Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Photo-triggered Self-catalyzed Fluoroalkylation/Cyclization of Unactivated Alkenes: Synthesis of Quinazolinones Containing CF_2R group

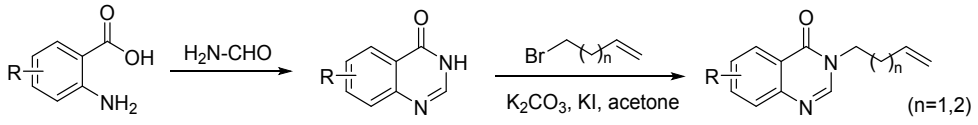
Jin Yang, Bin Sun, * Hao Ding, Pan-Yi Huang, Xiao-Li Tang, Rong-Cheng Shi, Zhi-Yang Yan, Chuan-Ming Yu, Can Jin*

I. General Information

Melting points were determined using a digital melting point apparatus and uncorrected. ^{1}H NMR spectra were recorded at 400 MHz using TMS as internal standard, ^{13}C NMR spectra were recorded at 100 MHz using TMS as internal standard. All chemical shifts were reported as δ values (ppm) relative to TMS and observed coupling constants (*J*) are given in Hertz (Hz). Mass spectra were measured with a HRMS-ESI instrument. Unless otherwise indicated, all reactions were carried out under N_2 atmosphere at room temperature with magnetic stirring. All reagents were purchased from commercial source and without prior purification. Column chromatography was performed on silica gel (200-300 mesh) and the elution was performed with *n*-hexane/ethyl acetate.

II. Preparation of substrate

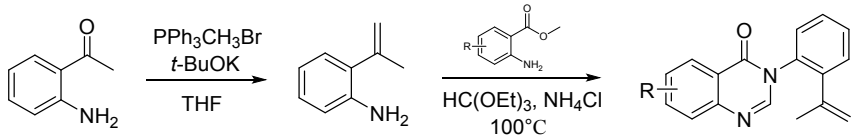
General procedure for the synthesis of equinazoline-4(3*H*)-one derivatives[1,2]



1 **2** n=1, **1a~1n** n=2, **1o~1s**

The mixtures of anthranilic acid (**1**) (1 mmol) and an excess of formamide (10 mmol) in a round-bottom flask were heated at 120 °C with stirring for 3-5 h. The reaction was checked by TLC. After the starting materials completely disappeared, the resulting mixtures were cooled to room temperature and then poured into ice-cold water. The light or dark brown precipitates were formed. The precipitates were filtered and washed three times with water (20 ml each) and dried to give quinazoline-4(3*H*)-one derivatives (**2**). These intermediates were used for the next step without further purification.

To a solution of each respective quinazoline-4(3*H*)-one intermediate (**2**) (1 mmol) in acetone (10 mL) were added K_2CO_3 (207 mg, 1.5 mmol).The resulting mixture was heated at 60 °C with stirring for 30 min. KI (16.6 mg,0.1 mmol) was added and after stirring for further 15 min, brominated olefins (0.13 mL, 1.2 mmol) diluted with acetone (1 mL) was dropwise added into the mixture. The reaction mixture was further stirred at 60 °C for 3 h. After the reaction completed, the resulting mixture was cooled and poured into ice-cold water. The solids were formed, filtered and dried to give the corresponding product (**1a~1n**, **1o~1s)**.

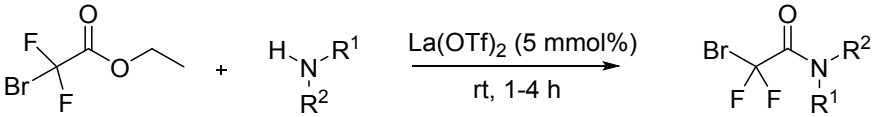


3 **4** **1t~1x**

A round-bottom flask was charged with methyltriphenylphosphonium bromide (5.36 g, 15 mmol) and dry THF (20 mL) under N_2 atmosphere, followed by the addition of potassium tert-butoxide (1.68 g, 15 mmol) at 0 °C. The reaction mixture was allowed to warm to ambient temperature and stir for 0.5 h. Next, 2-aminoacetophenone (**3**) (1.21 g, 10 mmol) was added. The reaction mixture was stirred at room temperature overnight. After completion, the reaction was quenched with saturated $NaHCO_3$ solution, and extracted with EtOAc (100 mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The reaction mixture was purified via column chromatography to give **4**.

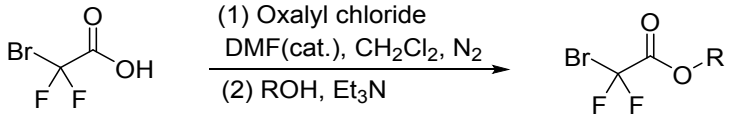
A mixture of 2-amino-benzoic acid esters (1.0 mmol), amines **4** (1.2 mmol), ortho esters (1.5 mmol) and NH_4Cl (21.0 mg, 0.4 mmol) was heated with stirring at 100 °C for 2 h. After cooling, H_2O was added and the product was extracted with CH_2Cl_2 (2×5 mL). The organic layer was dried ($MgSO_4$) and evaporated, and the residue was purified through flash column chromatography or recrystallized from EtOH-hexane to afford the pure product.

General procedure for the synthesis of α-bromo-α,α-difluoroacetamides from ethyl bromodifluoroacetate[3]



A 20 mL tube equipped with a magnetic stir bar was charged with lanthanum trifluoromethanesulfonate (0.25 mmol, 5.0 mol %). The tube was backfilled with argon, then ethyl bromodifluoroacetate (6.0 mmol) and amine (5.0 mmol) were added. The mixture was stirred at the room temperature and monitored by TLC. After the amine was exhausted, the mixture was purified by silica gel column chromatography to give the target amide.

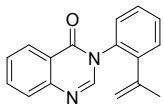
General procedure for the synthesis of α-bromo-α, α-difluoroesters from the corresponding alcohol[4]



α-bromo-α, α-difluoroacetic acid (1 equiv.) was dissolved in dry CH_2Cl_2 (c = 0.45 M) in a dry round bottom flask under an atmosphere of nitrogen. Oxalyl chloride (1.1 equiv.) was then added followed by two drops of DMF. The solution was then stirred at room temperature for 2 hours or until no more gas evolved. The corresponding alcohol (2 equiv.) and triethylamine (1.1 equiv.) was then added dropwise as a solution in CH_2Cl_2 (c = 0.2 M) at 0 °C over 20 min. The cooling was removed and stirring was continued for 2 hours. The crude reaction was then diluted with water and extracted for three times with CH_2Cl_2. The combined organic phases were washed with saturated bicarbonate and dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was then filtered through a short plug of silica (eluent: pentane) and the fractions containing product were concentrated to afford the α-bromo-α, α-difluoroester as a colorless oil.

Characterization data of some raw materials

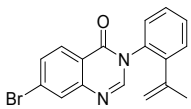
3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1t**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 7.9 Hz, 1H), 8.00 (s, 1H), 7.81 (q, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.53 – 7.43 (m, 3H), 7.38 (d, *J* = 8.2 Hz, 1H), 5.12 (s, 1H), 4.94 (s, 1H), 1.95 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.99 (s), 148.00 (s), 146.70 (s), 141.85 (s), 141.76 (s), 134.51 (s), 134.46 (s), 129.58 (s), 129.55 (s), 128.71 (s), 128.30 (s), 127.60 (s), 127.46 (s), 127.19 (s), 122.44 (s), 117.25 (s), 23.38 (s).

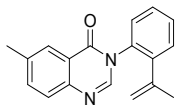
7-bromo-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1u**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.5 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.50 (dt, *J* = 13.3, 6.9 Hz, 3H), 7.37 (d, *J* = 7.5 Hz, 1H), 5.13 (s, 1H), 4.92 (s, 1H), 1.95 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.51 (s), 148.94 (s), 147.82 (s), 141.78 (s) , 141.64 (s), 134.12 (s), 130.87 (s), 130.35 (s), 129.73 (s), 129.62 (s), 129.31 (s), 128.68 (s), 128.54 (s), 128.36 (s), 121.24 (s), 117.32 (s), 23.39 (s).

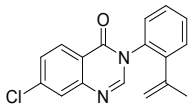
6-methyl-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1v**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.95 (s, 1H), 7.72 -7.61 (m, 2H), 7.54 - 7.43 (m, 3H), 7.40 - 7.35 (m, 1H), 5.11 (s, 1H), 4.93 (s, 1H), 2.54 (s, 3H), 1.95 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.02 (s), 145.93 (s), 141.83 (d, *J* = 7.6 Hz), 137.75 (s), 135.91 (s), 134.59 (s), 129.51 (d, *J* = 6.2 Hz), 128.71 (s), 128.27 (s), 127.40 (s), 126.61 (s), 122.14 (s), 117.15 (s), 23.34 (s), 21.32 (s).

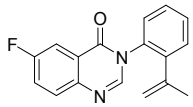
7-chloro-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1w**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.5, 3.3 Hz, 1H), 8.00 (s, 1H), 7.78 (s, 1H), 7.55 -7.43 (m, 4H), 7.37 (d, *J* = 8.1 Hz, 1H), 5.13 (s, 1H), 4.92 (s, 1H), 1.95 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.38 (s), 148.97 (s), 147.87 (s), 141.79 (s), 141.66 (s), 140.77 (s), 134.14 (s), 129.71 (s), 129.61 (s), 128.67 (s), 128.58 (s), 128.35 (s), 128.07 (s), 127.20 (s), 120.89 (s), 117.31 (s), 23.40 (s).

6-fluoro-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1x**)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.4, 2.7 Hz, 1H), 7.97 (s, 1H), 7.81 (dd, *J* = 8.9, 4.8 Hz, 1H), 7.59 -7.45 (m, 4H), 7.38 (d, *J* = 7.4 Hz, 1H), 5.13 (s, 1H), 4.93 (s, 1H), 1.96 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.43 (d, *J* = 225.9 Hz), 160.07 (s), 146.03 (s), 144.62 (s), 141.84 (s), 141.67 (s), 134.21 (s), 130.00 (d, *J* = 8.2 Hz), 129.65 (d, *J* = 8.1 Hz), 128.57 (s), 128.36 (s), 123.14 (s), 122.90 (s), 117.25 (s), 112.31 (s), 112.08 (s), 23.38 (s).

Reference:

1. Huan, L. C.; Tran, P. T.; Phuong, C. V.; Duc, P. H.; Anh, D. T.; Hai, P. T.; Huong, L. T. T.; Thuan, N. T.; Lee, H. J.; Park, E. J.; Kang, J. S.; Linh, N. P.; Hieu, T. T.; Oanh, D. T. K.; Han, S. B.; Nam, N. H., *Bioorg Chem* **2019,** *92*, 103202.

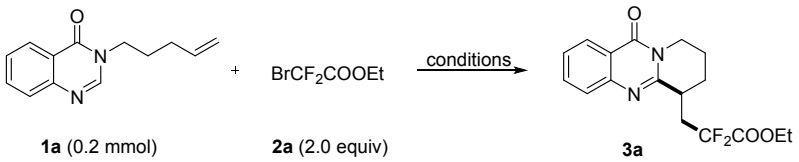
2. G. Huang, B. Liu, M. Teng, Y. Chen, *Synth. Commun.* **2014**, *44*, 1786-1794.

3. L. Wang, X. J. Wei, W. L. Jia, J. J. Zhong, L. Z. Wu, Q. Liu, *Org. Let.* **2014**, *16*, 5842-5845

4. T. L. Andersen, M. W. Frederiksen, K. Domino, T. Skrydstrup, *Angew. Chem., Int. Ed.***2016**, *55*, 10396-10400

III. Optimization of the reaction conditions

Table S1. Variations from standard conditions [a]

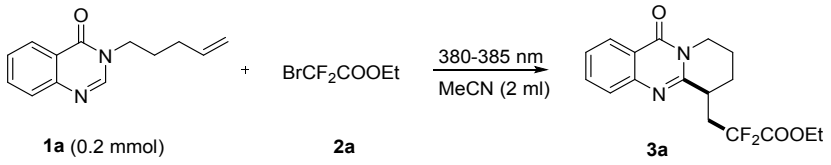


1a (0.2 mmol) **2a** (2.0 equiv) **3a**

Entry	Light source	Additive (2.0 eq.)	Solvent (2ml)	Yield [b] **3a** (%)
1	430-435 nm	TMEDA	MeCN	32
2	400-405 nm	TMEDA	MeCN	66
3	380-385 nm	TMEDA	MeCN	73
4	365-368 nm	TMEDA	MeCN	72
5	380-385 nm	Et_3N	MeCN	0
6	380-385 nm	PMDETA	MeCN	34
7	380-385 nm	Cs_2CO_3	MeCN	22
8	380-385 nm	Na_2CO_3	MeCN	18
9	380-385 nm	K_2HPO_4	MeCN	72
10	380-385 nm	-	MeCN	82
11	380-385 nm	-	MeOH	0
12	380-385 nm	-	DMSO	trace
13	380-385 nm	-	EA	80
14	380-385 nm	-	DCE	56
15	380-385 nm	-	THF	68
16[c]	450-455 nm	-	MeCN	0
17	380-385 nm		MeCN	0
18	-	-	MeCN	0

[a] Conditions: 3-(pent-4-en-1-yl)quinazolin-4(3*H*)-one (**1a**) (0.2 mmol), $BrCF_2COOEt$ (2.0 equiv.), additive (2.0 equiv.), solvent (2 mL), room temperature, N_2, 12 h. [b] Determined by ^{1}HNMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. [c] Under air.

Table S2. Screening of **2a**

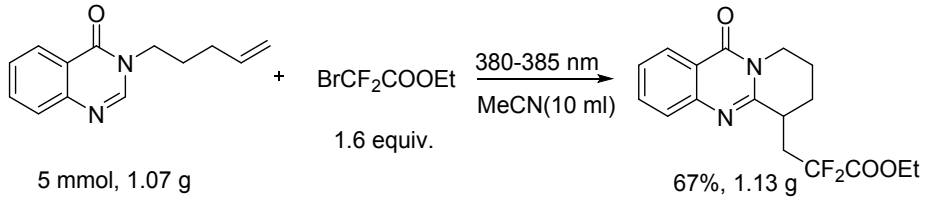


1a (0.2 mmol) **2a** **3a**

Entry	**2a**	Yield (%)
1	1.0 eq.	78
2	1.5 eq.	82
3	2.0 eq.	82
4	3.0 eq.	74

The results showed that 1.5 ~ 2.0 equivalent **2a** is optimum condition.

IV. Gram scale procedure for the synthesis of 3a



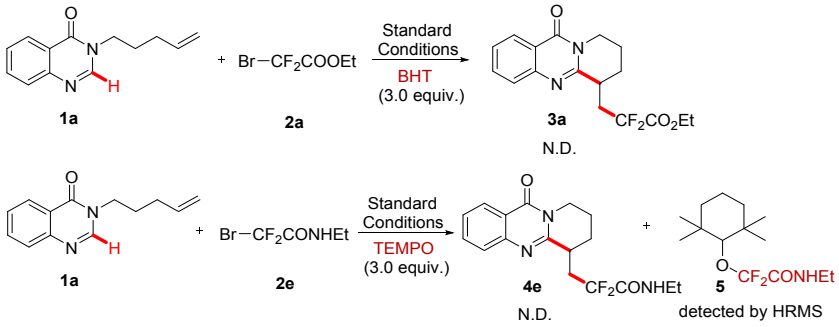
5 mmol, 1.07 g

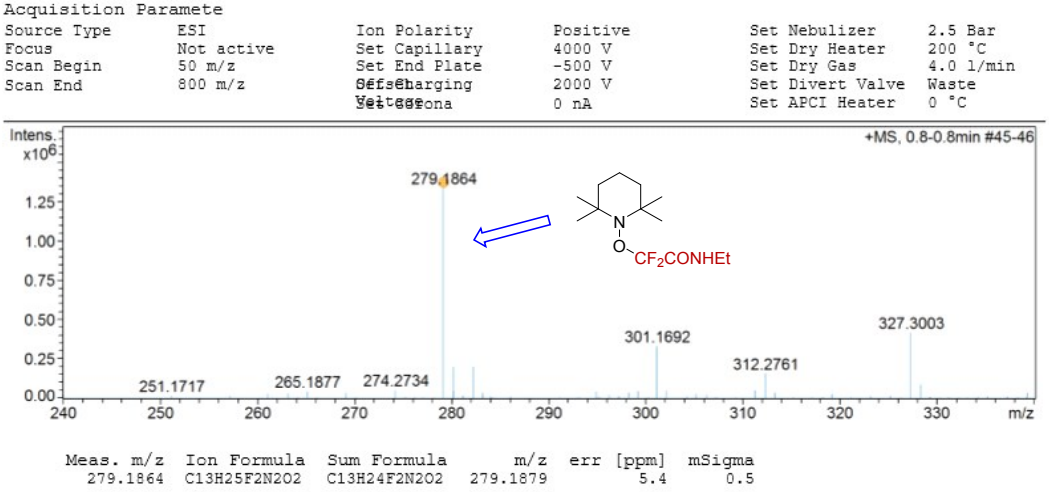
67%, 1.13 g

To a 15 mL Schlenk-tube was charged with quinazoline-4(3*H*)-one **1a** (1.07g, 5.0 mmol), $BrCF_2COOEt$ **2a** (1.62g, 8.0 mmol) and DMSO (10.0 mL). The tube was evacuated and backfilled with N_2 for three times. The mixture was then irradiated by380 nm light (10 w) for 12 h. The reaction mixture was then quenched with water (20 mL) and extracted with DCM (30 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel column (ethyl acetate/hexane, 1:10) to afford **3a** (1.13 g, 67%) as a colorless oil.

V. Control experiments

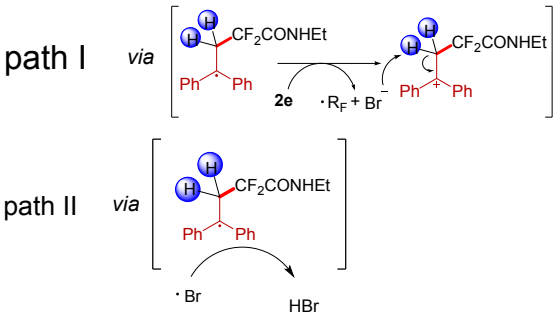
(1)





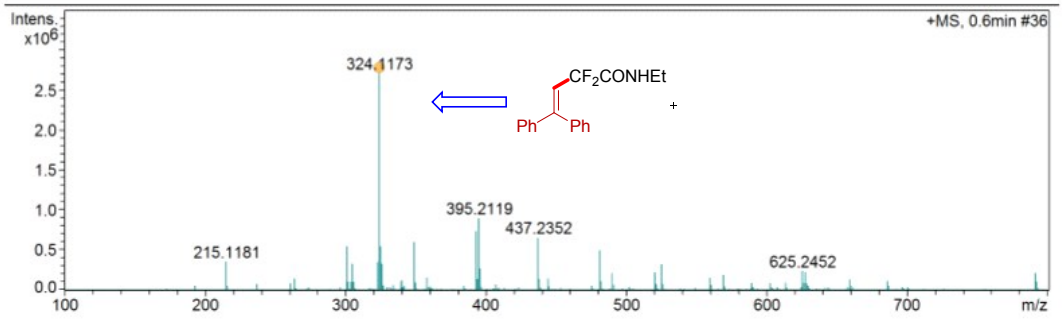
Meas. m/z	Ion Formula	Sum Formula	m/z	err [ppm]	mSigma
279.1864	C13H25F2N2O2	C13H24F2N2O2	279.1879	5.4	0.5

The reaction was completely inhibited by free radical inhibitors, and the radical adducts **5** was detected by HRMS ($[M+H]^+$=279.1864)



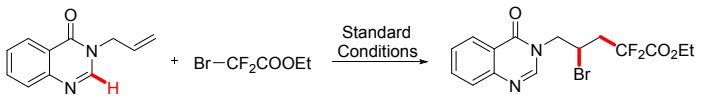
Acquisition Paramete

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.5 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate	-500 V	Set Dry Gas	4.0 l/min
Scan End	800 m/z	Set Charging	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



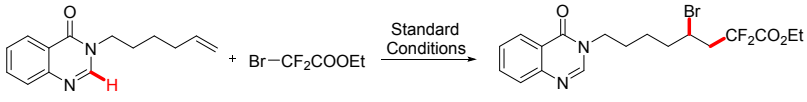
Meas. m/z	Ion Formula	Sum Formula	m/z	err [ppm]	mSigma
324.1173	C18H17F2NNaO	C18H17F2NO	324.1170	-0.7	58.0

(2)



6 **2a** **7**

detected by HRMS

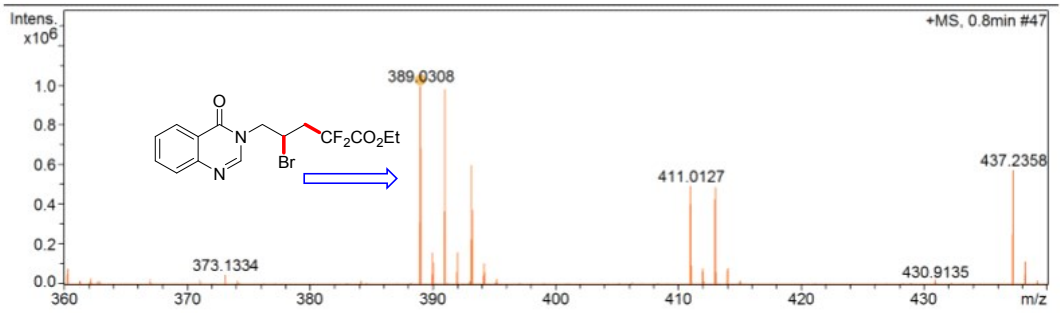


8 **2a** **9**

detected by HRMS

Acquisition Paramete

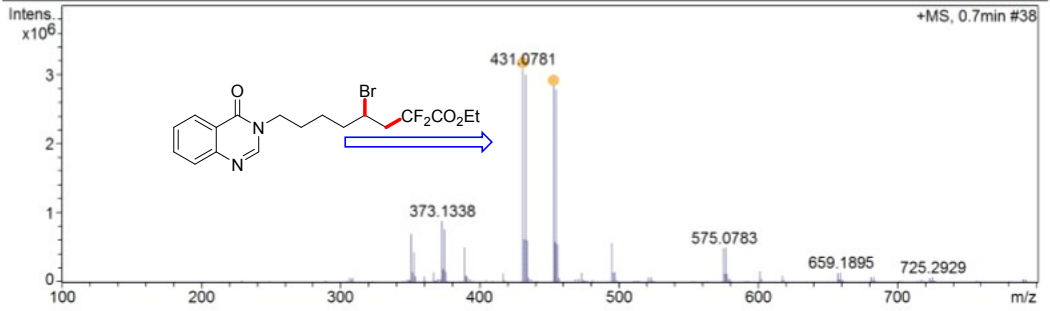
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.5 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate	-500 V	Set Dry Gas	4.0 l/min
Scan End	800 m/z	Set Charging	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	Ion Formula	Sum Formula	m/z	err [ppm]	mSigma
389.0308	C15H16BrF2N2O3	C15H15BrF2N2O3	389.0307	-0.3	7.1

Acquisition Paramete

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.5 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate	-500 V	Set Dry Gas	4.0 l/min
Scan End	800 m/z	Set Charging	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	Ion Formula	Sum Formula	m/z	err [ppm]	mSigma
431.0781	C18H22BrF2N2O3	C18H21BrF2N2O3	431.0776	-1.1	12.4
453.0601	C18H21BrF2N2NaO3		453.0596	-1.0	8.5

The 1,2-difunctionalization products were determined by HRMS, and these results indicated that $BrCF_2COOEt$ underwent a rapid C-Br bond homolysis.

VI. UV-visible absorption Spectra

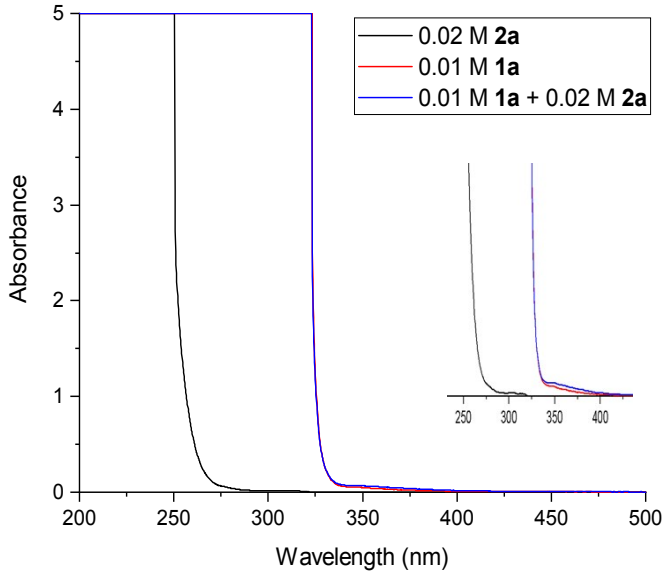


Figure S1. Absorption spectra of **1a** and **2a** (dissolved in MeCN).

VII. Luminescence Quenching Screening Studies

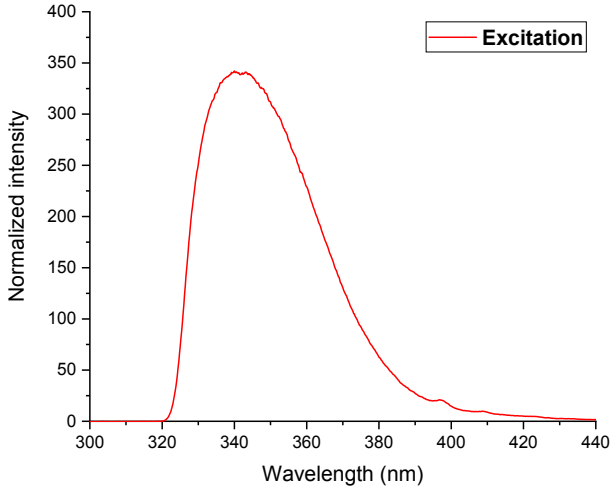


Figure S2. Excitation spectrum of **1a** (0.01 M in MeCN) measured by Fluorescence spectrophotometer. (base on optimum emission wavelength: 433 nm)

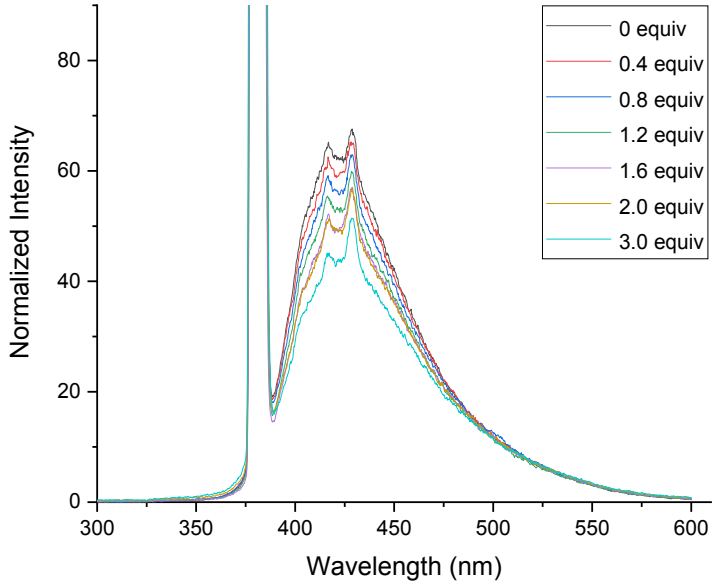


Figure S3. Quenching of the **1a** (0.01 M in MeCN) emission in the presence of increasing amount of ethyl bromodifluoroacetate reagent. (Excitation wavelength: 380 nm)

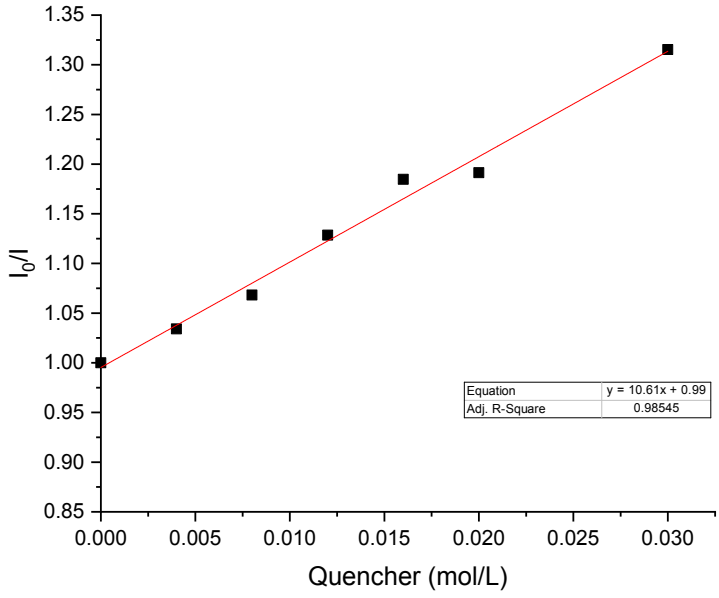


Figure S4. Stern-Volmer plot of Fluorescence quenching of **1a** by **2a**

VIII. Quantum Yield Measurements

Determination of the light intensity at 365 nm.

According to the procedure of Yoon[5] the photon flux of the LED (λ_{max} = 365 nm) was determined

by standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (0.737 g) in H_2SO_4 (10 mL of a 0.05 M solution). A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (5.0 mg) and sodium acetate (1.13 g) in H_2SO_4 (5.0 mL of a 0.5 M solution). Both solutions were stored in the dark. To determine the photon flux of the LED, the ferrioxalate solution (3.0 mL) was placed in a cuvette and irradiated for 90 seconds at λ_{max} = 365 nm. After irradiation, the phenanthroline solution (0.525 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 h to allow the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was measured at 510 nm. A nonirradiated sample was also prepared and the absorbance at 510 nm was measured. Conversion was calculated using eq 1.

	Non-irrad	Irrad 1	Irrad 2	Irrad 3
A_{510nm}	0.284	1.966	1.981	1.924
Average A_{510nm} of irradiation samples		1.957		

$$\textbf{mol } Fe^{2+} = (V \times \Delta A)/ (l \times \varepsilon) \quad (1)$$

$$\textbf{mol } Fe^{2+} = [3.525\times10^{-3}\ L \times (1.957-0.284)]/ (1\ cm \times 11100\ L\ mol^{-1}cm^{-1}) = 5.313\times10^{-7}\ mol$$

V is the total volume (0.003525 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.00 cm), and ε is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 $Lmol^{-1}cm^{-1}$)[6].S2 The photon flux can be calculated using eq 2.

$$\textbf{photo flux} = \text{mol } Fe^{2+}/ (\Phi \times t \times f) \quad (2)$$

$$\textbf{photo flux} = 5.313\times10^{-7} / (1.21 \times 90 \times 1) = 4.879 \times 10^{-9}\ \text{einstein}\ s^{-1}$$

Where Φ is the quantum yield for the ferrioxalate actinometer (1.21 at λ = 365 nm)[7] is the irradiation time (90 s), and f is the fraction of light absorbed at 365 nm by the ferrioxalate actinometer. This value is calculated using eq 3 where $A_{365\ nm}$ is the absorbance of the ferrioxalate solution at 365 nm. An absorption spectrum gave an $A_{365\ nm}$ value of >5, indicating that the fraction of absorbed light (f) is 1.

$$f = 1 - 10^{-A365\ nm} \quad (3)$$

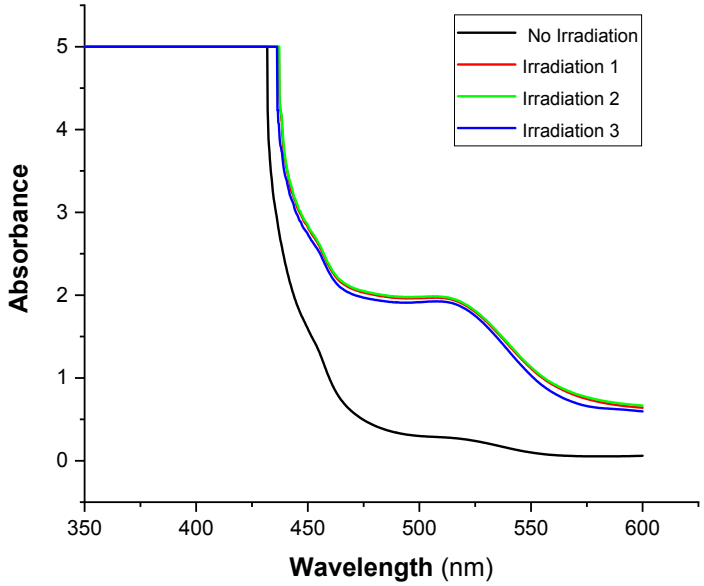
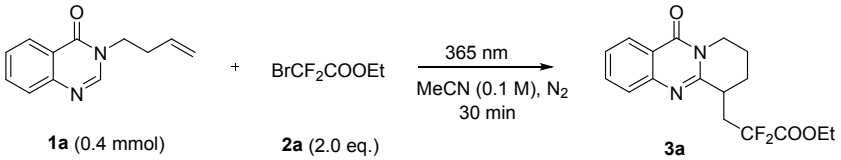


Figure S5. Absorption spectra of three irradiation experiments and non-irradiation experiment

Determination of the reaction quantum yield.



1a (0.4 mmol) **2a** (2.0 eq.) **3a**

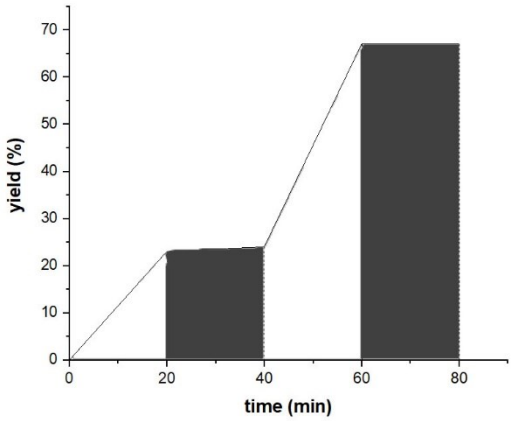
The reaction mixture was stirred and irradiated by blue LED (λ_{max} = 365 nm) for 1800 s. The yield of product was determined by ^{1}H NMR analysis using 1,3,5-Trimethoxybenzene as an internal standard. The yield of **3a** was determined to be 32.3% (0.129×10^{-3} mol of **3a**). The reaction quantum yield (Φ) was determined using eq 4 where the photon flux is 4.879×10^{-9} einsteins s^{-1} (determined by actinometry as described above), t is the reaction time (1800 s) and f is the fraction of incident light absorbed by the catalyst, determined using eq 3.

$$\textbf{Quantum Yield} = \text{moles of product formed}/ (\text{flux} \times f \times t) \quad (4)$$

$$= 0.129 \times 10^{-3} /(4.879 \times 10^{-9} \times 1 \times 1800)$$

$$= 14.69$$

IX. Light-dark cycle experiment



Time (min)	Yield (**3a**)
0	0
20	23
40	24
60	67
80	67

(white represents light, grey represents dark)

Figure S6. Light-dark cycle experiment for the model reaction. The yield of **3a** was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Reference:

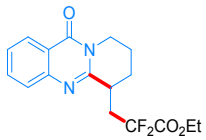
5. Cismesia, M. A.; Yoon, T. P. *Chem. Sci.*, **2015**, *6*, 5426.

6. Kuhn, H. J.; Braslavsky, S. E.; Schmidt, R. *Pure Appl. Chem.*, **2004**, *76*, 2105.

7. Demas, J. N.; Bowman, W. D.; Zalewski, E. F.; Velapoldi, R. A. *J. Phys. Chem.*, **1981**, *85*, 2766.

X. Compound Characterizations

ethyl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3a**)



Colorless oil, yield 82% (110 mg);

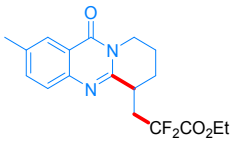
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 6.9 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 4.39 -4.31 (m, 1H), 4.30 -4.22 (m, 2H), 3.97 -3.88 (m, 1H), 3.47 -3.30 (m, 1H), 3.27 -3.18 (m, 1H), 2.43 -2.29 (m, 2H), 2.06 -1.98 (m, 2H), 1.77 -1.66 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.10 (t, *J* = 32.7 Hz), 161.85 (s), 155.54 (s), 146.86 (s), 134.10 (s), 126.82 (s), 126.63 (s), 126.45 (s), 120.21 (s), 116.06 (t, *J* = 252.0Hz), 62.94 (s), 41.08 (s), 36.82 (t, *J* = 23.1 Hz), 35.12 (t, *J* = 3.7 Hz), 25.78 (d, *J* = 12.5 Hz), 20.63 (d, *J* = 9.5 Hz), 13.90 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.33, -101.02, -105.47, -106.15.

HRMS: $C_{17}H_{18}F_2N_2O_3$ $[M+H]^+$;calculated: 337.1358, found: 337.1342.

ethyl 2,2-difluoro-3-(2-methyl-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3b**)



White solid, yield 56% (78 mg), 70.6 -75.3 °C;

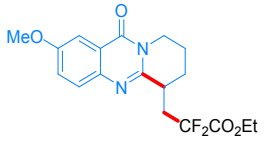
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 0.6 Hz, 1H), 7.55 -7.49 (m, 2H), 4.35 (dt, *J* = 13.8, 6.3 Hz, 1H), 4.29 -4.22 (m, 2H), 3.96 -3.88 (m, 1H), 3.44 -3.30 (m, 1H), 3.25 -3.17 (m, 1H), 2.47 (s, 3H), 2.41 -2.28 (m, 2H), 2.05 -1.97 (m, 2H), 1.75 -1.65 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.12 (t, *J* = 32.7 Hz), 161.87 (s), 154.63 (s), 144.88 (s), 136.60 (s), 135.62 (s), 126.64 (s), 126.01 (s), 119.94 (s), 116.07 (t, *J* = 251.5 Hz), 62.92 (s), 41.04 (s), 36.84 (t, *J* = 23.1 Hz), 35.03 (t, *J* = 3.7 Hz), 25.88 (s), 21.30 (s), 20.73 (s), 13.91 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.16, -103.85, -106.55, -107.24.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1510.

ethyl 2,2-difluoro-3-(2-methoxy-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3c**)



Colorless oil, yield 92% (135 mg);

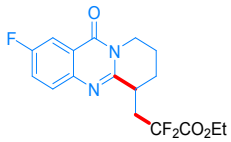
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 2.9 Hz, 1H), 7.52 (d, *J* = 8.9 Hz, 1H), 7.29 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.37 -4.30 (m, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.98 -3.93 (m, 1H), 3.90 (s, 3H), 3.44 -3.27 (m, 1H), 3.24 -3.16 (m, 1H), 2.40 -2.29 (m, 2H), 2.05 -1.98 (m, 2H), 1.75 -1.64 (m, 1H), 1.31 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07 (t, *J* = 32.7 Hz), 161.65 (s), 158.05 (s), 153.14 (s), 141.54 (s), 128.39 (s), 124.42 (s), 120.85 (s), 116.09 (t, *J* = 251.5 Hz), 105.77 (s), 62.88 (s), 55.72 (s), 41.18 (s), 36.84 (t, *J* = 23.0 Hz), 34.92 (t, *J* = 3.7 Hz), 25.89 (s), 20.71 (s), 13.87 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.34, -101.03, -105.41, -106.10.

HRMS: $C_{18}H_{20}F_2N_2O_4$ $[M+H]^+$;calculated: 367.1464, found: 367.1459.

ethyl 2,2-difluoro-3-(2-fluoro-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3d**)



White solid, yield 58% (82 mg), 103.2 -104 °C;

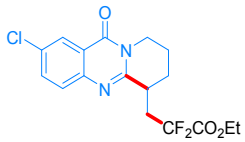
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 -7.82 (m, 1H), 7.65 -7.58 (m, 1H), 7.47 -7.39 (m, 1H), 4.34 (dd, *J* = 14.1, 6.3 Hz, 1H), 4.27 (dd, *J* = 14.1, 7.0 Hz, 2H), 3.98 -3.89 (m, 1H), 3.45 -3.28 (m, 1H), 3.27 -3.17 (m, 1H), 2.45 -2.28 (m, 2H), 2.08 -1.99 (m, 2H), 1.76 -1.65 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.08 (t, *J* = 32.7 Hz), 161.20 (d, *J* = 3.5 Hz), 160.59 (d, *J* = 247.7 Hz), 154.86 (d, *J* = 2.1 Hz), 143.58 (s), 129.28 (d, *J* = 8.1 Hz), 122.75 (d, *J* = 24.2 Hz), 121.35 (d, *J* = 8.7 Hz), 117.25 (t, *J* = 250.2 Hz), 111.33 (d, *J* = 23.5 Hz), 62.96 (s), 41.25 (s), 36.76 (t, *J* = 23.0 Hz), 35.06 (t, *J* = 3.7 Hz), 25.82 (s), 20.65 (s), 13.91 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.46, -101.15, -105.68, -106.37, -113.09.

HRMS: $C_{17}H_{18}F_3N_2O_3[M+H]^+$;calculated: 355.1264, found: 355.1263.

ethyl 3-(2-chloro-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3e**)



White solid, yield 65% (96 mg), 65.9 -70.6 °C;

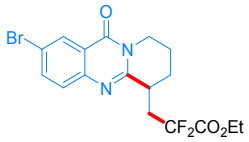
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 2.4 Hz, 2H), 7.64 (dd, *J* = 8.7, 2.4 Hz, 2H), 7.56 (d, *J* = 8.7 Hz, 2H), 4.40 -4.21 (m, 6H), 4.00 -3.86 (m, 2H), 3.48 -3.12 (m, 4H), 2.48 -2.24 (m, 4H), 2.12 -1.94 (m, 4H), 1.88 -1.46 (m, 3H), 1.32 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07 (t, *J* = 32.6 Hz), 160.87 (s), 155.91 (s), 145.38 (s), 134.57 (s), 132.17 (s), 128.57 (s), 125.99 (s), 121.23 (s), 115.96 (t, *J* = 249.4 Hz), 62.98 (s), 41.31 (s), 36.74 (t, *J* = 23.1 Hz), 35.18 (t, *J* = 3.6 Hz), 25.79 (s), 20.65 (s), 13.93 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.53, -101.22, -105.53, -106.22.

HRMS: $C_{17}H_{17}ClF_2N_2O_3[M+H]^+$;calculated: 371.0968, found: 371.0969.

ethyl 3-(2-bromo-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3f**)



White solid, yield 64% (106 mg), 87.8 -90.0 °C;

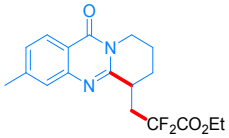
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 -8.33 (m, 1H), 7.83 -7.73 (m, 1H), 7.56 -7.45 (m, 1H), 4.40 -4.25 (m, 3H), 4.00 -3.90 (m, 1H), 3.45 -3.30 (m, 1H), 3.27 -3.16 (m, 1H), 2.44 -2.30 (m, 2H), 2.09 -2.00 (m, 2H), 1.78 -1.67 (m, 1H), 1.37 -1.29 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07 (t, *J* = 32.6 Hz), 160.71 (s), 156.08 (s), 145.70 (s), 137.30 (s), 129.18 (s), 128.74 (s), 121.58 (s), 119.88 (s), 115.97 (t, *J* = 252.0Hz), 62.99 (s), 41.33 (s), 36.74 (t, *J* = 28.8 Hz), 35.21 (t, *J* = 3.6 Hz), 25.75 (s), 20.64 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.52, -101.20, -105.56, -106.25.

HRMS: $C_{17}H_{17}BrF_2N_2O_3[M+H]^+$;calculated: 415.0463, found: 415.0455

ethyl 2,2-difluoro-3-(3-methyl-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3g**)



White solid, yield 64% (90 mg), 99.0 -104 °C;

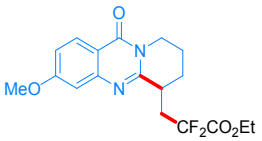
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 1H), 7.43 (s, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 4.40-4.32 (m, 1H), 4.32 -4.24 (m, 2H), 3.97 -3.89 (m, 1H), 3.46 -3.32 (m, 1H), 3.27 -3.18 (m, 1H), 2.50 (s, 3H), 2.42 -2.31 (m, 2H), 2.06 -1.98 (m, 2H), 1.76 -1.66 (m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.13 (t, *J* = 32.7 Hz), 161.82 (s), 155.56 (s), 147.00 (s), 145.07 (s), 128.11 (s), 126.54 (s), 126.49 (s), 117.85 (s), 116.08 (t, *J* = 251.5 Hz), 62.94 (s), 40.95 (s), 36.83 (t, *J* = 23.1 Hz), 35.10 (t, *J* = 3.6 Hz), 25.88 (s), 21.86 (s), 20.72 (s), 13.90 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.45, -101.13, -105.46, -106.14.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1512.

ethyl 2,2-difluoro-3-(3-methoxy-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3h**)



Colorless oil, yield 52% (76 mg);

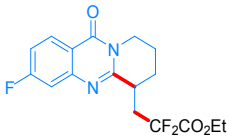
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 2H), 4.38 -4.26 (m, 3H), 3.97 -3.90 (m, 4H), 3.47 -3.32 (m, 1H), 3.28 -3.18 (m, 1H), 2.43 -2.31 (m, 2H), 2.07 -1.99 (m, 2H), 1.77 -1.67 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.12 (t, *J* = 33.9 Hz), 161.41 (s), 156.27 (s), 149.05 (s), 128.24 (s), 116.79 (s), 116.04 (t, *J* = 251.8 Hz), 113.81 (s), 107.25 (s), 62.96 (s), 55.65 (s), 40.94 (s), 36.85 (t, *J* = 23.1 Hz), 35.13 (s), 25.82 (s), 20.68 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.72, -101.41, -105.16, -105.85.

HRMS: $C_{18}H_{20}F_2N_2O_4$ $[M+H]^+$;calculated: 367.1464, found: 367.1453.

ethyl 2,2-difluoro-3-(3-fluoro-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3i**)



White solid, yield 52% (74 mg), 100.0 -103.1 °C;

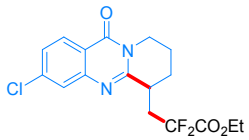
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 8.9, 6.2 Hz, 1H), 7.29 -7.25 (m, 1H), 7.17 (td, *J* = 8.6, 2.5 Hz, 1H), 4.42 -4.25 (m, 3H), 4.03 -3.85 (m, 1H), 3.50 -3.29 (m, 1H), 3.29 -3.17 (m, 1H), 2.50 -2.28 (m, 2H), 2.13 -1.98 (m, 2H), 1.77 -1.67 (m, 1H), 1.35 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.39 (d, *J* = 253.9 Hz), 164.08 (t, *J* = 32.7 Hz), 161.16 (s), 156.98 (s), 148.98 (d, *J* = 13.1 Hz), 129.43 (d, *J* = 10.7 Hz), 116.98 (d, *J* = 1.9 Hz), 115.98 (t, *J* =252.8 Hz), 115.35 (d, *J* = 23.7 Hz), 112.02 (d, *J* = 21.7 Hz), 63.00 (s), 41.12 (s), 36.74 (t, *J* = 23.0 Hz), 35.23 (t, *J* = 3.6 Hz), 25.78 (s), 20.66 (s), 13.93 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.52, -101.21, -103.76, -105.58, -106.27.

HRMS: $C_{17}H_{18}F_3N_2O_3$ $[M+H]^+$;calculated: 355.1264, found: 355.1254.

ethyl 3-(3-chloro-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3j**)



White solid, yield 60% (89 mg), 68.2 -71.0 °C;

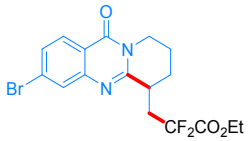
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.35-4.25 (m, 3H), 3.96 -3.88 (m, 1H), 3.42 -3.28 (m, 1H), 3.26-3.17 (m, 1H), 2.42 -2.31 (m, 2H), 2.06 -1.99 (m, 2H), 1.70 (m, 1H), 1.34 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07 (t, *J* = 32.6 Hz), 161.26 (s), 156.98 (s), 147.79 (s), 140.30 (s), 128.18 (s), 127.11 (s), 126.38 (s), 118.67 (s), 115.95 (t, *J* = 252.0Hz), 63.02 (s), 41.19 (s), 36.71 (t, *J* = 23.0 Hz), 35.24 (t, *J* = 3.6 Hz), 25.75 (s), 20.64 (s), 13.93 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.58, -101.27, -105.55, -106.24.

HRMS: $C_{17}H_{17}ClF_2N_2O_3[M+Na]^+$;calculated: 393.0788, found: 393.0794.

ethyl 3-(3-bromo-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3k**)



White solid, yield 62% (103 mg), 90.0 -93.2 °C;

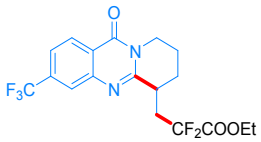
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.82 (dd, *J* = 10.7, 1.6 Hz, 1H), 7.54 (m, 1H), 4.35-4.23 (m, 3H), 3.96 -3.86 (m, 1H), 3.42 -3.27 (m, 1H), 3.26 -3.16 (m, 1H), 2.36 (dt, *J* = 12.0, 5.4 Hz, 2H), 2.06 -1.97 (m, 2H), 1.77-1.64 (m, 1H), 1.34 (td, *J* = 7.2, 1.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.07 (t, *J* = 32.6 Hz), 161.38 (s), 156.96 (s), 147.81 (s), 129.90 (s), 129.53 (s), 128.84 (d, *J* = 7.4 Hz), 128.19 (s), 119.02 (s), 115.94 (t, *J* = 252.0Hz), 63.04 (s), 41.22 (s), 36.71 (t, *J* = 22.3 Hz), 35.20 (s), 25.73 (s), 20.63 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.59, -101.27, -105.58, -106.27.

HRMS: $C_{17}H_{17}BrF_2N_2O_3[M+H]^+$;calculated: 415.0463, found: 415.0456

ethyl 2,2-difluoro-3-(11-oxo-3-(trifluoromethyl)-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3l**)



White solid, yield 62% (100 mg), 62.2 -67.9 °C;

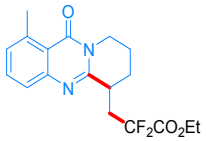
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.3 Hz, 1H), 7.95 (s, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 4.44 -4.25 (m, 3H), 4.07 -3.90 (m, 1H), 3.49 -3.33 (m, 1H), 3.32 -3.18 (m, 1H), 2.51 -2.33 (m, 2H), 2.12 -2.00 (m, 2H), 1.83 -1.67 (m, 1H), 1.37 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.11 (t, *J* = 32.5 Hz), 161.11 (s), 157.19 (s), 146.78 (s), 136.30 -136.23 (m), 135.98 (d, *J* = 29.4 Hz), 135.51 (s), 135.18 (s), 127.89 (s), 124.50 (s), 122.41 (d, *J* = 3.7 Hz), 115.94 (t, *J* = 253.4 Hz), 63.09 (s), 41.38 (s), 36.86 (s), 36.74 (t, *J* = 23.1 Hz), 35.27 (d, *J* = 3.4 Hz), 25.70 (s), 20.61 (s), 13.92 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -63.21 (d, *J* = 4.6 Hz), -100.66 (s), -101.35 (s), -105.40 – -105.50 (m), -106.11 – -106.19 (m).

HRMS: $C_{18}H_{17}F_5N_2O_3[M+H]^+$;calculated: 405.1215, found: 405.1232

ethyl 2,2-difluoro-3-(1-methyl-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3m**)



White solid, yield 46% (64 mg), 125.0 -126.2 °C;

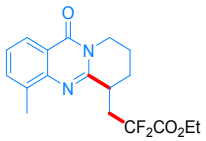
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, *J* = 7.7 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 4.29 -4.20 (m, 3H), 3.93 -3.85 (m, 1H), 3.45 -3.28 (m, 1H), 3.18 (dt, *J* = 11.1, 7.1 Hz, 1H), 2.86 (s, 3H), 2.42 -2.27 (m, 2H), 2.05 -1.97 (m, 2H), 1.72 -1.65 (m, 1H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.14 (t, *J* = 32.7 Hz), 162.46 (s), 155.09 (s), 148.42 (s), 140.86 (s), 133.20 (s), 129.02 (s), 125.05 (s), 118.77(s), 116.11 (t, *J* = 251.5Hz), 62.94 (s), 40.97 (s), 36.87 (t, *J* = 23.2 Hz), 35.08 (t, *J* = 3.7 Hz), 25.90 (s), 23.08 (s), 20.87 (s), 13.91 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.34, -101.03, -105.53, -106.22.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1500.

ethyl 2,2-difluoro-3-(4-methyl-11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**3n**)



Colorless oil, yield 48% (67 mg);

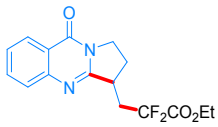
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 4.37 -4.30 (m, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.98 -3.89 (m, 1H), 3.54 -3.39 (m, 1H), 3.27 -3.15 (m, 1H), 2.57 (s, 3H), 2.47 -2.32 (m, 2H), 2.06 -1.97 (m, 2H), 1.76 - 1.64 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.14 (t, *J* = 32.7 Hz), 162.26 (s), 154.16 (s), 145.32 (s), 135.51 (s), 134.64 (s), 126.07 (s), 124.28 (s), 120.09 (s), 116.15 (t, *J* = 252.0 Hz), 62.97 (s), 41.00 (s), 36.65 (t, *J* = 22.9 Hz), 35.31 (t, *J* = 3.6 Hz), 25.89 (s), 20.88 (s), 17.12 (s), 13.88 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.32, -102.01, -104.72, -105.40.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1519.

ethyl 2,2-difluoro-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**3o**)



White solid, yield 61% (78 mg), 91.3 -95.6 °C;

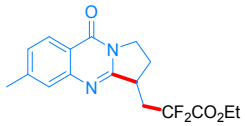
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 4.47 -4.34 (m, 3H), 4.04 -3.90 (m, 1H), 3.65 -3.50 (m, 1H), 3.34 -3.15 (m, 1H), 2.80 -2.64 (m, 1H), 2.41 -2.20 (m, 1H), 2.15 -1.98 (m, 1H), 1.41 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.74 (t, *J* = 32.4 Hz), 160.72 (s), 159.28 (s), 148.89 (s), 134.17 (s), 126.99 (s), 126.52 (s), 126.40 (s), 120.79 (s), 115.58 (t, *J* = 251.2 Hz), 63.20 (s), 44.78 (s), 37.99 (s), 36.40 (t, *J* = 23.0 Hz), 27.82 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.09, -103.79, -106.47, -107.17.

HRMS: $C_{16}H_{16}F_2N_2O_3$ $[M+H]^+$;calculated: 323.1202, found: 323.1190.

ethyl 2,2-difluoro-3-(6-methyl-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**3p**)



Colorless oil, yield 48% (65 mg);

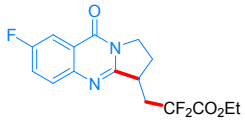
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.1 Hz, 1H), 7.48 (s, 1H), 7.29 (s, 2H), 4.45 -4.33 (m, 3H), 4.00 -3.87 (m, 1H), 3.60 -3.49 (m, 1H), 3.29 -3.12 (m, 1H), 2.77 -2.62 (m, 1H), 2.52 (s, 3H), 2.39 -2.20 (m, 1H), 2.12 -1.95 (m, 1H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.76 (t, *J* = 32.3 Hz), 160.69 (s), 159.33 (s), 149.04 (s), 145.17 (s), 128.08 (s), 126.77 (s), 126.21 (s), 118.39 (s), 115.60 (t, *J* = 252.5 Hz), 63.18 (s), 44.69 (s), 37.97 (s), 36.43 (t, *J* = 23.0 Hz), 27.83 (s), 21.80 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.15, -103.84, -106.51, -107.20.

HRMS: $C_{17}H_{18}F_2N_2O_3[M+H]^+$;calculated: 337.1358, found: 337.1343.

ethyl 2,2-difluoro-3-(7-fluoro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**3q**)



White solid, yield 44% (60 mg), 105.0 -108.2 °C;

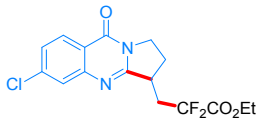
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.5, 3.0 Hz, 1H), 7.68 (dd, *J* = 9.0, 4.8 Hz, 1H), 7.46 (ddd, *J* = 8.9, 8.1, 3.0 Hz, 1H), 4.43 -4.33 (m, 3H), 3.99 -3.91 (m, 1H), 3.60 -3.50 (m, 1H), 3.28 -3.11 (m, 1H), 2.75 -2.66 (m, 1H), 2.38 -2.20 (m, 1H), 2.13 -1.99 (m, 1H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.71 (t, *J* = 32.3 Hz), 160.74 (d, *J* = 248.0 Hz), 160.01 (d, *J* = 3.5 Hz), 158.74 (d, *J* = 2.2 Hz), 145.54 (s), 129.30 (d, *J* = 8.2 Hz), 122.65 (d, *J* = 24.1 Hz), 122.11 (d, *J* = 8.6 Hz), 116.79 (t, *J* = 251.2 Hz), 111.37 (d, *J* = 23.6 Hz),63.22 (s), 44.87 (s), 37.93 (s), 36.41 (t, *J* = 23.0 Hz), 27.89 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.05, -103.74, -106.34, -107.04, -113.20.

HRMS: $C_{16}H_{15}F_3N_2O_3[M+H]^+$;calculated: 341.1108, found: 341.1099.

ethyl 3-(6-chloro-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)-2,2-difluoropropanoate (**3r**)



White solid, yield 52% (74 mg), 118.6 -119.5 °C;

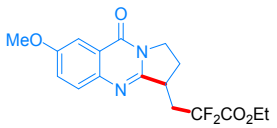
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.6 Hz, 1H), 7.69 (s, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 4.47 -4.32 (m, 3H), 4.00 -3.88 (m, 1H), 3.66 -3.52 (m, 1H), 3.34 -3.09 (m, 1H), 2.80 -2.63 (m, 1H), 2.42 -2.19 (m, 1H), 2.14 -1.97 (m, 1H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.69 (t, *J* = 32.6 Hz), 160.65 (s), 160.11 (s), 149.90 (s), 140.37 (s), 127.82 (s), 127.13 (s), 126.64 (s), 119.30 (s), 115.50 (t, *J* = 251.5 Hz), 63.25 (s), 44.90 (s), 38.12 (s), 36.30 (t, *J* = 23.5 Hz), 27.81 (s), 13.95 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.13, -103.82, -106.51, -107.20.

HRMS: $C_{16}H_{15}ClF_2N_2O_3[M+H]^+$;calculated: 357.0812, found: 357.0817.

ethyl 2,2-difluoro-3-(7-methoxy-9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**3s**)



White solid, yield 54% (76 mg), 110.2 -111.5 °C

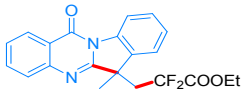
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 2.8 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.36 (dd, *J* = 8.9, 2.9 Hz, 1H), 4.43 -4.37 (m, 3H), 3.98 -3.94 (m, 4H), 3.62 -3.51 (m, 1H), 3.31 -3.12 (m, 1H), 2.77 -2.65 (m, 1H), 2.39 -2.23 (m, 1H), 2.11 -2.01 (m, 1H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.77 (t, *J* = 32.4 Hz), 160.58 (s), 158.24 (s), 157.08 (s), 143.42 (s), 128.45 (s), 124.33 (s), 121.56 (s), 115.61 (t, *J* = 251.2 Hz), 105.97 (s), 63.19 (s), 55.81 (s), 44.82 (s), 37.75 (s), 36.48 (t, *J* = 22.9 Hz), 27.95 (s), 13.94 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.07, -103.76, -106.46, -107.16.

HRMS: $C_{17}H_{18}F_2N_2O_4[M+H]^+$;calculated: 353.1307, found: 353.1303.

ethyl 2,2-difluoro-3-(6-methyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)propanoate (**3t**)



White solid, yield 78% (120 mg), 88.7 -89.8 °C;

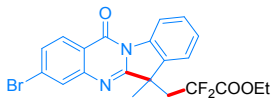
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.0 Hz, 1H), 8.48 (d, *J* = 7.9 Hz, 1H), 7.86 -7.79 (m, 2H), 7.60 -7.55 (m, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 4.01 -3.91 (m, 1H), 3.90 -3.80 (m, 1H), 3.23 (q, *J* = 14.4 Hz, 1H), 3.14 -3.00 (m, 1H), 1.71 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.43 (t, *J* = 32.3 Hz), 162.03 (s), 159.95 (s), 147.23 (s), 139.17 (s), 134.33 (s), 132.97 (s), 129.15 (s), 127.29 (s), 126.93 (s), 126.13 (s), 123.70 (s), 121.47 (s), 117.39 (s), 114.49 (t, *J* = 251.0 Hz), 62.99 (s), 45.48 (s), 42.93 (t, *J* = 23.3 Hz), 27.94 (s), 13.57 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.63, -99.34, -104.63, -105.34.

HRMS: $C_{21}H_{18}F_2N_2O_3[M+H]^+$;calculated: 385.1358, found: 385.1355.

ethyl 3-(3-bromo-6-methyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3u**)



Light yellow solid, yield 81% (150 mg), 132.5 -133.6 °C;

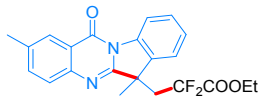
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.31 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 1.2 Hz, 1H), 7.67 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 4.05 -3.79 (m, 2H), 3.35 -2.96 (m, 2H), 1.70 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.43 (s), 163.371 (t, *J* = 31.9 Hz), 159.44 (s), 148.31 (s), 138.97 (s), 132.84 (s), 130.23 (s), 130.17 (s), 129.24 (s), 129.03 (s), 128.33 (s), 126.33 (s), 123.77 (s), 120.33 (s), 117.40 (s), 116.98 (t, *J* = 250.5 Hz), 63.05 (s), 45.59 (s), 42.90 (t, *J* = 22.9 Hz), 27.87 (s), 13.60 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.58 (s), -99.29 (s), -105.04 (s), -105.75 (s).

HRMS: $C_{21}H_{17}BrF_2N_2O_3$ $[M+H]^+$;calculated: 463.0463, found: 463.0467.

ethyl 3-(2,6-dimethyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3v**)



White solid, yield 74% (118 mg), 114.1 -115.7 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 -8.26 (m, 1H), 7.79 -7.65 (m, 2H), 7.52 -7.43 (m, 1H), 4.36 (dd, *J* = 13.8, 6.7 Hz, 5H), 4.03 -3.88 (m, 1H), 3.78 -3.63 (m, 1H), 3.37 -3.14 (m, 1H), 2.82 -2.66 (m, 1H), 2.42 -2.18 (m, 1H), 2.15 -1.98 (m, 1H), 1.49 -1.42 (m, 6H).

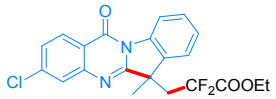
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.44 (t, *J* = 35.4 Hz), 161.06 (s), 160.01 (s), 145.32 (s), 139.25 (s), 137.08 (s), 135.69 (s), 133.06 (s), 129.08 (s), 127.12 (s), 126.40 (s), 126.01 (s), 123.66 (s), 121.21 (s),

117.37 (s), 114.51 (t, J = 251.5 Hz), 62.95 (s), 45.30 (s), 42.98 (t, J = 23.4 Hz), 27.95 (s), 21.30 (s), 13.56 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.66, -99.37, -104.47, -105.18.

HRMS: $C_{22}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 399.1515, found: 399.1515.

ethyl 3-(3-chloro-6-methyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)-2,2-difluoropropanoate (**3w**)



White solid, yield 82% (137 mg), 116.2 -117.2 °C;

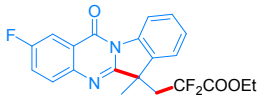
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, J = 8.1 Hz, 1H), 8.38 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 1.4 Hz, 1H), 7.51 (t, J = 7.2 Hz, 2H), 7.46 (d, J = 7.3 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 4.07 -3.93 (m, 1H), 3.92 -3.81 (m, 1H), 3.31 -2.99 (m, 2H), 1.70 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.47 (s), 163.3 (t, J = 32.3 Hz), 159.31 (s), 148.31 (s), 140.51 (s), 138.97 (s), 132.84 (s), 129.23 (s), 128.31 (s), 127.44 (s), 127.01 (s), 126.30 (s), 123.76 (s), 119.96 (s), 117.18 (s), 114.47 (t, J = 246.9 Hz), 63.04 (s), 45.61 (s), 42.87 (t, J = 23.3 Hz), 27.86 (s), 13.60 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.59, -99.30, -104.96, -105.67.

HRMS: $C_{21}H_{17}ClF_2N_2O_3$ $[M+H]^+$;calculated: 419.0969, found: 419.0976.

ethyl 2,2-difluoro-3-(2-fluoro-6-methyl-12-oxo-6,12-dihydroindolo[2,1-*b*]quinazolin-6-yl)propanoate (**3x**)



White solid, yield 77% (124 mg), 114.3 -115.2 °C;

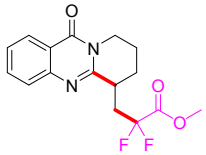
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 -8.22 (m, 1H), 7.76 -7.67 (m, 1H), 7.67 -7.58 (m, 1H), 7.50 -7.40 (m, 1H), 5.08 -4.91 (m, 1H), 4.39 -4.27 (m, 1H), 4.02 -3.89 (m, 1H), 3.59 -3.40 (m, 1H), 3.21 (s, 1H), 2.46 -2.26 (m, 3H), 2.07 -1.94 (m, 3H), 1.82 -1.67 (m, 3H), 1.41 -1.32 (m, 1H), 1.29 -1.22 (m, 1H), 1.09 -0.97 (m, 1H), 0.92 -0.83 (m, 8H), 0.80 -0.78 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.37 (t, J = 31.9 Hz), 161.82 (d, J = 78.3 Hz), 161.41 (s), 159.74 (s), 159.13 (d, J = 3.3 Hz), 143.97 (s), 138.92 (s), 133.00 (s), 129.62 (d, J = 8.2 Hz), 129.19 (s), 126.34 (s), 123.76 (s), 122.83 (d, J = 7.1 Hz), 122.56 (s), 117.56 -116.91 (m), 114.50 (d, J = 5.9 Hz), 112.01 (s), 111.78 (s), 63.01 (s), 45.39 (d, J = 5.0 Hz), 43.07 (t, J = 22.3 Hz), 27.89 (s), 13.58 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.59, -99.30, -104.82, -105.53, -112.73.

HRMS: $C_{21}H_{17}F_3N_2O_3$ $[M+H]^+$;calculated: 403.1264, found: 403.1263.

methyl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**4a**)



Colorless oil, yield 78% (100 mg);

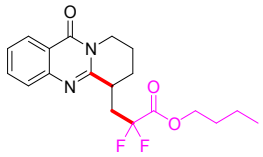
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 -8.22 (m, 1H), 7.77 -7.69 (m, J = 5.3, 3.2, 2.1 Hz, 1H), 7.66 -7.60 (m, 1H), 7.48 -7.41 (m, 1H), 4.42 -4.31 (m, 1H), 3.99 -3.90 (m, 1H), 3.83 (s, 3H), 3.47 -3.30 (m, 1H), 3.29 -3.18 (m, 1H), 2.44 -2.30 (m, 2H), 2.10 -1.99 (m, 2H), 1.78 -1.66 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.61 (t, J = 32.9 Hz), 161.87 (s), 155.51 (s), 146.87 (s), 134.16 (s), 126.84 (s), 126.69 (s), 126.51 (s), 120.24 (s), 116.09 (t, J = 251.5 Hz), 53.45 (s), 41.06 (s), 36.93 (t, J = 23.1 Hz), 35.09 (t, J = 3.8 Hz), 25.95 (s), 20.74 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.78, -100.46, -105.62, -106.31.

HRMS: $C_{16}H_{16}F_2N_2O_3$ $[M+H]^+$;calculated: 323.1202, found: 323.1189.

butyl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**4b**)



Colorless oil, yield 64% (93 mg);

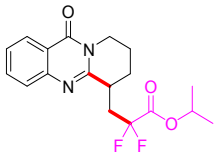
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.76 -7.70 (m, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.49 -7.42 (m, 1H), 4.37 (dt, *J* = 14.0, 6.3 Hz, 1H), 4.24 -4.16 (m, 2H), 4.00 -3.90 (m, 1H), 3.50 -3.32 (m, 1H), 3.30 -3.18 (m, 1H), 2.44 -2.30 (m, 2H), 2.07 -1.99 (m, 2H), 1.78 -1.62 (m, 3H), 1.42 -1.32 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.20 (t, *J* = 32.7 Hz), 161.87 (s), 155.52 (s), 146.86 (s), 134.13 (s), 126.86 (s), 126.66 (s), 126.49 (s), 120.23 (s), 116.12 (t, *J* = 252.0 Hz), 66.75 (s), 41.07 (s), 37.09 (s), 36.86 (t, *J* = 23.2 Hz), 36.63 (s), 35.14 (t, *J* = 3.7 Hz), 30.25 (s), 25.88 (s), 20.72 (s), 18.91 (s), 13.59 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.11, -100.79, -105.49, -106.17.

HRMS: $C_{19}H_{22}F_2N_2O_3$ $[M+H]^+$;calculated: 365.1671, found: 365.1670.

isopropyl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate **(4c)**



White solid, yield 68% (95 mg), 82.5 -91.0 °C;

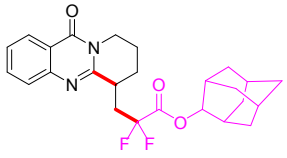
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 5.10 (dt, *J* = 12.5, 6.3 Hz, 1H), 4.39 -4.29 (m, 1H), 3.98 -3.88 (m, 1H), 3.48 -3.33 (m, 1H), 3.27 -3.17 (m, 1H), 2.44 -2.30 (m, 2H), 2.08 -1.96 (m, 2H), 1.76 -1.64 (m, 1H), 1.34 -1.27 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.61 (t, *J* = 32.6 Hz), 161.89 (s), 155.52 (s), 146.91 (s), 134.07 (s), 126.89 (s), 126.63 (s), 126.43 (s), 120.24 (s), 117.31 (t, *J* = 250.4 Hz), 71.25 (s), 41.10 (s), 36.75 (t, *J* = 23.0 Hz), 35.16 (t, *J* = 3.6 Hz), 25.82 (s), 21.49 (d, *J* = 4.8 Hz), 20.66 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.88, -101.57, -105.72, -106.41.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1508.

(1*r*,3*r*,5*r*,7*r*)-adamantan-2-yl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**4d**)



White solid, yield 61% (108 mg), 113.5 -115.5 °C;

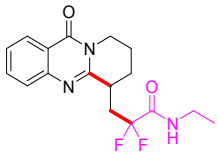
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.77 -7.70 (m, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.49 -7.42 (m, 1H), 5.03 (s, 1H), 4.43 -4.28 (m, 1H), 4.01 -3.90 (m, 1H), 3.61 -3.34 (m, 1H), 3.30 -3.15 (m, 1H), 2.50 -2.32 (m, 2H), 2.09 -1.96 (m, 6H), 1.90 -1.83 (m, 4H), 1.78 -1.70 (m, 5H), 1.59 (d, *J* = 11.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.45 (t, *J* = 32.5 Hz), 161.94 (s), 155.47 (s), 146.88 (s), 134.11 (s), 126.88 (s), 126.64 (s), 126.47 (s), 120.21 (s), 116.19 (t, *J* = 251.9 Hz), 80.28 (s), 41.14 (s), 37.13 (s), 36.91 (s), 36.68 (s), 36.12 (s), 36.11 (s), 35.44 -35.04 (m), 31.65 (s), 31.64 (s), 31.56 (s), 27.01 (s), 26.74 (s), 25.84 (s), 20.72 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.12, -100.80, -105.31, -105.99.

HRMS: $C_{25}H_{28}F_2N_2O_3$ $[M+Na]^+$;calculated: 465.1960, found: 465.1950.

2,2-difluoro-*N*-methyl-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanamide (**4e**)



White solid, yield 72% (96 mg), 113.6 -114.3 °C;

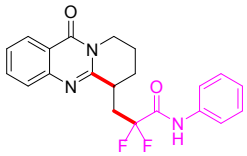
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.9 Hz, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 6.67 (s, 1H), 4.41 -4.28 (m, 1H), 4.07 -3.87 (m, 1H), 3.50 -3.32 (m, 3H), 3.32 -3.21 (m, 1H), 2.60 -2.30 (m, 2H), 2.12 -1.94 (m, 2H), 1.82 -1.64 (m, 1H), 1.24 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.00 (t, *J* = 28.7 Hz), 161.95 (s), 155.73 (s), 146.92 (s), 134.08 (s), 126.83 (s), 126.64 (s), 126.40 (s), 120.20 (s), 116.59 (t, *J* = 252.8 Hz), 41.10 (s), 36.30 (t, *J* = 22.9 Hz), 35.16 (s), 34.55 (s), 25.71 (s), 20.55 (s), 14.44 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.70, -102.37, -105.25, -105.92.

HRMS: $C_{17}H_{19}F_2N_2O_3$ $[M+H]^+$;calculated: 336.1518, found: 336.1528

2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-b]quinazolin-6-yl)-*N*-phenylpropanamide (**4f**)



White solid, yield 64% (98 mg), 156.9 -159.0 °C;

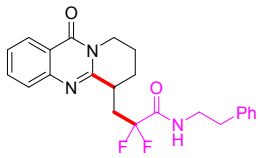
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.26 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.67 -7.62 (m, 1H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.45 -7.40 (m, 1H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 4.34 (dt, *J* = 14.0, 6.2 Hz, 1H), 4.04 -3.93 (m, 1H), 3.59 -3.41 m, 1H), 3.39 -3.29 (m, 1H), 2.61 -2.45 (m, 1H), 2.39 (td, *J* = 12.8, 6.3 Hz, 1H), 2.10 -1.99 (m, 2H), 1.82 -1.73 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.94 (t, *J* = 28.8 Hz), 155.60 (s), 146.75 (s), 136.19 (s), 134.08 (s), 129.18 (s), 126.78 (s), 126.63 (s), 126.47 (s), 125.50 (s), 120.23 (s), 120.18 (s), 117.77 (t, *J* = 255.3 Hz), 115.24 (s), 41.20 (s), 36.59 (t, *J* = 23.2 Hz), 35.25 (s), 25.87 (s), 20.50 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.99, -100.66, -104.10, -104.78.

HRMS: $C_{21}H_{19}F_2N_3O_2$ $[M+H]^+$;calculated: 384.1518, found: 384.1513.

2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-*N*-phenethylpropanamide (**4g**)



White solid, yield 60% (99 mg), 143.9 -147.6 °C;

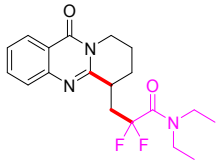
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.1 Hz, 2H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.72 (s, 1H), 4.34 -4.27 (m, 1H), 3.99 -3.91 (m, 1H), 3.62 (ddq, *J* = 19.8, 13.5, 6.7 Hz, 2H), 3.46 -3.30 (m, 1H), 3.21 -3.12 (m, 1H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.47 -2.29 (m, 2H), 2.04 -1.95 (m, 2H), 1.75 -1.64 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.09 (t, *J* = 28.9 Hz), 161.94 (s), 155.72 (s), 146.86 (s), 138.11 (s), 134.13 (s), 128.71 (s),126.79 (s), 126.74(s), 126.67 (s), 126.45 (s), 120.22 (s), 117.79 (t, *J* = 252.7 Hz), 41.19 (s), 40.62 (s), 36.42 (t, *J* = 22.9 Hz), 35.21 (s), 35.16 (t, *J* = 3.3 Hz), 25.79 (s), 25.59 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.03, -101.71, -105.00, -105.68.

HRMS: $C_{23}H_{23}F_2N_3O_2$ $[M+H]^+$;calculated: 412.1831, found: 412.1833.

N,*N*-diethyl-2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanamide (**4h**)



White solid, yield 65% (94 mg), 62.8 -68.1 °C;

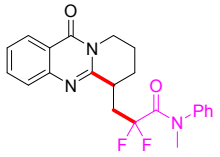
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H), 7.81 -7.66 (m, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 4.45 -4.30 (m, 1H), 4.04 -3.89 (m, 1H), 3.69 -3.58 (m, 3H), 3.50 -3.41 (m, 2H), 3.40 -3.26 (m, 1H), 2.75 -2.63 (m, 1H), 2.51 -2.33 (m, 1H), 2.18 -2.01 (m, 1H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.77 (t, *J* = 28.9 Hz), 162.04 (s), 156.17 (s), 147.03 (s), 134.04 (s), 126.94 (s), 126.63 (s), 126.32 (s), 120.21 (s), 119.42 (t, *J* = 255.5 Hz), 42.06 (t, *J* = 6.1 Hz), 41.63 (s), 41.01 (s), 36.85 (s, *J* = 22.7 Hz), 35.22 (t, *J* = 3.3 Hz), 25.92 (s), 20.58 (s), 14.37 (s), 12.36 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.33, -97.05, -98.90, -99.62.

HRMS: $C_{19}H_{23}F_2N_3O_2$ $[M+H]^+$;calculated: 364.1831, found: 364.1833.

2,2-difluoro-*N*-methyl-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)-*N*-phenylpropanamide (**4i**)



White solid, yield 63% (100 mg), 133.6 -135.0 °C;

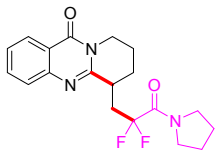
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.9 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.47 -7.42 (m, 3H), 7.42 -7.33 (m, 3H), 4.38 -4.26 (m, 1H), 3.97 -3.87 (m, 1H), 3.71 -3.34 (m, 2H), 3.30 (s, 3H), 3.24 -3.12 (m, 1H), 2.38 -2.24 (m, 2H), 2.01 -1.91 (m, 2H), 1.72 -1.60 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.37 (t, *J* = 28.8 Hz), 161.95 (s), 156.03 (s), 147.00 (s), 142.48 (s), 134.02 (s), 129.25 (s), 128.24 (s), 127.52 (s), 126.81 (s), 126.68 (s), 126.31 (s), 120.26 (s), 118.78 (t, *J* = 256.5 Hz), 41.04 (s), 40.07 (s), 37.60 (t, *J* = 23.8 Hz), 35.26 (s), 25.81 (s), 20.54 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -92.33, -93.03, -96.26, -96.97.

HRMS: $C_{22}H_{21}F_2N_3O_2$ $[M+H]^+$;calculated: 398.1675, found: 398.1679.

6-(2,2-difluoro-3-oxo-3-(pyrrolidin-1-yl)propyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4j**)



White solid, yield 66% (95 mg), 131.4 -133.4 °C;

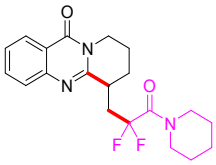
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 -8.22 (m, 1H), 7.72 -7.67 (m, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.45 -7.40 (m, 1H), 4.35 (m, 1H), 3.98 -3.89 (m, 1H), 3.75 (t, *J* = 6.1 Hz, 2H), 3.54 -3.38 (m, 3H), 3.32 -3.24 (m, 1H), 2.52 -2.32 (m, 2H), 2.04 -1.94 (m, 4H), 1.89 -1.79 (m, 2H), 1.75 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.14 (t, *J* = 29.8 Hz), 161.98 (s), 156.11 (s), 147.04 (s), 133.97 (s), 126.87 (s), 126.67 (s), 126.28 (s), 120.26 (s), 118.89 (t, *J* = 254.5Hz), 47.45 (s), 46.69 (t, *J* = 6.2 Hz), 41.04 (s), 36.33 (t, *J* = 22.7 Hz), 35.26 (t, *J* = 3.4 Hz), 26.55 (s), 25.85 (s), 23.27 (s), 20.63 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -98.95, -99.67, -101.66, -102.38.

HRMS: $C_{19}H_{21}F_2N_3O_2$ $[M+H]^+$;calculated: 362.1675, found: 362.1673

6-(2,2-difluoro-3-oxo-3-(piperidin-1-yl)propyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4k**)



White solid, yield 61% (92 mg), 116.0 -118.1 °C;

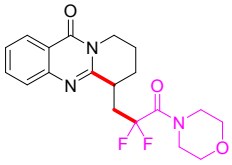
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.78 -7.68 (m, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.47 -7.42 (m, 1H), 4.39 (dt, *J* = 14.0, 6.2 Hz, 1H), 3.98 -3.90 (m, 1H), 3.73 (d, *J* = 4.7 Hz, 2H), 3.65 -3.49 (m, 3H), 3.35 -3.25 (m, 1H), 2.49 -2.34 (m, 2H), 2.10 -1.95 (m, 2H), 1.76 -1.63 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.02 (s), 161.77(t, *J* = 28.7 Hz), 161.49 (s), 156.15 (s), 147.07 (s), 134.01 (s), 126.65 (t, *J* = 33.3 Hz), 120.24 (s), 47.02 (t, *J* = 6.3 Hz), 44.51 (s), 41.02 (s), 37.16 (s), 36.94 (s), 36.72 (s), 35.26 (t, *J* = 3.2 Hz), 26.55 (s), 26.02 (s), 25.65 (s), 24.48 (s), 20.65 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.85, -96.57, -98.38, -99.10.

HRMS: $C_{20}H_{23}F_2N_3O_2$ $[M+H]^+$;calculated: 376.1831, found: 376.1813.

6-(2,2-difluoro-3-morpholino-3-oxopropyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4l**)



White solid, yield 75% (113 mg), 116.1 -119.3 °C;

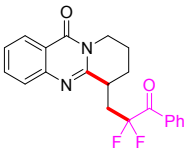
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 4.41 -4.33 (m, 1H), 3.98 -3.90 (m, 1H), 3.81 (d, *J* = 4.4 Hz, 2H), 3.74 (dd, *J* = 10.7, 5.2 Hz, 4H), 3.64 (m, 2H), 3.60 -3.47 (m, 1H), 3.34 -3.23 (m, 1H), 2.50 -2.34 (m, 2H), 2.07 -1.98 (m, 2H), 1.80 -1.67 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.01 (t, *J* = 29.2 Hz), 161.72 (s), 155.96 (s), 147.00 (s), 134.05 (s), 126.89 (s), 126.66 (s), 126.35 (s), 120.24 (s), 119.31 (t, *J* = 255.0 Hz), 66.76 (s), 66.72(s), 46.66 (t, *J* = 6.1 Hz), 43.43 (s), 41.02 (s), 36.74 (t, *J* = 22.2 Hz), 35.17 (t, *J* = 3.2 Hz), 26.07 (s), 20.63 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.61, -96.34, -98.36, -99.09.

HRMS: $C_{19}H_{21}F_2N_3O_2$ $[M+H]^+$;calculated: 378.1624, found: 378.1610.

6-(2,2-difluoro-3-oxo-3-phenylpropyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4m**)



White solid, yield 61% (90 mg), 130.1 -133.7 °C;

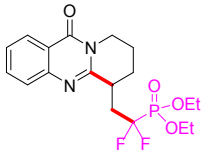
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.9 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 2H), 7.69 (q, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 4.49 -4.36 (m, 1H), 4.08 -3.90 (m, 1H), 3.61 (dtd, *J* = 23.1, 15.9, 4.5 Hz, 1H), 3.37 (td, *J* = 11.2, 6.8 Hz, 1H), 2.70 -2.51 (m, 1H), 2.51 -2.38 (m, 1H), 2.15 -2.00 (m, 2H), 1.86 -1.71 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.20 (t, *J* = 30.4 Hz), 161.78 (s), 161.24 (d, *J* = 3.5 Hz), 159.32 (s), 155.09 (d, *J* = 2.1 Hz), 143.46 (s), 134.32 (s), 132.07 (s), 130.26 (t, *J* = 3.3 Hz), 129.16 (d, *J* = 8.2 Hz), 128.69 (s), 122.75 (s), 122.51 (s), 121.35 (d, *J* = 8.8 Hz), 118.36 (t, *J* = 254.2 Hz), 111.43 (s), 111.19 (s), 41.20 (s), 36.59 (t, *J* = 22.5 Hz), 35.07 (t, *J* = 3.6 Hz), 26.02 (s), 20.70 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -95.78, -96.52, -99.56, -100.30.

HRMS: $C_{21}H_{18}F_2N_2O_2$ $[M+H]^+$;calculated: 369.1409, found: 369.1410.

diethyl (1,1-difluoro-2-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)ethyl)phosphonate (**4n**)



White solid, yield 56% (90 mg), 46.0 -47.3 °C;

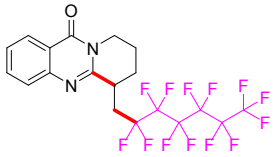
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 -8.18 (m, 1H), 7.78 -7.69 (m, 1H), 7.67 -7.61 (m, 1H), 7.54 -7.40 (m, 1H), 4.45 -4.27 (m, 5H), 4.02 -3.91 (m, 1H), 3.67 -3.44 (m, 1H), 3.44 -3.33 (m, 1H), 2.56 -2.41 (m, 1H), 2.42 -2.23 (m, 1H), 2.11 -1.97 (m, 2H), 1.76 -1.63 (m, 1H), 1.44 (t, *J* = 7.0 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.99 (s), 155.79 (s), 146.95 (s), 134.06 (s), 126.93 (s), 126.64 (s), 126.38 (s), 124.77 (s), 122.62 (s), 122.17 (s), 124.80 -117.10 (m), 120.11 (d, *J* = 15.9 Hz), 64.65 (d, *J* = 6.6 Hz), 41.16 (s), 35.80 (dd, *J* = 35.2, 19.5 Hz), 34.83 -34.57 (m), 26.02 (s), 20.70 (s), 16.45 (d, *J* = 5.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -106.81 (s), -107.09 (s), -107.60 (s), -107.88 (s), -111.84 (s), -112.12 (s), -112.62 (s), -112.91 (s).

HRMS: $C_{18}H_{23}F_2N_2O_4P$ $[M+Na]^+$;calculated: 423.1256, found: 423.1245.

6-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4o**)



White solid, yield 54% (115 mg), 124.1 -125.2 °C;

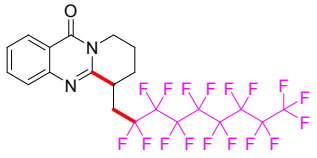
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.9 Hz, 1H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 4.47 -4.31 (m, 1H), 4.10 -3.95 (m, 1H), 3.76 -3.52 (m, 1H), 3.42 -3.25 (m, 1H), 2.62 -2.24 (m, 2H), 2.17 -2.02 (m, 2H), 1.86 -1.66 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.85 (s), 154.92 (s), 146.70 (s), 134.20 (s), 126.95 (s), 126.63 (s), 121.62 -105.01 (m), 120.16 (s), 41.06 (s), 34.32 (d, *J* = 3.3 Hz), 32.66 (t, *J* = 20.4 Hz), 25.87 (d, *J* = 3.0 Hz), 20.68 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.72– -80.88 (m), -109.71 – -110.04 (m), -110.43 – -110.75 (m), -113.97 – -114.22 (m), -114.68 – -114.93 (m), -121.26 – -122.07 (m), -122.40 – -123.20 (m), -123.27 – -123.68 (m), -125.90 – -126.28 (m).

HRMS: $C_{19}H_{13}F_{13}N_2O$ $[M+H]^+$;calculated: 533.0893, found: 533.0898

6-(2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononyl)-6,7,8,9-tetrahydro-11*H*-pyrido[2,1-*b*]quinazolin-11-one (**4p**)



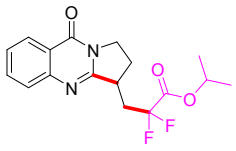
White solid, yield 43% (109 mg), 132.2 -133.7 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 6.5 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 4.49 -4.30 (m, 1H), 4.10 -3.91 (m, 1H), 3.74 -3.53 (m, 1H), 3.41 -3.26 (m, 1H), 2.54 -2.26 (m, 2H), 2.14 -1.99 (m, 2H), 1.85 -1.64 (m, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.83 (t, *J* = 10.0 Hz), -109.74 – -110.02 (m), -110.45 – -110.76 (m), -114.10 (t, *J* = 13.4 Hz), -114.81 (t, *J* = 13.5 Hz), -121.48 (s), -121.86 (s), -122.69 (s), -123.40 (s), -125.92 – -126.31 (m).

HRMS: $C_{21}H_{13}F_{17}N_2O$ $[M+H]^+$;calculated: 633.0829, found: 633.0825.

isopropyl 2,2-difluoro-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**4q**)



White solid, yield 65% (87 mg), 94.8 -96.2 °C;

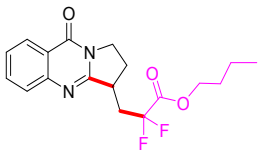
^{1}H NMR (400 MHz, CDCl3) δ 8.33 (d, *J* = 7.8 Hz, 1H), 7.78 (t, *J* = 7.3 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 5.29 -5.12 (m, 1H), 4.51 -4.34 (m, 1H), 4.05 -3.92 (m, 1H), 3.66 -3.52 (m, 1H), 3.32 -3.14 (m, 1H), 2.78 -2.67 (m, 1H), 2.42 -2.22 (m, 1H), 2.16 -2.02 (m, 1H), 1.41 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.61 (t, *J* = 32.6 Hz), 161.89 (s), 155.52 (s), 146.91 (s), 134.07 (s), 126.89 (s), 126.63 (s), 126.43 (s), 120.24 (s), 116.07 (t, *J* = 252.0 Hz), 71.25 (s), 41.10 (s), 36.75 (t, *J* = 23.0 Hz), 35.16 (t, *J* = 3.6 Hz), 25.82 (s), 21.49 (d, *J* = 4.8 Hz), 20.66 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.39, -104.08, -106.66, -107.35.

HRMS: $C_{17}H_{18}F_2N_2O_3$ $[M+H]^+$;calculated: 337.1358, found: 337.1353.

butyl 2,2-difluoro-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanoate (**4r**)



Colorless oil, yield 63% (88 mg);

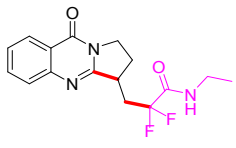
^{1}H NMR (400 MHz, CDCl3) δ 8.29 (d, *J* = 7.9 Hz, 1H), 7.75 (t, *J* = 7.3 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 4.44 -4.29 (m, 3H), 4.00 -3.90 (m, 1H), 3.62 -3.51 (m, 1H), 3.32 -3.13 (m, 1H), 2.75 -2.64 (m, 1H), 2.40 -2.22 (m, 1H), 2.12 -1.99 (m, 1H), 1.81 -1.69 (m, 2H), 1.53 -1.38 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.81 (t, *J* = 32.2 Hz), 160.70 (s), 159.31 (s), 148.81 (s), 134.18 (s), 126.95 (s), 126.54 (s), 126.40 (s), 120.78 (s), 115.64 (t, *J* = 251.2 Hz), 66.96 (s), 44.81 (s), 38.02 (s), 36.44 (t, *J* = 23.0 Hz), 30.28 (s), 27.80 (s), 18.90 (s), 13.57 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -102.92, -103.61, -106.36, -107.05.

HRMS: $C_{18}H_{20}F_2N_2O_3$ $[M+H]^+$;calculated: 351.1515, found: 351.1503.

N-ethyl-2,2-difluoro-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanamide (**4s**)



White solid, yield 67% (86 mg), 109.8 -110.7 °C;

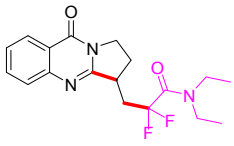
^{1}H NMR (400 MHz, CDCl3) δ 8.32 (d, *J* = 7.8 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 6.58 (s, 1H), 4.47 -4.33 (m, 1H), 4.05 -3.92 (m, 1H), 3.72 -3.58 (m, 1H), 3.49 -3.39 (m, 2H), 3.32 -3.13 (m, 1H), 2.79 -2.65 (m, 1H), 2.50 -2.31 (m, 1H), 2.19 -2.03 (m, 1H), 1.28 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.58 (t, *J* = 28.2 Hz), 160.72 (s), 159.66 (s), 148.59 (s), 134.27 (s), 126.81 (s), 126.61 (s), 126.45 (s), 120.72 (s), 117.40 (t, *J* = 254.0 Hz), 44.94 (s), 38.18 (s), 36.16 (t, *J* = 23.3 Hz), 34.62 (s), 27.79 (s), 14.43 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -103.57, -104.25, -106.13, -106.81.

HRMS: $C_{16}H_{17}F_2N_3O_2$ $[M+Na]^+$;calculated: 344.1181, found: 344.1184.

N,*N*-diethyl-2,2-difluoro-3-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)propanamide (**4t**)



White solid, yield 59% (82 mg), 127.1 -127.8 °C;

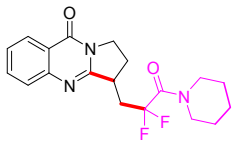
^{1}H NMR (400 MHz, CDCl3) δ 8.31 (d, *J* = 8.0 Hz, 1H), 7.81 -7.66 (m, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 4.45 -4.30 (m, 1H), 4.04 -3.89 (m, 1H), 3.69 -3.58 (m, 3H), 3.44 (q, *J* = 7.0 Hz, 2H), 3.40 -3.26 (m, 1H), 2.75 -2.63 (m, 1H), 2.51 -2.33 (m, 1H), 2.18 -2.01 (m, 1H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.30 (t, *J* = 28.8 Hz), 160.89 (s), 159.90 (s), 149.08 (s), 134.05 (s), 127.14 (s), 126.34 (s), 121.80 (s), 120.81 (s), 119.26 (s), 44.80 (s), 41.92 (t, *J* = 6.2 Hz), 41.59 (s), 38.39 (t, *J* = 3.6 Hz), 36.99 (t, *J* = 22.7 Hz), 28.19 (s), 14.30 (s), 12.33 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -97.06, -97.80, -99.78, -100.52.

HRMS: $C_{18}H_{21}F_2N_3O_2$ $[M+Na]^+$;calculated: 372.1494, found: 372.1491.

3-(2,2-difluoro-3-oxo-3-(piperidin-1-yl)propyl)-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**4u**)



Colorless oil, yield 60% (87 mg);

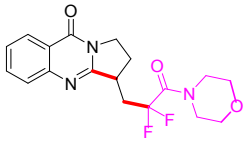
^{1}H NMR (400 MHz, CDCl3) δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.85 -7.74 (m, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 4.50 -4.41 (m, 1H), 4.08 -3.96 (m, 1H), 3.85 -3.76 (m, 2H), 3.75 -3.62 (m, 3H), 3.51 -3.32 (m, 1H), 2.81 -2.70 (m, 1H), 2.58 -2.38 (m, 1H), 2.22 -2.07 (m, 1H), 1.82 -1.70 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.26 (t, *J* = 30.6 Hz), 160.93 (s), 159.87 (s), 149.09 (s), 134.08 (s), 127.15 (s), 126.36 (s), 126.33 (s), 120.76 (s), 119.26 (t, *J* = 256.0 Hz), 46.91 (t, *J* = 6.4 Hz), 44.80 (s), 44.49 (s), 38.38 (s), 36.99 (t, *J* = 22.9 Hz), 28.21 (s), 26.54 (s), 25.62 (s), 24.42 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.38, -97.12, -99.17, -99.91.

HRMS: $C_{19}H_{21}F_2N_3O_2$ $[M+H]^+$;calculated: 362.1675, found: 362.1674.

3-(2,2-difluoro-3-morpholino-3-oxopropyl)-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**4v**)



White solid, yield 62% (90 mg), 121.2 -121.9 °C;

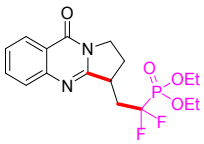
^{1}H NMR (400 MHz, CDCl3) δ 8.31 (d, J = 7.9 Hz, 1H), 7.75 (t, J = 7.5 Hz, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 4.48 -4.30 (m, 1H), 3.99 -3.89 (m, 1H), 3.85 -3.80 (m, 2H), 3.79 -3.74 (m, 4H), 3.74 -3.65 (m, 2H), 3.65 -3.58 (m, 1H), 3.47 -3.25 (m, 1H), 2.75 -2.60 (m, 1H), 2.51 -2.31 (m, 1H), 2.16 -1.99 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.51 (t, *J* = 29.1 Hz), 160.86 (s), 159.69 (s), 149.04 (s), 134.11 (s), 127.14 (s), 126.41 (s), 126.36 (s), 120.80 (s), 119.20 (t, *J* = 256.5 Hz), 66.74 (d, *J* = 6.3 Hz), 46.56 (t, *J* = 6.0 Hz), 44.78 (s), 43.44 (s), 38.25 (s), 36.85 (d, *J* = 22.5 Hz), 36.51 (s), 28.22 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -96.22, -96.97, -99.23, -99.97.

HRMS: $C_{18}H_{19}F_2N_3O_3$ $[M+H]^+$;calculated: 364.1467, found: 364.1472.

diethyl (1,1-difluoro-2-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-3-yl)ethyl)phosphonate (**4w**)



White solid, yield 52% (80 mg), 77.8 -80.1 °C;

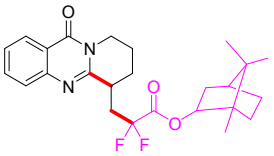
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 -8.26 (m, 1H), 7.79 -7.65 (m, 2H), 7.52 -7.43 (m, 1H), 4.41 -4.31 (m, 5H), 4.03 -3.88 (m, 1H), 3.78 -3.63 (m, 1H), 3.37 -3.14 (m, 1H), 2.82 -2.66 (m, 1H), 2.42 -2.18 (m, 1H), 2.15 -1.98 (m, 1H), 1.49 -1.42 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.86 (s), 159.63 (s), 149.04 (s), 134.16 (s), 127.10 (s), 126.48 (s), 126.43 (s), 120.84 (s), 124.62 -111.94 (m), 65.03 -64.52 (m), 44.88 (s), 37.78 (s), 36.33 -35.70 (m), 28.23 (s), 16.47 (d, J = 5.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -108.26, -108.54, -109.05, -109.33, -112.52, -112.81, -113.31, -113.60.

HRMS: $C_{17}H_{21}F_2N_2O_4P$ $[M+Na]^+$;calculated: 409.1099, found: 409.1089

(4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**4x**)



White solid, yield 60% (107 mg), 88.2 -90.3 °C;

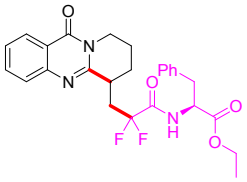
^{1}H NMR (400 MHz, CDCl3) δ 8.31 -8.22 (m, 1H), 7.76 -7.67 (m, 1H), 7.67 -7.58 (m, 1H), 7.50 -7.40 (m, 1H), 5.08 -4.91 (m, 1H), 4.39 -4.27 (m, 1H), 4.02 -3.89 (m, 1H), 3.59 -3.40 (m, 1H), 3.27 -3.13 (m, 1H), 2.46 -2.26 (m, 3H), 2.07 -1.94 (m, 3H), 1.82 -1.67 (m, 3H), 1.41 -1.32 (m, 1H), 1.29 -1.22 (m, 1H), 1.09 -0.97 (m, 1H), 0.92 -0.83 (m, 8H), 0.80 -0.78 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.46 (s), 164.12 (t, J = 32.3 Hz), 161.44 (s), 156.25 (s), 149.09 (s), 128.23 (s), 116.77 (s), 116.04 (t, J = 252.5 Hz), 113.82 (s), 107.28 (s), 62.95 (s), 55.64 (s), 40.94 (s), 36.86 (t, J = 23.1 Hz), 35.15 (s), 31.93 (s), 29.70 (s), 29.37 (s), 25.83 (s), 22.70 (s), 20.69 (s), 14.12 (s), 13.93 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.98 (d, J = 65.6 Hz), -100.08 – -100.27 (m), -100.57, -100.75, -105.13, -105.46, -105.82, -106.14.

HRMS: $C_{25}H_{30}F_2N_2O_3$ $[M+H]^+$;calculated: 445.2297, found: 445.2291.

ethyl (2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoyl)-*L*-phenylalaninate (**4y**)



White solid, yield 53% (102 mg), 119.9 -122.6 °C;

^{1}H NMR (400 MHz, CDCl3) δ 8.27 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 9.2 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.33 -7.29 (m, 1H), 7.27 -7.21 (m, 2H), 7.16 -7.10 (m, 2H), 7.10 -7.04 (m, 1H), 4.86 (dd, J = 13.2, 6.8 Hz, 1H), 4.38 -4.29 (m, 1H), 4.26 -4.18 (m, 2H), 3.97 -3.87 (m, 1H), 3.47 -3.32 (m, 1H), 3.27 -3.07 (m, 3H), 2.39 -2.27 (m, 2H), 2.02 -1.95 (m, 2H), 1.72 -1.61 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H).

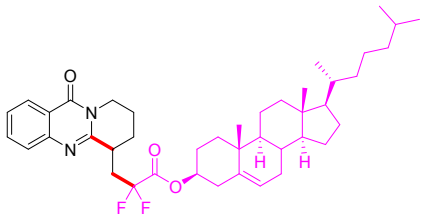
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.53 (s), 163.62 (t, J = 12.0 Hz), 161.92 (s), 155.64 (s), 146.83 (s), 135.23 (s), 134.10 (s), 129.26 (d, J = 4.5 Hz), 128.65 (d, J = 6.7 Hz), 127.31 (d, J = 7.3 Hz), 126.87 (s),

126.66 (s), 126.43 (s), 120.22 (s), 116.39 (t, J = 253.7 Hz), 61.93 (s), 53.14 (d, J = 18.3 Hz), 41.05 (d, J = 3.6 Hz), 37.64 (d, J = 5.3 Hz), 36.59 -35.80 (m), 35.13 -34.86 (m), 25.67 (s), 20.56 (s), 14.10 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -99.95, -100.63, -102.72, -103.40, -104.42, -105.10, -105.75, -106.44.

HRMS: $C_{26}H_{27}F_2N_3O_4$ $[M+Na]^+$;calculated: 506.1862, found: 506.1872.

(3*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[a]phenanthren-3-yl 2,2-difluoro-3-(11-oxo-6,8,9,11-tetrahydro-7*H*-pyrido[2,1-*b*]quinazolin-6-yl)propanoate (**4z**)



White solid, yield 21% (57 mg), 130.1 -132.5 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.5 Hz, 1H), 5.41 -5.25 (m, 1H), 4.78 -4.66 (m, 1H), 4.43 -4.32 (m, 1H), 4.01 -3.90 (m, 1H), 3.51 -3.32 (m, 1H), 3.24 (d, J = 6.4 Hz, 1H), 2.44 -2.34 (m, 3H), 2.08 -1.97 (m, 4H), 1.91 -1.81 (m, 3H), 1.78 -1.66 (m, 3H), 1.60 -1.44 (m, 6H), 1.42 -1.24 (m, 5H), 1.20 -1.07 (m, 7H), 1.05 -1.01 (m, 4H), 0.97 -0.91 (m, 4H), 0.90 -0.86 (m, 6H), 0.69 (s, 3H).

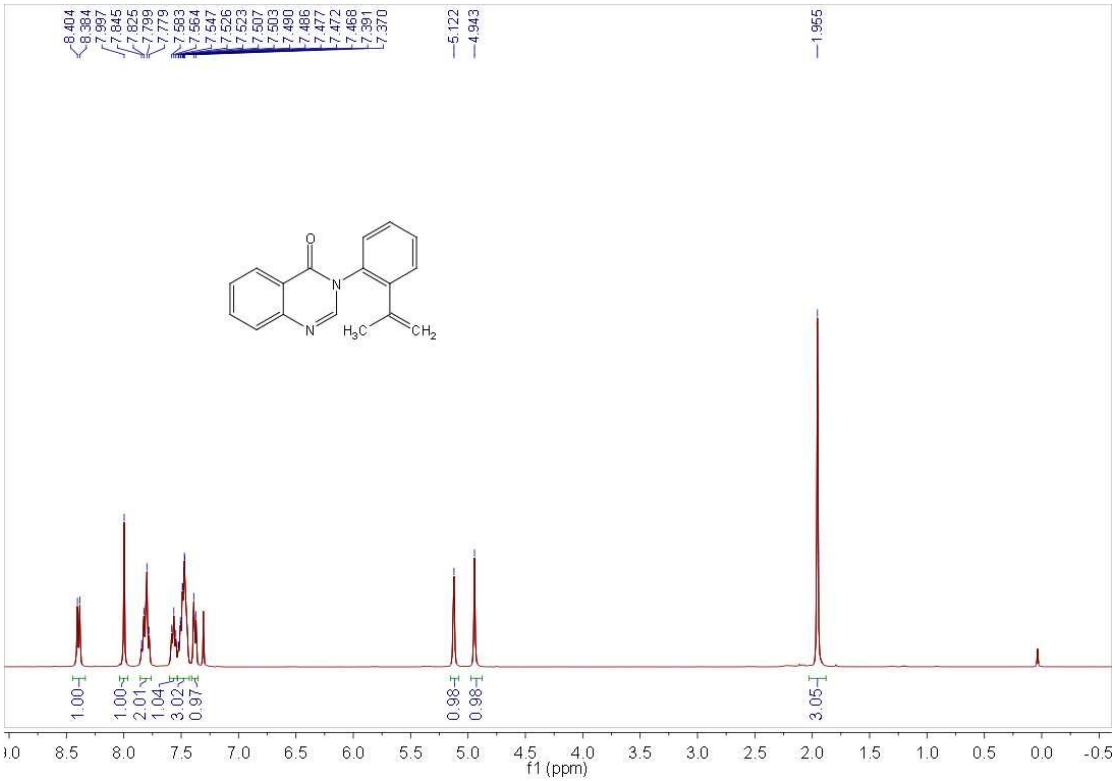
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.53 (t, J = 32.5 Hz), 161.90 (s), 155.57 (s), 146.85 (s), 138.78 (d, J = 6.0 Hz), 134.15 (s), 126.88 (s), 126.58 (d, J = 18.2 Hz), 123.38 (d, J = 3.5 Hz), 120.24 (s), 114.81 (t, J = 252.0 Hz), 56.66 (s), 56.14 (s), 49.96 (s), 42.31 (s), 41.11 (d, J = 6.0 Hz), 39.61 (d, J = 17.3 Hz), 37.65 (d, J = 4.6 Hz), 36.79 (d, J = 2.7 Hz), 36.53 (s), 36.19 (s), 35.79 (s), 35.18 (s), 31.84 (d, J = 6.3 Hz), 28.12 (d, J = 19.9 Hz), 27.45 (d, J = 3.8 Hz), 25.83 (s), 24.28 (s), 23.83 (s), 22.82 (s), 22.57 (s), 21.03 (s), 20.69 (s), 19.27 (s), 18.72 (s), 11.86 (s).

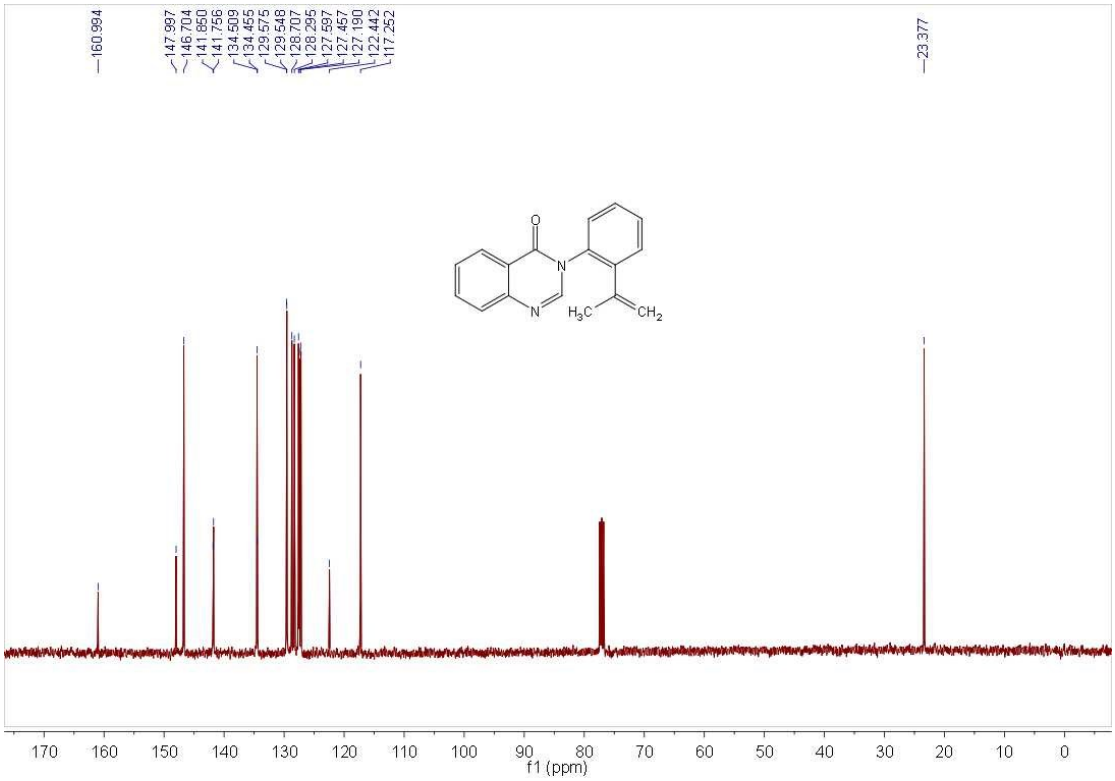
^{19}F NMR (376 MHz, $CDCl_3$) δ -100.47 (d, J = 37.1 Hz), -101.15 (d, J = 37.2 Hz), -105.52 (d, J = 17.3 Hz), -106.20 (d, J = 17.2 Hz).

HRMS: $C_{42}H_{58}F_2N_2O_3$ $[M+H]^+$;calculated: 677.4488, found: 677.4493.

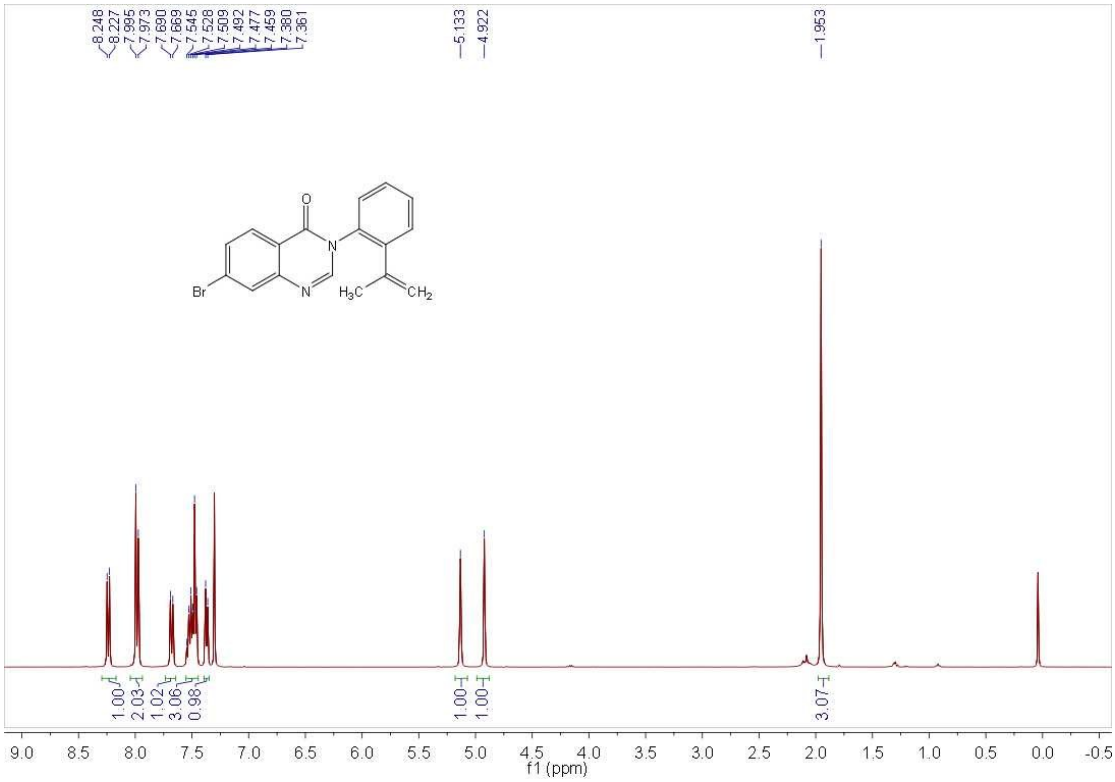
XI. Copies of NMR Spectra of some raw materials

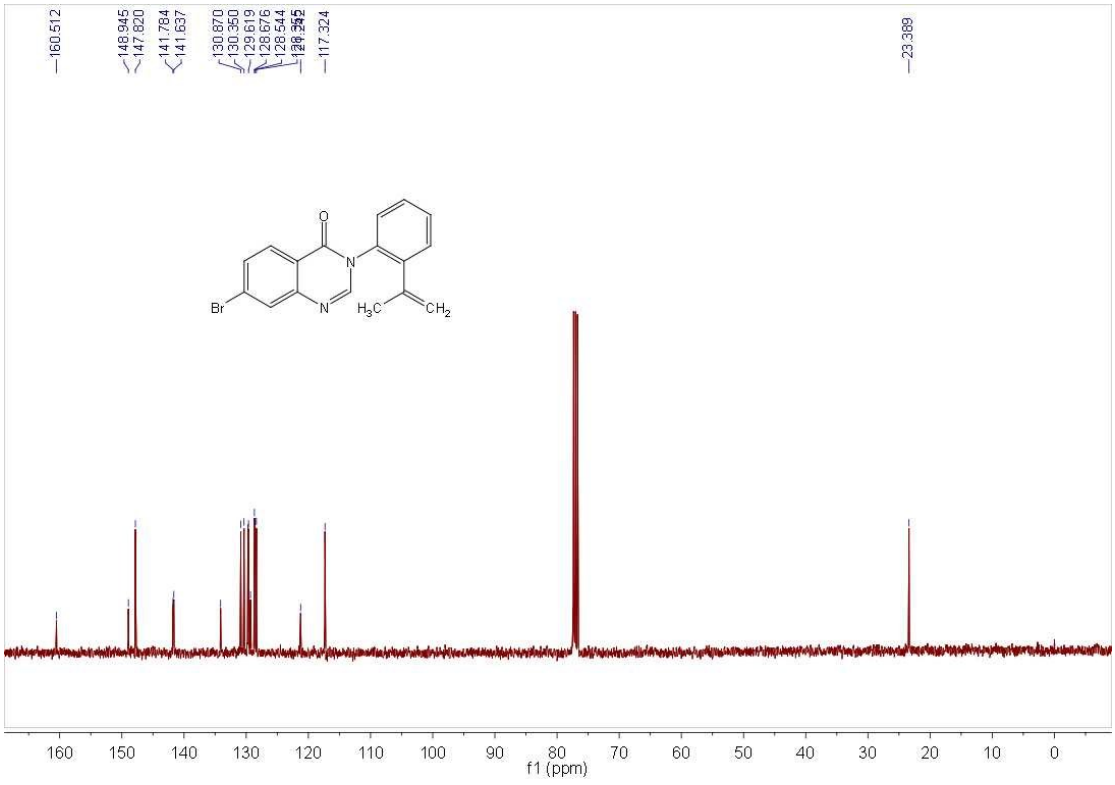
3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1t**)



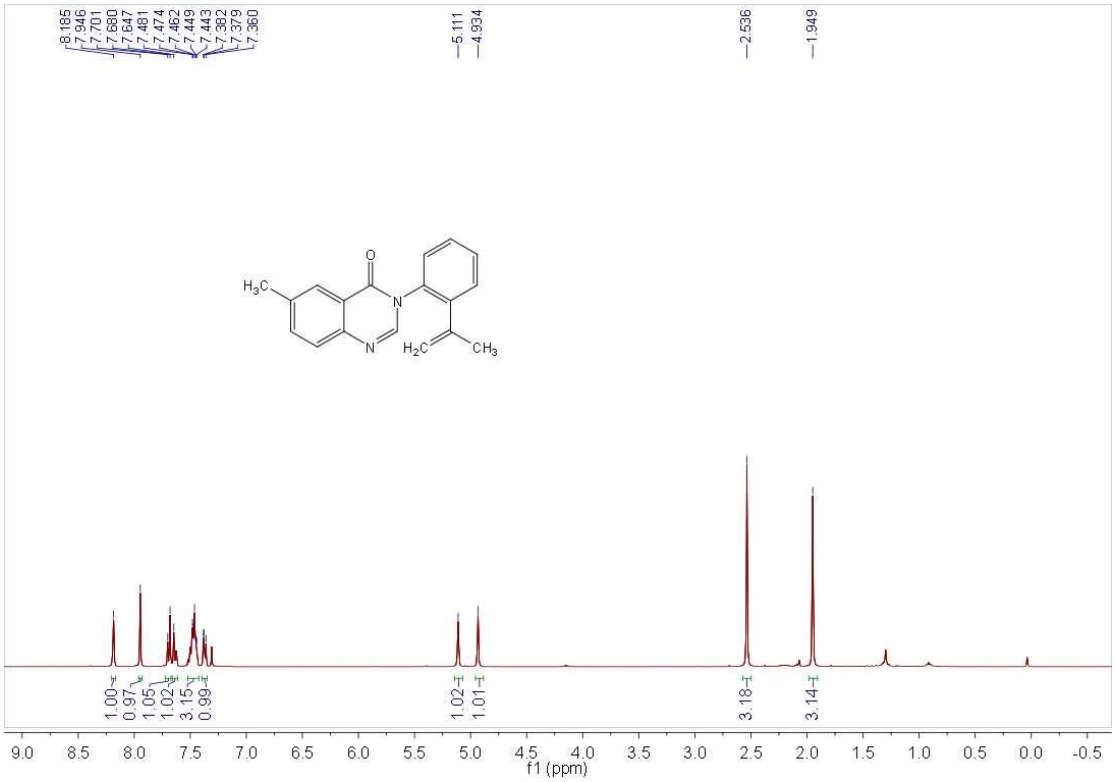


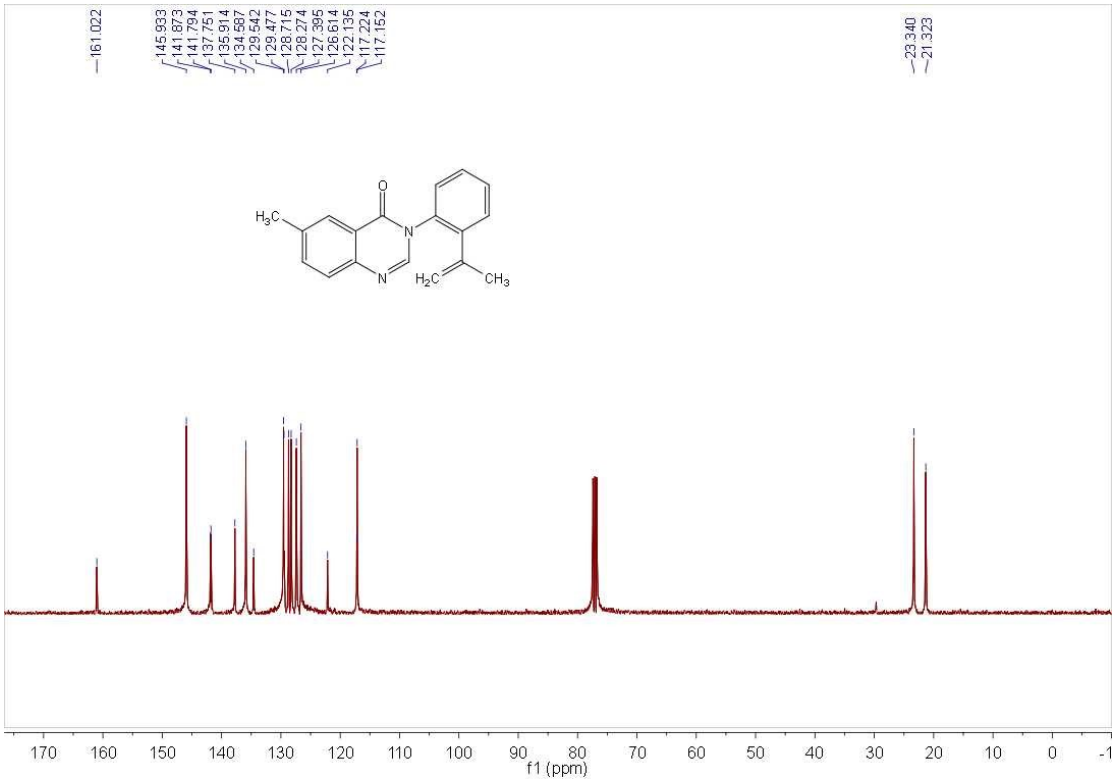
7-bromo-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1u**)



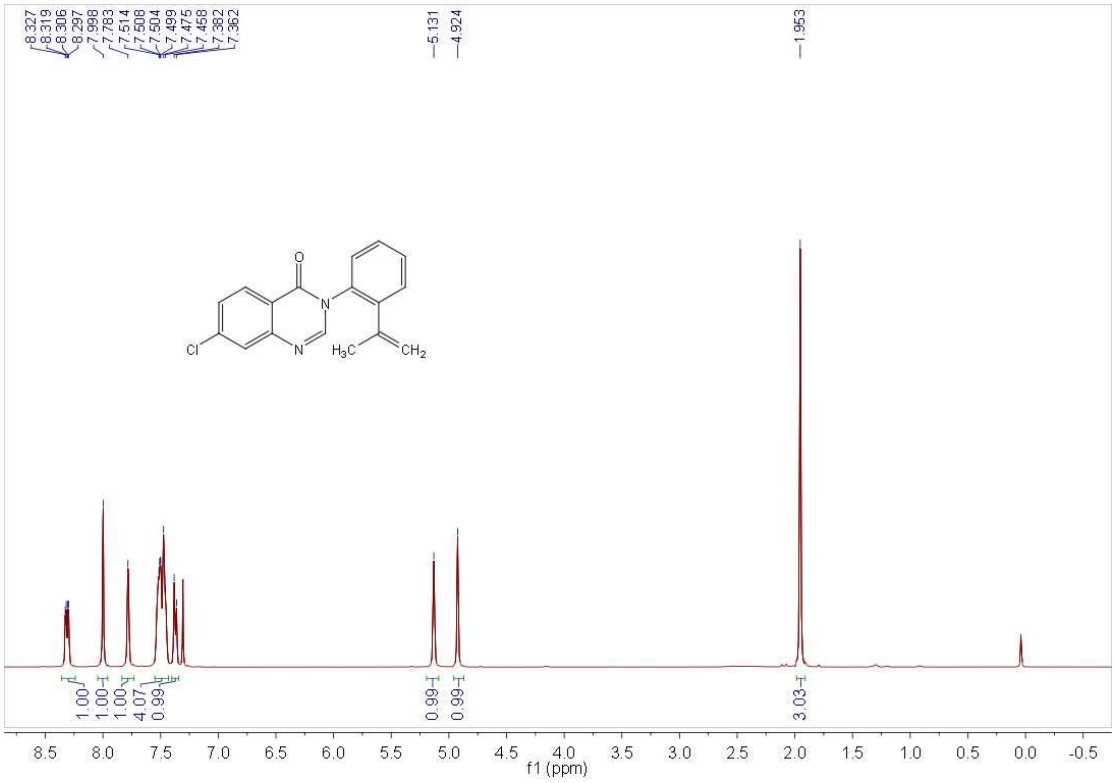


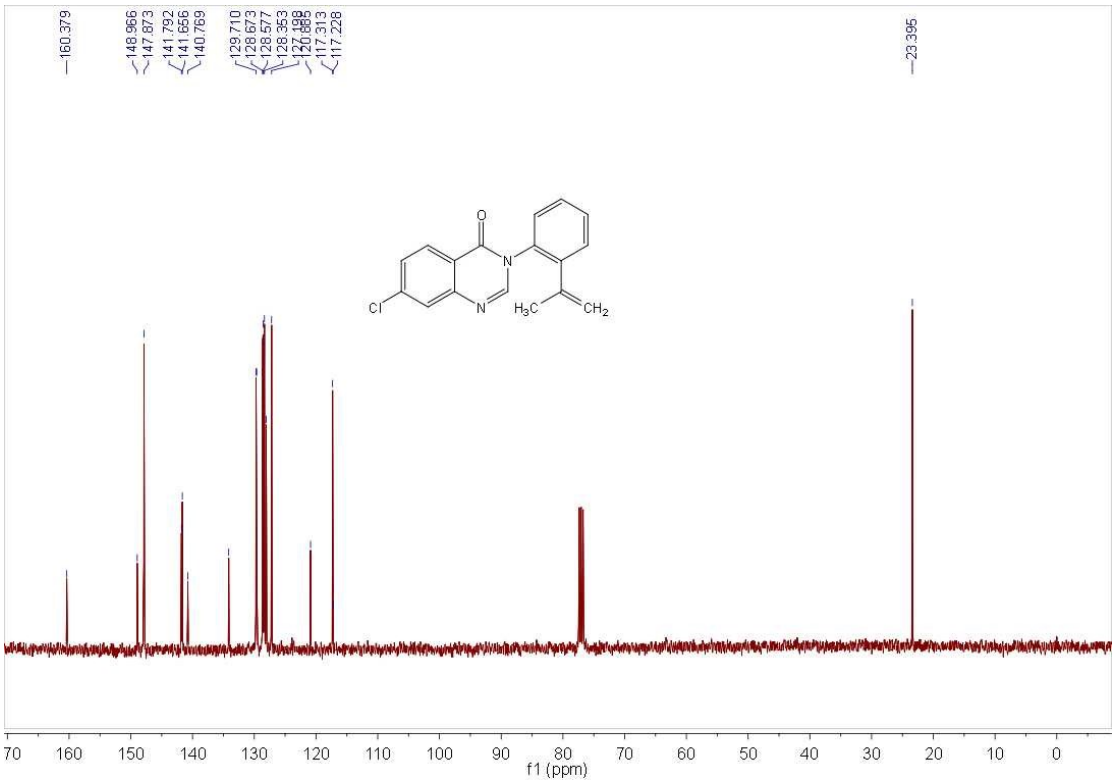
6-methyl-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1v**)



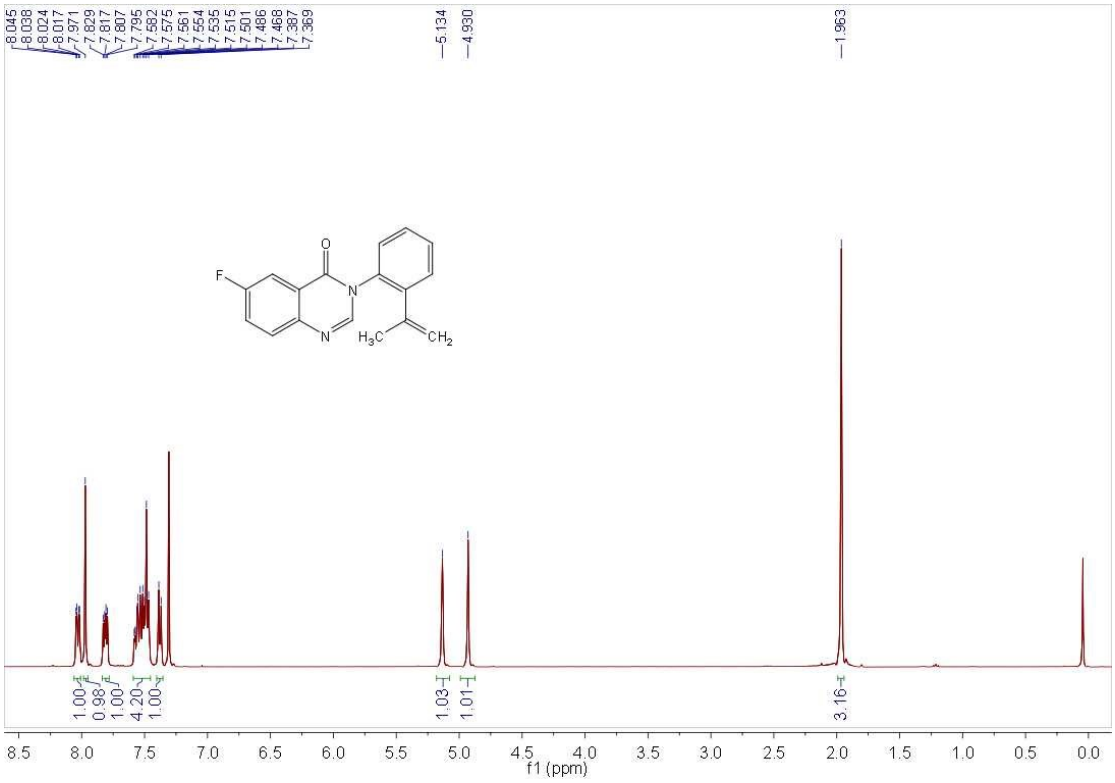


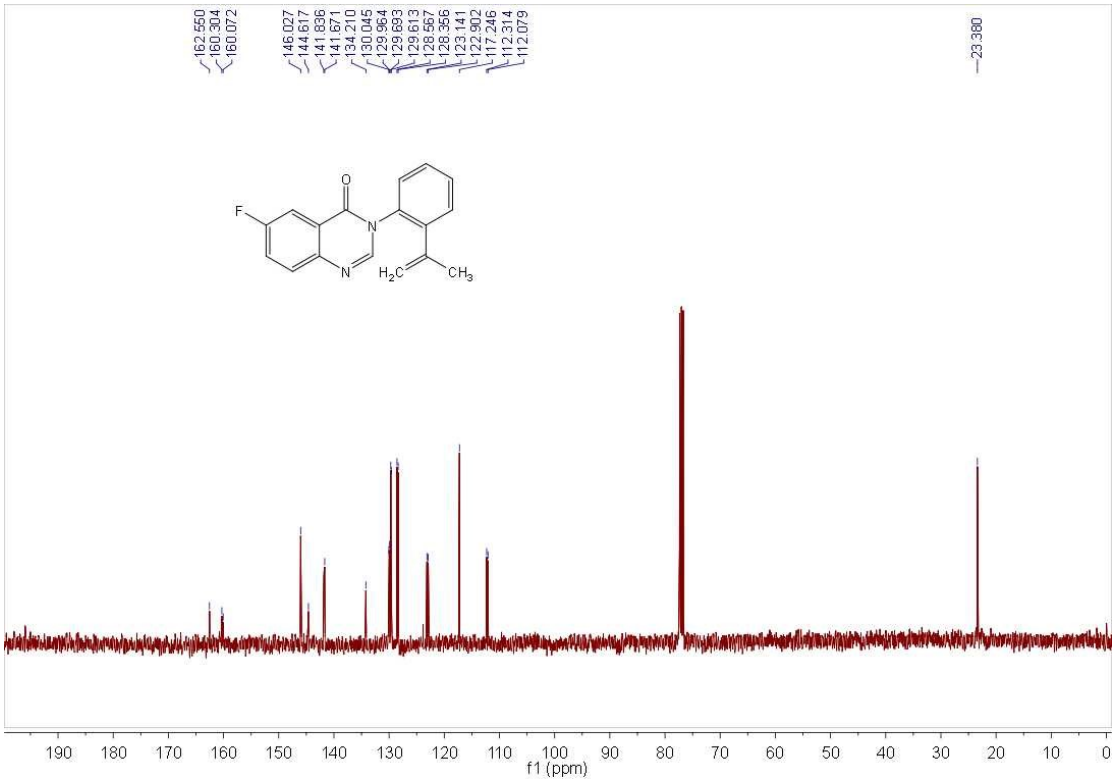
7-chloro-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1w**)





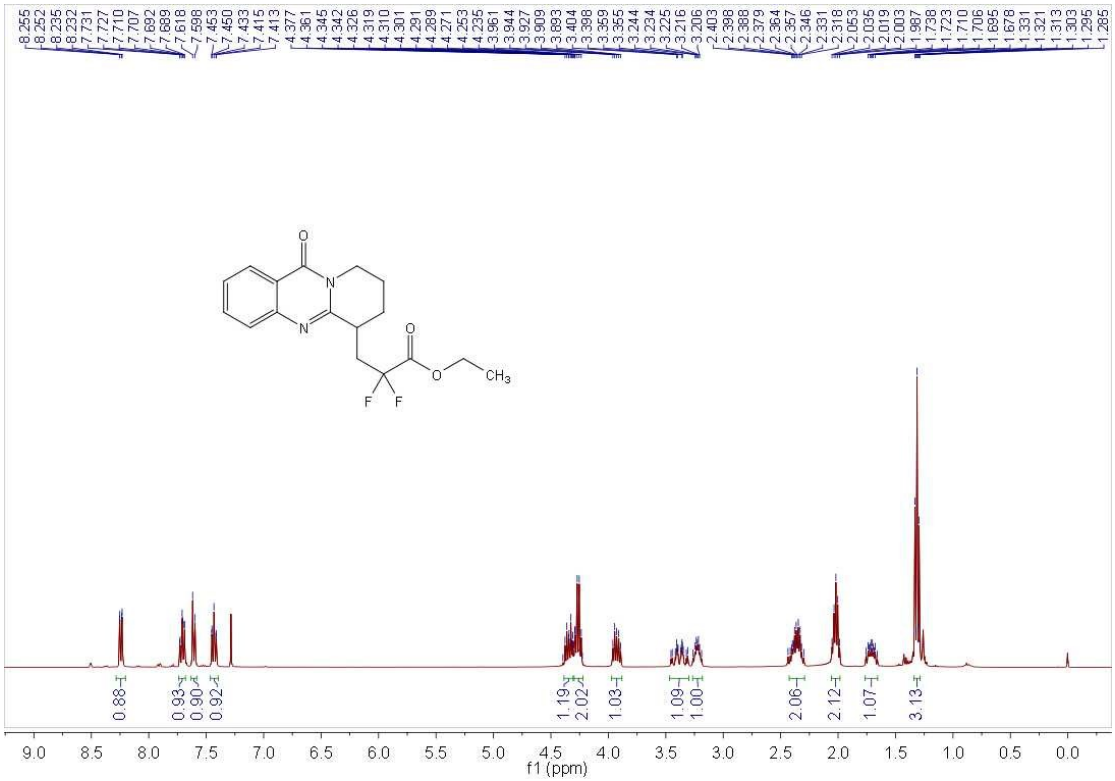
6-fluoro-3-(2-(prop-1-en-2-yl)phenyl)quinazolin-4(3*H*)-one (**1x**)

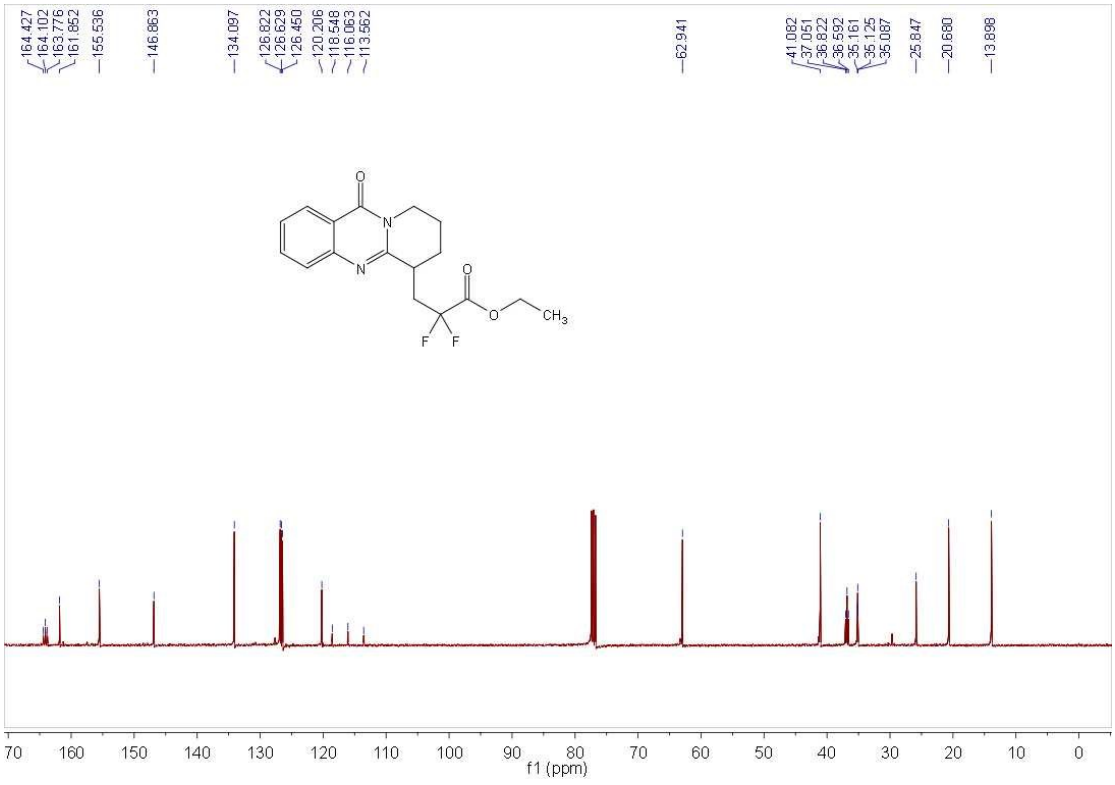


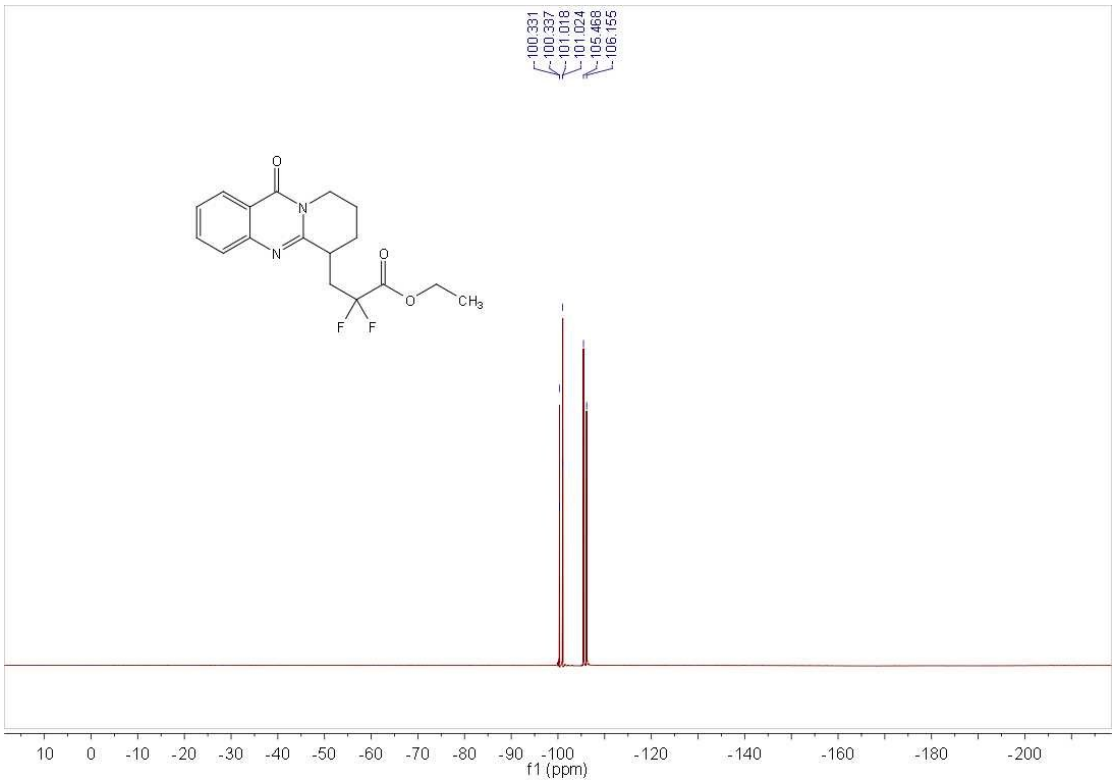


XII. Copies of NMR Spectra of products

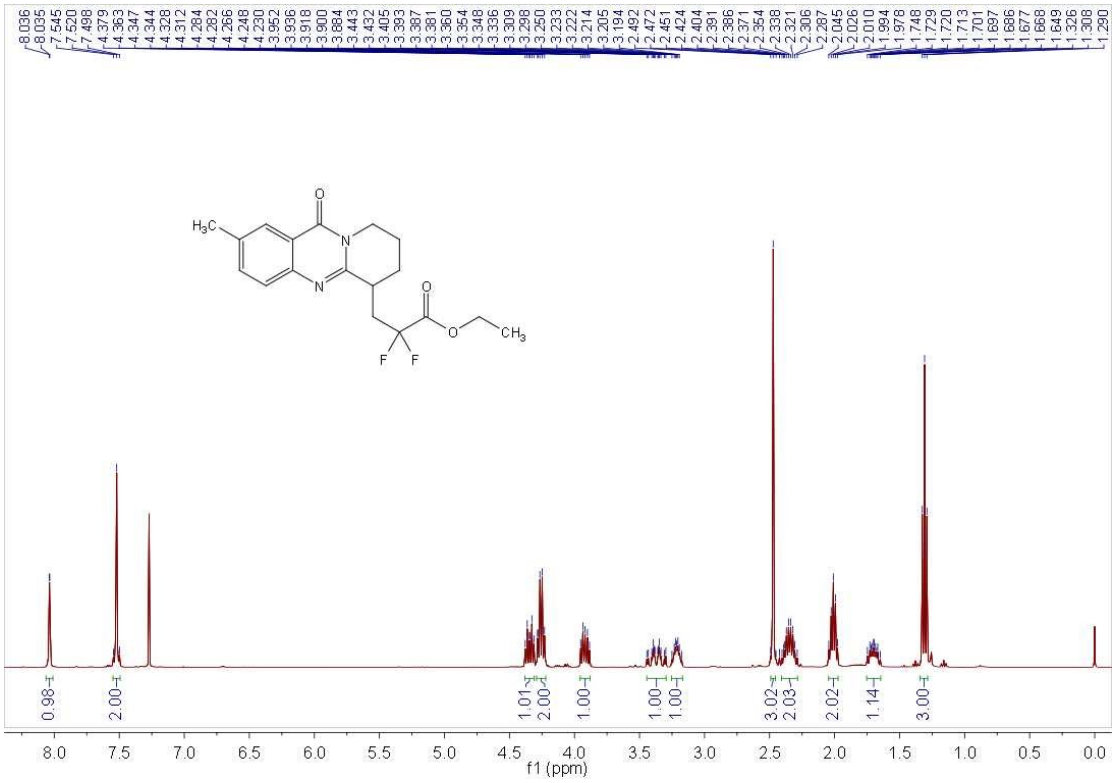
3a

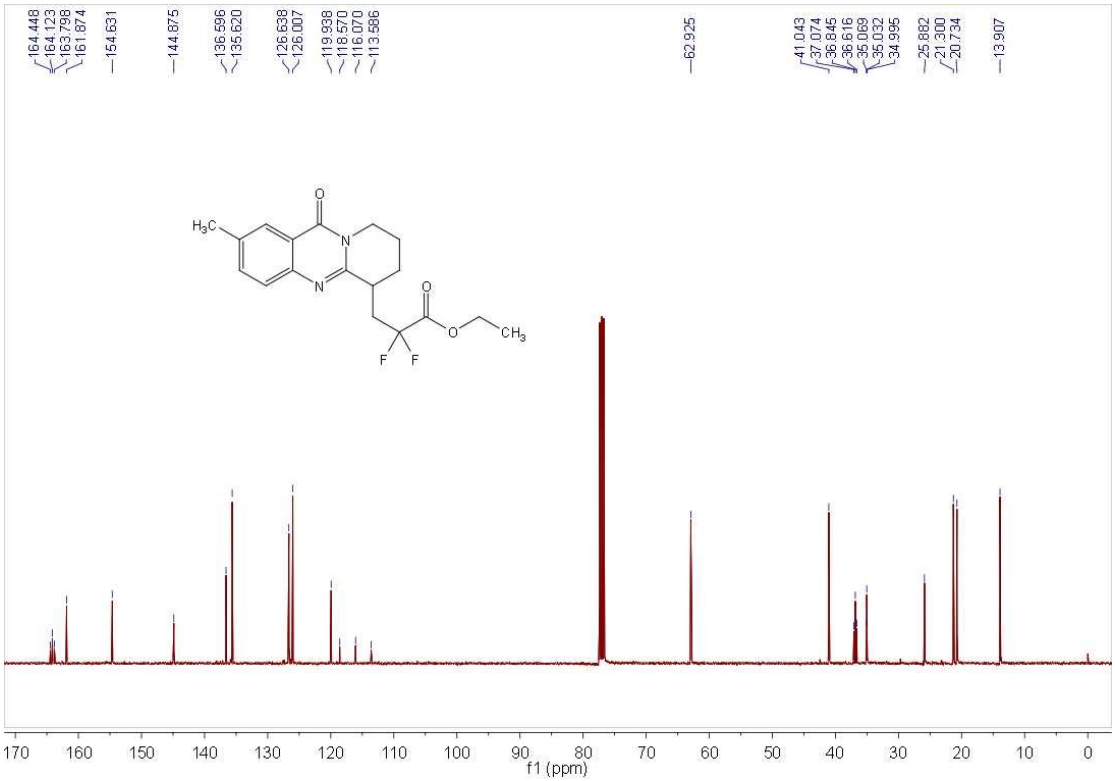

8.255
8.252
8.235
8.232
7.731
7.727
7.710
7.707
7.692
7.689
7.618
7.598
7.453
7.450
7.433
7.415
7.413
4.377
4.361
4.345
4.342
4.326
4.319
4.310
4.301
4.291
4.289
4.271
4.253
4.235
3.961
3.944
3.927
3.909
3.893
3.404
3.398
3.359
3.355
3.244
3.234
3.225
3.216
3.206
2.403
2.398
2.388
2.379
2.364
2.357
2.346
2.331
2.318
2.053
2.035
2.019
2.003
1.987
1.738
1.723
1.710
1.706
1.695
1.678
1.331
1.321
1.313
1.303
1.295
1.285
O
N
N
O
O
CH3
F
F
0.88
0.93
0.90
0.92
1.19
2.02
1.03
1.09
1.00
2.06
2.12
1.07
3.13
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

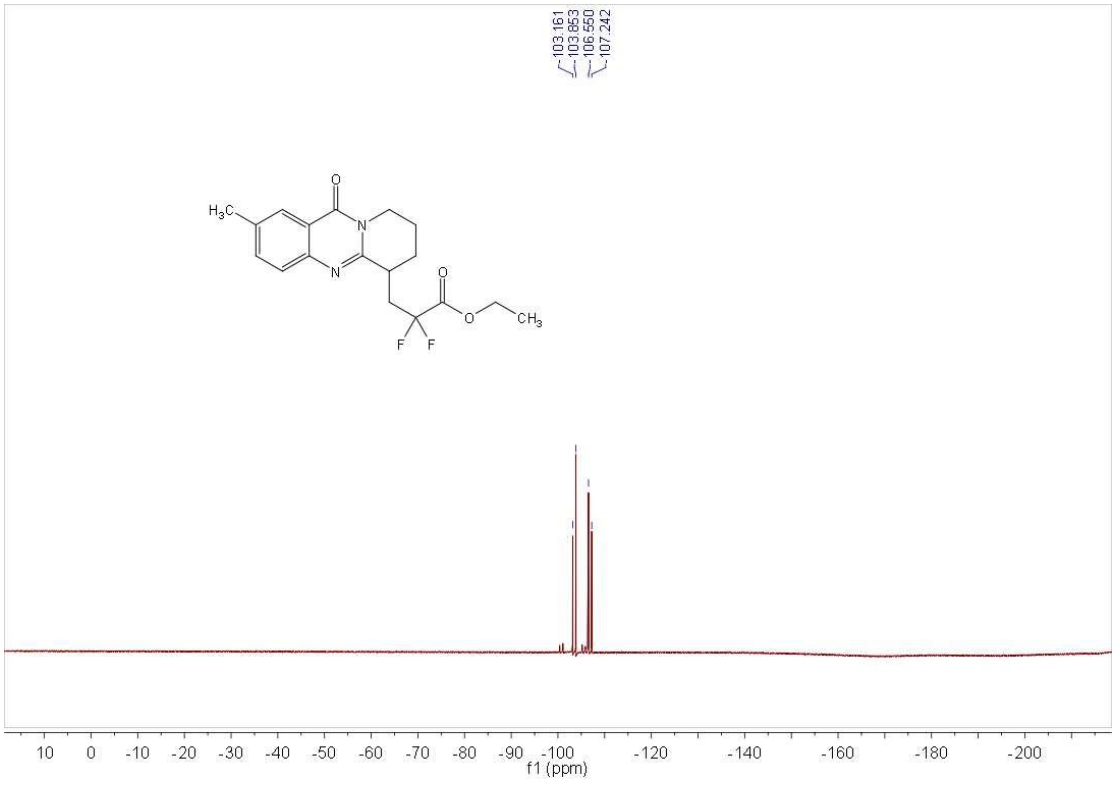

164.427
164.102
163.776
161.882
155.536
146.863
134.097
126.822
126.629
126.450
120.206
118.548
116.063
113.562
62.941
41.082
37.051
36.822
36.592
35.161
35.125
35.087
25.847
20.680
13.898
O
N
N
O
O
CH3
F
F
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


100.331
100.337
101.018
101.024
105.468
106.155
O
N
N
O
O
F
F
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

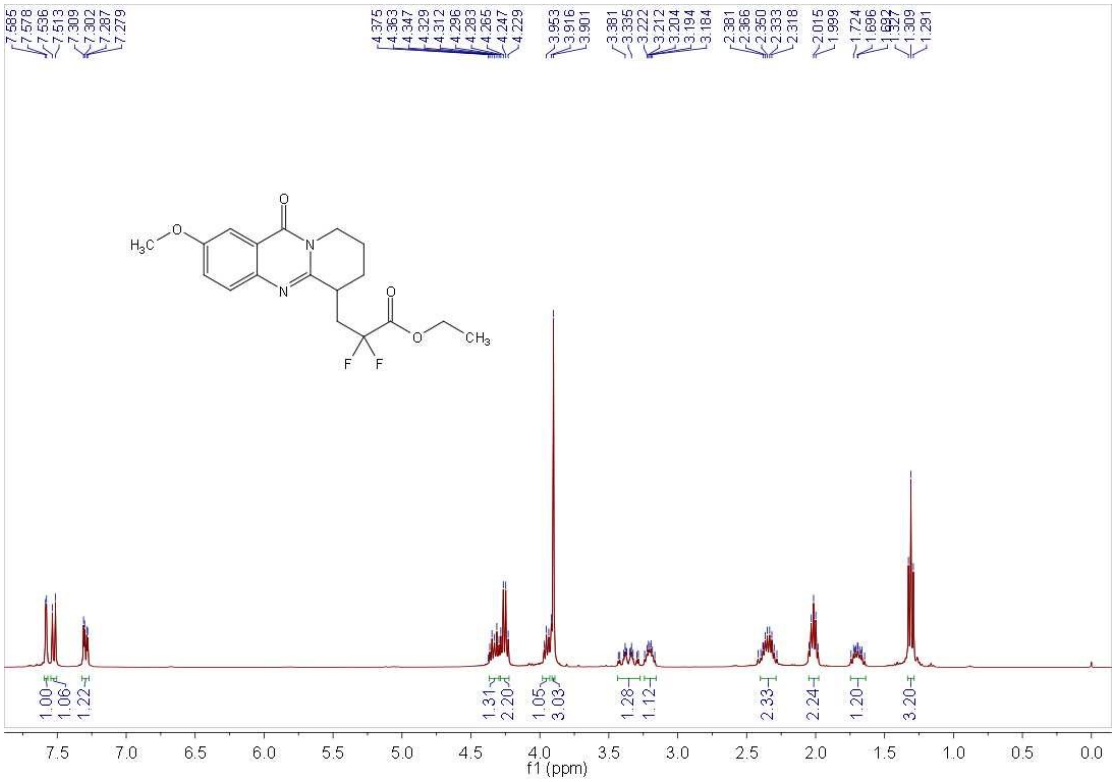
3b

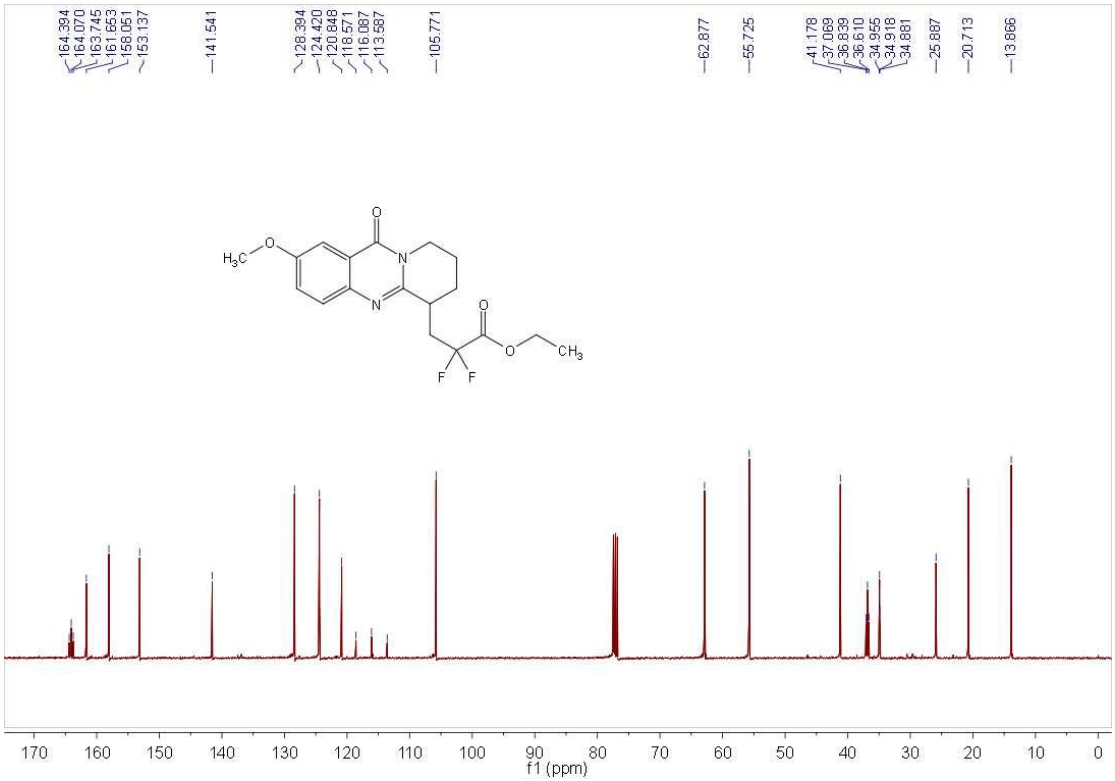

8.036
8.035
7.545
7.520
7.498
4.379
4.363
4.347
4.344
4.328
4.312
4.284
4.282
4.266
4.248
4.230
3.952
3.936
3.918
3.900
3.884
3.443
3.432
3.405
3.393
3.387
3.381
3.360
3.354
3.348
3.336
3.309
3.298
3.250
3.233
3.222
3.214
3.205
3.194
2.492
2.472
2.451
2.424
2.404
2.391
2.386
2.371
2.354
2.338
2.321
2.306
2.287
2.045
2.026
2.010
1.994
1.978
1.748
1.729
1.720
1.713
1.701
1.697
1.686
1.677
1.668
1.649
1.326
1.308
1.290
H3C
O
N
N
O
O
F
F
CH3
0.98
2.00
1.01
2.00
1.00
1.00
1.00
3.02
2.03
2.02
1.14
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

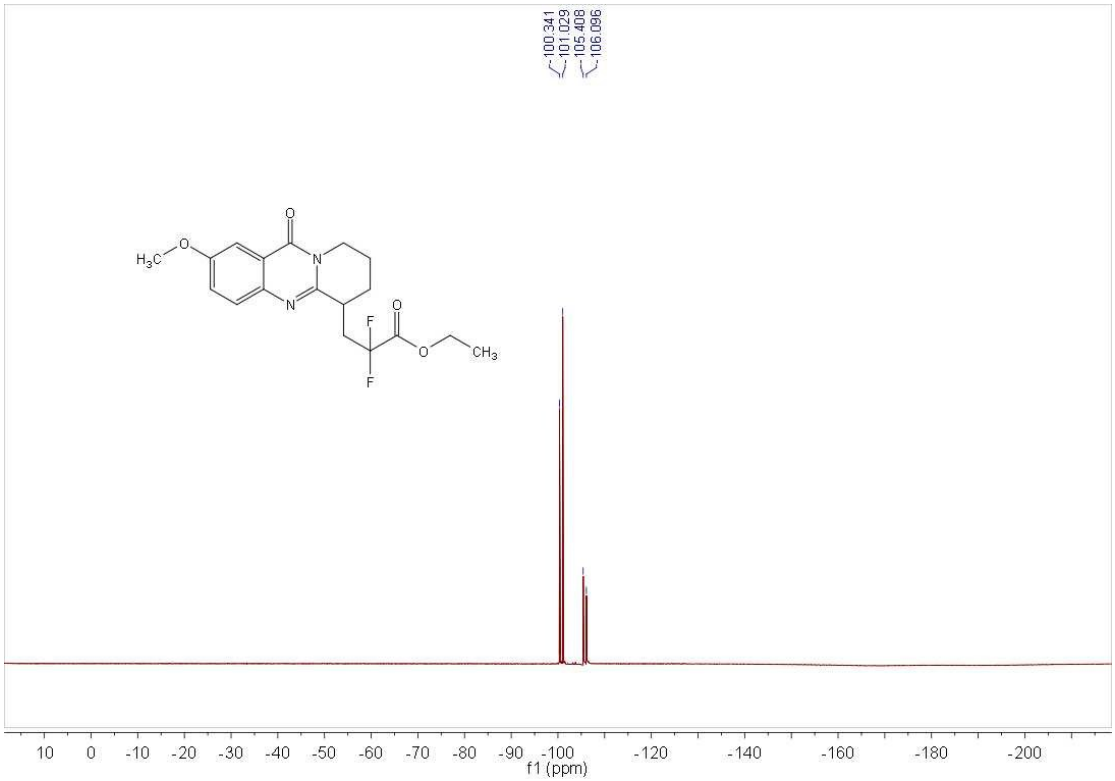

164.448
164.123
163.798
161.874
154.631
144.875
136.596
135.620
126.638
126.007
119.938
118.570
116.070
113.886
62.925
41.043
37.074
36.845
36.616
35.069
35.032
34.995
25.882
21.300
20.734
13.907
H3C
O
N
N
O
O
CH3
F
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


103.161
103.853
106.550
107.242
H3C
O
N
N
O
O
CH3
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

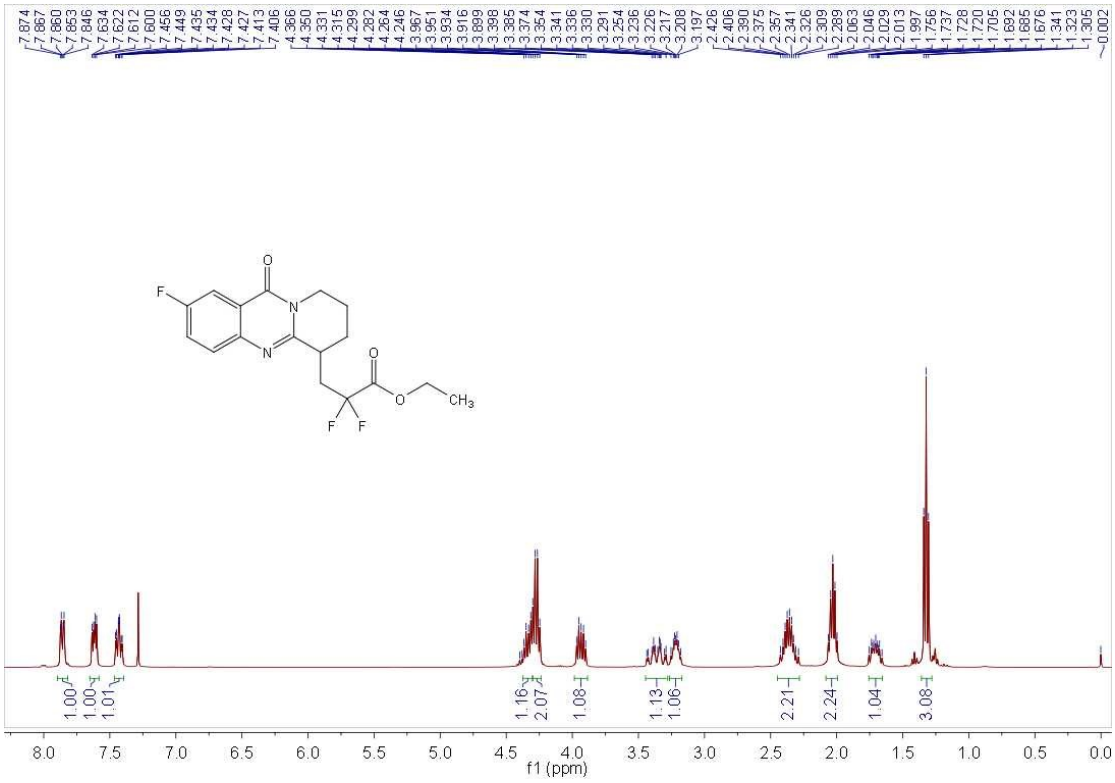
3c

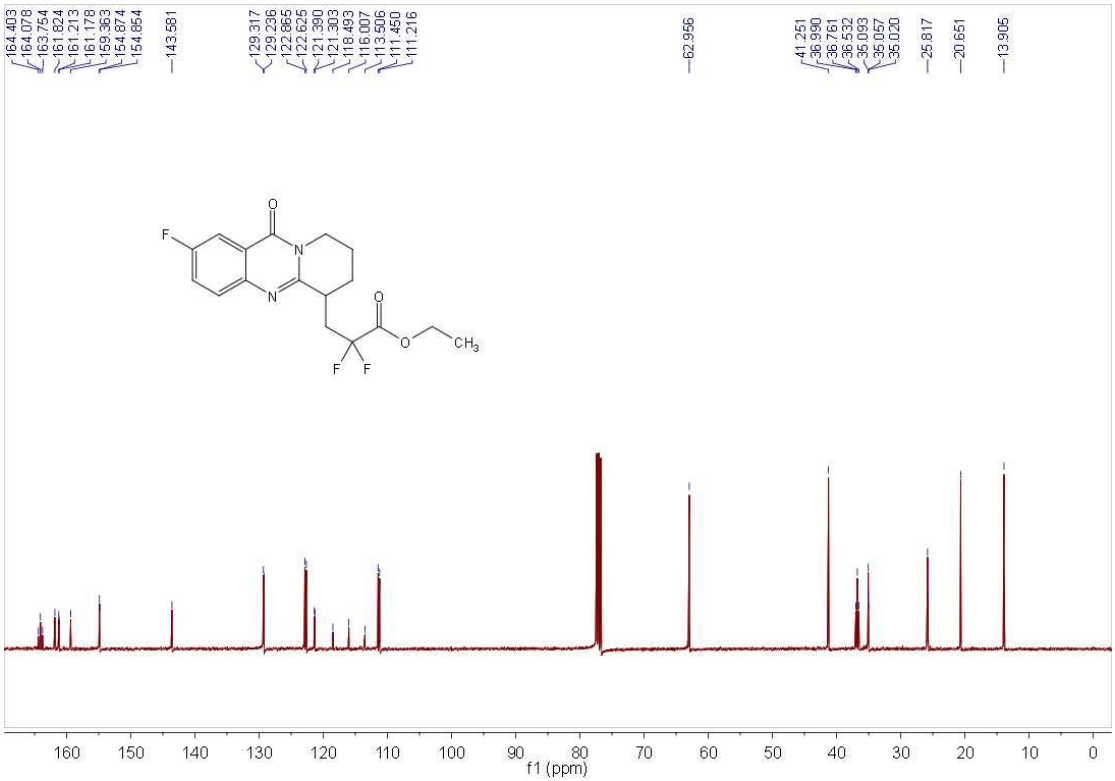

7.585
7.578
7.536
7.513
7.309
7.302
7.287
7.279
4.375
4.363
4.347
4.329
4.312
4.296
4.283
4.265
4.247
4.229
3.953
3.916
3.901
3.381
3.335
3.222
3.212
3.204
3.194
3.184
2.381
2.366
2.350
2.333
2.318
2.015
1.999
1.724
1.696
1.309
1.291
1.00
1.06
1.22
1.31
2.20
1.05
3.03
1.28
1.12
2.33
2.24
1.20
3.20
f1 (ppm)

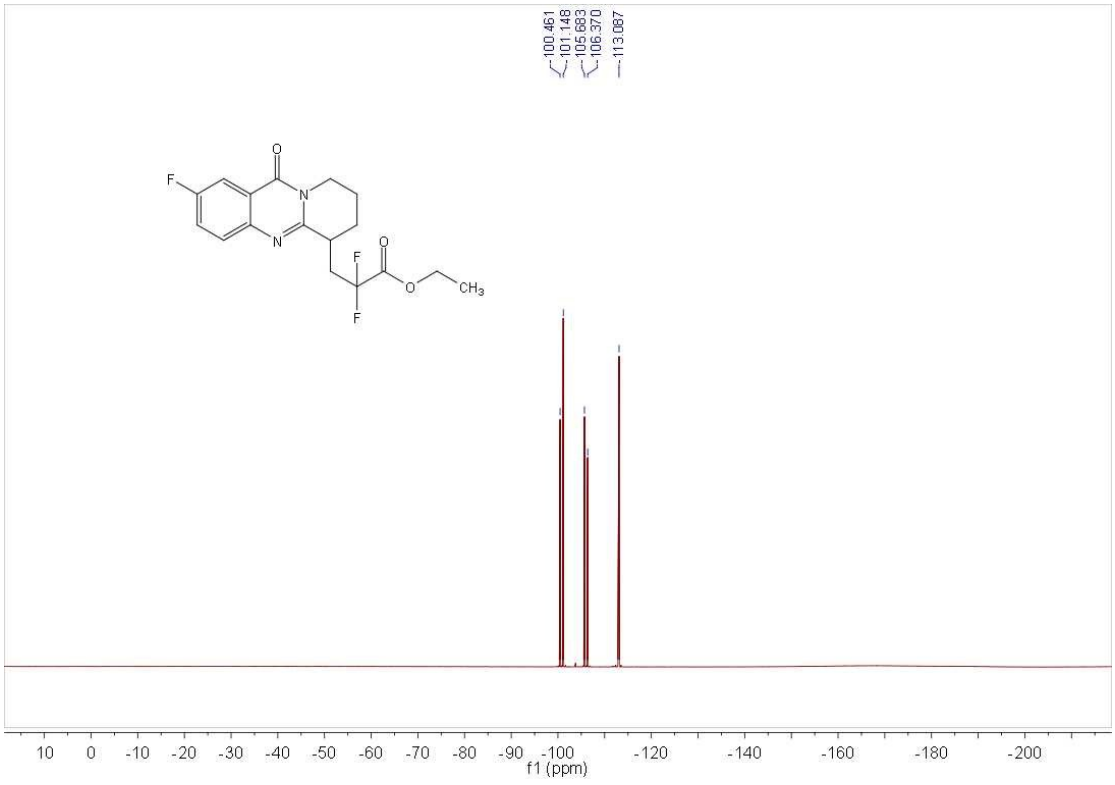

164.394
164.070
163.745
161.653
158.051
153.137
141.541
128.394
124.420
120.848
118.571
116.087
113.587
105.771
62.877
55.725
41.178
37.069
36.839
36.610
34.955
34.918
34.881
25.887
20.713
13.866
f1 (ppm)



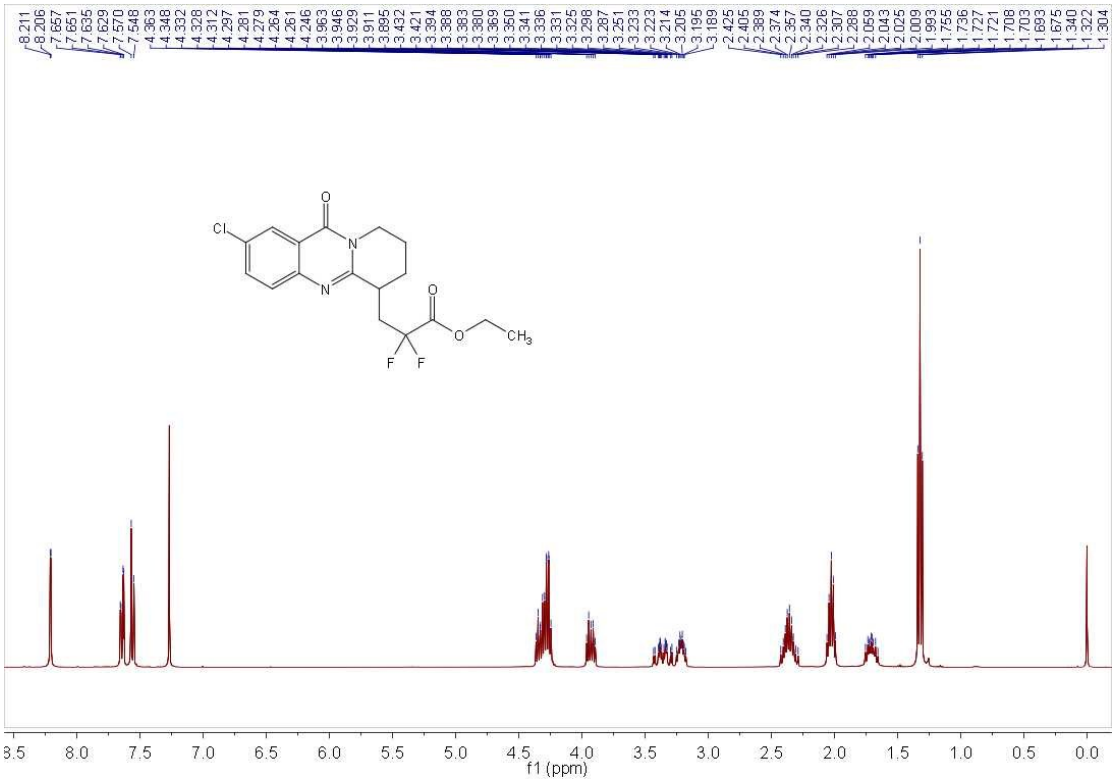
3d

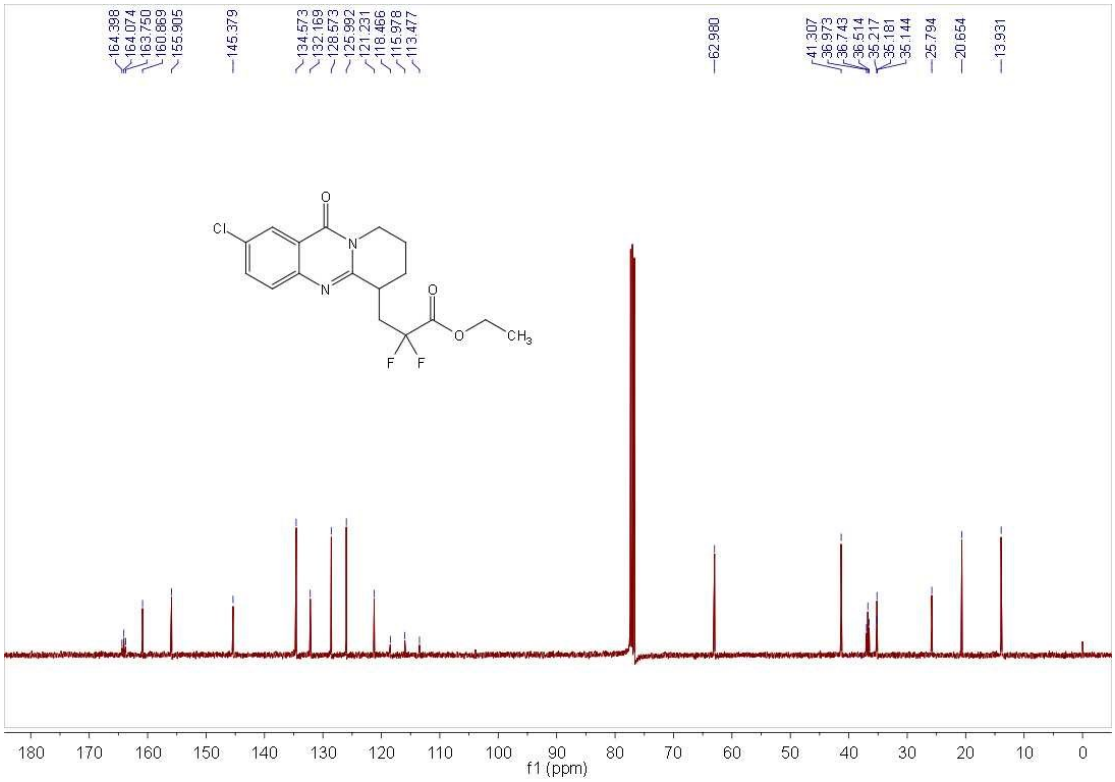


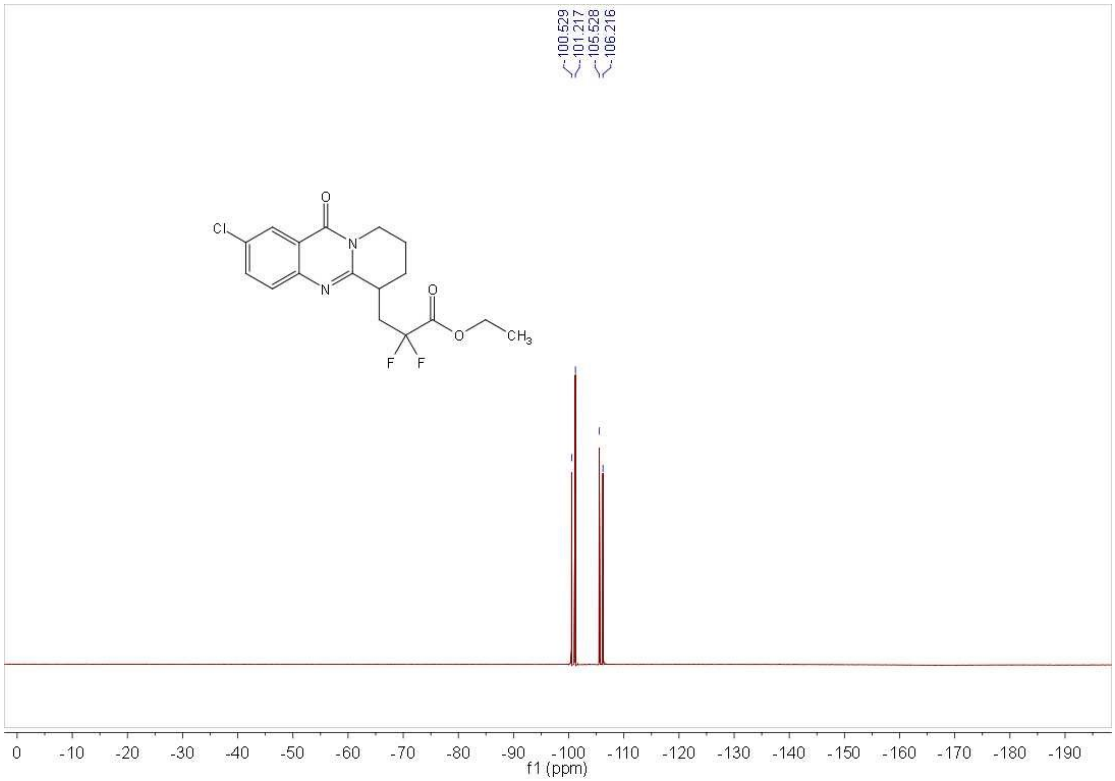

164.403
164.078
163.754
161.824
161.213
161.178
159.363
154.874
154.854
143.581
129.317
129.236
122.865
122.625
121.390
121.303
118.493
116.007
113.506
111.450
111.216
62.956
41.251
36.990
36.761
36.532
35.093
35.057
35.020
25.817
20.651
13.905
O
F
N
N
O
O
CH3
F
F
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


100.461
101.148
105.683
106.370
113.067
O
F
N
N
F
O
O
CH3
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

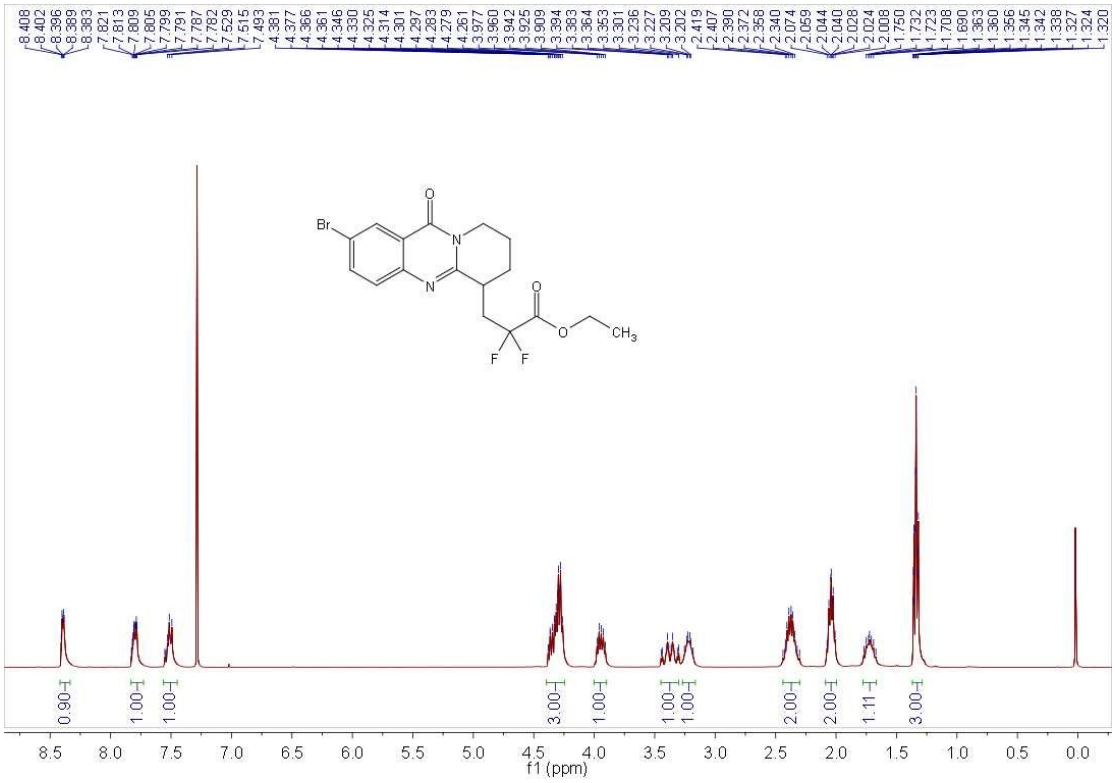
3e

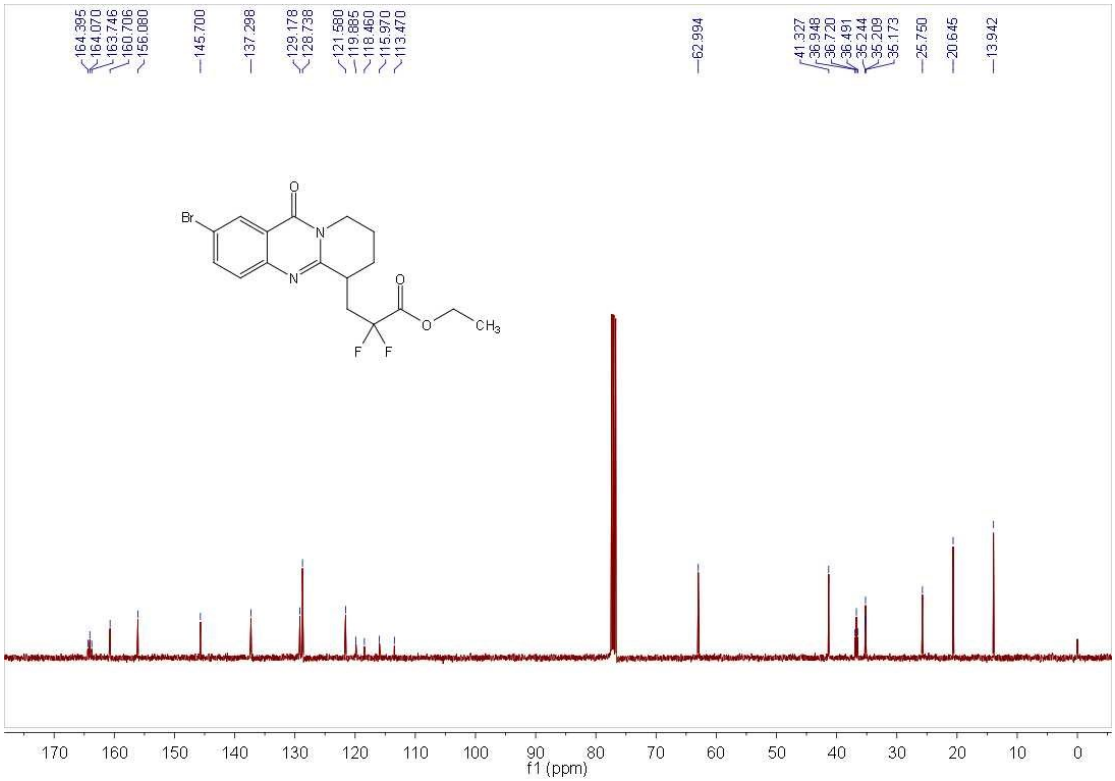

8.211
8.206
7.657
7.651
7.635
7.629
7.570
7.548
4.363
4.348
4.332
4.328
4.312
4.297
4.281
4.279
4.264
4.261
4.246
3.963
3.946
3.929
3.911
3.895
3.432
3.421
3.394
3.388
3.383
3.380
3.369
3.350
3.341
3.336
3.331
3.325
3.298
3.287
3.251
3.233
3.223
3.214
3.205
3.195
3.189
2.425
2.405
2.389
2.374
2.357
2.340
2.326
2.307
2.288
2.059
2.043
2.025
2.009
1.993
1.755
1.736
1.727
1.721
1.708
1.703
1.693
1.675
1.340
1.322
1.304
Cl
O
N
N
O
O
CH3
F
F
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

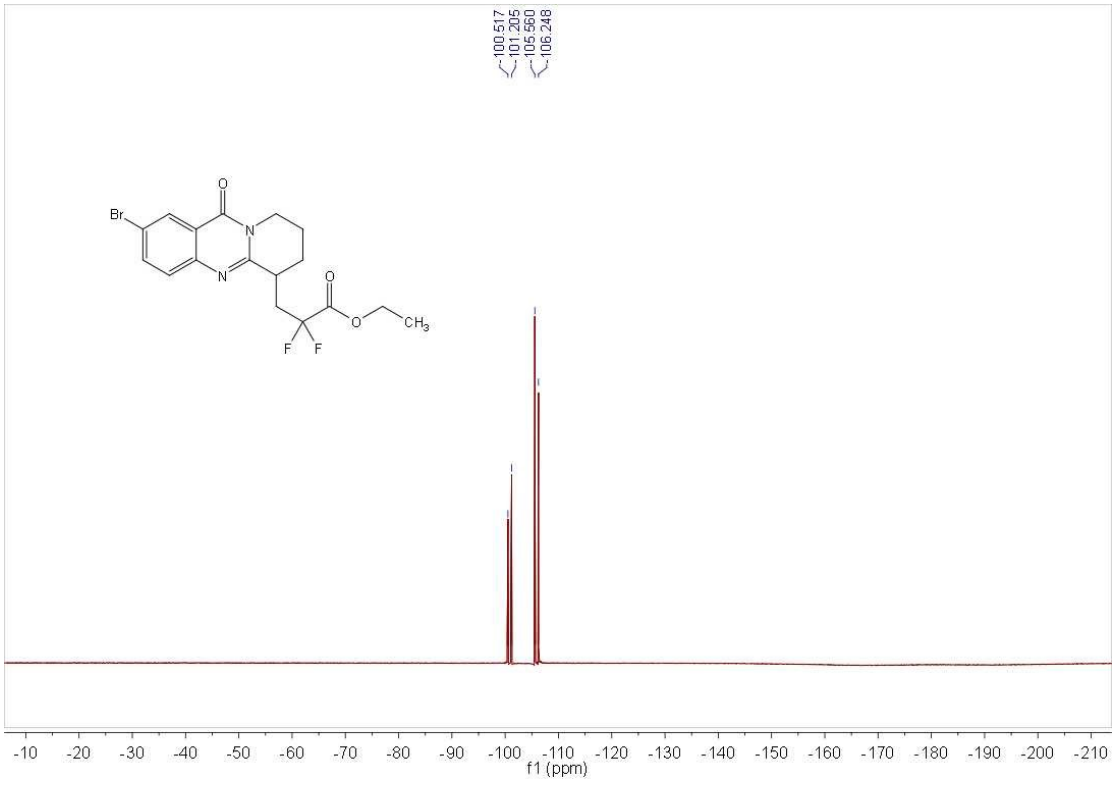

164.398
164.074
163.750
160.869
155.905
145.379
134.573
132.169
128.573
125.992
121.231
118.466
115.978
113.477
62.980
41.307
36.973
36.743
36.514
35.217
35.181
35.144
25.794
20.654
13.931
Cl
O
N
N
O
O
CH3
F
F
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-100.529
-101.217
-105.528
-106.216
Cl
O
N
N
O
O
CH3
F
F
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

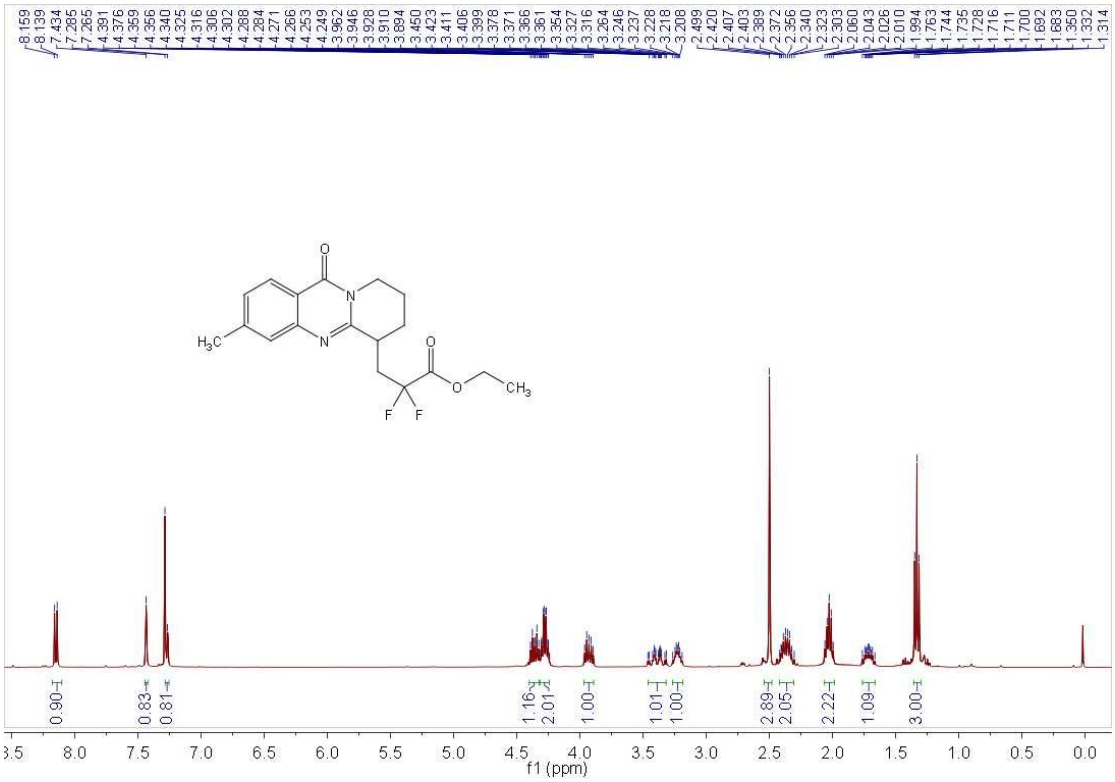
3f

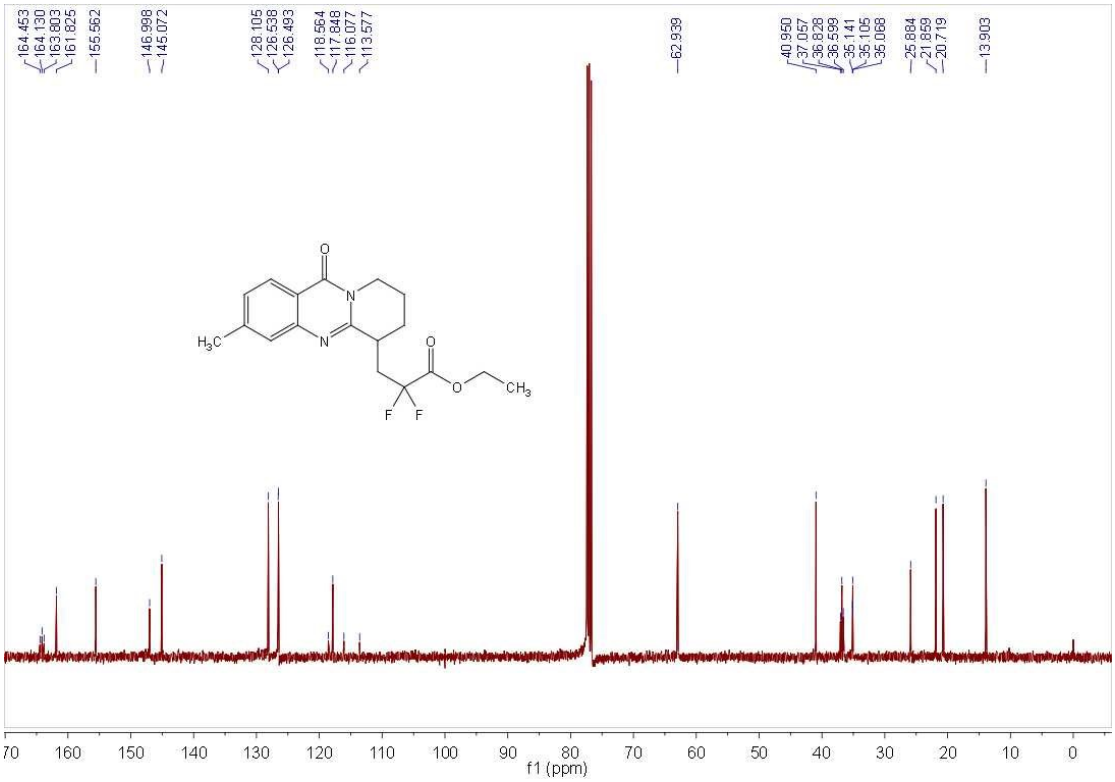

Br
O
N
N
O
O
CH3
F
F
0.90
1.00
1.00
3.00
1.00
1.00
1.00
2.00
2.00
1.11
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

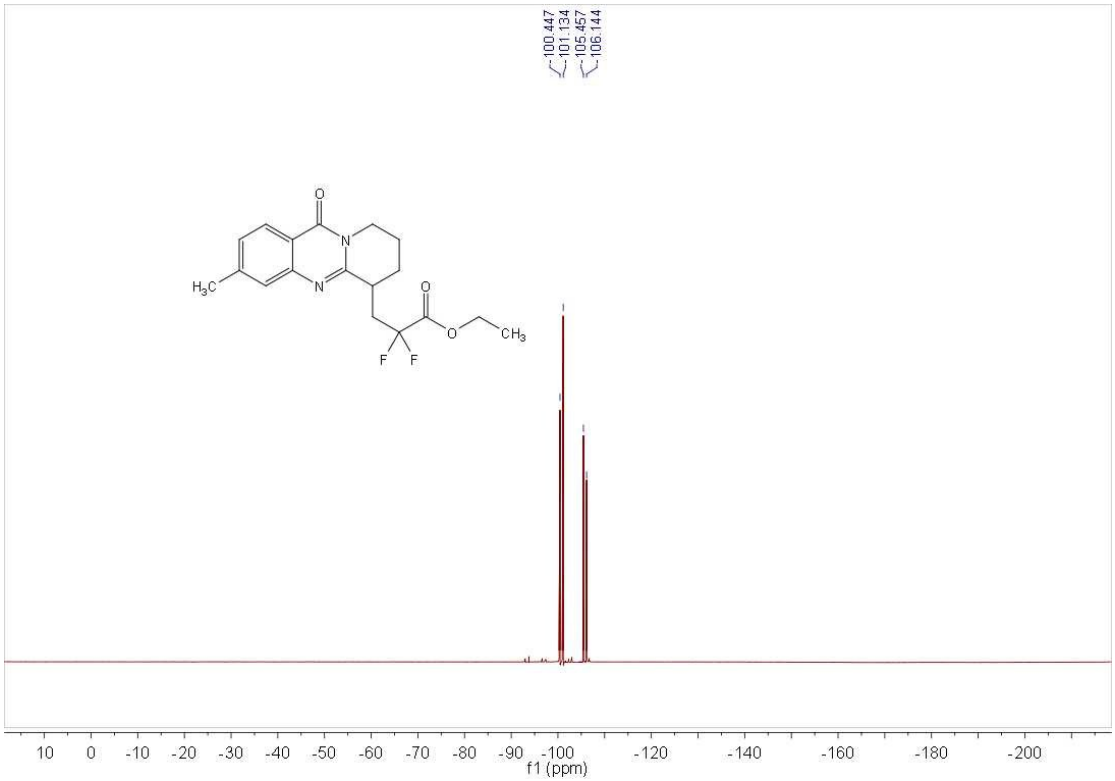

164.395
164.070
163.746
160.706
156.080
145.700
137.298
129.178
128.738
121.580
119.885
118.460
115.970
113.470
62.994
41.327
36.948
36.720
36.491
35.244
35.209
35.173
25.750
20.645
13.942
Br
O
N
N
O
O
CH3
F
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


100.517
101.205
105.560
106.248
Br
O
N
N
O
O
CH3
F
F
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

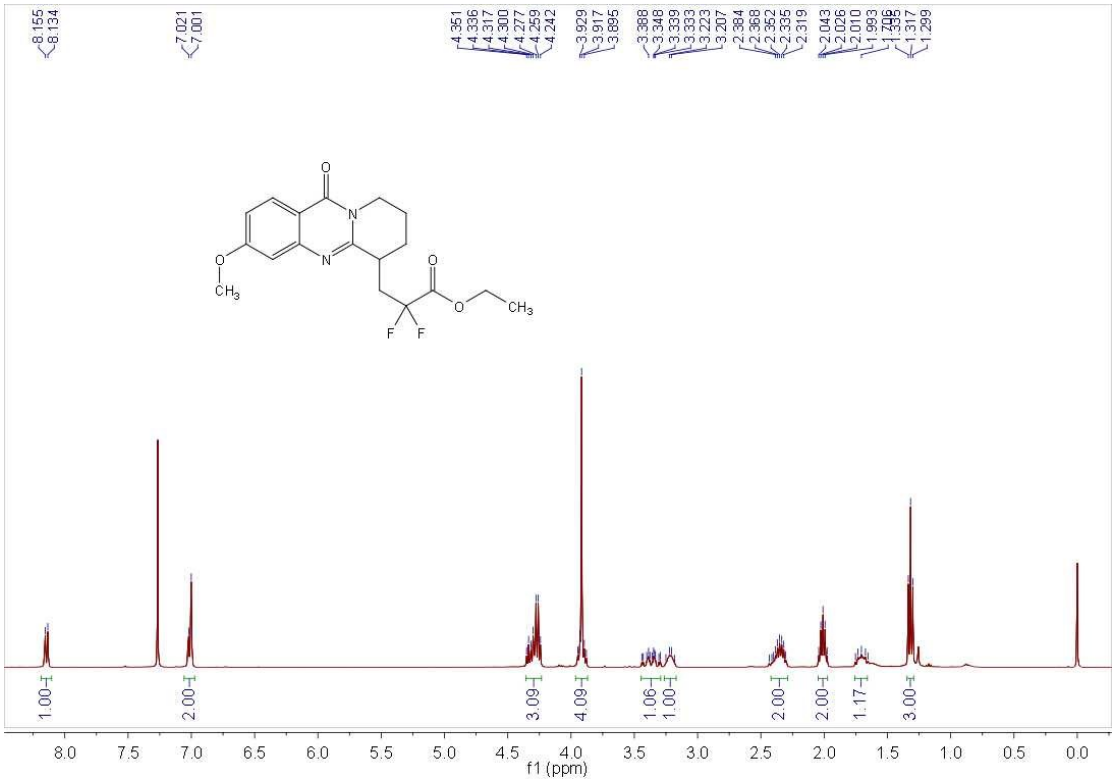
3g

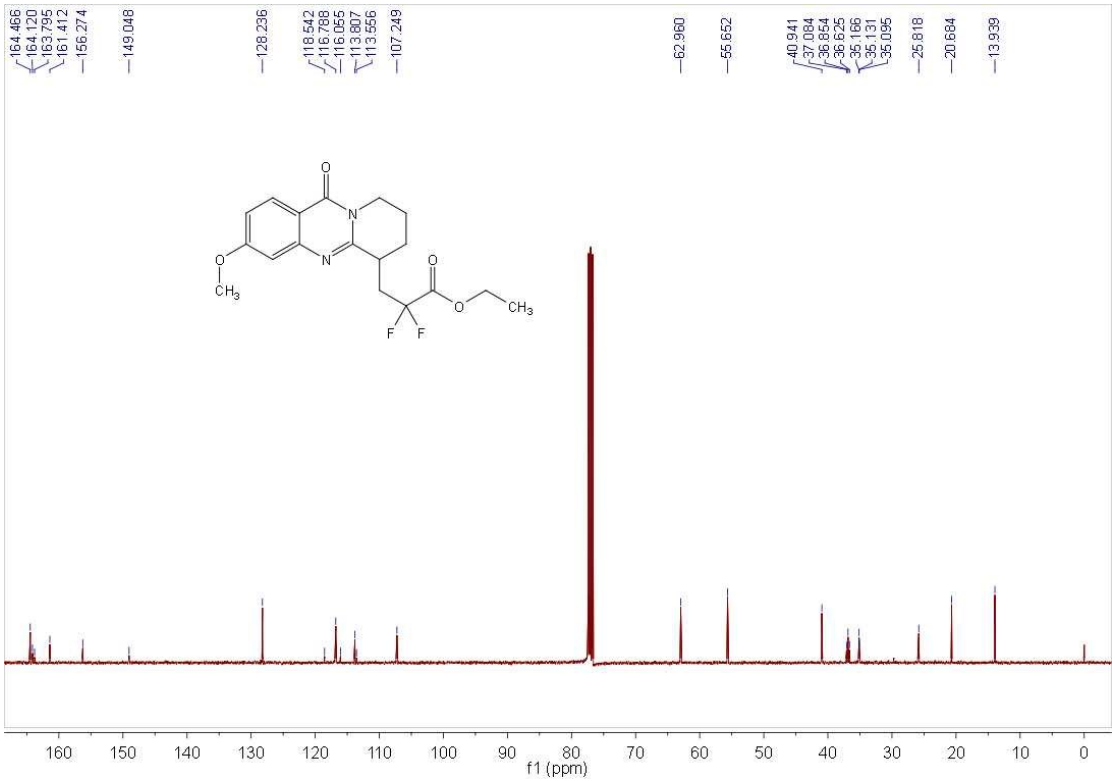


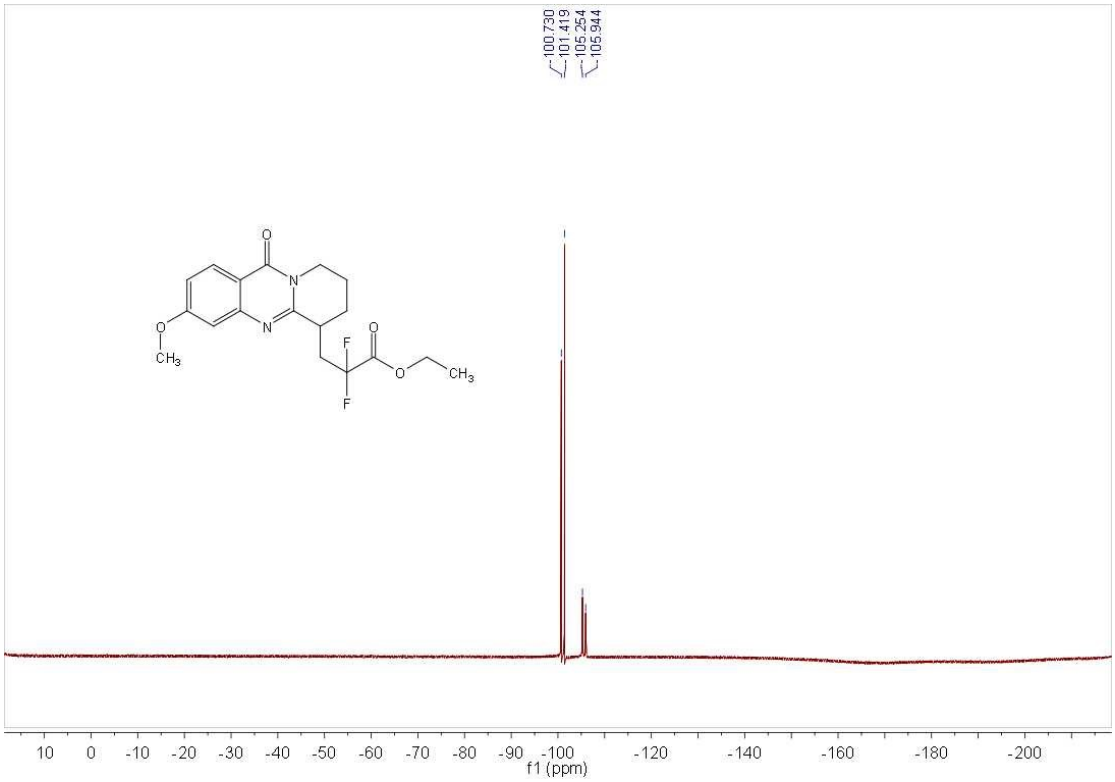



-100.447
-101.134
-105.457
-106.144
f1 (ppm)

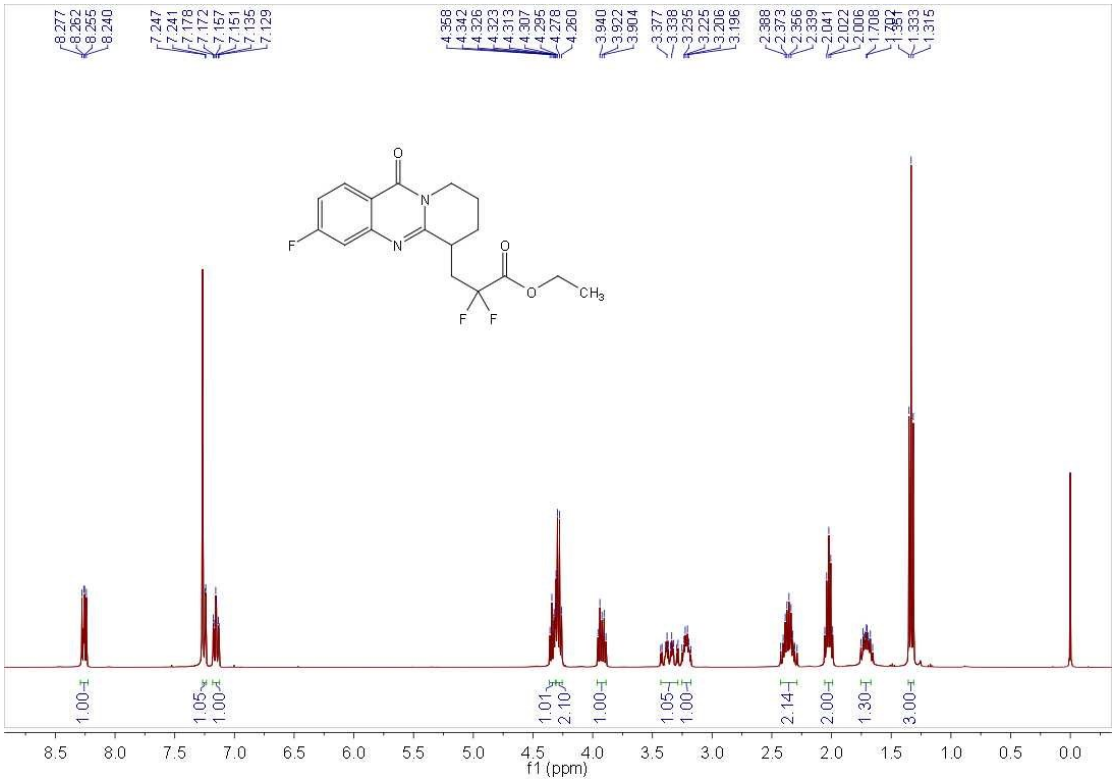
3h

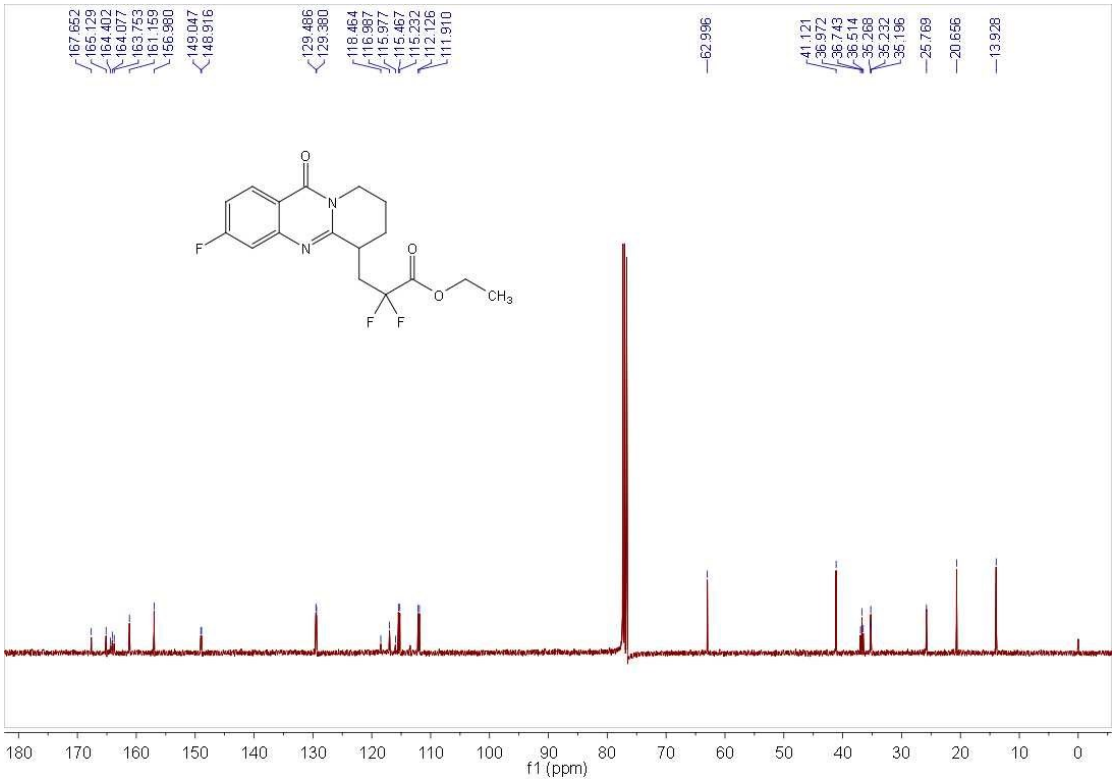

8.155
8.134
7.021
7.001
4.351
4.336
4.317
4.300
4.277
4.259
4.242
3.929
3.917
3.895
3.388
3.348
3.339
3.333
3.223
3.207
2.384
2.368
2.352
2.335
2.319
2.043
2.026
2.010
1.993
1.317
1.299
1.00
2.00
3.09
4.09
1.06
1.00
2.00
2.00
1.17
3.00
f1 (ppm)

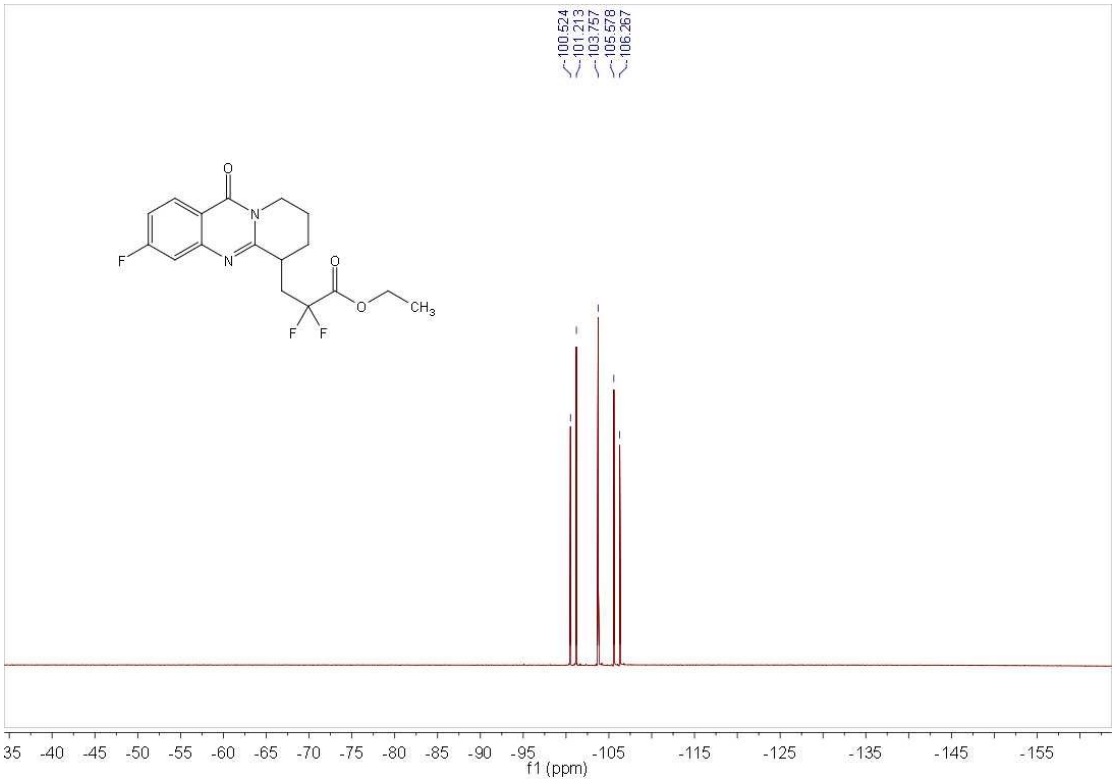

164.466
164.120
163.795
161.412
156.274
149.048
128.236
118.542
116.788
116.055
113.807
113.556
107.249
62.960
55.652
40.941
37.084
36.854
36.625
35.166
35.131
35.095
25.818
20.684
13.939
O
N
N
O
CH3
O
O
CH3
F
F
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


100.730
101.419
105.254
105.944
O
N
N
O
CH3
F
O
O
CH3
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

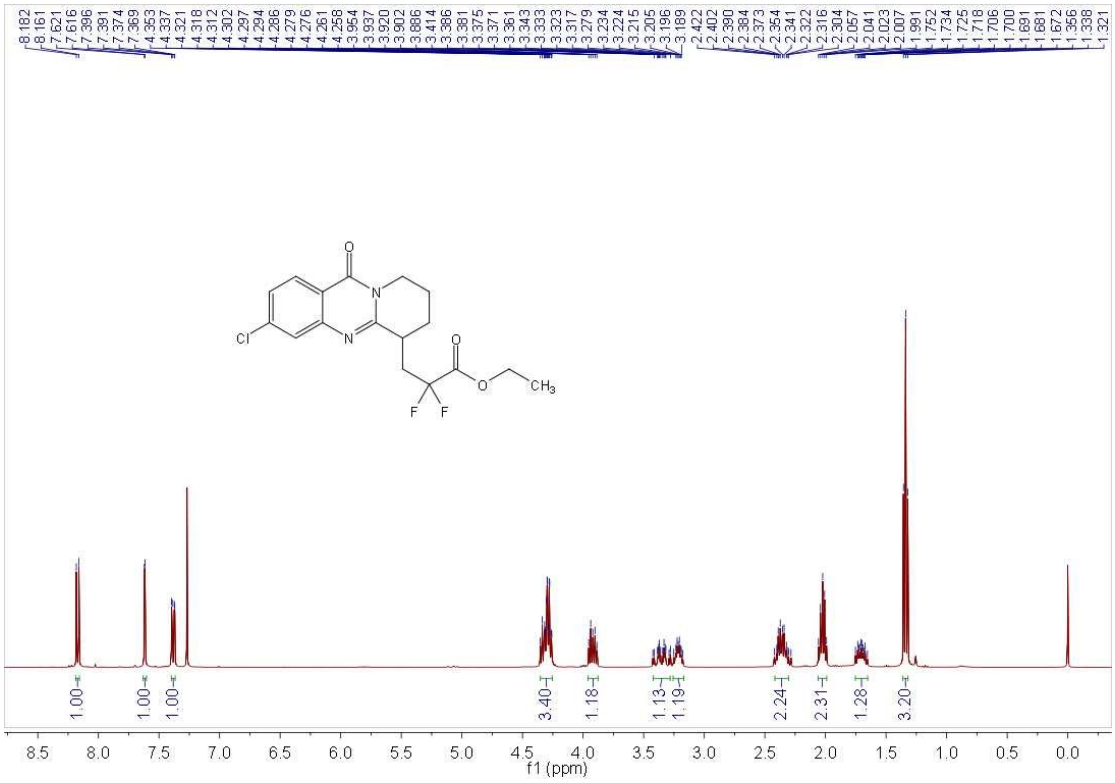
3i

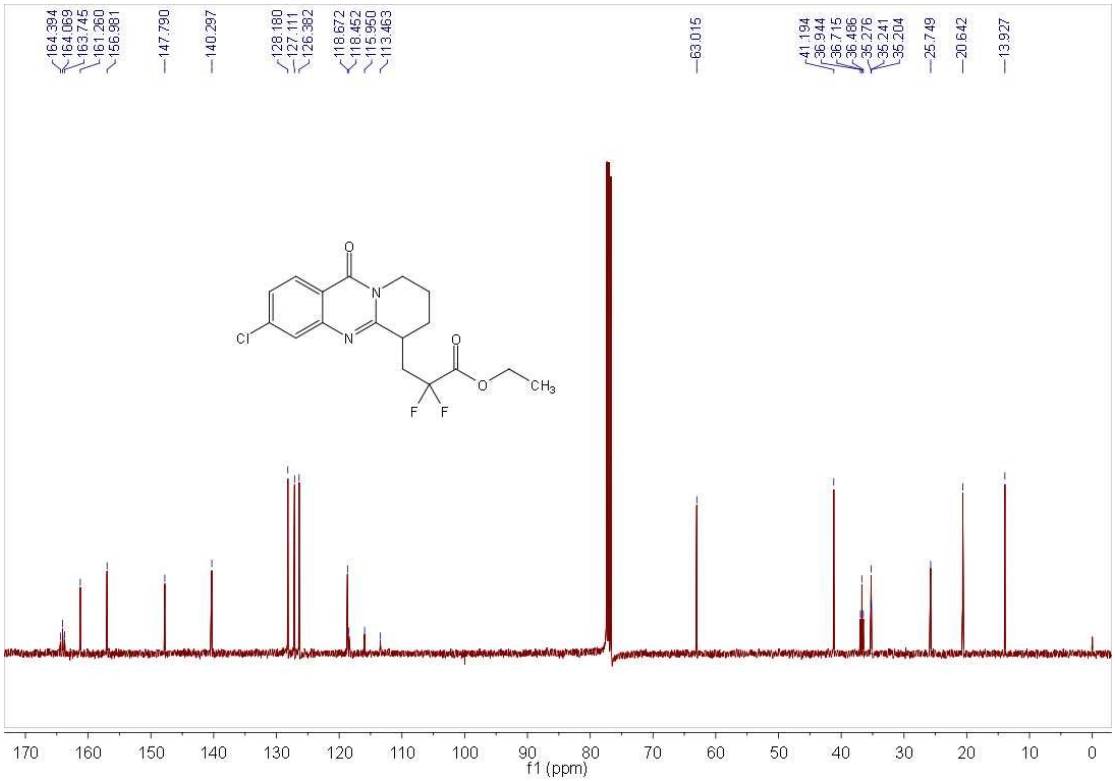

8.277
8.262
8.255
8.240
7.247
7.241
7.178
7.172
7.157
7.151
7.135
7.129
4.358
4.342
4.326
4.323
4.313
4.307
4.295
4.278
4.260
3.940
3.922
3.904
3.377
3.338
3.235
3.225
3.206
3.196
2.388
2.373
2.356
2.339
2.041
2.022
2.006
1.708
1.351
1.333
1.315
1.00
1.05
1.00
1.01
2.10
1.00
1.05
1.00
2.14
2.00
1.30
3.00
f1 (ppm)

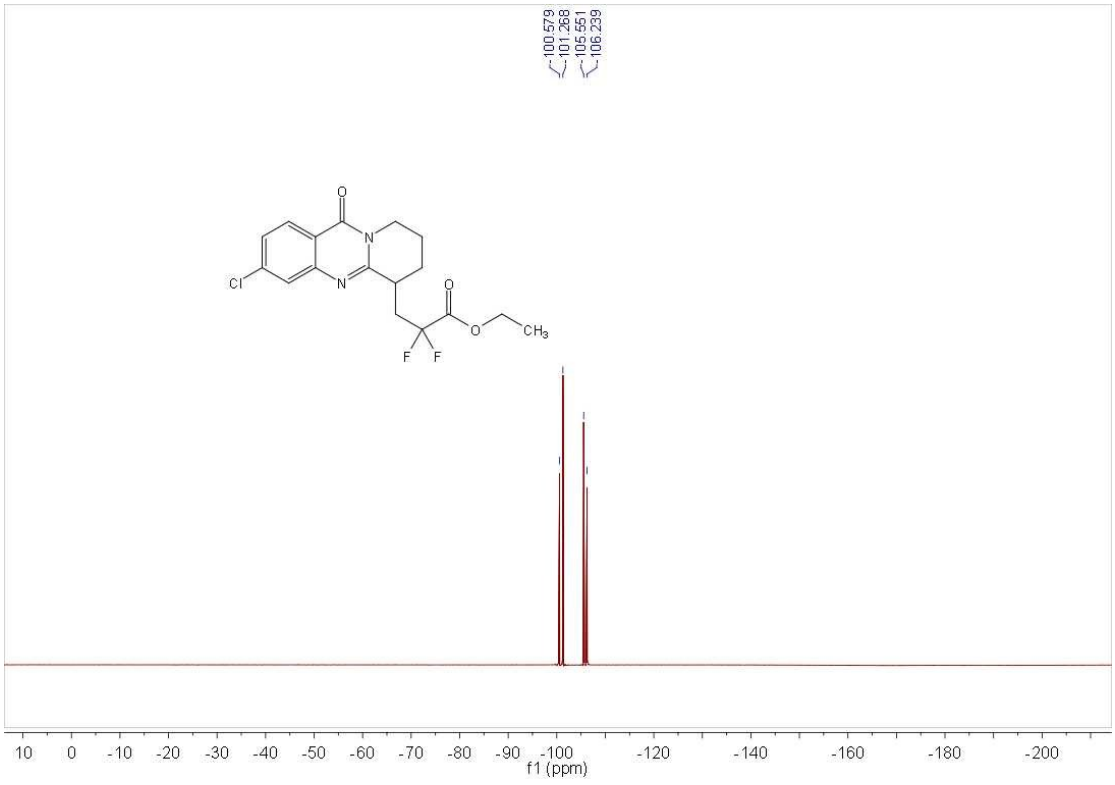

167.652
165.129
164.402
164.077
163.753
161.159
156.980
149.047
148.916
129.486
129.380
118.464
116.987
115.977
115.467
115.232
112.126
111.910
62.996
41.121
36.972
36.743
36.514
35.268
35.232
35.196
25.769
20.656
13.928
f1 (ppm)


-100.524
-101.213
-103.757
-105.578
-106.267
F
O
N
N
O
O
CH3
F
F
35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145 -155
f1 (ppm)

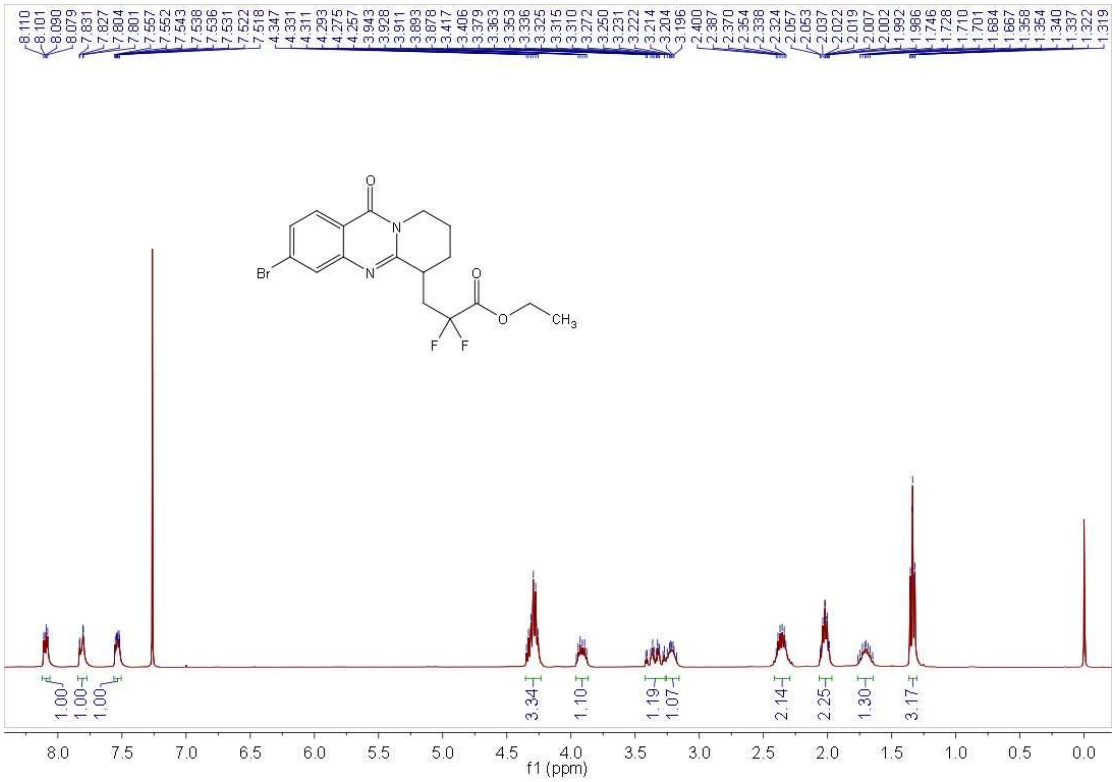
3j

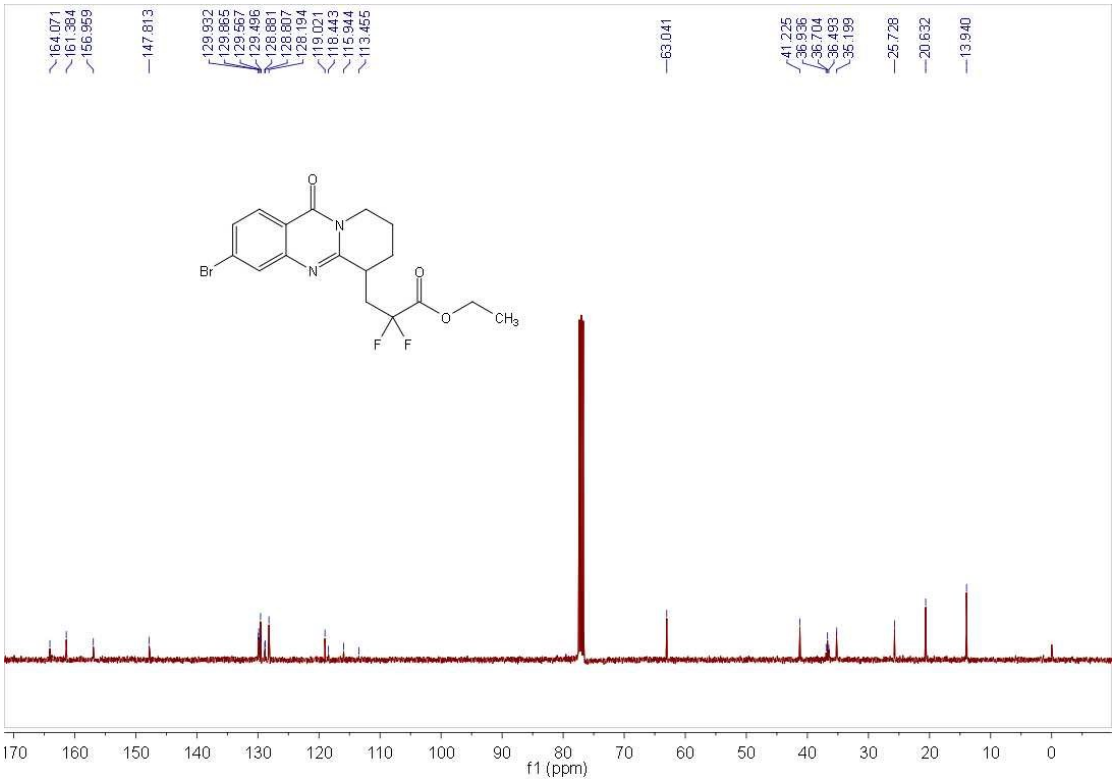

8.182
8.161
7.621
7.616
7.396
7.391
7.374
7.369
4.353
4.337
4.321
4.318
4.312
4.302
4.297
4.294
4.286
4.279
4.276
4.261
4.258
3.954
3.937
3.920
3.902
3.886
3.414
3.386
3.381
3.375
3.371
3.361
3.343
3.333
3.323
3.317
3.279
3.234
3.224
3.215
3.205
3.196
3.189
2.422
2.402
2.390
2.384
2.373
2.354
2.341
2.322
2.316
2.304
2.057
2.041
2.023
2.007
1.991
1.752
1.734
1.725
1.718
1.706
1.700
1.691
1.681
1.672
1.356
1.338
1.321
Cl
O
N
N
O
O
CH3
F
F
1.00
1.00
1.00
3.40
1.18
1.13
1.19
2.24
2.31
1.28
3.20
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

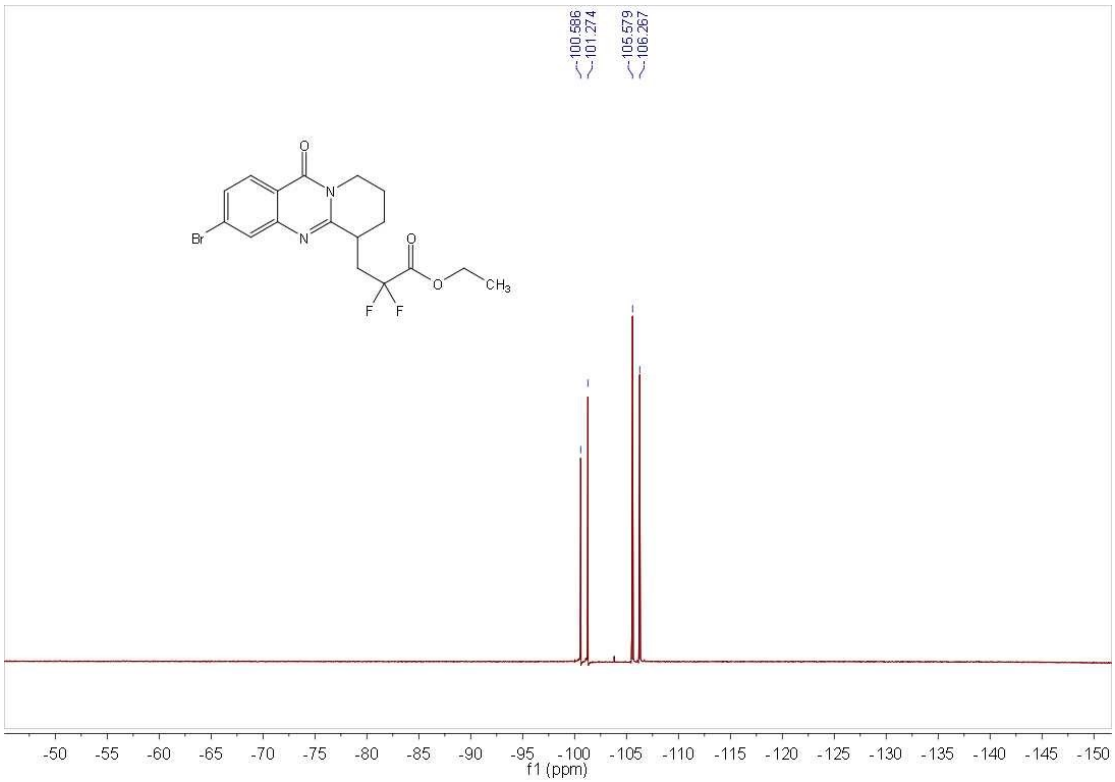

164.394
164.069
163.745
161.260
156.981
147.790
140.297
128.180
127.111
126.382
118.672
118.452
115.950
113.463
63.015
41.194
36.944
36.715
36.486
35.276
35.241
35.204
25.749
20.642
13.927
Cl
N
O
F
F
CH3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


100.579
101.268
105.551
106.239
Cl
N
O
F
F
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

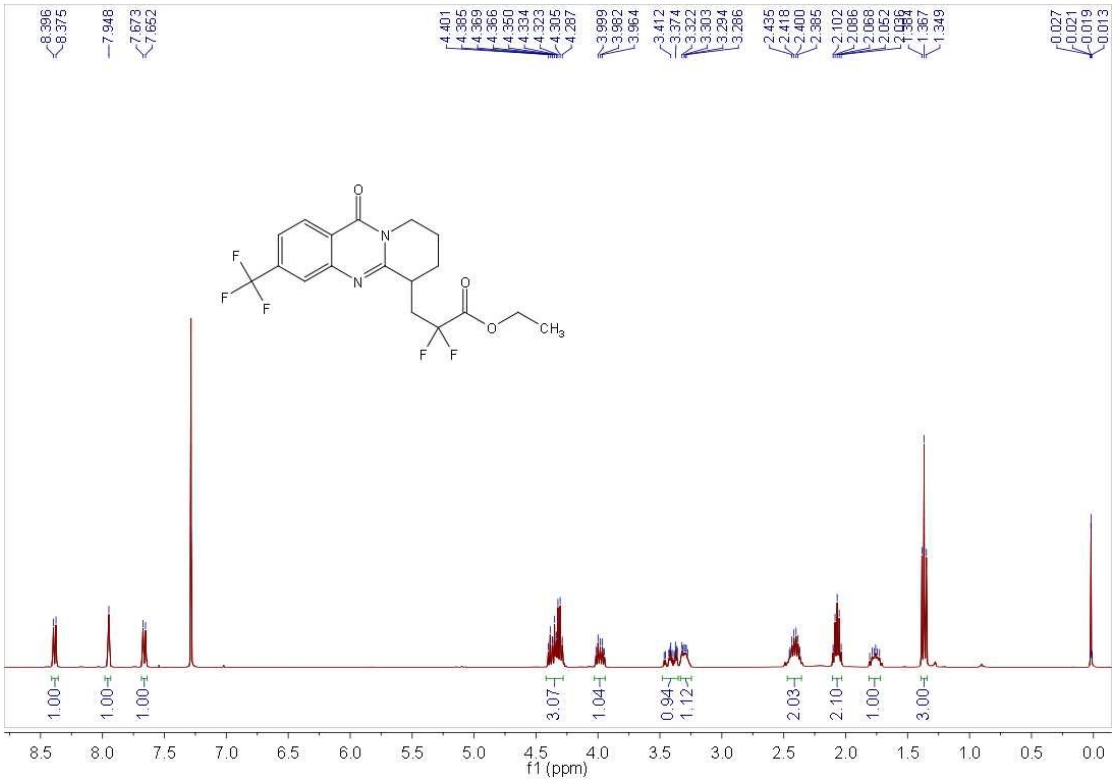
3k

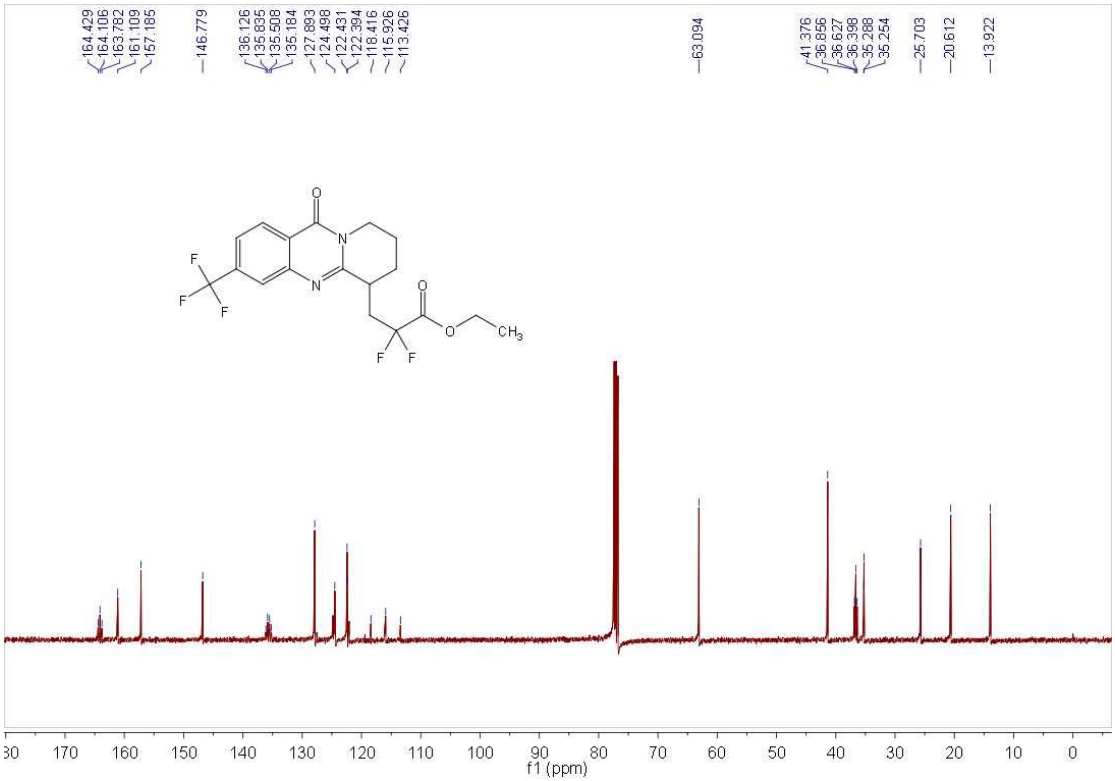

8.110
8.101
8.090
8.079
7.831
7.827
7.804
7.801
7.557
7.552
7.543
7.538
7.536
7.531
7.522
7.518
4.347
4.331
4.311
4.293
4.275
4.257
3.943
3.928
3.911
3.893
3.878
3.417
3.406
3.379
3.363
3.353
3.336
3.325
3.315
3.310
3.272
3.250
3.231
3.222
3.214
3.204
3.196
2.400
2.387
2.370
2.354
2.338
2.324
2.057
2.053
2.037
2.022
2.019
2.007
2.002
1.992
1.986
1.746
1.728
1.710
1.701
1.684
1.667
1.358
1.354
1.340
1.337
1.322
1.319
Br
O
N
N
O
O
CH3
F
F
1.00
1.00
1.00
3.34
1.10
1.19
1.07
2.14
2.25
1.30
3.17
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

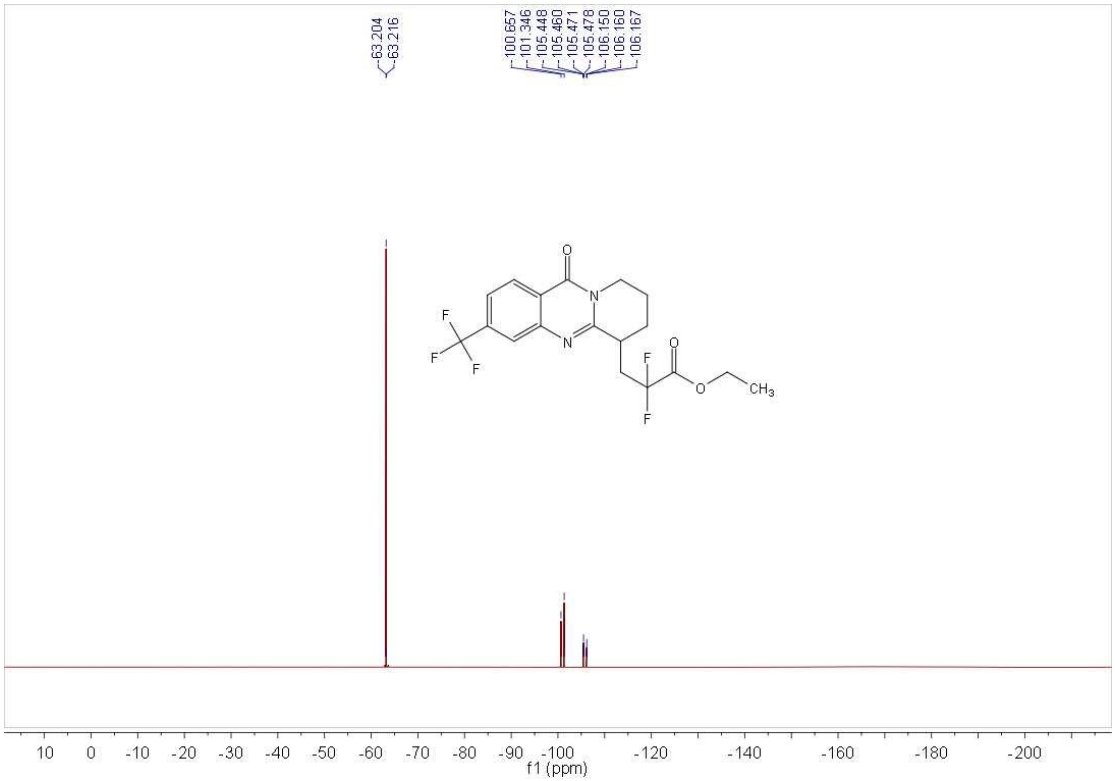

164.071
161.384
156.959
147.813
129.932
129.865
129.567
129.496
128.881
128.807
128.194
119.021
118.443
115.944
113.455
63.041
41.225
36.936
36.704
36.493
35.199
25.728
20.632
13.940
Br
O
N
N
O
O
CH3
F
F
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-100.586
-101.274
-105.579
-106.267
Br
O
N
N
O
O
CH3
F
F
-50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
f1 (ppm)

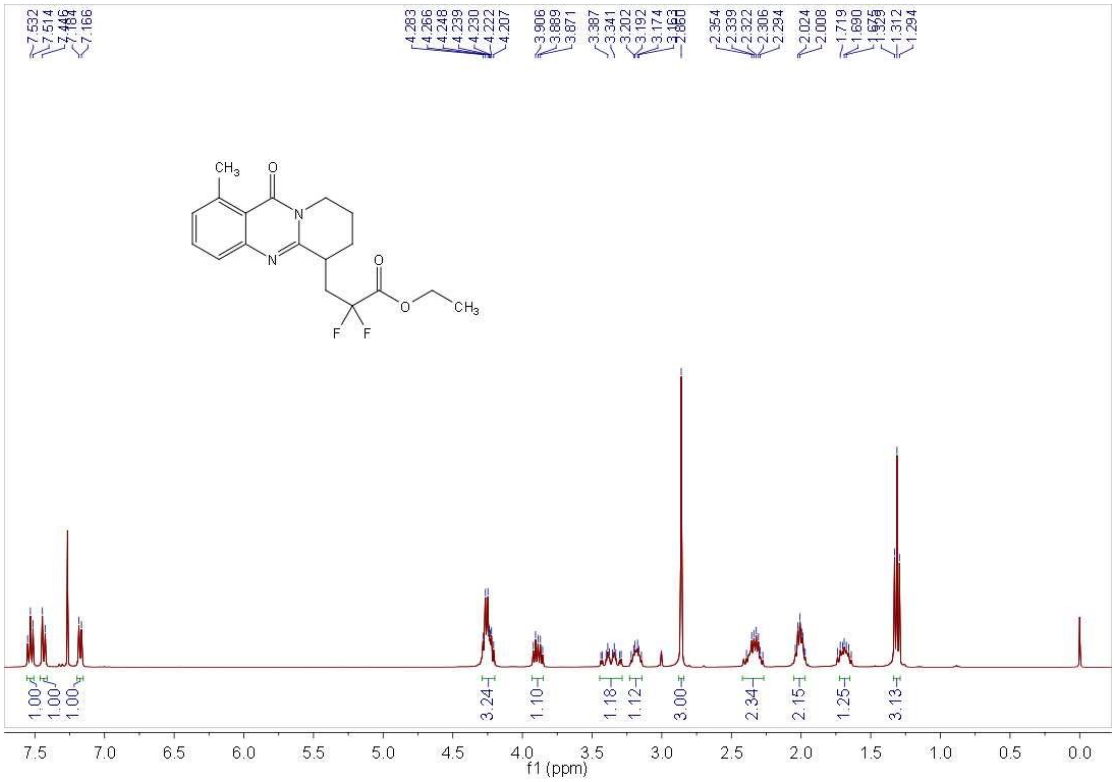
3l

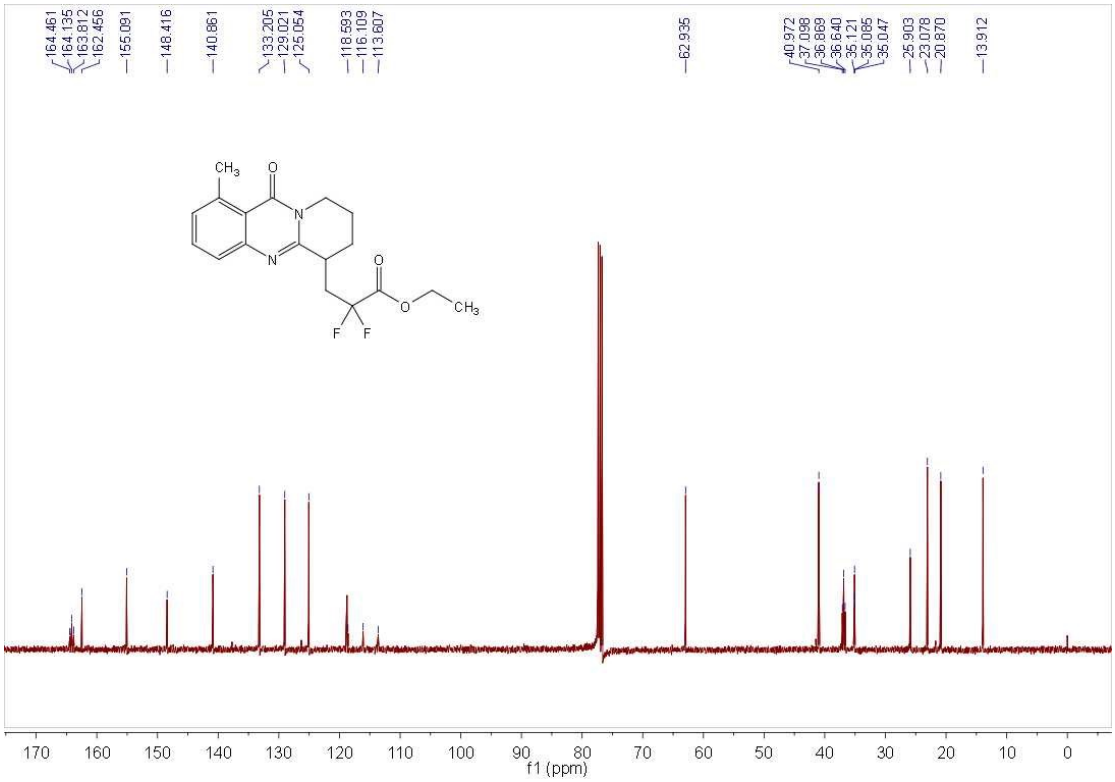

8.396
8.375
7.948
7.673
7.652
4.401
4.385
4.369
4.366
4.350
4.334
4.323
4.305
4.287
3.999
3.982
3.964
3.412
3.374
3.322
3.303
3.294
3.286
2.435
2.418
2.400
2.385
2.102
2.086
2.068
2.052
1.367
1.349
0.027
0.021
0.019
0.013
F
F
F
O
N
N
O
O
CH3
F
F
1.00
1.00
1.00
3.07
1.04
0.94
1.12
2.03
2.10
1.00
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

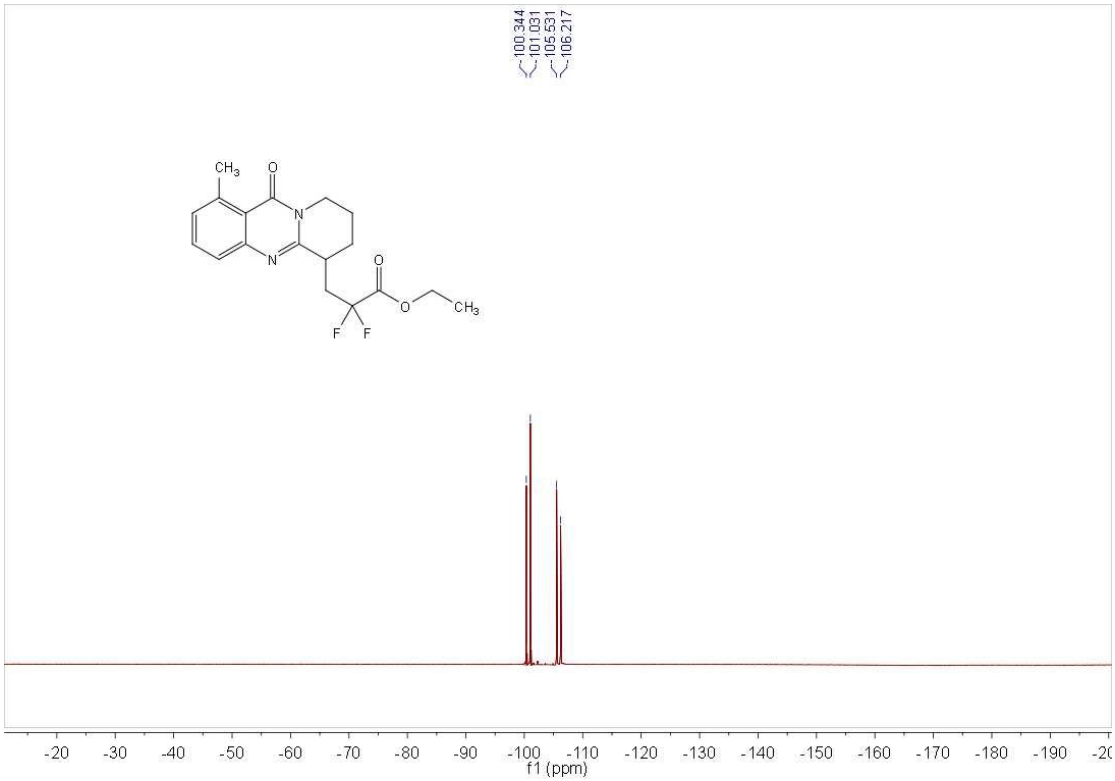

164.429
164.106
163.782
161.109
157.185
146.779
136.126
135.835
135.508
135.184
127.893
124.498
122.431
122.394
118.416
115.926
113.426
63.094
41.376
36.856
36.627
36.398
35.288
35.254
25.703
20.612
13.922
f1 (ppm)


63.204
63.216
100.667
101.346
105.448
105.460
105.471
105.478
106.150
106.160
106.167
f1 (ppm)

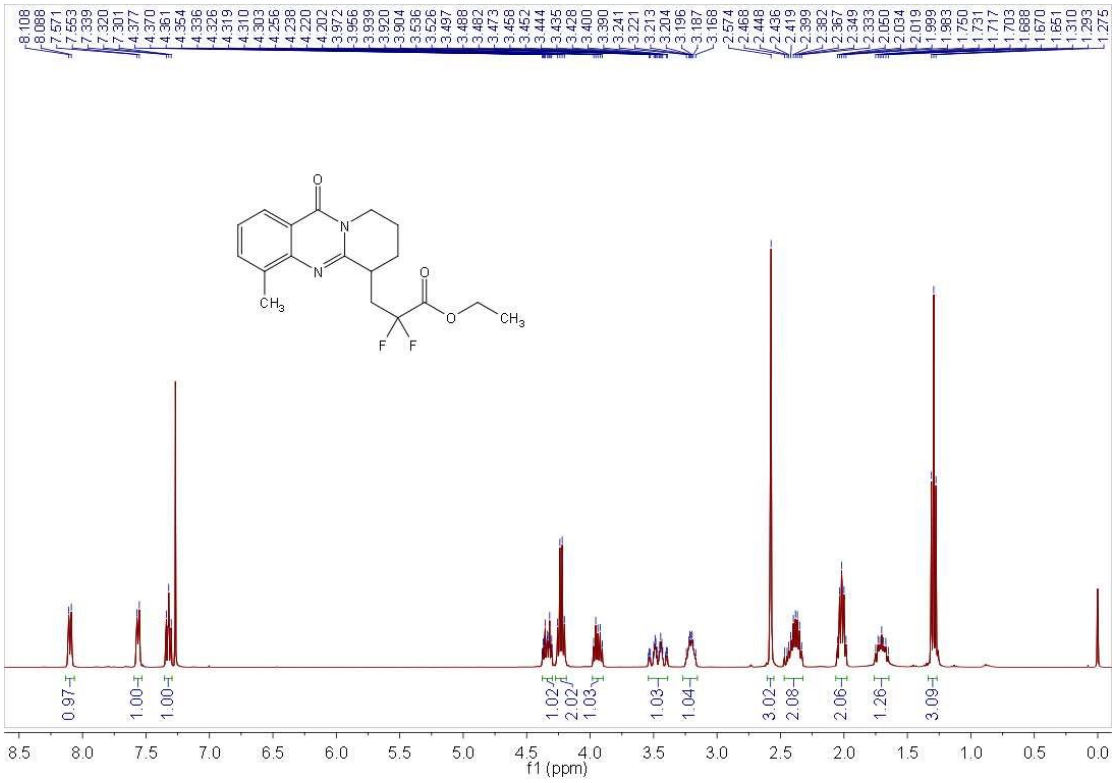
3m

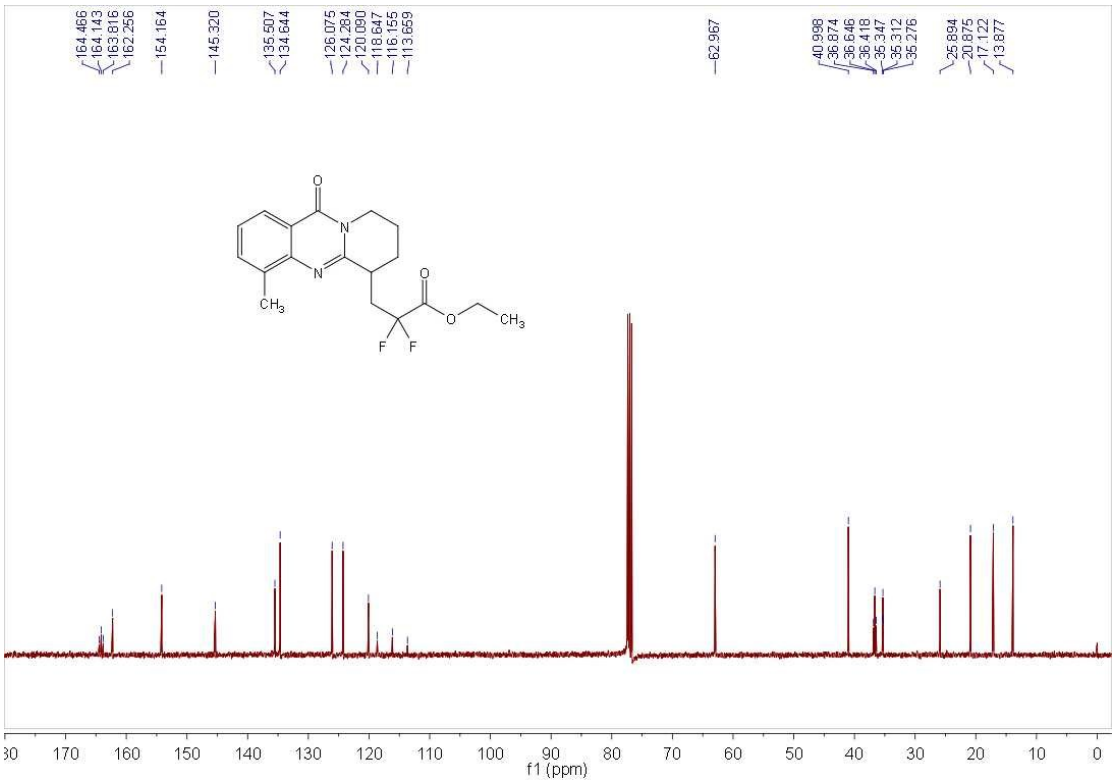

7.532
7.514
7.166
4.283
4.266
4.248
4.239
4.230
4.222
4.207
3.906
3.889
3.871
3.387
3.341
3.202
3.192
3.174
3.163
2.354
2.339
2.322
2.306
2.294
2.024
2.008
1.719
1.690
1.312
1.294
CH3
O
N
N
O
O
CH3
F
F
1.00
1.00
1.00
3.24
1.10
1.18
1.12
3.00
2.34
2.15
1.25
3.13
f1 (ppm)

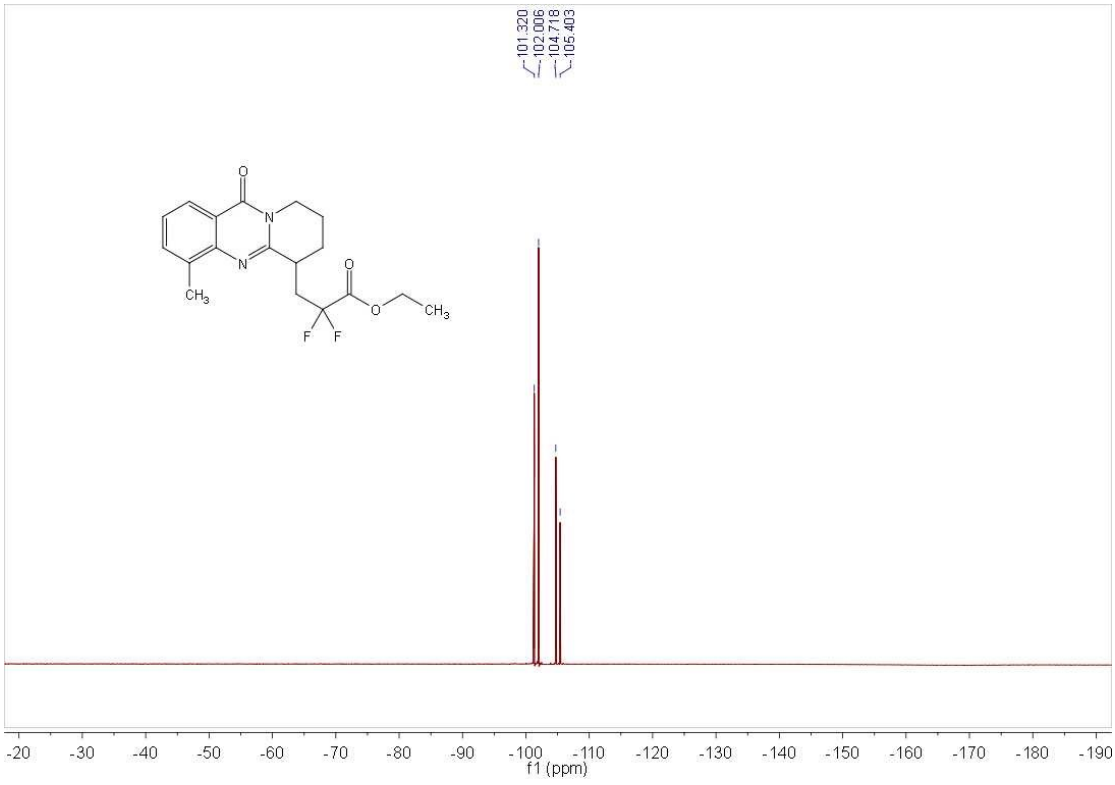

164.461
164.135
163.812
162.456
155.091
148.416
140.861
133.205
129.021
125.054
118.593
116.109
113.607
62.935
40.972
37.098
36.869
36.640
35.121
35.085
35.047
25.903
23.078
20.870
13.912
CH3
O
N
N
O
O
CH3
F
F
f1 (ppm)


100.344
101.031
105.531
106.217
CH3
O
N
N
O
O
CH3
F
F
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

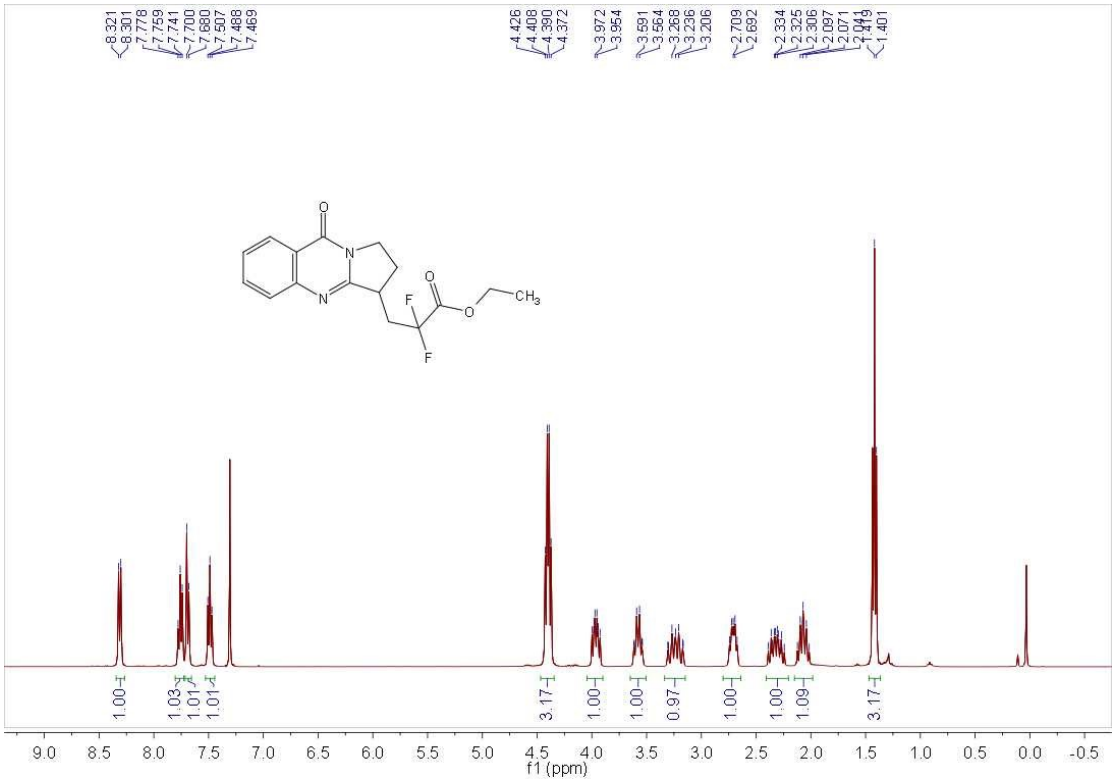
3n

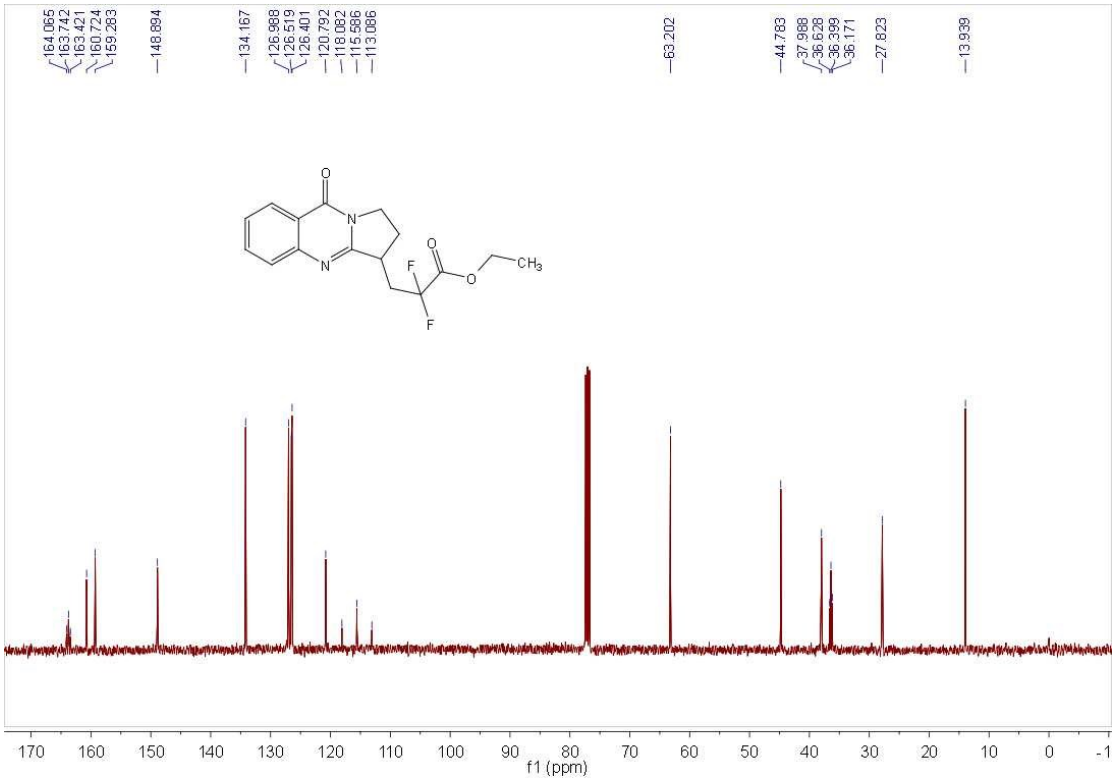

8.108
8.088
7.571
7.553
7.339
7.320
7.301
4.377
4.370
4.361
4.354
4.336
4.326
4.319
4.310
4.303
4.256
4.238
4.220
4.202
3.972
3.966
3.939
3.920
3.904
3.536
3.526
3.497
3.488
3.482
3.473
3.458
3.452
3.444
3.435
3.428
3.400
3.390
3.241
3.221
3.213
3.204
3.196
3.187
3.168
2.574
2.468
2.448
2.436
2.419
2.399
2.382
2.367
2.349
2.333
2.050
2.034
2.019
1.999
1.983
1.750
1.731
1.717
1.703
1.688
1.670
1.651
1.310
1.293
1.275
O
N
N
CH3
O
O
CH3
F
F
0.97
1.00
1.00
1.02
2.02
1.03
1.03
1.04
3.02
2.08
2.06
1.26
3.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

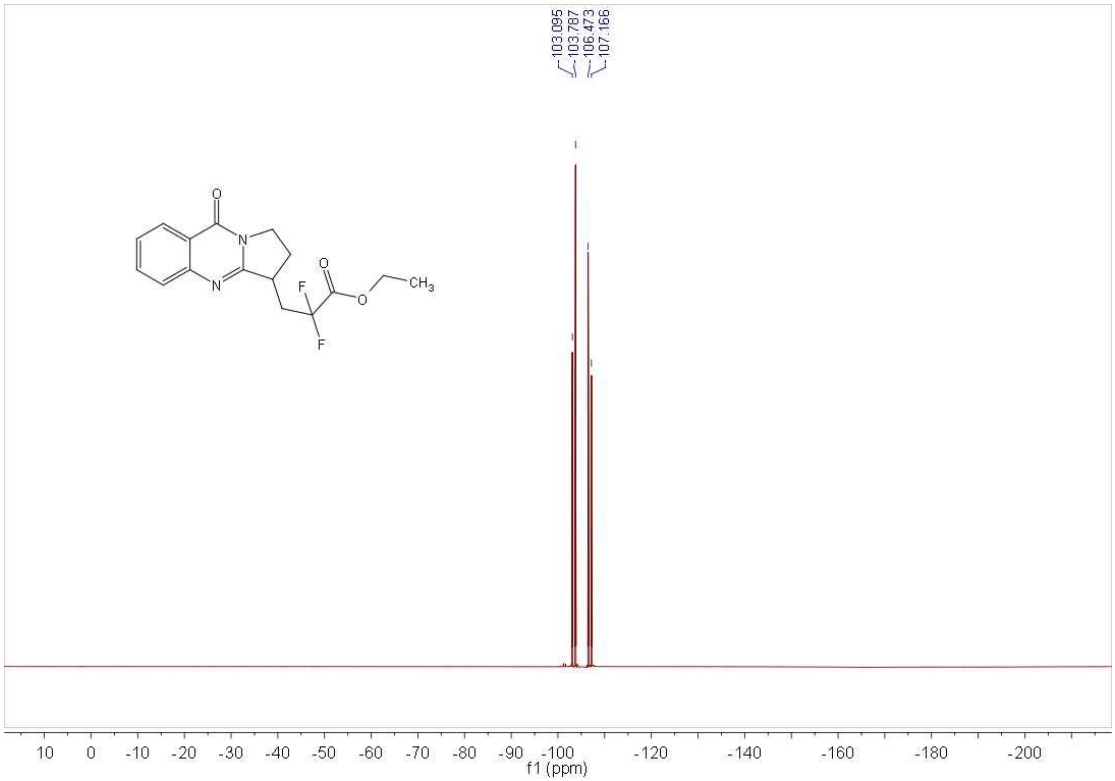

164.466
164.143
163.816
162.256
154.164
145.320
135.507
134.644
126.075
124.284
120.090
118.647
116.155
113.659
62.967
40.998
36.874
36.646
36.418
35.347
35.312
35.276
25.894
20.875
17.122
13.877
O
N
N
CH3
O
O
CH3
F
F
f1 (ppm)


101.320
102.006
104.718
105.403
O
N
N
CH3
O
O
CH3
F
F
f1 (ppm)

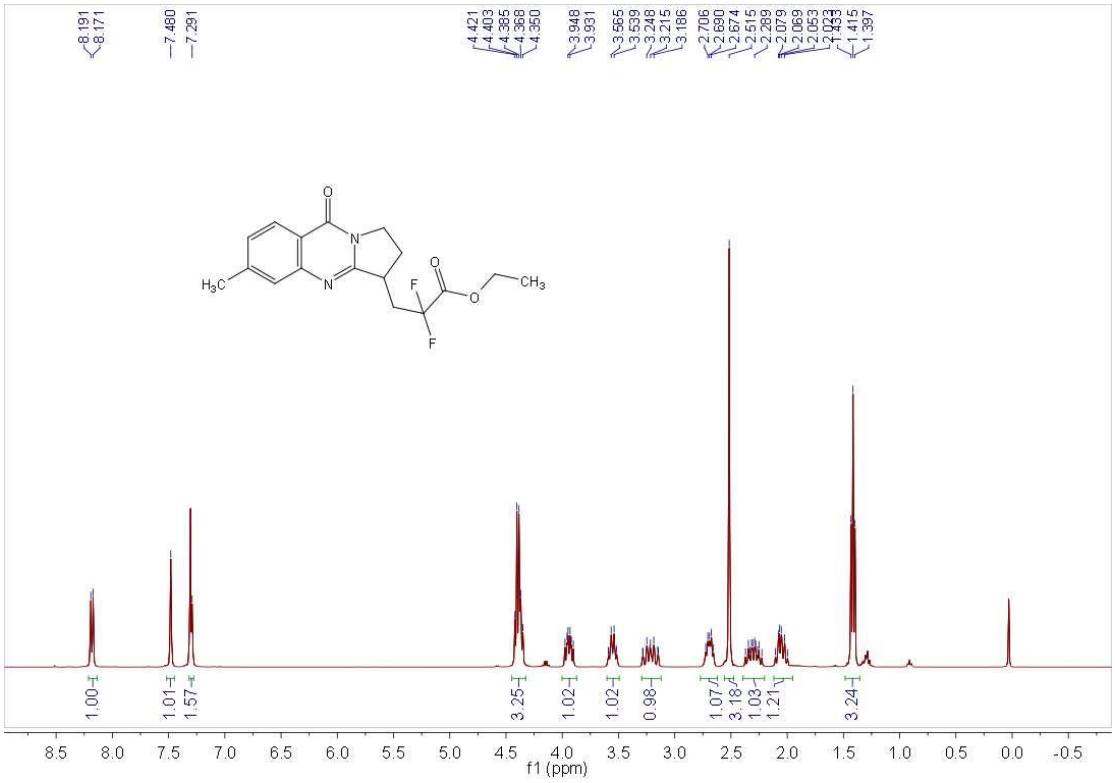
3o

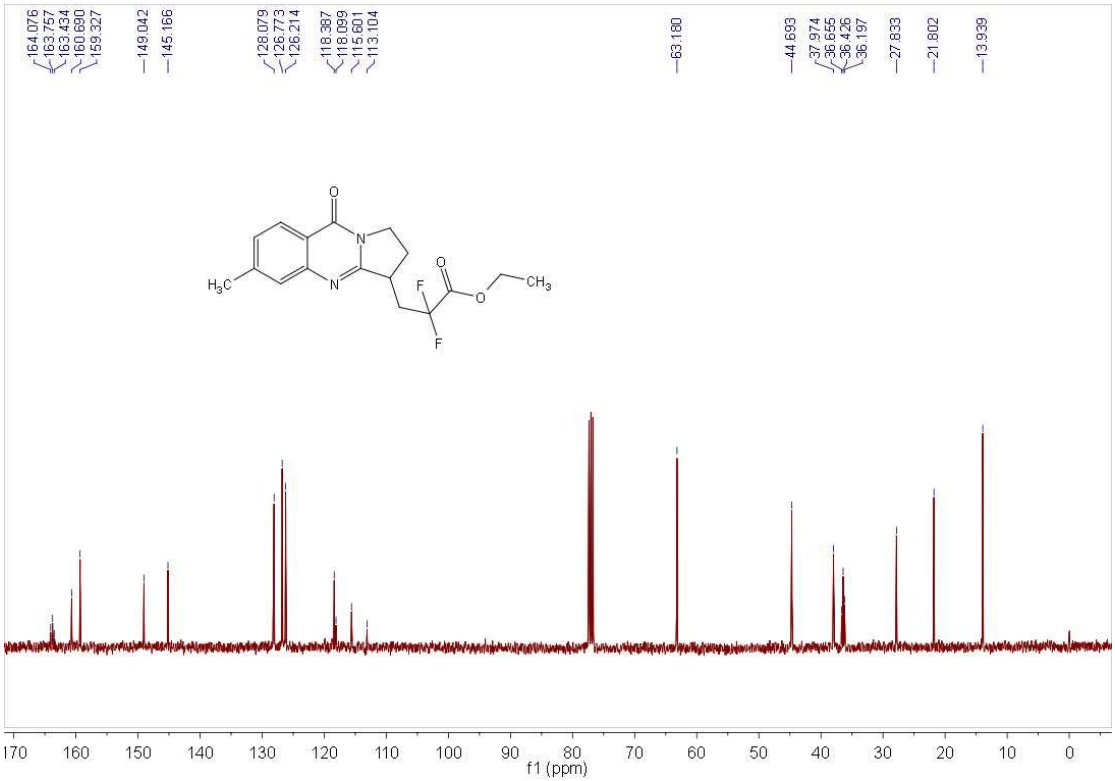

8.321
8.301
7.778
7.759
7.741
7.700
7.680
7.507
7.488
7.469
4.426
4.408
4.390
4.372
3.972
3.954
3.591
3.564
3.268
3.236
3.206
2.709
2.692
2.334
2.325
2.306
2.097
2.071
1.419
1.401
1.00
1.03
1.01
1.01
3.17
1.00
1.00
0.97
1.00
1.00
1.09
3.17
f1 (ppm)

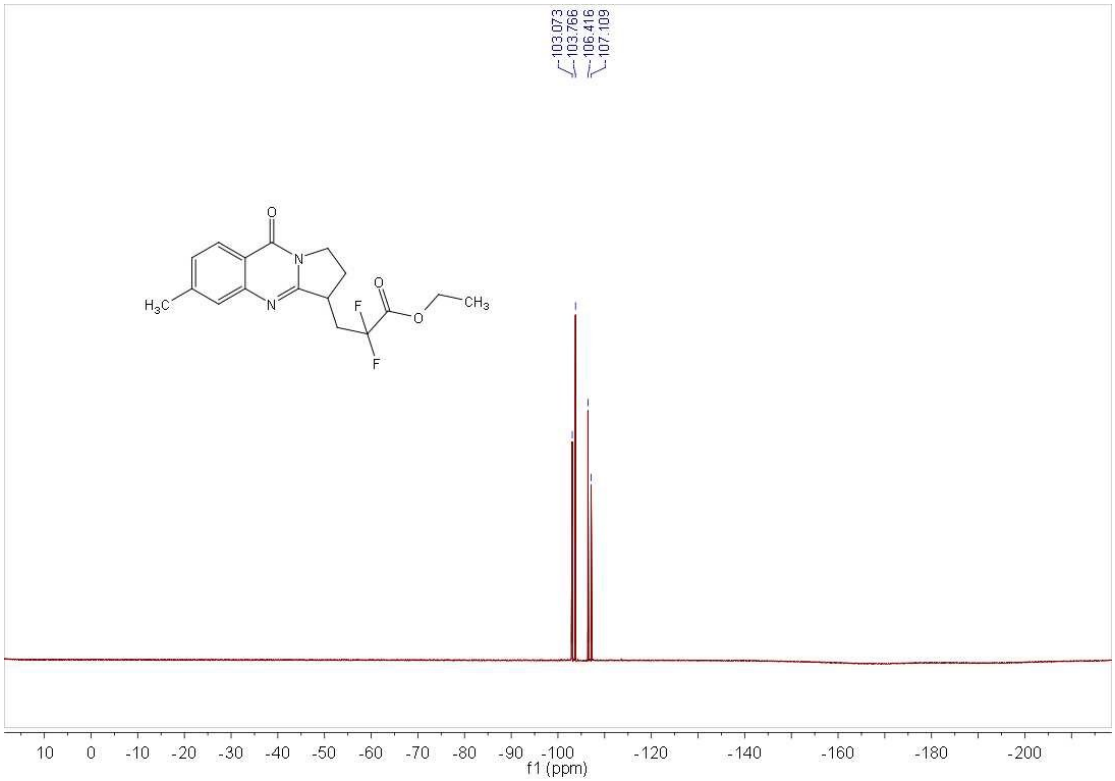

164.065
163.742
163.421
160.724
159.283
148.894
134.167
126.988
126.519
126.401
120.792
118.082
115.586
113.086
63.202
44.783
37.988
36.628
36.399
36.171
27.823
13.939
f1 (ppm)


103.095
103.787
106.473
107.166
f1 (ppm)

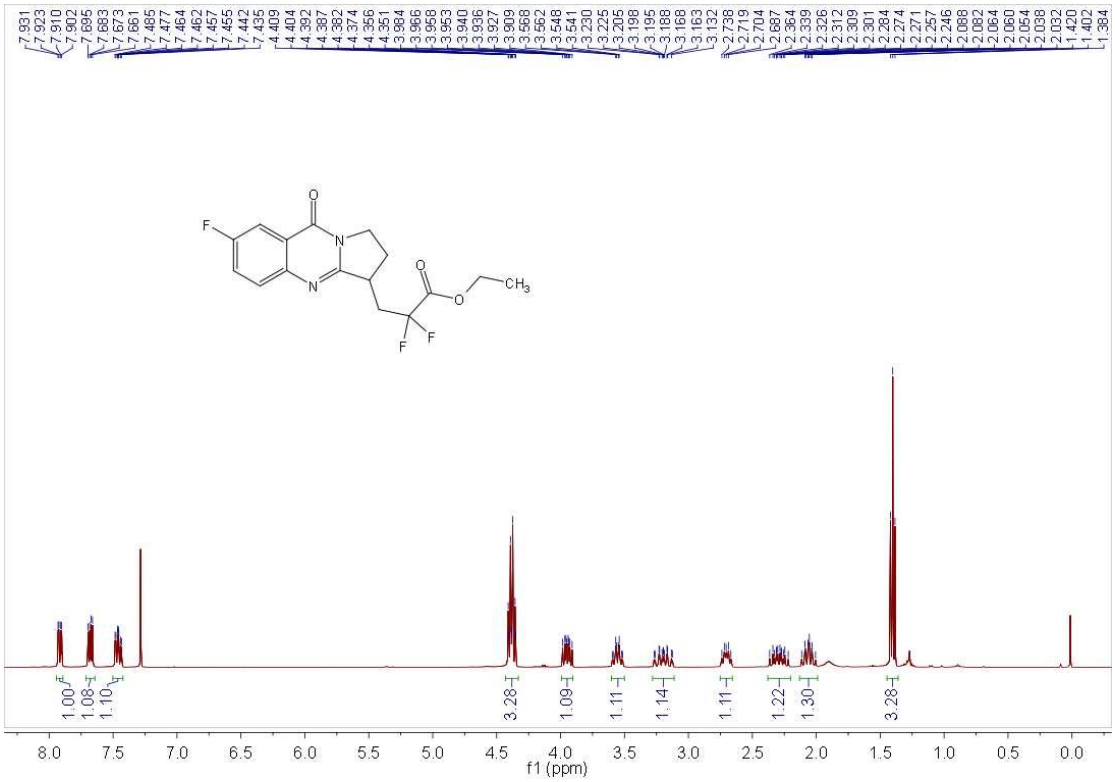
3p

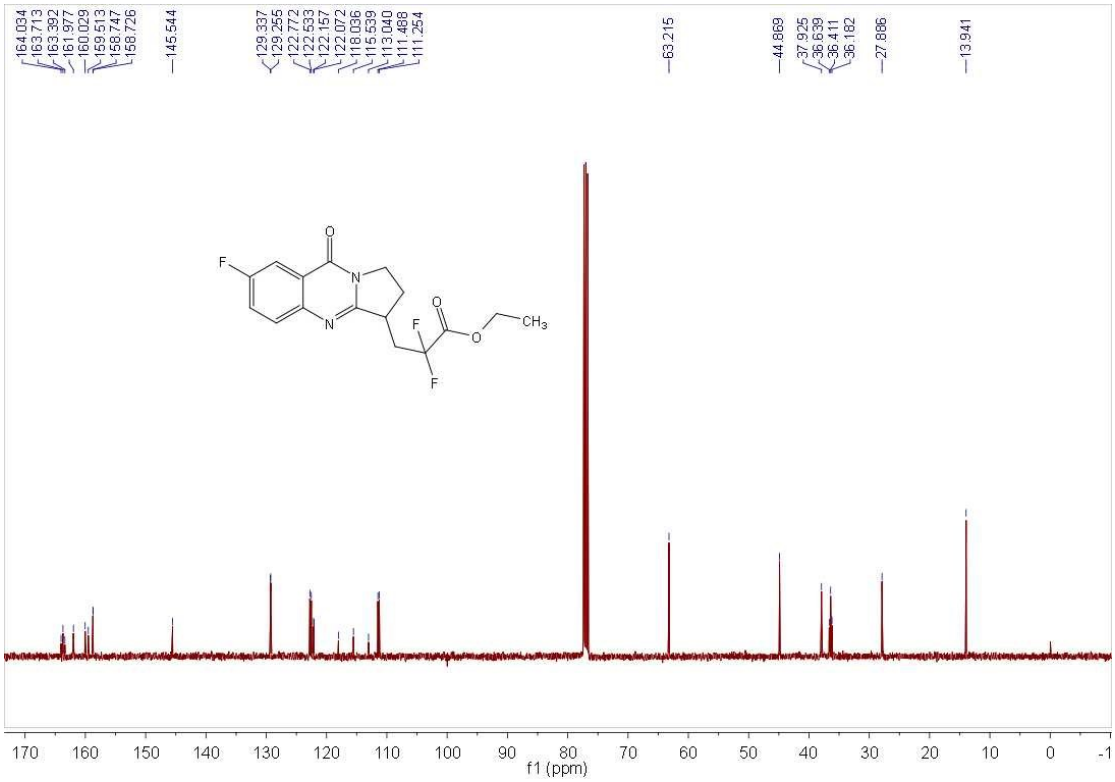

8.191
8.171
7.480
7.291
4.421
4.403
4.385
4.368
4.350
3.948
3.931
3.565
3.539
3.248
3.215
3.186
2.706
2.690
2.674
2.515
2.289
2.079
2.069
2.053
2.033
1.433
1.415
1.397
1.00
1.01
1.57
3.25
1.02
1.02
0.98
1.07
3.18
1.03
1.21
3.24
f1 (ppm)

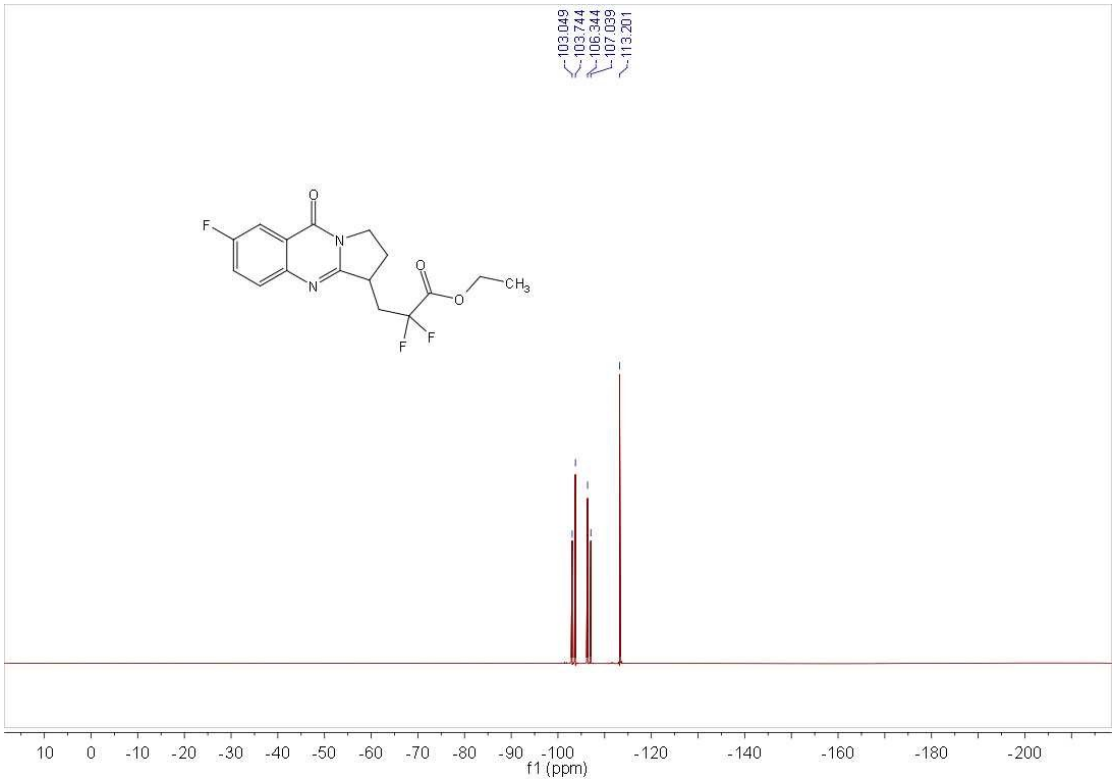

164.076
163.757
163.434
160.890
159.327
149.042
145.166
128.079
126.773
126.214
118.387
118.099
115.801
113.104
63.180
44.693
37.974
36.655
36.426
36.197
27.833
21.802
13.939
O
N
N
H3C
O
O
CH3
F
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


103.073
103.766
106.416
107.109
O
N
N
H3C
O
O
CH3
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

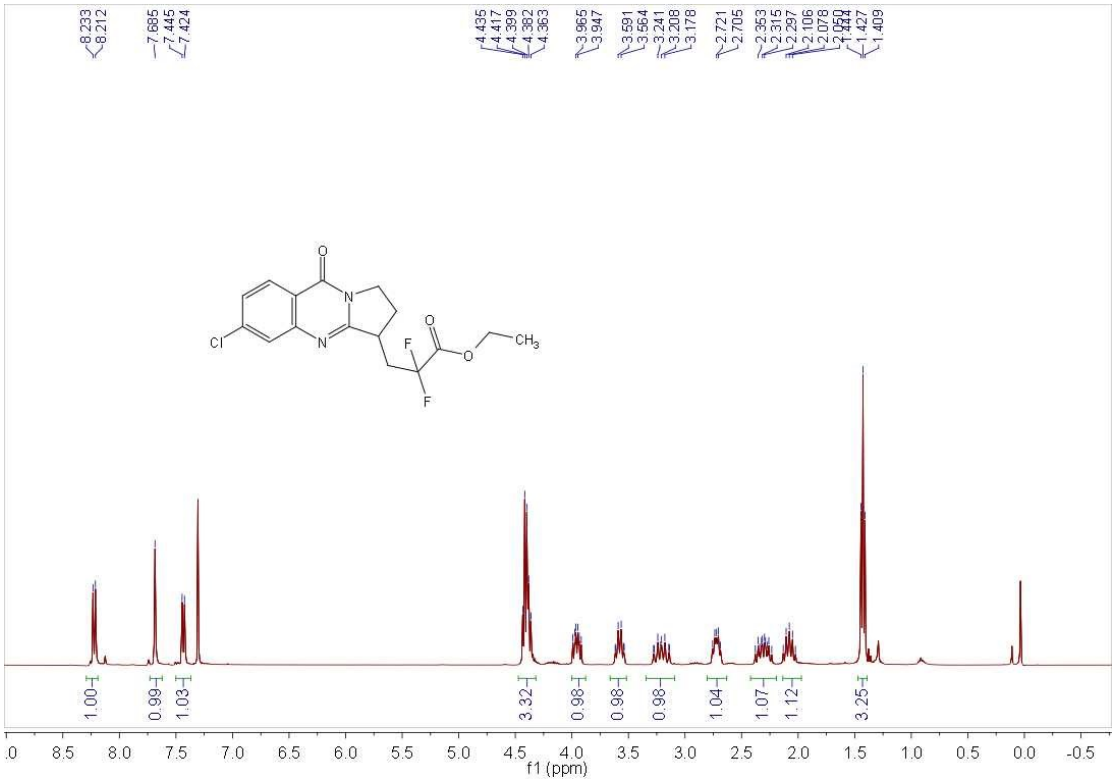
3q

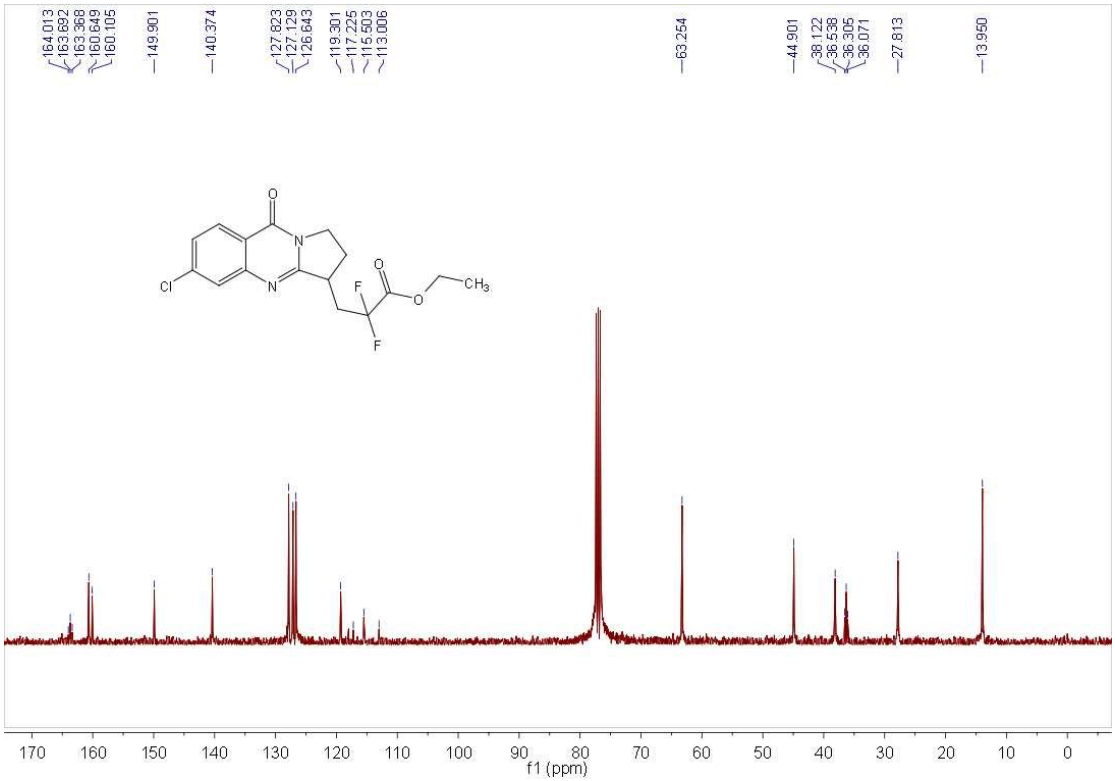

7.931
7.923
7.910
7.902
7.895
7.883
7.673
7.661
7.485
7.477
7.464
7.462
7.457
7.455
7.442
7.435
4.409
4.404
4.392
4.387
4.382
4.374
4.356
4.351
3.984
3.966
3.958
3.953
3.940
3.936
3.927
3.909
3.568
3.562
3.548
3.541
3.230
3.225
3.205
3.198
3.195
3.188
3.168
3.163
3.132
2.738
2.719
2.704
2.687
2.364
2.339
2.326
2.312
2.309
2.301
2.284
2.274
2.271
2.257
2.246
2.088
2.082
2.064
2.060
2.054
2.038
2.032
1.420
1.402
1.384
F
O
N
N
O
O
CH3
F
F
1.00
1.08
1.10
3.28
1.09
1.11
1.14
1.11
1.22
1.30
3.28
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

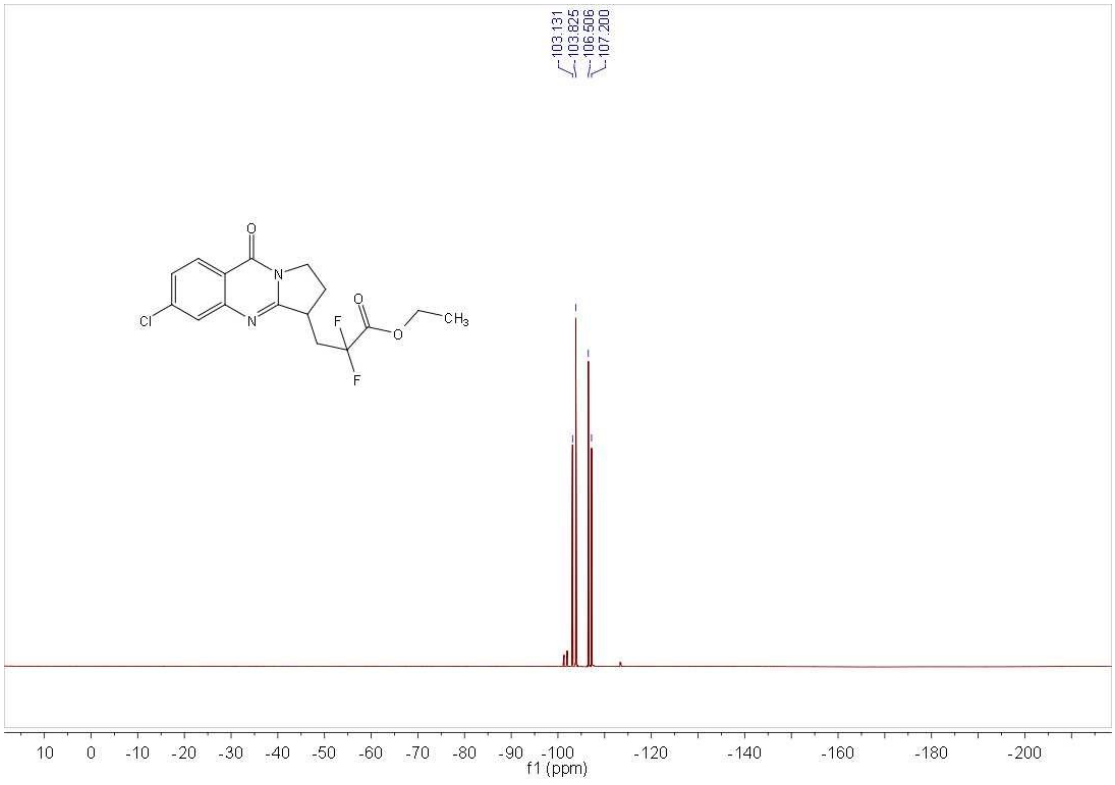

164.034
163.713
163.392
161.977
160.029
159.513
158.747
158.726
145.544
129.337
129.255
122.772
122.533
122.157
122.072
118.036
115.539
113.040
111.488
111.254
63.215
44.869
37.925
36.639
36.411
36.182
27.886
13.941
F
O
N
N
O
O
CH3
F
F
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


-103.049
-103.744
-106.344
-107.039
-113.201
F
O
N
N
O
O
CH3
F
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

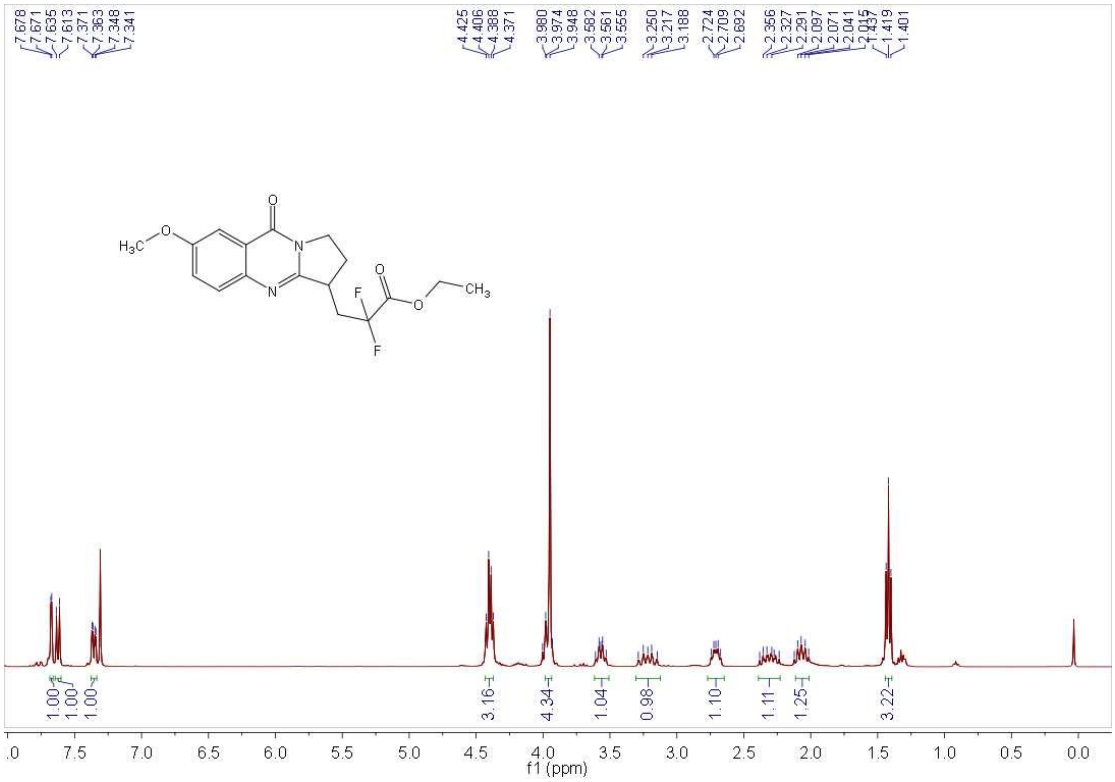
3r

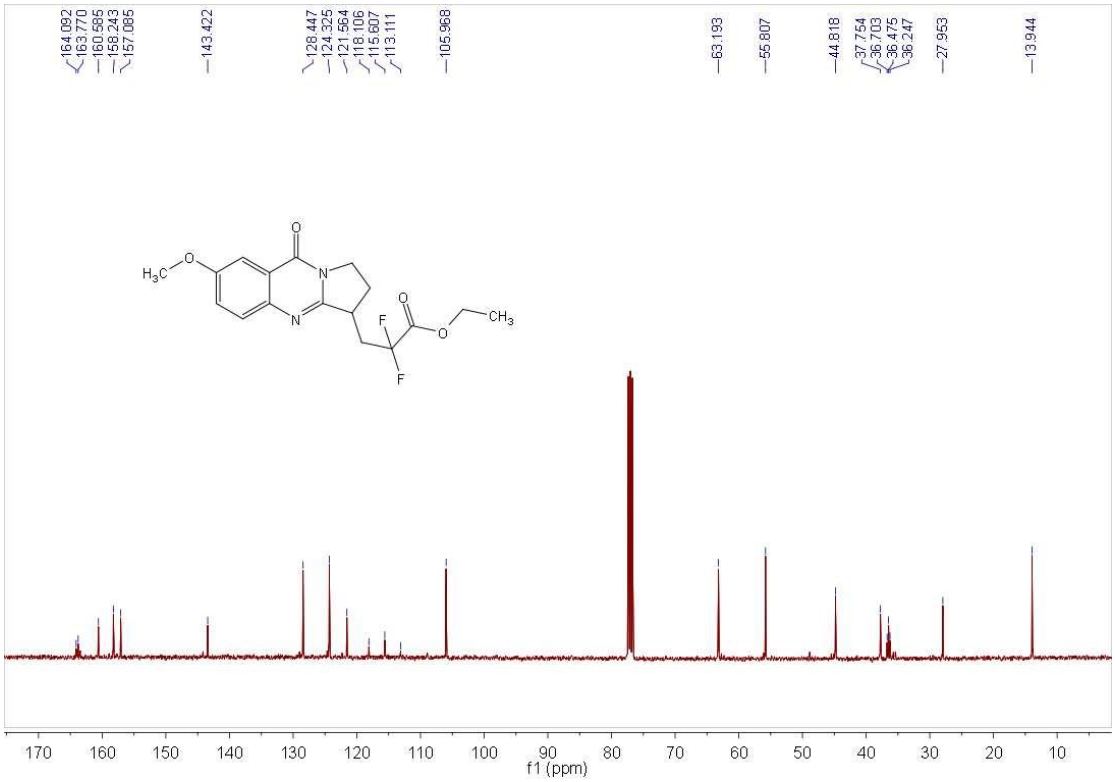

8.233
8.212
7.685
7.445
7.424
4.435
4.417
4.399
4.382
4.363
3.965
3.947
3.591
3.564
3.241
3.208
3.178
2.721
2.705
2.353
2.315
2.297
2.106
2.078
2.050
1.444
1.427
1.409
Cl
N
N
O
O
O
CH3
F
F
1.00
0.99
1.03
3.32
0.98
0.98
0.98
1.04
1.07
1.12
3.25
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

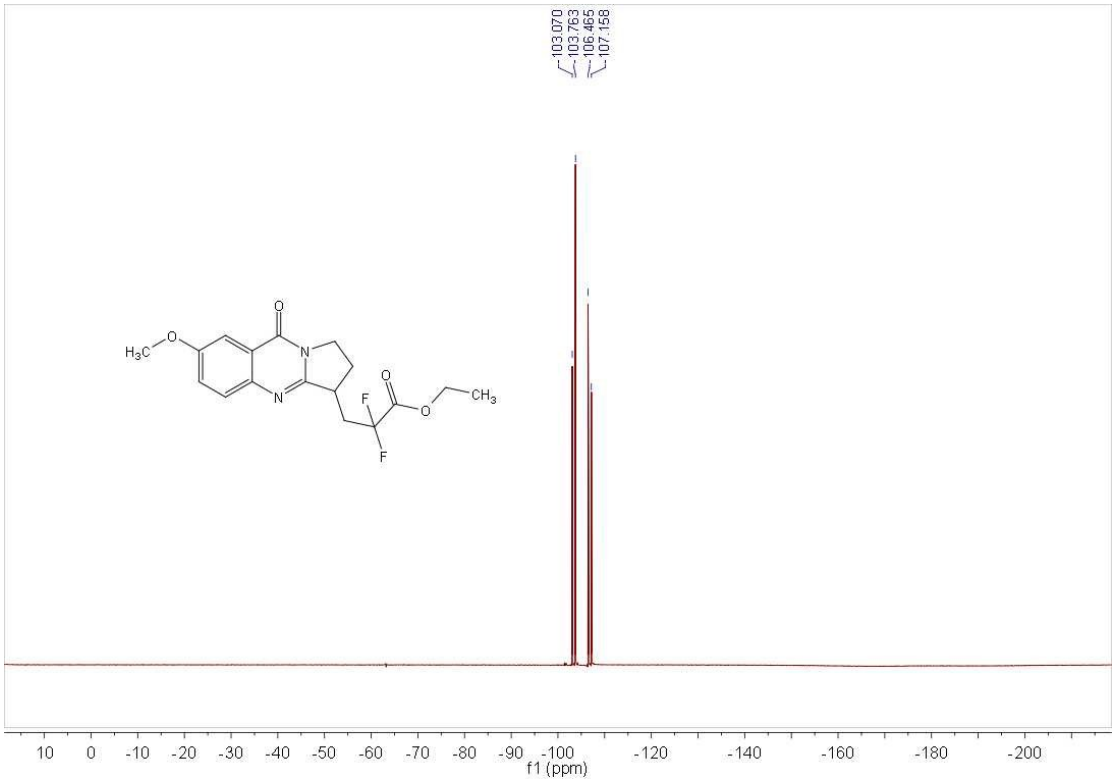

164.013
163.692
163.368
160.649
160.105
149.901
140.374
127.823
127.129
126.643
119.301
117.225
115.503
113.006
63.254
44.901
38.122
36.538
36.305
36.071
27.813
13.950
f1 (ppm)


103.131
103.825
106.506
107.200
f1 (ppm)

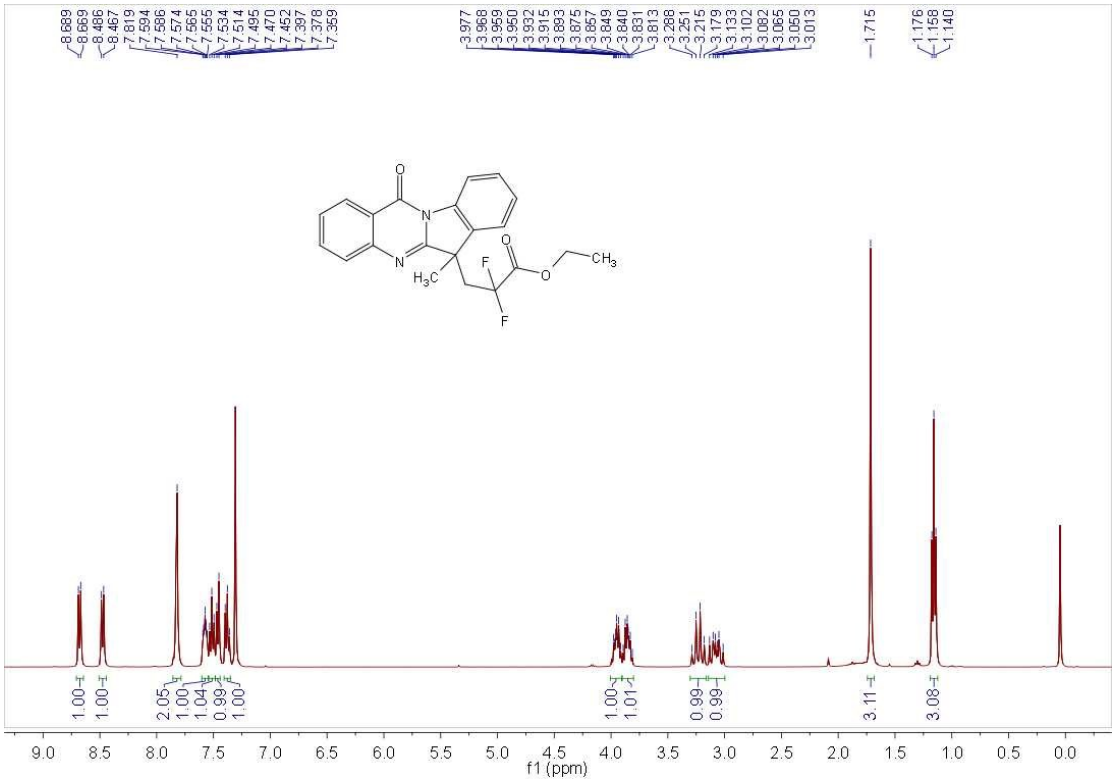
3s

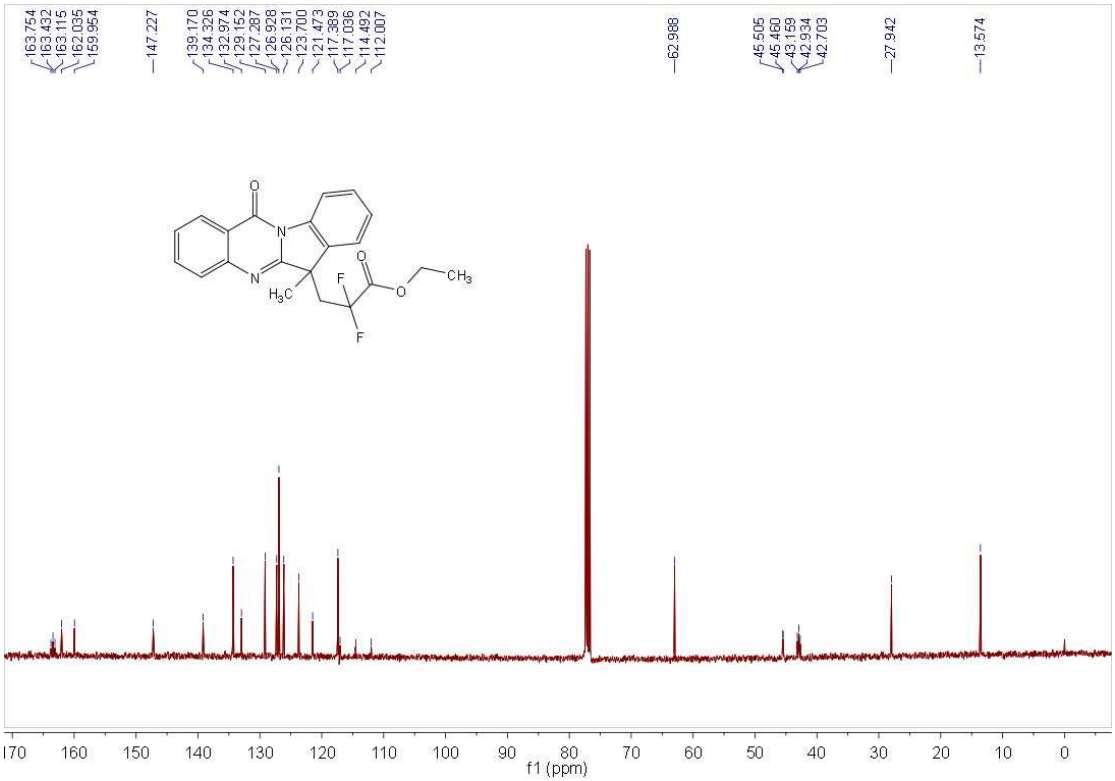

7.678
7.671
7.635
7.613
7.371
7.363
7.348
7.341
4.425
4.406
4.388
4.371
3.980
3.974
3.948
3.582
3.561
3.555
3.250
3.217
3.188
2.724
2.709
2.692
2.356
2.327
2.291
2.097
2.071
2.041
2.015
1.437
1.419
1.401
1.00
1.00
1.00
3.16
4.34
1.04
0.98
1.10
1.11
1.25
3.22
f1 (ppm)

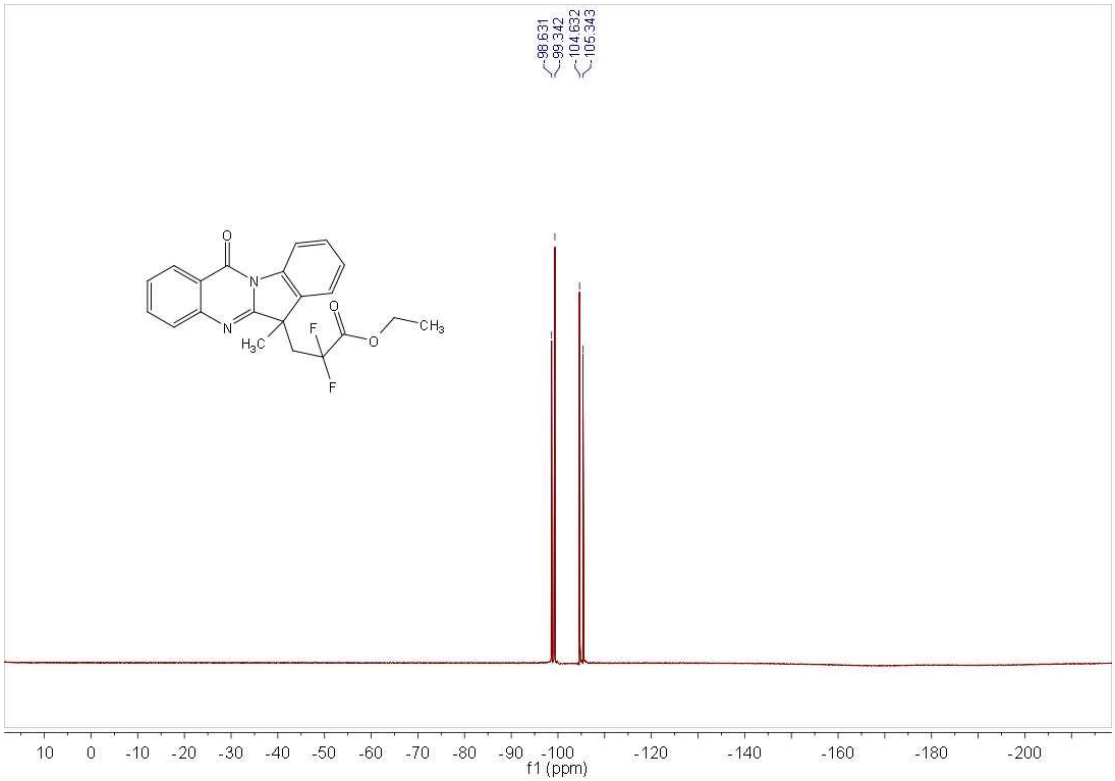

164.092
163.770
160.585
158.243
157.085
143.422
128.447
124.325
121.564
118.106
115.607
113.111
105.968
63.193
55.807
44.818
37.754
36.703
36.475
36.247
27.953
13.944
f1 (ppm)


103.070
103.763
106.465
107.158
O
H3C
O
N
N
O
F
F
O
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

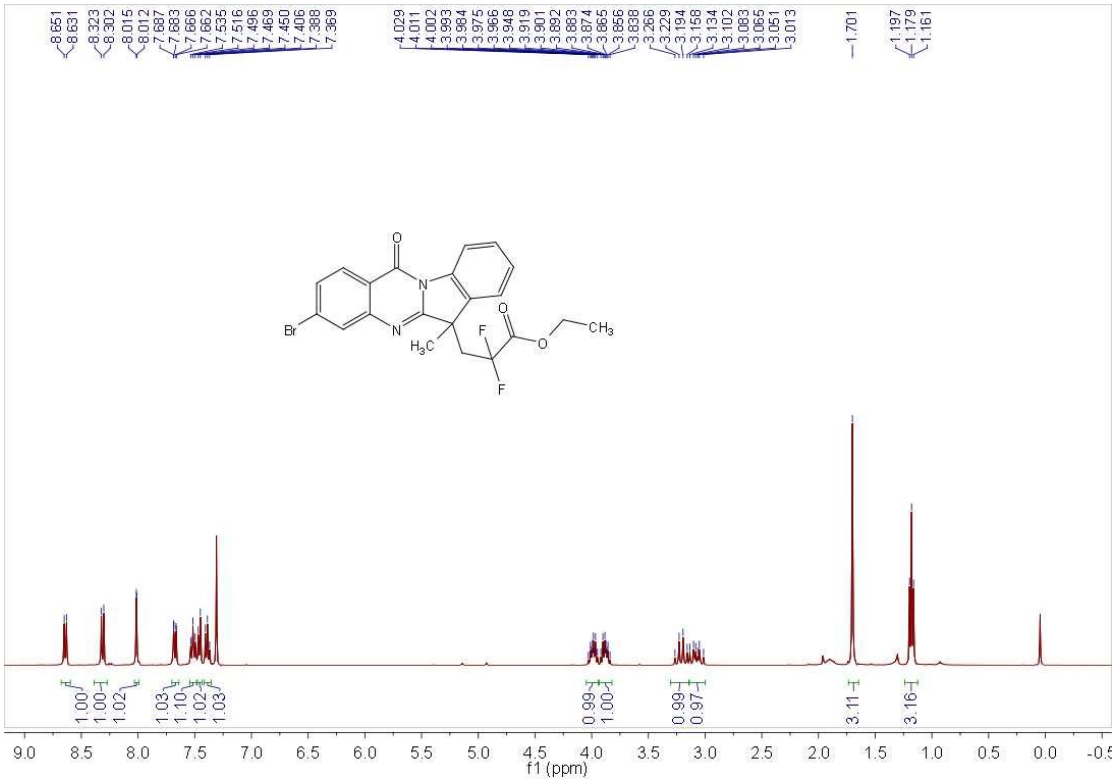
3t

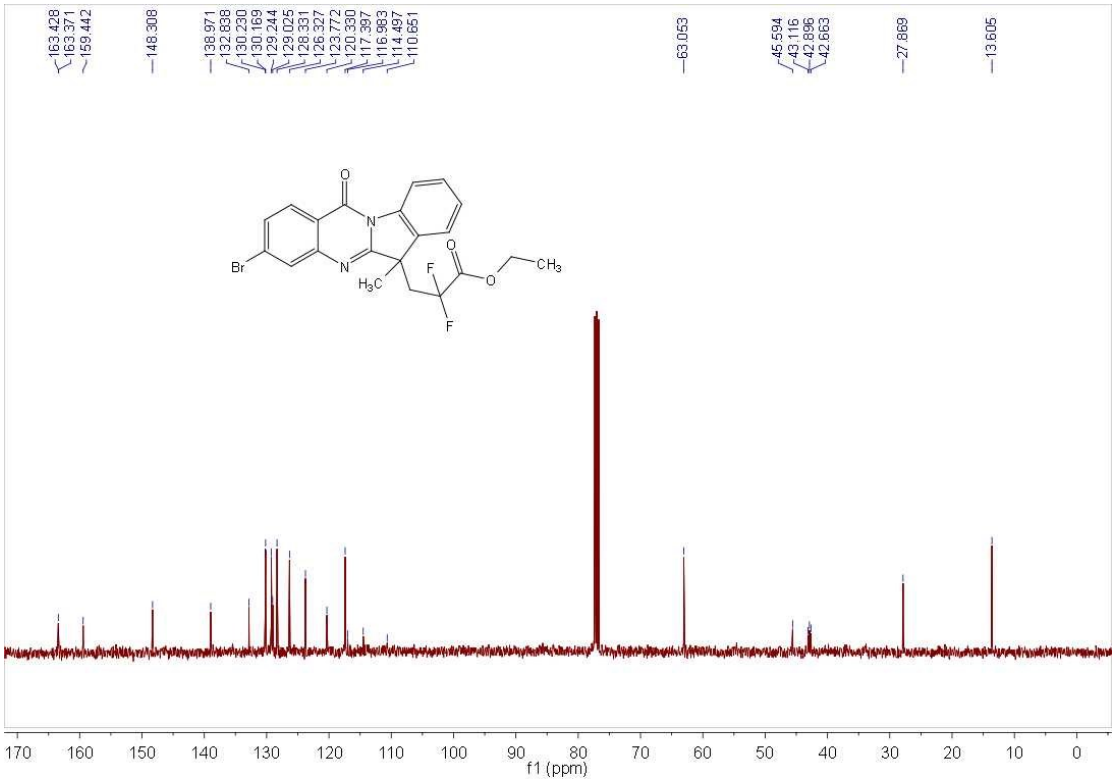

8.689
8.669
8.486
8.467
7.819
7.594
7.586
7.574
7.565
7.555
7.534
7.514
7.495
7.470
7.452
7.397
7.378
7.359
3.977
3.968
3.959
3.950
3.932
3.915
3.893
3.875
3.857
3.849
3.840
3.831
3.813
3.288
3.251
3.215
3.179
3.133
3.102
3.082
3.065
3.050
3.013
1.715
1.176
1.158
1.140
O
N
N
H3C
F
F
O
O
CH3
1.00
1.00
2.05
1.00
1.04
0.99
1.00
1.00
1.01
0.99
0.99
3.11
3.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

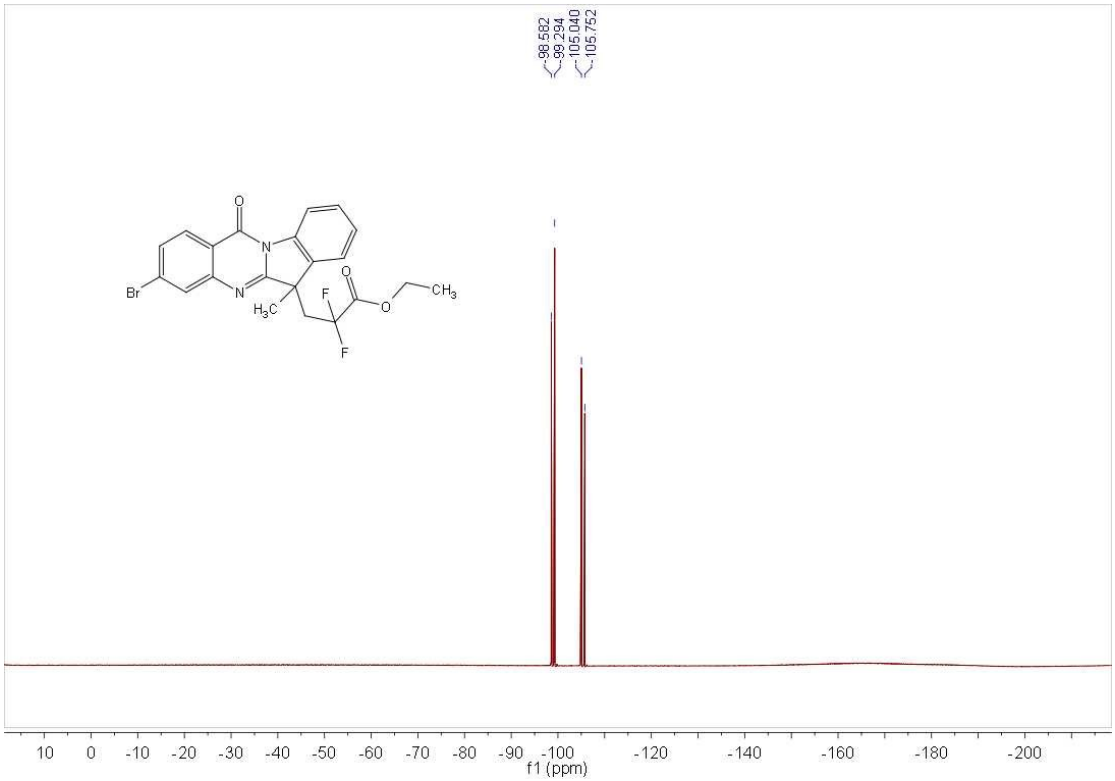

163.754
163.432
163.115
162.035
159.954
147.227
139.170
134.326
132.974
129.152
127.287
126.928
126.131
123.700
121.473
117.389
117.036
114.492
112.007
62.988
45.505
45.460
43.159
42.934
42.703
27.942
13.574
f1 (ppm)


98.631
99.342
104.632
105.343
f1 (ppm)

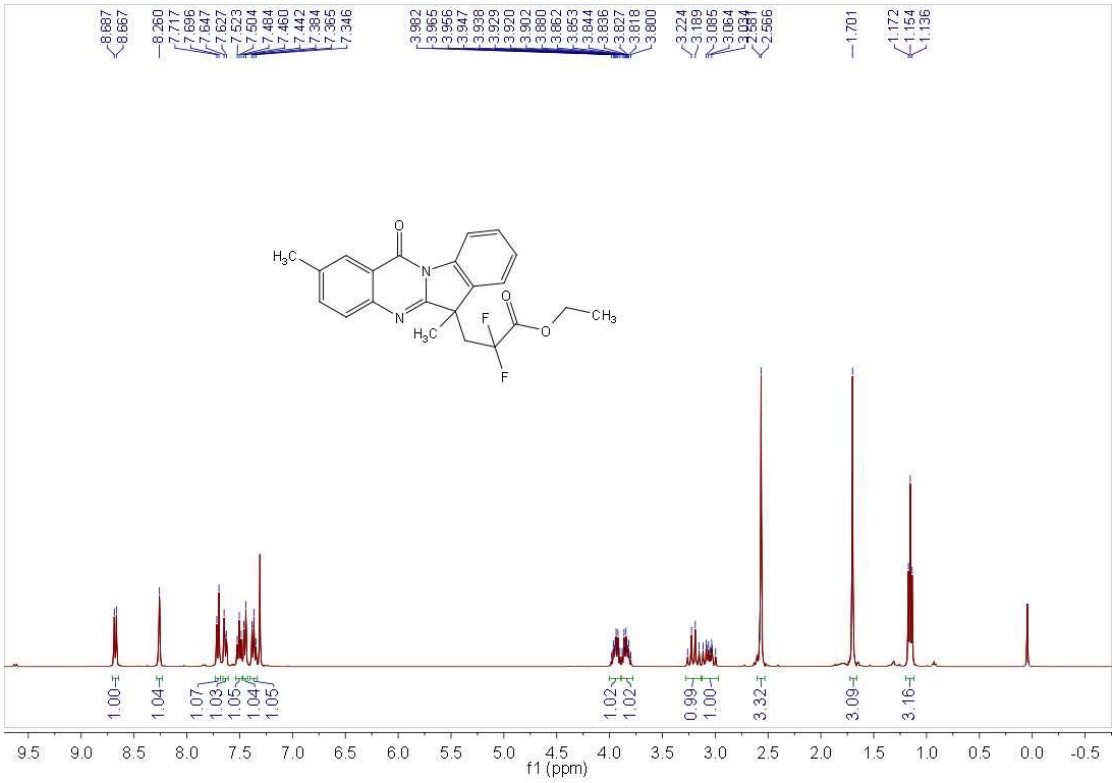
3u

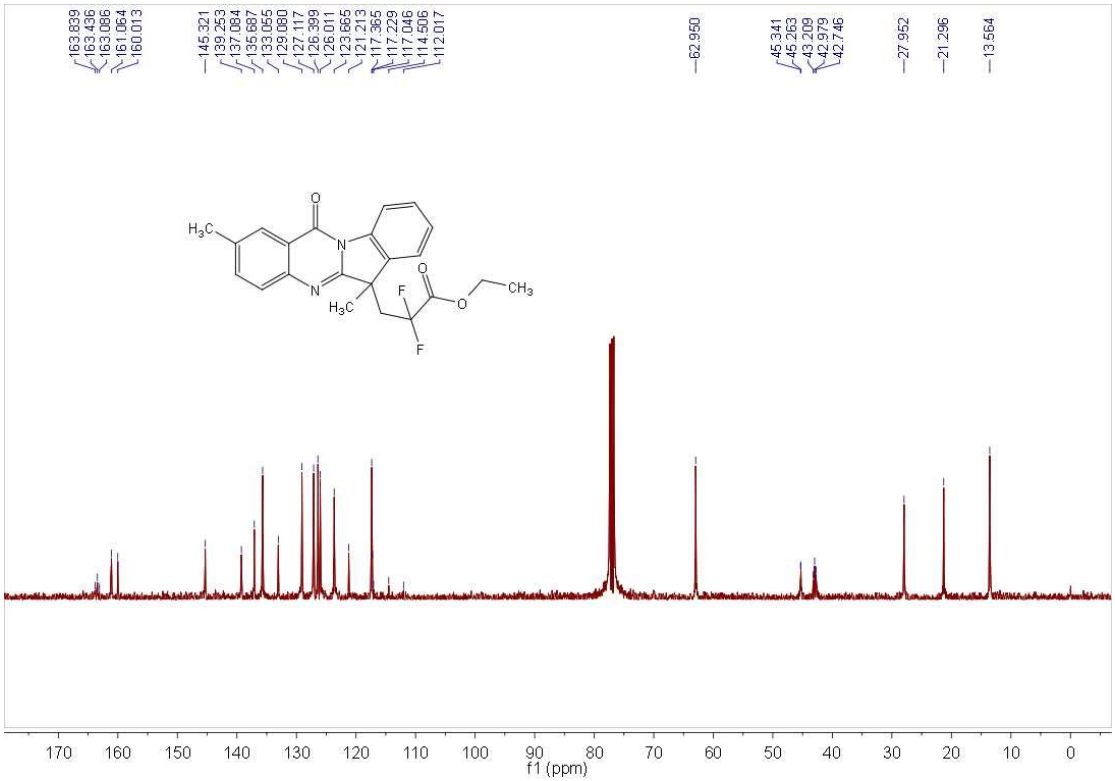

8.651
8.631
8.323
8.302
8.015
8.012
7.887
7.883
7.666
7.662
7.535
7.516
7.496
7.469
7.450
7.406
7.388
7.369
4.029
4.011
4.002
3.993
3.984
3.975
3.966
3.948
3.919
3.901
3.892
3.883
3.874
3.865
3.856
3.838
3.266
3.229
3.194
3.158
3.134
3.102
3.083
3.065
3.051
3.013
1.701
1.197
1.179
1.161
1.00
1.00
1.02
1.03
1.10
1.02
1.03
0.99
1.00
0.99
0.97
3.11
3.16
f1 (ppm)

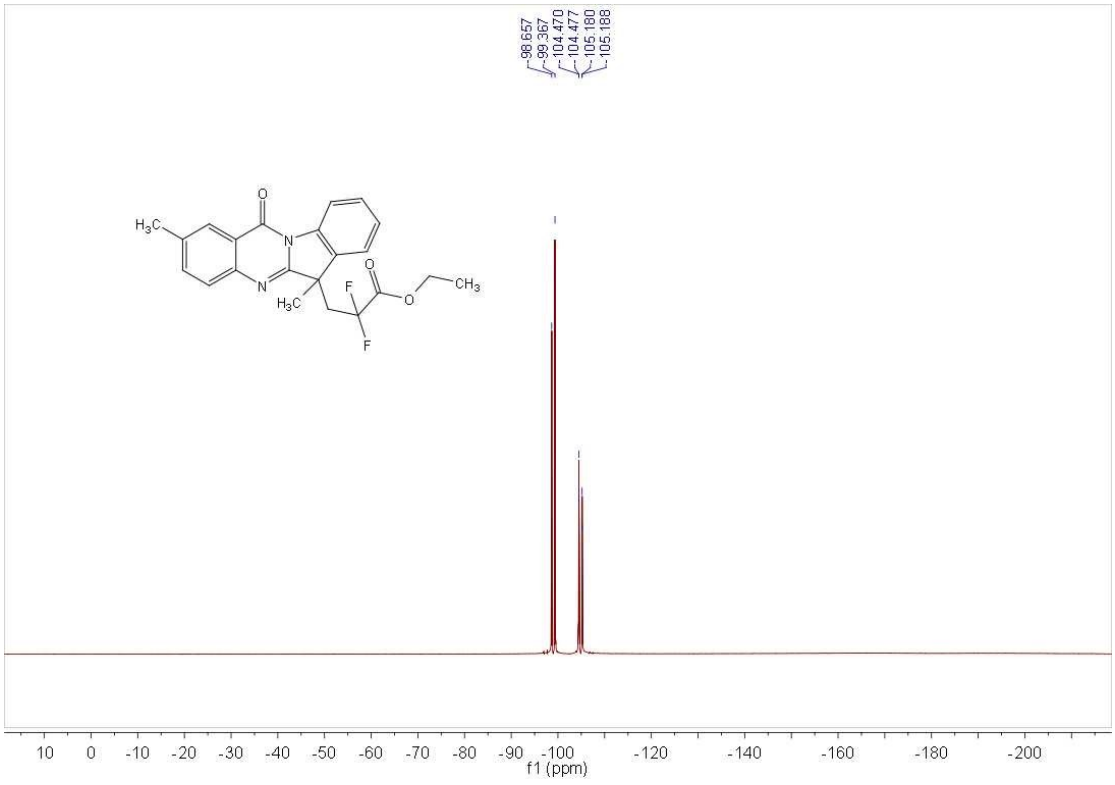

163.428
163.371
159.442
148.308
138.971
132.838
130.230
130.169
129.244
129.025
128.331
126.327
123.772
120.330
117.397
116.983
114.497
110.651
63.053
45.594
43.116
42.896
42.663
27.869
13.605
f1 (ppm)


-98.582
-99.294
-105.040
-105.752
Br
O
N
N
H3C
F
F
O
O
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

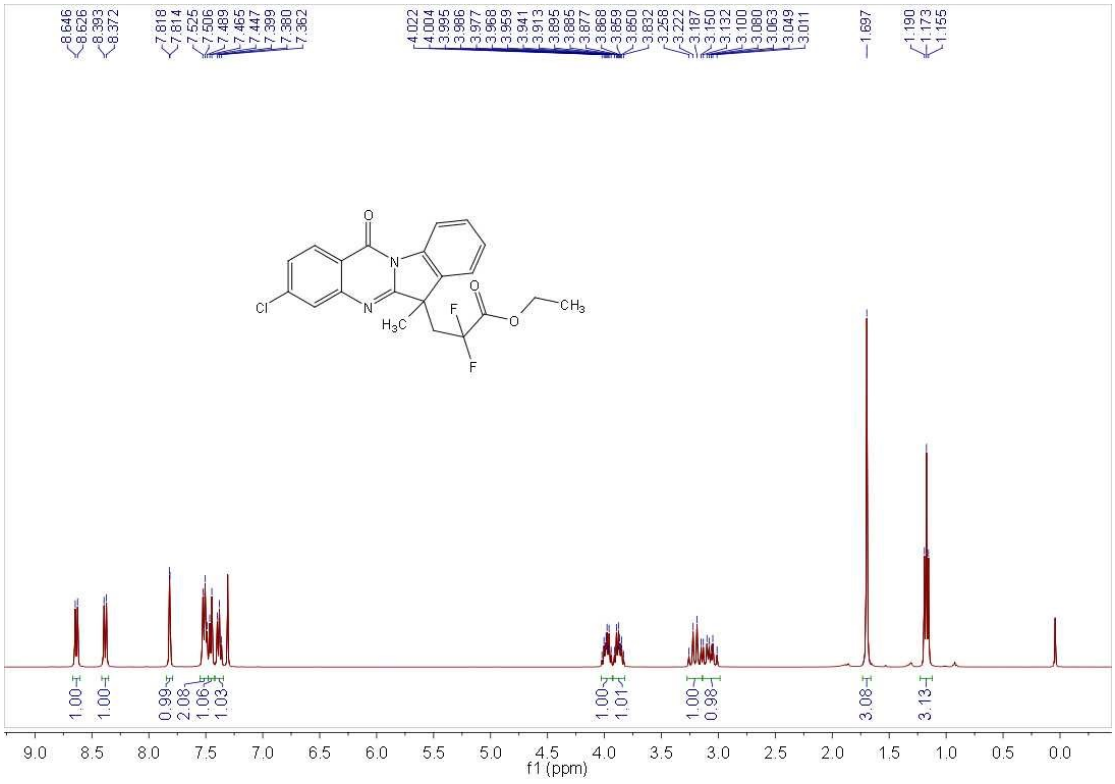
3v

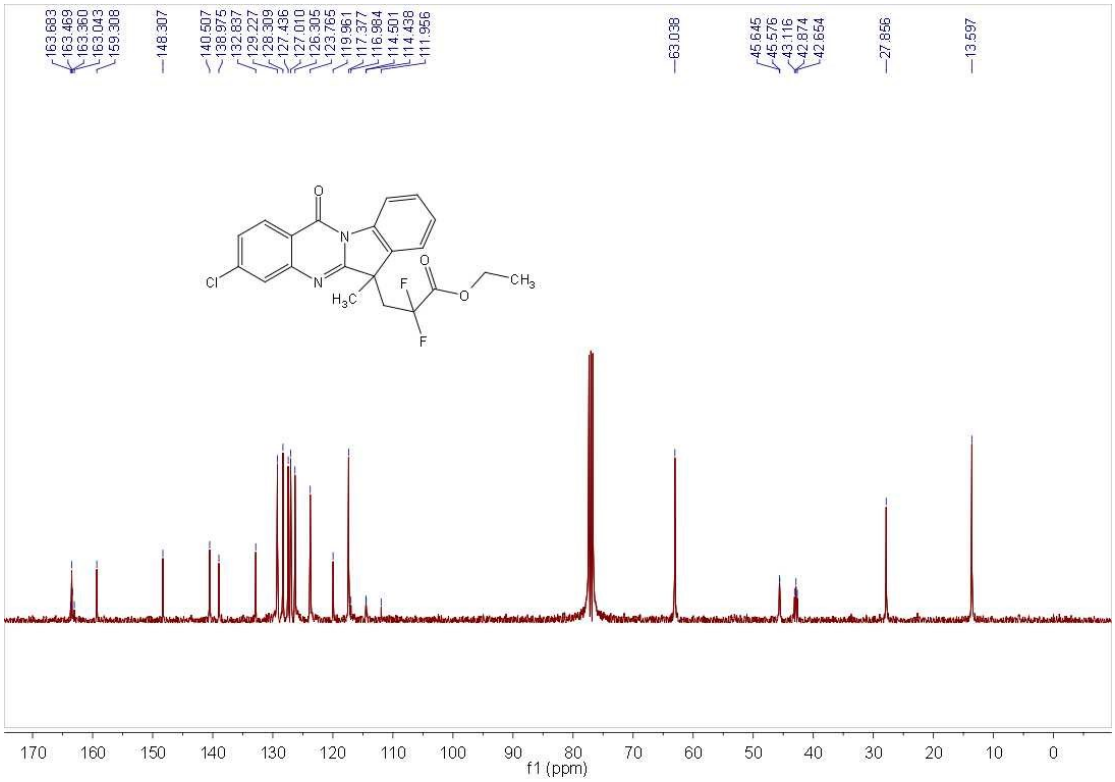

8.687
8.667
8.260
7.717
7.696
7.647
7.627
7.523
7.504
7.464
7.460
7.442
7.384
7.365
7.346
3.982
3.965
3.956
3.947
3.938
3.929
3.920
3.902
3.880
3.862
3.853
3.844
3.836
3.827
3.818
3.800
3.224
3.189
3.085
3.064
2.566
1.701
1.172
1.154
1.136
H3C
O
N
N
H3C
F
F
O
O
CH3
1.00
1.04
1.07
1.03
1.05
1.04
1.05
1.02
1.02
0.99
1.00
3.32
3.09
3.16
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
f1 (ppm)

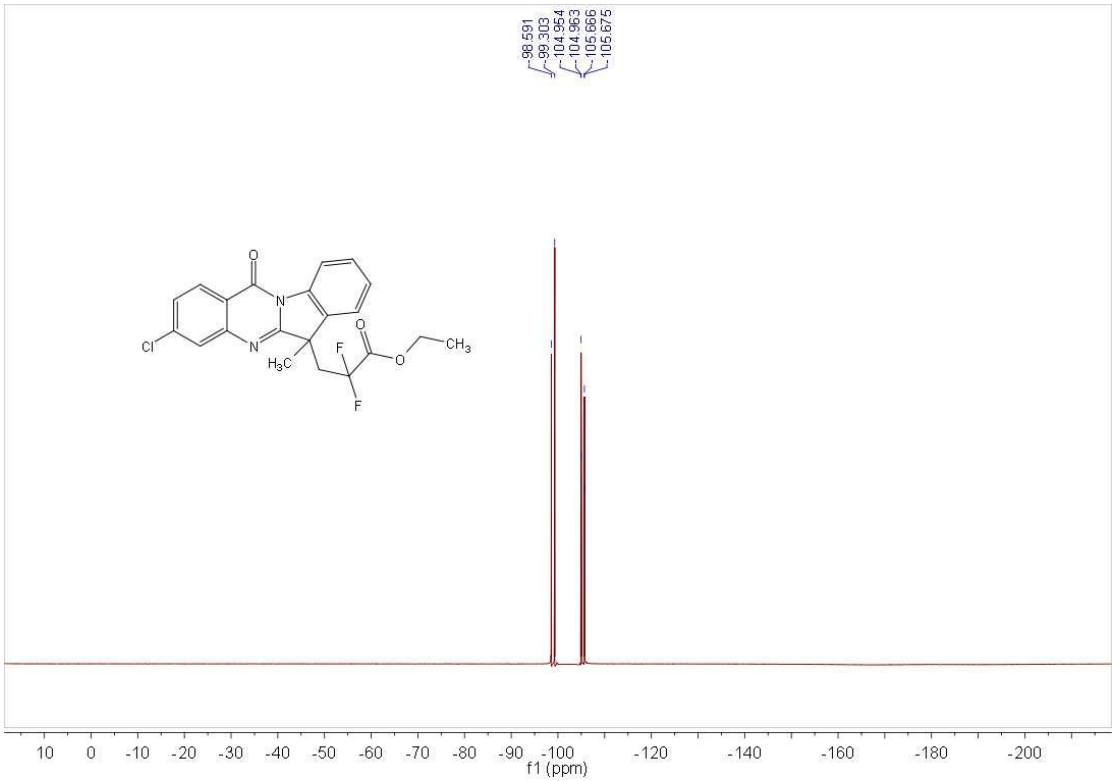

163.839
163.436
163.086
161.064
160.013
145.321
139.253
137.084
135.687
133.055
129.080
127.117
126.399
126.011
123.865
121.213
117.365
117.229
117.046
114.506
112.017
62.950
45.341
45.263
43.209
42.979
42.746
27.952
21.296
13.564
O
H3C
N
N
H3C
F
F
O
O
CH3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


98.657
99.367
104.470
104.477
105.180
105.188
O
H3C
N
N
H3C
F
F
O
O
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

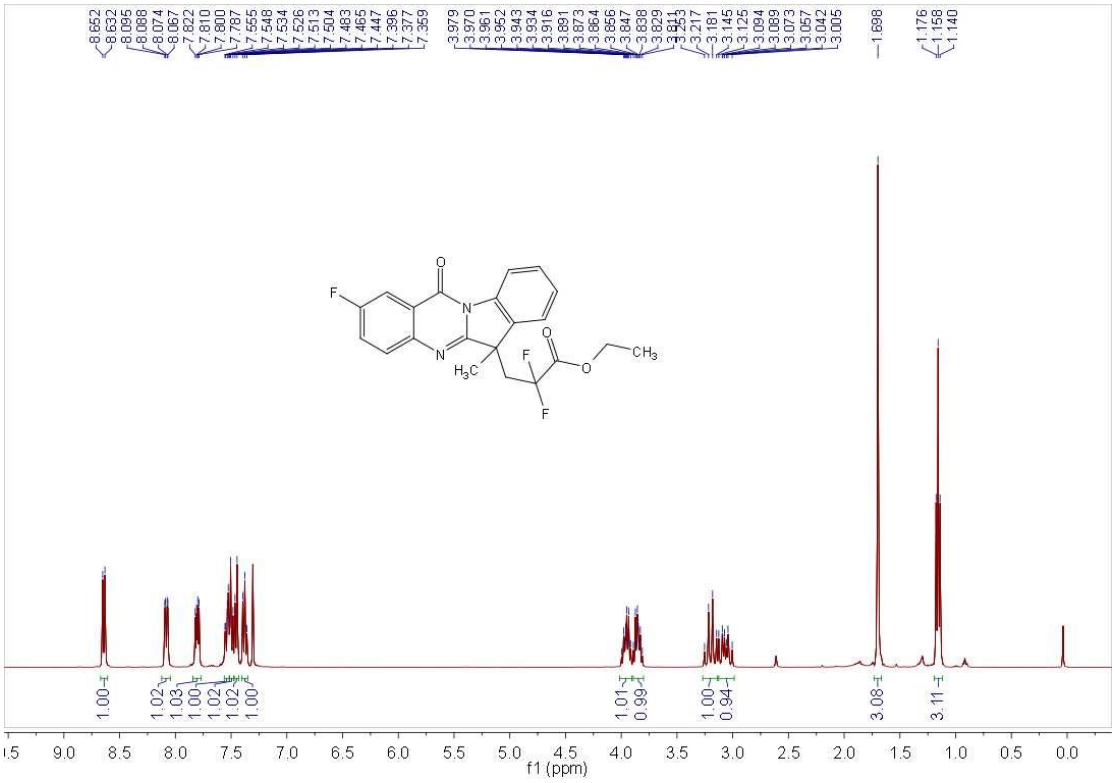
3w

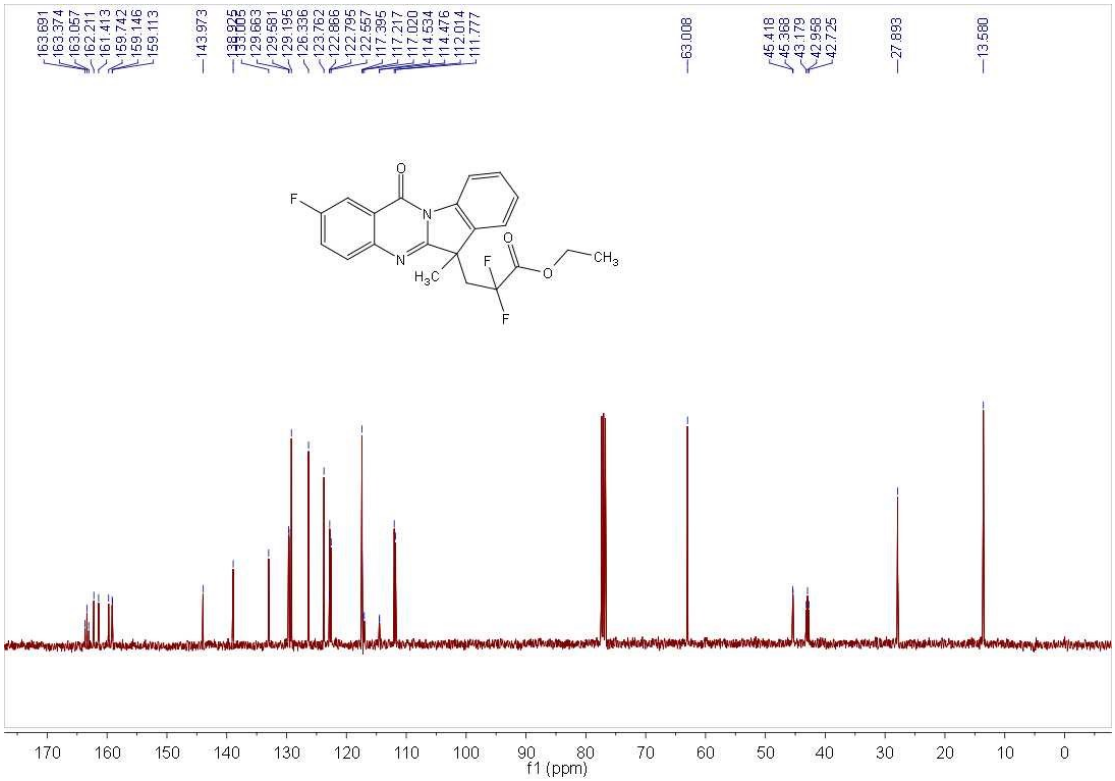

8.646
8.626
8.393
8.372
7.818
7.814
7.525
7.506
7.489
7.465
7.447
7.399
7.380
7.362
4.022
4.004
3.995
3.986
3.977
3.968
3.959
3.941
3.913
3.895
3.885
3.877
3.868
3.859
3.850
3.832
3.258
3.222
3.187
3.150
3.132
3.100
3.080
3.063
3.049
3.011
1.697
1.190
1.173
1.155
1.00
1.00
0.99
2.08
1.06
1.03
1.00
1.01
1.00
0.98
3.08
3.13
f1 (ppm)

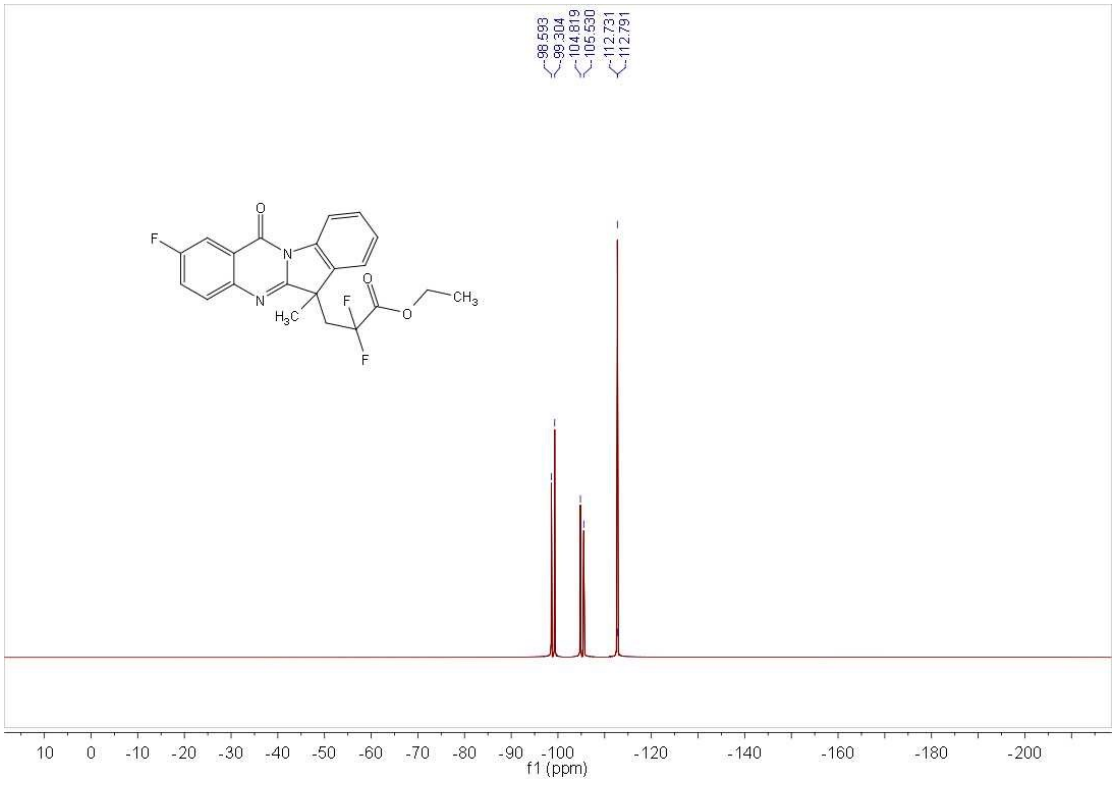

163.683
163.469
163.360
163.043
159.308
148.307
140.507
138.975
132.837
129.227
128.309
127.436
127.010
126.305
123.765
119.961
117.377
116.984
114.501
114.438
111.956
63.038
45.645
45.576
43.116
42.874
42.654
27.856
13.597
f1 (ppm)


98.591
99.303
104.954
104.963
105.666
105.675
Cl
N
O
F
F
CH3
H3C
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

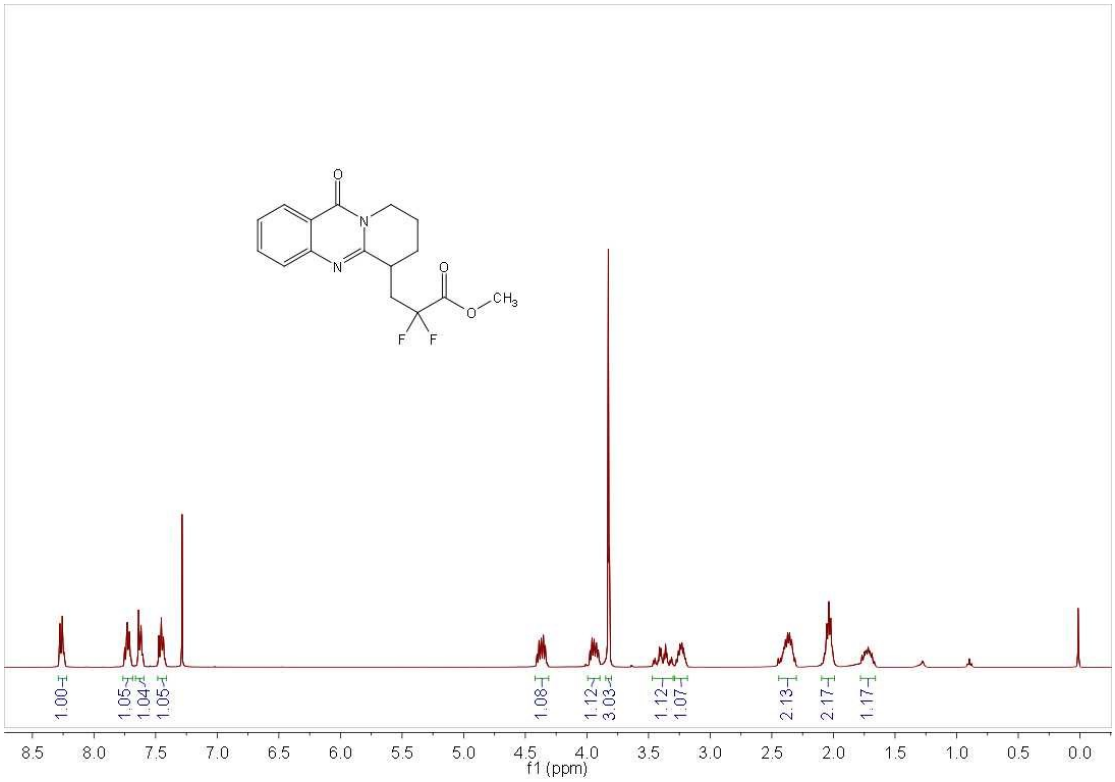
3x

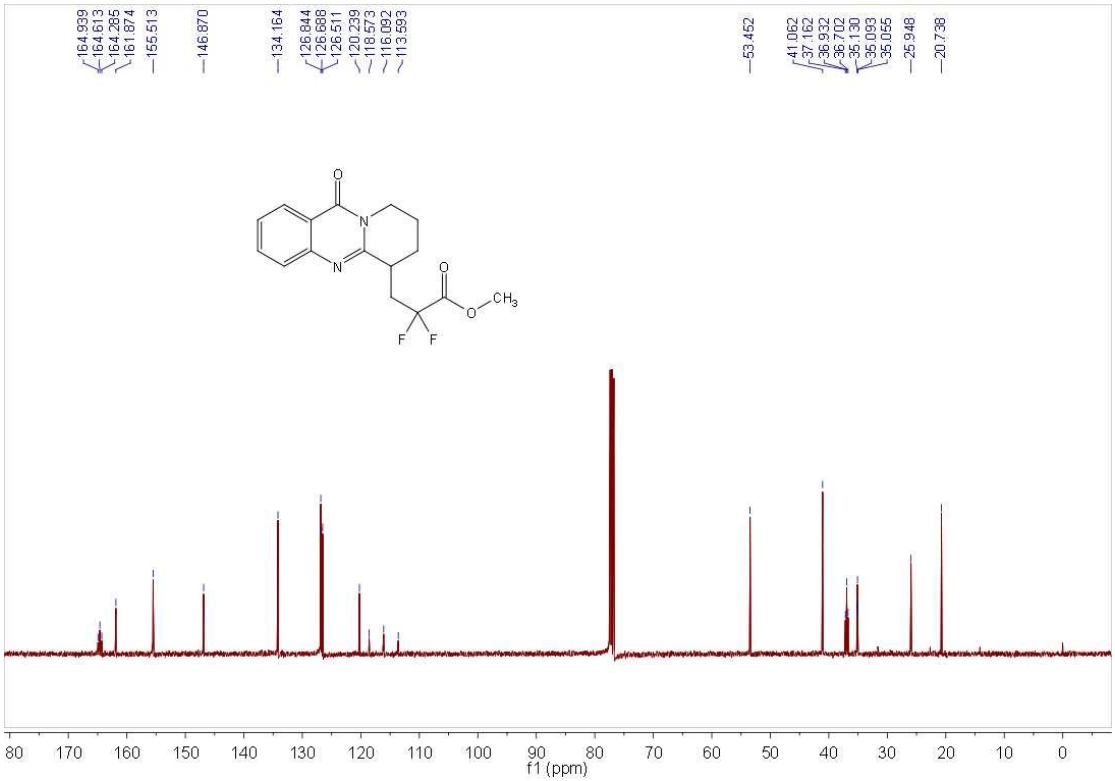

8.652
8.632
8.095
8.068
8.074
8.067
7.822
7.810
7.800
7.787
7.555
7.548
7.534
7.526
7.513
7.504
7.483
7.465
7.447
7.396
7.377
7.359
3.979
3.970
3.961
3.952
3.943
3.934
3.916
3.891
3.873
3.864
3.856
3.847
3.838
3.829
3.811
3.217
3.181
3.145
3.125
3.094
3.089
3.073
3.057
3.042
3.005
1.698
1.176
1.158
1.140
F
N
O
F
F
CH3
H3C
1.00
1.02
1.03
1.00
1.02
1.02
1.00
1.01
0.99
1.00
0.94
3.08
3.11
f1 (ppm)

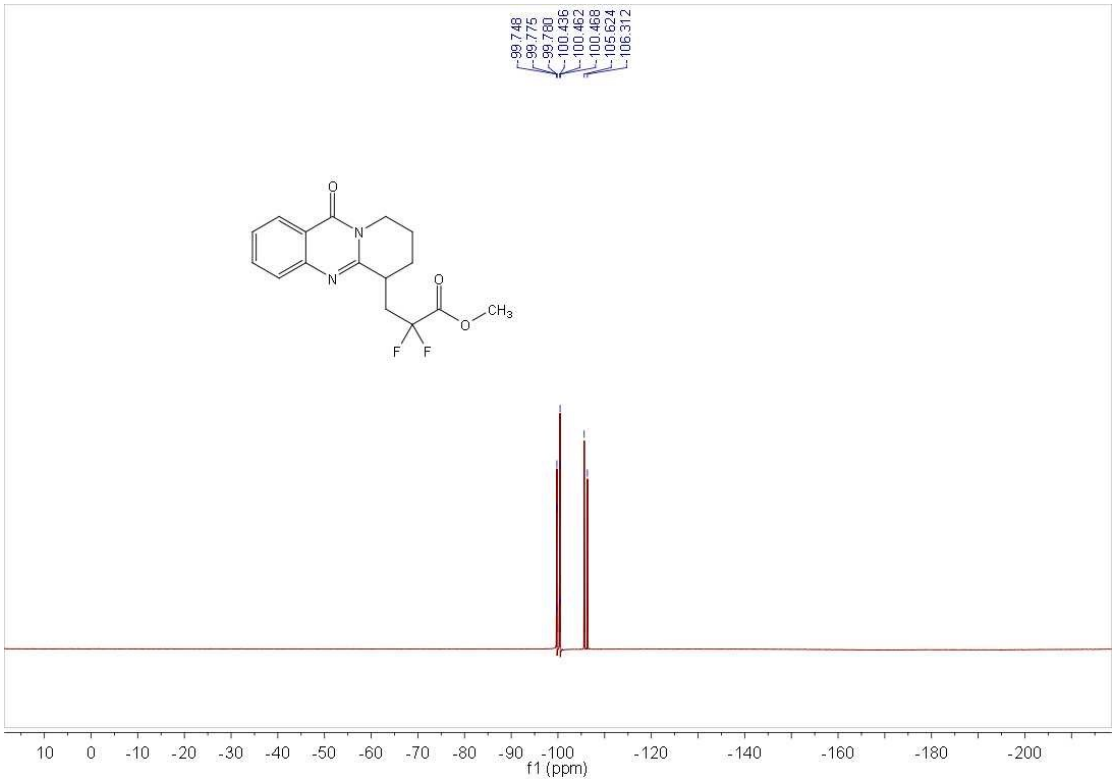

163.691
163.374
163.057
162.211
161.413
159.742
159.146
159.113
143.973
138.025
135.005
129.663
129.581
129.195
126.336
123.762
122.866
122.795
122.557
117.395
117.217
117.020
114.534
114.476
112.014
111.777
63.008
45.418
45.368
43.179
42.998
42.725
27.893
13.580
F
O
N
N
H3C
F
F
O
O
CH3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


98.593
99.304
104.819
105.530
112.731
112.791
F
O
N
N
H3C
F
F
O
O
CH3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

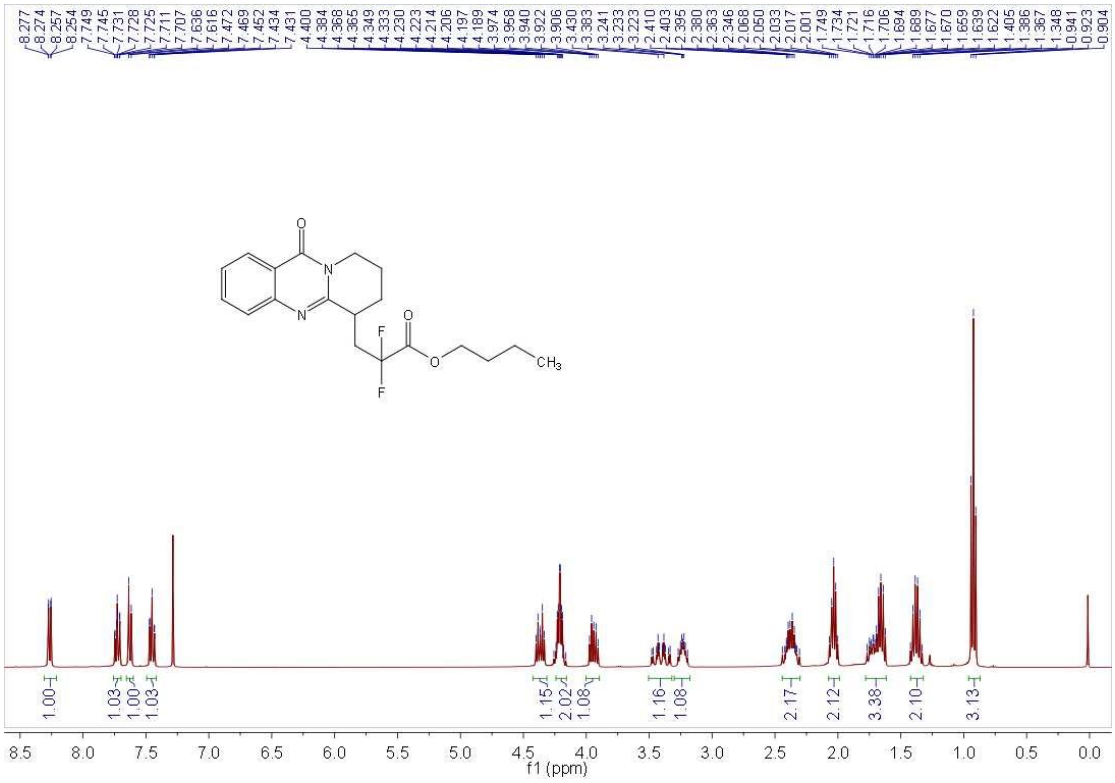
4a

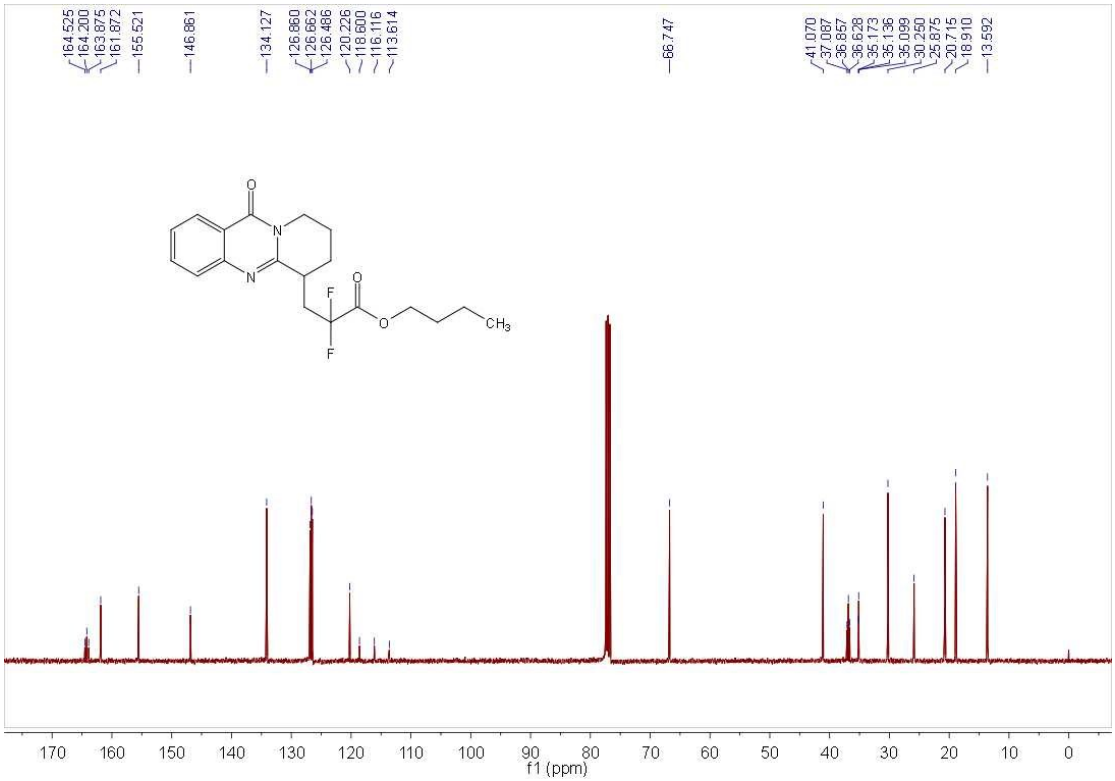

1.00
1.05
1.04
1.05
1.08
1.12
3.03
1.12
1.07
2.13
2.17
1.17
f1 (ppm)

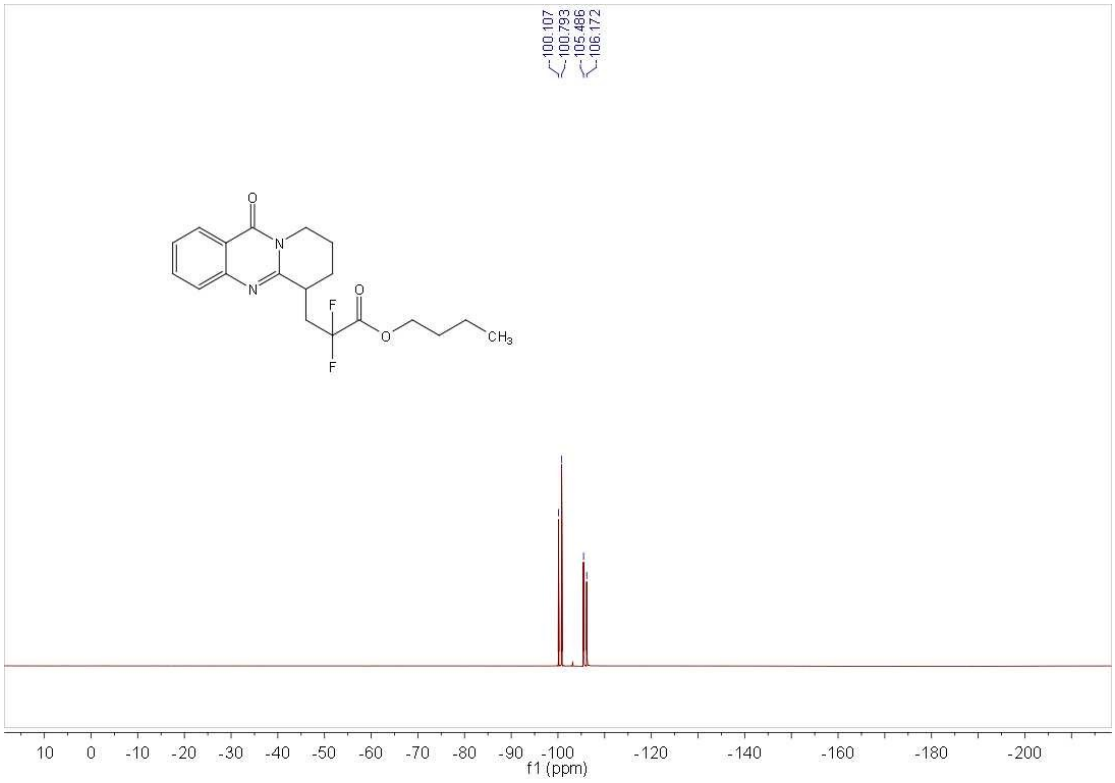

164.939
164.613
164.295
161.874
155.513
146.870
134.164
126.844
126.688
126.511
120.239
118.573
116.092
113.593
53.452
41.062
37.162
36.932
36.702
35.130
35.093
35.055
25.948
20.738
f1 (ppm)


99.748
99.775
99.790
100.436
100.462
100.468
105.624
106.312
O
N
N
O
O
CH3
F
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

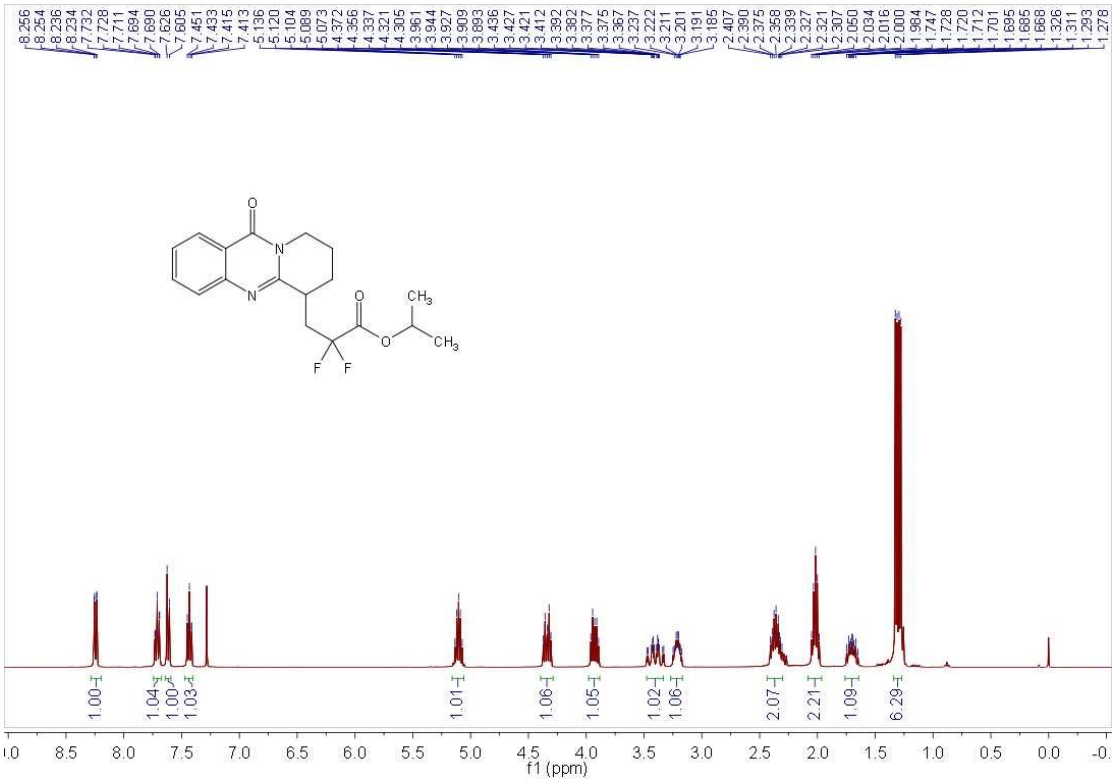
4b

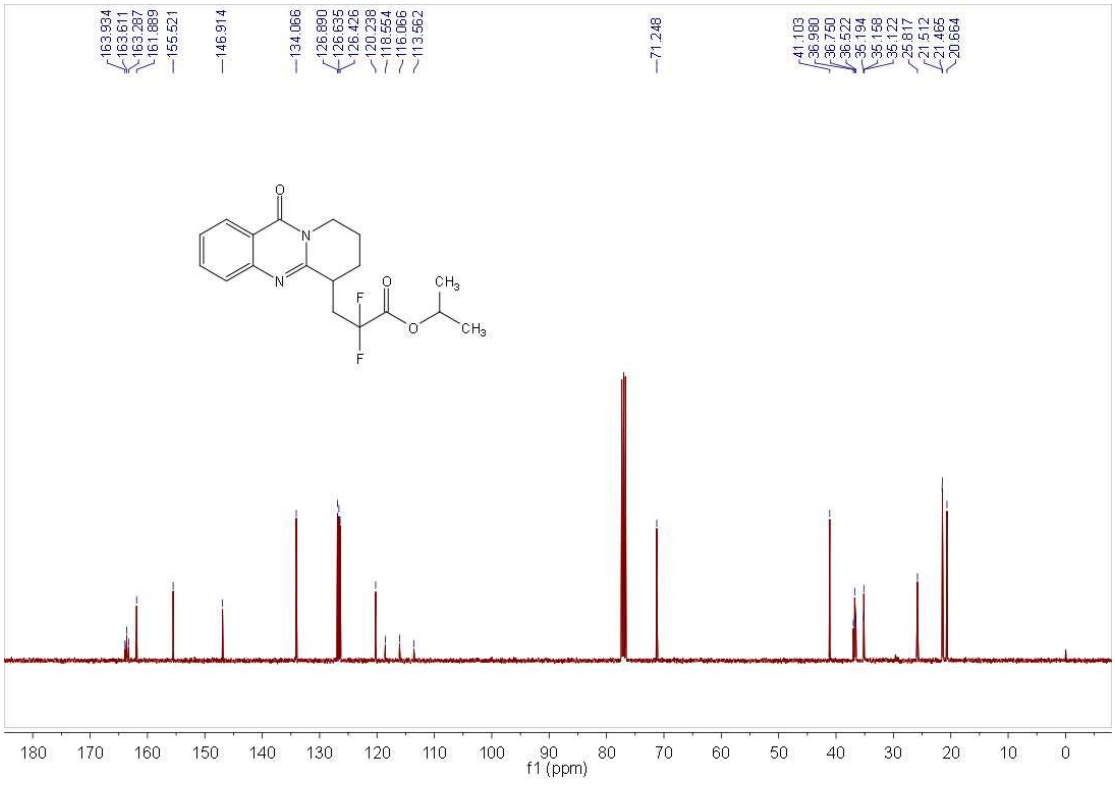

8.277
8.274
8.257
8.254
7.749
7.745
7.731
7.728
7.725
7.711
7.707
7.636
7.616
7.472
7.469
7.452
7.434
7.431
4.400
4.384
4.368
4.365
4.349
4.333
4.230
4.223
4.214
4.206
4.197
4.189
3.974
3.968
3.940
3.922
3.906
3.430
3.383
3.241
3.233
3.223
2.410
2.403
2.395
2.380
2.363
2.346
2.068
2.050
2.033
2.017
2.001
1.749
1.734
1.721
1.716
1.706
1.694
1.689
1.677
1.670
1.659
1.639
1.622
1.405
1.386
1.367
1.348
0.941
0.923
0.904
O
N
N
O
O
CH3
F
F
1.00
1.03
1.00
1.03
1.15
2.02
1.08
1.16
1.08
2.17
2.12
3.38
2.10
3.13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

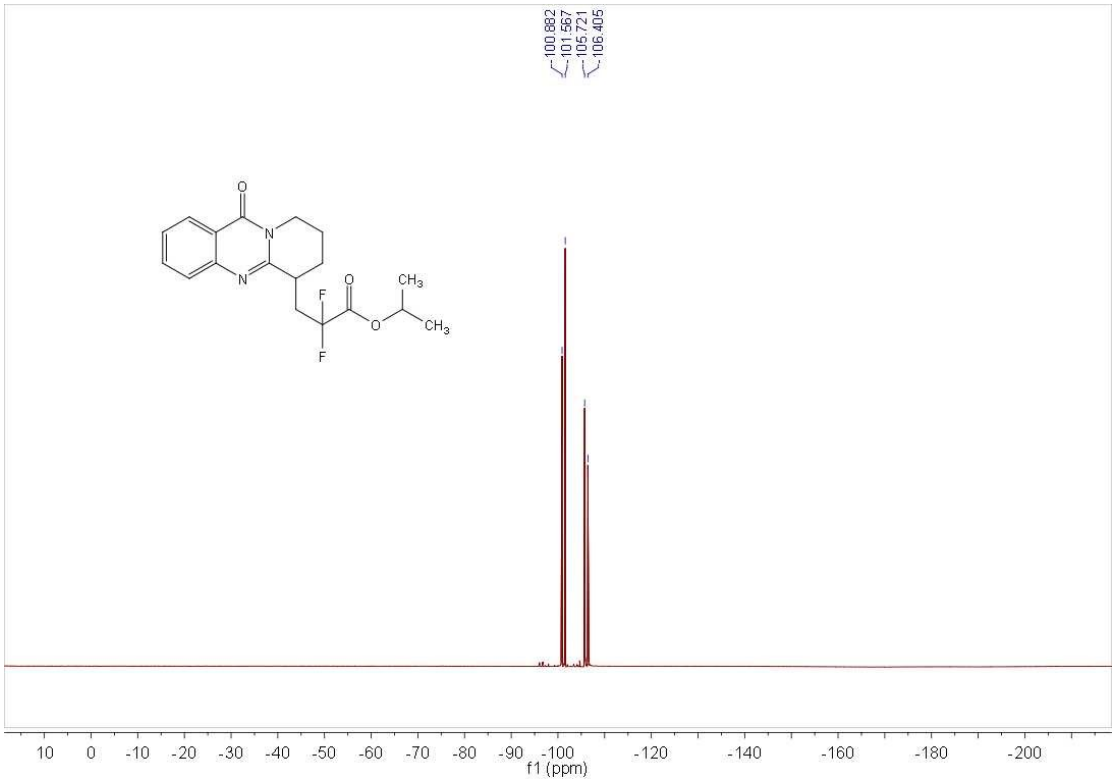

164.525
164.200
163.875
161.872
155.521
146.861
134.127
126.860
126.662
126.486
120.226
118.800
116.116
113.614
66.747
41.070
37.087
36.857
36.628
35.173
35.136
35.099
30.250
25.875
20.715
18.910
13.592
O
N
N
F
O
F
O
CH3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


100.107
100.793
105.486
106.172
O
N
N
F
O
F
O
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

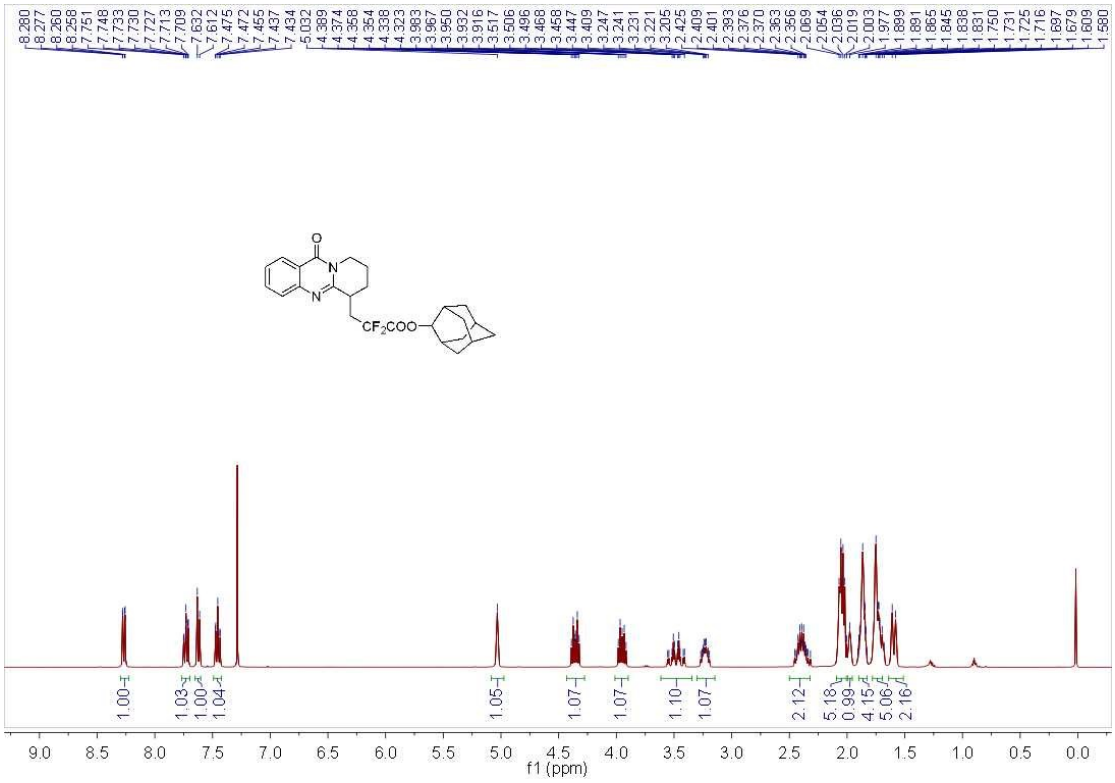
4c

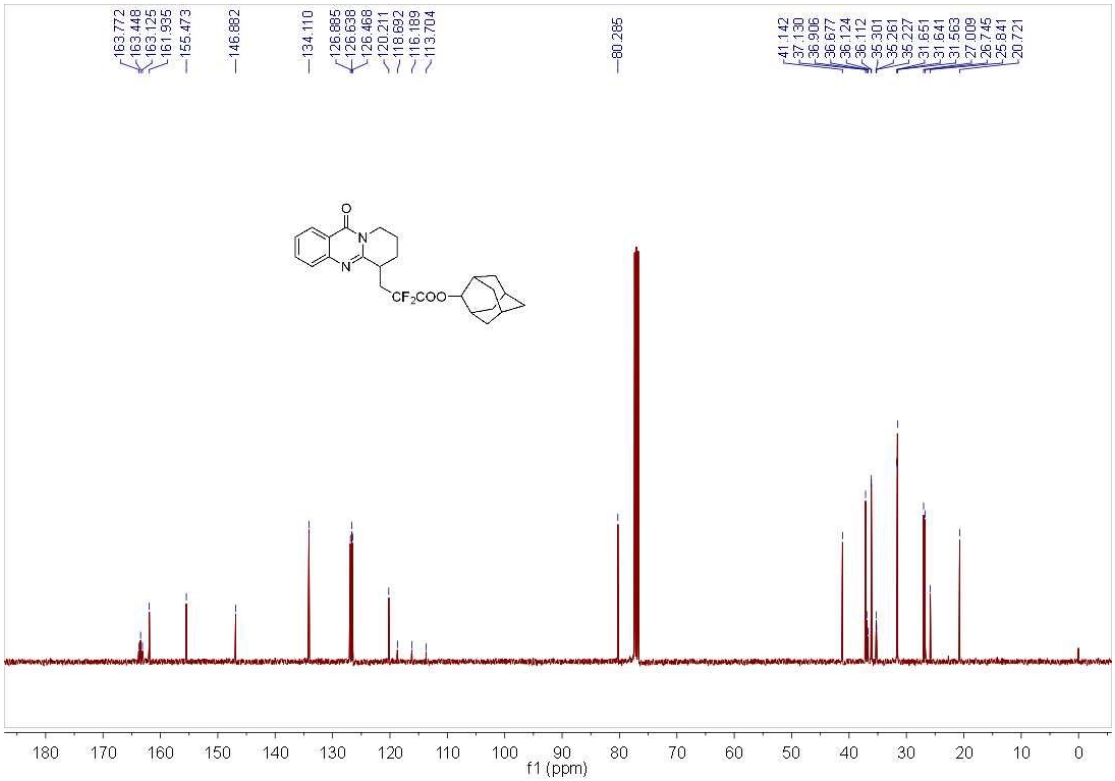

8.256
8.254
8.236
8.234
7.732
7.728
7.711
7.694
7.690
7.626
7.605
7.451
7.433
7.415
7.413
5.136
5.120
5.104
5.089
5.073
4.372
4.356
4.337
4.321
4.305
3.961
3.944
3.927
3.909
3.893
3.436
3.427
3.421
3.412
3.392
3.382
3.377
3.375
3.367
3.237
3.222
3.211
3.201
3.191
3.185
2.407
2.390
2.375
2.358
2.339
2.327
2.321
2.307
2.050
2.034
2.016
2.000
1.984
1.747
1.728
1.720
1.712
1.701
1.695
1.685
1.668
1.326
1.311
1.293
1.278
O
N
N
O
O
CH3
CH3
F
F
1.00
1.04
1.00
1.03
1.01
1.06
1.05
1.02
1.06
2.07
2.21
1.09
6.29
f1 (ppm)

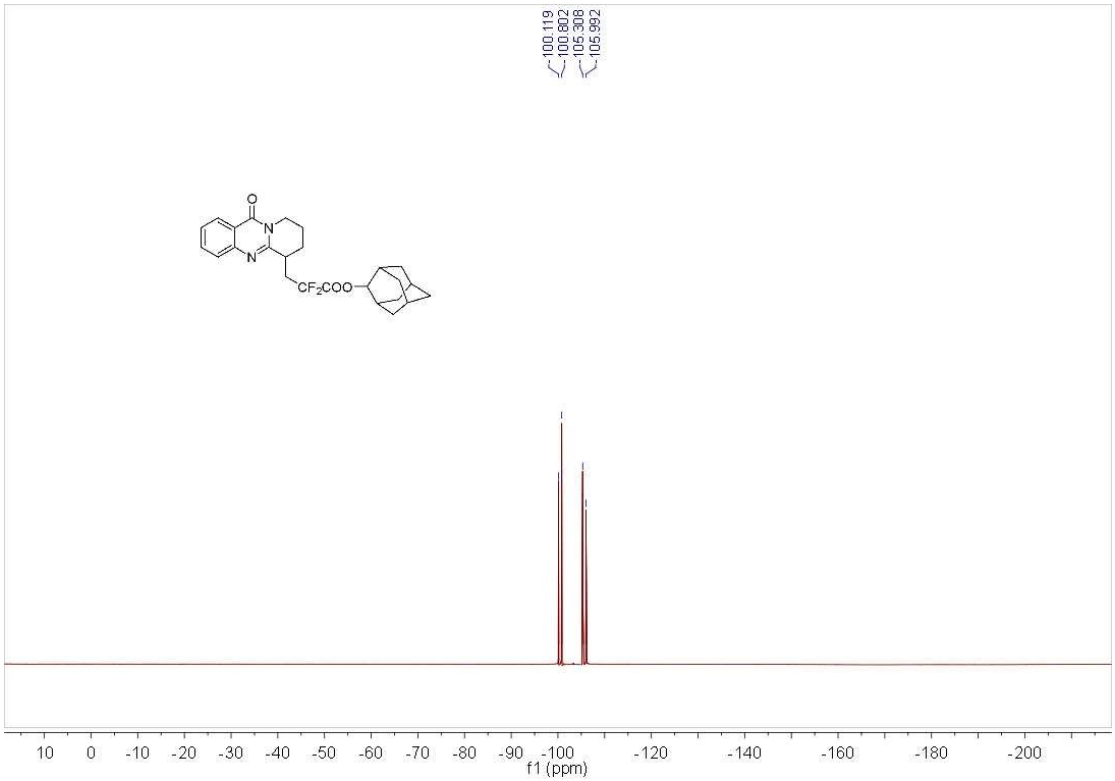

163.934
163.611
163.287
161.889
155.521
146.914
134.066
126.890
126.635
126.426
120.238
118.554
116.066
113.562
71.248
41.103
36.980
36.750
36.522
35.194
35.158
35.122
25.817
21.512
21.465
20.664
O
N
N
O
O
CH3
CH3
F
F
f1 (ppm)



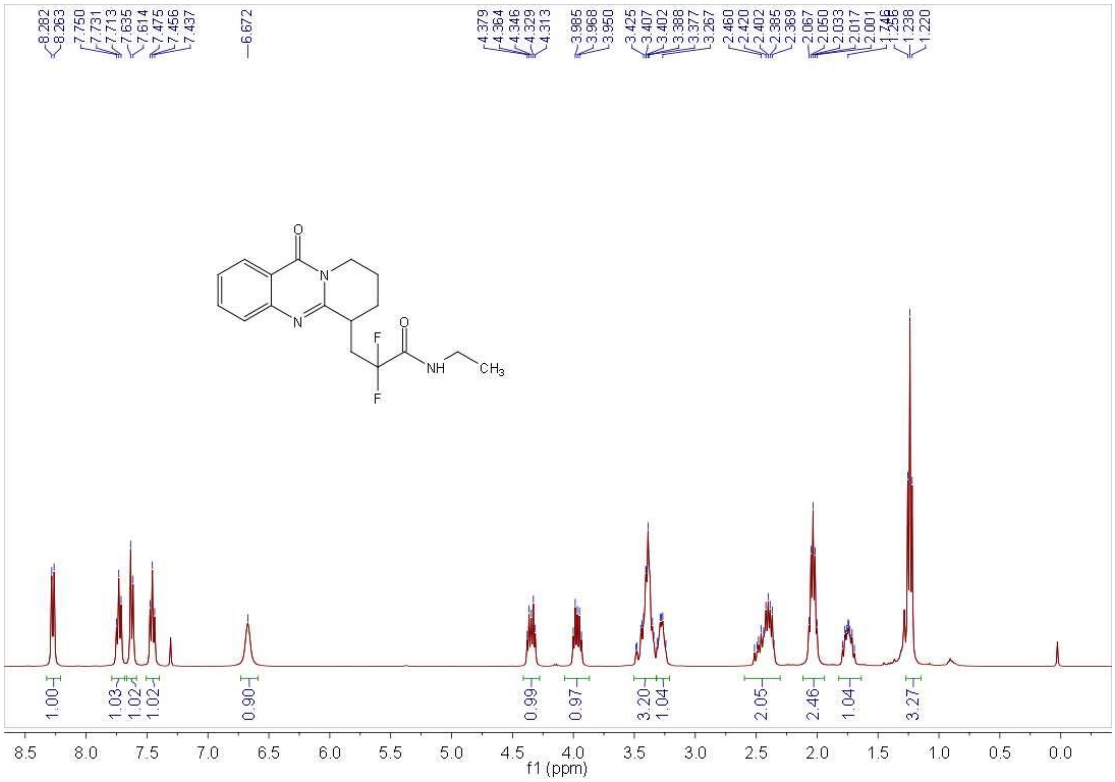
4d

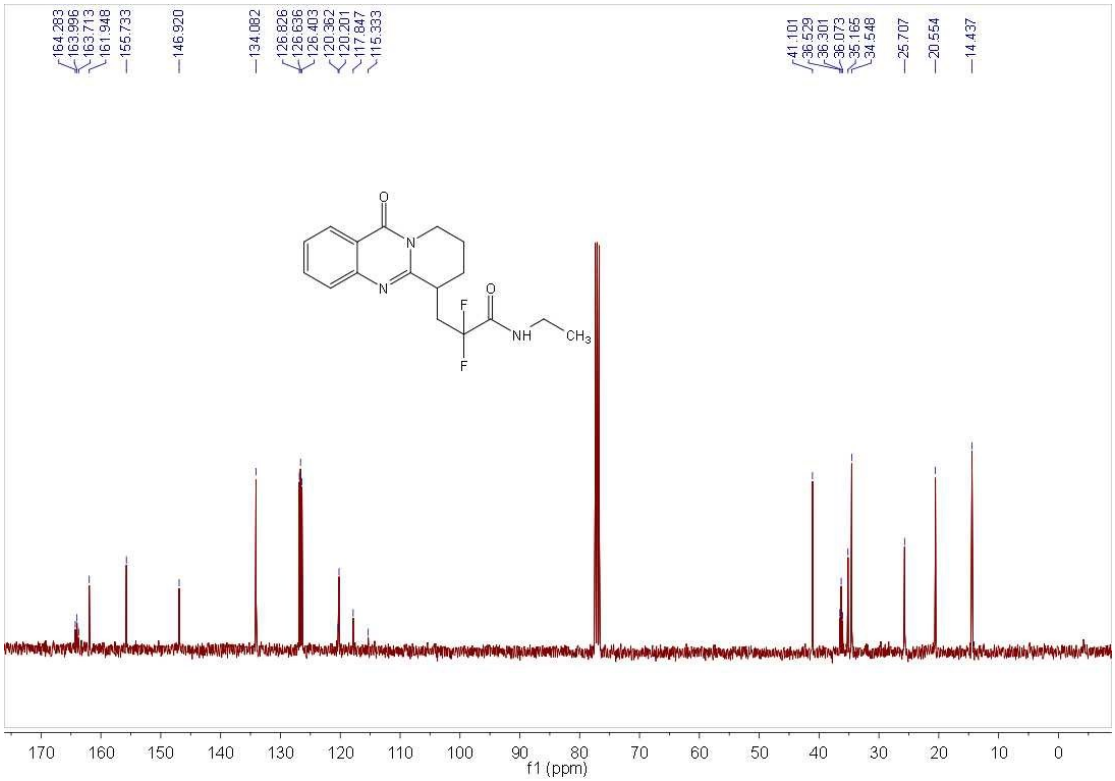


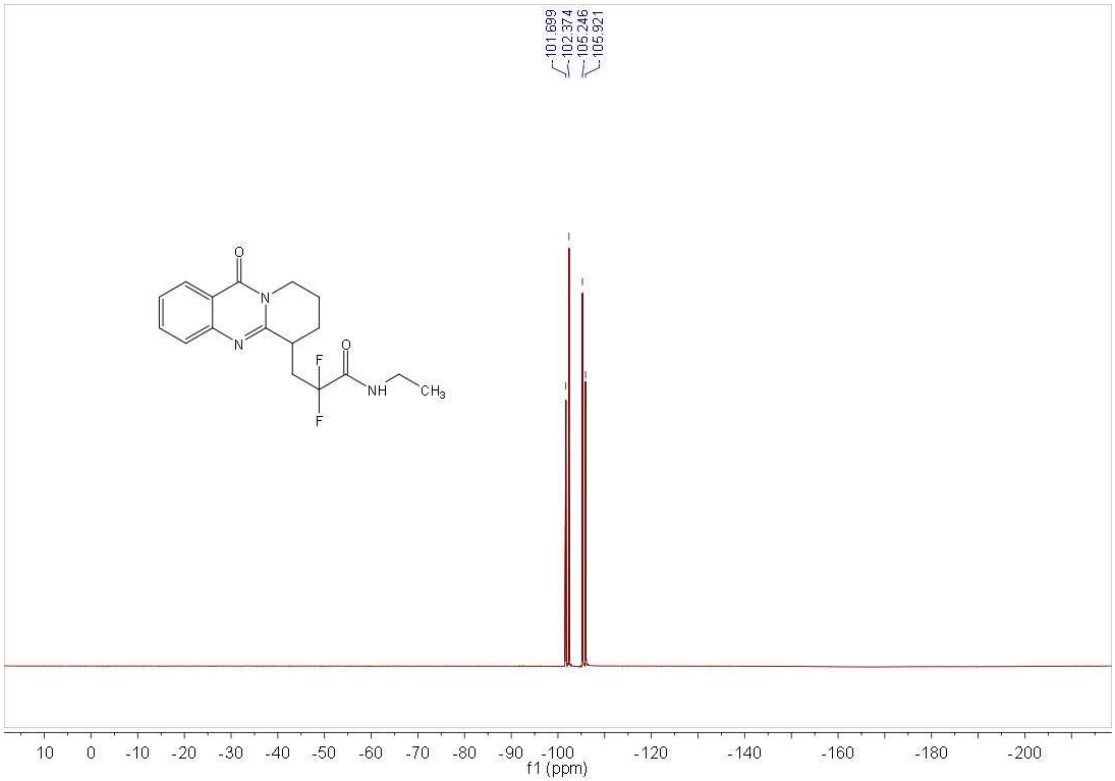

163.772
163.448
163.125
161.935
155.473
146.882
134.110
126.885
126.638
126.468
120.211
118.892
116.189
113.704
80.285
41.142
37.130
36.906
36.677
36.124
36.112
35.301
35.261
35.227
31.651
31.641
31.563
27.009
26.745
25.841
20.721
O
N
N
CF2COO
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


100.119
100.802
105.308
105.992
O
N
N
CF2COO
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

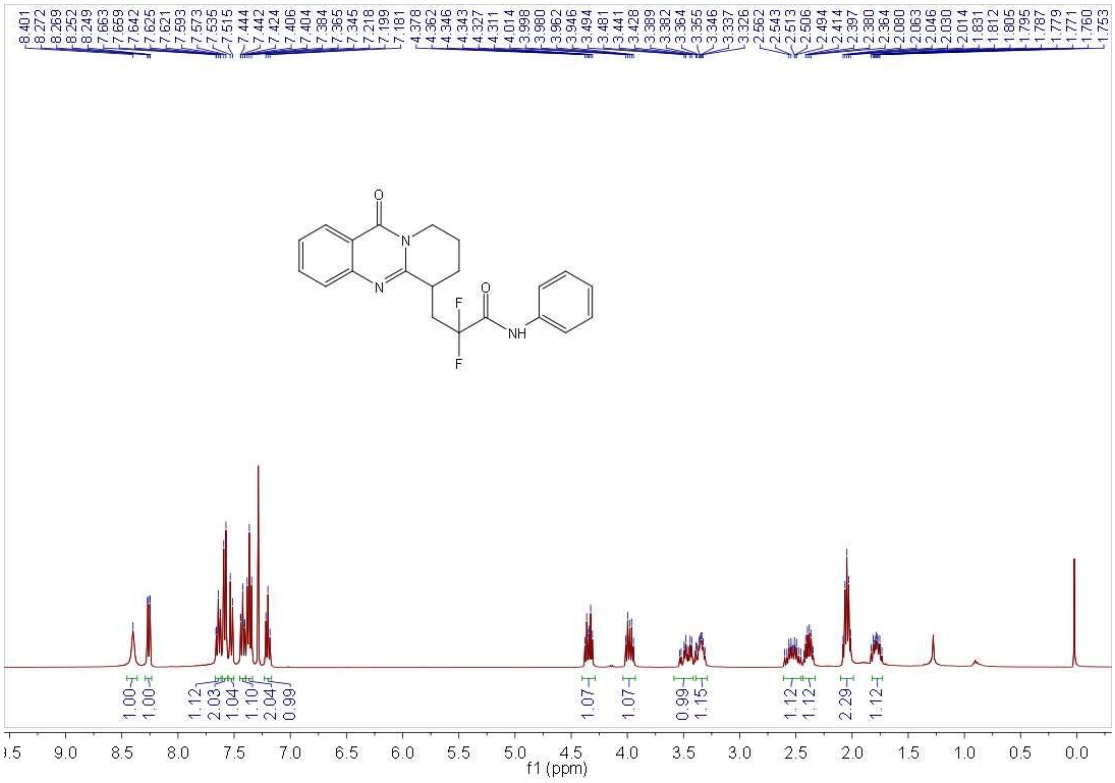
4e

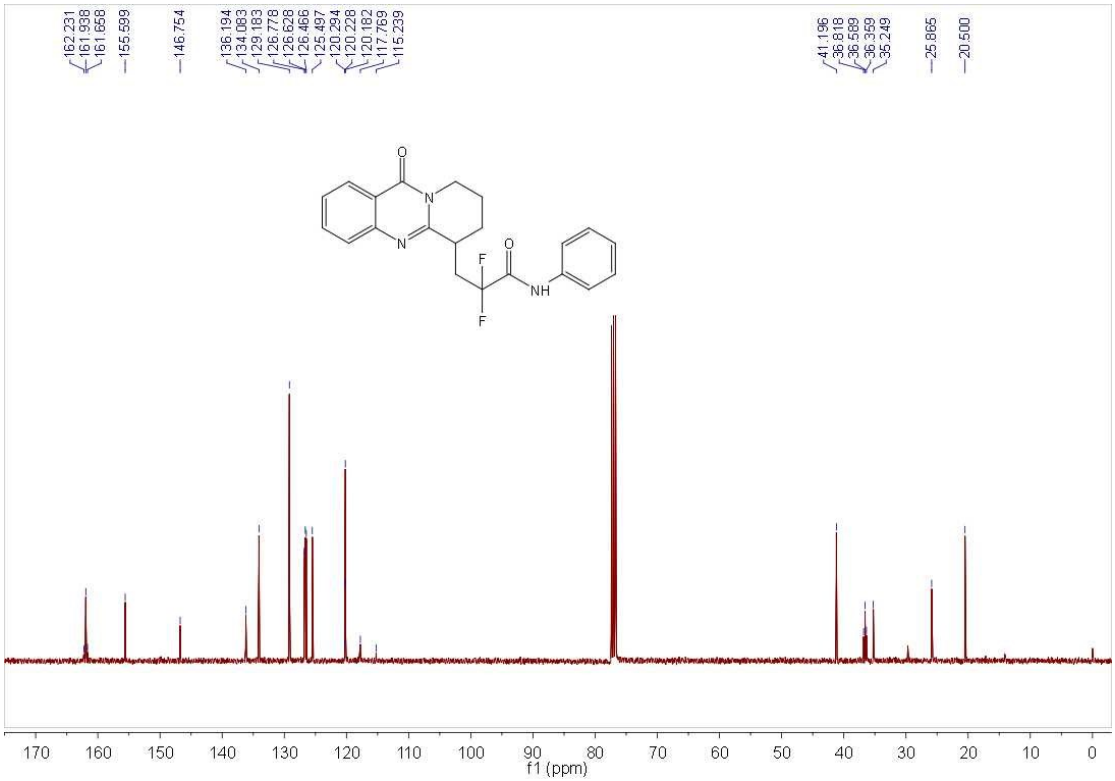

8.282
8.263
7.750
7.731
7.713
7.635
7.614
7.475
7.456
7.437
6.672
4.379
4.364
4.346
4.329
4.313
3.985
3.968
3.950
3.425
3.407
3.402
3.388
3.377
3.267
2.460
2.420
2.402
2.385
2.369
2.067
2.050
2.033
2.017
2.001
1.238
1.220
1.00
1.03
1.02
1.02
0.90
0.99
0.97
3.20
1.04
2.05
2.46
1.04
3.27
f1 (ppm)


164.283
163.996
163.713
161.948
155.733
146.920
134.082
126.826
126.636
126.403
120.362
120.201
117.847
115.333
41.101
36.529
36.301
36.073
35.165
34.548
25.707
20.554
14.437
f1 (ppm)


101.699
102.374
105.246
105.921
O
N
N
F
F
O
NH
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

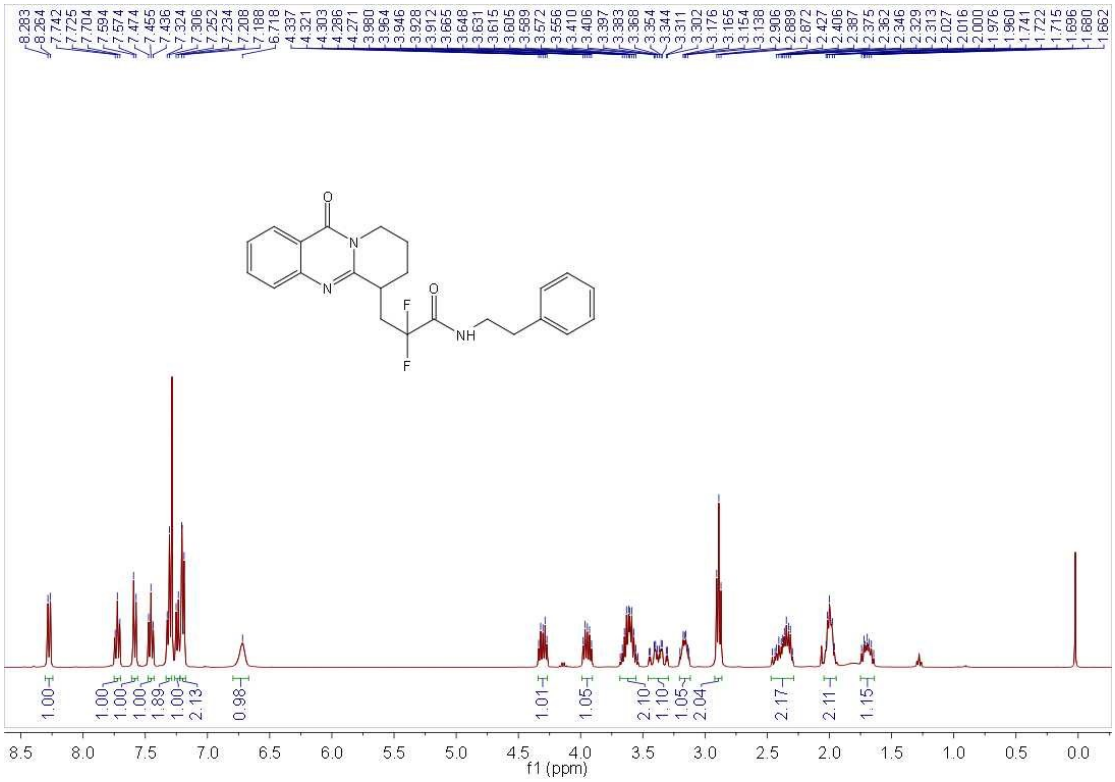
4f

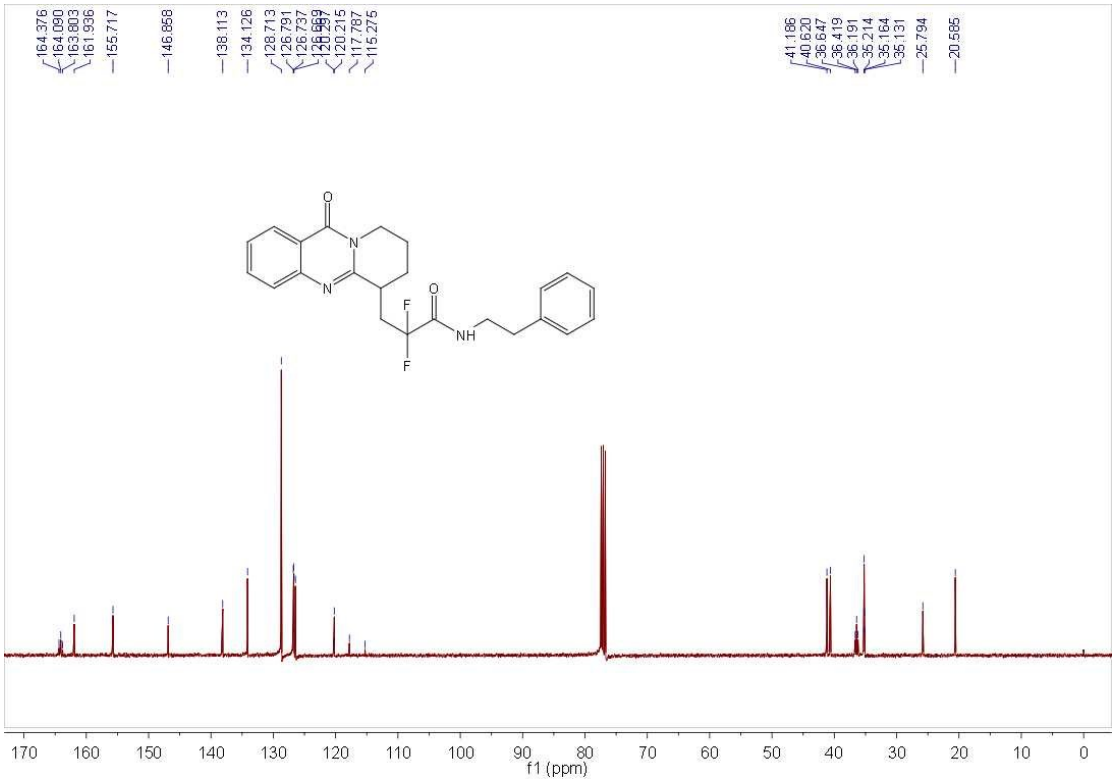

8.401
8.272
8.269
8.252
8.249
7.663
7.659
7.642
7.625
7.621
7.593
7.573
7.536
7.515
7.444
7.442
7.424
7.406
7.404
7.384
7.365
7.345
7.218
7.199
7.181
4.378
4.362
4.346
4.343
4.327
4.311
4.014
3.998
3.980
3.962
3.946
3.494
3.481
3.441
3.428
3.389
3.382
3.364
3.355
3.346
3.337
3.326
2.562
2.543
2.513
2.506
2.494
2.414
2.397
2.380
2.364
2.080
2.063
2.046
2.030
2.014
1.831
1.812
1.805
1.795
1.787
1.779
1.771
1.760
1.753
O
N
N
F
F
O
NH
1.00
1.00
1.12
2.03
1.04
1.10
2.04
0.99
1.07
1.07
0.99
1.15
1.12
1.12
2.29
1.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

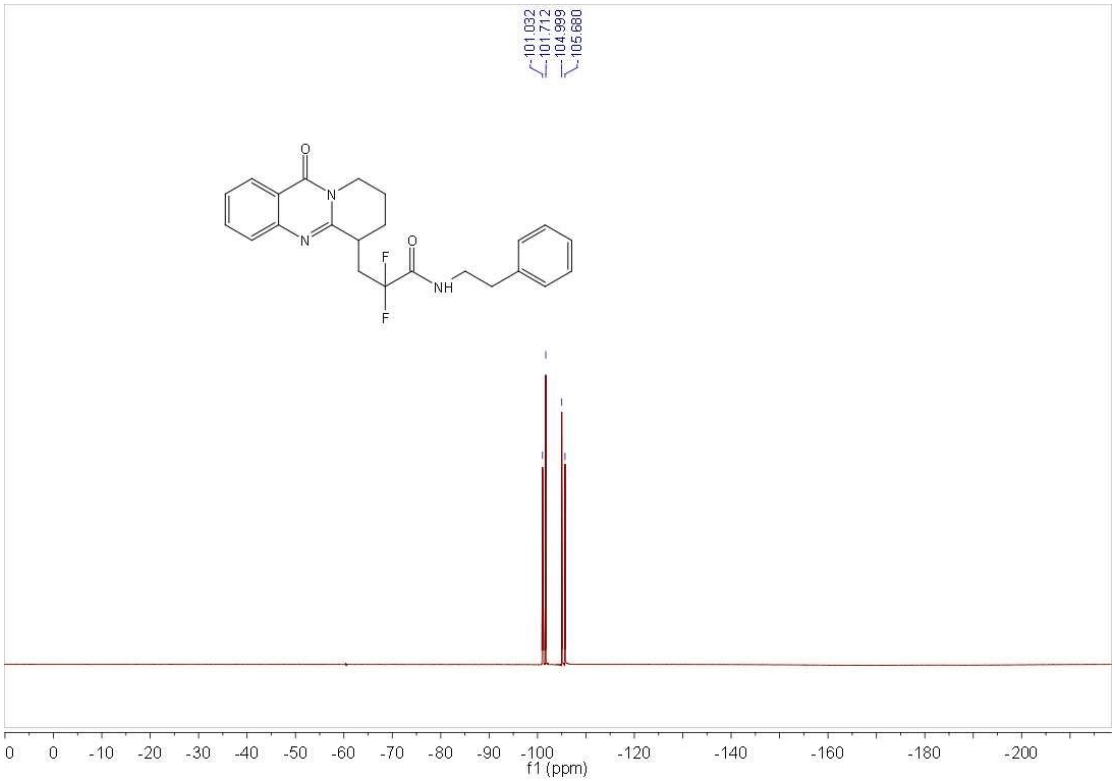

162.231
161.938
161.658
155.599
146.754
136.194
134.083
129.183
126.778
126.628
126.466
125.497
120.294
120.228
120.182
117.769
115.239
41.196
36.818
36.589
36.359
35.249
25.865
20.500
O
N
N
O
F
F
NH
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


99.985
100.663
104.103
104.780
O
N
N
O
F
F
NH
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

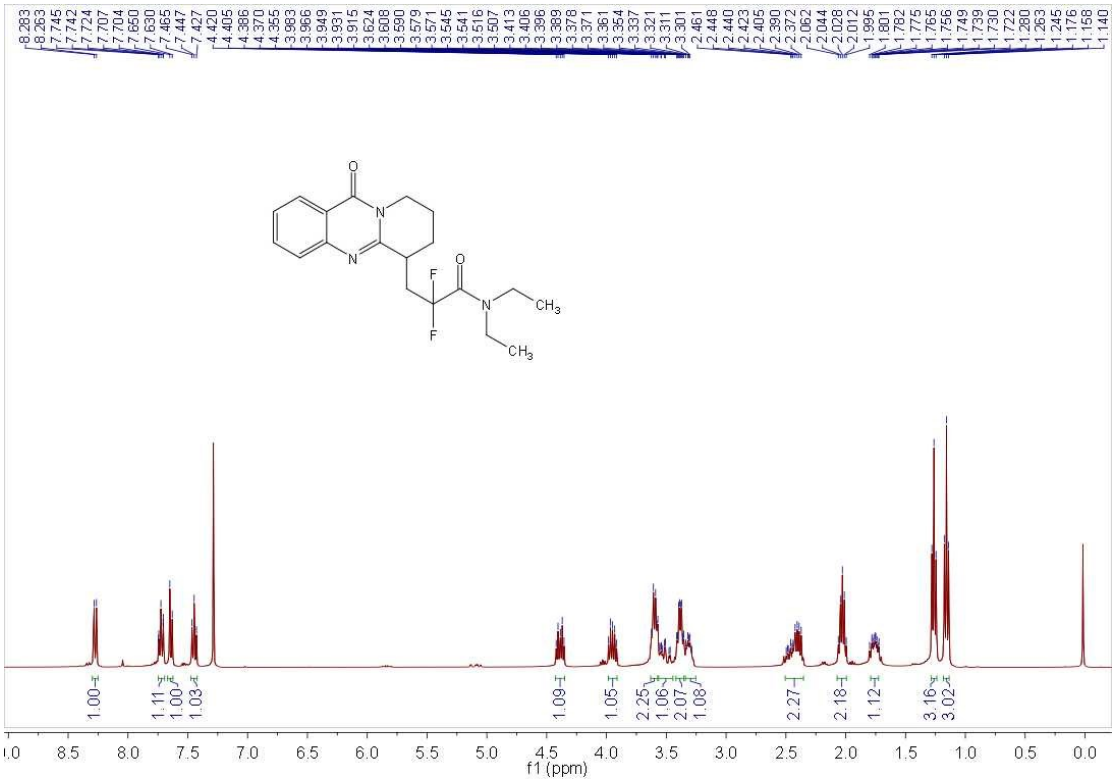
4g

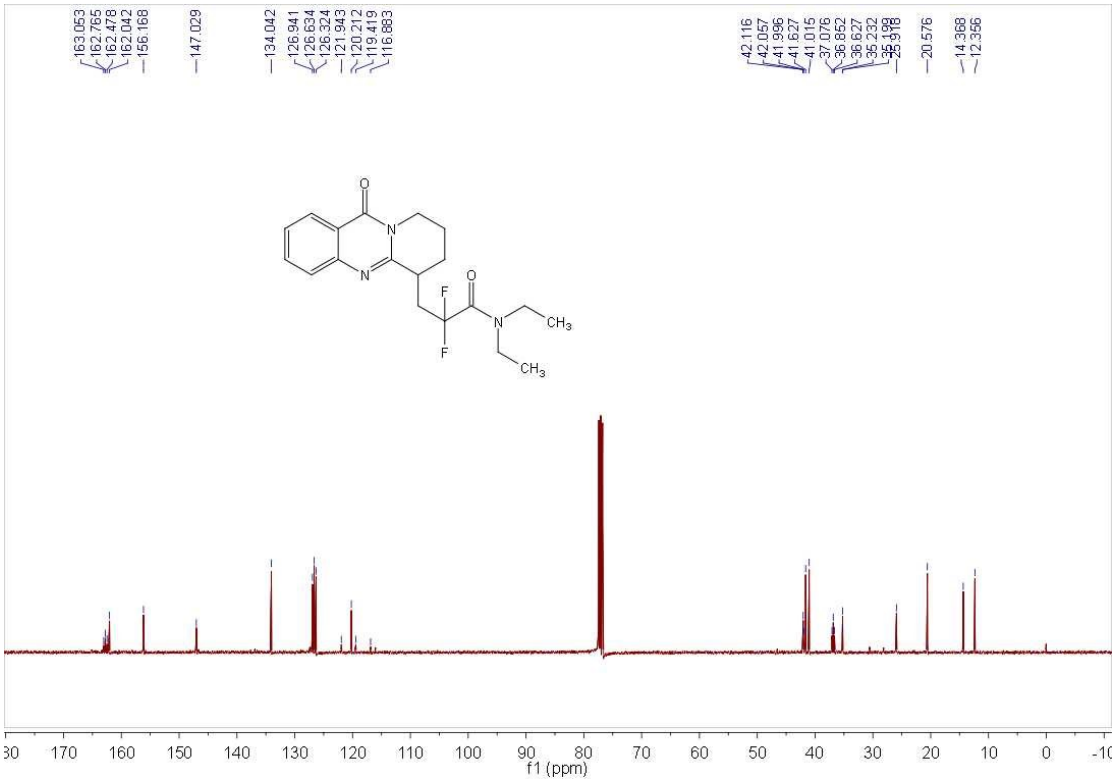

8.283
8.264
7.742
7.725
7.704
7.594
7.574
7.474
7.455
7.436
7.324
7.306
7.252
7.234
7.208
7.188
6.718
4.337
4.321
4.303
4.286
4.271
3.980
3.964
3.946
3.928
3.912
3.665
3.648
3.631
3.615
3.605
3.589
3.572
3.556
3.410
3.406
3.397
3.383
3.368
3.354
3.344
3.311
3.302
3.176
3.165
3.154
3.138
2.906
2.889
2.872
2.427
2.406
2.387
2.375
2.362
2.346
2.329
2.313
2.027
2.016
2.000
1.976
1.960
1.741
1.722
1.715
1.696
1.680
1.662
O
N
N
F
O
NH
F
1.00
1.00
1.00
1.00
1.89
1.00
2.13
0.98
1.01
1.05
2.10
1.10
1.05
2.04
2.17
2.11
1.15
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

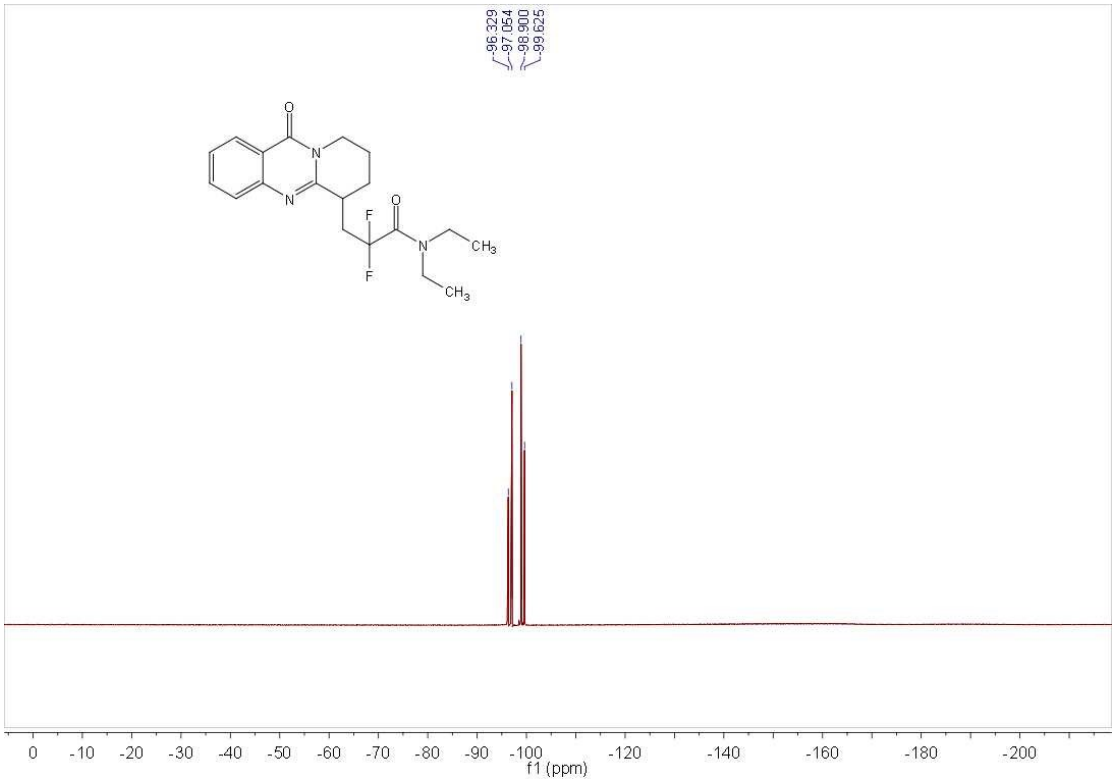

164.376
164.090
163.803
161.936
155.717
146.858
138.113
134.126
128.713
126.791
126.737
120.215
117.787
115.275
41.186
40.620
36.647
36.419
36.191
35.214
35.164
35.131
25.794
20.585
O
N
N
F
O
NH
F
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-101.032
-101.712
-104.999
-105.680
O
N
N
F
O
NH
F
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

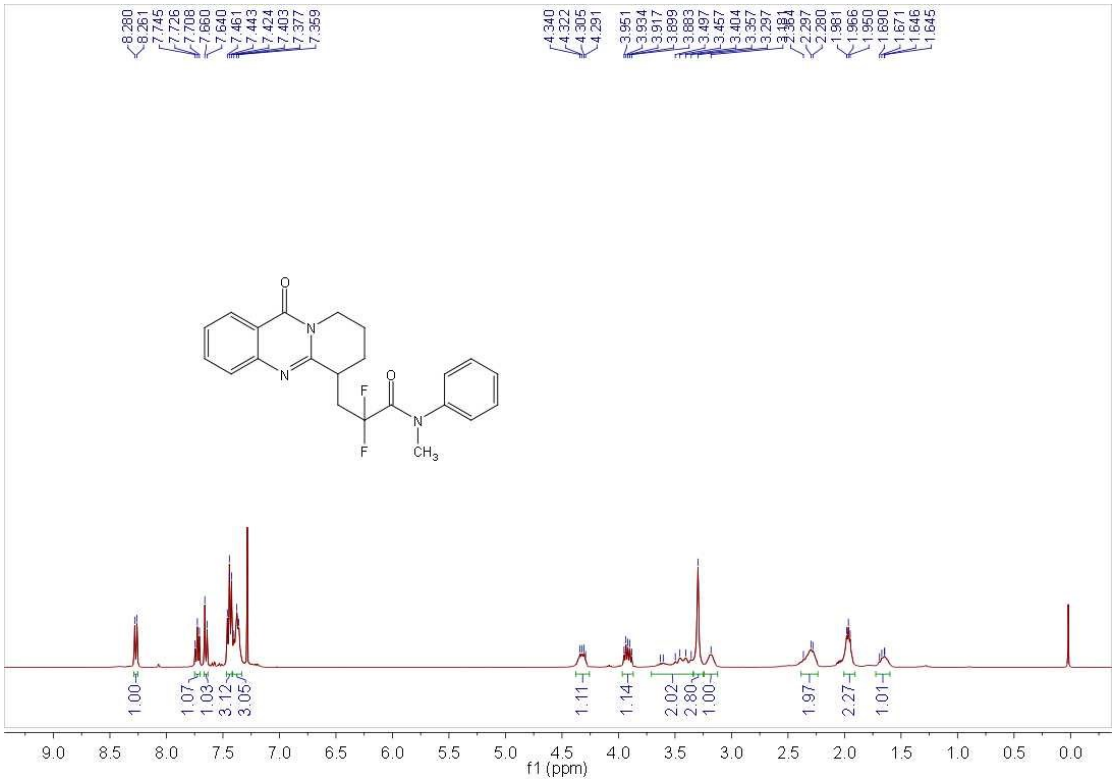
4h

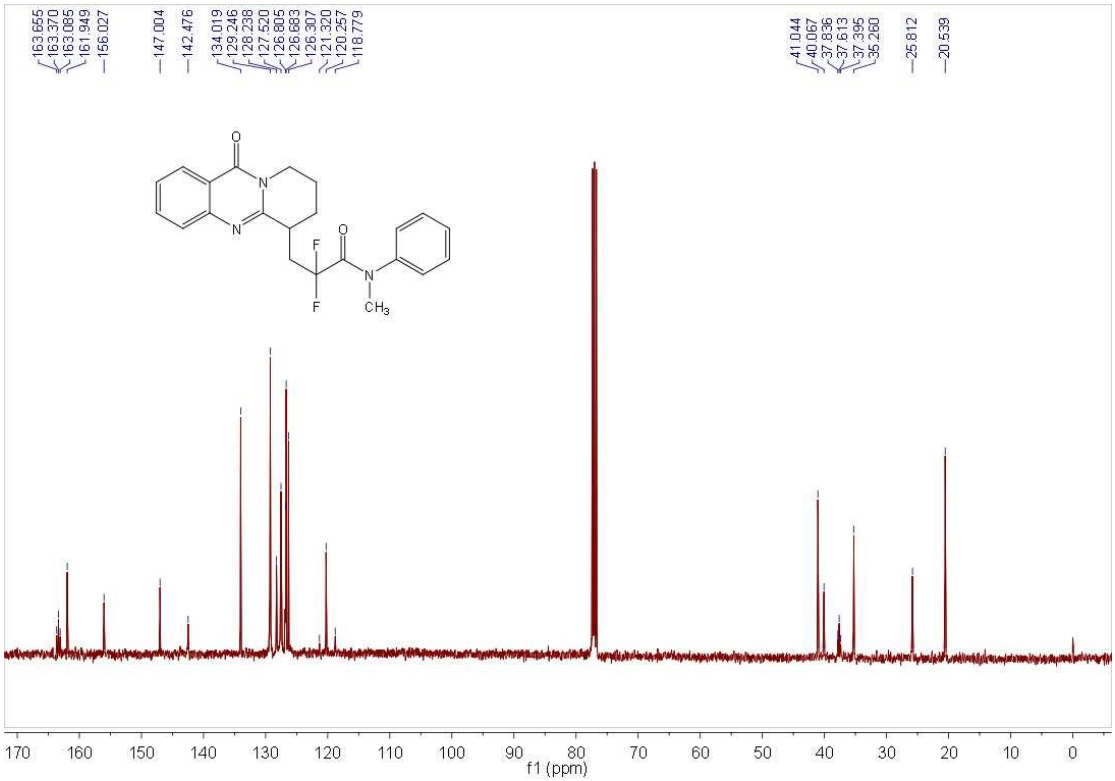

O
N
N
F
O
N
CH3
F
CH3
1.00
1.11
1.00
1.03
1.09
1.05
2.25
1.06
2.07
1.08
2.27
2.18
1.12
3.16
3.02
1.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

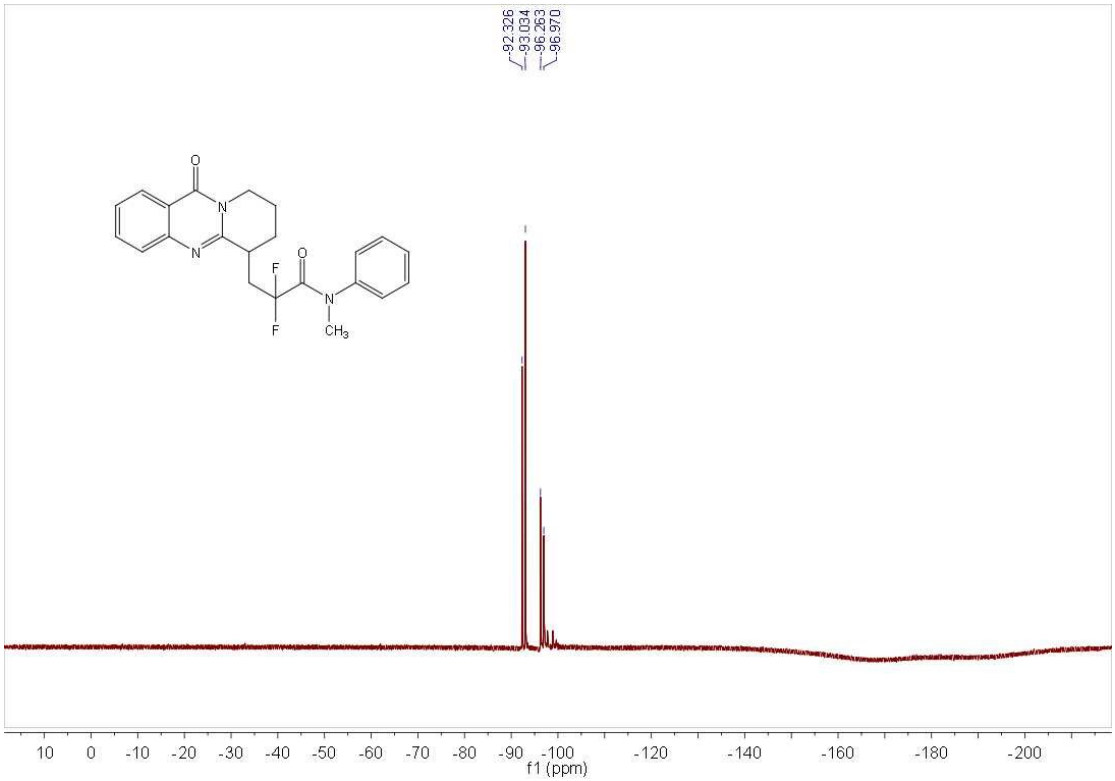

163.053
162.765
162.478
162.042
156.168
147.029
134.042
126.941
126.634
126.324
121.943
120.212
119.419
116.883
42.116
42.057
41.996
41.627
41.015
37.076
36.852
36.627
36.232
20.576
14.368
12.356
O
N
N
F
F
O
N
CH3
CH3
f1 (ppm)


96.329
97.054
98.900
99.625
O
N
N
F
F
O
N
CH3
CH3
f1 (ppm)

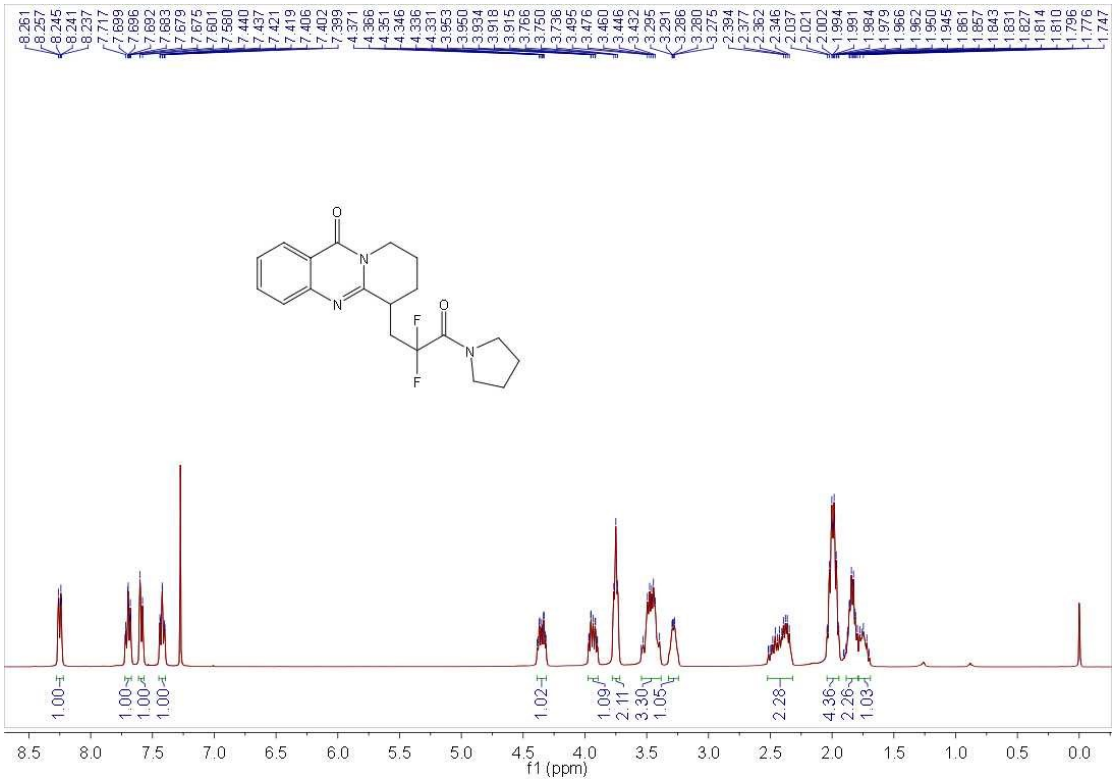
4i

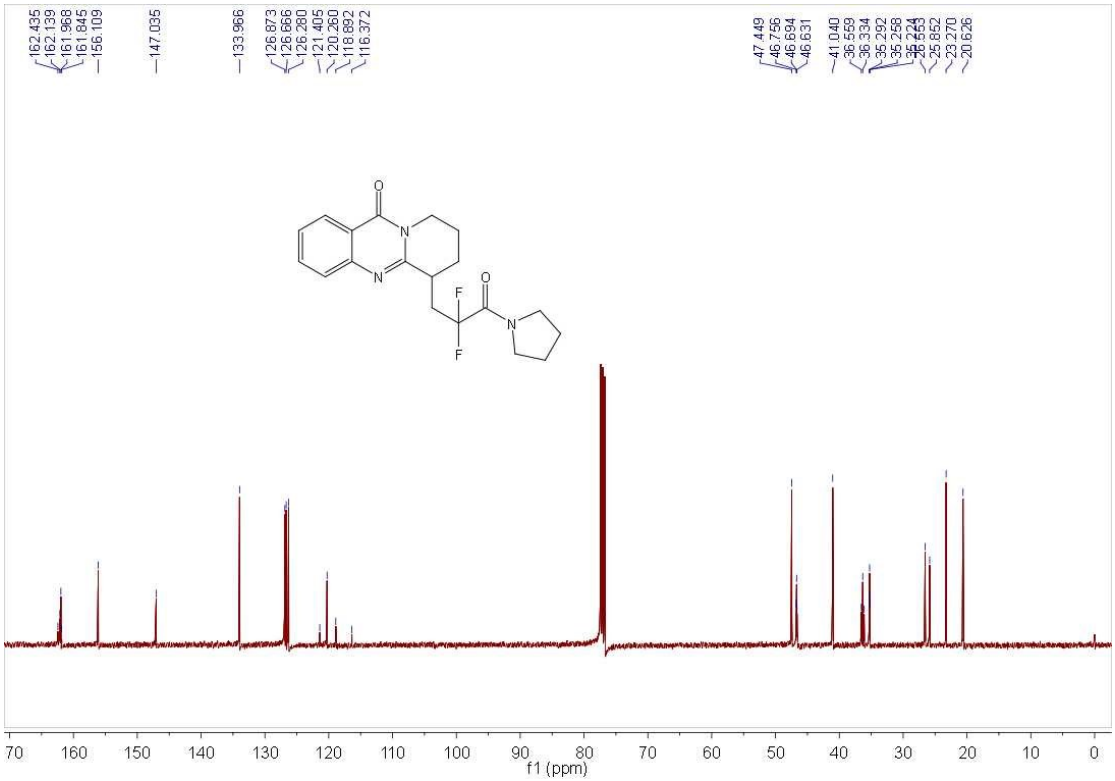

8.280
9.261
7.745
7.726
7.708
7.660
7.640
7.461
7.443
7.424
7.403
7.377
7.359
4.340
4.322
4.305
4.291
3.951
3.934
3.917
3.899
3.883
3.497
3.457
3.404
3.357
3.297
3.181
2.384
2.297
2.280
1.981
1.966
1.950
1.690
1.671
1.646
1.645
O
N
N
O
F
F
N
CH3
1.00
1.07
1.03
3.12
3.05
1.11
1.14
2.02
2.80
1.00
1.97
2.27
1.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

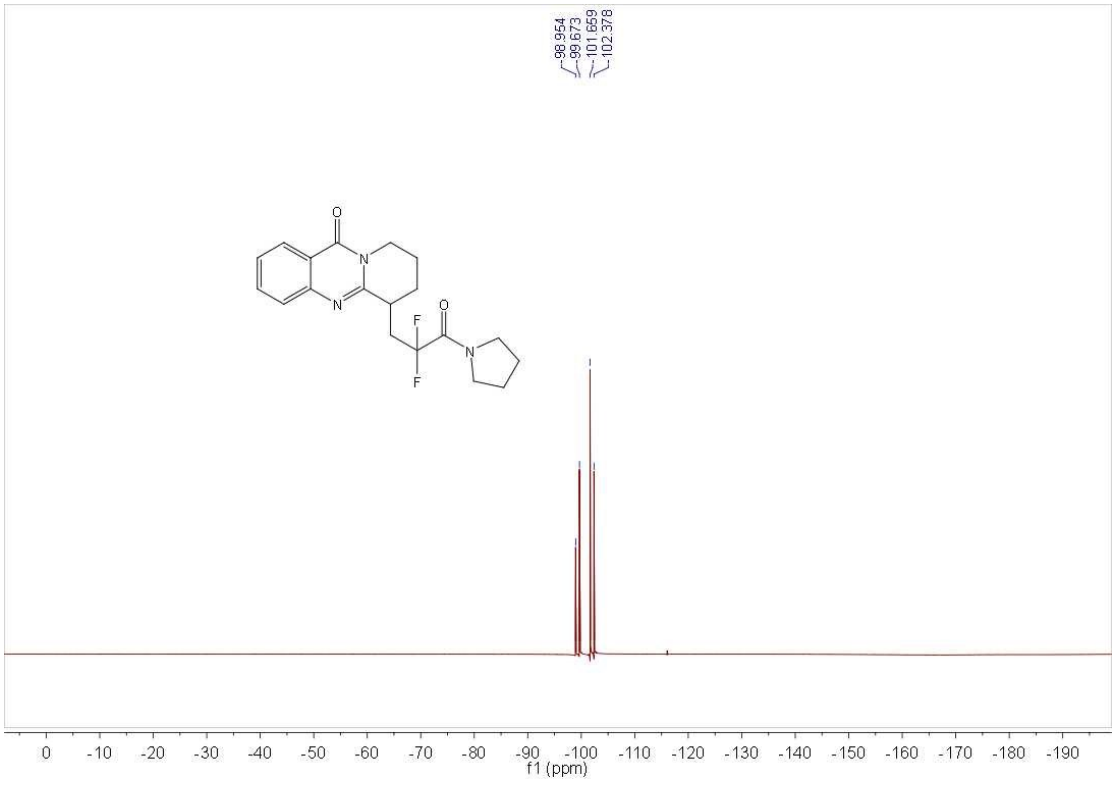

163.655
163.370
163.085
161.949
156.027
147.004
142.476
134.019
129.246
128.238
127.520
126.805
126.683
126.307
121.320
120.257
118.779
41.044
40.067
37.836
37.613
37.395
35.260
25.812
20.539
O
N
N
O
F
F
N
CH3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-92.326
-93.034
-96.263
-96.970
O
N
N
F
O
F
N
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

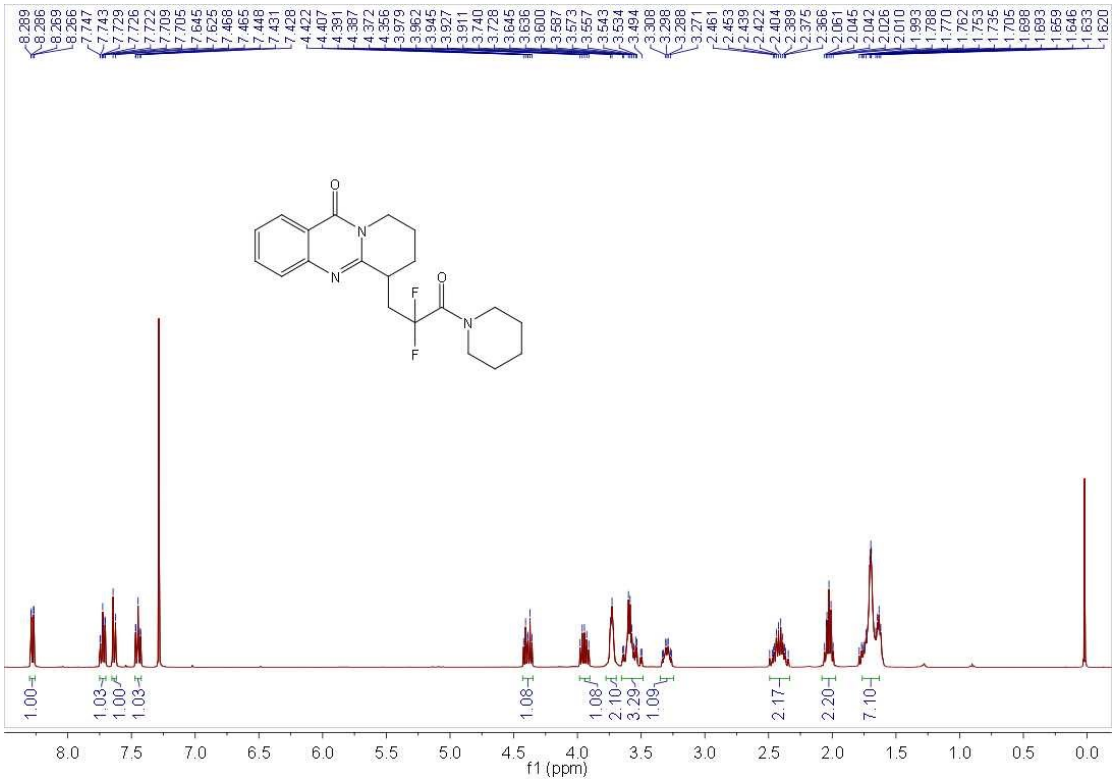
4j

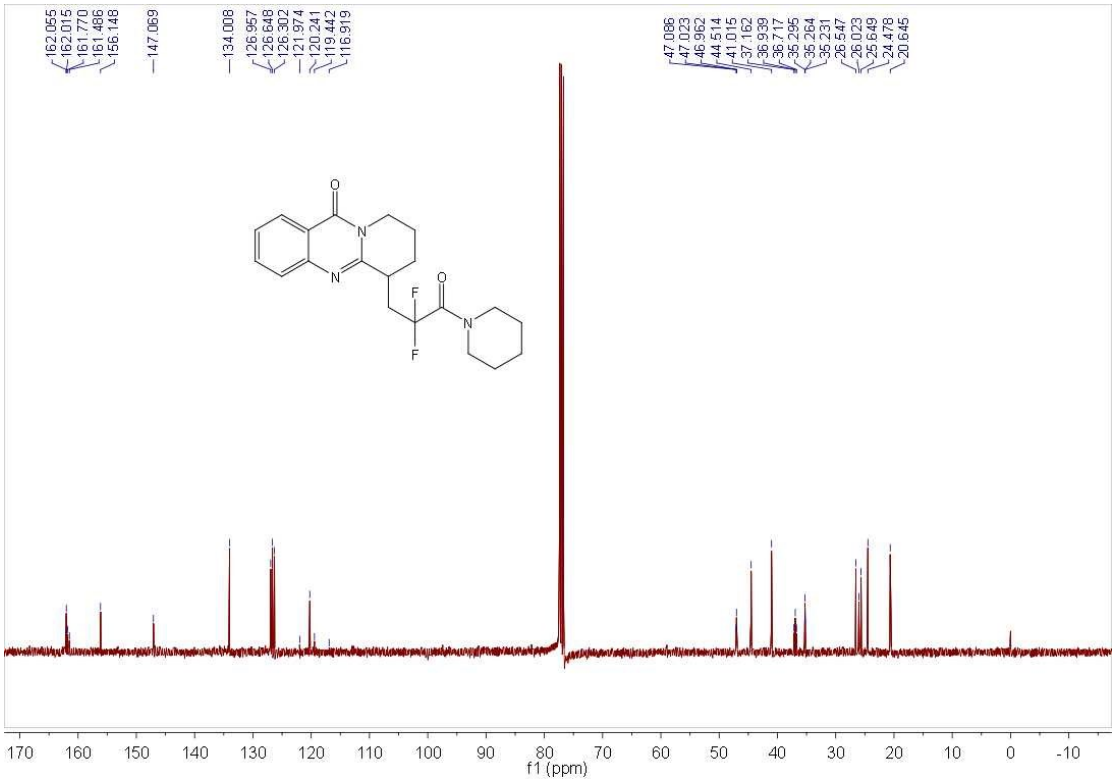

8.261
8.257
8.245
8.241
8.237
7.717
7.699
7.696
7.692
7.683
7.679
7.675
7.601
7.580
7.440
7.437
7.421
7.419
7.406
7.402
7.399
4.371
4.366
4.351
4.346
4.336
4.331
3.953
3.950
3.934
3.918
3.915
3.766
3.750
3.736
3.495
3.476
3.460
3.446
3.432
3.295
3.291
3.286
3.280
3.275
2.394
2.377
2.362
2.346
2.037
2.021
2.002
1.994
1.991
1.984
1.979
1.966
1.962
1.950
1.945
1.861
1.857
1.843
1.831
1.827
1.814
1.810
1.796
1.776
1.747
O
N
N
F
O
F
N
1.00
1.00
1.00
1.00
1.02
1.09
2.11
3.30
1.05
2.28
4.36
2.26
1.03
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

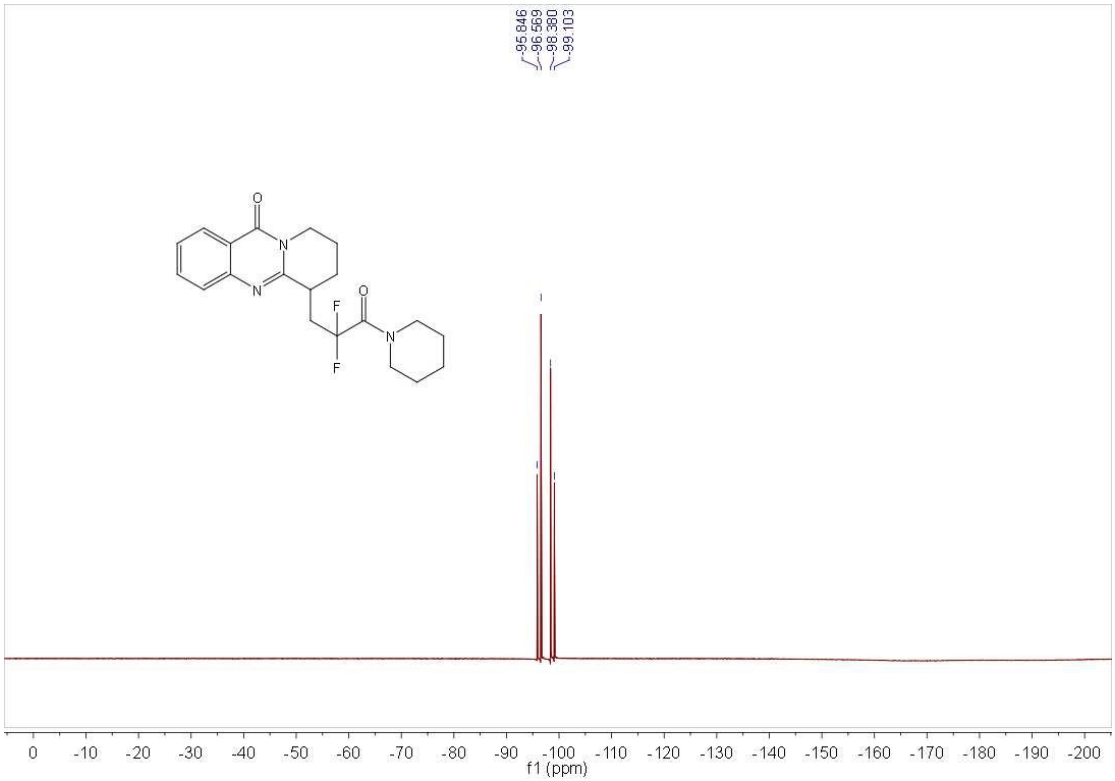

162.435
162.139
161.968
161.845
156.109
147.035
133.966
126.873
126.666
126.280
121.405
120.260
118.892
116.372
47.449
46.756
46.694
46.631
41.040
36.559
36.334
35.292
35.258
25.852
23.270
20.626
O
N
N
F
F
O
N
70 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-98.954
-99.673
-101.659
-102.378
O
N
N
F
F
O
N
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

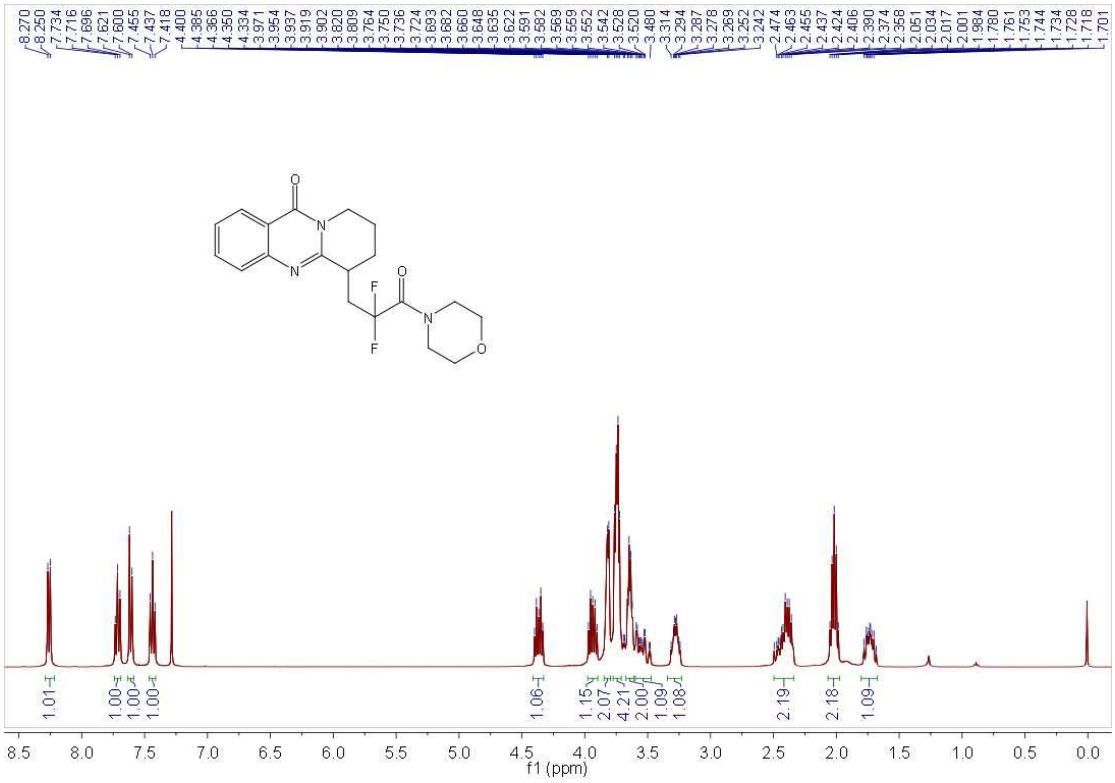
4k

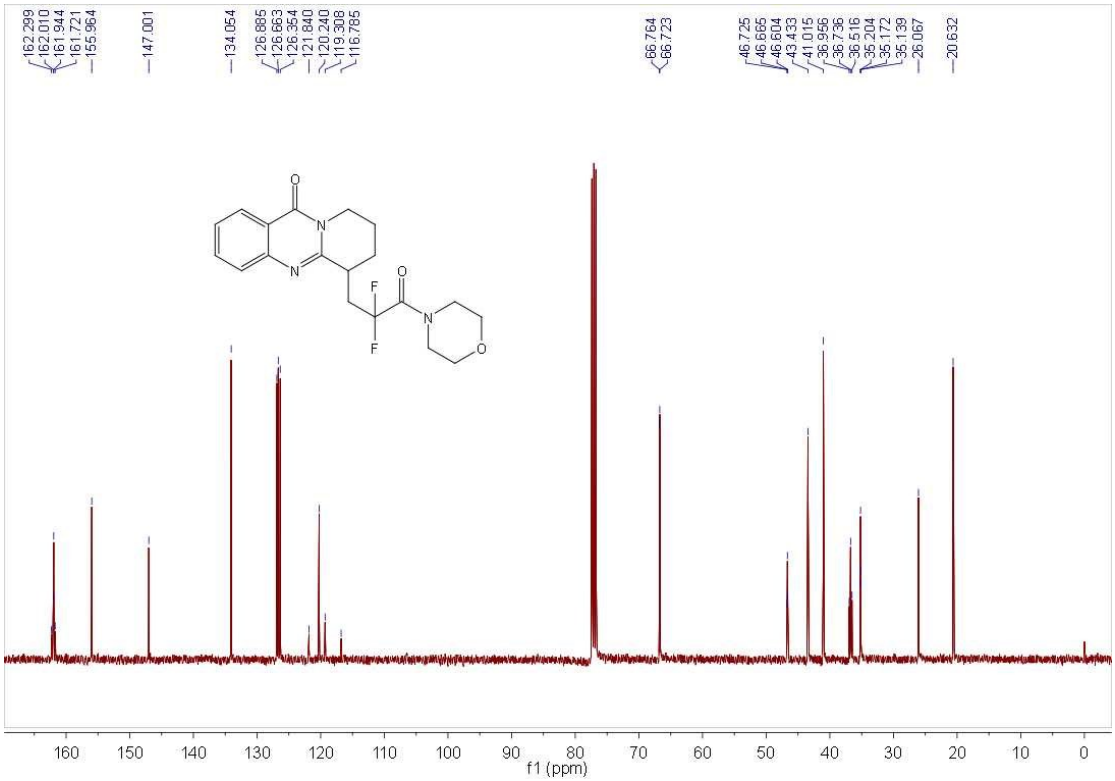


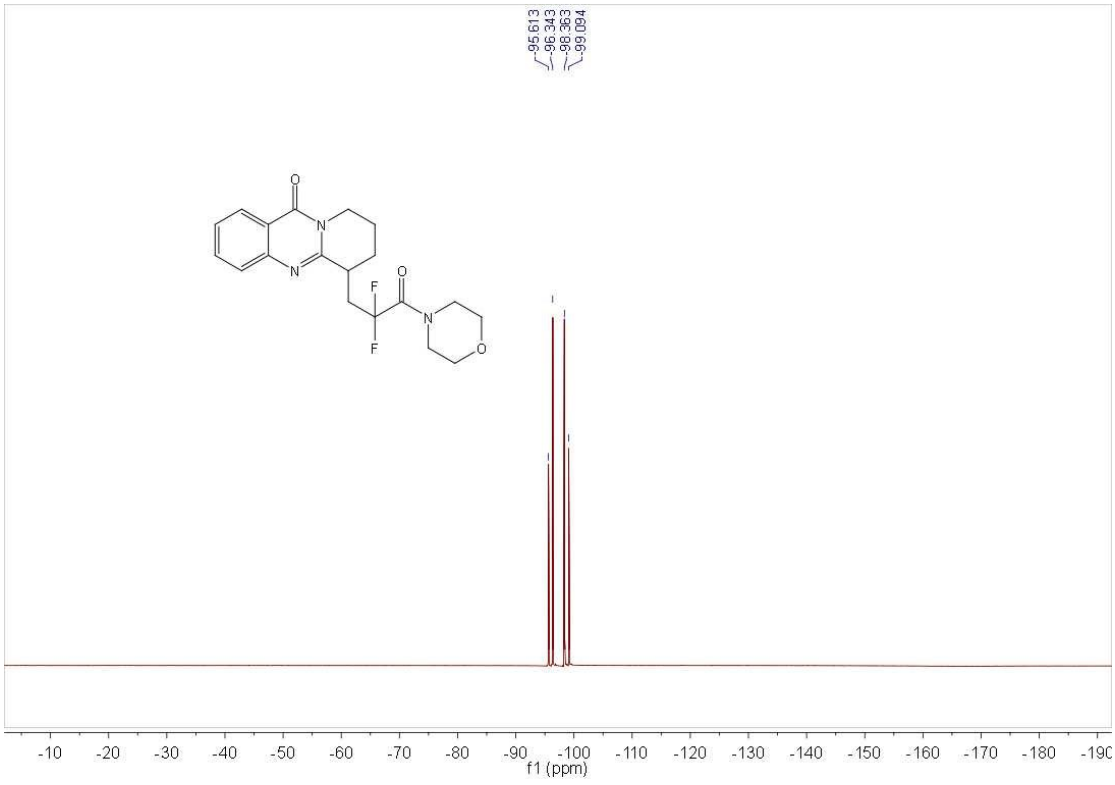



-95.846
-96.569
-98.390
-99.103
O
N
N
F
O
F
N
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

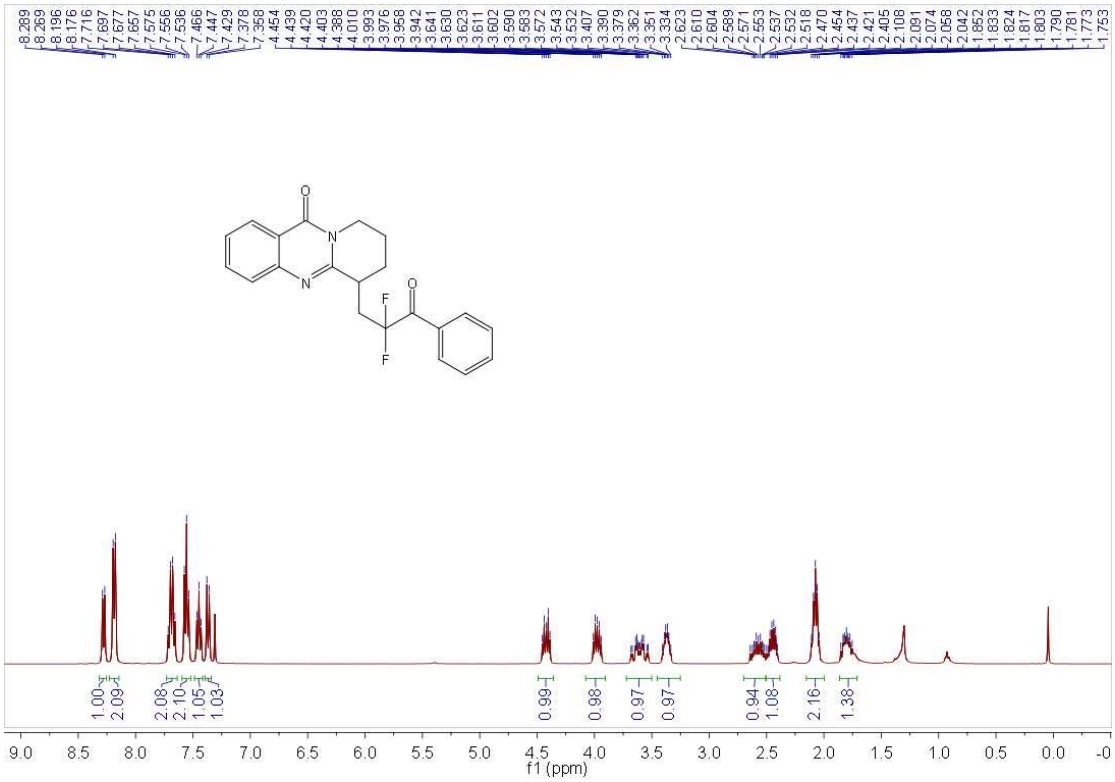
4l

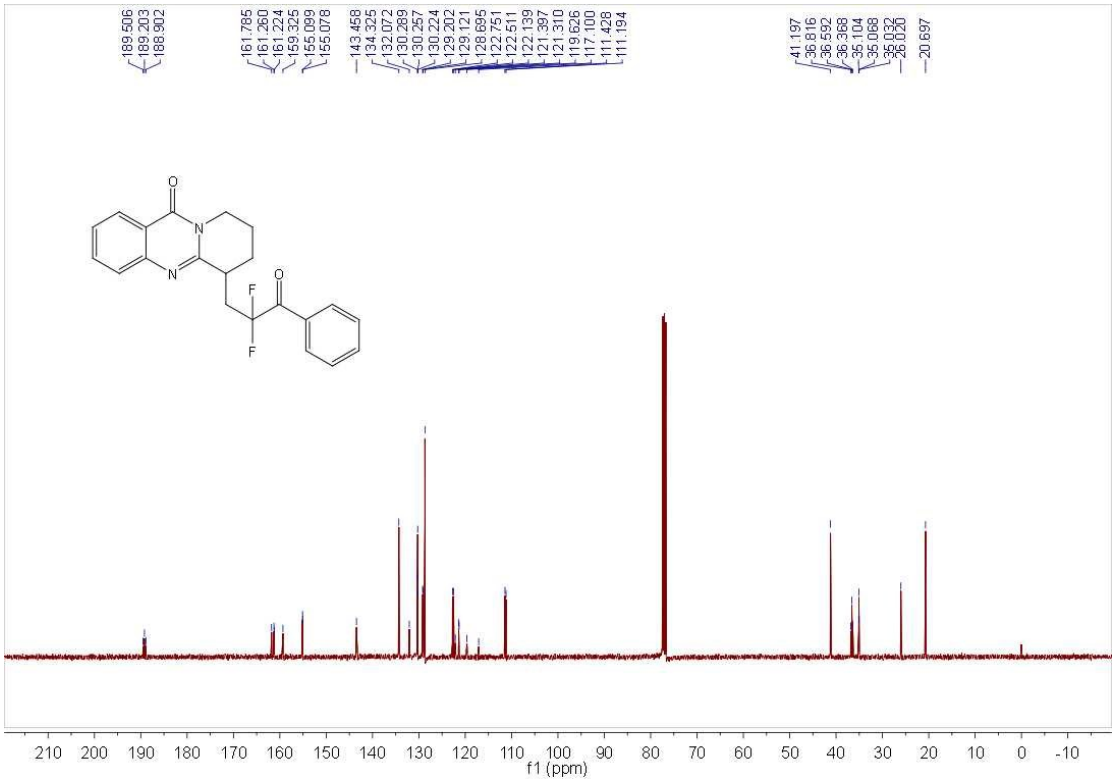

8.270
8.250
7.734
7.716
7.696
7.621
7.600
7.455
7.437
7.418
4.400
4.385
4.366
4.350
4.334
3.971
3.954
3.937
3.919
3.902
3.820
3.809
3.764
3.750
3.736
3.724
3.693
3.682
3.660
3.648
3.635
3.622
3.591
3.582
3.569
3.559
3.552
3.542
3.528
3.520
3.480
3.314
3.294
3.287
3.278
3.269
3.252
3.242
2.474
2.463
2.455
2.437
2.424
2.406
2.390
2.374
2.358
2.051
2.034
2.017
2.001
1.984
1.780
1.761
1.753
1.744
1.734
1.728
1.718
1.701
O
N
N
F
O
F
N
O
1.01
1.00
1.00
1.00
1.06
1.15
2.07
4.21
2.00
1.09
1.08
2.19
2.18
1.09
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

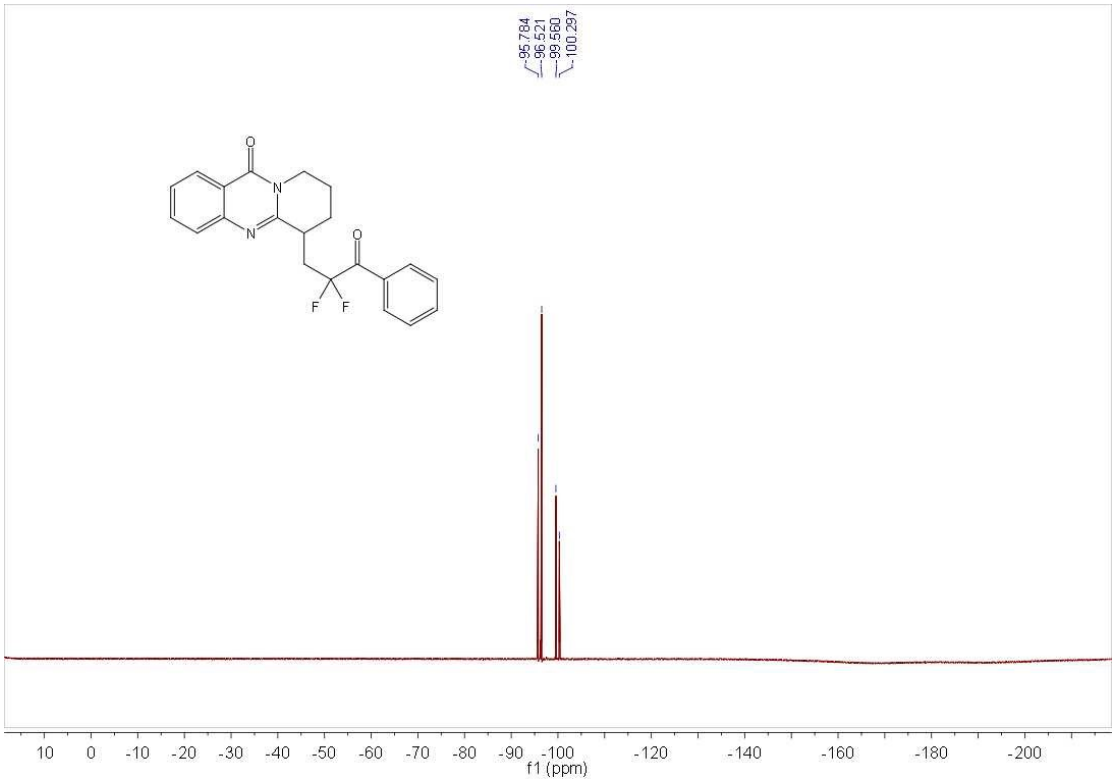

162.299
162.010
161.944
161.721
155.964
147.001
134.054
126.885
126.663
126.354
121.840
120.240
119.308
116.785
66.764
66.723
46.725
46.665
46.604
43.433
41.015
36.956
36.736
36.516
35.204
35.172
35.139
26.067
20.632
O
N
N
F
F
O
N
O
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-95.613
-96.343
-98.363
-99.094
O
N
N
F
F
O
N
O
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

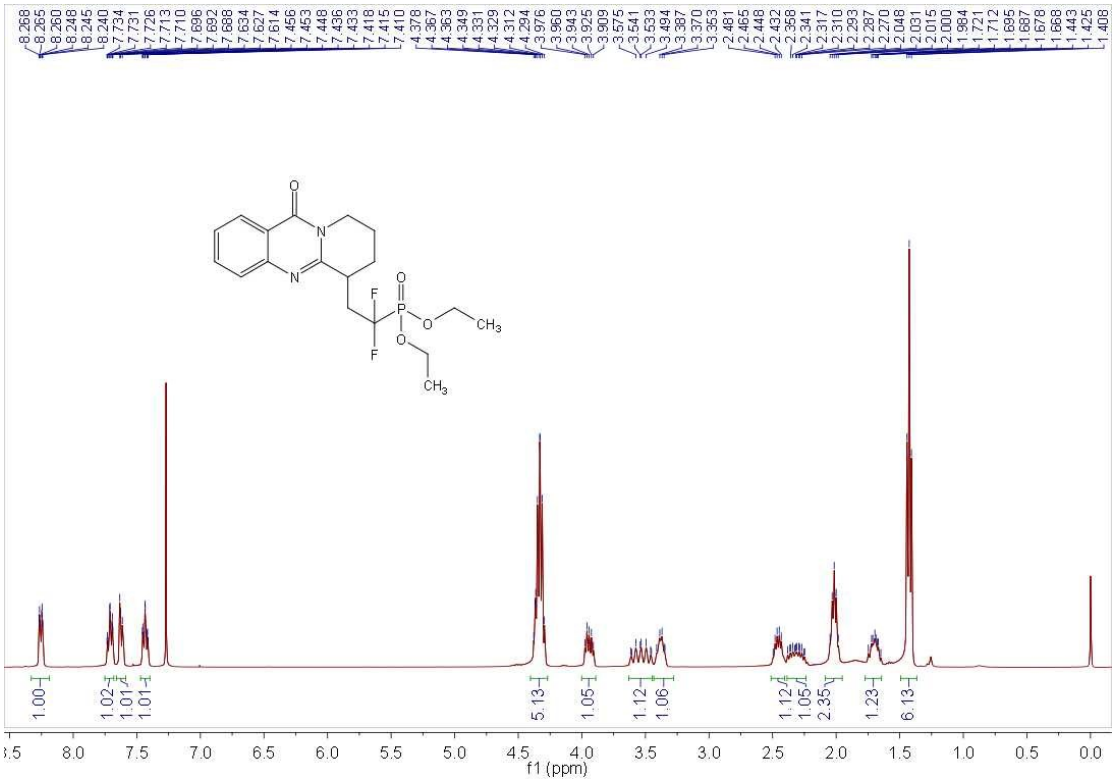
4m

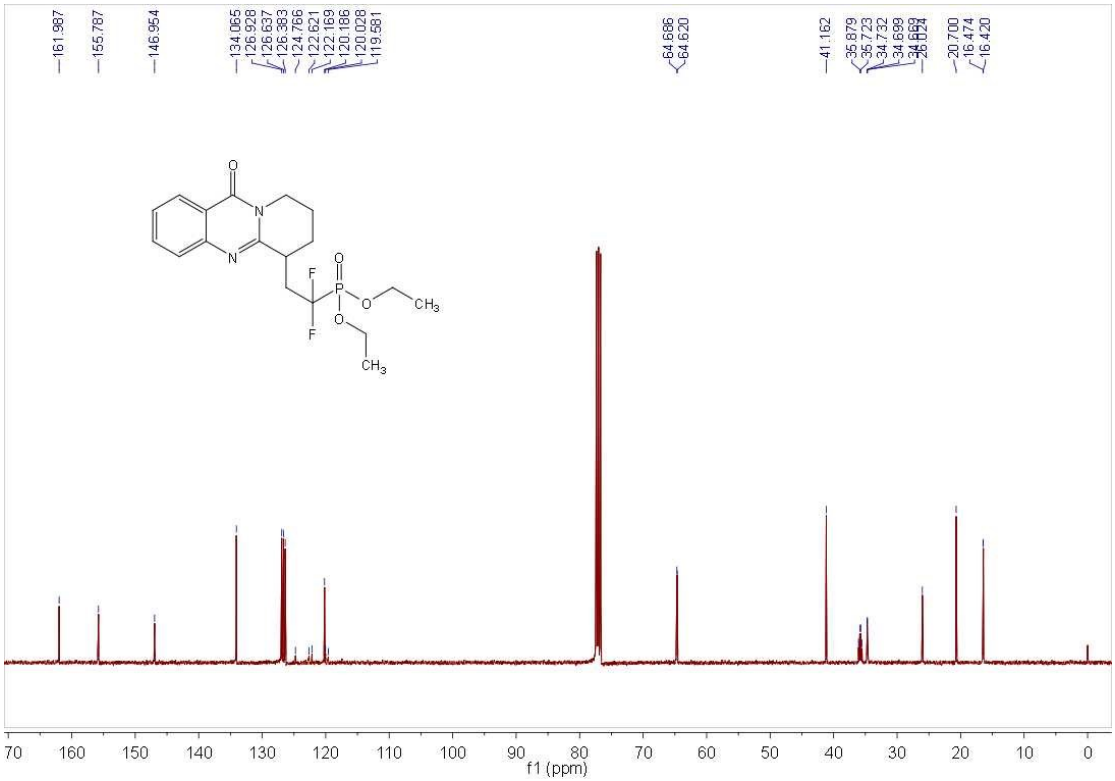

8.289
8.269
8.196
8.176
7.716
7.697
7.677
7.657
7.575
7.556
7.536
7.466
7.447
7.429
7.378
7.358
4.454
4.439
4.420
4.403
4.388
4.010
3.993
3.976
3.958
3.942
3.641
3.630
3.623
3.611
3.602
3.590
3.583
3.572
3.543
3.532
3.407
3.390
3.379
3.362
3.351
3.334
2.623
2.610
2.604
2.589
2.571
2.553
2.537
2.532
2.518
2.470
2.454
2.437
2.421
2.405
2.108
2.091
2.074
2.058
2.042
1.852
1.833
1.824
1.817
1.803
1.790
1.781
1.773
1.753
O
N
N
F
O
F
1.00
2.09
2.08
2.10
1.05
1.03
0.99
0.98
0.97
0.97
0.94
1.08
2.16
1.38
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
f1 (ppm)

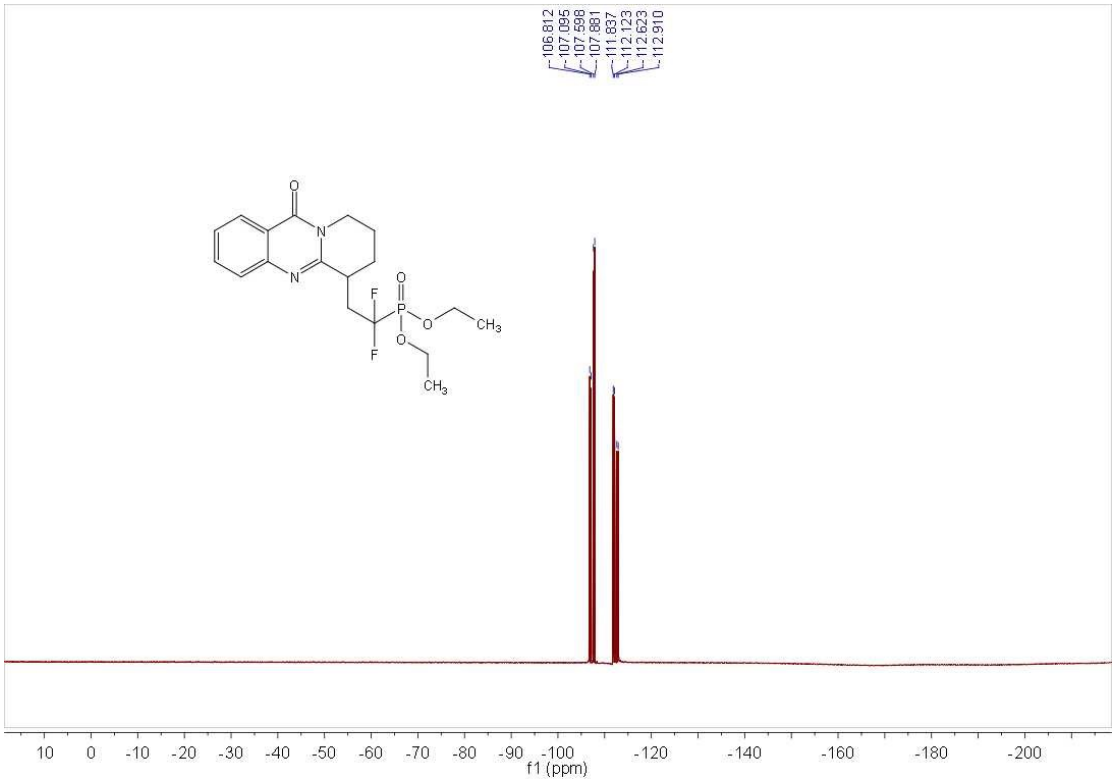

189.506
189.203
188.902
161.785
161.260
161.224
159.325
155.099
155.078
143.458
134.325
132.072
130.289
130.257
130.224
129.202
129.121
128.695
122.751
122.511
122.139
121.397
121.310
119.626
117.100
111.428
111.194
41.197
36.816
36.592
36.368
35.104
35.068
35.032
26.020
20.697
O
N
N
F
O
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


95.784
96.521
99.560
100.297
O
N
N
O
F
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

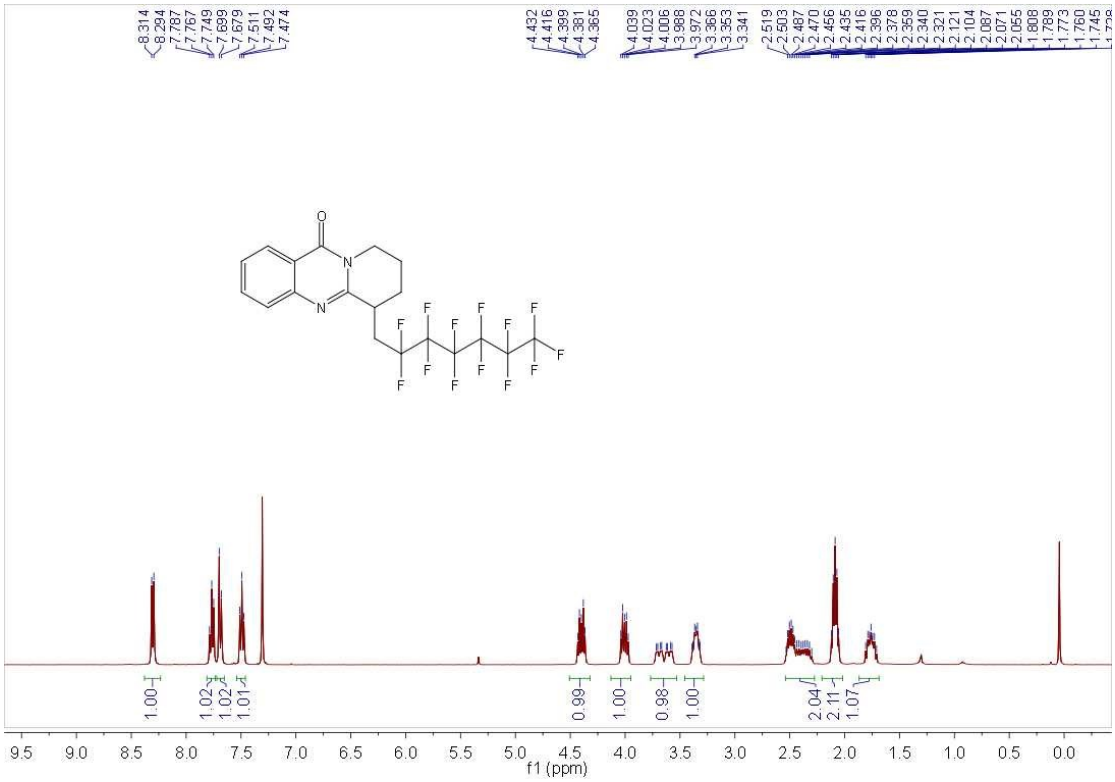
4n

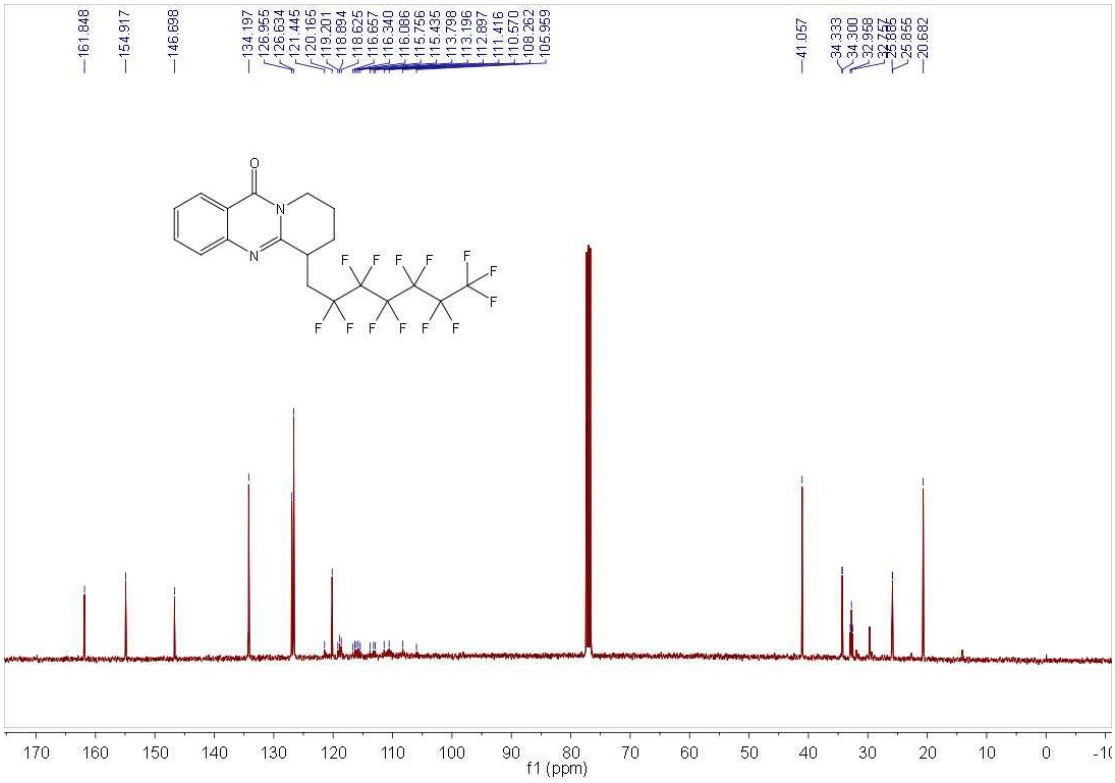

O
N
N
F
F
O
P
O
CH3
O
CH3
1.00
1.02
1.01
1.01
5.13
1.05
1.12
1.06
1.12
1.05
2.35
1.23
6.13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

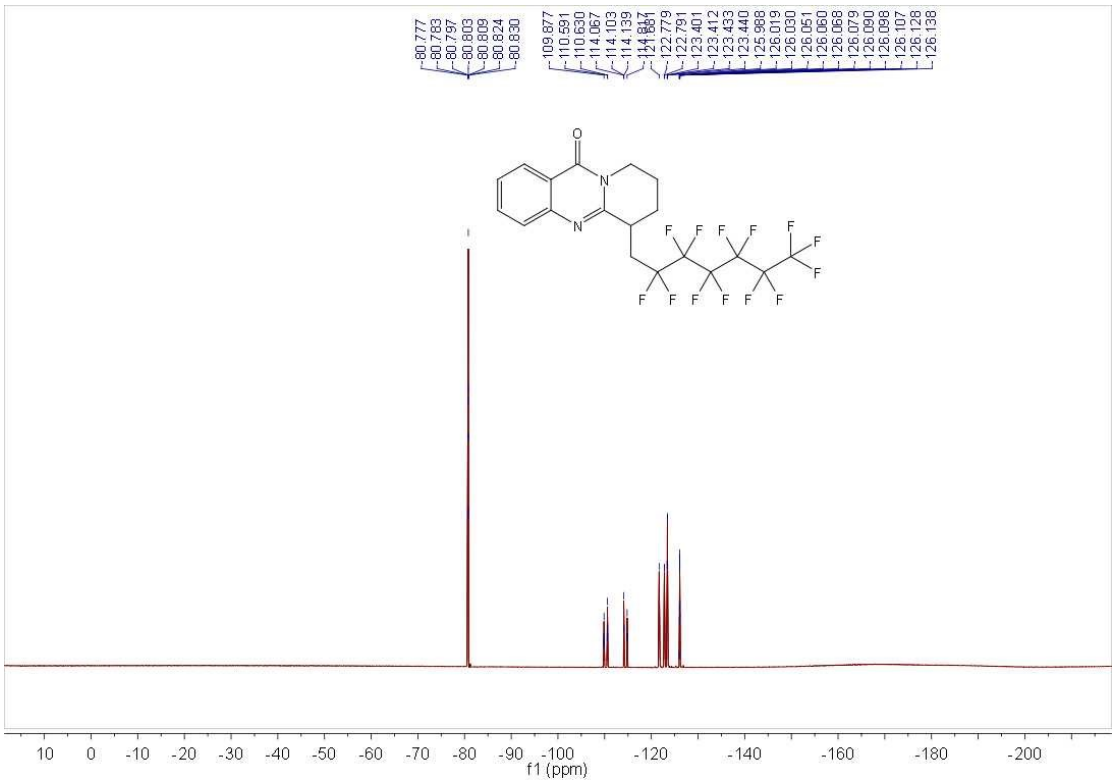

161.987
155.787
146.954
134.065
126.928
126.637
126.383
124.766
122.621
122.169
120.186
120.028
119.581
64.686
64.620
41.162
35.879
35.723
34.732
34.699
20.700
16.474
16.420
f1 (ppm)


106.812
107.095
107.598
107.881
111.837
112.123
112.623
112.910
f1 (ppm)

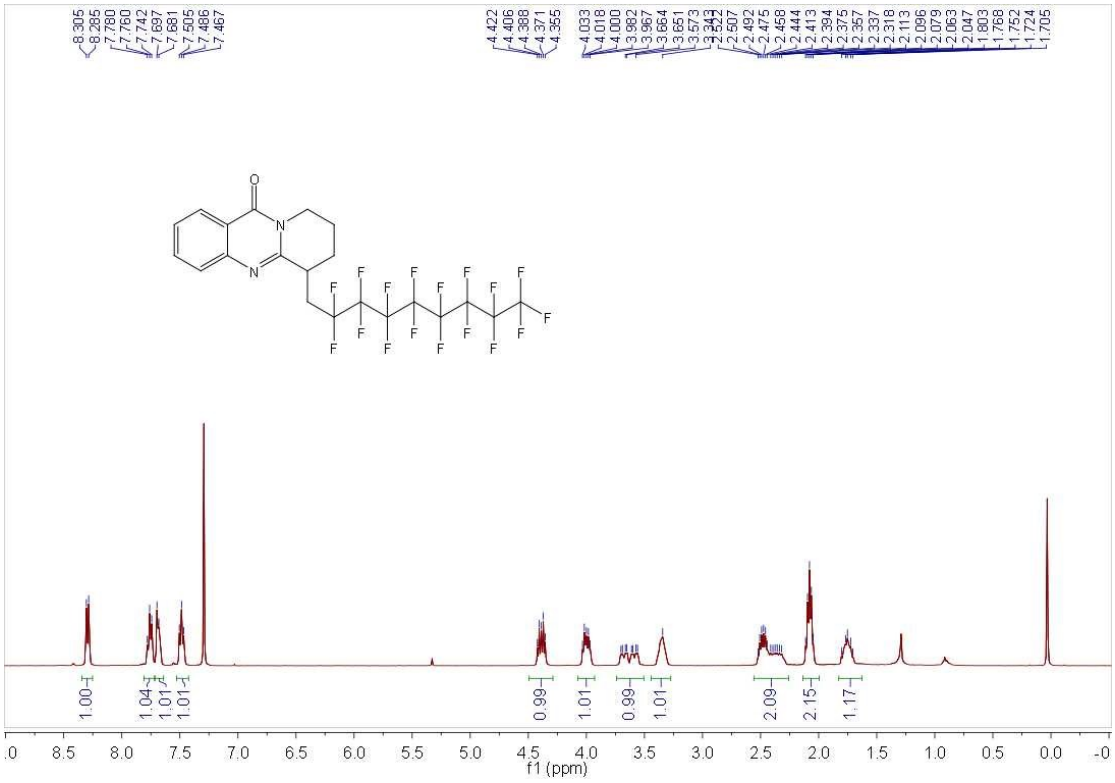
4o

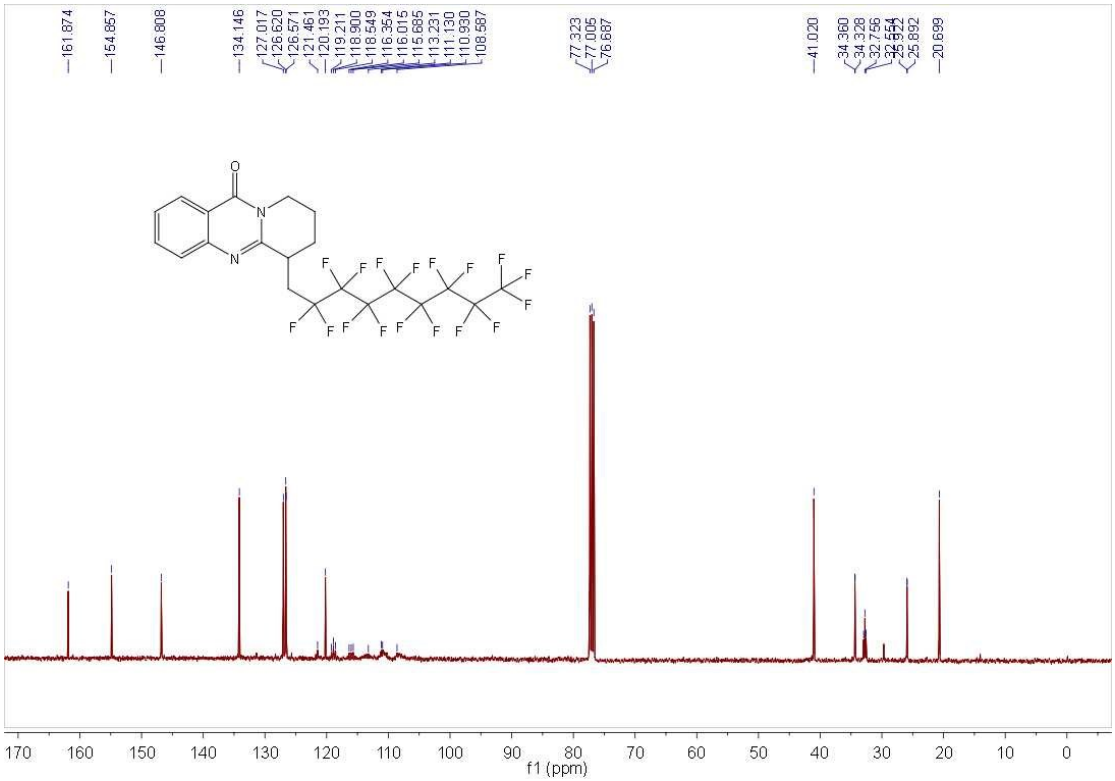

8.314
8.294
7.787
7.767
7.749
7.699
7.679
7.511
7.492
7.474
4.432
4.416
4.399
4.381
4.365
4.039
4.023
4.006
3.988
3.972
3.366
3.353
3.341
2.519
2.503
2.487
2.470
2.456
2.435
2.416
2.396
2.378
2.359
2.340
2.321
2.121
2.104
2.087
2.071
2.055
1.808
1.789
1.773
1.760
1.745
1.00
1.02
1.02
1.01
0.99
1.00
0.98
1.00
2.04
2.11
1.07
f1 (ppm)

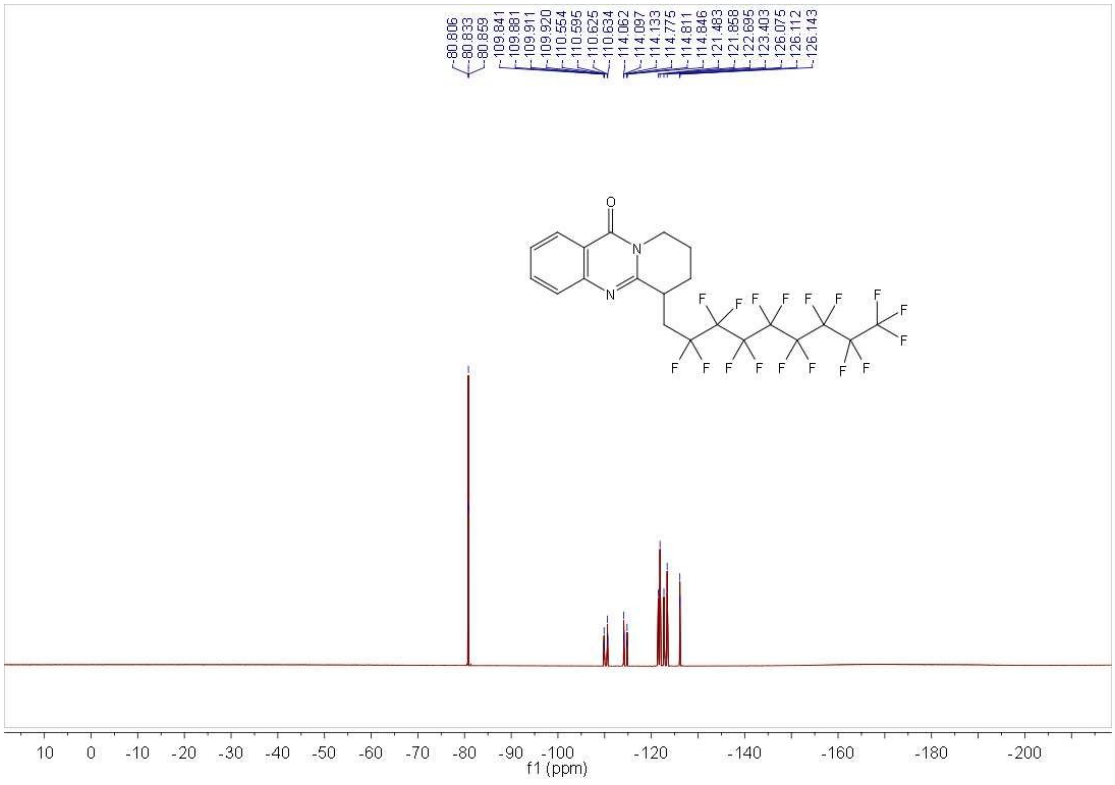

161.848
154.917
146.698
134.197
126.955
126.634
121.445
120.165
119.201
118.894
118.625
116.657
116.340
116.086
115.756
115.435
113.798
113.196
112.897
111.416
110.570
108.262
105.959
41.057
34.333
34.300
32.958
32.757
25.885
25.855
20.682
f1 (ppm)


80.777
80.783
80.797
80.803
80.809
80.824
80.830
109.877
110.591
110.630
114.067
114.103
114.139
121.881
122.779
122.791
123.401
123.412
123.433
123.440
125.988
126.019
126.030
126.051
126.060
126.068
126.079
126.090
126.098
126.107
126.128
126.138
O
N
N
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

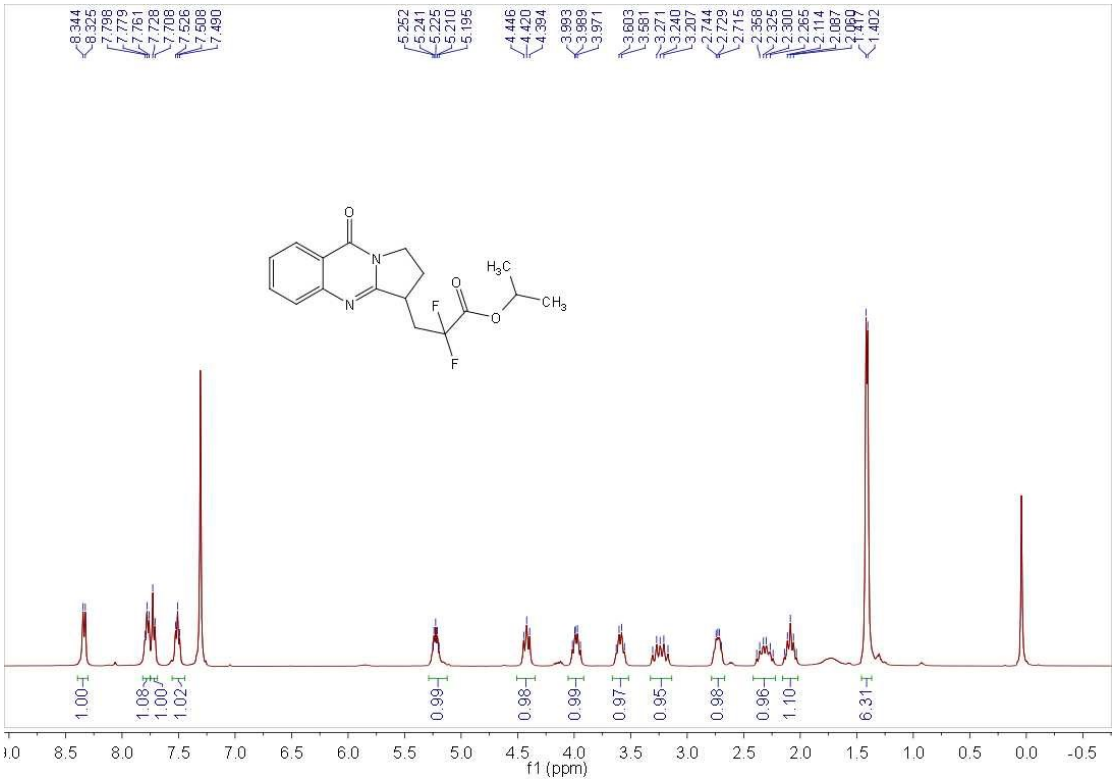
4p

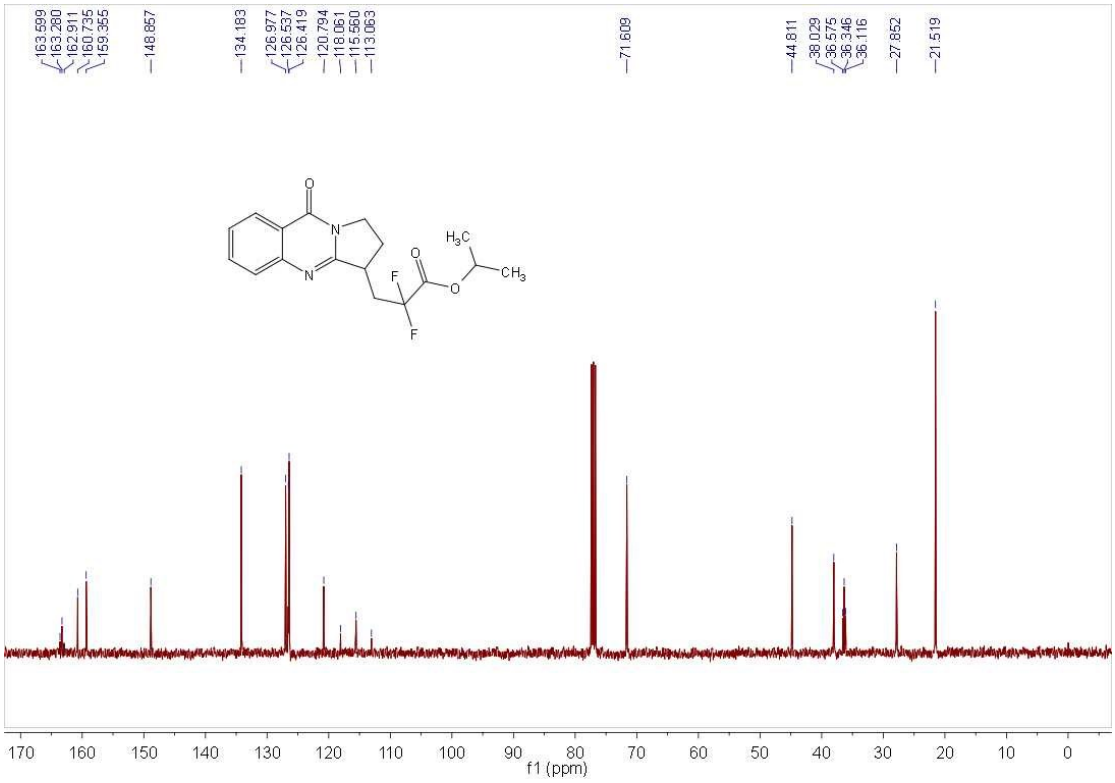

8.305
8.285
7.780
7.760
7.742
7.697
7.681
7.505
7.486
7.467
4.422
4.406
4.388
4.371
4.355
4.033
4.018
4.000
3.982
3.967
3.684
3.651
3.573
2.507
2.492
2.475
2.458
2.444
2.413
2.394
2.375
2.357
2.337
2.318
2.113
2.096
2.079
2.063
2.047
1.803
1.768
1.752
1.724
1.705
O
N
N
F
1.00
1.04
1.01
1.01
0.99
1.01
0.99
1.01
2.09
2.15
1.17
.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
f1 (ppm)

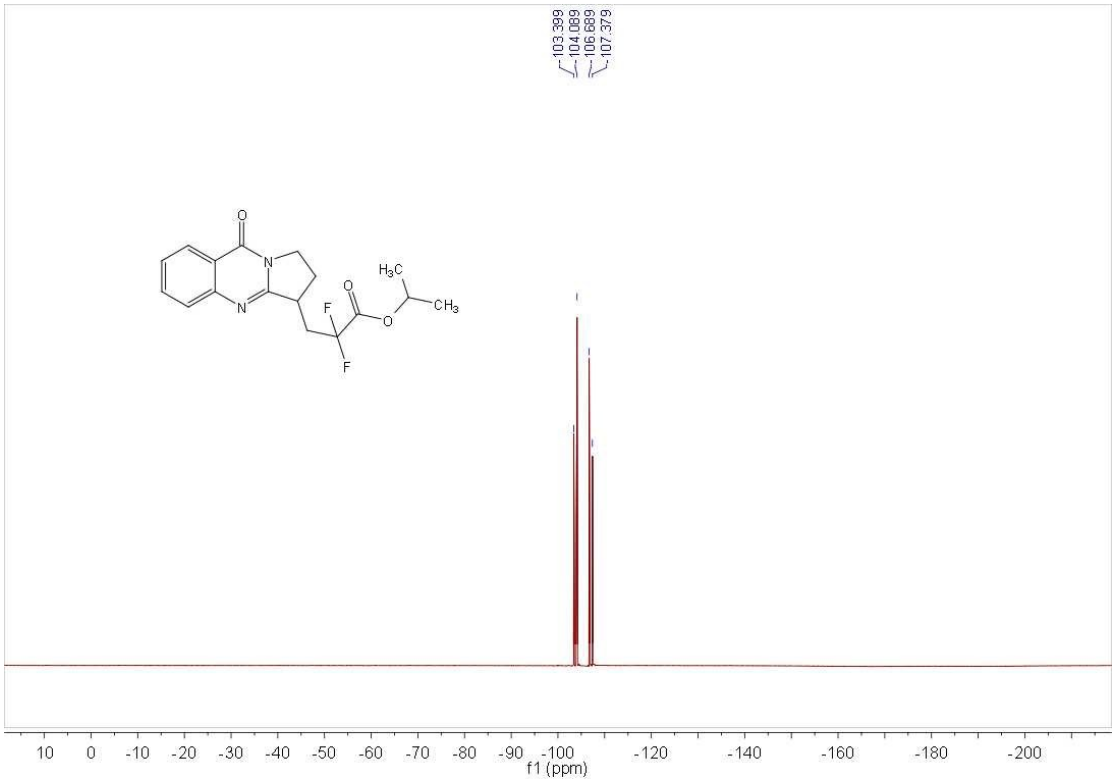

161.874
154.857
146.808
134.146
127.017
126.620
126.571
121.461
120.193
119.211
118.900
118.549
116.354
116.015
115.685
113.231
111.130
110.930
108.587
77.323
77.005
76.687
41.020
34.360
34.328
32.756
32.554
25.922
25.892
20.699
O
N
N
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


80.806
80.833
80.859
109.841
109.881
109.911
109.920
110.554
110.595
110.625
110.634
114.062
114.097
114.133
114.775
114.811
114.846
121.483
121.658
122.695
123.403
126.075
126.112
126.143
O
N
N
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

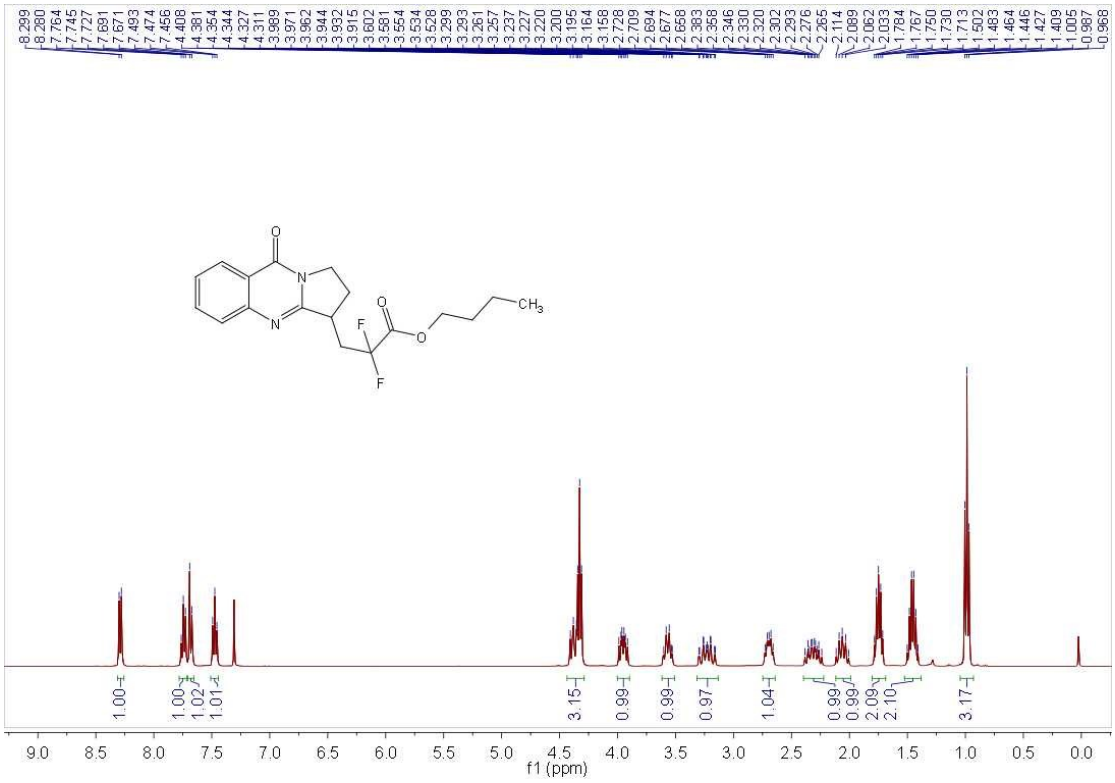
4q

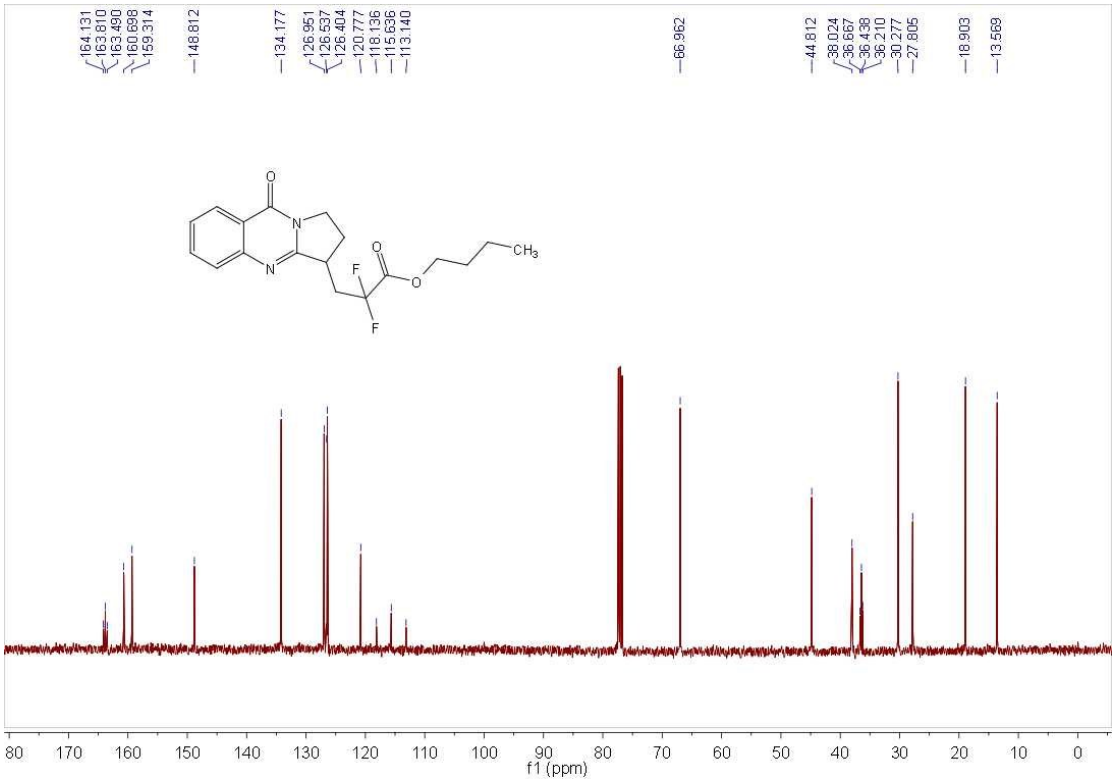

8.344
8.325
7.798
7.779
7.761
7.728
7.708
7.526
7.508
7.490
5.252
5.241
5.225
5.210
5.195
4.446
4.420
4.394
3.993
3.989
3.971
3.603
3.581
3.271
3.240
3.207
2.744
2.729
2.715
2.358
2.325
2.300
2.265
2.114
2.087
2.069
1.417
1.402
1.00
1.08
1.00
1.02
0.99
0.98
0.99
0.97
0.95
0.98
0.96
1.10
6.31
f1 (ppm)

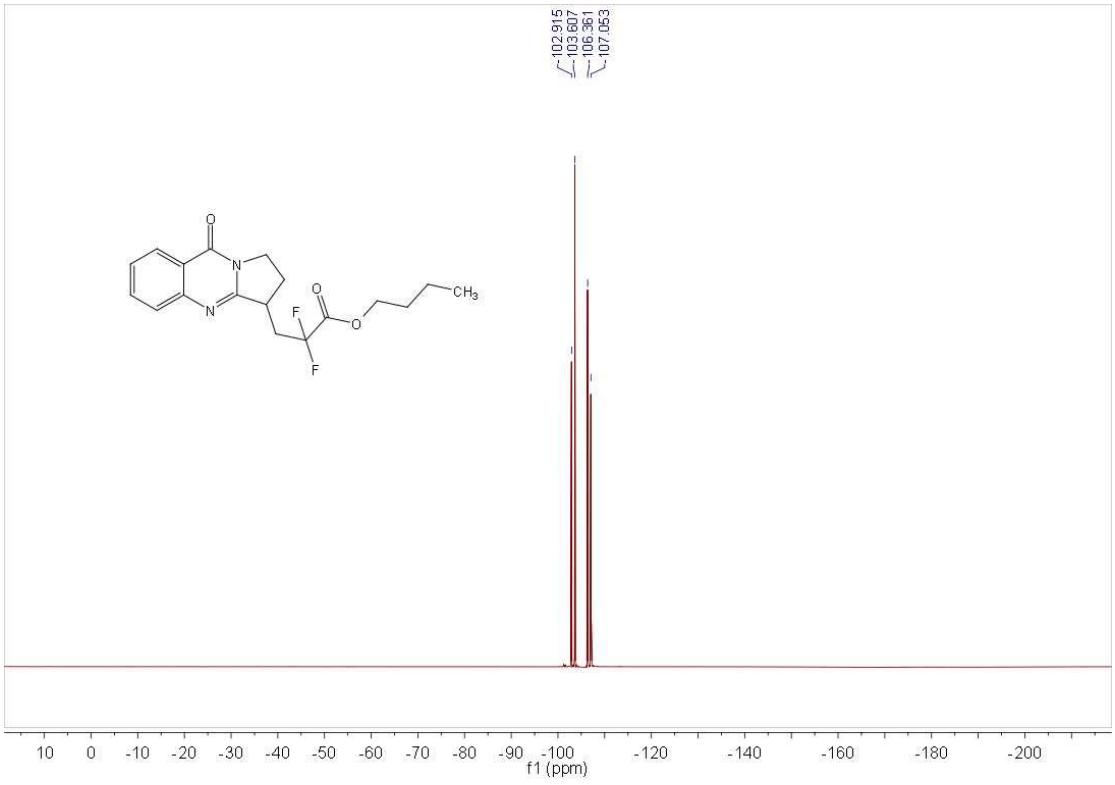

163.599
163.280
162.911
160.735
159.355
148.857
134.183
126.977
126.537
126.419
120.794
118.061
115.560
113.063
71.609
44.811
38.029
36.575
36.346
36.116
27.852
21.519
f1 (ppm)



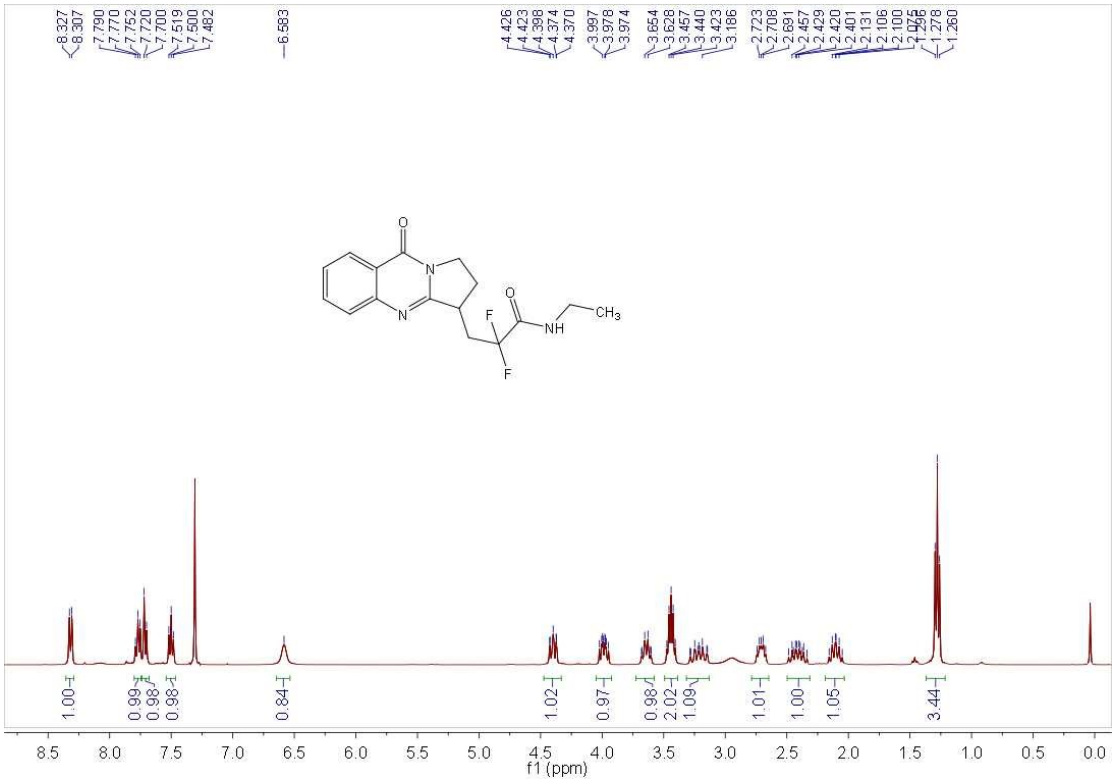
4r

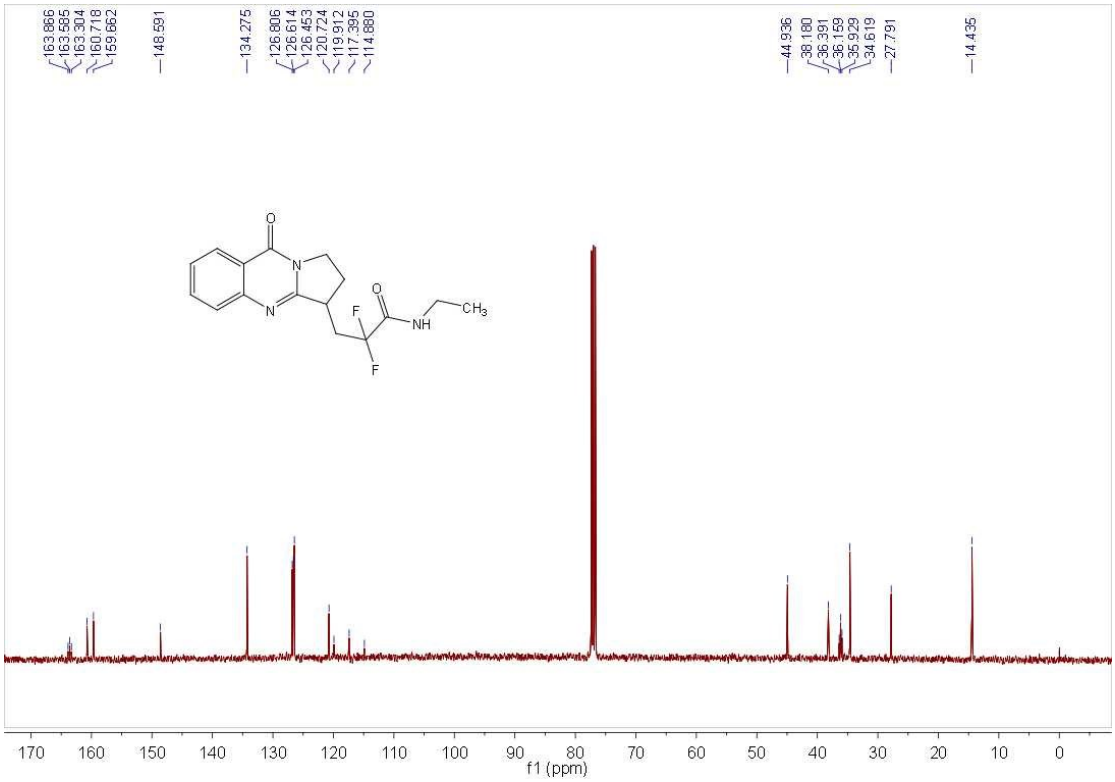


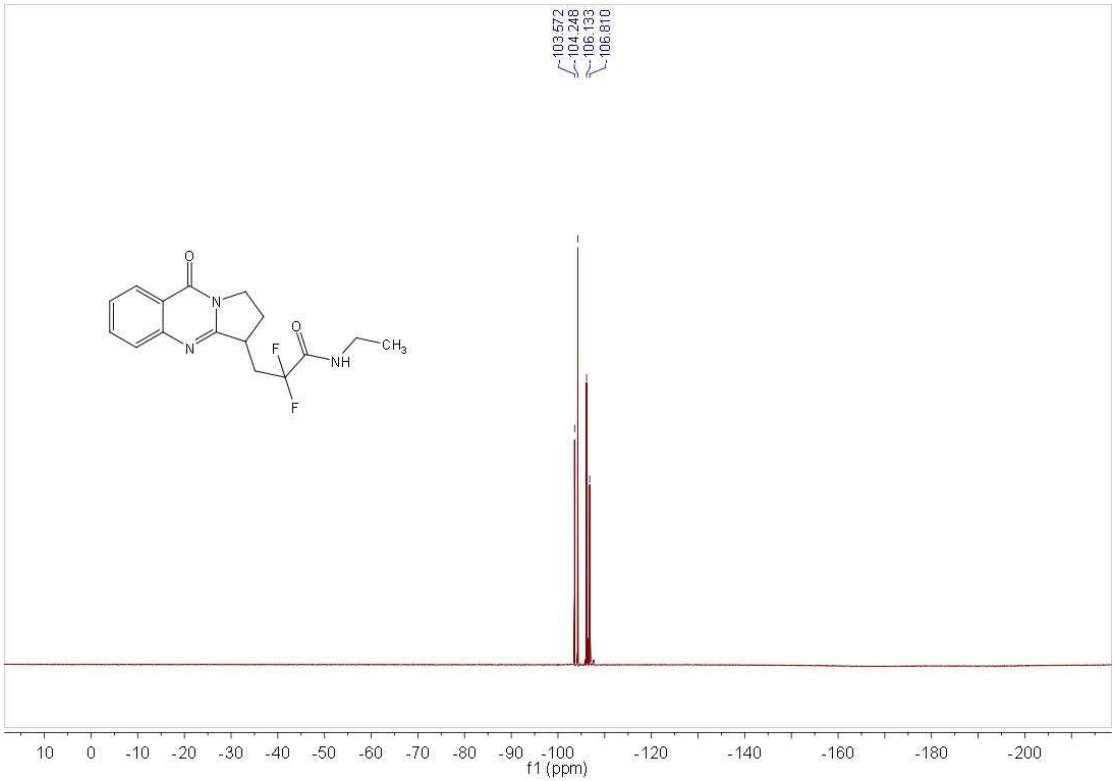

164.131
163.810
163.490
160.698
159.314
148.812
134.177
126.951
126.537
126.404
120.777
118.136
115.636
113.140
66.962
44.812
38.024
36.667
36.438
36.210
30.277
27.805
18.903
13.569
O
N
N
O
O
F
F
CH3
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


102.915
103.607
106.361
107.053
O
N
N
O
O
F
F
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

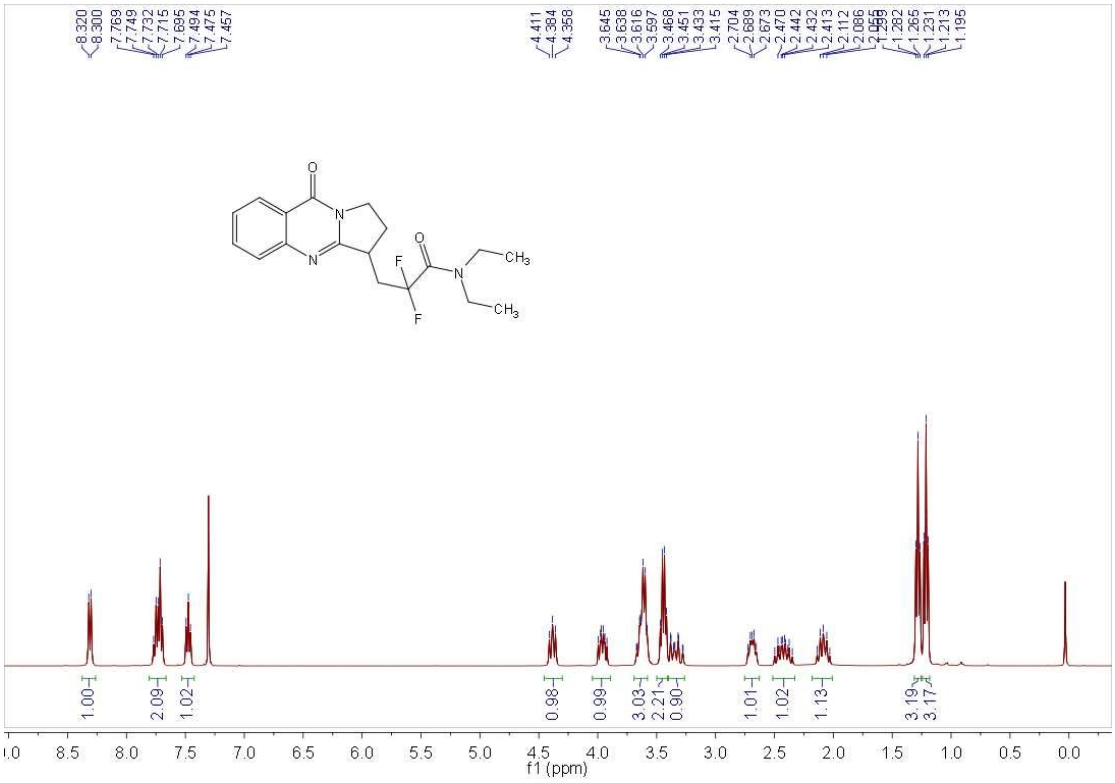
4s

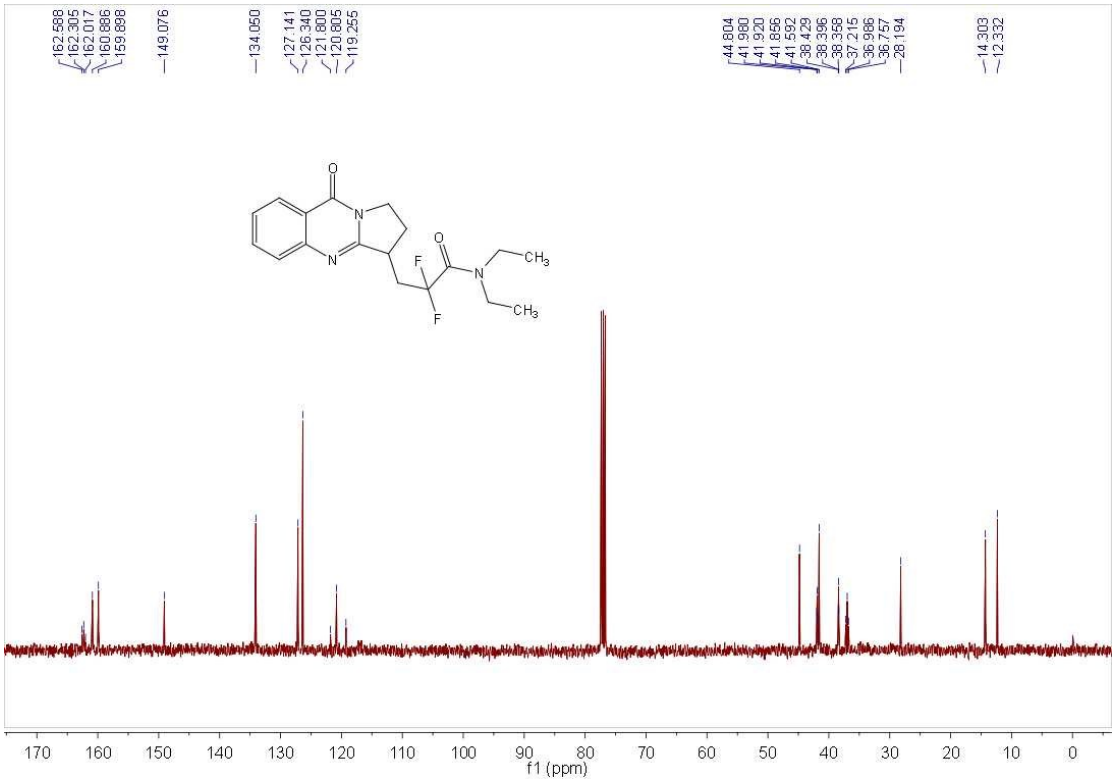

8.327
8.307
7.790
7.770
7.752
7.720
7.700
7.519
7.500
7.482
6.583
4.426
4.423
4.398
4.374
4.370
3.997
3.978
3.974
3.654
3.628
3.457
3.440
3.423
3.186
2.723
2.708
2.691
2.457
2.429
2.420
2.401
2.131
2.106
2.100
1.278
1.260
1.00
0.99
0.98
0.98
0.84
1.02
0.97
0.98
2.02
1.09
1.01
1.00
1.05
3.44
f1 (ppm)

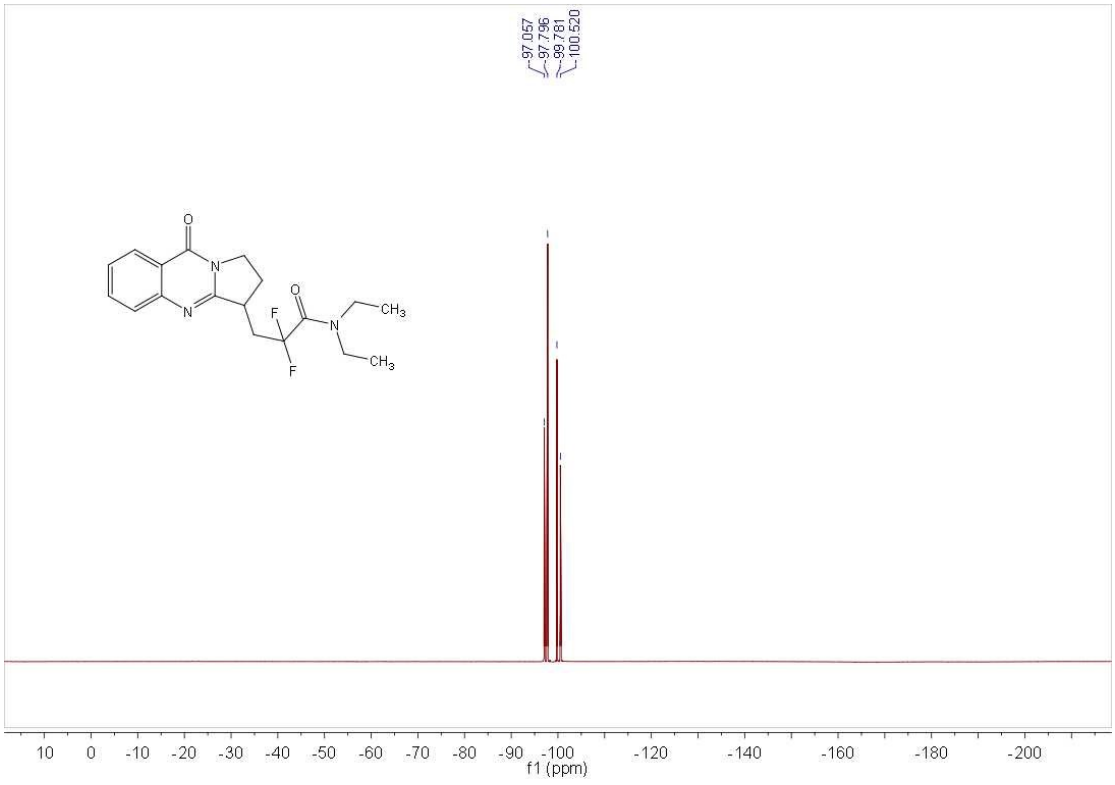

163.866
163.585
163.304
160.718
159.662
148.591
134.275
126.806
126.614
126.453
120.724
119.912
117.395
114.880
44.936
38.180
36.391
36.159
35.929
34.619
27.791
14.435
f1 (ppm)


103.572
104.248
106.133
106.810
O
N
N
O
F
F
NH
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

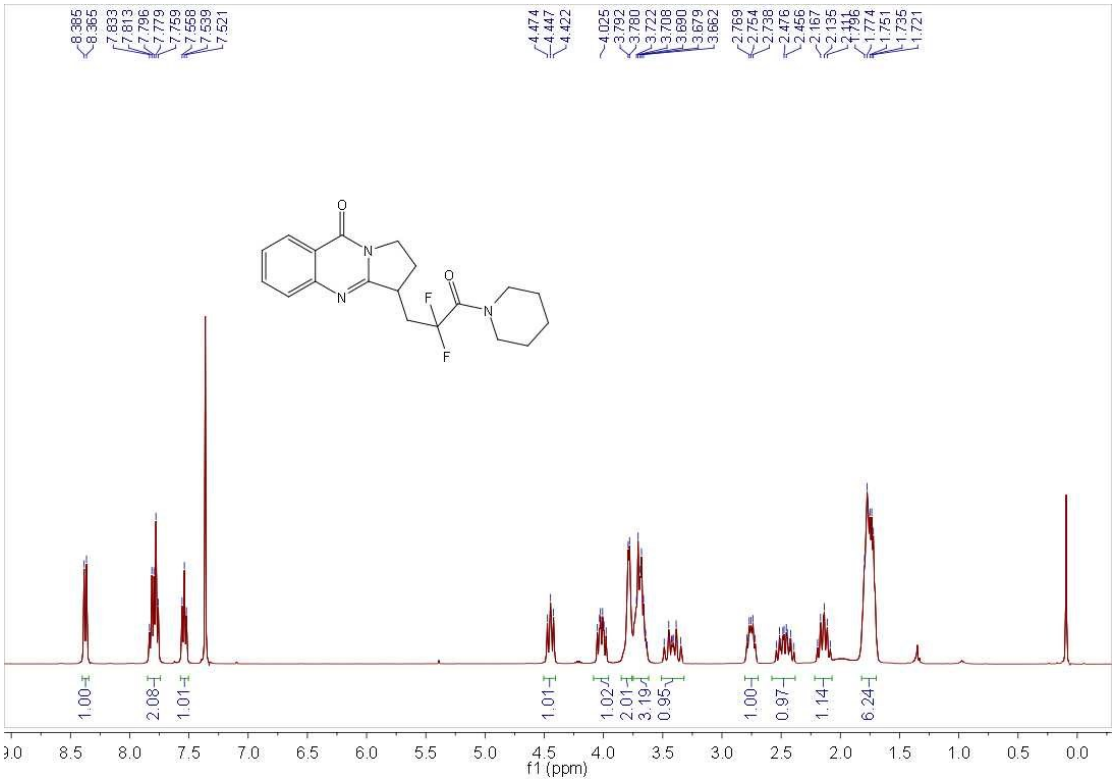
4t

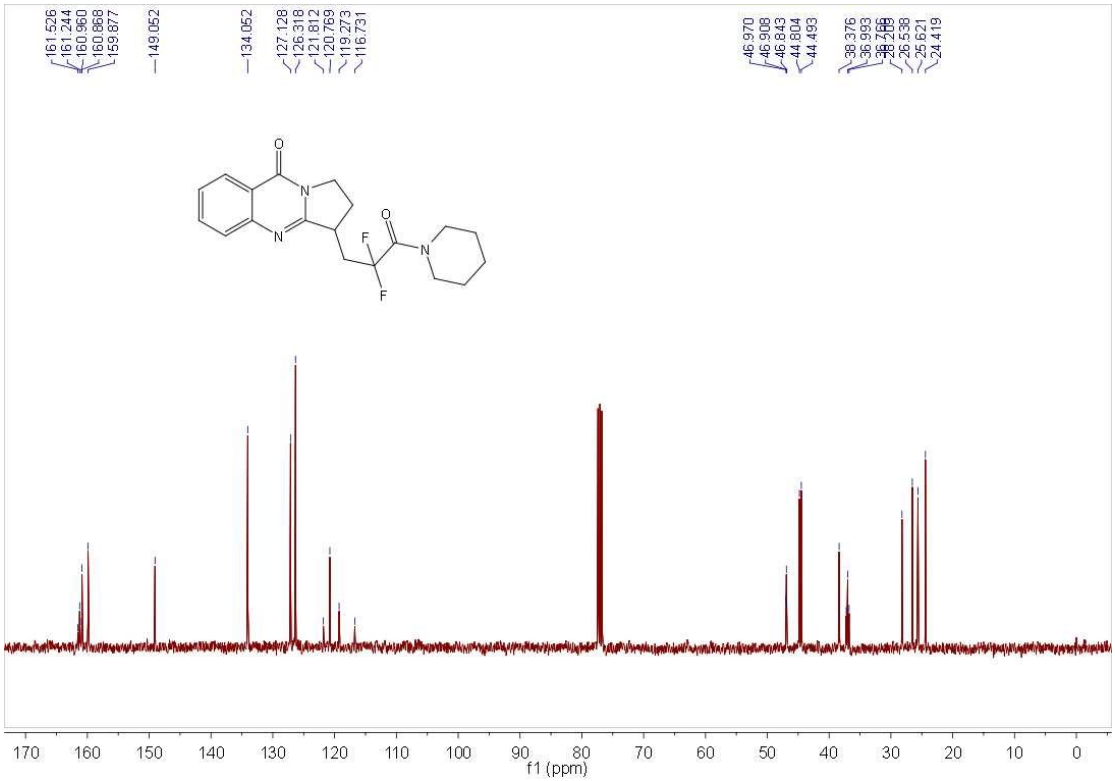

8.320
8.300
7.769
7.749
7.732
7.715
7.695
7.494
7.475
7.457
4.411
4.384
4.358
3.645
3.638
3.616
3.597
3.468
3.451
3.433
3.415
2.704
2.689
2.673
2.470
2.442
2.432
2.413
2.112
2.086
1.282
1.265
1.231
1.213
1.195
O
N
N
O
F
F
N
CH3
CH3
1.00
2.09
1.02
0.98
0.99
3.03
2.21
0.90
1.01
1.02
1.13
3.19
3.17
1.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

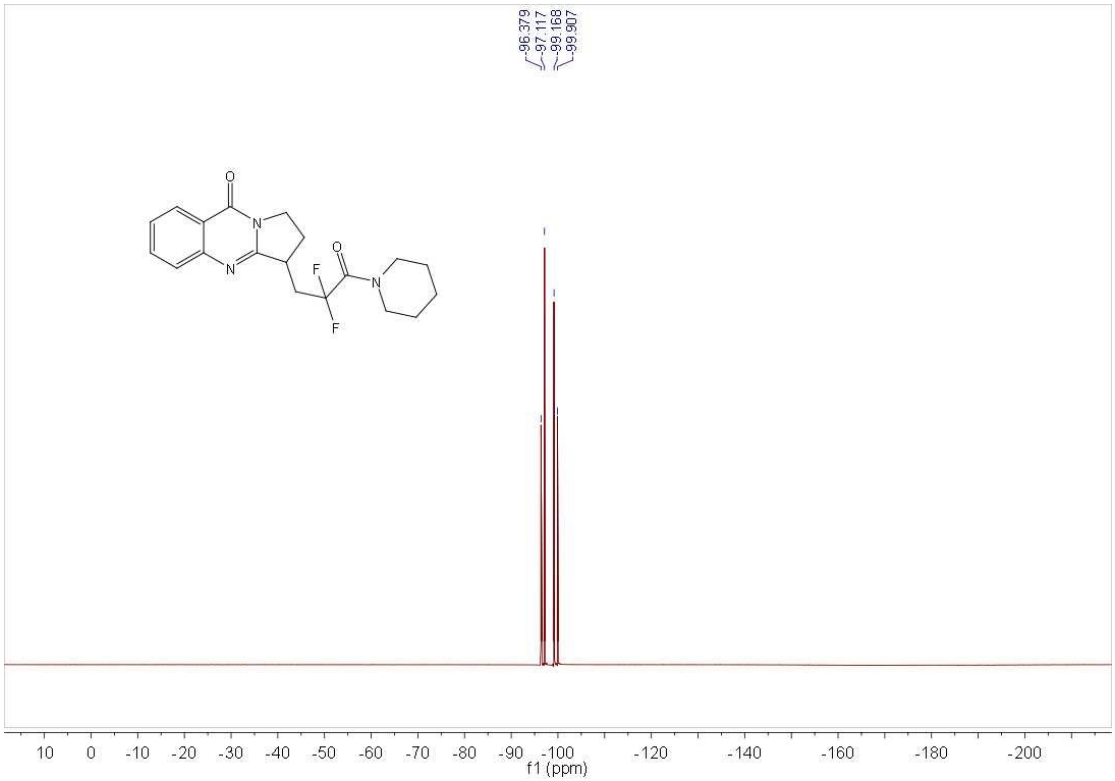

162.588
162.305
162.017
160.886
159.898
149.076
134.050
127.141
126.340
121.800
120.805
119.255
44.804
41.980
41.920
41.856
41.592
38.429
38.396
38.358
37.215
36.986
36.757
28.194
14.303
12.332
O
N
N
O
F
F
N
CH3
CH3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


97.057
97.796
99.781
100.520
O
N
N
O
F
F
N
CH3
CH3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

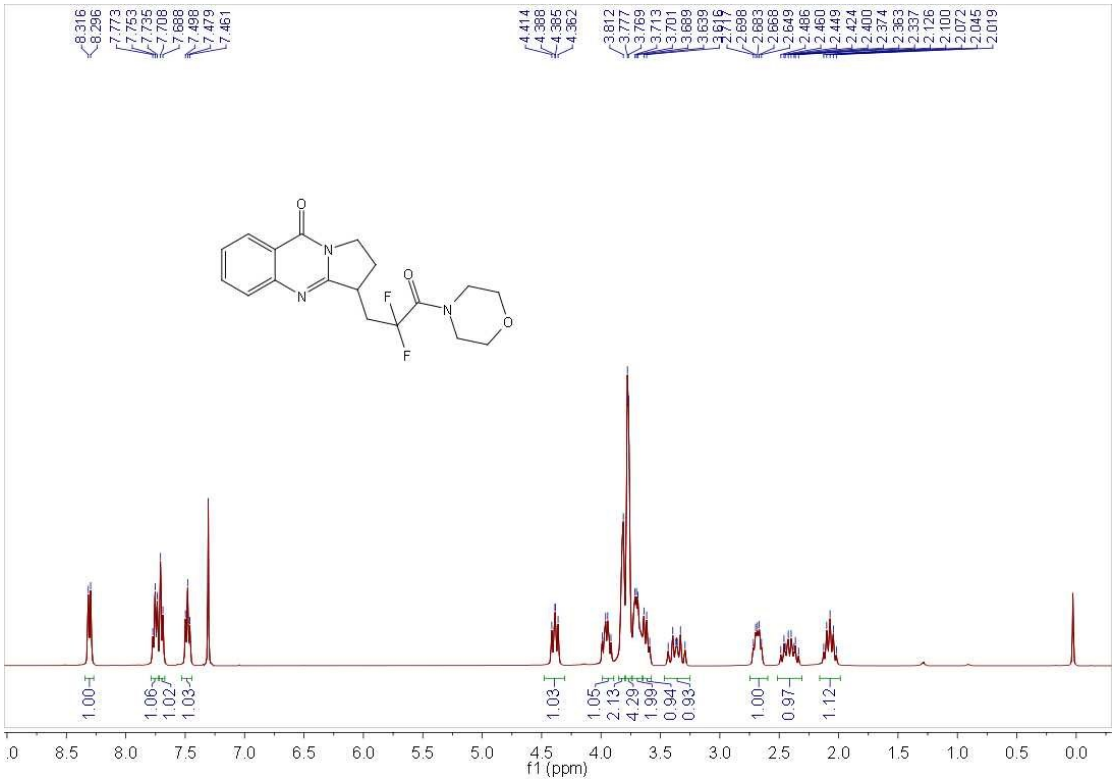
4u

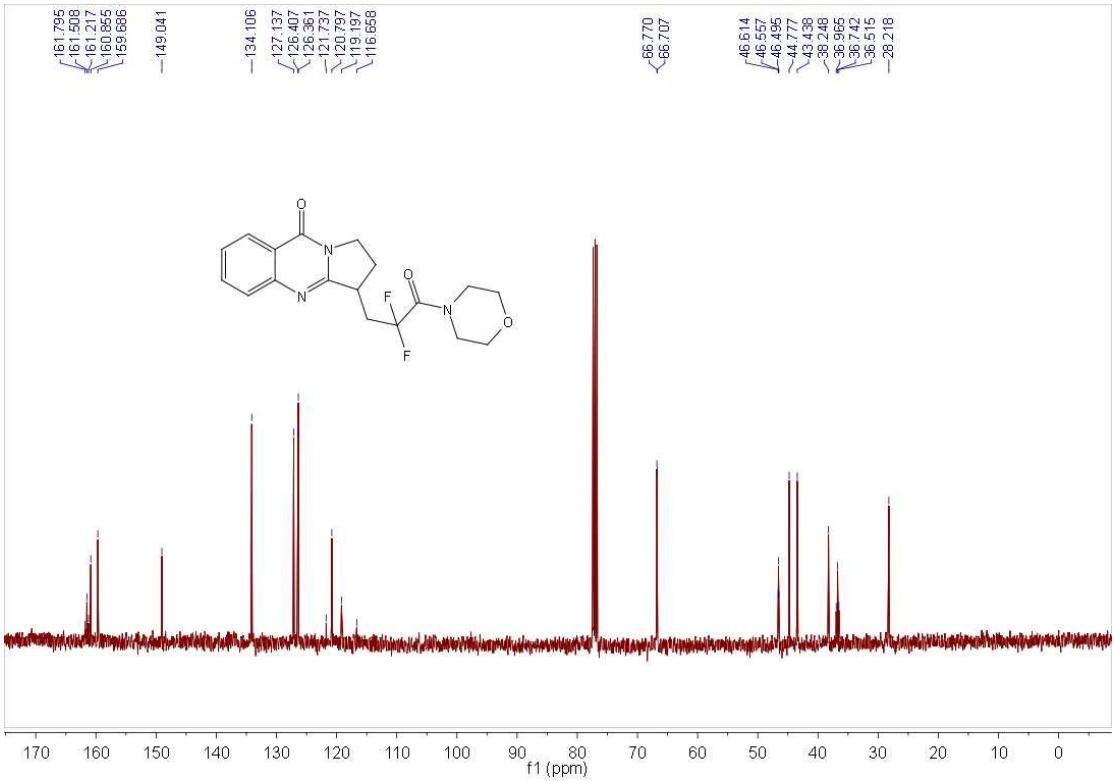

8.385
8.365
7.833
7.813
7.796
7.779
7.759
7.558
7.539
7.521
4.474
4.447
4.422
4.025
3.792
3.780
3.722
3.708
3.690
3.679
3.662
2.769
2.754
2.738
2.476
2.456
2.167
2.135
2.116
1.774
1.751
1.735
1.721
1.00
2.08
1.01
1.01
1.02
2.01
3.19
0.95
1.00
0.97
1.14
6.24
f1 (ppm)

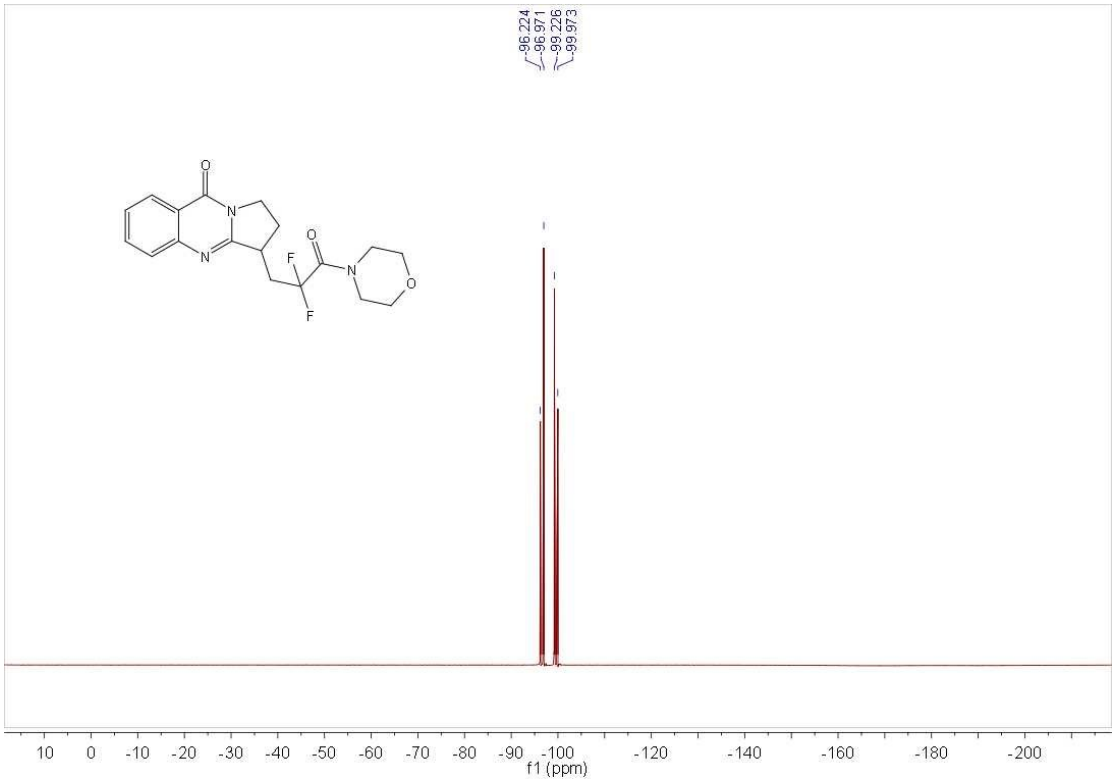

161.526
161.244
160.960
160.868
159.877
149.052
134.052
127.128
126.318
121.812
120.769
119.273
116.731
46.970
46.908
46.843
44.804
44.493
38.376
36.993
26.538
25.621
24.419
f1 (ppm)


-96.379
-97.117
-99.168
-99.907
O
N
N
O
F
F
N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

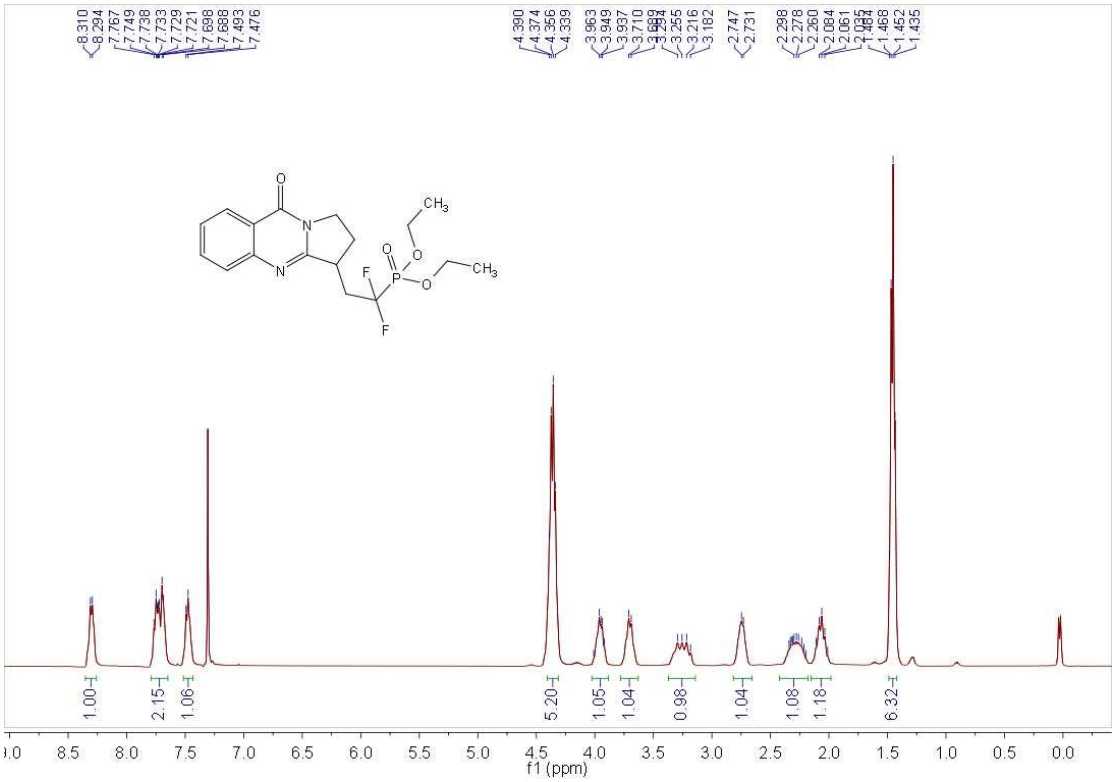
4v

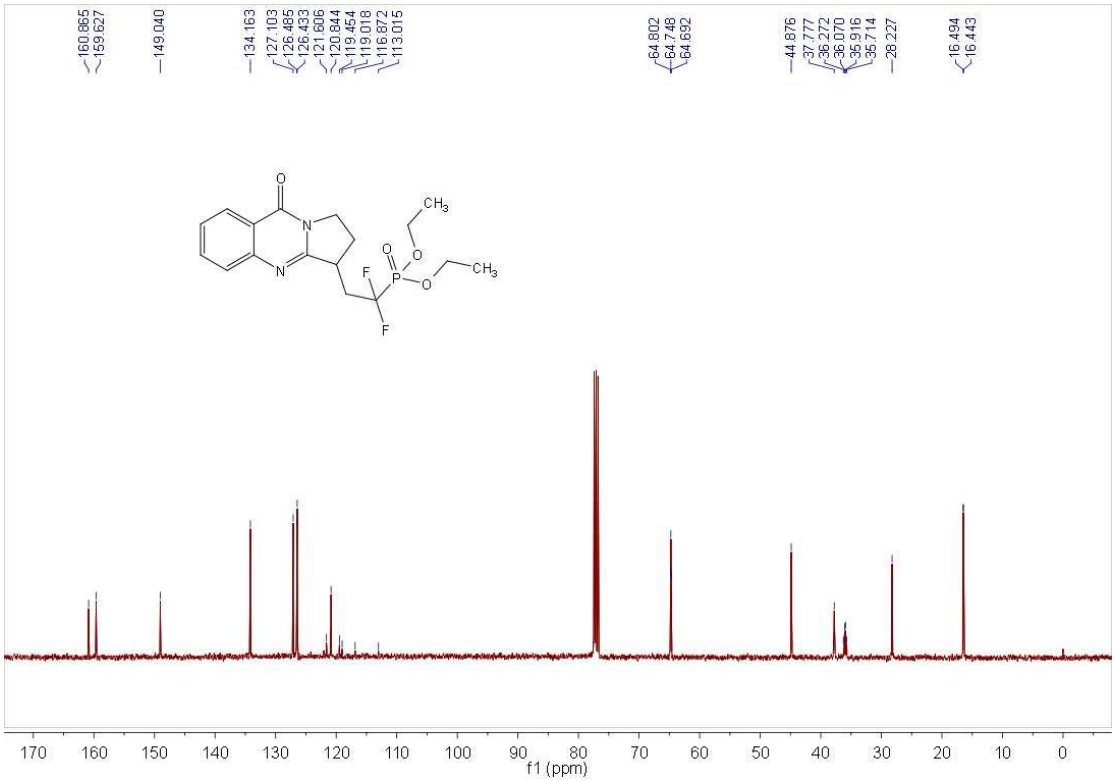

8.316
8.296
7.773
7.753
7.735
7.708
7.688
7.498
7.479
7.461
4.414
4.388
4.385
4.362
3.812
3.777
3.769
3.713
3.701
3.689
3.639
2.698
2.683
2.668
2.649
2.486
2.460
2.449
2.424
2.400
2.374
2.363
2.337
2.126
2.100
2.072
2.045
2.019
O
N
N
O
F
F
N
O
1.00
1.06
1.02
1.03
1.03
1.05
2.13
4.29
1.99
0.94
0.93
1.00
0.97
1.12
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

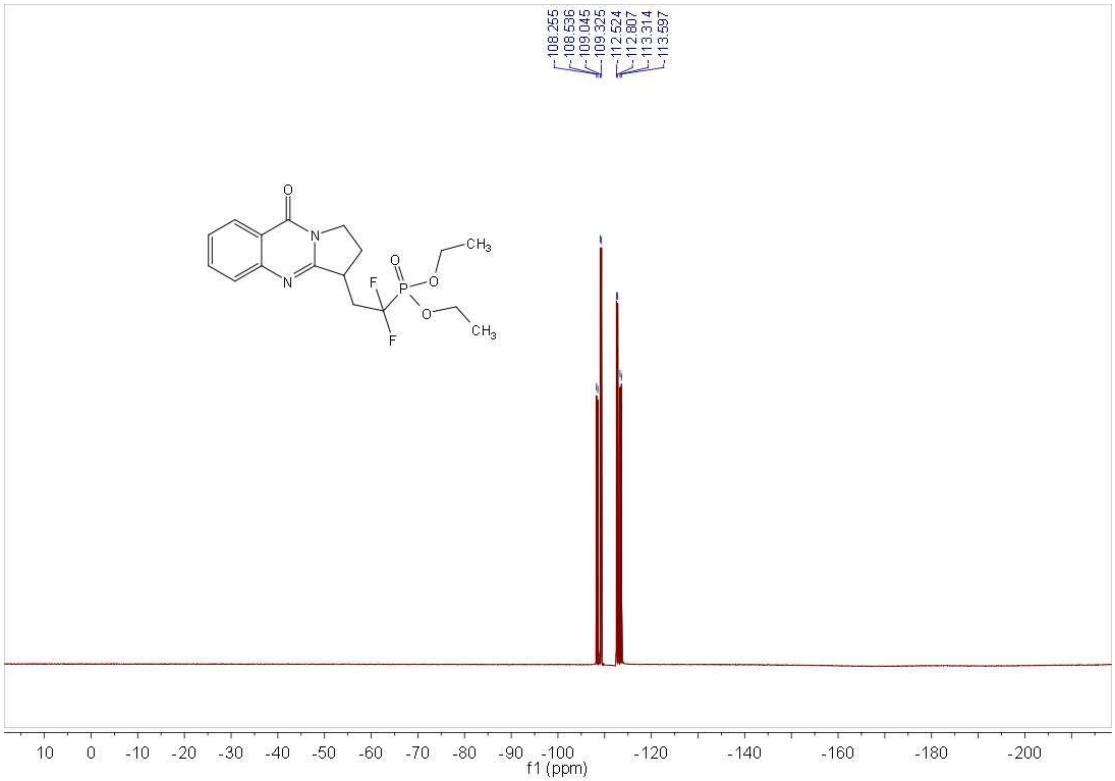

161.795
161.508
161.217
160.855
159.686
149.041
134.106
127.137
126.407
126.361
121.737
120.797
119.197
116.658
66.770
66.707
46.614
46.557
46.495
44.777
43.438
38.248
36.965
36.742
36.515
28.218
O
N
N
O
F
F
O
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-96.224
-96.971
-99.226
-99.973
O
N
N
O
F
F
O
N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

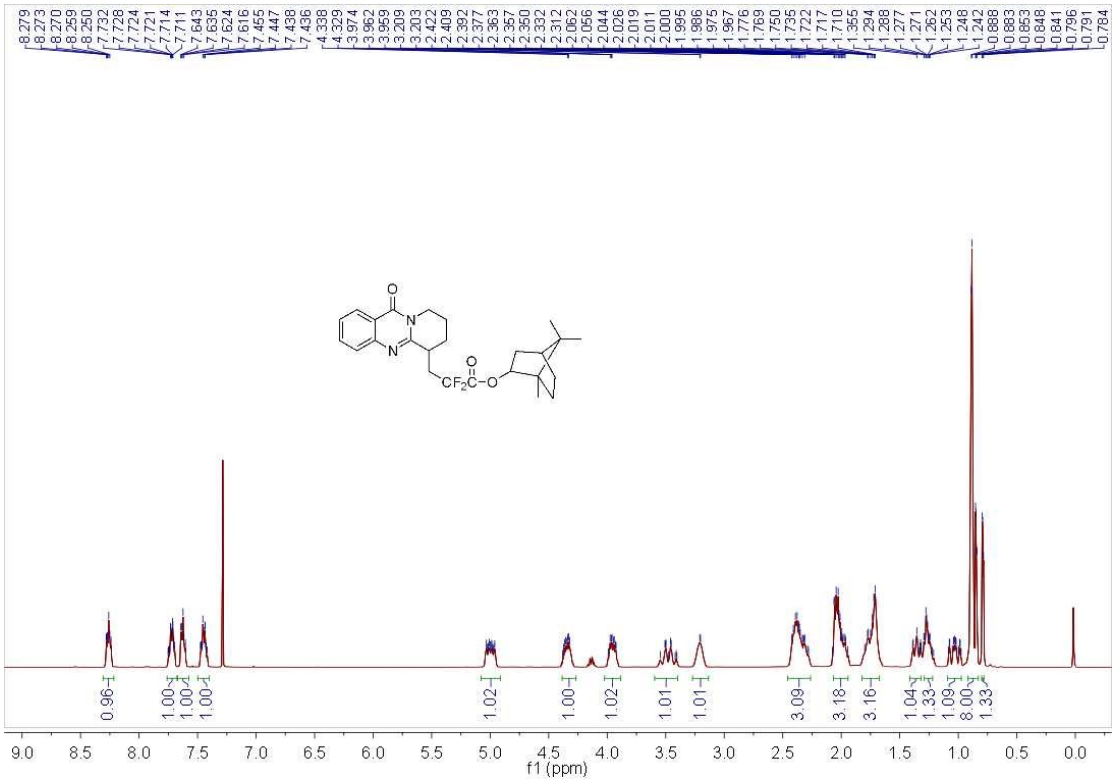
4w

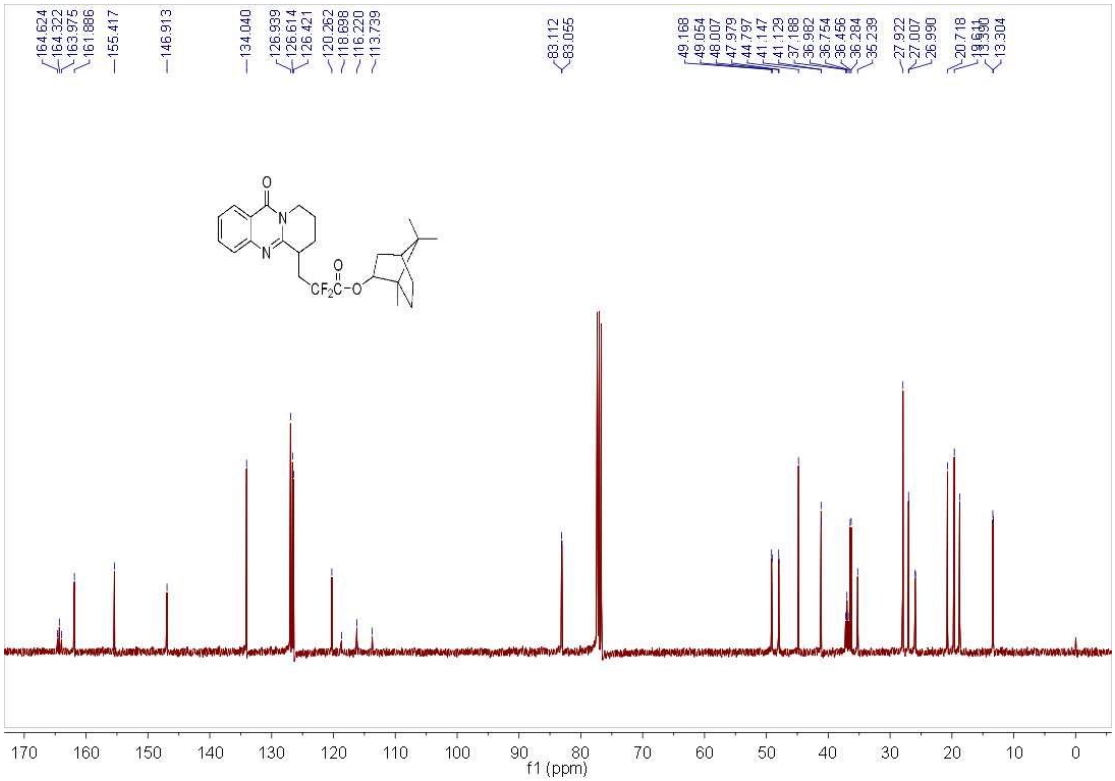

8.310
8.294
7.767
7.749
7.738
7.733
7.729
7.721
7.698
7.688
7.493
7.476
4.390
4.374
4.356
4.339
3.963
3.949
3.937
3.710
3.255
3.216
3.182
2.747
2.731
2.298
2.278
2.260
2.084
2.061
1.468
1.452
1.435
1.00
2.15
1.06
5.20
1.05
1.04
0.98
1.04
1.08
1.18
6.32
f1 (ppm)

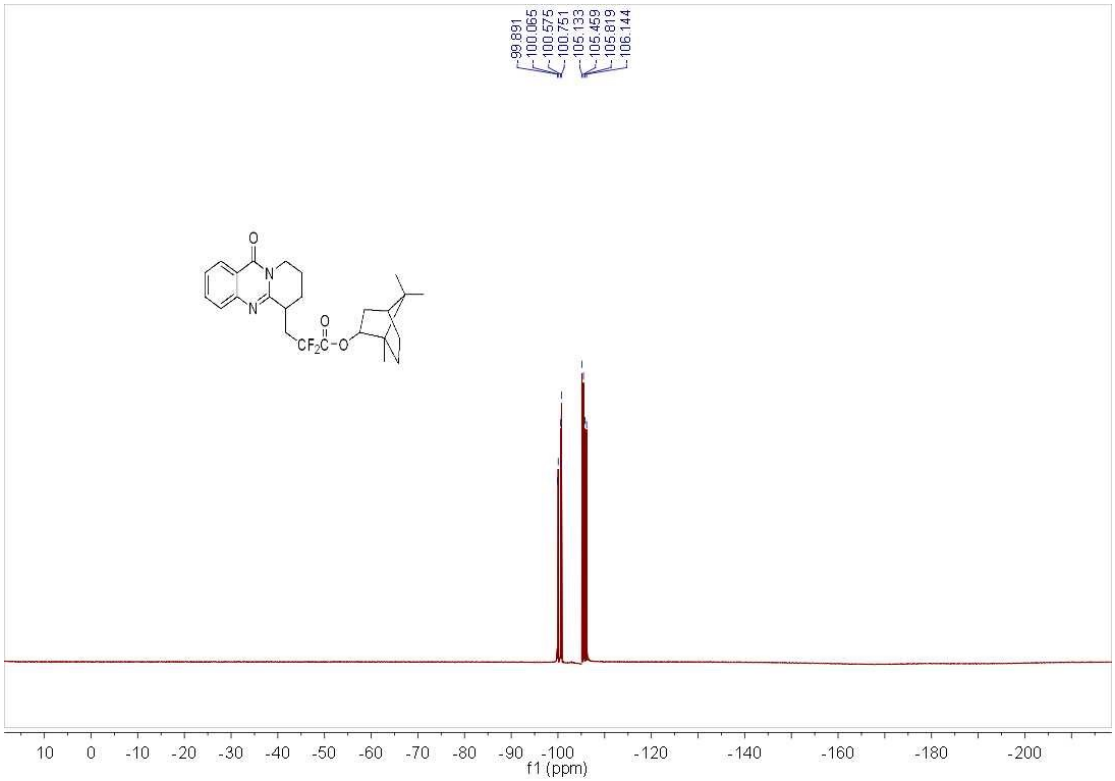

160.865
159.627
149.040
134.163
127.103
126.485
126.433
121.606
120.844
119.454
119.018
116.872
113.015
64.802
64.748
64.692
44.876
37.777
36.272
36.070
35.916
35.714
28.227
16.494
16.443
f1 (ppm)


108.255
108.536
109.045
109.325
112.524
112.807
113.314
113.597
f1 (ppm)

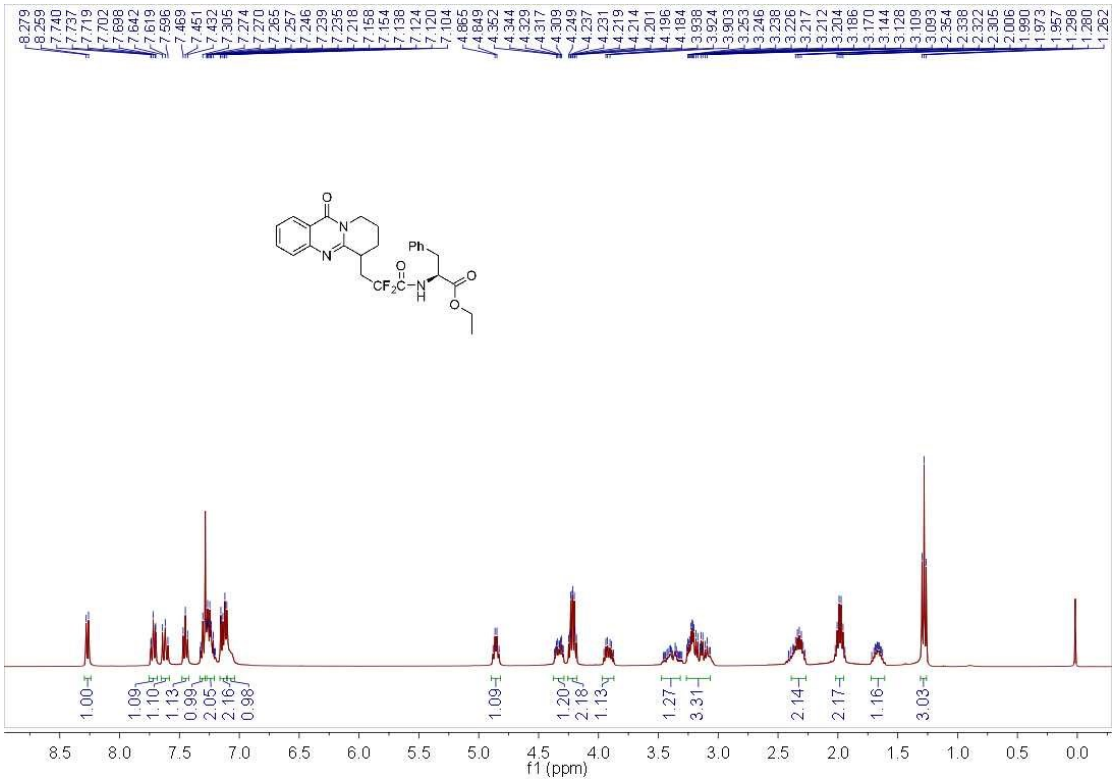
4x

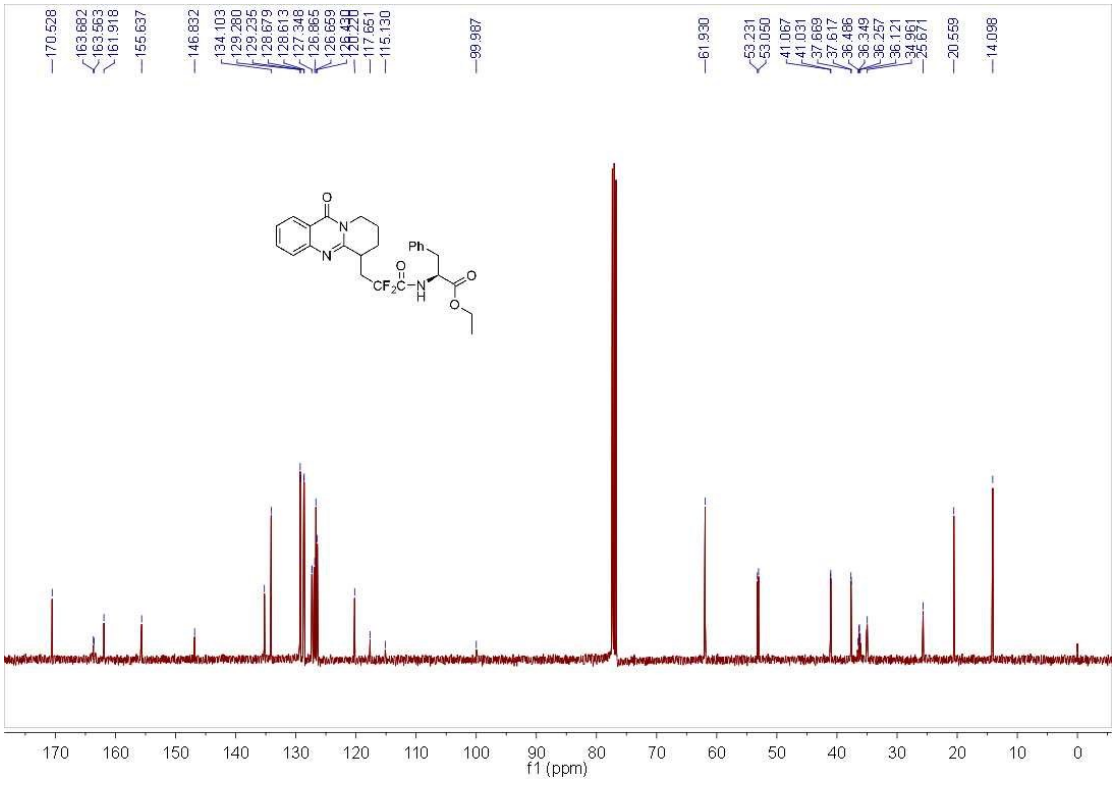

f1 (ppm)

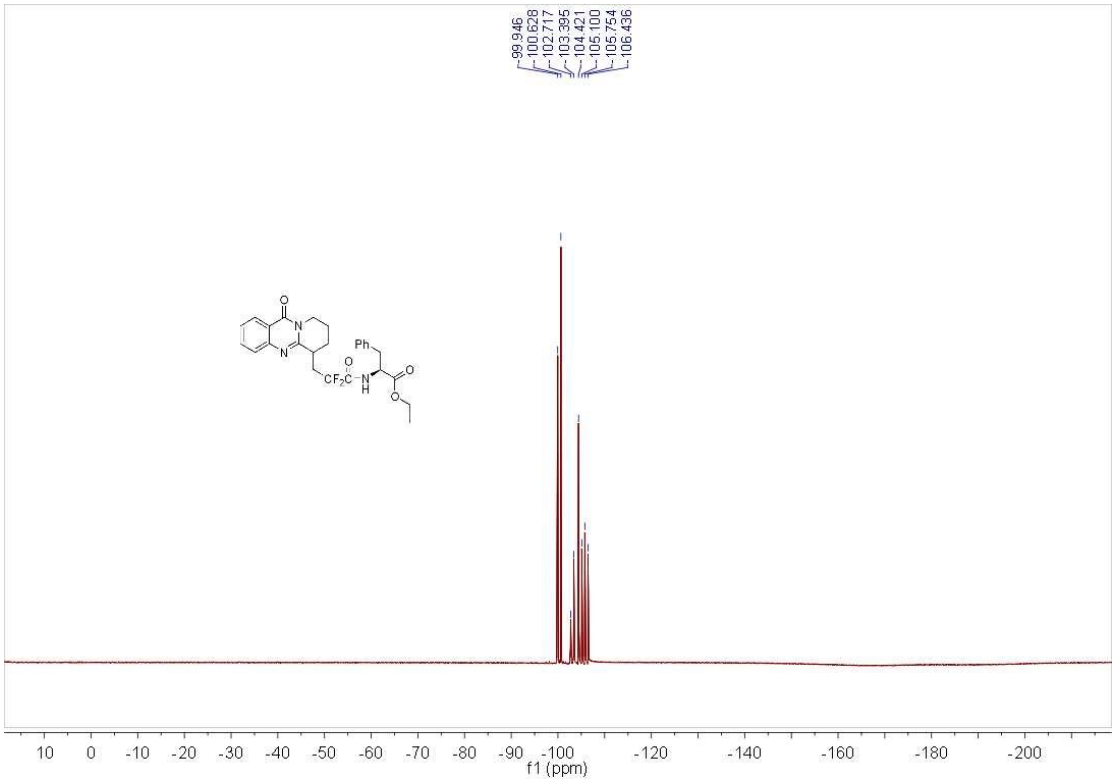

164.624
164.322
163.975
161.886
155.417
146.913
134.040
126.939
126.614
126.421
120.262
118.698
116.220
113.739
83.112
83.055
49.168
49.054
48.007
47.379
44.797
41.147
41.129
37.188
36.982
36.754
36.456
36.284
35.239
27.922
27.007
26.990
20.718
19.641
19.390
13.304
O
N
N
O
CF2C
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


99.891
100.065
100.575
100.751
105.133
105.459
105.819
106.144
O
N
N
O
CF2C
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

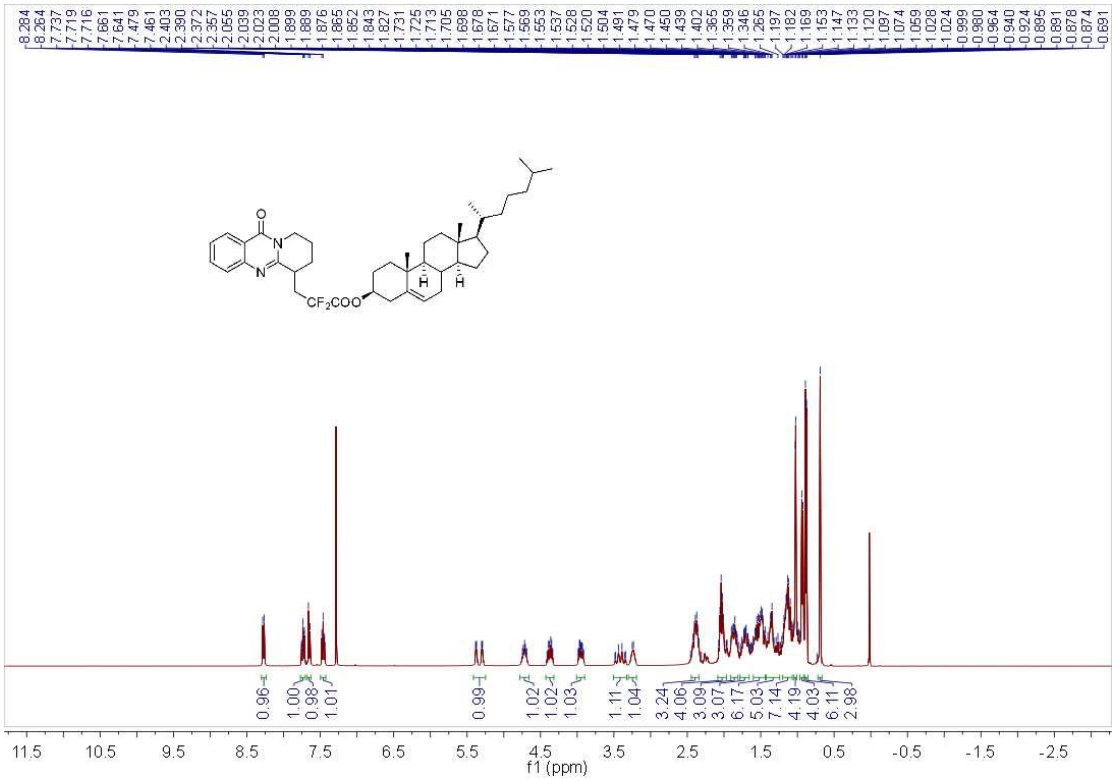
4y

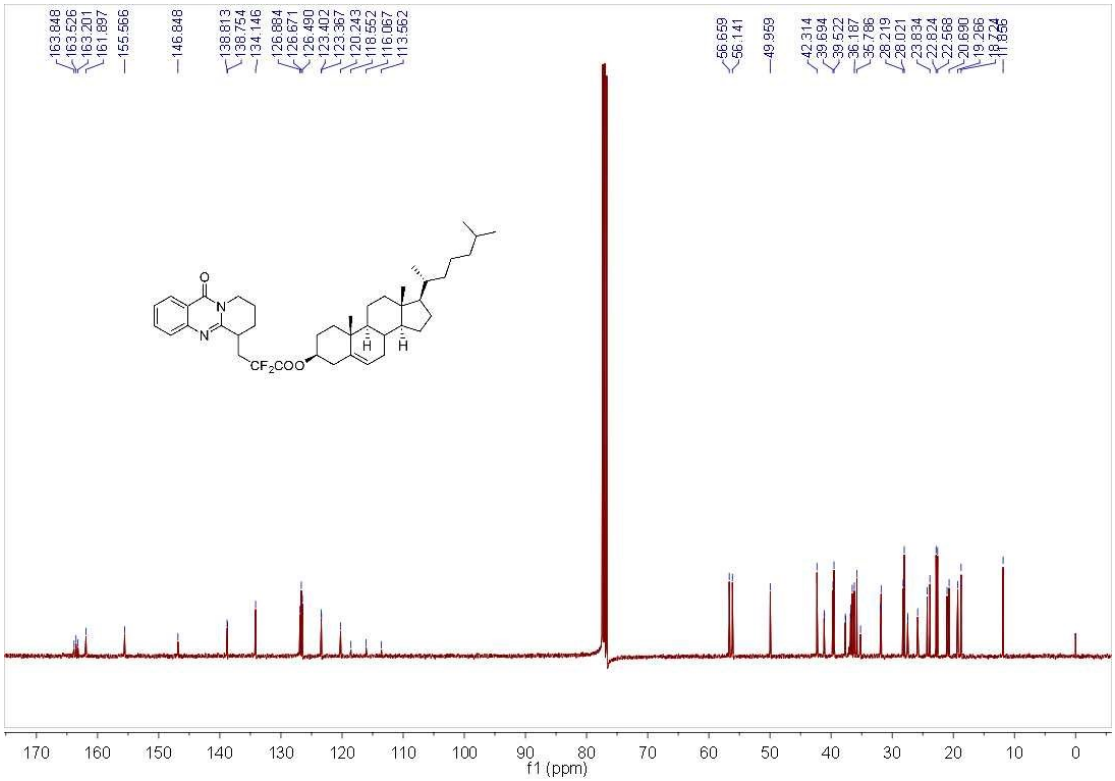

8.279
8.259
7.740
7.737
7.719
7.702
7.698
7.642
7.619
7.596
7.469
7.451
7.432
7.305
7.274
7.270
7.265
7.257
7.246
7.239
7.235
7.218
7.158
7.154
7.138
7.124
7.120
7.104
4.865
4.849
4.352
4.344
4.329
4.317
4.309
4.249
4.237
4.231
4.219
4.214
4.201
4.196
4.184
3.938
3.924
3.903
3.253
3.246
3.238
3.226
3.217
3.212
3.204
3.186
3.170
3.144
3.128
3.109
3.093
2.354
2.338
2.322
2.305
2.006
1.990
1.973
1.957
1.298
1.280
1.262
Ph
O
N
CF2
C
N
H
O
O
1.00
1.09
1.10
1.13
0.99
2.05
2.16
0.98
1.09
1.20
2.18
1.13
1.27
3.31
2.14
2.17
1.16
3.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

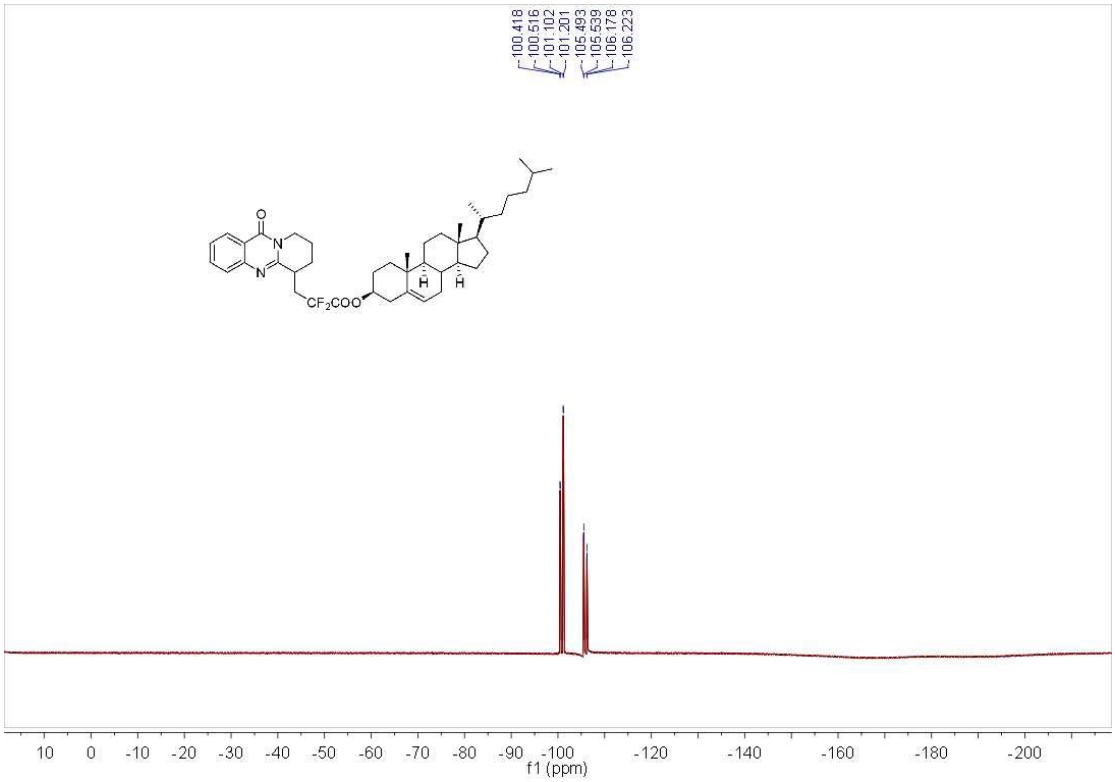

170.528
163.682
163.563
161.918
155.637
146.832
134.103
129.280
129.235
128.679
128.613
127.348
126.865
126.659
117.651
115.130
99.987
61.930
53.231
53.050
41.067
41.031
37.669
37.617
36.486
36.349
36.257
36.121
34.961
25.671
20.559
14.098
Ph
O
N
CF2
C
N
H
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


99.946
100.628
102.717
103.395
104.421
105.100
105.754
106.436
Ph
CF2
f1 (ppm)

4z


CF2COO
0.96
1.00
0.98
1.01
0.99
1.02
1.02
1.03
1.11
1.04
3.24
4.06
3.09
3.07
6.17
5.03
7.14
4.19
4.03
6.11
2.98
f1 (ppm)


163.848
163.526
163.201
161.897
155.566
146.848
138.813
138.754
134.146
126.884
126.671
126.490
123.402
123.367
120.243
118.552
116.067
113.562
56.659
56.141
49.959
42.314
39.694
39.522
36.187
35.786
28.219
28.021
23.834
22.824
22.568
20.690
19.266
18.724
11.856
CF2COO
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


100.418
100.516
101.102
101.201
105.493
105.539
106.178
106.223
CF2COO
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)