Supporting Information

Photocatalytic difluoroalkylation/cyclization of *N*-cinnamyl-*N*-cyanobenzamides with difluoroalkyl bromides toward C2-difluoroalkylated pyrroloquinazolinones

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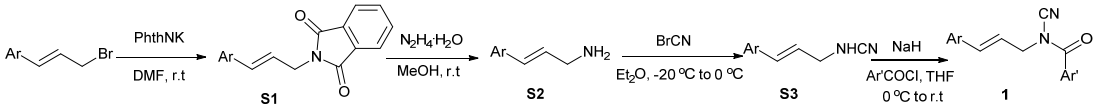
1. General Considerations

General Information: Unless otherwise noted, all chemicals were purchased and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 400 MHz NMR spectrometer (101 MHz for ^{13}C). ^{19}F NMR spectra were recorded at ambient temperature on a 300 or 400 MHz NMR spectrometer (282 or 376 MHz for ^{19}F). NMR experiments are reported in δ units, parts per million (ppm). The coupling constants J are given in Hz. Column chromatography was performed using EM Silica gel 60 (300-400 mesh). HRMS were recorded on a TOF LC/MS equipped with electrospray ionization (ESI) probe operating in positive ion mode. Emission intensities were recorded using a FS5 spectrophotometer.

2. General Synthetic Procedures

2.1 General procedure for synthesis of substrates 1



To a solution of the crude cinnamyl bromide (6 mmol) in DMF (20 mL) was added phthalimide potassium salt (6.6 mmol), and the suspension was stirred at room temperature for 2 h. The resulting mixture was quenched with H_2O (30 mL). Then, white solid **S1** was collected after filtering the solution and washing by petroleum ether (2×20 mL), which was used without further purification.

To a solution of 2-cinnamylisoindoline-1,3-dione (**S1**, 5 mmol) in MeOH (30 mL), was charged hydrazine monohydrate (20 mmol) at room temperature. The mixture was stirred 16 h at room temperature. The resulting residue was diluted with CH_2Cl_2 (20 mL) and KOH (1 M, 30 mL). The aqueous phase was extracted into EtOAc (2×20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure to give cinnamylamine **S2** which was used without further purification.

To a solution of cyanogen bromide (4 mmol) in Et_2O (10 mL) was added cinnamylamine (4 mmol) and Na_2CO_3 (8 mmol) at –20 ºC. The reaction mixture was kept at –20 ºC for additional 1 hour and then warmed to 0 ºC for additional 3 hours. The mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed in *vacuo,* and the resulting intermediates **S3** was used without further purification.

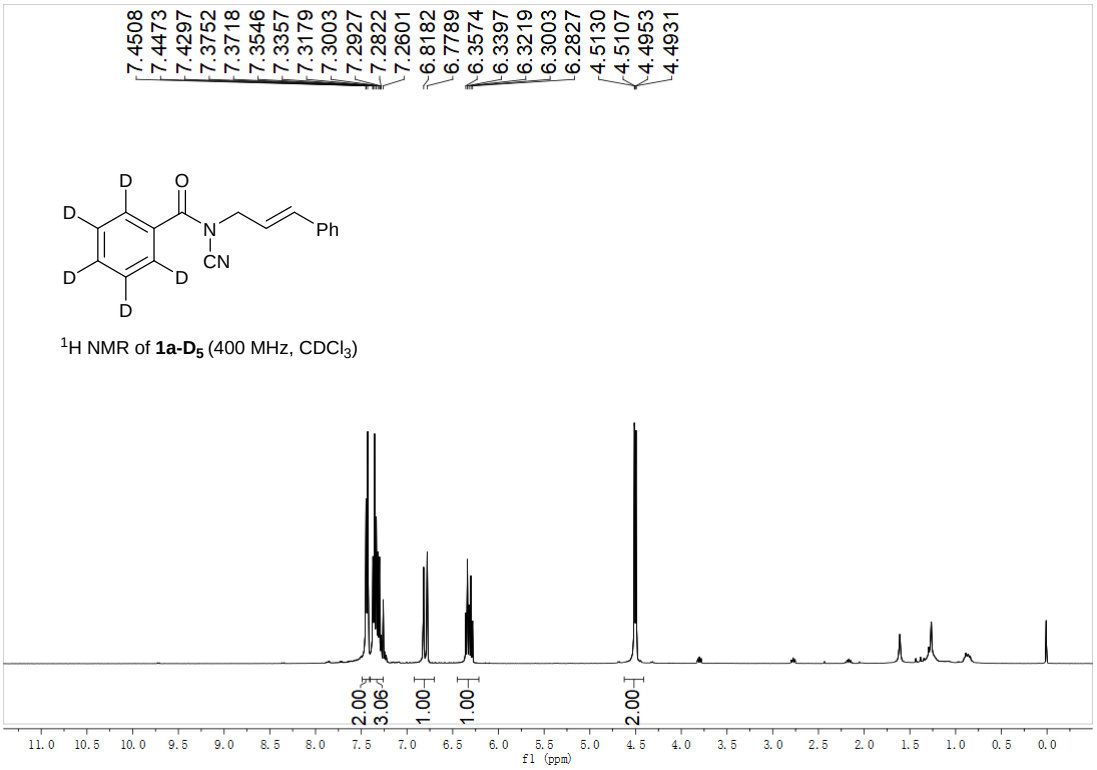
To a solution of intermediates **S3** (3 mmol) in THF (6 mL) was added NaH (6 mmol) at 0 ºC. After stirring at this temperature for 30 minutes, the corresponding acyl chloride (4.5 mmol) was added. The reaction was gradually warmed to room temperature for additional 5 hours. Then, it was quenched with water and the aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with brine, and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel to give the desired *N*-cinnamylbenzamide **1**.

2.2 The procedure for synthesis of compound 1a-D_5

A round-bottom flask equipped with a stir bar and a condenser was charged with D_8-toluene (99.9% atom D) (0.5 g, 5 mmol), $KMnO_4$ (2 g, 12.5 mmol), Na_2CO_3 (0.26g, 2.5 mmol), and H_2O (15 mL). The reaction mixture was refluxed for 8 h and then cooled to room temperature. The mixture was filtered and the filtrate was acidified with concentrated hydrochloric acid and extracted by DCM. The organic layer was washed with H_2O and concentrated under reduced pressure to give white solid D_5-PhCOOH, which was used without further purification.

A flask with round bottom was added D_5-PhCOOH (3 mmol, 381.3 mg) dissolved in 6 mL of DCM. The solution was cooled to 0 °C and oxalyl chloride (4.5 mmol) was added in portions. The resulting suspension was warmed to room temperature and stirred for 2 h. The mixture was concentrated under reduced pressure to obtain the D_5-PhCOCl, which was used without further purification.

To a solution of *N*-cinnamylcyanamide (2 mmol, 316.2 mg) in THF (4 mL) was added NaH (4 mmol) at 0 ºC. After stirring at this temperature for 30 minutes, the D_5-PhCOCl (3 mmol) was added. The reaction was gradually warmed to room temperature for additional 5 hours. Then, it was quenched with water and the aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with brine, and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography on silica gel to give the compound **1a-D_5**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H), 7.37-7.28 (m, 3H), 6.80 (d, J = 15.7 Hz, 1H), 6.36-6.28 (m, 1H), 4.50 (dd, J = 7.1, 0.9 Hz, 2H).



2.3 The procedure for photo-induced difluoroalkylation/cyclization of *N*-cinnamylbenzamide towards CF_2COR-containing quinazolinones

The mixture of *N*-cinnamylbenzamide **1** (0.2 mmol), bromodifluoroacetamides **2** (0.4 mmol), 4CzIPN (2 mol%, 3.2 mg), $NaHCO_3$ (0.4 mmol, 33.6 mg) and DMSO (2 mL) were added to a Schlenk tube. The tube was evacuated and backfilled with nitrogen (repeated five times) and then sealed. The mixture was stirred at room temperature under 30W 450-460 nm blue LEDs for 12 hours. The mixture was added with water and extracted with ethyl acetate. The combined organic layers were washed with brine and dried over Na_2SO_4. Then, the solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography (eluent: petroleum ether/ethyl acetate) to obtain the product **3**. The photoreactor is shown in Figure S1.

Figure S1. Photoreactor used in this work (30 W blue LEDs, λmax = 454 nm).

The Light Source and the Material of the Irradiation Vessel:

The photochemical reaction was carried out under visible light irradiation by a 30W 450-460 nm blue LED at room temperature. This blue LED was purchased from taobao (link: https://shop152143906.taobao.com/?spm=pc_detail.29232929/evo365560b447259.shop_block.dshopinfo.6cef7dd6EDPjwB). The blue LED's energy peak wavelength is 454 nm, the peak width at half-height is 17.0 nm, and irradiance@20 W is 38.51 mW/cm^2. The reaction vessel is a borosilicate glass tube. The distance between the tube and lamp is about 2 cm, and no filter is applied.

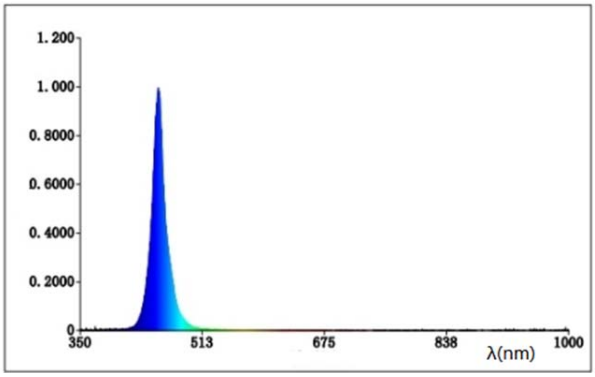


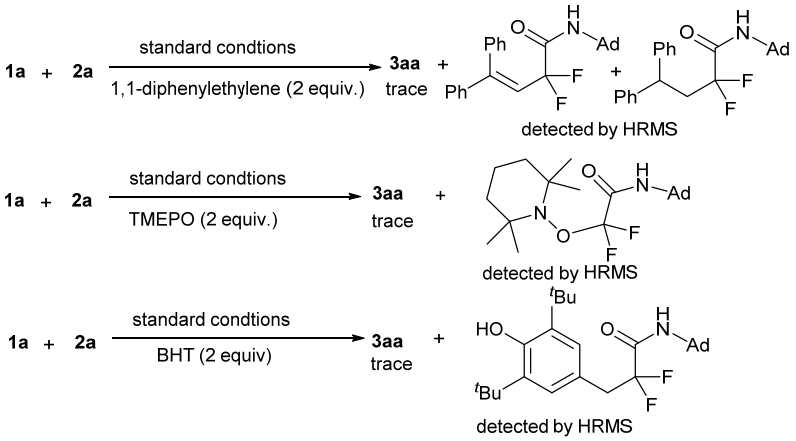
Figure S2. The spectral distribution of 30 W 450-460 nm blue LED

1 mmol scale preparation of 3aa

The mixture of *N*-cinnamylbenzamide **1a** (1 mmol, 262.1 mg), bromodifluoroacetamides **2** (2 mmol, 646.1 mg), 4CzIPN (2 mol%, 16 mg), $NaHCO_3$ (2 mmol, 168 mg) and DMSO (10 mL) were added to a Schlenk tube. The tube was evacuated and backfilled with nitrogen (repeated five times) and then sealed. The mixture was stirred at room temperature under 30W 450-460 nm blue LEDs for 12 hours. The mixture was added with water and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4. Then, the solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography (eluent: petroleum ether/ethyl acetate) to obtain the product **3aa** (77%, 376.7 mg).

3. Mechanism studies

3.1 Radical inhibition experiment for the reaction of **1a** with **2a**



The mixture of **1a** (0.1 mmol, 26.2 mg), **2a** (0.2 mmol, 61.4 mg), 4CzIPN (2 mol%, 1.6 mg), $NaHCO_3$ (0.2 mmol, 16.8 mg), 1,1-diphenylethylene (0.2 mmol, 36 mg), TEMPO (0.2 mmol, 31.2 mg) or BHT (0.2 mmol, 44 mg) and DMSO (1 mL) was added to a Schlenk tube. The tube was evacuated and backfilled with nitrogen (repeated five times). The reaction mixture was irradiated with 30W 450-460 nm blue LEDs at ambient temperature for 12 h. Radical trapped adducts were detected by

HRMS (Figure S3-S5).

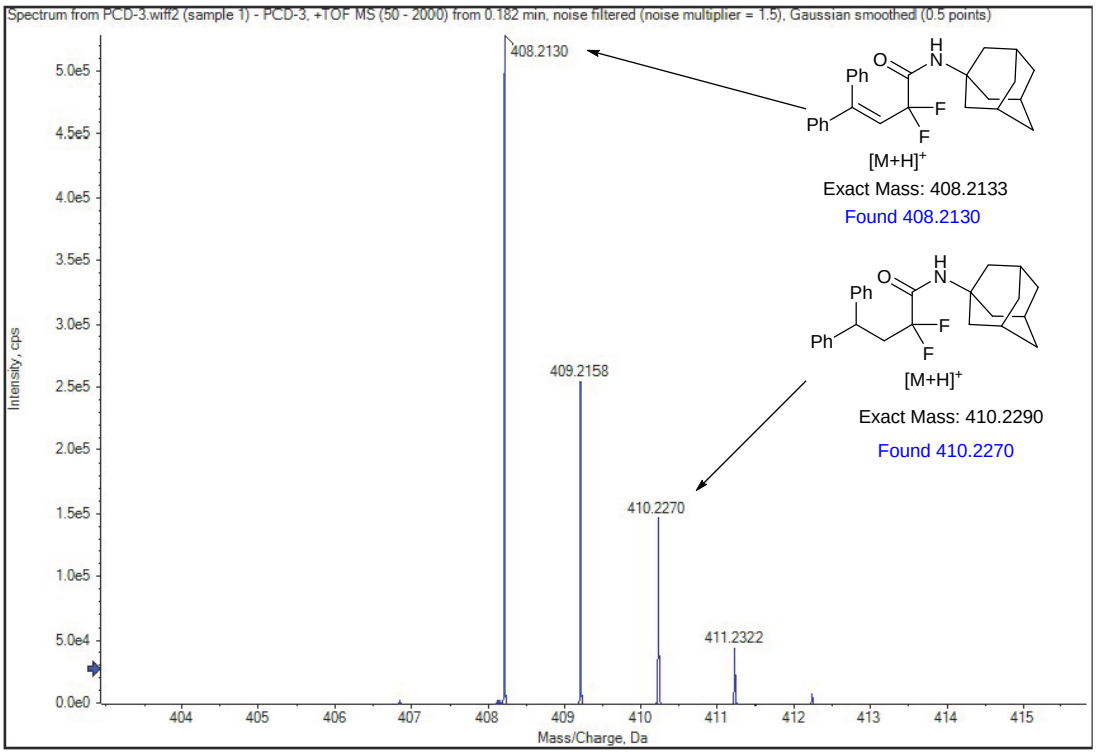


Figure S3. The HRMS spectra for the radical-trapping experiment with 1,1-diphenylethylene.

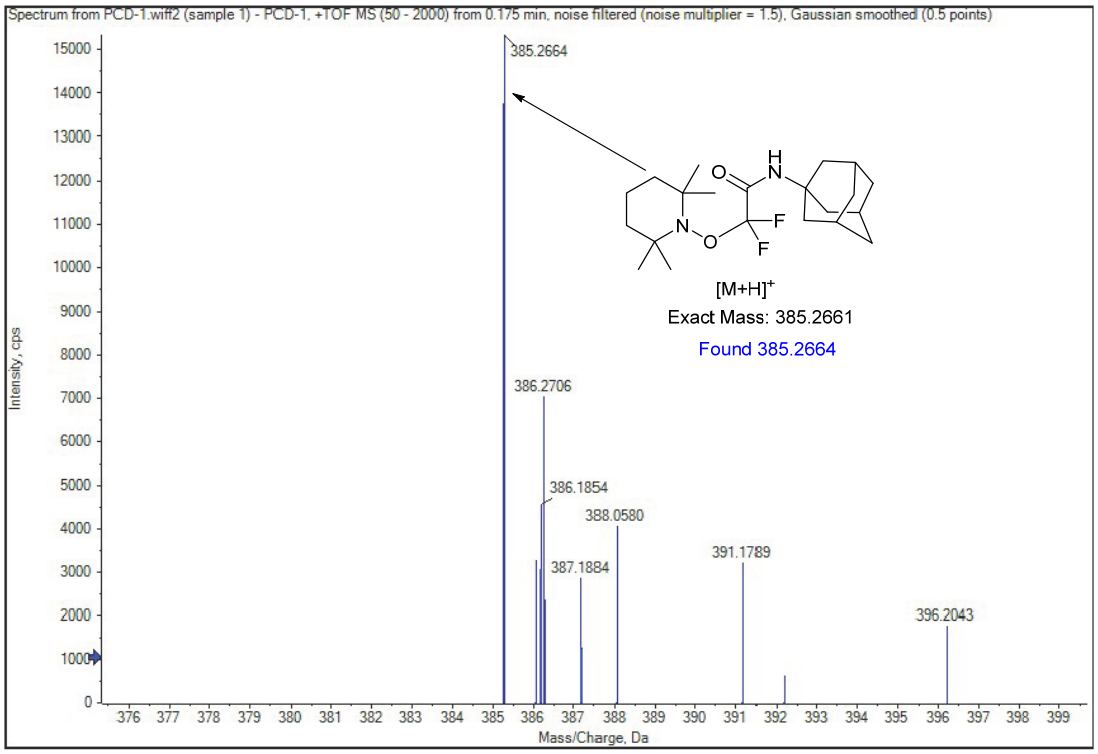


Figure S4. The HRMS spectra for the radical-trapping experiment with TEMPO.

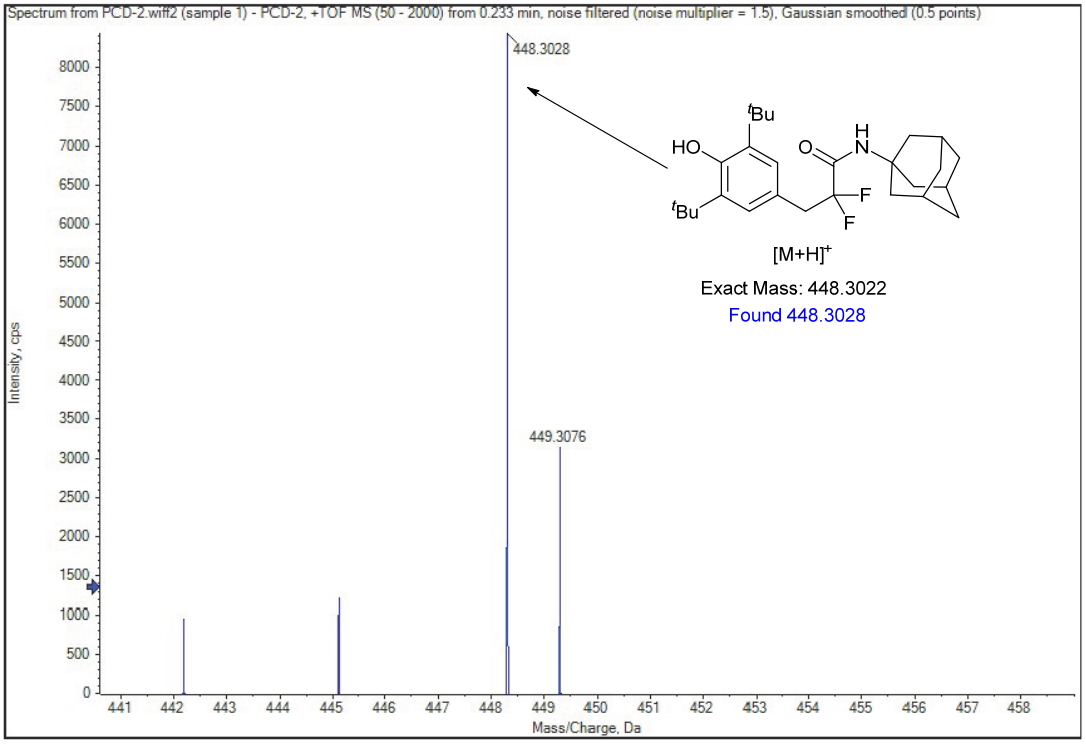
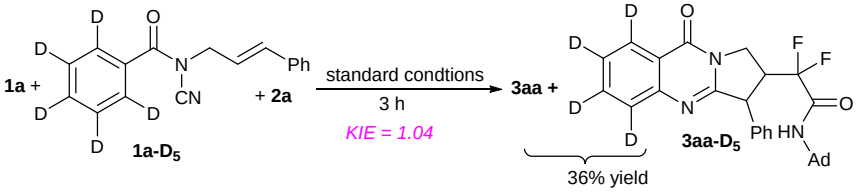
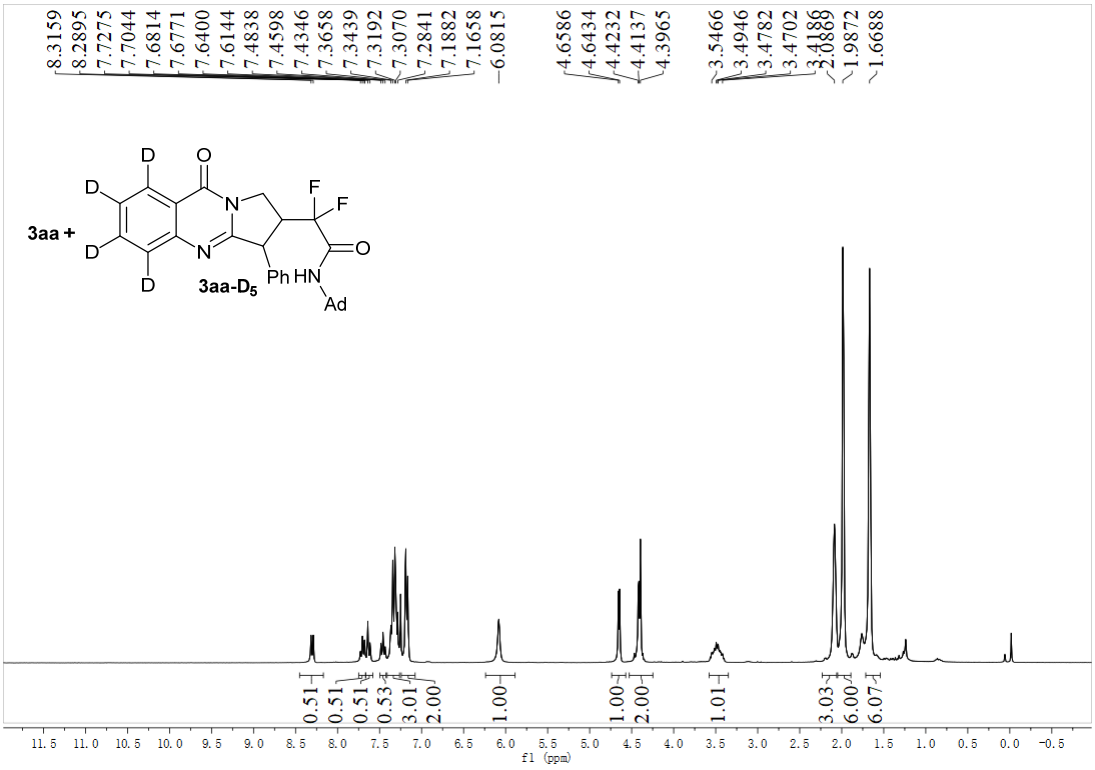


Figure S5. The HRMS spectra for the radical-trapping experiment with BHT.

3.2 Intermolecular competition experiment with isotopically labeled **1a-D$_5$**



The mixture of **1a** (0.05 mmol, 13.1 mg), **1a-D$_5$** (0.05 mmol, 13.4 mg), **2a** (0.2 mmol, 61.4 mg), 4CzIPN (2 mol%, 1.6 mg), $NaHCO_3$ (0.2 mmol, 16.8 mg) and DMSO (1 mL) was added to a Schlenk tube. The tube was evacuated and backfilled with nitrogen (repeated five times). The reaction mixture was irradiated with 30W 450-460 nm blue LEDs at ambient temperature for 3 h. The mixture was added with water and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4. Then, the solvent was evaporated under reduced pressure, and the residue was purified by silica gel flash column chromatography (eluent: petroleum ether/ethyl acetate) to obtain the product **3aa**+**3aa-D$_5$** in 36% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J = 7.9 Hz, 0.51H), 7.70 (t, J = 6.9 Hz, 0.51H), 7.63 (d, J = 7.7 Hz, 0.51H), 7.46 (t, J = 7.6 Hz, 0.53H), 7.37-7.28 (m, 3H), 7.19-7.17 (m, 2H), 6.08 (s, 1H), 4.65 (d, J = 4.6 Hz, 1H), 4.42-4.39 (m, 2H), 3.56-3.42 (m, 1H), 2.09 (s, 3H), 1.99 (s, 6H), 1.67 (s, 6H).



3.3 Stern–Volmer luminescence-quenching experiments

Fluorescence quenching experiments were measured on an Agilent Cary Eclipse Spectrophotometer. The excitation wavelength of 4CzIPN was fixed at 378 nm with emission spectrum λ_{max} = 560 nm. The emission spectrum of a 3×10^{-5} M solution of 4CzIPN in DMSO was collected.

1a: A stock solution of **1a** (0.05 M) was prepared. The emission intensity of 4CzIPN (3×10^{-5} M in DMSO) was collected with the gradient concentration of **1a** and the results were presented.

2a: A stock solution of **2a** (0.05 M) was prepared. The emission intensity of 4CzIPN (3×10^{-5} M in DMSO) was collected with the gradient concentration of **2a** and the results were presented.

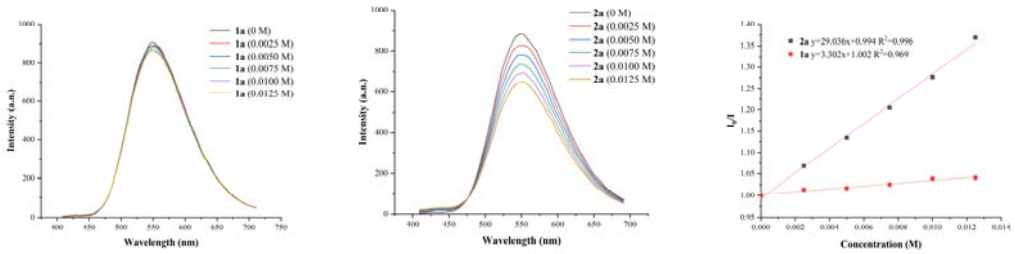


Figure S6. Luminescence quenching of excited 4CzIPN by **1a** or **2a** and the Stern-Volmer plots.

3.4 Light ON/OFF experiment

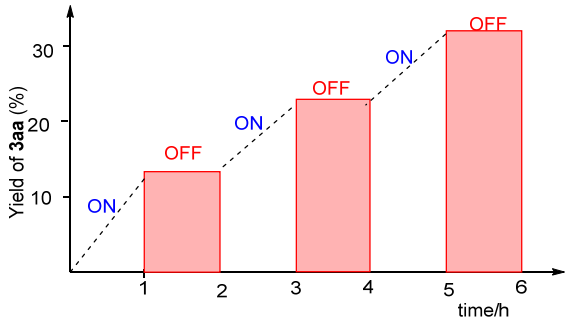
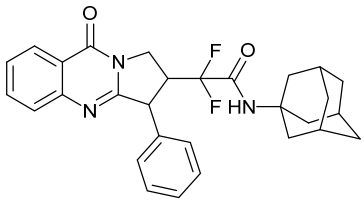
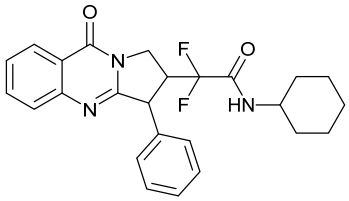


Figure S7. Light ON/OFF experiment

4. Characterization Data for the Substrates

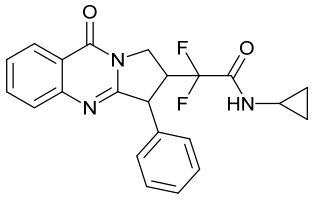


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3aa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (82%, 80.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.1 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.36-7.28 (m, 3H), 7.19-7.17 (m, 2H), 6.13 (s, 1H), 4.65 (d, J = 4.6 Hz, 1H), 4.42-4.37 (m, 2H), 3.54-3.42 (m, 1H), 2.08 (s, 3H), 1.98 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 27.1 Hz), 160.6, 158.9, 149.2, 138.7, 134.3, 129.2, 127.9, 127.6, 127.4, 126.7, 126.3, 120.5, 116.8 (t, $J_{C\text{-}F}$ = 259.7 Hz), 53.1, 50.2 (t, $J_{C\text{-}F}$ = 2.6 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.2 Hz), 44.9 (t, $J_{C\text{-}F}$ = 4.5 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.75, -110.67, -111.24, -112.16; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{30}F_2N_3O_2$ 490.2301; Found 490.2305.

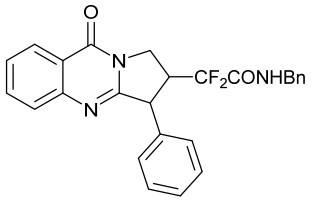


2N-cyclohexyl-2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ab**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave yellowish solid (81%, 70.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 7.9 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.35-7.26 (m, 3H), 7.18 (t, J = 6.9 Hz, 2H), 6.46 (s, 1H), 4.67 (d, J = 4.8 Hz, 1H), 4.46-4.35 (m, 2H), 3.77-3.70 (m, 1H), 3.56-3.44 (m, 1H), 1.96-1.83 (m, 2H), 1.73-1.70 (m, 2H), 1.63-1.60 (m, 1H), 1.39-1.29 (m, 2H), 1.24-1.10 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5 (t, $J_{C\text{-}F}$ = 29.9 Hz), 161.1 (t,

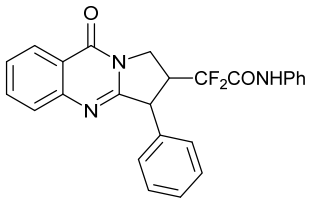
$J_{C\text{-}F}$ = 3.6 Hz), 158.9, 149.2, 138.6, 134.4, 129.2, 127.9, 127.7, 127.4, 126.7, 126.3, 120.5, 116.9 (t, $J_{C\text{-}F}$ = 258.3 Hz), 50.2 (t, $J_{C\text{-}F}$ = 3.4 Hz), 49.0, 45.4 (t, $J_{C\text{-}F}$ = 23.0 Hz), 44.9 (t, $J_{C\text{-}F}$ = 5.3 Hz), 32.6, 25.2, 24.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.59, -111.28, -111.57, -112.26; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{26}F_2N_3O_2$ 438.1988; Found 438.1985.



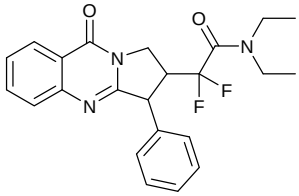
N-cyclopropyl-2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ac**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave yellowish solid (70%, 55.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz, 1H), 7.62-7.57 (m, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.28-7.19 (m, 3H), 7.11-7.09 (m, 2H), 6.91 (s, 1H), 4.57 (d, J = 5.0 Hz, 1H), 4.38-4.25 (m, 2H), 3.47-3.35 (m, 1H), 2.67-2.60 (m, 1H), 0.75-0.69 (m, 2H), 0.51-0.43 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7 (t, $J_{C\text{-}F}$ = 28.3 Hz), 160.7, 158.8, 149.2, 138.4, 134.4, 129.2, 128.0, 127.7, 127.4, 126.8, 126.3, 120.4, 116.9 (t, $J_{C\text{-}F}$ = 258.7 Hz), 50.1 (t, $J_{C\text{-}F}$ = 3.2 Hz), 45.4 (t, $J_{C\text{-}F}$ = 22.7 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.8 Hz), 22.7, 6.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.50, -111.20, -111.59, -112.29; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{20}F_2N_3O_2$ 396.1518; Found 396.1513.



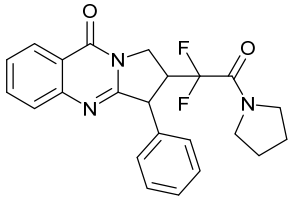
N-benzyl-2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ad**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (77%, 68.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.67-7.63 (m, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.42-7.38 (m, 1H), 7.35-7.20 (m, 9H), 7.17-7.14 (m, 2H), 4.66 (d, J = 4.5 Hz, 1H), 4.43-4.32 (m, 4H), 3.54-3.42 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (t, $J_{C\text{-}F}$ = 28.6 Hz), 160.7, 158.8, 149.2, 138.5, 136.5, 134.4, 129.2, 128.9, 128.0, 127.9, 127.8, 127.4, 126.8, 126.4, 120.4, 116.9 (t, $J_{C\text{-}F}$ = 258.4 Hz), 50.1, 45.5 (t, $J_{C\text{-}F}$ = 23.0 Hz), 44.9 (t, $J_{C\text{-}F}$ = 4.9 Hz), 43.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.27, -110.97, -111.44, -112.14; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{22}F_2N_3O_2$ 446.1675; Found 446.1671.



2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-N-phenylacetamide (**3ae**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (71%, 61.2 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.17 (d, J = 7.7 Hz, 1H), 8.17 (t, J = 7.6 Hz, 1H), 7.55-7.47 (m, 3H), 7.42-7.25 (m, 7H), 7.15 (t, J = 7.2 Hz, 1H), 4.80 (d, J = 8.0 Hz, 1H), 4.63-4.57 (m, 1H), 4.28-4.23 (m, 1H), 3.83-3.78 (m, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.1 (t, $J_{C\text{-}F}$ = 30.7 Hz), 160.2, 160.1, 149.4, 139.2, 137.2, 134.7, 129.3, 129.1, 129.0, 127.9, 127.4, 126.9, 126.2, 125.6, 121.6, 120.8, 119.7, 118.6 (t, $J_{C\text{-}F}$ = 261.2 Hz), 50.1, 45.8 (t, $J_{C\text{-}F}$ = 23.2 Hz), 45.1 (t, $J_{C\text{-}F}$ = 3.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.41, -109.31, -110.14, -111.03; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}F_2N_3O_2$ 432.1518; Found 432.1527.

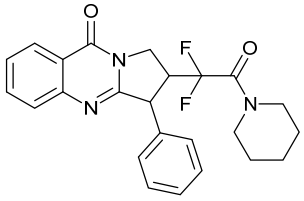


N,N-diethyl-2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3af**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 4/1) gave yellowish oil (53%, 43.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.9 Hz, 1H), 7.61 (t, J = 7.1 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.29-7.16 (m, 5H), 4.67 (d, J = 4.4 Hz, 1H), 4.51-4.45 (m, 1H), 4.31-4.27 (m, 1H), 3.55-3.41 (m, 3H), 3.35-3.23 (m, 2H), 1.12-1.05 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ161.1 (t, $J_{C\text{-}F}$ = 28.3 Hz), 160.8, 159.6, 149.4, 139.8, 134.2, 129.2, 127.8, 127.7, 127.4, 126.5, 126.3, 120.5, 119.3 (t, $J_{C\text{-}F}$ = 262.3 Hz), 50.4 (t, $J_{C\text{-}F}$ = 3.5 Hz), 46.5 (t, $J_{C\text{-}F}$ = 22.9 Hz), 46.2 (t, $J_{C\text{-}F}$ = 5.6 Hz), 41.7 (t, $J_{C\text{-}F}$ = 6.2 Hz), 14.2, 12.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -102.49, -103.51, -108.36, -109.38; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{24}F_2N_3O_2$ 412.1831; Found 412.1829.

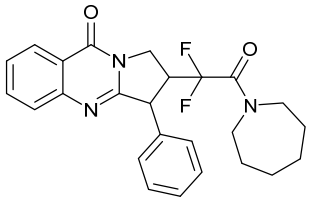


2-(1,1-difluoro-2-oxo-2-(pyrrolidin-1-yl)ethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3ag**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave yellowish oil (65%, 53.2 mg); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 8.31 (dd, J = 8.0, 1.0 Hz, 1H), 7.72-7.68 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.47-7.43 (m, 1H), 7.37-7.33 (m, 2H), 7.31-7.24 (m, 3H), 4.76 (d, J = 4.5 Hz, 1H), 4.57-4.51 (m, 1H), 4.42-4.38 (m, 1H), 3.73-3.62 (m, 2H), 3.61-3.49 (m, 3H), 1.98-1.91 (m, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 160.4 (t, J_{C-F} = 29.3 Hz), 159.5, 149.4, 139.5, 134.2, 129.1, 127.8, 127.7, 127.4, 126.5, 126.3, 120.5, 118.6 (t, J_{C-F} = 260.2 Hz), 50.3 (t, J_{C-F} = 3.1 Hz), 47.4, 46.4 (t, J_{C-F} = 5.9 Hz), 46.0 (t, J_{C-F} = 22.6 Hz), 45.8 (t, J_{C-F} = 5.2 Hz), 26.4, 25.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.50, -107.26, -110.87, -111.63; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}F_2N_3O_2$ 410.1675; Found 410.1673.

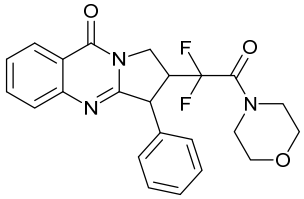


2-(1,1-difluoro-2-oxo-2-(piperidin-1-yl)ethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3ah**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (67%, 56.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.63-7.58 (m, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.38-7.34 (m, 1H), 7.29-7.24 (m, 2H), 7.22-7.15 (m, 3H), 4.67 (d, J = 4.4 Hz, 1H), 4.51-4.45 (m, 1H), 4.32-4.27 (m, 1H), 3.56-3.39 (m, 5H), 1.57-1.50 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 160.0 (t, J_{C-F} = 28.3 Hz), 159.6, 149.4, 139.8, 134.2, 129.2, 127.8, 127.7, 127.4, 126.5, 126.3, 120.5, 119.4 (t, J_{C-F} = 262.1 Hz), 50.4 (t, J_{C-F} = 3.3 Hz), 46.7 (t, J_{C-F} = 6.3 Hz), 46.6 (t, J_{C-F} = 22.8 Hz), 46.2 (t, J_{C-F} = 5.6 Hz), 44.5, 26.5, 25.6, 24.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -101.79, -102.81, -107.71, -108.73; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{24}F_2N_3O_2$ 424.1831; Found 424.1826.

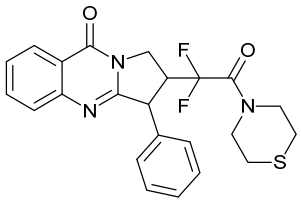


2-(2-(azepan-1-yl)-1,1-difluoro-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3ai**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (61%, 53.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 8.0, 1.1 Hz, 1H), 7.72-7.68 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.48-7.44 (m, 1H), 7.38-7.34 (m, 2H), 7.31-7.24 (m, 3H), 4.76 (d, J = 4.5 Hz, 1H), 4.60-4.54 (m, 1H), 4.39-4.35 (m, 1H), 3.68-3.49 (m, 5H), 1.75-1.71 (m, 4H), 1.58-1.53 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4 (t, J_{C-F} = 28.4 Hz), 160.8, 159.6, 149.4, 139.8, 134.2, 129.2, 127.8, 127.7, 127.4, 126.5, 126.3, 120.5, 119.4 (t, J_{C-F} = 262.3 Hz), 50.4 (t, J_{C-F} = 3.6 Hz), 48.2, 47.5 (t, J_{C-F} = 6.1 Hz), 46.6 (t, J_{C-F} = 23.0 Hz), 46.2 (t, J_{C-F} = 5.6 Hz), 29.5, 27.5, 26.3, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ

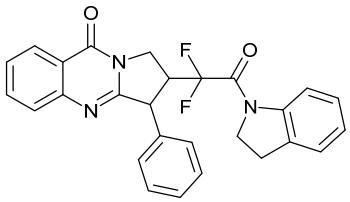
-102.14, -102.91, -107.98, -108.75; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{26}F_2N_3O_2$ 438.1988; Found 438.1982.



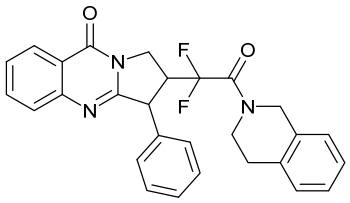
2-(1,1-difluoro-2-morpholino-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3aj**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (65%, 55.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, J = 8.0, 1.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.37-7.34 (m, 1H), 7.28-7.24 (m, 2H), 7.22-7.15 (m, 3H), 4.66 (d, J = 4.6 Hz, 1H), 4.51-4.45 (m, 1H), 4.30-4.26 (m, 1H), 3.61-3.39 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 160.3 (t, $J_{C\text{-}F}$ = 28.9 Hz), 159.4, 149.4, 139.6, 134.3, 129.2, 127.8, 127.7, 127.4, 126.6, 126.3, 120.5, 119.2 (t, $J_{C\text{-}F}$ = 261.2 Hz), 66.6 (d, $J_{C\text{-}F}$ = 5.5 Hz), 50.3 (t, $J_{C\text{-}F}$ = 3.4 Hz), 46.3 (t, $J_{C\text{-}F}$ = 5.9 Hz), 46.0 (t, $J_{C\text{-}F}$ = 5.4 Hz), 43.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ -101.54, -102.57, -107.39, -108.42; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}F_2N_3O_3$ 426.1624; Found 426.1637.



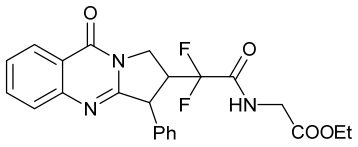
2-(1,1-difluoro-2-oxo-2-thiomorpholinoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3ak**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave yellowish oil (68%, 60.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, J = 8.0, 1.1 Hz, 1H), 7.72-7.68 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.47-7.43 (m, 1H), 7.38-7.34 (m, 2H), 7.32-7.24 (m, 3H), 4.74 (d, J = 4.6 Hz, 1H), 4.60-4.55 (m, 1H), 4.38-4.33 (m, 1H), 3.99-3.81 (m, 4H), 3.61-3.48 (m, 1H), 2.65 (t, J = 4.7 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 160.4 (t, $J_{C\text{-}F}$ = 29.2 Hz), 159.4, 149.4, 139.6, 134.3, 129.2, 127.9, 127.7, 127.4, 126.6, 126.3, 120.5, 118.6 (t, $J_{C\text{-}F}$ = 262.7 Hz), 50.3 (t, $J_{C\text{-}F}$ = 3.0 Hz), 47.4, 46.4 (t, $J_{C\text{-}F}$ = 5.7 Hz), 46.6 (t, $J_{C\text{-}F}$ = 22.6 Hz), 46.0, 45.9 (t, $J_{C\text{-}F}$ = 5.9 Hz), 28.1, 27.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.85, -102.62, -107.76, -108.53; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}F_2N_3O_2S$ 442.1395; Found 442.1385.



2-(1,1-difluoro-2-(indolin-1-yl)-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3al**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (85%, 77.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.0 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 7.69 (t, J = 8.2 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.39-7.35 (m, 2H), 7.32-7.28 (m, 3H), 7.25-7.21 (m, 2H), 7.12 (t, J = 7.5 Hz, 1H), 4.83 (d, J = 4.7 Hz, 1H), 4.67-4.61 (m, 1H), 4.48-4.43 (m, 1H), 4.32 (t, J = 8.1 Hz, 1H), 3.72-3.59 (m, 1H), 3.17 (d, J = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 159.5 (t, $J_{C\text{-}F}$ = 29.3 Hz), 159.4, 149.4, 142.2, 139.6, 134.3, 131.8, 129.2, 127.9, 127.8, 127.6, 127.4, 126.6, 126.3, 125.6, 124.8, 120.6, 119.1 (t, $J_{C\text{-}F}$ = 261.8 Hz), 117.9, 50.4, 47.6 (t, $J_{C\text{-}F}$ = 7.4 Hz), 46.1 (t, $J_{C\text{-}F}$ = 22.9 Hz), 46.1 (t, $J_{C\text{-}F}$ = 22.9 Hz), 46.0 (t, $J_{C\text{-}F}$ = 5.69 Hz), 28.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.62, -106.40, -111.20, -111.97; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{22}F_2N_3O_2$ 458.1675; Found 458.1674.

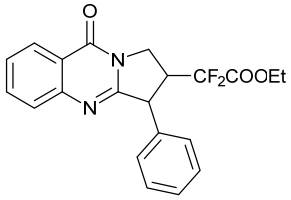


2-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-1,1-difluoro-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3am**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (63%, 59.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.0 Hz, 1H), 7.71-7.67 (m, 1H), 7.62 (t, J = 8.2 Hz, 1H), 7.45 (t, J = 7.1 Hz, 1H), 7.35-7.32 (m, 1H), 7.30-7.23 (m, 3H), 7.21-7.18 (m, 2H), 7.13-7.07 (m, 2H), 4.84-4.73 (m, 3H), 4.61-4.55 (m, 1H), 4.42-4.36 (m, 1H), 3.95-3.92 (m, 1H), 3.85-3.79 (m, 1H), 3.63-3.52 (m, 1H), 2.93-2.87 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 160.7 (t, $J_{C\text{-}F}$ = 30.5 Hz), 160.6 (t, $J_{C\text{-}F}$ = 30.2 Hz), 159.5, 159.4, 149.4, 149.3, 139.7, 139.6, 134.2, 134.1, 133.5, 132.1, 131.7, 129.2, 128.6, 127.8, 127.7, 127.4, 126.9, 126.7, 126.6, 126.5, 126.3, 126.0, 120.5, 119.3 (t, $J_{C\text{-}F}$ = 263.3 Hz), 50.4, 46.9 (t, $J_{C\text{-}F}$ = 6.8 Hz), 46.6 (t, $J_{C\text{-}F}$ = 22.9 Hz), 46.1 (t, $J_{C\text{-}F}$ = 5.3 Hz), 45.6, 43.2 (t, $J_{C\text{-}F}$ = 6.7 Hz), 41.8, 29.4, 27.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ -102.25, -102.51, -103.27, -103.54, -107.77, 107.86, -108.79, 108.89; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{28}H_{24}F_2N_3O_2$ 472.1831; Found 472.1829.

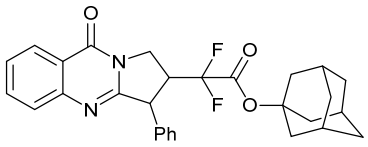


ethyl (2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetyl)glycinate (**3an**). Flash column chromatography on silica gel (petroleum ether/ethyl

acetate 2/1) gave yellowish solid (72%, 63.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.9 Hz, 1H), 7.61-7.57 (m, 2H), 7.51 (d, J = 8.2 Hz, 1H), 7.34 (d, J = 6.9 Hz, 1H), 7.26-7.18 (m, 3H), 7.10 (d, J = 7.1 Hz, 2H), 4.64 (d, J = 5.0 Hz, 1H), 4.34-4.29 (m, 2H), 4.13-4.08 (m, 2H), 3.89-3.87 (m, 2H), 3.47-3.35 (m, 1H), 1.19-1.16 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 162.9 (t, $J_{C\text{-}F}$ = 28.9 Hz), 160.6, 158.8, 149.2, 138.5, 134.4, 129.2, 128.0, 127.8, 127.4, 126.8, 126.3, 120.4, 116.8 (t, $J_{C\text{-}F}$ = 257.9 Hz), 61.9, 49.9 (q, $J_{C\text{-}F}$ = 3.2 Hz), 45.4 (t, $J_{C\text{-}F}$ = 22.8 Hz), 44.7 (t, $J_{C\text{-}F}$ = 4.6 Hz), 41.2, 14.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ -110.87, -111.80, -112.11, -113.04; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{22}F_2N_3O_4$ 442.1573; Found 442.1572.

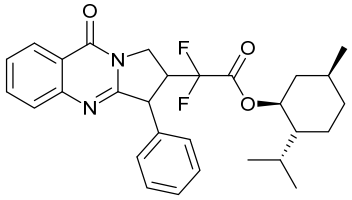


ethyl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3ao**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 5/1) gave yellow solid (79%, 60.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, J = 8.0, 1.2 Hz, 1H), 7.72-7.68 (m, 1H), 7.61 (d, J = 7.7 Hz, 1H), 7.48-7.44 (m, 1H), 7.40-7.30 (m, 5H), 7.22-7.19 (m, 2H), 4.64 (d, J = 6.6 Hz, 1H), 4.55-4.49 (m, 1H), 4.39-4.34 (m, 1H), 4.20-4.12 (m, 1H), 4.10-4.02 (m, 1H), 3.49-3.36 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4 (t, $J_{C\text{-}F}$ = 31.8 Hz), 160.6, 158.6, 149.2, 138.0, 134.4, 129.2, 128.2, 128.1, 127.5, 126.8, 126.3, 120.5, 114.8 (t, $J_{C\text{-}F}$ = 255.1 Hz), 63.6, 50.1 (q, $J_{C\text{-}F}$ = 2.5 Hz), 46.4 (t, $J_{C\text{-}F}$ = 23.2 Hz), 44.5 (t, $J_{C\text{-}F}$ = 4.9 Hz), 13.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.57, -110.51, -112.64, -113.58; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{19}F_2N_2O_3$ 385.1358; Found 385.1355.

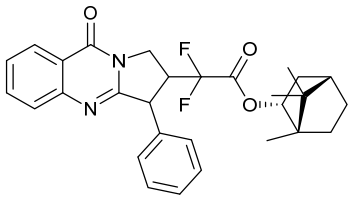


(3s,5s,7s)-adamantan-1-yl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3ap**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 5/1) gave yellow solid (70%, 68.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.9 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.38-7.31 (m, 3H), 7.21 (d, J = 7.1 Hz, 2H), 4.67 (d, J = 5.5 Hz, 1H), 4.51-4.36 (m, 2H), 4.43-4.32 (m, 1H), 2.13 (s, 3H), 2.02-1.95 (m, 6H), 1.63-1.55 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (t, $J_{C\text{-}F}$ = 31.3 Hz), 160.6, 158.8, 149.3, 138.6, 134.4, 129.3, 128.1, 127.9, 127.5, 126.8, 126.3, 120.5, 114.7 (t, $J_{C\text{-}F}$ = 255.9 Hz), 86.1, 50.2

(q, $J_{C\text{-}F}$ = 3.5 Hz), 46.1 (t, $J_{C\text{-}F}$ = 23.6 Hz), 44.9 (t, $J_{C\text{-}F}$ = 5.1 Hz), 40.7, 35.7, 30.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.25, -109.42, -111.03, -111.97; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}F_2N_2O_3$ 491.2141; Found 491.2143.

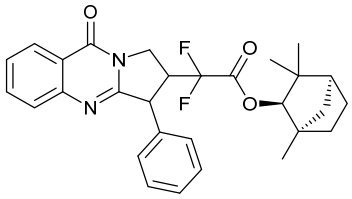


2-isopropyl-5-methylcyclohexyl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3aq**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 5/1) gave white solid (73%, 72.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.0 Hz, 1H), 7.70-7.66 (m, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.37-7.28 (m, 3H), 7.21 (d, J = 7.0 Hz, 2H), 4.82-4.68 (m, 2H), 4.54-4.37 (m, 2H), 3.46-3.33 (m, 1H), 1.84-1.54 (m, 4H), 1.45-1.33 (m, 2H), 1.05-0.69 (m, 13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (dt, $J_{C\text{-}F}$ = 32.2 Hz), 160.6, 158.8, 158.6, 149.3, 138.7, 138.5, 134.4, 129.3, 129.2, 128.2, 128.1, 128.0, 127.7, 127.5, 126.8, 126.3, 120.5, 120.4, 115.1 (dt, $J_{C\text{-}F}$ = 255.6 Hz), 78.6, 78.5, 50.2 (t, $J_{C\text{-}F}$ = 3.9 Hz), 50.1 (t, $J_{C\text{-}F}$ = 3.4 Hz), 46.6, 46.5, 46.1 (d, $J_{C\text{-}F}$ = 23.0 Hz), 46.0 (t, $J_{C\text{-}F}$ = 23.4 Hz), 44.9 (t, $J_{C\text{-}F}$ = 5.5 Hz), 44.7 (t, $J_{C\text{-}F}$ = 5.1 Hz), 33.8, 31.3, 31.2, 26.2, 23.2, 21.7, 20.6, 20.5, 16.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.56, -109.58, -110.33, -110.35, -110.51, 110.53, -111.25, 112.19; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{33}F_2N_2O_3$ 495.2454; Found 495.2445.

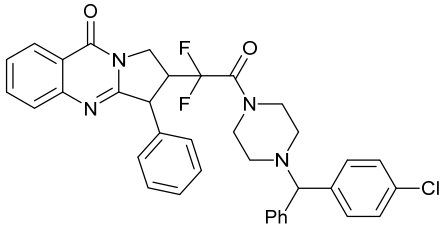


1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3ar**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 5/1) gave white solid (71%, 69.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.8 Hz, 1H), 7.69 (t, J = 8.1 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.45 (t, J = 7.4 Hz, 2H), 7.38-7.29 (m, 3H), 7.22-7.20 (m, 2H), 4.94-4.91 (m, 0.5H), 4.87-4.84 (m, 0.5H), 4.69-4.66 (m, 1H), 4.55-4.49 (m, 1H), 4.43-4.37 (m, 1H), 3.49-3.34 (m, 1H), 2.40-2.32 (m, 0.5H), 2.26-2.18 (m, 0.5H), 1.87-1.63 (m, 3H), 1.33-1.10 (m, 2.5H), 0.99-0.95 (m, 0.5H), 0.86 (s, 6H), 0.83 (s, 1.5H), 0.73 (s, 1.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 (t, $J_{C\text{-}F}$ = 31.1 Hz), 162.8 (t, $J_{C\text{-}F}$ = 31.1 Hz), 160.6, 158.6, 149.3, 138.4, 138.3, 134.4, 129.3, 128.7 (t, $J_{C\text{-}F}$ = 10.3 Hz), 128.2, 128.1, 128.0, 127.9, 127.5, 126.8, 126.3, 120.5, 115.1 (t, $J_{C\text{-}F}$ = 256.0 Hz), 115.0 (t, $J_{C\text{-}F}$ = 255.1 Hz), 84.2, 84.0,

50.2 (t, $J_{C\text{-}F}$ = 7.6 Hz), 49.1, 49.0, 48.1, 47.9, 46.23 (d, $J_{C\text{-}F}$ = 22.8 Hz), 46.20 (t, $J_{C\text{-}F}$ = 23.0 Hz), 44.67, 44.62, 33.4, 35.9, 27.8, 27.7, 26.9, 26.8, 19.6, 18.8, 18.7, 13.5, 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.72, -110.17, -110.43, -110.88, -111.70, 112.18, -112.41, 112.89; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{31}F_2N_2O_3$ 493.2297; Found 493.2281.

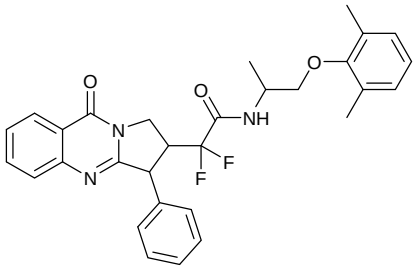


(1R,2R,4S)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3as**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 5/1) gave white solid (77%, 75.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.9 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.61 (t, J = 8.1 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.38-7.28 (m, 2H), 7.23-7.21 (m, 2H), 4.73 (d, J = 4.8 Hz, 1H), 4.55-4.47 (m, 1.5H), 4.44-4.37 (m, 1.5H), 3.47-3.33 (m, 1H), 1.74-1.64 (m, 3H), 1.59-1.55 (m, 1H), 1.51-1.40 (m, 1H), 1.24-1.19 (m, 1H), 1.51-1.40 (m, 1H), 1.11-1.02 (m, 5.5H), 0.92 (s, 1.5H), 0.79 (s, 1.5H), 0.72 (s, 1.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2 (t, $J_{C\text{-}F}$ = 31.6 Hz), 163.1 (t, $J_{C\text{-}F}$ = 31.9 Hz), 160.6 (t, $J_{C\text{-}F}$ = 3.6 Hz), 158.7, 149.3, 138.74, 138.70, 134.4, 129.3, 128.1, 127.9, 127.5, 126.7, 126.3, 120.5, 115.4 (t, $J_{C\text{-}F}$ = 256.1 Hz), 115.3 (t, $J_{C\text{-}F}$ = 256.9 Hz), 90.2, 90.0, 50.12, 50.10, 48.6, 48.3, 48.2, 48.1, 46.0 (t, $J_{C\text{-}F}$ = 23.1 Hz), 45.9 (t, $J_{C\text{-}F}$ = 23.2 Hz), 45.1 (q, $J_{C\text{-}F}$ = 5.2 Hz), 41.2, 39.7, 39.6, 29.6, 26.4, 26.3, 25.6, 20.0, 19.9, 19.3, 19.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.29, -109.84, -110.26, -110.79, -110.80, -111.38, 111.77, -112.33; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{31}F_2N_2O_3$ 493.2297; Found 493.2298.

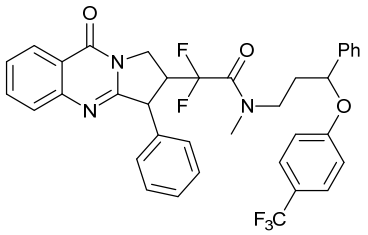


2-(2-(4-((4-chlorophenyl)(phenyl)methyl)piperazin-1-yl)-1,1-difluoro-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3at**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (66%, 82.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.2 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.36-7.35 (m, 6H), 7.30-7.18 (m, 8H), 4.73 (d, J = 4.4 Hz, 1H), 4.58-4.52 (m, 1H), 4.39-4.21 (m, 1H), 4.21 (s, 1H), 3.70-3.45 (m, 5H), 2.40-2.39 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 160.1 (t, $J_{C\text{-}F}$ = 28.3 Hz), 159.4, 149.4, 141.3, 140.5, 139.7, 134.3, 132.9, 129.2,

129.1, 128.9, 128.8, 127.8, 127.75, 127.73, 127.5, 127.4, 126.6, 126.3, 120.5, 119.2 (t, $J_{C\text{-}F}$ = 262.1 Hz), 75.1, 51.9, 51.3, 50.3 (t, $J_{C\text{-}F}$ = 3.2 Hz), 46.5 (t, $J_{C\text{-}F}$ = 22.6 Hz), 46.1 (t, $J_{C\text{-}F}$ = 5.6 Hz), 45.8 (t, $J_{C\text{-}F}$ = 6.1 Hz), 43.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -101.44, -101.47, -102.46, -102.49, -107.24, 108.27; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{32}ClF_2N_4O_2$ 625.2176; Found 625.2177.

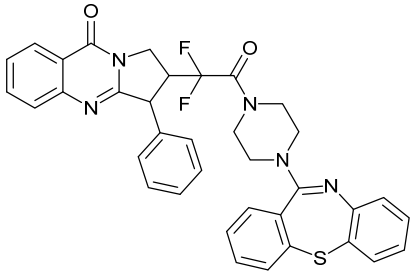


2-(1,1-difluoro-2-oxo-2-thiomorpholinoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3au**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (63%, 65.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32-8.28 (m, 1H), 7.71-7.67 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.47-7.42 (m, 1H), 7.37-7.28 (m, 3H), 7.24-7.24 (m, 2H), 7.12 (s, 1H), 7.00 (d, J = 7.3 Hz, 2H), 6.95-6.92 (m, 1H), 4.76-4.72 (m, 1H), 4.53-4.39 (m, 2H), 4.34-4.27 (m, 1H), 3.82-3.75 (m, 1H), 3.74-3.72 (m, 1H), 3.62-3.50 (m, 1H), 2.24 (s, 6H), 1.45-1.43 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (dt, $J_{C\text{-}F}$ = 28.1 Hz), 160.7, 160.6, 158.85, 158.83, 154.5, 154.4, 149.3, 149.2, 138.6, 138.5, 134.4, 130.62, 130.60, 129.24, 127.21, 129.1, 128.05, 128.02, 127.8, 127.7, 127.5, 127.4, 126.75, 126.74, 126.34, 126.33, 124.4, 120.52, 120.50, 116.9 (t, $J_{C\text{-}F}$ = 258.9 Hz), 73.0, 72.9, 50.2 (tt, $J_{C\text{-}F}$ = 18.5 Hz), 46.2, 46.1, 45.5 (tt, $J_{C\text{-}F}$ = 23.1 Hz), 44.9 (q, $J_{C\text{-}F}$ = 5.5 Hz), 17.4, 17.3, 16.2, 16.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.30, -109.75, -110.24, -110.68, -111.64, -111.88, -112.57, -112.81; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{30}F_2N_3O_3$ 518.2250; Found 518.2251.

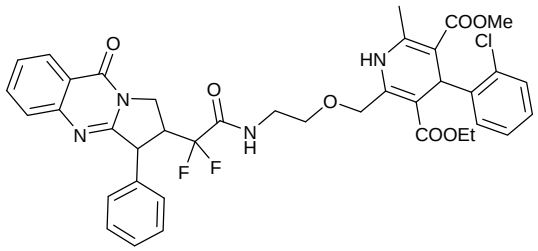


2,2-difluoro-N-methyl-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-N-(3-phenyl-3-(4-(trifluoromethyl)phenoxy)propyl)acetamide (**3av**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (77%, 99.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 7.62-7.52 (m, 2H), 7.37-7.30 (m, 3H), 7.26-7.09 (m, 10H), 6.80-6.75 (m, 2H), 5.13-5.06 (m, 1H), 4.64-4.62 (m, 1H), 4.48-4.42 (m, 1H), 4.27-4.19 (m, 1H), 3.65-3.37 (m, 3H), 3.06 (s, 2H), 2.88 (s, 1H), 2.22-2.10 (m, 1H), 2.06-1.98 (m, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7 (t, $J_{C\text{-}F}$ = 28.7 Hz), 160.8, 160.1, 160.0, 259.5, 149.5, 140.2, 140.1, 139.9, 139.8, 139.7, 139.69, 139.67, 139.66, 134.3, 129.2, 129.0, 128.9, 128.2, 127.8, 127.77, 127.77, 127.70, 127.4, 128.9, 126.6, 126.4, 125.7, 125.6, 123.0 (t, $J_{C\text{-}F}$ = 19.4 Hz), 122.9 (t, $J_{C\text{-}F}$ = 17.1 Hz), 119.2 (t, $J_{C\text{-}F}$ = 262.1 Hz), 115.8, 115.7, 78.2 (d, $J_{C\text{-}F}$ = 11.3 Hz), 77.8 (d, $J_{C\text{-}F}$ = 14.4 Hz), 77.8, 50.4 (t, $J_{C\text{-}F}$ = 3.8 Hz), 47.0 (d, $J_{C\text{-}F}$ = 7.4 Hz), 46.7 (t, $J_{C\text{-}F}$ = 23.1 Hz), 46.5 (t, $J_{C\text{-}F}$ = 22.9 Hz), 37.5, 35.5, 35.3 (t, $J_{C\text{-}F}$ = 6.6 Hz), 34.8 (d, $J_{C\text{-}F}$ = 2.9 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ -61.47, 61.50, 61.51, -101.56, -101.80, -102.52, -102.58, -108.82, -103.55, -103.85, -107.41, -107.48, -108.41, -108.50, -108.93, -109.44, 109.97; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{31}F_5N_3O_3$ 648.2280; Found 648.2258.

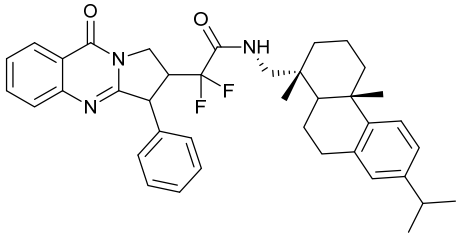


2-(2-(4-(dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl)-1,1-difluoro-2-oxoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3aw**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave yellow solid (59%, 74.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.46-7.23 (m, 10H), 7.18-7.16 (m, 1H), 7.09-7.07 (m, 1H), 6.93-6.89 (m, 1H), 4.76 (d, J = 4.4 Hz, 1H), 4.58-4.55 (m, 1H), 4.40-4.36 (m, 1H), 3.91-3.26 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ 160.8, 160.5,* 160.2 (t, $J_{C\text{-}F}$ = 34.1 Hz), 159.4, 149.4, 148.3, 140.1, 139.6, 134.3, 133.7, 132.4, 132.3, 131.2, 129.2, 128.8, 128.6, 127.9, 127.8, 127.7, 127.4, 126.6, 126.3, 125.3, 123.5, 120.5, 119.2 (t, $J_{C\text{-}F}$ = 261.5 Hz), 50.4, 46.6 (t, $J_{C\text{-}F}$ = 21.1 Hz), 46.1 (t, $J_{C\text{-}F}$ = 4.4 Hz), 45.4 (t, $J_{C\text{-}F}$ = 5.1 Hz), 42.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ -101.28, -101.44, -102.30, -102.46, -107.03, -107.23, -108.05, -108.26; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{30}F_2N_5O_2S$ 634.2083; Found 634.2084.

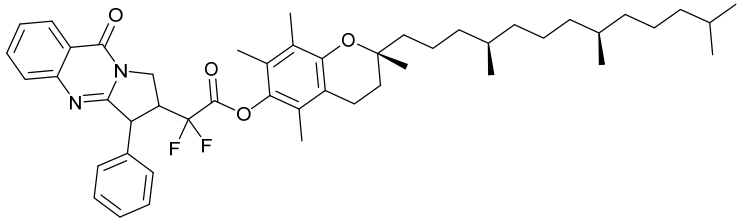


3-ethyl 5-methyl 4-(2-chlorophenyl)-2-((2-(2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamido)ethoxy)methyl)-6-methyl-1,4-dihydropyridine-3,5-d

icarboxylate (**3ax**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 1/1) gave white solid (47%, 55.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 6.9 Hz, 1H), 7.39-7.28 (m, 7H), 7.25-7.13 (m, 4H), 4.86-4.76 (m, 2H), 4.71 (d, J = 4.9 Hz, 1H), 4.54-4.33 (m, 2H), 3.97 (q, J = 7.0 Hz, 2H), 3.59-3.45 (m, 9H), 2.64 (s, 3H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 166.8, 158.9, 156.5, 155.5, 149.2, 145.2, 138.5, 134.7, 134.4, 132.8, 132.7, 130.15, 130.13, 129.9, 129.14, 129.11, 128.5, 127.9, 127.8, 127.4, 126.7, 126.3, 126.2, 120.5, 116.7 (t, $J_{C\text{-}F}$ = 256.6 Hz), 72.9, 68.8, 61.6, 52.3, 50.1, 45.6 (t, $J_{C\text{-}F}$ = 22.2 Hz), 44.8 (d, $J_{C\text{-}F}$ = 6.2 Hz), 39.5, 23.2, 13.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ -110.42, -111.35, -111.73, -112.66; HRMS (ESI) *m/z*: $[M\text{-}H]^+$ Calcd for $C_{39}H_{36}ClF_2N_4O_7$ 745.2246; Found 745.2235.

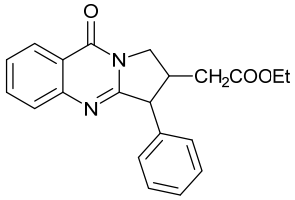


2-(1,1-difluoro-2-oxo-2-thiomorpholinoethyl)-3-phenyl-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**3ay**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (76%, 94.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.38-7.30 (m, 3H), 7.22-7.18 (m, 3H), 7.02 (d, J = 8.0 Hz, 1H), 6.92 (s, 1H), 6.65 (s, 1H), 4.73 (d, J = 2.8 Hz, 1H), 4.51-4.38 (m, 2H), 4.61-4.44 (m, 1H), 3.36-3.16 (m, 2H), 2.97-2.78 (m, 3H), 2.32 (d, J = 12.7 Hz, 1H), 1.85-1.68 (m, 4H), 1.49-1.38 (m, 3H), 1.25-1.23 (m, 11H), 0.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (t, $J_{C\text{-}F}$ = 28.6 Hz), 160.7, 158.9, 149.3, 146.8, 145.7, 138.7, 134.5, 134.4, 129.2, 128.0, 127.7, 127.5, 126.95, 126.7, 126.3, 124.2, 124.0, 120.5, 117.2 (t, $J_{C\text{-}F}$ = 258.3 Hz), 50.3 (d, $J_{C\text{-}F}$ = 2.7 Hz), 50.2 (t, $J_{C\text{-}F}$ = 3.6 Hz), 46.1 (d, $J_{C\text{-}F}$ = 3.9 Hz), 46.1 (t, $J_{C\text{-}F}$ = 27.5 Hz), 45.0 (q, $J_{C\text{-}F}$ = 4.2 Hz), 38.2, 37.6, 37.5, 36.2, 33.5, 30.2, 25.4, 24.0, 19.1, 18.5, 18.49, 18.45; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.23, -110.17, -110.39, -110.52, -111.04, -111.05, -111.97, -111.99; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{39}H_{44}F_2N_3O_2$ 624.3396; Found 624.3391.

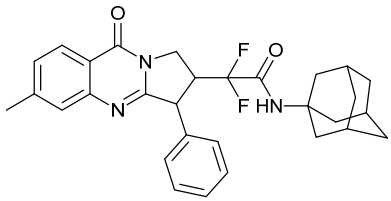


(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 2,2-difluoro-2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acet

ate (**3az**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 4/1) gave white solid (53%, 79.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, J = 8.1, 1.2 Hz, 1H), 7.74-7.69 (m, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.49-7.45 (m, 1H), 7.41-7.33 (m, 3H), 7.28 (d, J = 7.1 Hz, 2H), 4.87 (d, J = 4.8 Hz, 1H), 4.64-4.52 (m, 2H), 3.65-3.53 (m, 1H), 2.60 (t, J = 6.5 Hz, 2H), 2.11 (s, 3H), 1.99 (s, 3H), 1.95 (s, 3H), 1.87-1.74 (m, 2H), 1.61-1.23 (m, 18H), 1.18-1.03 (m, 7H), 0.89-0.86 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5 (t, $J_{C\text{-}F}$ = 32.3 Hz), 160.7, 158.7, 150.2, 149.3, 139.5, 138.8, 134.4, 129.4, 128.1, 127.8, 127.5, 126.8, 126.4, 125.9, 124.4, 123.6, 120.5, 117.8, 115.8 (t, $J_{C\text{-}F}$ = 257.2 Hz), 75.4, 50.3, 45.9 (t, $J_{C\text{-}F}$ = 22.5 Hz), 45.1 (d, $J_{C\text{-}F}$ = 4.8 Hz), 39.3, 37.5, 37.4, 37.3, 32.8, 32.7, 32.7, 30.9 (d, $J_{C\text{-}F}$ = 5.1 Hz), 28.0, 24.8, 24.5, 23.9, 22.8, 22.7, 21.0, 20.6, 19.8, 19.7, 19.6, 12.8, 11.9, 11.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ -105.75, -105.85, -108.25, -109.24, -110.71, -111.71; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{48}H_{63}F_2N_2O_4$ 769.4750; Found 769.4747.

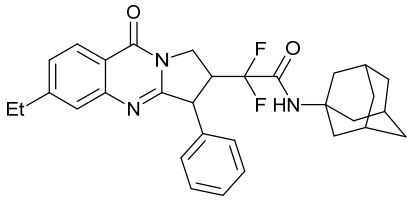


ethyl 2-(9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetate (**3aaa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 4/1) gave white solid (46%, 32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.0 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 7.47 (t, J = 7.1 Hz, 1H), 7.42-7.32 (m, 3H), 7.25 (t, J = 7.4 Hz, 2H), 4.69-4.64 (m, 1H), 4.18-4.08 (m, 3H), 3.87-3.81 (m, 1H), 3.00-2.90 (m, 1H), 2.74-2.68 (m, 1H), 2.61-2.55 (m, 1H), 1.24 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 160.8, 159.6, 149.2, 137.5, 134.2, 129.1, 128.6, 127.9, 127.5, 126.6, 126.4, 120.8, 63.0, 55.8, 49.7, 40.5, 36.5, 14.2; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{21}N_2O_3$ 349.1547; Found 349.1545.

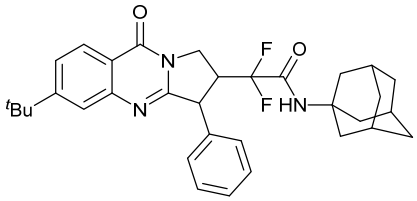


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(6-methyl-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ba**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (80%, 80.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz, 1H), 7.42 (s, 1H), 7.36-7.26 (m, 4H), 7.18 (d, J = 7.5 Hz, 2H), 6.11 (s, 1H), 4.64 (d, J = 4.5 Hz, 1H), 4.44-4.36 (m, 2H), 3.52-3.43 (m, 1H), 2.44 (s, 3H), 2.08 (s, 3H), 1.99 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 28.1 Hz), 158.9, 149.4, 145.4, 138.7, 129.2,

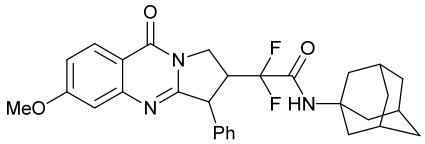
128.3, 127.9, 127.6, 127.2, 126.1, 118.1, 116.8 (t, $J_{C\text{-}F}$ = 259.5 Hz), 53.1, 50.4 (t, $J_{C\text{-}F}$ = 3.1 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.3 Hz), 44.8 (t, $J_{C\text{-}F}$ = 3.8 Hz), 41.0, 36.0, 29.3, 21.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.83, -110.75, -111.20, -112.12; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_2$ 504.2457; Found 504.2465.



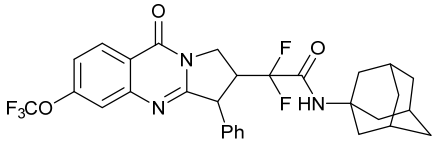
N-((3s,5s,7s)-adamantan-1-yl)-2-(6-ethyl-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3ca**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave yellow solid (85%, 87.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.2 Hz, 1H), 7.44 (s, 1H), 7.35-7.25 (m, 4H), 7.17 (d, *J* = 7.1 Hz, 2H), 6.15 (s, 1H), 4.63 (d, *J* = 4.6 Hz, 1H), 4.44-4.34 (m, 2H), 3.53-3.42 (m, 1H), 2.72 (q, *J* = 7.5 Hz, 2H), 2.08 (s, 3H), 1.98 (s, 6H), 1.66 (s, 6H), 1.24 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 26.9 Hz), 160.6, 158.9, 151.5, 149.5, 138.8, 129.2, 127.9, 127.6, 127.3, 126.2, 125.9, 118.3, 116.8 (t, $J_{C\text{-}F}$ = 259.7 Hz), 53.1, 50.2 (t, $J_{C\text{-}F}$ = 3.0 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.0 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.5 Hz), 40.9, 36.0, 29.3, 29.0, 14.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.82, -110.74, -111.34, -112.26; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{34}F_2N_3O_2$ 518.2614; Found 518.2612.



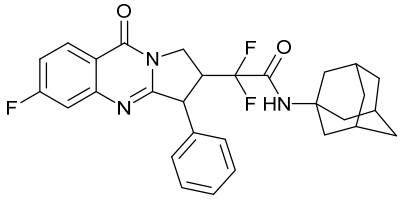
N-((3s,5s,7s)-adamantan-1-yl)-2-(6-(tert-butyl)-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3da**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (76%, 82.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.64 (s, 1H), 7.52 (d, *J* = 6.0 Hz, 1H), 7.35-7.27 (m, 3H), 7.17 (d, *J* = 7.2 Hz, 2H), 6.13 (s, 1H), 4.64 (d, *J* = 3.5 Hz, 1H), 4.41 (s, 2H), 3.55-3.37 (m, 1H), 2.08 (s, 3H), 1.98 (s, 6H), 1.66 (s, 6H), 1.33 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 27.7 Hz), 158.9, 158.4, 149.3, 138.8, 129.2, 127.9, 127.6, 125.9, 124.9, 123.7, 117.9, 116.8 (t, $J_{C\text{-}F}$ = 259.6 Hz), 53.1, 50.3, 45.3 (t, $J_{C\text{-}F}$ = 23.5 Hz), 44.8 (t, $J_{C\text{-}F}$ = 3.7 Hz), 40.9, 36.0, 35.4, 31.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.69, -110.60, -111.57, -112.49; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{38}F_2N_3O_2$ 546.2927; Found 546.2921.



N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(6-methoxy-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ea**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (79%, 82.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.14 (m, 1H), 7.35-7.32 (m, 2H), 7.29-7.27 (m, 1H), 7.18 (d, J = 7.1 Hz, 2H), 7.00-6.98 (m, 2H), 6.23 (s, 1H), 4.64 (d, J = 4.9 Hz, 1H), 4.44-4.32 (m, 2H), 3.81 (s, 3H), 3.53-3.41 (m, 1H), 2.08 (s, 3H), 1.99 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 161.1 (t, $J_{C\text{-}F}$ = 27.1 Hz), 160.2, 159.7, 151.6, 138.7, 129.2, 127.9, 127.7, 116.81, 116.80 (t, $J_{C\text{-}F}$ = 260.8 Hz), 113.9, 108.1, 55.6, 53.1, 50.3 (t, $J_{C\text{-}F}$ = 3.1 Hz), 45.4 (t, $J_{C\text{-}F}$ = 23.2 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.1 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.88, -110.80, -111.10, -112.02; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_3$ 520.2406; Found 520.2411.

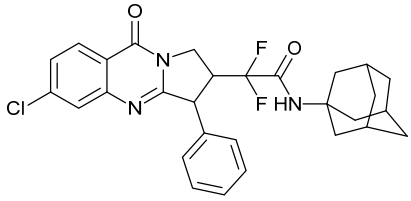


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(9-oxo-3-phenyl-6-(trifluoromethoxy)-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3fa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (68%, 79.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 1H), 7.47 (s, 1H), 7.39-7.26 (m, 4H), 7.20 (d, J = 7.2 Hz, 2H), 6.13 (s, 1H), 4.67 (d, J = 4.9 Hz, 1H), 4.49-4.37 (m, 2H), 3.58-3.46 (m, 1H), 2.09 (s, 3H), 1.99 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0 (t, $J_{C\text{-}F}$ = 26.9 Hz), 160.6, 159.8, 153.5, 150.9, 138.3, 129.3, 128.6, 128.1, 127.7, 121.6 (q, $J_{C\text{-}F}$ = 260.4 Hz), 119.2, 118.8, 117.9 (t, $J_{C\text{-}F}$ = 257.8 Hz), 117.7, 53.3, 50.4 (t, $J_{C\text{-}F}$ = 3.4 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.2 Hz), 45.1 (t, $J_{C\text{-}F}$ = 4.8 Hz), 41.0, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -57.6, -109.56, -110.48, -110.81, -111.73; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{29}F_5N_3O_3$: 574.2124; Found: 574.2122.

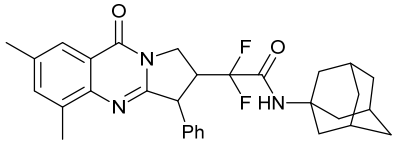


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(6-fluoro-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ga**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (62%, 62.9 mg); ^{1}H

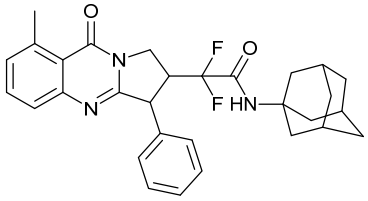
NMR (400 MHz, $CDCl_3$) δ 8.19 (t, J = 6.6 Hz, 1H), 7.28-7.16 (m, 4H), 7.12-7.04 (m, 3H), 6.09 (s, 1H), 4.57 (d, J = 4.9 Hz, 1H), 4.38-4.27 (m, 2H), 3.48-3.36 (m, 1H), 2.00 (s, 3H), 1.90 (s, 6H), 1.59 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4 (d, $J_{C\text{-}F}$ = 255.2 Hz), 161.1 (t, $J_{C\text{-}F}$ = 26.9 Hz), 160.4, 151.5 (d, $J_{C\text{-}F}$ = 13.2 Hz), 138.4, 129.3, 128.9 (d, $J_{C\text{-}F}$ = 10.6 Hz), 128.1, 127.7, 117.2 (d, $J_{C\text{-}F}$ = 1.4 Hz), 116.7 (t, $J_{C\text{-}F}$ = 259.3 Hz), 115.4 (d, $J_{C\text{-}F}$ = 23.6 Hz), 112.8 (d, $J_{C\text{-}F}$ = 22.3 Hz), 53.1, 50.3 (t, $J_{C\text{-}F}$ = 3.0 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.3 Hz), 45.0 (t, $J_{C\text{-}F}$ = 5.3 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -103.23, -109.62, -110.54, -110.82, -111.74; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}F_3N_3O_2$ 508.2206; Found 508.2207.



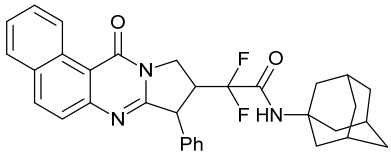
N-((3s,5s,7s)-adamantan-1-yl)-2-(6-chloro-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3ha**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (58%, 60.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.6 Hz, 1H), 7.61 (t, J = 1.9 Hz, 1H), 7.40-7.28 (m, 4H), 7.18 (d, J = 7.0 Hz, 2H), 6.11 (s, 1H), 4.65 (d, J = 5.0 Hz, 1H), 4.46-4.34 (m, 2H), 3.56-3.44 (m, 1H), 2.09 (s, 3H), 1.98 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 26.9 Hz), 160.3, 160.0, 150.3, 140.6, 138.4, 129.3, 128.1, 127.7, 127.6, 127.3, 127.1, 119.0, 116.7 (t, $J_{C\text{-}F}$ = 259.7 Hz), 53.2, 50.3 (t, $J_{C\text{-}F}$ = 3.2 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.2 Hz), 45.0 (t, $J_{C\text{-}F}$ = 4.5 Hz), 41.0, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.59, -110.52, -110.75, -111.67; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}ClF_2N_3O_2$ 524.1911; Found 524.1917.



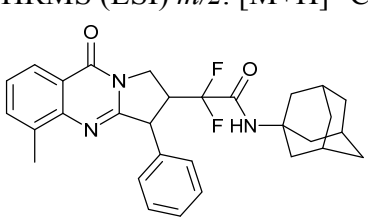
N-((3s,5s,7s)-adamantan-1-yl)-2-(5,7-dimethyl-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3ia**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (74%, 76.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.37-7.26 (m, 4H), 7.20 (d, J = 7.4 Hz, 2H), 6.16 (s, 1H), 4.67 (d, J = 4.3 Hz, 1H), 4.38 (d, J = 6.5 Hz, 1H), 3.57-3.45 (m, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.09 (s, 3H), 2.00 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3 (t, $J_{C\text{-}F}$ = 26.9 Hz), 161.1, 156.5, 146.0, 139.1, 136.5, 136.2, 135.7, 128.9, 127.7, 127.6, 123.3, 120.2, 116.9 (t, $J_{C\text{-}F}$ = 259.6 Hz), 53.1, 49.8 (t, $J_{C\text{-}F}$ = 3.0 Hz), 45.0 (t, $J_{C\text{-}F}$ = 23.1 Hz), 44.7 (t, $J_{C\text{-}F}$ = 4.5 Hz), 41.0, 36.1, 29.3, 21.2, 17.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ -110.01, -110.93, -110.98, -111.90; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{34}F_2N_3O_2$ 518.2614; Found 518.2616.



N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(8-methyl-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ja**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (63%, 63.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, J = 7.8 Hz, 1H), 7.35 (d, J = 7.9 Hz, 1H), 7.25-7.16 (m, 3H), 7.09 (d, J = 7.2 Hz, 3H), 6.12 (s, 1H), 4.53 (d, J = 4.4 Hz, 1H), 4.27-4.25 (m, 2H), 3.42-3.33 (m, 1H), 2.79 (s, 3H), 1.98 (s, 3H), 1.89 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 161.2 (t, $J_{C\text{-}F}$ = 27.1 Hz), 158.5, 150.9, 140.9, 138.8, 133.4, 129.3, 129.2, 127.9, 127.6, 125.6, 118.9, 116.9 (t, $J_{C\text{-}F}$ = 259.6 Hz), 53.1, 50.1 (t, $J_{C\text{-}F}$ = 3.0 Hz), 45.2 (t, $J_{C\text{-}F}$ = 22.8 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.6 Hz), 40.9, 36.0, 29.3, 22.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.94, -110.96; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_2$ 504.2457; Found 504.2450.

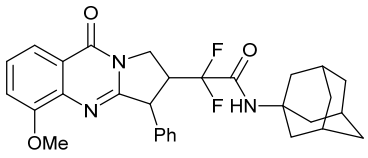


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(12-oxo-8-phenyl-8,9,10,12-tetrahydrobenzo[f]pyrrolo[2,1-b]quinazolin-9-yl)acetamide (**3ka**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (42%, 45.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.07 (d, J = 8.9 Hz, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.77-7.73 (m, 1H), 7.66-7.59 (m, 2H), 7.38-7.28 (m, 3H), 7.21 (d, J = 8.2 Hz, 2H), 6.14 (s, 1H), 4.77 (d, J = 4.6 Hz, 1H), 4.59-4.51 (m, 2H), 3.62-3.47 (m, 1H), 2.09 (s, 3H), 2.01 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (t, $J_{C\text{-}F}$ = 27.2 Hz), 160.9, 159.5, 151.8, 138.7, 135.7, 131.8, 130.9, 129.3, 128.7, 128.3, 128.0, 127.7, 126.9, 126.7, 126.1, 116.9 (t, $J_{C\text{-}F}$ = 259.8 Hz), 114.0, 53.2, 50.5 (t, $J_{C\text{-}F}$ = 3.0 Hz), 45.6 (t, $J_{C\text{-}F}$ = 4.5 Hz), 45.3 (t, $J_{C\text{-}F}$ = 23.1 Hz), 41.0, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.94, -110.86, -111.16, -112.08; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{32}F_2N_3O_2$ 540.2457; Found 540.2447.

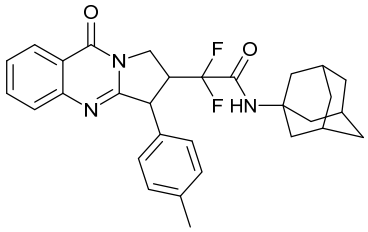


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(5-methyl-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3la**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (66%, 66.4 mg); ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.5 Hz, 1H), 7.54 (d, J = 7.2 Hz, 1H), 7.36-7.28 (m, 4H), 7.23-7.20 (m, 2H), 6.15 (s, 1H), 4.69 (d, J = 4.4 Hz, 1H), 4.39 (d, J = 6.5 Hz, 2H), 3.58-3.46 (m, 1H), 2.48 (s, 3H), 2.09 (s, 3H), 2.00 (s, 6H), 1.68 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (t, J_{C-F} = 27.1 Hz), 161.1, 157.3, 147.9, 138.9, 136.0, 134.9, 129.0, 127.7, 127.6, 126.2, 123.9, 120.4, 116.9 (t, J_{C-F} = 261.9 Hz), 53.1, 49.9 (t, J_{C-F} = 3.1 Hz), 44.9 (t, J_{C-F} = 23.2 Hz), 44.7 (t, J_{C-F} = 4.6 Hz), 42.0, 36.1, 29.3, 17.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.98, -110.90, -111.38, -112.30; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_2$ 504.2457; Found 504.2460.

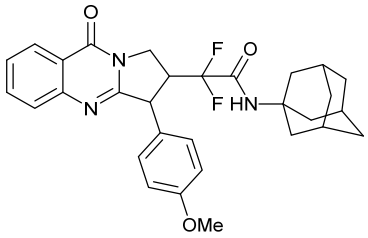


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(5-methoxy-9-oxo-3-phenyl-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3ma**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave white solid (71%, 73.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.9 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.33-7.25 (m, 3H), 7.19-7.13 (m, 3H), 6.17 (s, 1H), 4.72 (d, J = 1.8 Hz, 1H), 4.52-4.48 (m, 1H), 4.36-4.31 (m, 1H), 3.94 (s, 3H), 3.52-3.42 (m, 1H), 2.11 (s, 3H), 2.03 (s, 6H), 1.69 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (t, J_{C-F} = 26.8 Hz), 160.5, 157.9, 154.4, 139.8, 138.9, 129.2, 127.7, 127.2, 127.0, 121.7, 117.6, 117.0 (t, J_{C-F} = 259.9 Hz), 114.3, 56.2, 53.1, 50.2 (t, J_{C-F} = 3.5 Hz), 45.1 (t, J_{C-F} = 22.8 Hz), 44.6 (t, J_{C-F} = 4.7 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -108.99, -109.92, -113.68, -114.61; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_3$ 520.2406; Found 520.2408.

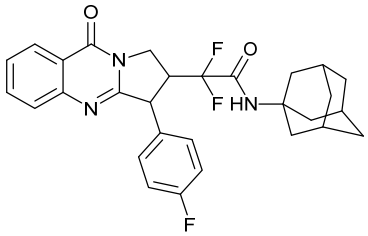


N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(9-oxo-3-(p-tolyl)-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3na**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (88%, 88.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 7.4 Hz, 1H), 7.68 (t, J = 7.7 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.14 (s, 1H), 4.61 (d, J = 4.7 Hz, 1H), 4.45-4.36 (m, 2H), 3.51-3.42 (m, 1H), 2.31 (s, 3H), 2.07 (s, 3H), 1.98 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, J_{C-F} = 26.8 Hz), 159.1, 149.3, 137.7, 135.6, 134.3, 129.9, 127.5, 127.4, 126.6, 126.3, 120.5, 116.8 (t, J_{C-F} = 259.6 Hz), 53.1, 49.8, 45.4 (t, J_{C-F} = 23.0 Hz), 44.9 (t, J_{C-F} = 5.1 Hz), 40.9, 36.0, 29.3, 21.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.67, -110.59, -111.30, -112.22; HRMS (ESI)

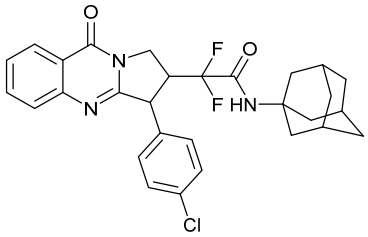
m/z: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_2$ 504.2457; Found 504.2454.



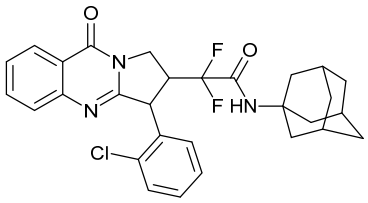
N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(3-(4-methoxyphenyl)-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3oa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 2/1) gave yellow solid (77%, 77.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 8.3 Hz, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.09 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.15 (s, 1H), 4.58 (d, J = 5.1 Hz, 1H), 4.44-4.32 (m, 2H), 3.74 (s, 3H), 3.50-3.38 (m, 1H), 2.06 (s, 3H), 1.97 (s, 6H), 1.65 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, $J_{C\text{-}F}$ = 26.9 Hz), 160.6, 159.2, 159.1, 149.3, 134.3, 130.6, 128.8, 127.4, 126.6, 126.3, 120.5, 116.8 (t, $J_{C\text{-}F}$ = 259.7 Hz), 114.6, 55.3, 53.1, 49.5 (t, $J_{C\text{-}F}$ = 2.6 Hz), 45.4 (t, $J_{C\text{-}F}$ = 22.9 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.7 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.51, -110.43, -111.42, -112.34; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{32}F_2N_3O_3$ 520.2406; Found 520.2412.



N-((3s,5s,7s)-adamantan-1-yl)-2,2-difluoro-2-(3-(4-fluorophenyl)-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)acetamide (**3pa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (74%, 75.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (t, J = 8.0 Hz, 1H), 7.68-7.64 (m, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.9 Hz, 1H), 7.18-7.15 (m, 2H), 7.01 (t, J = 8.6 Hz, 2H), 6.17 (s, 1H), 4.63 (d, J = 5.4 Hz, 1H), 4.44-4.38 (m, 1H), 4.34-4.29 (m, 1H), 3.51-3.38 (m, 1H), 2.06 (s, 3H), 1.96 (s, 6H), 1.65 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3 (d, $J_{C\text{-}F}$ = 247.7 Hz), 161.0 (t, $J_{C\text{-}F}$ = 27.5 Hz), 160.5, 158.6, 149.1, 134.4, 129.5 (d, $J_{C\text{-}F}$ = 8.3 Hz), 127.4, 126.8, 126.3, 120.4, 116.7 (t, $J_{C\text{-}F}$ = 259.7 Hz), 116.1 (d, $J_{C\text{-}F}$ = 23.6 Hz), 112.8 (d, $J_{C\text{-}F}$ = 21.7 Hz), 53.1, 49.5 (t, $J_{C\text{-}F}$ = 3.1 Hz), 45.4 (t, $J_{C\text{-}F}$ = 22.9 Hz), 44.8 (t, $J_{C\text{-}F}$ = 4.5 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.67, -110.36, -111.10, -111.80, 114.04; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}F_3N_3O_2$ 508.2206; Found 508.2216.

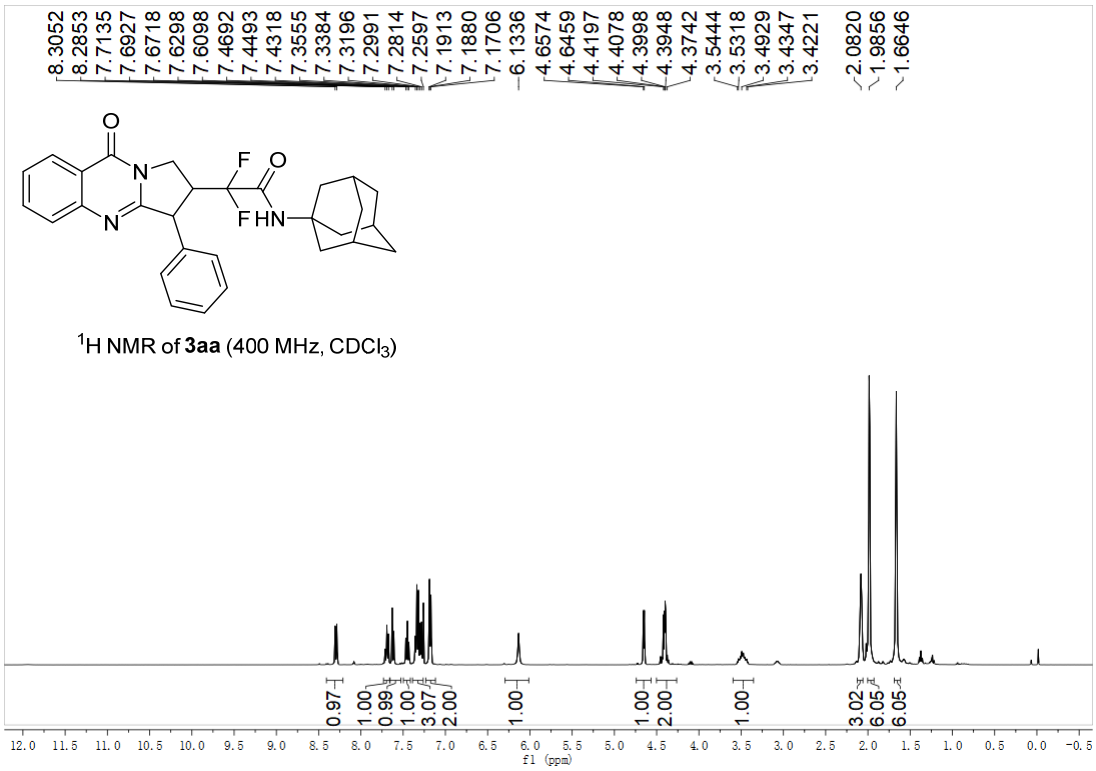


N-((3s,5s,7s)-adamantan-1-yl)-2-(3-(4-chlorophenyl)-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3qa**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (71%, 74.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 7.9 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 6.12 (s, 1H), 4.64 (d, J = 5.5 Hz, 1H), 4.45-4.39 (m, 1H), 4.35-4.31 (m, 1H), 3.50-3.40 (m, 1H), 2.08 (s, 3H), 1.97 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (t, J_{C-F} = 26.9 Hz), 160.6, 158.4, 149.1, 136.9, 134.4, 133.9, 129.4, 129.3, 127.4, 126.8, 126.4, 120.5, 116.6 (t, J_{C-F} = 259.9 Hz), 53.6, 49.6 (t, J_{C-F} = 3.5 Hz), 45.3 (t, J_{C-F} = 23.3 Hz), 44.8 (t, J_{C-F} = 4.7 Hz), 40.9, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -109.42, -110.34, -110.84, -111.76; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}ClF_2N_3O_2$ 524.1911; Found 524.1916.

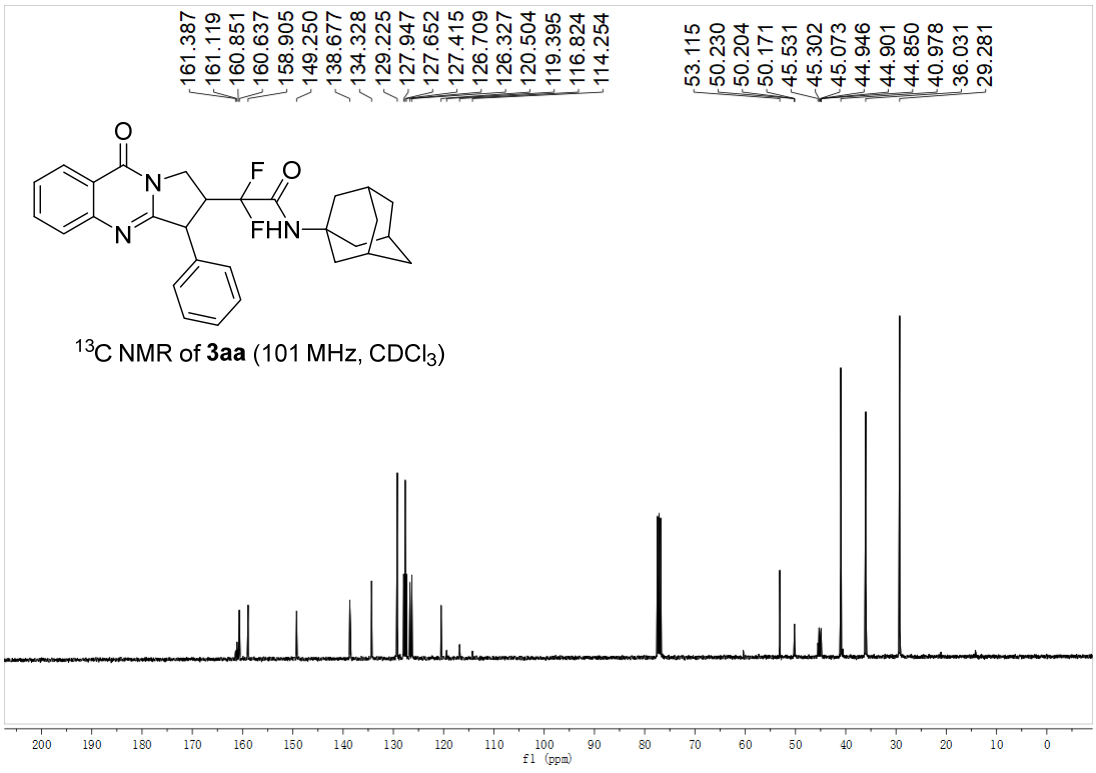


N-((3s,5s,7s)-adamantan-1-yl)-2-(3-(2-chlorophenyl)-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-2-yl)-2,2-difluoroacetamide (**3ra**). Flash column chromatography on silica gel (petroleum ether/ethyl acetate 3/1) gave white solid (50%, 52.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, J = 8.0, 1.2 Hz, 1H), 7.71-7.66 (m, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.47-7.43 (m, 1H), 7.41-7.39 (m, 2H), 7.31-7.22 (m, 3H), 6.11 (s, 1H), 5.03 (d, J = 7.2 Hz, 1H), 4.61-4.55 (m, 1H), 4.34-4.28 (m, 1H), 3.72-3.59 (m, 1H), 2.09 (s, 3H), 1.97 (s, 6H), 1.67 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1 (t, J_{C-F} = 27.1 Hz), 160.7, 158.3, 149.3, 135.9, 134.3, 133.6, 131.4, 130.5, 129.6, 127.5, 127.4, 126.6, 126.3, 120.5, 116.7 (t, J_{C-F} = 258.9 Hz), 53.1, 48.8 (t, J_{C-F} = 4.5 Hz), 45.4 (t, J_{C-F} = 5.4 Hz), 43.7 (t, J_{C-F} = 24.2 Hz), 41.0, 36.0, 29.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ -108.14, -109.06, -110.74, -111.66; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{29}ClF_2N_3O_2$ 524.1911; Found 524.1918.

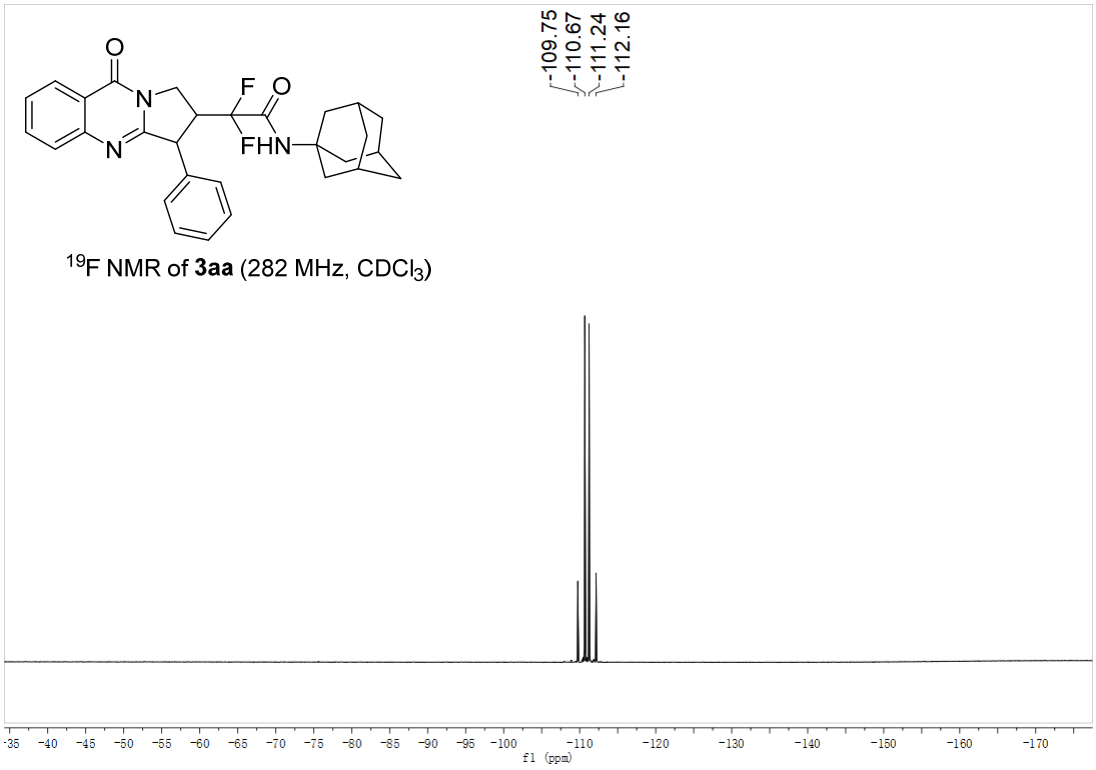
5. Copies of the ^{1}H NMR and ^{13}C NMR Spectra



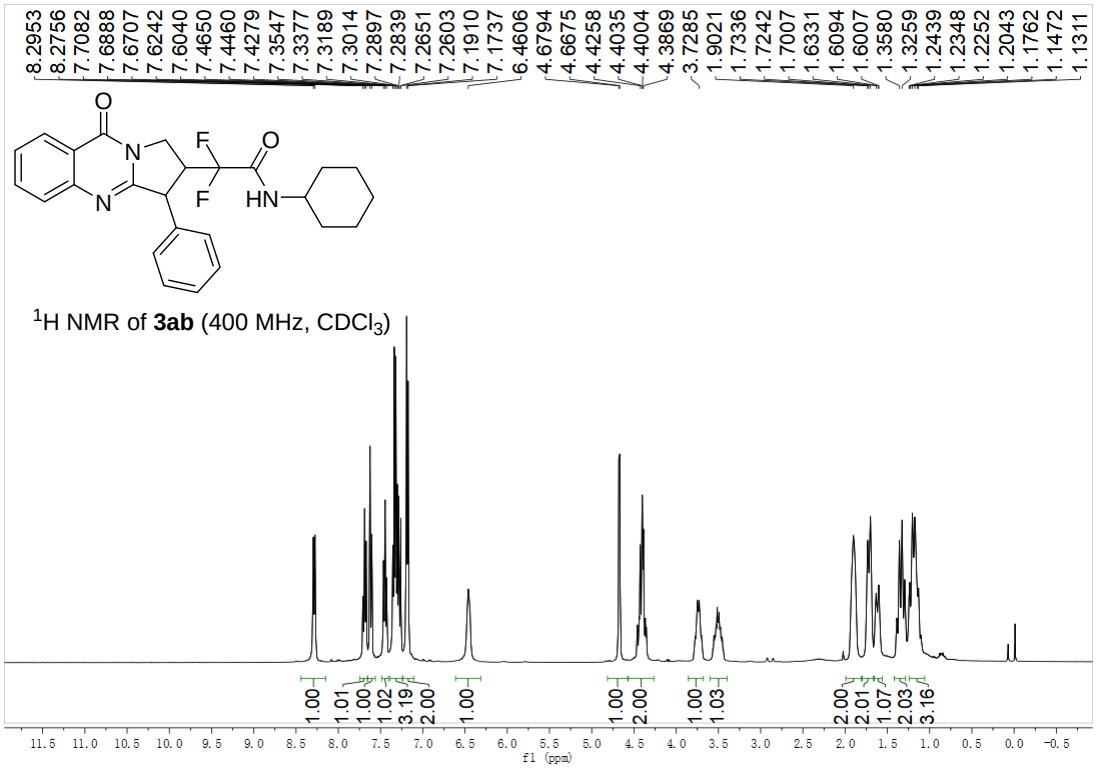
^{1}H NMR of **3aa** (400 MHz, $CDCl_3$)



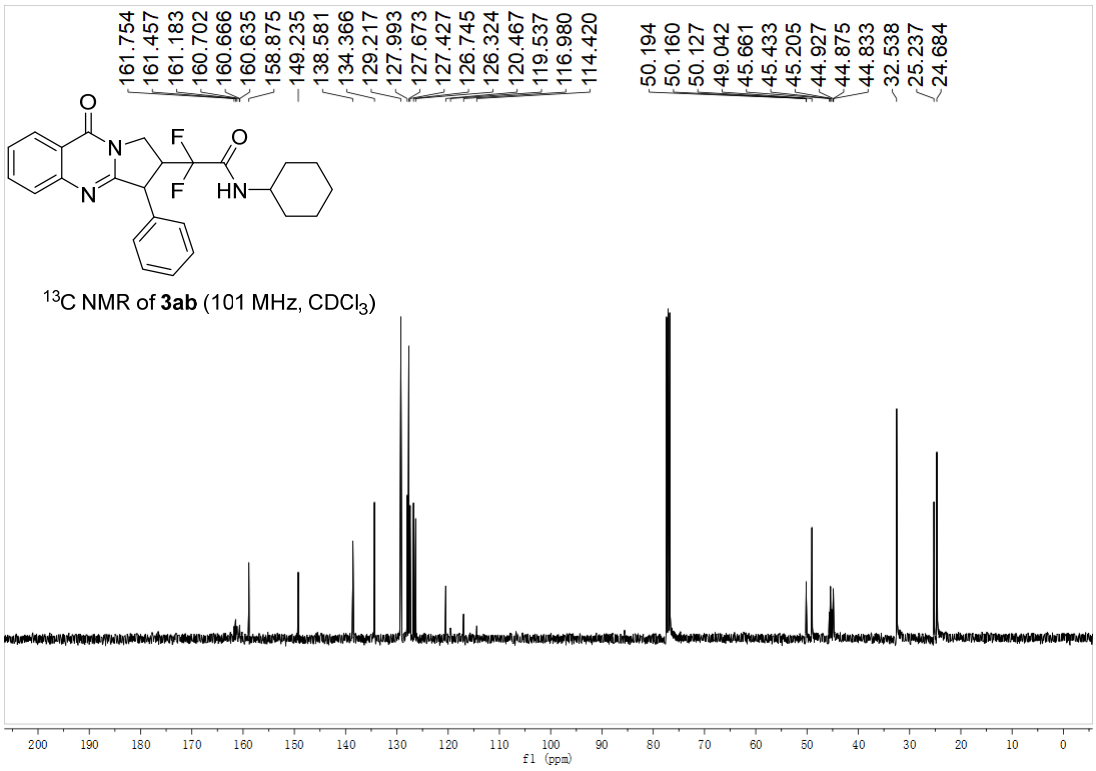
^{13}C NMR of **3aa** (101 MHz, $CDCl_3$)



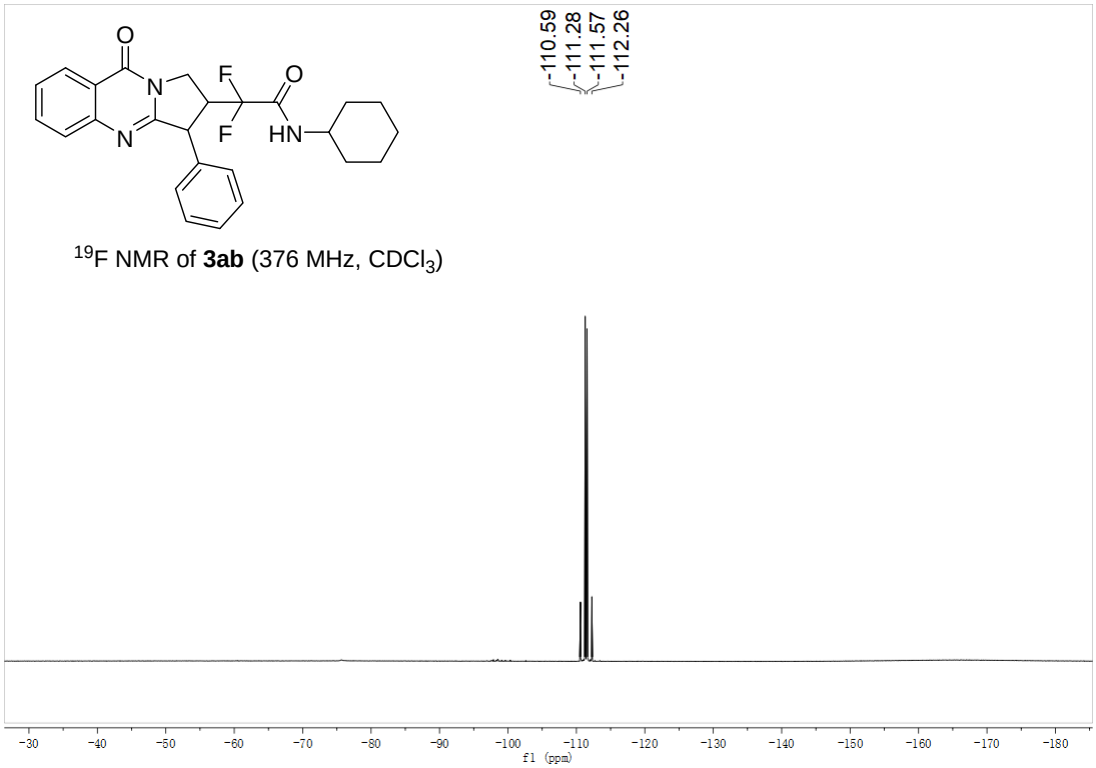
^{19}F NMR of **3aa** (282 MHz, $CDCl_3$)



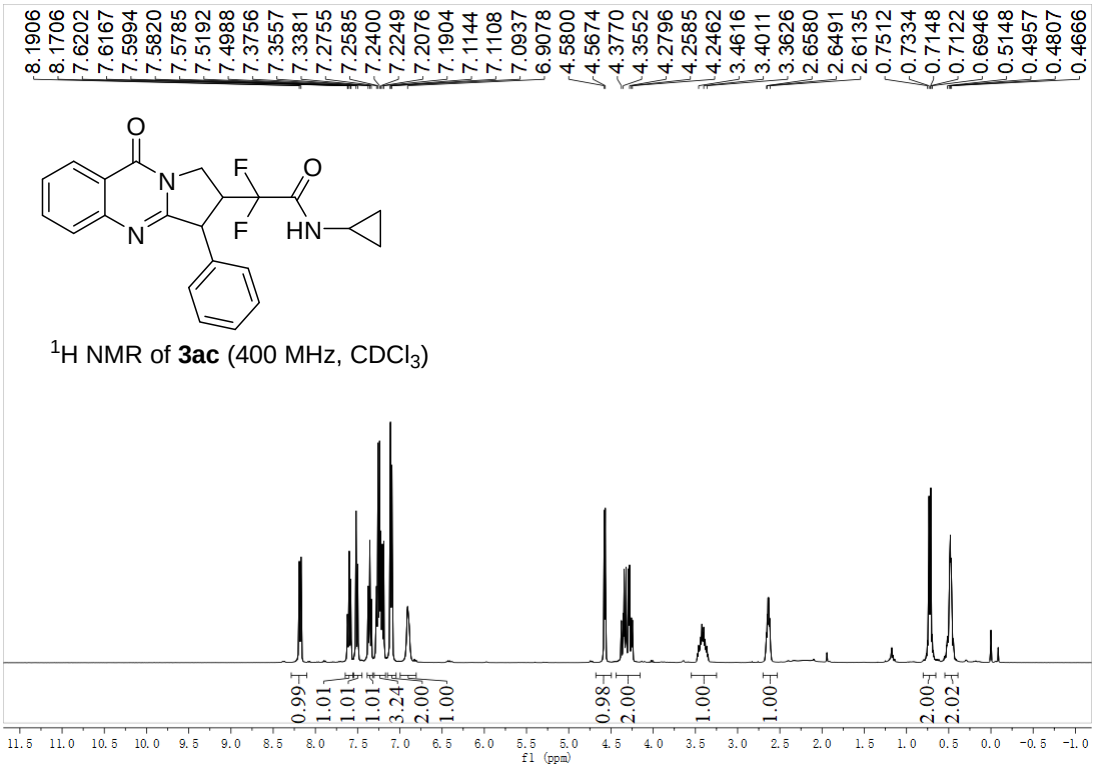
^{1}H NMR of **3ab** (400 MHz, $CDCl_3$)



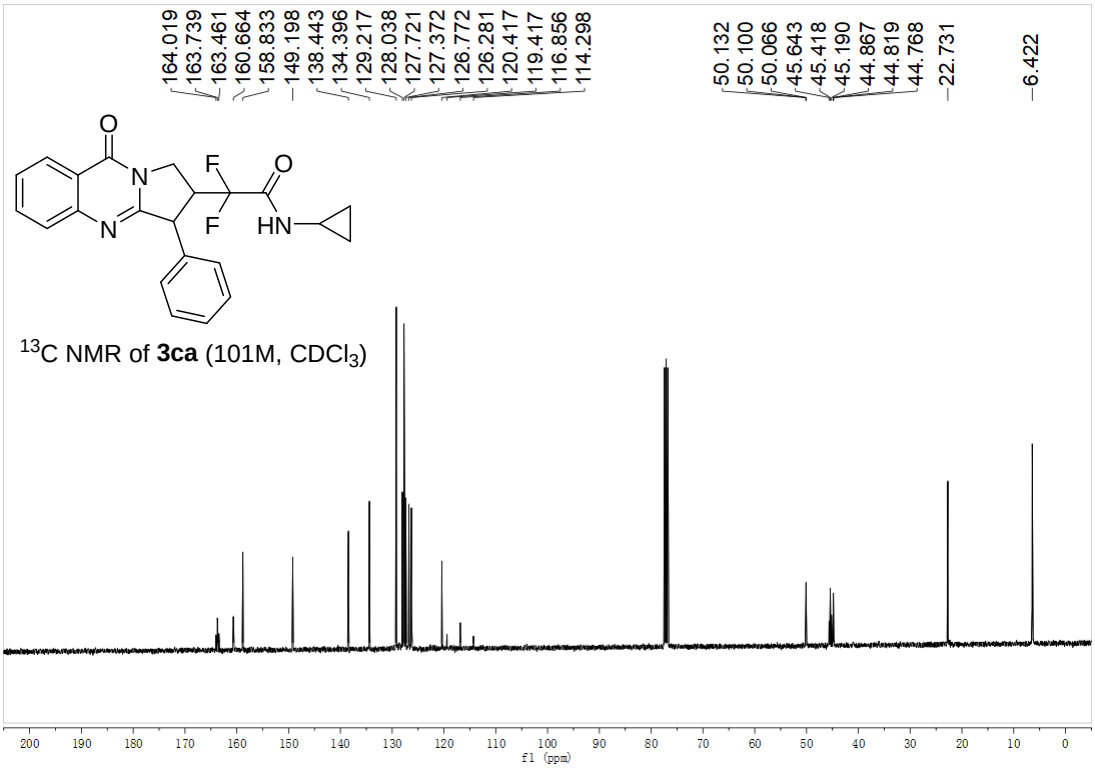
^{13}C NMR of **3ab** (101 MHz, $CDCl_3$)



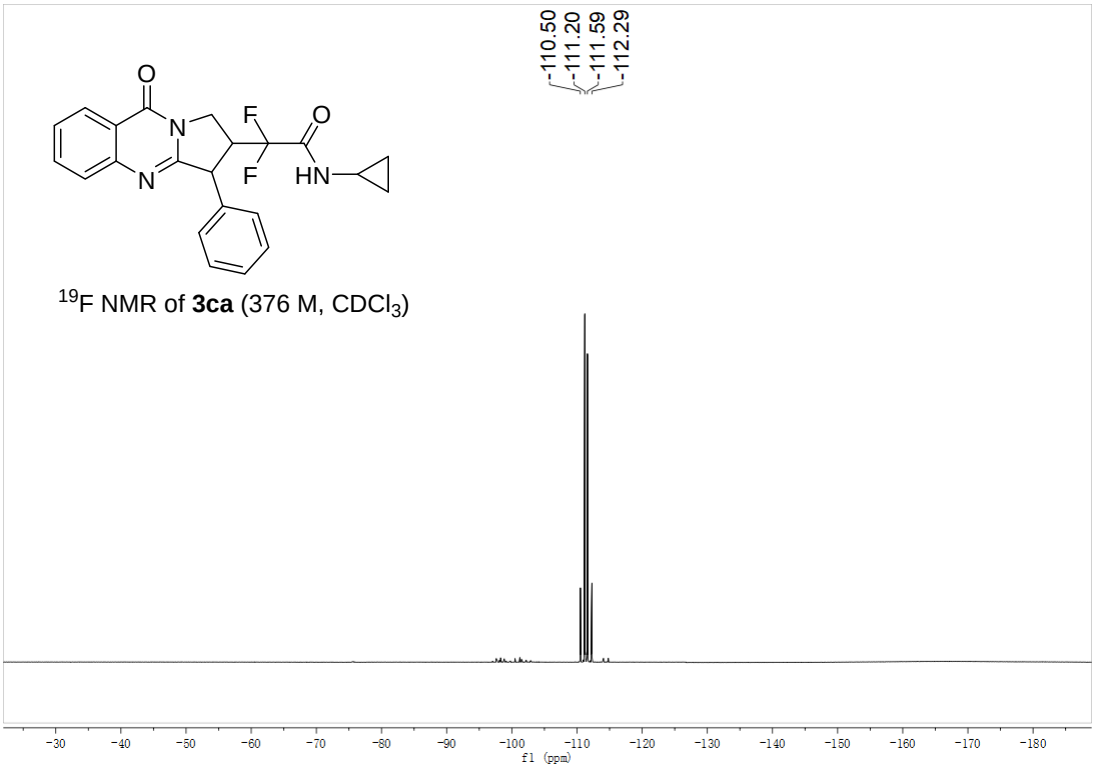
^{19}F NMR of **3ab** (376 MHz, $CDCl_3$)



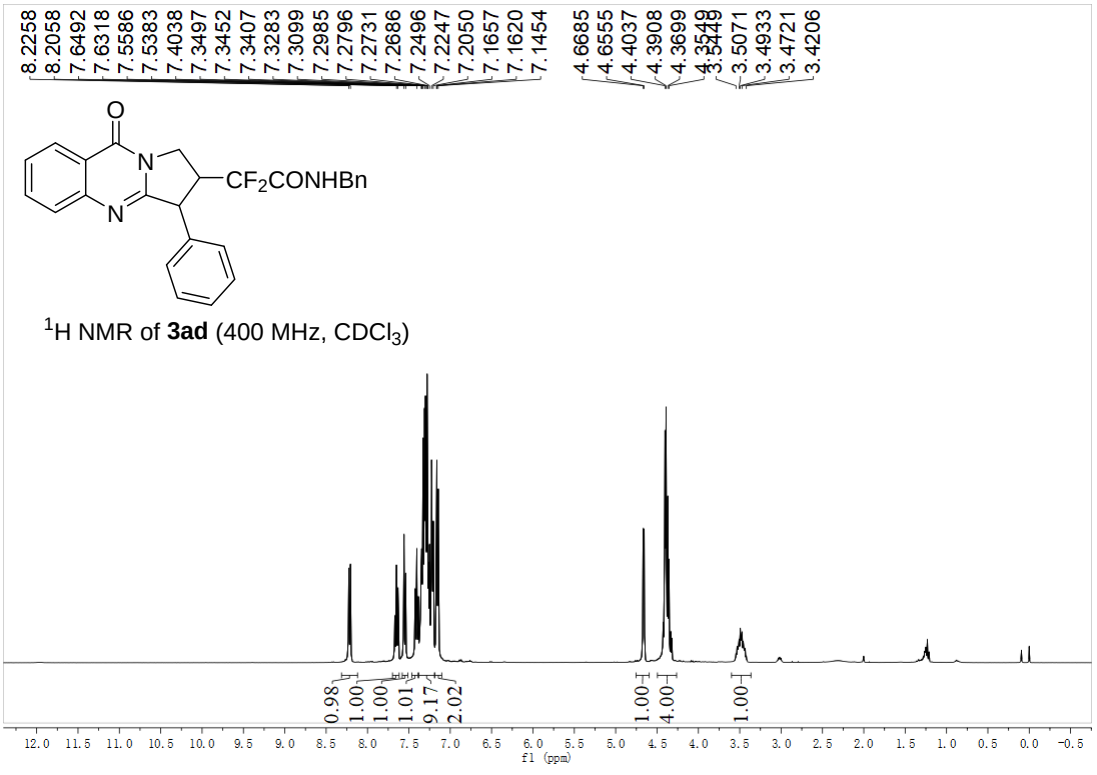
^{1}H NMR of **3ac** (400 MHz, $CDCl_3$)



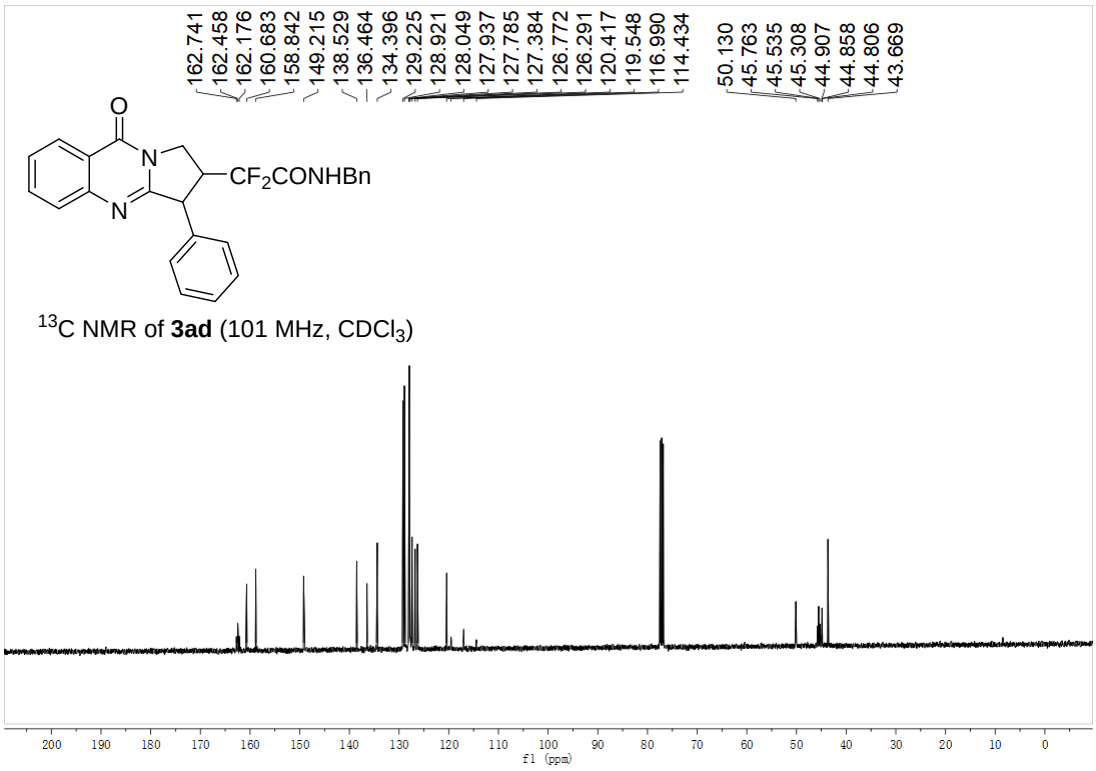
^{13}C NMR of **3ca** (101M, $CDCl_3$)



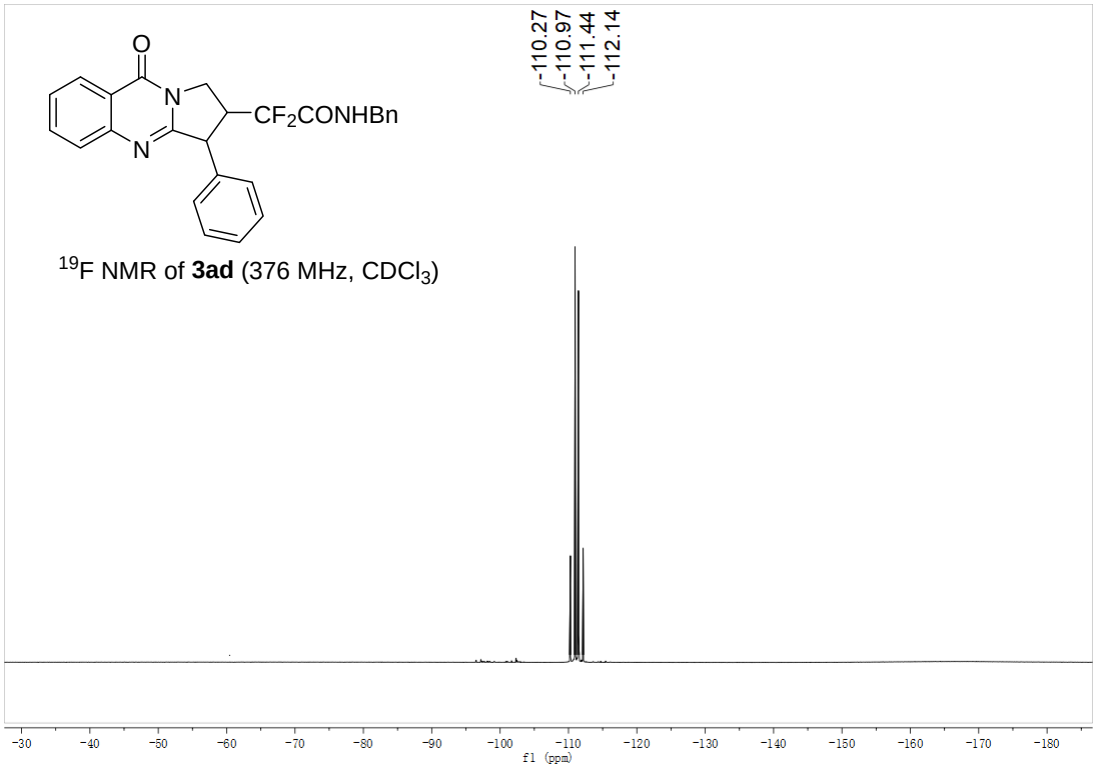
^{19}F NMR of **3ca** (376 M, $CDCl_3$)



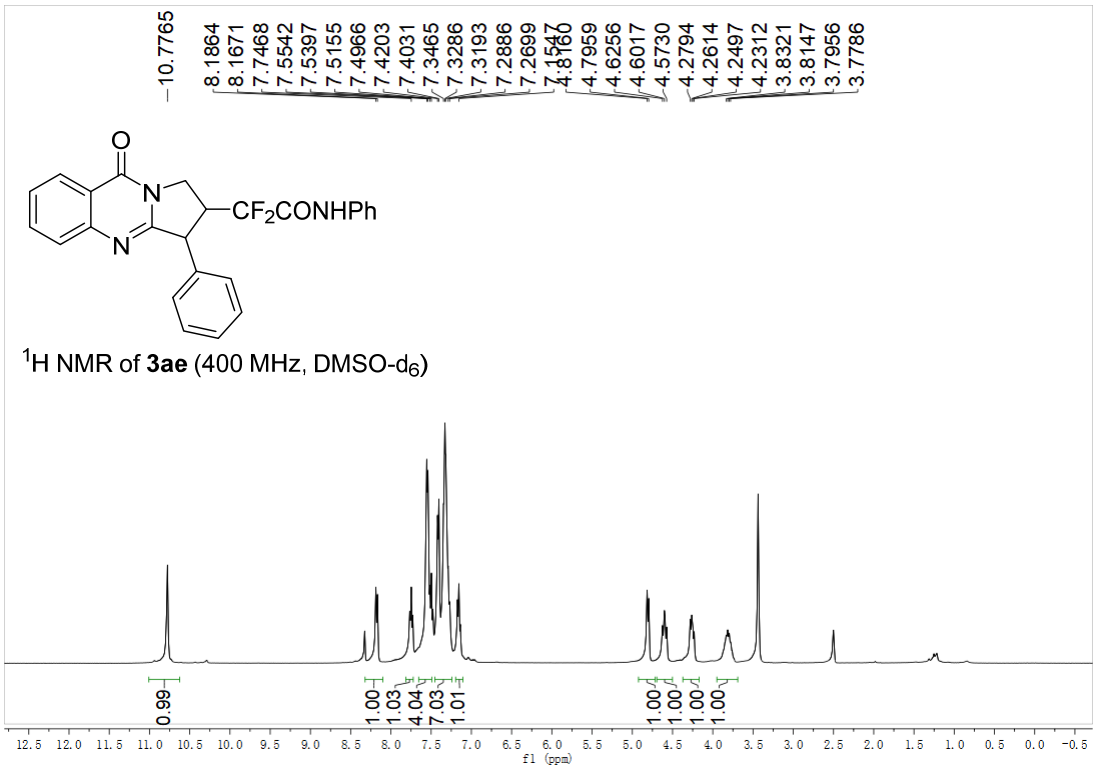
^{1}H NMR of **3ad** (400 MHz, $CDCl_3$)



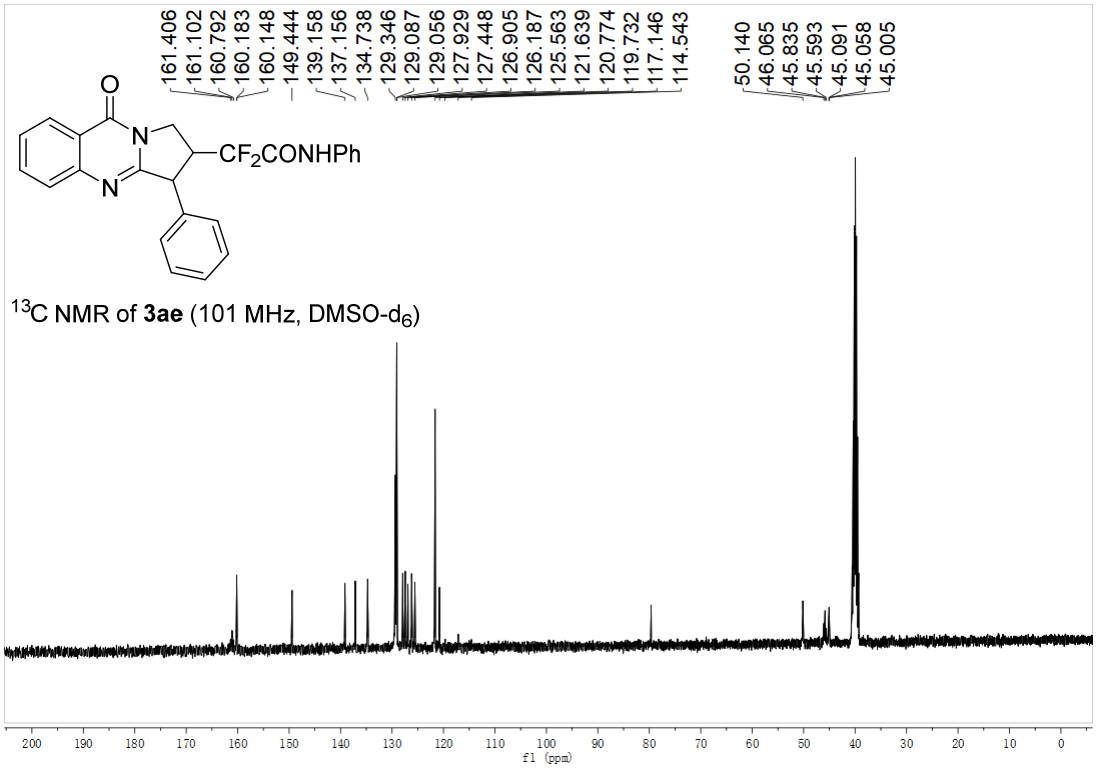
^{13}C NMR of **3ad** (101 MHz, $CDCl_3$)



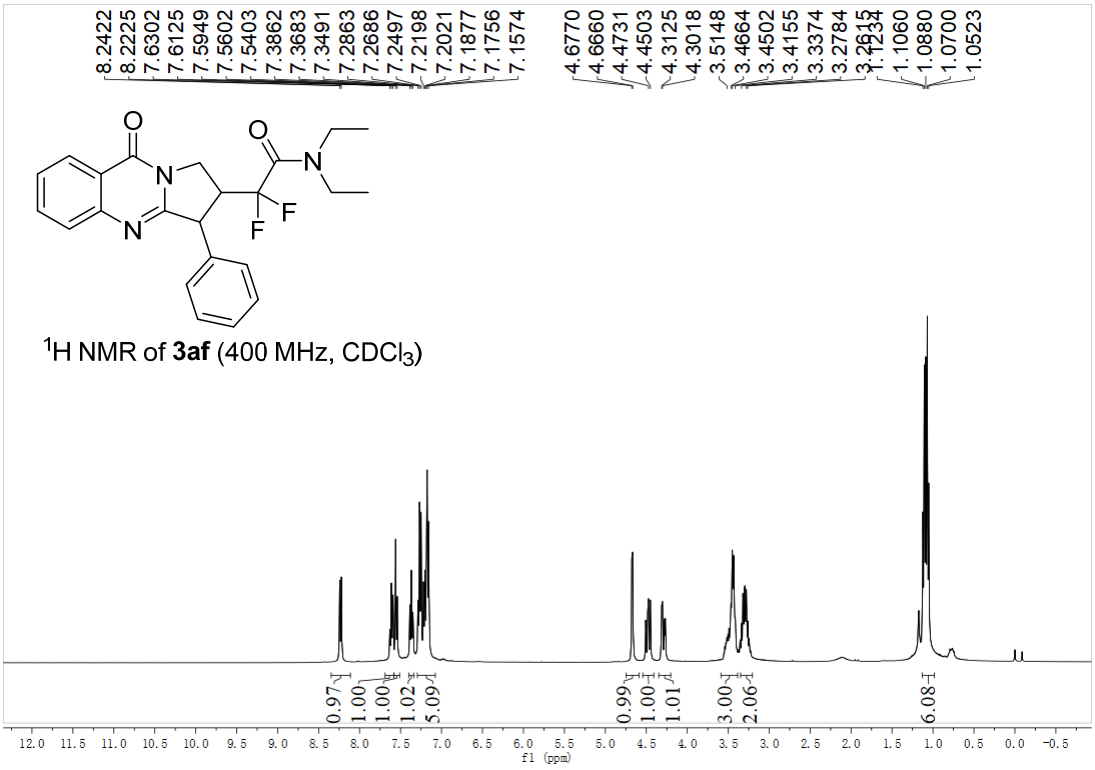
^{19}F NMR of **3ad** (376 MHz, $CDCl_3$)



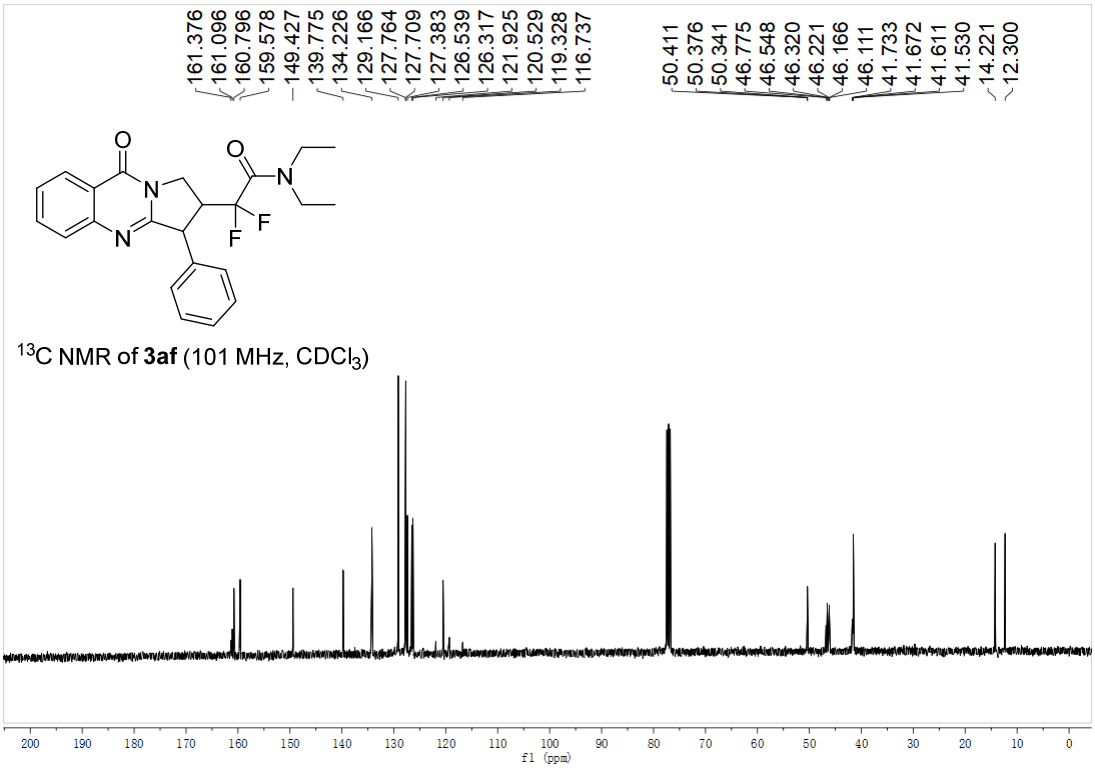
^{1}H NMR of **3ae** (400 MHz, DMSO-d_6)



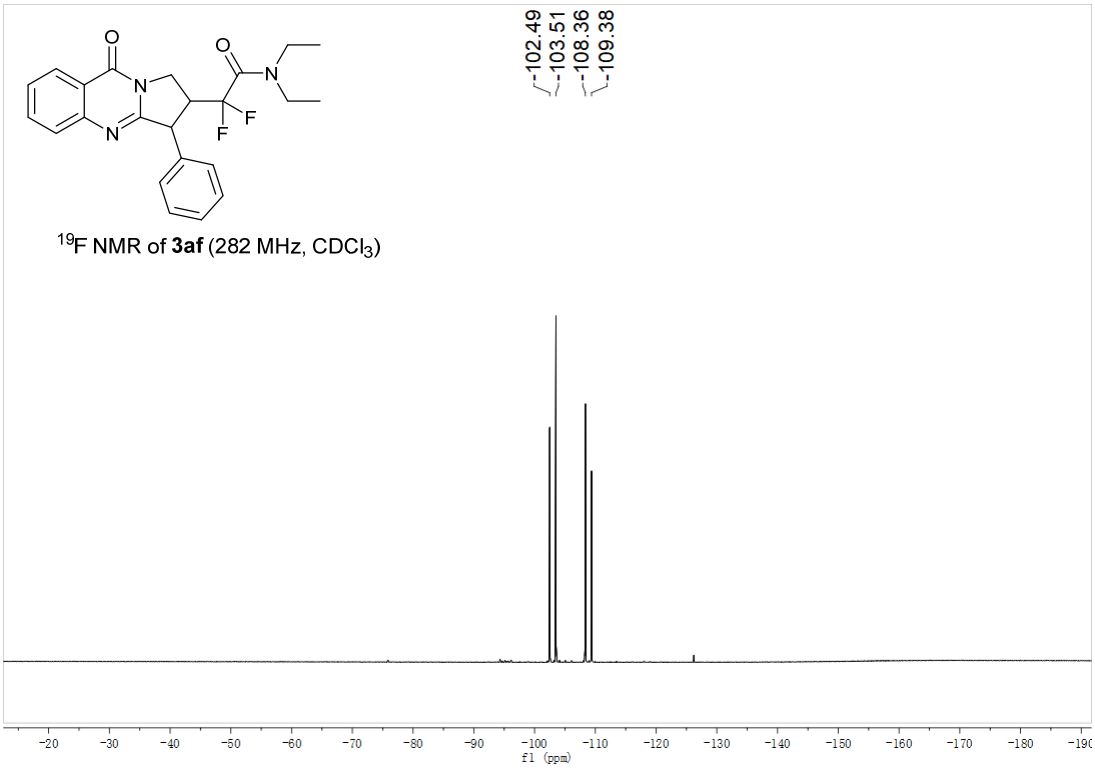
^{13}C NMR of **3ae** (101 MHz, DMSO-d_6)



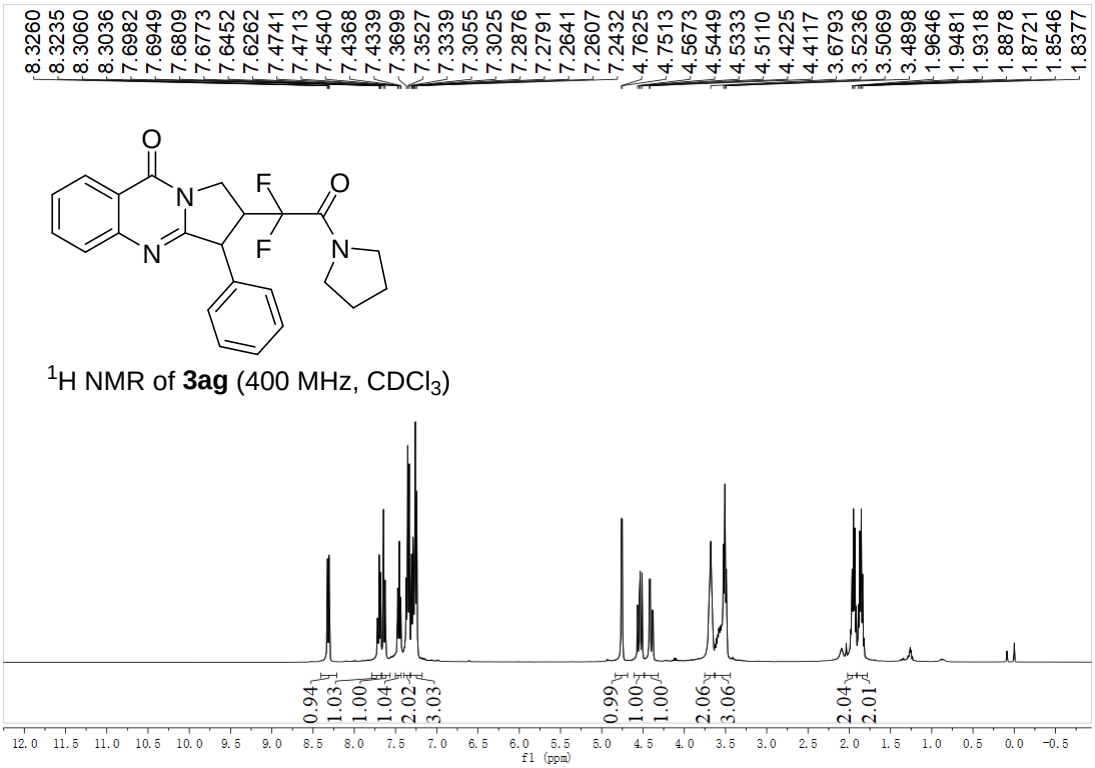
^{1}H NMR of **3af** (400 MHz, $CDCl_3$)



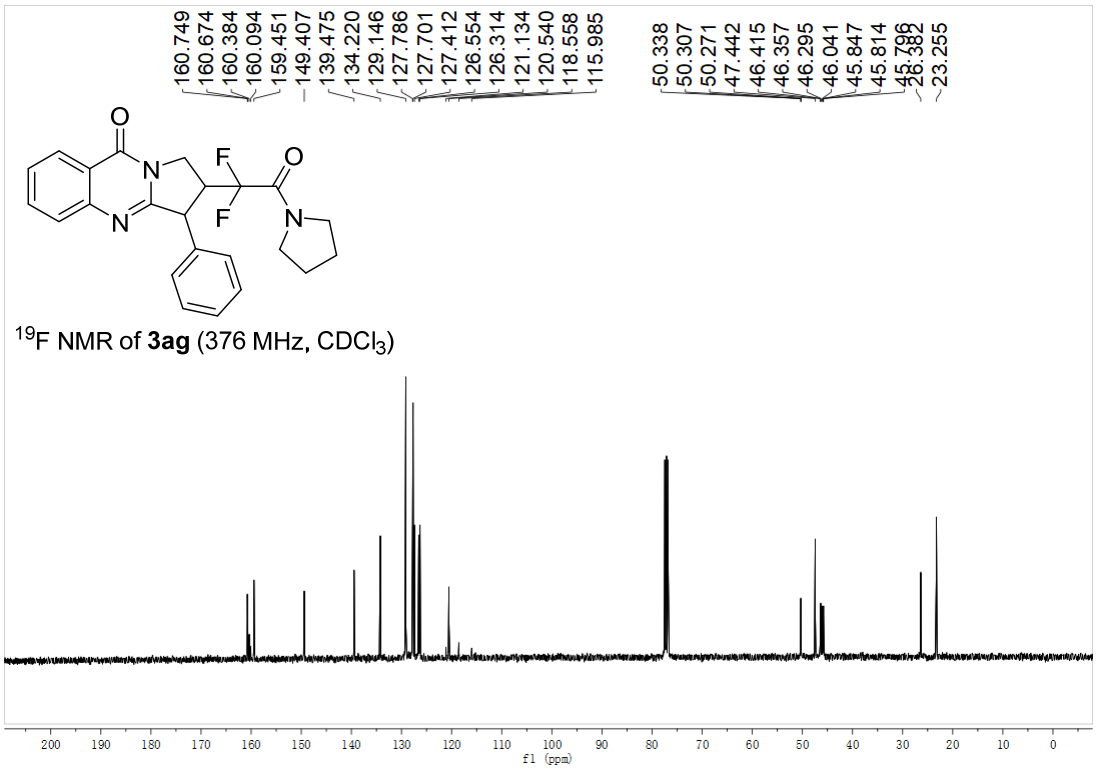
^{13}C NMR of **3af** (101 MHz, $CDCl_3$)



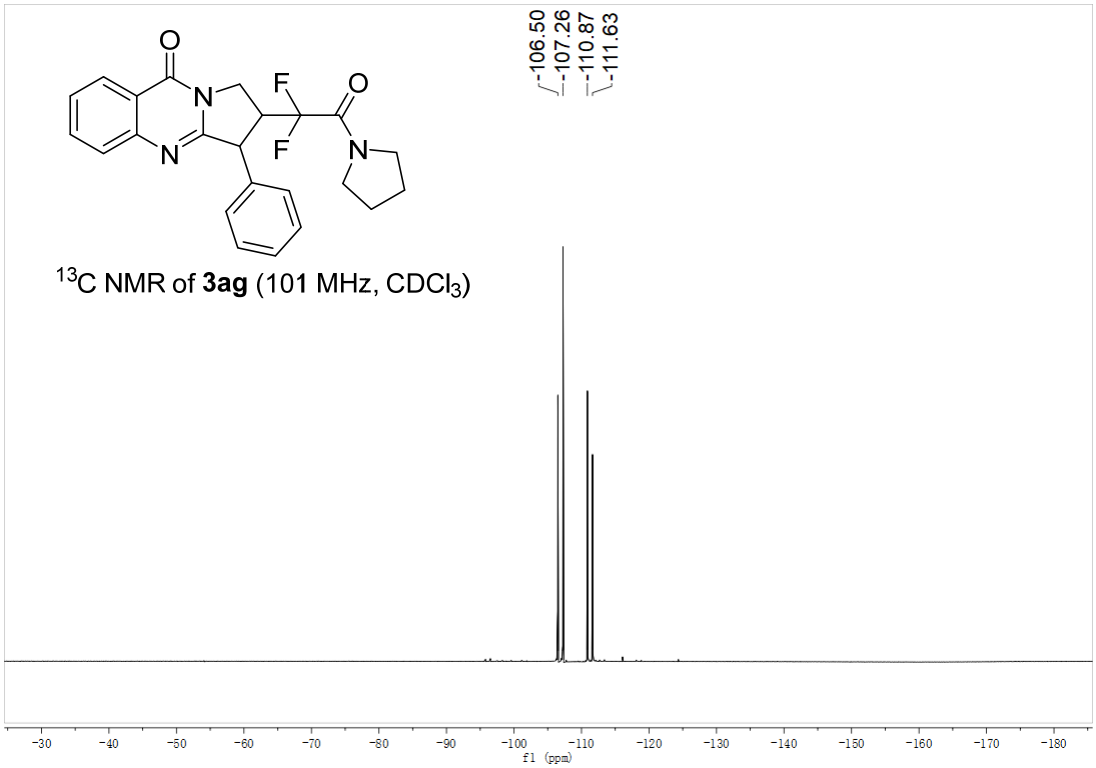
^{19}F NMR of **3af** (282 MHz, $CDCl_3$)



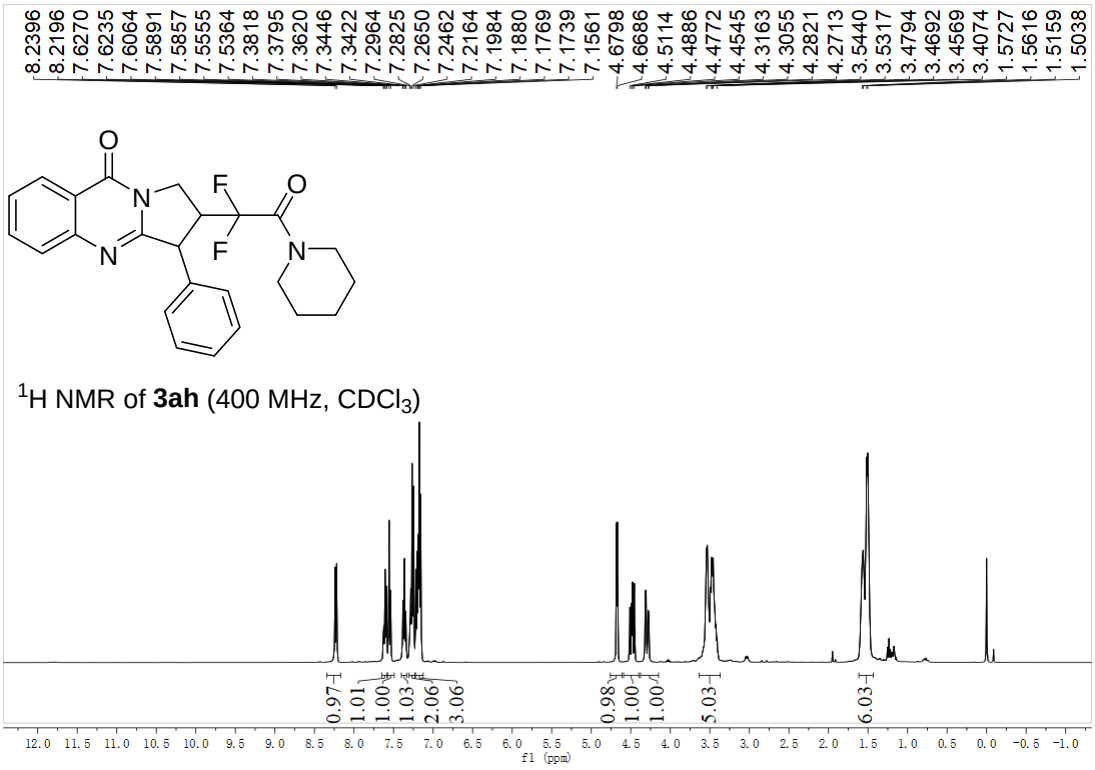
^{1}H NMR of **3ag** (400 MHz, $CDCl_3$)



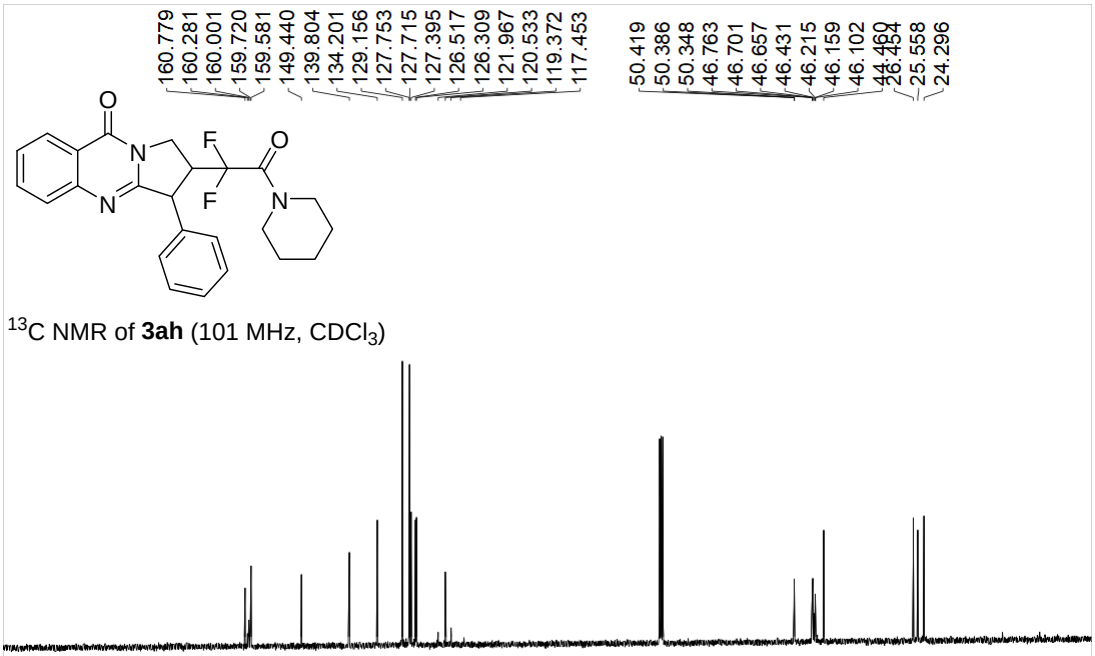
^{19}F NMR of **3ag** (376 MHz, $CDCl_3$)



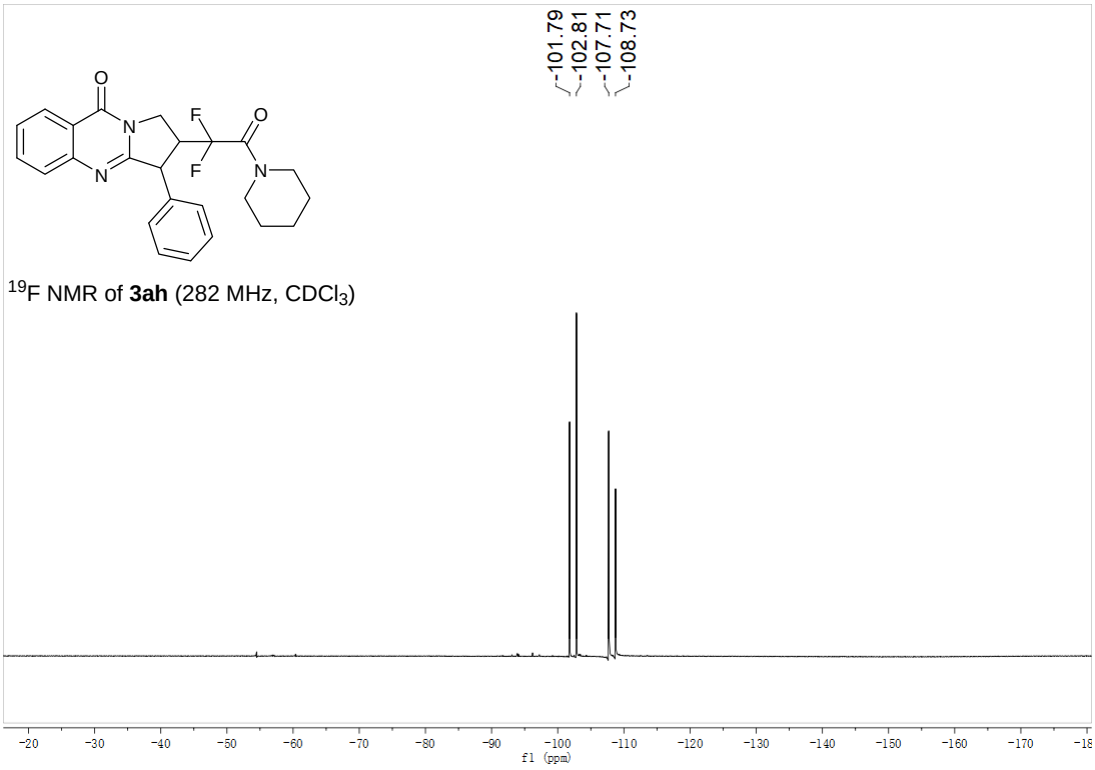
^{13}C NMR of **3ag** (101 MHz, $CDCl_3$)



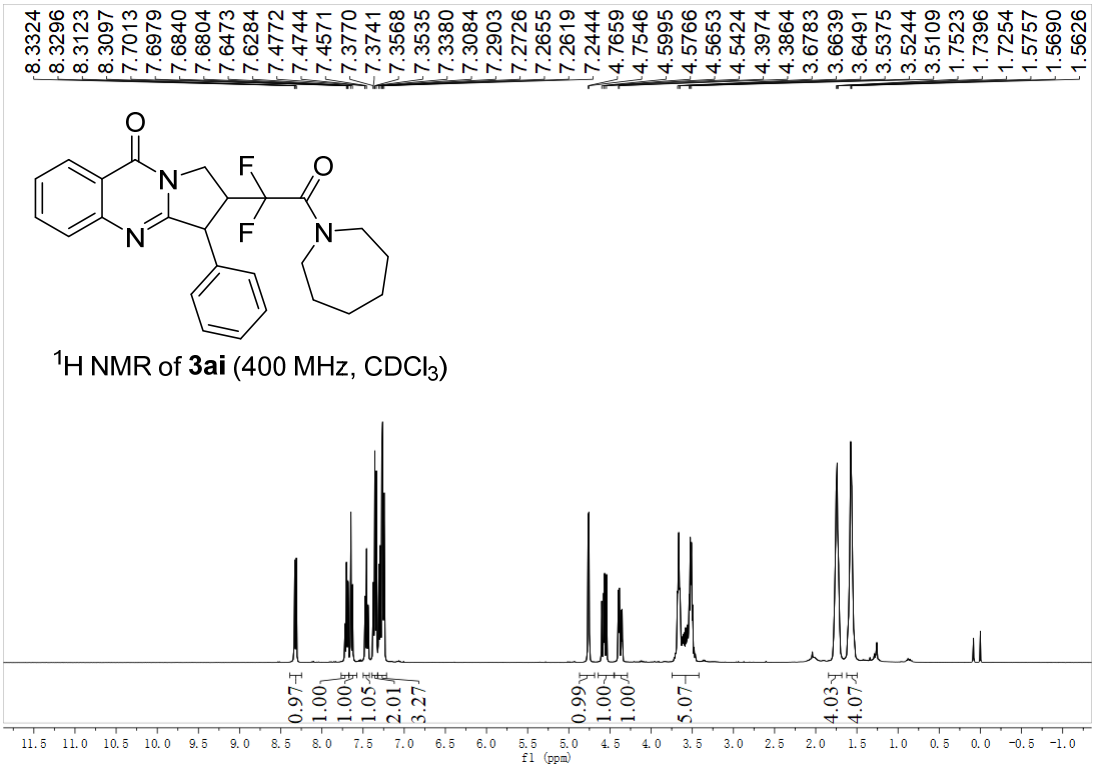
^{1}H NMR of **3ah** (400 MHz, $CDCl_3$)



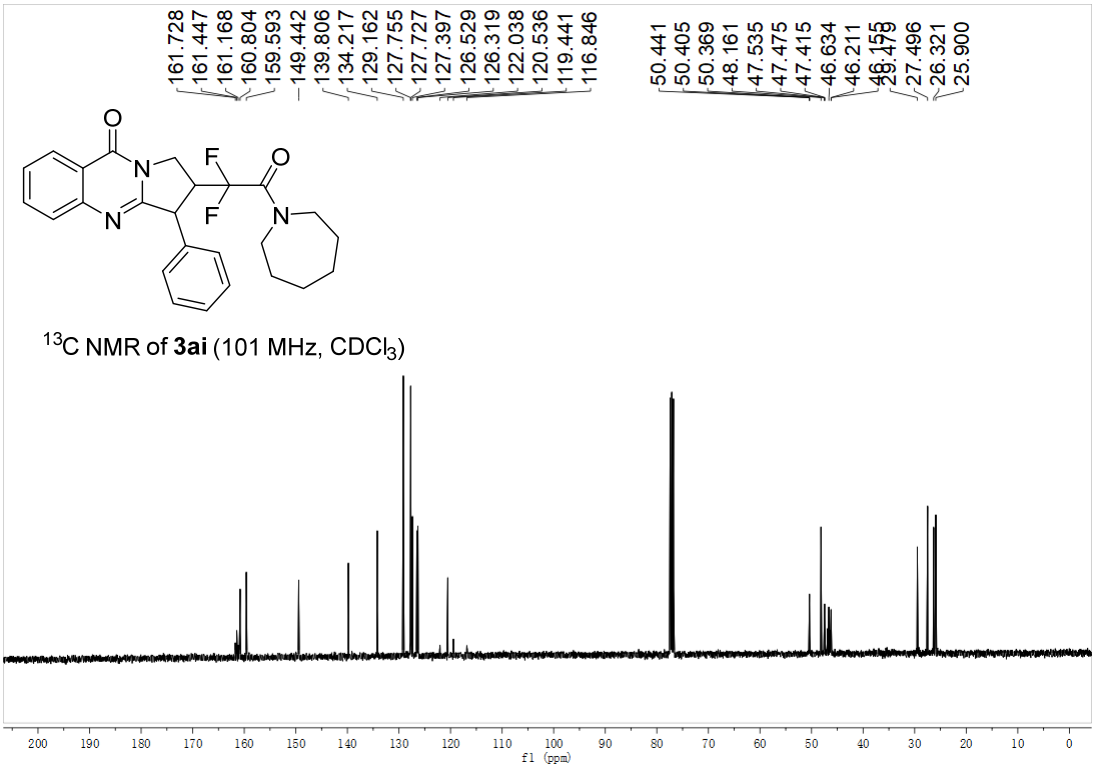
^{13}C NMR of **3ah** (101 MHz, $CDCl_3$)



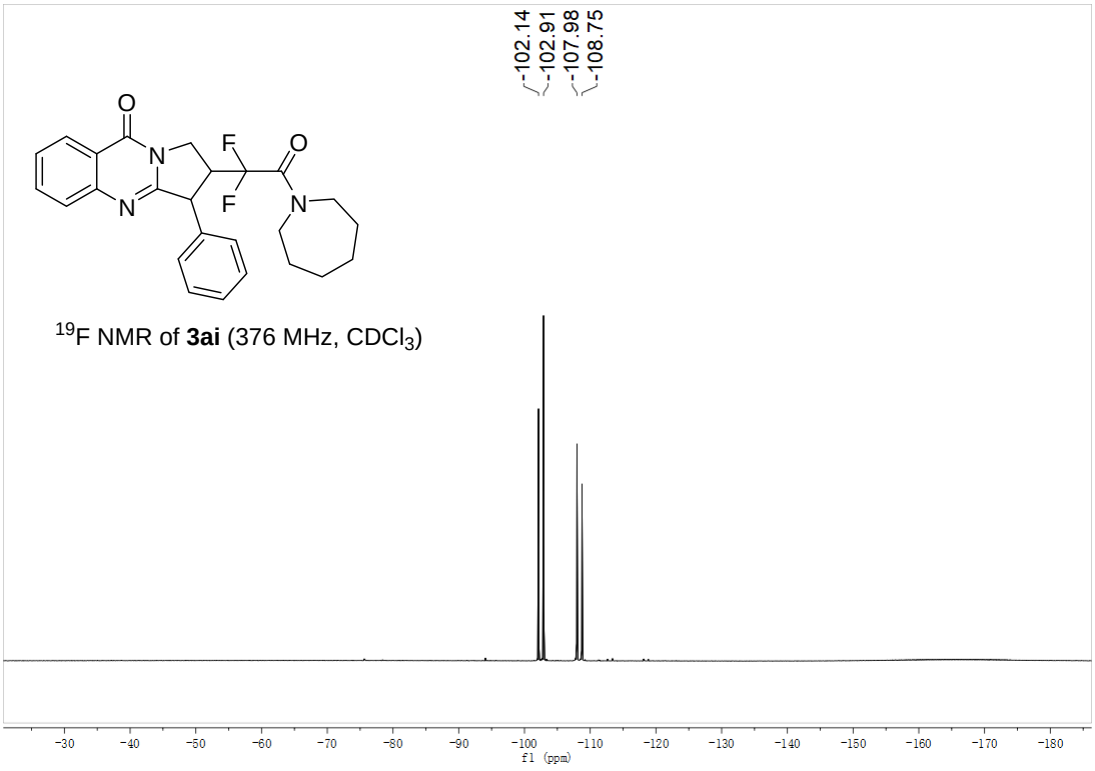
^{19}F NMR of **3ah** (282 MHz, $CDCl_3$)



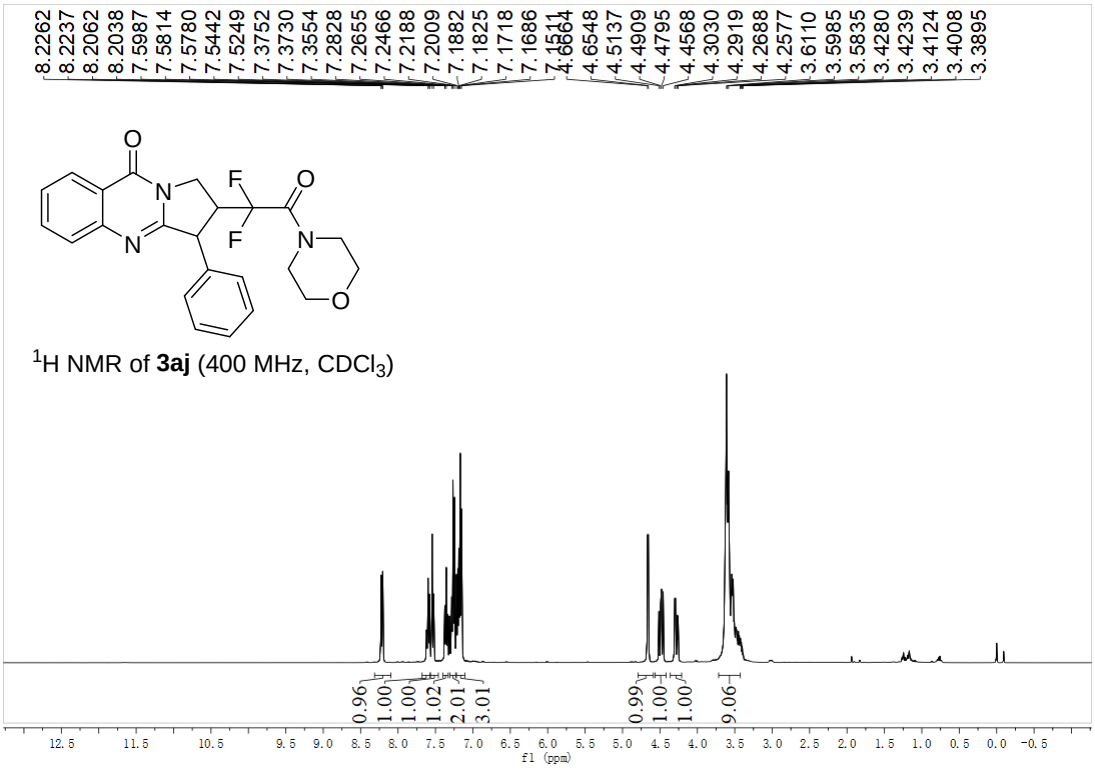
^{1}H NMR of **3ai** (400 MHz, $CDCl_3$)



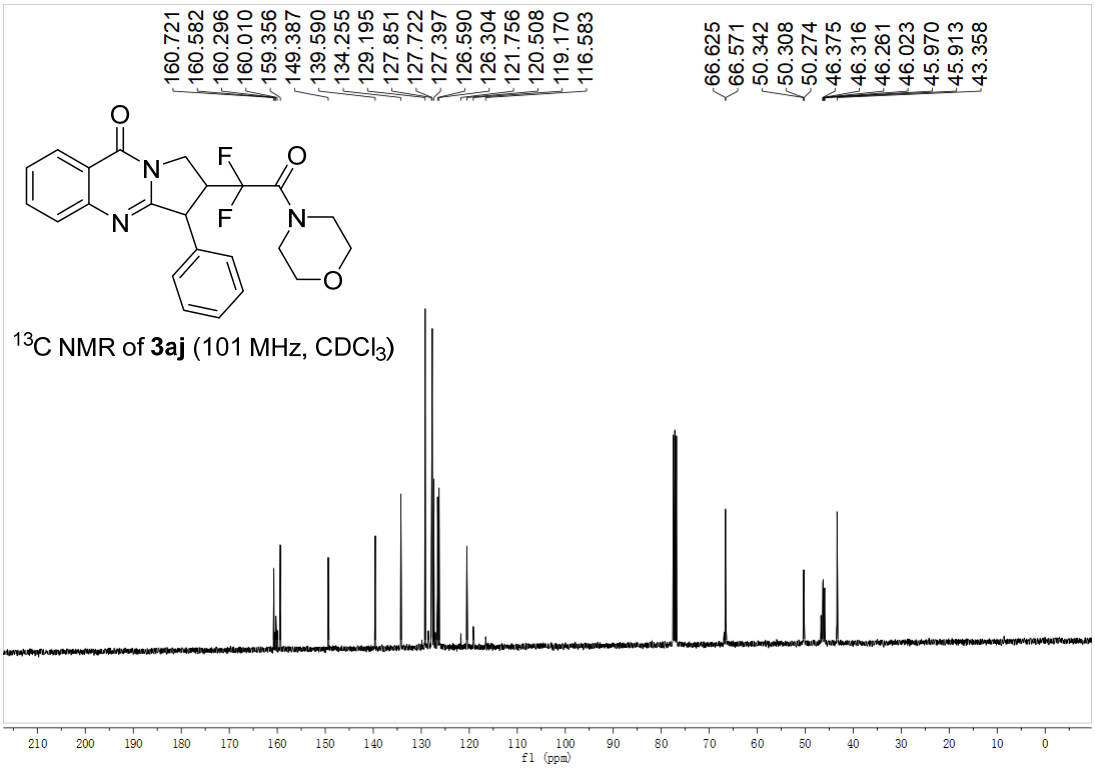
^{13}C NMR of **3ai** (101 MHz, $CDCl_3$)



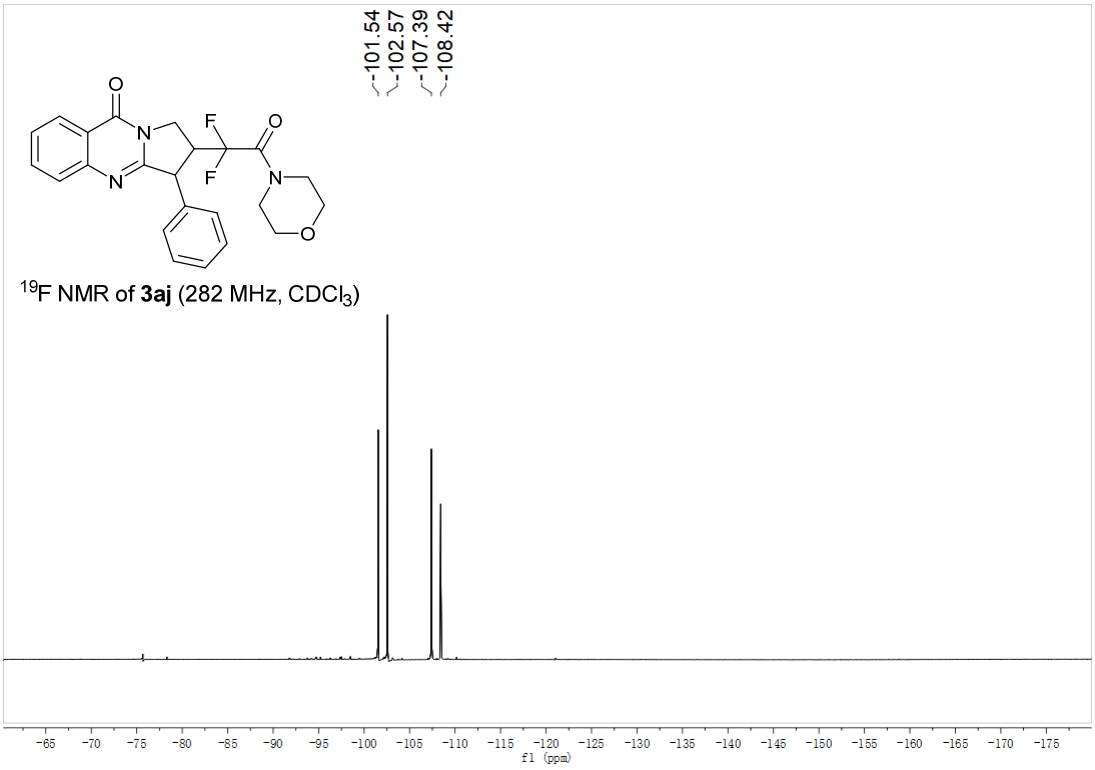
^{19}F NMR of **3ai** (376 MHz, $CDCl_3$)

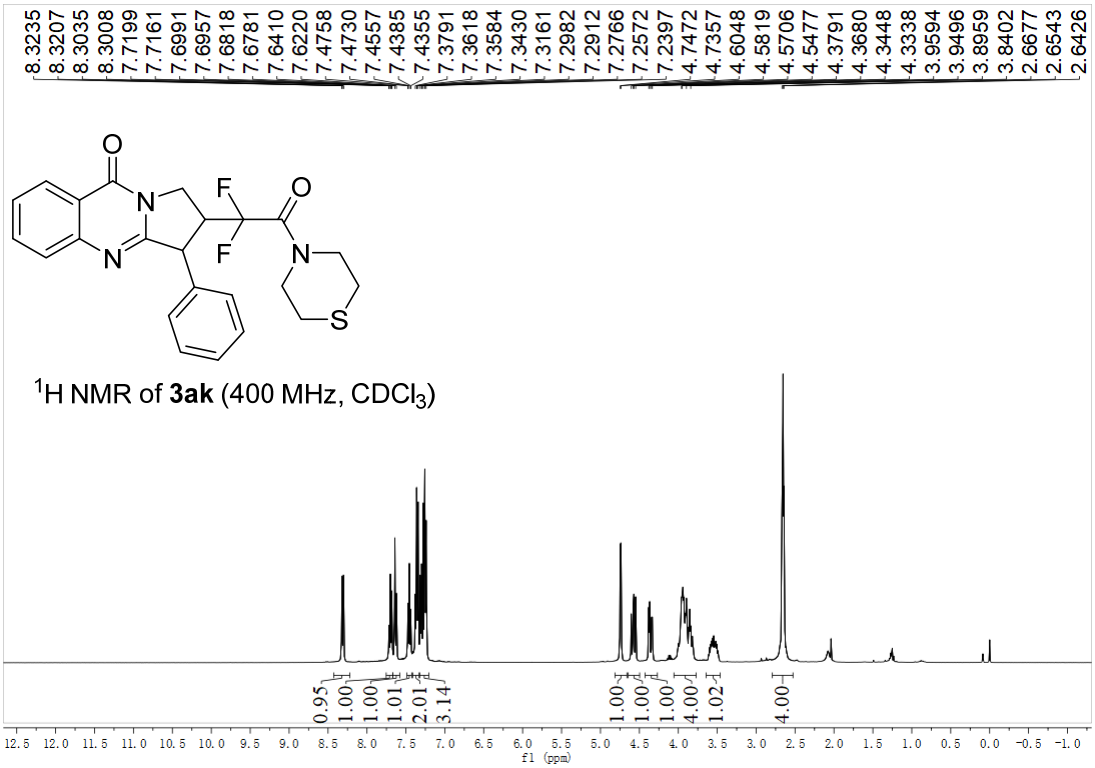


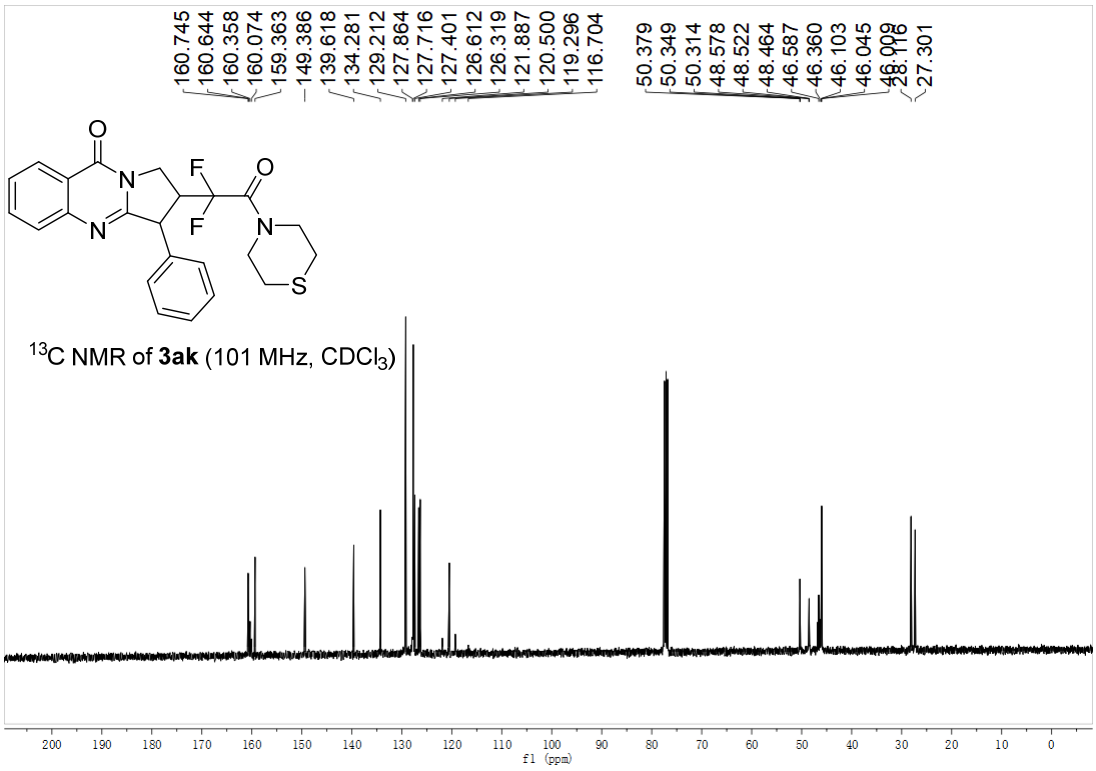
^{1}H NMR of **3aj** (400 MHz, $CDCl_3$)

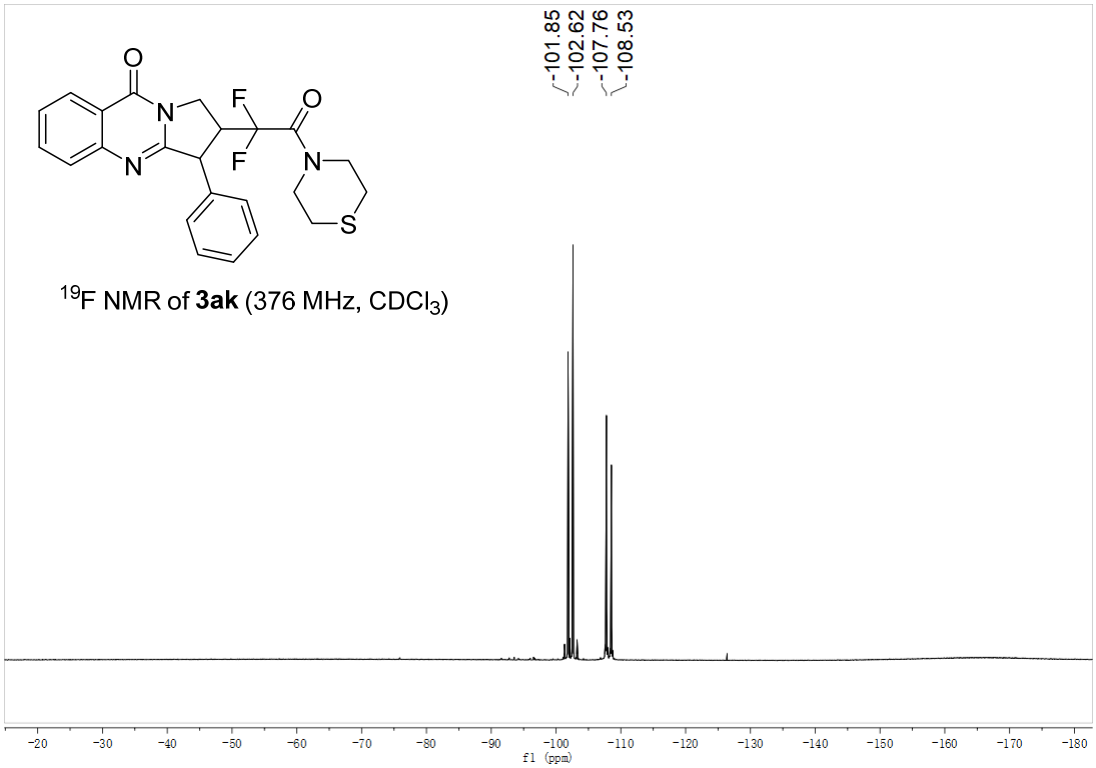


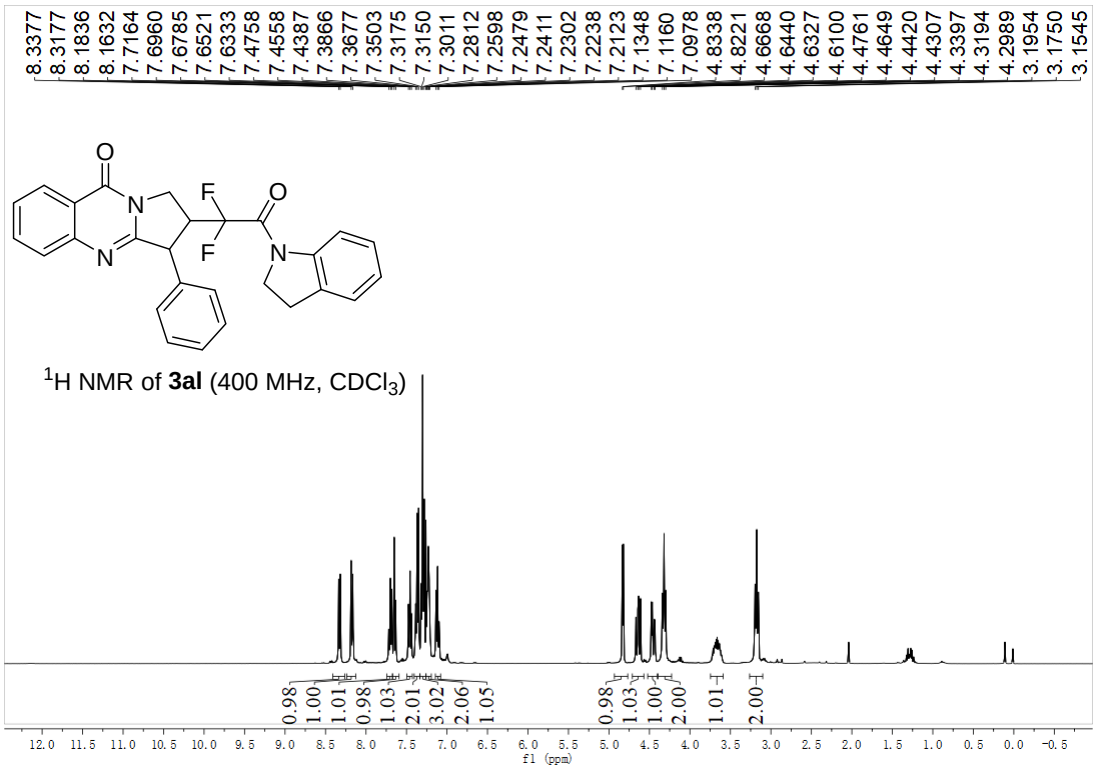
^{13}C NMR of **3aj** (101 MHz, $CDCl_3$)


-101.54
-102.57
-107.39
-108.42
O
N
F
F
O
N
N
O
19F NMR of 3aj (282 MHz, CDCl3)
-65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175
f1 (ppm)

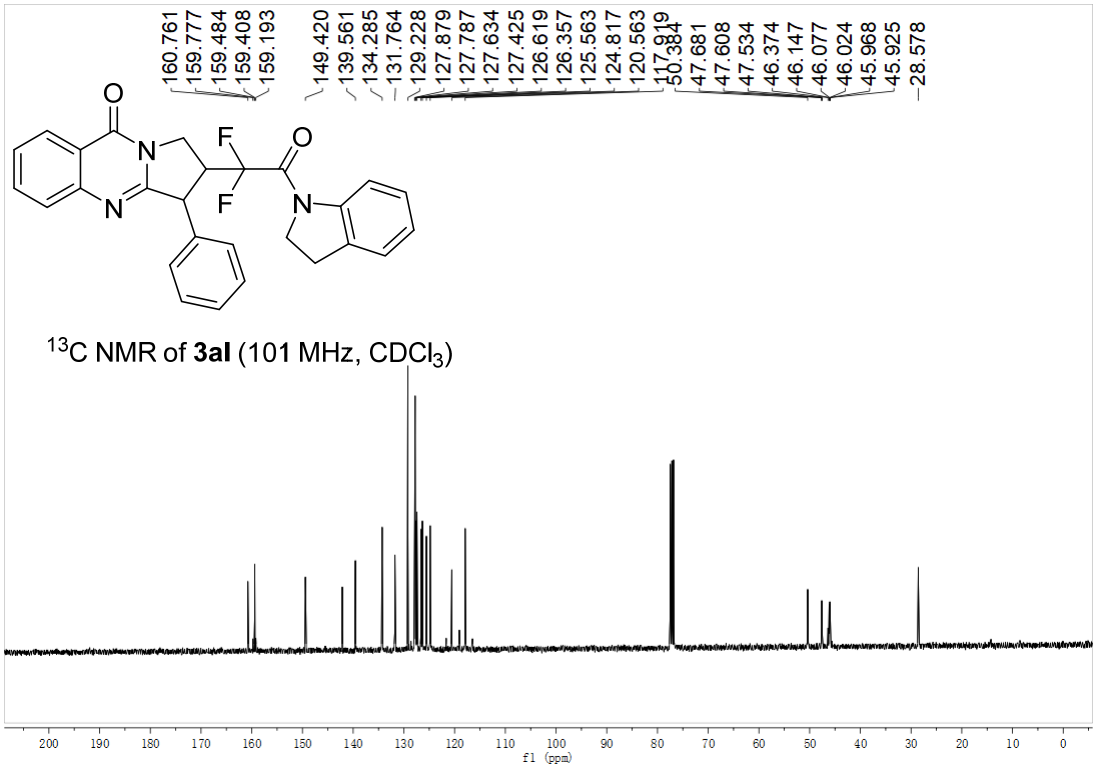

8.3235
8.3207
8.3035
8.3008
7.7199
7.7161
7.6991
7.6957
7.6818
7.6781
7.6410
7.6220
7.4758
7.4730
7.4557
7.4385
7.4355
7.3791
7.3618
7.3584
7.3430
7.3161
7.2982
7.2912
7.2766
7.2572
7.2397
4.7472
4.7357
4.6048
4.5819
4.5706
4.5477
4.3791
4.3680
4.3448
4.3338
3.9594
3.9496
3.8959
3.8402
2.6677
2.6543
2.6426
O
N
F
F
O
N
N
S
1H NMR of 3ak (400 MHz, CDCl3)
0.95
1.00
1.00
1.01
2.01
3.14
1.00
1.00
1.00
4.00
1.02
4.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


160.745
160.644
160.358
160.074
159.363
149.386
139.618
134.281
129.212
127.864
127.716
127.401
126.612
126.319
121.887
120.500
119.296
116.704
50.379
50.349
50.314
48.578
48.522
48.464
46.587
46.360
46.103
46.045
28.116
27.301
O
N
N
F
F
O
N
S
^{13}C NMR of **3ak** (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

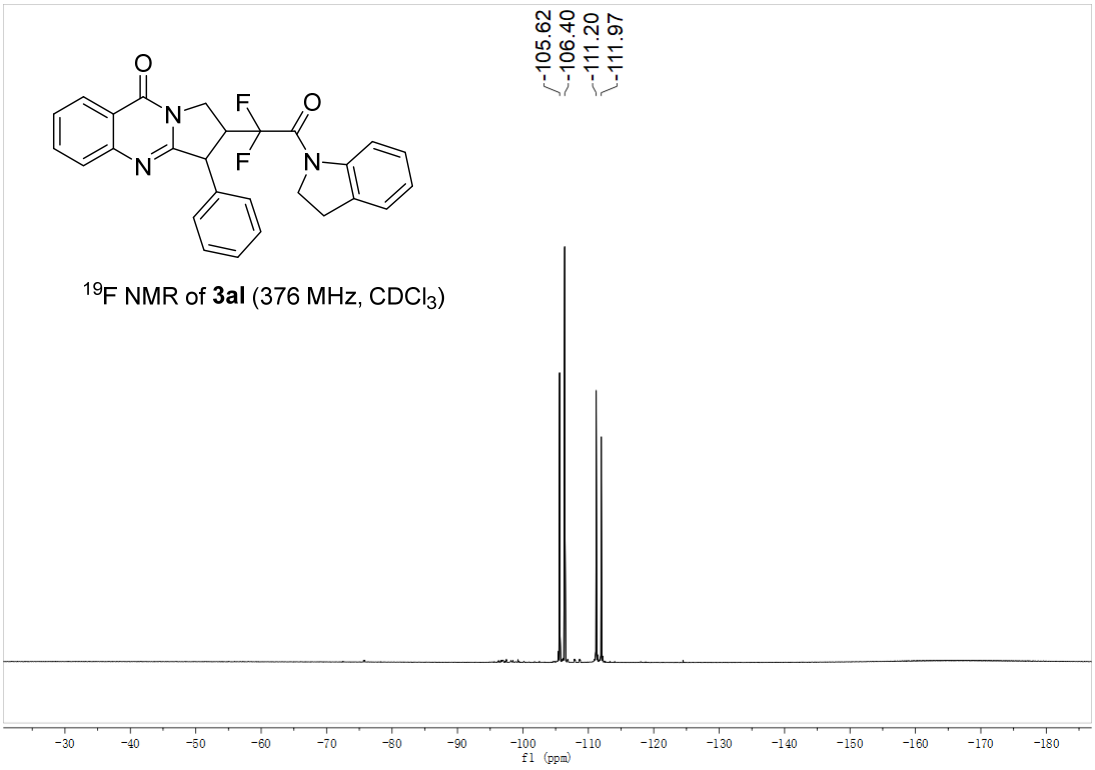

-101.85
-102.62
-107.76
-108.53
O
N
N
F
F
O
N
S
^{19}F NMR of **3ak** (376 MHz, $CDCl_3$)
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)



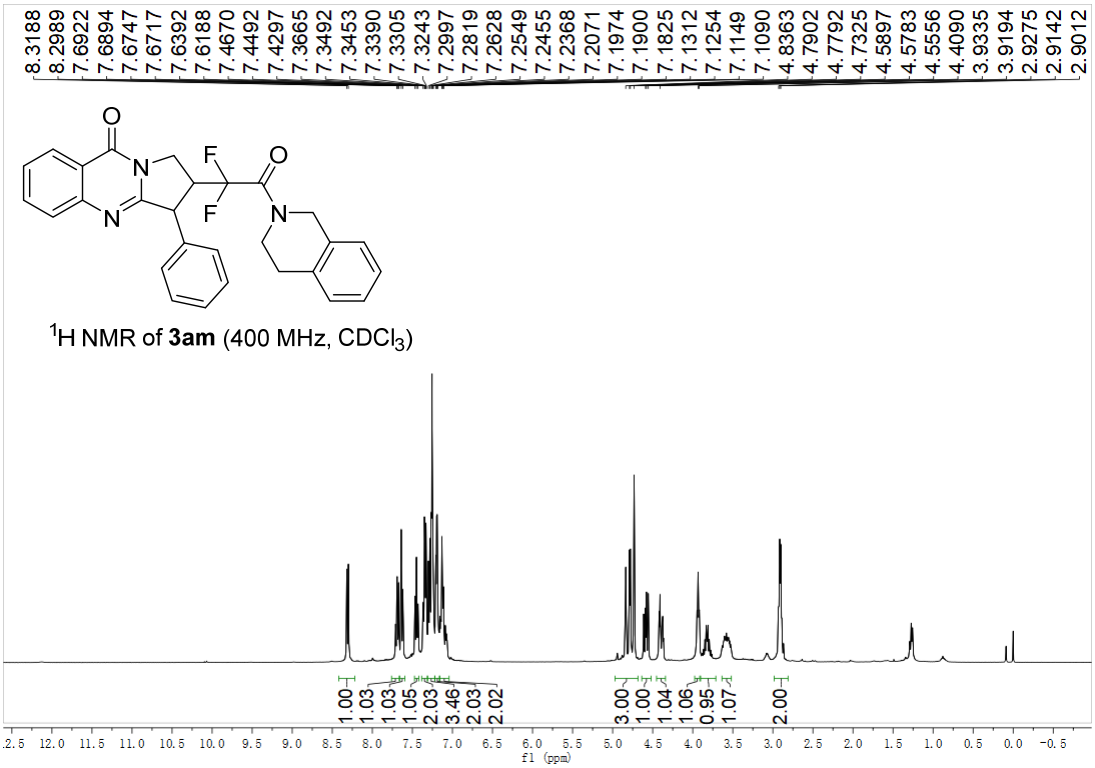
^{1}H NMR of **3al** (400 MHz, $CDCl_3$)



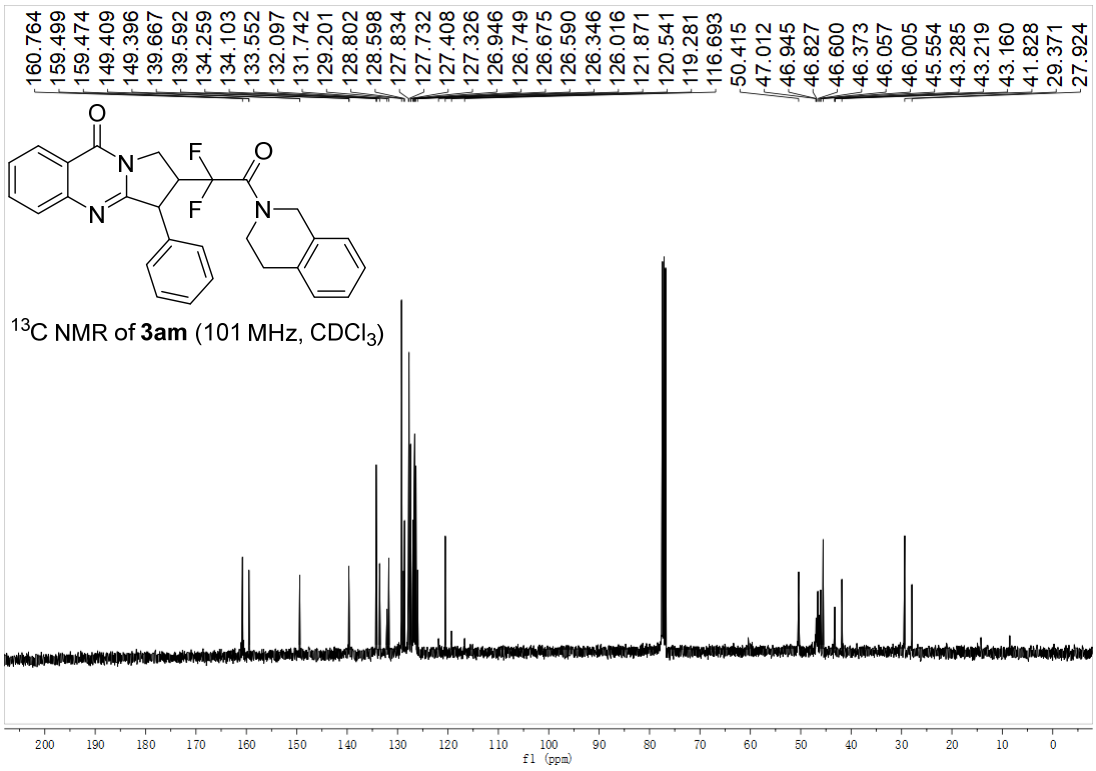
^{13}C NMR of **3al** (101 MHz, $CDCl_3$)



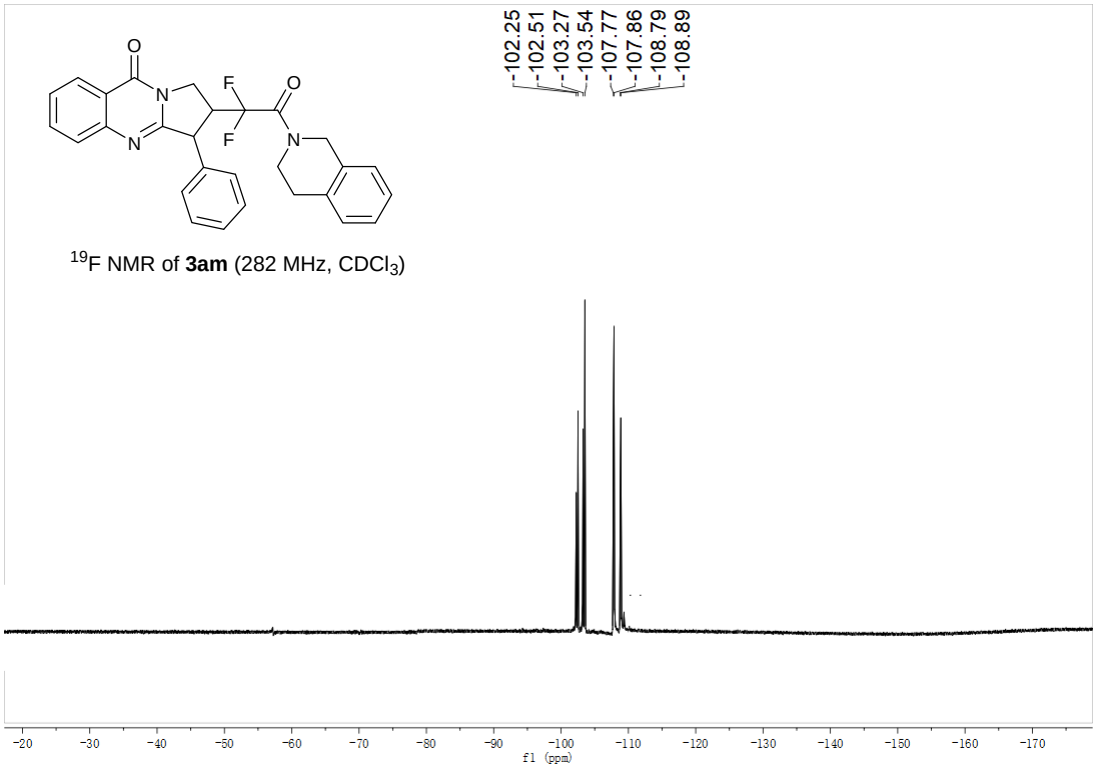
^{19}F NMR of **3al** (376 MHz, $CDCl_3$)



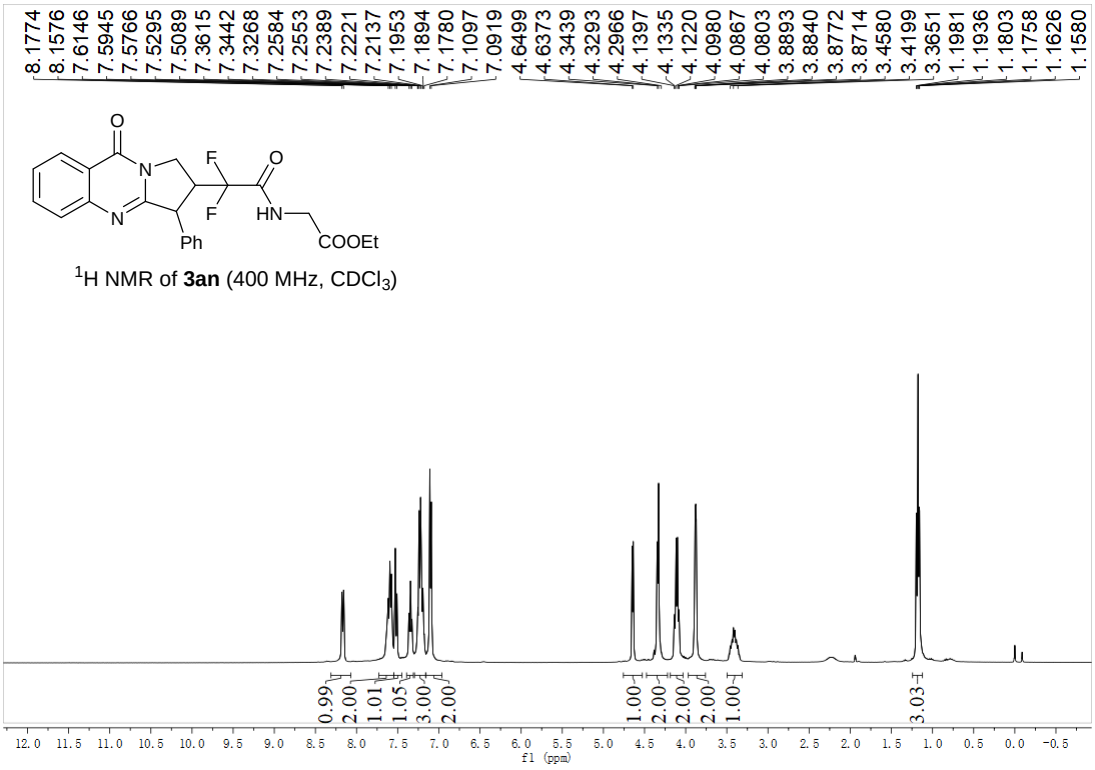
^{1}H NMR of **3am** (400 MHz, $CDCl_3$)



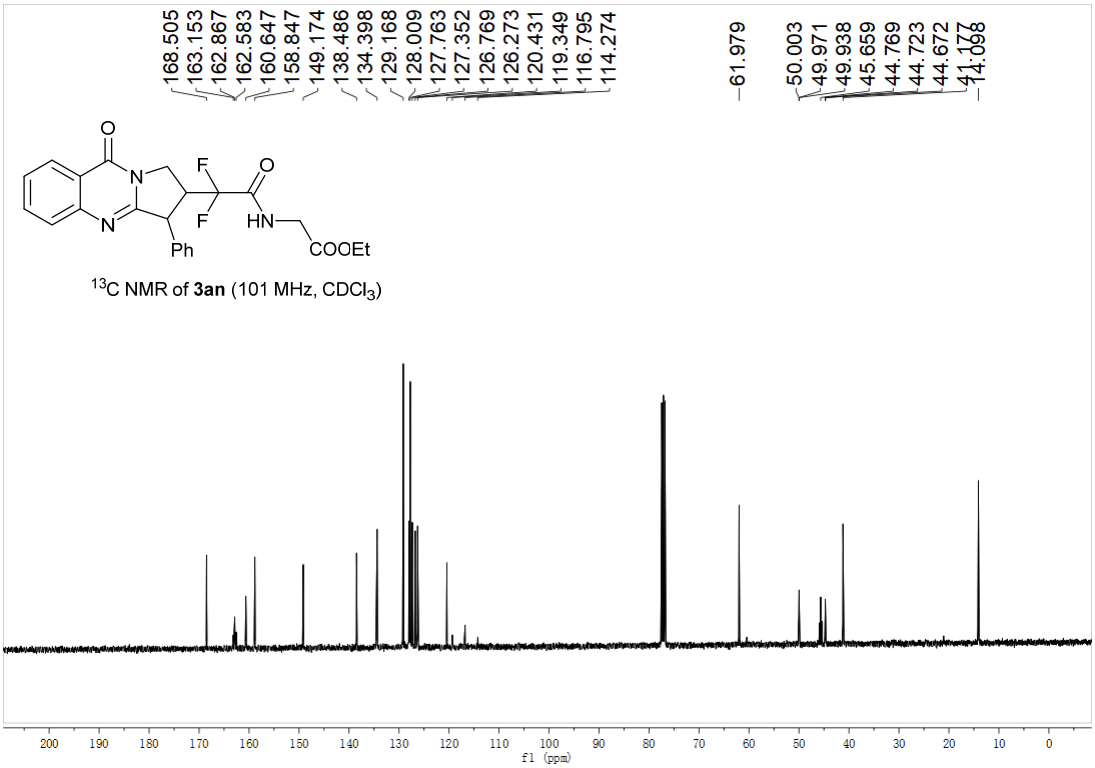
^{13}C NMR of **3am** (101 MHz, $CDCl_3$)



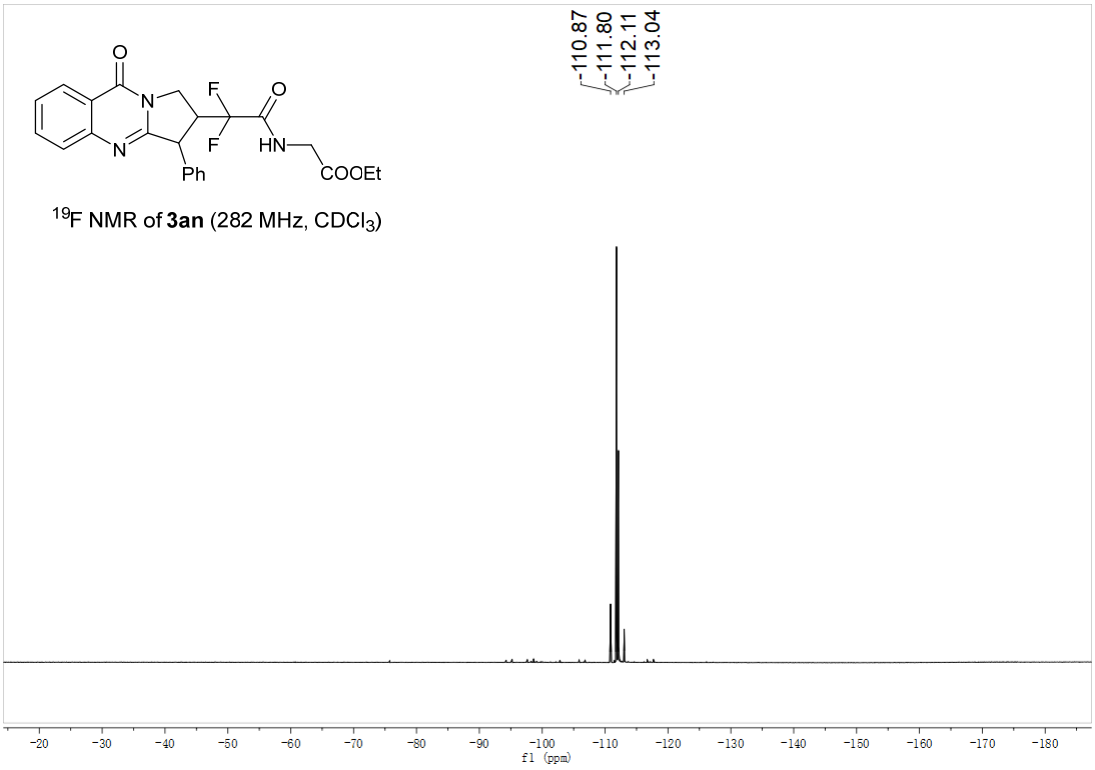
^{19}F NMR of **3am** (282 MHz, $CDCl_3$)



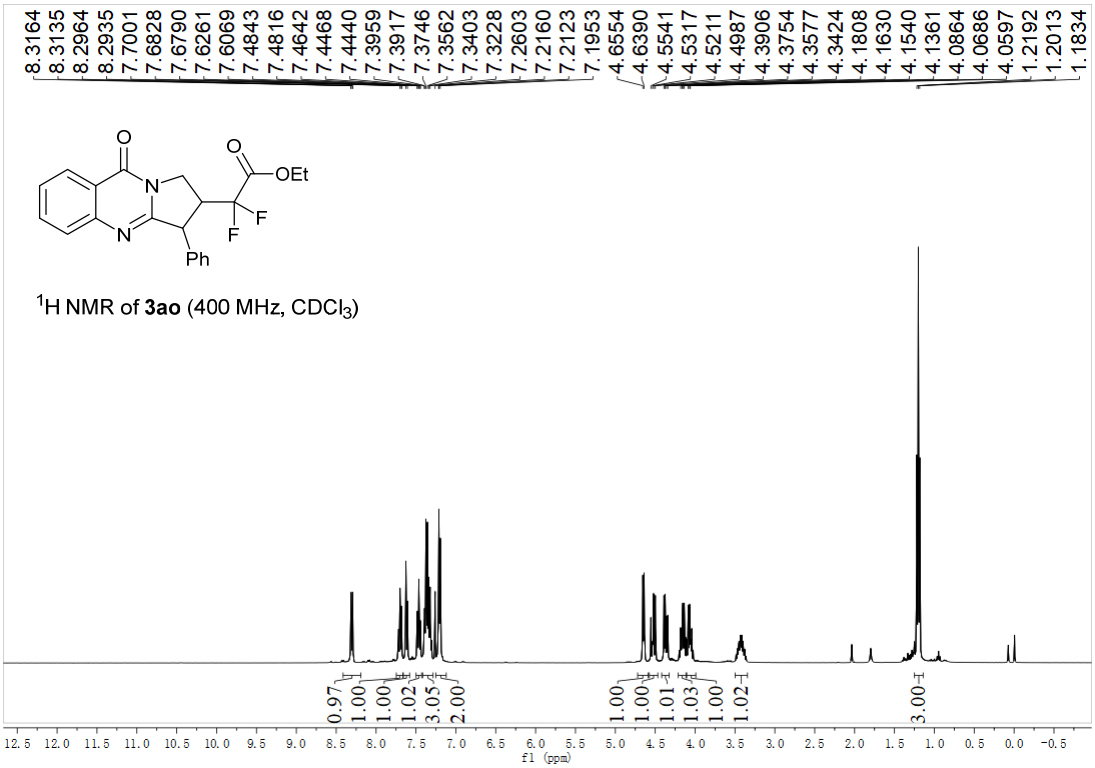
^{1}H NMR of **3an** (400 MHz, $CDCl_3$)



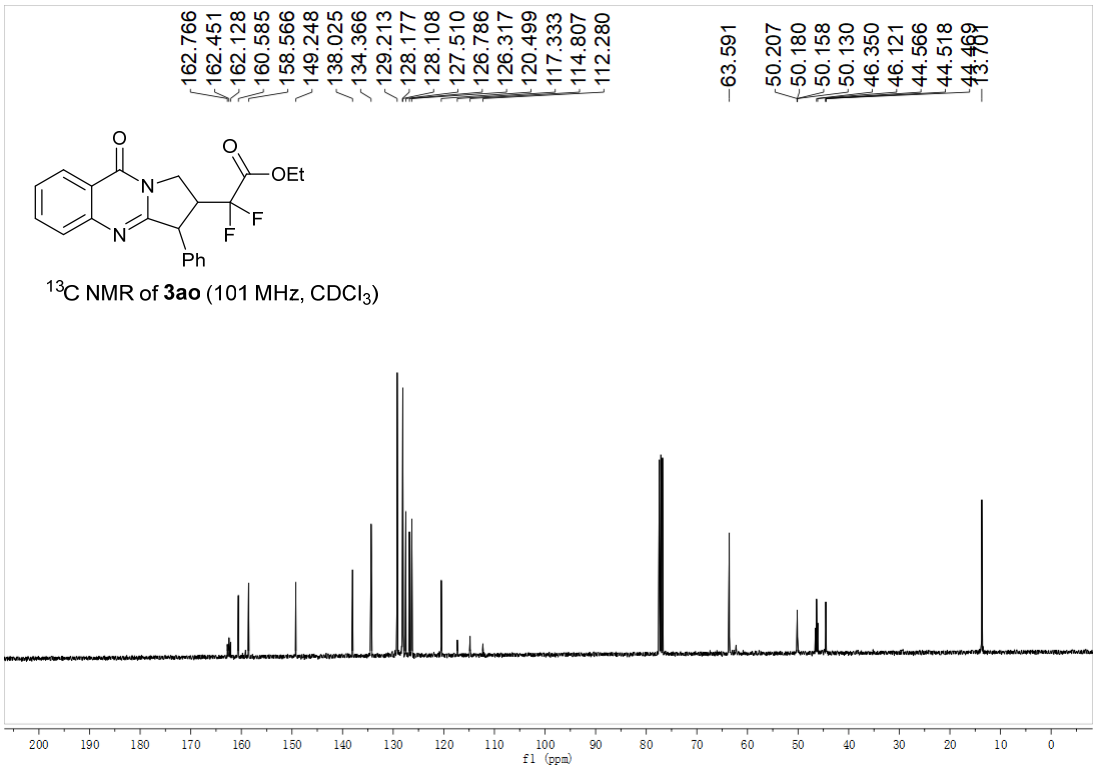
^{13}C NMR of **3an** (101 MHz, $CDCl_3$)



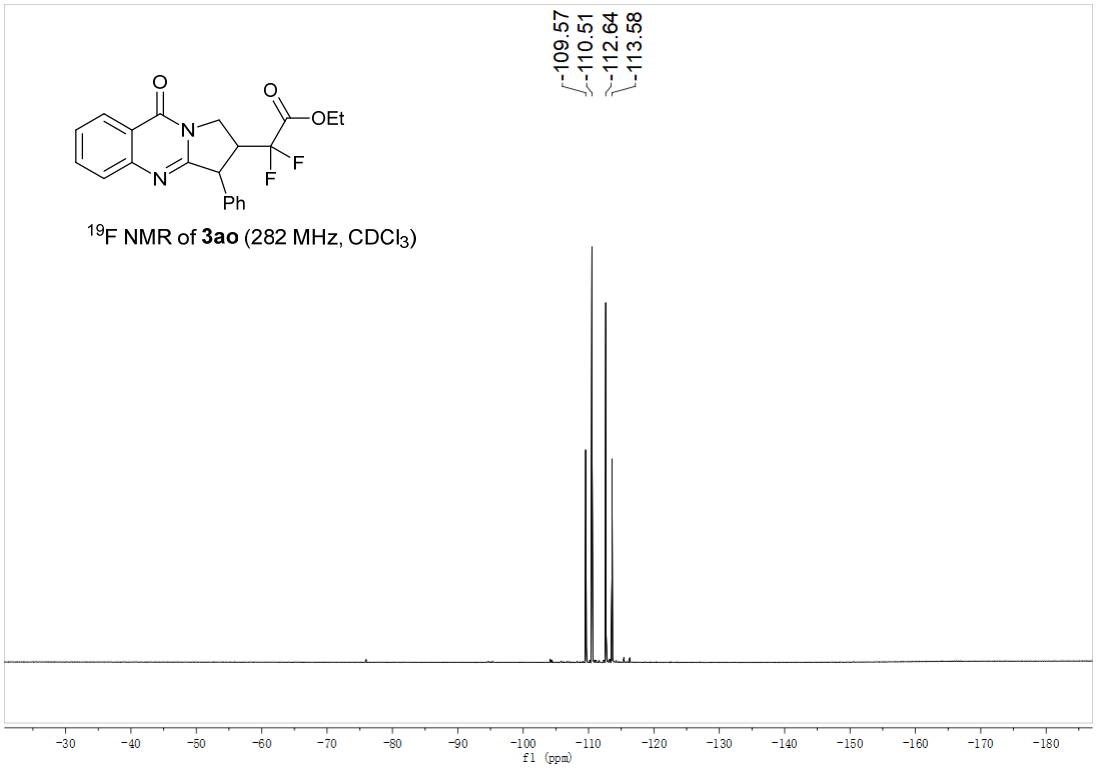
^{19}F NMR of **3an** (282 MHz, $CDCl_3$)



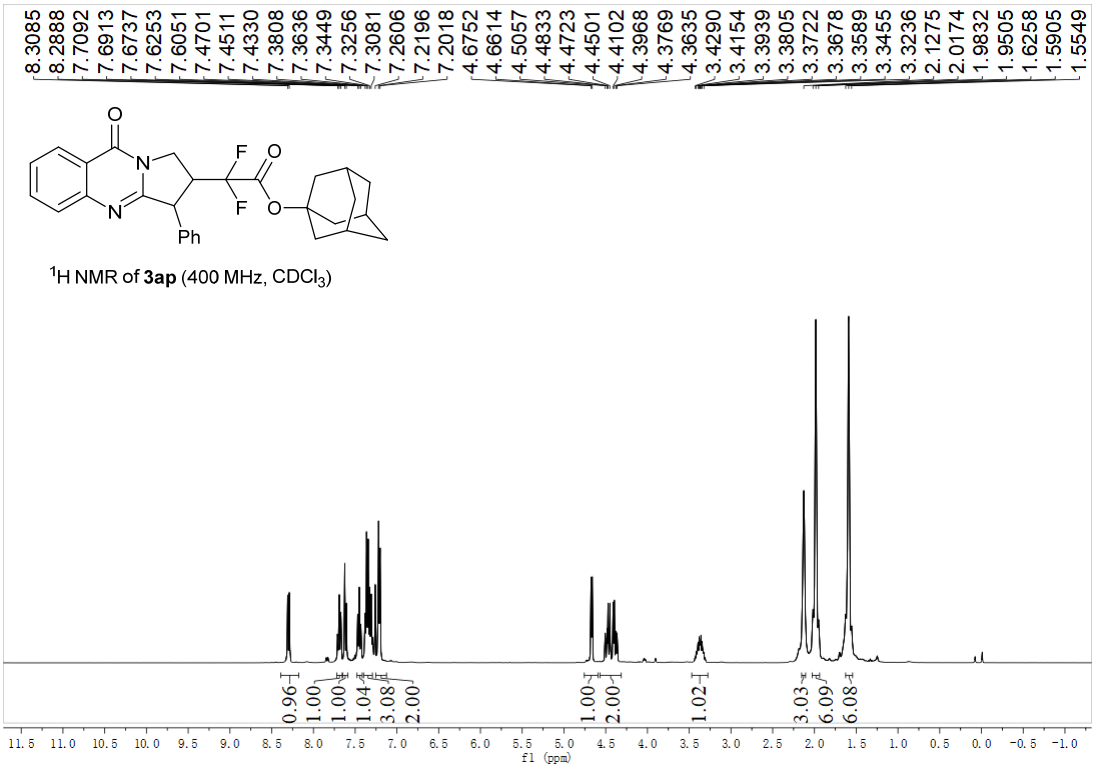
^{1}H NMR of **3ao** (400 MHz, $CDCl_3$)



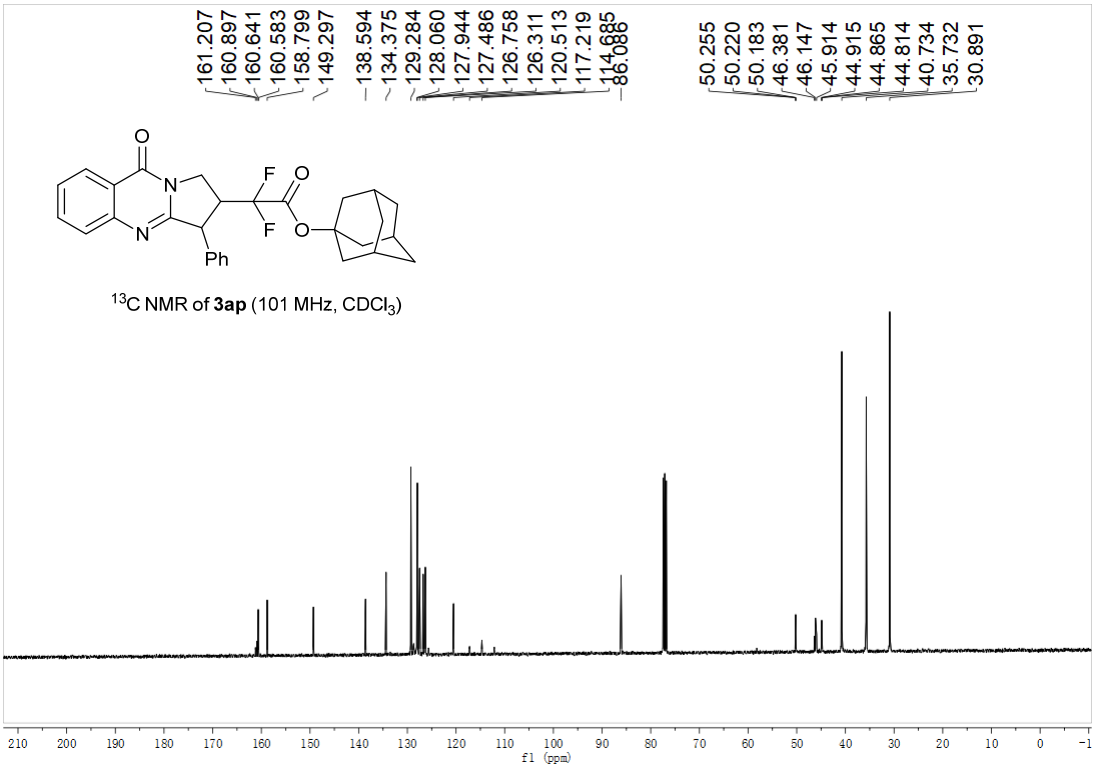
^{13}C NMR of **3ao** (101 MHz, $CDCl_3$)



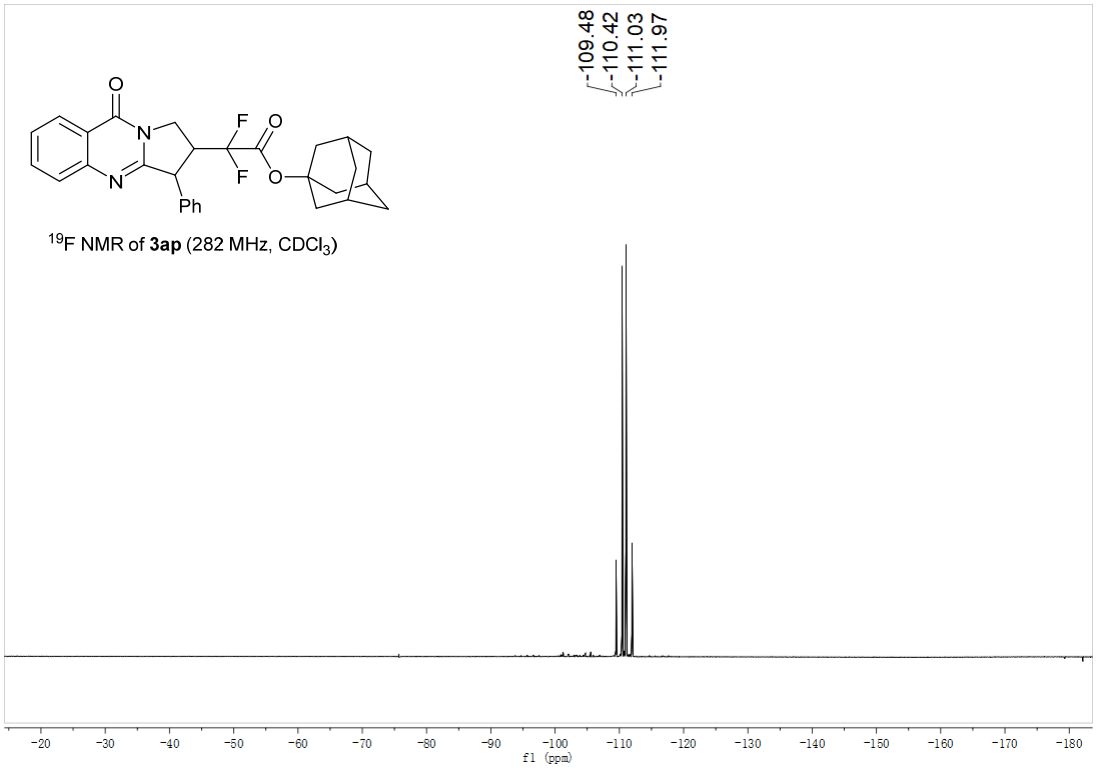
^{19}F NMR of **3ao** (282 MHz, $CDCl_3$)



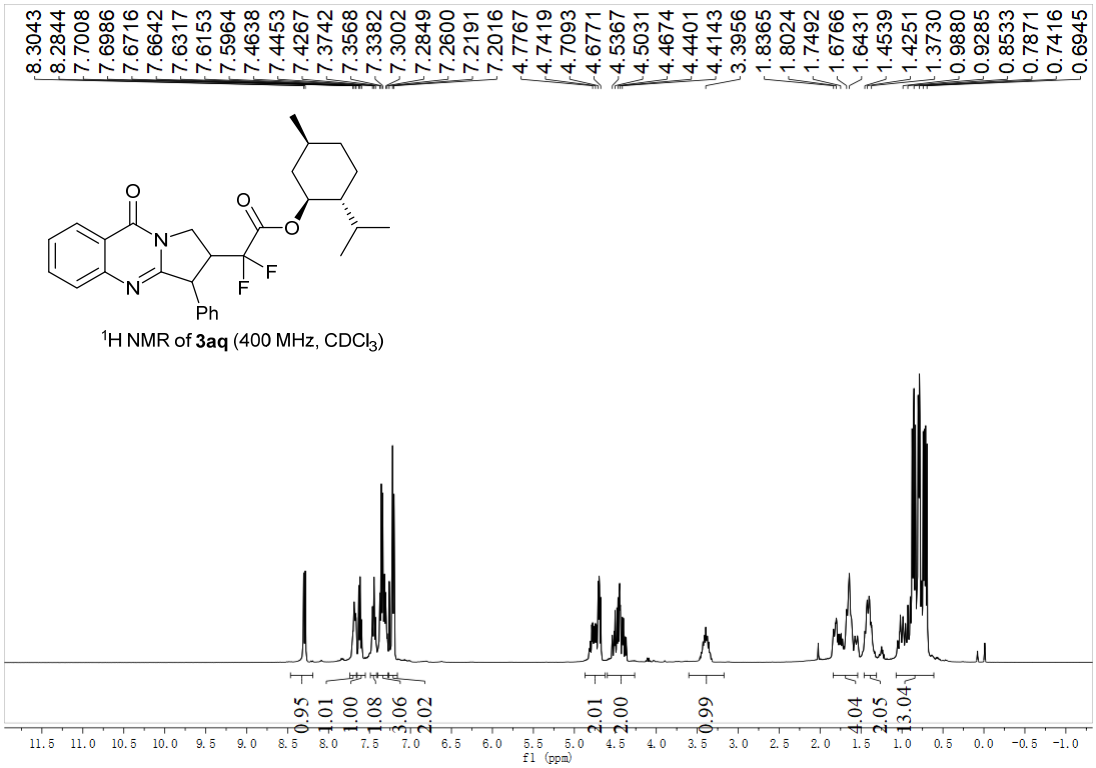
^{1}H NMR of **3ap** (400 MHz, $CDCl_3$)



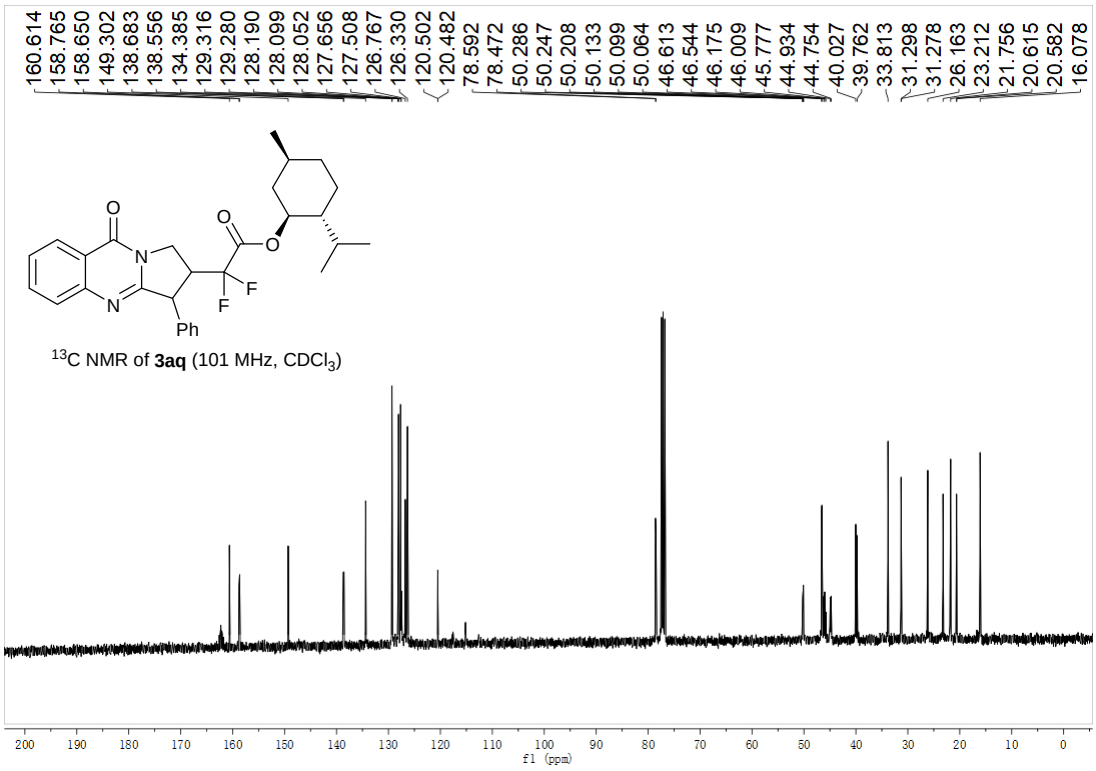
^{13}C NMR of **3ap** (101 MHz, $CDCl_3$)



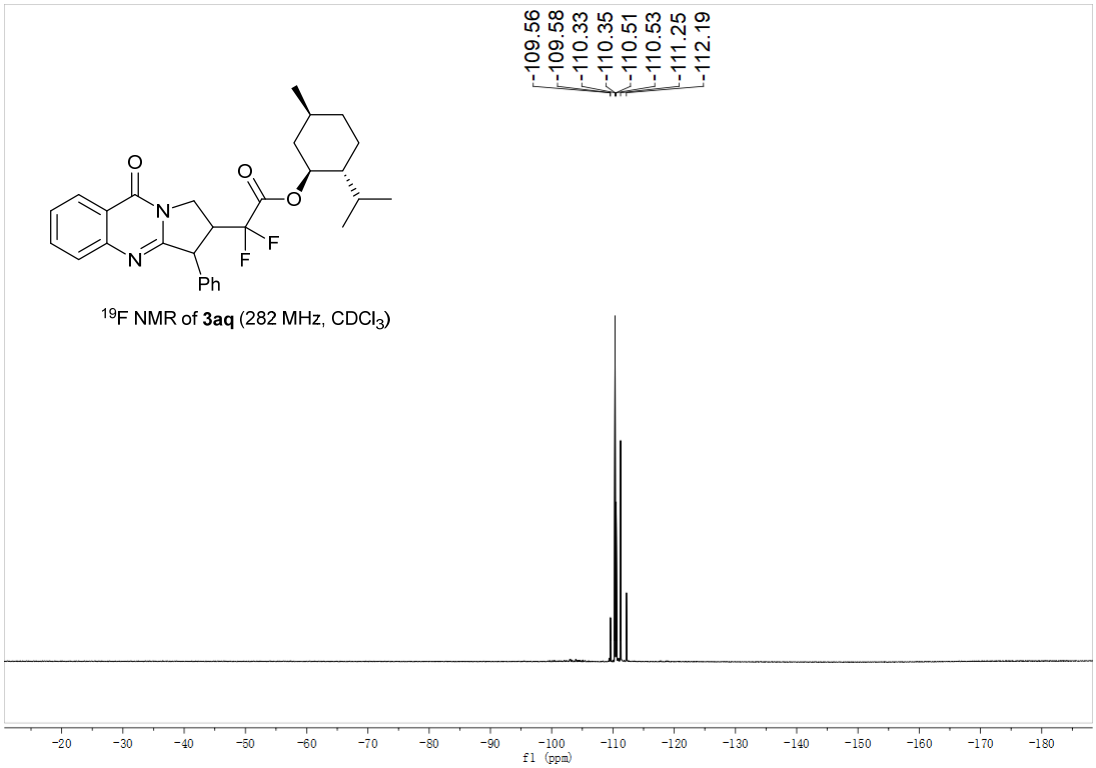
^{19}F NMR of **3ap** (282 MHz, $CDCl_3$)



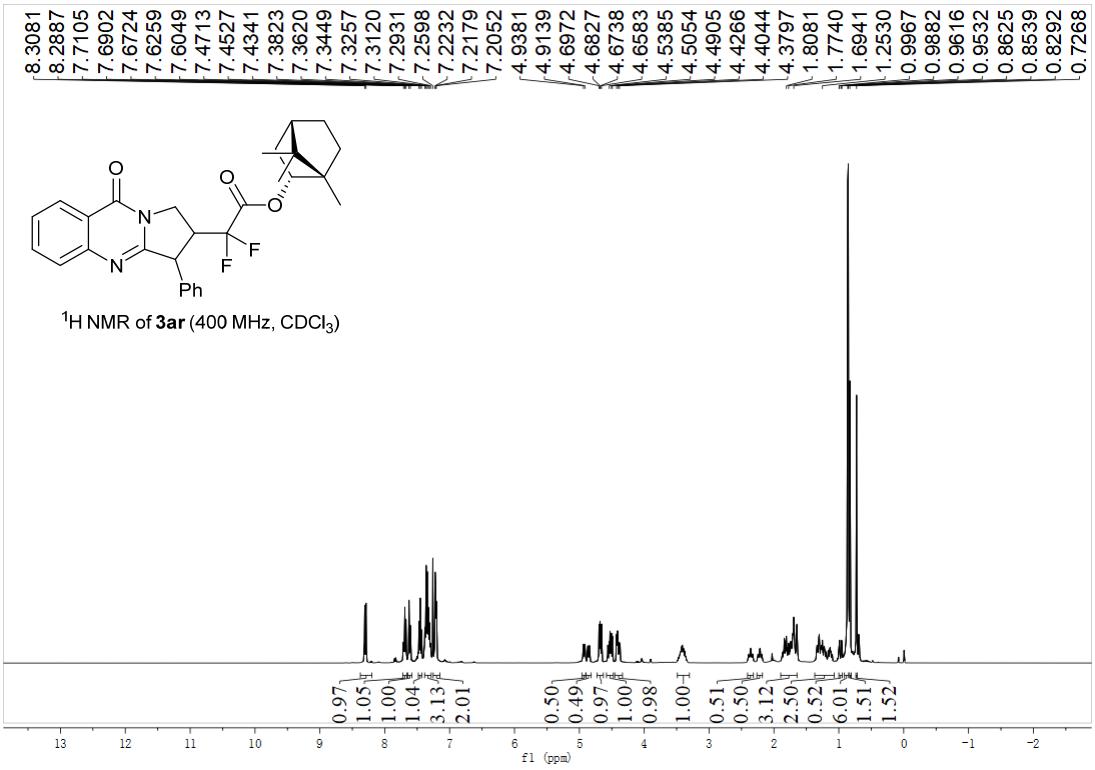
^{1}H NMR of **3aq** (400 MHz, $CDCl_3$)



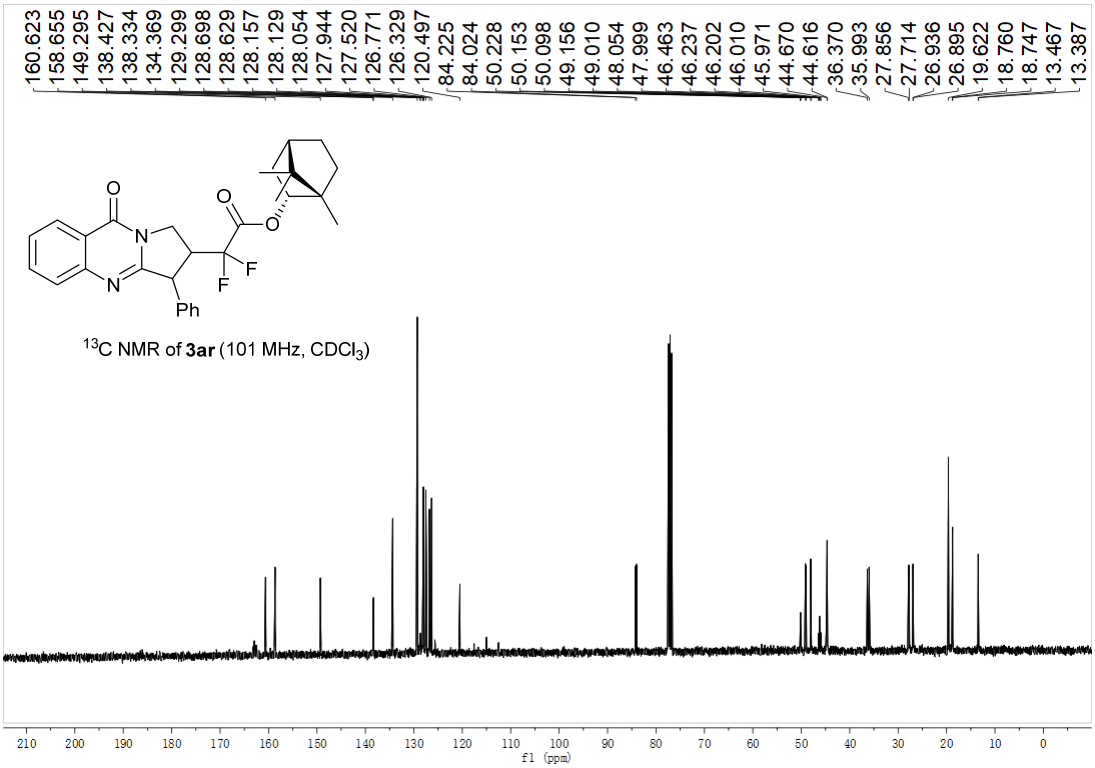
^{13}C NMR of **3aq** (101 MHz, $CDCl_3$)



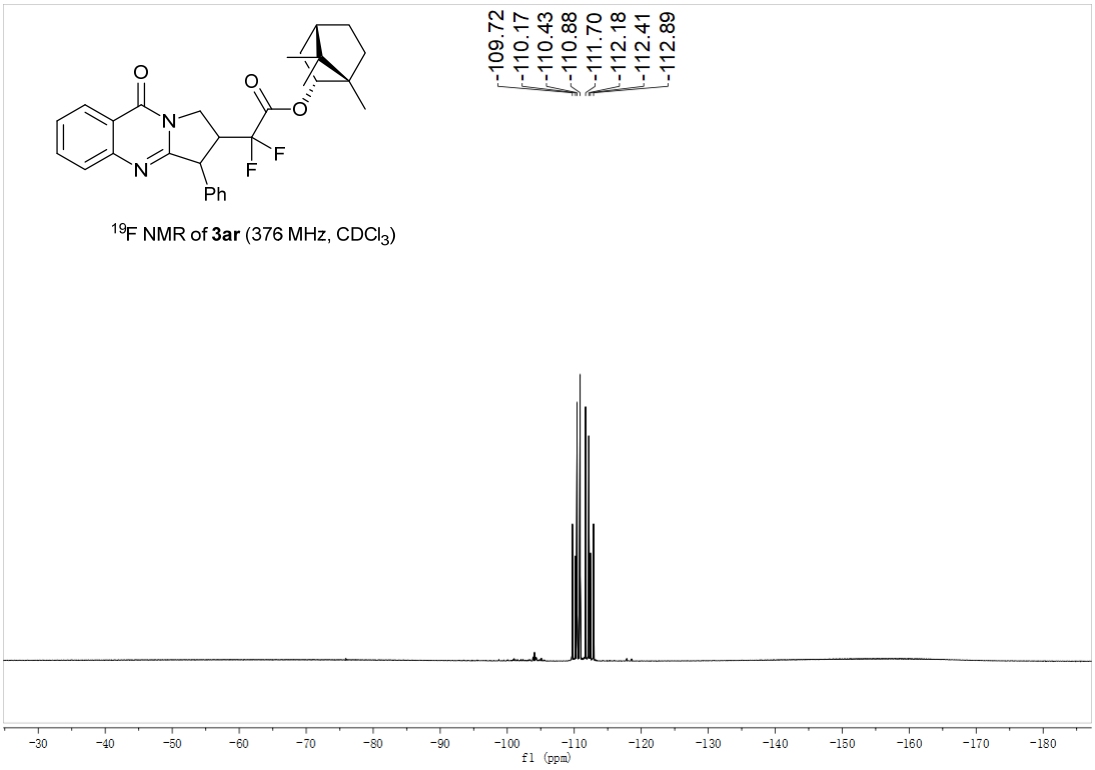
^{19}F NMR of **3aq** (282 MHz, $CDCl_3$)



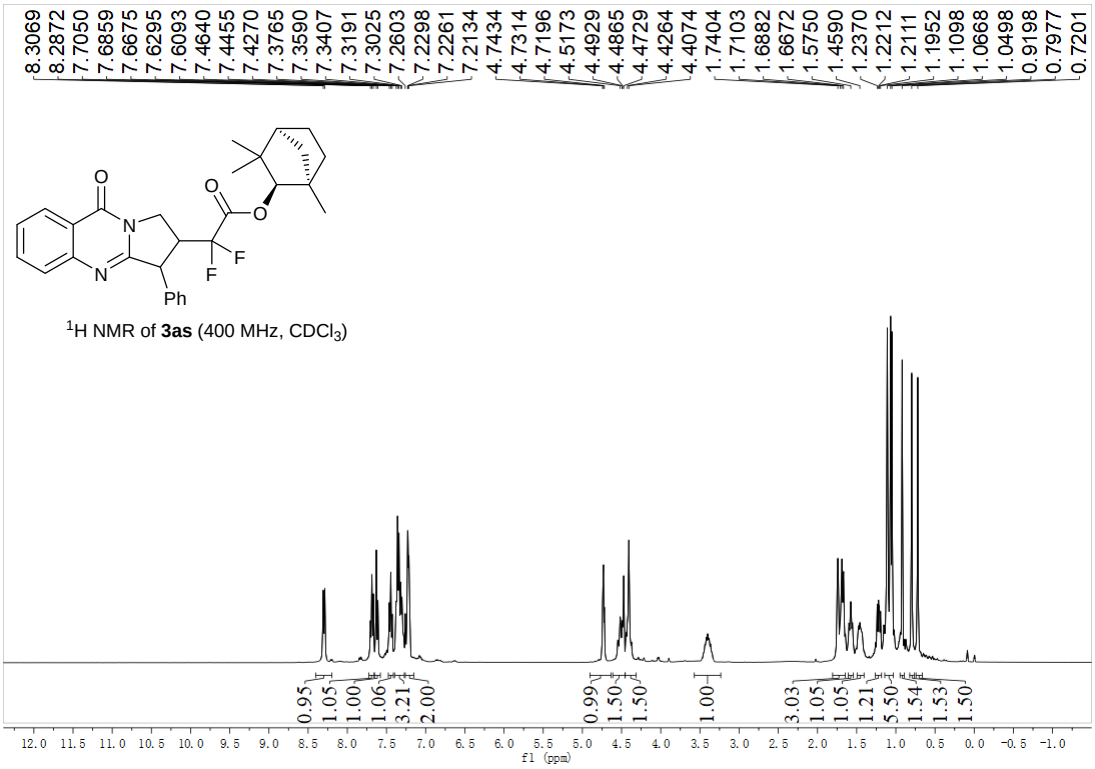
^{1}H NMR of **3ar** (400 MHz, $CDCl_3$)



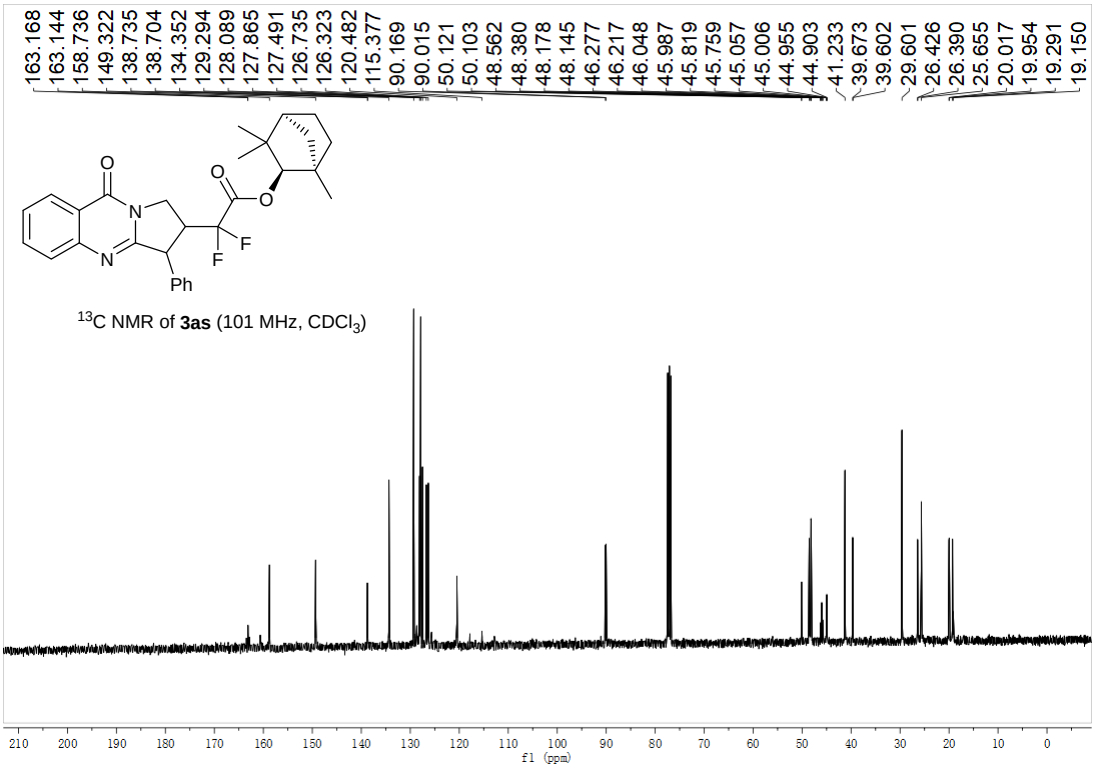
^{13}C NMR of **3ar** (101 MHz, $CDCl_3$)



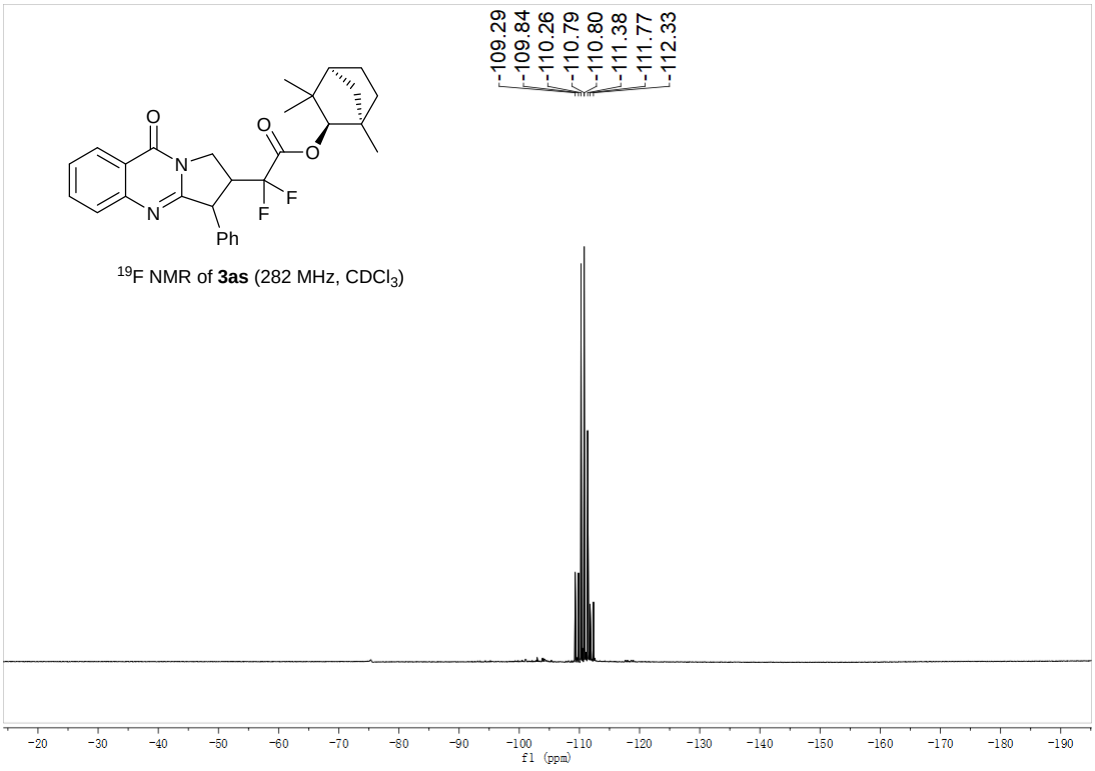
^{19}F NMR of **3ar** (376 MHz, $CDCl_3$)



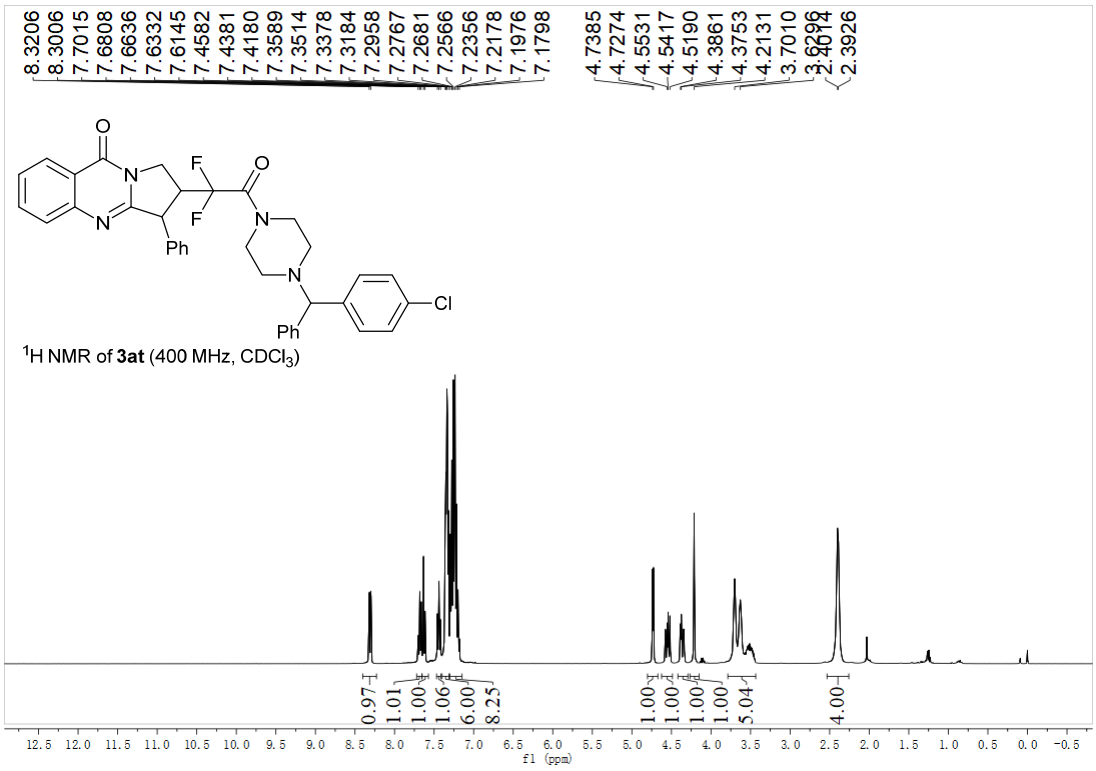
^{1}H NMR of **3as** (400 MHz, $CDCl_3$)



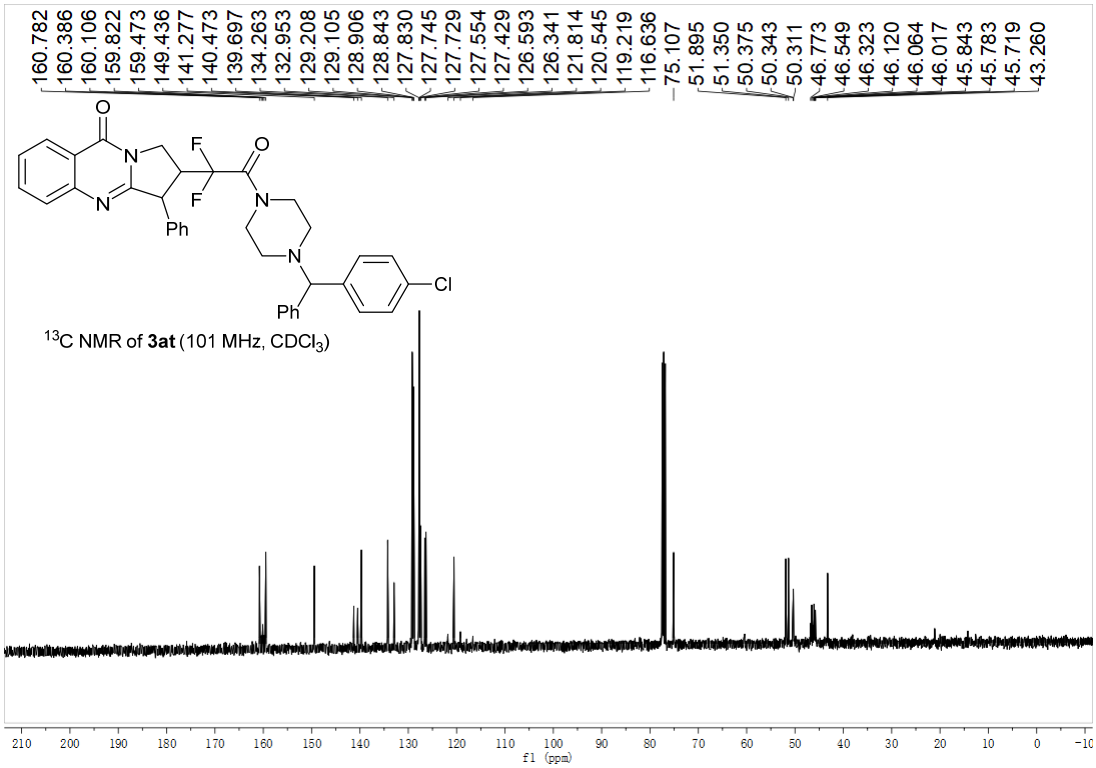
^{13}C NMR of **3as** (101 MHz, $CDCl_3$)



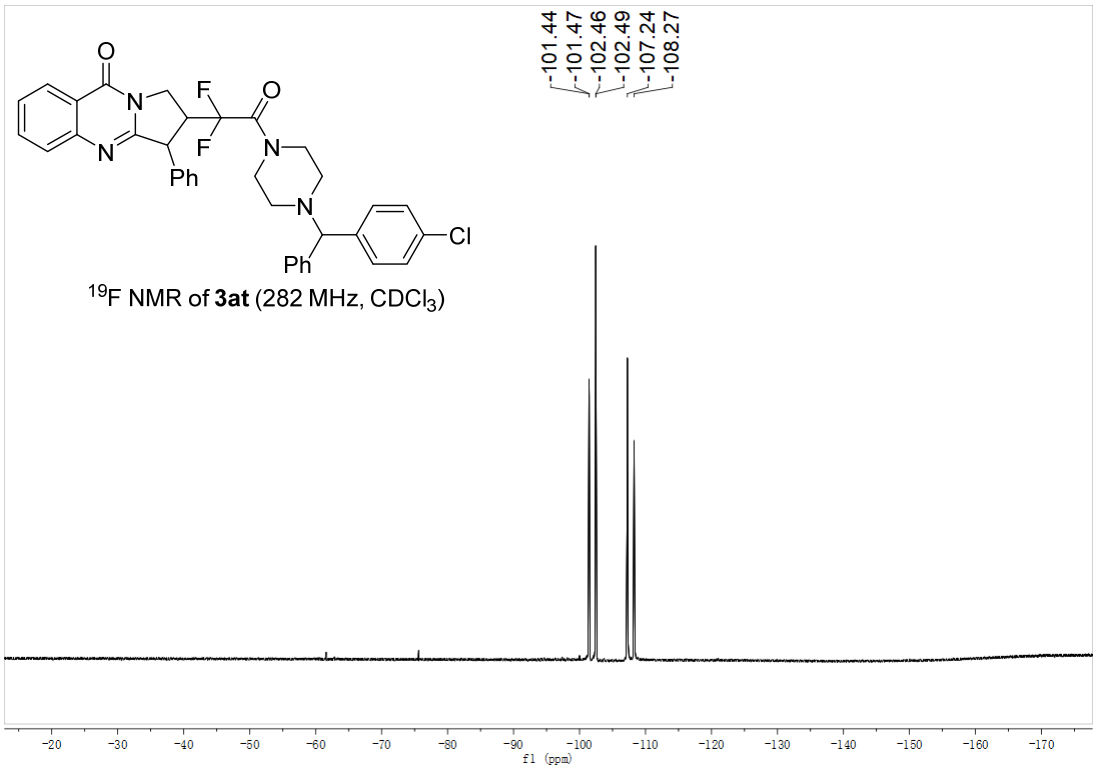
^{19}F NMR of **3as** (282 MHz, $CDCl_3$)



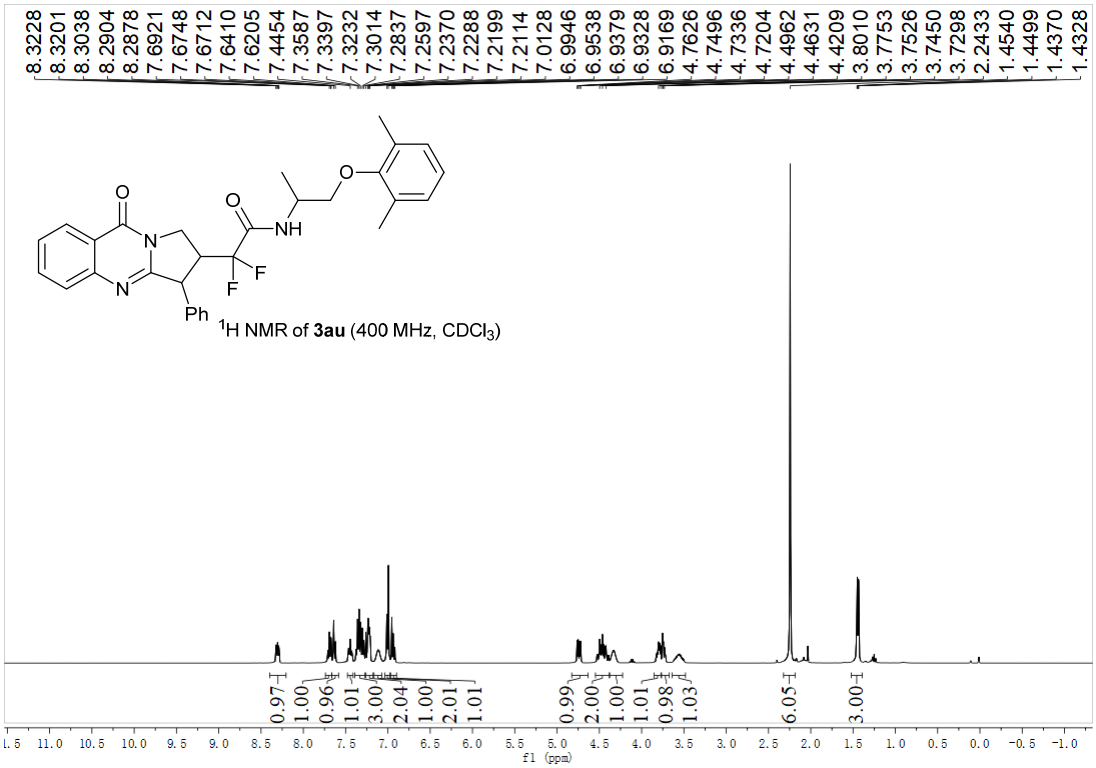
^{1}H NMR of **3at** (400 MHz, $CDCl_3$)



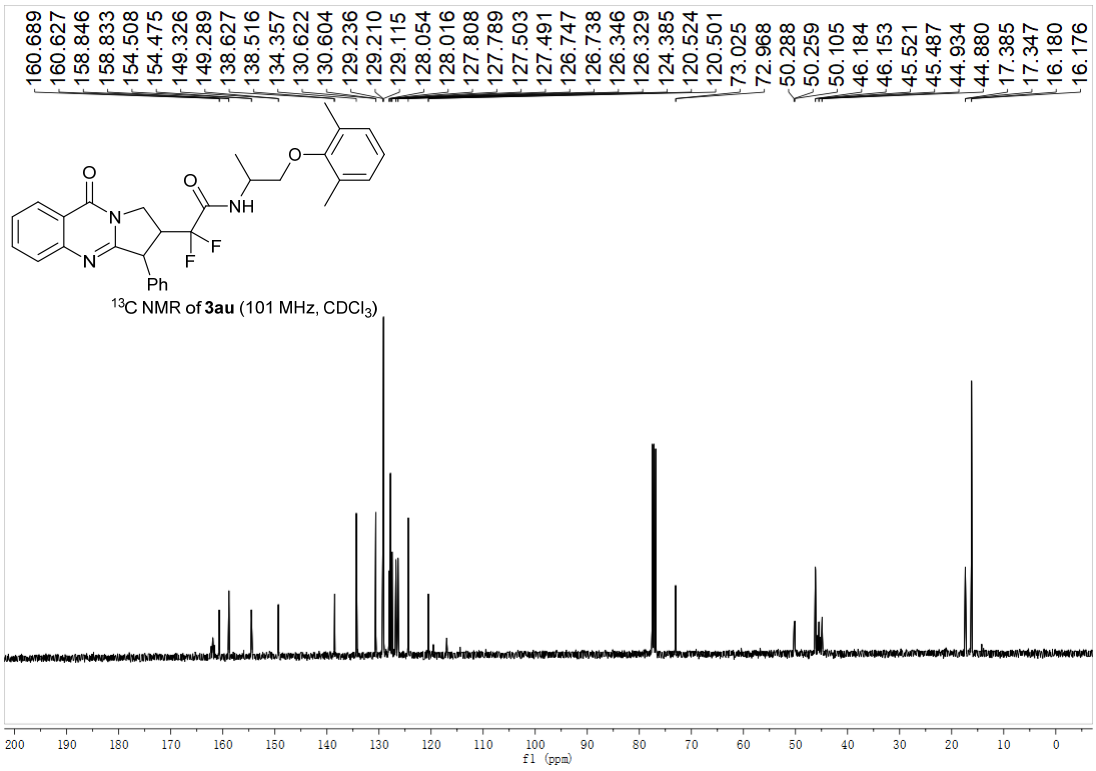
^{13}C NMR of **3at** (101 MHz, $CDCl_3$)



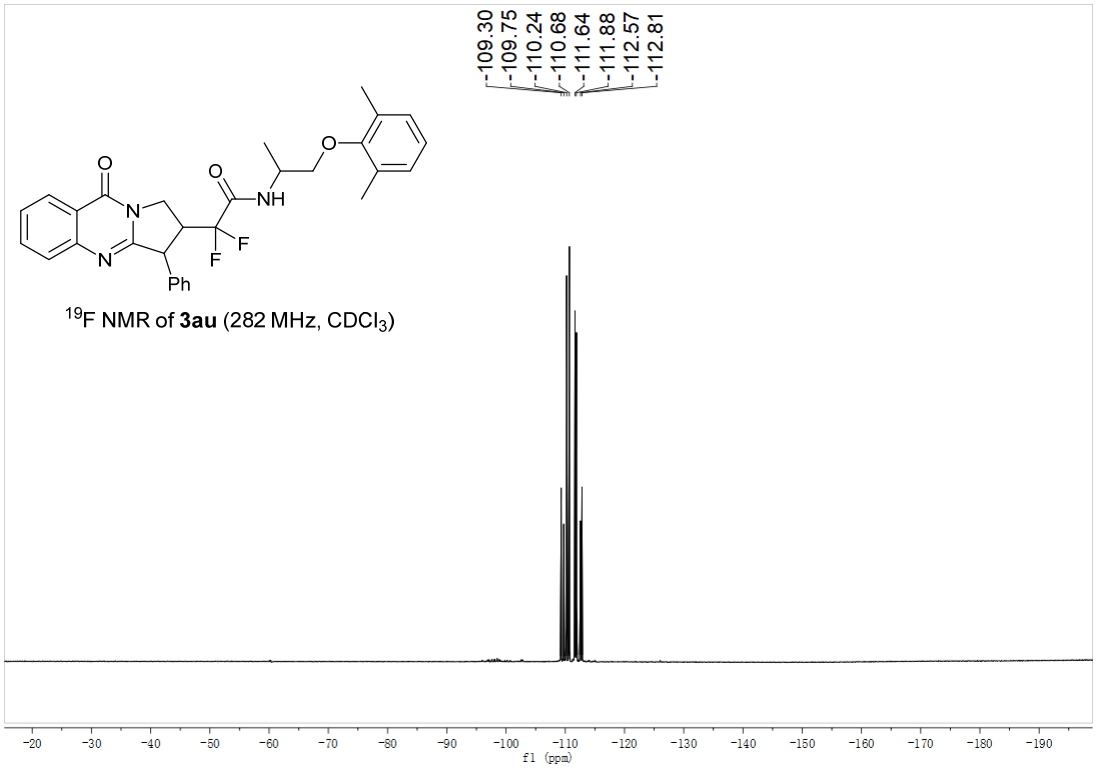
^{19}F NMR of **3at** (282 MHz, $CDCl_3$)



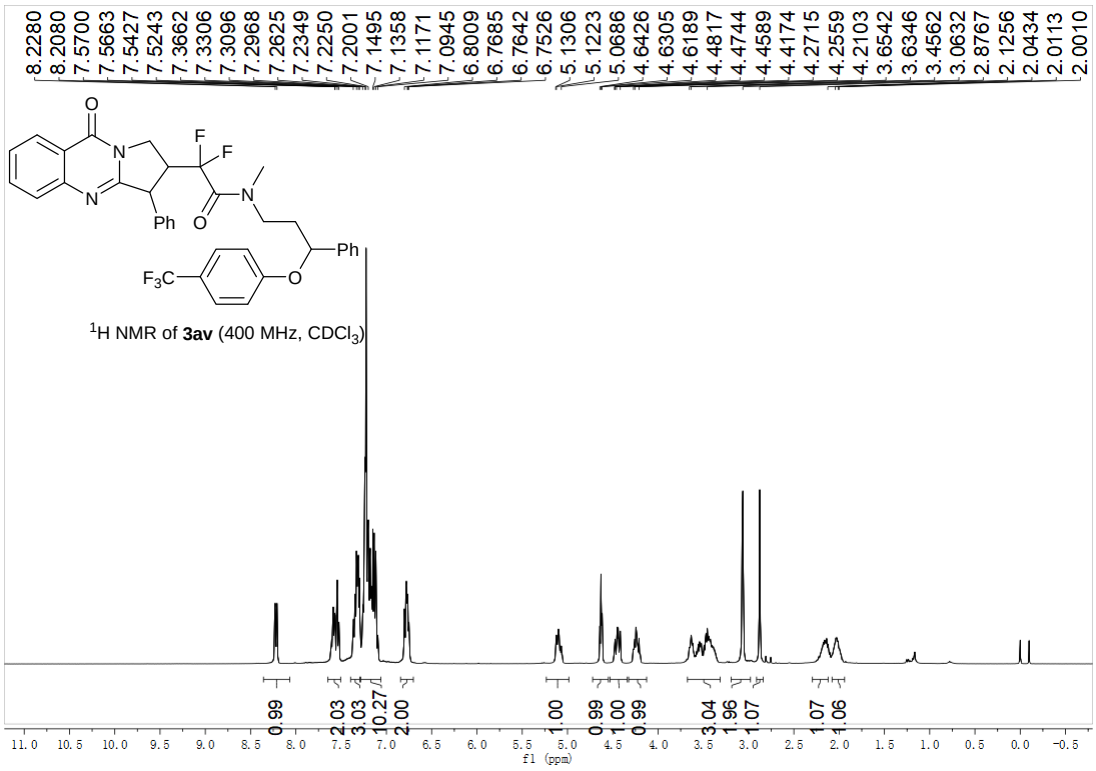
^{1}H NMR of **3au** (400 MHz, $CDCl_3$)



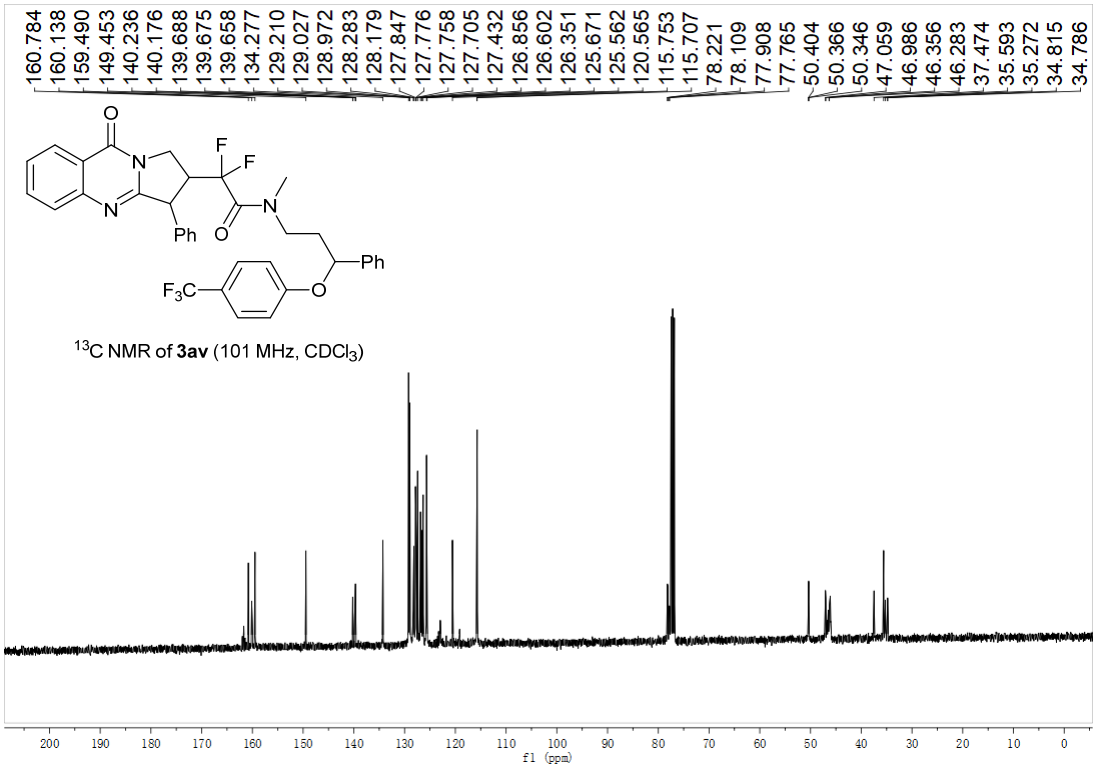
^{13}C NMR of **3au** (101 MHz, $CDCl_3$)



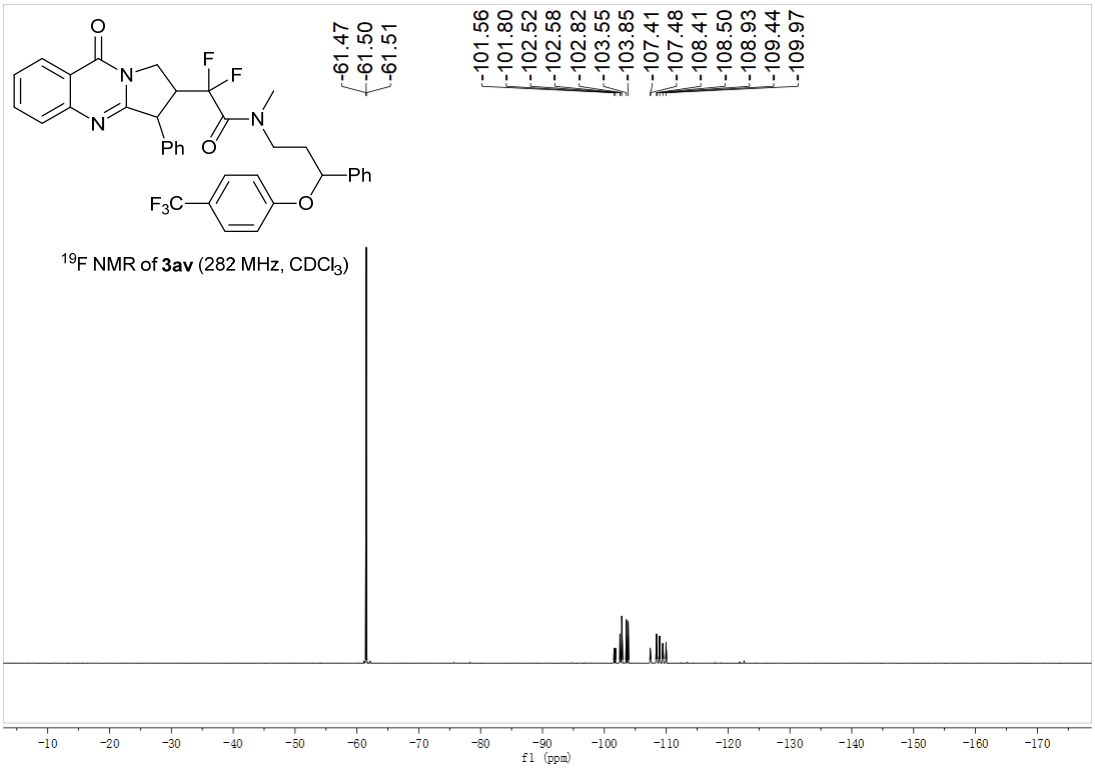
^{19}F NMR of **3au** (282 MHz, $CDCl_3$)

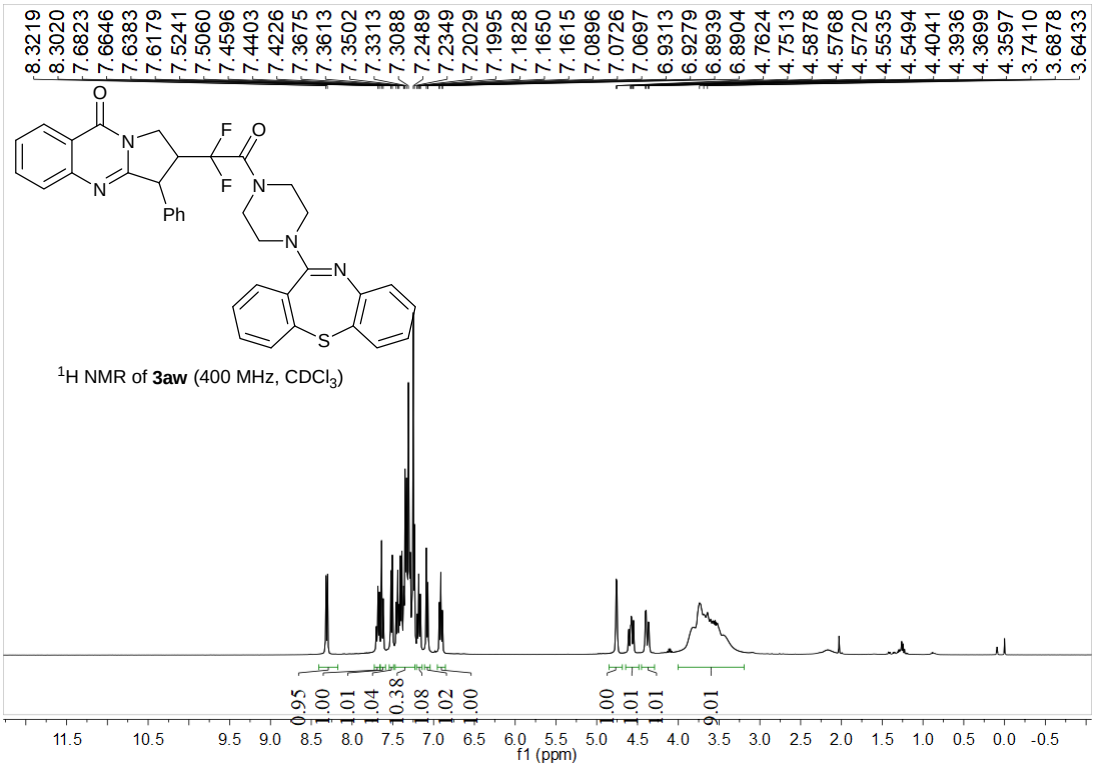


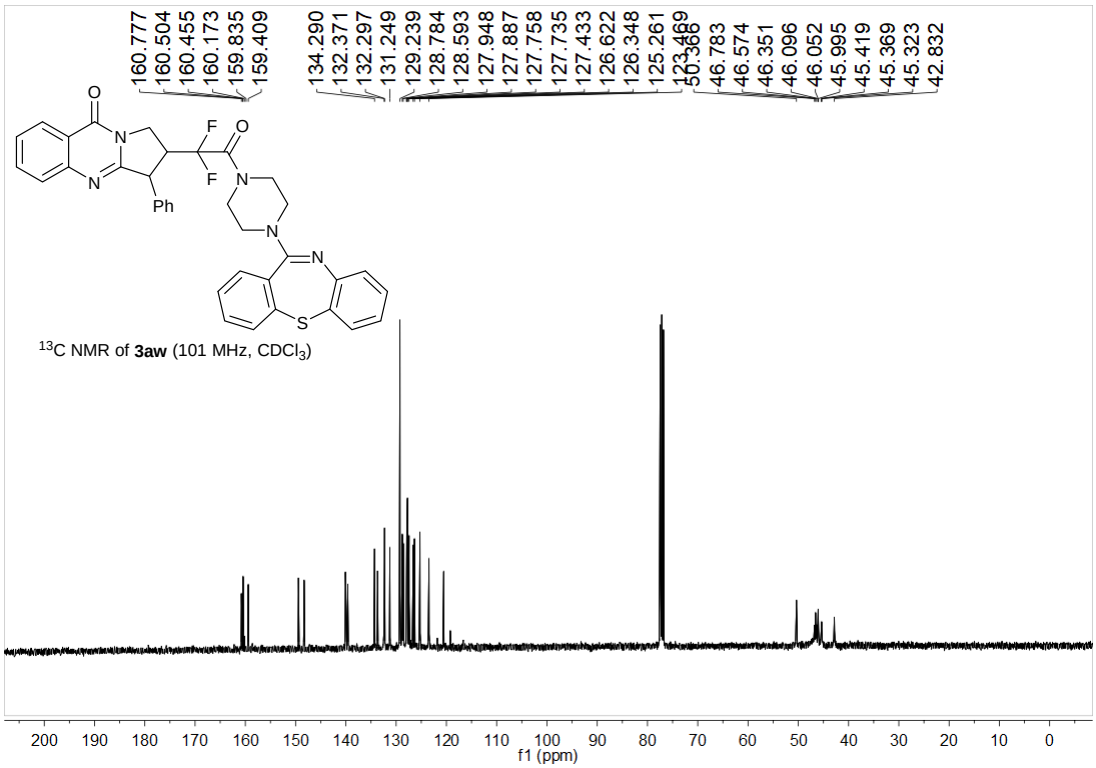
^{1}H NMR of **3av** (400 MHz, $CDCl_3$)



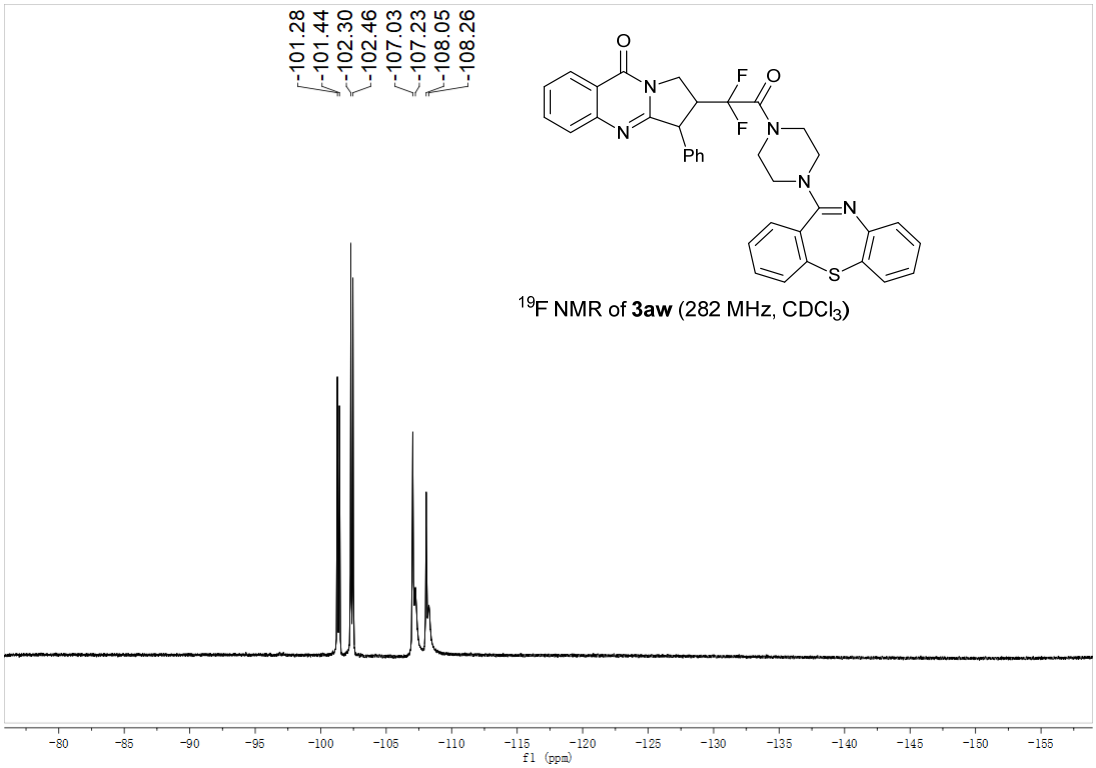
^{13}C NMR of **3av** (101 MHz, $CDCl_3$)


-61.47
-61.50
-61.51
-101.56
-101.80
-102.52
-102.58
-102.82
-103.55
-103.85
-107.41
-107.48
-108.41
-108.50
-108.93
-109.44
-109.97
F
F
O
N
N
Ph
O
N
Ph
F3C
O
19F NMR of 3av (282 MHz, CDCl3)
f1 (ppm)

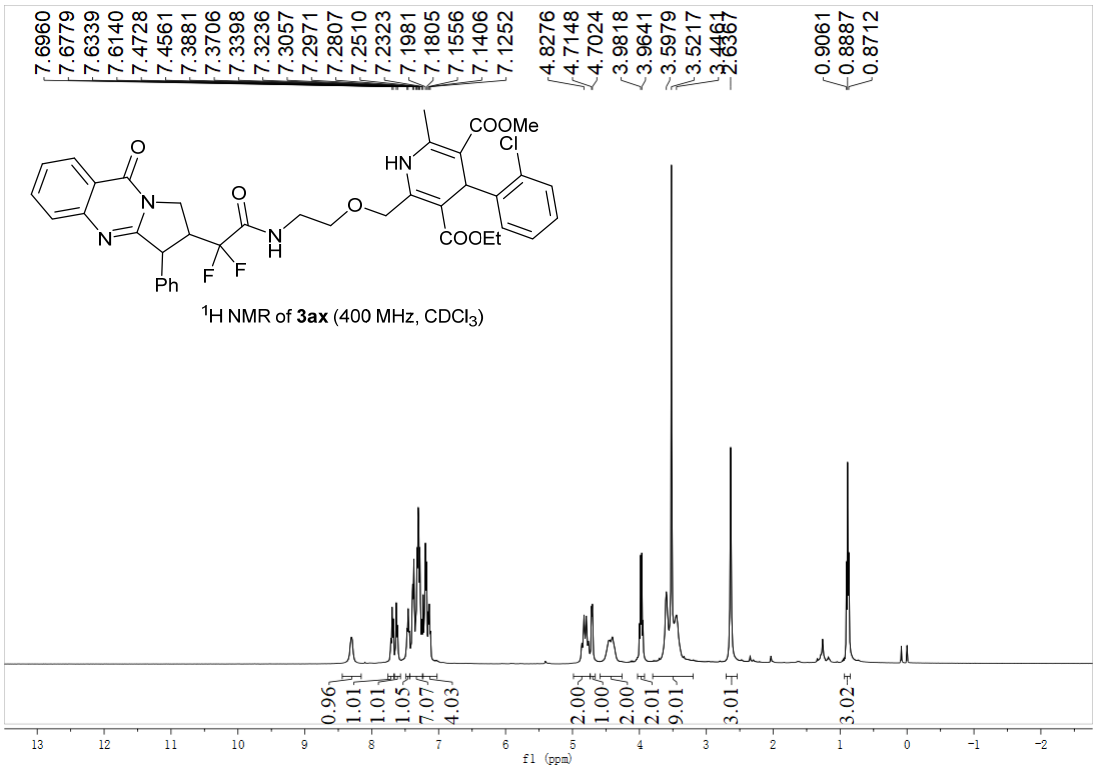

8.3219
8.3020
7.6823
7.6646
7.6383
7.6179
7.5241
7.5060
7.4596
7.4403
7.4226
7.3675
7.3613
7.3502
7.3313
7.3088
7.2489
7.2349
7.2029
7.1995
7.1828
7.1650
7.1615
7.0896
7.0726
7.0697
6.9313
6.9279
6.8939
6.8904
4.7624
4.7513
4.5878
4.5768
4.5720
4.5535
4.5494
4.4041
4.3936
4.3699
4.3597
3.7410
3.6878
3.6433
O
N
N
Ph
F
F
O
N
N
N
S
1H NMR of 3aw (400 MHz, CDCl3)
0.95
1.00
1.01
1.04
10.38
1.08
1.02
1.00
1.00
1.01
1.01
9.01
f1 (ppm)



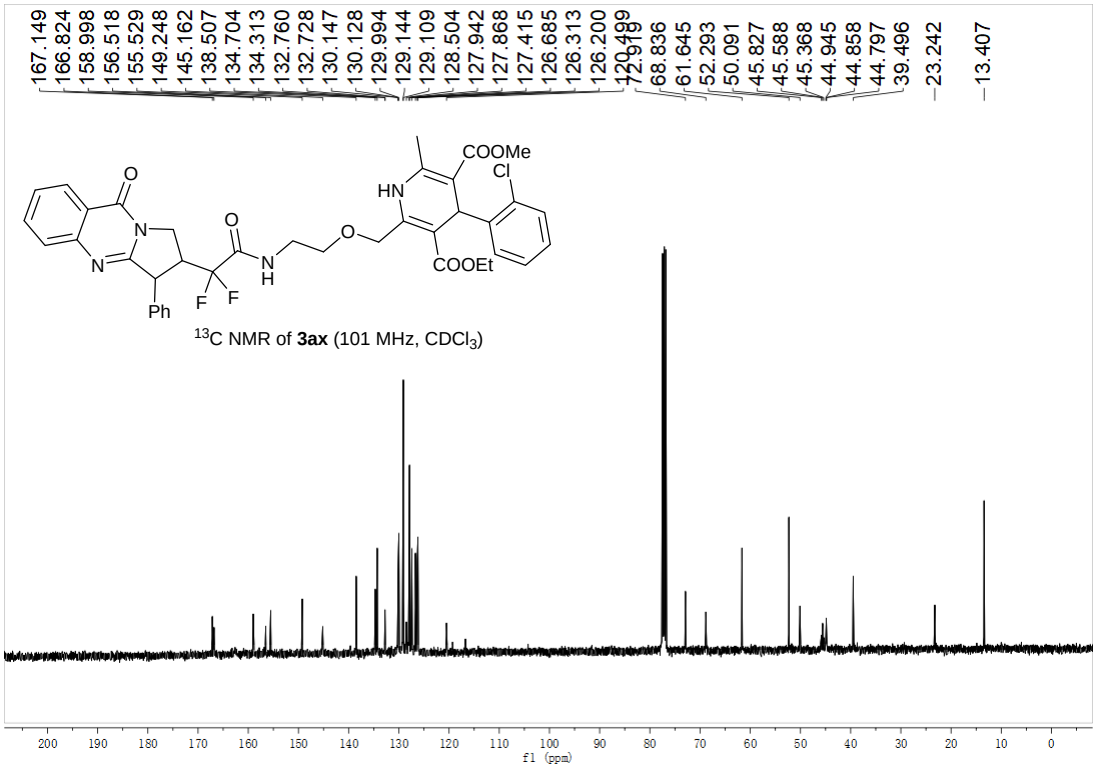
^{13}C NMR of **3aw** (101 MHz, $CDCl_3$)



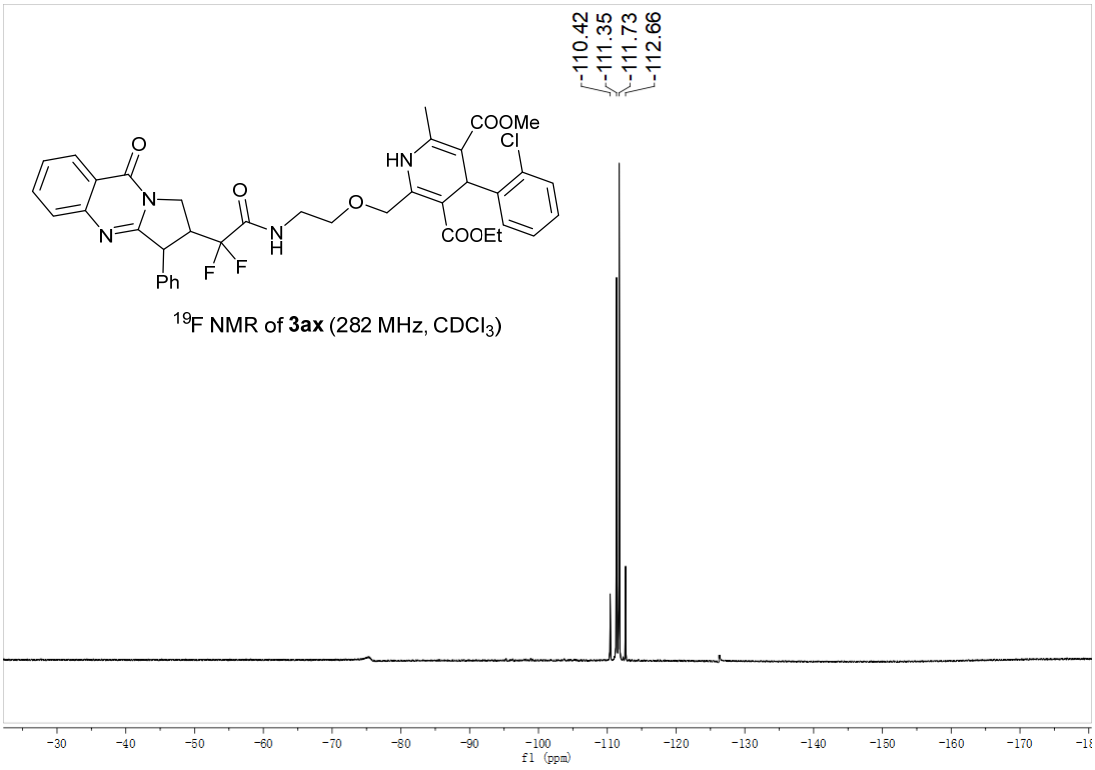
^{19}F NMR of **3aw** (282 MHz, $CDCl_3$)



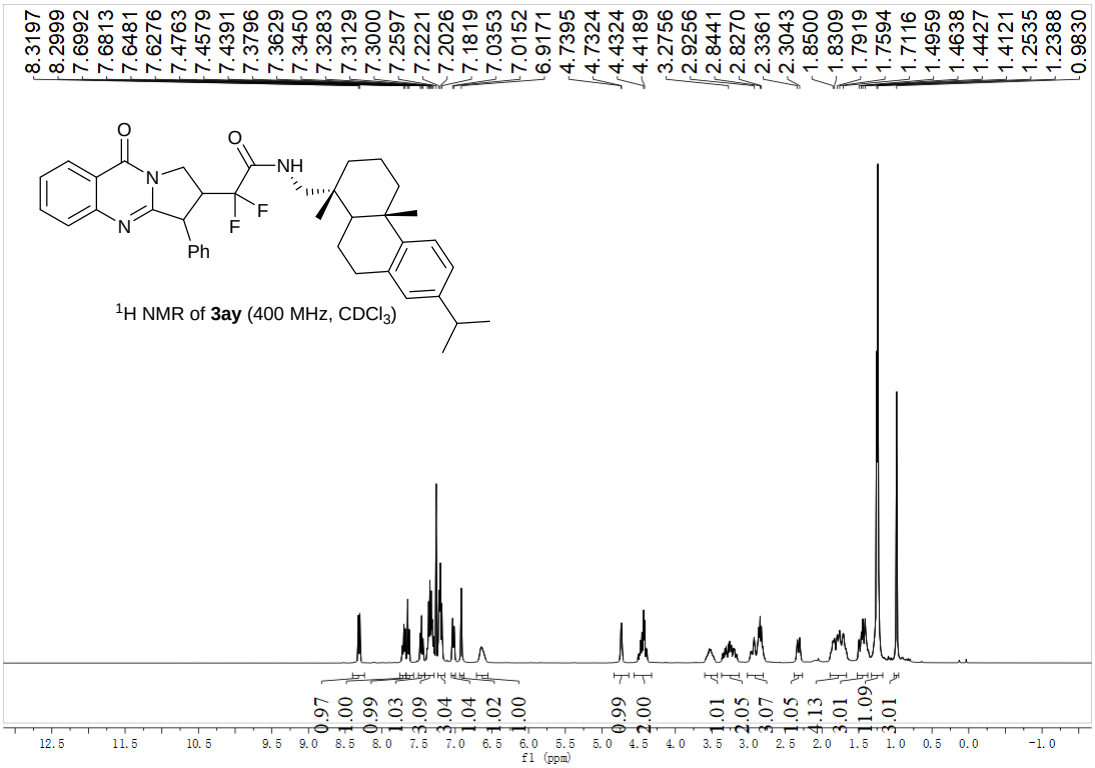
^{1}H NMR of **3ax** (400 MHz, $CDCl_3$)



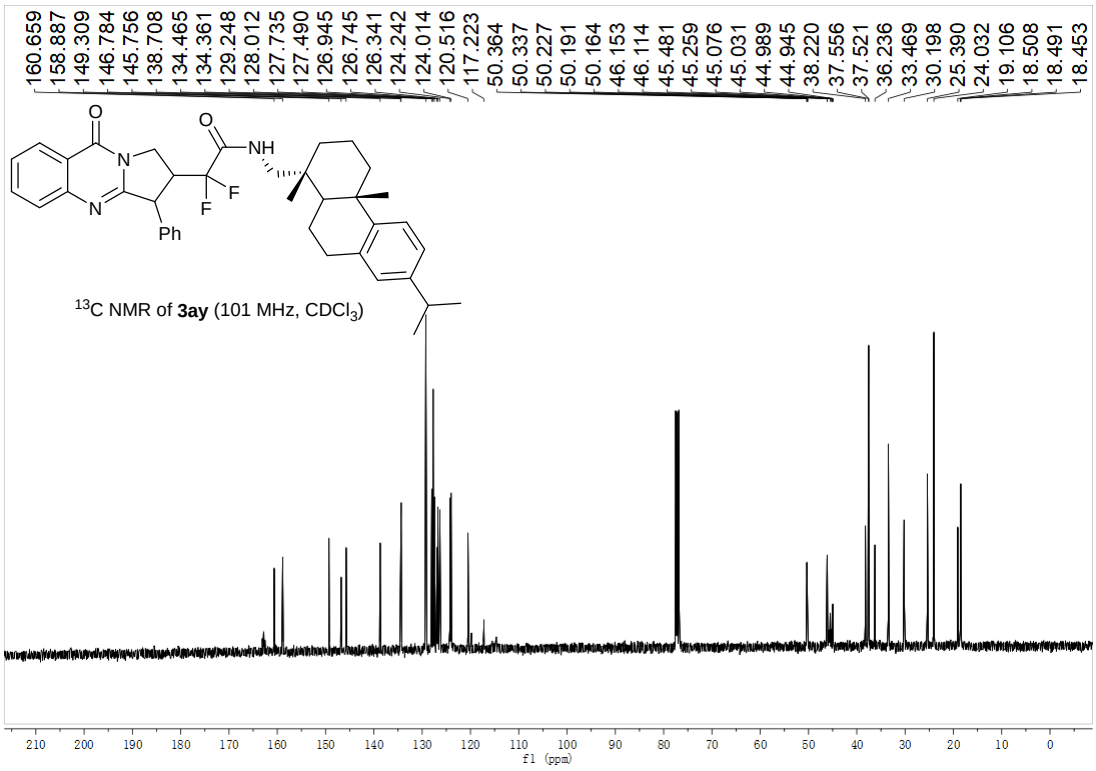
^{13}C NMR of **3ax** (101 MHz, $CDCl_3$)



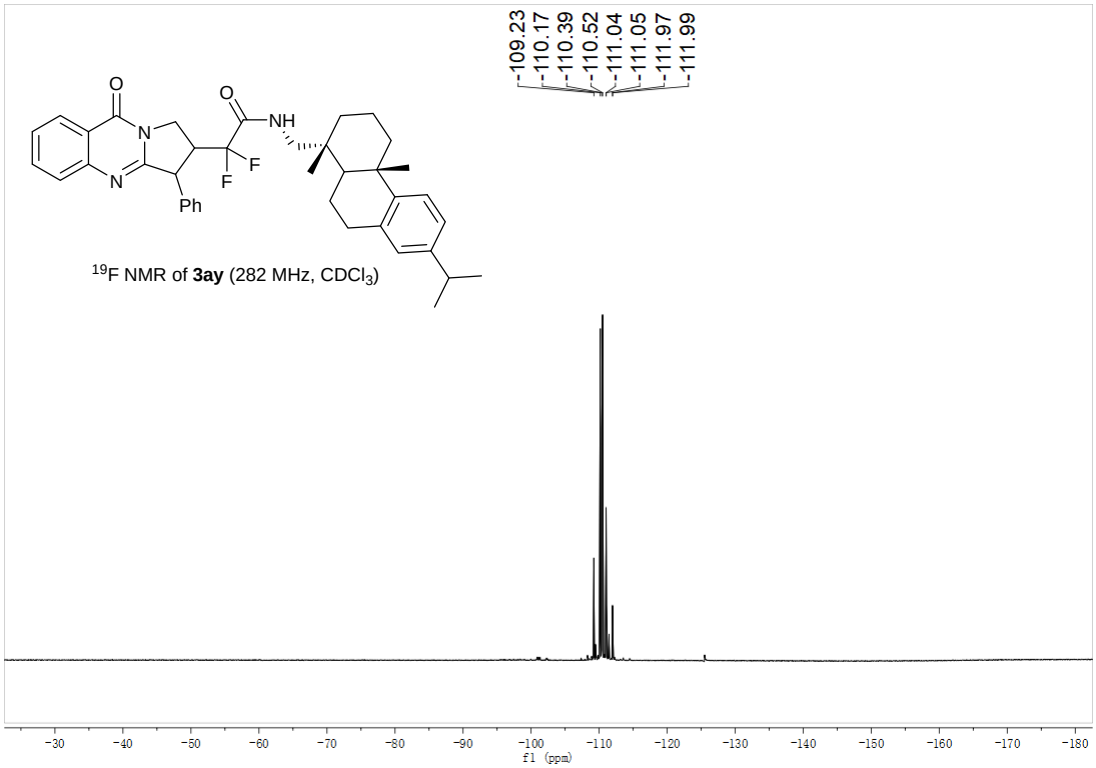
^{19}F NMR of **3ax** (282 MHz, $CDCl_3$)



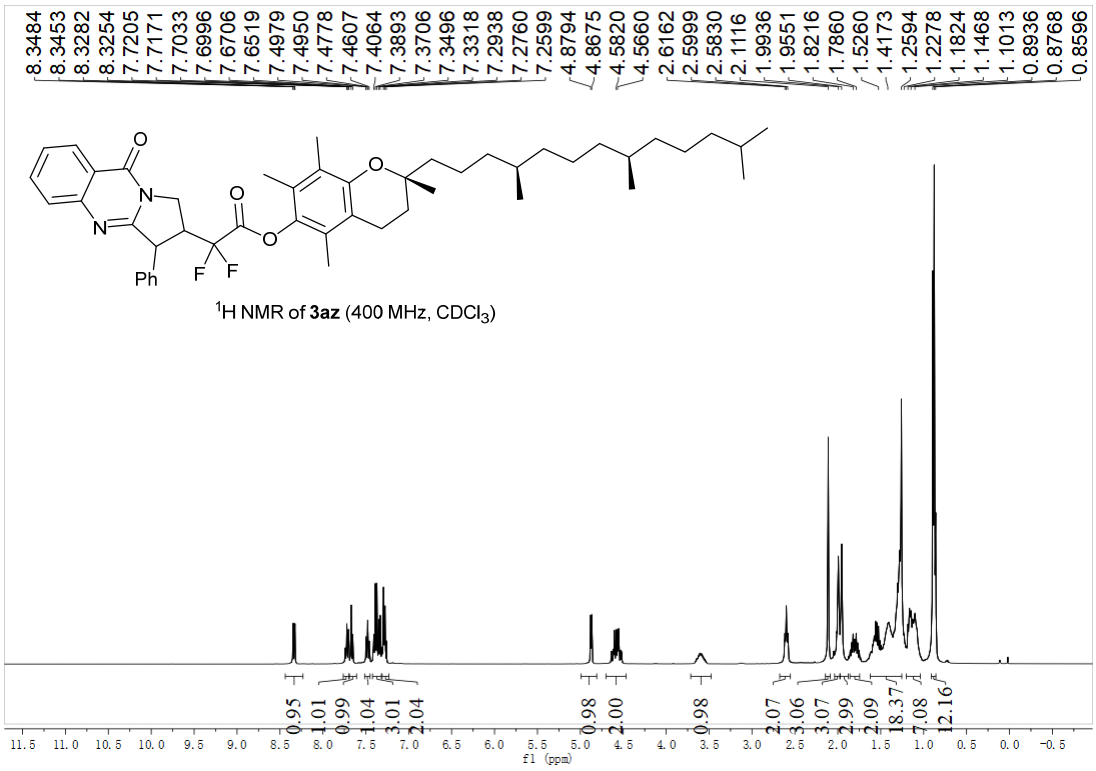
^{1}H NMR of **3ay** (400 MHz, $CDCl_3$)



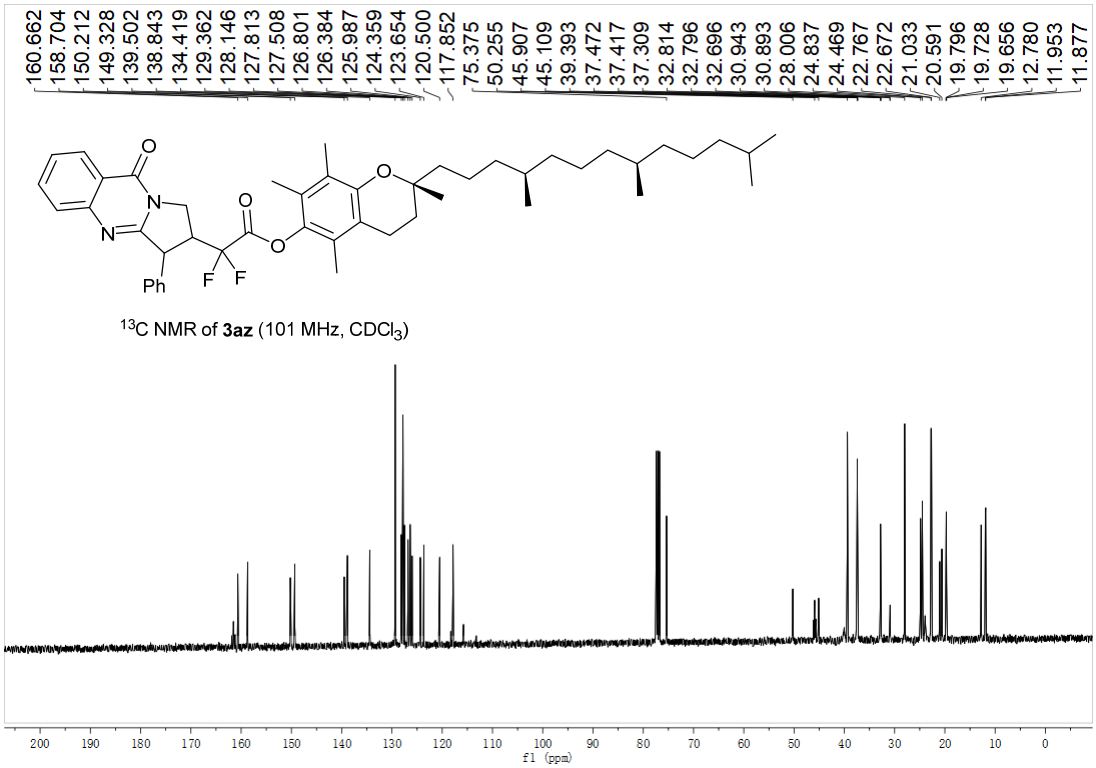
^{13}C NMR of **3ay** (101 MHz, $CDCl_3$)



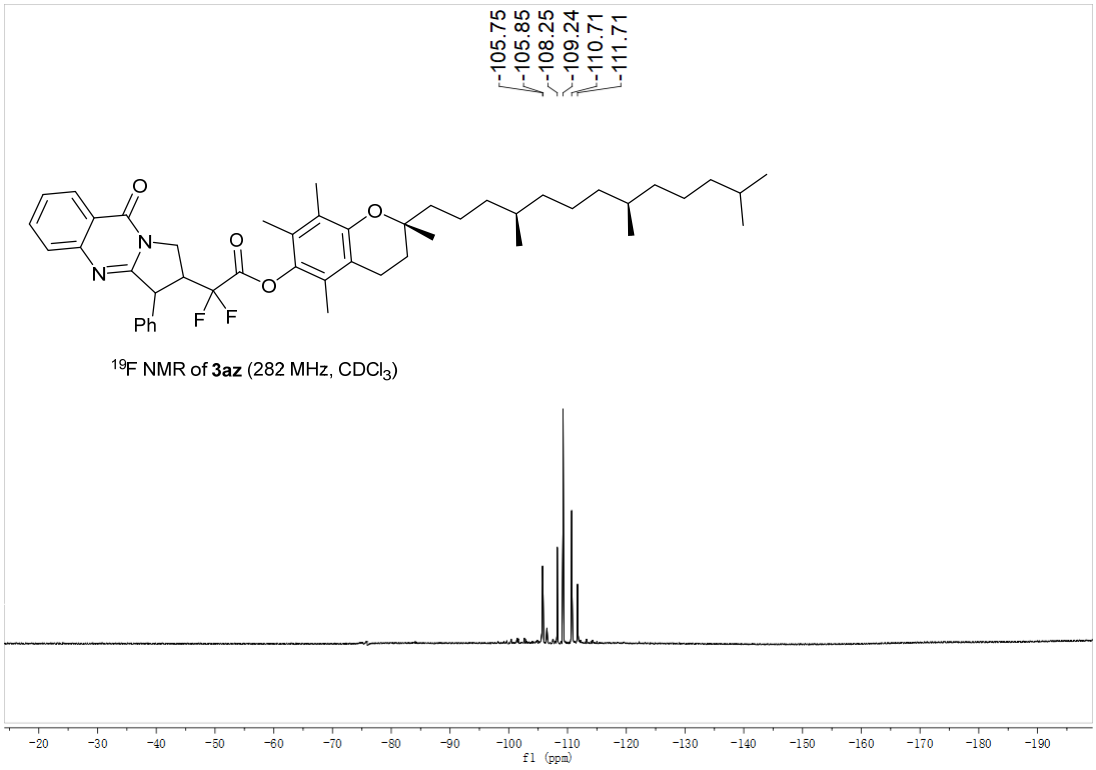
^{19}F NMR of **3ay** (282 MHz, $CDCl_3$)



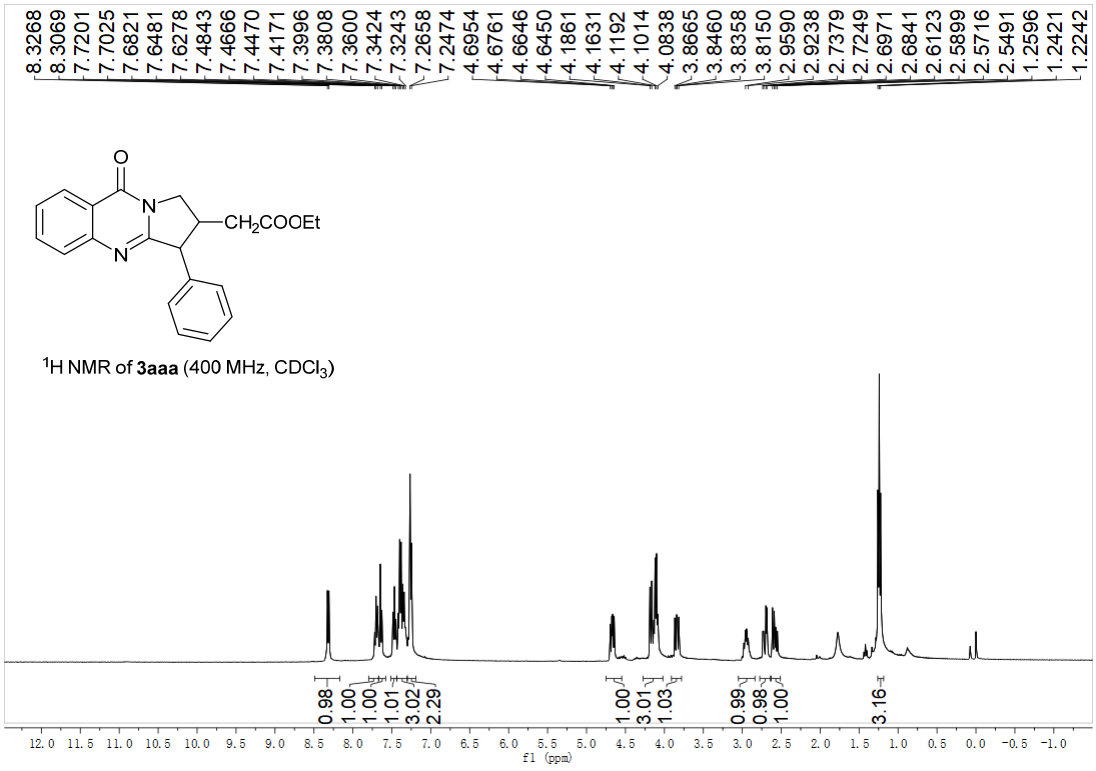
^{1}H NMR of **3az** (400 MHz, $CDCl_3$)



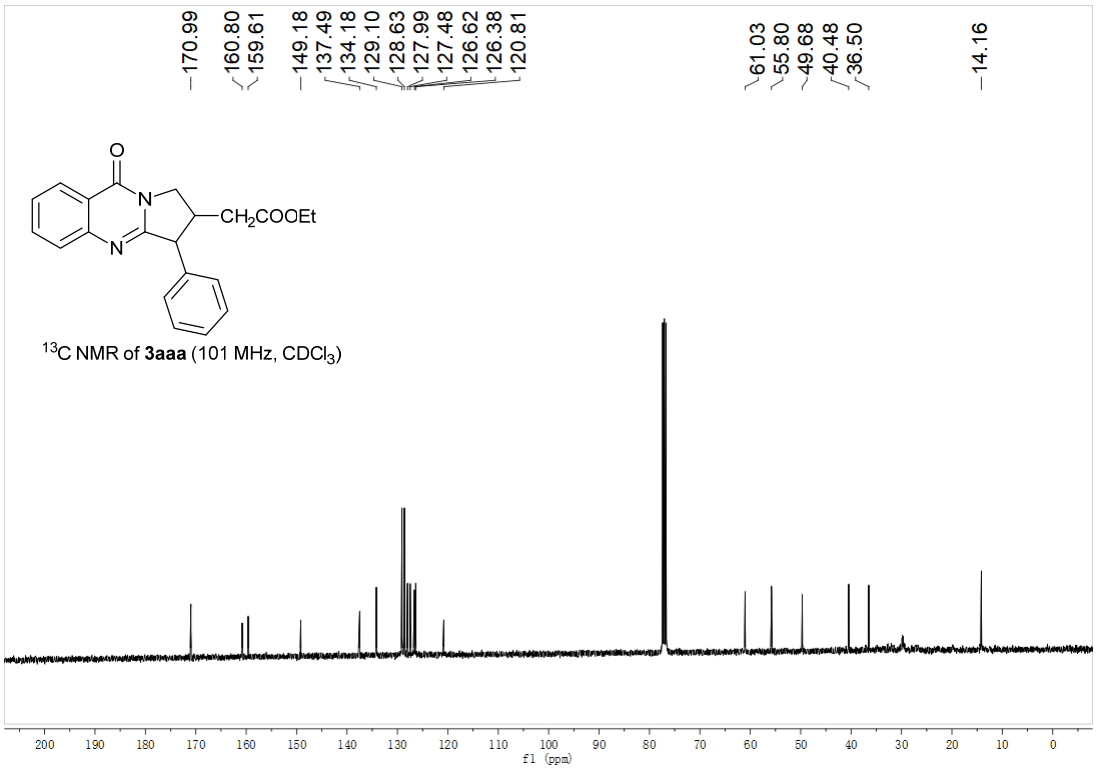
^{13}C NMR of **3az** (101 MHz, $CDCl_3$)



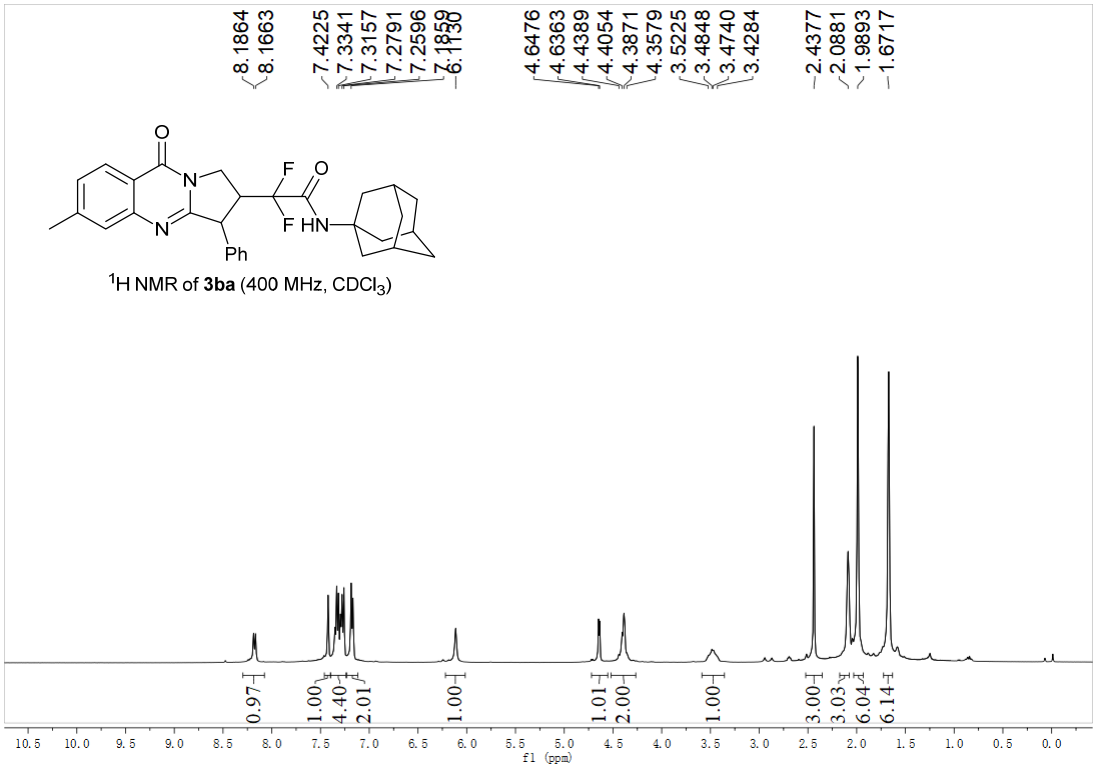
^{19}F NMR of **3az** (282 MHz, $CDCl_3$)



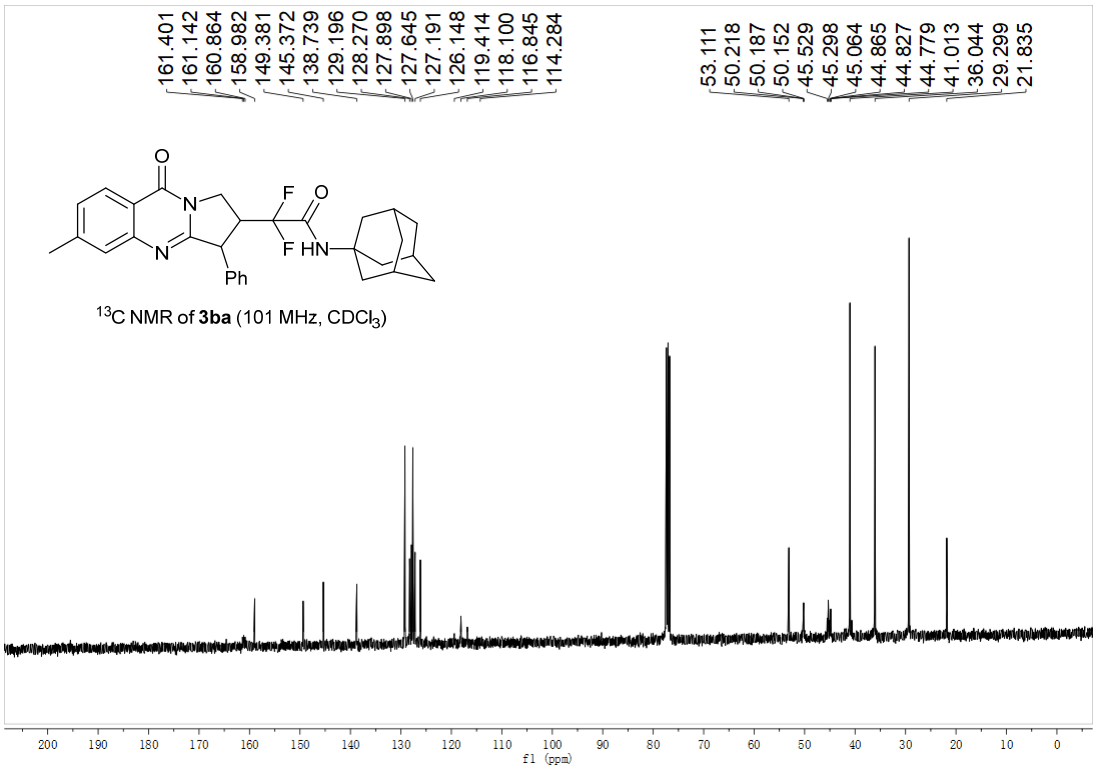
^{1}H NMR of **3aaa** (400 MHz, $CDCl_3$)



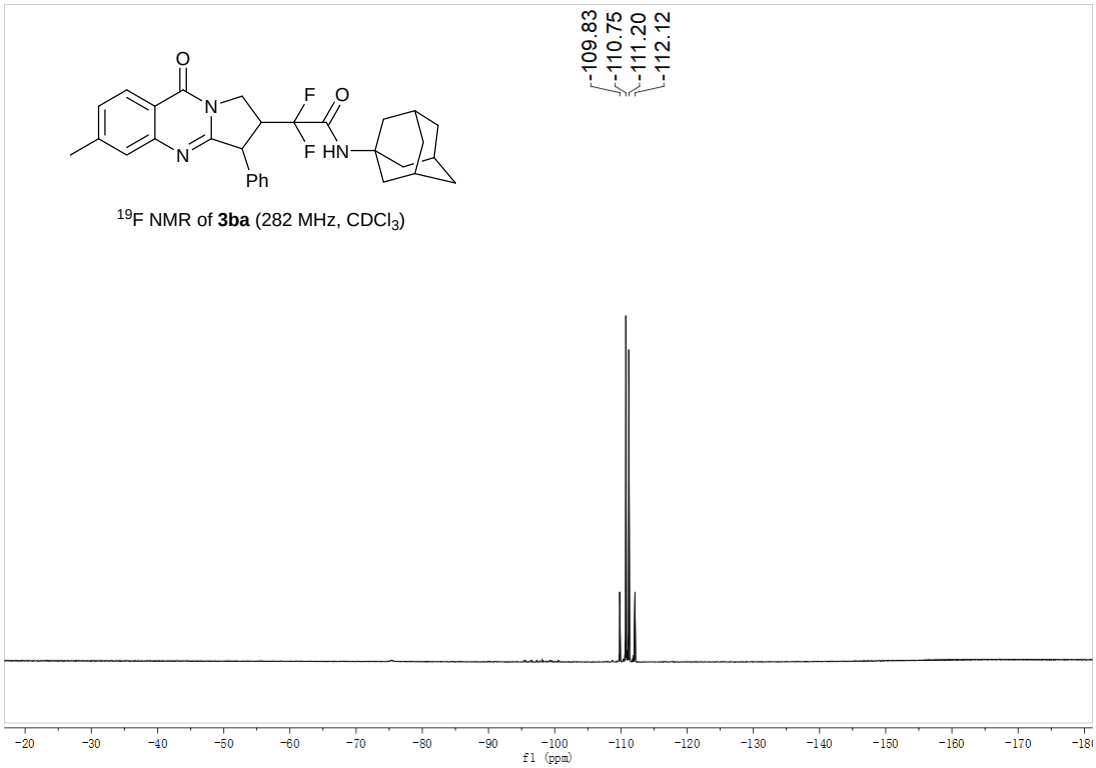
^{13}C NMR of **3aaa** (101 MHz, $CDCl_3$)



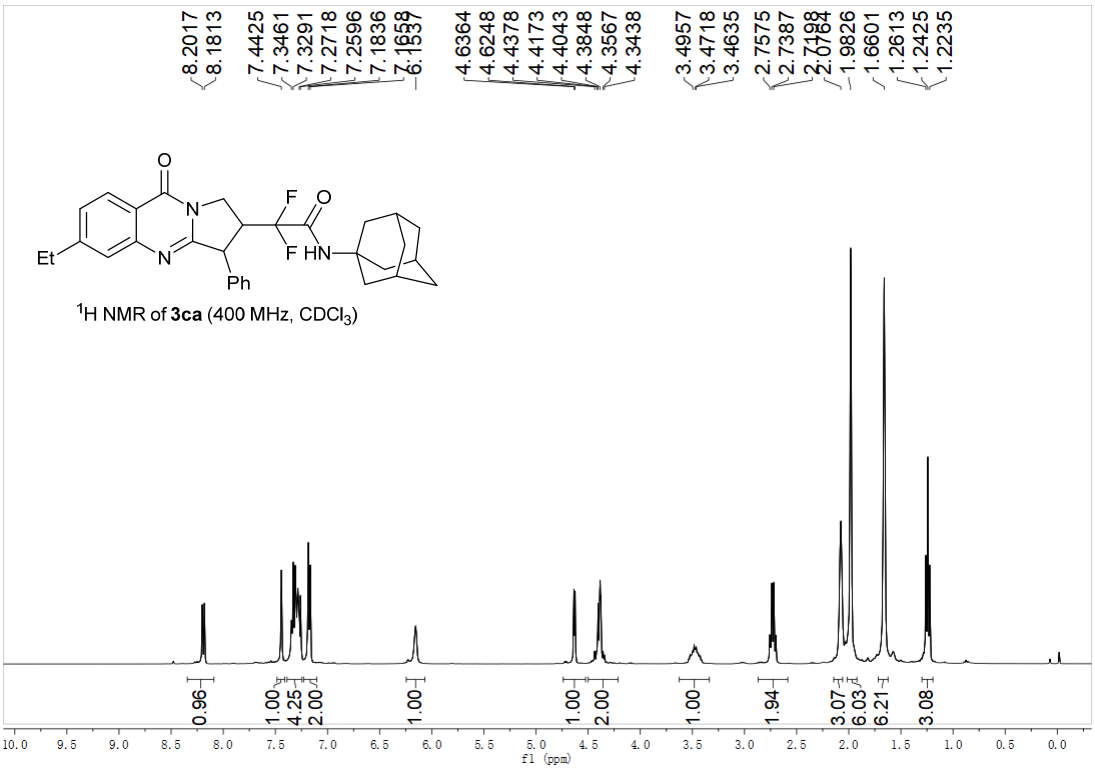
^{1}H NMR of **3ba** (400 MHz, $CDCl_3$)



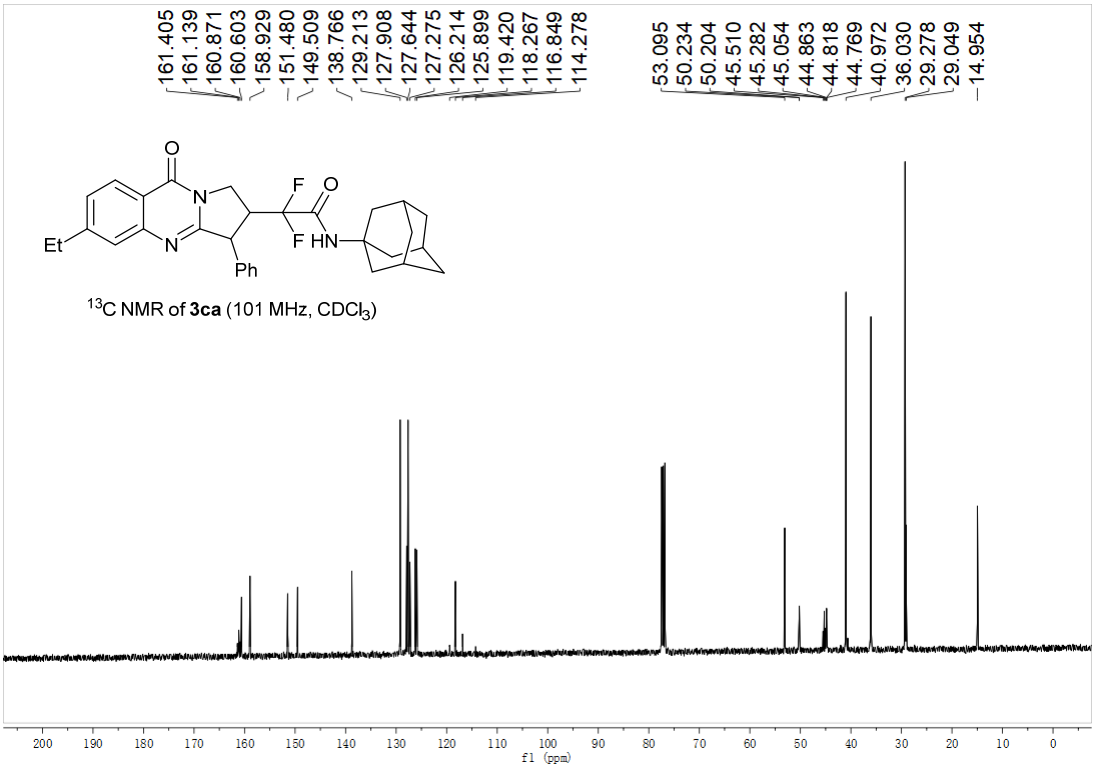
^{13}C NMR of **3ba** (101 MHz, $CDCl_3$)



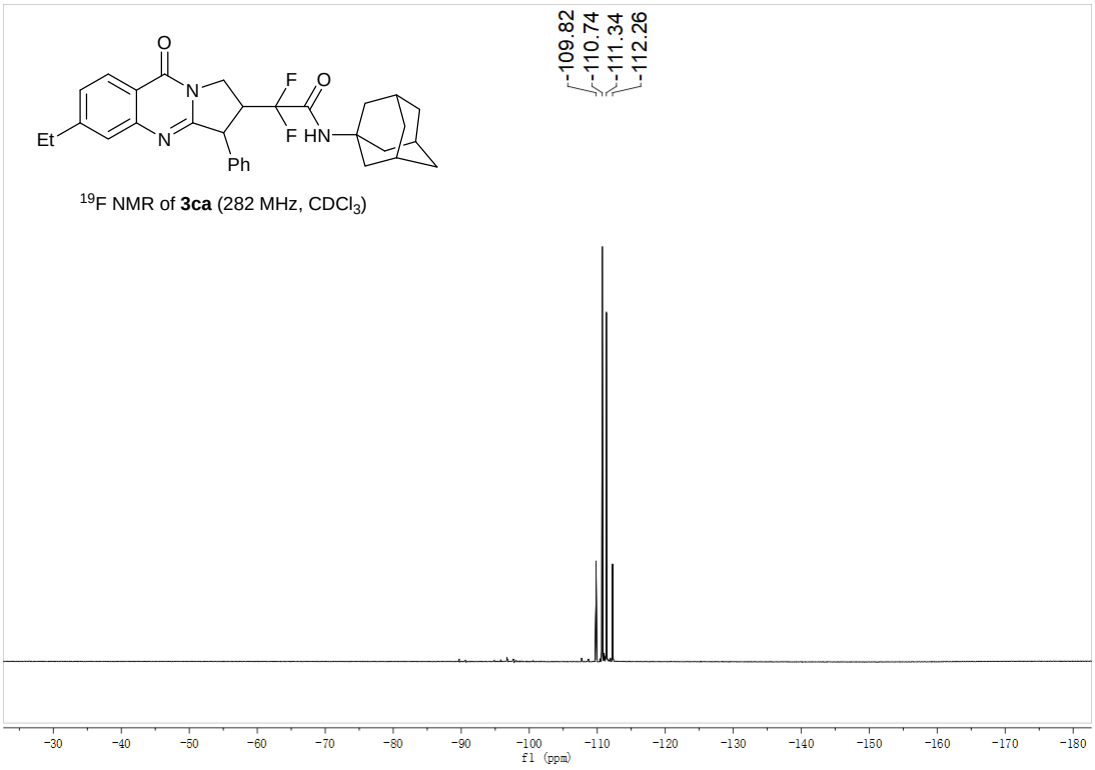
^{19}F NMR of **3ba** (282 MHz, $CDCl_3$)



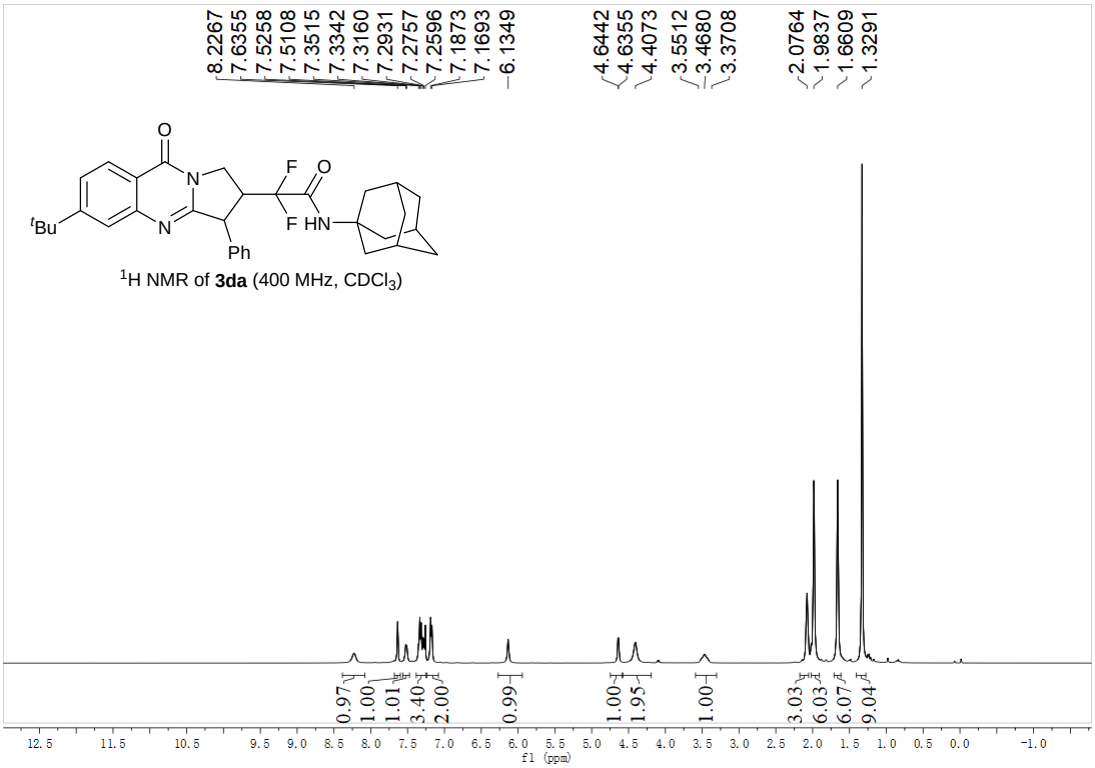
^{1}H NMR of **3ca** (400 MHz, $CDCl_3$)



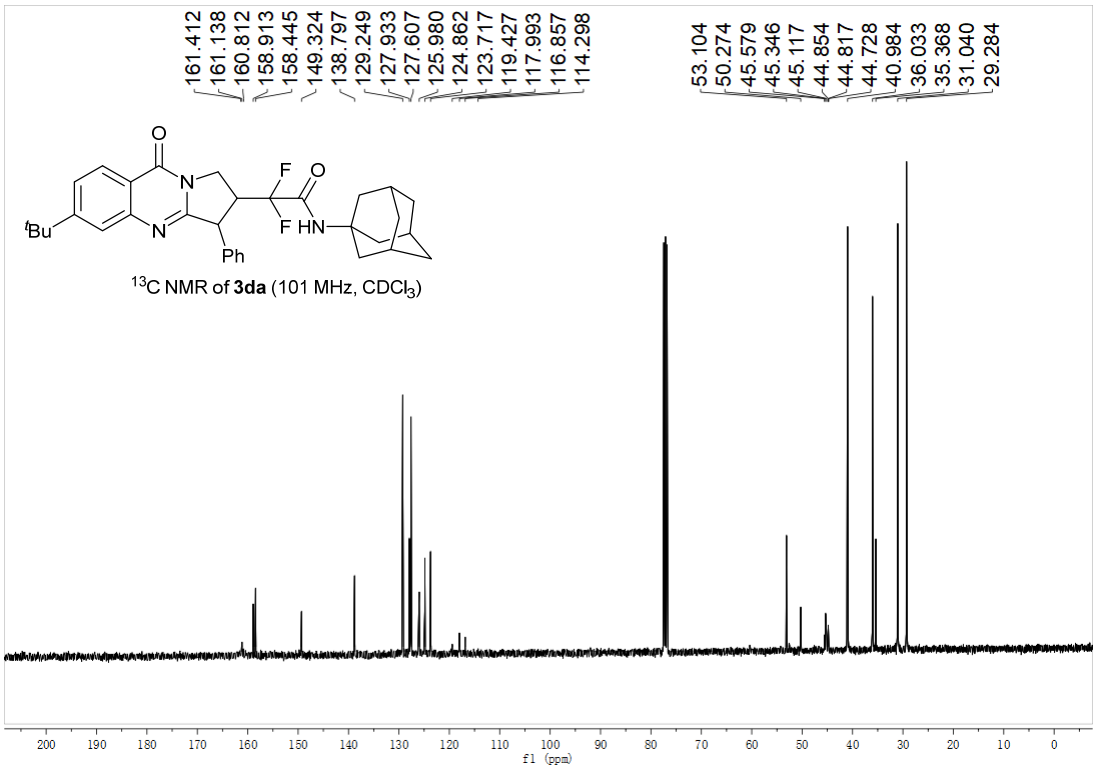
^{13}C NMR of **3ca** (101 MHz, $CDCl_3$)



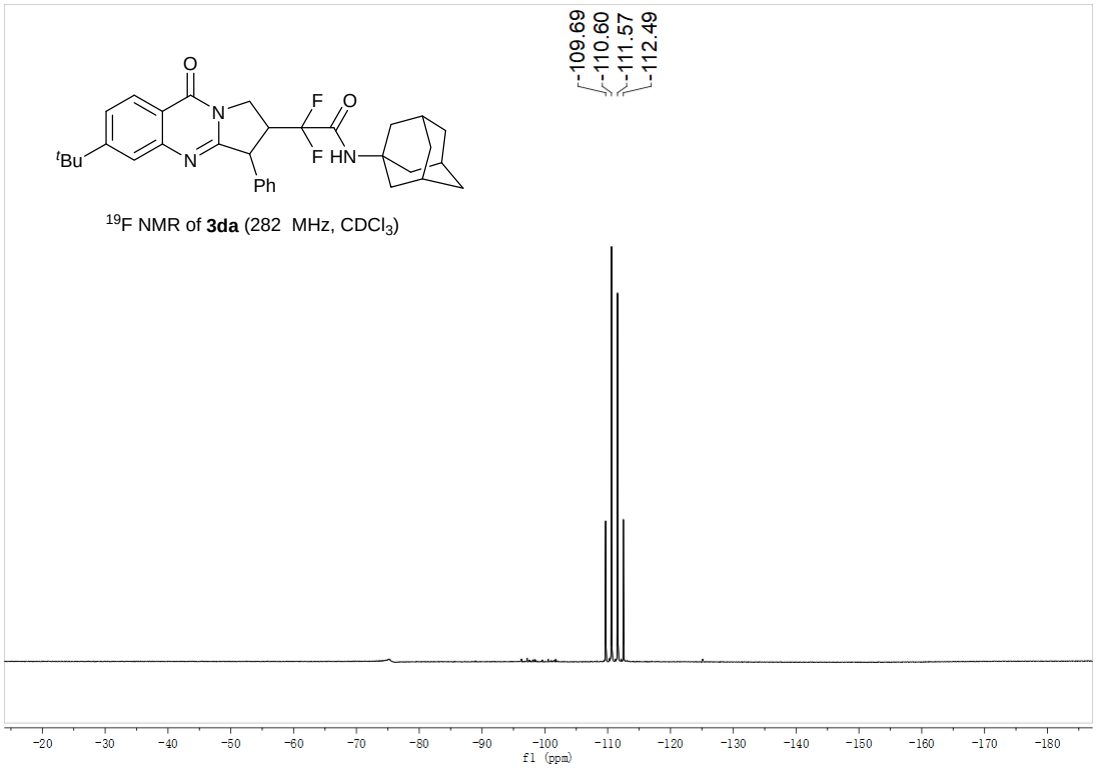
^{19}F NMR of **3ca** (282 MHz, $CDCl_3$)



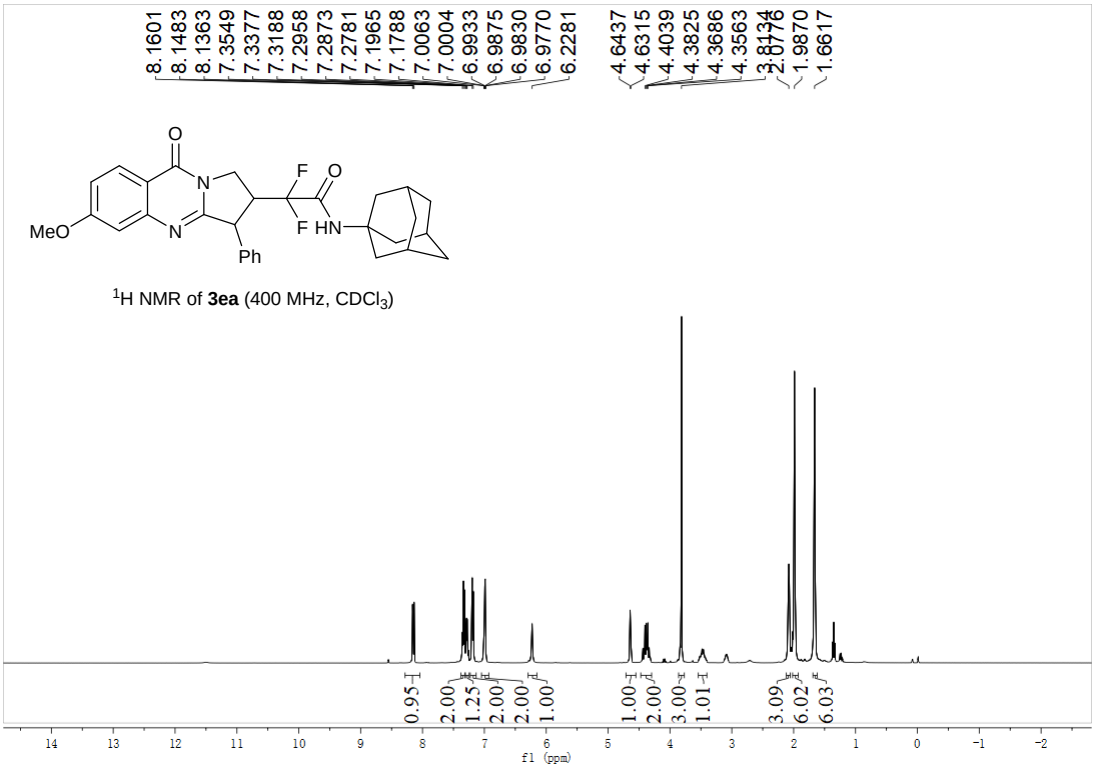
^{1}H NMR of **3da** (400 MHz, $CDCl_3$)



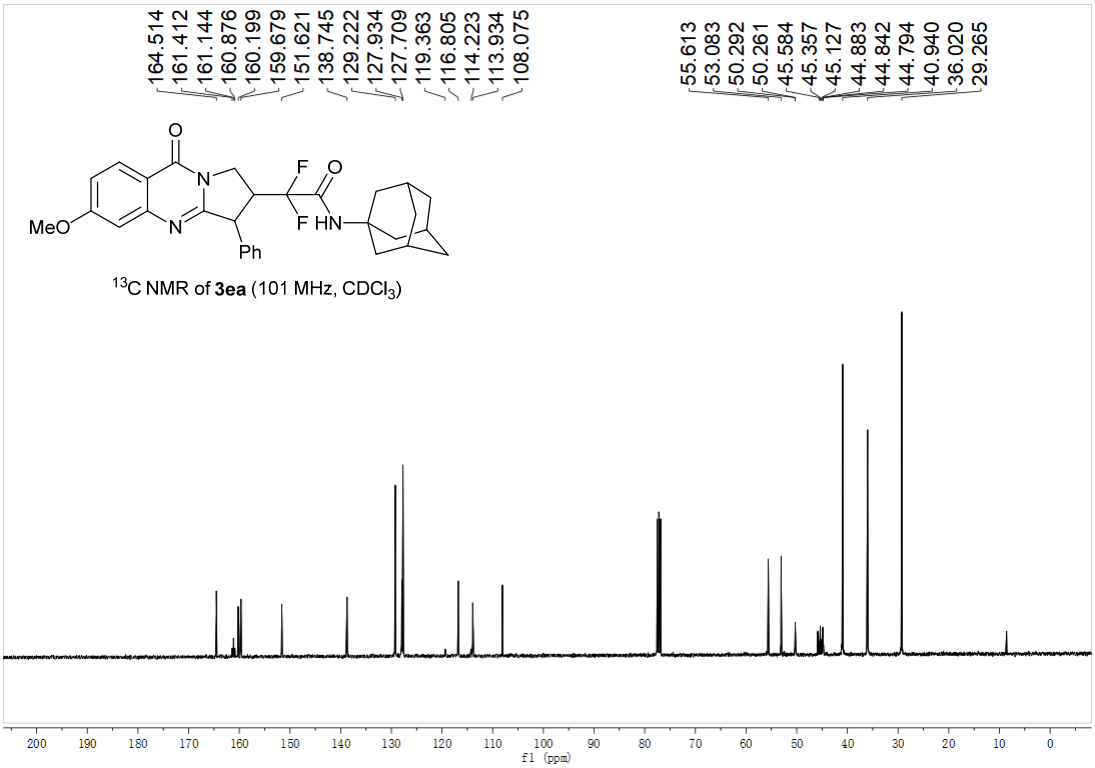
^{13}C NMR of **3da** (101 MHz, $CDCl_3$)



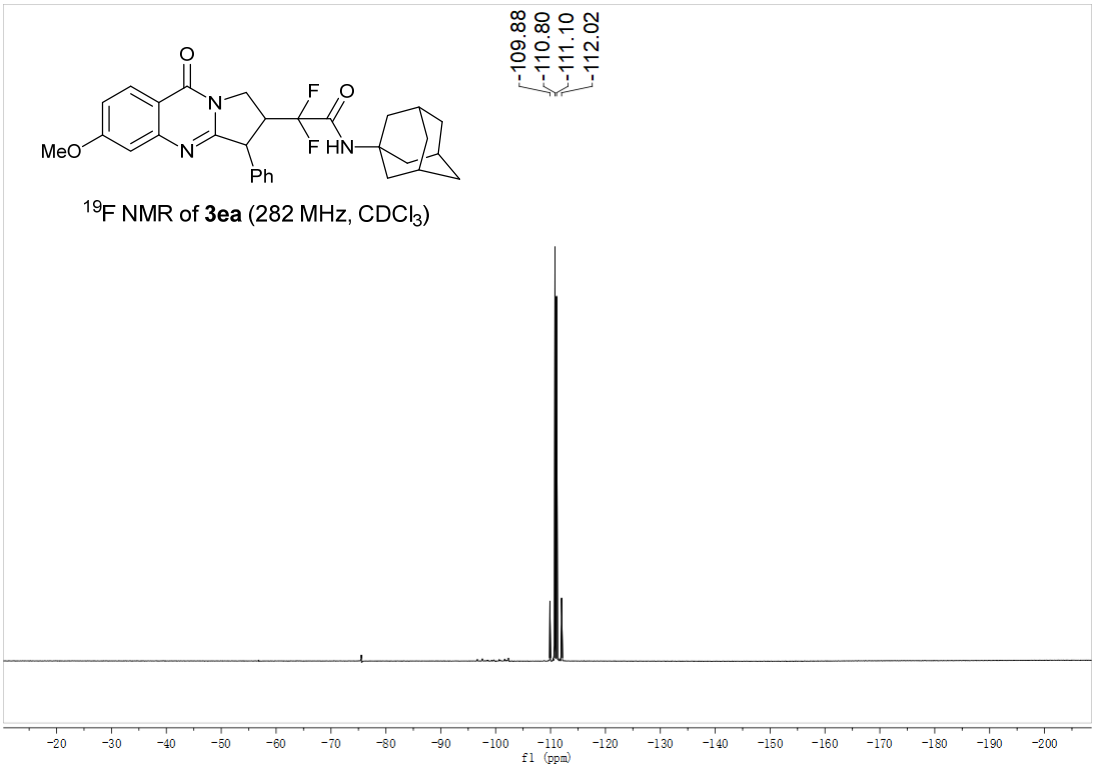
^{19}F NMR of **3da** (282 MHz, $CDCl_3$)



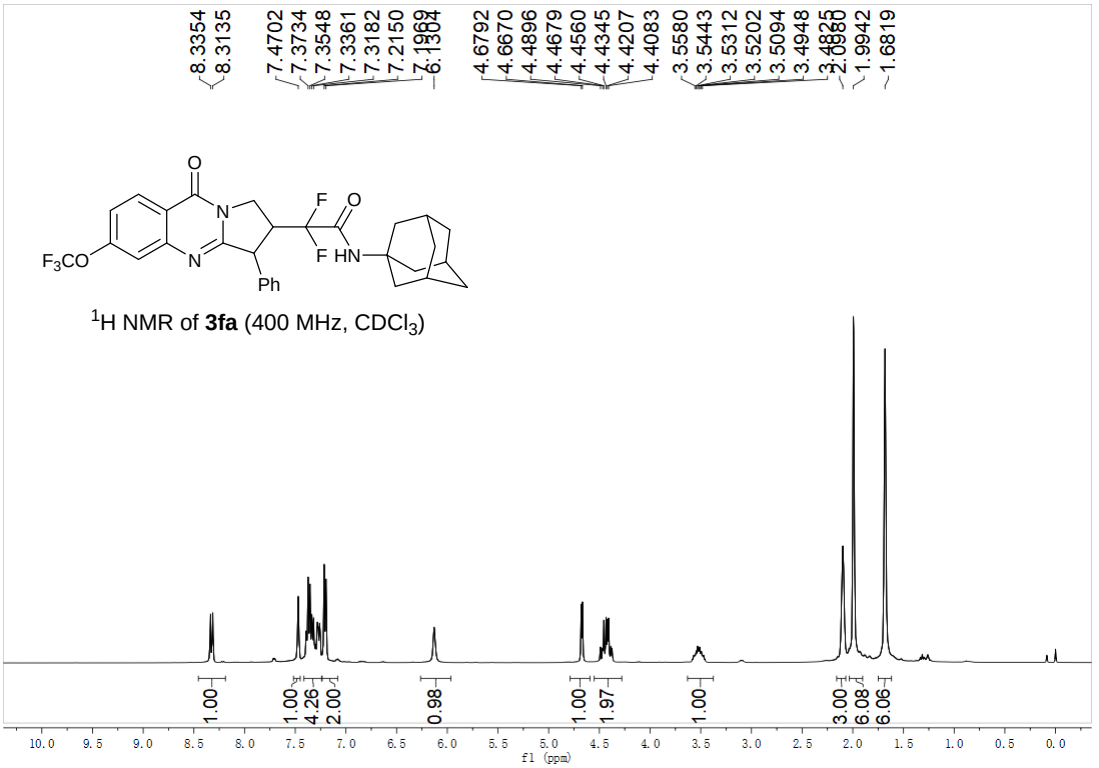
^{1}H NMR of **3ea** (400 MHz, $CDCl_3$)



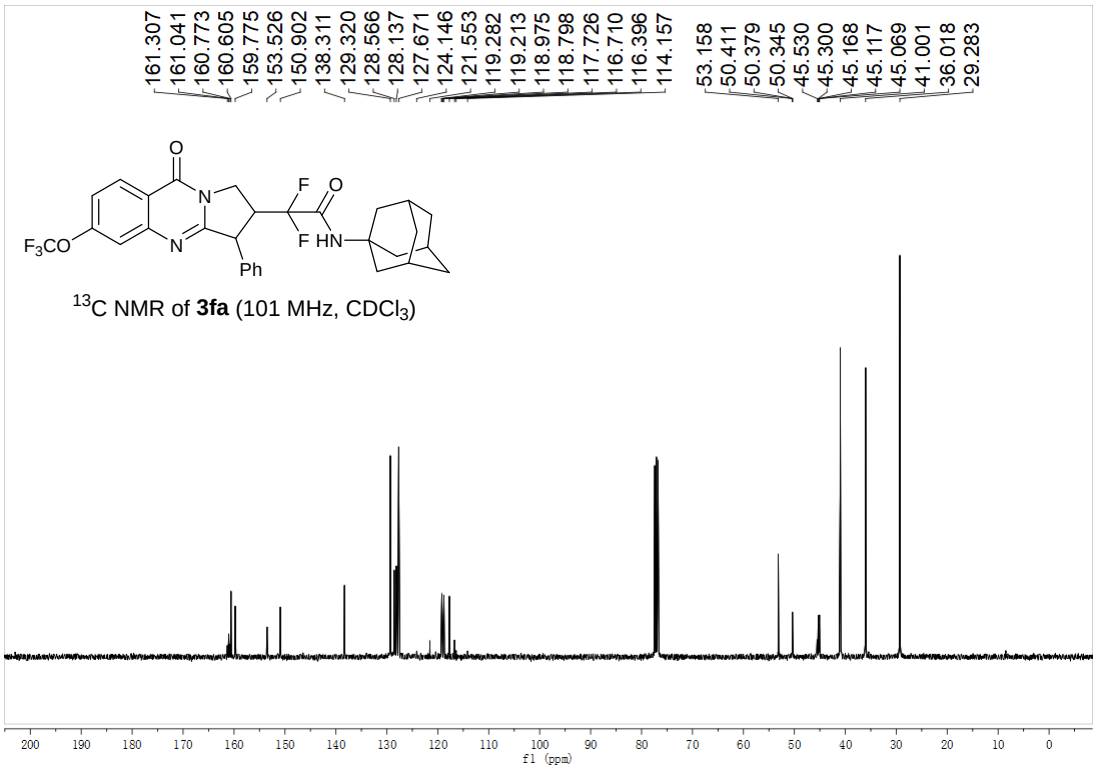
^{13}C NMR of **3ea** (101 MHz, $CDCl_3$)



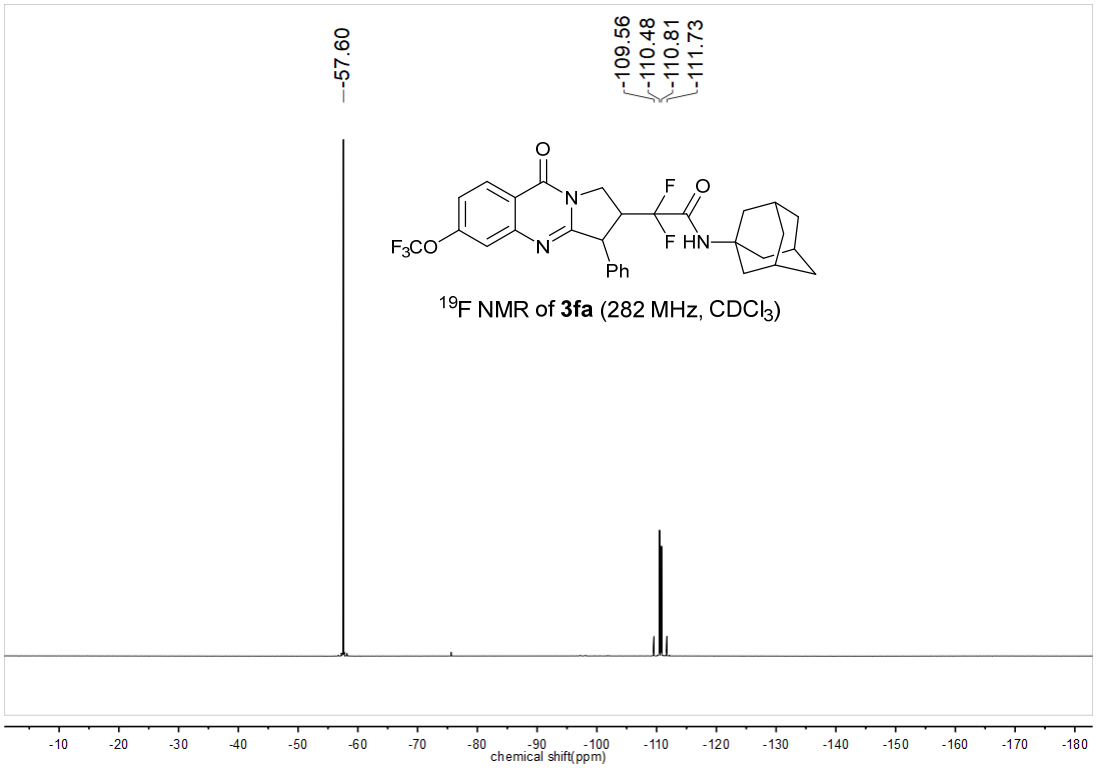
^{19}F NMR of **3ea** (282 MHz, $CDCl_3$)



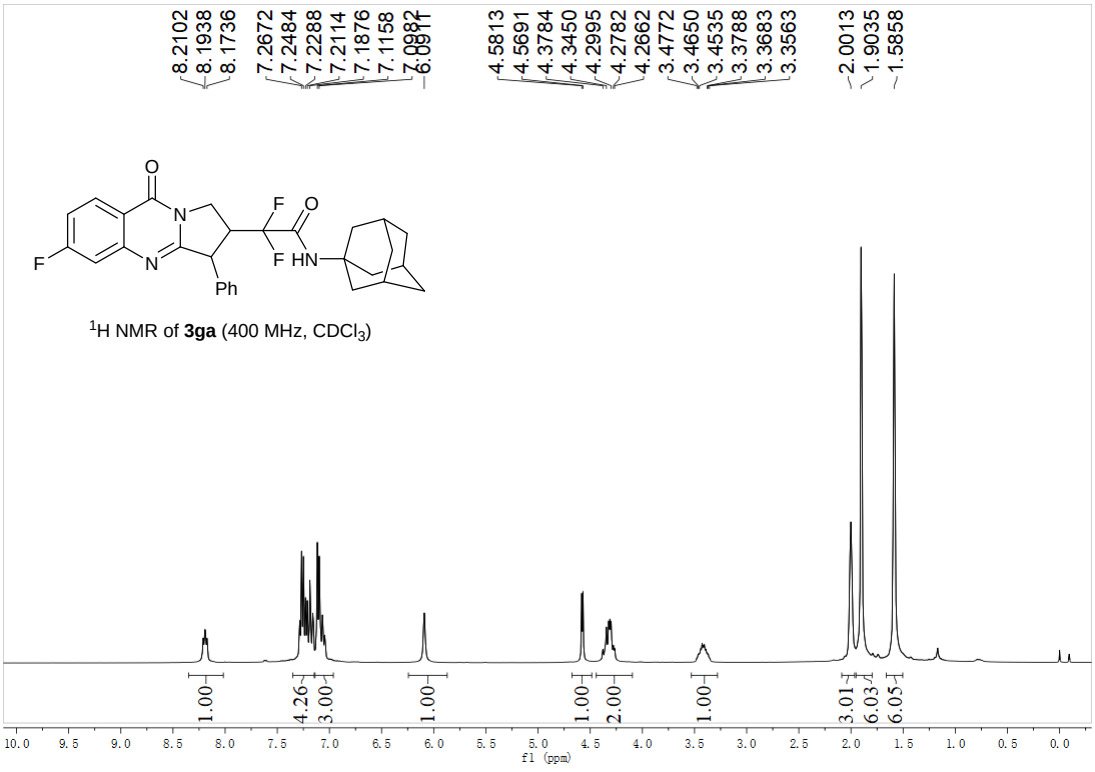
^{1}H NMR of **3fa** (400 MHz, $CDCl_3$)



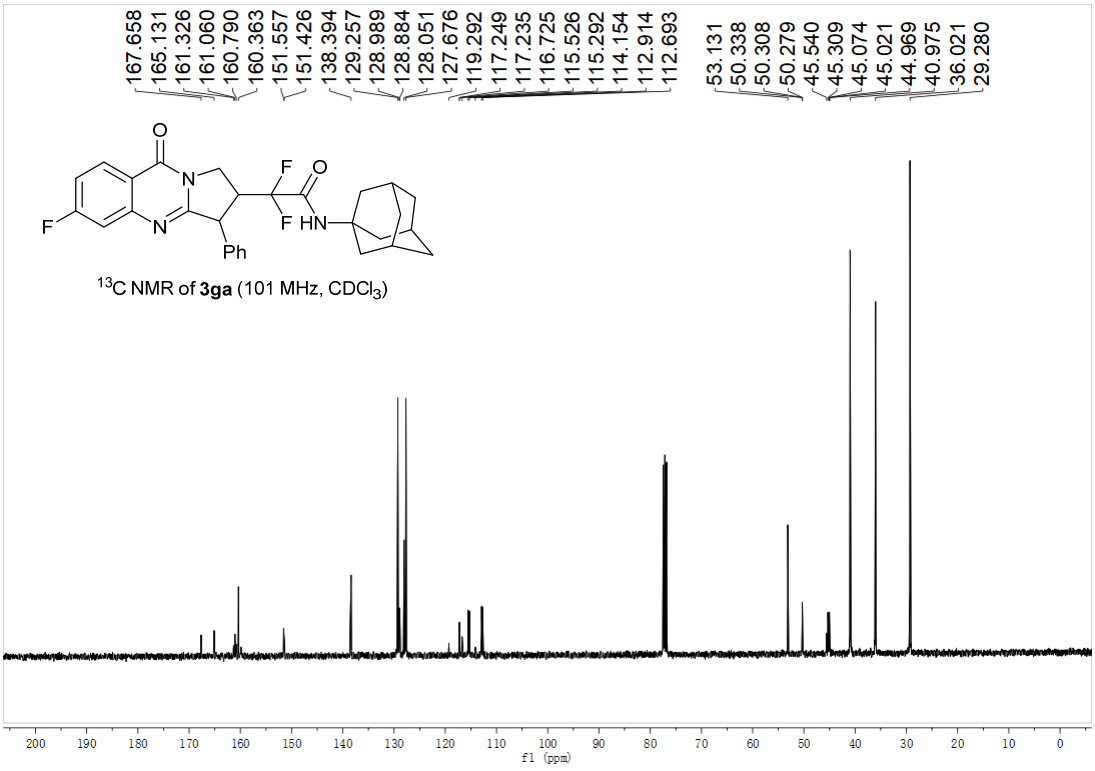
^{13}C NMR of **3fa** (101 MHz, $CDCl_3$)



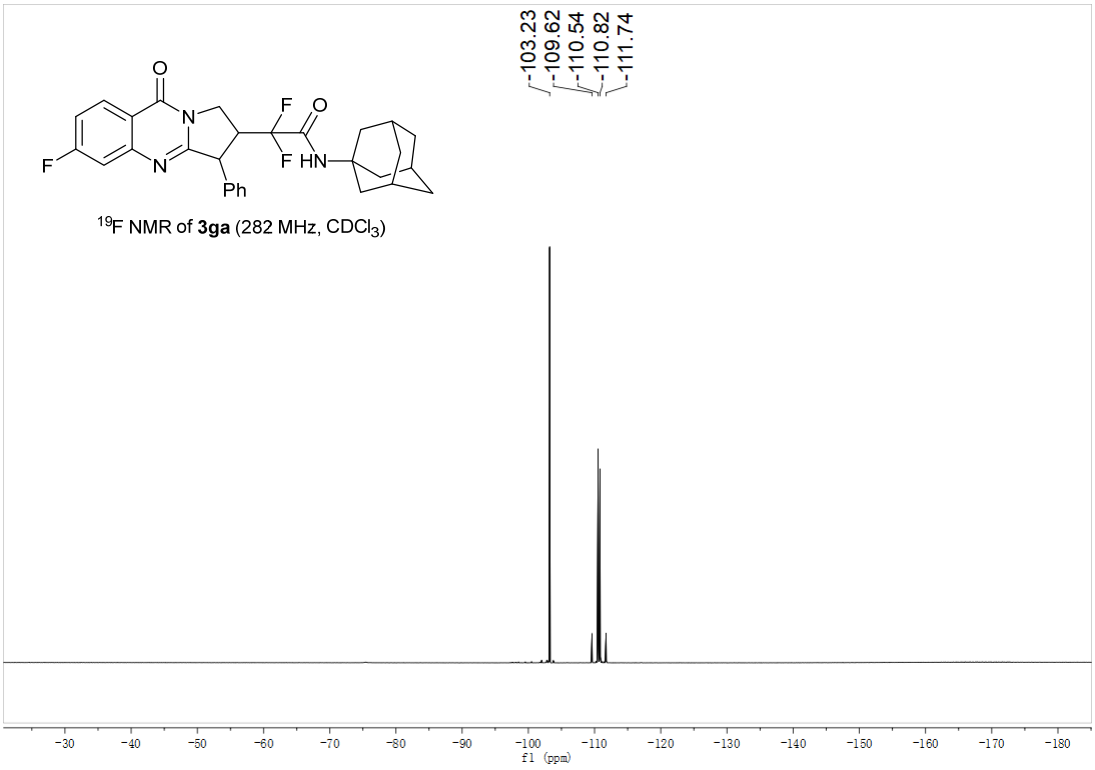
^{19}F NMR of **3fa** (282 MHz, $CDCl_3$)



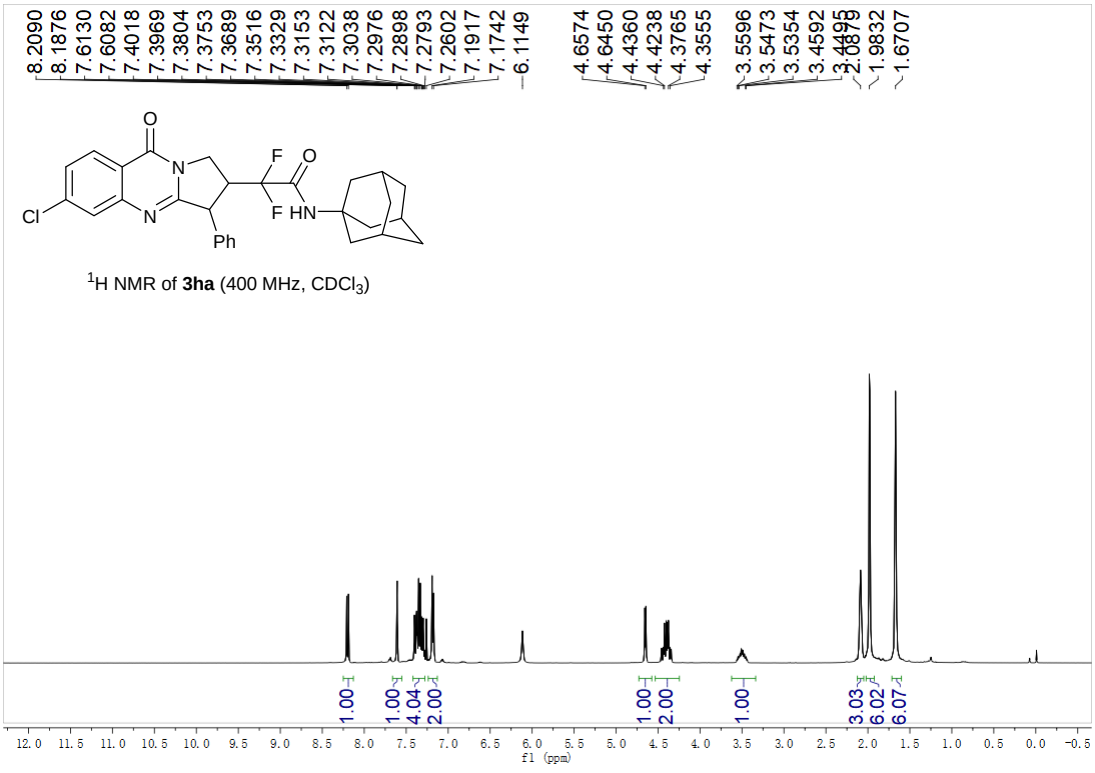
^{1}H NMR of **3ga** (400 MHz, $CDCl_3$)



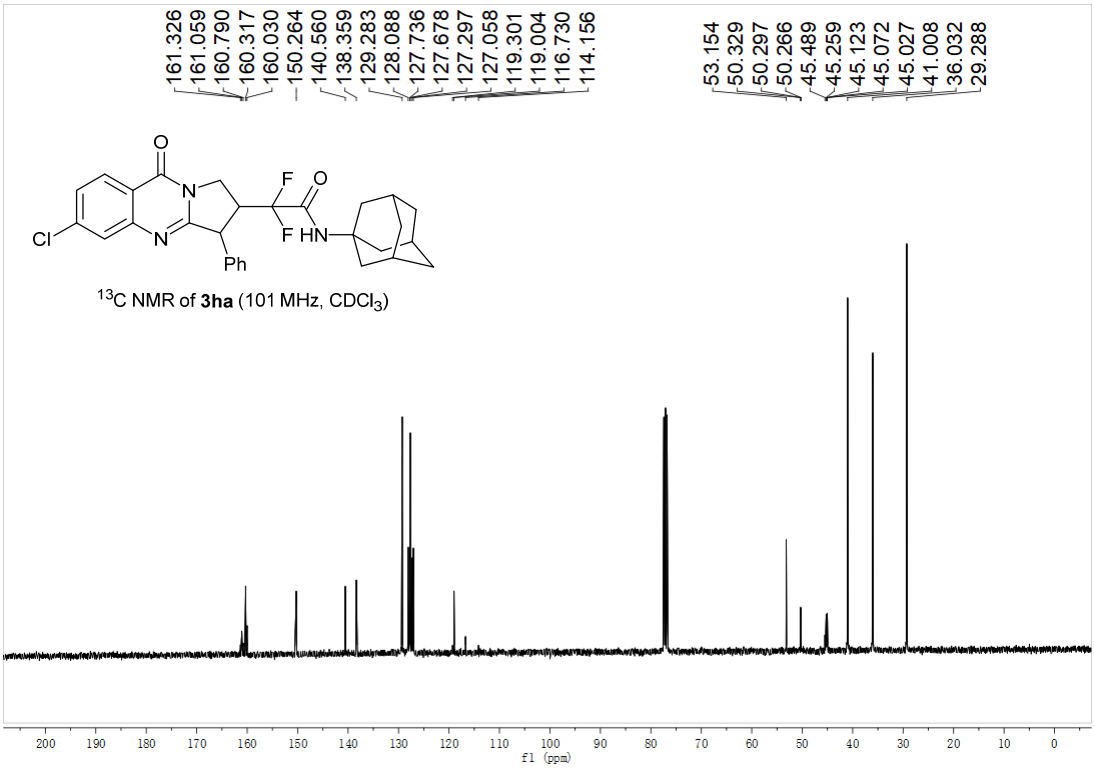
^{13}C NMR of **3ga** (101 MHz, $CDCl_3$)



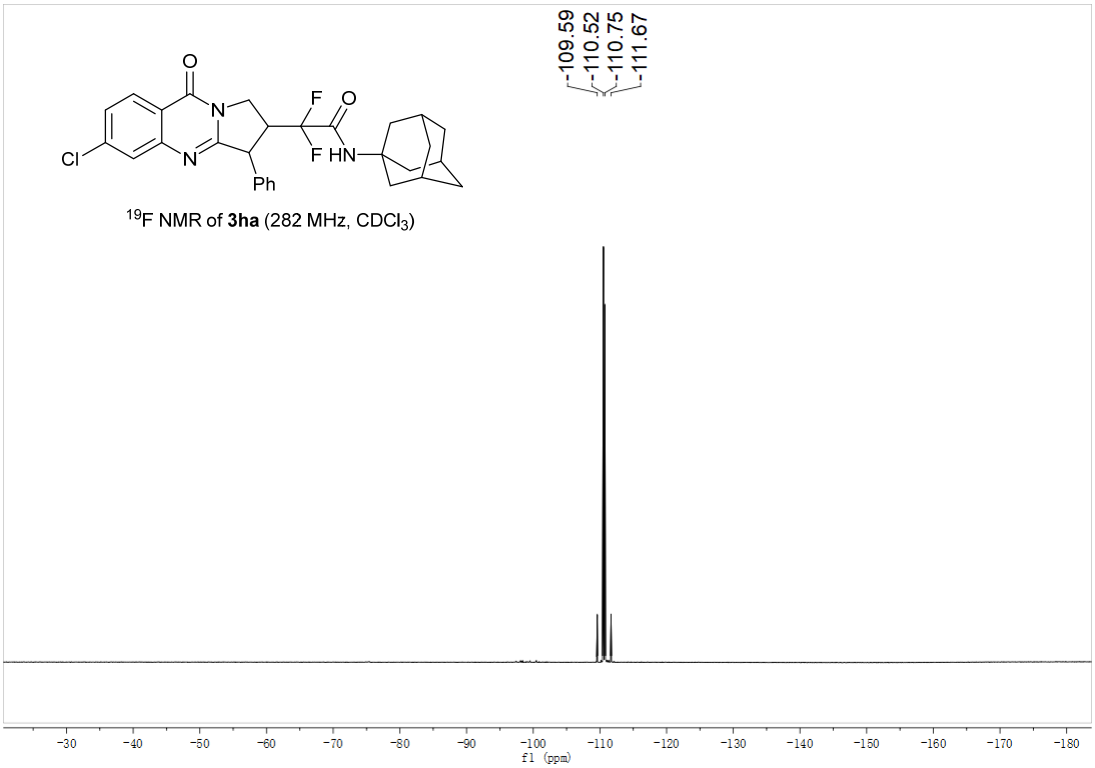
^{19}F NMR of **3ga** (282 MHz, $CDCl_3$)



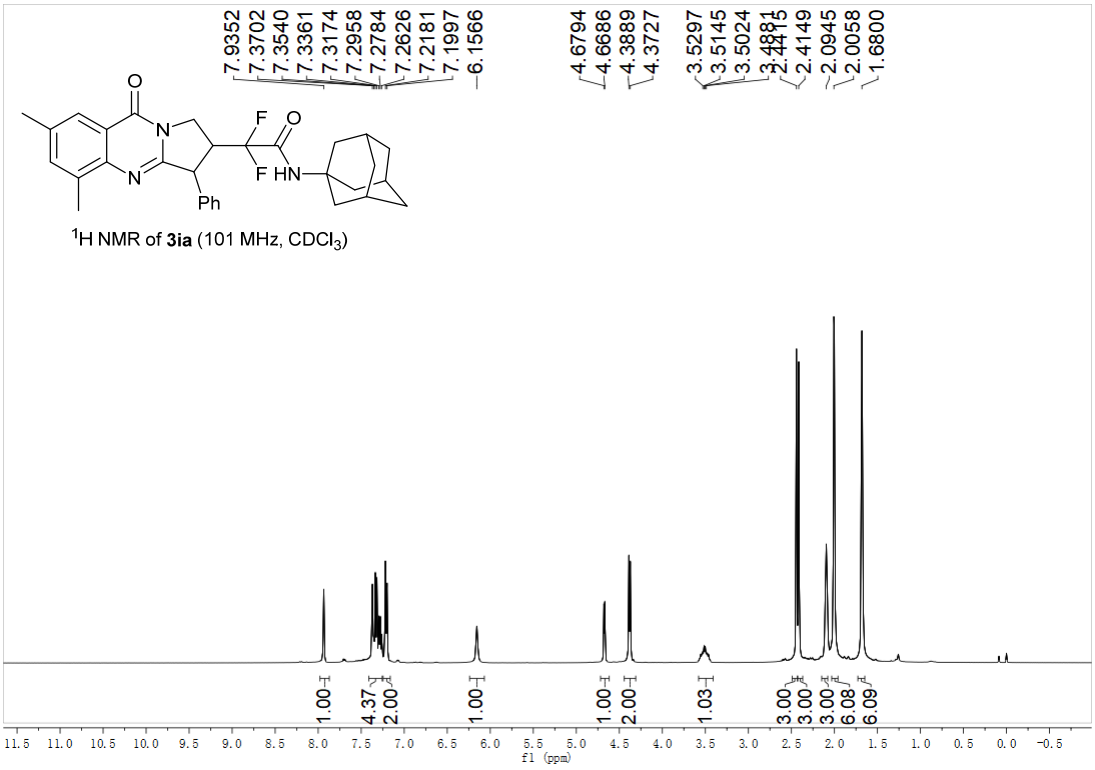
^{1}H NMR of **3ha** (400 MHz, $CDCl_3$)



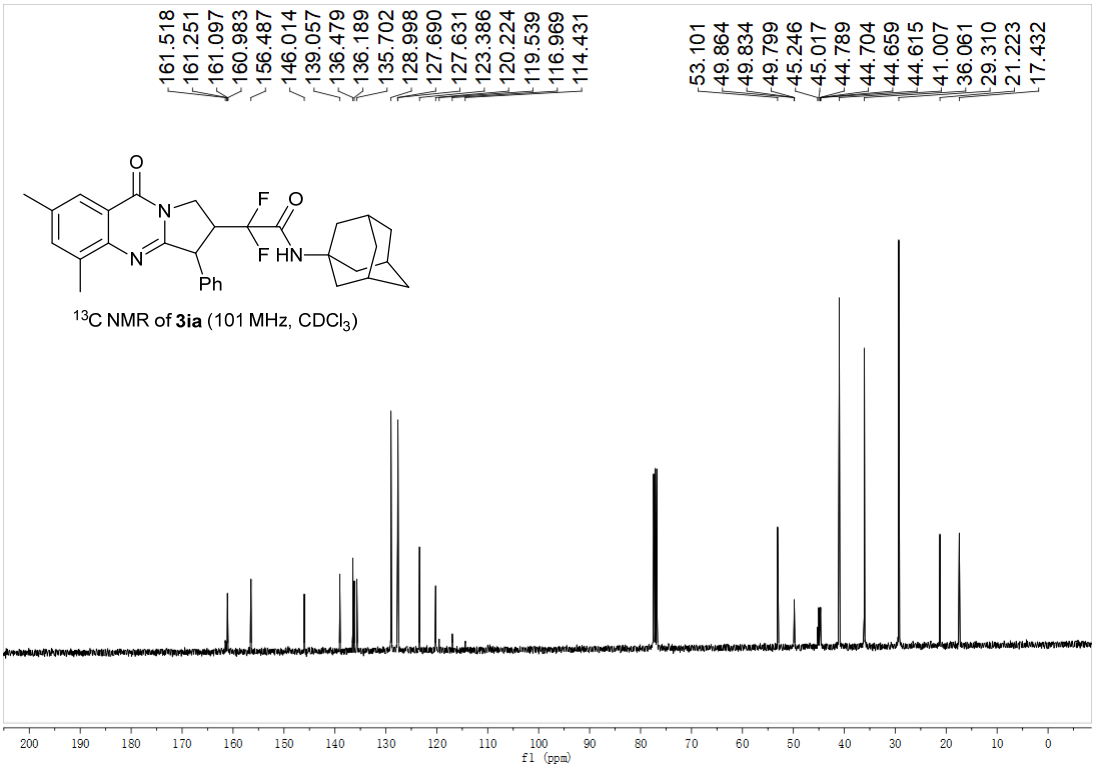
^{13}C NMR of **3ha** (101 MHz, $CDCl_3$)



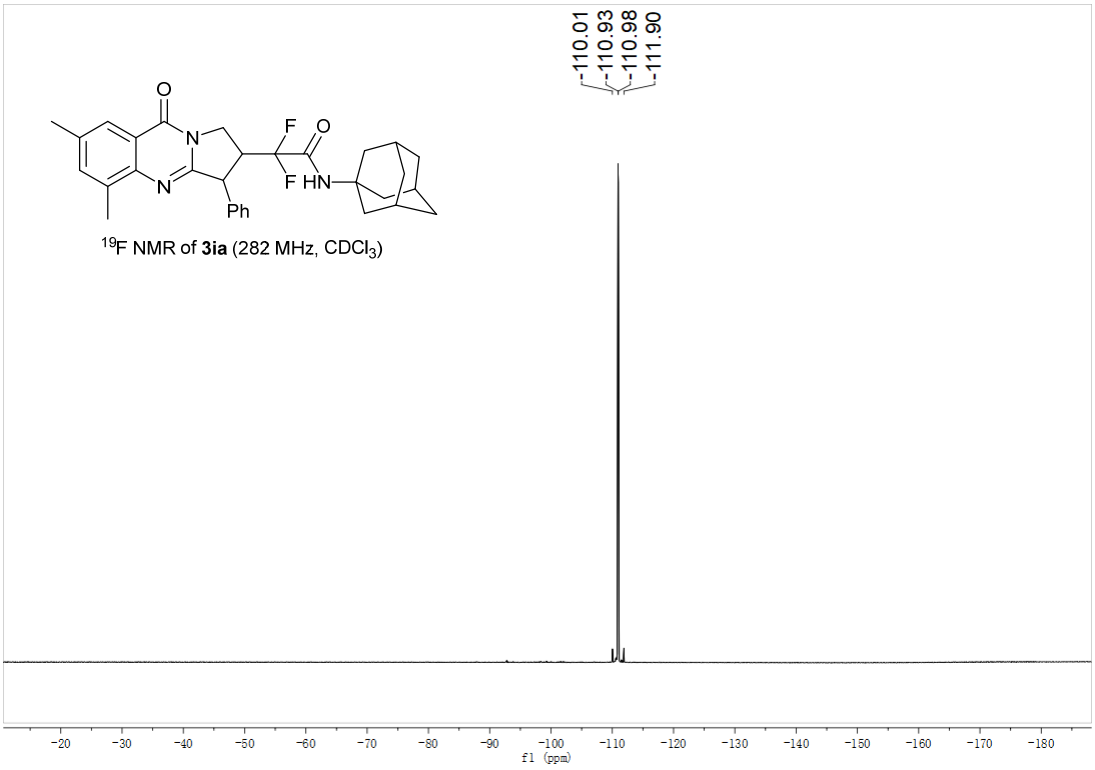
^{19}F NMR of **3ha** (282 MHz, $CDCl_3$)



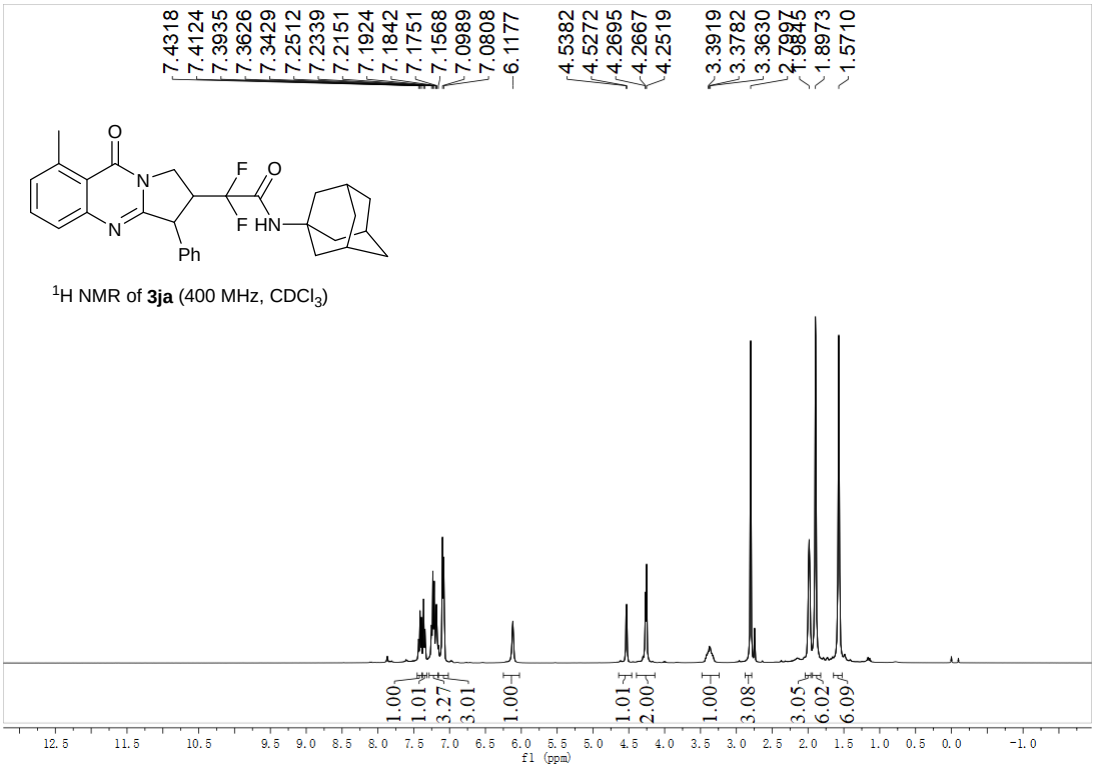
^{1}H NMR of **3ia** (101 MHz, $CDCl_3$)



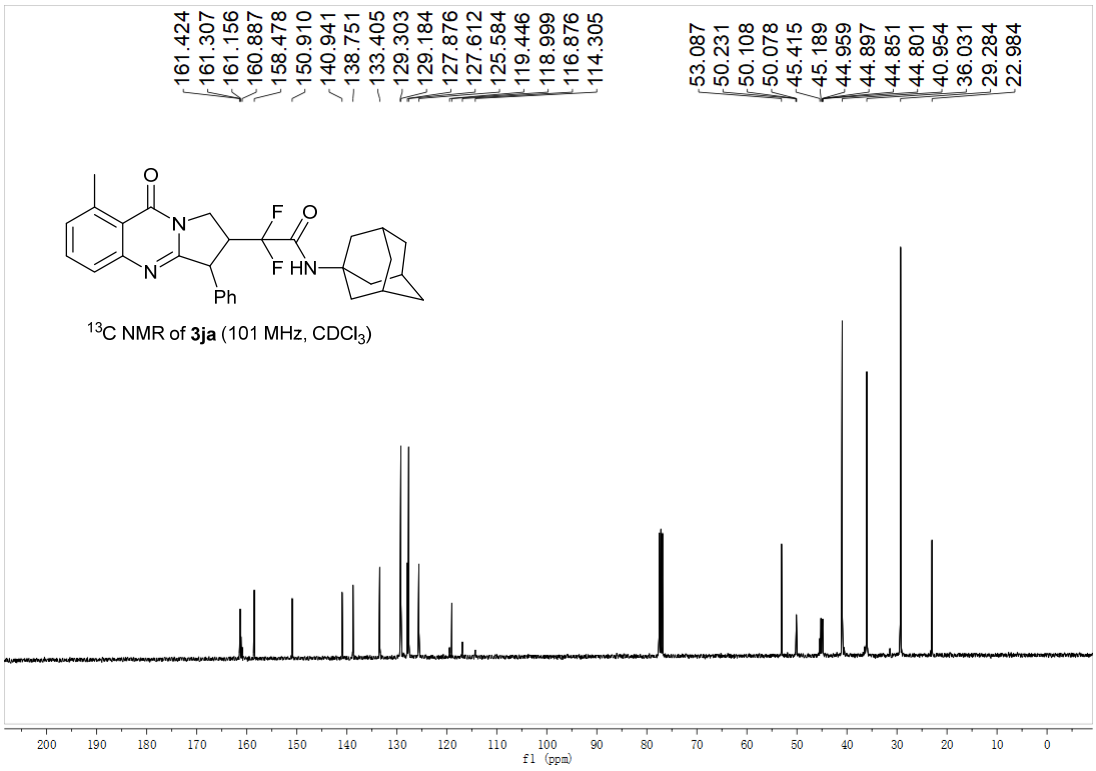
^{13}C NMR of **3ia** (101 MHz, $CDCl_3$)



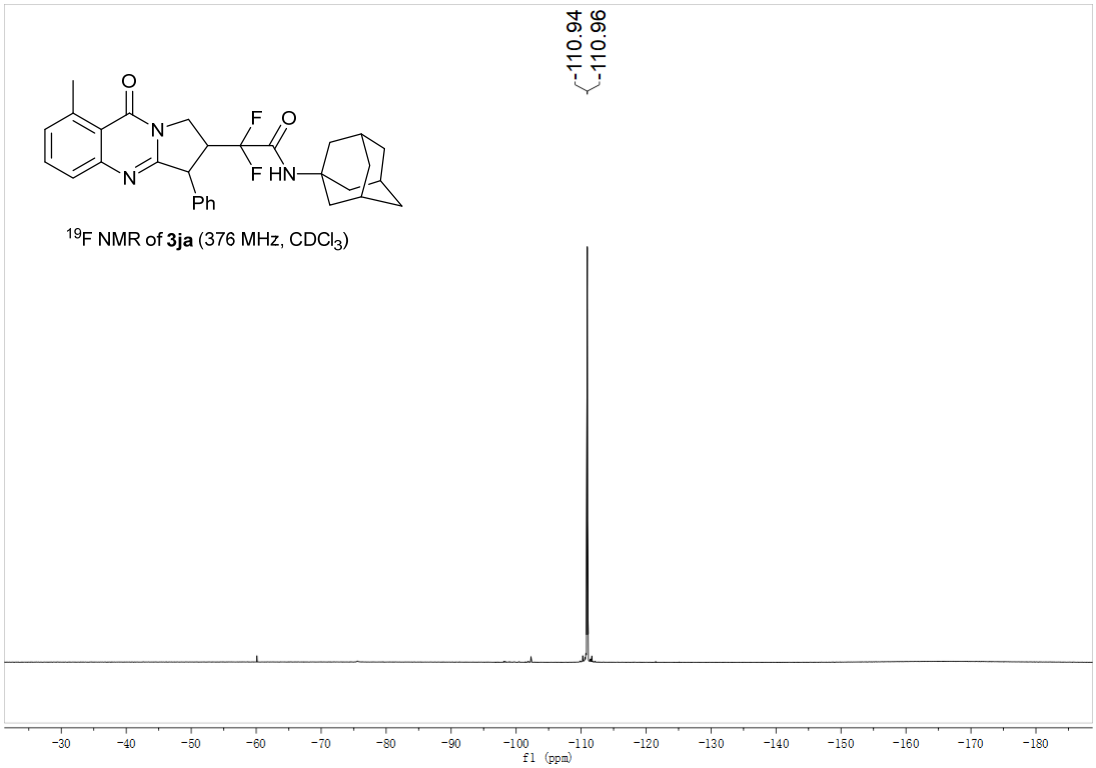
^{19}F NMR of **3ia** (282 MHz, $CDCl_3$)



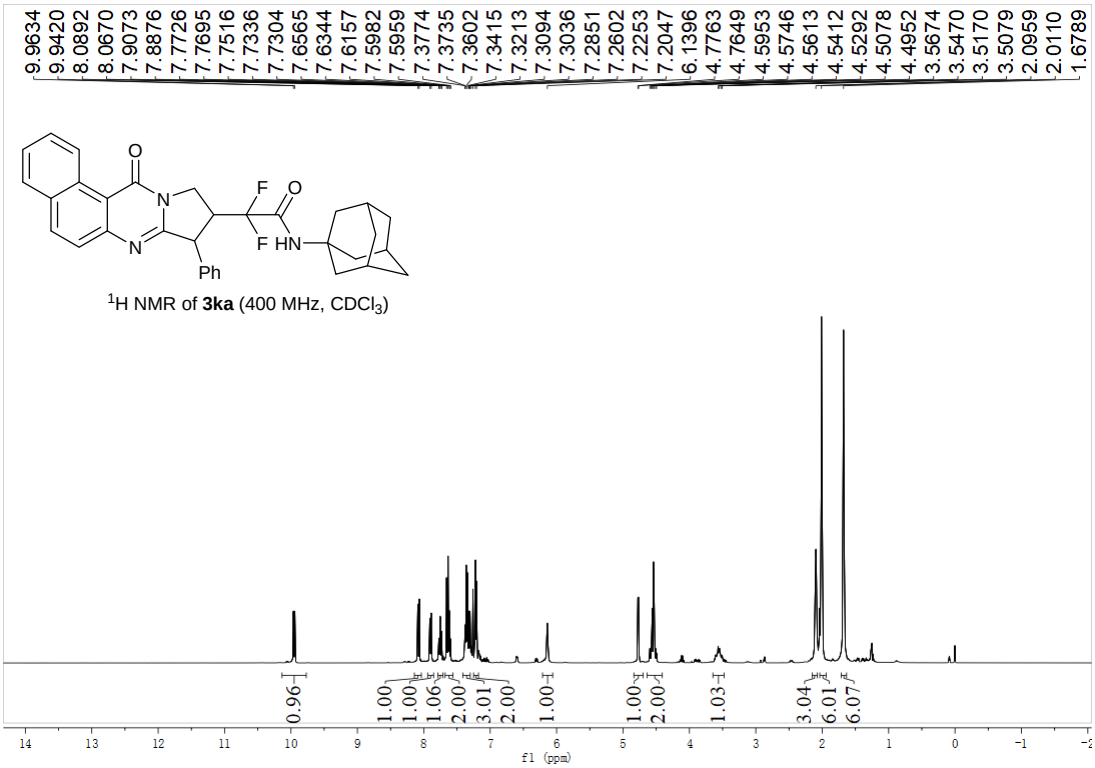
^{1}H NMR of **3ja** (400 MHz, $CDCl_3$)



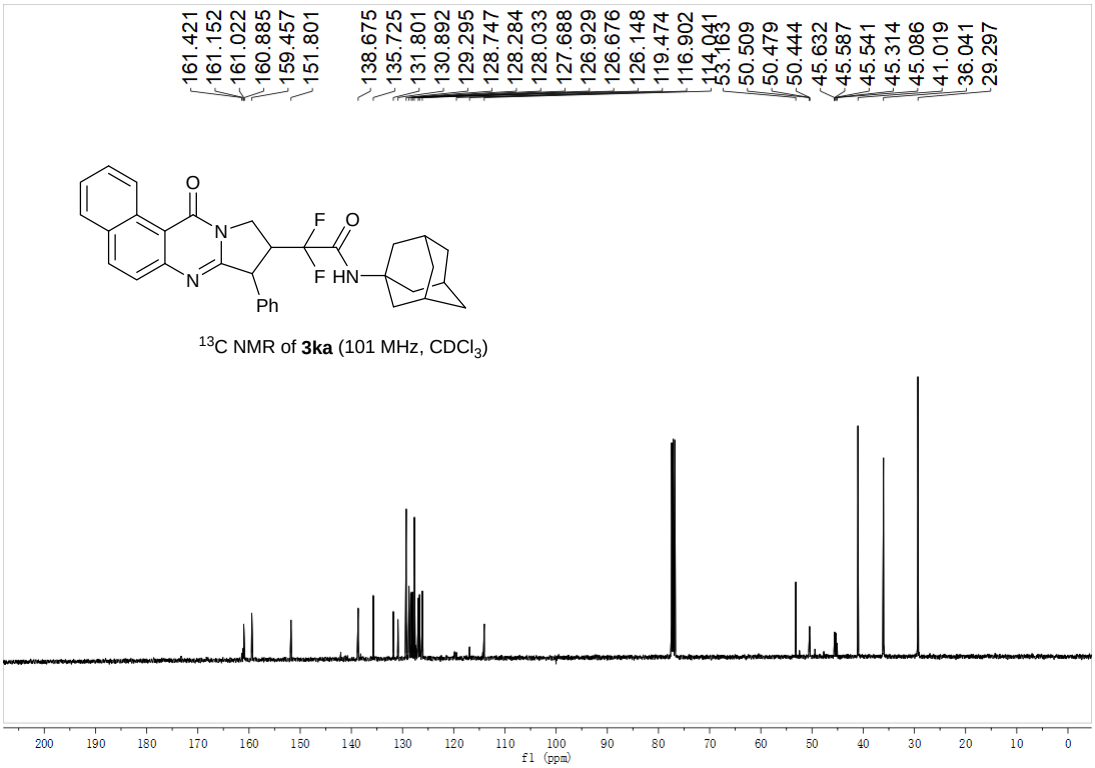
^{13}C NMR of **3ja** (101 MHz, $CDCl_3$)



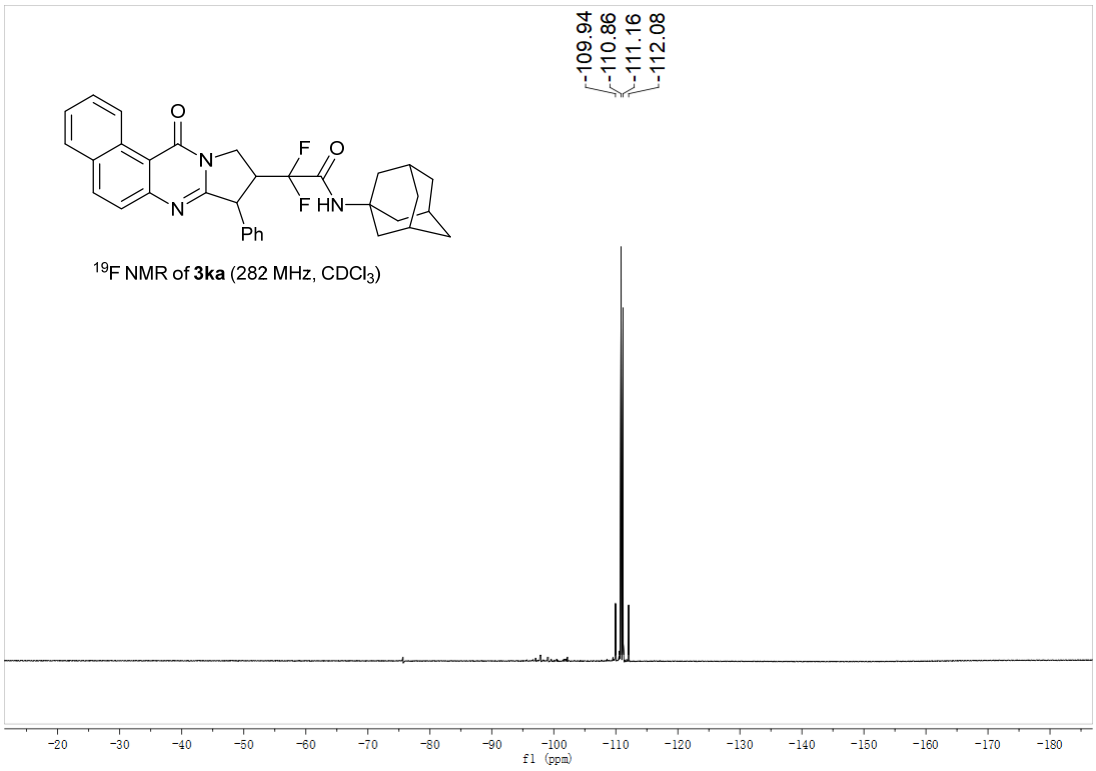
^{19}F NMR of **3ja** (376 MHz, $CDCl_3$)



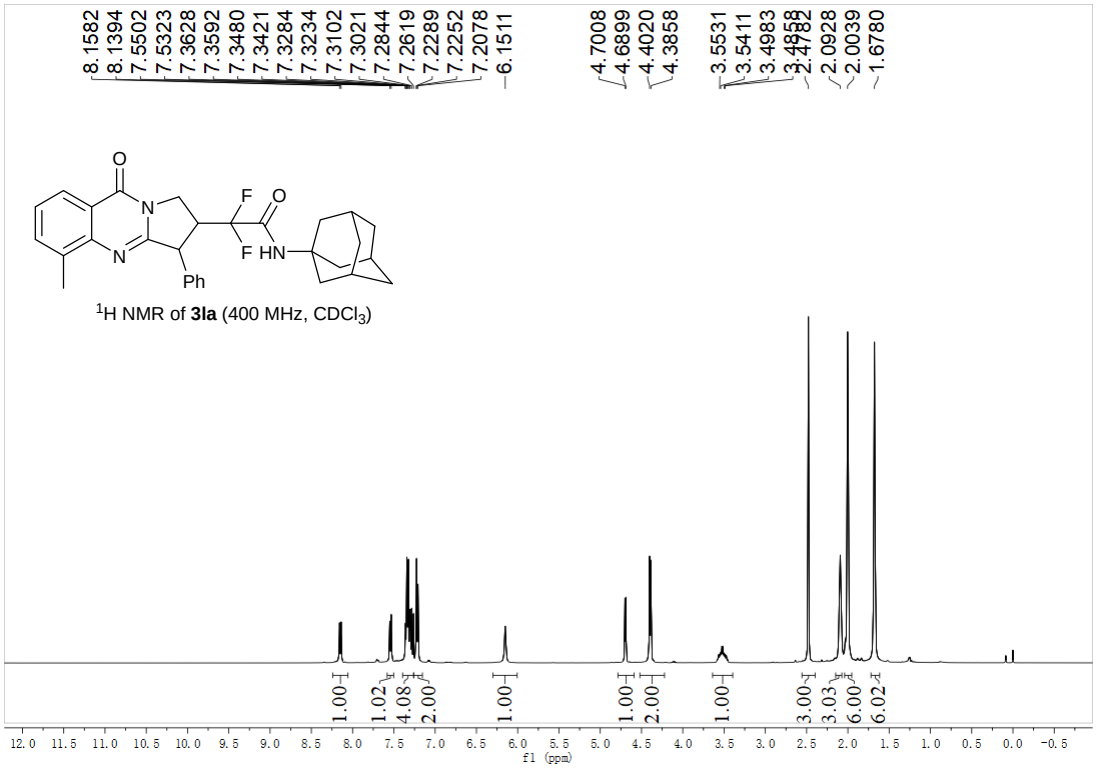
^{1}H NMR of **3ka** (400 MHz, $CDCl_3$)



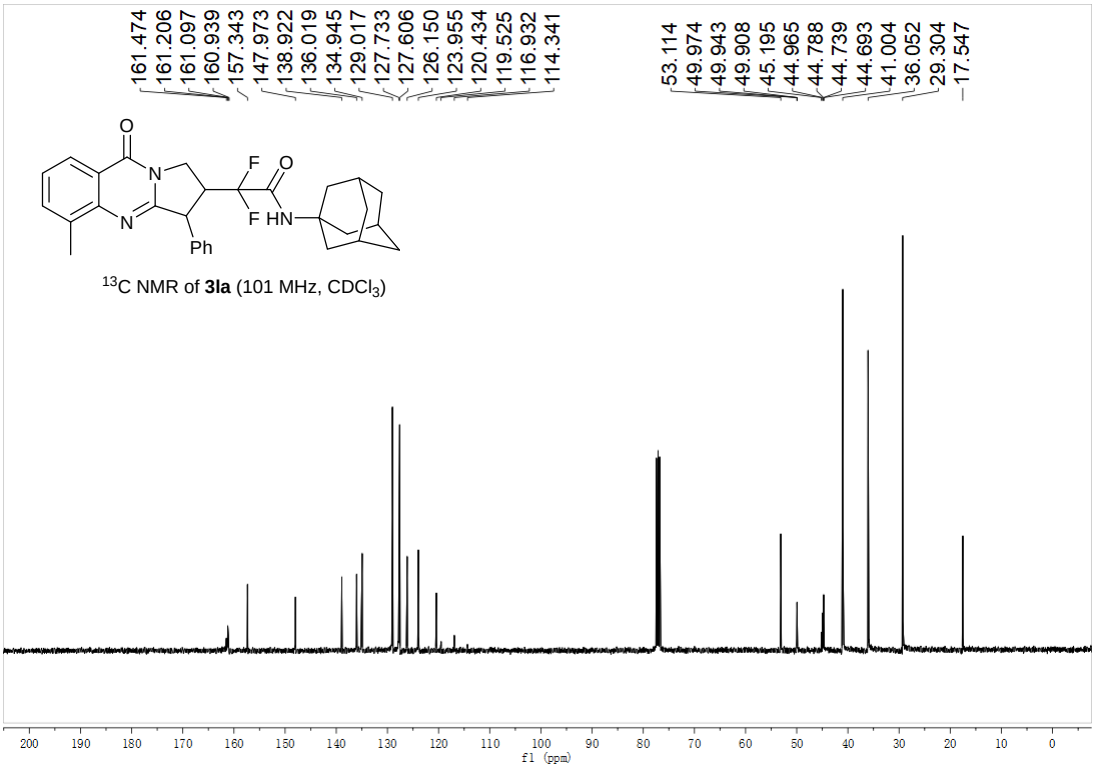
^{13}C NMR of **3ka** (101 MHz, $CDCl_3$)



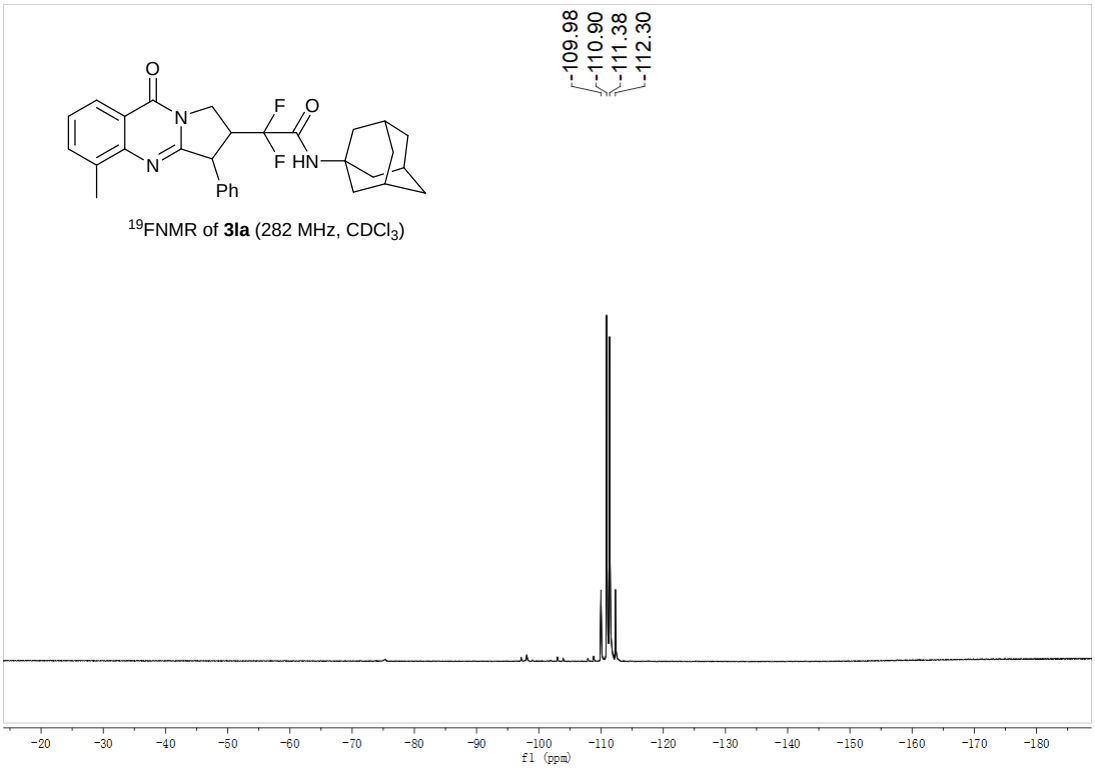
^{19}F NMR of **3ka** (282 MHz, $CDCl_3$)



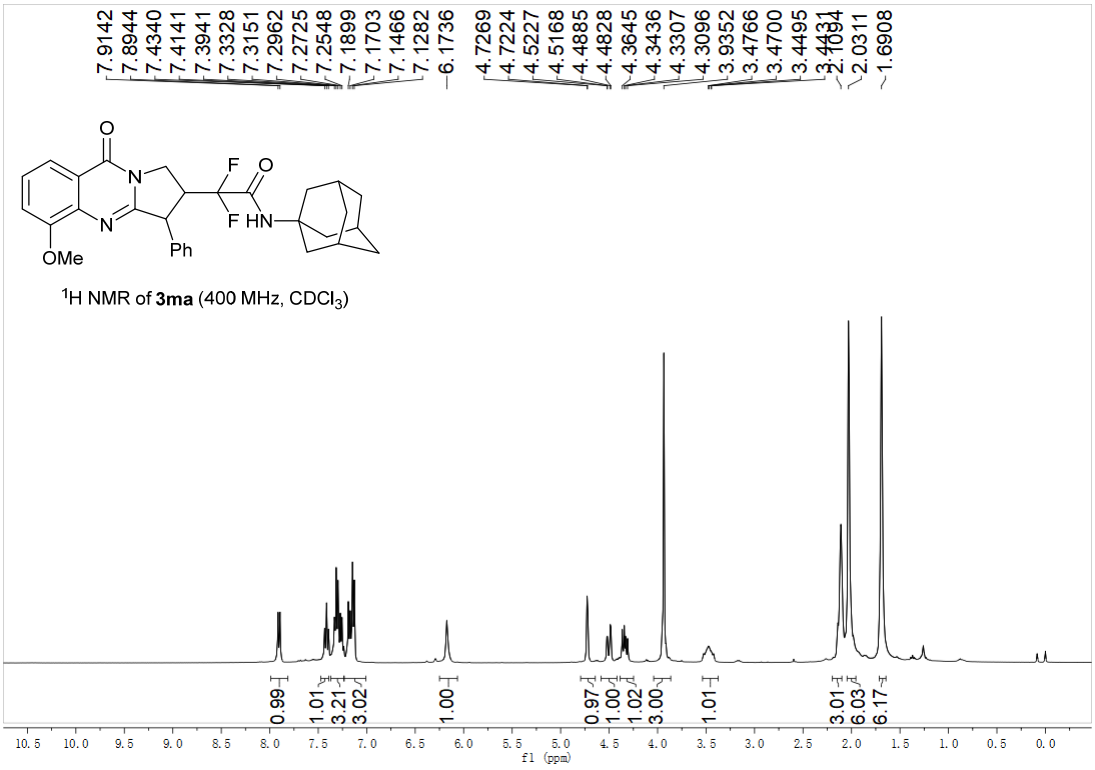
^{1}H NMR of **3la** (400 MHz, $CDCl_3$)



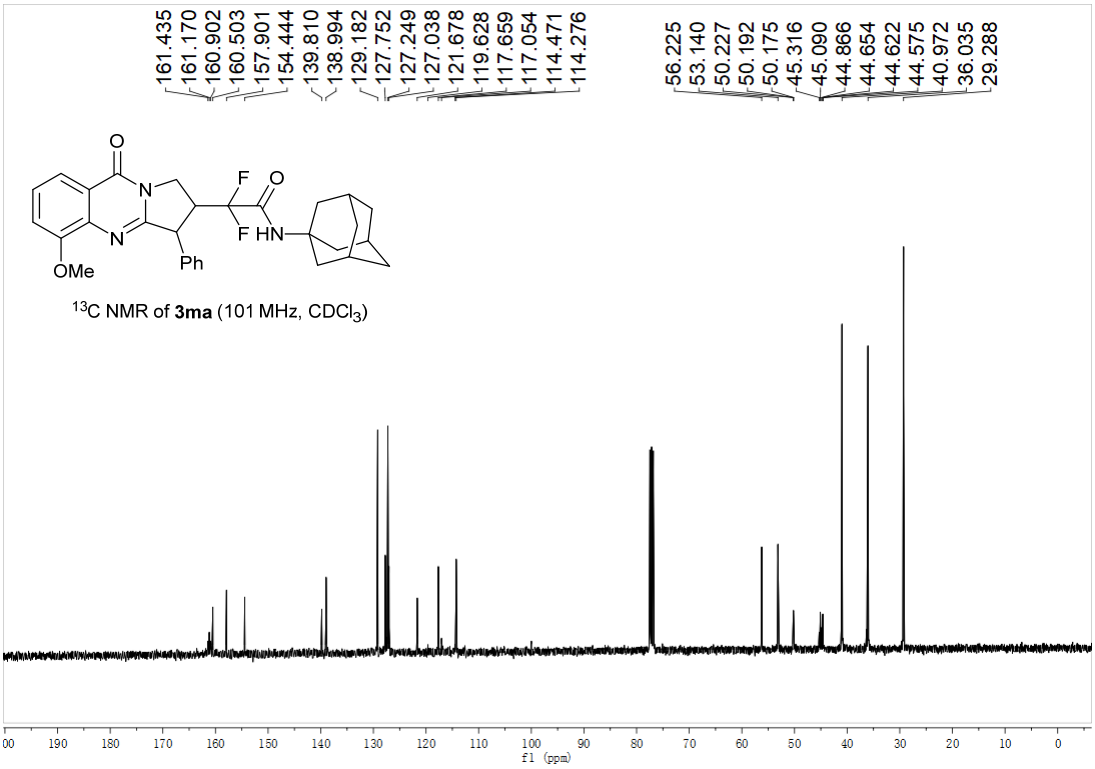
^{13}C NMR of **3la** (101 MHz, $CDCl_3$)



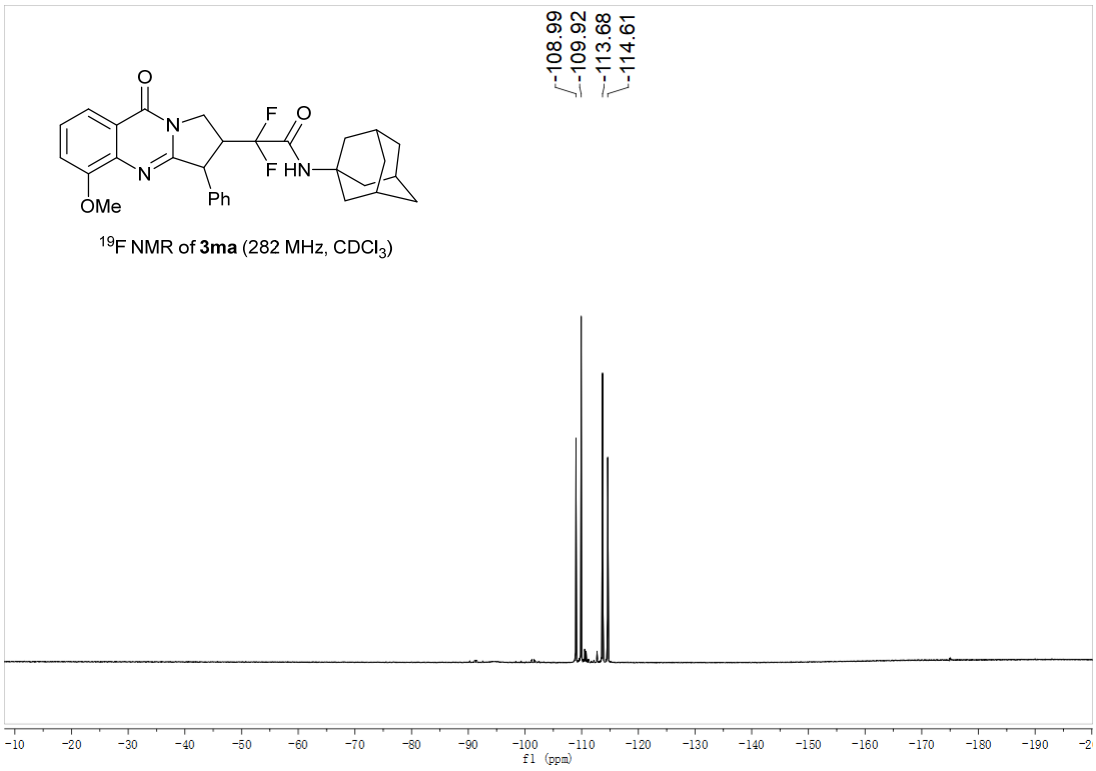
^{19}FNMR of **3la** (282 MHz, $CDCl_3$)



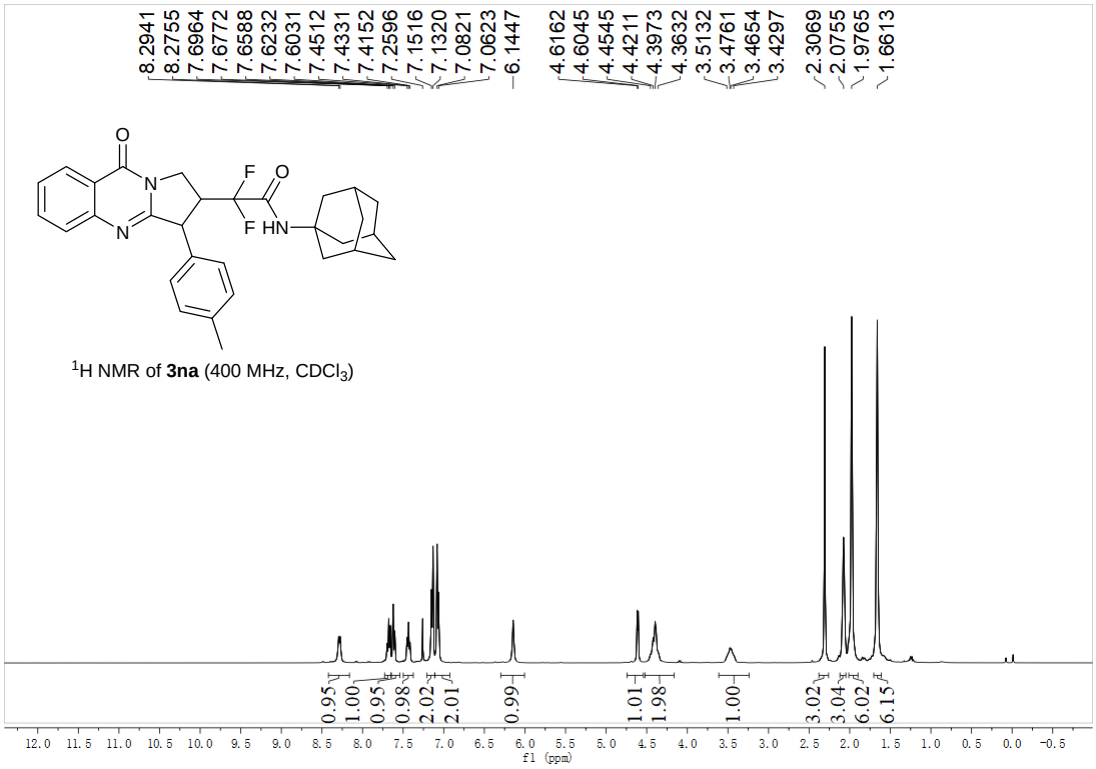
^{1}H NMR of **3ma** (400 MHz, $CDCl_3$)



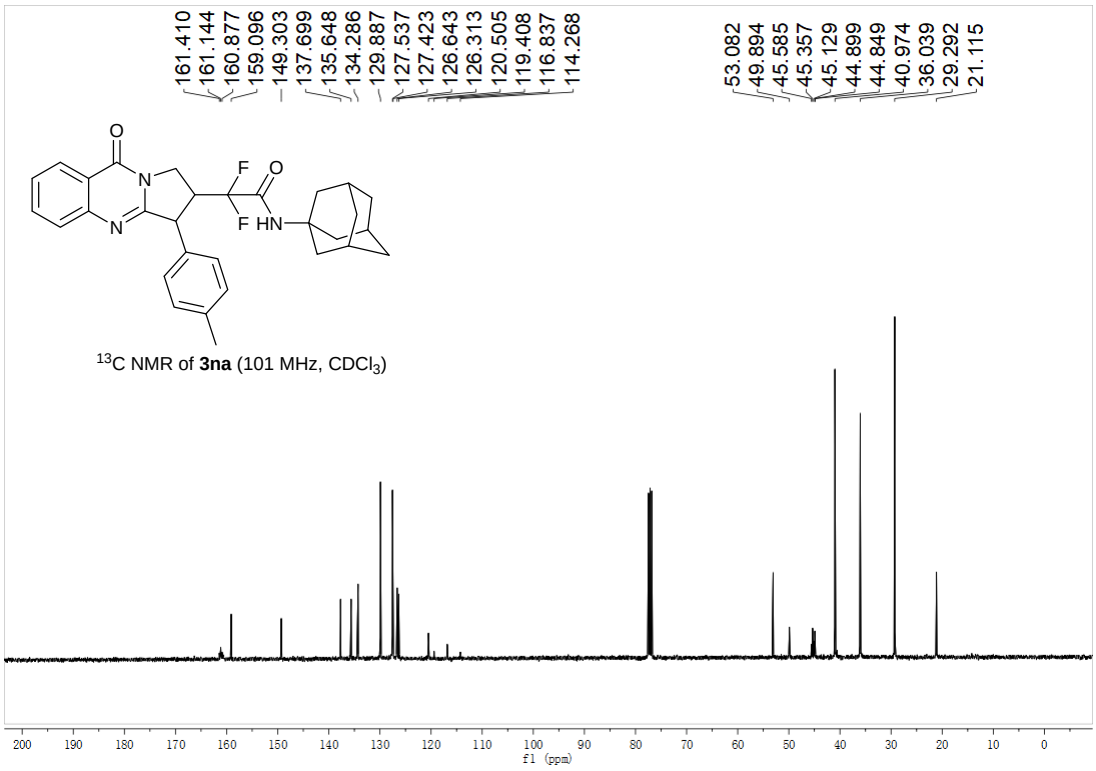
^{13}C NMR of **3ma** (101 MHz, $CDCl_3$)



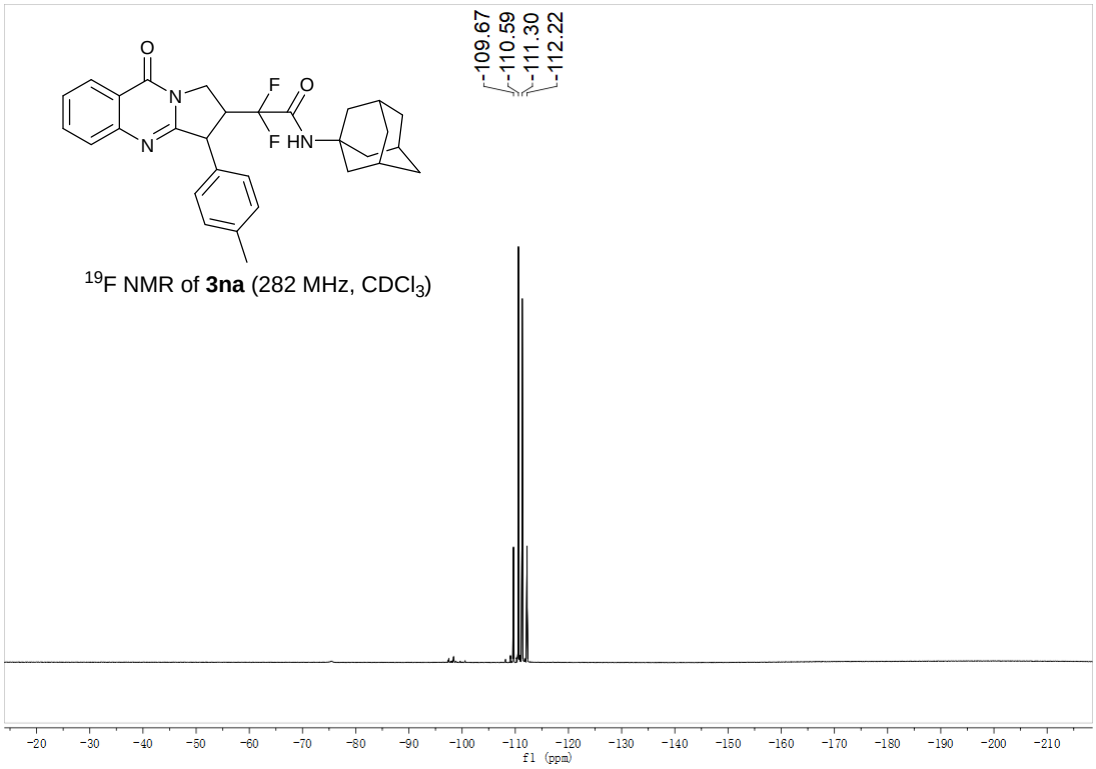
^{19}F NMR of **3ma** (282 MHz, $CDCl_3$)



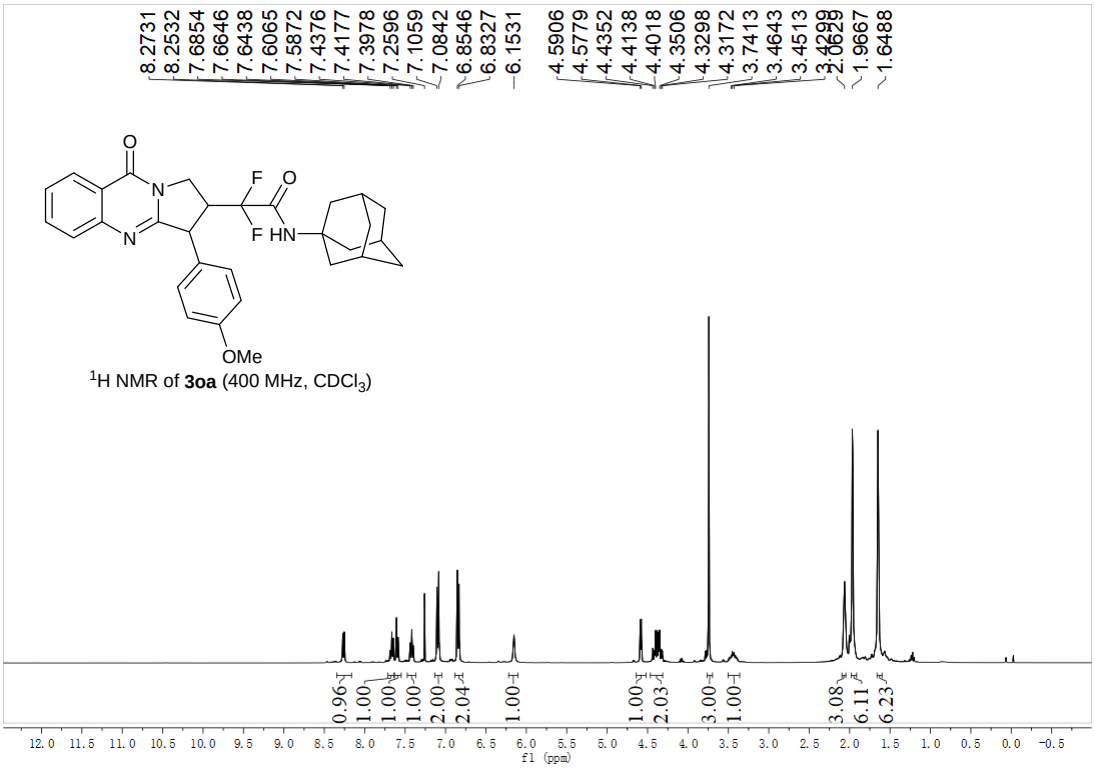
^{1}H NMR of **3na** (400 MHz, $CDCl_3$)



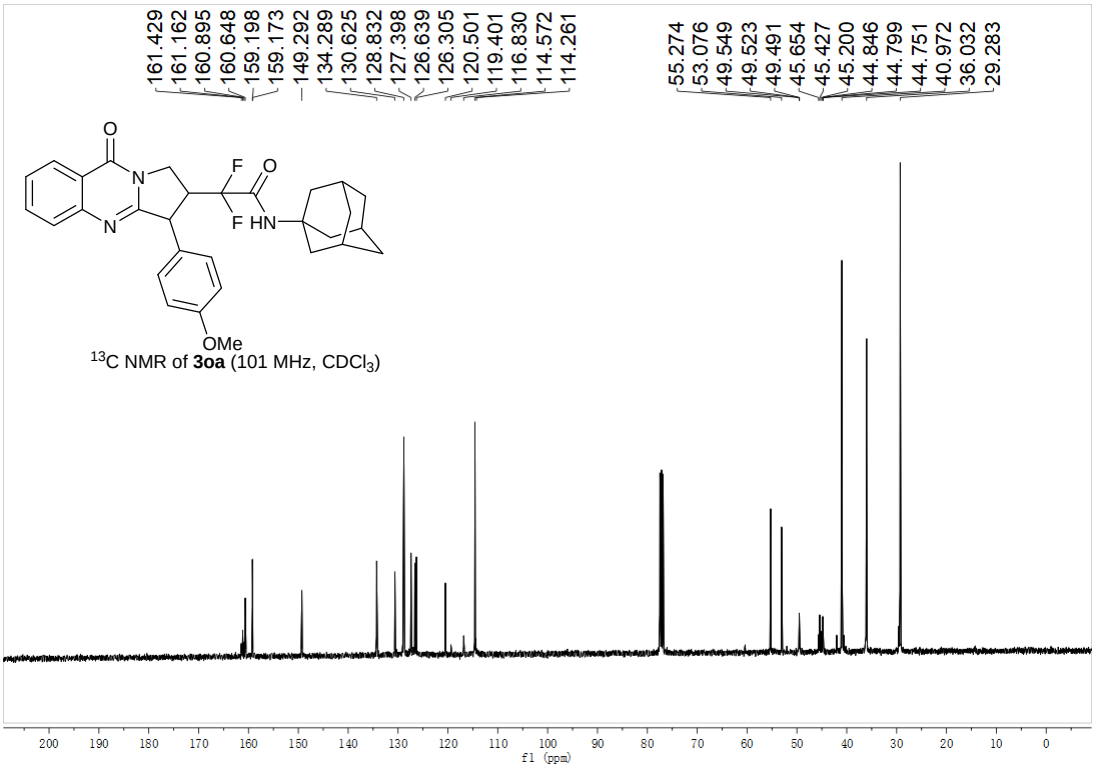
^{13}C NMR of **3na** (101 MHz, $CDCl_3$)



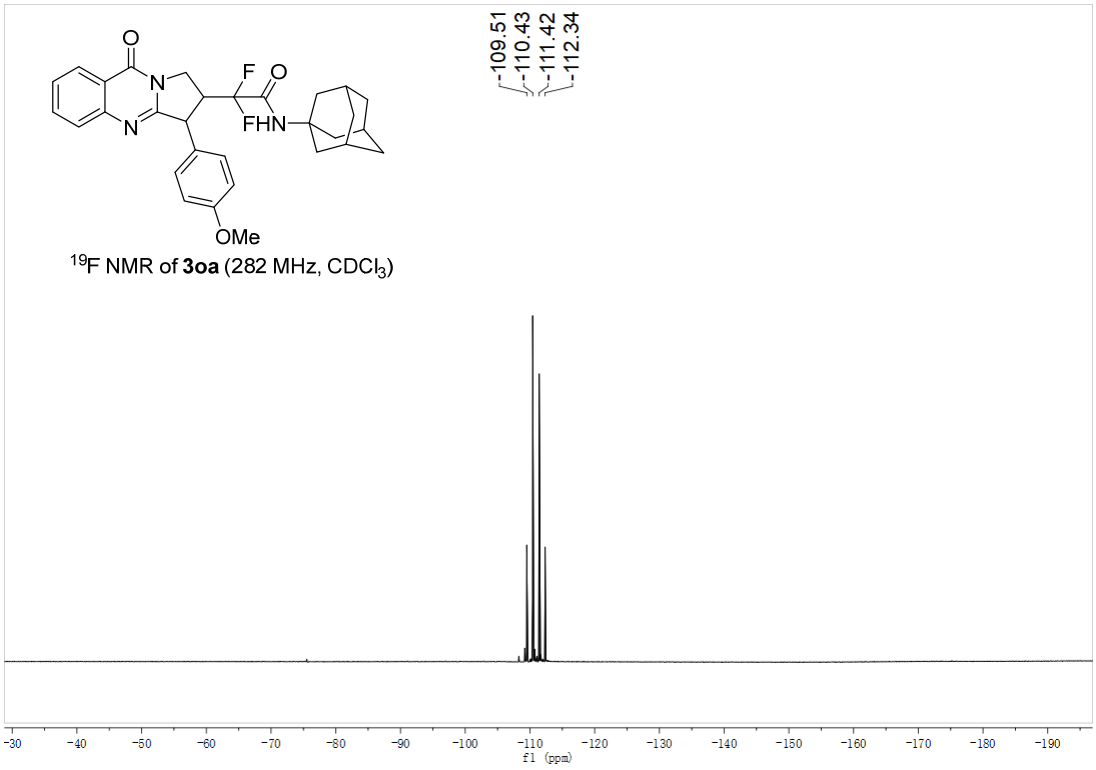
^{19}F NMR of **3na** (282 MHz, $CDCl_3$)



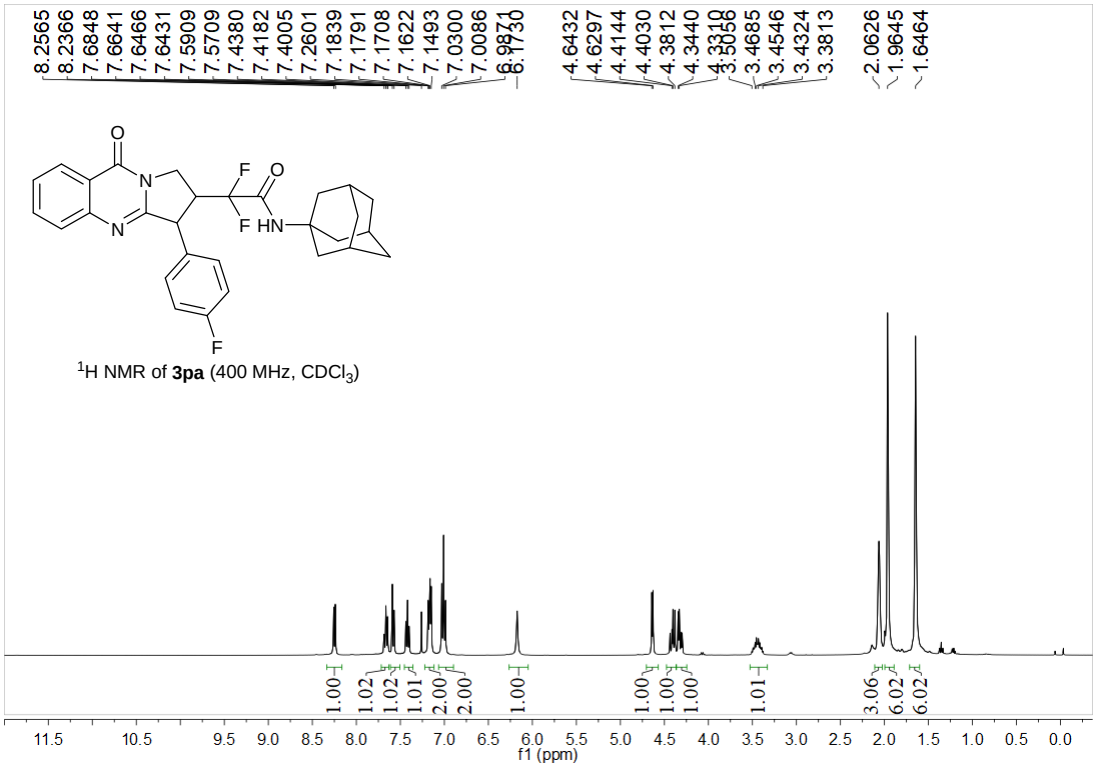
^{1}H NMR of **3oa** (400 MHz, $CDCl_3$)



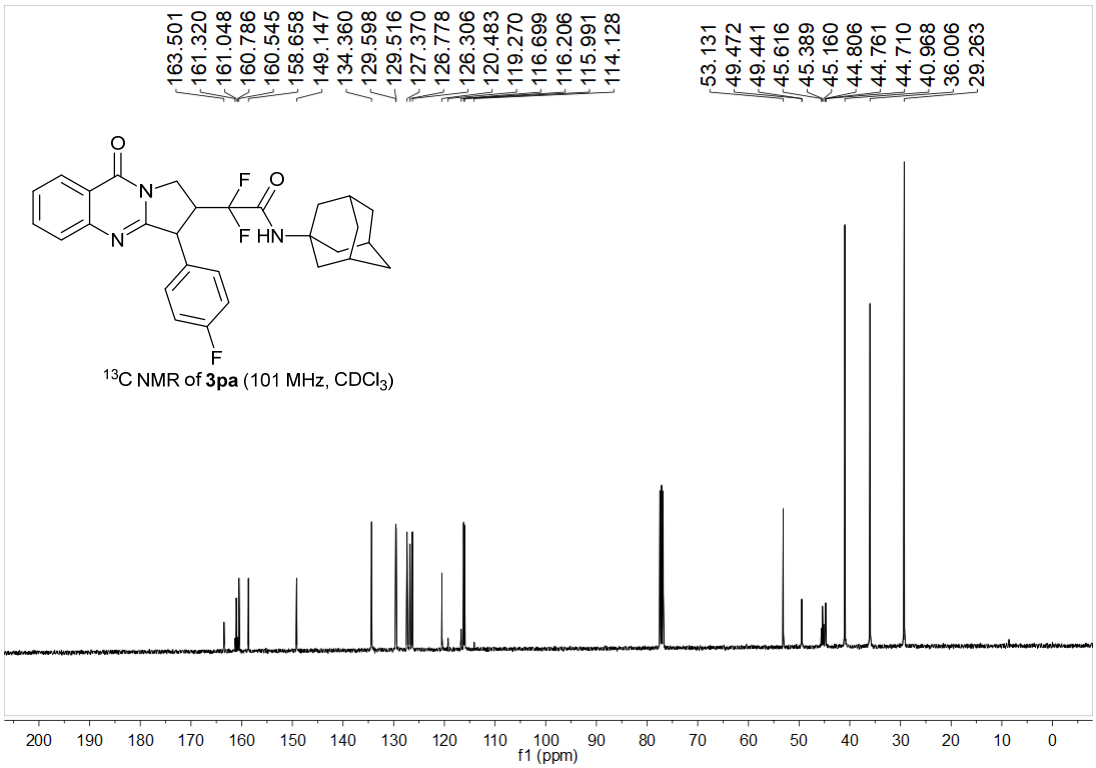
^{13}C NMR of **3oa** (101 MHz, $CDCl_3$)



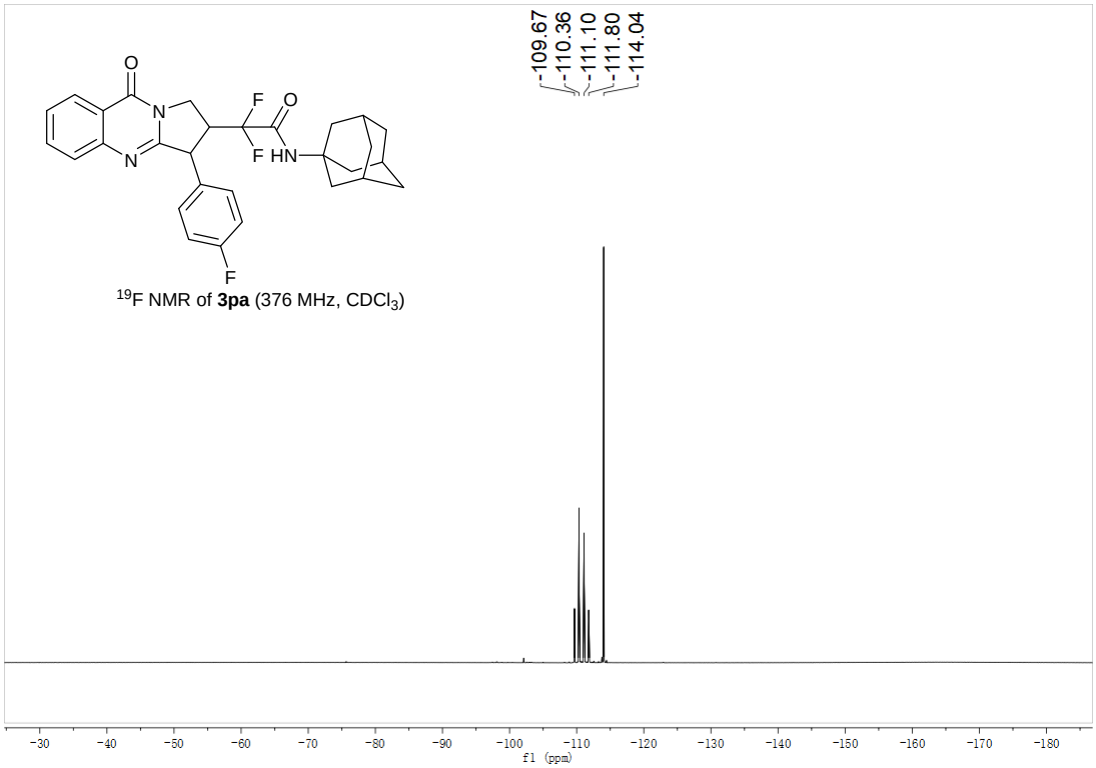
^{19}F NMR of **3oa** (282 MHz, $CDCl_3$)



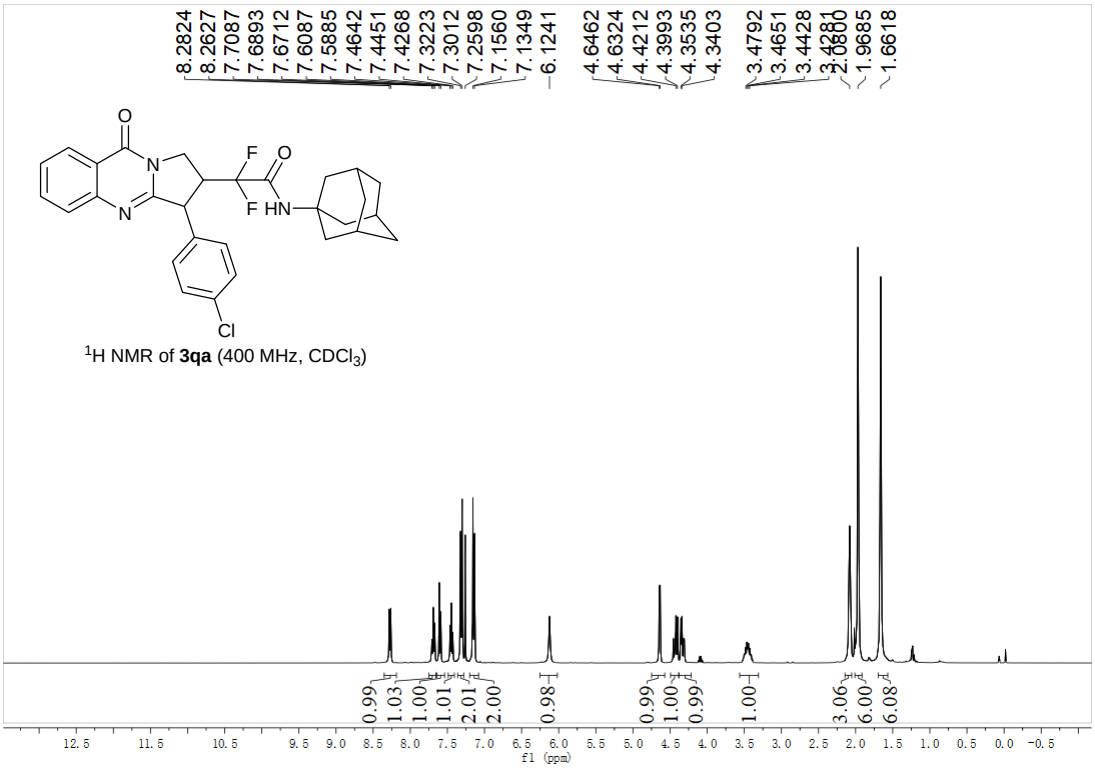
^{1}H NMR of **3pa** (400 MHz, $CDCl_3$)



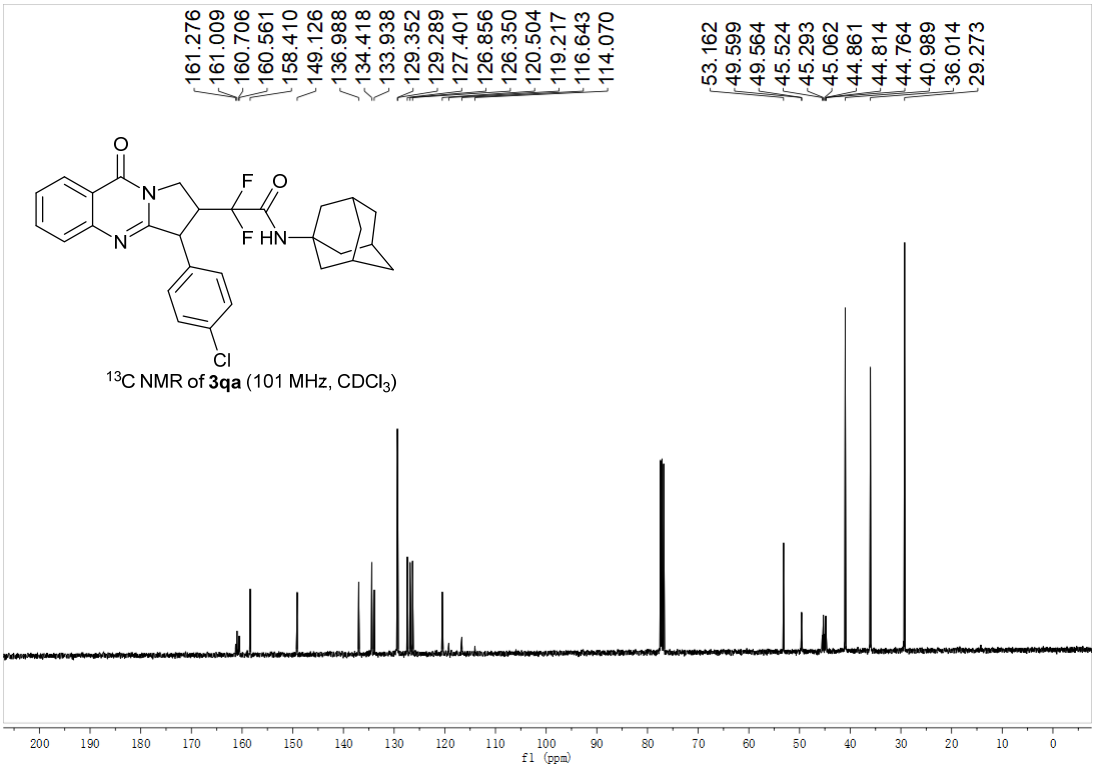
^{13}C NMR of **3pa** (101 MHz, $CDCl_3$)



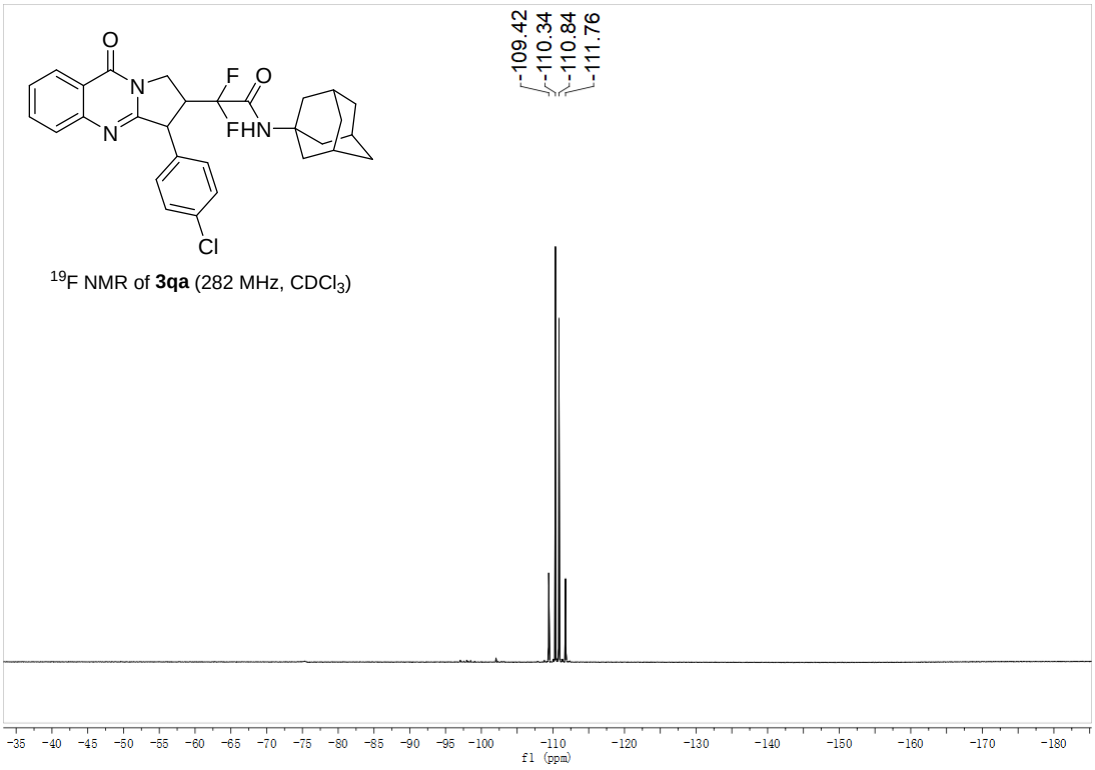
^{19}F NMR of **3pa** (376 MHz, $CDCl_3$)



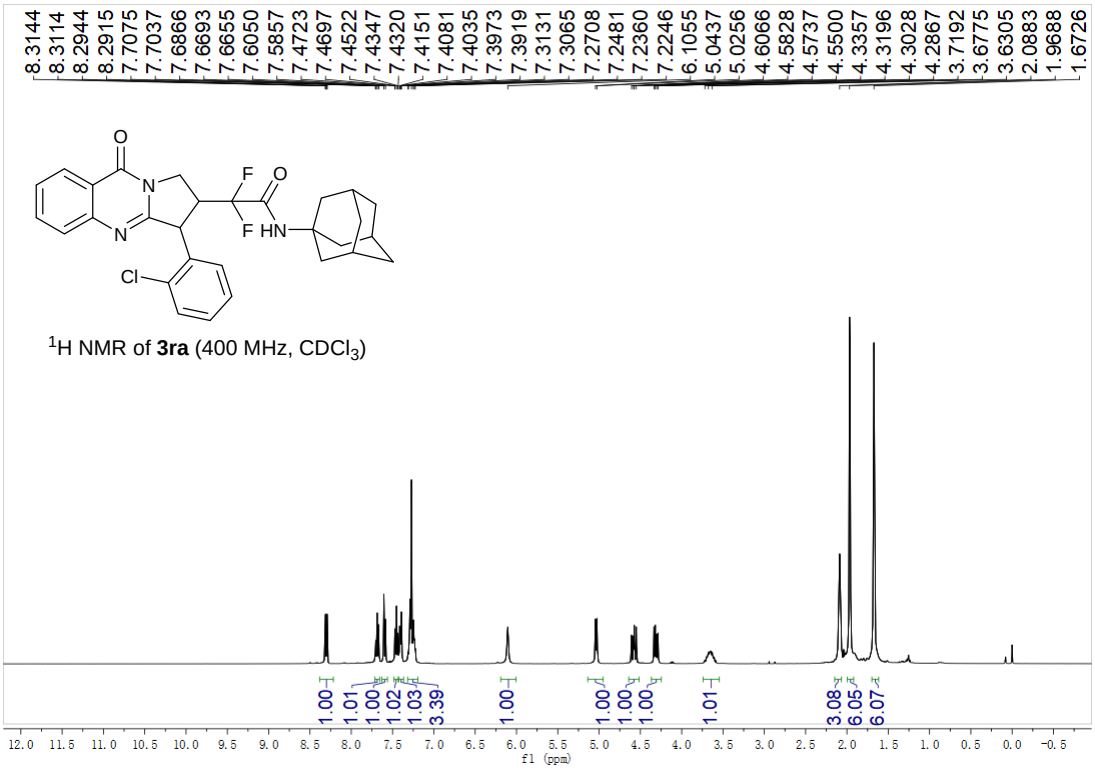
^{1}H NMR of **3qa** (400 MHz, $CDCl_3$)



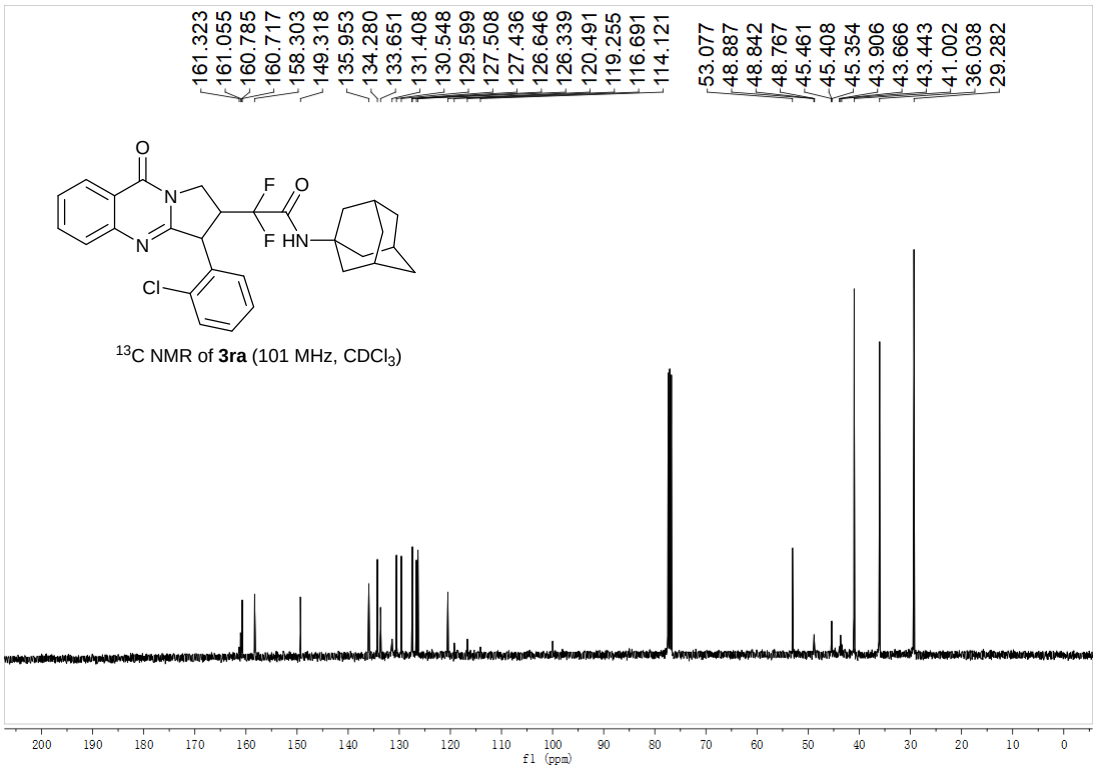
^{13}C NMR of **3qa** (101 MHz, $CDCl_3$)



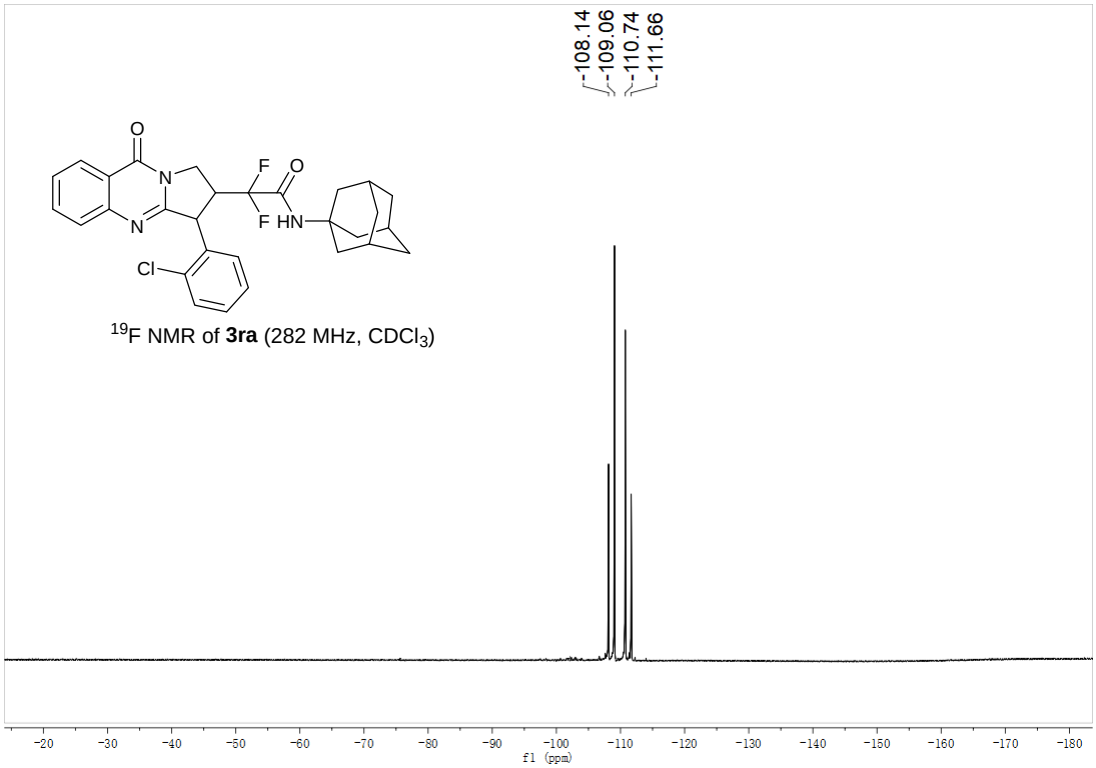
^{19}F NMR of **3qa** (282 MHz, $CDCl_3$)



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



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



^{19}F NMR of **3ra** (282 MHz, $CDCl_3$)