Supporting Information

Catalyst-Free Cyclization of Anthranils and Cyclic Amines: One-step Synthesis of Rutaecarpine

Jian Li,* Zheng-Bing Wang, Yue Xu, Xue-Chen Lu, Shang-Rong Zhu, Li Liu

† Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Pharmaceutical Engineering & Life Sciences, Changzhou University, Changzhou, 213164, China

Table of content:

General Information

All reactions were carried out under an air atmosphere condition. Solvents and reagents were purchased from commercial source and used without further purification. Flash column chromatography was performed using silica gel (200-300 mesh). Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). NMR spectra were recorded in $CDCl_3$ on Bruker NMR-300 (300 MHz) and NMR-400 (400 MHz) with TMS as an internal reference. HRMS were performed on Agilent 6540 Q-TOF mass spectrometer (ESI). X-ray crystallographic data were collected using a SMART APEX II X-ray diffractometer.

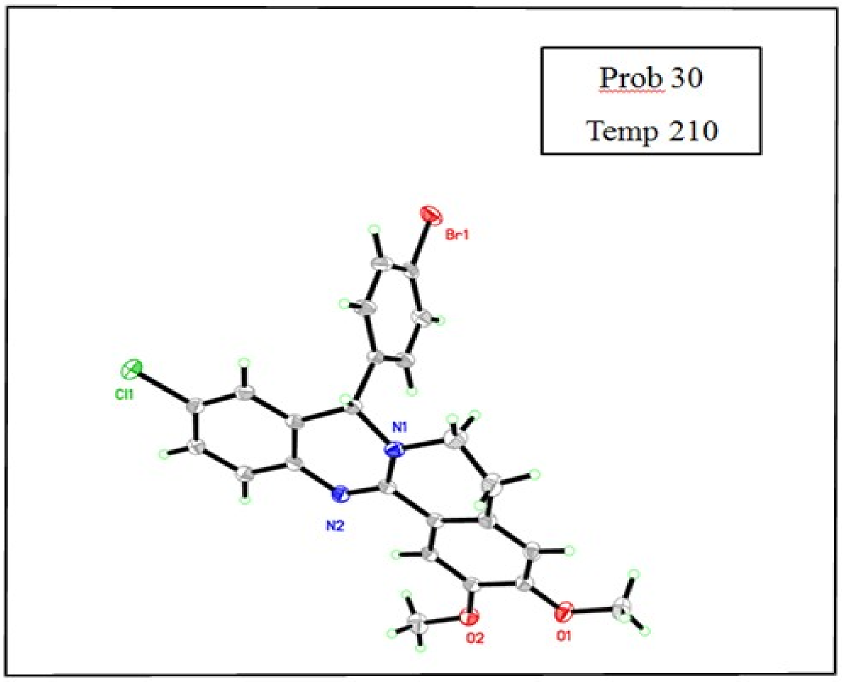


Figure S1. ORTEP drawing (30%) of the crystal structure **4q**

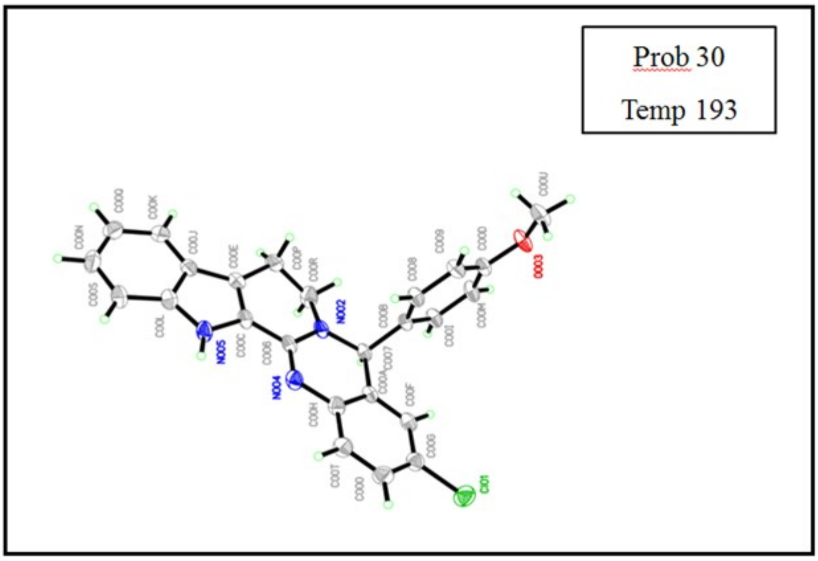
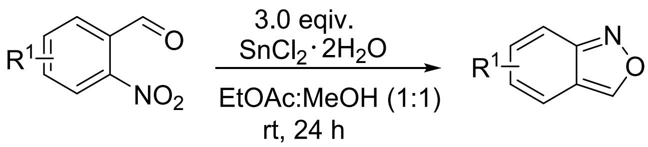


Figure S2. ORTEP drawing (30%) of the crystal structure **6j**

Table S1. Crystal data parameter for compound **4o, 6j**		
	4o	**6j**
Formula unit	$C_{24}H_{20}BrClN_2O_2$	$C_{25}H_{20}ClN_3O$
Formula wt.	483.78	413.89
Crystal system	monoclinic	monoclinic
T [K]	210	193
a [Å]	11.4651(6)	31.8664(15)
b [Å]	10.5710(5)	8.9719(5)
c [Å]	17.7266(9)	16.6944(8)
α [º]	90	90
β[º]	105.480(2)	110.086(2)
γ [º]	90	90
Volume [Å3]	2070.48(18)	4482.7(4)
Space group	P 21/n	C 2/c
Z	4	8
Reflns. Collected	16566	2136
R_1 [I>2σ(I)], wR_2	0.0445, 0.1207	0.0696, 0.1014
GOF	1.058	0.922
CCDC Reference NO.	1943441	1940471

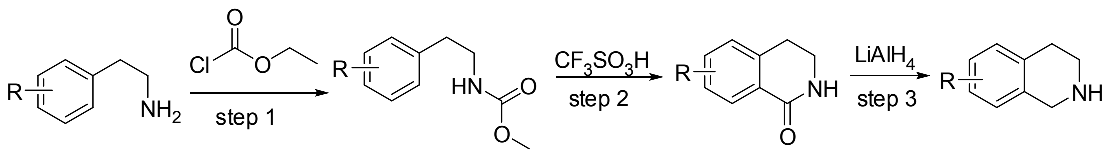
Synthesis of substituted anthranils 1[1]



Scheme S3. Synthesis of anthranils

To a solution of 2-nitroacylbenzene (2.0 mmol) in Ethyl acetate/Methanol 1:1 (10 mL) was added $SnCl_2 \cdot 2H_2O$ (1.35 g, 6.0 mmol). The reaction mixture was stirred at room temperature for 24 h. The reaction was quenched by saturated $NaHCO_3$, and filtered and washed with DCM. Organic layer was then washed with water and saturated brine solution, dried over $MgSO_4$ and concentrated. Crude product was then purified by flash chromatography on silica gel using (EA/Hexane = 1:50) to give substituted anthranils in 78-90% yield.

Synthesis of 1,2,3,4-tetrahydroisoquinoline derivatives [2]



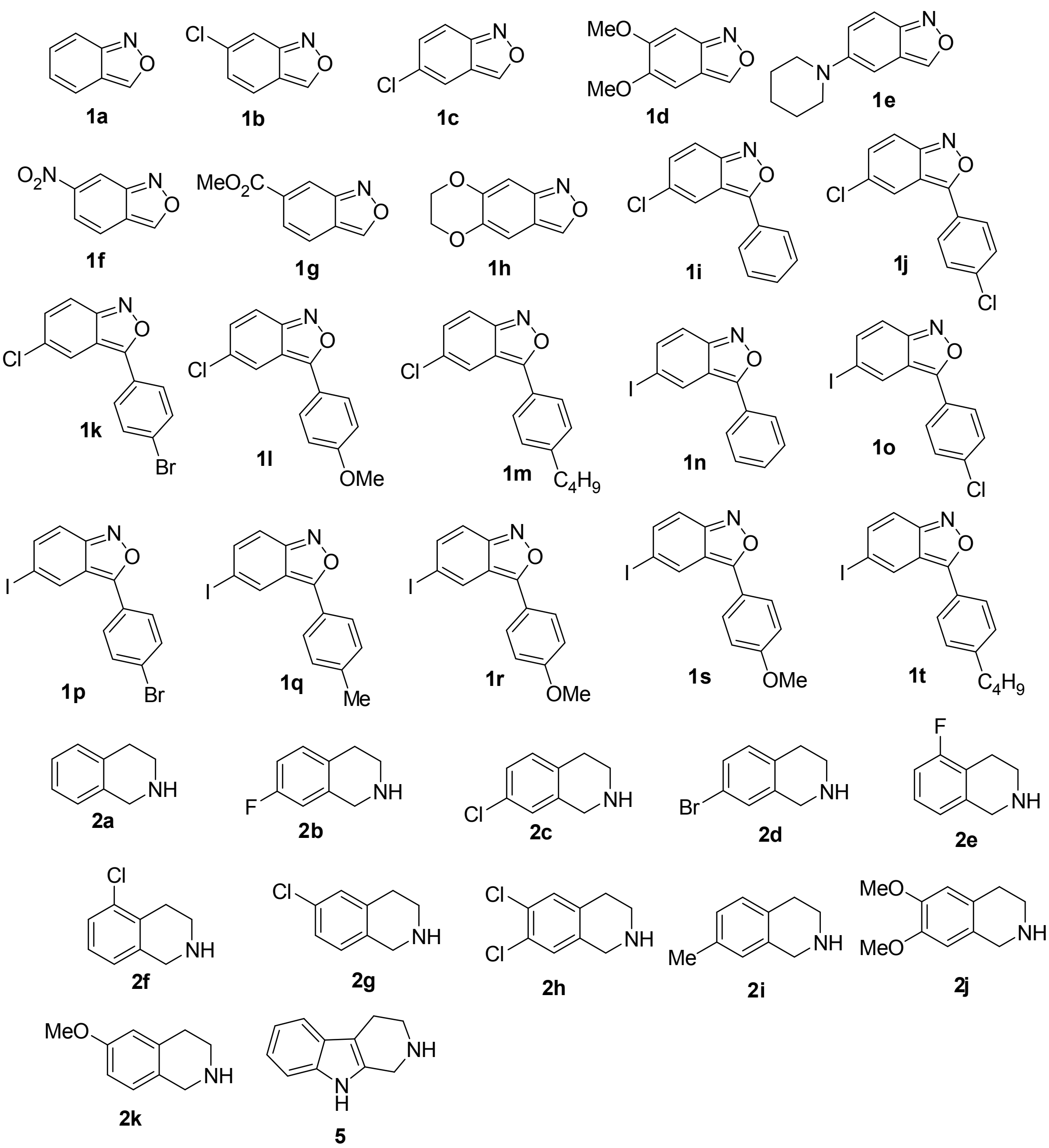
Scheme S4. Synthesis of 1,2,3,4-tetrahydroisoquinoline

Synthesis of ethyl phenethylcarbamate derivatives (step 1). To a solution of substituted phenethylamine (8.0 mmol) and triethylamine (1.2 mL, 8.8 mmol, 1.1 equiv) in CH_2Cl_2 (25 mL) was added ethyl chloroformate (0.68 mL, 8.8 mmol, 1.1 equiv) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, then water was added and extracted with ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give the residue, which was used in the next step without further purification.

Synthesis of substituted 3,4-dihydro isoquinolin -1(2H)one (step 2). Trifluoromethanesulfonic acid (5.30 mL, 50.0 equiv) was slowly added to the obtained ethyl phenethylcarbamate derivatives (5.0 mmol) at 20°C, and trifluoromethanesulfonic acid (5.30 mL, 50.0 equiv) was added in portions over 10 min. was slowly added to the obtained chlorophenylethylcarbamic acid methyl ester (5.0 mmol) at 20 °C. After stirred at 70 °C for 16 h, the whole was poured into ice-water (100 mL) and was extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over

Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford substituted 3,4-dihydro isoquinolin -1(2H)one.

Synthesis of 1,2,3,4-tetrahydroisoquinoline derivatives (step 3). An Universal Path: Under a N_2 atmosphere, a solution of $LiAlH_4$ in THF (1.0 M, 1.5 equiv) was added rapidly to a solution of 3,4-dihydro-2H-isoquinolin-1-one (1.0 equiv) in THF (100 mL). The reaction mixture was stirred under reflux for 12 h. After cooling to room temperature, 1.0 M NaOH was added slowly to the whole for quenching the excess $LiAlH_4$, after filtering out the aluminum salts, the filtrate was washed with brine and then dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 1,2,3,4-tetrahydroisoquinoline derivatives as a pale yellow oil (46~67% yield).



Scheme S5. Substrates employed for the synthesis of quinazolinone derivatives

Synthesis of target Compound 3-4

To a stirred solution of 1,2,3,4-tetrahydroisoquinoline derivatives (0.5 mmol) was added benzo[*c*]isoxazole derivatives (0.5 mmol). The mixture was heated at 130°C in a sealed tube for 1 h. After cooling to room temperature, water was added and extracted with DCM. The organic phase was washed with brine, dried over Na_2SO_4. The solvent was evaporated under reduced pressure and purification of the crude product by column chromatography, the product was obtained as a white or light yellow solid in 65%-96% yield.

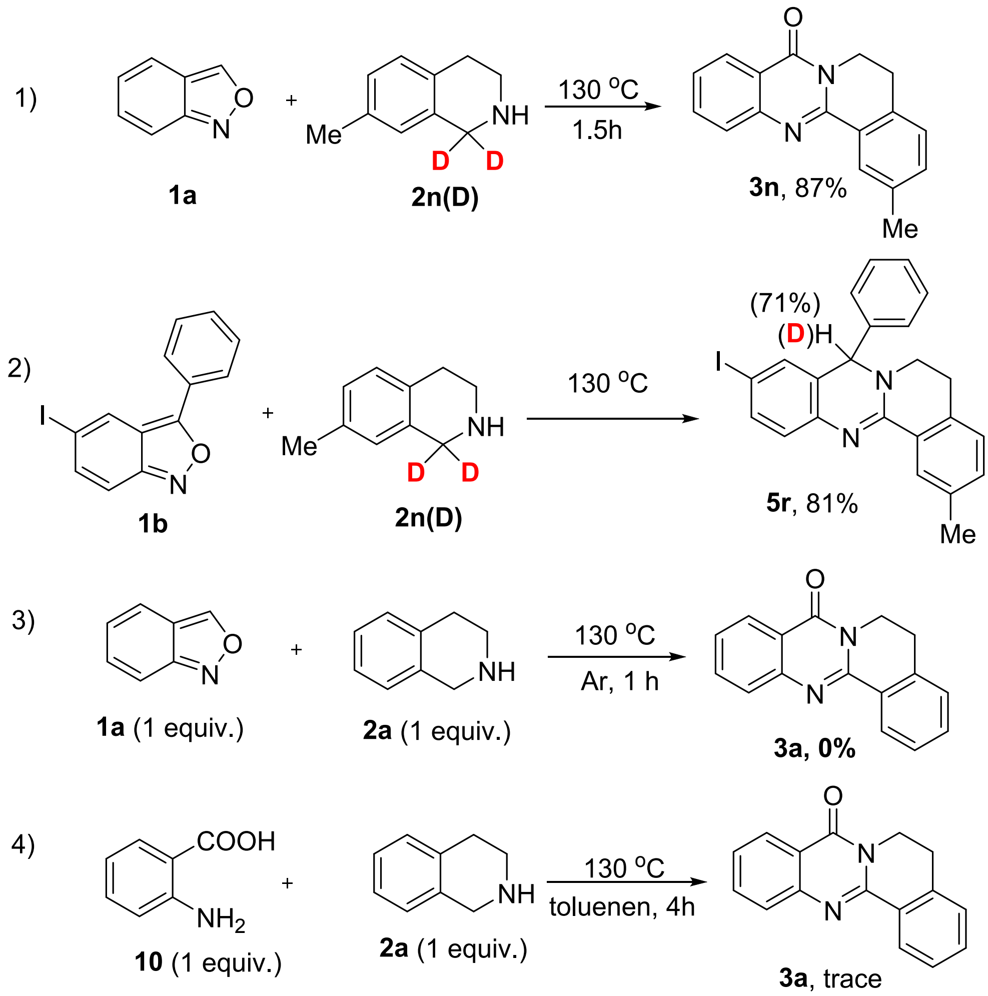
Synthesis of target Compound 5

To a stirred solution of 2,3,4,9-tetrahrdro-1*H*-pyrido[3,4-*b*]indole (0.5 mmol) in toluene (2 mL) was added benzo[*c*]isoxazole derivatives (0.5 mmol). The mixture was heated at 130°C in a sealed tube for 1 h. After cooling to room temperature, water was added and extracted with DCM. The organic phase was washed with brine, dried over Na_2SO_4. The solvent was evaporated under reduced pressure and purification of the crude product by column chromatography, the product was obtained as a white or light yellow solid in 52%-71% yield.

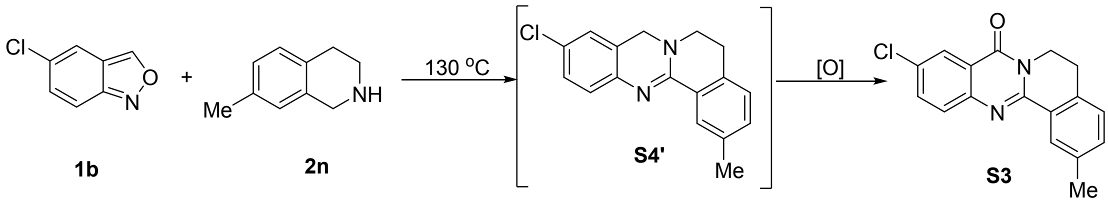
Synthesis of target Compound 9

To a stirred solution of Rutaecarpine (0.5 mmol) in DMF (2 mL) was added NaH (0.75 mmol, 60%), followed by benzyl 5-bromopentanoate **7** (1.0 mmol), the mixture was heated at reflux in a tube for 4 h, most of DMF was distilled off. After cooling to room temperature, water was added and extracted with EA. The organic phase was washed with brine, dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give a brown oil, which was added sodium hydroxide (1 mL, 2 mol/L) and THF (1 mL), the liquid was heated to reflux for 8 h. After cooling to room temperature, water was added, precipitate was formed and collected, the product **9** was obtained as a light yellow solid in 95% yield.

Control Experiments



Scheme S6. Control experiments



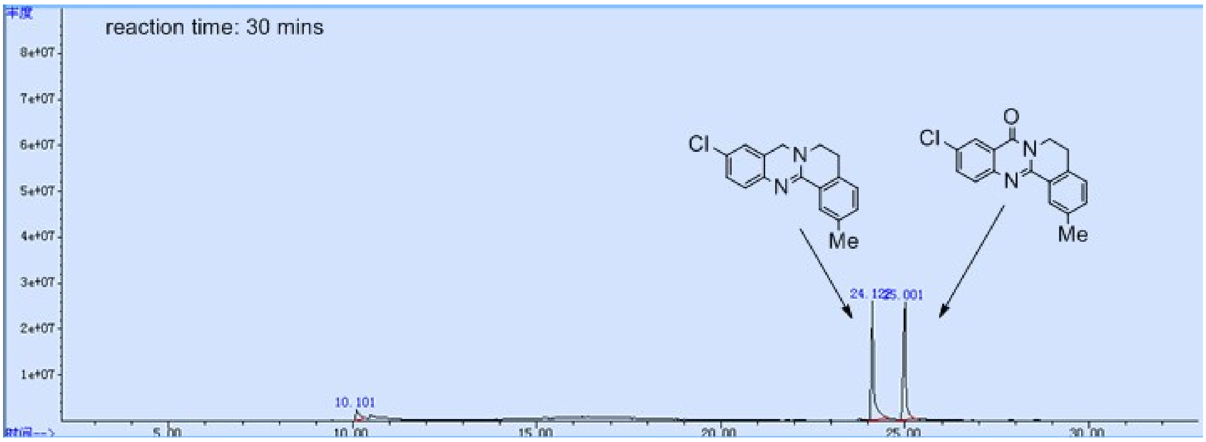


Figure S1. Detection of intermediate 4'

GC-MS:7890A/5975C

Column: HP-5MS 5% Phenyl Methyl Silox 325 °C: 30 m x 250 μm x 0.25 μm

Detection method: Initial temperature 80°C keep 3 mins

Heating rate 10 °C /min Final temperature 280 °C keep 10 mins

Split ratio 20:1

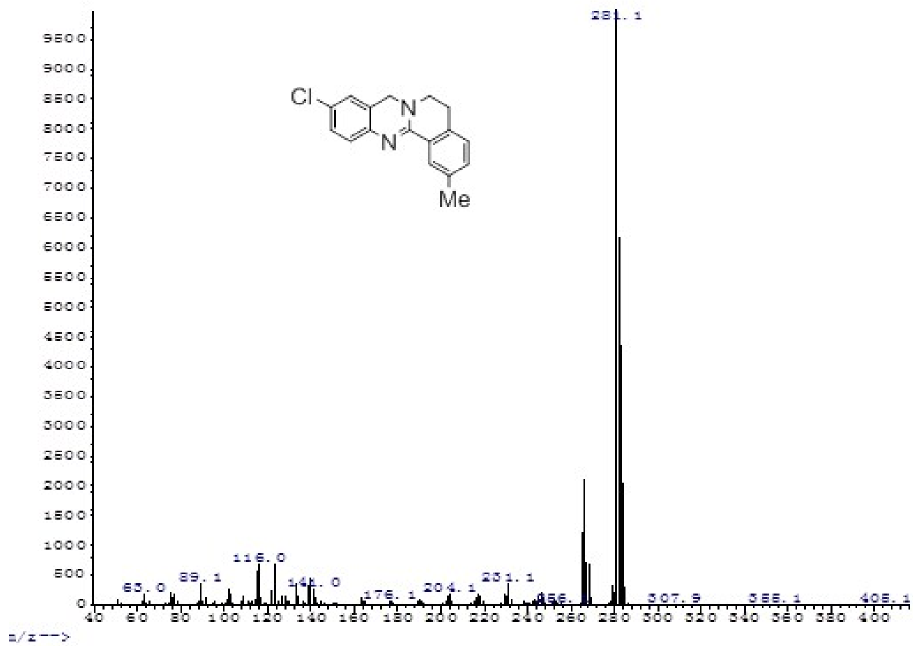


Figure S2. MS of Intermediate 4'(24.122min)

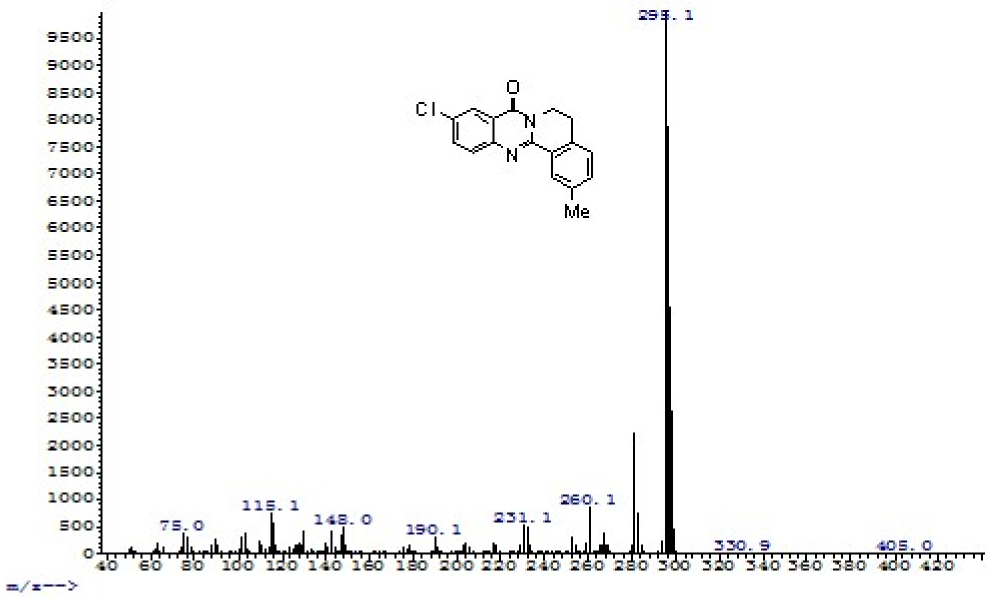
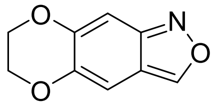
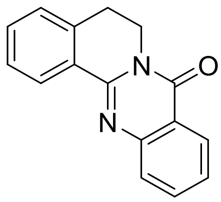


Figure S2. MS of Product 3(25.001min)

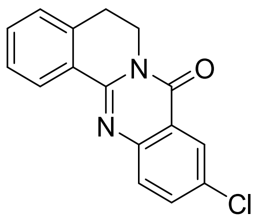
Characterization Data



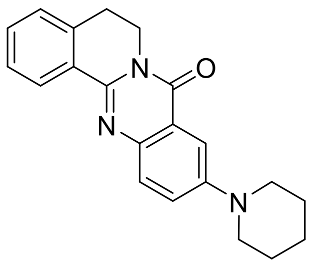
1f. Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 6.88 (s, 1H), 6.80 (s, 1H), 4.27-4.20 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.5, 149.4, 144.0, 114.8, 101.0, 65.2, 64.5. HRMS (ESI) calcd for $C_9H_8NO_3$ ($[M+H]^+$): 178.0499 found 178.0452.



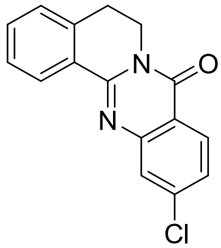
3a, white solid. Spectral data for this compound was consistent with those previously reported [3]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 7.4 Hz, 1H), 8.33 (d, J = 7.7 Hz, 1H), 7.81-7.77 (m, 2H), 7.50-7.46 (m, 3H), 7.31 (d, J = 7.2 Hz, 1H), 4.44 (t, J = 6.4 Hz, 2H), 3.13 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 149.8, 146.8, 137.2, 134.5, 132.3, 127.8, 127.6, 127.0, 126.9, 126.8, 120.5, 39.7, 27.4.



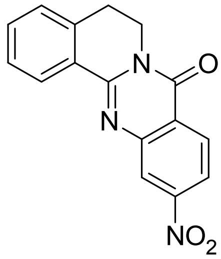
3b, white solid. Spectral data for this compound was consistent with those previously reported [3]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 2.3 Hz, 1H), 7.71-7.69 (m, 1H), 7.62-7.59 (m, 1H), 7.45-7.35 (m, 2H), 7.22 (d, J = 7.3 Hz, 1H), 4.33 (t, J = 6.5 Hz, 2H), 3.04 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 150.7, 137.1, 134.8, 132.4, 132.2, 129.1, 128.2, 127.8, 127.6, 126.3, 121.6, 39.8, 27.4.



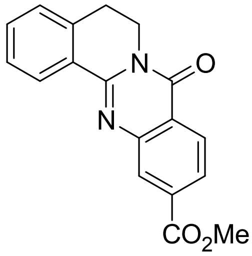
3c, light yellow solid. ^{1}H NMR (300 MHz, DMSO-d6) δ 8.31 (dd, J = 7.6, 1.2 Hz, 1H), 7.63-7.57 (m, 2H), 7.54-7.38 (m, 4H), 4.29 (t, J = 6.5 Hz, 2H), 3.30-3.27 (m, 4H), 3.09 (t, J = 6.5 Hz, 2H), 1.66-1.57 (m, 6H). ^{13}C NMR (75 MHz, DMSO-d6) δ 160.9, 150.4, 146.6, 140.3, 137.6, 131.5, 129.9, 128.7, 128.2, 127.6, 124.7, 121.5, 108.7, 49.6, 27.1, 25.5, 24.3. HRMS (ESI) calcd for $C_{21}H_{22}N_3O^+$ ($[M+H]^+$): 332.1757 found 332.1762.



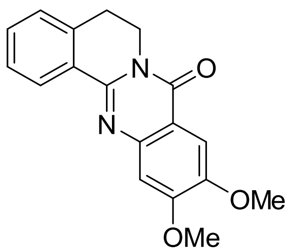
3d, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 7.73 (d, J = 1.9 Hz, 1H), 7.46-7.32 (m, 3H), 7.22 (d, J = 7.3 Hz, 1H), 4.33 (t, J = 6.4 Hz, 2H), 3.04 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 150.7, 148.5, 140.5, 137.2, 132.3, 128.4, 128.3, 127.8, 127.6, 127.2, 126.9, 119.1, 39.7, 27.3.



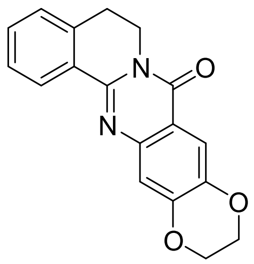
3e, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.19-8.16 (m, 1H), 7.45-7.42 (m, 1H), 7.36-7.32 (m, 2H), 7.29-7.26 (m, 2H), 4.75 (t, J = 6.9 Hz, 2H), 3.28 (t, J = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 147.6, 147.3, 133.6, 130.9, 128.3, 128.2, 125.7, 119.7, 118.4, 117.6, 114.8, 43.4, 28.1. HRMS (ESI) calcd for $C_{16}H_{12}N_3O_3^+$ ([M+H]$^+$): 294.0873 found 294.0879.



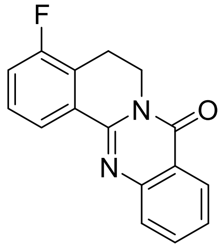
3f, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.48 (m, 2H), 8.30 (d, J = 8.3 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.48-7.39 (m, 2H), 7.24 (d, J = 7.2 Hz, 1H), 4.36 (t, J = 6.4 Hz, 2H), 3.93 (s, 3H), 3.06 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 160.8, 150.7, 146.3, 137.3, 135.7, 132.8, 128.8, 128.7, 128.0, 127.7, 127.4, 126.9, 123.2, 52.7, 39.9, 27.3. HRMS (ESI) calcd for $C_{18}H_{15}N_2O_3^+$ ([M+H]$^+$): 307.1077 found 307.1079.



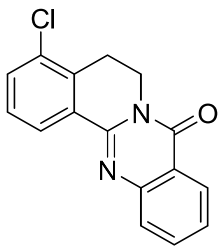
3g, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 7.2 Hz, 1H), 7.56 (s, 1H), 7.40-7.36 (m, 2H), 7.21 (d, J = 7.1 Hz, 1H), 7.15 (s, 1H), 4.34 (t, J = 6.4 Hz, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 3.03 (t, J = 6.3 Hz, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 160.6, 155.2, 149.2, 148.7, 136.9, 131.9, 128.0, 127.8, 113.9, 107.4, 105.8, 56.5, 39.7, 27.5.



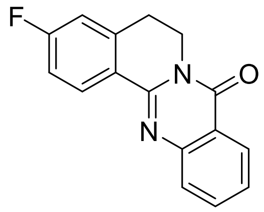
3h, white solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.38 (d, J = 7.4 Hz, 1H), 7.69 (s, 1H), 7.41-7.34 (m, 2H), 7.22-7.19 (m, 2H), 4.33-4.30 (m, 4H), 4.28-4.26 (m, 2H), 3.01 (t, J = 6.4 Hz, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 160.7, 149.8, 148.4, 143.7, 136.9, 131.7, 127.7, 127.5, 113.6, 64.6, 64.2, 39.6, 37.5. HRMS (ESI) calcd for $C_{18}H_{15}N_2O_3^+$ ([M + H]$^+$): 307.1077 found 307.1080.



3i, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25-8.22 (m, 2H), 7.69-7.68 (m, 2H), 7.42-7.38 (m, 1H), 7.34-7.31 (m, 1H), 7.14 (t, J = 8.2 Hz, 1H), 4.34 (t, J = 6.5 Hz, 2H), 3.06 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 161.5, 158.4 (d, J = 244.1 Hz), 148.5, 147.4, 134.4, 131.5, 128.4 (d, J = 8.1 Hz), 127.6, 126.9, 124.3 (d, J = 19.8 Hz), 123.6, 120.8, 118.2 (d, J = 21.3 Hz), 38.9, 20.1.

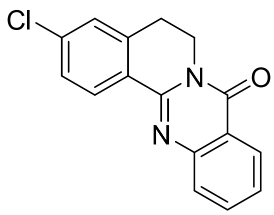


3j, white solid. Spectral data for this compound was consistent with those previously reported [2b] ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.41 (d, J = 7.8 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.75-7.70 (m, 2H), 7.49(dd, J = 7.9, 1.1 Hz,1H), 7.44-7.41 (m, 1H), 7.33 (t, J = 7.9 Hz, 1H), 4.35 (t, J = 6.5 Hz, 2H), 3.16 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 161.1, 149.1, 146.3, 136.2, 134.8, 133.0, 132.8, 130.4, 137.3, 127.2, 127.0, 126.9, 120.4, 39.0, 24.5.

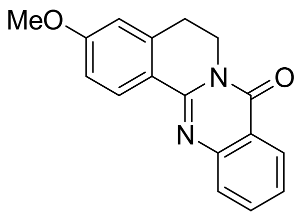


3k, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.43 (dd, J = 8.8, 5.7 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.69-7.65 (m, 2H), 7.41-7.37

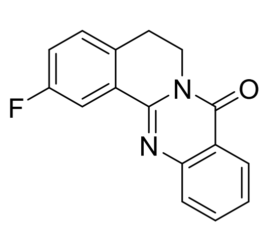
(m, 1H), 7.05 (dt, J = 5.2, 2.5 Hz, 1H), 6.91 (dd, J = 8.6, 2.4 Hz, 1H), 4.35 (t, J = 6.4 Hz, 2H), 3.02 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0 (d, J = 246.5 Hz), 161.6, 148.7, 139.7 (d, J = 8.8 Hz), 134.4, 130.8 (d, J = 9.1 Hz), 127.4, 126.9, 126.6, 120.6.



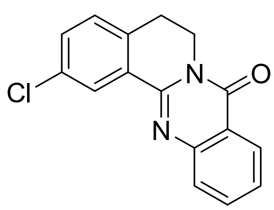
3l, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41(d, J = 8.2 Hz, 1H), 8.23 (dd, J = 7.8, 0.9 Hz, 1H), 7.76-7.67 (m, 2H), 7.43-7.39 (m, 1H), 7.35 (dd, J = 8.5, 1.5 Hz, 1H), 7.23 (d, J = 1.8 Hz, 1H), 4.35 (t, J = 6.4 Hz, 2H), 3.02 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 149.2, 138.8, 134.8, 130.2, 128.3, 127.7, 127.1, 126.7, 120.3, 39.5, 27.2.



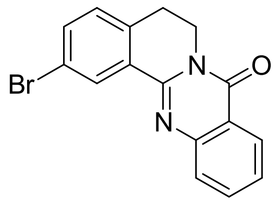
3m, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.77-7.75 (m, 1H), 7.66 (t, J = 8.0 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 6.89 (dd, J = 8.8, 2.4 Hz, 1H), 6.70-6.69 (m, 1H), 4.32 (t, J = 6.4 Hz, 2H), 3.81 (s, 3H), 2.99 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 161.5, 149.8, 139.3, 134.4, 130.5, 126.9, 126.8, 126.3, 120.2, 113.8, 112.4, 55.6, 39.6, 27.7.



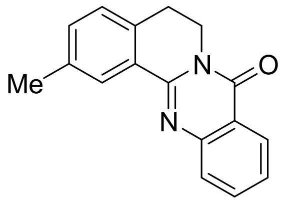
3n, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.0 Hz, 1H), 8.13 (dd, J = 9.5, 2.6 Hz, 1H), 7.74-7.67 (m, 2H), 7.43-7.39 (m, 1H), 7.22-7.20 (m, 1H), 7.12 (dt, J = 8.2, 2.7 Hz, 1H), 4.34 (t, J = 6.4 Hz, 2H), 3.01 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d, J = 244.1 Hz), 161.4, 148.5, 147.1, 134.5, 132.8, 131.0, 129.2 (d, J = 7.7 Hz), 127.5, 127.0 (d, J = 6.6 Hz), 120.7, 119.3, 118.9, 114.7 (d, J = 24.1 Hz), 39.7, 26.8.



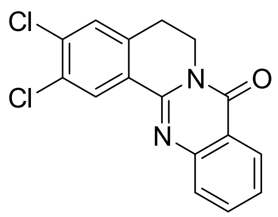
3o, white solid. Spectral data for this compound was consistent with those previously reported [2b] . ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 2.2 Hz, 1H), 8.26-8.23 (m, 1H), 7.75-7.68 (m, 2H), 7.45-7.37 (m, 2H), 7.18-7.16 (m, 1H), 4.34(t, J = 6.4 Hz, 2H), 3.01 (t, J = 6.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 148.4, 146.9, 135.4, 134.6, 133.7, 131.9, 130.6, 128.9, 128.1, 127.4, 126.9, 120.7, 39.6, 26.9.



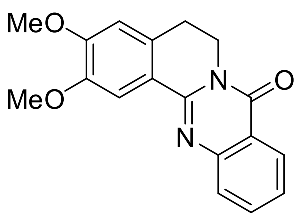
3p, white solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 2.0 Hz, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.76-7.71 (m, 2H), 7.53 (dd, J = 8.0, 2.0 Hz, 1H), 7.45-7.40 (m, 1H), 7.11 (d, J = 8.1 Hz, 1H), 4.34 (t, J = 6.3 Hz, 2H), 3.00 (t, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 148.2, 146.9, 135.8, 134.8, 134.6, 131.0, 130.9, 129.2, 127.4, 127.1, 126.9, 121.5, 120.7, 39.5, 27.1. HRMS (ESI) calcd for $C_{16}H_{12}BrN_2O$ ([M + H]$^+$): 327.0128 found 327.0125.



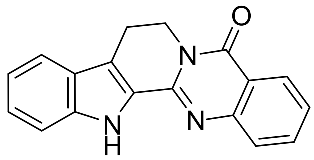
3q, white solid, Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.23 (m, 2H), 7.78-7.76 (m, 1H), 7.69 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.23 (d, J = 7.7 Hz, 1H), 7.11 (d, J = 7.7 Hz, 1H), 4.33 (d, J = 6.4 Hz, 2H), 2.99 (t, J = 6.4 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 149.8, 137.5, 134.4, 134.3, 132.9, 128.4, 127.5, 127.3, 126.9, 126.6, 120.6, 39.8, 27.1, 21.3.



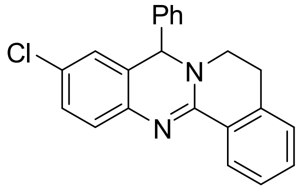
3r, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.22 (d, J = 7.8 Hz, 1H), 7.70-7.69 (m, 2H), 7.43-7.40 (m, 1H), 7.33 (s, 1H), 4.33 (t, J = 6.5 Hz, 2H), 3.00 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 147.5, 147.3, 136.4, 135.9, 134.5, 132.1, 129.8, 129.4, 127.7 127.1, 126.9, 120.8, 39.3, 26.8. HRMS (ESI) calcd for $C_{16}H_{11}Cl_2N_2O$ ([M + H]$^+$): 317.0243 found 317.0248.



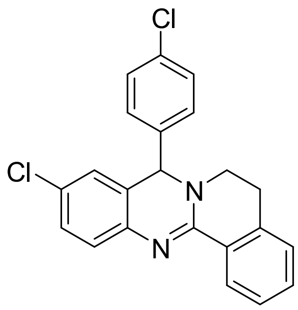
3s, white solid. Spectral data for this compound was consistent with those previously reported [2b]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = .8 Hz, 1H), 7.92 (s, 1H), 7.68-7.67 (m, 2H), 7.36 (t, J = 8.0 Hz, 1H), 6.66 (s, 1H), 4.33 (t, J = 6.4 Hz, 2H), 3.97 (s, 3H), 3.89 (s, 3H), 2.96 (t, J = 6.4 Hz, 2H).



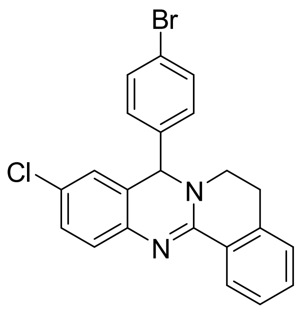
light yellow solid. Spectral data for this compound was consistent with those previously reported.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (br, 1H), 8.24 (d, J = 8.0 Hz, 1H), 7.64-7.63 (m, 2H), 7.55 (d, J = .8 Hz, 1H), 7.37-7.36 (m, 1H), 7.32-7.30 (m, 1H), 7.26 (t, J = 7.8 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H), 4.52 (t, J = 6.9 Hz, 2H), 3.17 (t, J = 6.9 Hz, 2H).



4a, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (br, 1H), 7.30-7.28 (m, 2H), 7.23-7.19 (m, 5H), 7.07-7.04 (m, 2H), 6.71 (d, J = 2.2 Hz, 1H), 5.45 (s, 1H), 3.29-3.23 (m, 1H), 3.17-3.11 (m, 1H), 2.94-2.86 (m, 1H), 2.76-2.70 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 142.7, 136.3, 130.9, 129.2, 128.6, 127.6, 127, 127.2, 126.9, 126.2, 125.9, 65.2, 46.5, 28.4. HRMS (ESI) calcd for $C_{22}H_{18}ClN_2$ ([M+H]$^+$): 345.1153 found 345.1148.

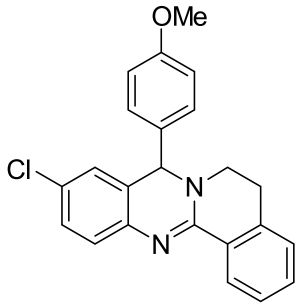


4b, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (br, 1H), 7.40 (t, J = 3.6 Hz, 2H), 7.31-7.26 (m, 4H), 7.18-7.14 (m, 2H), 6.78 (d, J = 2.2 Hz, 1H), 5.54 (s, 1H), 3.39-3.33 (m, 1H), 3.26-3.19 (m, 1H), 3.04-2.97 (m, 1H), 2.87-2.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 141.2, 136.2, 134.5, 131.1, 129.5, 129.4, 128.8, 128.3, 127.6, 127.3, 127.2, 126.1, 125.5, 64.5, 46.5, 28.4. HRMS (ESI) calcd for $C_{22}H_{17}Cl_2N_2$ ([M+H]$^+$): 379.0763 found 379.0761.

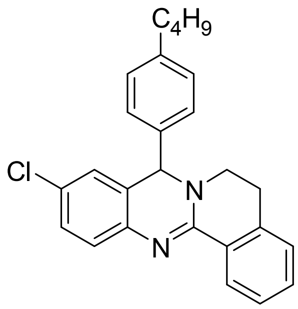


4c, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.36 (d, J = 8.3 Hz, 2H), 7.31 (t, J = 2.6 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.08-7.04 (m, 2H), 6.67 (d, J = 2.1 Hz, 1H), 5.47 (s, 1H), 3.31-3.27 (m, 1H), 3.16-3.10 (m, 1H), 2.95-2.88 (m, 1H), 2.78-2.72 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 141.7, 136.2, 132.3, 131.0, 129.4, 128.7, 128.6, 127.6, 127.3, 126.2, 126.1, 125.5, 122.6, 64.5, 46.5, 28.4. HRMS

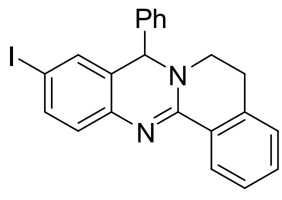
(ESI) calcd for $C_{22}H_{17}BrClN_2$ ([M+H]$^+$): 423.0258 found 423.0254.



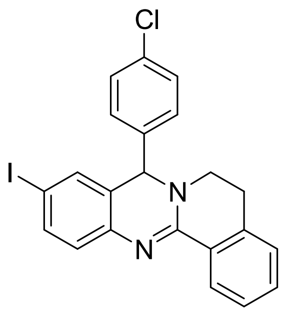
4d, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.48 (s, 1H), 7.40-7.38 (m, 2H), 7.25 (d, J = 8.6 Hz, 3H), 7.16-7.14 (m, 2H), 6.84 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 2.2 Hz, 1H), 5.52 (s, 1H), 3.77 (s, 3H), 3.38-3.34 (m, 1H), 3.29-3.22 (m, 1H), 3.02-2.96 (m, 1H), 2.86-2.81 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.8, 151.6, 136.3, 132.3, 128.6, 128.3, 127.8, 127.3, 126.2, 114.5, 113.7, 64.5, 55.3, 46.4, 28.3. HRMS (ESI) calcd for $C_{23}H_{20}ClN_2O$ ([M+H]$^+$): 375.1259 found 375.1263.



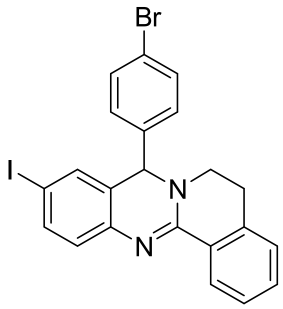
4e, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.43 (br, 1H), 7.32-7.30 (m, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.3 Hz, 3H), 7.07-7.05 (m, 2H), 6.73 (d, J = 2.2 Hz, 1H), 5.46 (s, 1H), 3.31-3.27 (m, 1H), 3.22-3.19 (m, 1H), 2.97-2.89 (m, 1H), 2.79-2.74 (m, 1H),1.19 (s, 9H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.7, 151.6, 139.4, 136.3, 131.1, 128.5, 127.8, 127.2, 126.6, 126.2, 126.1, 64.8, 46.5, 34.6, 31.3, 28.4. HRMS (ESI) calcd for $C_{26}H_{26}ClN_2$ ([M+H]$^+$): 401.1779 found 401.1777.



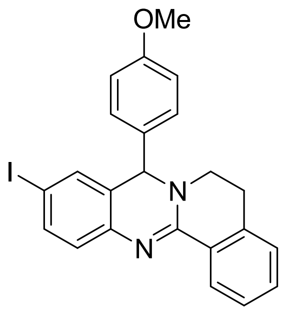
4f, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.56 (br, 1H), 7.49 (dd, J = 8.4, 1.8 Hz, 1H), 7.40 (t, J = 4.2 Hz, 2H), 7.33-7.29 (m, 5H), 7.15 (s, 3H), 5.53 (s, 1H), 3.40-3.34 (m, 1H), 3.29-3.22 (m, 1H), 3.04-2.97 (m, 1H), 2.87-2.80 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.9, 142.7, 137.4, 136.3, 134.9, 130.9, 129.2, 128.6, 127.6, 127.2, 126.9, 64.8, 46.6, 28.4. HRMS (ESI) calcd for $C_{22}H_{18}IN_2$ ([M+H]$^+$): 437.0509 found 437.0512.



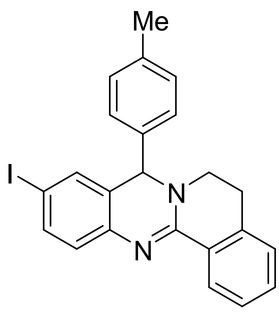
4g, light yellow solid. [1]H NMR (400 MHz, $CDCl_3$) δ 8.47 (br, 1H), 7.49 (dd, J = 8.4, 1.9 Hz, 1H), 7.43-7.38 (m, 2H), 7.31-7.29 (m, 2H), 7.27-7.25 (m, 2H), 7.15-7.13 (m, 1H), 7.11 (d, J = 1.7 Hz, 1H), 5.56 (s, 1H), 3.41-3.35 (m, 1H), 3.26-3.19 (m, 1H), 3.05-2.97 (m, 1H), 2.86-2.80 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 141.0, 137.7, 136.2, 134.9, 134.5, 129.4, 128.4, 127.7, 127.3, 87.9, 64.1, 46.6, 28.3. HRMS (ESI) calcd for $C_{22}H_{17}ClIN_2$ ([M+H]$^+$): 471.0119 found 471.0123.



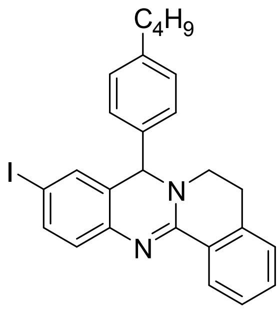
4h, light yellow solid. [1]H NMR (400 MHz, $CDCl_3$) δ 8.48 (br, 1H), 8.50 (dd, J = 8.4, 1.9 Hz, 1H), 7.47-7.45 (m, 2H), 7.42-7.40 (m, 2H), 7.22-7.20 (m, 2H), 7.16-7.14 (m, 1H), 7.11 (d, J = 1.6 Hz, 1H), 5.56 (s, 1H), 3.39-3.37 (m, 1H), 3.27-3.21 (m, 1H), 3.05-2.98 (m, 1H), 2.87-2.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 141.4, 137.7, 136.2, 134.9, 132.4, 128.7, 127.3, 122.8, 64.2, 46.7, 28.3. HRMS (ESI) calcd for $C_{22}H_{17}BrIN_2$ ([M+H]$^+$): 514.9614 found 514.9608.



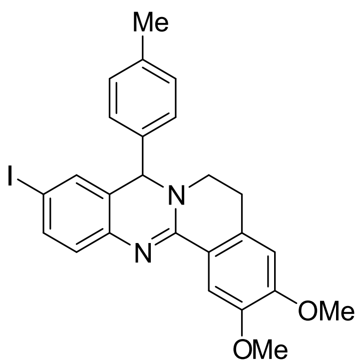
4i, light yellow solid. [1]H NMR (400 MHz, $CDCl_3$) δ 8.53 (br, 1H), 7.49 (dd, J = 8.4, 1.9 Hz, 1H), 7.42-7.40 (m, 2H), 7.25-7.23 (m, 2H), 7.15-7.12 (m, 3H), 6.86-6.84 (m, 2H), 5.55 (s, 1H), 3.78 (s, 3H), 3.42-3.38 (m, 1H), 3.30-3.23 (m, 1H), 3.04-2.97 (m, 1H), 2.86-2.79 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 151.8, 137.5, 136.4, 135.0, 128.4, 128.0, 127.4, 114.5, 64.1, 55.3, 46.5, 28.2. HRMS (ESI) calcd for $C_{23}H_{20}IN_2O$ ([M+H]$^+$): 467.0615 found 467.0612.



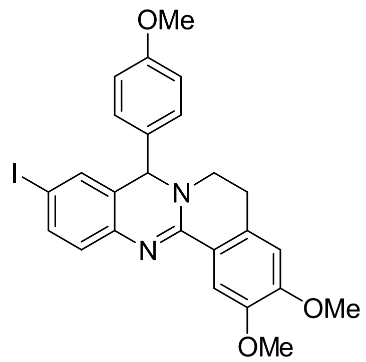
4j, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.49 (dd, J = 8.4, 1.9 Hz, 1H), 7.41 (t, J = 4.3 Hz, 2H), 7.22-7.20 (m, 2H), 7.15-7.12 (m, 5H), 5.53 (s, 1H), 3.41-3.23 (m, 1H), 3.30-3.23 (m, 1H), 3.04-2.96 (m, 1H), 2.86-2.79 (m, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 139.6, 138.5, 137.5, 136.6, 134.9, 129.8, 129.1, 127.8, 127.2, 126.9, 64.5, 46.5, 28.3, 21.1. HRMS (ESI) calcd for $C_{23}H_{20}IN_2$ ([M+H]$^+$): 451.0666 found 451.0671.



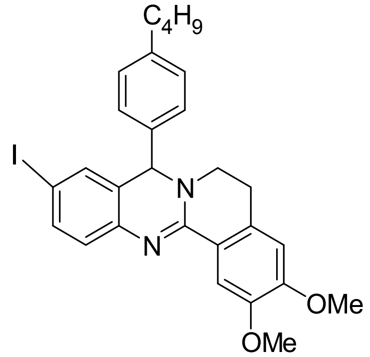
4k, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (br, 1H), 7.41 (dd, J = 8.4, 1.6 Hz, 1H), 7.34 (br, 2H), 7.25-7.23 (m, 3H), 7.15-7.13 (m, 2H), 7.08-7.06 (m, 2H), 5.48 (s, 1H), 3.34-3.30 (m, 1H), 3.24-3.18 (m, 1H), 2.99-2.91 (m, 1H), 2.78-2.72 (m, 1H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 137.6, 136.4, 134.9, 127.3, 126.7, 126.2, 64.5, 46.7, 34.6, 31.2. HRMS (ESI) calcd for $C_{26}H_{26}IN_2$ ([M+H]$^+$): 493.1135 found 493.1131.



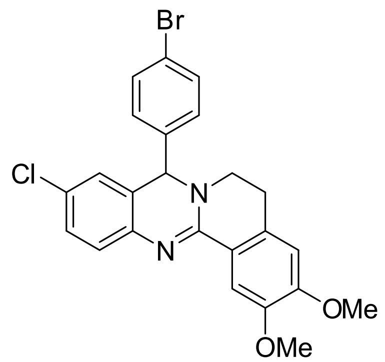
4l, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (br, 1H), 7.37 (dd, J = 8.4, 1.6 Hz, 1H), 7.12 (d, J = 8.0 Hz, 3H), 7.03 (d, J = 8.1 Hz, 3H), 6.50 (s, 1H), 5.36 (s, 1H), 3.96 (s, 3H), 3.82 (s, 3H), 3.26-3.23 (m, 1H), 3.17-3.10 (m, 1H), 2.85-2.78 (m, 1H), 2.69-2.62 (m, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 148.0, 138.3, 137.3, 134.9, 129.9, 126.9, 109.5, 64.4, 56.0, 46.6, 27.9, 21.2. HRMS (ESI) calcd for $C_{25}H_{24}IN_2O_2$ ([M+H]$^+$): 511.0877 found 511.0882.



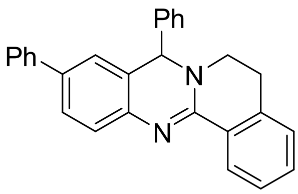
4m, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (br, 1H), 7.39 (dd, J = 8.4, 1.7 Hz, 1H), 7.18 (d, J = 6.8 Hz, 3H), 7.02 (d, J = 1.6 Hz, 1H), 6.75 (d, J = 8.6 Hz, 2H), 6.51 (s, 1H), 5.37 (s, 1H), 3.97 (s, 3H), 3.82 (s, 3H), 3.69 (s, 3H), 3.28-3.24 (m, 1H), 3.18-3.11 (m, 1H), 2.84-2.79 (m, 1H), 2.70-2.65 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.7, 151.8, 148.1, 137.4, 134.9, 128.3, 128.1, 114.5, 113.5, 109.6, 64.1, 55.1, 55.3, 49.8, 46.6. HRMS (ESI) calcd for $C_{25}H_{24}IN_2O_3$ ([M+H]$^+$): 527.0826 found 527.0823.



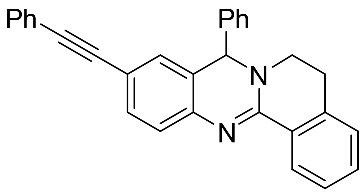
4n, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (br, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 1.5 Hz, 1H), 6.52 (s, 1H), 5.42 (s, 1H), 4.01 (s, 3H), 3.83 (s, 3H), 3.37-3.26 (m, 1H), 3.21-3.15 (m, 1H), 2.91-2.83 (m, 1H), 2.72-2.65 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.9, 137.5, 134.9, 126.6, 125.4, 109.6, 85.9, 64.5, 56.1, 34.6, 31.2, 27.7. HRMS (ESI) calcd for $C_{28}H_{30}IN_2O_2$ ([M + H]$^+$): 553.1346 found 553.1351.



4o, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (br, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.1 Hz, 3H), 7.07-7.05 (m, 1H), 6.67 (s, 1H), 6.51 (s, 1H), 5.44 (s, 1H), 3.97 (s, 3H), 3.82 (s, 3H), 3.28-3.26 (m, 1H), 3.15-3.10 (m, 1H), 2.87-2.83 (m, 1H), 2.70-2.66 (m, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.6, 148.2, 132.4, 128.6, 126.1, 109.6, 64.5, 56.1, 46.7, 27.8. HRMS (ESI) calcd for $C_{24}H_{21}BrClN_2O_2$ ([M+H]$^+$): 483.0469 found 483.0471.

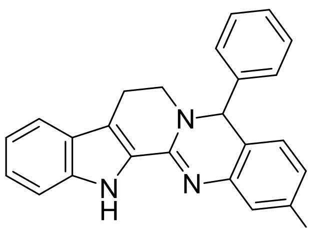


4p, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (br, 1H), 7.39-7.34 (m, 5H), 7.31-7.27 (m, 5H), 7.23-7.19 (m, 4H), 7.08-7.06 (m, 1H), 6.98 (d, J = 2.4 Hz, 1H), 5.64 (s, 1H), 3.39-3.36 (m, 1H), 3.26-3.20 (m, 1H), 2.99-2.92 (m, 1H), 2.80-2.74 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 140.3, 136.4, 129.2, 128.2, 127.5, 127.4, 127.3, 126.7, 124.9, 65.7, 46.8, 28.2. HRMS (ESI) calcd for $C_{28}H_{23}ClN_3O$ ([M+H]$^+$): 387.1856 found 387.1859.

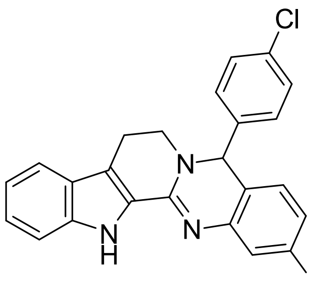


251-2

4q, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (br, 1H), 7.49-7.47 (m, 2H), 7.42-7.38 (m, 4H), 7.36-7.35 (m, 2H), 7.33-7.29 (m, 6H), 7.17-7.14 (m, 1H), 7.03 (s, 1H), 5.60 (s, 1H), 3.43-3.37 (m, 1H), 3.31-3.25 (m, 1H), 3.06-2.98 (m, 1H), 2.88-2.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 142.9, 136.3, 132.0, 131.5, 129.7, 129.1, 128.5, 128.3, 128.1, 127.8, 127.2, 127.0, 124.5, 123.4, 89.7, 89.4, 65.3, 46.6, 28.4. HRMS (ESI) calcd for $C_{30}H_{23}N_2$ ([M+H]$^+$): 411.1856 found 411.1862.

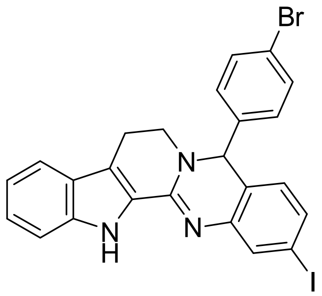


6a, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.15 (br, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.45-7.34 (m, 6H), 7.26-7.17 (m, 3H), 7.11-7.04 (m, 2H), 5.60 (s, 1H), 3.67-3.60 (m, 1H), 3.43-3.37 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 143.0, 138.1, 137.6, 135.5, 129.3, 128.7, 127.1, 125.4, 124.9, 120.1, 119.5, 112.4, 87.7, 63.9, 48.1, 20.6. HRMS (ESI) calcd for $C_{24}H_{19}IN_3$ ([M+H]$^+$): 476.0618 found 476.0621.

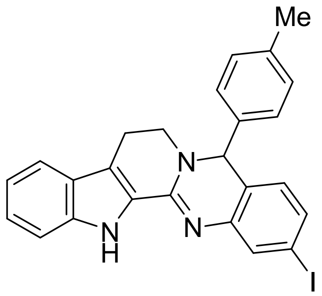


6b, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.76 (br, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.44 (dd, J = 8.4, 1.8 Hz, 1H), 7.36-7.33 (m, 5H), 7.29-7.25 (m, 1H), 7.13-7.10 (m, 3H), 5.61 (s, 1H), 3.71-3.64 (m, 1H), 3.42-3.36 (m, 1H), 3.09-2.95 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 140.6, 138.5, 137.9, 135.4, 134.9, 129.7, 128.5, 125.9, 124.9, 120.6, 119.8, 112.7, 63.2, 48.2, 20.4. HRMS (ESI) calcd for $C_{24}H_{18}ClIN_3$

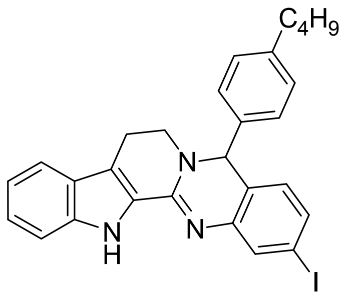
([M+H]$^+$): 510.0228 found 510.0226.



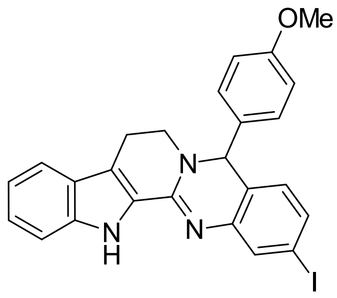
6c light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.59 (br, 1H), 7.42 (d, J = 8.0 Hz,3H), 7.38-7.35 (m, 1H), 7.28-7.26 (m, 1H), 7.19-7.16 (m, 3H), 7.05-7.01 (m, 3H), 5.49 (s, 1H), 3.61-3.55 (m, 1H), 3.33-3.27 (m, 1H), 3.00-2.85 (m, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 147.4, 140.7, 138.8, 138.1, 135.5, 132.7, 128.9, 126.5, 124.5,123.4, 120.8, 119.9, 112.8, 63.3, 48.3, 20.4. HRMS (ESI) calcd for $C_{24}H_{18}BrIN_3$ ([M+H]$^+$): 553.9723 found 553.9719.



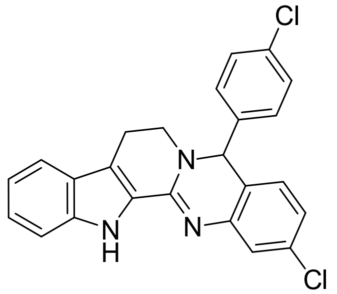
6d, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.73 (br, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.20-7.18 (m, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.04-7.00 (m, 3H), 5.47 (s, 1H), 3.59-3.53 (m, 1H), 3.36-3.30 (m, 1H), 2.97-2.88 (m, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 147.8, 139.4, 138.9, 137.7, 135.5, 130.1, 127.1, 126.7, 124.9, 120.5, 119.7, 112.7, 63.6, 48.1, 21.2. HRMS (ESI) calcd for $C_{25}H_{21}IN_3$ ([M+H]$^+$): 490.0775 found 490.0778.



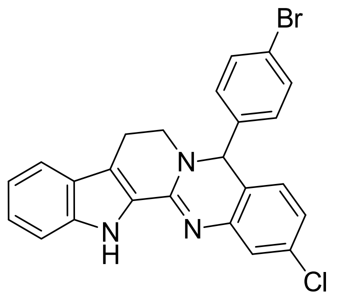
6e, light yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.96 (br, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.32 (dd, J = 8.4, 1.9 Hz, 1H), 7.28-7.20 (m, 5H), 7.13-7.09 (m, 2H), 7.01-6.96 (m, 2H), 5.45 (s, 1H), 3.56-3.49 (m, 1H), 3.35-3.29 (m, 1H), 2.93-2.90 (m, 2H), 1.21 (s, 9H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 151.5, 148.5, 139.9m 137.9, 137.4, 135.4, 129.9, 126.6, 126.1, 125.6, 125.5, 125.4, 124.6, 119.9, 119.5, 116.4, 112.3, 87.5, 63.5, 47.9, 34.6, 31.3, 20.6. HRMS (ESI) calcd for $C_{28}H_{27}IN_3$ ([M+H]$^+$): 532.1244 found 532.1246.



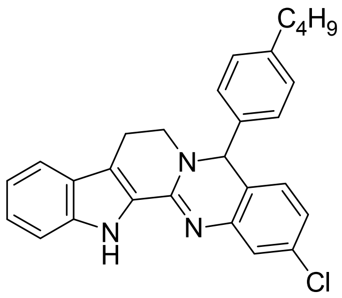
6f, light yellow solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.87 (br, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.44 (dd, J = 8.4, 1.7 Hz, 1H), 7.37-7.30 (m, 3H), 7.26-7.24 (m, 1H), 7.13-7.10 (m, 3H), 6.89 (d, J = 8.6 Hz, 2H), 5.55 (s, 1H), 3.81(s, 3H), 3.67-3.60 (m, 1H), 3.45-3.38 (m, 1H), 3.06-2.98 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 148.0, 138.1, 137.5, 135.5, 135.0, 128.4, 125.3, 125.1, 120.2, 119.6, 114.6, 112.4, 87.8, 63.2, 55.4, 47.9, 20.6. HRMS (ESI) calcd for $C_{25}H_{21}IN_3O$ ([M+H]$^+$): 506.0724 found 506.0721.



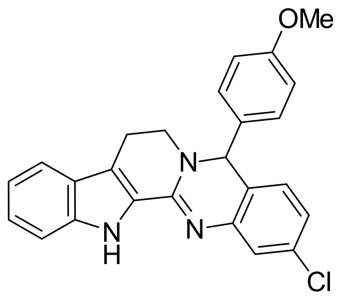
6g, light yellow solid Compound**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br, 1H),7.42 (d, J = 7.6 Hz, 1H), 7.30-7.25 (m, 4H), 7.16-7.12 (m, 3H), 7.03-6.99 (m, 2H), 6.70 (d, J = 2.0 Hz, 1H), 5.51 (s, 1H), 3.56-3.50 (m, 1H), 3.31-3.24 (m, 1H), 2.98-2.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 141.5, 137.9, 134.5, 129.5, 128.9, 128.5, 126.6, 125.4, 120.1, 119.6, 112.4, 63.6, 48.1, 20.6. HRMS (ESI) calcd for $C_{24}H_{18}Cl_2N_3$ ([M+H]$^+$): 418.0872 found 418.0872.



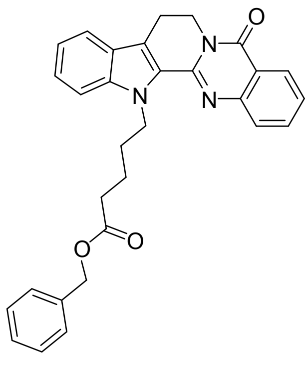
6h, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (br, 1H), 7.44-7.40 (m, 3H), 7.22 (d, J = 8.0 Hz, 2H), 7.15-7.12(m, 3H), 7.03-6.99 (m, 2H), 6.70 (br, 1H), 5.48 (s, 1H), 3.55-3.48 (m, 1H), 3.30-3.24 (m, 1H), 2.97-2.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 142.1, 137.8, 132.4, 128.8, 126.6, 125.5, 124.8, 122.6, 120.1, 119.6, 112.2, 63.7, 48.0, 20.7. HRMS (ESI) calcd for $C_{24}H_{18}BrClN_3$ ([M+H]$^+$): 462.0367 found 462.0362 .



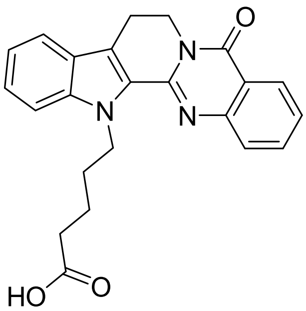
6i, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (br, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.34-7.28 (m, 4H), 7.22-7.18 (m, 3H), 7.05-7.01 (M, 2H), 6.74 (d, J = 2.2 Hz, 1H), 5.50 (s, 1H), 3.62-3.55 (m, 1H), 3.42-3.33 (m, 1H), 3.02-2.86 (m, 2H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 147.3, 138.7, 138.6, 130.5, 128.9, 126.4, 126.1, 124.7, 120.6, 119.8, 112.9, 63.9, 48.2, 34.7, 31.2, 20.4. HRMS (ESI) calcd for $C_{28}H_{27}ClN_3$ ([M+H]$^+$): 440.1888 found 440.1888.



6j, light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.3 (br, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.26 (d, J = 8.6 Hz, 2H), 7.11-7.04 (m, 3H), 6.99-6.93 (m, 2H), 6.79 (d, J = 8.6 Hz, 2H), 6.71 (d, J = 2.2 Hz, 1H), 5.46 (s, 1H), 3.70 (s, 3H), 3.53-3.47 (m, 1H), 3.33-3.26 (m, 1H), 2.91-2.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.3, 138.1, 135.4, 129.3, 128.4, 127.4, 126.8, 126.6, 125.4, 124.8, 124.8, 124.6, 119.9, 119.5, 116.4, 114.5, 112.5, 63.7, 55.4, 47.9, 20.7. HRMS (ESI) calcd for $C_{25}H_{21}ClN_3O$ ([M+H]$^+$): 414.1368 found 414.1374.



8, Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.7 Hz, 1H), 7.76-7.70 (m, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.47-7.45 (m, 2H), 7.39 (J = 7.2 Hz, 1H), 7.36-7.31 (m, 5H), 7.20 (t, J = 7.5 Hz, 1H), 5.08 (s, 2H), 4.90 (t, J = 7.2 Hz, 2H), 4.55 (t, J = 6.6 Hz, 2H), 3.19 (t, J = 6.7 Hz, 2H), 2.46 (t, J = 7.4 Hz, 2H), 2.00-1.96 (m, 2H), 1.82-1.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ173.2, 161.6, 146.9, 145.3, 140.0, 135.9, 134.3, 128.5, 128.2, 127.1, 126.9, 125.5, 124.2, 120.7, 120.4, 120.2, 110.5, 66.2, 44.8, 40.9, 34.0, 22.4, 19.8.



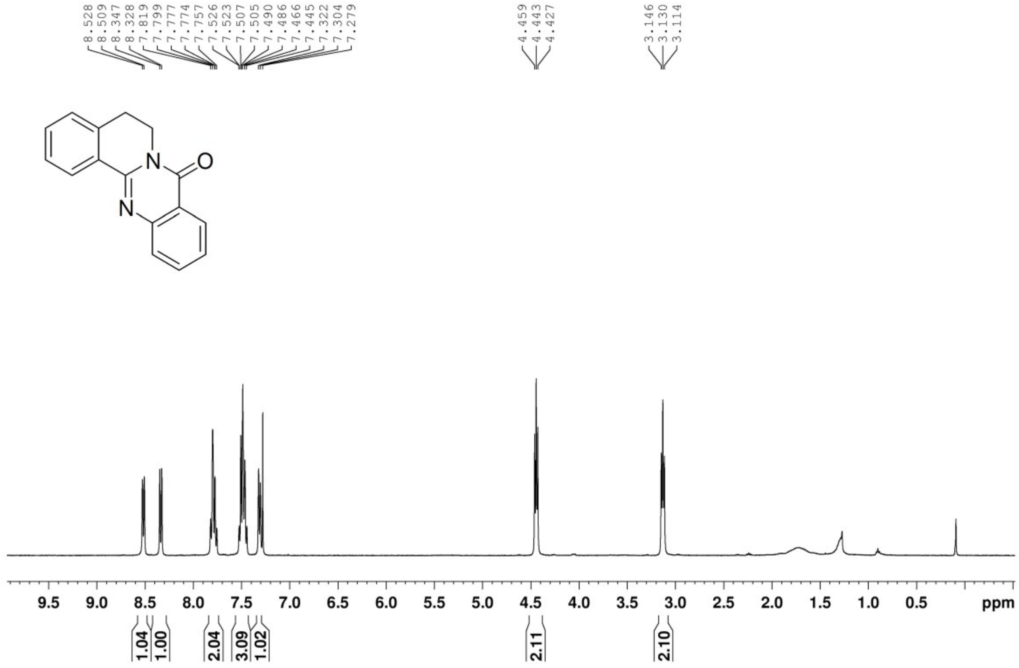
9, white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 7.0 Hz, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.5 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 7.25 (t, J = 7.3 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 4.73 (t, J = 7.2 Hz, 2H), 4.33 (t, J = 6.7 Hz, 2H), 3.06 (t, J = 6.7 Hz, 2H), 2.12 (t, J = 7.0 Hz, 2H), 1.76-1.73 (m, 2H), 1.54-1.50 (m, 2H).

References:

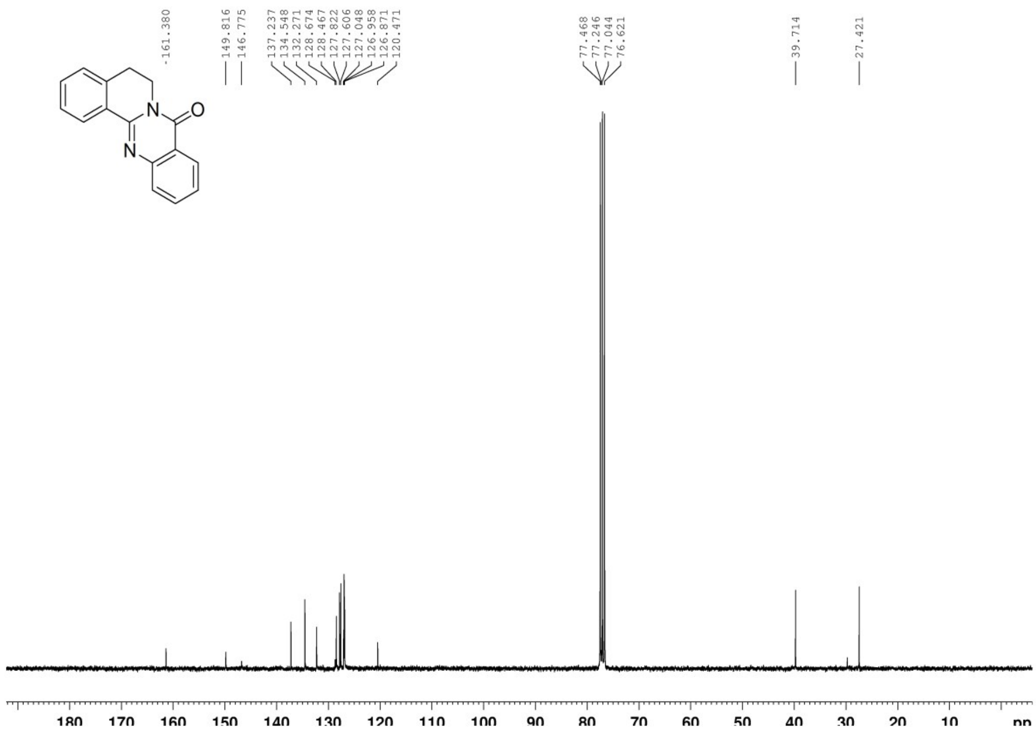
[1] (a) Biswas, A.; Karmakar, U.; Nandi, S.; Samanta, R. *J Org. Chem.* **2017,** 82, 8933-8942. (b) Cheng, Q.; Xie, J-H.; Weng, Y.-C.; You, S-L. *Angew. Chem. Int. Ed.,* **2019,** *58,* 5739-5743. (c) Li, L.; Wang, H.; Yu, S.; Yang, X.; Li, X. *Org. Let.* **2016,** *18,* 3662-3665.

[2] (a) Murashige, R.; Ohtsuka, Y.; Sagisawa, K.; Shiraishi, M. *Tetrahedron Lett.* **2015,** *56,* 3410-3412. (b) Lu, C.; Su, Z.; Jing, D.; Jin, S.; Xie, L.; Li, L.; Zheng, K. *Org. Lett.* **2019,** *21,* 1438-1443.

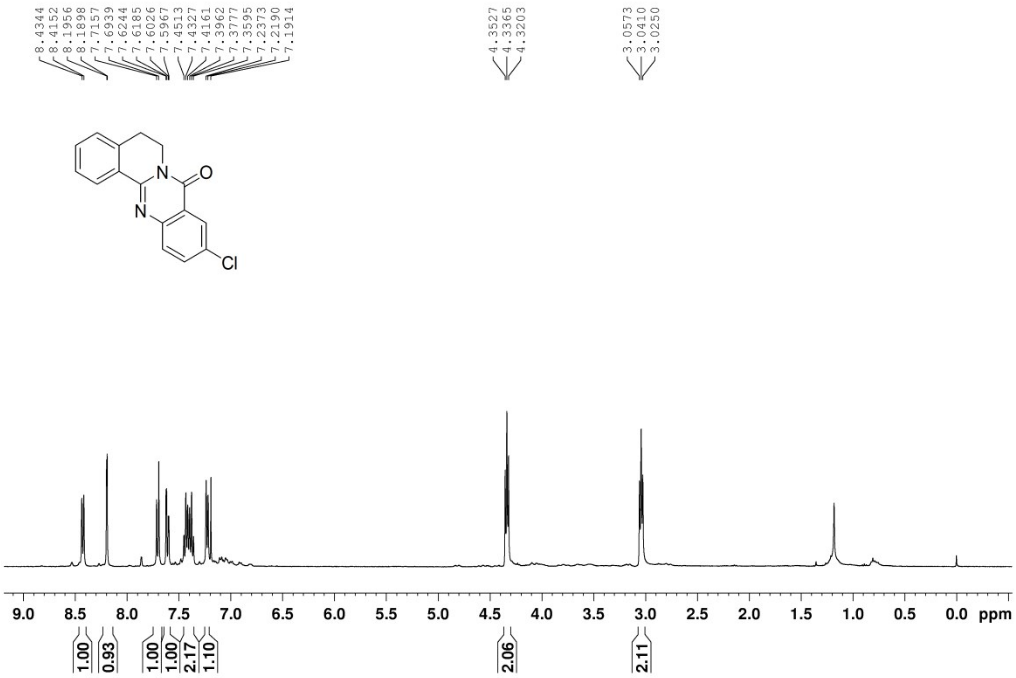
[3] Xie, F.; Chen, Q.; Xie, R.; Jiang, H.; Zhang, M. *ACS Catal,* **2018,** *8,* 5869-5874.



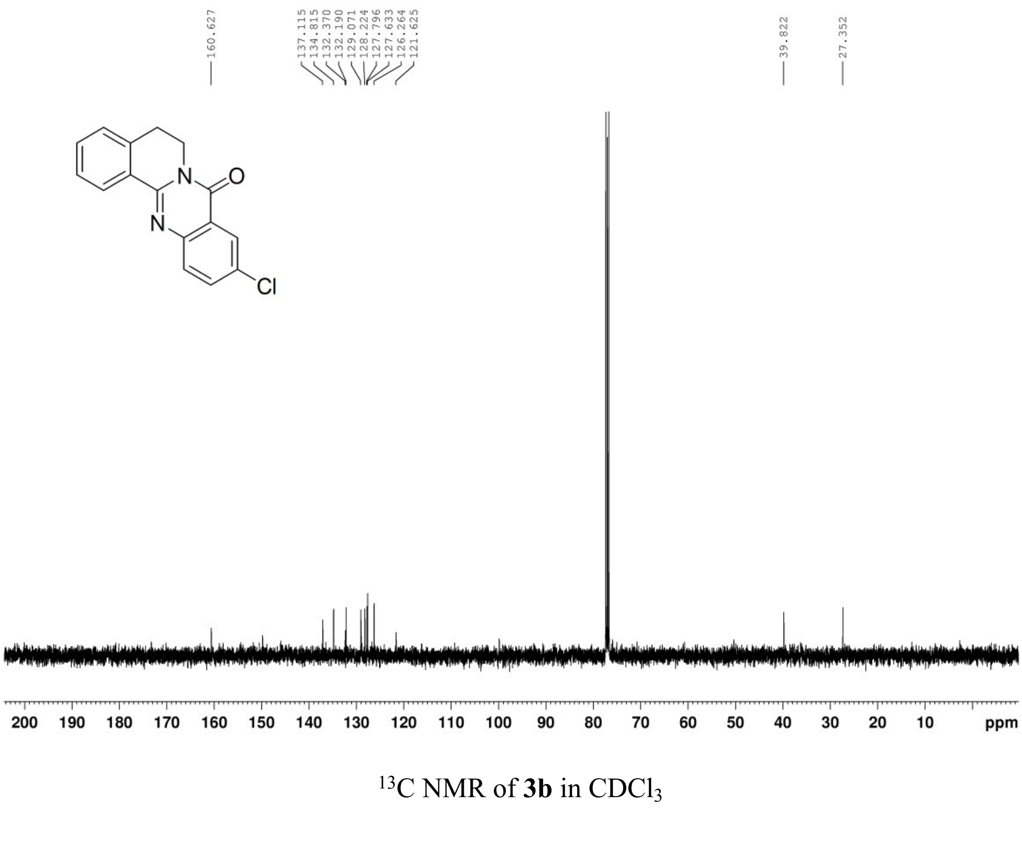
^{1}H NMR of **3a** in $CDCl_3$



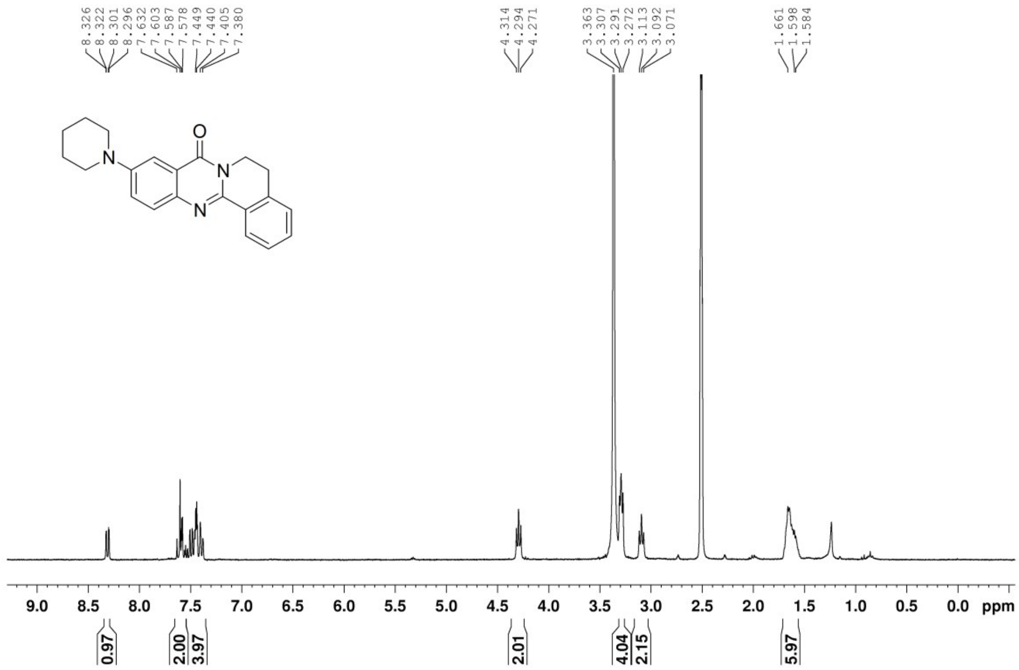
^{13}C NMR of **3a** in $CDCl_3$



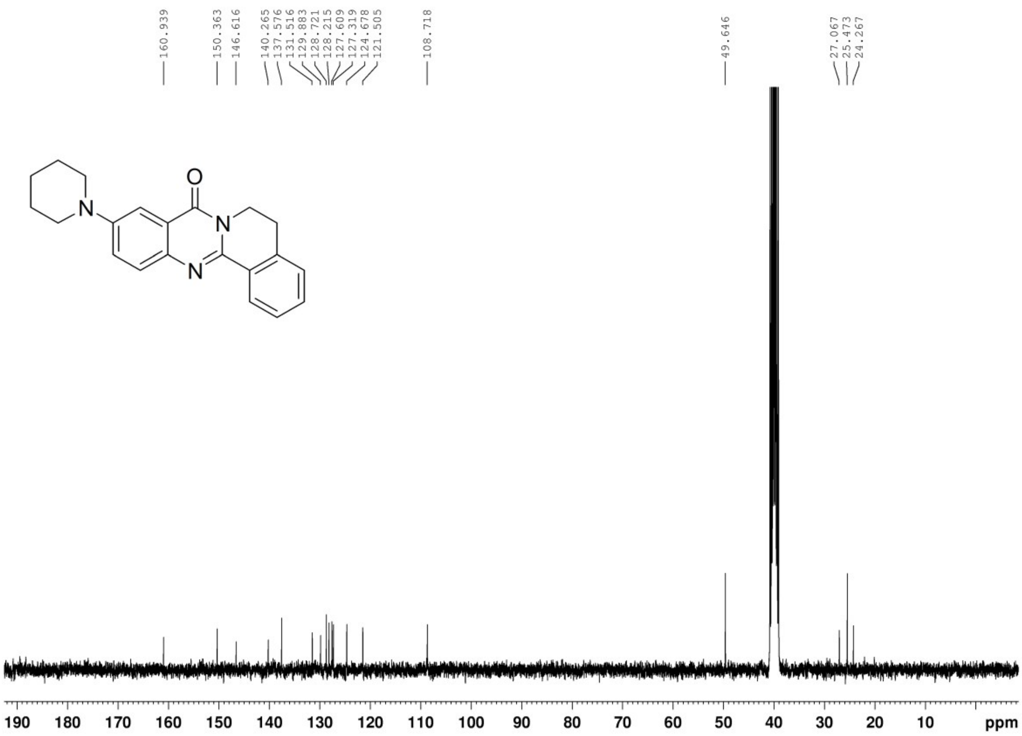
^{1}H NMR of **3b** in $CDCl_3$



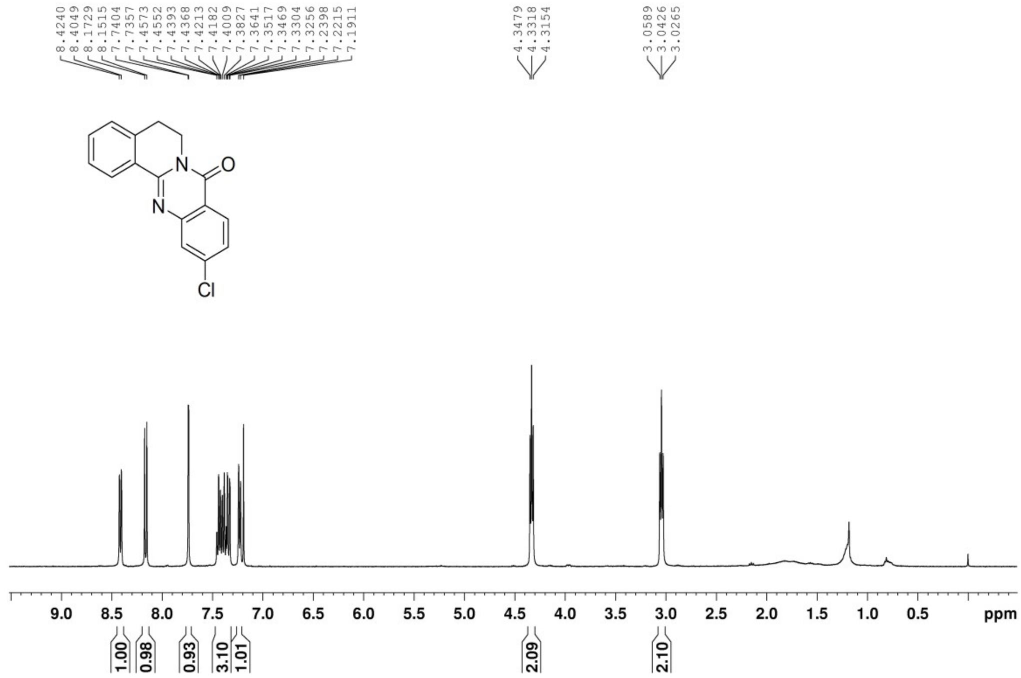
^{13}C NMR of **3b** in $CDCl_3$



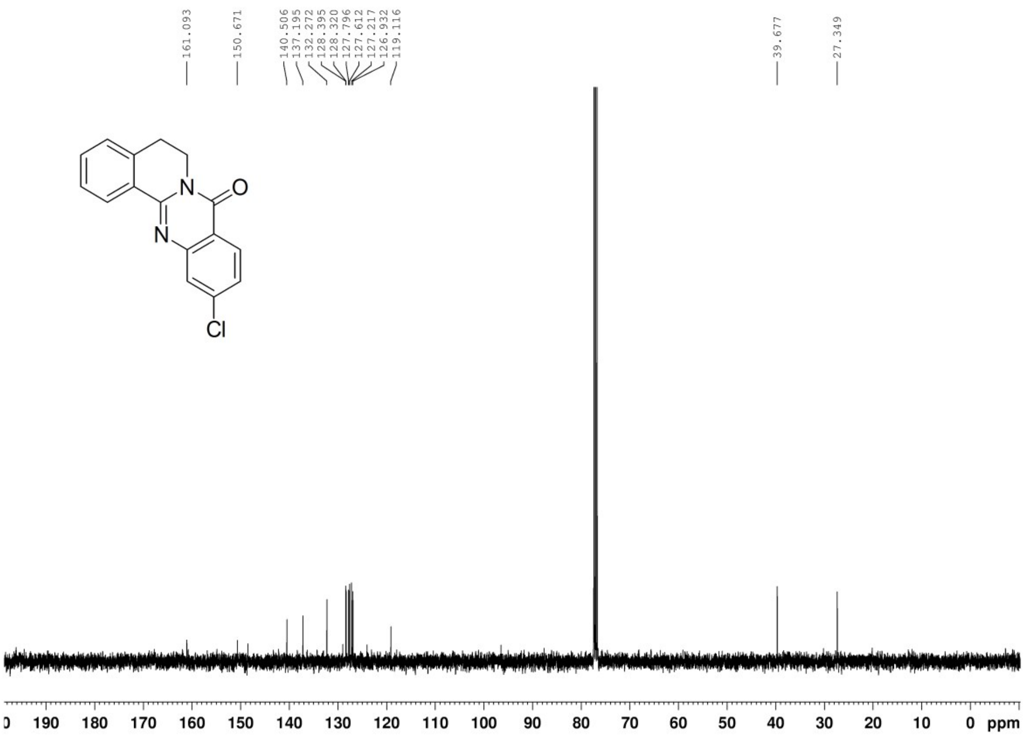
^{1}H NMR of **3c** in DMSO-d6



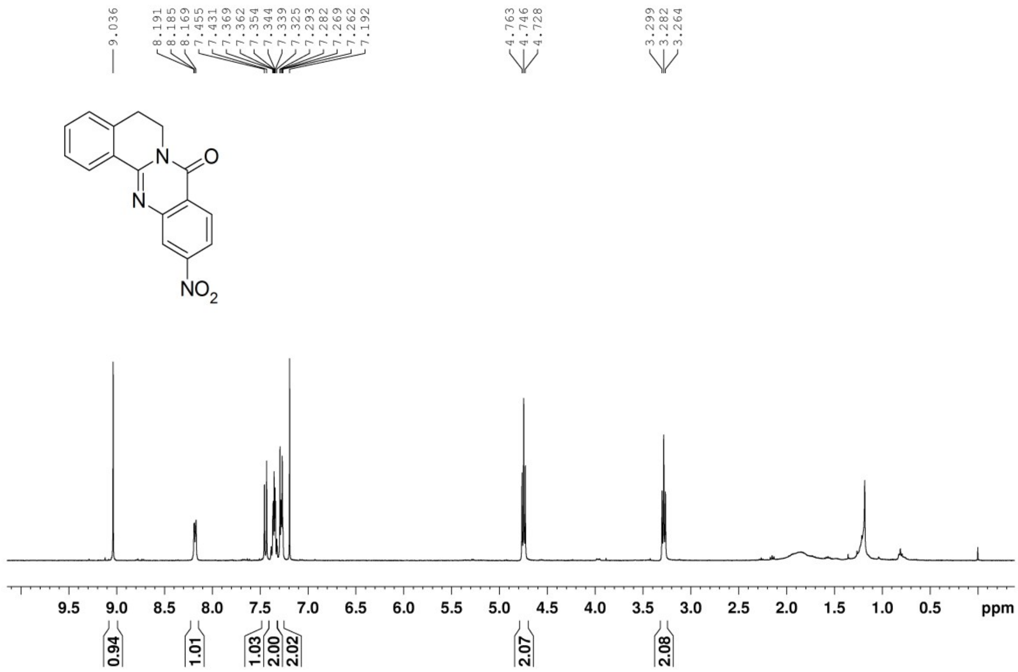
^{13}C NMR of **3c** in DMSO-d6



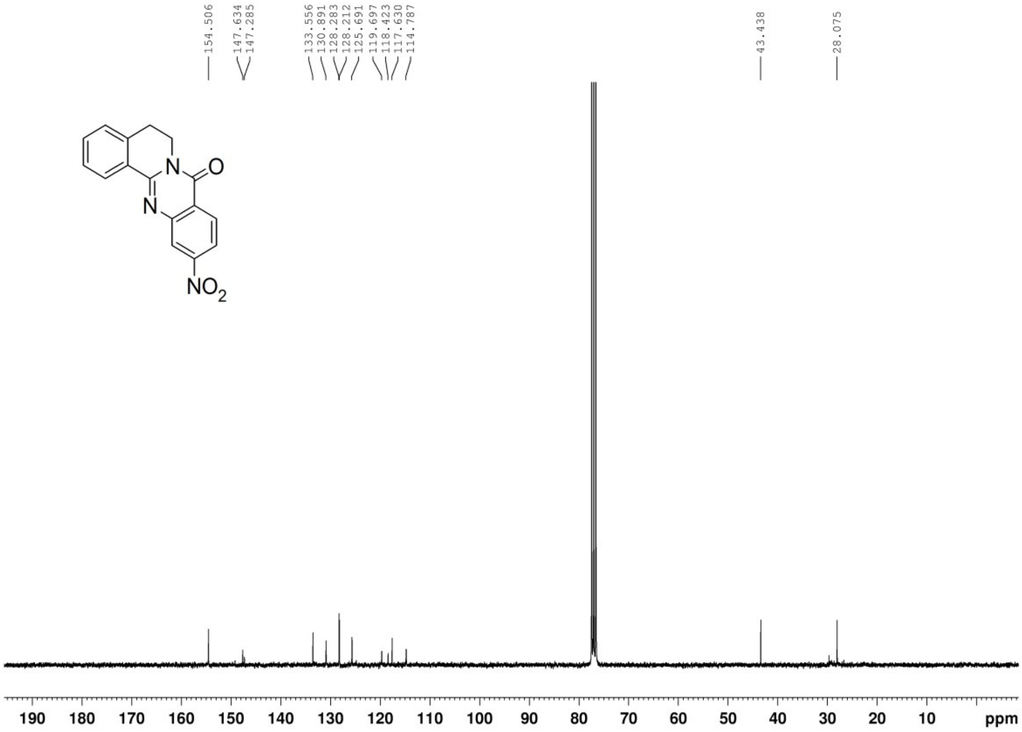
^{1}H NMR of **3d** in $CDCl_3$



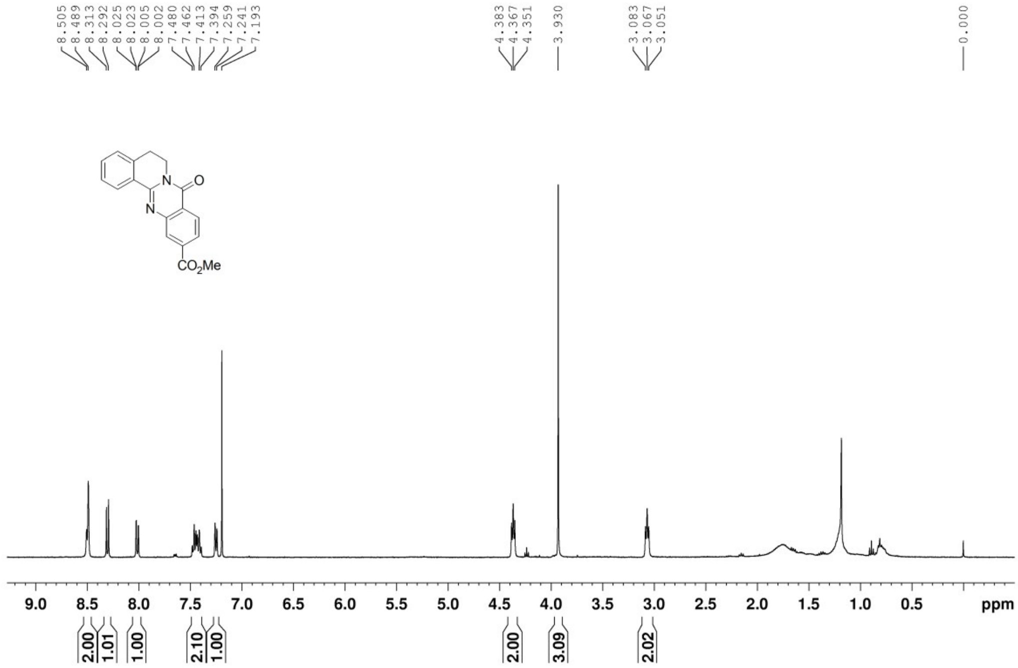
^{13}C NMR of **3d** in $CDCl_3$



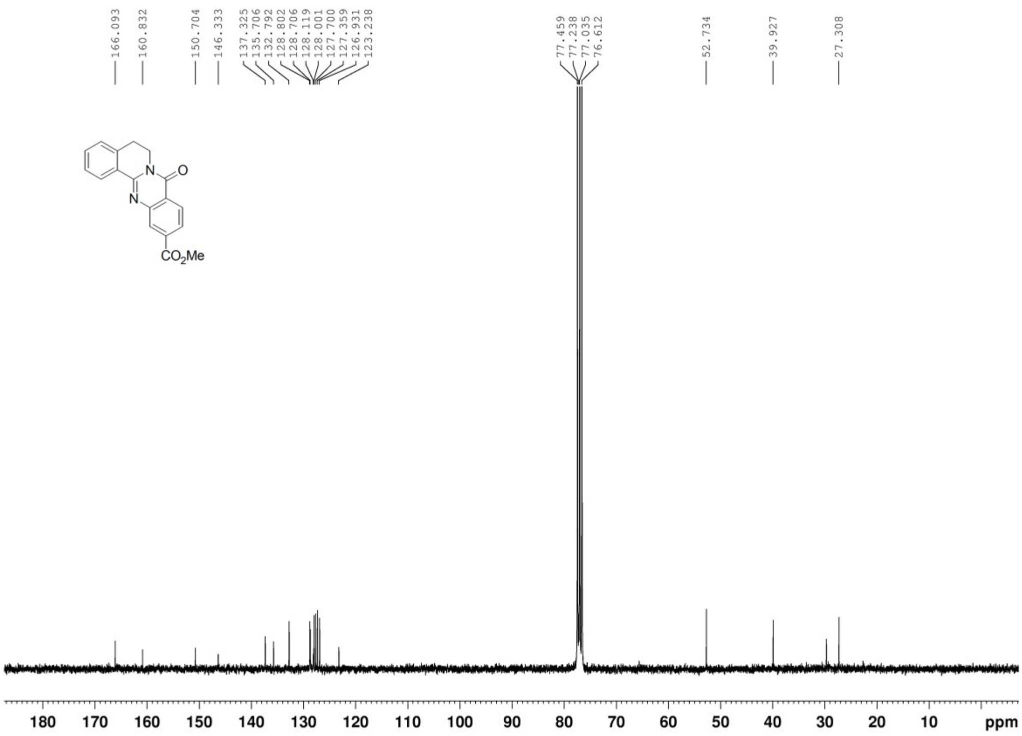
^1H NMR of **3e** in $CDCl_3$



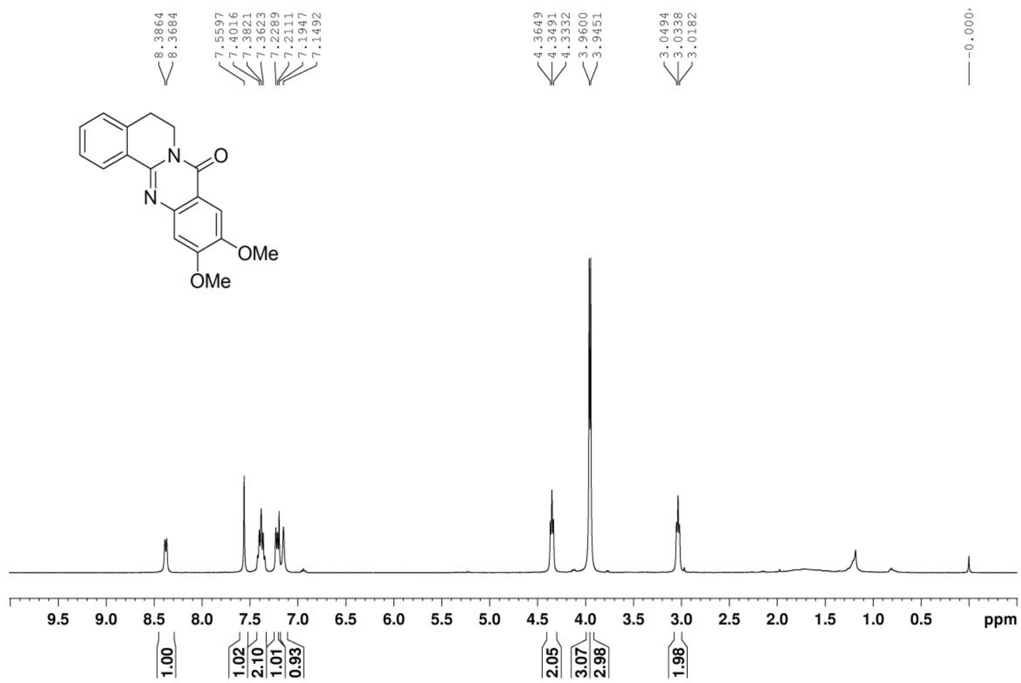
^{13}C NMR of **3e** in $CDCl_3$



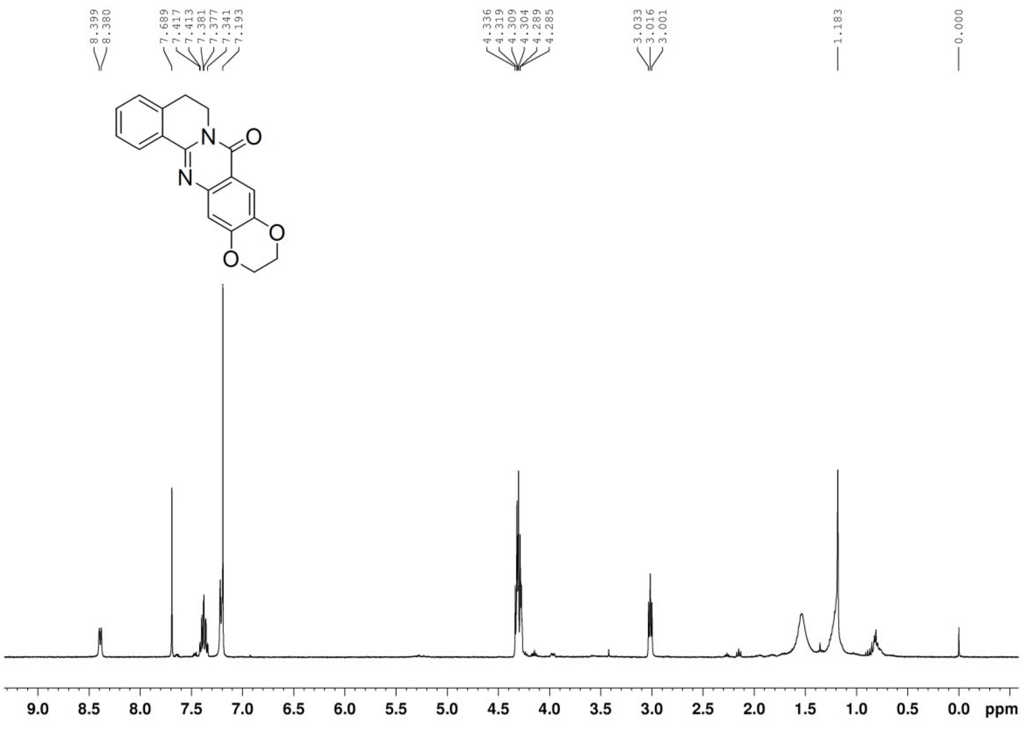
^1H NMR of **3f** in $CDCl_3$



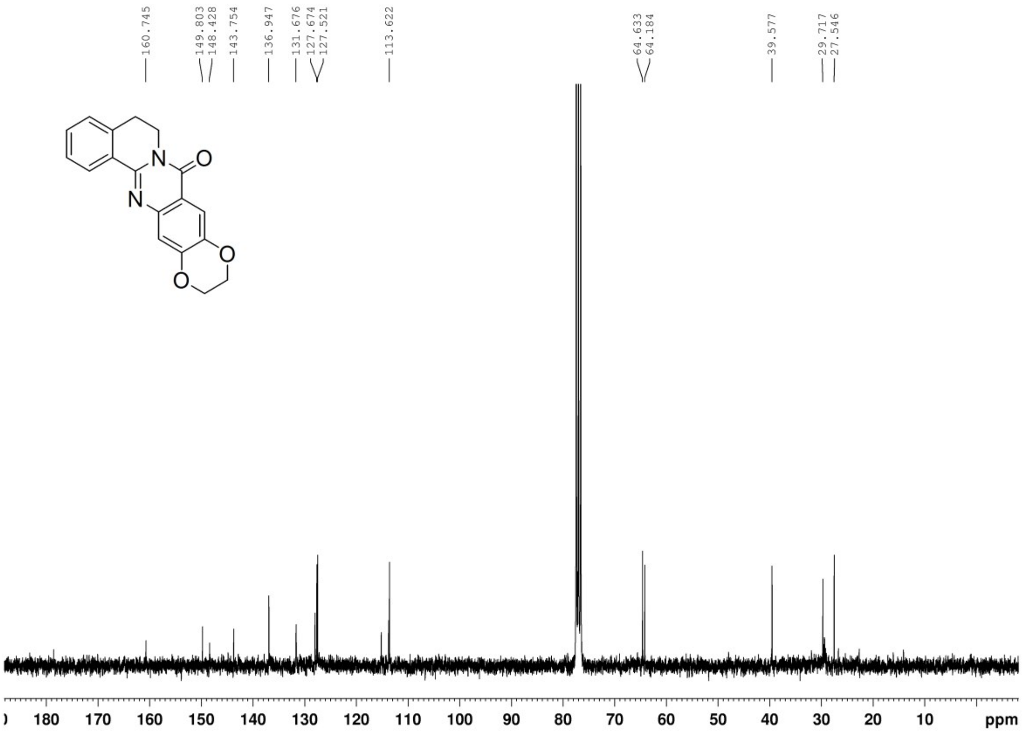
^{13}C NMR of **3f** in $CDCl_3$



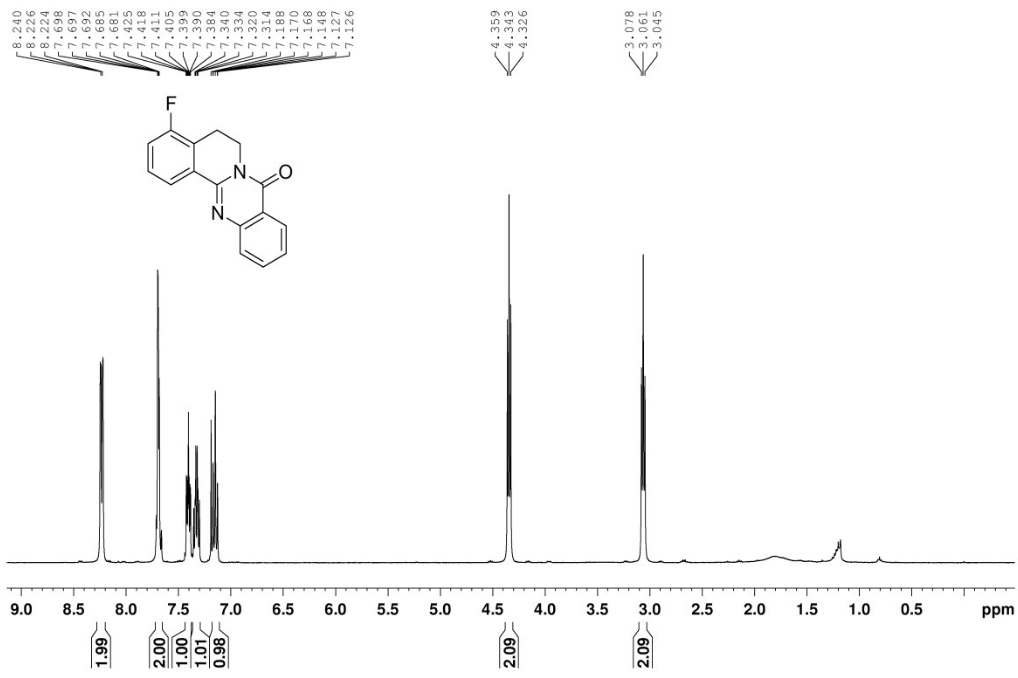
^{1}H NMR of **3g** in $CDCl_3$



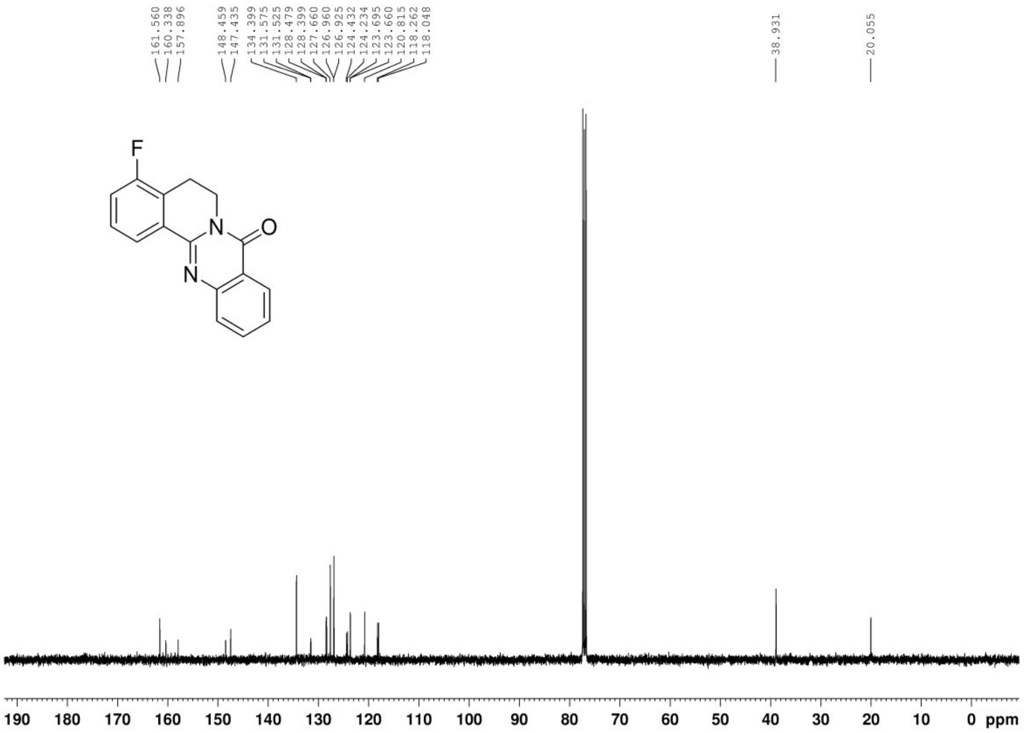
^{1}H NMR of **3h** in $CDCl_3$



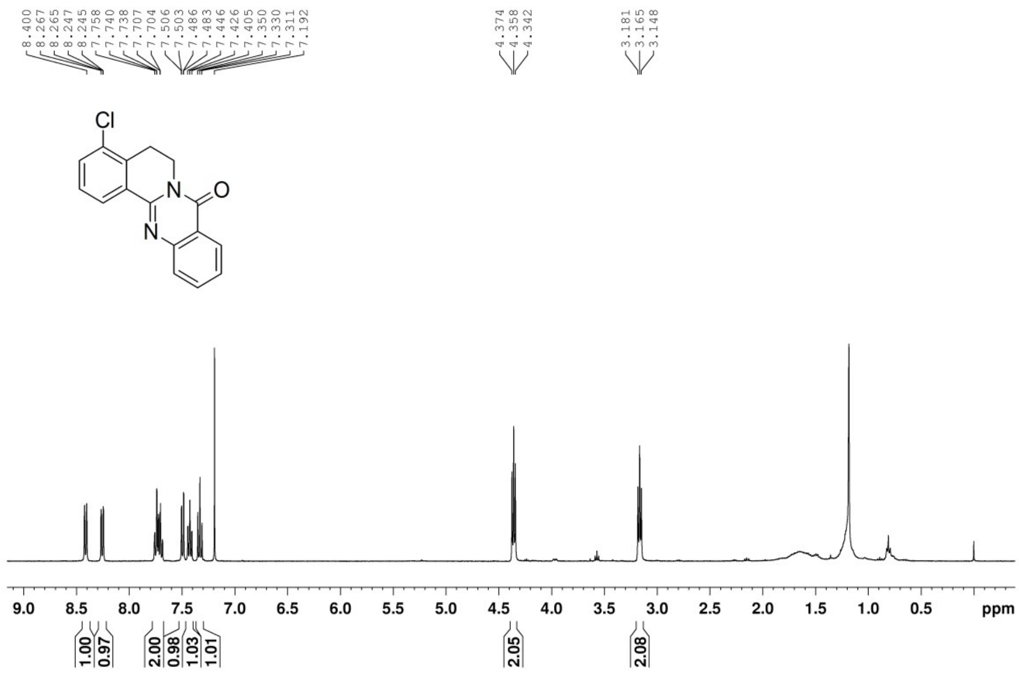
^{13}C NMR of **3h** in $CDCl_3$



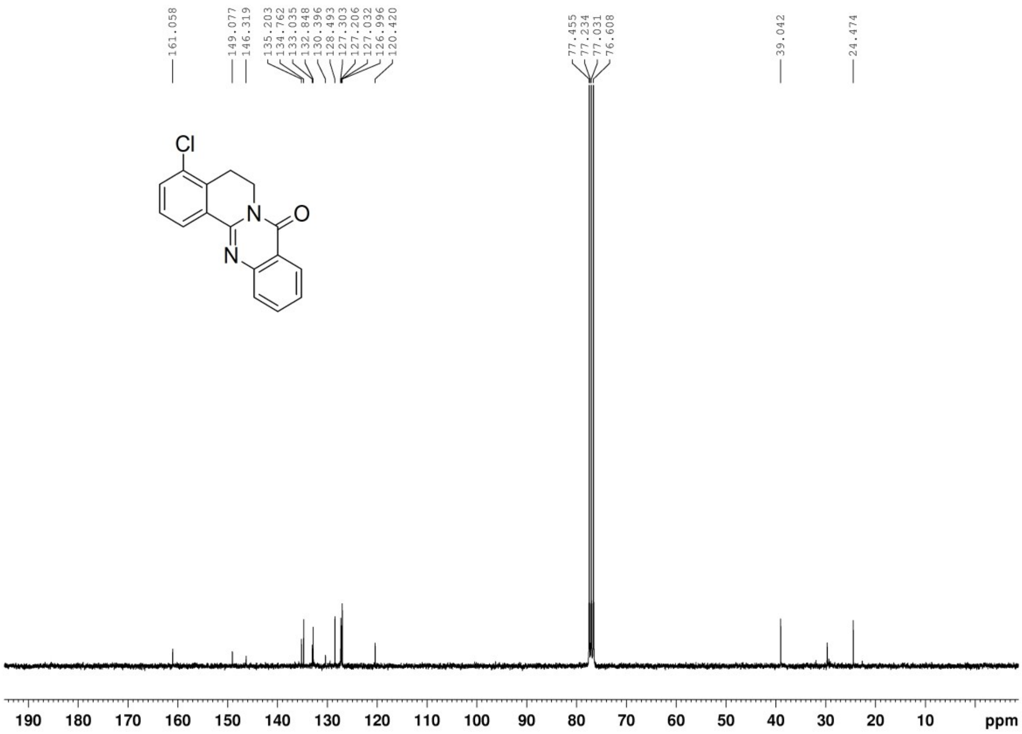
^{1}H NMR of **3i** in $CDCl_3$



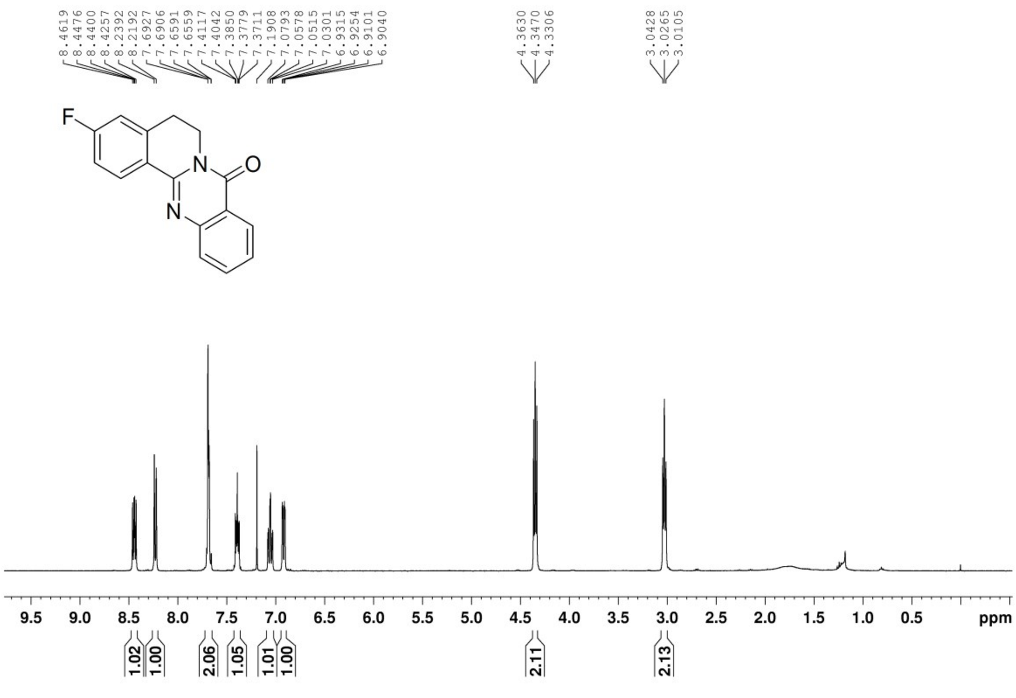
^{13}C NMR of **3i** in $CDCl_3$



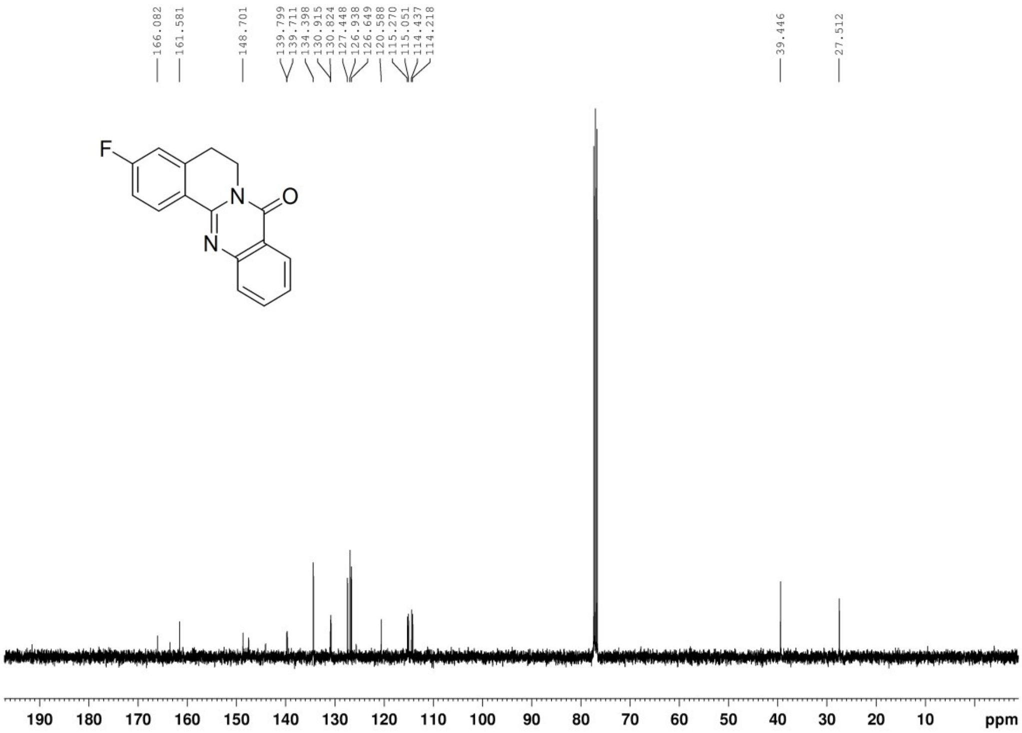
^{1}H NMR of **3j** in $CDCl_3$



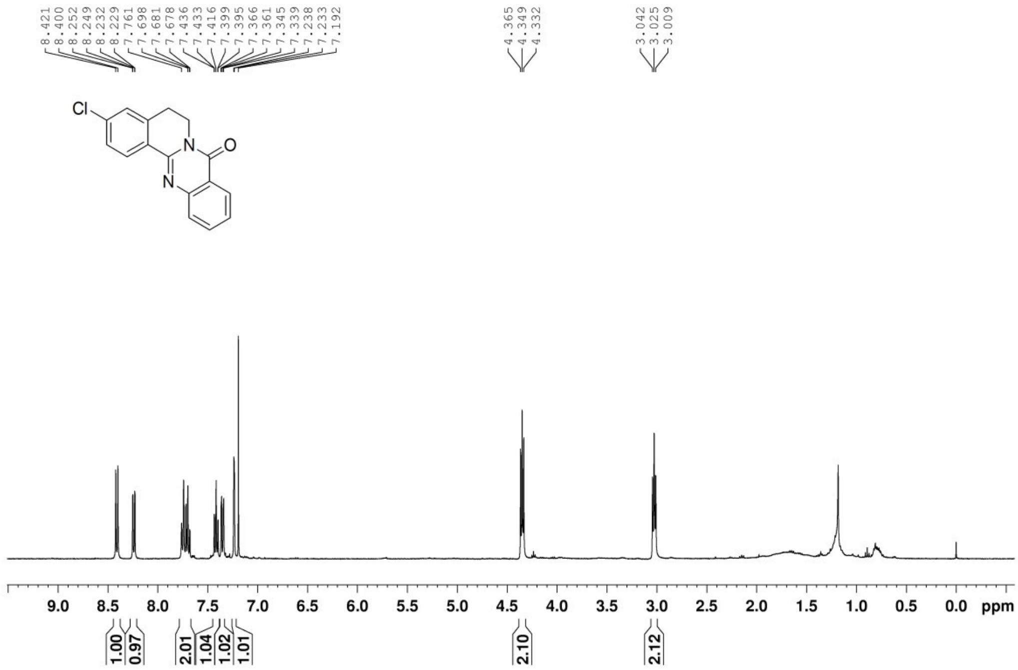
^{13}C NMR of **3j** in $CDCl_3$



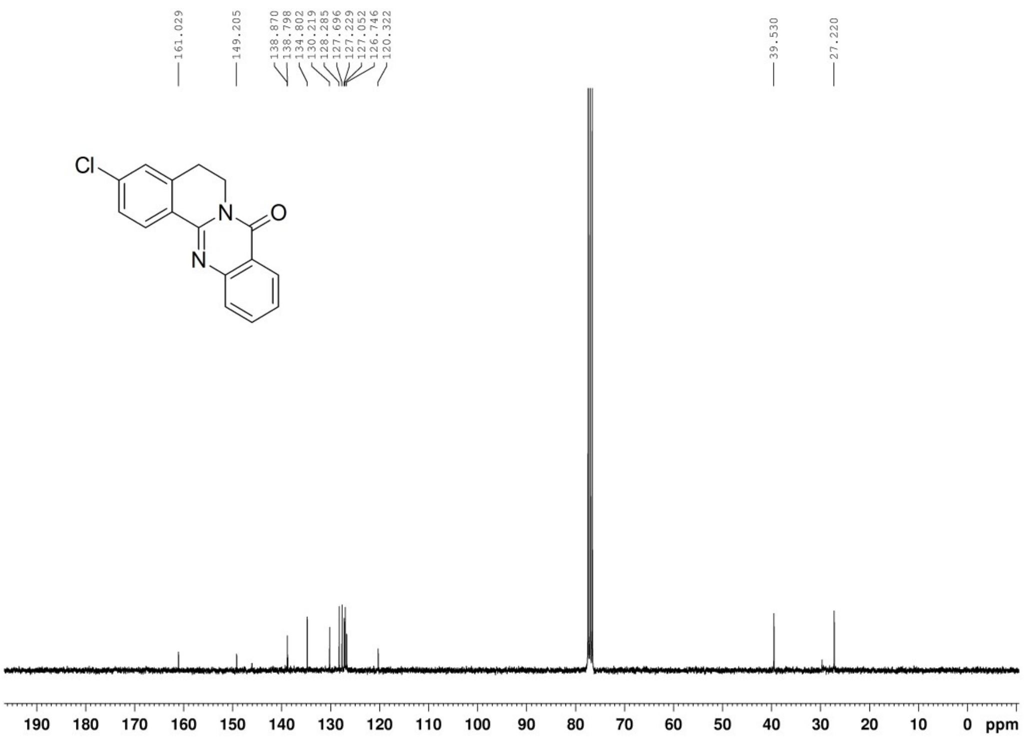
^{1}H NMR of **3k** in $CDCl_3$



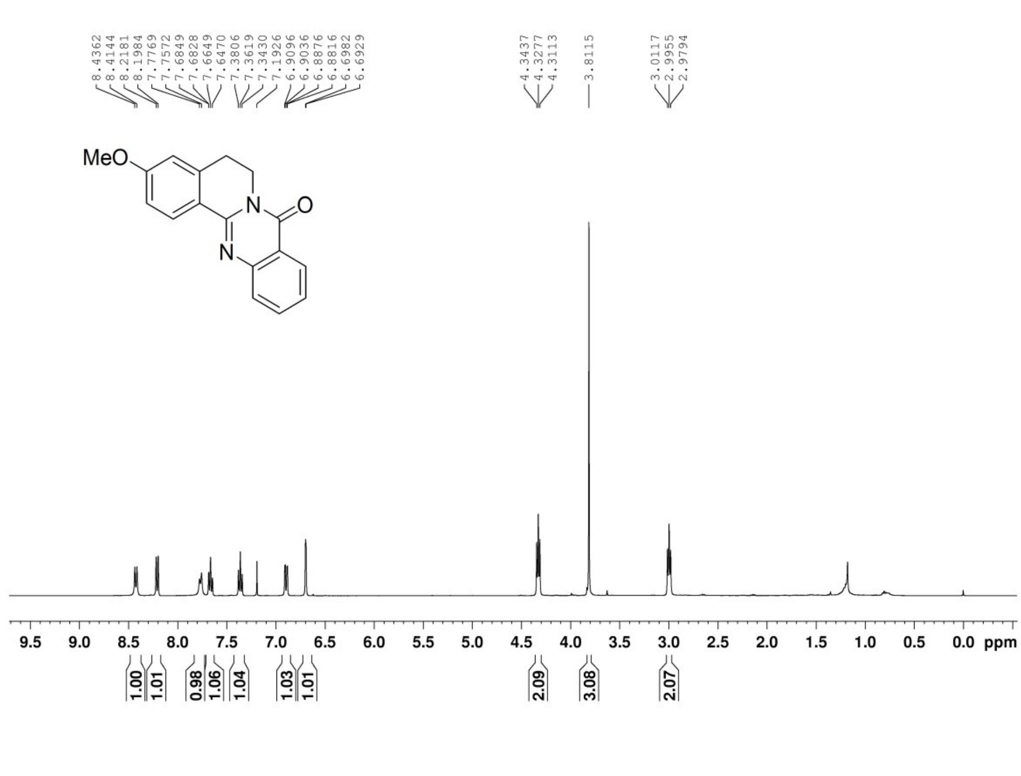
^{13}C NMR of **3k** in $CDCl_3$



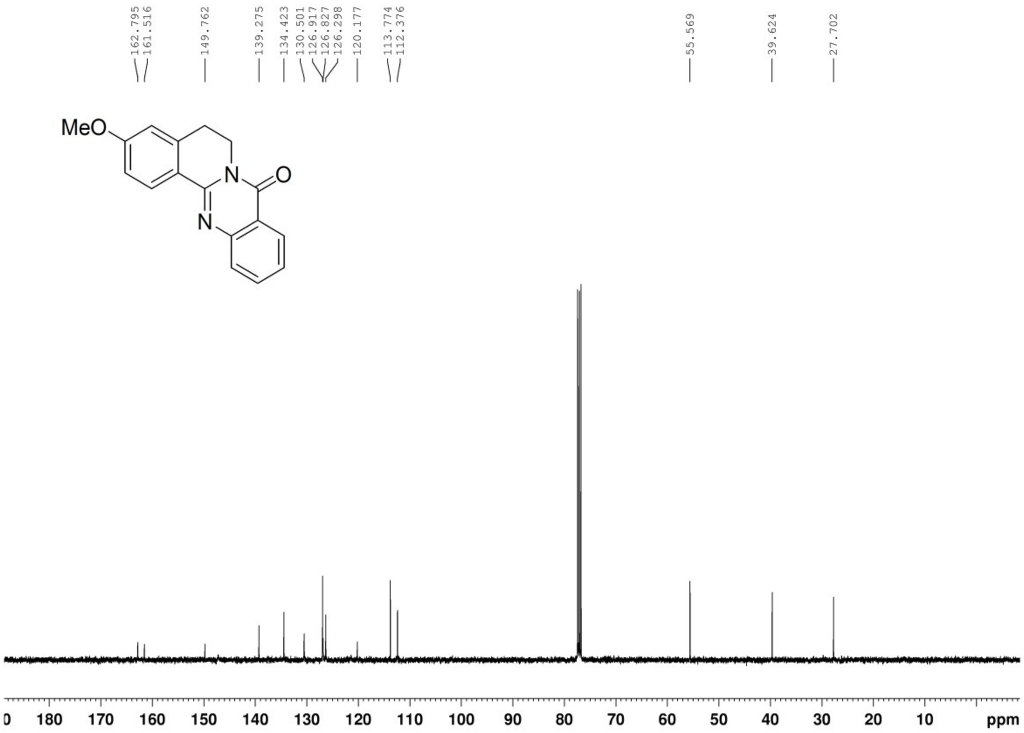
^{1}H NMR of 3**l** in $CDCl_3$



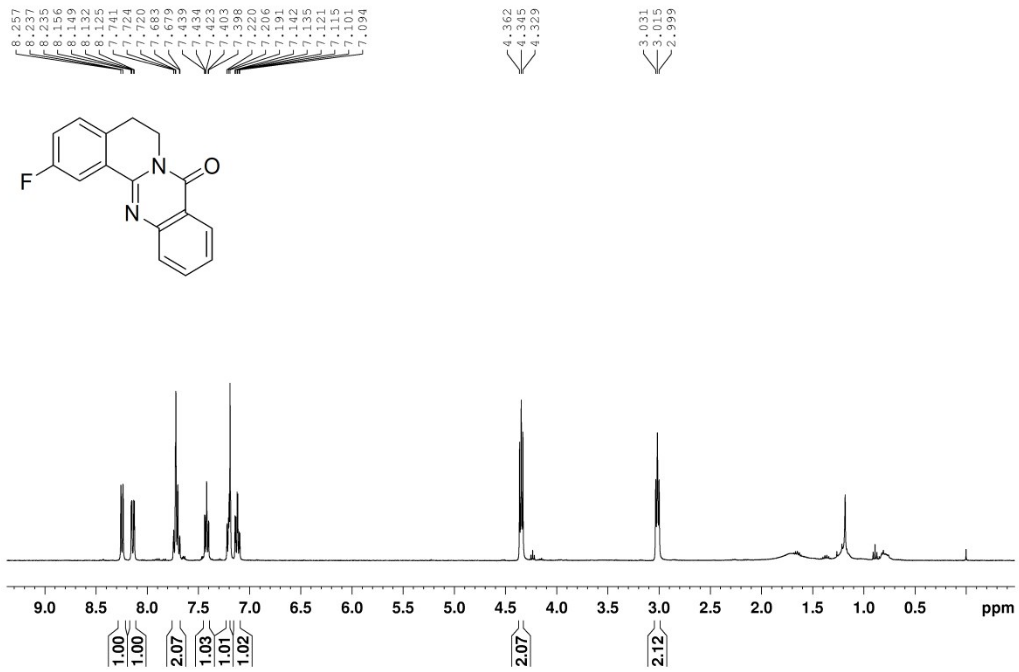
^{13}C NMR of **3l** in $CDCl_3$



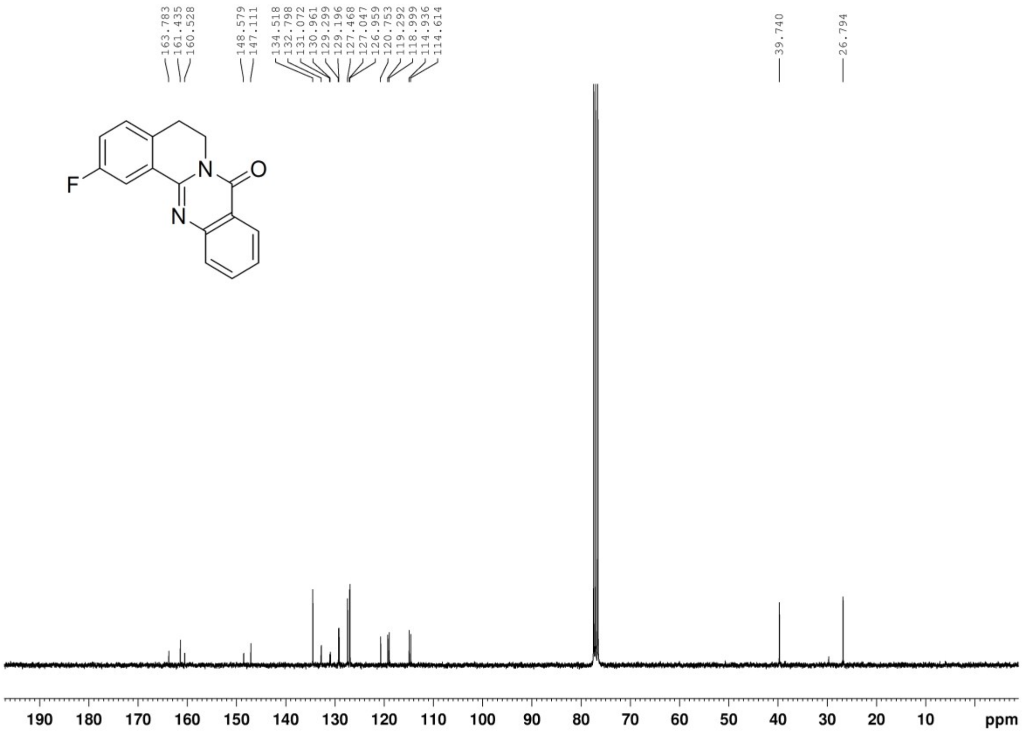
^{1}H NMR of **3m** in $CDCl_3$



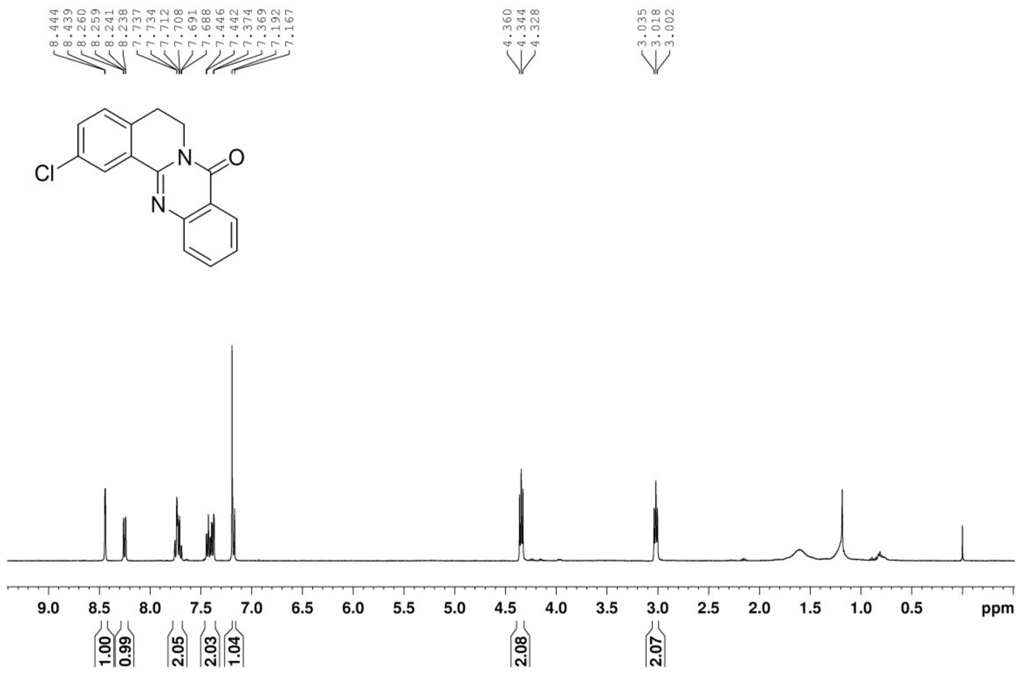
^{13}C NMR of **3m** in $CDCl_3$



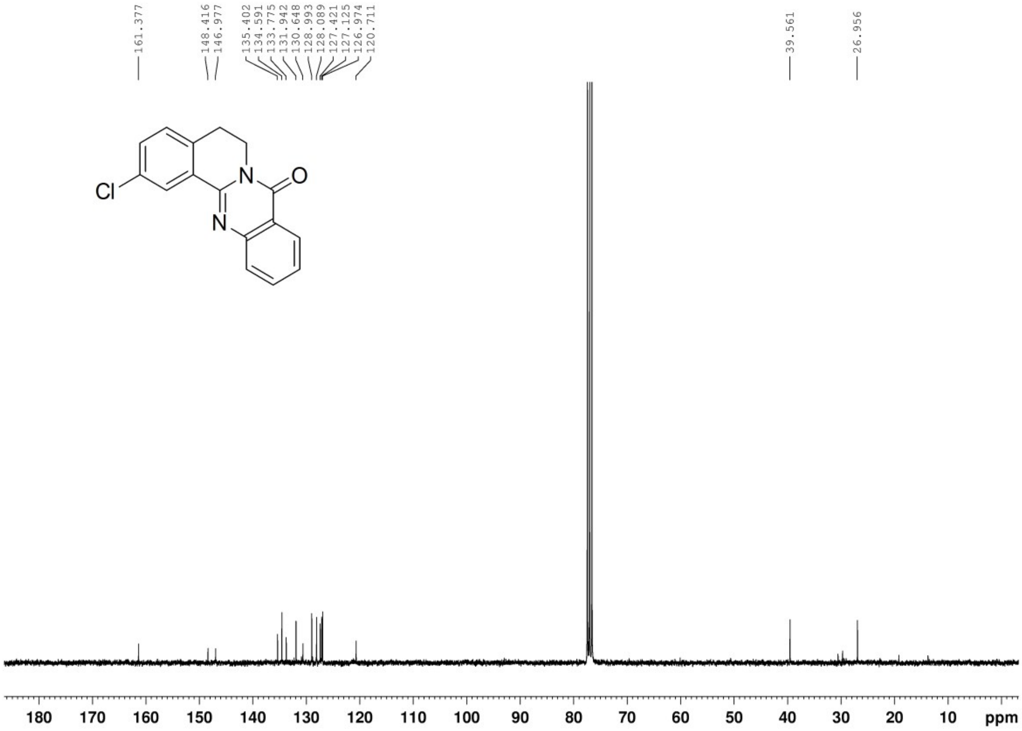
^{1}H NMR of **3n** in $CDCl_3$



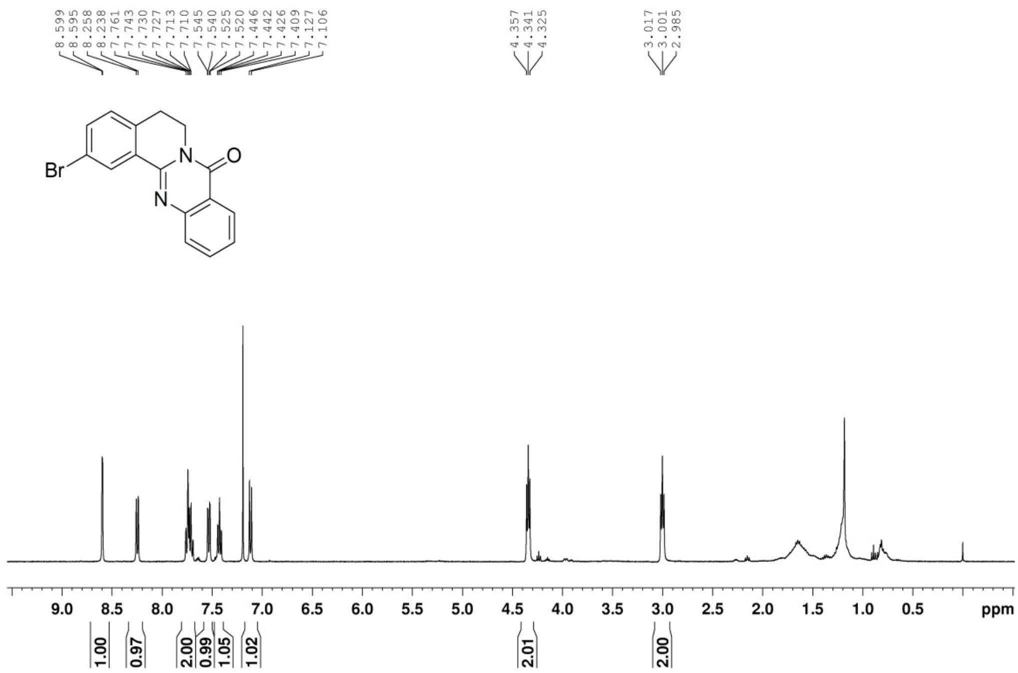
^{13}C NMR of **3n** in $CDCl_3$



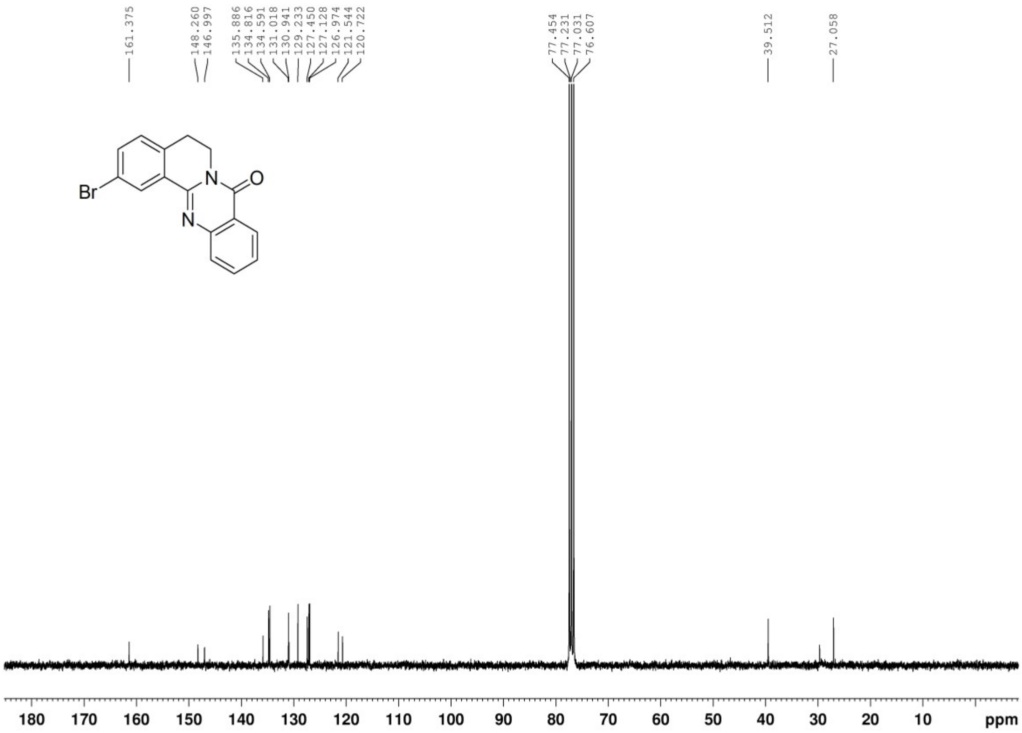
^{1}H NMR of **3o** in $CDCl_3$



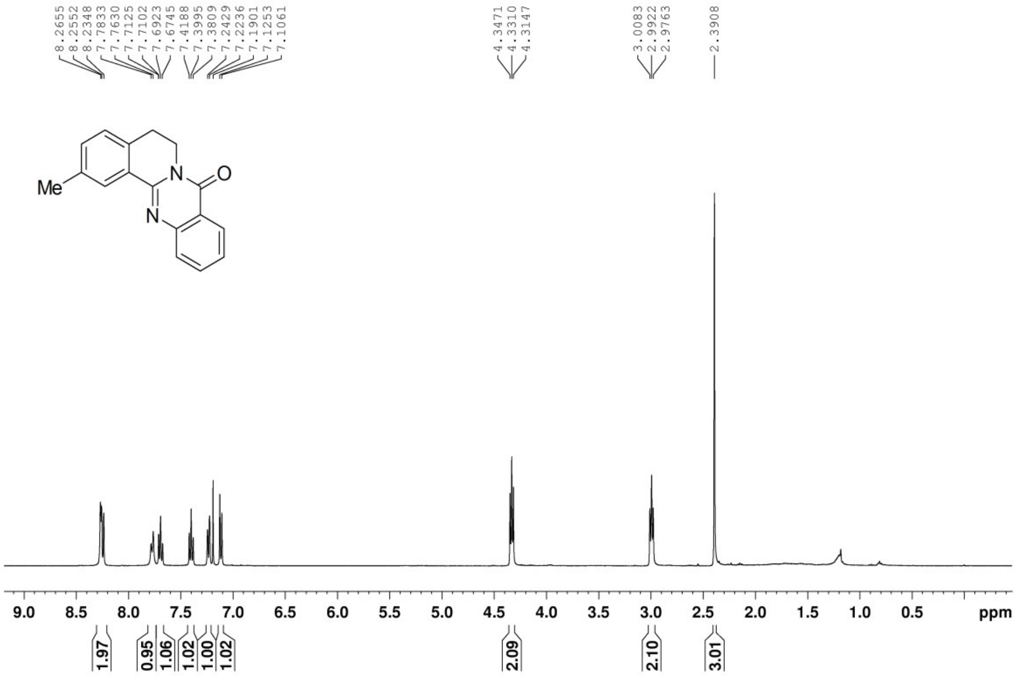
^{13}C NMR of **3o** in $CDCl_3$



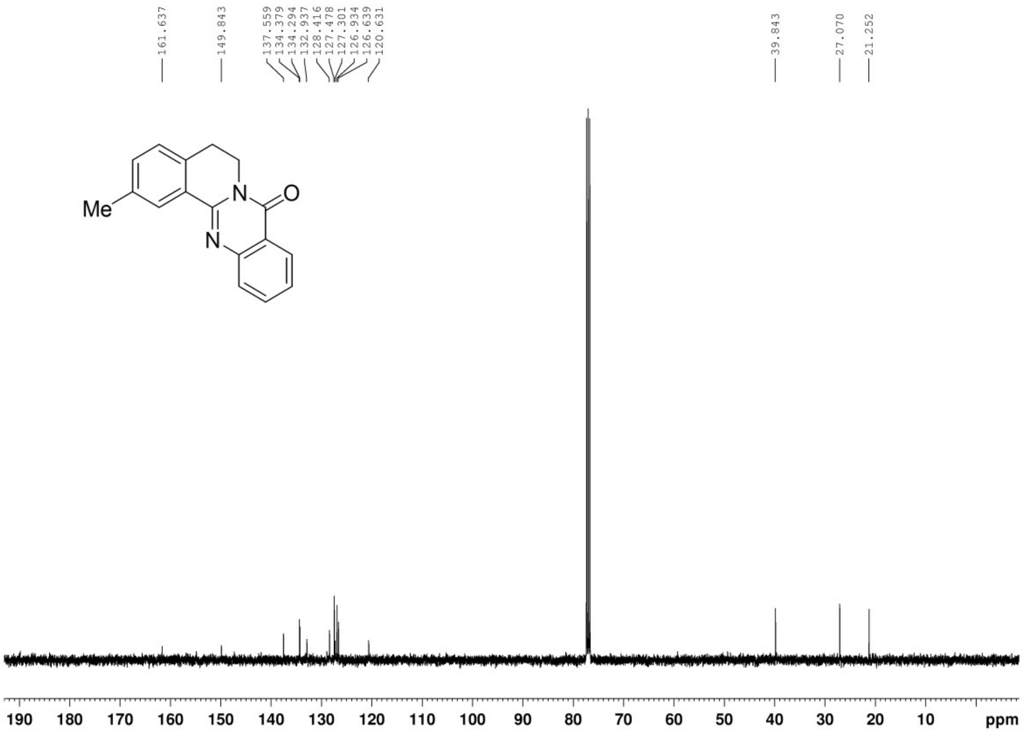
^{1}H NMR of **3p** in $CDCl_3$



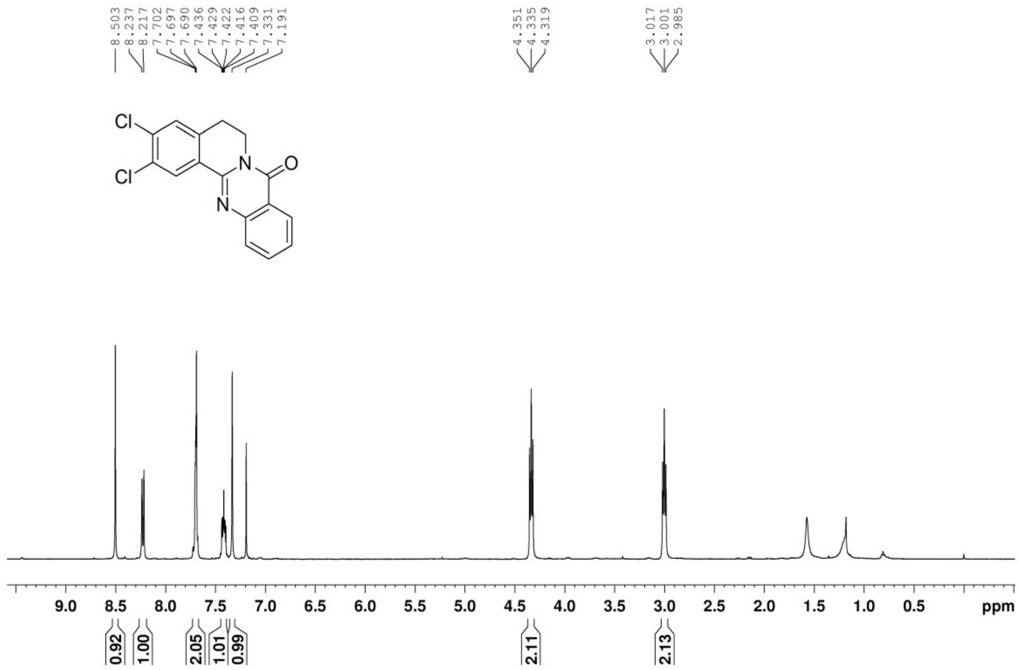
^{13}C NMR of **3p** in $CDCl_3$



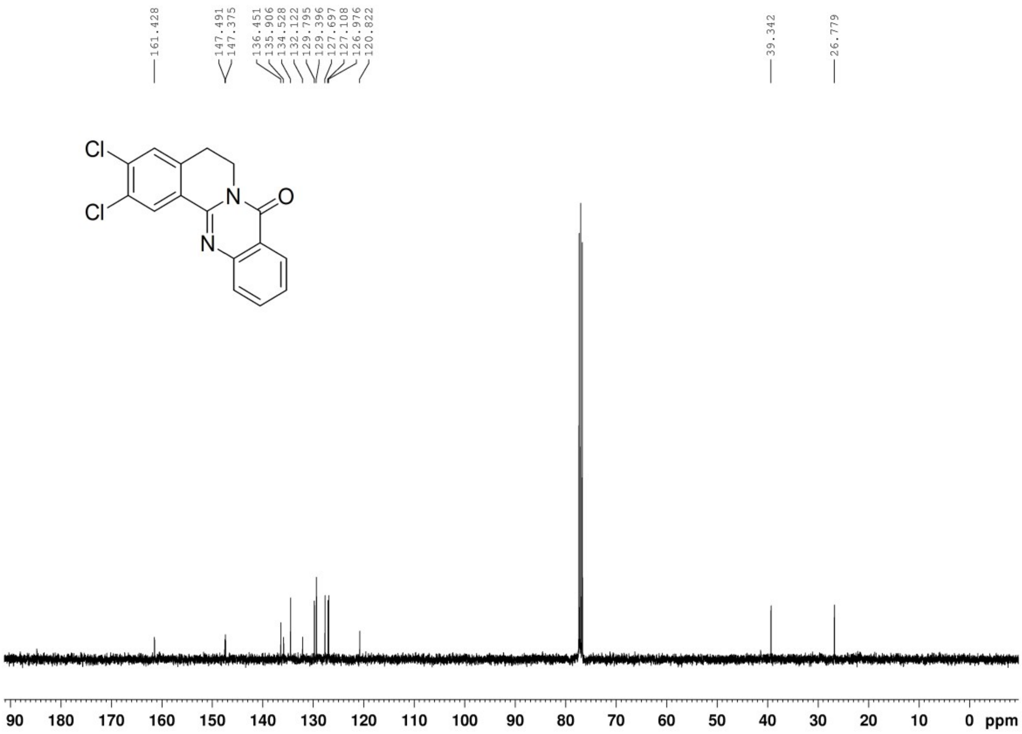
^{1}H NMR of **3q** in $CDCl_3$



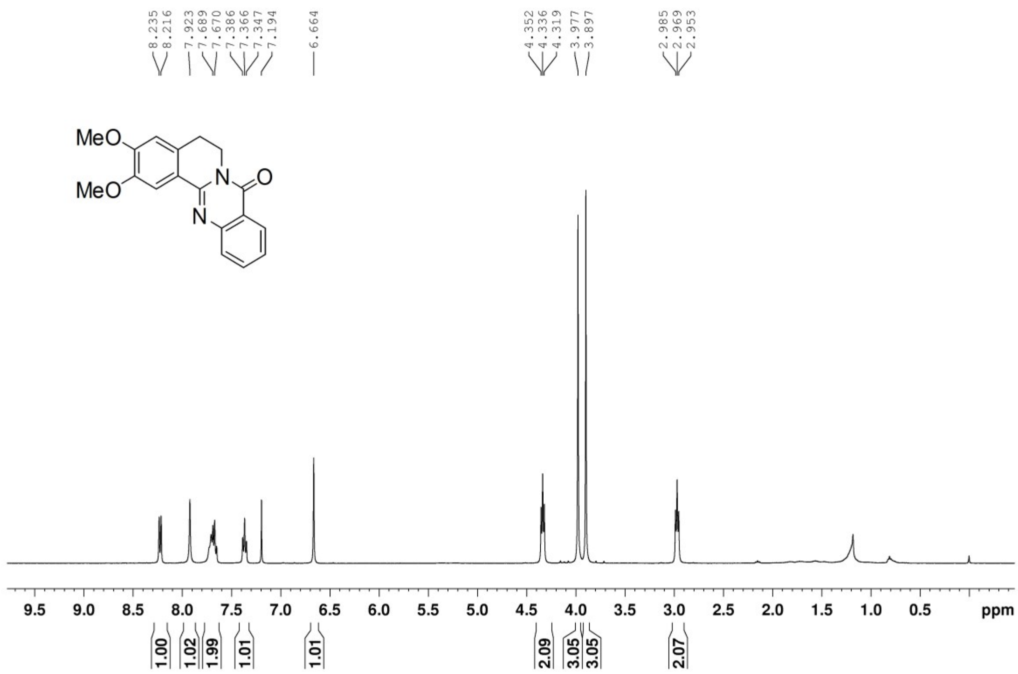
^{13}C NMR of **3q** in $CDCl_3$



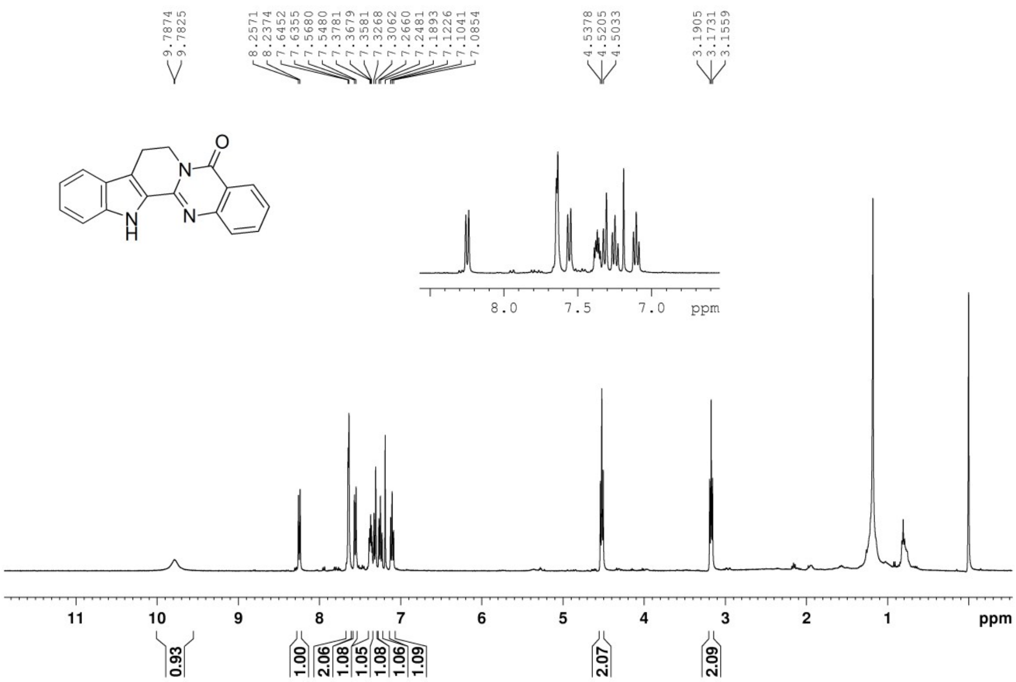
^{1}H NMR of **3r** in $CDCl_3$



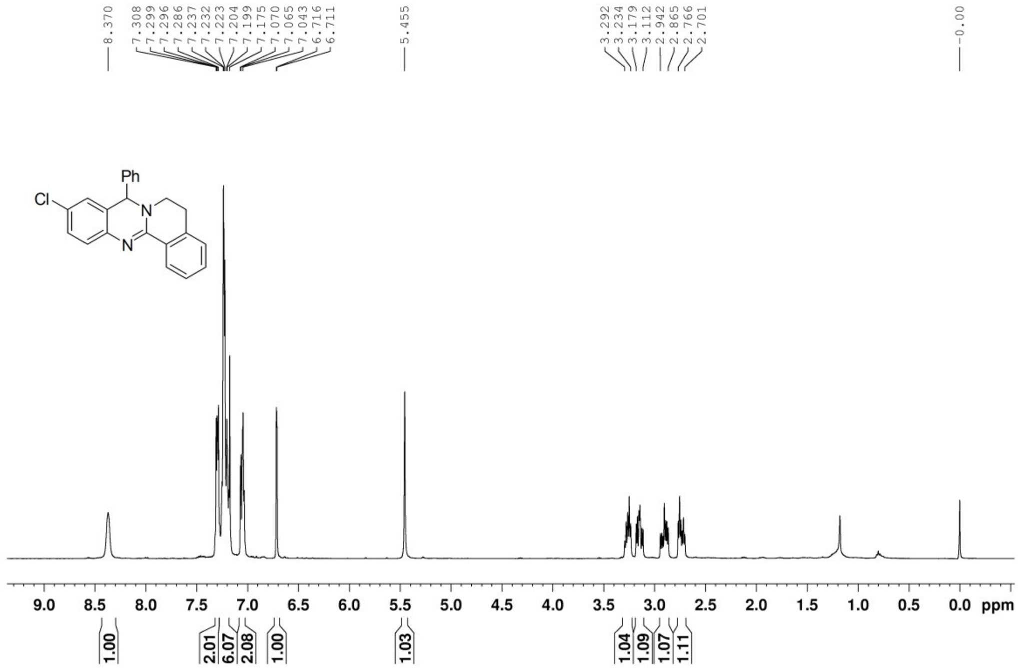
^{13}C NMR of **3r** in $CDCl_3$



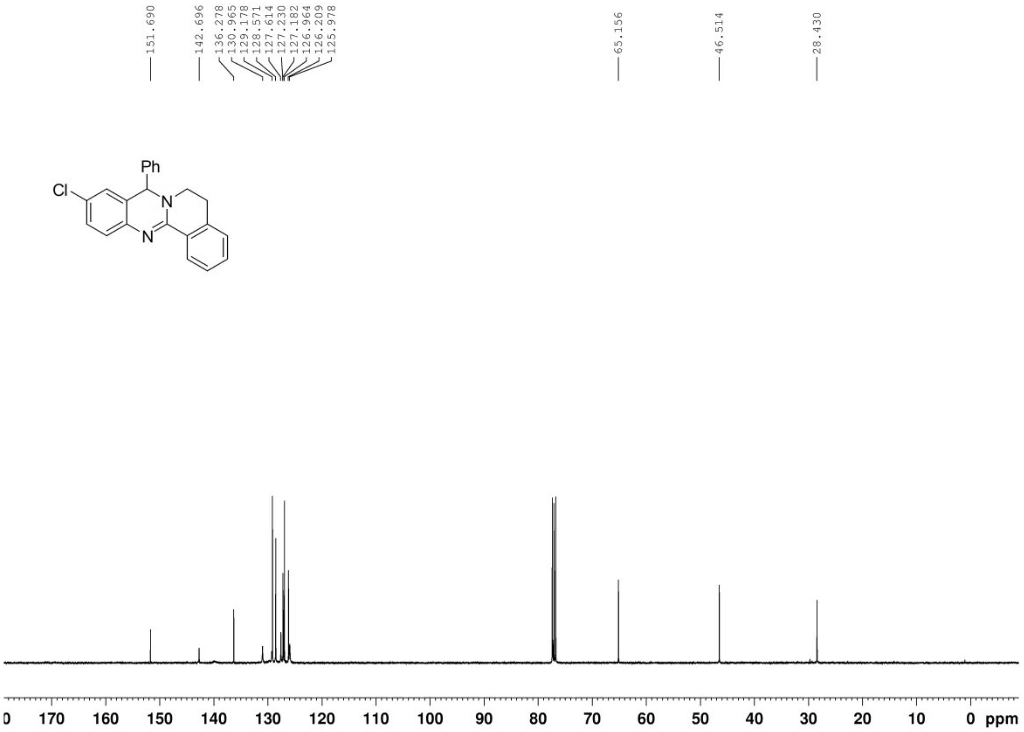
^{1}H NMR of **3s** in $CDCl_3$



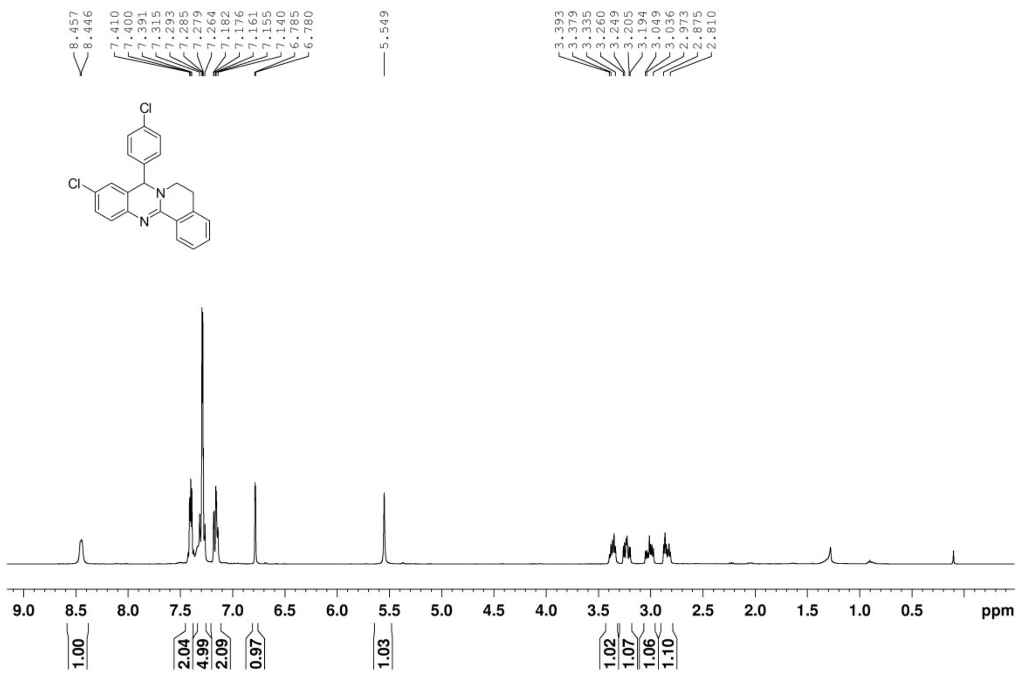
^{1}H NMR of Rutaecarpine in $CDCl_3$



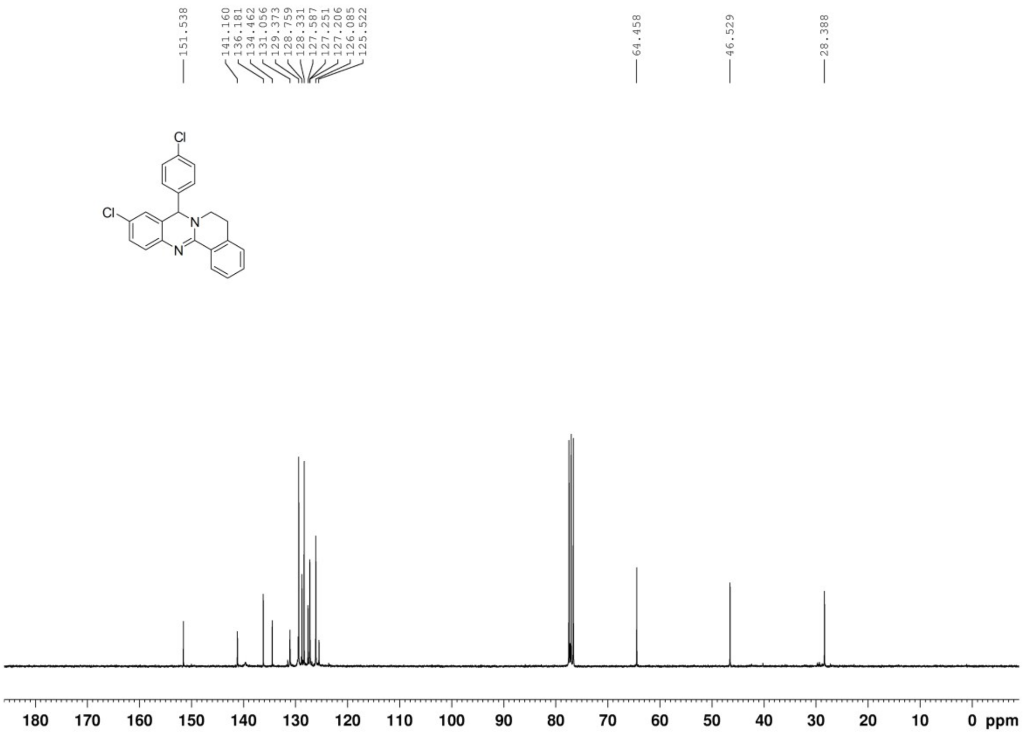
^{1}H NMR of **4a** in $CDCl_3$



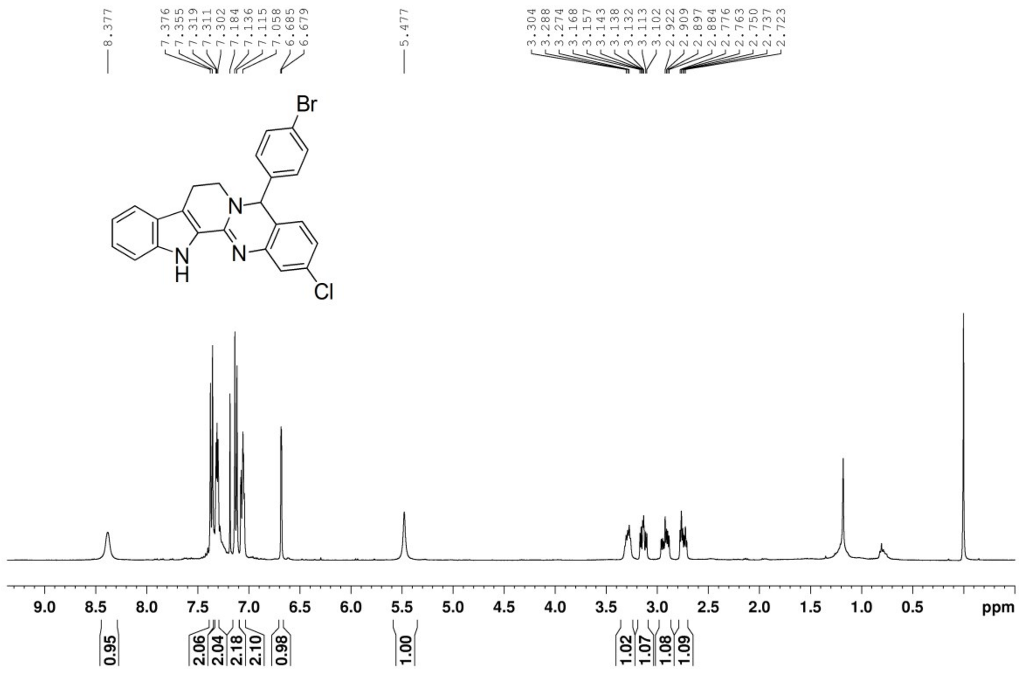
^{13}C NMR of **4a** in $CDCl_3$



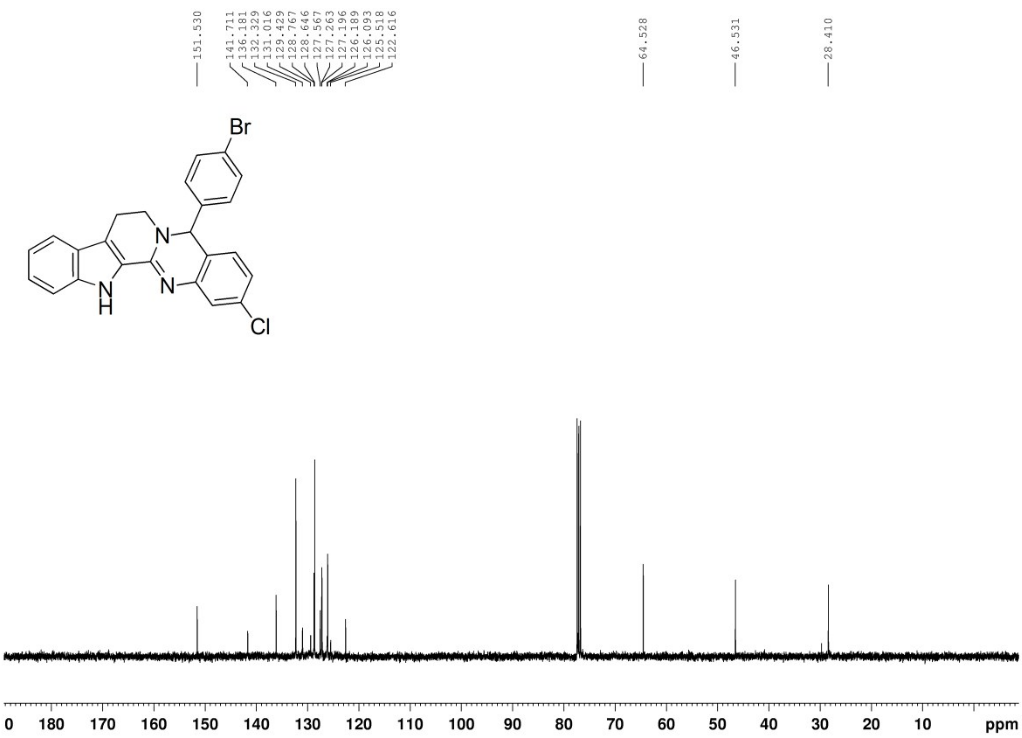
^{1}H NMR of **4b** in $CDCl_3$



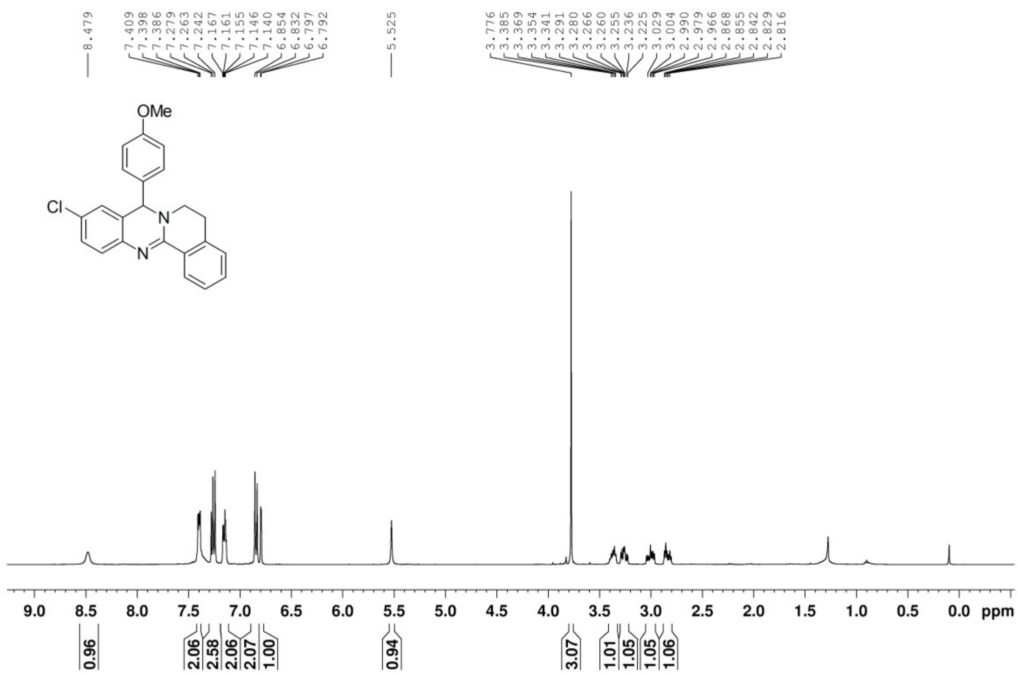
^{13}C NMR of **4b** in $CDCl_3$



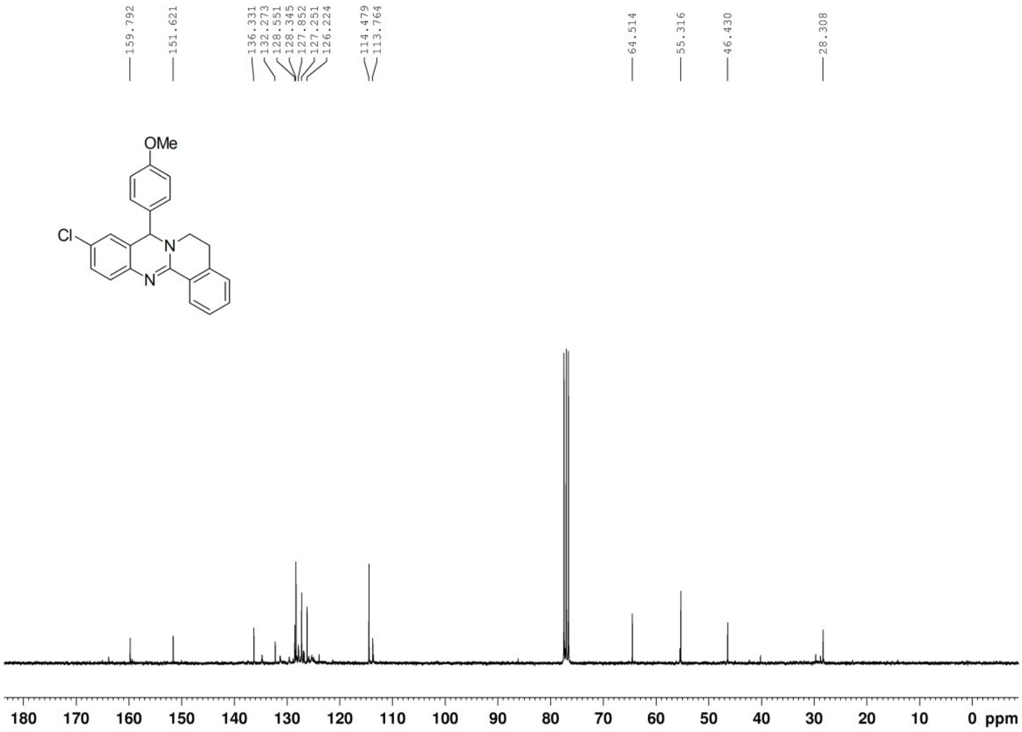
^{1}H NMR of **4c** in $CDCl_3$



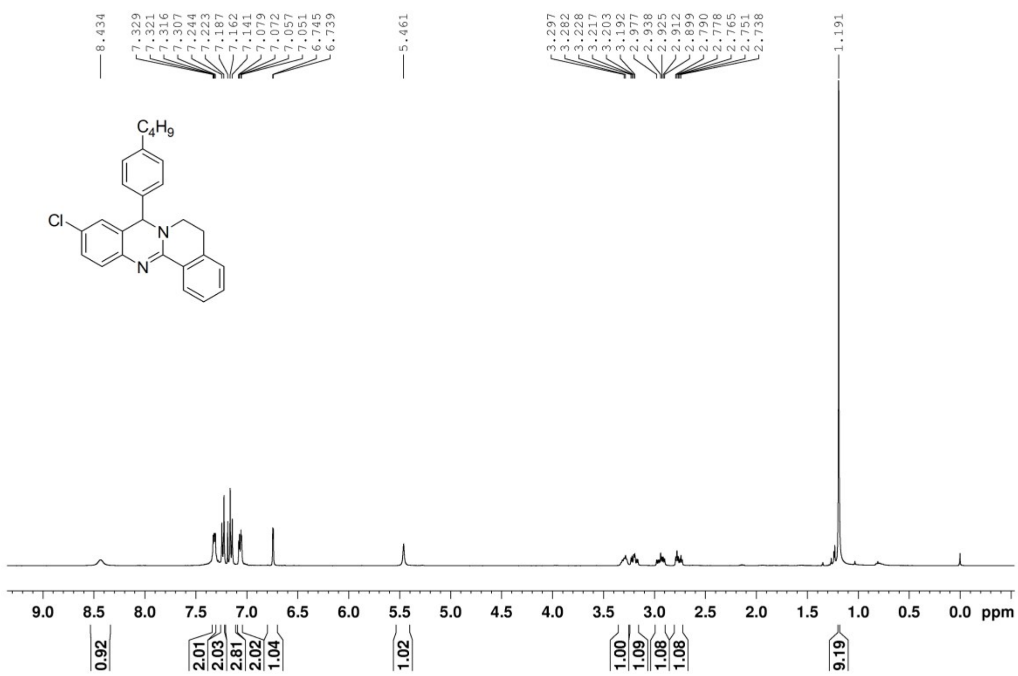
^{13}C NMR of **4c** in $CDCl_3$



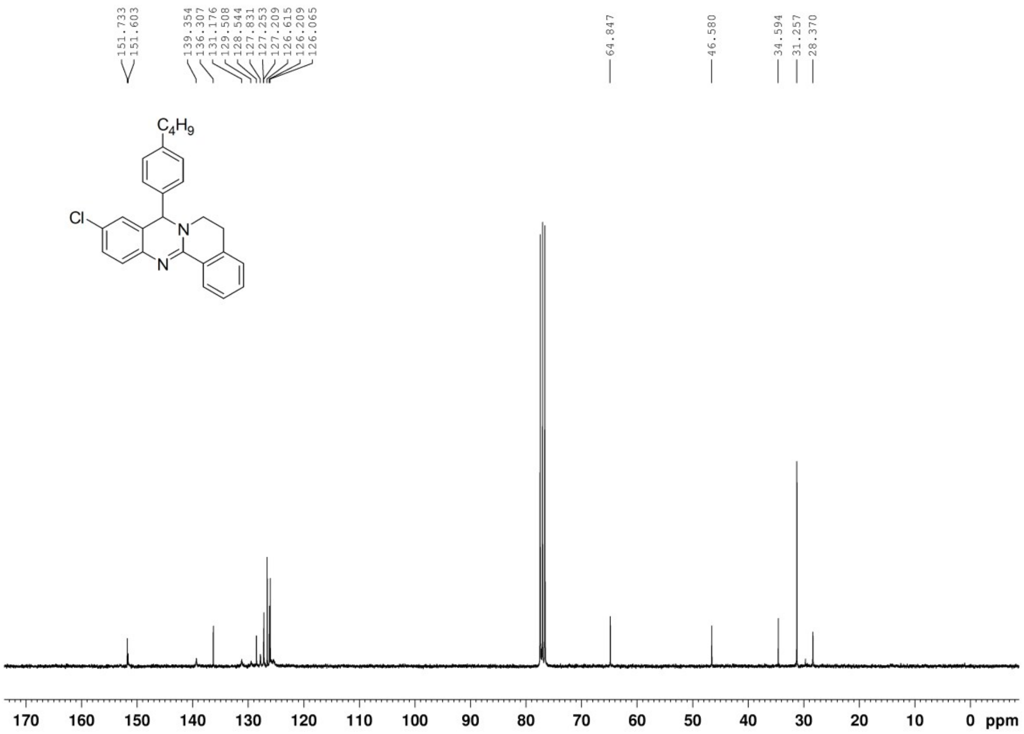
^{1}H NMR of **4d** in $CDCl_3$



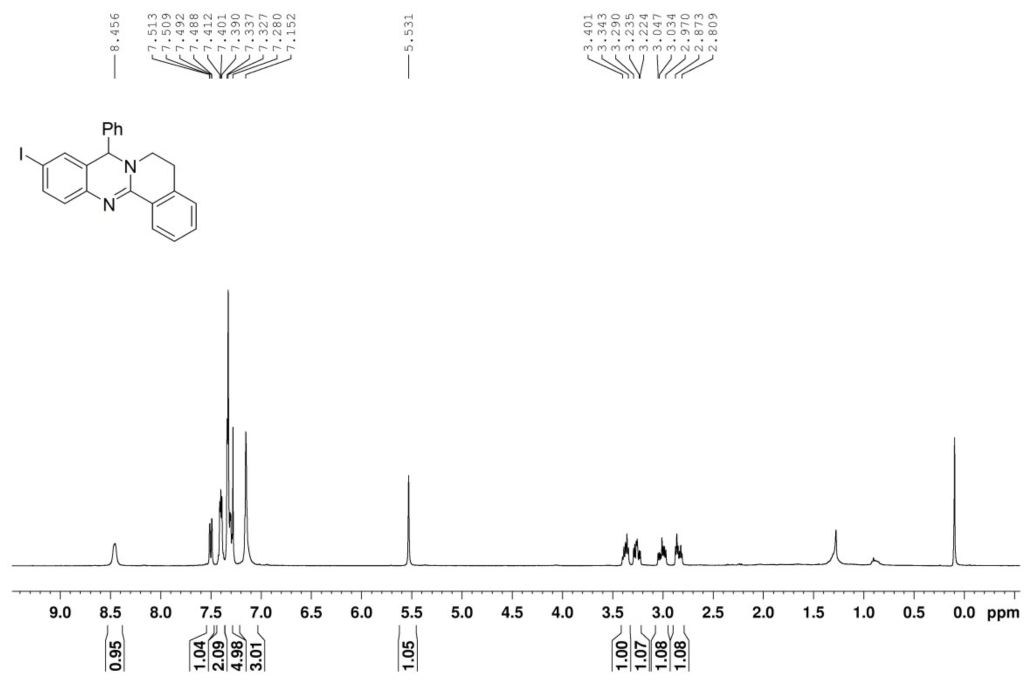
^{13}C NMR of **4d** in $CDCl_3$



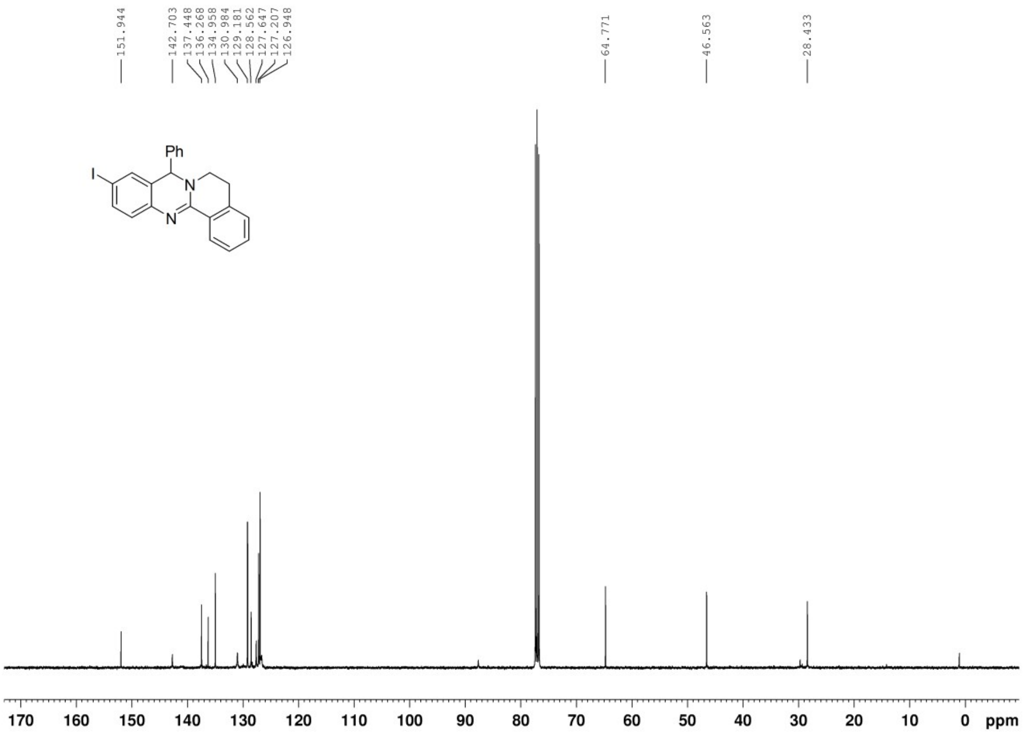
^{1}H NMR of **4e** in $CDCl_3$



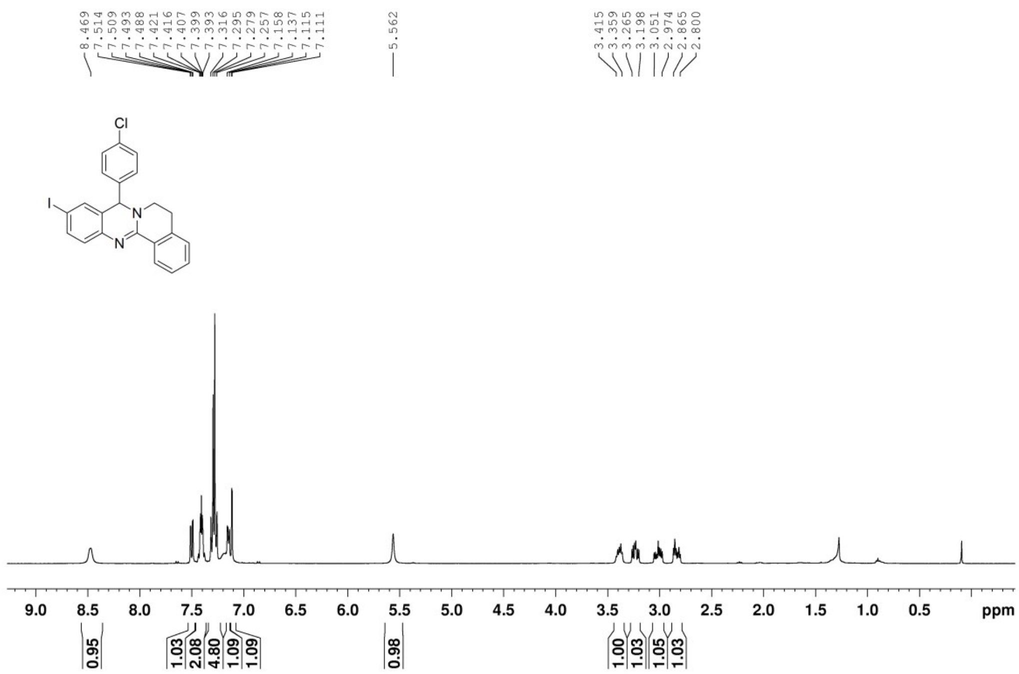
^{13}C NMR of **4e** in $CDCl_3$



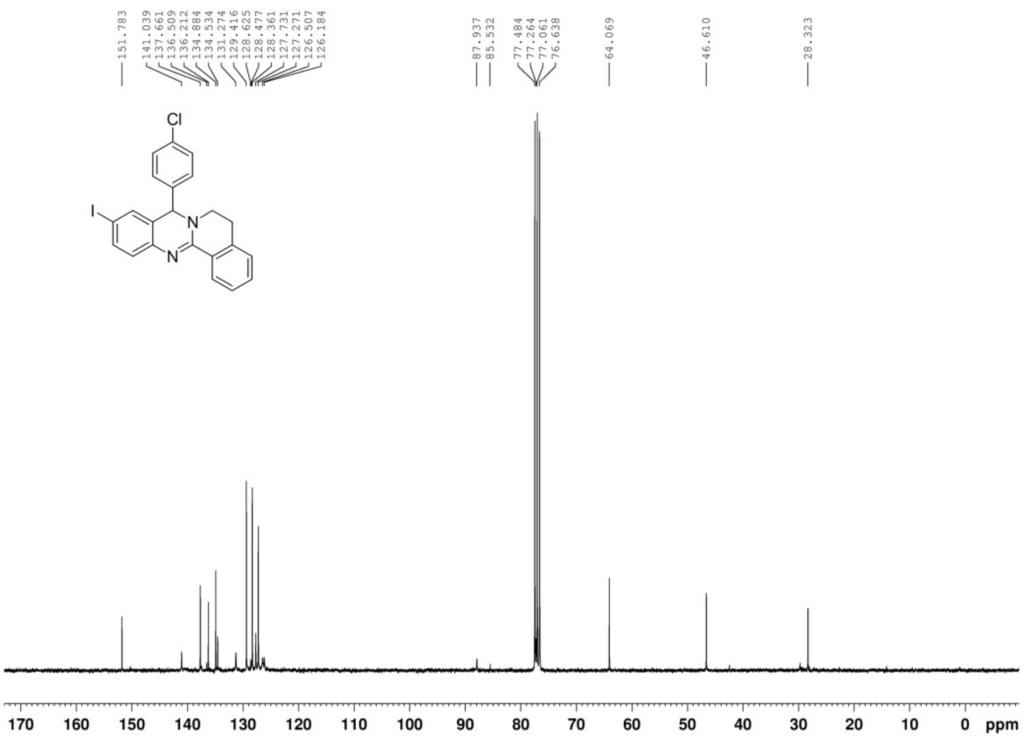
^{1}H NMR of **4f** in $CDCl_3$



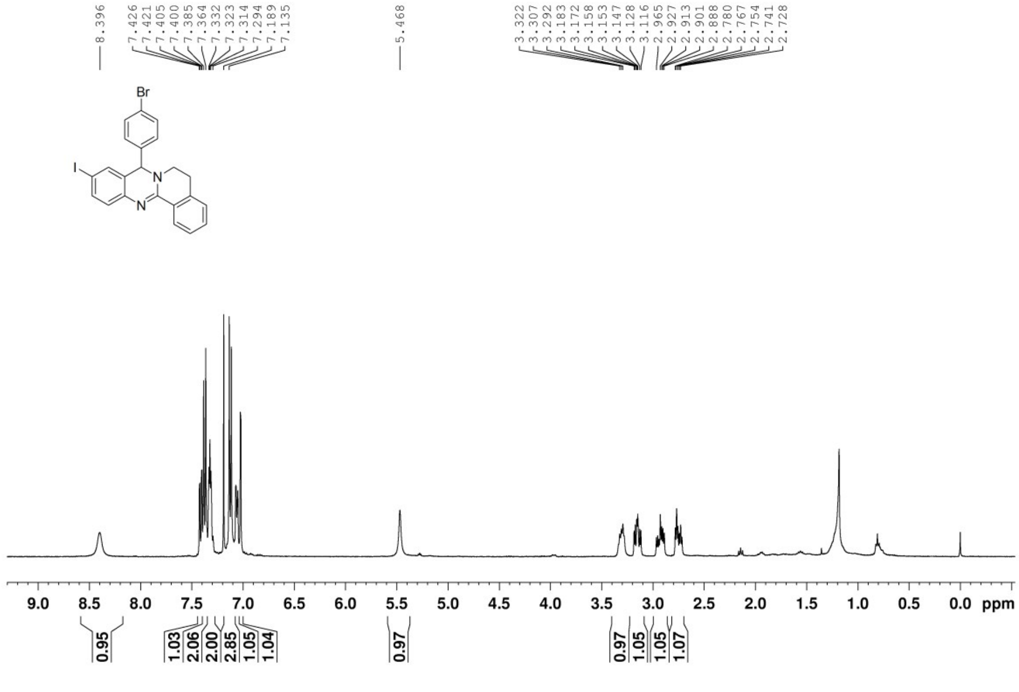
^{13}C NMR of **4f** in $CDCl_3$



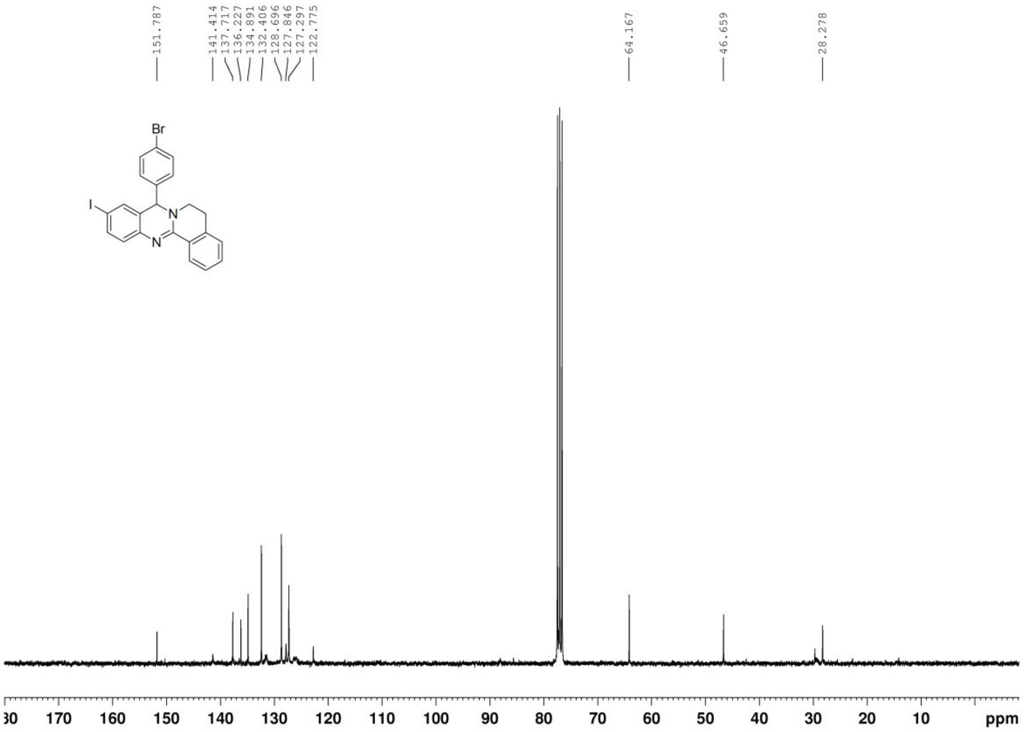
^{1}H NMR of **4g** in $CDCl_3$



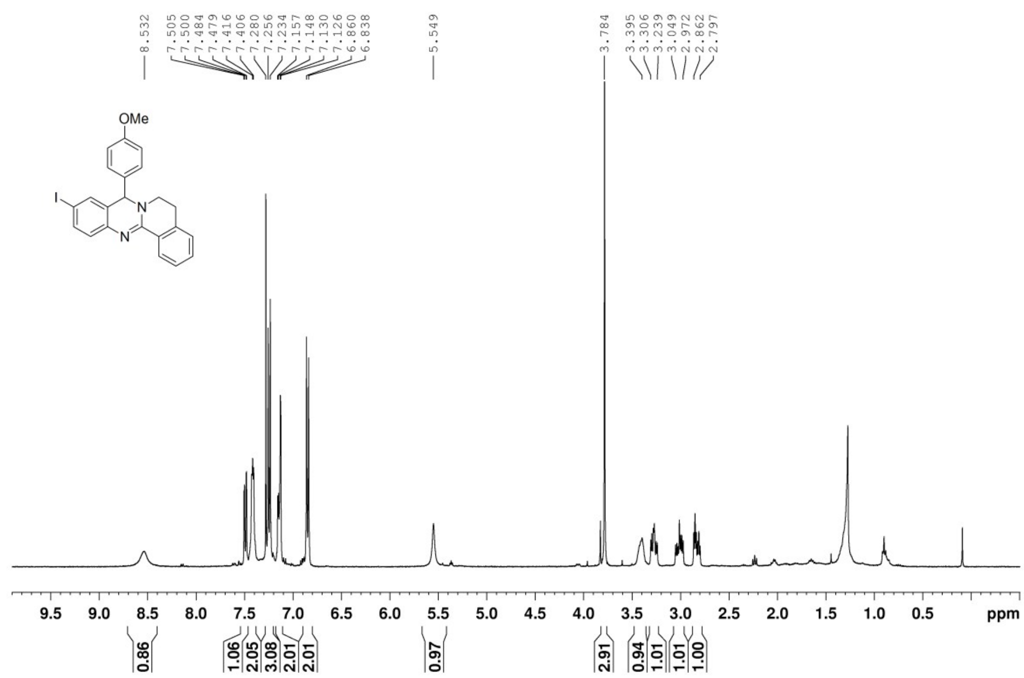
^{13}C NMR of **4g** in $CDCl_3$



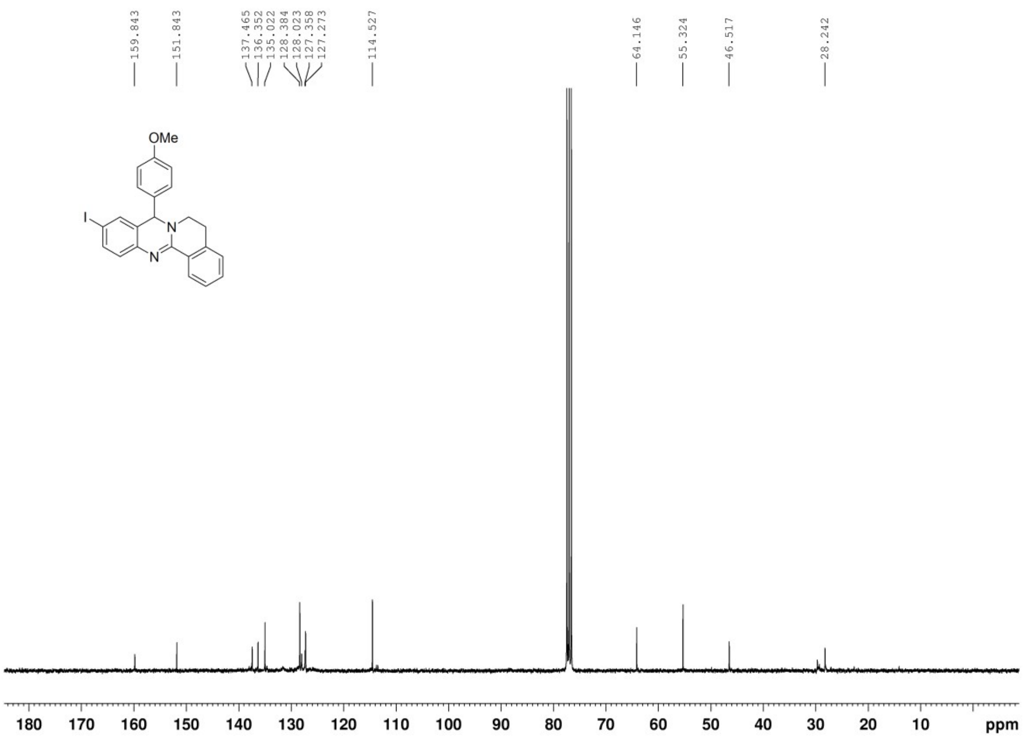
^{1}H NMR of **4h** in $CDCl_3$



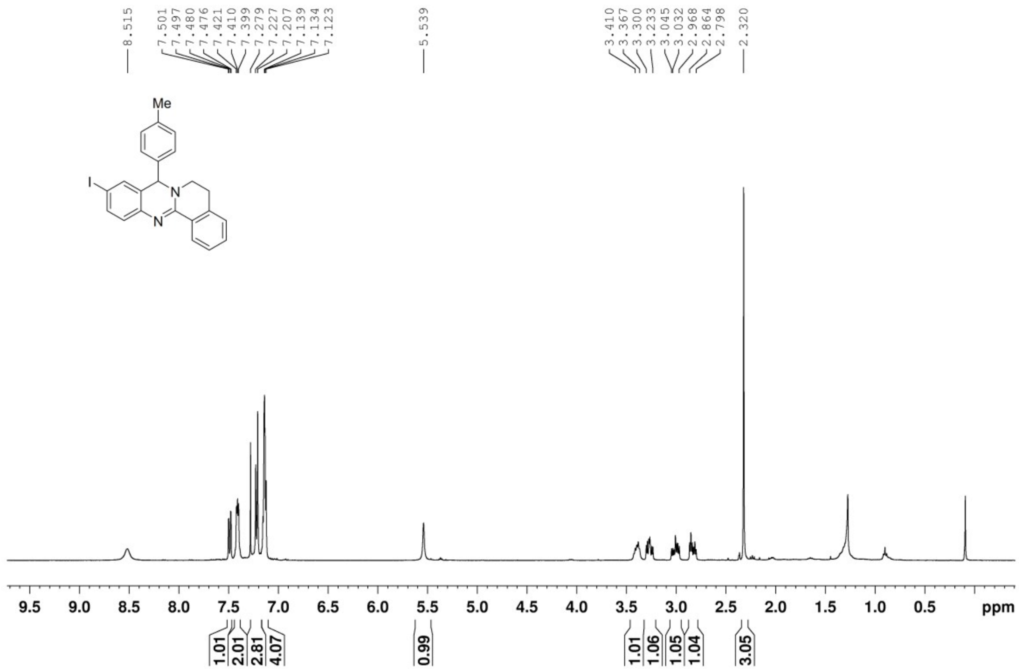
^{13}C NMR of **4h** in $CDCl_3$



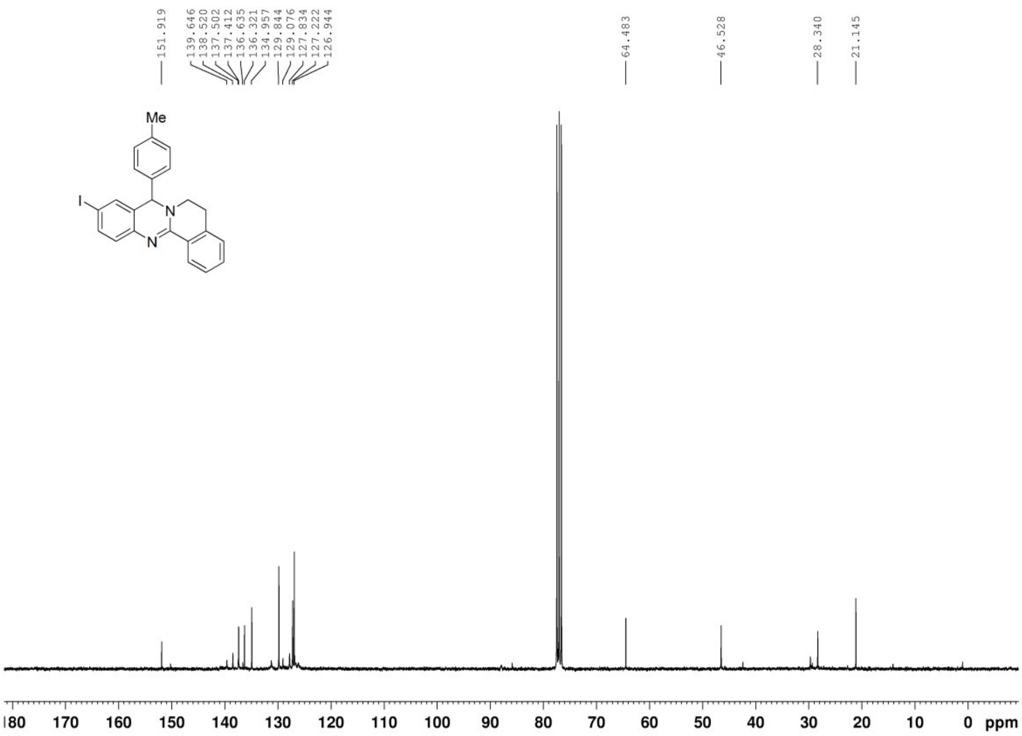
^{1}H NMR of **4i** in $CDCl_3$



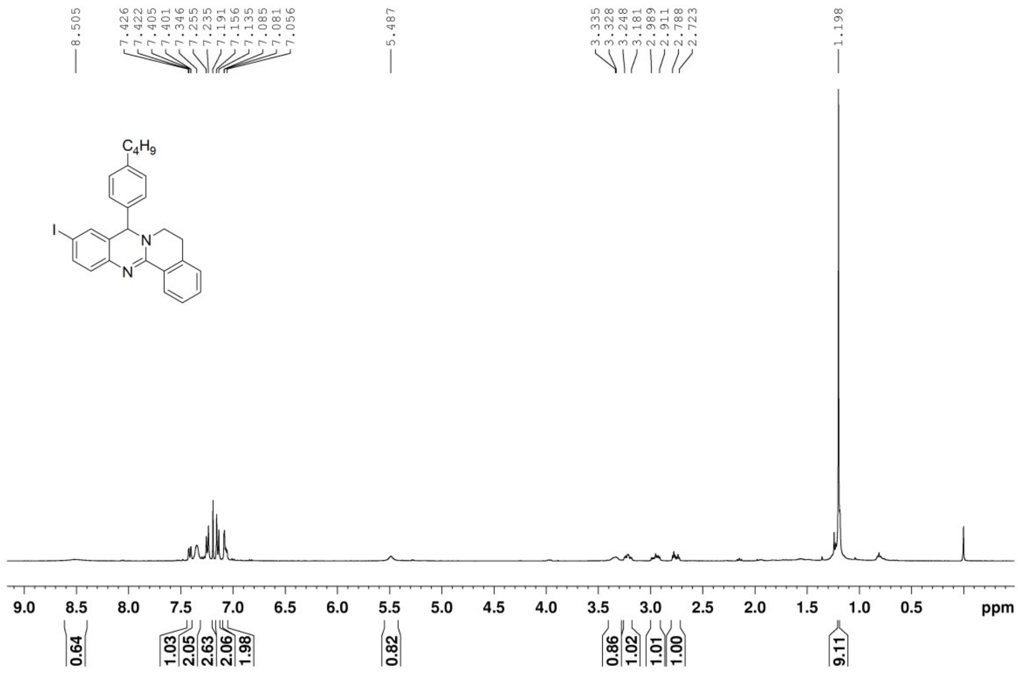
^{13}C NMR of **4i** in $CDCl_3$



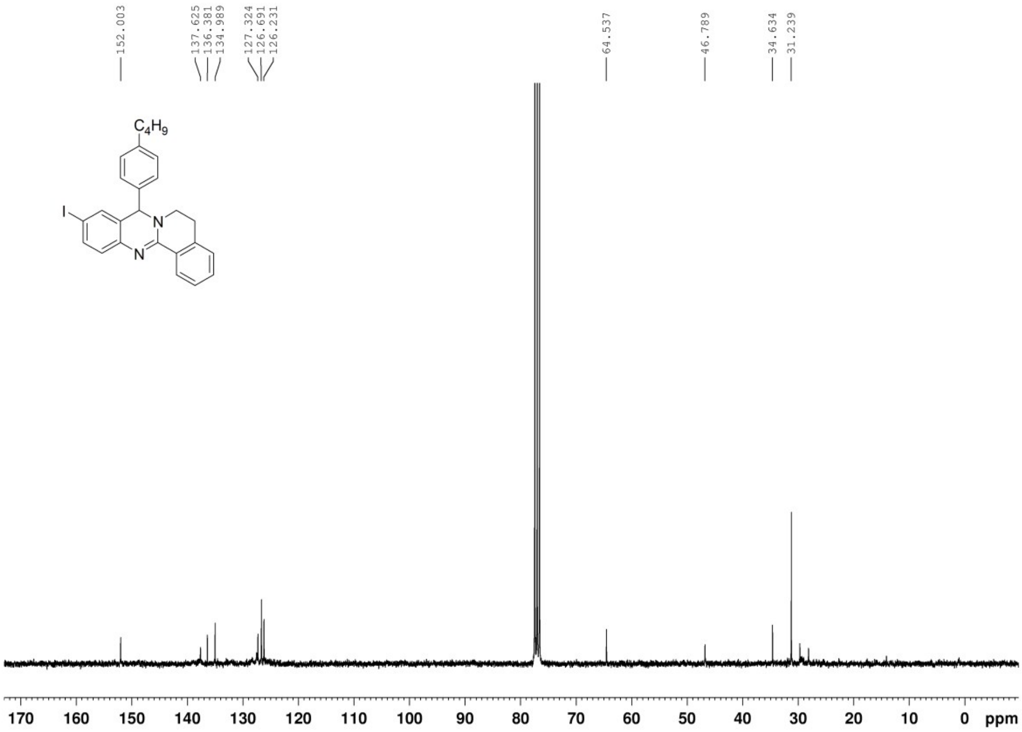
^{1}H NMR of **4j** in $CDCl_3$



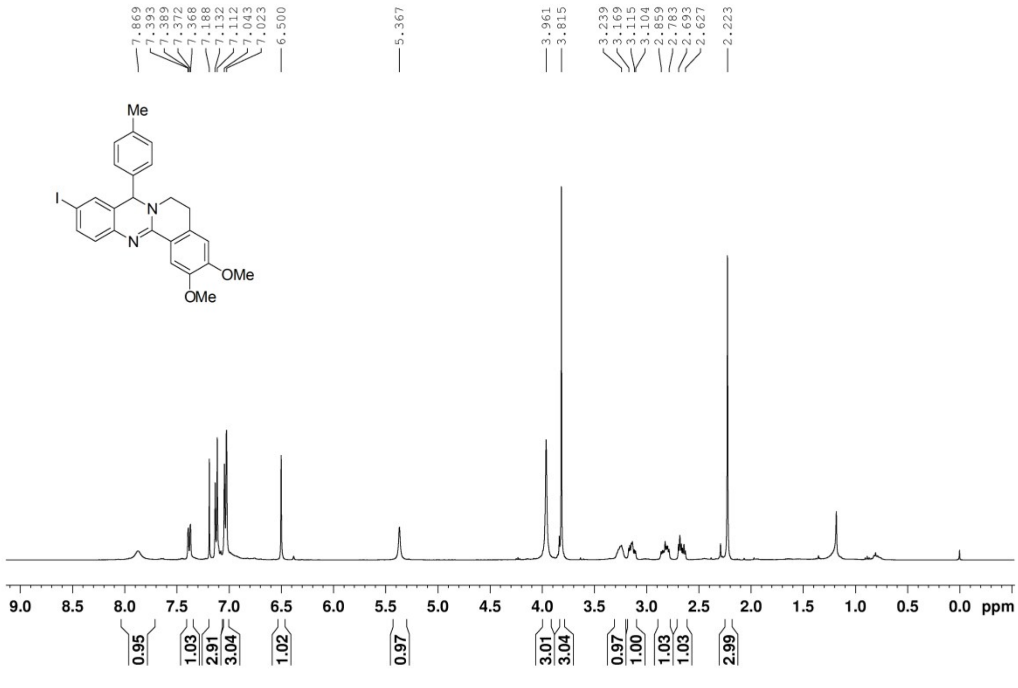
^{13}C NMR of **4j** in $CDCl_3$



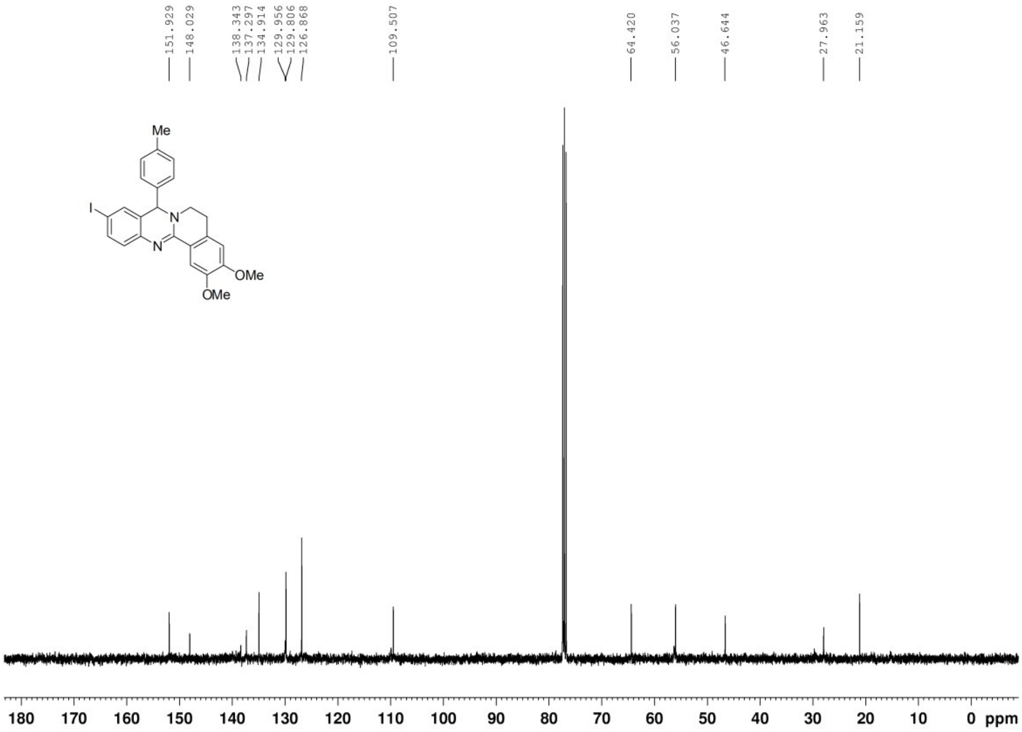
^{1}H NMR of **4k** in $CDCl_3$



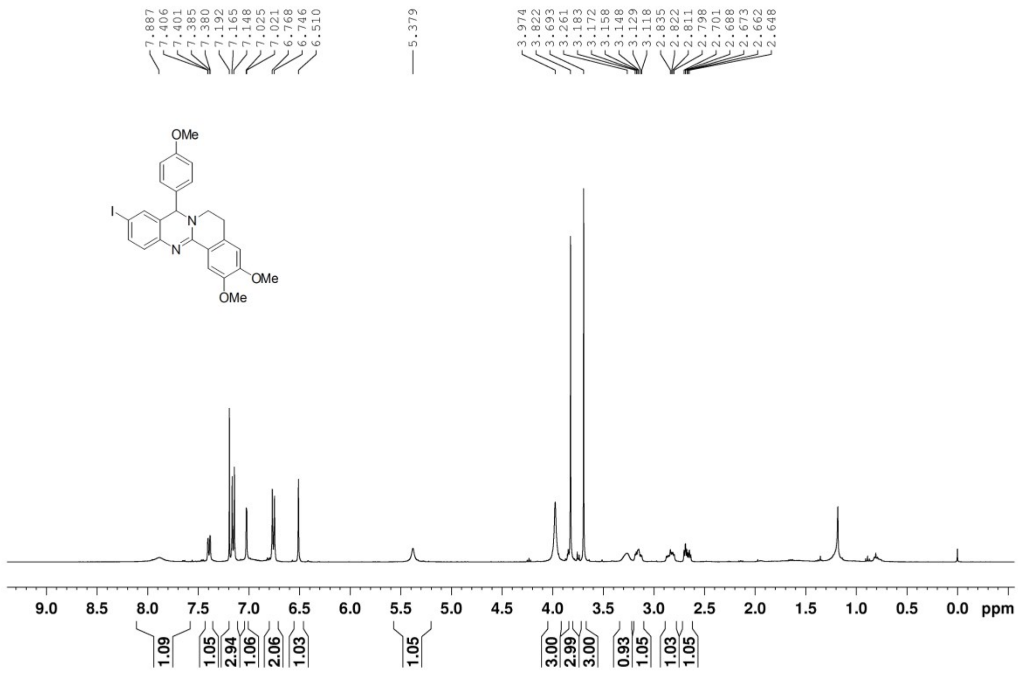
^{13}C NMR of **4k** in $CDCl_3$



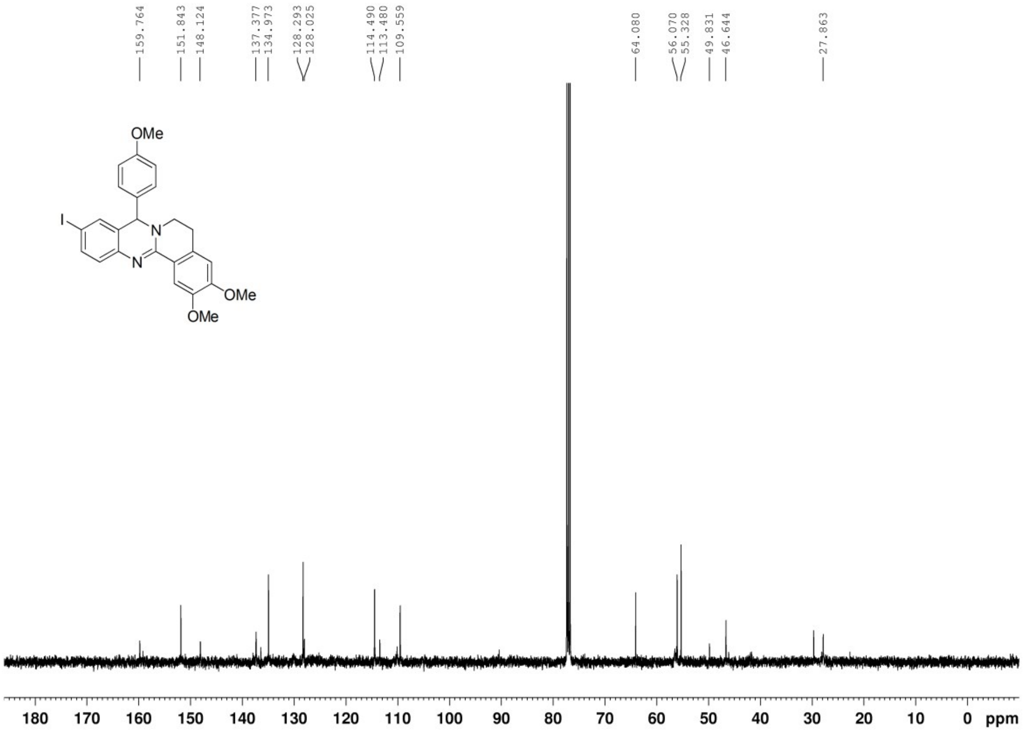
^{1}H NMR of **4l** in $CDCl_3$



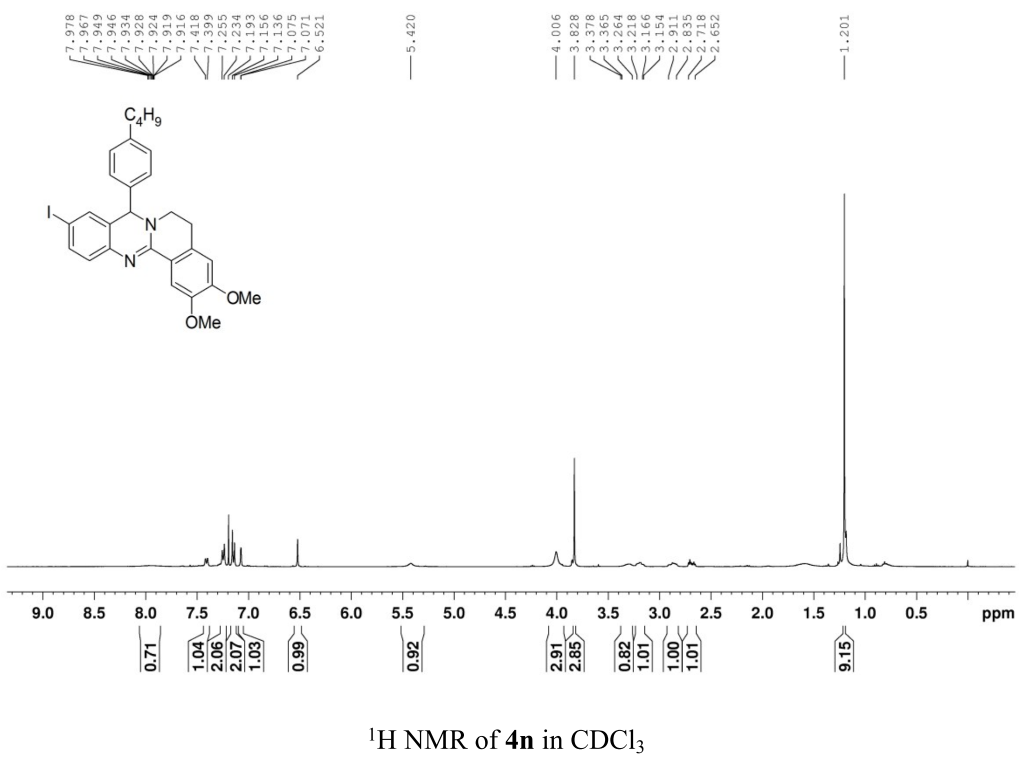
^{13}C NMR of **4l** in $CDCl_3$



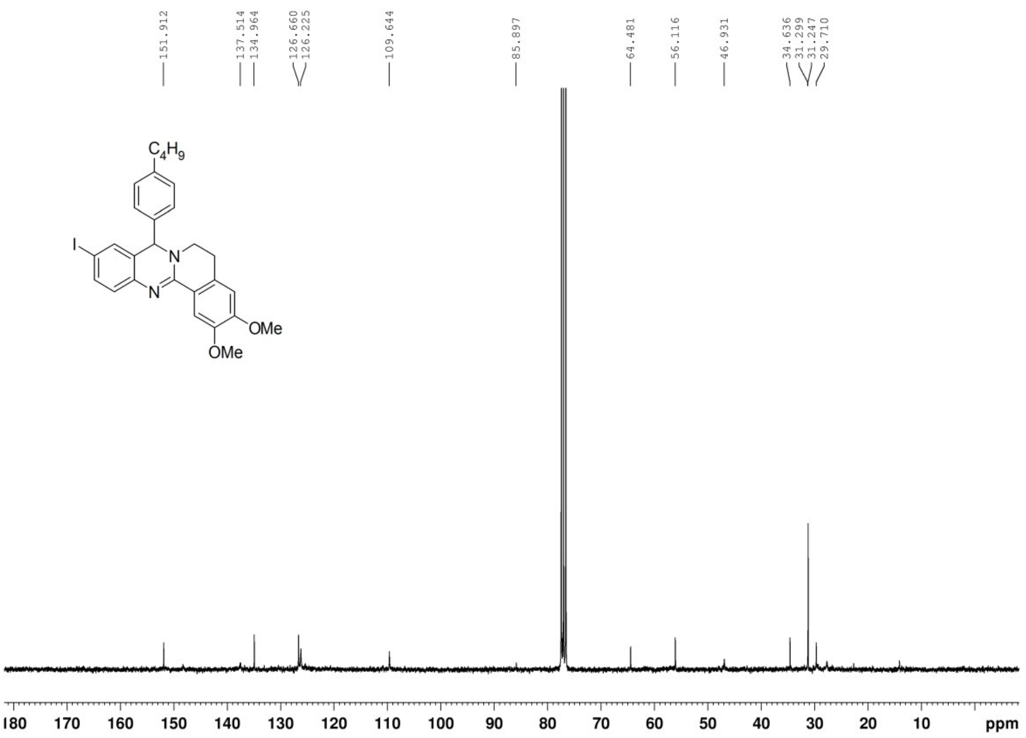
^{1}H NMR of **4m** in $CDCl_3$



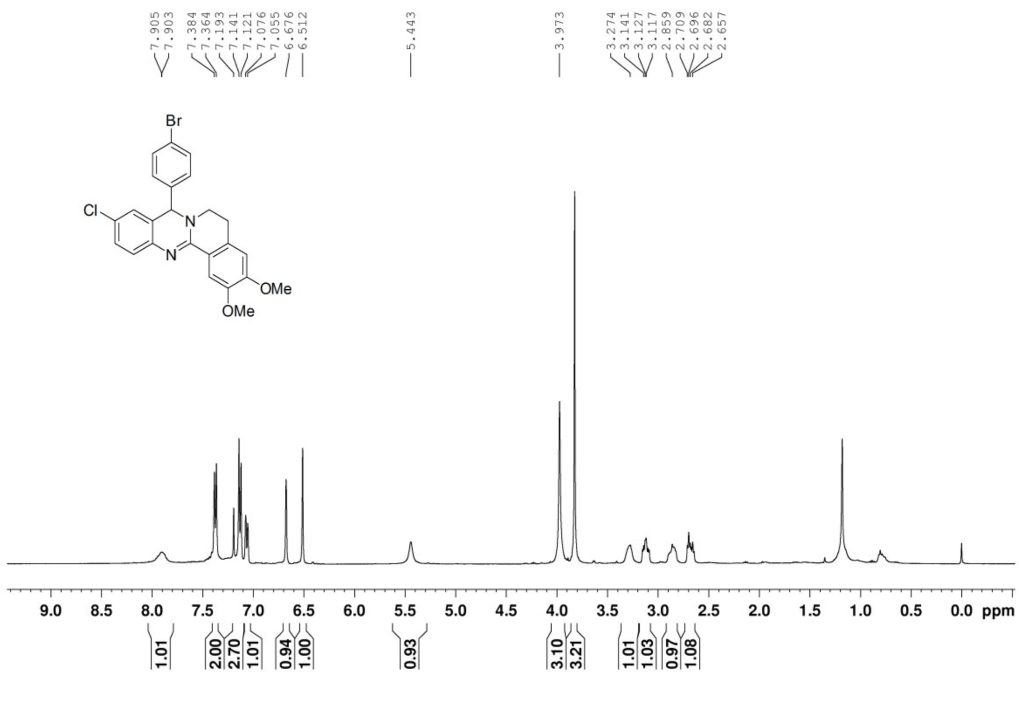
^{13}C NMR of **4m** in $CDCl_3$



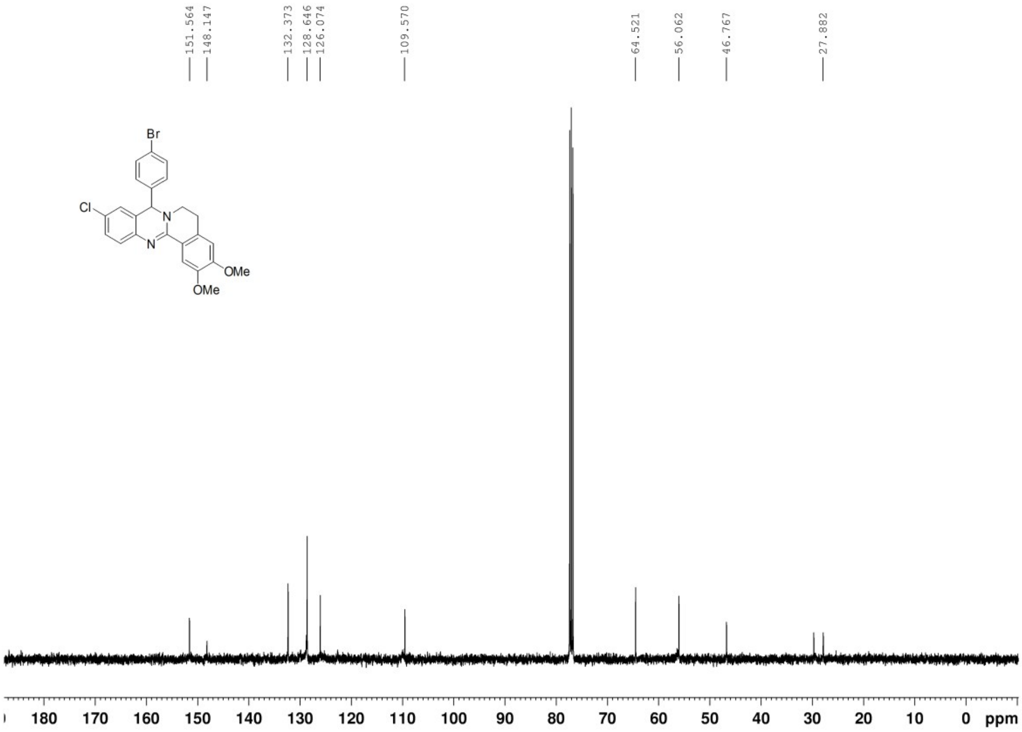
^{1}H NMR of **4n** in $CDCl_3$



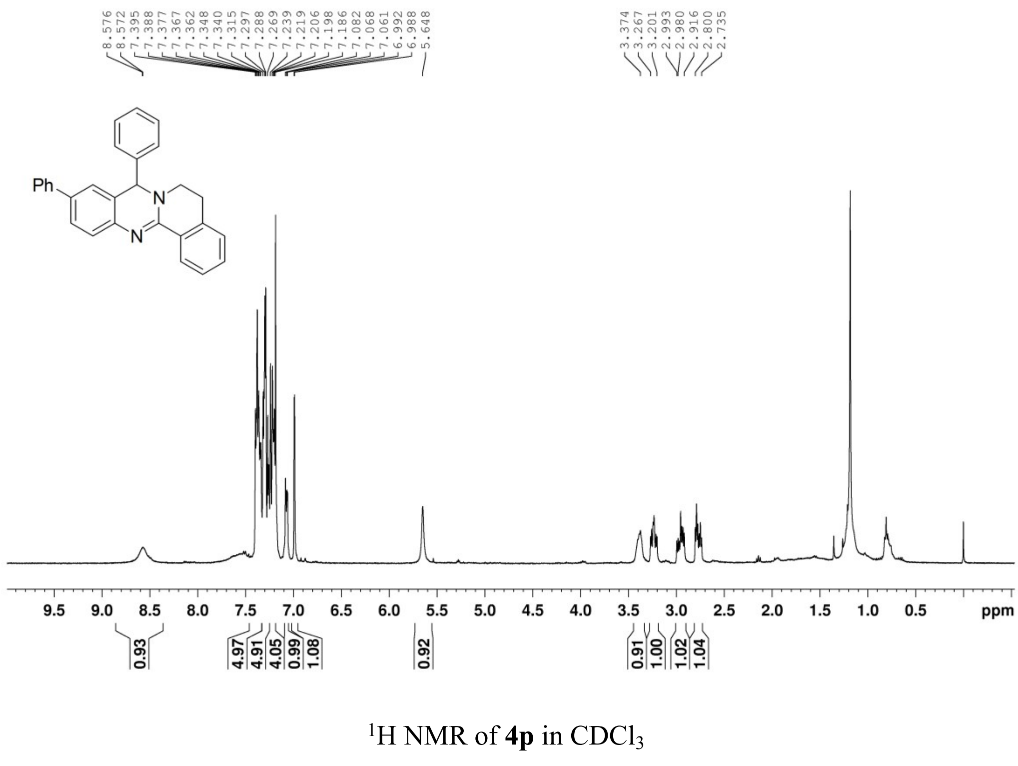
^{13}C NMR of **4n** in $CDCl_3$



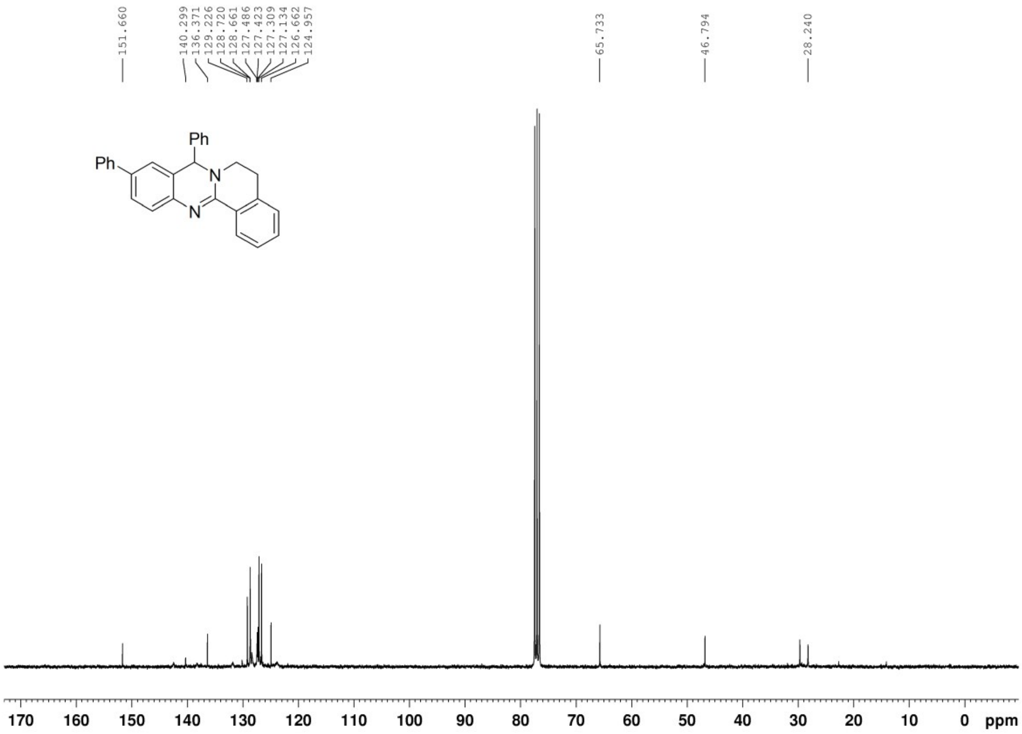
^{1}H NMR of **4o** in $CDCl_3$



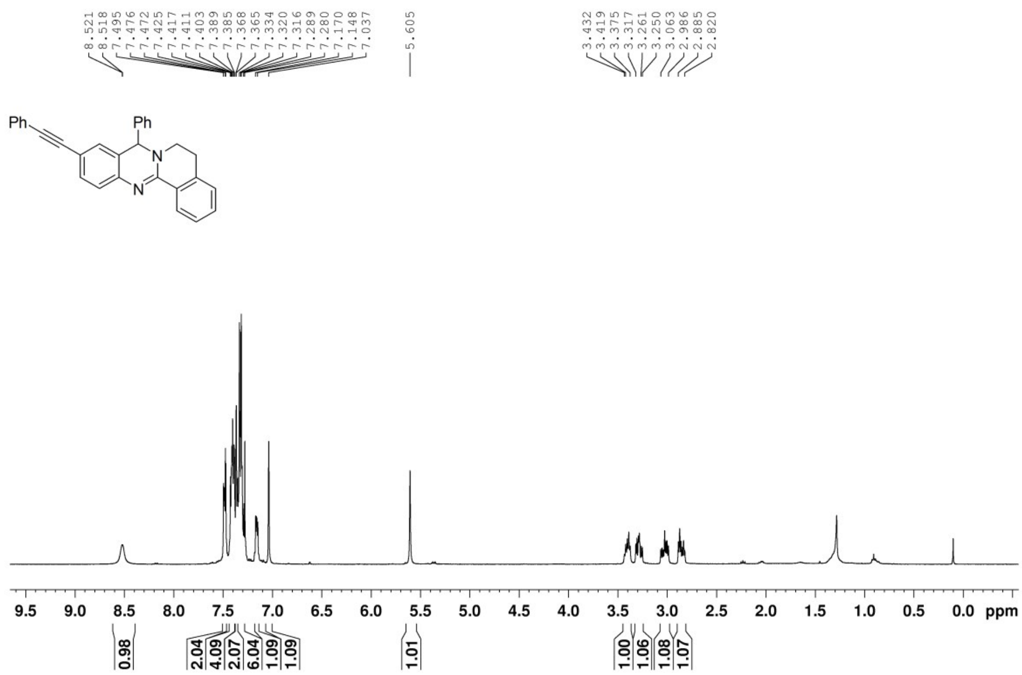
^{13}C NMR of **4o** in $CDCl_3$



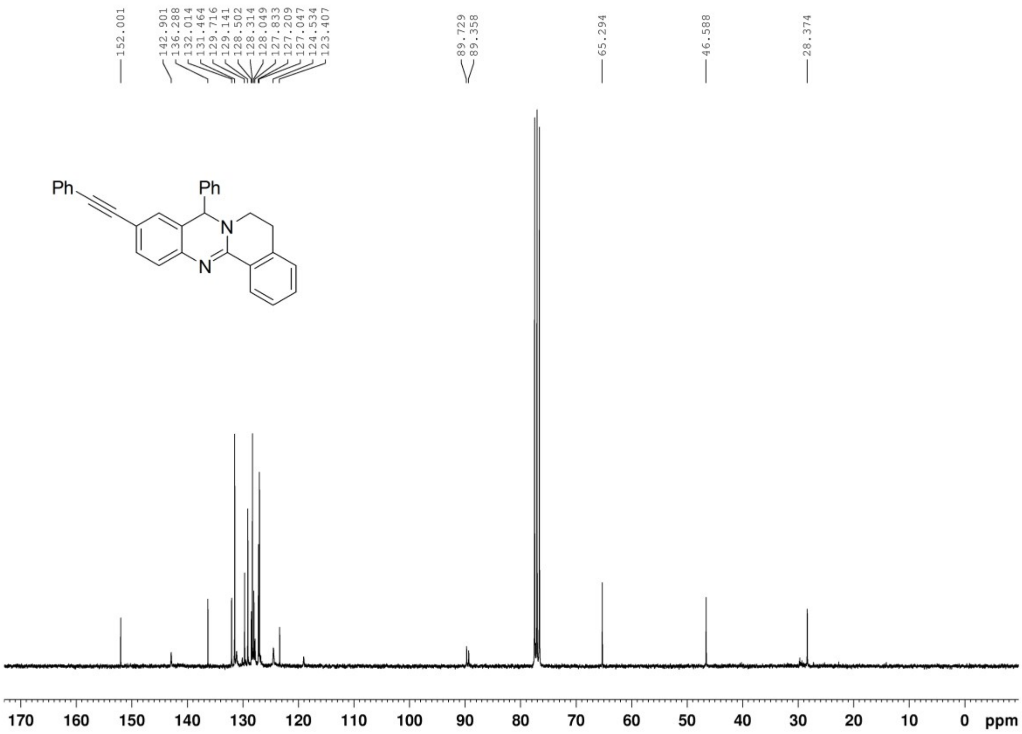
^{1}H NMR of **4p** in $CDCl_3$



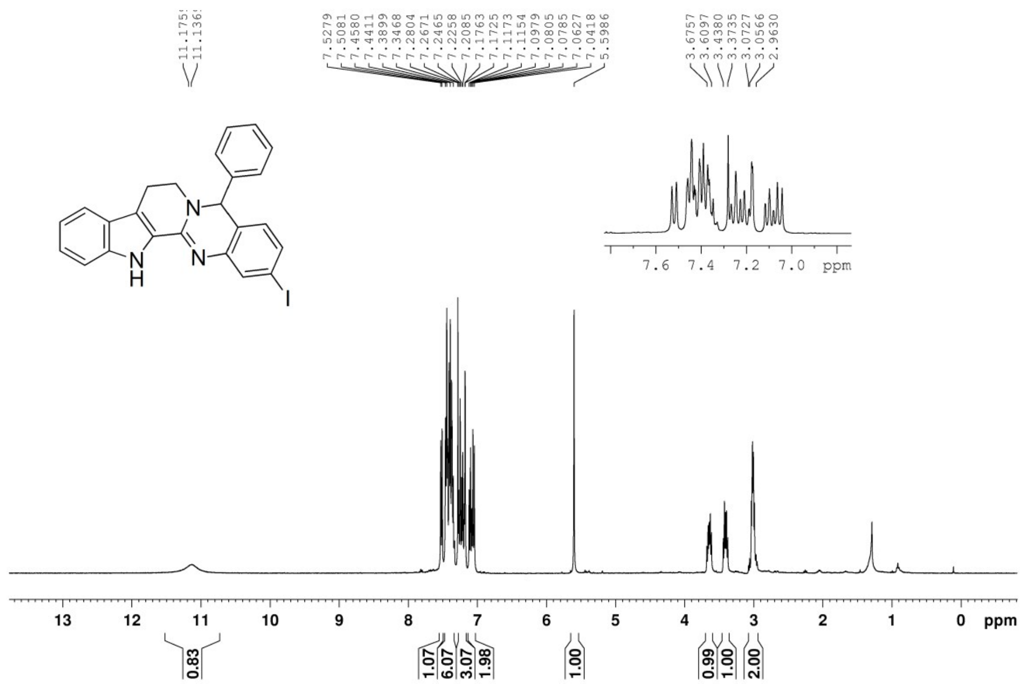
^{13}C NMR of **4p** in $CDCl_3$



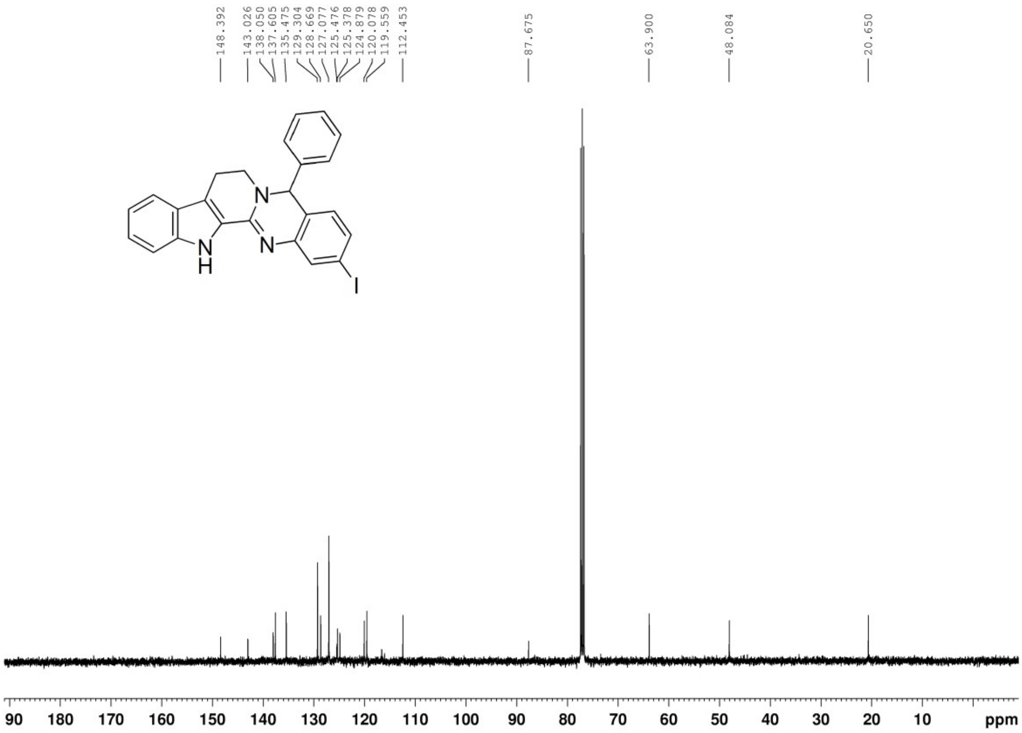
^{1}H NMR of **4q** in $CDCl_3$



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

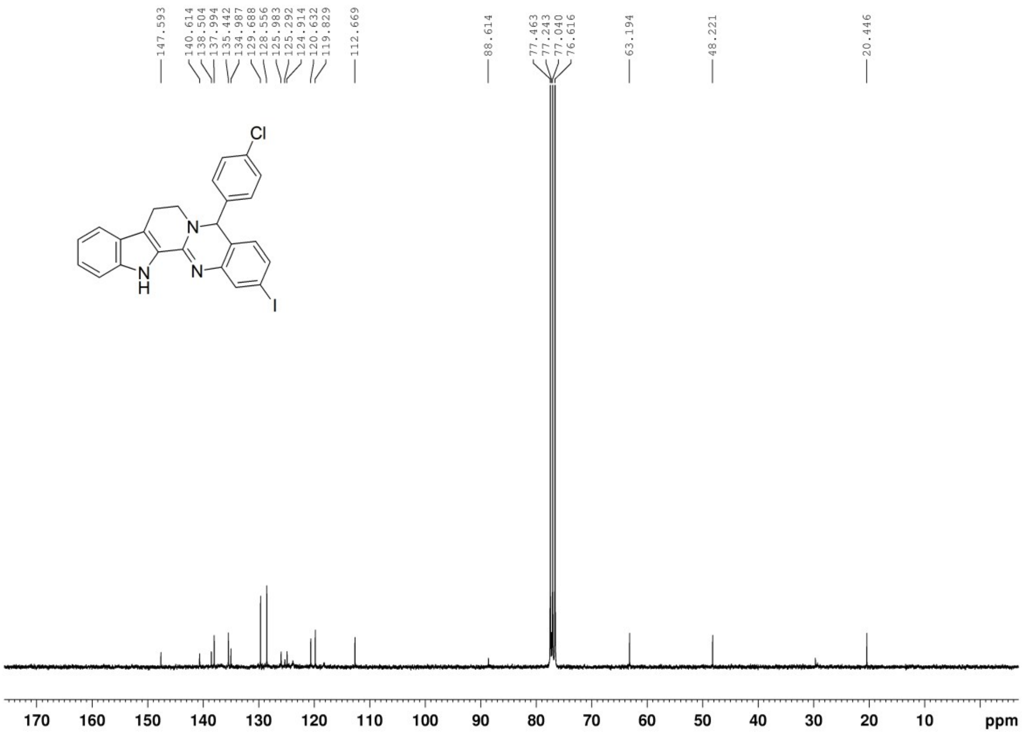


^{1}H NMR of **6a** in $CDCl_3$

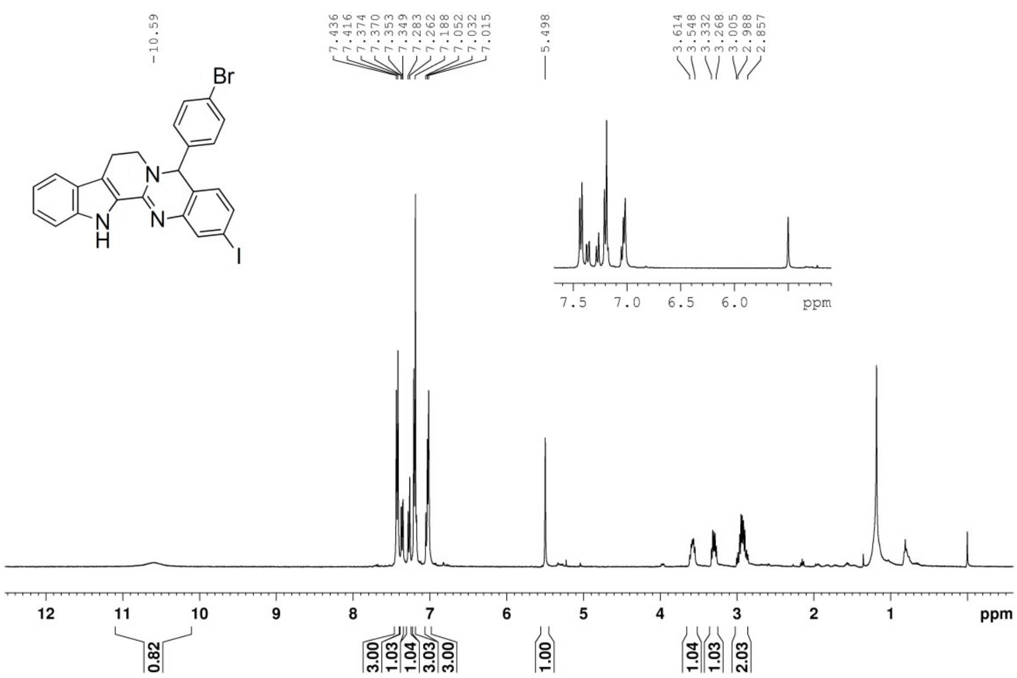


^{13}C NMR of **6a** in $CDCl_3$

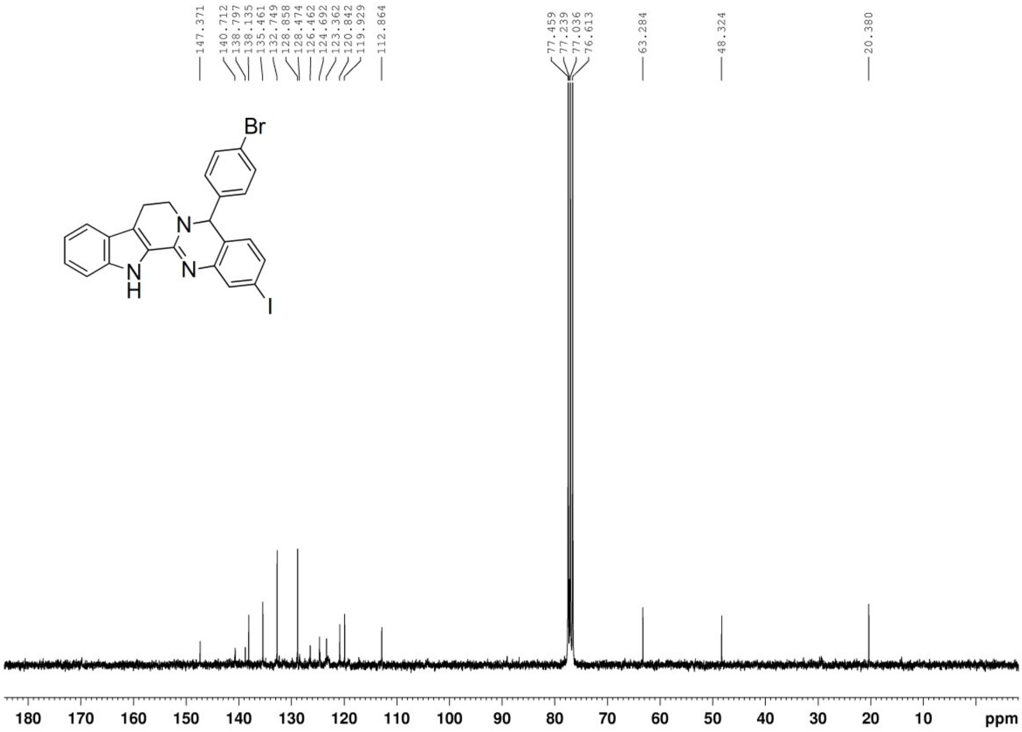
^{1}H NMR of **6b** in $CDCl_3$



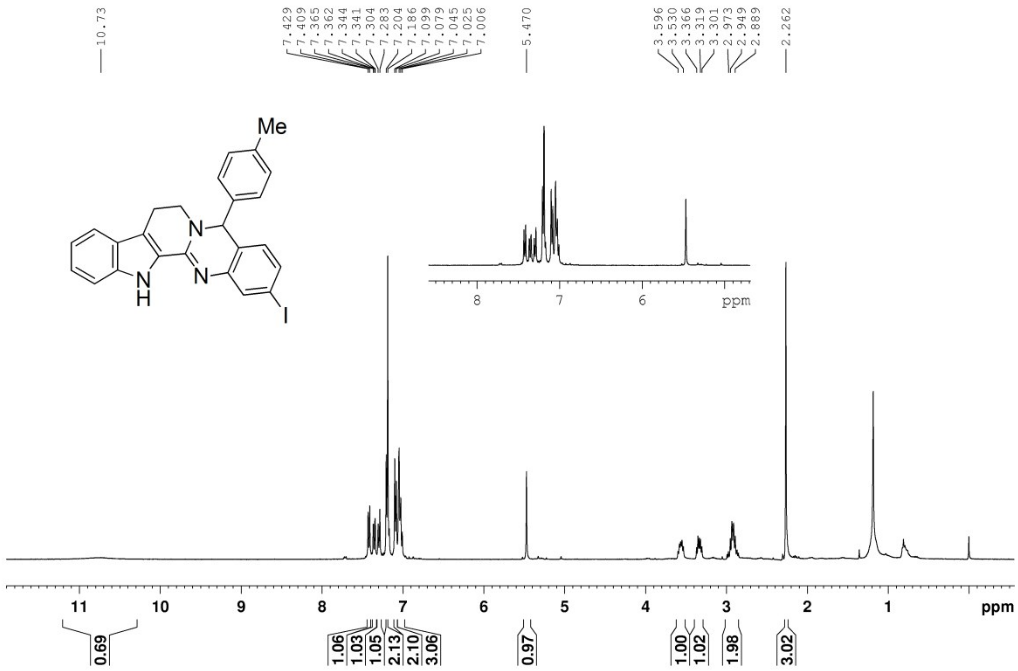
^{13}C NMR of **6b** in $CDCl_3$



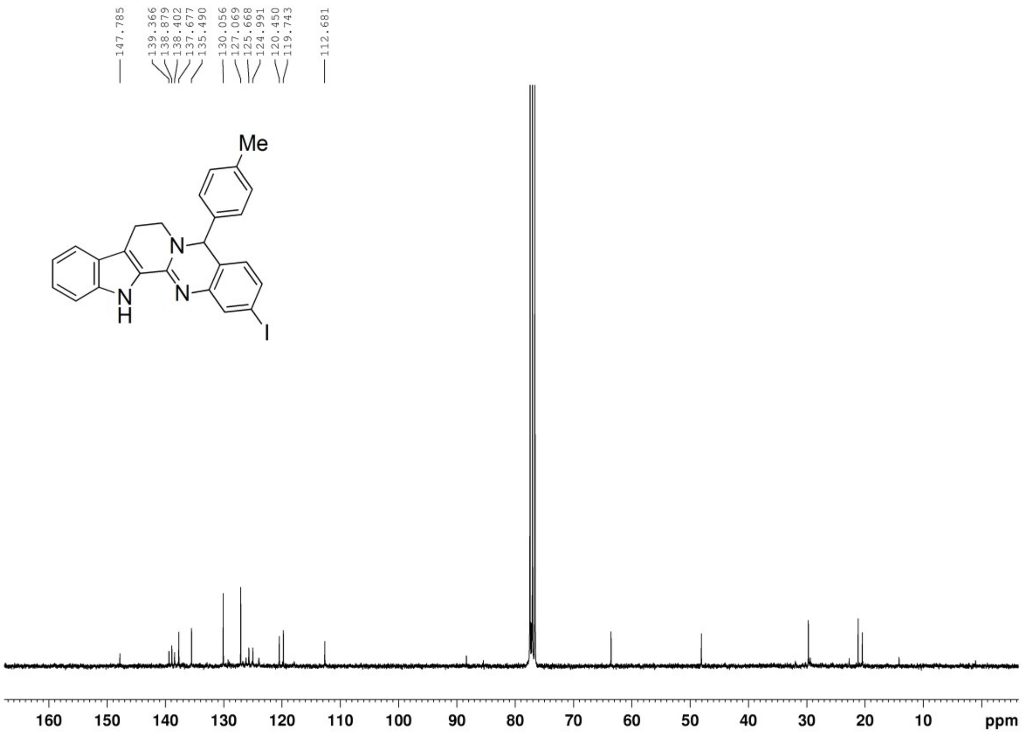
^{1}H NMR of **6c** in $CDCl_3$



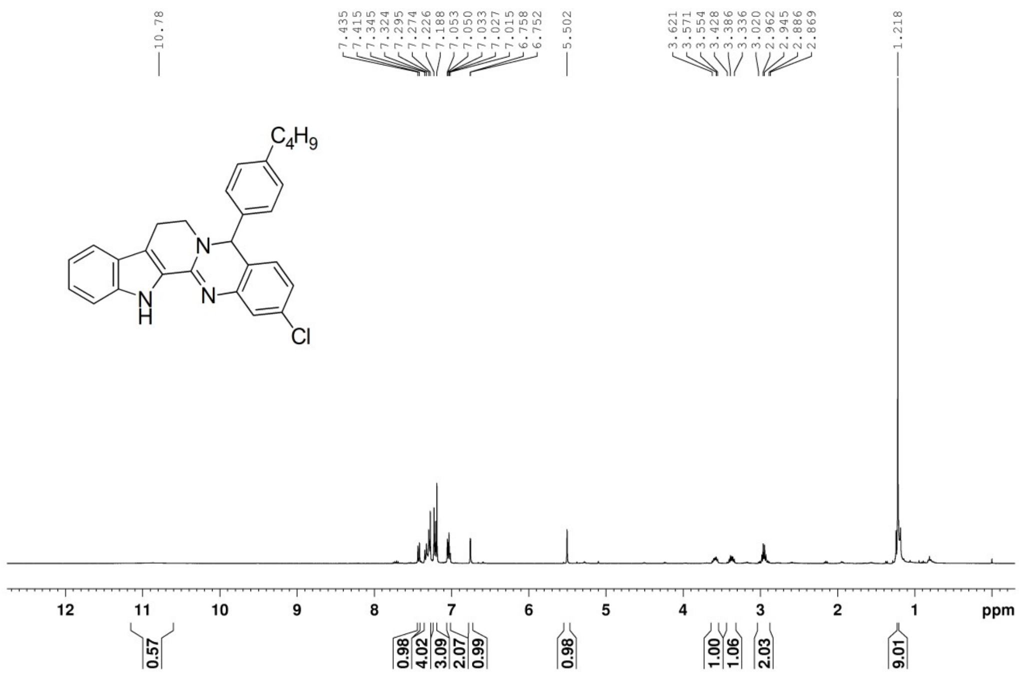
^{13}C NMR of **6c** in $CDCl_3$



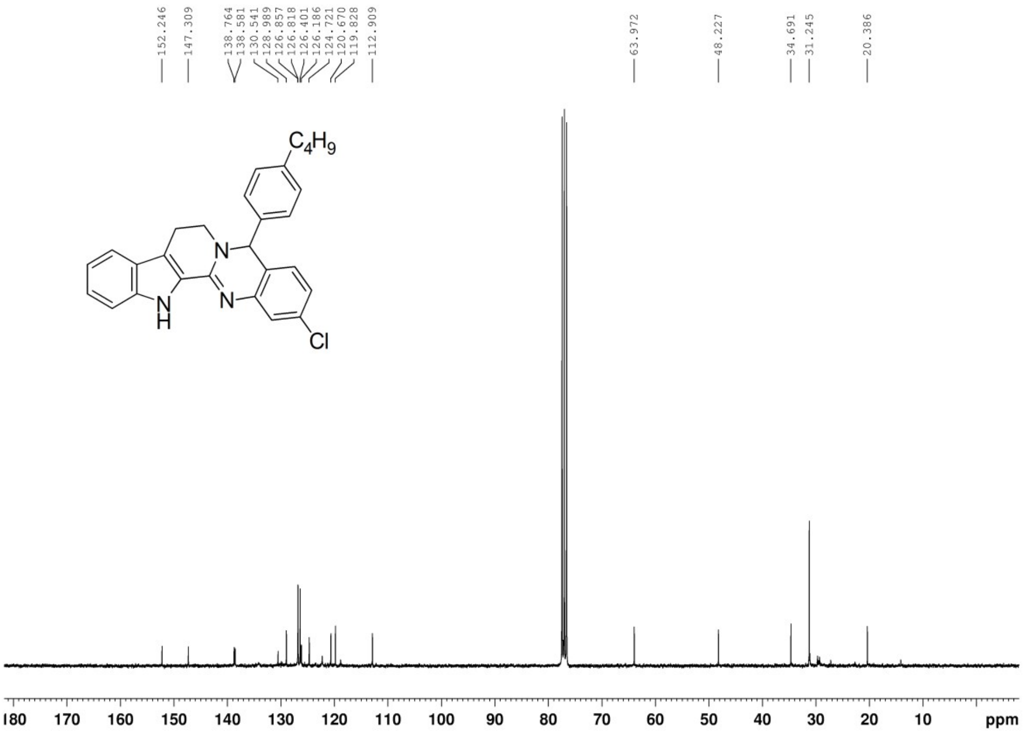
^{1}H NMR of **6d** in $CDCl_3$



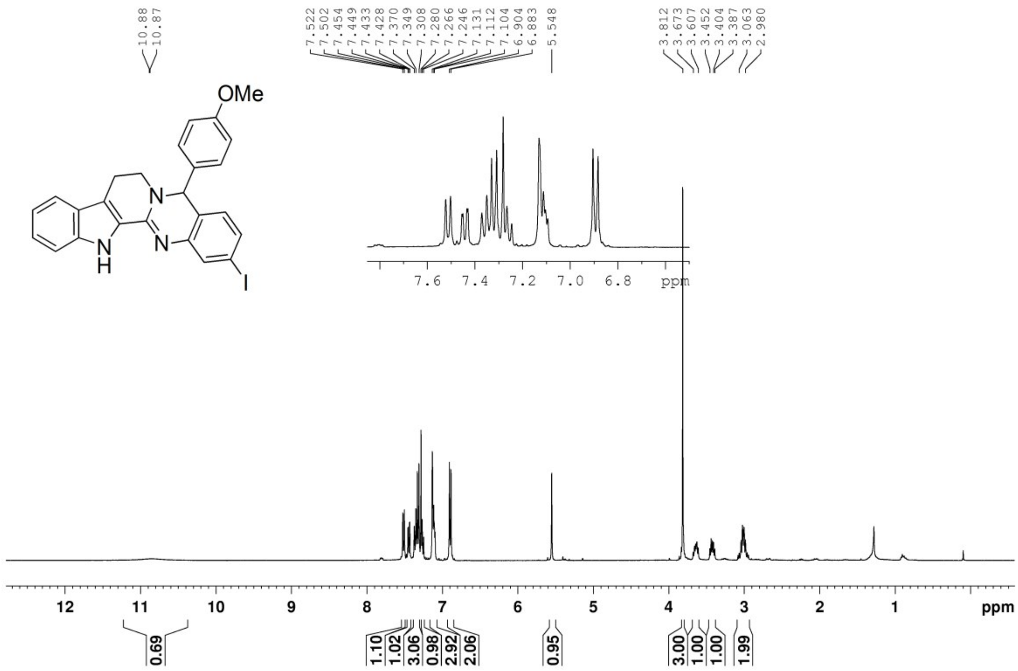
^{13}C NMR of **6d** in $CDCl_3$



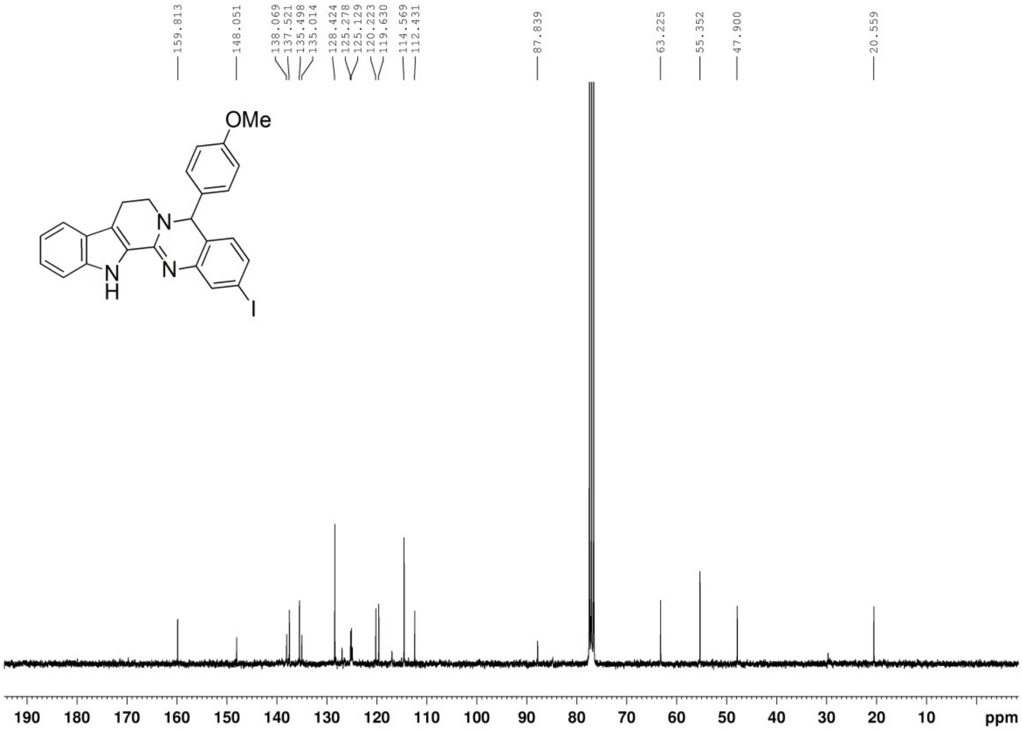
^{1}H NMR of **6e** in $CDCl_3$



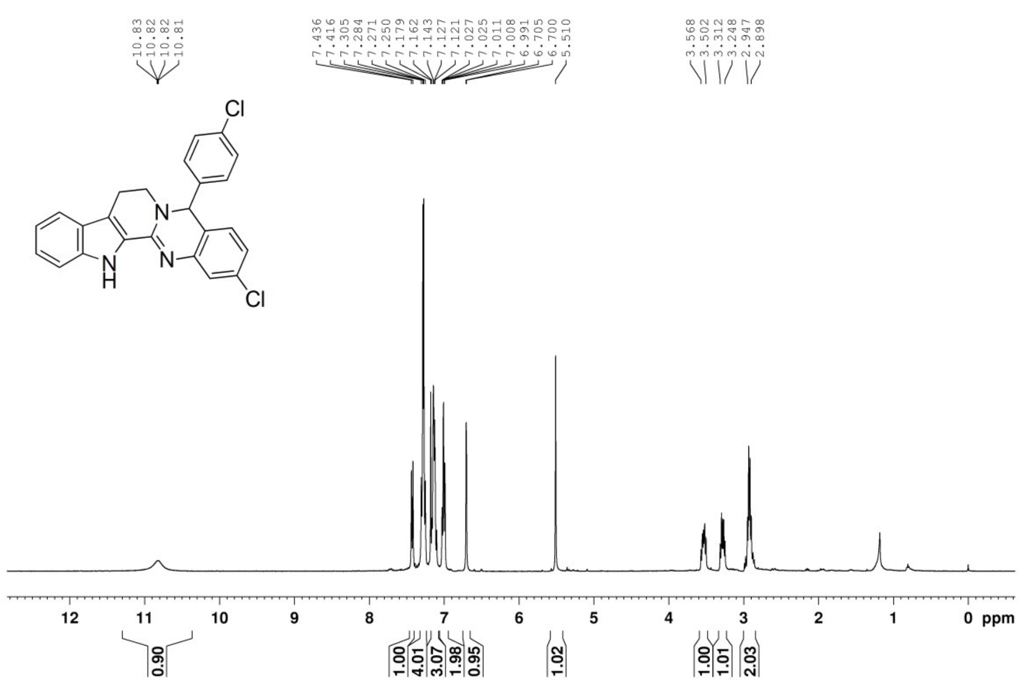
^{13}C NMR of **6e** in $CDCl_3$



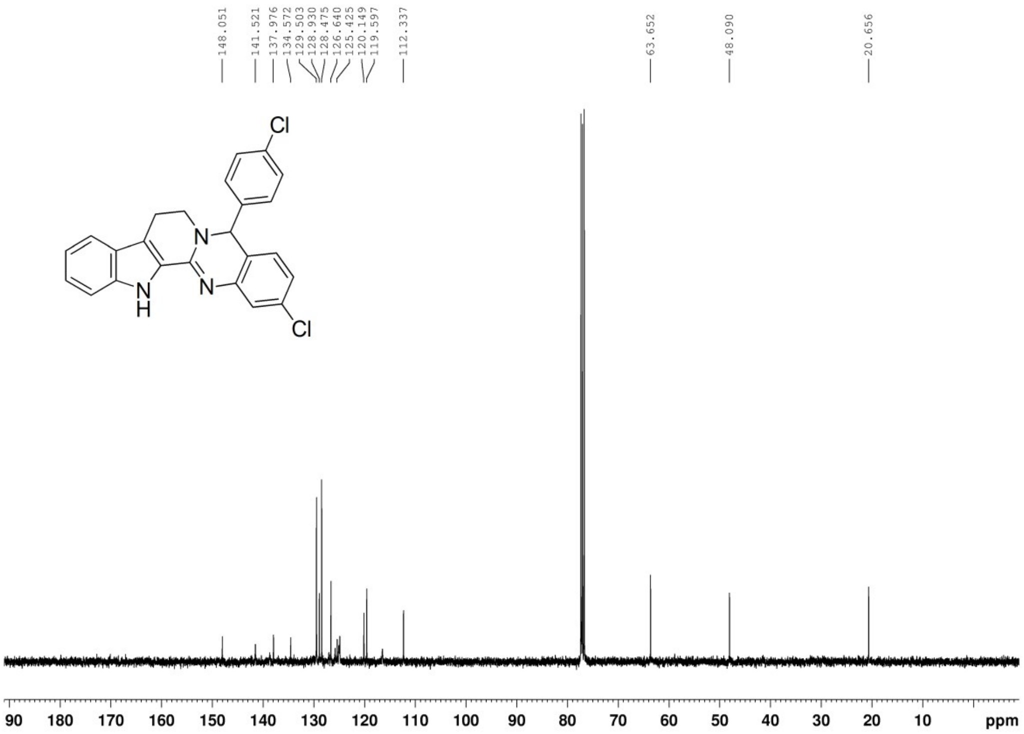
^{1}H NMR of **6f** in $CDCl_3$



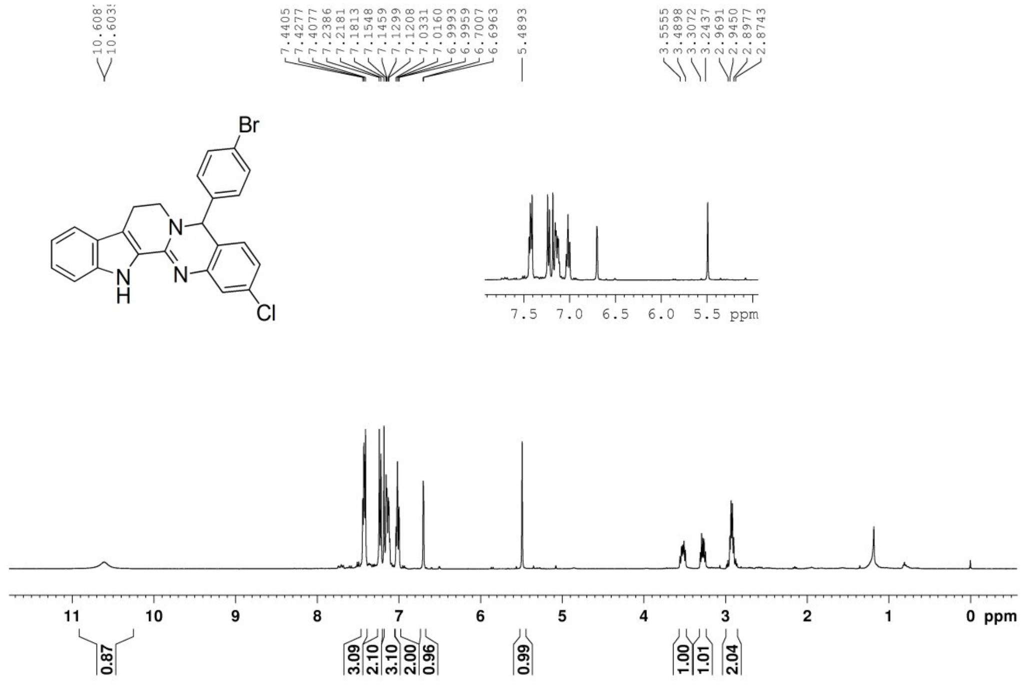
^{13}C NMR of **6f** in $CDCl_3$



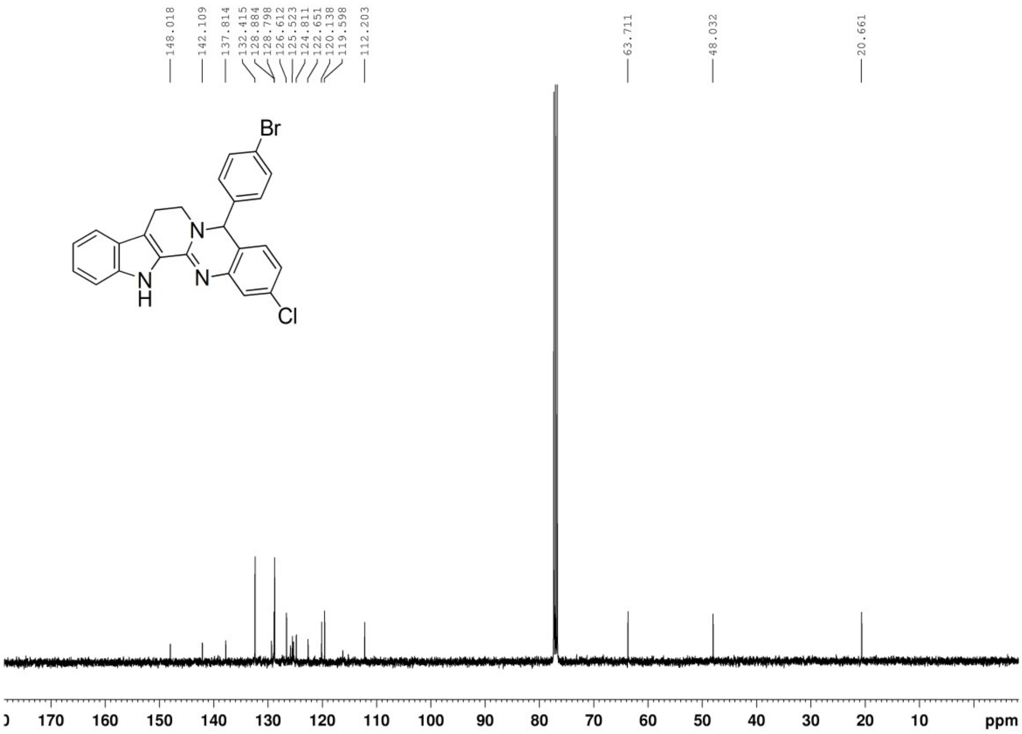
[1]H NMR of **6g** in $CDCl_3$



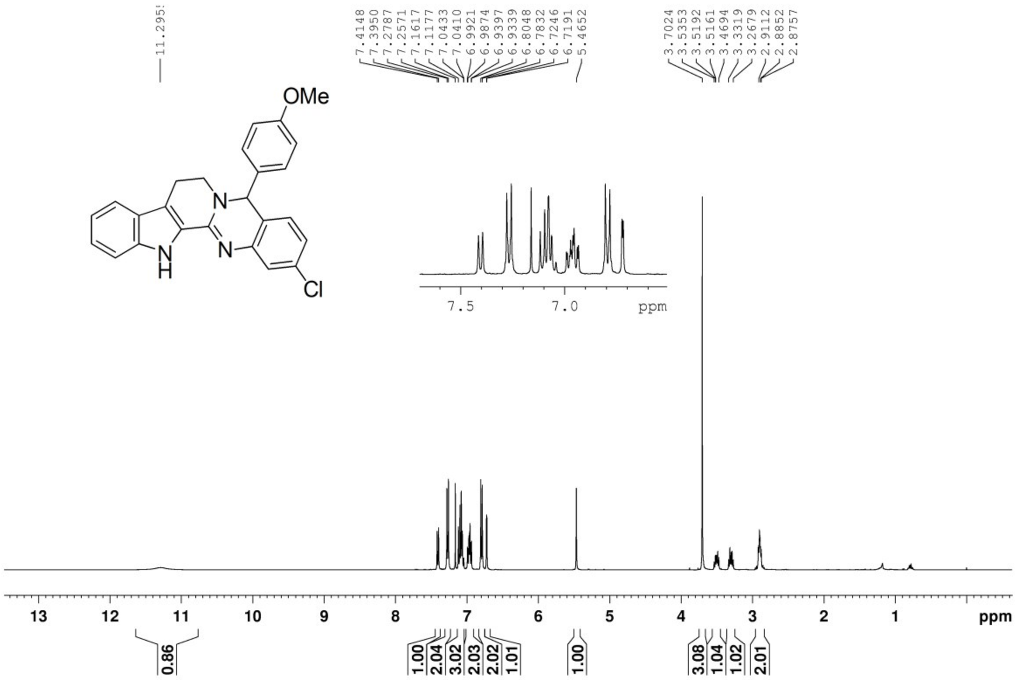
[13]C NMR of **6g** in $CDCl_3$



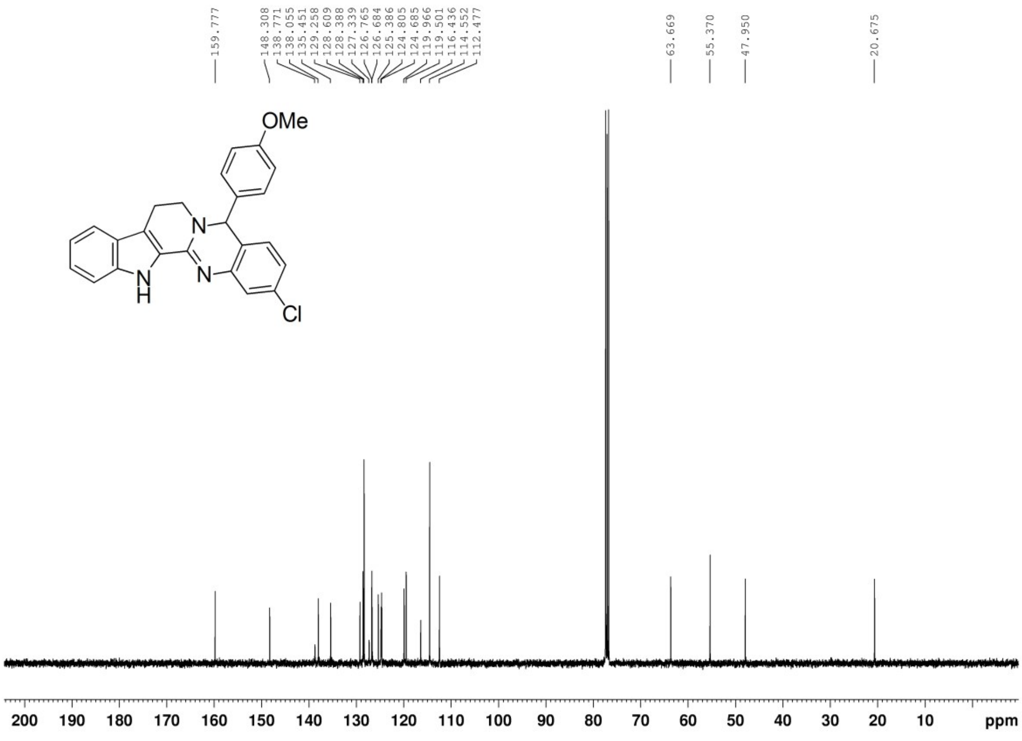
^{1}H NMR of **6h** in $CDCl_3$



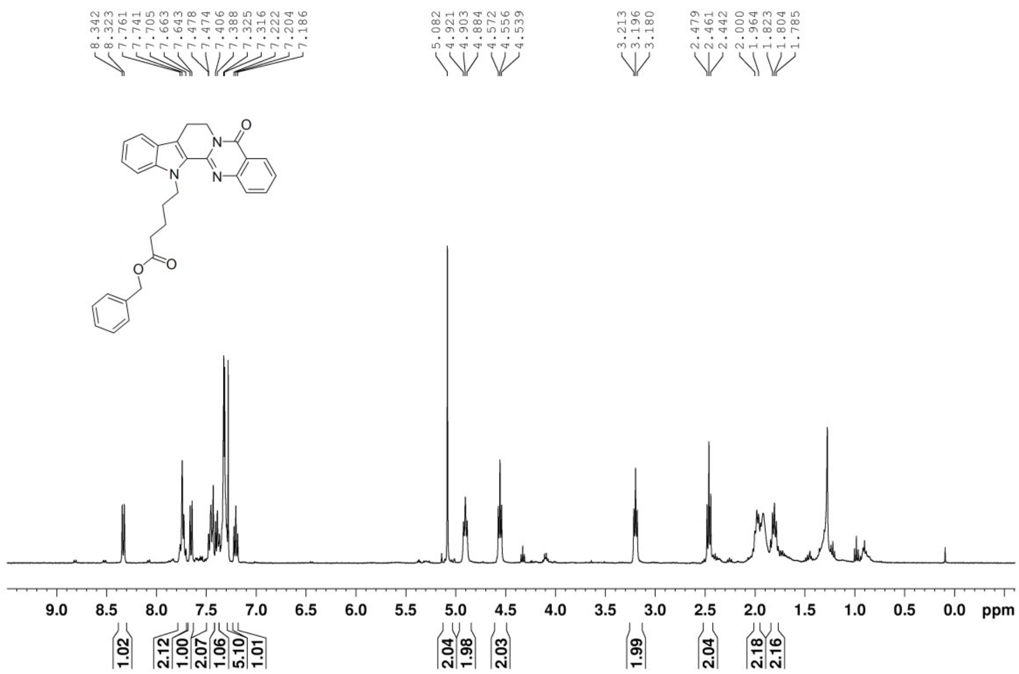
^{13}C NMR of **6h** in $CDCl_3$



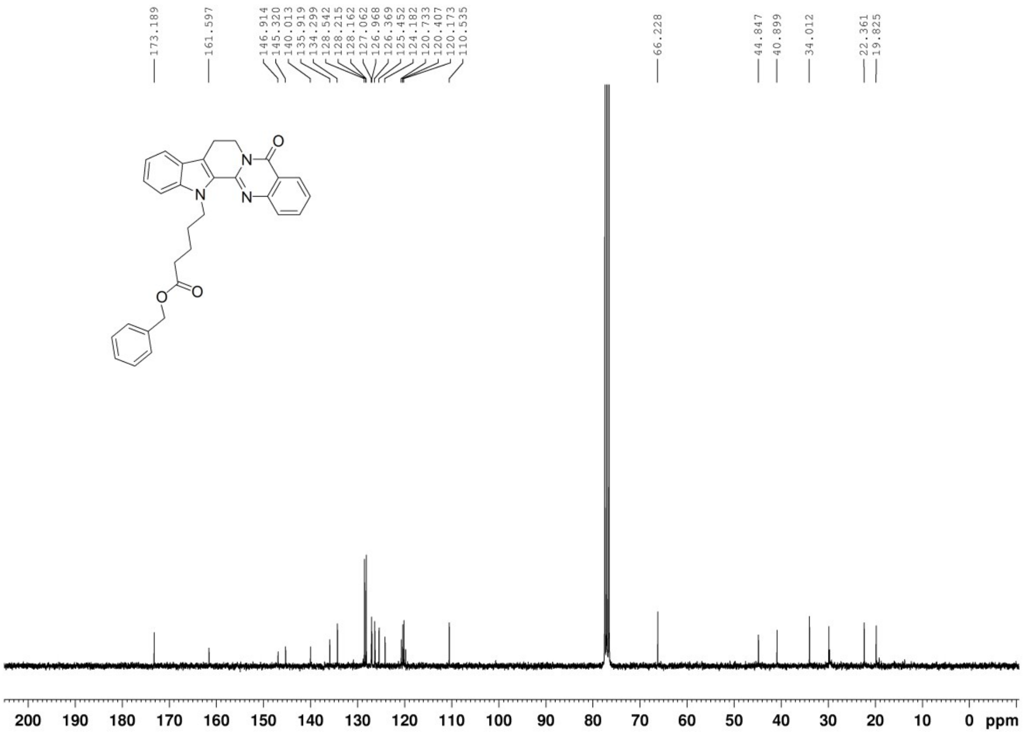
^{1}H NMR of **6j** in $CDCl_3$



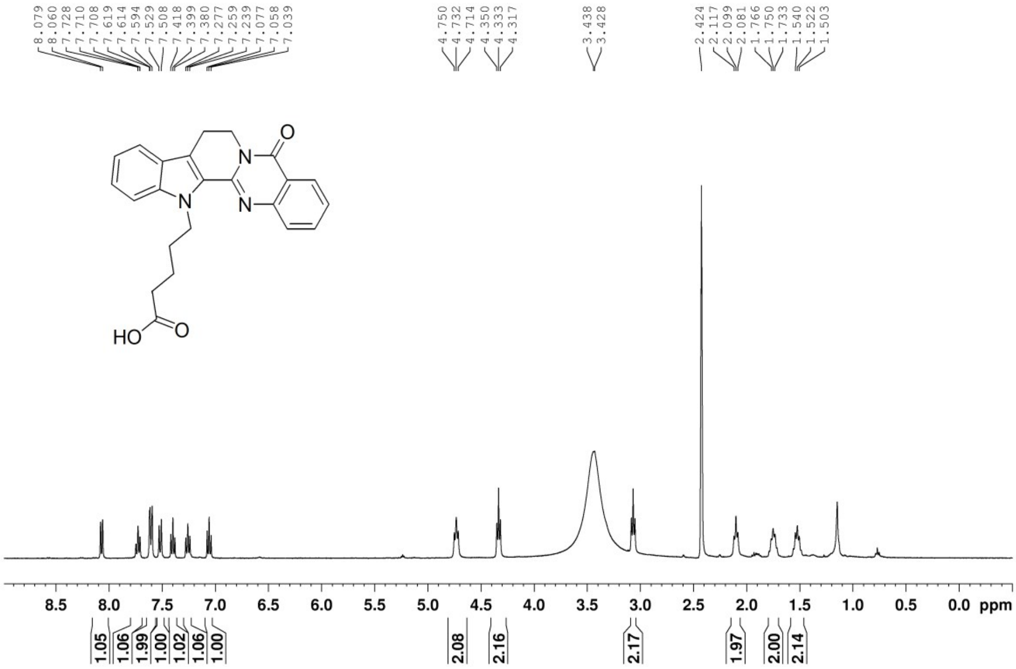
^{13}C NMR of **6j** in $CDCl_3$



^{1}H NMR of **8** in $CDCl_3$



^{13}C NMR of **8** in $CDCl_3$



^{1}H NMR of **9** in DMSO-d_6