Ruthenium-Catalyzed Late-Stage C–H Alkenylation of *N*-arylpyridazino [4,5-*b*]quinolin-1(2*H*)-ones

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1. General Information.

All chemicals were purchased from Sigma-Aldrich and TCI Chemicals Ltd. and used directly without further purification. Other reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. Analytical thin-layer chromatography was performed on 0.25 mm silica gel 60 F254 Merck pre-coated aluminium-backed silica gel plates. **^{1}H NMR** spectra were recorded on a Bruker AVANCE-III (400 MHz) spectrometer using $CDCl_3$ as the solvent. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz. **^{13}C NMR** spectra were recorded on a Bruker AVANCE-III (101 MHz) spectrometer using $CDCl_3$ and were fully decoupled by broadband proton decoupling. Chemical shifts were referenced to the appropriate residual solvent peaks. After completion of the reaction, the reaction mixture was extracted with water and CH_2Cl_2, and the organic extracts were passed over anhydrous Na_2SO_4. The crude reaction mixture was purified by manual column chromatography on silica gel (100-200 mesh, Merck Ltd.) using petroleum ether and ethyl acetate as the mobile phase. High-resolution mass spectra (**HR-MS**) were recorded on a WATERS-XEVOG2-XS-QToF using ESI-TOF (a positive electrospray ionization time-of-flight). **FT-IR** spectra were recorded using a Shimadzu IR Tracer-100 spectrometer (ATR). Single Crystal X-ray were recorded at Single Crystal X-ray Diffractometer (**SC-XRD**) model Bruker D8 Quest, and Specific Optical rotation (**SOR**) were recorded at Rudolph Research Analytical model Autopol III S2.

2. Experimental Section

2.1) Preparation of starting materials

General procedure for the synthesis of methyl 2-methyl-4-phenylquinoline-3-carboxylate **(3a)** from the literature[1-2],

Figure S1: Starting materials

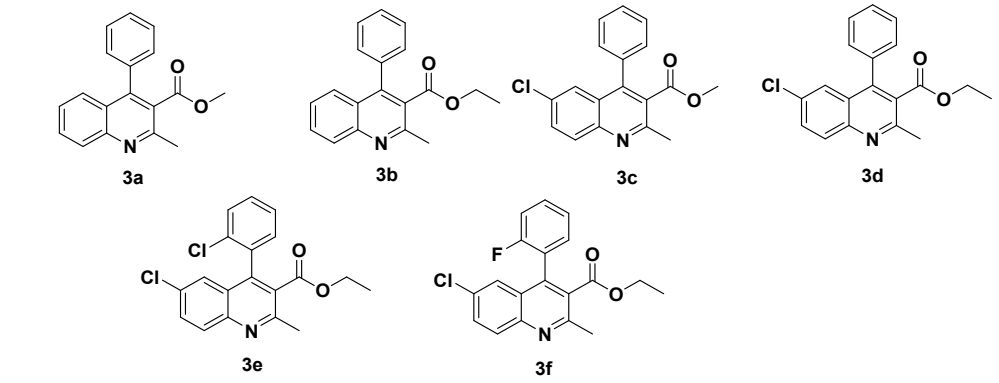
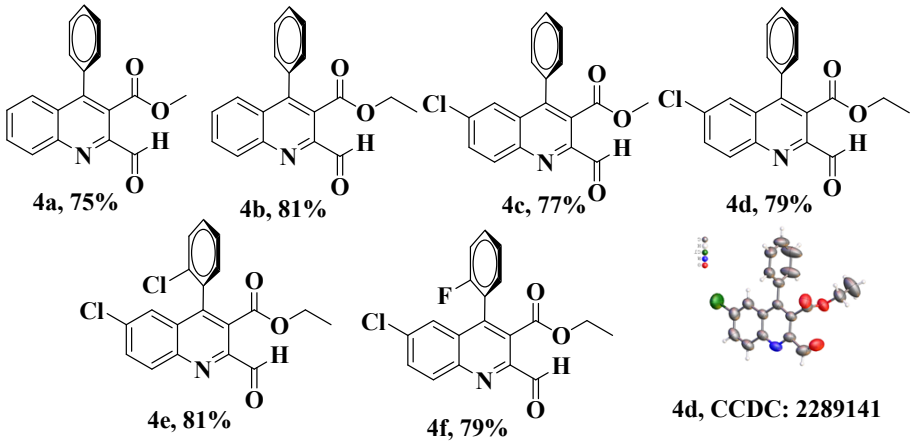
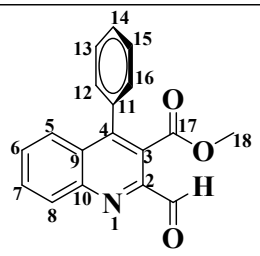


Figure S2: Scope of quinoline-3-carboxylate

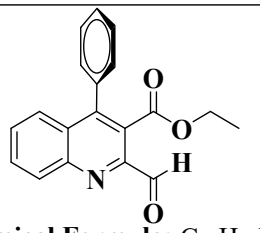


In an oven dried vial was filled with quinoline-esters (**3a,** 0.3 mmol, 98 mg), and then [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%, 6 mg), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol, 30 mg), DCE 3 mL under atmospheric air the reaction mixture is heated for 8h at 100 °C and monitored by TLC. Once the reaction was completed, the reaction mixture was quenched with water and extracted with ethyl acetate (15 mL x 2). The combined organic layer was passed over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resultant crude product was purified by column chromatography to obtain the pure compound of results with high yield, confirmed through NMR, FT-IR, Mass and also confirmed through Single crystal XRD analysis for compound **4d CCDC: 2289141**.



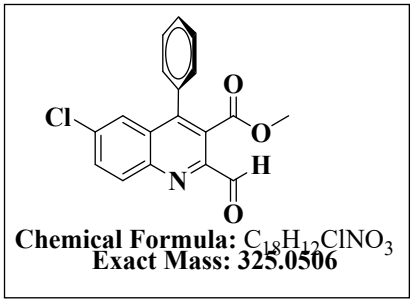
Chemical Formula: $C_{18}H_{13}NO_3$
Exact Mass: 291.0895

Methyl 2-formyl-4-phenylquinoline-3-carboxylate (4a), 75% yield, off white solid, melting point 98-100 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.31 (d, *J* = 8.5 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.72 – 7.60 (m, 2H), 7.55 – 7.46 (m, 3H), 7.37 (dd, *J* = 6.4, 2.9 Hz, 2H), 3.71 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6 (–CHO, C19), 167.6 (C=O, C17), 148.4 (C_q, C2), 147.7 (C_q, C10), 147.7 (C_q, C4), 134.2 (C_q, C11), 131.2 (CH, C7), 130.7 (CH, C8), 130.1 (CH, C6), 129.5 (CH, C14), 129.1 (CH, C13,C15), 128.5 (CH, C12, C16), 128.3 (CH, C5), 126.9 (C_q, C9), 125.1 (C_q, C3), 52.7(CH_3, C18) ppm. **FT-IR**(ATR): *ν*(cm^{-1}) 2951, 2824, 1732, 1705, 1431, 1315, 1219, 1072, 875, 763, 702. **GC-MS [M+H]$^+$:** Chemical formula $C_{18}H_{14}NO_3$, calculated 292.0968, found 292.2782.



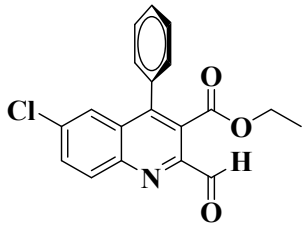
Chemical Formula: $C_{19}H_{15}NO_3$
Exact Mass: 305.1052

Ethyl 2-formyl-4-phenylquinoline-3-carboxylate (4b), 81% yield, off white solid, melting point 92-94 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.86 (ddd, *J* = 8.3, 6.6, 1.6 Hz, 1H), 7.71 – 7.58 (m, 2H), 7.56 – 7.46 (m, 3H), 7.38 (dt, *J* = 6.6, 3.5 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.07 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6(–CHO, C20), 167.1 (C=O, C17), 148.5 (C_q, C2), 147.7 (C_q, C10), 134.2 (C_q, C4), 131.2 (C_q, C11), 130.7 (CH, C7), 130.0 (CH, C8), 129.6 (CH, C6), 129.1 (CH, C13, C14, C15), 128.4 (CH, C12, 16), 128.4 (CH, C5), 126.9 (C_q, C9), 125.5 (C_q, C3), 61.9 (–CH_2–, C18), 13.8 (–CH_3, C19) ppm. **FT-IR**(ATR): *ν*(cm^{-1}) 2848, 1739, 1710, 1400, 1210, 1070, 832, 700. **GC-MS[M+H]$^+$:** Chemical formula $C_{19}H_{16}NO_3$, calculated 306.1125, found 306.224.



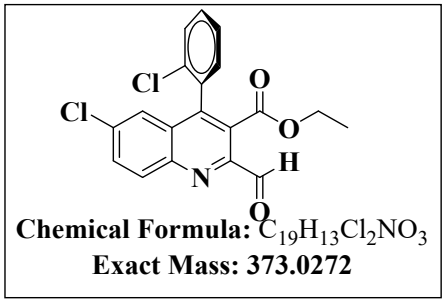
Chemical Formula: $C_{18}H_{12}ClNO_3$
Exact Mass: 325.0506

Methyl 6-chloro-2-formyl-4-phenylquinoline-3-carboxylate (4c), 77% yield, off white solid, melting point 96-98 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.26 (d, *J* = 9.0 Hz, 1H), 7.80 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.63 (d, *J* = 2.2 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.36 (dt, *J* = 5.2, 3.6 Hz, 2H), 3.70 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1 (–CHO, C19), 167.1 (C=O, C17), 148.5 (C_q, C2), 146.8 (C_q, C10), 145.9 (C_q, C4), 136.3 (C_q, C11), 133.4 (CH, C7), 132.2 (CH, C8), 132.2 (C_q, C6), 129.3 (CH, C13, C14, C15), 129.0 (CH, C12, C16), 128.6 (CH, C5), 125.8 (C_q, C9), 125.6 (C_q, C3), 52.7 (CH_3, C18) ppm. **FT-IR**(ATR): *v*(cm^{-1}) 2947, 2855, 1744, 1713, 1207, 1069, 875, 709. **GC-MS[M+H]$^+$:** Chemical formula $C_{18}H_{13}ClNO_3$, calculated 326.0579, found 326.1559.



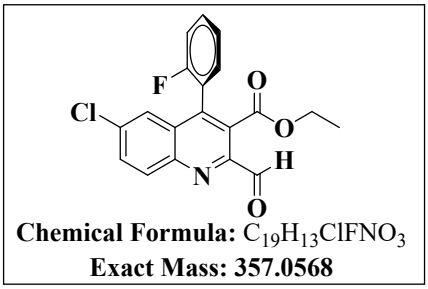
Chemical Formula: $C_{19}H_{14}ClNO_3$
Exact Mass: 339.0662

Ethyl 6-chloro-2-formyl-4-phenylquinoline-3-carboxylate (4d), 79% yield, off white solid, melting point 94-96 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 7.78 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.36 (dd, *J* = 6.3, 2.7 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.14 – 0.98 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.1 (–CHO, C20), 167.5 (C=O, C17), 148.5 (C_q, C2), 146.8 (C_q, C10), 145.9 (C_q, C4), 136.3 (C_q, C11), 133.4 (CH, C7), 132.1 (CH, C8), 129.4 (C_q, C6), 129.3 (CH, C13, C14, C15), 129.0 (CH, C12, C16), 128.6 (CH, C5), 126.1 (C_q, C9), 125.6 (C_q, C3), 61.9 (–CH_2, C18), 13.7 (–CH_3, C19) ppm. **FT-IR**(ATR): *v*(cm^{-1}) 2847, 1737, 1708, 1403, 1209, 1081, 833, 699. **GC-MS [M+H]$^+$:** Chemical formula $C_{19}H_{15}ClNO_3$, calculated 340.0735, found 340.2054.



Chemical Formula: $C_{19}H_{13}Cl_2NO_3$
Exact Mass: 373.0272

Ethyl 6-chloro-4-(2-chlorophenyl)-2-formylquinoline-3-carboxylate (4e), 81% yield, pale yellow solid, melting point 110-112 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.27 (d, *J* = 9.0 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.42 (dd, *J* = 13.6, 4.8 Hz, 2H), 7.33 – 7.28 (m, 1H), 4.22 – 4.13 (m, 2H), 1.06 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.8 (–CHO, C20), 166.1 (C=O, C17), 148.9 (C_q, C2), 145.8 (C_q, C10), 144.3 (C_q, C4), 136.7 (C_q, C11), 133.7 (CH, C7), 132.5(CH, C8), 132.4 (C_q, C12), 132.3 (C_q, C6), 131.3 (CH, C14), 130.9 (CH, C13), 129.9(CH, C16), 128.6(CH, C15), 126.9(CH, C5), 126.3(C_q, C9), 125.1(C_q, C3), 61.9(–CH_2–, C18), 13.7(CH_3, C19) ppm. **FT-IR**(ATR): *ν*(cm^{-1}) 2916, 1767, 1724, 1597, 1246, 1026, 756, 702. **GC-MS[M+H]$^+$:** Chemical formula $C_{19}H_{14}Cl_2NO_3$, calculated 374.0345, found 374.1009.

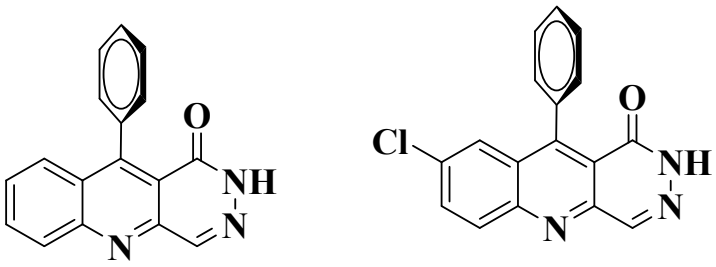


Chemical Formula: $C_{19}H_{13}ClFNO_3$
Exact Mass: 357.0568

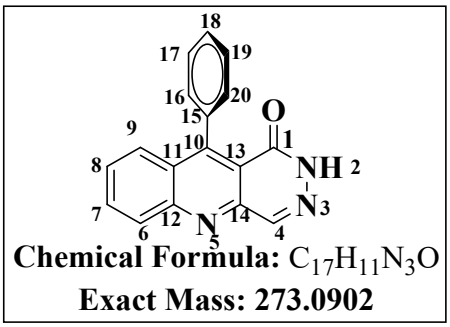
Ethyl 6-chloro-4-(2-fluorophenyl)-2-formylquinoline-3-carboxylate (4f), 79% yield, pale yellow solid, melting point 108-110 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.28 (d, *J* = 9.0 Hz, 1H), 7.82 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.33 (dt, *J* = 12.1, 6.0 Hz, 2H), 7.28 (s, 1H), 4.27 – 4.18 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.9 (–CHO, C20), 166.3 (C=O, C17), 161.0 (C_q, C2), 158.5 (C_q, *J* = 249.2 Hz, C12), 148.8 (C_q, C10), 145.8 (C_q, C4), 141.3 (CH, C7), 136.8(C_q, C11), 132.5(CH, C8), 132.3(C_q, C6), 131.9(CH, C14), 131.8(CH, C14), 131.5(CH, C16), 128.9(CH, C16), 127.0(CH, C5), 125.2(CH, C15), 124.5(C_q, C9), 124.5(C_q, C9), 121.3(C_q, C3), 121.1(C_q, C3), 116.2(C_q, C13), 116.0(C_q, C13), 62.1(–CH_2–, C18), 13.8(CH_3, C19) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -112.3, -112.4, -112.4, -112.4 (m) ppm. **FT-IR**(ATR): *ν*(cm^{-1})

2859, 1740, 1713, 1393, 1207, 1072, 879, 709. **GC-MS[M+H]$^+$:** Chemical formula $C_{19}H_{14}ClFNO_3$, calculated 358.0641, found 358.0882.

Figure S3: Intramolecular cyclization

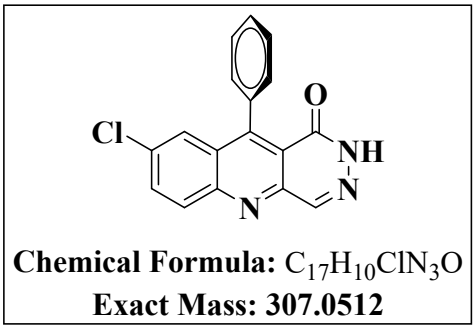


In a dry round-bottom flask was filled with quinoline-esters (**3a,** 0.3 mmol), and then [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol), DCE 3mL under atmospheric air the reaction mixture is heated for 8h at 100 °C, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) were added to the reaction mixture continued stirring for 1h at 100 °C and monitored by TLC. Once the reaction was completed, the reaction mixture was quenched with water and extracted with ethyl acetate (15mL x 2). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resultant crude product was purified by column chromatography to obtain the pure compound of results with high yield.



10-Phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (5a), 79% yield, yellow colour solid, melting point = 278-280 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.43 (s, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.54 – 7.44 (m, 4H), 7.23 (d, *J* = 3.6 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.8 (C=O, C1), 152.6(C_q, C14), 151.0(C_q, C12), 146.4(C_q, C10), 141.5(C_q, C15), 136.3(CH, C4), 132.9(CH, C7), 130.0(CH, C17, C18, C19), 128.9(CH, C6), 128.5(CH, C8), 128.4(CH, C16), 128.4(C_q, C20), 128.2(C_q, C13), 128.1(C_q, C11), 118.4(CH, C9) ppm. **FT-IR**(ATR): *v*(cm^{-1}) 3185, 1658, 1546,

1266, 993, 756, 523. **GC-MS:** Chemical formula $C_{17}H_{11}N_3O$, calculated 273.0902, found 273.1003.

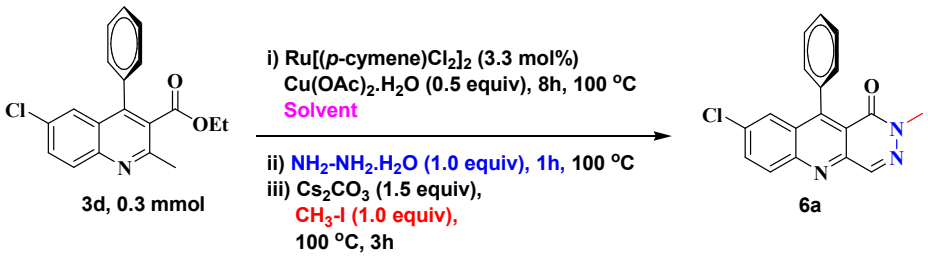


Chemical Formula: $C_{17}H_{10}ClN_3O$
Exact Mass: 307.0512

8-Chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (5b), 75% yield, yellow colour solid, melting point = 272 – 274 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.47 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 7.84 (dd, *J* = 9.1, 1.6 Hz, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.31 – 7.27 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.6 (C=O, C1), 151.7(C_q, C14), 149.3(C_q, C12), 146.4(C_q, C10), 141.2(C_q, C15), 135.5(CH, C4), 134.9(CH, C7), 134.0(CH, C17, C18, C19), 131.6(CH, C6), 129.5(C_q, C8), 128.8(C_q, C13), 128.4(CH, C16), 128.3(CH, C20), 126.5(C_q, C11), 119.0(CH, C9) ppm. **FT-IR**(ATR): *ν*(cm^{-1}) 3324, 1668, 1463, 1435, 1082, 981, 696, 595. **GC-MS:** Chemical formula $C_{17}H_{10}ClN_3O$, calculated 307.0512, found 307.5870.

2.2) Synthesis of N-H alkylated products[a]

Table S1: Screening of Different Solvents[a]

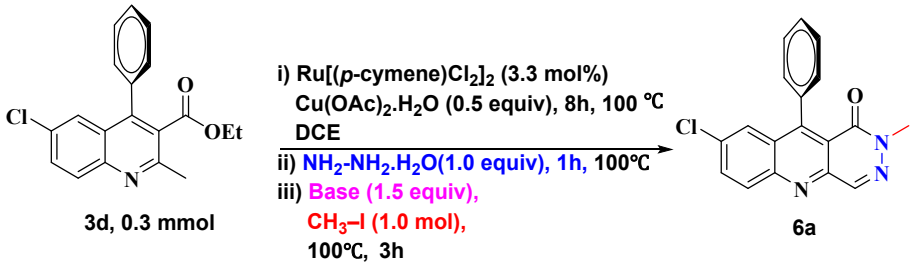


entry	solvents	yield[b] (%) 6a
1	MeCN	0
2	Acetone	0
3	dioxane	trace
4	DMF	21
5	DMSO	37
6	Toluene	trace

7	DCE	73

[a]**Reaction condition:** A mixture of **3d** (0.3 mmol) [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL of **Solvent** stirred at 100 ºC for 8h, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) added and continued stirring for 1h, followed by sequential addition of Cs_2CO_3 (1.5 equiv, 0.45 mmol), **methyl iodide** (1.0 equiv, 0.3 mmol) was stirred at 100 ºC for 3h. [b]Isolated yields.

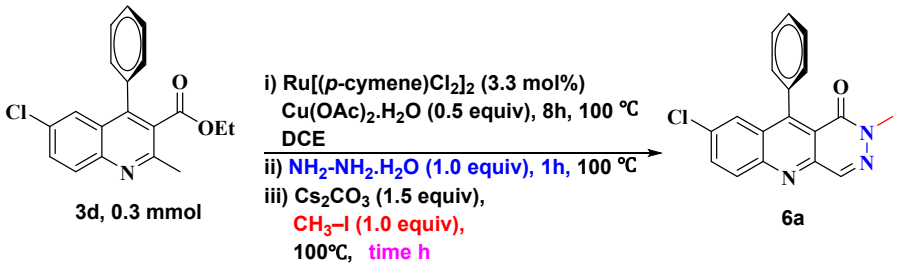
Table S2: Screening of Different bases[a]



entry	**base**	**yield[b] (%) 6a**
1	none	0
2	NaOH	31
3	NaOAc	trace
4	DBU	50
5	K_3PO_4	trace
6	$NaHCO_3$	trace
7	^{t}BuOK	62
8	Cs_2CO_3	73

[a]**Reaction condition:** A mixture of **3d** (0.3 mmol) [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mol) in 3 mL of DCE stirred at 100 ºC for 8h, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) added and continued stirring for 1h, followed by sequential addition of **Base** (1.5 equiv, 0.45 mmol), **methyl iodide** (1.0 equiv, 0.3 mmol) was stirred at 100 ºC for 3h. [b]Isolated yields.

Table S3: Screening of Different Time[a]

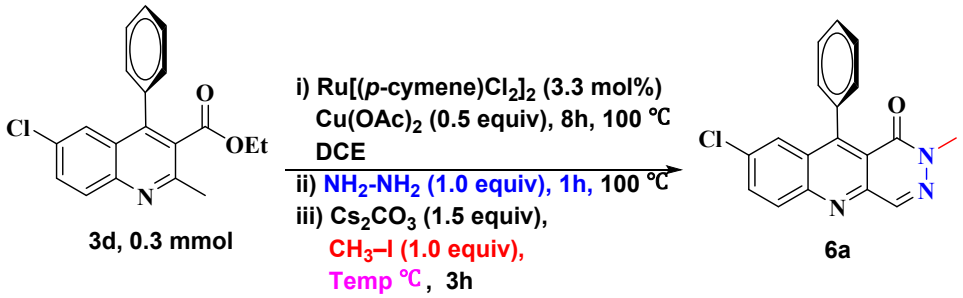


entry	**time**	**yield[b] (%) 6a**

1	After adding alkyl halides 45 mins	0
2	60 mins	21
3	120 mins	37
4	150 mins	51
5	180 mins	73
6	210 mins	73

[a]**Reaction condition:** A mixture of **3d** (0.3 mmol) [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL of DCE stirred at 100 ºC for 8h, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) added and continued stirring for 1h, followed by sequential addition of Cs_2CO_3 (1.5 equiv, 0.45 mmol), **methyl iodide** (1.0 equiv, 0.3 mmol) was stirred at 100 ºC for **time h**. [b]Isolated yields.

Tabel S4: Screening of Different Temperature[a]



entry	**Temperature ºC**	**yield[b] (%) 6a**
1	50	0
2	60	29
3	70	43
4	80	51
5	90	67
6	100	73
7	120	73

[a]**Reaction condition:** A mixture of **3d** (0.3 mmol) [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL of DCE stirred at 100 ºC for 8h, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) added and continued stirring for 1h, followed by sequential addition of Cs_2CO_3 (1.5 equiv, 0.45 mmol), **methyl iodide** (1.0 equiv, 0.3 mmol) was stirred at **Temperature ºC** for 12h. [b]Isolated yields.

General Procedure for sequential N–Alkylated synthesis of pyridazino[4,5-*b*]quinoline-1(2*H*)-one.

Initially, **3d** (0.3 mmol, 98 mg) with [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%, 6 mg) with Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol, 30 mg), stirred at 100 ºC for 8h which converts the methyl into carbonyl which identified in NMR spectra , further addition of NH_2-NH_2.H_2O

(1.0 equiv, 0.3 mmol, 15 mg) in the reaction mixture continued stirring at 100 ºC for 1h, further addition of base Cs_2CO_3 (1.5 equiv, 0.45 mmol, 146 mg), alkyl halides (1.0 equiv, 0.3 mmol) reaction mixture stirred at 100 °C for 3h gives N–H alkylation product with good yield.

Figure S4: Used alkyl halides

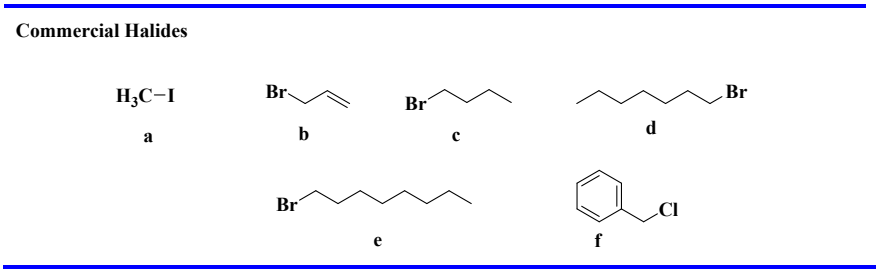
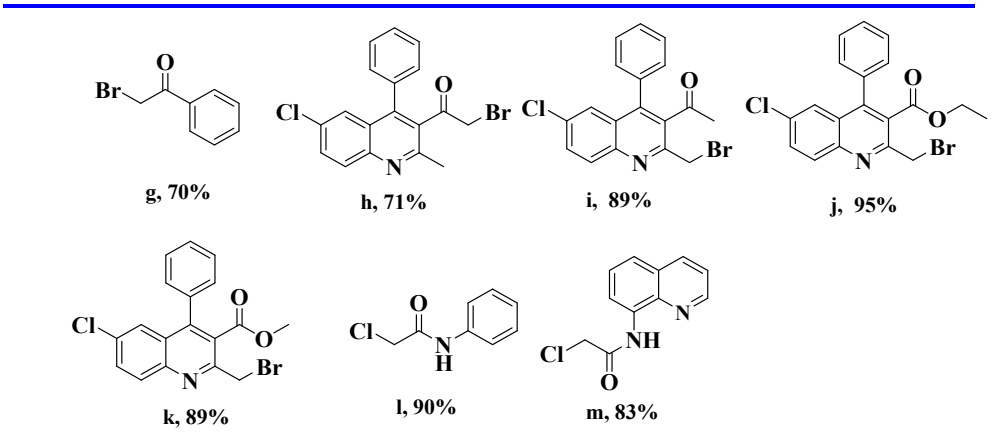


Figure S5: The following alkyl halides were prepared



Synthesis of corresponding halides

2-Bromo-1-phenylethan-1-one (g), in a dry round-bottom flask was filled with acetophenone (1.0 mmol), and then 5 mL of acetonitrile with *p*-TSA (15 mol%) with NBS (1.0 equiv) were added and under refluxed at 80 °C for 2 h and monitored by TLC. Once the reaction was completed by confirmed by TLC, the reaction mixture was quenched with ice water and exacted with ethyl acetate (20 mL x 2). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resultant mixture was purified by column chromatography to obtain the pure compound with good yield. Similar method for the preparation of **2-Bromo-1-(6-chloro-2-methyl-4-phenylquinolin-3-yl)ethan-1-one (h)**.

2-Bromo-1-(6-chloro-2-methyl-4-phenylquinolin-3-yl)ethan-1-one (h), 71% yield. Reddish white colour solid: melting point = 130-132 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03

(d, *J* = 8.9 Hz, 1H), 7.68 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.62 – 7.52 (m, 4H), 7.41 – 7.32 (m, 2H), 3.49 (s, 2H), 2.73 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.0, 155.3, 146.3, 143.8, 134.2, 132.7, 132.0, 131.5, 130.7, 129.8, 129.3, 125.4, 124.9, 34.9, 23.9 ppm.

1-(2-(Bromomethyl)-6-chloro-4-phenylquinolin-3-yl)ethan-1-one (i),

ethyl 2-(Bromomethyl)-6-chloro-4-phenylquinoline-3-carboxylate (j), and

methyl 2-(Bromomethyl)-6-chloro-4-phenylquinoline-3-carboxylate (k) were synthesized by following procedure.

In a reaction vial from PerkinElmer (screw-type), charged with a magnetic stir-bar, 1-(6-chloro-2-methyl-4-phenylquinolin-3-yl)ethan-1-one (1.0 mmol), NBS (1.0 equiv), and AIBN (10 mol%) were taken in CCl_4 (2 mL). The reaction mixture was stirred under Visible light (Kessil A160W Blue light) for 6 hours. After the reaction was complete (checked by TLC), the solvent was evaporated under reduced pressure. The reaction mixture was extracted with ethyl acetate (30 mL) and water (10 mL). The organic layer was dried over anhydrous Na_2SO_4, and the crude mixture was evaporated and purified by column chromatography using silica gel (100-200 mesh) and a petroleum ether/ethyl acetate (94/4) mixture as the eluent, yielding 87-95%. Followed for other substrates to give excellent yields.[3]

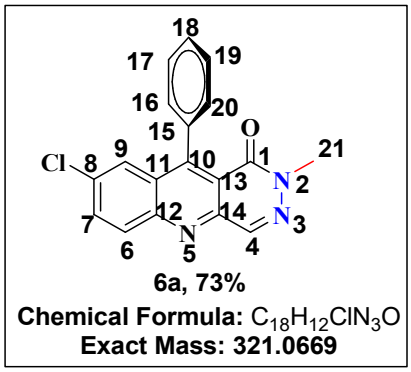
1-(2-(Bromomethyl)-6-chloro-4-phenylquinolin-3-yl)ethan-1-one (i) 89% of yield, colourless powder, melting point 160-162 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.9 Hz, 1H),7.70 (dd, *J* = 8.9, 2.3 Hz, 1H),7.63 (d, *J* = 2.2 Hz, 1H), 7.56 (dd, *J* = 10.0, 6.6 Hz, 3H), 7.35 (dt, *J* = 7.4, 3.2 Hz, 2H), 4.81 (s, 2H), 2.00 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.9, 153.3, 145.5, 144.7, 134.6, 134.3, 134.0, 131.5, 131.2, 129.9, 129.5, 129.1, 126.6, 124.9, 32.5, 31.7 ppm.

Ethyl 2-(bromomethyl)-6-chloro-4-phenylquinoline-3-carboxylate (j) 95% of yield, colourless powder, melting point = 116 – 118 °C; **^{1}H NMR** (400 MHz, CDCl3) δ 8.06 (d, *J* = 9.0 Hz, 1H), 7.70 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.39 – 7.30 (m, 2H), 4.89 (s, 2H), 4.14 – 3.95 (m, 2H), 0.91 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, CDCl3) δ 167.3, 153.6, 147.3, 145.8, 135.0, 133.8, 131.7, 131.1, 129.1, 128.8, 128.4, 127.1, 126.9, 125.3, 61.7, 32.1, 13.4 ppm.

Methyl 2-(bromomethyl)-6-chloro-4-phenylquinoline-3-carboxylate (k) 89% of yield, colourless powder, melting point = 126 – 128 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, *J* =

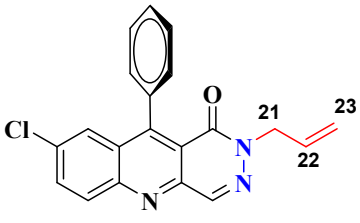
9.0 Hz, 1H), 7.74 – 7.67 (m, 1H), 7.59 (d, *J* = 2.2 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.33 (dd, *J* = 6.4, 3.0 Hz, 2H), 4.88 (s, 2H), 3.56 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.8, 153.5, 147.4, 145.8, 134.9, 133.9, 131.7, 131.1, 129.0, 128.9, 128.5, 126.9, 126.8, 125.4, 52.4, 32.1 ppm.

2-Chloro-N-phenylacetamide (l), and **2-chloro-N-(quinolin-8-yl)acetamide (m)** substituted were prepared according to the literature procedures[4]



6a, 73%
Chemical Formula: $C_{18}H_{12}ClN_3O$
Exact Mass: 321.0669

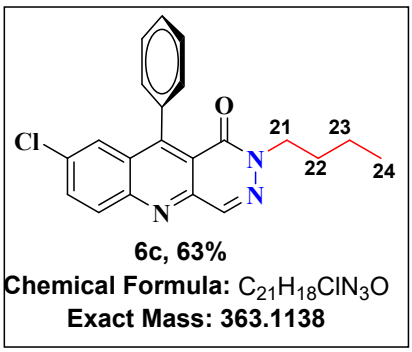
8-Chloro-2-methyl-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6a): yellow solid (73% yield); melting point 168-170 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.22 (d, *J* = 9.1 Hz, 1H), 7.83 (d, *J* = 9.1, 2.2 Hz, 1H), 7.60-7.58 (m, 4H), 7.28-77.27 (d, *J* = 3.9 Hz, 2H), 3.72 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.8 (C=O, C1), 151.3(C_q, C14), 149.1(C_q, C12), 146.0(C_q, C10), 139.7(C_q, C15), 136.1(CH, C4), 134.5(CH, C7), 133.7(CH, C17, C18, C19), 131.4(CH, C6), 129.5(C_q, C8), 128.5(CH, C16), 128.3(C_q, C20), 128.0(CH, C9), 126.4(C_q, C11), 118.4(C_q, C13), 39.5(CH_3, C21) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 2852, 1727, 1665, 1472, 1302, 1182, 1086, 983, 841, 710; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{18}H_{13}ClN_3O$, calculated 322.0742; Found 322.0748.



6b, 69%
Chemical Formula: $C_{20}H_{14}ClN_3O$
Exact Mass: 347.0825

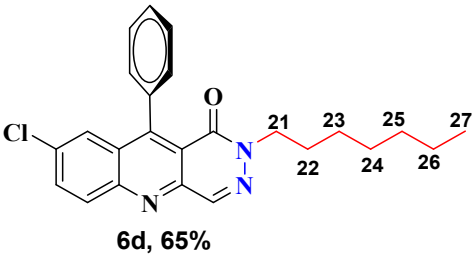
2-Allyl-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6b): yellow solid (69% yield); melting point 176-178 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.14 (d, *J* = 9.1 Hz, 1H), 7.75 (dd, *J* = 9.1, 1.7 Hz, 1H), 7.50 (m, 4H), 7.21 (s, 2H), 5.91 (ddd, *J* = 16.3,

11.2, 5.9 Hz, 1H), 5.25 – 5.10 (m, 2H), 4.64 (d, *J* = 5.8 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2(C=O, C1), 151.5(C_q, C14), 149.0(C_q, C12), 145.9(C_q, C10), 140.0(C_q, C15), 136.0(CH, C4), 134.4(CH, C7), 133.6(=CH, C22), 132.4(CH, C6), 131.3(CH, C17, C18, C19), 128.4(C_q, C8), 128.2(CH, C9), 128.0(CH, C16, C20), 126.3(C_q, C13), 118.5(C_q, C13), 118.2(=CH_2, C23), 53.1 (CH_2, C21) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 2921, 2836, 1727, 1659, 1472, 1312, 1176, 1074, 908, 830, 690, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{20}H_{15}ClN_3O$, calculated 348.0898; found 348.0908.



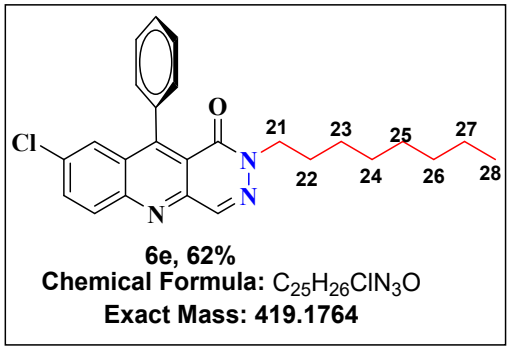
6c, 63%
Chemical Formula: $C_{21}H_{18}ClN_3O$
Exact Mass: 363.1138

2-Butyl-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6c): yellow solid (63% yield); melting point = 182-184 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.21 (d, *J* = 9.1 Hz, 1H), 7.81 (d, *J* = 9.1, 2.2 Hz, 1H), 7.57 (m, *J* = 5.5, 3.2 Hz, 4H), 7.27 (d, *J* = 4.6 Hz, 2H), 4.13 – 4.04 (m, 2H), 1.75 (dt, *J* = 15.3, 7.6 Hz, 2H), 1.35 (dt, *J* = 14.9, 7.5 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2(C=O, C1), 151.4(C_q, C14), 148.9(C_q, C12), 145.9(C_q, C10), 139.5(C_q, C15), 136.2(CH, C4), 134.3, (CH, C7) 133.5(CH, C17, C18, C19), 131.3(CH, C6), 129.5(C_q, C8), 128.4(CH, C16), 128.3(CH, C20), 128.0(CH, C9), 126.3(C_q, C11), 118.6(C_q, C13), 50.8 (CH_2, C21), 30.4(CH_2, C22), 20.0(CH_2, C23),13.7(CH_3, C24) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 3307, 3222, 2921, 2858, 1733, 1654, 1466, 1381, 1165, 1040, 989, 824, 710, 597; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{21}H_{19}ClN_3O$, calculated 364.1211; found 364.1222.



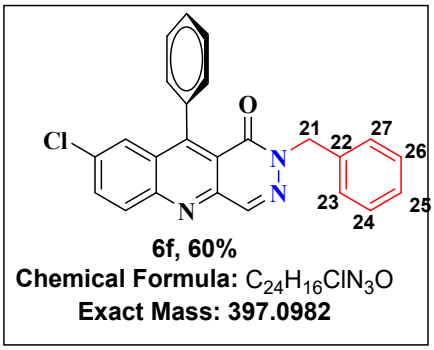
6d, 65%
Chemical Formula: $C_{24}H_{24}ClN_3O$
Exact Mass: 405.1608

8-Chloro-2-heptyl-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6d): yellow solid (65% yield); melting point = 190-192 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) 8.51 (s, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.59-7.57 (m, 4H), 7.28-7.27 (m, 2H), 4.11 – 4.04 (t, 2H), 1.78-1.73 (m, 2H), 1.34-1.26 (m, 8H), 0.88-0.85 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 151.4(C_q, C14), 149.0(C_q, C12), 145.5(C_q, C10), 139.0(C_q, C15), 136.2(CH, C4), 134.4(CH, C7), 133.5(CH, C17, C18, C19), 131.3(CH, C6), 129.5(C_q, C8), 128.4(CH, C16), 128.3(CH, C20), 128.1(CH, C9), 126.3(C_q, C11), 118.6(C_q, C13), 51.1(CH_2, 21), 31.5(CH_2, C25), 29.7(CH_2, C24), 28.4(CH_2, C23), 26.4(CH_2, C22), 22.5(CH_2, C26), 14.0(CH_3, C27) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 2920, 2847, 1654, 1548, 1478, 1329, 1080, 835, 700, 598; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{24}H_{25}ClN_3O$, calculated 406.1681; found 406.1676.



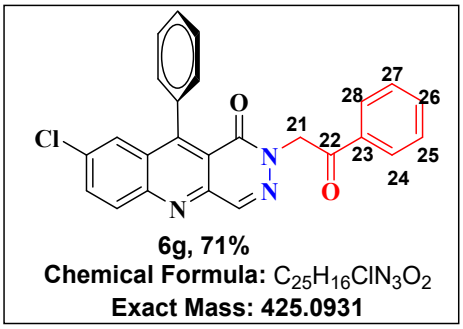
6e, 62%
Chemical Formula: $C_{25}H_{26}ClN_3O$
Exact Mass: 419.1764

8-Chloro-2-octyl-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6e): yellow solid (62% yield); melting point = 194-196 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.20 (d, *J* = 9.1 Hz, 1H), 7.81 (d, *J* = 9.1, 2.1 Hz, 1H), 7.61 – 7.53 (m, 4H), 7.27 (d, *J* = 3.9 Hz, 2H), 4.12 – 4.03 (m, 2H), 1.78-1.74 (m, *J* = 14.4, 7.2 Hz, 2H), 1.29-1.24 (m, *J* = 14.3, 5.9 Hz, 10H), 0.87-0.84 (m, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2(C=O, C1), 151.4(C_q, C14), 148.9(C_q, C12), 145.9(C_q, C10), 139.4(C_q, C15), 136.1(CH, C4), 134.3(CH, C7), 133.5(CH, C17, C18, C19), 131.3(CH, C6), 129.4(C_q, C8), 128.4(CH, C16), 128.2(CH, C20), 128.0(CH, C9), 126.3(C_q, C11), 118.5(C_q, C13), 51.1 (CH_2, C21), 31.7(CH_2, C26), 29.2(CH_2, C25), 29.1(CH_2, C24), 28.4(CH_2, C23), 26.7(CH_2, C22), 22.5(CH_2, C27), 14.0(CH_3, C28) ppm. **FT-IR**(ATR): *ν*(cm^{-1}) 2915, 2849, 1731, 1654, 1540, 1472, 1324, 1239, 1080, 835, 694, 593; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{25}H_{27}ClN_3O$, calculated 420.1837, found 420.1851.



6f, 60%
Chemical Formula: $C_{24}H_{16}ClN_3O$
Exact Mass: 397.0982

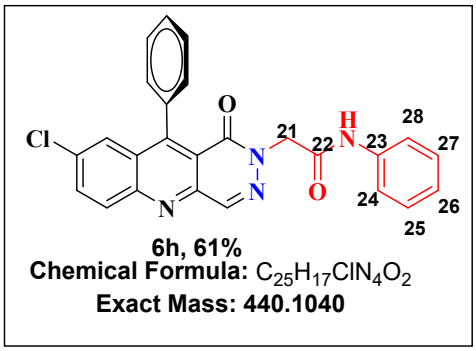
2-Benzyl-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6f): yellow solid (60% yield solid; melting point 300-302 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.20 (d, *J* = 9.1 Hz, 1H), 7.81 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.63 – 7.52 (m, 5H), 7.38 (d, *J* = 6.9 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.29 – 7.26 (m, 2H), 5.28 (s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 151.6(C_q, C14), 149.0(C_q, C12), 145.9(C_q, C10), 140.1(C_q, C15), 136.9(CH, C4), 136.1(CH, C7), 134.5(C_q, C22), 133.6(CH, C4), 131.4(CH, C17, C18, C19), 129.5(CH, C6), 128.6(CH, C16, C20), 128.5(C_q, C11), 128.4(CH, C23, C27), 128.3(CH, C25), 128.1(CH, C9), 127.7(C_q, C8), 126.4(CH, C24, C26), 118.7(Cq, C13), 53.8(CH_2, C21) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 2910, 2851, 1705, 1648, 1540, 1471, 1315, 1217, 1071, 1031, 885, 758, 689, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{24}H_{17}ClN_3O$, calculated 398.1055, found 398.1064.



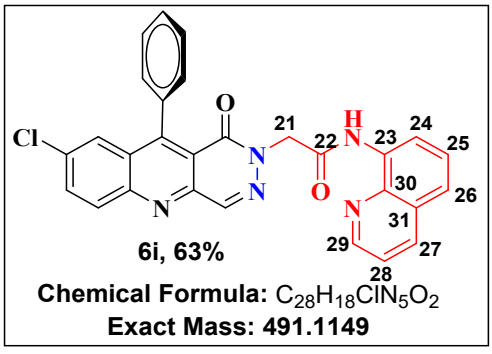
6g, 71%
Chemical Formula: $C_{25}H_{16}ClN_3O_2$
Exact Mass: 425.0931

8-Chloro-2-(2-oxo-2-phenylethyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6g); yellow solid (71% yield); melting point 302-304 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.24 (t, *J* = 7.2 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.85 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.64 – 7.54 (m, 5H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.33 – 7.26 (m, 2H), 5.57 (s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.0(–CH_2–C=O, C22), 158.8(C_q, C1), 151.6(C_q, C14), 149.1(C_q, C12), 146.1(C_q, C10), 140.5(C_q, C15), 135.9(CH, C4), 134.8(CH, C7), 134.6(CH, C6), 133.8(C_q, C23), 133.7(CH, C26), 131.4(CH, C17, C18, C19), 129.4(C_q, C11), 128.7(CH, C16), 128.5(CH, C20), 128.2(CH, C24, C28), 128.1(CH, C25, C27), 127.9(CH, C9), 126.4(C_q, C8),

118.4(C_q, C13), 57.0(CH_2, C21) ppm; **FT-IR**(ATR): ν(cm^{-1}) 3063, 2921, 2841, 1699, 1659, 1540, 1472, 1313, 1222, 1086, 1072, 881, 835, 760, 682, 583; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{25}H_{17}ClN_3O_2$, calculated 426.1004, found 426.1017.

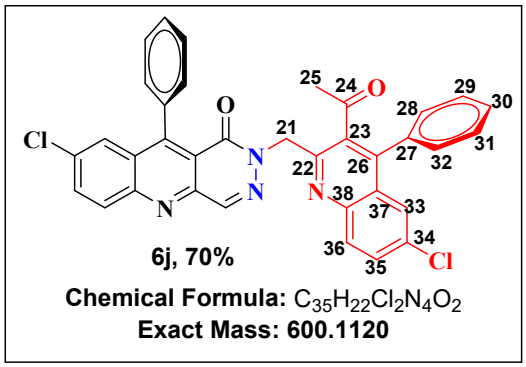


2-(8-Chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)-*N*-phenylacetamide (6h); yellow solid (61% yield); melting point 312 – 314 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 8.09 (s, 1H), 7.85 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.58 (m, *J* = 7.8 Hz, 5H), 7.54 – 7.50 (m, 2H), 7.25 (d, *J* = 2.8 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 4.82 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4 (–CH_2–C=O, C22), 159.0 (C=O, C1), 151.8(C_q, C14), 149.2(C_q, C12), 148.3(C_q, C10), 146.2(C_q, C23), 140.9(C_q, C15), 138.4(CH, C4), 136.4(CH, C7), 133.4 (CH, C6), 133.9(CH, C17, C18, C19), 131.6(C_q, C8), 128.4(C_q, C11), 128.3(CH, C16, C20), 127.4(CH, C25, C27), 126.5(CH, C26), 122.0(CH, C9), 121.7(CH, C24, C28), 116.8(C_q, C13), 54.9(CH_2, C21) ppm; **FT-IR**(ATR): ν(cm^{-1}) 3274, 1670, 1551, 1404, 1329, 1256, 1074, 835, 756, 699, 585; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{25}H_{18}ClN_4O_2$, calculated 441.1113, found 441.1128.

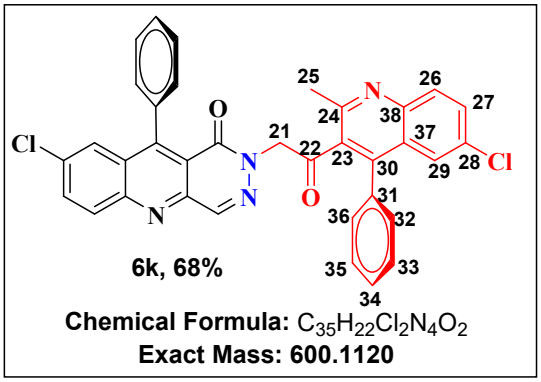


2-(8-Chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)-*N*-(quinolin-8-yl) acetamide (6i); brownish yellow solid (63% yield); melting point 302-304°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.66 (dd, *J* = 8.6, 4.3 Hz, 2H), 8.61 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 8.13 (dd, *J* = 12.9, 4.7 Hz, 1H), 7.84 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.59 (d, *J* = 2.1 Hz, 1H), 7.54 (dd, *J* = 8.6, 6.1 Hz, 3H), 7.47 (t, *J* = 6.7 Hz, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H),

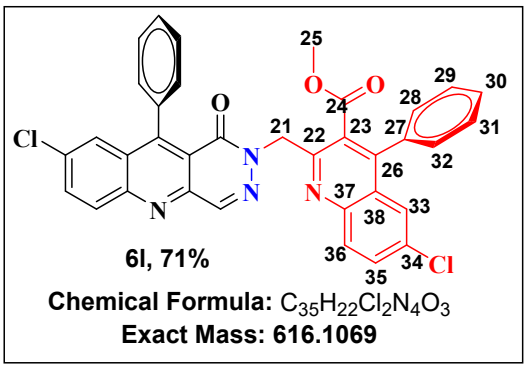
7.29 (dd, J = 6.4, 2.8 Hz, 2H), 5.11 (s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.4(–CH_2–C=O, C22), 159.0(C=O, C1), 151.8(C_q, C14), 149.2(CH, C29), 148.3(C_q, C12), 146.2(C_q, C10), 140.9(C_q, C15), 138.4(C_q, C30), 136.4(CH, C27), 135.9(CH, C7), 134.8(C_q, C23), 134.0(CH, C4), 133.9(CH, C17, C18, C19), 131.6(CH, C6), 129.6(C_q, C31), 128.6(CH, C16,C20), 128.4(C_q, C11), 128.3(CH, C25), 127.4(C_q, C8), 126.5(CH, C9), 122.2(CH, C28), 121.7(CH, C24), 118.6(C_q, C13), 116.9(CH, C26), 54.9(CH_2, C21) ppm; **FT-IR**(ATR): ν(cm^{-1}) 3271, 1664, 1545, 1303, 830, 744, 697; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{19}ClN_5O_2$, calculated 492.1222, found 492.1224.



2-((3-Acetyl-6-chloro-4-phenylquinolin-2-yl)methyl)-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (6j); brownish red solid (70% yield); melting point 298-300°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.24 (d, J = 9.1 Hz, 1H), 7.84 (d, J = 8.9 Hz, 2H), 7.60 (d, J = 2.1 Hz, 1H), 7.60 – 7.52 (m, 8H), 7.35 – 7.28 (m, 4H), 5.57 (s, 2H), 1.86 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.9(CH_3–C=O, C24), 159.3(C=O, C1), 152.1(C_q, C22), 152.0(C_q, C38), 149.6(C_q, C14), 146.7(C_q, C12), 146.3(C_q, C10), 144.6(C_q, C27), 140.4(C_q, C26), 136.4(C_q, C15), 135.1(CH, C7), 134.9(CH, C35), 134.5(CH, C6), 134.0(CH, C36), 133.5(CH, C17, C18, C19, C29, C30, C31), 131.9(CH, C9), 131.3(CH, C4), 130.4(C_q, C8), 129.9(CH, C16, C20), 129.8(CH, C28, C32), 129.4(C_q, C11), 128.8(C_q, C34), 128.7(C_q, C23), 126.8(CH, C33), 125.3(C_q, C37), 119.1(C_q, C13), 54.8(CH_2, C21), 32.2(CH_3, C25) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1669, 1551, 1480, 1324, 1062, 1013, 837, 700, 583; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{35}H_{23}Cl_2N_4O_2$, calculated 601.1193, found 601.1212.

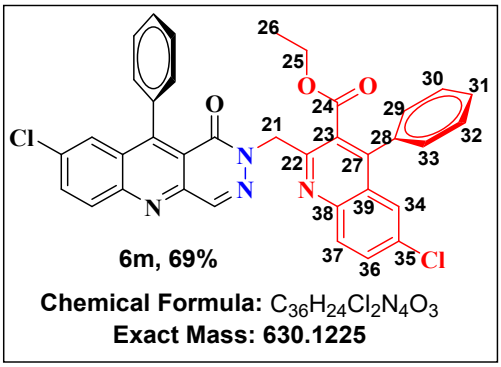


8-Chloro-2-(2-(6-chloro-2-methyl-4-phenylquinolin-3-yl)-2-oxoethyl)-10-phenyl pyridazino[4,5-*b*]quinolin-1(2*H*)-one (6k); brownish red solid (68% yield); melting point 296-298°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.20 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.9 Hz, 1H), 7.82 (d, *J* = 9.3 Hz, 1H), 7.66 (d, *J* = 9.1 Hz, 1H), 7.58 (s, 6H), 7.55 (s, 2H), 7.35 (d, *J* = 5.7 Hz, 2H), 7.19 (d, *J* = 5.7 Hz, 2H), 4.40 (s, 2H), 2.64 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.7(–CH_2–C=O, C22), 158.8(C=O, C1), 156.3(C_q, C24), 151.7(C_q, C14), 149.2(C_q, C38), 146.3(C_q, C12), 146.1(C_q, C10), 144.6(C_q, C15), 140.4(C_q, C31), 134.8(C_q, C30), 134.2(CH, C7), 133.9(CH, C4), 132.7(CH, C27), 131.6(CH, C17, C18, C19, C33, C34, C35), 130.7(C_q, C8), 130.4(CH, C9), 129.9(CH, C26), 129.5(CH, C16, C20), 129.4(CH, C32, C36), 128.6(CH, C6), 128.3(C_q, C37), 128.3(C_q, C28), 126.5(C_q, C11), 125.7(C_q, C23), 125.1(CH, C29), 118.3(C_q, C13), 61.0(CH_2, C21), 29.8(CH_3, C25) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 2924, 1669, 1551, 1473, 1385, 1317, 1082, 1023, 837, 700, 585; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$: Chemical formula $C_{35}H_{23}Cl_2N_4O_2$, calculated 601.1193, found 601.1211.



Methyl 6-chloro-2-((8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)methyl)-4-phenylquinoline-3-carboxylate (6l); brownish yellow solid (71% yield); melting point 280-282°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.47 (s, 1H), 8.24 (dd, *J* = 9.0, 5.2 Hz, 1H), 7.91 – 7.83 (m, 4H), 7.63 – 7.56 (m, 4H), 7.50 – 7.45 (m, 2H), 7.35 – 7.28 (m, 4H),

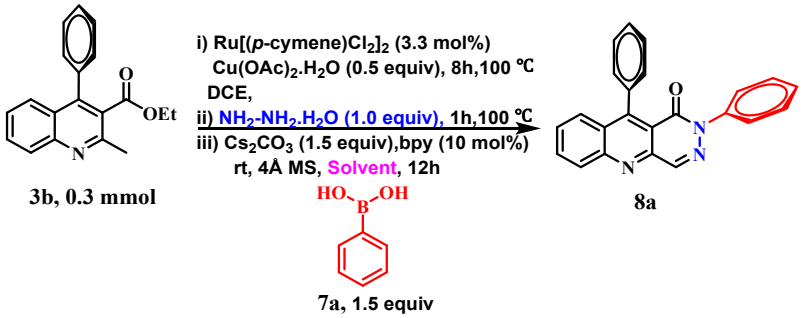
5.72 (s, 2H), 3.44 (s, 3H) ppm, **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.5(–O–C=O, C24), 158.9(C=O, C1), 152.2(C_q, C22), 151.6(C_q, C14), 149.1(C_q, C37), 146.0(C_q, C12), 141.1(C_q, C10, C26), 140.2(C_q, C15, C27), 136.1(CH, C7), 134.5(CH, C4), 133.9(CH, C35), 133.6(CH, C6), 133.0(CH, C36), 131.4(CH, C17. C18, C19, C29, C30, C31), 131.2(CH, C9), 129.1(C_q, C8), 128.5(CH, C33), 128.3(CH, C16, C20), 128.3(CH, C28, 32), 128.2(C_q, C11), 128.1(C_q, C34), 126.4(C_q, C23), 125.3(C_q, C38), 118.6(C_q, C13), 54.3(CH_2, C21), 52.3(CH_3, C25) ppm; **FT-IR**(ATR): ν(cm^{-1}) 3387, 2918, 1723, 1674, 1576, 1478, 1331, 1224, 1140, 1058, 843, 696; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{35}H_{23}Cl_2N_4O_3$, calculated 617.1142, found 617.1163.



Ethyl 6-chloro-2-((8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)methyl)-4-phenylquinoline-3-carboxylate (6m); brownish yellow solid (69% yield); melting point 268-270°C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.25 (d, J = 9.1 Hz, 1H), 7.84 (dd, J = 9.0, 2.8 Hz, 2H), 7.60 (d, J = 2.2 Hz, 1H), 7.57 (d, J = 2.3 Hz, 1H), 7.55 (d, J = 2.3 Hz, 1H), 7.53 (d, J = 1.3 Hz, 1H), 7.52 (d, J = 2.1 Hz, 2H), 7.51 (d, J = 2.2 Hz, 1H), 7.49 – 7.46 (m, 3H), 7.29 (dd, J = 6.3, 3.1 Hz, 3H), 5.73 (s, 2H), 3.90 (q, J = 7.1 Hz, 2H), 0.82 (t, J = 7.1 Hz, 3H) ppm, **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.0(–O–C=O, C24), 158.9(C=O, C1), 152.2(C_q, C22), 151.6(C_q, C14), 149.1(C_q, C38), 146.7(C_q, C12), 146.2(C_q, C10, C27), 140.1(C_q, C15, 28), 136.1(CH, C7), 134.4(CH, C4), 133.6(CH, C36), 132.9(CH, C6), 131.4(CH, C37), 131.1(CH, C17, C18, C19, C30, C31, C32), 129.2(CH, C9), 128.7(C_q, C8), 128.4(CH, C34), 128.2(CH, C16, C20), 128.1(CH, C29, C33) 126.7(C_q, C11), 126.4(C_q, C35), 126.2(C_q, C23), 125.2(C_q, C39), 118.6(C_q, C13), 61.5(–CH_2, C25), 54.4(–CH_2, C21), 13.4(CH_3, C26) ppm; **FT-IR**(ATR): ν(cm^{-1}) 2971, 2852, 1727, 1659, 1581, 1473, 1317, 1219, 1053, 857, 691, 603; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{36}H_{25}Cl_2N_4O_3$, calculated 631.1298, found 631.1320.

2.3) Sequential N–H arylation using boronic acids

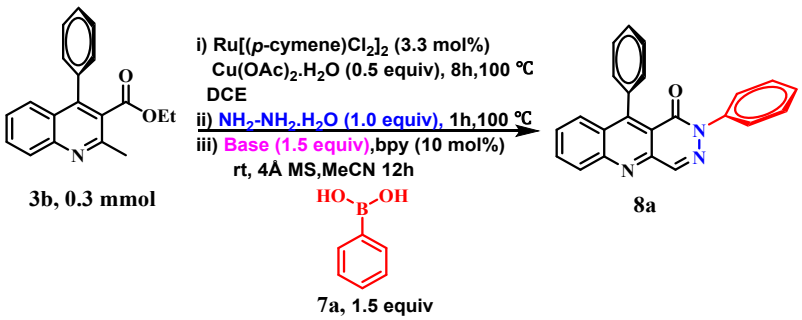
Table S5: Evaluation of solvents for Chan-Lam reaction[a]



entry	Solvent	8a yield[b] (%)
1	toluene	0
2	**MeCN**	**75**
3	dioxane	20
4	DMF	trace
5	DMSO	21
6	DCE	57
7	DMA	21
8	DCB	trace

[a]**Reaction conditions**: **3b** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL DCE for 8h at 100 ºC, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) for 1h at 100 ºC, followed by the addition of Cs_2CO_3 (1.5 equiv, 0.45 mmol), bpy (10 mol%, 0.03 mmol), **7a** aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS added stirred at room temperature in Solvent (3 mL) for 12h to give **8a**. [b]Isolated yields.

Table S6: Evaluation of bases for Chan-Lam reaction[a]

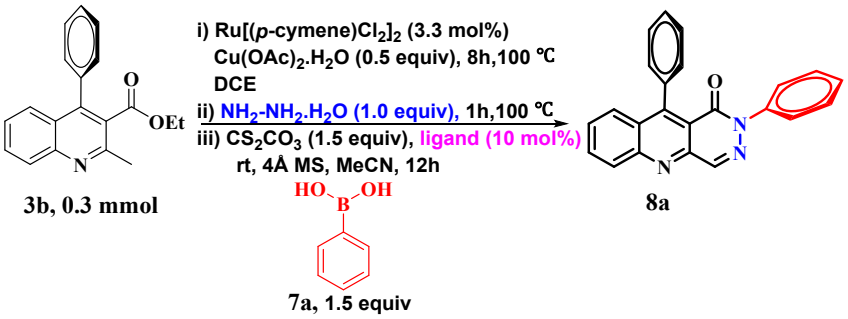


entry	Bases	8a yield[b] (%)
1	none	0

2	NaOH	0
3	KOH	0
4	NaOAc	trace
5	K_2CO_3	21
6	K_3PO_4	trace
7	$NaHCO_3$	16
8	^{t}BuOK	29
9	**Cs_2CO_3 (1.5 equiv)**	**73**
10	Cs_2CO_3 (1.0 equiv)	40
11	Cs_2CO_3 (1.75 equiv)	75
12	Cs_2CO_3 (2.0 equiv)	75
13	DBU (1.5 equiv)	43

[a]**Reaction conditions**: **3b** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL DCE for 8h at 100 ºC, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) at 100ºC for 1h, Base (1.5 equiv, 0.45 mmol), bpy (10 mol%, 0.03 mmol), aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS added stirred at room temperature in MeCN (3 mL) for 12h to give **8a**. [b]Isolated yields.

Table S7: Evaluation of ligands for Chan-Lam reaction[a]

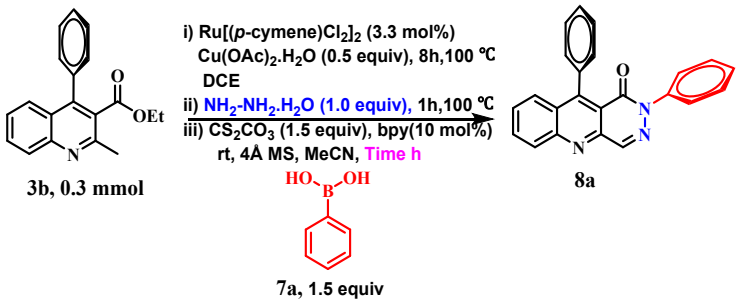


entry	**Ligands**	**8a yield[b] (%)**
1	none	0
2	1,10 phenanthroline	21
3	Pyridine	0
4	2,2'-bipyridine	75
5	2,2'-bipyridine (5 mol%)	31
6	**2,2'-bipyridine (15 mol%)**	**75**

[a]**Reaction conditions**: **3b** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL DCE for 8h at 100 ºC, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) at 100 ºC for 1h, Cs_2CO_3 (1.5 equiv,

0.45 mmol), Ligand (5-10 mmol%), aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS added stirred at room temperature using MeCN (3 mL) for 12h to give **8a**. [b]Isolated yields.

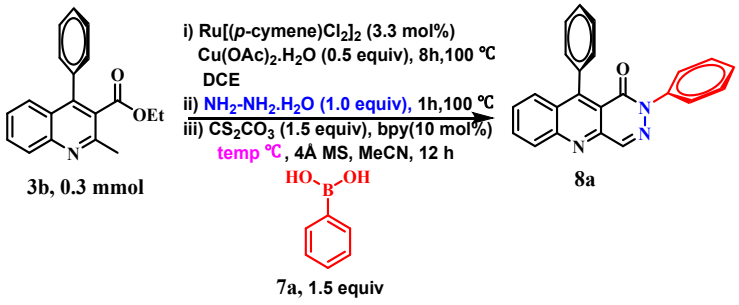
Table S8: Evaluation of reaction time for Chan-Lam reaction[a]



entry	Time h	8a yield[b] (%)
1	10	23
2	11	31
3	**12**	**75**
4	13	75

[a]**Reaction conditions**: **3b** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL DCE for 8h at 100ºC, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) at 100ºC for 1h, Cs_2CO_3 (1.5 equiv, 0.45 mmol), bpy (10 mol%), aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS added stirred at room temperature using (3 mL) for Time h to give **8a**. [b]Isolated yields.

Table S9: Evaluation of Temperature for Chan-Lam reaction[a]



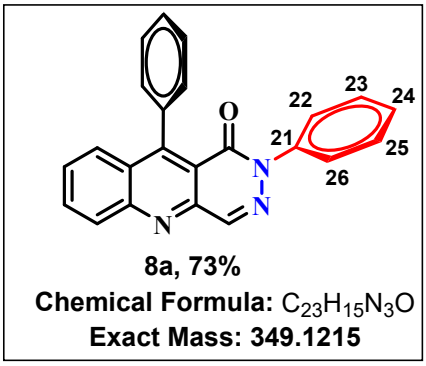
entry	Temperature ºC	8a yield[b] (%)
1	100	0
2	90	0
3	80	0
4	70	0
5	60	Trace
6	50	27

7	**Room temperature**	**75**

[a]**Reaction conditions**: **3b** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%), Cu(OAc)$_2$.H_2O (0.5 equiv, 0.15 mmol) in 3 mL DCE for 8h at 100ºC, further NH_2-NH_2.H_2O (1.0 equiv, 0.3 mmol) at 100 ºC for 1h, Cs_2CO_3 (1.5 equiv, 0.45 mmol), bpy (10 mol%), aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS added stirred temperature (ºC) using (3 mL) for 12h to give **8a**. [b]Isolated yields.

A General Procedure for the sequential N-H arylation

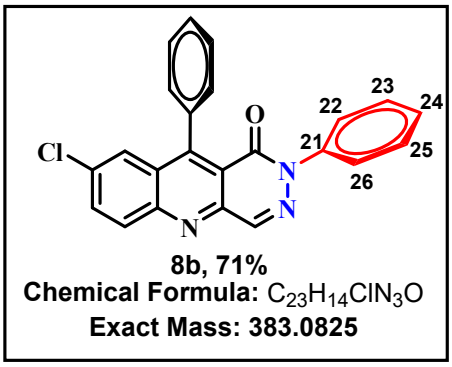
In an oven-dried glass vial, a mixture of **3b** (0.3 mmol, 88 mg), [Ru(*p*-cymene)Cl_2]$_2$ (3.3 mol%, 6 mg), and Cu(OAc)$_2$·H_2O (0.5 equiv, 0.15 mmol, 30 mg) in DCE (3 mL) was stirred at 100 °C for 8 h. Subsequently, NH_2NH_2·H_2O (1.0 equiv, 0.3 mmol, 15 mg) was added, and the reaction mixture was heated at 100 °C for an additional 1 h. The excess DCE was evaporated under reduced pressure, and the residue was treated with Cs_2CO_3 (1.5 equiv, 0.45 mmol, 147 mg), bpy (10 mol%, 16 mg), arylboronic acid (1.5 equiv, 0.45 mmol, 55 mg), and 4 Å molecular sieves (5 pellets) in MeCN (3 mL). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction (monitored by TLC), the mixture was quenched with ice water and extracted with ethyl acetate (2 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography to afford the desired compound in good yield.



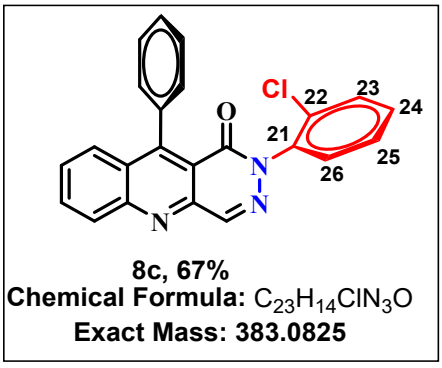
8a, 73%
Chemical Formula: $C_{23}H_{15}N_3O$
Exact Mass: 349.1215

2,10-Diphenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8a); reddish white solid (75% yield); melting point 208-210 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.31 (d, *J* = 8.6 Hz, 1H), 7.98 – 7.87 (m, 1H), 7.66 – 7.59 (m, 2H), 7.56 – 7.48 (m, 5H), 7.42 (dd, *J* = 10.6, 5.0 Hz, 2H), 7.34 – 7.27 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.7(C=O, C1), 153.1(C_q, C14), 150.9(C_q, C12), 145.9(C_q, C21), 141.8(C_q, C10), 140.8(C_q, C15), 136.8(CH, C4), 132.8(CH, C7), 129.9(CH, C17, C18, C19), 129.3(CH, C23, C25), 128.9(CH, C6), 128.4(CH, C24), 128.3(CH, C8), 128.2(CH, C9), 128.2(CH, C16, C20), 127.8(C_q, C11), 126.2(CH, C22, C26), 118.7(C_q, C13) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 1687, 1501, 1227, 978,

839, 745, 595; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{16}N_3O$, calculated 350.1288, found 350.1289. $[\alpha]_D^{20}$ = -14 (Concentration 0.5, $CHCl_3$).

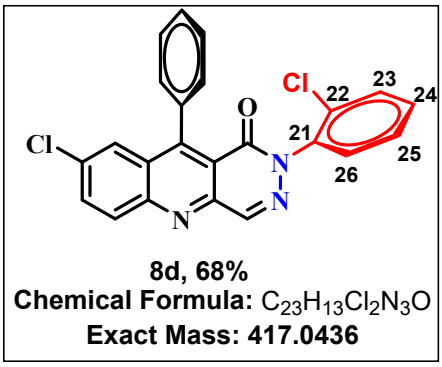


8-Chloro-2,10-diphenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8b); reddish white solid (71% yield); melting point 202-204 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 7.84 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.57 (d, *J* = 2.2 Hz, 1H), 7.53 (dd, *J* = 6.9, 5.8 Hz, 5H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.28 (dd, *J* = 7.4, 2.0 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4(C=O, C1), 152.3(C_q, C14), 149.2(C_q, C12), 145.9(C_q, C21), 141.7(C_q, C10), 140.5(C_q, C15), 136.0(CH, C4), 134.7(CH, C7), 133.9(CH, C17, C18, C19), 131.5(CH, C23, C25), 129.8(CH, C6), 128.9(CH, C24), 128.5(CH, C16), 128.5(CH, C20), 128.2(C_q, C8), 127.9(CH, C9), 126.6(C_q, C11), 126.1(CH, C22, C26), 119.2(C_q, C13) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 1697, 1468, 1310, 1081, 797, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{15}ClN_3O$, calculated 384.0898, found 384.0902. $[\alpha]_D^{20}$ = -17 (Concentration 0.5, $CHCl_3$).



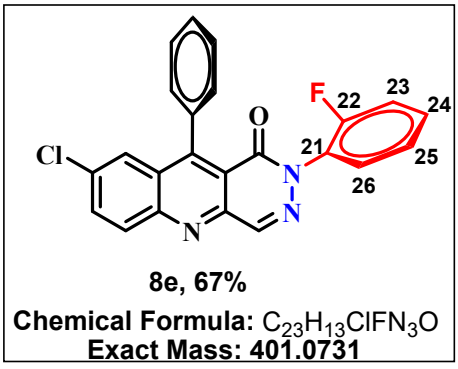
2-(2-Chlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8c); brownish white solid (67% yield); melting point 208-210 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 7.93 (t, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.48 (ddd, *J* = 8.9, 6.6, 4.1 Hz, 5H), 7.38 – 7.28 (m, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.5(C=O, C1), 153.1(C_q, C14), 150.9(C_q, C12), 146.0(C_q, C10), 141.1(C_q, C15),

139.4(C_q, C21), 136.4(CH, C4), 132.8(CH, C7), 132.3(CH, C24), 130.4(C_q, C22), 130.0(CH, C17, C18, C19), 129.9(CH, C23), 129.6(CH, C6), 129.1(CH, C8, CH, C9), 128.5(CH, C16, C20), 128.3(CH, C25), 128.1(C_q, C11), 127.8(C_q, C26), 118.5(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 2916, 1730, 1678, 1471, 1046, 700, 569; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{15}ClN_3O$, calculated 384.0898, found 384.0899, $[\alpha]_D^{20}$ = -23 (Concentration 0.5, $CHCl_3$).



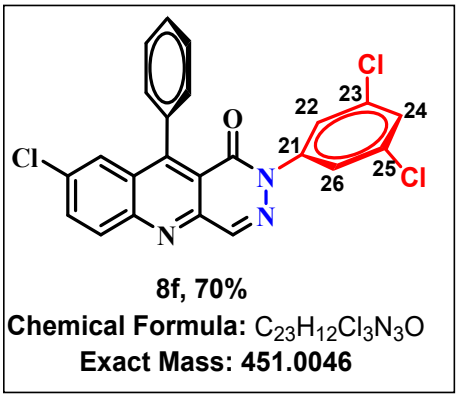
8d, 68%
Chemical Formula: $C_{23}H_{13}Cl_2N_3O$
Exact Mass: 417.0436

8-Chloro-2-(2-chlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8d); brownish white solid (68% yield); melting point 212-214 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.85 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.52 (q, *J* = 5.6 Hz, 3H), 7.46 (m, *J* = 6.8, 4.3, 2.8 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.31 – 7.26 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2(C=O, C1), 152.2(C_q, C14), 149.3(C_q, C12), 146.1(C_q, C10), 140.8(C_q, C15), 139.3(C_q, C21), 135.6(CH, C7), 134.9(CH, C4), 133.9(CH, C24), 132.2(C_q, C22), 131.6(CH, C23), 130.4(CH, C6), 130.1(CH, C17, C18, C19), 129.7(CH, C9), 129.6(C_q, C8), 128.6(CH, C16, C20), 128.4(C_q, C11), 127.8(CH, C25), 126.6(CH, C26), 119.0(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1671, 1476, 1303, 1076, 970, 824, 699, 593; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}Cl_2N_3O$, calculated 418.0508, found 418.0506. $[\alpha]_D^{20}$ = -25 (Concentration 0.5, $CHCl_3$).



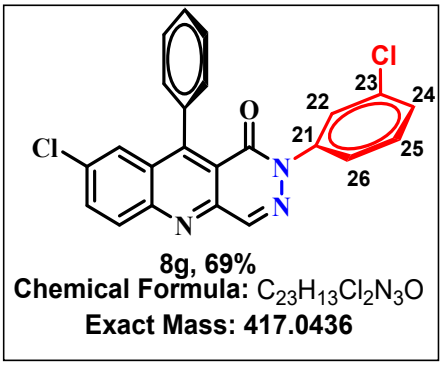
8e, 67%
Chemical Formula: $C_{23}H_{13}ClFN_3O$
Exact Mass: 401.0731

8-Chloro-2-(2-fluorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8e); off white solid (67% yield); melting point 226-228 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.84 (dt, *J* = 14.6, 7.3 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.48 – 7.43 (m, 1H), 7.35 (ddd, *J* = 9.8, 6.3, 1.7 Hz, 1H), 7.29 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.17 (dd, *J* = 16.6, 6.9 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.7(C_q, *J* = 61.3 Hz, C22), 158.1 (C=O, C1), 156.2(C_q, C14), 152.2(C_q, C12), 149.3(C_q, C10), 146.1(C_q, C15), 141.1(CH, C7), 135.7(CH, C4), 134.9(CH, C6), 133.9(C_q, C17, C18, C19), 131.6(CH, C24), 130.4(C_q, C13), 130.3(CH, C9), 129.8(C_q, C8), 129.0(CH, C16, C20), 128.6(CH, C25), 128.5(CH, C25), 128.2(C_q, C11), 126.6(C_q, C21), 124.7(CH, C26), 124.6(CH, C26), 118.9(C_q, C13),116.8 (CH, C23), 116.6(CH, C23) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -119.6 (ddd, *J* = 10.0, 7.4, 5.1 Hz); **FT-IR**(ATR): *ν*(cm^{-1}) 1680, 1495, 1223, 1078, 972, 752, 596; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}ClFN_3O$, calculated 402.0804, found 402.804. **$[\alpha]_D^{20}$** = -26 (Concentration 0.5, $CHCl_3$).



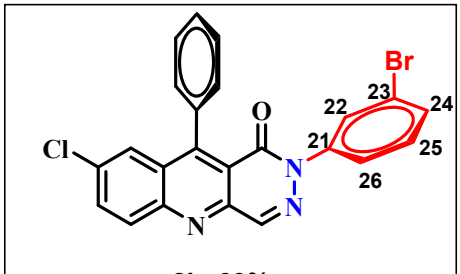
8f, 70%
Chemical Formula: $C_{23}H_{12}Cl_3N_3O$
Exact Mass: 451.0046

8-Chloro-2-(3,5-dichlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8f); off brown solid (70% yield); melting point 208-210 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.87 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.62 – 7.55 (m, 4H), 7.52 (d, *J* = 1.6 Hz, 2H), 7.28 (dd, *J* = 10.0, 6.5 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2(C=O, C1), 152.5(C_q, C14), 149.4(C_q, C12), 145.6(C_q, C21), 143.1(C_q, C10), 141.4(C_q, C15), 135.8(CH, C7), 135.2(CH, C4), 134.9(CH, C6), 134.2(CH, C17, C18, C19), 131.6(C_q, C23, C25), 129.9(C_q, C8), 128.8(CH, C16), 128.6(CH, C20), 128.1(CH, C9), 127.9(C_q, C11), 126.6(CH, C24), 124.7(CH, C22, C26), 118.9(C_q, C13) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 1673, 1468, 1316, 1071, 978, 820, 680; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{13}Cl_3N_3O$, calculated 452.0119, found 452.0119. **$[\alpha]_D^{20}$** = -19 (Concentration 0.5, $CHCl_3$).



8g, 69%
Chemical Formula: $C_{23}H_{13}Cl_2N_3O$
Exact Mass: 417.0436

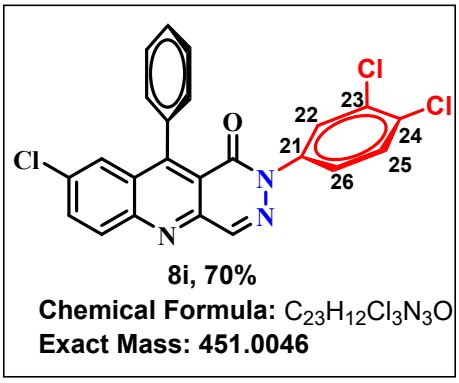
8-Chloro-2-(3-chlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8g); off white solid (69% yield); melting point 212-214 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.7 Hz, 1H), 8.24 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.84 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.63 – 7.53 (m, 5H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.30 (dtd, *J* = 10.5, 7.7, 1.8 Hz, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 152.4(C_q, C14), 149.3(C_q, C12), 145.8(C_q, C21), 142.7(C_q, C10), 141.0(C_q, C15), 135.9(CH, C7), 135.0(CH, C4), 134.4(CH, C6), 134.1(CH, C24), 134.0 (C_q, C23) 131.6(CH, C17, C18, C19), 129.8(CH, C25), 128.7 (Cq, C8), 128.6(CH, C9), 128.1(CH, C16, C20), 126.7(C_q, C11), 126.5(CH, C26), 124.4(CH, C22), 119.1(C_q, C13) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 1690, 1470, 1303, 1071, 838, 673, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}Cl_2N_3O$, calculated 418.0508, found 418.0503. **$[\alpha]_D^{20}$** = -17 (Concentration 0.5, $CHCl_3$).



8h, 69%
Chemical Formula: $C_{23}H_{13}BrClN_3O$
Exact Mass: 460.9931

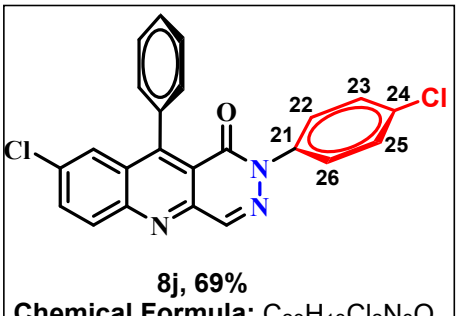
2-(3-Bromophenyl)-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8h); brownish white solid (69% yield); melting point 218-220 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.72 – 8.56 (m, 1H), 8.26 (dd, *J* = 12.6, 9.1 Hz, 1H), 7.94 – 7.84 (m, 1H), 7.81 – 7.69 (m, 1H), 7.67 – 7.52 (m, 5H), 7.46 (dd, *J* = 14.2, 9.5 Hz, 1H), 7.39 – 7.24 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 152.4(C_q, C14), 149.3(C_q, C12), 145.8(C_q, C21), 142.8(C_q, C10), 141.0(C_q, C15), 141.0 (CH, C7) 135.9(CH, C4), 135.0(CH, C6), 134.1(CH, C25) 131.6(CH, C17, C18, C19), 131.0(CH, C9), 130.1(C_q, C8), 129.3(CH, C16, C20),

128.5(C_q, C11), 128.1(CH, C24), 126.7(CH, C26), 124.7(C_q, C23), 122.2(CH, C22), 119.0(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1678, 1473, 1303, 1076, 838, 781, 674, 594; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}BrClN_3O$, calculated 462.0003, found 462.0008. $[\alpha]_D^{20}$ = -20 (Concentration 0.5, $CHCl_3$).



8i, 70%
Chemical Formula: $C_{23}H_{12}Cl_3N_3O$
Exact Mass: 451.0046

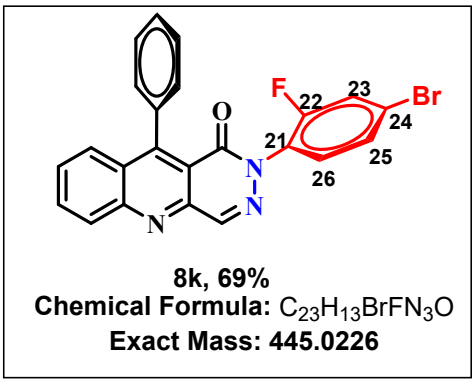
8-Chloro-2-(3,4-dichlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8i); off brown solid (70% yield); melting point 210-212 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.24 (d, J = 9.1 Hz, 1H), 7.86 (dd, J = 9.1, 2.3 Hz, 1H), 7.74 – 7.65 (m, 1H), 7.59 – 7.56 (m, 2H), 7.56 (d, J = 2.2 Hz, 2H), 7.47 (t, J = 4.3 Hz, 2H), 7.30 – 7.26 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 152.4(C_q, C14), 149.3(C_q, C12), 145.7(C_q, C10), 141.3(C_q, C15), 140.8(C_q, C21), 135.8(CH, C7), 135.1(CH, C4), 134.2(C_q, C23), 132.6(CH, C6), 131.6(CH, C17, C18, C19), 130.3(C_q, C24), 129.9(CH, C25), 128.7(CH, C9), 128.5(C_q, C8), 128.1(CH, C16, C20), 127.9(C_q, C11), 126.6(CH, C26), 125.3(CH, C22), 118.9(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1680, 1468, 1074, 984, 813, 678, 538; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{13}Cl_3N_3O$, calculated 452.0119, found 452.0115. $[\alpha]_D^{20}$ = -18 (Concentration 0.5, $CHCl_3$).



8j, 69%
Chemical Formula: $C_{23}H_{13}Cl_2N_3O$
Exact Mass: 417.0436

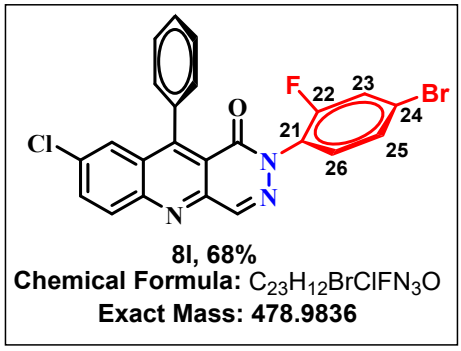
8-Chloro-2-(4-chlorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8j); brown solid (69% yield); melting point 214-216 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.62 (s, 1H),

8.25 (d, J = 9.1 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.53 (dd, J = 22.1, 10.7 Hz, 7H), 7.37 (d, J = 8.5 Hz, 2H), 7.27 (s, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 152.4(C_q, C14), 149.3(C_q, C12), 145.8(C_q, C21), 140.9(C_q, C10), 140.2(C_q, C15), 136.0(CH, C7), 135.0(CH, C4), 134.1(CH, C6), 133.5(C_q, C24), 131.6(CH, C17, C18, C19), 129.9(CH, C9), 129.0(CH, C23, C25), 128.5(CH, C16, C20), 128.1(C_q, C8), 127.4(C_q, C11), 126.6(CH, C22, C26), 119.1(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1678, 1464, 1303, 1077, 823, 700, 595; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}Cl_2N_3O$, calculated 418.0508, found 418.0506. **$[\alpha]_D^{20}$** = -13 (Concentration 0.5, $CHCl_3$).



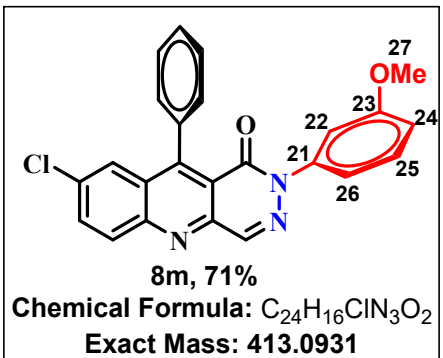
8k, 69%
Chemical Formula: $C_{23}H_{13}BrFN_3O$
Exact Mass: 445.0226

2-(4-Bromo-2-fluorophenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8k); off white solid (69% yield); melting point 224-226 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H), 7.92 (dd, J = 11.1, 4.1 Hz, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.58 (dd, J = 11.4, 3.9 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.36 (dd, J = 8.9, 2.6 Hz, 2H), 7.29 (dd, J = 13.5, 7.9 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.5(C_q, J = 26.9 Hz, C22), 158.3 C=O, C1), 155.9(C_q, C14), 153.1(C_q, C12), 150.8(C_q, C10), 145.8(C_q, C15), 141.6(CH, C7), 136.3(CH, C4), 132.9(CH, C6), 130.2(CH, C17, C18, C19), 129.9(CH, C8), 129.1(CH, C9), 128.9(CH, C16, C20), 128.6(CH, C25), 128.4(CH, C25), 128.2(C_q, C21), 128.2(C_q, C21), 128.1(C_q, C11), 127.9(CH, C26), 127.8(CH, C26), 122.6(CH, C23), 122.5(CH, C23), 120.5(C_q, C24), 120.2(C_q, C24), 118.2(C_q, C13) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -115.79 – -116.01 (m) ppm; **FT-IR**(ATR): ν(cm^{-1}) 1687, 1489, 1326, 965, 856, 762, 702, 590; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{14}BrFN_3O$, calculated 446.0299, found 446.0299. **$[\alpha]_D^{20}$** = -10 (Concentration 0.3, $CHCl_3$).



8l, 68%
Chemical Formula: $C_{23}H_{12}BrClFN_3O$
Exact Mass: 478.9836

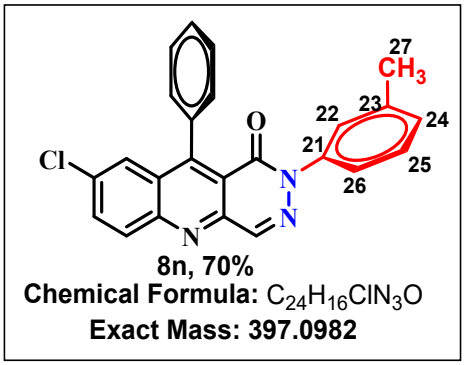
2-(4-Bromo-2-fluorophenyl)-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8l); off white solid (68% yield); melting point 230-232 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.86 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.56 – 7.50 (m, 3H), 7.38 – 7.33 (m, 2H), 7.33 – 7.31 (m, 1H), 7.30 – 7.26 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.5(C_q, *J* = 52.0 Hz, C22), 157.9 (C=O, C1), 155.9(C_q, C14), 152.3(C_q, C12), 149.3(C_q, C10), 145.9(C_q, C15), 141.4(CH, C7), 135.6(CH, C4), 135.1(CH, C6), 134.1(CH, C17, C18, C19), 131.6(C_q, C8), 130.1(CH, C9), 129.8(CH, C16, C20), 128.8(CH, C25), 128.7(CH, C25), 128.5(C_q, C21), 128.2(C_q, C21), 128.0(C_q, C11), 127.9(CH, C26), 126.6(CH, C26), 122.8(CH, C23), 122.7(CH, C23), 120.5(C_q, C24), 120.3(C_q, C24), 118.8(C_q, C13) ppm, **^{19}F NMR** (377 MHz, $CDCl_3$) δ -115.73 – -116.14 (m) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 1678, 1493, 1310, 1081, 976, 839, 698; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{23}H_{13}BrClFN_3O$, calculated 479.9909, found 479.9909. **$[\alpha]_D^{20}$** = -14(Concentration 0.5, $CHCl_3$).



8m, 71%
Chemical Formula: $C_{24}H_{16}ClN_3O_2$
Exact Mass: 413.0931

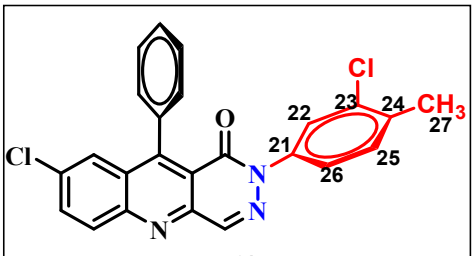
8-Chloro-2-(3-methoxyphenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8m); off brown solid (71% yield); melting point 258-260 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 7.84 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.57 (t, *J* = 2.4 Hz, 1H), 7.52 (ddd, *J* = 11.8, 6.2, 2.5 Hz, 3H), 7.29 (ddd, *J* = 10.6, 7.0, 4.9 Hz, 3H), 7.15 – 7.09 (m, 1H), 7.05 (t, *J* = 2.2 Hz, 1H), 6.91 – 6.83 (m, 1H), 3.80 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$)

δ 160.1 (C_q, C23), 158.3(C=O, C1), 152.3(C_q, C14), 149.3(C_q, C12), 145.9(C_q, C10), 142.7(C_q, C15), 140.5(CH, C7), 136.0(CH, C4), 134.8(CH, C6), 133.9(CH, C17, C18, C19), 131.5(C_q, C8), 129.6(CH, C9), 128.5(C_q, C11), 128.4(CH, C16, C20), 128.1(CH, C25), 126.6(CH, C26), 119.2(CH, C24), 118.7(C_q, C13), 113.9(C_q, C21), 112.1(C_q, C21), 55.5(–OCH_3, C27) ppm; **FT-IR**(ATR): ν(cm^{-1}) 2919, 1665, 1597, 1467, 1284, 1218, 988, 937, 684, 585; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{24}H_{17}ClN_3O_2$, calculated 414.1004, found 414.1005. $[\alpha]_D^{20}$ = -17 (Concentration 0.5, $CHCl_3$).



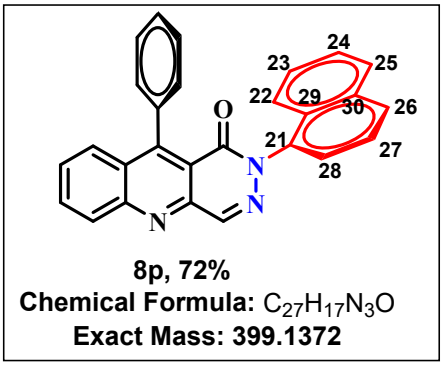
8n, 70%
Chemical Formula: $C_{24}H_{16}ClN_3O$
Exact Mass: 397.0982

8-Chloro-10-phenyl-2-(*m*-tolyl)pyridazino[4,5-*b*]quinolin-1(2*H*)-one (8n); off white solid (70% yield); melting point 249-250 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 7.84 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.57 (t, *J* = 3.2 Hz, 1H), 7.52 (t, *J* = 8.8 Hz, 3H), 7.28 (dd, *J* = 12.4, 3.3 Hz, 5H), 7.13 (d, *J* = 3.1 Hz, 1H), 2.36 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4(C=O, C1), 152.2(C_q, C14), 149.3(C_q, C12), 146.0(C_q, C10), 141.6(C_q, C23), 140.4(C_q, C15), 138.9(C_q, C21), 136.1(CH, C7), 134.7(CH, C4), 133.9(CH, C6), 131.5(CH, C17, C18, C19), 128.8(CH, C25), 128.7(CH, C9), 128.5(C_q, C8), 128.4(C_q, C11), 128.2(CH, C16, C20), 126.8(CH, C24), 126.6(CH, C26), 126.6(CH, C26), 123.3(CH, C22), 119.2(C_q, C13), 21.5(CH_3, C27) ppm; **FT-IR**(ATR): ν(cm^{-1}) 2925, 1682, 1467, 1299, 1081, 870, 697, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{24}H_{17}ClN_3O$, (calculated 398.1055, found 398.1053. $[\alpha]_D^{20}$ = -19 (Concentration 0.5, $CHCl_3$).



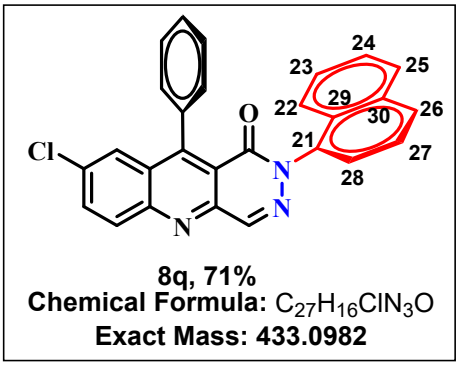
8o, 73%
Chemical Formula: $C_{24}H_{15}Cl_2N_3O$
Exact Mass: 431.0592

8-Chloro-2-(3-chloro-4-methylphenyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8o); Brownish white solid (73% yield); melting point 240-242 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 13.3 Hz, 1H), 8.25 (d, *J* = 9.1 Hz, 1H), 7.84 (dt, *J* = 17.0, 8.5 Hz, 1H), 7.55 (tt, *J* = 13.1, 5.6 Hz, 5H), 7.35 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.27 (dd, *J* = 3.8, 2.2 Hz, 2H), 7.24 (s, 1H), 2.37 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.3(C=O, C1), 152.3(C_q, C14), 149.3(C_q, C12), 145.9(C_q, C10), 140.8(C_q, C15), 140.3(C_q, C21), 135.9(C_q, C23), 135.9(CH, C7), 134.9(CH, C4), 134.3(C_q, C24), 134.0(CH, C25), 131.6(CH, C6), 130.9(CH, C17, C18, C19), 129.9(CH, C9), 128.6(C_q, C8), 128.5(CH, C16, C20), 128.1(C_q, C11), 126.7(CH, C26), 126.6(CH, C26), 124.3(CH, C22), 119.1(C_q, C13), 19.8, (CH_3, C27) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 1668, 1477, 1296, 1087, 976, 845, 707, 591; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{24}H_{16}Cl_2N_3O$, calculated 432.0665, found 432.0664. **$[\alpha]_D^{20}$** = -19 (Concentration 0.5, $CHCl_3$).



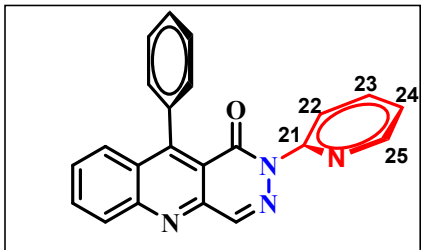
8p, 72%
Chemical Formula: $C_{27}H_{17}N_3O$
Exact Mass: 399.1372

2-(Naphthalen-2-yl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8p); brown solid (72% yield); melting point 232-234 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 8.05 (s, 1H), 7.97 – 7.90 (m, 1H), 7.89 – 7.78 (m, 3H), 7.67 – 7.61 (m, 2H), 7.59 (d, J = 7.3 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 3H), 7.49 – 7.43 (m, 2H), 7.35 – 7.29 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.8(C=O, C1), 153.1(C_q, C14), 150.9(C_q, C12), 145.9(C_q, C21), 140.9(C_q, C10), 139.3(C_q, C15), 136.8(C_q, C30), 133.3(CH, C7), 132.8(CH, C4), 132.6 (CH, C17, C18, C19), 129.9(CH, C6, C25), 129.3(CH, C8), 128.6(CH, C27), 128.4(CH, C9), 128.2(CH, C16, C20), 128.2(C_q, C11), 127.7(CH, C23), 126.5(C_q, C29), 126.4(CH, C22), 124.7(CH, C26), 124.3(CH, C28), 118.7(C_q, C13) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 2918, 2847, 1678, 1460, 1311, 1112, 813, 746, 702; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{27}H_{18}N_3O$, calculated 400.1444, found 400.1445. **$[\alpha]_D^{20}$** = -21 (Concentration 0.5, $CHCl_3$).



8q, 71%
Chemical Formula: $C_{27}H_{16}ClN_3O$
Exact Mass: 433.0982

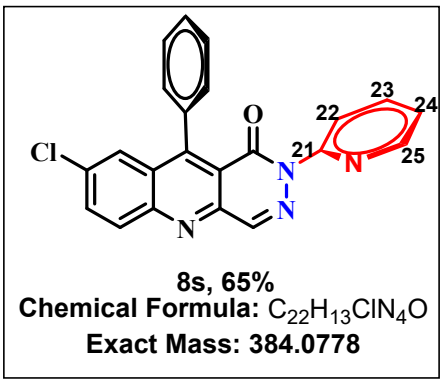
8-Chloro-2-(naphthalen-2-yl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (8q); brown solid (71% yield); melting point 240-242 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.25 (t, *J* = 9.4 Hz, 1H), 8.07 – 7.99 (m, 1H), 7.90 – 7.79 (m, 4H), 7.63 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.58 (t, *J* = 3.6 Hz, 1H), 7.53 (t, *J* = 6.1 Hz, 3H), 7.50 – 7.44 (m, 2H), 7.33 – 7.28 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.6(C=O, C1), 152.3(C_q, C14), 149.3(C_q, C12), 145.9(C_q, C21), 140.7(C_q, C10), 139.2(C_q, C15), 136.1(C_q, C30), 134.8(CH, C7), 133.9(CH, C4), 133.3(CH, C6), 132.6(CH, C17, C18, C19), 131.5(C_q, C8,), 129.8(C_q, C11), 128.7(CH, C25), 128.6(CH, C16, C20), 128.5(CH, C27), 128.4(CH, C9), 128.2(CH, C24), 127.7(CH, C23), 126.6(C_q, C29), 126.5(CH, C22), 124.7(CH, C26), 124.2(CH, C28), 119.2(C_q, C13) ppm; **FT-IR**(ATR): *ν*(cm^{-1}) 2914, 2848, 1731, 1673, 1303, 1103, 756, 703; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$: Chemical formula $C_{27}H_{17}ClN_3O$, calculated 434.1055, found 434.1057. **$[\alpha]_D^{20}$** = -21 (Concentration 0.5, $CHCl_3$).



8r, 67%
Chemical Formula: $C_{22}H_{14}N_4O$
Exact Mass: 350.1168

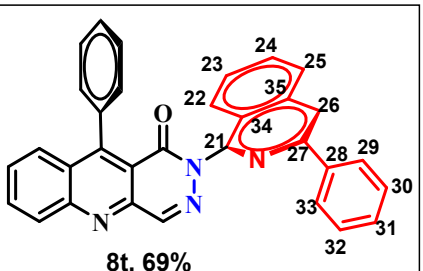
10-Phenyl-2-(pyridin-2-yl)pyridazino[4,5-*b*]quinolin-1(2*H*)-one (8r); brown solid (67% yield); melting point 258-260 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.63 (dd, *J* = 4.8, 0.9 Hz, 1H), 8.31 (d, *J* = 8.6 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.78 (td, *J* = 8.0, 1.8 Hz, 1H), 7.60 (dd, *J* = 11.7, 6.3 Hz, 3H), 7.55 – 7.48 (m, 3H), 7.34 – 7.28 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.8(C=O, C1), 153.4(C_q, C21), 153.2(C_q, C14), 150.9(CH, C25), 149.4(C_q, C12), 145.9(C_q, C10), 141.4(CH, C23), 138.0(C_q, C15), 136.6(CH, C7), 132.9(CH,

C4), 129.9(CH, C17, C19), 129.2(CH, C18), 128.5(CH, C6), 128.3(CH, C8), 128.2(CH, C9), 128.2(CH, C16, C20), 128.2(C_q, C11), 123.3(CH, C24), 121.9(CH, C22), 118.6(C_q, C13) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 1681, 1496, 1223, 973, 833, 750, 594; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{22}H_{15}N_4O$, calculated 351.1240, found 351.1242. $[\alpha]_D^{20}$ = -41 (Concentration 0.5, $CHCl_3$).



8s, 65%
Chemical Formula: $C_{22}H_{13}ClN_4O$
Exact Mass: 384.0778

8-Chloro-10-phenyl-2-(pyridin-2-yl)pyridazino[4,5-*b*]quinolin-1(2*H*)-one (8s); brown solid (65% yield); melting point 268-270 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.57 – 8.53 (m, 1H), 8.18 (d, *J* = 9.1 Hz, 1H), 7.78 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.71 (td, *J* = 7.9, 1.8 Hz, 1H), 7.53 – 7.41 (m, 5H), 7.25 – 7.18 (m, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.6(C=O, C1), 153.3(C_q, C21), 152.3(C_q, C14), 149.4(CH, C25), 149.3(C_q, C12), 145.9(C_q, C10), 141.2(CH, C23), 138.1(C_q, C15), 135.9(CH, C4), 134.9(CH, C7), 134.0(CH, C17, C19), 131.6(CH, C18), 129.8(CH, C6), 128.6(C_q, C8), 128.4(CH, C9), 128.1(CH, C16, C20), 126.6(C_q, C11), 123.4(CH, C24), 121.8(CH, C22), 119.1(C_q, C13) ppm; **FT-IR**(ATR): *v*(cm^{-1}) 1682, 1466, 1305, 1075, 790, 588; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{22}H_{14}ClN_4O$, calculated 385.0851, found 385.0853. $[\alpha]_D^{20}$ = -44 (Concentration 0.5, $CHCl_3$).

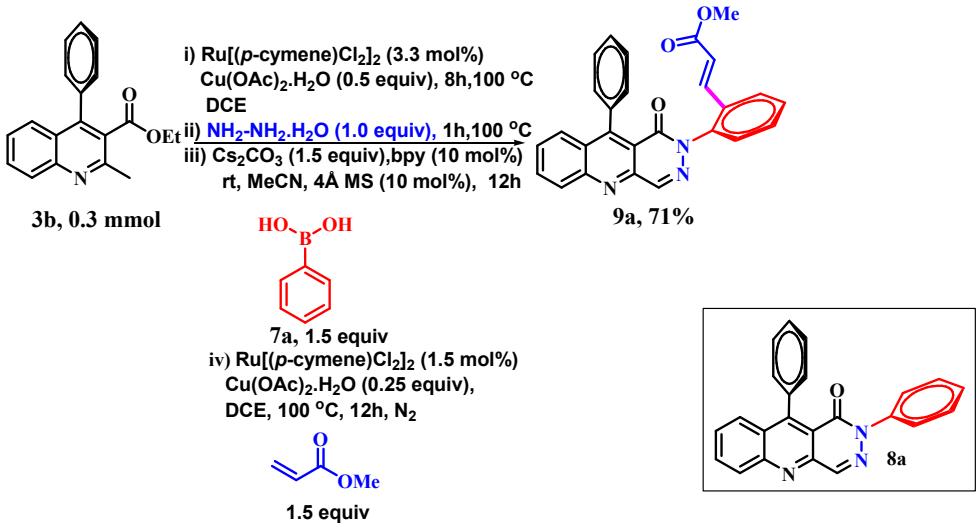


8t, 69%
Chemical Formula: $C_{32}H_{20}N_4O$
Exact Mass: 476.1637

10-Phenyl-2-(3-phenylisoquinolin-1-yl)pyridazino[4,5-*b*]quinolin-1(2*H*)-one (8t); off white to yellow solid (69% yield); melting point 288-290 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 8.12 (s, 1H), 8.07 (d, *J* = 7.5 Hz, 2H), 8.00 – 7.90 (m,

2H), 7.74 – 7.66 (m, 3H), 7.64 – 7.59 (m, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.44 (dd, J = 12.2, 6.1 Hz, 5H), 7.39 (d, J = 7.3 Hz, 1H), 7.33 (d, J = 6.9 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.3(C=O, C1), 153.1(C_q, C21), 152.8(C_q, C27), 151.0(C_q, C14), 150.9(C_q, C12), 146.3(C_q, C10), 141.2(C_q, C28), 139.3(C_q, C35), 138.9(C_q, C15), 136.3(CH, C7), 132.9(CH, C4), 131.0(CH, C24), 130.1(CH, C17, C18, C19), 129.3(CH, C30, C32), 128.8(CH, C6), 128.8(CH, C9), 128.6(CH, C31), 128.4(CH, C25), 128.3(CH, C16, C20), 128.2(C_q, C11), 128.2(CH, C23), 127.5(CH, C29, C33), 127.5(CH, C8), 124.7(CH, C22), 124.1(C_q, C34), 118.7(CH, C26), 118.5(C_q, C13) ppm; **FT-IR**(ATR): ν(cm^{-1}) 2914, 2846, 1730, 1671, 1467, 1304, 1102, 756, 702; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{32}H_{21}N_4O$, calculated 477.1710, found 477.1711. **$[\alpha]_D^{20}$** = -55 (Concentration 0.5, $CHCl_3$).

2.4) Table S10: Sequential C–H alkenylation[a]

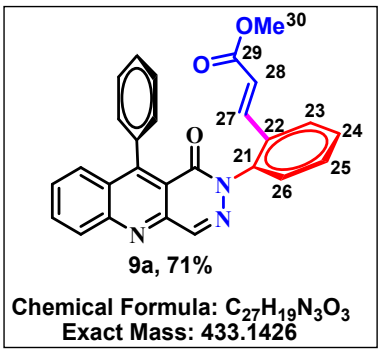


Entry	Deviation from standard condition after formation of 8a[a]	9a yield[b] (%)
1	Added excess of Ru (1.5 mol%)	61
2	Added excess oxidant Cu (0.25 equiv)	65
3	**Added excess of both Ru (1.5 mol%) and Cu (0.25 equiv)**	**71**
4	Temperature 80ºC, 90ºC, 120ºC	47, 51,71
5	Time 10h, 11h, 13h	39, 47, 71
6	Without N_2	37

[a]**Reaction conditions: 3b** (0.3 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (3.3 mol%), $Cu(OAc)_2.H_2O$ (0.5 equiv, 0.15 mmol), in 3 mL of DCE for 8h at 100 ºC, then NH_2-$NH_2.H_2O$ (1.0 equiv, 0.3 mmol) at 100 ºC for 1h, evaporated the DCE, followed by the addition of Cs_2CO_3 (1.5 equiv, 0.45 mmol), bpy (10 mol%, 0.03 mmol), aryl boronic acids (1.5 equiv, 0.45 mmol) and 4Å MS (10 mol%) were stirred at room temperature using MeCN (3 mL) for 12h to give **8a** with 73% of yield, further addition of $[Ru(p\text{-cymene})Cl_2]_2$ (1.5 mol%), $Cu(OAc)_2.H_2O$ (0.25 equiv, 0.075 mmol) and methyl acrylate (1.5 equiv, 0.45 mmol) in DCE (3 mL) at 100 ºC for 12h under Nitrogen atmosphere to give **9a** with 71% of yield. [b]Isolated yields.

Sequential *ortho*-C-H Olefination towards 9a (Fujiwara-Moritani-type alkenylation)

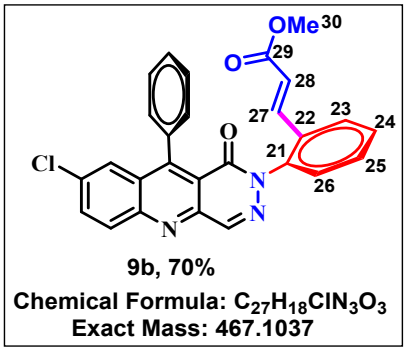
In an oven-dried glass vial, **3b** (0.3 mmol, 88 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (3.3 mol%, 6 mg), and $Cu(OAc)_2 \cdot H_2O$ (0.5 equiv, 0.15 mmol, 30 mg) were added to DCE (3 mL) and the mixture was stirred at 100 °C for 8 h. Subsequently, $NH_2NH_2 \cdot H_2O$ (1.0 equiv, 0.3 mmol, 15 mg) was added, and the reaction mixture was heated at 100 °C for an additional 1 h. The excess DCE was removed under reduced pressure, and MeCN (3 mL) was added, followed by Cs_2CO_3 (1.5 equiv, 0.45 mmol, 147 mg), bpy (10 mol%, 16 mg), arylboronic acid (1.5 equiv, 0.45 mmol, 55 mg), and 4 Å molecular sieves (5 pellets). The mixture was stirred at room temperature for 12 h. After completion of the Chan–Lam coupling (monitored by TLC), the solvent was evaporated under reduced pressure and DCE (3 mL) was added. To this, $[Ru(p\text{-cymene})Cl_2]_2$ (1.5 mol%, 3 mg), $Cu(OAc)_2 \cdot H_2O$ (0.25 equiv, 0.075 mmol, 15 mg), and methyl acrylate (1.5 equiv, 0.45 mmol, 38 mg) were added via syringe, and the vial was sealed with a screw-type septum cap. The reaction mixture was evacuated and purged with nitrogen three times, then stirred at 100 °C for 12 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 and filtered through Celite. The filtrate was concentrated, and the crude product, **9a** was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to afford the pure product. The same procedure was applied to other derivatives to obtain the corresponding products in good to excellent yields.



9a, 71%

Chemical Formula: $C_{27}H_{19}N_3O_3$
Exact Mass: 433.1426

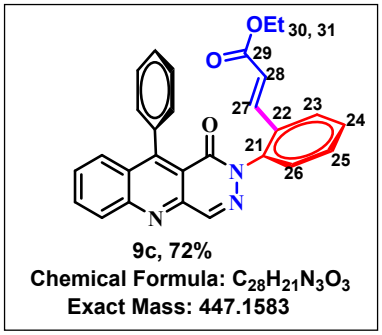
Methyl (*E*)-3-(2-(1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)(*S*)phenyl)acrylate (9a); pale yellow solid (71% yield); melting point 168-170 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.95 (ddd, *J* = 8.4, 6.7, 1.3 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.63 – 7.52 (m, 2H), 7.48 (dd, *J* = 5.1, 1.7 Hz, 3H), 7.45 – 7.37 (m, 3H), 7.31 (dd, *J* = 6.5, 3.0 Hz, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 3.74 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1 (–O–C=O, C29), 159.0(C=O, C1), 153.2(C_q, C14), 151.0(C_q, C12), 145.9(–CH=, C27), 141.4(C_q, C10), 141.2(C_q, C15), 139.9(C_q, C21), 136.4(CH, C7), 132.9(CH, C4), 131.7(CH, C25), 130.9(CH, C17, C18, C19), 130.0(CH, C6), 129.2(C_q, C22), 129.0(CH, C8), 128.6(CH, C16, C20), 128.3(C_q, C13), 128.3(C_q, C11), 128.2(CH, C23), 128.2(CH, C24), 127.3(CH, C26), 120.3(CH, C9), 118.5(–CH=, C28), 51.8(CH_3, C30) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{27}H_{20}N_3O_3$, calculated 434.1499, found 434.1499. Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.652 min and SOR **$[\alpha]_D^{20}$** = -21 (Concentration 0.5, $CHCl_3$).



9b, 70%
Chemical Formula: $C_{27}H_{18}ClN_3O_3$
Exact Mass: 467.1037

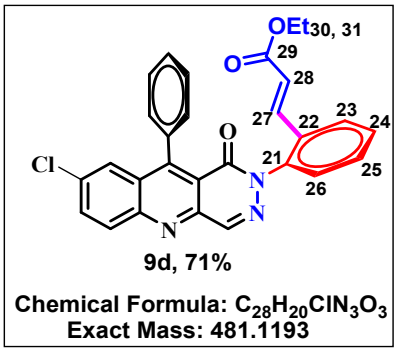
Methyl (*E*)-3-(2-(8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl) acrylate (9b) ; pale yellow solid (70% yield); melting point 174-176 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.27 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.64 (s, 1H), 7.50 (dd, *J* = 27.4, 16.6 Hz, 5H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.29 (s, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 3.74 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.1(–O–C=O, C29), 158.7(C=O, C1), 152.3, (C_q, C14) 149.4(C_q, C12), 146.1(–CH=, C27), 141.1(C_q, C10), 141.0(C_q, C15), 139.8(C_q, C21), 135.7(CH, C7), 134.9(CH, C4), 134.0(CH, C25), 131.6(CH, C17, C18, C19), 131.0(CH, C6), 129.7(C_q, C22), 129.1(C_q, C8), 128.6(CH, C16, C20), 128.5(CH, C9), 128.4(C_q, C11), 128.3(CH, C23), 127.3(CH, C24), 126.6(CH, C26), 120.3(C_q, C13), 118.9(–CH=, C28), 51.8(CH_3, C30) ppm; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{27}H_{19}ClN_3O_3$, calculated 468.1109; found 468.1108. Atropisomeric

nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 8.943 min and with SOR $[\alpha]_D^{20}$ = -43 (Concentration 0.5, $CHCl_3$).

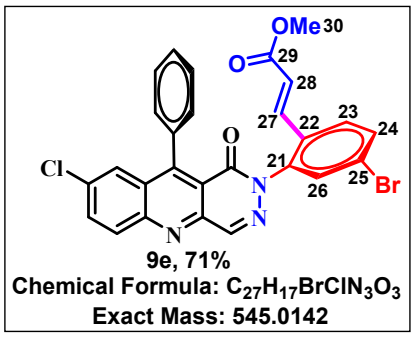


9c, 72%
Chemical Formula: $C_{28}H_{21}N_3O_3$
Exact Mass: 447.1583

Ethyl (*E*)-3-(2-(1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl)acrylate (9c); pale yellow solid (72% yield); melting point 162-164 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 7.98 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.65 – 7.60 (m, 1H), 7.50 (d, *J* = 5.3 Hz, 4H), 7.47 – 7.37 (m, 3H), 7.35 – 7.31 (m, 2H), 6.42 (d, *J* = 15.9 Hz, 1H), 4.27 – 4.17 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7(–O–C=O, C29), 159.1(C=O, C1), 153.2(C_q, C14), 151.0(C_q, C12), 146.0(–CH=, C27), 141.4(C_q, C10), 141.2(C_q, C15), 139.7(C_q, C21), 136.4(CH, C7), 132.9(CH, C4), 131.8(CH, C25), 130.9(CH, C17, C18, C19), 130.0(CH, C6), 129.2(C_q, C22), 129.0(CH, C8), 128.6(CH, C16, C20), 128.4(CH, C9), 128.3(C_q, C11), 128.2(CH, C23), 128.2(CH, C24), 127.2(CH, C26), 120.7(C_q, C13), 118.4(–CH=, C28), 60.6 (CH_2, C30), 14.4(CH_3, C31) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{22}N_3O_3$, calculated 448.1656, found 448.1657. Atropisomeric nature was determined with **HPLC** using using a C18 column with a mobile phase of MeOH/H_2O = 80:20, flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 15.872 min and **HPLC** using a Chiralcel OD-H (cellulose-3) column with a mobile phase of acetonitrile/isopropanol (80:20), flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 3.522 min and SOR $[\alpha]_D^{20}$ = -20 (Concentration 0.5, $CHCl_3$).

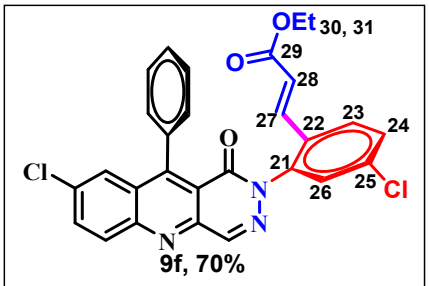


Ethyl(*E*)-3-(2-(8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl) acrylate (9d); off white solid (71% yield); melting point 172-174 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.28 (d, *J* = 9.1 Hz, 1H), 7.87 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 1.9 Hz, 1H), 7.55 – 7.48 (m, 4H), 7.45 (d, *J* = 6.5 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.32 – 7.27 (m, 2H), 6.40 (d, *J* = 15.9 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7(–O–C=O, C29), 158.7(C=O, C1), 152.3(C_q, C14), 149.4(C_q, C12), 146.1(–CH=, C27), 141.1(C_q, C10), 141.0(C_q, C15), 139.6(C_q, C21), 135.7(CH, C7), 134.1(CH, C4), 131.7(CH, C25), 131.7(CH, C17, C18, C19), 130.9(CH, C6), 129.7(C_q, C22), 129.1(C_q, C8), 128.6(CH, C16, C20), 128.5(CH, C9), 128.4(C_q, C11), 128.3(CH, C23), 127.3(CH, C24), 126.6(CH, C26), 120.8(C_q, C13), 119.0(–CH=, C28), 60.7(CH_2, C30), 14.4(CH_3, C31) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{21}ClN_3O_3$ calculated 482.1266; found 482.1276. **$[\alpha]_D^{20}$** = -27 (Concentration 0.5, $CHCl_3$).



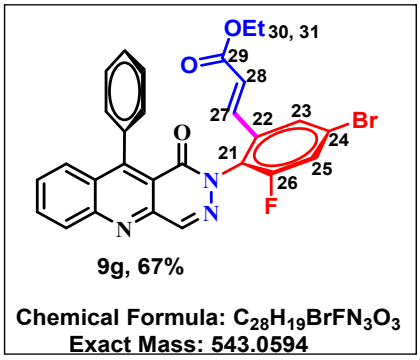
Methyl (*E*)-3-(2-bromo-6-(8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl)acrylate (9e); pale yellow solid (71 % yield); melting point 158-160 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 12.2 Hz, 1H), 8.21 (d, *J* = 9.1 Hz, 1H), 7.81 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.50 (s, 1H), 7.46 (s, 2H), 7.45 – 7.42 (m, 2H), 7.37 (d, *J* = 15.9 Hz, 1H), 7.23 – 7.20 (m, 2H), 7.19 (s, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 3.66 (d, *J* = 11.5 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.9(–O–C=O, C29), 158.6(C=O, C1),

152.4(C_q, C14), 149.4(C_q, C12), 145.9(–CH=, C27), 141.8(C_q, C10), 141.5(C_q, C15), 138.8(C_q, C21), 135.5(CH, C7), 135.2(CH, C4) 134.2(CH, C6), 132.4(CH, C17, C18, C19), 131.7(CH, C23), 131.7(CH, C9) 130.8(C_q, C8), 129.8(CH, C16, C20), 128.8(C_q, C11), 128.5(CH, C24), 128.2(C_q, C22), 126.6(C_q, C25), 124.3(CH, C26), 120.8(C_q, C13), 118.9(–CH=, C28), 51.9(CH_3, C30) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{27}H_{18}BrClN_3O_3$, calculated 546.0215, found 546.0217. $[\alpha]_D^{20}$ = -47 (Concentration 0.5, $CHCl_3$).



Chemical Formula: $C_{28}H_{19}Cl_2N_3O_3$
Exact Mass: 515.0803

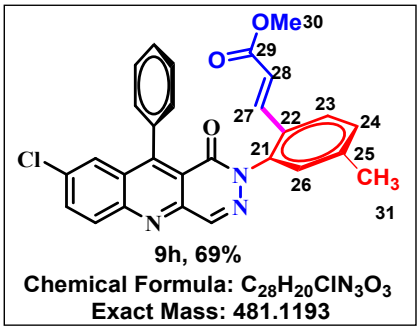
Ethyl (*E*)-3-(2-chloro-6-(8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl)acrylate (9f); pale yellow solid (70% yield); melting point 162-164 °C, **^{1}H NMR** (400 MHz, CDCl3) δ 8.56 (s, 1H), 8.20 (t, *J* = 9.6 Hz, 1H), 7.81 (dd, *J* = 9.0, 1.7 Hz, 1H), 7.56 (s, 1H), 7.43 (s, 3H), 7.40 – 7.34 (m, 2H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.22 (s, 2H), 7.19 (s, 1H), 6.27 (t, *J* = 19.8 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 6.5 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.5(–O–C=O, 29), 158.7(C=O, C1), 152.4(C_q, C14), 149.5(C_q, C12), 146.6(–CH=, C27), 141.5(C_q, C10), 138.5(C_q, C15), 136.3(C_q, C21), 135.6(CH, C7), 135.2(CH, C4), 134.2(C_q, C25), 131.7(CH, C6), 130.5(CH, C17, C18, C19), 129.8(CH, 23) 129.4(CH, C9), 128.9(C_q, C8), 128.8(CH, C16, C20), 128.5(C_q, C11), 128.3(CH, C24), 128.2(C_q, C22), 126.6(CH, C26), 121.2(C_q, C13), 118.9(–CH=, C28), 60.8(CH_2, C30), 14.4(CH_3, C31) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{20}Cl_2N_3O_3$, calculated 516.0876; found 516.0876. $[\alpha]_D^{20}$ = -43 (Concentration 0.5, $CHCl_3$).



9g, 67%

Chemical Formula: $C_{28}H_{19}BrFN_3O_3$
Exact Mass: 543.0594

Ethyl (*E*)-3-(5-bromo-3-fluoro-2-(1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl) phenyl)acrylate (9g); off white solid (67% yield); melting point 164-166 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 7.89 (t, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 11.9 Hz, 3H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 5.9 Hz, 2H), 7.19 (s, 1H), 6.34 (d, *J* = 15.9 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.0(–O–C=O, C29), 158.7(C_q, C26), 153.3(C=O, C1), 151.1(C_q, C14), 145.9(–CH=, C27), 142.3(C_q, C12), 137.0(C_q, C10), 136.2(C_q, C15), 133.1(C_q, C22), 130.1(CH, C7), 129.2(CH, C4), 128.8(CH, C17, C18, C19), 128.5(CH, C6), 128.4(CH, C8), 128.3(CH, C9), 125.9(CH, C16, C20), 125.8(C_q, C11), 123.4(CH, C23), 123.1 (C_q, C21) ,123.0(C_q, C24), 121.3(CH, C25), 121.0(C_q, C13), 118.1(–CH=, C28), 60.9(CH_2, C30), 14.3(CH_3, C31) ppm; **^{19}F NMR** (377 MHz, $CDCl_3$) δ -116.6, -116.6 (d) ppm. **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{20}BrFN_3O_3$, calculated 544.0667, found 544.0667. Atropisomeric nature was determined with **HPLC** using a C18 column with a mobile phase of MeOH/H_2O = 80:20, flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 20.864 min and SOR **$[\alpha]_D^{20}$** = -57 (Concentration 0.5, $CHCl_3$).

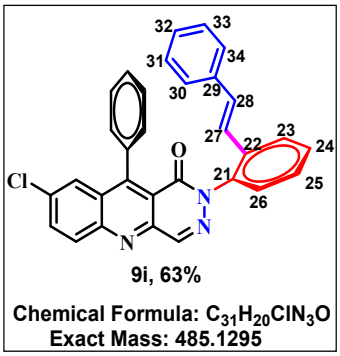


9h, 69%

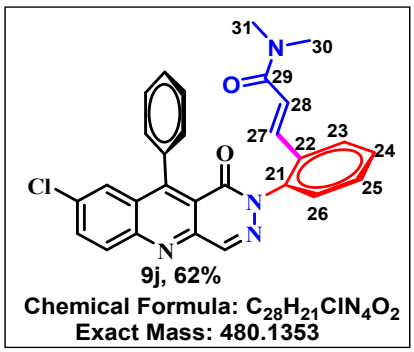
Chemical Formula: $C_{28}H_{20}ClN_3O_3$
Exact Mass: 481.1193

Methyl (*E*)-3-(2-(8-chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)-6-methyl phenyl)acrylate (9h); pale yellow solid (69% yield); melting point 168-170 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 13.5 Hz, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.8 Hz,

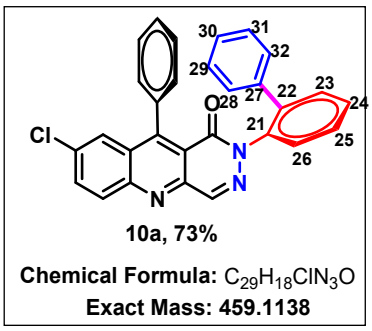
1H), 7.68 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 9.0 Hz, 5H), 7.33 (d, *J* = 12.2 Hz, 3H), 6.41 (d, *J* = 15.8 Hz, 1H), 3.75 (d, *J* = 22.8 Hz, 3H), 2.42 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.3(–O–C=O, C29), 158.8(C=O. C1), 152.3(C_q, C14), 149.4(C_q, C12), 146.1(–CH=, C27), 141.9(C_q, C10), 141.0(C_q, C15), 139.7(C_q, C23), 135.7(C_q, C21), 135.0(CH, C7), 134.1(CH, C4), 131.7(CH, C17, C18, C19), 130.1(CH, C6), 129.8 (CH, C9), 129.0(C_q, C8), 128.8 (C_q, C16, C20), 128.6(C_q, C22), 128.4(CH, C24), 128.3(C_q, C11), 127.1(CH, C25), 126.6(CH, C26), 119.3(–CH=, C28), 119.0 (C_q, C13), 51.8(CH_2, C30), 21.4(CH_3, C31) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{21}ClN_3O_3$, calculated 482.1266, found 482.1267. Atropisomeric nature was determined with **HPLC conditions:** Enantiomeric excess was determined using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.130 min and **$[\alpha]_D^{20}$** = -43 (Concentration 0.5, $CHCl_3$).



(*E*)-8-Chloro-10-phenyl-2-(2-styrylphenyl)pyridazino[4,5-*b*]quinolin-1(2*H*)-one (9i); yellow solid (63% yield); melting point 158-160 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.38 (d, *J* = 8.9 Hz, 1H), 8.21 (d, *J* = 8.9 Hz, 1H), 7.78 (s, 1H), 7.55 (s, 3H), 7.53 (d, *J* = 5.8 Hz, 4H), 7.46 (d, *J* = 7.0 Hz, 2H), 7.43 – 7.39 (m, 4H), 7.33 (d, *J* = 6.1 Hz, 2H), 7.22 (s, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.7(C=O, C1), 153.1(C_q, C14), 150.3(C_q, C12), 145.8(C_q, C10), 141.9(C_q, C15), 141.0(C_q, C29), 140.8(C_q, C21), 139.8(CH, C7), 139.7(CH, C4), 136.7(CH, C6), 132.8(CH, C25), 130.7 (C_q, C22), 130.4(CH, C17, C18, C19), 129.6(CH, C23), 129.2(CH, C9), 128.9(CH, C31, C33), 128.7(CH, C30, 34), 128.5(C_q, C8), 128.3(CH, C16, C20), 128.2(C_q, C11), 127.9(–CH=, C28), 127.6(CH, C32), 126.6(CH, C24), 126.2(CH, C26), 125.4(C_q, C13), 119.0(–CH=, C27) ppm. **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{31}H_{21}ClN_3O$, calculated 486.13368, found 486.1362. **$[\alpha]_D^{20}$** = -34 (Concentration 0.5, $CHCl_3$).

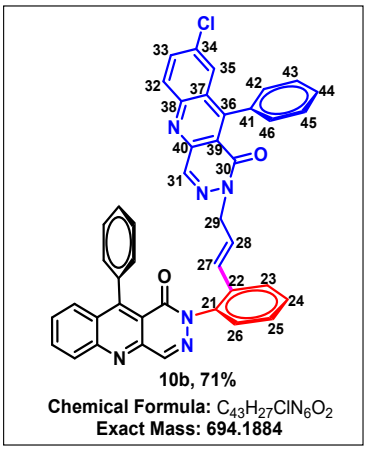


(*E*)-3-(2-(8-Chloro-1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl)-*N*,*N*-dimethylacrylamide (9j); brown solid (62% yield); melting point 154-156 °C, **^{1}H NMR** (400 MHz, CDCl3) δ 8.63 (d, *J* = 6.4 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.63 (s, 1H), 7.51 (dd, *J* = 12.5, 9.5 Hz, 4H), 7.42 (dd, *J* = 16.0, 9.0 Hz, 3H), 7.32 (s, 2H), 6.85 (d, *J* = 15.3 Hz, 1H), 3.14 (s, 3H), 3.03 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2(–N–C=O, C29), 158.7(C=O, C1), 152.2(C_q, C14), 149.3(C_q, C12), 146.1(–CH=, C27), 141.0(C_q, C10), 137.4(C_q, C15), 135.8(C_q, C21), 134.8(CH, C7), 133.9(CH, C4), 132.9(CH, C25), 131.6(CH, C6), 130.3(CH, C17, C18, C19), 129.7(CH, C9), 129.0(C_q, C8), 128.5(C_q, C22), 128.3(C_q, C11), 128.2(CH, C16, C20), 127.9(CH, C23), 127.1(CH, C24), 126.6(CH, C26), 120.2(C_q, C13), 119.1(–CH=, C28), 37.5(CH_3, C30), 35.9(CH_3, C31) ppm; **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{28}H_{22}ClN_4O_2$, calculated 481.1426, found 481.1421. Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.565 min and SOR **$[\alpha]_D^{20}$** = -29 (Concentration 0.5, $CHCl_3$).



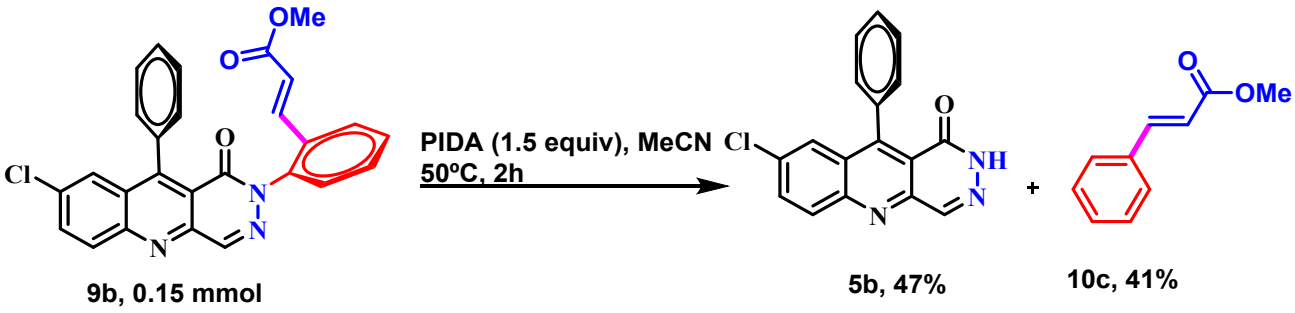
2-([1,1'-Biphenyl]-2-yl)-8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (10a): brown solid 73% yield, melting point = 172-174 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 7.71 (s, 1H), 7.49 – 7.44 (m, 5H), 7.39 – 7.33 (m, 5H), 7.26 (d, *J* = 5.4 Hz, 2H), 7.17 (d, *J* = 14.2 Hz, 2H) ppm. **^{13}C NMR** (101

MHz, $CDCl_3$) δ 158.7(C=O, C1), 153.1(C_q, C14), 150.3(C_q, C12), 141.9(C_q, C27), 140.8(C_q, C10), 139.7(C_q, C15), 136.7(C_q, C21), 134.0 (CH, C7), 132.8(CH, C4), 130.4(CH, C6), 129.6 (CH, C9), 129.2(C_q, C17, C18, C19), 128.9(CH, C29, C31), 128.7(CH, C28, C32), 128.5(C_q, C8), 128.3(CH, C25), 128.3(CH, C30), 128.2(C_q, C11), 127.9(CH, C16, C20), 127.6(CH, C24), 126.5 (C_q, C22), 126.2(CH, C23), 125.4(CH, C26), 119.0(C_q, C13) ppm; **HRMS**(ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{29}H_{19}ClN_3O$, calculated 460.1211, found 460.1281. $[\alpha]_D^{20}$ = -27 (Concentration 0.5, $CHCl_3$).



(*E*)-8-Chloro-2-(3-(2-(1-oxo-10-phenylpyridazino[4,5-*b*]quinolin-2(1*H*)-yl)phenyl)allyl)-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (10b): pale yellow solid 71% yield, melting point 244-246 °C, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.41 – 8.40 (m, 1H), 8.26 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 8.6 Hz, 1H), 7.79 (s, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.47 (t, *J* = 17.6 Hz, 9H), 7.38 (s, 3H), 7.22 (s, 2H), 7.15 (s, 4H), 6.29 (t, *J* = 19.2 Hz, 1H), 4.65 (s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.0 (C=O, C1, C30), 150.8(C_q, C14, C40), 145.8(C_q, C12), 140.7(C_q, C38), 140.0(C_q, C10), 139.7(C_q, C36), 136.4(C_q, C15, C41), 136.0(C_q, C21), 134.6(CH, C33), 134.1(CH, C4, C31), 133.7(CH, C7), 132.6(CH, C25, –CH=, C28), 131.5(CH, C32), 129.9(C–CH=, C27), 129.5(CH, C17, C18, C19, C43, C44, C45), 129.1(CH, C23, C6), 129.0(C_q, C39), 128.6(C_q, C34), 128.6(CH, C8), 128.4(CH, C16, C20, C42, C46), 128.2(CH, C9, C26), 128.1(C_q, C11), 127.2(CH, C35), 126.8(CH, C24), 126.4(C_q, C13, C37), 29.8(CH_2, C29) ppm. **HRMS** (ESI/Q-TOF) m/z: $[M+H]^+$**:** Chemical formula $C_{43}H_{28}ClN_6O_2$, calculated 695.1957, found 695.1959. $[\alpha]_D^{20}$ = -26 (Concentration 0.5, $CHCl_3$).

2.5)Removal of the Directing group (C–N bond cleavage)

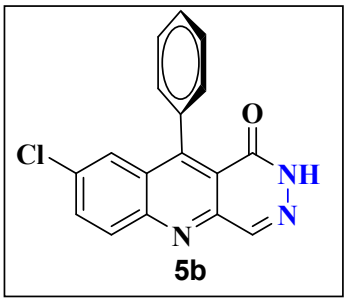


9b, 0.15 mmol

5b, 47%

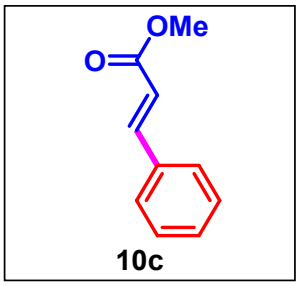
10c, 41%

In an oven dried reaction vial **9b** (0.15 mmol, 70mg) is dissolved in 3 mL of acetonitrile, followed by the addition of PIDA (1.5 equiv, 0.225 mmol, 73 mg) the mixture is stirred at 50 °C for 2h. The completion of reaction in monitored by TLC, then excesses of solvent is reduced under pressure. The reaction mixture was washed with water 10 mL and ethyl acetate (15 mL x 2) the combined organic layer was passed over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resultant crude was purified by column chromatography to pure compound.



5b

8-chloro-10-phenylpyridazino[4,5-*b*]quinolin-1(2*H*)-one (5b), yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.49 (s, 1H), 8.26 (d, J = 9.1 Hz, 1H), 7.87 (dd, J = 9.1, 2.2 Hz, 1H), 7.63 (d, J = 2.1 Hz, 1H), 7.59 (d, J = 2.5 Hz, 3H), 7.30 (d, J = 3.5 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, CDCl3) δ 159.5(C=O, C1), 151.7(C_q, C14), 149.3(C_q, C12), 146.4(C_q, C10), 141.3(C_q, C15), 135.5(CH, C4), 134.9(CH, C7), 134.0(CH, C17, C18, C19), 131.6(CH, C6), 129.5(C_q, C8), 128.8(CH, C9), 128.4(CH, C16), 128.3(CH, C20), 126.5(C_q, C11), 118.9(C_q, C13) ppm.



methyl cinnamate (10c), pale yellow liquid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 16.0 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.43 – 7.35 (m, 3H), 6.51 – 6.30 (m, 1H), 3.81 (d, *J* = 3.3 Hz, 3H) ppm. **^{13}C NMR** (125 MHz, CDCl3) δ 167.3(–O–C=O), 144.8(–CH=), 134.4(C_q), 130.3(C_q), 128.9(C_q), 128.1(C_q), 117.8(–CH=), 51.8(CH_3) ppm.

3) MECHANISTIC STUDIES

3.1) H/D studies

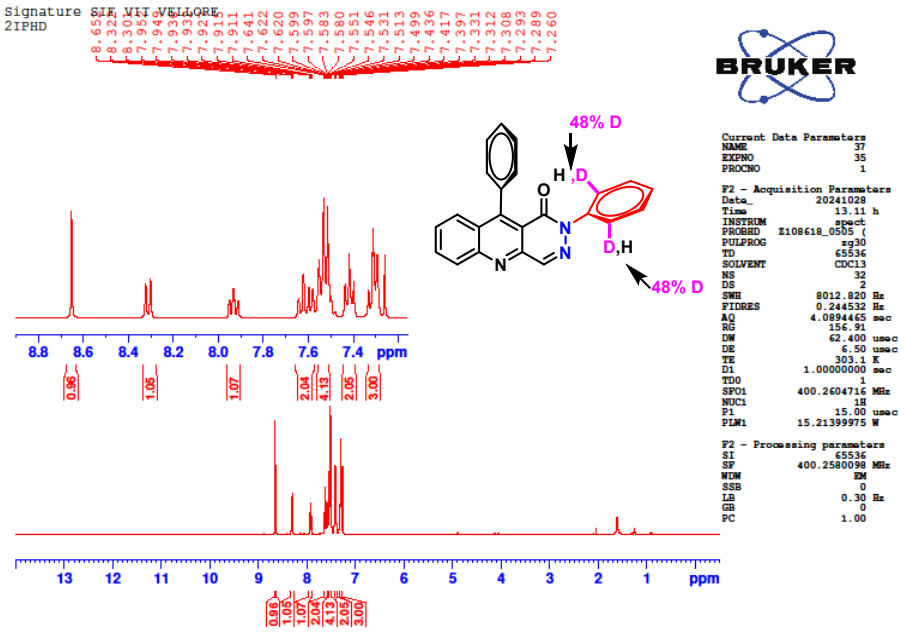


Figure S6: H/D studies

3.2) Identified HR-MS

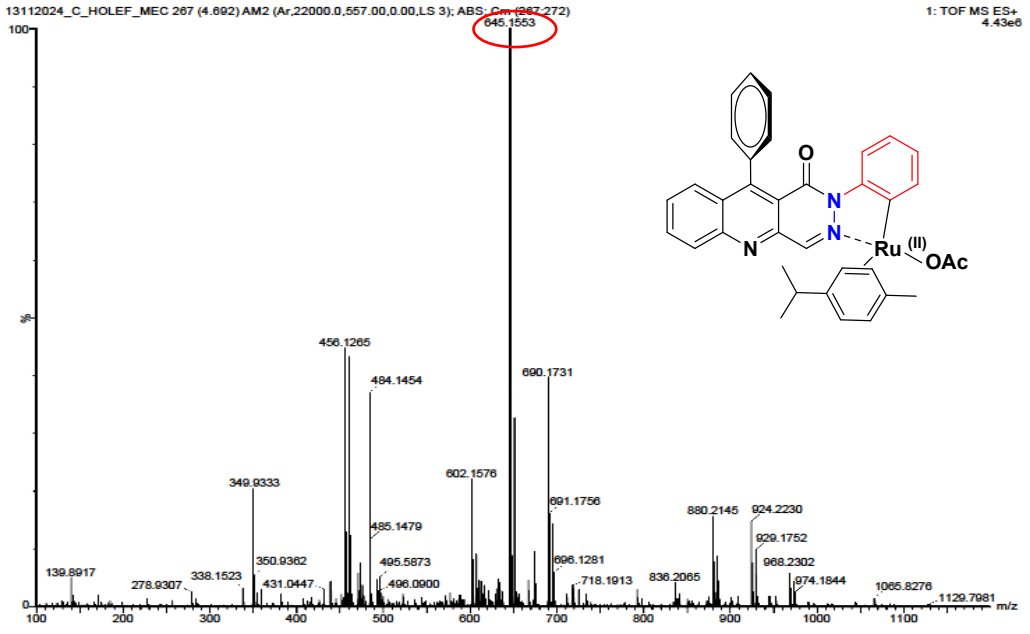


Figure S7: HR-MS for complex-1

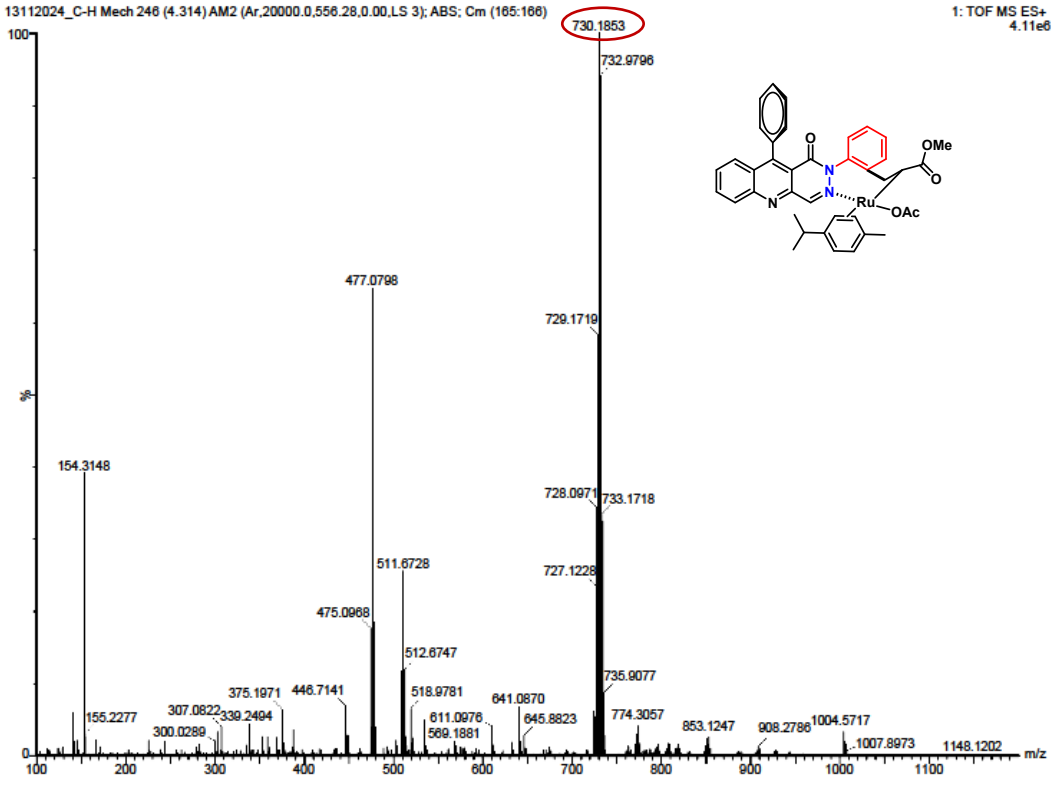


Figure S8: HR-MS for complex-2

3.3) Reaction process overtime

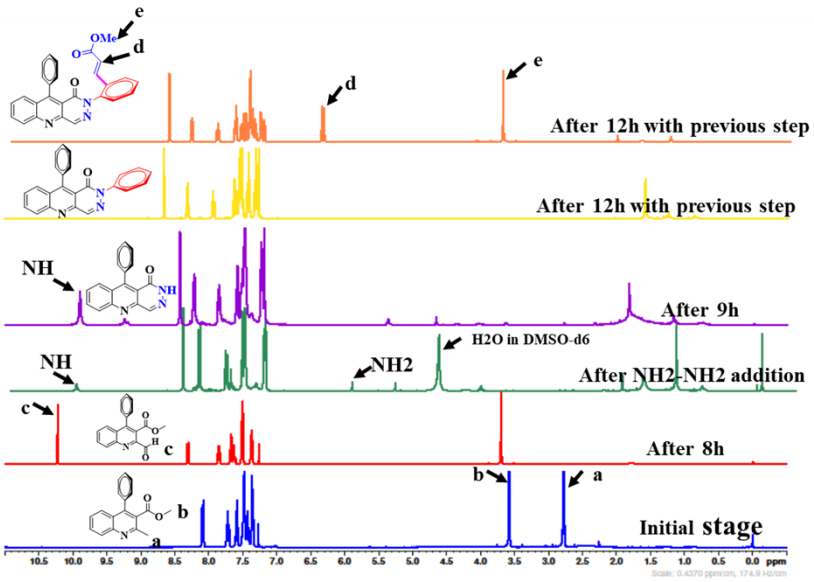


Figure S9: Reaction process overtime

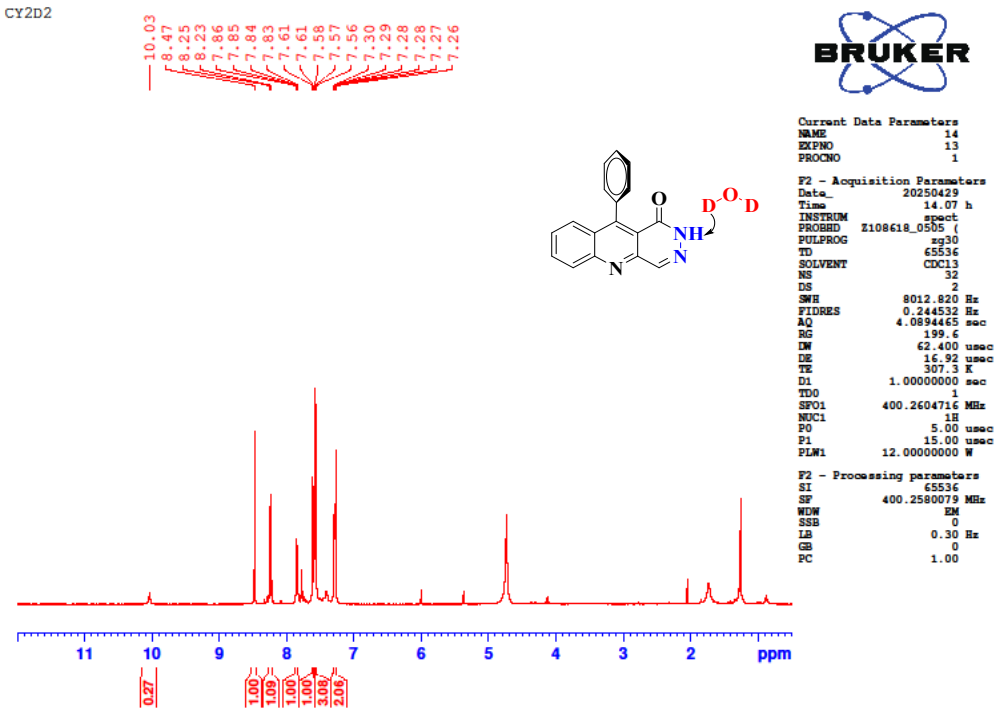
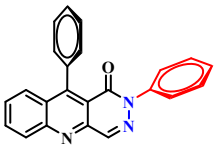
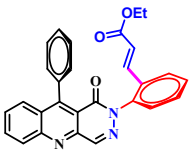


Figure S10: NH population decreases while adding D_2O

3.4) Specific Optical Rotation





Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-14.000	13.4164	10.000	-20.000

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE II	05:26:27 PM	-20.00	SR	-0.02	589	100.00	24.8
2	SAMPLE II	05:26:37 PM	10.00	SR	0.01	589	100.00	24.8
3	SAMPLE II	05:26:48 PM	-20.00	SR	-0.02	589	100.00	24.8
4	SAMPLE II	05:26:59 PM	-20.00	SR	-0.02	589	100.00	24.8
5	SAMPLE II	05:27:10 PM	-20.00	SR	-0.02	589	100.00	24.9

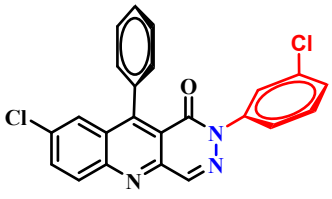
Figure S11: SOR for 8a

Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-20.000	0.0000	-20.000	-20.000

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-9	05:33:57 PM	-20.00	SR	-0.02	589	100.00	25.1
2	SAMPLE-9	05:34:09 PM	-20.00	SR	-0.02	589	100.00	25.0
3	SAMPLE-9	05:34:20 PM	-20.00	SR	-0.02	589	100.00	25.0
4	SAMPLE-9	05:34:32 PM	-20.00	SR	-0.02	589	100.00	25.0
5	SAMPLE-9	05:34:44 PM	-20.00	SR	-0.02	589	100.00	25.0

Figure S12: SOR for 9a

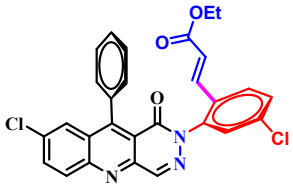


Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-28.889	6.0857	-22.222	-33.333

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-5	05:17:44 PM	-33.33	SR	-0.03	589	100.00	25.1
2	SAMPLE-5	05:17:56 PM	-33.33	SR	-0.03	589	100.00	25.1
3	SAMPLE-5	05:18:08 PM	-22.22	SR	-0.02	589	100.00	25.1
4	SAMPLE-5	05:18:20 PM	-33.33	SR	-0.03	589	100.00	25.0
5	SAMPLE-5	05:18:33 PM	-22.22	SR	-0.02	589	100.00	25.0

Figure S13: SOR for 8g

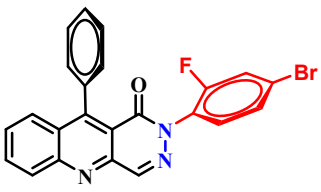


Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-42.857	10.1017	-28.571	-57.143

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-7	05:28:25 PM	-28.57	SR	-0.02	589	100.00	24.9
2	SAMPLE-7	05:28:37 PM	-57.14	SR	-0.04	589	100.00	24.9
3	SAMPLE-7	05:28:49 PM	-42.86	SR	-0.03	589	100.00	24.9
4	SAMPLE-7	05:29:01 PM	-42.86	SR	-0.03	589	100.00	24.9
5	SAMPLE-7	05:29:13 PM	-42.86	SR	-0.03	589	100.00	24.9

Figure S14: SOR for 9f

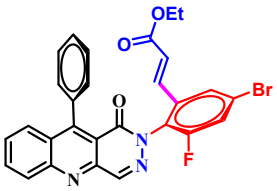


Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-10.000	0.0000	-10.000	-10.000

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-3	04:54:59 PM	-10.00	SR	-0.02	589	100.00	25.0
2	SAMPLE-3	04:55:11 PM	-10.00	SR	-0.02	589	100.00	25.0
3	SAMPLE-3	04:55:24 PM	-10.00	SR	-0.02	589	100.00	25.0
4	SAMPLE-3	04:55:35 PM	-10.00	SR	-0.02	589	100.00	25.0
5	SAMPLE-3	04:55:47 PM	-10.00	SR	-0.02	589	100.00	25.0

Figure S15: SOR for 8k

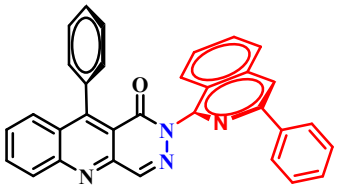


Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-57.143	0.0000	-57.143	-57.143

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-8	05:23:35 PM	-57.14	SR	-0.02	589	100.00	25.1
2	SAMPLE-8	05:23:47 PM	-57.14	SR	-0.02	589	100.00	25.1
3	SAMPLE-8	05:23:59 PM	-57.14	SR	-0.02	589	100.00	25.1
4	SAMPLE-8	05:24:11 PM	-57.14	SR	-0.02	589	100.00	25.1
5	SAMPLE-8	05:24:22 PM	-57.14	SR	-0.02	589	100.00	25.1

Figure S16: SOR for 9g

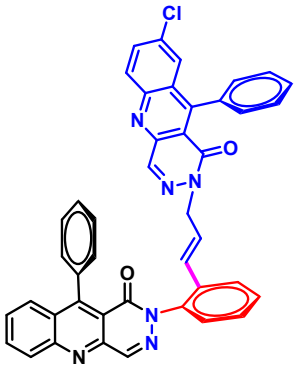


Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-55.000	11.1803	-50.000	-75.000

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-4	05:11:50 PM	-75.00	SR	-0.03	589	100.00	25.1
2	SAMPLE-4	05:12:02 PM	-50.00	SR	-0.02	589	100.00	25.1
3	SAMPLE-4	05:12:14 PM	-50.00	SR	-0.02	589	100.00	25.0
4	SAMPLE-4	05:12:26 PM	-50.00	SR	-0.02	589	100.00	25.1
5	SAMPLE-4	05:12:38 PM	-50.00	SR	-0.02	589	100.00	25.0

Figure S17: SOR for 8t



Set Temperature [TempTrol] : 25.0
Temperature Correction : OFF

n	Average	Std.Dev.	Maximum	Minimum
5	-25.714	6.3884	-14.286	-28.571

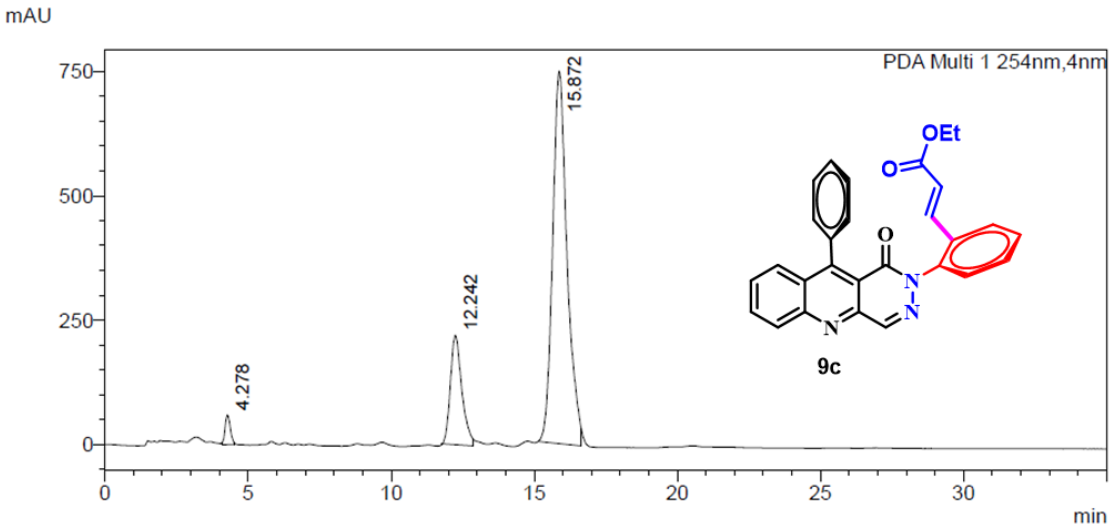
S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG	Lg.mm	Temp.
1	SAMPLE-11	05:43:47 PM	-28.57	SR	-0.02	589	100.00	25.0
2	SAMPLE-11	05:43:59 PM	-28.57	SR	-0.02	589	100.00	25.0
3	SAMPLE-11	05:44:11 PM	-14.29	SR	-0.01	589	100.00	25.0
4	SAMPLE-11	05:44:23 PM	-28.57	SR	-0.02	589	100.00	24.9
5	SAMPLE-11	05:44:34 PM	-28.57	SR	-0.02	589	100.00	25.0

Figure S18: SOR for 10b

4) HPLC ANALAYIS

Initially, to identify the enantiomers of the system, we performed HPLC analysis using a C18 column for preliminary separation. Based on these results, further analyses were carried out using chiral columns (Daicel Chiralpak and Cellulose-3) to achieve enantioresolution and determine the enantiomeric composition.

Atropisomeric nature was determined with **HPLC** using a C18 column with a mobile phase of MeOH/H_2O = 80:20, flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 15.872 min.



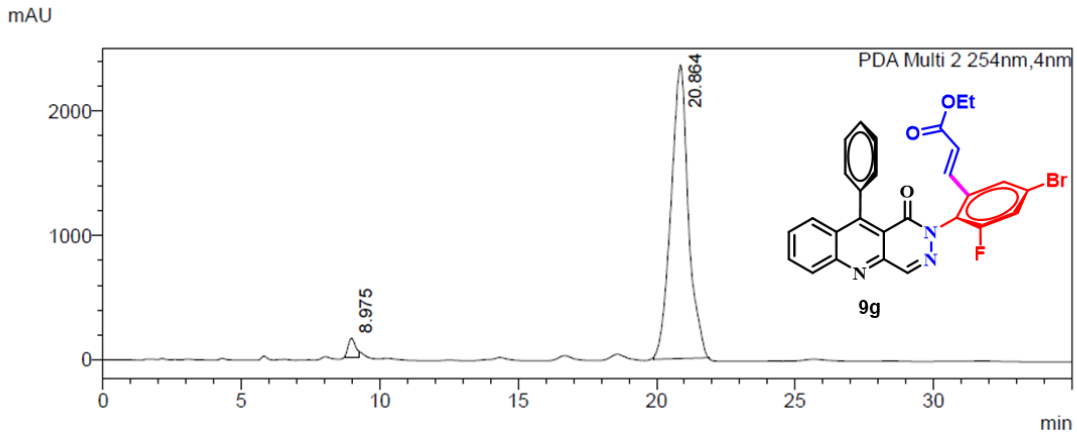
<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Conc.	Peak Start	Peak End	Area%
1	4.278	754074	59556	2.279	4.107	4.512	2.279
2	12.242	6107344	219618	18.460	11.755	12.864	18.460
3	15.872	26223676	748032	79.261	15.157	16.640	79.261
Total		33085094	1027207				100.000

Height%	Area/Height
5.798	12.662
21.380	27.809
72.822	35.057
100.000	

Atropisomeric nature was determined with **HPLC** using a C18 column with a mobile phase of MeOH/H_2O = 80:20, flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 20.864 min.

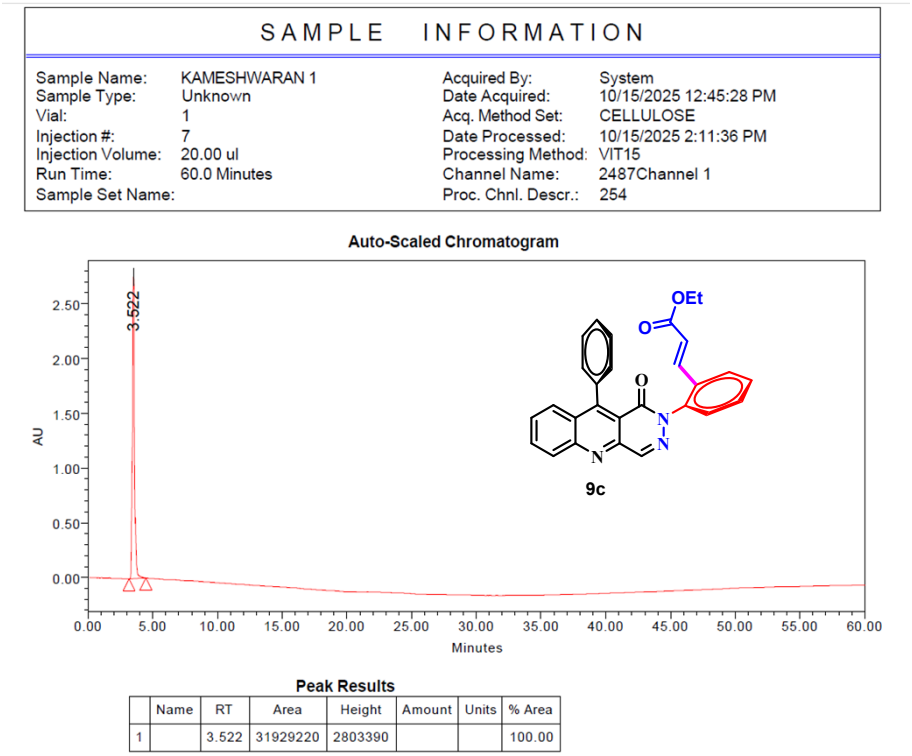


<Peak Table>

PDA Ch1 254nm

Ret. Time	Area	Height	Conc.	Name	Area%
8.975	3860333	160283	3.559		3.559
20.864	104612097	2372735	96.441		96.441
	108472430	2533017			100.000

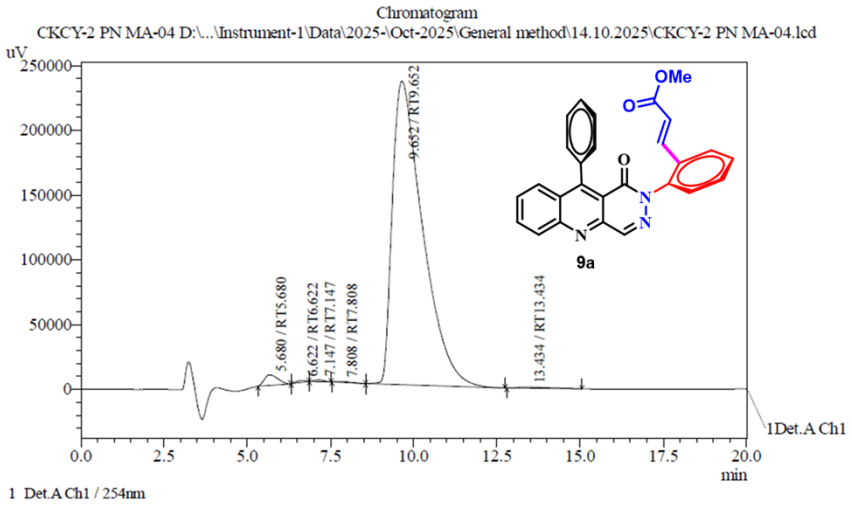
Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (cellulose-3) column with a mobile phase of acetonitrile/isopropanol (80:20), flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 3.522 min.



Peak Results

	Name	RT	Area	Height	Amount	Units	% Area
1		3.522	31929220	2803390			100.00

Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.652 min.

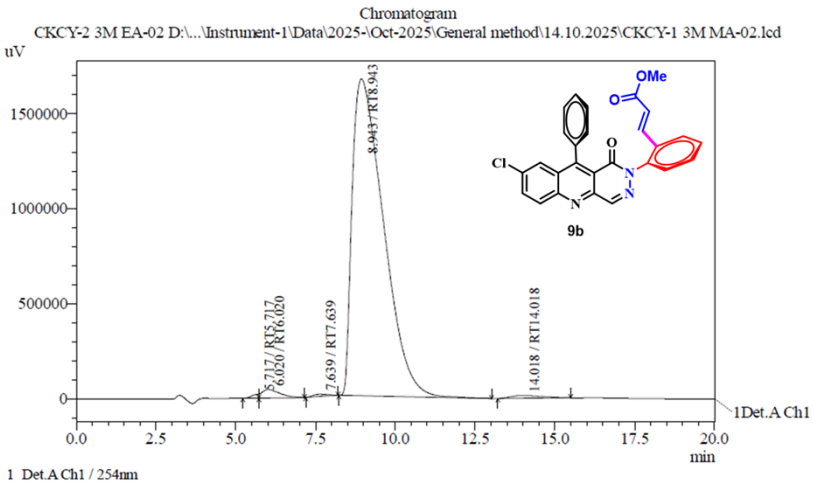


1 Det.A Ch1 / 254nm

PeakTable
Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	RT5.680	5.680	227939	8170	1.495
2	RT6.622	6.622	27074	1485	0.178
3	RT7.147	7.147	23464	1213	0.154
4	RT7.808	7.808	20840	695	0.137
5	RT9.652	9.652	14874510	234591	97.547
	RT13.434	13.434	74757	1078	0.490
Total			15248584	247232	100.000

Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 8.943 min.

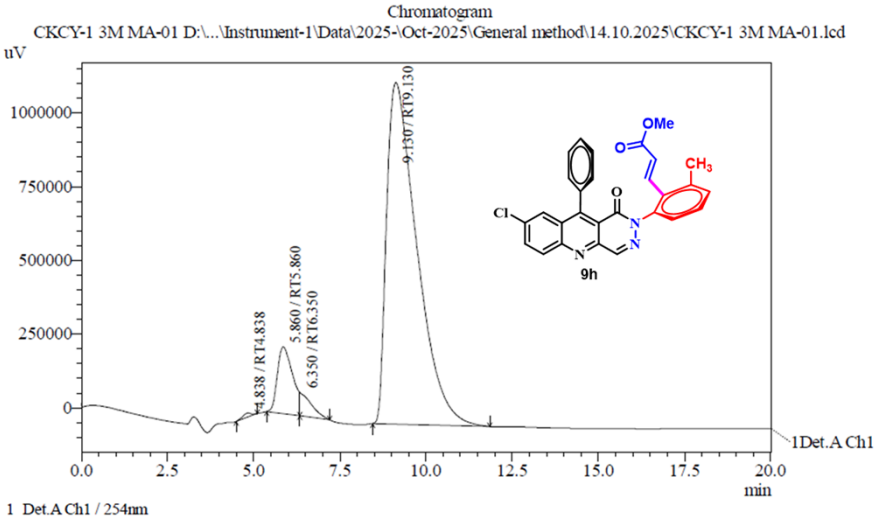


1 Det.A Ch1 / 254nm

PeakTable
Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	RT5.717	5.717	273835	20014	0.234
2	RT6.020	6.020	1723444	44490	1.472
3	RT7.639	7.639	371547	12073	0.317
4	RT8.943	8.943	113696635	1665962	97.138
	RT14.018	14.018	980956	14550	0.838
Total			117046417	1757088	100.000

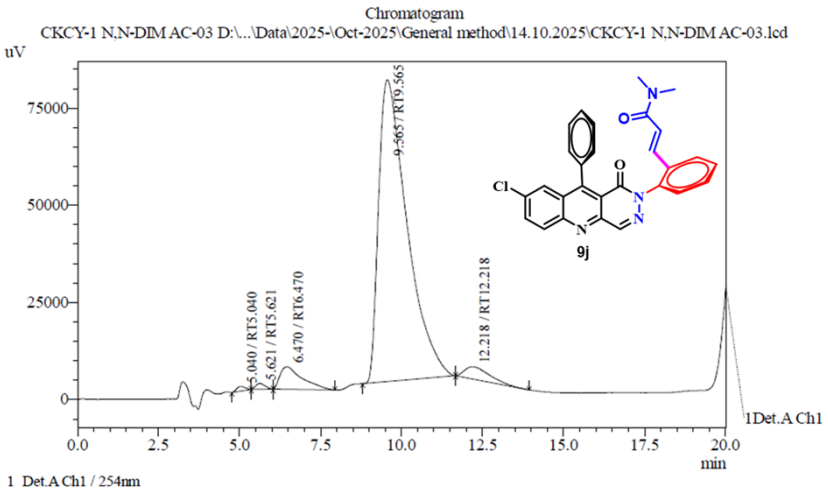
Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.130 min.



PeakTable
Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	RT4.838	4.838	243624	13315	0.305
2	RT5.860	5.860	7029328	226524	8.790
3	RT6.350	6.350	1839362	79071	2.300
4	RT9.130	9.130	70854602	1159351	88.605
Total			79966916	1478261	100.000

Atropisomeric nature was determined with **HPLC** using a Chiralcel OD-H (Diacel Chiral IA, 250 X 4.6 mm, 5) column with a mobile phase A: Hexane/IPA: 80/20 v/v; flow rate = 1.0 mL/min, detection at λ = 254 nm; *t* (major) = 9.565 min.

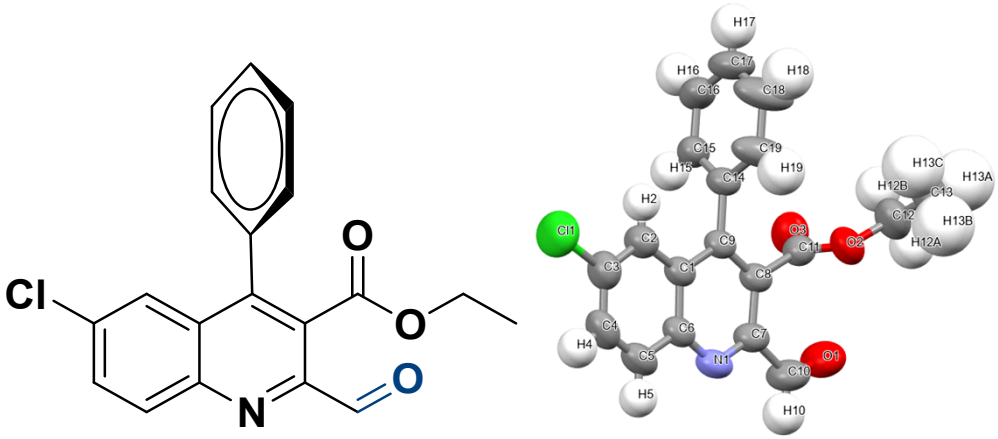


PeakTable
Detector A Ch1 254nm

Peak#	Name	Ret. Time	Area	Height	Area %
1	RT5.040	5.040	21977	1174	0.418
2	RT5.621	5.621	30330	1505	0.577
3	RT6.470	6.470	278635	5809	5.301
4	RT9.565	9.565	4749446	77646	90.359
	RT12.218	12.218	175826	3219	3.345
Total			5256214	89353	100.000

The compounds exhibit chirality in solution, as evidenced by their specific optical rotations and chiral HPLC analyses. However, single-crystal X-ray diffraction (SC-XRD) studies reveal that both crystallize as racemates in centrosymmetric space groups ($P2_1/n$ and C2/c), consistent with their achiral solid-state nature. The crystal packing is stabilized through multiple weak intermolecular interactions, including hydrogen bonding and π–π stacking between the quinoline rings. Representative partial packing diagrams illustrating these racemic arrangements are shown in the accompanying figures.

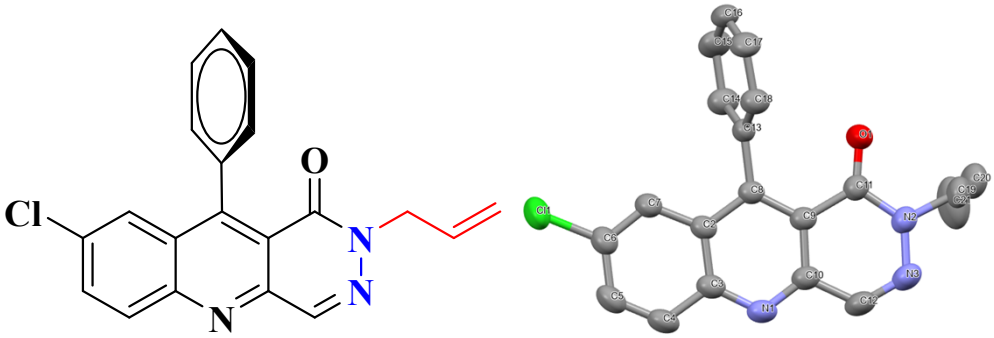
5) X- RAY CRYSTAL STRUCTURES



The crystal was obtained through slow evaporation of CH_2Cl_2 solution at room temperature (r.t). The structure of was then determined by X-ray crystallography (**4d**, **CCDC No: 2289141**)

Identification code	work_CKHA	
Chemical formula	$C_{19}H_{14}ClNO_3$	
Formula weight	339.76 g/mol	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 12.782(19) Å	α = 90°
	b = 15.878(18) Å	β = 93.91(5)°
	c = 8.643(11) Å	γ = 90°
Volume	1750.(4) $Å^3$	

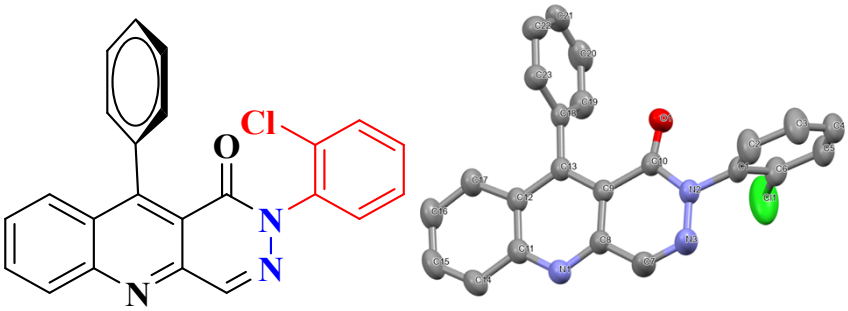
Z	4
Density (calculated)	1.290 g/cm^3
Absorption coefficient	0.234 mm^{-1}
F(000)	704



The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**6b, CCDC No: 2381375**)

Identification code	2B_140824_0m_a
Empirical formula	$C_{20}H_{14}ClN_3O$
Formula weight	347.806
Temperature/K	300.00
Crystal system	triclinic
Space group	P-1
a/Å	9.7967(16)
b/Å	9.9850(17)
c/Å	10.4267(18)
α/°	100.814(5)
β/°	104.185(5)
γ/°	117.719(5)
Volume/Å^3	819.5(3)
Z	2
ρ_{calc}g/cm^3	1.409
μ/mm^{-1}	0.246
F(000)	360.5

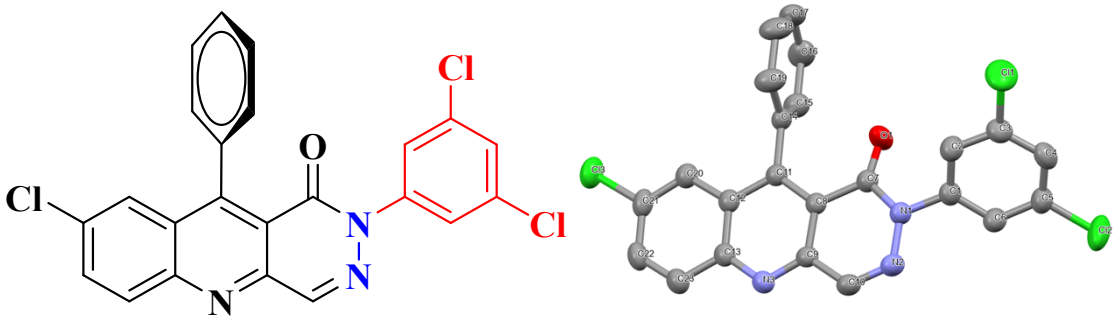
Crystal size/mm^3	0.27 × 0.183 × 0.104
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.3 to 56.5
Index ranges	-12 ≤ h ≤ 13, -13 ≤ k ≤ 13, -13 ≤ l ≤ 13
Reflections collected	20366
Independent reflections	4054 [R_{int} = 0.0418, R_{sigma} = 0.0389]
Data/restraints/parameters	4054/0/226
Goodness-of-fit on F^2	1.015
Final R indexes [I>=2σ (I)]	R_1 = 0.0551, wR_2 = 0.2081
Final R indexes [all data]	R_1 = 0.0960, wR_2 = 0.2818
Largest diff. peak/hole / e Å^{-3}	0.38/-0.61



The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**8c, CCDC No: 2387930**)

Identification code	NH2CL	
Chemical formula	$C_{23}H_{14}ClN_3O$	
Formula weight	383.82 g/mol	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal size	0.122 x 0.141 x 0.273 mm	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 14.9493(11) Å	α = 90°
	b = 7.5272(6) Å	β = 92.674(3)°
	c = 16.2680(12) Å	γ = 90°

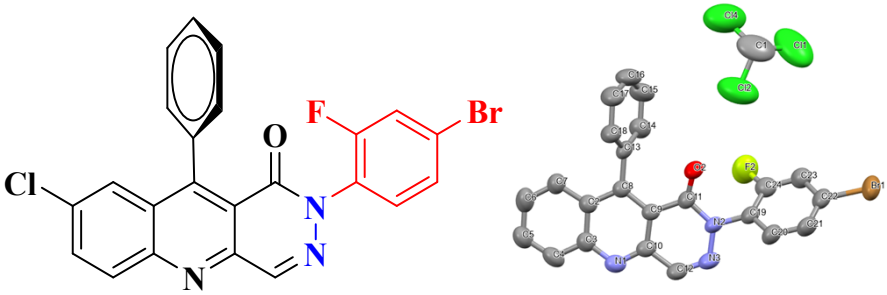
Volume	1828.6(2) Å^3
Z	4
Density (calculated)	1.394 g/cm^3
Absorption coefficient	0.228 mm^{-1}
F(000)	792



The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**8f, CCDC No: 2376044)**

Identification code	CKCY_1_270724_0m_a
Empirical formula	$C_{23}H_{12}Cl_3N_3O$
Formula weight	452.71
Temperature/K	300.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.925(3)
b/Å	11.551(3)
c/Å	14.849(4)
α/°	90
β/°	97.201(8)
γ/°	90
Volume/Å^3	2029.3(10)
Z	4
ρ_{calc}g/cm^3	1.482

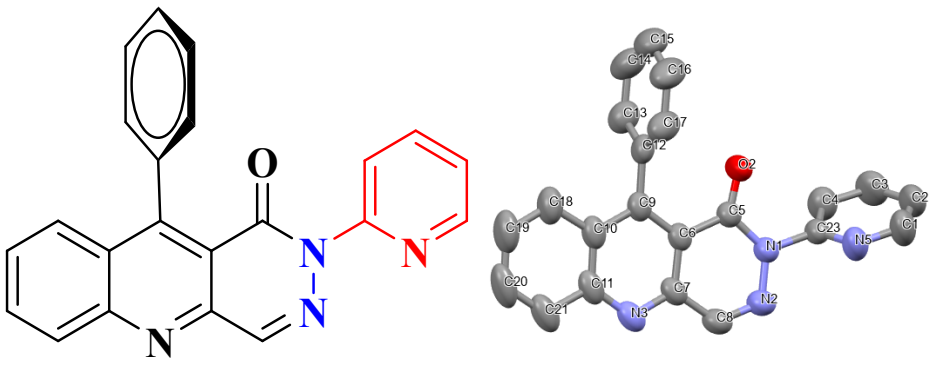
μ/mm^{-1}	0.473
F(000)	920.0
Crystal size/mm^3	0.252 × 0.207 × 0.179
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.136 to 56.554
Index ranges	-15 ≤ h ≤ 15, -15 ≤ k ≤ 15, -19 ≤ l ≤ 19
Reflections collected	38870
Independent reflections	5008 [R_{int} = 0.0389, R_{sigma} = 0.0275]
Data/restraints/parameters	5008/0/271
Goodness-of-fit on F^2	1.132
Final R indexes [I>=2σ (I)]	R_1 = 0.0587, wR_2 = 0.1626
Final R indexes [all data]	R_1 = 0.0730, wR_2 = 0.1756
Largest diff. peak/hole / e Å^{-3}	0.75/-0.78



The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**8k, CCDC No: 2388359)**

Identification code	CKCY_2_270724_0m_a
Empirical formula	$C_{24}H_{14}BrCl_3FN_3O$
Formula weight	565.64
Temperature/K	300.00
Crystal system	triclinic
Space group	P-1
a/Å	9.9616(9)
b/Å	10.8396(10)
c/Å	11.1734(10)

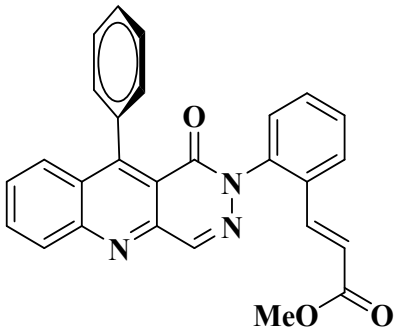
α/°	92.854(4)
β/°	99.122(4)
γ/°	92.843(4)
Volume/Å^3	1187.74(19)
Z	2
ρ_{calc}g/cm^3	1.582
μ/mm^{-1}	2.098
F(000)	564.0
Crystal size/mm^3	0.35 × 0.21 × 0.062
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.698 to 54.36
Index ranges	-12 ≤ h ≤ 12, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14
Reflections collected	31645
Independent reflections	5289 [R_{int} = 0.0790, R_{sigma} = 0.0767]
Data/restraints/parameters	5289/62/382
Goodness-of-fit on F^2	1.001
Final R indexes [I>=2σ (I)]	R_1 = 0.0552, wR_2 = 0.1247
Final R indexes [all data]	R_1 = 0.1407, wR_2 = 0.1530
Largest diff. peak/hole / e Å^{-3}	0.34/-0.64

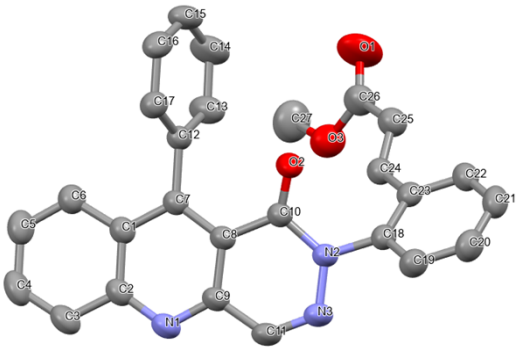


The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**8r, CCDC No: 2421395)**

Identification code	work_HA_3_2HPYI
Chemical formula	$C_{22}H_{14}N_4O$

Formula weight	350.37 g/mol	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal size	0.134 x 0.186 x 0.237 mm	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 13.3290(6) Å	α = 90°
	b = 6.8873(3) Å	β = 100.513(2)°
	c = 19.3643(9) Å	γ = 90°
Volume	1747.82(14) $Å^3$	
Z	4	
Density (calculated)	1.332 g/cm^3	
Absorption coefficient	0.085 mm^{-1}	
F(000)	728	

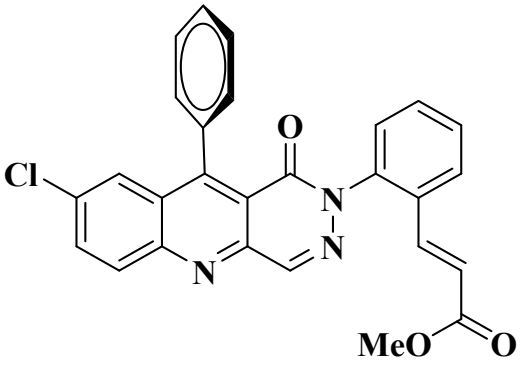


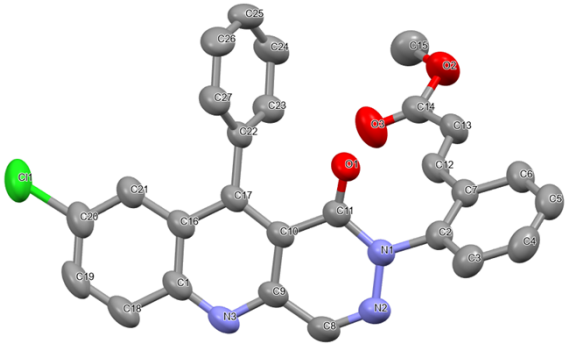


The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**9a, CCDC No: 2402442)**

Identification code	work_CY_2_Phma
Chemical formula	$C_{27}H_{19}N_3O_3$
Formula weight	433.45 g/mol
Temperature	300(2) K
Wavelength	0.71073 Å
Crystal size	0.135 x 0.192 x 0.291 mm
Crystal system	monoclinic

Space group	P 1 21/n 1	
Unit cell dimensions	a = 10.4666(6) Å	α = 90°
	b = 13.6900(8) Å	β = 100.902(2)°
	c = 14.9463(9) Å	γ = 90°
Volume	2103.0(2) $Å^3$	
Z	4	
Density (calculated)	1.369 g/cm^3	
Absorption coefficient	0.091 mm^{-1}	
F(000)	904	





The crystal was obtained through slow evaporation of CH_2Cl_2 solution at r.t. The structure of was then determined by X-ray crystallography (**9b, CCDC No: 2387931)**

Identification code	CHOL	
Chemical formula	$C_{27}H_{18}ClN_3O_3$	
Formula weight	467.89 g/mol	
Temperature	300(2) K	
Wavelength	0.71073 Å	
Crystal size	0.085 x 0.175 x 0.189 mm	
Crystal system	monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 24.6996(9) Å	α = 90°
	b = 12.4147(4) Å	β = 126.0450(10)°
	c = 18.1999(6) Å	γ = 90°

Volume	4512.4(3) $Å^3$
Z	8
Density (calculated)	1.377 g/cm^3
Absorption coefficient	0.205 mm^{-1}
F(000)	1936

6) References

1) Prameela, Soda, and Fazlur-Rahman Nawaz Khan. "Ru-Catalyzed Sequential Dehydrogenative Friedlander Reaction/sp3 C–H Activation/Knovenagel Condensation in the Regioselective Synthesis of Chimanine B Analogues." *European Journal of Organic Chemistry* 2020.19 (2020): 2888-2903.
2) Prameela, Soda, and Fazlur-Rahman Nawaz Khan. "Ir (I)-Catalyzed Synthesis of (E)-4-Benzylidenylacridines and (E)-2-Styrylquinoline-3-carboxamide through Sequential Suzuki–Miyaura Coupling, Dehydrogenative Friedländer Reaction, and sp3-C–H Activation." *European Journal of Organic Chemistry* 2020.33 (2020): 5394-5410.
3) K. Chinnagounder and F.-R. N. Khan, Visible-Light-Driven Synthesis of Pyrrolo[3,4-b]quinolin-1-one Imines Exhibiting Aggregation-Induced Enhanced Emission, *Chem. Asian J.*, **2025**, *e00770*.
4) Singh, Nisha Kumari, and Swastika Ganguly. "Synthesis, Characterization, and Biological Evaluation of New Oxadiazole Analogues: A Comprehensive Experimental and Computational Investigation." *ChemistrySelect* 10.17 (2025): e202500769.

7) Spectra Details

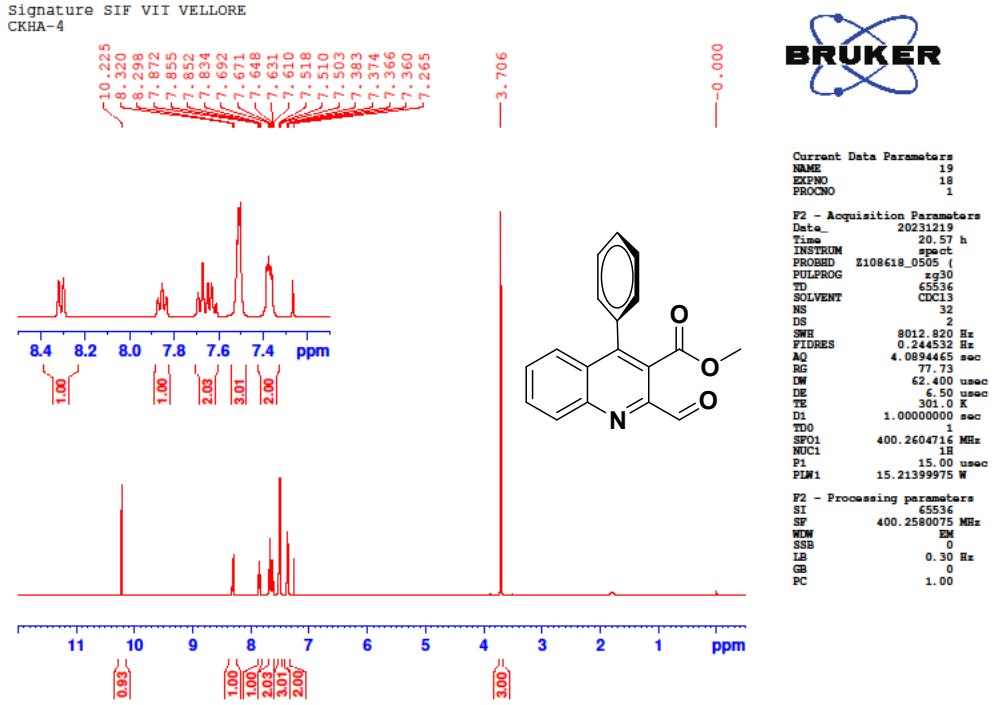


Figure S19: ^{1}H NMR of compound 4a

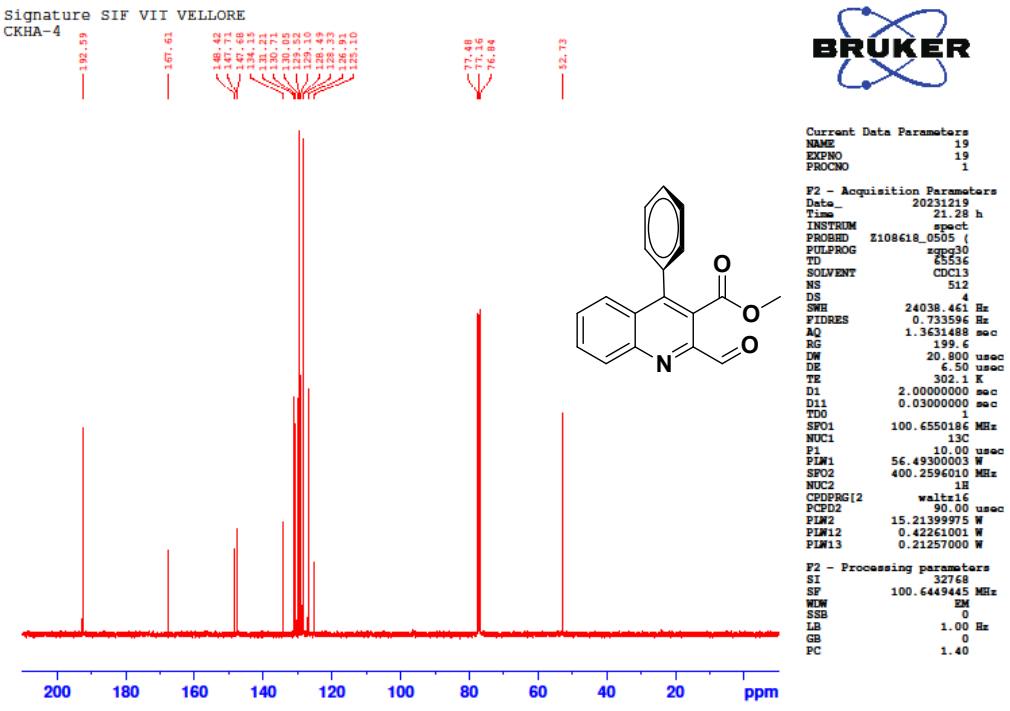


Figure S20: ^{13}C NMR of compound 4a

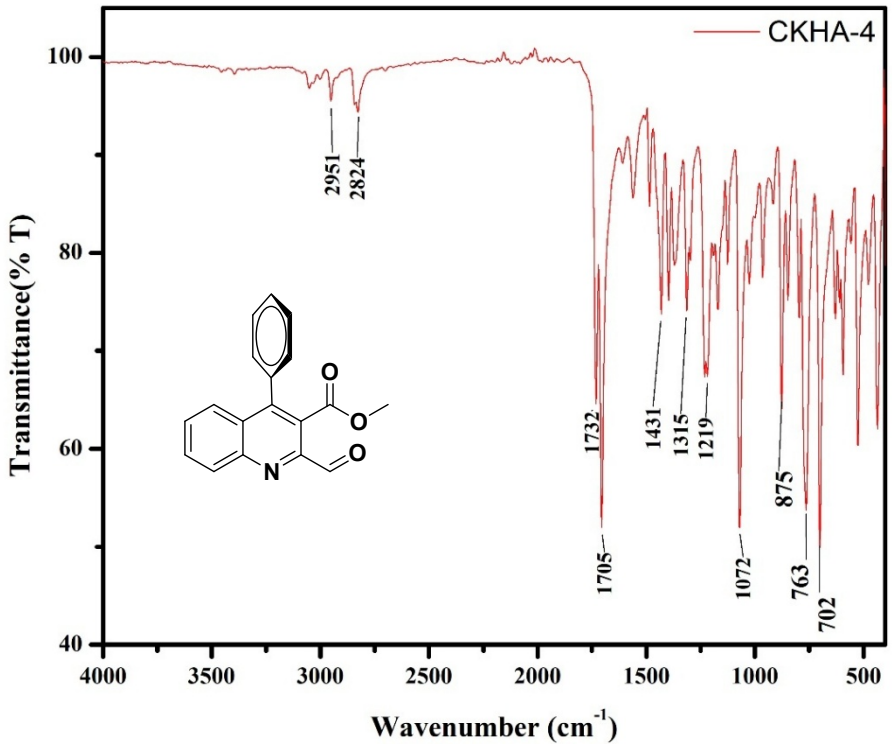


Figure S21: IR spectra of compound 4a

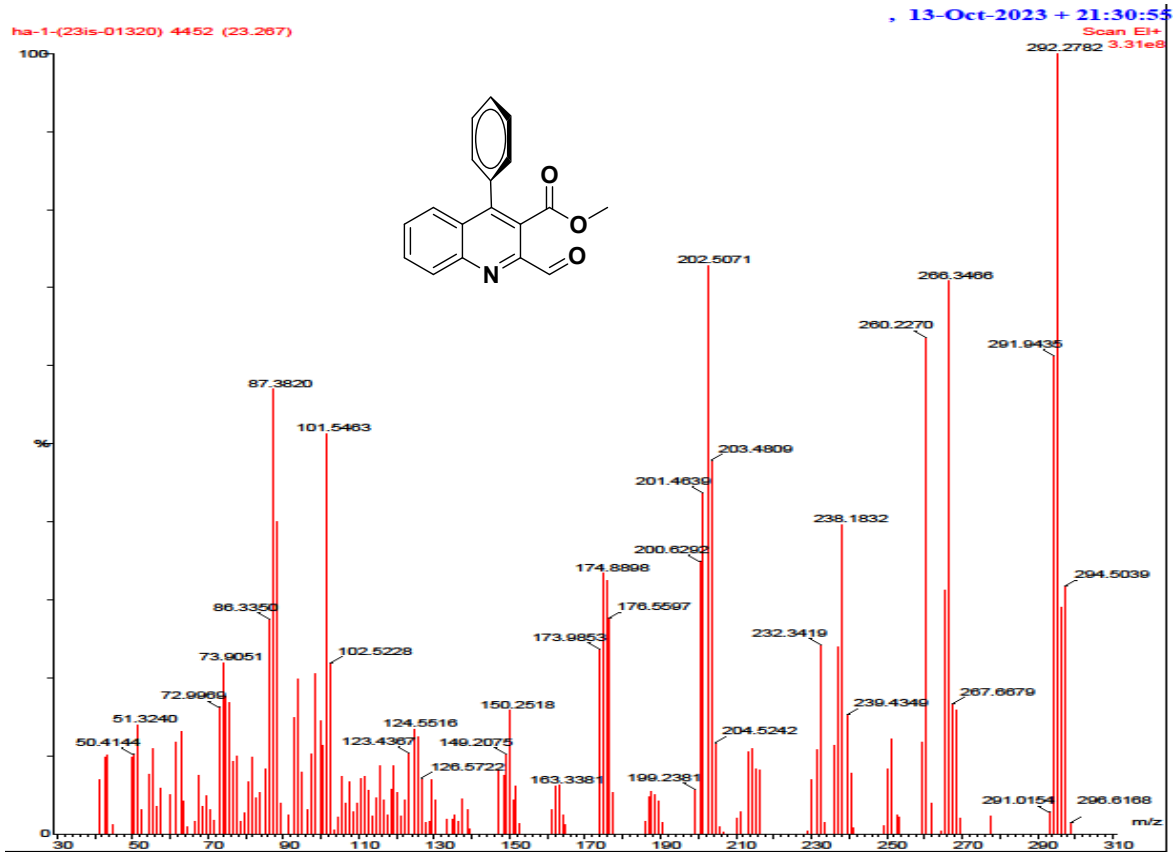


Figure S22: GC-MS spectra of compound 4a

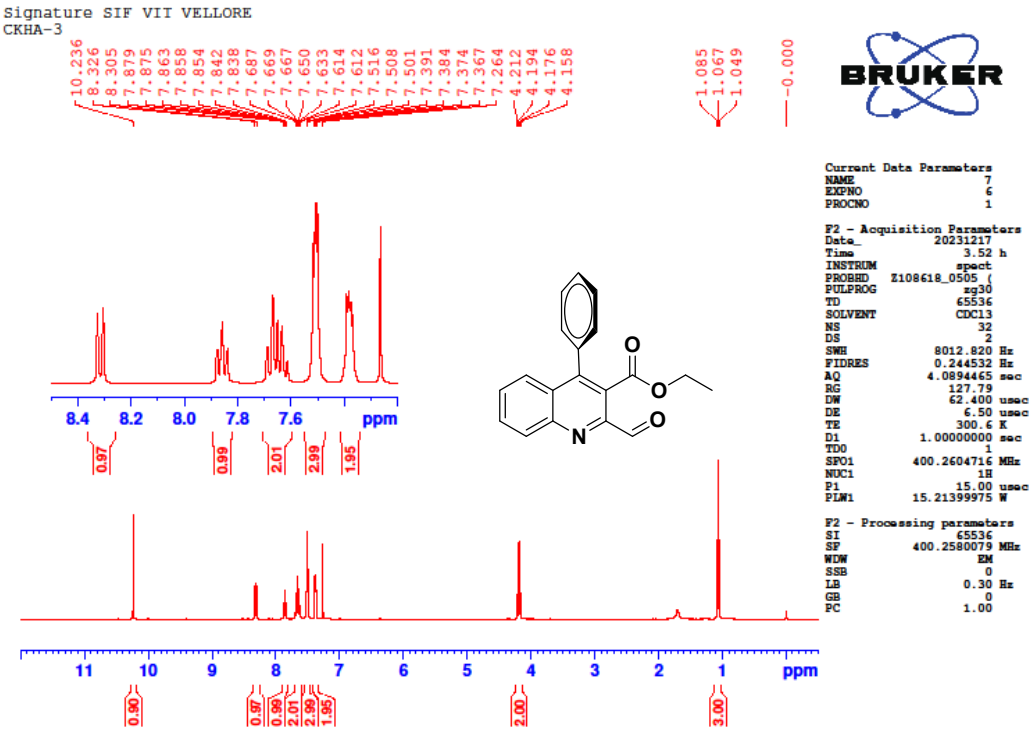


Figure S23: ^{1}H NMR of compound 4b

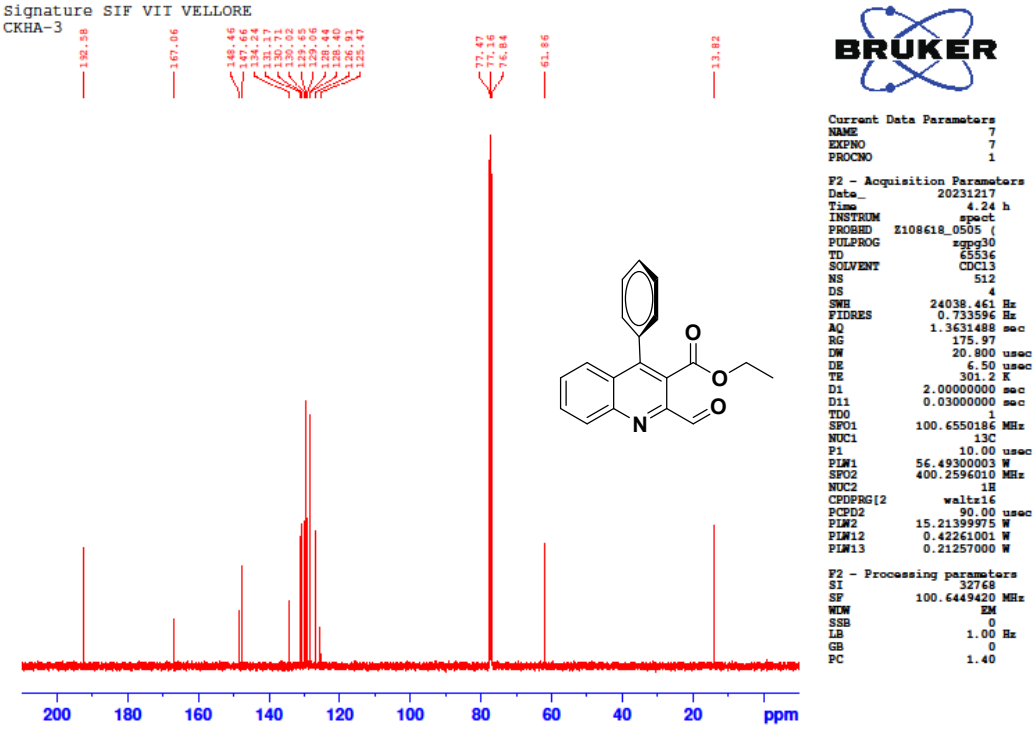


Figure S24: ^{13}C NMR of compound 4b

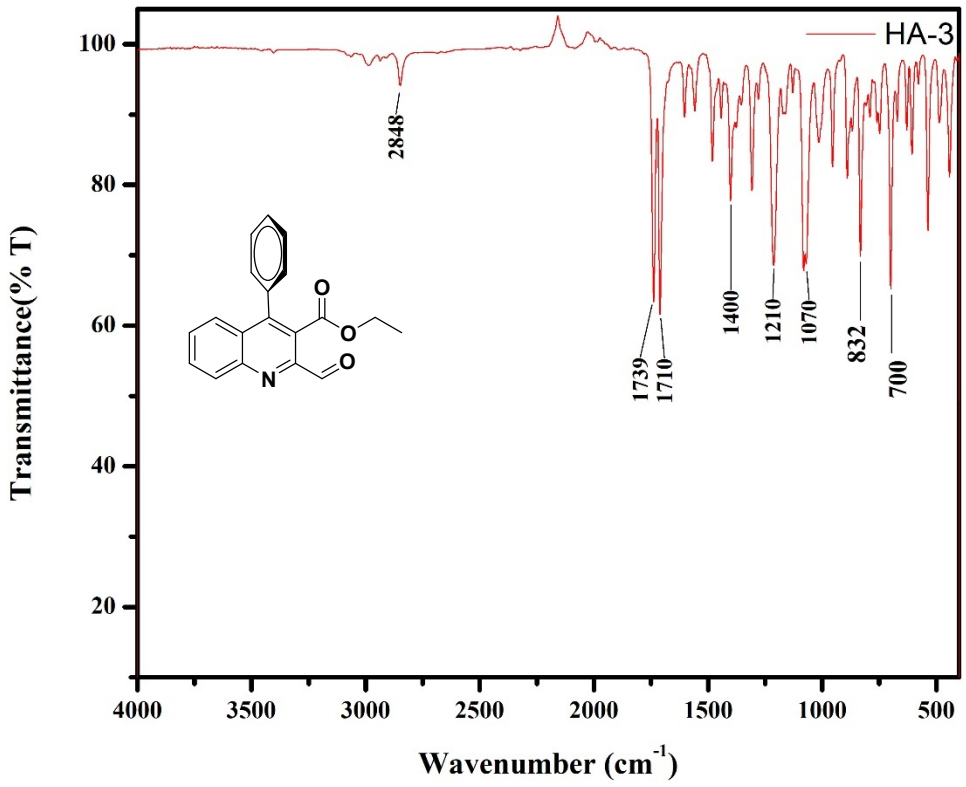


Figure S25: IR spectra of compound 4b

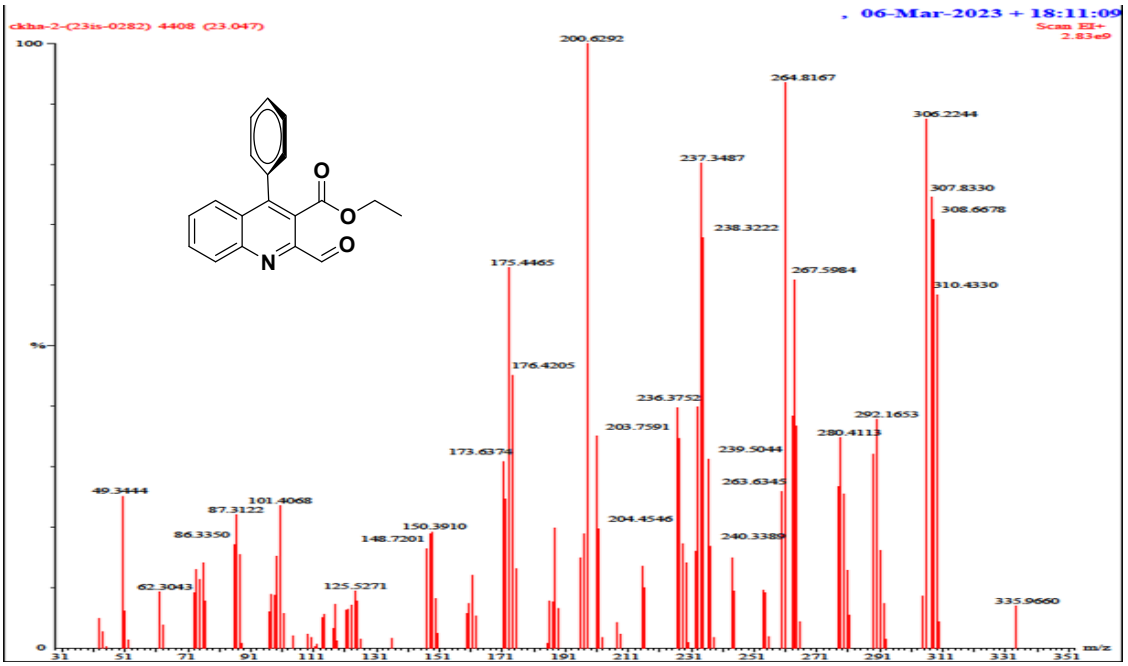


Figure S26: GC-MS spectra of compound 4b

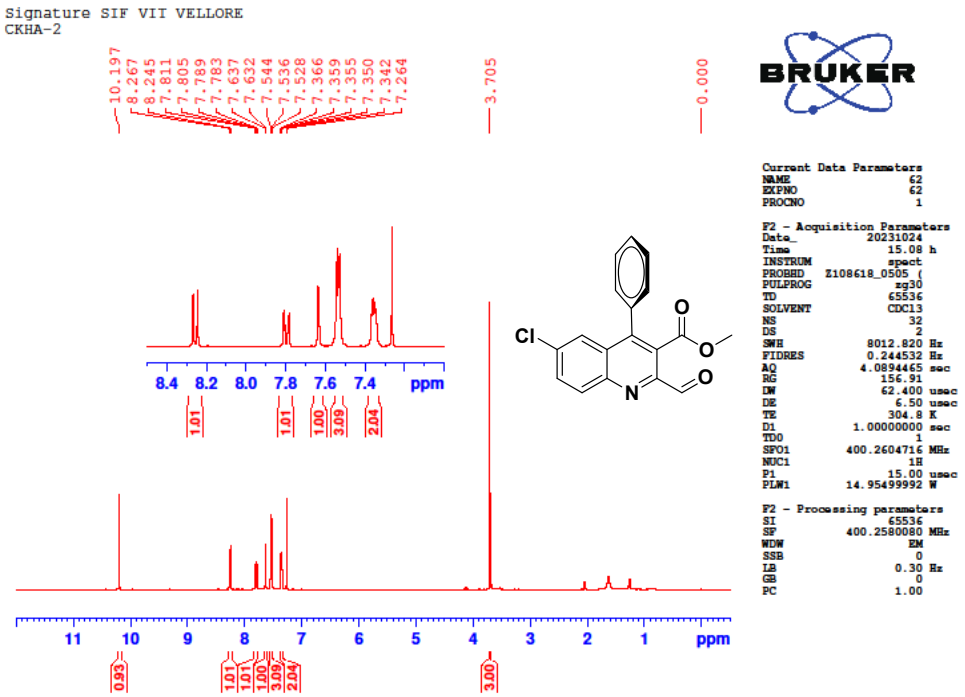


Figure S27: ^{1}H NMR of compound 4c

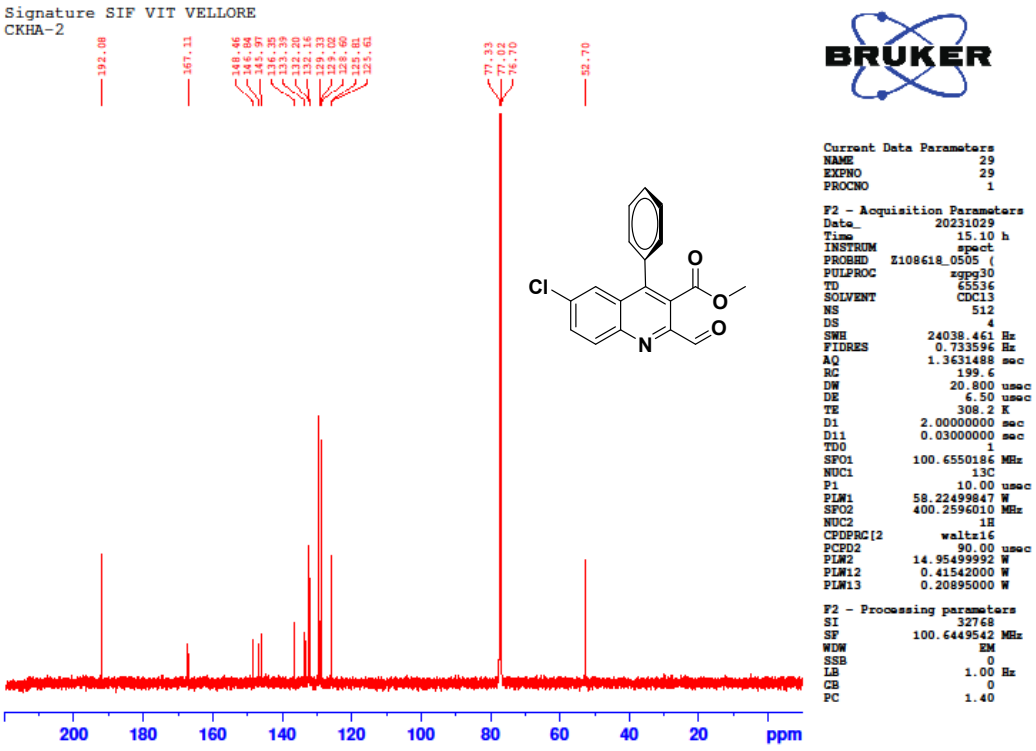


Figure S28: ^{13}C NMR of compound 4c

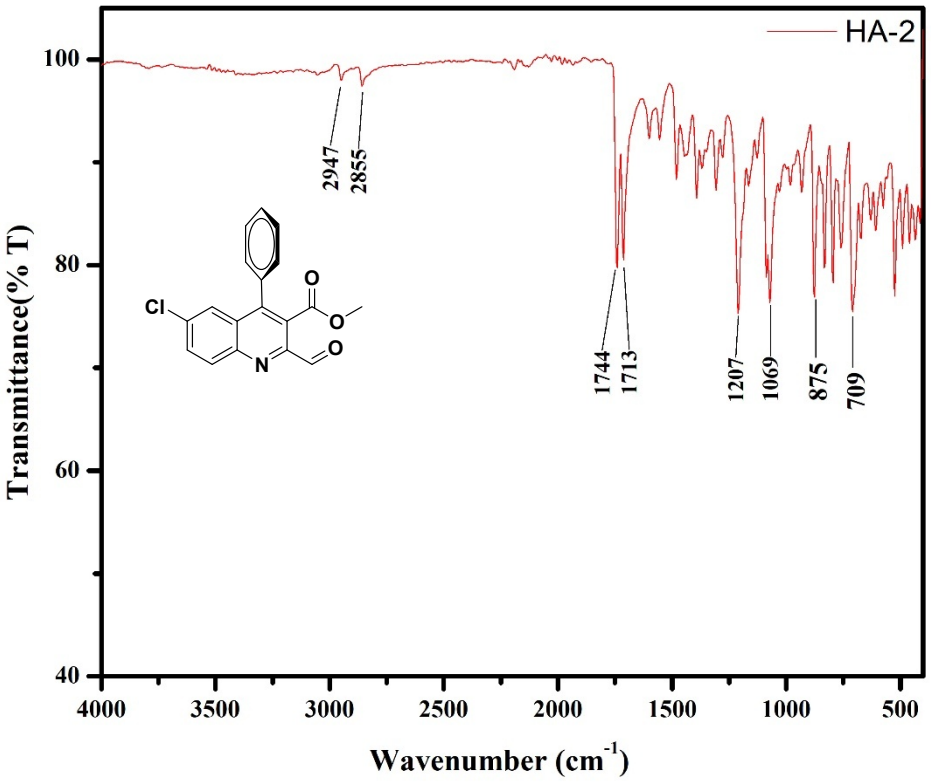


Figure S29: IR spectra of compound 4c

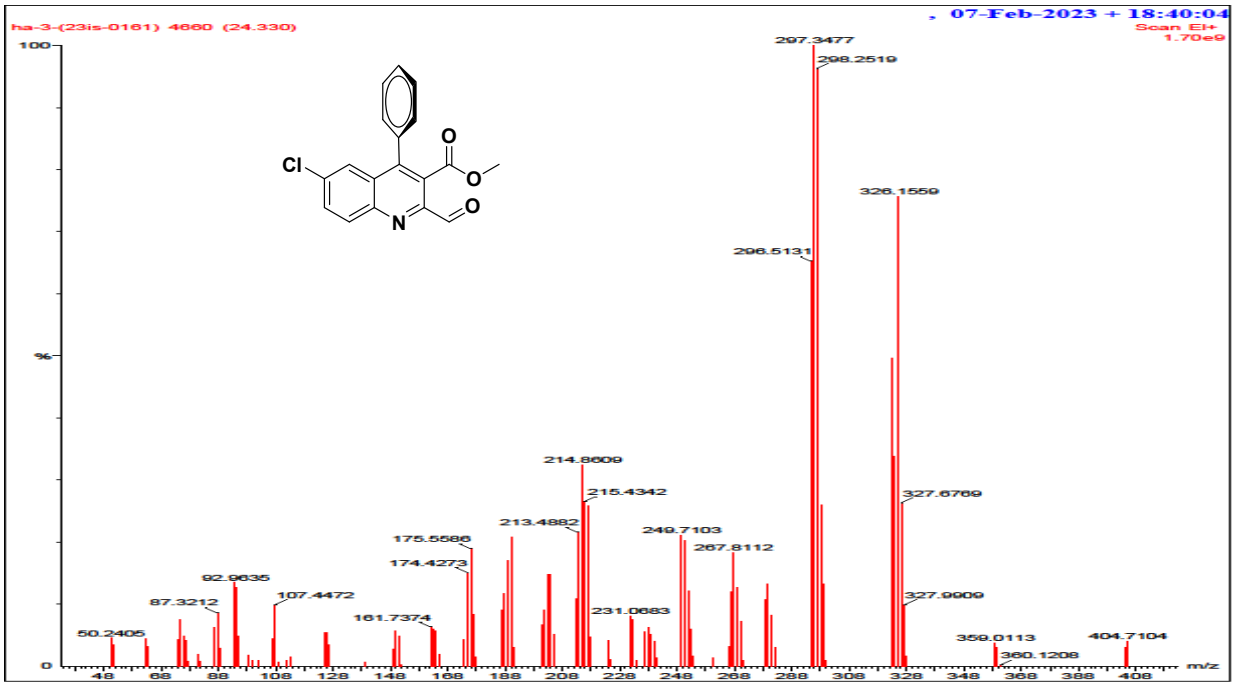


Figure S30: GC-MS spectra of compound 4c

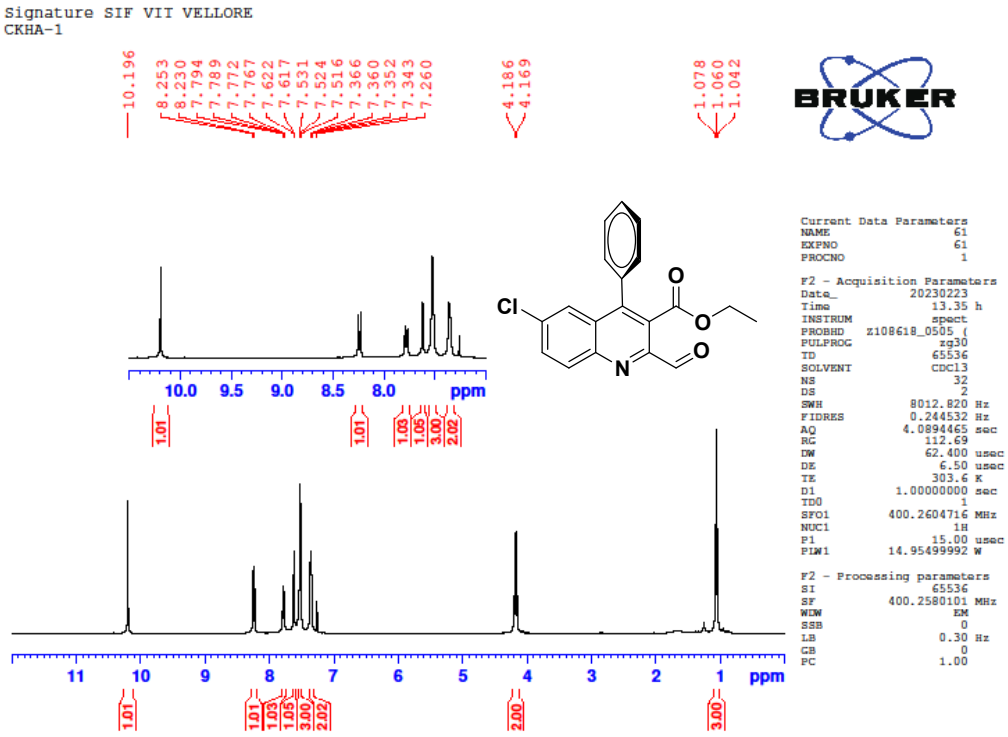


Figure S31: ^{1}H NMR of compound 4d

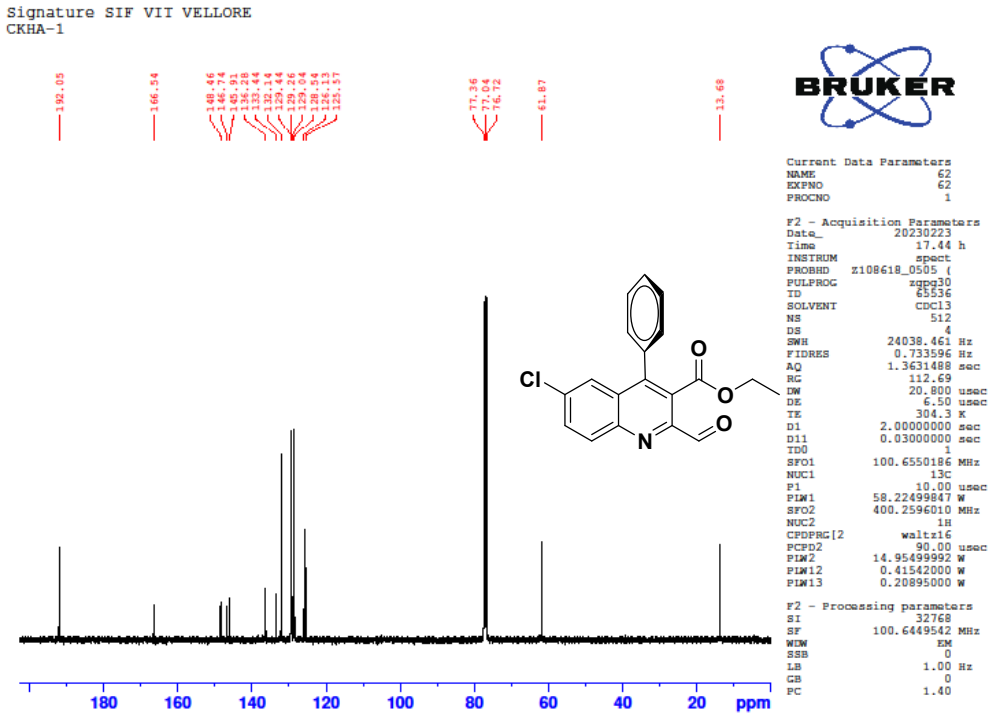


Figure S32: ^{13}C NMR of compound 4d

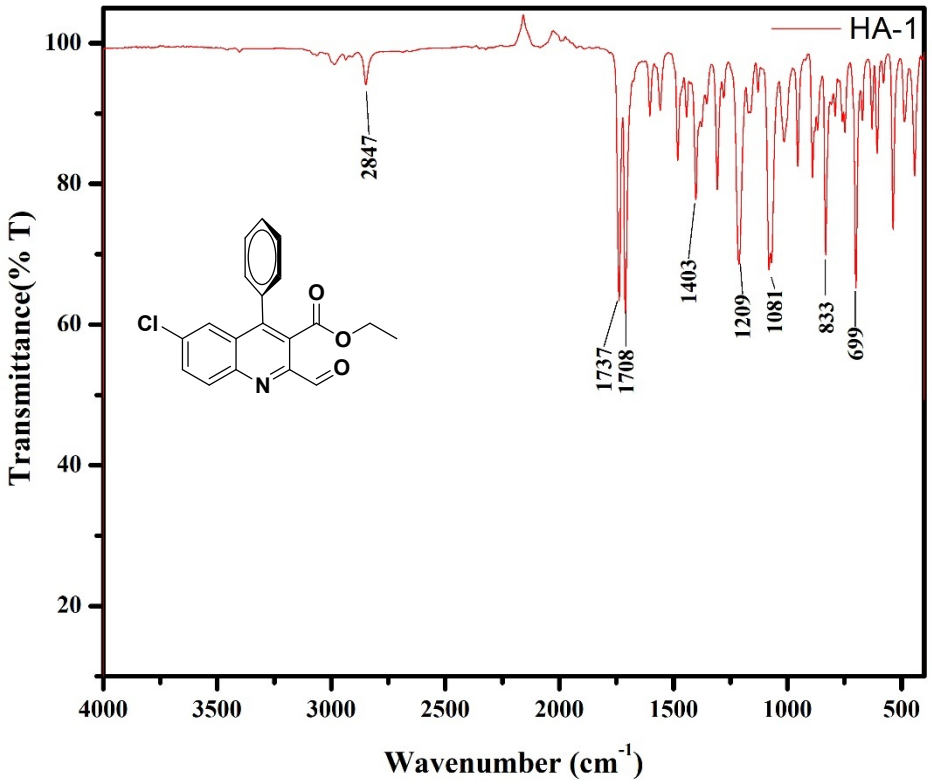


Figure S33: IR spectra of compound 4d

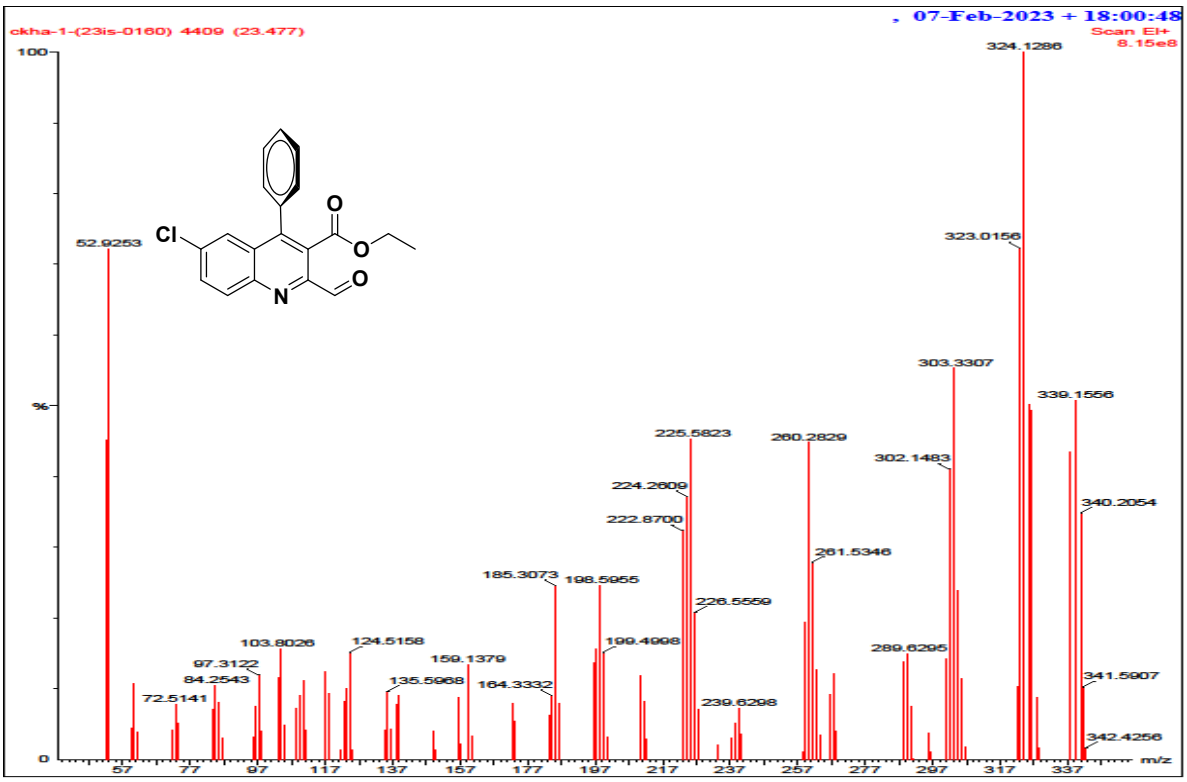


Figure S34: GC-MS spectra of compound 4d

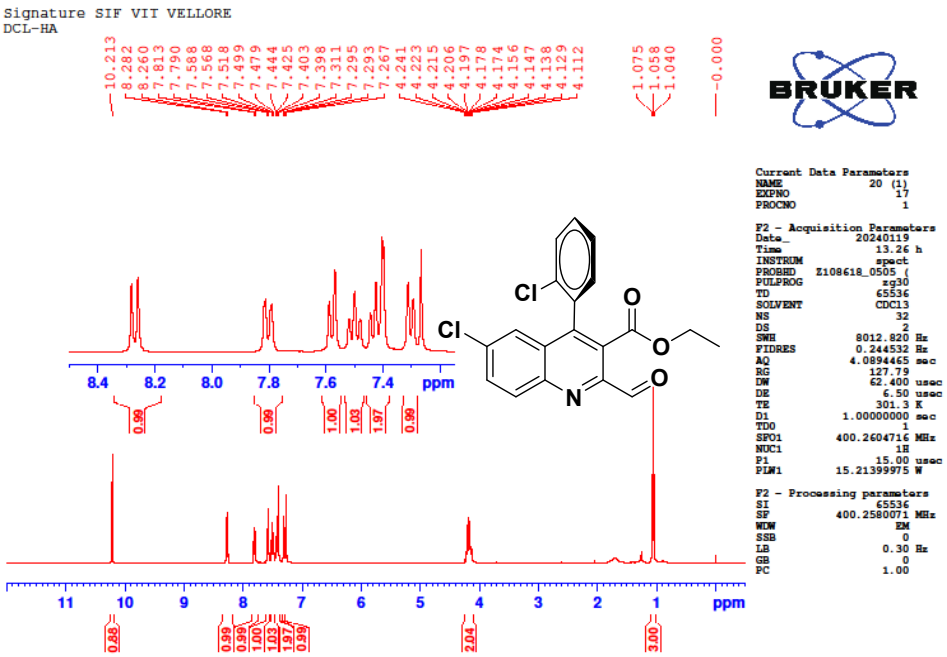


Figure S35: ^{1}H NMR of compound 4e

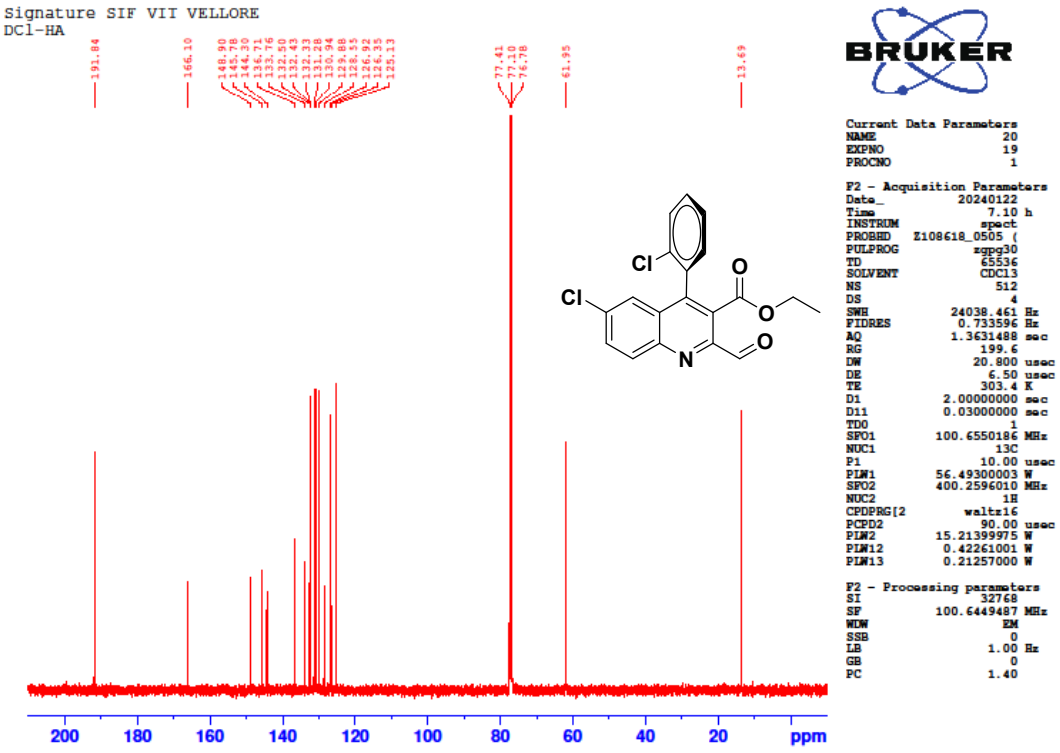


Figure S36: ^{13}C NMR of compound 4e

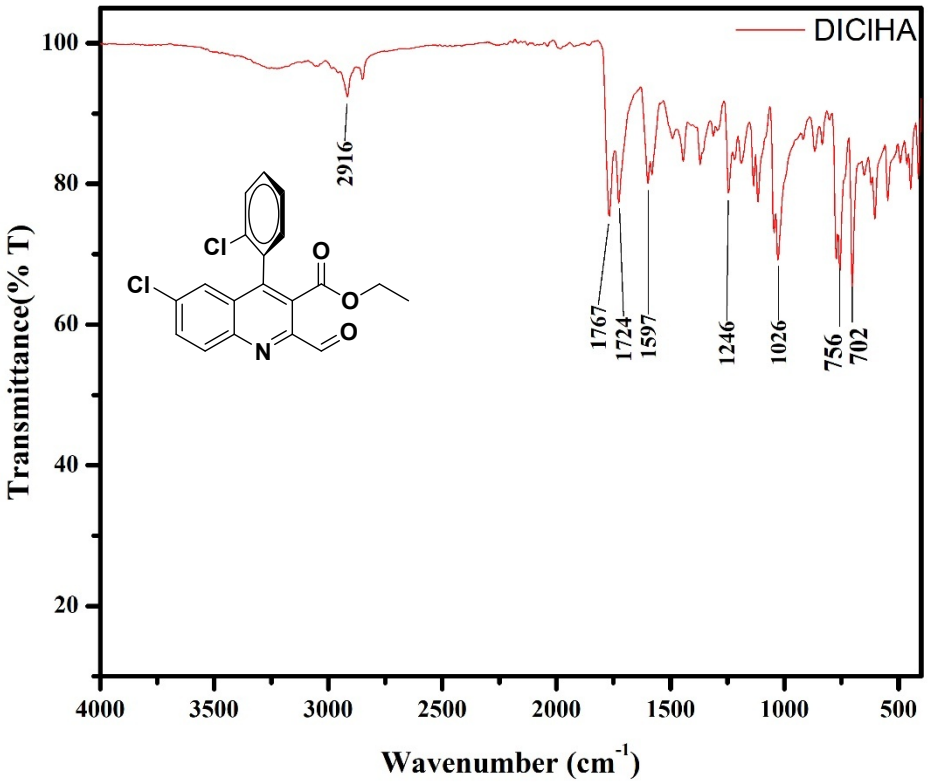


Figure S37: IR spectra of compound 4e

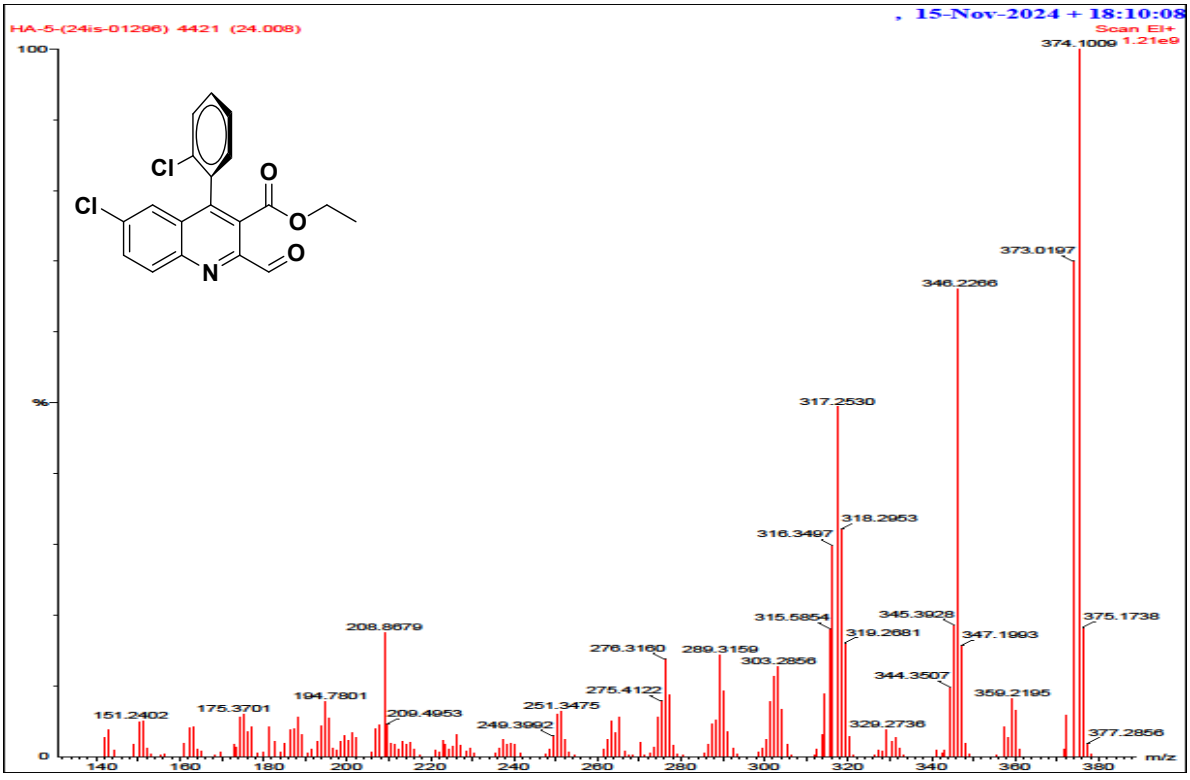


Figure S38: GC-MS spectra of compound 4e

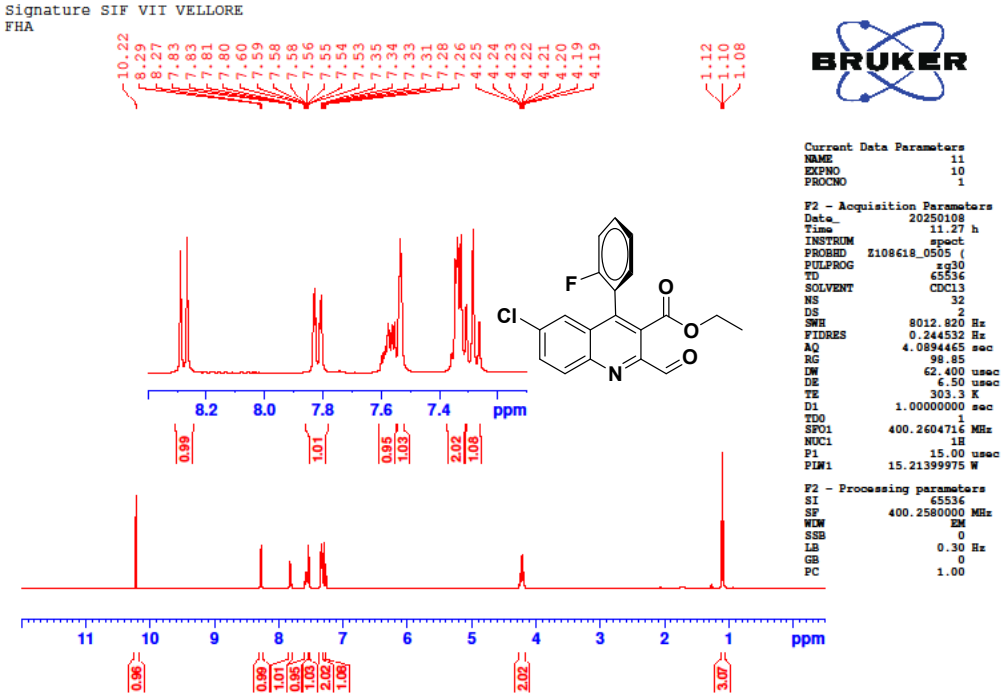


Figure S39: ^{1}H NMR of compound 4f

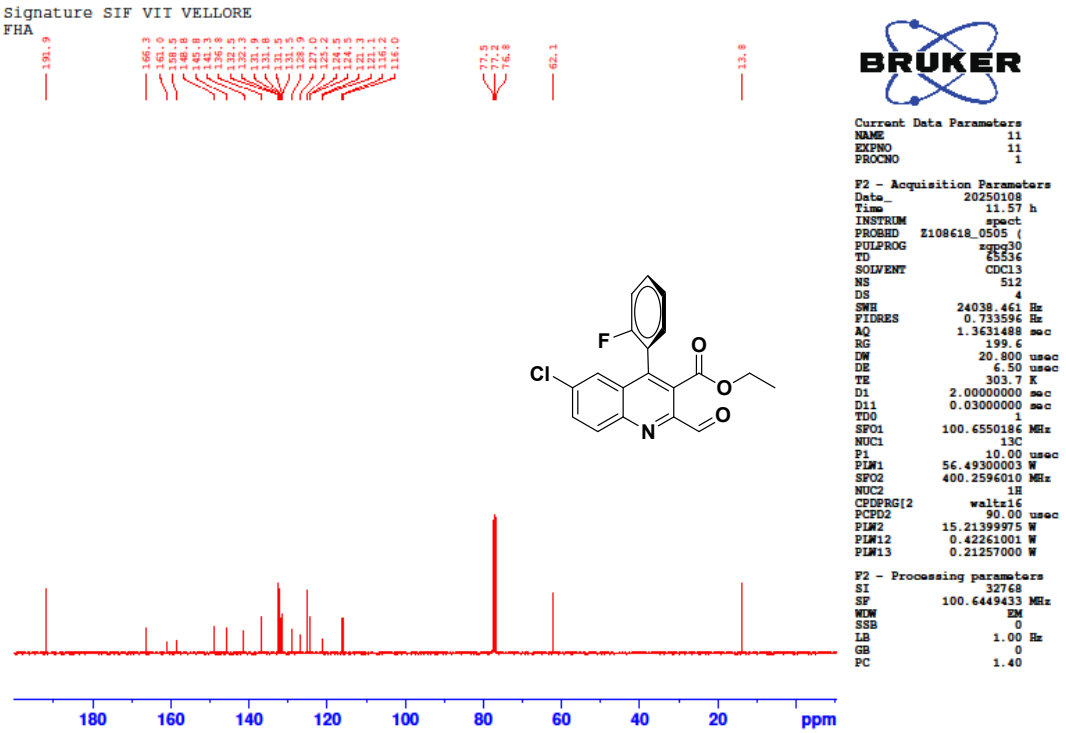


Figure S40: ^{13}C NMR of compound 4f

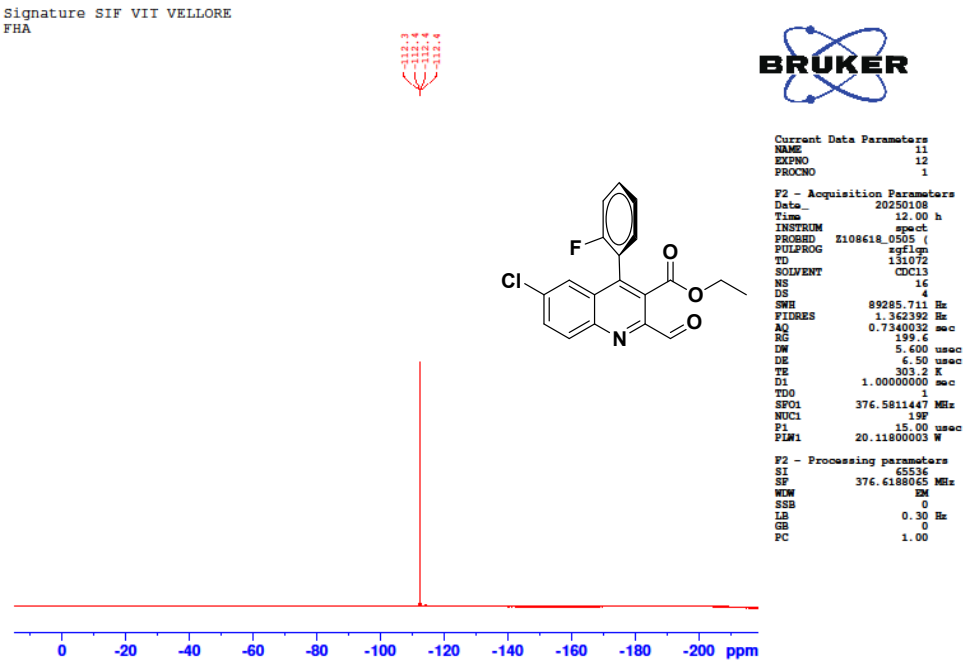


Figure S41: ^{19}F NMR of compound 4f

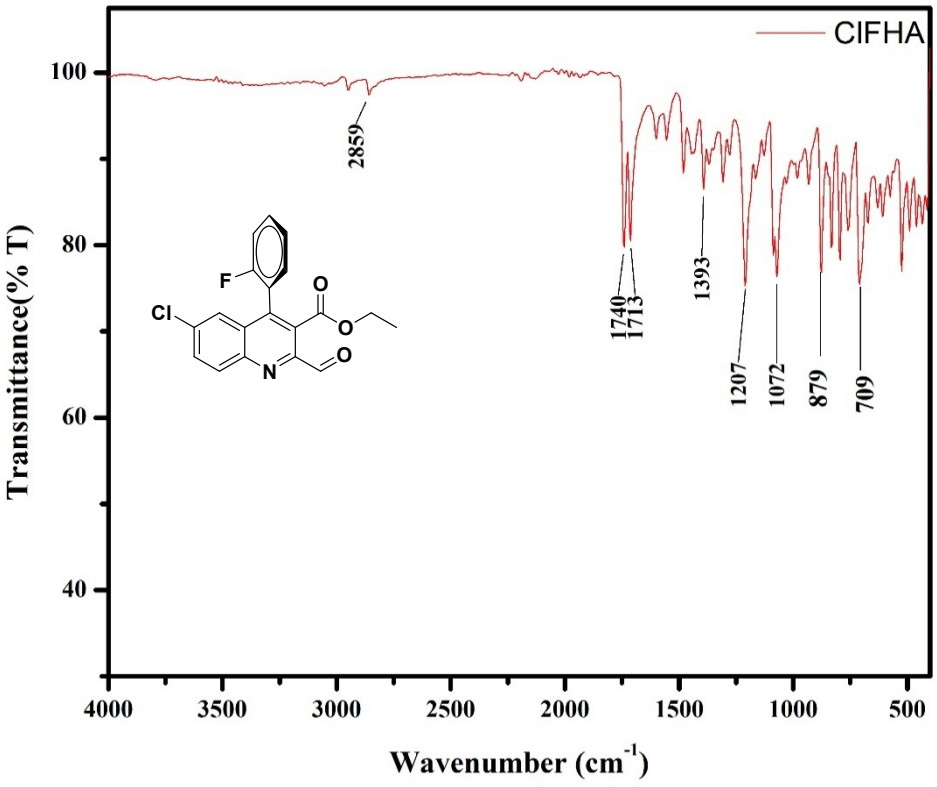


Figure S42: IR spectra of compound 4f

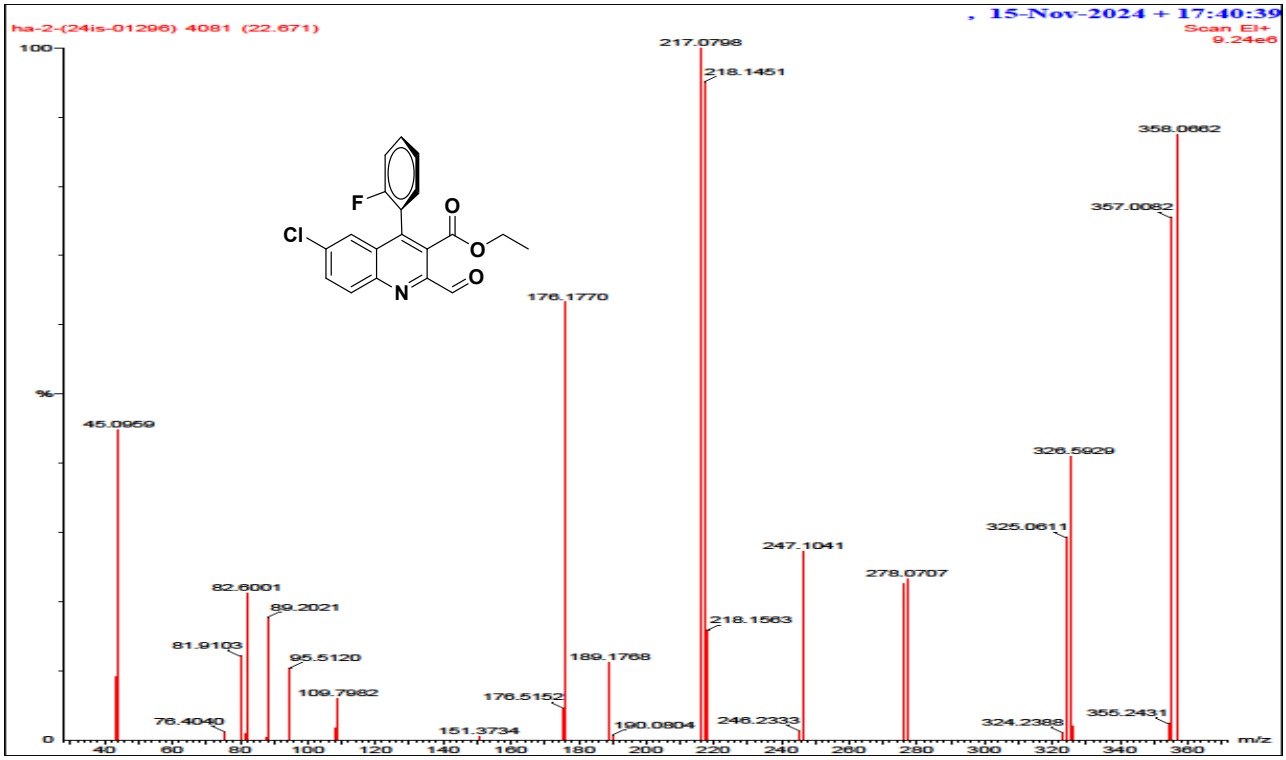


Figure S43: GC-MS spectra of compound 4f

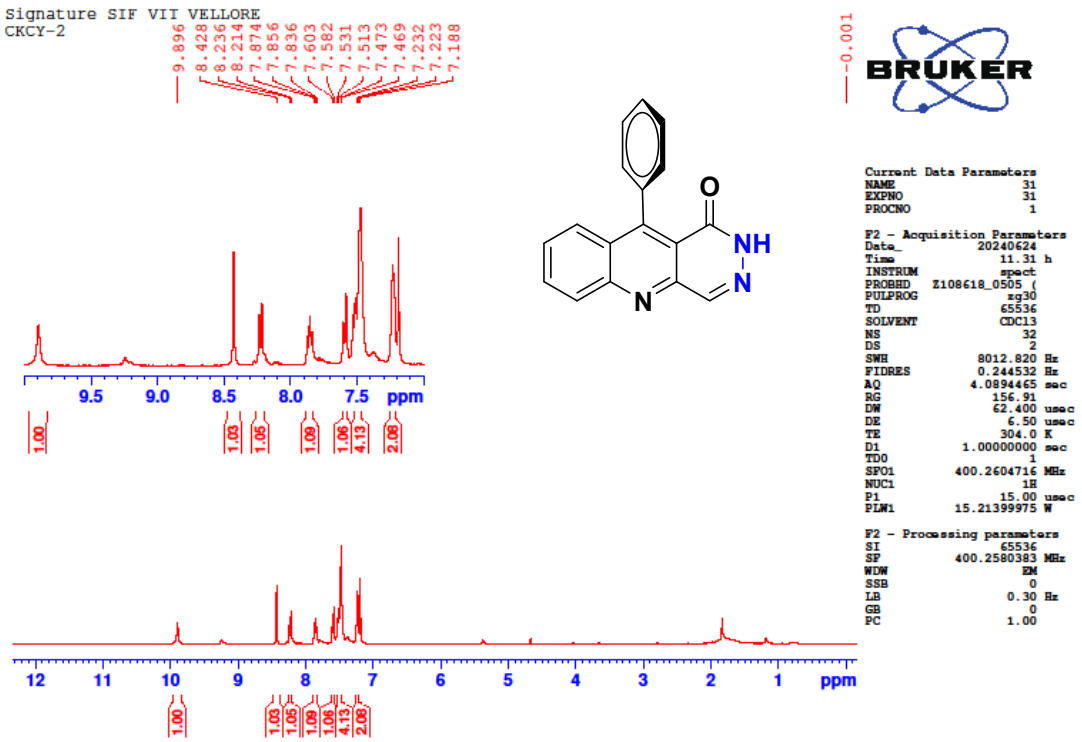


Figure S44: ^{1}H NMR of compound 5a

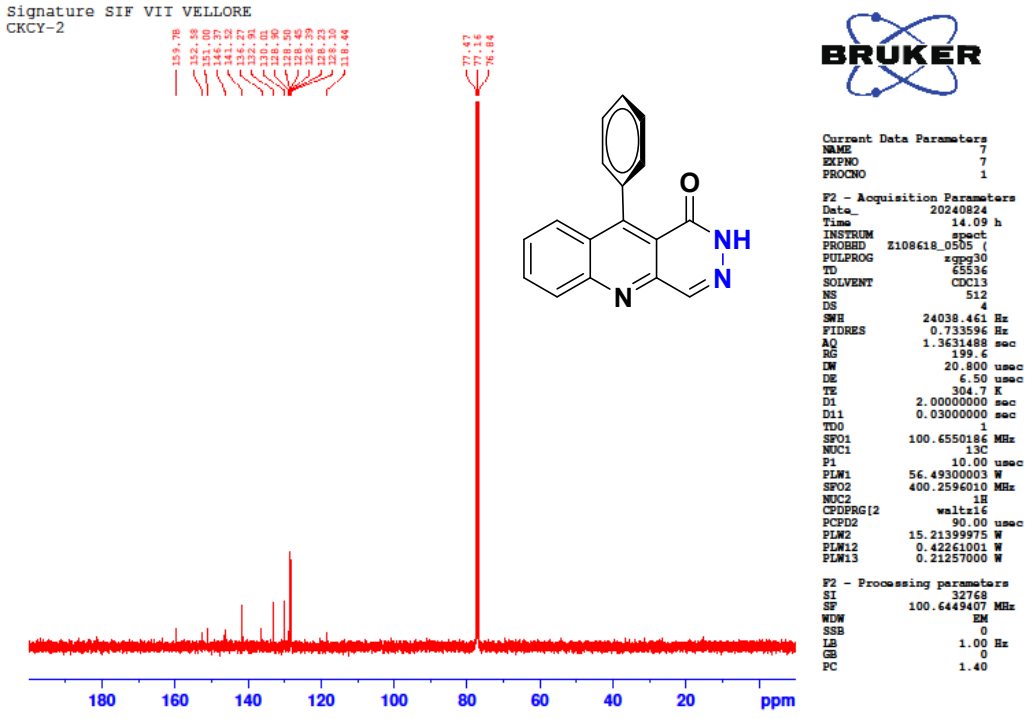


Figure S45: ^{13}C NMR of compound 5a

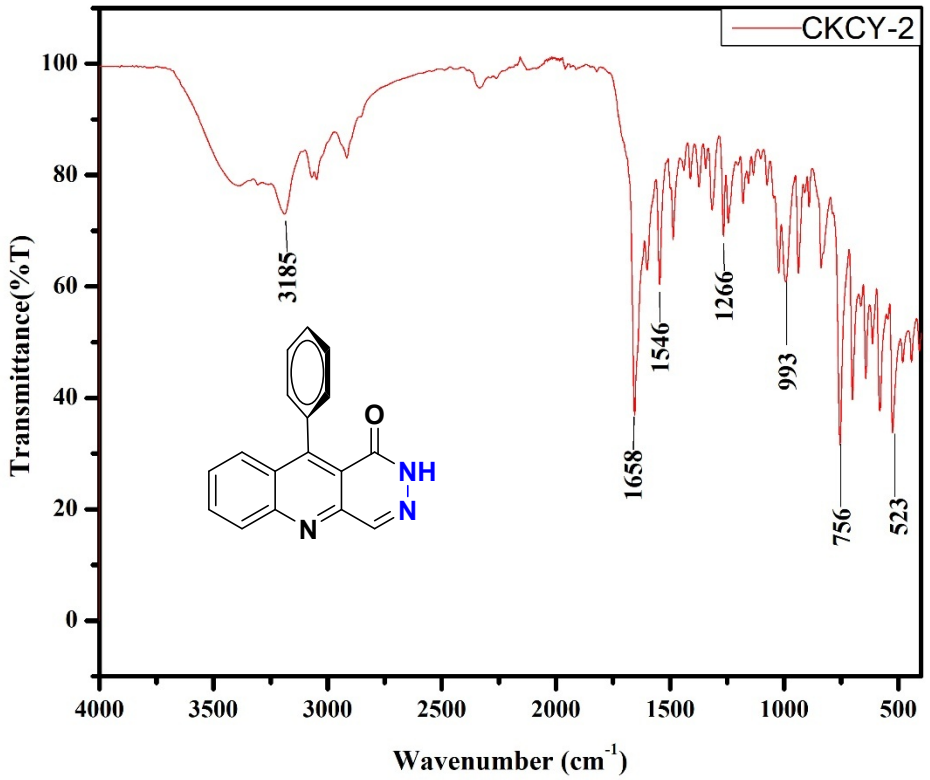


Figure S46: IR spectra of compound 5a

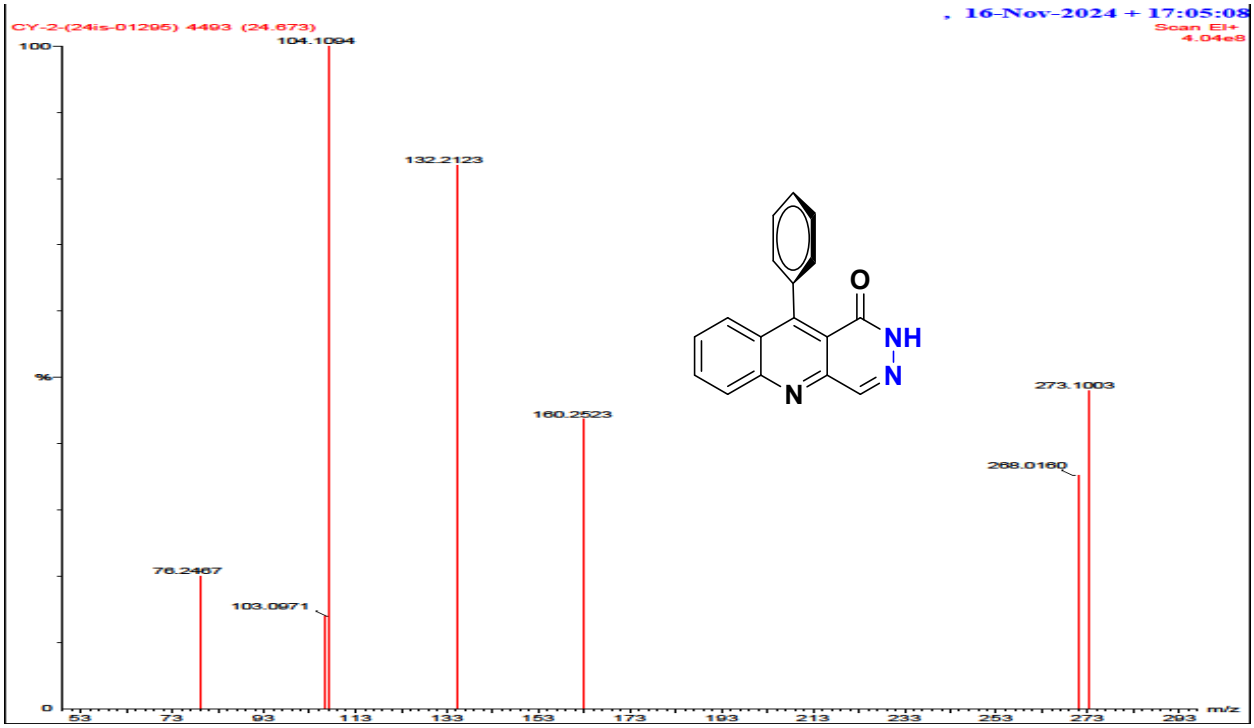


Figure S47: GC-MS spectra of compound 5a

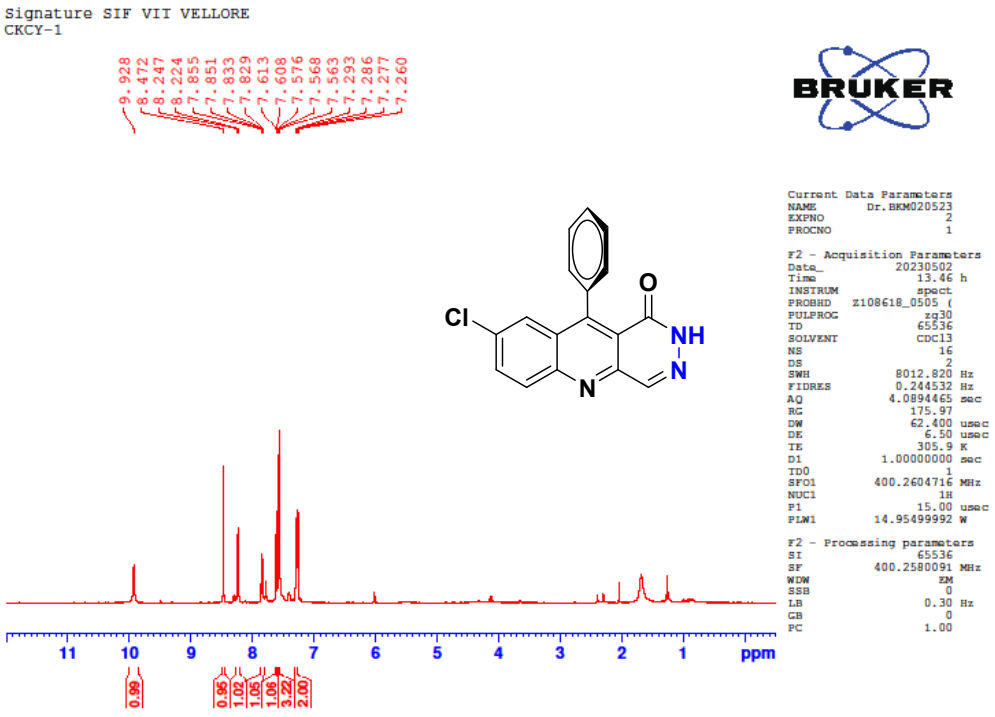


Figure S48: ^{1}H NMR of compound 5b

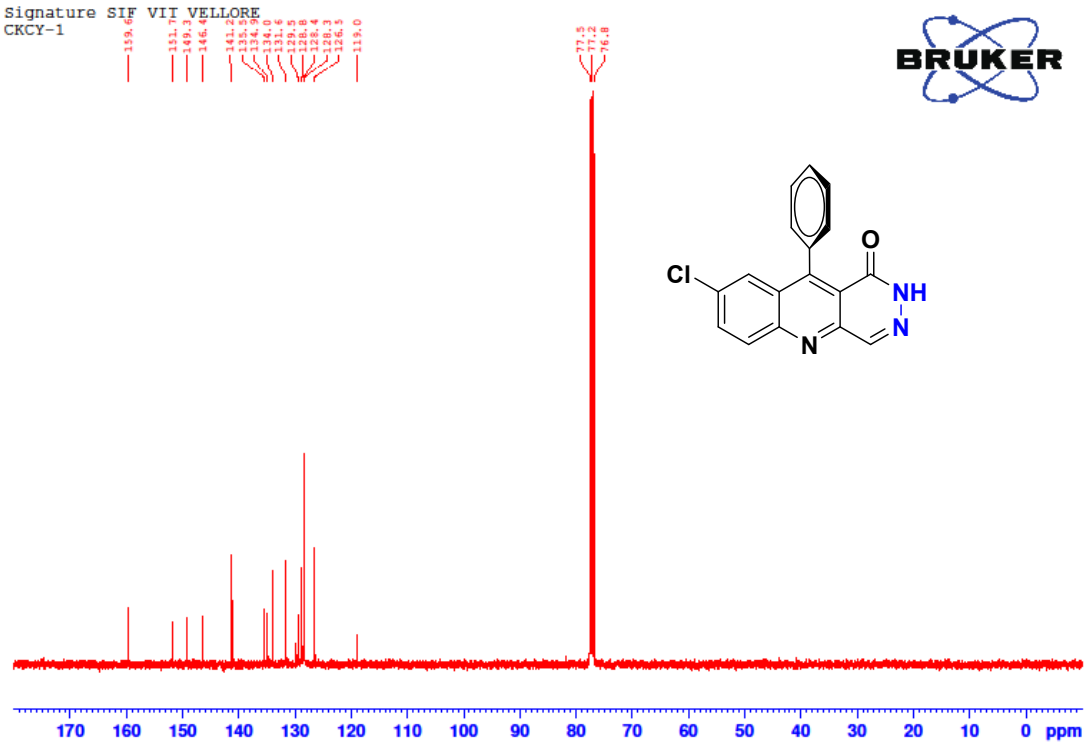


Figure S49: ^{13}C NMR of compound 5b

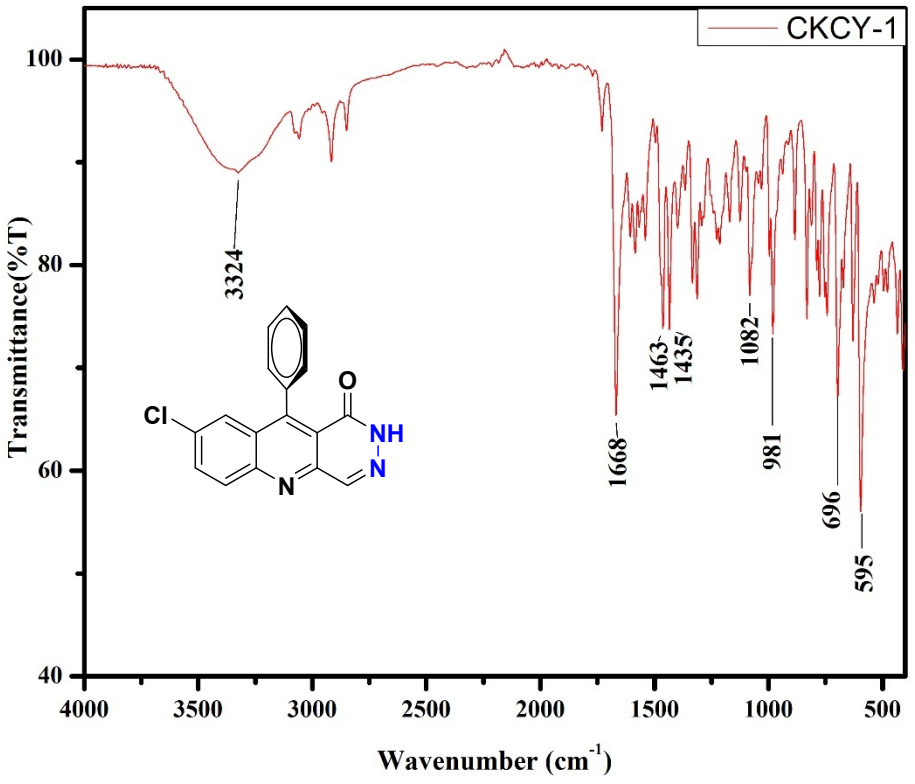


Figure S50: IR spectra of compound 5b

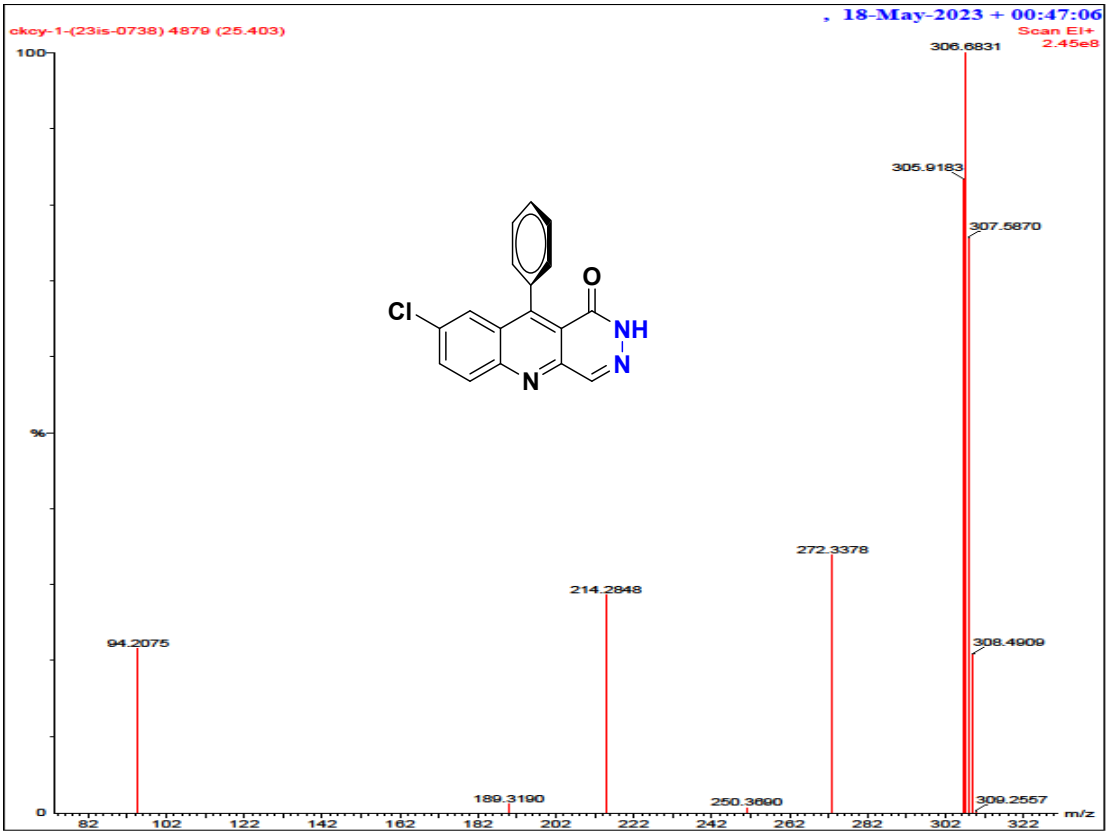


Figure S51: GC-MS spectra of compound 5b

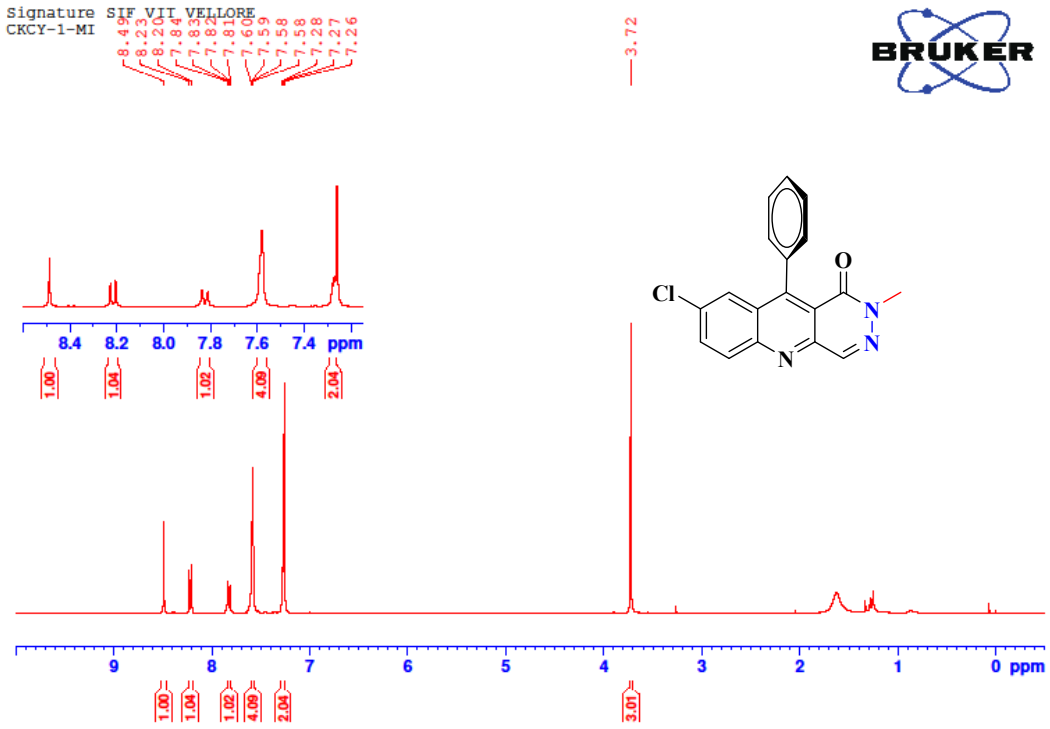


Figure S52: ^{1}H NMR of compound 6a

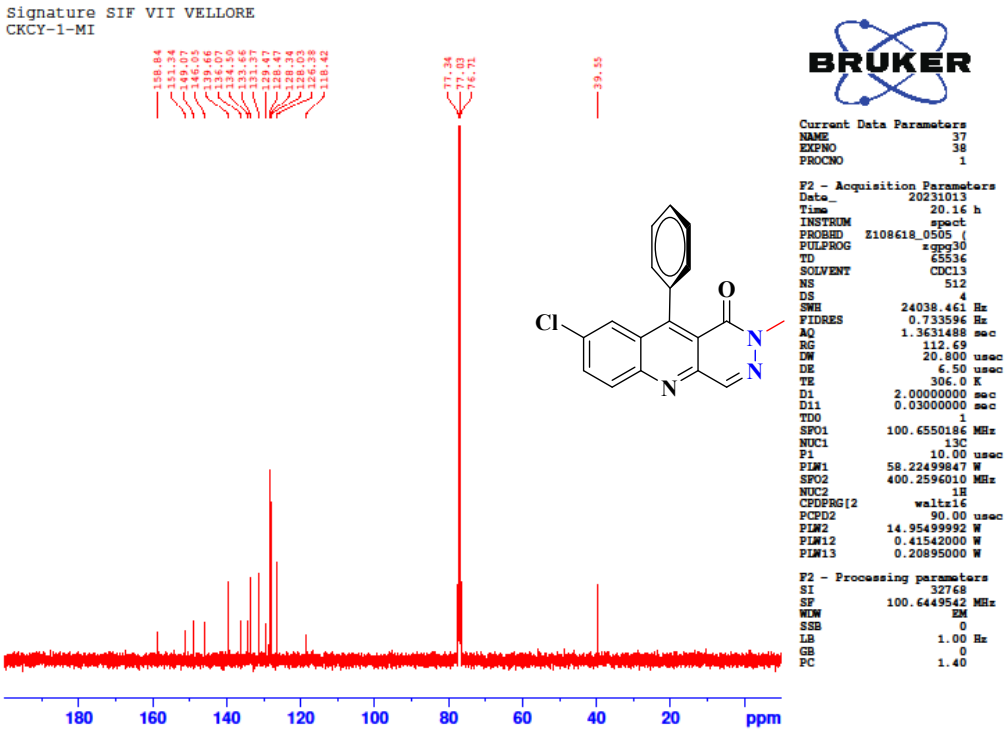


Figure S53: ^{13}C NMR of compound 6a

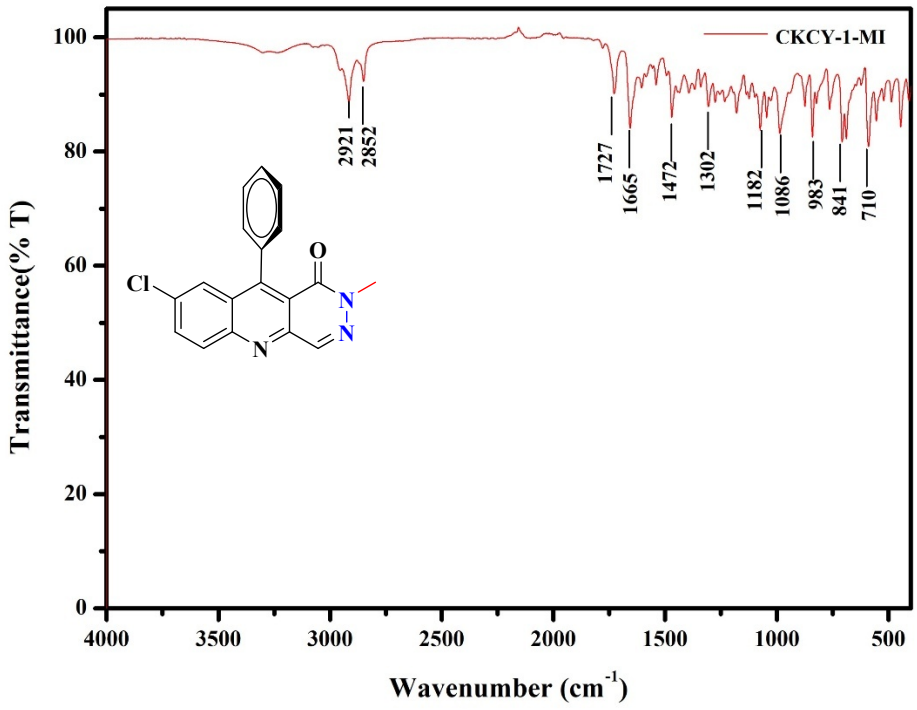


Figure S54: IR spectra of compound 6a

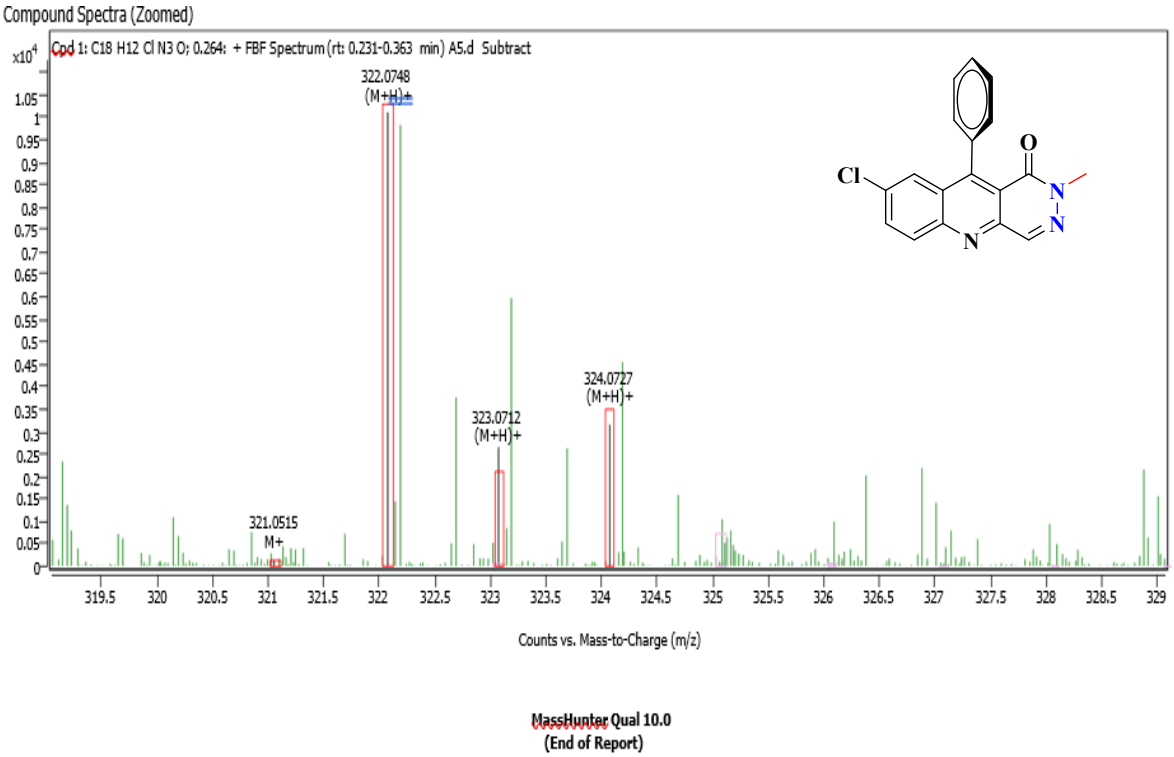


Figure S55: HR-MS spectra of compound 6a

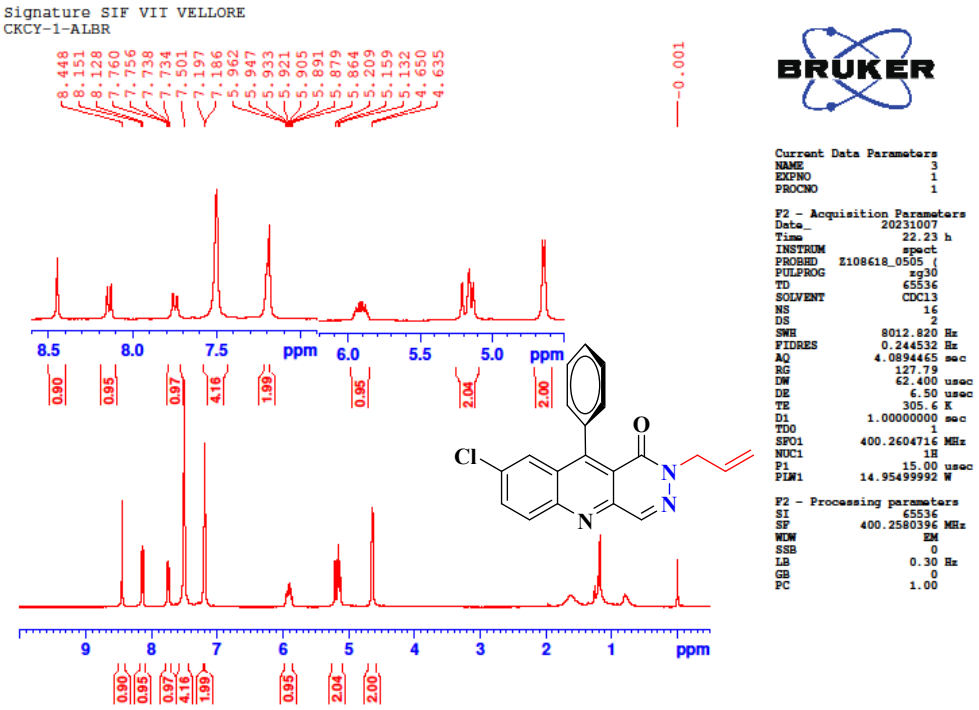


Figure S56: ^{1}H NMR of compound 6b

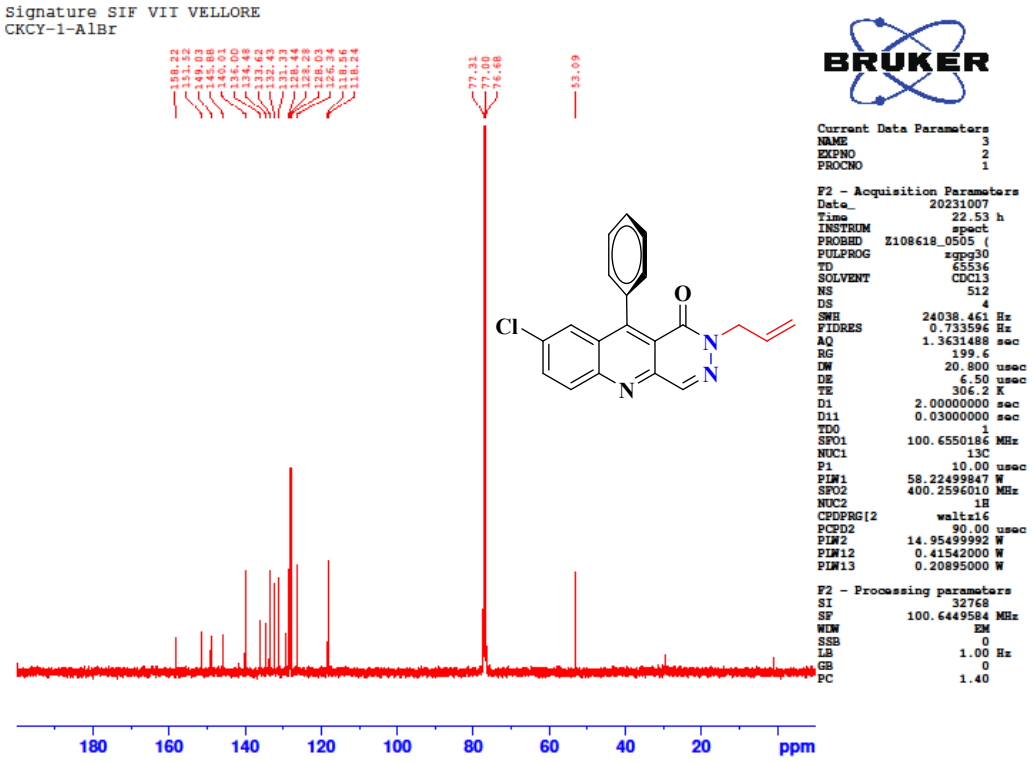


Figure S57: ^{13}C NMR of compound 6b

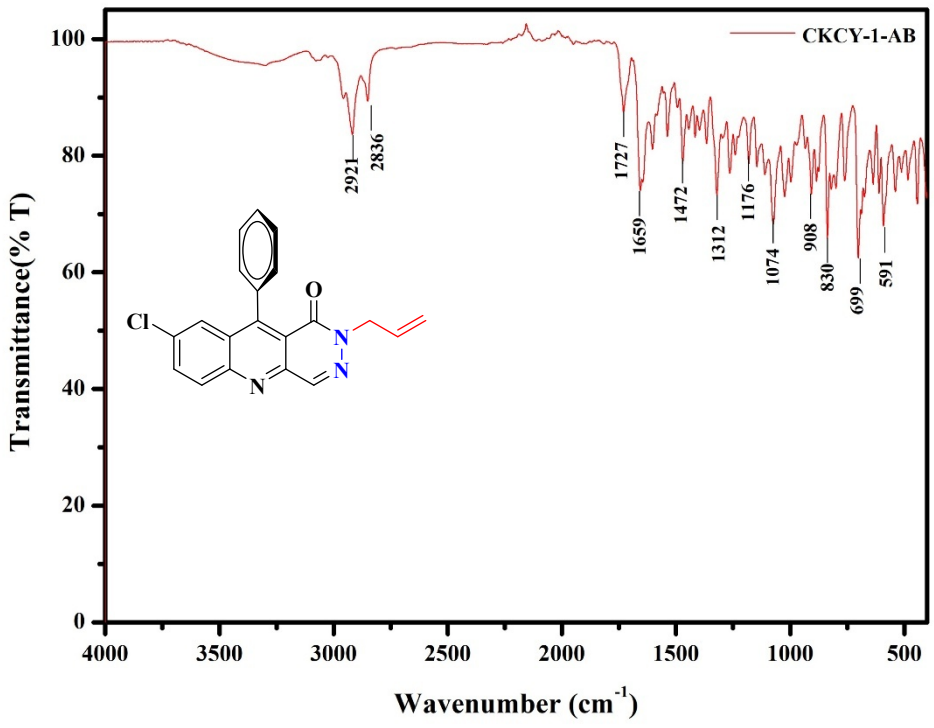


Figure S58: IR spectra of compound 6b

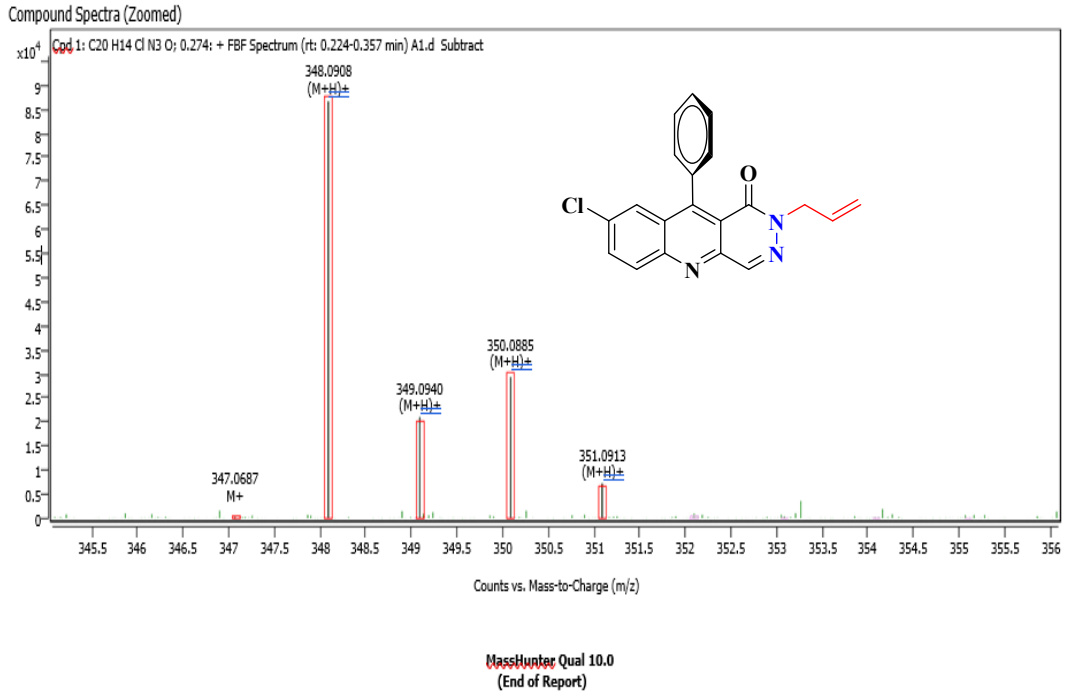


Figure S59: HR-MS spectra of compound 6b

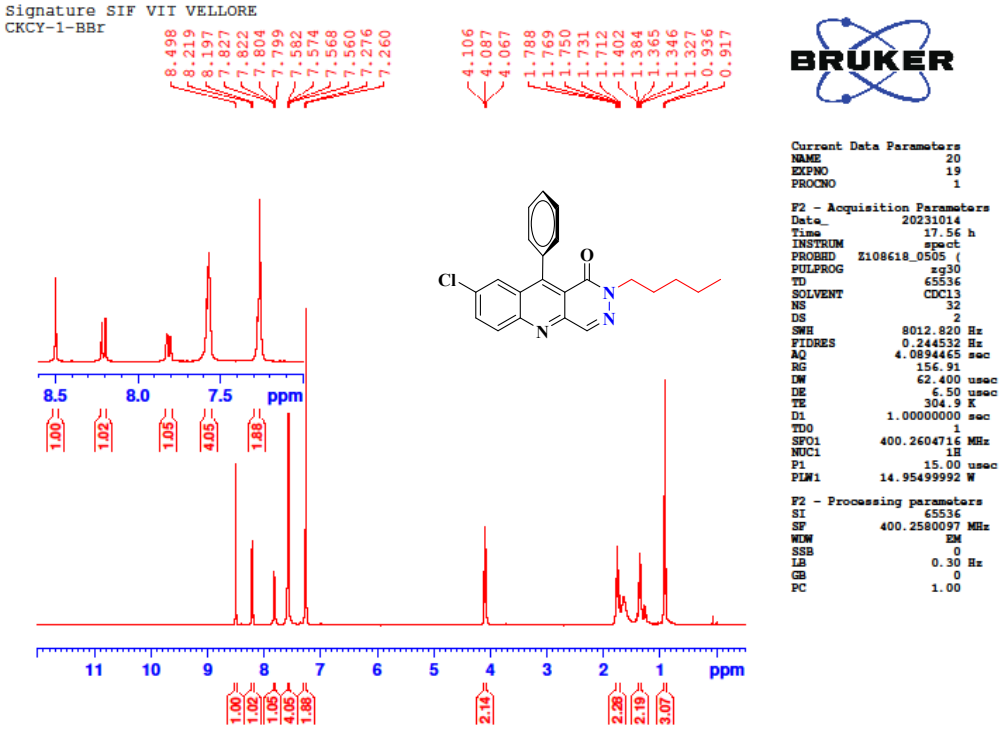


Figure S60: ^{1}H NMR of compound 6c

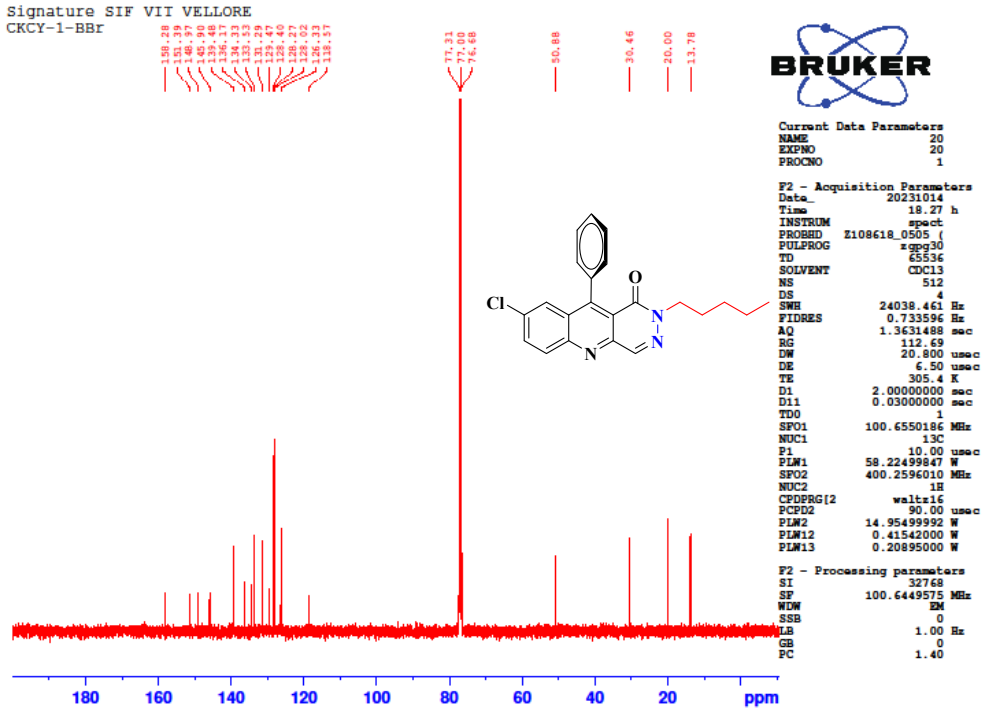


Figure S61: ^{13}C NMR of compound 6c

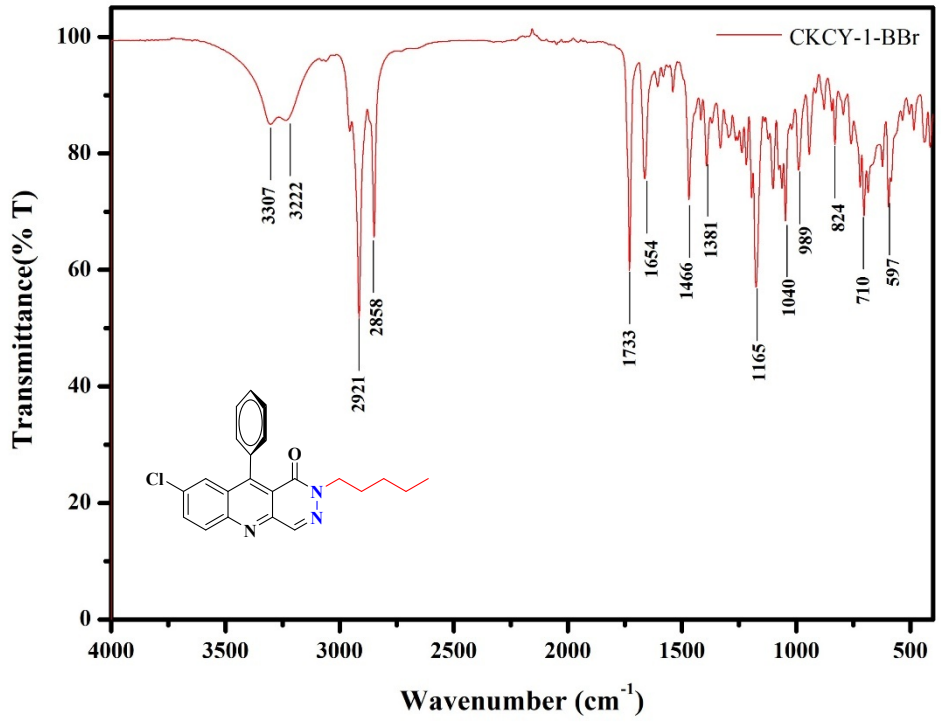


Figure S62: IR spectra of compound 6c

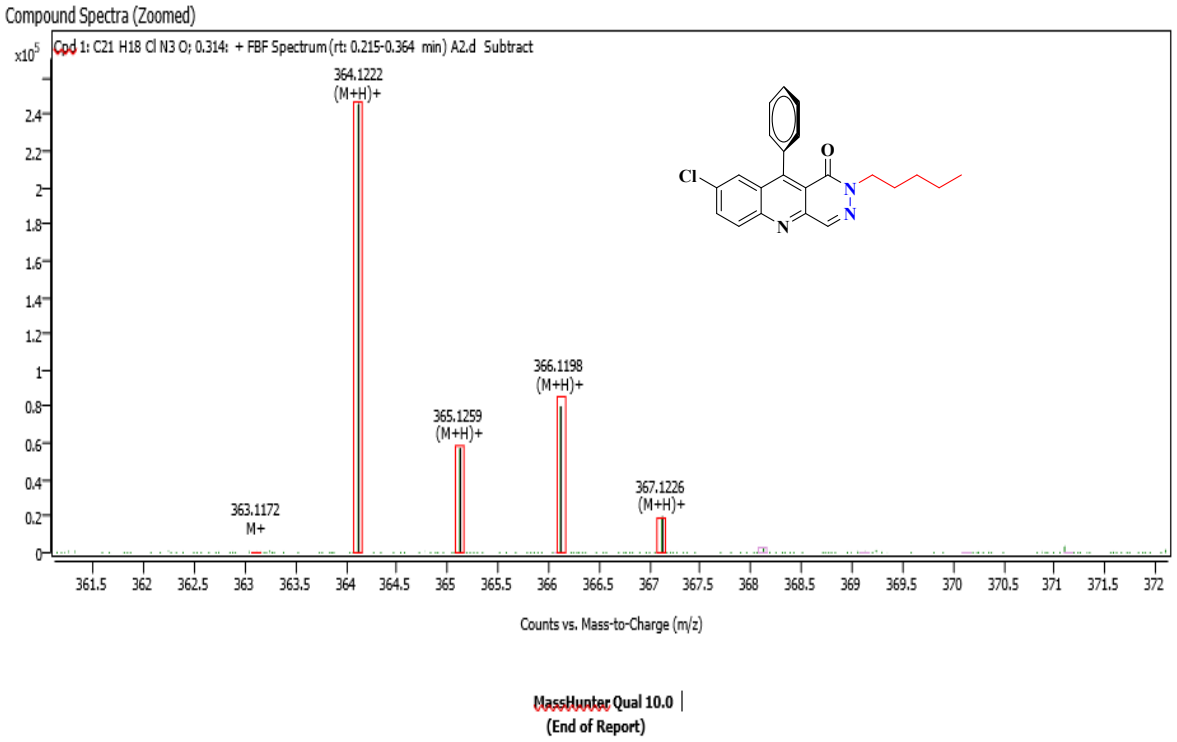


Figure S63: HR-MS spectra of compound 6c

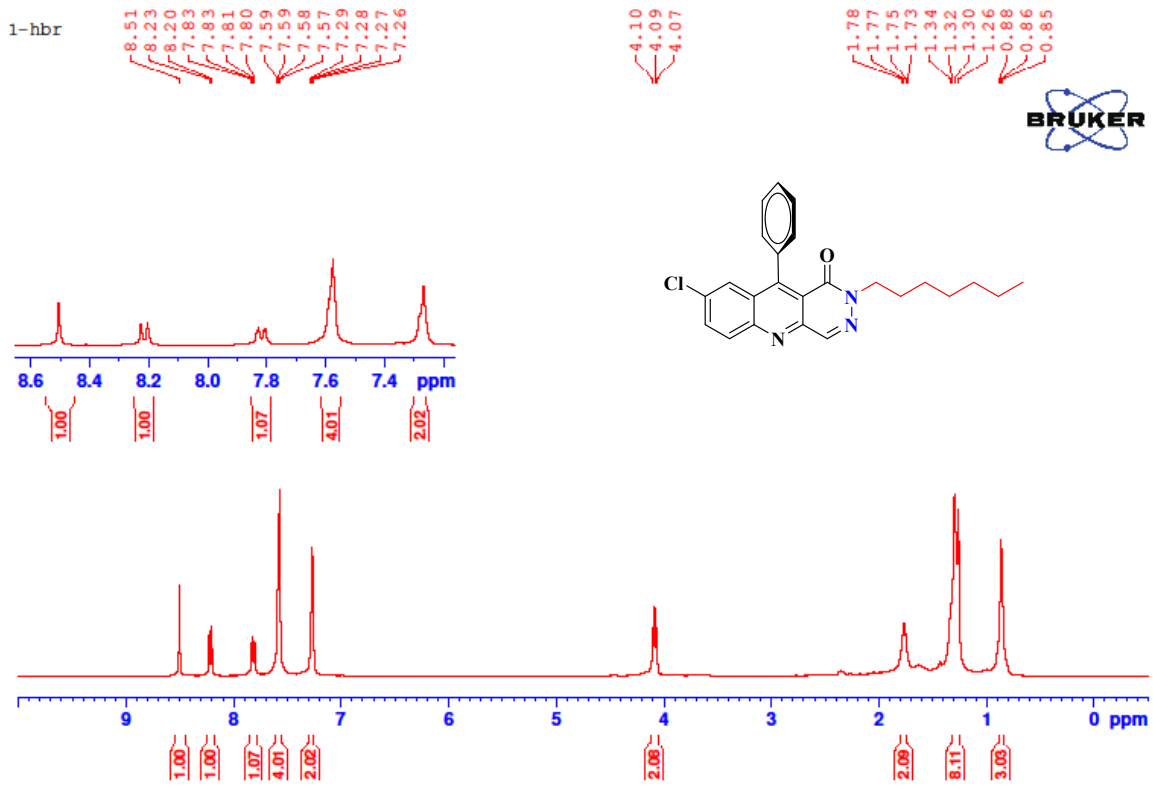


Figure S64: ^{1}H NMR of compound 6d

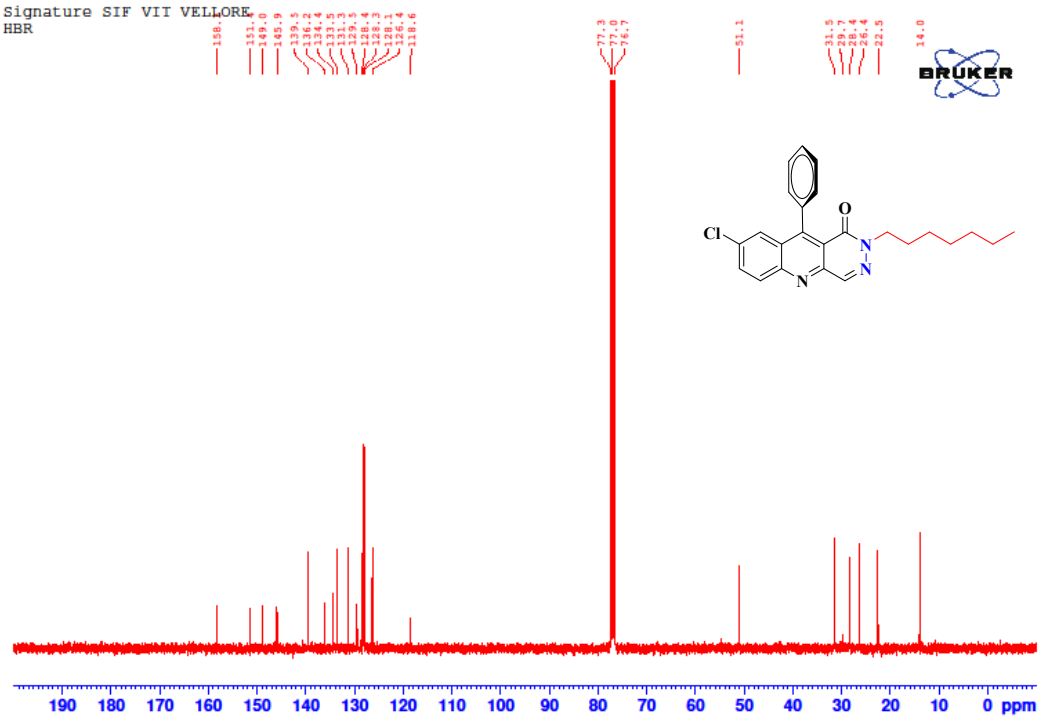


Figure S65: ^{13}C NMR of compound 6d

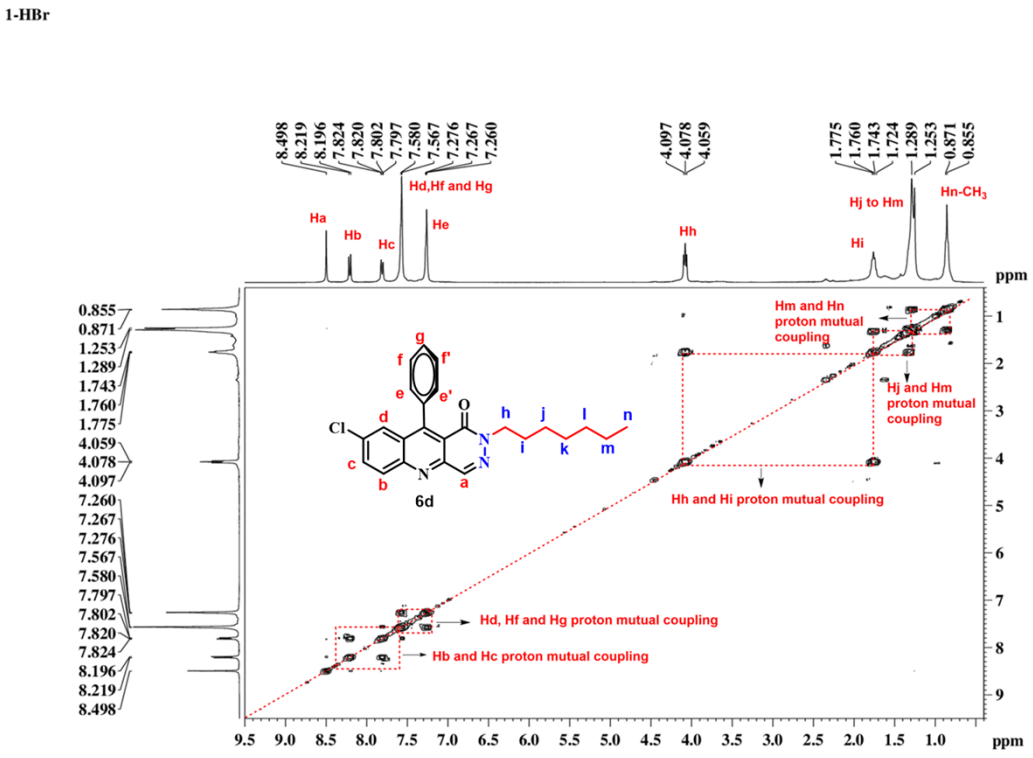


Figure S66: COSY NMR of compound 6d

1-HBr_HSQC

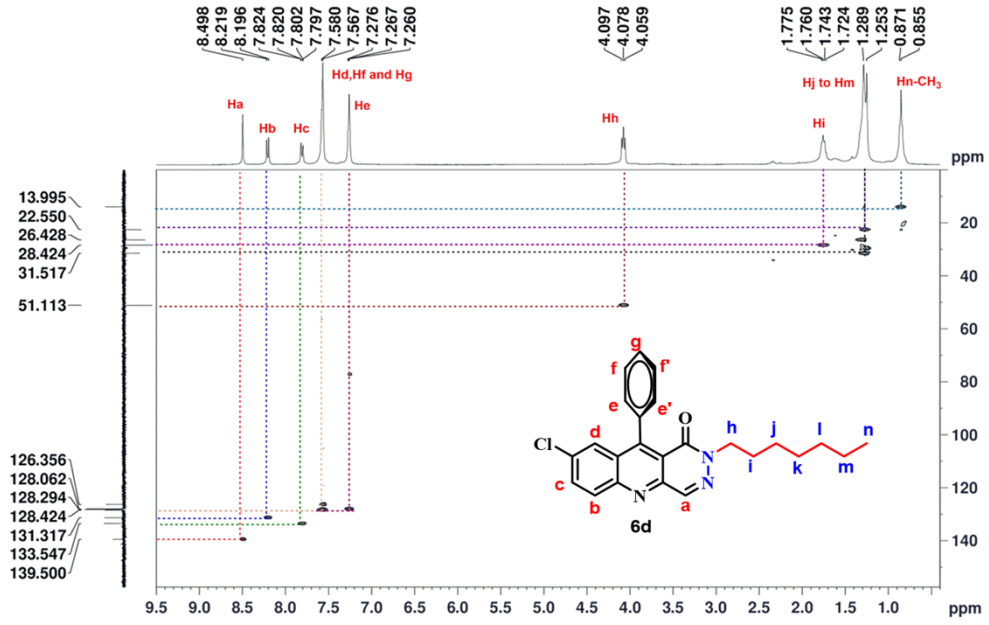


Figure S67: HSQC NMR of compound 6d

1-HBr-HMBC

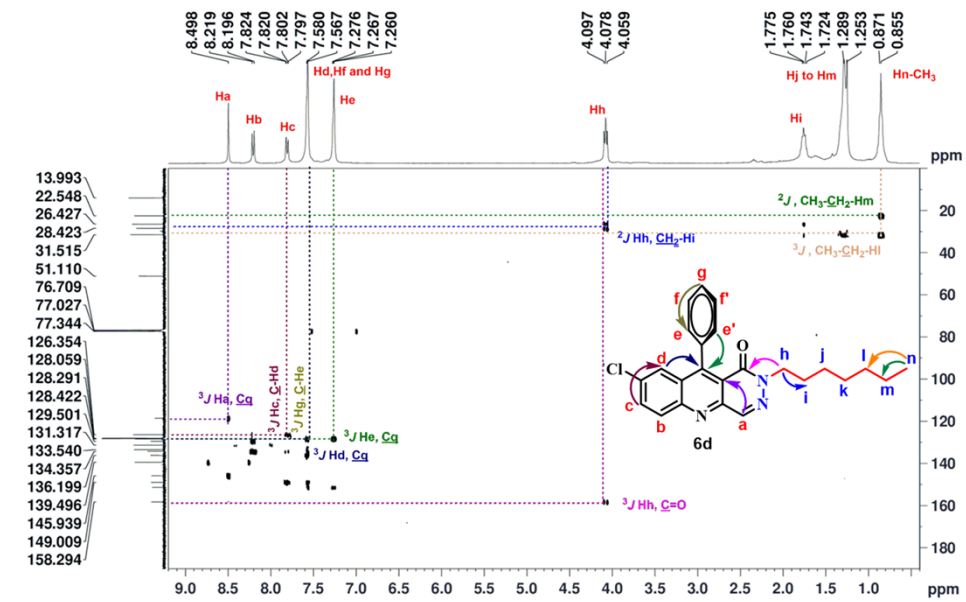


Figure S68: HMBC NMR of compound 6d

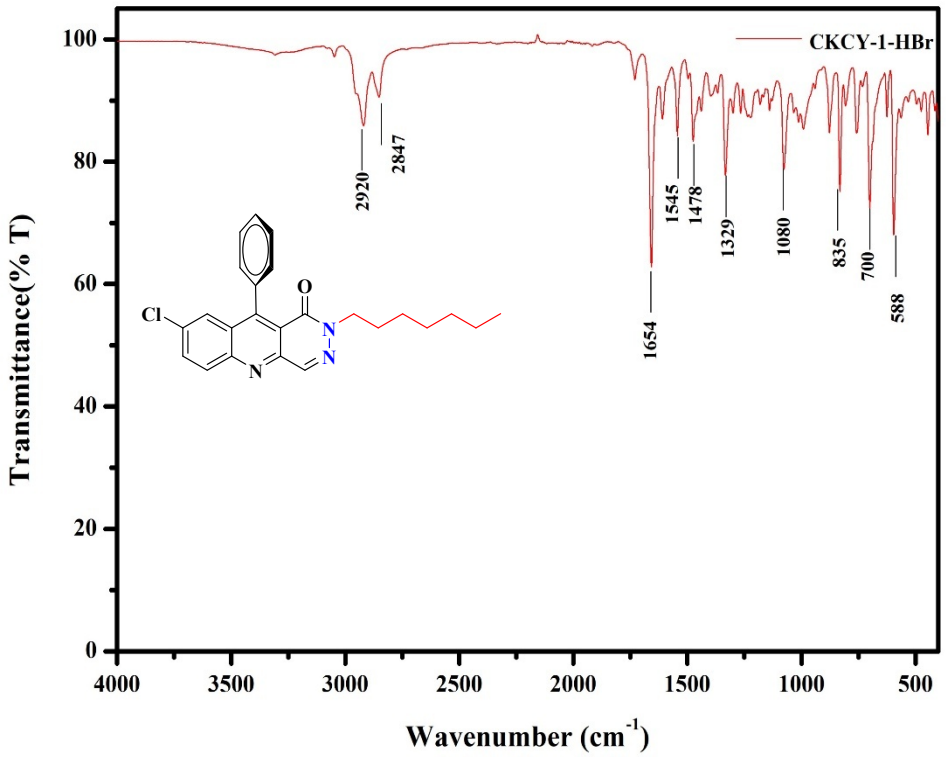


Figure S69: IR spectra of compound 6d

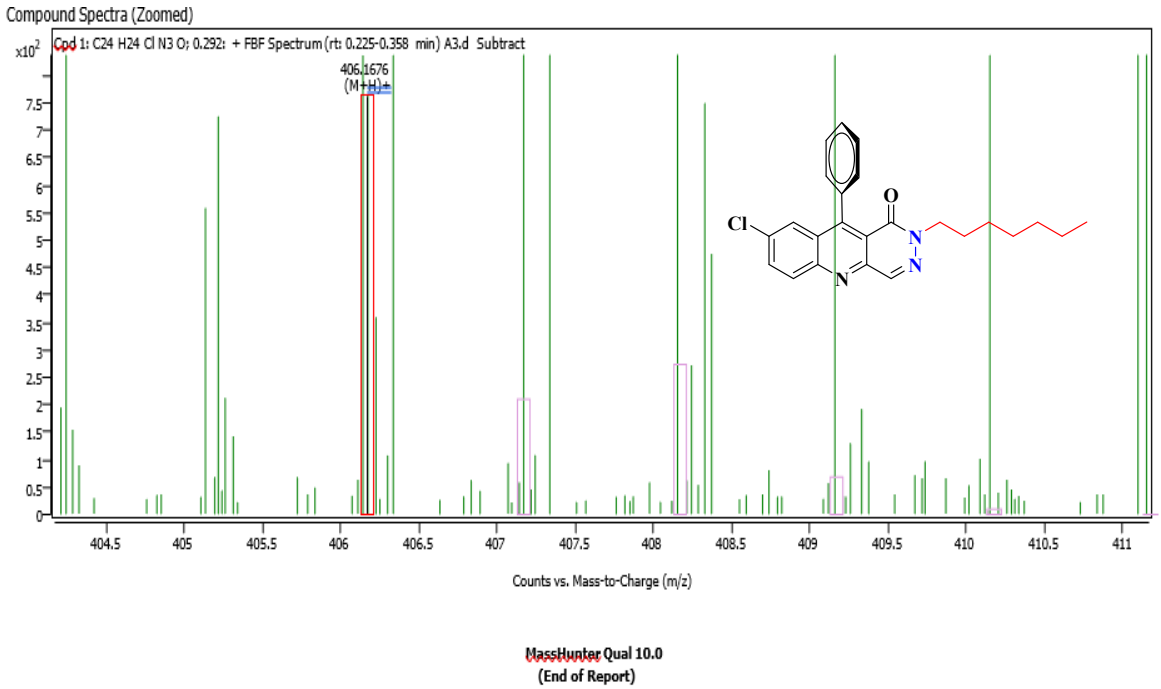


Figure S70: HR-MS spectra of compound 6d

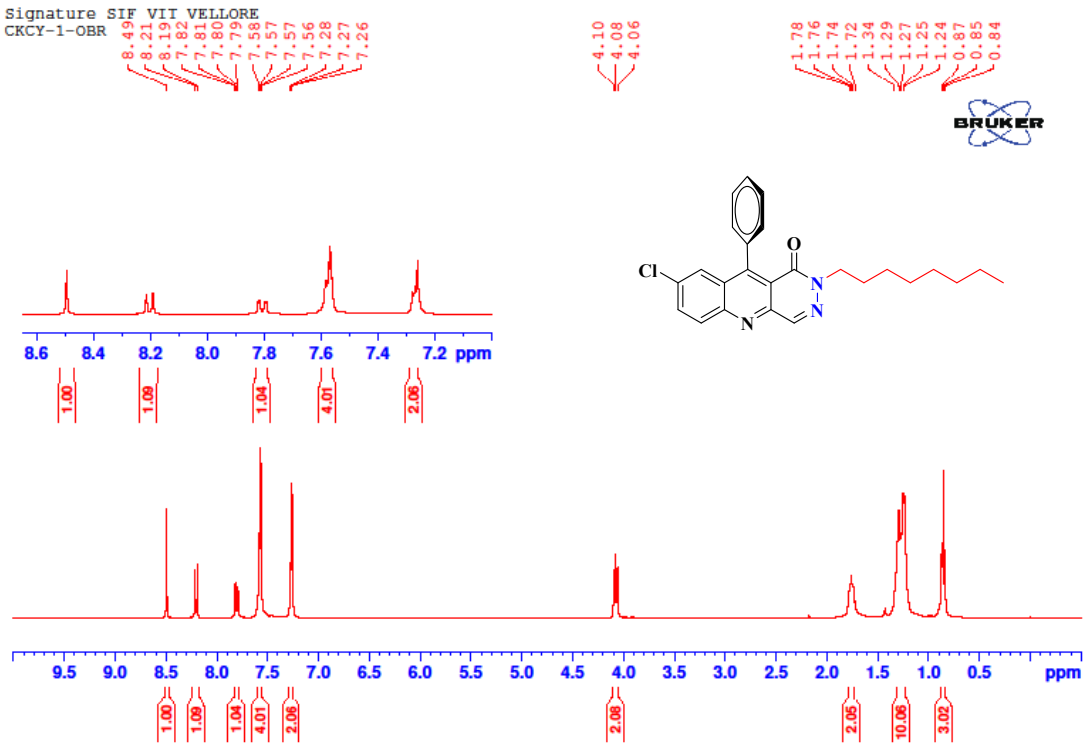


Figure S71: ^{1}H NMR of compound 6e

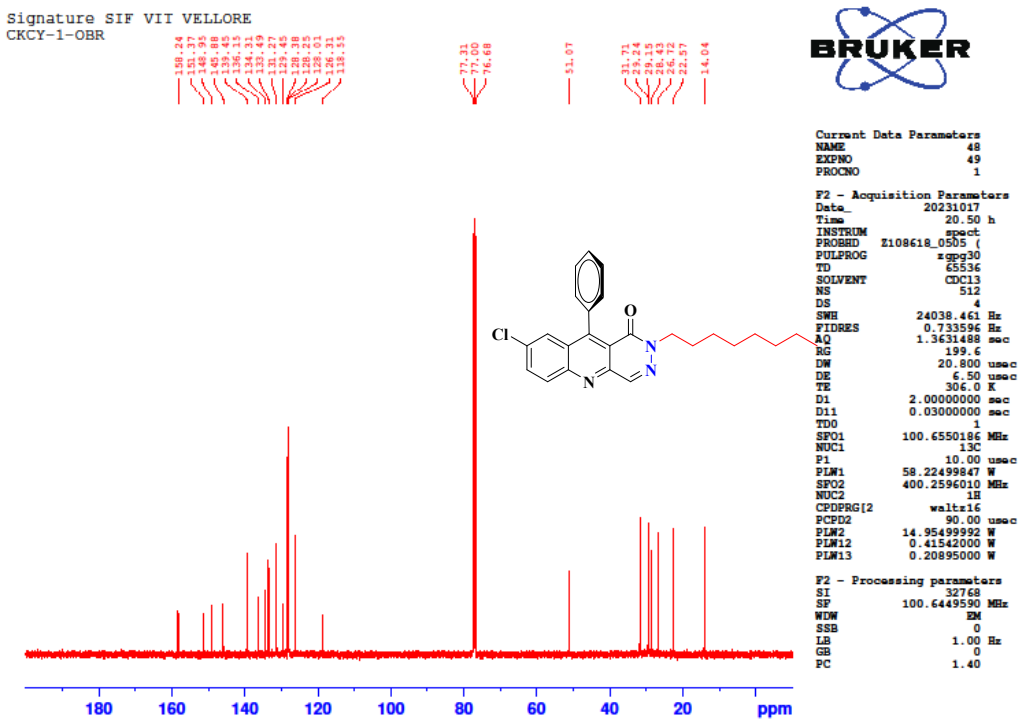


Figure S72: ^{13}C NMR of compound 6e

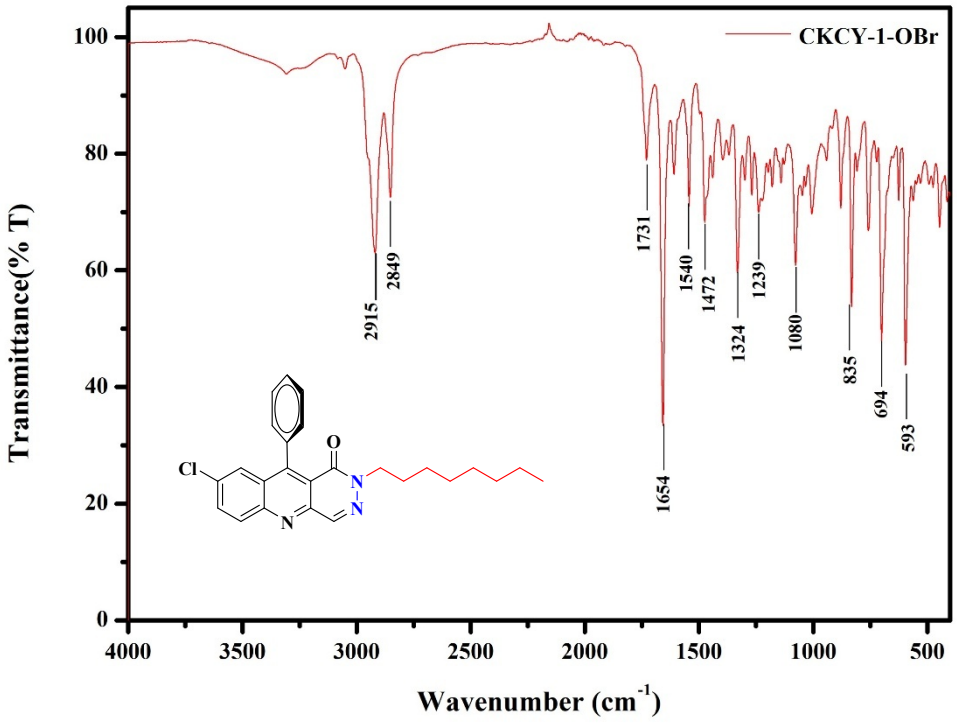


Figure S73: IR spectra of compound 6e

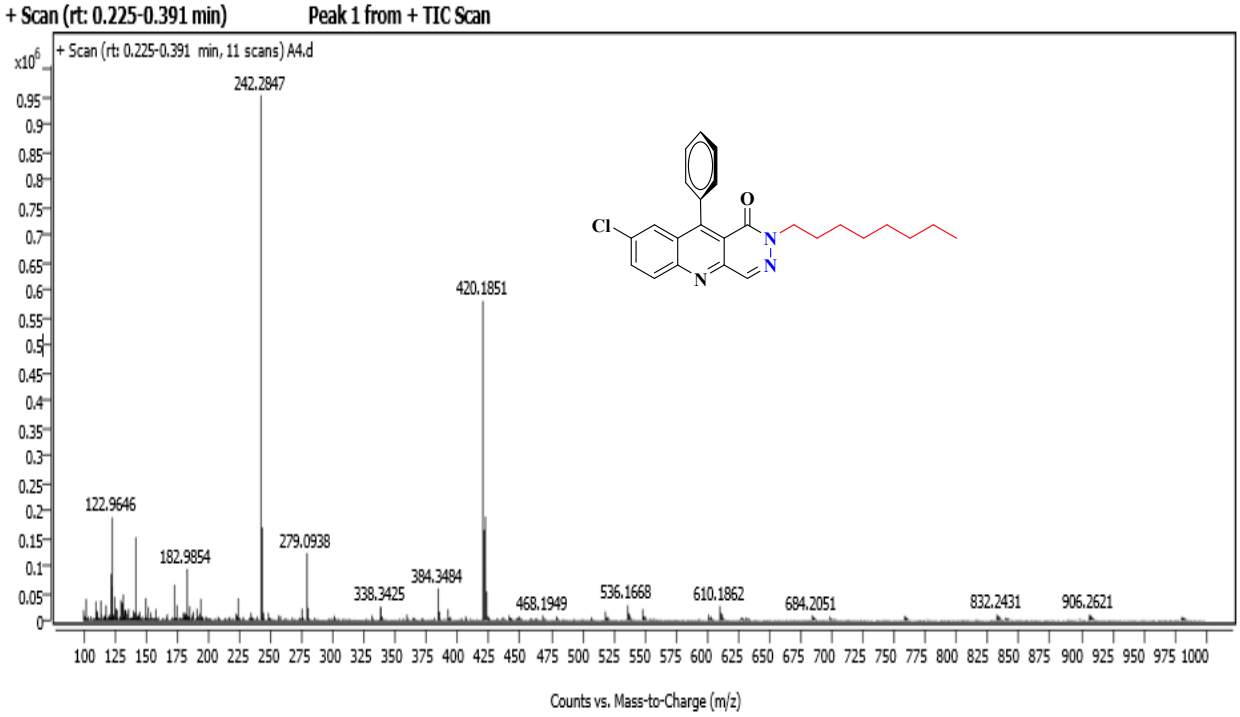


Figure S74: HR-MS spectra of compound 6e

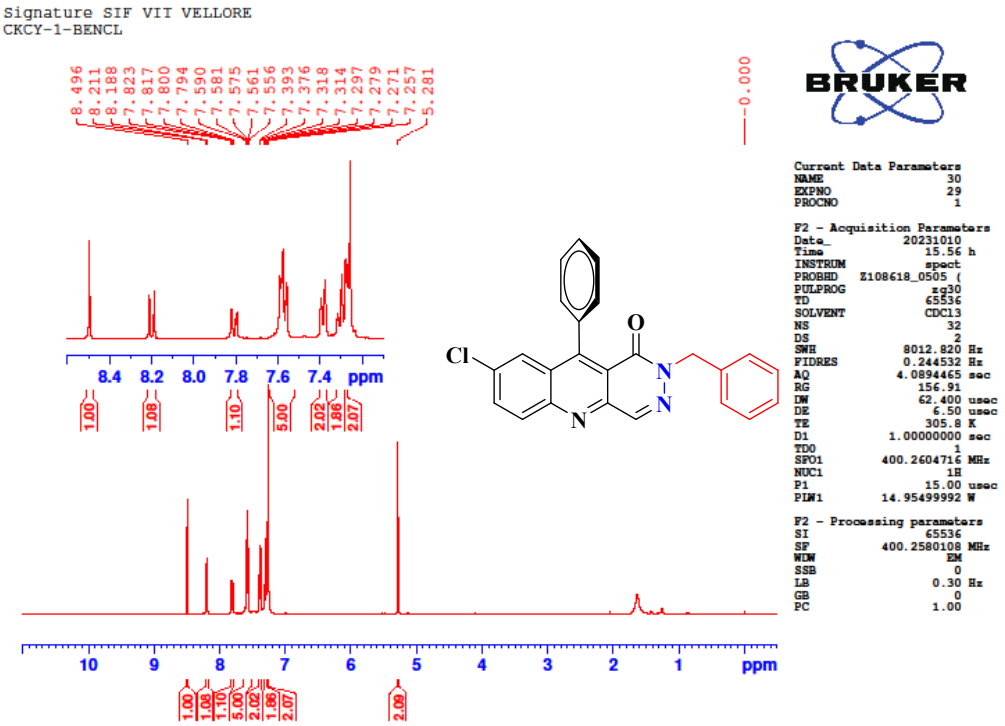


Figure S75: ^{1}H NMR of compound 6f

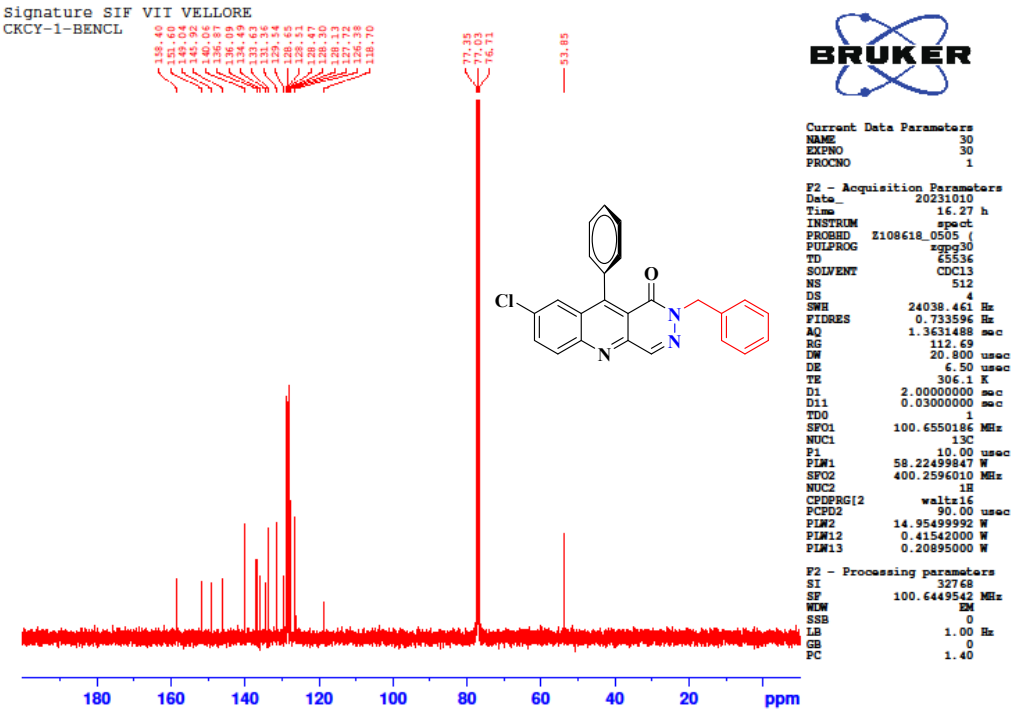


Figure S76: ^{13}C NMR of compound 6f

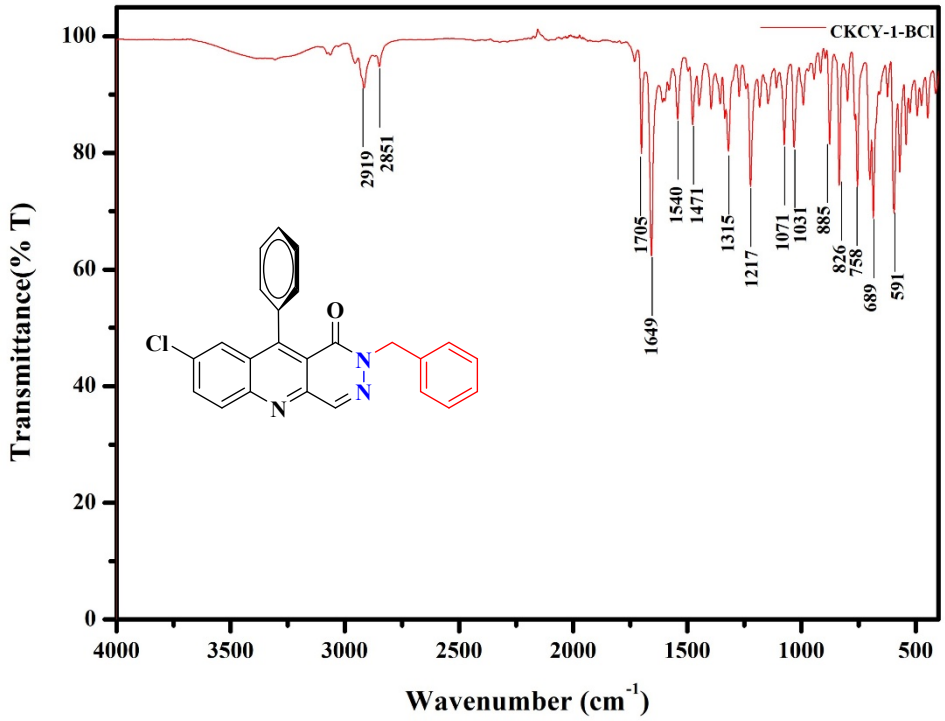


Figure S77: IR spectra of compound 6f

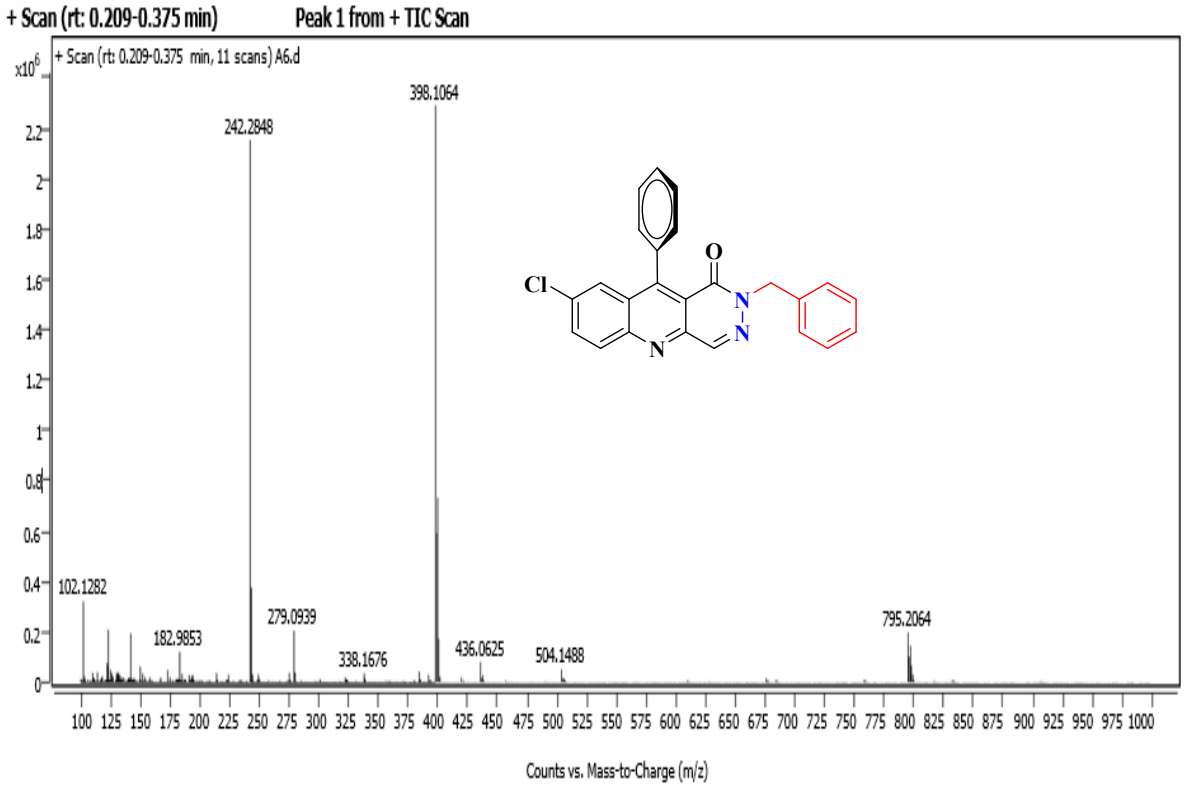


Figure S78: HR-MS spectra of compound 6f

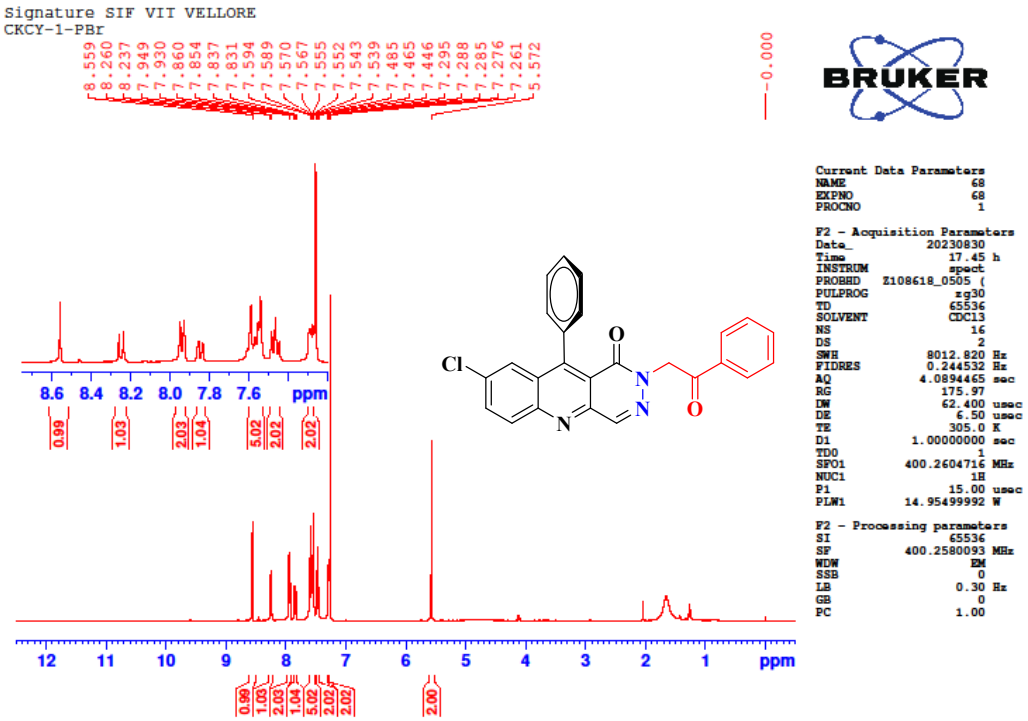


Figure S79: ^{1}H NMR of compound 6g

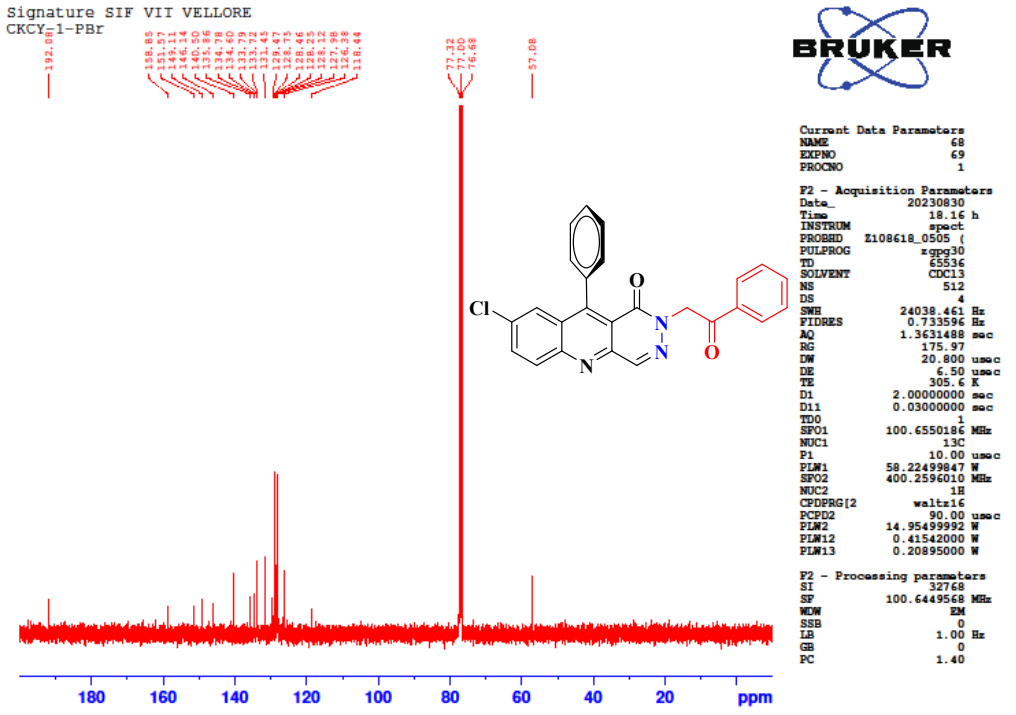


Figure S80: ^{13}C NMR of compound 6g

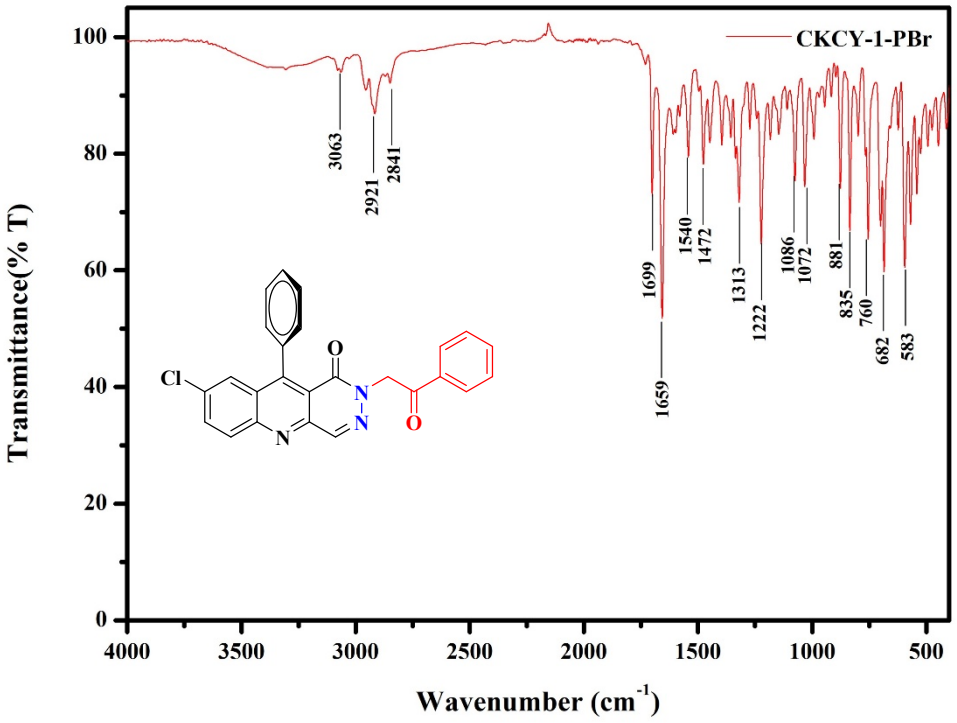


Figure S81: IR spectra of compound 6g

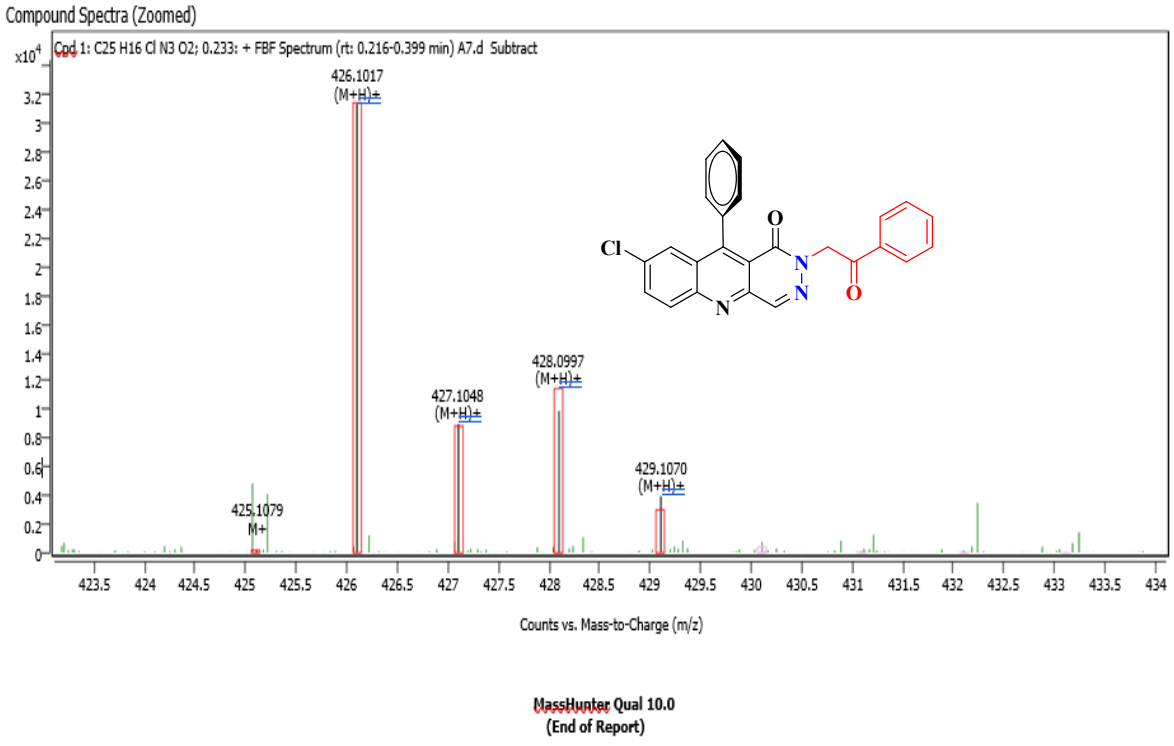


Figure S82: HR-MS spectra of compound 6g

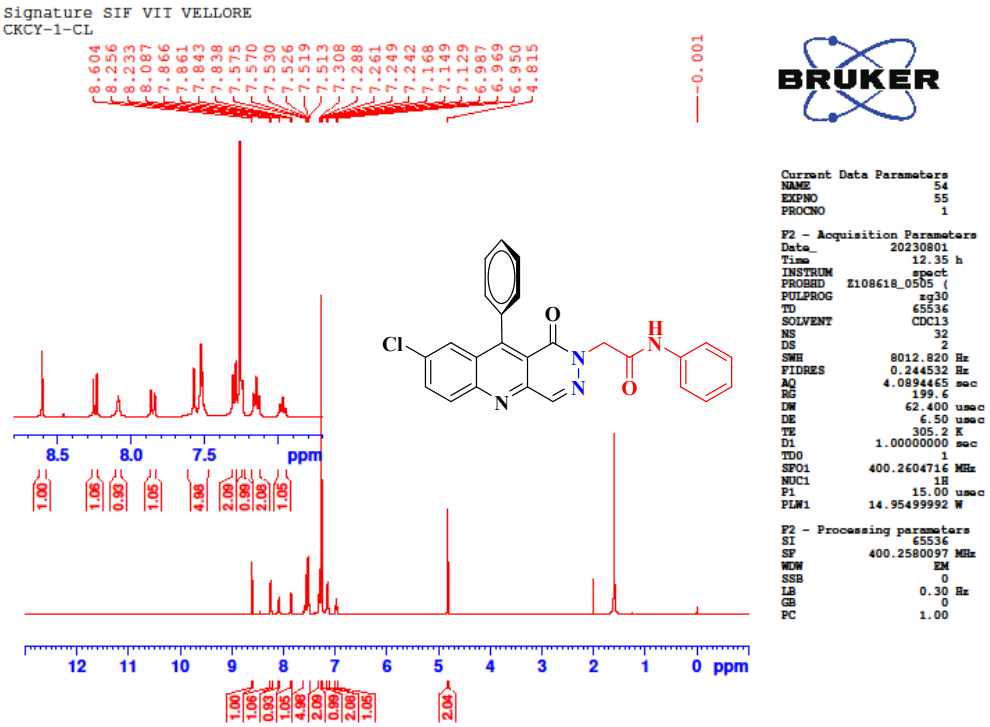


Figure S83: ^{1}H NMR of compound 6h

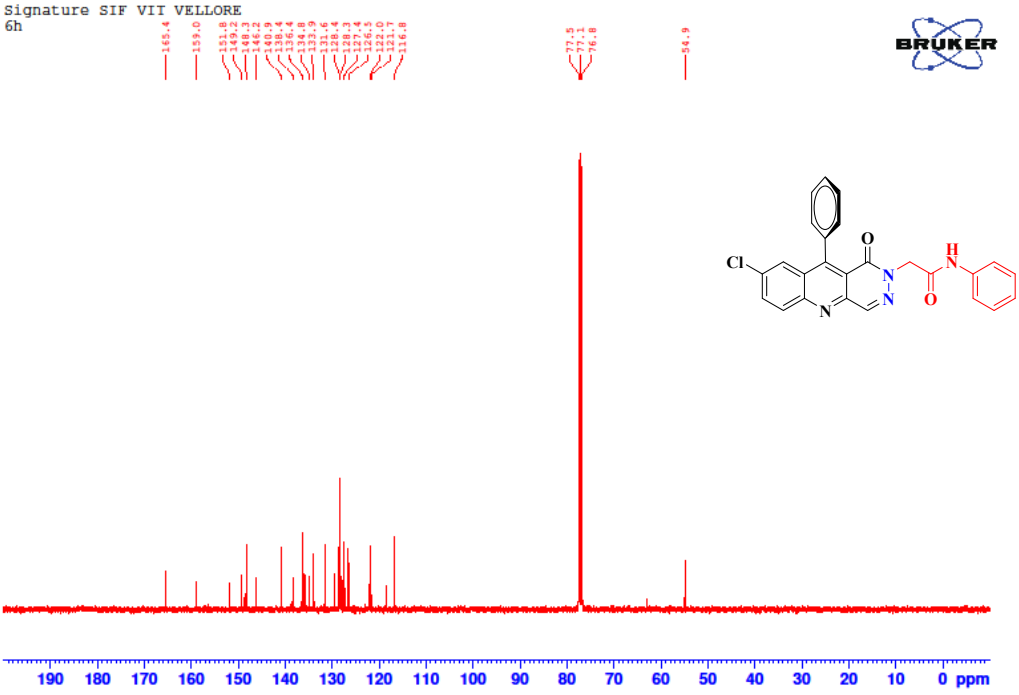


Figure S84: ^{13}C NMR of compound 6h

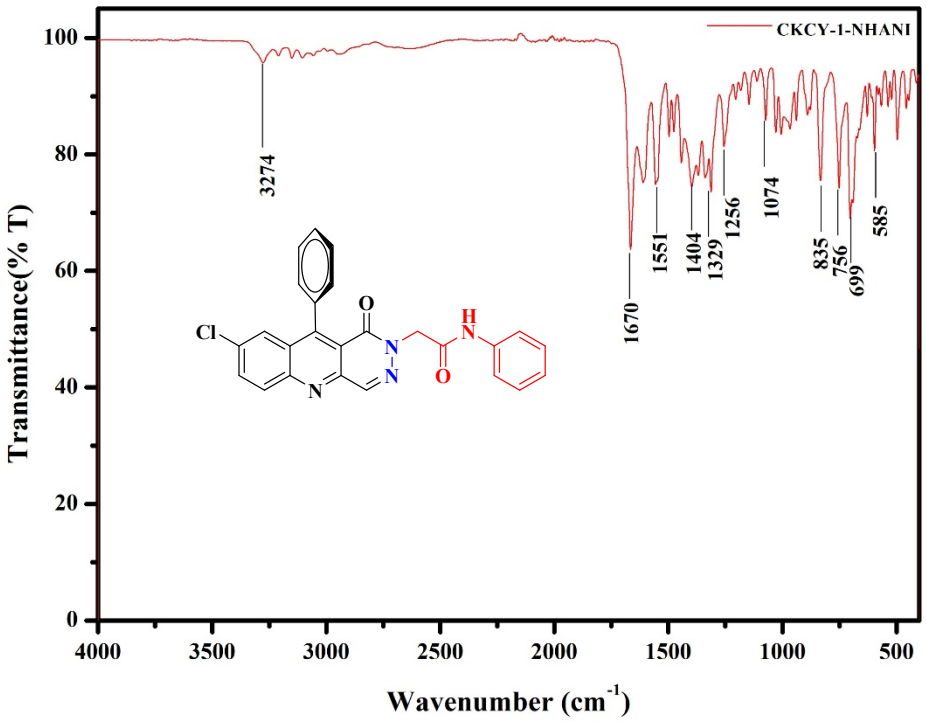


Figure S85: IR spectra of compound 6h

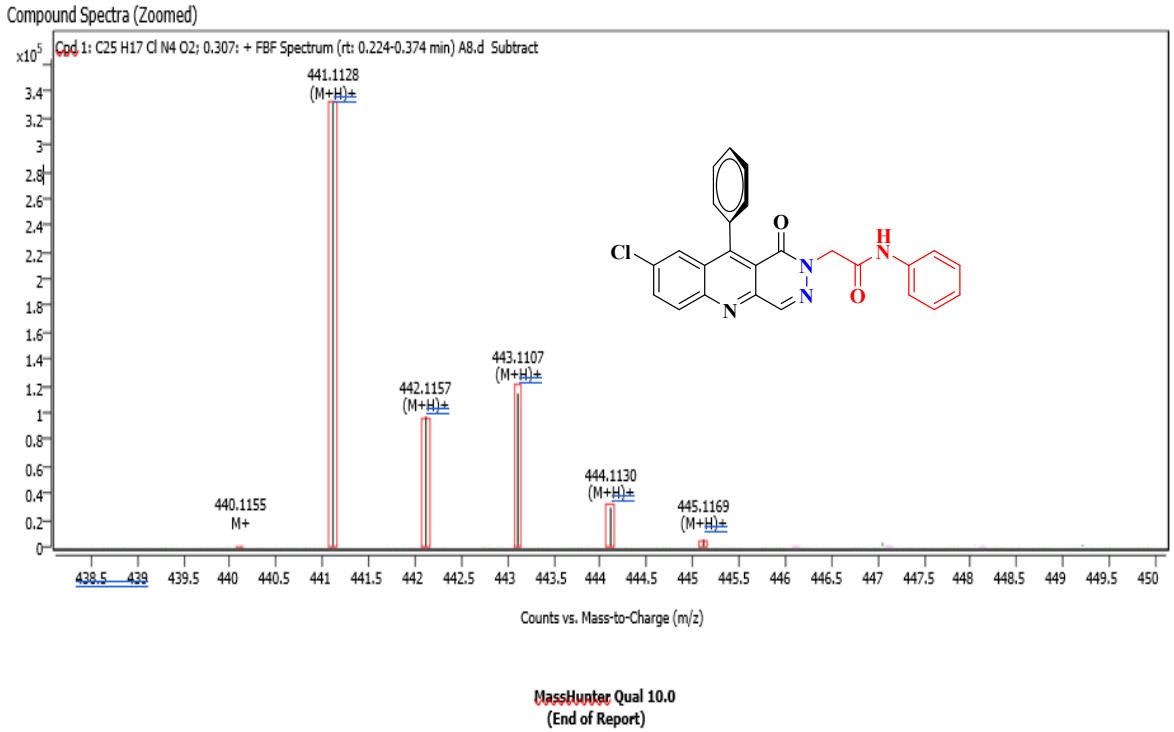


Figure S86: HR-MS spectra of compound 6h

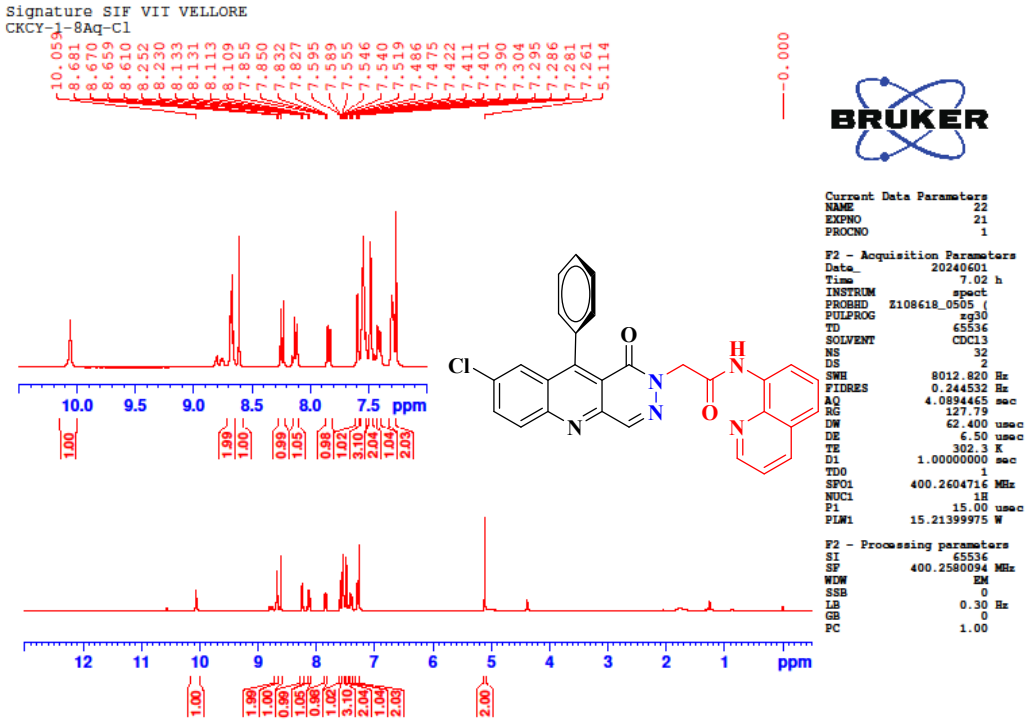


Figure S87: ^{1}H NMR of compound 6i

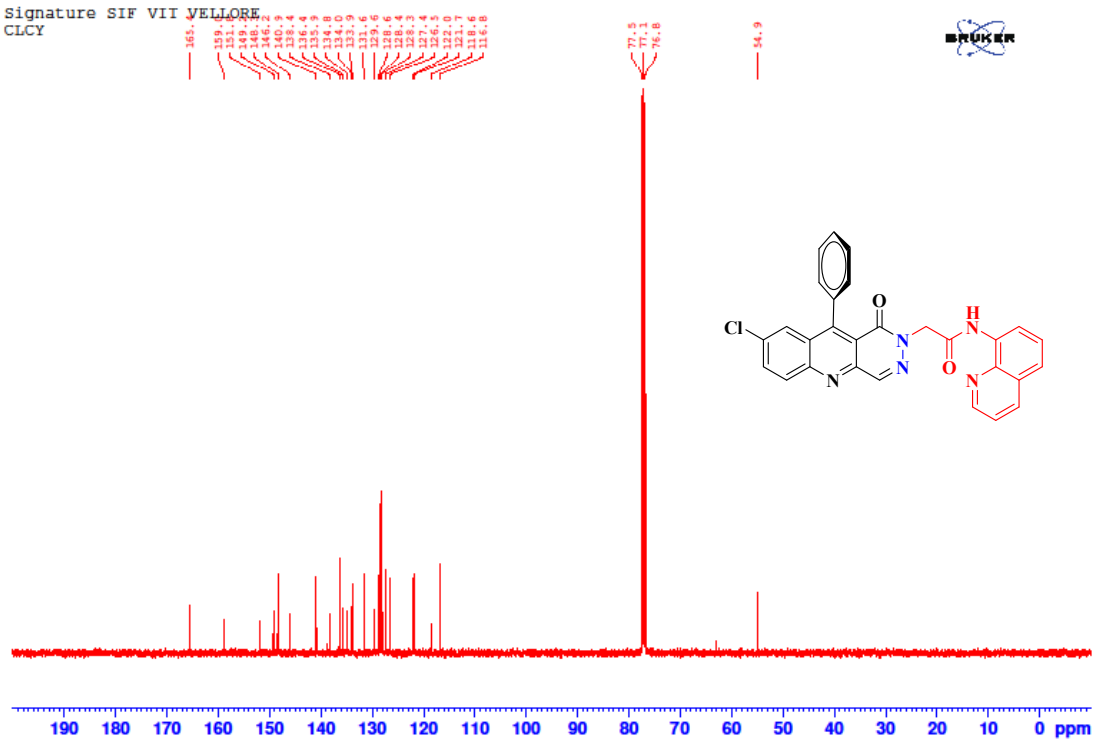


Figure S88: ^{13}C NMR of compound 6i

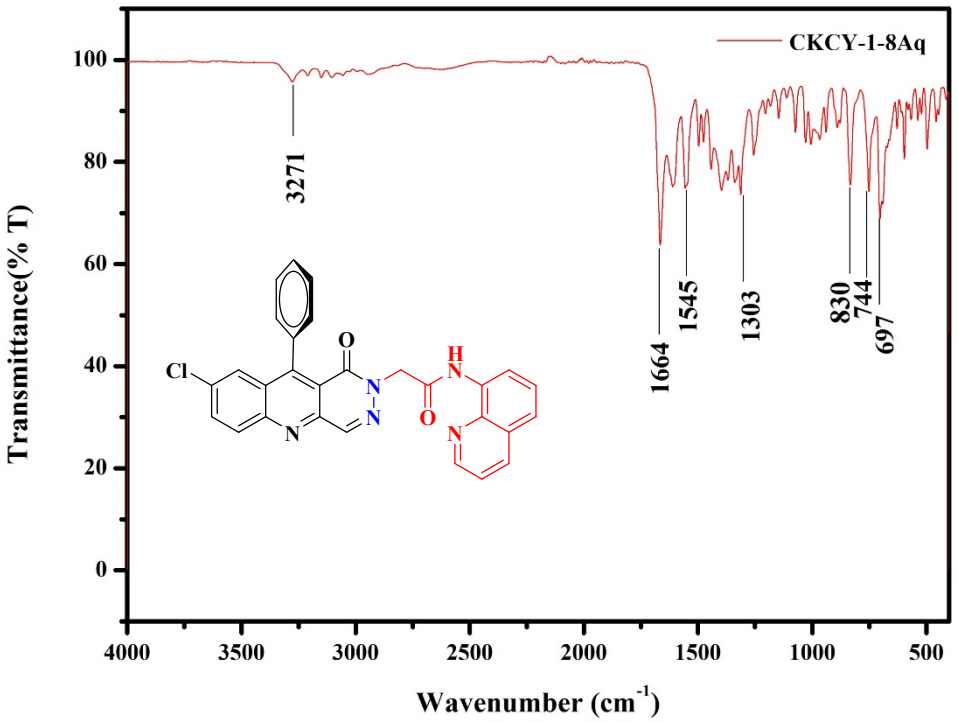


Figure S89: IR spectra of compound 6i

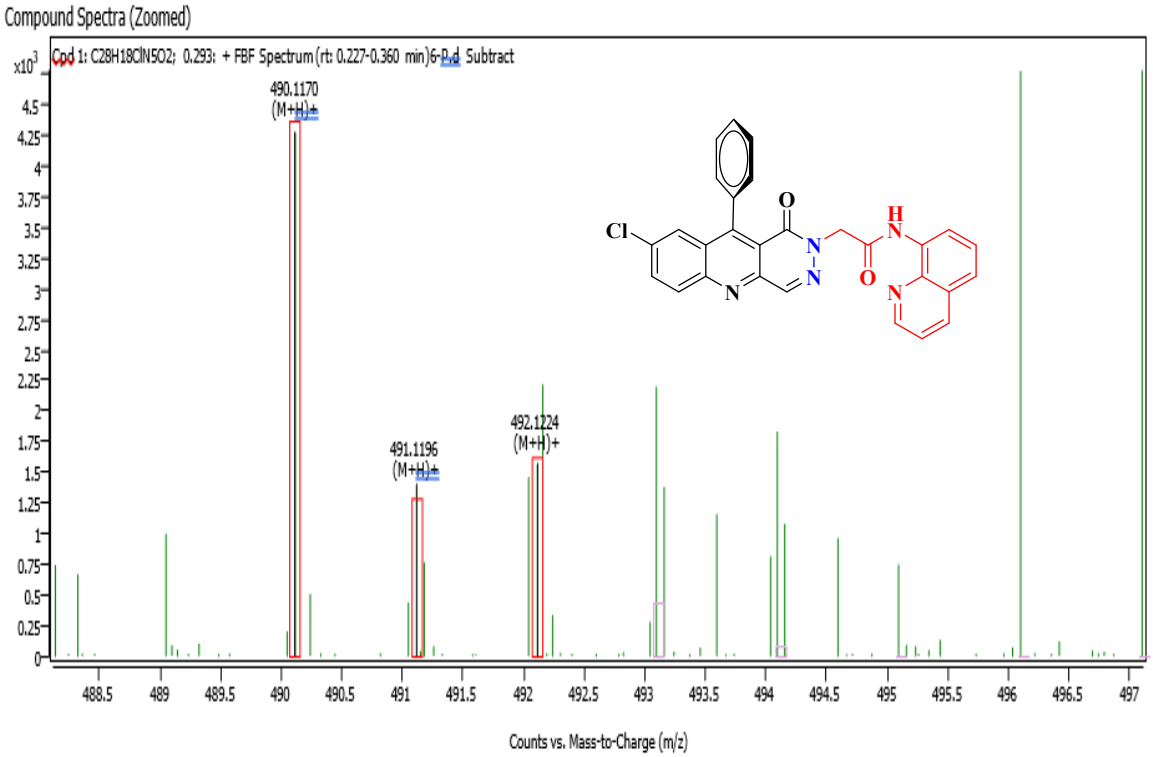


Figure S90: HR-MS spectra of compound 6i

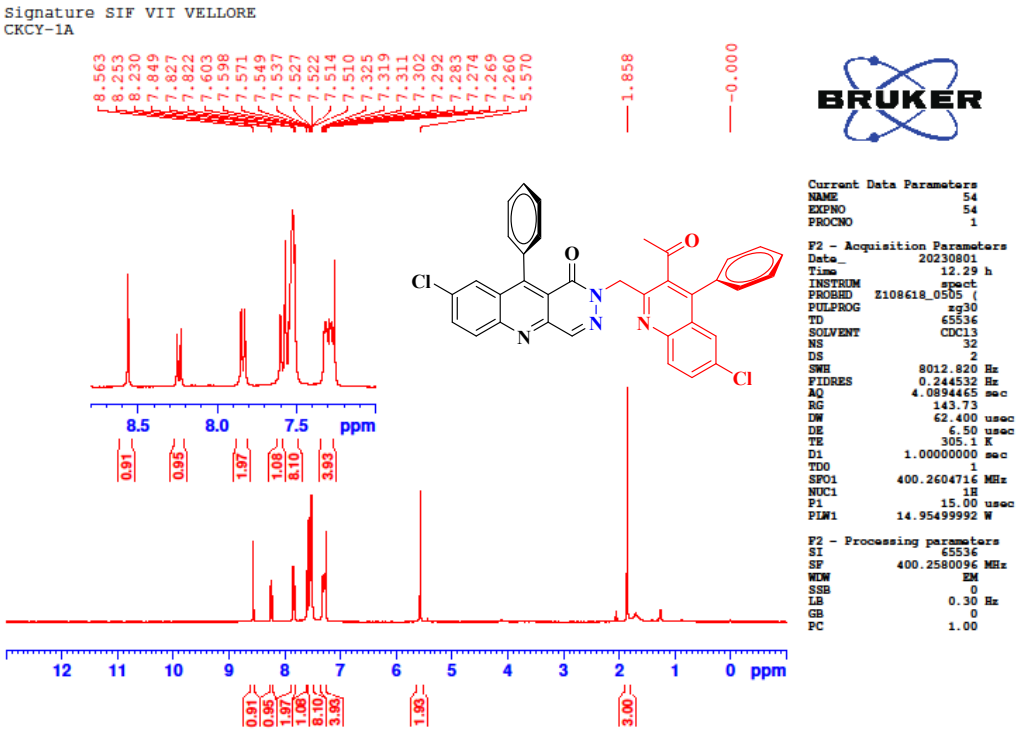


Figure S91: ^{1}H NMR of compound 6j

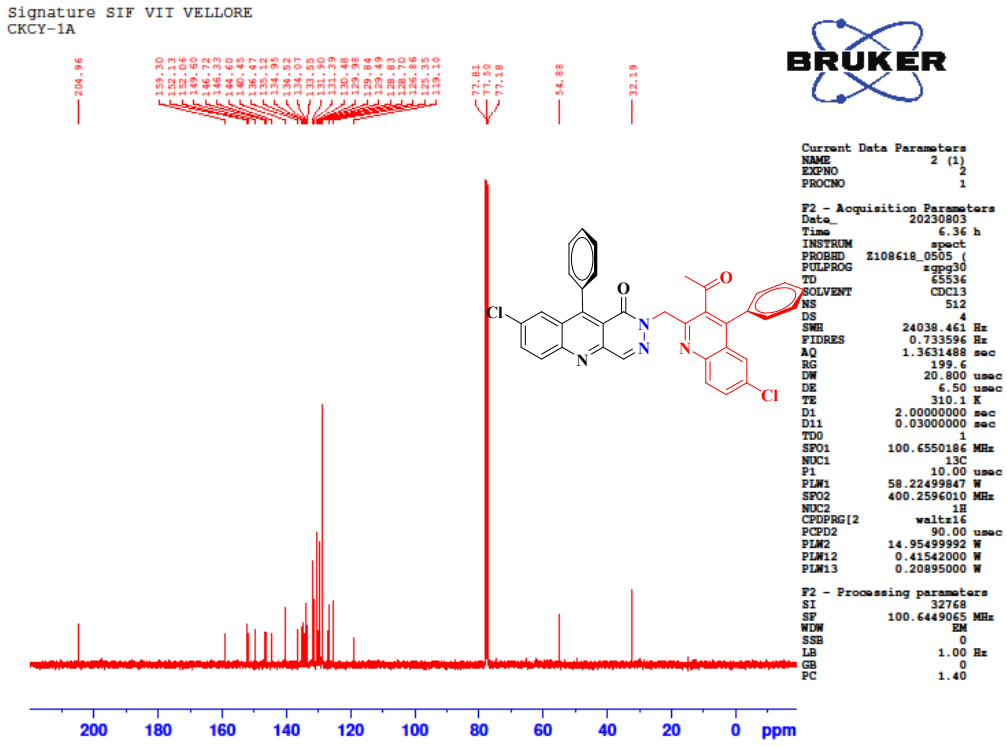


Figure S92: ^{13}C NMR of compound 6j

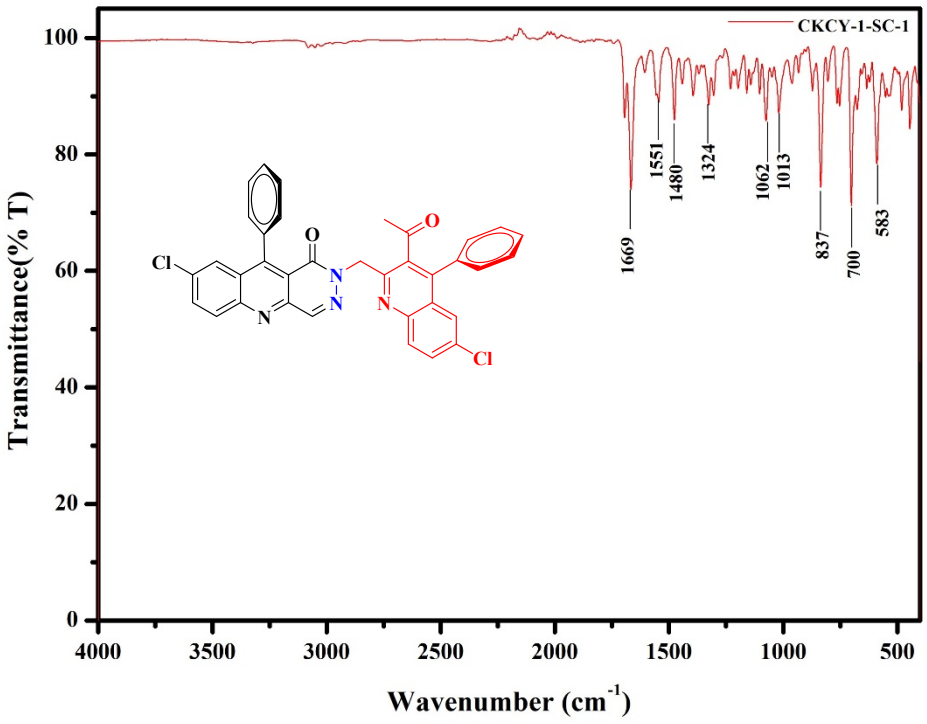


Figure S93: IR spectra of compound 6j

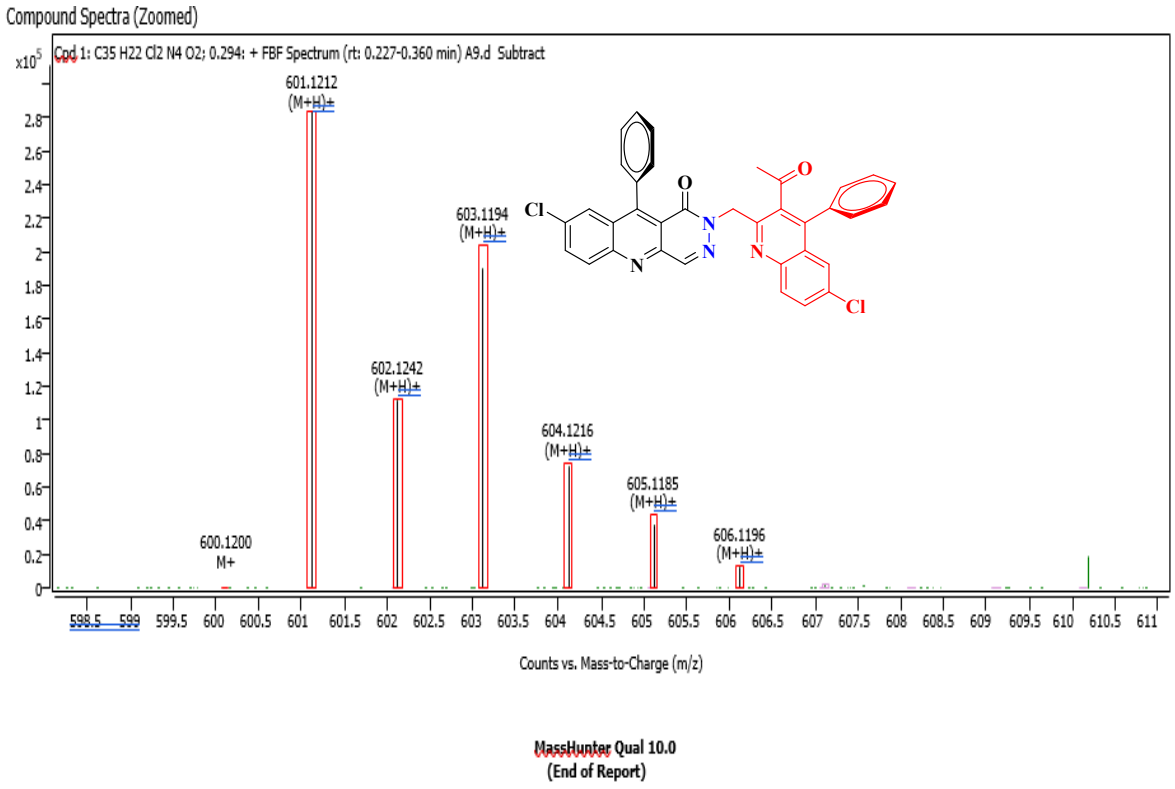


Figure S94: HR-MS spectra of compound 6j

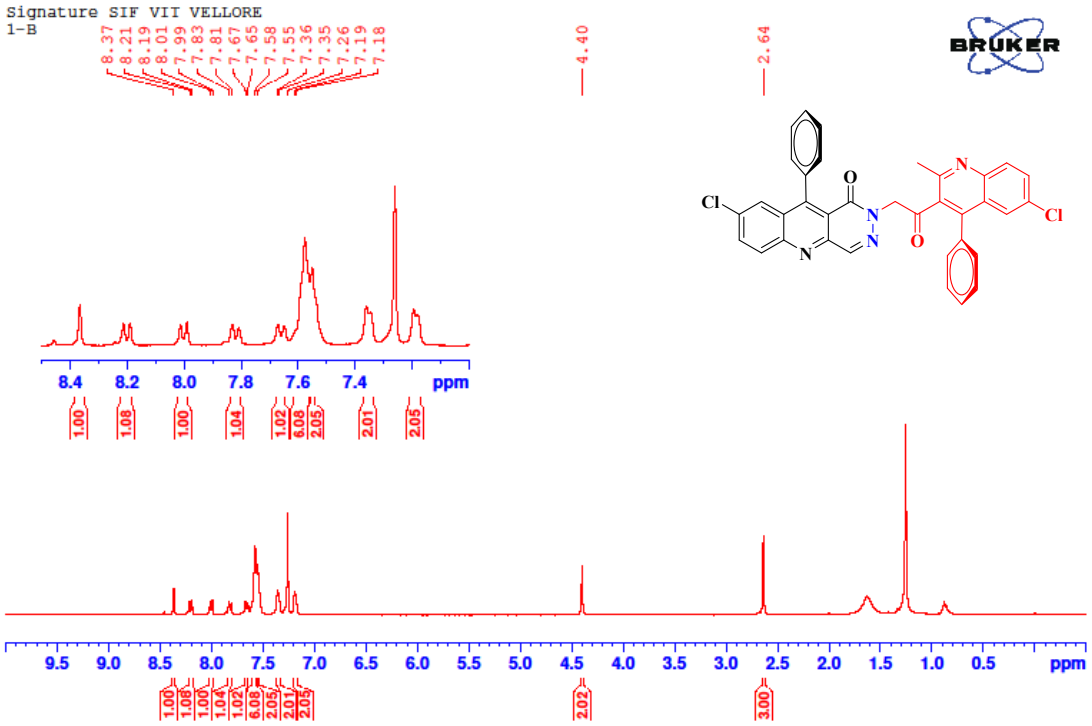


Figure S95: ^{1}H NMR of compound 6k

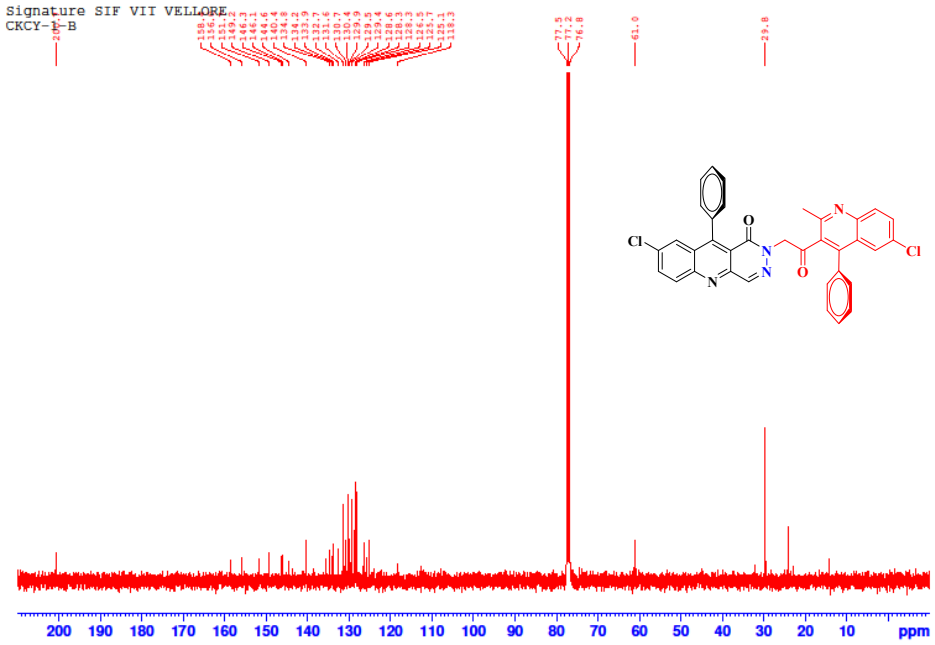


Figure S96: ^{13}C NMR of compound 6k

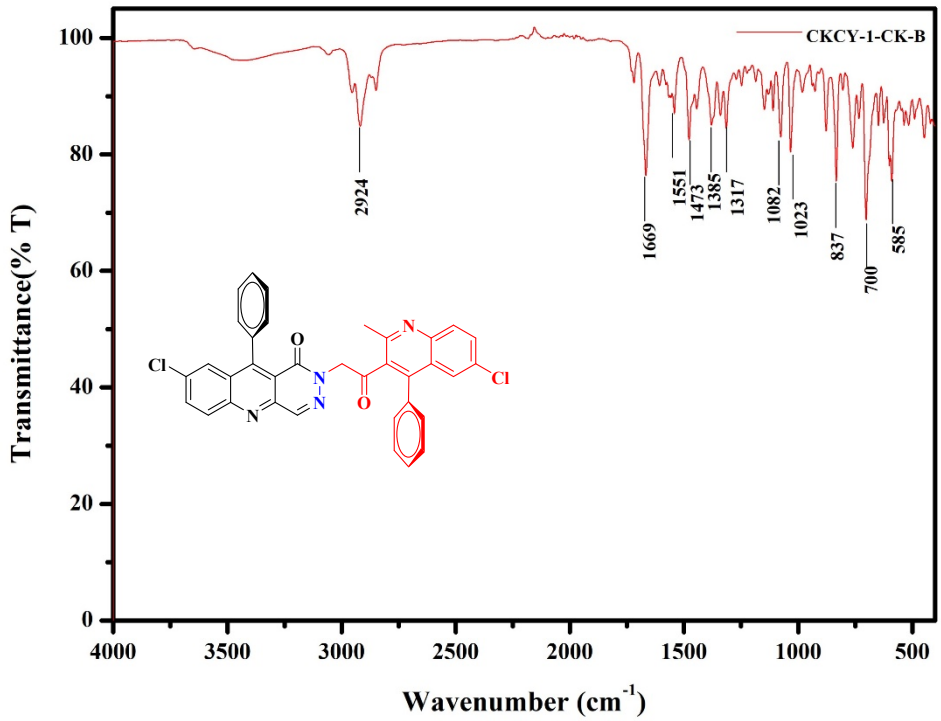


Figure S97: IR spectra of compound 10

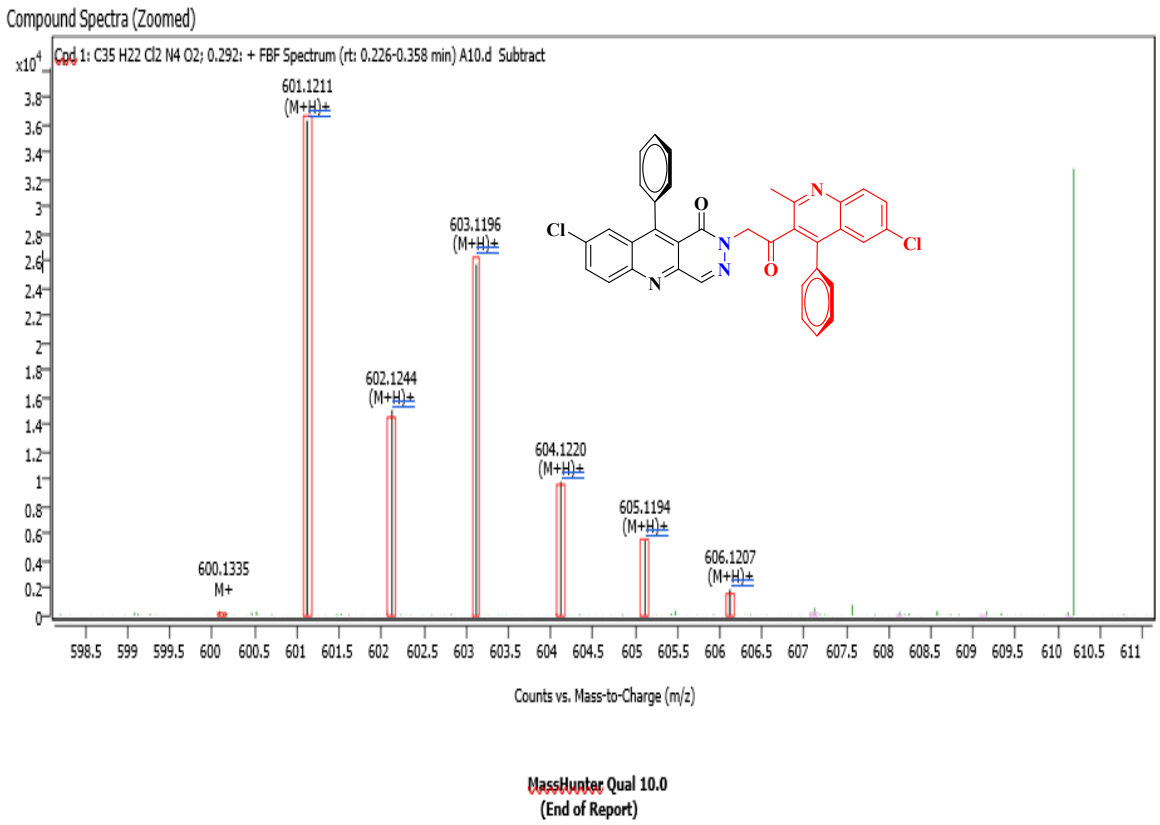


Figure S98: HR-MS spectra of compound 6k

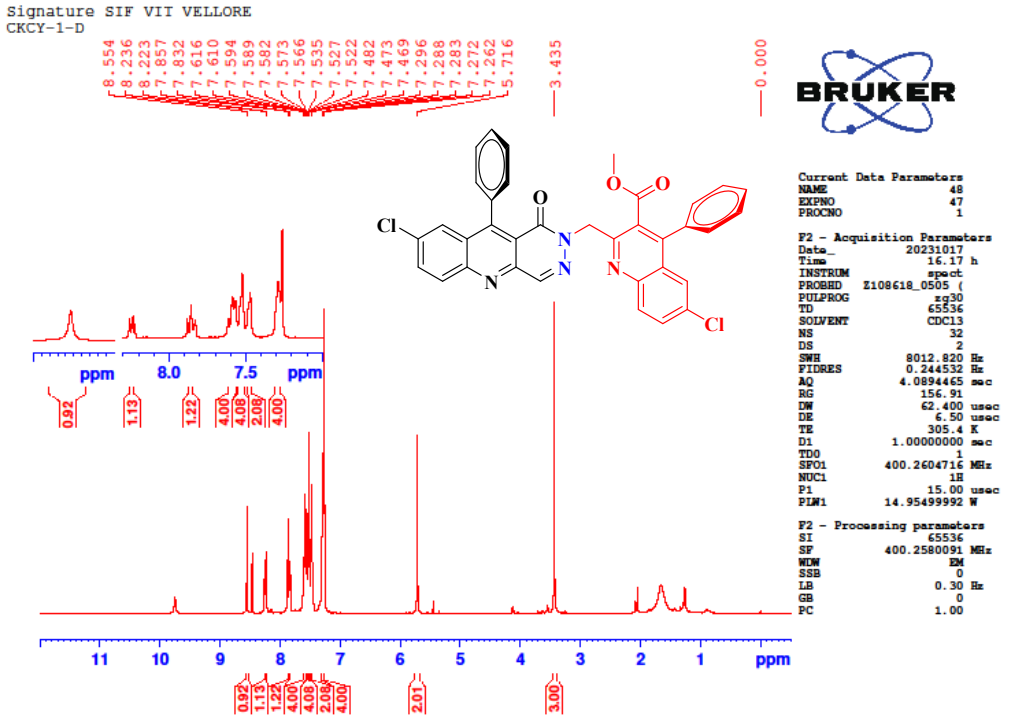


Figure S99: ^{1}H NMR of compound 6l

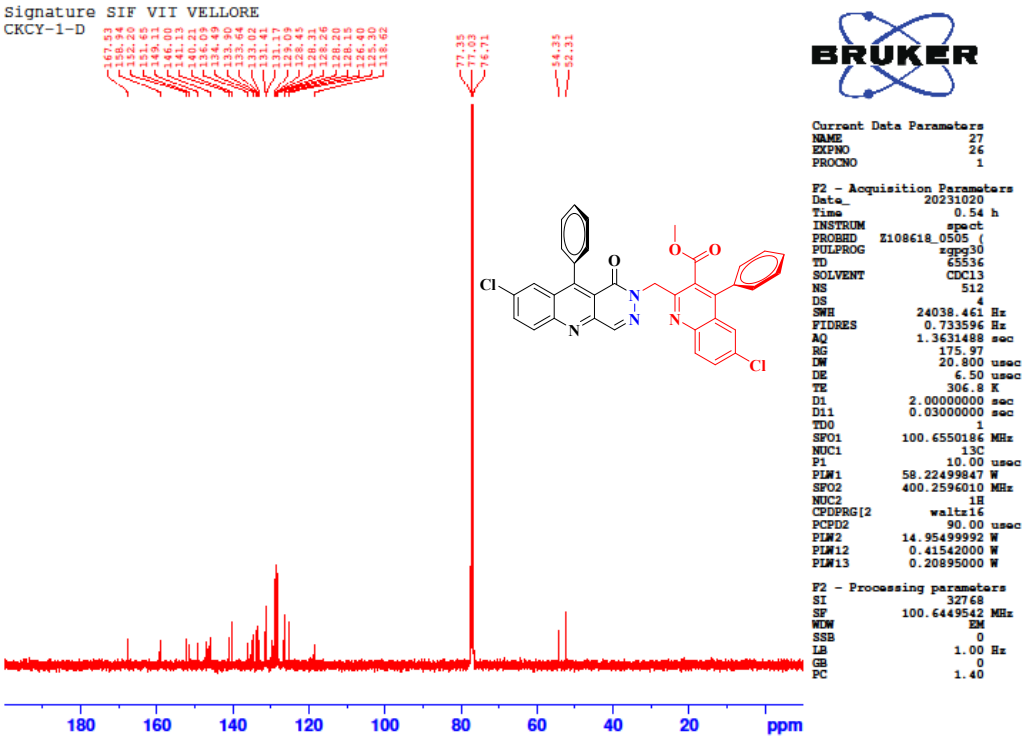


Figure S100: ^{13}C NMR of compound 6l

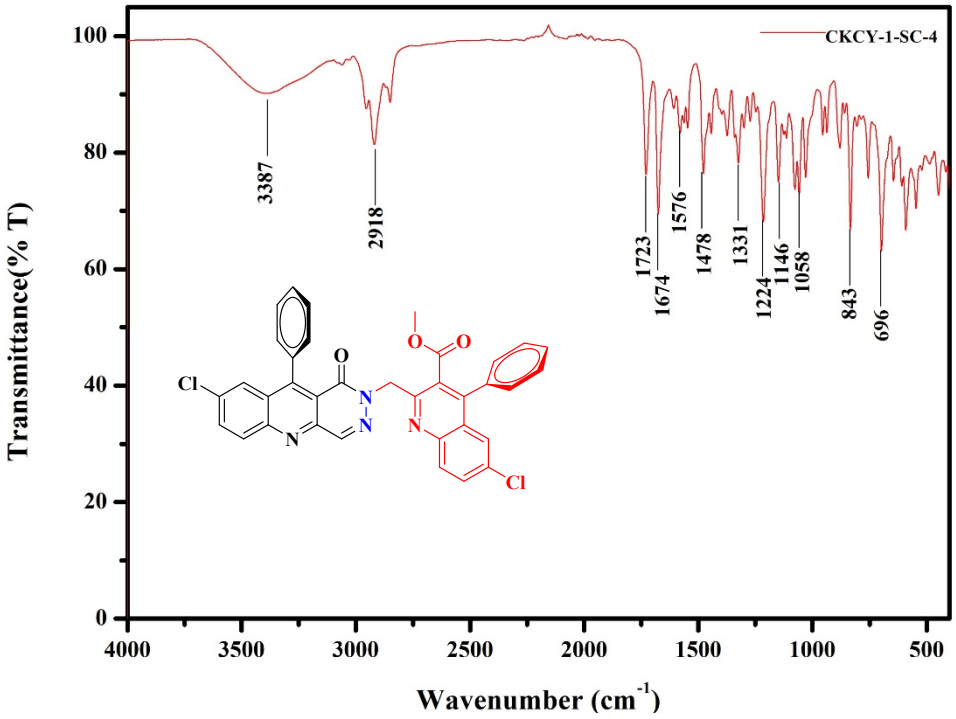


Figure S101: IR spectra of compound 6l

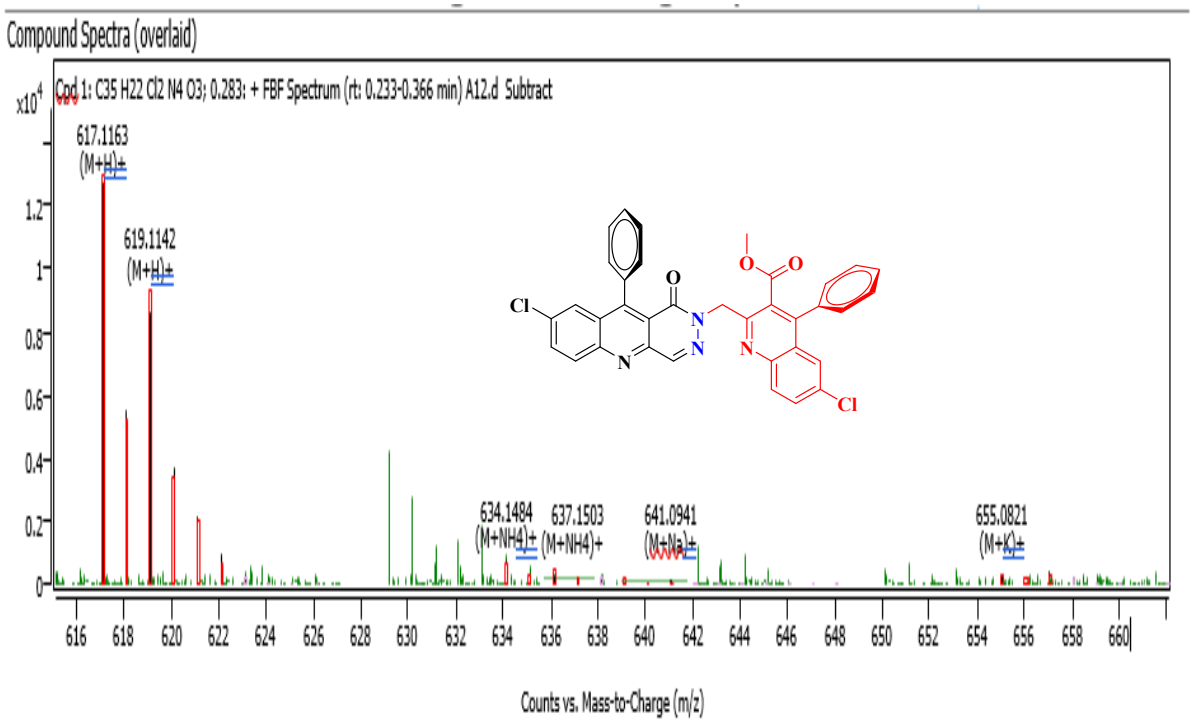


Figure S102: HR-MS spectra of compound 6l

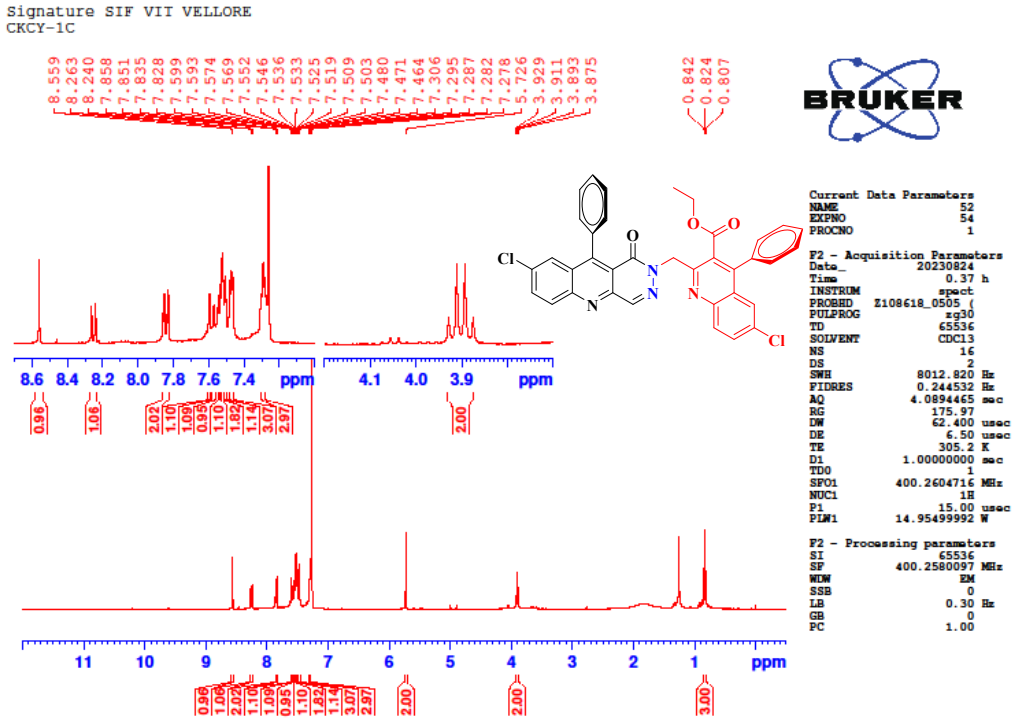


Figure S103: ^{1}H NMR of compound 6m

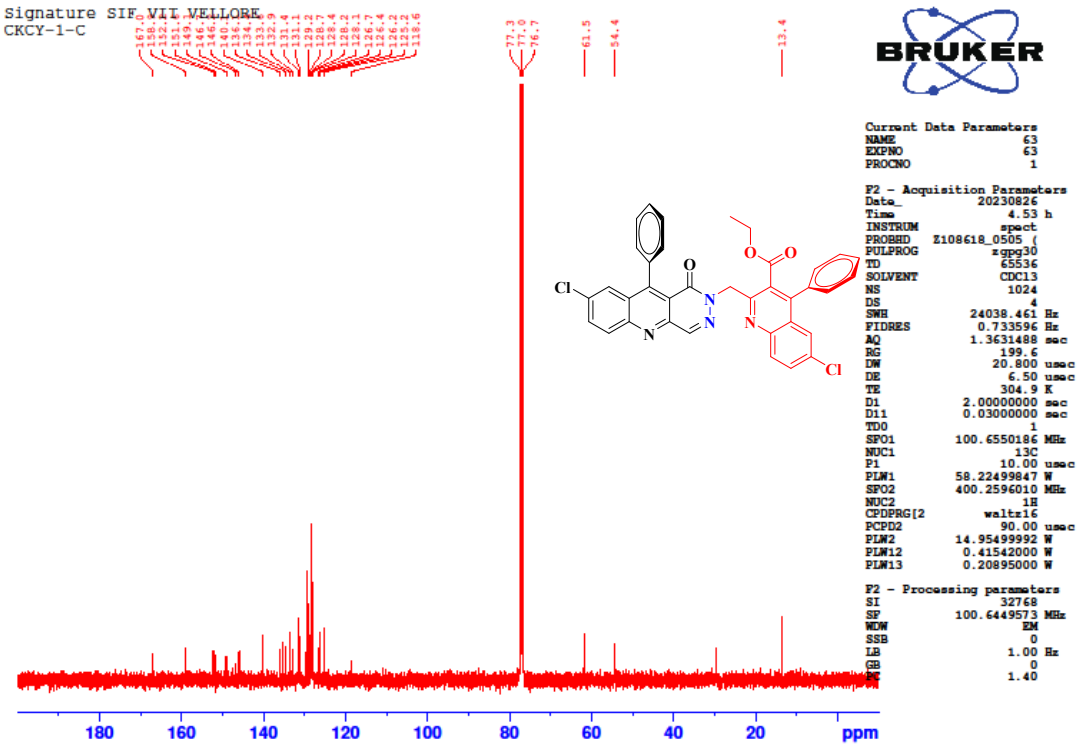


Figure S104: ^{13}C NMR of compound 6m

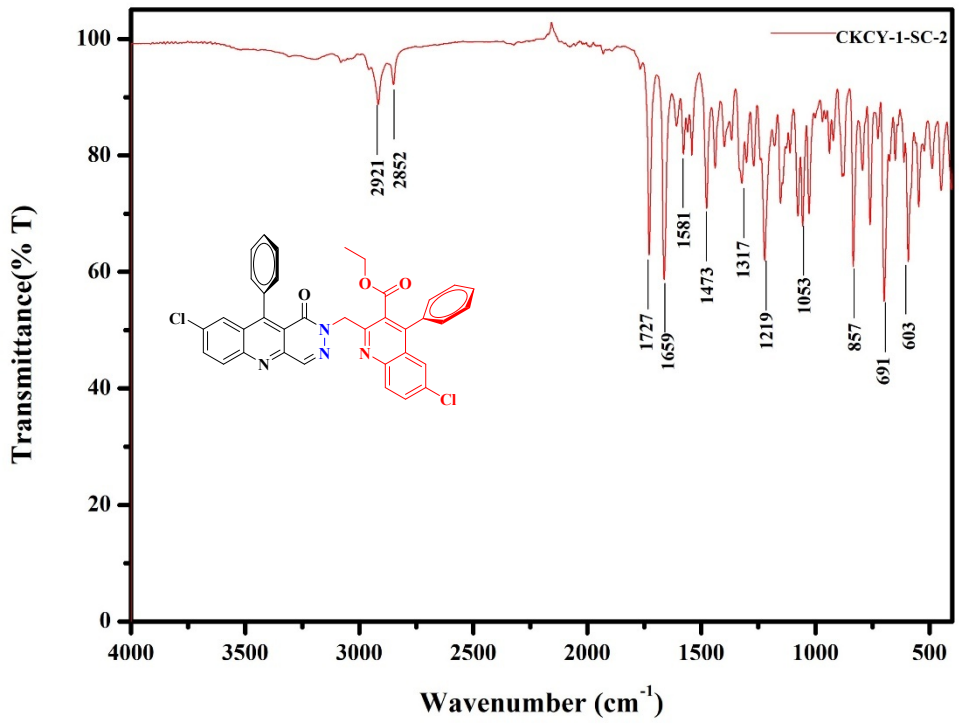


Figure S105: IR spectra of compound 6m

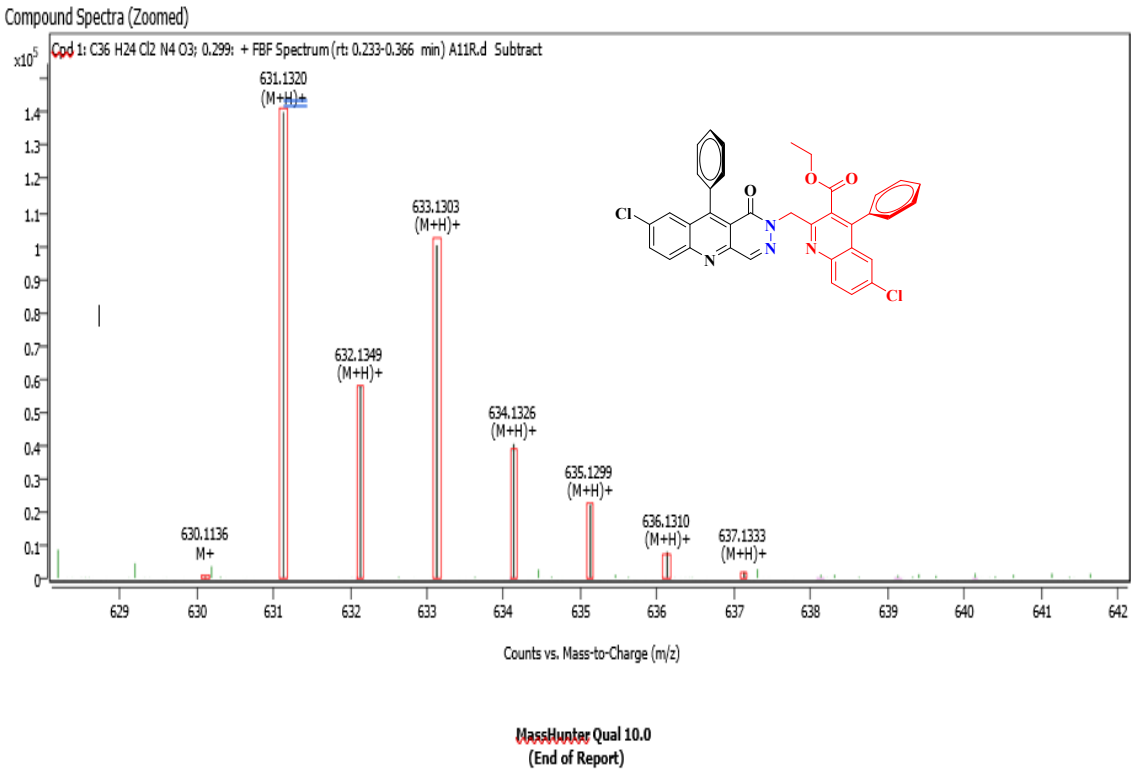


Figure S106: HR-MS spectra of compound 6m

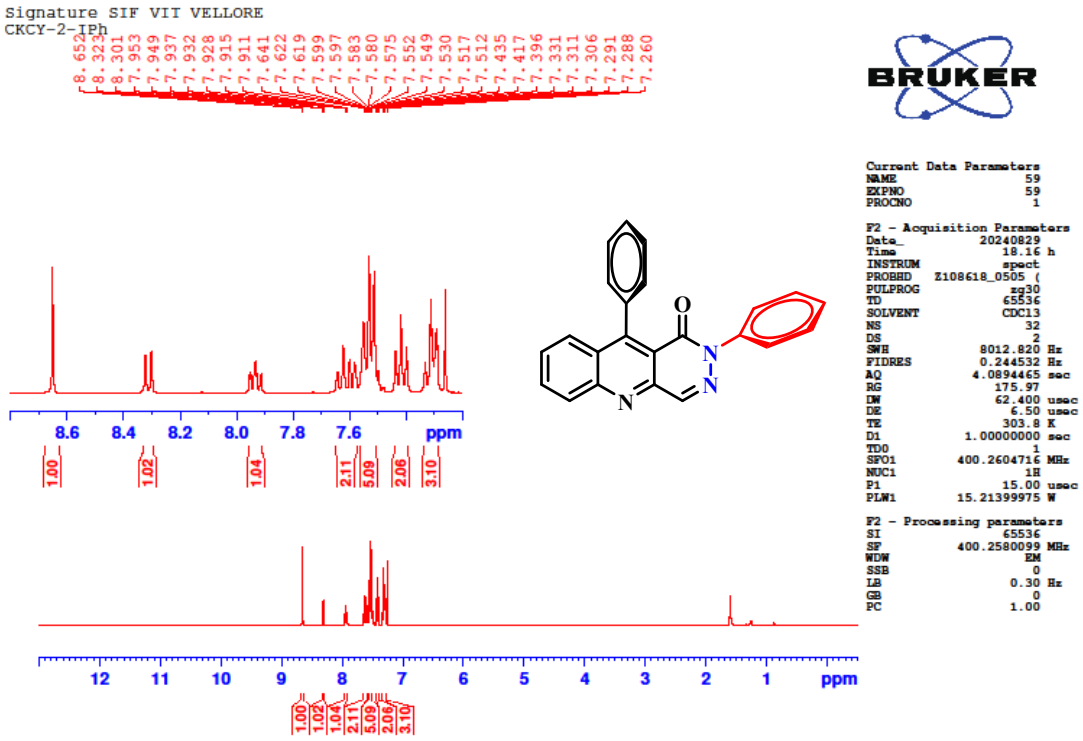


Figure S107: ^{1}H NMR of compound 8a

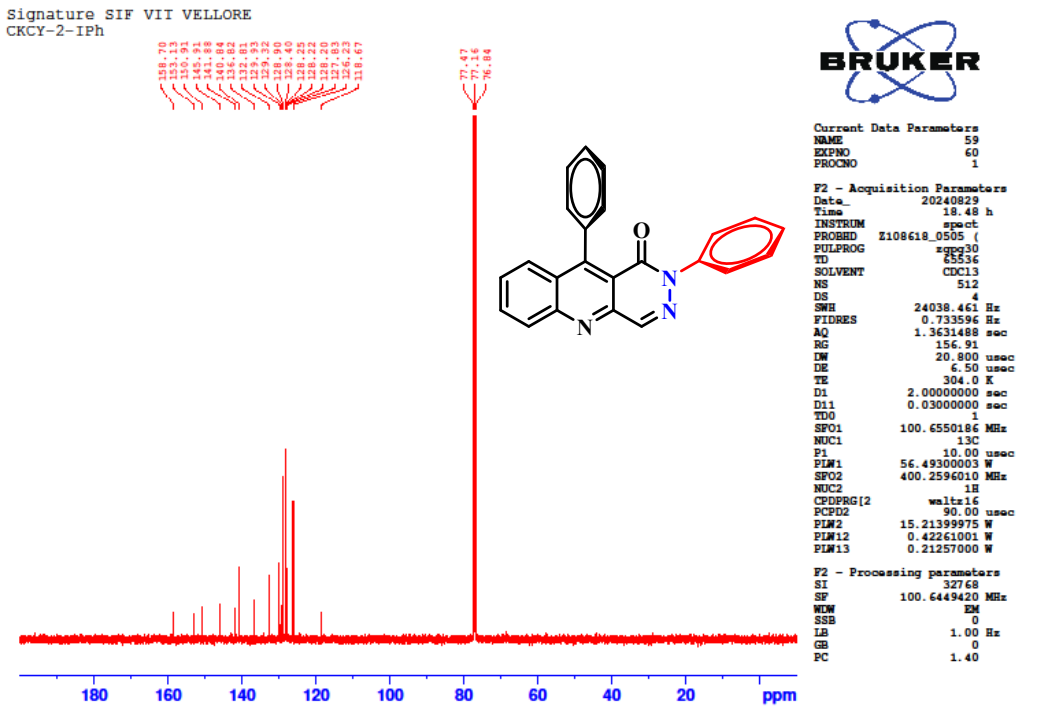


Figure S108: ^{13}C NMR of compound 8a

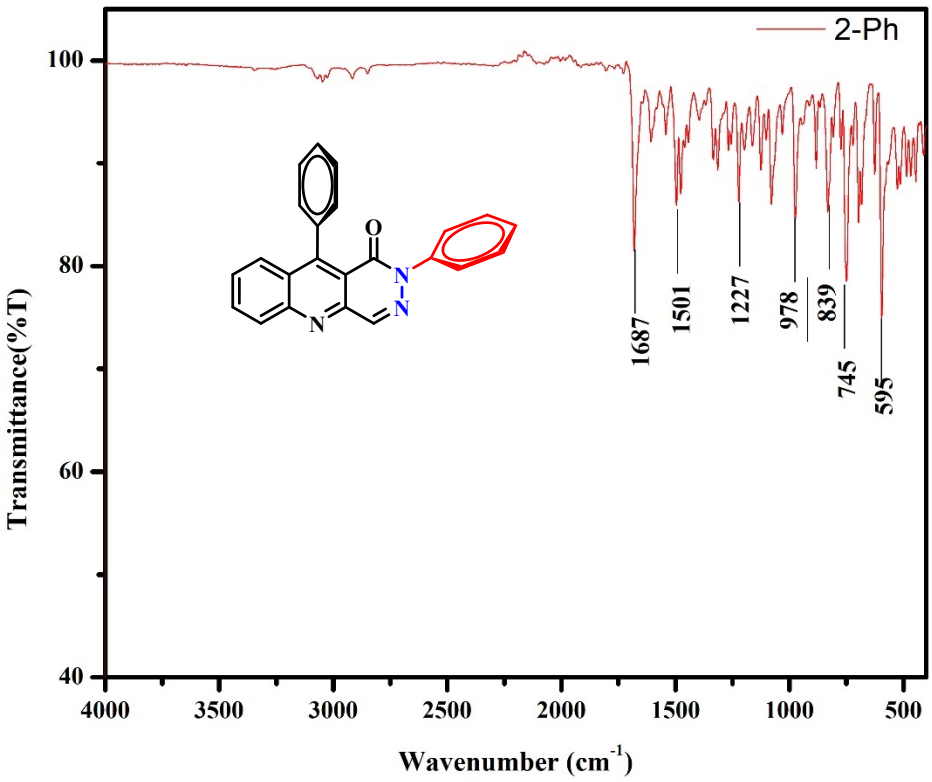


Figure S109: IR spectra of compound 8a

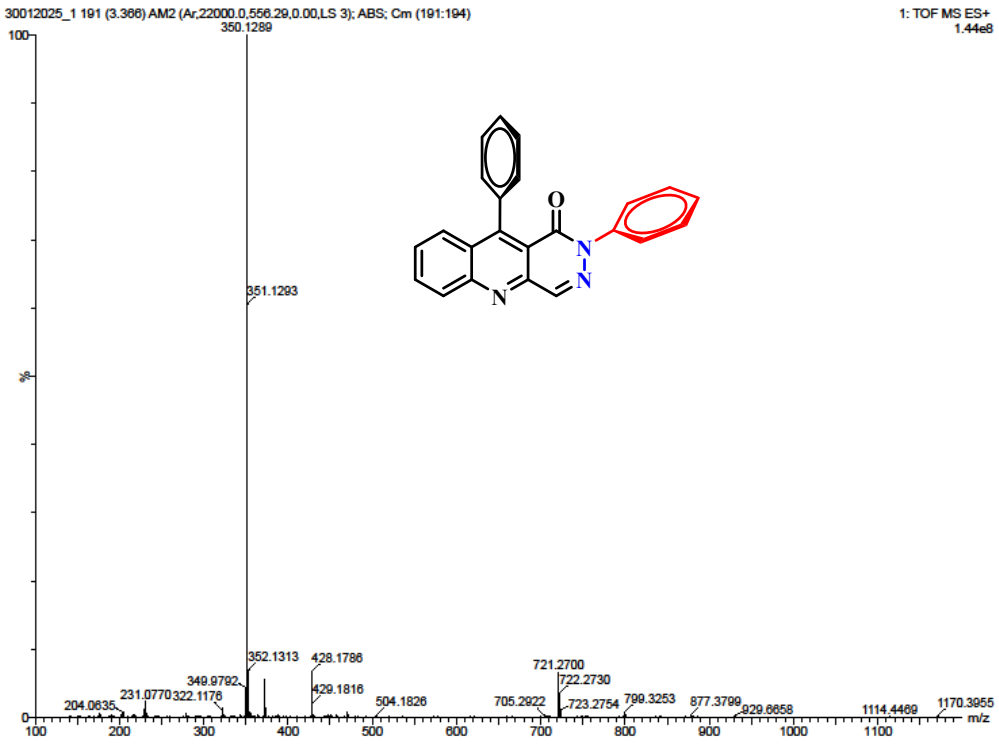


Figure S110: HR-MS spectra of compound 8a

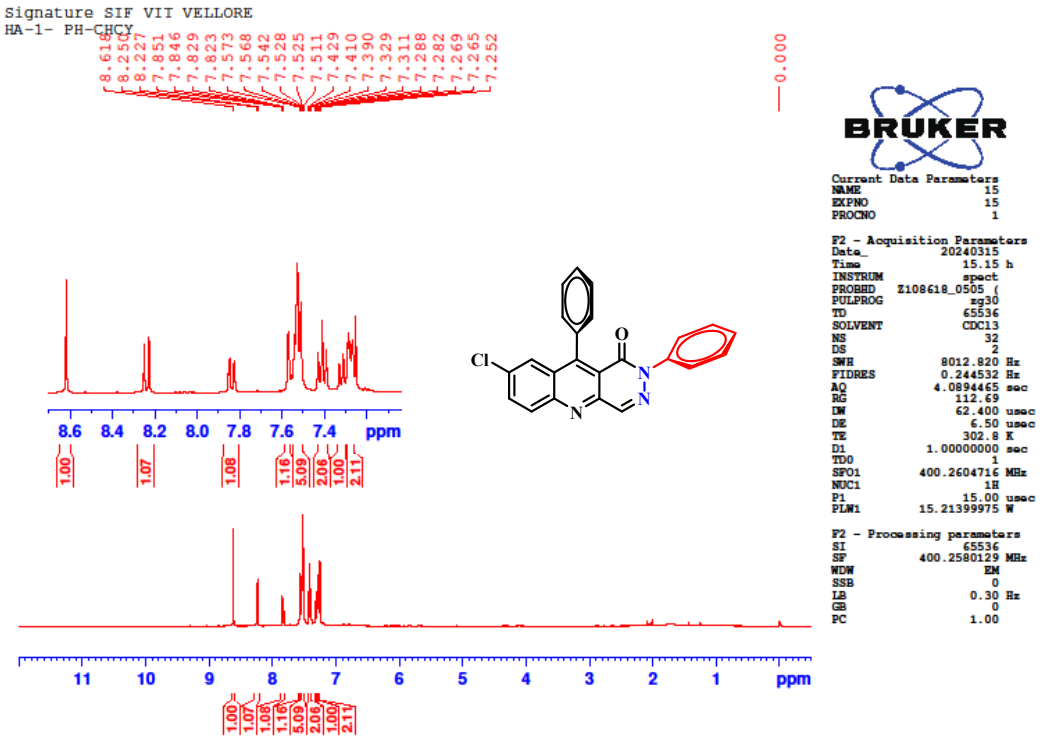


Figure S111: ^{1}H NMR of compound 8b

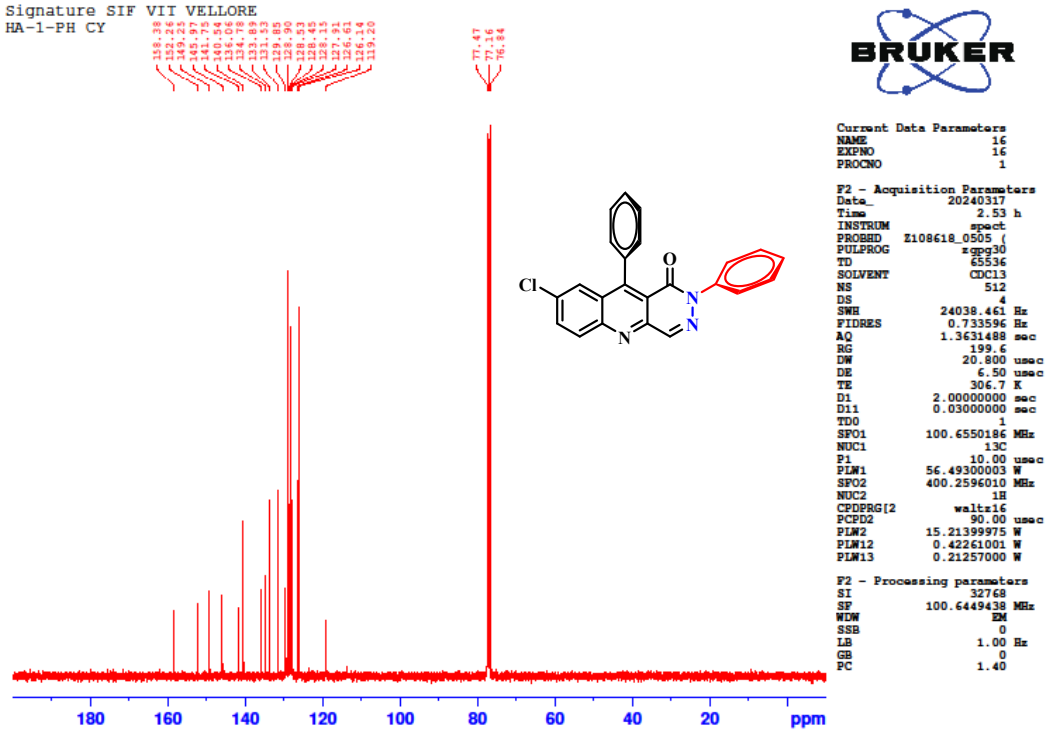


Figure S112: ^{13}C NMR of compound 8b

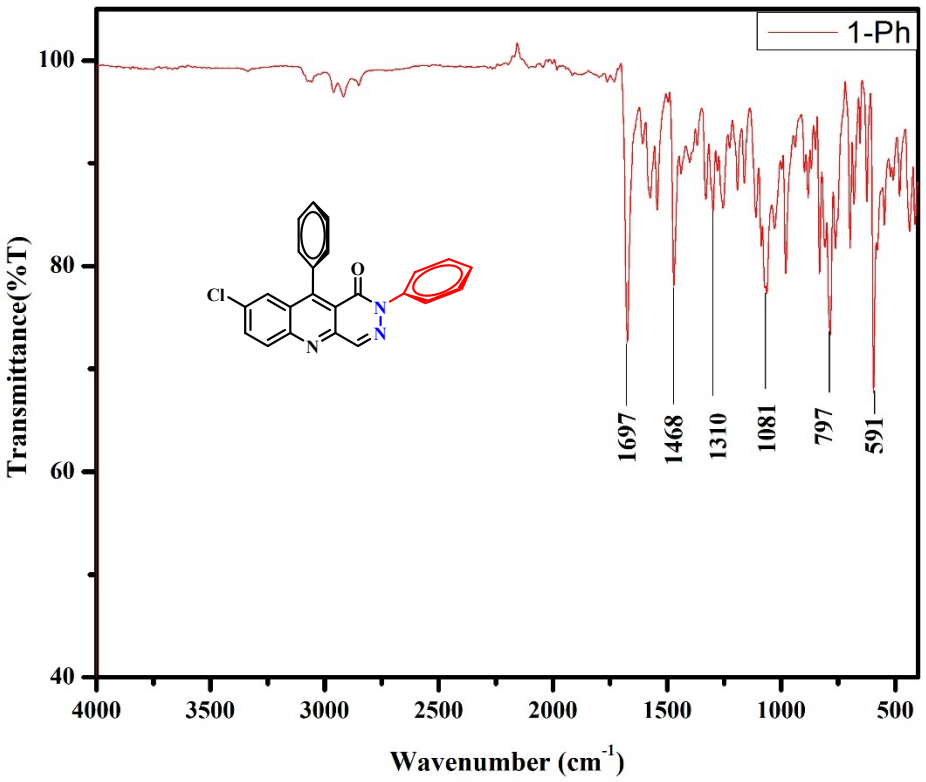


Figure S113: IR spectra of compound 8b

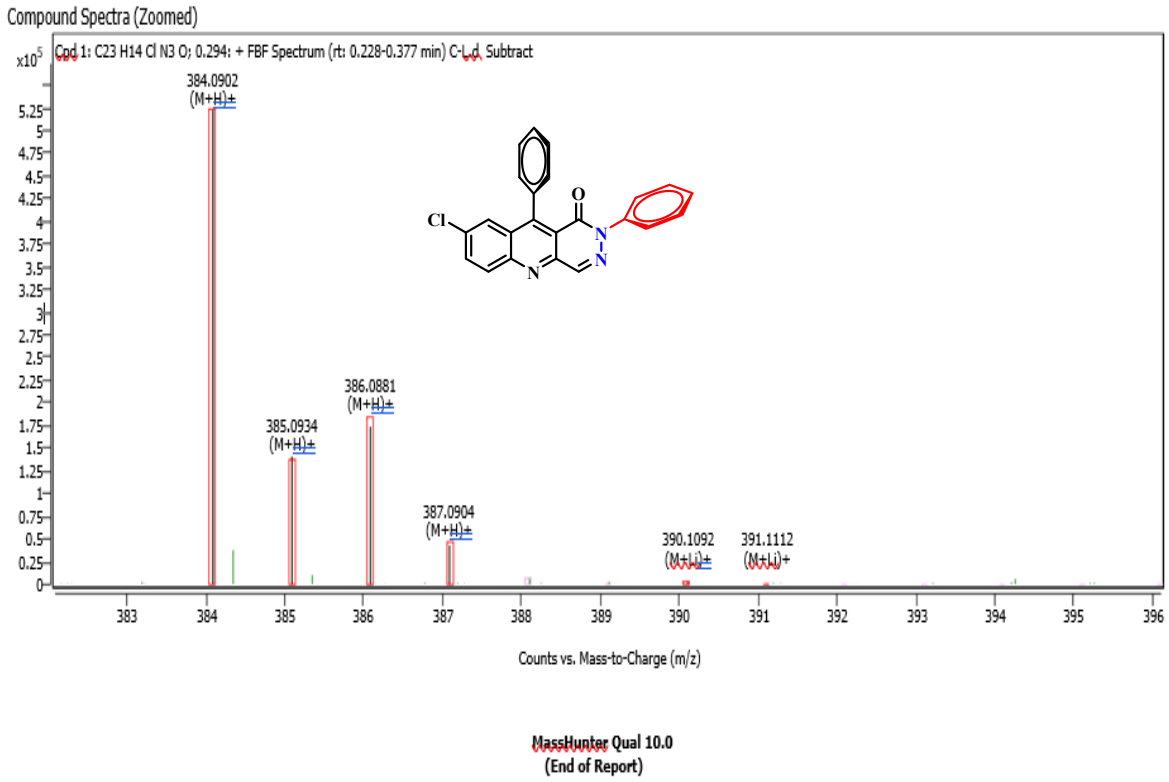


Figure S114: HR-MS spectra of compound 8b

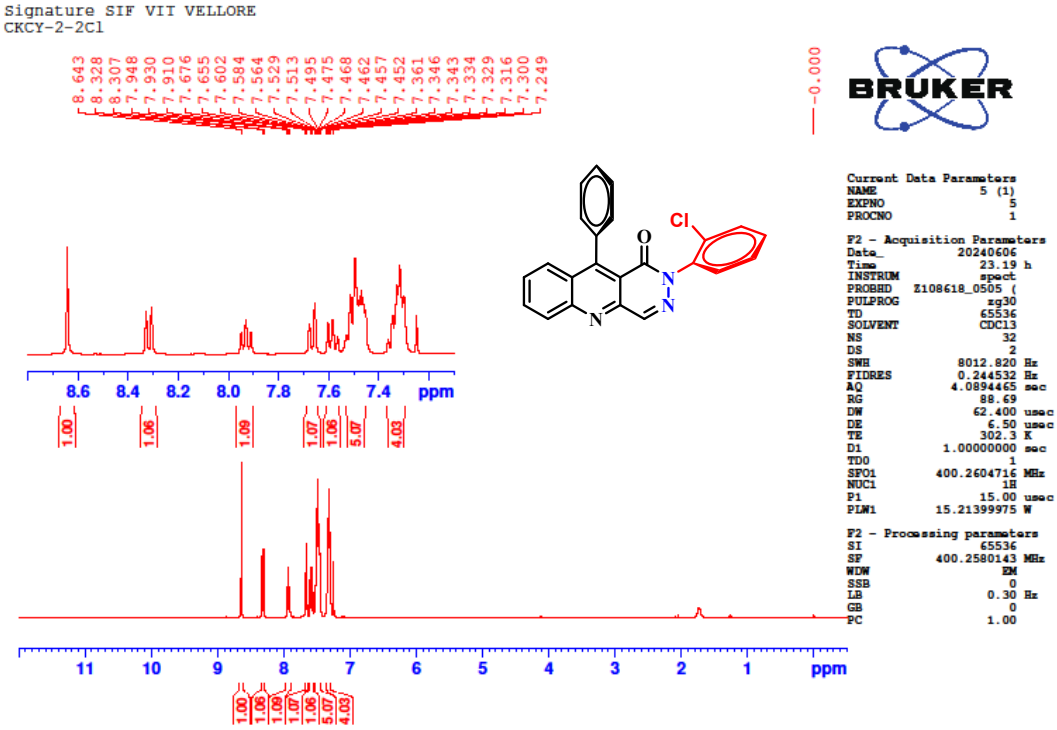


Figure S115: ^{1}H NMR of compound 8c

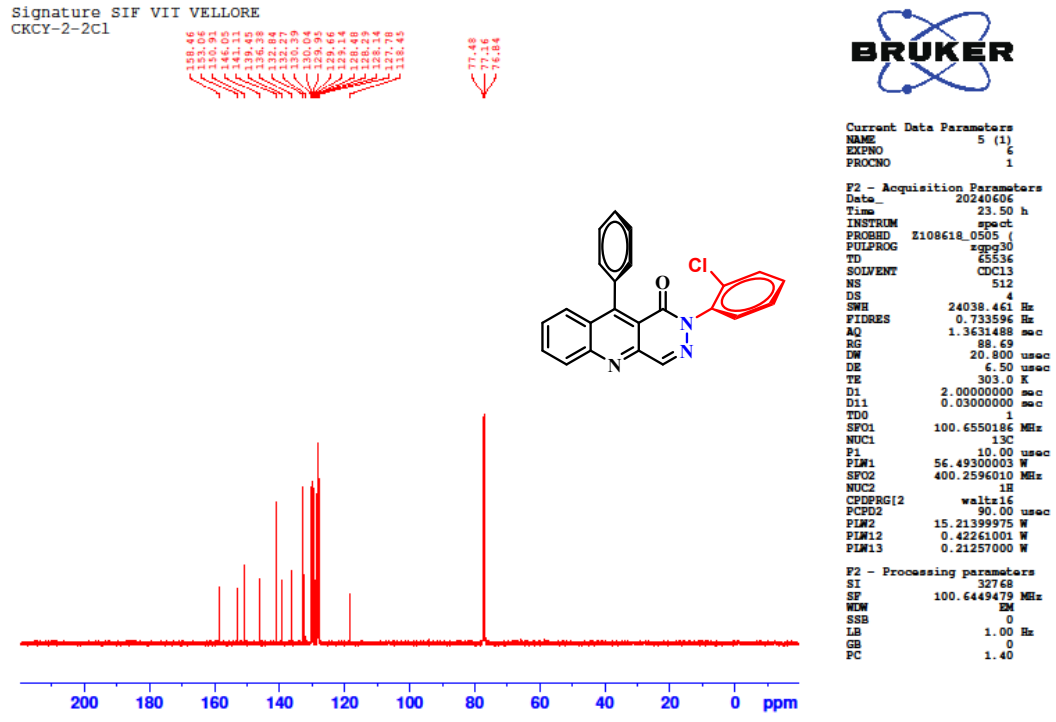


Figure S116: ^{13}C NMR of compound 8c

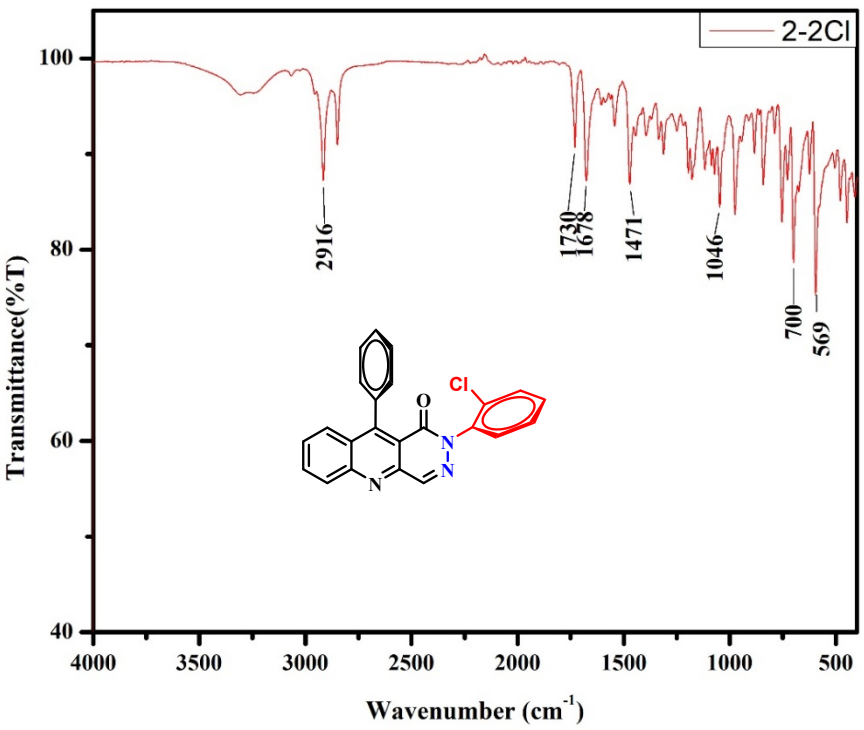


Figure S117: IR spectra of compound 8c

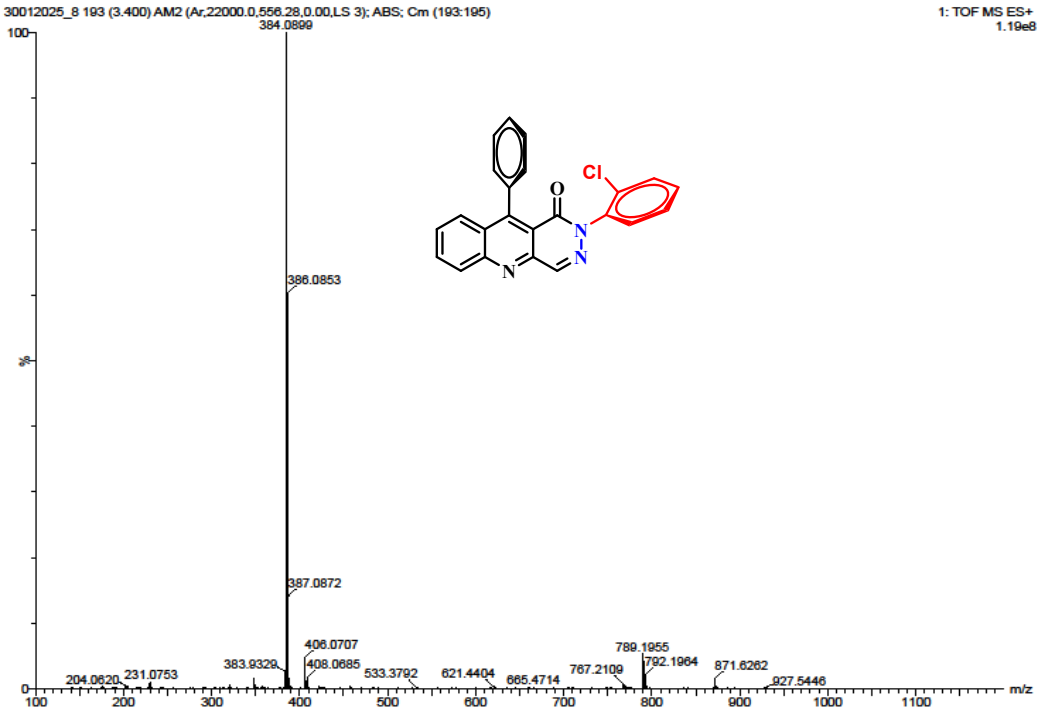


Figure S118: HR-MS spectra of compound 8c

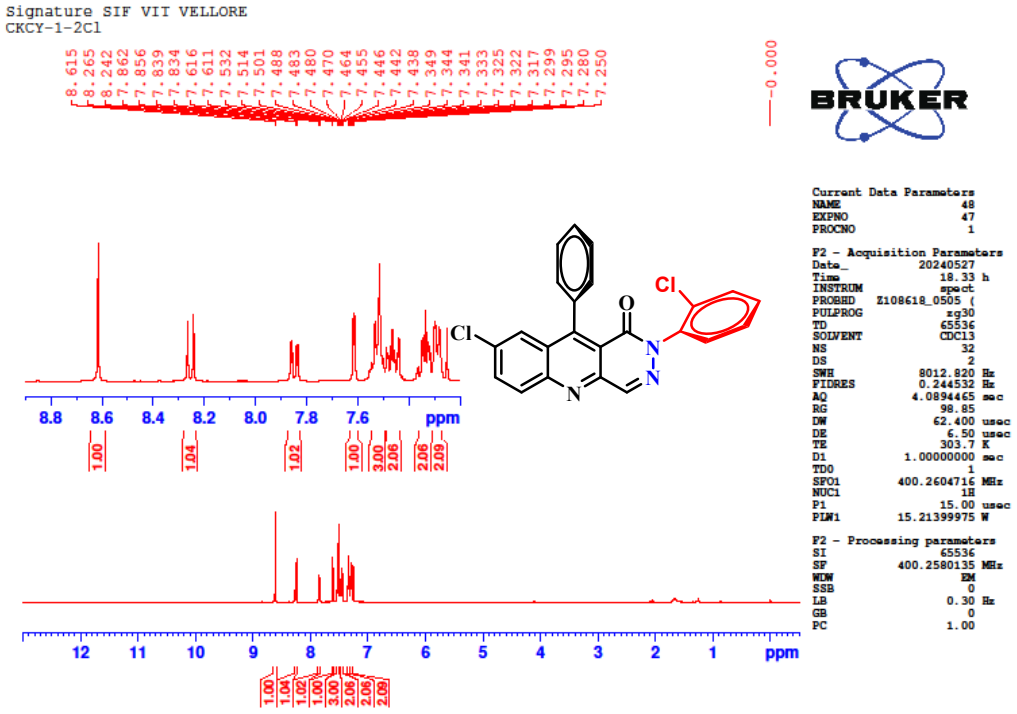


Figure S119: ^{1}H NMR of compound 8d

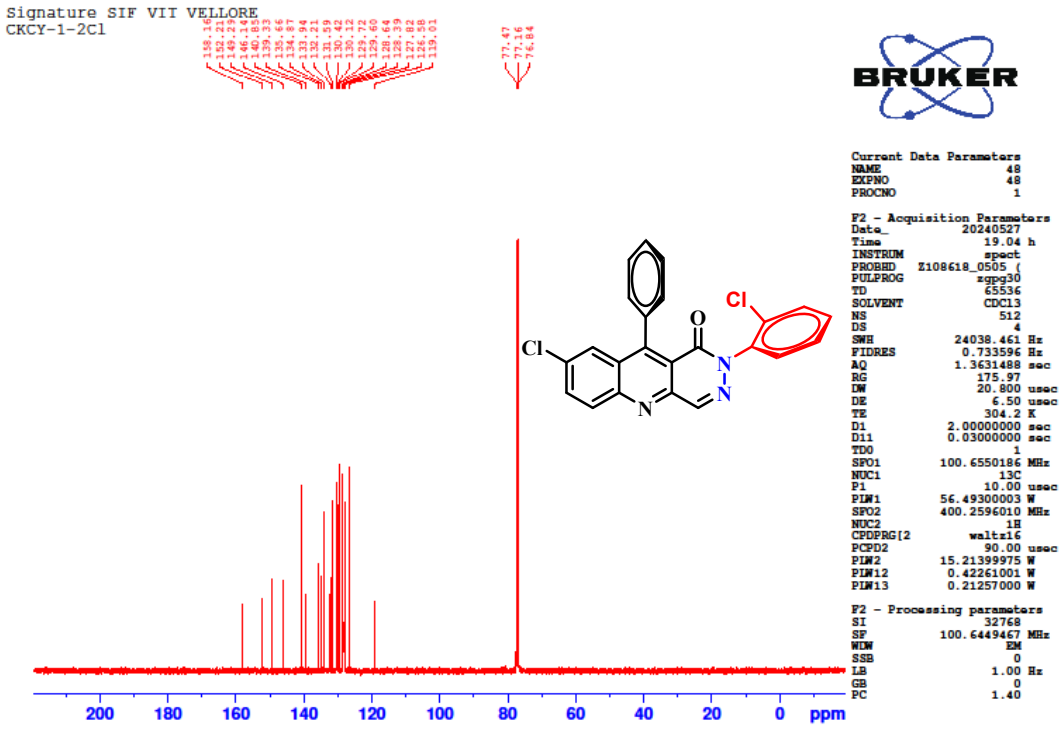


Figure S120: ^{13}C NMR of compound 8d

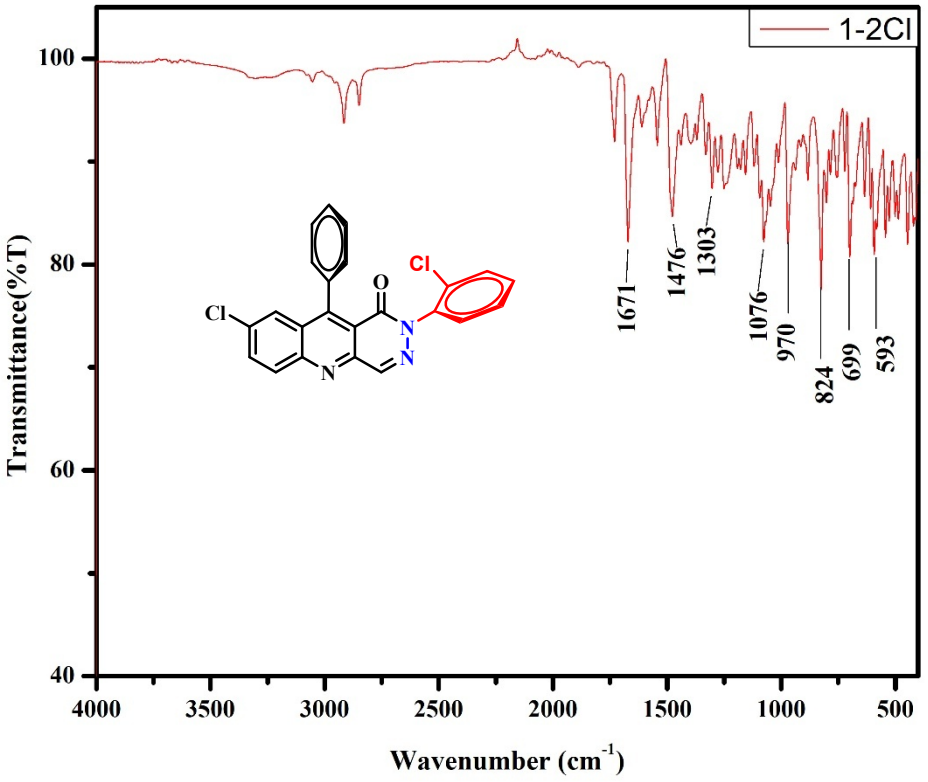


Figure S121: IR spectra of compound 8d

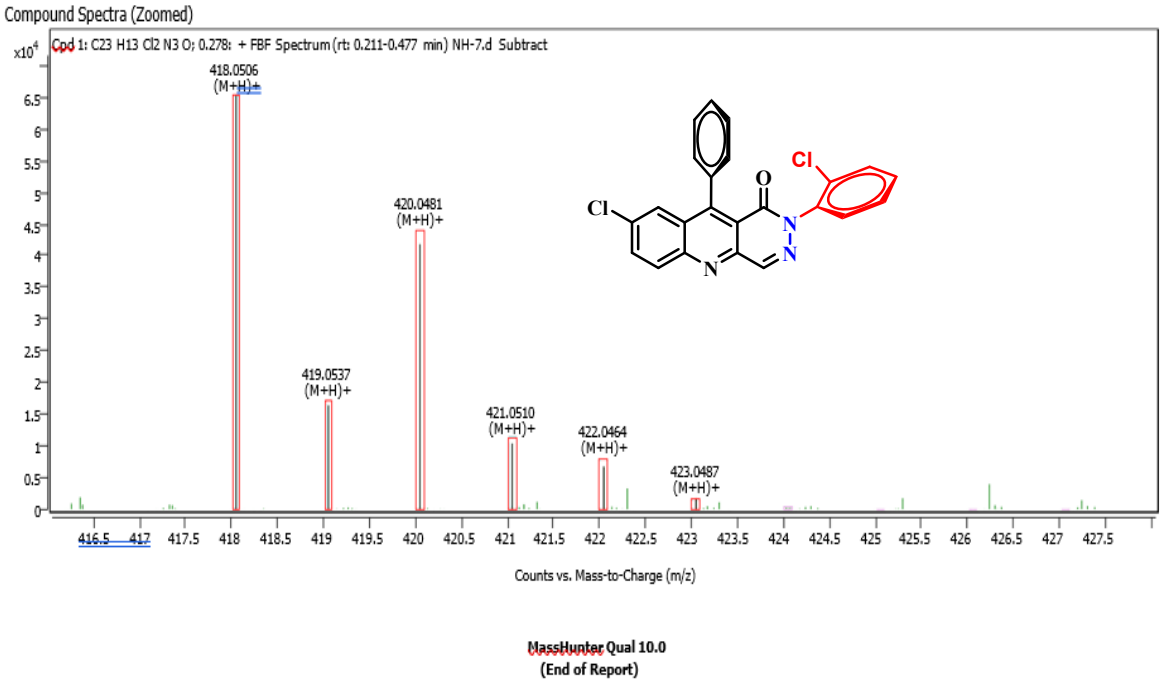


Figure S122: HR-MS spectra of compound 8d

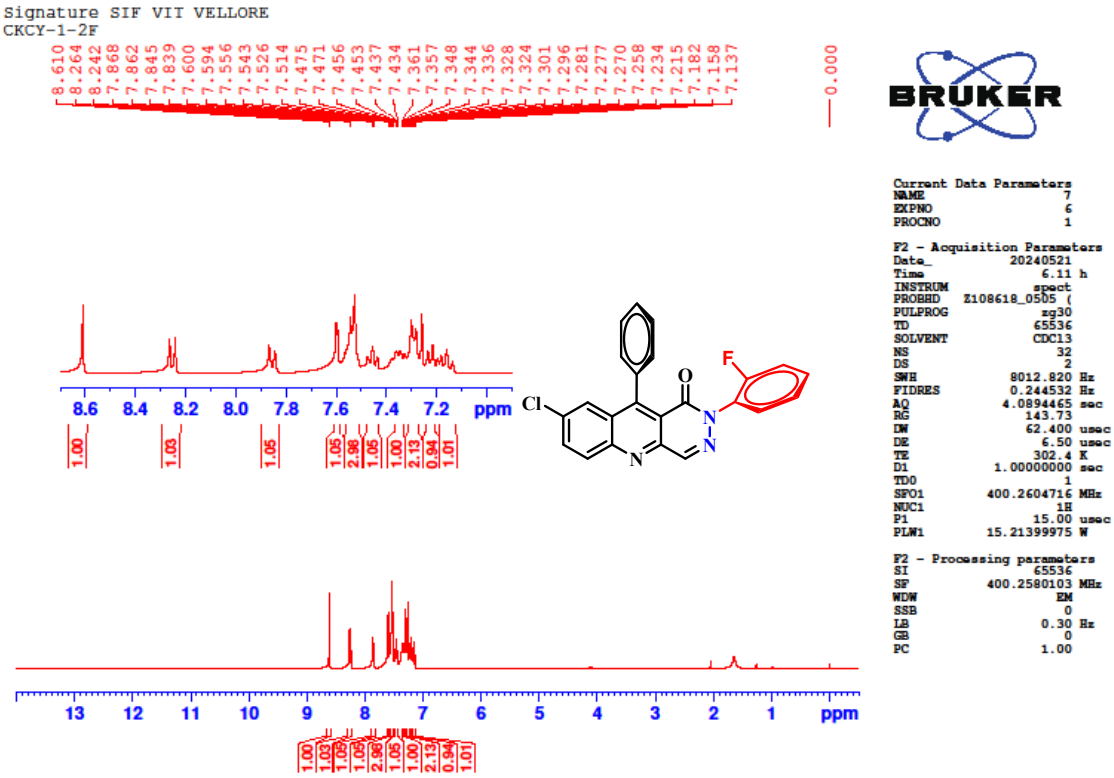


Figure S123: ^{1}H NMR of compound 8e

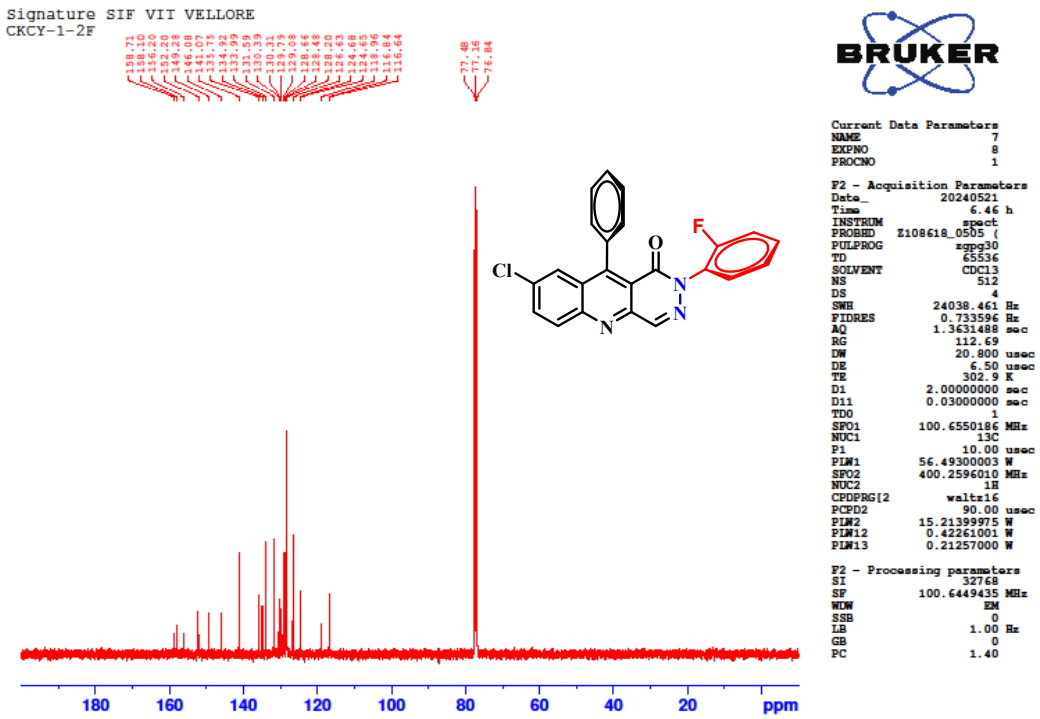


Figure S124: ^{13}C NMR of compound 8e

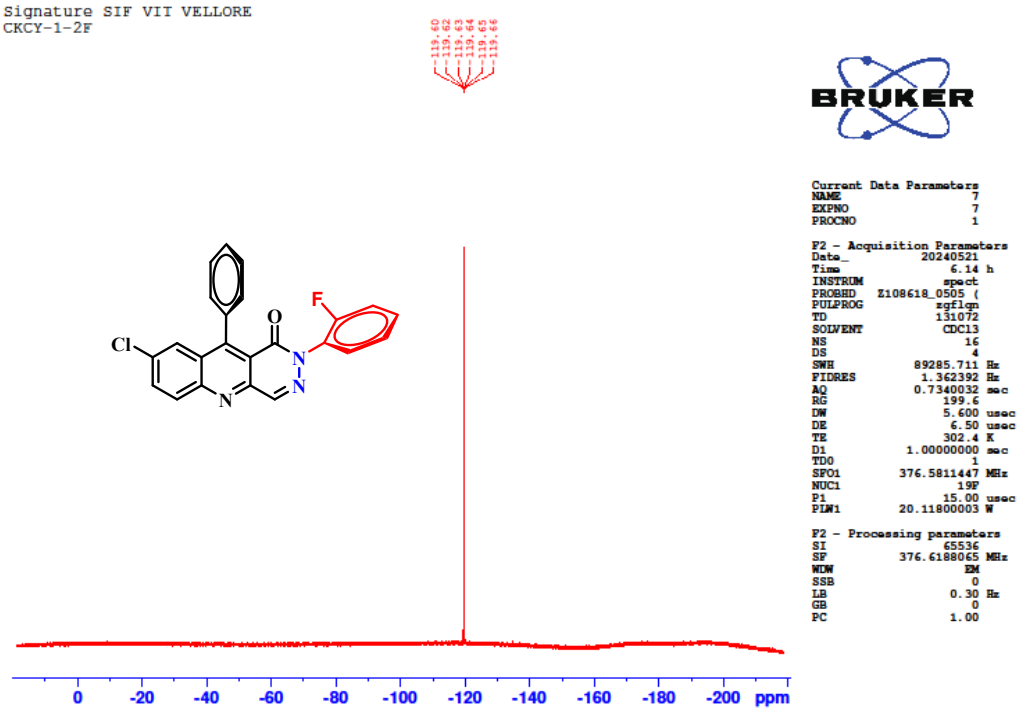


Figure S125: ^{19}F NMR of compound 8e

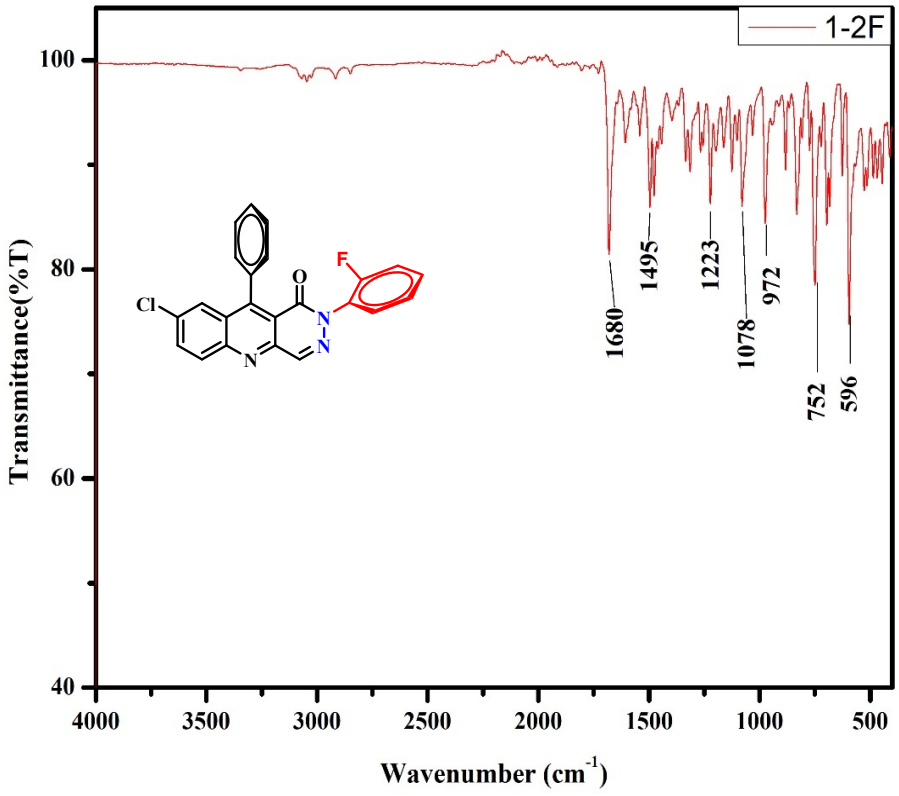


Figure S126: IR spectra of compound 8e

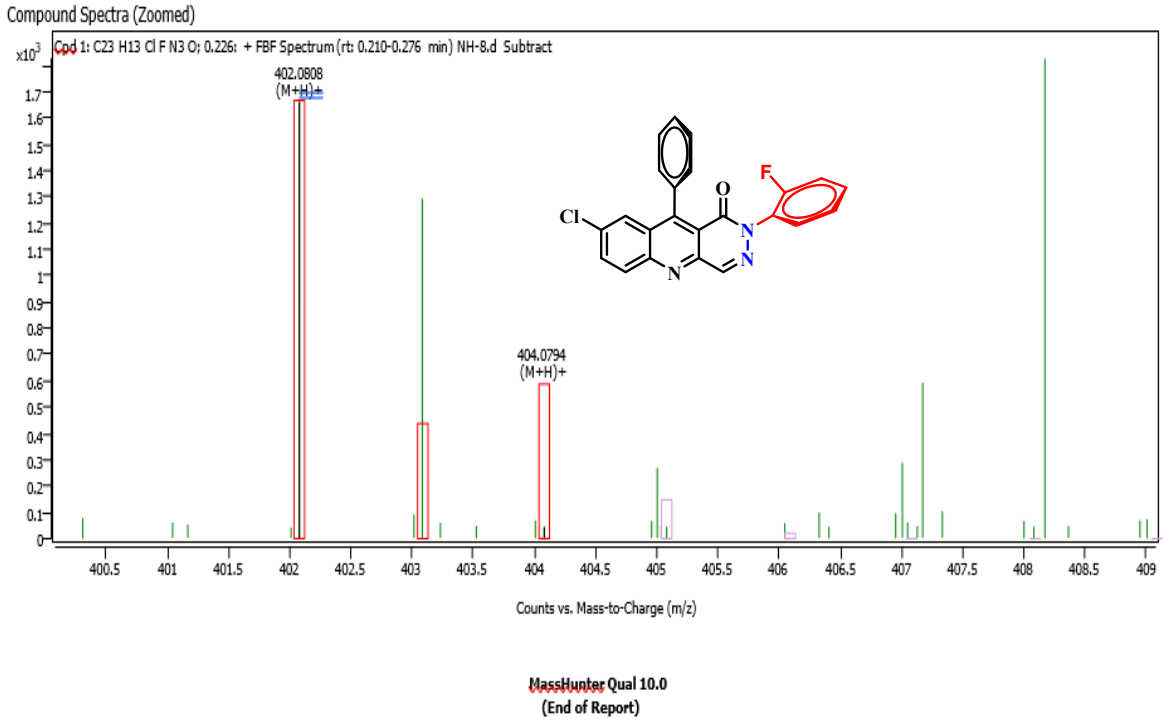


Figure S127: HR-MS spectra of compound 8e

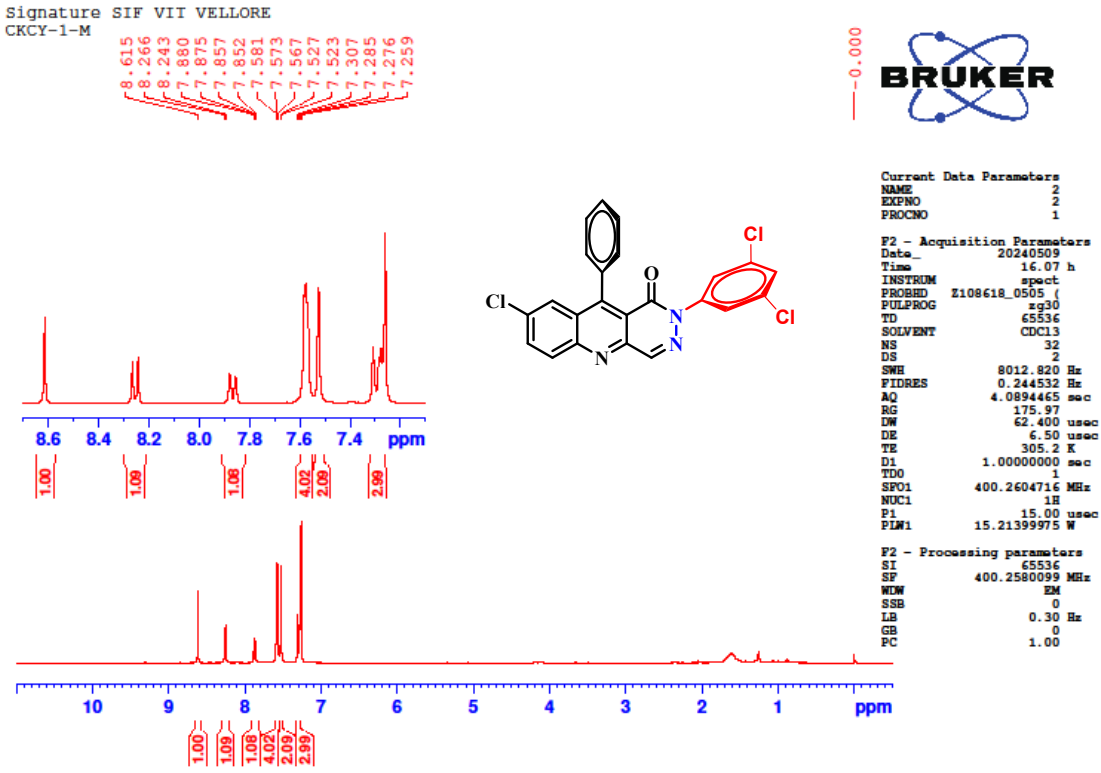


Figure S128: ^{1}H NMR of compound 8f

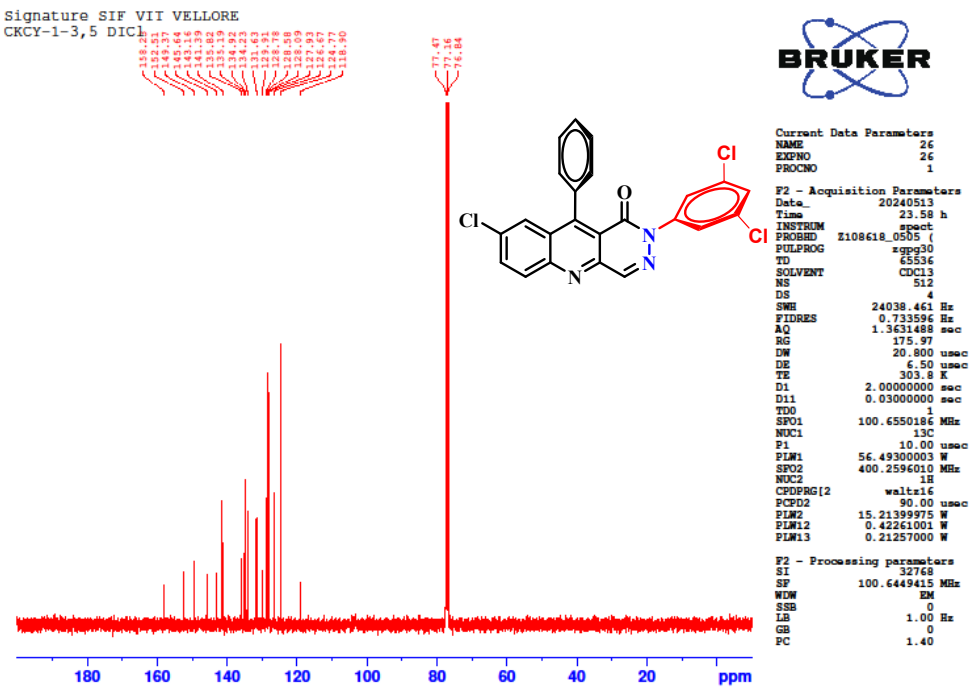


Figure S129: ^{13}C NMR of compound 8f

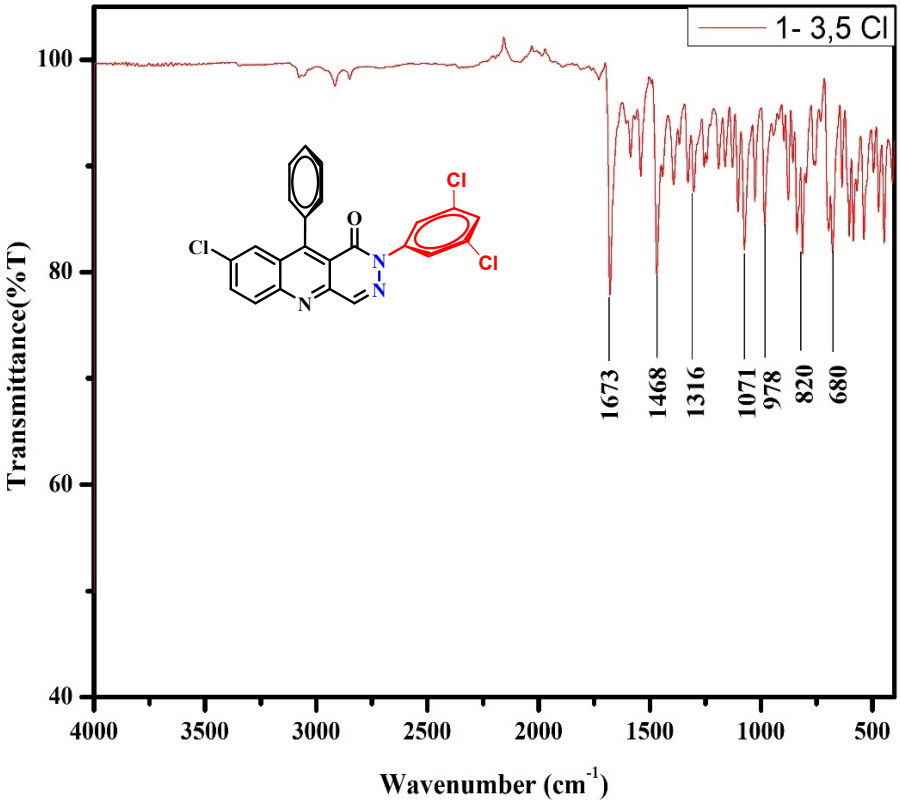


Figure S130: IR spectra of compound 8f

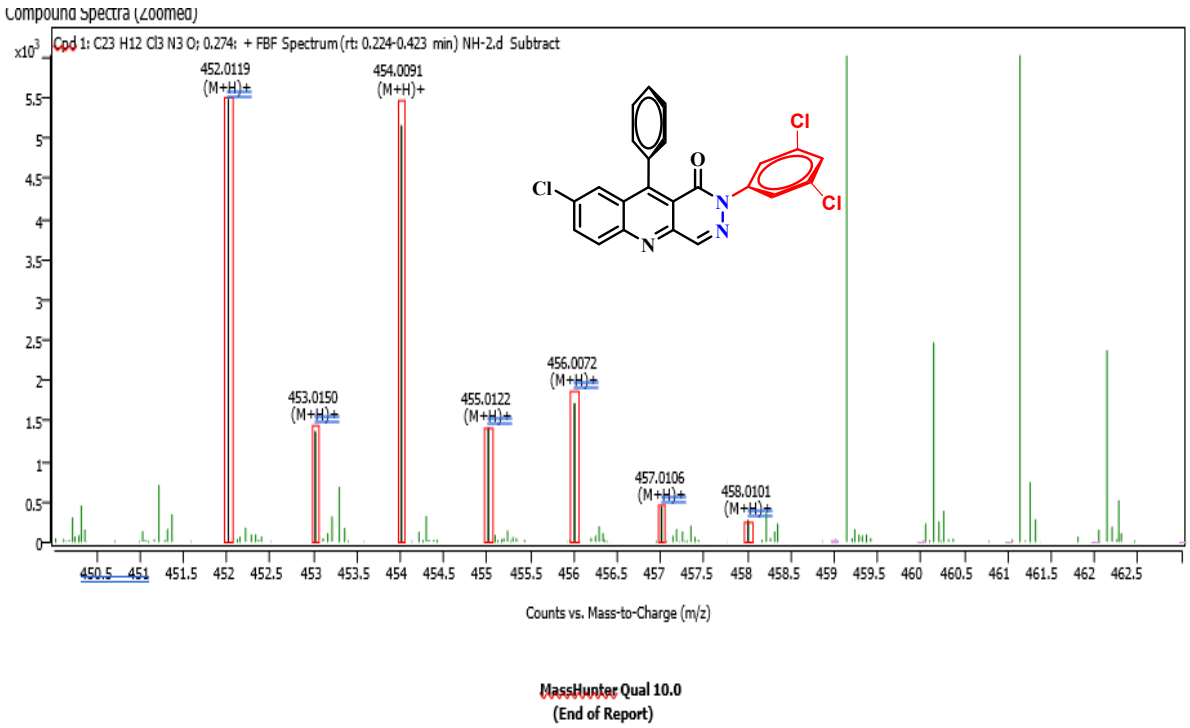


Figure S131: HR-MS spectra of compound 8f

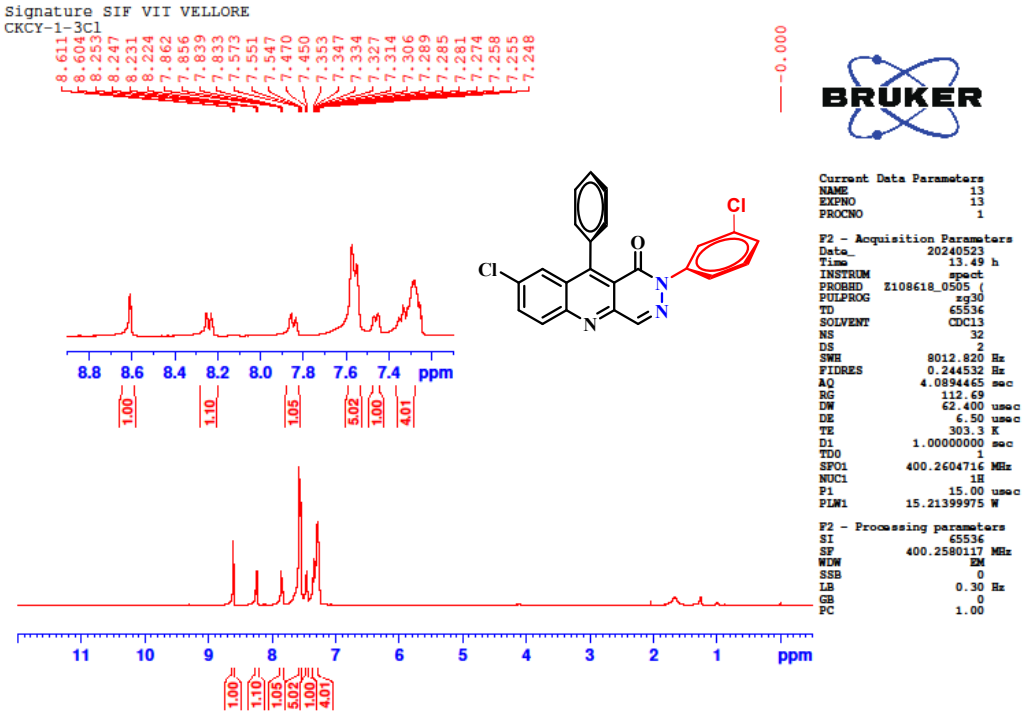


Figure S132: ^{1}H NMR of compound 8g

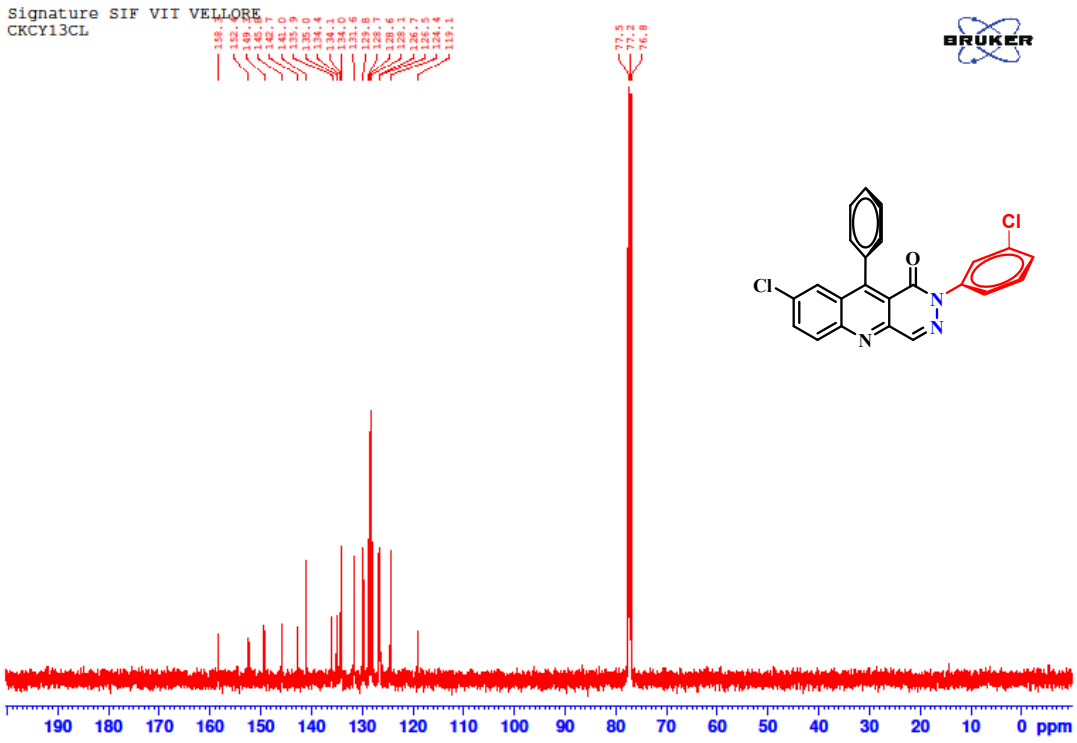


Figure S133: ^{13}C NMR of compound 8g

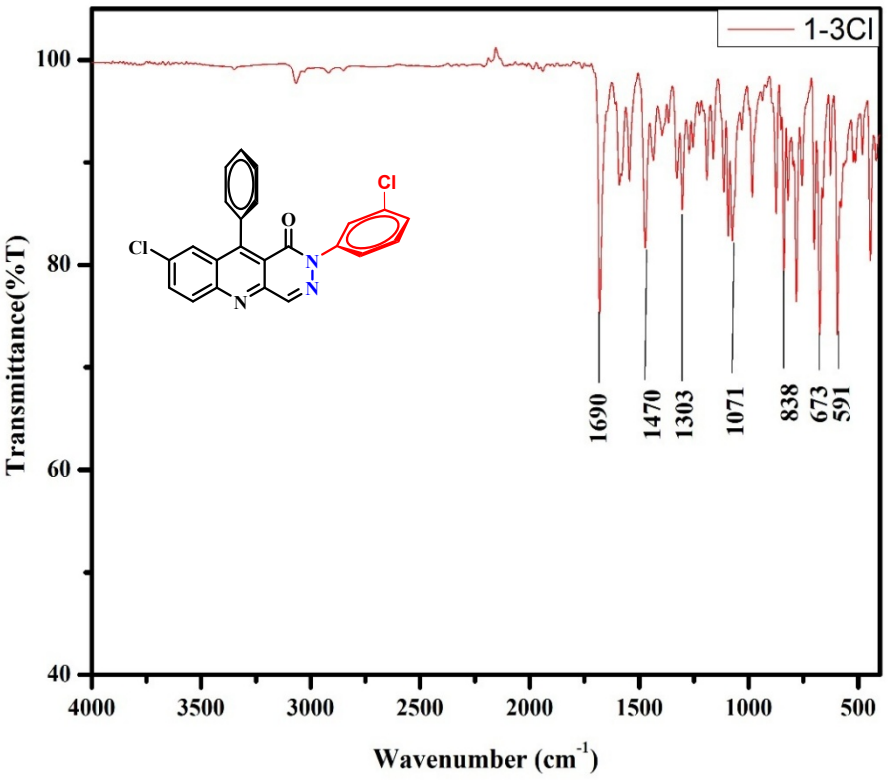


Figure S134: IR spectra of compound 8g

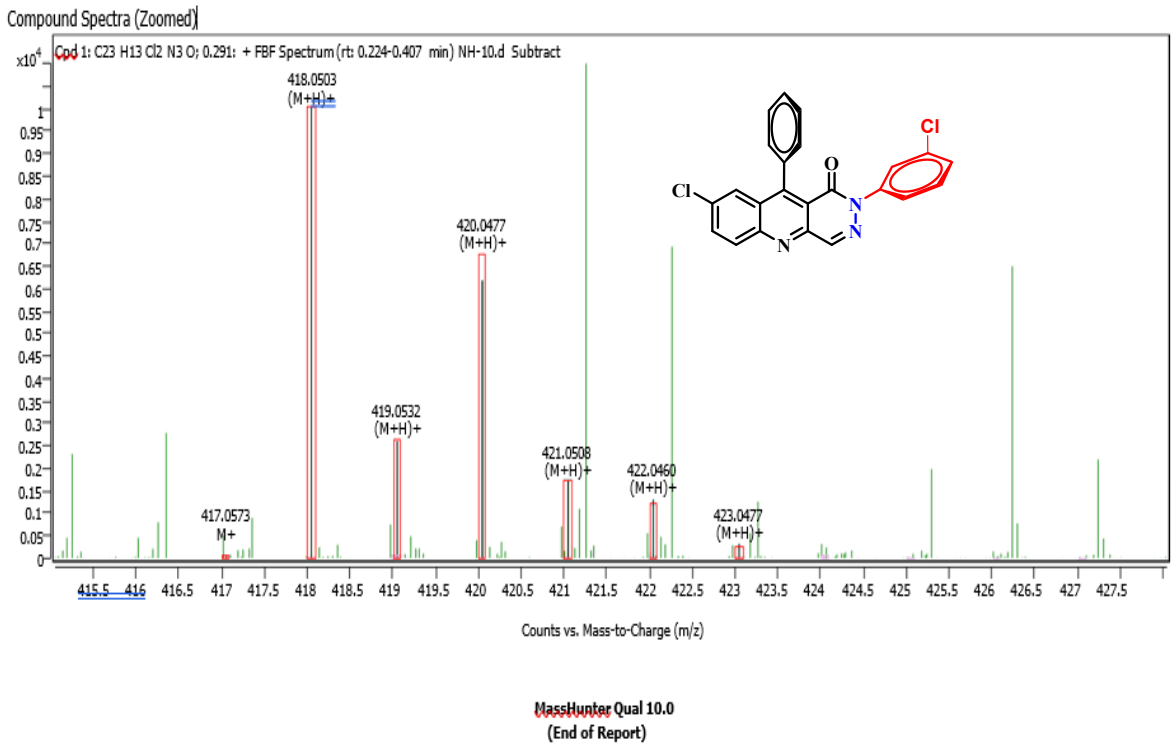


Figure S135: HR-MS spectra of compound 8g

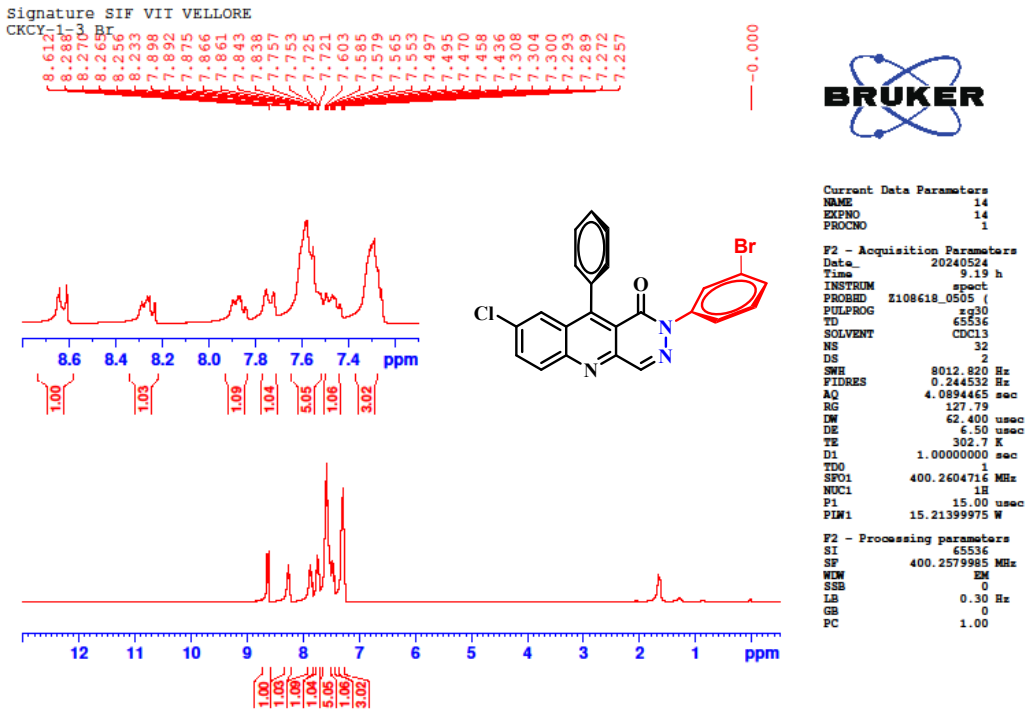


Figure S136: ^{1}H NMR of compound 8h

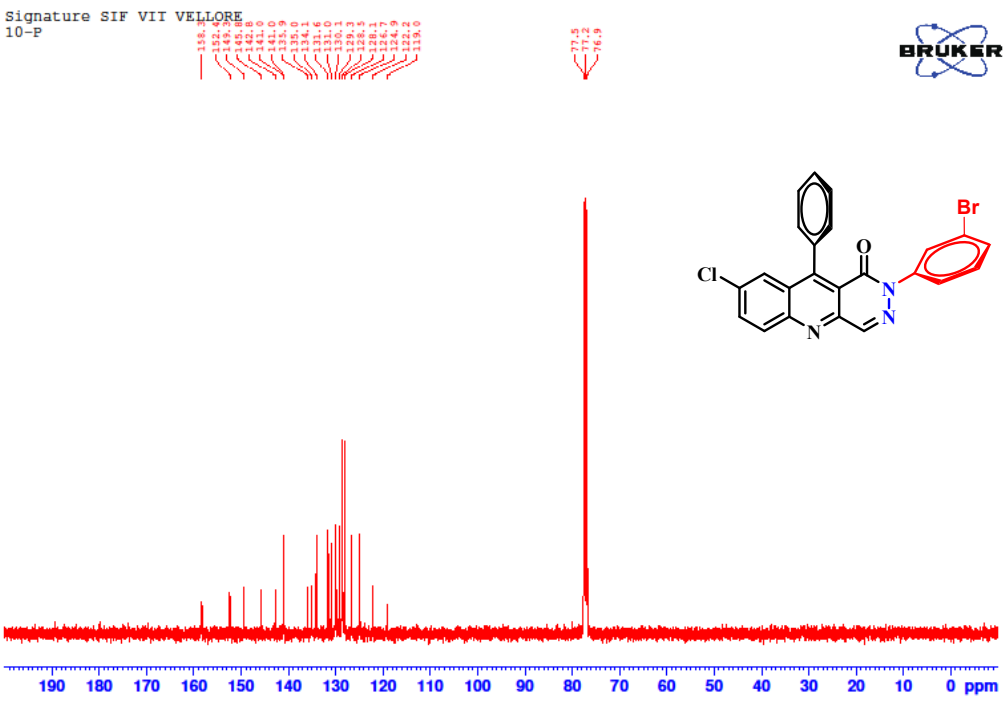


Figure S137: ^{13}C NMR of compound 8h

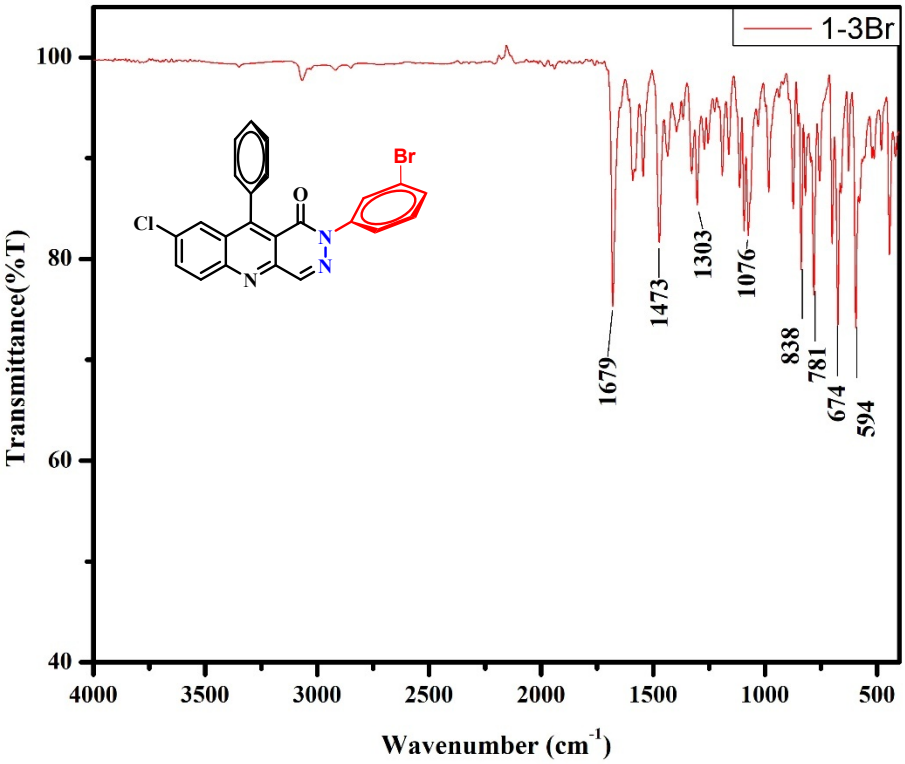


Figure S138: IR spectra of compound 8h

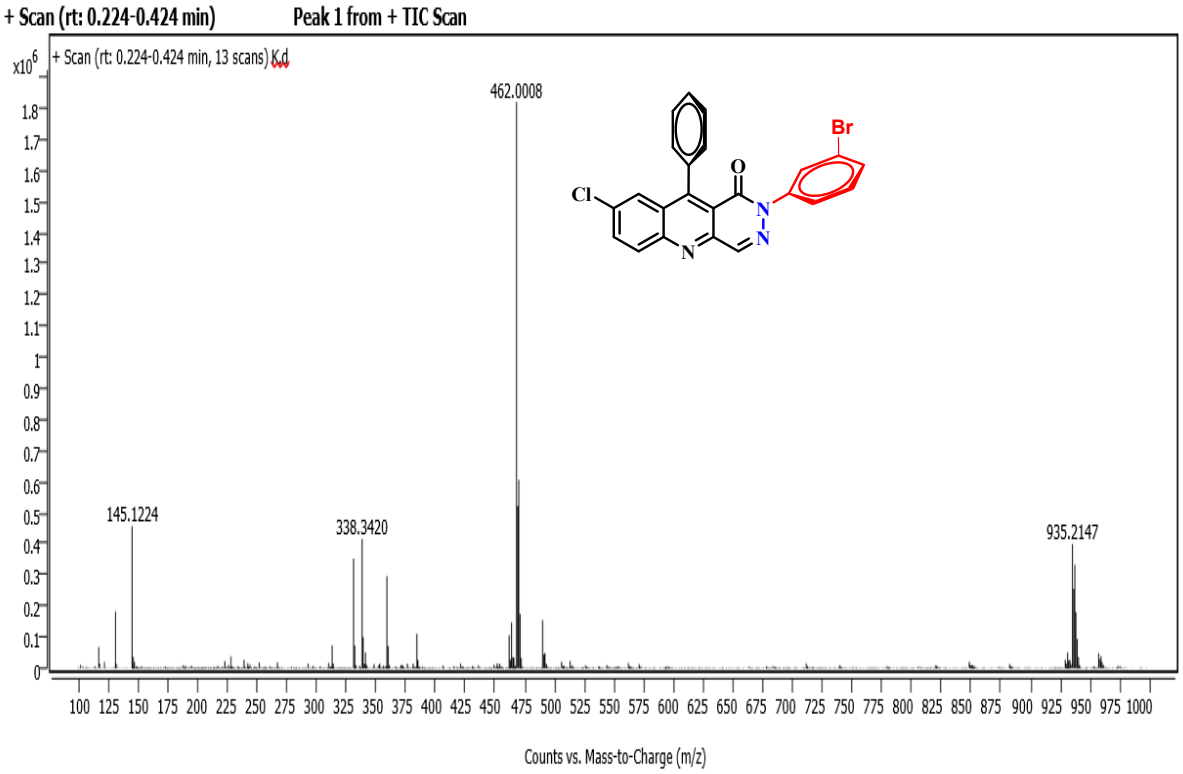


Figure S139: HR-MS spectra of compound 8h

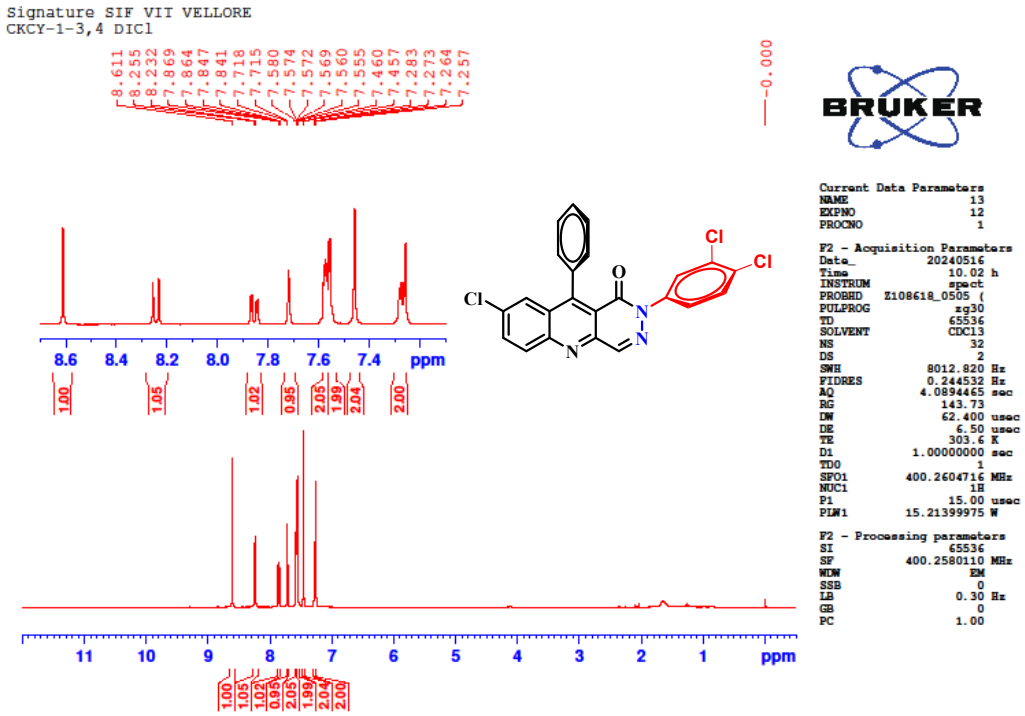


Figure S140: ^{1}H NMR of compound 8i

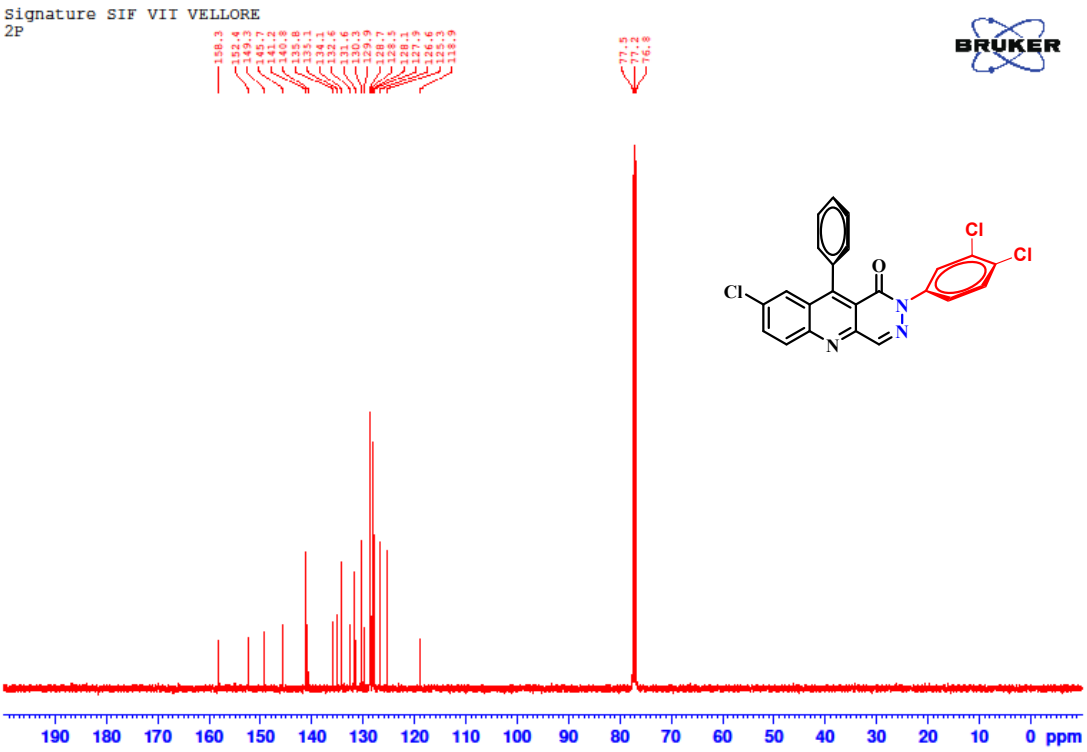


Figure S141: ^{13}C NMR of compound 8i

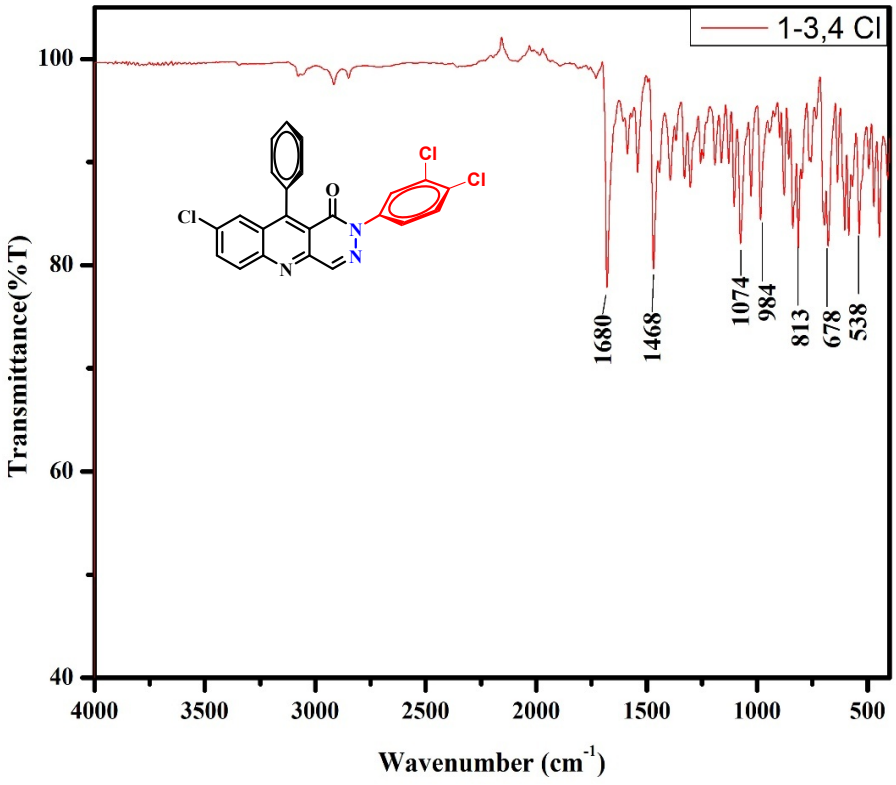


Figure S142: IR spectra of compound 8i

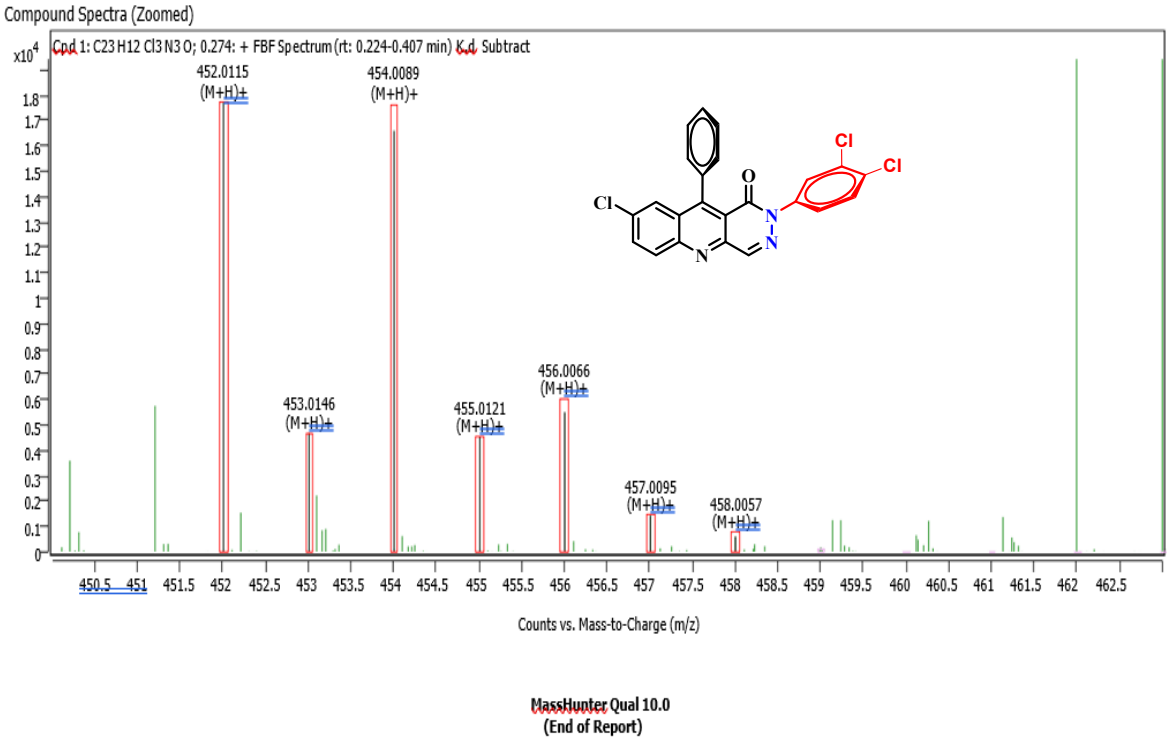


Figure S143: HR-MS spectra of compound 8i

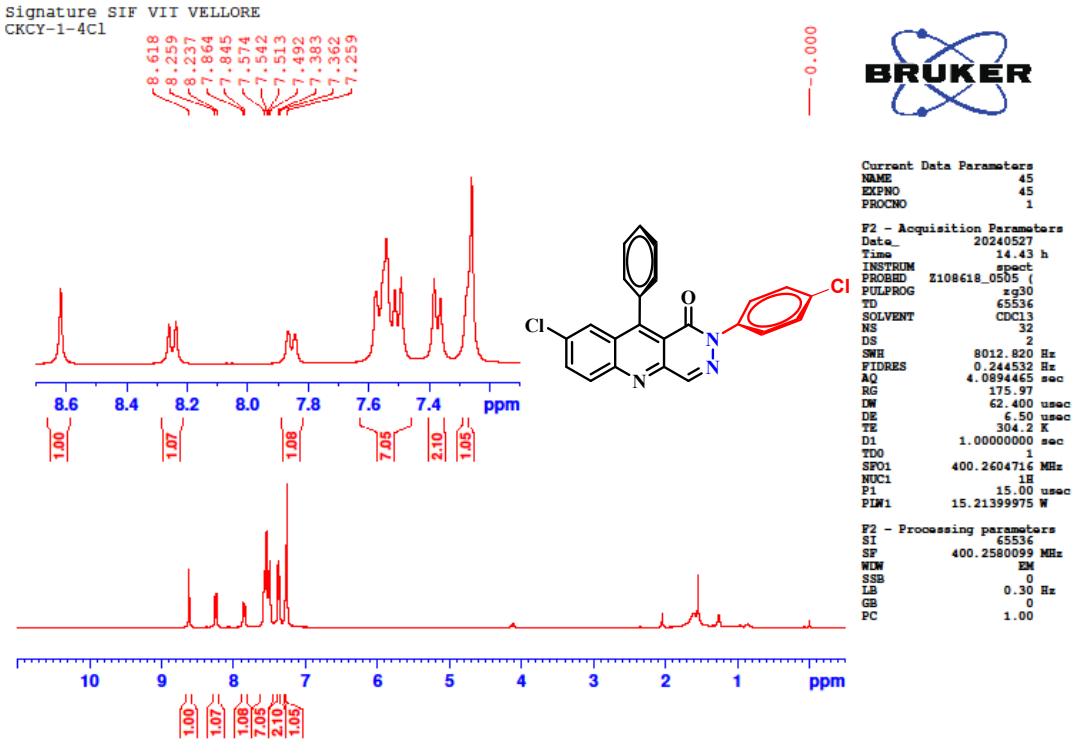


Figure S144: ^{1}H NMR of compound 8j

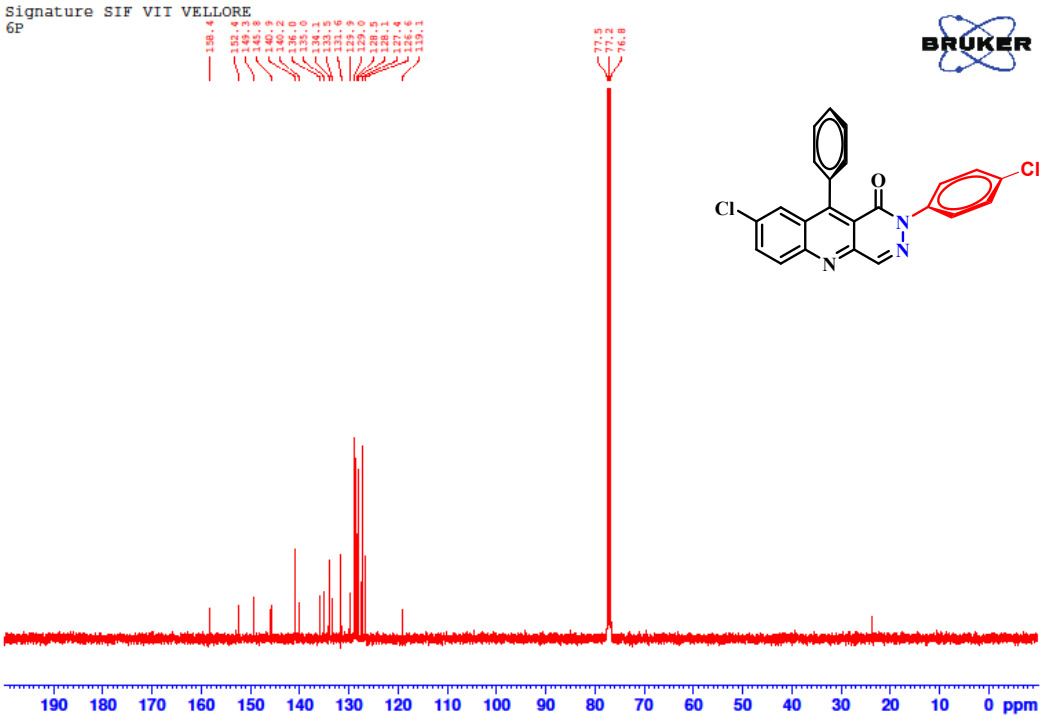


Figure S145: ^{13}C NMR of compound 8j

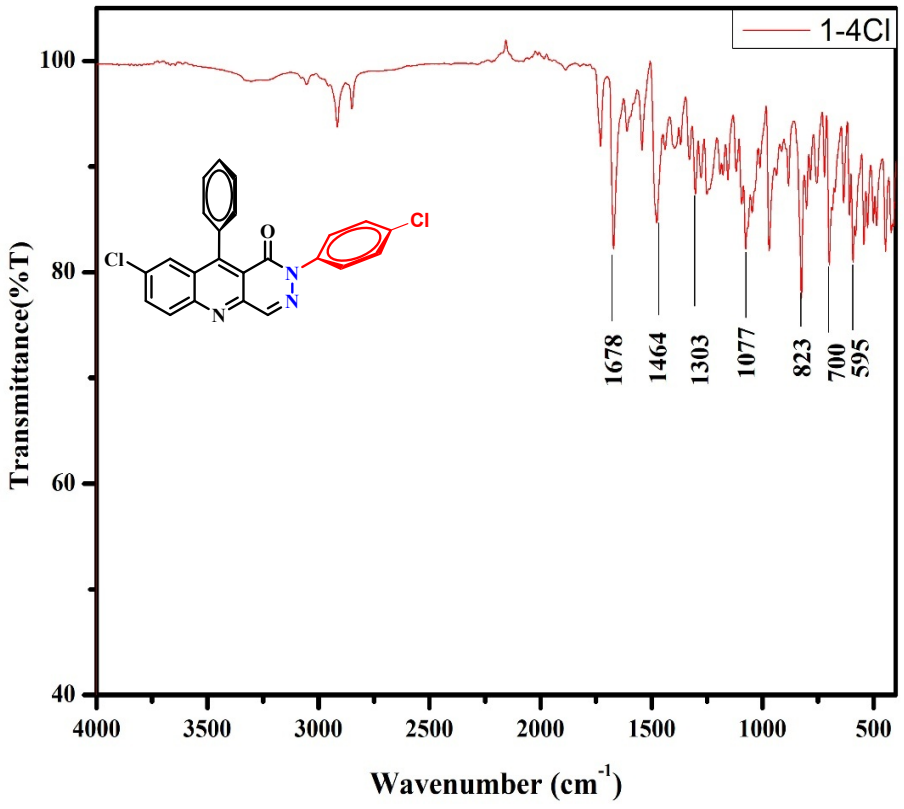


Figure S146: IR spectra of compound 8j

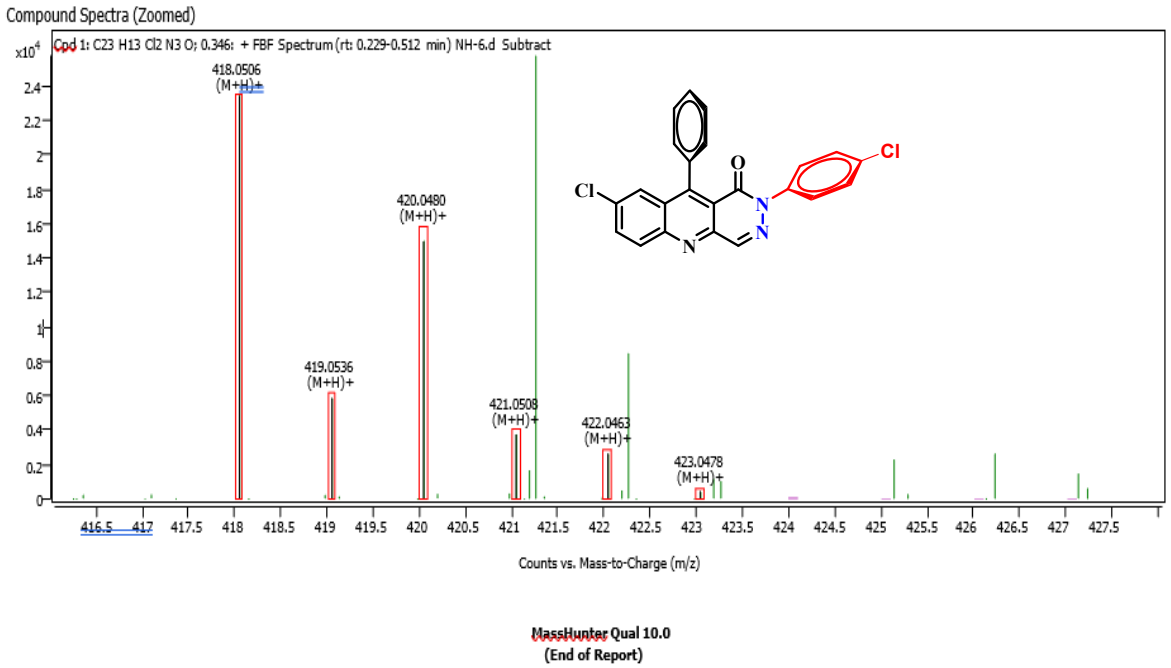


Figure S147: HR-MS spectra of compound 8j

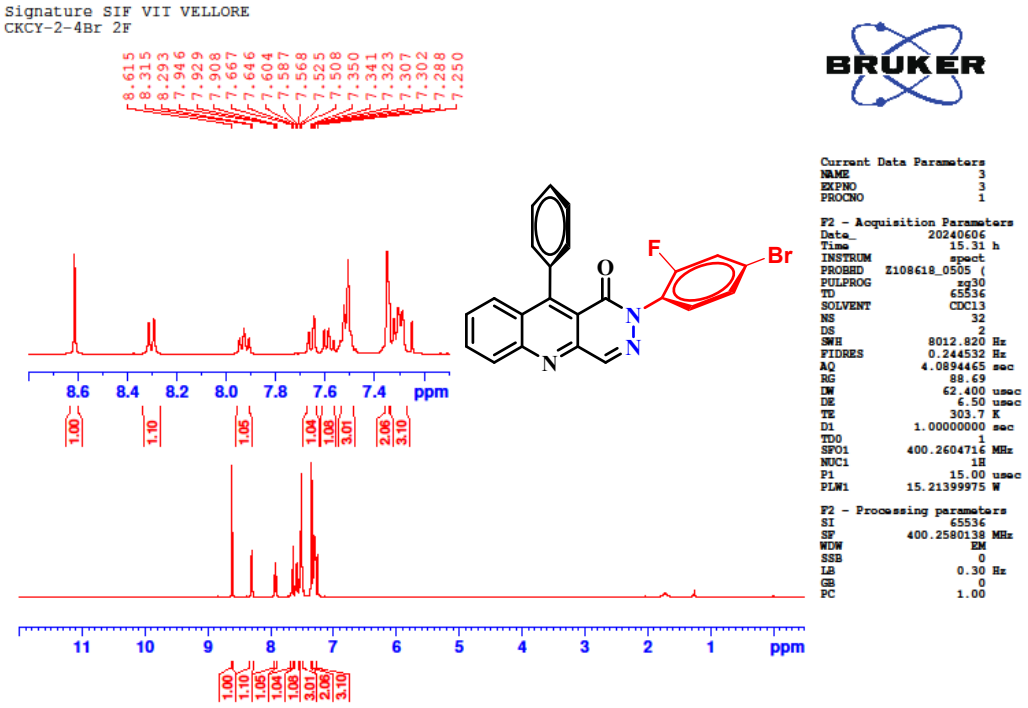


Figure S148: ^{1}H NMR of compound 8k

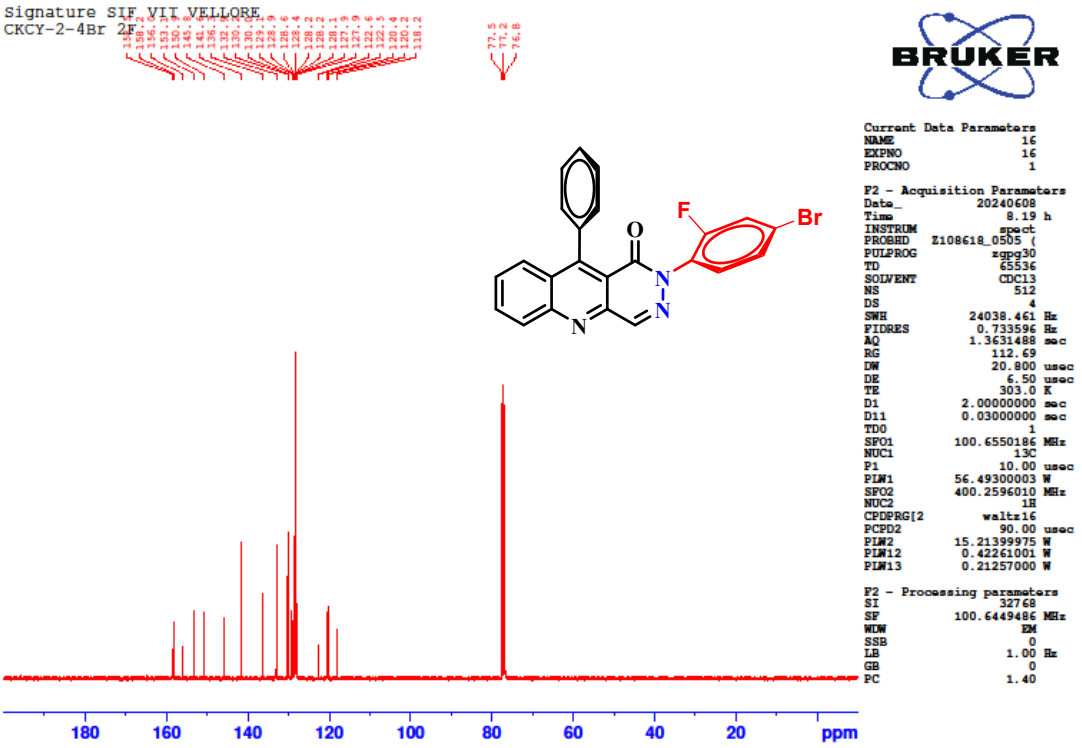


Figure S149: ^{13}C NMR of compound 8k

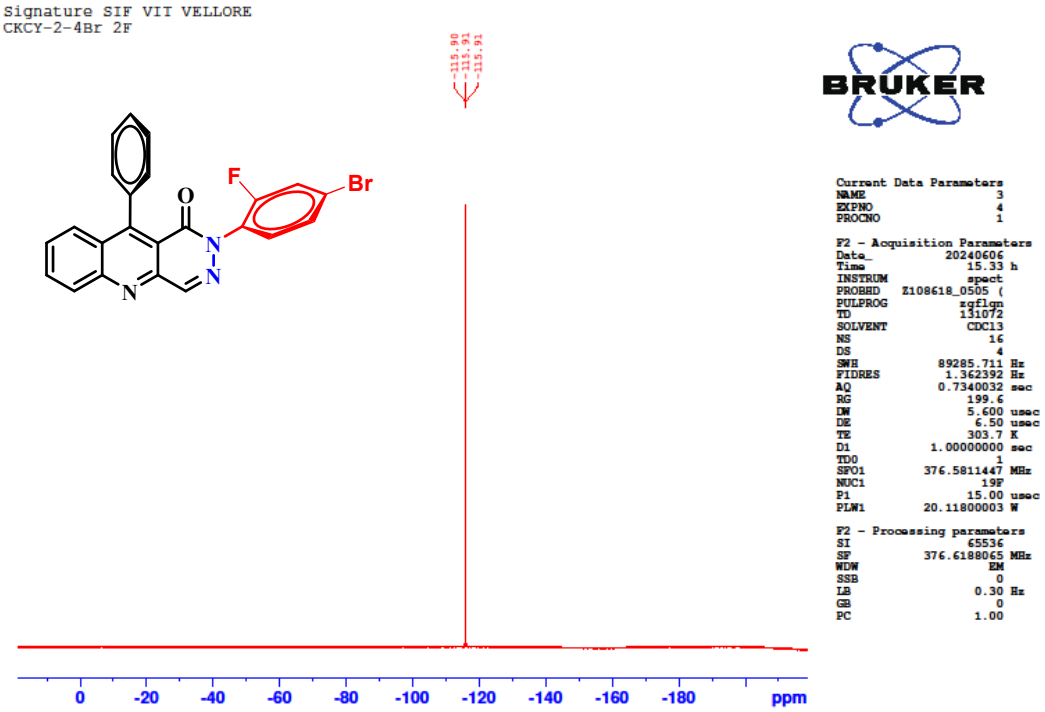


Figure S150: ^{19}F NMR of compound 8k

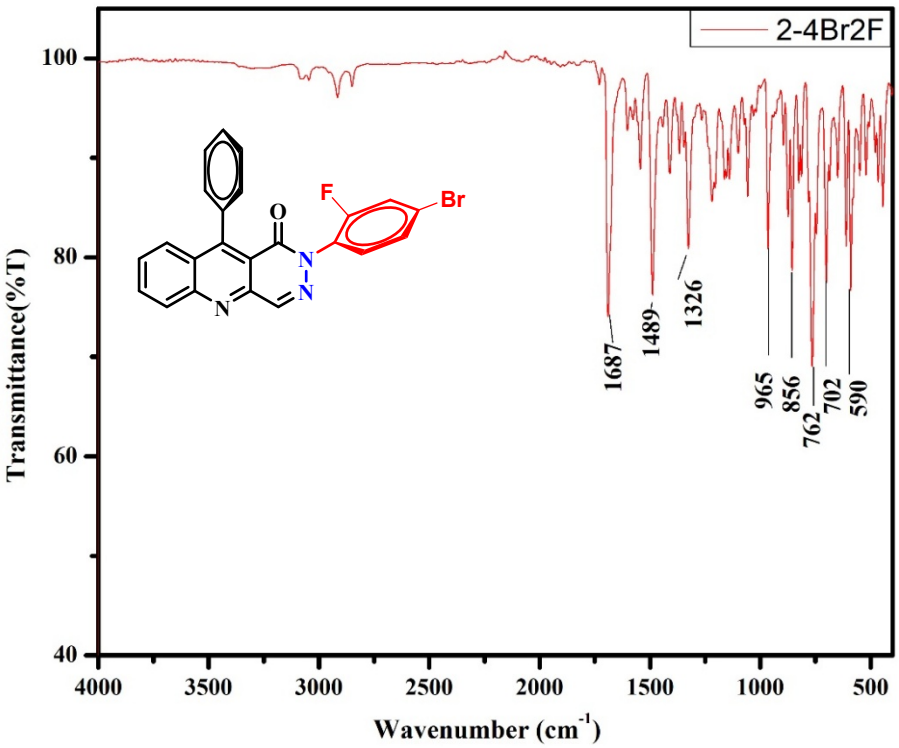


Figure S151: IR spectra of compound 8k

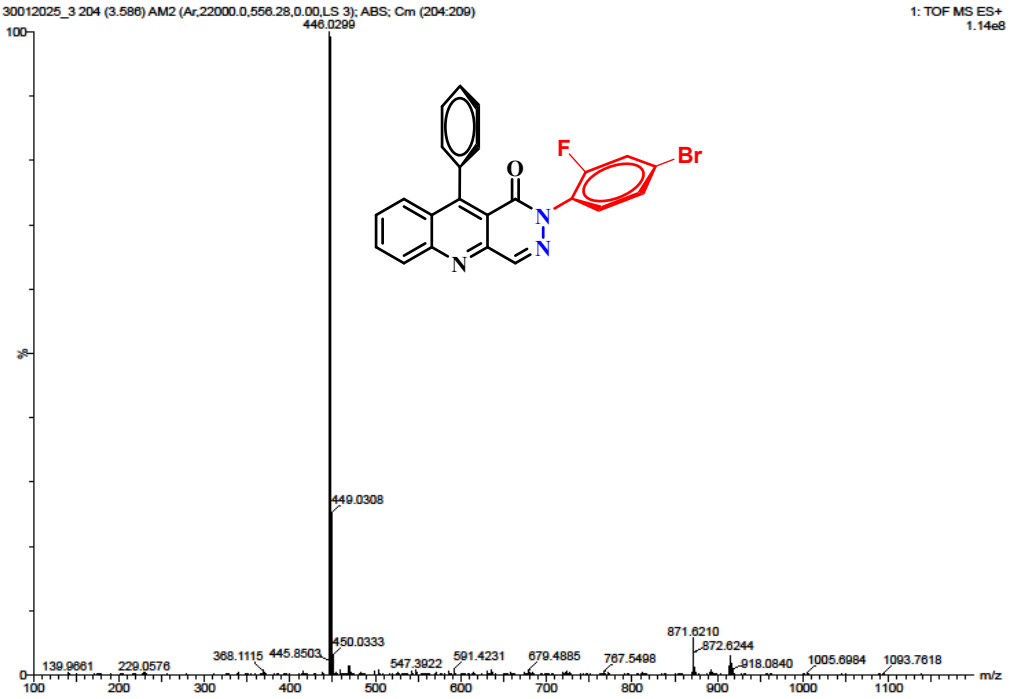


Figure S152: HR-MS spectra of compound 8k

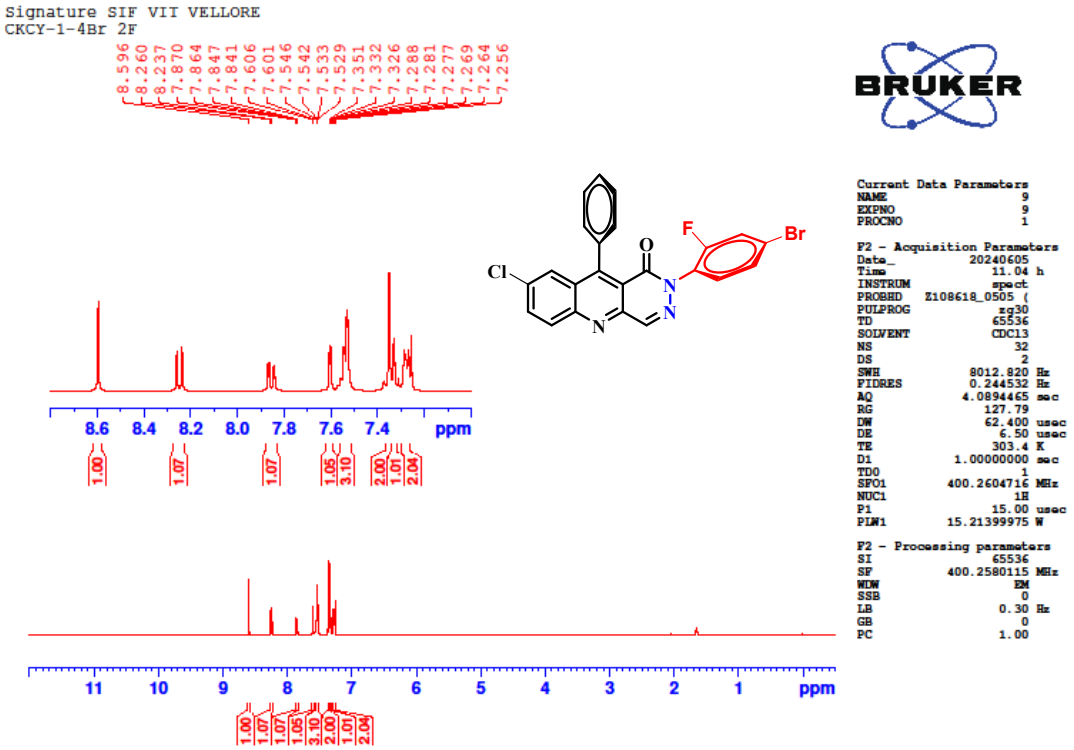


Figure S153: ^{1}H NMR of compound 8l

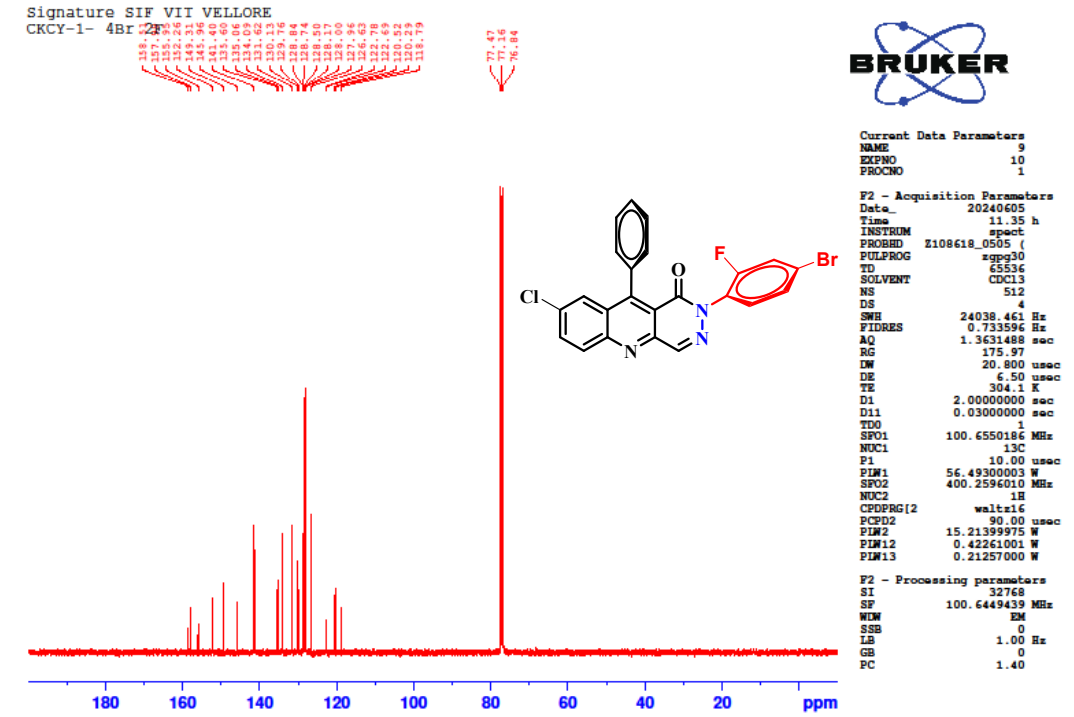


Figure S154: ^{13}C NMR of compound 8l

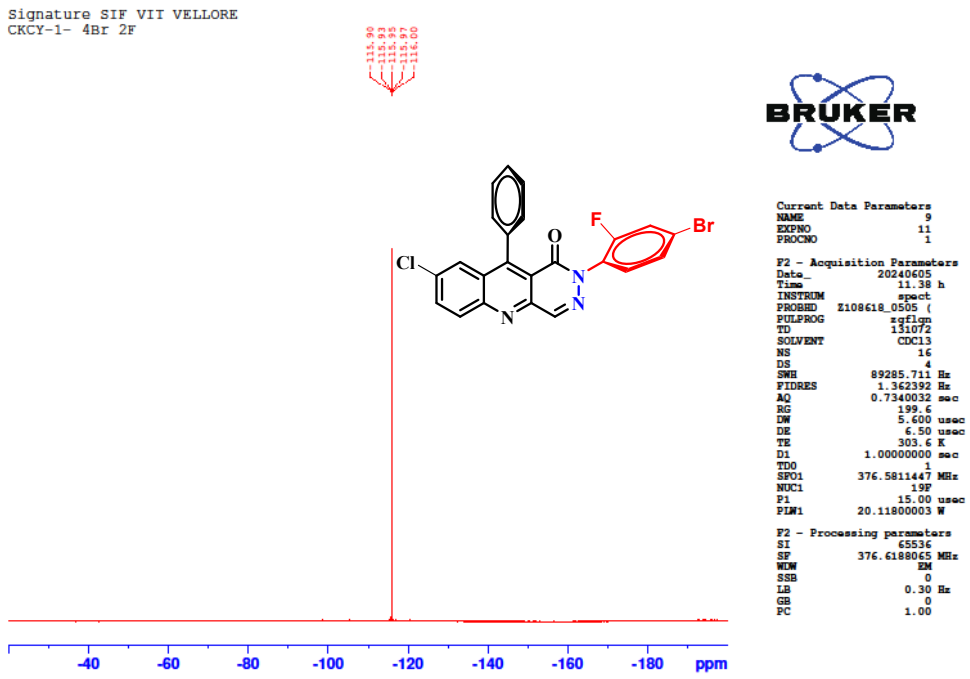


Figure S155: ^{19}F NMR of compound 8l

1-4-Br-2F_COSY

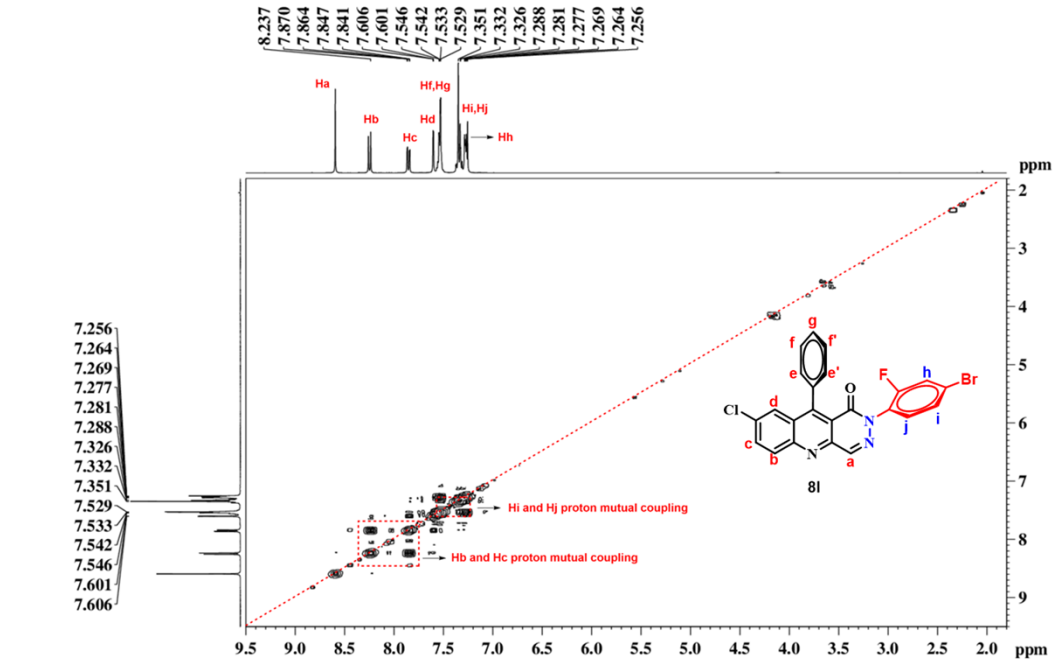


Figure S156: COSY NMR of compound 8l

1-4-Br-2-F_HSQC

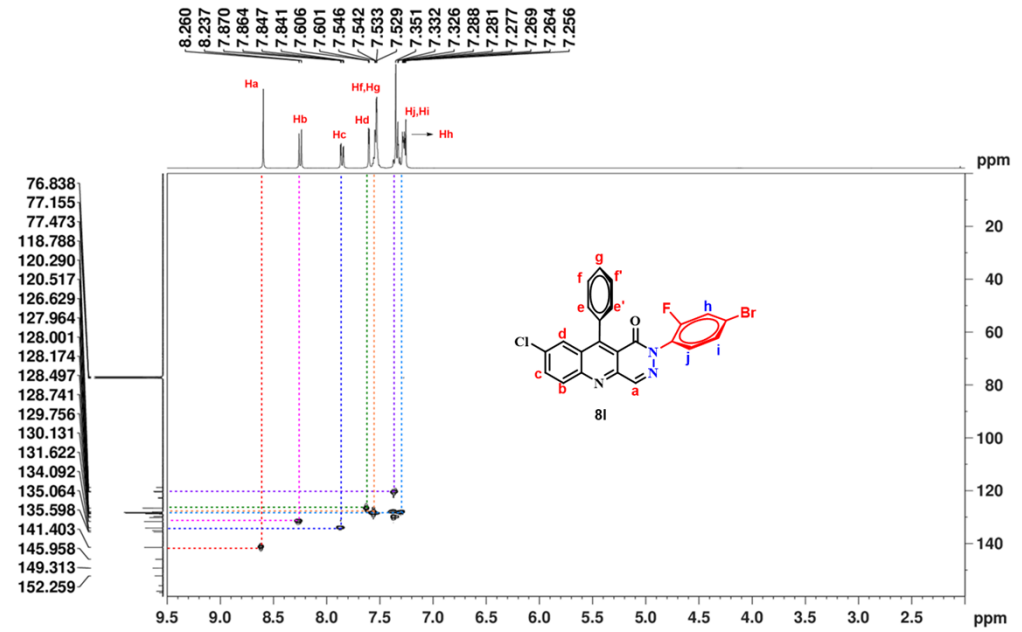


Figure S157: HSQC NMR of compound 8l

1-HBr_HMBC

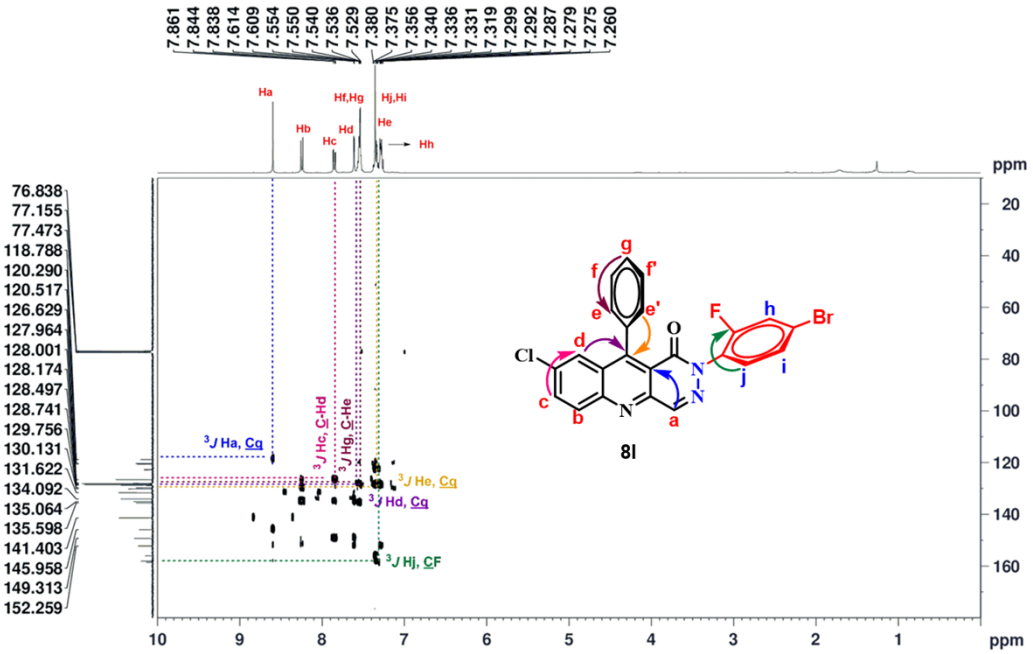


Figure S158: HMBC NMR of compound 8l

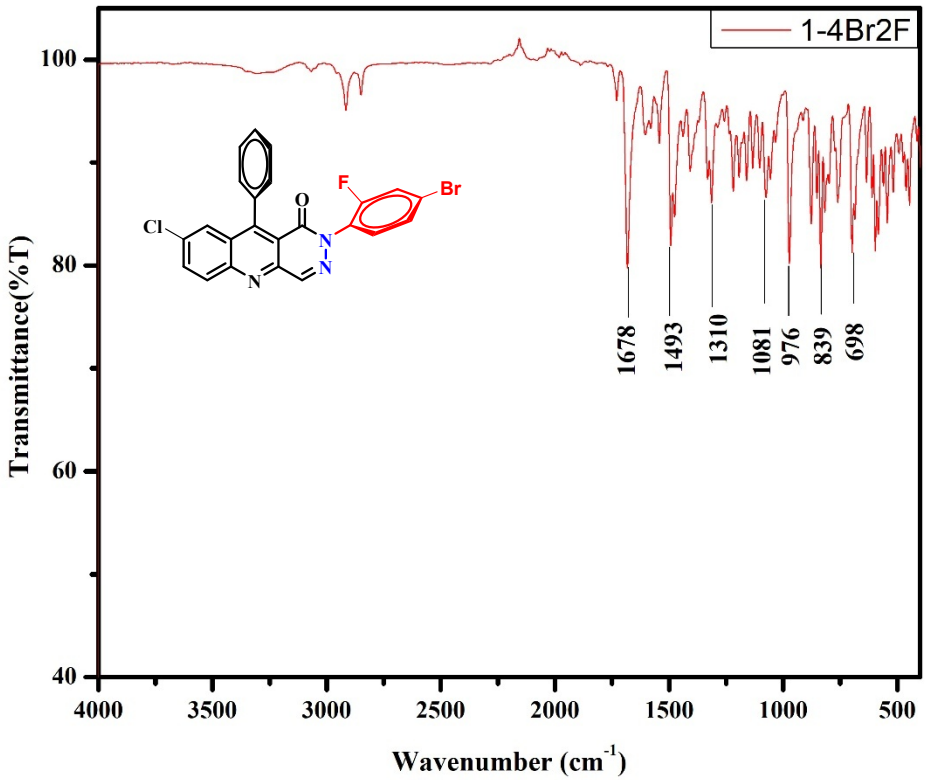


Figure S159: IR spectra of compound 8l

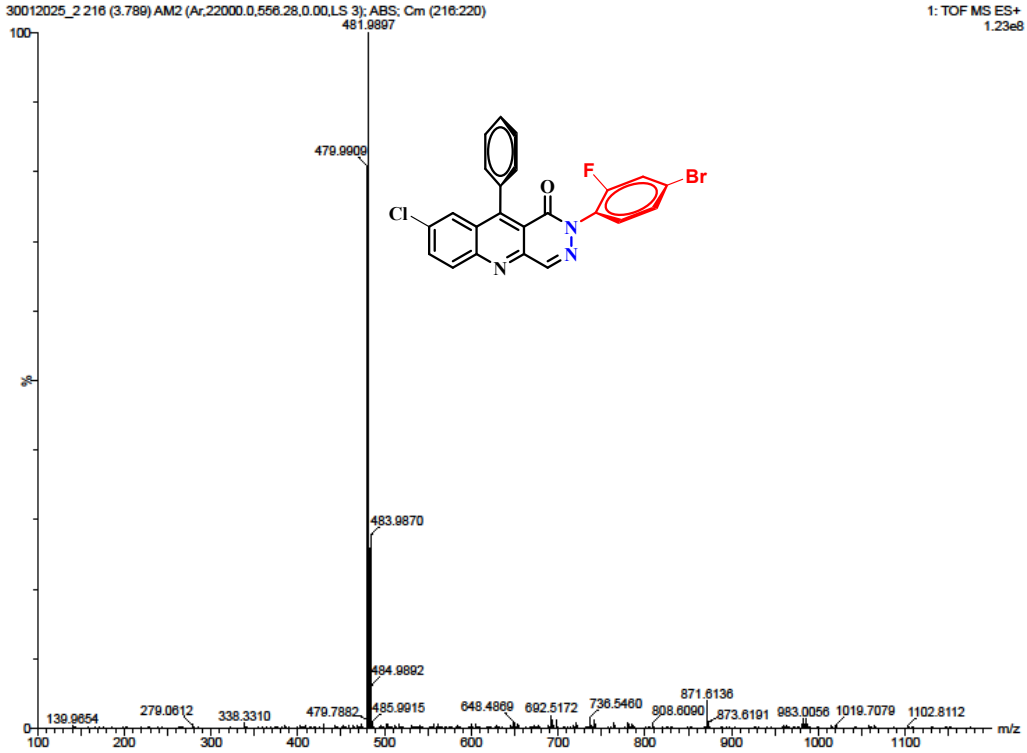


Figure S160: HR-MS spectra of compound 8l

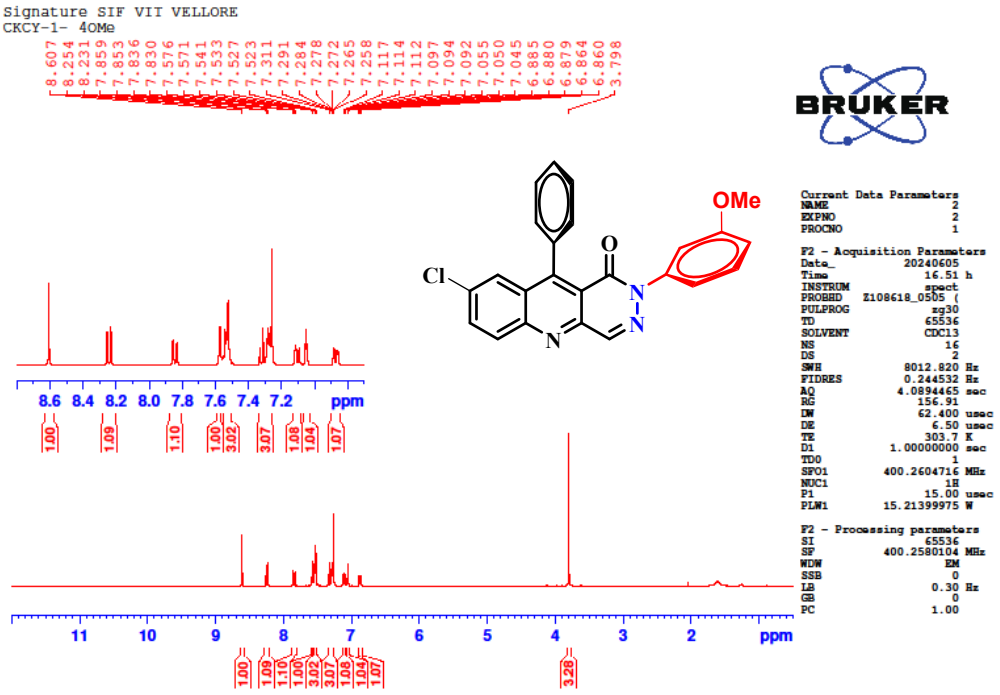


Figure S161: ^{1}H NMR of compound 8m

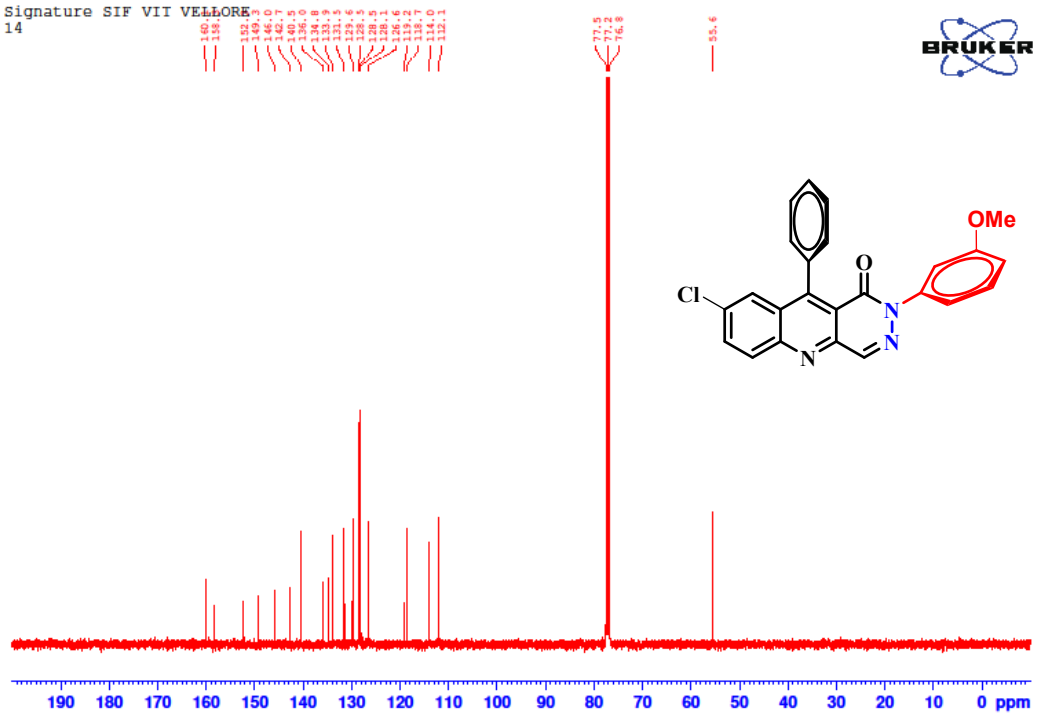


Figure S162: ^{13}C NMR of compound 8m

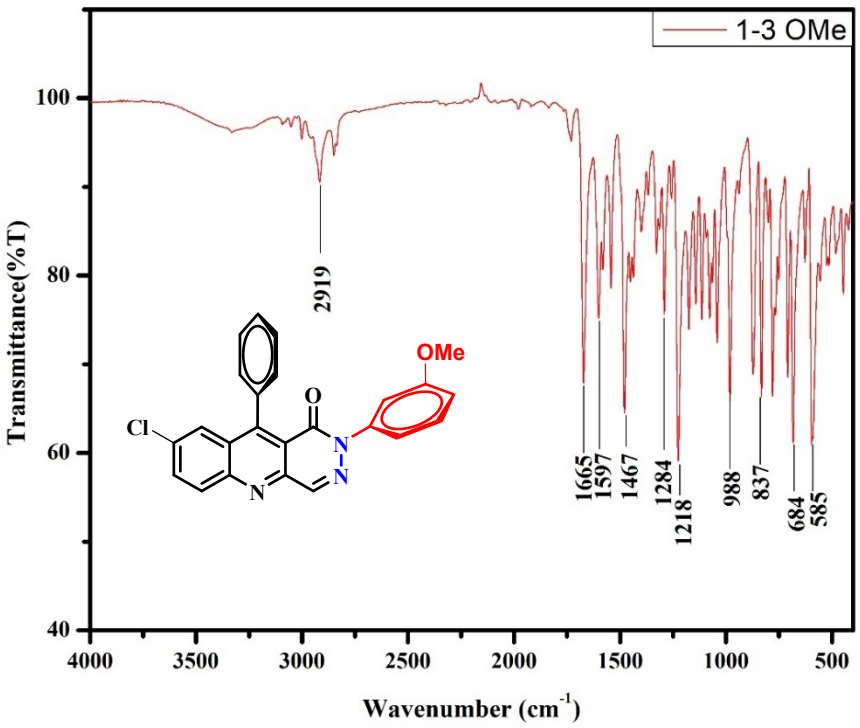


Figure S163: IR spectra of compound 8m

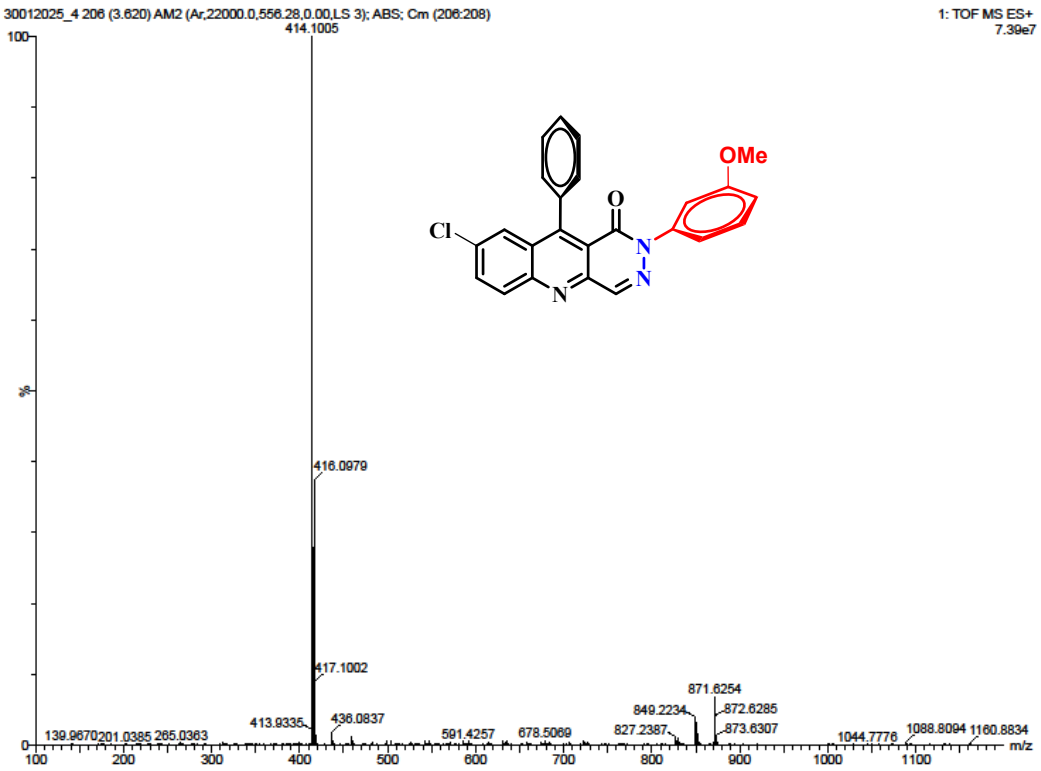


Figure S164: HR-MS spectra of compound 8m

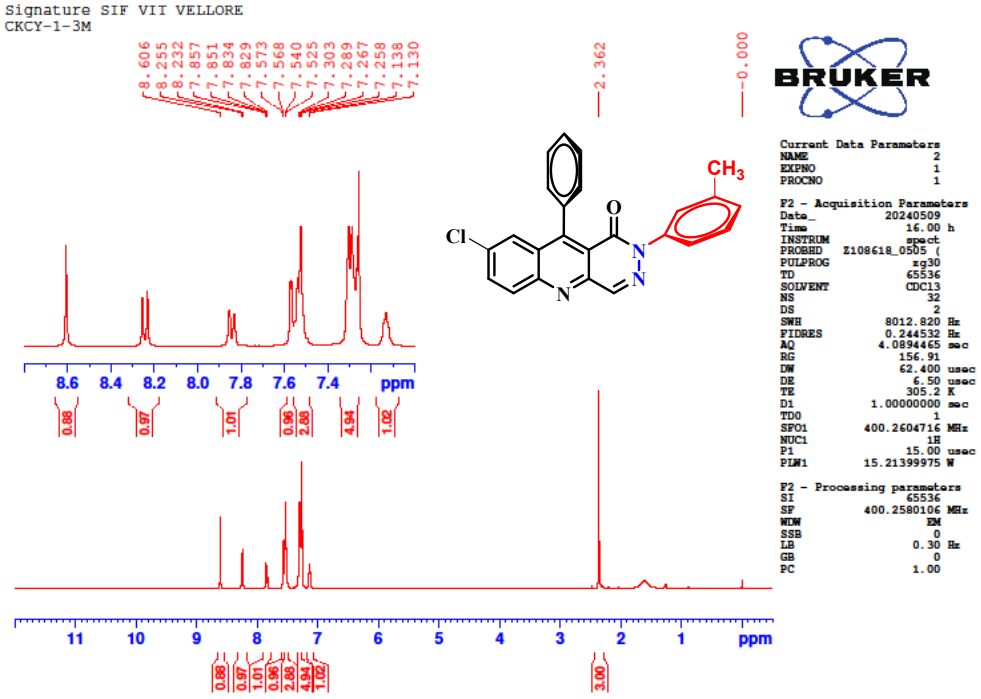


Figure S165: ^{1}H NMR of compound 8n

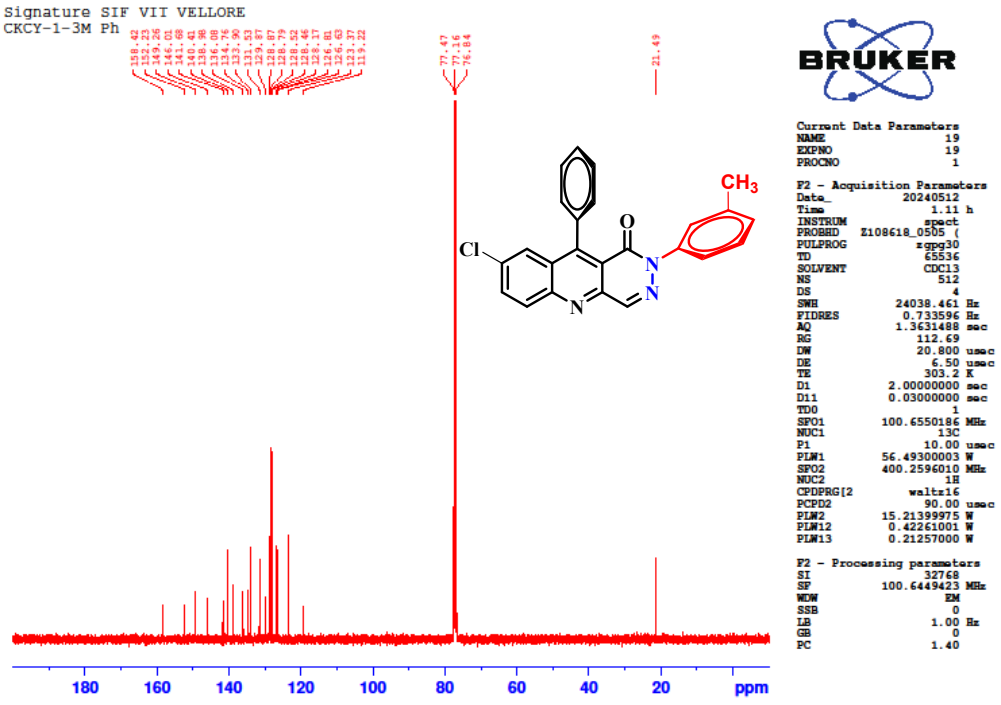


Figure S166: ^{13}C NMR of compound 8n

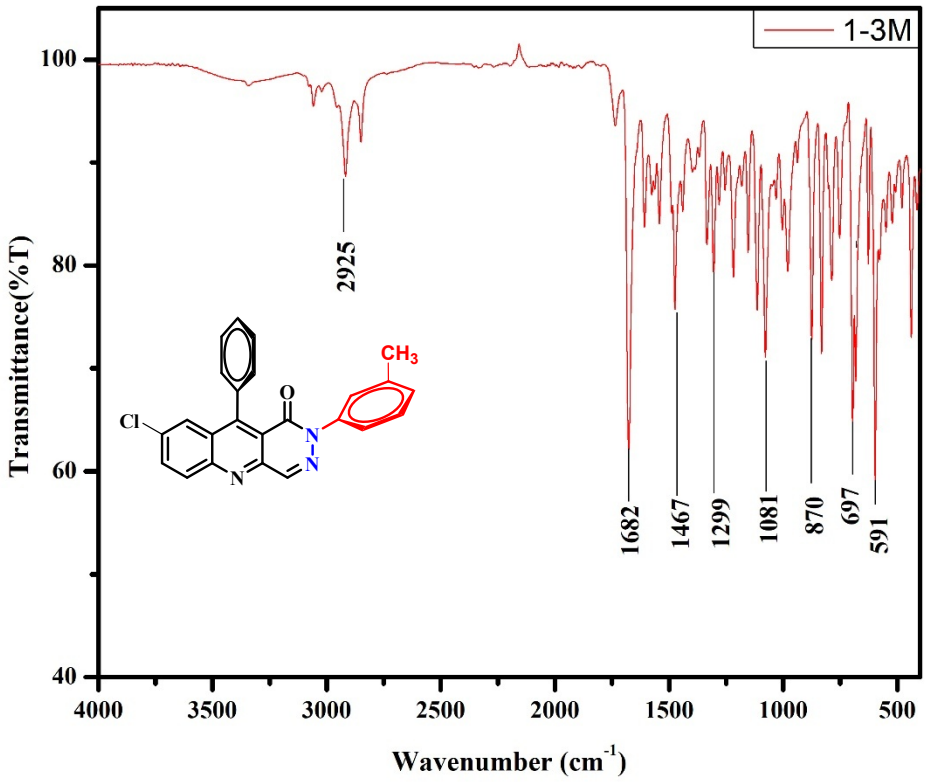


Figure S167: IR spectra of compound 8n

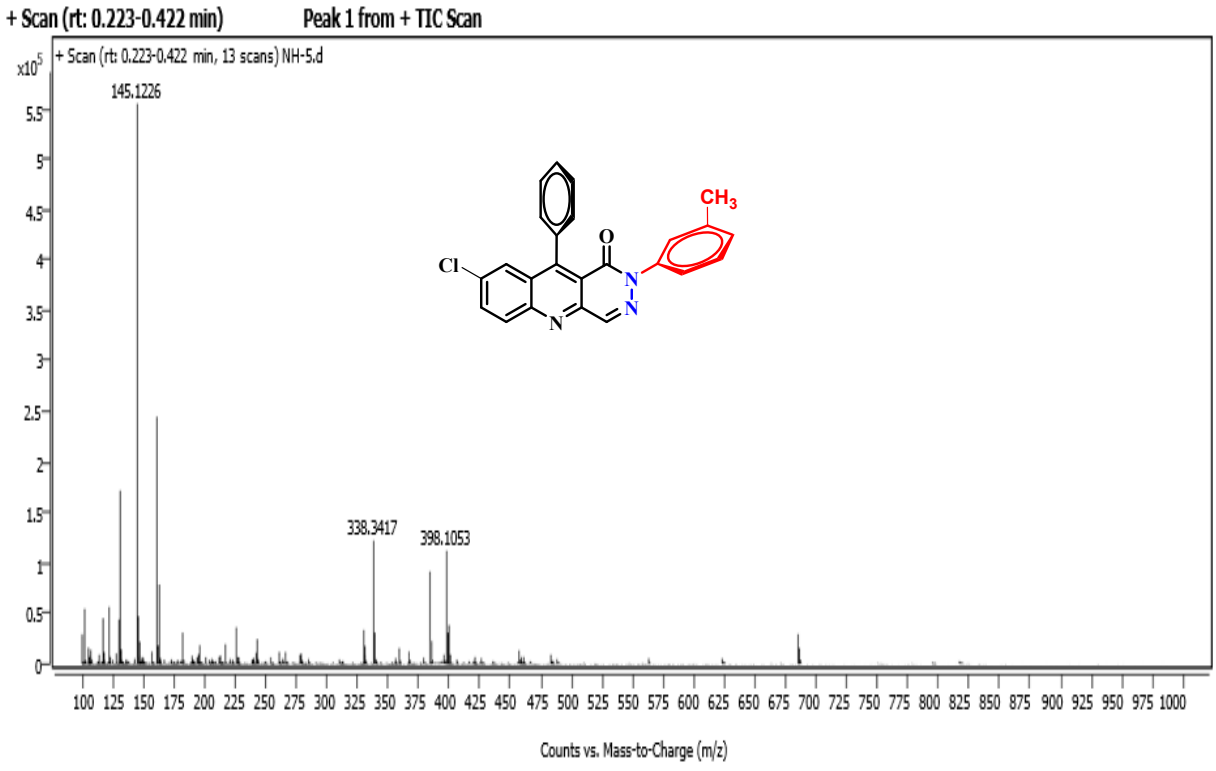


Figure S168: HR-MS spectra of compound 8n

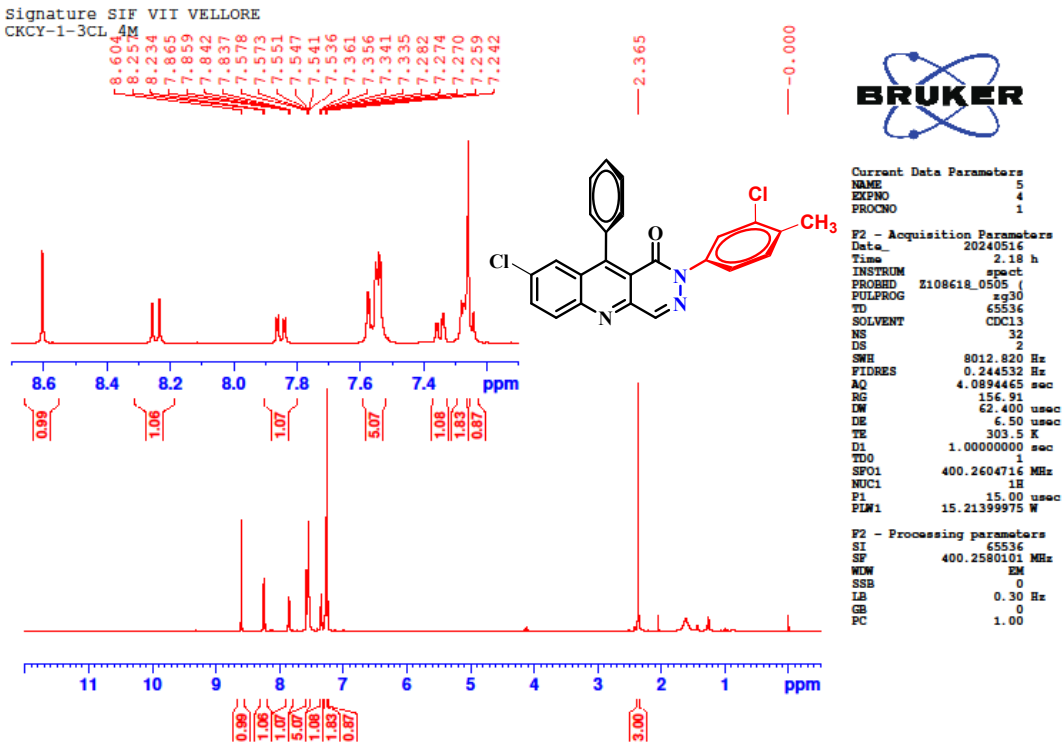


Figure S169: ^{1}H NMR of compound 8o

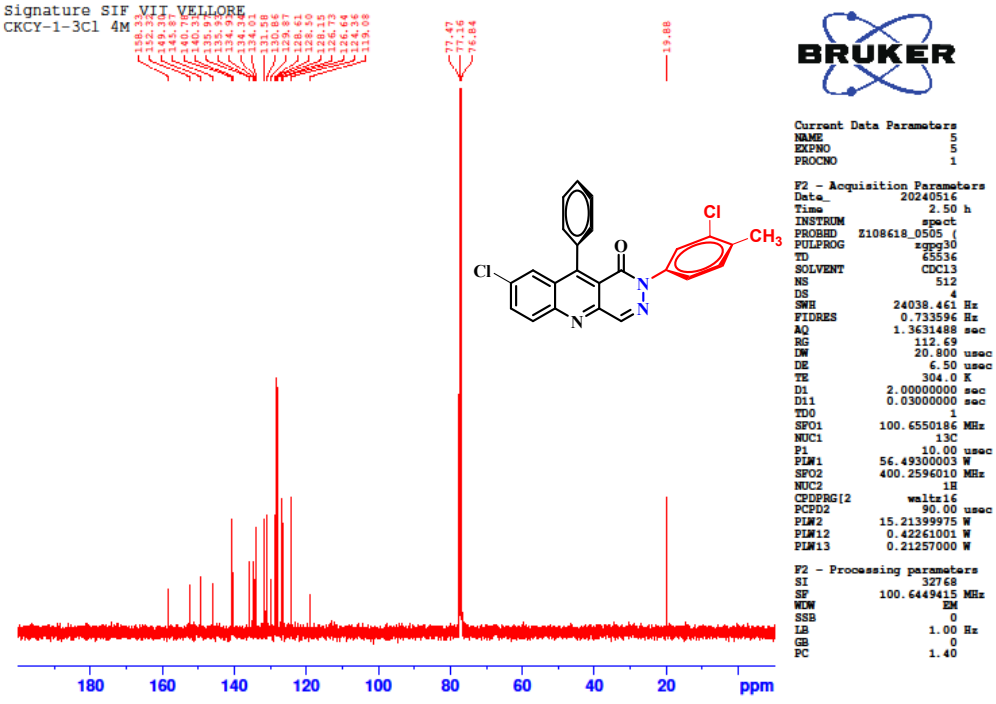


Figure S170: ^{13}C NMR of compound 8o

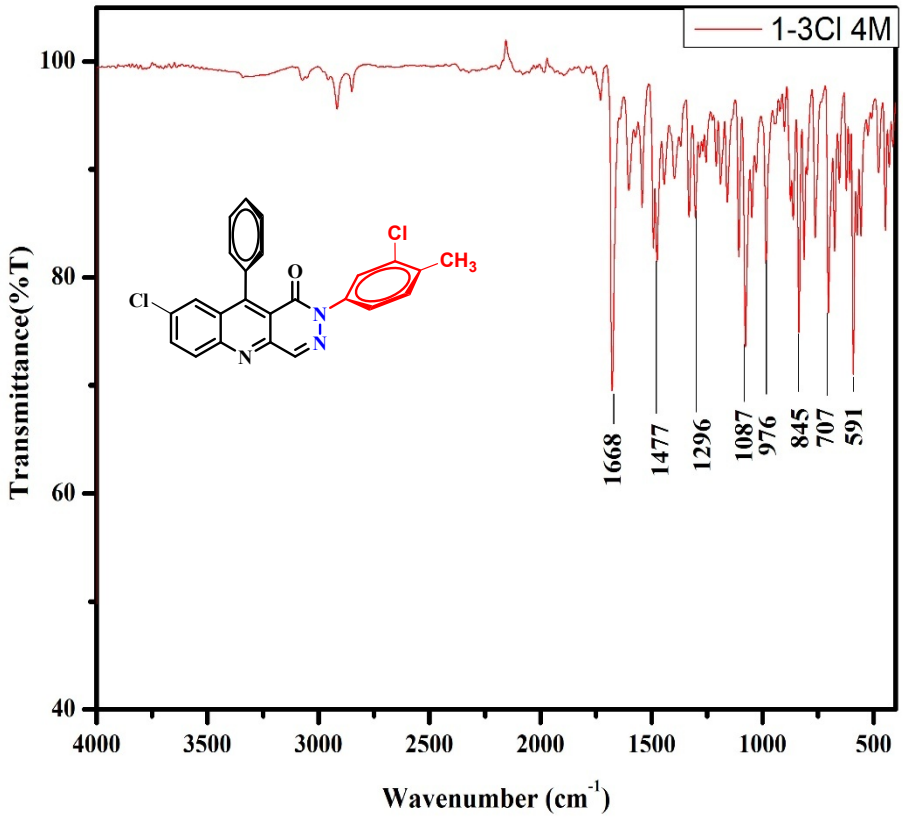


Figure S171: IR spectra of compound 8o

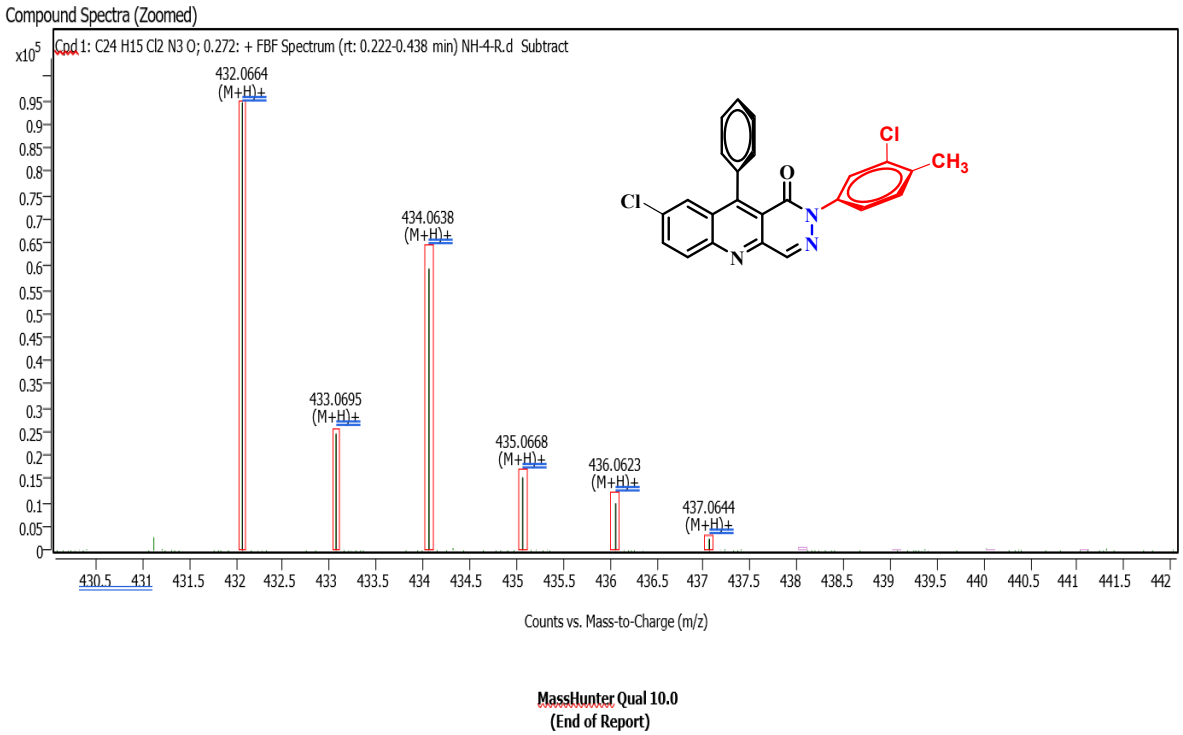


Figure S172: HR-MS spectra of compound 8o

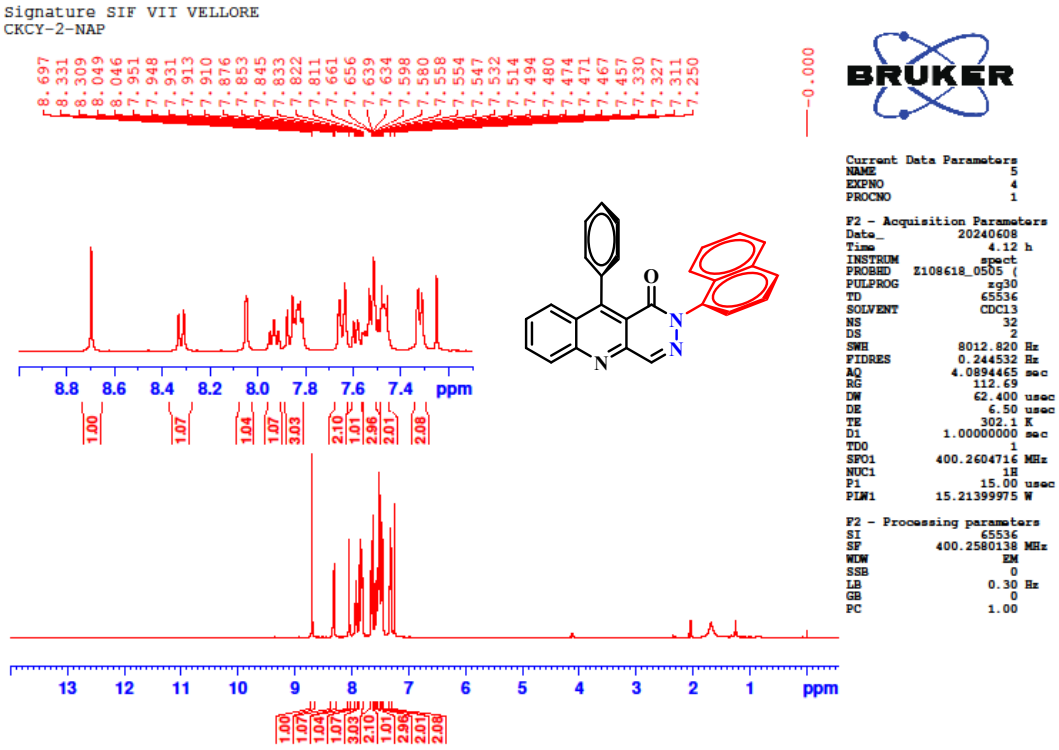


Figure S173: ^{1}H NMR of compound 8p

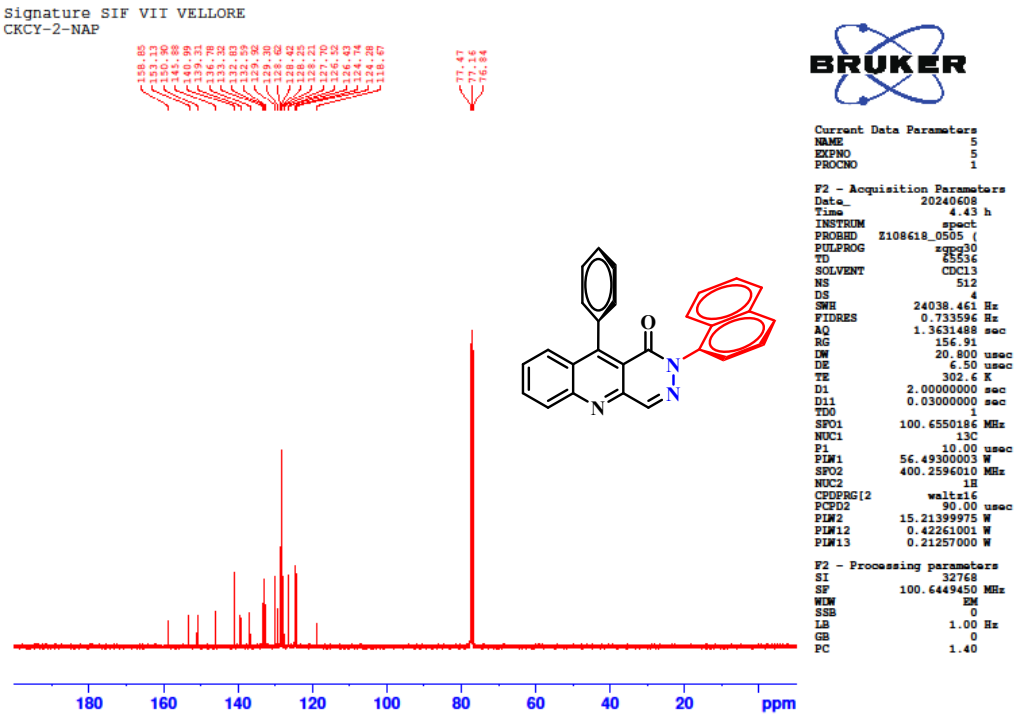


Figure S174: ^{13}C NMR of compound 8p

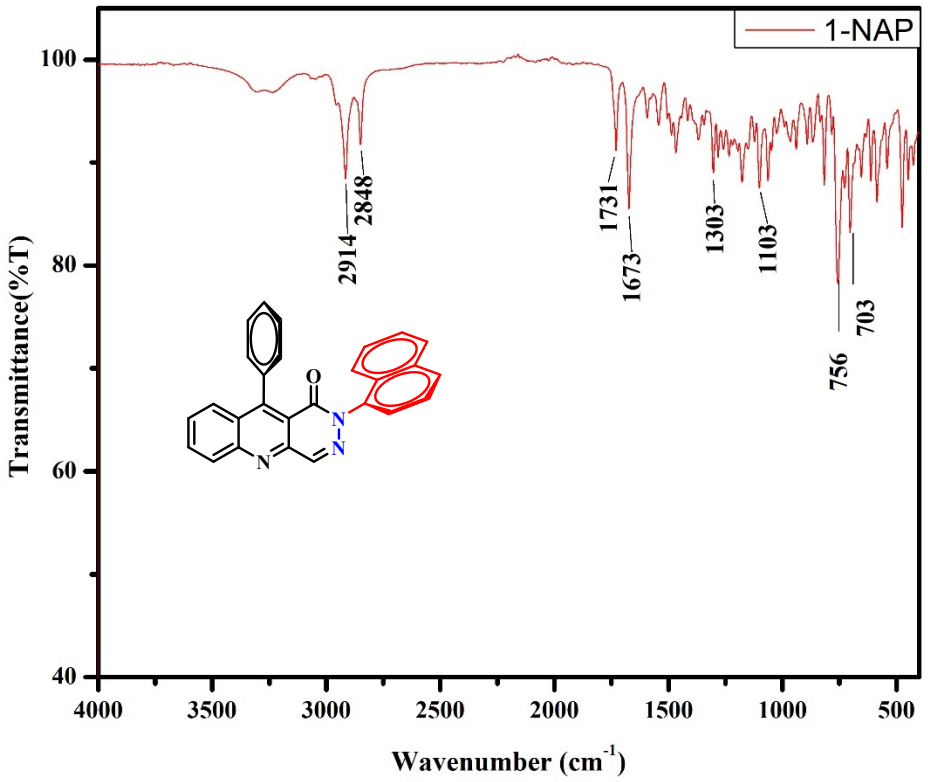


Figure S175: IR spectra of compound 8p

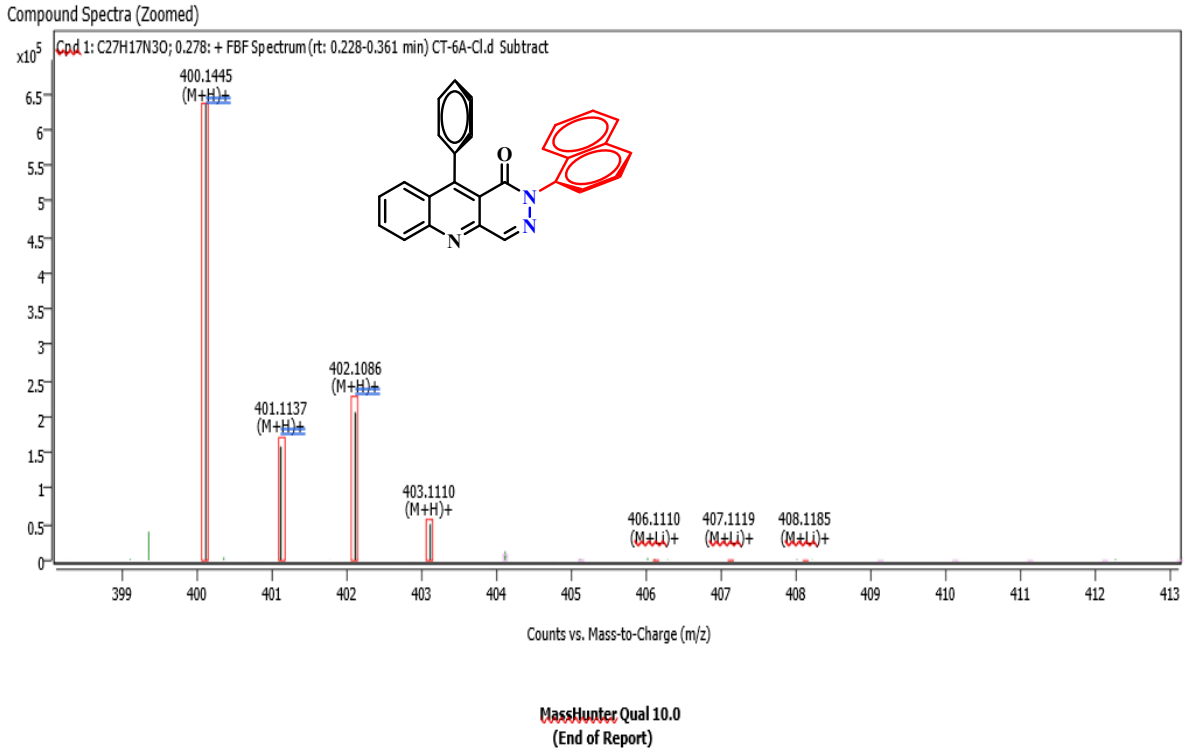


Figure S176: HR-MS spectra of compound 8p

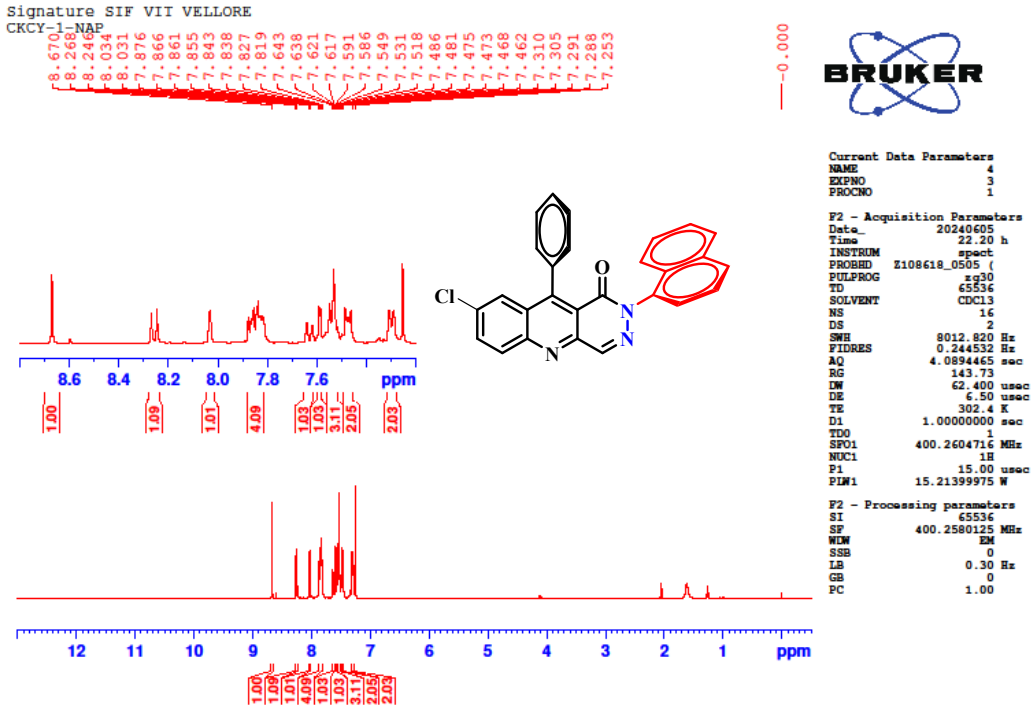


Figure S177: ^{1}H NMR of compound 8q

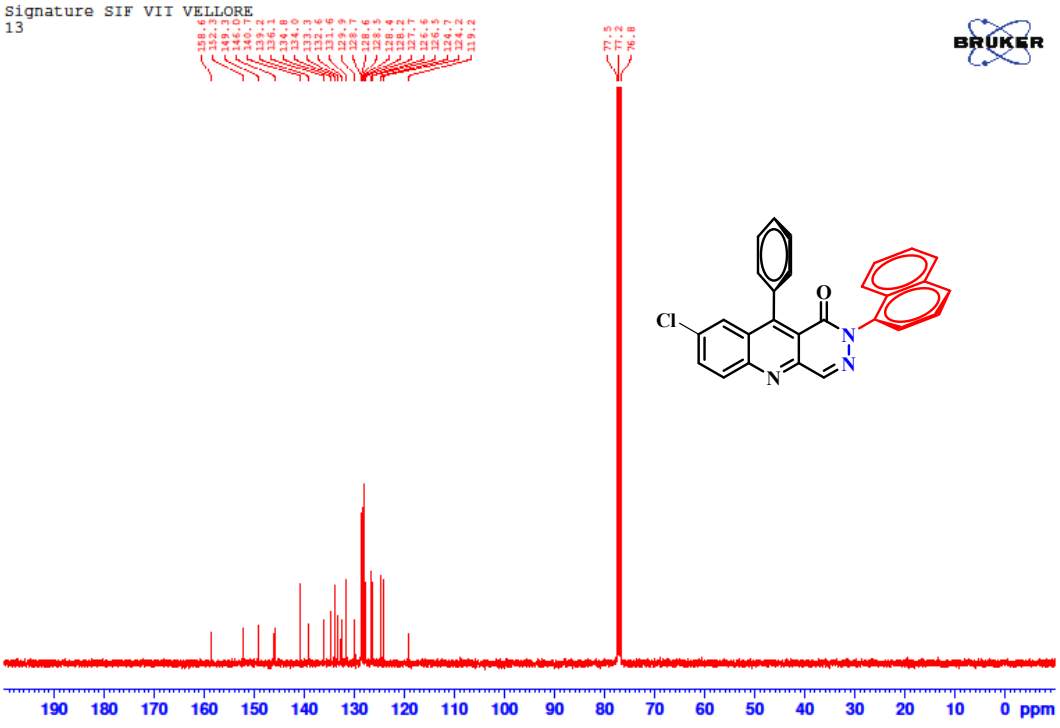


Figure S178: ^{13}C NMR of compound 8q

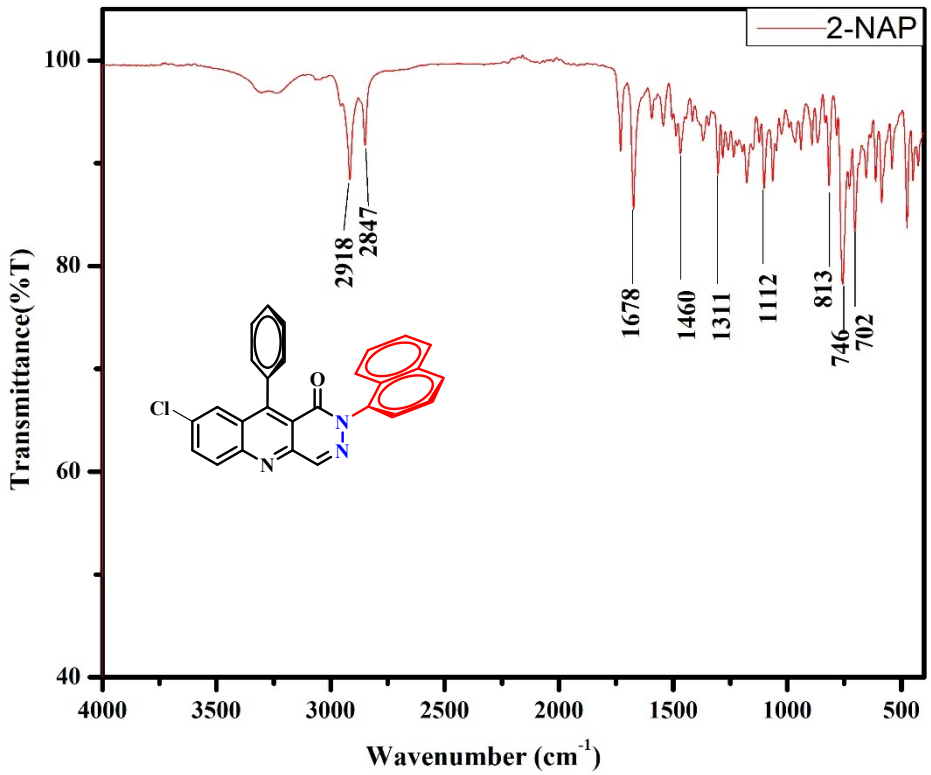


Figure S179: IR spectra of compound 8q

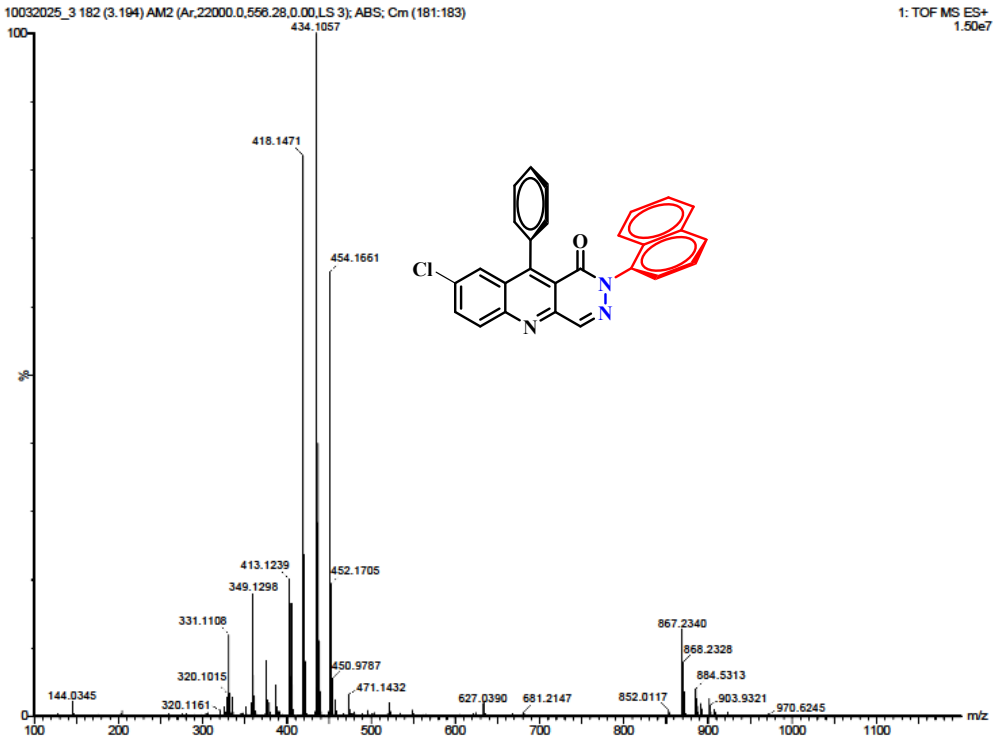


Figure S180: HR-MS spectra of compound 8q

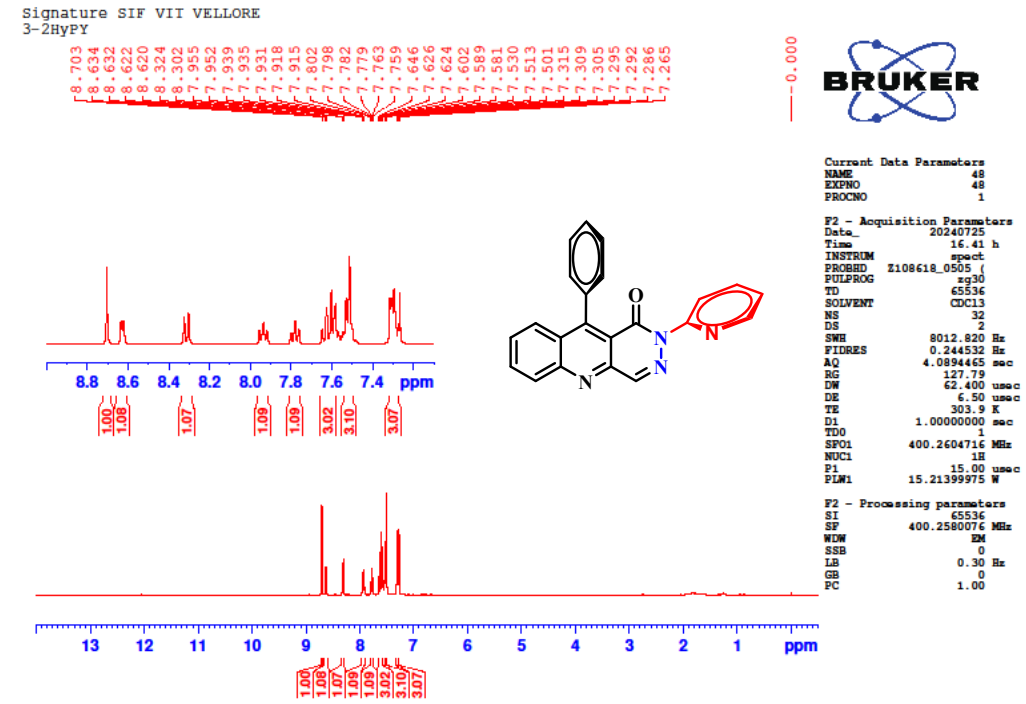


Figure S181: ^{1}H NMR of compound 8r

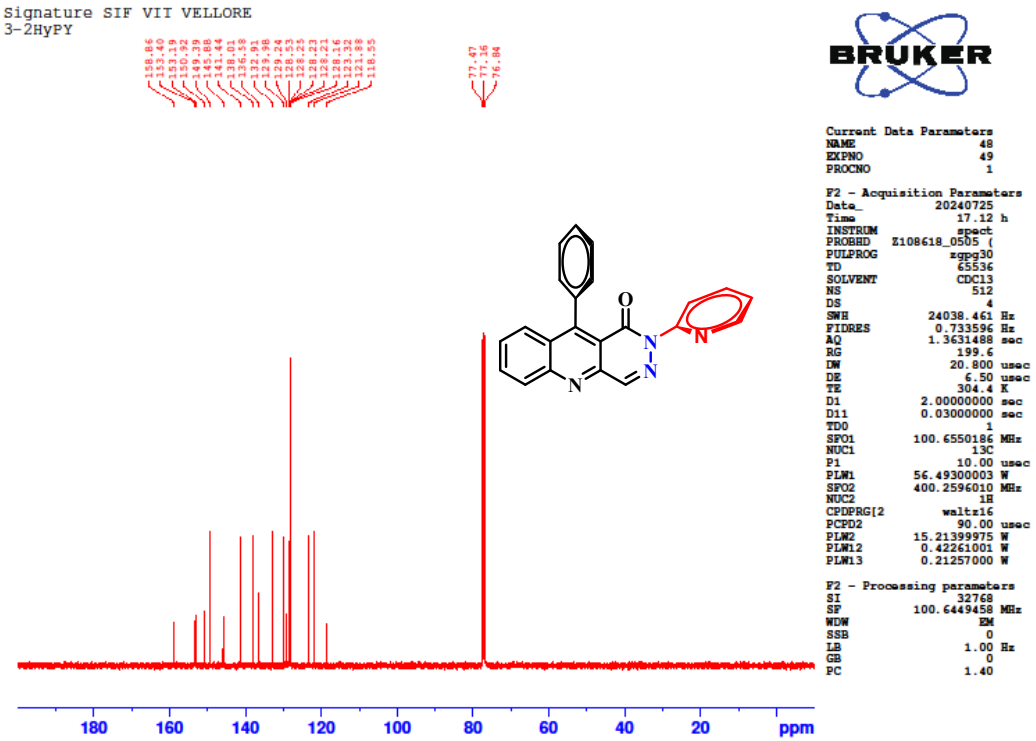


Figure S182: ^{13}C NMR of compound 8r

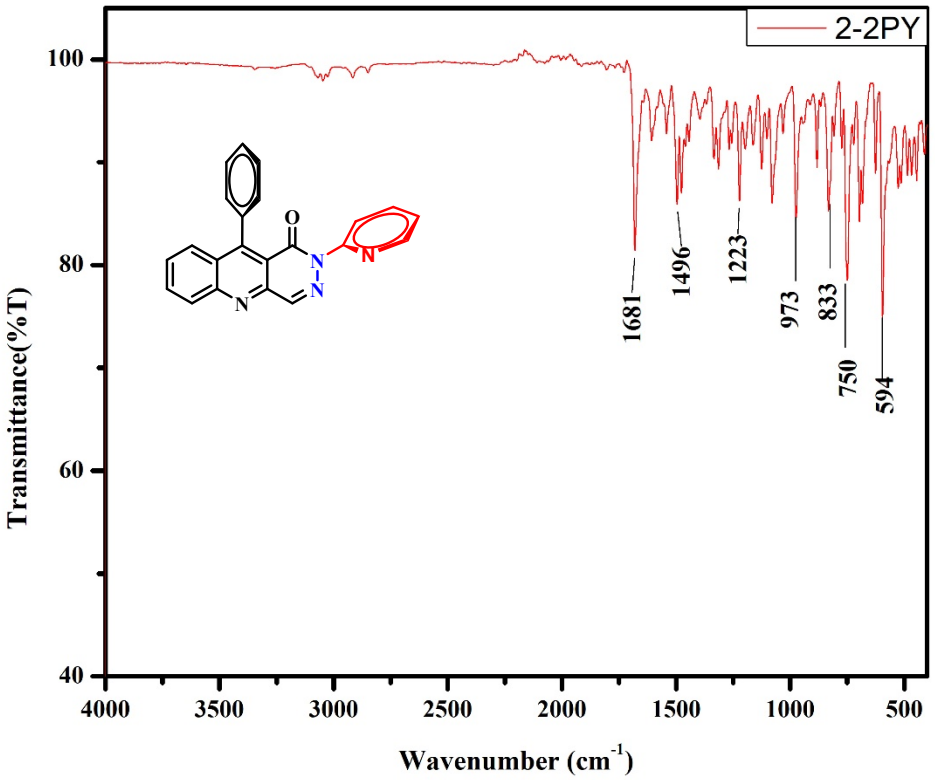


Figure S183: IR spectra of compound 8r

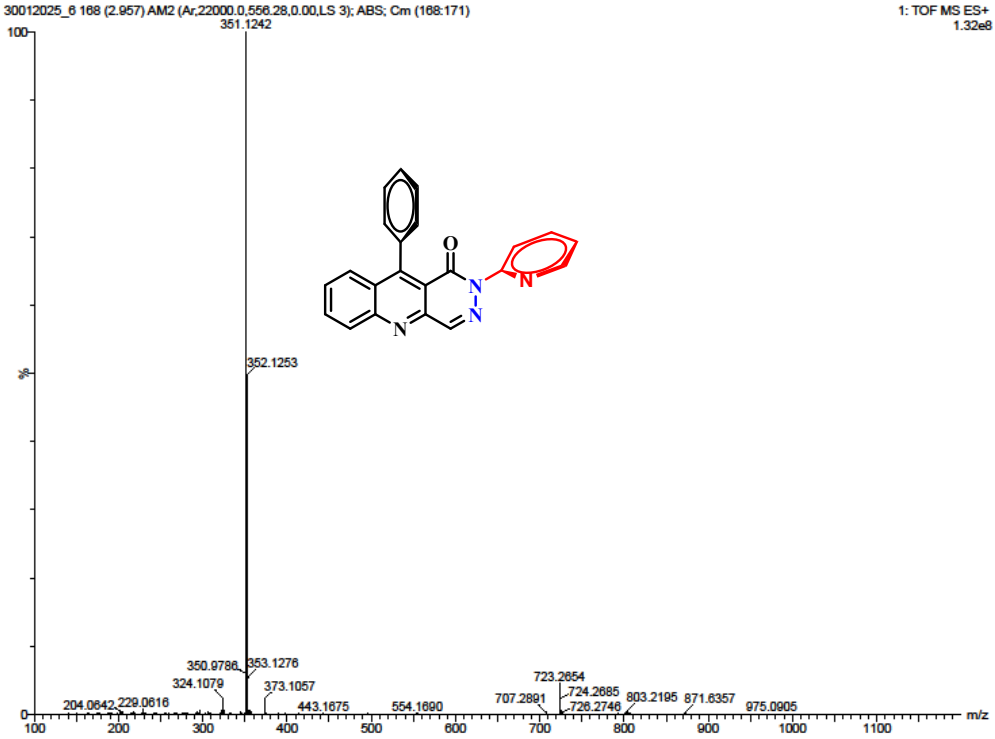


Figure S184: HR-MS spectra of compound 8r

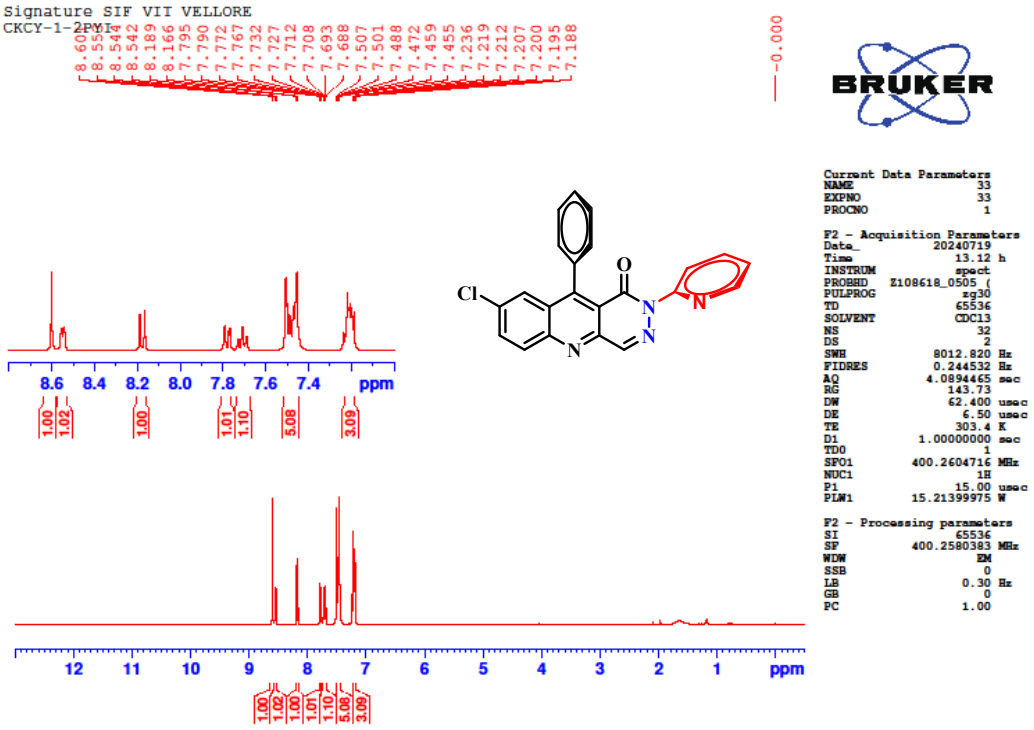


Figure S185: ^{1}H NMR of compound 8s

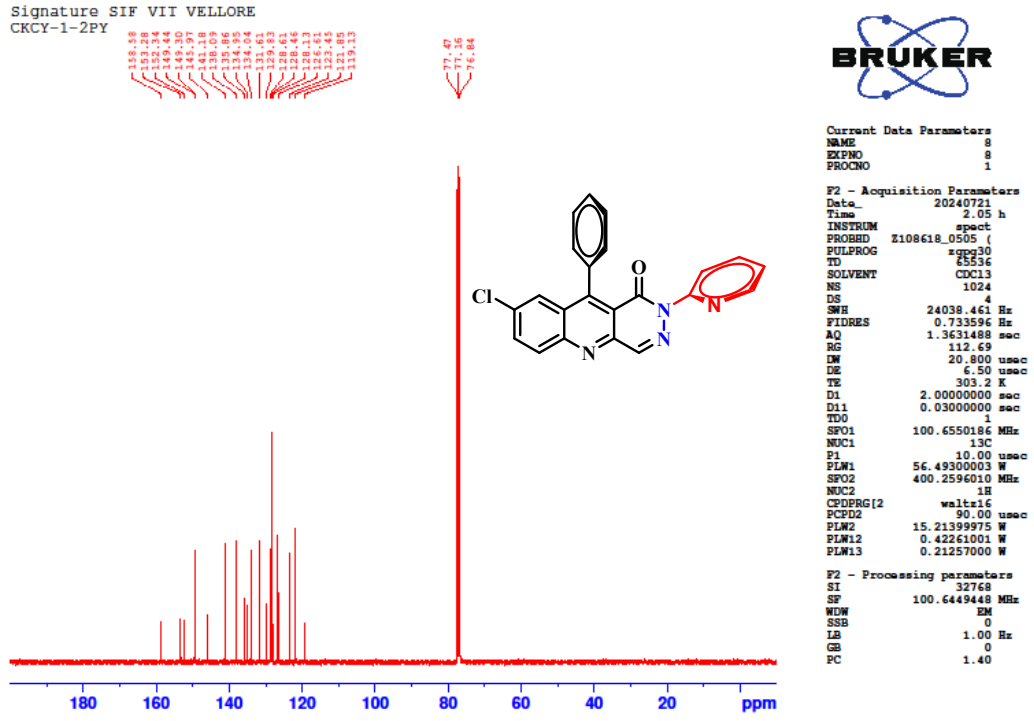


Figure S186: ^{13}C NMR of compound 8s

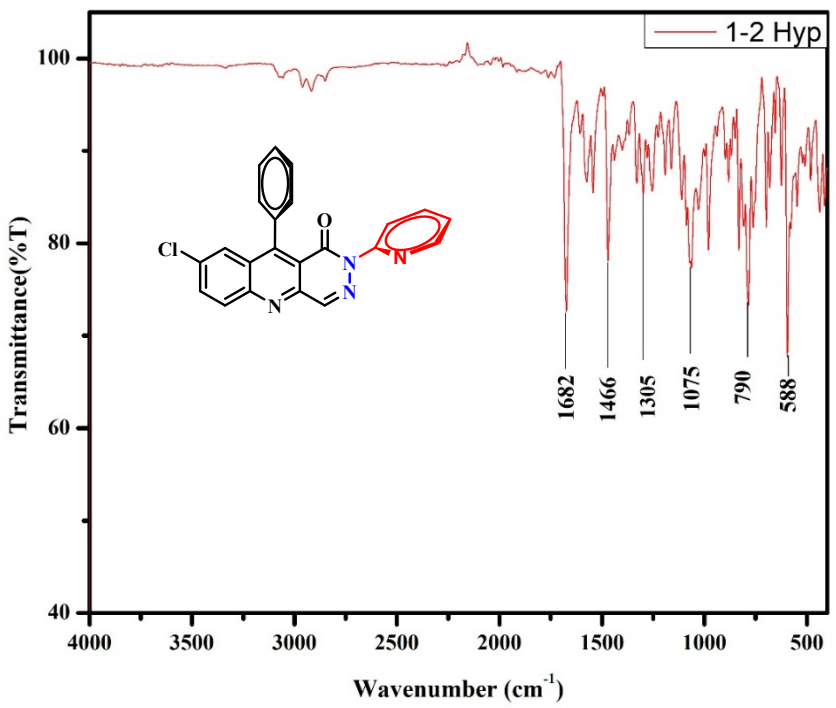


Figure S187: IR spectra of compound 8s

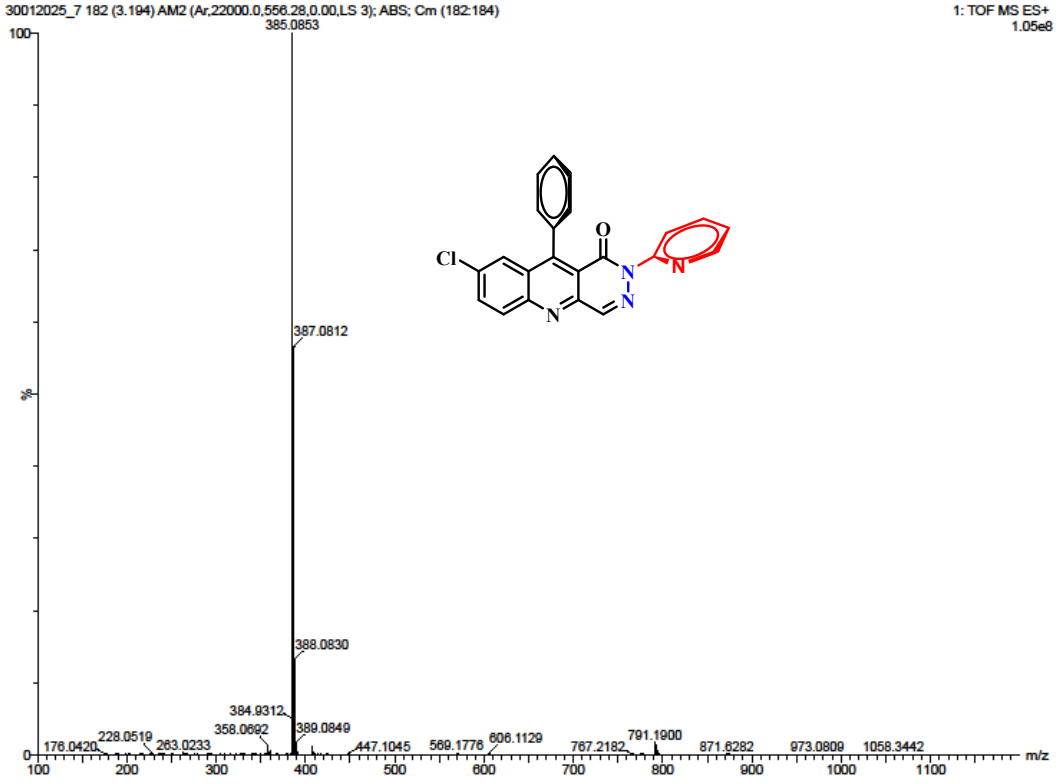


Figure S188: HR-MS spectra of compound 8s

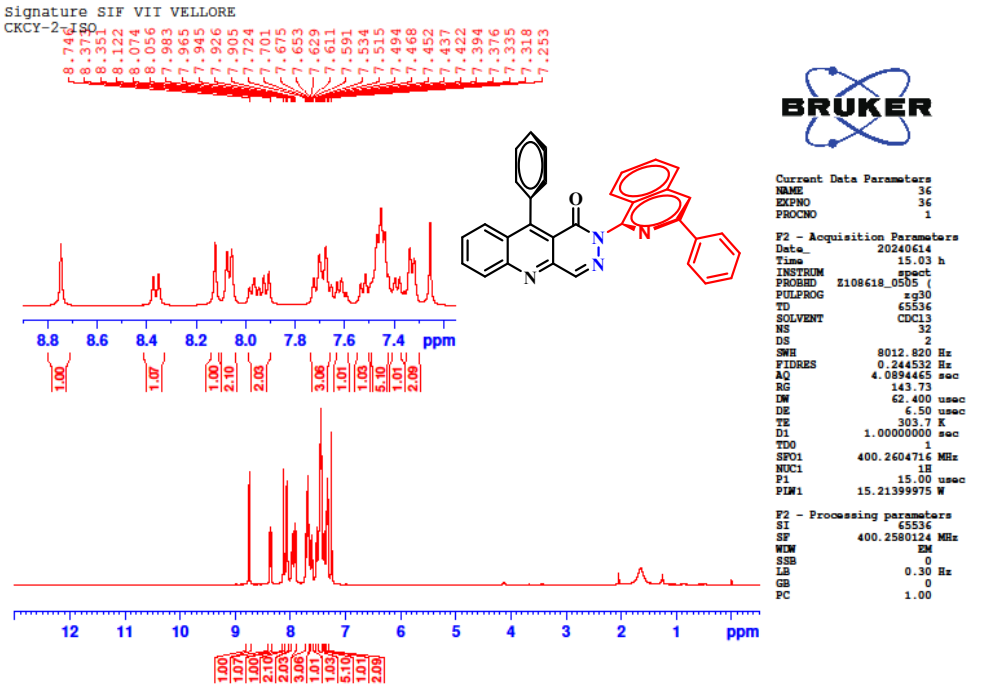


Figure S189: ^{1}H NMR of compound 8t

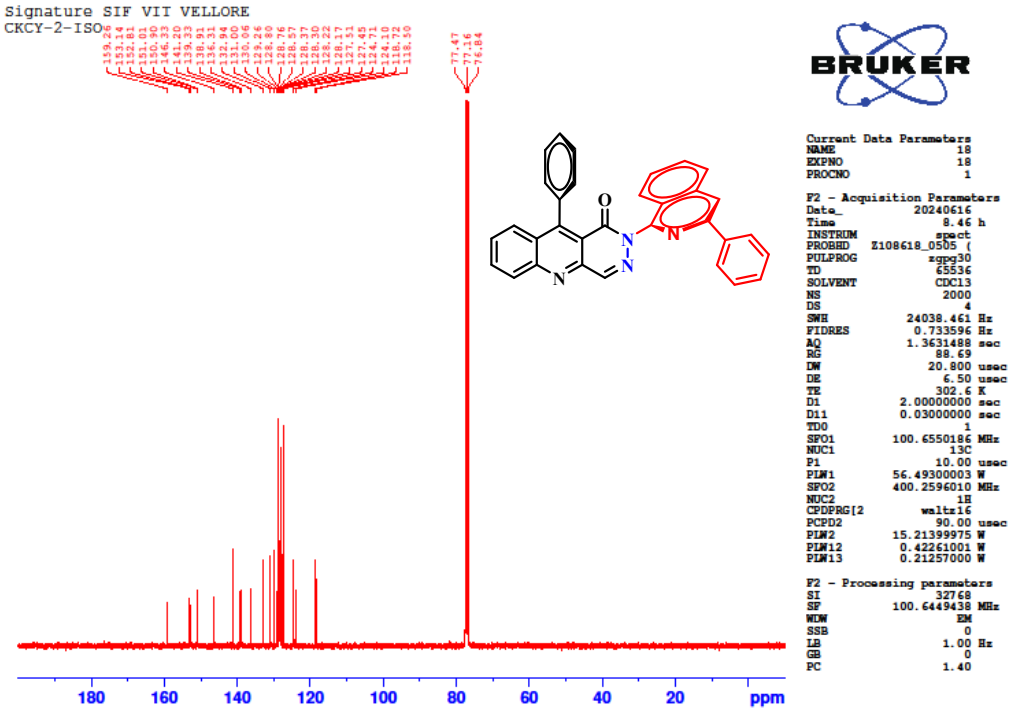


Figure S190: ^{13}C NMR of compound 8t

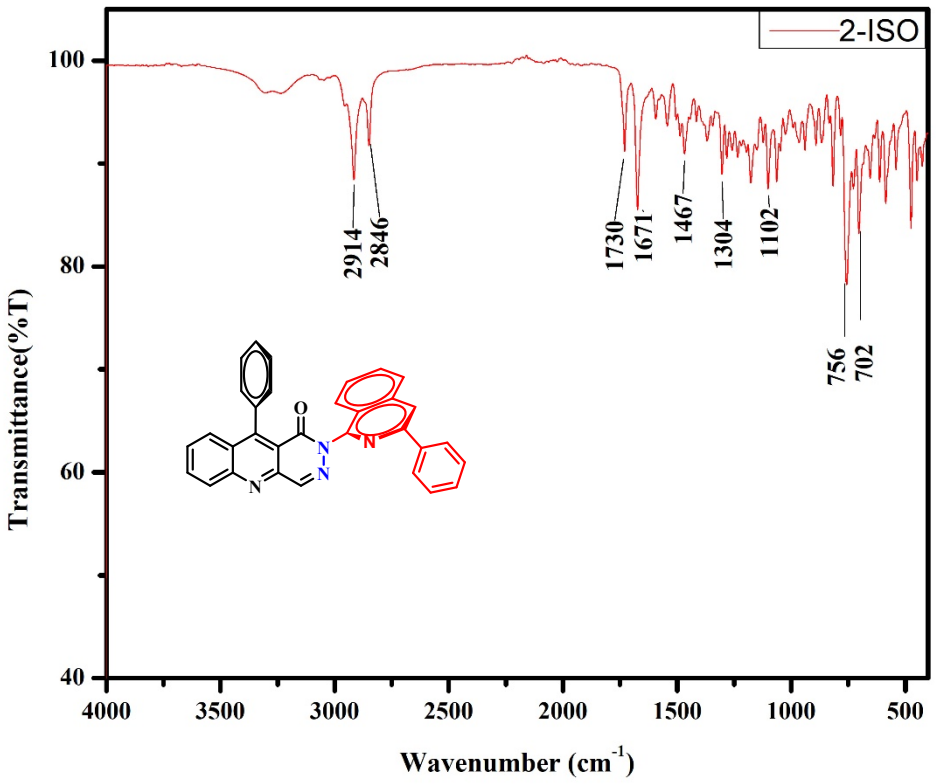


Figure S191: IR spectra of compound 8t

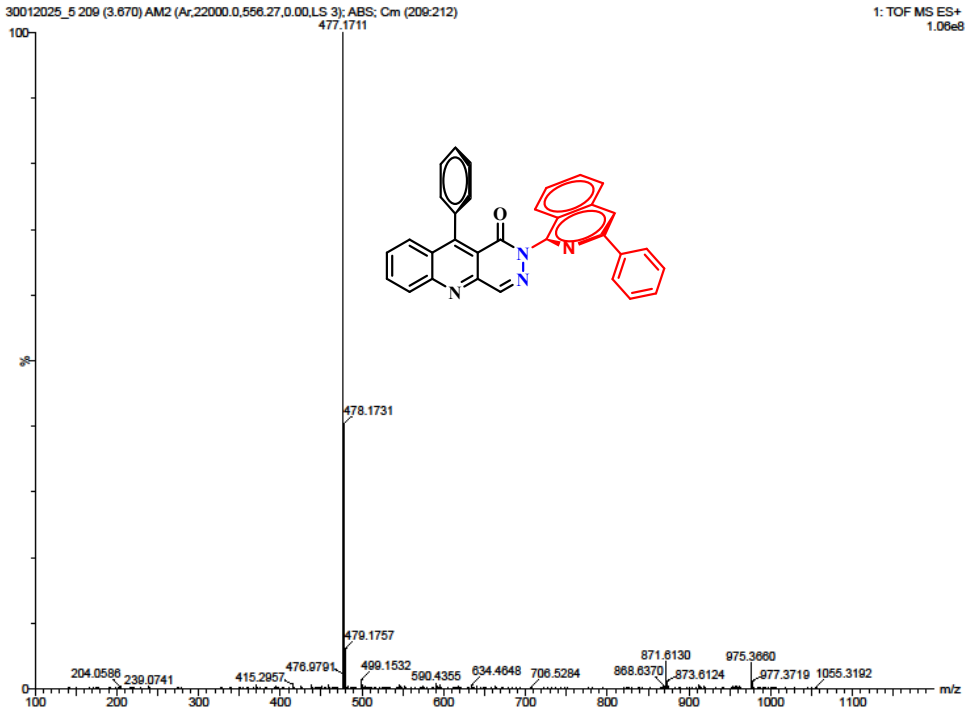


Figure S192: HR-MS spectra of compound 8t

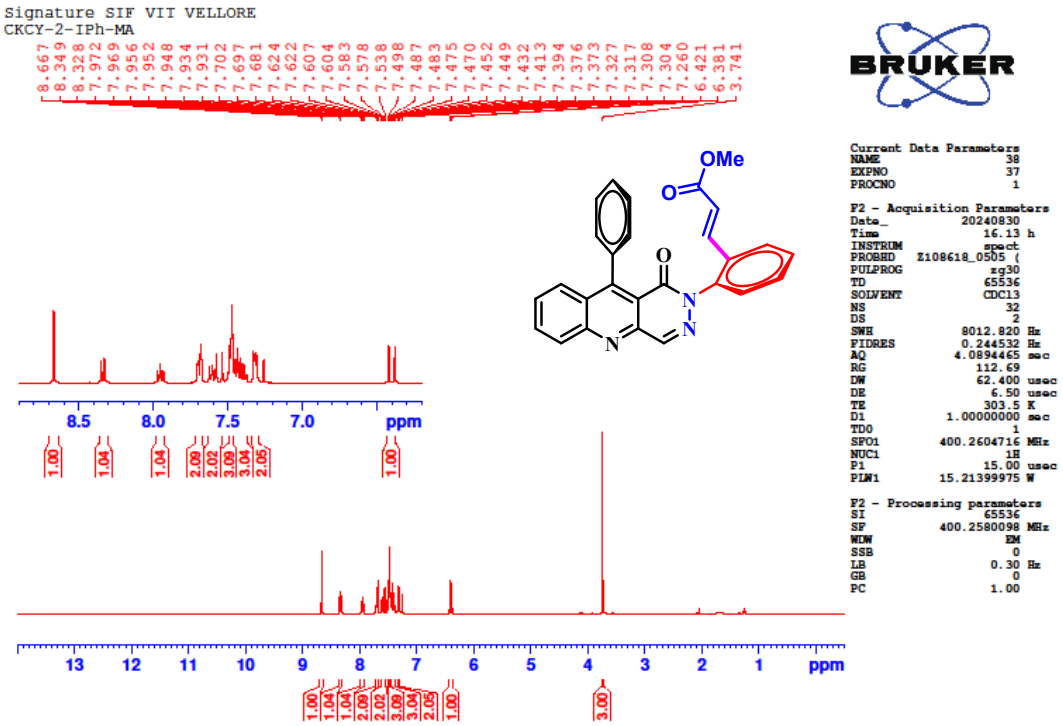


Figure S193: ^{1}H NMR of compound 9a

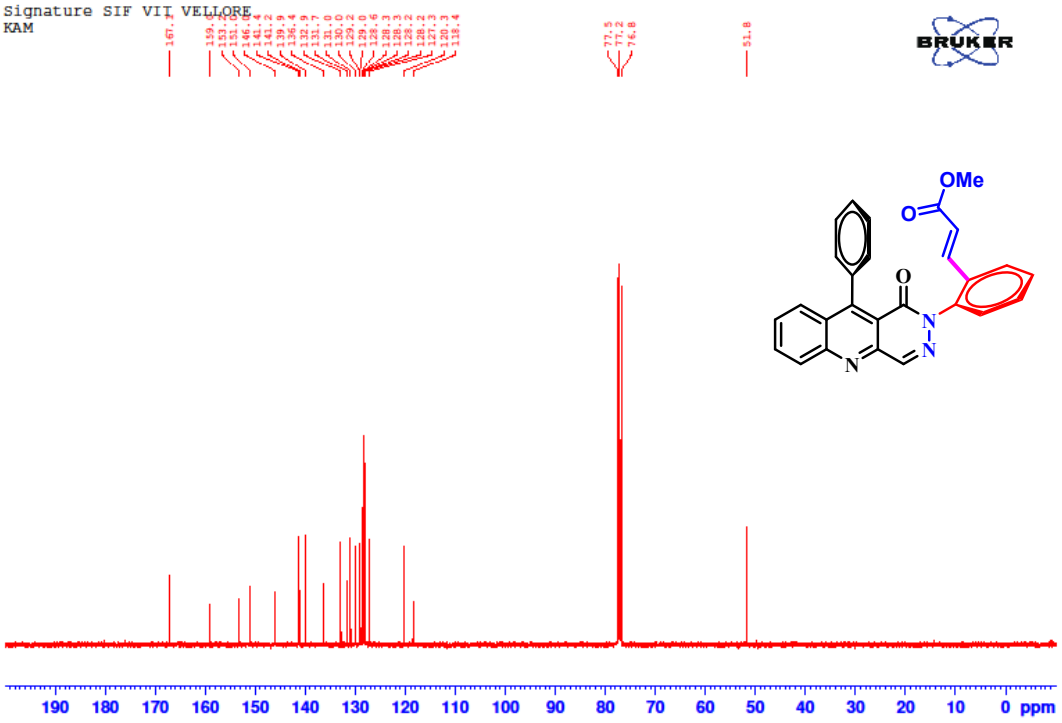


Figure S194: ^{13}C NMR of compound 9a

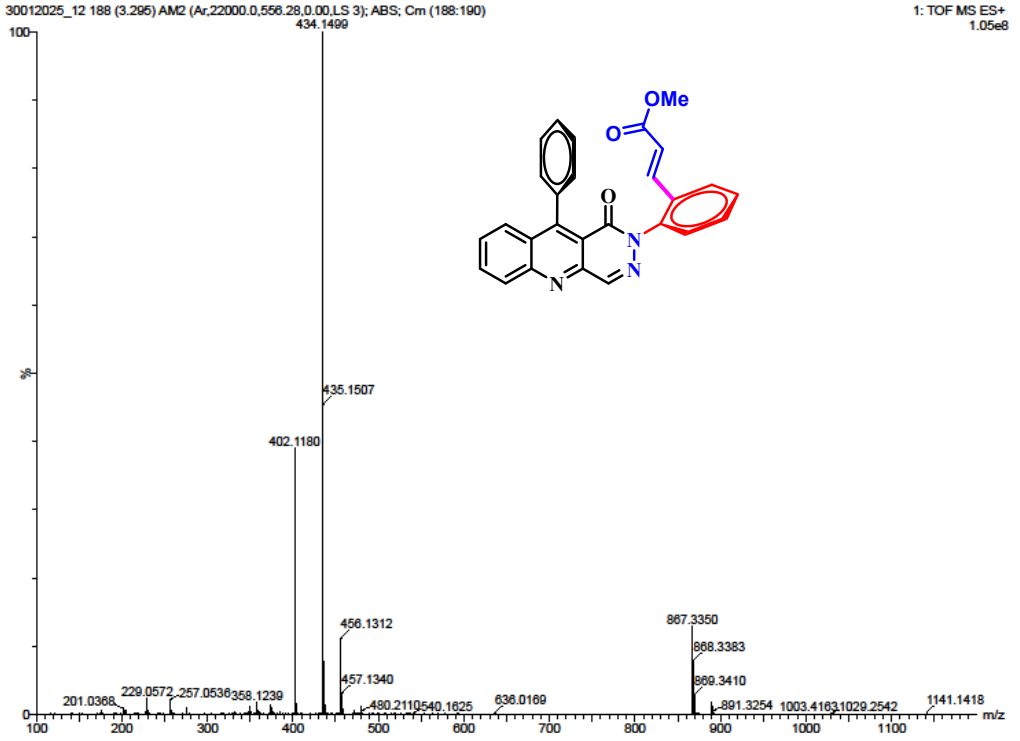


Figure S195: HR-MS spectra of compound 9a

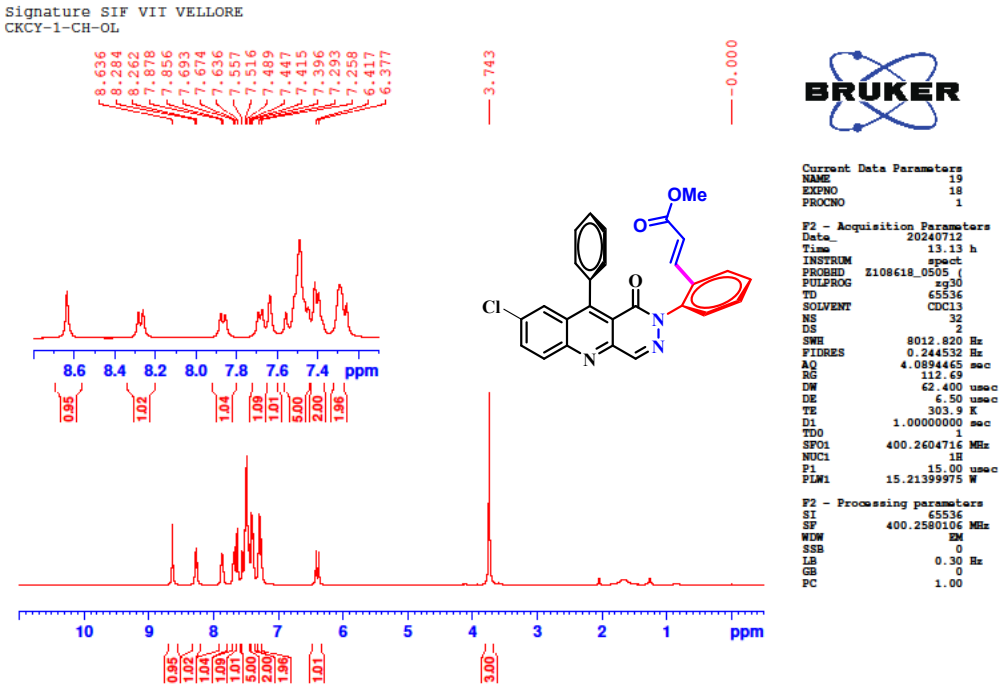
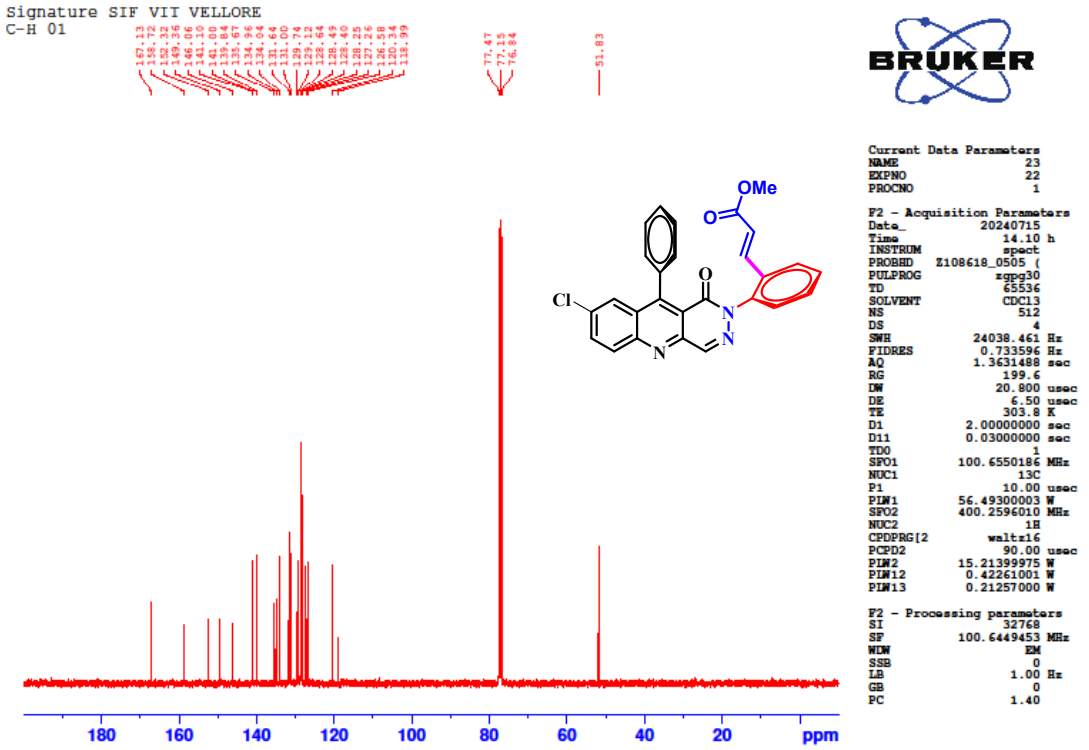


Figure S196: ^{1}H NMR of compound 9b



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PROCNO 1

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DE 6.50 usec
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P1 10.00 usec
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SFO2 400.2596010 MHz
NUC2 1H
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PLW13 0.21257000 W

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Figure S197: ^{13}C NMR of compound 9b

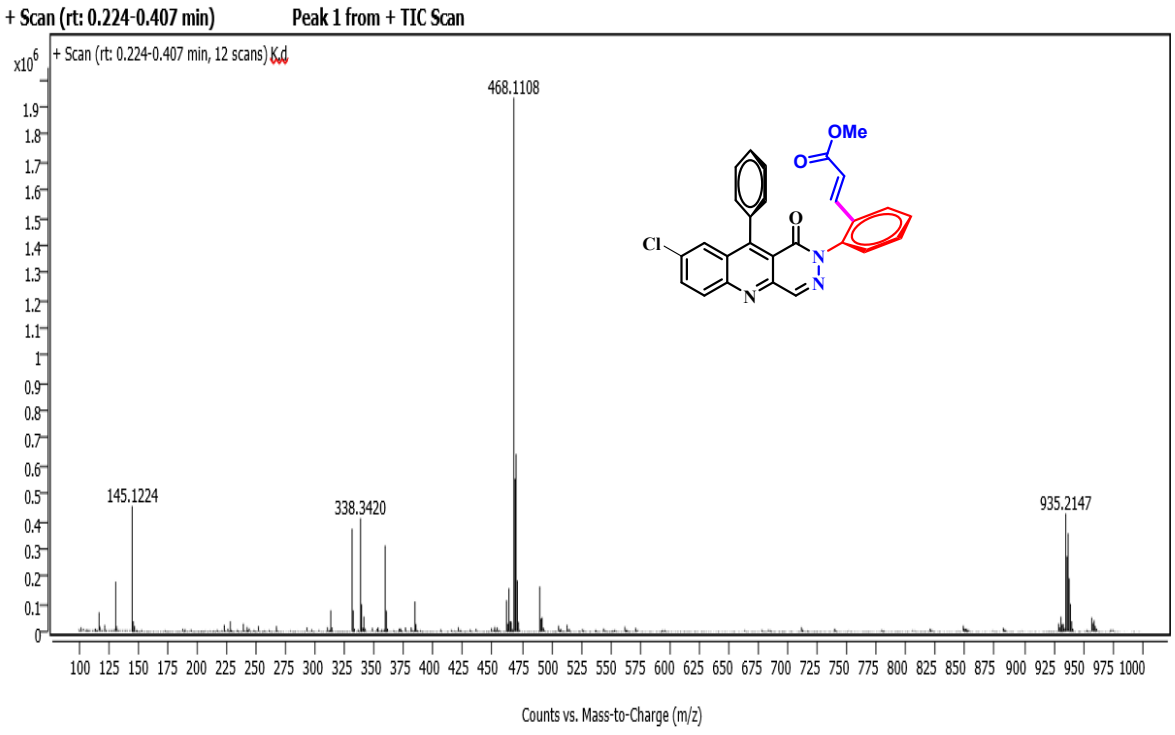

Figure S198: HR-MS spectra of compound 9b

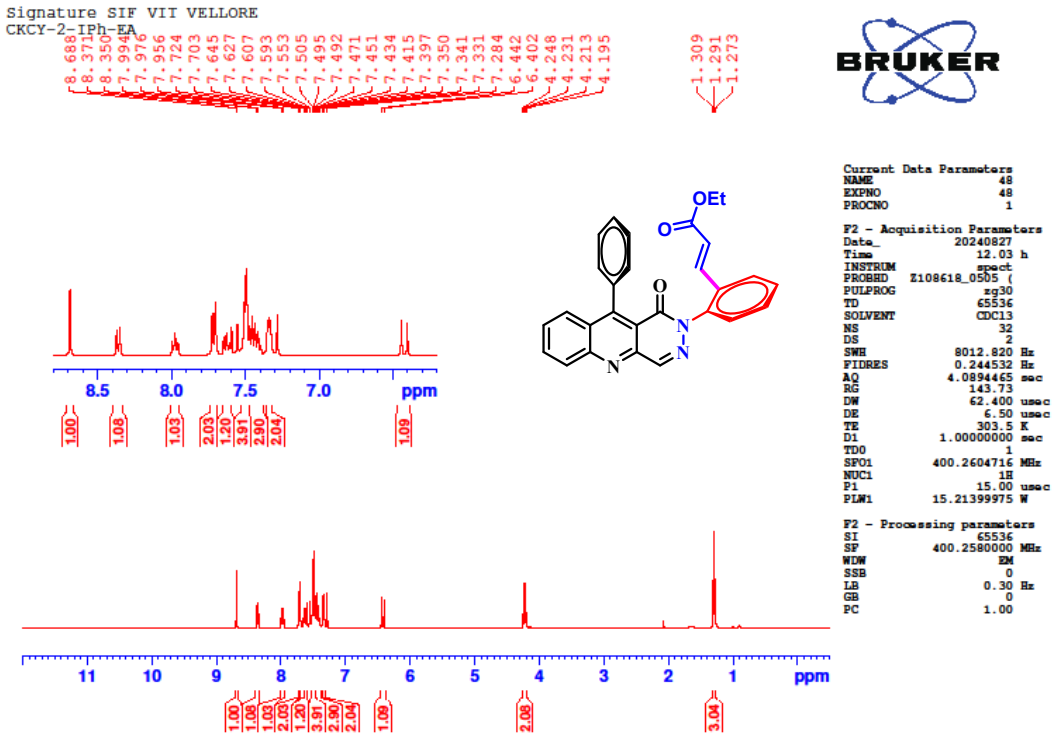

Figure S199: ^{1}H NMR of compound 9c

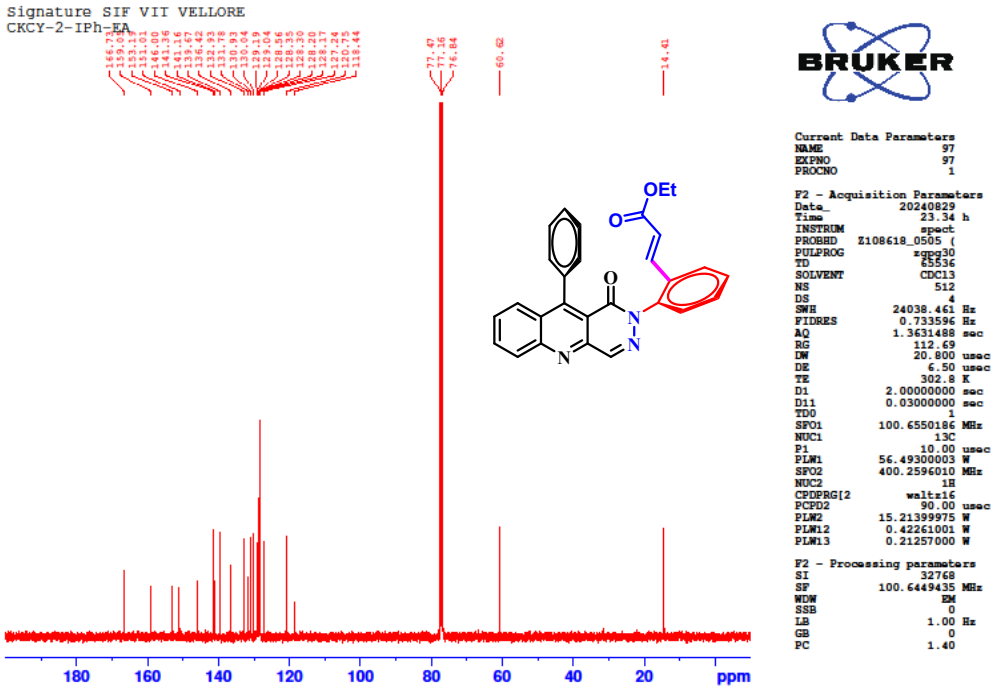

Figure S200: ^{13}C NMR of compound 9c

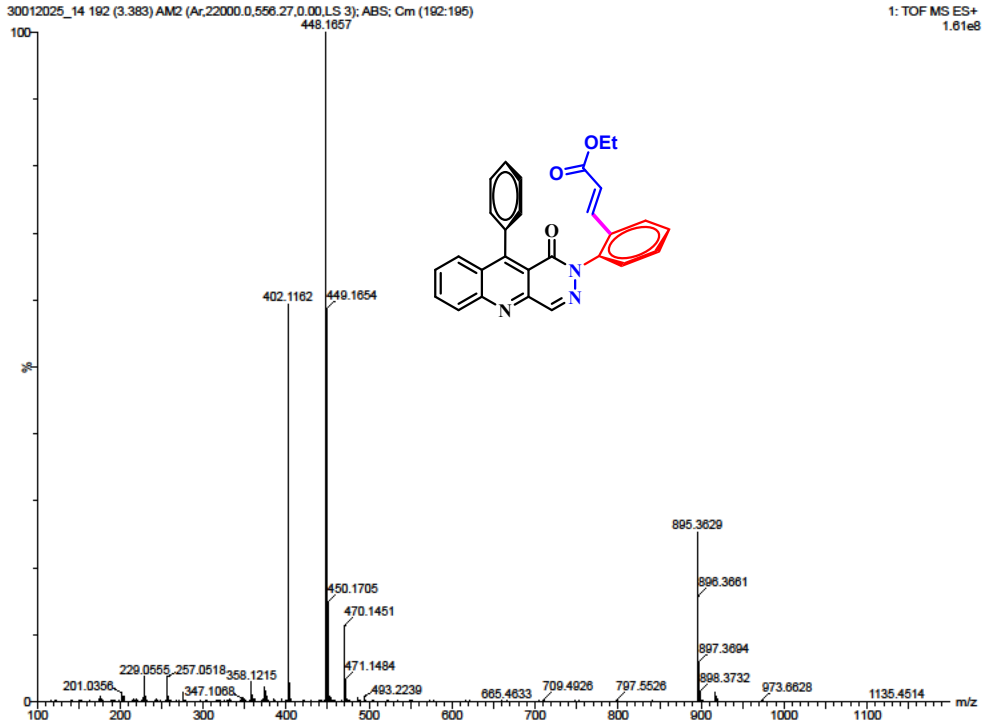

Figure S201: HR-MS spectra of compound 9c

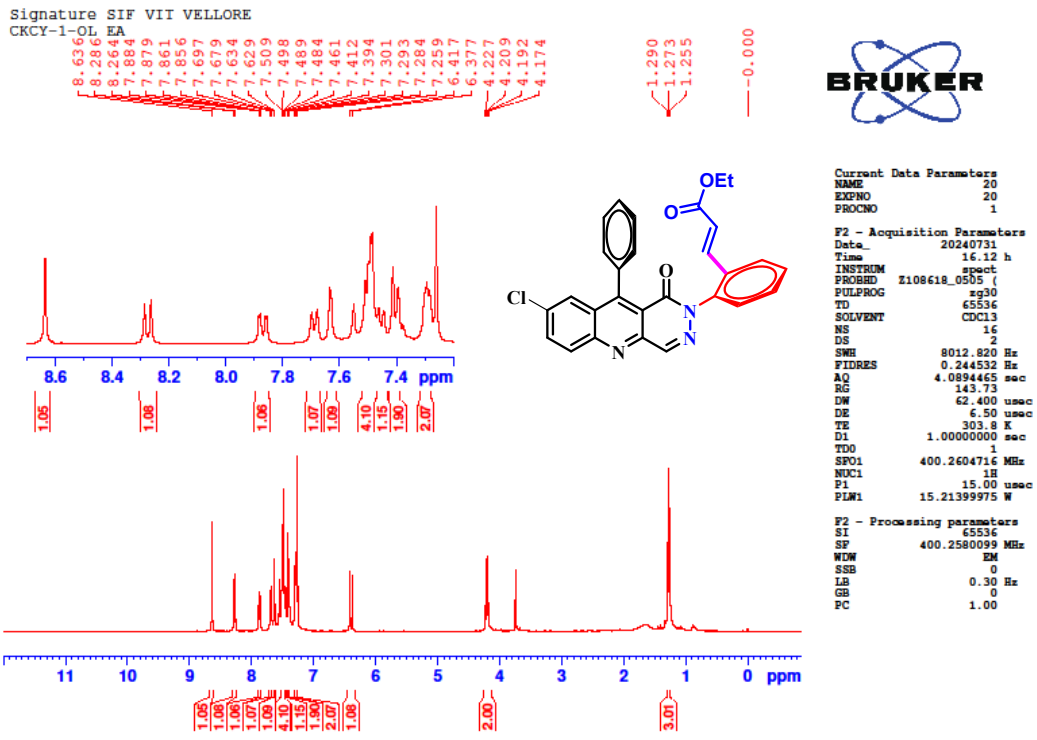

Figure S202: ^{1}H NMR of compound 9d

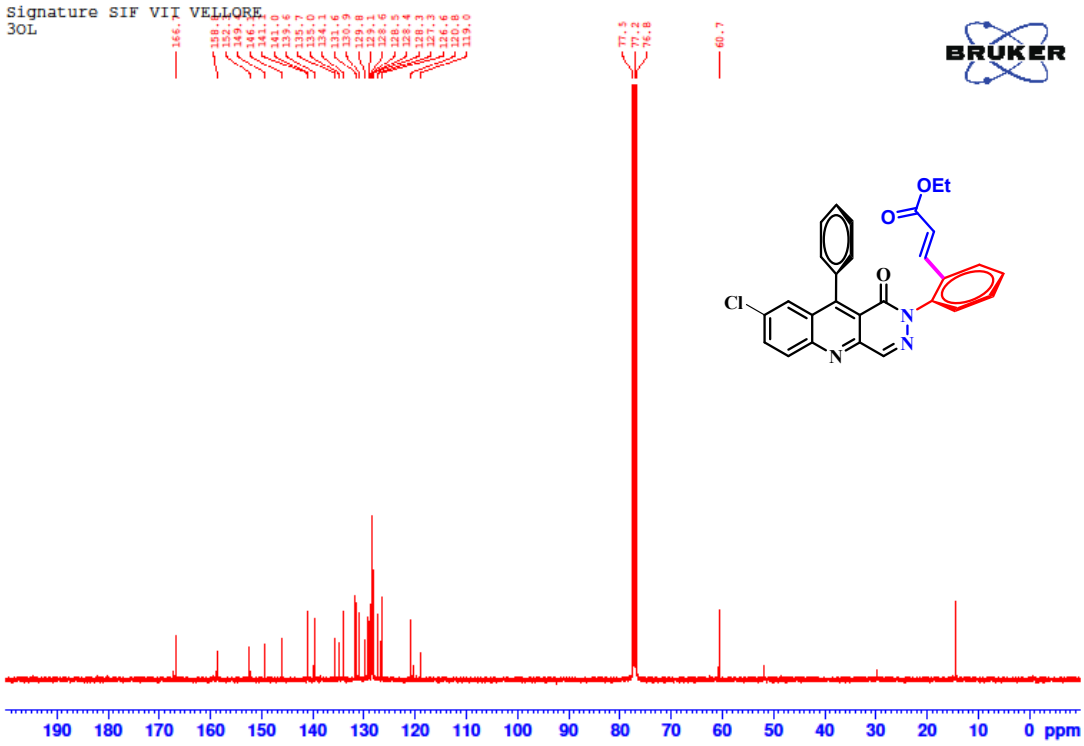

Figure S203: ^{13}C NMR of compound 9d

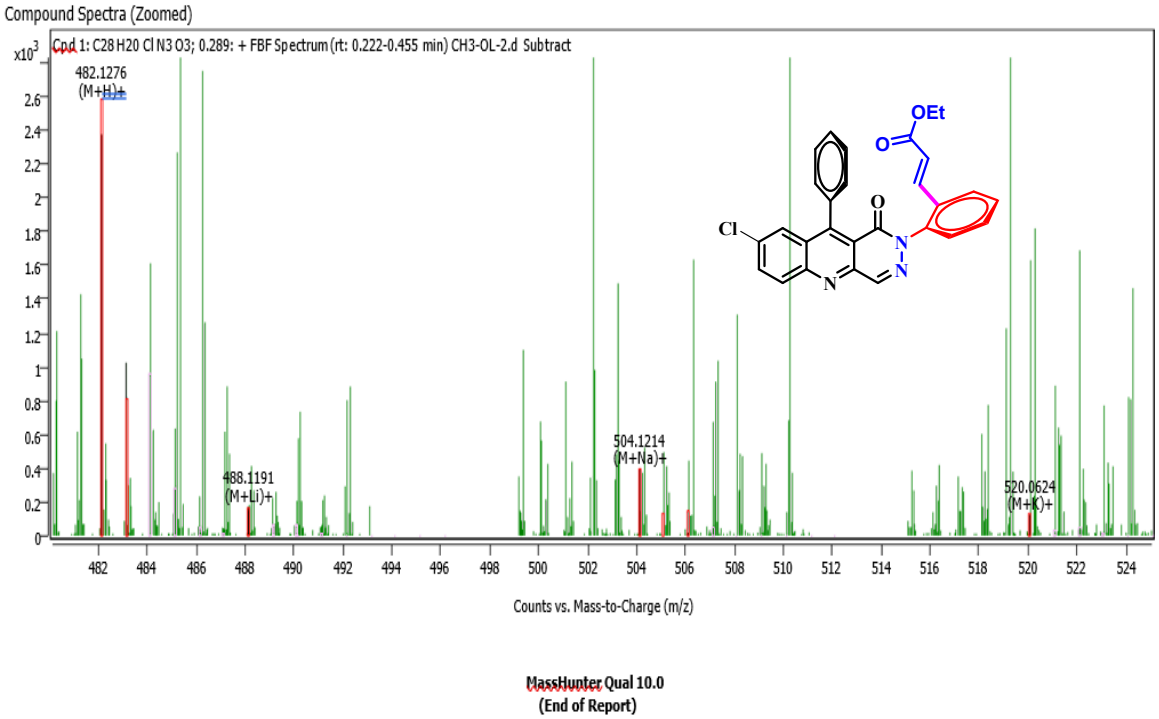

Figure S204: HR-MS spectra of compound 9d

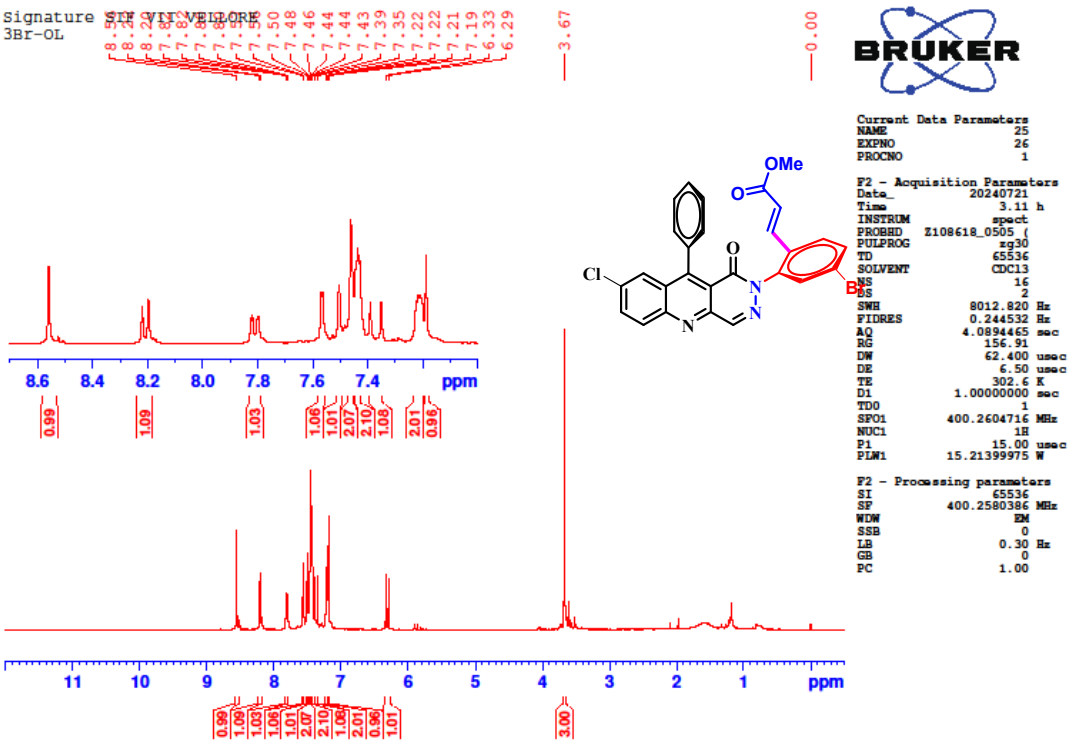

Figure S205: ^{1}H NMR of compound 9e

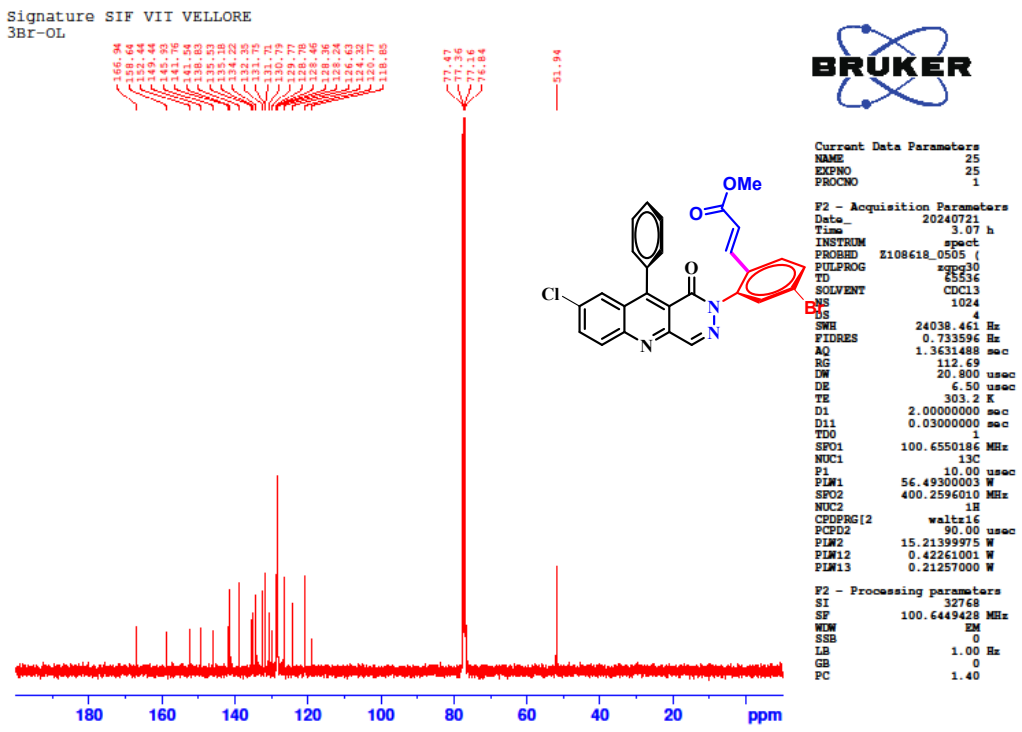

Figure S206: ^{13}C NMR of compound 9e

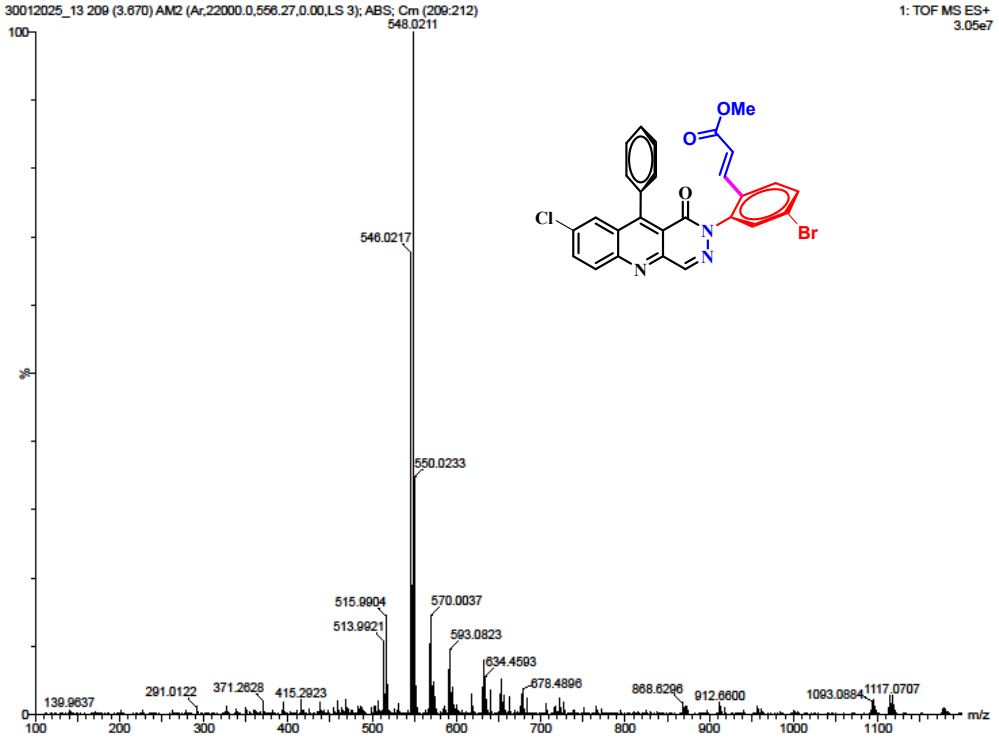

Figure S207: HR-MS spectra of compound 9e

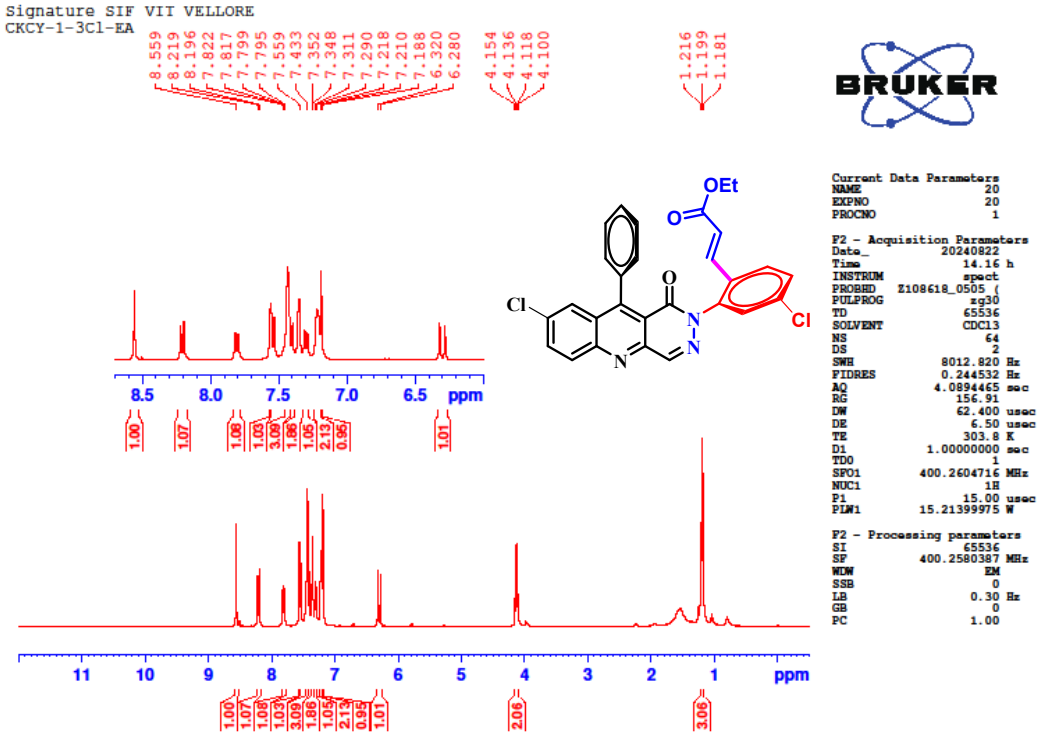

Figure S208: ^{1}H NMR of compound 9e

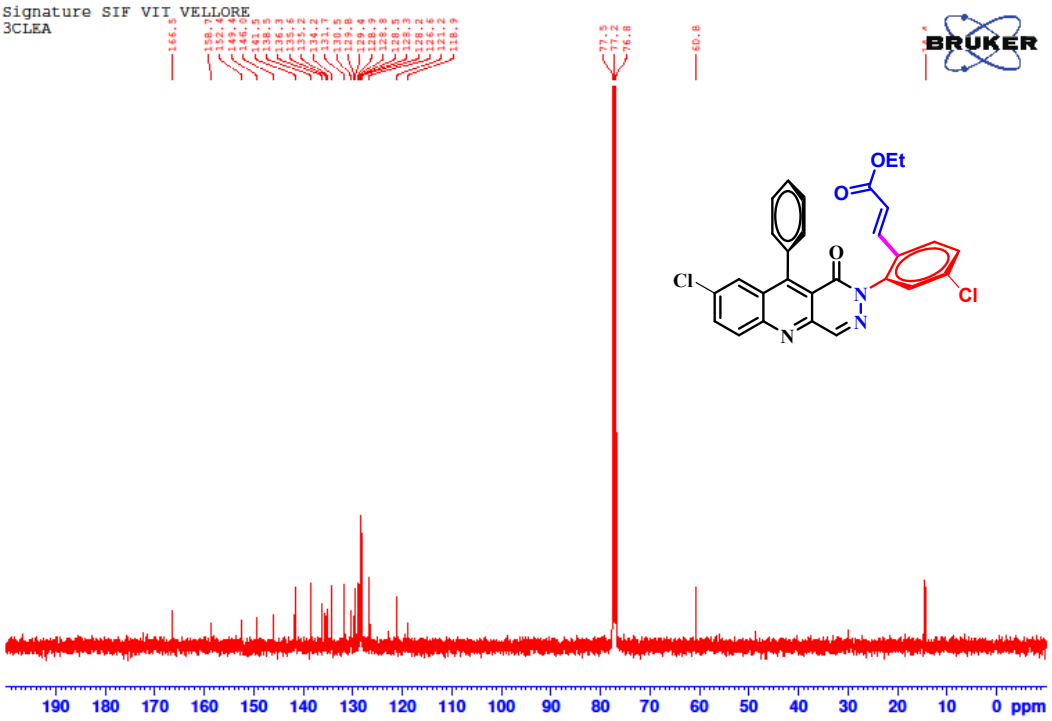

Figure S209: ^{13}C NMR of compound 9f

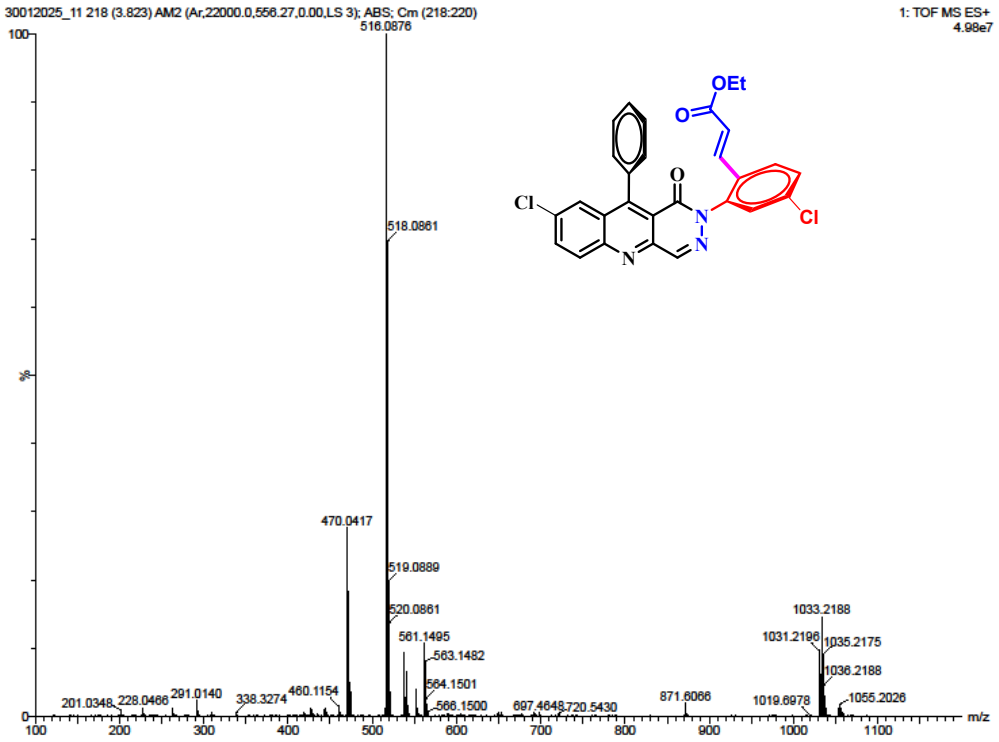

Figure S210: HR-MS spectra of compound 9f

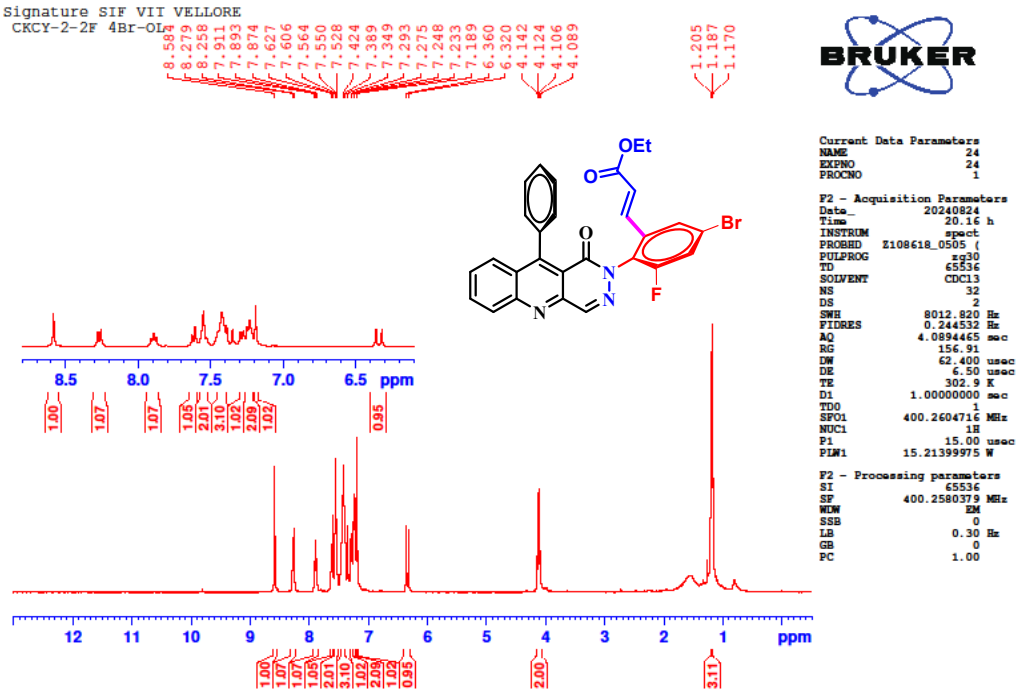

Figure S211: ^{1}H NMR of compound 9g

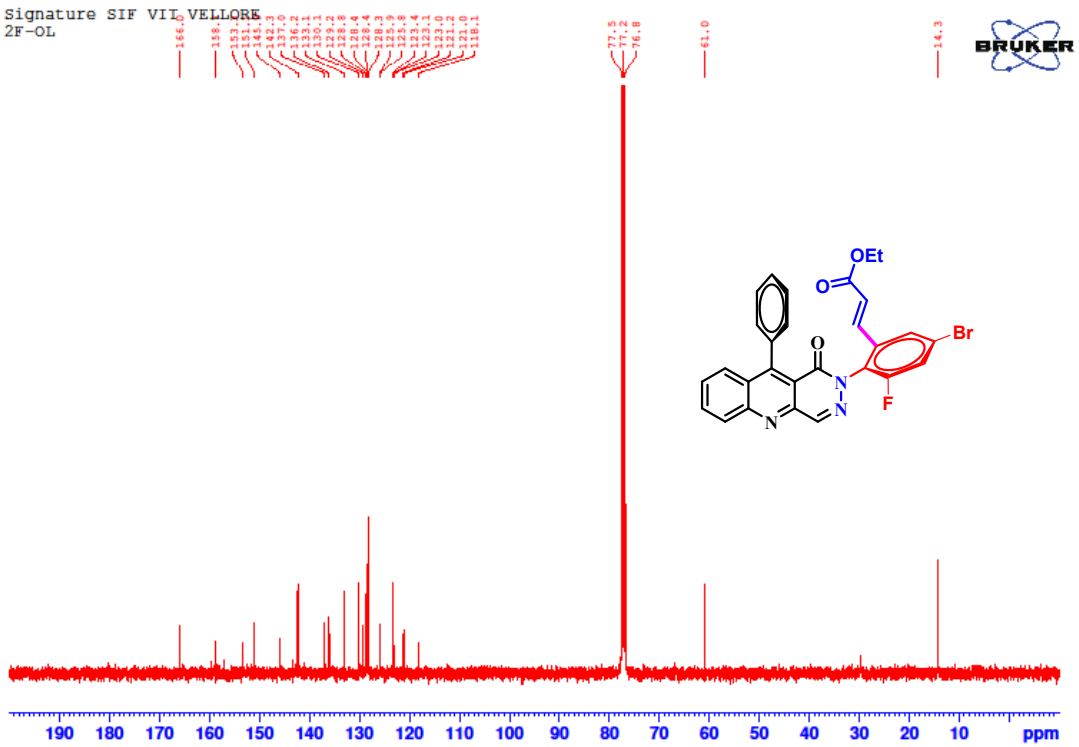

Figure S212: ^{13}C NMR of compound 9g

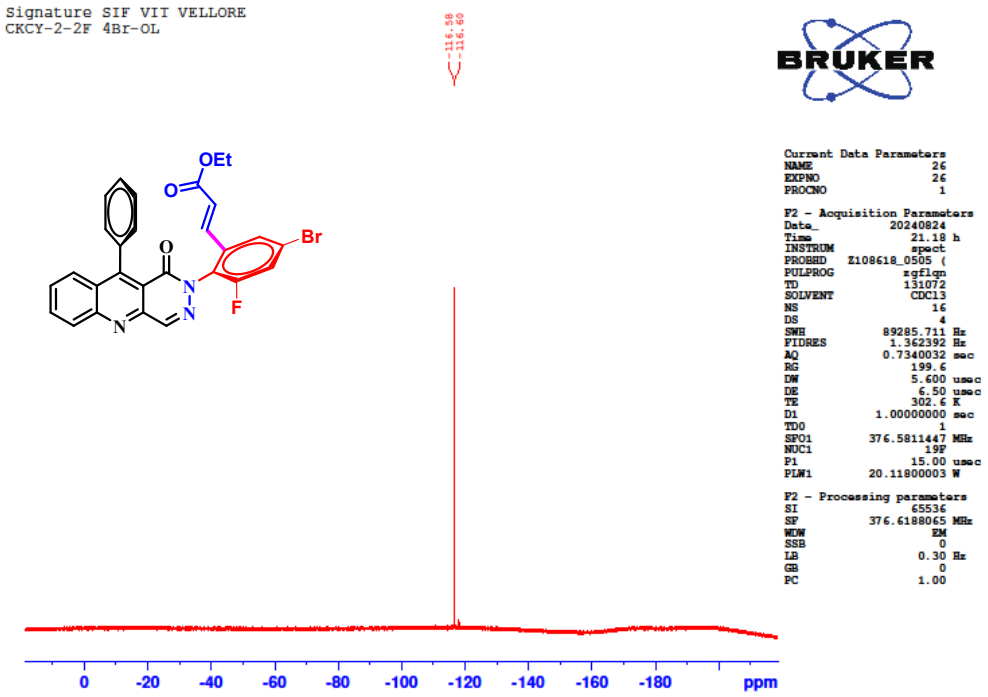

Figure S213: ^{19}F NMR of compound 9g

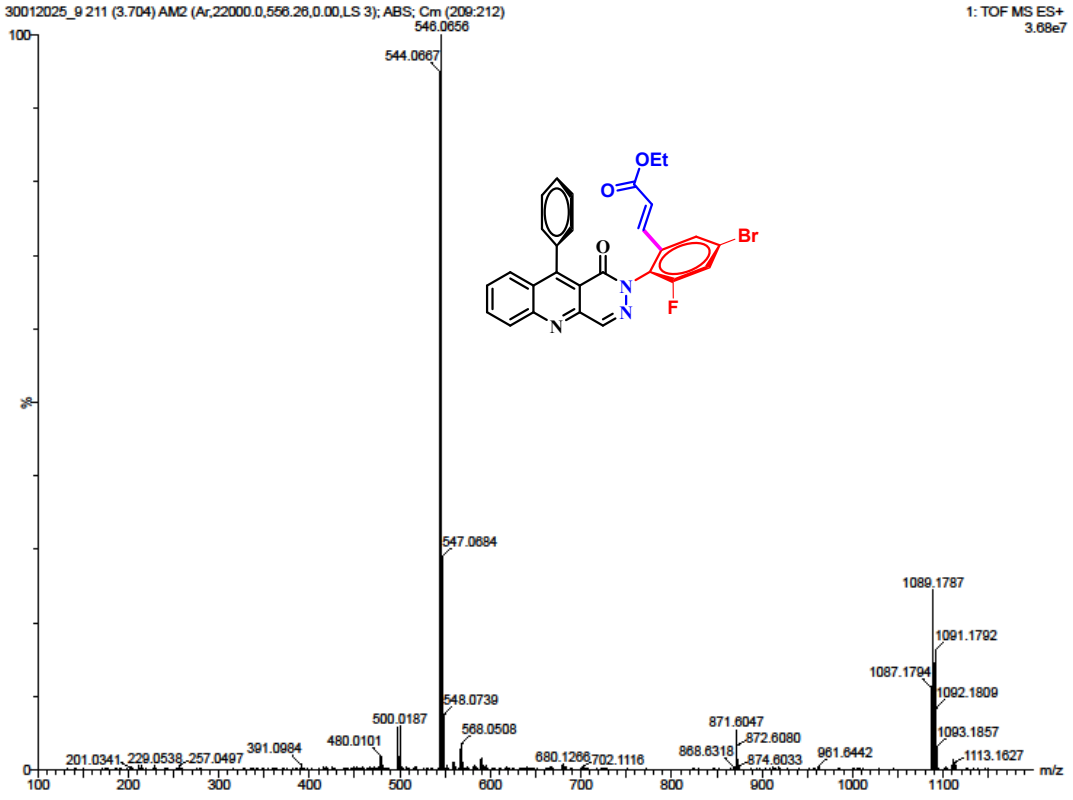

Figure S214: HR-MS spectra of compound 9g

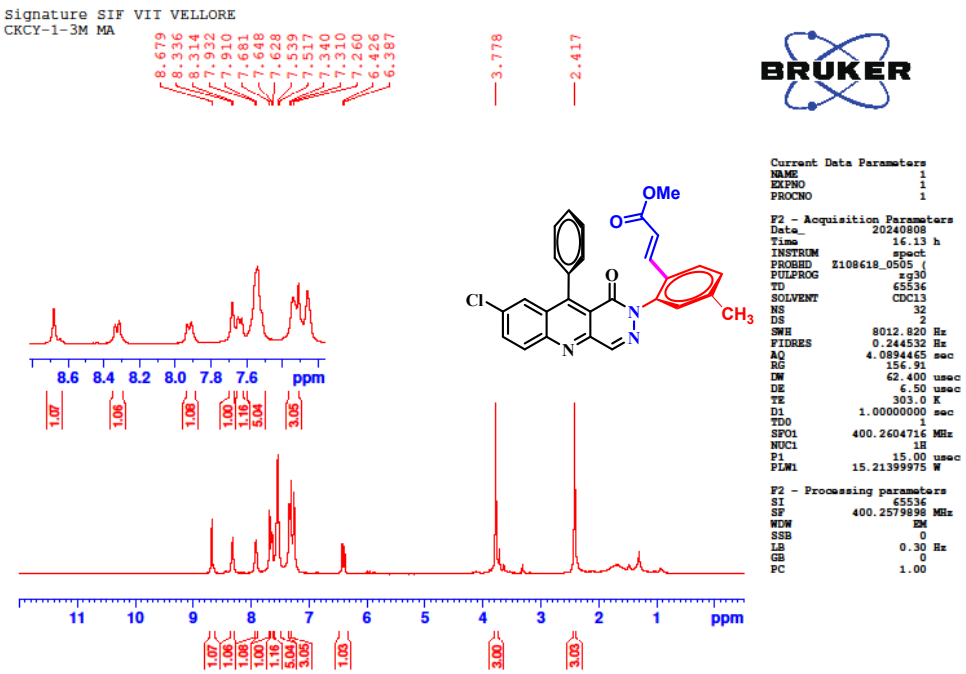

Figure S215: ^{1}H NMR of compound 9h

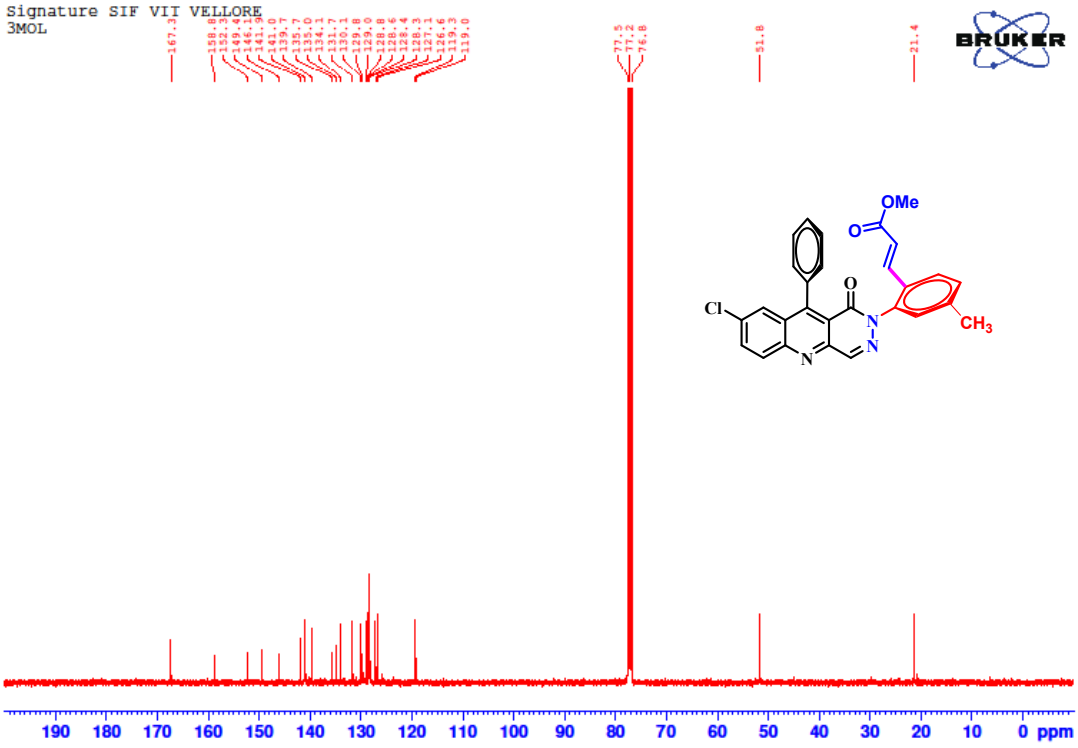

Figure S216: ^{13}C NMR of compound 9h

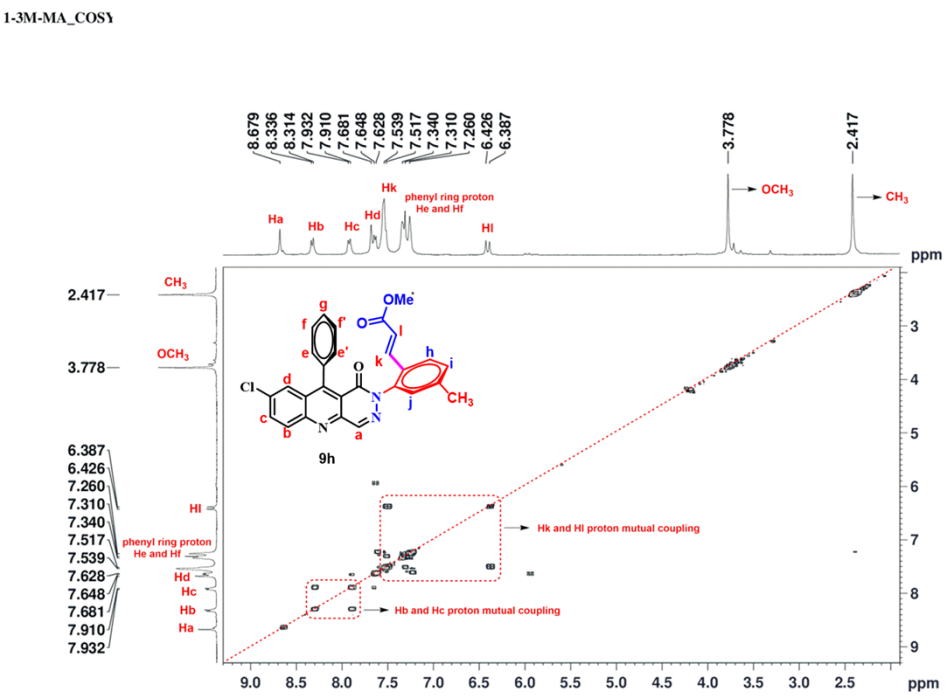

Figure S217: COSY NMR of compound 9h

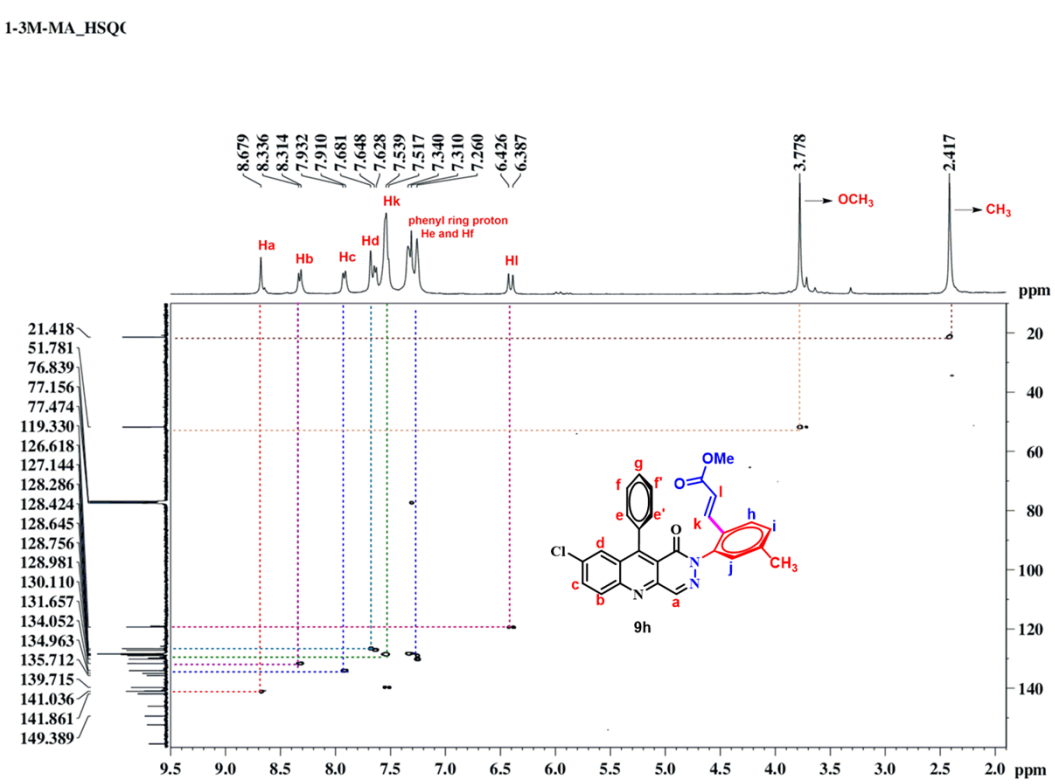

Figure S218: HSQC NMR of compound 9h

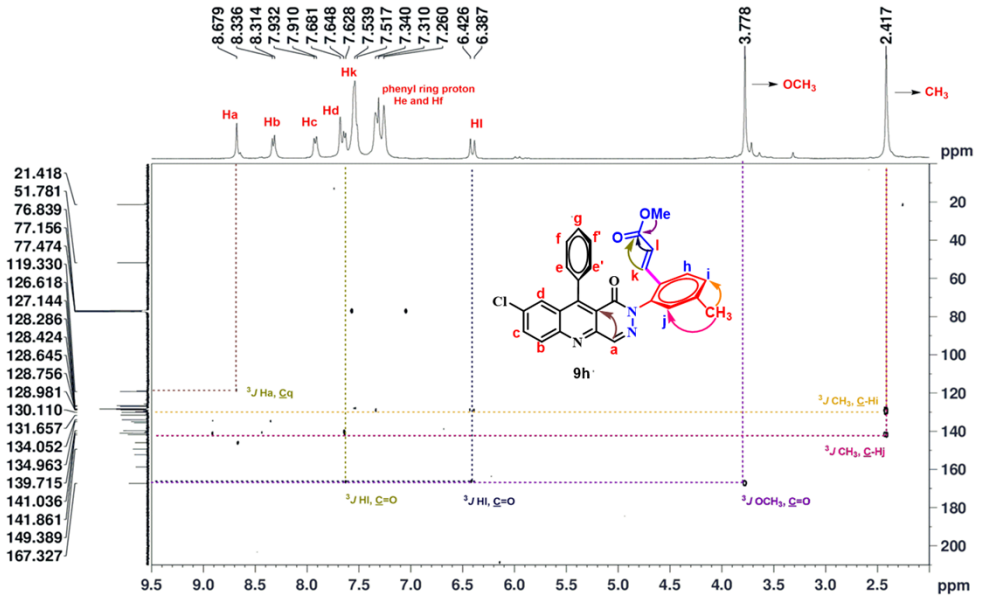

Figure S219: HMBC NMR of compound 9h

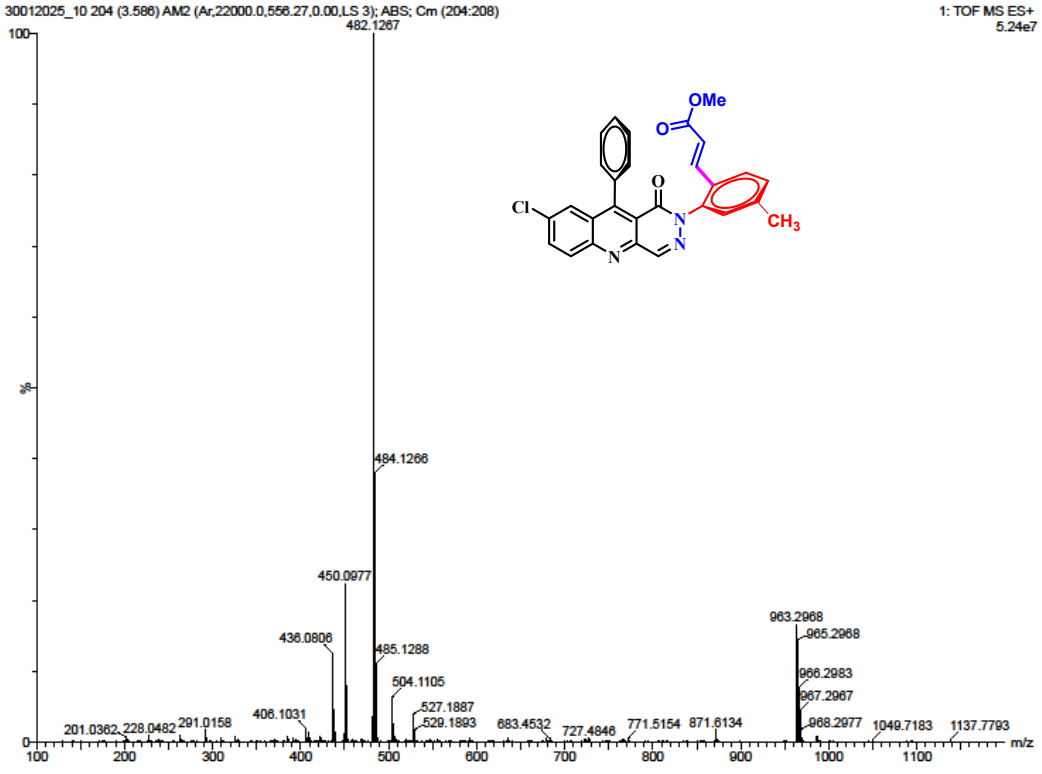

Figure S220: HR-MS spectra of compound 9h

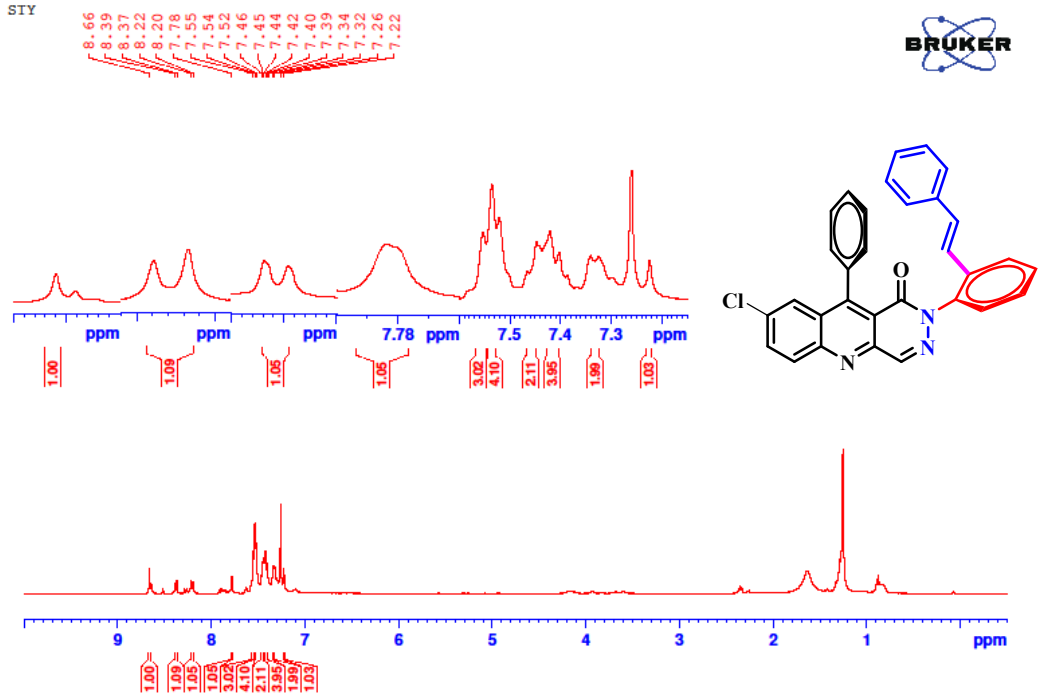

Figure S221: ^{1}H NMR of compound 9i

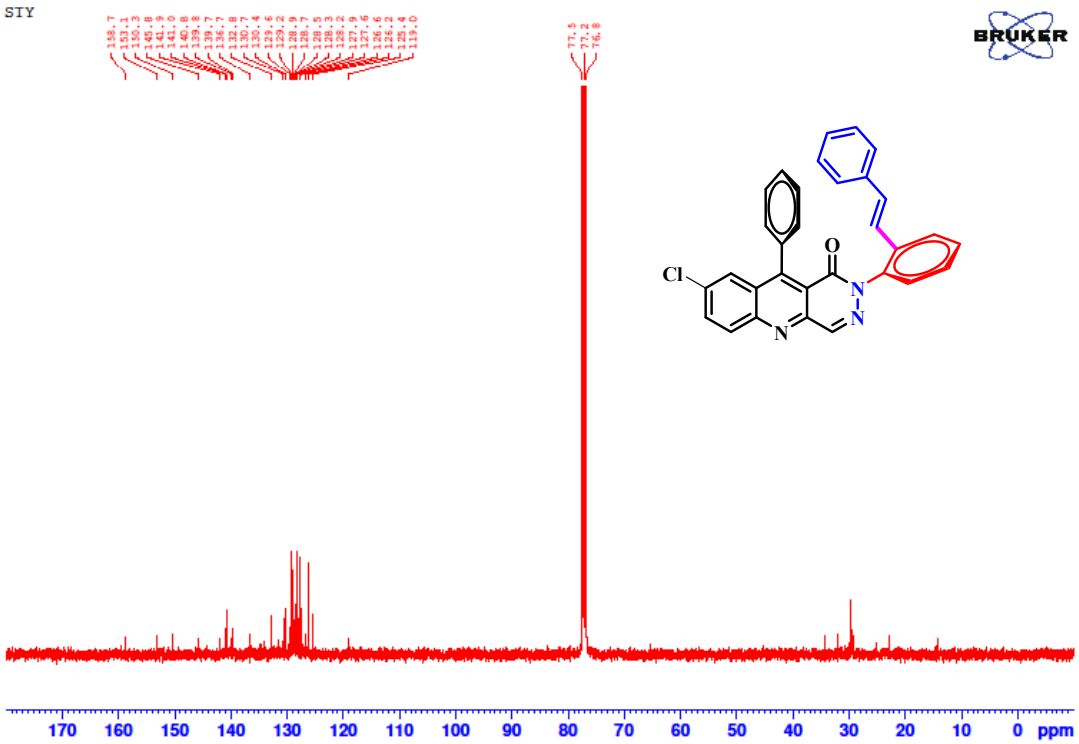

Figure S222: ^{13}C NMR of compound 9i

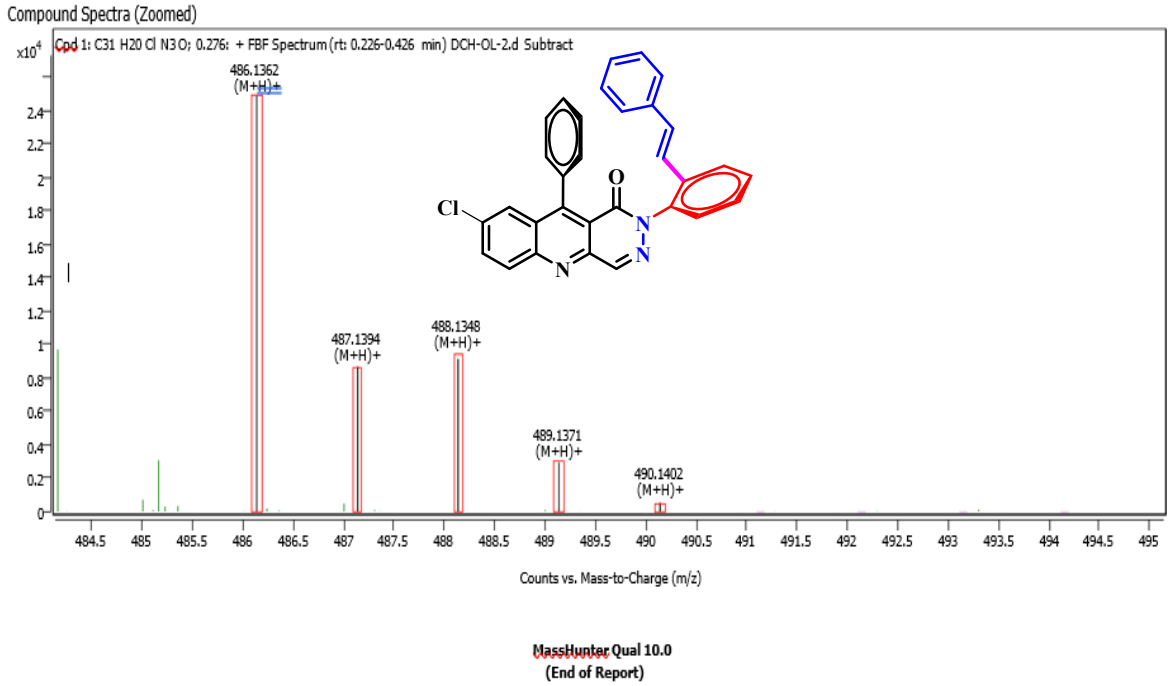

Figure S223: HR-MS spectra of compound 9i

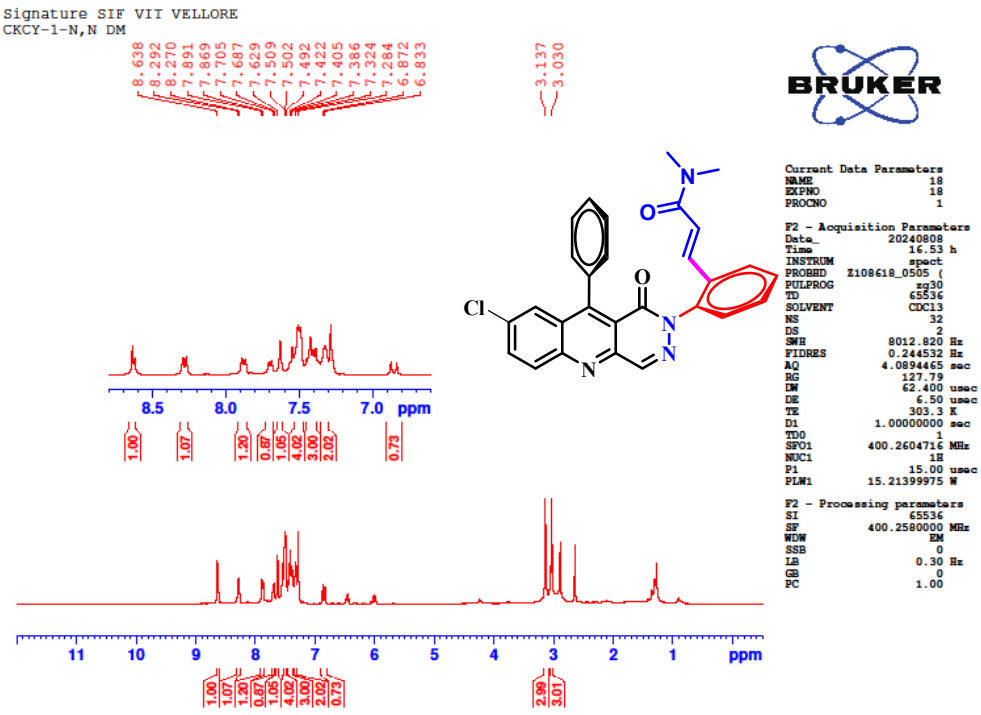

Figure S224: ^{1}H NMR of compound 9j

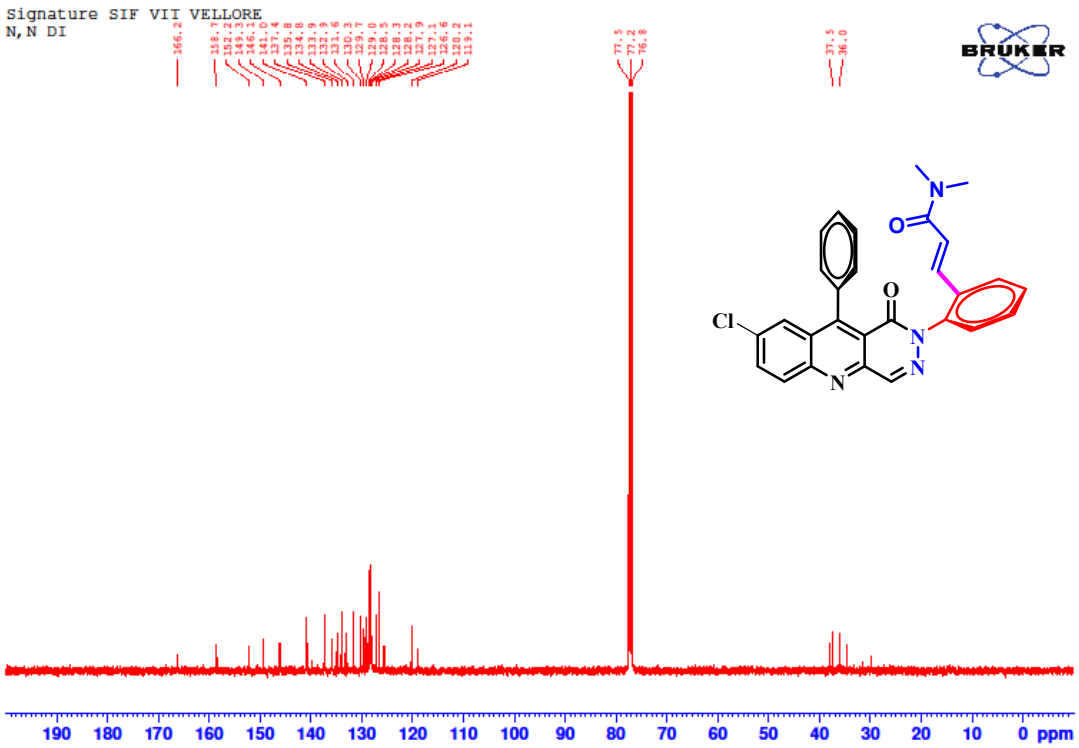

Figure S225: ^{13}C NMR of compound 9j

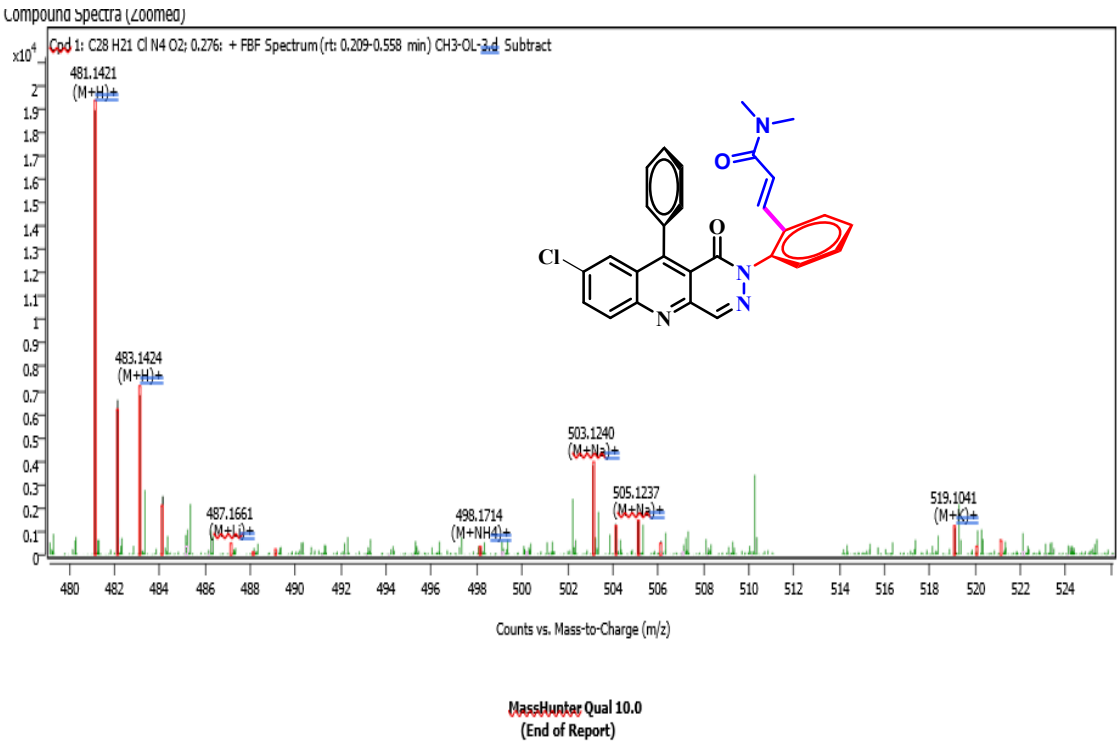

Figure S226: HR-MS spectra of compound 9j

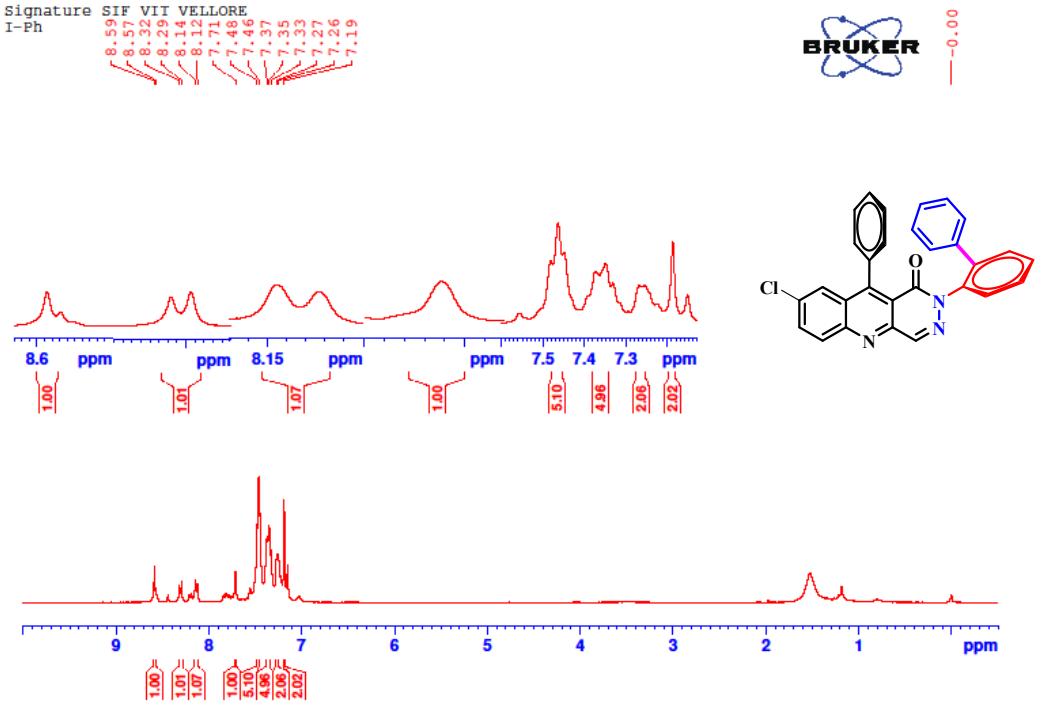

Figure S227: ^{1}H NMR of compound 10a

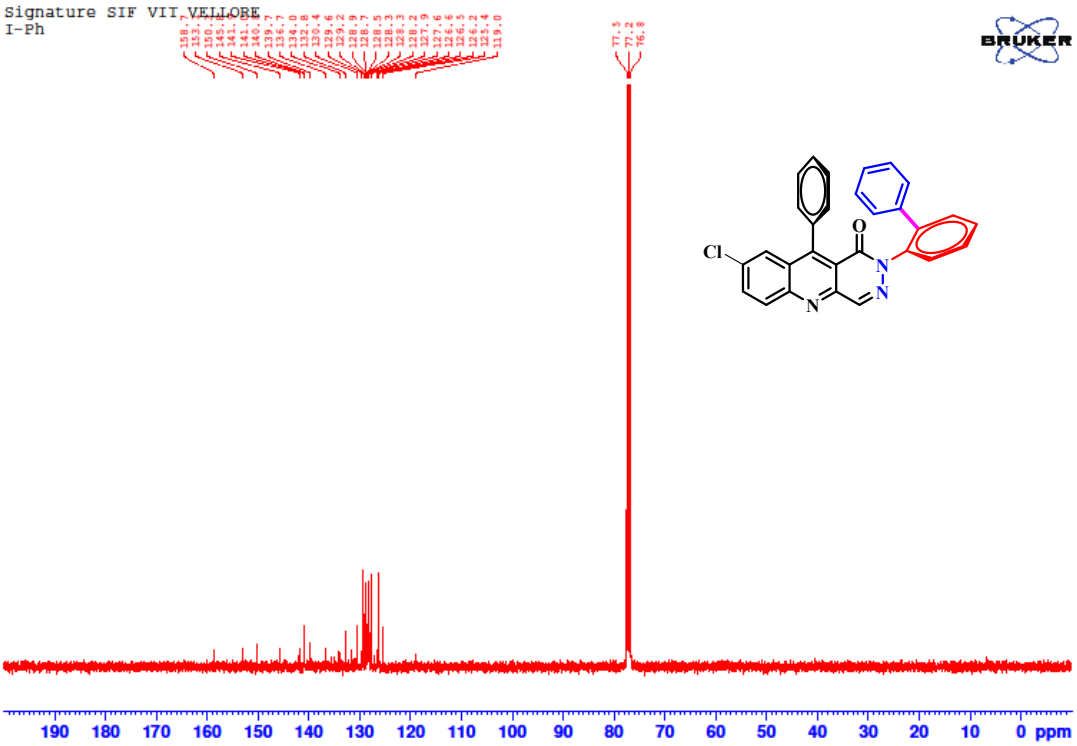

Figure S228: ^{13}C NMR of compound 10a

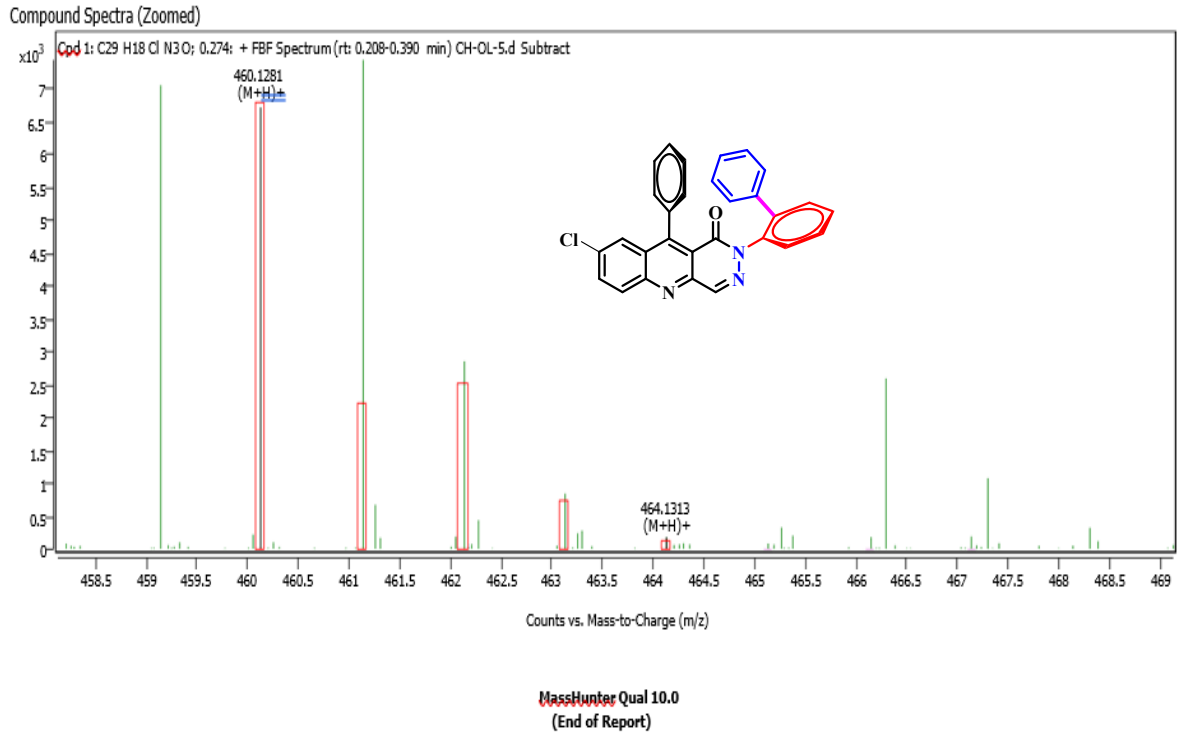

Figure S229: HR-MS spectra of compound 10a

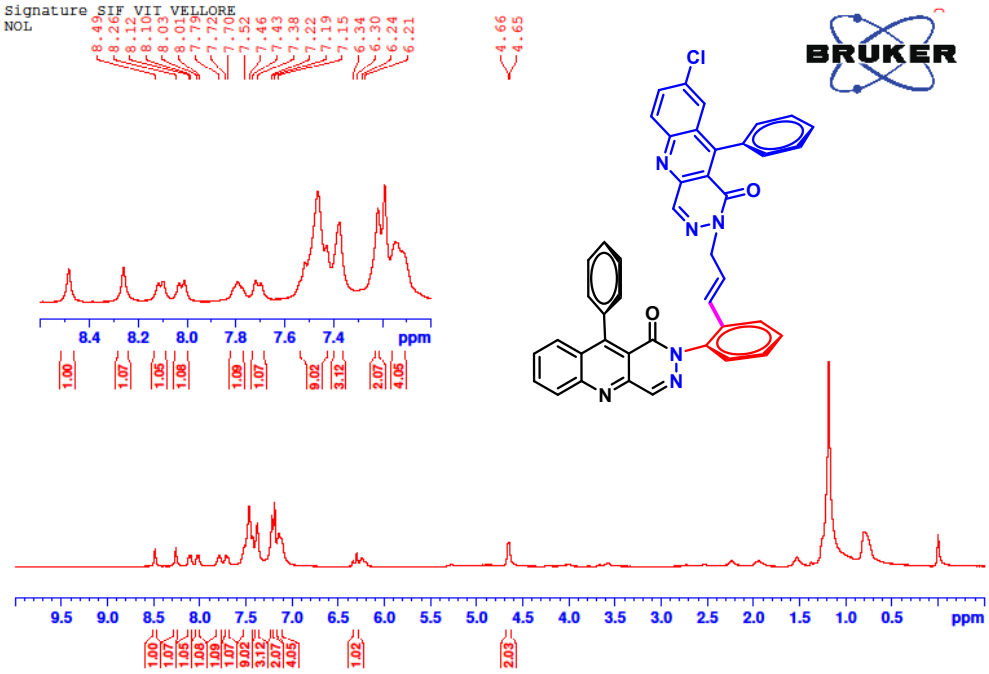

Figure S230: ^{1}H NMR of compound 10b

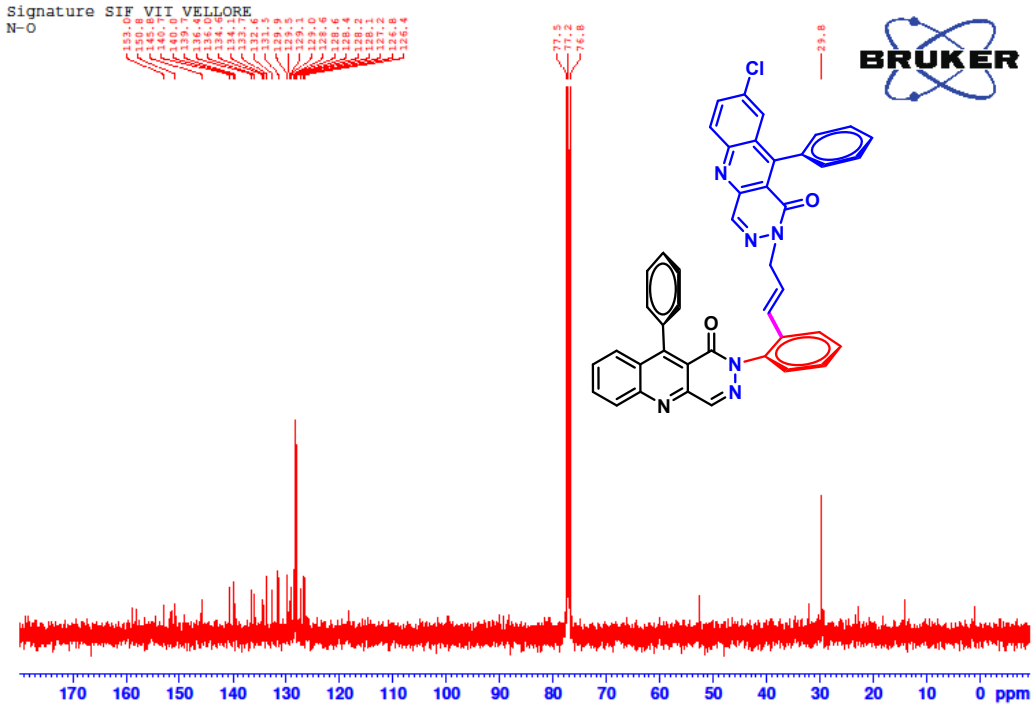

Figure S231: ^{13}C NMR of compound 10b

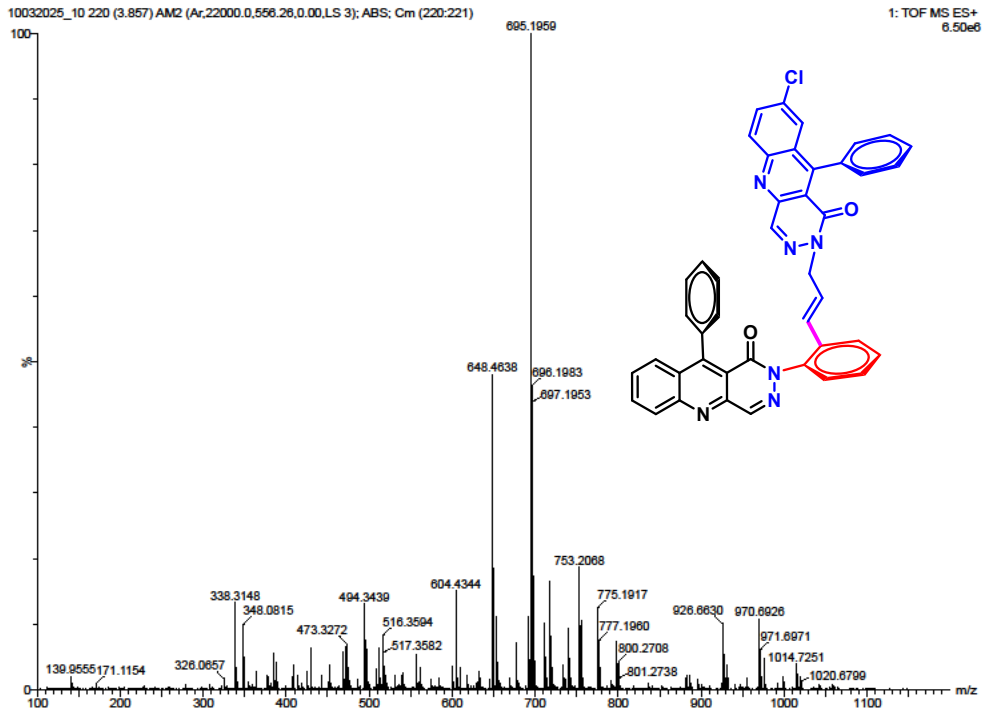

Figure S232: HR-MS spectra of compound 10b

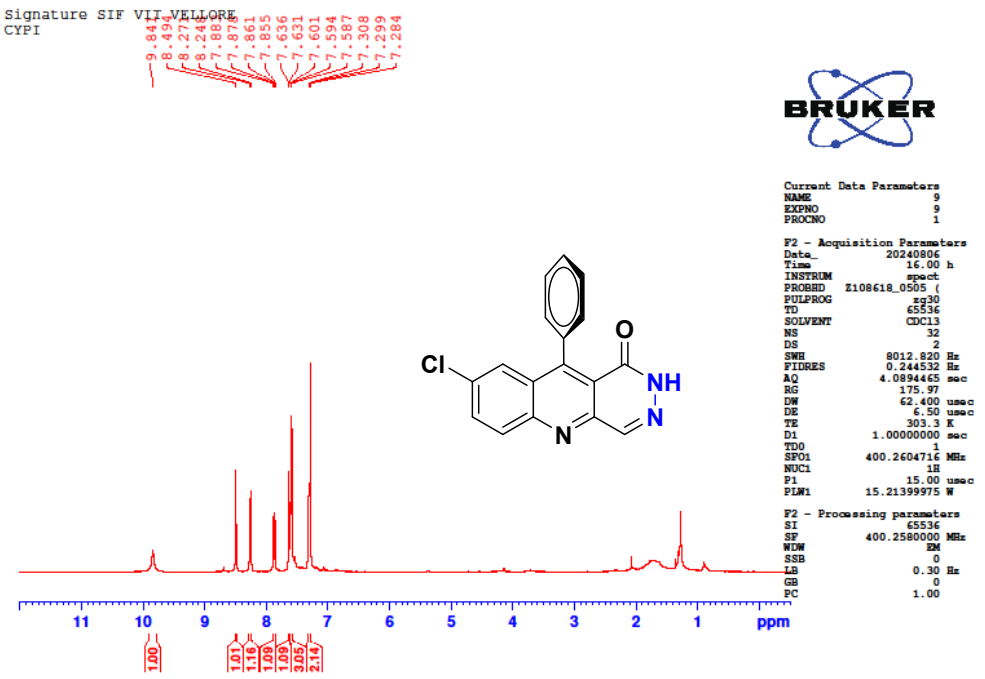

Figure S233: ^{1}H NMR of compound 5b

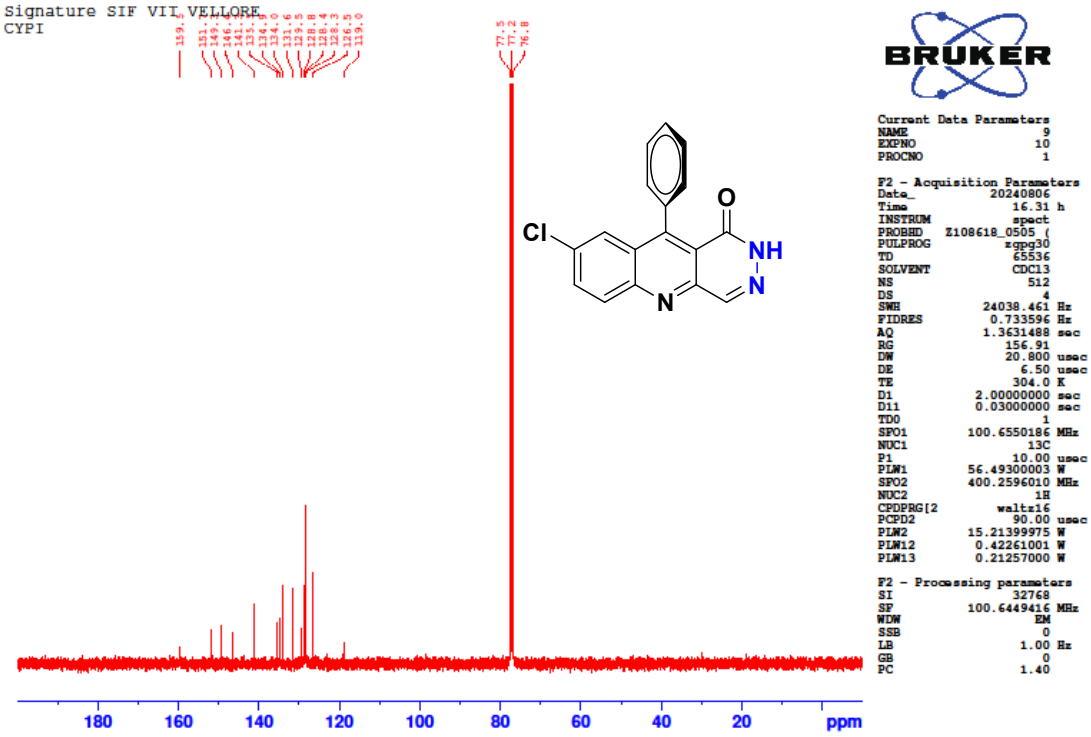

Figure S234: ^{13}C NMR of compound 5b

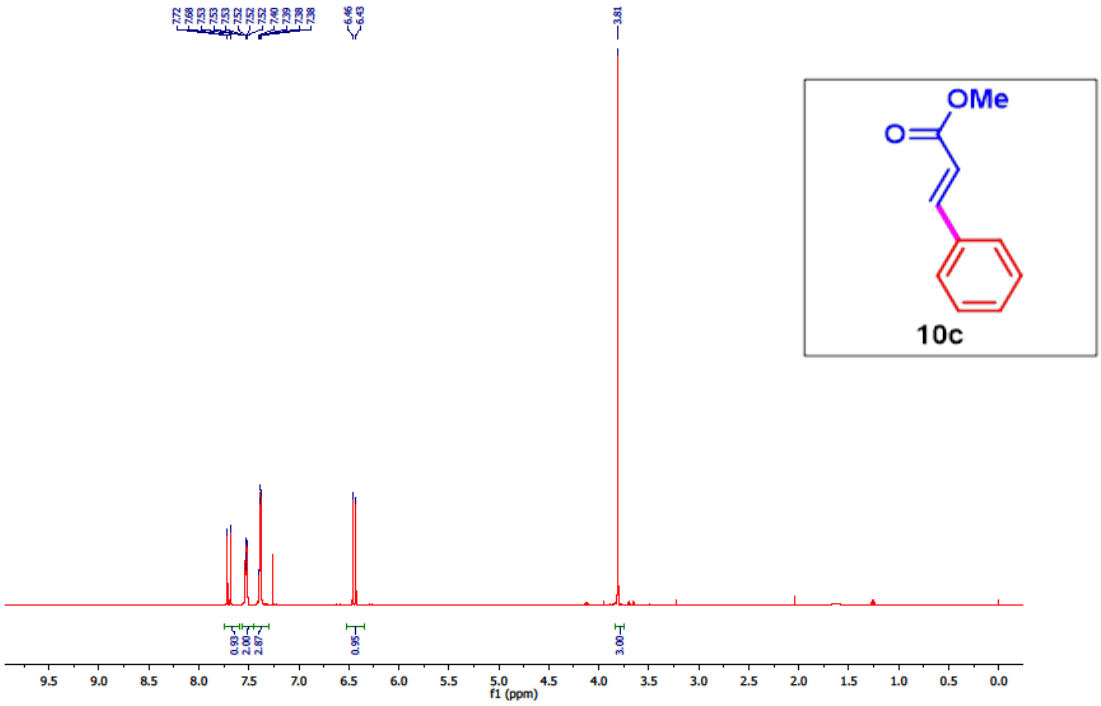

Figure S235: ^{1}H NMR of compound 10c

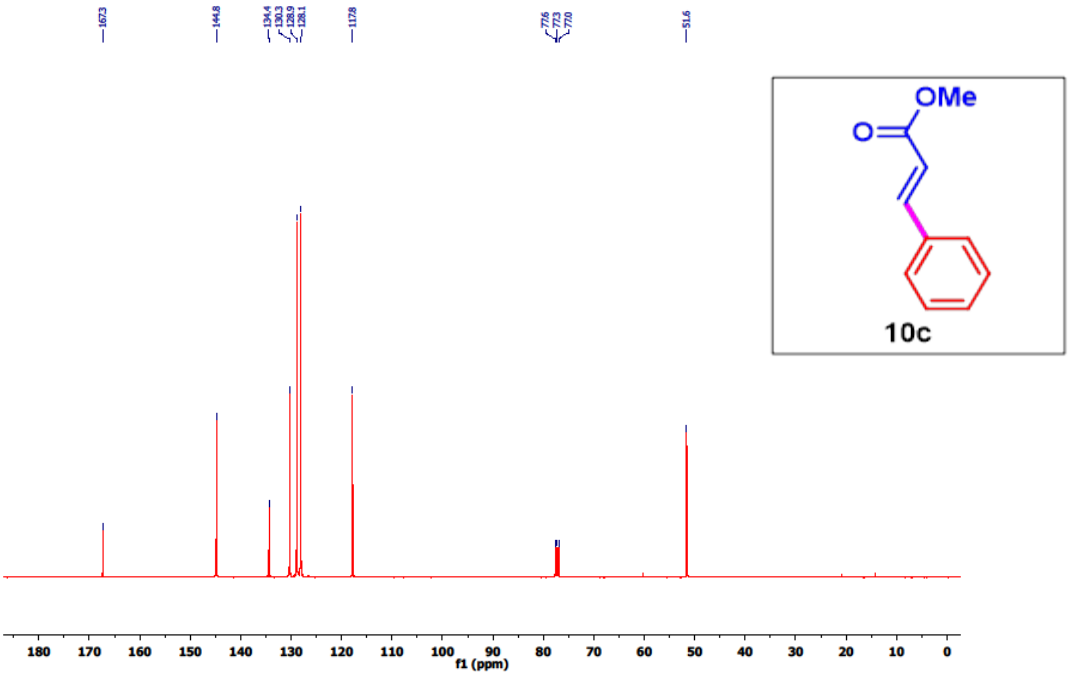

Figure S236: ^{13}C NMR of compound 10c

8) Comparison of SOR values

The N-aryl substitution in pyridazino[4,5-*b*]quinolin-1(2*H*)-one introduces significant steric hindrance, which restricts free rotation around the C–N single bond (partially endowed with C=N character due to the amide functionality, the phenyl ring, and *ortho*-bulky substituents). As a result, the molecule exhibits inherent atropisomerism, as confirmed by specific optical rotation (SOR) studies. Furthermore, alkenylation at the ortho-position increases this rotational restriction, leading to the formation of distinct atropisomeric products, as evidenced by chiral HPLC analysis and SOR measurements.

<table>
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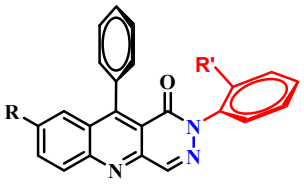
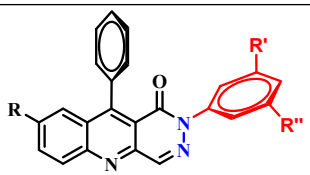
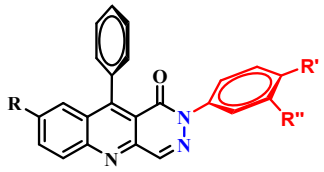
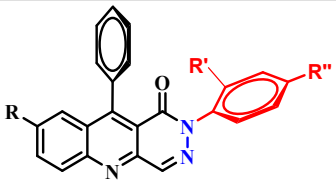
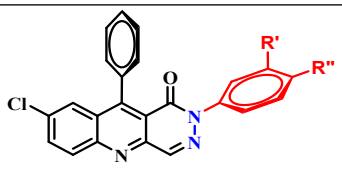
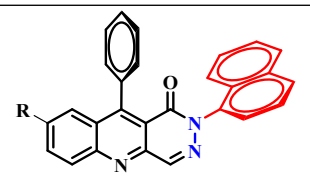
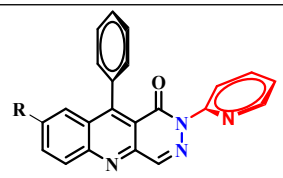
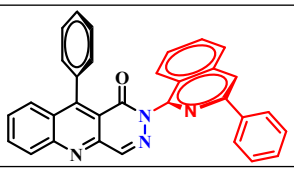
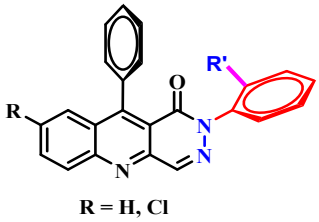
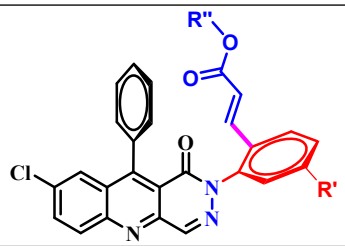
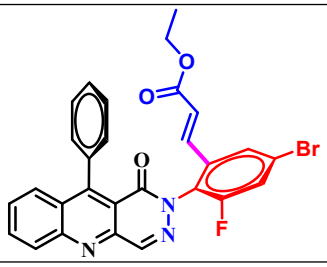
<tr><td rowspan="2"> 
R = H, Cl</td><td>R = H</td><td>R^I = H, [α]_D²⁰ = -14 (8a)
R^I = Cl, [α]_D²⁰ = -23 (8c)</td></tr>
<tr><td>R = Cl</td><td>R^I = H, [α]_D²⁰ = -17 (8b)
R^I = Cl, [α]_D²⁰ = -25 (8d)
R^I = F, [α]_D²⁰ = -26 (8e)</td></tr>
<tr><td rowspan="2"> 
R = H, Cl</td><td colspan="2"></td></tr>
<tr><td>R = Cl</td><td>R^I = Cl, R^{II} = Cl, [α]_D²⁰ = -19 (8f)
R^I = Cl, R^{II} = H, [α]_D²⁰ = -17 (8g)
R^I = Br, R^{II} = H, [α]_D²⁰ = -20 (8h)</td></tr>
<tr><td rowspan="2"> 
R = H, Cl</td><td colspan="2"></td></tr>
<tr><td>R = Cl</td><td>R^I = Cl, R^{II} = Cl, [α]_D²⁰ = -18 (8i)
R^I = Cl, R^{II} = H, [α]_D²⁰ = -13 (8j)</td></tr>
<tr><td rowspan="2"> 
R = H, Cl</td><td>R = H</td><td>R^I = F, R^{II} = Br, [α]_D²⁰ = -10 (8k)</td></tr>
<tr><td>R = Cl</td><td>R^I = F, R^{II} = Br, [α]_D²⁰ = -14 (8l)</td></tr>
<tr><td>  </td><td colspan="2">R^I = OCH₃, R^{II} = H [α]_D²⁰ = -17 (8m)
R^I = CH₃, R^{II} = H
[α]_D²⁰ = -19 (8n)
R^I = Cl, R^{II} = CH₃
[α]_D²⁰ = -19 (8o)</td></tr>
<tr><td> 
R = H, Cl</td><td colspan="2">R = H, [α]_D²⁰ = -21 (8p)

R = Cl, [α]_D²⁰ = -21 (8q)</td></tr>
</table>

 R = H, Cl	**R = H, $[\alpha]_D^{20}$ = -41 (8r)** **R = Cl, $[\alpha]_D^{20}$ = -44 (8s)**
	**$[\alpha]_D^{20}$ = -55 (8t)**

Compound structure	SOR values
 R = H, Cl	**R = H, $R^I = C_4H_5O_2$, $[\alpha]_D^{20}$ = -21 (9a)** **R = Cl, $R^I = C_4H_5O_2$, $[\alpha]_D^{20}$ = -43 (9b)** **R = H, $R^I = C_5H_7O_2$, $[\alpha]_D^{20}$ = -20 (9c)** **R = Cl, $R^I = C_5H_7O_2$, $[\alpha]_D^{20}$ = -27 (9d)** **R = Cl, $R^I = C_8H_7$, $[\alpha]_D^{20}$ = -34 (9i)** **R = Cl, $R^I = C_5H_8NO$, $[\alpha]_D^{20}$ = -29 (9j)** **R = Cl, R^I = Ph, $[\alpha]_D^{20}$ = -27 (10a)** **R = Cl, $R^I = C_{19}H_{13}ClN_3O$, $[\alpha]_D^{20}$ = -26 (10b)**
	**R^I = Br, $R^{II} = CH_3$, $[\alpha]_D^{20}$ = -47 (9e)** **R^I = Br, R^{II} = Et, $[\alpha]_D^{20}$ = -43 (9f)** **$R^I = CH_3$, $R^{II} = CH_3$, $[\alpha]_D^{20}$ = -43 (9h)**
	**$[\alpha]_D^{20}$ = -57 (9g)**