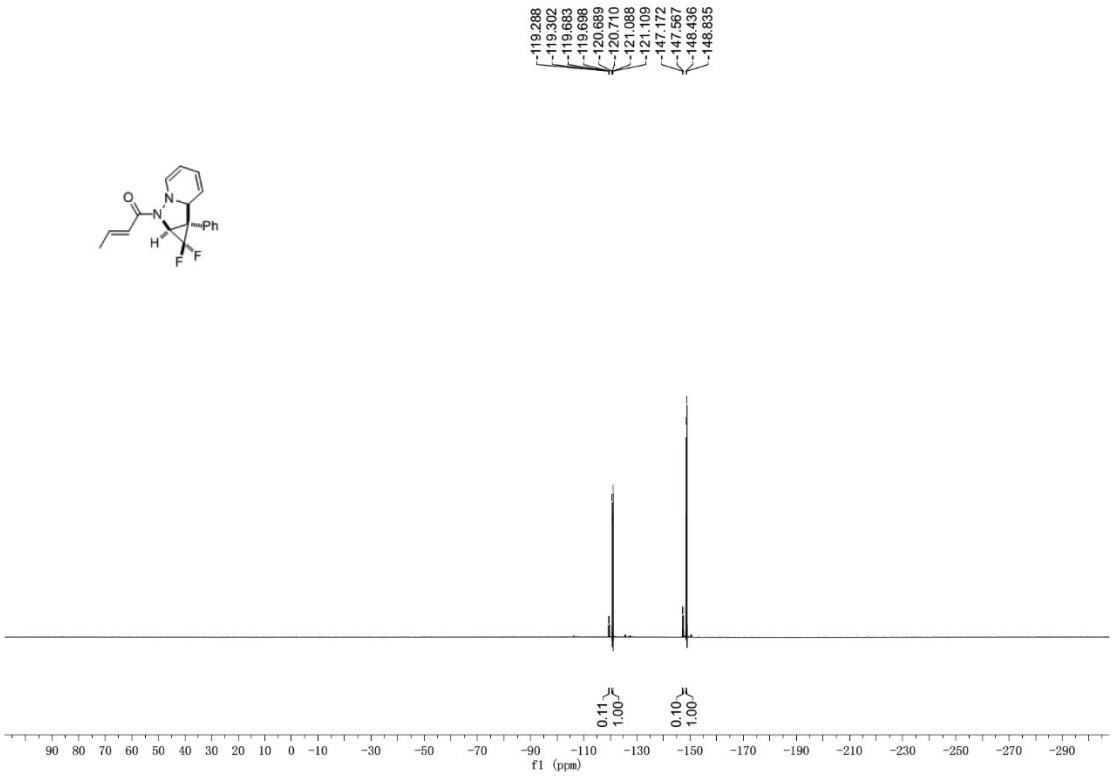
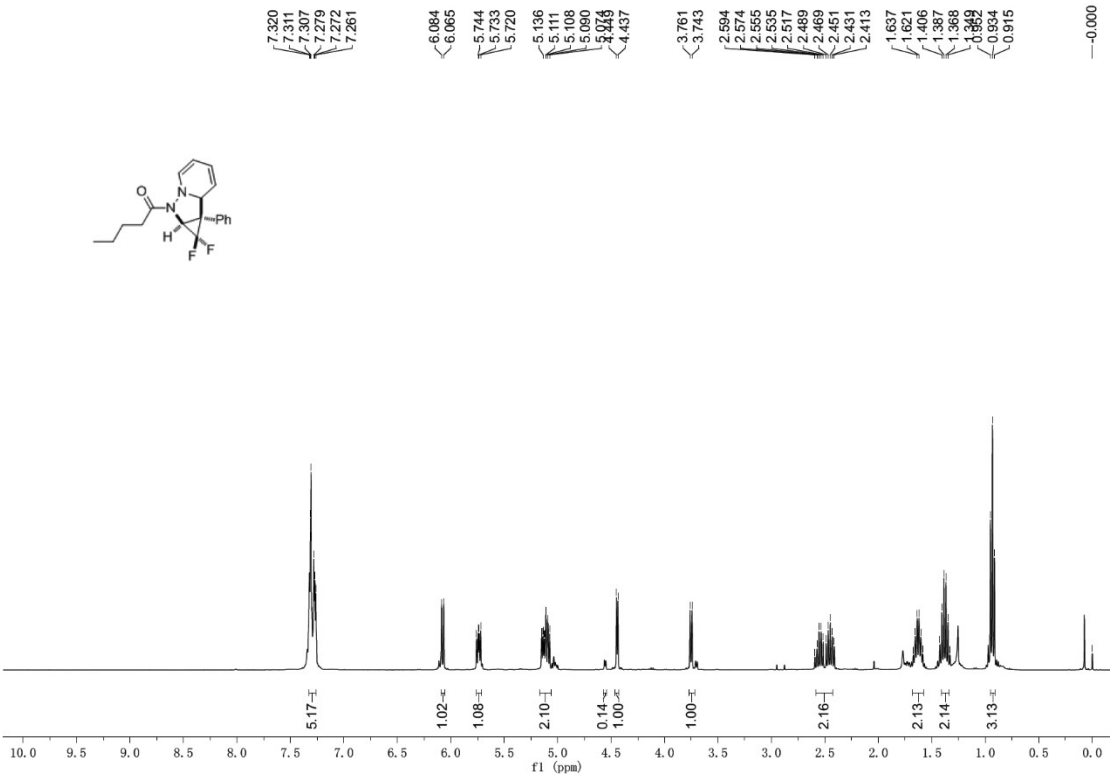


3ca-^{19}F NMR (376 MHz, $CDCl_3$)



3da-^{1}H NMR (400 MHz, $CDCl_3$)



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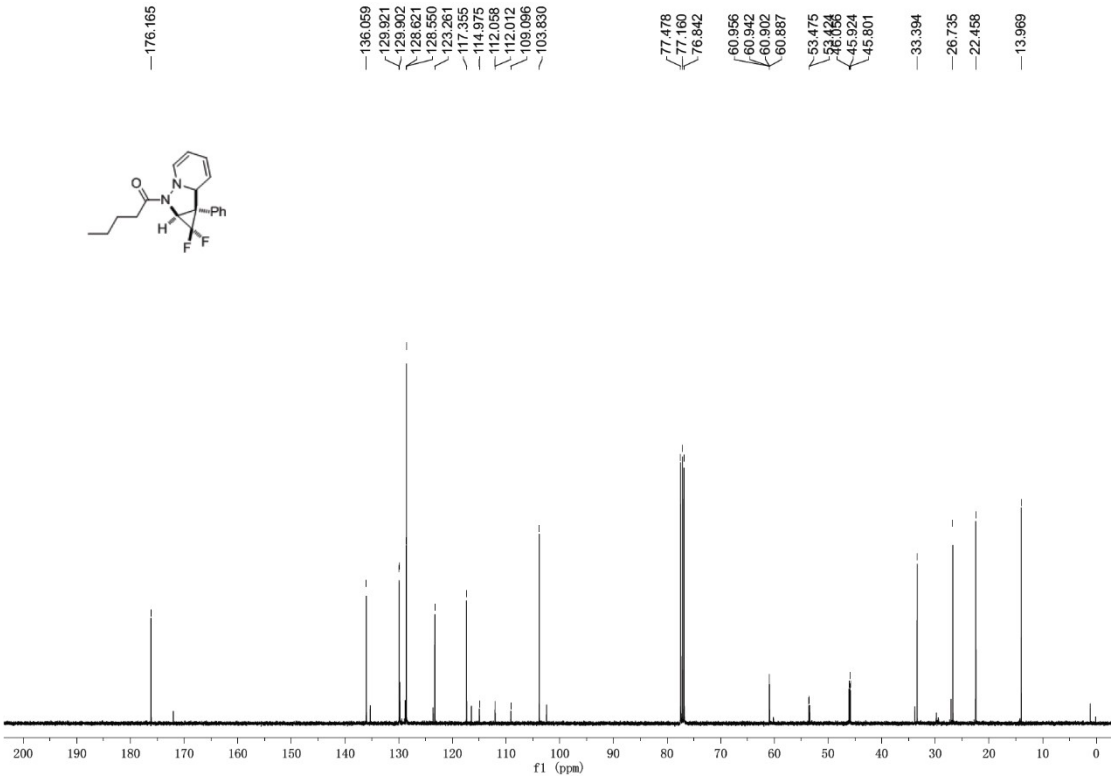
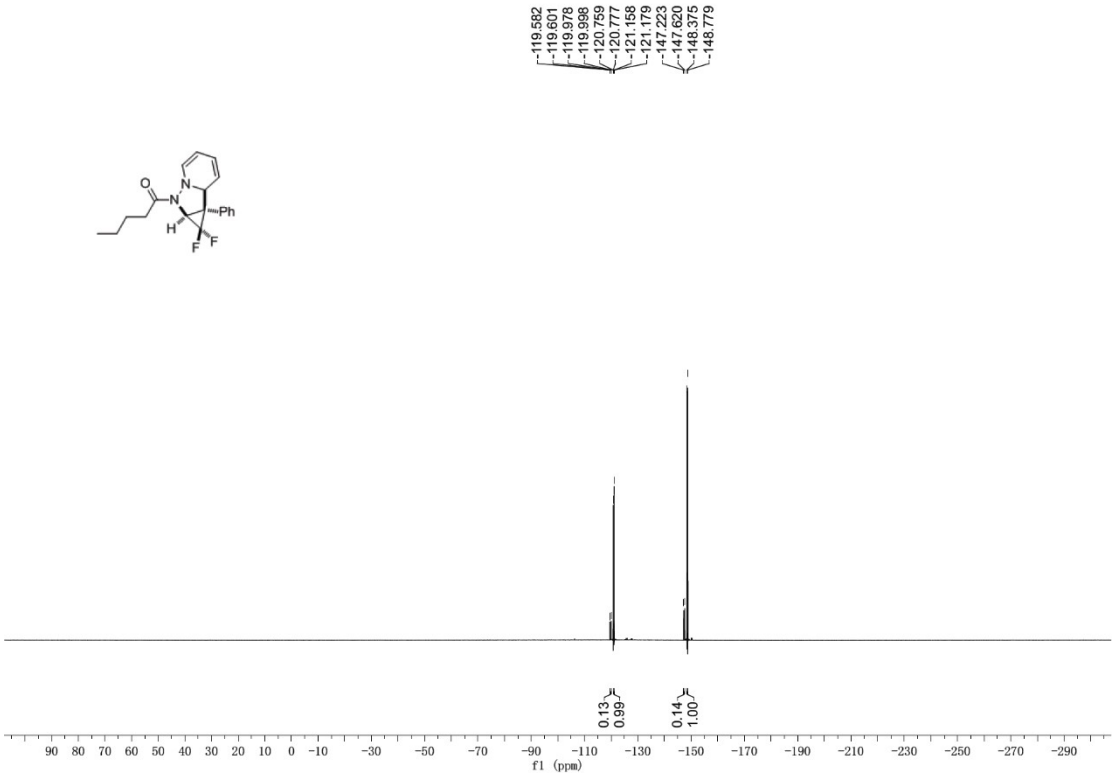
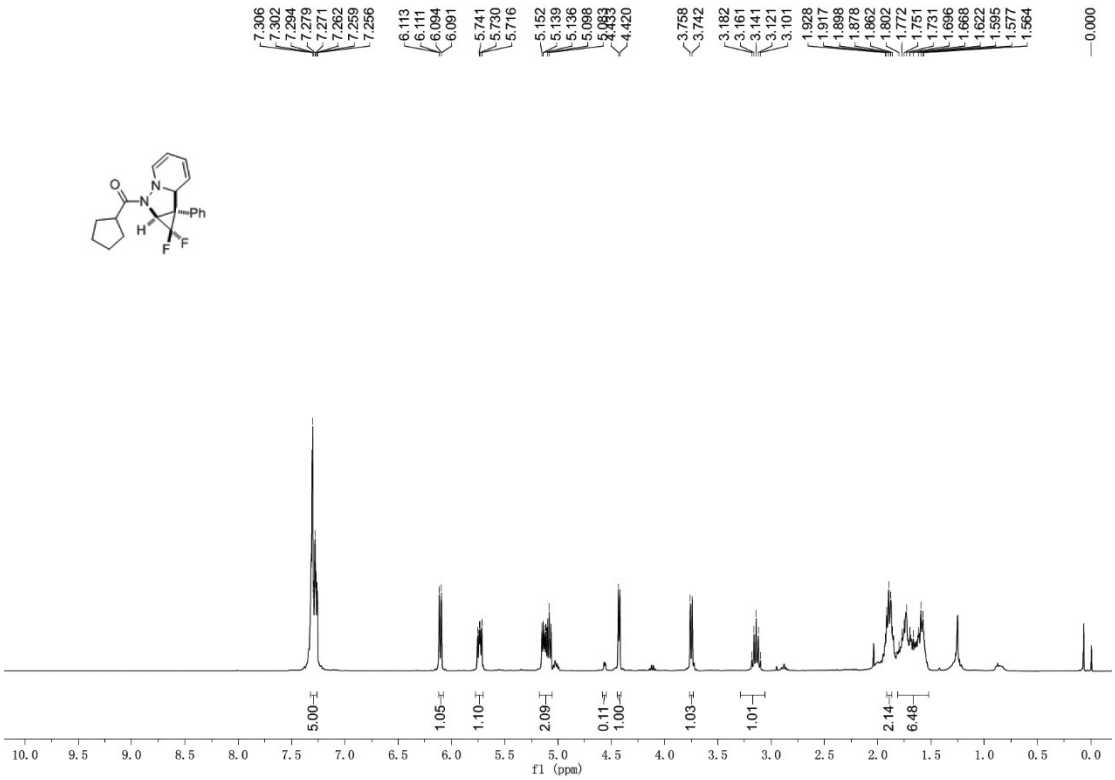


3da-^{19}F NMR (376 MHz, $CDCl_3$)



3ea-^{1}H NMR (400 MHz, $CDCl_3$)



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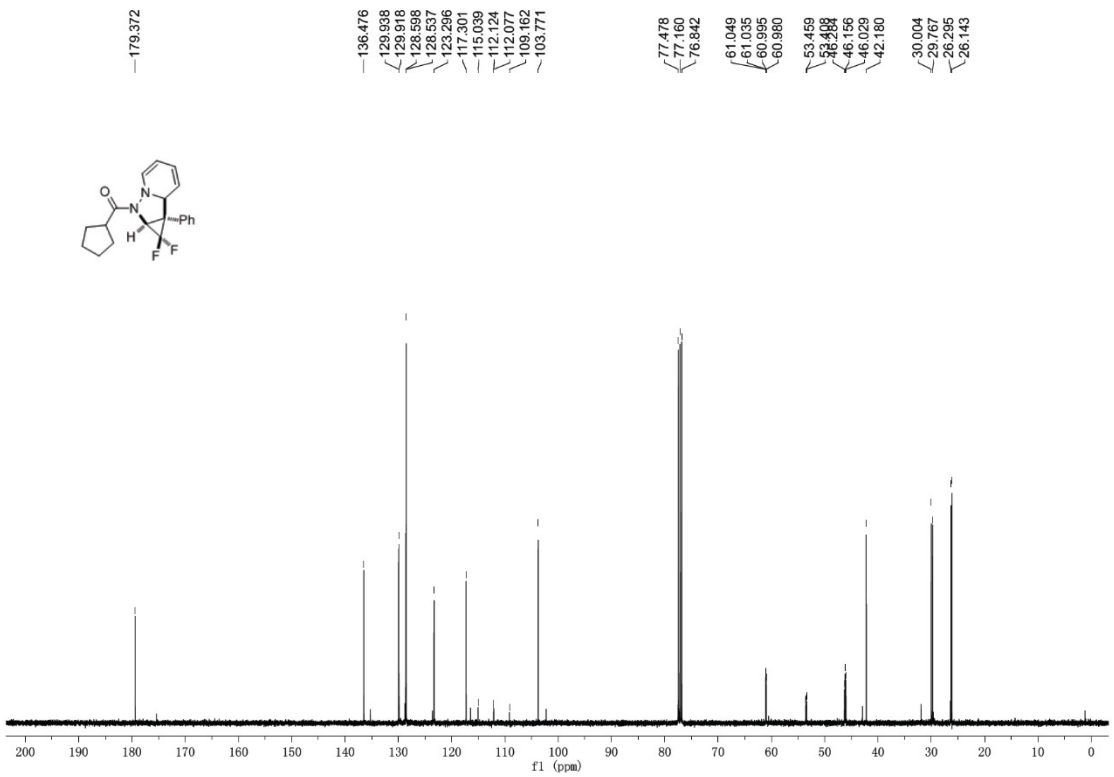
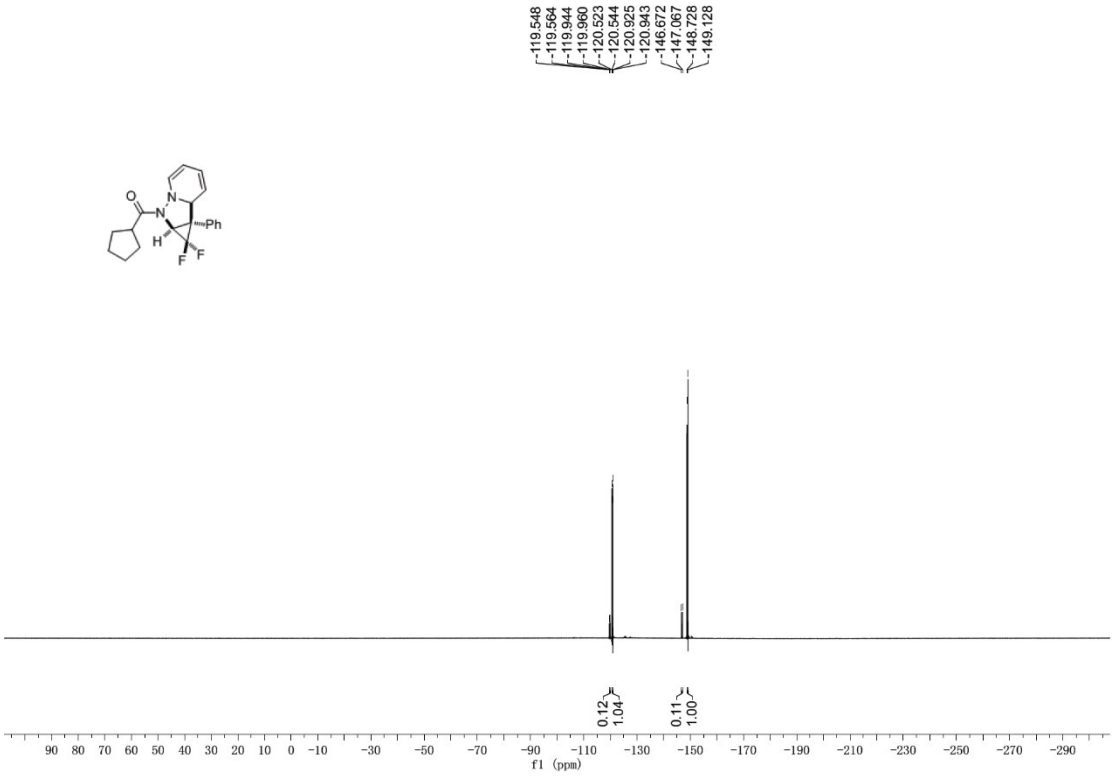
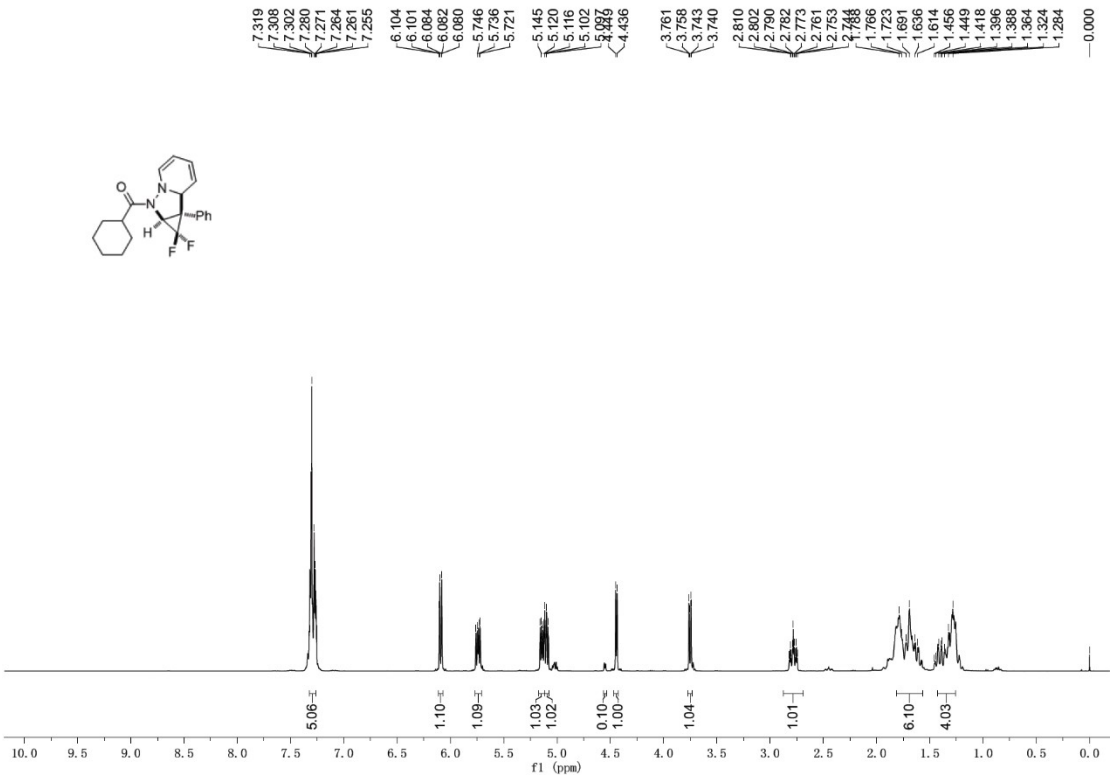


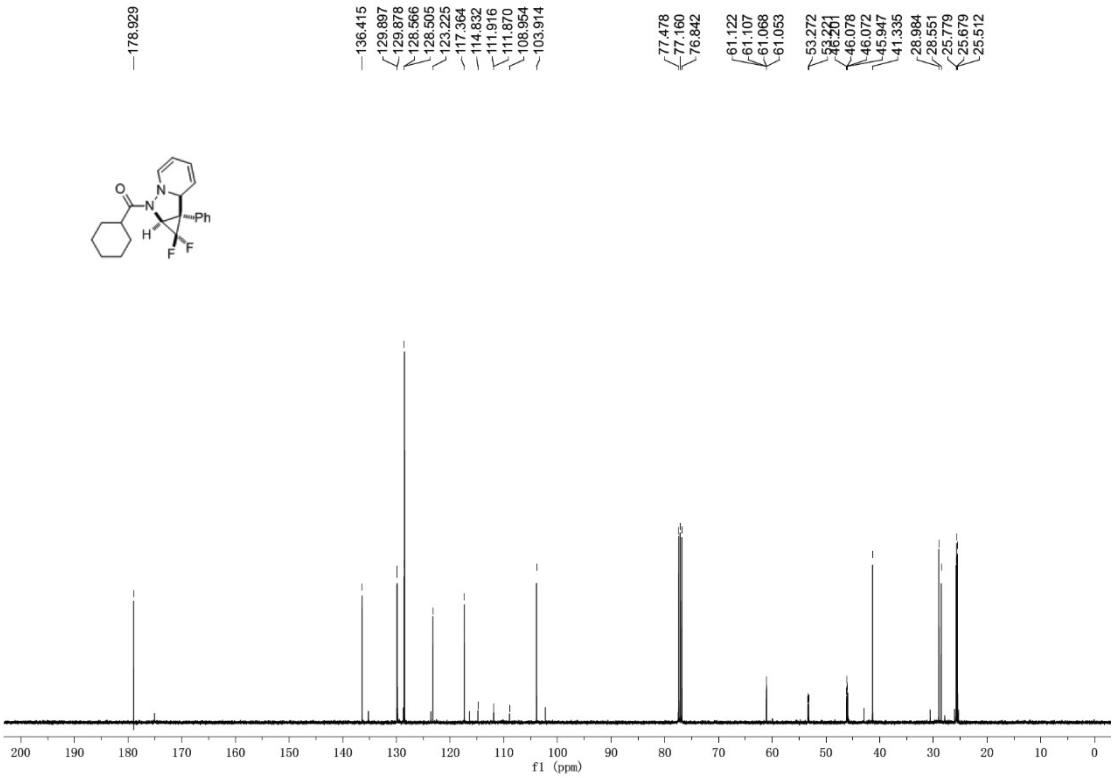
3ea-^{19}F NMR (376 MHz, $CDCl_3$)



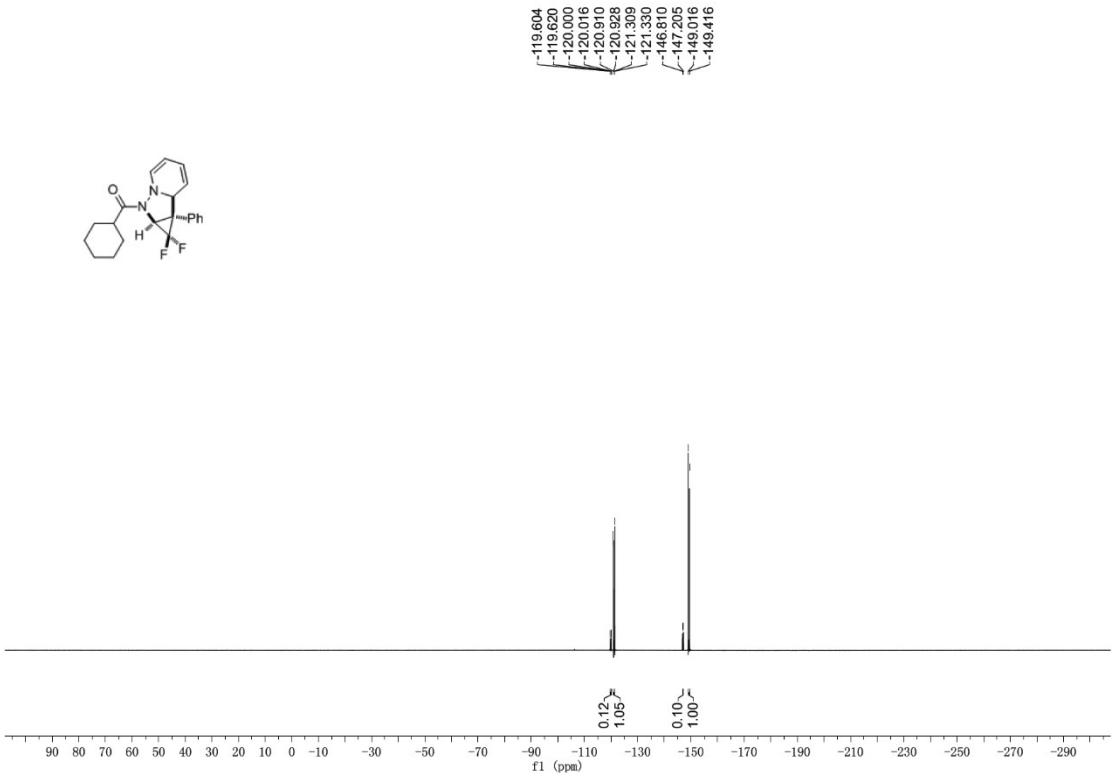
3fa-^{1}H NMR (400 MHz, $CDCl_3$)



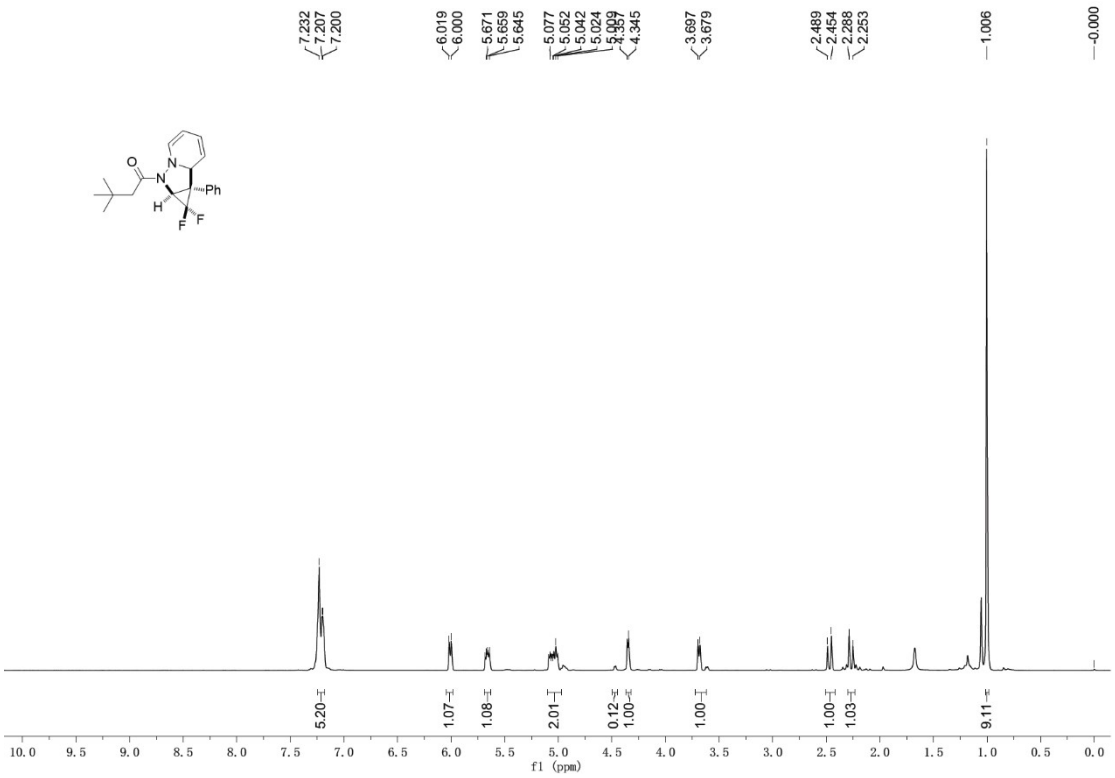
3fa-^{13}C NMR (100 MHz, $CDCl_3$)



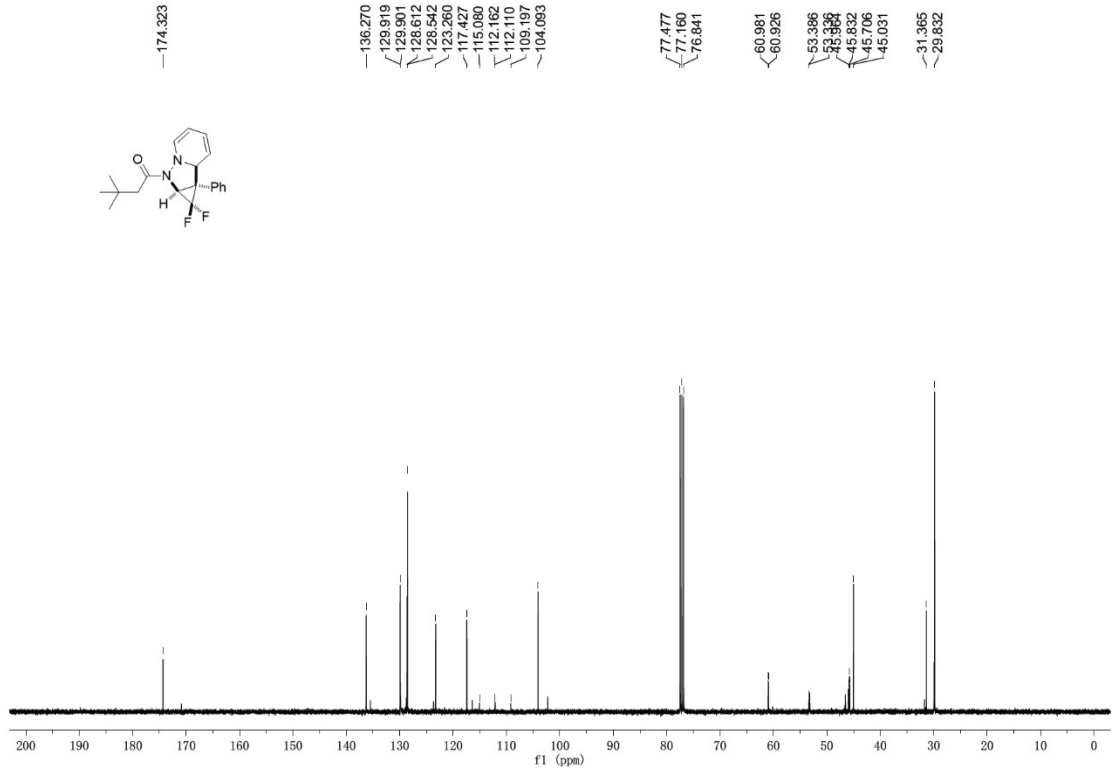
3fa-^{19}F NMR (376 MHz, $CDCl_3$)



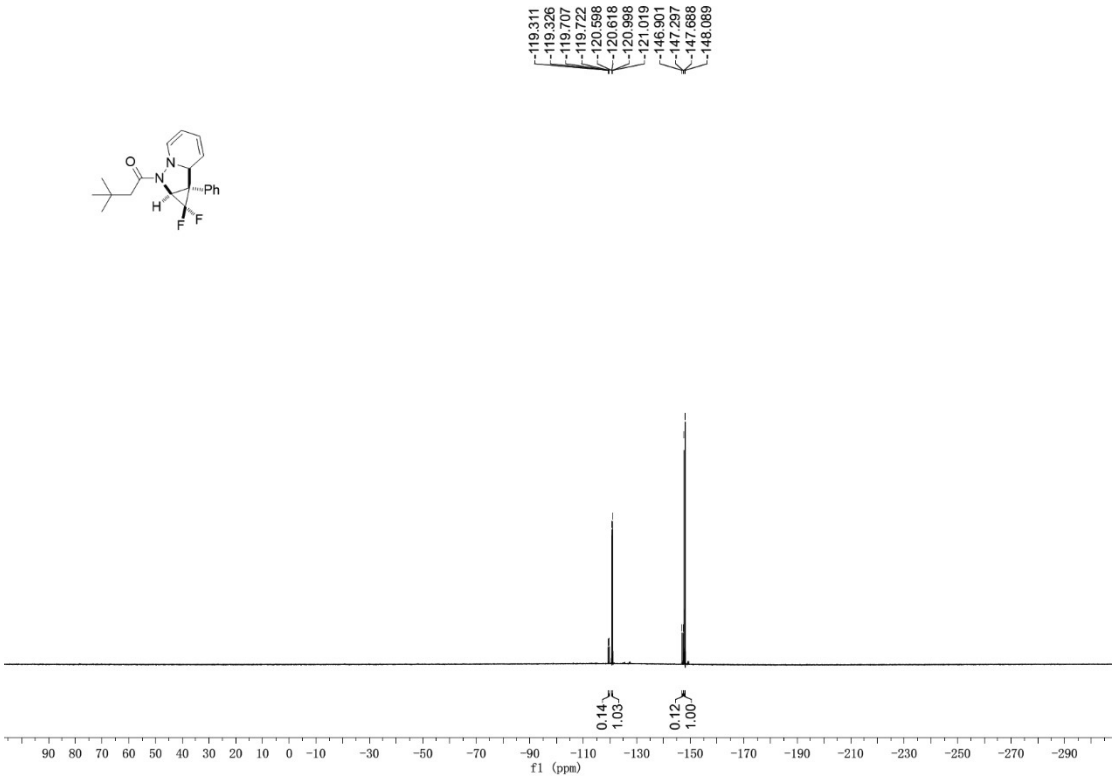
3ga-^{1}H NMR (400 MHz, $CDCl_3$)



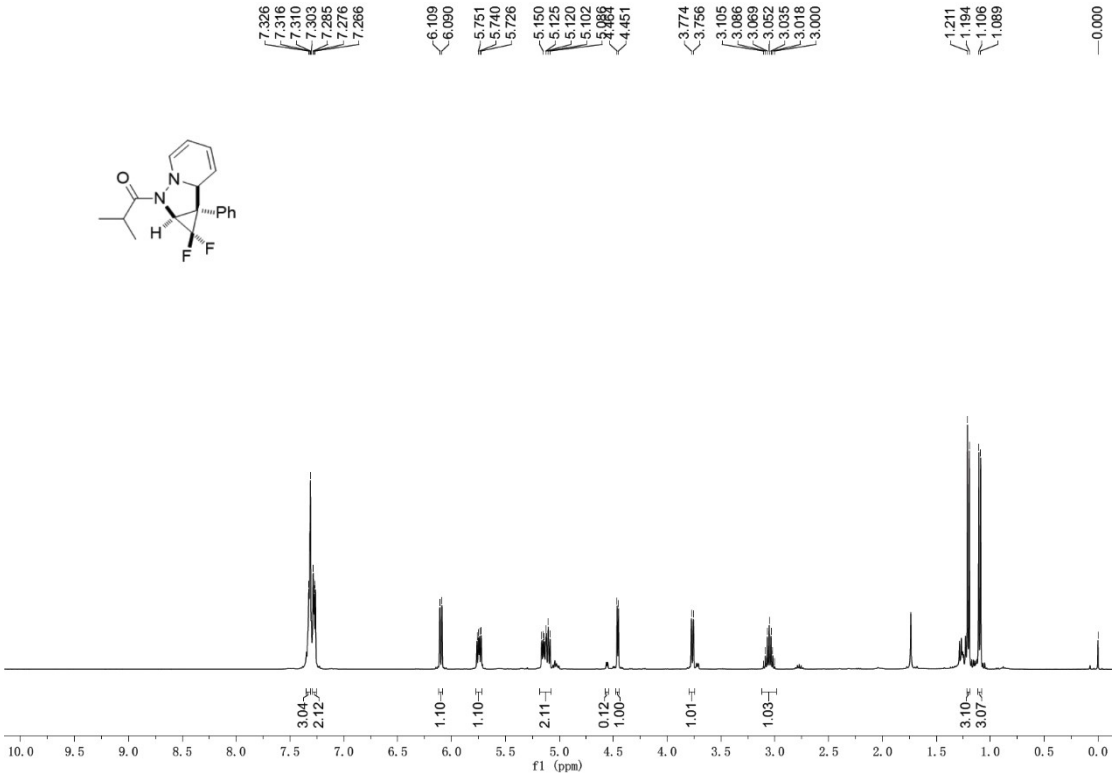
3ga-^{13}C NMR (100 MHz, $CDCl_3$)



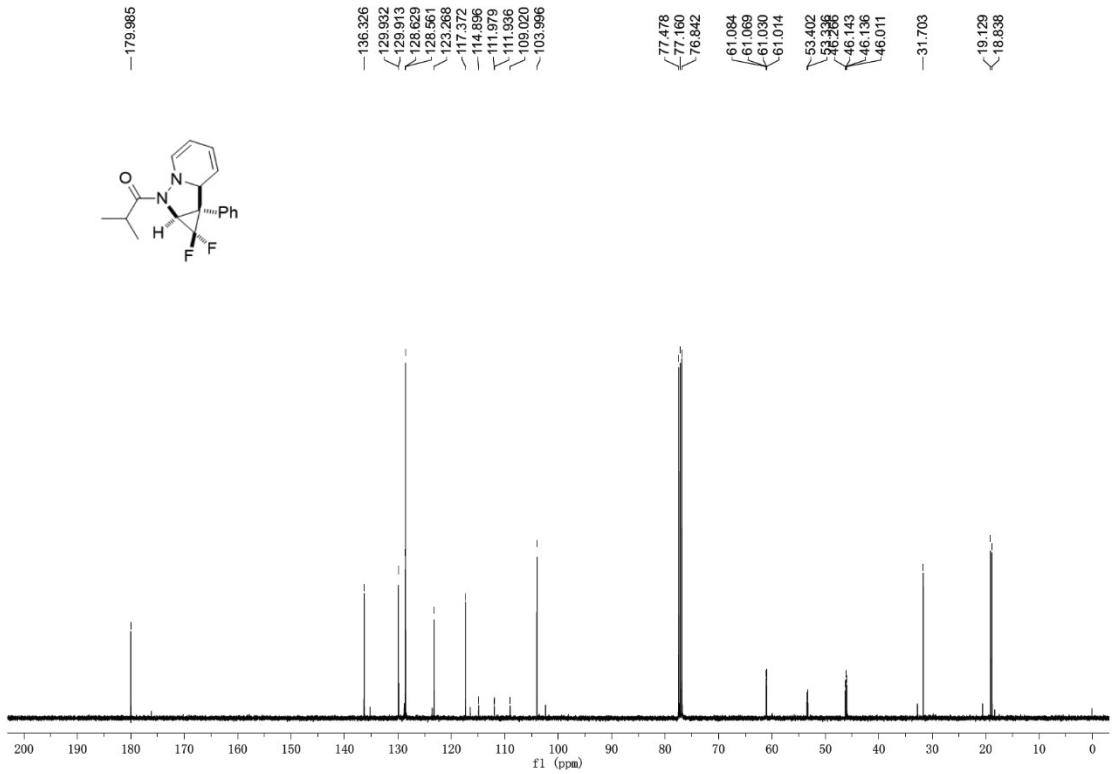
3ga-^{19}F NMR (376 MHz, $CDCl_3$)



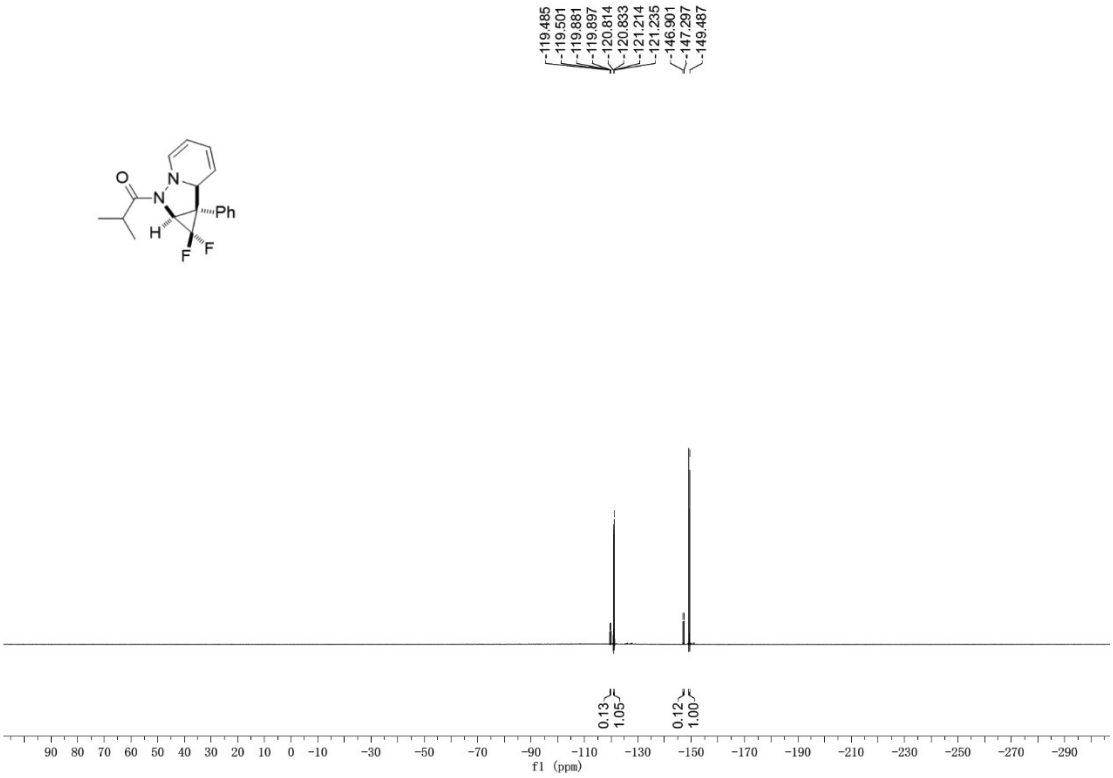
3ha-^{1}H NMR (400 MHz, $CDCl_3$)



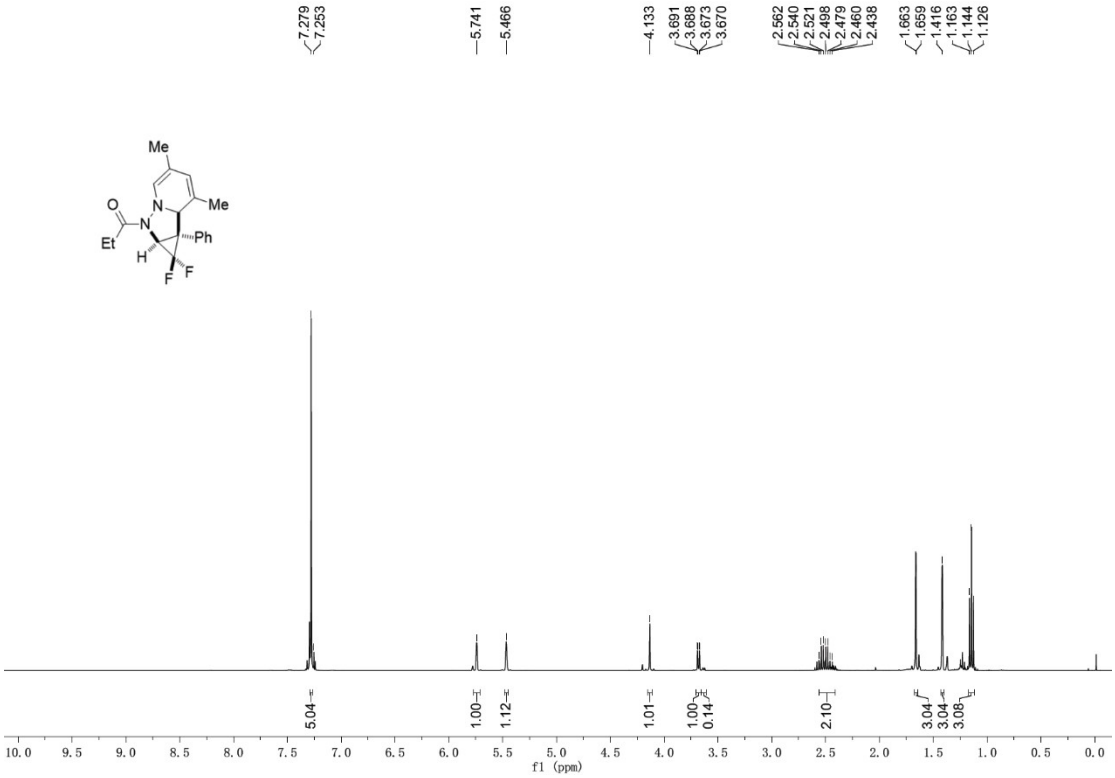
3ha-^{13}C NMR (100 MHz, $CDCl_3$)



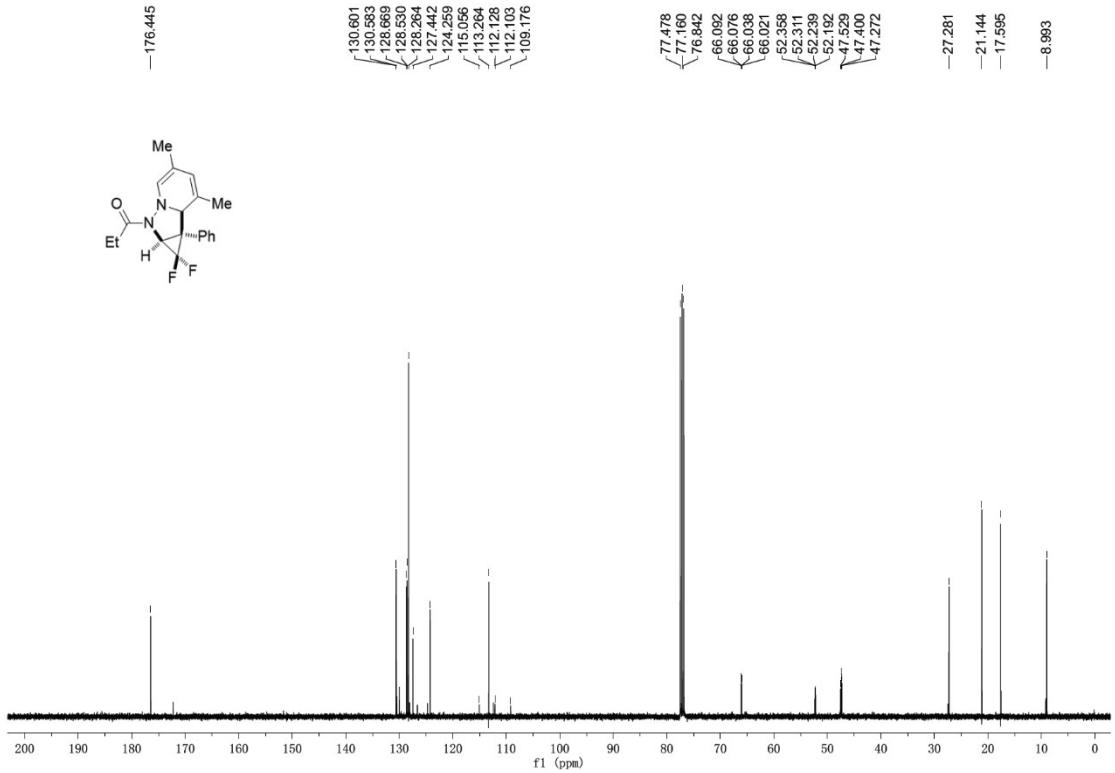
3ha-^{19}F NMR (376 MHz, $CDCl_3$)



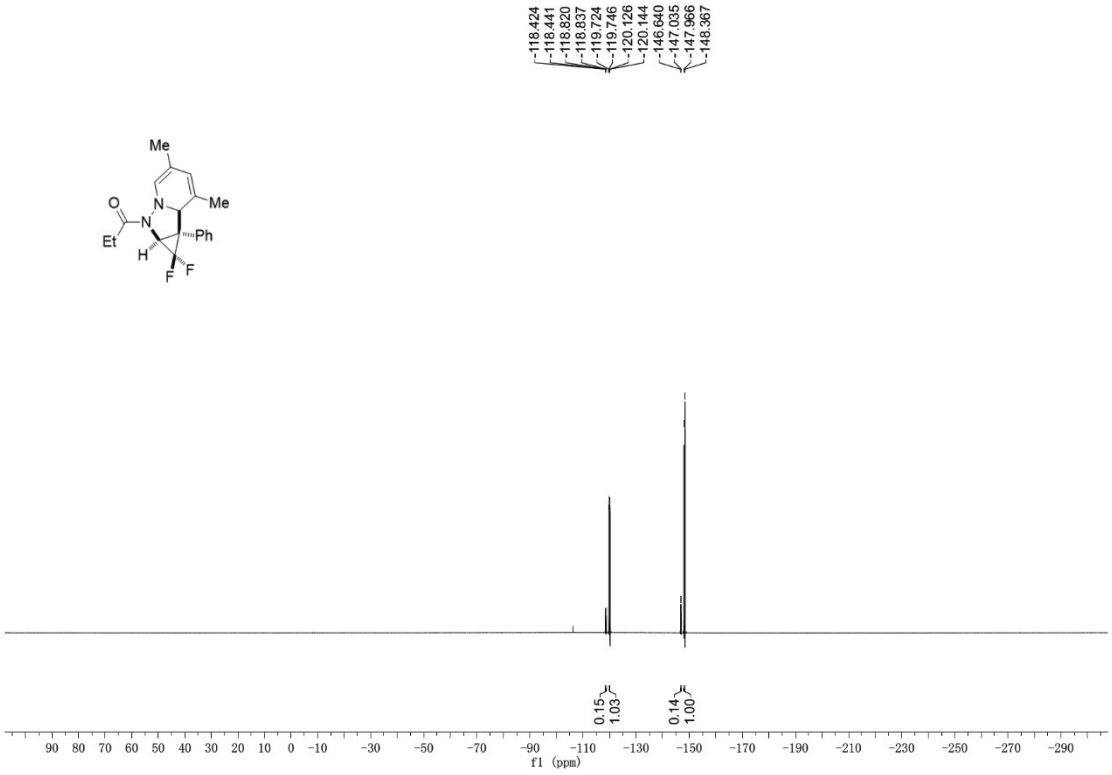
3ia-^{1}H NMR (400 MHz, $CDCl_3$)



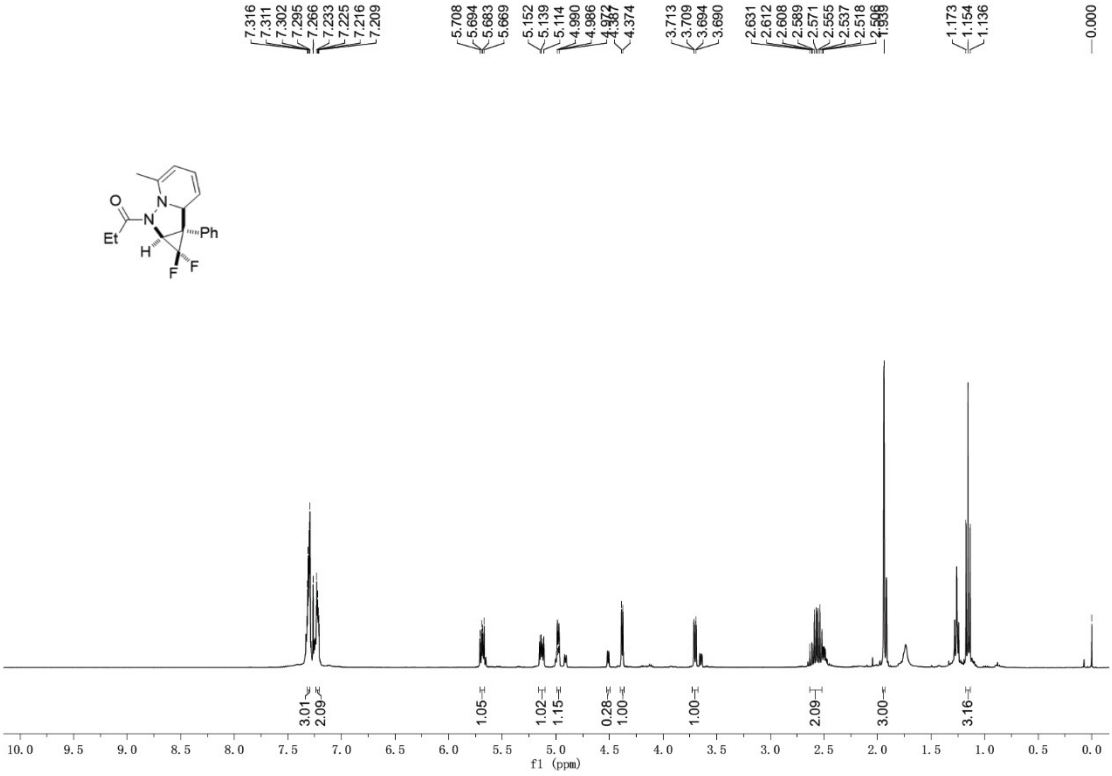
3ia-^{13}C NMR (100 MHz, $CDCl_3$)



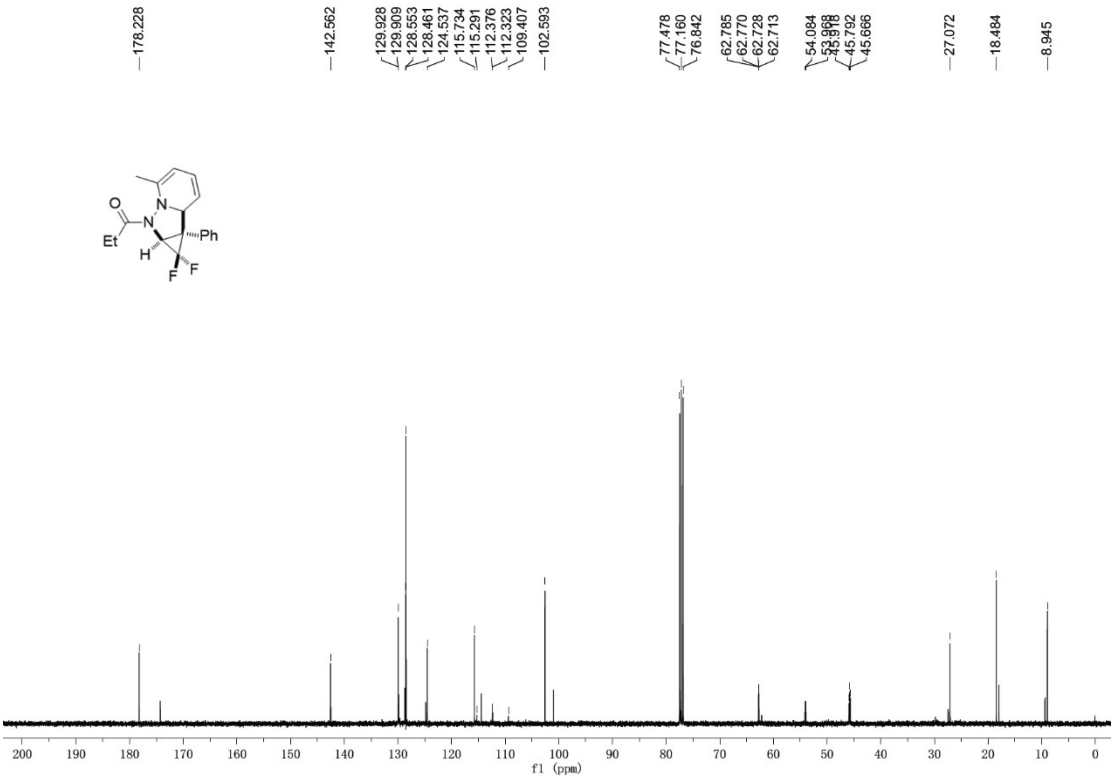
3ia-^{19}F NMR (376 MHz, $CDCl_3$)



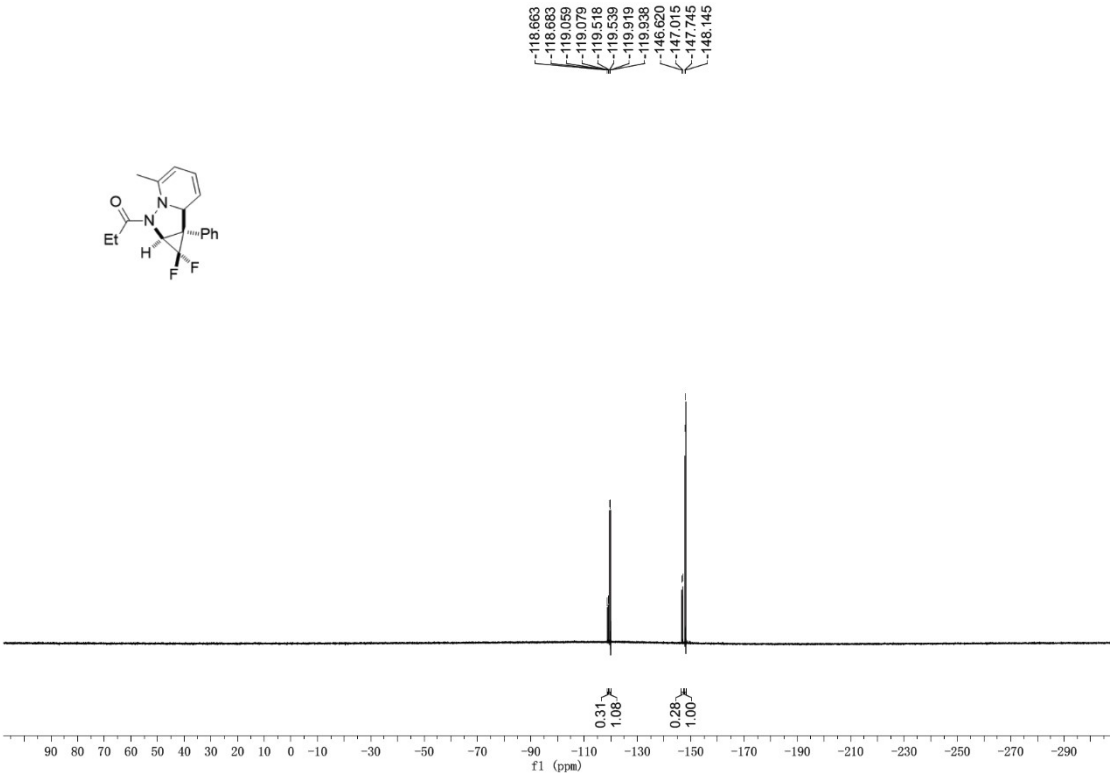
3ja-^{1}H NMR (400 MHz, $CDCl_3$)



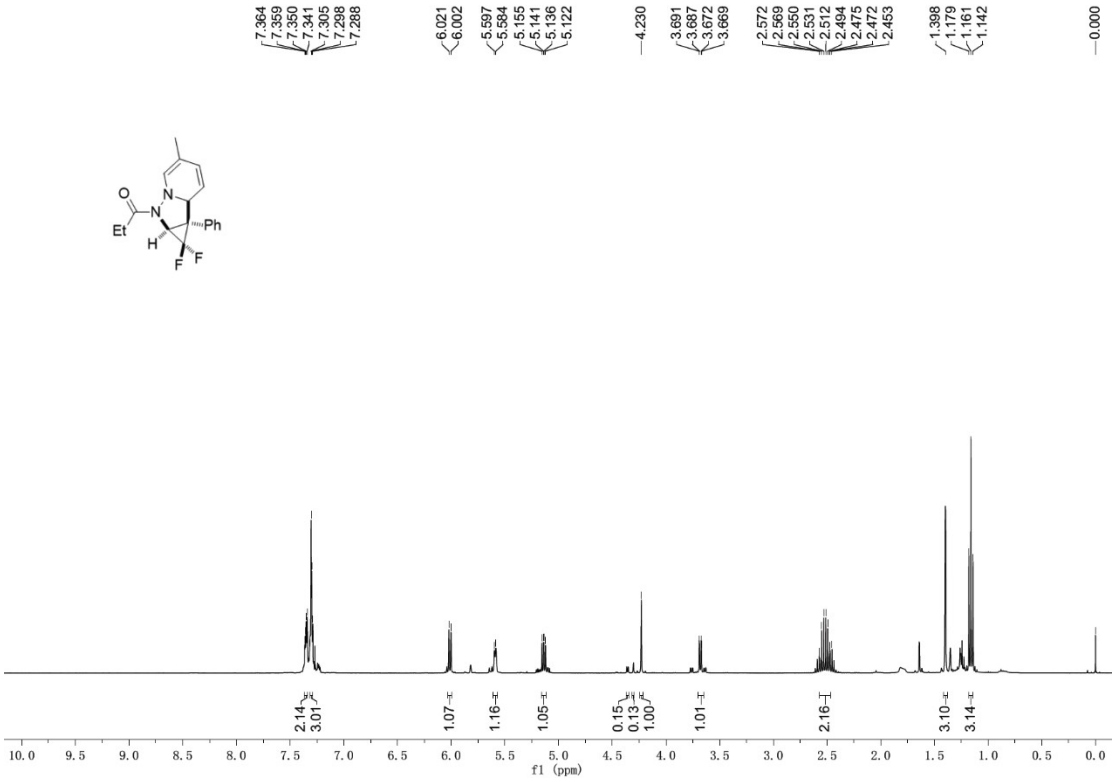
3ja-^{13}C NMR (100 MHz, $CDCl_3$)



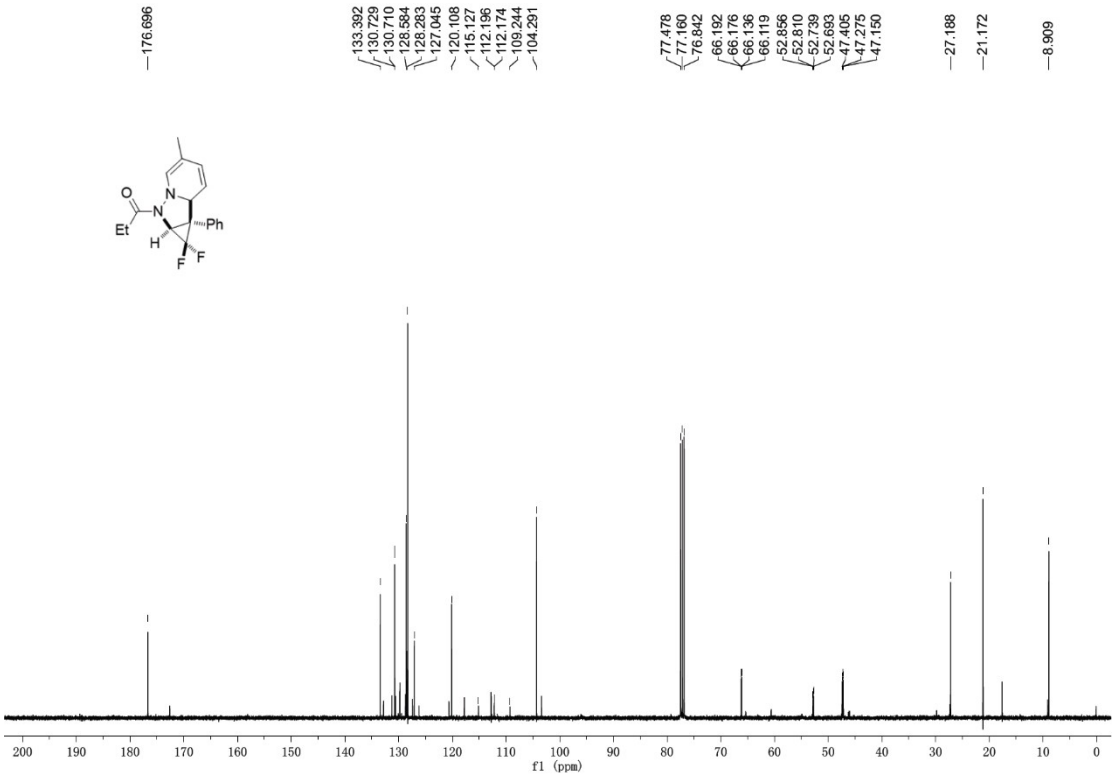
3ja-^{19}F NMR (376 MHz, $CDCl_3$)



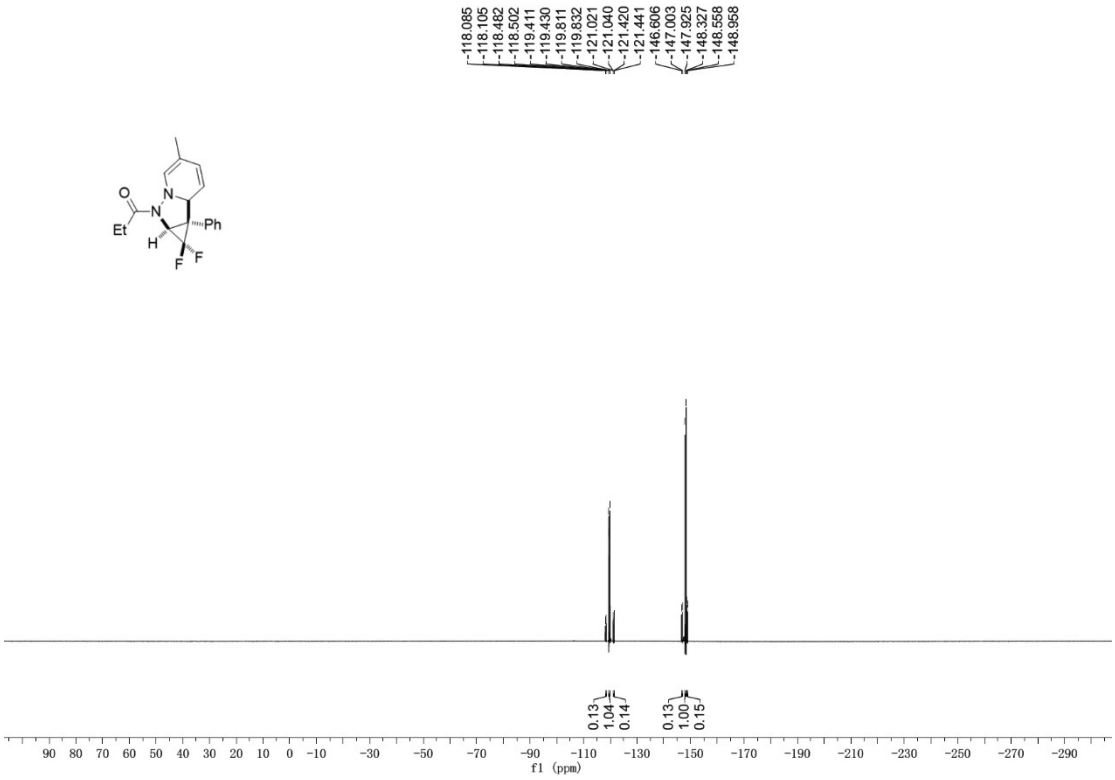
3ka-^{1}H NMR (400 MHz, $CDCl_3$)



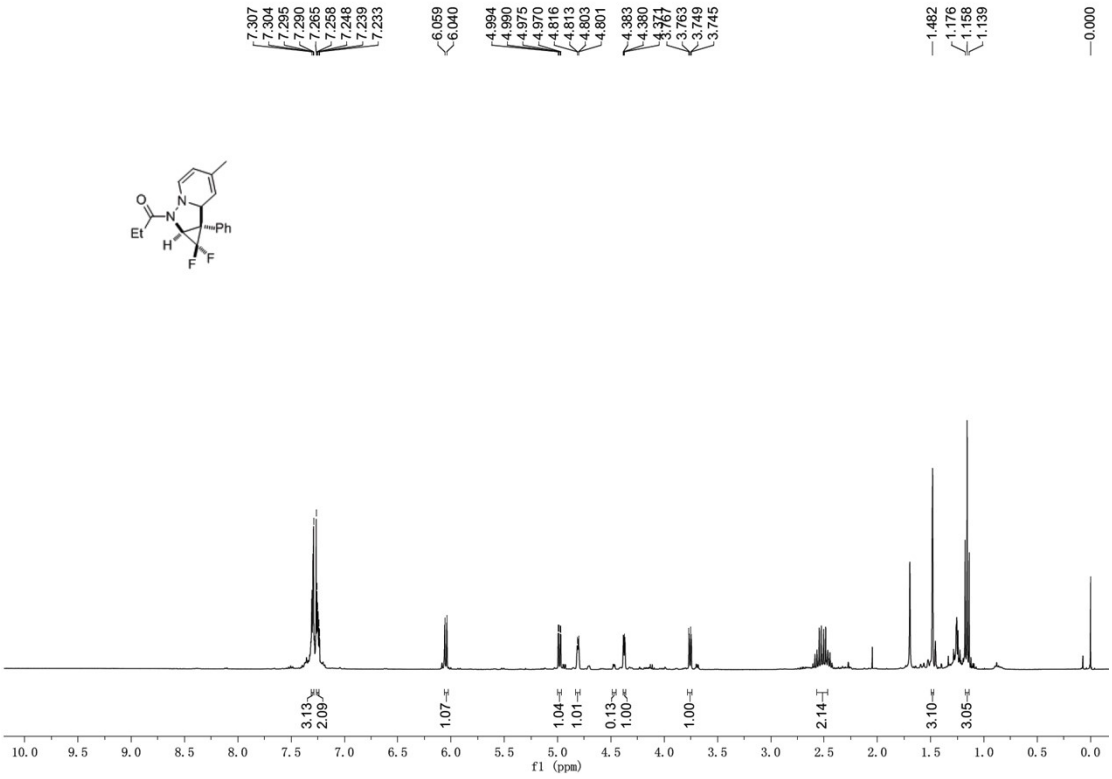
3ka-^{13}C NMR (100 MHz, $CDCl_3$)



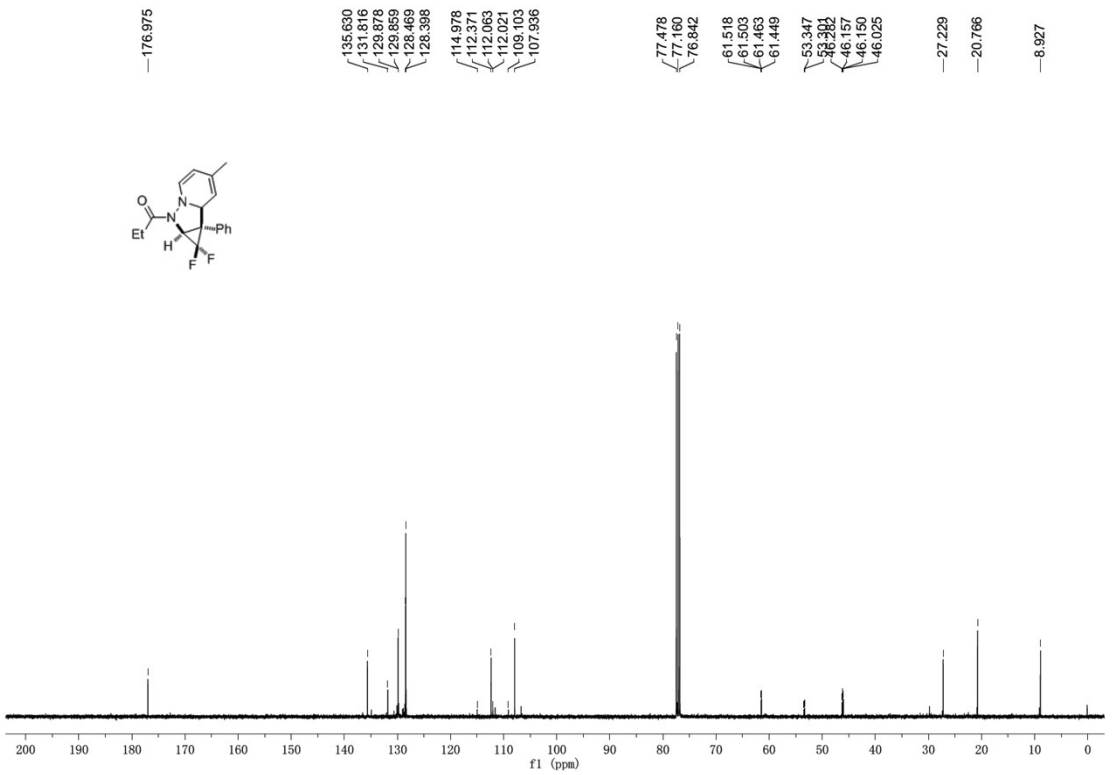
3ka-^{19}F NMR (376 MHz, $CDCl_3$)



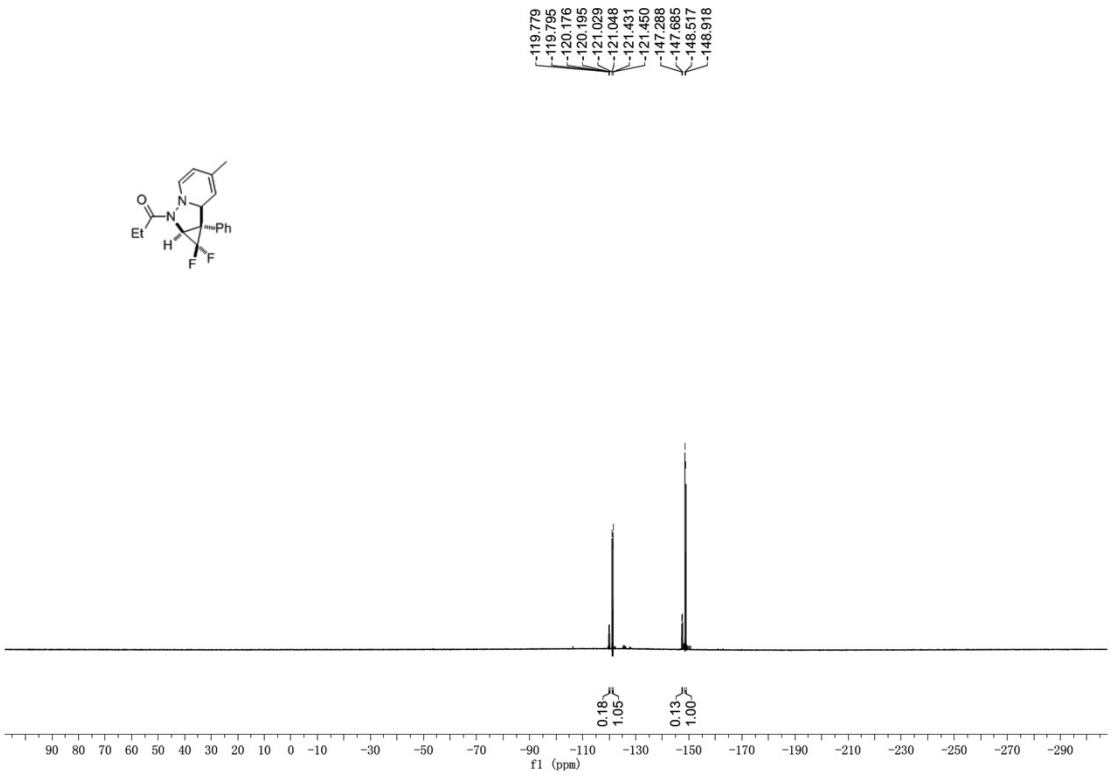
3la-^{1}H NMR (400 MHz, $CDCl_3$)



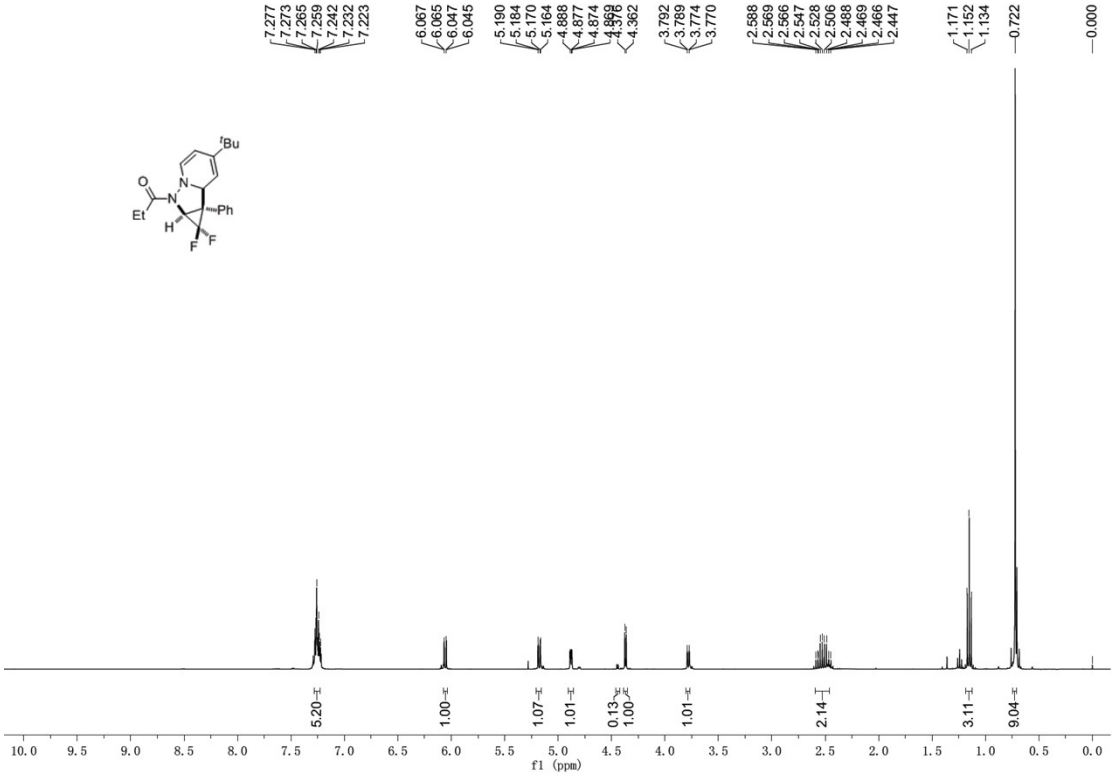
3la-^{13}C NMR (100 MHz, $CDCl_3$)



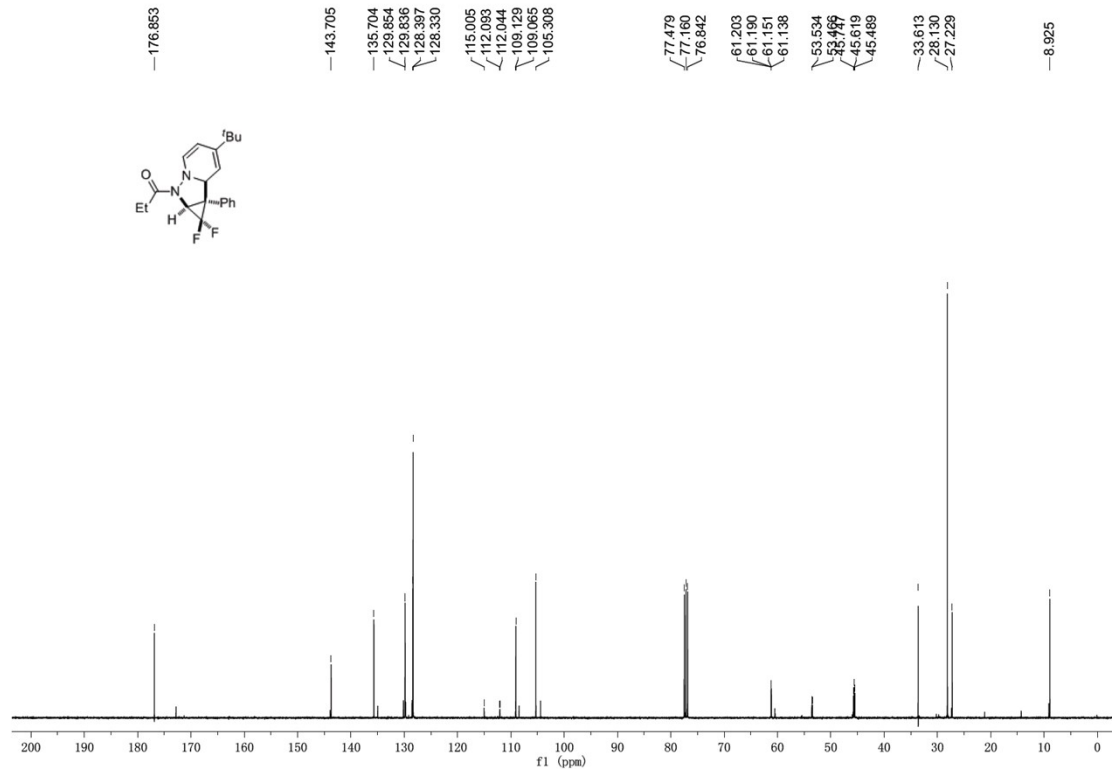
3la-^{19}F NMR (376 MHz, $CDCl_3$)



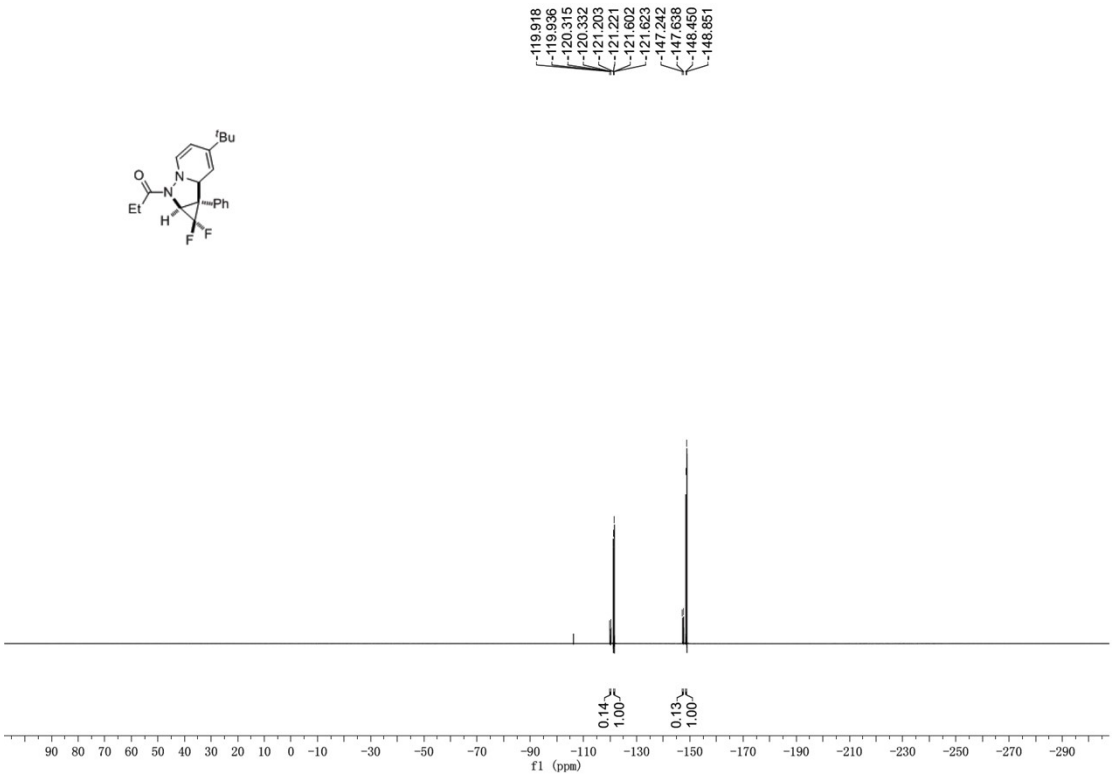
3ma-^{1}H NMR (400 MHz, $CDCl_3$)



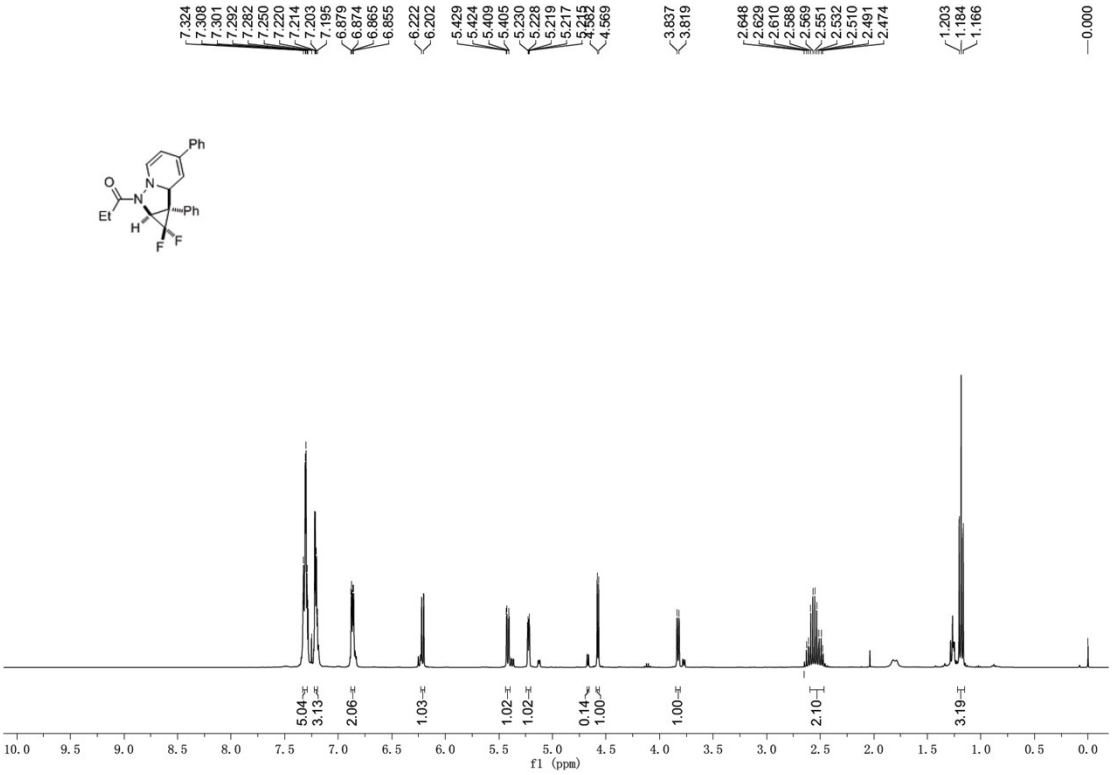
3ma-^{13}C NMR (100 MHz, $CDCl_3$)



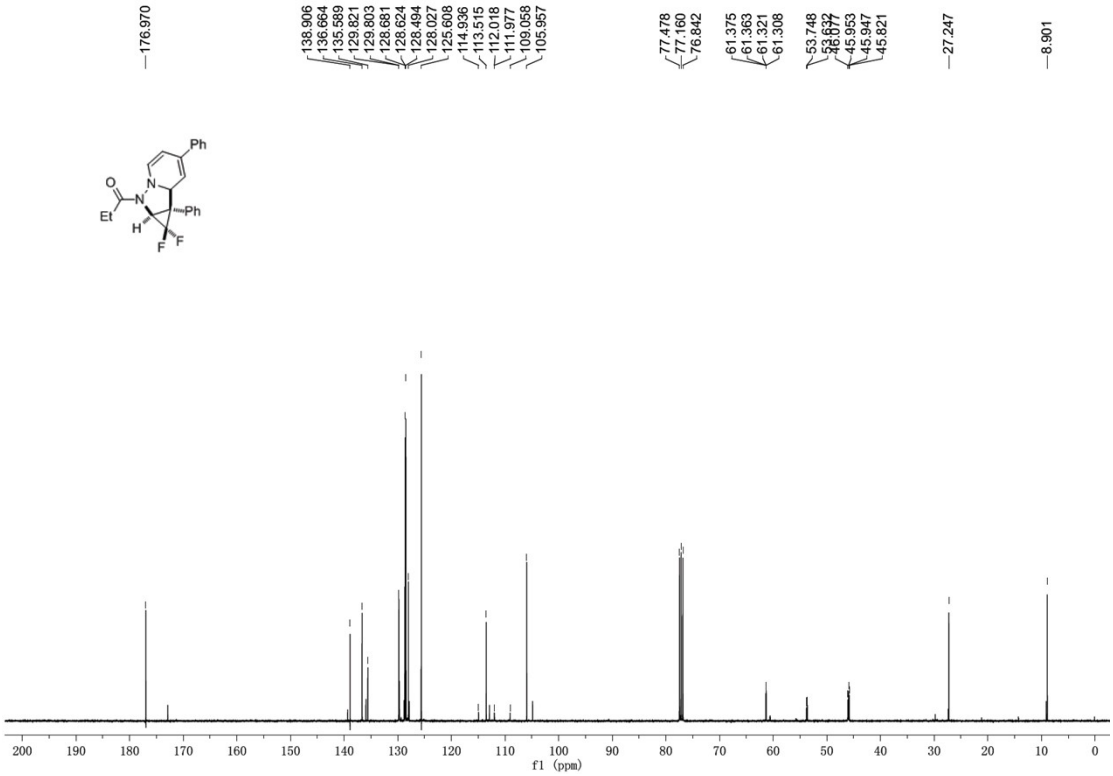
3ma-^{19}F NMR (376 MHz, $CDCl_3$)



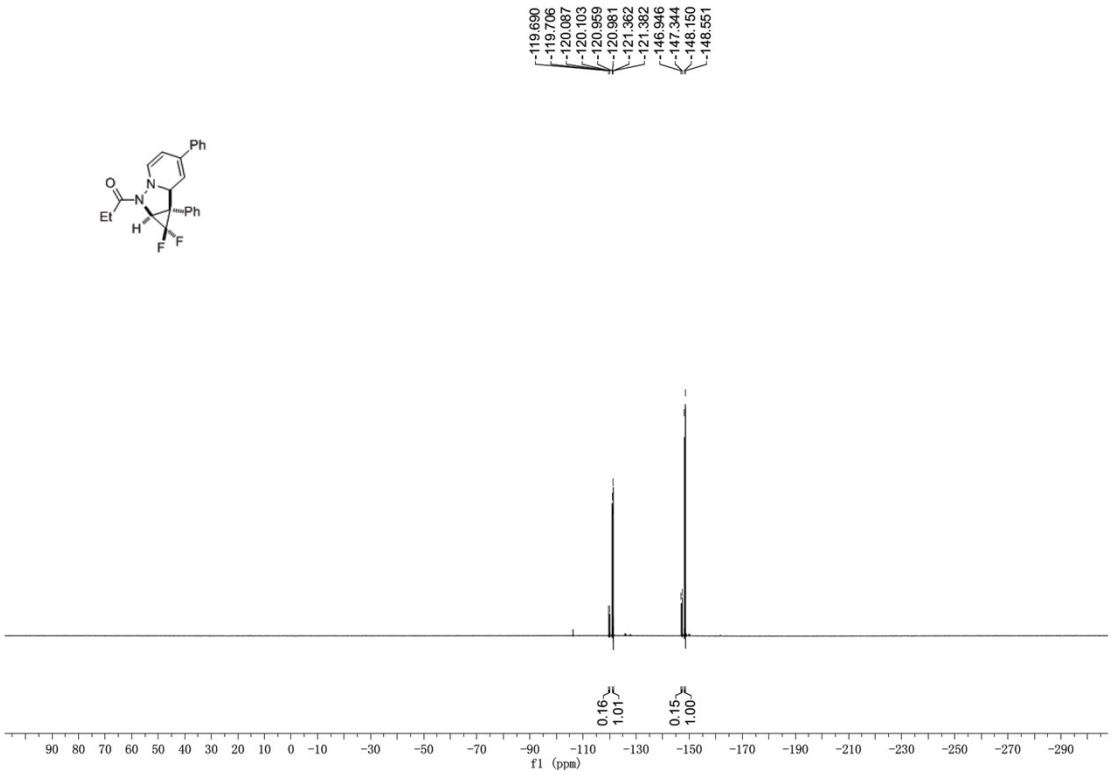
3na-^{1}H NMR (400 MHz, $CDCl_3$)



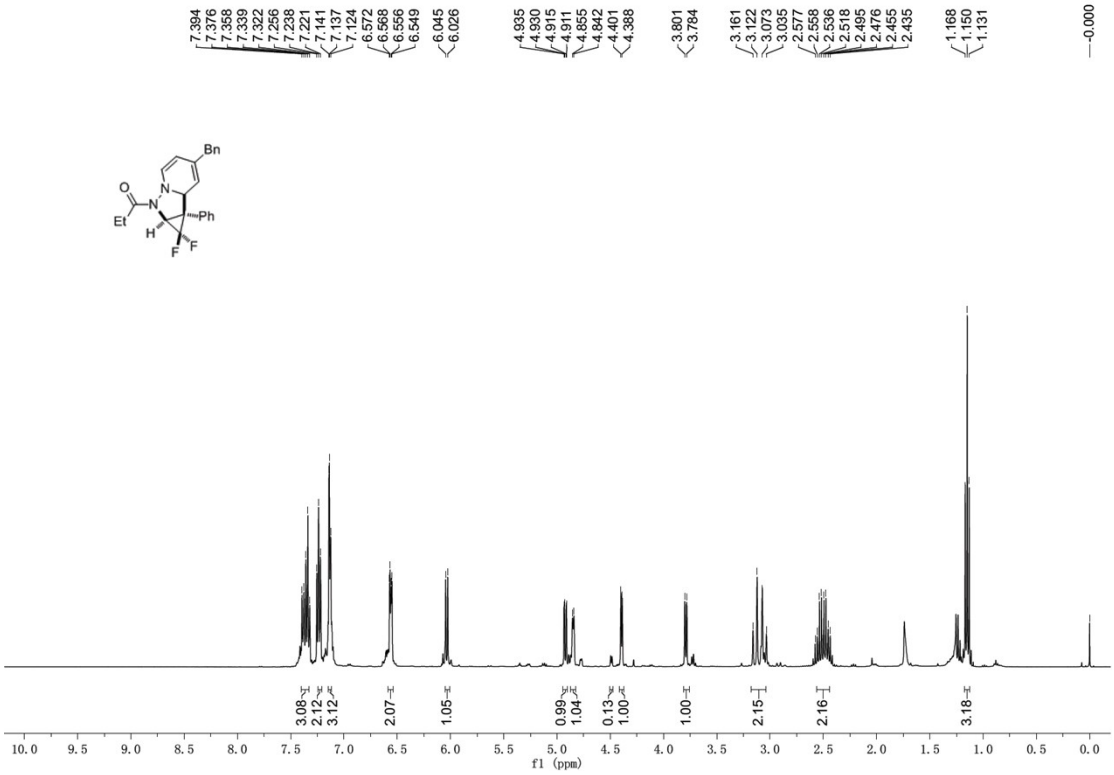
3na-^{13}C NMR (100 MHz, $CDCl_3$)



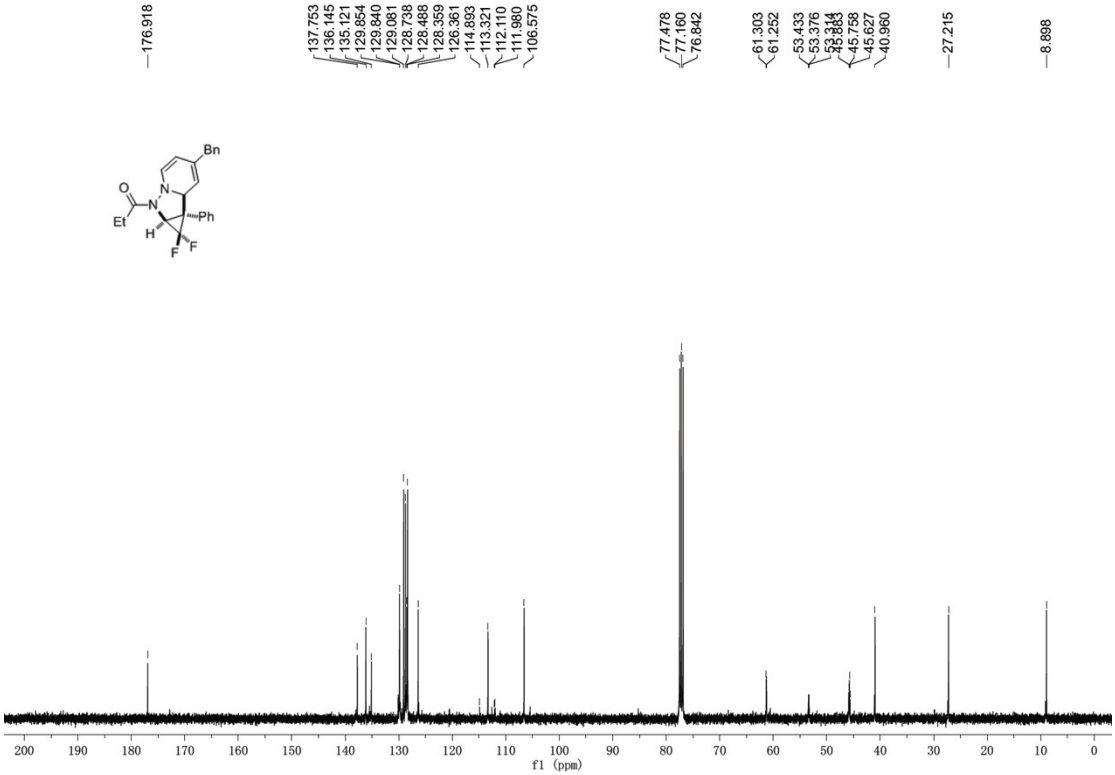
3na-^{19}F NMR (376 MHz, $CDCl_3$)



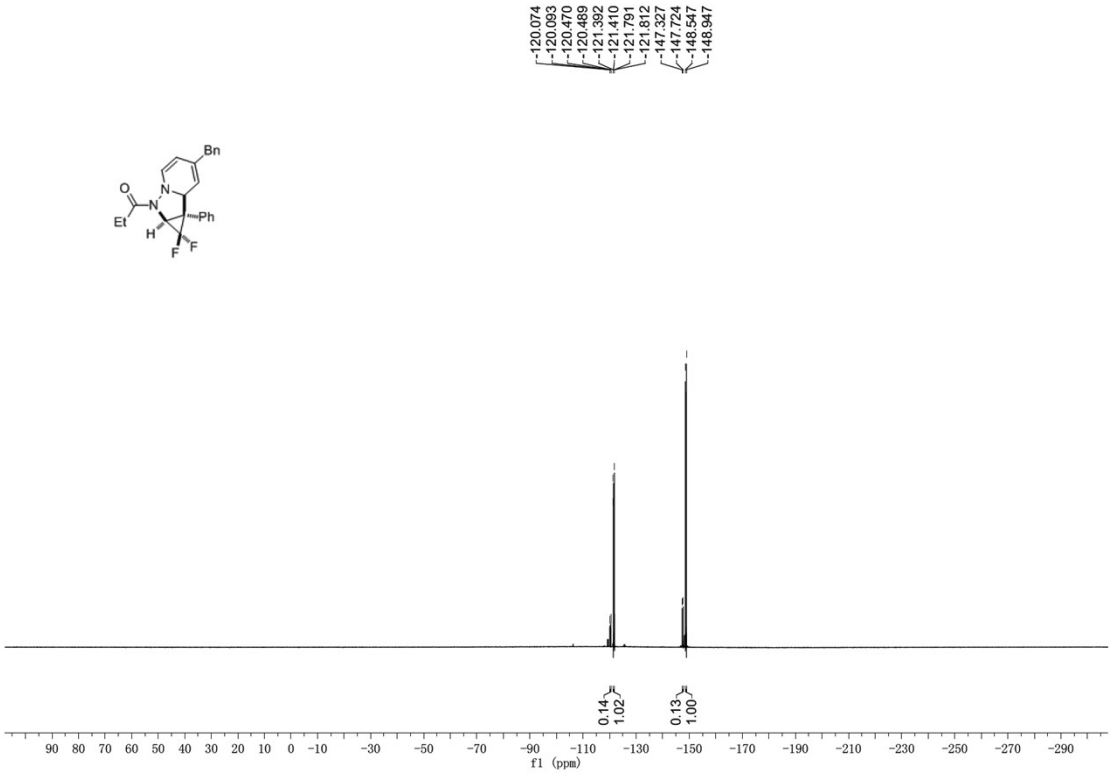
3oa-^{1}H NMR (400 MHz, $CDCl_3$)



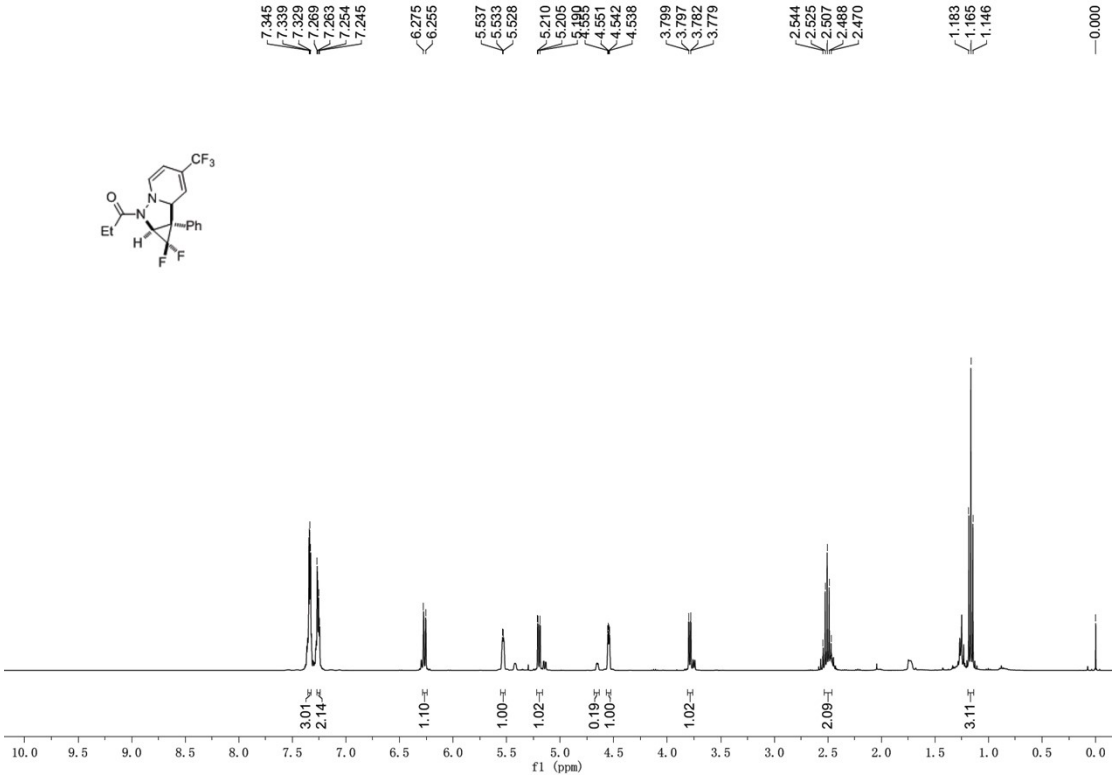
3oa-^{13}C NMR (100 MHz, $CDCl_3$)



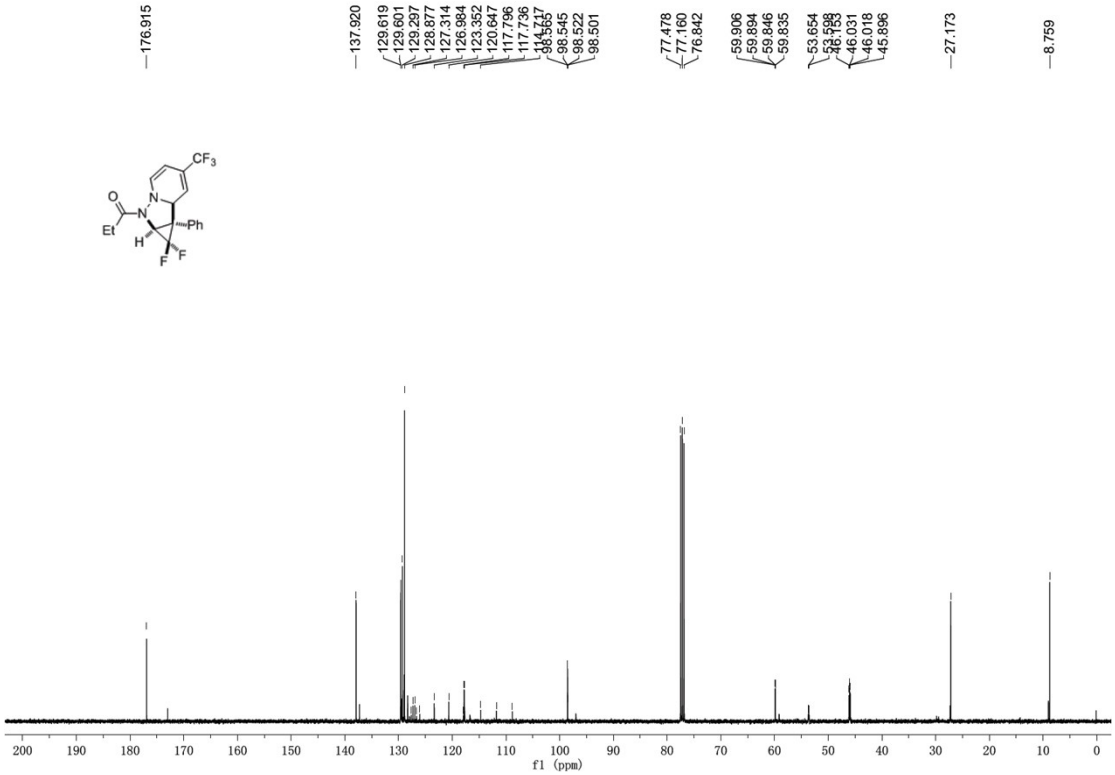
3oa-^{19}F NMR (376 MHz, $CDCl_3$)



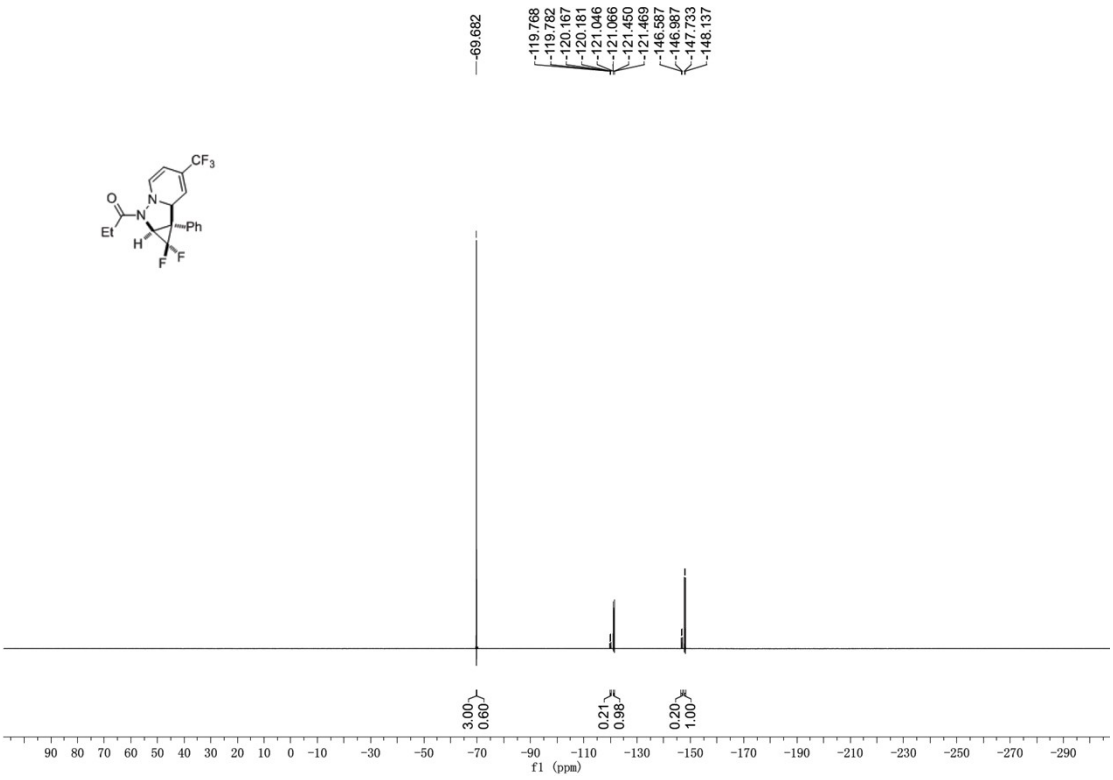
3pa-^{1}H NMR (400 MHz, $CDCl_3$)



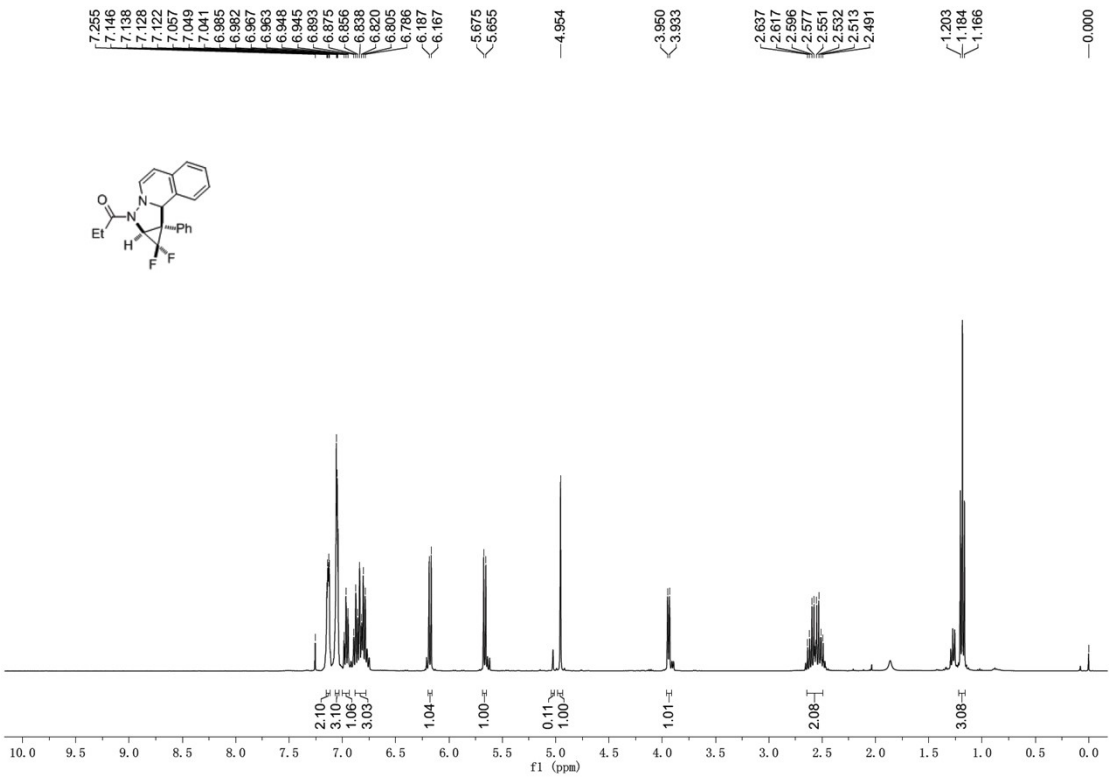
3pa-^{13}C NMR (100 MHz, $CDCl_3$)



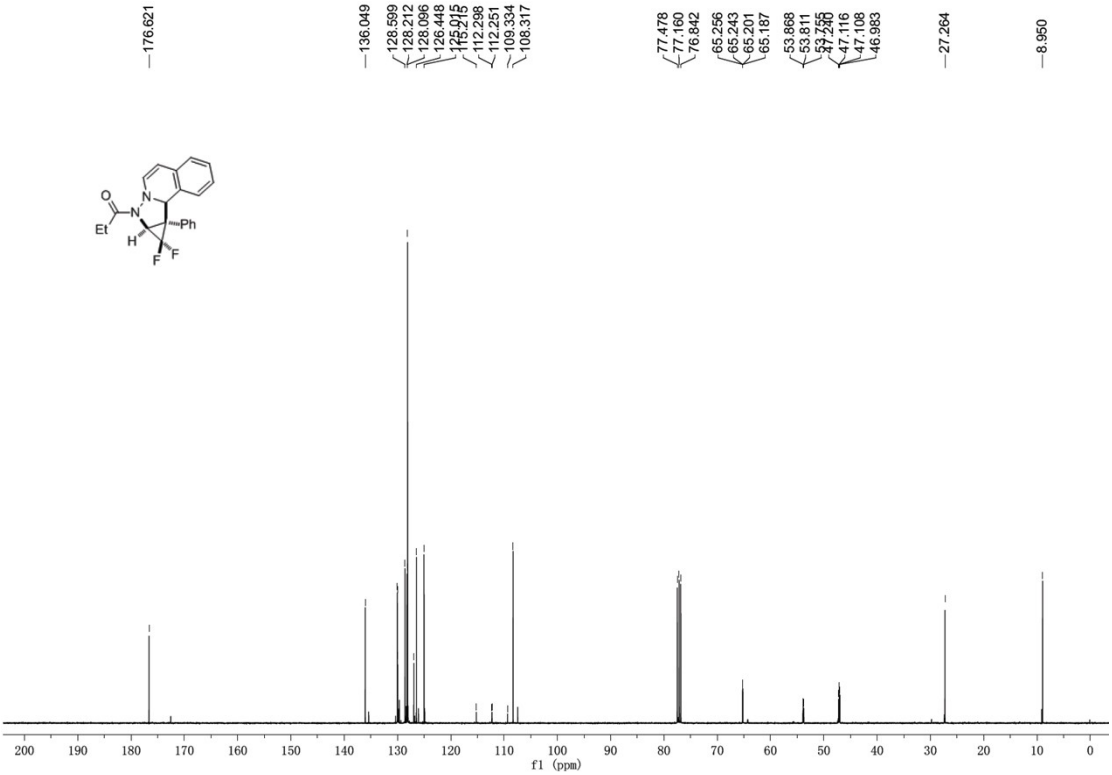
3pa-^{19}F NMR (376 MHz, $CDCl_3$)



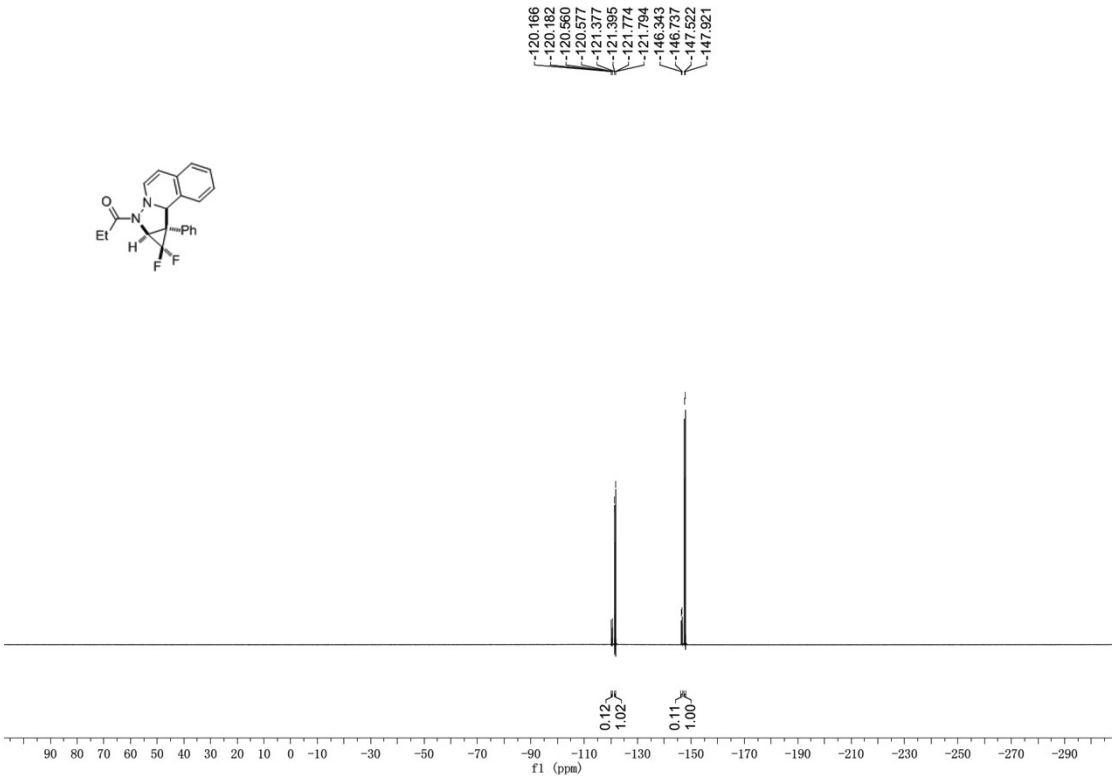
4aa-^{1}H NMR (400 MHz, $CDCl_3$)



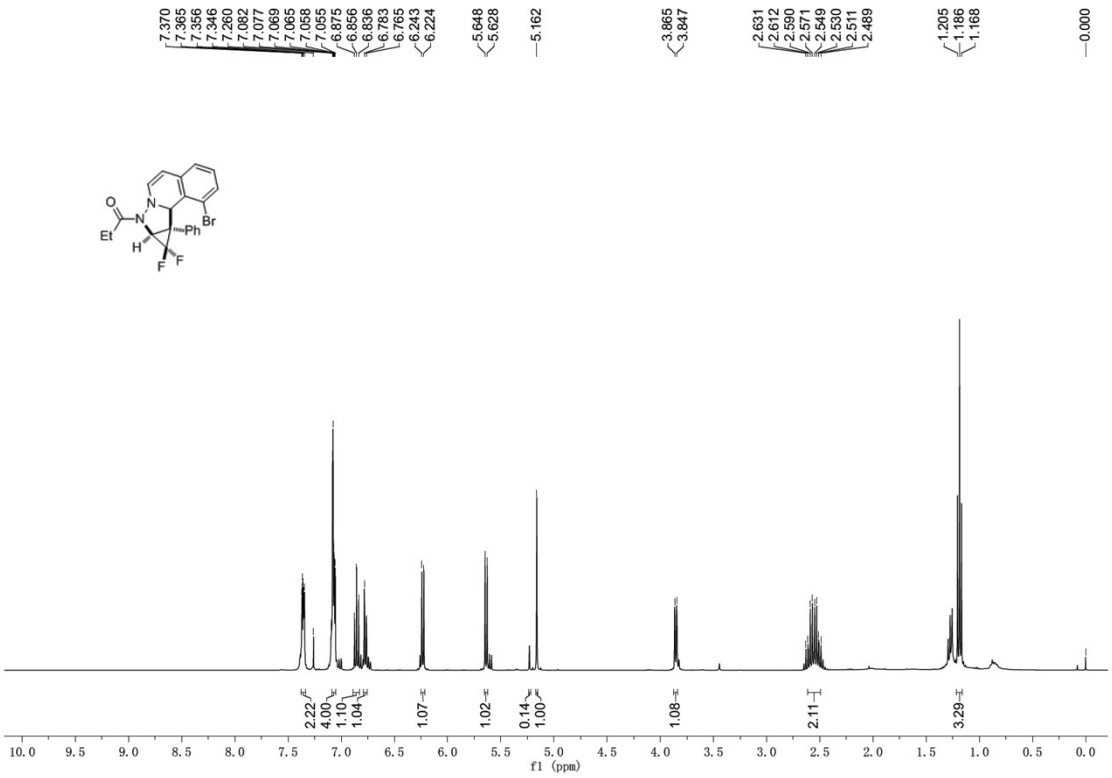
4aa-^{13}C NMR (100 MHz, $CDCl_3$)



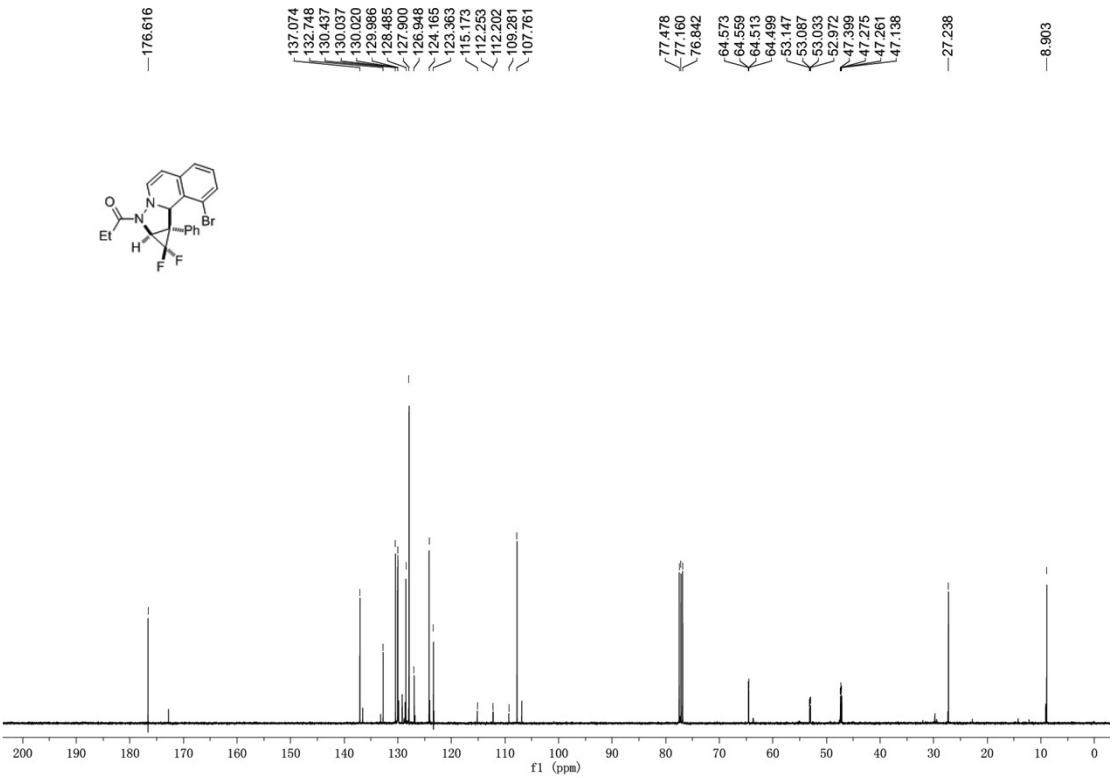
4aa-^{19}F NMR (376 MHz, $CDCl_3$)



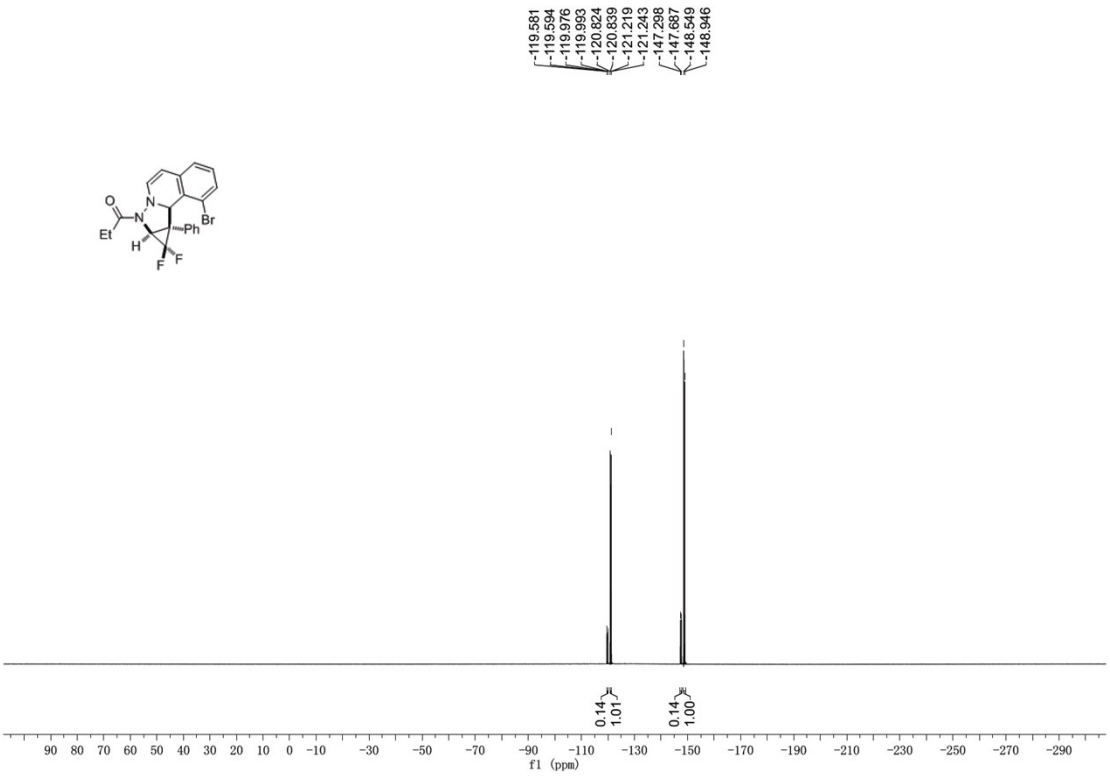
4ba-^{1}H NMR (400 MHz, $CDCl_3$)



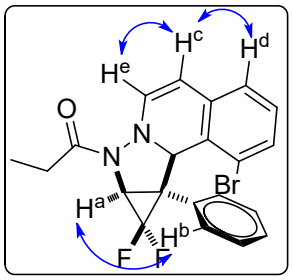
4ba-^{13}C NMR (100 MHz, $CDCl_3$)

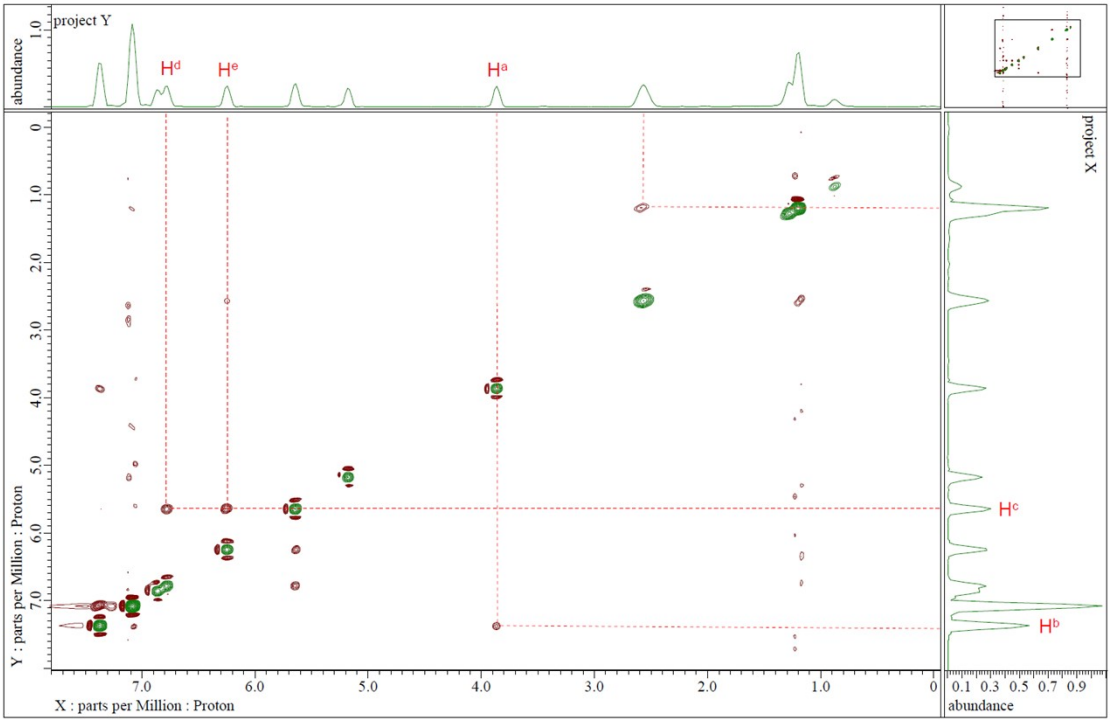


4ba-^{19}F NMR (376 MHz, $CDCl_3$)

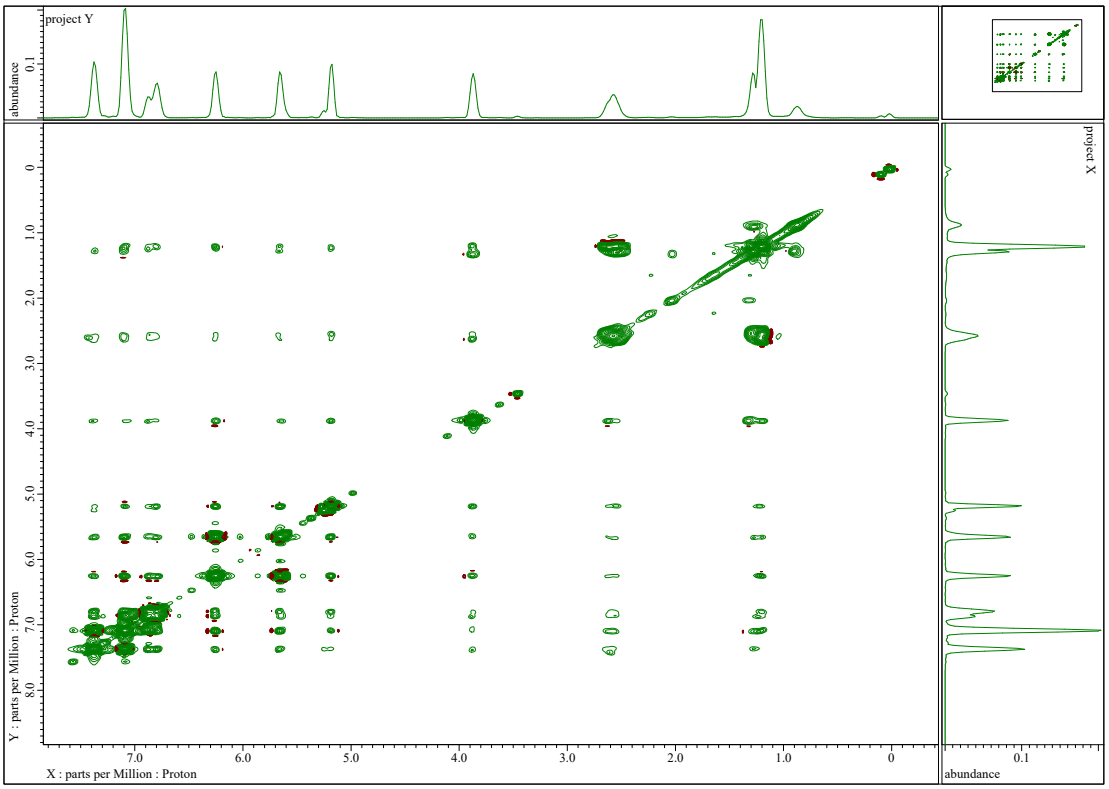


4ba-^{1}H-^{1}H NOESY (400 MHz, $CDCl_3$)

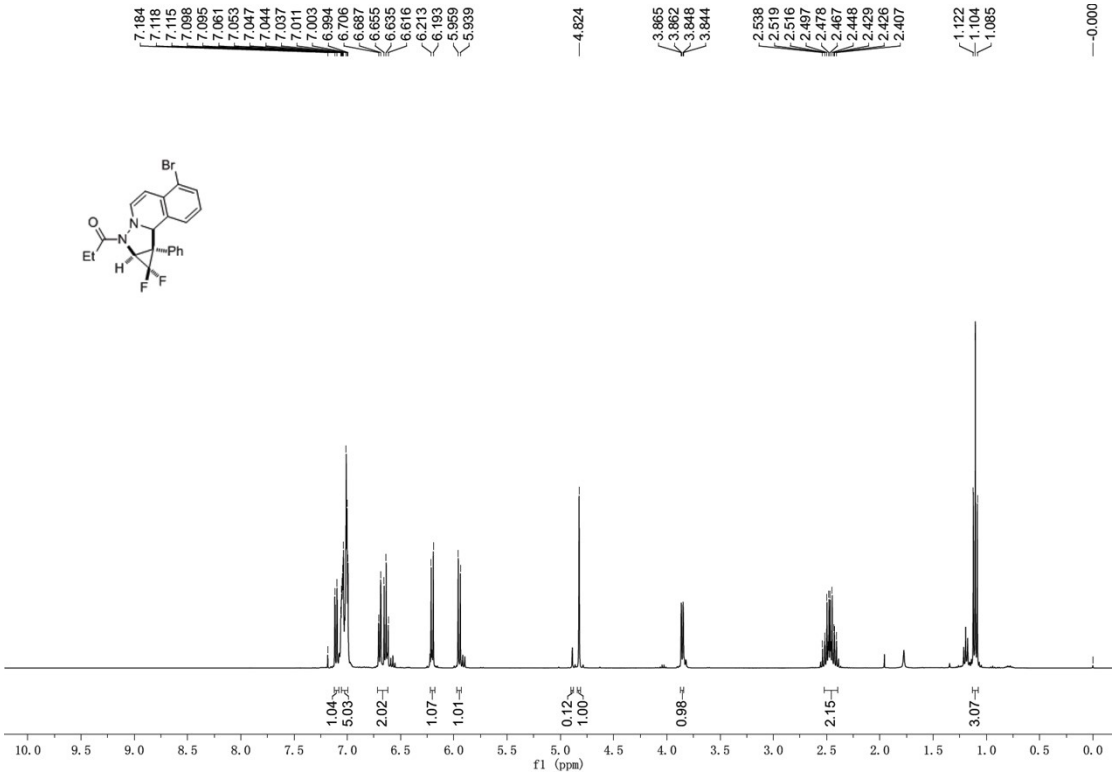




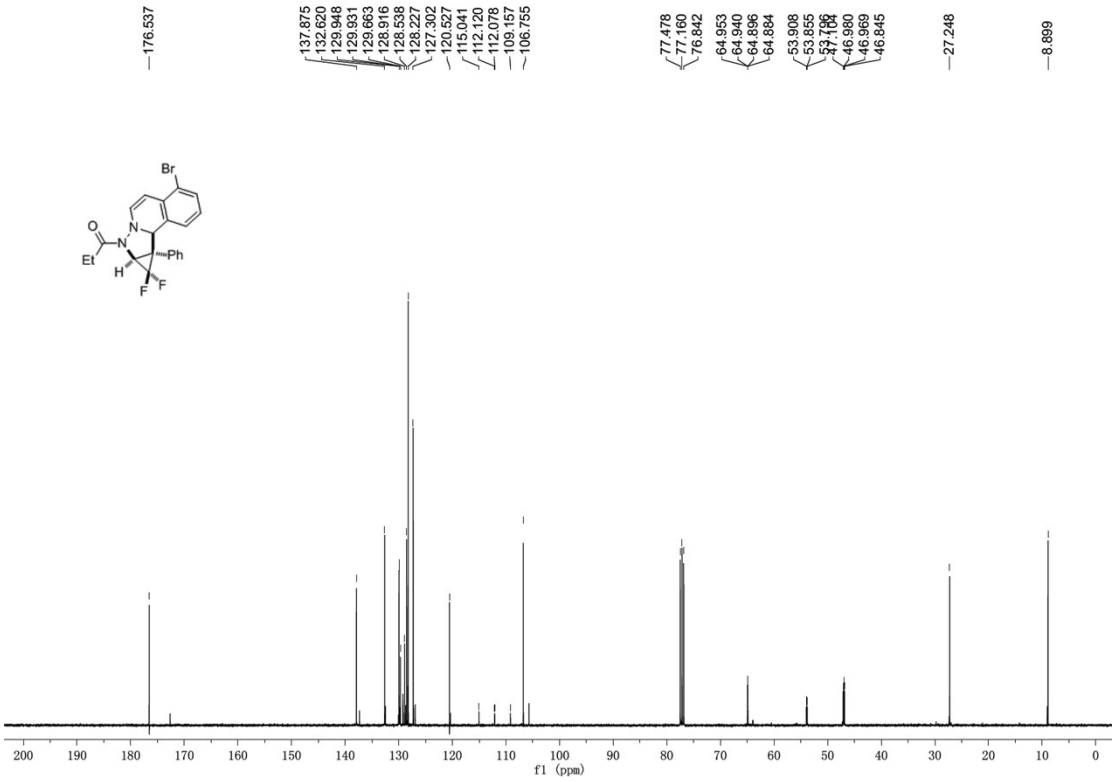
4ba-^{1}H-^{1}H COSY (400 MHz, $CDCl_3$)



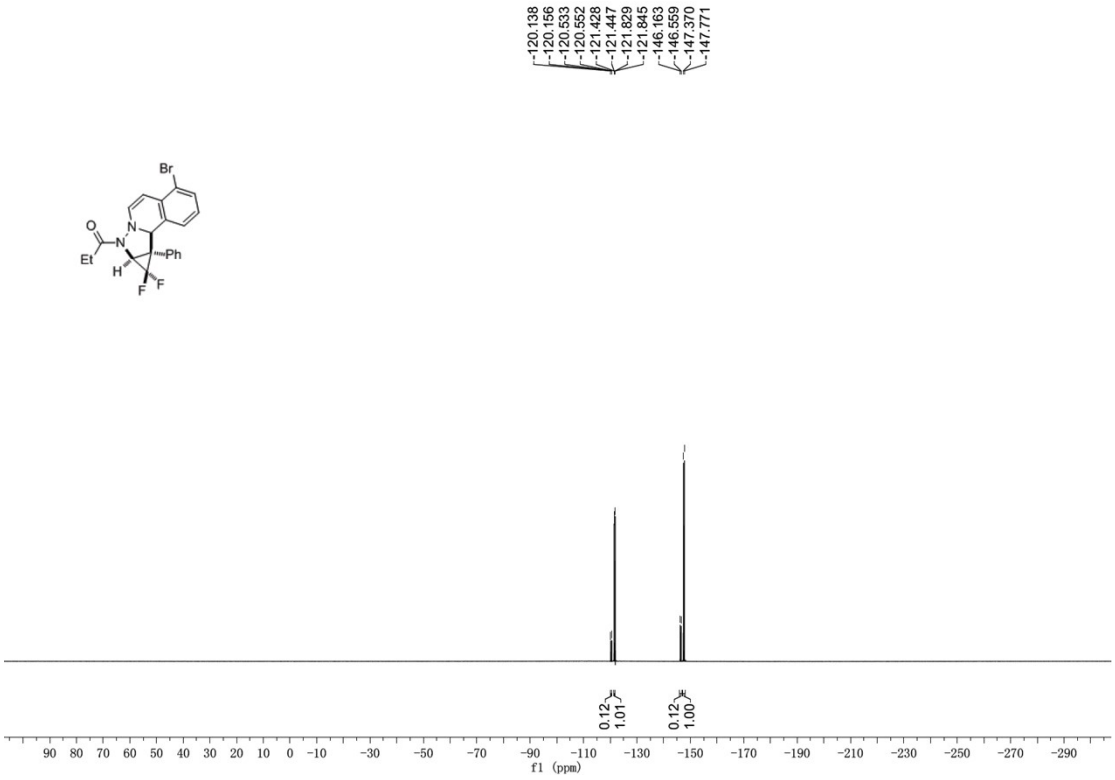
4ca-^{1}H NMR (400 MHz, $CDCl_3$)



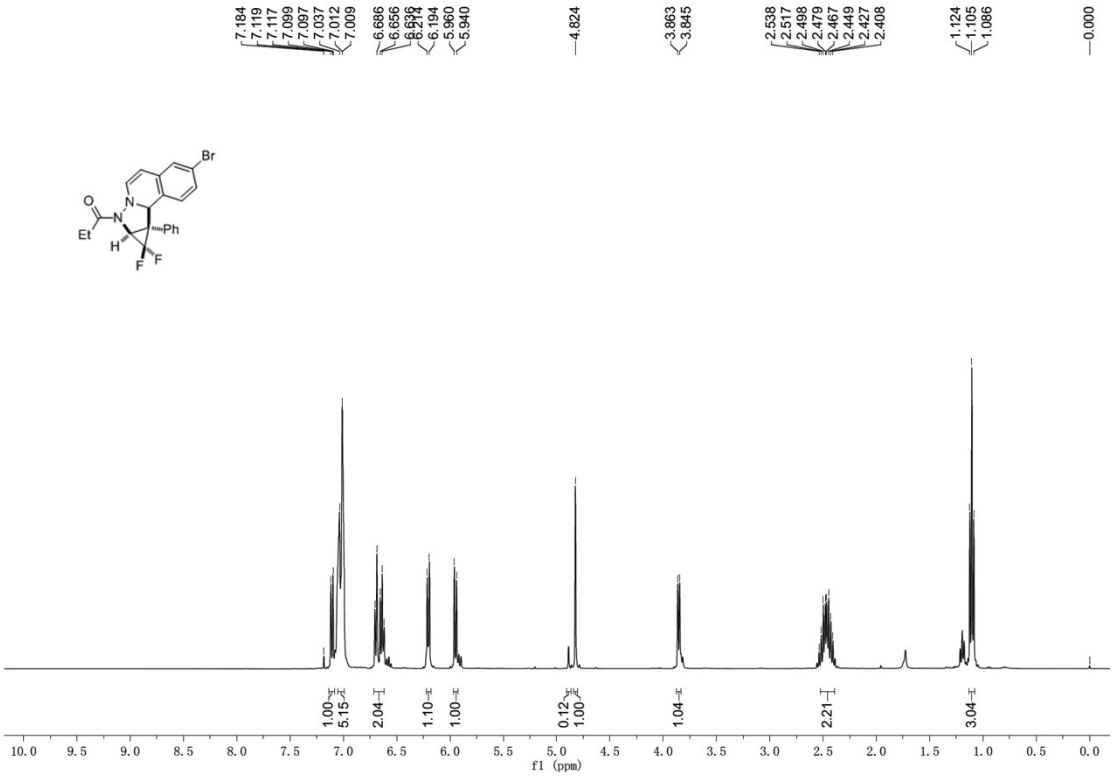
4ca-^{13}C NMR (100 MHz, $CDCl_3$)



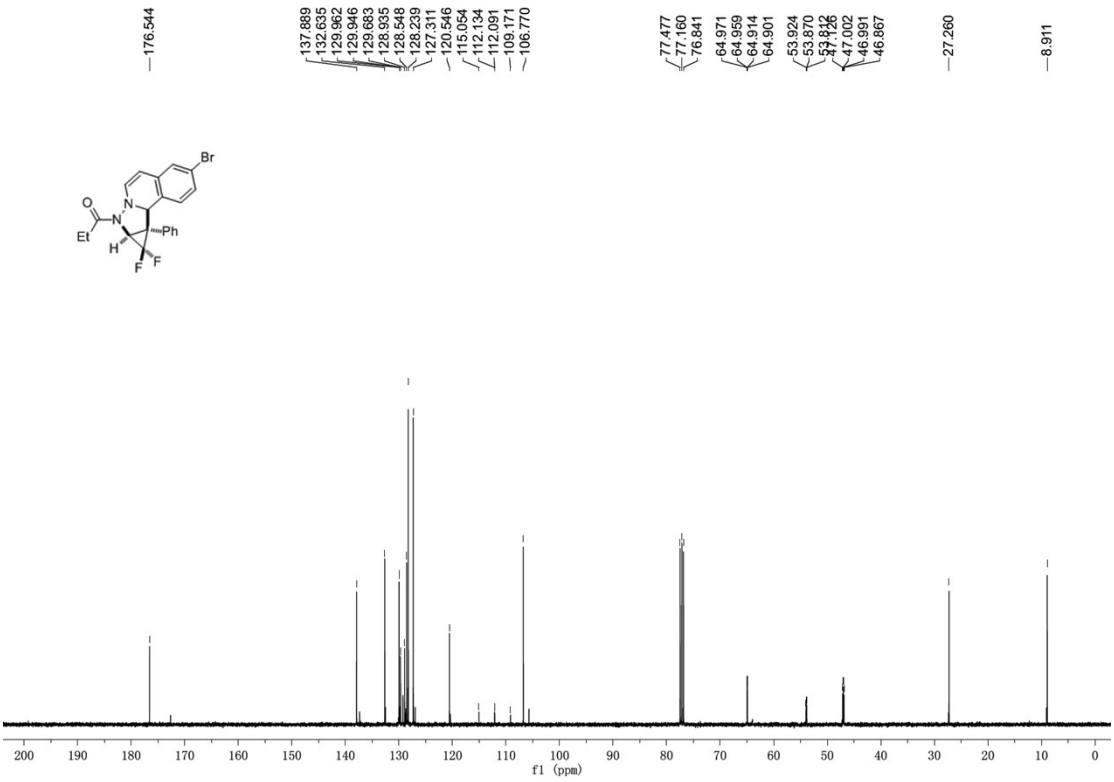
4ca-^{19}F NMR (376 MHz, $CDCl_3$)



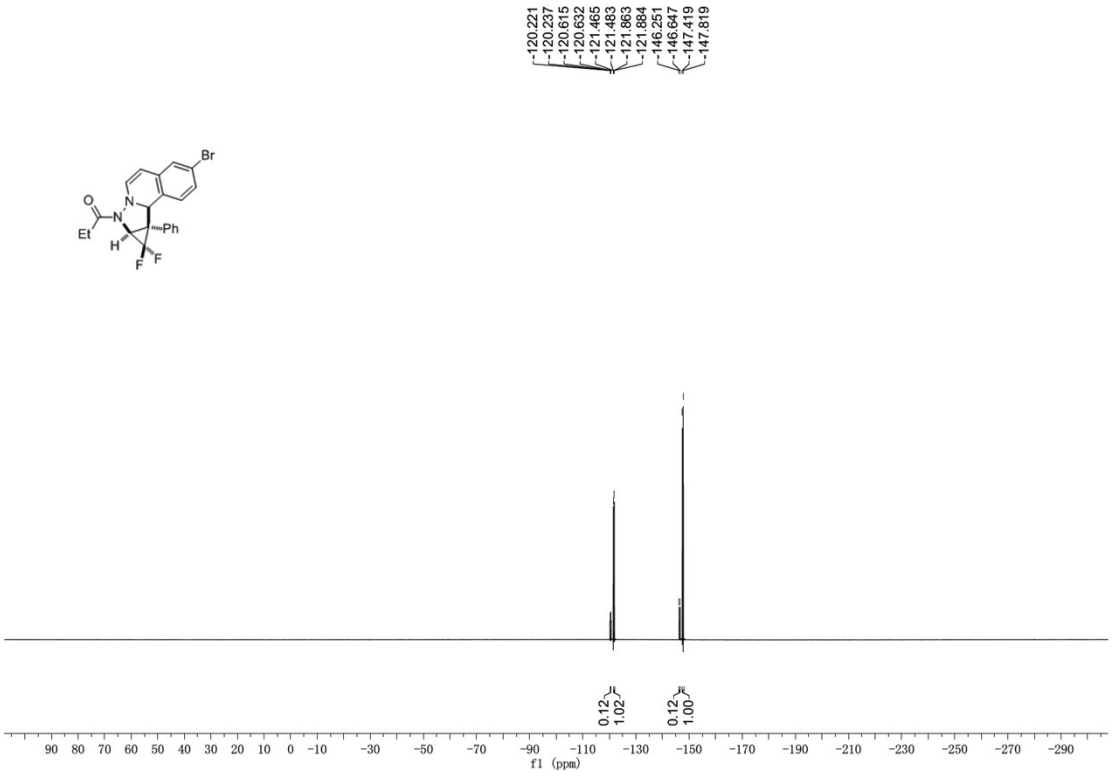
4da-^{1}H NMR (400 MHz, $CDCl_3$)



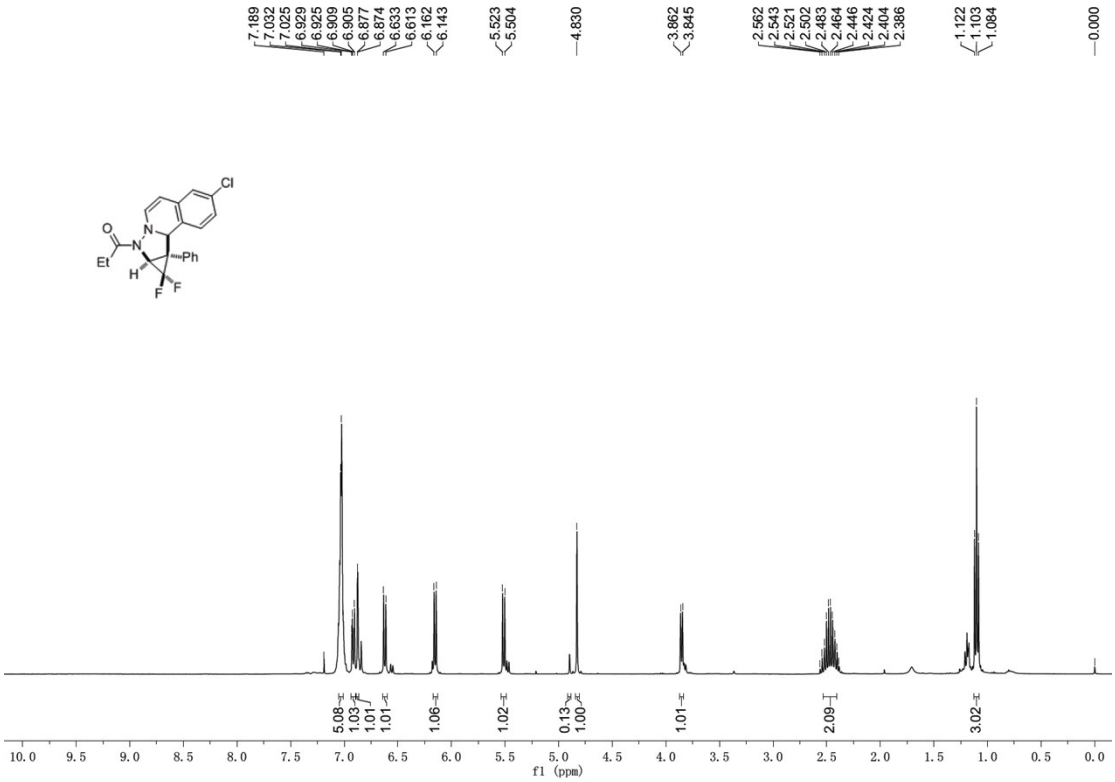
4da-^{13}C NMR (100 MHz, $CDCl_3$)



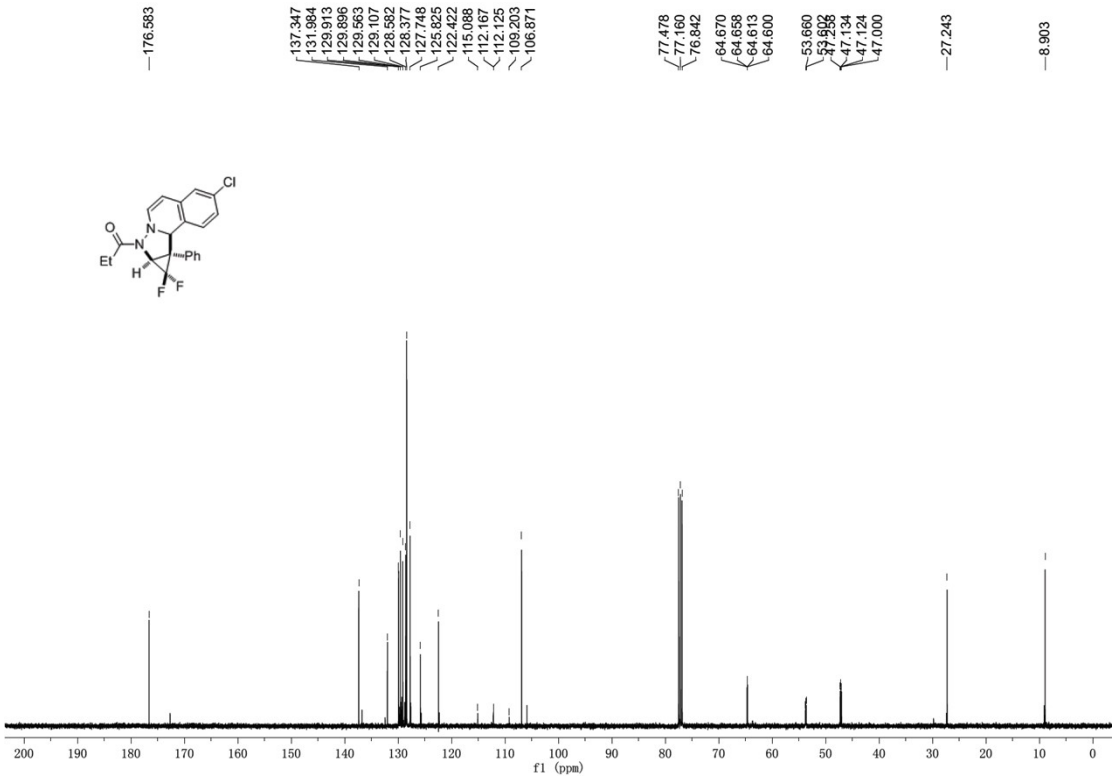
4da-^{19}F NMR (376 MHz, $CDCl_3$)



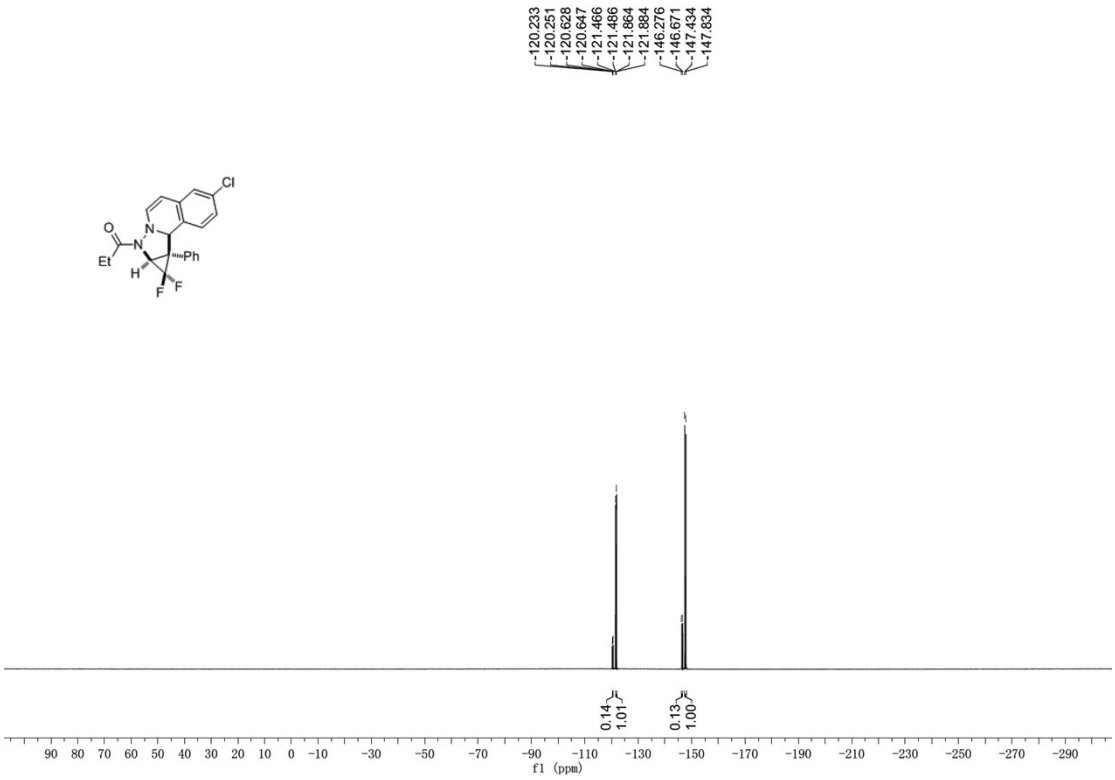
4ea-^{1}H NMR (400 MHz, $CDCl_3$)



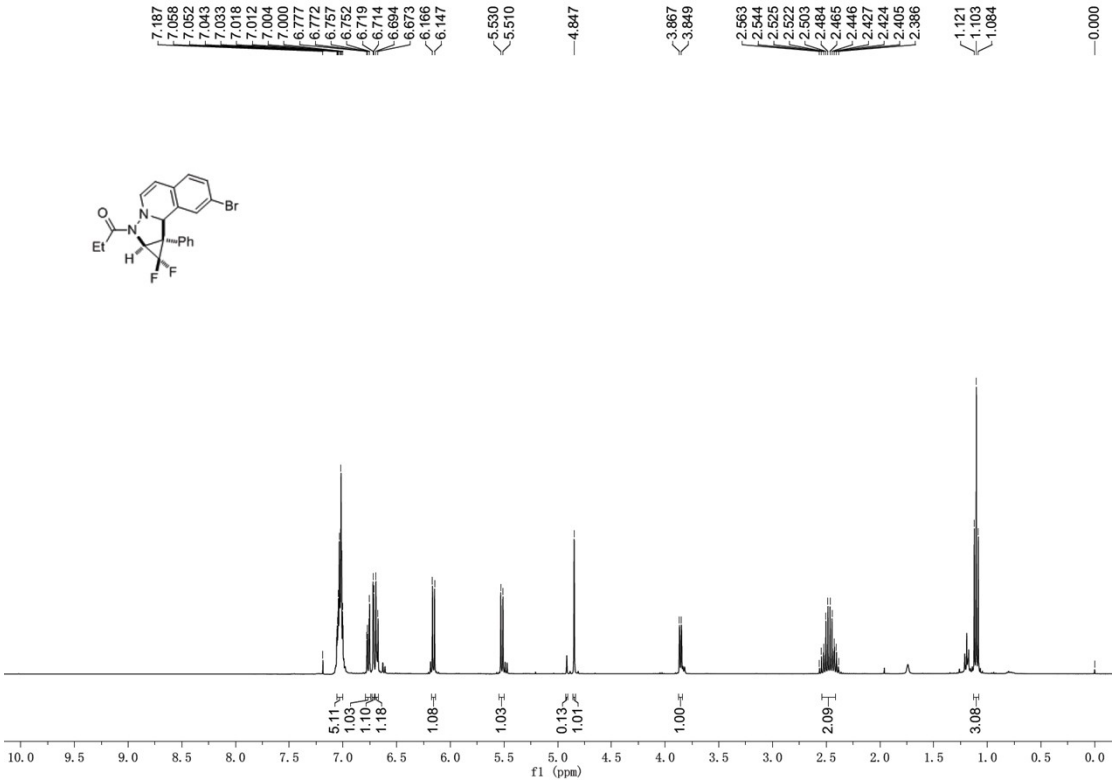
4ea-^{13}C NMR (100 MHz, $CDCl_3$)



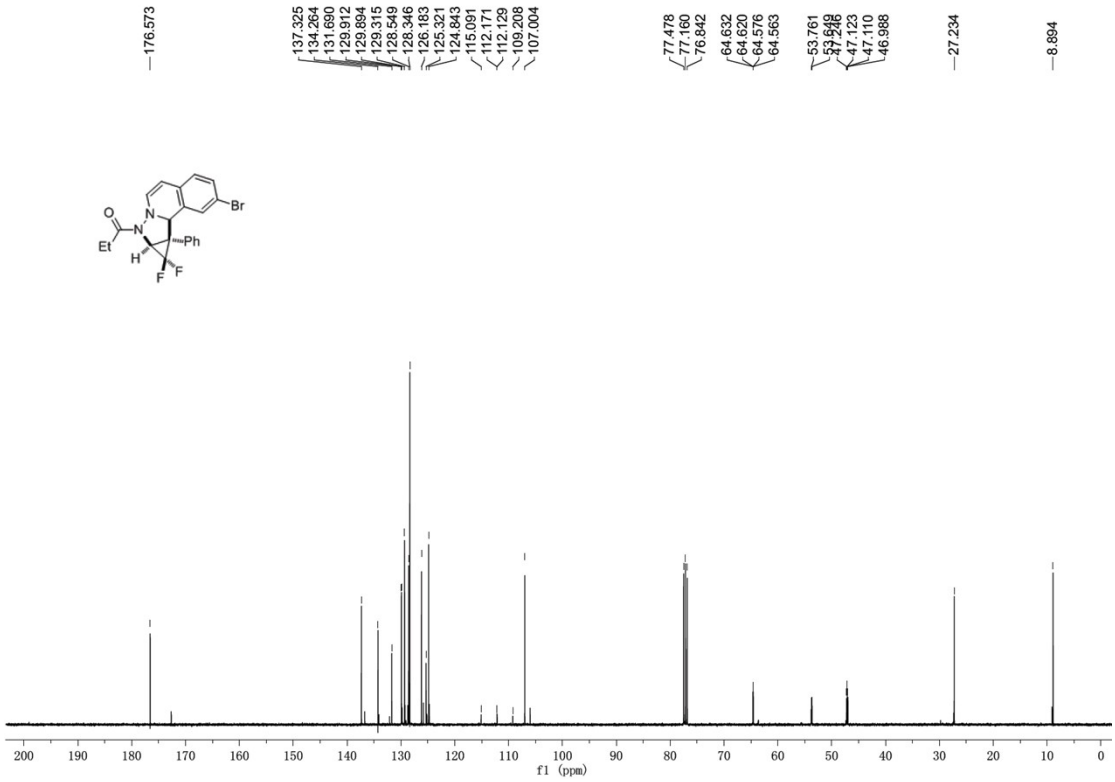
4ea-^{19}F NMR (376 MHz, $CDCl_3$)



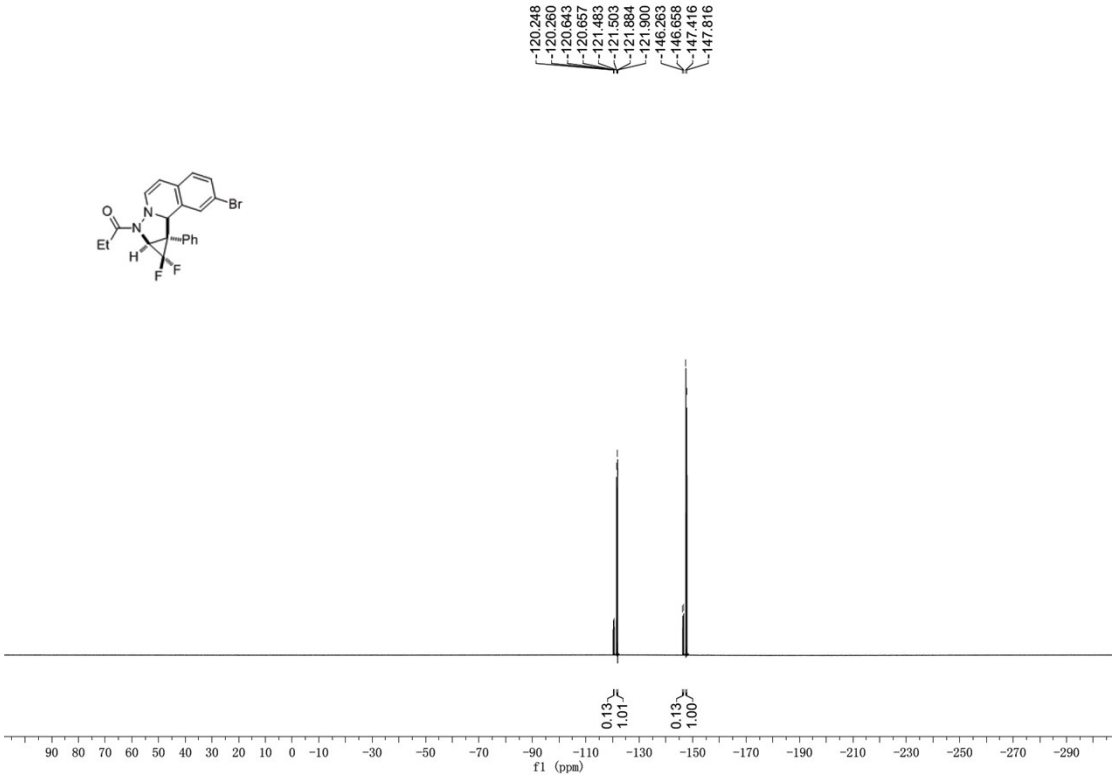
4fa-^{1}H NMR (400 MHz, $CDCl_3$)



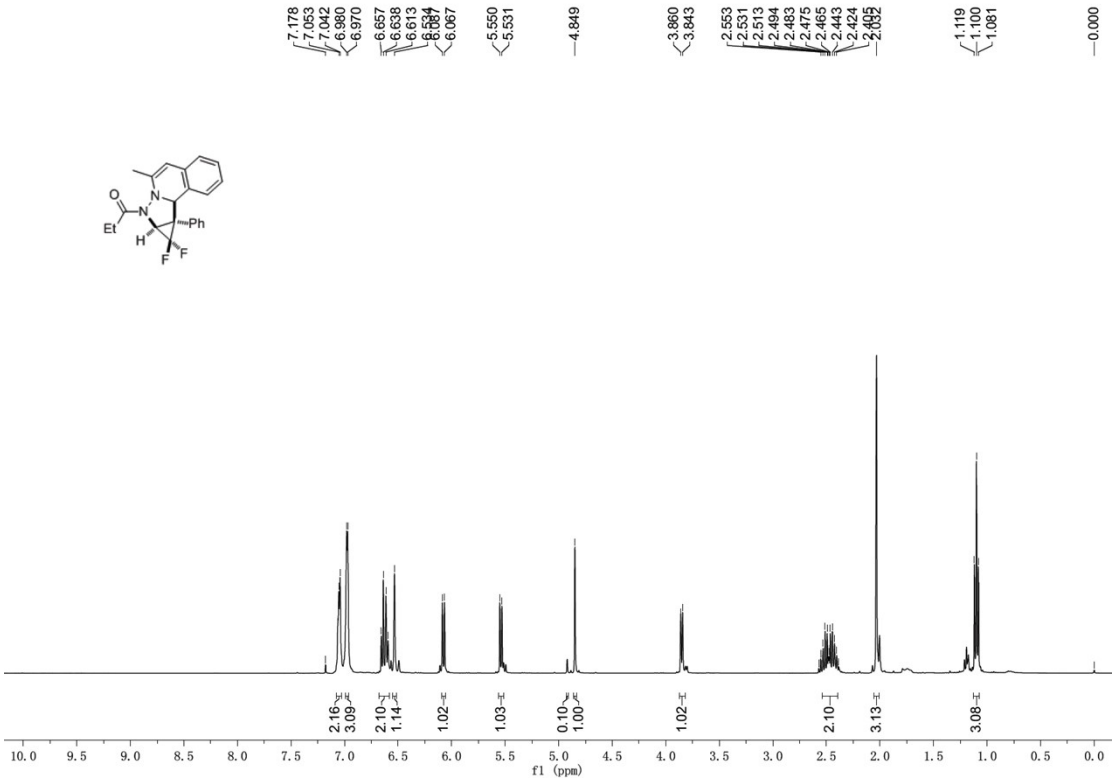
4fa-^{13}C NMR (100 MHz, $CDCl_3$)



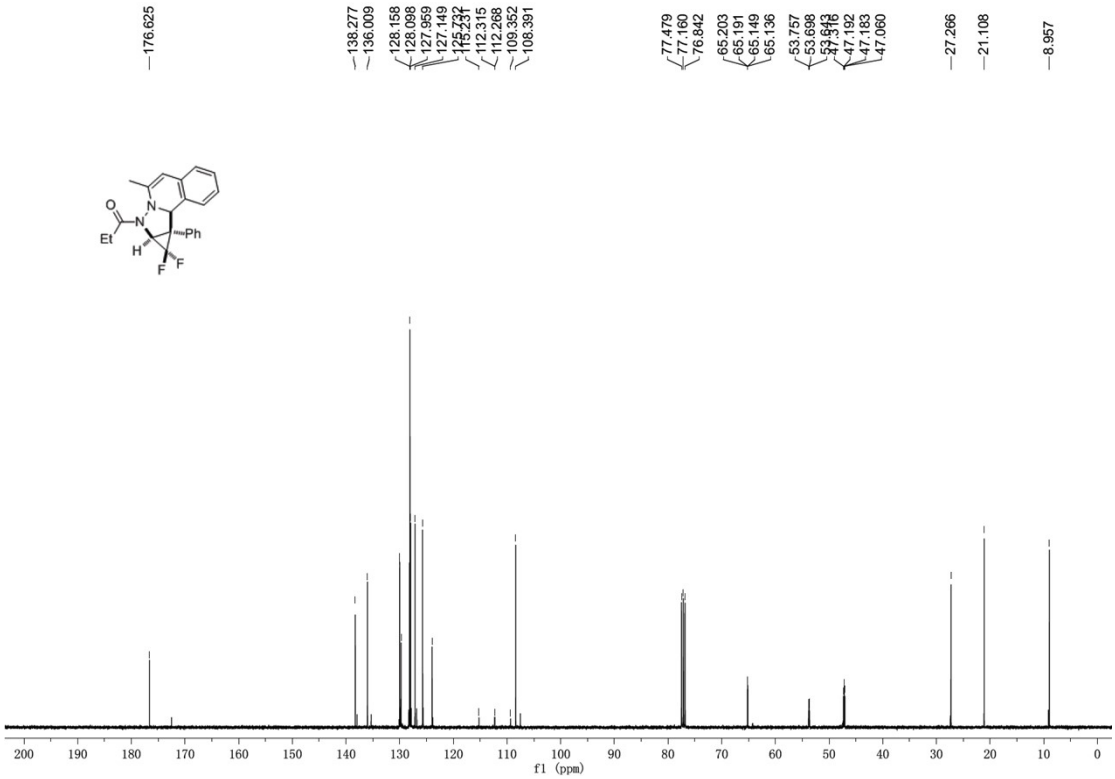
4fa-^{19}F NMR (376 MHz, $CDCl_3$)



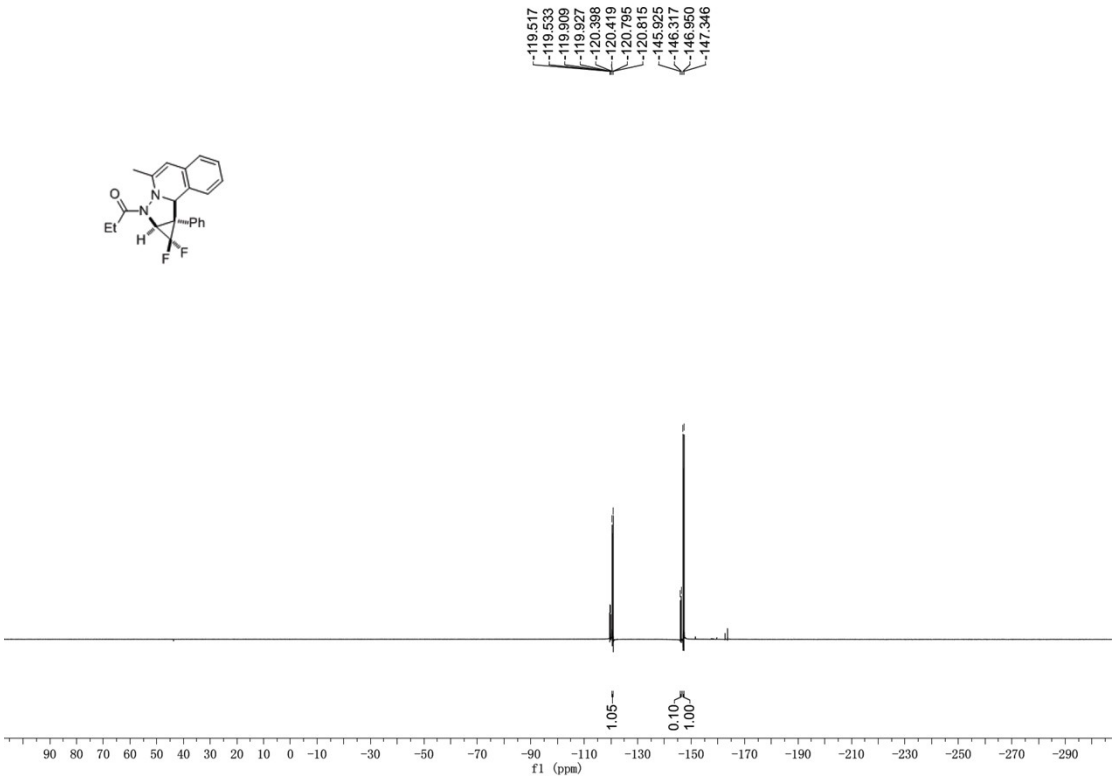
4ga-^{1}H NMR (400 MHz, $CDCl_3$)



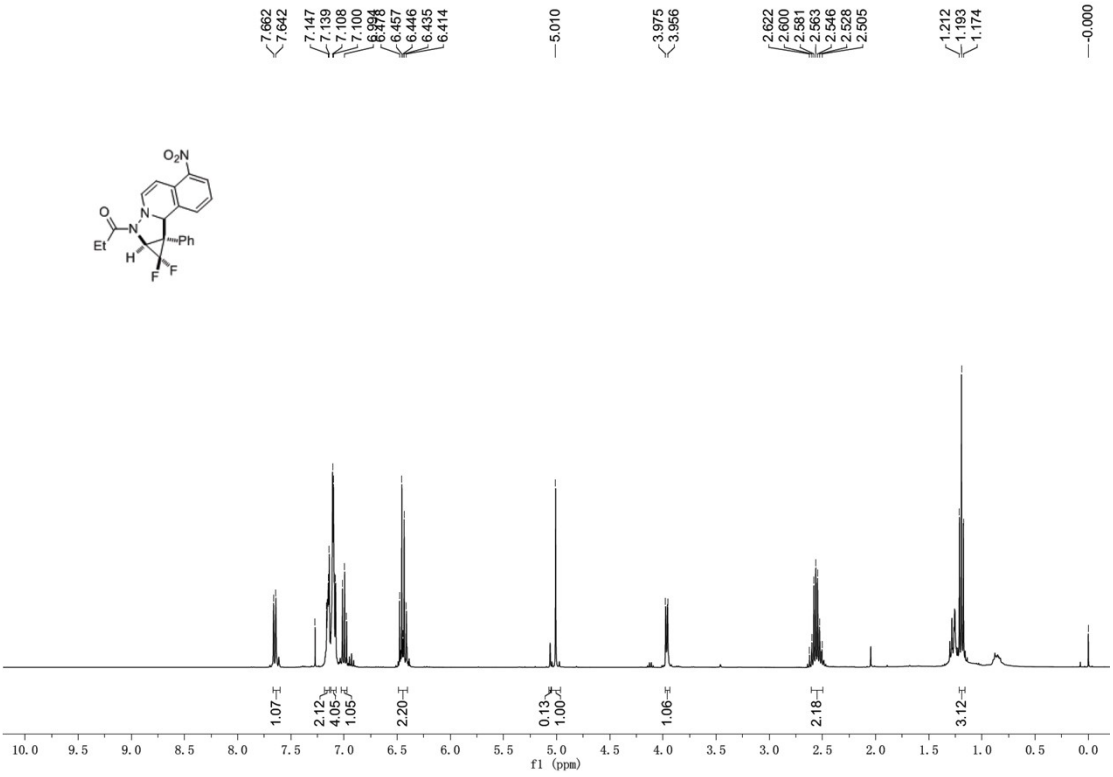
4ga-^{13}C NMR (100 MHz, $CDCl_3$)



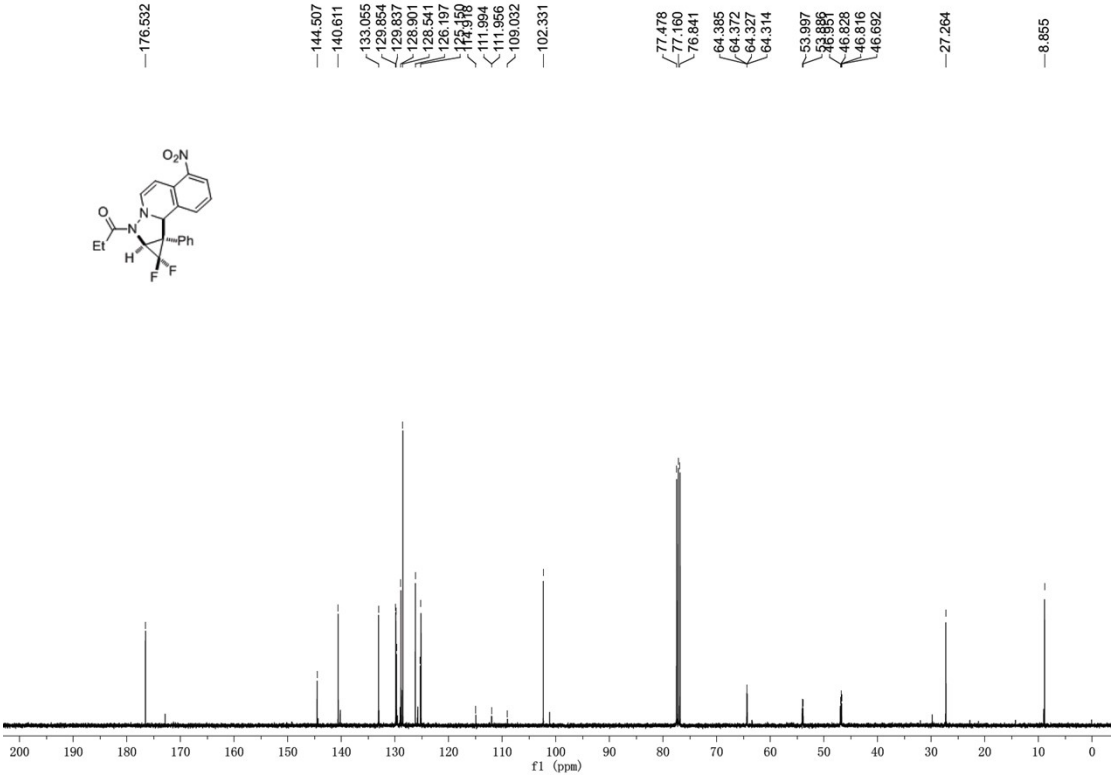
4ga-^{19}F NMR (376 MHz, $CDCl_3$)



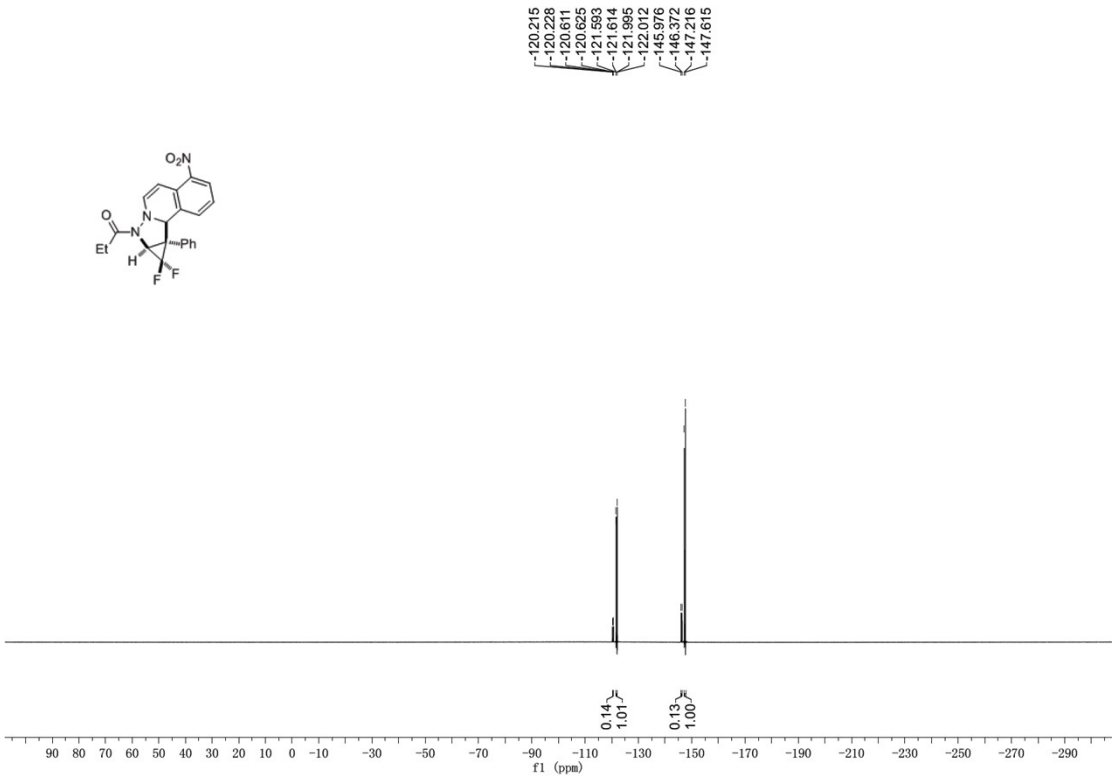
4ha-^{1}H NMR (400 MHz, $CDCl_3$)



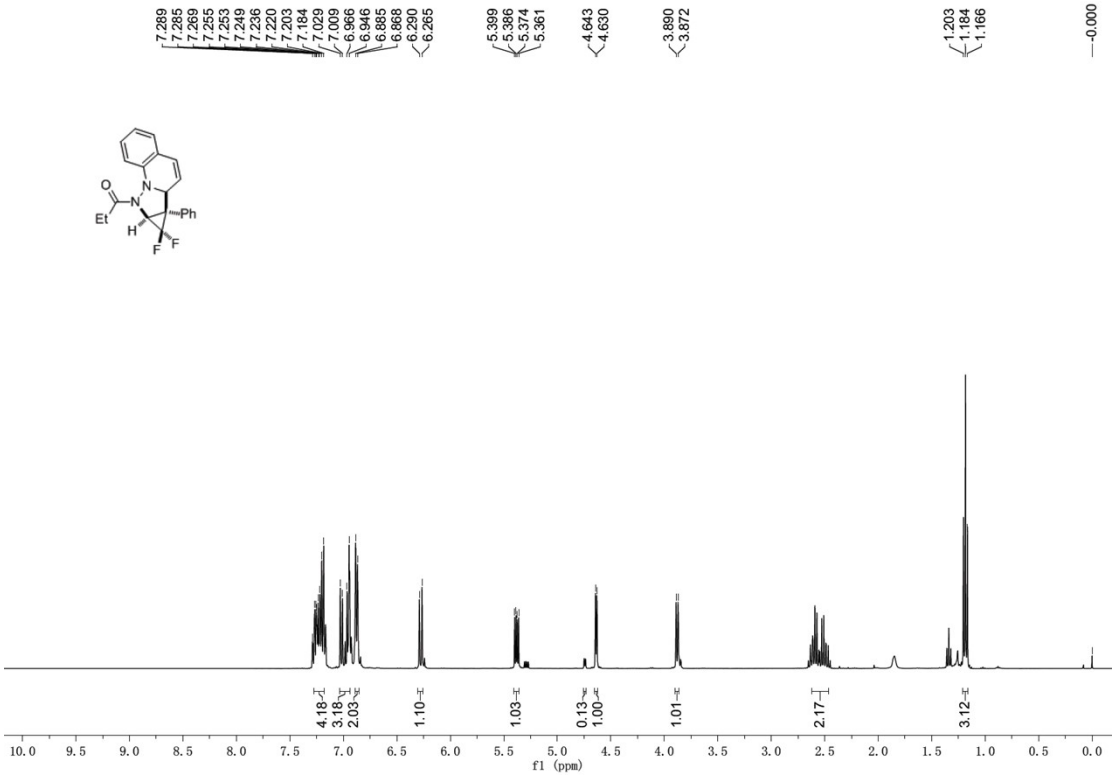
4ha-^{13}C NMR (100 MHz, $CDCl_3$)



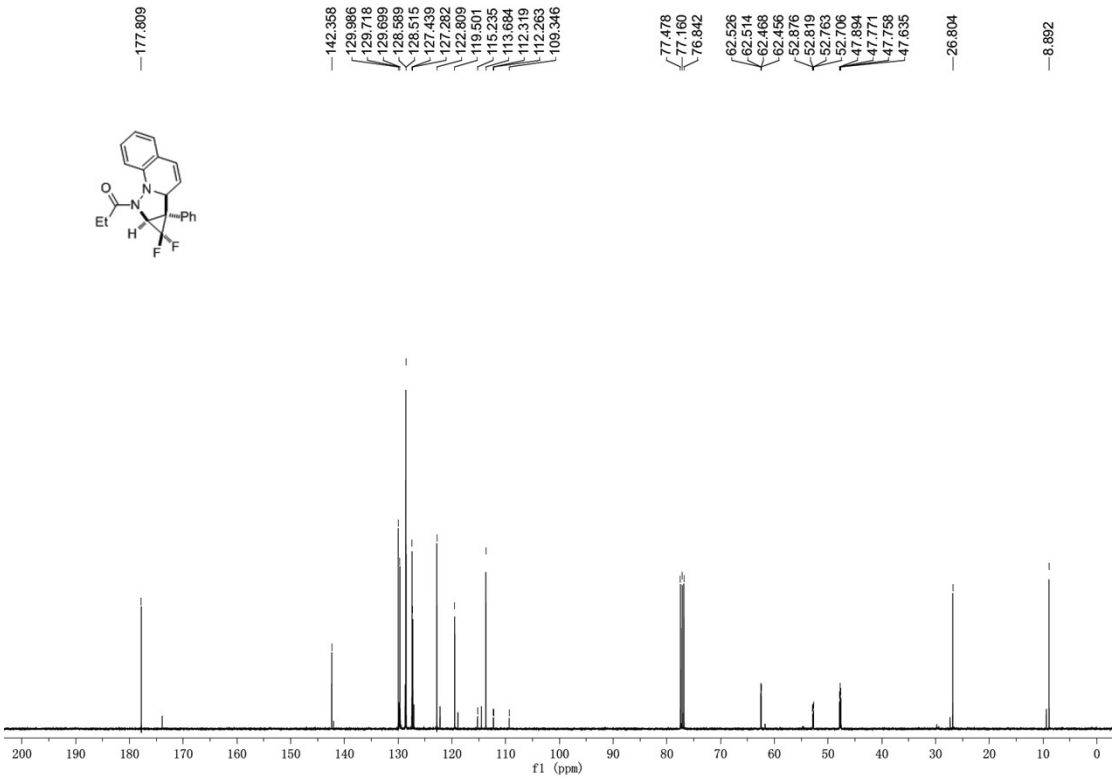
4ha-^{19}F NMR (376 MHz, $CDCl_3$)



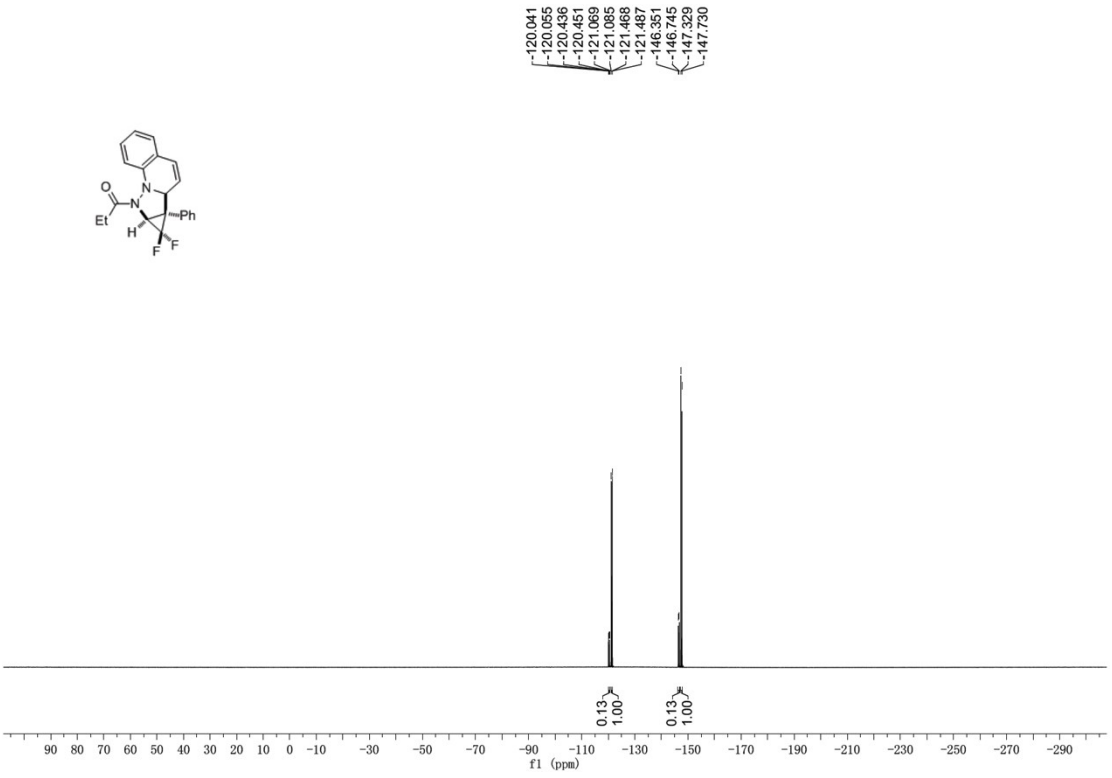
5aa-^{1}H NMR (400 MHz, $CDCl_3$)



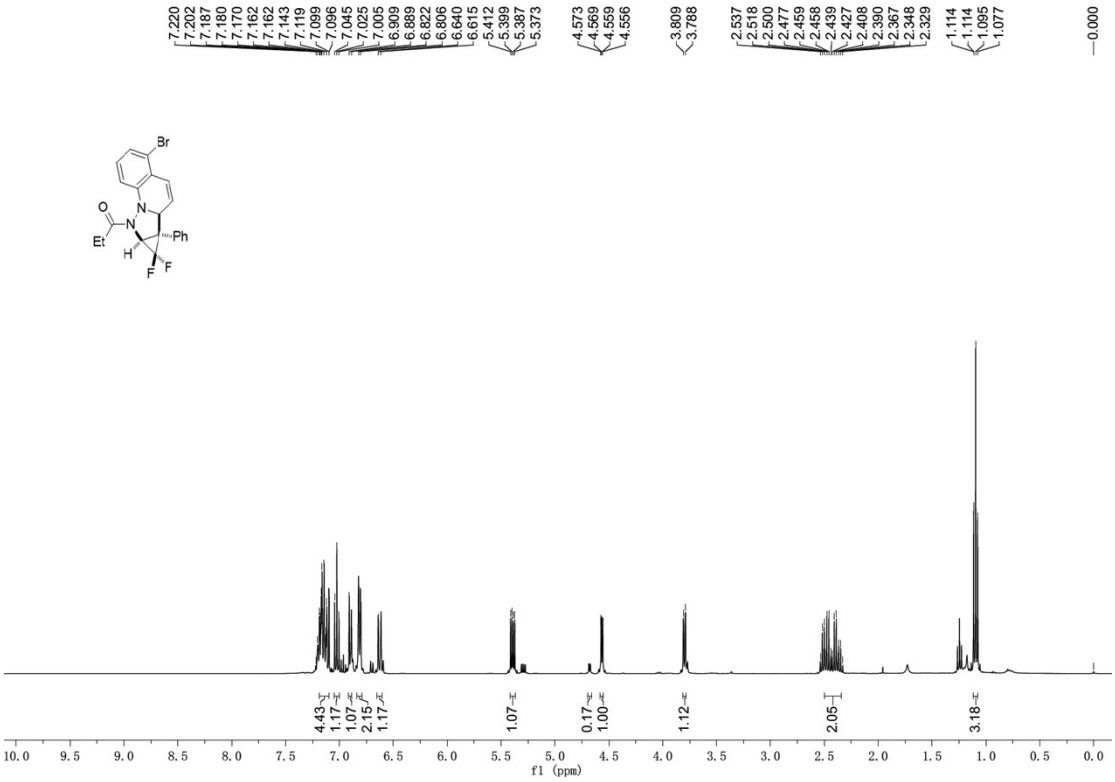
5aa-^{13}C NMR (100 MHz, $CDCl_3$)



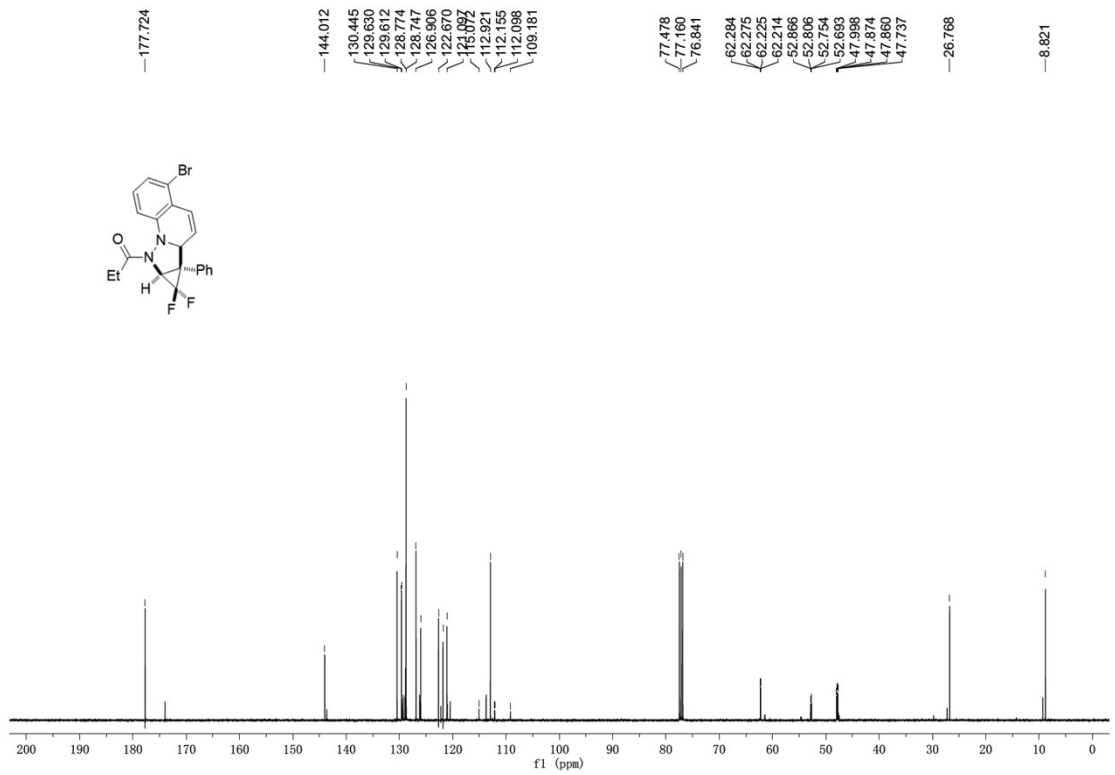
5aa-^{19}F NMR (376 MHz, $CDCl_3$)



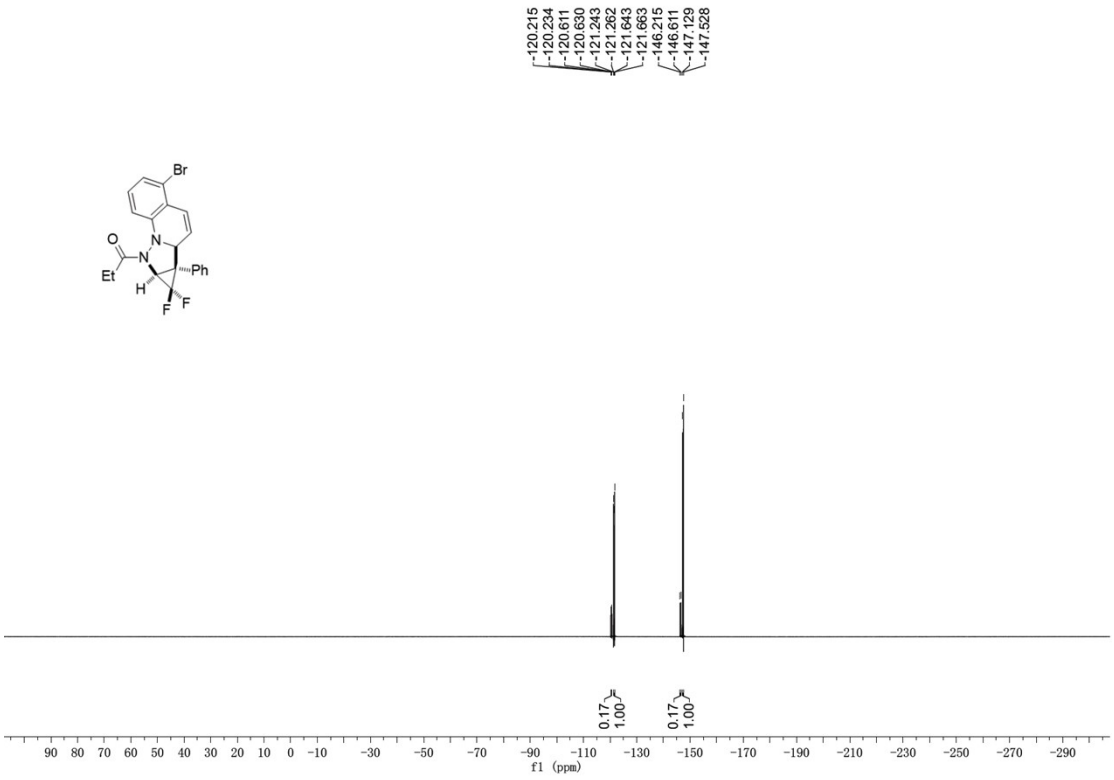
5ba-^{1}H NMR (400 MHz, $CDCl_3$)



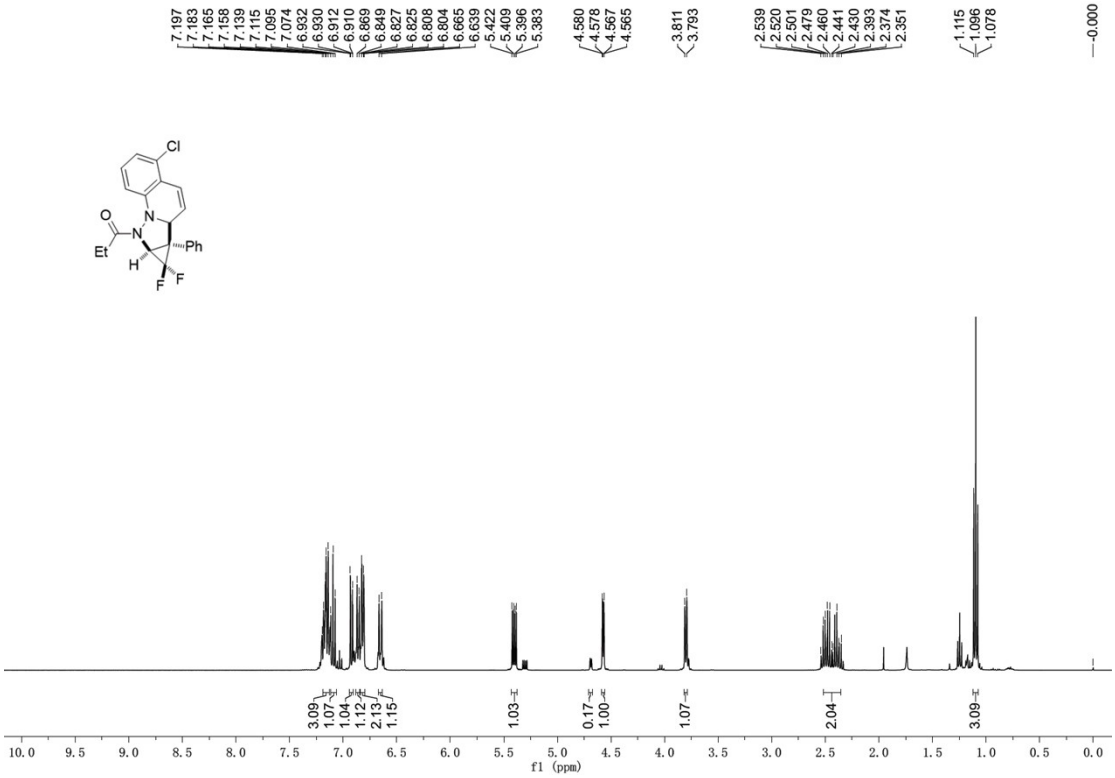
5ba-^{13}C NMR (100 MHz, $CDCl_3$)



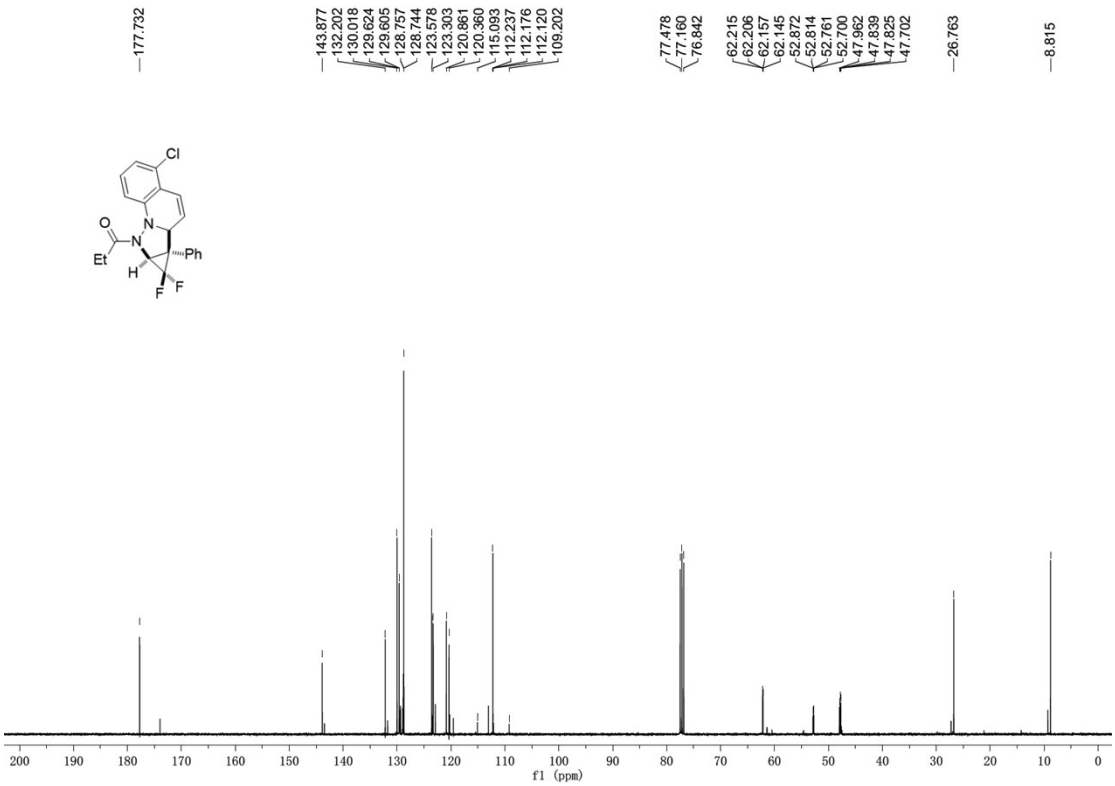
5ba-^{19}F NMR (376 MHz, $CDCl_3$)



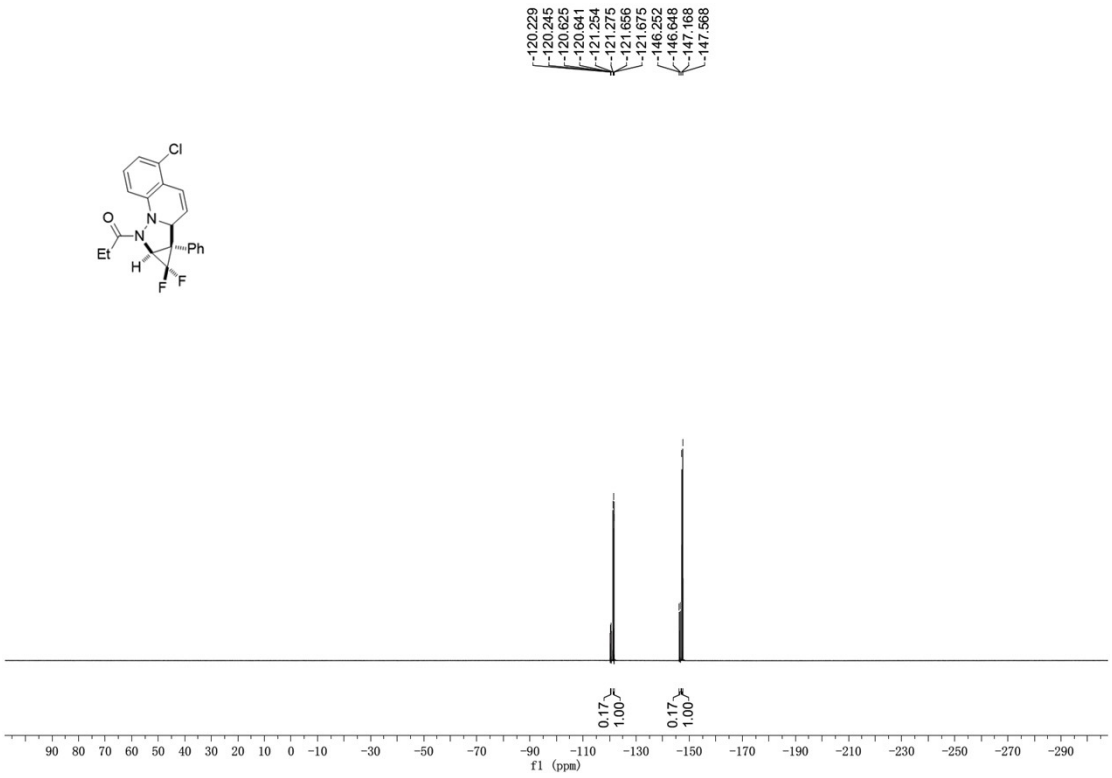
5ca-^{1}H NMR (400 MHz, $CDCl_3$)



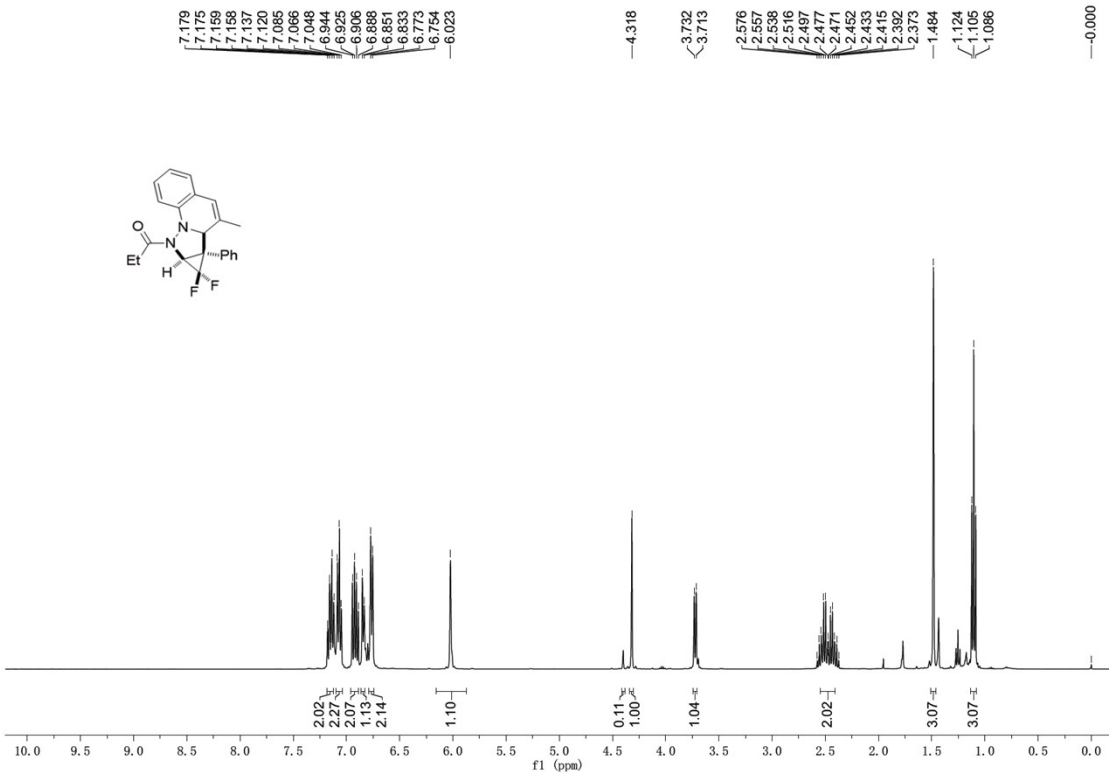
5ca-^{13}C NMR (100 MHz, $CDCl_3$)



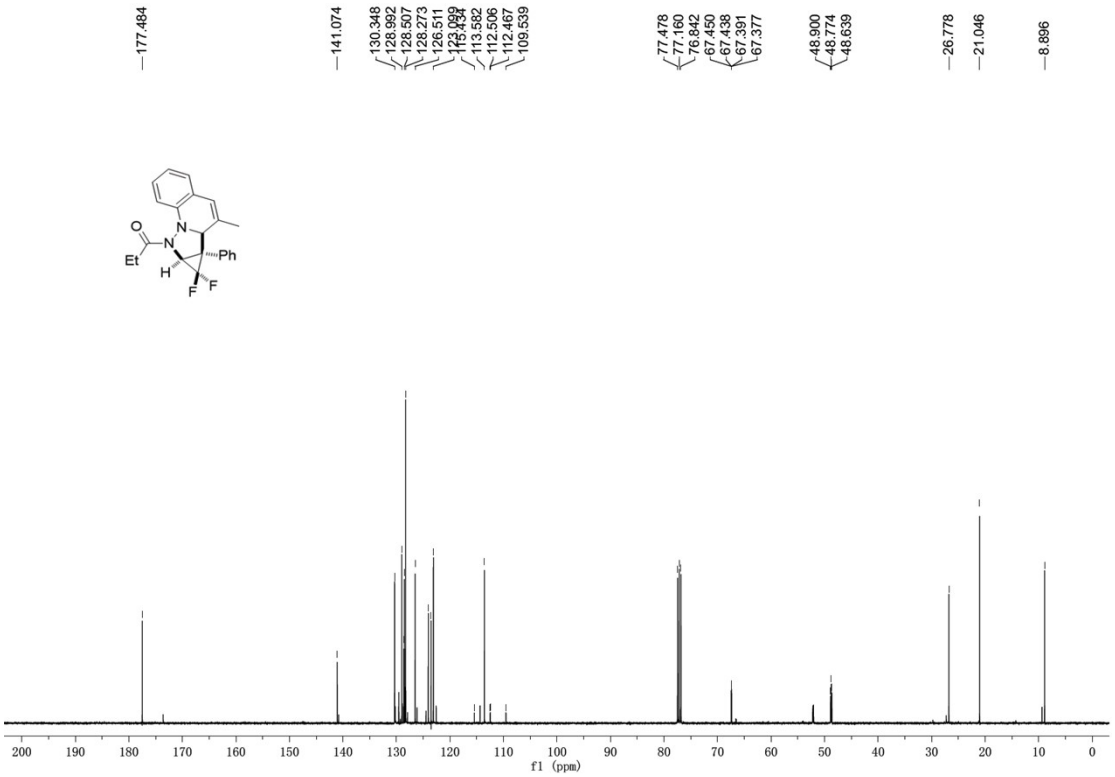
5ca-^{19}F NMR (376 MHz, $CDCl_3$)



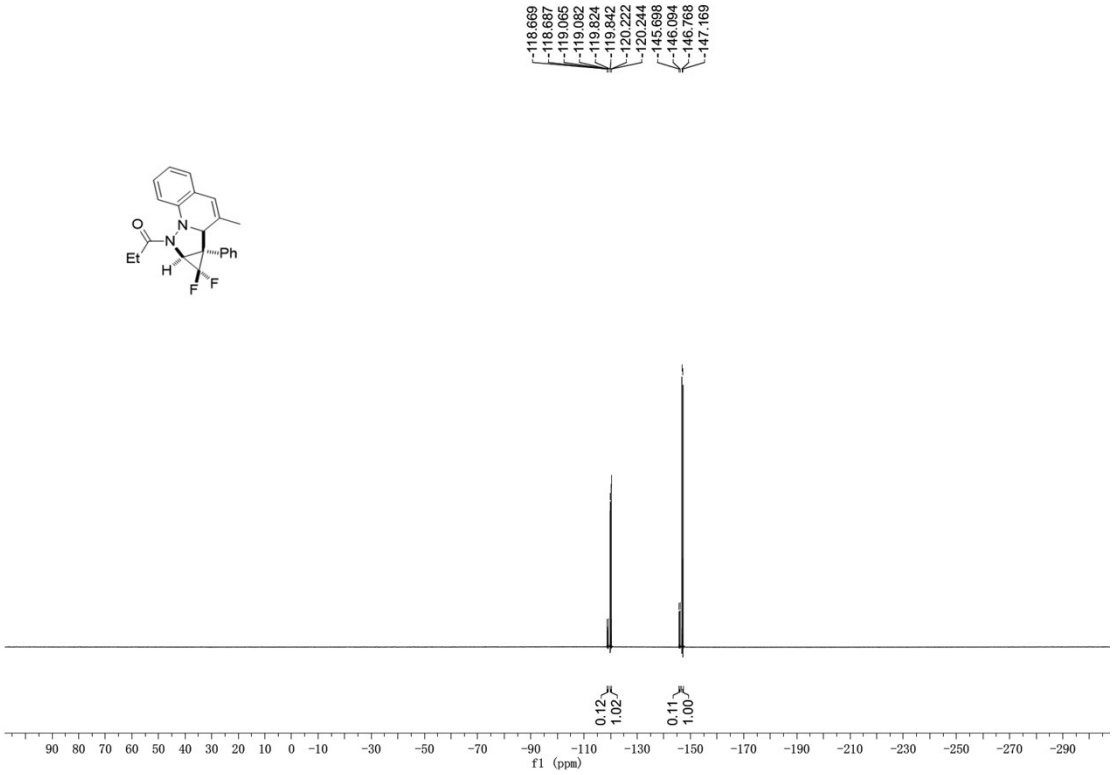
5da-^{1}H NMR (400 MHz, $CDCl_3$)



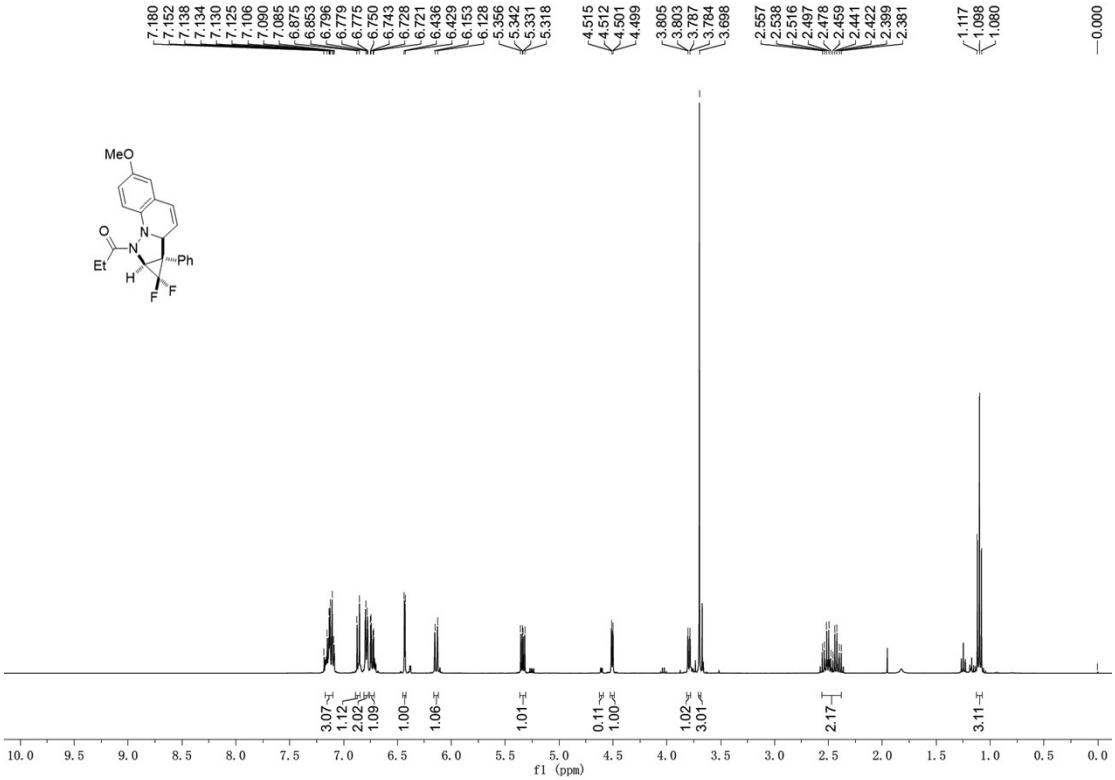
5da-^{13}C NMR (100 MHz, $CDCl_3$)



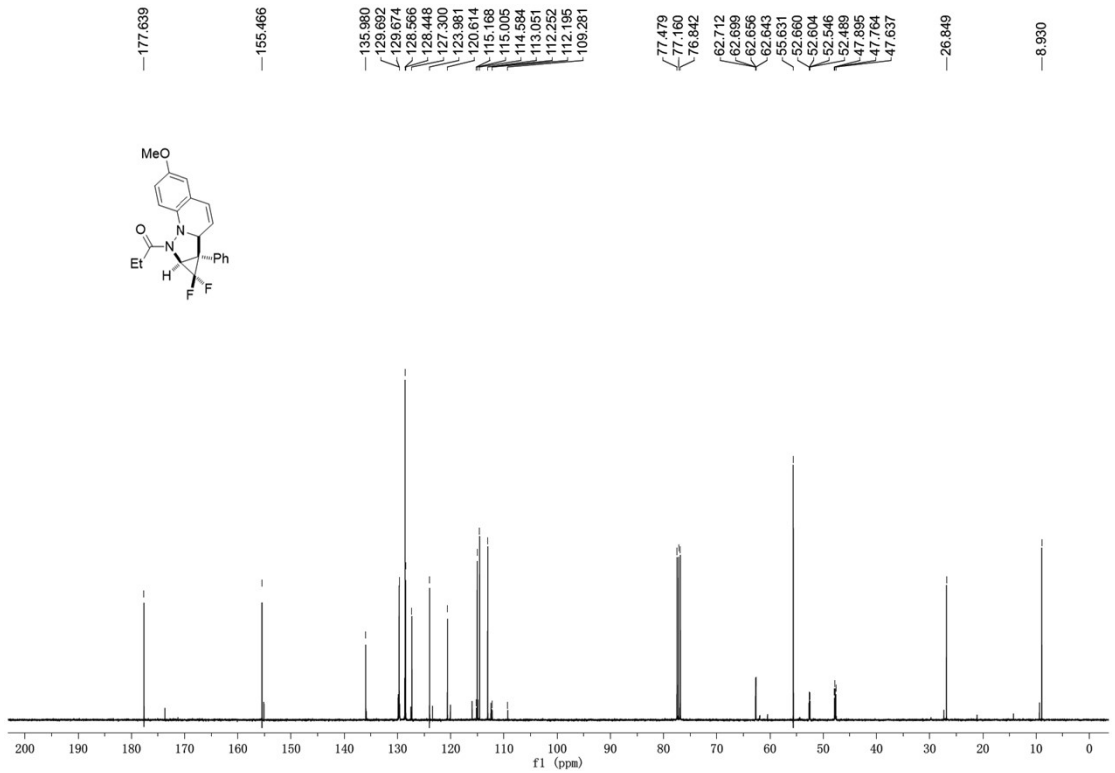
5da-^{19}F NMR (376 MHz, $CDCl_3$)



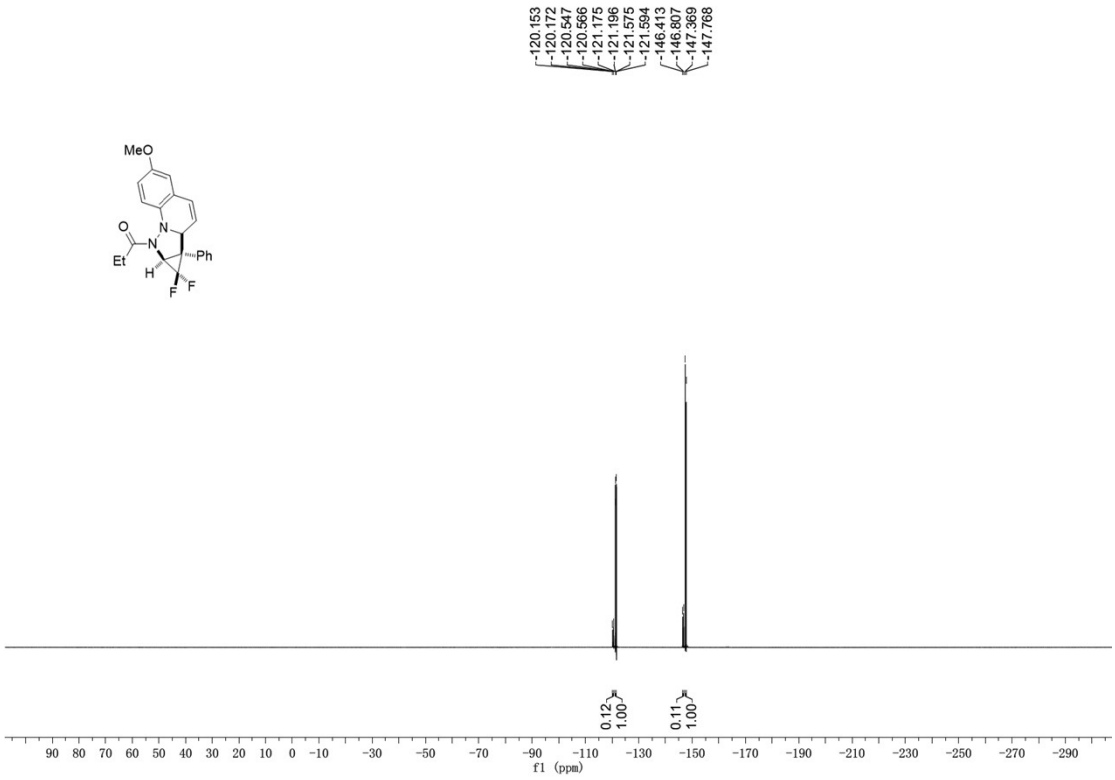
5ea-^{1}H NMR (400 MHz, $CDCl_3$)



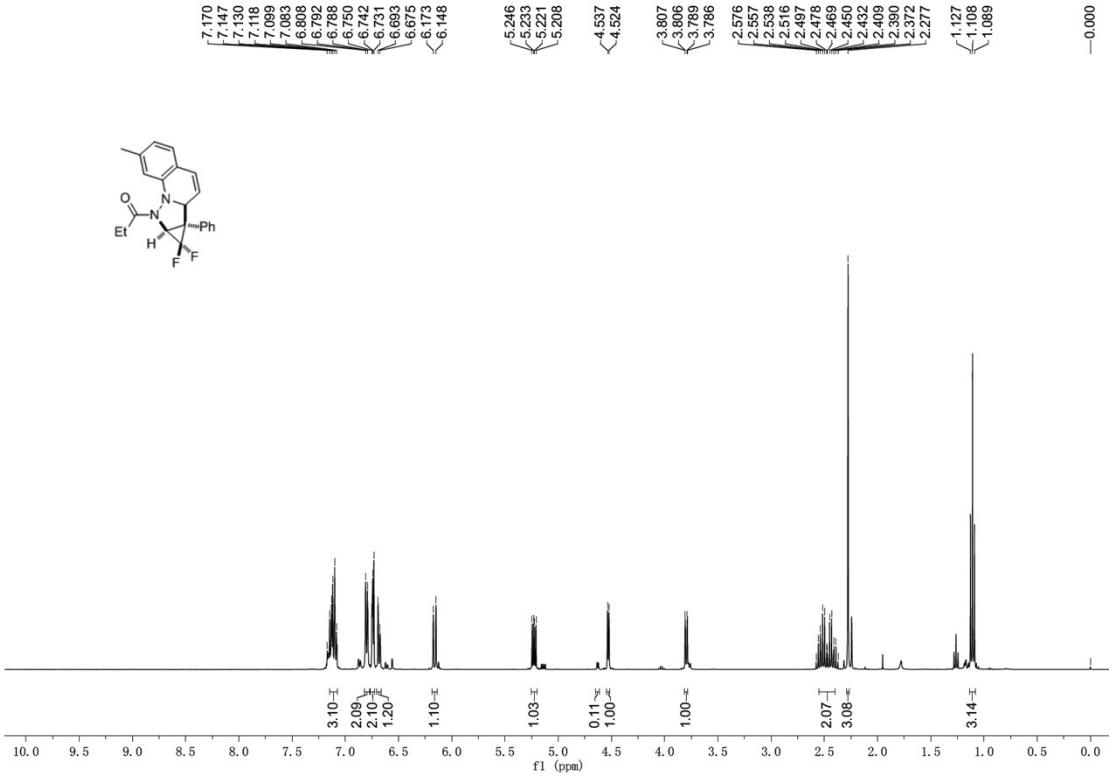
5ea-^{13}C NMR (100 MHz, $CDCl_3$)



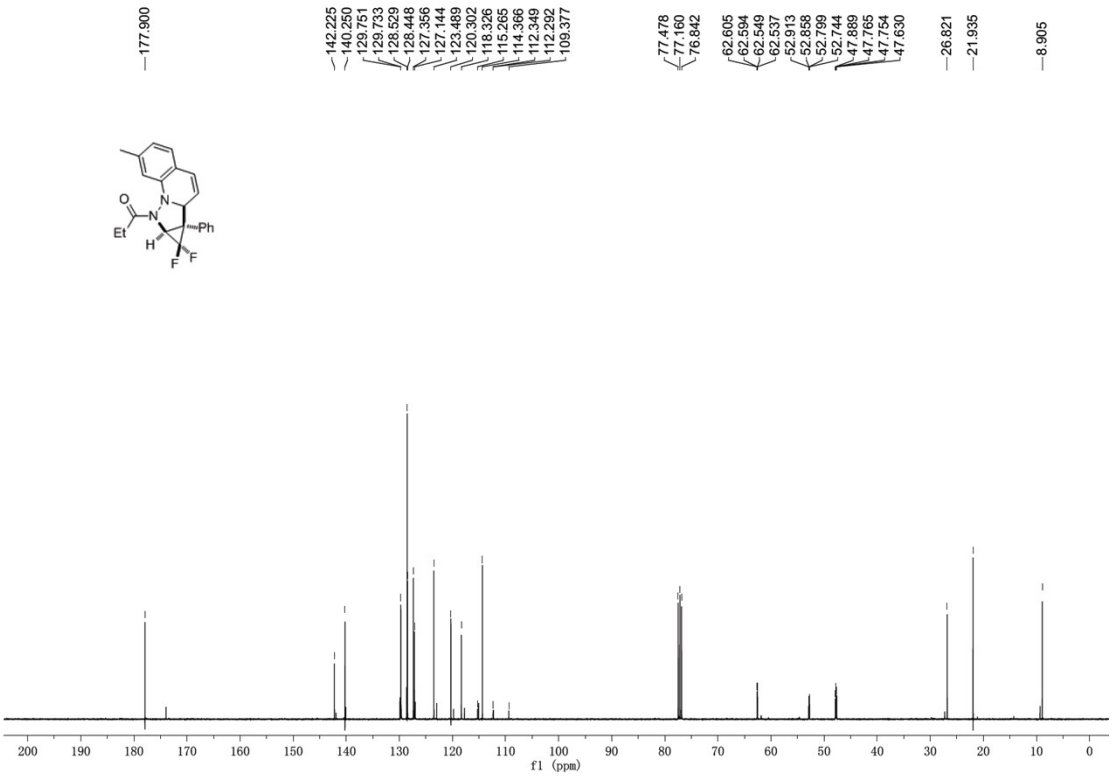
5ea-^{19}F NMR (376 MHz, $CDCl_3$)



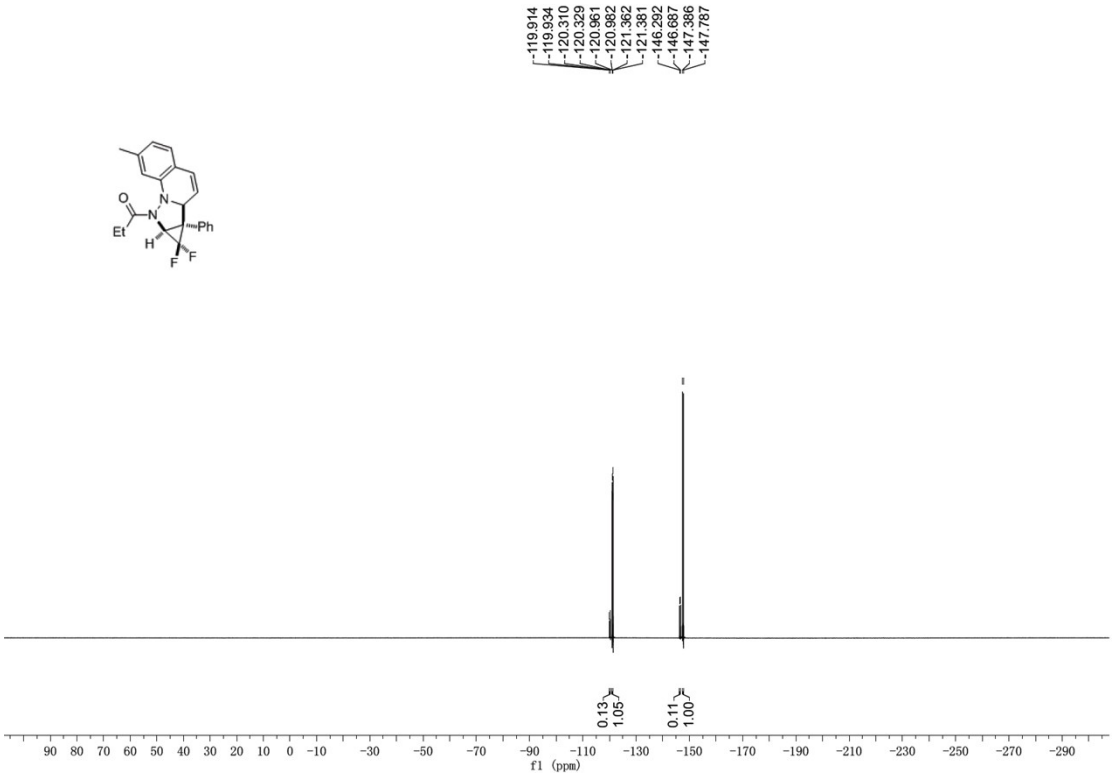
5fa-^{1}H NMR (400 MHz, $CDCl_3$)



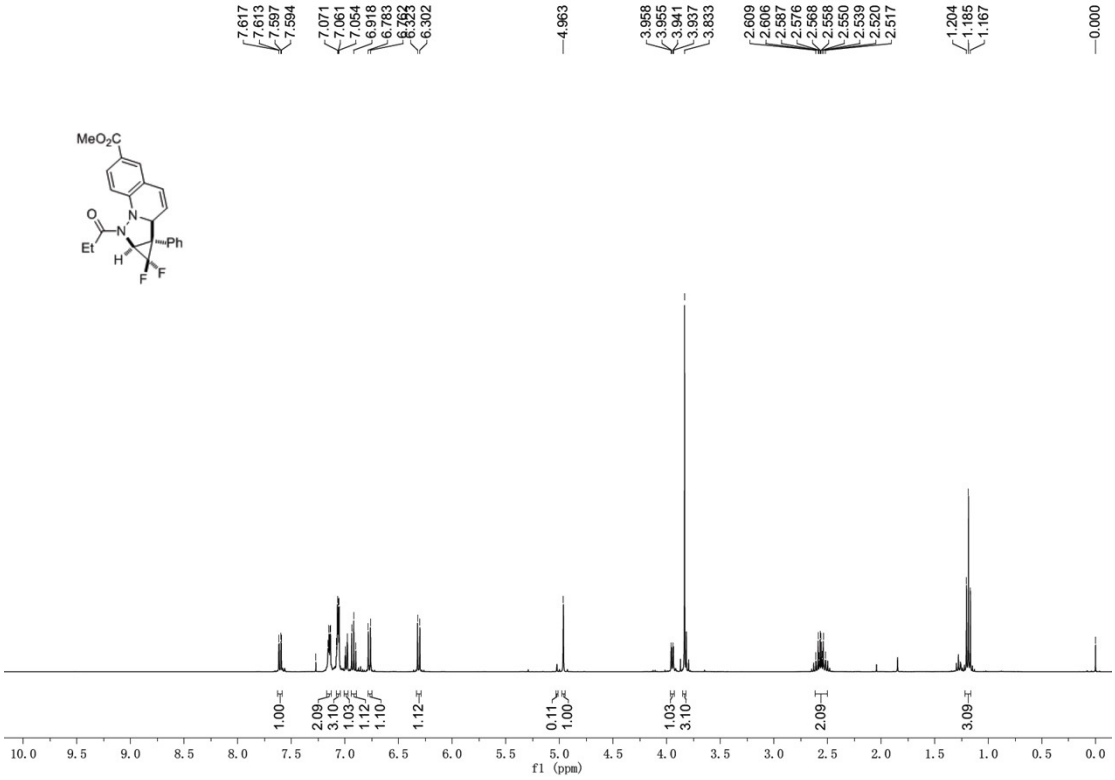
5fa-^{13}C NMR (100 MHz, $CDCl_3$)



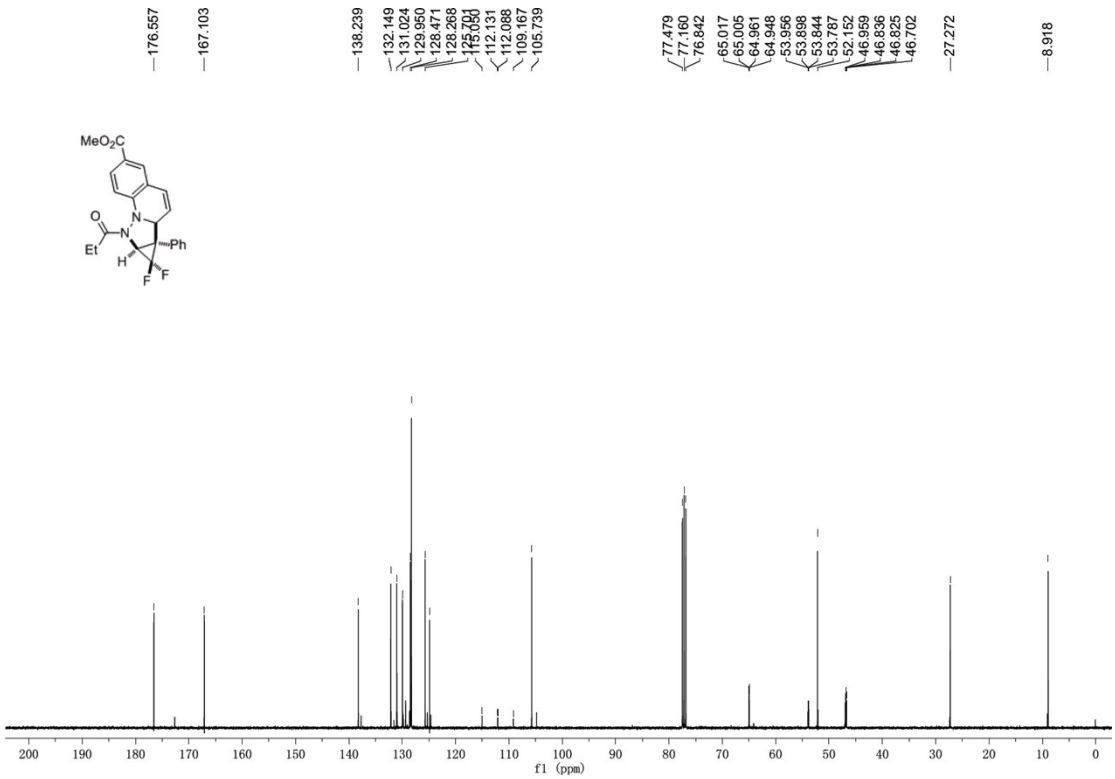
5fa-^{19}F NMR (376 MHz, $CDCl_3$)



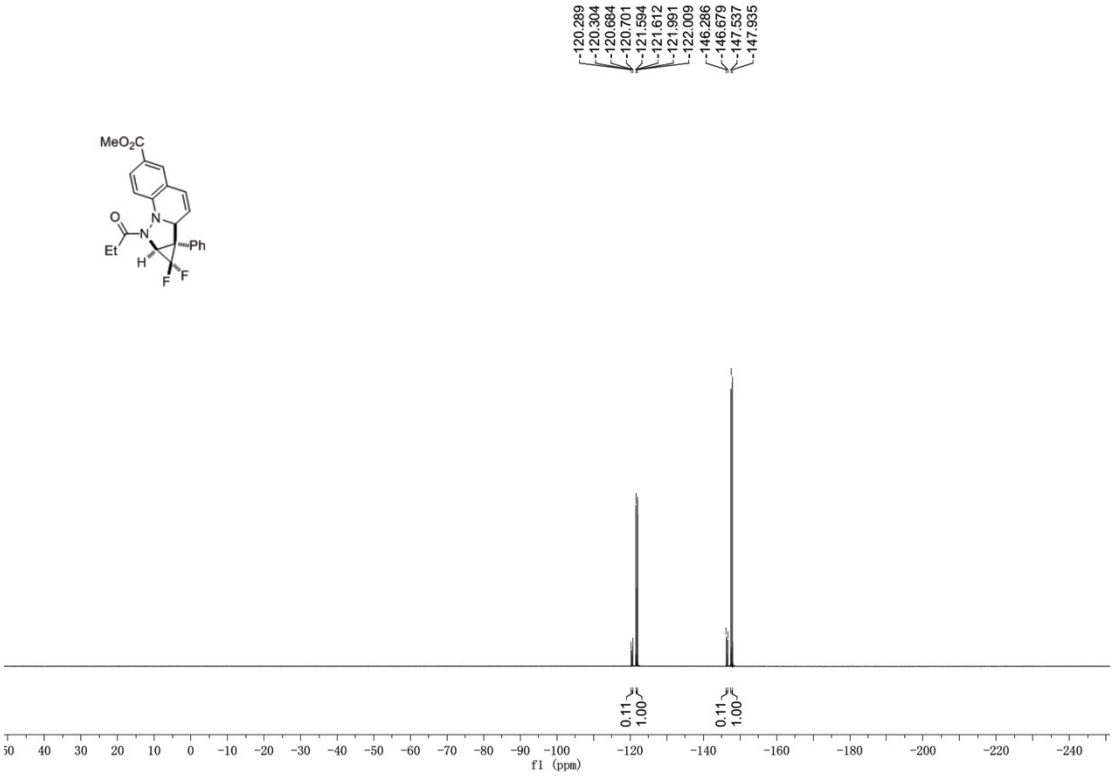
5ga-^{1}H NMR (400 MHz, $CDCl_3$)



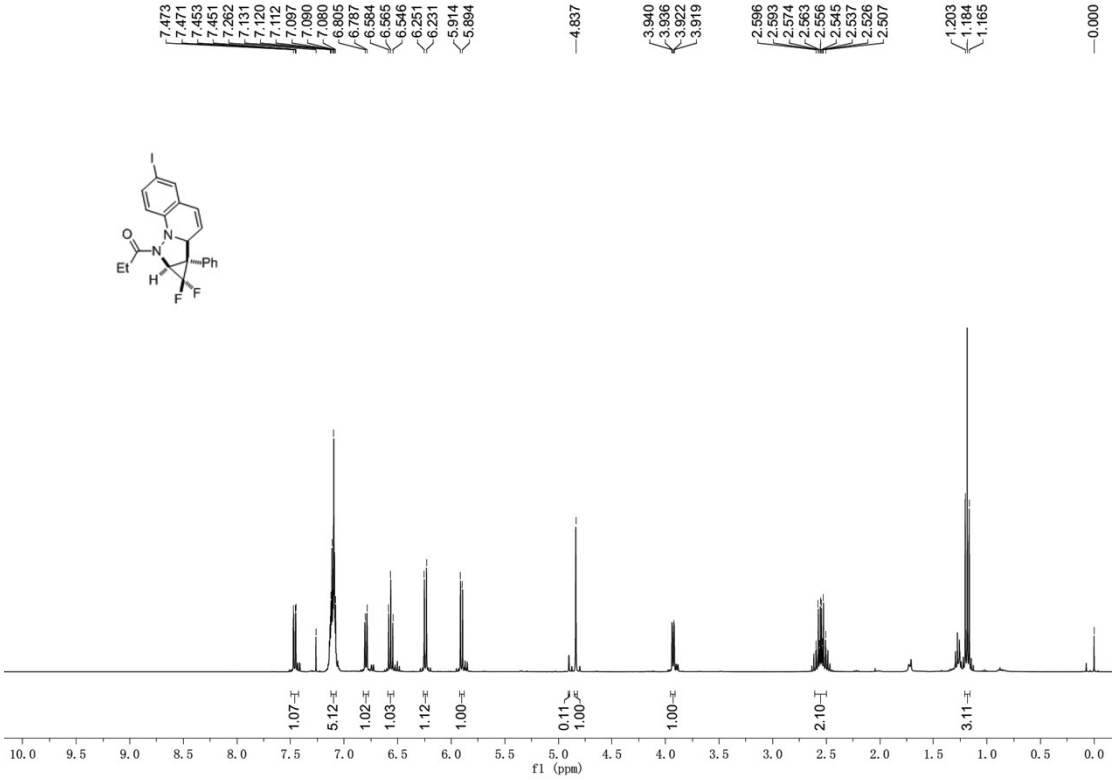
5ga-^{13}C NMR (100 MHz, $CDCl_3$)



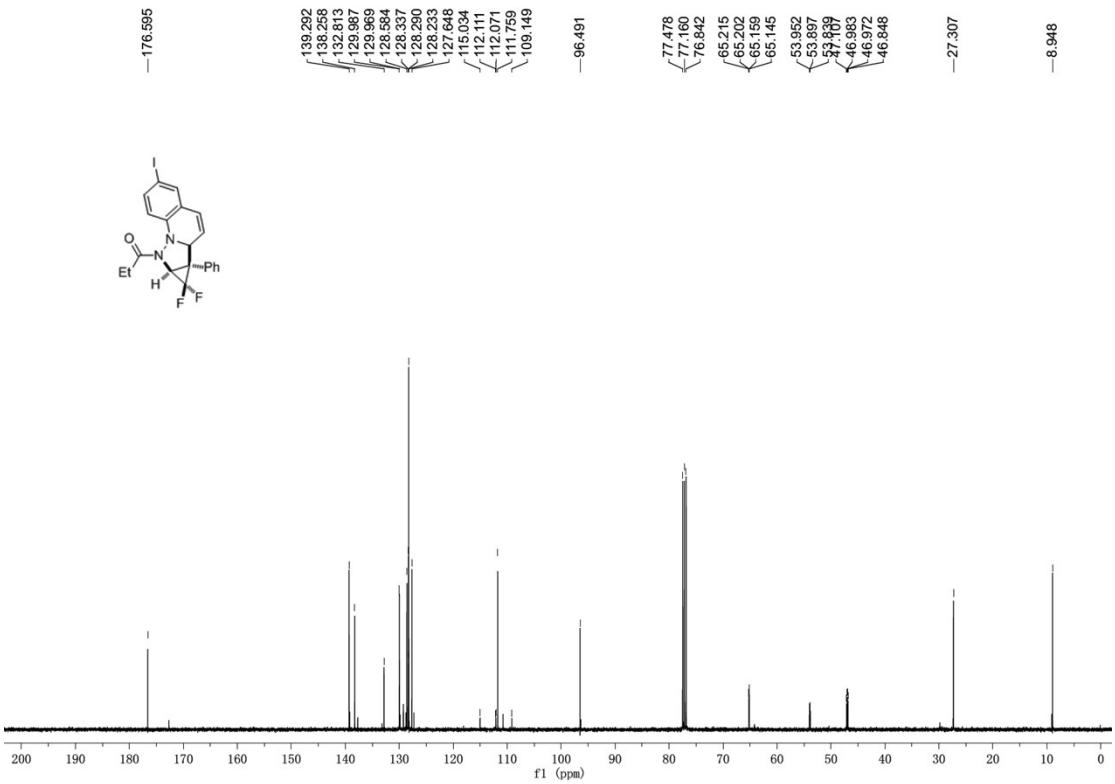
5ga-^{19}F NMR (376 MHz, $CDCl_3$)



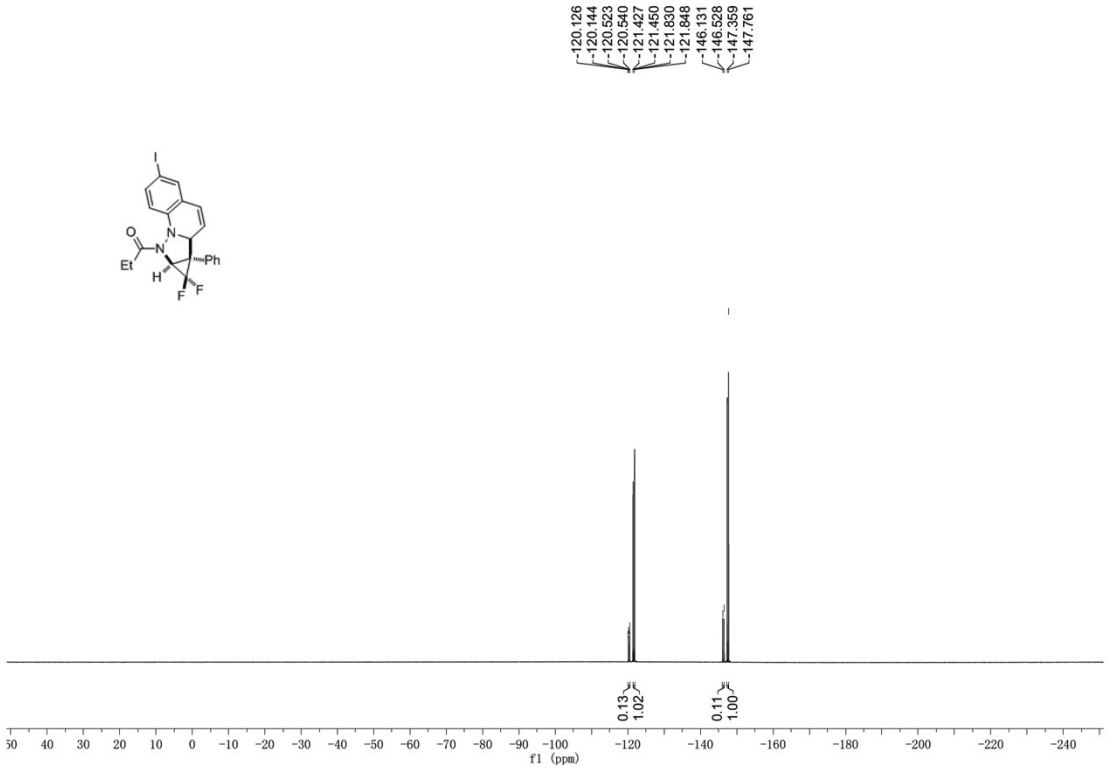
5ha-^{1}H NMR (400 MHz, $CDCl_3$)



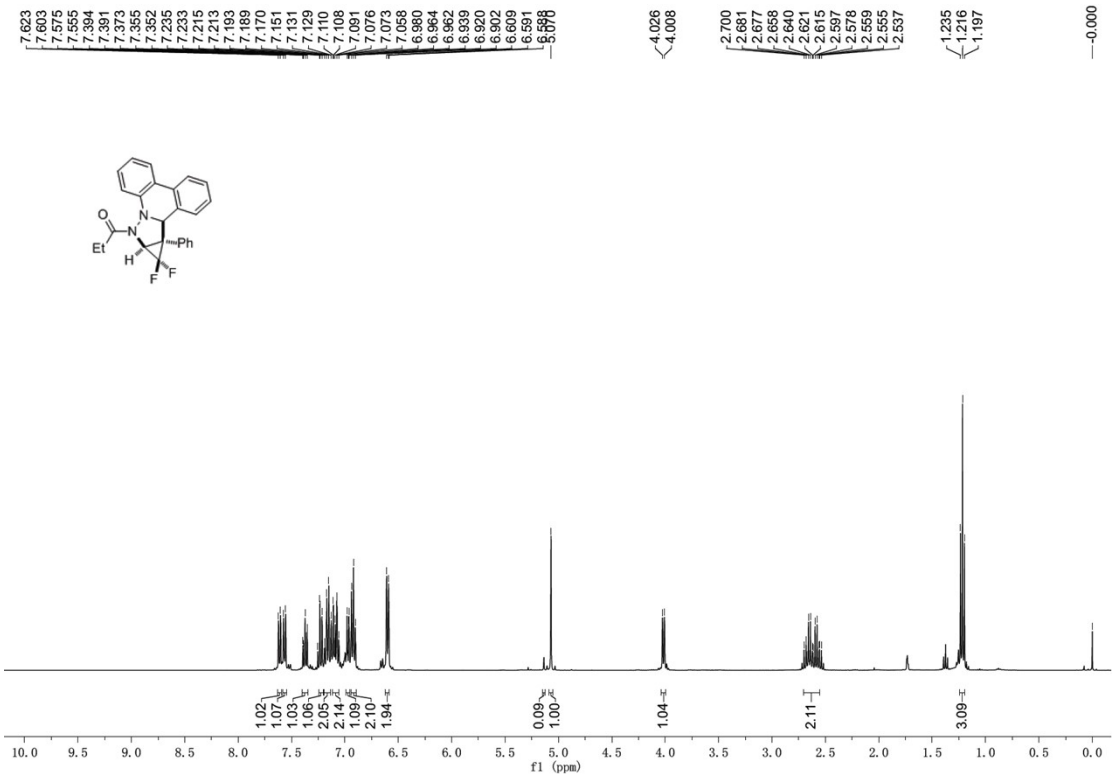
5ha-^{13}C NMR (100 MHz, $CDCl_3$)



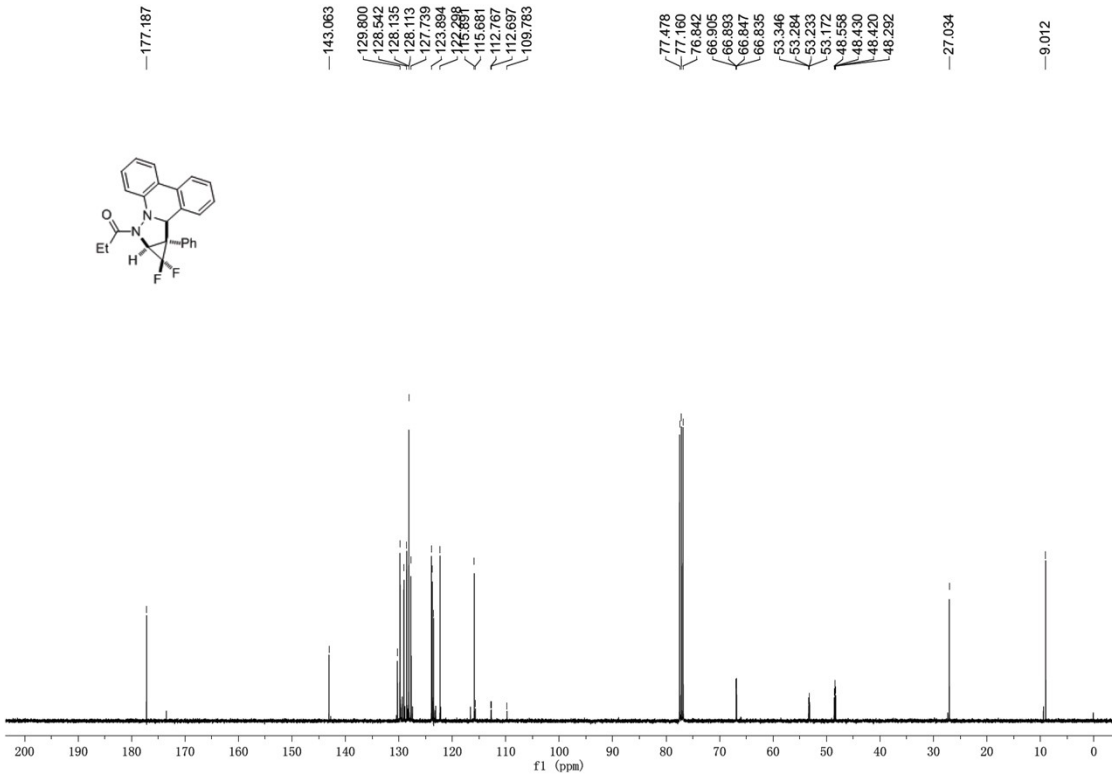
5ha-^{19}F NMR (376 MHz, $CDCl_3$)



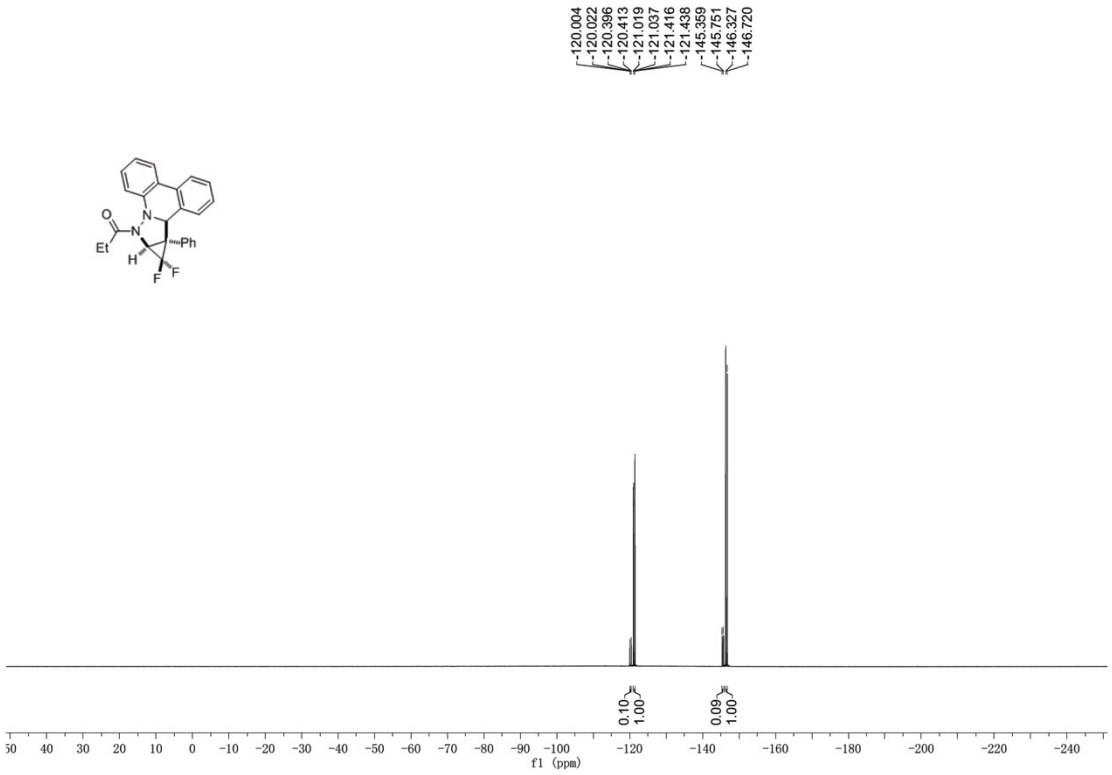
6-^{1}H NMR (400 MHz, $CDCl_3$)



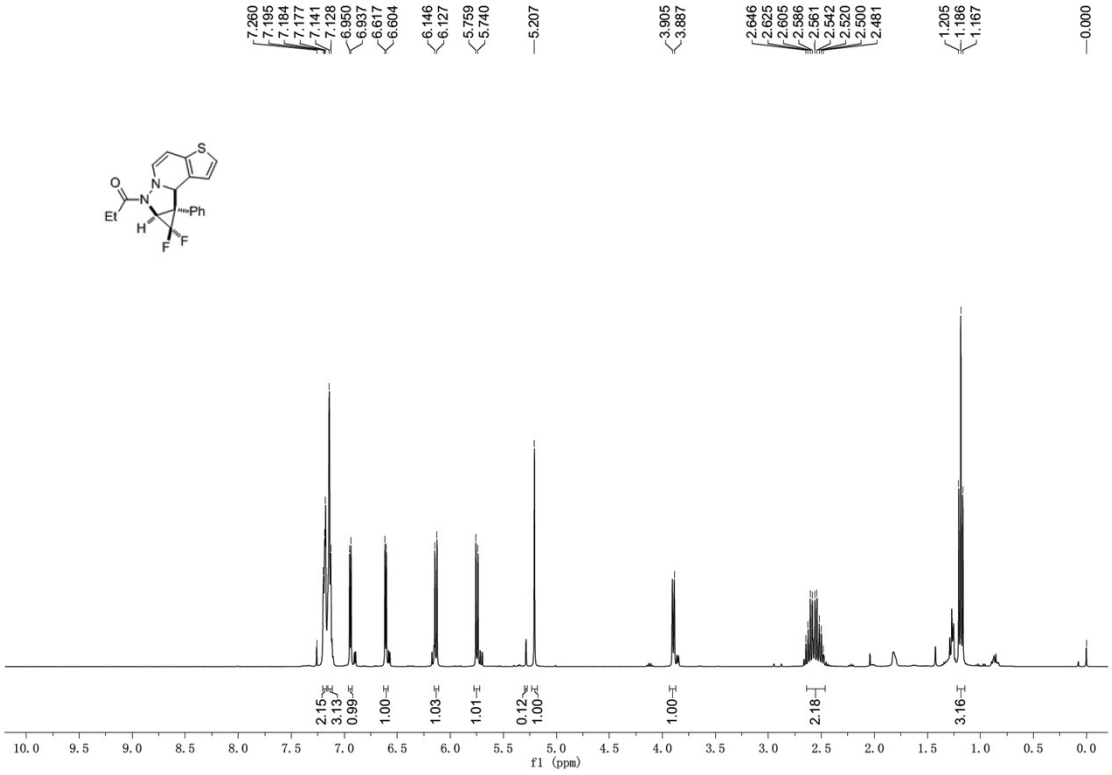
6-^{13}C NMR (100 MHz, $CDCl_3$)



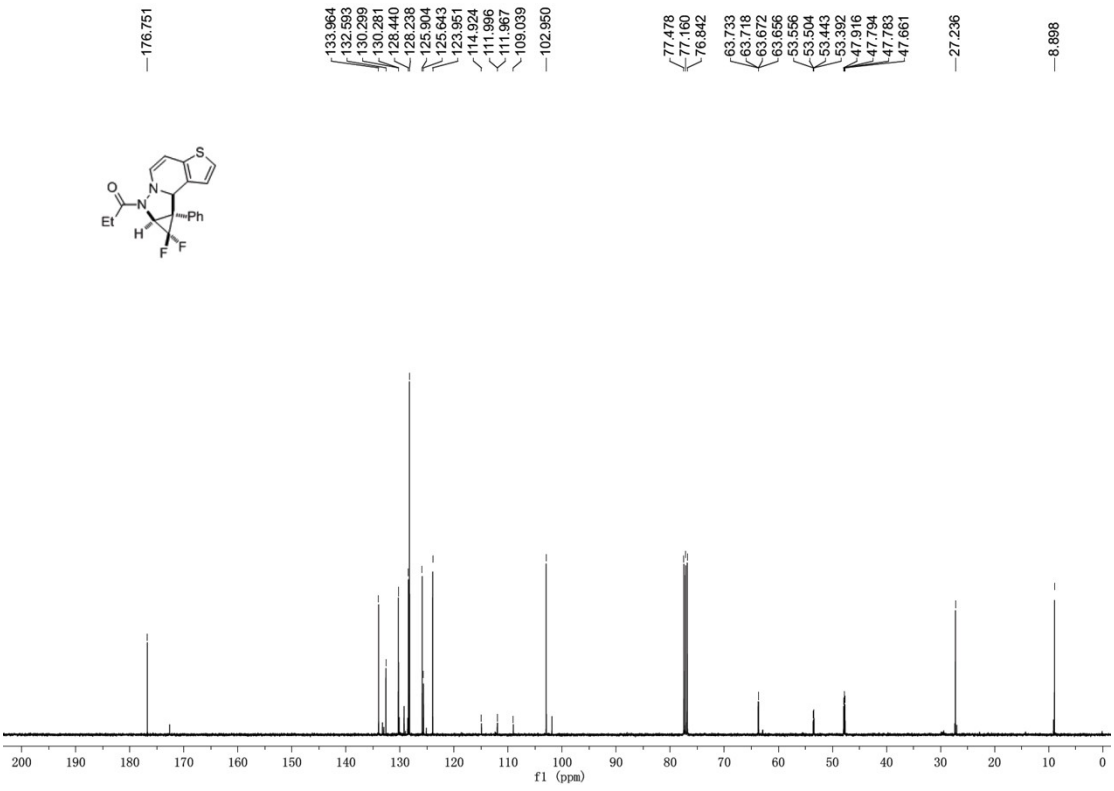
6-^{19}F NMR (376 MHz, $CDCl_3$)



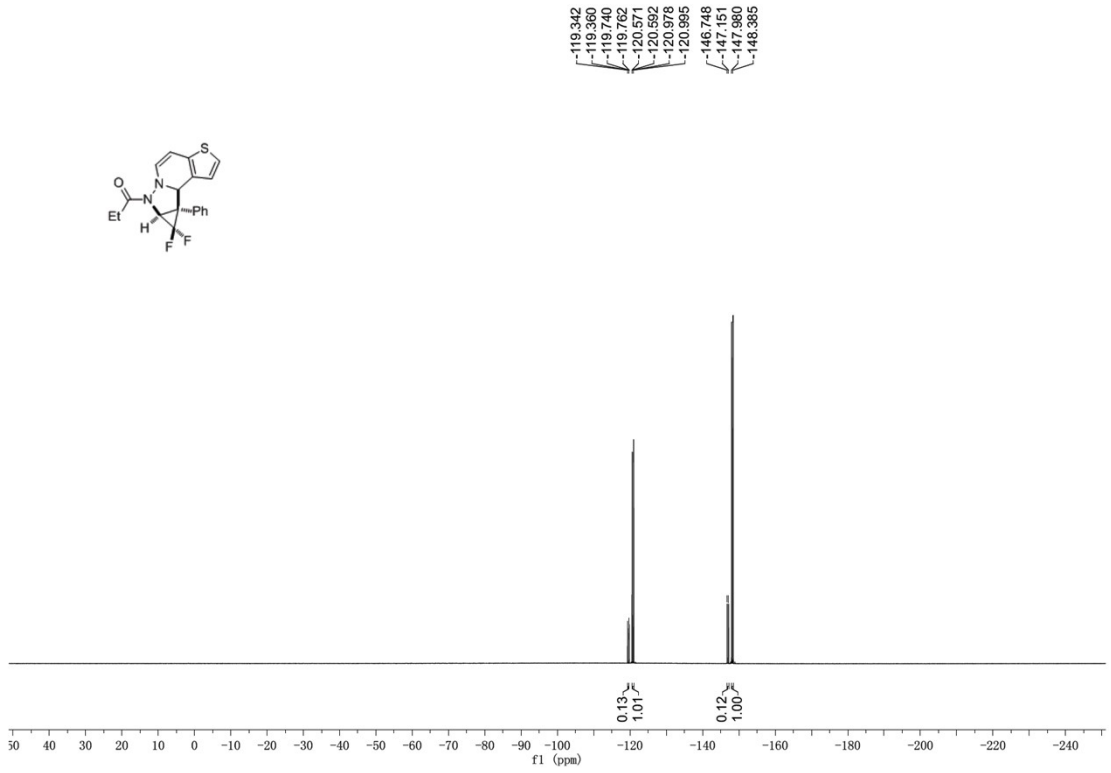
7-^{1}H NMR (400 MHz, $CDCl_3$)



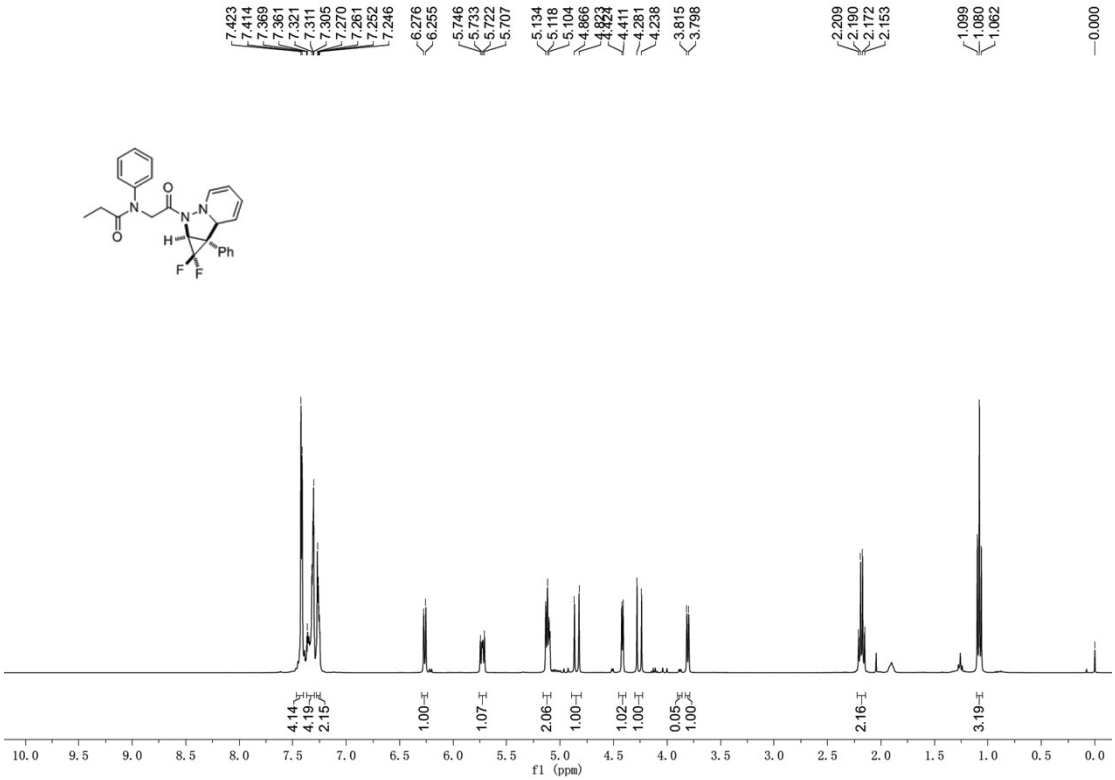
7-^{13}C NMR (100 MHz, $CDCl_3$)



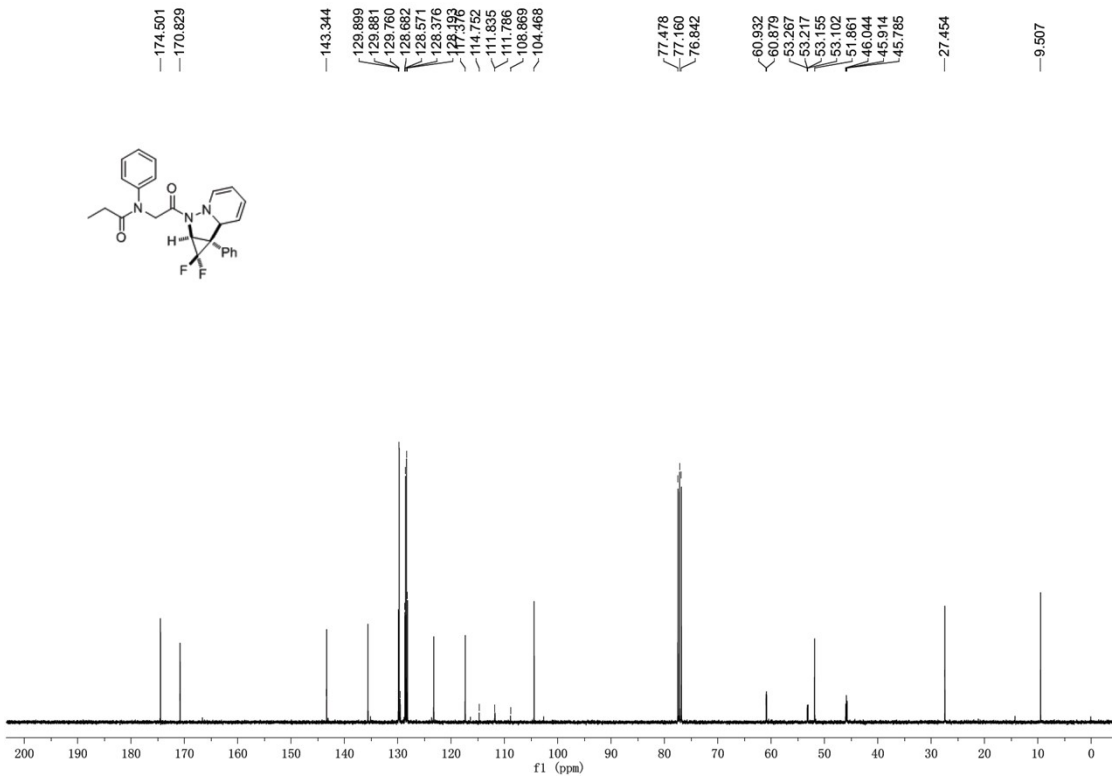
7-^{19}F NMR (376 MHz, $CDCl_3$)



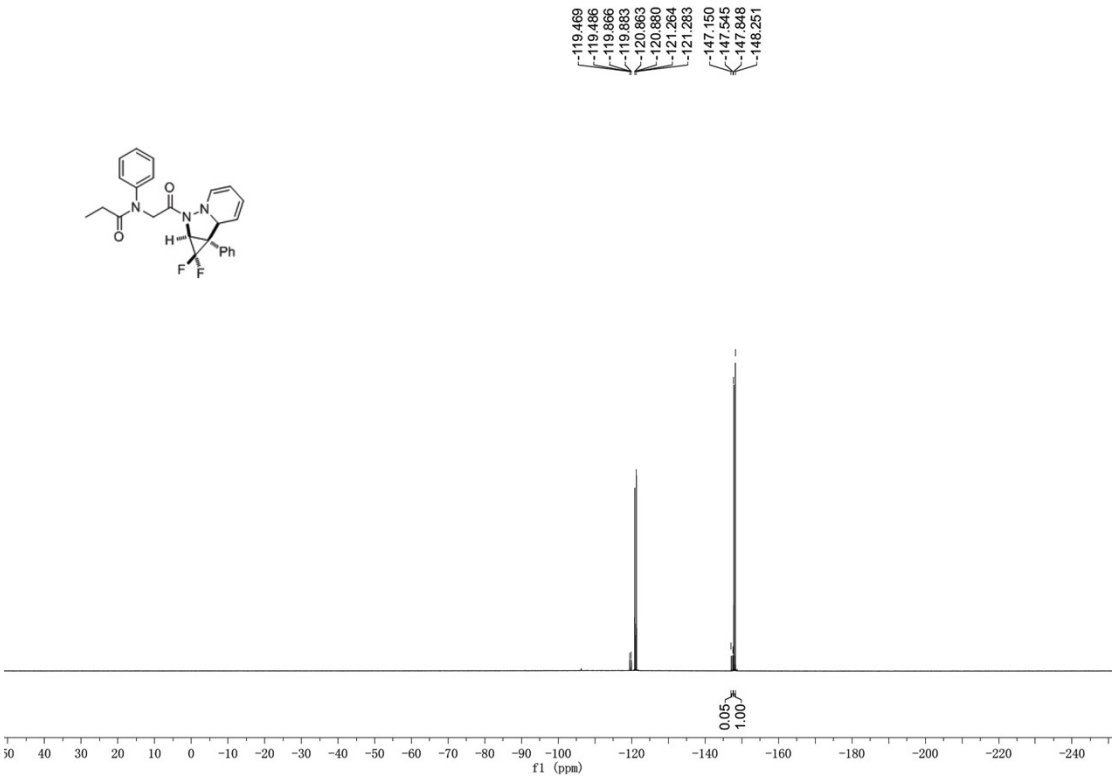
8a-^{1}H NMR (400 MHz, $CDCl_3$)



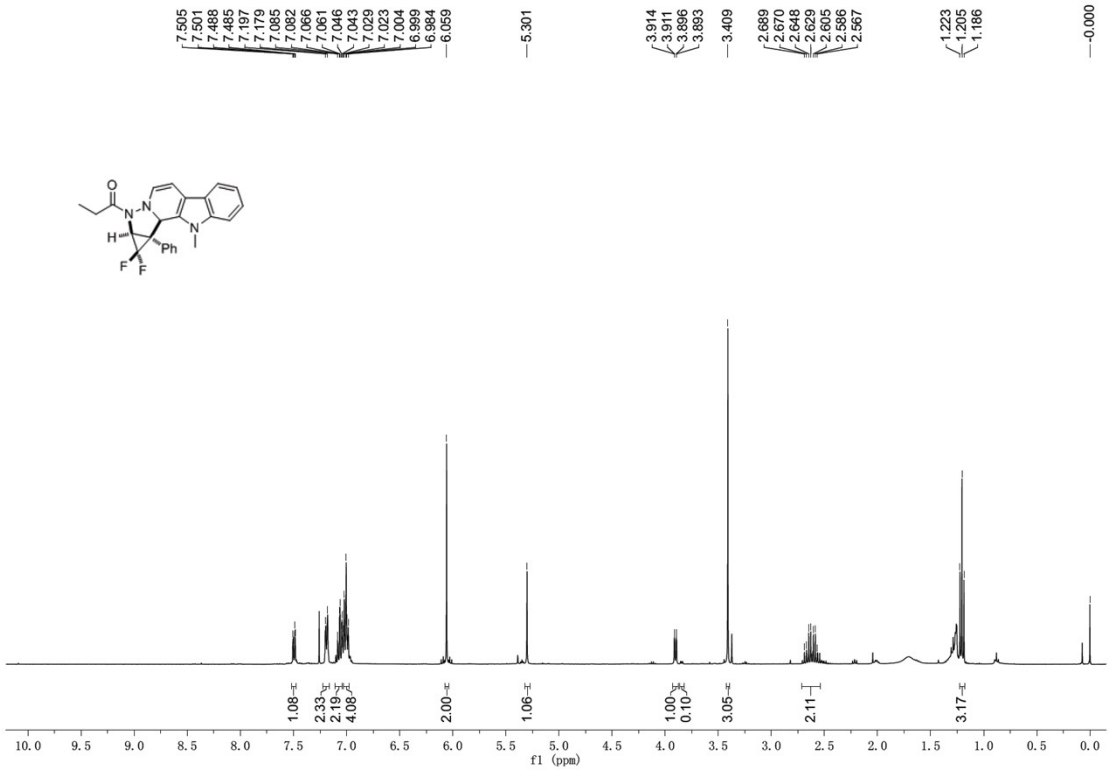
8a-^{13}C NMR (100 MHz, $CDCl_3$)



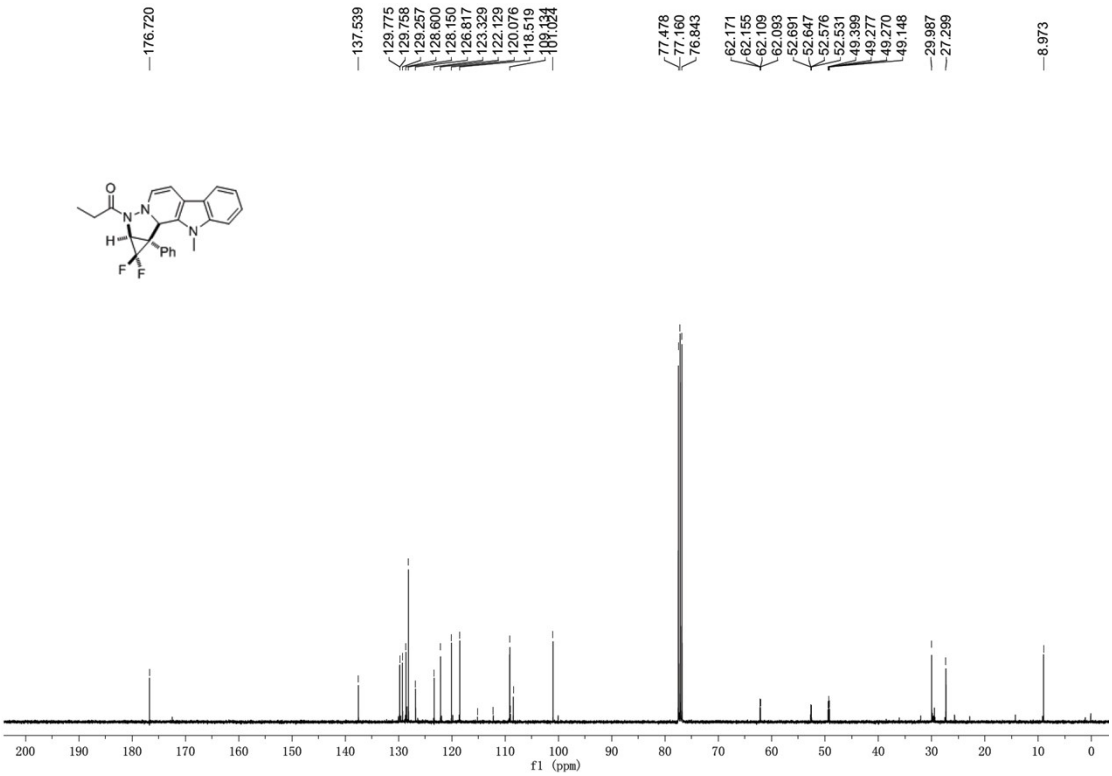
8a-^{19}F NMR (376 MHz, $CDCl_3$)



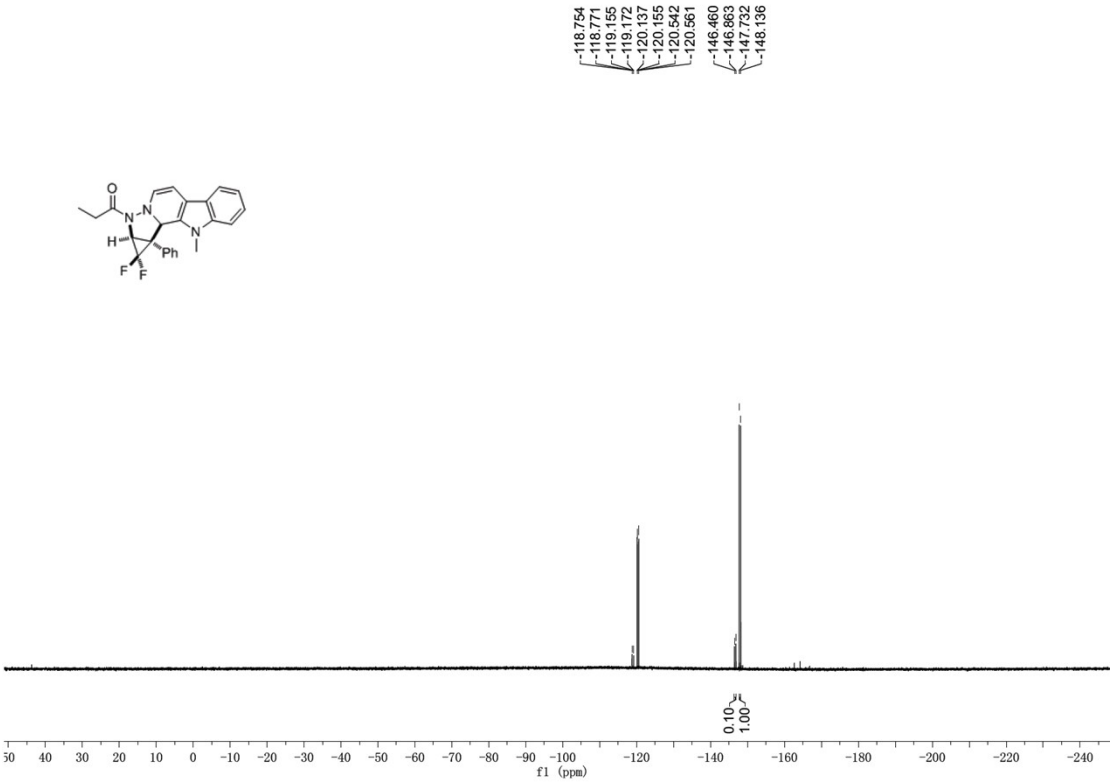
8b-^{1}H NMR (400 MHz, $CDCl_3$)



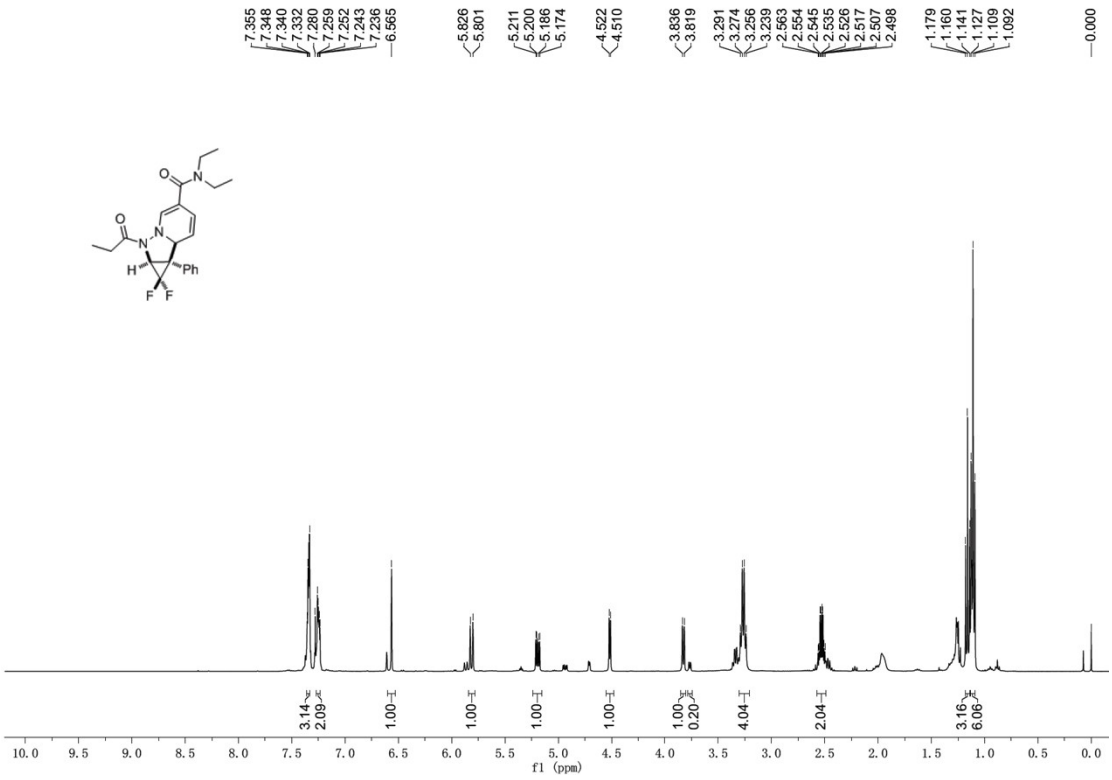
8b-^{13}C NMR (100 MHz, $CDCl_3$)



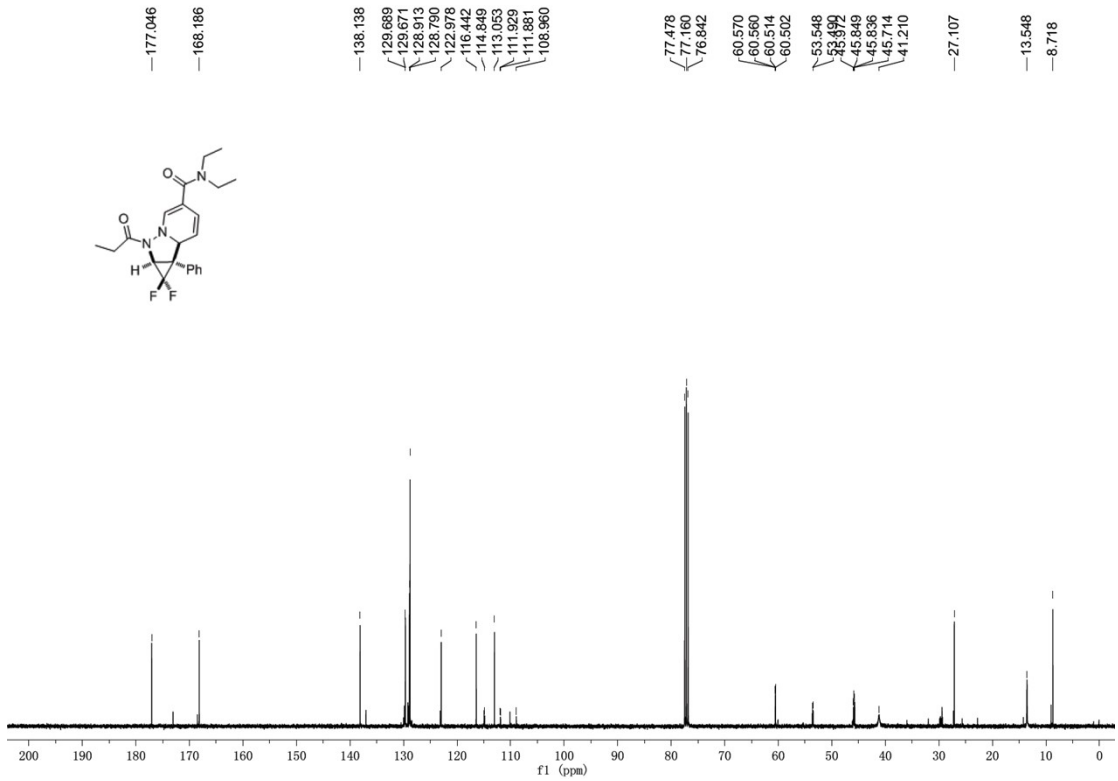
8b-^{19}F NMR (376 MHz, $CDCl_3$)



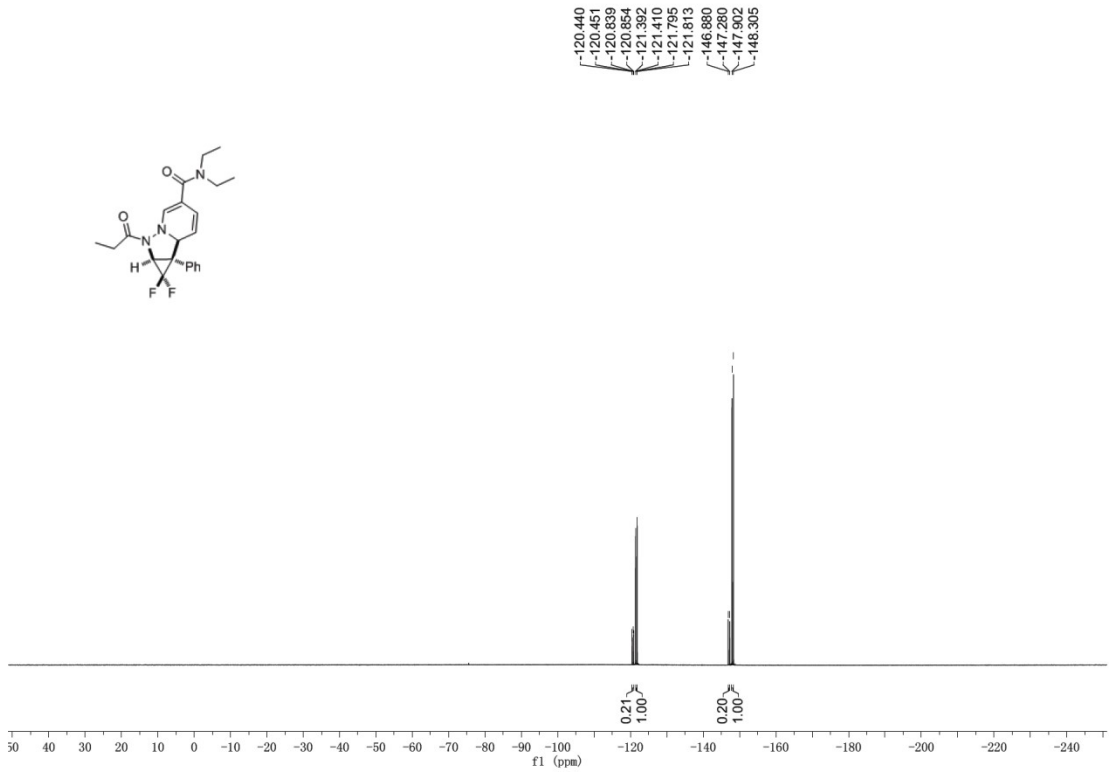
8c-^{1}H NMR (400 MHz, $CDCl_3$)



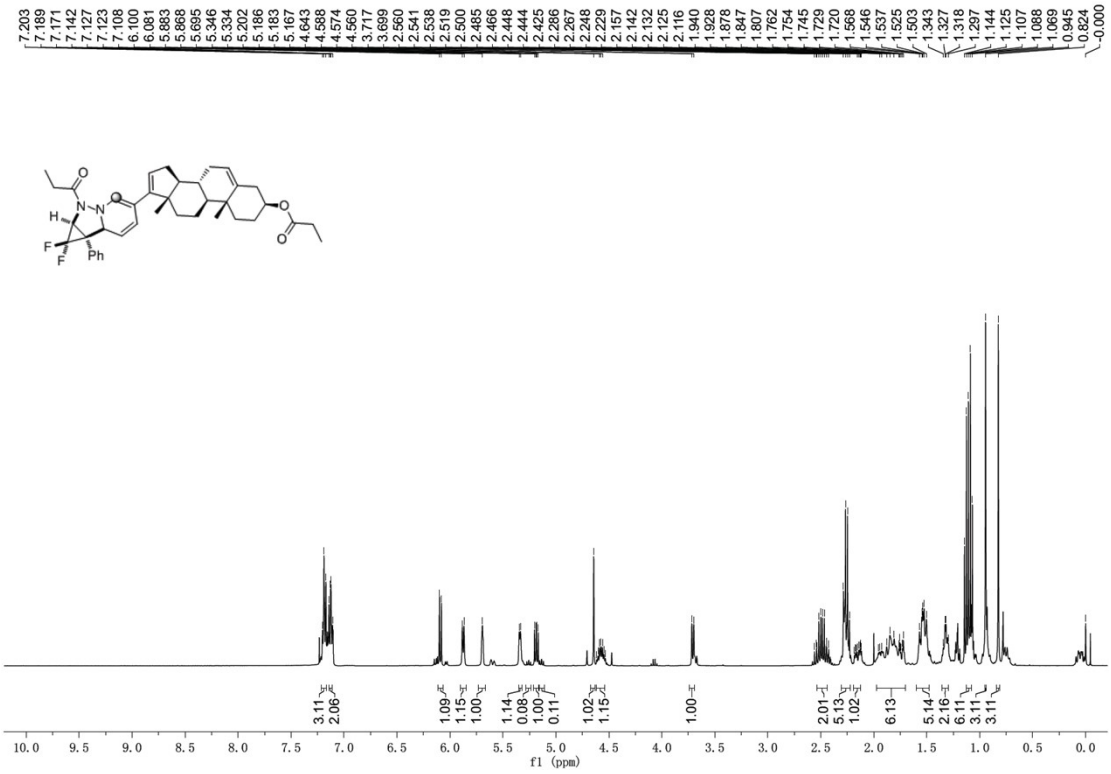
8c-^{13}C NMR (100 MHz, $CDCl_3$)



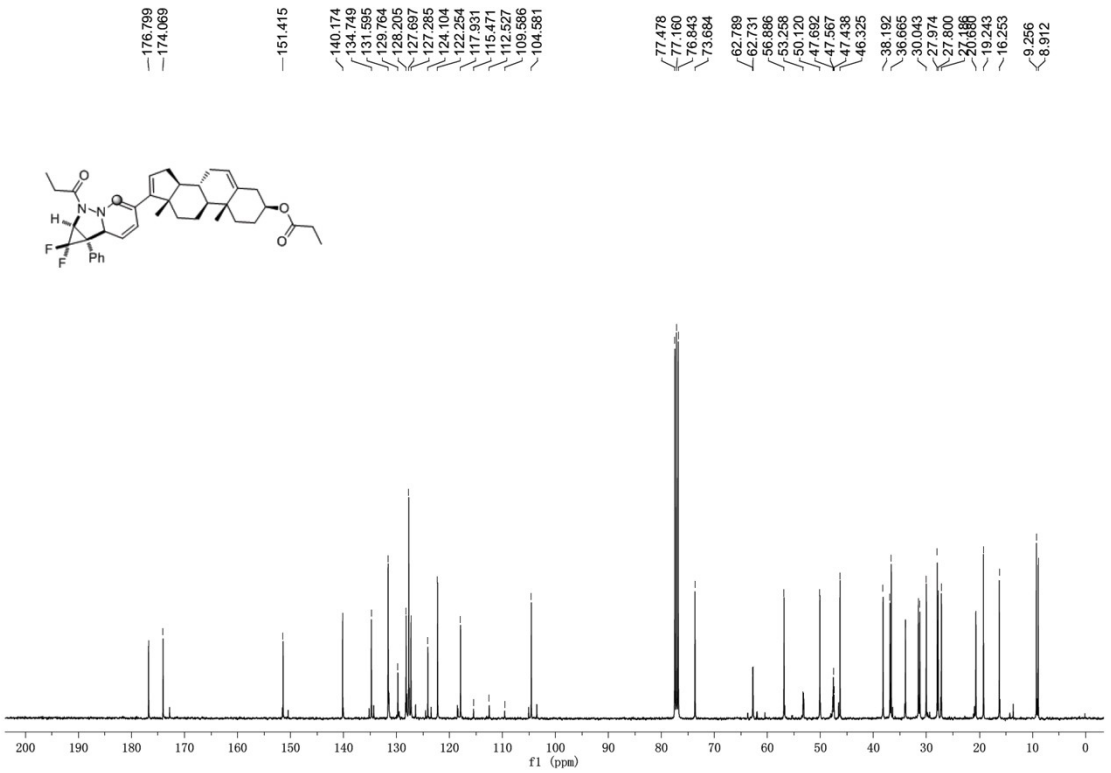
8c-^{19}F NMR (376 MHz, $CDCl_3$)



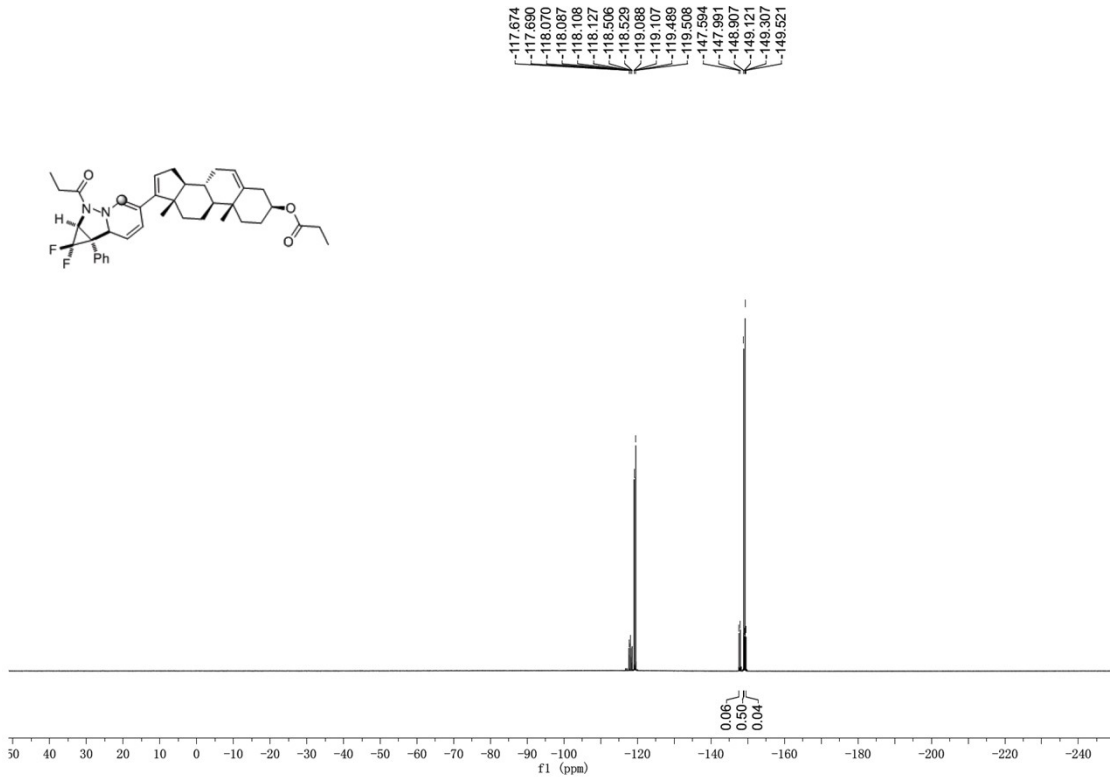
8d-^{1}H NMR (400 MHz, $CDCl_3$)



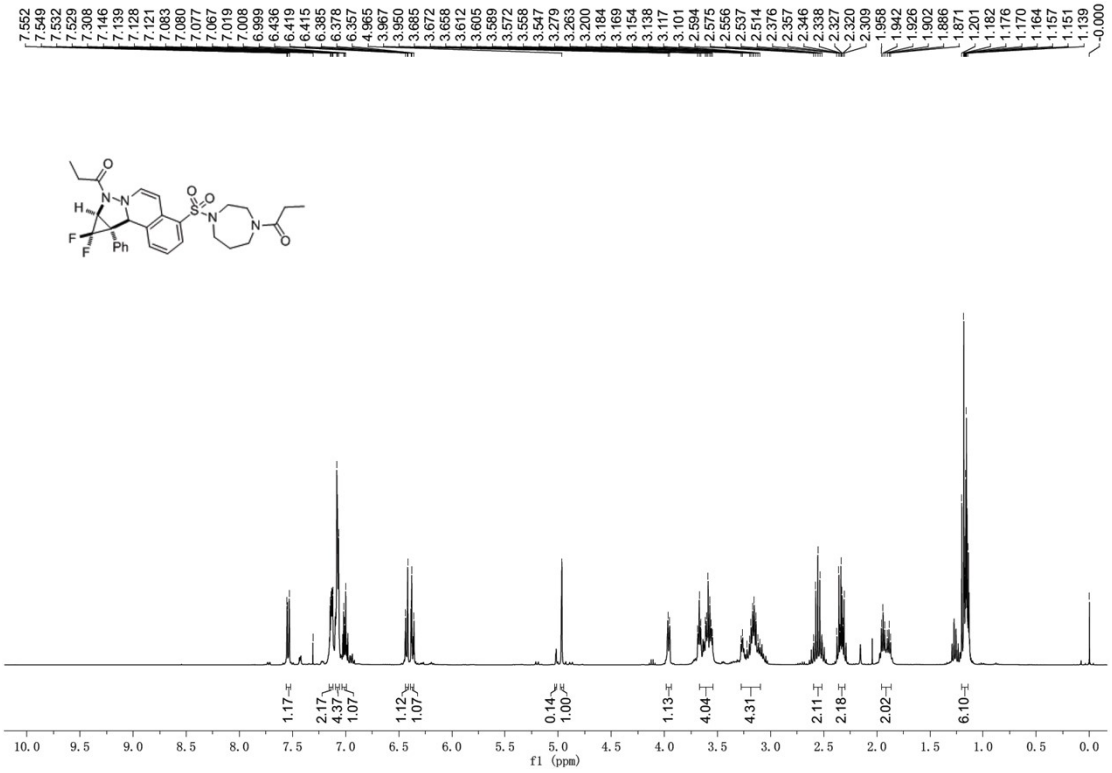
8d-^{13}C NMR (100 MHz, $CDCl_3$)



8d-^{19}F NMR (376 MHz, $CDCl_3$)



8e-^{1}H NMR (400 MHz, $CDCl_3$)



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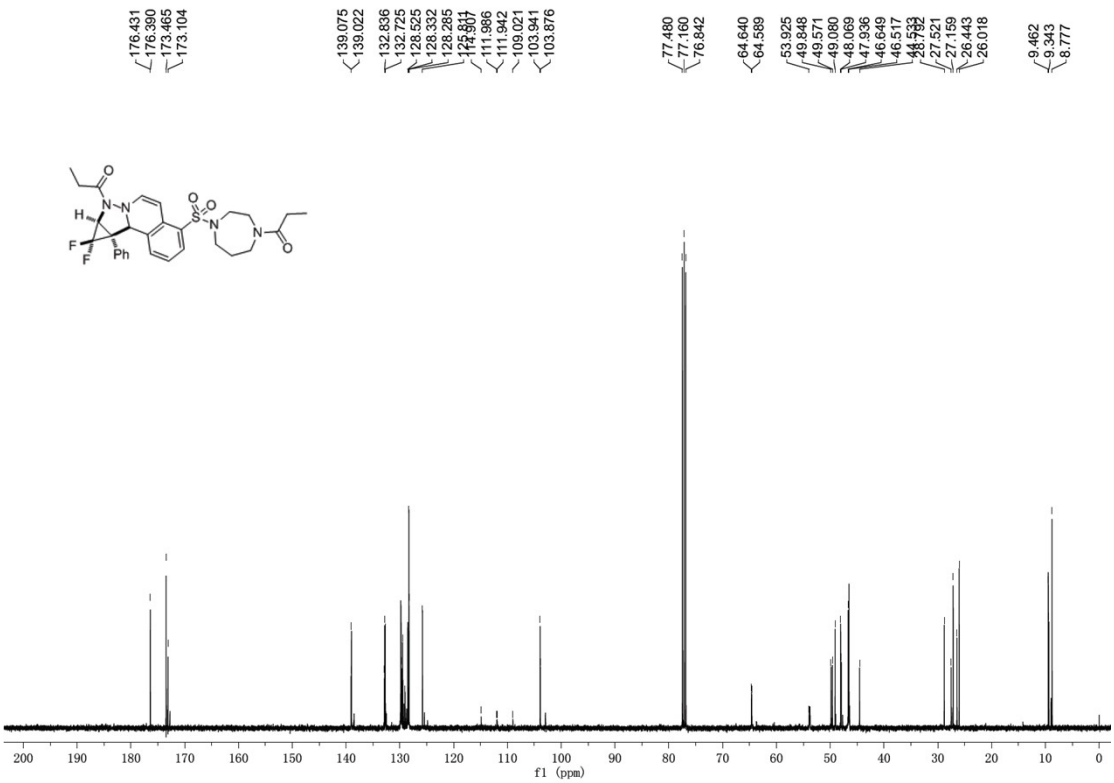
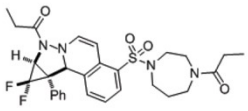
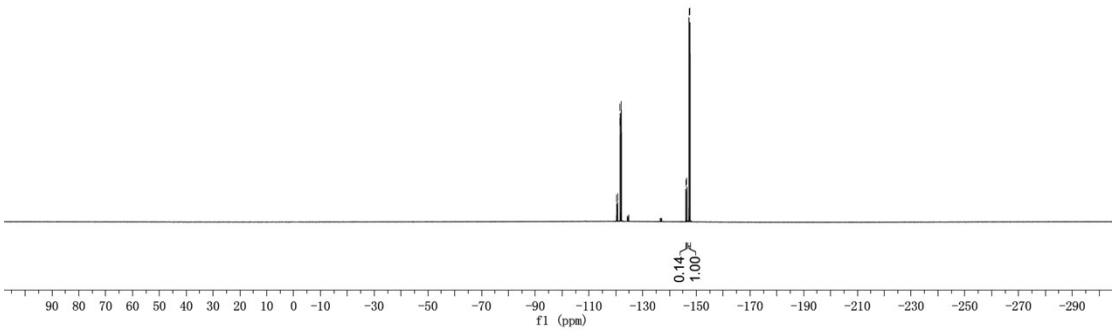
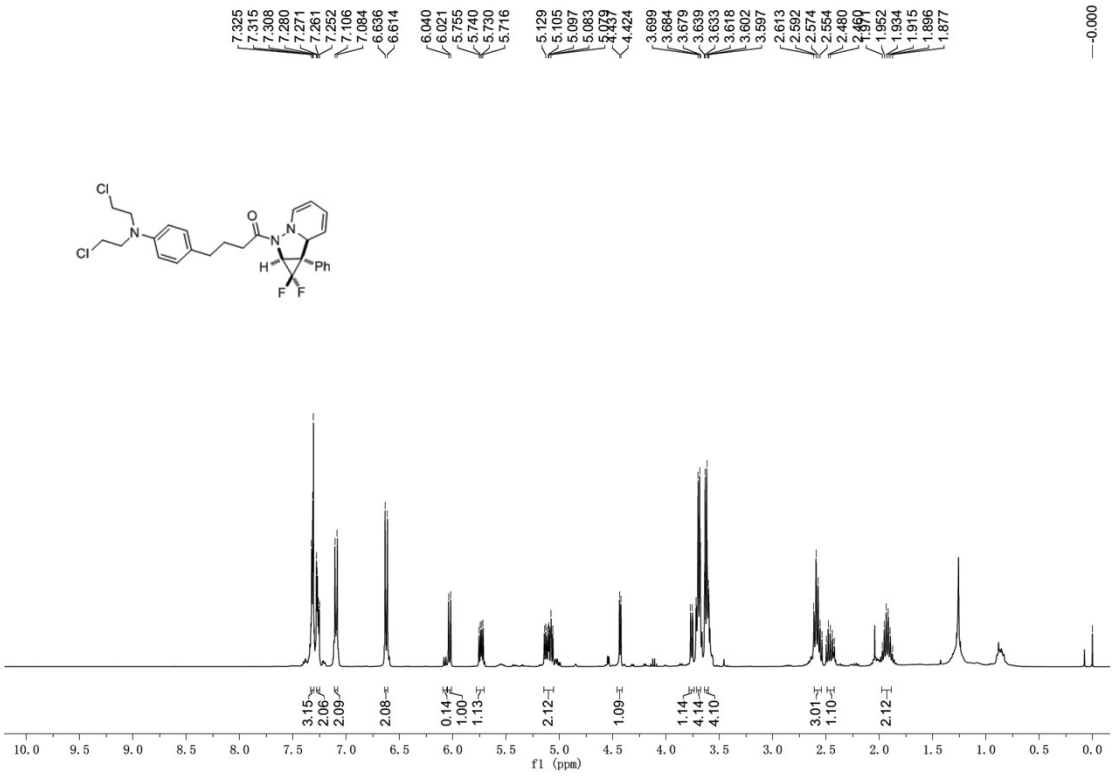


8e-^{19}F NMR (376 MHz, $CDCl_3$)

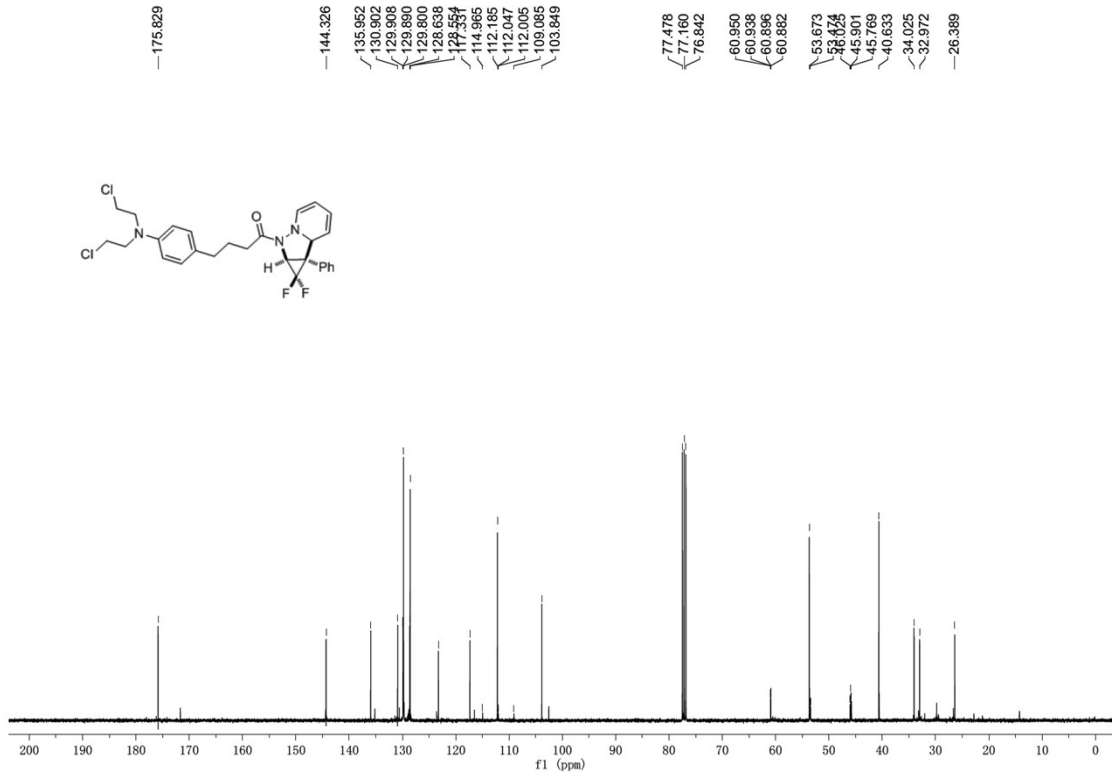




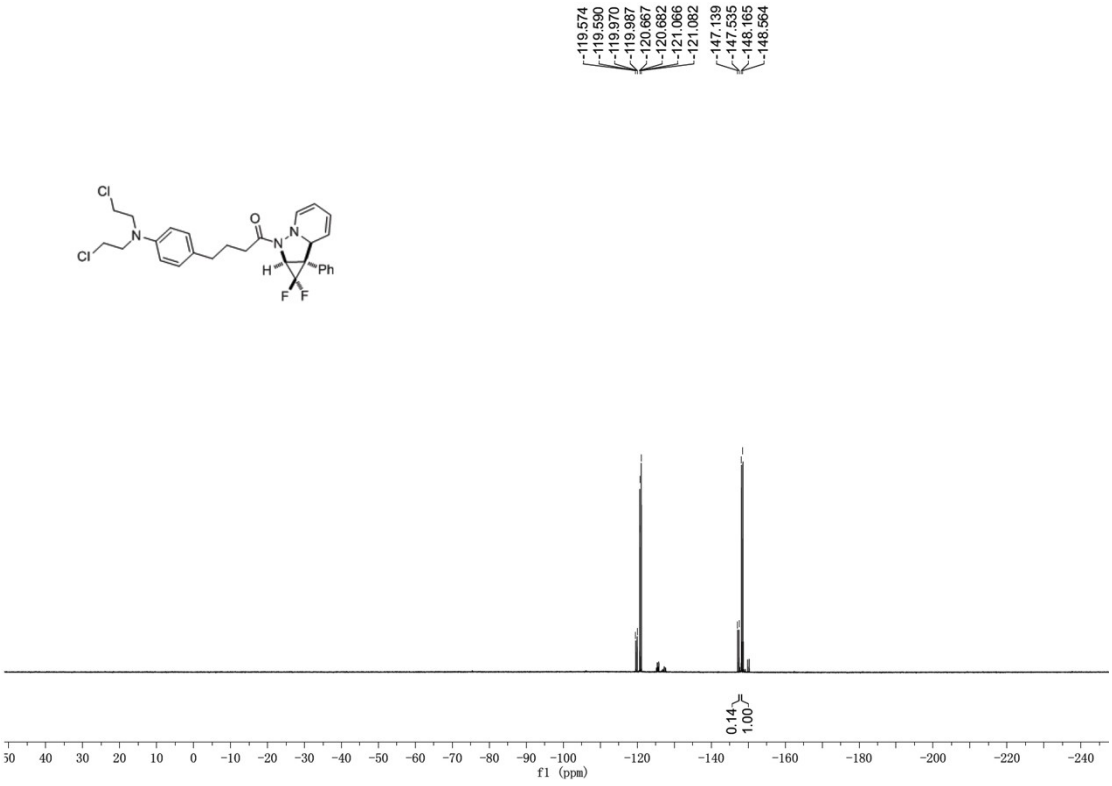
8f-^{1}H NMR (400 MHz, $CDCl_3$)



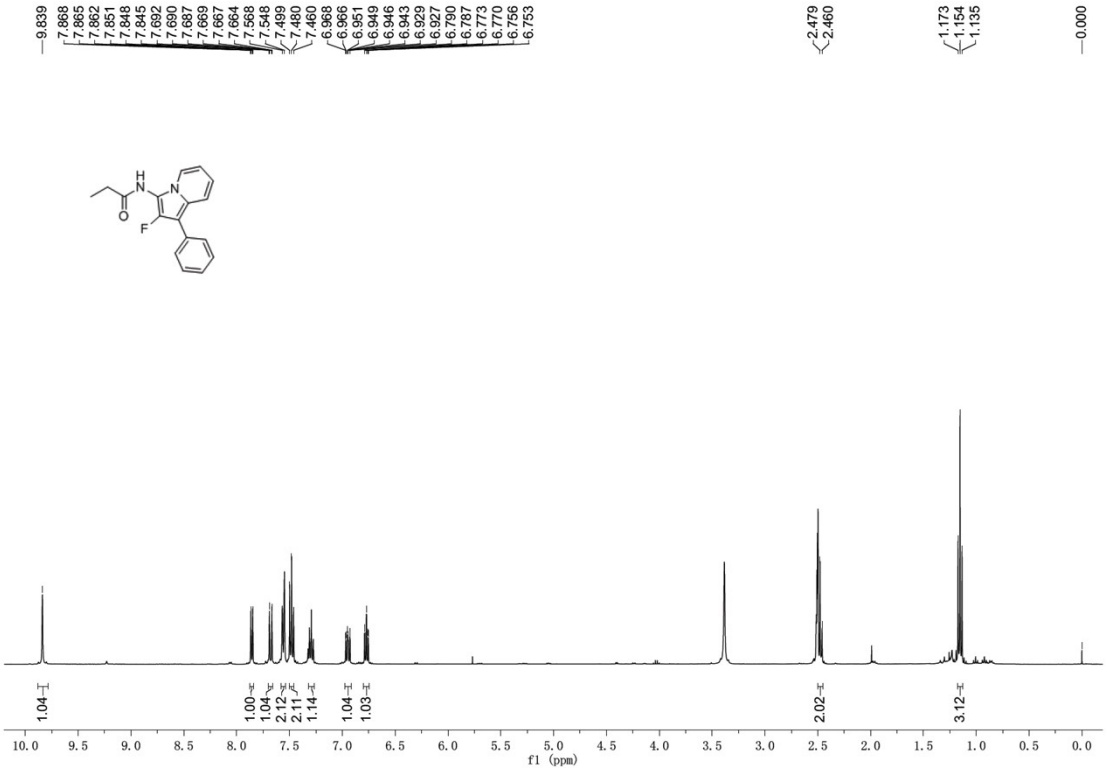
8f-^{13}C NMR (100 MHz, $CDCl_3$)



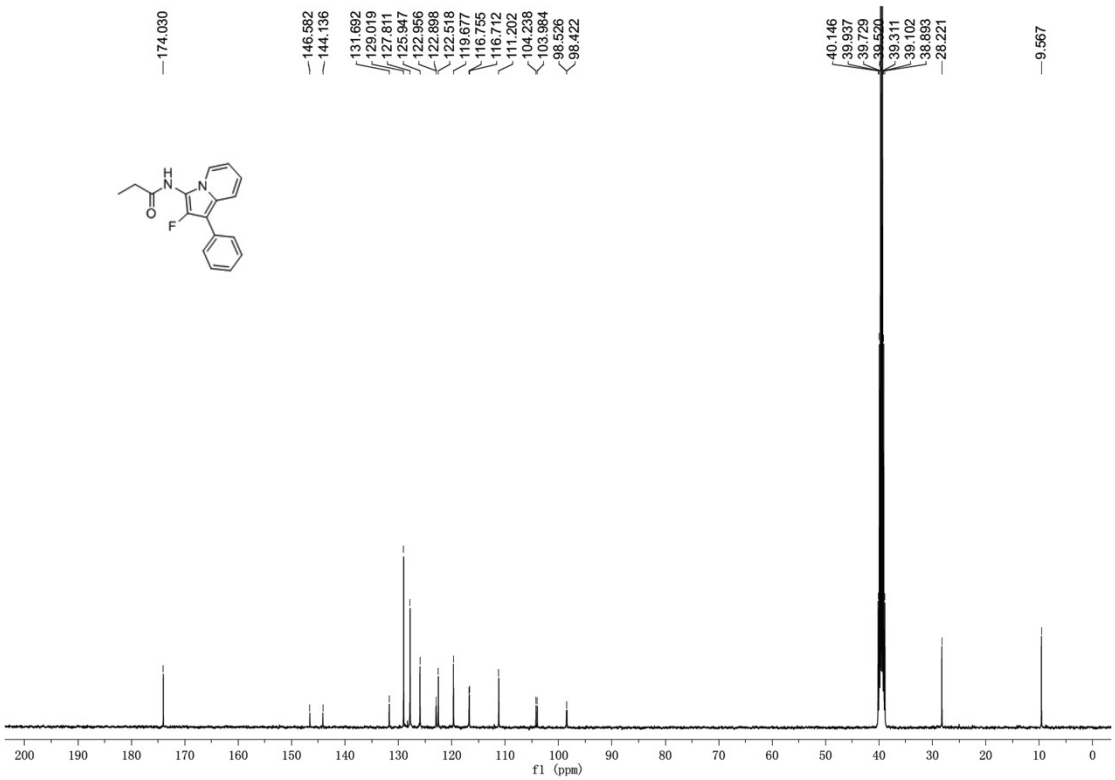
8f-^{19}F NMR (376 MHz, $CDCl_3$)



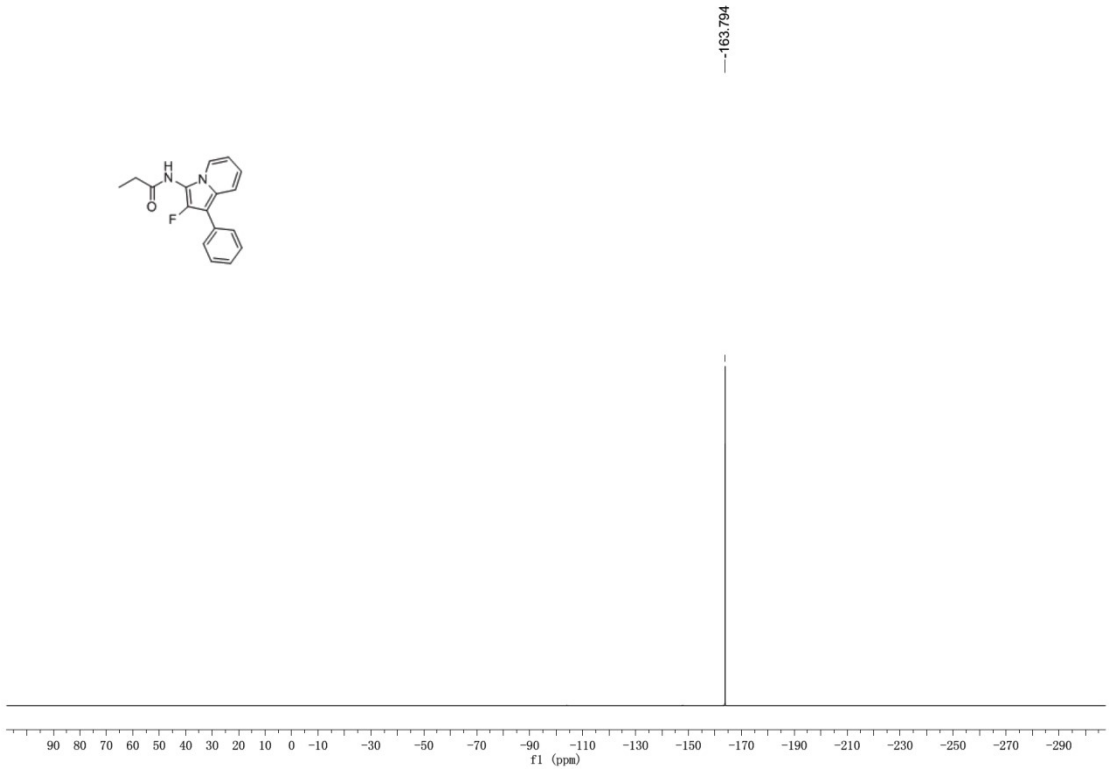
9a-^{1}H NMR (400 MHz, DMSO-d_6)



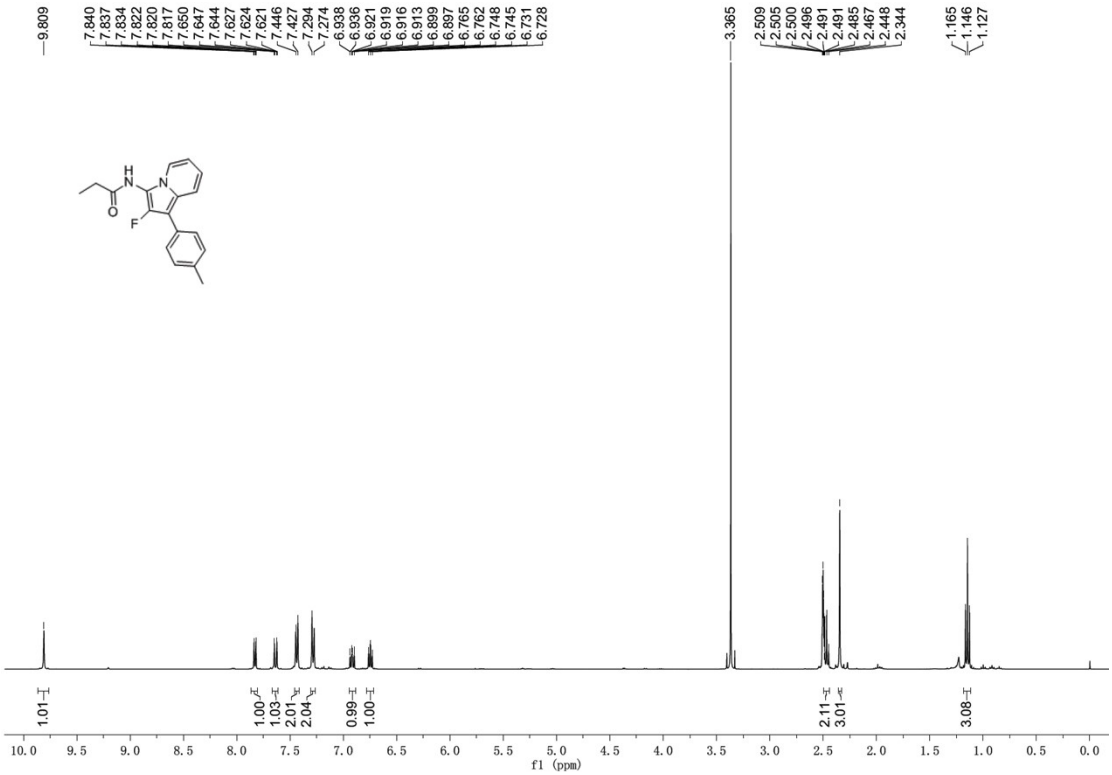
9a-^{13}C NMR (100 MHz, DMSO-d_6)



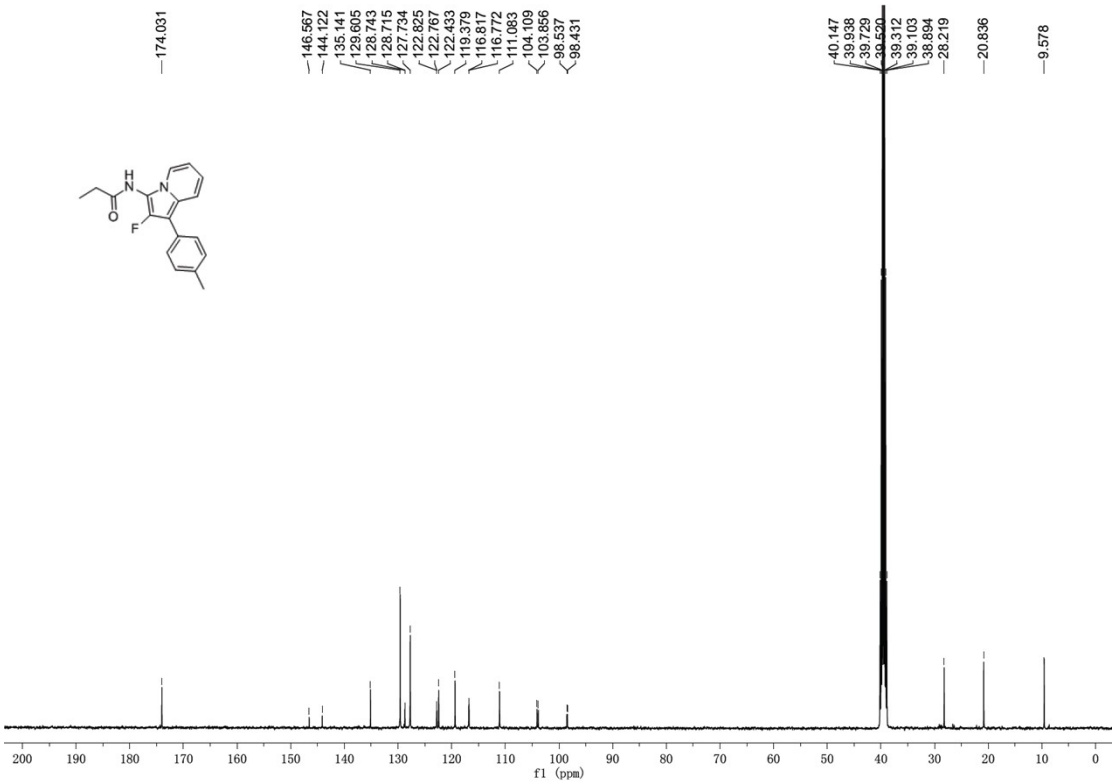
9a-^{19}F NMR (376 MHz, DMSO-d_6)



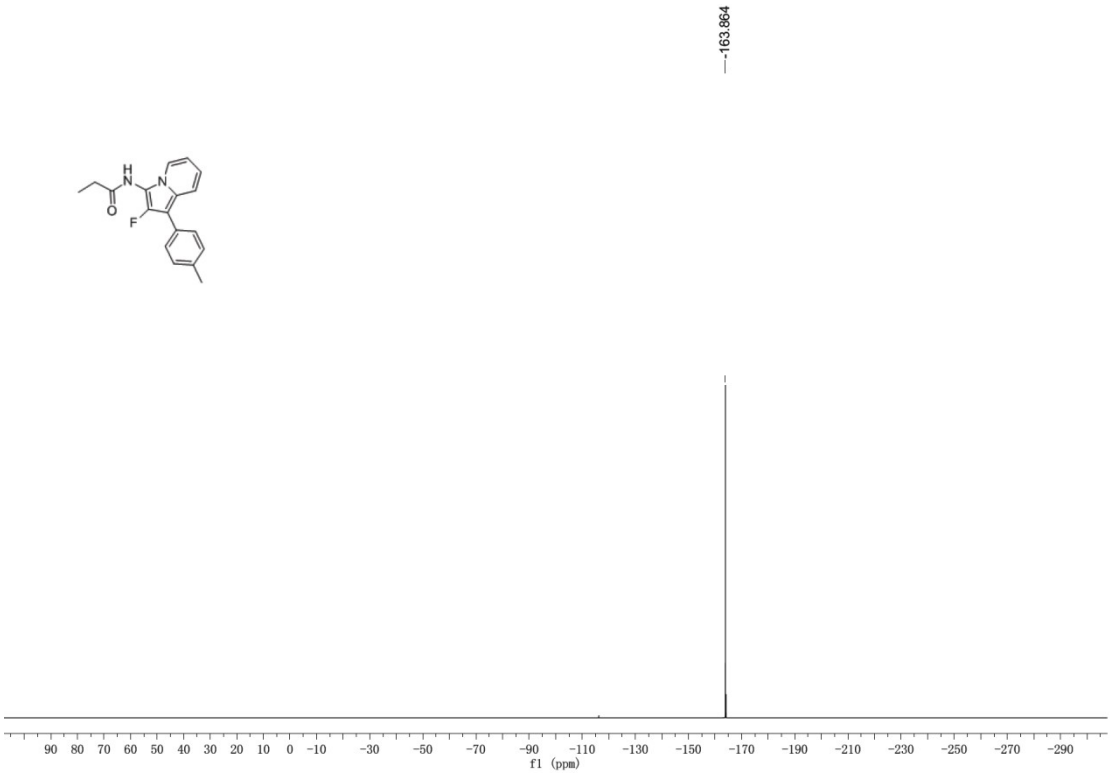
9b-^{1}H NMR (400 MHz, DMSO-d_6)



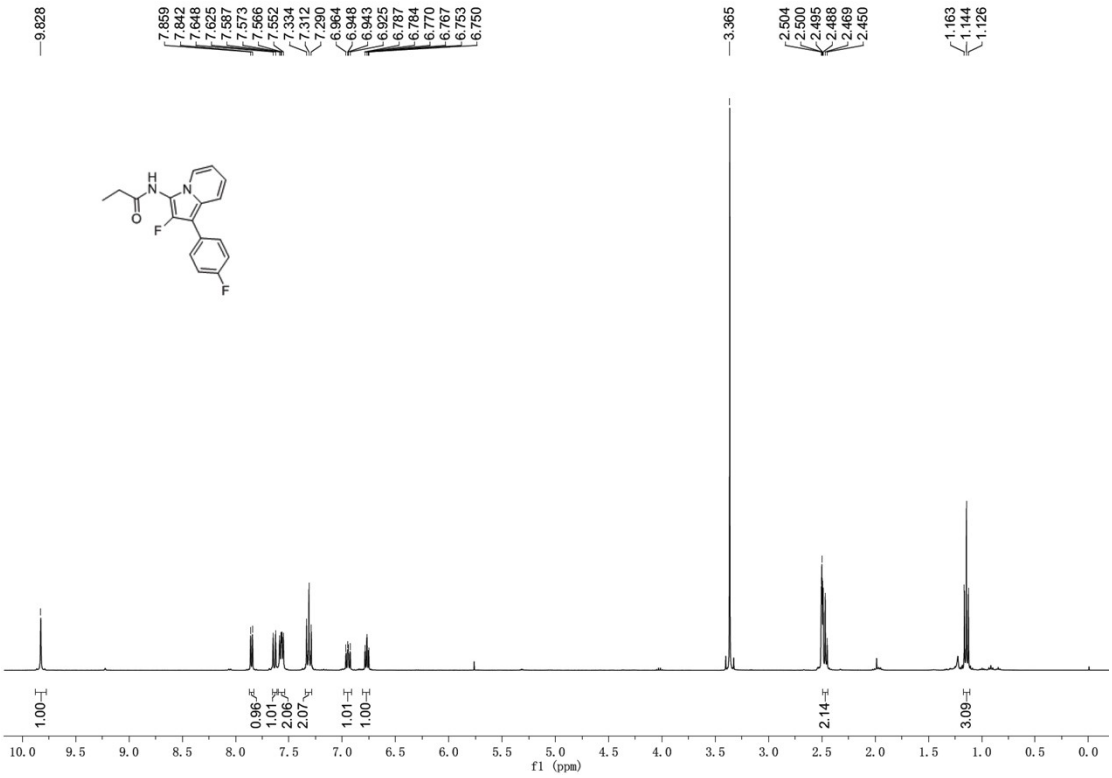
9b-^{13}C NMR (100 MHz, DMSO-d_6)



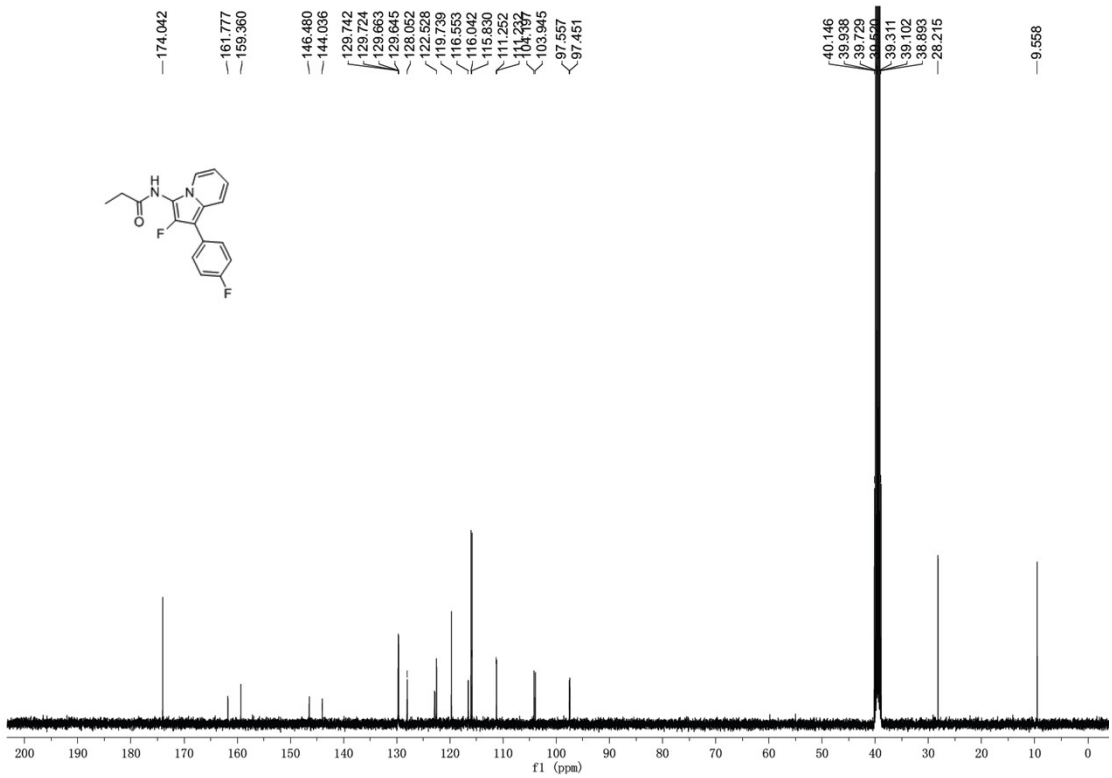
9b-^{19}F NMR (376 MHz, DMSO-d_6)



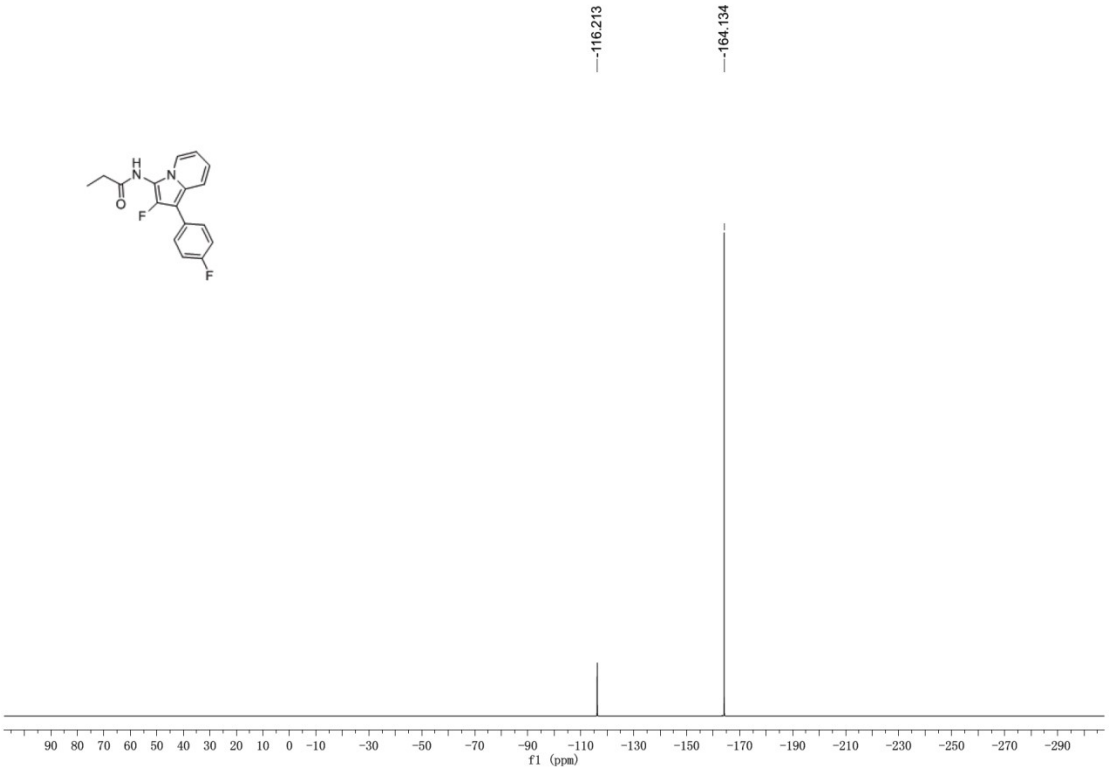
9c-^{1}H NMR (400 MHz, DMSO-d_6)



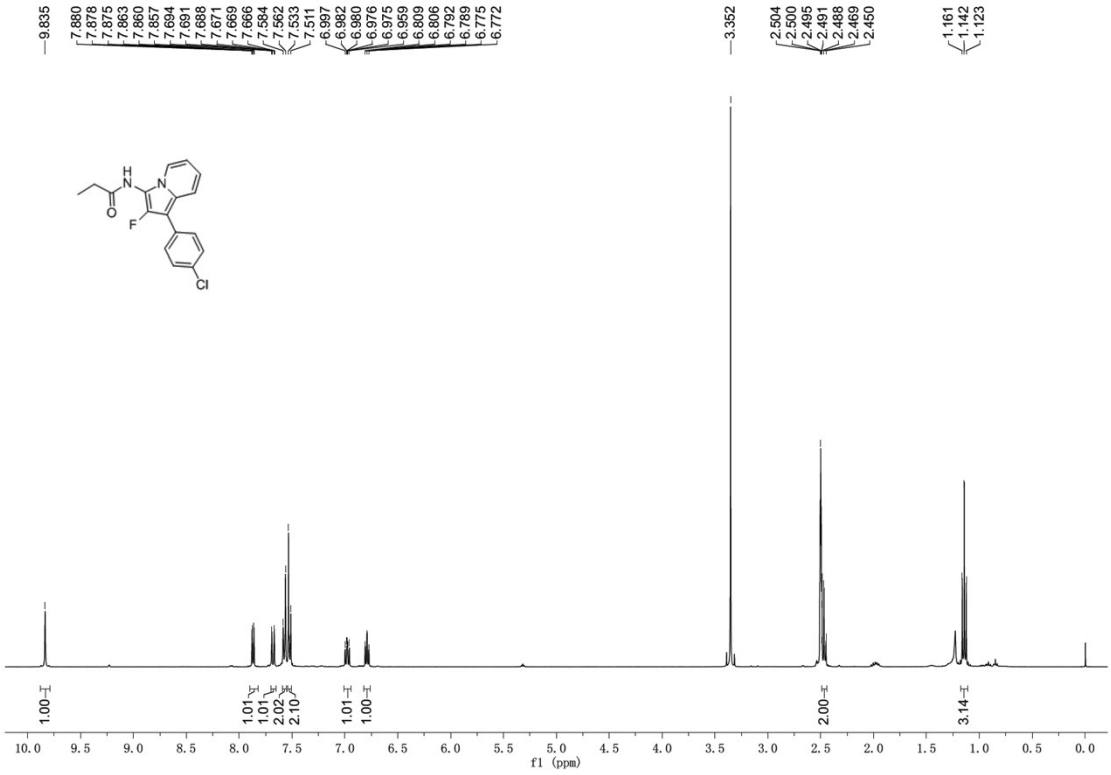
9c-^{13}C NMR (100 MHz, DMSO-d_6)



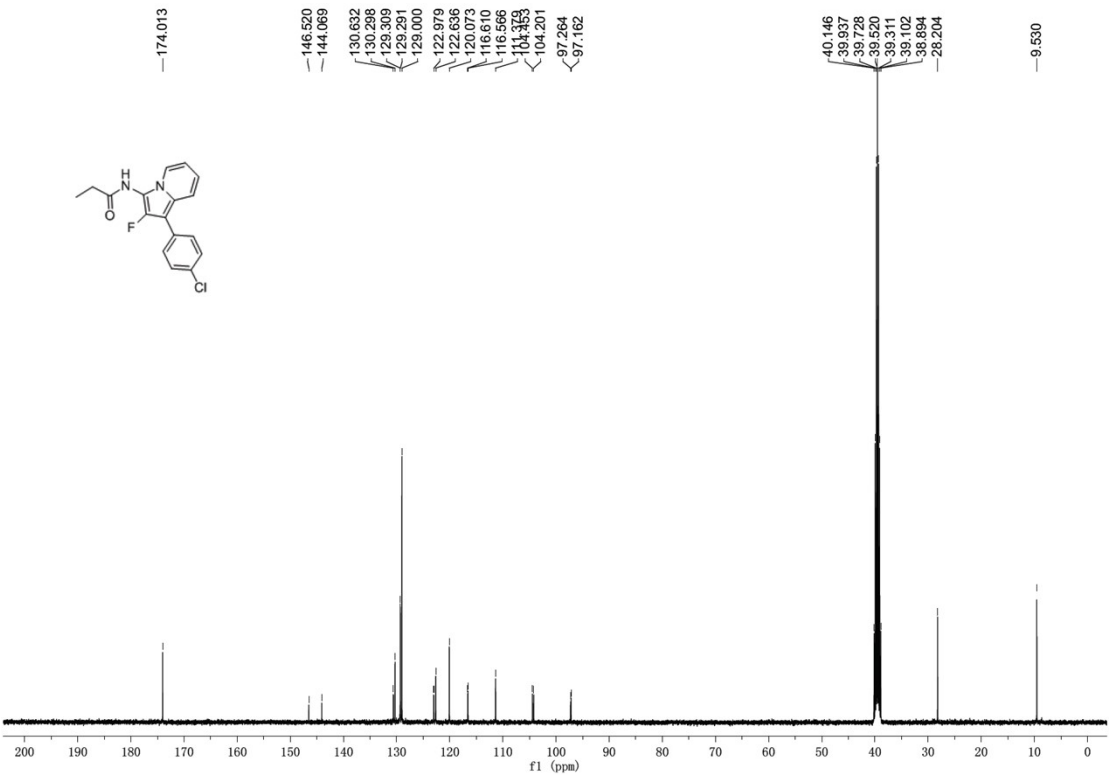
9c-^{19}F NMR (376 MHz, DMSO-d_6)



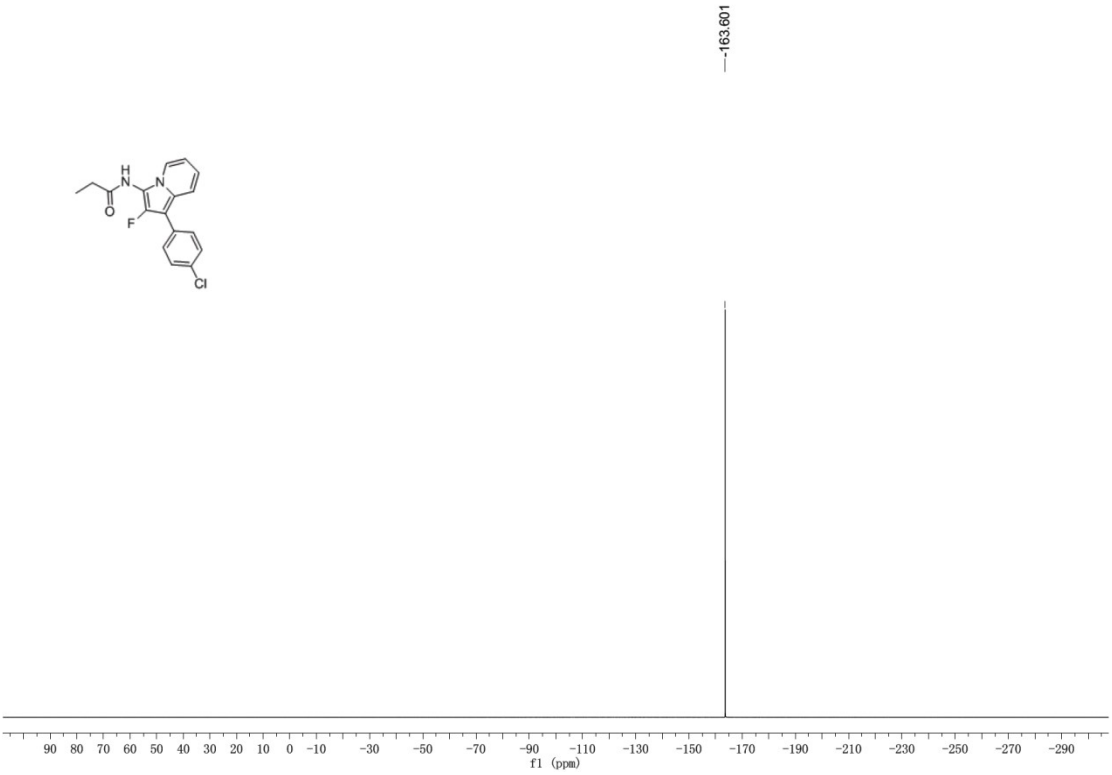
9d-^{1}H NMR (400 MHz, DMSO-d_6)



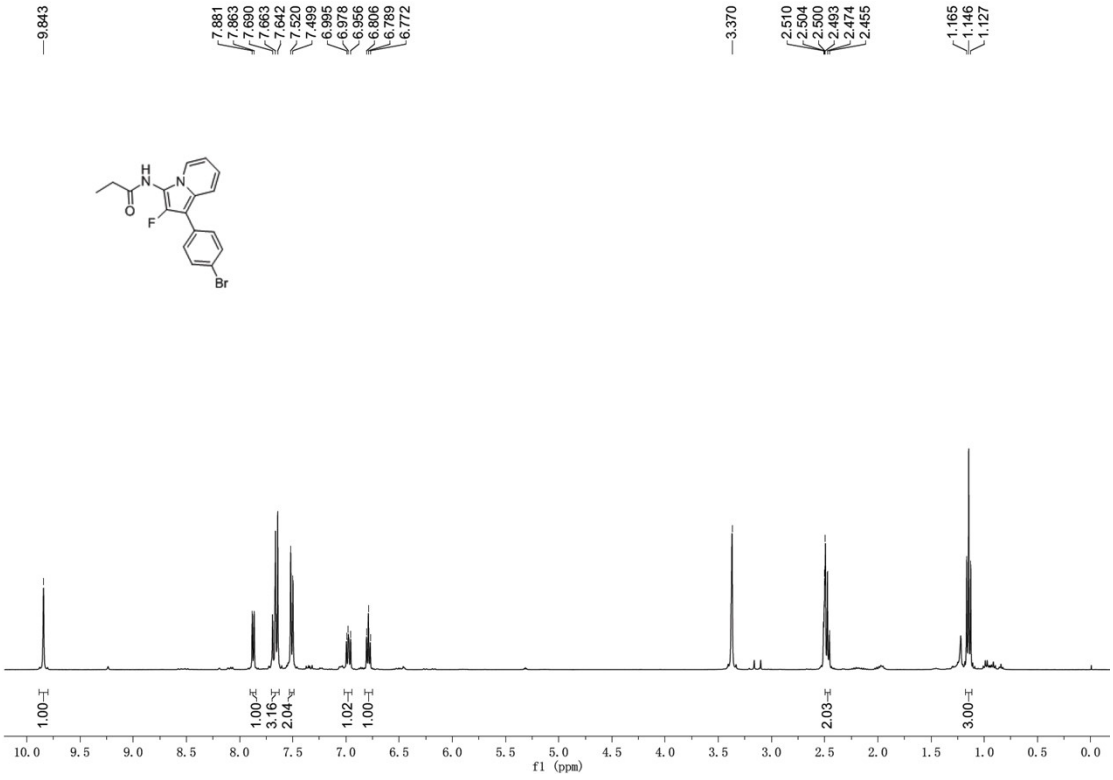
9d-^{13}C NMR (100 MHz, DMSO-d_6)



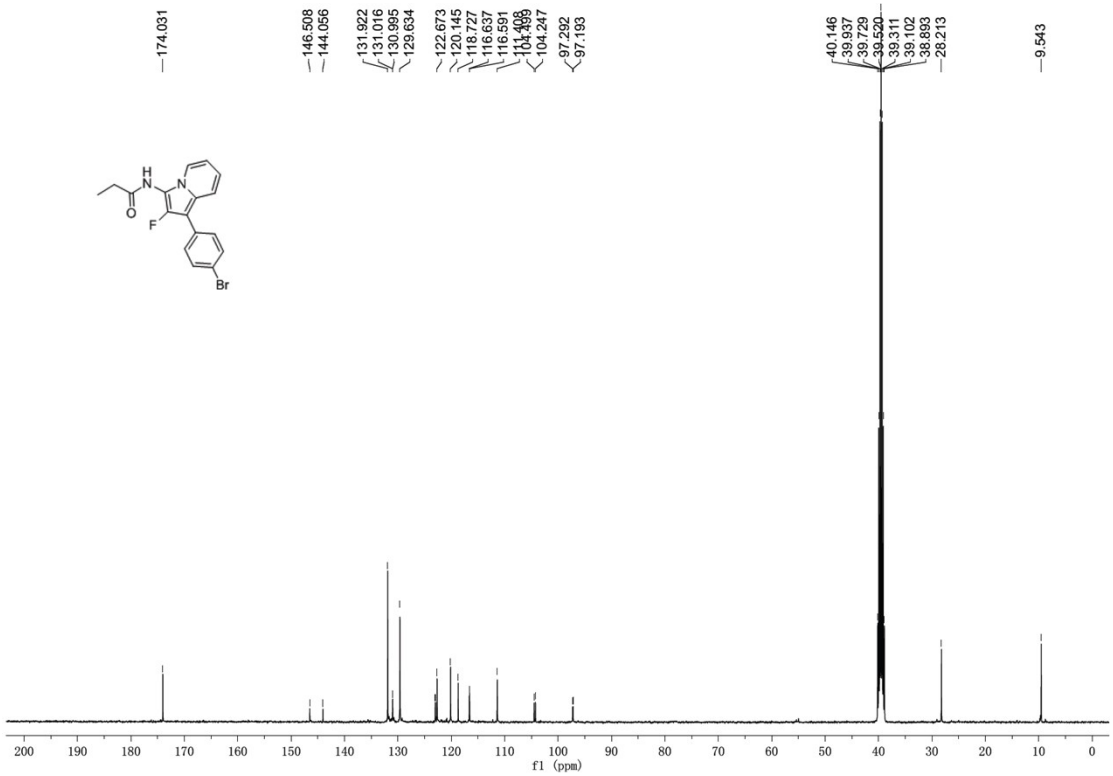
9d-^{19}F NMR (376 MHz, DMSO-d_6)



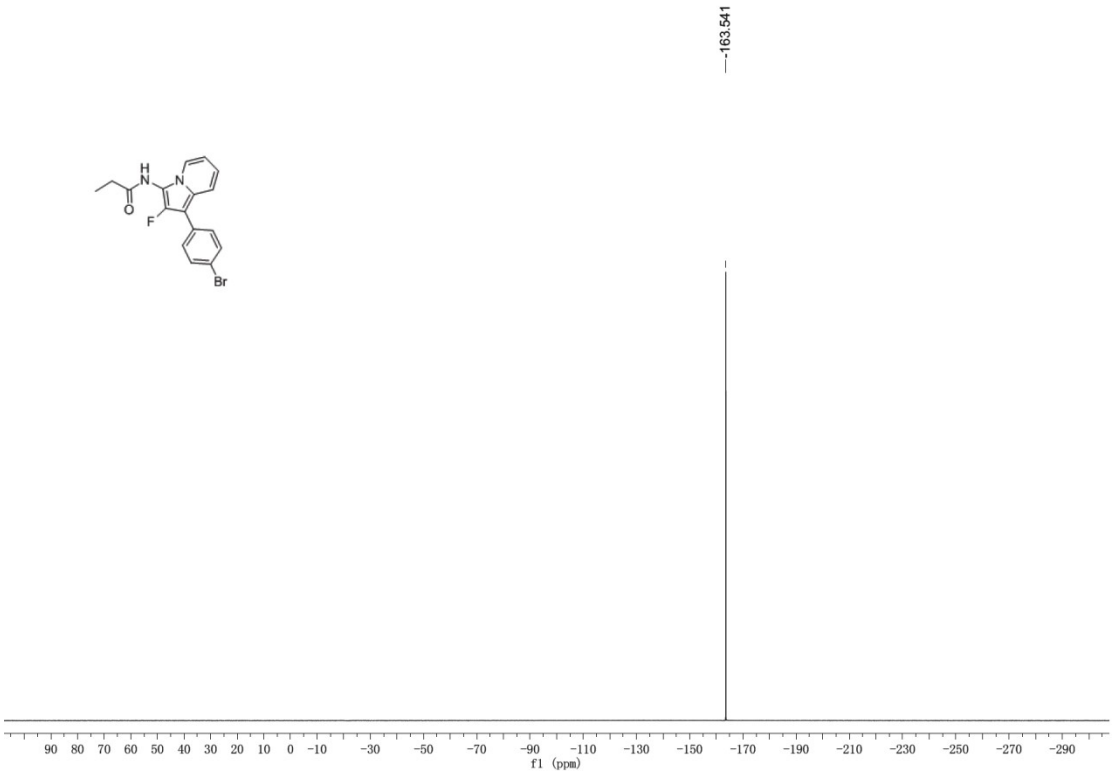
9e-^{1}H NMR (400 MHz, DMSO-d_6)



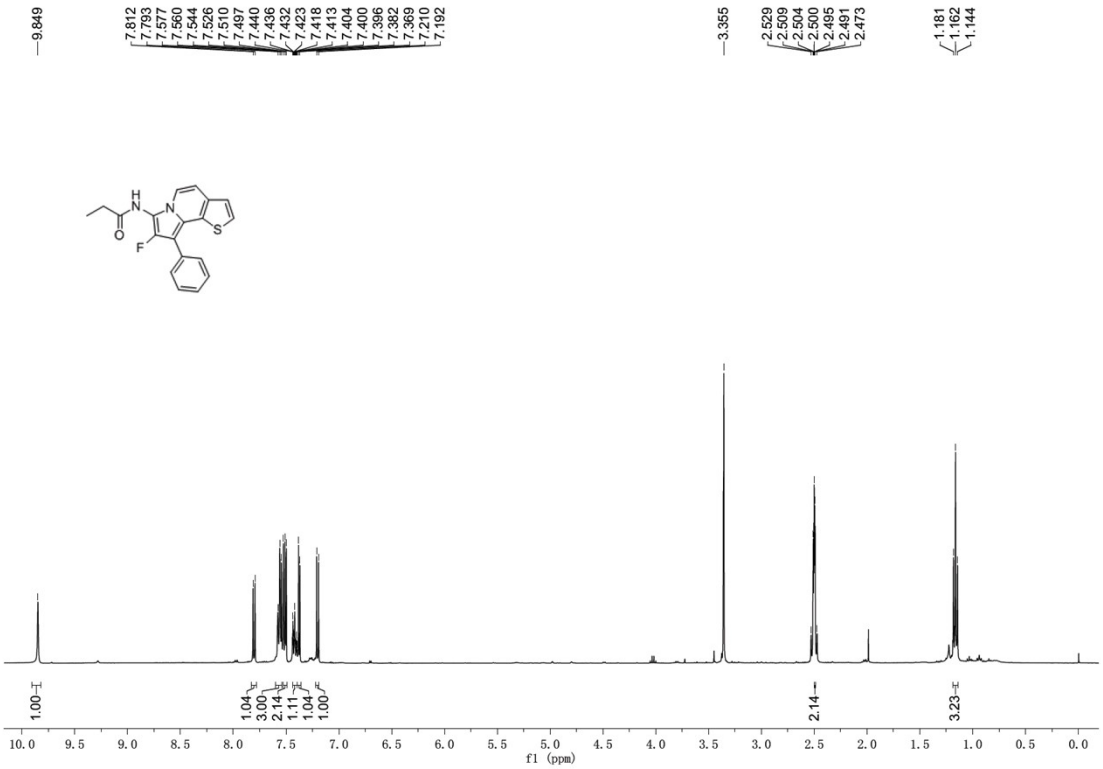
9e-^{13}C NMR (100 MHz, DMSO-d_6)



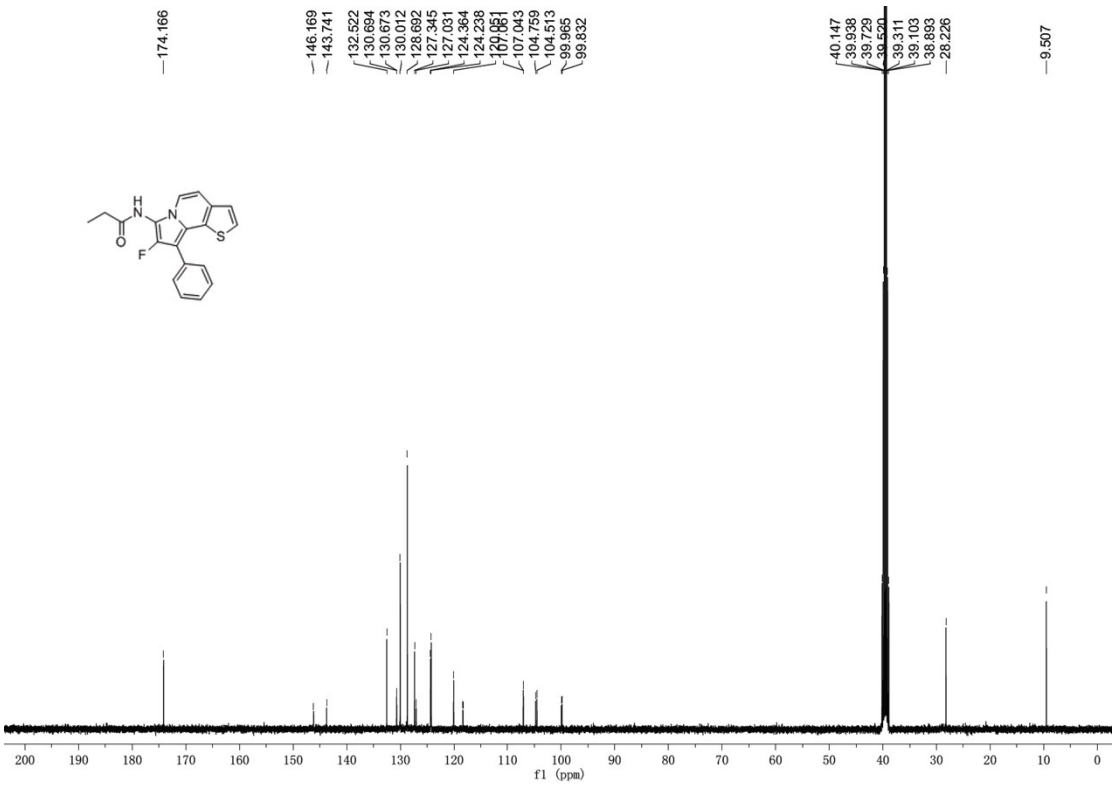
9e-^{19}F NMR (376 MHz, DMSO-d_6)



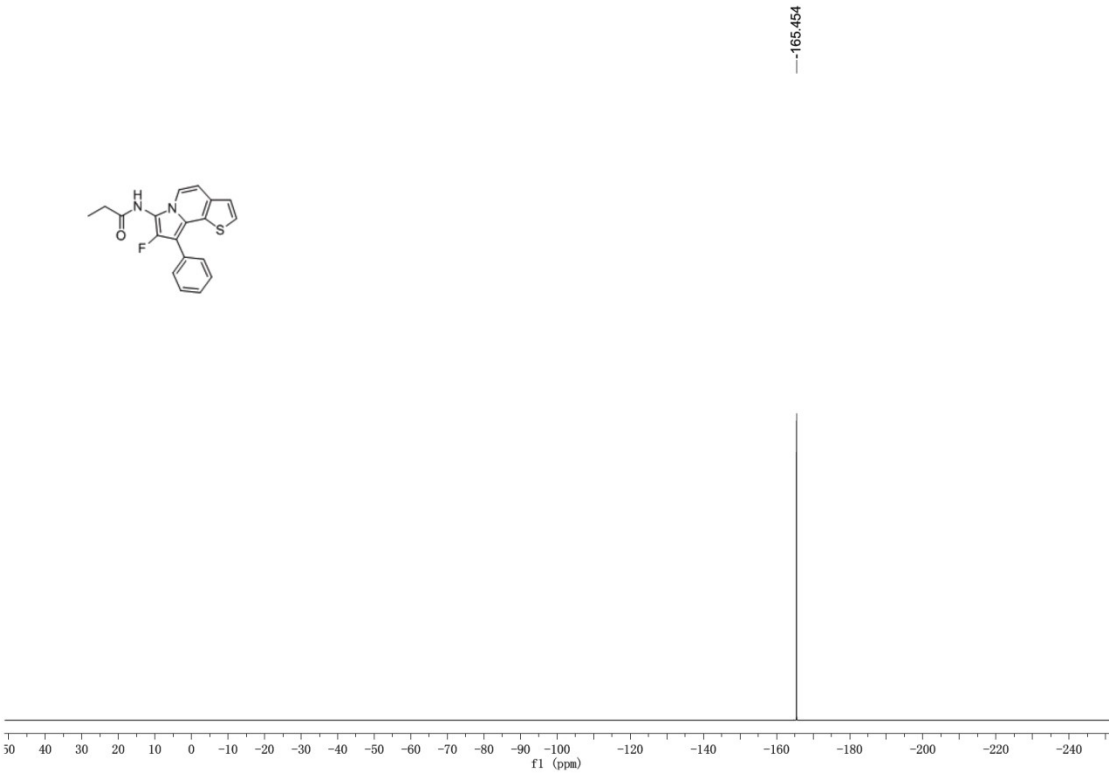
9f-^{1}H NMR (100 MHz, DMSO-d_6)



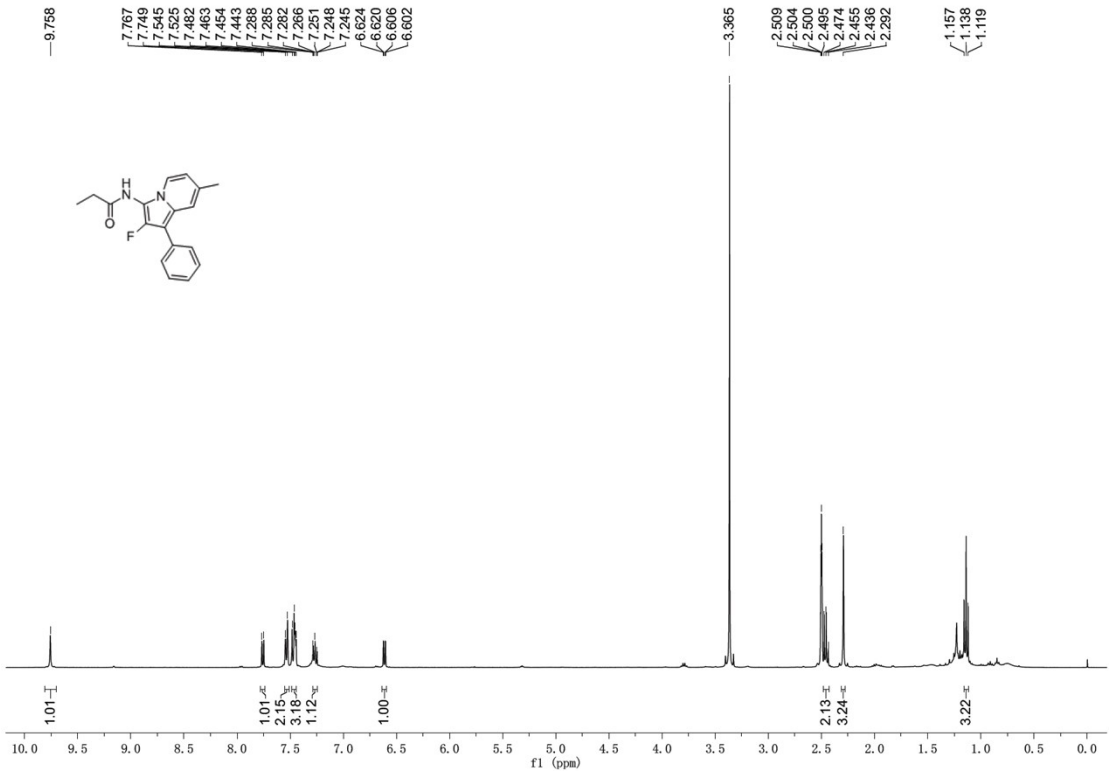
9f-^{13}C NMR (100 MHz, DMSO-d_6)



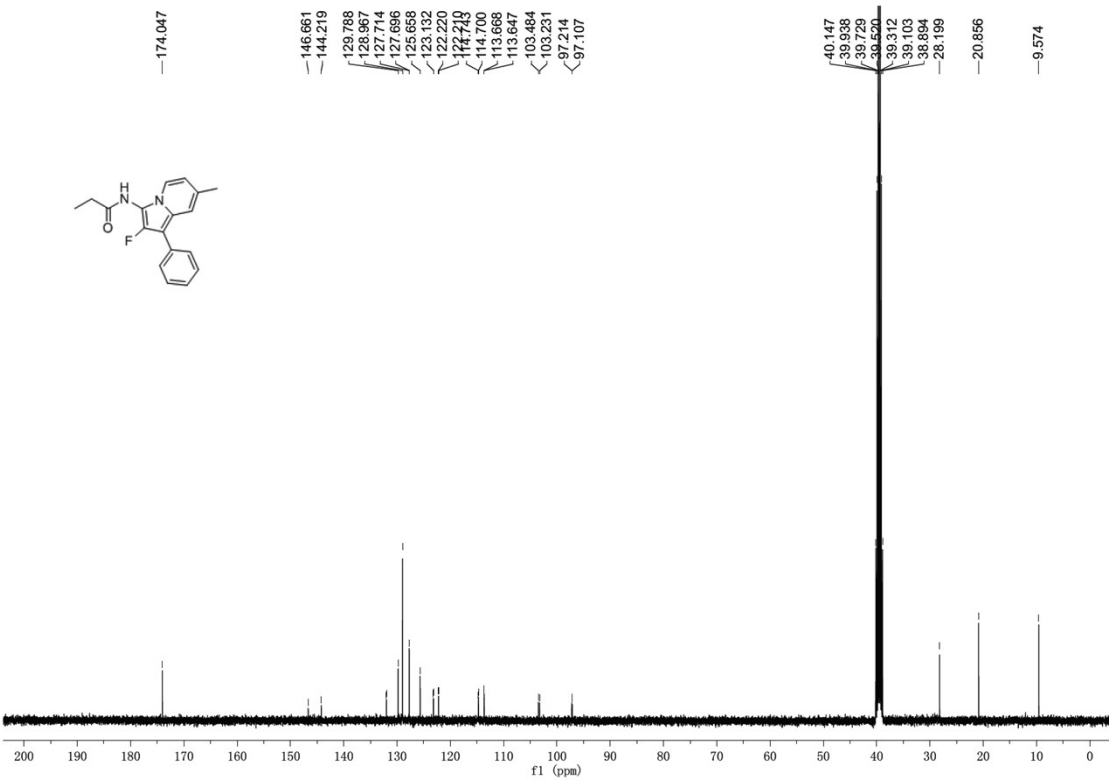
9f-^{19}F NMR (376 MHz, DMSO-d_6)



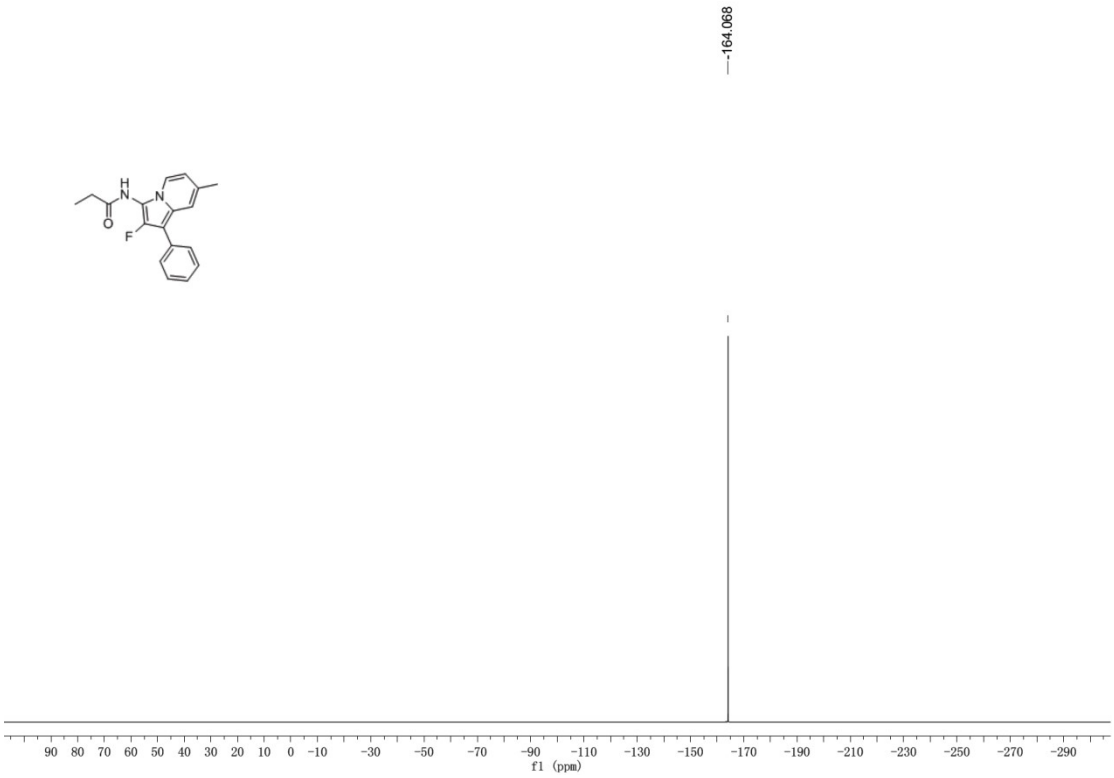
9g-^{1}H NMR (400 MHz, DMSO-d_6)



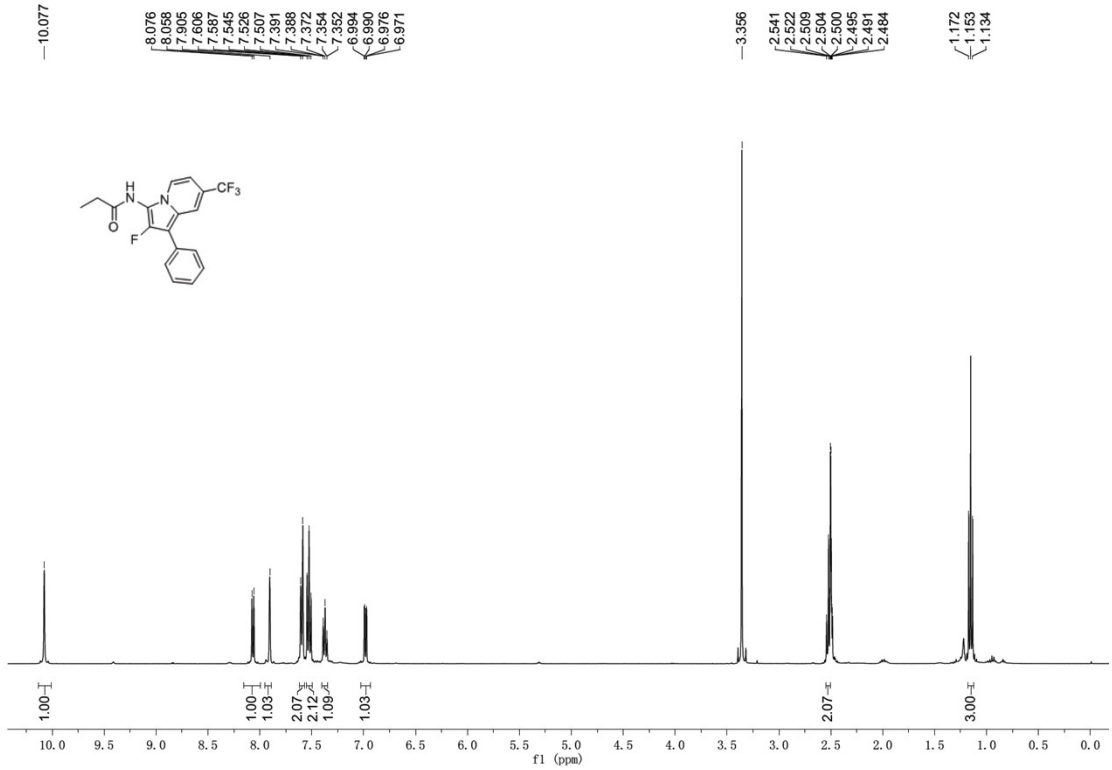
9g-^{13}C NMR (100 MHz, DMSO-d_6)



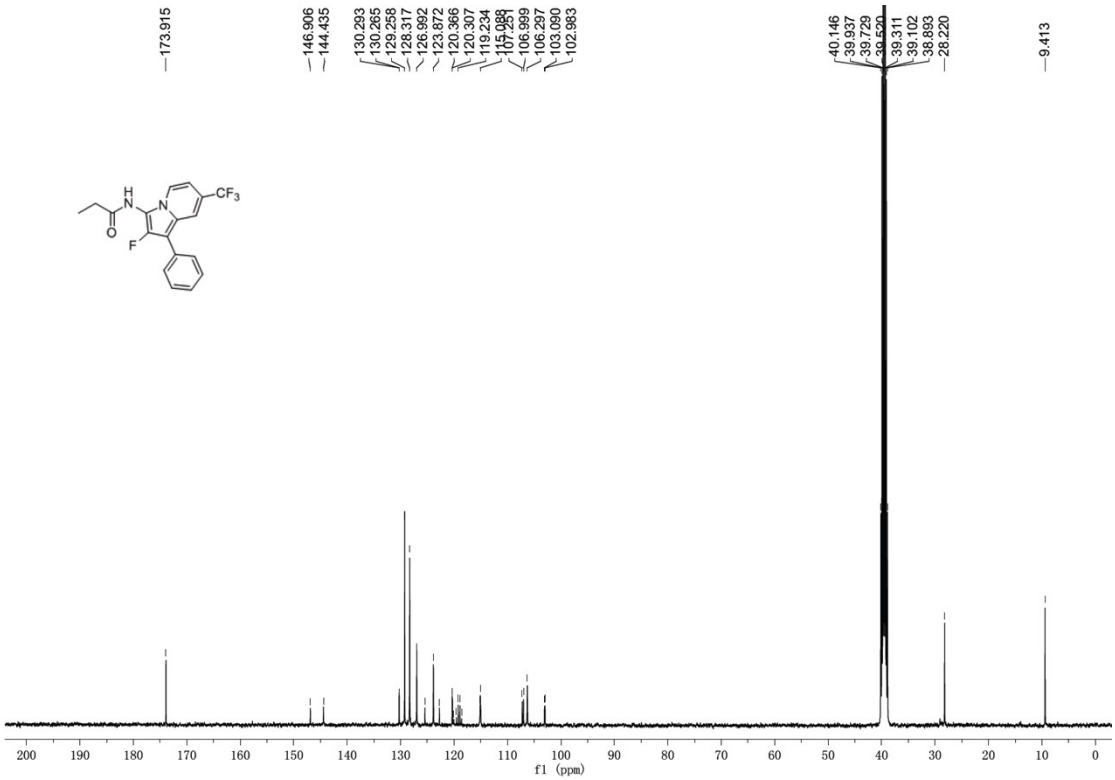
9g-^{19}F NMR (376 MHz, DMSO-d_6)



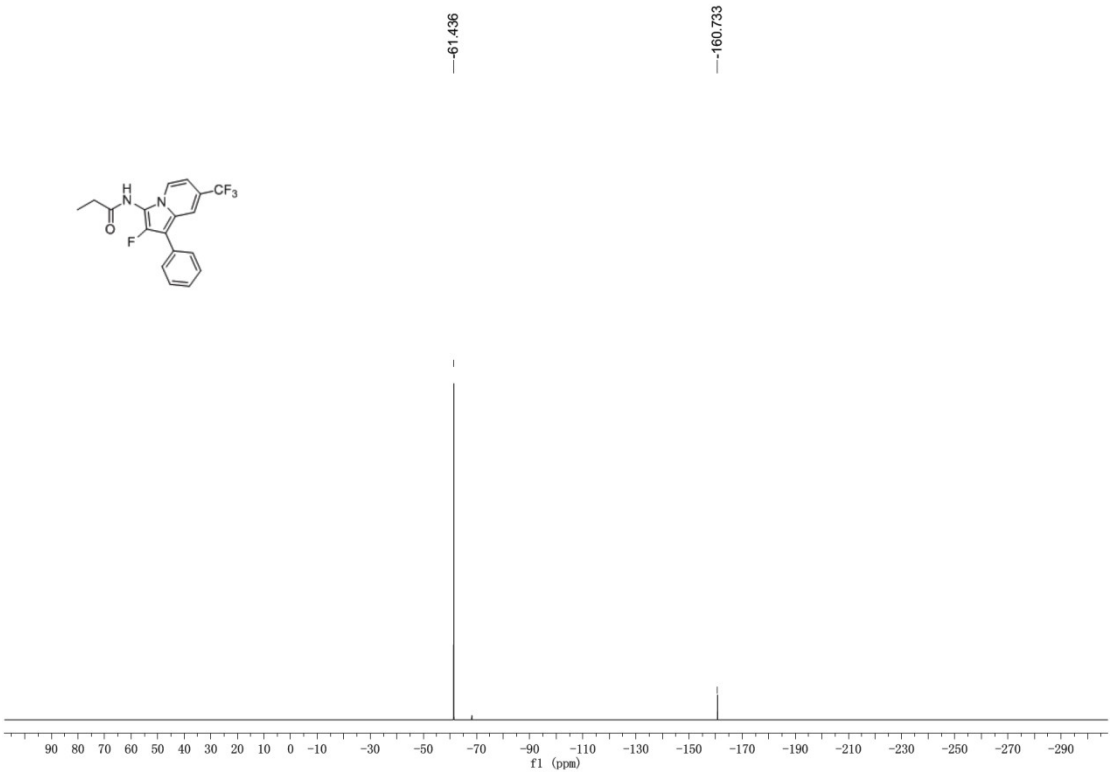
9h-^{1}H NMR (400 MHz, DMSO-d_6)



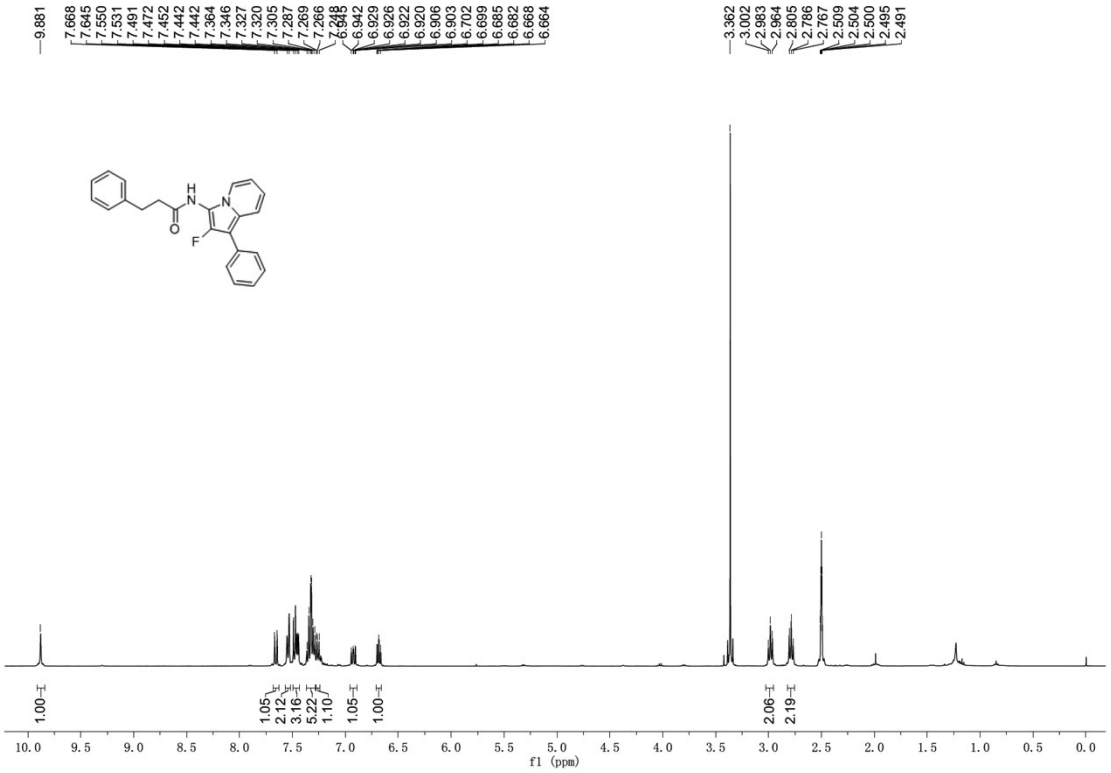
9h-^{13}C NMR (100 MHz, DMSO-d_6)



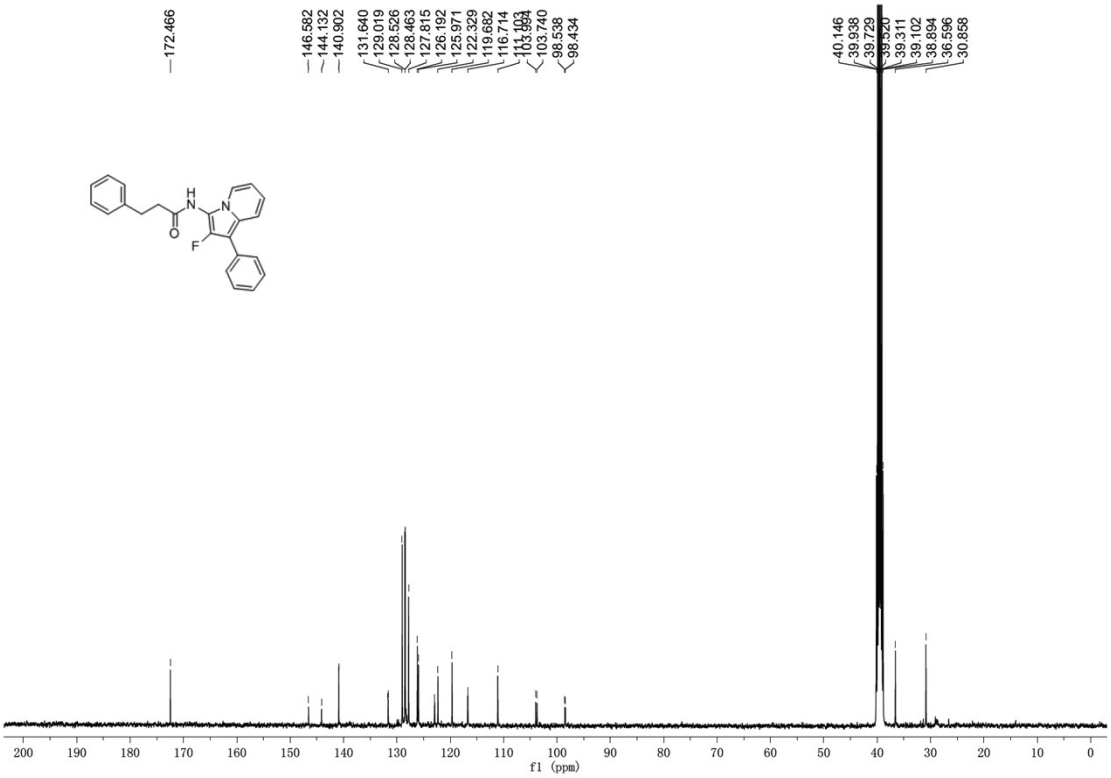
9h-^{19}F NMR (376 MHz, DMSO-d_6)



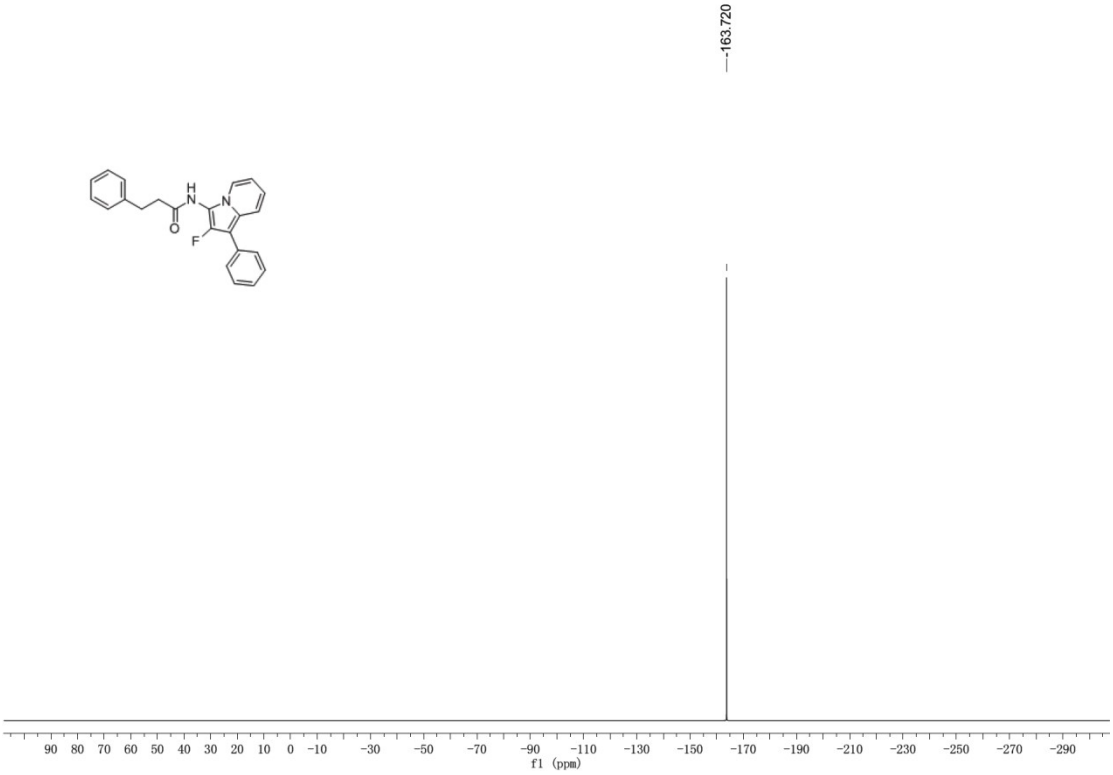
9i-^{1}H NMR (400 MHz, DMSO-d_6)



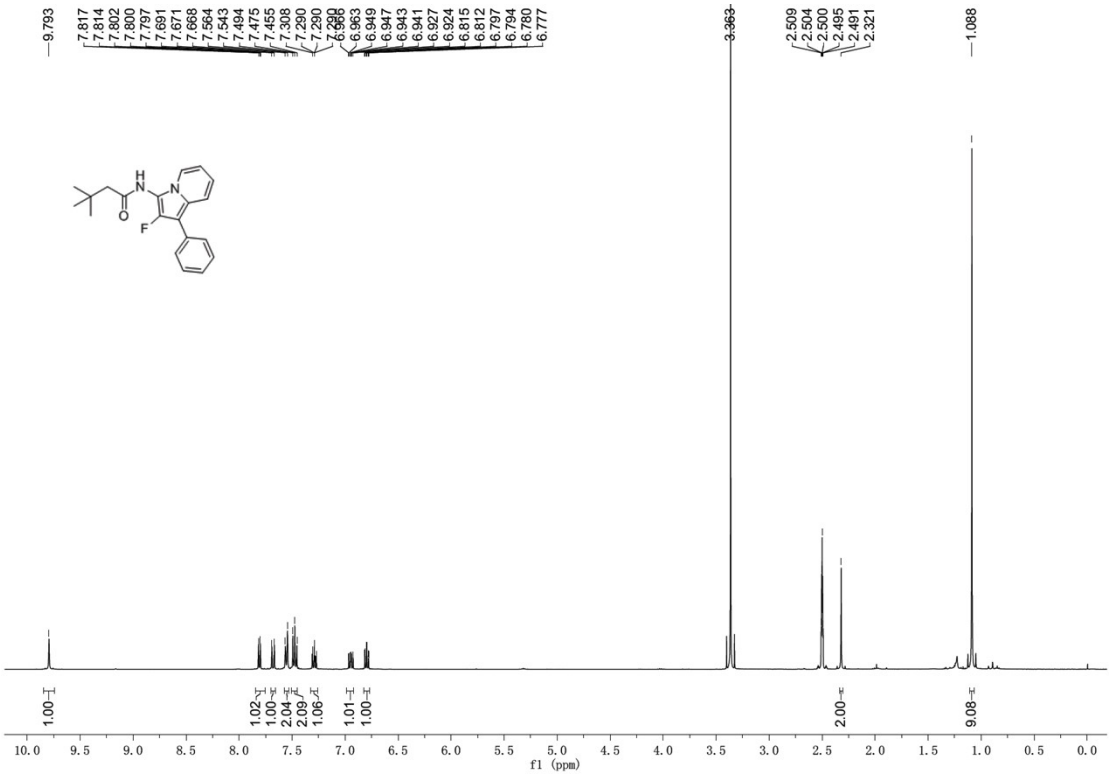
9i-^{13}C NMR (100 MHz, DMSO-d_6)



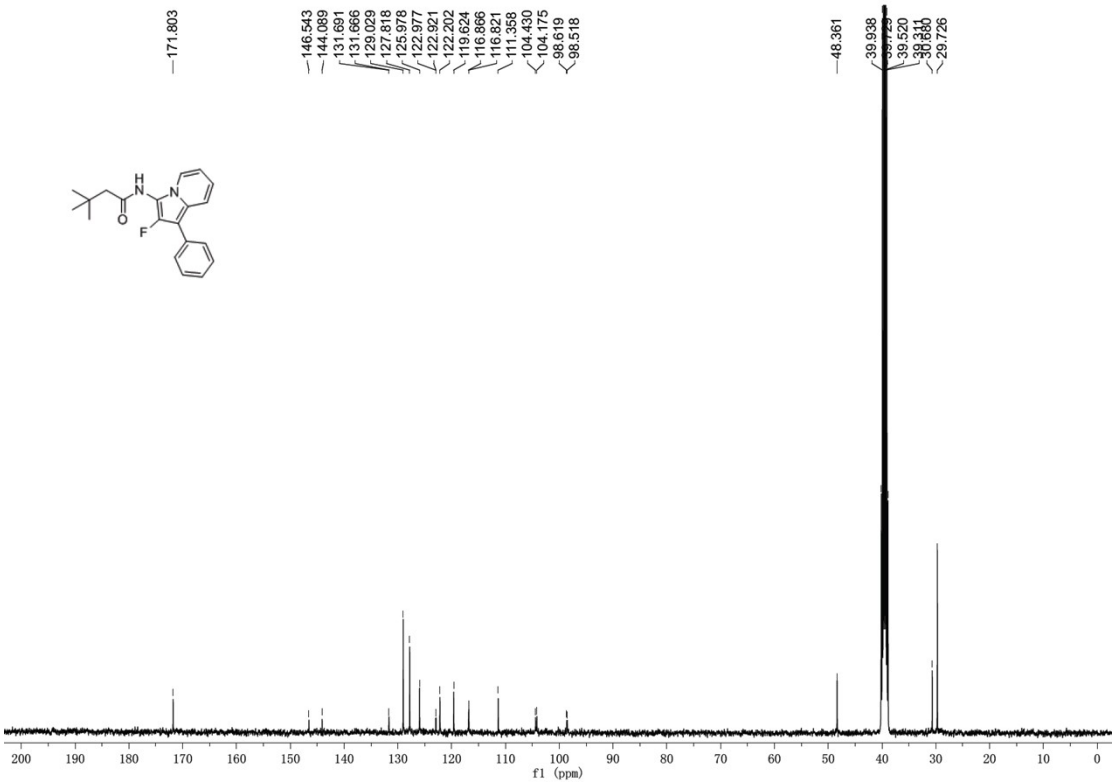
9i-^{19}F NMR (376 MHz, DMSO-d_6)



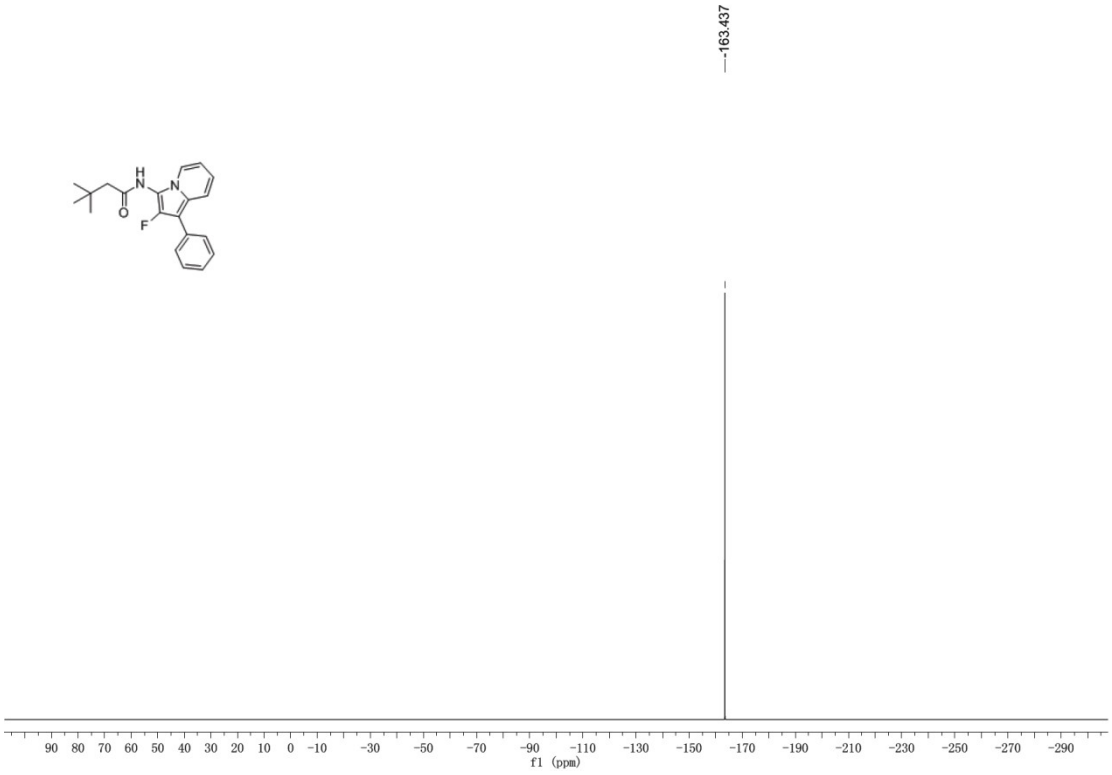
9j-^{1}H NMR (400 MHz, DMSO-d_6)



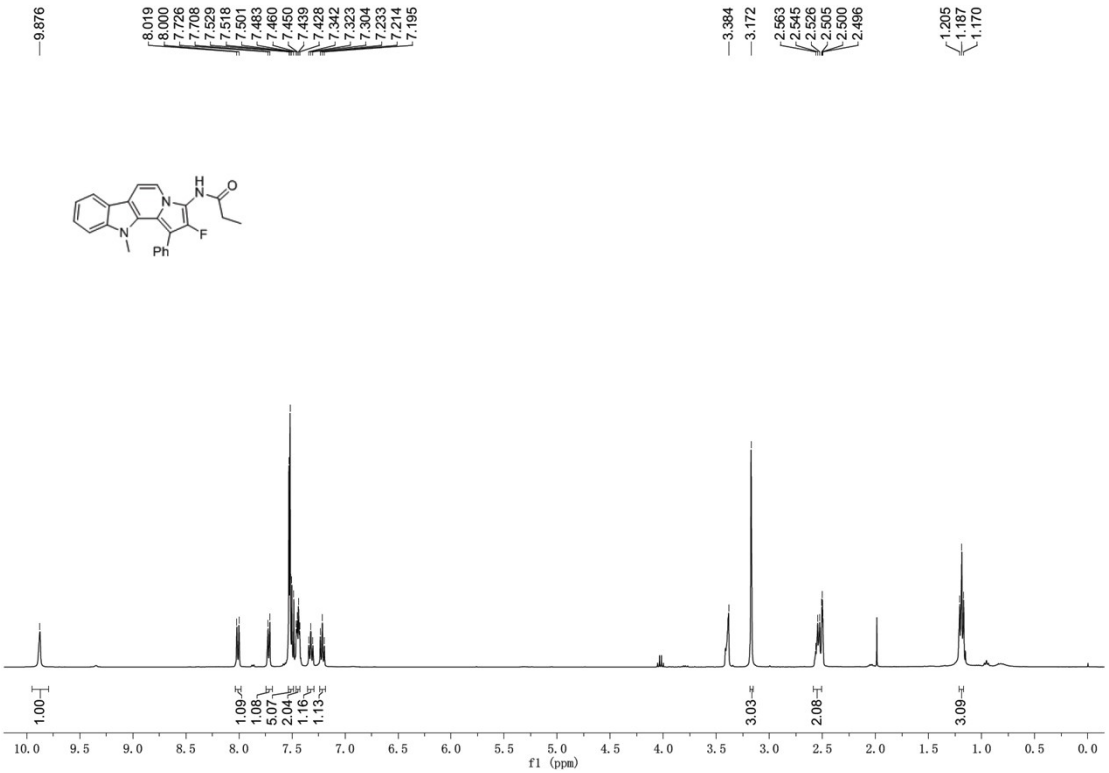
9j-^{13}C NMR (100 MHz, DMSO-d_6)



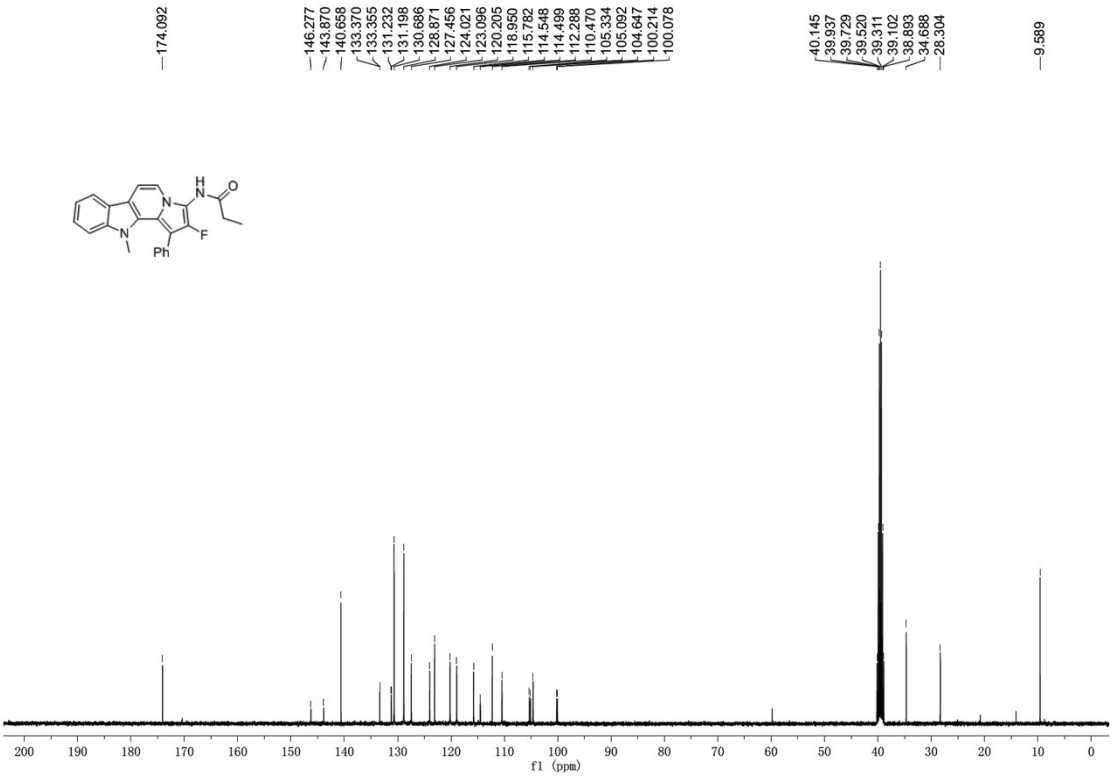
9j-^{19}F NMR (376 MHz, DMSO-d_6)



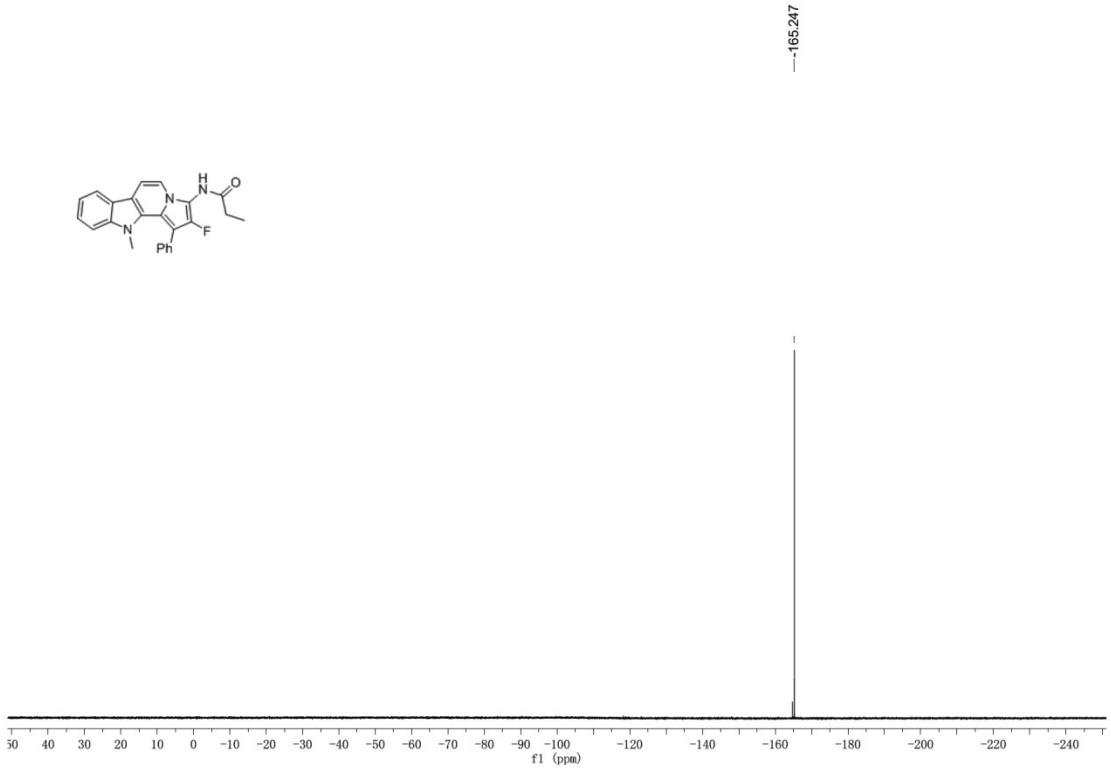
9k-^{1}H NMR (400 MHz, DMSO-d_6)



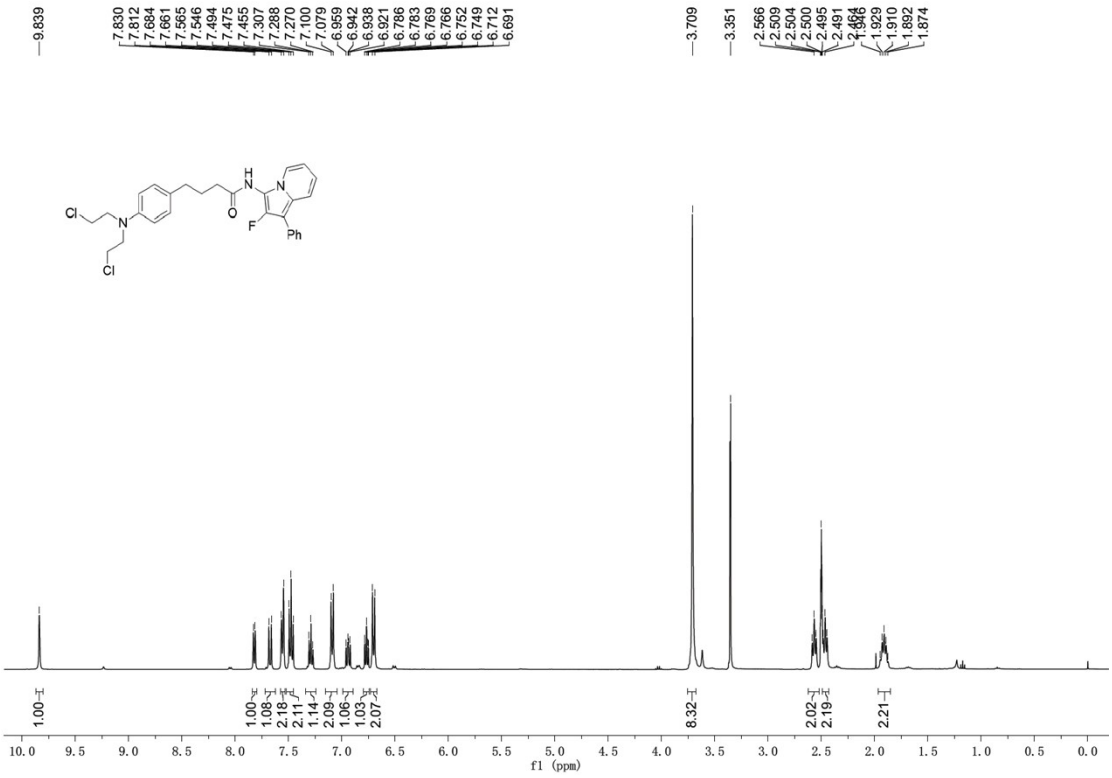
9k-^{13}C NMR (100 MHz, DMSO-d_6)



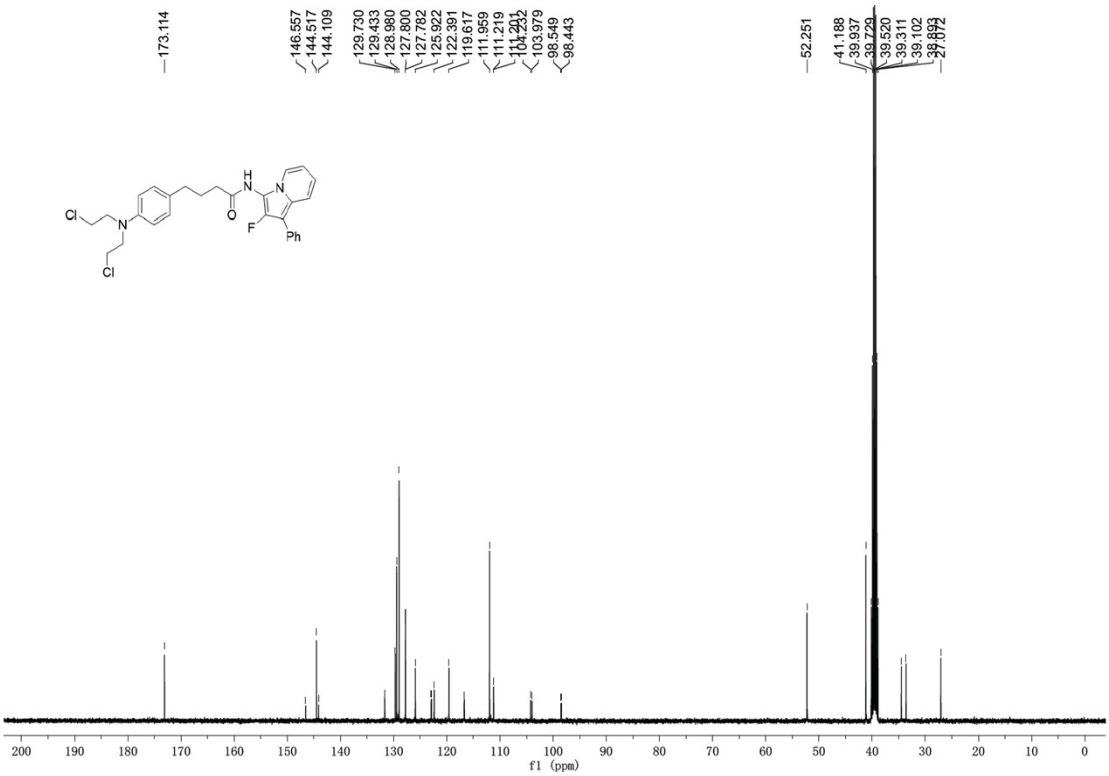
9k-^{19}F NMR (376 MHz, DMSO-d_6)



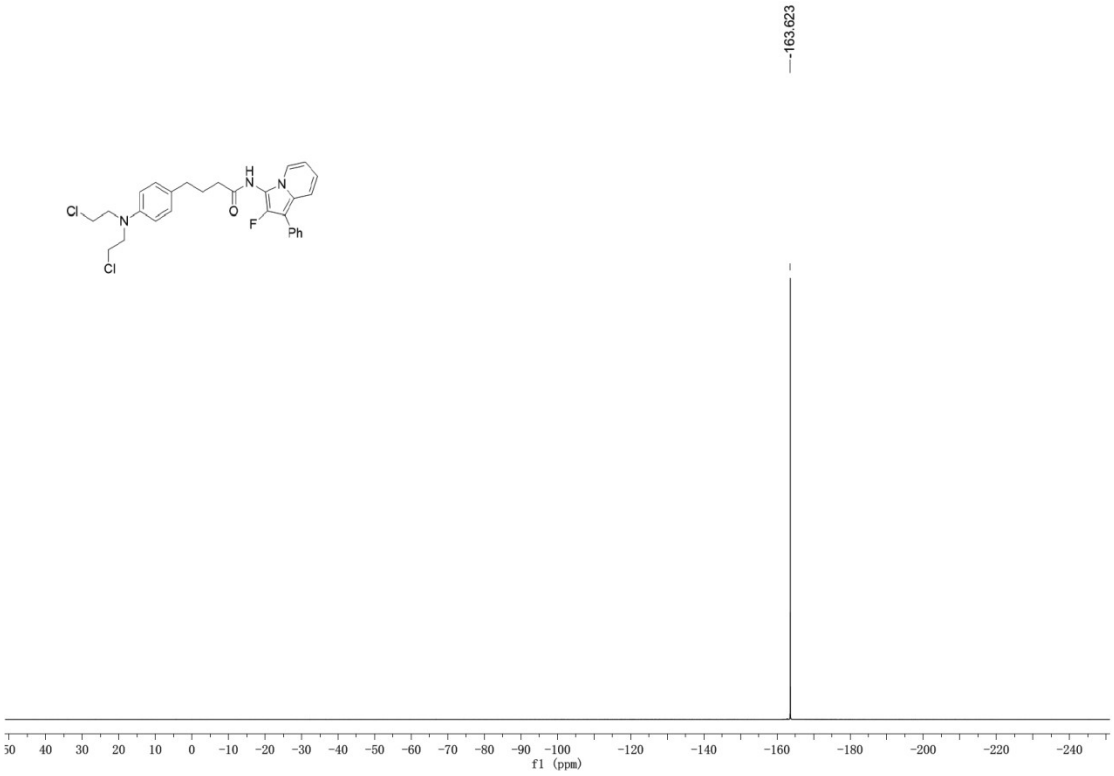
9l-^{1}H NMR (400 MHz, DMSO-d_6)



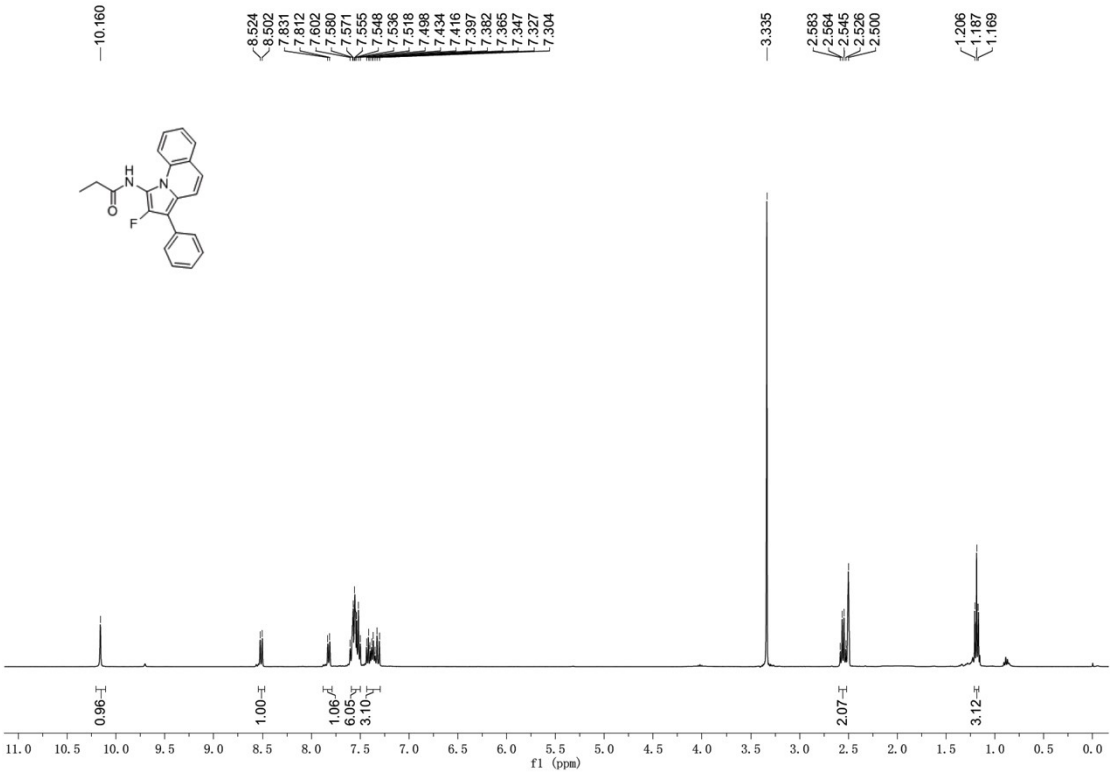
9l-^{13}C NMR (100 MHz, DMSO-d_6)



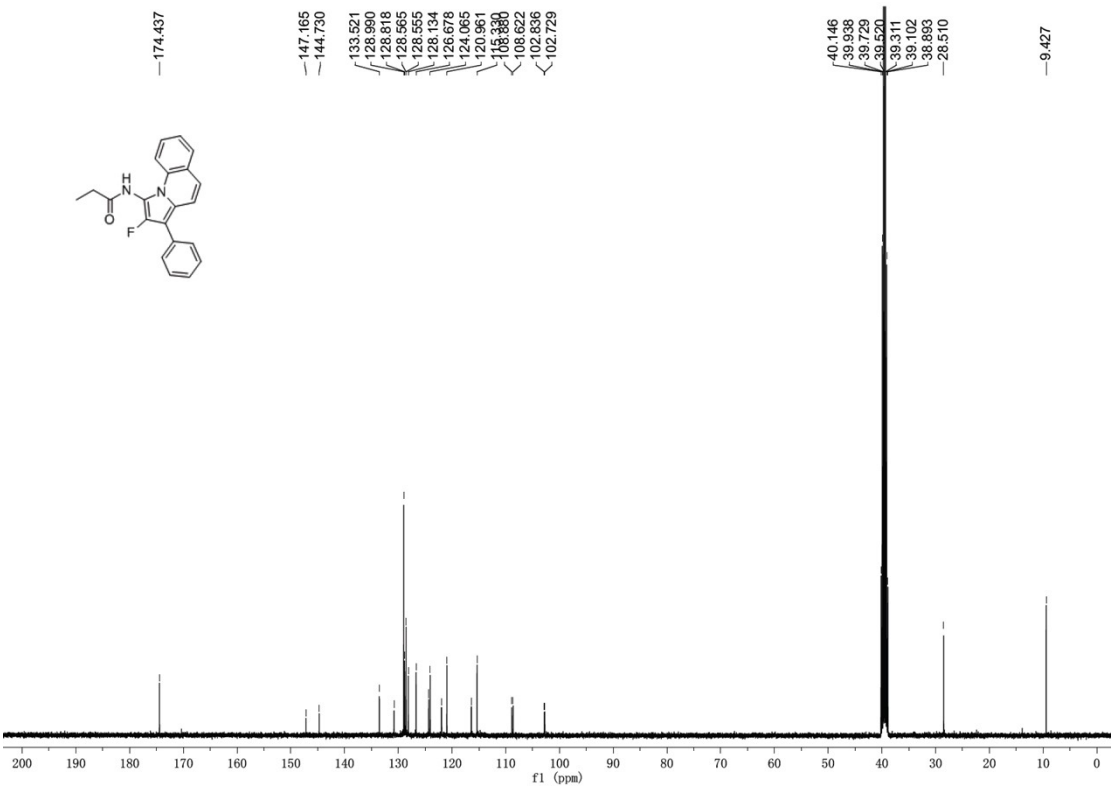
9l-^{19}F NMR (376 MHz, DMSO-d_6)



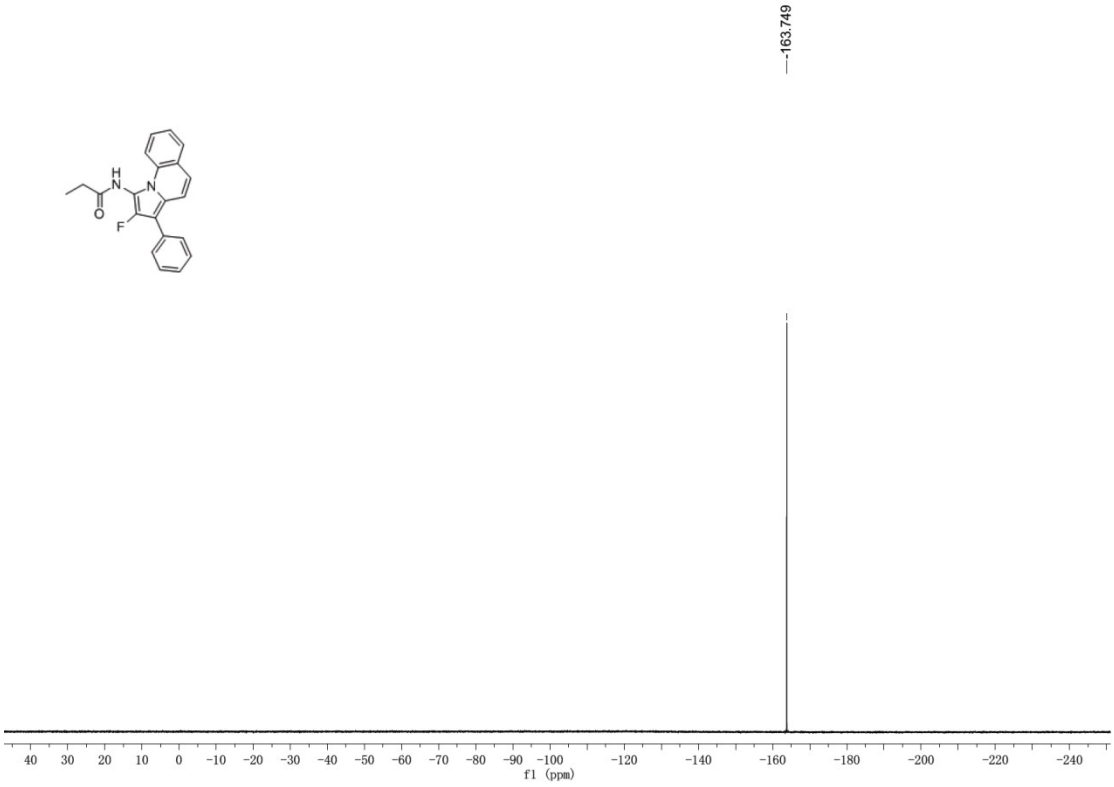
9m-^{1}H NMR (400 MHz, DMSO-d_6)



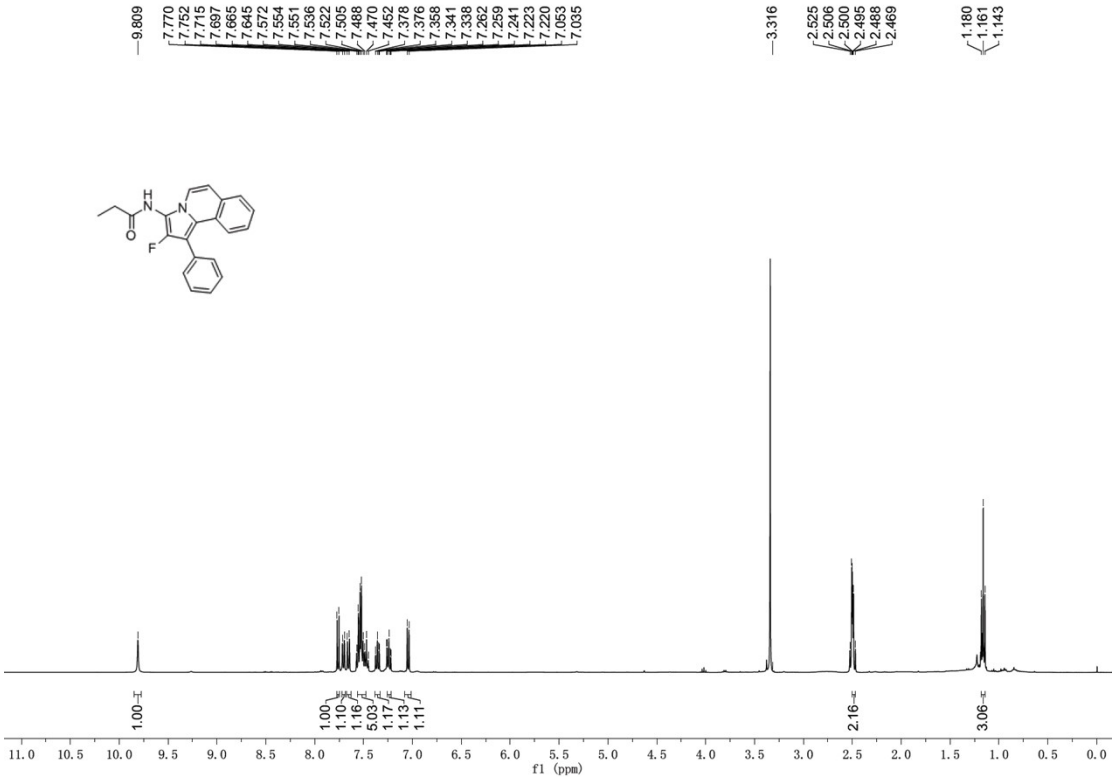
9m-^{13}C NMR (100 MHz, DMSO-d_6)



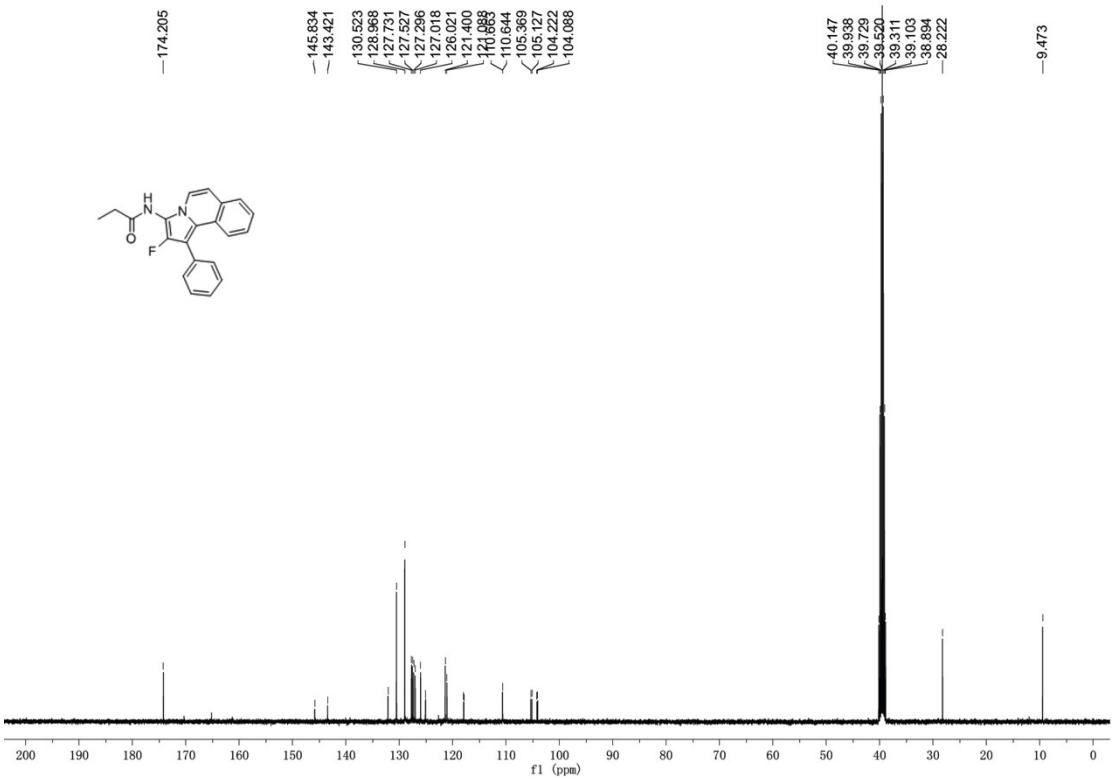
9m-^{19}F NMR (376 MHz, DMSO-d_6)



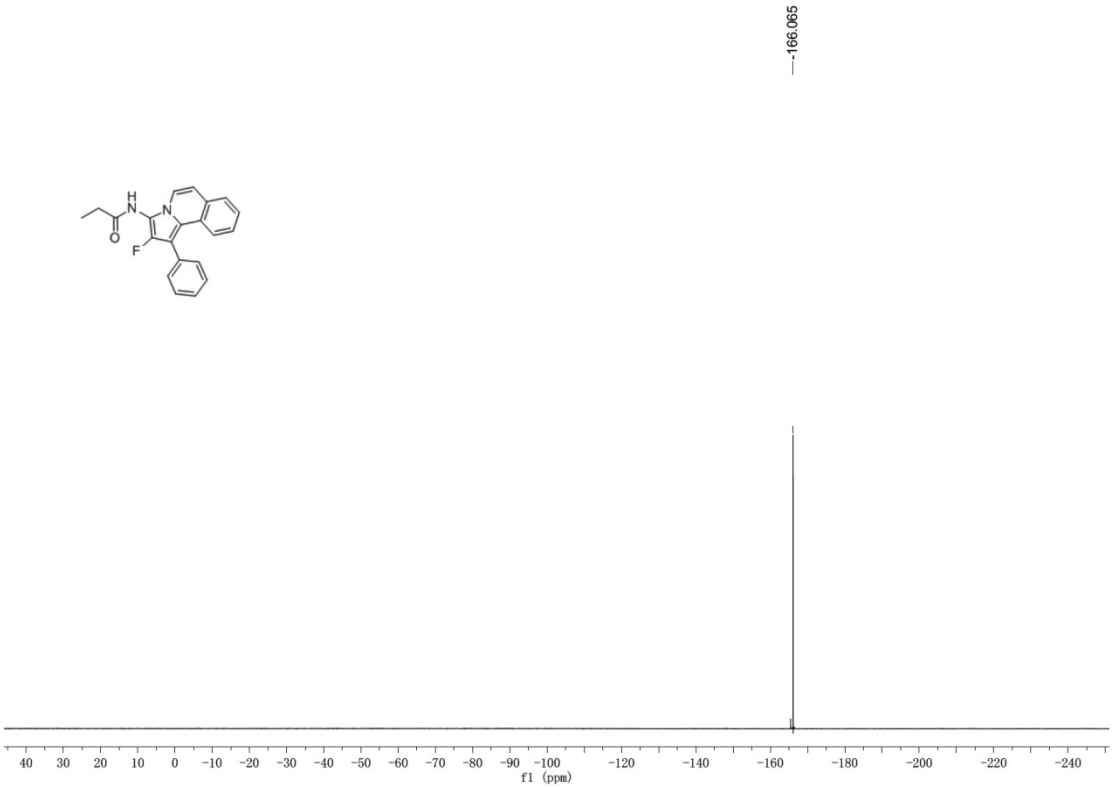
9n-^{1}H NMR (400 MHz, DMSO-d_6)



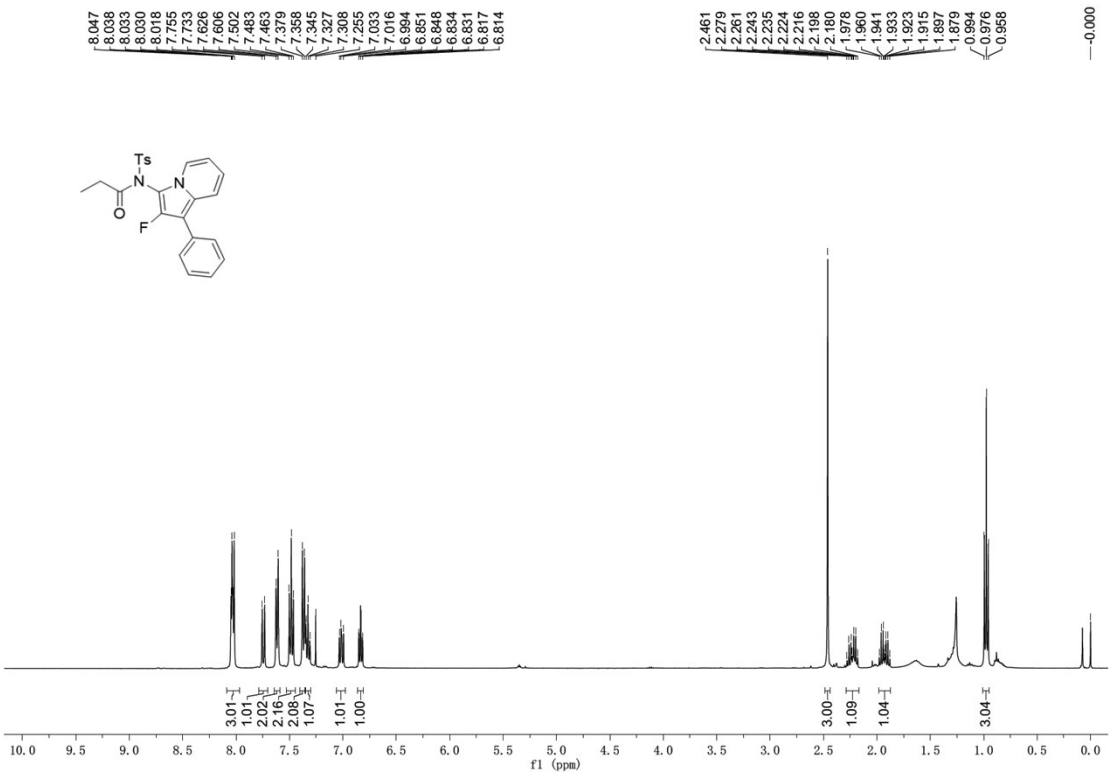
9n-^{13}C NMR (100 MHz, DMSO-d_6)



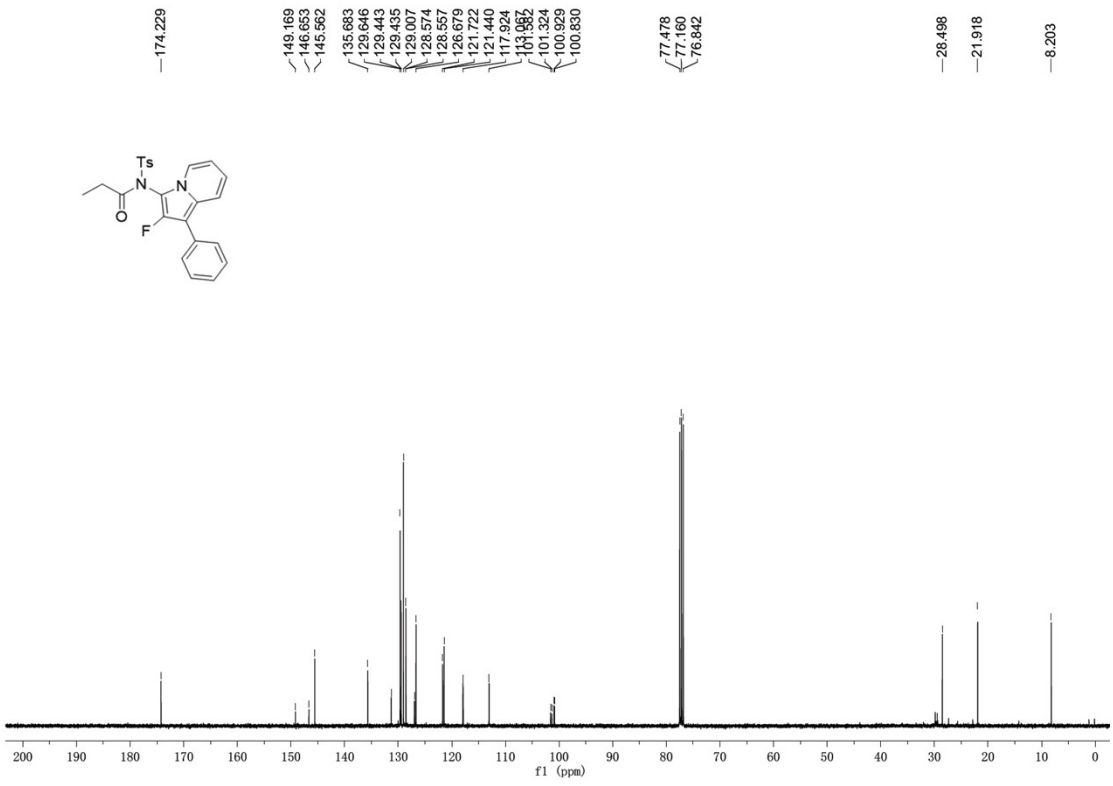
9n-^{19}F NMR (376 MHz, DMSO-d_6)



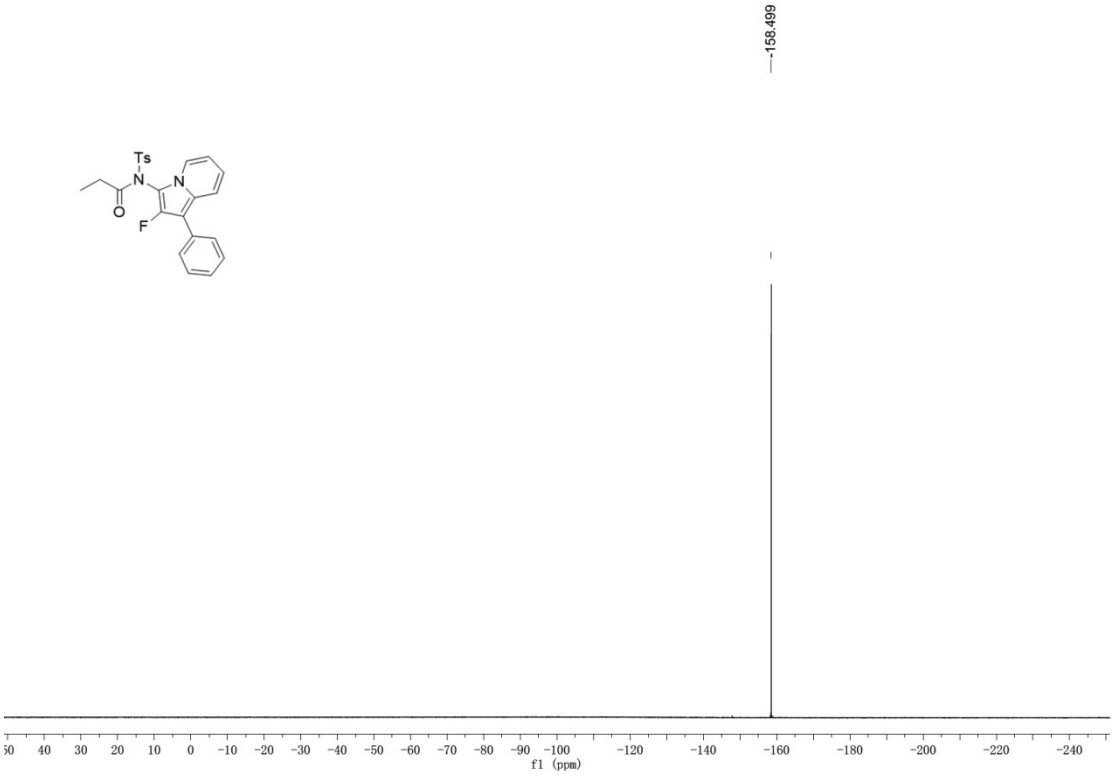
10-^{1}H NMR (400 MHz, $CDCl_3$)



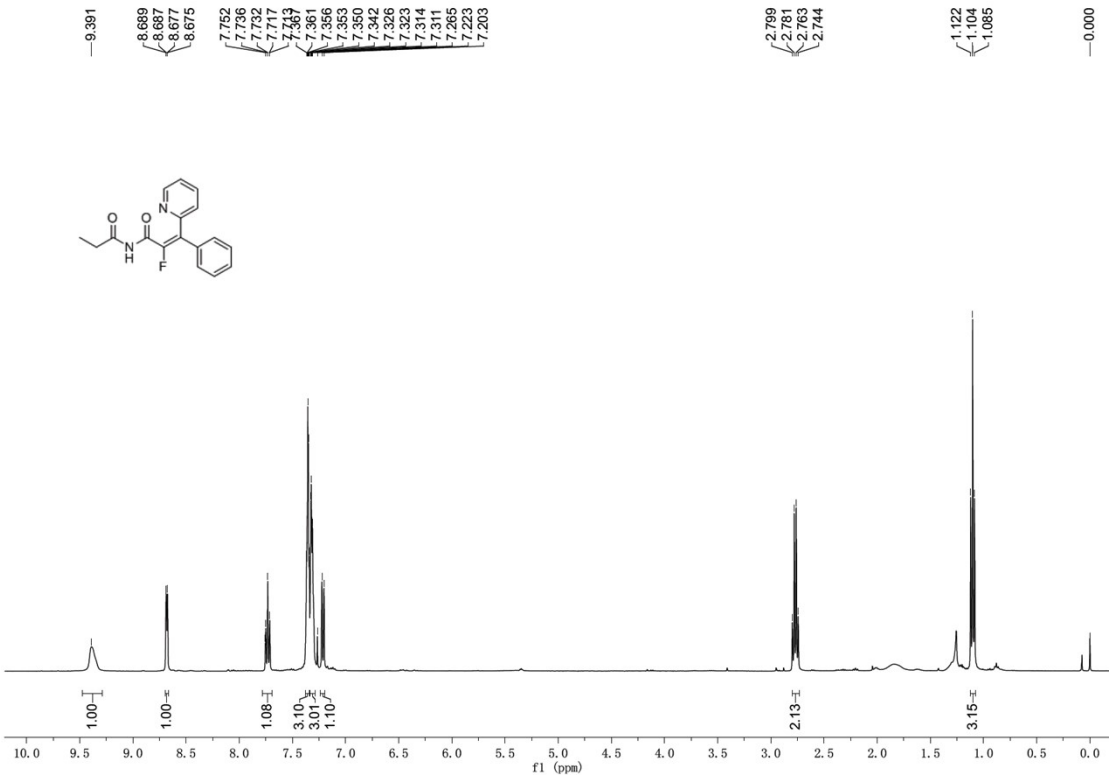
10-^{13}C NMR (100 MHz, $CDCl_3$)



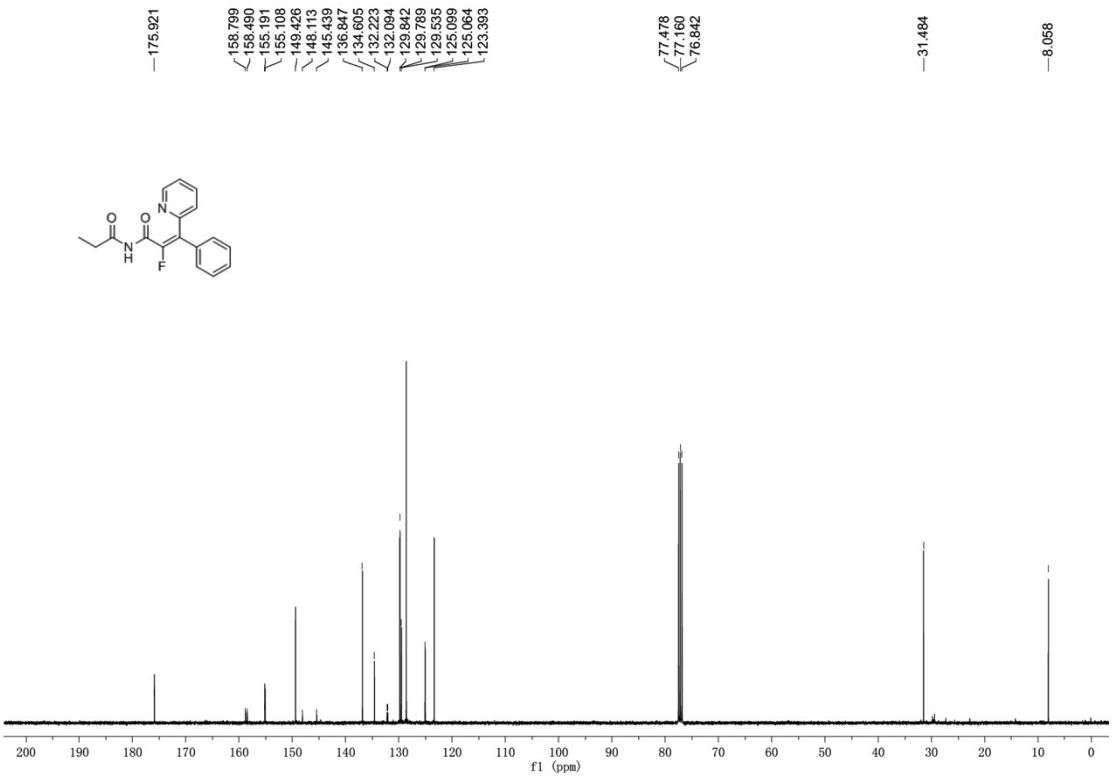
10-^{19}F NMR (376 MHz, $CDCl_3$)



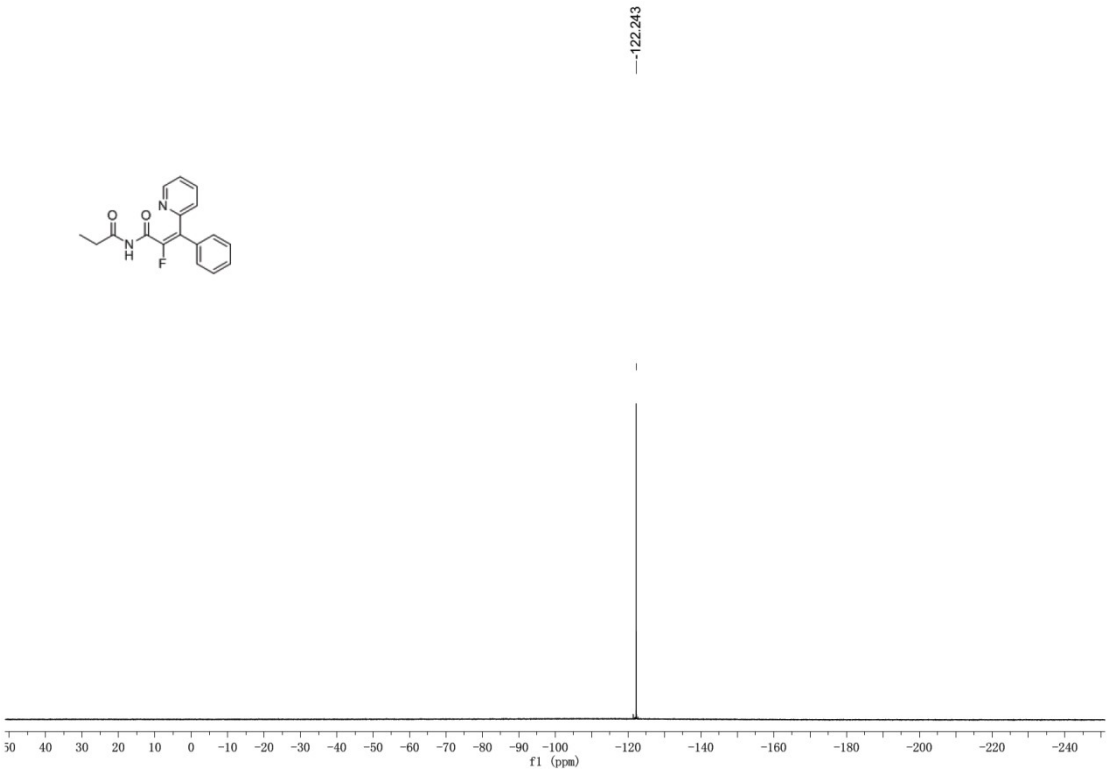
11a-^{1}H NMR (400 MHz, $CDCl_3$)



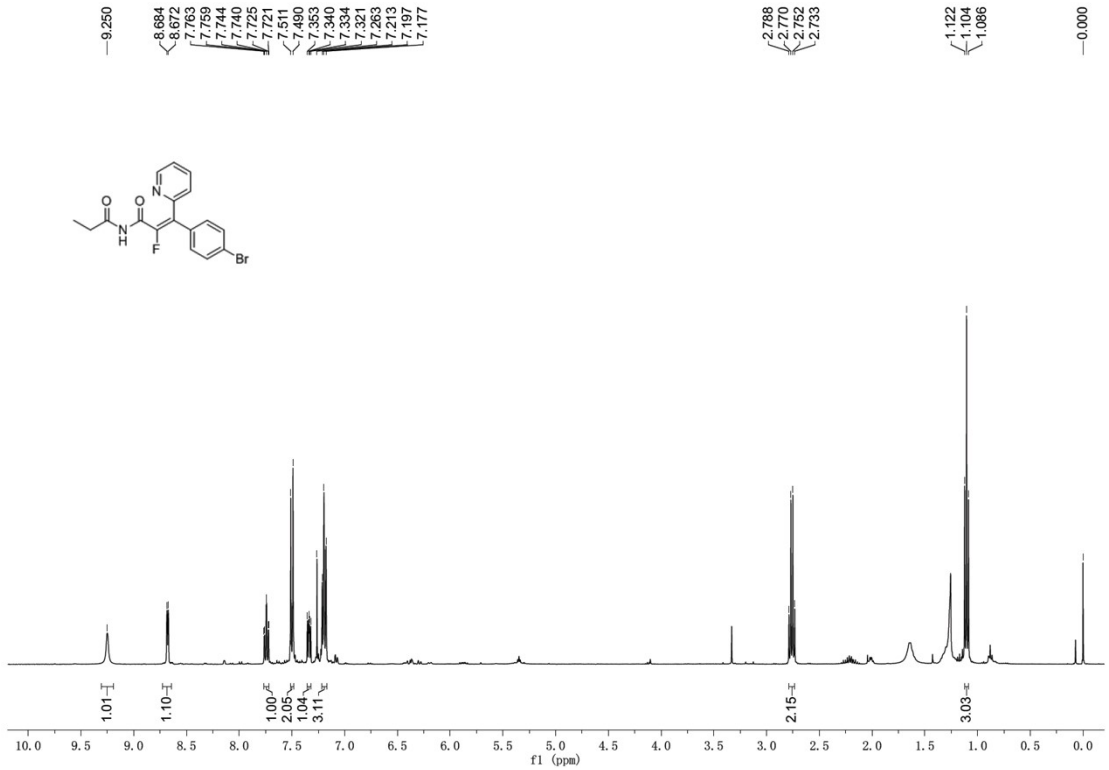
11a-^{13}C NMR (100 MHz, $CDCl_3$)



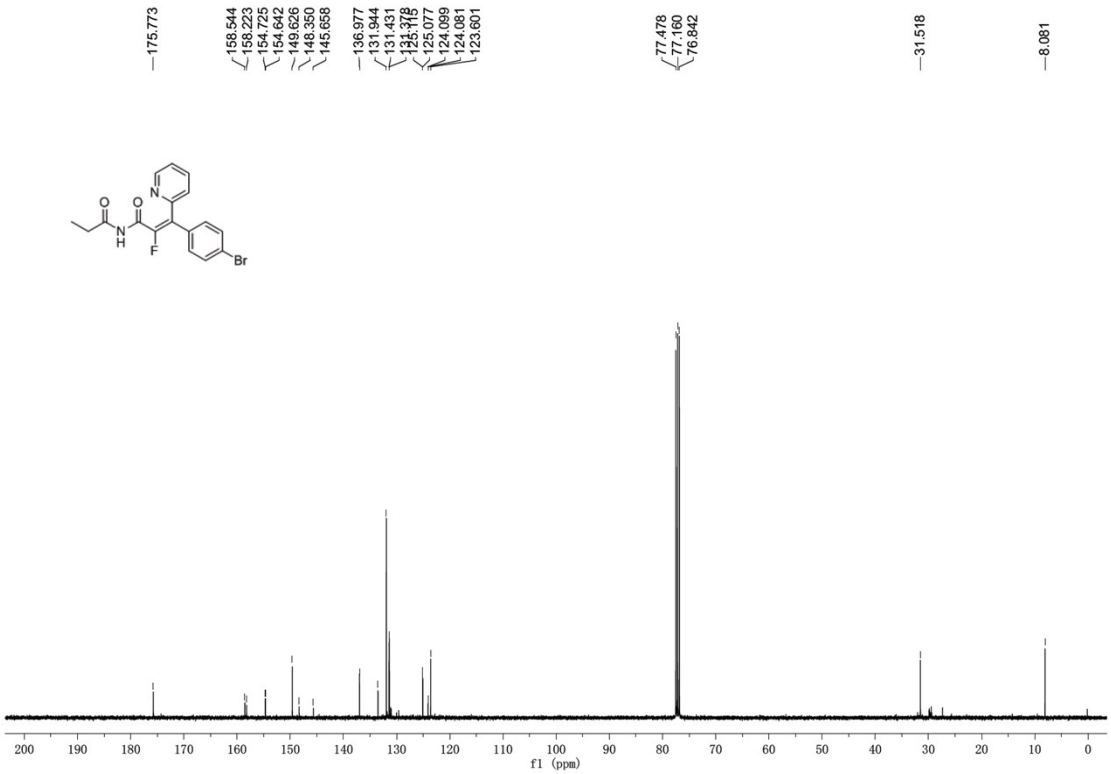
11a-^{19}F NMR (376 MHz, $CDCl_3$)



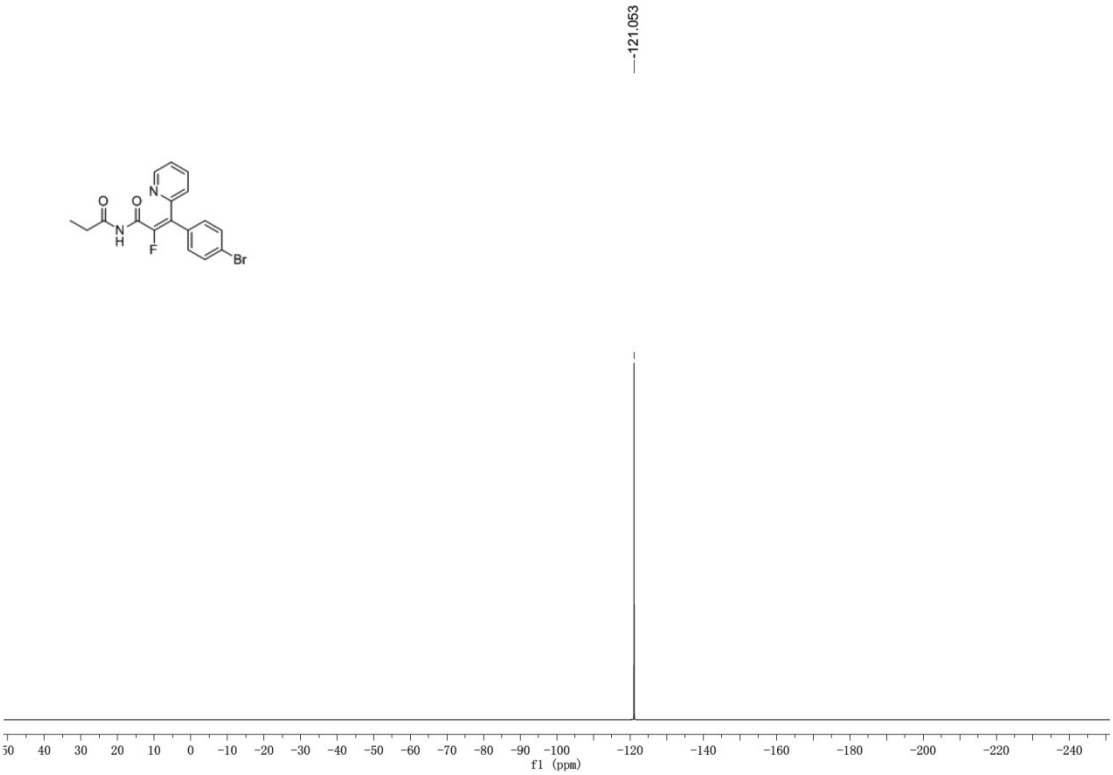
11b-^{1}H NMR (400 MHz, $CDCl_3$)



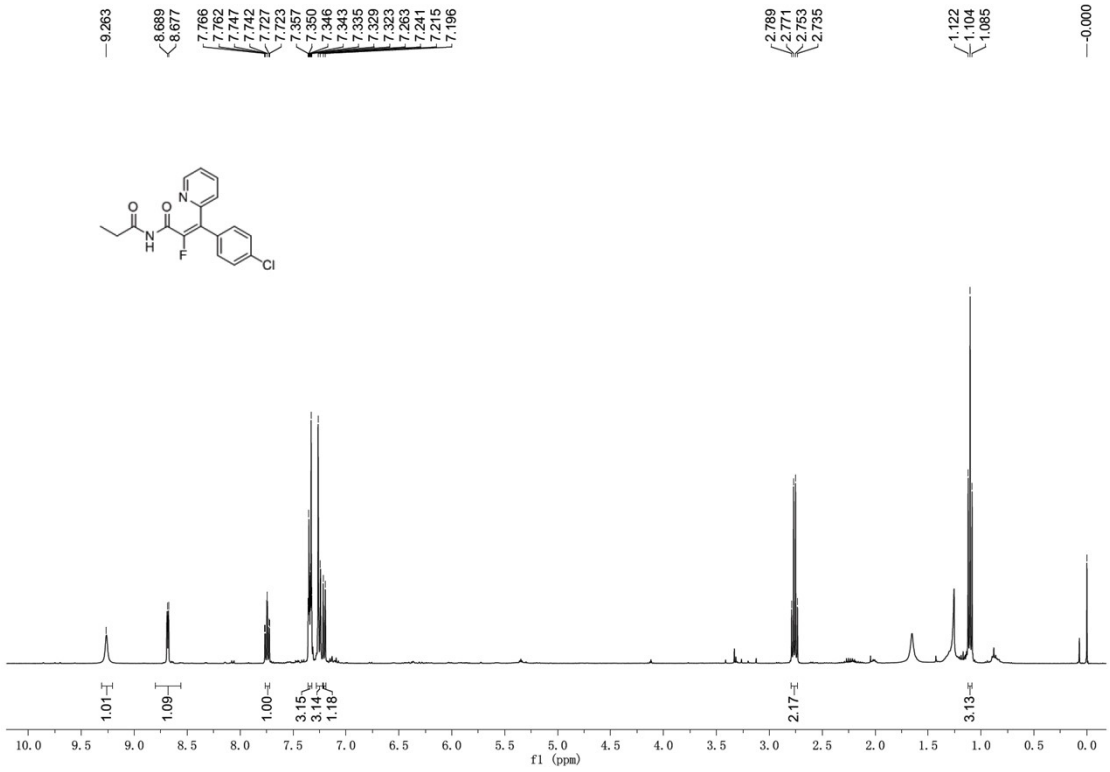
11b-^{13}C NMR (100 MHz, $CDCl_3$)



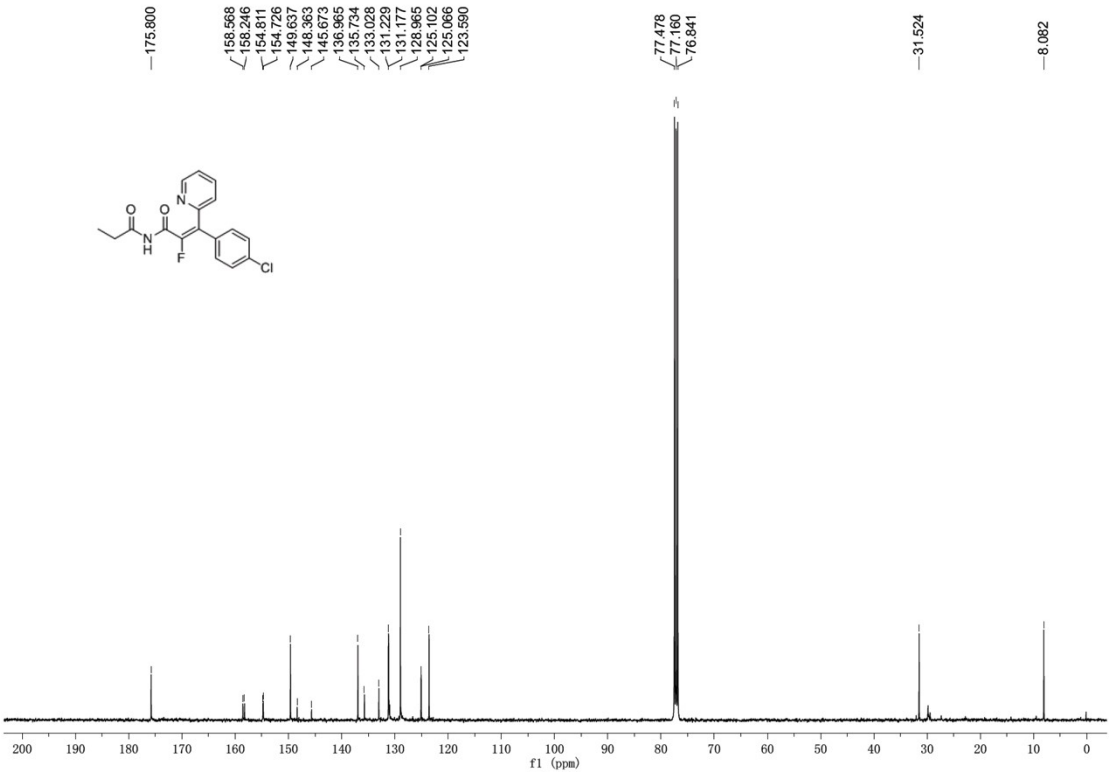
11b-^{19}F NMR (376 MHz, $CDCl_3$)



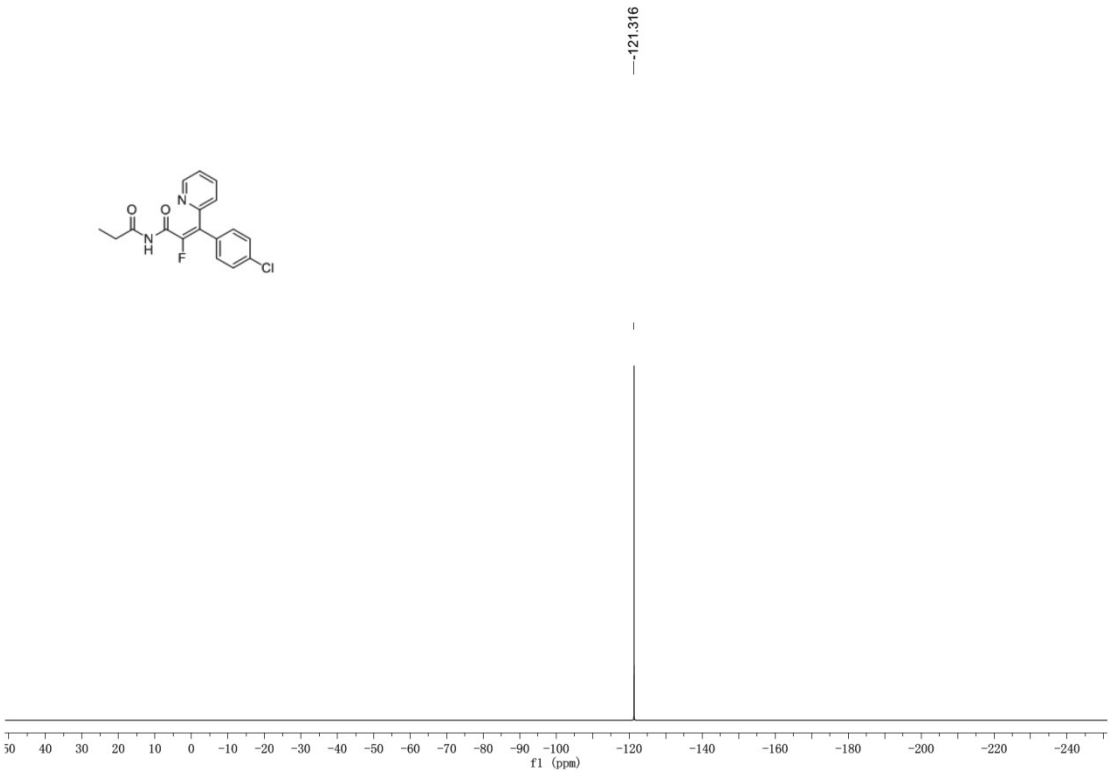
11c-^{1}H NMR (400 MHz, $CDCl_3$)



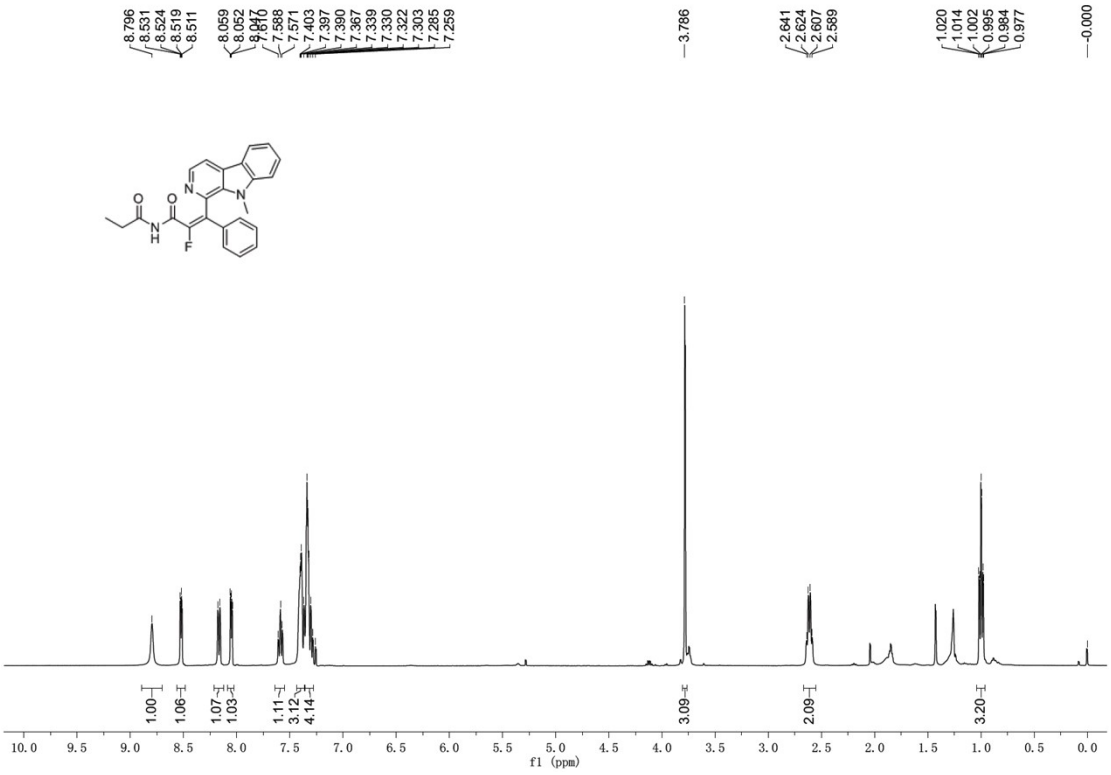
11c-^{13}C NMR (100 MHz, $CDCl_3$)



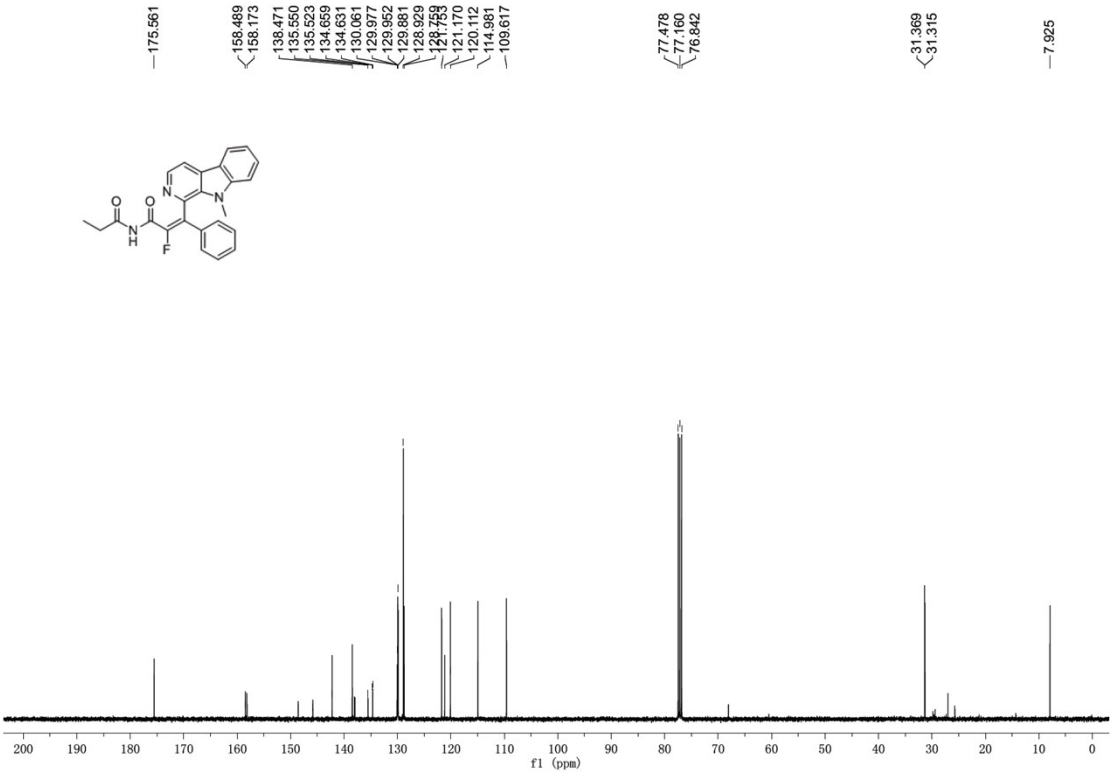
11c-^{19}F NMR (376 MHz, $CDCl_3$)



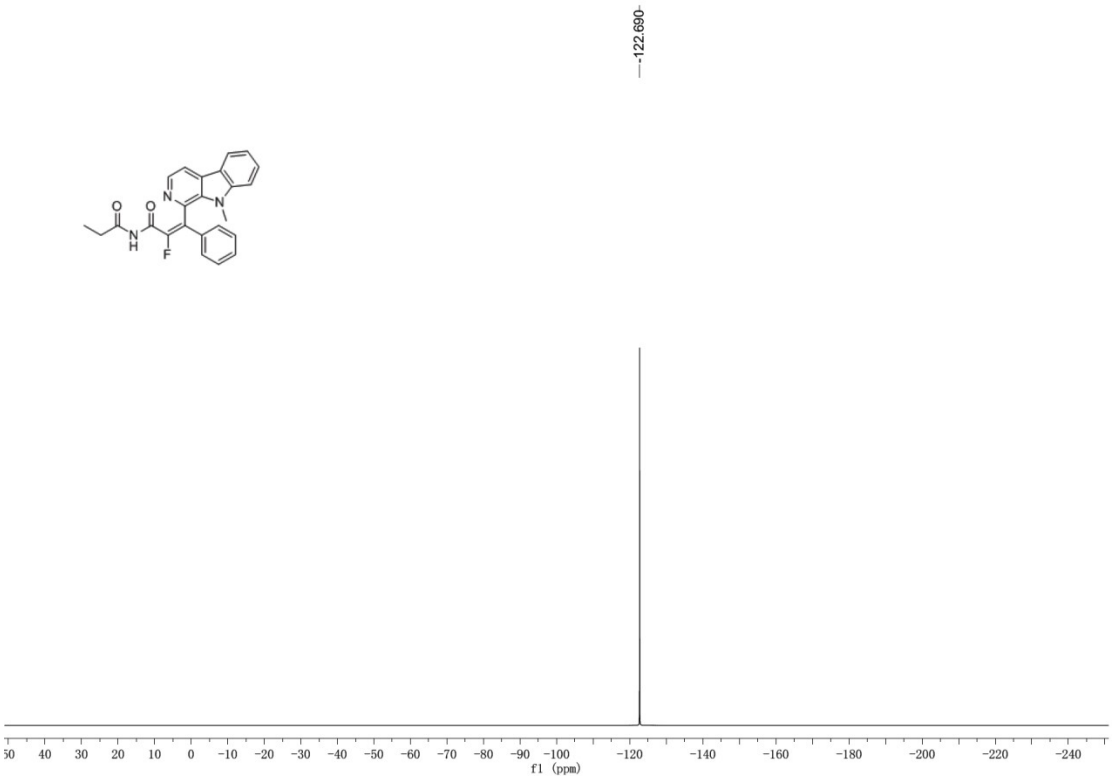
11d-^{1}H NMR (400 MHz, $CDCl_3$)



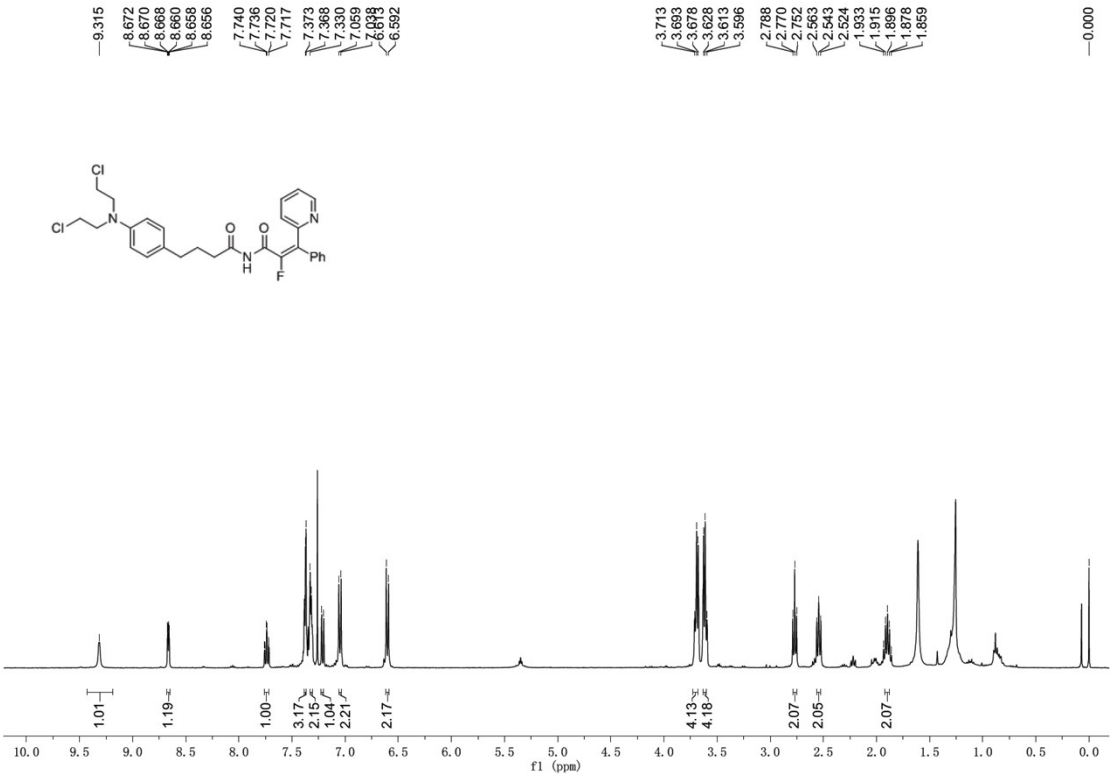
11d-^{13}C NMR (100 MHz, $CDCl_3$)



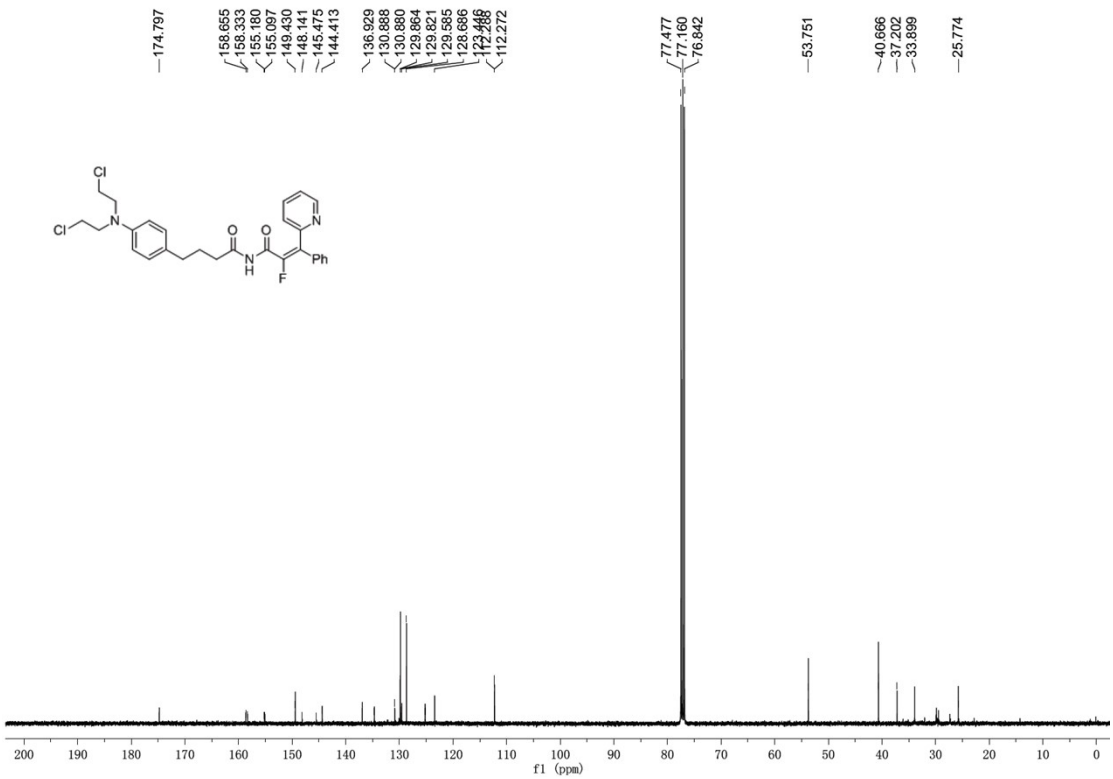
11d-^{19}F NMR (376 MHz, $CDCl_3$)



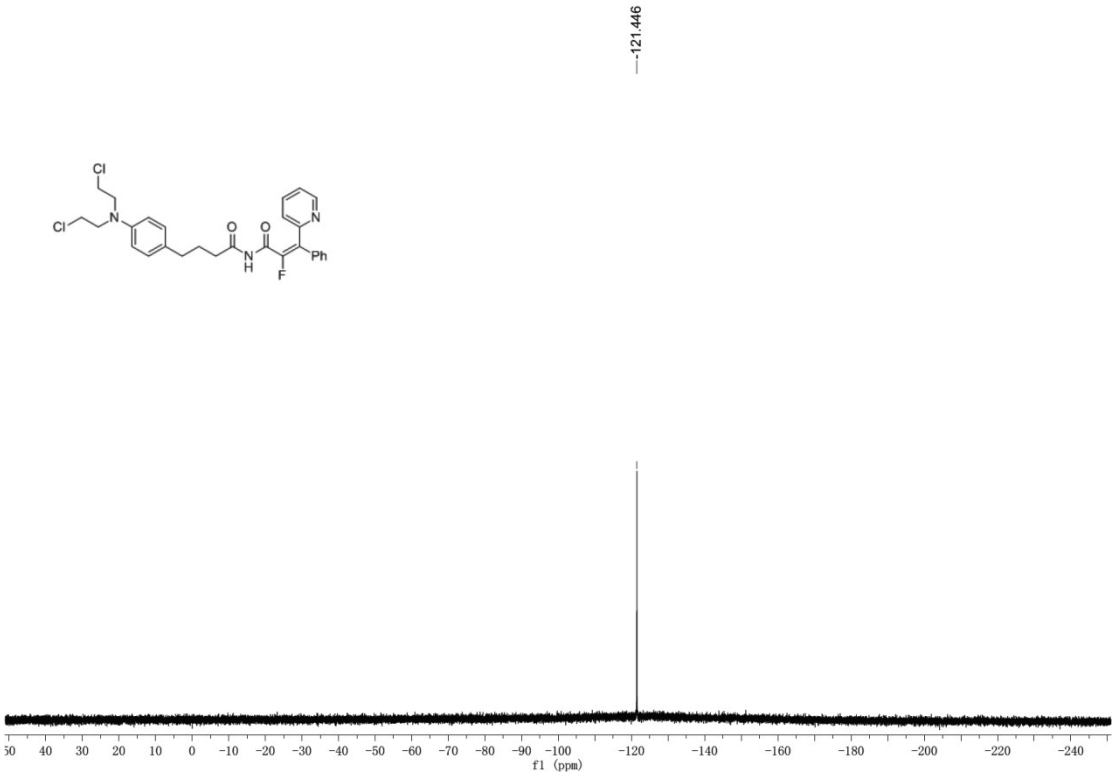
11e-^{1}H NMR (400 MHz, $CDCl_3$)



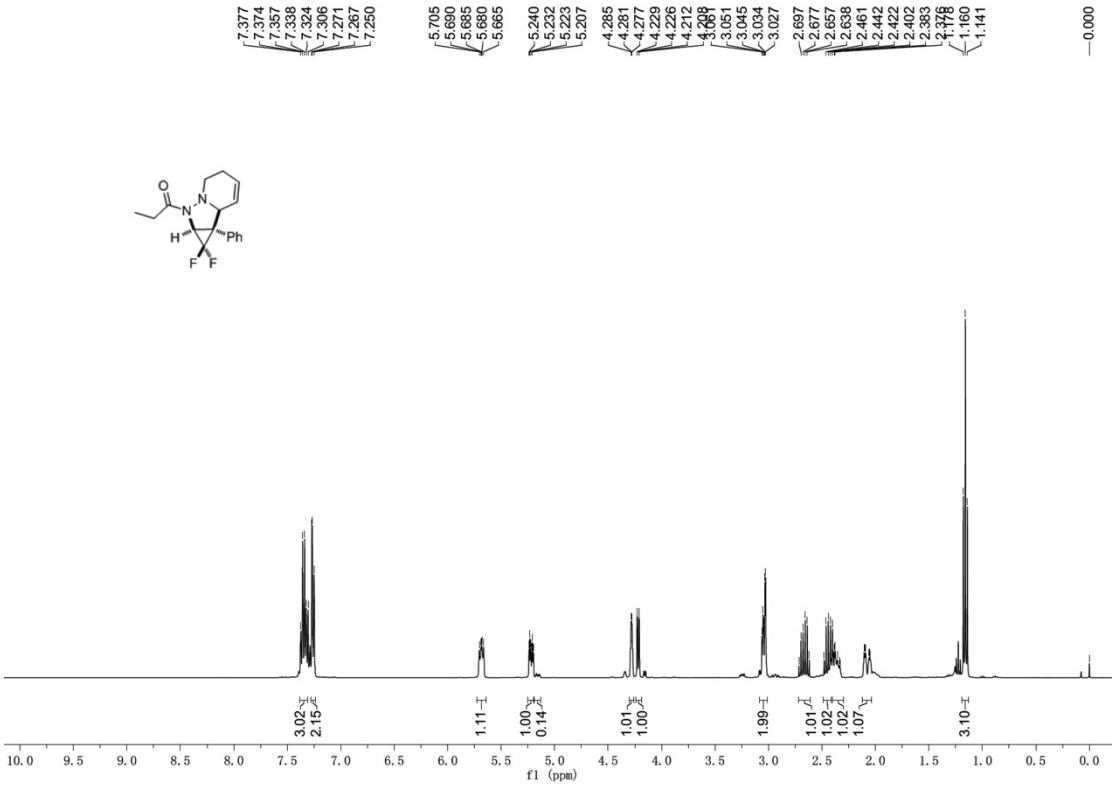
11e-^{13}C NMR (100 MHz, $CDCl_3$)



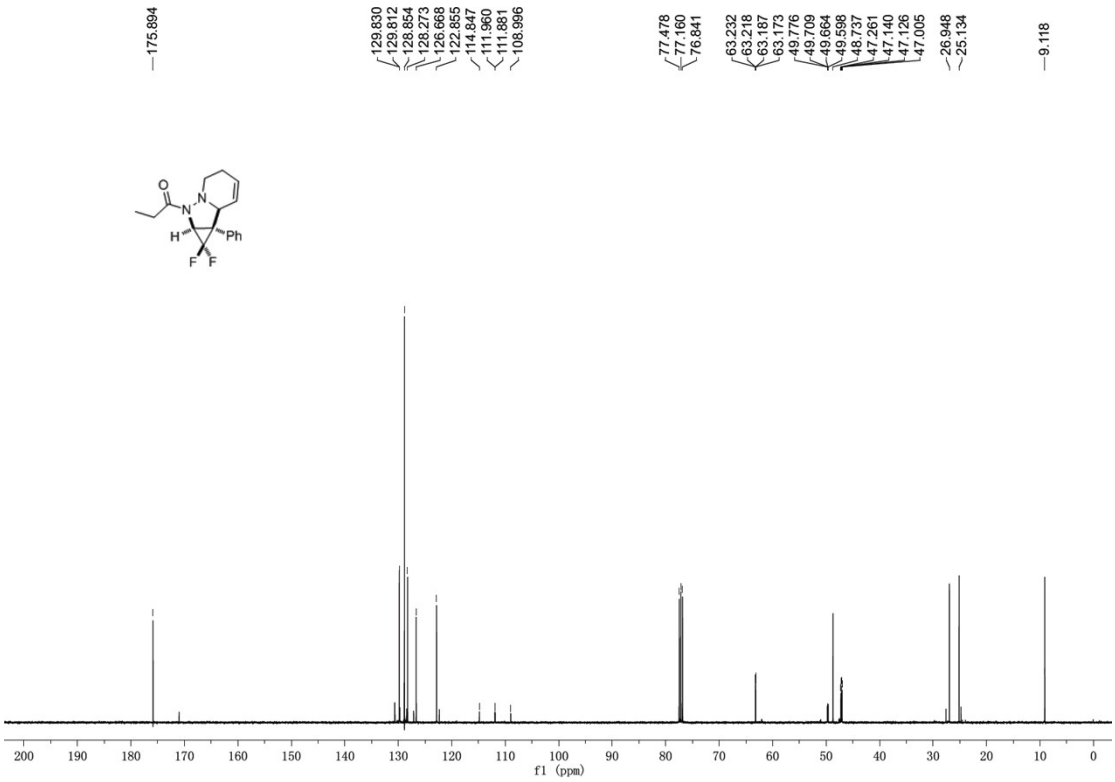
11e-^{19}F NMR (376 MHz, $CDCl_3$)



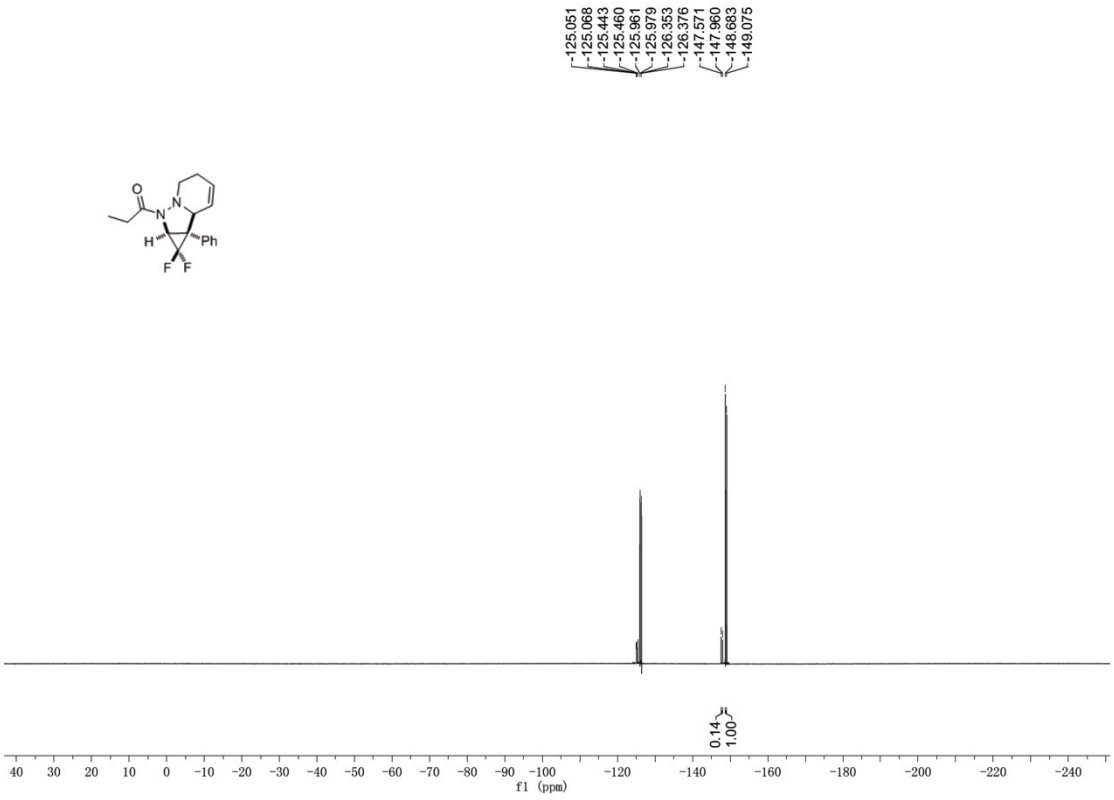
12-^{1}H NMR (400 MHz, $CDCl_3$)



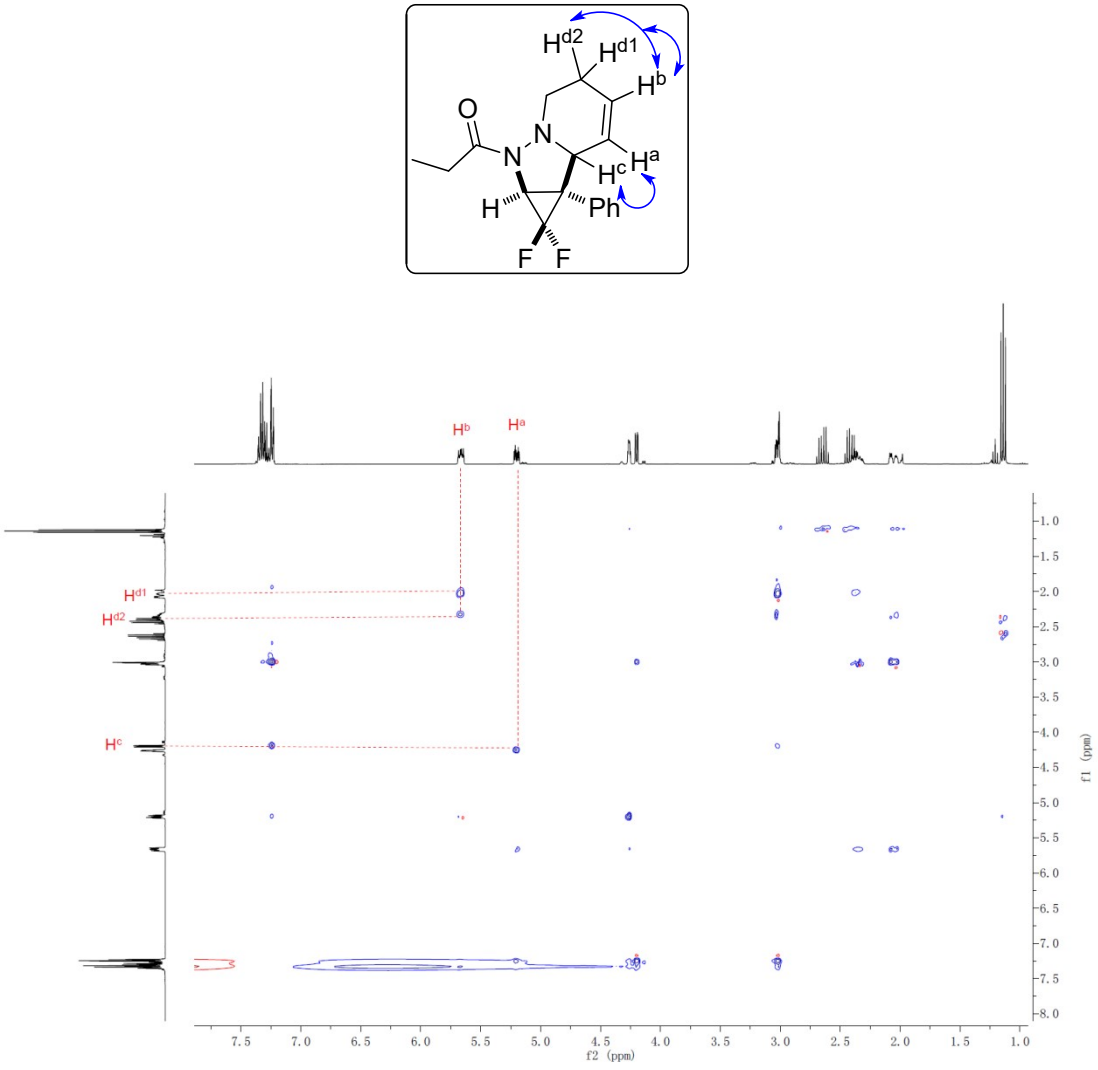
12-^{13}C NMR (100 MHz, $CDCl_3$)



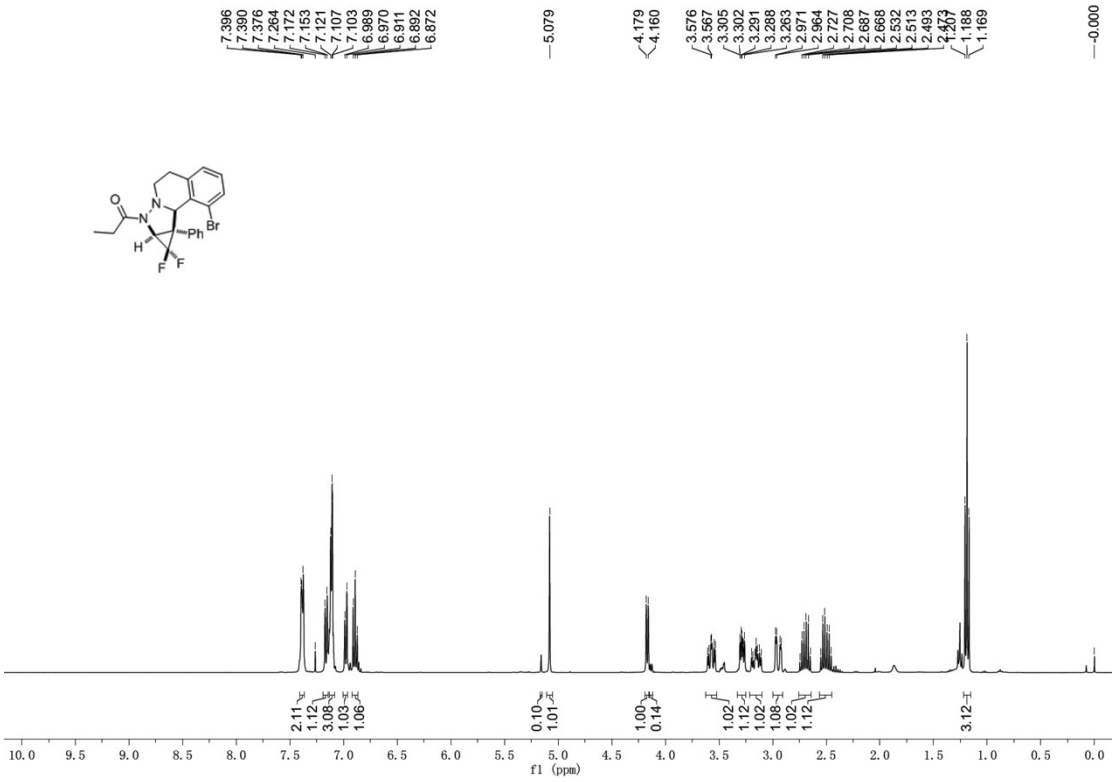
12-^{19}F NMR (376 MHz, $CDCl_3$)



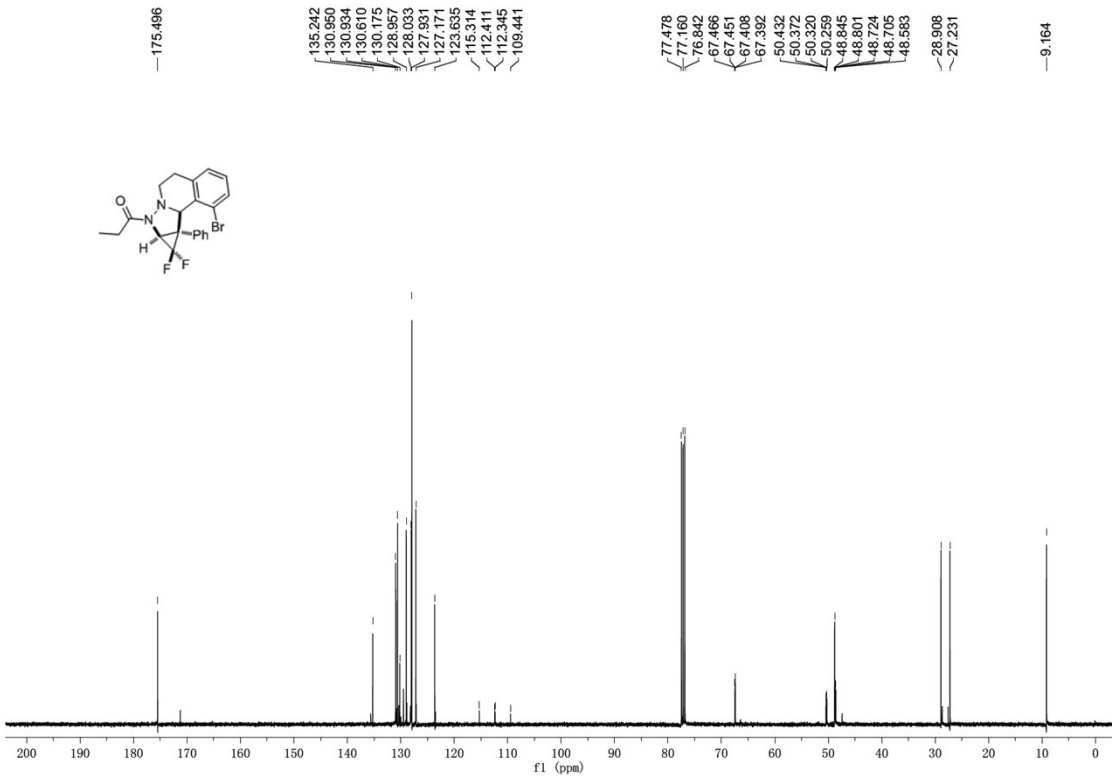
12-^{1}H-^{1}H NOESY (400 MHz, $CDCl_3$)



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



13-^{13}C NMR (100 MHz, $CDCl_3$)



13-^{19}F NMR (376 MHz, $CDCl_3$)