Supporting Information for:

Visible-light-induced Annulation of 4-Aminocoumarins to Tetrahydropyrimidine-Fused Coumarins and Evaluation of Their Antitumor Activities

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Table of Content

1. General Information

Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 500 MHz and ^{13}C NMR spectra were recorded at 125 MHz by using a Bruker Avance 500 spectrometer in $CDCl_3$ with TMS as internal standard. The chemical shifts (δ) were expressed in ppm and J values were given in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectral (HRMS) analysis was performed on a Bruker micr OTOF-Q II instrument using ESI techniques. Cyclic voltammetric investigations were performed on the CHI-660E electrochemical workstation (Shanghai Chenhua Instrument Co., Ltd., China). TLC analysis was performed using precoated glass plates. Column chromatography was performed on silica gel (200-300 mesh). 4-anilinocoumarins and N-arylglycines were prepared according to literature.[1-3]

The Light Source and the Material of the Irradiation Vessel

Manufacturer: Beijing Rogertech Ltd.
Model: OHSP-350 UV
Value: 3536.956 μW/cm²/nm
Energy peak wavelength: 519.0 nm
Peak width at half-height: 33.2 nm
Material of the irradiation vessel: Schlenk flask

Not use any filters

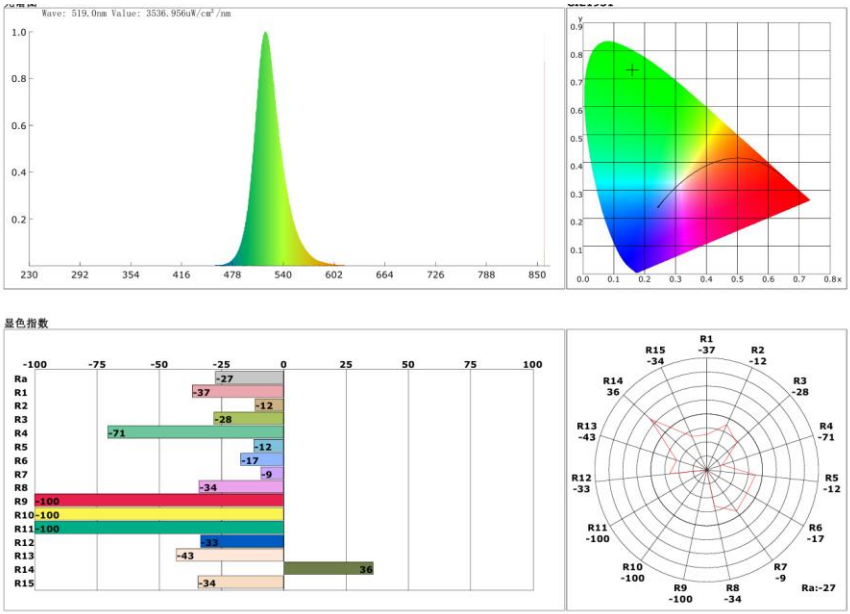


Figure S1 LED spectrum test report

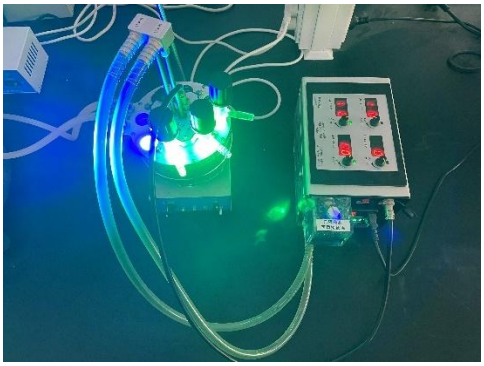


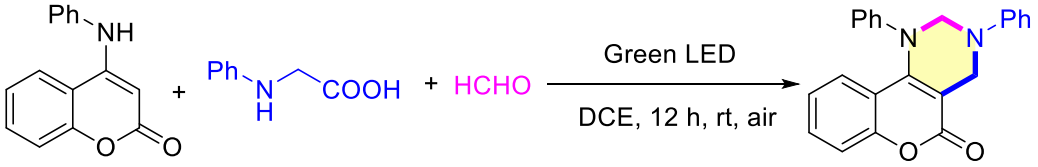
Figure S2 (Photographed by author Ningbo Li)

2. Experimental Section

2.1 Typical Procedure for Annulation of 4-Anilinocoumarins:

A 10 ml Schlenk tube equipped with a magnetic stirring bar was charged with 4-anilinocoumarin **1a** (0.2 mmol), *N*-phenylglycine **2a** (0.24 mmol), formaldehyde **3a** (0.24 mmol) and 1,2-dichloroethane (2 mL). The solution was stirred at room temperature with the irradiation of a 10 W Green LED lamp for 6 h. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 6/1-3/1) to give the desired products **4a**.

2.2 Procedure for Gram-scale Synthesis of 4a



1a, 5 mmol **2a**, 6 mmol **3**, 6 mmol **4a,** 1.27 g, 81%

A 25 ml Schlenk tube equipped with a magnetic stirring bar was charged with 4-aminocoumarin (**1a**, 5 mmol), *N*-phenylglycine (**2a**, 6 mmol), formaldehyde (**3**, 6 mmol) and 1,2-dichloroethane (15 mL). The solution was stirred at room temperature with the irradiation of a 10 W Green LED lamp for 12 h. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 5/1) to give the desired products **4a** (1.27 g, 81% yield).

2.3 Experiments of investigations on the mechanism

To get insight into the contribution of different active species to the reaction, radical trapping and active species trapping experiments were performed. The commonly used scavengers 2,2,6,6-tetramethylpiperidinooxy (TEMPO) or 1,1-diphenylethylene were used in the model reaction, respectively. In a typical experiment: A 10 ml Schlenk tube equipped with

a magnetic stirring bar was charged with 4-anilinocoumarins **1a** (0.2 mmol), *N*-phenylglycine **2a** (0.24 mmol), formaldehyde **3** (0.24 mmol), 1,1-diphenylethylene (3 equiv.) and DCE (2 mL). The solution was stirred at room temperature with the irradiation of a 10 W green LED lamp for 6 h. Afterwards, 30 μL of the mixture was quickly taken out into a small tube and analyzed by LC-MS.

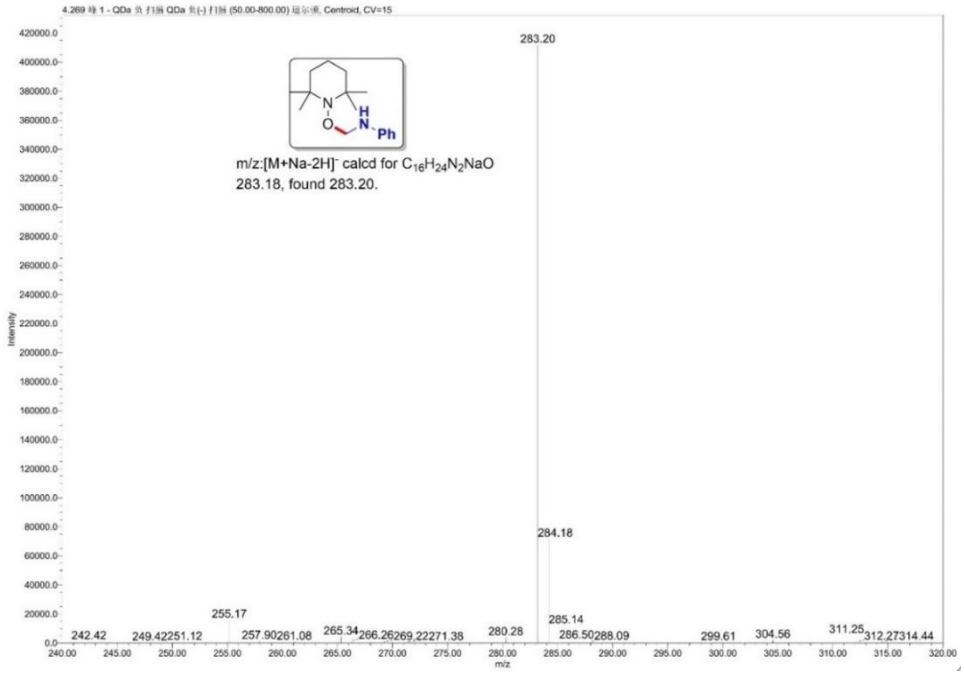


Figure S3 MS of **5**

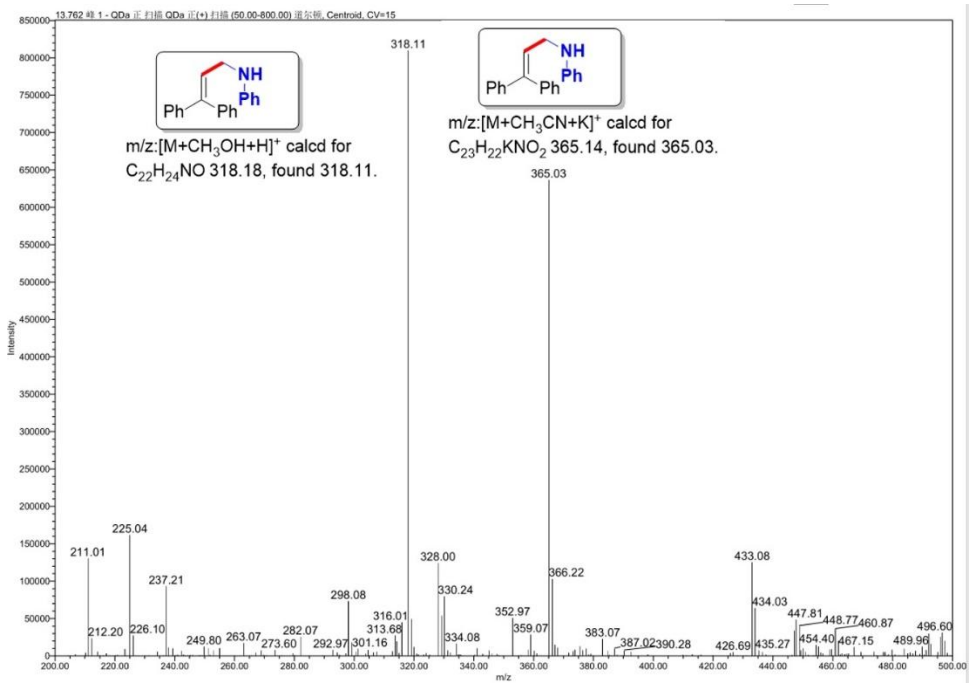


Figure S4 MS of **6**

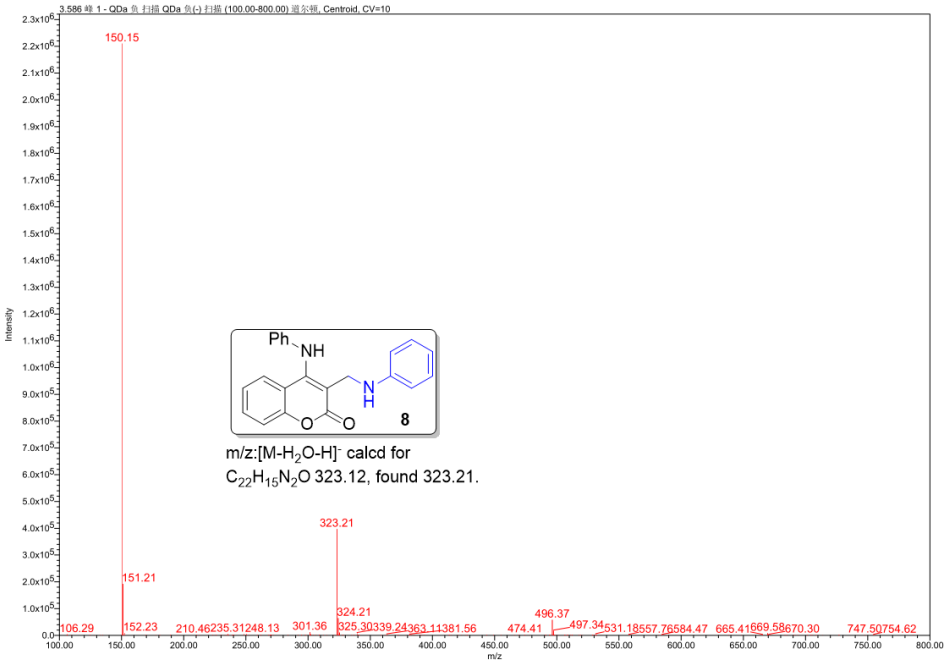


Figure S5 MS of **7**

2.4 UV/Vis Absorption Experiment

The UV/Vis absorption spectra of 4-anilinocoumarin (**1a**, 0.020 M) and 1,3-diphenyl-1,2,3,4-tetrahydro-5*H*-chromeno[4,3-*d*]pyrimidin-5-one (**4a**, 0.020 M) in 1, 2-dichloroethane were recorded in 1 cm path quartz cuvettes by using a SHIMADZU UV-5300 UV-visible spectrophotometer, respectively. The obtained bands in UV/vis absorption spectra were shown in Figure S6.

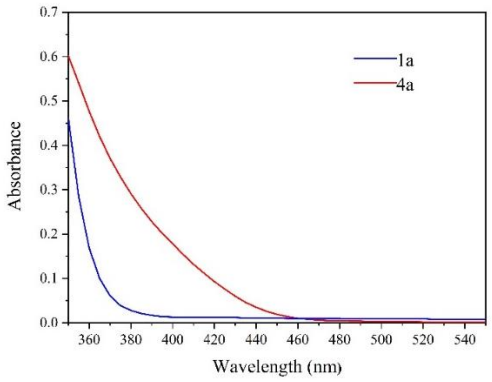


Figure S6 UV-Vis absorption spectra of **1a** and **4a**

2.5 Fluorescence quenching studies

The fluorescence emission intensities were recorded on a HITACHI Fluormax-7100 spespectrofluorimeter. The excitation wavelength was fixed at 288 nm, and the emission wavelength was measured at 525 nm (emission maximum). The samples were prepared by mixing by 4-aminocoumarin **1a** (5.0×10^{-4} mol/L) and different amount of *N*-phenylglycine **2a**

in 1, 2-dichloroethane (total volume = 0.2 mL) in a light path quartz fluorescence cuvette. The concentration of N-phenylglycine stock solution is 1.0×10^{-4} mol/L in 1, 2-dichloroethane. For each quenching experiment, 0.1 mL different concentration of N-phenylglycine stock solution was titrated to a mixed solution of 0.1 mL 4-aminocoumarin **1a** (in a total volume = 0.2 mL). Then the emission intensity was collected and the results were presented in Figure S7. The linear relationship between I_0/I (I_0 and I are the fluorescence intensities before and after adding the various concentration of **2a**) and the concentration.

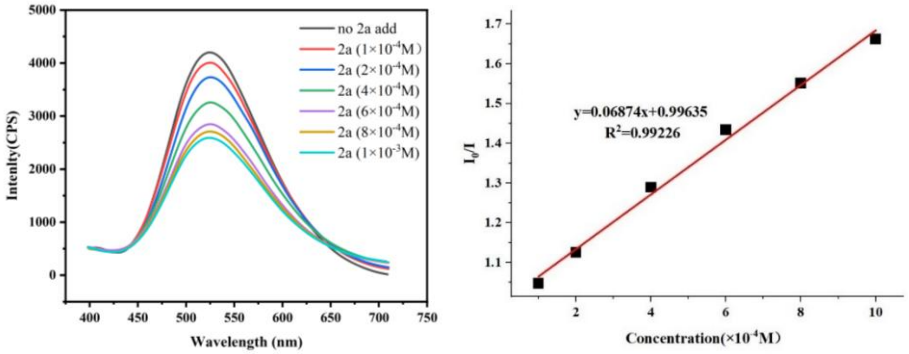


Figure S7 Fluorescence quenching experiment

2.6 2.8 Cyclic Voltammetry of 1a and N-phenylglycine

Cyclic voltammetric investigations were performed on the CHI-660E electrochemical workstation (Shanghai Chenhua Instrument Co., Ltd., China) with the conventional threeelectrode system. A glassy carbon electrode was used as the working electrode; a Ag/AgCl electrode (SCE) and a platinum wire were used as the reference electrode and counter electrode, respectively. 4-aminocoumarin **1a** (0.02 M) and *N*-phenylglycine **2a** (0.02 M) was solved in 1,2-dichloroethane and experiment were conducted in the presence of tetrabutylammonium hexafluorophosphate (0.1 M) as supporting electrolyte at a scan rate of 100 mV/s.

2.7 Effect of Visible Light Irradiation

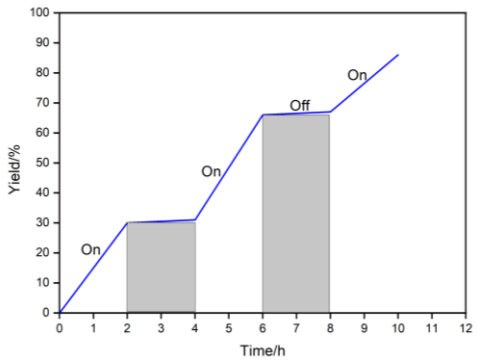


Figure S8 Visible light on/off experiments

2.8 Calculation of Apparent Quantum Yield

$$E_{photon} = \frac{hc}{\lambda_{inc}(520\ nm)} = \frac{6.63x10^{-34}\ J.Sx3x\ 10^{8}\ m.s^{-1}}{520\ x\ 10^{-9}\ m} = 3.83x10^{-19}\ J$$

$$E_{total}=P(10\ W)St = 6.99x\ 10^{-3}\ W.cm^{-2}*3.14\ cm^{2}\ *6x3600s = 4.74x10^{2}\ J$$

$$\text{Number of incident photons} = \frac{E_{total}}{E_{photon}*N_A} = \frac{4.74x10^{2}\ J}{3.83x10^{-19}\ J} = 1.24\ x10^{21}\ *N_A^{-1} = 2.060\ mmol$$

$$A.Q.Y(\%) = \frac{\text{Number of Product}}{\text{Number of incident photons}} = \frac{0.174\ mmol}{2.060\ mmol} = 8.44\ \% < 1$$

2.9. Bioactivity Experiments

Materials and Methods

Two Human cancer cell lines HCT 116 (colorectal carcinoma) and HepG2 (hepatoma) were kindly provided by Stem Cell Bank, Chinese Academy of Sciences (Shanghai, China). These two cell lines were cultured in Dulbecco's Modified Eagle Medium (DMEM, Biological Industres) supplemented with 10% Fetal Bovine Serum (FBS) (Biological Industres, China). Cell lines were maintained at 37 °C in a humidified 5% CO_2 incubator.

Cell viability assay

To determine cell viability, the cells were seeded in 96-well plates (100 μL per well) and incubated 24 h, then they were treated with a designated chemical compound for 24 h. The test concentrations for HCT-116 and HepG2 are 100 μM. Following the treatment, cell viability was evaluated using the Cell Counting Kit (CCK) (Seven Biotech, Beijing, China) according to the manufacturer's protocol. Briefly, the cells were exposed to 10 μL of the CCK-8 reagent for 4 h at 37 °C in a humidified 5% CO_2 incubator. The optical density of viable cells was measured at 450 nm using a microplate reader.

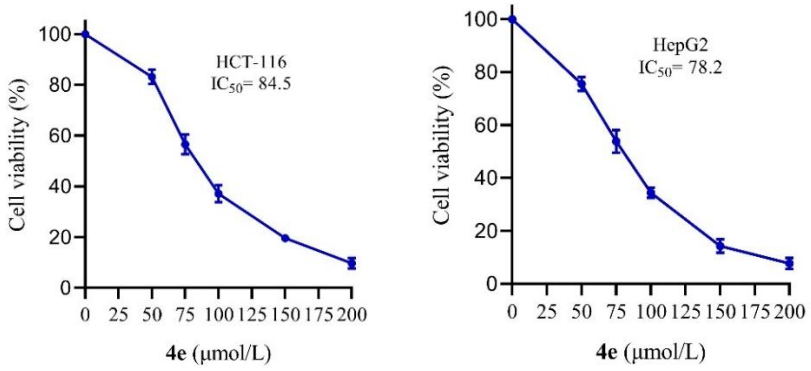
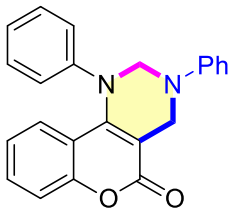
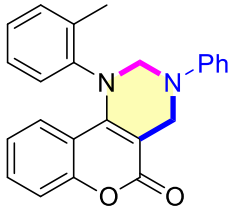


Figure S9 Antitumor activities.

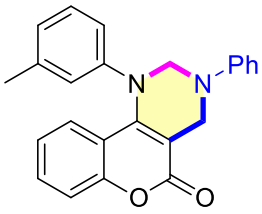
3. Characterization data of products



1,3-diphenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4a)**: Yellow solid; 61.6 mg, 87% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (t, *J* = 7.50 Hz, 1H), 7.25 (t, *J* = 7.50 Hz, 3H), 7.14-7.10 (m, 3H), 7.01 (d, *J* = 7.50 Hz, 2H), 6.95 (d, *J* = 8.50 Hz, 1H), 6.85 (t, *J* = 7.50 Hz, 1H), 6.76 (t, *J* = 9.25 Hz, 3H), 4.92 (s, 2H), 4.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 152.0, 149.8, 146.5 ,146.3, 129.7, 128.7, 128.3, 124.7, 124.6, 123.8, 122.2, 119.5, 116.3, 115.2, 114.8, 106.6, 70.7, 45.6; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{23}H_{19}N_2O_2$ 355.1441, found 355.1442.

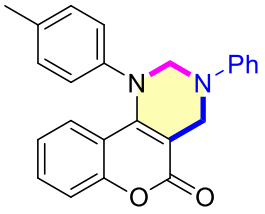


3-phenyl-1-(o-tolyl)-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4b)**: Yellow solid; 60.4 mg, 82% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.22 (m, 3H), 7.14 (t, *J* = 7.75 Hz, 3H), 6.99 (t, *J* = 7.50 Hz, 1H), 6.81-6.67 (m, 5H), 6.68 (d, *J* = 8.00 Hz, 1H), 4.81-4.72 (q, 2H), 4.47 (d, *J* = 17.00 Hz, 1H), 4.29 (d, *J* = 17.00 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 153.0, 151.3, 147.7, 145.6, 133.8, 131.9, 130.6, 129.3, 127.4, 127.3, 127.2, 124.8, 123.3, 120.8, 117.4, 116.7, 116.0, 104.2, 70.9, 46.4, 18.2; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1600.

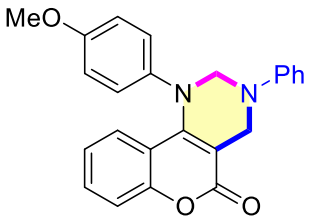


3-phenyl-1-(m-tolyl)-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4c)**: Yellow solid; 60.8 mg, 84% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.24 (m, 2H), 7.12 (t, *J* = 7.75 Hz, 3H), 6.95 (t, *J* = 9.25 Hz, 2H), 6.87-6.76 (m, 6H), 4.90 (s, 2H), 4.34 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 152.0, 149.9, 146.5, 146.2, 129.6,

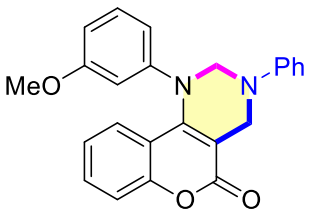
128.5, 128.2, 125.7, 124.6, 124.5, 122.2, 121.0, 119.5, 116.2, 115.3, 106.1, 70.7, 45.6, 20.4; HRMS: calcd for $C_{24}H_{21}N_2O_2$ $[M+H]^+$ 369.1598, found 369.1599.



3-phenyl-1-(p-tolyl)-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4d)**: Yellow solid; 64.1 mg, 87% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (t, *J* = 7.50 Hz, 1H), 7.23 (t, *J* = 8.00 Hz, 1H), 7.12 (t, *J* = 8.00 Hz, 2H), 7.04 (d, *J* = 8.00 Hz, 2H), 6.96 (d, *J* = 8.00 Hz, 1H), 6.90 (d, *J* = 8.50 Hz, 2H), 6.85 (t, *J* = 7.75 Hz, 1H), 6.77 (t, *J* = 6.50 Hz, 3H), 4.87 (s, 2H), 4.33 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 153.0, 151.0, 147.6, 144.7, 135.7, 130.6, 130.4, 129.3, 125.7, 124.8, 123.2, 120.5, 117.3, 116.2, 116.0, 106.9, 70.8, 46.6, 21.0; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1600.

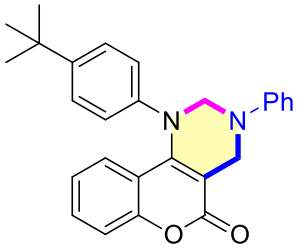


1-(4-methoxyphenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4e)**: Yellow solid; 67.6 mg, 88% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (t, *J* =7.50 Hz, 1H), 7.23 (d, *J* = 8.00 Hz, 1H), 7.13 (t, *J* = 8.00 Hz, 2H), 6.97 (t, *J* = 6.75 Hz, 3H), 6.86 (t, *J* = 7.50 Hz, 1H), 6.77 (d, *J* = 8.50 Hz, 5H), 4.84 (s, 2H), 4.33 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 157.7, 153.1, 151.0, 147.6, 140.3, 130.6, 129.3, 126.4, 125.6, 123.2, 120.6, 117.3, 116.3, 116.0, 115.0, 106.3, 72.1, 55.5, 46.6; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{21}N_2O_3$ 385.1547, found 385.1548.



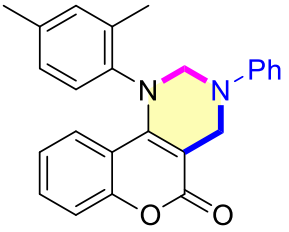
1-(3-methoxyphenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4f)**: Yellow solid; 65.3 mg, 85% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (t, *J* =

7.75 Hz, 1H), 7.25 (d, *J* = 8.50 Hz, 1H), 7.16-7.10 (m, 3H), 7.00 (d, *J* = 8.00 Hz, 1H), 6.88 (t, *J* = 7.75 Hz, 1H), 6.77 (d, *J* = 7.00 Hz, 2H), 6.67 (d, *J* = 8.50 Hz, 1H), 6.60 (d, *J* = 8.00 Hz, 1H),6.53 (s, 1H), 4.91 (s, 2H), 4.34 (s, 2H); 3.67 (s, 3H),^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 159.5, 151.9, 149.8, 146.4 , 129.7, 129.4, 128.3, 124.5, 122.3, 119.5, 116.2, 115.2, 114.9, 110.1, 109.8, 106.5, 70.6, 54.4, 45.5; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{21}N_2O_3$ 385.1547, found 385.1549.



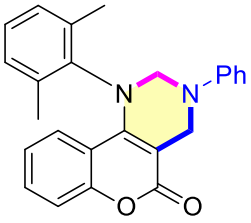
1-(4-(tert-butyl)phenyl)-3-phenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one

(4g): Yellow solid; 60.7 mg, 74% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (t, *J* = 7.50 Hz, 1H), 7.24 (d, *J* = 8.50 Hz, 3H), 7.12 (t, *J* = 7.75 Hz, 2H), 6.97 (d, *J* = 8.00 Hz, 1H), 6.93 (d, *J* = 8.50 Hz, 2H), 6.86 (t, *J* = 7.50 Hz, 1H), 6.76 (d, *J* = 8.50 Hz, 3H), 4.88 (s, 2H), 4.33 (s, 2H); 1.23 (s, 9H),^{13}C NMR (125 MHz, $CDCl_3$): δ 161.3, 153.0, 151.0, 148.9, 147.6 ,144.5, 130.6, 129.3, 126.6, 125.7, 124.3, 123.2, 120.4, 117.3, 116.2, 116.0, 107.0, 71,5, 46.7, 34.5, 31.3; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{27}H_{27}N_2O_2$ 411.2067, found 411.2068.

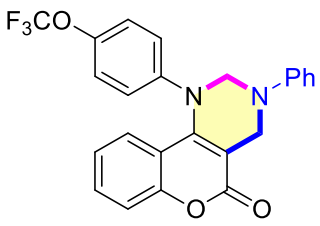


1-(2,4-dimethylphenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one

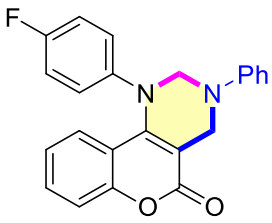
(4h): Yellow solid; 63.4 mg, 83% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (t, *J* = 7.50 Hz, 1H), 7.22 (d, *J* = 8.00 Hz, 1H), 7.15 (t, *J* = 8.00 Hz, 2H), 7.08 (s, 1H), 6.80 (t, *J* = 7.00 Hz, 5H), 6.71(d, *J* = 8.50 Hz, 1H), 6.66 (d, *J* = 8.00 Hz, 1H), 4.78-4.70 (m, 2H) ,4.46 (d, *J*= 16.50 Hz, 1H), 4.28 (d, *J* = 16.50 Hz, 1H), 2.27 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$):δ 160.3, 152.0, 150.4, 146.7, 141.8, 136.2, 132.5, 131.5, 129.5, 128.3, 127.0, 125.9, 123.8, 122.2, 119.7, 116.4, 115.7, 114.9, 102.3, 70.0, 45.4, 20.0, 17.0; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{25}H_{23}N_2O_2$ 383.1754, found 383.1756.



1-(2,6-dimethylphenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4i)**: Yellow solid; 60.3 mg, 79% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (t, *J* = 7.50 Hz, 1H), 7.14 (t, *J* = 7.00 Hz, 2H), 7.06 (d, *J* = 7.00 Hz, 2H), 6.90 (d, *J* = 8.00 Hz, 2H), 6.85 (t, *J* = 7.25 Hz, 1H), 6.73-6.69 (m, 2H), 6.56 (d, *J* = 8.00 Hz, 1H), 6.51 (d, *J* = 8.00 Hz, 1H), 4.78 (s, 2H), 4.42 (s, 2H), 2.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 151.9, 149.7, 146.7, 141.6, 135.1, 129.8, 128.7, 128.4, 127.3, 122.4, 120.1, 117.8, 116.7, 116.1, 114.4, 112.2, 95.8, 69.6, 45.1, 21.7, 17.4; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{25}H_{23}N_2O_2$ 383.1754, found 383.1757.

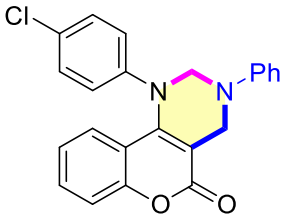


1-phenyl-1-(4-(trifluoromethoxy)phenyl)-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4j)**: Yellow solid; 71.0 mg, 81% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.00 Hz, 1H), 7.27 (d, *J* = 8.00 Hz, 1H), 7.13-7.07 (m, 4H), 7.00 (d, *J* = 8.50 Hz, 2H), 6.91 (t, *J* = 7.50 Hz, 2H), 6.79-6.73 (m, 3H), 4.91 (s, 2H), 4.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9, 152.0, 149.5, 146.3, 144.9, 129.9, 128.3, 124.8, 124.2, 122.5, 121.2, 119.8, 116.4, 115.3, 114.6, 107.7, 70.9, 45.5; ^{19}F NMR (471 MHz, $CDCl_3$): δ -58.04 ppm; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{18}F_3N_2O_3$ 439.1264, found 439.1265.

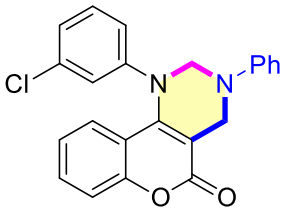


1-(4-fluorophenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4k)**: Yellow solid; 54.3 mg, 73% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (t, *J* = 7.50 Hz, 1H), 7.26 (d, *J* = 8.00 Hz, 1H), 7.13 (t, *J* = 7.75 Hz, 2H), 7.00-6.89 (m, 6H), 6.80-6.74 (m, 3H), 4.89 (s, 2H), 4.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1, 153.0, 150.8, 147.4, 143.5, 130.9, 130.8, 129.3, 126.5 (d, *J* = 8.25 Hz), 125.4, 123.4, 120.7, 117.4, 116.7,

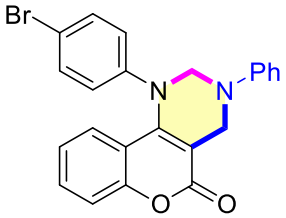
116.6, 116.3, 115.7, 107.8, 72.2, 46.6; ^{19}F NMR (471 MHz, $CDCl_3$): δ -115.72 ppm; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{23}H_{18}FN_2O_2$ 373.1347, found 373.1349.



1-(4-chlorophenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4l)**: Yellow solid; 59.0 mg, 76% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (t, *J* = 7.75 Hz, 1H), 7.26 (d, *J* = 8.00 Hz, 1H), 7.19 (d, *J* = 8.00 Hz, 2H), 7.13 (t, *J* = 7.75 Hz, 2H), 6.94-6.89 (m, 4H), 6.80-6.73 (m, 3H), 4.89 (s, 2H), 4.33 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 153.0, 150.5, 147.3, 146.0, 131.2, 130.9, 129.9, 129.4, 125.9, 125.3, 123.4, 120.8, 117.4, 116.3, 115.6, 108.5, 71.9, 46.5; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{23}H_{18}ClN_2O_2$ 389.1051, found 389.1053.

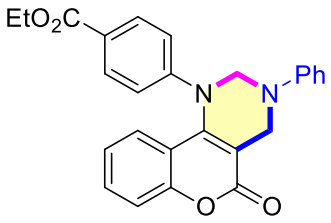


1-(3-chlorophenyl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4m)**: Yellow solid; 57.4 mg, 74% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (t, *J* = 7.00 Hz, 1H), 7.27 (d, *J* = 8.50 Hz, 1H), 7.15-7.09 (m, 4H), 7.02 (s, 1H), 6.96-6.91 (m, 2H), 6.85 (d, *J* = 8.00 Hz, 1H), 6.80-6.74 (m. 3H), 4.91 (s, 2H), 4.33 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 151.9, 149.3, 147.5, 146.3, 134.3, 129.9, 129.6, 128.3, 124.8, 124.2, 123.7, 122.5, 121.9, 119.8, 116.4, 115.3, 114.6, 107.9, 70.8, 45.5; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{23}H_{18}N_2O_2$ 389.1051, found 389.1053.

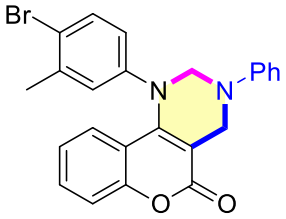


1-(4-bromophenyl)-3-phenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one **(4n)**: Yellow solid; 67.4 mg, 78% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.00 Hz, 2H), 7.27 (d, *J* = 7.50 Hz, 2H), 7.13 (t, *J* = 7.50 Hz, 3H), 6.95 (d, *J* = 8.00 Hz, 2H),

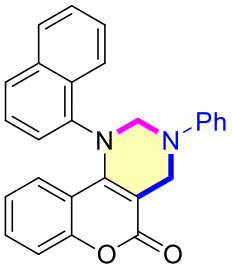
6.88 (d, J = 8.00 Hz, 2H), 6.74 (d, J = 8.00 Hz, 2H), 4.89 (s, 2H), 4.32 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 153.0, 150.5, 147.3, 146.5, 132.8, 131.0, 129.4, 126.2, 125.3, 123.5, 120.8, 117.4, 116.3, 108.6, 71.9, 46.5; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{23}H_{18}BrN_2O_2$ 433.0546, found 433.0547.



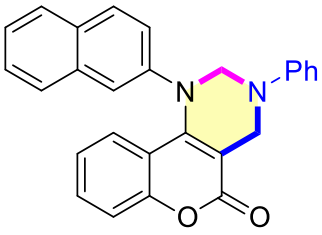
***Ethyl 4-(5-oxo-3-phenyl-2,3,4,5-tetrahydro-1H-chromeno[4,3-d]pyrimidin-1-yl)benzoate* (4o)**: Light yellow solid; 63.9 mg, 75% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.50 Hz, 2H),7.34 (t, J = 7.25 Hz, 1H), 7.28 (d, J = 8.50 Hz, 1 H), 7.10 (t, J = 7.75 Hz, 2H), 7.01 (d, J = 8.50 Hz, 2H), 6.90 (t, J = 8.25 Hz, 2H), 6.78-6.73 (m, 3H), 5.00 (s, 2H), 4.30-4.27(m, 4H), 1.31 (t, J =7.00 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.9, 159.9, 151.9, 150.1, 149.2, 146.1, 130.1, 130.0, 128.3, 126.0, 124.2, 122.6, 122.4, 119.8, 116.4, 115.2, 114.5, 108.4, 70.5, 60.1, 46.5; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{26}H_{23}N_2O_4$ 427.1652, found 427.1652.



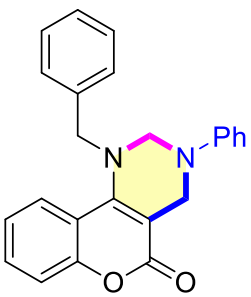
***1-(4-bromo-3-methylphenyl)-3-phenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one* (4p)**: Yellow solid; 63.3 mg, 71% yield; PE/EA = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, J = 8.50 Hz, 1H), 7.33 (t, J = 7.50 Hz, 1H), 7.26 (d, J = 8.00 Hz, 1H), 7.13 (t, J = 8.00 Hz, 3H), 6.96 (d, J = 8.00 Hz, 1H), 6.91 (t, J = 7.50 Hz, 1H), 4.85 (s, 1H), 4.80 (d, J = 7.50 Hz, 1H),6.76 (t, J = 6.75 Hz, 3H), 6.71 (d, J = 8.50 Hz, 1H), 4.87 (s, 2H), 4.32 (s, 2H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 151.9, 149.5, 146.3, 145.5, 138.5, 134.2, 132.4, 129.8, 128.3, 125.8, 124.4, 124.0, 122.6, 122.4, 120.6, 119.7, 116.3, 115.3, 114.7, 107.1, 70.8, 45.5, 21.7; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{24}H_{20}BrN_2O_2$ 447.0703, found 447.0702.



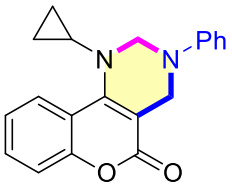
1-(naphthalen-1-yl)-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4q)**: Yellow solid; 66.3 mg, 82% yield; PE/EA = 3:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.00 Hz, 1H), 7.94 (d, *J* = 7.50 Hz, 1H), 7.72 (d, *J* = 8.00 Hz, 1H), 7.63-7.59 (m, 2H), 7.25(d, *J* = 7.50 Hz, 2H), 7.18 (t, *J* = 7.50 Hz, 1H), 7.07 (t, *J* = 7.75 Hz, 2H), 6.91 (d, *J* = 7.00 Hz, 1H), 6.75 (t, *J* = 7.25 Hz, 1H), 6.70-6.64 (m, 4H), 4.96 (d, *J* = 12.00 Hz, 1H), 4.85 (d, *J* = 12.00 Hz, 1H), 4.54 (d, *J* = 17.00 Hz, 1H), 4.31 (d, *J* = 17.00 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 153.0, 152.0, 147.6, 143.1, 135.1, 130.7, 129.3, 129.2, 129.1, 127.5, 127.4, 126.9, 125.8, 124.9, 124.4, 123.5, 122.6, 120.6, 117.3, 116.3, 115.9, 71.0, 46.4; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{27}H_{21}N_2O_2$ 405.1598, found 405.1599.



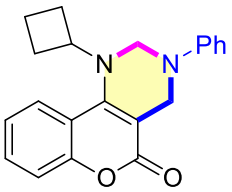
1-(naphthalen-2-yl)-3-phenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one **(4r)**: Yellow solid; 60.6 mg, 75% yield; PE/EA = 3:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.00 Hz, 2H), 7.62 (t, *J* = 7.50 Hz, 1H), 7.41-7.38 (m, 3H), 7.27 (s, 2H), 7.21 (d, *J* = 8.50 Hz, 1H), 7.08 (t, *J* = 8.00 Hz, 1H), 6.96 (d, *J* = 8.00 Hz, 2H), 6.79-6.72 (m, 4H), 5.02 (s, 2H), 4.38 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 152.0, 149.8, 146.4, 143.7, 132.8, 130.2, 129.7, 129.0, 126.8, 126.6, 125.8, 124.9, 124.5, 122.6, 122.3, 121.4, 119.6, 116.3, 115.2, 114.8, 106.9, 71.8, 45.6; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{27}H_{21}N_2O_2$ 405.1598, found 405.1597.



1-benzyl-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4s)**: Yellow solid; 57.4 mg, 78% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.25 Hz, 1H), 7.51 (t, *J* = 6.50 Hz, 1H), 7.44 (t, *J* = 7.75 Hz, 3H), 7.35 (d, *J* = 7.50 Hz, 1H), 7.31 (d, *J* = 8.00 Hz, 1H), 7.21-7.14 (m, 4H), 6.82-6.79 (m, 3H),4.52 (s, 2H), 4.30 (s, 2H), 4.17 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1, 154.0, 152.0, 136.1, 130.2, 128.4, 128.2, 127.0, 126.1, 123.1, 122.1, 119.3, 116.6, 115.6, 114.5, 108.1, 64.9, 55.2, 45.2; HRMS(ESI-TOF) m/z:$[M+H]^+$ calcd for $C_{24}H_{211}N_2O_2$ 369.1598, found 369.1599.



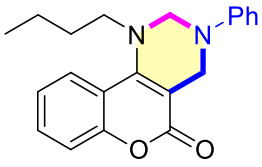
1-cyclopropyl-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4t)**: Yellow solid; 52.8 mg, 78% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.00 Hz, 1H), 7.42 (t, *J* = 7.00 Hz, 1H), 7.27 (t, *J* = 7.75 Hz, 3H), 7.19 (s, 1H), 6.99 (d, *J* = 7.50 Hz, 2H), 6.87 (t, *J* = 6.25 Hz, 1H), 4.59 (s, 2H), 4.07 (s, 2H), 3.28 (t, *J* = 5.25 Hz, 1H), 1.35-1.31 (m, 2H), 0.82-0.79 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 151.9, 151.2, 146.6, 129.8, 128.4, 124.8, 122.0, 119.5, 116.4, 114.9, 102.2, 67.5, 45.1, 35.6, 8.2; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{20}H_{19}N_2O_2$ 319.1441, found 319.1442.



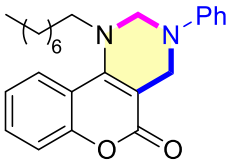
Ethyl4-(5-oxo-3-phenyl-3,4-dihydro-2H-chromeno[4,3-d]pyrimidin-1(5H)-yl)benzoate **(4u)**: Yellow solid; 61.2 mg, 92% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.00 Hz, 1H),7.44 (t, *J* = 7.75 Hz, 1H), 7.30 (t, *J* = 7.75 Hz, 3 H), 7.23 (t, *J* = 7.50 Hz, 1H), 7.0 (d, *J* = 8.00 Hz, 2H), 6.87 (t, *J* = 7.25 Hz, 1H), 4.51 (s, 2H), 4.37-4.30 (m, 1H), 4.12 (s, 2H), 2.34-2.26 (m, 2H), 2.19-2.14(m, 2H), 1.67-1.64(m, 1H), 1.53-1.47(m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 152.3, 152.1, 146.5, 130.0, 128.5, 123.1, 122.6, 119.0, 116.5, 115.6, 113.7, 105.8, 59.1, 56.2, 45.1, 13.3; HRMS(ESI-TOF)m/z:$[M+H]^+$ calcd for $C_{21}H_{21}N_2O_2$ 333.1598, found 333.1600.

Crystal Data for **4u** $C_{21}H_{20}N_2O_2$ (*M* =332.39 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 7.7577(2) Å, *b* = 9.9027(3) Å, *c* = 21.2760(5) Å, *β* = 93.666(2)°, *V* = 1631.12(8) Å^3, *Z* = 4, *T* = 100.0(2) K, μ(Cu Kα) = 0.700 mm^{-1}, *Dcalc* = 1.354 g/cm^3, 7708 reflections measured (8.328° ≤ 2Θ ≤ 133.196°), 2834 unique (R_{int} = 0.1025, R_{sigma} = 0.1035)

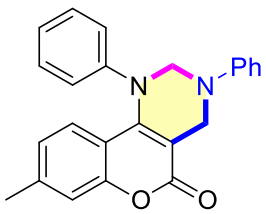
which were used in all calculations. The final R_1 was 0.0846 (I > 2σ(I)) and wR_2 was 0.2437 (all data).



1-butyl-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4v)**: Yellow solid; 59.5 mg, 89% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 7.50 Hz, 1H), 7.44 (t, J = 7.25 Hz, 1 H), 7.31-7.22 (m, 4H), 6.95 (d, J = 8.00 Hz, 2H), 6.86 (t, J = 7.00 Hz, 1H), 4.37 (s, 2H), 4.12 (s, 2H), 3.24 (t, J =7.75 Hz, 2H), 1.85 (t, J = 7.75 Hz, 2H), 1.40 (d, J = 7.50 Hz, 2H), 0.97 (t, J = 7.50 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 154.3, 152.0, 147.2, 130.0, 128.5, 122.8, 122.5, 119.2, 116.5, 115.8, 114.5, 107.1, 64.5, 51.9, 45.2, 30.3, 19.3, 13.0; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{21}H_{23}N_2O_2$ 335.1754, found 335.1755.

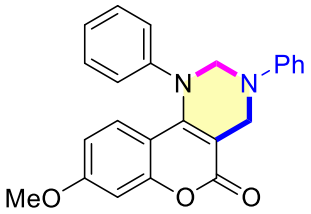


1-octyl-3-phenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one**(4w)**: Light yellow solid; 71.0 mg, 91% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 8.00 Hz, 1H), 7.44 (t, J = 7.50 Hz, 1H), 7.30-7.219 (m, 5H), 6.95 (d, J = 8.00 Hz, 2H), 6.86 (t, J = 7.25 Hz, 1H), 4.37 (s, 2H), 4.12 (s, 2H), 3.23 (t, J = 8.00 Hz, 2H), 1.89-1.83 (m, 2H), 1.37-1.31 (m, 4H), 1.28-1.18 (m, 6H), 0.85-0.79 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 154.3, 152.0, 147.2, 130.0, 128.5, 122.8, 122.5, 119.2, 116.5, 115.8, 114.5, 107.0, 64.6, 52.1, 45.2, 30.8, 28.7, 28.4, 28.2, 26.0, 21.6, 13.0; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{25}H_{31}N_2O_2$ 391.2380, found 391.2381.

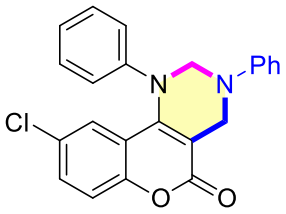


8-methyl-1,3-diphenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one**(4x)**: Yellow solid; 58.9 mg, 80% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (t, J = 7.75 Hz, 2H), 7.13-7.09 (m, 3H), 7.04 (s, 1H), 7.00 (d, J = 7.50 Hz, 2H), 6.80-6.74 (m, 4H), 6.66 (d, J = 8.00 Hz, 1H), 4.91 (s, 2H), 4.33 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4, 153.1, 151.0, 147.6, 147.3, 141, 8, 129.7, 129.3, 125.7, 125.3, 124.8, 124.5, 120.5, 117.4,

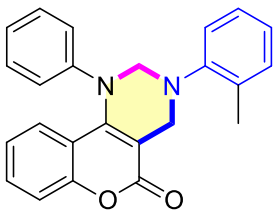
116.3, 106.4, 71.7, 46.6, 21.4; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1600.



8-methoxy-1,3-diphenyl-1,2,3,4-tetrahydro-5H-chromeno[4,3-d]pyrimidin-5-one **(4y)**: Yellow solid; 63.8 mg, 83% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (t, *J* = 7.50 Hz, 2H), 7.14-7.09 (m, 3H), 7.00 (d, *J* = 8.00 Hz, 2H), 6.82-6.72 (m, 5H), 6.42 (d, *J* = 7.20 Hz, 1H), 4.91 (s, 2H), 4.32 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 153.7, 150.1, 146.6, 146.3, 128.7, 128.2, 125.6, 124.7, 123.9, 119.5, 115.3, 110.5, 108.0, 103.3, 99.8, 70.7, 54.6, 45.5; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{24}H_{21}N_2O_3$ 385.1547, found 385.1548.

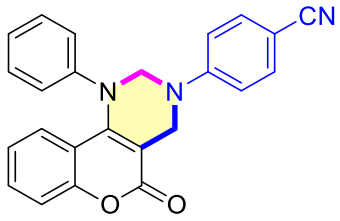


9-chloro-1,3-diphenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one **(4z)**: Yellow solid; 54.3 mg, 70% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.24 (m, 3H), 7.18 (t, *J* = 7.50 Hz, 2H), 7.18 (t, *J* = 7.75 Hz, 2H), 7.01 (d, *J* = 8.00 Hz, 2H), 6.86 (s, 1H), 6.79 (d, *J* = 7.50 Hz, 1H), 6.75 (d, *J* = 8.00 Hz, 2H), 4.91 (s, 2H), 4.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.6, 150.4, 148.8, 146.3, 145.6, 129.7, 128.9, 128.3, 125.3, 124.2, 123.8, 119.7, 117.7, 115.3, 107.1, 70.8, 45.6; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{23}H_{18}ClN_2O_2$ 389.1051, found 389.1053.

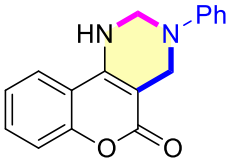


1-phenyl-3-(o-tolyl)-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one **(4aa)**: Yellow solid; 59.6 mg, 81% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (t, *J* = 7.5 Hz, 1H), 7.25-7.19 (m, 3H), 7.10 (t, *J* = 7.50 Hz, 1H),7.05 (d, *J* = 7.50 Hz, 2H), 7.01 (d, *J* = 8.00

Hz, 3H),6.92 (t, *J* = 7.75 Hz, 2H), 6.84 (t, *J* = 7.50 Hz, 1H), 4.59 (s, 2H), 4.18 (s, 2H), 1.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2, 152.0, 149.3, 146.6, 146.1, 132.0, 130.3, 129.5, 128.5, 125.6, 124.7, 124.2, 123.3, 122.1, 119.1, 116.3, 114.8, 106.7, 72.2, 47.9, 16.7; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1599.



4-(5-oxo-1-phenyl-1H-chromeno[4,3-d]pyrimidin-3(2H,4H,5H)-yl)benzonitrile **(4ab)**: Yellow solid; 47.8 mg, 63% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.50 Hz, 3H), 7.28 (t, *J* = 7.50 Hz, 3H), 7.16 (d, *J* = 7.25 Hz, 1H), 7.02 (d, *J* = 7.25 Hz, 2H), 6.98 (d, *J* = 8.00 Hz, 1H), 6.90 (t, *J* = 6.75 Hz, 1H), 6.63 (d, *J* = 9.00 Hz, 3H), 5.00 (s, 2H), 4.42 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.8, 151.9, 150.0, 149.2, 145.8, 132.6, 130.1, 129.1, 125.2, 124.4, 123.4, 122.5, 116.4, 114.7, 113.4, 106.8, 68.0, 44.8; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{24}H_{18}N_3O_2$ 380.1394, found 380.1395.



3-phenyl-3,4-dihydro-1H-chromeno[4,3-d]pyrimidin-5(2H)-one **(4ac)**: Yellow solid; 45.6 mg, 82% yield; PE/EA = 4:1; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.41 (m, 1H), 7.28 (d, *J* = 7.00 Hz, 1H),7.24 (d, *J* = 7.25 Hz, 1H), 7.18-7.15 (m, 1H), 6.98 (d, *J* = 8.00 Hz, 2H), 6.85 (t, *J* = 7.25 Hz, 2H), 5.53 (s, 1H), 4.85 (s, 2H), 4.37 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1, 149.4, 147.4, 130.4, 128.4, 127.8, 122.5, 120.3, 118.8, 116.9, 116.7, 112.6, 92.7, 59.7, 44.9; HRMS(ESI-TOF)m/z:[M+H]$^+$ calcd for $C_{17}H_{15}N_2O_2$ 279.1128, found 279.1130.

4. References

[1] Y. Y. Weng, H. Zhou, C. Sun, Y. Y. Xie, W. K. Su, J. Org. Chem., 2017, 82, 9047−9053.

[2] Y. Y. Weng, H. T. Chen, N. H. Li, L. Yang, L. Ackermann, Adv. Synth. Catal. 2021, 363, 1-6.

[3] Y. Duan, M. Zhang, R. Ruzi, Z. Wu, C. Zhu, Org. Chem. Front. 2017, 4 (4), 525-528.

5. X-ray Crystallographic Data for 4u

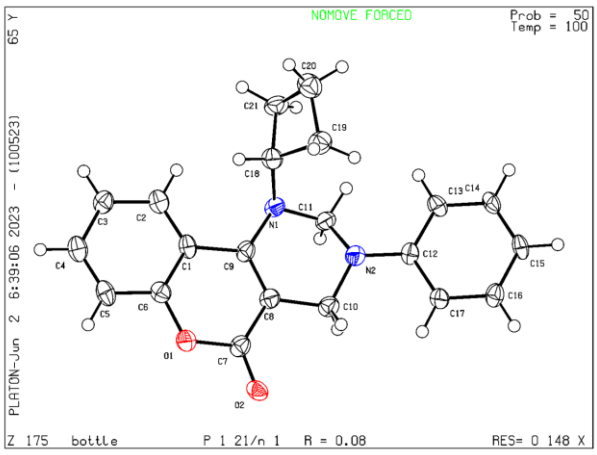


Figure S10. X-Ray crystal structure of **4u**

Table S1 Crystal data and structure refinement for 4u.

Identification code	**4u**
Empirical formula	$C_{21}H_{20}N_2O_2$
Formula weight	332.39
Temperature/K	*100.0(2)*
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.7577(2)
b/Å	9.9027(3)
c/Å	21.2760(5)
α/°	90
β/°	93.666(2)
γ/°	90
Volume/Å^3	1631.12(8)
Z	4
ρ_{calc}g/cm^3	1.354
μ/mm^{-1}	0.700
F(000)	704.0
Crystal size/mm^3	0.14 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.328 to 133.196
Index ranges	$-9 \le h \le 6$, $-11 \le k \le 11$, $-25 \le l \le 25$
Reflections collected	7708
Independent reflections	2834 [R_{int} = 0.1025, R_{sigma} = 0.1035]
Data/restraints/parameters	2834/0/226
Goodness-of-fit on F^2	2.225
Final R indexes [I>=2σ (I)]	R_1 = 0.0846, wR_2 = 0.1799
Final R indexes [all data]	R_1 = 0.1078, wR_2 = 0.2437
Largest diff. peak/hole / e Å^{-3}	0.48/-0.50

CCDC-2267263 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S2 Bond Lengths for 4u

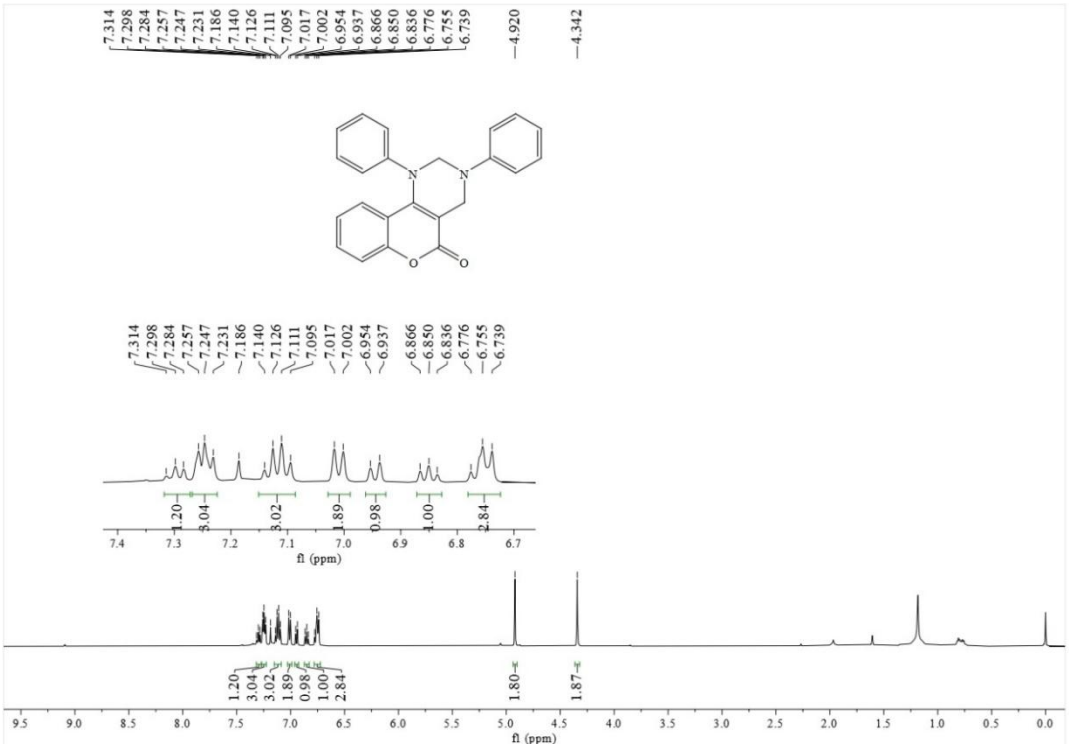
Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C6	1.394(6)	C11	H11A	0.99
O1	C7	1.392(6)	C11	H11B	0.99
O2	C7	1.207(6)	C12	C13	1.408(6)
N1	C9	1.388(6)	C12	C17	1.404(8)
N1	C11	1.451(6)	C13	H13	0.95
N1	C18	1.481(6)	C13	C14	1.385(6)
N2	C10	1.454(6)	C14	H14	0.95
N2	C11	1.445(6)	C14	C15	1.383(8)
N2	C12	1.390(6)	C15	H15	0.95
C1	C2	1.380(7)	C15	C16	1.394(6)
C1	C6	1.385(6)	C16	H16	0.95
C1	C9	1.476(6)	C16	C17	1.409(6)
C2	H2	0.95	C17	H17	0.95
C2	C3	1.399(7)	C18	H18	1
C3	H3	0.95	C18	C19	1.568(6)
C3	C4	1.403(7)	C18	C21	1.525(7)
C4	H4	0.95	C19	H19A	0.99
C4	C5	1.354(7)	C19	H19B	0.99
C5	H5	0.95	C19	C20	1.537(8)
C5	C6	1.395(6)	C20	H20A	0.99
C7	C8	1.447(6)	C20	H20B	0.99
C8	C9	1.349(7)	C20	C21	1.531(7)
C8	C10	1.506(6)	C21	H21A	0.99
C10	H10A	0.99	C21	H21B	0.99
C10	H10B	0.99			

Table S3 Bond Angles for 4u

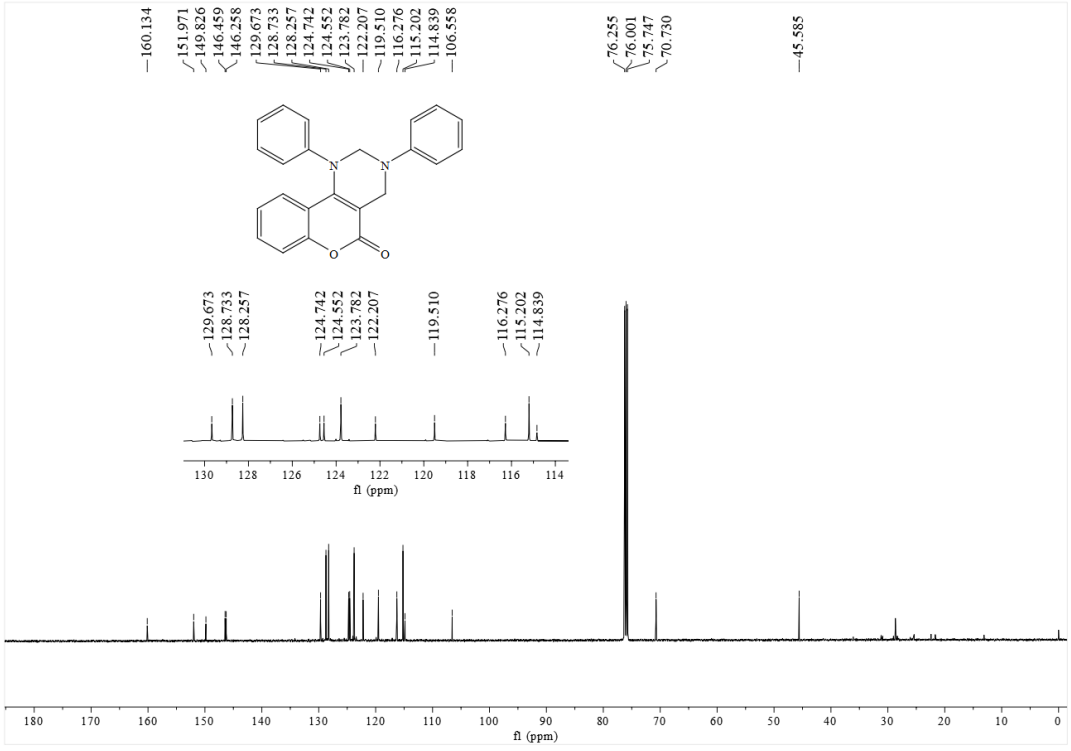
Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C7	O1	C6	121.5(4)	H11A	C11	H11B	108
C9	N1	C11	112.5(4)	N2	C12	C13	121.0(4)
C9	N1	C18	119.6(3)	N2	C12	C17	121.2(4)
C11	N1	C18	117.4(4)	C17	C12	C13	117.7(4)
C11	N2	C10	110.7(4)	C12	C13	H13	119.5
C12	N2	C10	119.1(4)	C14	C13	C12	120.9(5)
C12	N2	C11	122.3(4)	C14	C13	H13	119.5
C2	C1	C6	118.2(4)	C13	C14	H14	119.4
C2	C1	C9	125.3(4)	C15	C14	C13	121.2(4)
C6	C1	C9	116.3(4)	C15	C14	H14	119.4
C1	C2	H2	119.5	C14	C15	H15	120.4
C1	C2	C3	120.9(4)	C14	C15	C16	119.3(4)
C3	C2	H2	119.5	C16	C15	H15	120.4
C2	C3	H3	120.5	C15	C16	H16	120

C2	C3	C4	119.0(5)	C15	C16	C17	119.9(4)
C4	C3	H3	120.5	C17	C16	H16	120
C3	C4	H4	119.7	C12	C17	C16	120.9(4)
C5	C4	C3	120.7(4)	C12	C17	H17	119.6
C5	C4	H4	119.7	C16	C17	H17	119.6
C4	C5	H5	120.3	N1	C18	H18	109.2
C4	C5	C6	119.4(4)	N1	C18	C19	120.2(4)
C6	C5	H5	120.3	N1	C18	C21	117.5(4)
O1	C6	C5	115.8(4)	C19	C18	H18	109.2
C1	C6	O1	122.3(4)	C21	C18	H18	109.2
C1	C6	C5	121.8(5)	C21	C18	C19	89.9(4)
O1	C7	C8	117.2(4)	C18	C19	H19A	114.3
O2	C7	O1	115.5(4)	C18	C19	H19B	114.3
O2	C7	C8	127.3(4)	H19A	C19	H19B	111.4
C7	C8	C10	114.4(4)	C20	C19	C18	86.1(4)
C9	C8	C7	121.5(4)	C20	C19	H19A	114.3
C9	C8	C10	124.0(4)	C20	C19	H19B	114.3
N1	C9	C1	119.0(4)	C19	C20	H20A	113.5
C8	C9	N1	119.9(4)	C19	C20	H20B	113.5
C8	C9	C1	120.9(4)	H20A	C20	H20B	110.8
N2	C10	C8	110.2(4)	C21	C20	C19	90.9(4)
N2	C10	H10A	109.6	C21	C20	H20A	113.5
N2	C10	H10B	109.6	C21	C20	H20B	113.5
C8	C10	H10A	109.6	C18	C21	C20	87.9(4)
C8	C10	H10B	109.6	C18	C21	H21A	114
H10A	C10	H10B	108.1	C18	C21	H21B	114
N1	C11	H11A	109.3	C20	C21	H21A	114
N1	C11	H11B	109.3	C20	C21	H21B	114
N2	C11	N1	111.5(4)	H21A	C21	H21B	111.2
N2	C11	H11A	109.3	H11A	C11	H11B	108
N2	C11	H11B	109.3				

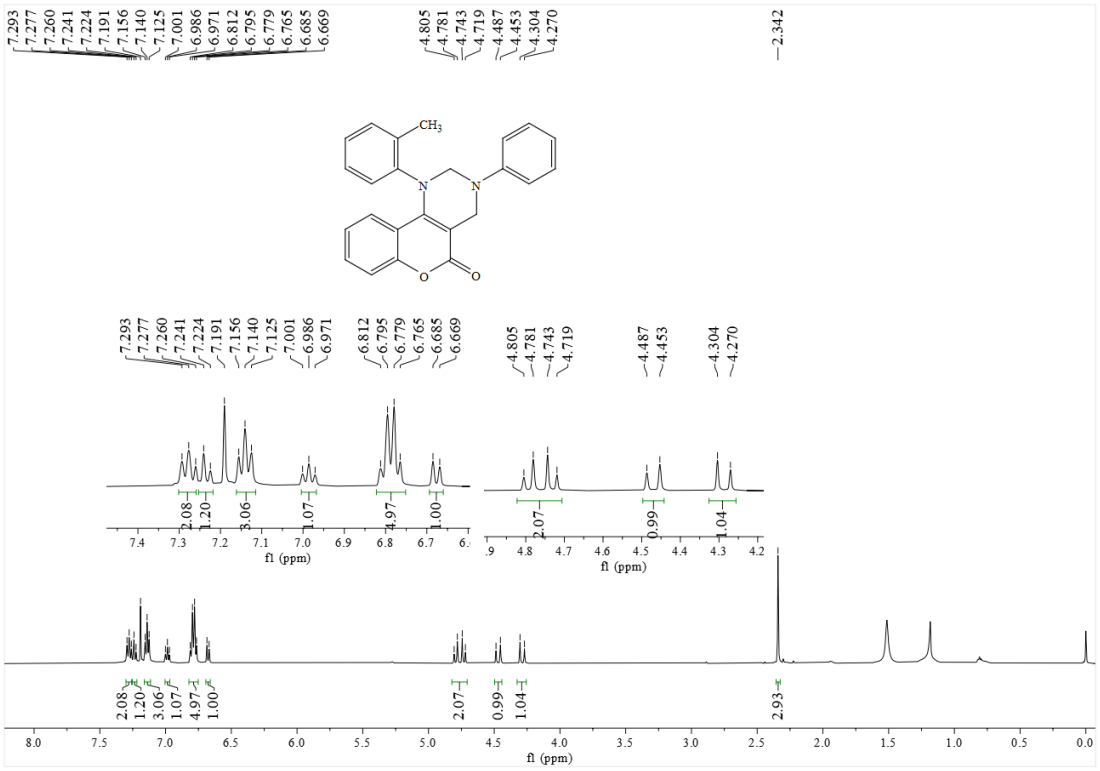
6. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of products



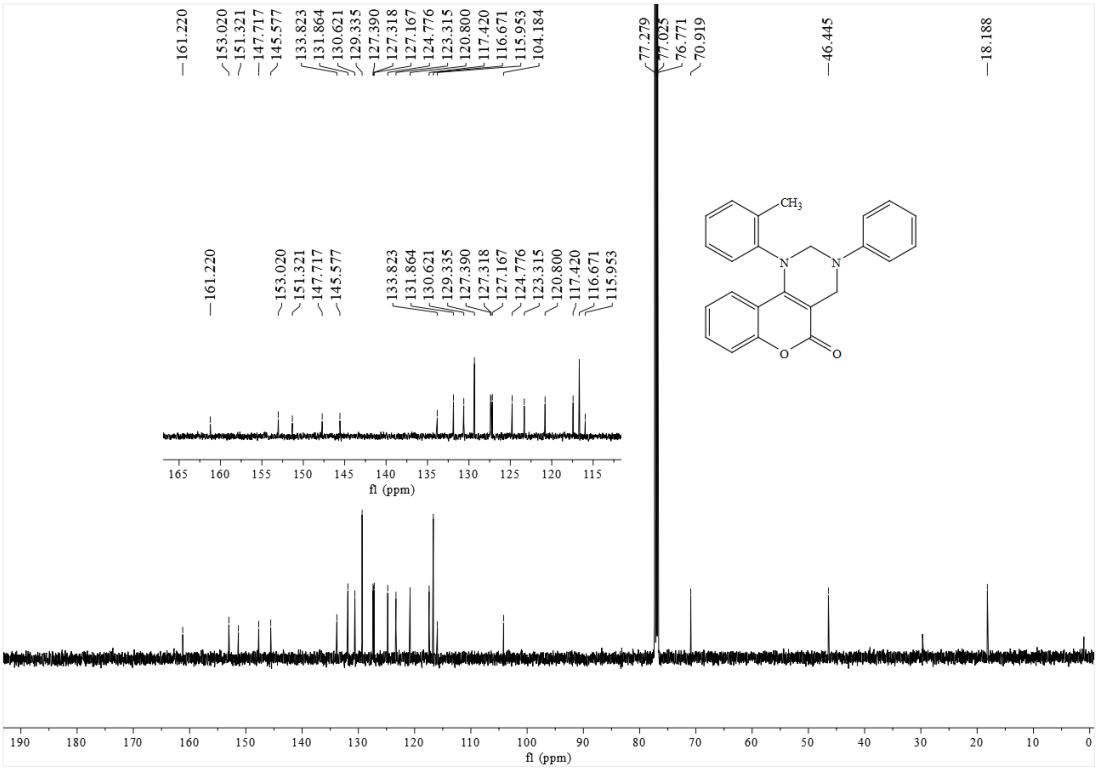
^{1}H NMR of **4a** in $CDCl_3$



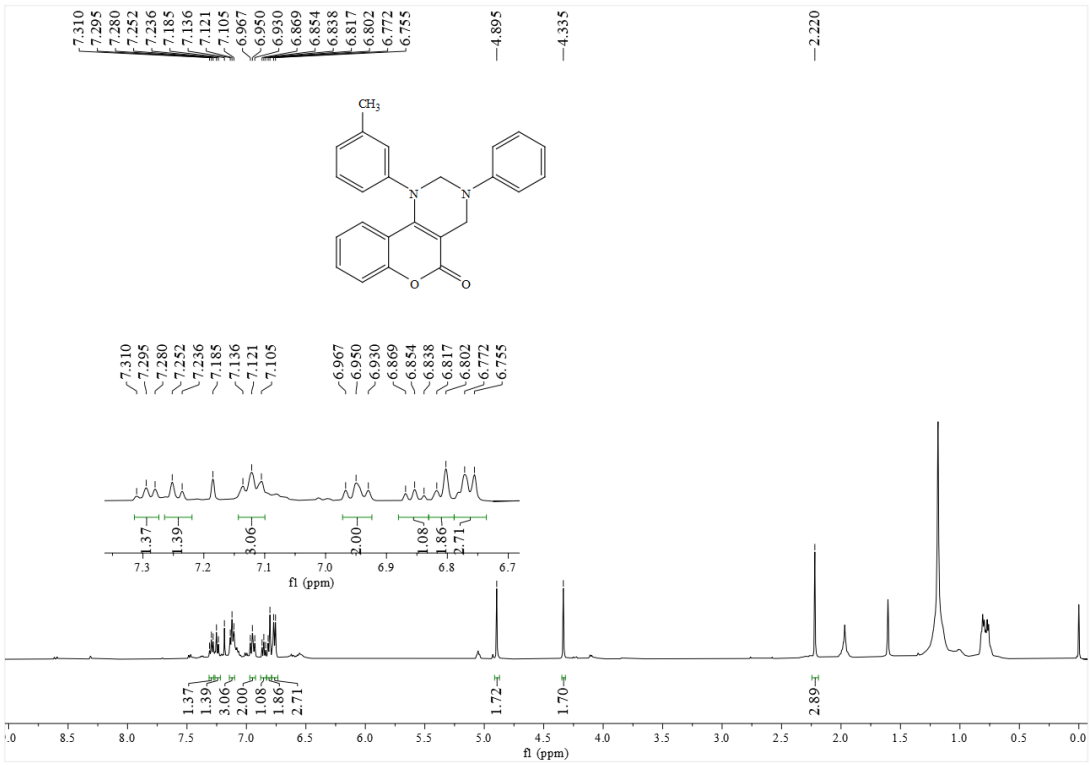
^{13}C NMR of **4a** in $CDCl_3$



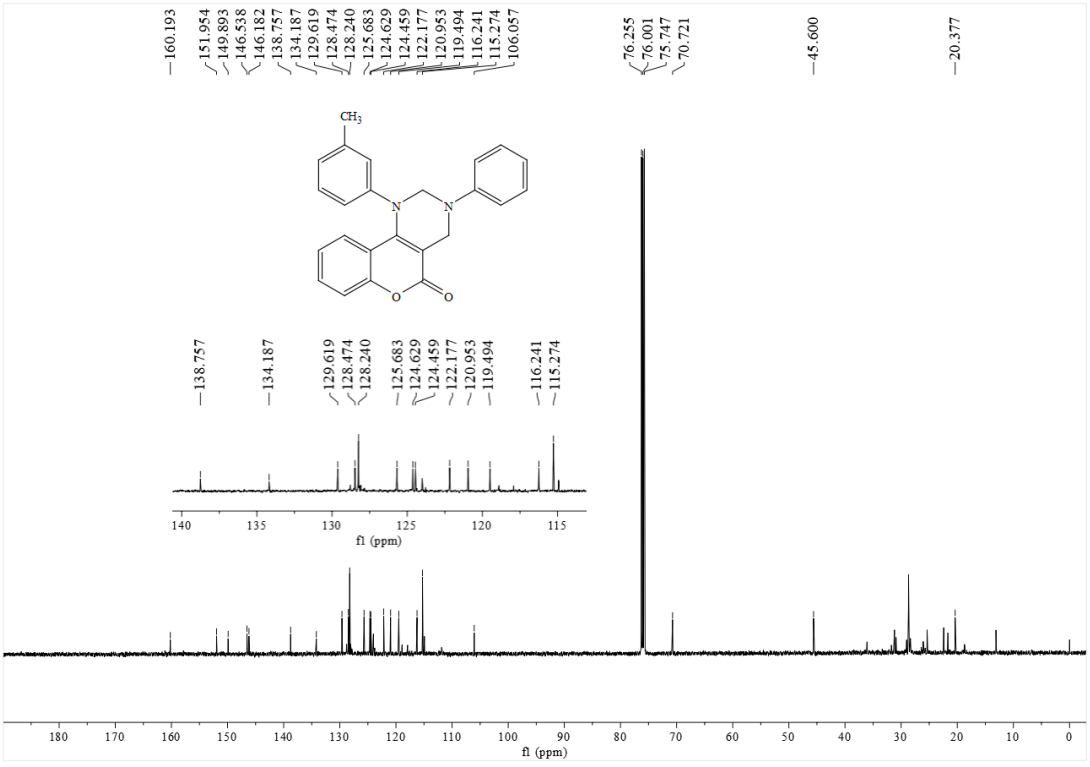
^{1}H NMR of **4b** in $CDCl_3$



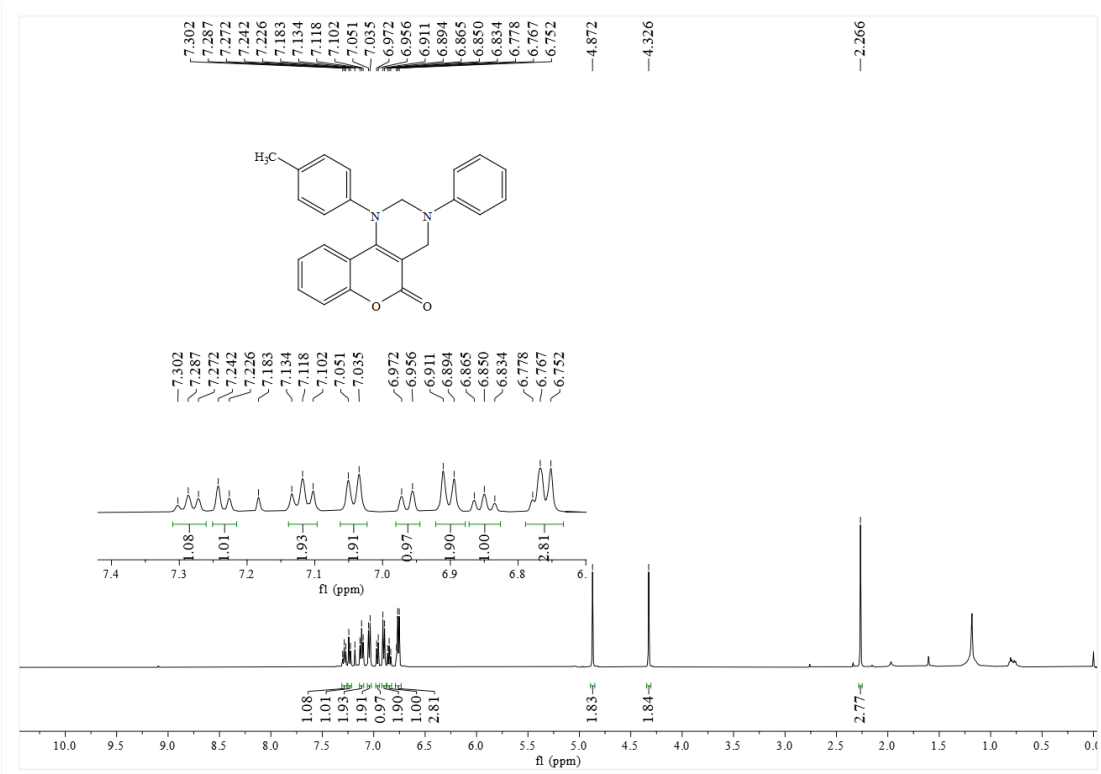
^{13}C NMR of **4b** in $CDCl_3$



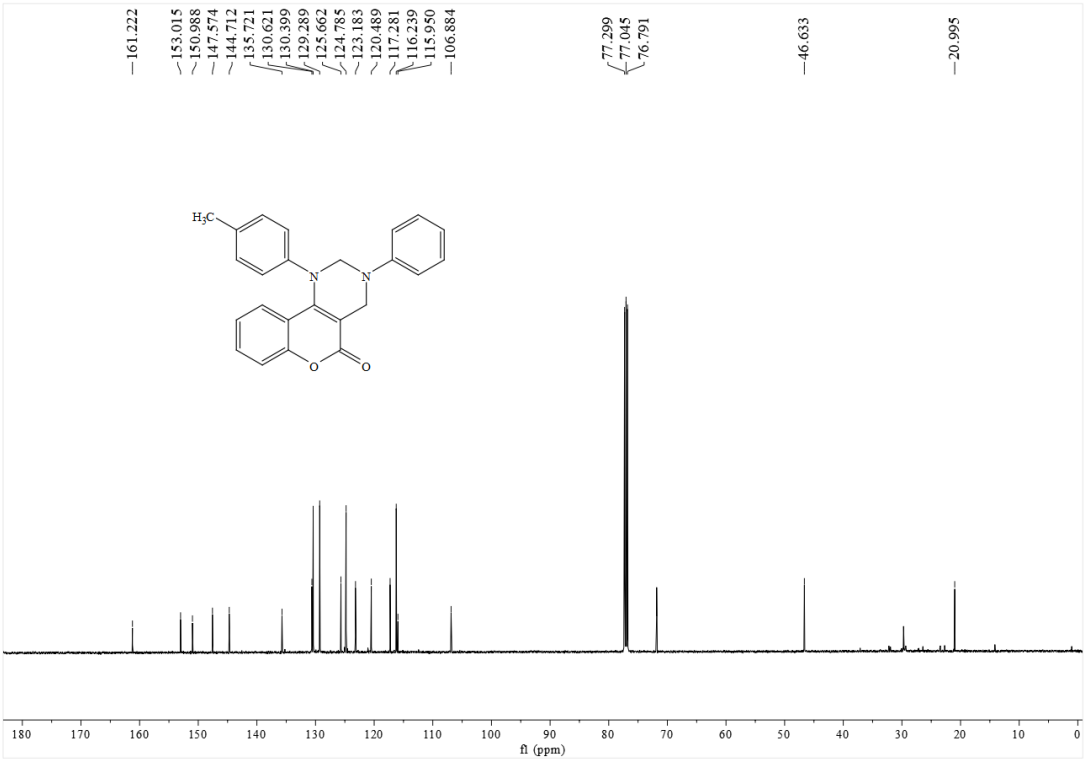
^{1}H NMR of **4c** in $CDCl_3$



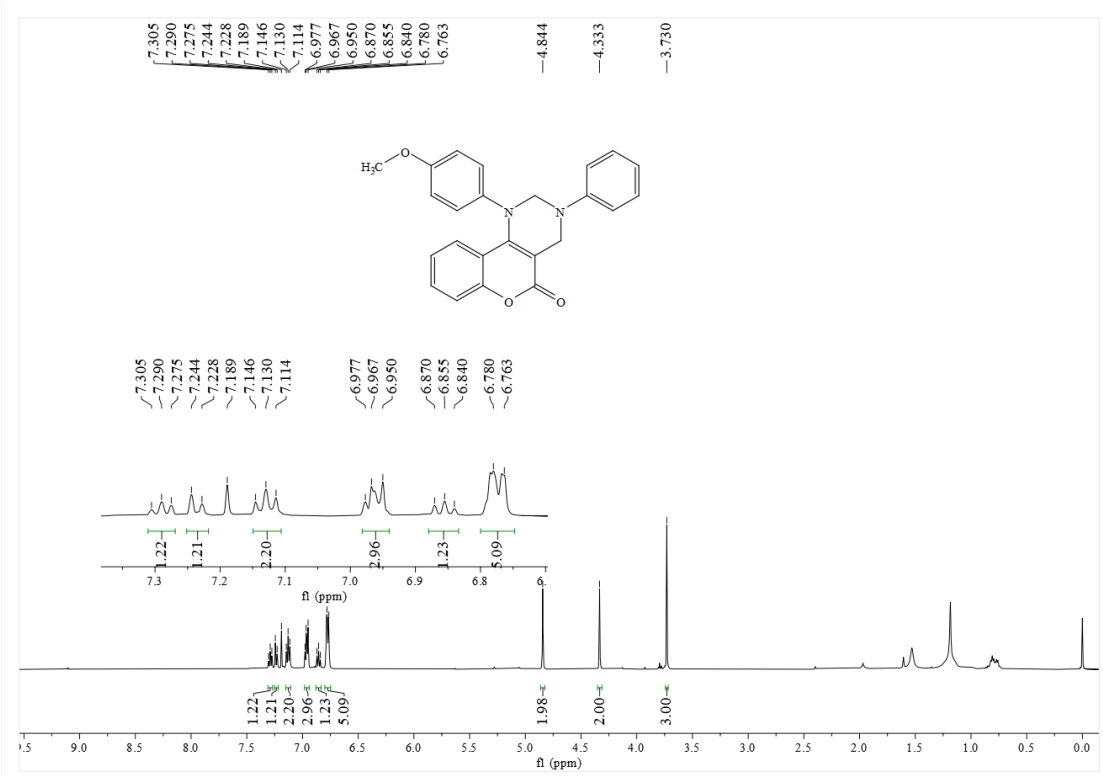
^{13}C NMR of **4c** in $CDCl_3$



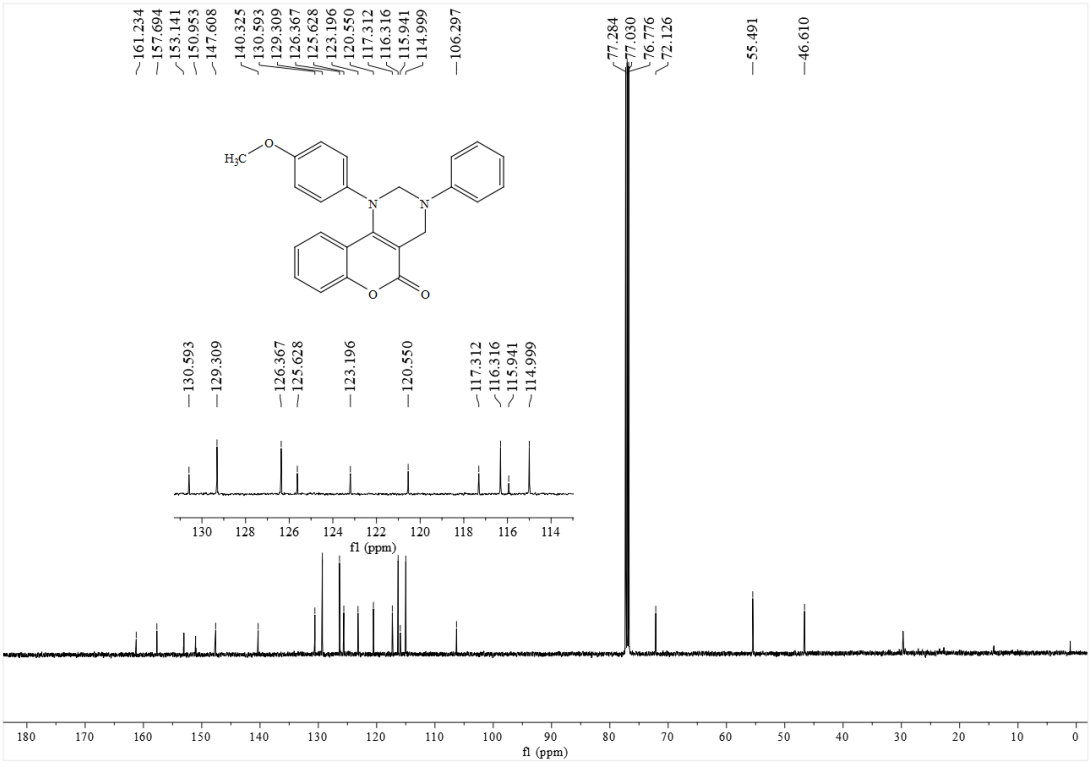
^{1}H NMR of **4d** in $CDCl_3$



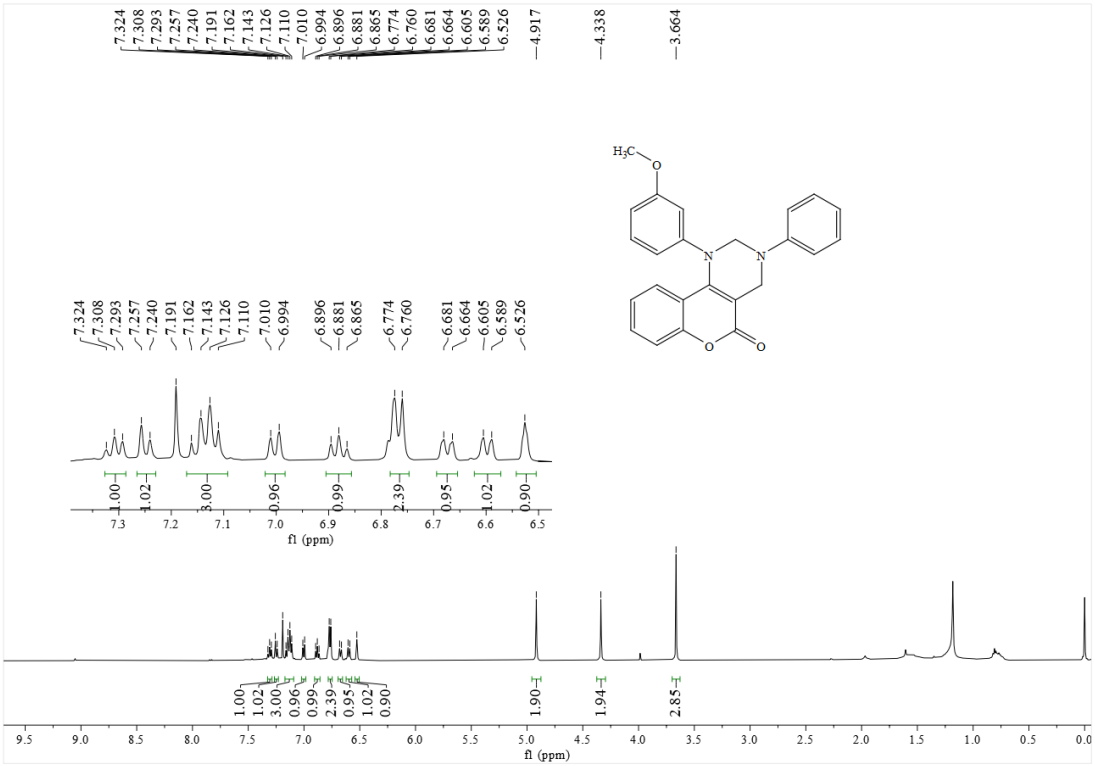
^{13}C NMR of **4d** in $CDCl_3$



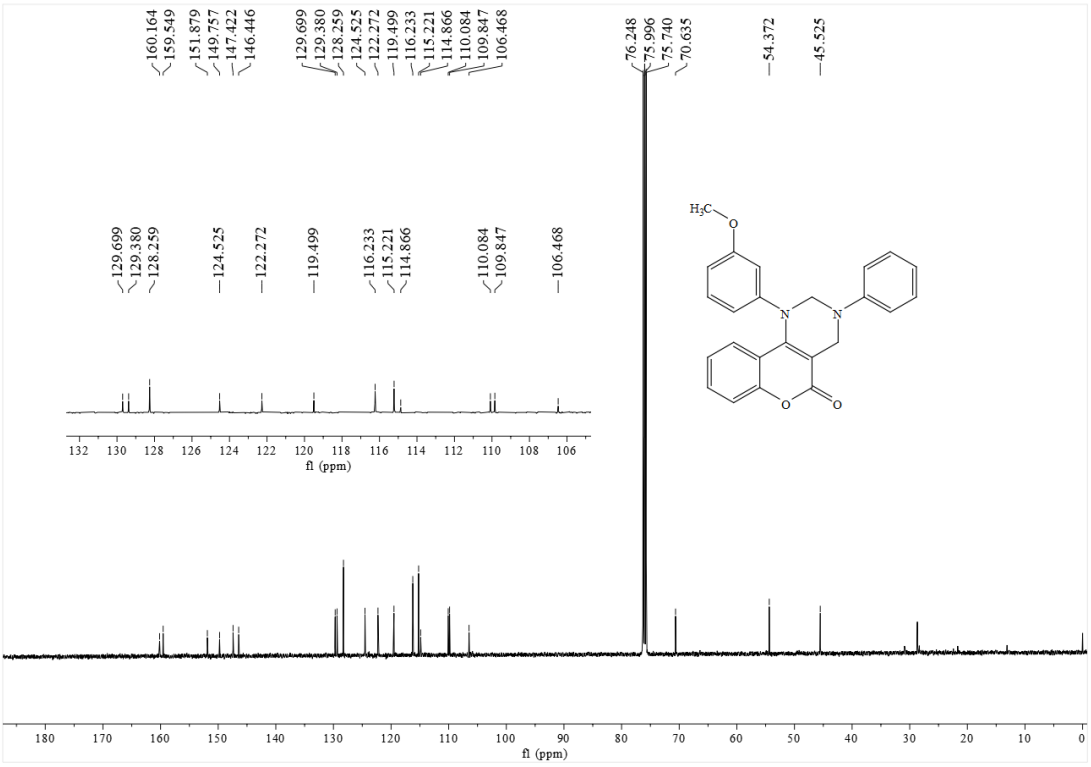
^{1}H NMR of **4e** in $CDCl_3$



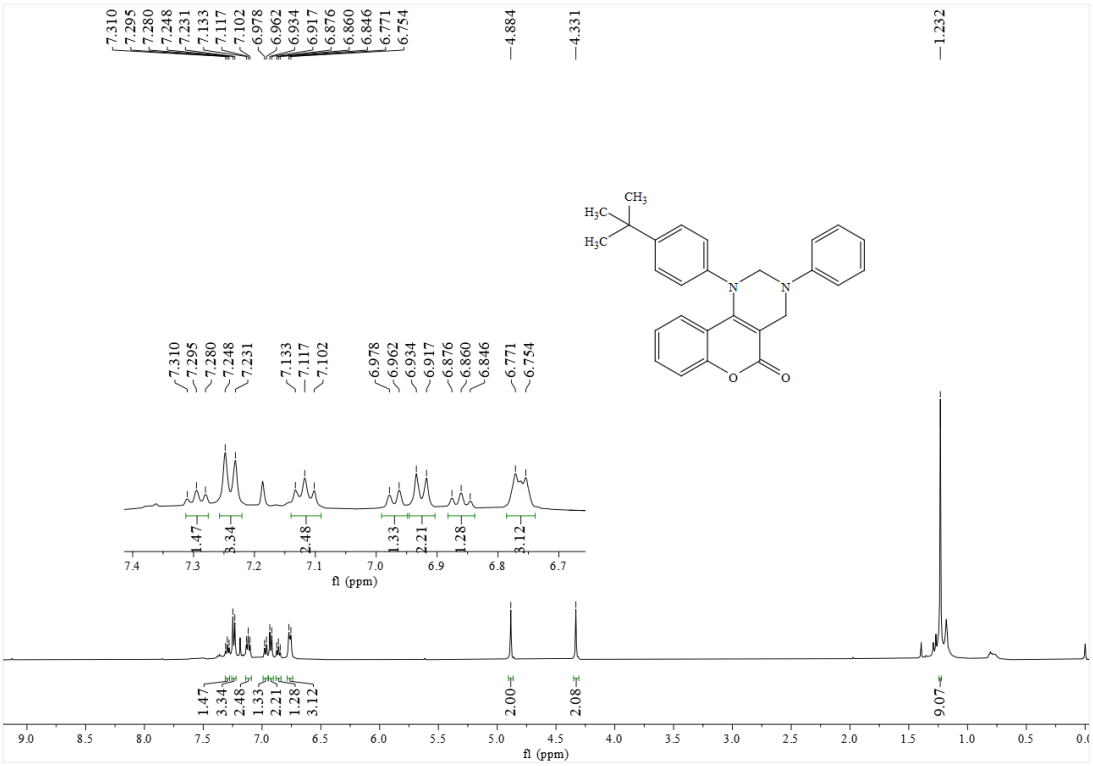
^{13}C NMR of **4e** in $CDCl_3$



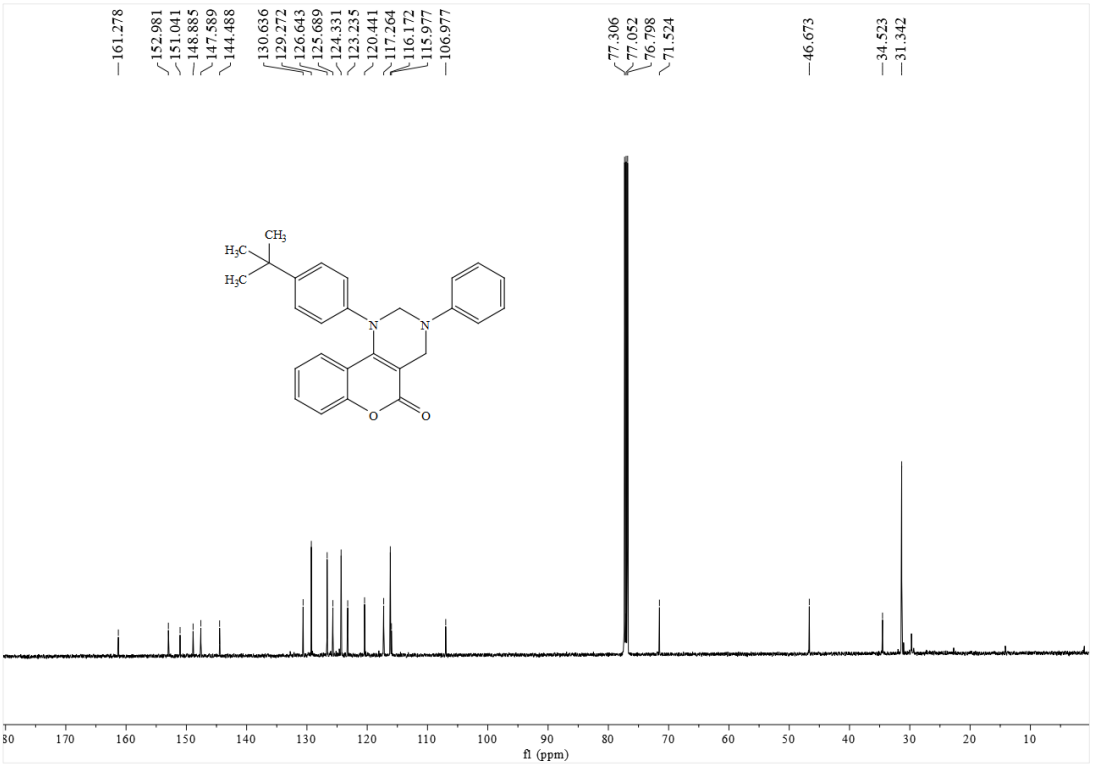
^{1}H NMR of **4f** in $CDCl_3$



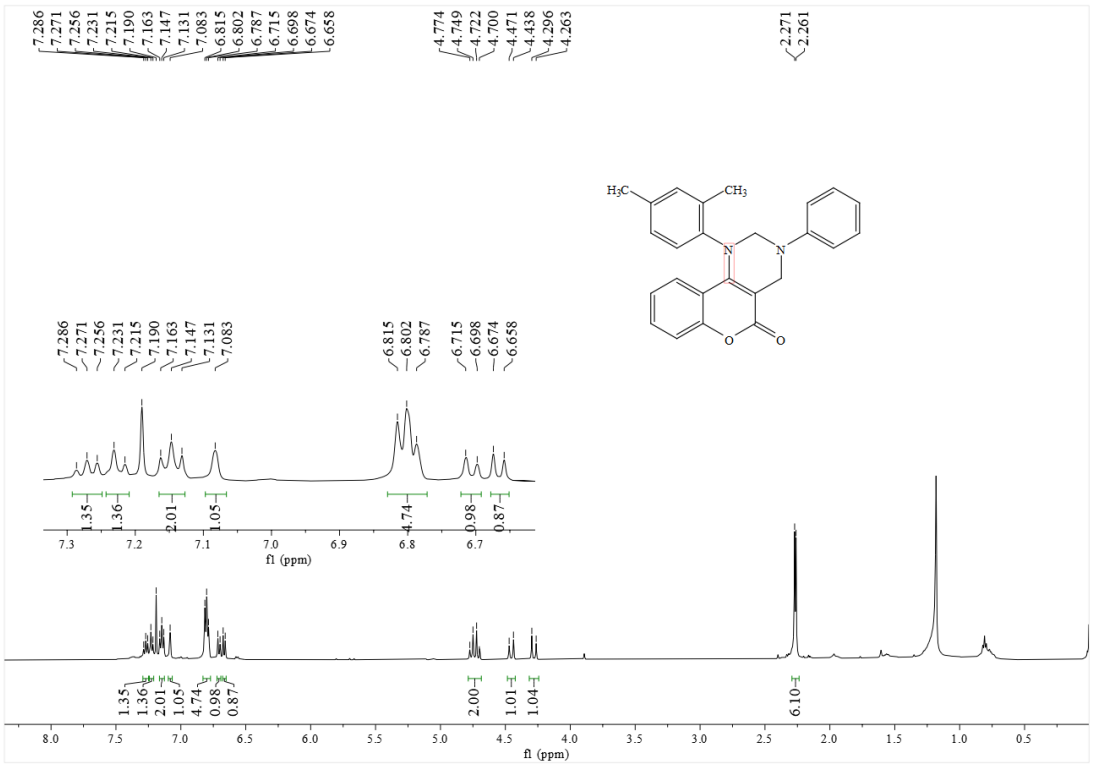
^{13}C NMR of **4f** in $CDCl_3$



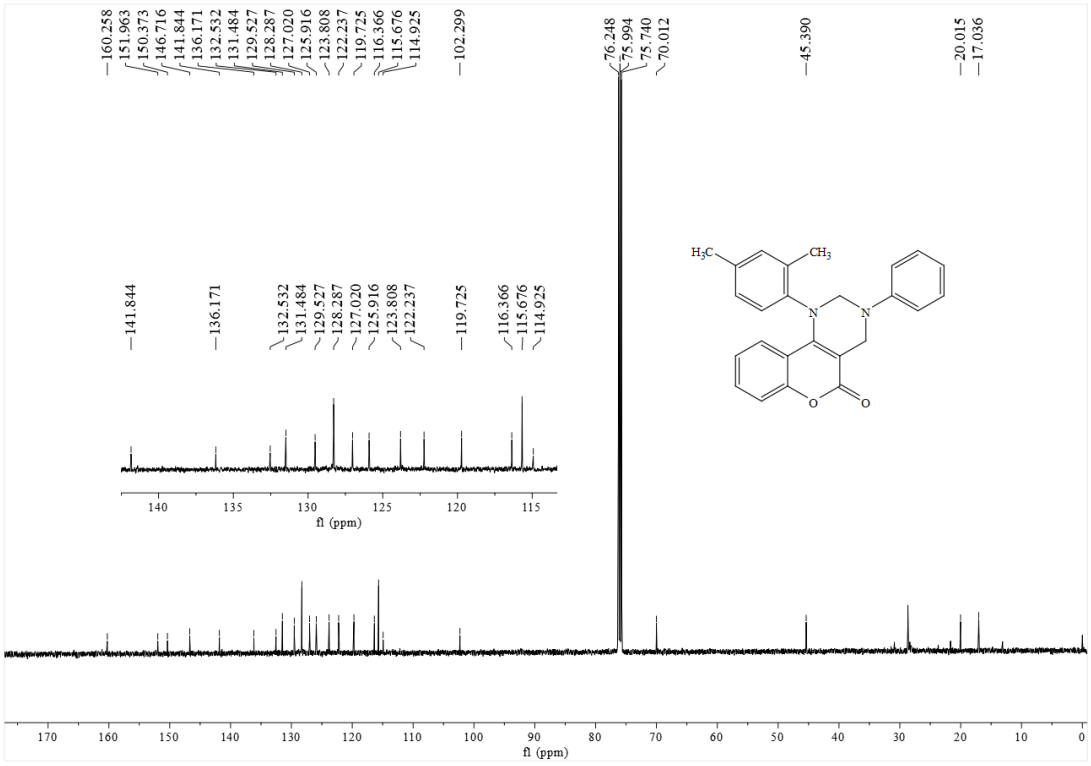
^{1}H NMR of **4g** in $CDCl_3$



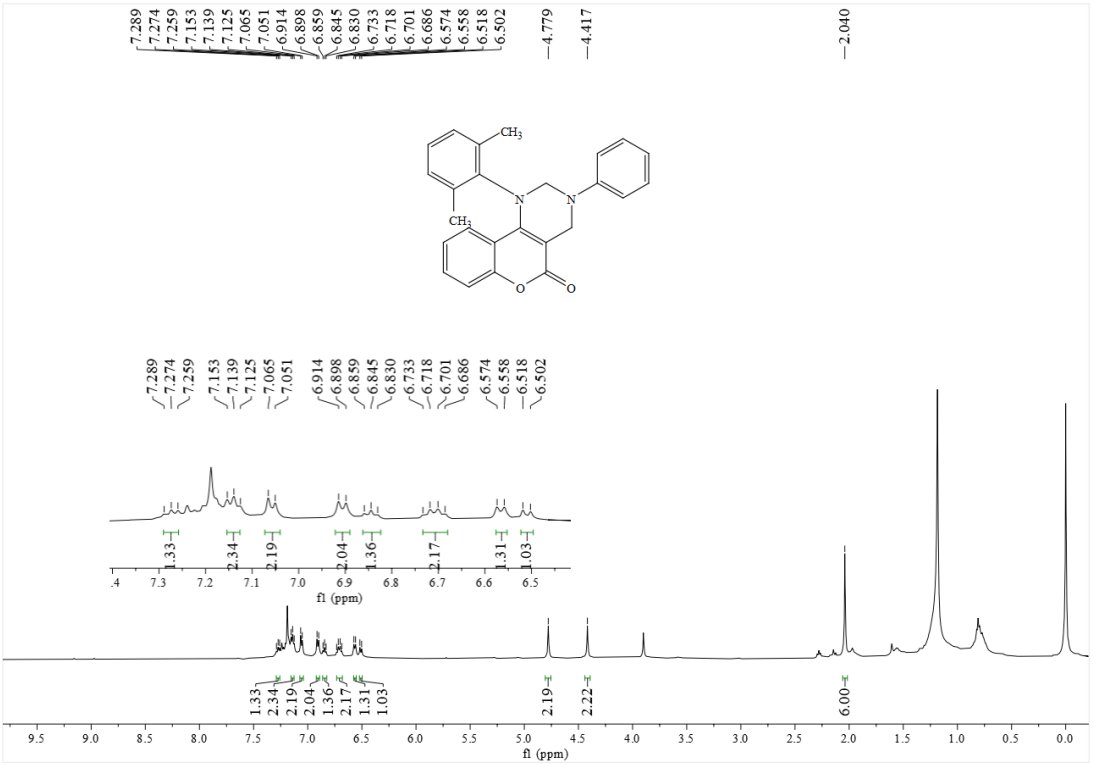
^{13}C NMR of **4g** in $CDCl_3$



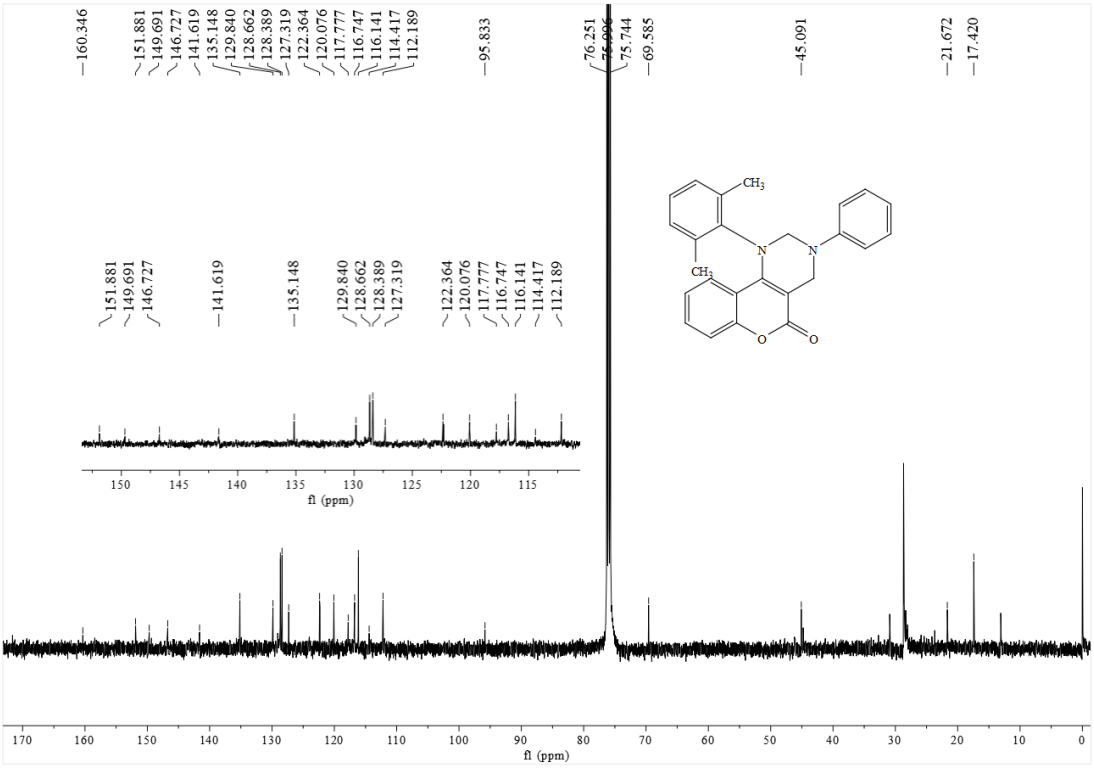
^{1}H NMR of **4h** in $CDCl_3$



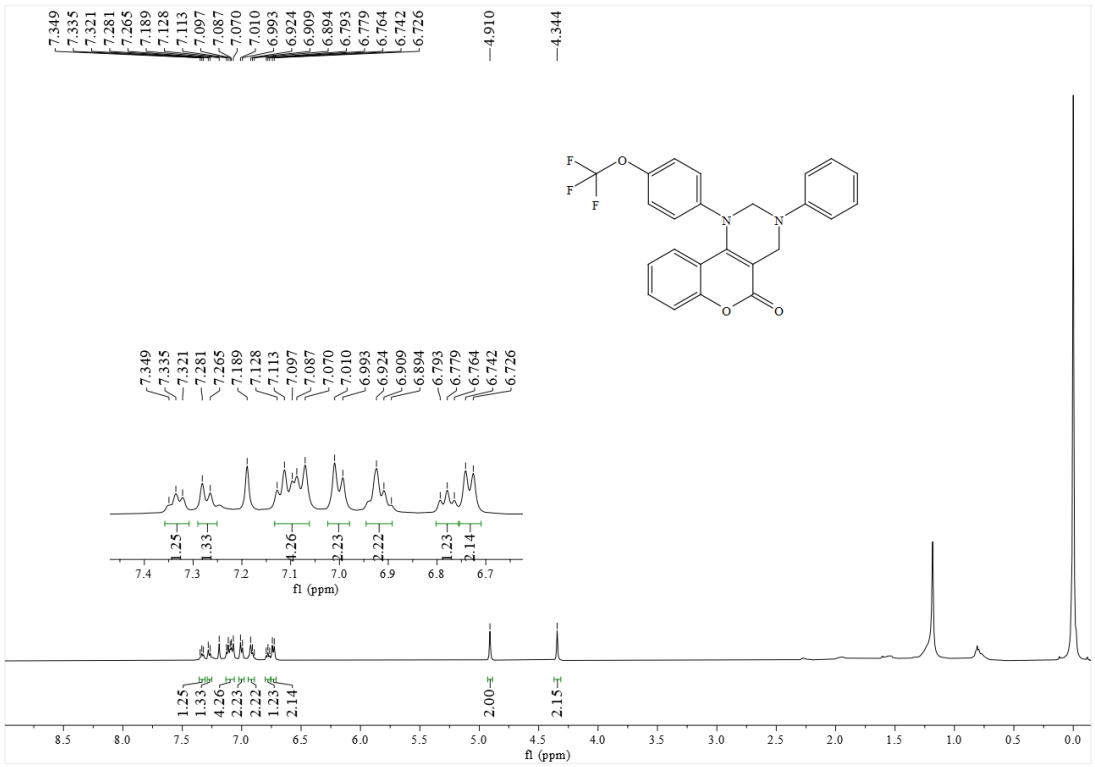
^{13}C NMR of **4h** in $CDCl_3$



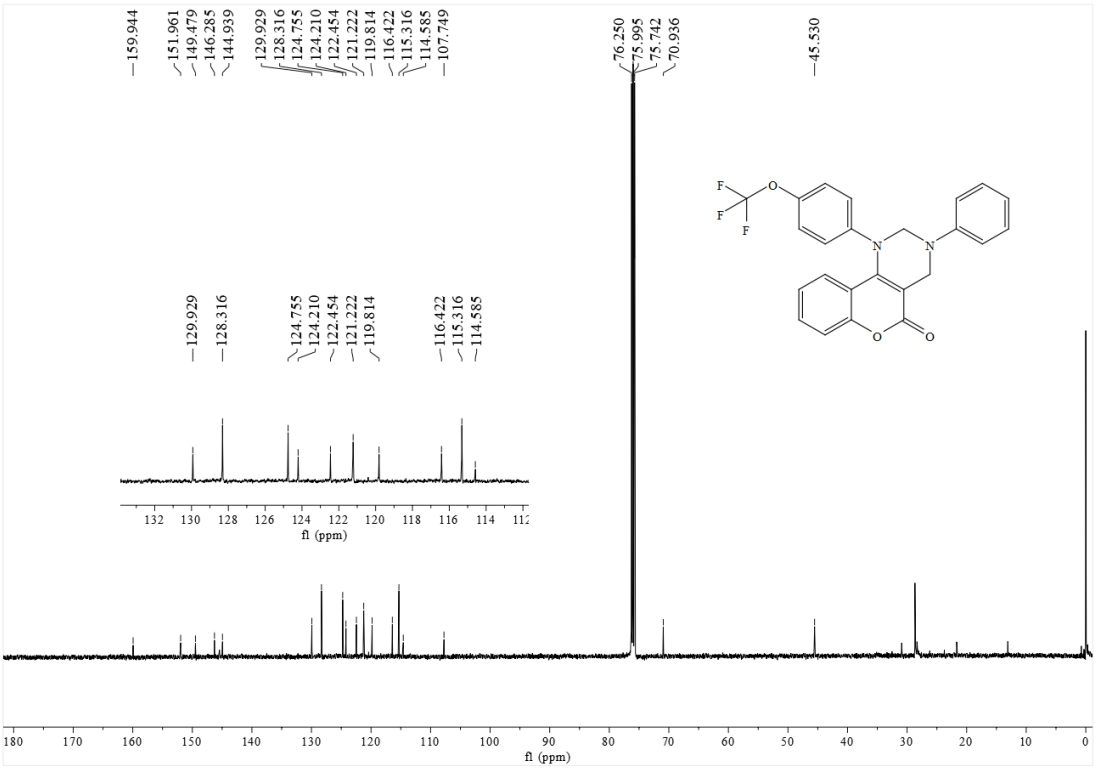
^{1}H NMR of **4i** in $CDCl_3$



^{13}C NMR of **4i** in $CDCl_3$

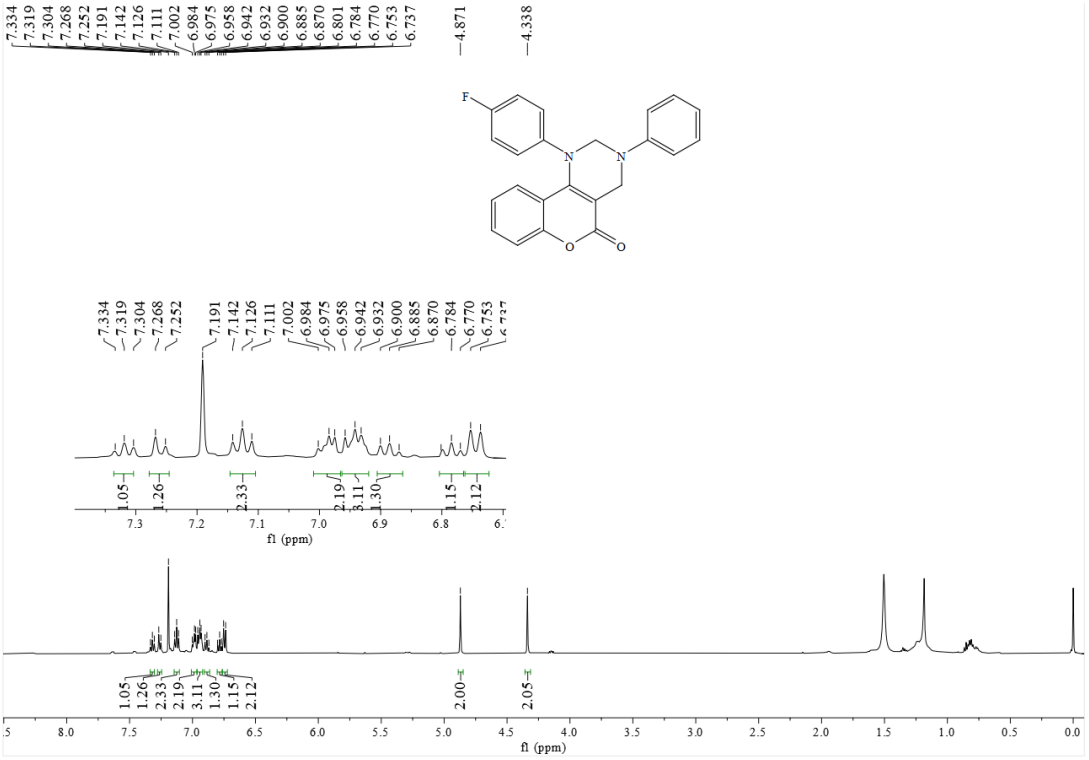


^{1}H NMR of **4j** in $CDCl_3$

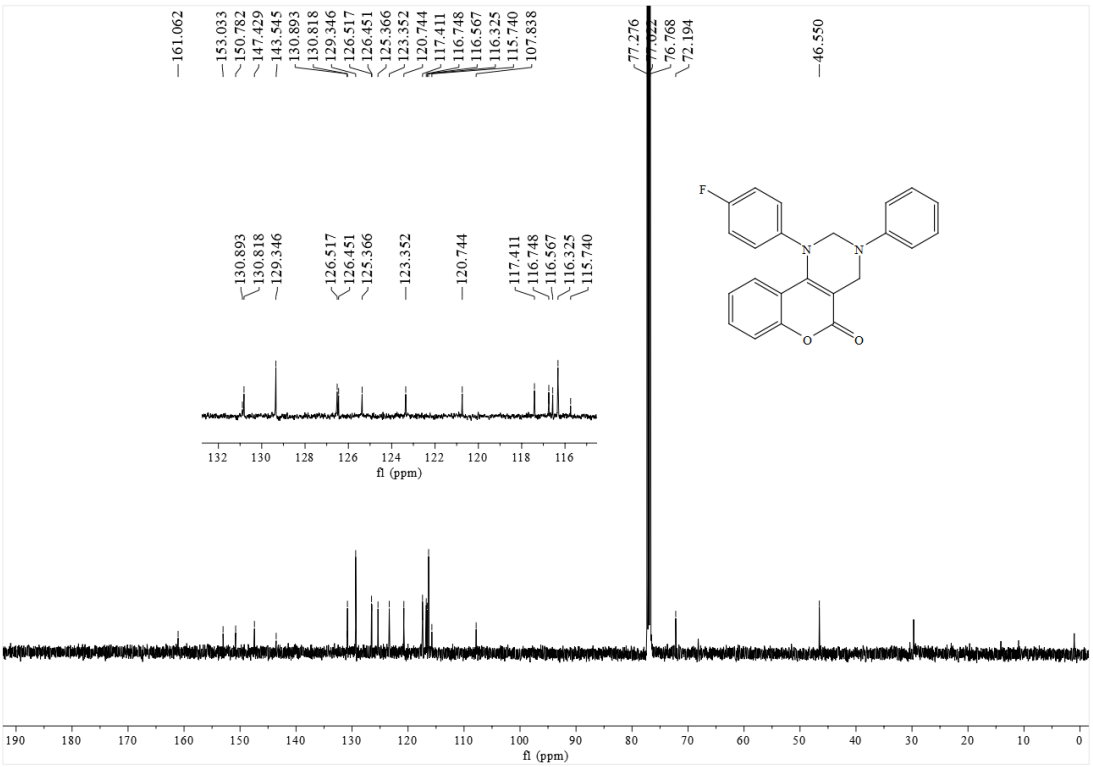


^{13}C NMR of **4j** in $CDCl_3$

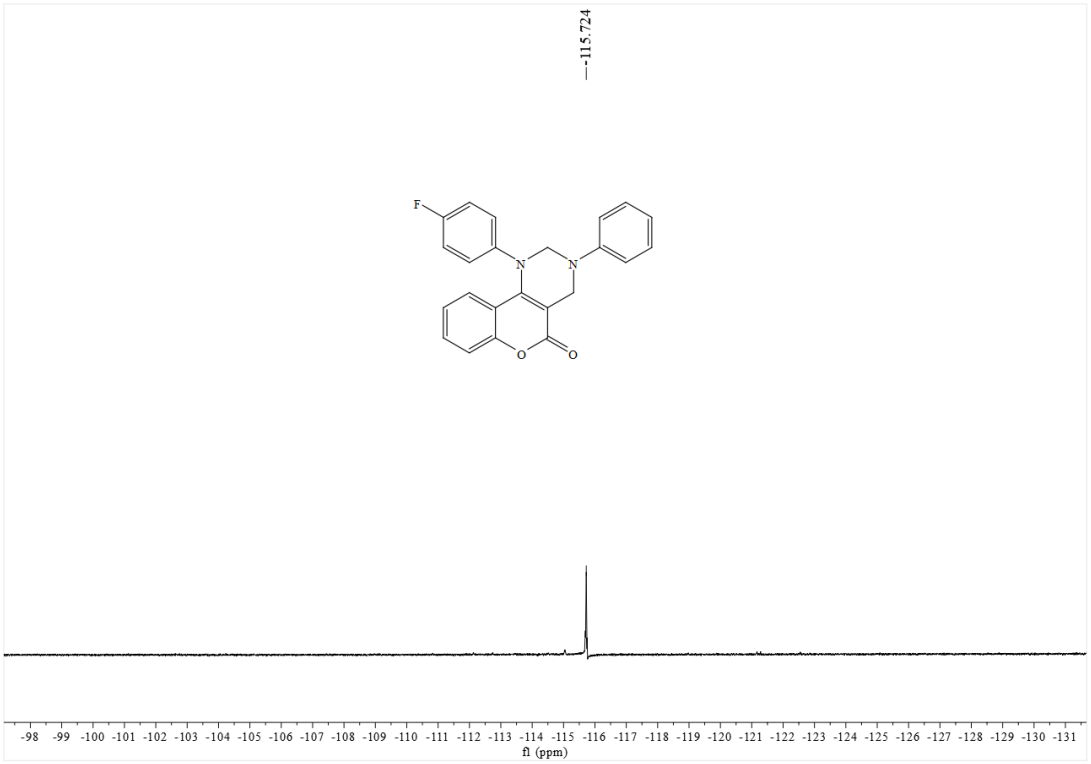
^{19}F NMR of **4i** in $CDCl_3$



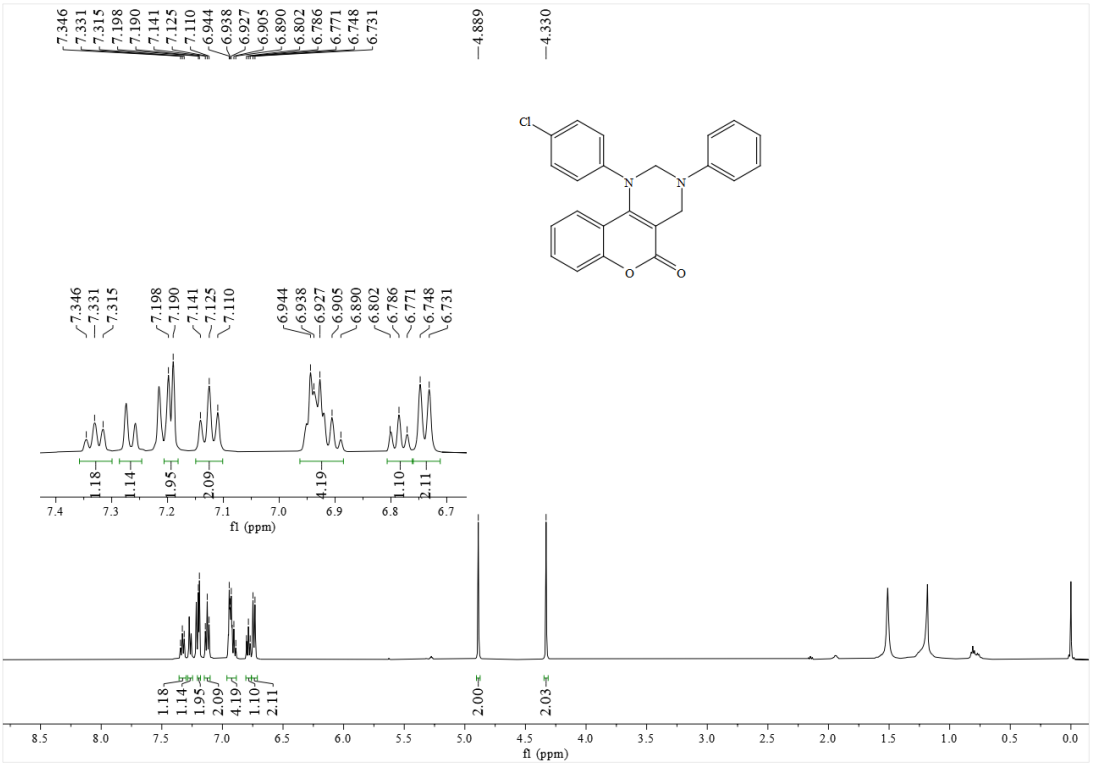
^{1}H NMR of **4k** in $CDCl_3$



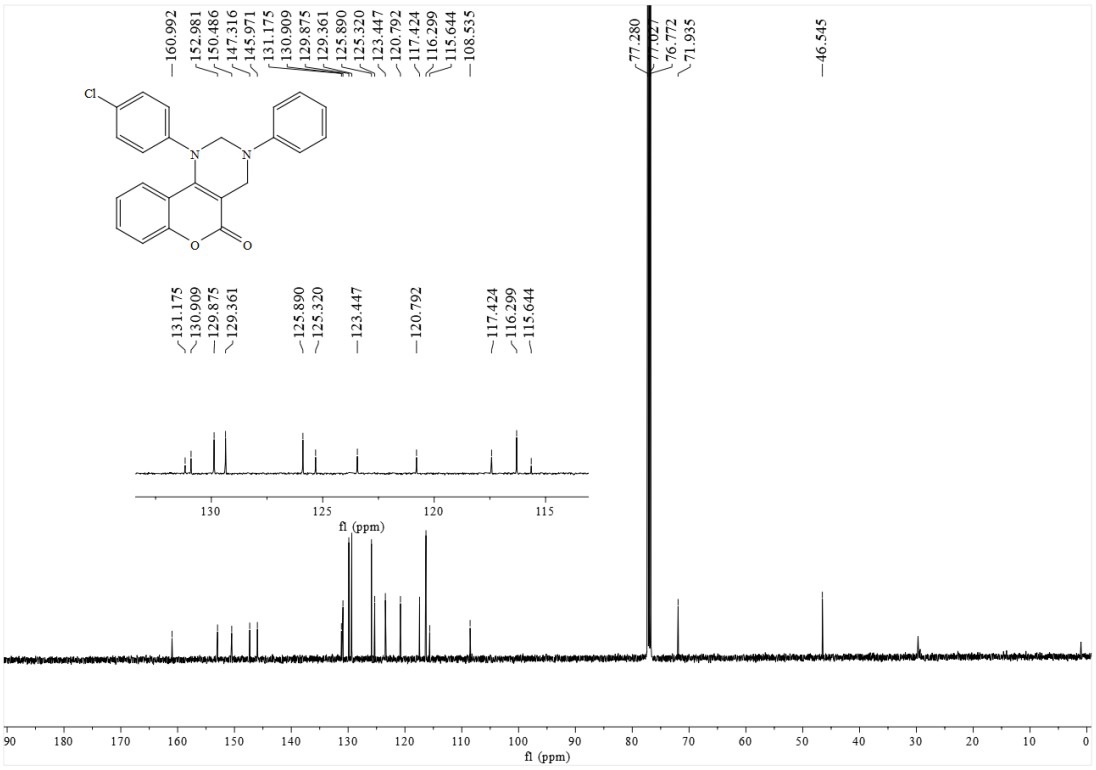
^{13}C NMR of **4k** in $CDCl_3$



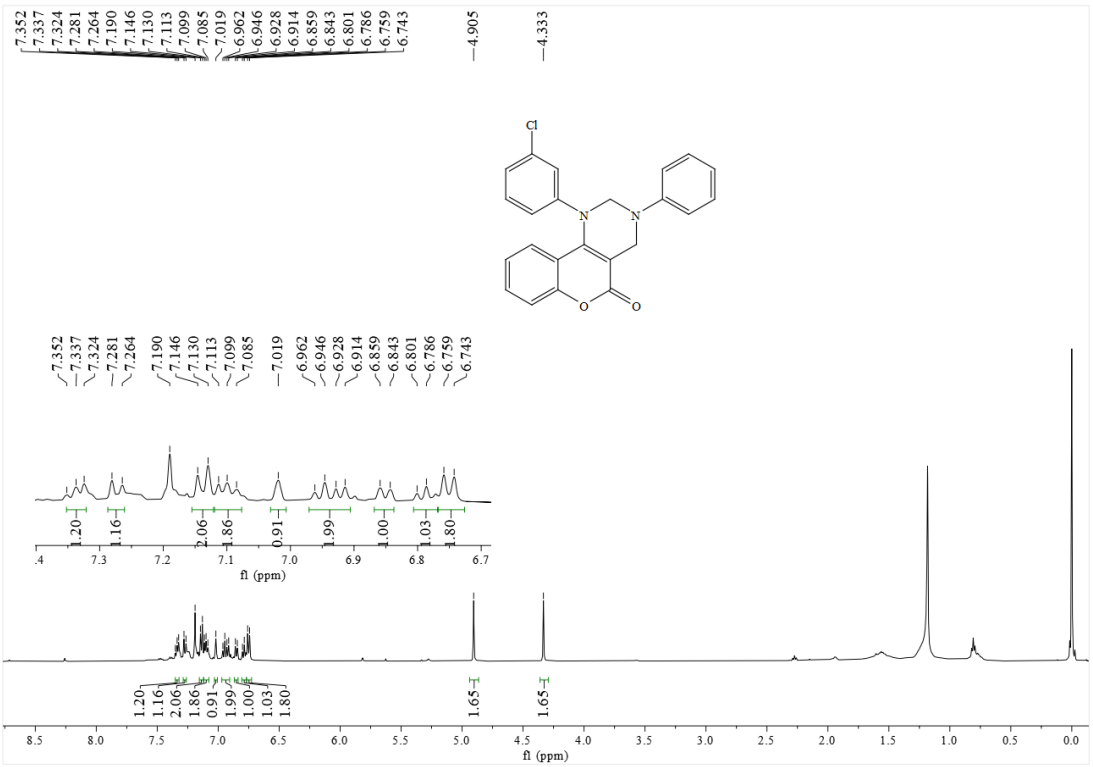
^{19}F NMR of **4k** in $CDCl_3$



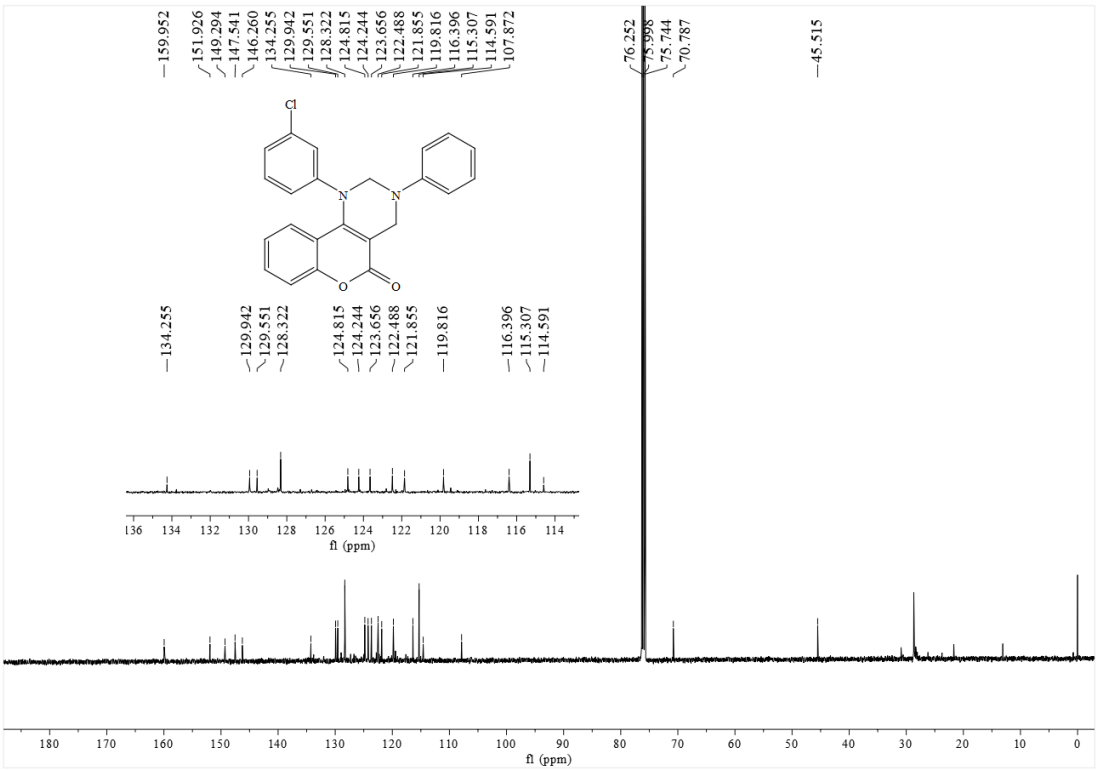
^{1}H NMR of **4l** in $CDCl_3$



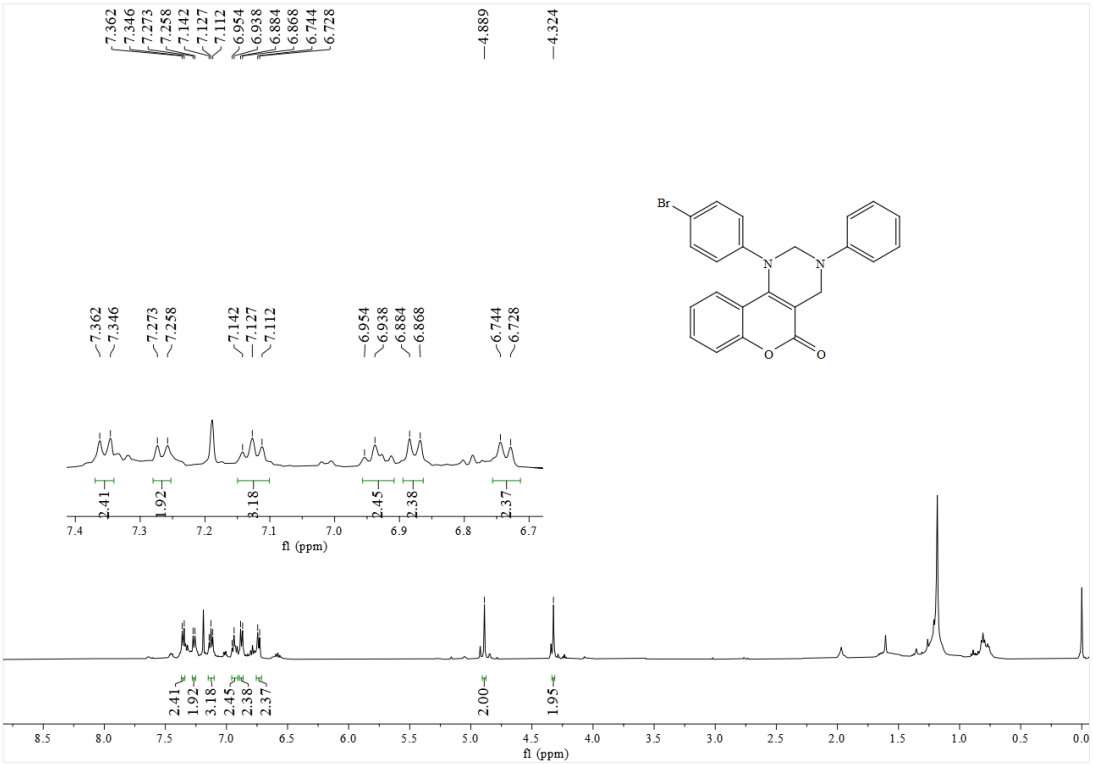
^{13}C NMR of **4l** in $CDCl_3$



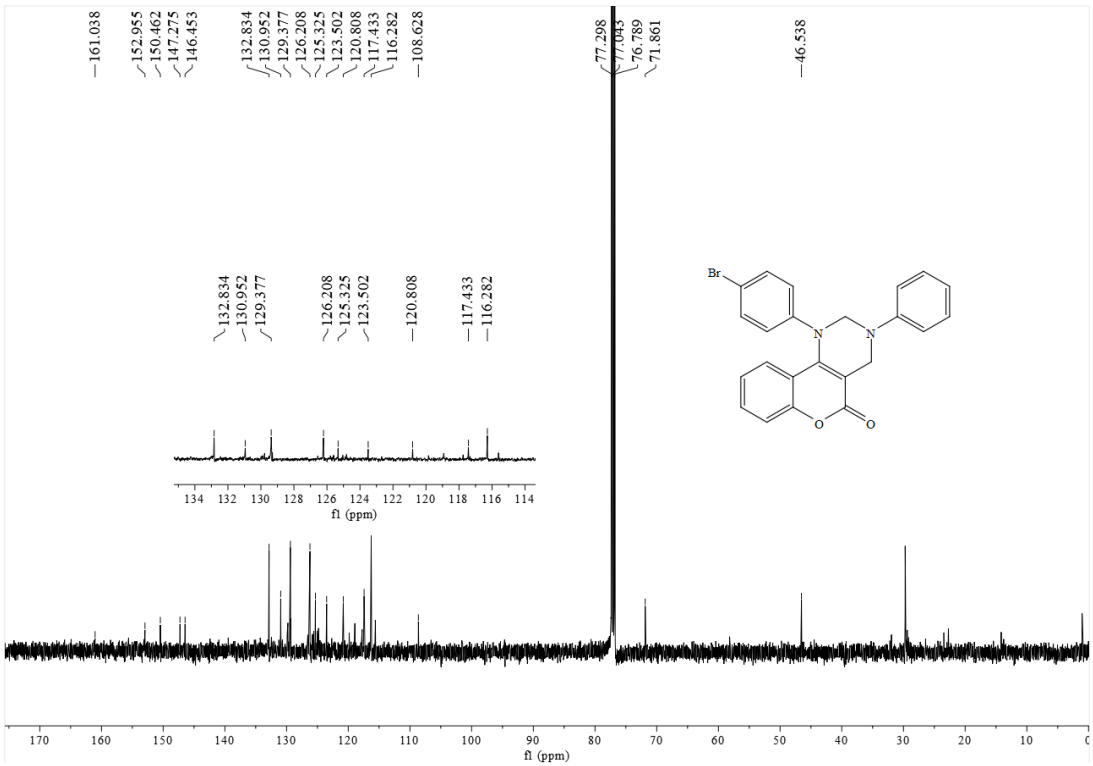
^{1}H NMR of **4m** in $CDCl_3$



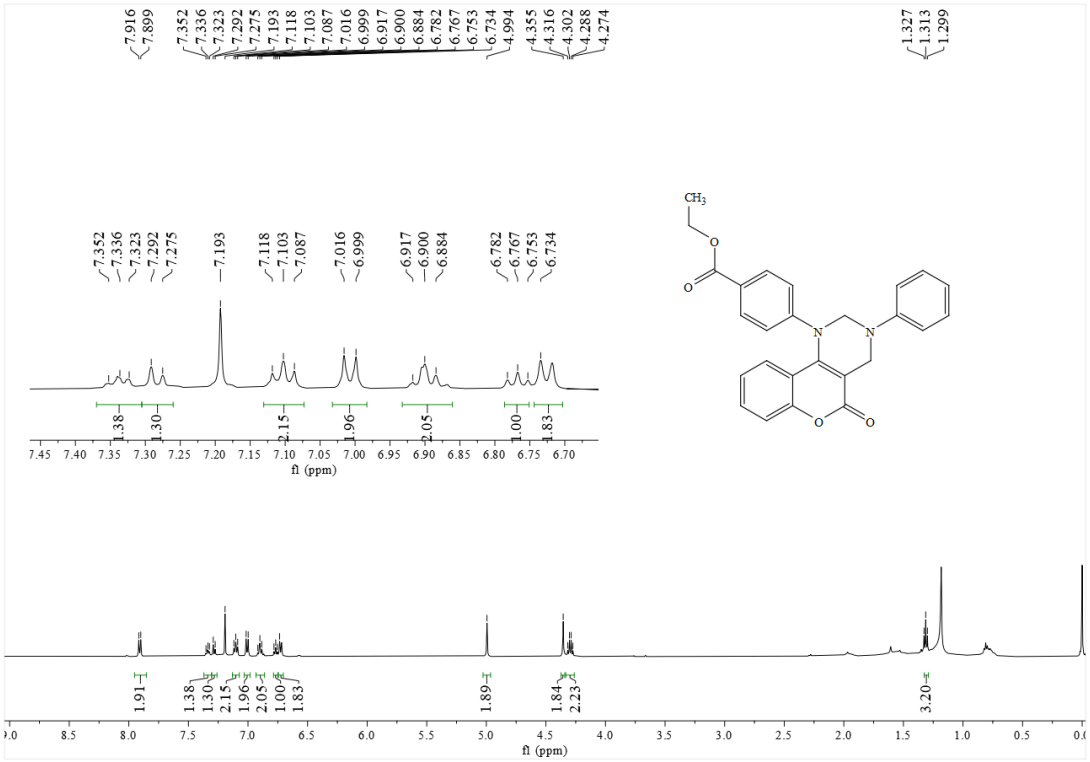
^{13}C NMR of **4m** in $CDCl_3$



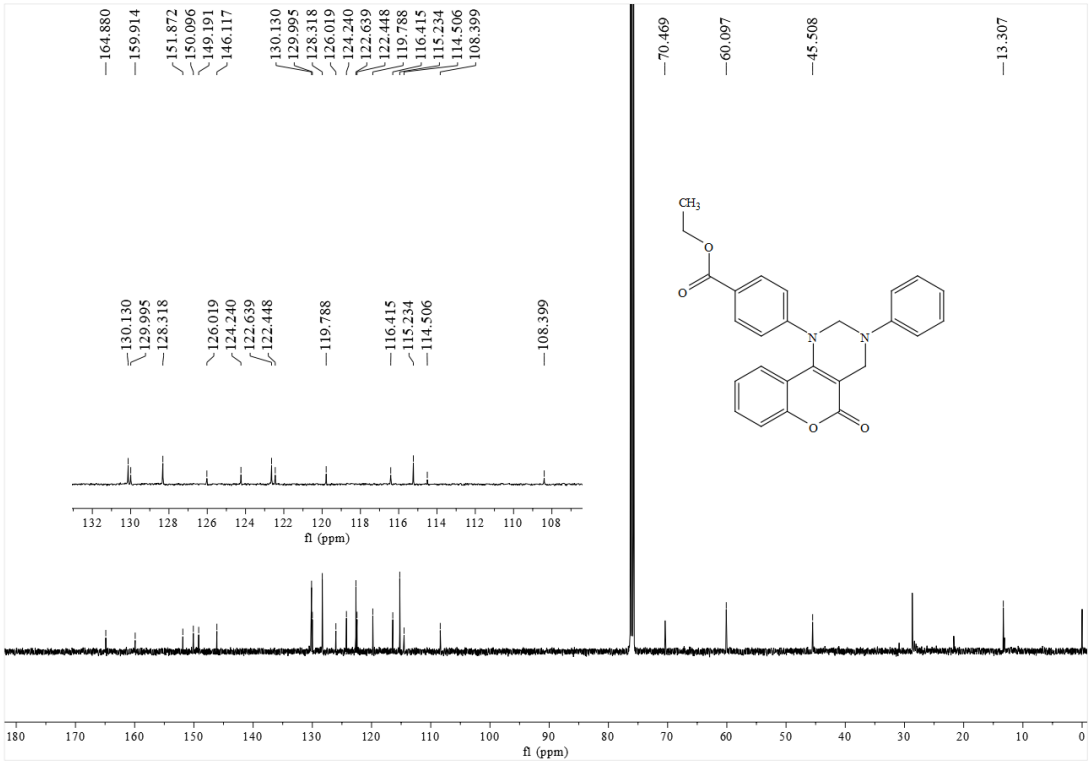
^{1}H NMR of **4n** in $CDCl_3$



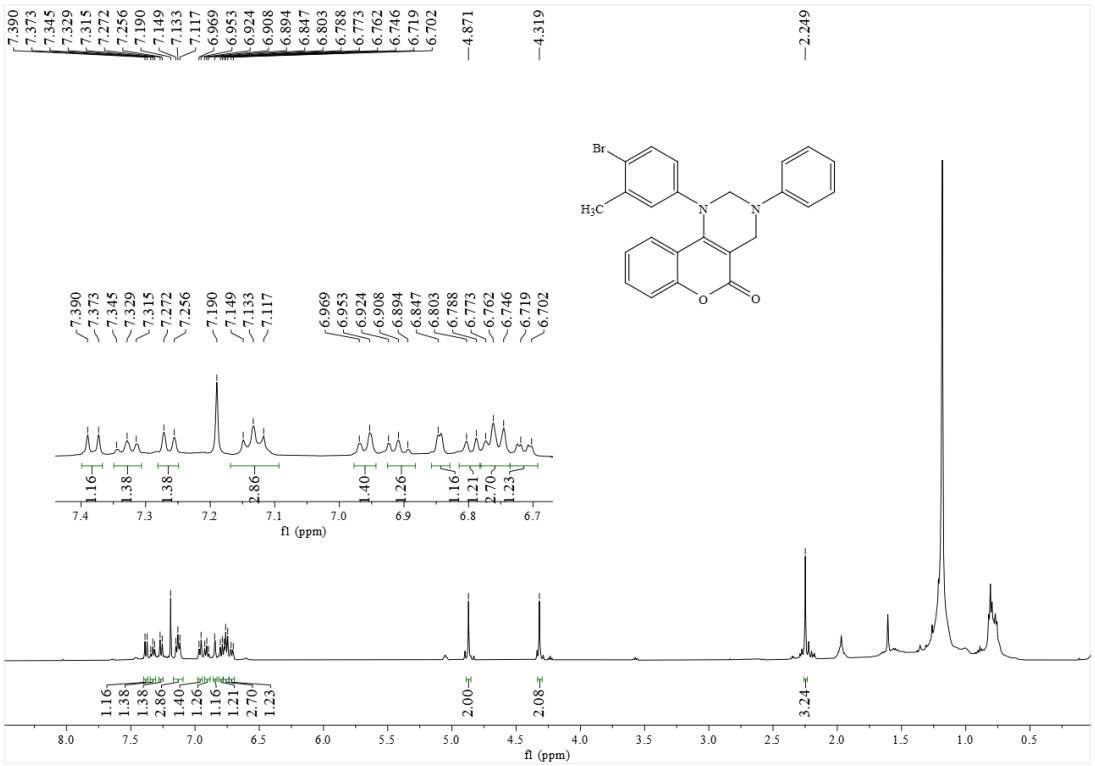
^{13}C NMR of **4n** in $CDCl_3$



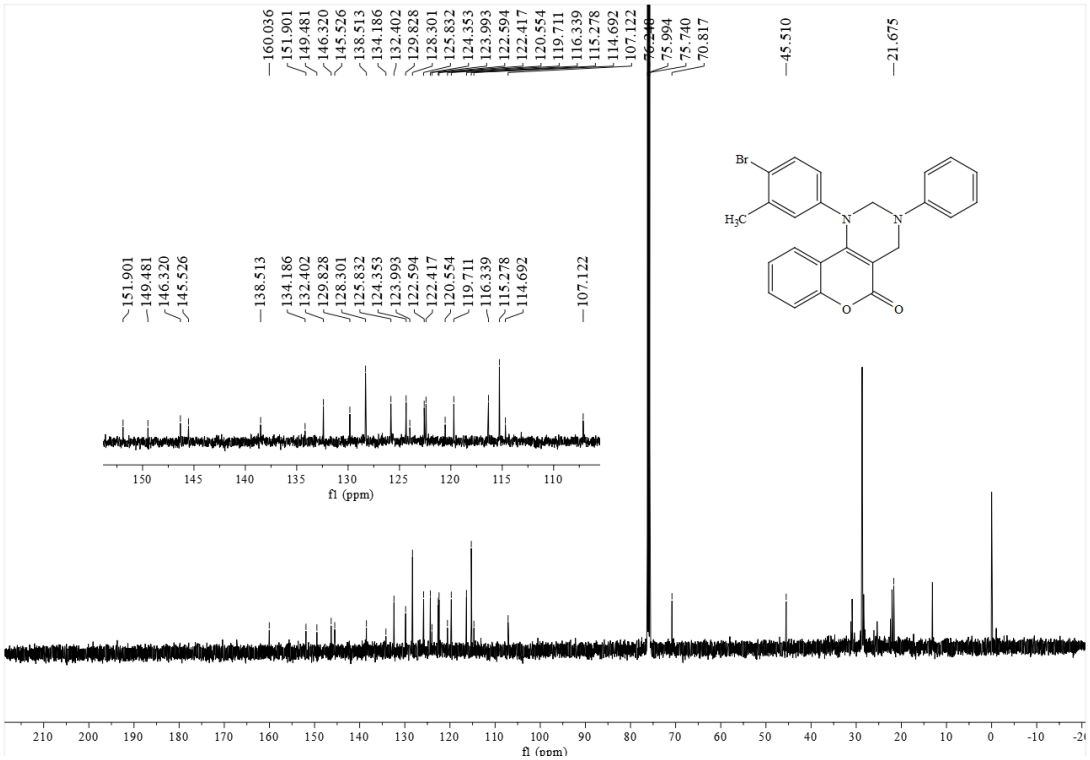
^{1}H NMR of **4o** in $CDCl_3$



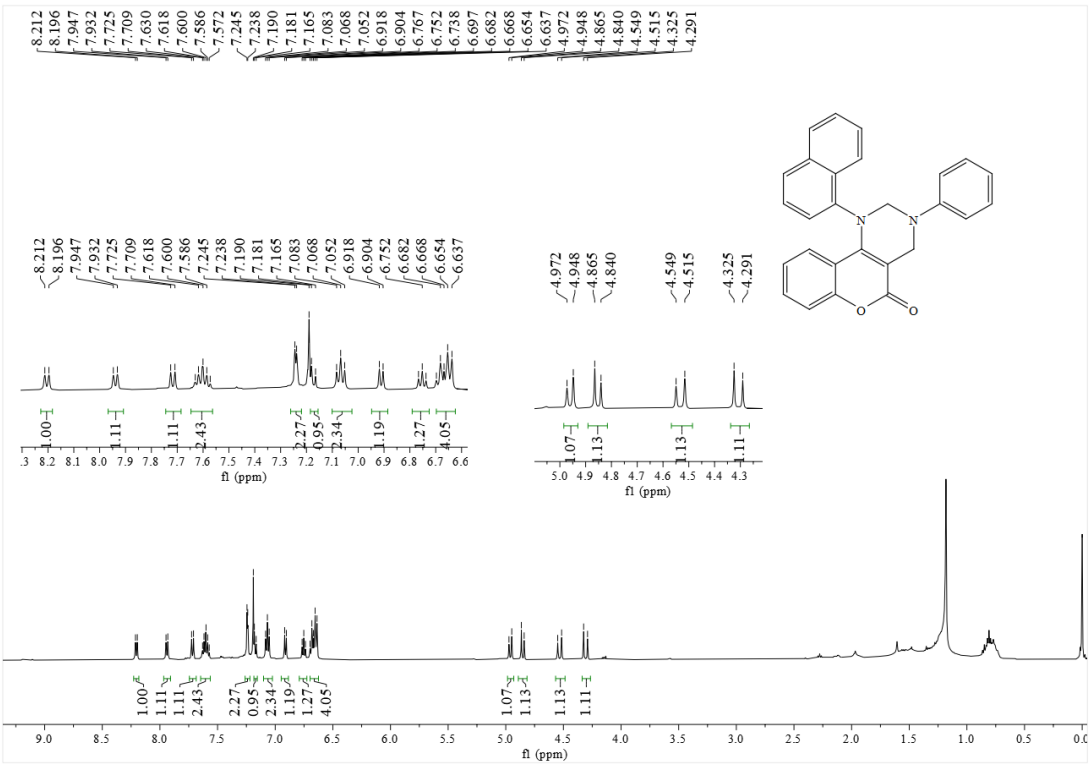
^{13}C NMR of **4o** in $CDCl_3$



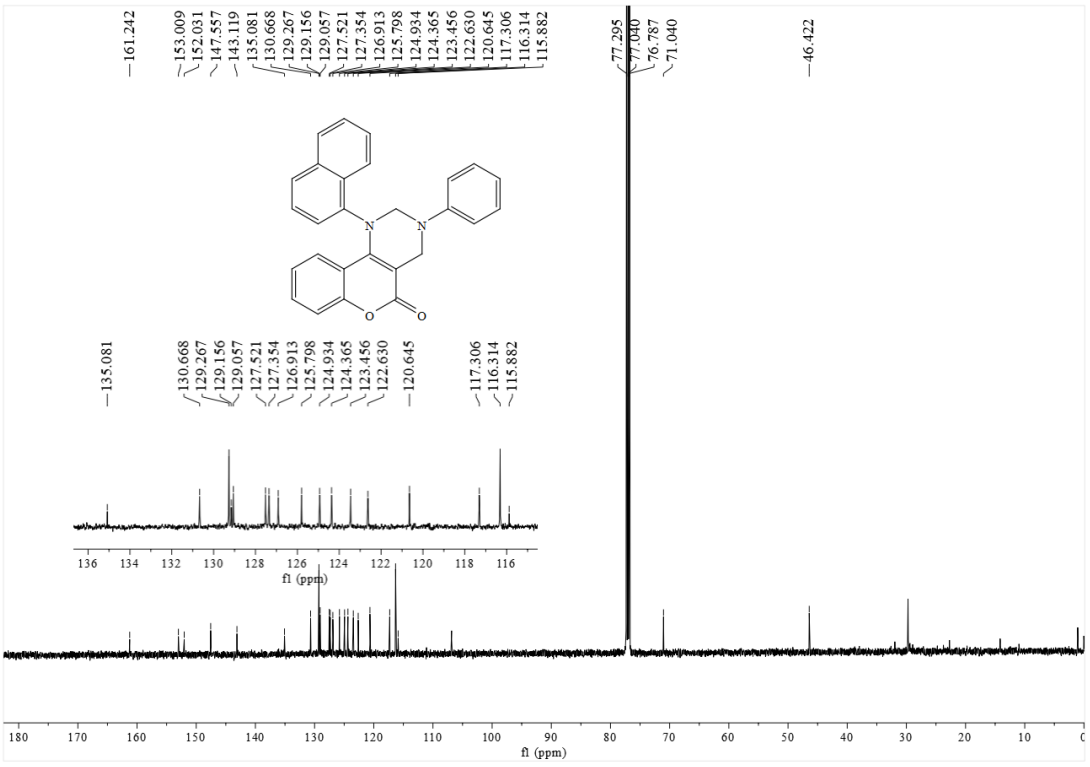
^{1}H NMR of **4p** in $CDCl_3$



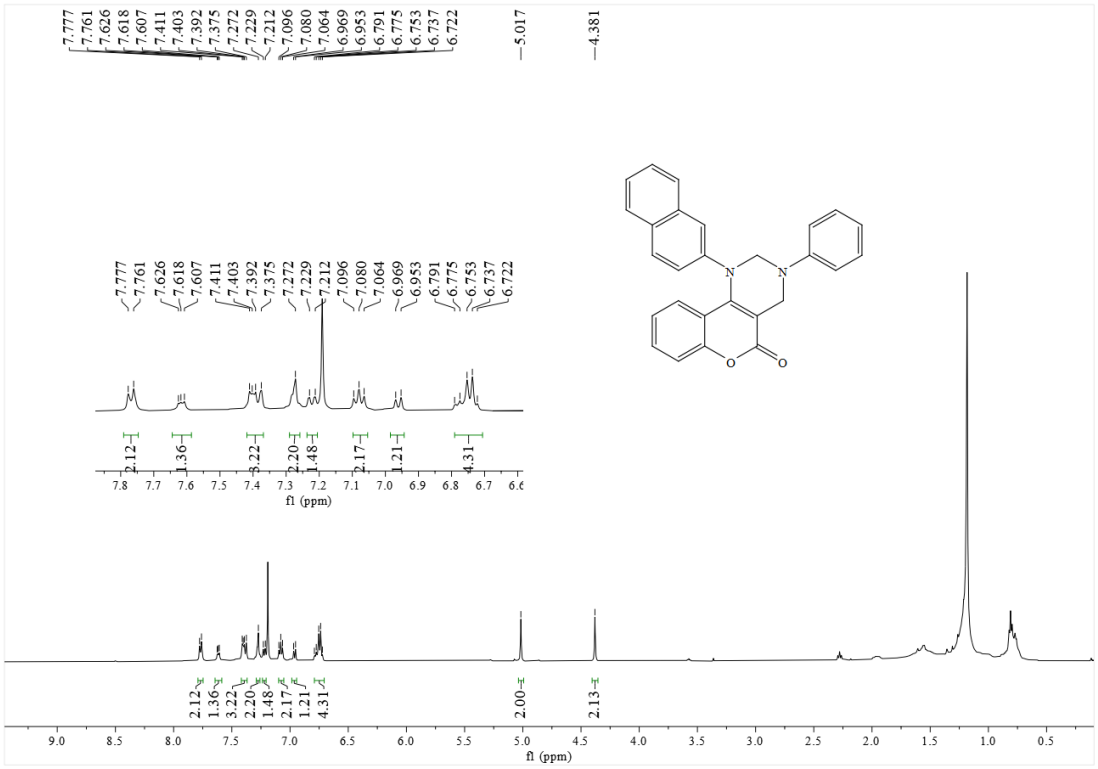
^{13}C NMR of **4p** in $CDCl_3$



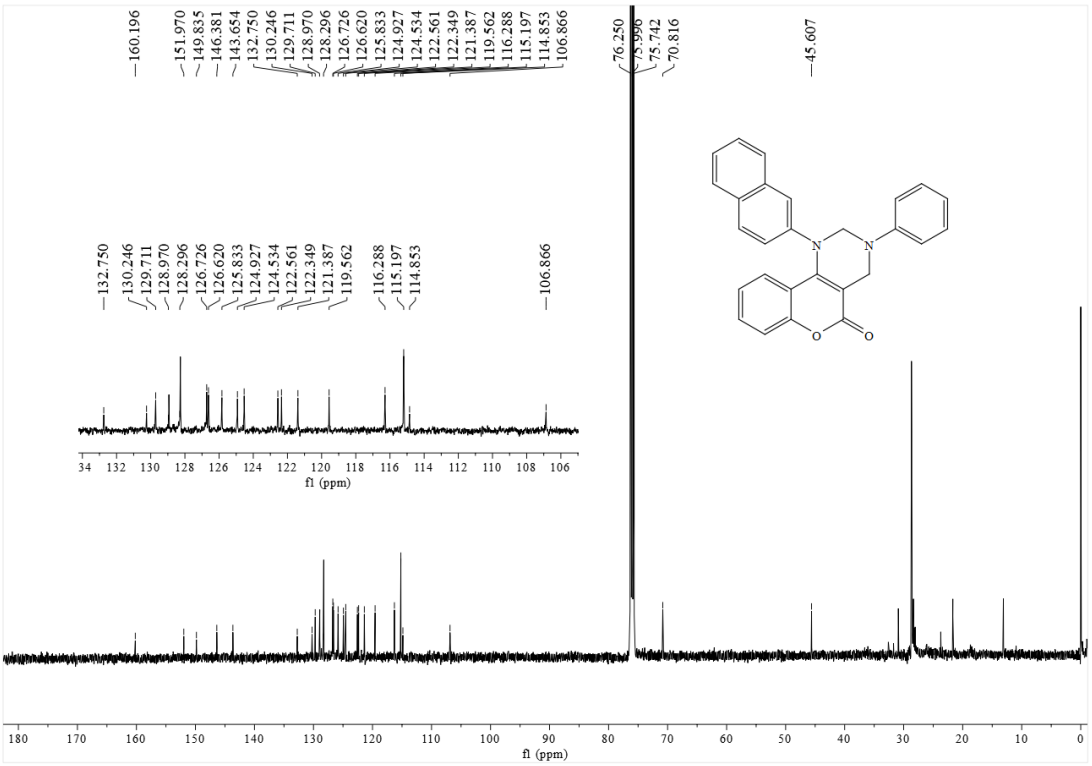
^{1}H NMR of **4q** in $CDCl_3$



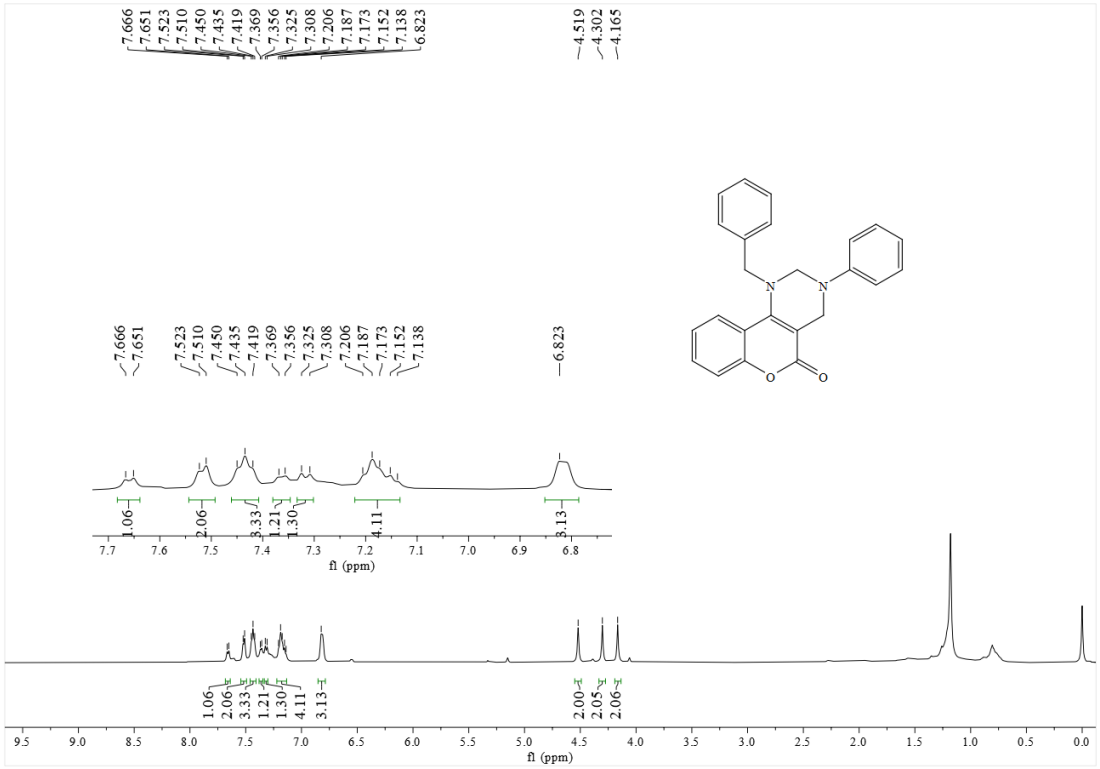
^{13}C NMR of **4q** in $CDCl_3$



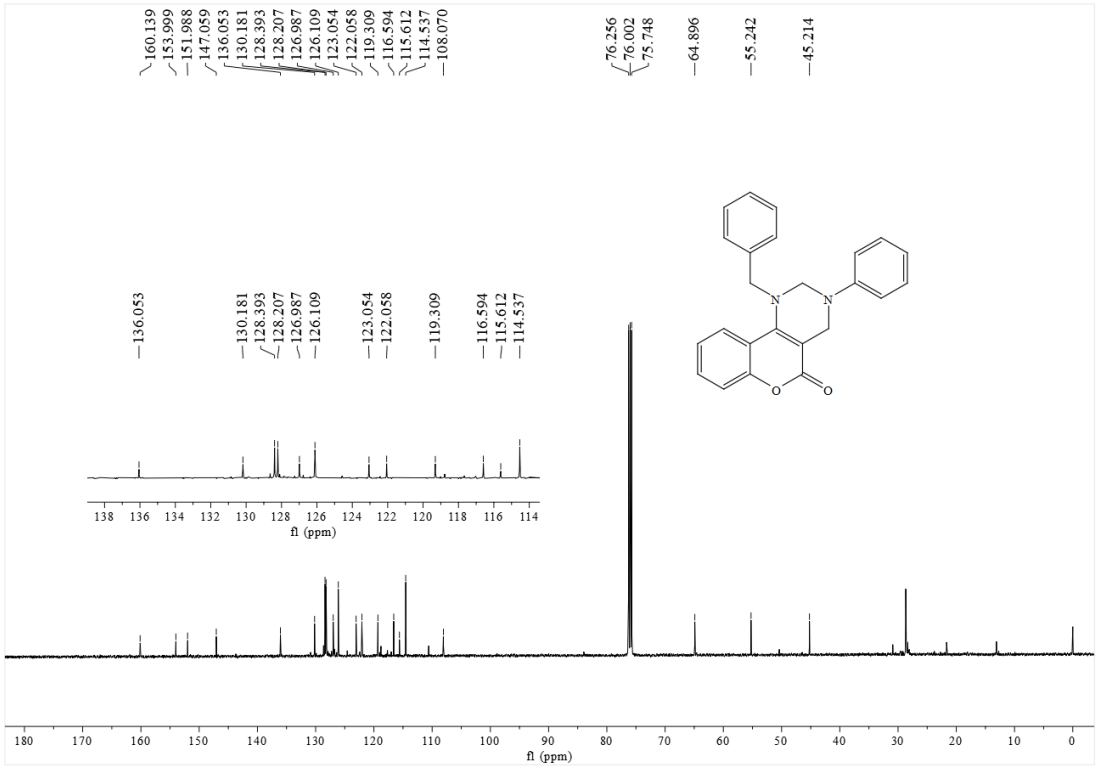
^{1}H NMR of **4r** in $CDCl_3$



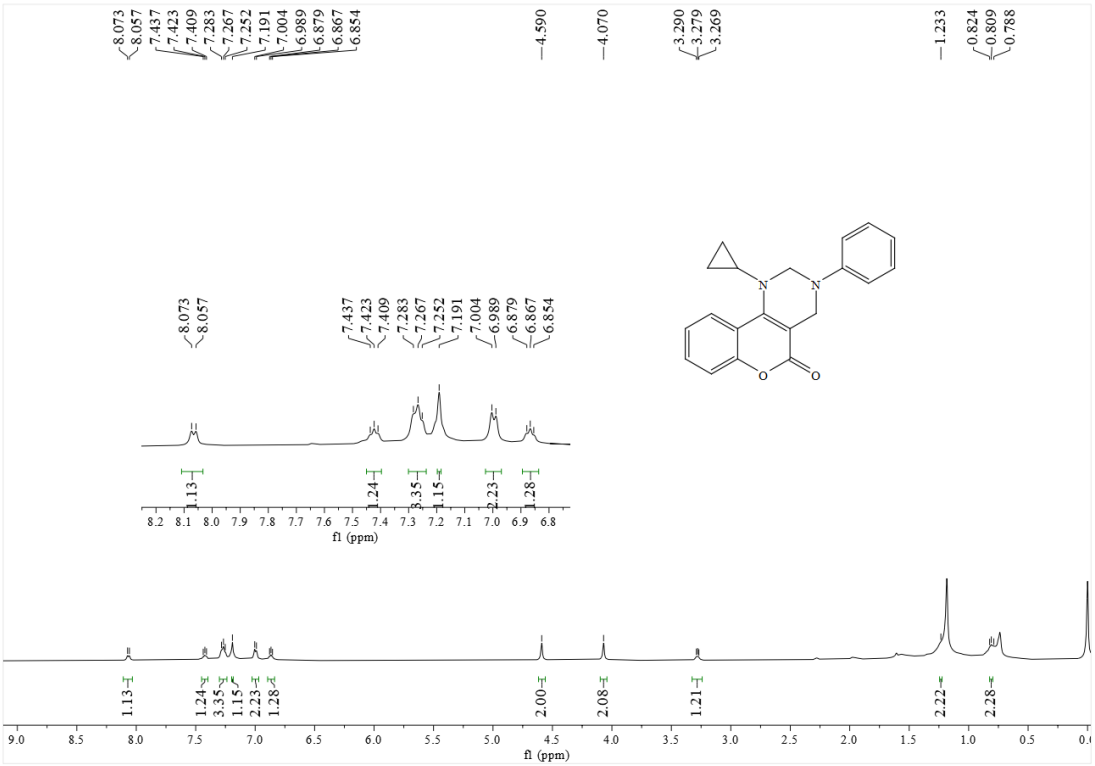
^{13}C NMR of **4r** in $CDCl_3$



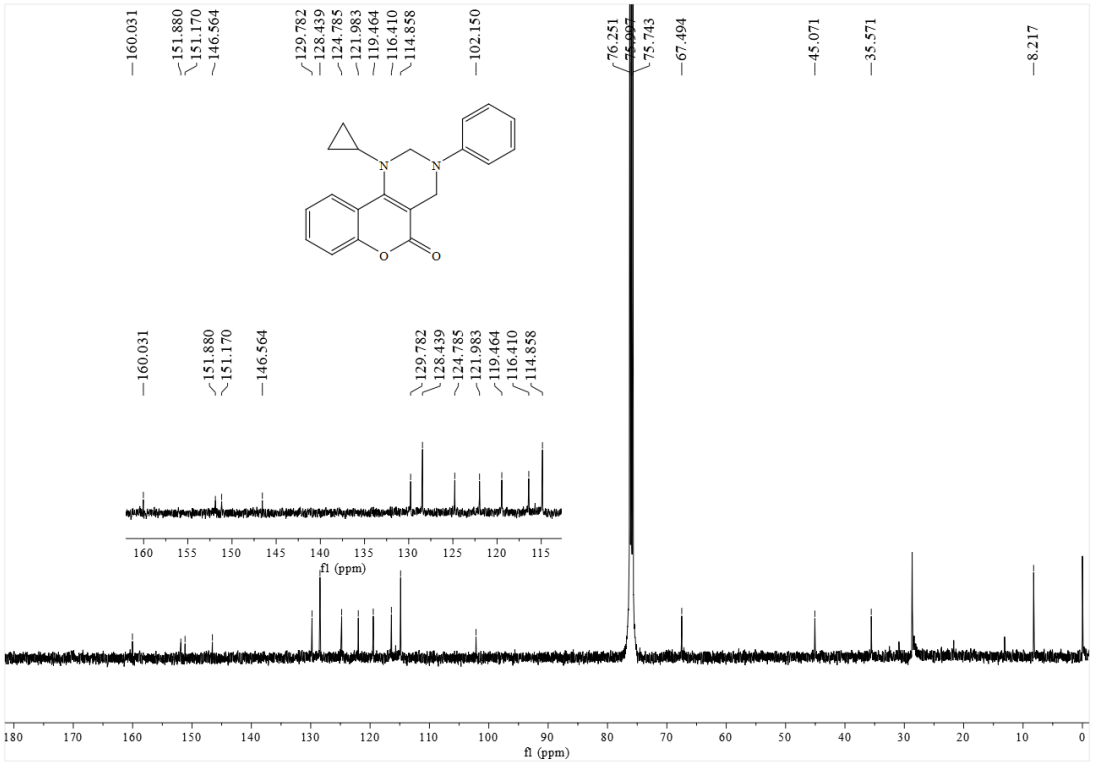
^{1}H NMR of **4s** in $CDCl_3$



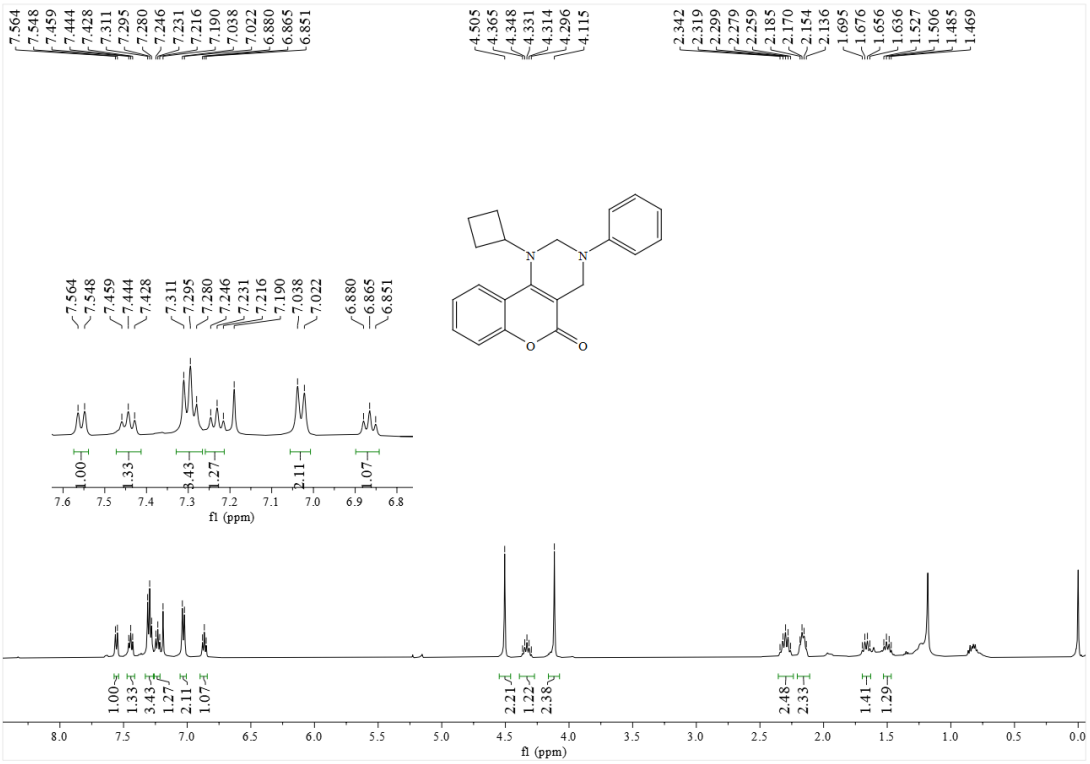
^{13}C NMR of **4s** in $CDCl_3$



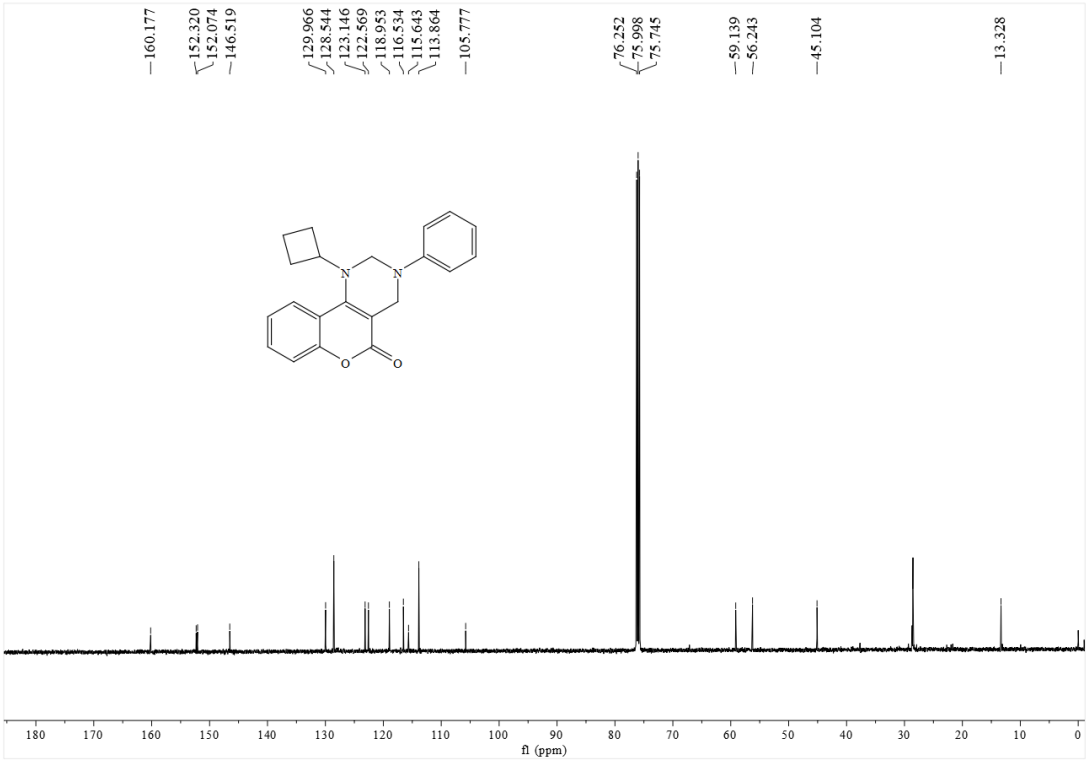
^{1}H NMR of **4t** in $CDCl_3$



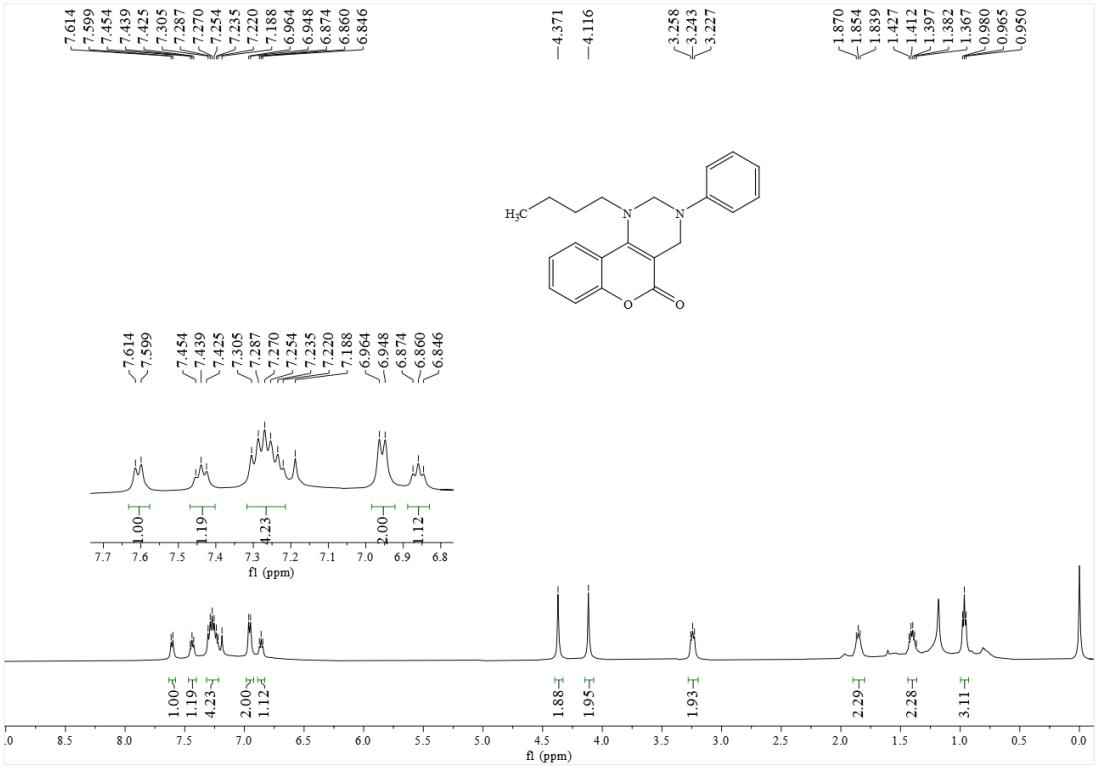
^{13}C NMR of **4t** in $CDCl_3$



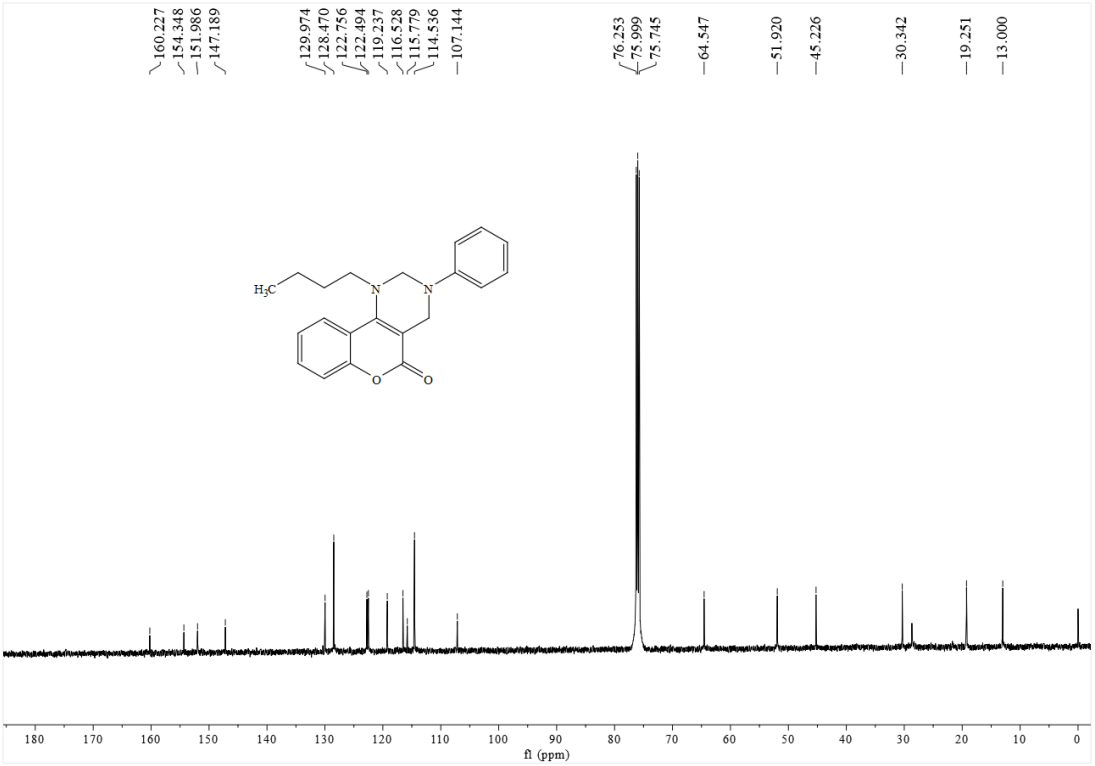
^{1}H NMR of **4u** in $CDCl_3$



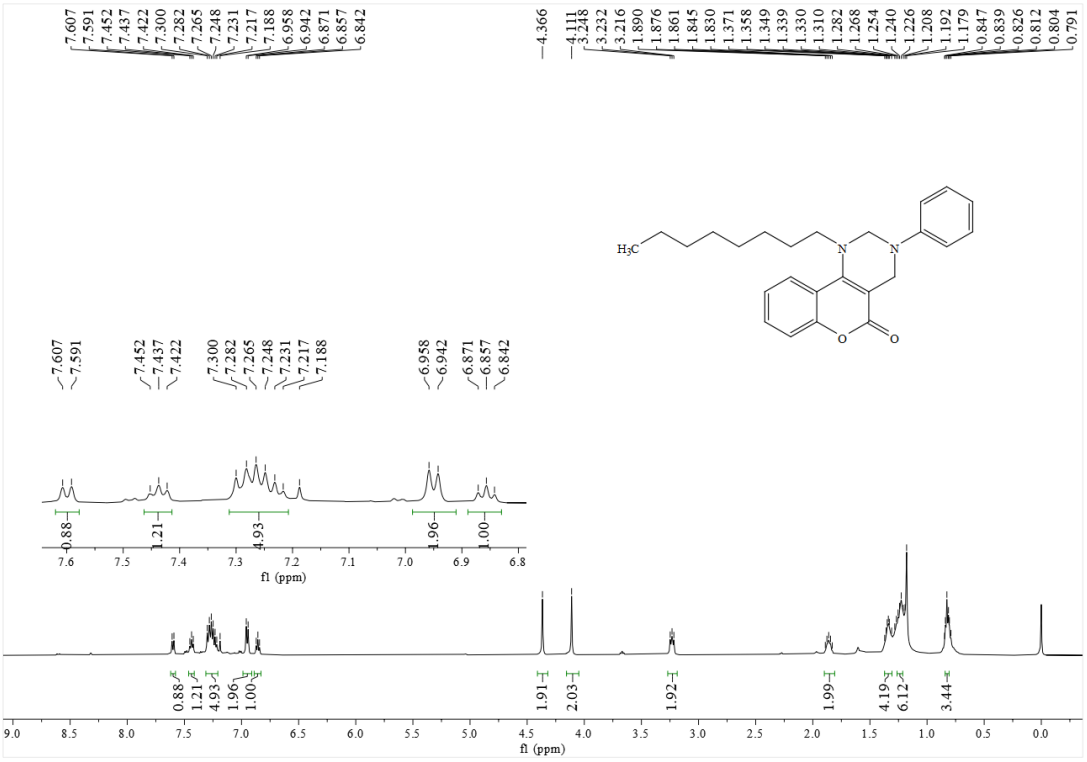
^{13}C NMR of **4u** in $CDCl_3$



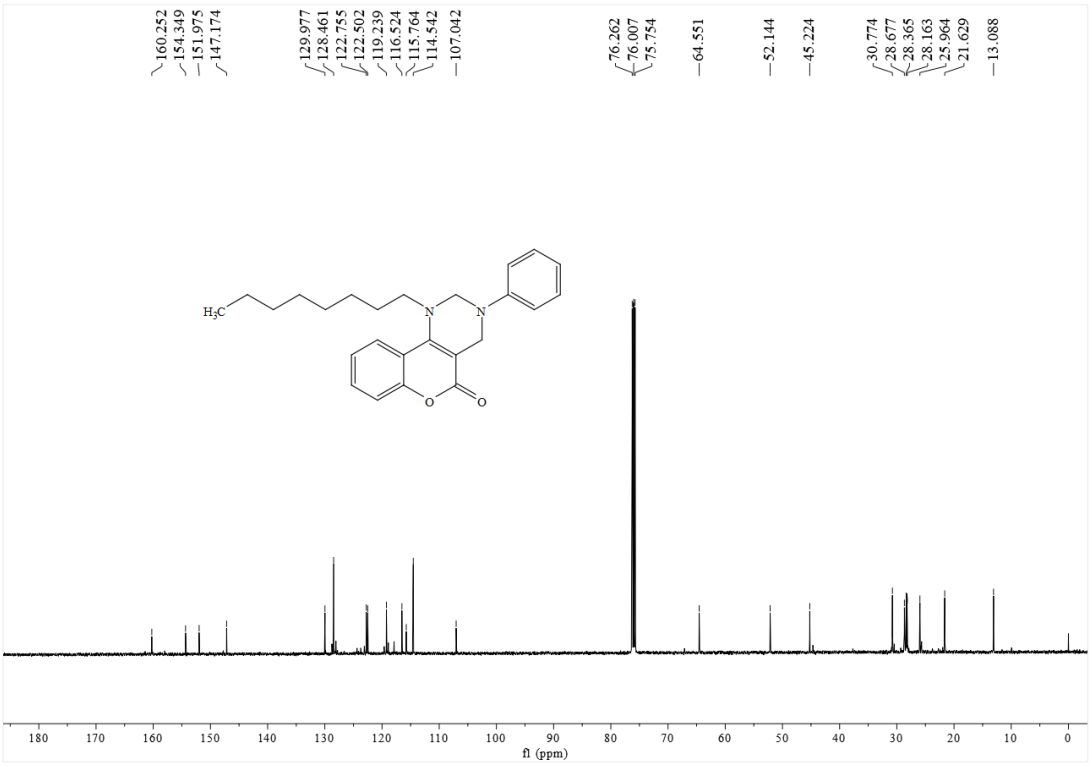
^{1}H NMR of **4v** in $CDCl_3$



^{13}C NMR of **4v** in $CDCl_3$

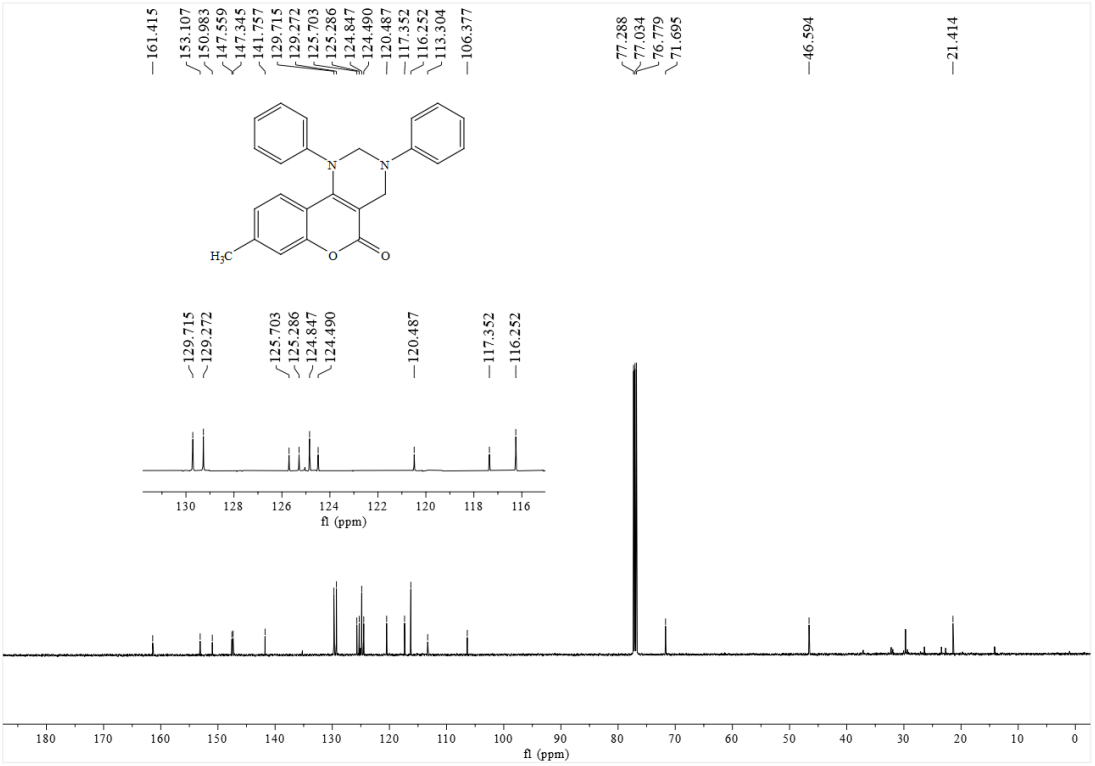


^{1}H NMR of **4w** in $CDCl_3$



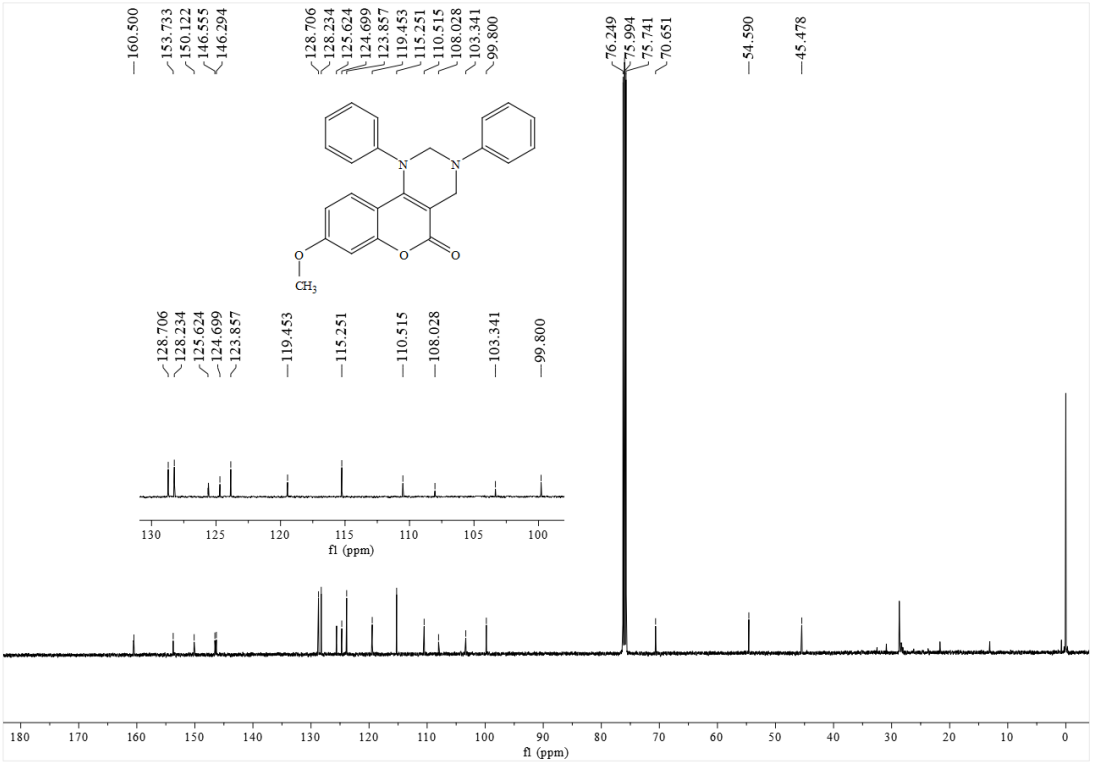
^{13}C NMR of **4w** in $CDCl_3$

^{1}H NMR of **4x** in $CDCl_3$

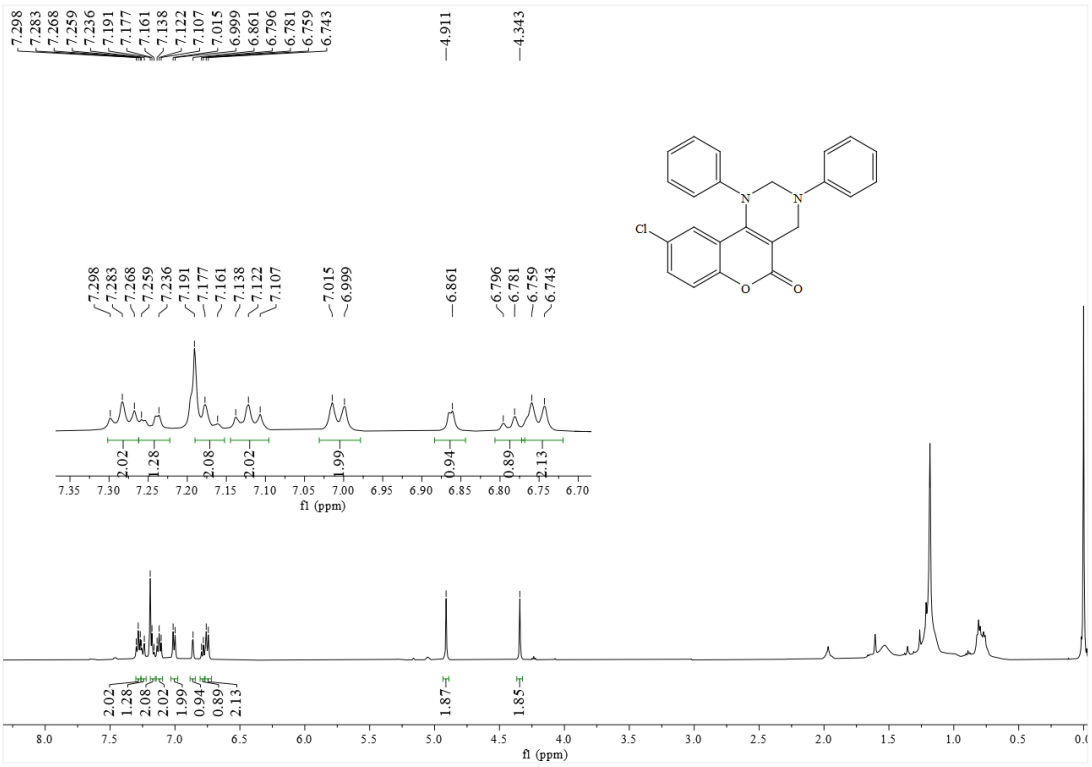


^{13}C NMR of **4x** in $CDCl_3$

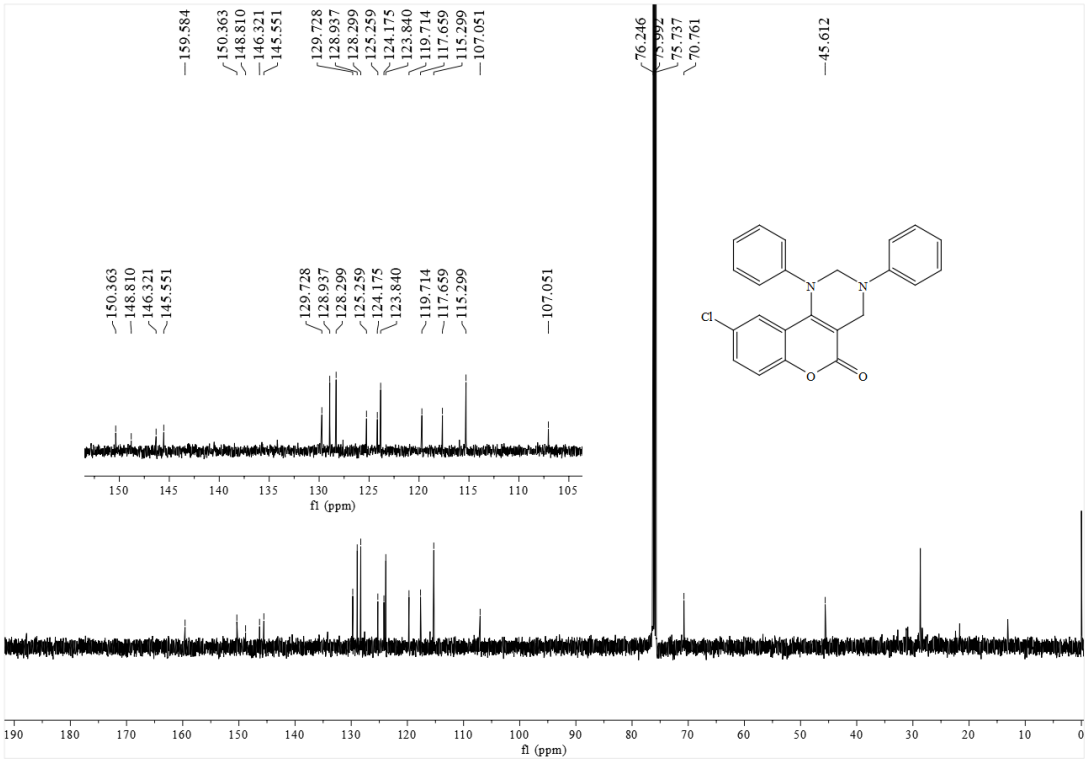
^{1}H NMR of **4y** in $CDCl_3$



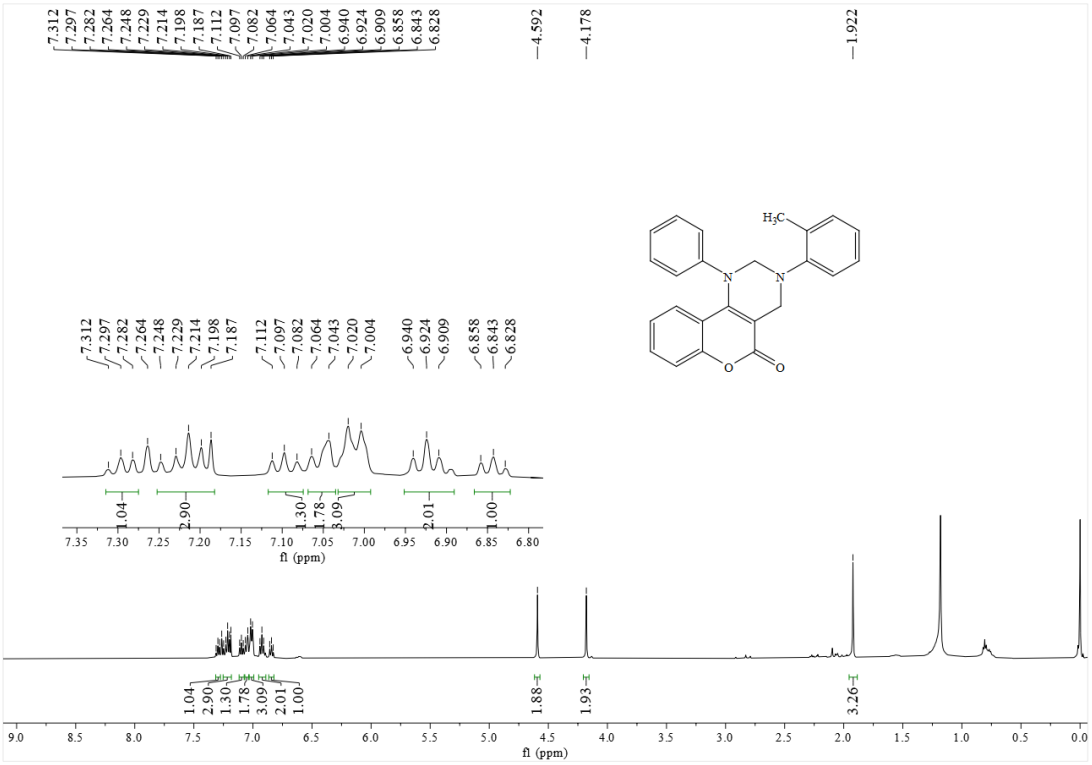
^{13}C NMR of **4y** in $CDCl_3$



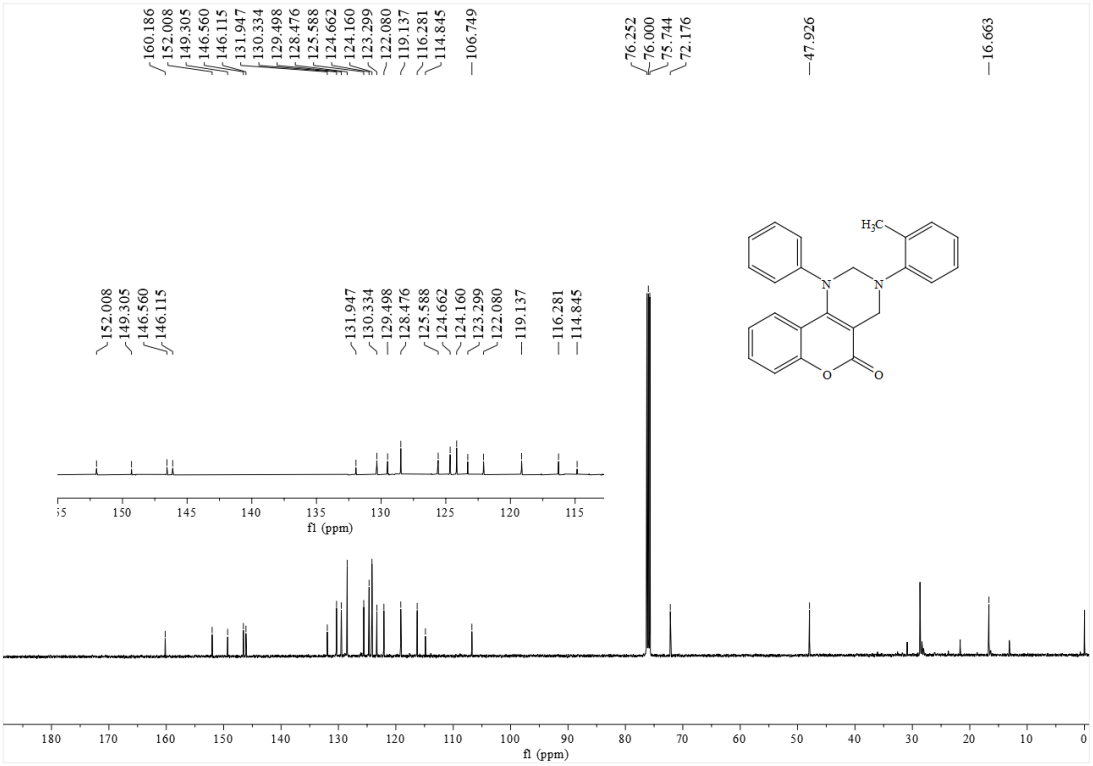
^{1}H NMR of **4z** in $CDCl_3$



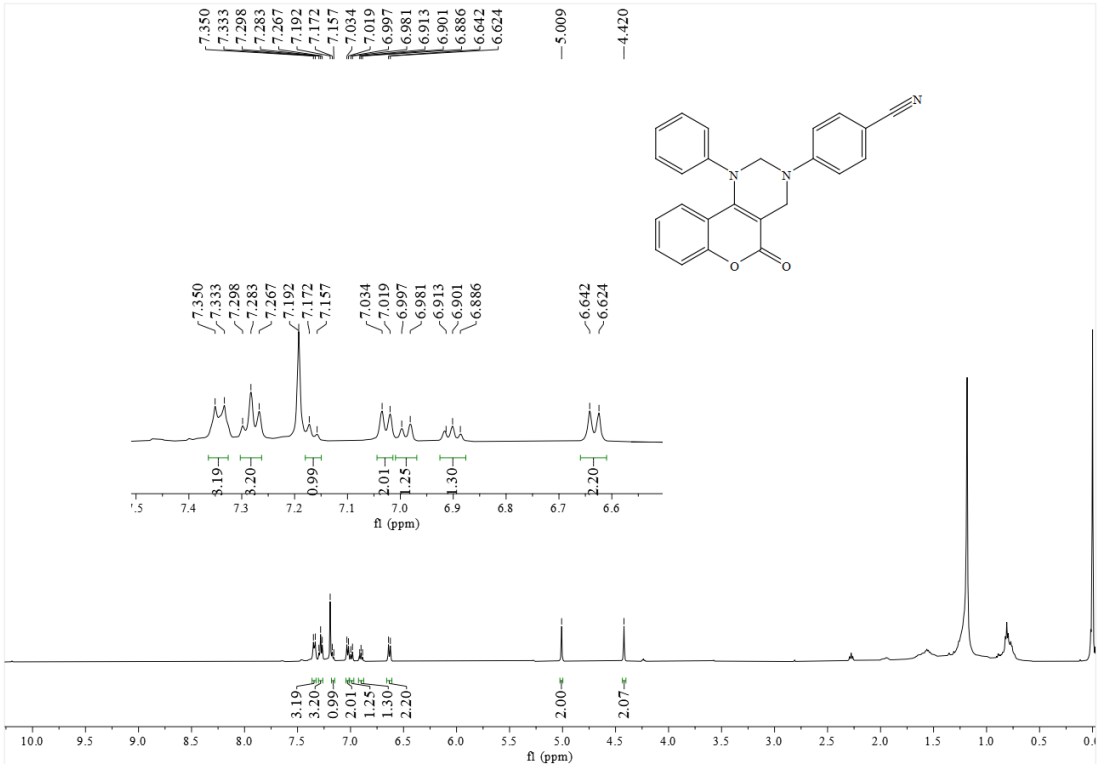
^{13}C NMR of **4z** in $CDCl_3$



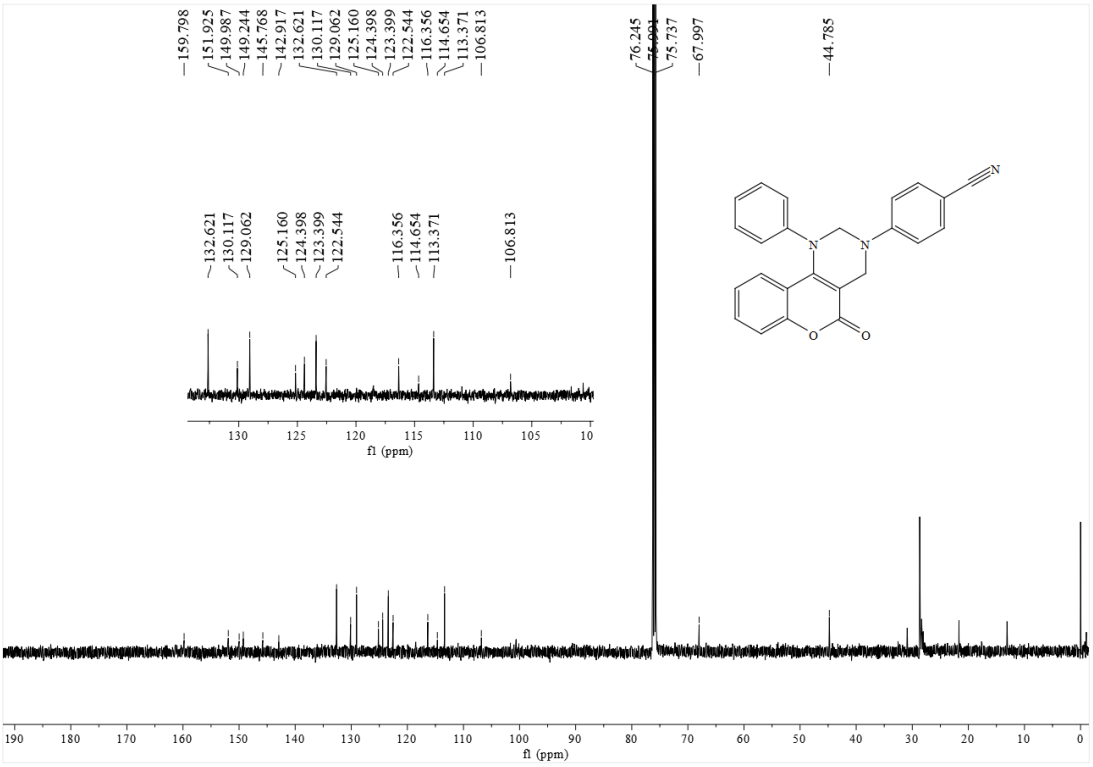
^{1}H NMR of **4aa** in $CDCl_3$



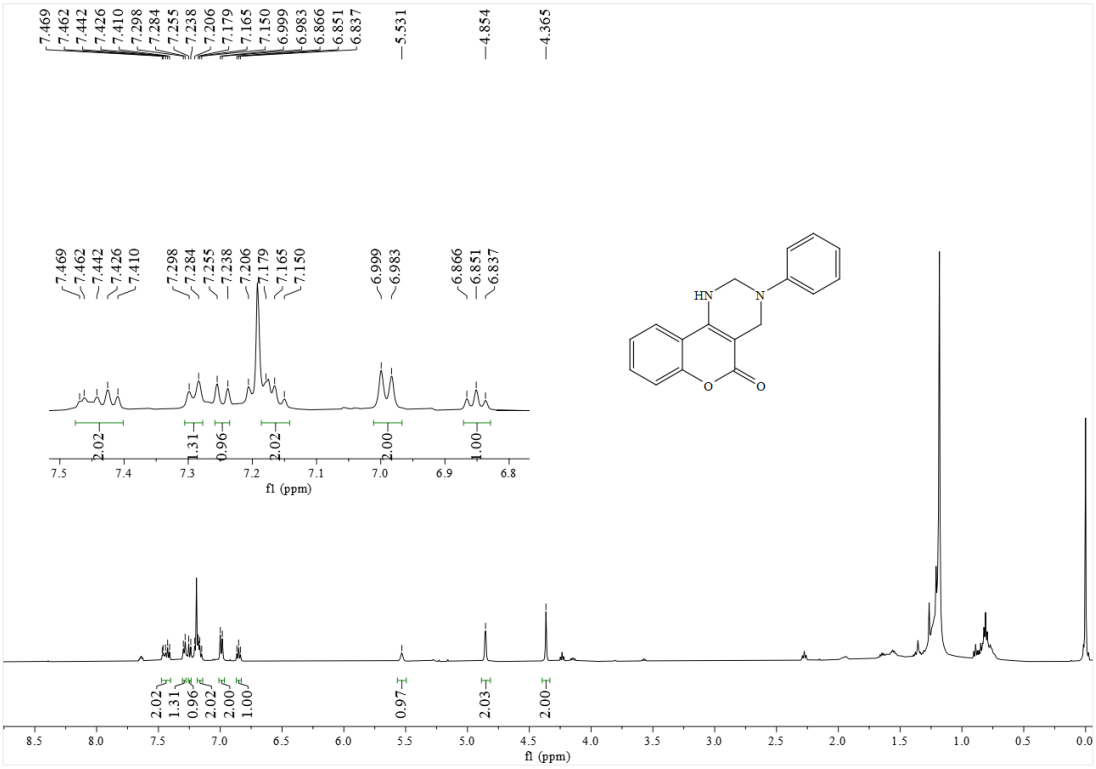
^{13}C NMR of **4aa** in $CDCl_3$



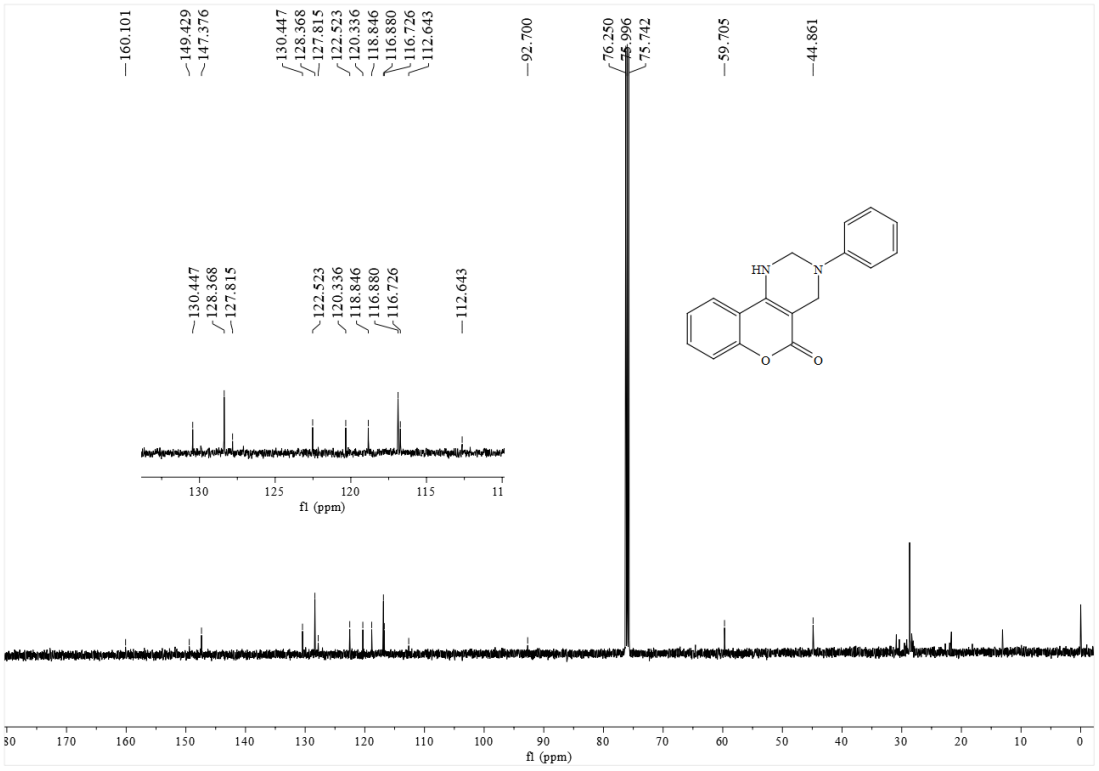
^{1}H NMR of **4ab** in $CDCl_3$



^{13}C NMR of **4ab** in $CDCl_3$



^{1}H NMR of **4ac** in $CDCl_3$



^{13}C NMR of **4ac** in $CDCl_3$