Photoinduced homolytic decarboxylative acylation/cyclization of unactivated alkenes with α-keto acid under external oxidant and photocatalyst free conditions: access to quinazolinone derivatives

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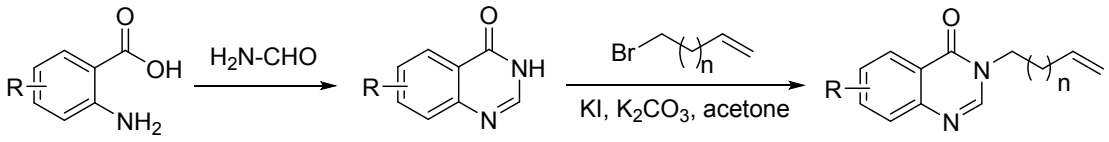
Supporting Information

1. 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. All chemical 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.

2. General procedure

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



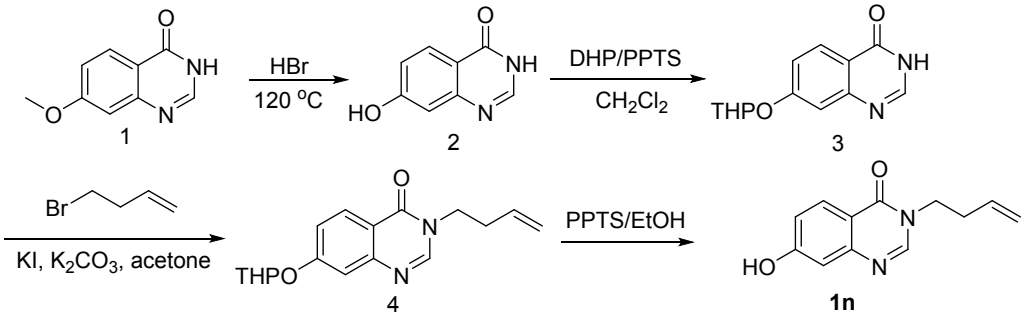
n=1, 1a-1o,1p

n=2, 2a-2h

The mixtures of anthranilic acid (1 mmol) and an excess of formamide (10 mmol) in a roundbottom 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 . These intermediates were used for the next step without further purification.

To a solution of each respective quinazoline-4(3*H*)-one intermediate (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.

The synthesis of 1n[2]

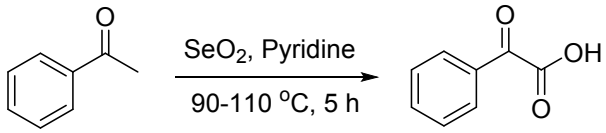


7-methoxy-3*H*-quinazolin -4-one (20 mmol) (1) was stirred in HBr, 48% (20mL) at 120 °C overnight. The mixture was cooled to room temperature and filtered. The filter cake was stirred in water and treated with ammonium hydroxide to pH = 8 and the mixture was filtered. The filter cake was stirred in acetone and the resulting mixture was filtered. The filter cake was washed with diethyl ether and dried giving the desired product (2).

To a solution of 1 (3.5mmol) in CH_2Cl_2 (10 mL) at room temperature was added 3,4- dihydro-2*H*-pyran (5.25mmol) and PPTS (0.08mmol). The solution was stirred at room temperature for 1 h and diluted with a 100 mL solution of (1:1) diethyl ether and ethyl acetate. The organic layer was separated, washed with H_2O, and the residue was chromatographed, eluting with hexane/ethyl acetate (20:1) to give the THP-ether (3).

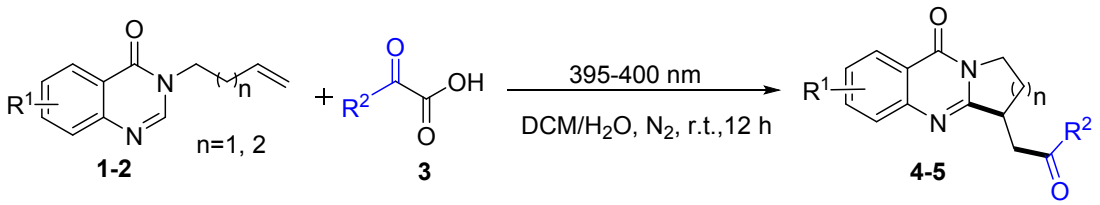
To an ethanol solution (30 mL) of THP ether (4) (5 mmol) was added PPTS (0.08 mmol) in one portion. The solution was refluxed for 1 h, cooled to room temperature, and diluted with a mixture of diethyl ether (100 mL) and H_2O (200 mL). The organic layer was washed with H_2O (200 mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by chromatography on silica gel, eluting with hexane/ethyl acetate (3:1) to give **1n**.

Synthesis of α-Keto acids[3]



Methyl ketones (5 mmol), SeO_2 (6 mmol), 20 mL of pyridine were added in a 50 mL roundbottom flask. The reaction mixture was stirred at 110 ºC for 1 h in an oil bath, then reduce the temperature to 90 ºC for 4 h. The desired products were isolated by flash chromatography on silica gel using (EA / petroleum ether = 1: 20) to give α-keto acids in 65-90% yield

General procedure for the synthesis of 4-5

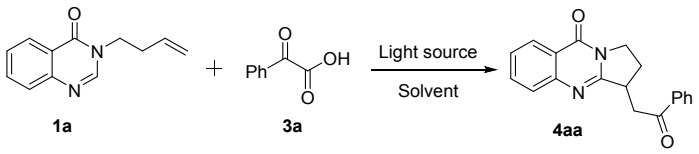


In a mixed solvent of DCE/H_2O (v/v, 5:1, 3 mL) was added **1 or 2** (0.3 mmol) and α-oxo carboxylic acid **3** (0.75 mmol). The reaction mixture was stirred at room temperature under the irradiation of a 10 W LED lamp (395-400 nm) in N_2 atmosphere for 12 h. After completion of the reaction, the resulting solution was extracted by methylene chloride (30 mL) and the organic phase was removed under vacuum for concentration. The residue was purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **4-5**.

3. Optimization of reaction conditions

To evaluate this hypothesis, the transformation between quinazolin-4(3*H*)-one **1a** and 2-oxo-phenylacetic acid **3a** was performed to optimize the reaction conditions (Table S1). The reaction was initially carried out in CH_3CN with irradiation of a 360-365 LED under N_2 atmosphere. To our delight, the desired product **4aa** was obtained in a yield of 39% (Table 1，entry 1). Based on the satisfactory result, the reaction parameters such as wavelength, solvent and additive were further screened. The yield of target product **4aa** could be sharply increased to 59% when the wavelength was adjusted to 395-400 nm. Other wavelength exhibited less reactivity towards the reaction in the following order: 395-400 nm > 405-410 nm > 375-380 nm > 415-420nm > 430-435 nm (Table 1, entries 2-6). The reaction was totally inhibited when it was performed with irradiation of a 450-455 nm LED or under dark condition (Table 1, entries 7-8). Subsequently, several other commonly used solvents were studied for this reaction, and the experiment results indicated that solvents played a vital role in this process. For example, an obviously increasing yield could be observed when the solvent was replaced by DCM. Besides, EtOAc, acetone, $CHCl_3$ and DCE could only give an inferior result, and the reaction even could not proceed at all when performed in DMSO or 1,4-dioxane (Table 1, entries 9-15). Unexpectedly, the mixed solvent DCM/H_2O (v/v, 5:1) could afford a better result than pure DCE, but no improvement in the yield of **4aa** could be obtained upon increasing the ratio of water (Table 1, entries 16-17). The transformation could not proceed well when adding K_2CO_3 (2 equiv.) into the system and exposing to air atmosphere (Table 1, entries 18-19). The contrast experiments showed that the irradiation and N_2 atmosphere were all indispensable for this reaction. Therefore, it could be concluded that the optimal reaction conditions of this transformation require the irradiation of 10 W UV light (395-400 nm) as light source in DCM/H_2O (v/v, 5:1) at room temperature under N_2 atmosphere for 12 h.

Table S1. Optimization of reaction conditions[a]



1a **3a** **4aa**

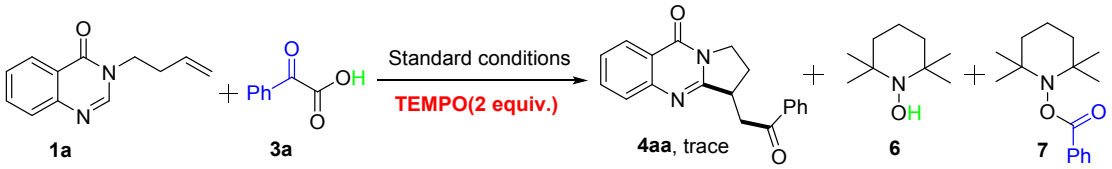
Entry	Light source	Solvent	Yield (%)
1	360-365nm	CH_3CN	39
2	375-380nm	CH_3CN	45
3	395-400nm	CH_3CN	59
4	405-410nm	CH_3CN	53
5	415-420nm	CH_3CN	30
6	430-435nm	CH_3CN	14
7	450-455nm	CH_3CN	trace
8	Darkness	CH_3CN	N.R.
9	395-400nm	DMSO	trace
10	395-400nm	EtOAc	13
11	395-400nm	1,4-dioxane	trace
12	395-400nm	DCM	65
13	395-400nm	Acetone	39
14	395-400nm	$CHCl_3$	35

15	395-400nm	DCE	53
16	**395-400nm**	**DCM/H_2O(5:1)**	**75**
17	395-400nm	DCM/H_2O(3:1)	55
18[b]	395-400nm	DCM/H_2O(5:1)	trace
19[c]	395-400nm	DCM/H_2O(5:1)	trace

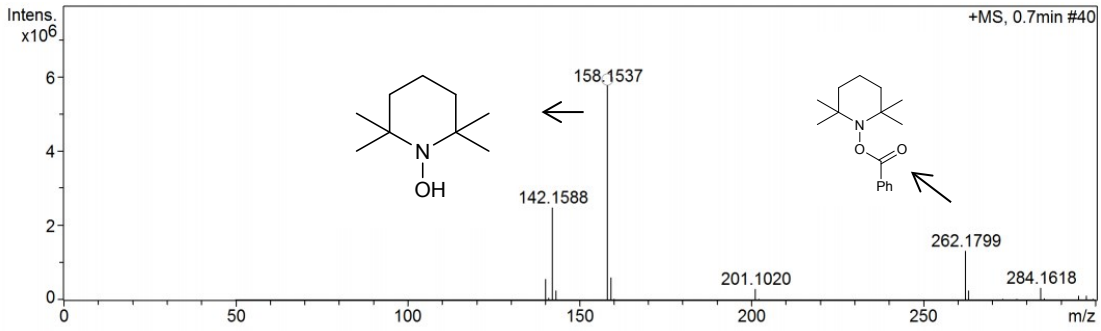
[a]Conditions: **1a** (0.3 mmol), **3a** (0.75 mmol), solvent (3 mL), under N_2 atmosphere for 12 h, r.t. ; [b]K_2CO_3 (2 equiv.); [C]air atmosphere;

4. Control experiments

Radical trapped experiment using TEMPO as radical scavenger



1a (20 mg, 0.1 mmol), 2-oxo-2-phenylacetic acid **3a** (37.8 mg, 0.25 mmol) and radical scavenger TEMPO (0.2 mmol) were added to a 10 mL Quartz tube. The reaction mixture was stirred and irradiated using a 10 W 395-400 nm LED for 12 h. After completion of the reaction, the resulting mixture was analyzed by HRMS. The TEMPO-trapped products **6** and **7** were found. **6** HRMS (ESI) m/z Calcd for $C_9H_{21}NO$ $[M+H]^+$: 158.1539, found: 158.1537; **7** HRMS (ESI) m/z Calcd for $C_{16}H_{24}NO_2$ $[M+H]^+$: 262.1802, found: 262.1799.



Luminescence Quenching Screening Studies

All **1a** solution was irradiated at 390 nm approximately and the emission intensity from 290 nm to 600 nm was recorded by F-7000 FL Spectrophotometer. A 5 mL solution of **1a** in DCM (0.01 mmol/mL) was added **3a** (0.1 equiv, 0.2 equiv, 0.4 equiv, 0.6 equiv in turn), and emission spectra of the sample were collected instantly after each addition.

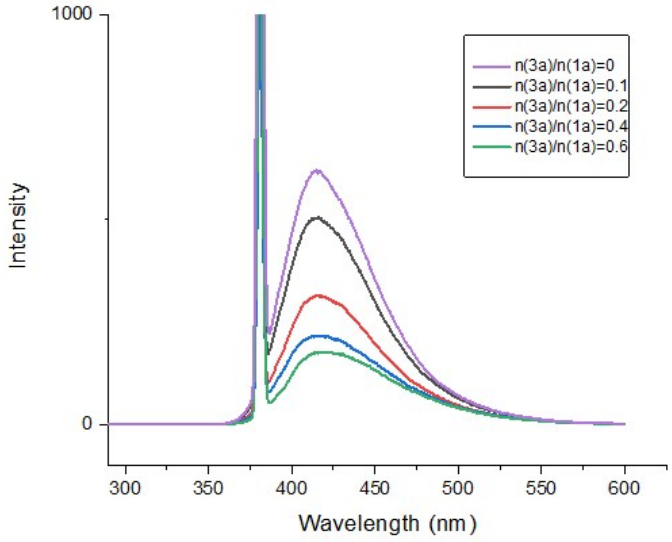


Figure S1 Fluorescence quenching experiment

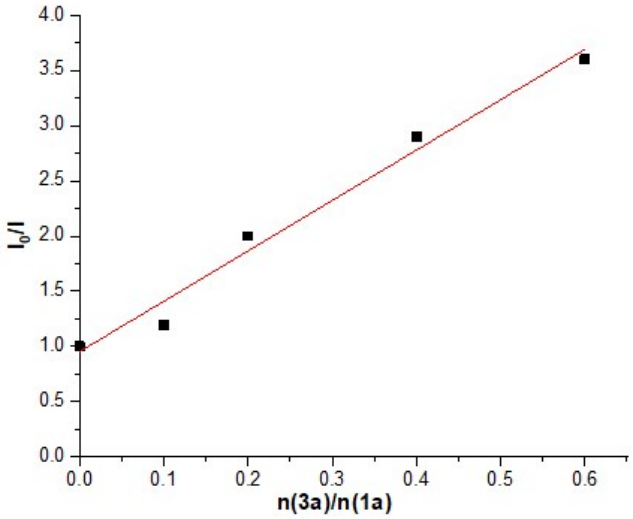


Figure S2 Stern-Volmer plot of Fluorescence quenching of 1a by 3a

UV/Vis Absorption Experiment

The UV/Vis absorption spectra of 4-(4-oxoquinazolin-3(4*H*)-yl)but-1-en-1-ylium (**1a**, 0.01 M) and 3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4aa**, 0.01 M) in CH_2Cl_2 were recorded in 1 cm path quartz cuvettes by using a UV-2600 UV-visible spectrophotometer, respectively. The obtained bands in UV/vis absorption spectra were shown in Figure S3.

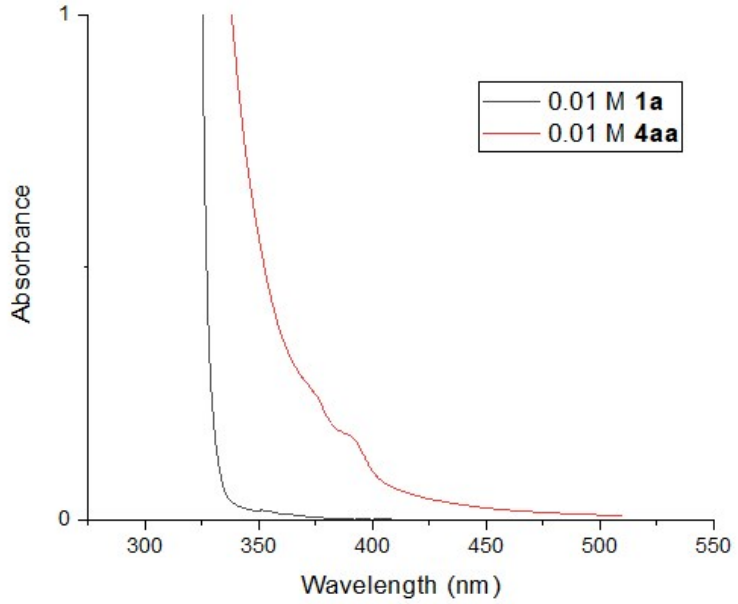


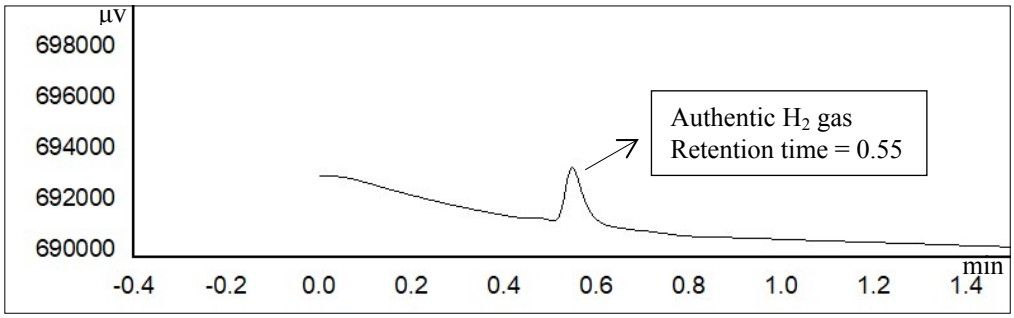
Figure S3 UV-Vis Spectroscopic Measurements on 1a and 4aa

Qualitative Analysis of Hydrogen

Under standard conditions the transformation of **1a** and **3a** was carried out in closed quartz tube. After 12 h, the gas was collected by the closed quartz tube with rubber plug and qualitatively analyzed by GC-TCD with a Carbon plot capillary column gas chromatography which showed the presence of H_2 gas (retention time 0.55 min). The retention time of H_2 is calibrated (0.54 min).

GC Conditions:

Gas chromatographic model：GC-9560-HD; Detection method: GB/T10628-2008; Detector: Thermal Conductivity Detector (TCD); Carrier gas: Argon; Make up flow Ar: 30 cm/min; Detector Temperature: 180 ℃; Column Temperature: 80 ℃ and oven temperature 80 ℃ at the time of injection.



5. Continuous-Flow Photochemical Reaction under sunlight

General Procedures

In an oven dried round bottom flask, **1a** (0.3 mmol) and **3a** (2.5 equiv.) were dissolved in CH_2Cl_2 (3 mL). The mixture solution was injected in the system with a total flow rate of 13.1 μL •min^{-1} (inner diameter ø = 1 mm and length L = 200 cm). After a residence time of 120 min, the product was collected in a closed and lucifugal flask (Figure S4). The solvent was removed under reduced pressure and the residue was purified by chromatography.

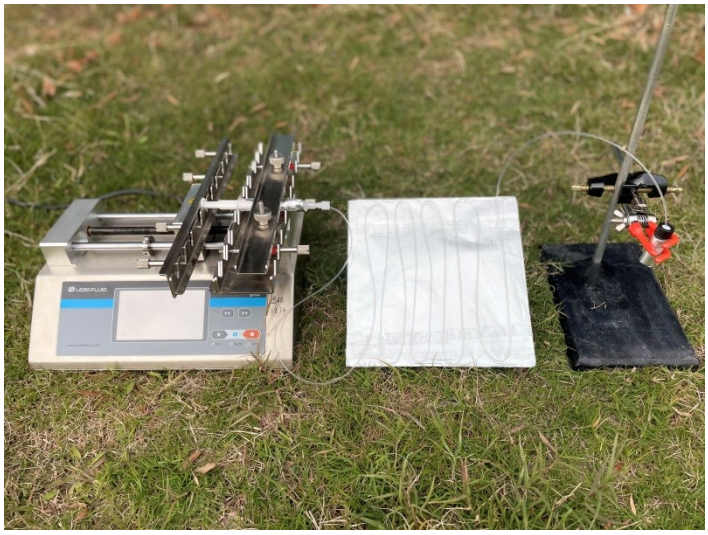
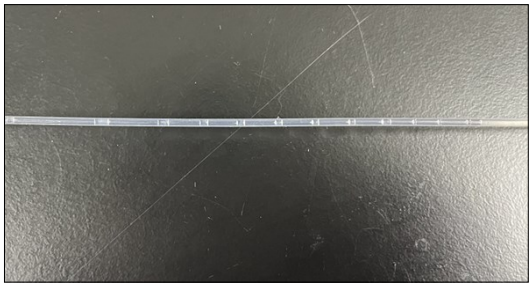


Figure S4 pictures of continuous-flow photochemical reactor



(1) (2)

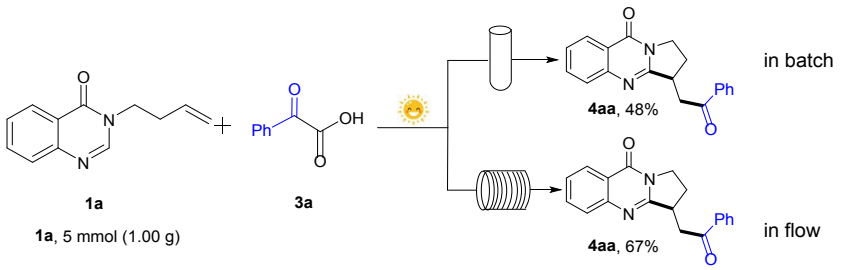
Figure S5 (1): Interface of injection pump;

(2) Gas generation during reaction of 1a and 3a in a capillary reactor

The Gram-scope reaction under sunlight

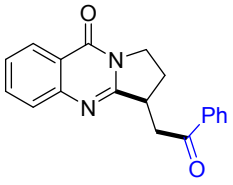
Conditions of the reaction in batch: 1a (5 mmol, 1 equiv.), **3a** (12.5 mmol, 2.5 equiv.), solvent (6 mL), sunlight as energy source, 8 h.

Conditions of the reaction in flow: 1a (5 mmol, 1 equiv.), **3a** (12.5 mmol, 2.5 equiv.), solvent (6 mL), sunlight as energy source, parameter of capillary reactor (inner diameter ø = 1 mm and length L = 200 cm), flow rate 13.1 μL •min^{-1}, residence time = 2 hours.



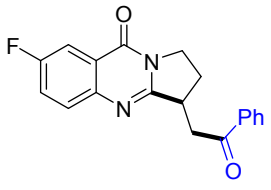
Scheme S1 Gram-scope reaction with sunlight irradiation in batch and flow

6. Characterization Data for the products



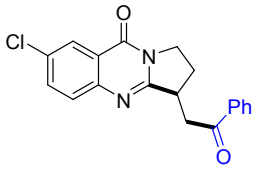
(**4aa**)

White solid, M.P.151.6-153.4 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 7.5 Hz, 2H), 7.77 (t, *J* = 7.3 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.58-7.46 (m, 3H), 4.41 (t, *J* = 10.2 Hz, 1H), 4.15-3.98 (m, 2H), 3.94 (dd, *J* = 17.1, 8.2 Hz, 1H), 3.40 (dd, *J* = 17.9, 9.2 Hz, 1H), 2.92-2.69 (m, 1H), 1.96 (dq, *J* = 19.0, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.41, 160.96, 149.14, 136.44, 134.10, 133.50, 128.73, 128.12, 126.88, 126.46, 126.28, 120.82, 44.97, 41.11, 39.56, 27.16. HRMS (ESI) m/z Calcd for $C_{19}H_{17}N_2O_2$ $[M+H]^+$: 305.1285, found: 305.1283.



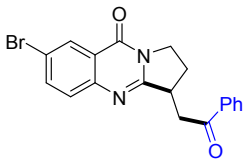
(**4ba**)

White solid, M.P.131.2-132.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.7 Hz, 2H), 7.97 (d, J = 7.7 Hz, 1H), 7.74-7.63 (m, 2H), 7.61-7.45 (m, 3H), 4.42 (t, J = 10.7 Hz, 1H), 4.16-4.04 (m, 1H), 4.04-3.88 (m, 2H), 3.43 (dd, J = 17.4, 8.5 Hz, 1H), 2.91-2.72 (m, 1H), 1.98 (dq, J = 19.0, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.33, 160.56 (d, J = 247.6 Hz), 160.40, 145.79, 136.37, 133.58, 129.16 (d, J = 8.2 Hz), 128.76, 128.12, 122.60 (d, J = 24.0 Hz), 122.08, 111.35 (d, J = 23.5 Hz), 45.05, 40.99, 39.40, 27.17. ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.03. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 323.1190, found: 323.1191.



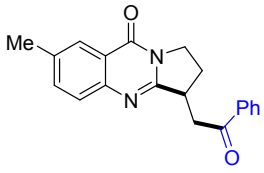
(**4ca**)

White solid, M.P.133.9-139.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 2.2 Hz, 1H), 8.06 (d, J = 7.5 Hz, 2H), 7.73-7.61 (m, 3H), 7.53 (t, J = 7.6 Hz, 2H), 4.41 (ddd, J = 12.0, 9.2, 2.5 Hz, 1H), 4.08 (dt, J = 12.3, 8.8 Hz, 1H), 4.03-3.97 (m, 1H), 3.95-3.87 (m, 1H), 3.41 (dd, J = 18.0, 8.9 Hz, 1H), 2.96-2.69 (m, 1H), 1.98 (dq, J = 12.7, 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.25, 161.39, 159.85, 147.56, 136.41, 134.46, 133.54, 132.05, 128.74, 128.46, 128.10, 125.83, 121.88, 45.16, 40.94, 39.57, 27.03. HRMS (ESI) m/z Calcd for $C_{19}H_{16}ClN_2O_2$ $[M+H]^+$: 339.0895, found: 339.0898.



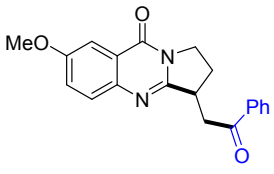
(**4da**)

White solid, M.P.143.6-146.5 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.91-7.75 (m, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.54 (dd, *J* = 14.1, 7.2 Hz, 3H), 4.41 (dd, *J* = 15.5, 5.8 Hz, 1H), 4.08 (dt, *J* = 12.2, 8.6 Hz, 1H), 3.98 (dt, *J* = 9.6, 4.8 Hz, 1H), 3.94-3.86 (m, 1H), 3.42 (dd, *J* = 18.0, 8.9 Hz, 1H), 2.86-2.73 (m, 1H), 2.04-1.92 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 197.25, 161.57, 159.69, 147.85, 147.55, 137.23, 136.40, 133.55, 129.01, 128.75, 128.62, 128.11, 122.23, 119.75, 117.23, 45.21, 40.93, 39.62, 27.00. HRMS (ESI) m/z Calcd for $C_{19}H_{16}BrN_2O_2$ $[M+H]^+$: 383.0390, found: 383.0395.



(**4ea**)

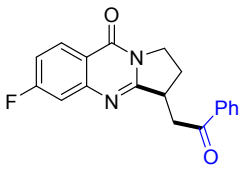
White solid, M.P.160.0-162.6 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.62 (dd, *J* = 13.1, 5.7 Hz, 1H), 7.58 (s, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.45-4.33 (m, 1H), 4.10-3.96 (m, 2H), 3.91 (qd, *J* = 9.4, 2.7 Hz, 1H), 3.36 (dd, *J* = 18.1, 9.5 Hz, 1H), 2.86-2.67 (m, 1H), 2.51 (s, 3H), 1.93 (dq, *J* = 12.6, 9.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.46, 160.95, 160.11, 147.06, 136.49, 136.42, 135.55, 133.46, 128.71, 128.12, 126.61, 125.90, 120.53, 44.93, 41.18, 39.47, 27.23, 21.23. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1449.



(**4fa**)

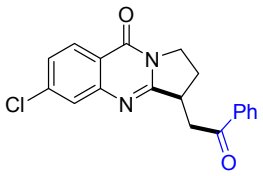
White solid, M.P.117.4-121.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (t, *J* = 11.7 Hz, 2H), 7.69 (d, *J* = 2.8 Hz, 1H), 7.62 (t, *J* = 8.4 Hz, 2H), 7.57-7.47 (m, 2H), 7.35 (dd, *J* = 8.9, 2.8 Hz, 1H), 4.39 (ddd, *J* = 11.9, 9.2, 2.4 Hz, 1H), 4.12-4.04 (m, 1H), 4.00 (dd, *J* = 18.1, 2.7 Hz, 1H), 3.95 (s, 3H), 3.93-3.85 (m, 1H), 3.36 (dd, *J* = 18.1, 9.4 Hz, 1H), 2.87-2.70 (m, 1H), 1.94 (dq, *J* = 12.6, 9.3 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 197.48, 160.74, 158.74, 158.04, 143.65, 136.49, 133.44, 128.70, 128.31, 128.10,

124.25, 121.53, 105.95, 55.81, 44.97, 41.18, 39.31, 27.30. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1391.



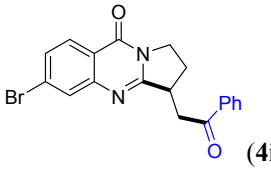
(**4ga**)

White solid, M.P.128.5-131.1 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 8.7, 6.3 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 1.9 Hz, 1H), 7.26-7.16 (m, 1H), 4.48-4.34 (m, 1H), 4.15-3.84 (m, 3H), 3.41 (dd, *J* = 18.0, 8.9 Hz, 1H), 2.79 (dt, *J* = 13.3, 5.2 Hz, 1H), 1.98 (dq, *J* = 18.8, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.28, 167.63, 165.11, 162.49, 160.17, 136.40, 133.55, 129.11, 129.01, 128.75, 128.11, 117.53, 115.12, 114.88, 112.28, 112.06, 45.09, 40.93, 39.70, 27.01. ^{19}F NMR (376 MHz, $CDCl_3$) δ -103.74. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 323.1190, found: 323.1191.



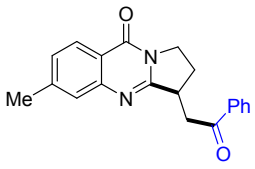
(**4ha**)

White solid, M.P.144.9-148.6 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.65 (dd, *J* = 14.6, 7.2 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 1H), 4.49-4.33 (m, 1H), 4.11-3.87 (m, 3H), 3.41 (dd, *J* = 17.9, 8.8 Hz, 1H), 2.88-2.70 (m, 1H), 1.98 (dd, *J* = 12.7, 9.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.26, 162.39, 160.29, 150.08, 140.24, 136.39, 133.56, 128.75, 128.10, 127.85, 126.85, 126.46, 119.29, 45.11, 40.88, 39.67, 26.99. HRMS (ESI) m/z Calcd for $C_{19}H_{16}ClN_2O_2$ $[M+H]^+$: 339.0895, found: 339.0898.



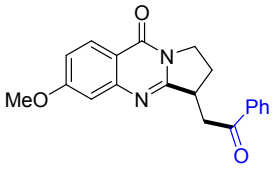
(**4ia**)

White solid, M.P.178.5-180.7 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 7.6 Hz, 2H), 7.86 (s, 1H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.60-7.50 (m, 3H), 4.39 (t, *J* = 9.8 Hz, 1H), 4.11-3.87 (m, 3H), 3.40 (dd, *J* = 17.9, 8.6 Hz, 1H), 2.86-2.69 (m, 1H), 2.05-1.89 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.24, 162.36, 160.40, 150.10, 136.40, 133.55, 129.61, 128.75, 128.10, 127.88, 119.66, 45.14, 40.88, 39.69, 26.98. HRMS (ESI) m/z Calcd for $C_{19}H_{16}BrN_2O_2$ $[M+H]^+$: 383.0390, found: 383.0395.



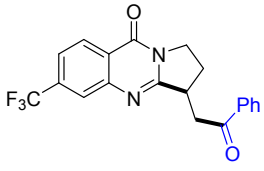
(**4ja**)

White solid, M.P.145.2-146.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.62-7.49 (m, 3H), 4.53-4.32 (m, 1H), 4.14-3.99 (m, 2H), 3.94 (d, *J* = 9.0 Hz, 1H), 3.57-3.32 (m, 1H), 2.91-2.70 (m, 1H), 2.54 (s, 3H), 1.97 (dd, *J* = 12.7, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.43, 161.03, 160.89, 149.23, 145.06, 136.48, 133.47, 128.71, 128.11, 127.86, 126.62, 126.27, 118.41, 44.89, 41.14, 39.56, 27.17, 21.85. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1451.



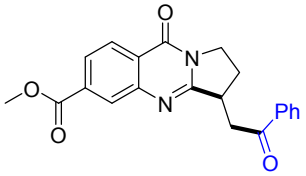
(**4ka**)

White solid, M.P.131.9-134.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39 (d, *J* = 9.7 Hz, 1H), 4.12-4.03 (m, 1H), 4.00 (d, *J* = 6.0 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 1H), 3.49-3.35 (m, 1H), 2.89-2.71 (m, 1H), 1.96 (dd, *J* = 12.5, 9.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.34, 164.44, 161.74, 160.52, 151.38, 136.46, 133.48, 128.71, 128.11, 127.92, 116.23, 114.33, 107.66, 55.60, 44.89, 41.12, 39.64, 27.13. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_3$ $[M+H]^+$: 335.1390, found: 335.1395.



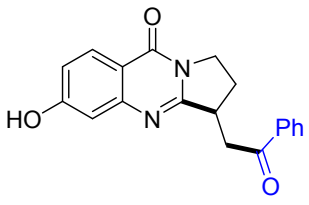
(**4la**)

White solid, M.P.156.2-157.8 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.3 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 2H), 7.98 (s, 1H), 7.67 (dd, *J* = 17.6, 8.1 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 4.53-4.36 (m, 1H), 4.11 (dt, *J* = 12.3, 8.7 Hz, 1H), 4.05-3.90 (m, 2H), 3.46 (dd, *J* = 18.0, 8.6 Hz, 1H), 2.82 (dt, *J* = 13.2, 5.1 Hz, 1H), 2.13-1.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.17, 162.61, 160.07, 149.02, 136.35, 133.61, 128.77, 128.10 , 127.61 , 124.44 (d, *J* = 3.9 Hz), 123.13 , 122.27 (d, *J* = 3.4 Hz), 45.28 , 40.79, 39.67, 26.89. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.10. HRMS (ESI) m/z Calcd for $C_{20}H_{16}F_3N_2O_2$ $[M+H]^+$: 373.1158, found: 373.1165.



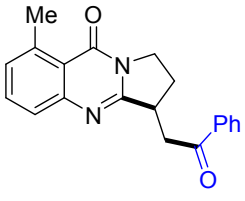
(**4ma**)

White solid, M.P.174.4-176.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40-8.33 (m, 2H), 8.08-8.02 (m, 3H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.40 (ddd, *J* = 12.0, 9.2, 2.5 Hz, 1H), 4.13-3.99 (m, 2H), 3.98 (s, 3H), 3.94-3.88 (m, 1H), 3.40 (dd, *J* = 18.1, 9.0 Hz, 1H), 2.78 (dtd, *J* = 10.7, 8.2, 2.5 Hz, 1H), 1.97 (dq, *J* = 12.8, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.29, 166.17, 161.89, 160.40, 148.97, 136.37, 135.17, 133.58, 128.80, 128.77, 128.12, 126.78, 126.30, 123.81, 52.58, 45.17, 40.92, 39.59, 27.07. HRMS (ESI) m/z Calcd for $C_{21}H_{19}N_2O_4$ $[M+H]^+$: 363.1339, found: 363.1332.



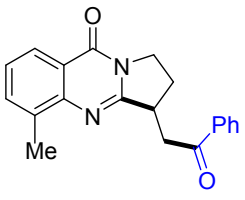
(**4na**)

White solid, M.P.240.7-242.8 ℃, ^{1}H NMR (400 MHz, DMSO) δ 10.79 (s, 1H), 8.04 (m, *J* = 7.1 Hz, 3H), 7.71 (t, *J* = 7.3 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.05-7.00 (m, 1H), 6.97 (s, 1H), 4.32-4.13 (m, 1H), 4.08-3.93 (m, 2H), 3.88 (m, *J* = 18.4 Hz, 1H), 3.69 (dd, *J* = 18.4, 8.2 Hz, 1H), 2.58 (m, *J* = 2.9 Hz, 1H), 2.09-1.89 (m, 1H).^{13}C NMR (100 MHz, DMSO) δ 197.89, 165.55, 164.08, 158.63, 145.13, 136.51, 134.12, 129.29, 128.98, 128.52, 117.70, 111.82, 106.60, 47.02, 40.61, 40.10, 25.88. HRMS (ESI) m/z Calcd for $C_{19}H_{17}N_2O_3$ $[M+H]^+$: 321.234, found: 321.1245.



(**4oa**)

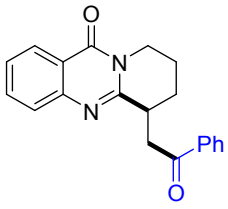
White solid, M.P.152.8-153.6 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.5 Hz, 2H), 7.64 (dd, *J* = 13.5, 6.2 Hz, 1H), 7.60-7.48 (m, 4H), 7.23 (d, *J* = 6.9 Hz, 1H), 4.36 (t, *J* = 10.6 Hz, 1H), 4.09-3.86 (m, 3H), 3.38 (dd, *J* = 17.6, 9.4 Hz, 1H), 2.94 (s, 3H), 2.84-2.72 (m, 1H), 2.00-1.86 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.50, 161.65, 160.63, 141.08, 136.42, 133.51, 133.27, 129.01, 128.73, 128.13, 127.09, 124.92, 119.25, 45.03, 41.15, 39.50, 27.01, 23.03. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1442.



(4**pa**)

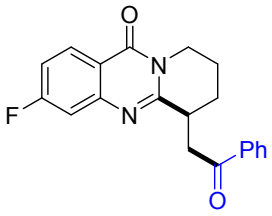
White solid, M.P.139.3-140.5 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.9 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.62-7.51 (m, 3H), 7.36 (t, *J* = 7.6 Hz, 1H), 4.49-4.32 (m, 1H), 4.16-3.84 (m, 3H), 3.34 (dd, *J* = 17.4, 8.4 Hz, 1H), 2.87-2.71 (m, 1H), 2.55 (d, *J* = 12.1 Hz, 3H), 1.96 (dq, *J* = 19.4, 9.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.76, 161.32, 159.51, 147.63, 136.70,

135.40, 134.68, 133.42, 128.72, 128.14, 125.75, 124.07, 120.68, 44.84, 41.11, 39.77, 27.34, 17.42. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1443.



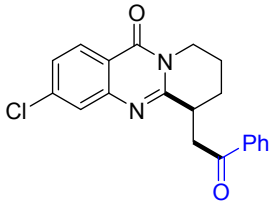
(**5aa**)

White solid, M.P.156.7-158.7 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.8 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 2H), 7.71 (dd, *J* = 15.2, 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 4.53-4.34 (m, 1H), 4.13 (ddd, *J* = 22.5, 14.9, 5.6 Hz, 2H), 3.75 (dq, *J* = 11.8, 5.9 Hz, 1H), 3.45-3.26 (m, 1H), 2.45-2.27 (m, 1H), 2.19-2.08 (m, 2H), 1.84-1.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.58, 161.97, 156.92, 137.43, 133.88, 133.00, 128.57, 128.19, 127.97, 127.08, 126.63, 126.09, 120.24, 41.44, 41.38, 36.91, 25.67, 21.20. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1449.



(**5ba**)

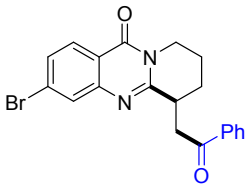
White solid, M.P.159.3-164.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 8.6, 6.4 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.13 (dd, *J* = 12.0, 5.0 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 4.44-4.26 (m, 1H), 4.21-4.06 (m, 1H), 3.99 (dd, *J* = 17.2, 5.4 Hz, 1H), 3.68 (dd, *J* = 11.4, 5.7 Hz, 1H), 3.34 (d, *J* = 15.5 Hz, 1H), 2.29 (td, *J* = 12.1, 5.8 Hz, 1H), 2.19-2.02 (m, 2H), 1.88-1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.43, 167.52, 165.00, 137.27, 133.12, 129.43, 129.33, 128.61, 128.15, 127.08, 116.94, 114.95 (d, *J* = 23.4 Hz), 111.82, 41.40, 41.34, 36.94, 25.55, 21.17. ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.19. HRMS (ESI) m/z Calcd for $C_{20}H_{18}FN_2O_2$ $[M+H]^+$: 337.1347, found: 337.1353.



(5ca)

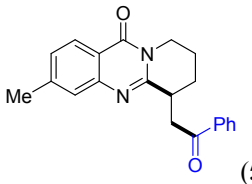
White solid, M.P.168.3-170.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 7.5 Hz, 2H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.46-7.34 (m, 2H), 4.46-4.25 (m, 1H), 4.15-4.06 (m, 1H), 3.99 (dd, *J* = 17.3, 5.2 Hz, 1H), 3.65 (dt, *J* = 11.3, 5.6 Hz, 1H), 3.33 (dd, *J* = 17.1, 5.3 Hz, 1H), 2.28 (dt, *J* = 11.7, 5.8 Hz, 1H), 2.17-2.01 (m, 2H), 1.85-1.62 (m, 1H). ^{13}C NMR (100

MHz, $CDCl_3$) δ 198.43, 167.52, 165.00, 137.27, 133.12, 129.38 (d, *J* = 10.6 Hz), 128.61, 128.15, 127.08, 116.94, 114.95 (d, *J* = 23.4 Hz), 111.82, 111.60, 41.40, 41.34, 36.94, 25.55, 21.17. HRMS (ESI) m/z Calcd for $C_{20}H_{18}ClN_2O_2$ $[M+H]^+$: 353.1051, found: 353.1057.



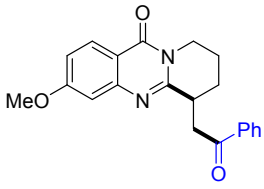
(**5da**)

White solid, M.P.171.4-172.9 ℃, ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.60 (s, 1H), 7.54 (dd, *J* = 15.8, 8.1 Hz, 3H), 4.49-4.26 (m, 1H), 4.16-4.06 (m, 1H), 3.99 (dd, *J* = 17.3, 5.3 Hz, 1H), 3.66 (dq, *J* = 11.7, 6.0 Hz, 1H), 3.35 (dd, *J* = 17.0, 5.0 Hz, 1H), 2.39-2.21 (m, 1H), 2.20-1.96 (m, 2H), 1.75 (ddd, *J* = 15.2, 12.6, 7.8 Hz, 1H).^{113}C NMR (100 MHz, $CDCl_3$) δ 198.32, 161.46, 158.49, 147.99, 137.19, 133.16, 129.47, 129.33, 128.63, 128.57, 128.14, 119.00, 41.51, 41.37, 36.86, 25.54, 21.15. HRMS (ESI) m/z Calcd for $C_{20}H_{18}BrN_2O_2$ $[M+H]^+$: 397.0546, found: 397.0549.



(**5ea**)

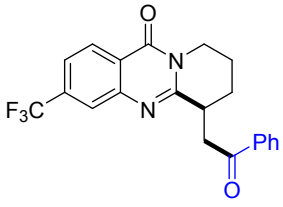
White solid, M.P.163.3-165.6 ℃, ^1H NMR (400 MHz, $CDCl_3$) ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 4.36 (dd, *J* = 13.2, 6.5 Hz, 1H), 4.11 (d, *J* = 5.2 Hz, 1H), 4.04 (dd, *J* = 17.3, 5.2 Hz, 1H), 3.69 (dd, *J* = 11.2, 5.6 Hz, 1H), 3.44-3.11 (m, 1H), 2.46 (s, 3H), 2.29 (dd, *J* = 12.8, 6.3 Hz, 1H), 2.16-1.99 (m, 2H), 1.82-1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.54, 161.93, 156.94, 144.78, 137.42, 132.99, 128.56, 128.19, 128.14, 128.05, 127.73, 127.09, 126.96, 126.47, 126.35, 117.87, 41.51, 41.28, 36.83, 25.70, 21.79, 21.19. HRMS (ESI) m/z Calcd for $C_{21}H_{21}N_2O_2$ $[M+H]^+$: 333.1598, found: 333.1600.



(**5fa**)

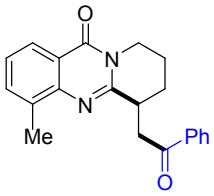
White solid, M.P.150.6-151.9 ℃, ^1H NMR (400 MHz, $CDCl_3$) ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.9 Hz, 1H), 8.11 (d, *J* = 7.5 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.07-6.96 (m, 1H), 6.77 (s, 1H), 4.41-4.26 (m, 1H), 4.15-4.06 (m, 1H), 4.02 (dd, *J* = 17.1, 5.3 Hz, 1H), 3.86 (s, 3H), 3.68 (dq, *J* = 11.4, 5.8 Hz, 1H), 3.32 (m, 1H), 2.39-2.22 (m, 1H), 2.18-2.03 (m, 2H), 1.79-1.67 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.50, 164.29, 161.48, 157.74, 137.42, 132.99, 128.54, 128.29, 128.21,

116.41, 113.78, 106.98, 106.93, 55.50, 41.57, 41.35, 37.02, 25.71, 21.19. HRMS (ESI) m/z Calcd for $C_{21}H_{21}N_2O_3$ $[M+H]^+$:349.1547, found: 349.1557.



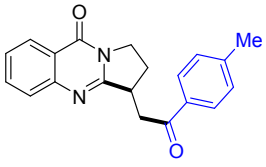
(**5ga**)

White solid, M.P.168.3-169.5 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.3 Hz, 1H), 8.13-7.97 (m, 2H), 7.67 (s, 1H), 7.66-7.57 (m, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 4.34 (dt, *J* = 13.6, 6.6 Hz, 1H), 4.22-4.03 (m, 1H), 3.98 (dd, *J* = 17.4, 5.3 Hz, 1H), 3.66 (td, *J* = 11.8, 6.0 Hz, 1H), 3.39 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.27 (dt, *J* = 12.1, 6.0 Hz, 1H), 2.10 (dt, *J* = 12.0, 6.1 Hz, 2H), 1.82-1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.30, 161.23, 158.65, 146.99, 137.11, 135.43 (d, *J* = 32.7 Hz), 133.25, 128.67, 128.15, 127.84, 124.31 (d, *J* = 4.2 Hz), 122.41, 121.99 (d, *J* = 3.4 Hz), 41.73, 41.31, 36.94, 25.51, 21.18. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.20. HRMS (ESI) m/z Calcd for $C_{21}H_{18}F_3N_2O_2$ $[M+H]^+$:387.1315, found: 387.1313.



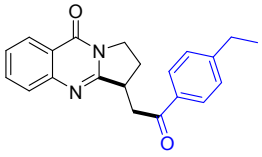
(**5ha**)

White solid, M.P.131.4-132.7 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.05 (m, 3H), 7.66-7.57 (m, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 15.2 Hz, 2H), 4.49-4.38 (m, 1H), 4.15-3.96 (m, 2H), 3.74 (dd, *J* = 11.8, 5.8 Hz, 1H), 3.16 (dd, *J* = 17.0, 5.5 Hz, 1H), 2.27 (dt, *J* = 12.6, 6.3 Hz, 1H), 2.21 (s, 3H), 2.09 (ddt, *J* = 16.5, 12.9, 6.4 Hz, 2H), 1.81-1.69 (m, 1H). ^{13}C NMR (101MHz, $CDCl_3$) δ 198.34, 198.09, 162.25, 155.55, 145.64, 137.24, 135.24, 134.39, 133.08, 128.60, 128.21, 124.27, 120.16, 41.09, 41.04, 36.85, 25.74, 21.28, 16.96. HRMS (ESI) m/z Calcd for $C_{21}H_{21}N_2O_2$ $[M+H]^+$: 333.1598, found: 333.1610.



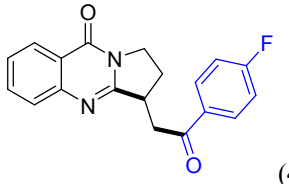
(**4ab**)

White solid, M.P.159.3-161.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 6.6 Hz, 2H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.55-7.39 (m, 3H), 4.41 (t, *J* = 10.5 Hz, 1H), 4.14-3.90 (m, 3H), 3.39 (dd, *J* = 17.8, 9.3 Hz, 1H), 2.88-2.74 (m, 1H), 2.47 (s, 3H), 1.96 (dd, *J* = 12.5, 9.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.60, 161.06, 160.97, 149.11, 138.56, 136.47, 134.27, 134.12, 128.63, 128.61, 126.85, 126.48, 126.29, 125.35, 120.81, 44.99, 41.16, 39.60, 27.14, 21.36. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1440.



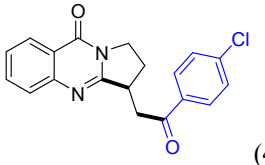
(**4ac**)

White solid, M.P.163.0-164.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 7.80-7.67 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.40 (ddd, *J* = 12.0, 9.2, 2.6 Hz, 1H), 4.15-3.88 (m, 3H), 3.38 (dd, *J* = 17.9, 9.3 Hz, 1H), 2.83-2.70 (m, 3H), 1.95 (dq, *J* = 12.7, 9.3 Hz, 1H), 1.29 (t, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.04, 161.14, 160.97, 150.57, 149.08, 134.21, 134.13, 128.36, 128.23, 126.83, 126.48, 126.30, 120.81, 45.01, 41.03, 39.64, 28.99, 27.14, 15.20. HRMS (ESI) m/z Calcd for $C_{21}H_{21}N_2O_2$ $[M+H]^+$: 333.1598, found: 333.1563.



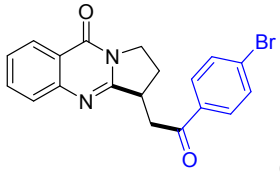
(**4ad**)

White solid, M.P.129.8-132.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.9 Hz, 1H), 8.11 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.83-7.68 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.21 (t, *J* = 8.5 Hz, 2H), 4.53-4.32 (m, 1H), 4.18-4.06 (m, 1H), 4.06-3.98 (m, 1H), 3.95 (d, *J* = 9.2 Hz, 1H), 3.55-3.37 (m, 1H), 2.88-2.73 (m, 1H), 1.98 (dd, *J* = 12.7, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.84, 167.25, 164.71, 160.98, 160.87, 134.23, 132.88, 130.86, 130.77, 126.69, 126.52, 126.43, 120.75, 115.99, 115.78, 45.08, 41.05, 39.55, 27.13. ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.33. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 323.1190, found: 323.1192.



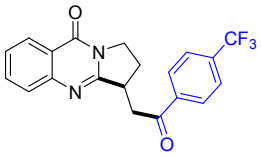
(**4ae**)

White solid, M.P.131.1-132.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.73-7.66 (m, 3H), 7.50 (t, *J* = 7.4 Hz, 1H), 4.49-4.34 (m, 1H), 4.14-3.87 (m, 3H), 3.35 (dd, *J* = 18.0, 9.1 Hz, 1H), 2.89-2.73 (m, 1H), 1.97 (dt, *J* = 9.6, 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.44, 160.92, 160.80, 148.99, 135.15, 134.19, 132.07, 129.64, 128.77, 126.80, 126.50, 126.40, 120.79, 45.00, 41.06, 39.49, 27.16. HRMS (ESI) m/z Calcd for $C_{19}H_{16}ClN_2O_2$ $[M+H]^+$: 339.0895, found: 339.0898.



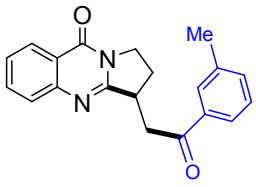
(**4af**)

White solid, M.P.99.6-103.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.78 (t, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.50 (dd, *J* = 11.5, 8.8 Hz, 4H), 4.44 (dd, *J* = 15.5, 5.8 Hz, 1H), 4.18-4.06 (m, 1H), 4.06-3.97 (m, 1H), 3.97-3.86 (m, 1H), 3.40 (dd, *J* = 17.3, 8.3 Hz, 1H), 2.82 (dt, *J* = 13.3, 5.2 Hz, 1H), 1.97 (dd, *J* = 12.7, 9.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.23, 160.90, 140.03, 134.76, 134.22, 131.46, 129.54, 129.07, 128.79, 126.70, 126.52, 126.43, 120.76, 45.06, 41.07, 39.53, 27.10. HRMS (ESI) m/z Calcd for $C_{19}H_{16}BrN_2O_2$ $[M+H]^+$: 383.0390, found: 383.0375.



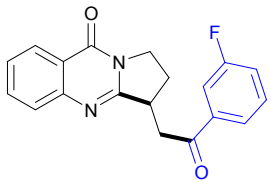
(**4ag**)

White solid, M.P.120.4-124.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.9 Hz, 1H), 8.19 (d, *J* = 8.1 Hz, 2H), 7.79 (dd, *J* = 15.1, 7.8 Hz, 4H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 4.45 (t, *J* = 10.7 Hz, 1H), 4.14 (d, *J* = 8.8 Hz, 1H), 4.07 (dd, *J* = 18.4, 3.0 Hz, 1H), 3.97 (d, *J* = 9.0 Hz, 1H), 3.49 (dd, *J* = 6.3, 4.5 Hz, 1H), 2.81 (dd, *J* = 11.8, 6.6 Hz, 1H), 1.99 (dd, *J* = 12.3, 9.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.55, 160.76 (d, J = 21.9 Hz), 160.54-160.07 (m), 148.88, 139.04, 134.63, 134.23, 128.50, 126.76, 126.49 (d, J = 6.1 Hz), 125.83 (d, J = 3.7 Hz), 124.87, 120.78, 45.02, 41.38, 39.45, 27.13. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.10. HRMS (ESI) m/z Calcd for $C_{20}H_{16}F_3N_2O_2$ $[M+H]^+$: 373.1158, found: 373.1157.



(**4ah**)

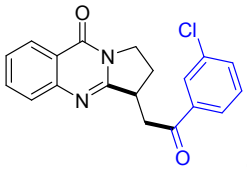
White solid, M.P.154.3-156.8 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.9 Hz, 1H), 8.19 (d, *J* = 8.1 Hz, 2H), 7.79 (dd, *J* = 15.1, 7.8 Hz, 3H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 4.45 (t, *J* = 10.7 Hz, 1H), 4.19-4.03 (m, 2H), 3.97 (d, *J* = 9.0 Hz, 1H), 3.57-3.38 (m, 1H), 2.81 (dd, *J* = 11.8, 6.6 Hz, 1H), 1.99 (dd, *J* = 12.3, 9.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.55, 160.87, 160.65, 148.88, 139.04, 134.23, 128.50, 126.76, 126.52, 126.46, 125.85, 125.81, 120.78, 45.02, 41.38, 39.45, 27.13. HRMS (ESI) m/z Calcd for $C_{20}H_{19}N_2O_2$ $[M+H]^+$: 319.1441, found: 319.1439.



(**4ai**)

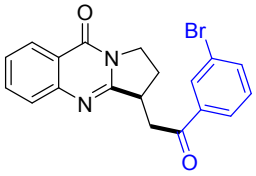
White solid, M.P.127.8-131.5 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.75 (dd, *J* = 22.2, 11.5 Hz, 3H), 7.61-7.47 (m, 2H), 7.35 (t, *J* = 8.2 Hz, 1H), 4.42 (t, *J* = 9.4 Hz, 1H), 4.19-3.87 (m, 3H), 3.38 (dd, *J* = 17.9, 8.9 Hz, 1H), 2.89-2.71 (m, 1H), 2.11-1.83 (m, 1H). ^{13}C NMR (100 MHz, CDCl3) δ 196.24, 164.11, 161.64, 160.82 (d, J = 18.4 Hz), 149.01, 149.01,

138.47 (d, J = 6.0 Hz), 138.47 (d, J = 6.0 Hz), 130.44 (d, J = 7.6 Hz), 126.82, 126.42 (d, J = 10.1 Hz), 123.91 (d, J = 2.8 Hz), 120.71 (d, J = 12.3 Hz), 120.44, 114.85 (d, J = 22.3 Hz), 44.98, 41.25, 39.45, 27.13. ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.45. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 323.1190, found: 323.1191.



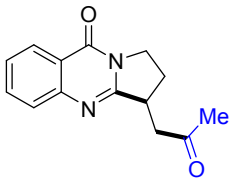
(**4aj**)

White solid, M.P.76.9-80.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.9 Hz, 1H), 8.06 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 1H), 7.79 (t, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.51 (dd, *J* = 14.5, 7.1 Hz, 2H), 4.44 (dd, *J* = 15.5, 5.8 Hz, 1H), 4.15-4.06 (m, 1H), 4.06-3.97 (m, 1H), 3.94 (d, *J* = 9.2 Hz, 1H), 3.38 (dd, *J* = 18.1, 9.1 Hz, 1H), 2.88-2.75 (m, 1H), 1.97 (dd, *J* = 12.6, 9.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.44, 160.93, 160.84, 148.97, 135.13, 134.20, 132.06, 131.72, 131.51, 129.64, 128.76, 126.78, 126.50, 126.41, 120.77, 45.02, 41.04, 39.48, 27.13. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 339.0895, found: 339.0895.



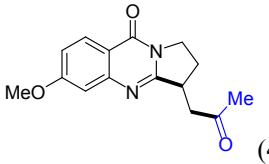
(**4ak**)

White solid, M.P.87.0-89.3, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 3H), 7.50 (t, *J* = 7.0 Hz, 1H), 4.42 (t, *J* = 10.3 Hz, 1H), 4.03 (ddd, *J* = 40.6, 18.9, 8.7 Hz, 3H), 3.35 (dd, *J* = 17.7, 8.9 Hz, 1H), 2.90-2.68 (m, 1H), 1.97 (dd, *J* = 20.2, 10.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.43, 160.92, 160.83, 148.96, 135.15, 134.19, 132.05, 131.75, 131.53, 129.63, 128.75, 126.77, 126.50, 126.40, 120.77, 45.01, 41.04, 39.49, 27.12. HRMS (ESI) m/z Calcd for $C_{19}H_{16}FN_2O_2$ $[M+H]^+$: 383.0382, found: 383.0390.



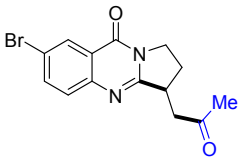
(**4al**)

White solid, M.P.93.0-95.6 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 7.4 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 1H), 4.36 (t, *J* = 10.4 Hz, 1H), 4.02 (dd, *J* = 20.1, 8.9 Hz, 1H), 3.72 (d, *J* = 7.7 Hz, 1H), 3.44 (d, *J* = 18.4 Hz, 1H), 2.86 (dd, *J* = 18.3, 8.7 Hz, 1H), 2.75-2.61 (m, 1H), 2.30 (s, 3H), 1.97-1.73 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.03, 160.85, 160.77, 148.89, 134.16, 126.75, 126.44, 126.34, 120.71, 45.52, 44.93, 39.22, 30.23, 27.00. HRMS (ESI) m/z Calcd for $C_{14}H_{15}N_2O_2$ $[M+H]^+$:243.1128, found: 243.1131.



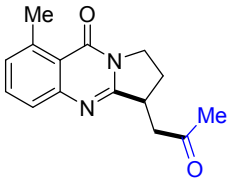
(**4am**)

White solid, M.P.97.2-99.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.4 Hz, 1H), 7.07 (s, 2H), 4.35 (t, *J* = 9.8 Hz, 1H), 4.08-3.98 (m, 1H), 3.95 (s, 3H), 3.71 (d, *J* = 7.3 Hz, 1H), 3.43 (d, *J* = 18.2 Hz, 1H), 2.85 (dd, *J* = 17.8, 8.7 Hz, 1H), 2.78-2.61 (m, 1H), 2.31 (s, 3H), 1.89 (dd, *J* = 19.9, 9.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.91, 164.41, 161.45, 160.46, 151.33, 127.88, 116.23, 114.26, 107.62, 55.62, 45.54, 44.78, 39.29, 30.19, 27.02. HRMS (ESI) m/z Calcd for $C_{15}H_{17}N_2O_3$ $[M+H]^+$:273.1234, found: 273.1232.



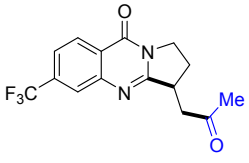
(**4an**)

White solid, M.P.89.7-91.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 4.36 (t, *J* = 10.5 Hz, 1H), 4.01 (dd, *J* = 19.5, 9.3 Hz, 1H), 3.69 (d, *J* = 8.0 Hz, 1H), 3.40 (d, *J* = 17.5 Hz, 1H), 2.85 (dd, *J* = 18.2, 8.6 Hz, 1H), 2.70 (dd, *J* = 11.6, 7.1 Hz, 1H), 2.30 (s, 3H), 1.96-1.87 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.81, 161.23, 159.67, 147.93, 137.21, 128.97, 128.67, 122.19, 119.71, 45.32, 45.05, 39.26, 30.21, 26.91. HRMS (ESI) m/z Calcd for $C_{14}H_{14}BrN_2O_2$ $[M+H]^+$:321.0233, found: 321.0232.



(**4ao**)

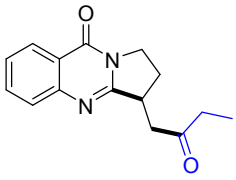
White solid, M.P.97.5-99.1 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.1 Hz, 1H), 4.30 (t, *J* = 9.9 Hz, 1H), 4.04 – 3.91 (m, 1H), 3.78-3.62 (m, 1H), 3.42 (dd, *J* = 18.4, 2.6 Hz, 1H), 2.91 (s, 3H), 2.81 (dd, *J* = 18.4, 9.2 Hz, 1H), 2.72-2.60 (m, 1H), 2.29 (s, 3H), 1.84 (dq, *J* = 19.1, 9.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.07, 161.62, 160.26, 150.69, 141.03, 133.21, 128.96, 125.00, 119.23, 45.55, 44.85, 39.16, 30.22, 26.92, 23.01. HRMS (ESI) m/z Calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$:257.1212, found: 257.1220.



(**4ap**)

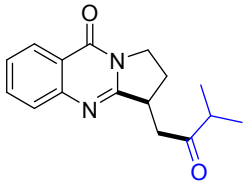
White solid, M.P.100.3-103.9 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.3 Hz, 1H), 7.95 (s, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 4.50-4.35 (m, 1H), 4.13-3.99 (m, 1H), 3.74 (qd, *J* = 9.0, 3.5 Hz, 1H), 3.42 (dd,

J = 18.5, 3.4 Hz, 1H), 2.89 (dd, *J* = 18.5, 8.5 Hz, 1H), 2.80-2.63 (m, 1H), 2.31 (s, 3H), 2.04-1.89 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.76, 162.26, 160.06, 149.09, 135.79, 135.46, 127.59, 124.49 (d, *J* = 4.0 Hz), 123.10, 122.26 (d, *J* = 3.4 Hz), 45.14, 45.13, 39.32, 30.23, 26.80. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.16. HRMS (ESI) m/z Calcd for $C_{15}H_{14}F_3N_2O_2$ $[M+H]^+$:310.0995, found: 310.0996.



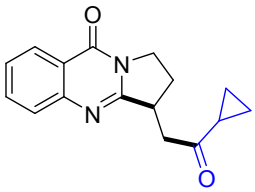
(4aq)

White solid, M.P.85.5-89.1 ℃， ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.9 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 4.38 (t, *J* = 10.5 Hz, 1H), 4.05 (dt, *J* = 12.1, 8.5 Hz, 1H), 3.77 (qd, *J* = 9.1, 3.3 Hz, 1H), 3.40 (d, *J* = 18.1 Hz, 1H), 2.88 (dd, *J* = 18.1, 8.8 Hz, 1H), 2.76-2.63 (m, 1H), 2.58 (dt, *J* = 14.9, 7.5 Hz, 2H), 1.90 (dq, *J* = 18.7, 9.3 Hz, 1H), 1.16 (t, *J* = 7.3 Hz, 3H), 0.96 (dd, *J* = 16.5, 9.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.90, 175.03, 161.33, 160.79, 148.40, 134.30, 126.51, 126.34, 120.57, 45.14, 44.19, 39.29, 36.19, 26.76, 7.75. HRMS (ESI) m/z Calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$:257.1212, found: 257.1214.



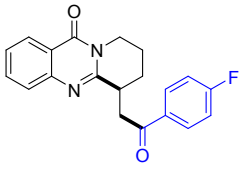
(4ar)

White solid, M.P.90.6-92.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 4.37 (t, *J* = 10.7 Hz, 1H), 4.09-3.98 (m, 1H), 3.80-3.69 (m, 1H), 3.43 (dd, *J* = 18.2, 2.3 Hz, 1H), 2.88 (dd, *J* = 18.1, 8.9 Hz, 1H), 2.81-2.62 (m, 2H), 1.95-1.80 (m, 1H), 1.24-1.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.19, 160.97, 160.91, 149.05, 134.11, 126.78, 126.44, 126.28, 120.73, 44.89, 42.41, 41.04, 39.32, 27.00, 18.28, 18.22. HRMS (ESI) m/z Calcd for $C_{16}H_{19}N_2O_2$ $[M+H]^+$:271.1441, found: 271.1441.



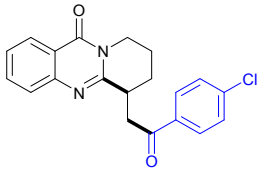
(4as)

White solid, M.P.90.6-92.2 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.9 Hz, 1H), 7.84-7.64 (m, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 4.37 (t, *J* = 9.6 Hz, 1H), 4.05 (d, *J* = 11.8 Hz, 1H), 3.76 (d, *J* = 8.6 Hz, 1H), 3.60 (dd, *J* = 18.2, 2.8 Hz, 1H), 3.03 (dd, *J* = 18.1, 10.3 Hz, 1H), 2.70 (dd, *J* = 8.6, 3.7 Hz, 1H), 2.11-2.00 (m, 1H), 1.90 (dd, *J* = 12.4, 9.5 Hz, 1H), 1.21-1.07 (m, 2H), 1.04-0.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.14, 170.93, 160.84, 134.19, 126.65, 126.49, 126.36, 120.70, 117.23, 45.41, 44.99, 39.33, 26.99, 20.81, 11.27, 11.05. HRMS (ESI) m/z Calcd for $C_{16}H_{17}N_2O_2$ $[M+H]^+$:269.1285, found: 269.1277.



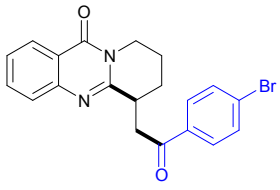
(**5ab**)

White solid, M.P.126.5-129.1℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.9 Hz, 1H), 8.22 (dd, *J* = 8.1, 5.6 Hz, 2H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.30 (t, *J* = 8.5 Hz, 2H), 4.56-4.41 (m, 1H), 3.78 (dq, *J* = 11.8, 6.0 Hz, 1H), 3.40-3.24 (m, 1H), 2.45-2.31 (m, 1H), 2.17 (dd, *J* = 12.5, 6.3 Hz, 2H), 1.90-1.76 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.09, 165.71 (d, *J* = 254.5 Hz), 161.99, 156.87, 146.98, 134.01, 133.74 (d, *J* = 2.8 Hz), 130.86 (d, *J* = 9.3 Hz), 126.67, 126.56, 126.21, 120.17, 115.68 (d, *J* = 21.8 Hz), 41.39, 41.26, 36.91), 25.61, 21.16. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.36. HRMS (ESI) m/z Calcd for $C_{20}H_{18}FN_2O_2$ $[M+H]^+$: 337.1247, found: 337.1251.



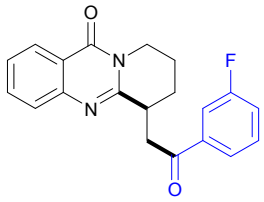
(**5ac**)

White solid, M.P.124.4-126.6 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.9 Hz, 1H), 8.06 (t, *J* = 7.1 Hz, 3H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.57-7.49 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 4.48-4.33 (m, 1H), 4.17-4.04 (m, 1H), 3.99 (dd, *J* = 17.1, 5.8 Hz, 1H), 3.71 (dd, *J* = 11.5, 5.9 Hz, 1H), 3.21 (m, 1H), 2.30 (dt, *J* = 12.4, 6.2 Hz, 1H), 2.10 (dd, *J* = 12.4, 6.1 Hz, 2H), 1.85-1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.49, 161.95, 156.78, 139.44, 135.72, 134.01, 131.51, 129.67, 128.89, 126.68, 126.54, 126.23, 120.20, 41.34, 41.30, 36.96, 25.63, 21.18. HRMS (ESI) m/z Calcd for $C_{20}H_{18}ClN_2O_2$ $[M+H]^+$: 353.1051, found: 353.1046.



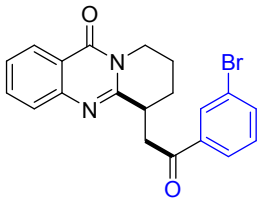
(**5ad**)

White solid, M.P.139.4-143.3, ^{1}H NMR (400 MHz, DMSO) δ 8.12 (d, *J* = 7.8 Hz, 1H), 8.01 (t, *J* = 10.1 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 4.19 (dt, *J* = 13.1, 6.4 Hz, 1H), 4.05-3.95 (m, 1H), 3.82 (dd, *J* = 17.1, 6.4 Hz, 1H), 3.60 (dq, *J* = 11.8, 6.0 Hz, 1H), 3.33-3.25 (m, 1H), 2.15 (td, *J* = 12.0, 5.8 Hz, 1H), 2.08-1.92 (m, 2H), 1.77-1.63 (m, 1H).^{13}C NMR (100 MHz, DMSO) δ 198.38, 161.30, 158.06, 147.13, 136.82, 134.54, 132.18, 130.49, 127.43, 126.71, 126.49, 126.46, 120.13, 41.60, 41.29, 37.17, 25.28, 20.98. HRMS (ESI) m/z Calcd for $C_{20}H_{18}BrN_2O_2$ $[M+H]^+$: 397.0546, found: 397.0545.



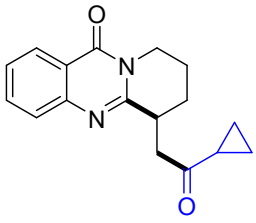
(**5ae**)

White solid, M.P.132.2-134.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.79 (d, *J* = 9.4 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.53 (dd, *J* = 13.6, 7.9 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.40-7.32 (m, 2H), 4.53-4.35 (m, 1H), 3.38-3.12 (m, 1H), 2.32 (dd, *J* = 12.5, 6.2 Hz, 1H), 2.19-1.99 (m, 2H), 1.75 (tt, *J* = 12.6, 8.0 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 197.44, 162.86 (d, *J* = 247.8 Hz), 161.93, 139.54 (d, *J* = 6.3 Hz), 133.95, 130.23 (d, *J* = 7.7 Hz), 126.65, 126.60, 126.18, 123.96 (d, *J* = 2.8 Hz), 120.16 (d, *J* = 13.4 Hz), 119.88, 115.00 (d, *J* = 22.3 Hz), 41.43, 41.29, 36.99, 25.62, 21.20. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.34. HRMS (ESI) m/z Calcd for $C_{20}H_{18}FN_2O_2$ $[M+H]^+$: 337.1247, found: 337.1249.



(**5af**)

White solid, M.P.140.0-141.7 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.68 (dd, *J* = 13.4, 7.9 Hz, 3H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 4.50-4.33 (m, 1H), 3.70 (dq, *J* = 12.1, 6.1 Hz, 1H), 3.19 (dd, *J* = 16.7, 4.5 Hz, 1H), 2.30 (dt, *J* = 12.3, 6.2 Hz, 1H), 2.19-1.99 (m, 2H), 1.75 (ddd, *J* = 12.0, 9.8, 6.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.69, 161.93, 156.72, 138.66, 136.15, 133.98, 131.88, 131.26, 129.78, 128.69, 128.14, 126.66, 126.59, 126.20, 120.20, 41.30, 41.23, 36.98, 25.62, 21.19. HRMS (ESI) m/z Calcd for $C_{20}H_{18}BrN_2O_2$ $[M+H]^+$: 397.0546, found: 397.0550.



(**5ag**)

White solid, M.P.103.2-105.0 ℃, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.9 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 4.46-4.26 (m, 1H), 4.11-3.94 (m, 1H), 3.52 (ddt, *J* = 22.8, 11.7, 5.7 Hz, 2H), 2.92 (dd, *J* = 16.4, 5.4 Hz, 1H), 2.21 (td, *J* = 12.1, 5.9 Hz, 1H), 2.16-2.09 (m, 1H), 2.09-1.98 (m, 2H), 1.70-1.58 (m, 1H), 1.20-1.07 (m, 2H), 1.06-0.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.00, 161.95, 156.86, 147.20, 133.92, 126.67, 126.08, 120.26, 45.70, 41.31, 36.47, 25.51, 21.23, 21.05, 10.78, 10.75. HRMS (ESI) m/z Calcd for $C_{17}H_{19}N_2O_2$ $[M+H]^+$: 283.1450, found: 283.1451.

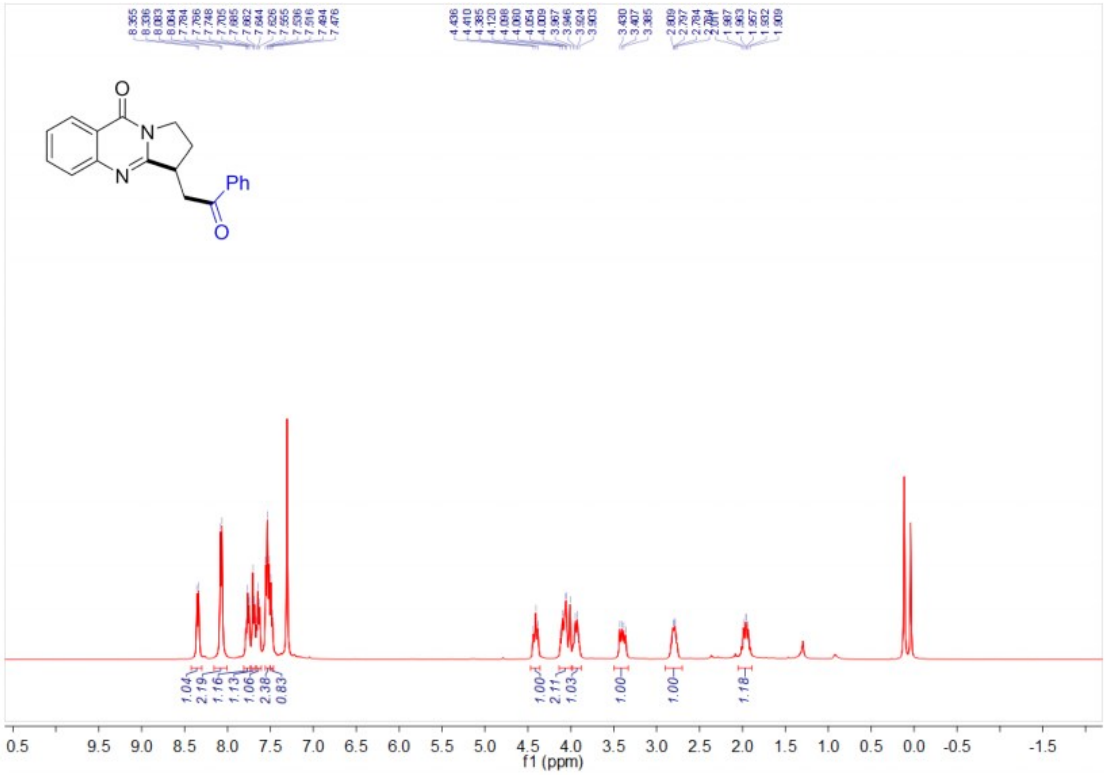
7. References

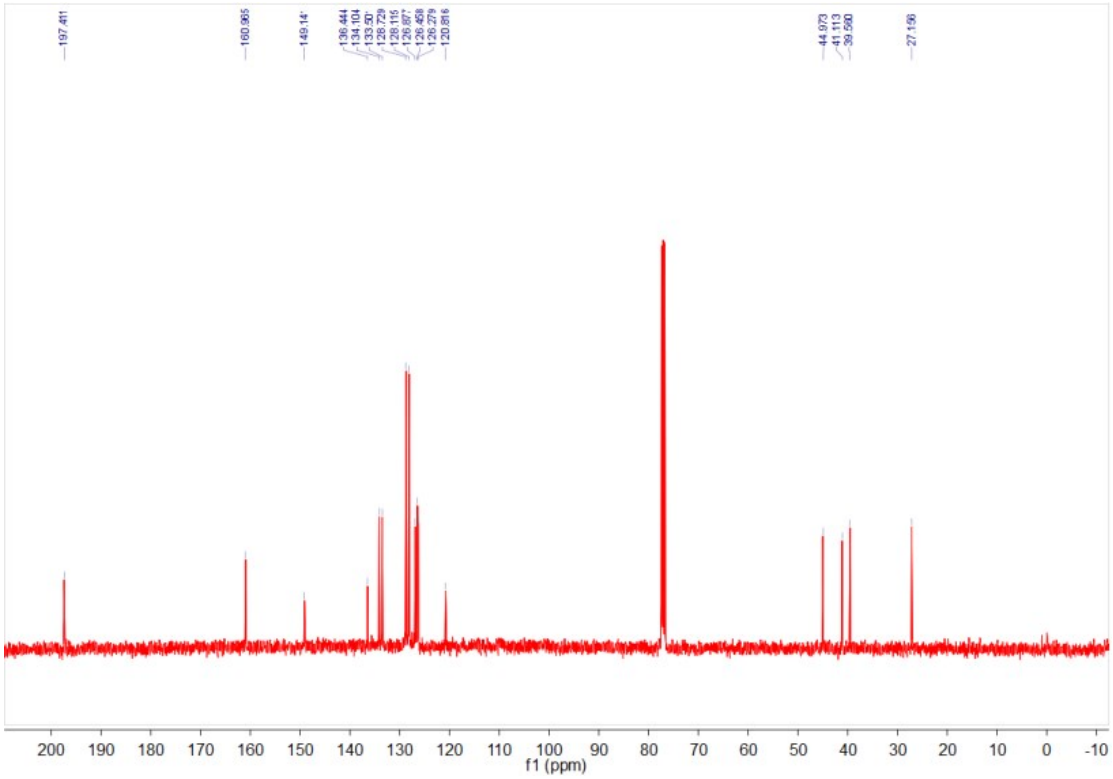
1. (a) D. T. Hieu, D. T. Anh, P. T. Hai, N. T. Thuan, L. T. Huong, E. J. Park, A. Young Ji, J. Soon Kang, P. T. Phuong Dung, S. B. Han and N. H. Nam, *Chem Biodivers*, 2019, **16**, e1800502; (b) J. Zhuang, C. Wang, F. Xie and W. Zhang, *Tetrahedron*, 2009, **65**, 9797-9800.

2. (a) M. Miyashita, A. Yoshikoshi and P. A. Grieco, *J. Org. Chem.*, 1977, **42**, 3772-3774; (b) C. Kim, B. P. Shah, P. Subramaniam and K.-B. Lee, *Mol. Pharmaceutics*, 2011, **8**, 1955-1961.

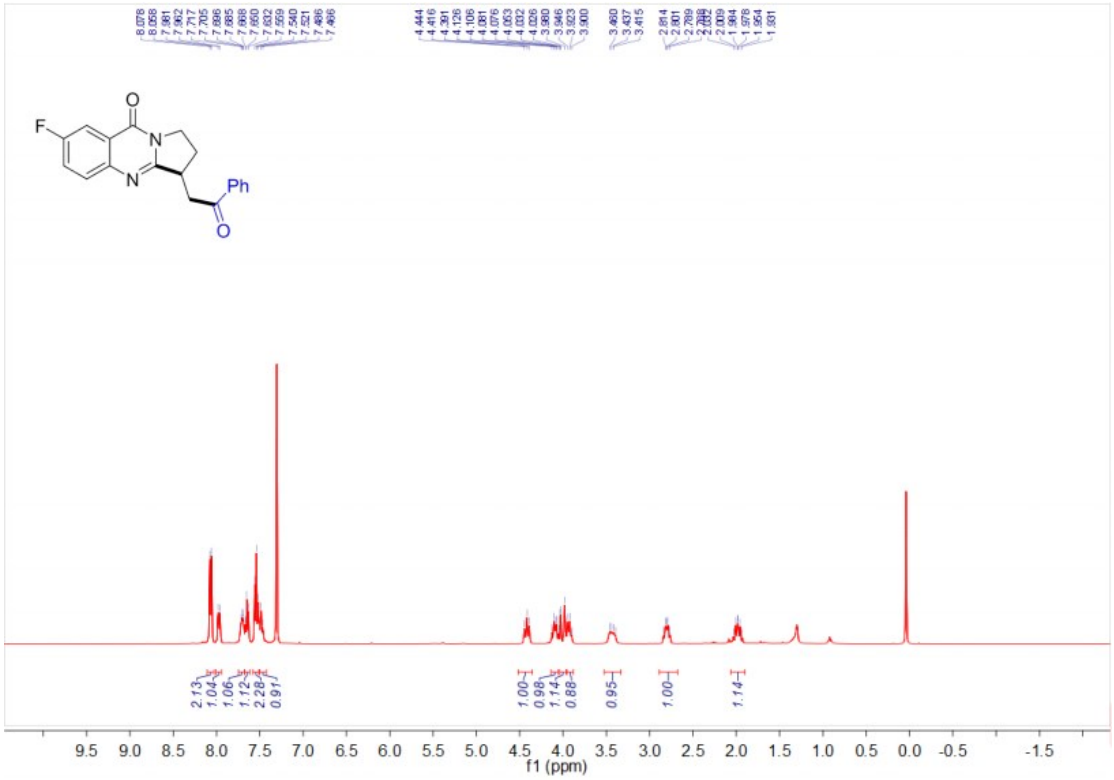
3. J. Li, X.-C. Lu, Y. Xu, J.-X. Wen, G.-Q. Hou and L. Liu, *Org. Lett.*, 2020, **22**, 9621-9626.

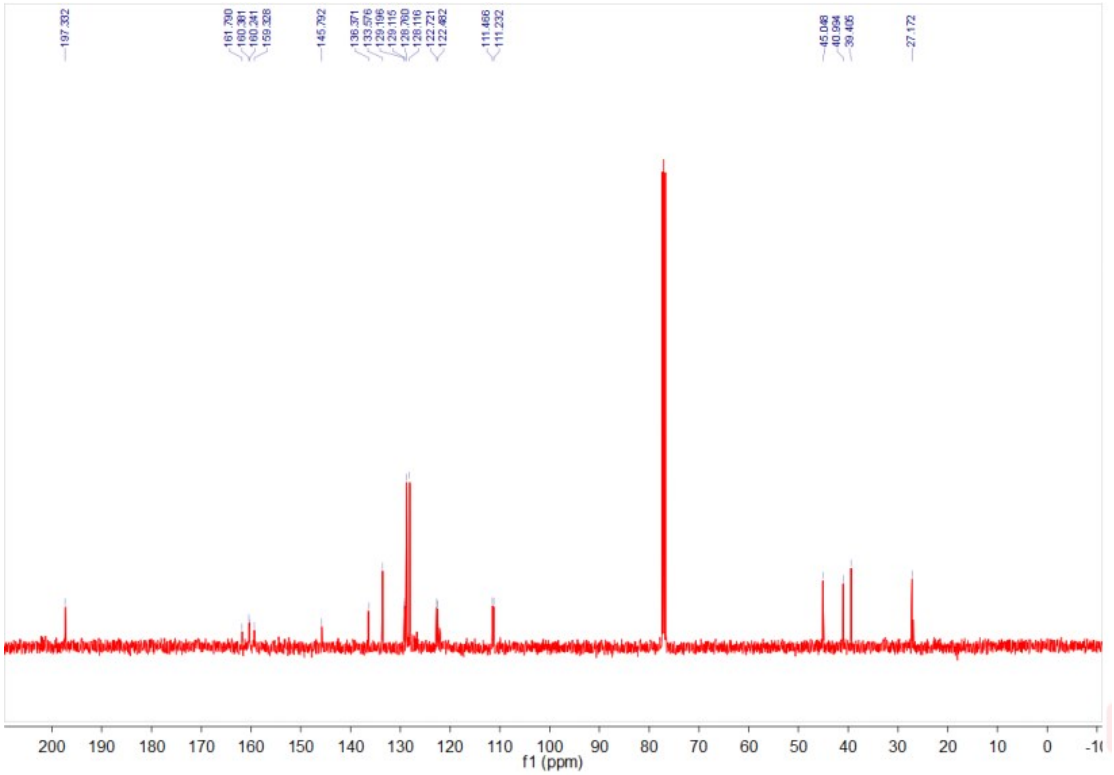
3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4aa)**

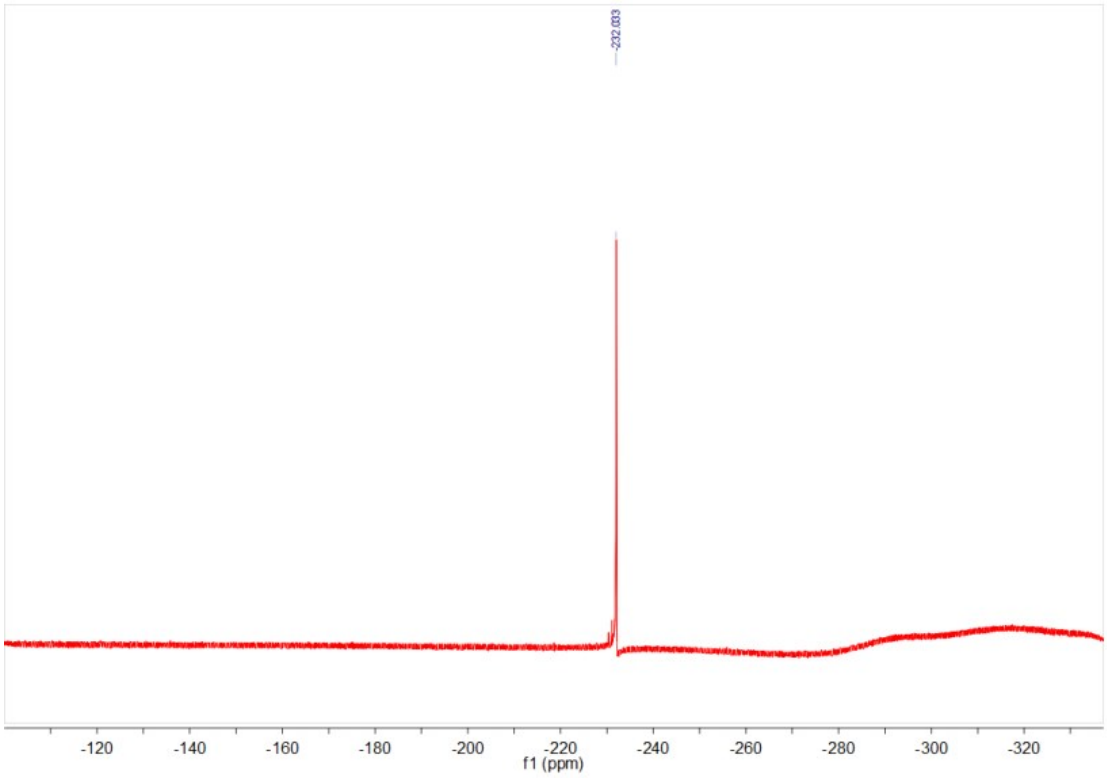




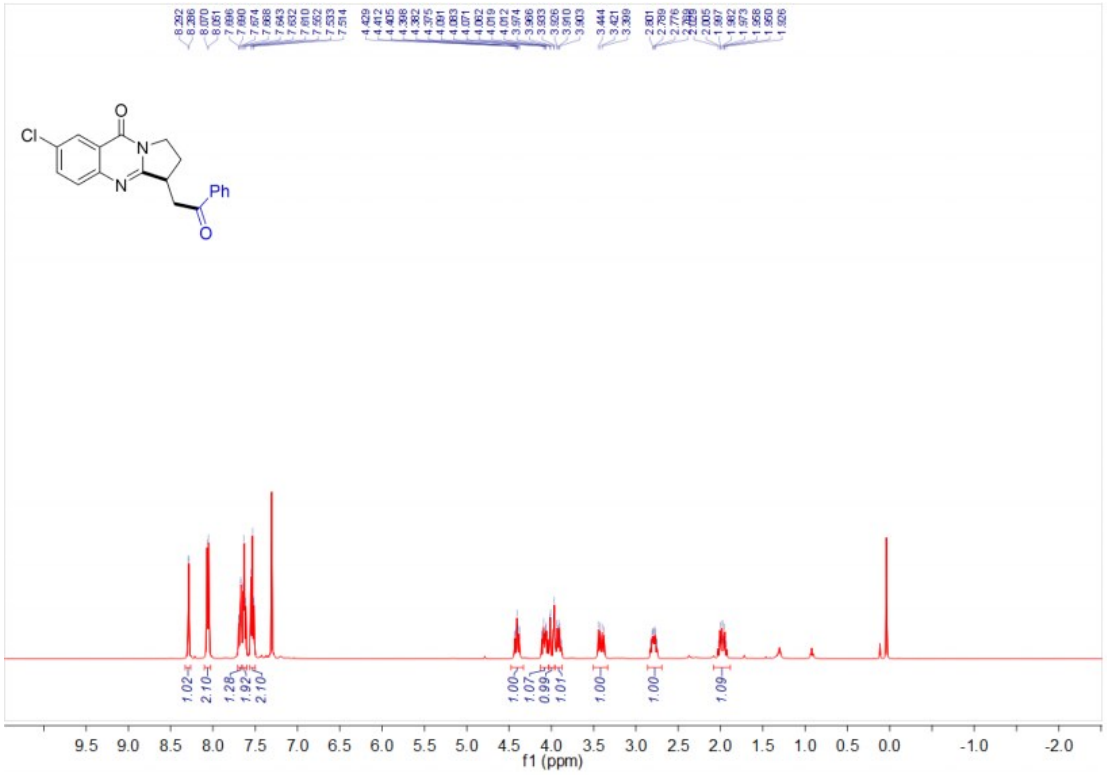
7-fluoro-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ba**)

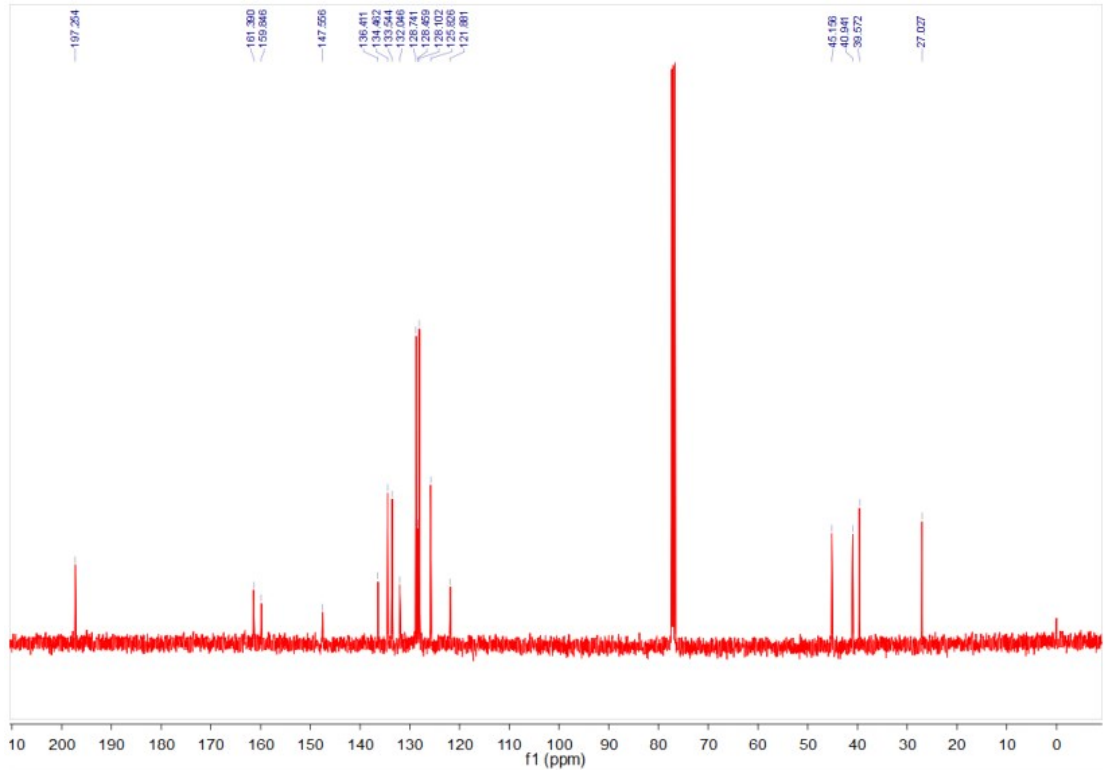




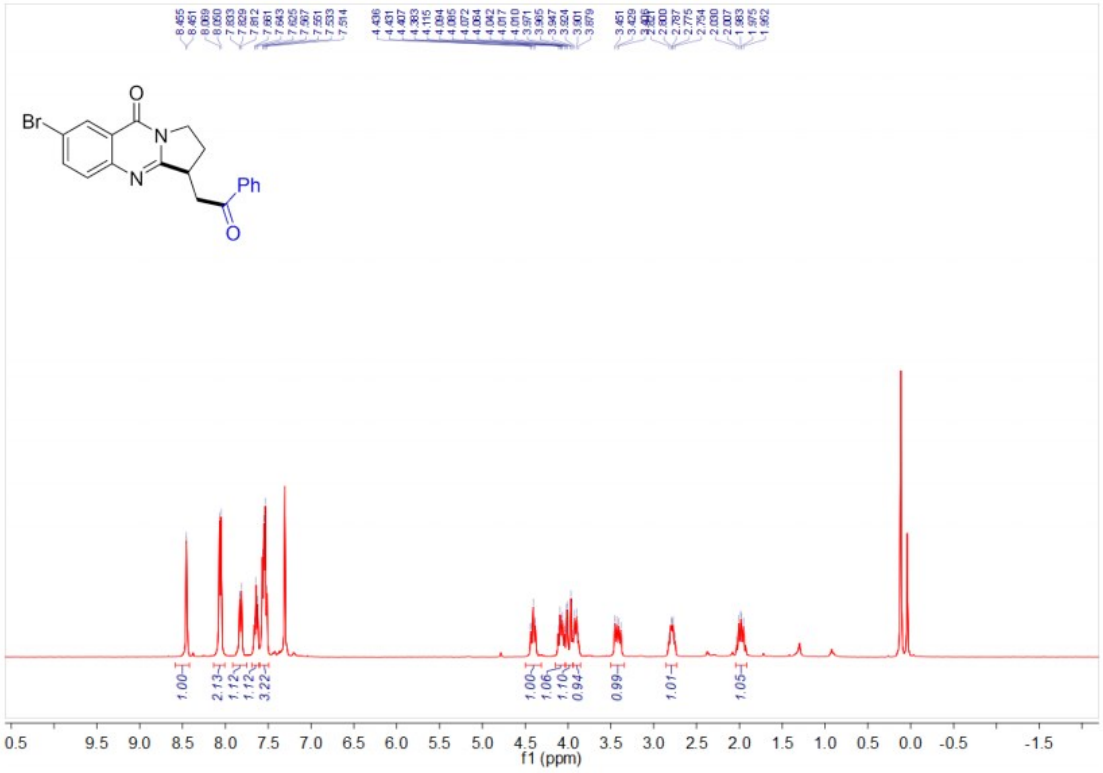

-232.033
-120
-140
-160
-180
-200
-220
-240
-260
-280
-300
-320
f1 (ppm)

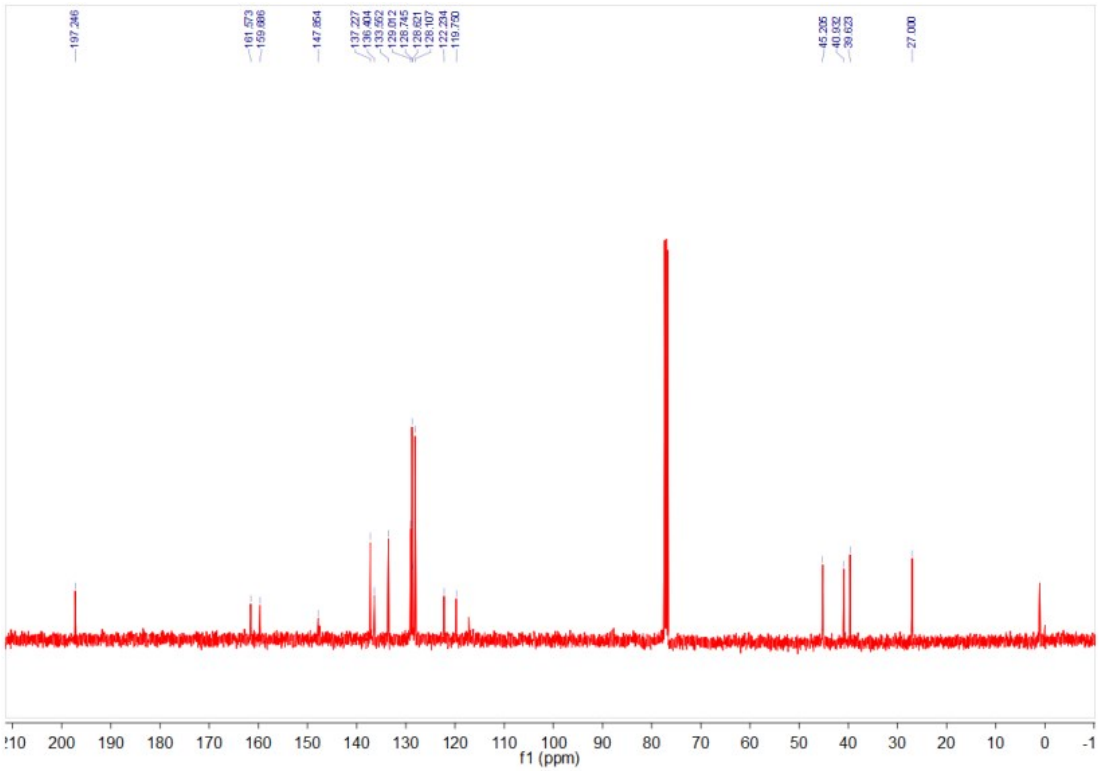
7-chloro-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H)*-one (**4ca**)



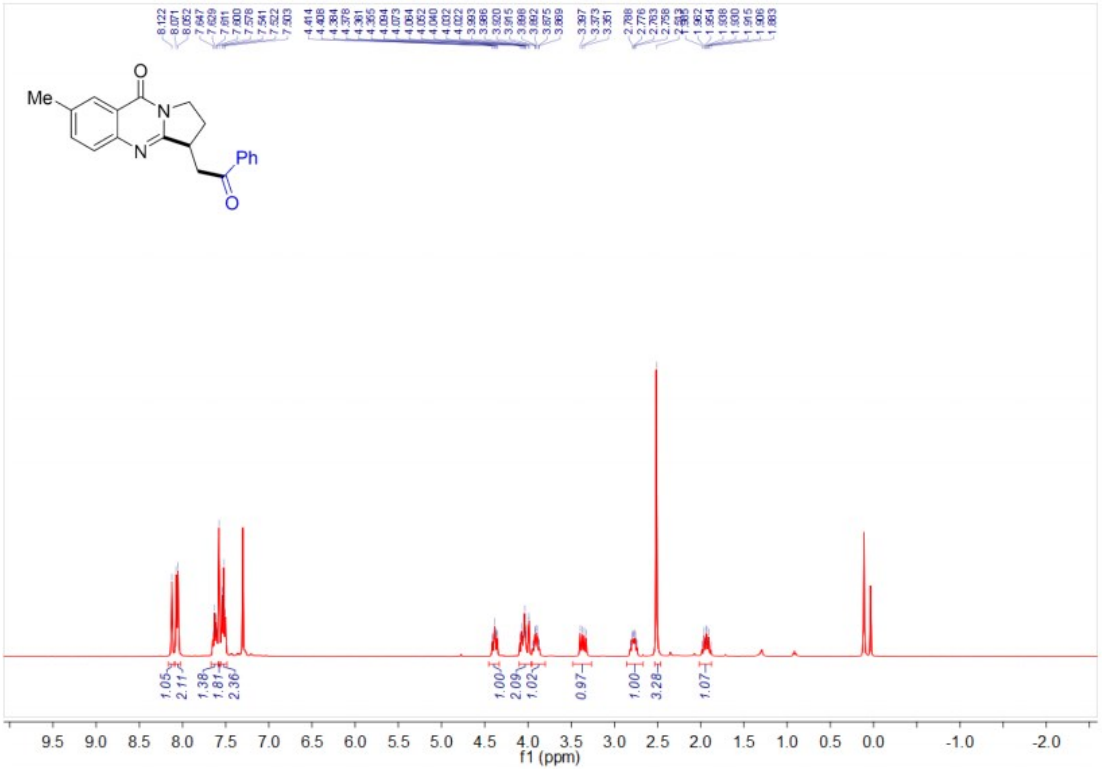


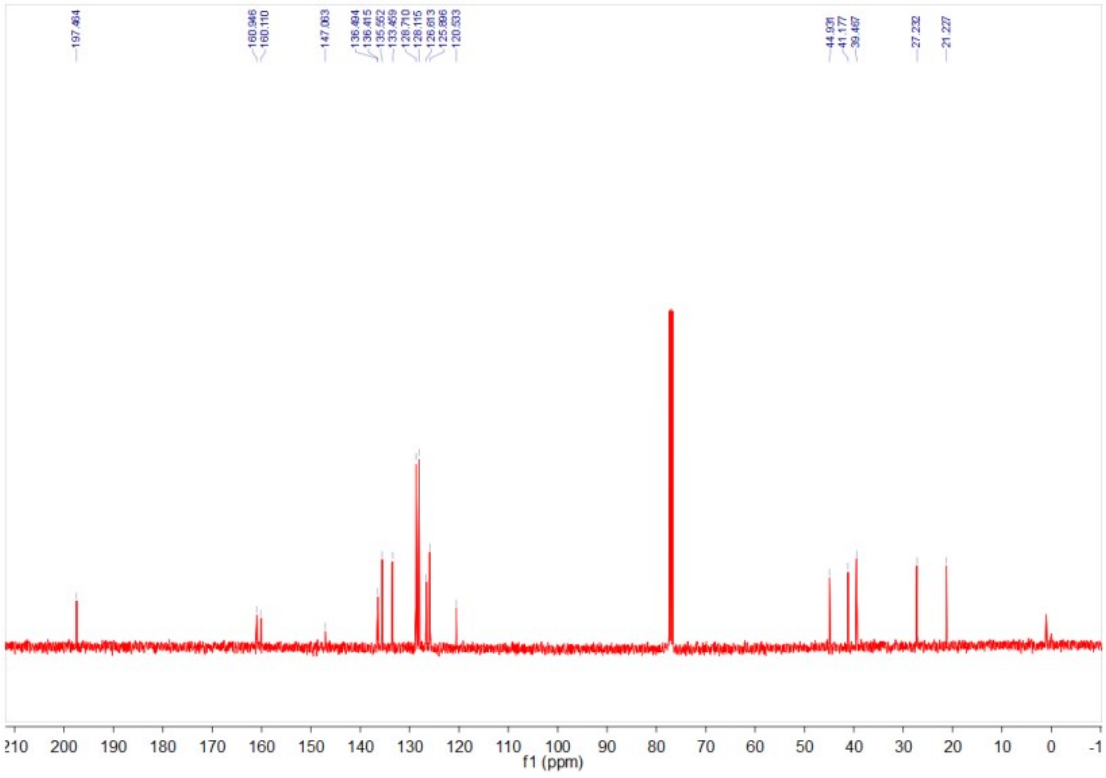
7-bromo-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4da**)



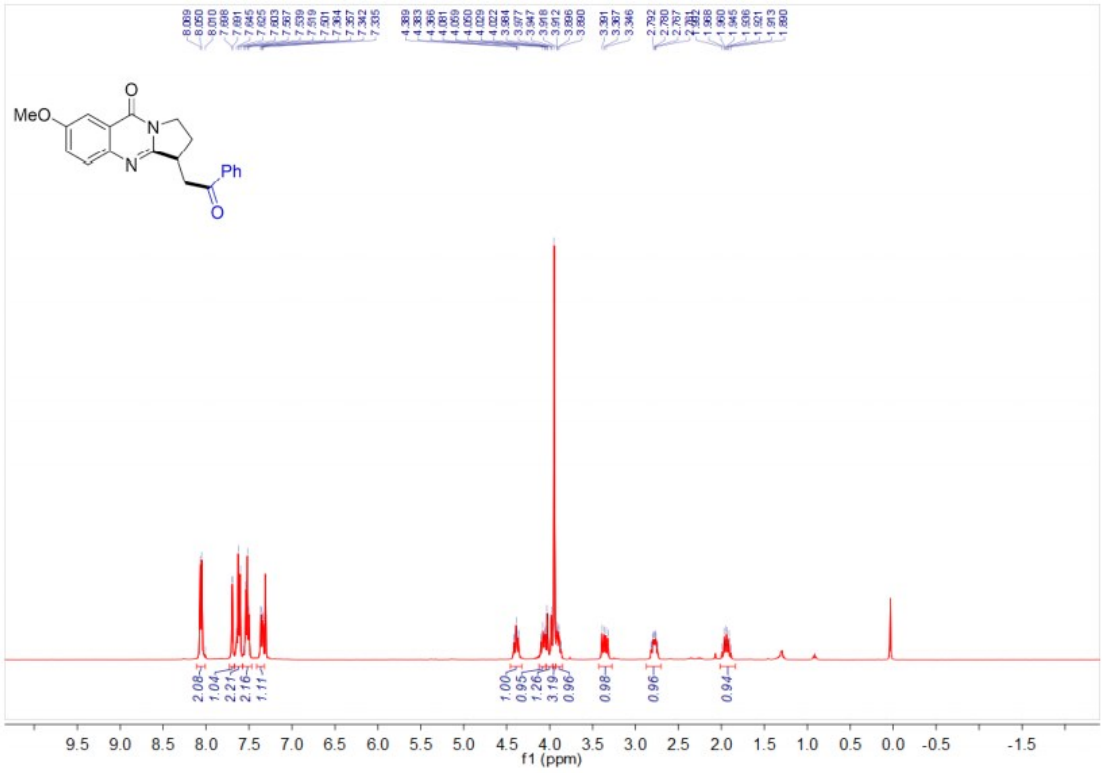


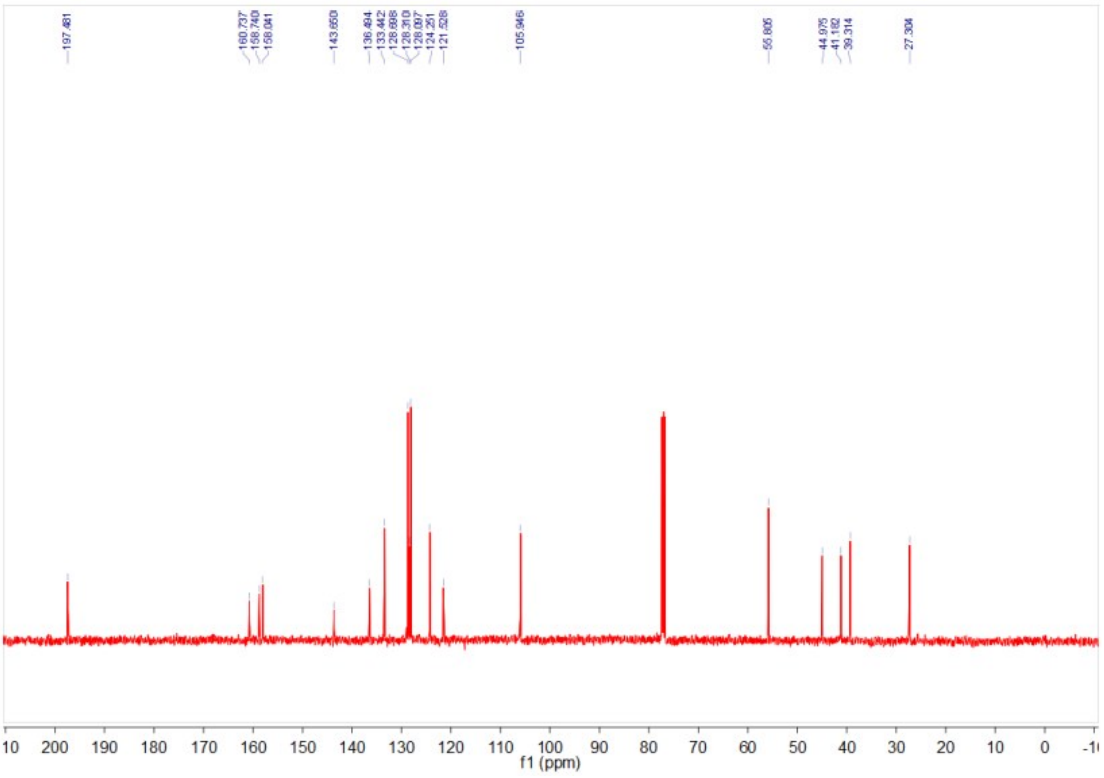
7-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ea)**



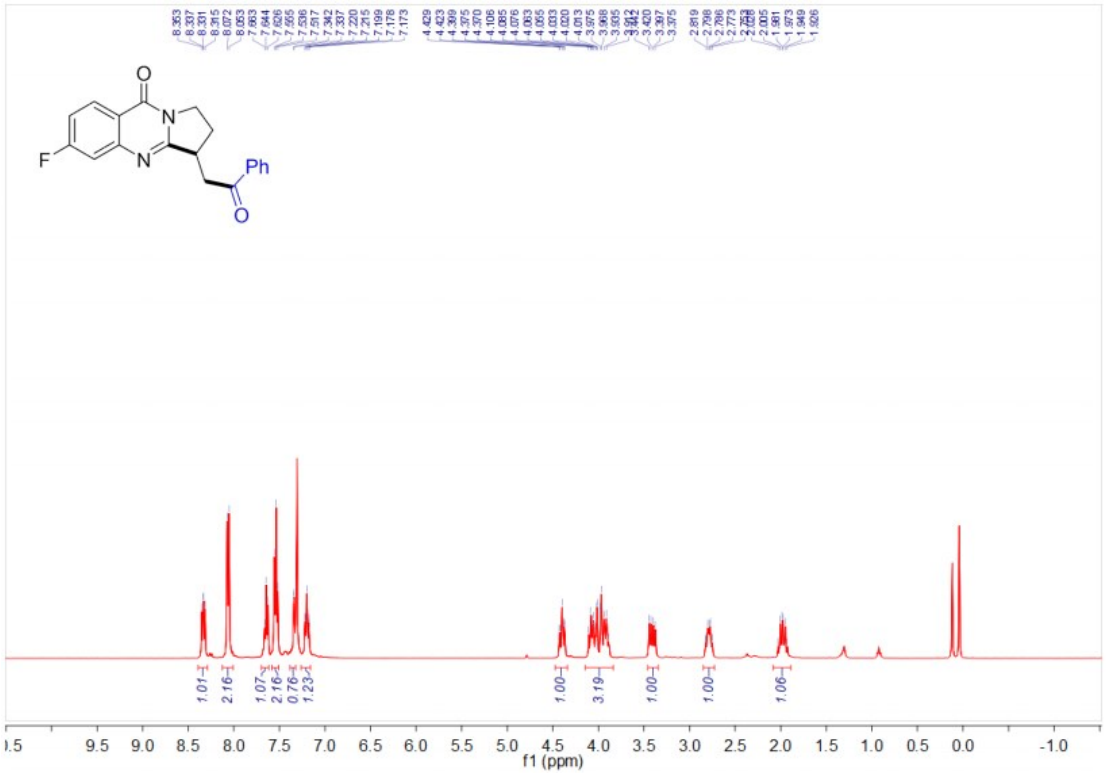


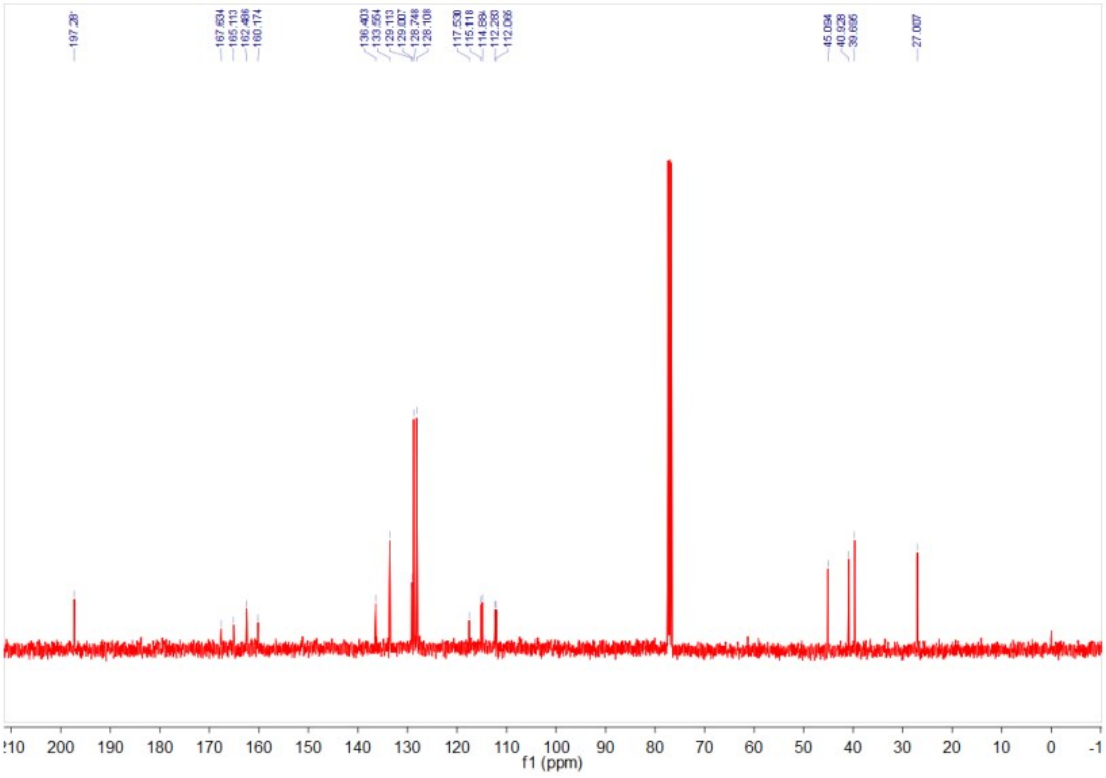
7-methoxy-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4fa**)

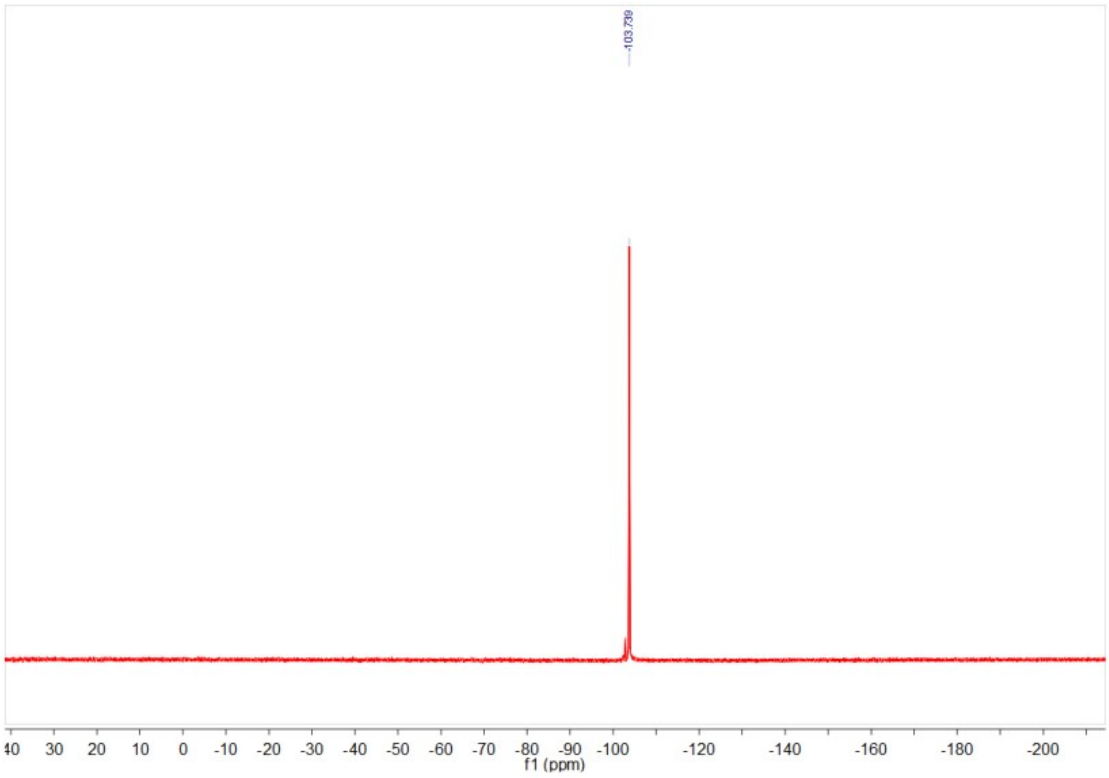




6-fluoro-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ga**)






-103.739
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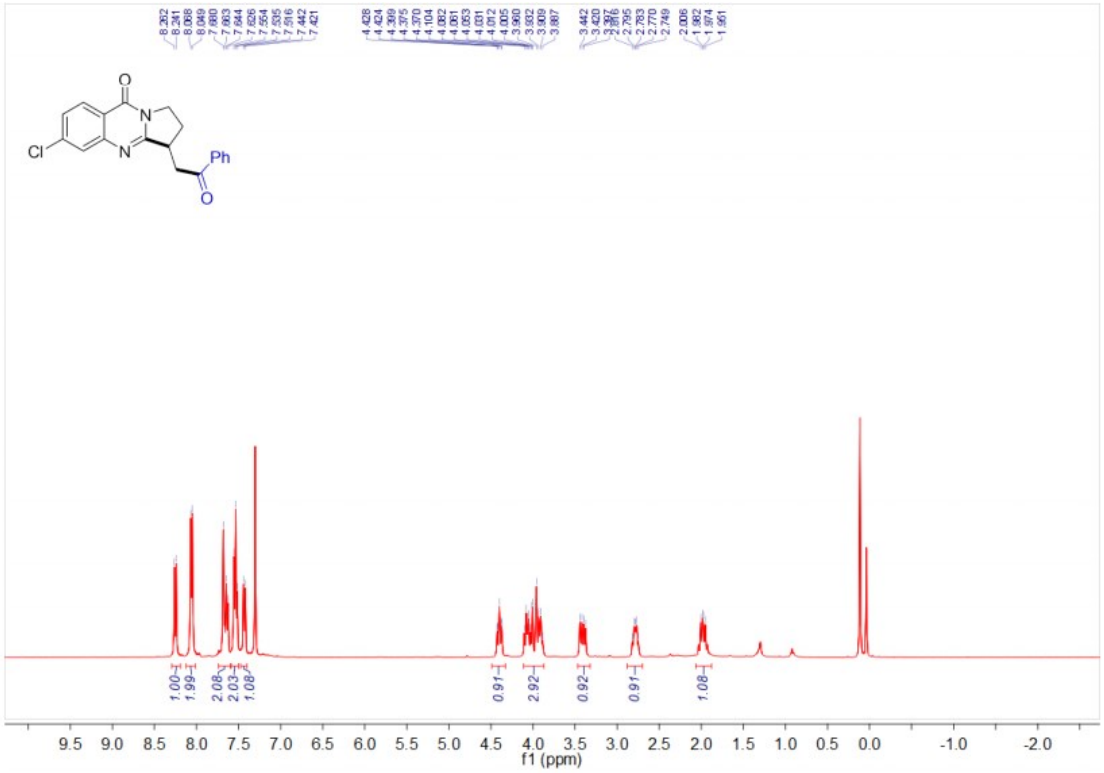
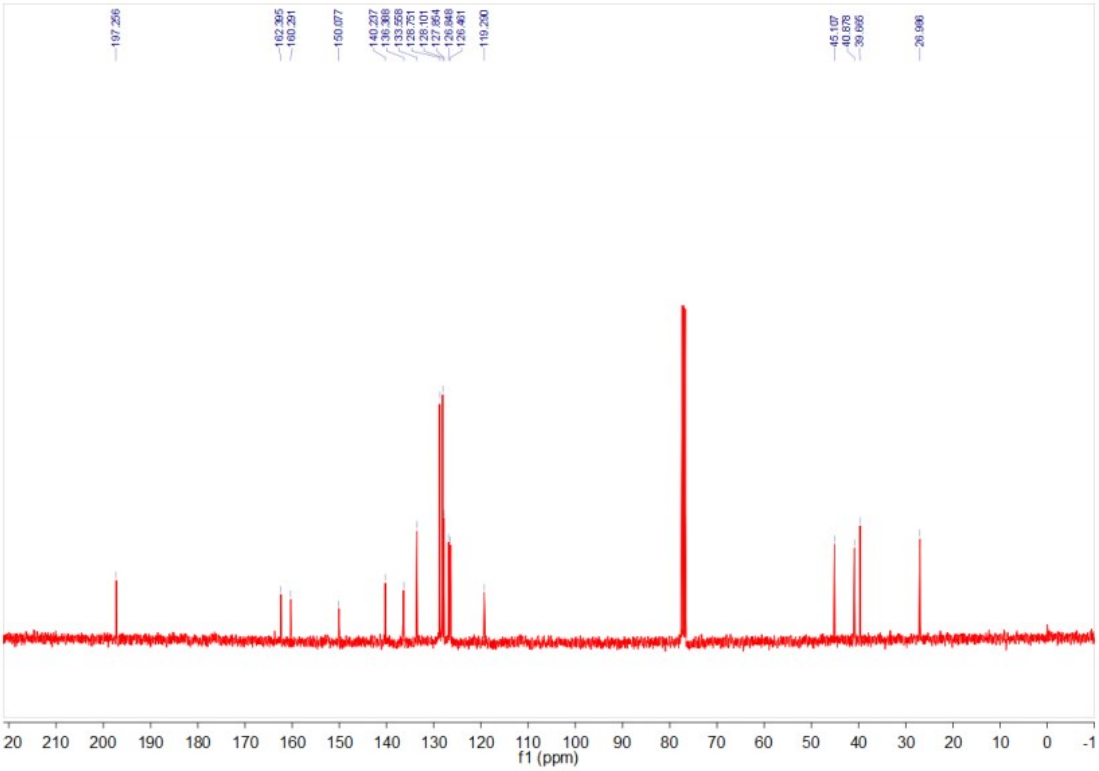
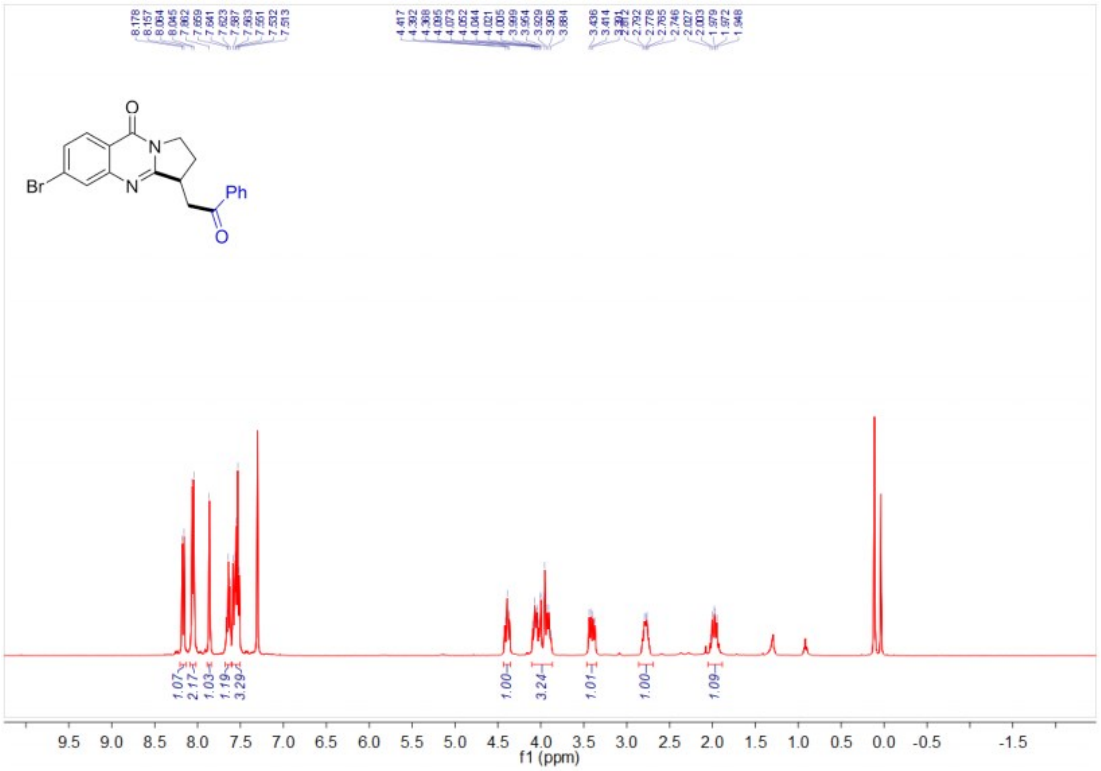
f1 (ppm)

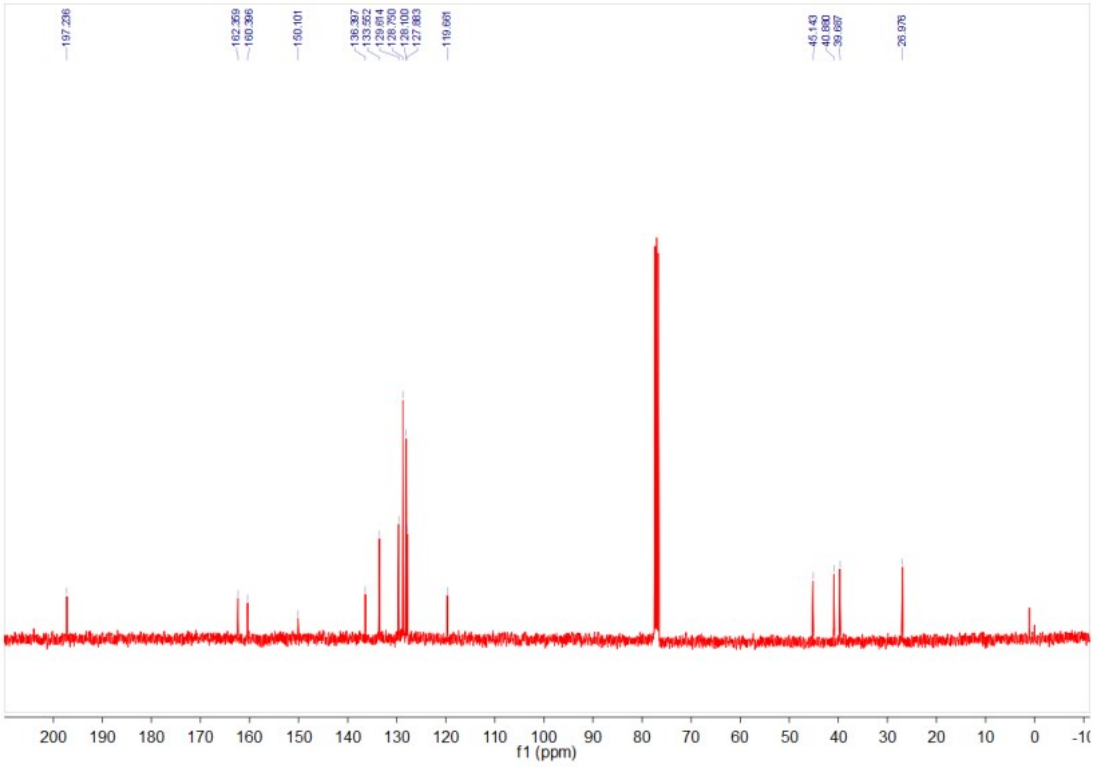
6-chloro-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ha**)



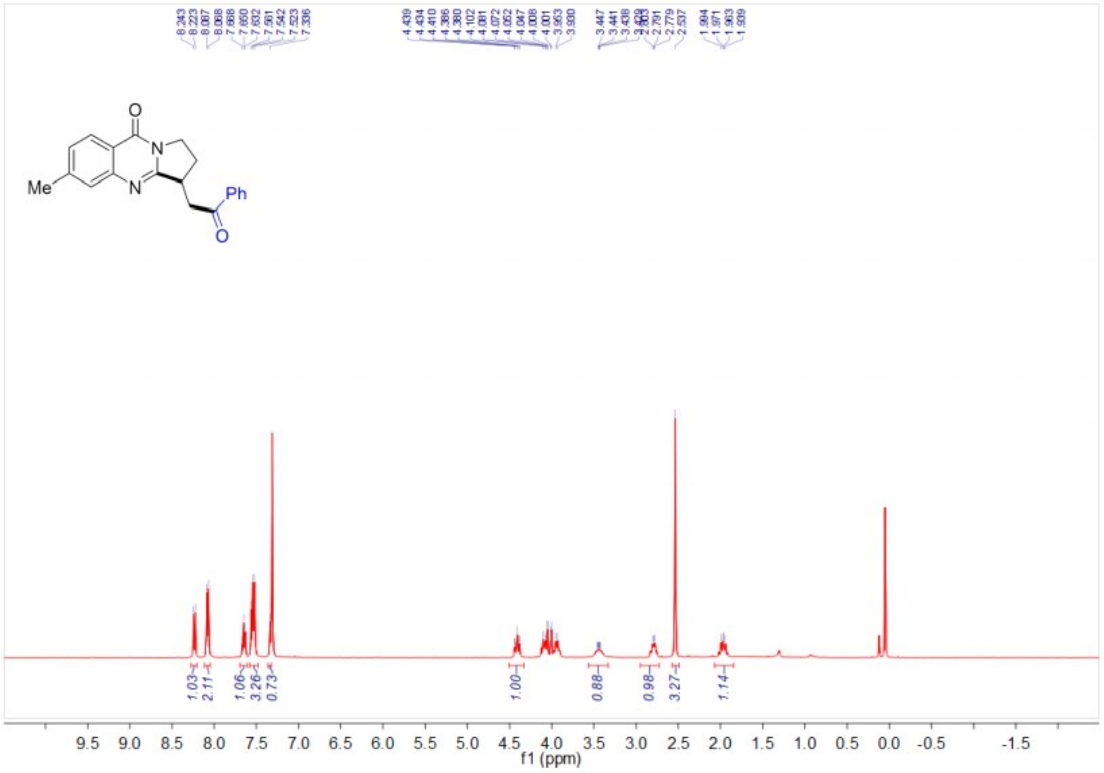


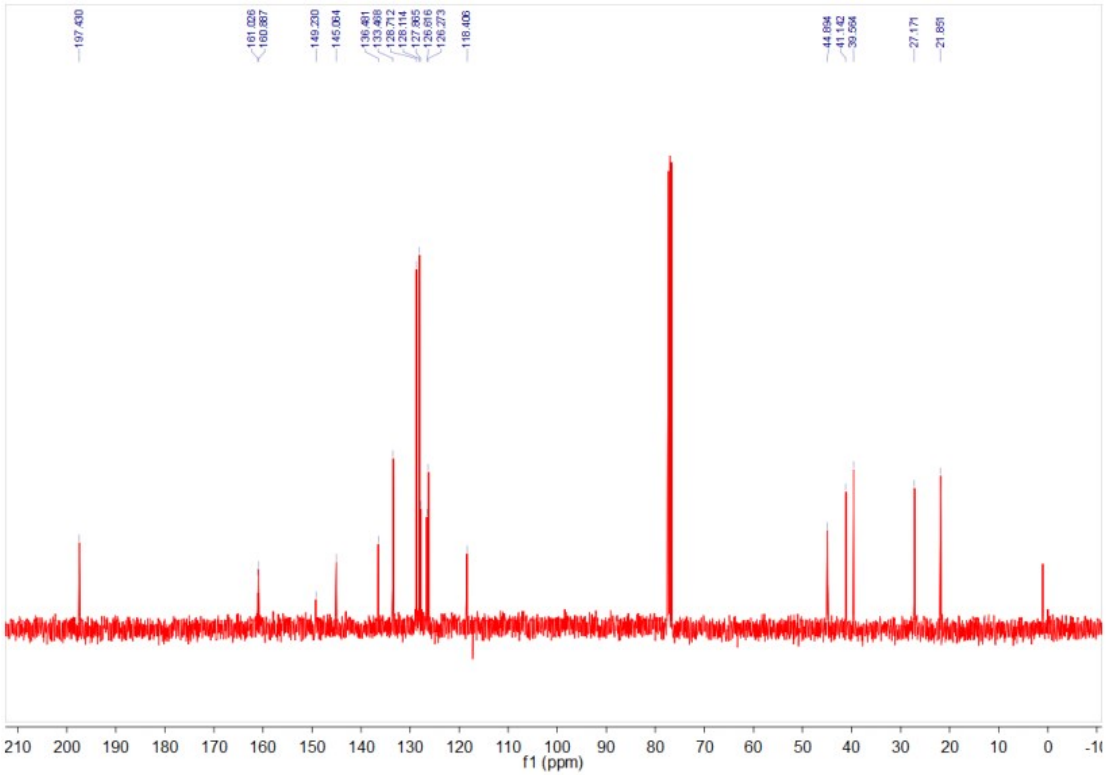
6-bromo-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ia**)



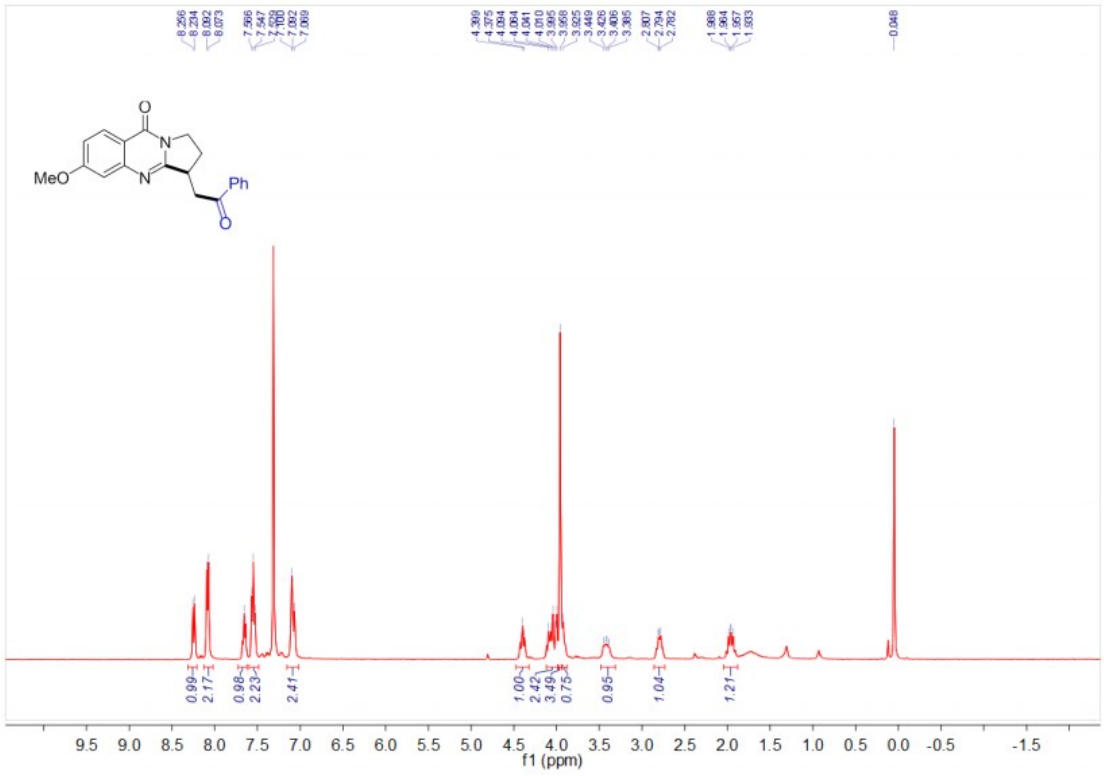


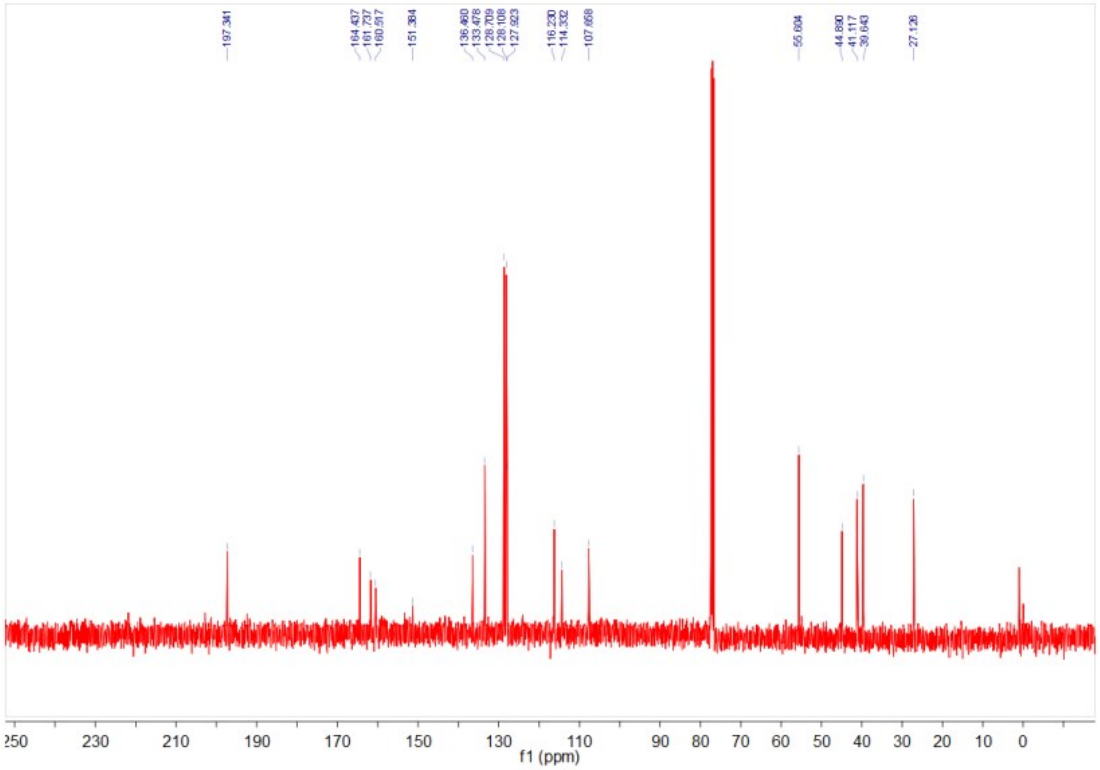
6-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ja)**



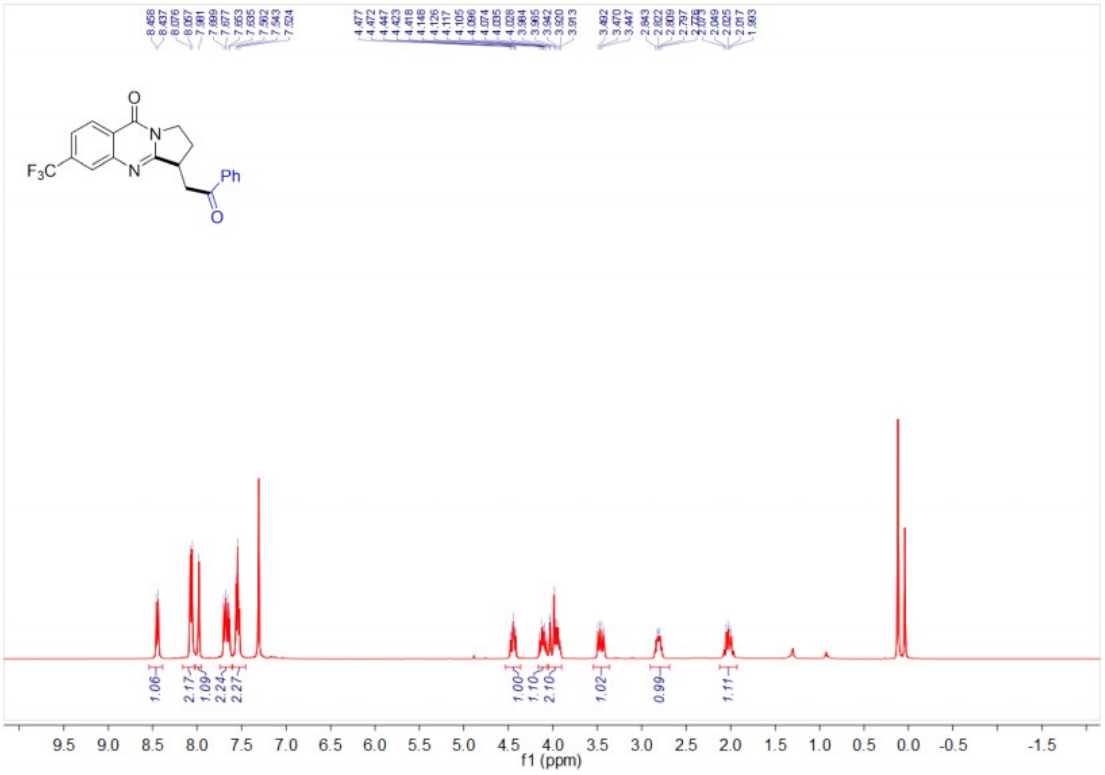


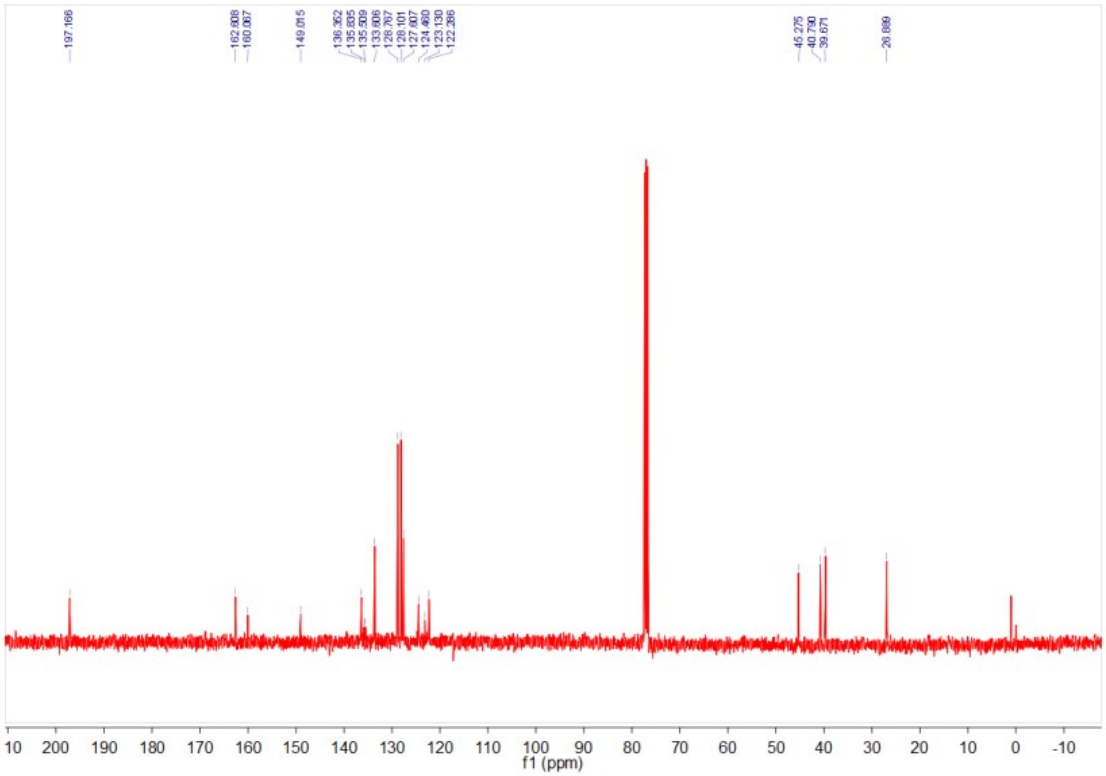
6-methoxy-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ka**)

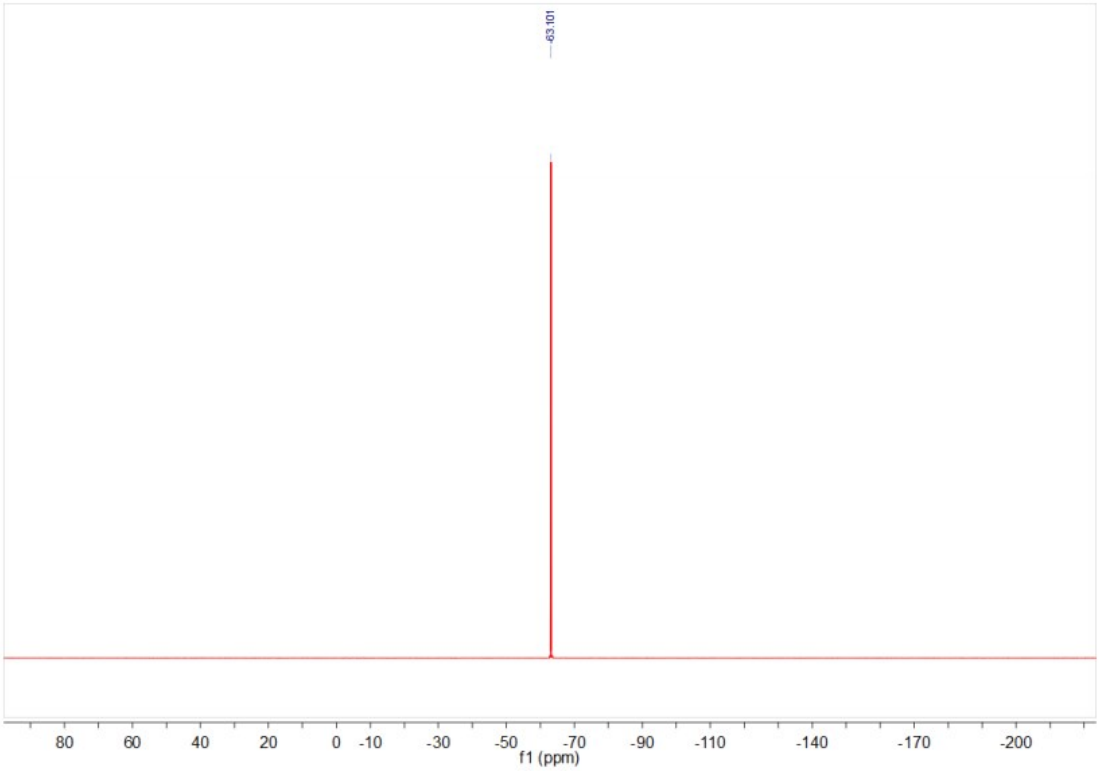




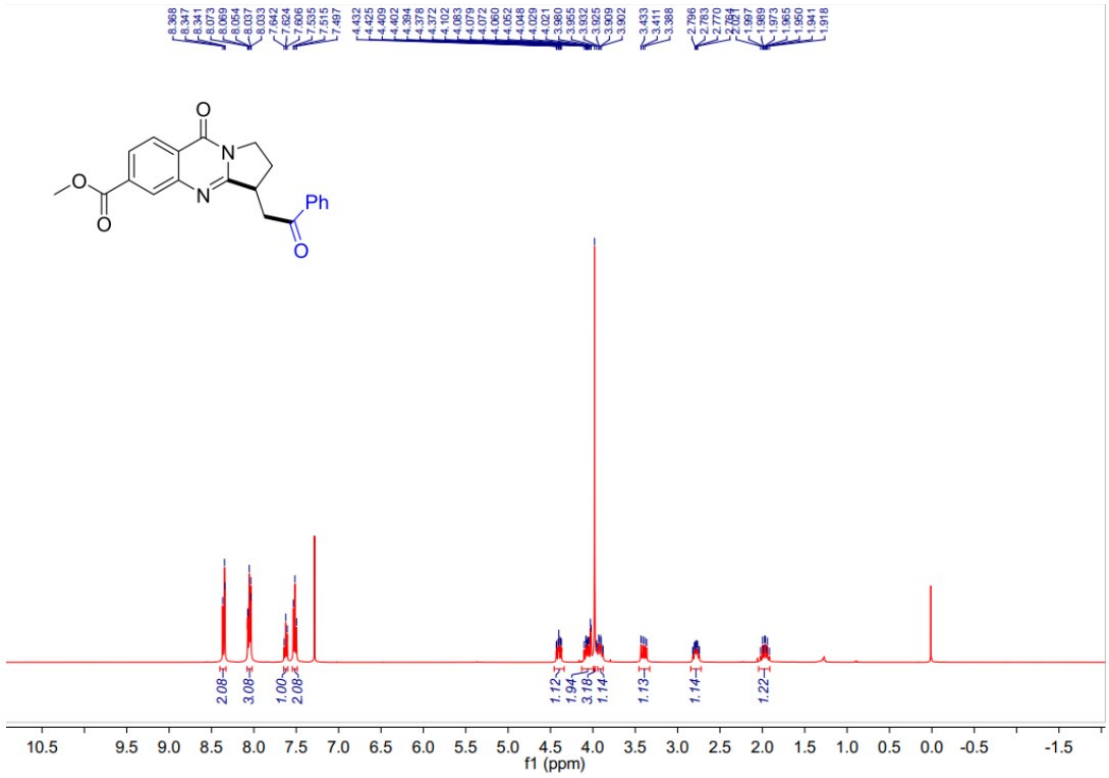
3-(2-oxo-2-phenylethyl)-6-(trifluoromethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4la**)

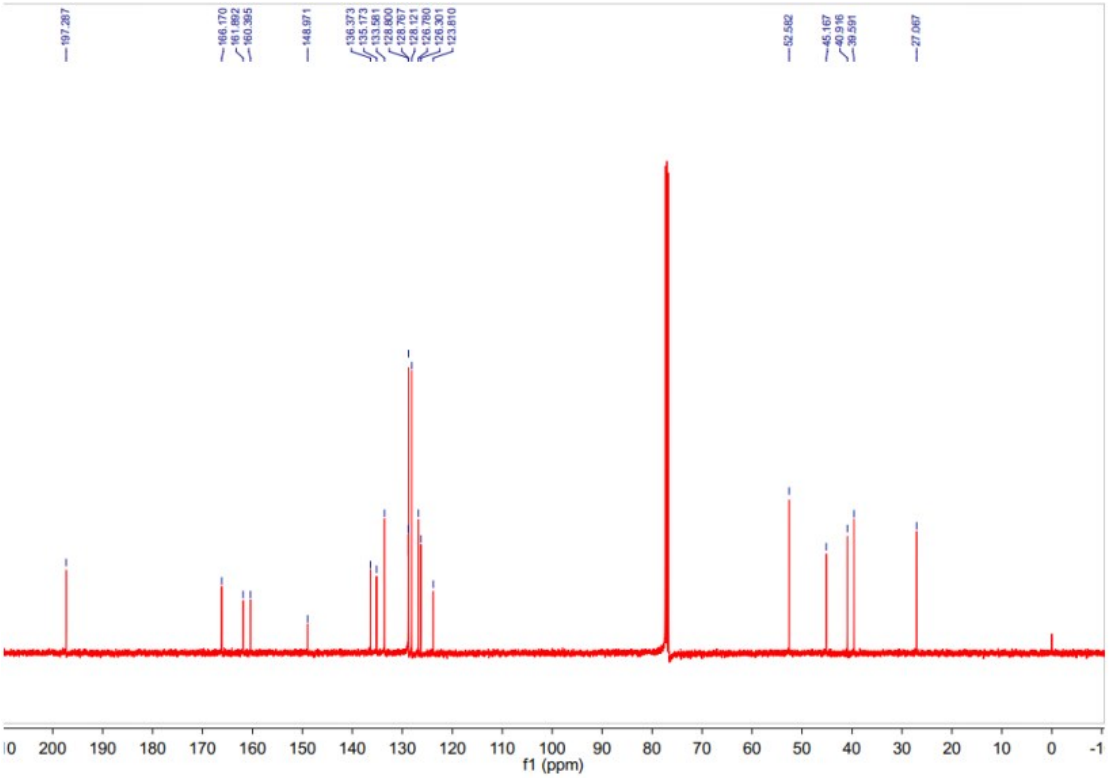




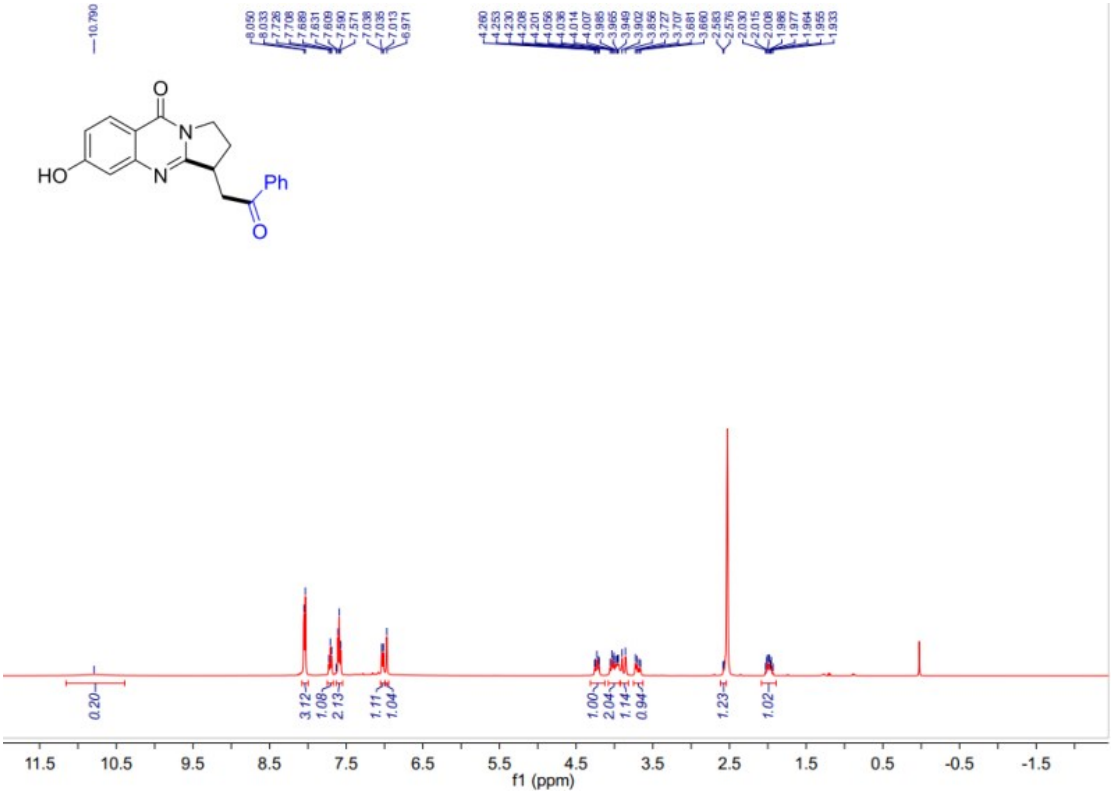

-63.101
80
60
40
20
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
f1 (ppm)

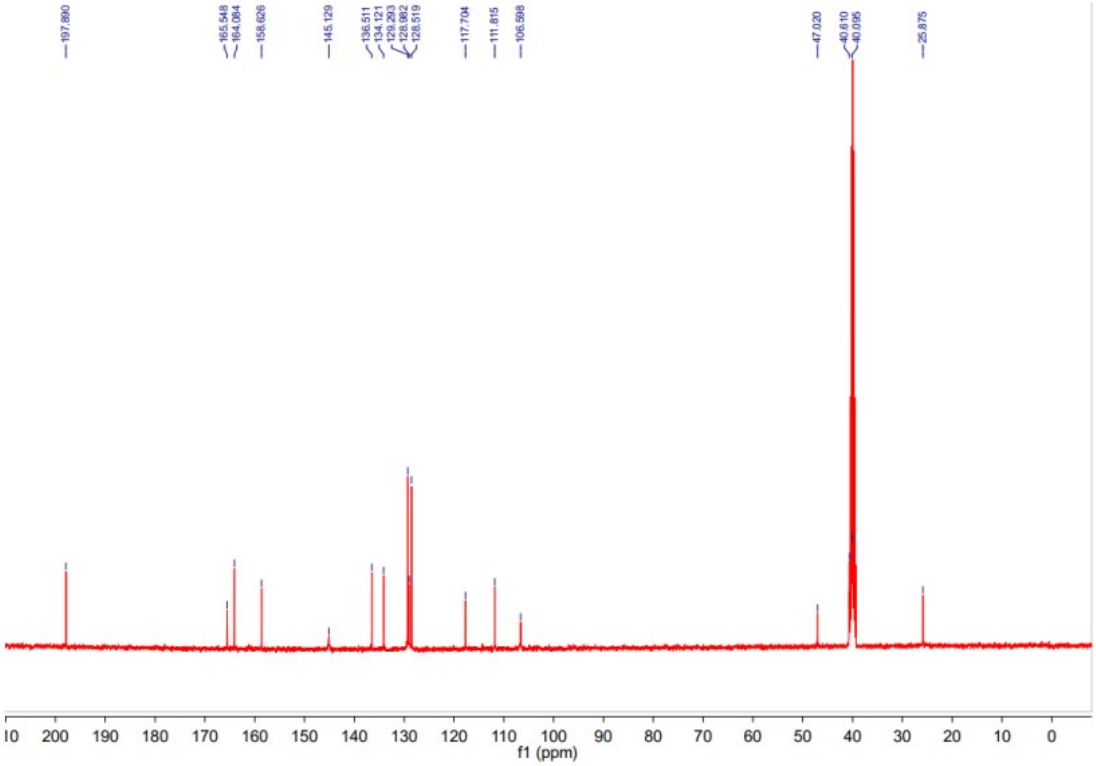
methyl 9-oxo-3-(2-oxo-2-phenylethyl)-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline-6-carboxylate (**4ma**)



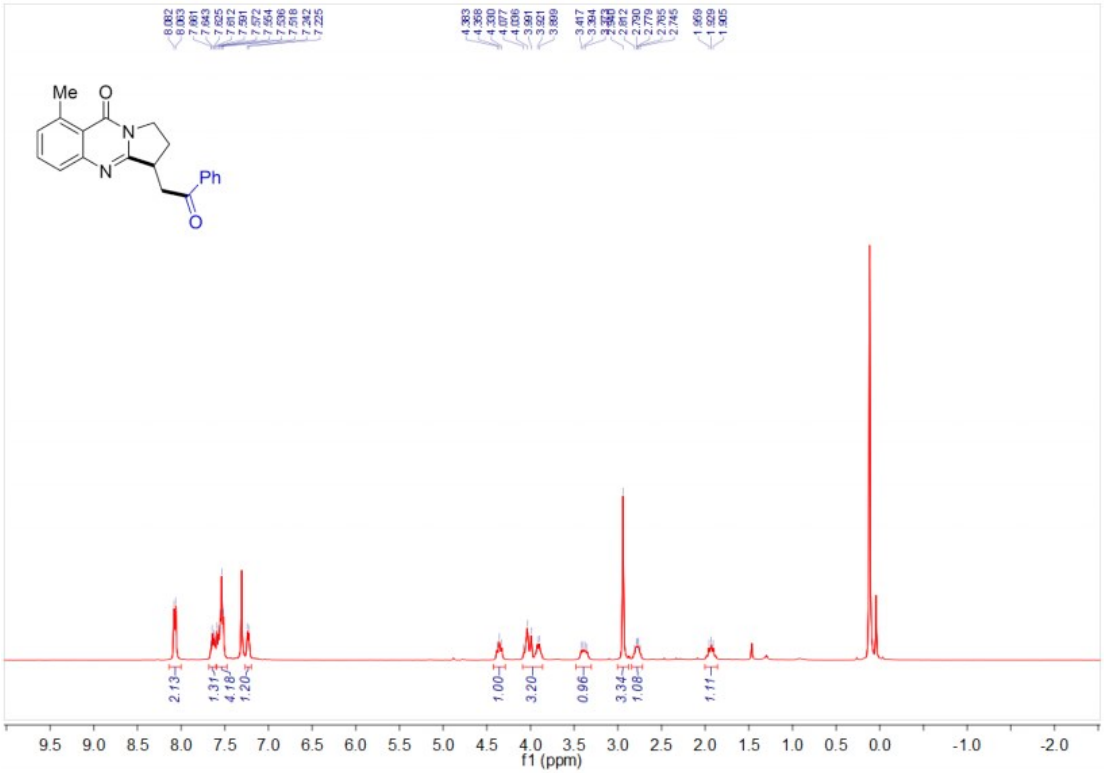


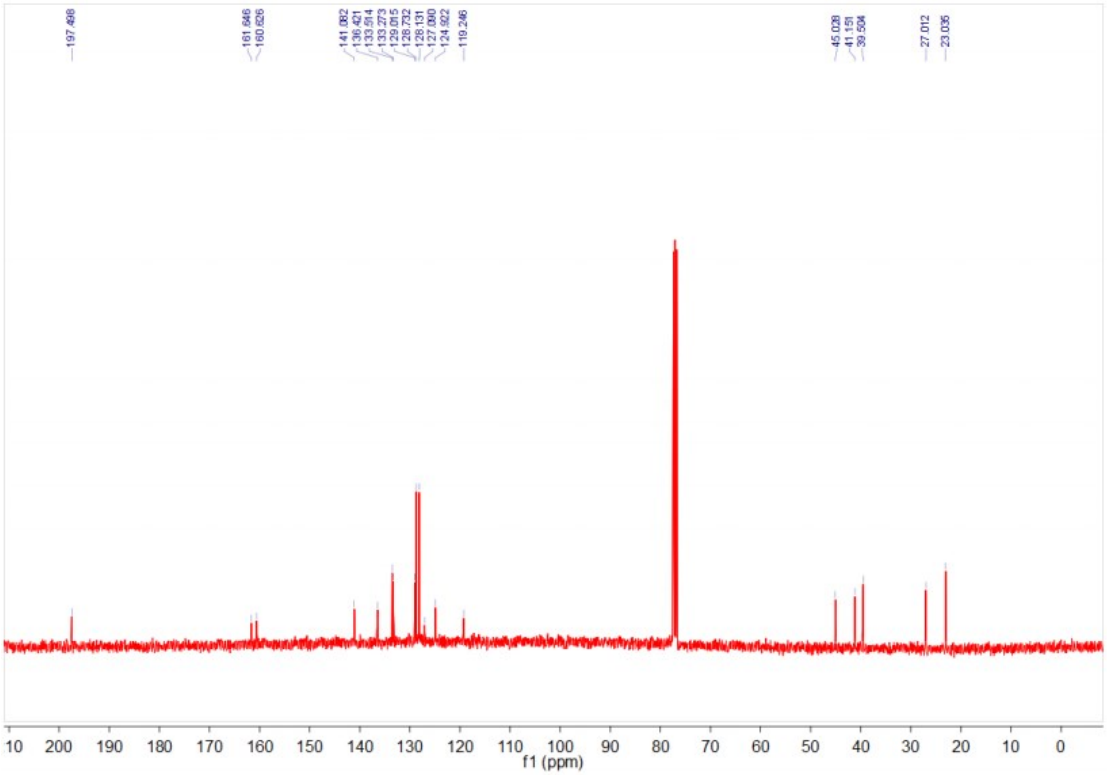
6-hydroxy-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4na**)



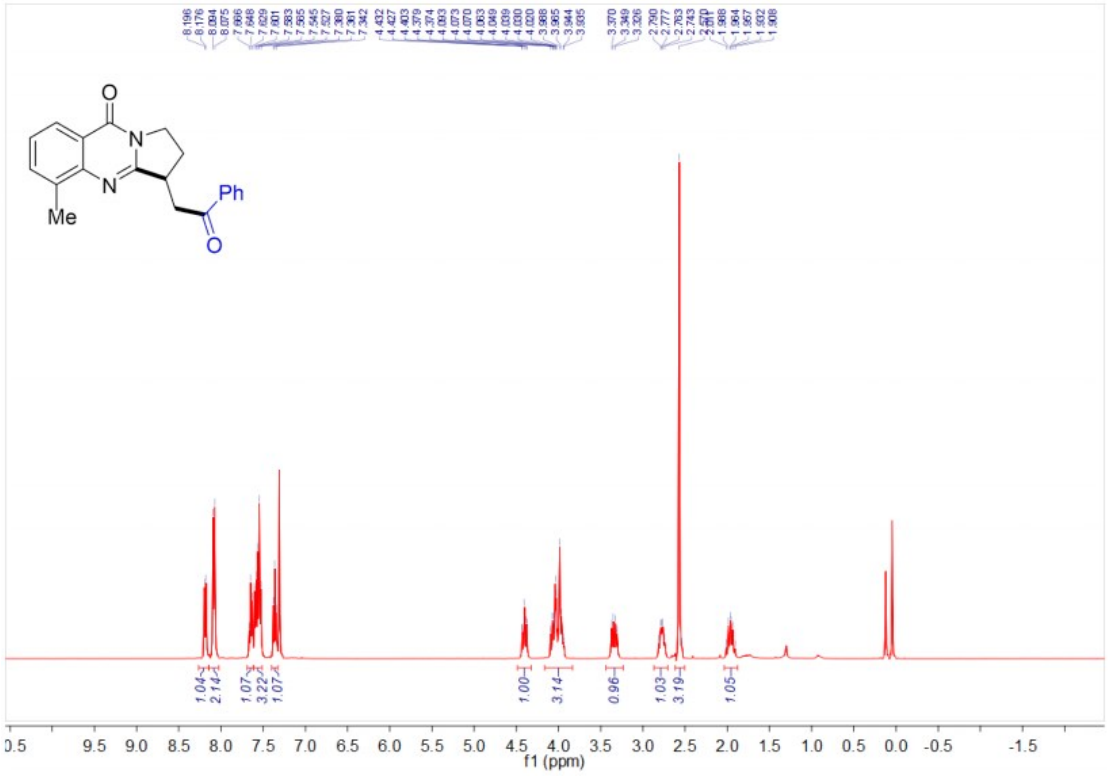


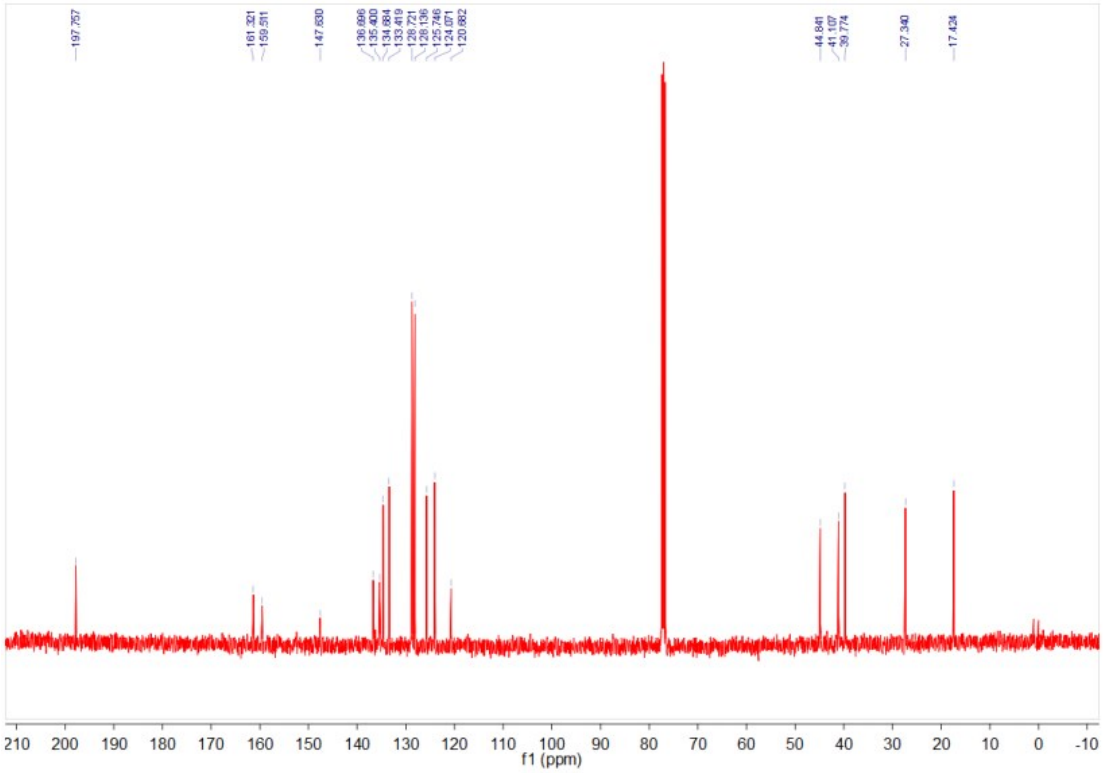
8-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4oa)**



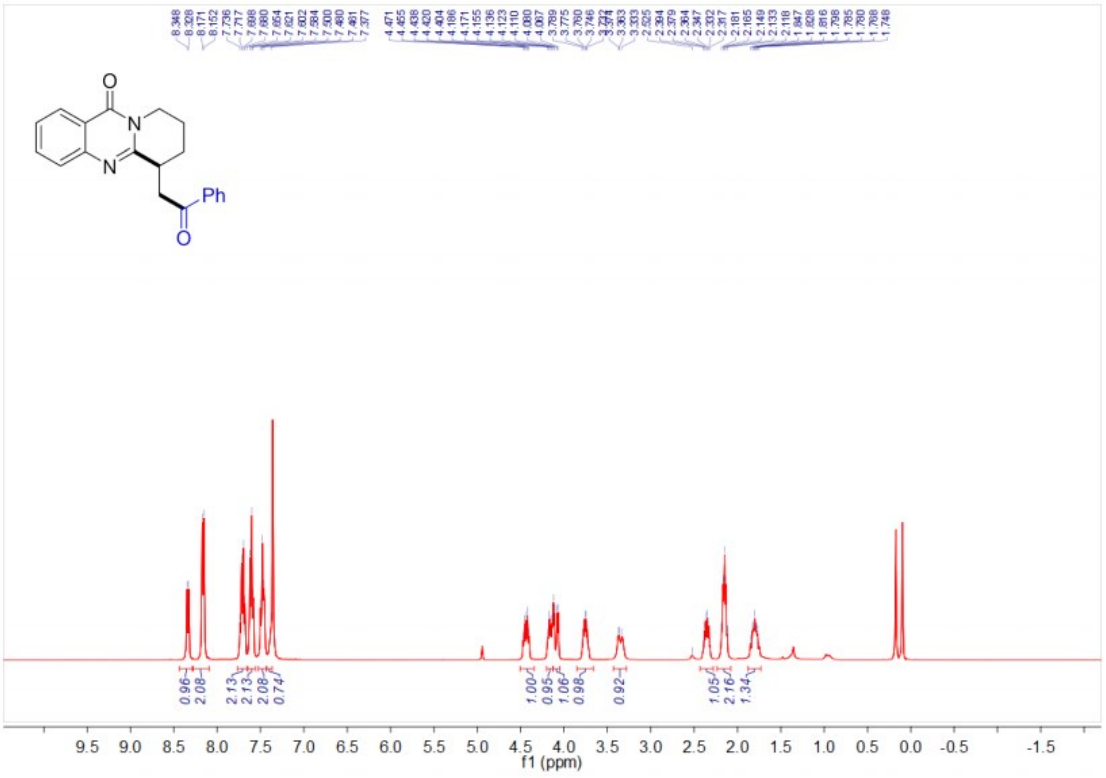


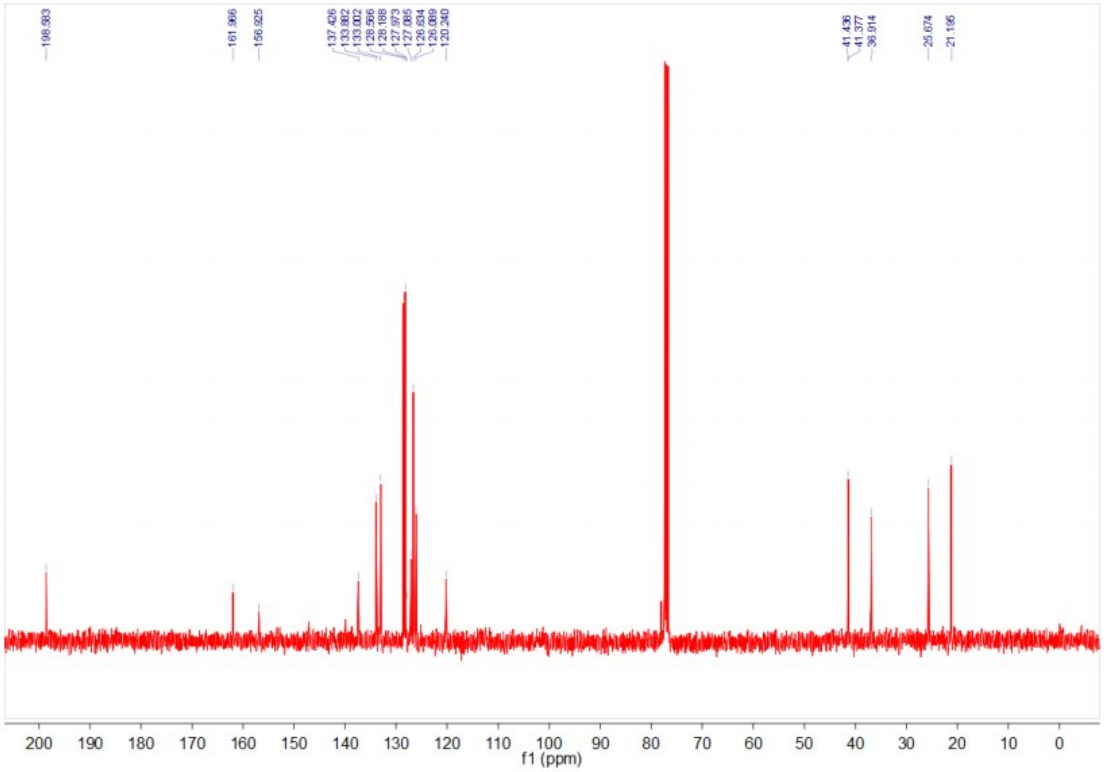
5-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4pa**)



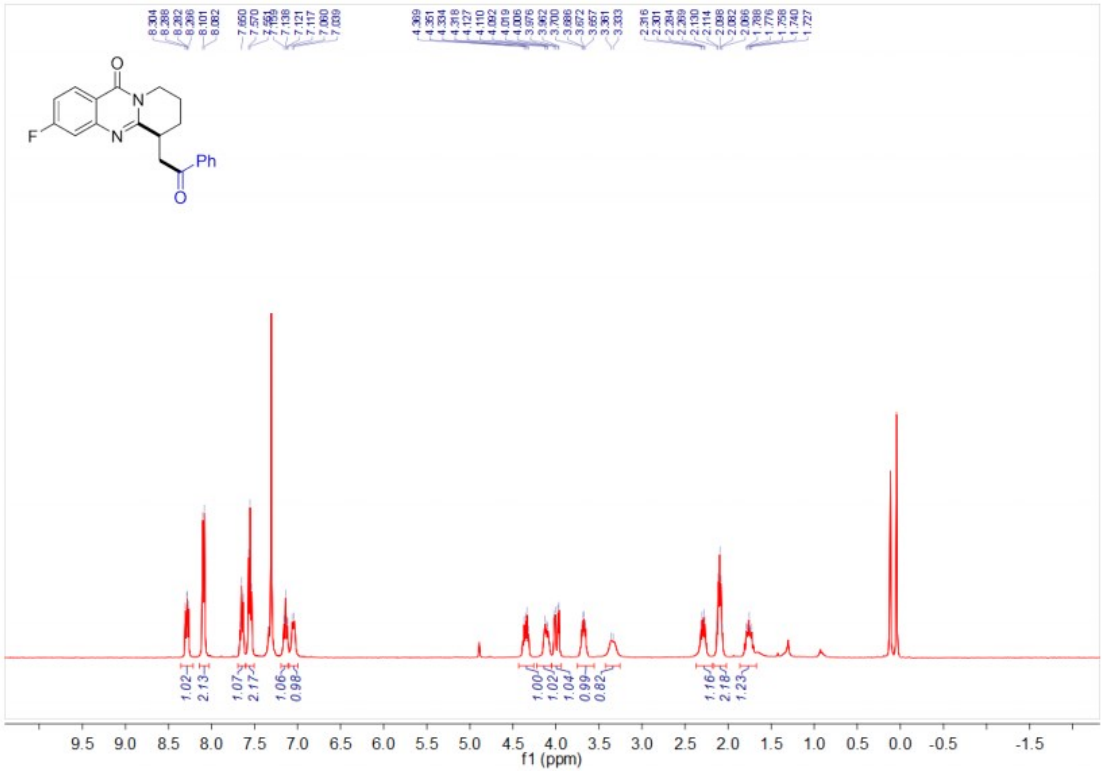


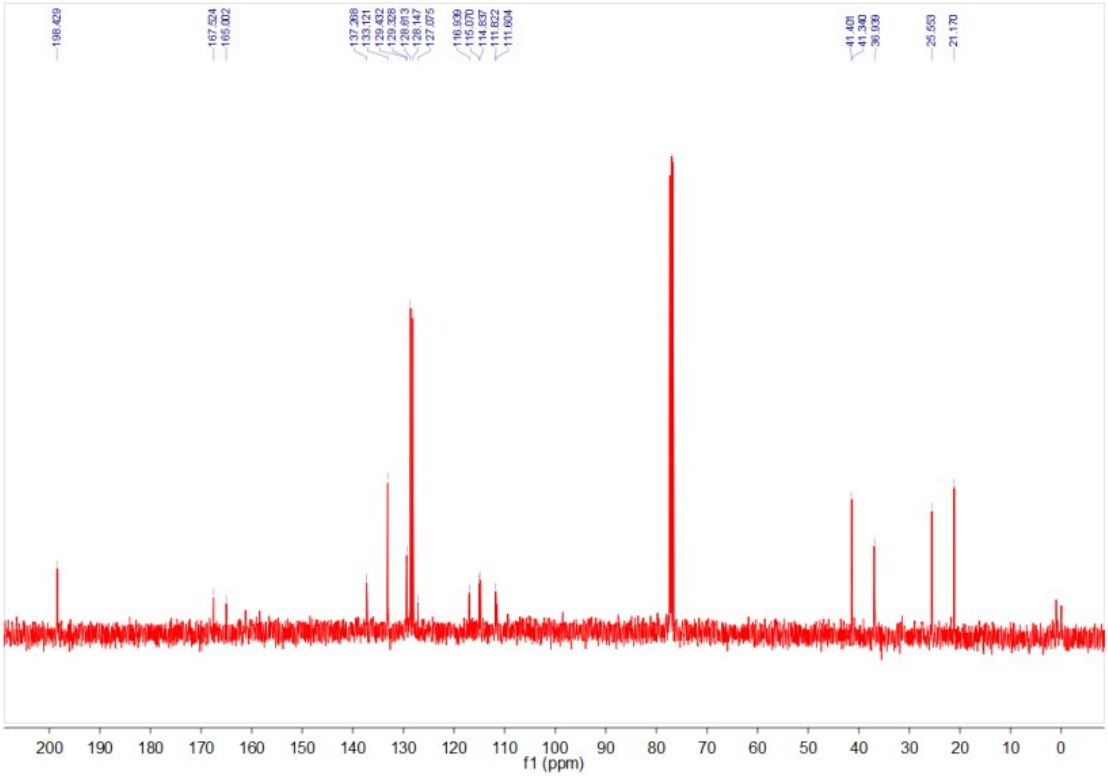
6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5aa**)

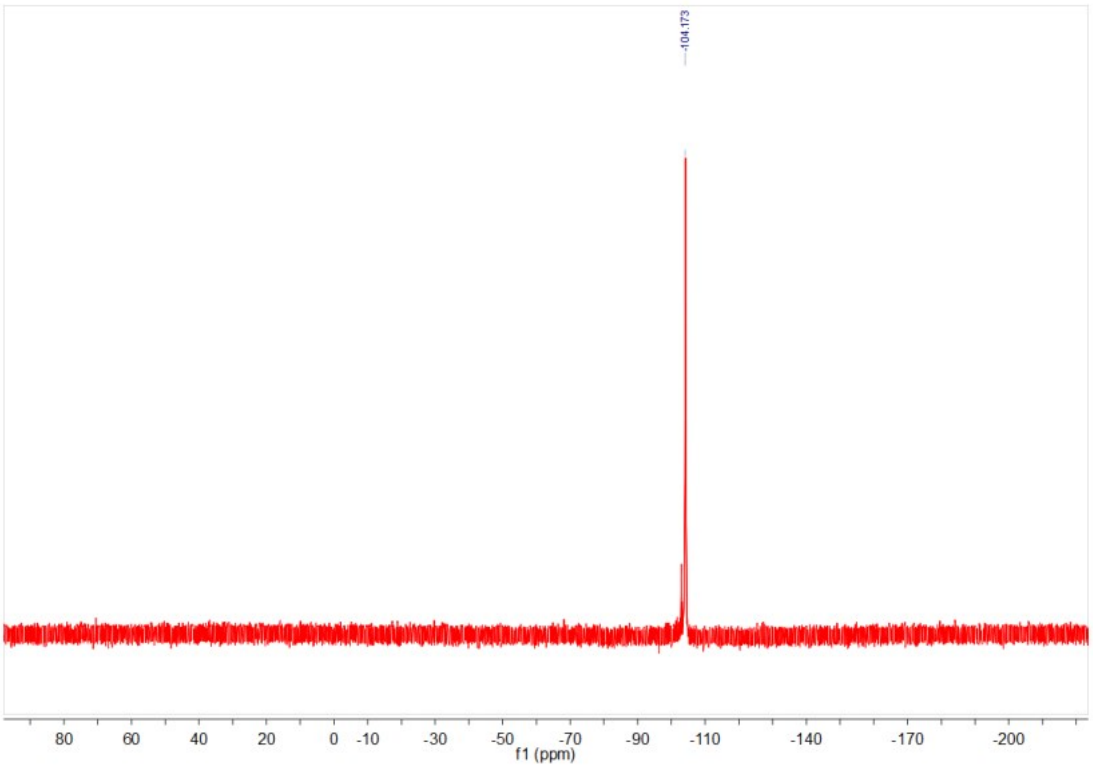




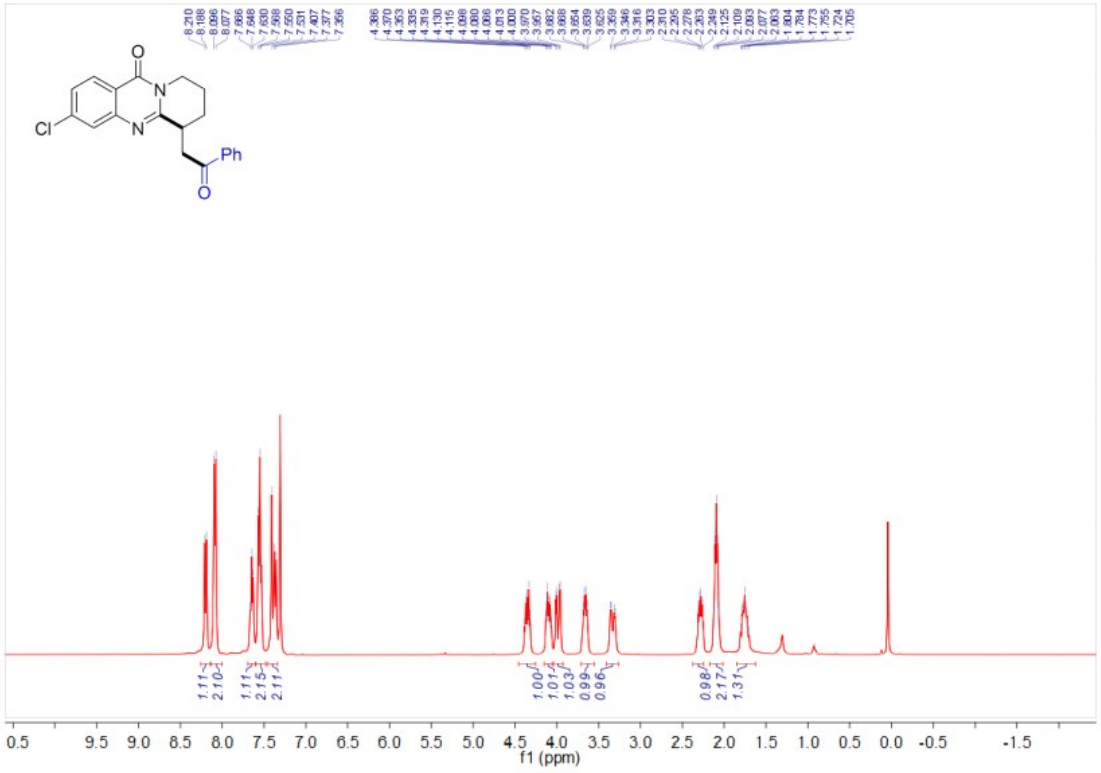
3-fluoro-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ba**)

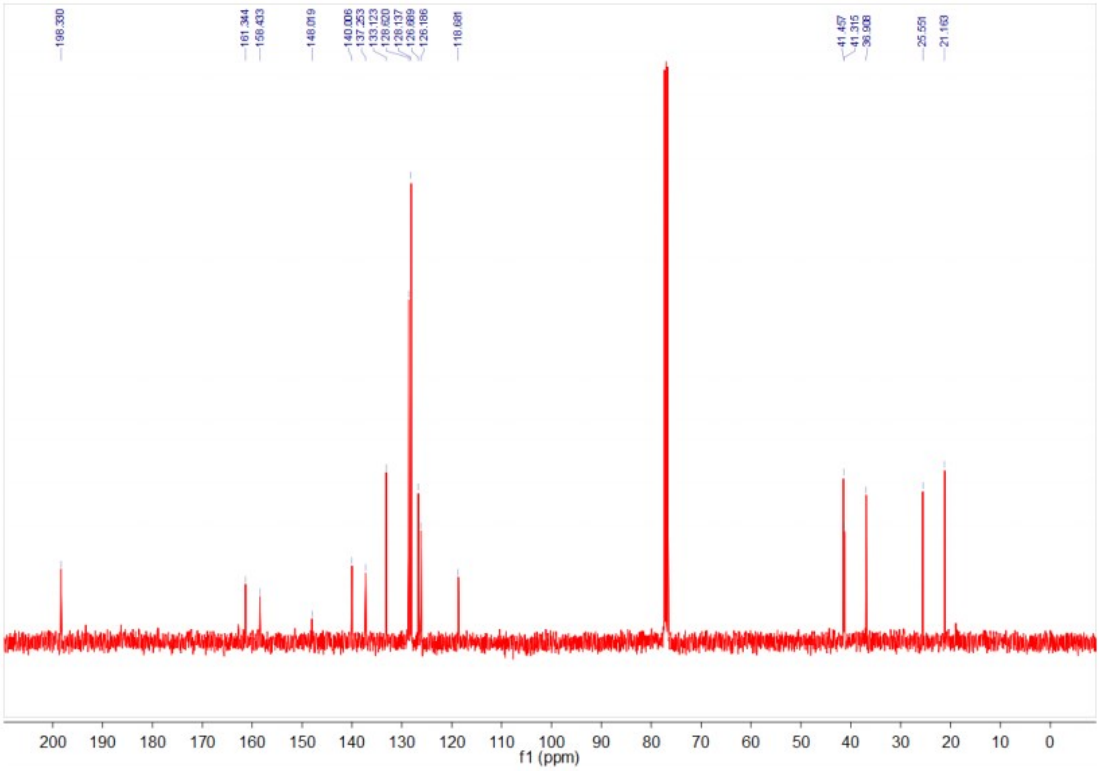




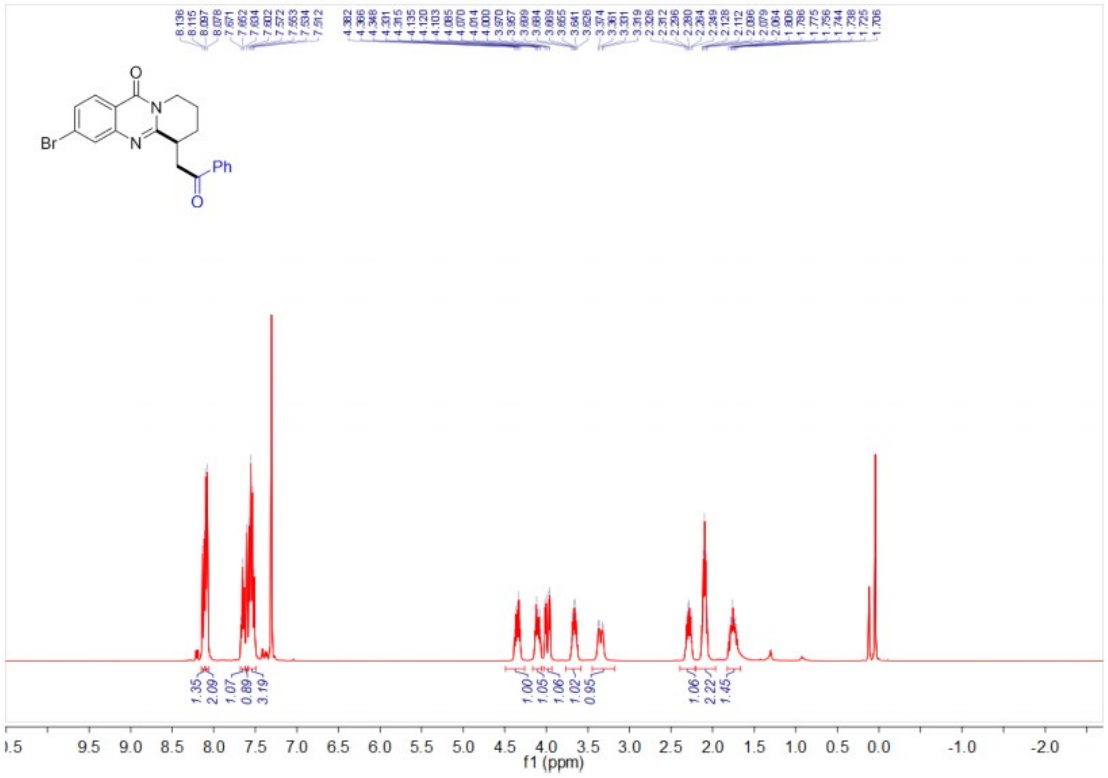

-104.173
80
60
40
20
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
f1 (ppm)

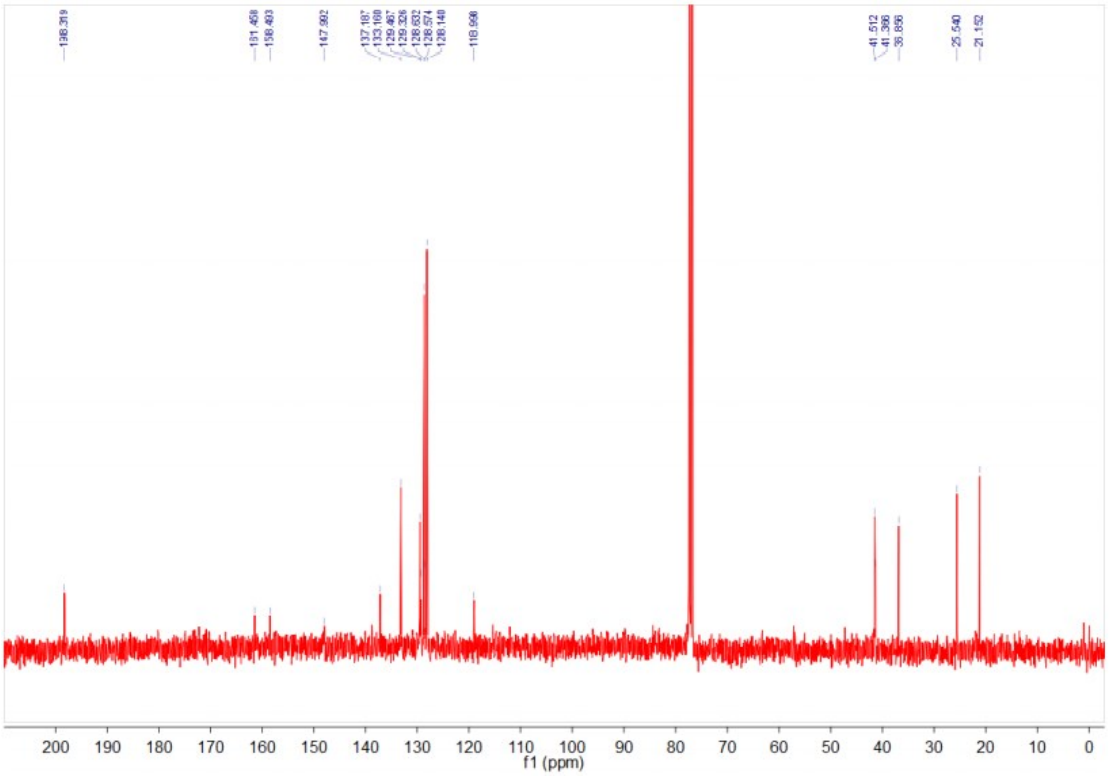
3-chloro-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ca**)



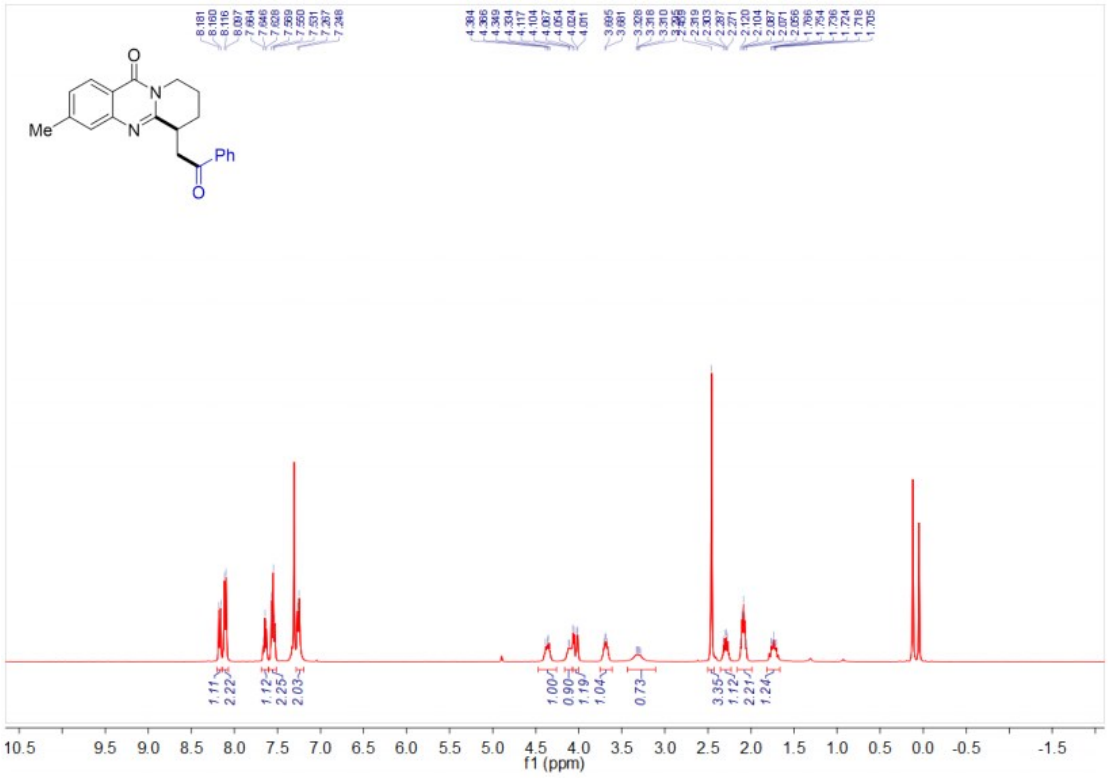


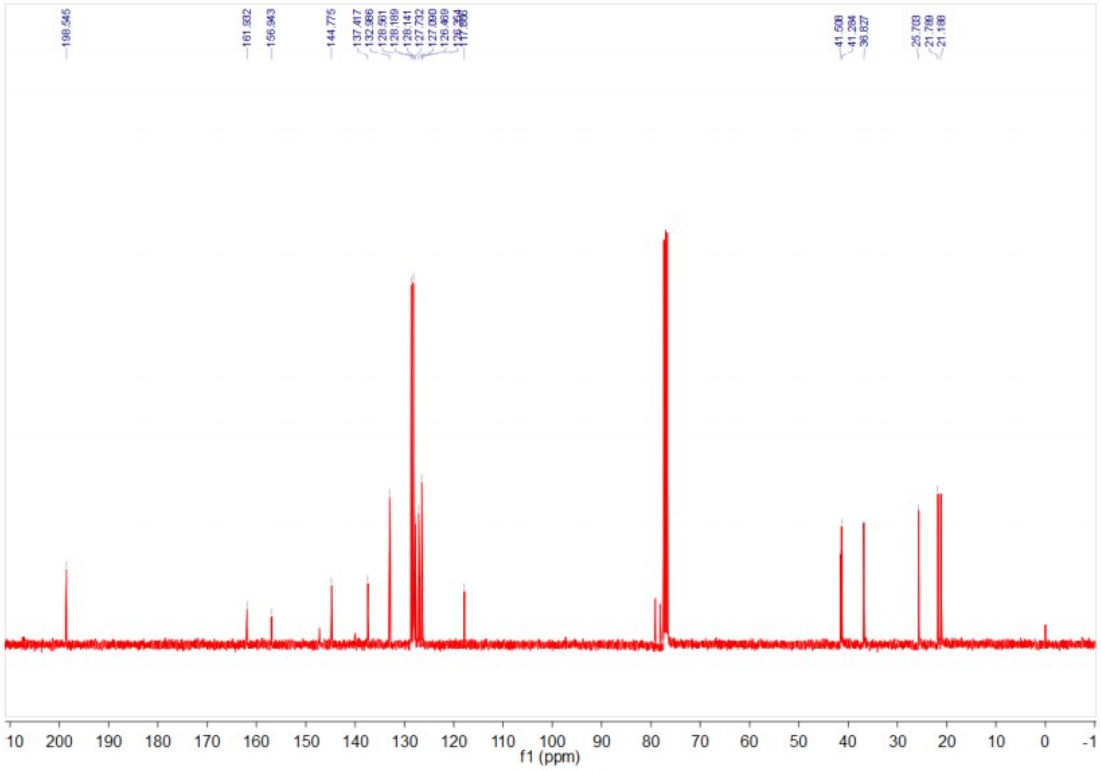
3-bromo-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5da**)



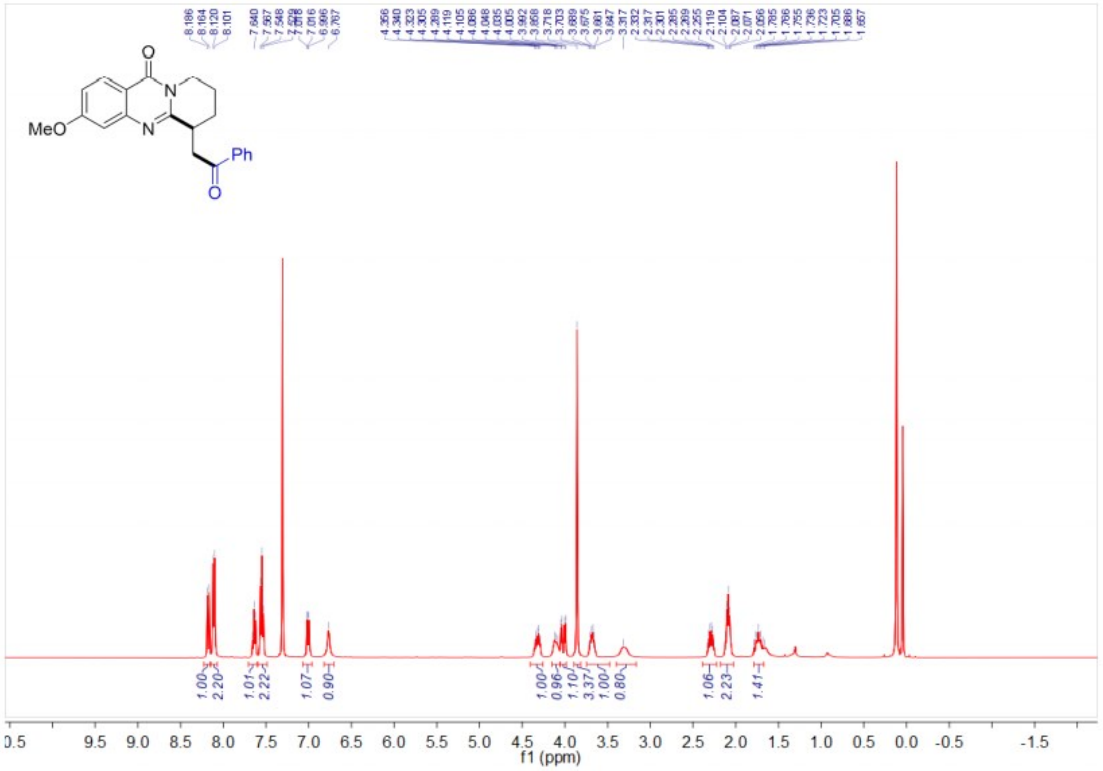


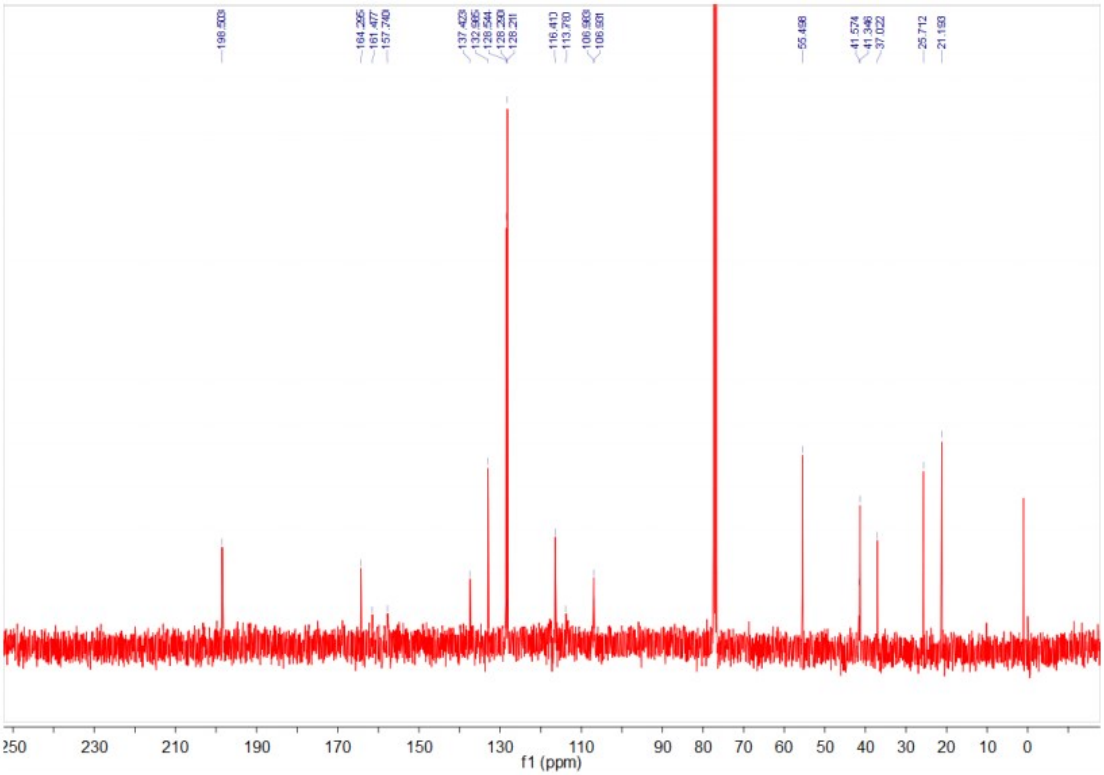
3-methyl-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ea**)



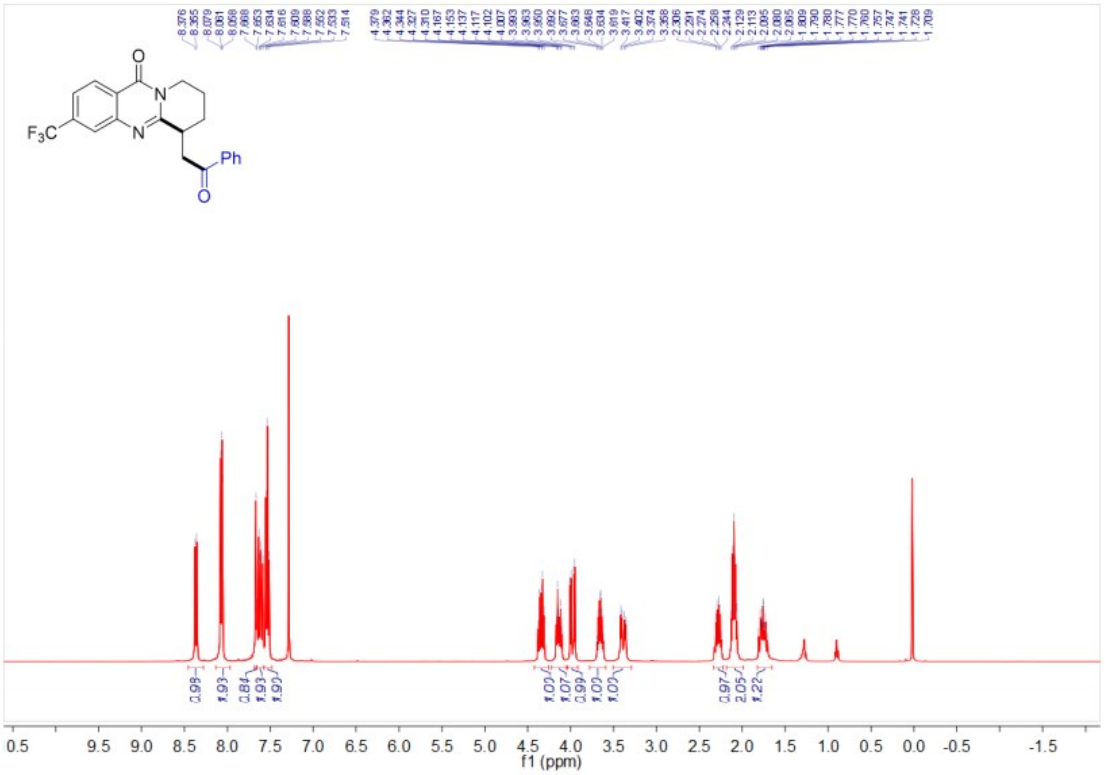


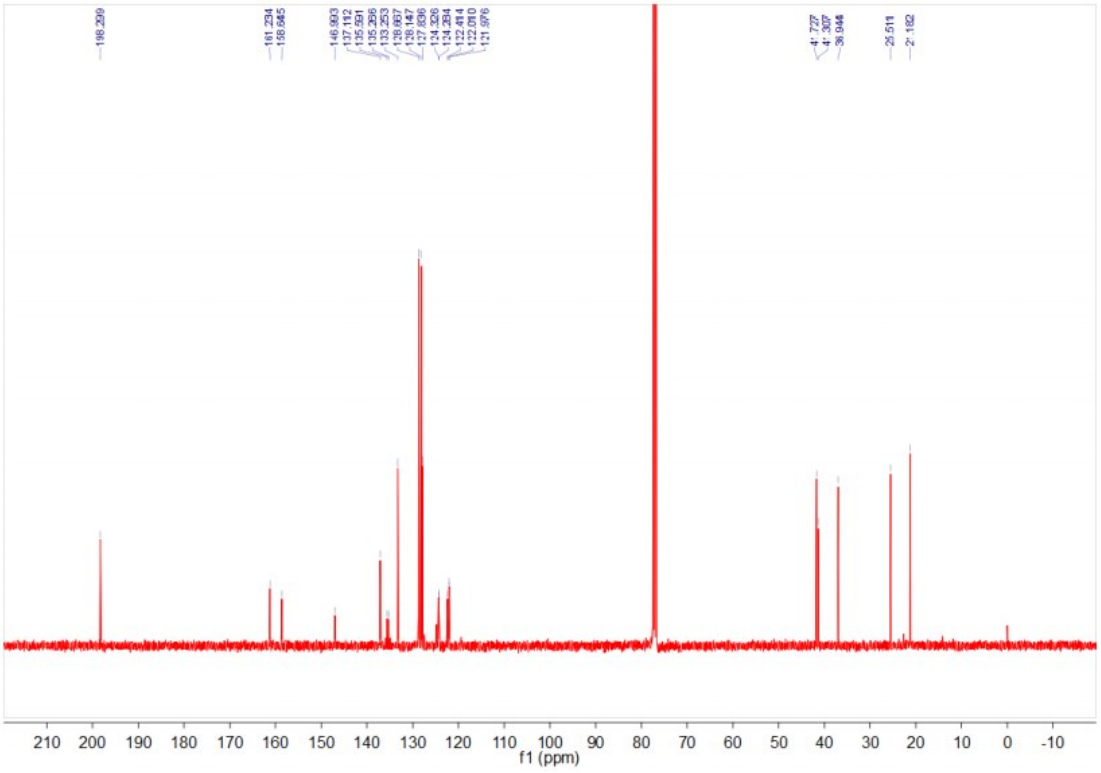
3-methoxy-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5fa**)

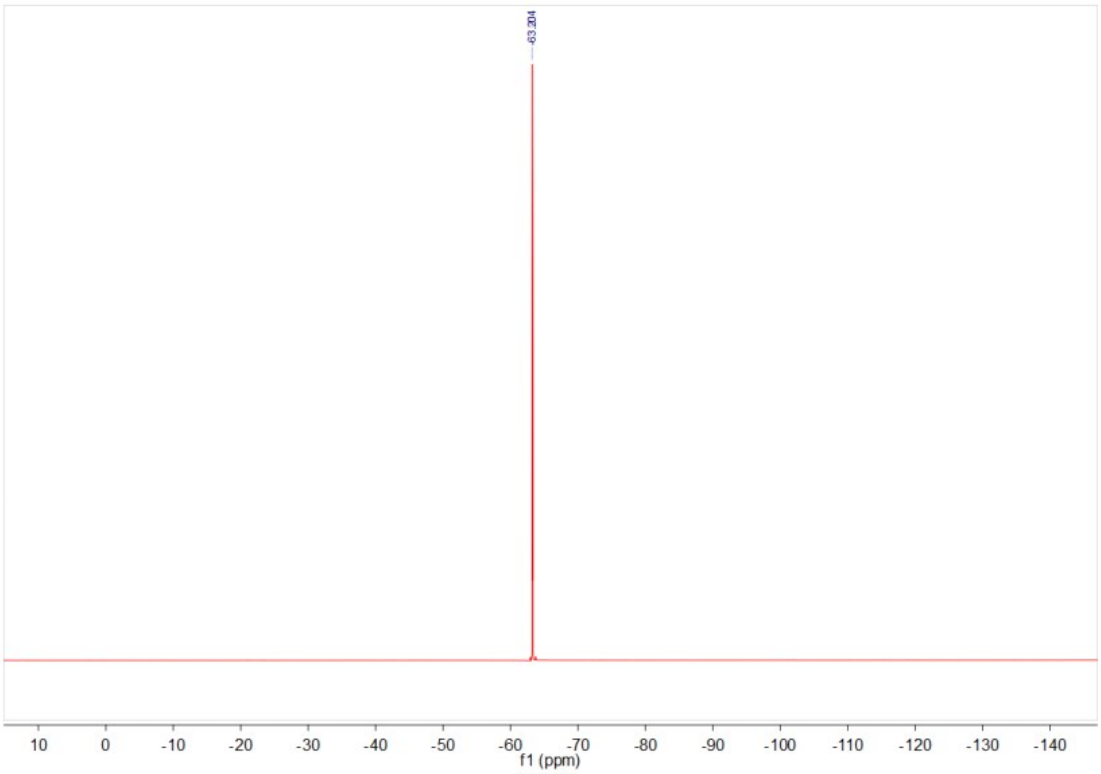




6-(2-oxo-2-phenylethyl)-3-(trifluoromethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ga**)



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-70
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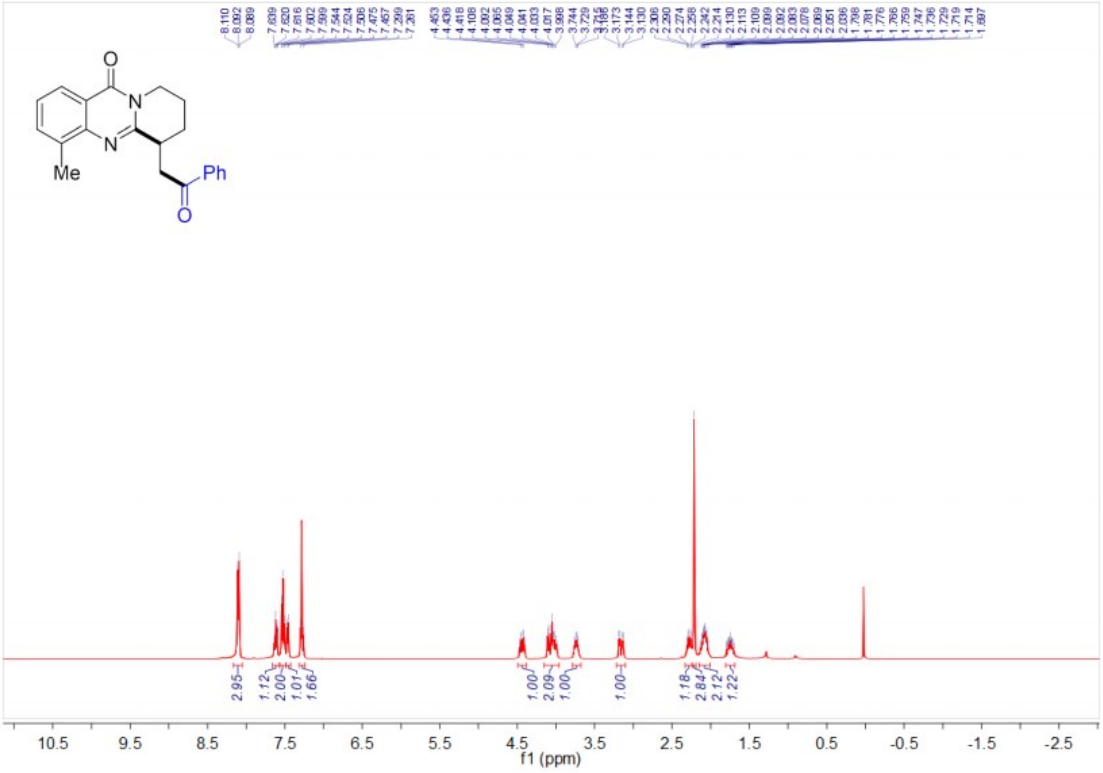
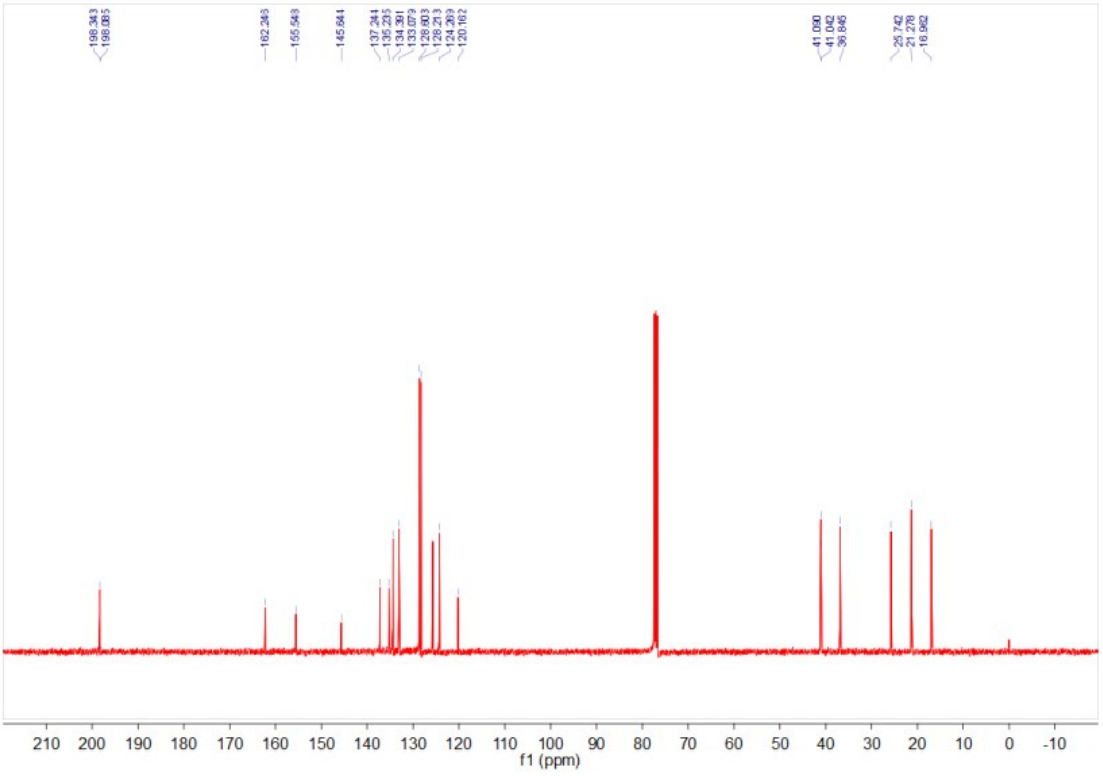
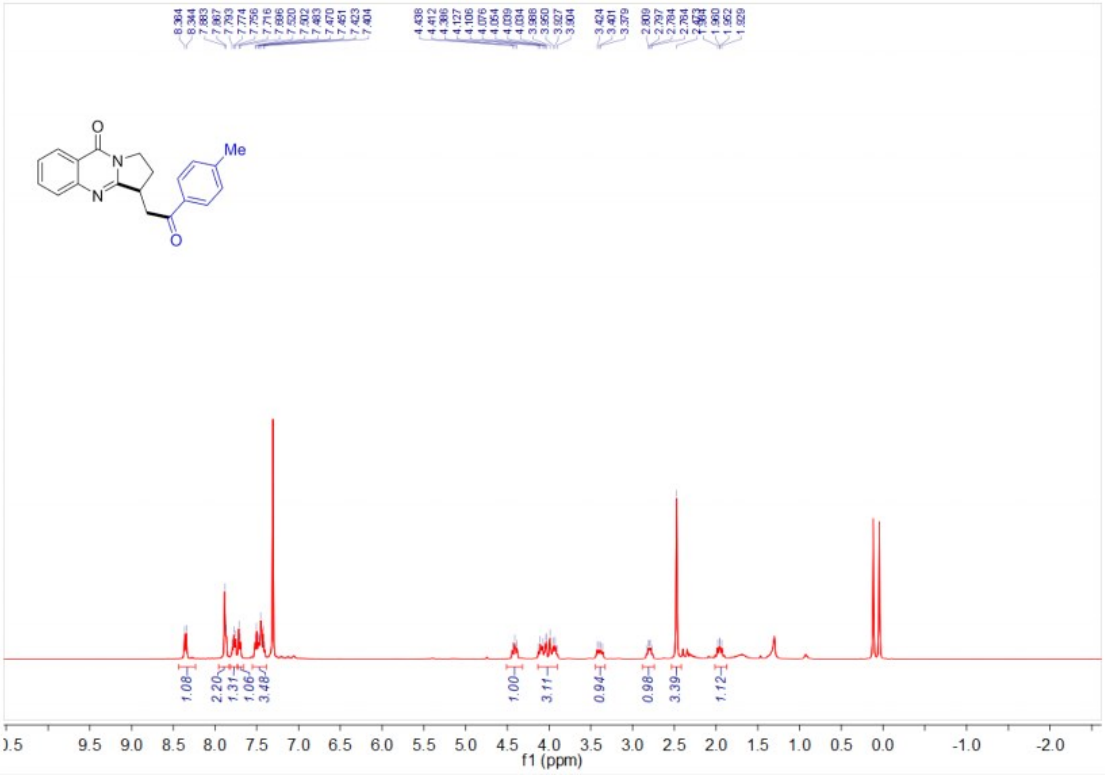
-120
-130
-140
f1 (ppm)

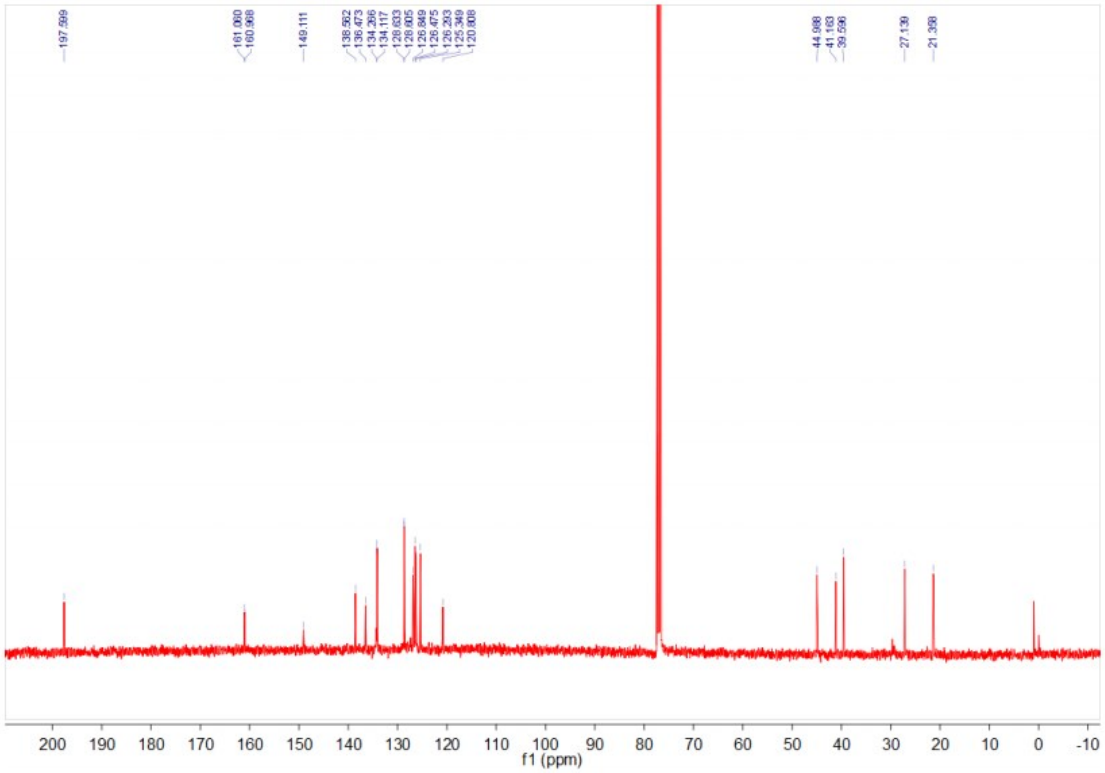
4-methyl-6-(2-oxo-2-phenylethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ha**)



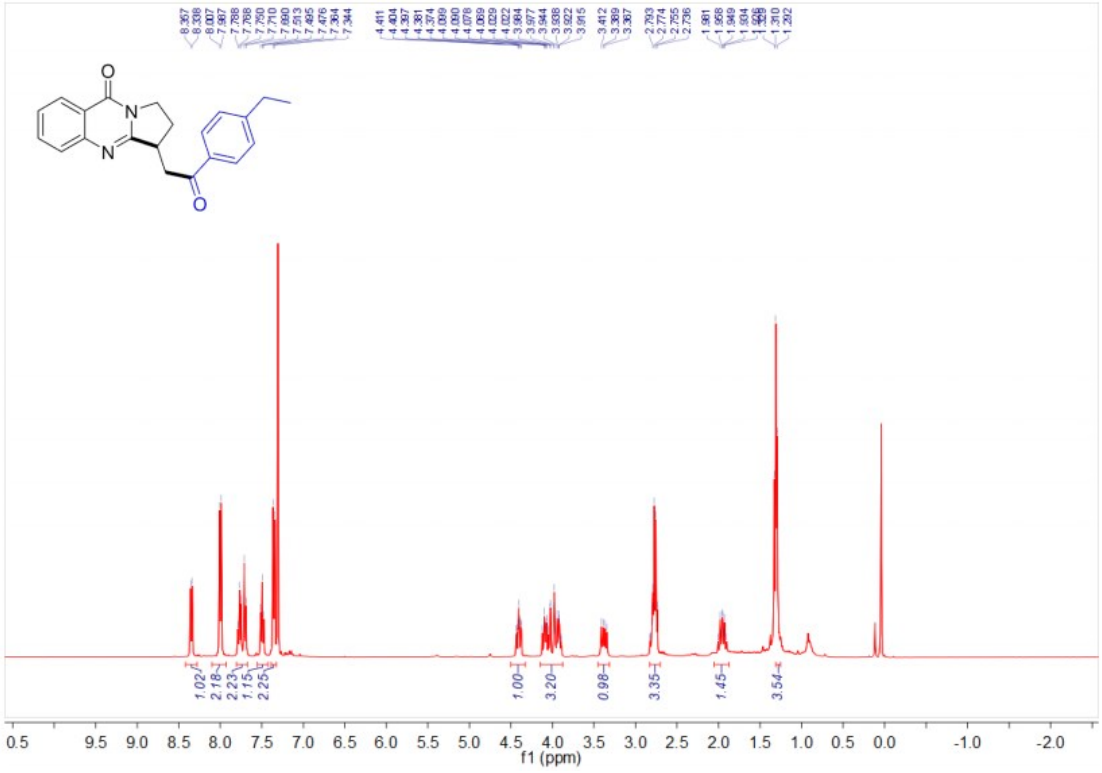


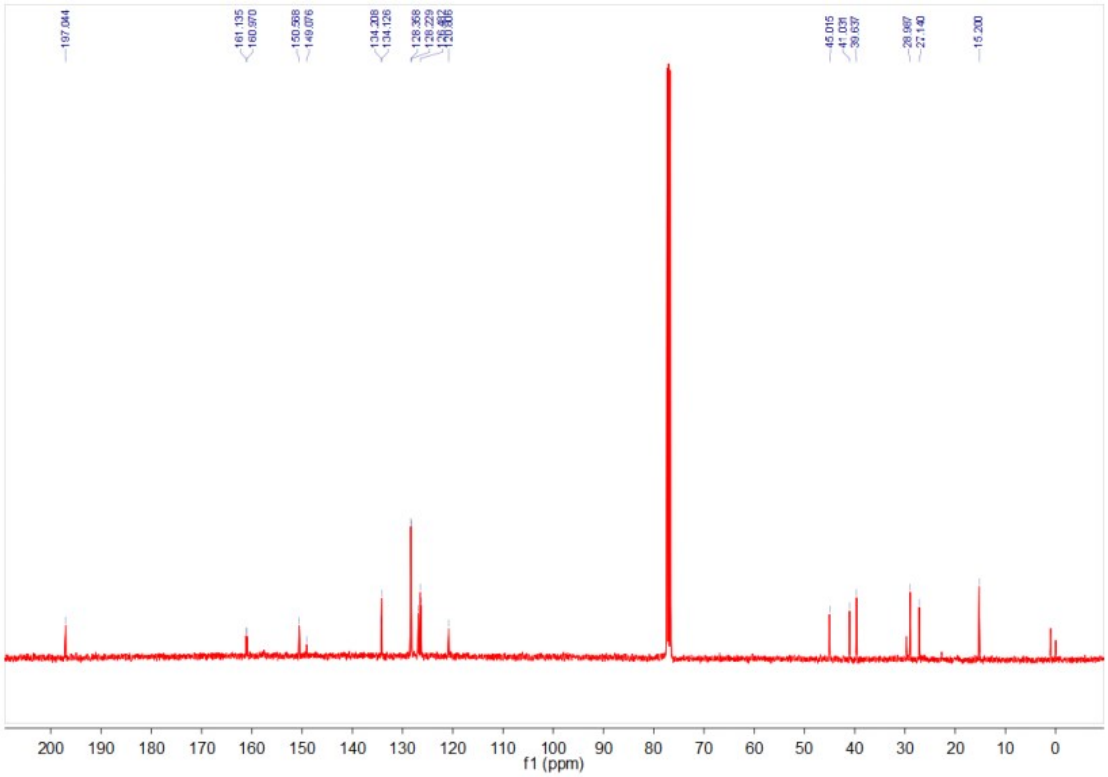
3-(2-oxo-2-(p-tolyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ab)**


Me
f1 (ppm)

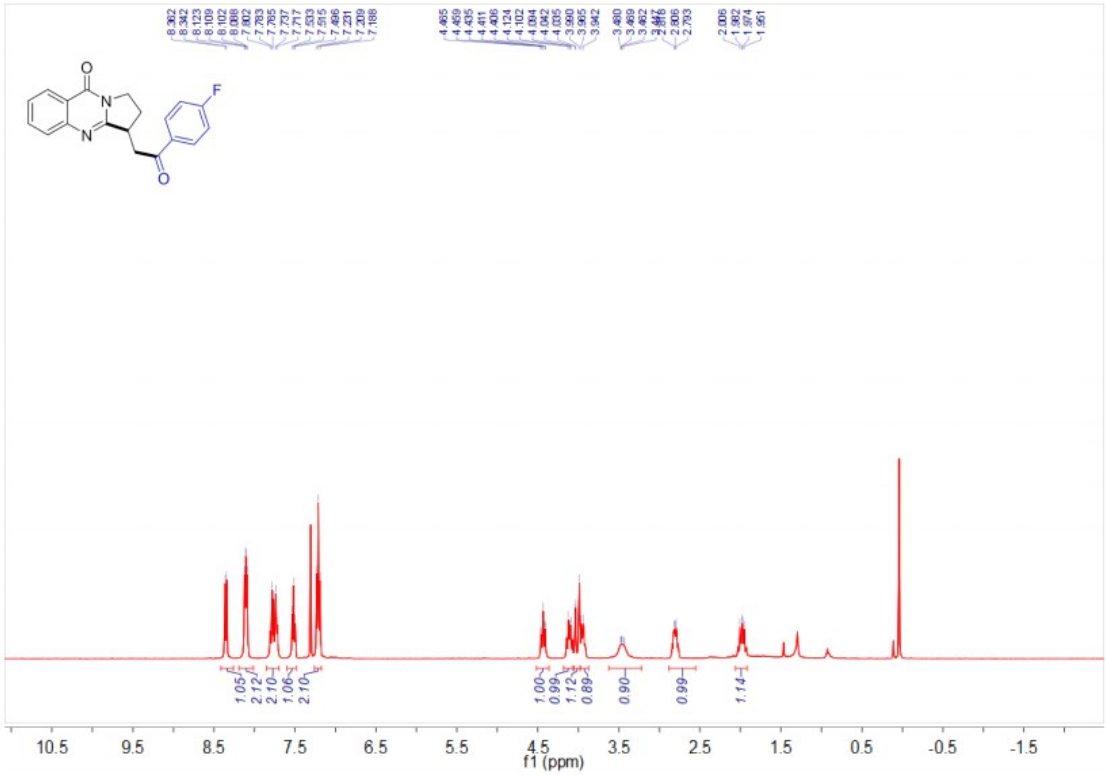

f1 (ppm)

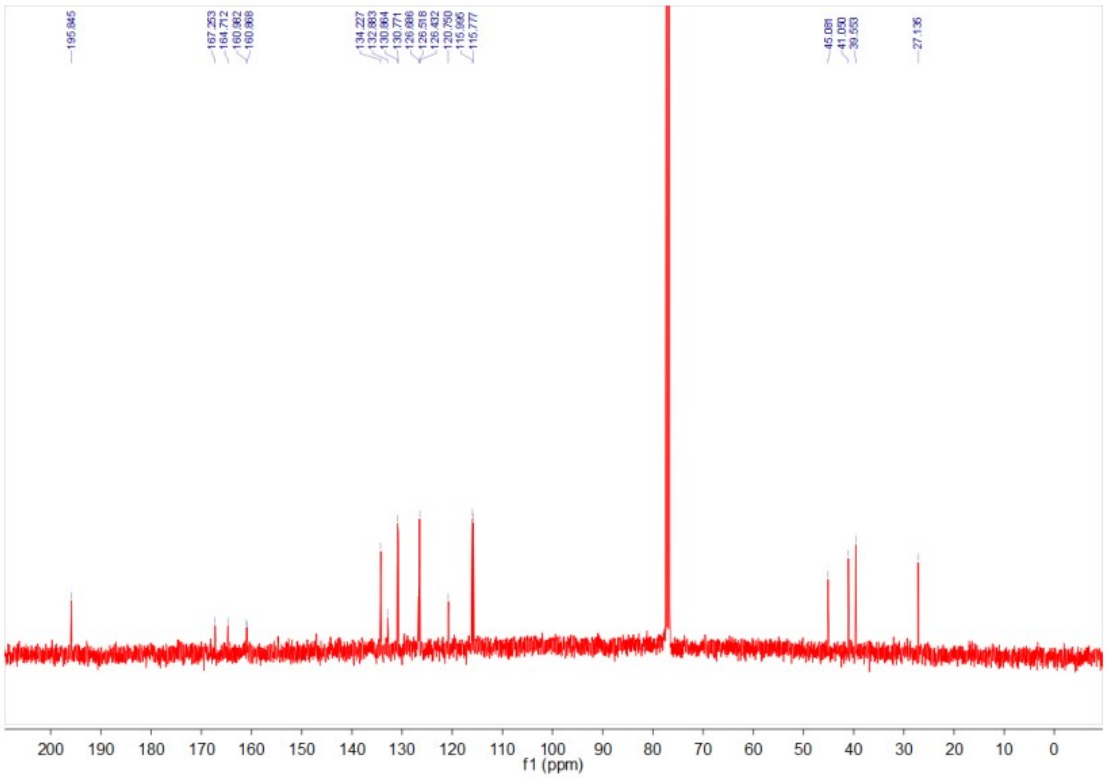
3-(2-(4-ethylphenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ac)**

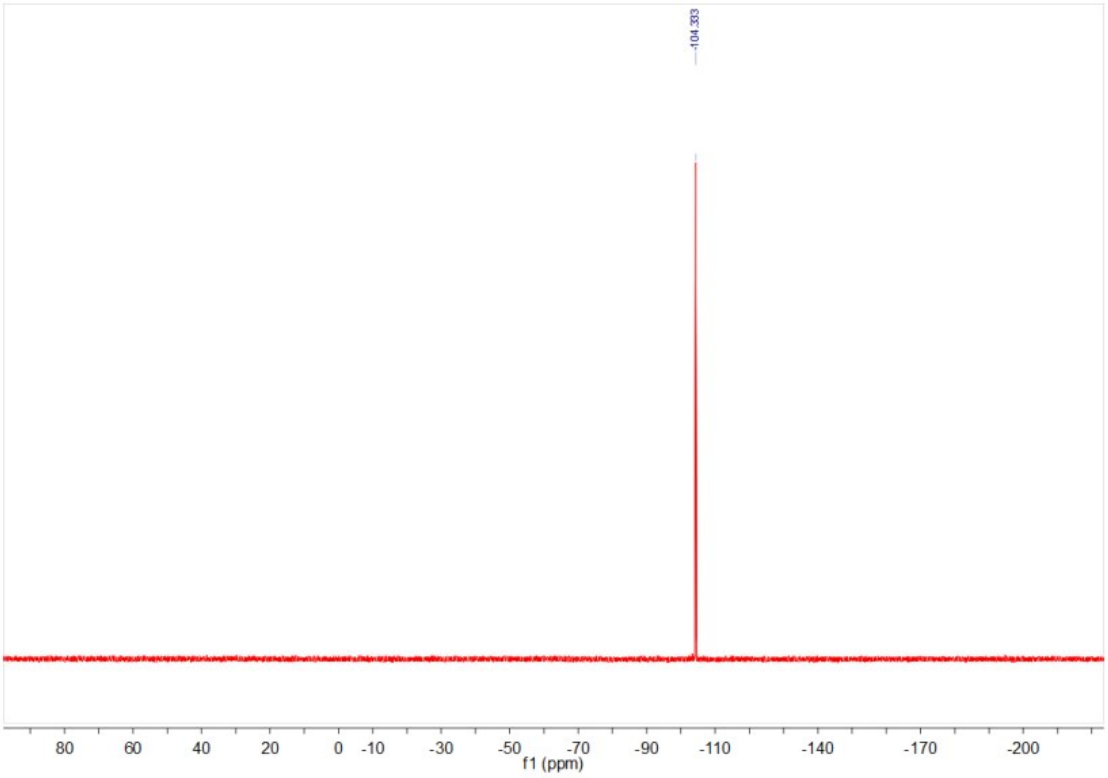




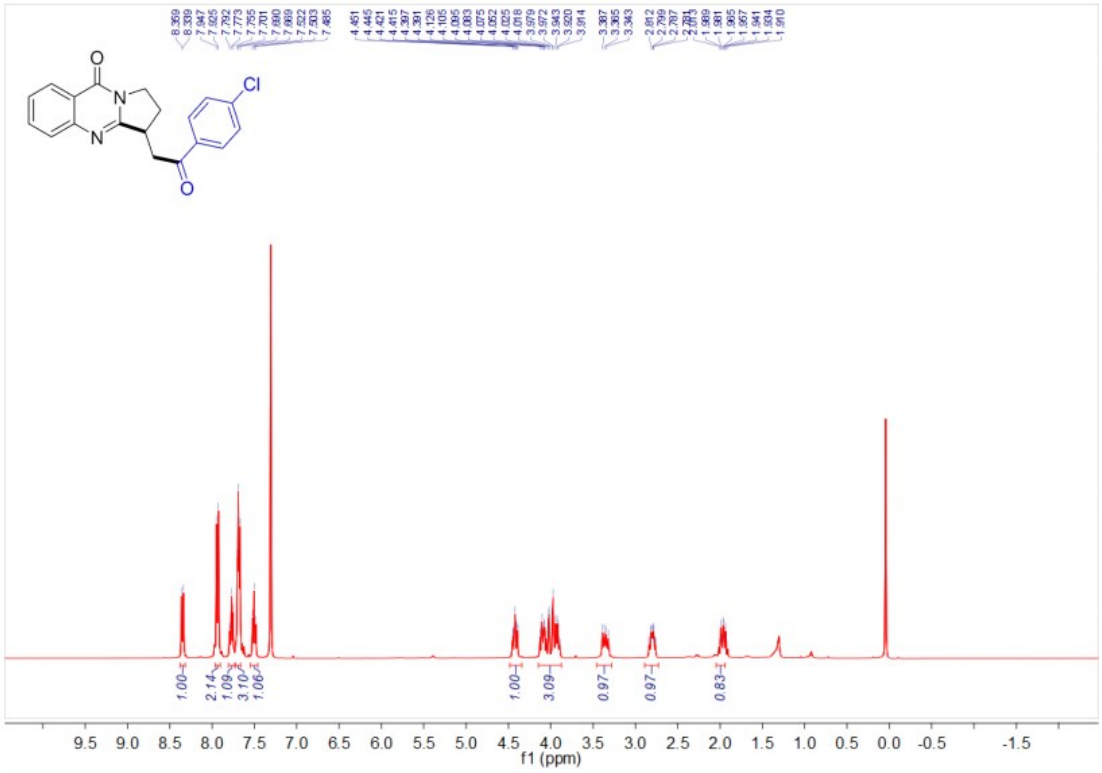
3-(2-(4-fluorophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ad)**

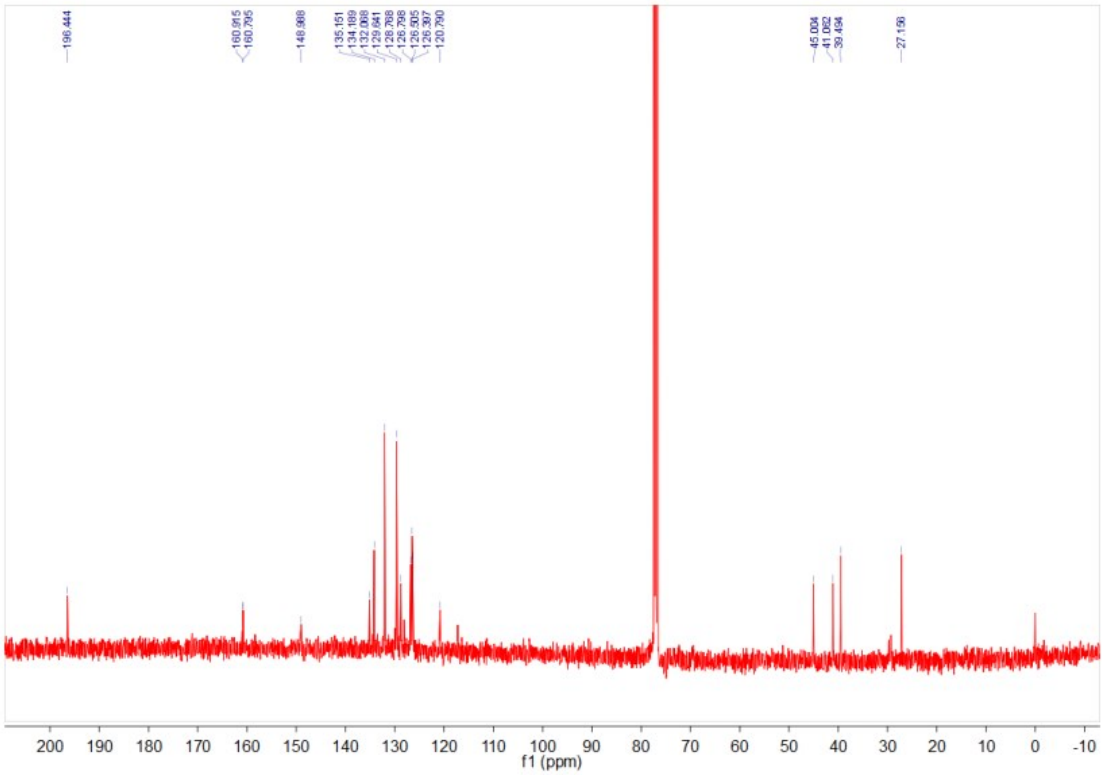




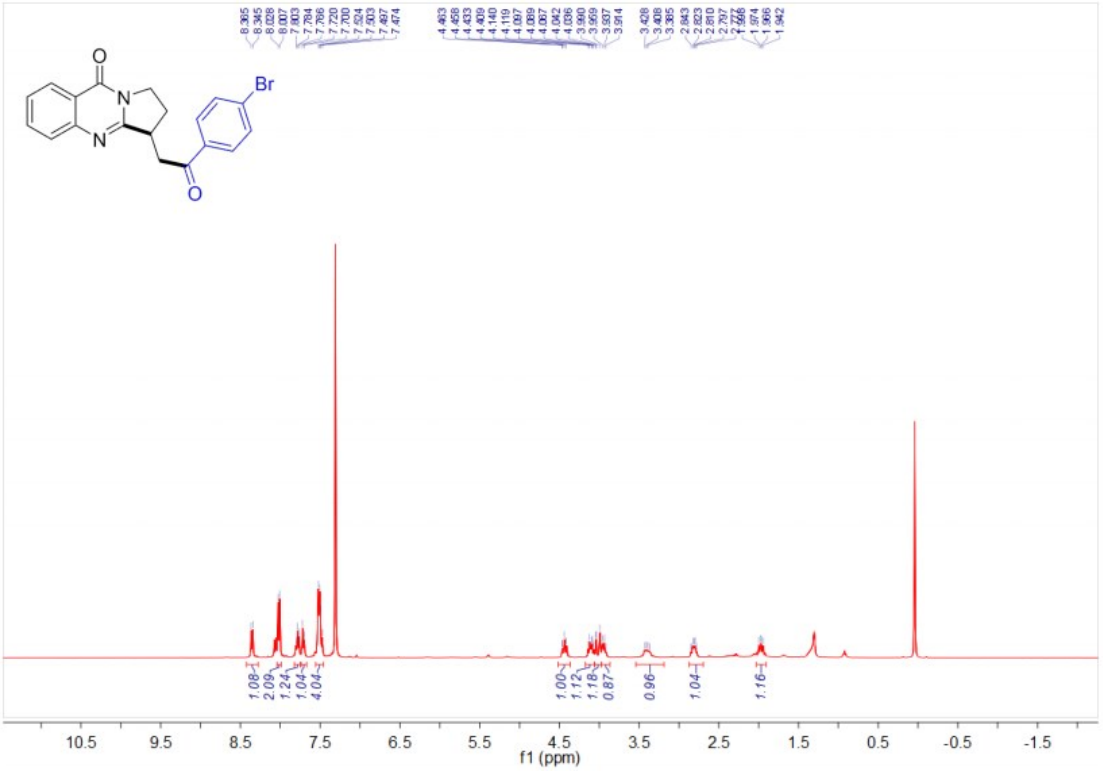

-104.333
80
60
40
20
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
f1 (ppm)

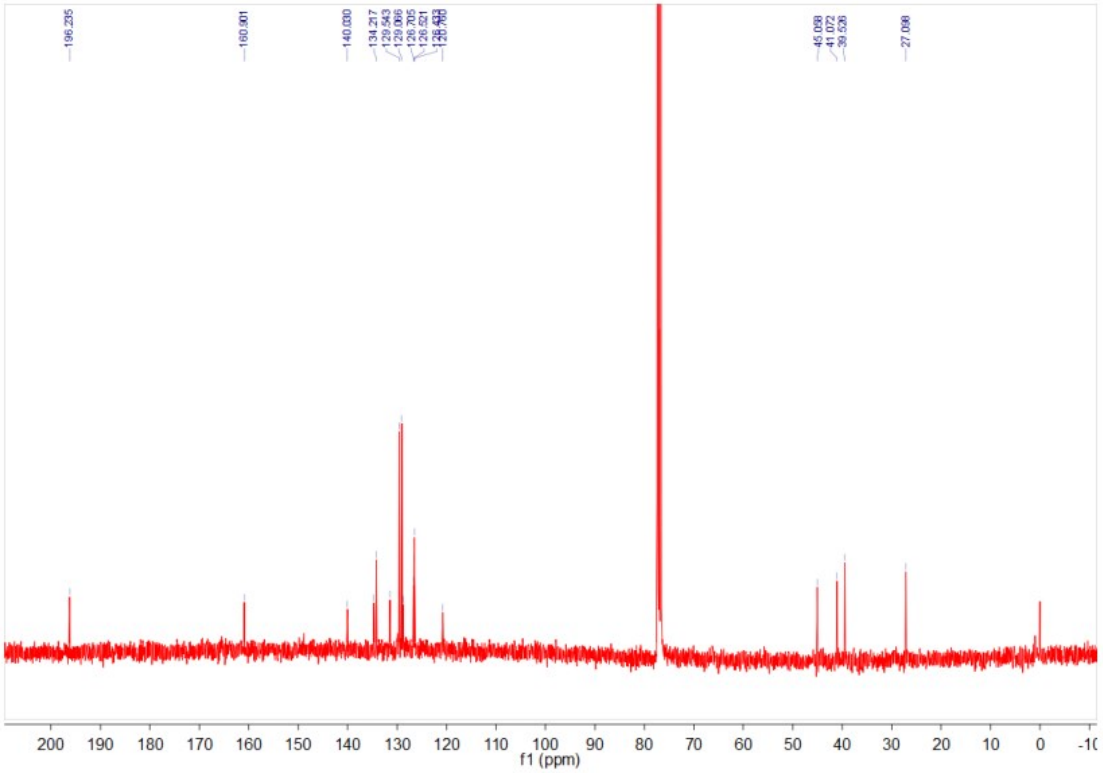
3-(2-(4-chlorophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ae)**



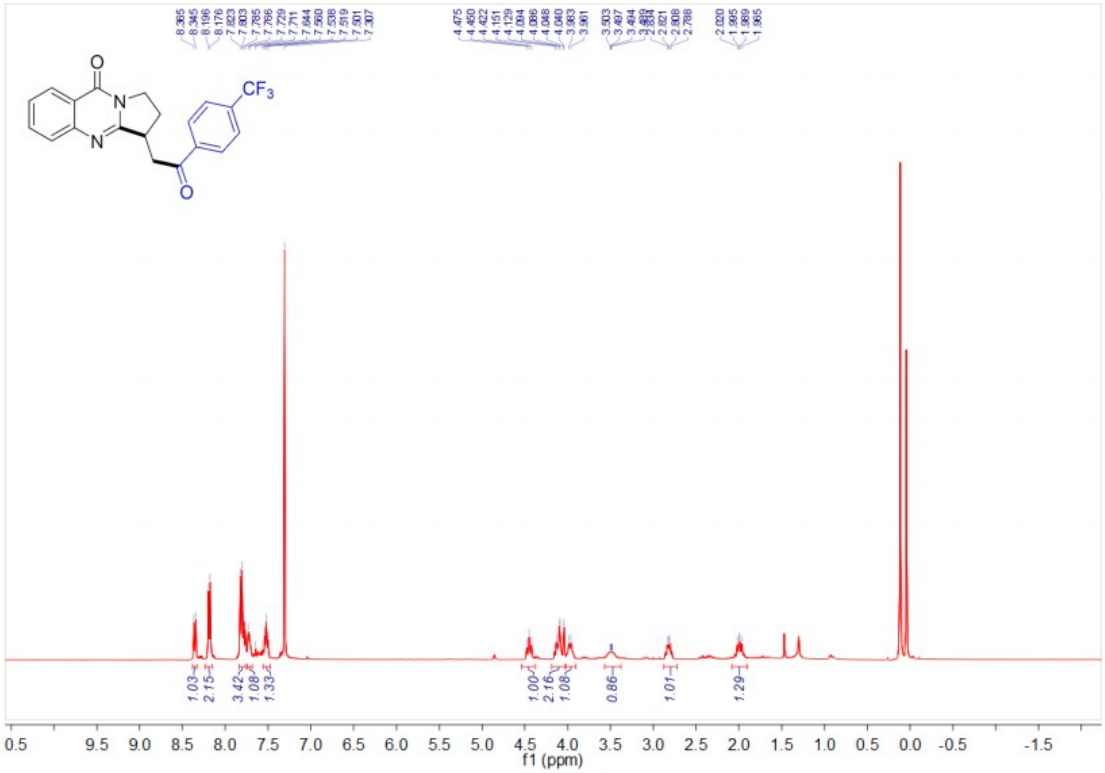


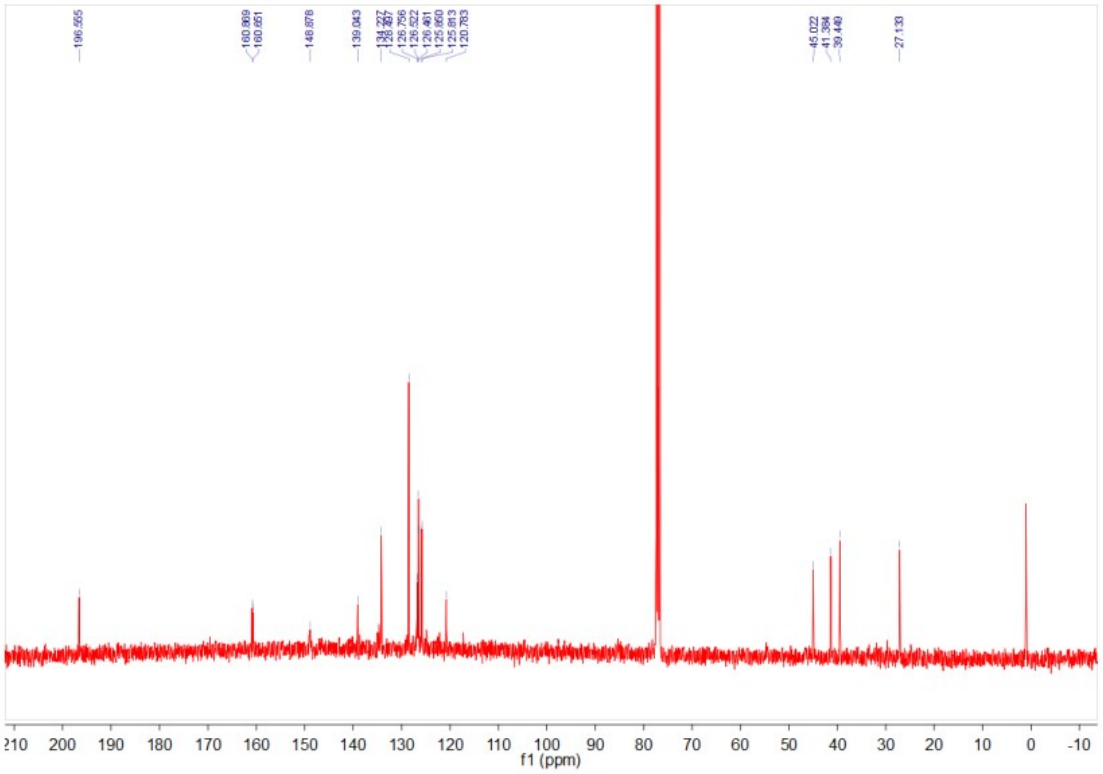
3-(2-(4-bromophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4af)**

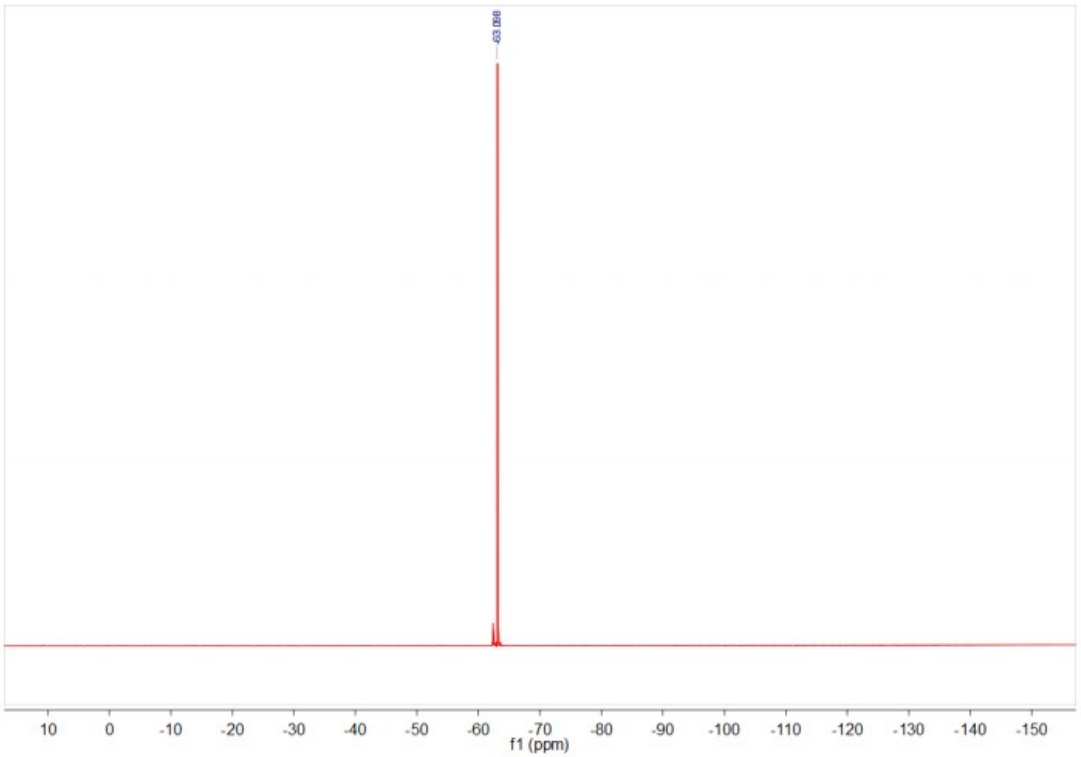




3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one **(4ag)**



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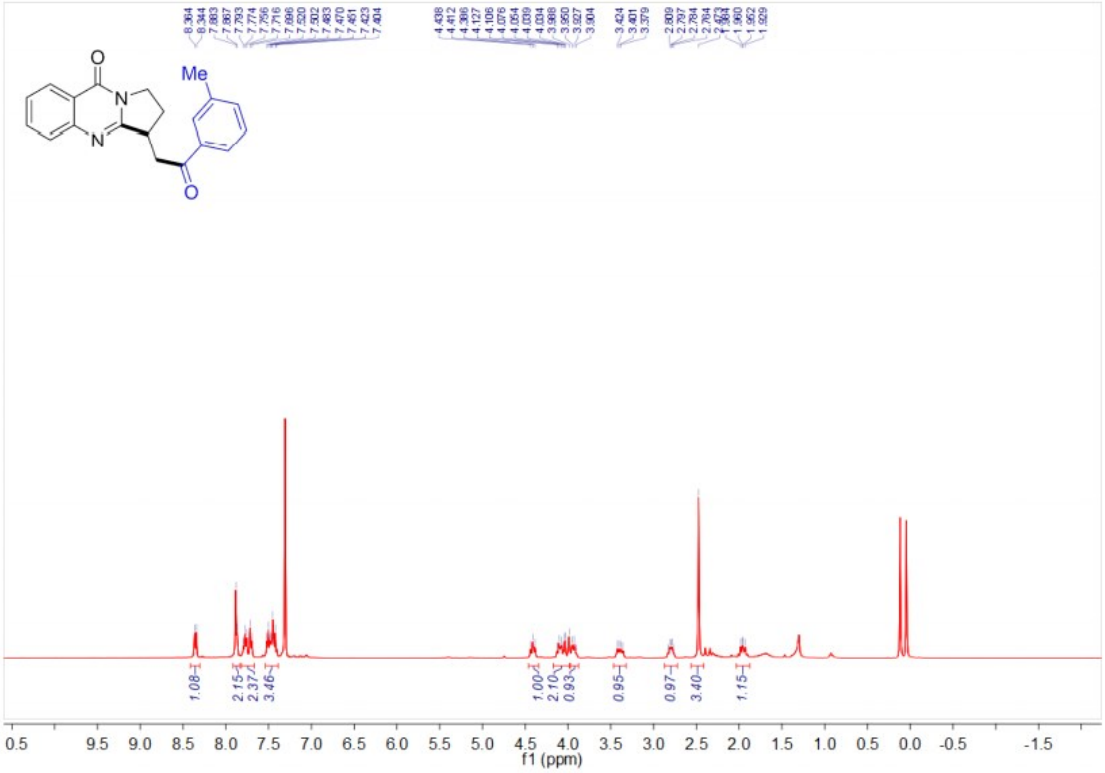
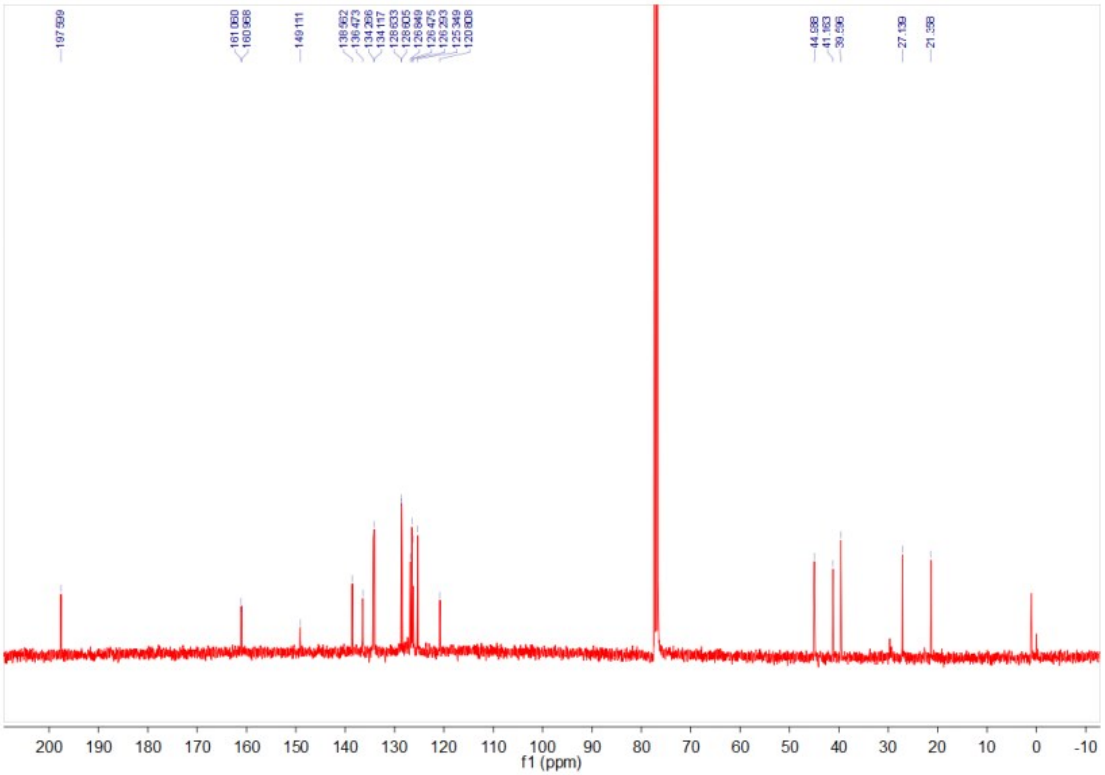
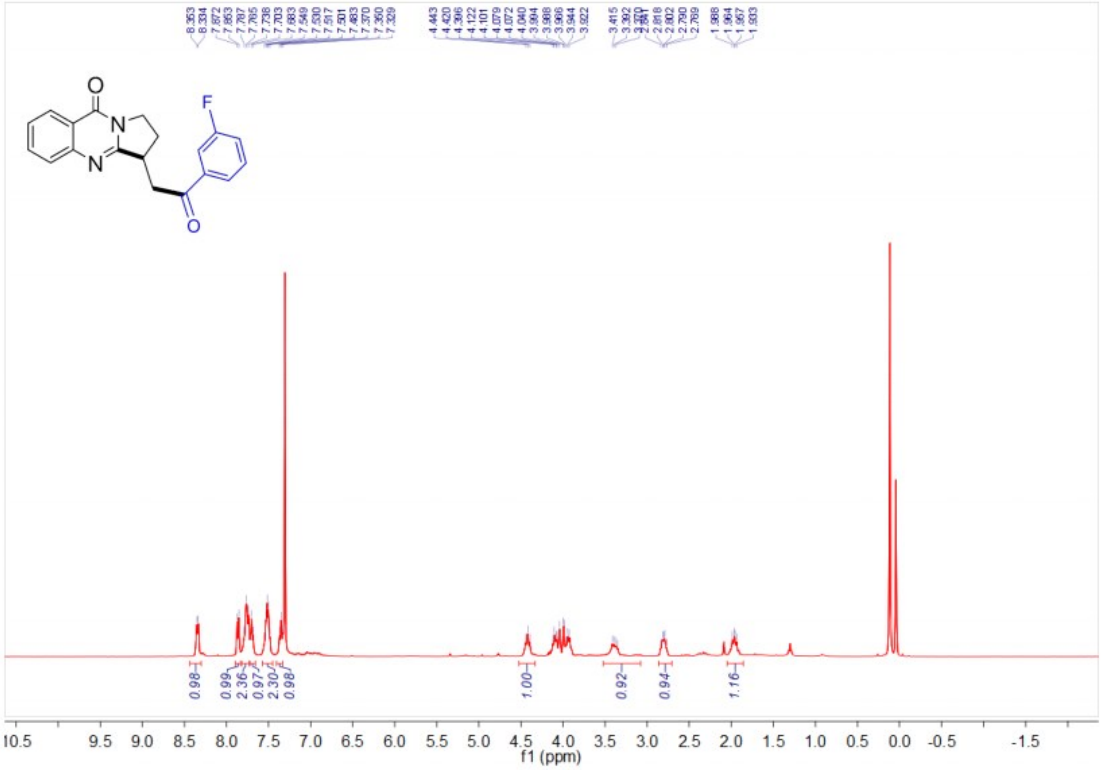
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

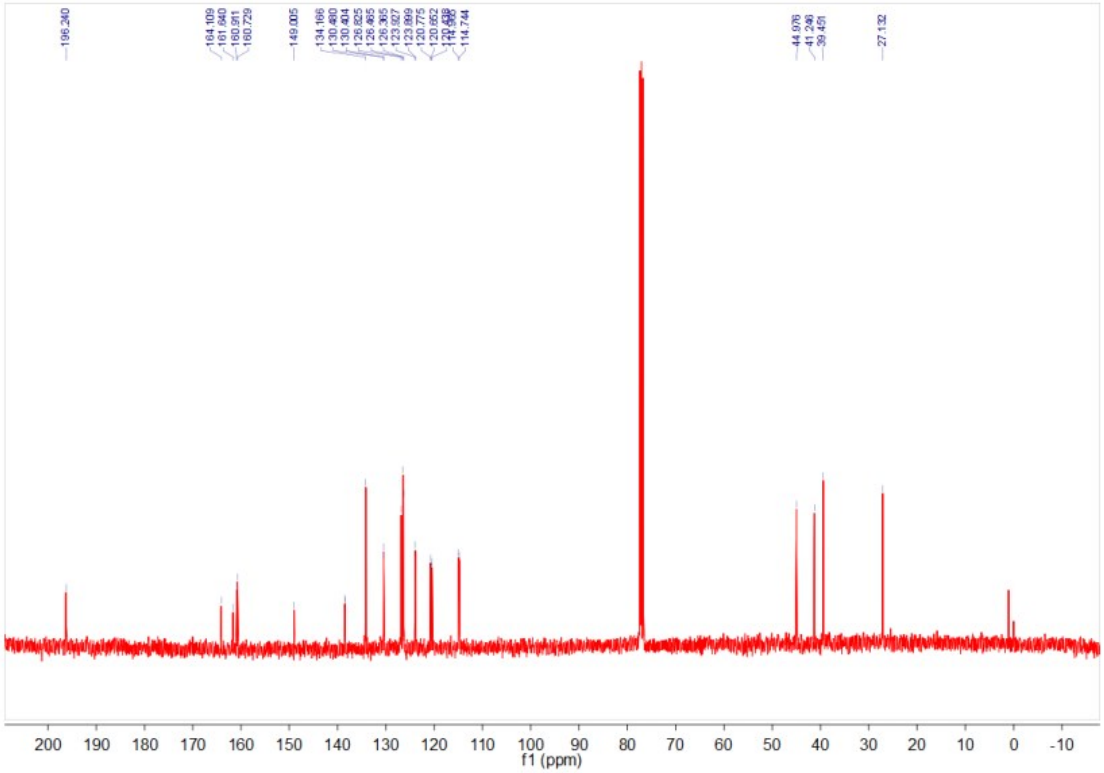
3-(2-oxo-2-(m-tolyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ah**)

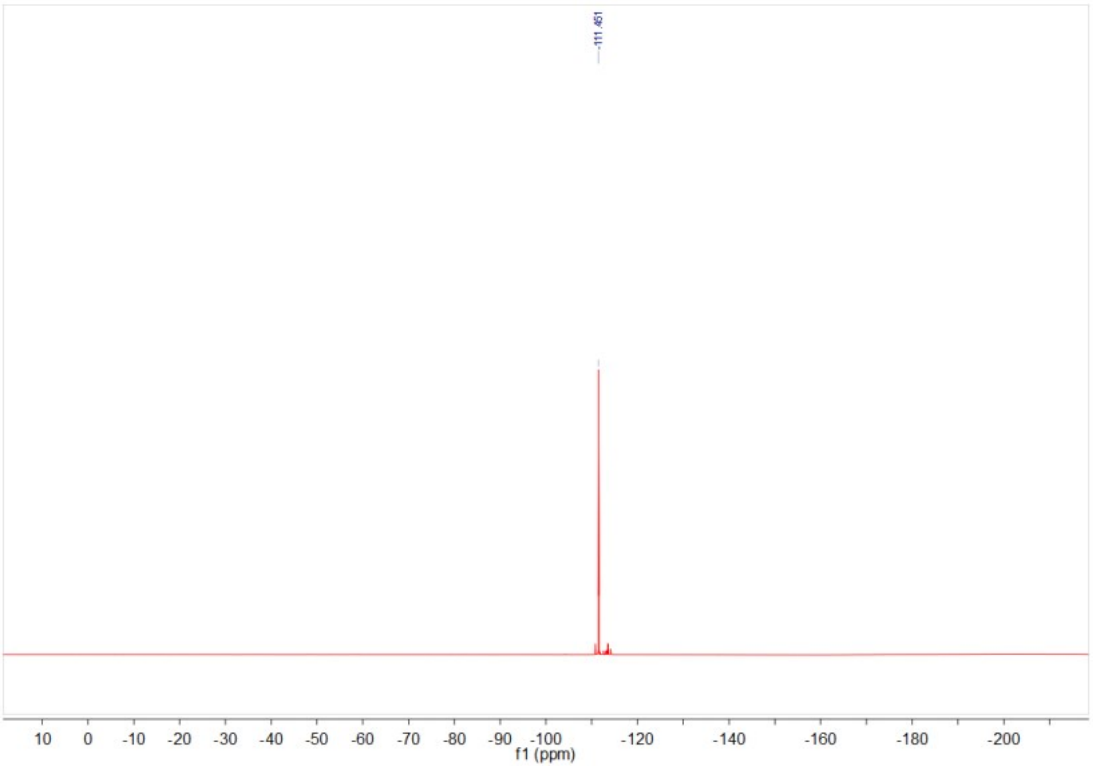




3-(2-(3-fluorophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (**4ai**)



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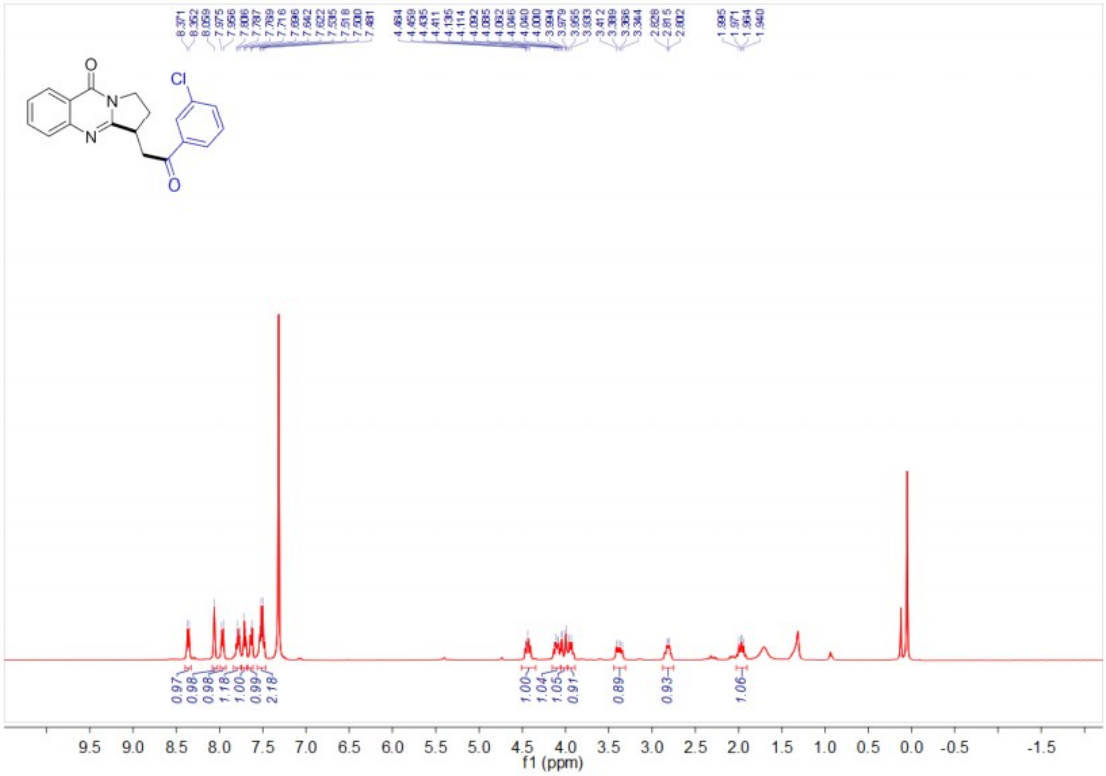
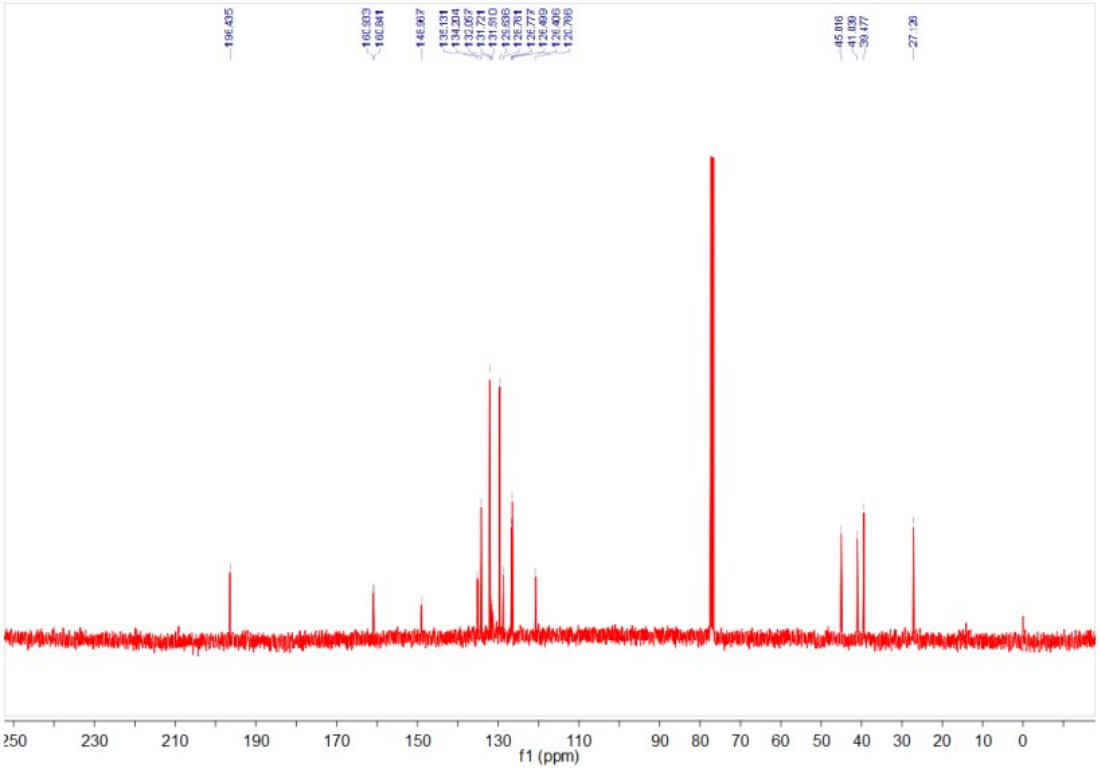
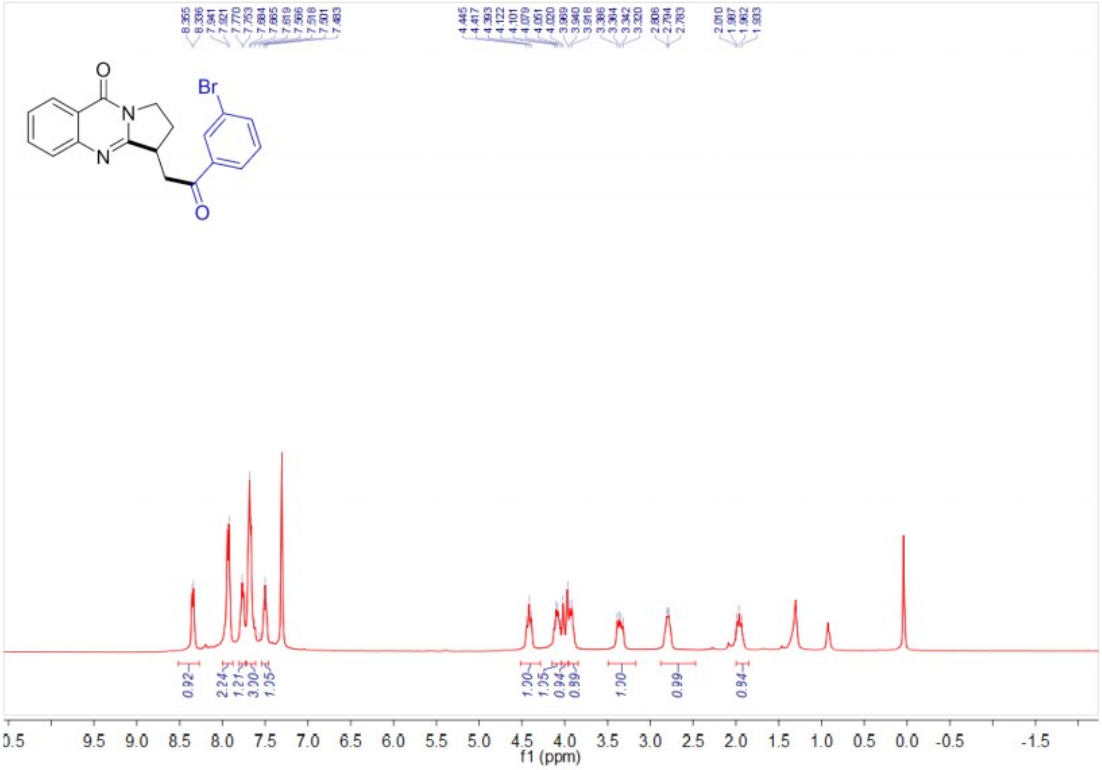
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

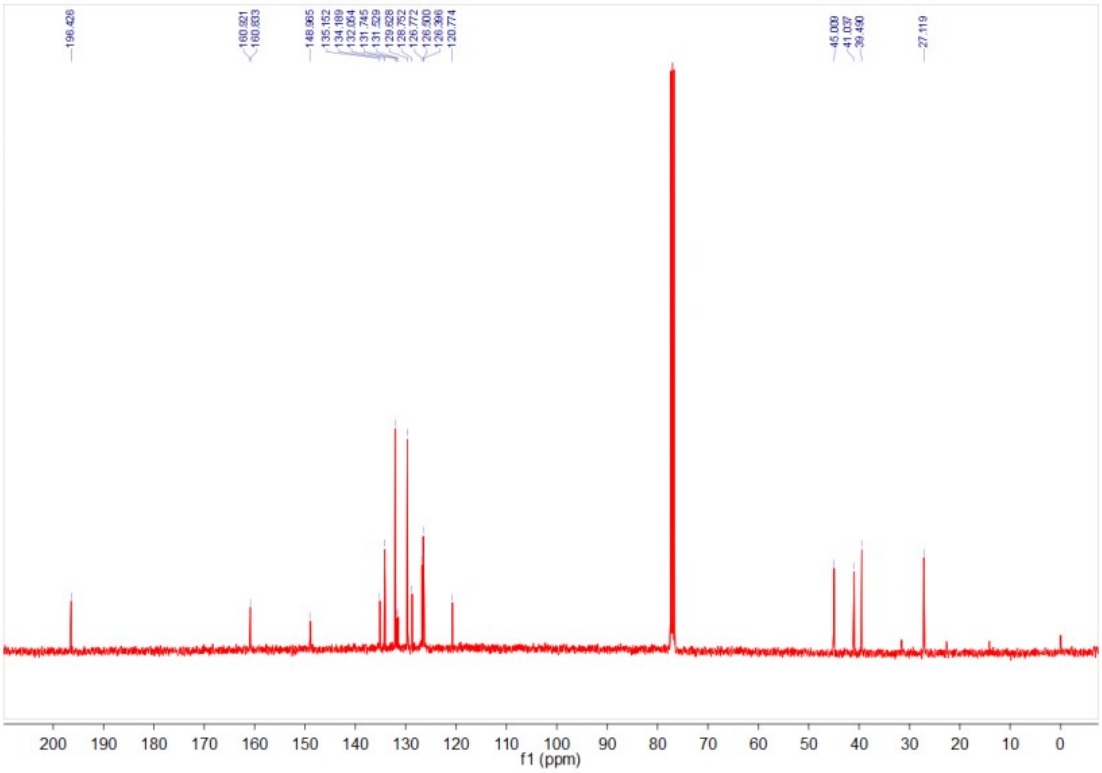
3-(2-(3-chlorophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4aj**)



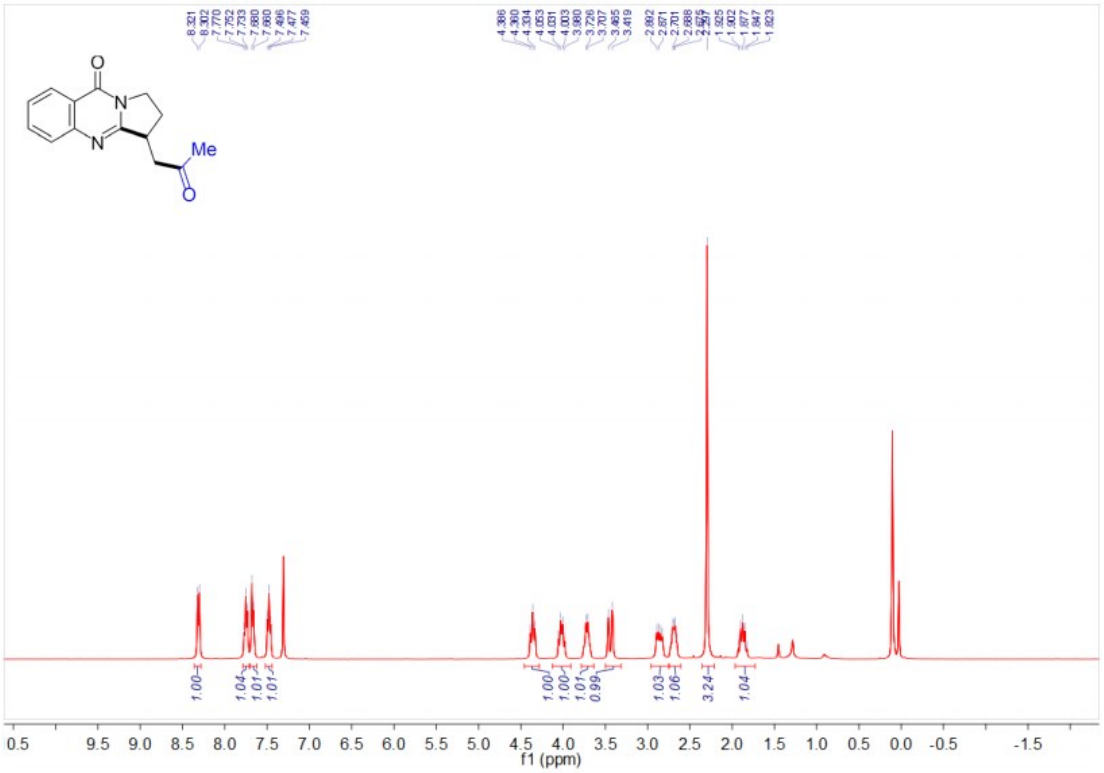


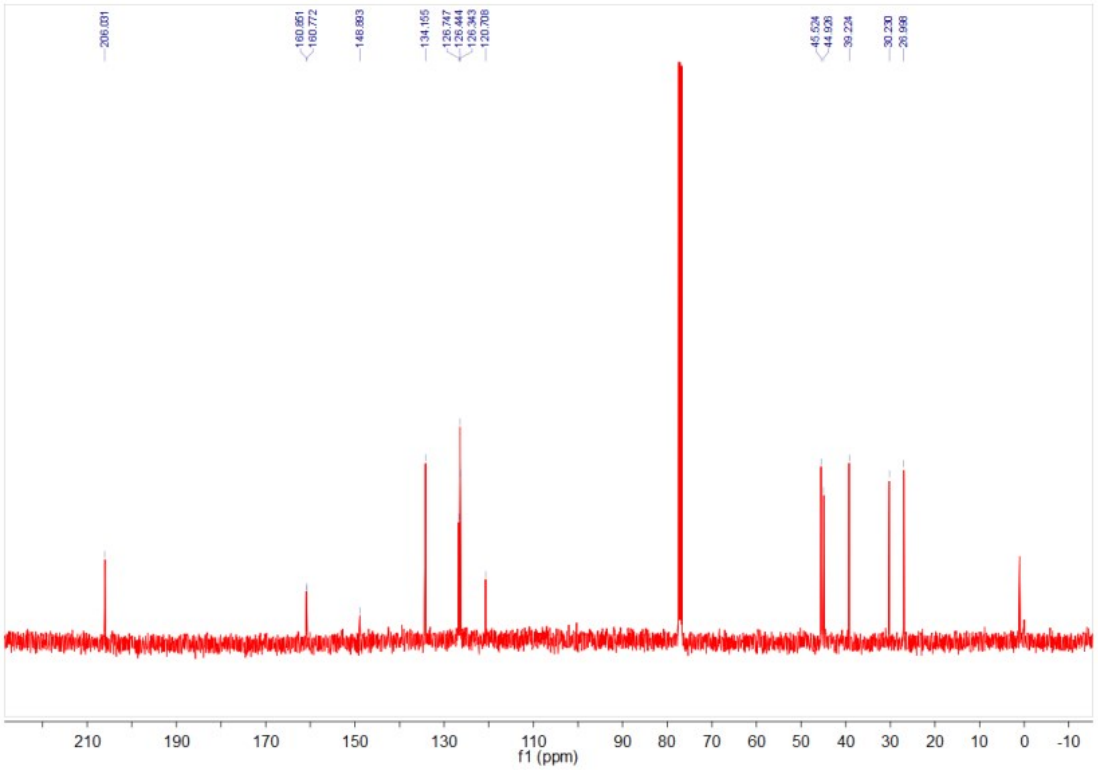
3-(2-(3-bromophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ak**)



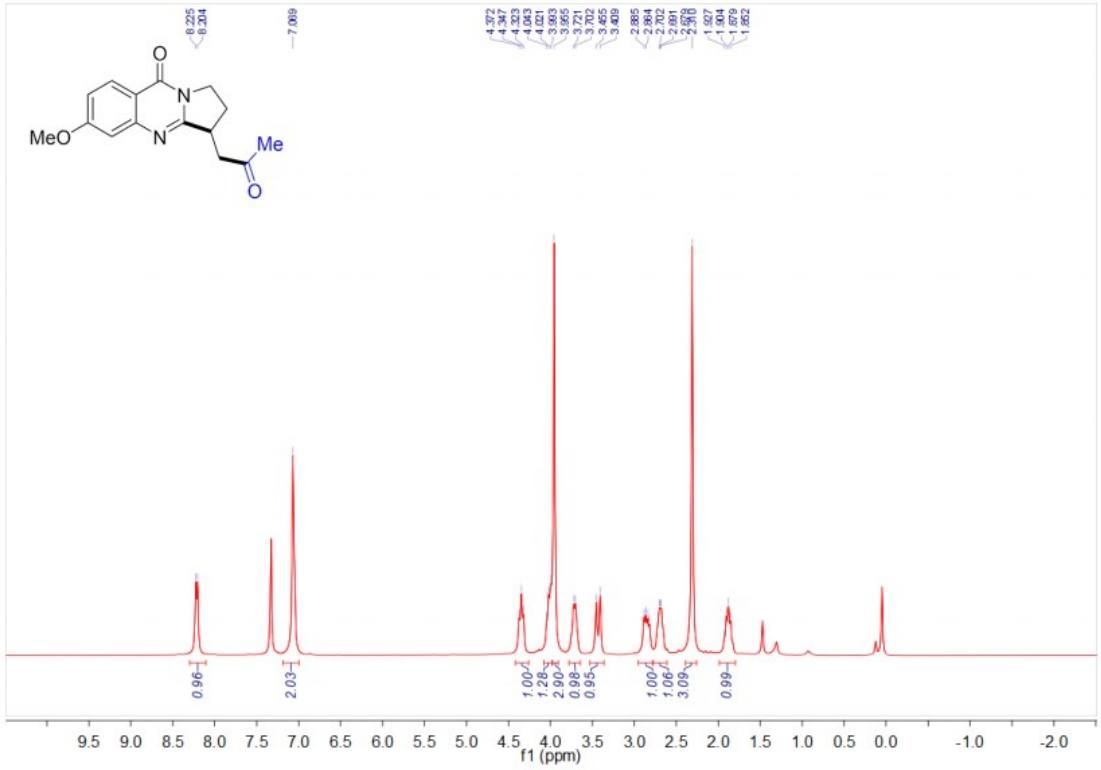


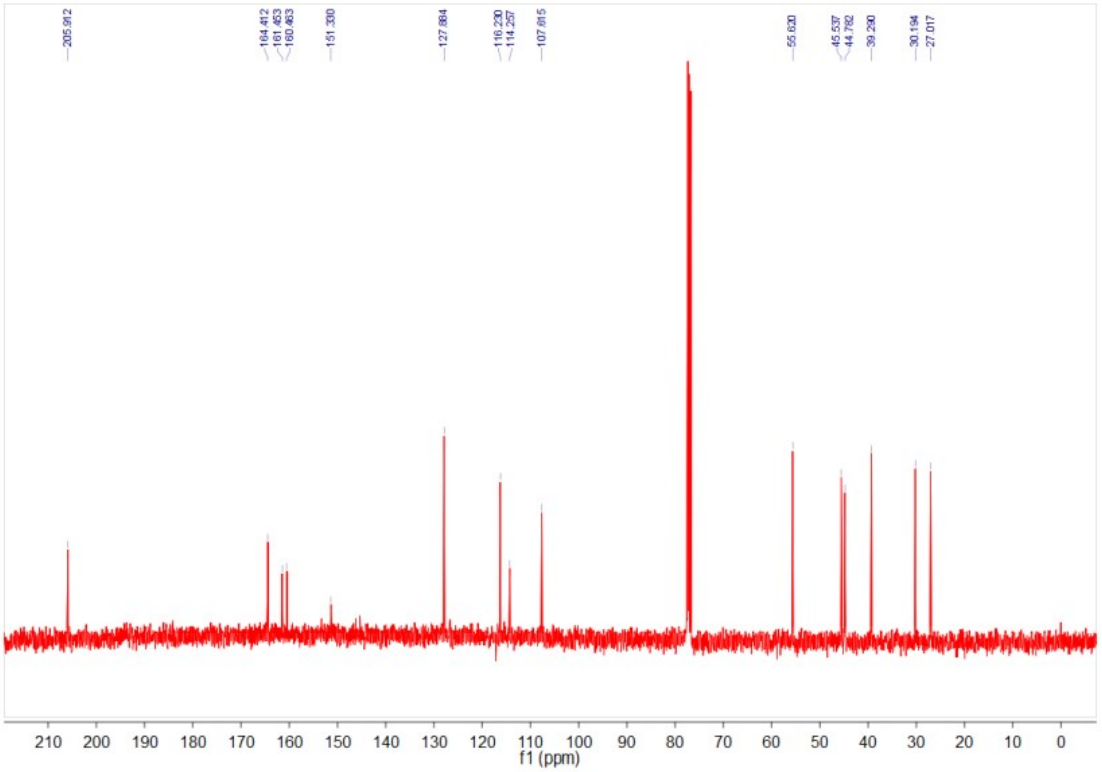
3-(2-oxopropyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4al**)



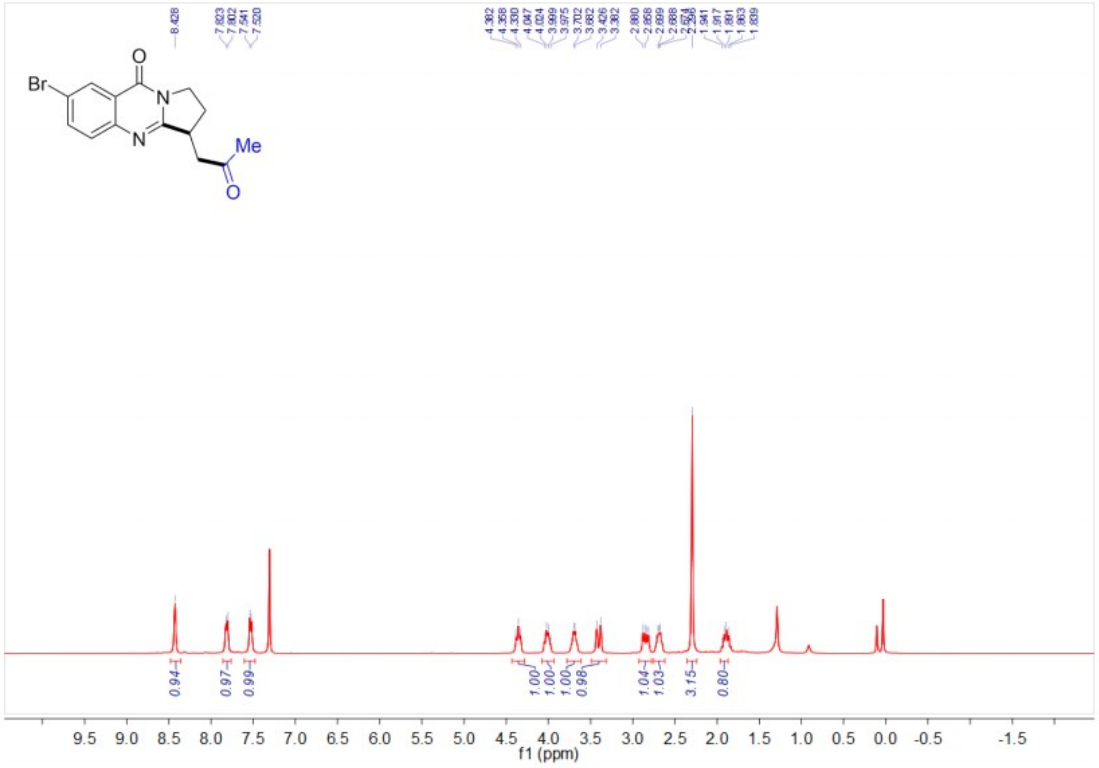


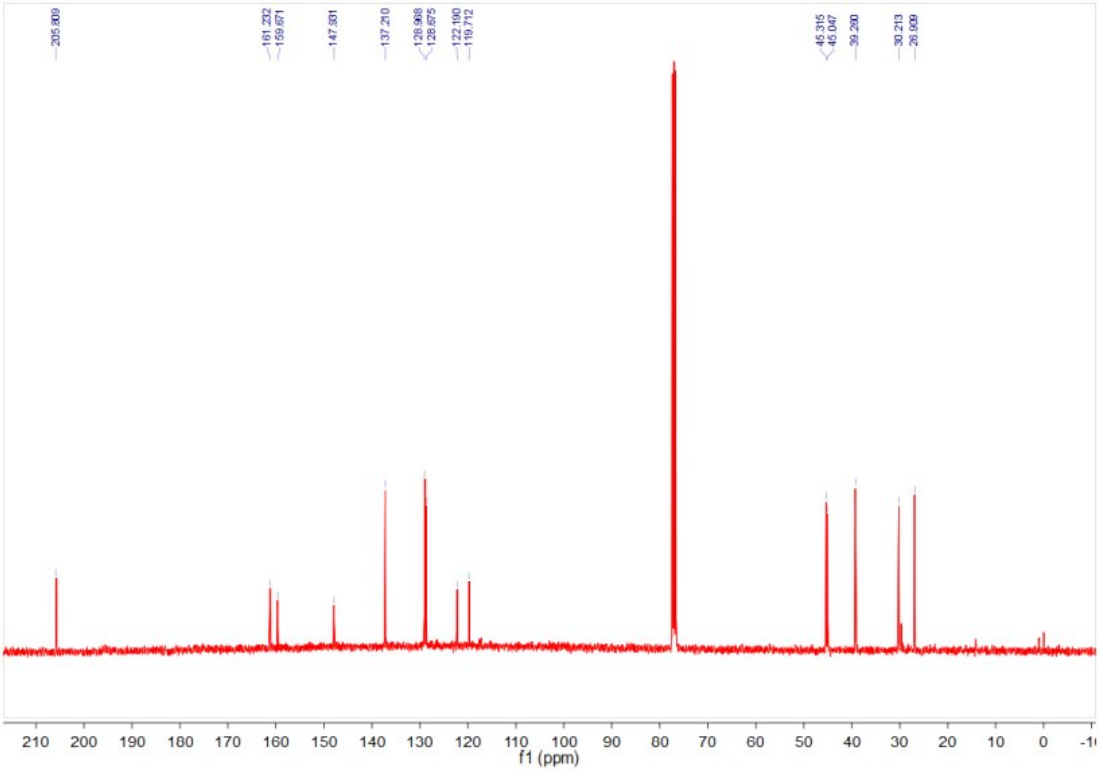
6-methoxy-3-(2-oxopropyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4am**)



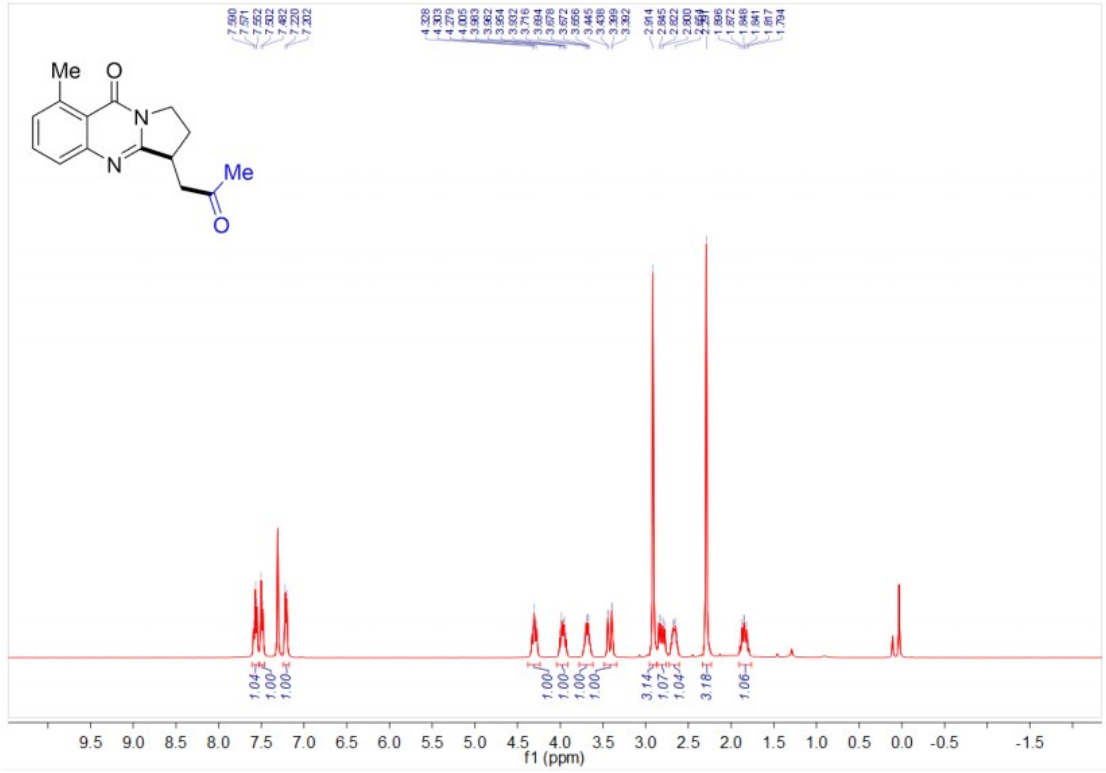


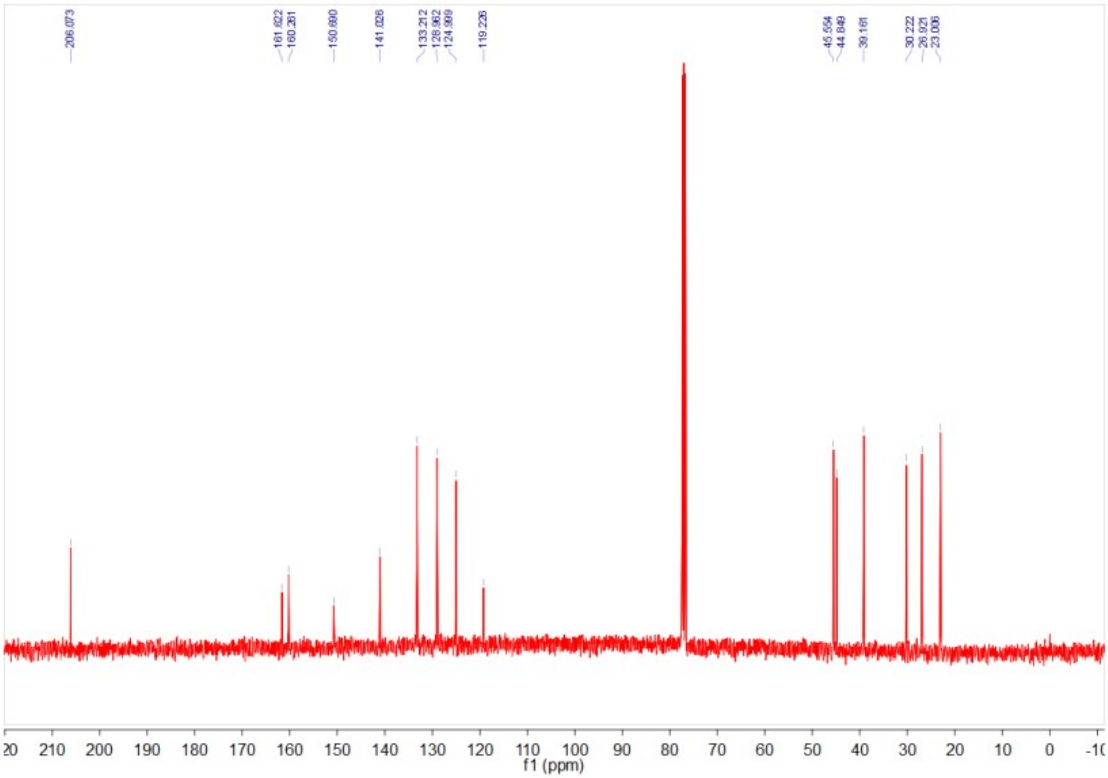
7-bromo-3-(2-oxopropyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4an**)



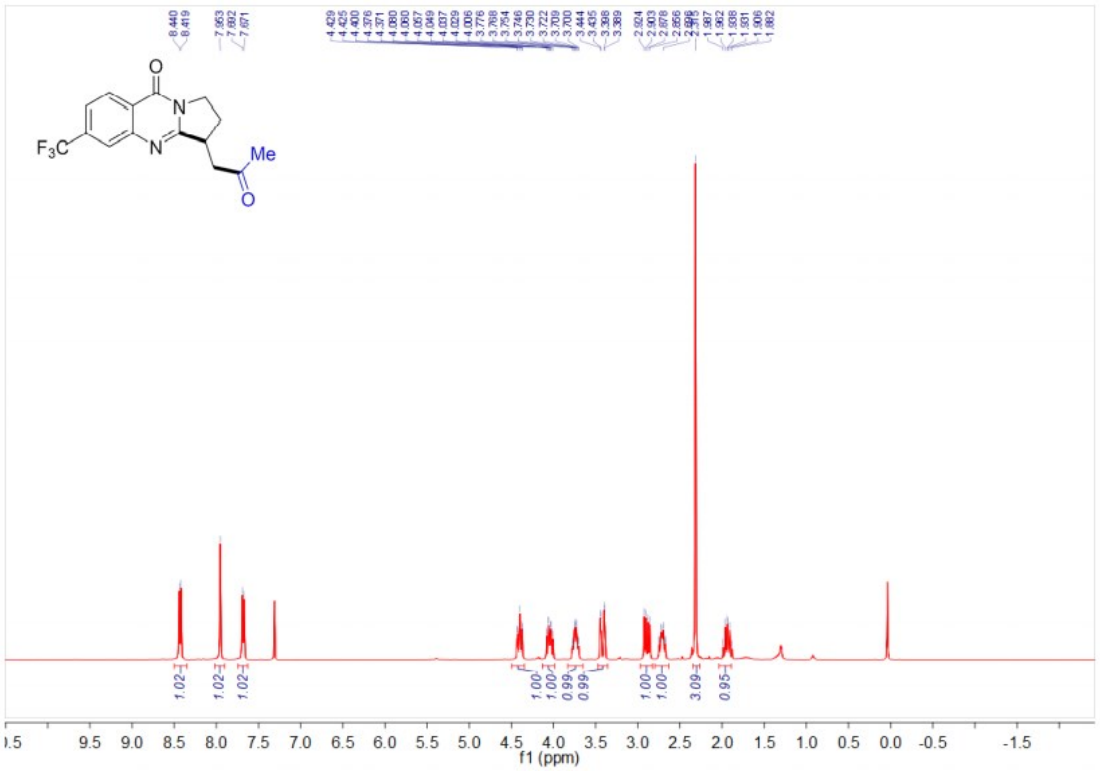


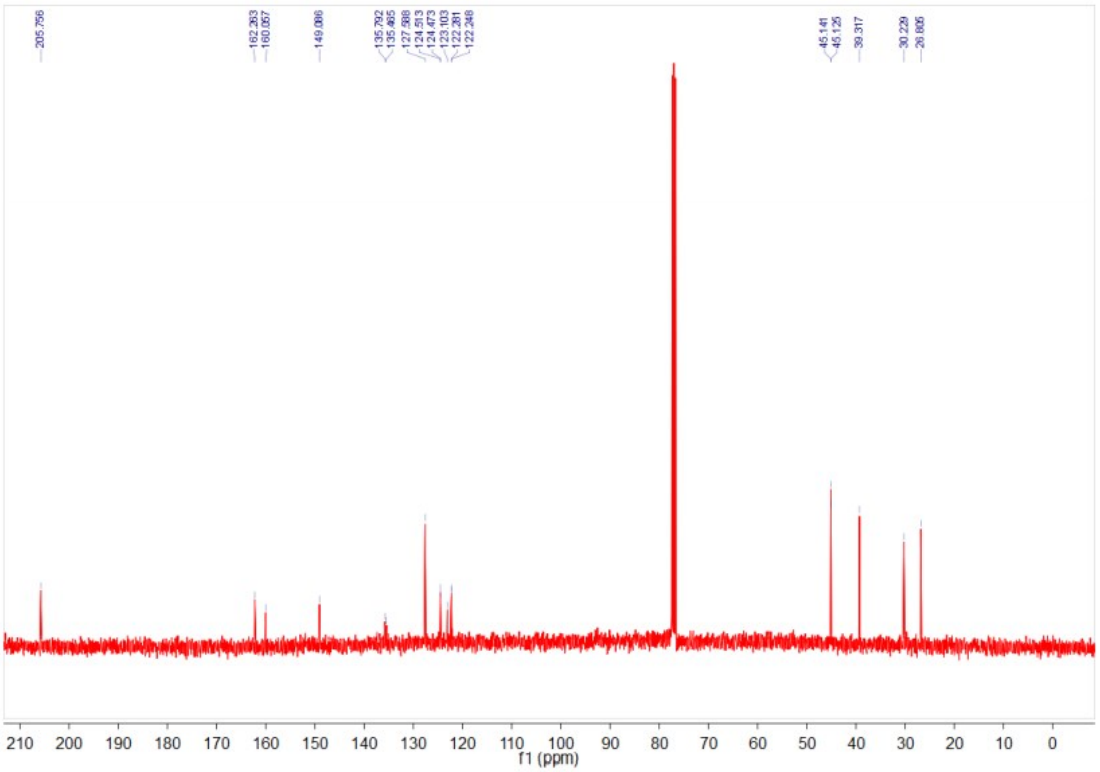
8-methyl-3-(2-oxopropyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ao**)

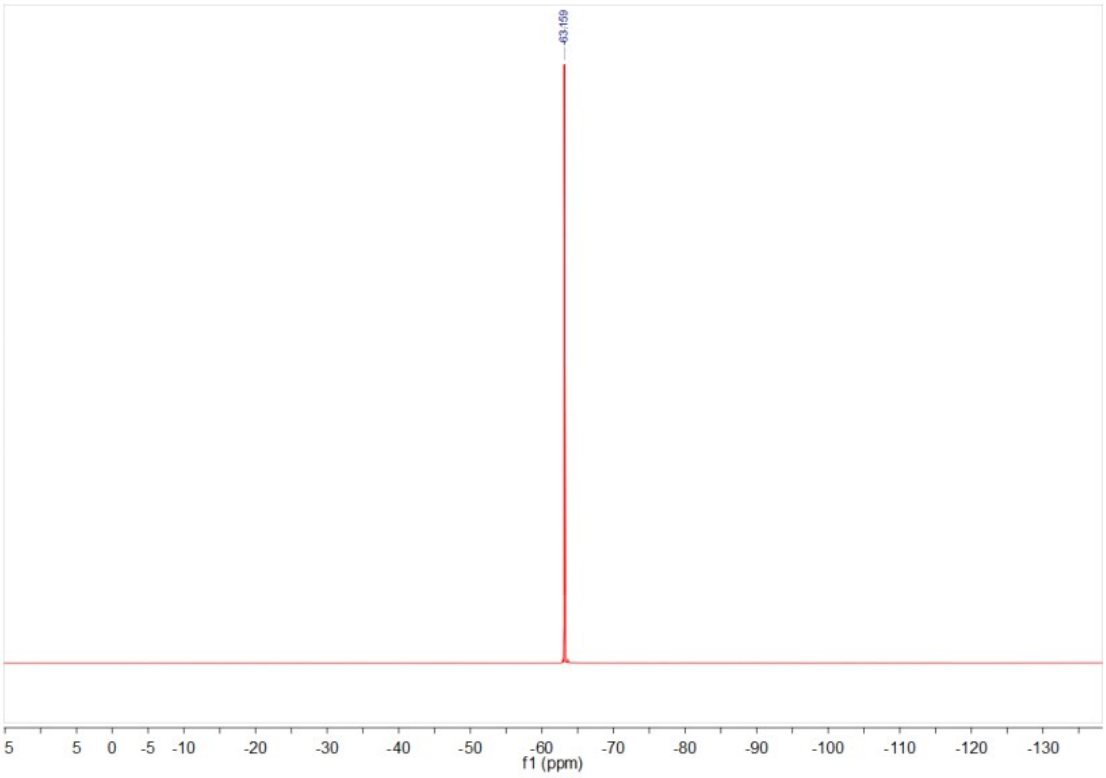




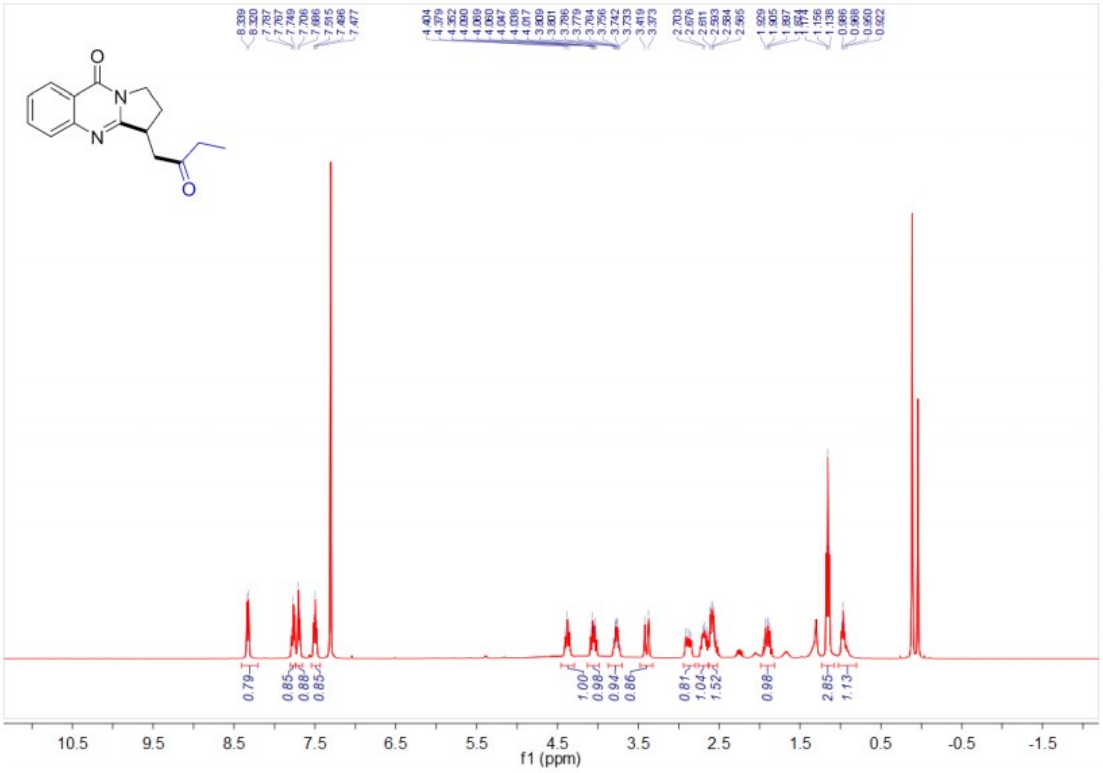
3-(2-oxopropyl)-6-(trifluoromethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ap**)

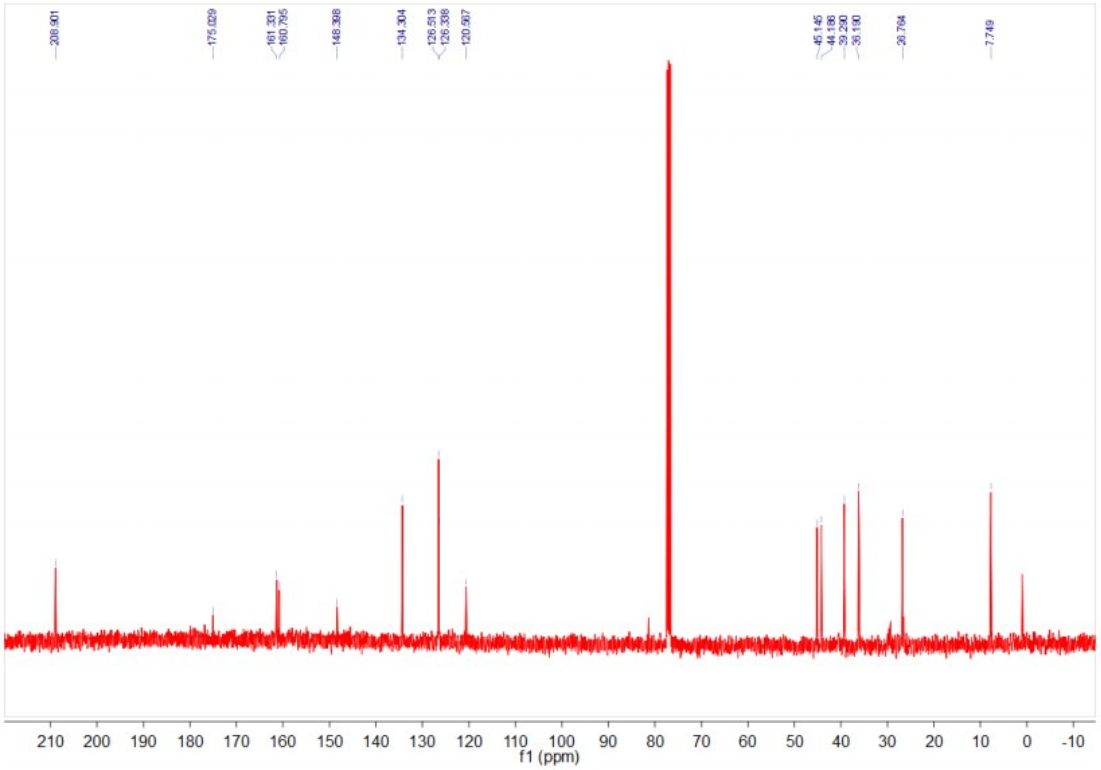




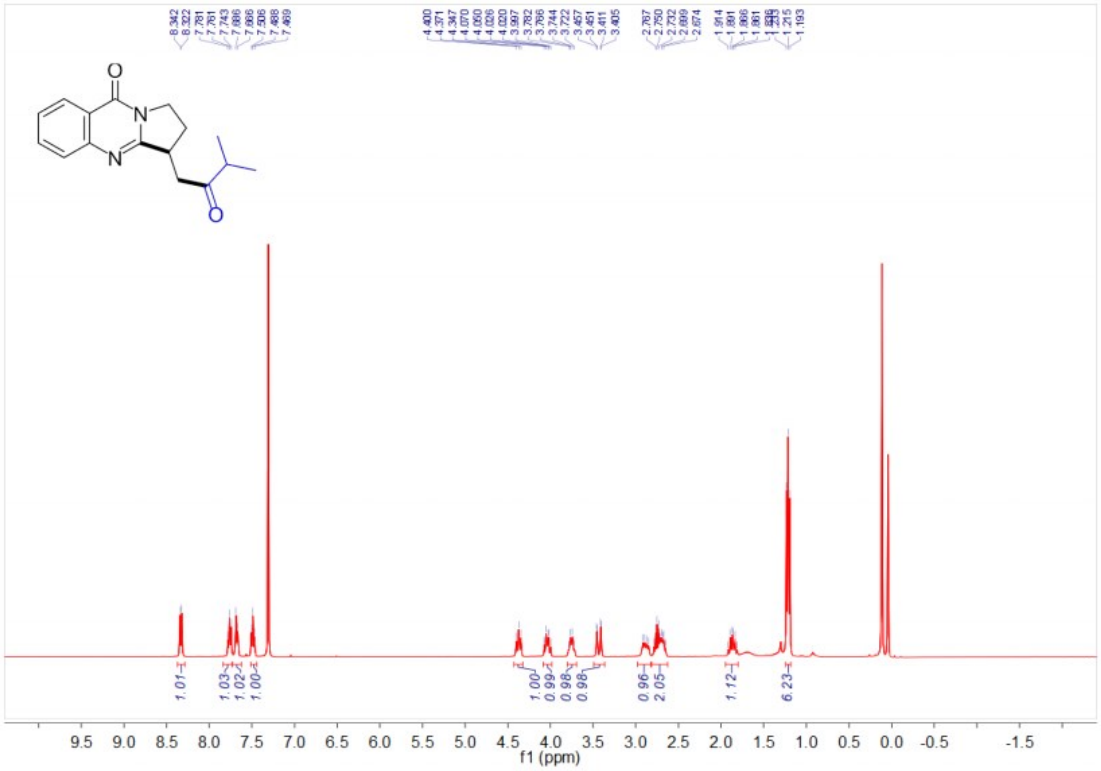

-63.159
5
5
0
-5
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
f1 (ppm)

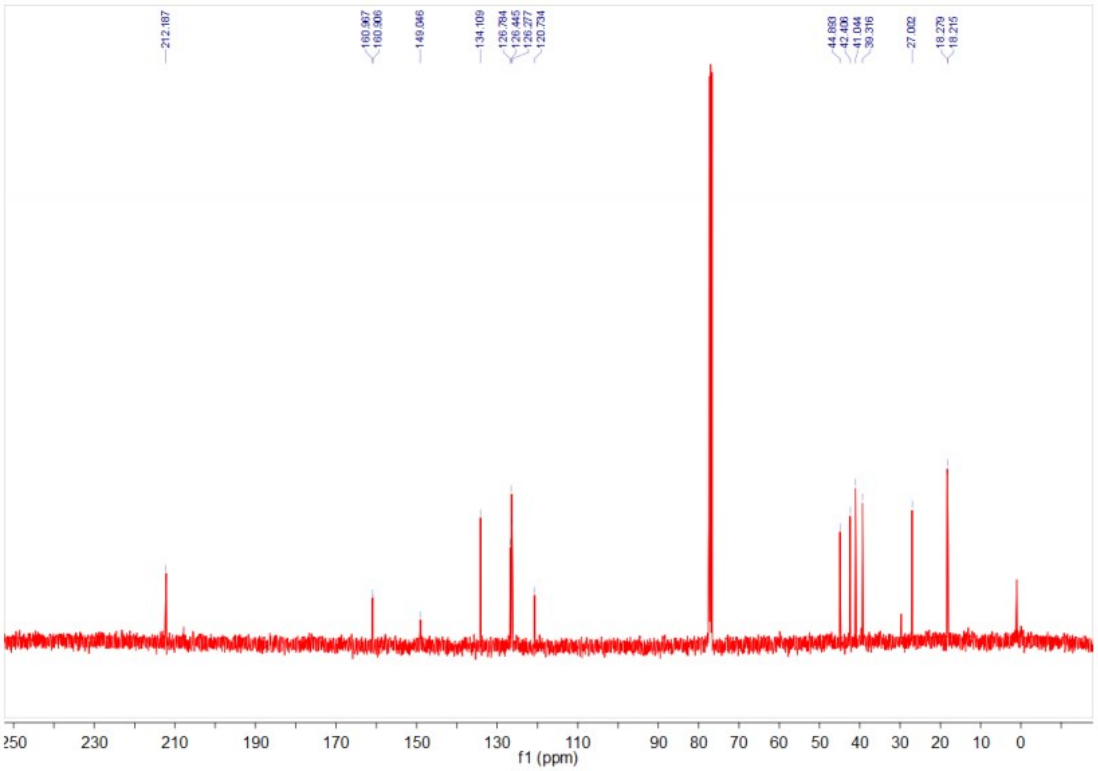
3-(2-oxobutyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4aq**)



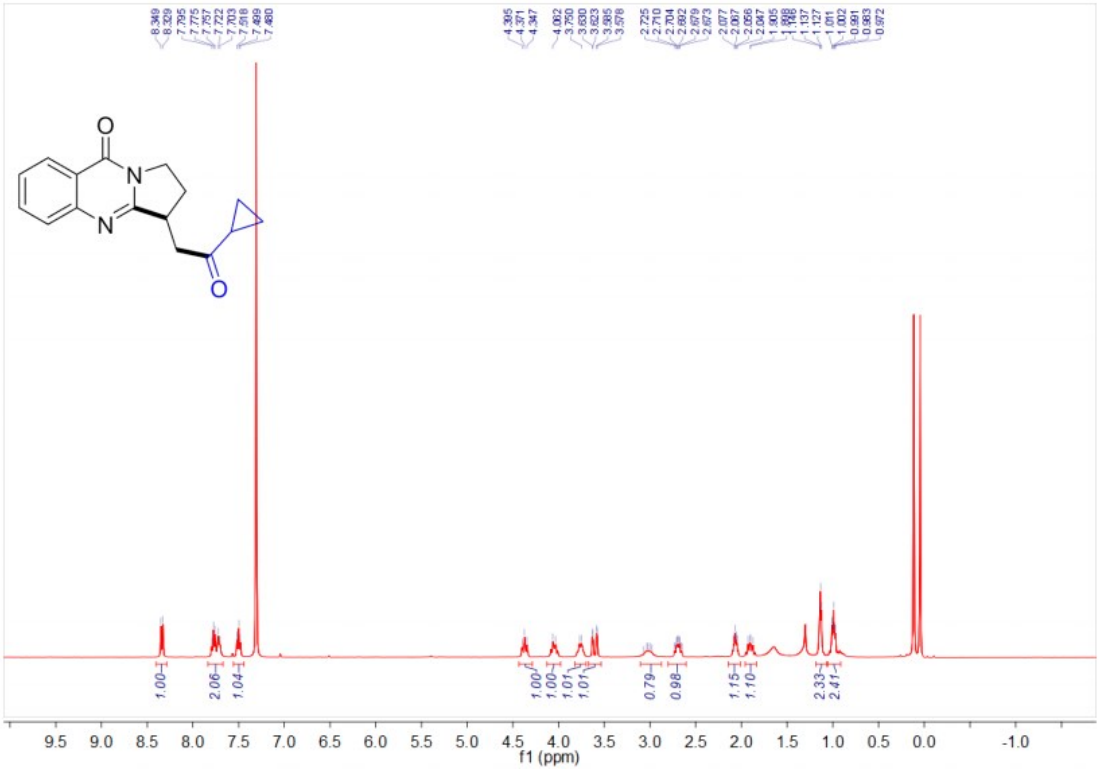


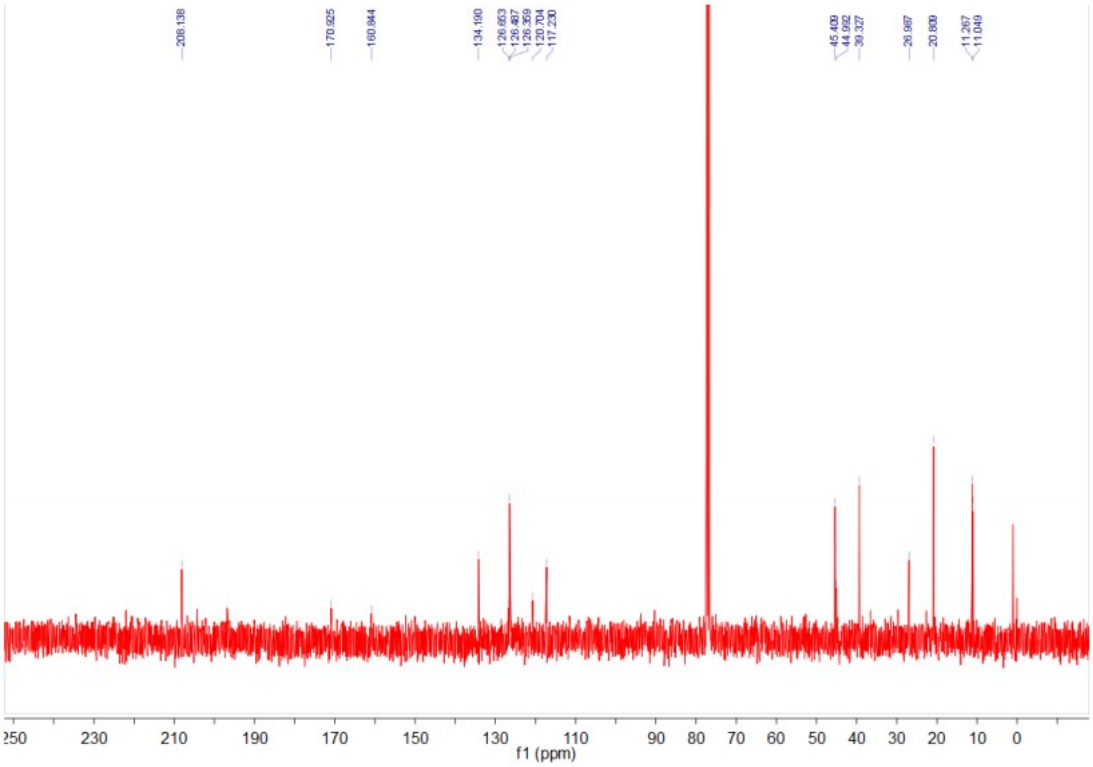
3-(3-methyl-2-oxobutyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4ar**)



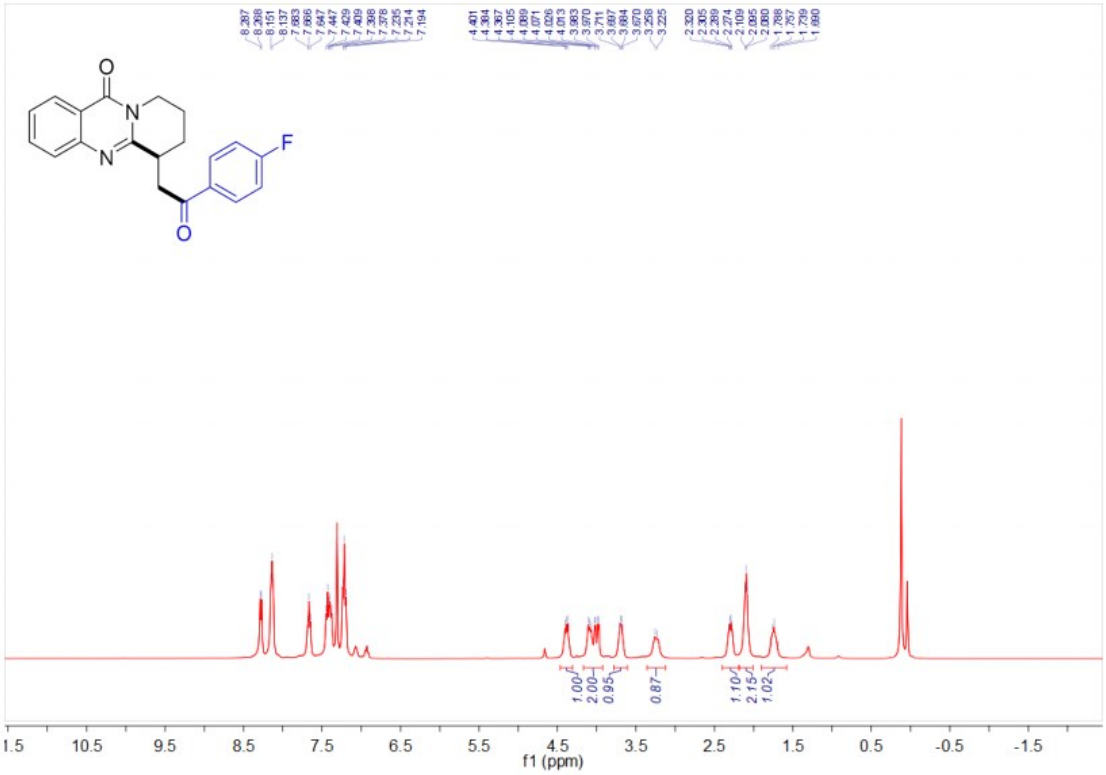


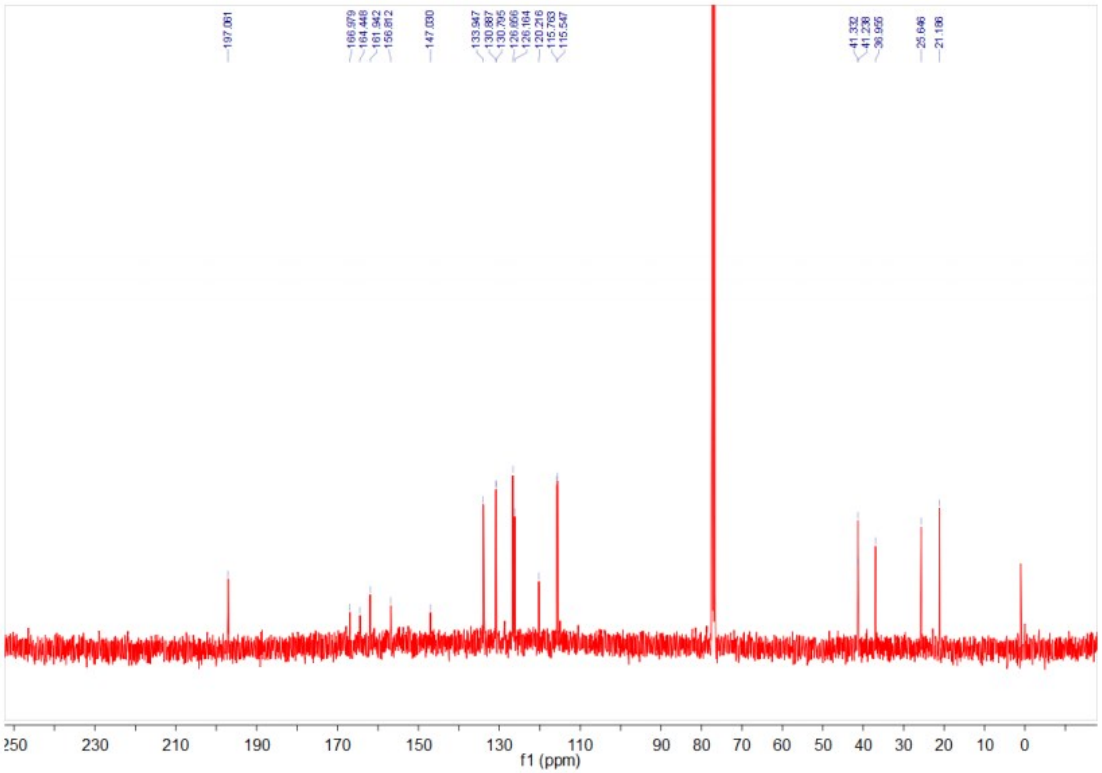
3-(2-cyclopropyl-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1*H*)-one (**4as**)

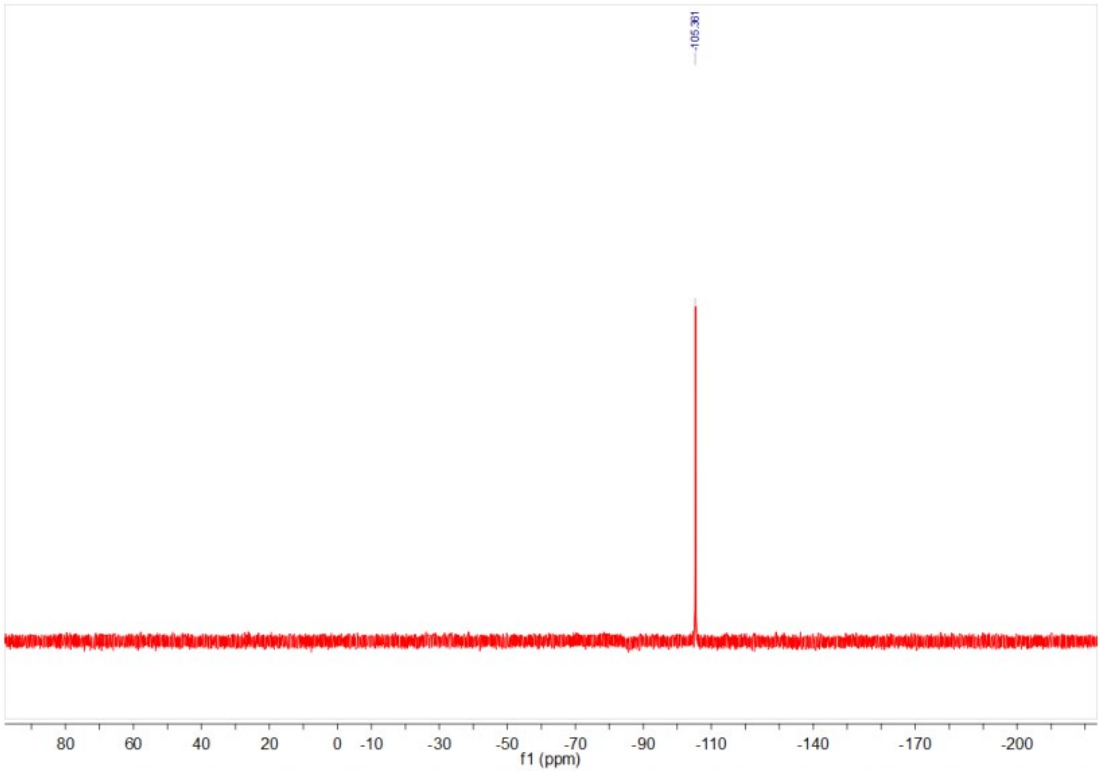




6-(2-(4-fluorophenyl)-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ab**)






-105.361
80
60
40
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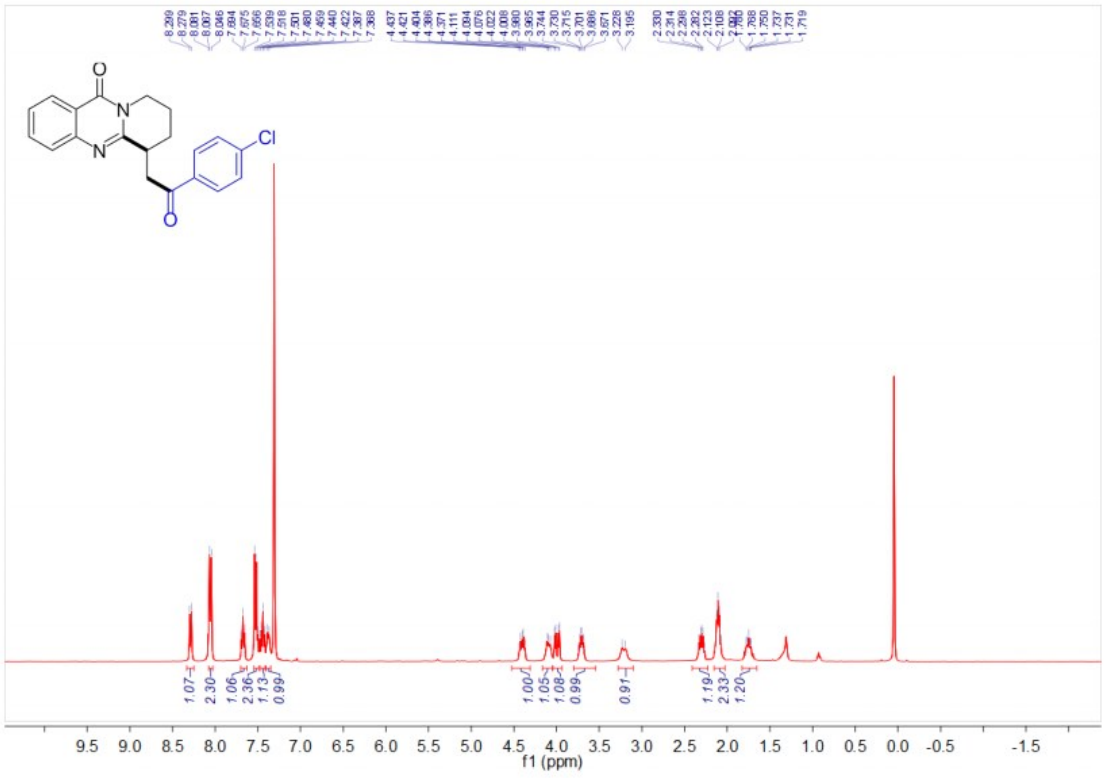
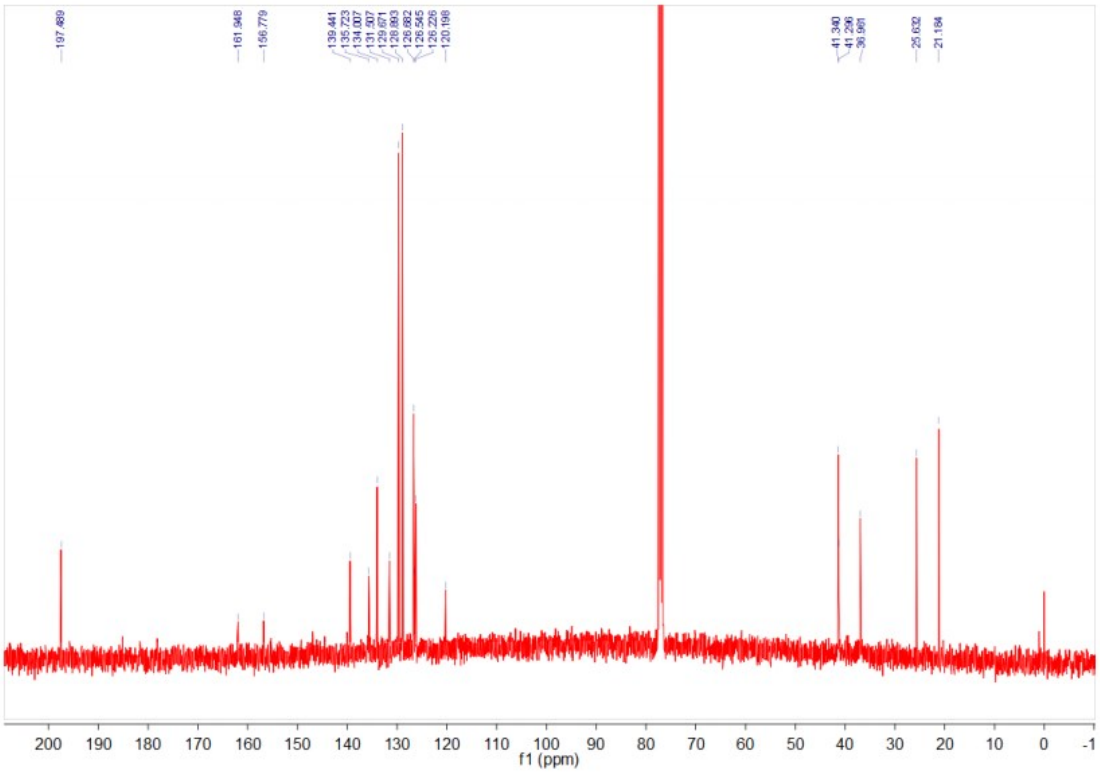
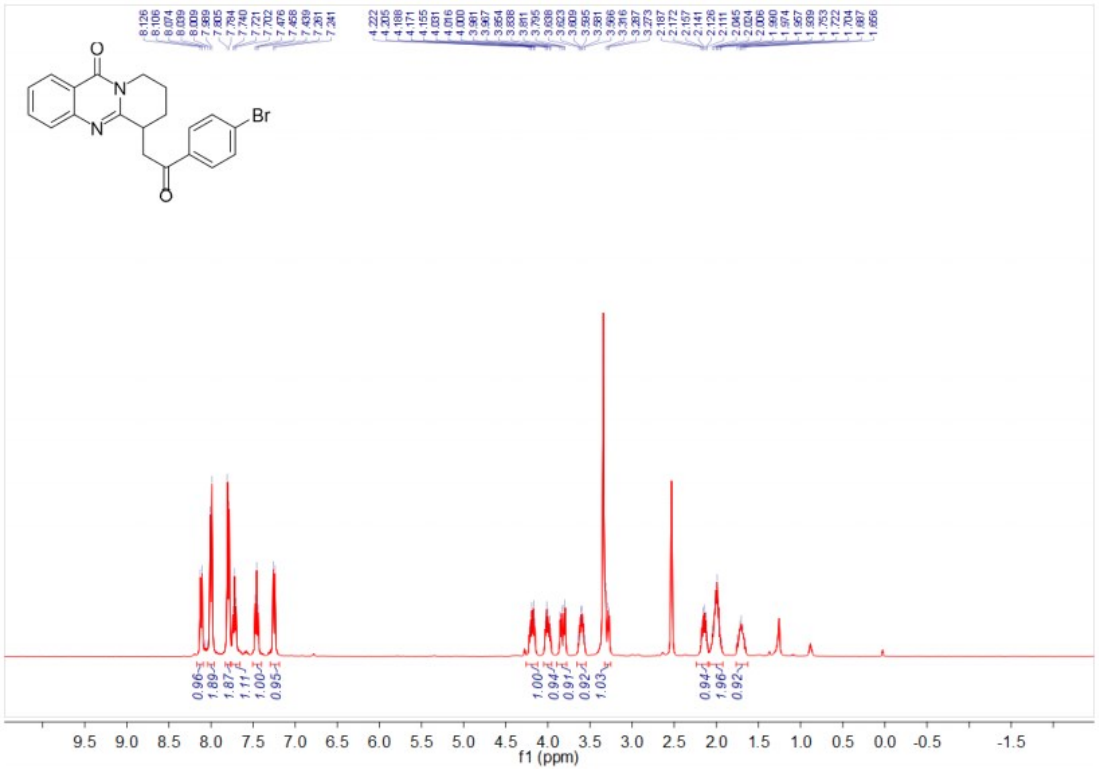
0
-10
-30
-50
-70
-90
-110
-140
-170
-200
f1 (ppm)

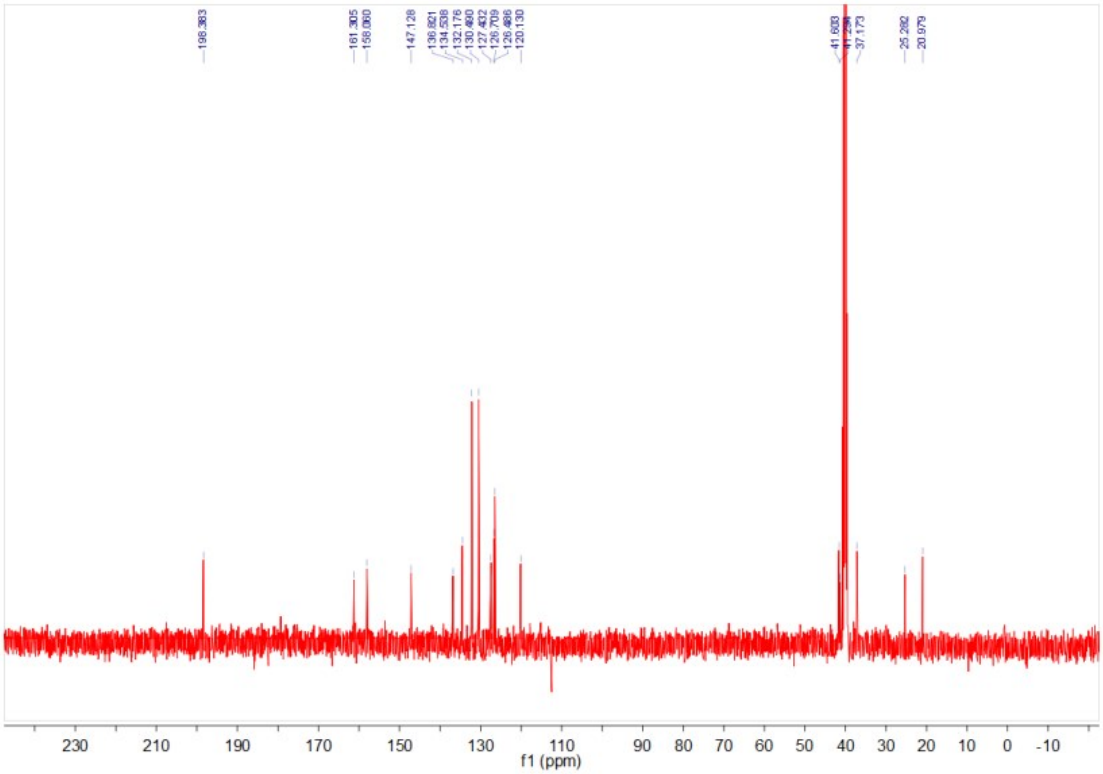
6-(2-(4-chlorophenyl)-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ac**)



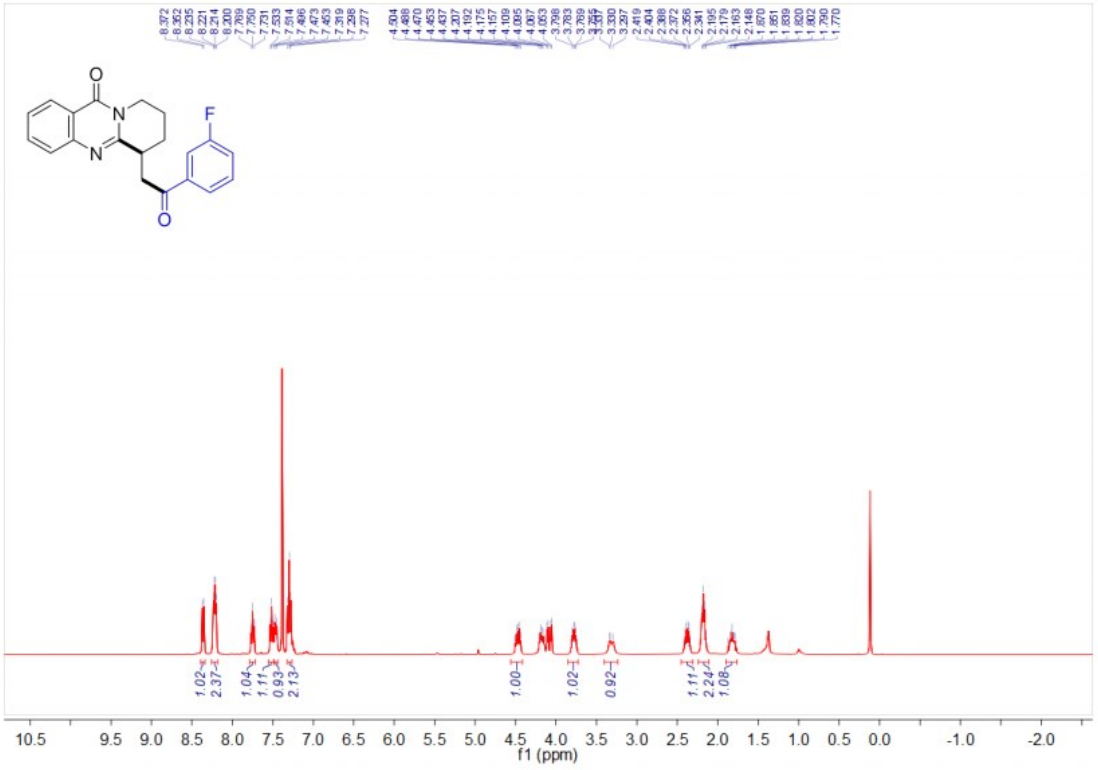


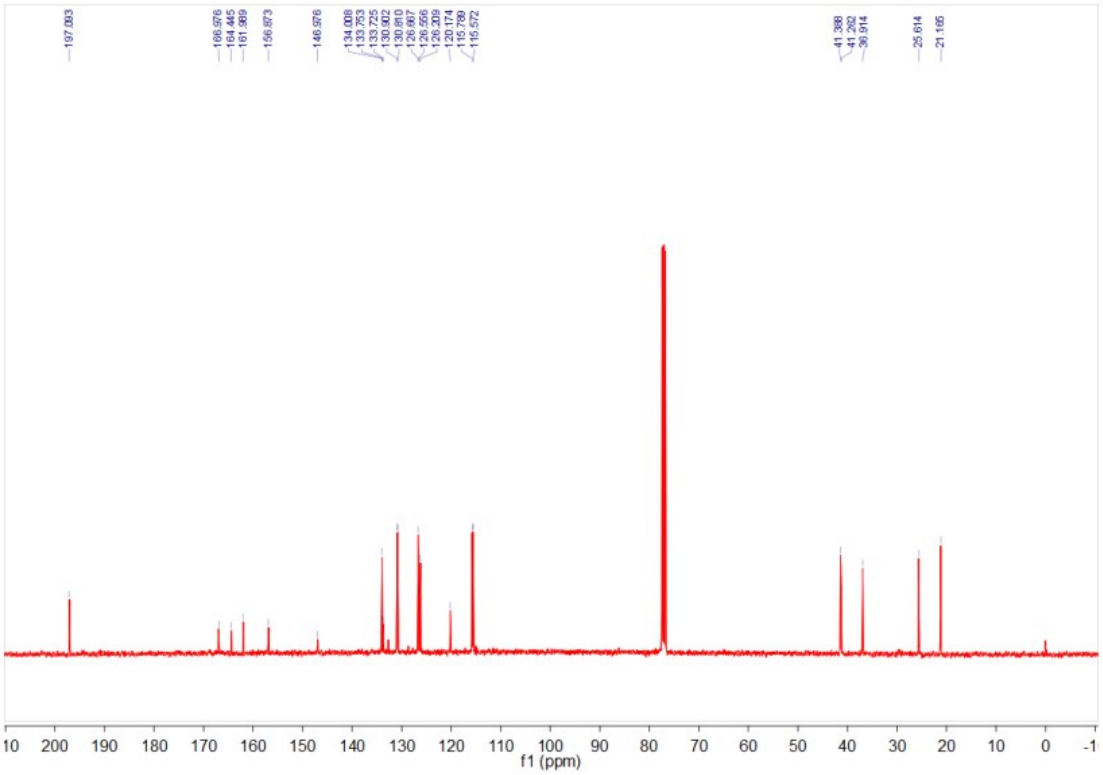
6-(2-(4-bromophenyl)-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ad**)

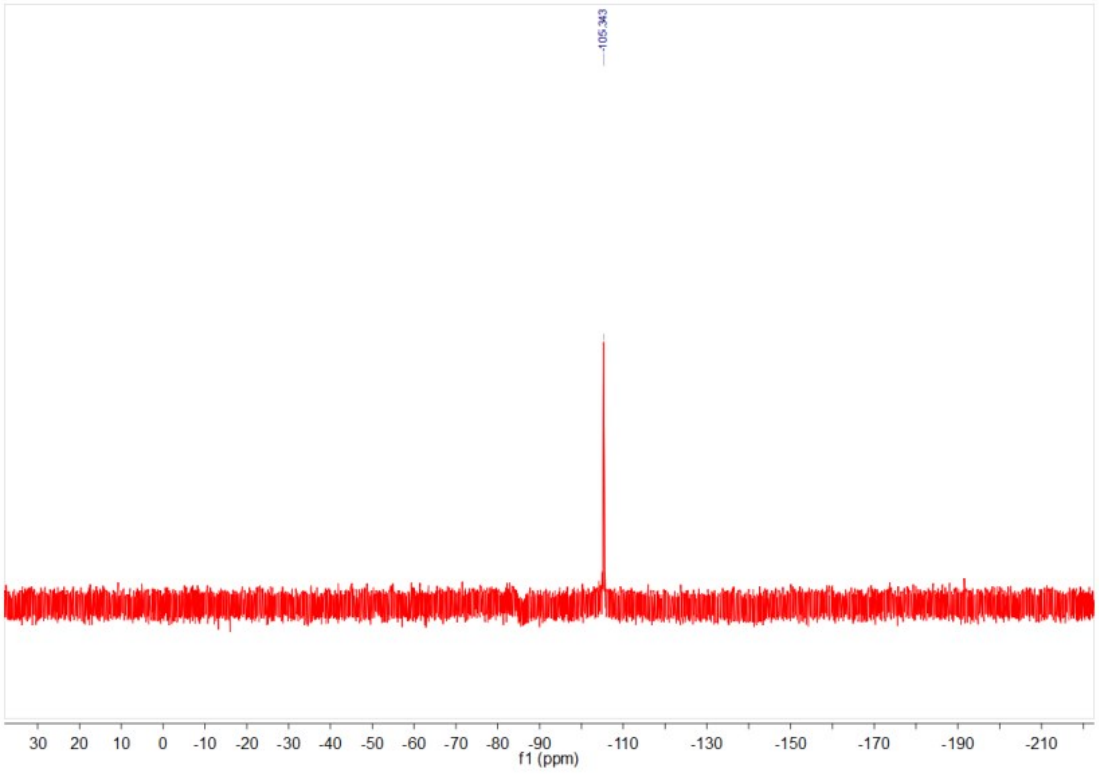




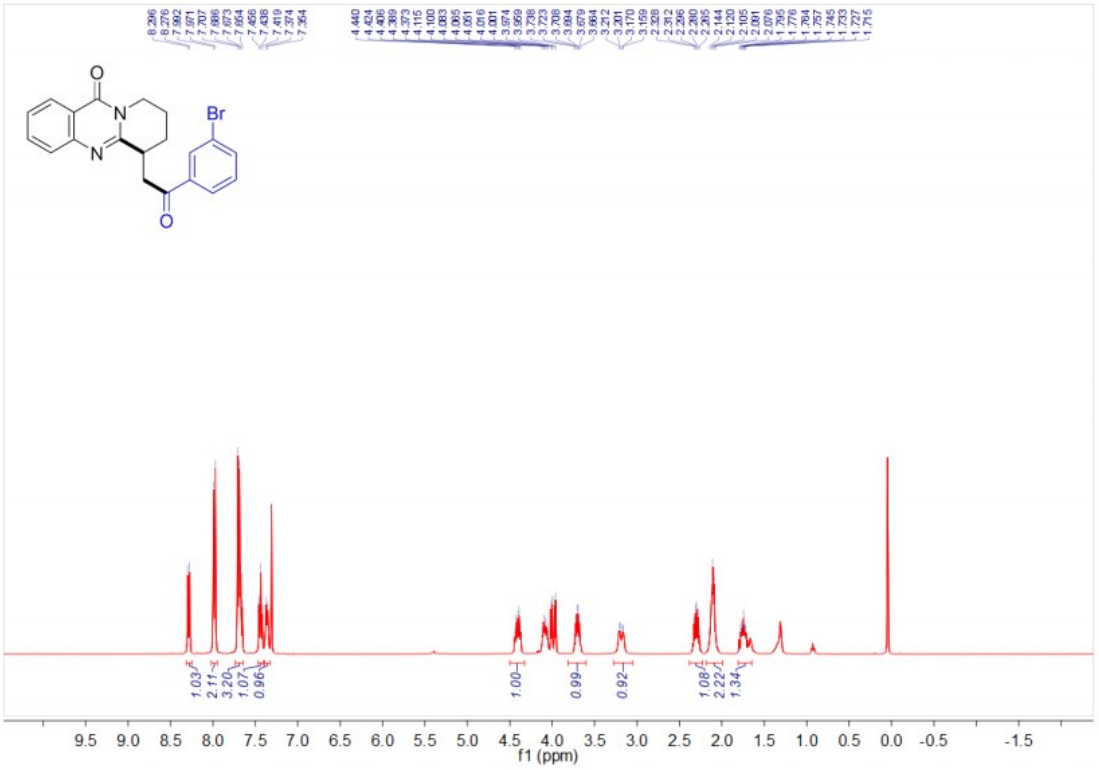
6-(2-(3-fluorophenyl)-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ae**)

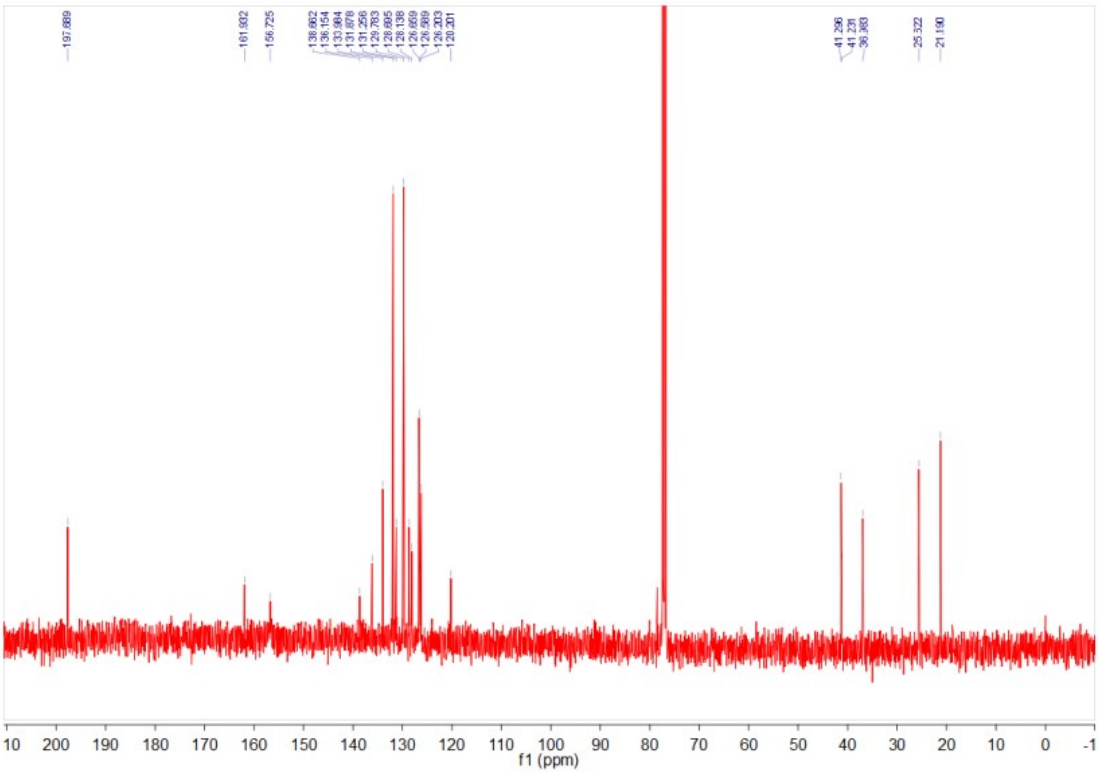





-105.343
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)

6-(2-(3-bromophenyl)-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5af**)





6-(2-cyclopropyl-2-oxoethyl)-6,7,8,9-tetrahydro-11H-pyrido[2,1-b]quinazolin-11-one (**5ag**)