Electronic Supporting Information

For

Visible-light triggered Cu-catalyzed C–H bond activation to afford isocoumarin and isoquinolinone scaffolds at room temperature

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General Information

Materials and Reagents:

All benzamide derivatives were synthesized following previously reported literature procedures. Malononitrile was obtained from TCI, while 3-oxo-3-phenylpropanenitrile was purchased from BLD pharma. Copper (II) acetate monohydrate ($Cu(OAc)_2.H_2O$) and dimethyl sulfoxide (DMSO) were purchased from SRL, and sodium carbonate (Na_2CO_3) was purchased from Merck. Dichloromethane (DCM) was distilled using calcium hydride under nitrogen atmosphere prior to use in reactions. Thin-layer chromatography (TLC) was performed on pre-

coated silica gel 60 F254 plates, and spots were visualized under UV light (254 nm). Column chromatography was carried out using silica gel (100-200 mesh) as the stationary phase and a mixture of ethyl acetate and hexane as the mobile phase.

Instrumentations:

^{1}H, ^{13}C and ^{19}F NMR spectra were obtained with BRUKER 300 MHz and 400 MHz FT-NMR spectrometers and the chemical shifts are reported in ppm, using tetramethylsilane as an internal standard and were referenced to the residual solvent as follows: $CDCl_3$ = 7.26 (^{1}H), 76.16 (^{13}C) ppm and DMSO-d_6 = 2.50 (^{1}H), 39.52 (^{13}C) at room temperature. For ^{1}H NMR, coupling constants *J* are given in Hz and the resonance multiplicity is described as s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet), td (triplet of doublet), tt (triplet of triplet), q (quartet). ^{13}C NMR spectra were fully decoupled by broadband proton decoupling. High-resolution mass spectra (HRMS) were obtained from Waters (Xevo G2 Q-TOF) mass spectrometer in electrospray ionization mode (ESI^{+}). GCMS was recorded in PerkinElmer Gas Chromatograph Clarus 590. GC was obtained using TCD and FID detector from Agilent 8860 (G2790A). Photocatalytic experiments were done by visible white CFL lamp 65 watt.


A
26.1
0270


B
26.5
0270


C
26.9
0280

Figure S1. Picture of the photoreaction setup (A) before light on (B) after 3h (C) after 6h. The photocatalytic reactions were performed on 65watt white visible light (CFL). Attached with cooling fan provides consistent temperature to each reaction. Distance between light source and quartz tube was approximately 1 cm and no filter was used for the reaction.

Light Source Details:

Model Number: SKYC44FHD

Model Name: SKYC65455D

Lumen Efficacy: 6500 lm/W

Light Colour temperature (Kelvins scale): 6500-7500K (cool daylight)

Experimental Section:

General procedure for preparation of benzamides[1]**:** Substrates were prepared from the corresponding carboxylic acids and 8-aminoquinoline (8-AQ). The carboxylic acid (5 mmol) was reacted with oxalyl chloride $(COCl)_2$, (6 mmol, 1.2 equiv,) and a catalytic amount of DMF (0.05 mL) in dichloromethane (DCM, 15 mL), at 0 ^oC then stirred at room temperature under a nitrogen atmosphere for 4 h. Then the excess oxalyl chloride and solvent were removed by evaporation. The resulting acyl chloride was dissolved in DCM (10 mL) for further use. To a stirring solution of 8-aminoquinoline (8-AQ, 5 mmol, 1.0 equiv.), triethylamine (Et_3N, 6 mmol), and 4-dimethylaminopyridine (DMAP, 0.5 mmol, 10 mol%) in DCM (8 mL), the acyl chloride solution in DCM was added drop wise at 0 ^oC under nitrogen. Following the addition, the reaction mixture was warmed to room temperature and stirred overnight. The reaction was quenched with water at 0 °C and further diluted with DCM (15 mL). The mixture was then washed with saturated aqueous sodium bicarbonate (10 mL) and brine (10 mL). The organic layer was dried over anhydrous sodium sulphate (Na_2SO_4) and then evaporated under vacuum. The crude product was purified by column chromatography, yielding the desired amide (75-85 %).

General procedure for the formation of isocoumarins with the coupling partner 2a/2b/2c: An oven-dried round-bottomed flask equipped with a stir bar was charged with $Cu(OAc)_2.H_2O$ (2 equiv, 2 mmol, 399.3 mg), Na_2CO_3 (1.5 equiv, 1.5 mmol, 159 mg) and 3-oxo-3-phenylpropanenitrile (**2a**) (1.5 equiv, 1.5 mmol, 217.7 mg) or 3-(furan-2-yl)-3-oxopropanenitrile (**2b**) (1.5 equiv, 1.5 mmol, 202.7 mg) or 3-oxo-3-(*p*-tolyl) propanenitrile (**2c**) (1.5 equiv, 1.5 mmol, 238.8 mg). DMSO (2 mL) was added to the reaction mixture followed by benzamide derivatives (1.0 equiv, 1.0 mmol). Then the reaction mixture was stirred for 18 h at room temperature in the presence of visible light (65 watt) under aerobic atmosphere. Upon

completion of the reaction, water was added to the reaction mixture and the product was extracted by washing with dichloromethane (3×20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography (EtOAc/pet ether 1:9–1:4) on silica gel (100–200 meshes) to afford the corresponding products **3aa – 3ic** with good to excellent yield.

General procedure for the formation of isos with the coupling partner 2d: An oven-dried round-bottomed flask equipped with a stir bar was charged with $Cu(OAc)_2.H_2O$ (2 equiv, 2 mmol, 399.3 mg), Na_2CO_3 (1.5 equiv, 1.5 mmol, 159 mg) and malononitrile (**2d**) (1.5 equiv, 1.5 mmol, 99.1 mg). DMSO (2 mL) was added to the reaction mixture followed by benzamide derivatives (1.0 equiv, 1.0 mmol). Then the reaction mixture was stirred for 6 h at room temperature in the presence of visible light (65 watt) under aerobic atmosphere. Upon completion of the reaction, water was added to the reaction mixture and the product was extracted by washing with dichloromethane (3×20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography (EtOAc/pet ether 3:2–7:3) on silica gel (100–200 meshes) to afford the corresponding products **4ad** – **4md** with excellent yield.

Gram-scale reaction: 3-methyl-N-(quinolin-8-yl)benzamide (**1k**) was used for multi-gram scale reaction. An oven-dried round-bottomed flask equipped with a stir bar was charged with $Cu(OAc)_2.H_2O$ (2 equiv, 7.62 mmol, 1.5 g) and Na_2CO_3 (1.5 equiv, 5.72 mmol, 605.7 mg). Then **1k** (1 equiv, 3.81 mmol, 1 g) and malononitrile (**2d**) (1.5 equiv, 5.72 mmol, 377 mg) were added to it. After that DMSO (10 mL) is added to the reaction mixture and the reaction mixture was stirred at room temperature for 6 h in the presence of visible light (65 watt) under aerobic atmosphere. Upon completion of the reaction, water was added to the reaction mixture and the product was extracted by washing with dichloromethane (3×50 mL) and water. The organic layer was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure.

The crude product was purified by column chromatography on silica gel (100-200 meshes) (EtOAc/pet ether 3:2 – 7:3) to afford the desired products **4kd** (932.57 mg, yield 75%).

Similar experiment was done for compound **3ba** using 4-methoxy-N-(quinolin-8-yl)benzamide (**1b**) (1 equiv, 3.59 mmol, 1 g) and 3-oxo-3-phenylpropanenitrile (**2a**) (1.5 equiv, 5.38 mmol, 781.7 mg). The corresponding crude product was purified by column chromatography on silica gel (100-200 meshes) (EtOAc/pet ether 1:9–1:4) to afford the desired product **3ba** (696.78 mg, yield 70%).

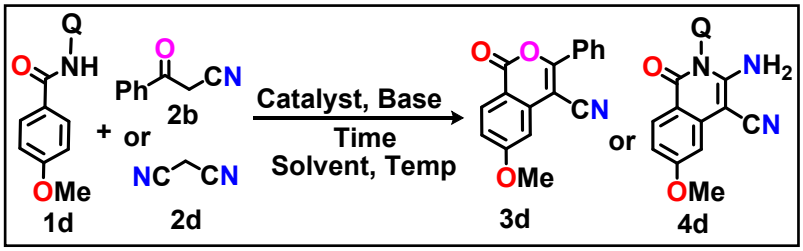
Radical trapping experiment: An oven-dried 10 mL Schlenk tube was charged with 4-methyl-N-(quinolin-8-yl)benzamide (**1a)** (1equiv,1 mmol, 262.3 mg), Na_2CO_3 (1.5 equiv, 1.5 mmol, 159 mg), and $Cu(OAc)_2.H_2O$ (2 equiv, 2 mmol, 399.3 mg) were mixed in DMSO (2 ml) at room temperature. Then 3-oxo-3-phenylpropanenitrile (**2a**) (1.5 equiv, 1.5 mmol, 217.7 mg) was added to it. Finally, TEMPO (3 equiv, 3 mmol, 468.7 mg) and BHT (3 equiv, 3 mmol, 661 mg) were added separately to this reaction mixture and the resulting reaction mixture was kept at room temperature and stirred for 18 h in the presence of visible light (65 watt) under aerobic atmosphere. Then a portion of the crude reaction mixture was analyzed directly by HRMS. The product was extracted with dichloromethane (3×10 mL) and water. Organic phase was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (100-200 meshes) (EtOAc/pet ether 1:9) to afford the corresponding product **5** (yield 50%, 181.7 mg).

Procedure for H/D scrambling experiment: An oven-dried 10 mL Schlenk tube was charged with N-(quinolin-8-yl)benzamide (**1g**) (1.0 equiv, 0.2 mmol, 50 mg) $Cu(OAc)_2.H_2O$ (2 equiv, 0.4 mmol, 79.86 mg), Na_2CO_3 (1.5 equiv, 0.3 mmol, 31.8 mg), D_2O (1.5 equiv, 0.3 mmol, 6 µL). Then DMSO (1 ml) was added and the reaction mixture was stirred in the presence of visible light (65 watts) under aerobic atmosphere. After 5 h, the reaction was stopped and the product was extracted by washing with dichloromethane (3×20 mL). The organic layer was

washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (100-200 meshes) (EtOAc/pet ether 1:9) to afford the desired products **1g-d$_n$** (<5 %) (59.68 mg, yield 95%). The deuterium incorporation (<5 %) was determined by ^{1}H NMR.

Kinetic Isotopic Effect (KIE) studies: An oven-dried 10 mL schlenk tube was charged with N-(quinolin-8-yl)benzamide (**1g**) (1.0 equiv, 0.2 mmol, 50 mg), D5-N-(quinolin-8-yl)benzamide (**1g-d$_5$**) (1.0 equiv, 0.2 mmol, 50.67 mg), malononitrile (**2d**) (1.5 equiv, 0.3 mmol, 19.81 mg), $Cu(OAc)_2.H_2O$ (2 equiv, 0.4 mmol, 79.86 mg), and Na_2CO_3 (1.5 equiv, 0.3 mmol, 31.8 mg). Then DMSO (2 ml) was added and the reaction mixture was stirred in the presence of visible light (65 watts) under aerobic atmosphere. After 6 h, the reaction was stopped and the product was extracted by washing with dichloromethane (3×20 mL). The organic layer was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (100-200 meshes) (EtOAc/pet ether 1:9) to afford the desired products **4g** and **[D]-4g** (41.1 mg, yield 65%). The KIE value calculated from ^{1}H NMR was found to be 5.77.

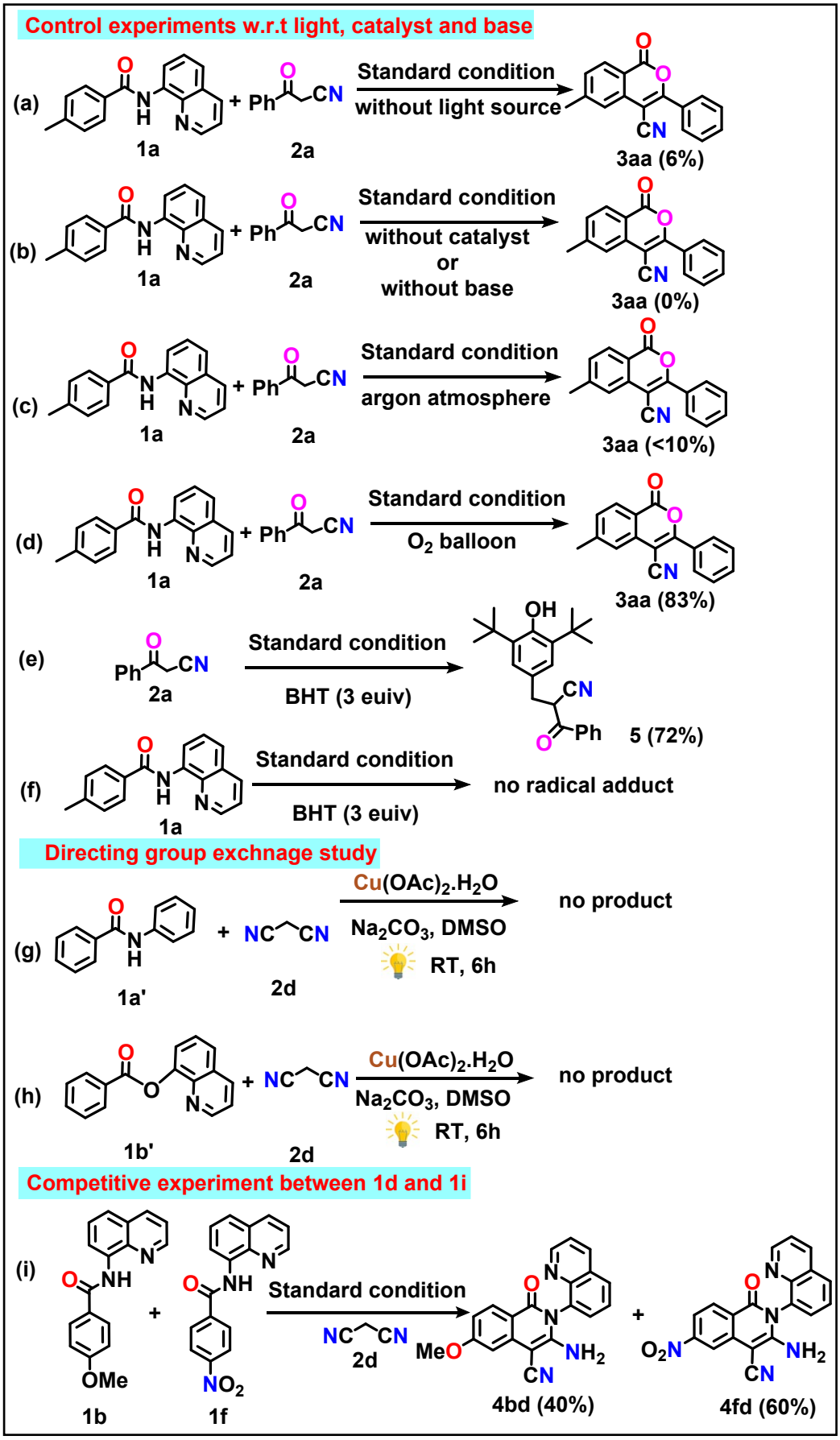
Table S1. Optimization of reaction conditions [a,b]



Entry	Catalyst (equiv)	Solvent	Base (equiv)	Visible light[c]	Time	Temp.	Yield[b] (%)
1	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	off	12 h	120 °C	<10
2	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	off	12 h	RT	<5

3	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	on	12 h	RT	70
4	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	on	10 h	RT	50
5	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	on	18 h	RT	84
6	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (2)	on	24 h	RT	84
7	$Cu(OAc)_2.H_2O$ (2)	DMSO	K_2CO_3 (2)	on	18 h	RT	50
8	$Cu(OAc)_2.H_2O$ (2)	DMSO	KO^tBu (2)	on	18 h	RT	5
9	$Cu(OAc)_2.H_2O$ (2)	DMSO	DBU (2)	on	18 h	RT	65
10[d]	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	84
11[e]	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (1.5)	on	6 h	RT	92
12	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (1)	on	18 h	RT	55
13	$Cu(OAc)_2.H_2O$ (2)	DCE	Na_2CO_3 (1.5)	on	18 h	RT	ND
14	$Cu(OAc)_2.H_2O$ (2)	CH_3CN	Na_2CO_3 (1.5)	on	18 h	RT	ND
15	$Cu(OAc)_2.H_2O$ (2)	DMF	Na_2CO_3 (1.5)	on	18 h	RT	10
16	$CuCl_2$ (2)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	68
17	CuI (2)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	ND
18	$Co(OAc)_2.4H_2O$ (2)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	ND
19	$Cu(OAc)_2.H_2O$ (1.5)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	65
20	$FeCl_3$	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	ND
21	$Ni(OAc)_2.4H_2O$	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	ND
22[f]	$Cu(OAc)_2.H_2O$ (2)	DMSO	Na_2CO_3 (1.5)	on	18 h	RT	<10%

[a]Catalytic conditions: **1a** (1 equiv), **2d** (1.5 equiv), Na_2CO_3 (1.5 equiv), $Cu(OAc)_2.H_2O$ (2 equiv.), RT = Room Temperature, 6 h, air; [b]Isolated yield based on column chromatography, [c]65 watt, [d]for **2a**, **2b**, **2c**, [e]for **2d**, [f]Argon atmosphere, ND: Not detected



Scheme S1. Control experiments

Characterizations of the products:

6-methyl-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3aa**): White solid (Isolated yield 83%, 216.88 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10-8.08 (m, 2H), 7.92 (s, 1H), 7.83 (s, 1H), 7.66-7.57 (m, 4H), 2.63 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 164.6, 156.3, 147.8, 137.6, 136.1, 133.2, 129.6, 129.3, 128.7, 117.0, 116.3, 114.7, 114.2, 90.0, 22.0. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{12}NO_2$, 262.0868, found 262.0886.

6-methoxy-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3ba**): White solid (Isolated yield 84%, 232.90 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 9 Hz, 1H), 8.07 (d, *J* = 6 Hz, 2H), 7.60-7.54 (m, 3H), 7.24 (s, 1H), 7.16 (d, *J* = 9 Hz, 1H), 4.00 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 165.9, 163.7, 159.3, 136.7, 132.5, 132.4, 130.4, 129.1, 128.6, 118.5, 115.5, 111.8, 106.8, 90.8, 56.2. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{12}NO_3$, 278.0817, found 278.0829.

6,7-dimethoxy-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3ca**)[2]: White solid (Isolated yield 85%, 261.20 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09-8.05 (m, 2H), 7.69 (s, 1H), 7.59-7.55 (m, 3H), 7.22 (s, 1H), 4.09 (s, 3H), 4.03 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 161.9, 159.6, 156.3, 151.1, 132.2, 130.5, 129.8, 129.1, 128.4, 115.7, 112.2, 109.9, 105.3, 90.5, 56.8, 56.7.

6-amino-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3da**): White solid (Isolated yield 81%, 212.43 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 9 Hz, 1H), 8.07-8.03 (m, 2H), 7.58-7.53 (m, 3H), 6.95 (d, *J* = 3 Hz, 1H), 6.83 (dd, J_1 = 3 Hz, J_2 = 9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 163.5, 159.5, 153.5, 136.5, 132.5, 132.3, 130.7, 129.0, 128.5, 116.8, 115.8, 108.7, 106.8, 90.5. HRMS (ESI, m/z) [M+H] calcd. for $C_{16}H_{11}N_2O_2$, 263.0820, found 263.0820.

6-chloro-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3ea**): White solid (Isolated yield 84%, 236.62 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 9 Hz, 1H), 8.08 (dd, J_1 = 7.5 Hz, J_2 = 3 Hz, 2H), 7.89 (d, *J* = 2.1 Hz, 1H), 7.63-7.54 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 164.1, 158.7, 143.5, 135.7, 132.9, 131.8, 130.5, 130.0, 129.2, 128.6, 124.5, 117.3, 114.8, 89.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{16}H_9NClO_2$, 282.0322, found 282.0322.

6-nitro-1-oxo-3-phenyl-1H-isochromene-4-carbonitrile (**3fa**)[2]: White solid (Isolated yield 80%, 233.80 mg), ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66 (s, 1H), 8.36 (d, *J* = 6 Hz, 1H), 8.22 (d, *J* = 3 Hz, 2H), 7.71 (d, *J* = 9 Hz, 1H), 7.61 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 164.8, 155.9, 145.5, 132.5, 129.6, 128.1, 127.0, 126.9, 122.3, 116.6, 113.1, 112.5, 88.9.

3-(furan-2-yl)-6-methyl-1-oxo-1H-isochromene-4-carbonitrile (**3ab**): White solid (Isolated yield 82%, 206.02 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = δ = 8.18 (d, *J* = 9 Hz, 1H), 7.74 (s, 1H), 7.65 (s, 1H), 7.42-7.39 (m, 2H), 6.67-6.65 (m, 1H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 158.8, 152.5, 147.9, 146.8, 144.9, 134.2, 131.0, 130.3, 124.6, 116.9, 116.4, 114.4, 113.0, 86.8, 22.3. HRMS (ESI, m/z) [M+H] calcd. for $C_{15}H_{10}NO_3$, 252.0661, found 252.0672.

3-(furan-2-yl)-6-methoxy-1-oxo-1H-isochromene-4-carbonitrile (**3bb**): White solid (Isolated yield 84%, 224.48 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 9 Hz, 1H), 7.75 (d, *J* = 3 Hz, 1H), 7.41 (d, *J* = 3 Hz, 1H), 7.21 (d, *J* = 3 Hz, 1H), 7.11 (dd, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 1H), 6.67-6.66 (m, 1H), 4.0 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 166.0, 158.5, 153.1, 146.9, 144.9, 136.7, 132.6, 118.3, 117.1, 114.5, 113.1, 111.7, 106.7, 100.1, 86.8, 56.2. HRMS (ESI, m/z) [M+H] calcd. for $C_{15}H_{10}NO_4$, 268.0610, found 268.0611.

6-amino-3-(furan-2-yl)-1-oxo-1H-isochromene-4-carbonitrile (**3db**): White solid (Isolated yield 82%, 206.82 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 9 Hz, 1H), 7.72 (s, 1H), 7.37 (d, *J* = 3 Hz, 1H), 6.92 (d, *J* = 2.4 Hz, 1H), 6.79 (dd, J_1 = 9 Hz, J_2 = 3 Hz, 1H), 6.65-6.63 (m, 1H), 4.54 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 158.7, 153.5, 152.9, 146.6, 145.1,

136.5, 132.6, 129.2, 116.7, 114.8, 112.9, 108.6, 106.7, 86.6. HRMS (ESI, m/z) [M+H] calcd. for $C_{14}H_9N_2O_3$, 253.0613, found 253.0612.

6-chloro-3-(furan-2-yl)-1-oxo-1H-isochromene-4-carbonitrile (**3eb**): White solid (Isolated yield 80%, 217.32 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 9 Hz, 1H), 7.85 (d, *J* = 3 Hz, 1H), 7.77 (d, *J* = 3 Hz, 1H), 7.56 (dd, J_1 = 9 Hz, J_2 = 3 Hz, 1H), 7.44 (d, *J* = 3 Hz, 1H), 6.69-6.68 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.9, 153.3, 147.4, 144.5, 143.6, 135.8, 131.9, 130.2, 124.3, 117.8, 117.0, 113.8, 113.2, 85.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{14}H_7NClO_3$, 272.0114, found 272.0114.

3-(furan-2-yl)-1-oxo-1H-isochromene-4-carbonitrile (**3gb**): White solid (Isolated yield 80%, 189.77 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 6 Hz, 1H), 7.88-7.87 (m, 2H), 7.76 (s, 1H), 7.64-7.60 (m, 1H), 7.41 (d, *J* = 3 Hz, 1H), 6.67 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 158.7, 152.5, 146.9, 144.8, 136.3, 134.2, 130.3, 129.7, 124.6, 118.9, 117.1, 114.2, 113.1, 86.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{14}H_8NO_3$, 238.0504, found 238.0505.

3-(furan-2-yl)-1-oxo-6-(trifluoromethyl)-1H-isochromene-4-carbonitrile (**3hb**): White solid (Isolated yield 81%, 247.22 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.43 (d, *J* = 9 Hz, 1H), 8.10 (s, 1H), 7.84-7.80 (m, 2H), 7.47 (d, *J* = 3 Hz, 1H), 6.71-6.69 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.6, 153.4, 147.7, 144.3, 135.0, 131.4, 125.9, 124.3, 121.8, 121.2, 118.2, 113.6, 113.4, 86.2. ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$): δ = -63.54. HRMS (ESI, m/z) [M+H] calcd. for $C_{15}H_7F_3NO_3$, 306.0378, found 306.0388.

6-methoxy-1-oxo-3-(p-tolyl)-1H-isochromene-4-carbonitrile (**3bc**): White solid (Isolated yield 85%, 247.60 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 6 Hz, 1H), 7.98 (d, *J* = 6 Hz, 2H), 7.36 (d, *J* = 9 Hz, 2H), 7.22 (s, 1H), 7.14 (d, *J* = 6 Hz, 1H), 3.99 (s, 3H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 165.9, 163.9, 159.4, 143.4, 136.9, 132.4, 129.8, 128.5,

127.6, 118.3, 115.7, 111.7, 106.6, 90.0, 56.2, 21.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{18}H_{14}NO_3$, 292.0974, found 292.0984.

6,7-dimethoxy-1-oxo-3-(p-tolyl)-1H-isochromene-4-carbonitrile (**3cc**): White solid (Isolated yield 84%, 269.69 mg). δ = 7.97 (d, *J* = 9 Hz, 2H), 7.67 (s, 1H), 7.35 (d, *J* = 9 Hz, 2H), 7.20 (s, 1H), 4.08 (s, 3H), 4.02 (s, 3H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 162.2, 159.7, 156.3, 150.9, 143.0, 130.0, 129.8, 128.3, 127.7, 115.9, 112.1, 109.8, 105.2, 89.8, 56.7, 21.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{19}H_{16}NO_4$, 322.1079, found 322.1078.

6-amino-1-oxo-3-(p-tolyl)-1H-isochromene-4-carbonitrile (**3dc**): White solid (Isolated yield 83%, 229.32 mg). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 9 Hz, 1H), 7.96 (d, *J* = 9 Hz, 2H), 7.33 (d, *J* = 9 Hz, 2H), 6.92 (d, *J* = 3 Hz, 1H), 6.82 (dd, J_1 = 9 Hz, J_2 = 3 Hz 1H), 4.54 (s, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 163.7, 159.7, 153.5, 143.1, 136.7, 132.4, 129.7, 129.2, 128.5, 125.4, 116.6, 108.6, 106.6, 89.7, 21.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{13}N_2O_2$, 277.0977, found 277.0980.

6-chloro-1-oxo-3-(p-tolyl)-1H-isochromene-4-carbonitrile (**3ec**): White solid (Isolated yield 84%, 248.40 mg). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 9 Hz, 1H), 7.99 (d, *J* = 9 Hz, 2H), 7.87 (d, *J* = 3 Hz, 1H), 7.59 (dd, J_1 = 9 Hz, J_2 = 3 Hz, 1H), 7.37 (d, *J* = 9 Hz 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 164.2, 158.9, 143.9, 136.0, 131.7, 129.9, 129.2, 128.6, 127.2, 125.4, 124.3, 117.2, 115.0, 89.2, 21.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{11}NClO_2$, 296.0478, found 296.0478.

6-bromo-1-oxo-3-(p-tolyl)-1H-isochromene-4-carbonitrile (**3ic**): White solid (Isolated yield 82%, 278.93 mg). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 9 Hz, 1H), 8.05 (s, 1H), 7.99 (d, *J* = 6 Hz, 2H), 7.75 (d, *J* = 6 Hz, 1H), 7.37 (d, *J* = 6 Hz 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 164.2, 159.0, 143.9, 135.9, 133.2, 132.1, 131.6, 129.9, 128.6, 127.4,

127.1, 117.5, 115.0, 89.0, 21.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{11}NBrO_2$, 339.9973, found 339.9973.

3-amino-6-methyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile(**4ad**): White solid (Isolated yield 92%, 300.2 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 3 Hz, 1H), 8.52 (d, *J* = 6 Hz, 1H), 8.19 (d, *J* = 6 Hz, 1H), 7.86 (d, *J* = 6 Hz, 1H), 7.77 (t, *J* = 6 Hz, 1H), 7.63-7.60 (m, 1H), 7.28 (s, 1H), 7.06 (d, *J* = 6Hz, 1H), 6.70 (s, 2H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 161.4, 154.7, 151.2, 144.7, 143.8, 137.0, 136.7, 132.3, 131.3, 130.5, 129.6, 128.1, 127.0, 124.5, 122.3, 120.5, 117.9, 116.4, 64.1, 21.7. HRMS (ESI, m/z) [M+H] calcd. for $C_{20}H_{15}N_4O$, 327.1245, found 327.1241 and [M+Na] calcd. for $C_{20}H_{14}N_4ONa$, 349.1065, found 349.1060.

3-amino-6-methoxy-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile(**4bd**): White solid (Isolated yield 90%, 308.1 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 3 Hz, 1H), 8.51 (d, *J* = 6 Hz, 1H), 8.18 (d, *J* = 6 Hz, 1H), 7.89-7.84 (m, 2H), 7.76 (t, *J* = 6 Hz, 1H), 7.63-7.60 (m, 1H), 6.83-6.81 (m, 2H), 6.73 (s, 2H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 164.2, 161.2, 155.1, 151.4, 144.0, 139.3, 136.9, 132.4, 131.5, 130.7, 130.6, 129.7, 127.2, 122.5, 118.1, 112.4, 112.3, 102.4, 64.5, 55.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{20}H_{15}N_4O_2$, 343.1195, found 343.1190.

3-amino-6,7-dimethoxy-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4cd**): White solid (Isolated yield 91%, 338.8 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 6 Hz, 1H), 8.51 (d, *J* = 9 Hz, 1H), 8.18 (d, *J* = 6 Hz, 1H), 7.84-7.76 (m, 2H), 7.61 (s, 1H), 7.35 (s, 1H), 6.85 (m, 1H), 6.51 (s, 2H), 3.94 (s, 3H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 161.2, 155.4, 154.2, 151.8, 146.7, 144.1, 137.2, 132.8, 132.7, 131.6, 131.0, 129.9, 127.5, 122.9, 118.6, 111.6, 108.8, 102.3, 64.8, 56.3, 56.1. HRMS (ESI, m/z) [M+Na] calcd. for $C_{21}H_{16}N_4O_3Na$, 395.1120, found 395.1116.

3,6-diamino-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4dd**): White solid (Isolated yield 92%, 301.1 mg), ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 6 Hz, 1H), 8.49 (d, *J* = 9 Hz, 1H), 8.15 (d, *J* = 9 Hz, 1H), 7.80-7.74 (m, 2H), 7.64-7.57 (m, 2H), 6.53 (s, 1H), 6.46 (d, *J* = 9 Hz, 1H), 6.37 (s, 2H), 6.12 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 160.9, 154.5, 154.0, 151.0, 144.1, 138.8, 136.6, 132.8, 131.4, 130.1, 129.7, 129.4, 126.9, 122.2, 122.1, 118.4, 111.7, 108.0, 63.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{19}H_{14}N_5O$, 328.1198, found 328.1199.

3-amino-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4gd**)[3]: White solid (Isolated yield 92%, 287.3 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 6 Hz, 1H), 8.52 (d, *J* = 6 Hz, 1H), 8.20 (d, *J* = 9 Hz, 1H), 7.96 (d, *J* = 6 Hz, 1H), 7.88 (d, *J* = 9 Hz, 1H), 7.80-7.71 (m, 1H), 7.64-7.60 (m, 1H), 7.48 (d, *J* = 6 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.75 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 161.4, 154.6, 151.1, 143.7, 136.9, 136.6, 134.3, 132.2, 131.3, 130.4, 129.5, 127.9, 126.9, 122.8, 122.2, 120.8, 118.4, 117.7, 64.1.

3-amino-5,7-dimethoxy-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4jd**): White solid (Isolated yield 91%, 338.8 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 6 Hz, 1H), 8.52 (d, *J* = 9 Hz, 1H), 8.19 (d, *J* = 9 Hz, 1H), 7.87-7.85 (m, 1H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.63-7.60 (m, 1H), 7.04 (s, 1H), 6.90 (s, 1H), 6.17 (s, 2H), 3.91 (s, 3H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ = 160.7, 156.0, 153.6, 151.3, 143.6, 136.7, 132.7, 131.1, 130.5, 129.5, 127.0, 122.3, 121.1, 119.9, 119.3, 105.1, 100.0, 61.2, 56.4, 55.4. HRMS (ESI, m/z) [M+H] calcd. for $C_{21}H_{17}N_4O_3$, 373.1301, found 373.1306.

3-amino-7-methyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile(**4kd**): White solid (Isolated yield 90%, 293.7 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.71 (s, 1H), 8.94 (d, *J* = 3 Hz, 1H), 8.86 (d, *J* = 3 Hz, 1H), 8.20 (d, *J* = 6 Hz, 1H), 7.90-7.87 (m, 2H), 7.61 (t, *J* = 6 Hz, 1H), 7.55 (d, *J* = 6 Hz, 1H), 7.50-7.47 (m, 1H), 7.44 (t, *J* = 6 Hz, 1H), 7.39 (s, 1H),

2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 165.9, 148.4, 138.9, 138.8, 136.7, 135.3, 134.8, 134.5, 132.7, 130.8, 128.8, 128.5, 128.2, 128.1, 127.7, 127.4, 124.4, 121.8, 116.9, 21.6. HRMS (ESI, m/z) [M+H] calcd. for $C_{20}H_{15}N_4O$, 327.1245, found 327.1241 and [M+Na] calcd. for $C_{20}H_{14}N_4ONa$, 349.1065, found 349.1061.

3-amino-6-chloro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4ed**): White solid (Isolated yield 95%, 329.4 mg). ^1H NMR (300 MHz, DMSO-d_6): δ = 8.83 (dd, J_1 = 7.5 Hz, J_2 = 1.8 Hz, 1H), 8.52 (dd, J_1 = 7.5 Hz, J_2 = 3 Hz, 1H), 8.20 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.95 (d, J = 9 Hz, 1H), 7.88 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.77 (t, J = 9 Hz, 1H), 7.64-7.60 (m, 1H), 7.40 (d, J = 1.8 Hz, 1H), 7.24 (dd, J_1 = 7.5 Hz, J_2 = 2.1 Hz, 1H), 6.99 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ = 160.8, 155.3, 151.2, 143.7, 139.4, 138.7, 136.7, 131.9, 131.2, 130.6, 130.4, 129.5, 127.0, 122.9, 122.3, 119.6, 117.2, 116.9, 63.6. HRMS (ESI, m/z) [M+H] calcd. for $C_{19}H_{12}ClN_4O$, 347.0700, found 343.0696.

3-amino-6-nitro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4fd**): Red solid (Isolated yield 95%, 339.45 mg). ^1H NMR (300 MHz, DMSO-d_6): δ = 8.83 (d, J = 3 Hz, 1H), 8.53 (d, J = 6 Hz, 1H), 8.21 (d, J = 6 Hz, 1H), 8.19-8.16 (m, 2H), 7.92-7.90 (m, 2H), 7.79 (t, J = 6 Hz, 1H), 7.64-7.61 (m, 1H), 7.20 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ = 160.9, 155.9, 151.7, 151.5, 143.9, 138.4, 137.1, 132.1, 131.6, 131.2, 130.9, 130.0, 127.5, 122.8, 122.1, 117.4, 116.6, 116.1, 64.9. HRMS (ESI, m/z) [M+H] calcd. for $C_{19}H_{12}N_5O_3$, 358.0940, found 358.0951.

3-amino-1-oxo-2-(quinolin-8-yl)-6-(trifluoromethyl)-1,2-dihydroisoquinoline-4-carbonitrile (**4hd**): green solid (Isolated yield 94%, 357.5 mg). ^1H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, J = 3 Hz, 1H), 8.52 (dd, J_1 = 7.5 Hz, J_2 = 3 Hz, 1H), 8.21 (d, J = 6 Hz, 1H), 8.16 (d, J = 6 Hz, 1H), 7.90 (d, J = 3 Hz, 1H), 7.78 (t, J = 6 Hz, 1H), 7.67 (s, 1H), 7.64-7.61 (m, 1H), 7.49 (d, J = 6 Hz, 1H), 7.11 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ = 160.8, 155.4, 151.3, 143.6,

137.5, 136.8, 134.1, 133.8, 131.8, 131.3, 130.7, 129.8, 129.6, 127.1, 125.2, 122.4, 120.7, 117.5, 117.2, 64.3. $^{19}F\{^{1}H\}$ NMR (282 MHz, DMSO-d_6): δ = -62.1. HRMS (ESI, m/z) [M+H] calcd. for $C_{20}H_{12}F_3N_4O$, 381.0963, found 381.0962.

3-amino-6-bromo-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinoline-4-carbonitrile (**4id**): White solid (Isolated yield 93%, 363.8 mg). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.82 (d, *J* = 3 Hz, 1H), 8.52 (d, *J* = 6 Hz, 1H), 8.20 (d, *J* = 6 Hz, 1H), 7.89-7.86 (m, 2H), 7.77 (t, *J* = 6 Hz, 1H), 7.63-7.60 (m, 1H), 7.56 (s, 1H), 7.37 (d, *J* = 6 Hz, 1H), 6.99 (s, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ = 161.4, 155.5, 151.7, 143.8, 139.1, 137.1, 132.1, 131.5, 131.1, 130.7, 129.8, 129.1, 127.4, 126.2, 123.0, 122.7, 117.6, 117.5, 63.8. HRMS (ESI, m/z) [M+H] calcd. for $C_{19}H_{12}BrN_4O$, 391.0194, found 391.0193.

3-amino-1-oxo-2-(quinolin-8-yl)-1,2-dihydro-2,7-naphthyridine-4-carbonitrile (**4ld**): White solid (Isolated yield 94%, 294.5 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (s, 1H), 8.83 (dd, J_1 = 3 Hz, J_2 = 3 Hz, 1H), 8.58 (d, *J* = 6 Hz, 1H), 8.52 (dd, J_1 = 12 Hz, J_2 = 3 Hz, 1H), 8.21 (dd, J_1 = 7.5 Hz, J_2 = 3 Hz,, 1H), 7.89 (dd, J_1 = 8.4 Hz, J_2 = 3 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.64-7.60 (m, 1H), 7.33-7.30 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ = 161.7, 157.2, 152.3, 151.9, 150.5, 143.9, 143.8, 137.4, 131.8, 131.7, 131.4, 130.0, 127.6, 123.0, 117.0, 115.0, 114.4, 64.4. HRMS (ESI, m/z) [M+H] calcd. for $C_{18}H_{12}N_5O$, 314.1042, found 314.1040.

6-amino-4-oxo-5-(quinolin-8-yl)-4,5-dihydrothieno[3,4-c]pyridine-7-carbonitrile(**4md**): White solid (Isolated yield 93%, 296.0 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.83 (d, *J* = 6 Hz, 1H), 8.51 (d, *J* = 6 Hz, 1H), 8.18 (d, *J* = 6 Hz, 1H), 7.84 (d, *J* = 6 Hz, 1H), 7.76 (t, *J* = 6Hz, 1H), 7.63-7.60 (m, 1H), 7.29-7.25 (m, 2H), 6.90 (s, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ = 157.7, 154.9, 151.3, 150.4, 143.8, 136.8, 132.2, 131.4, 130.6, 129.7, 127.2, 125.0, 122.4, 120.5, 120.1, 117.3, 64.3. HRMS (ESI, m/z) [M+H] calcd. for $C_{17}H_{11}N_4OS$, 319.0654, found 319.0655.

2-(3,5-di-tert-butyl-4-hydroxybenzyl)-3-oxo-3-phenylpropanenitrile (**5**): White solid (Isolated yield 50%, 181.7 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 6 Hz, 1H), 7.44 (s, 2H), 7.26 (d, *J* = 12 Hz, 2H), 7.05 (d, *J* = 6 Hz, 2H), 5.31 (s, 1H), 3.65 (d, *J* = 12 Hz, 1H), 5.31 (s, 1H), 3.33 (d, *J* = 12 Hz, 1H), 1.53 (s, 18H).

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3. Capdevila, L.; Andris, E.; Bris, A.; Tarrés, M.; Roldán-Gómez, S.; Roithova, J.; Ribas, X. Silver(I)-catalyzed C–X, C–C, C–N, and C–O cross-couplings using aminoquinoline directing group *via* elusive aryl-Ag(III) species. *ACS Catal.* **2018***, 8,* 10430−10436.

Table S2. Classification of synthesized compounds as known and unknown

Known	Unknown
3fa, 3ca, 4gd	**3aa, 3ba, 3da, 3ea, 3fa, 3ab, 3bb, 3db, 3eb, 3gb, 3hb, 3bc, 3cc, 3dc, 3ec, 3ic, 4ad, 4bd, 4cd, 4dd, 4gd, 4jd, 4kd, 4ed, 4fd, 4hd, 4id, 4ld, 4md**

^{1}H and ^{13}C NMR Spectra:

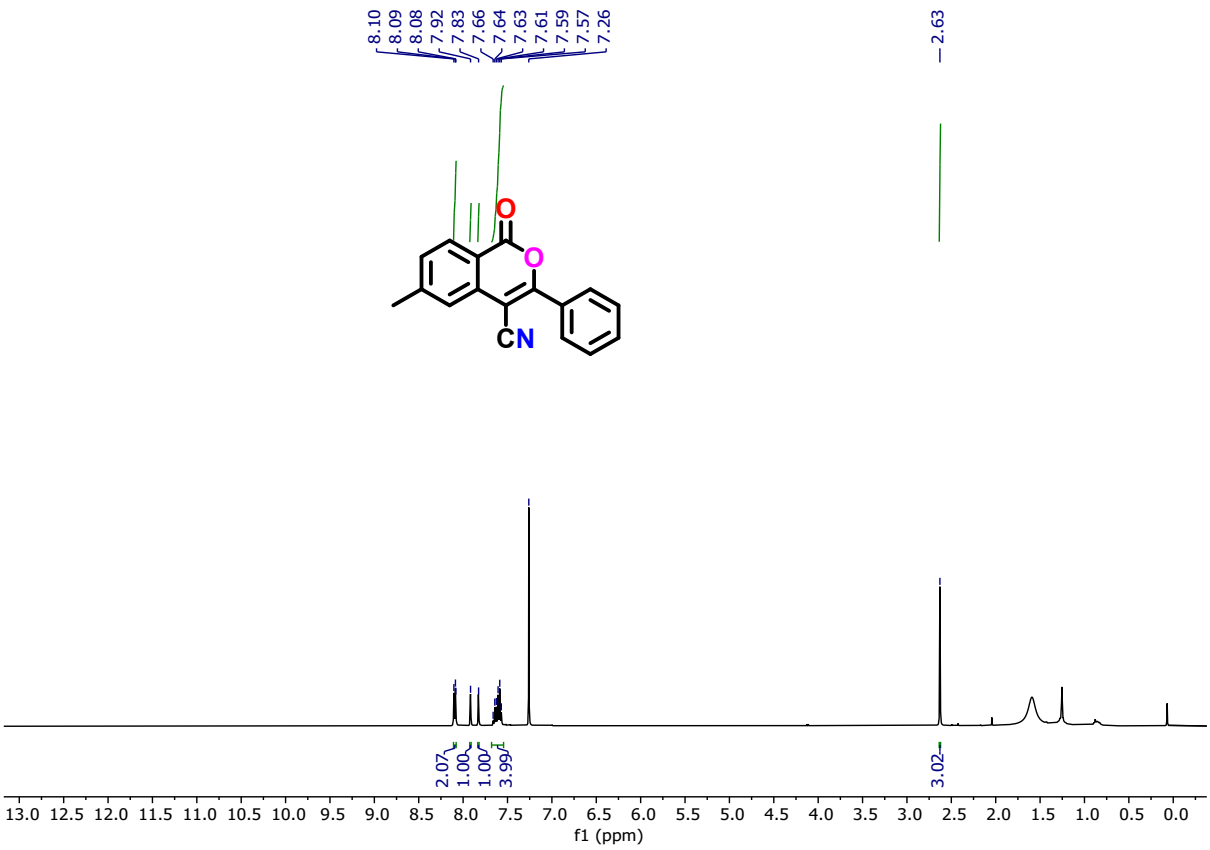


Figure S2. ^{1}H NMR (300 MHz) spectrum of **3aa** in $CDCl_3$.

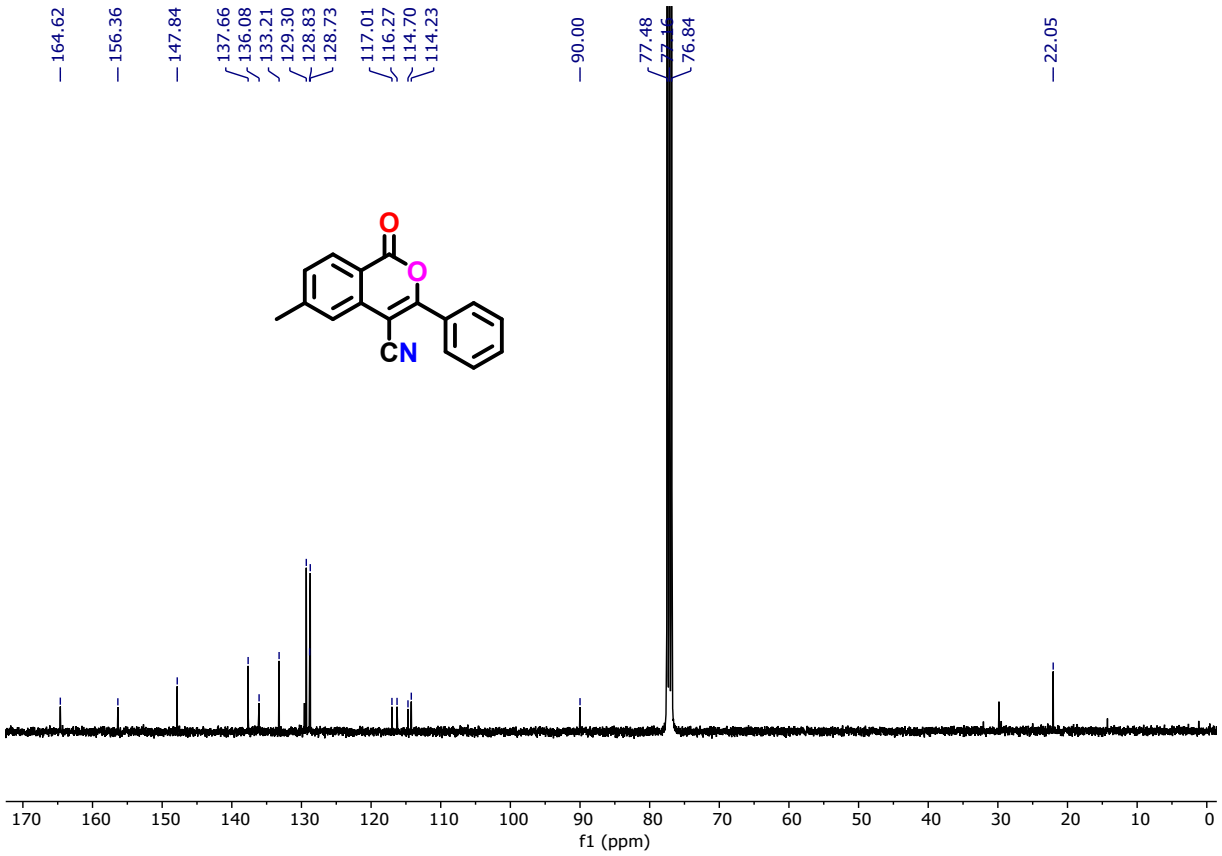


Figure S3. ^{13}C NMR (100 MHz) spectrum of **3aa** in $CDCl_3$.

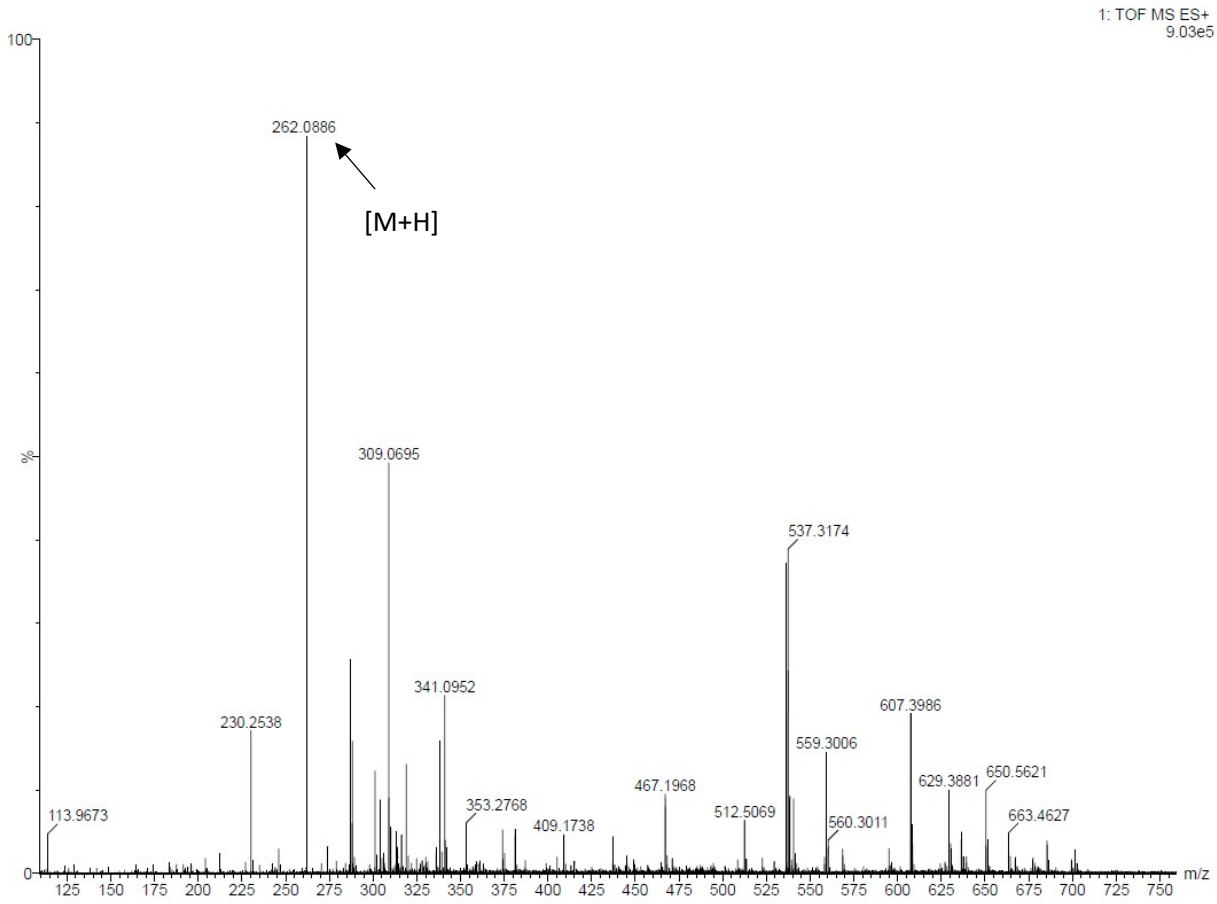


Figure S4. HRMS of **3aa**

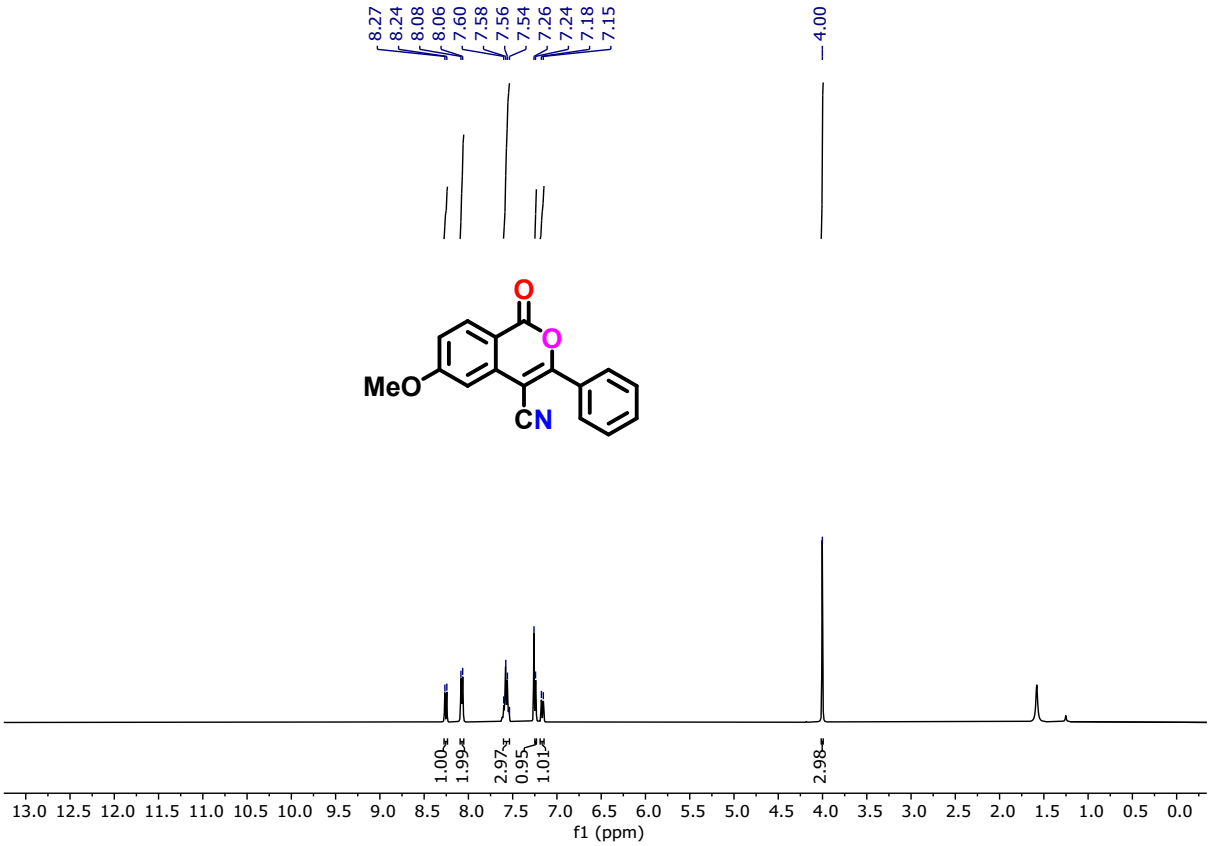


Figure S5. ^{1}H NMR (300 MHz) spectrum of **3ba** in $CDCl_3$.

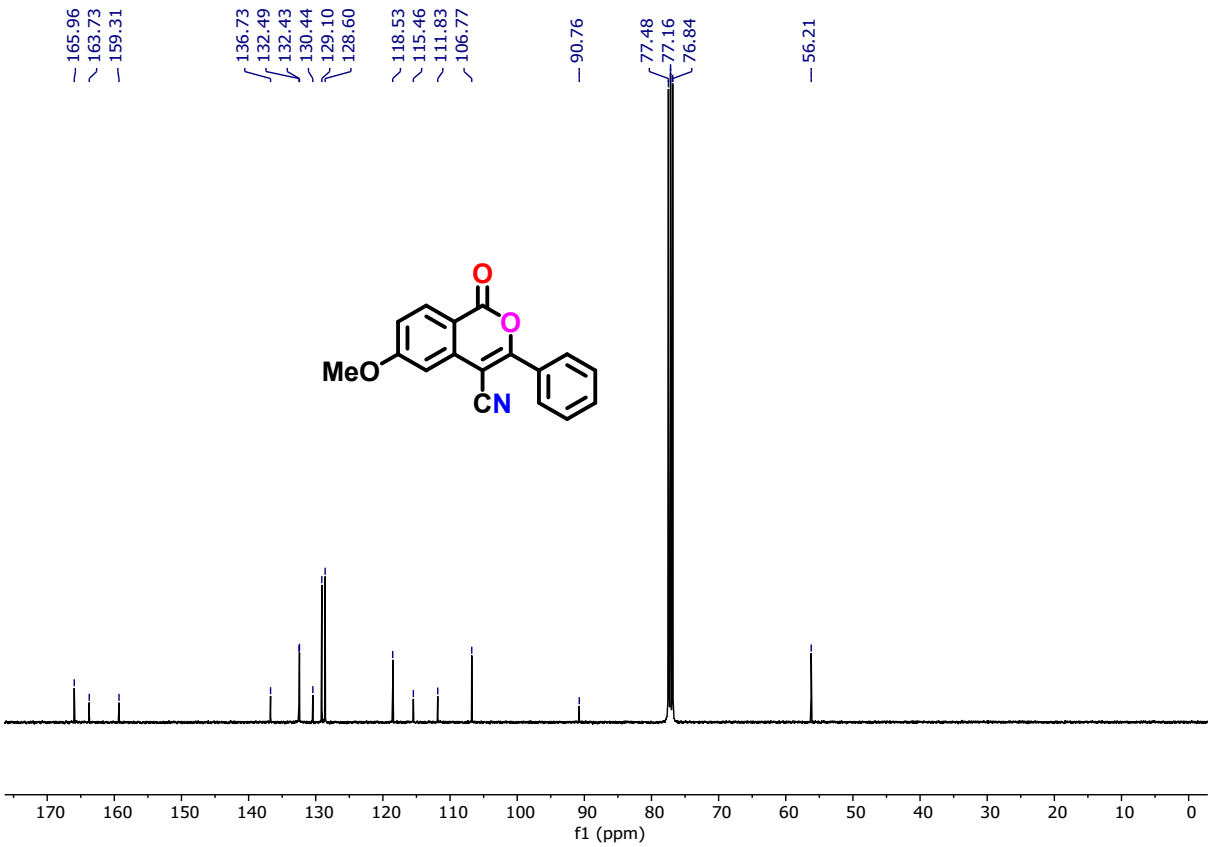


Figure S6. ^{13}C NMR (100 MHz) spectrum of **3ba** in $CDCl_3$.

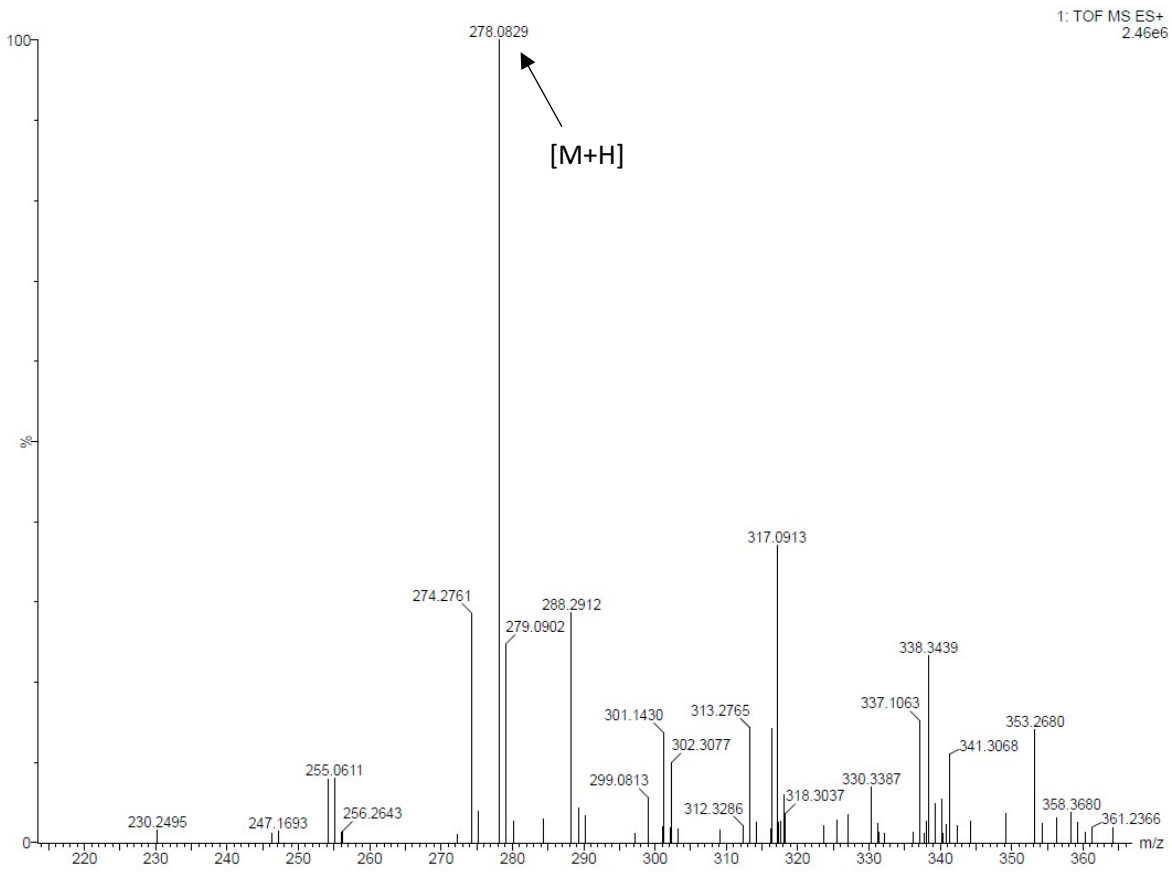


Figure S7. HRMS of **3ba**

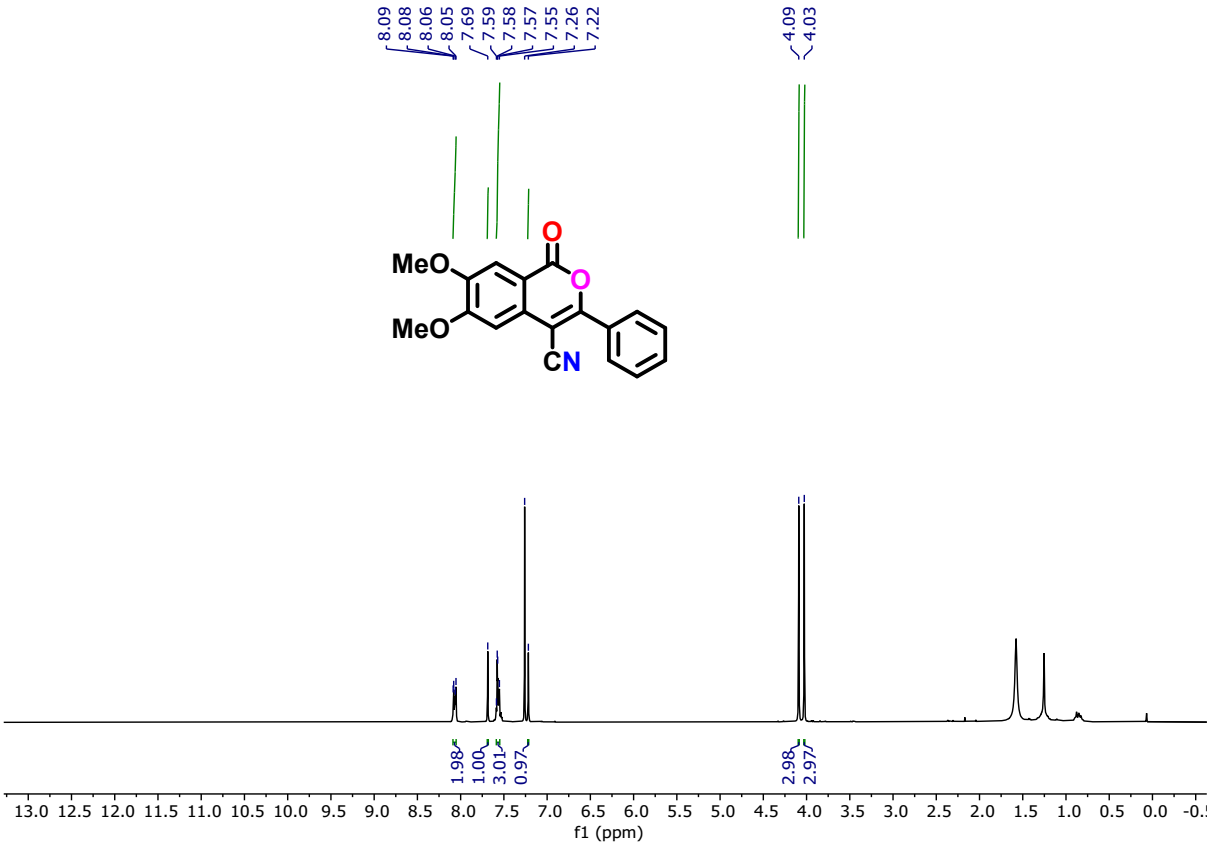


Figure S8. ^{1}H NMR (300 MHz) spectrum of **3ca** in $CDCl_3$.

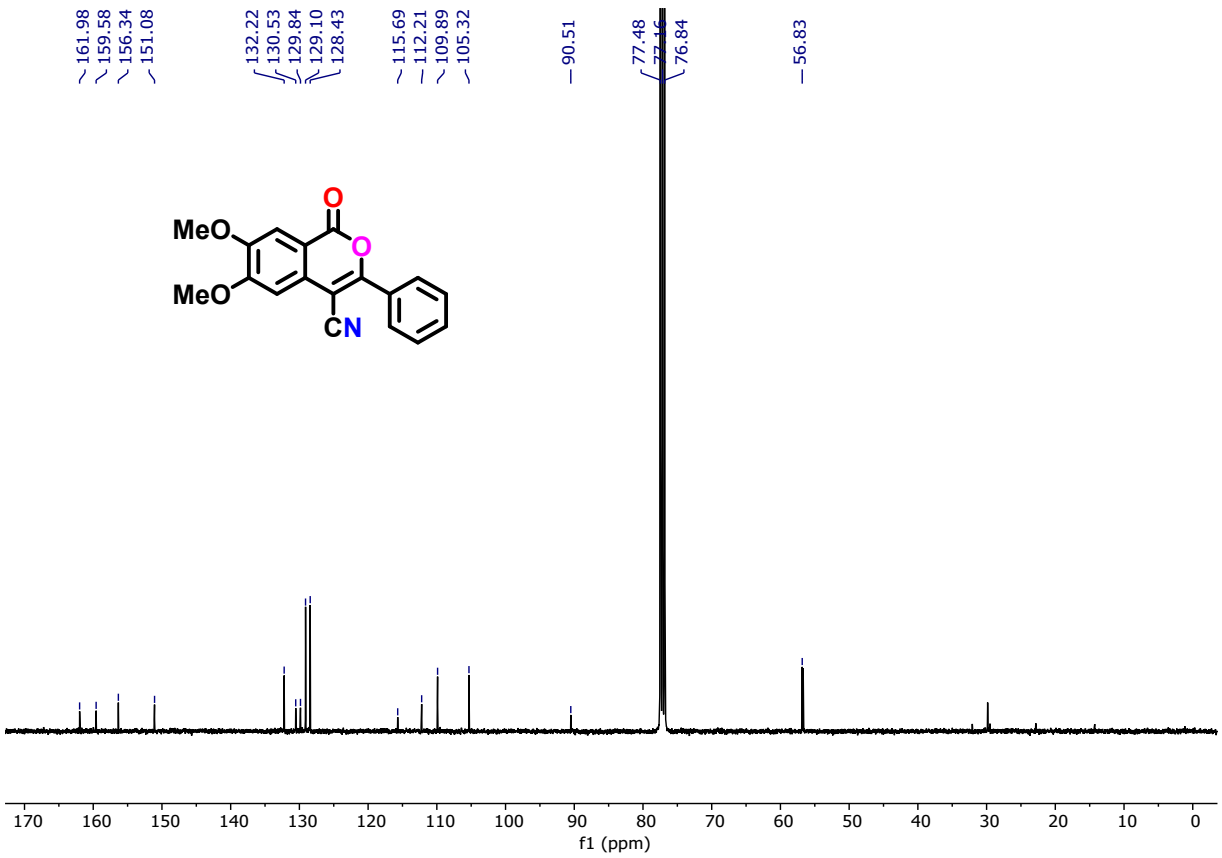


Figure S9. ^{13}C NMR (75 MHz) spectrum of **3ca** in $CDCl_3$.

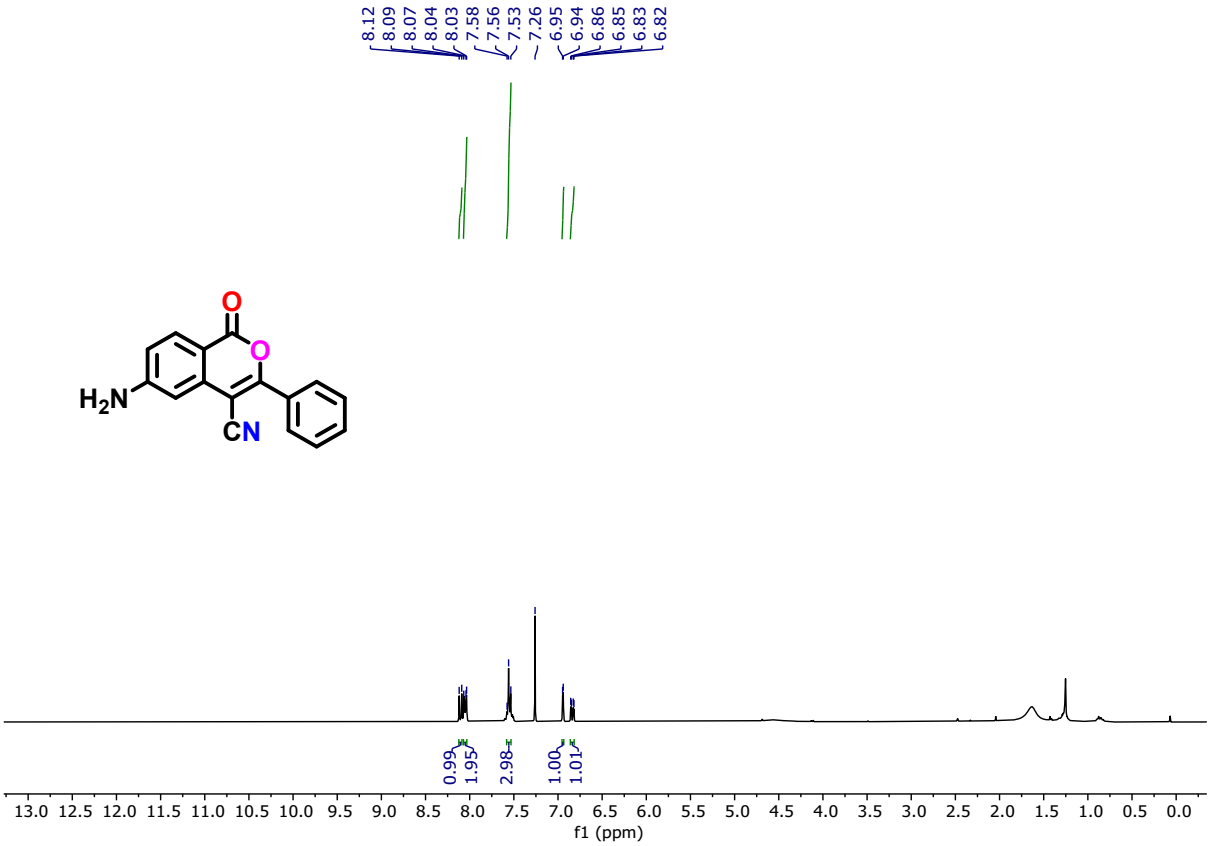


Figure S10. ^{1}H NMR (300 MHz) spectrum of **3da** in $CDCl_3$.

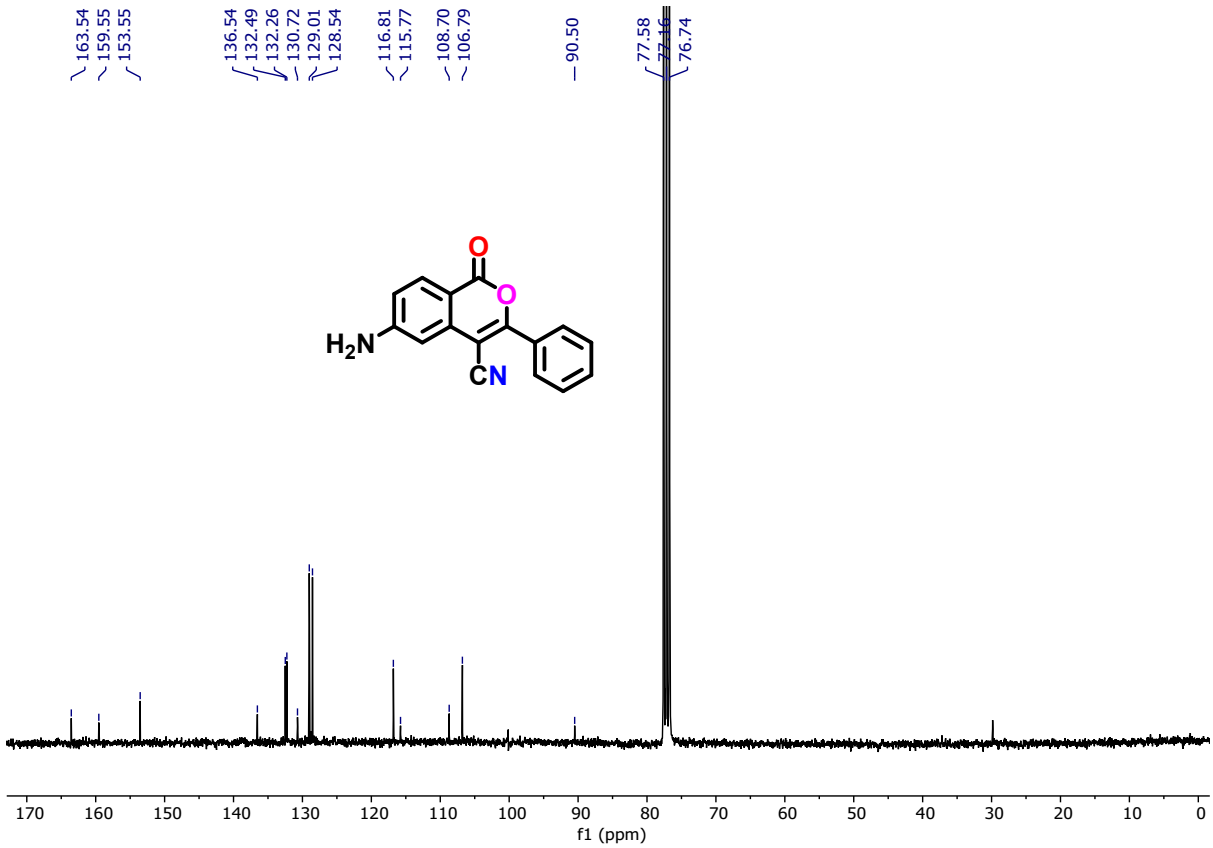


Figure S11. ^{13}C NMR (100 MHz) spectrum of **3da** in $CDCl_3$.

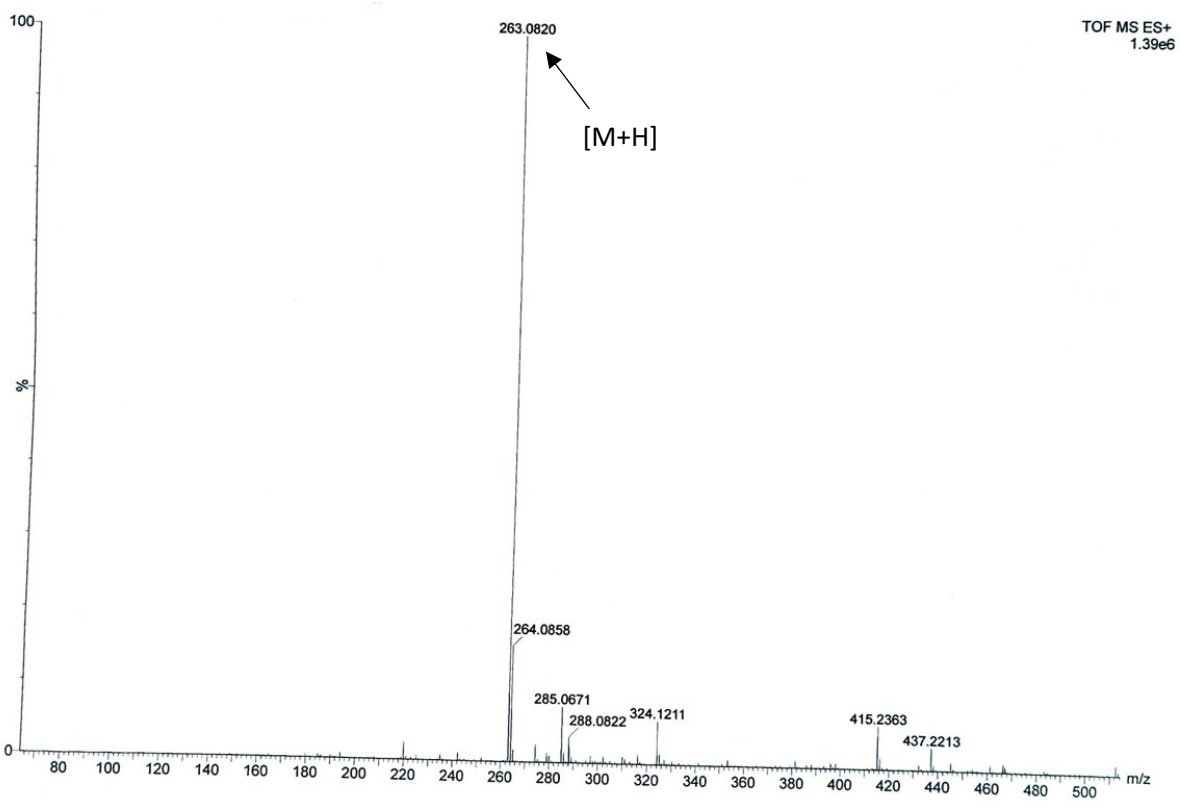


Figure S12. HRMS of **3da**

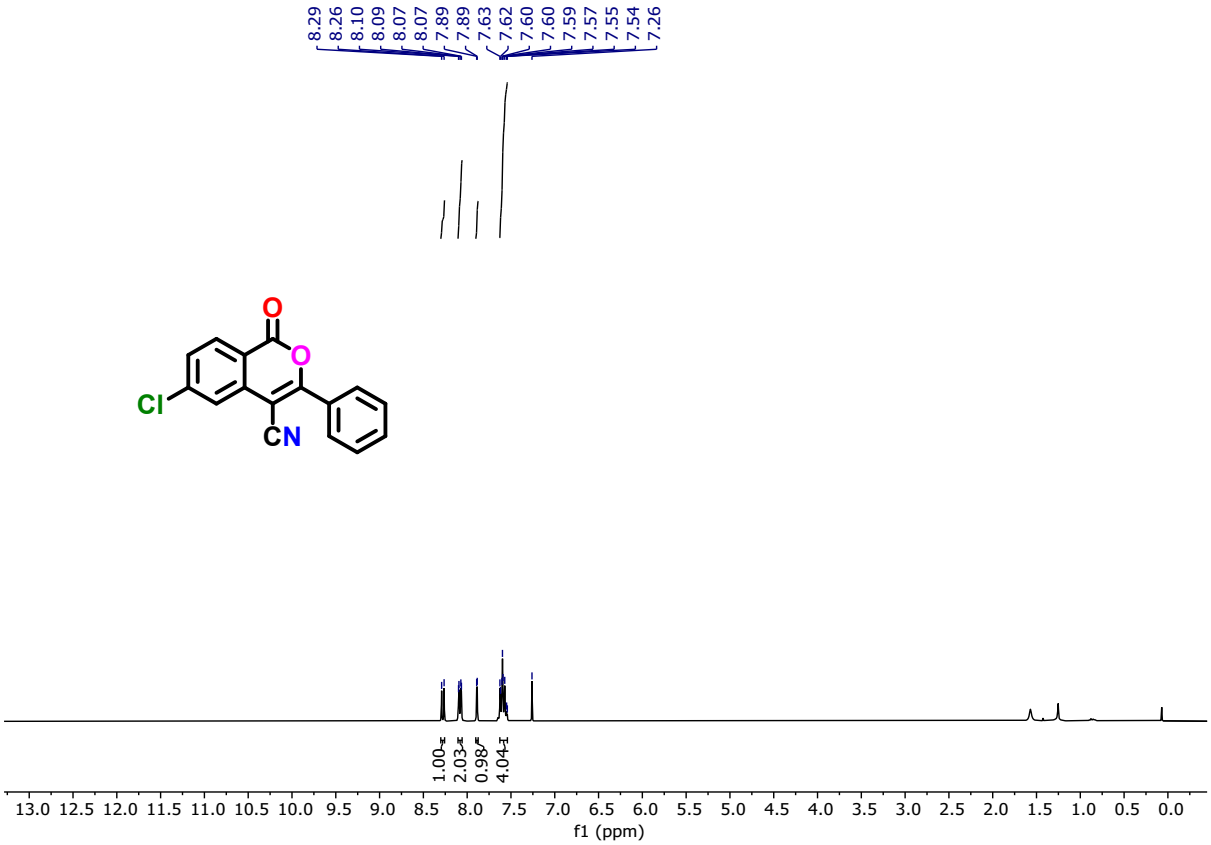


Figure S13. ^{1}H NMR (300 MHz) spectrum of **3ea** in $CDCl_3$.

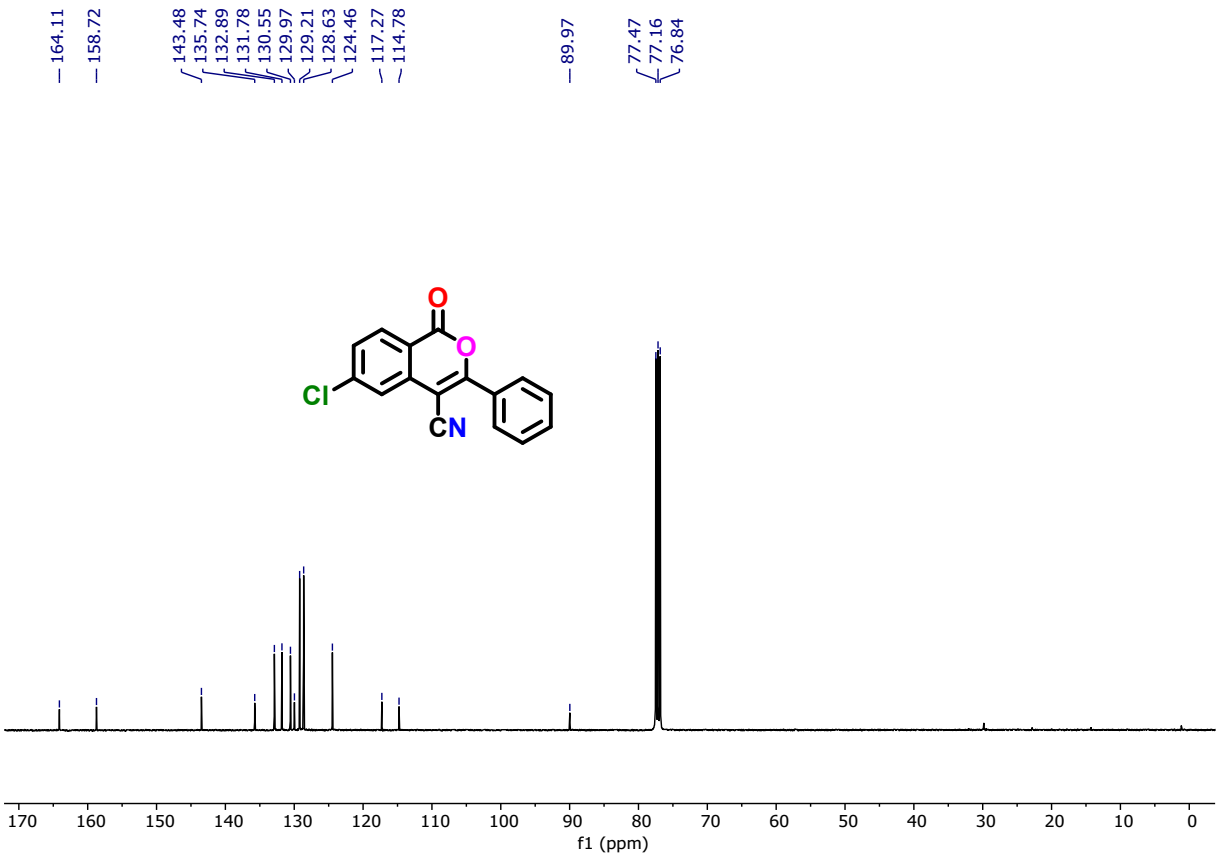


Figure S14. ^{13}C NMR (100 MHz) spectrum of **3ea** in $CDCl_3$.

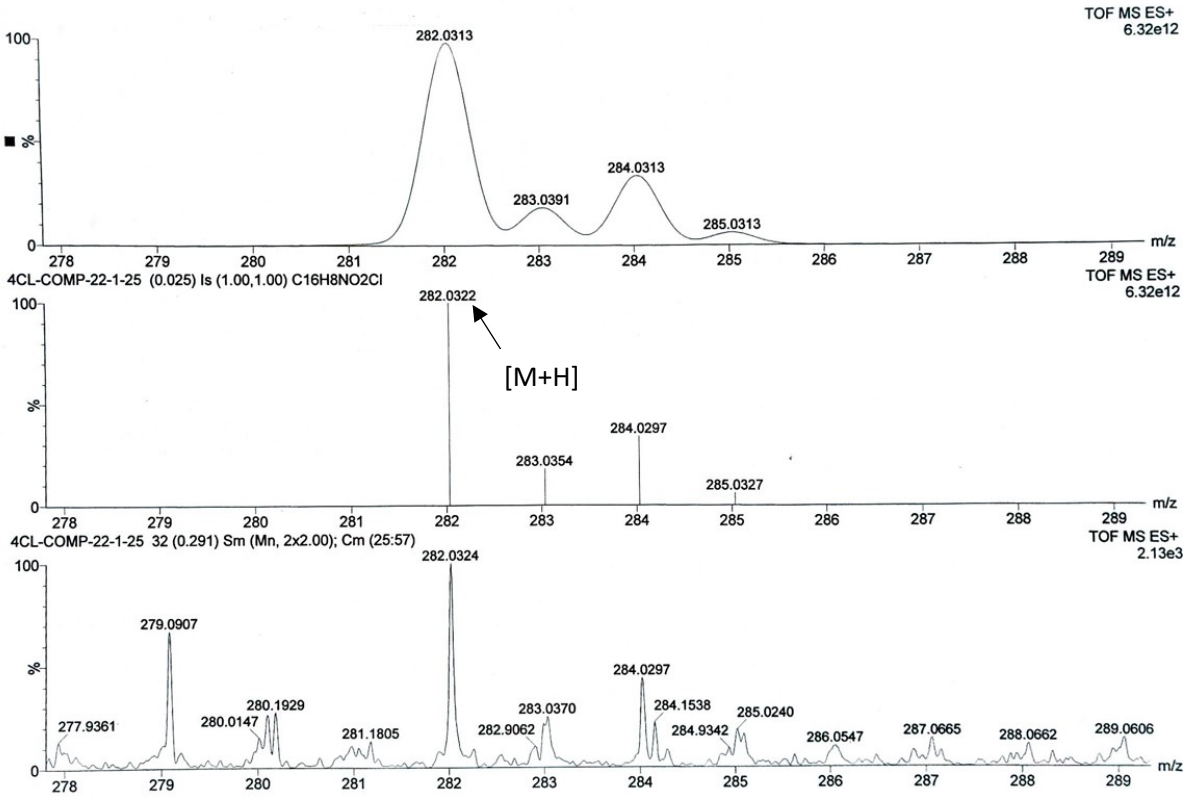


Figure S15. HRMS of **3ea**.

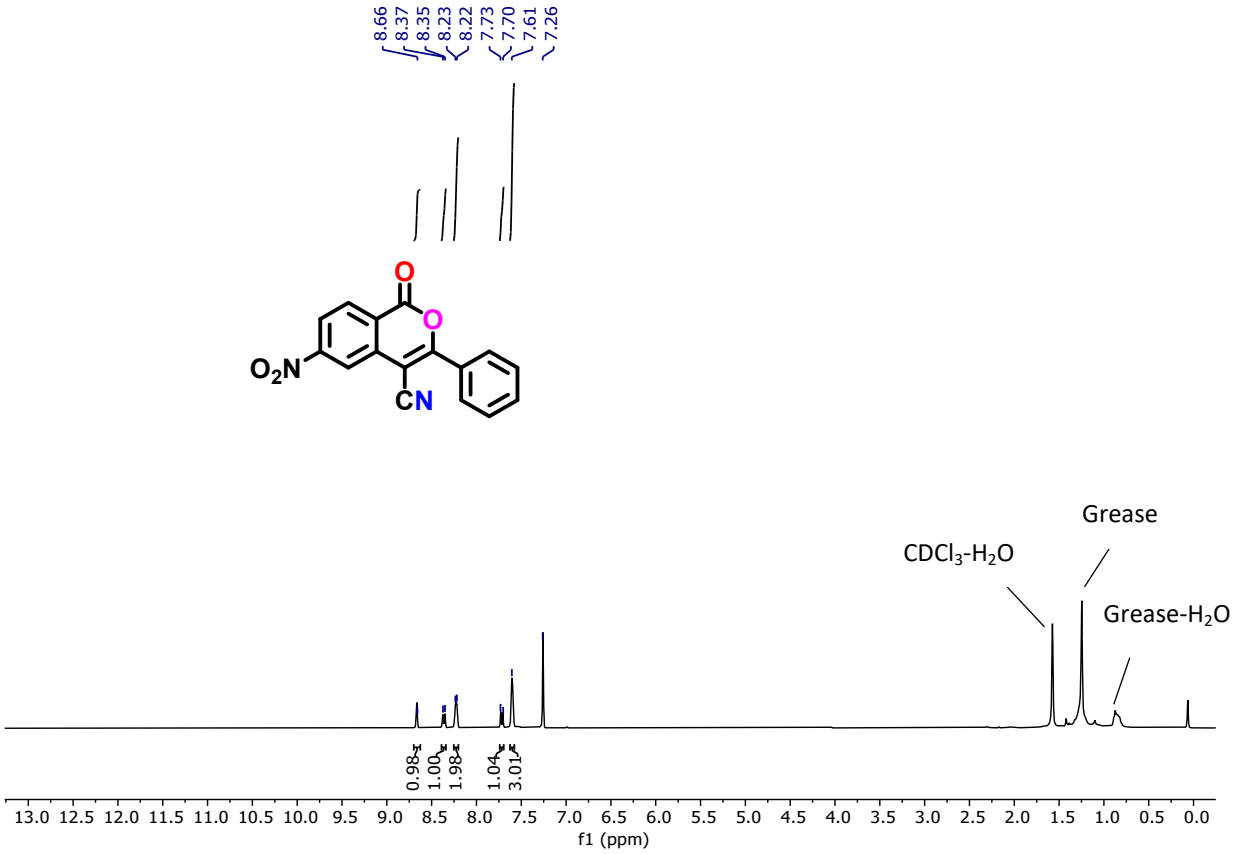


Figure S16. ^{1}H NMR (300 MHz) spectrum of **3fa** in $CDCl_3$.

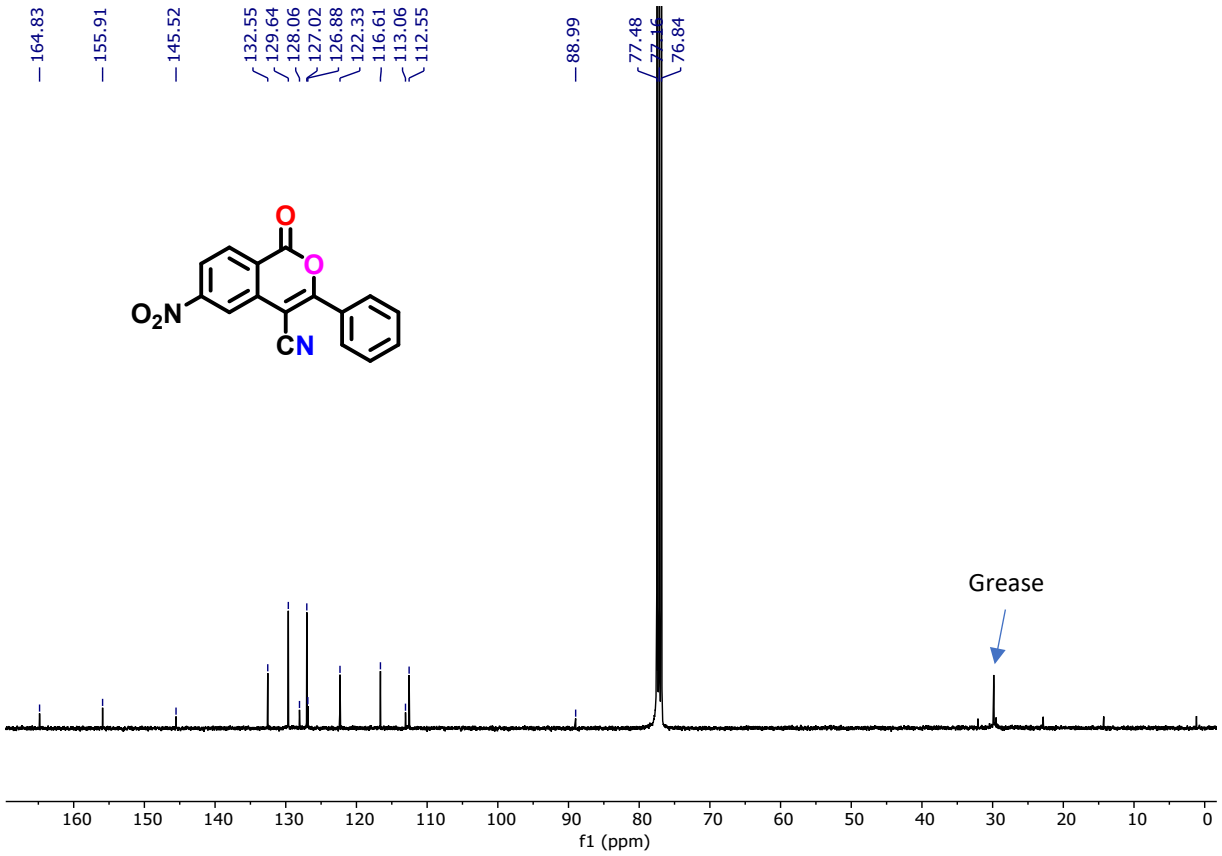


Figure S17. ^{13}C NMR (75 MHz) spectrum of **3fa** in $CDCl_3$.

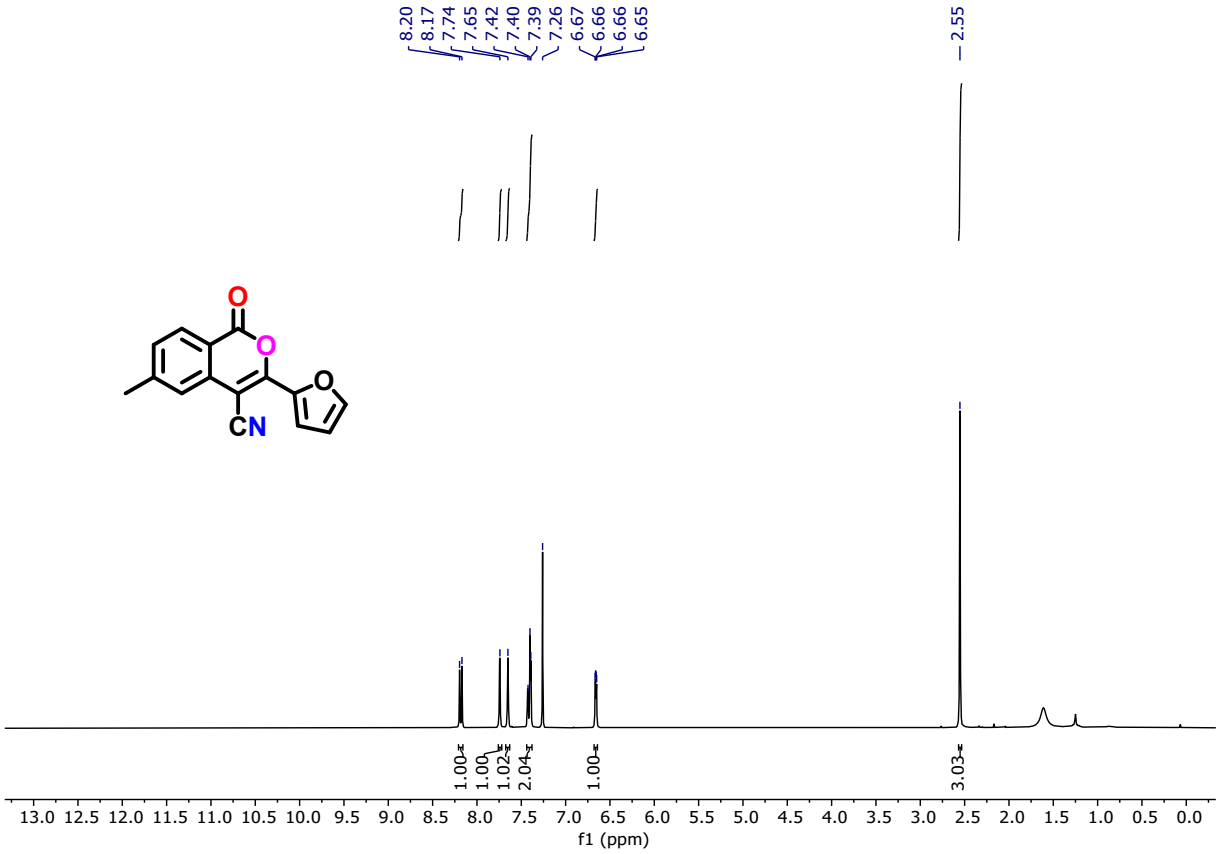


Figure S18. ^{1}H NMR (300 MHz) spectrum of **3ab** in $CDCl_3$.

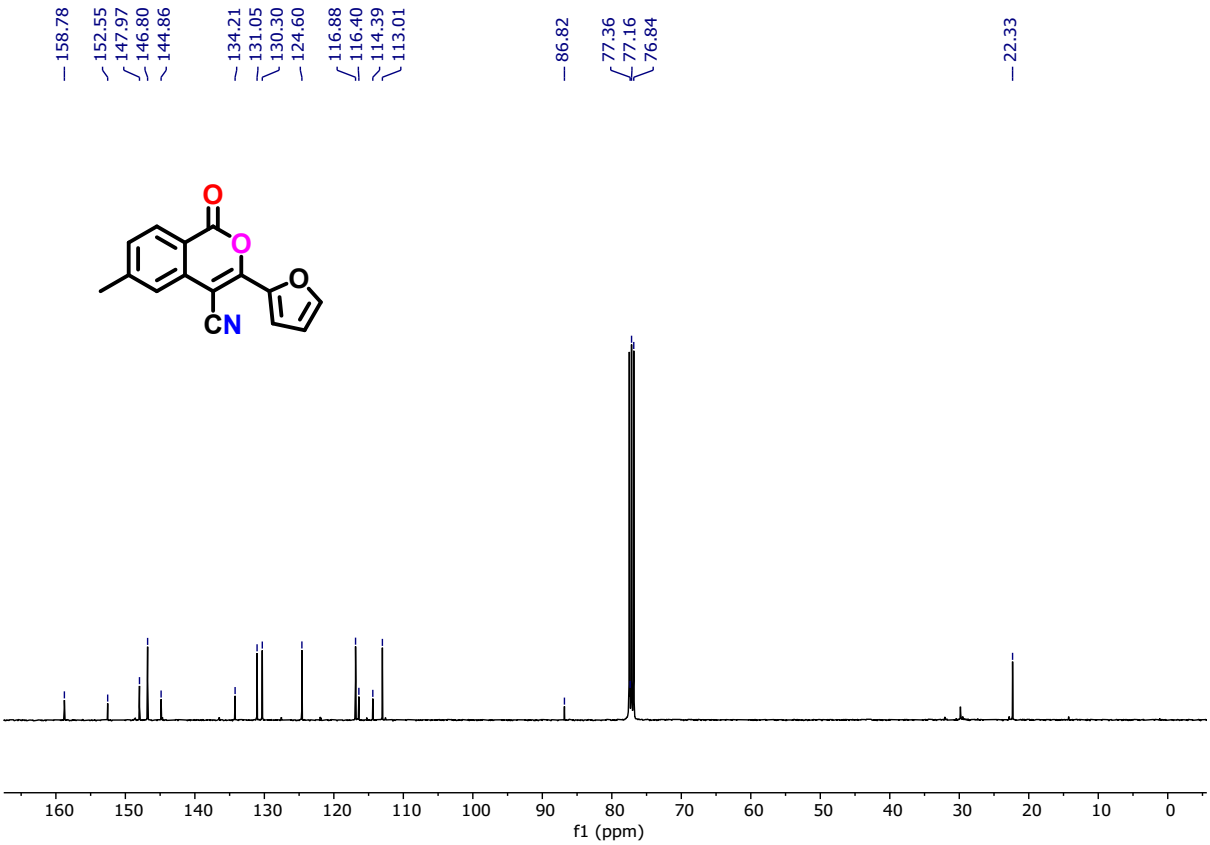


Figure S19. ^{13}C NMR (100 MHz) spectrum of **3ab** in $CDCl_3$.

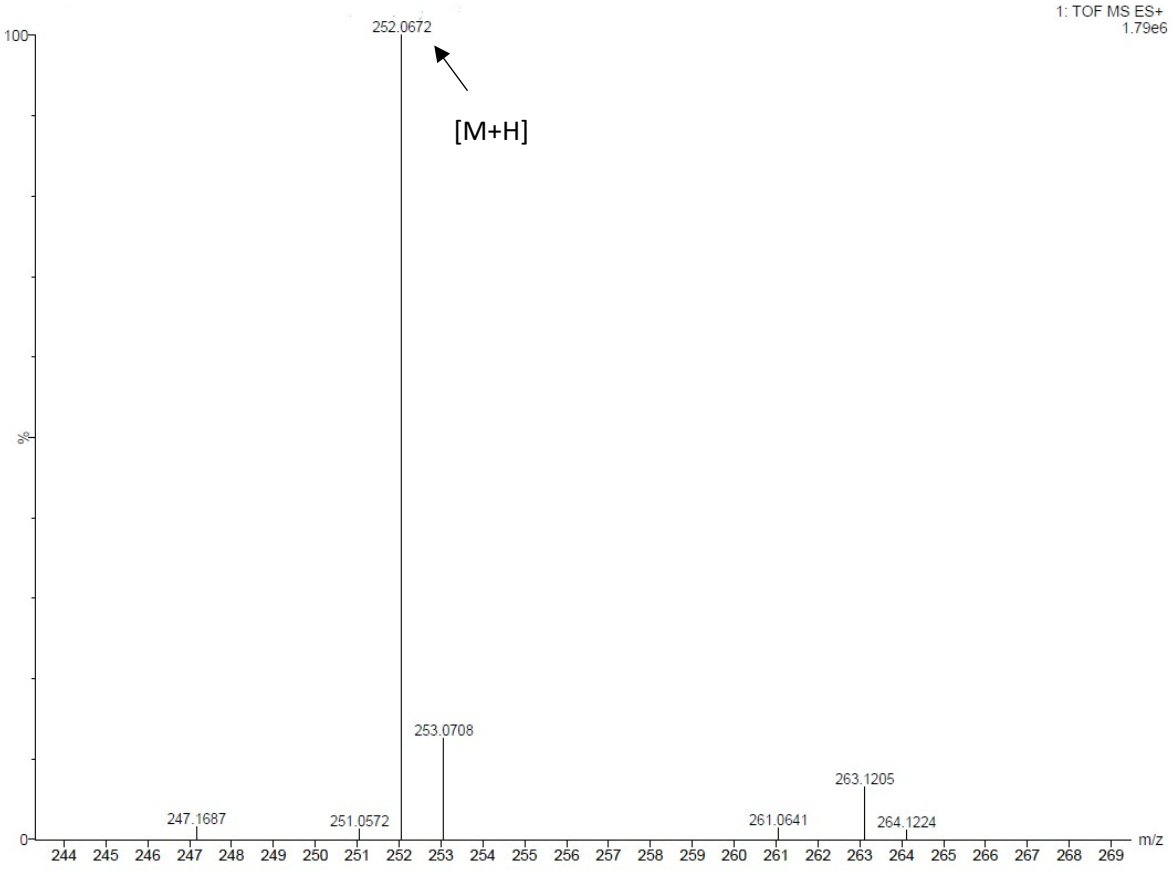


Figure S20. HRMS of **3ab**.

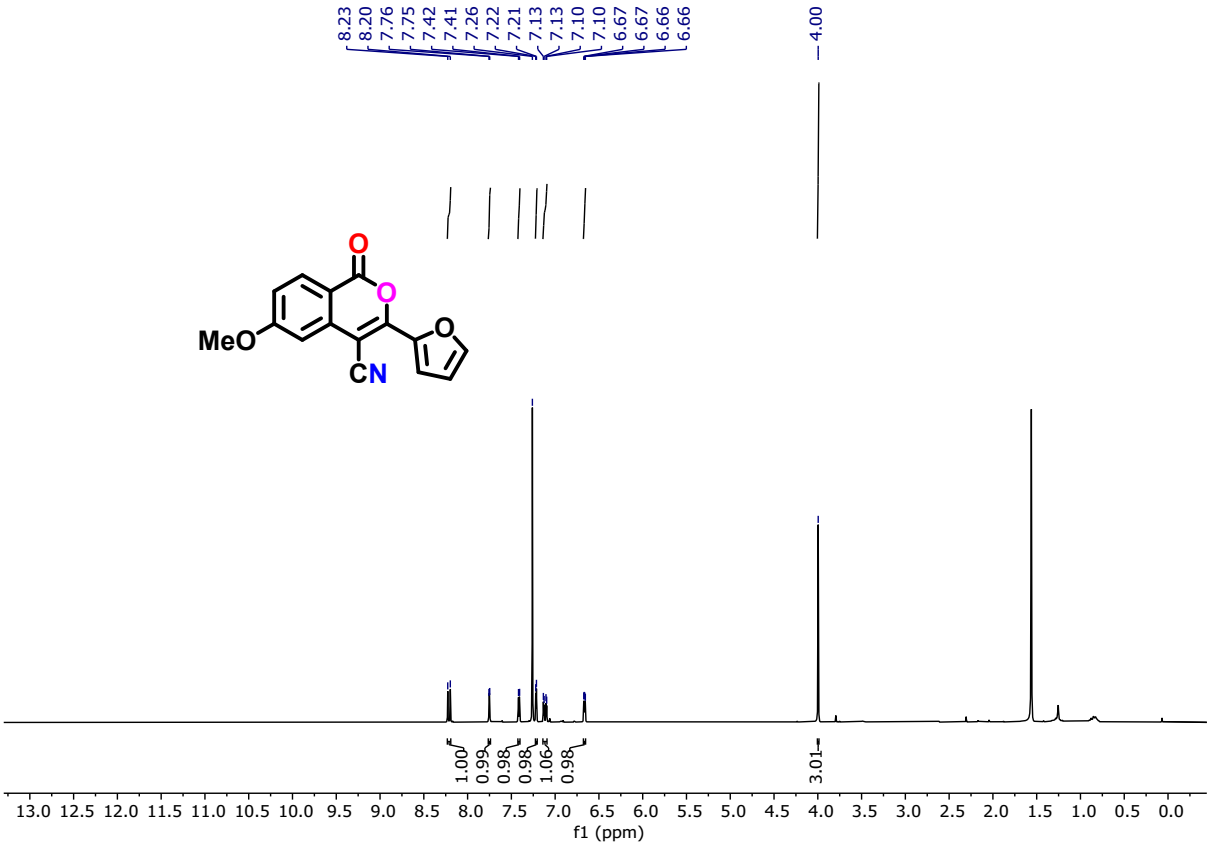


Figure S21. ^{1}H NMR (300 MHz) spectrum of **3bb** in $CDCl_3$.

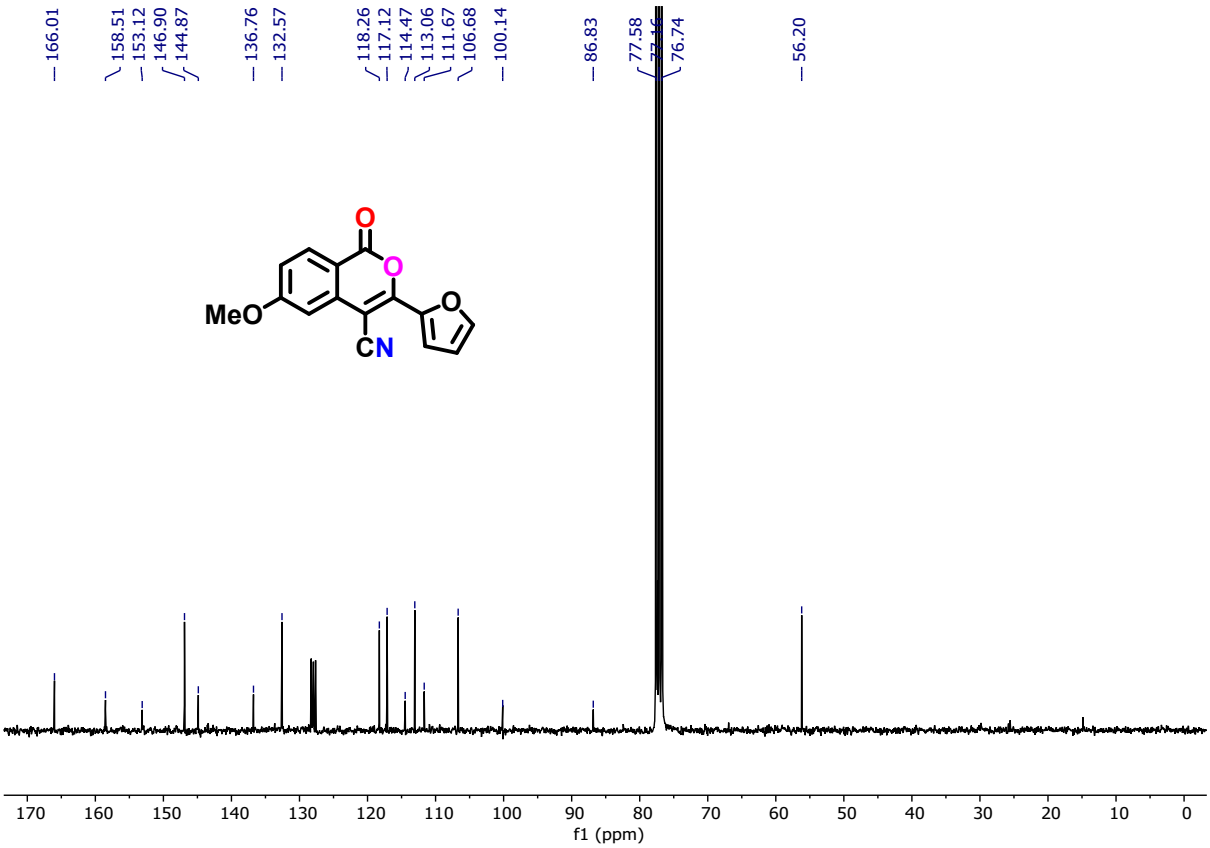


Figure S22. ^{13}C NMR (100 MHz) spectrum of **3bb** in $CDCl_3$.

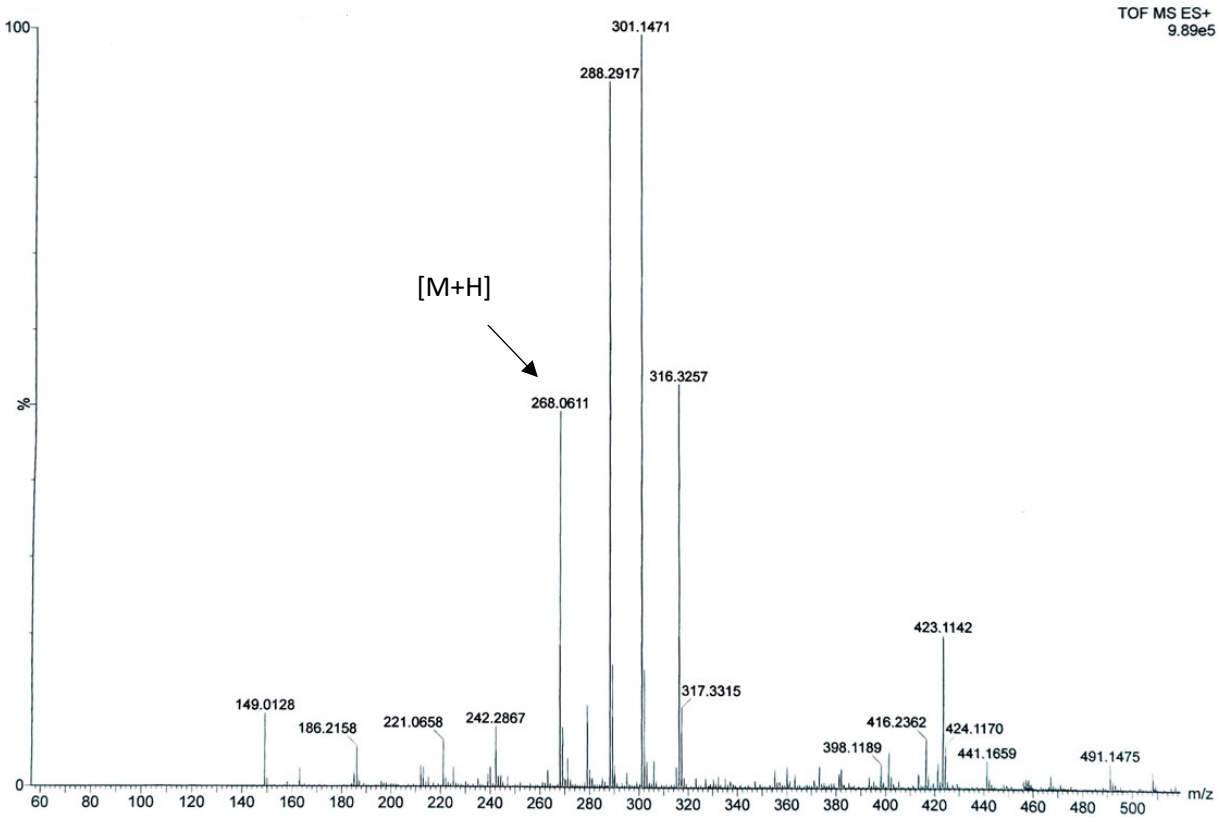


Figure S23. HRMS of **3bb**.

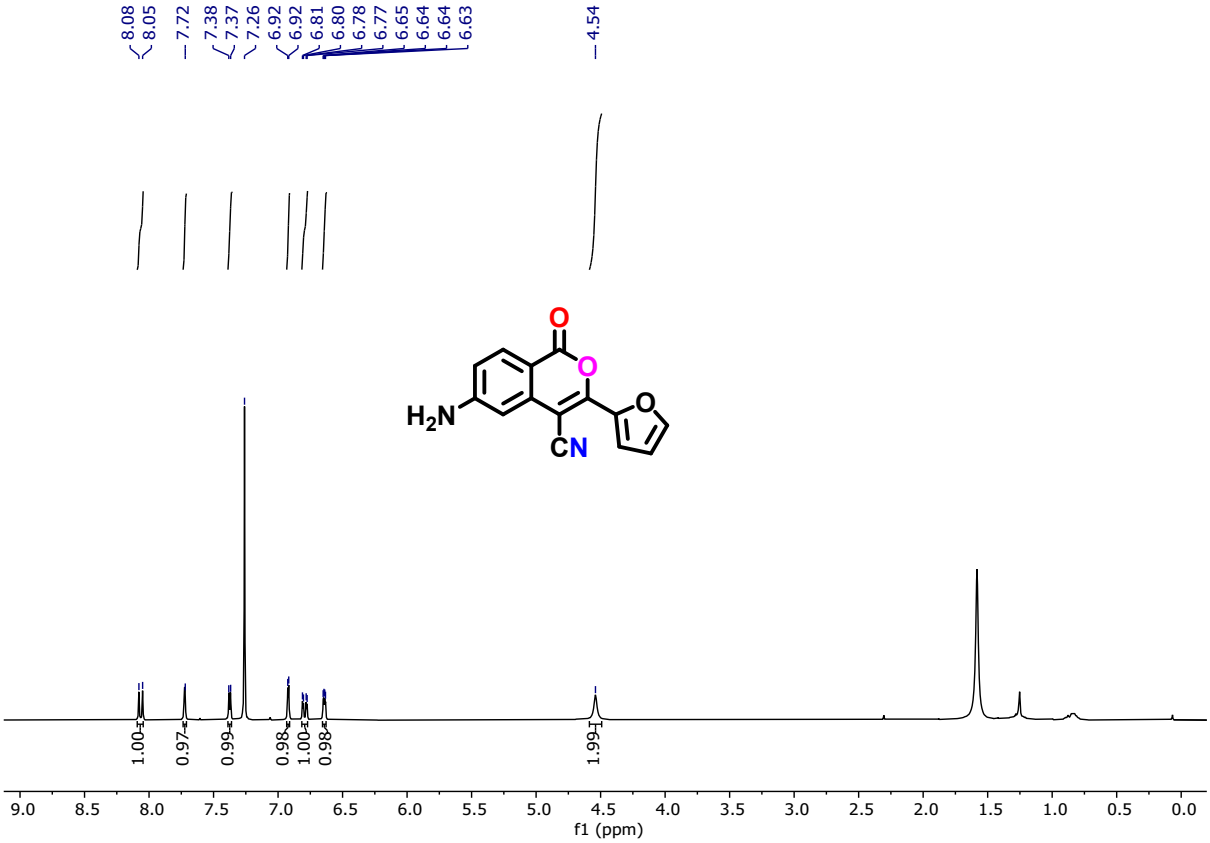


Figure S24. ^{1}H NMR (300 MHz) spectrum of **3db** in $CDCl_3$.

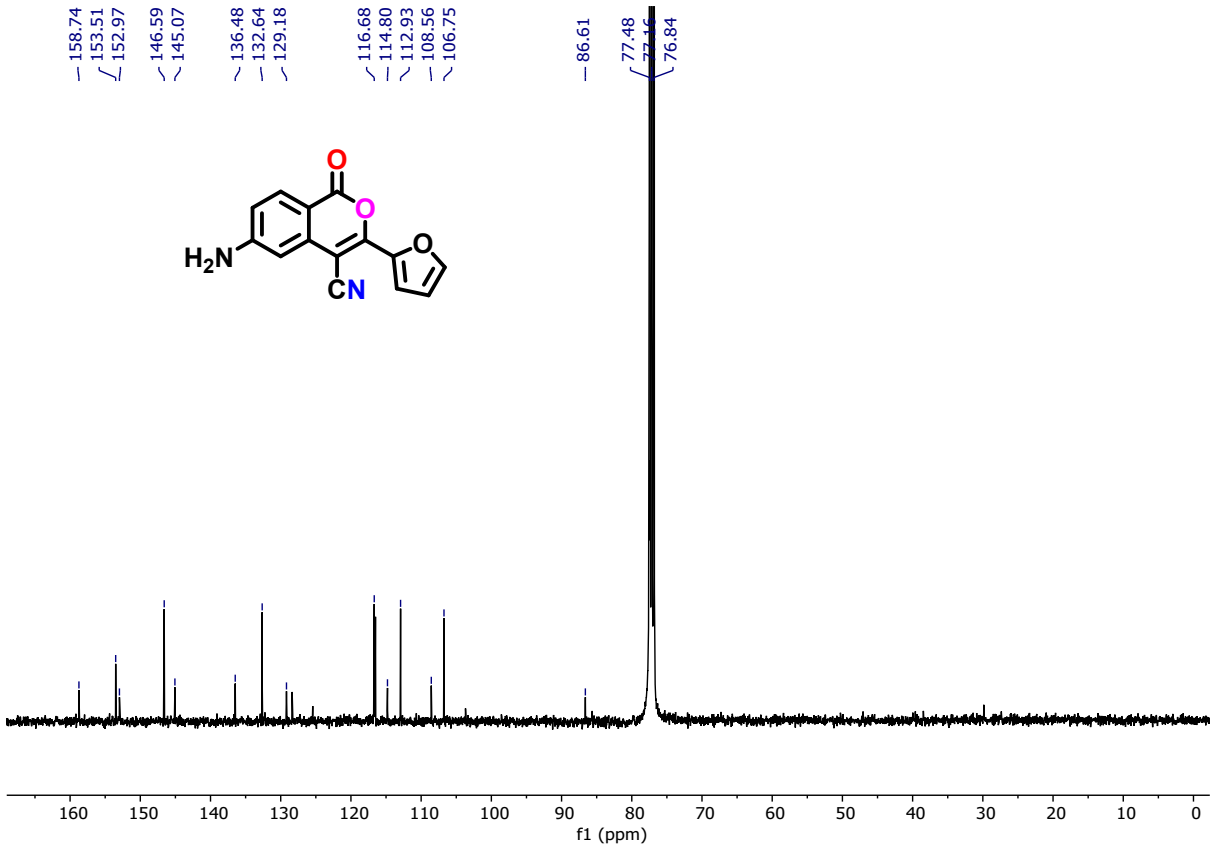


Figure S25. ^{13}C NMR (100 MHz) spectrum of **3db** in $CDCl_3$.

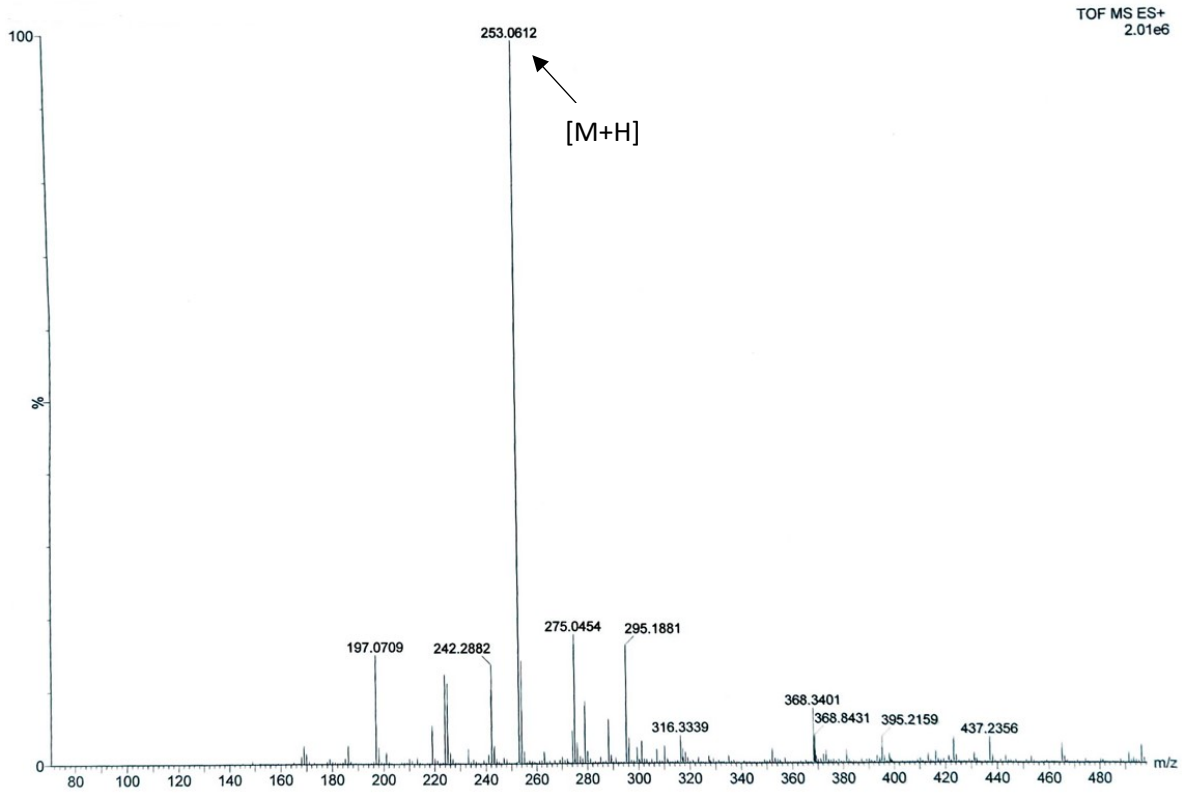


Figure S26. HRMS of **3db**.

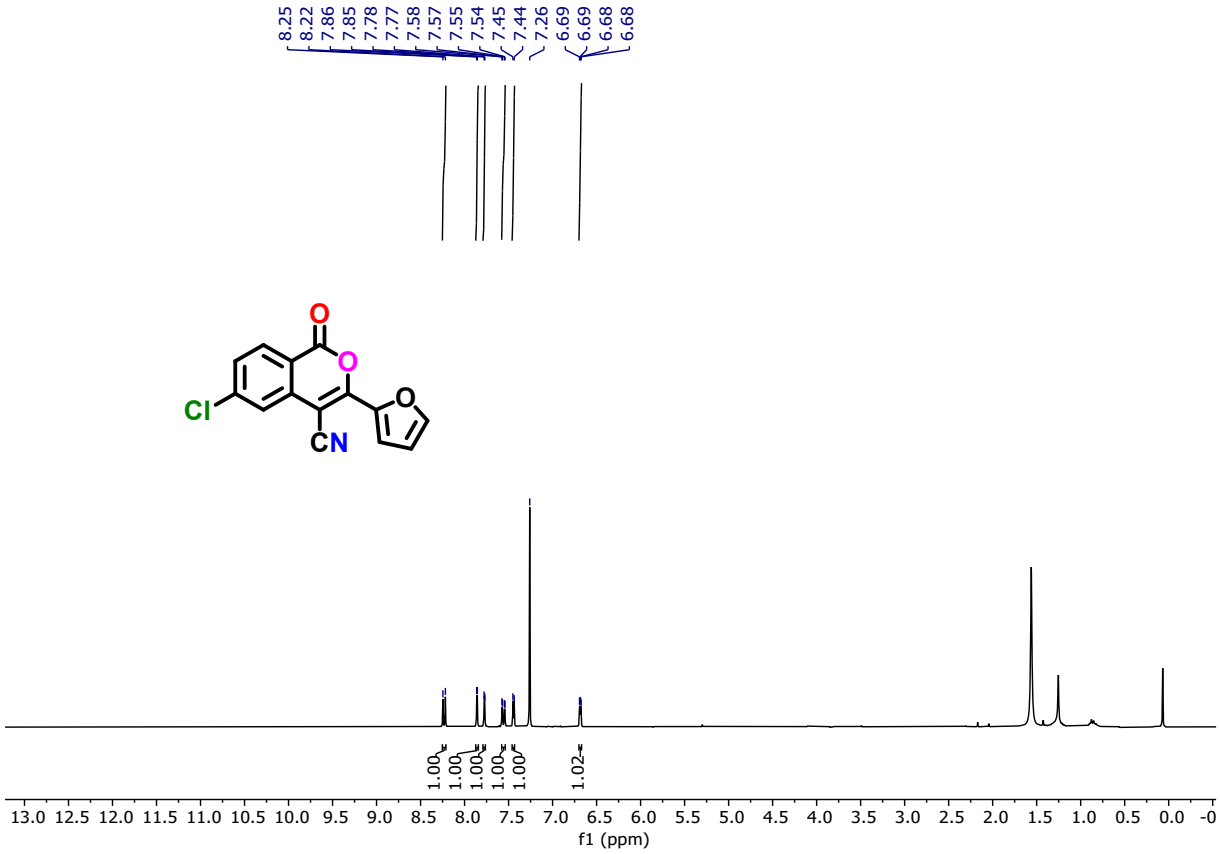


Figure S27. ^{1}H NMR (300 MHz) spectrum of **3eb** in $CDCl_3$.

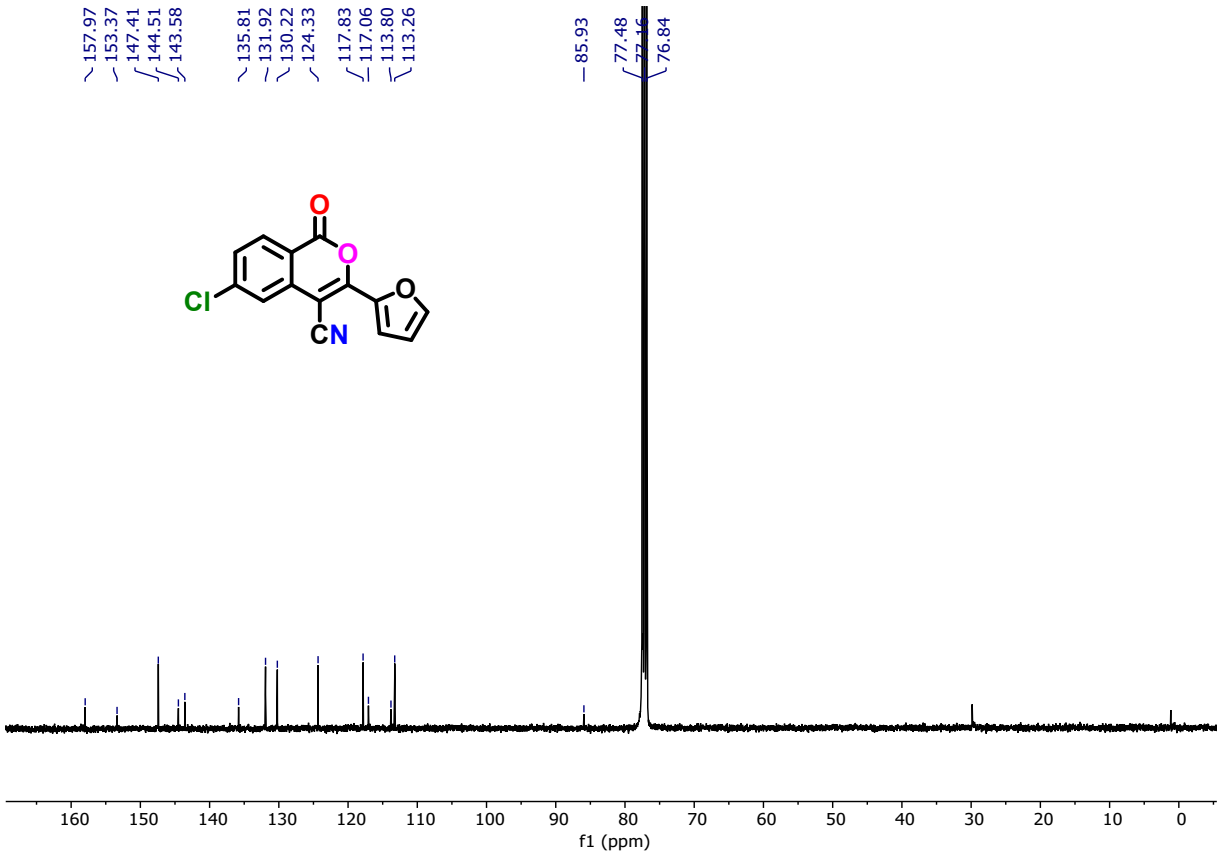


Figure S28. ^{13}C NMR (100 MHz) spectrum of **3eb** in $CDCl_3$.

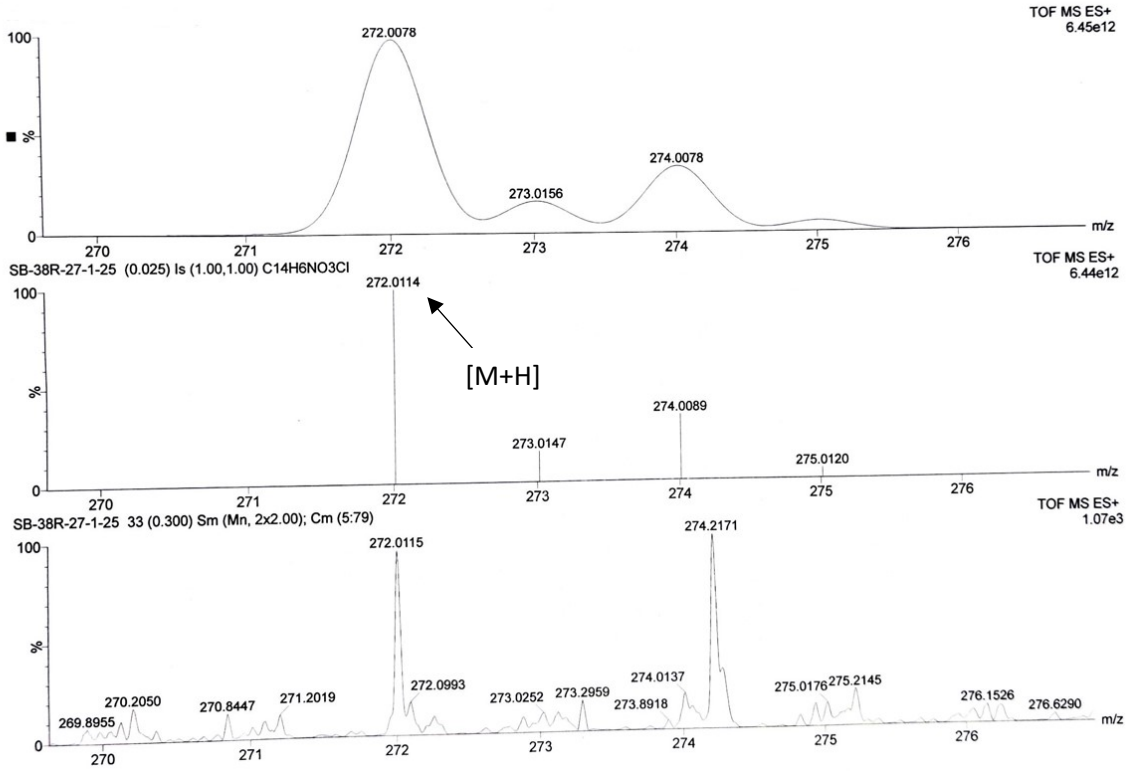


Figure S29. HRMS of **3eb**.

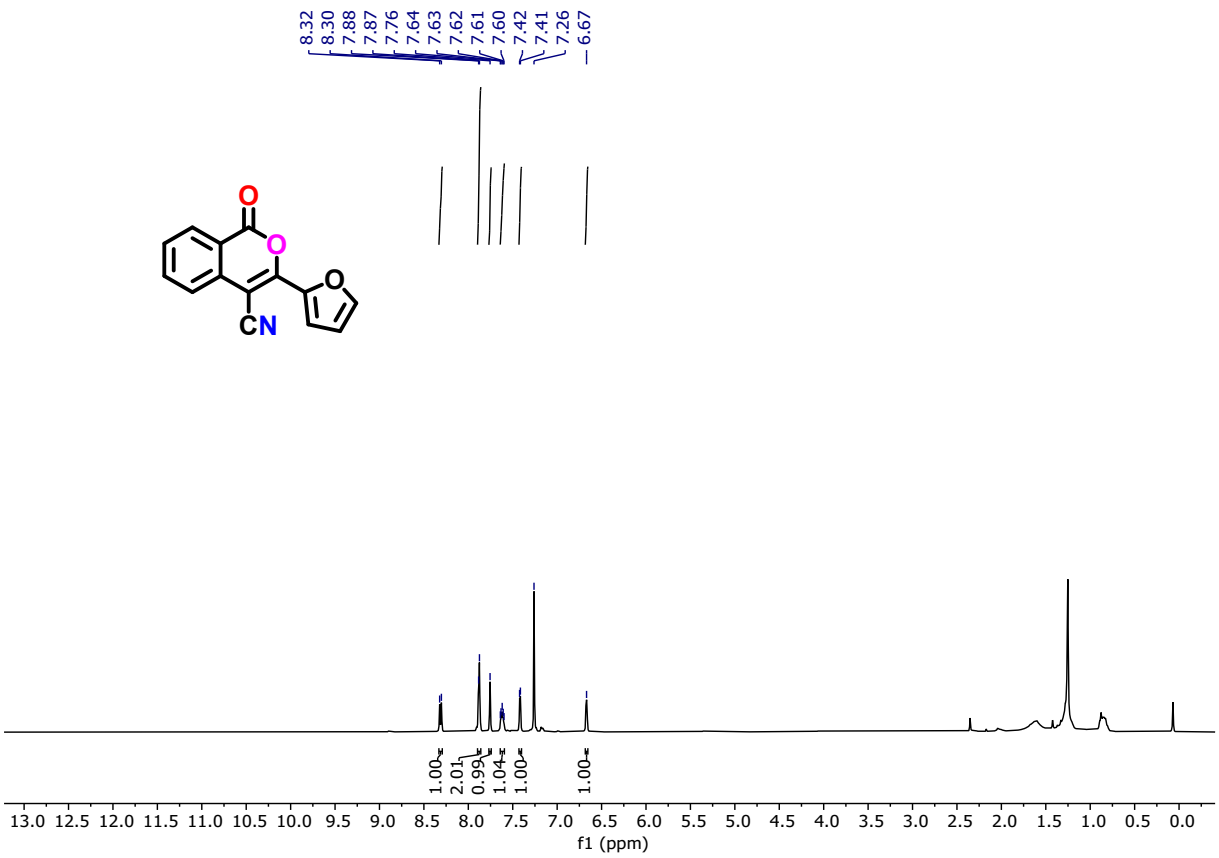


Figure S30. ^{1}H NMR (300 MHz) spectrum of **3gb** in $CDCl_3$.

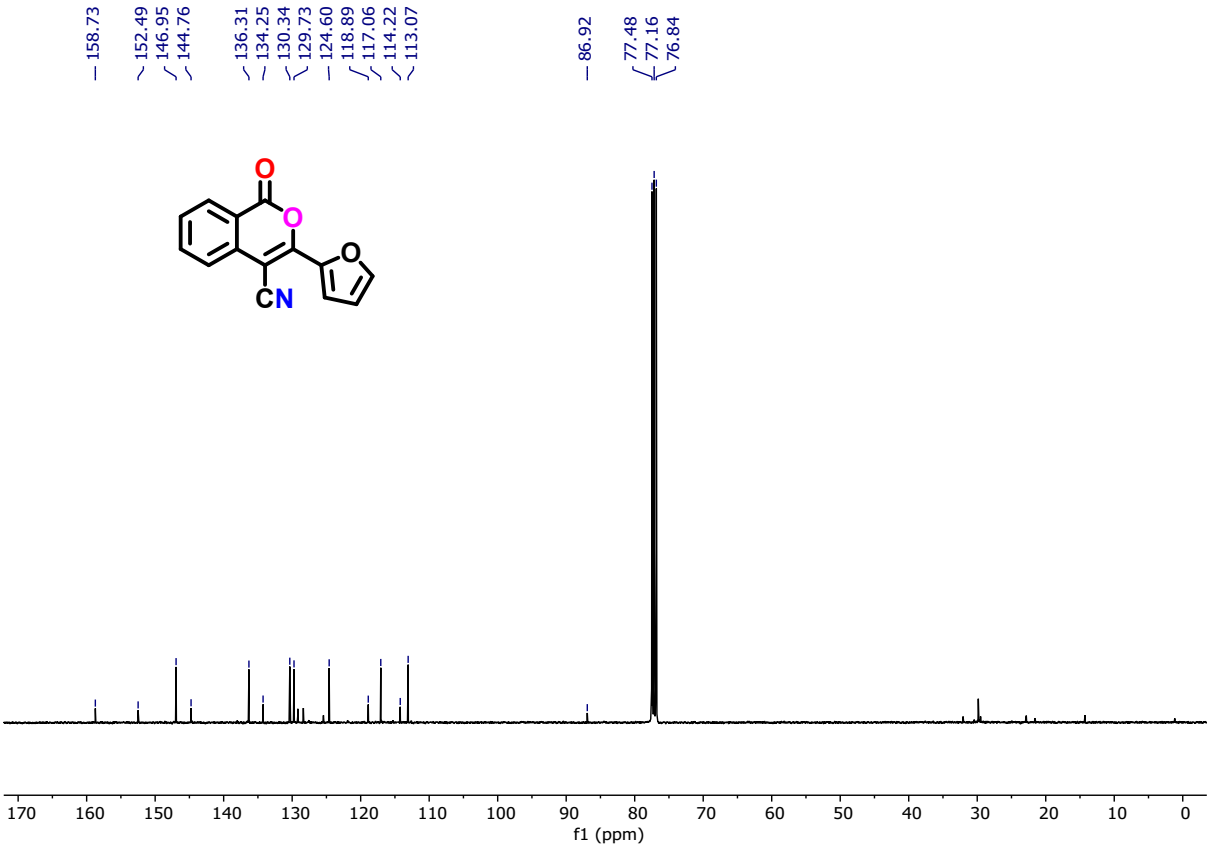


Figure S31. ^{13}C NMR (100 MHz) spectrum of **3gb** in $CDCl_3$.

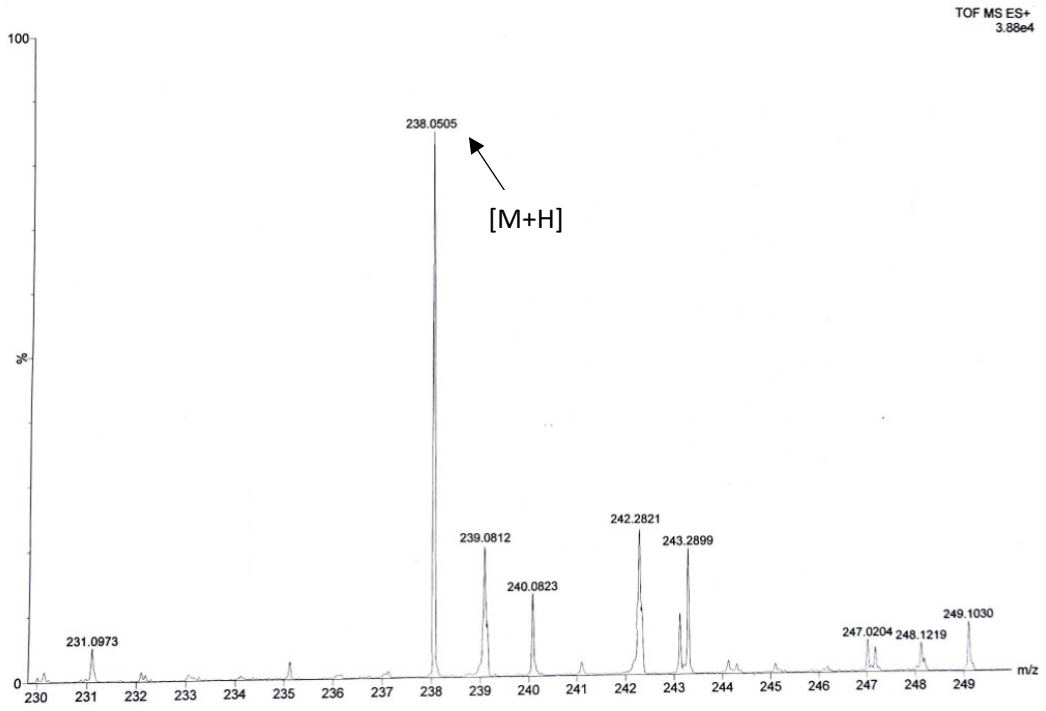


Figure S32. HRMS of **3gb**

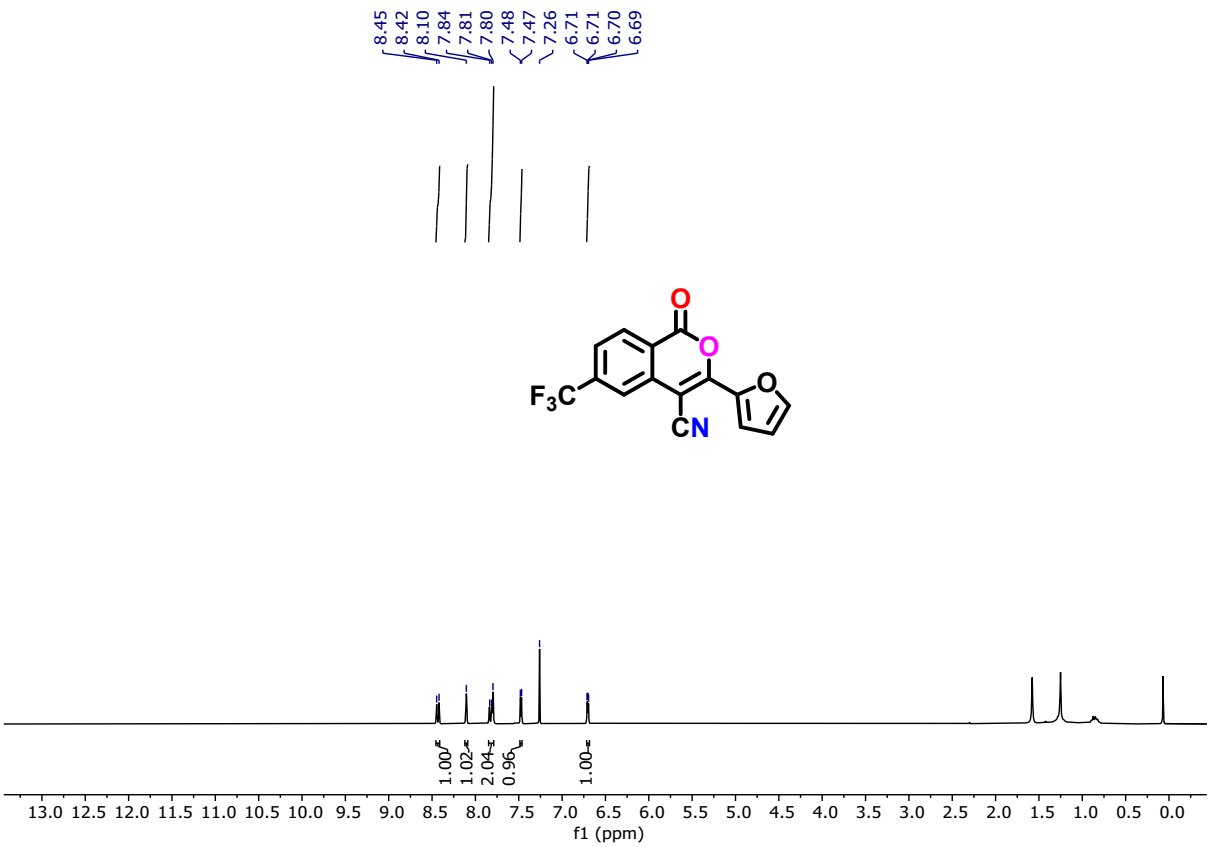


Figure S33. ^{1}H NMR (300 MHz) spectrum of **3hb** in $CDCl_3$.

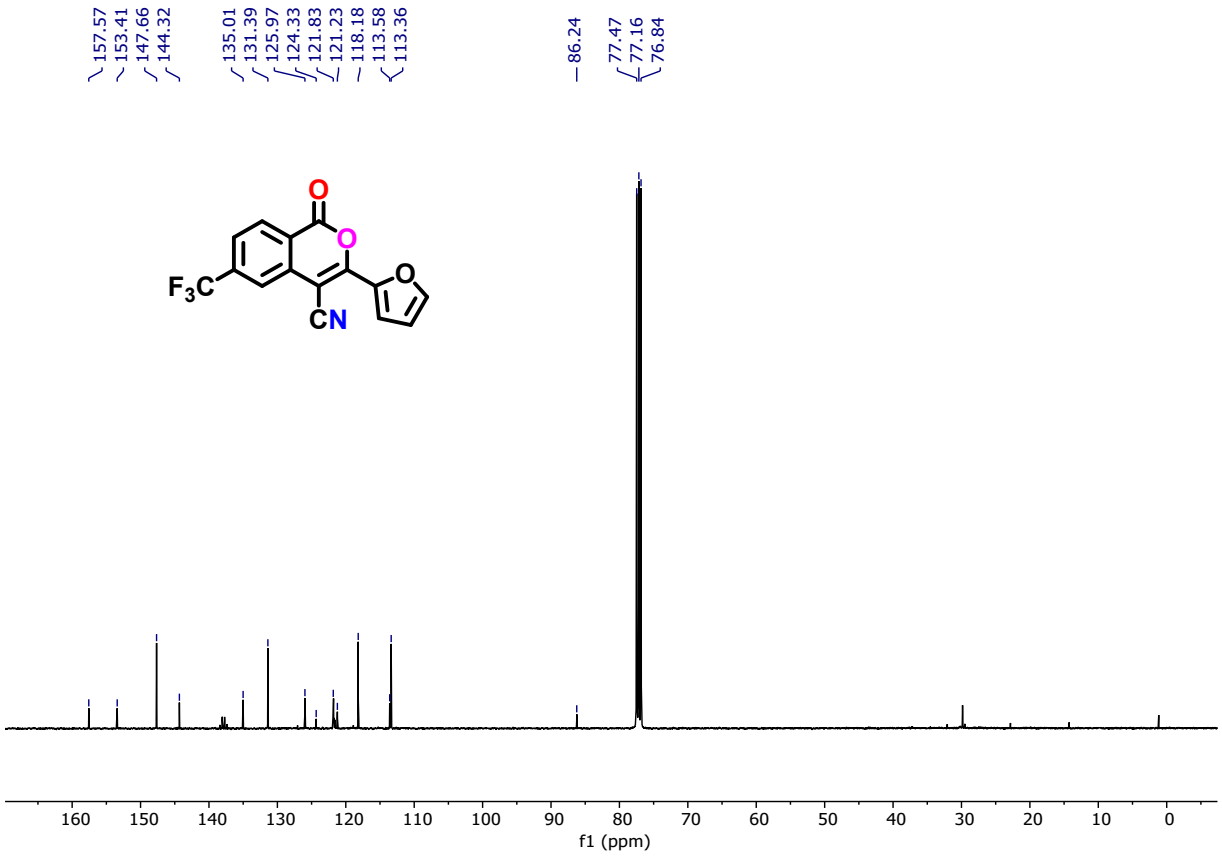


Figure S34. ^{13}C NMR (100 MHz) spectrum of **3hb** in $CDCl_3$.

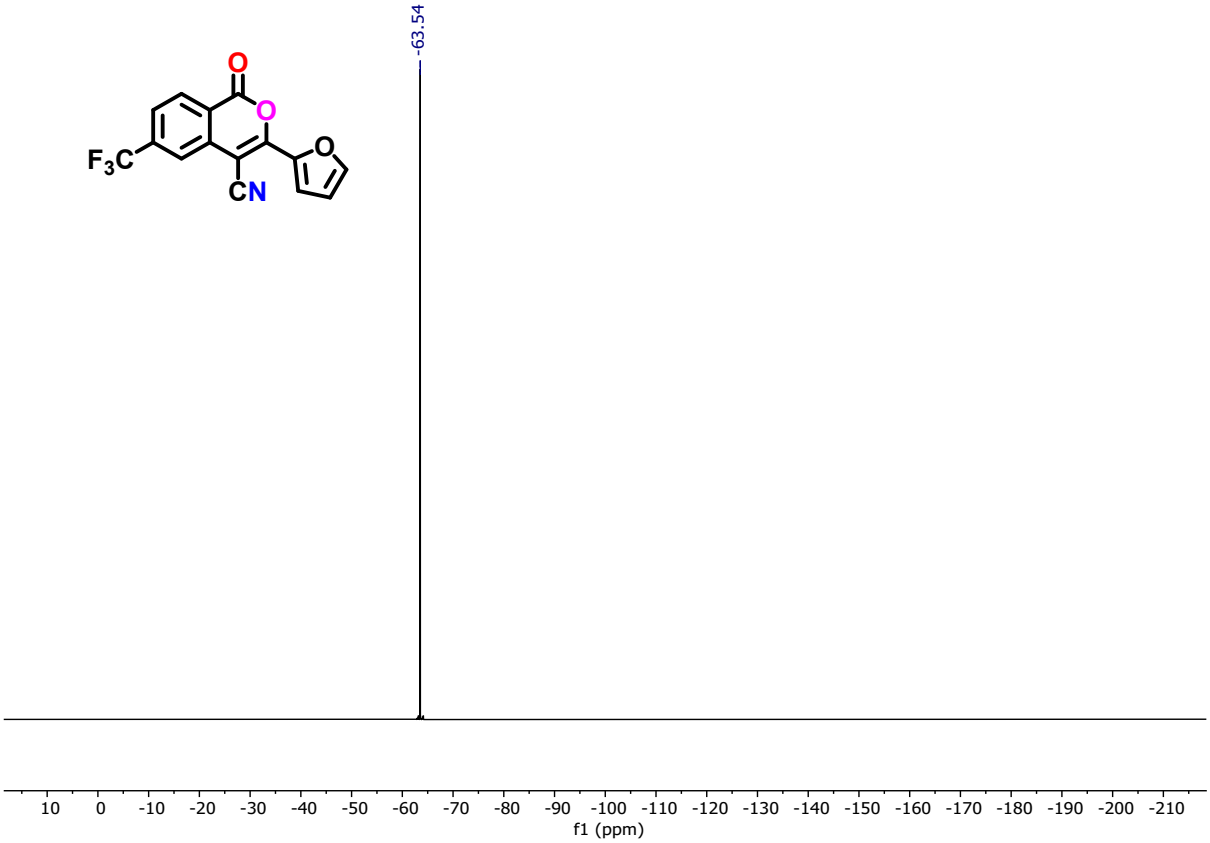


Figure S35. ^{19}F NMR (282 MHz) spectrum of **3hb** in $CDCl_3$.

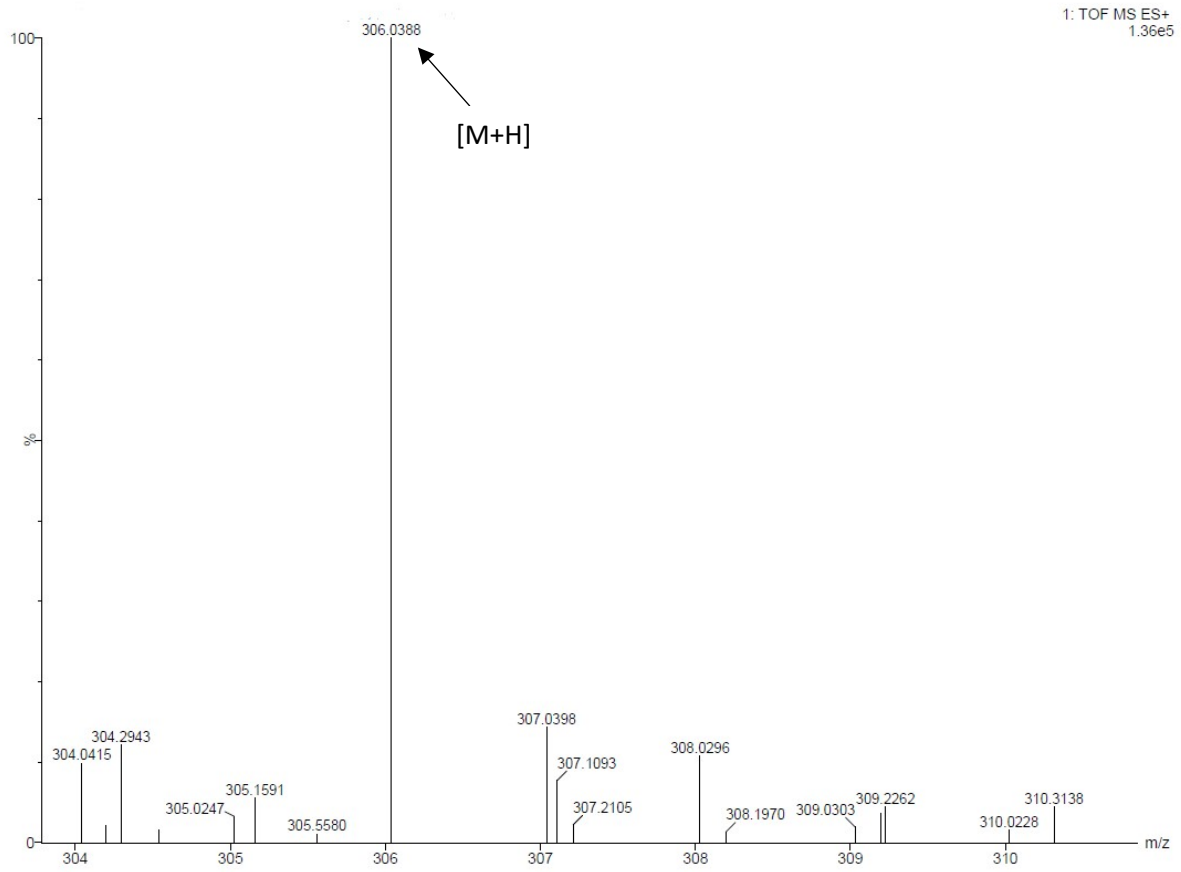


Figure S36. HRMS of compound **3hb**.

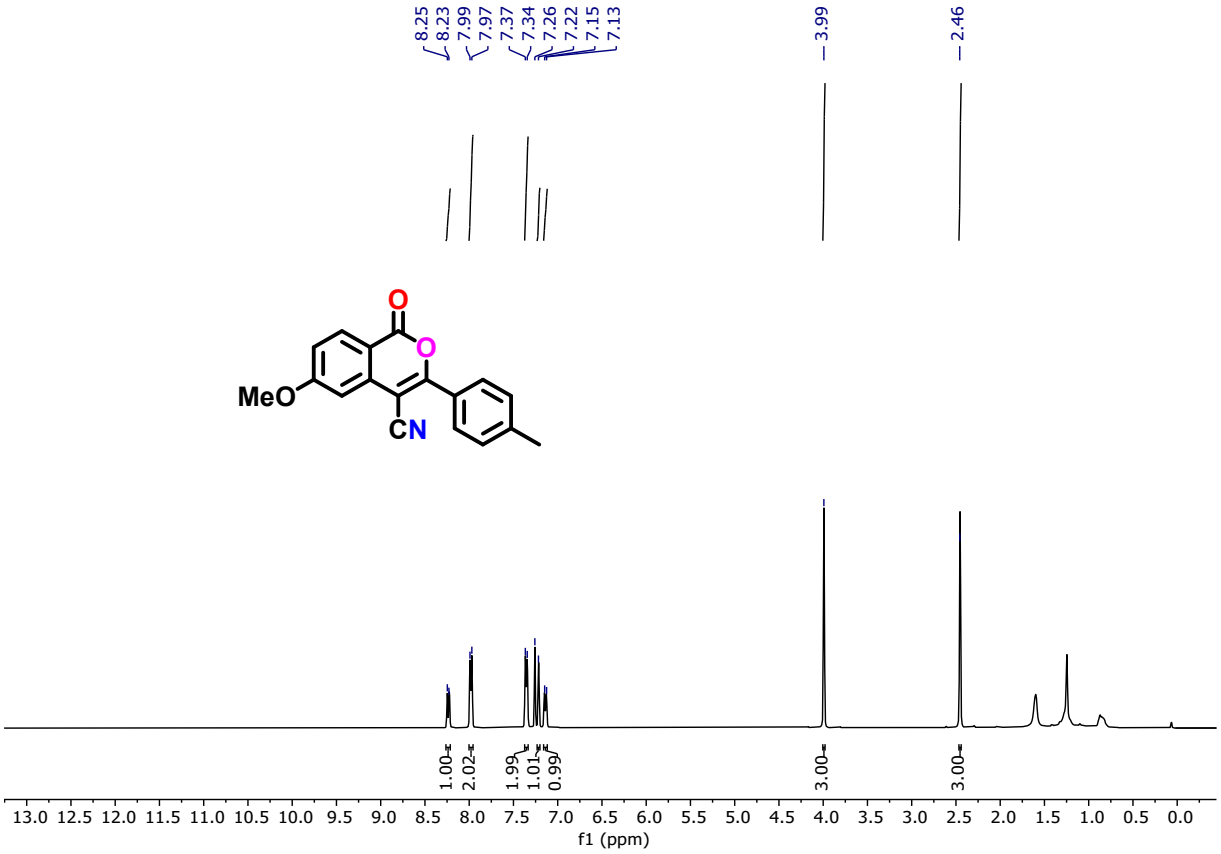


Figure S37. ^{1}H NMR (300 MHz) spectrum of **3bc** in $CDCl_3$.

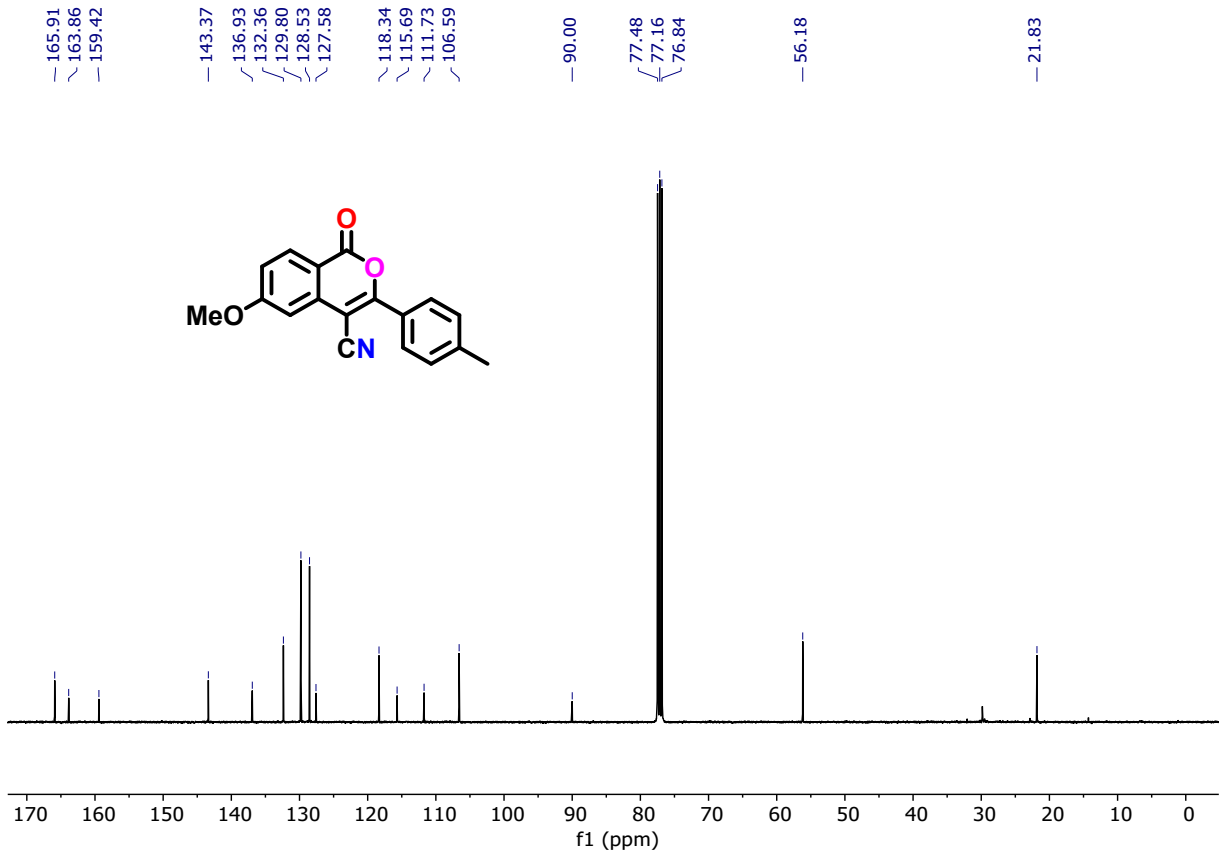


Figure S38. ^{13}C NMR (75 MHz) spectrum of **3bc** in $CDCl_3$.

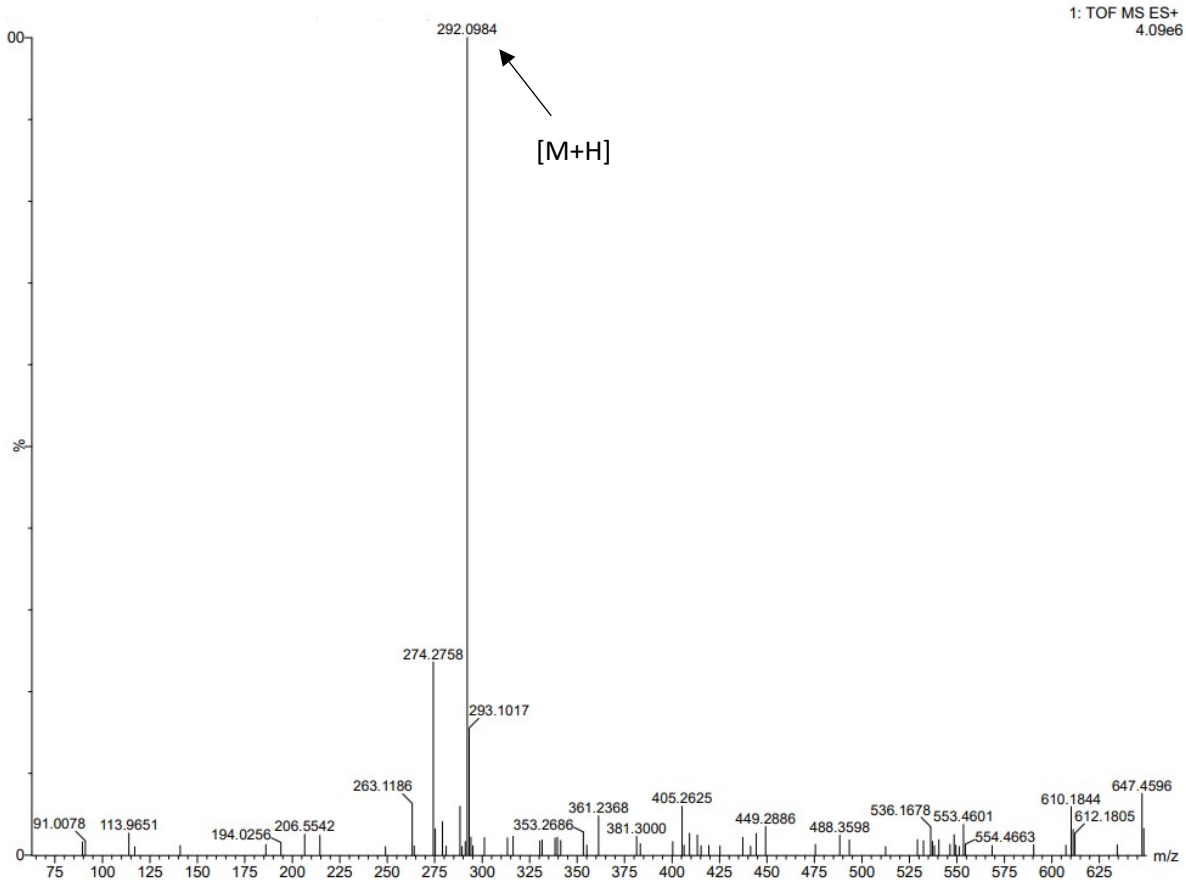


Figure S39. HRMS of **3bc**.

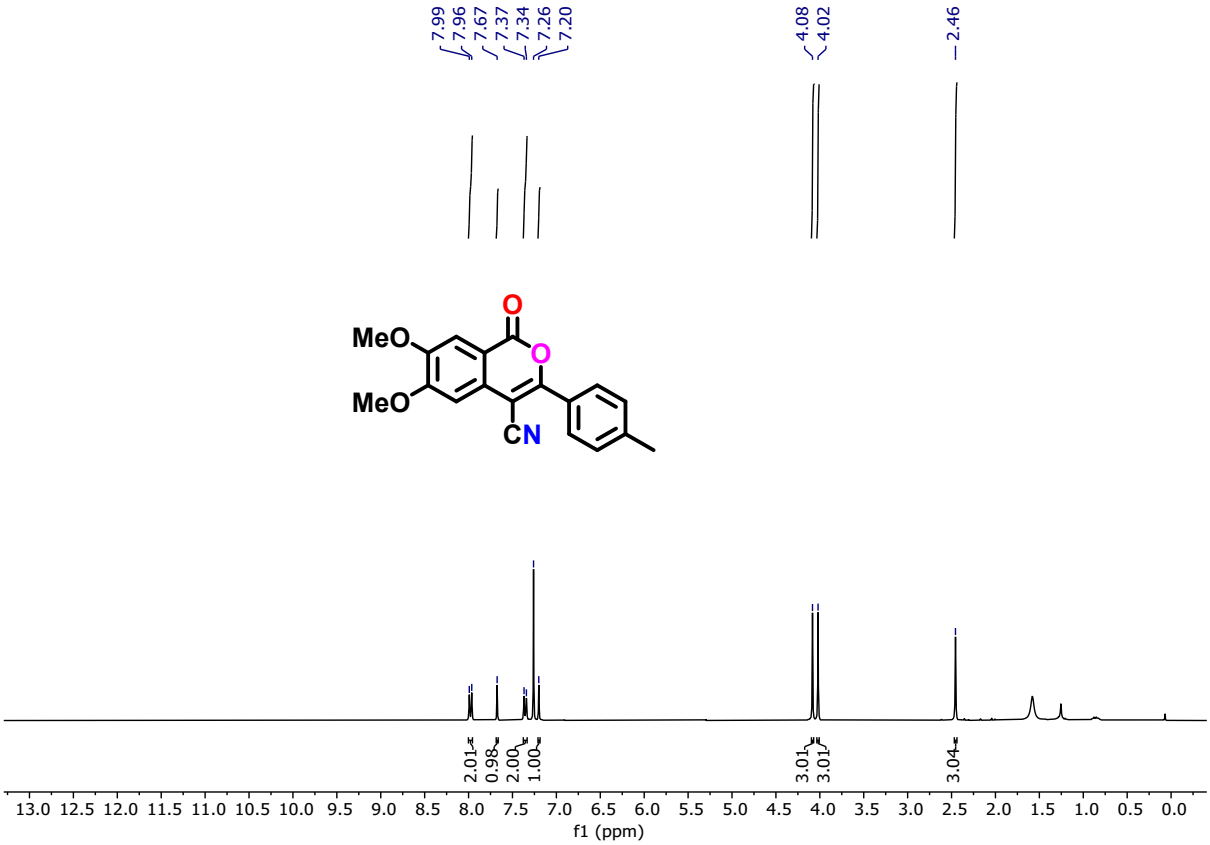


Figure S40. ^{1}H NMR (300 MHz) spectrum of **3cc** in $CDCl_3$.

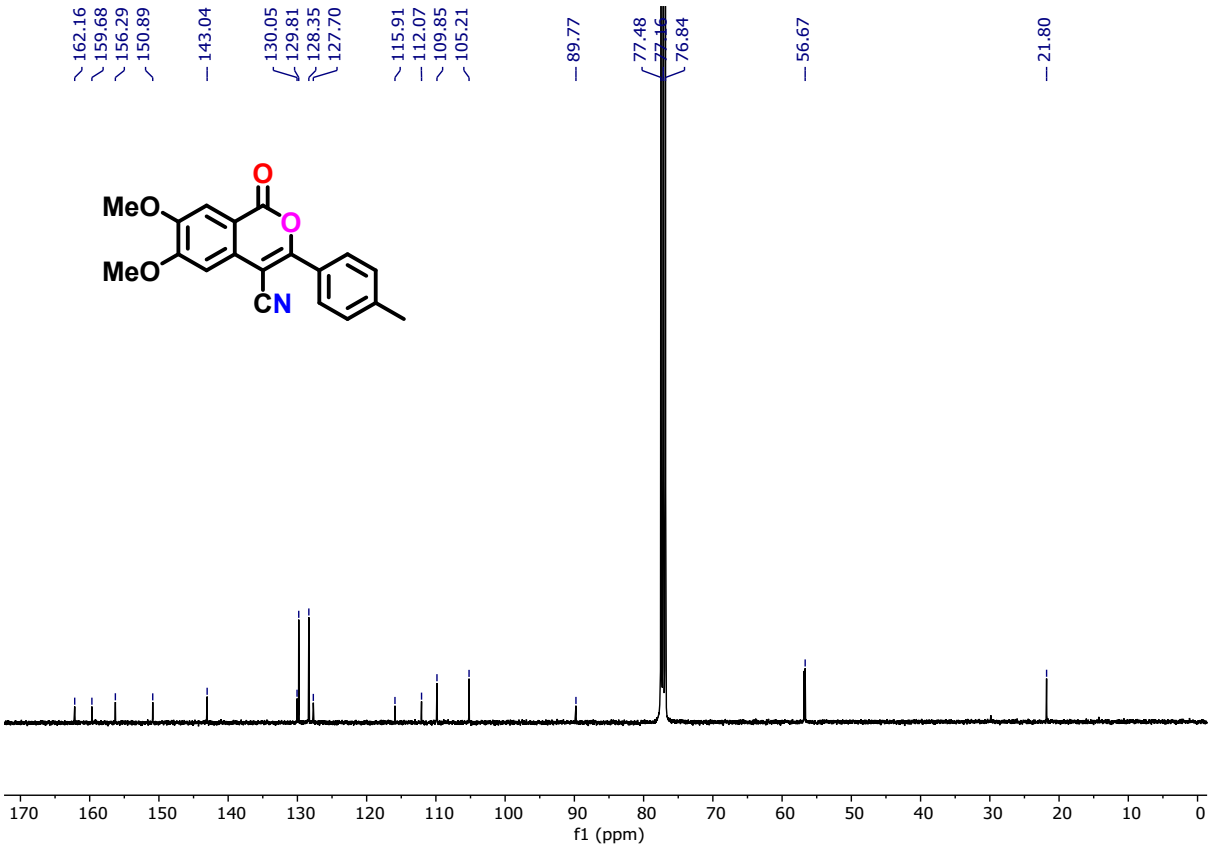


Figure S41. ^{13}C NMR (100 MHz) spectrum of **3cc** in $CDCl_3$.

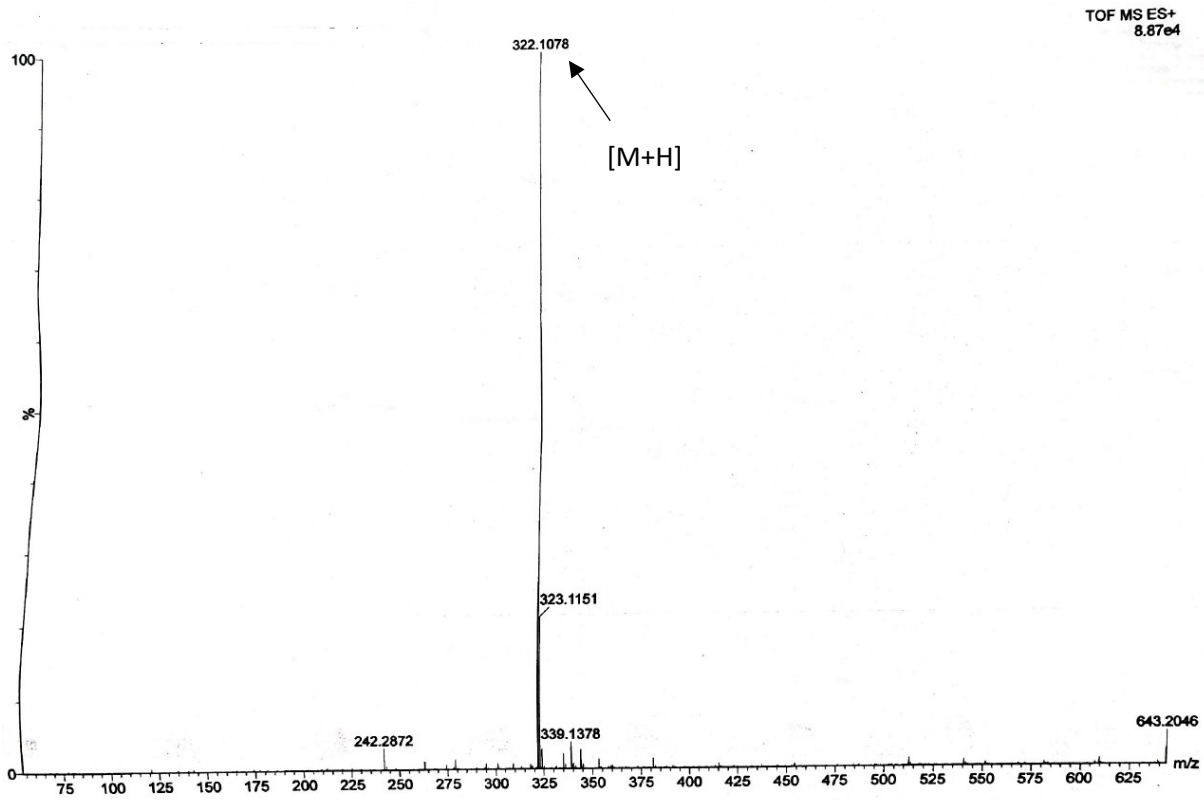


Figure S42. HRMS of **3cc**

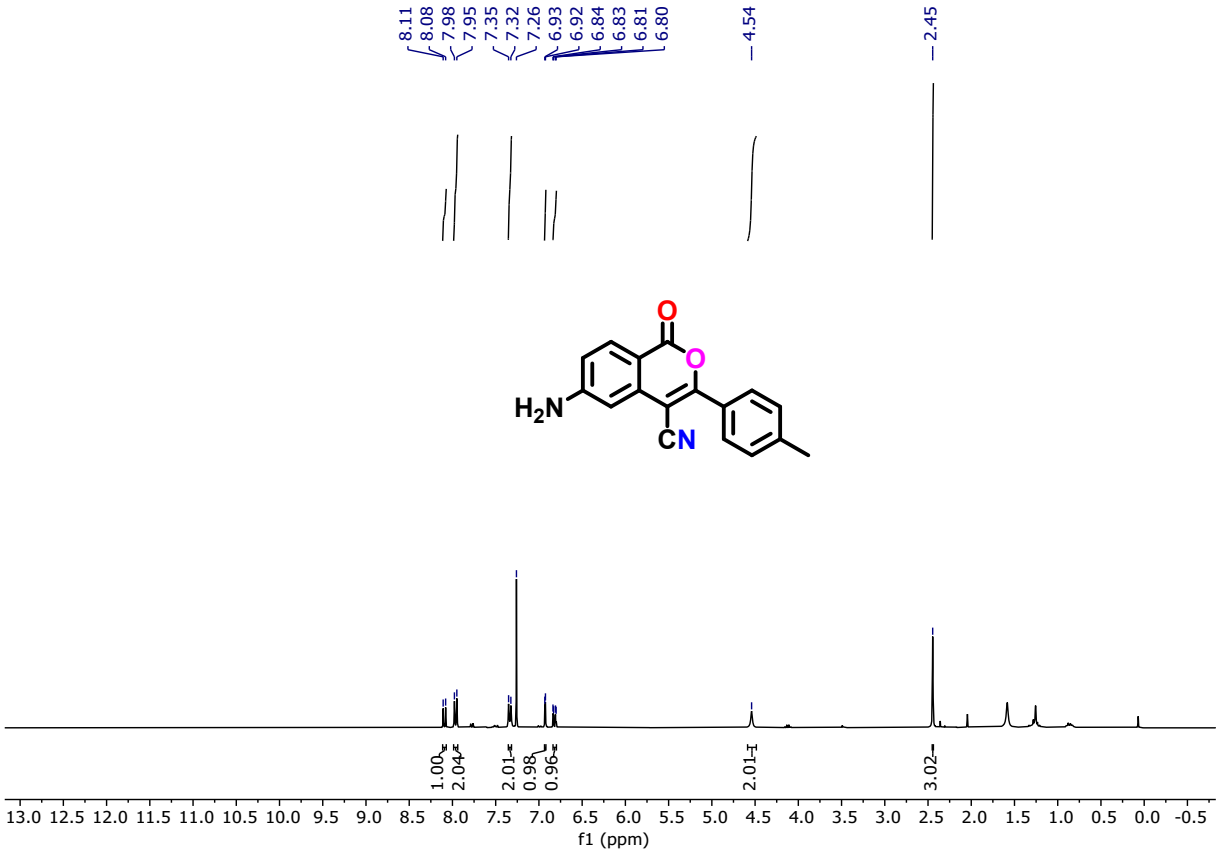


Figure S43. ^{1}H NMR (300 MHz) spectrum of **3dc** in $CDCl_3$.

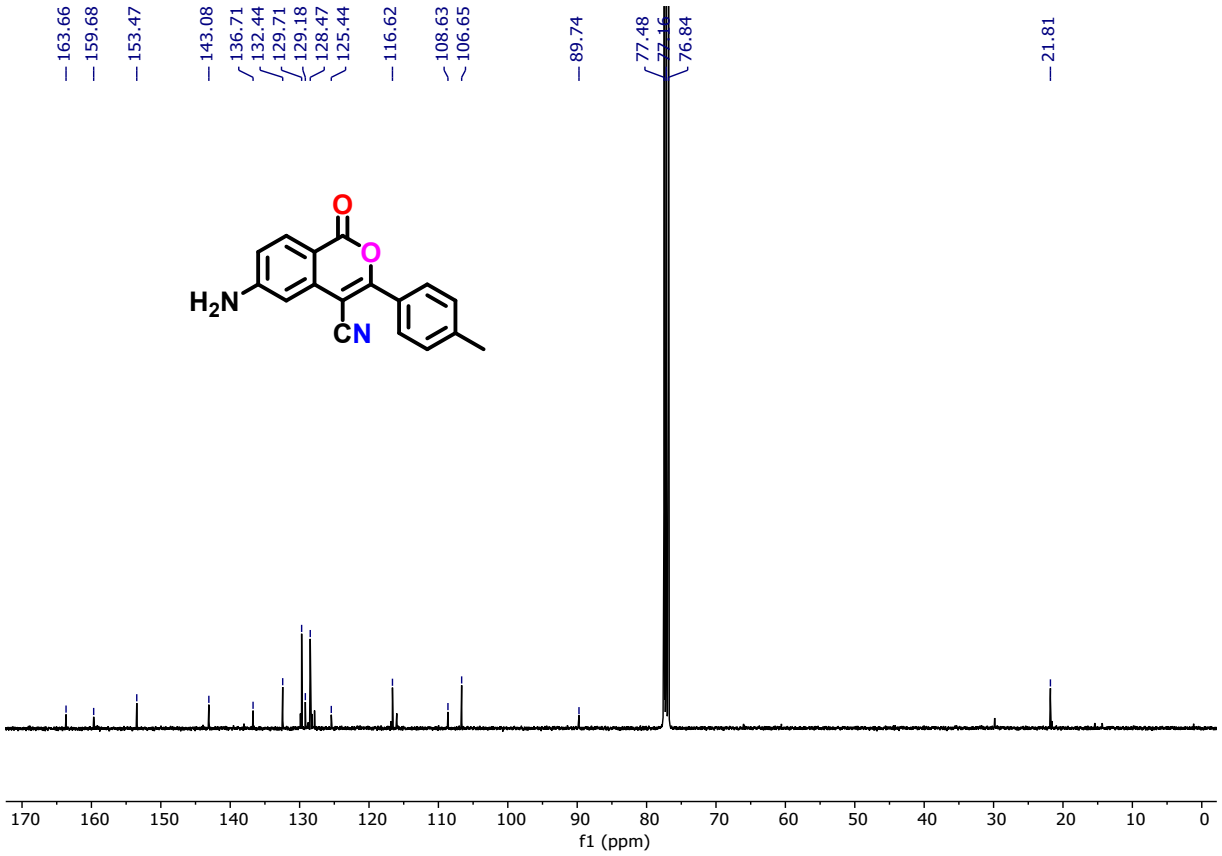


Figure S44. ^{13}C NMR (75 MHz) spectrum of **3dc** in $CDCl_3$.

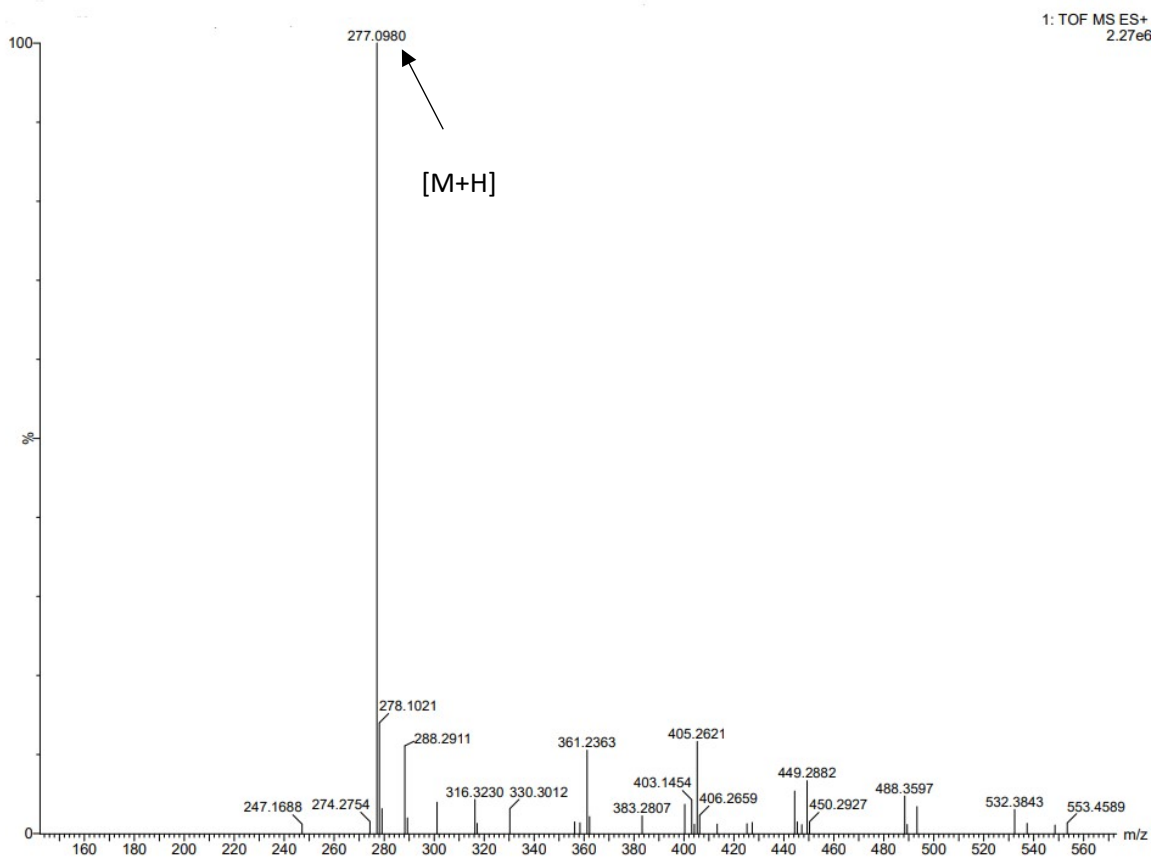


Figure S45. HRMS of **3dc**.

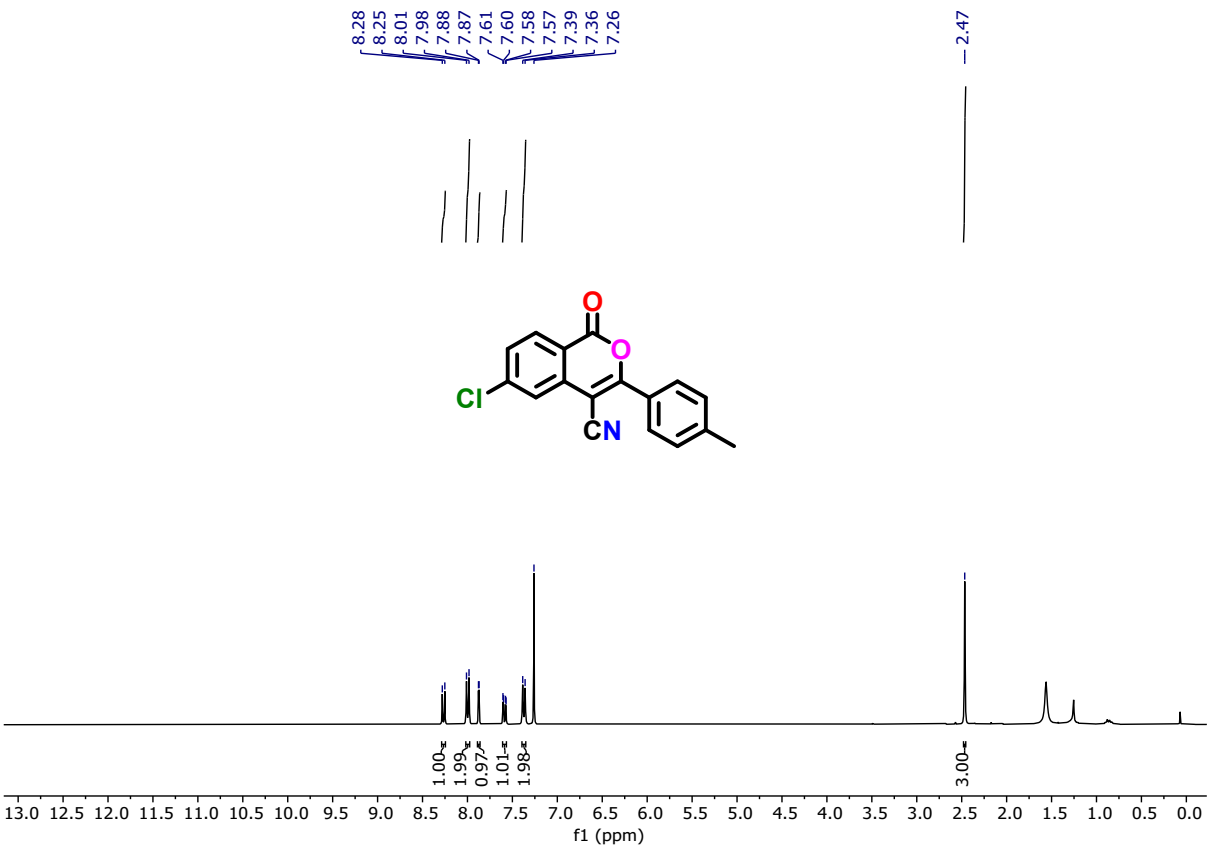


Figure S46. ^{1}H NMR (300 MHz) spectrum of **3ec** in $CDCl_3$.

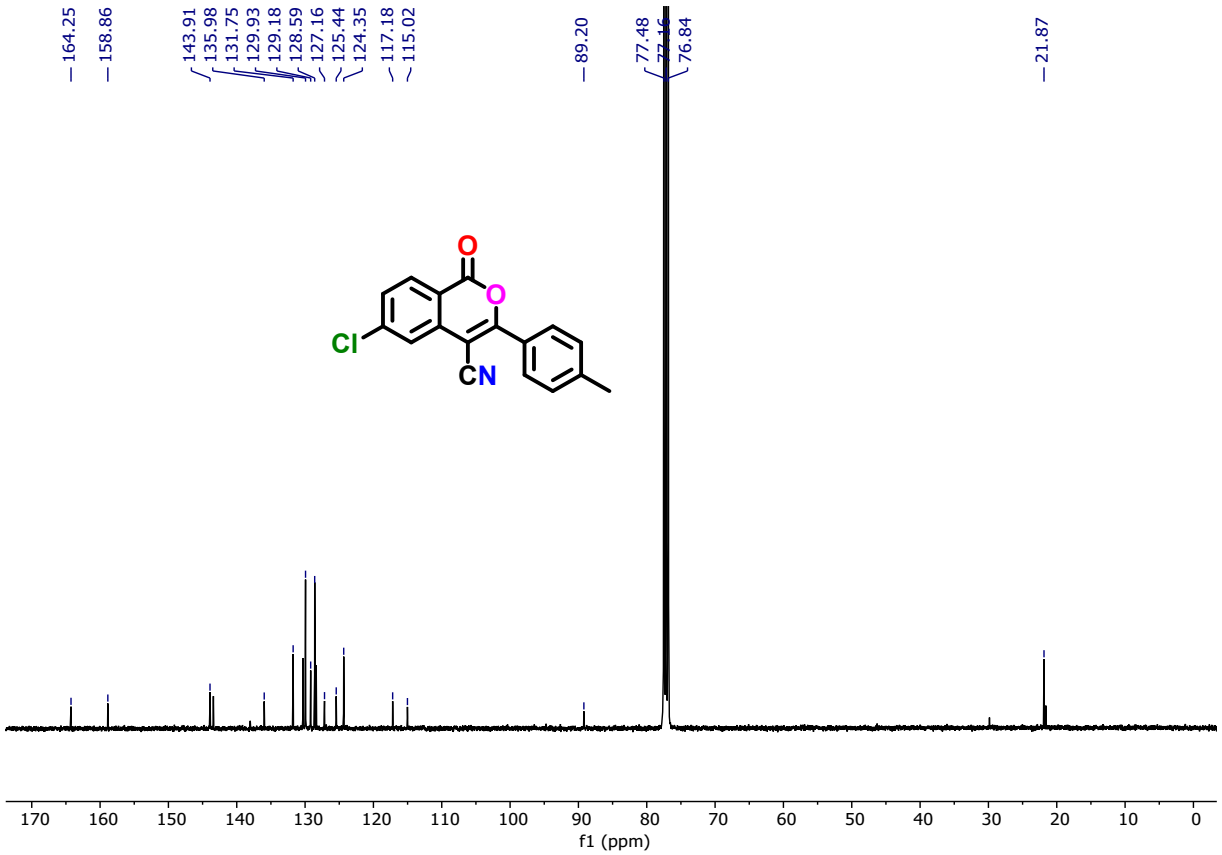


Figure S47. ^{13}C NMR (100 MHz) spectrum of **3ec** in $CDCl_3$.

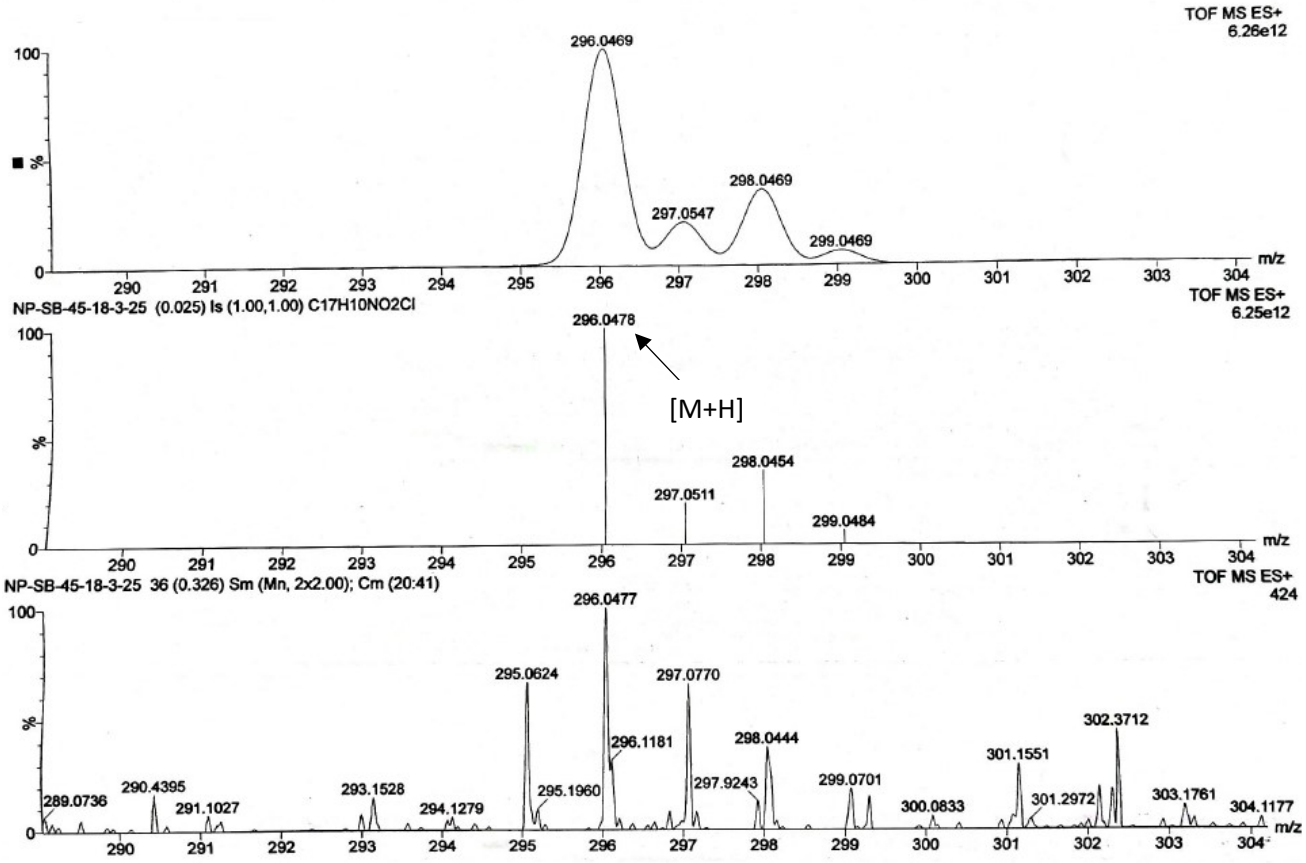


Figure S48. HRMS of **3ec**

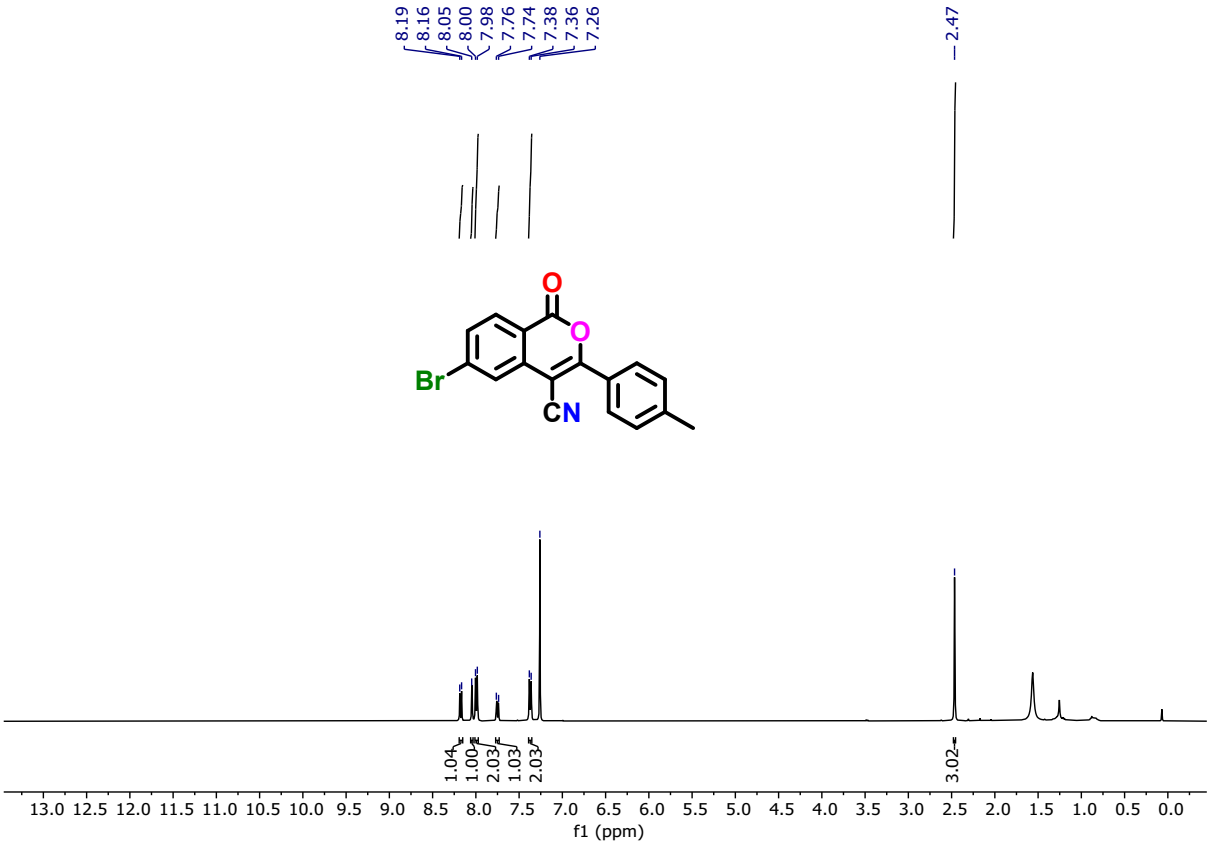


Figure S49. ^{1}H NMR (300 MHz) spectrum of **3ic** in $CDCl_3$.

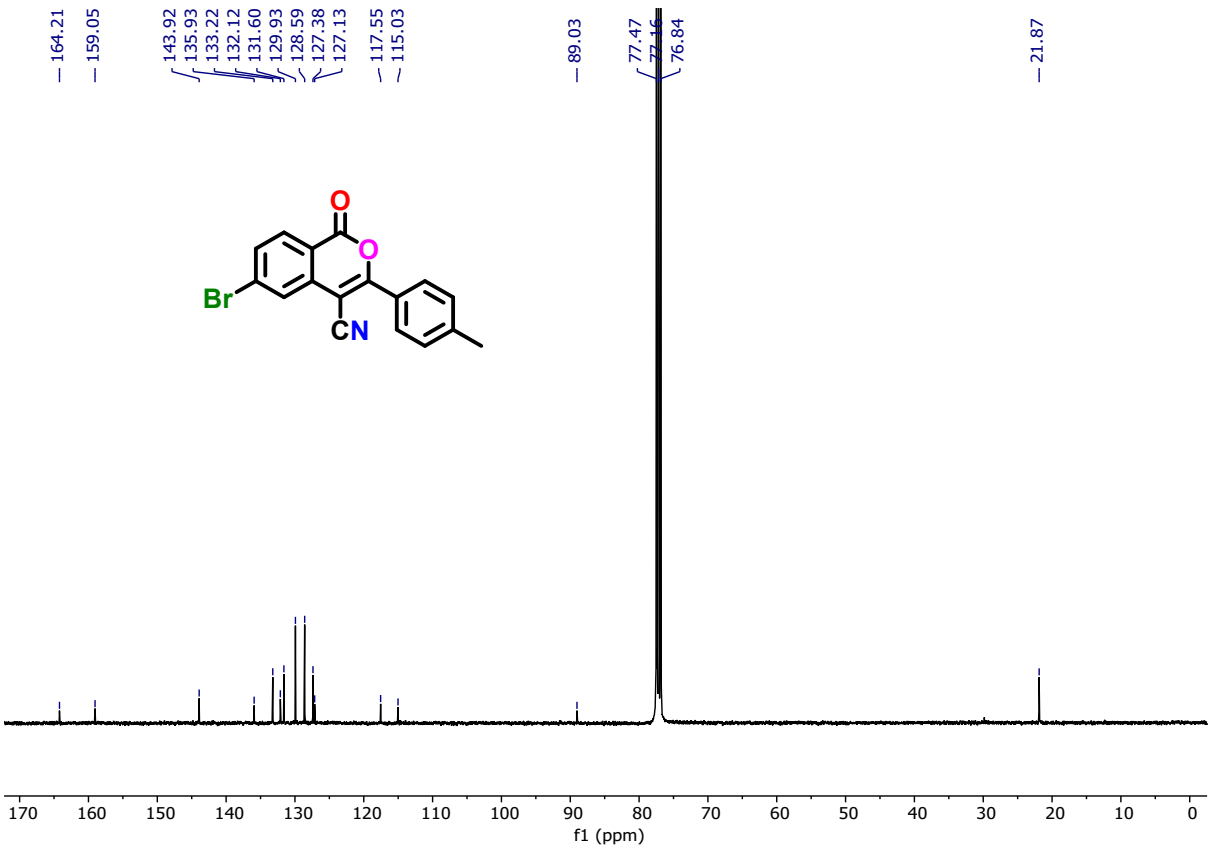


Figure S50. ^{13}C NMR (100 MHz) spectrum of **3ic** in $CDCl_3$.

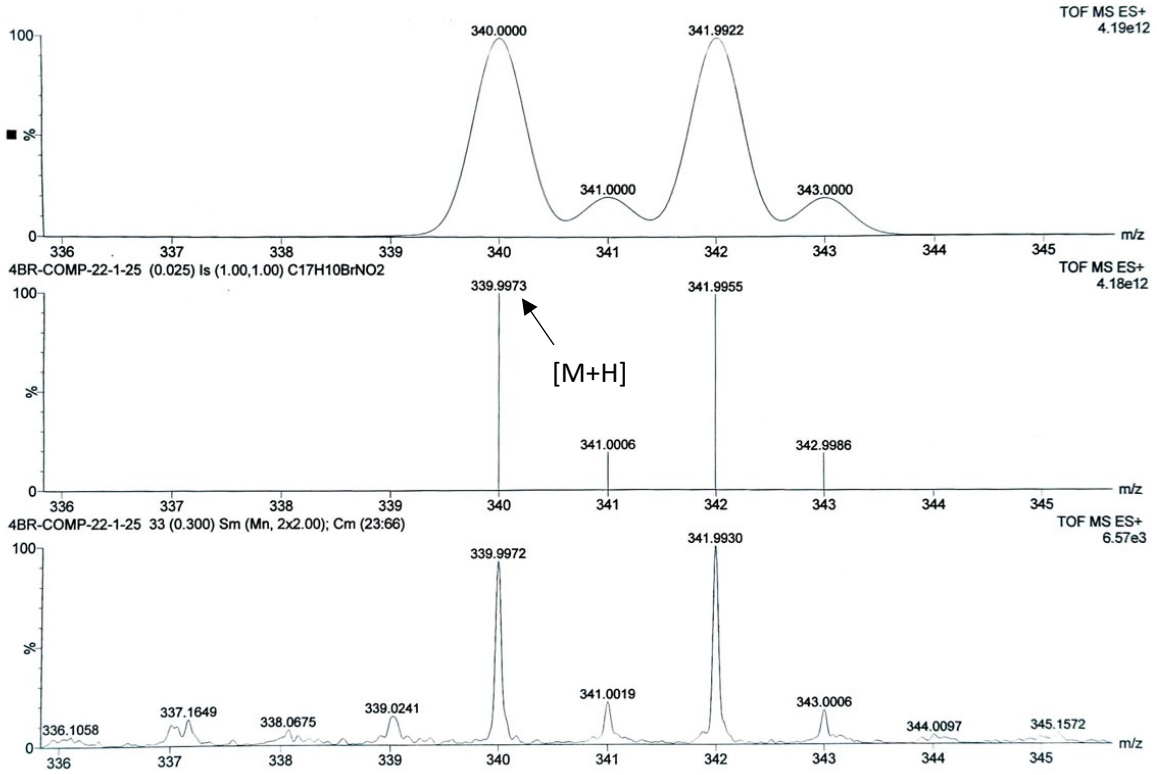


Figure S51. HRMS of **3ic**.

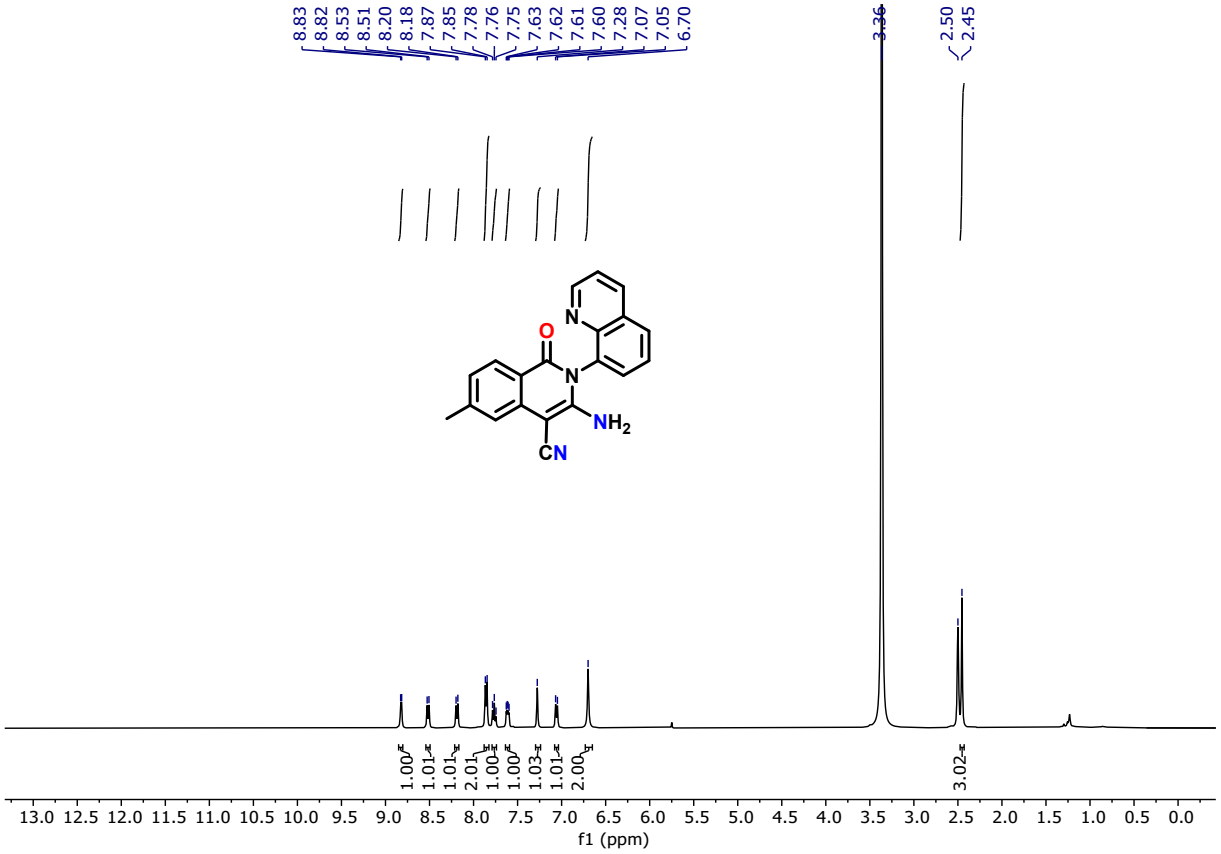


Figure S52. ^{1}H NMR (300 MHz) spectrum of **4ad** in DMSO-d_6.

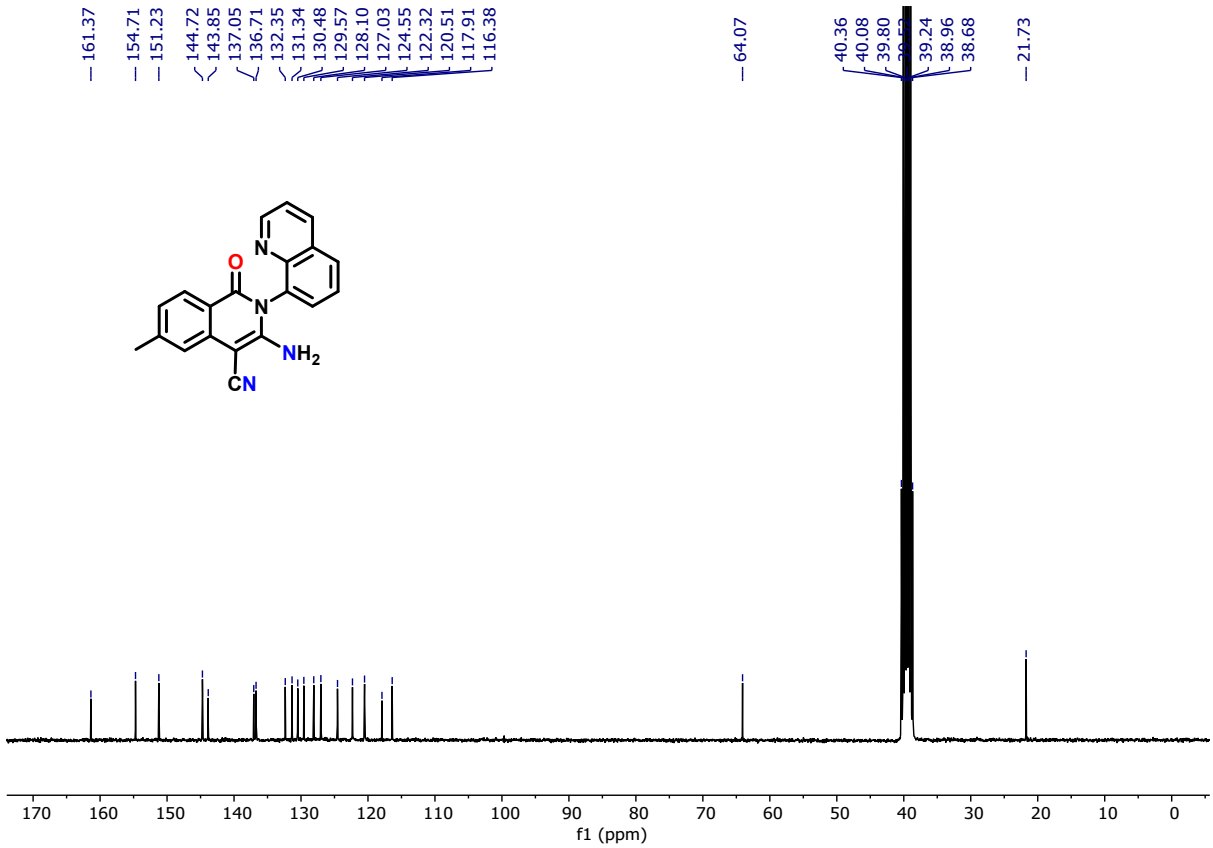


Figure S53. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4ad** in DMSO-d_6.

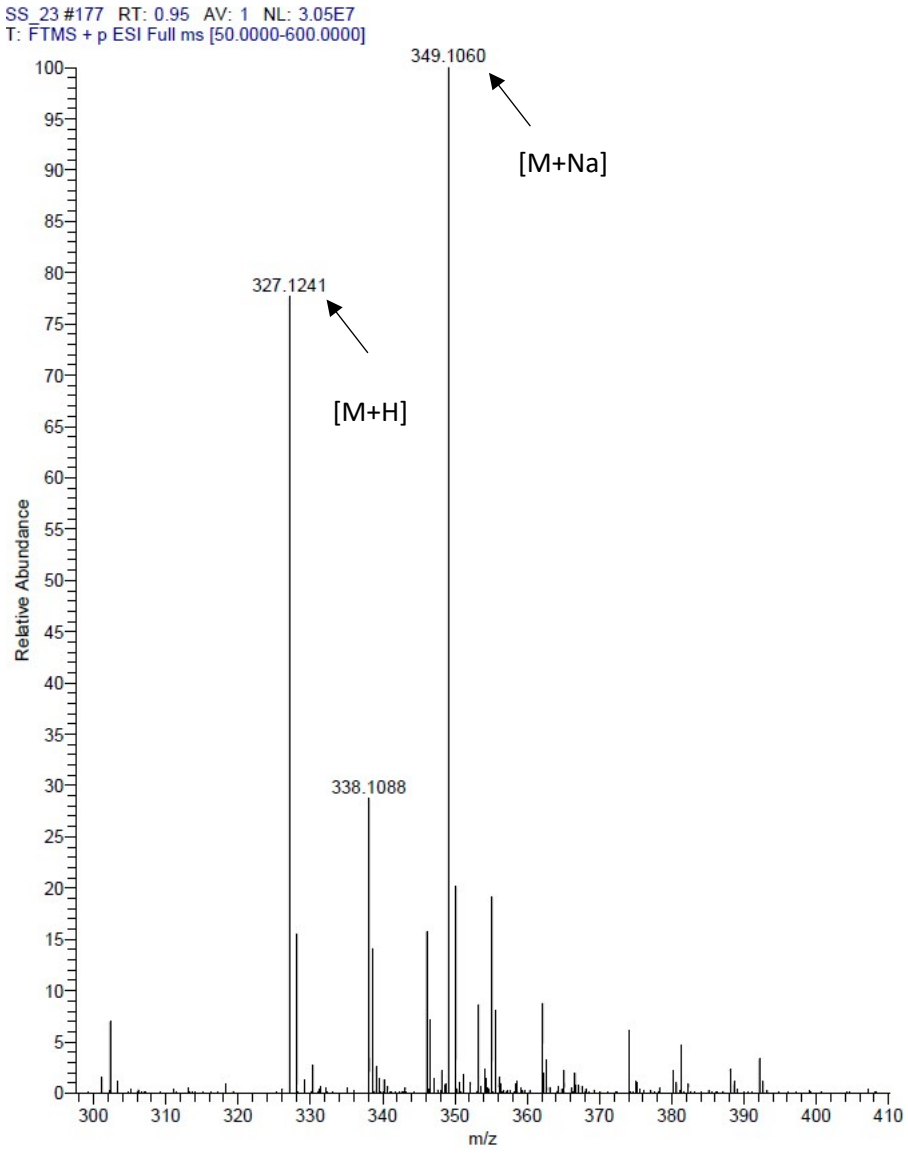


Figure S54: HRMS of compound **4ad**.

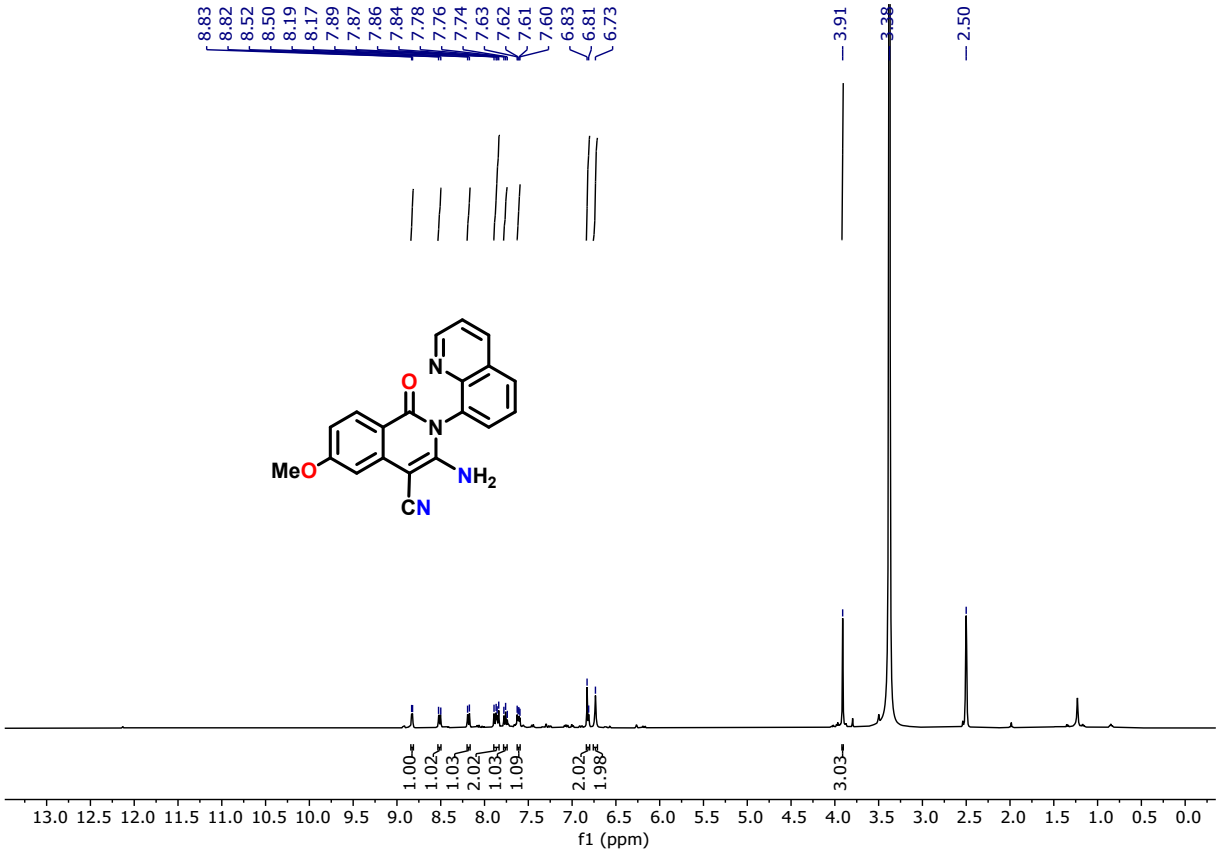


Figure S55. ^{1}H NMR (300 MHz) spectrum of **4bd** in DMSO-d_6.

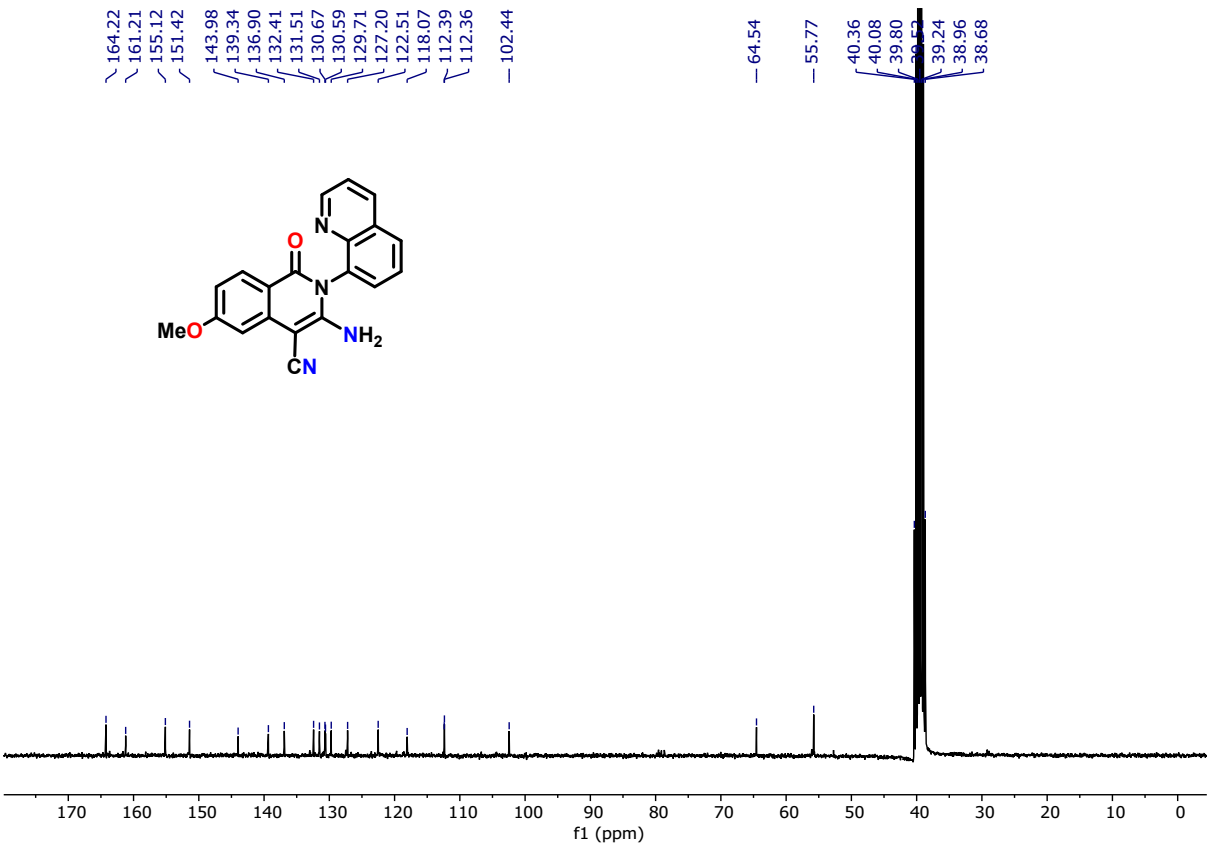


Figure S56. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4bd** in DMSO-d_6.

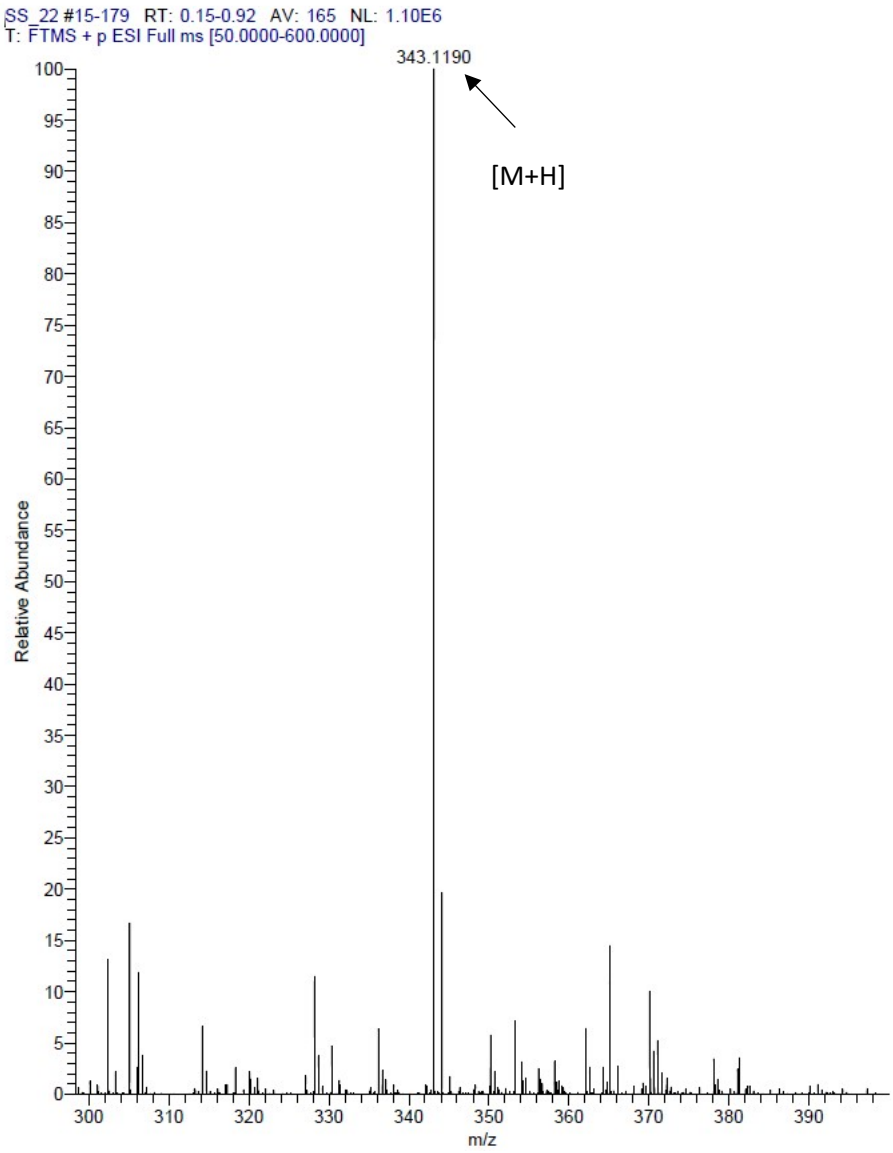


Figure S57. HRMS of compound **4bd**.

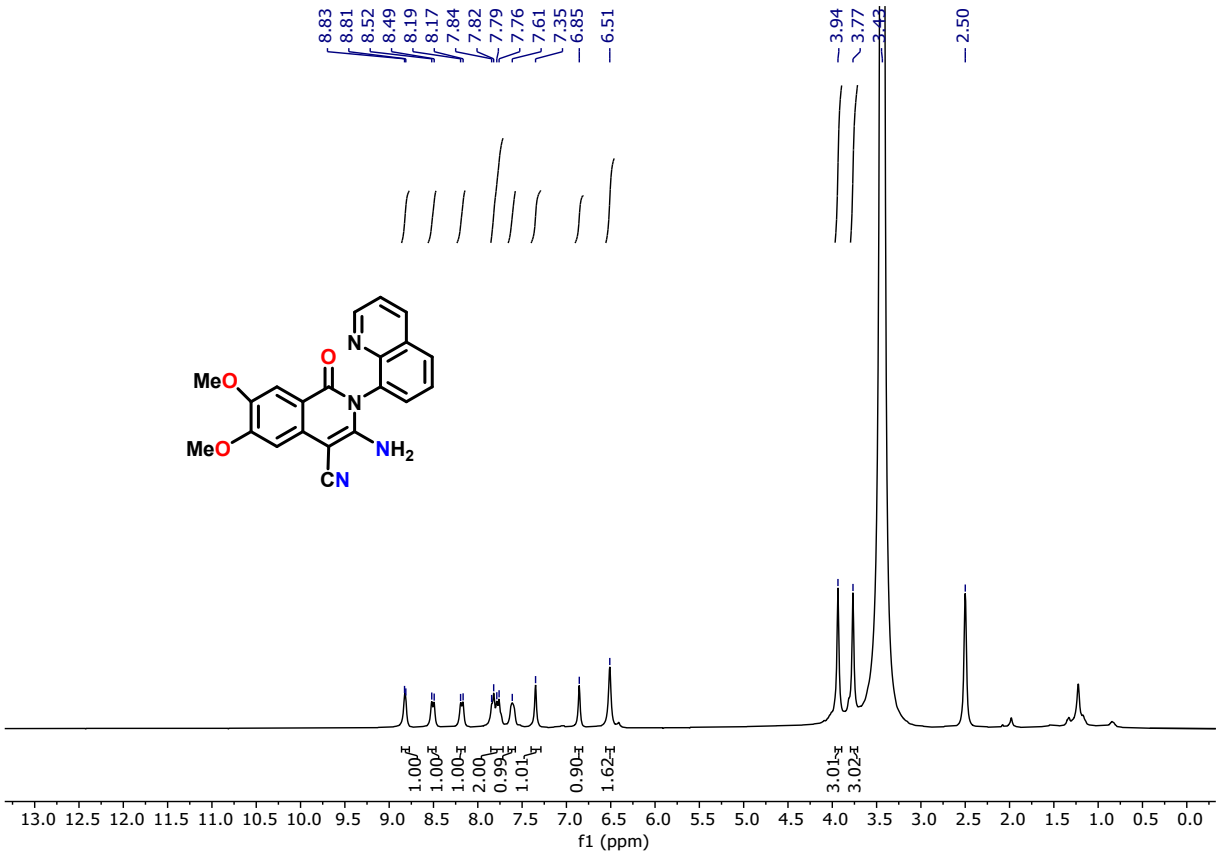


Figure S58. ^{1}H NMR (300 MHz) spectrum of **4cd** in DMSO-d_6.

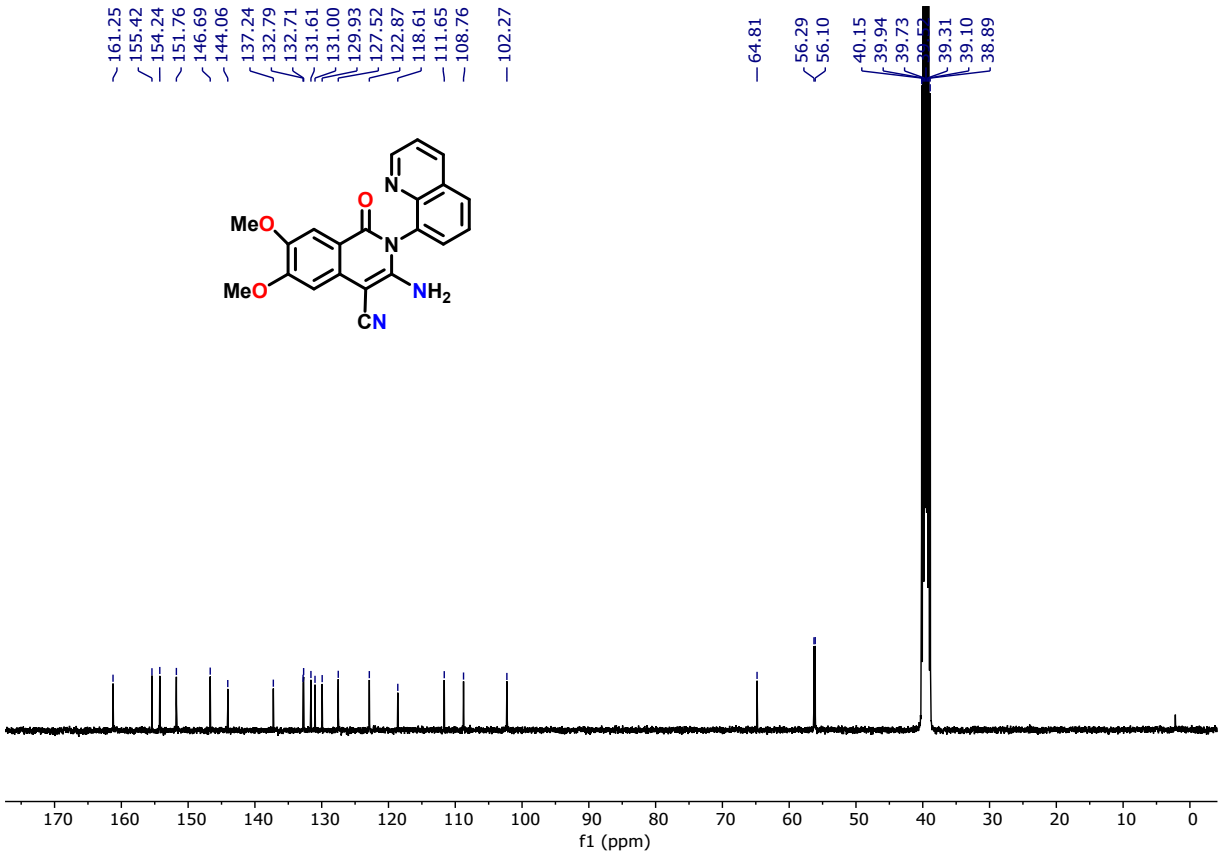


Figure S59. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4cd** in DMSO-d_6.

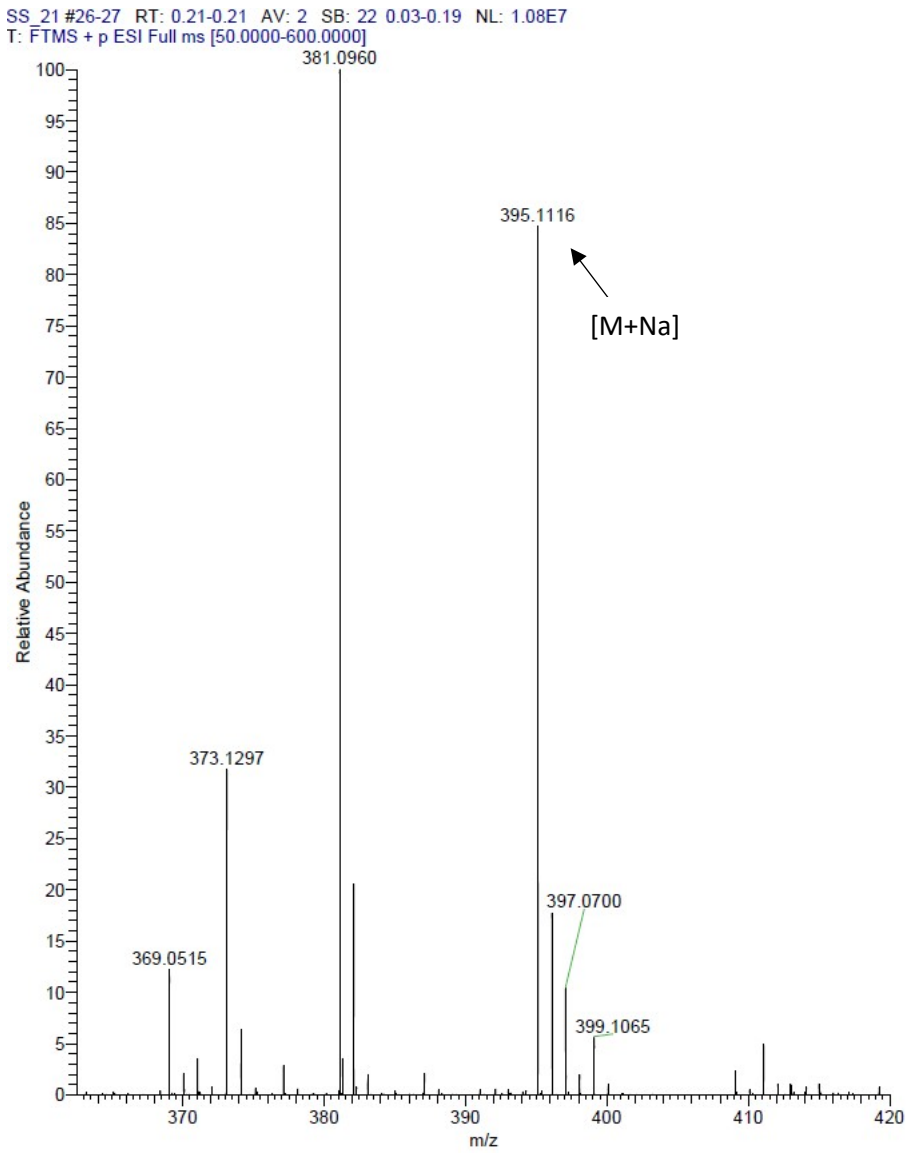


Figure S60: HRMS of compound **4cd**.

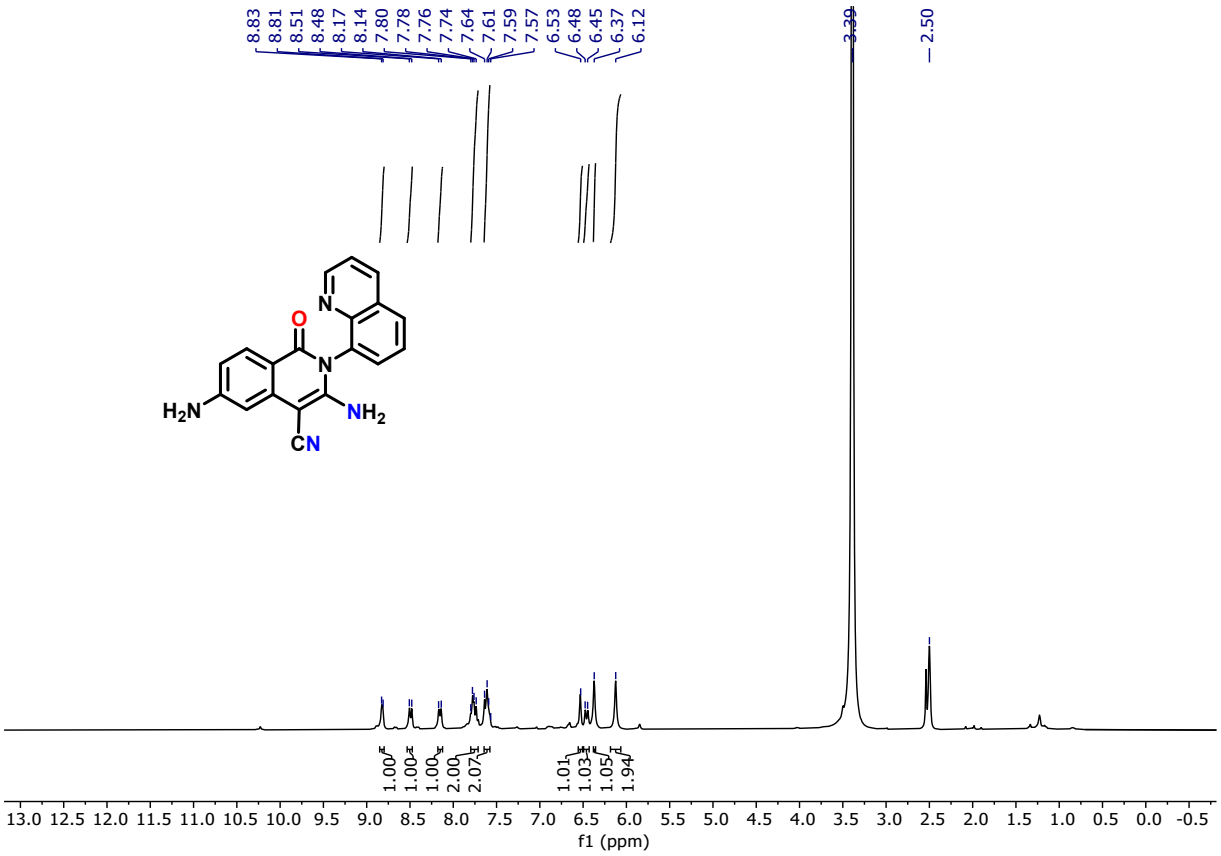


Figure S61. ^{1}H NMR (300 MHz) spectrum of **4dd** in DMSO-d_6.

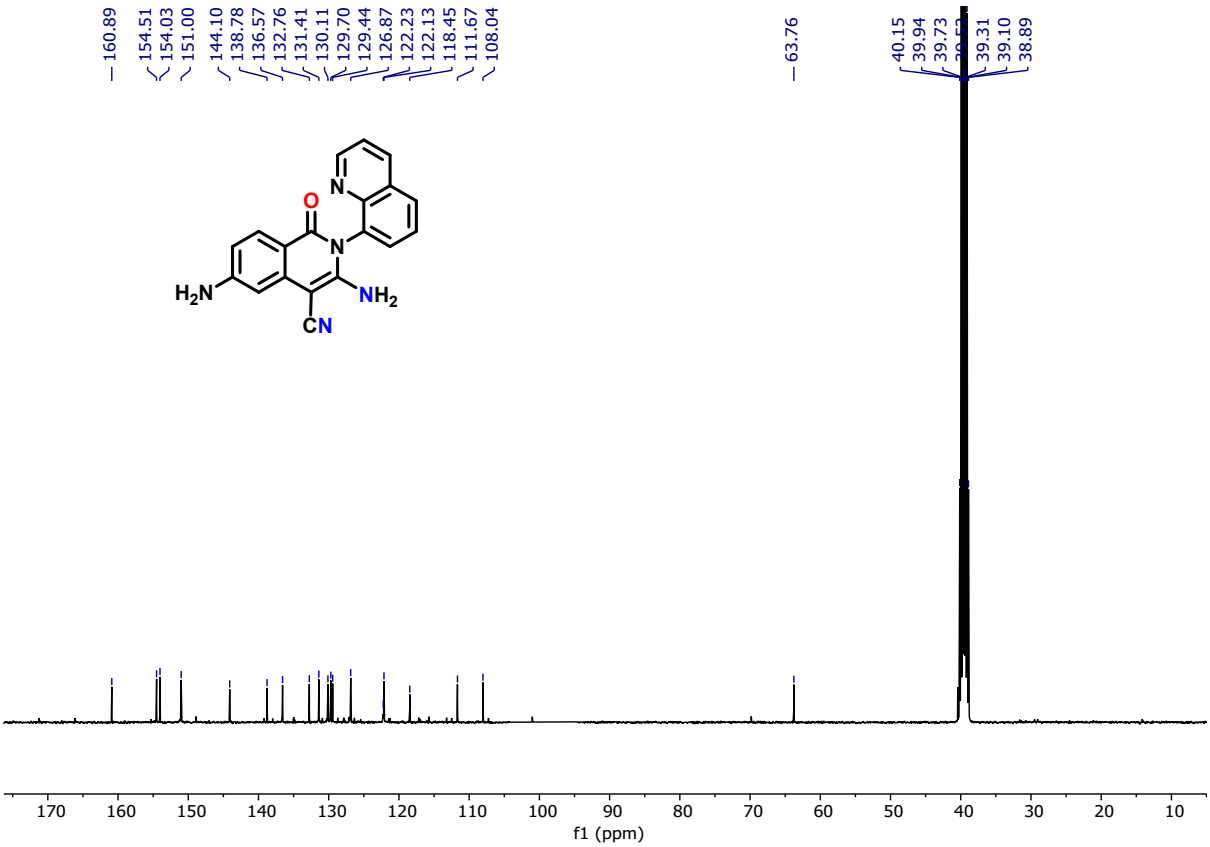


Figure S62. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4dd** in DMSO-d_6.

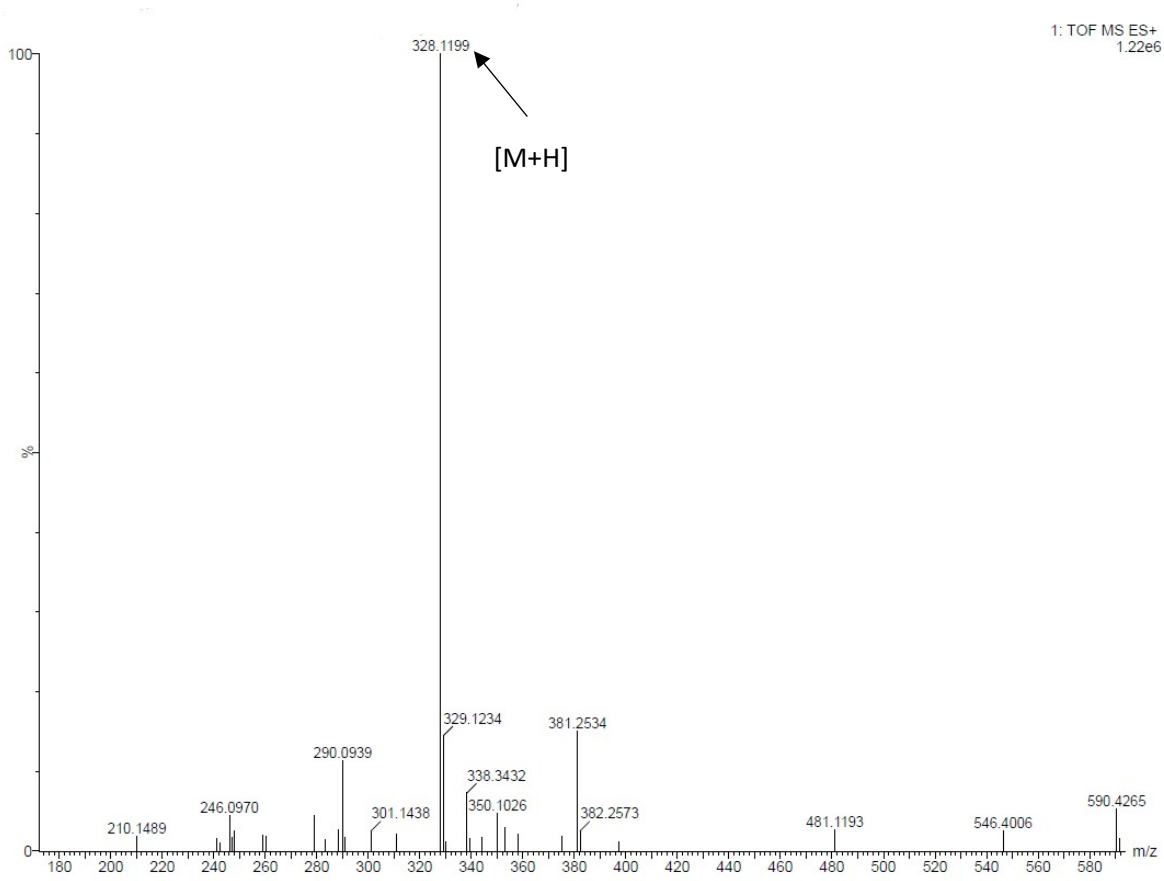


Figure S63. HRMS of compound **4dd**.

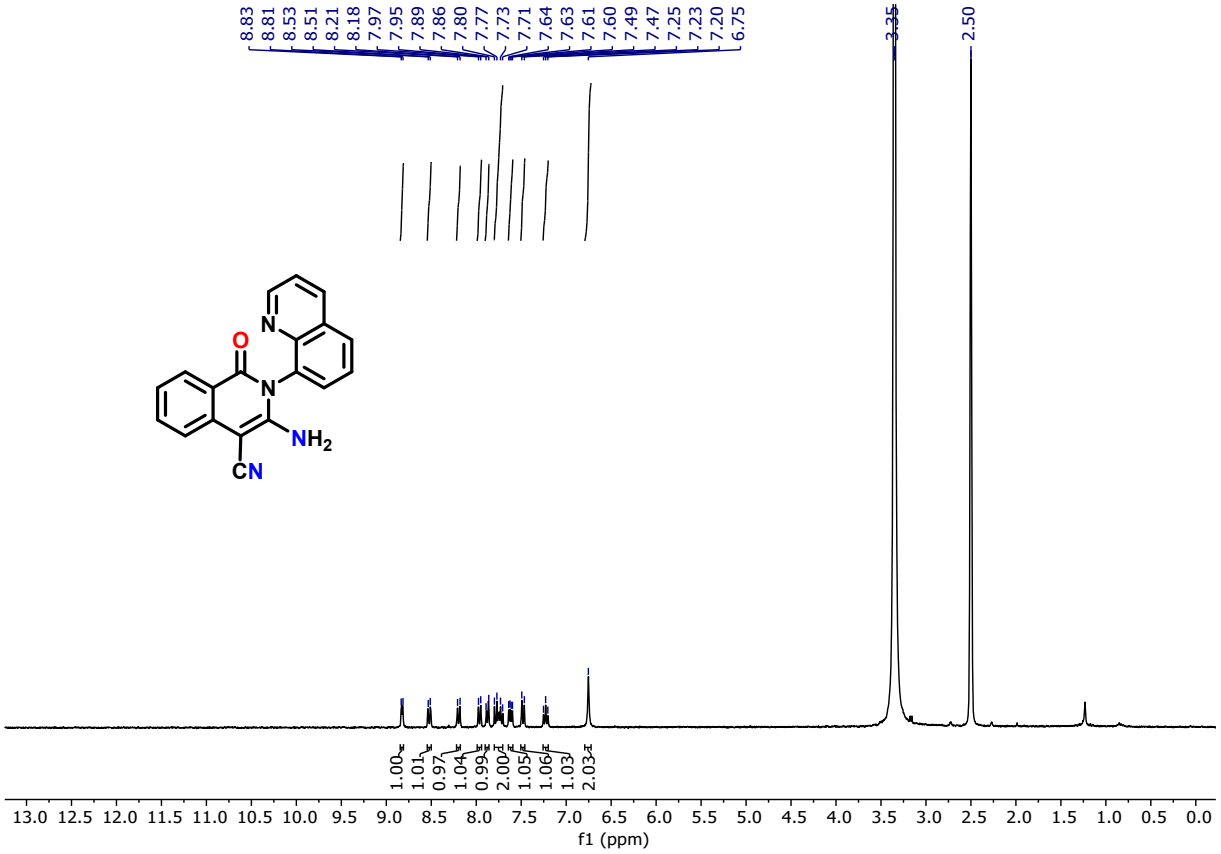


Figure S64. ^{1}H NMR (300 MHz) spectrum of **4gd** in DMSO-d_6.

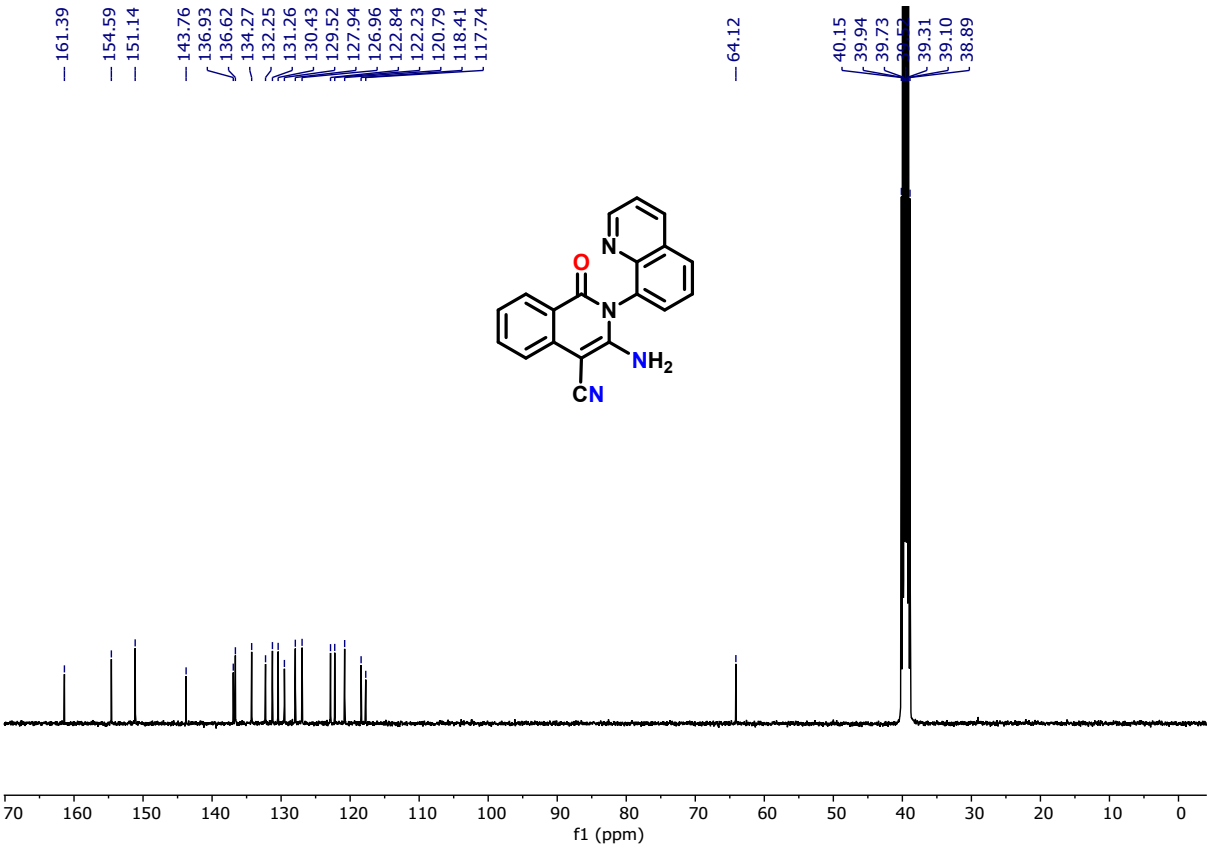


Figure S65. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4gd** in DMSO-d_6.

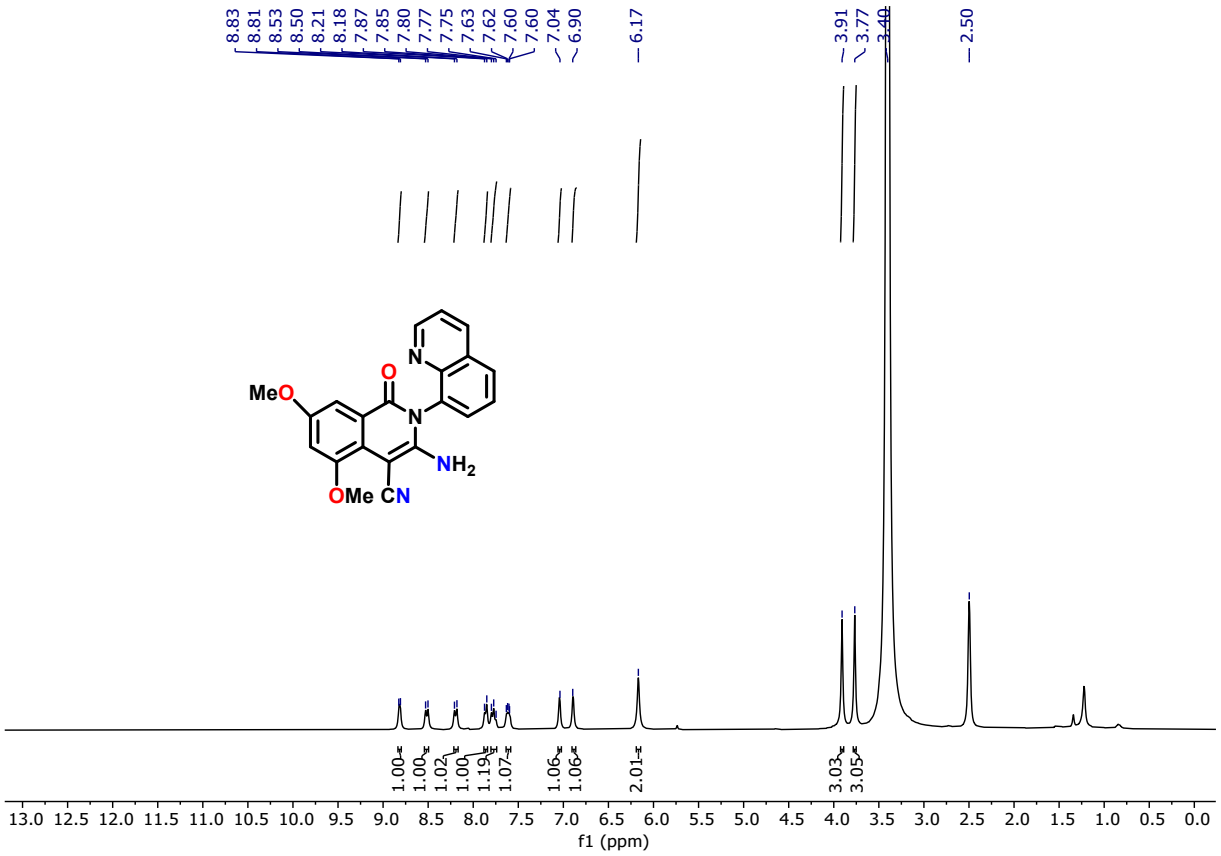


Figure S66. ^{1}H NMR (300 MHz) spectrum of **4jd** in DMSO-d_6.

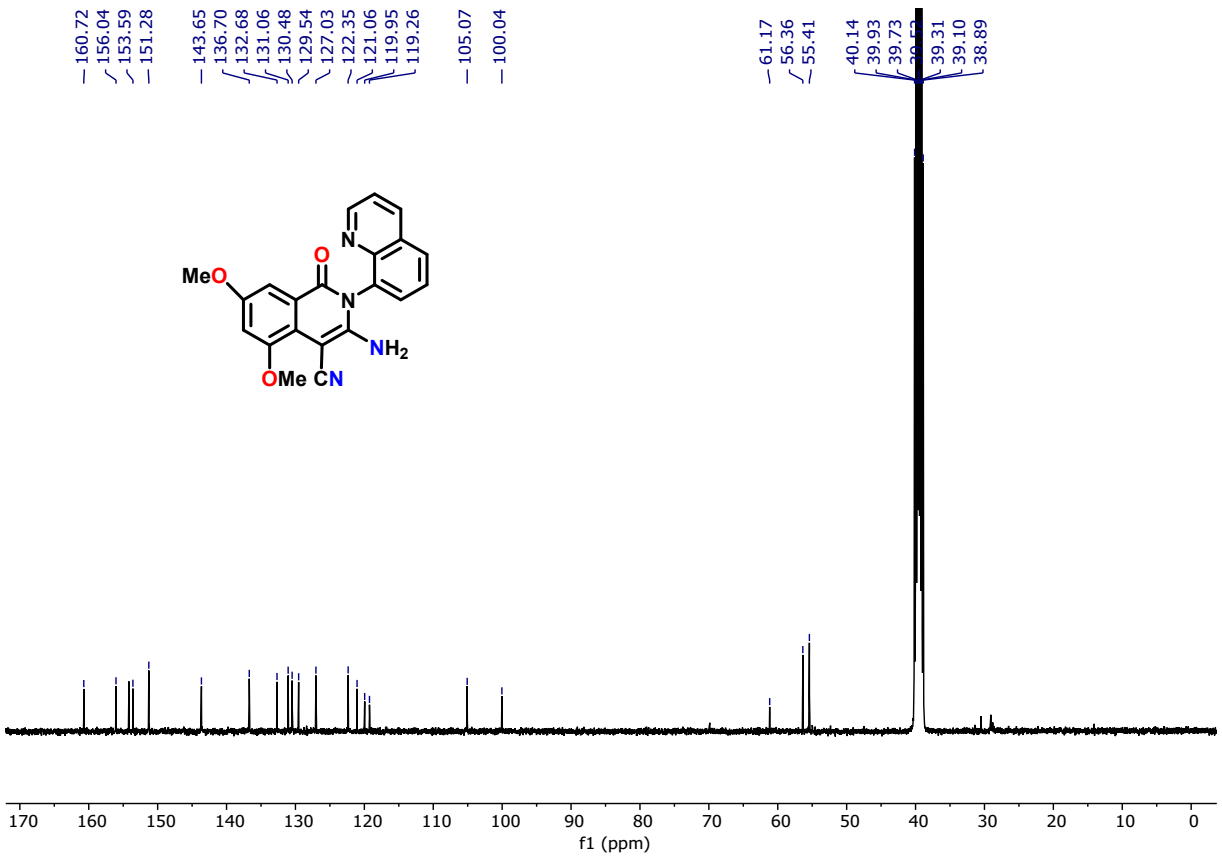


Figure S67. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4jd** in DMSO-d_6.

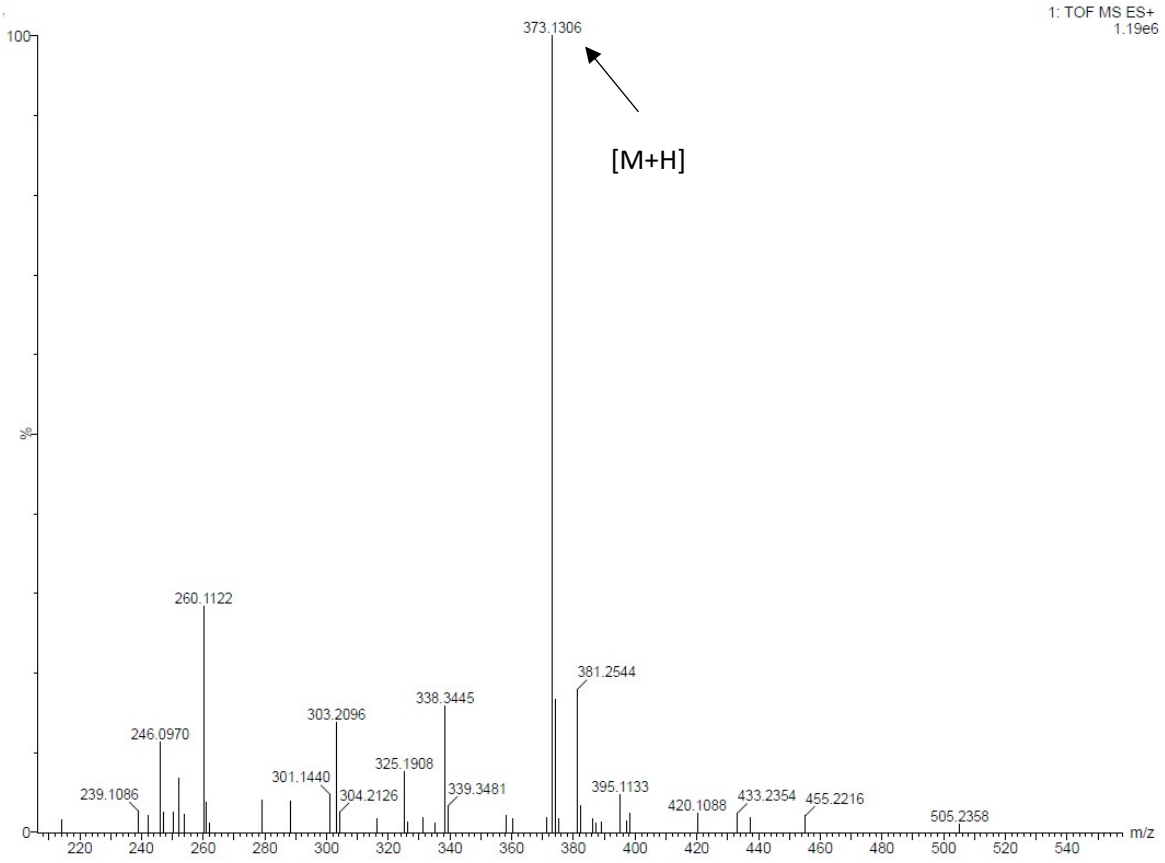


Figure S68. HRMS of **4jd** compound

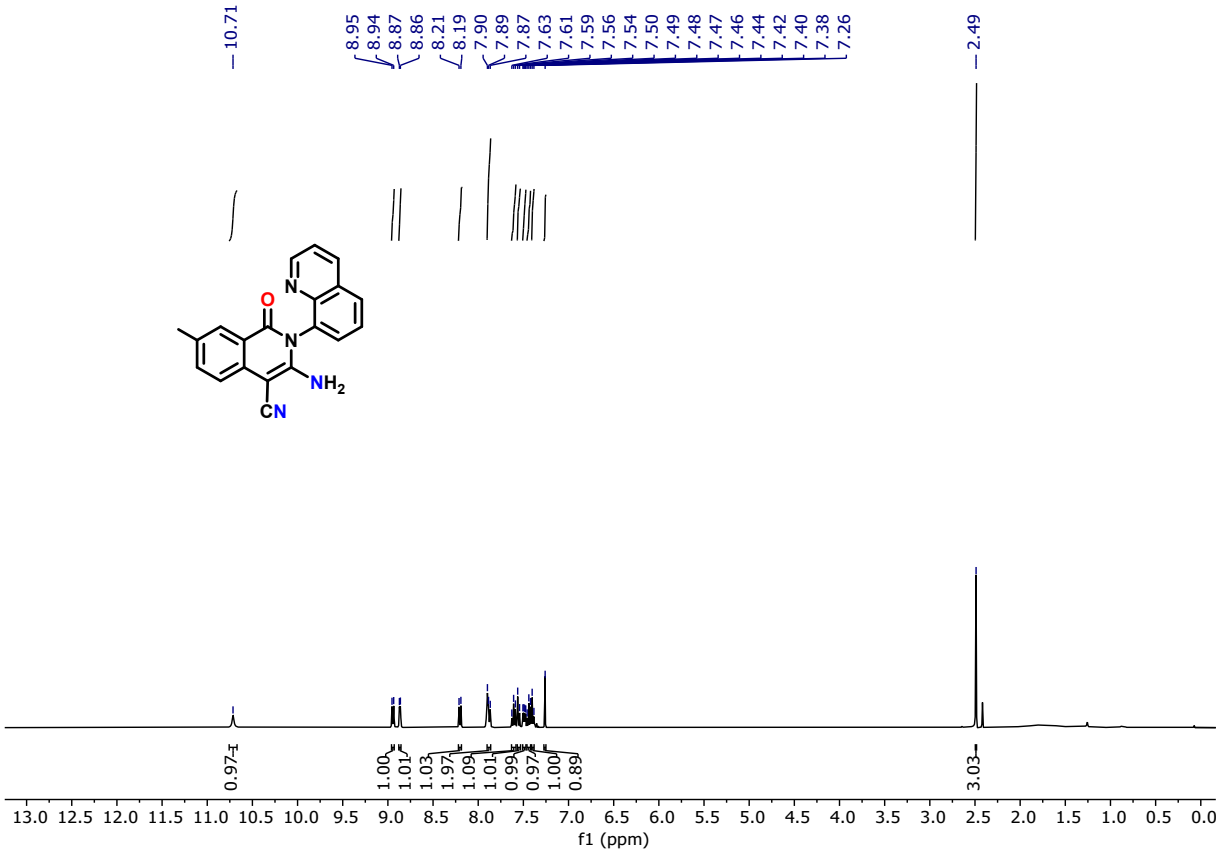


Figure S69. ^{1}H NMR (300 MHz) spectrum of **4kd** in $CDCl_3$.

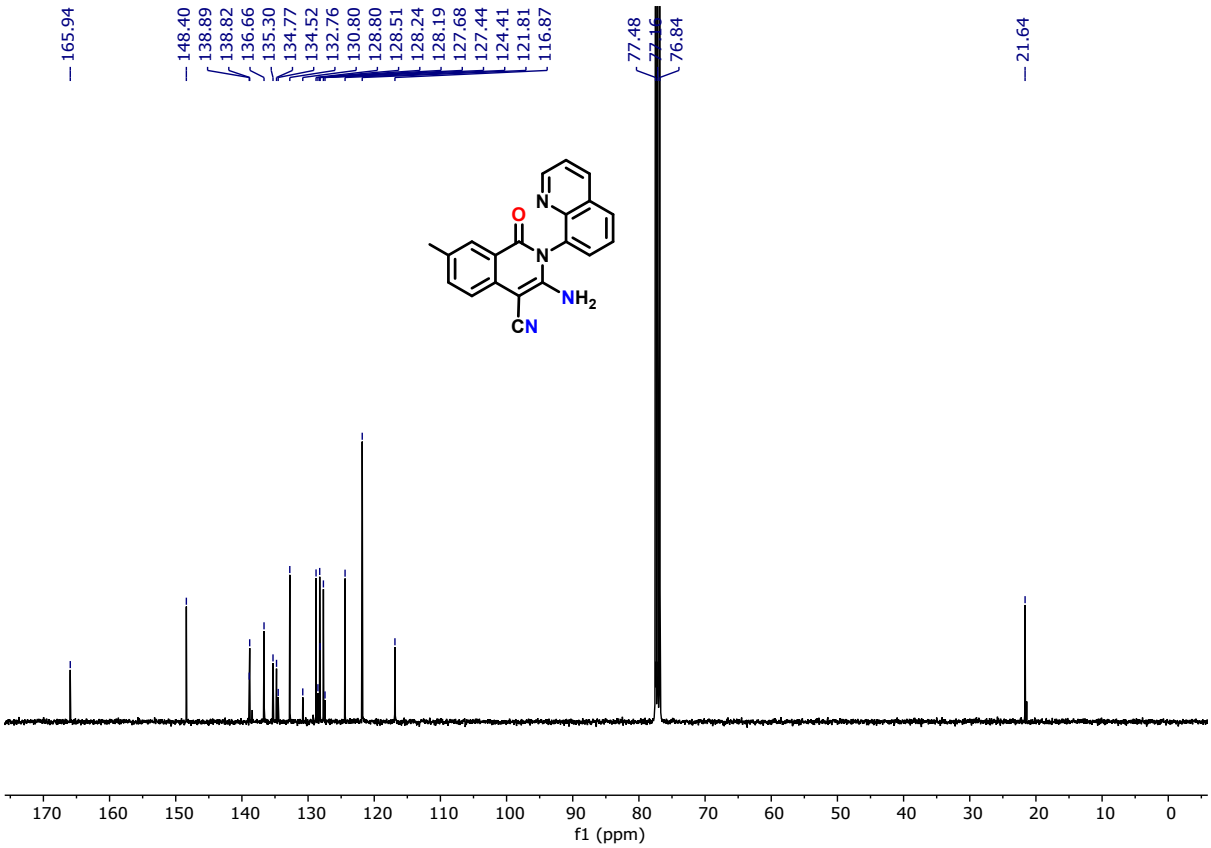


Figure S70. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4kd** in $CDCl_3$.

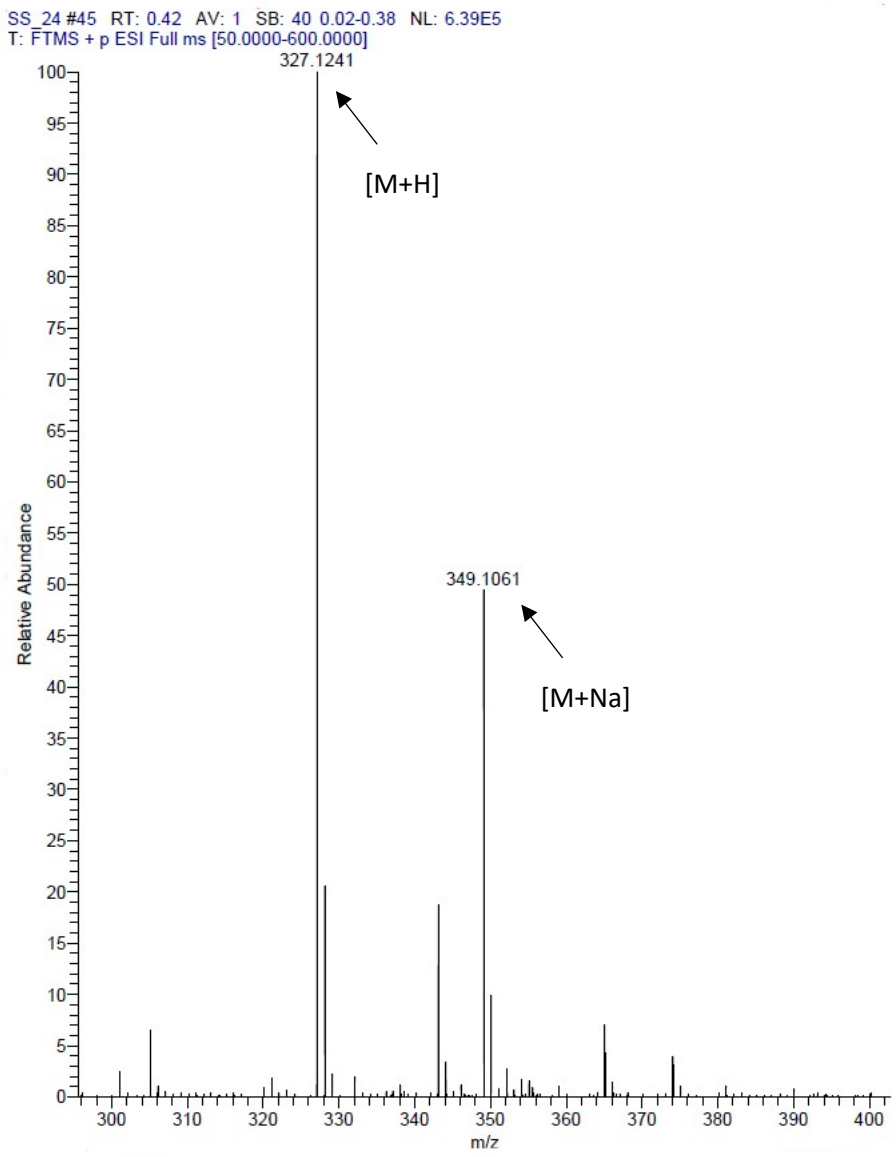


Figure S71. HRMS of compound **4kd**.

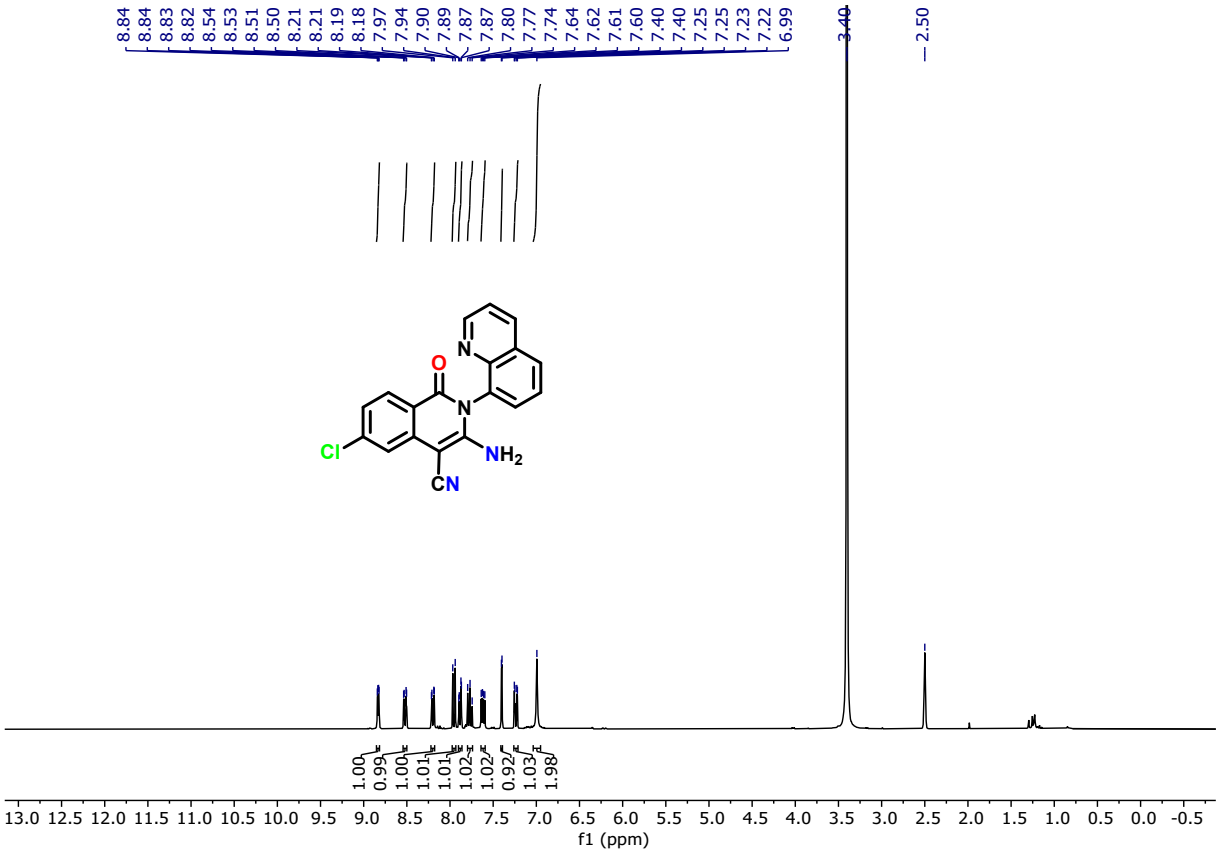


Figure S72. ^{1}H NMR (300 MHz) spectrum of **4ed** in DMSO-d_6.

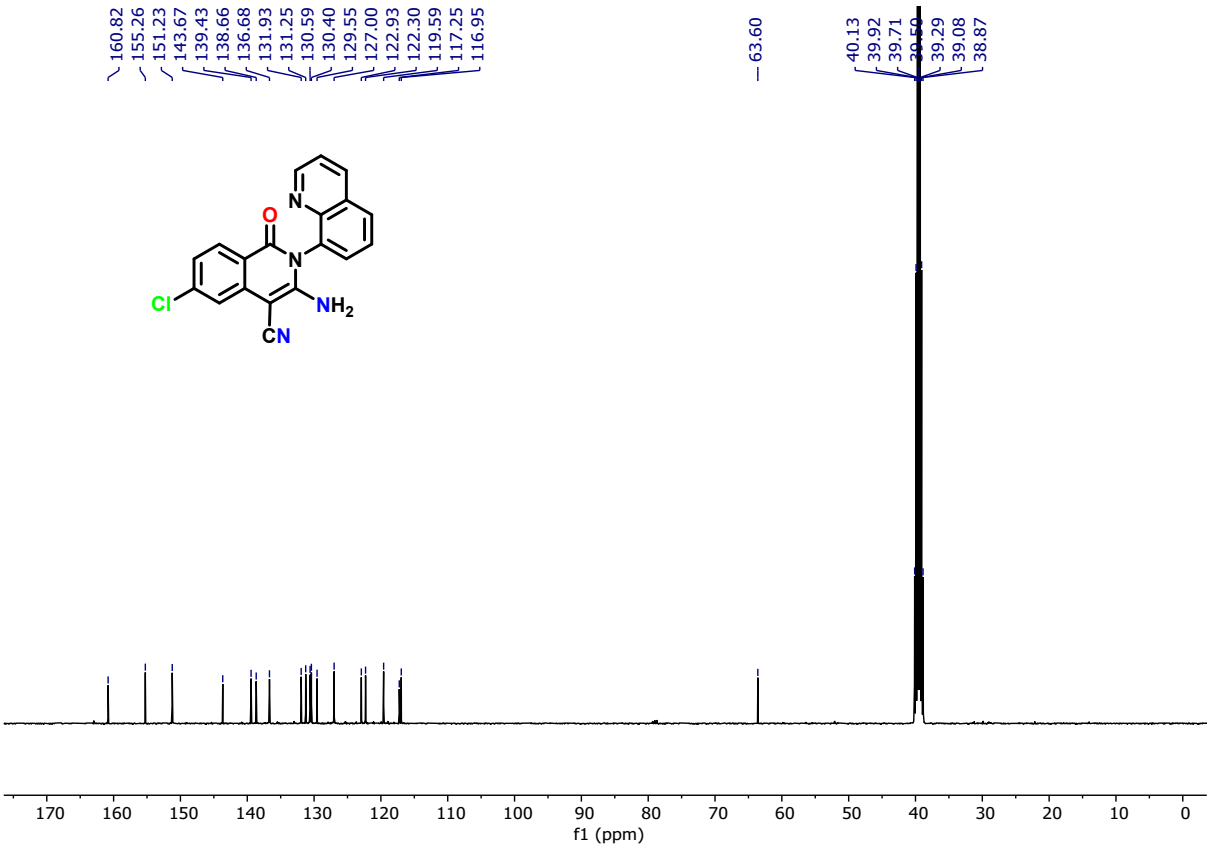


Figure S73. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4ed** in DMSO-d_6.

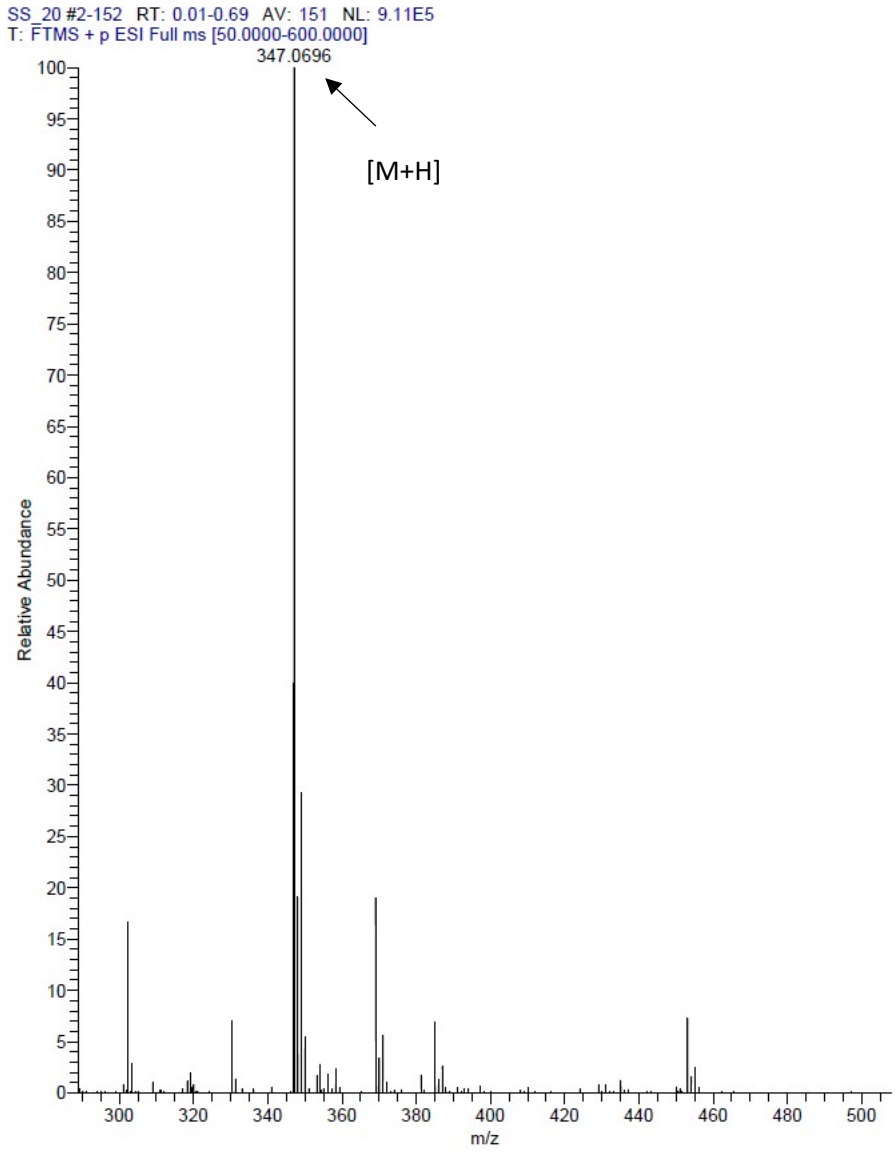


Figure S74: HRMS of compound **4ed**.

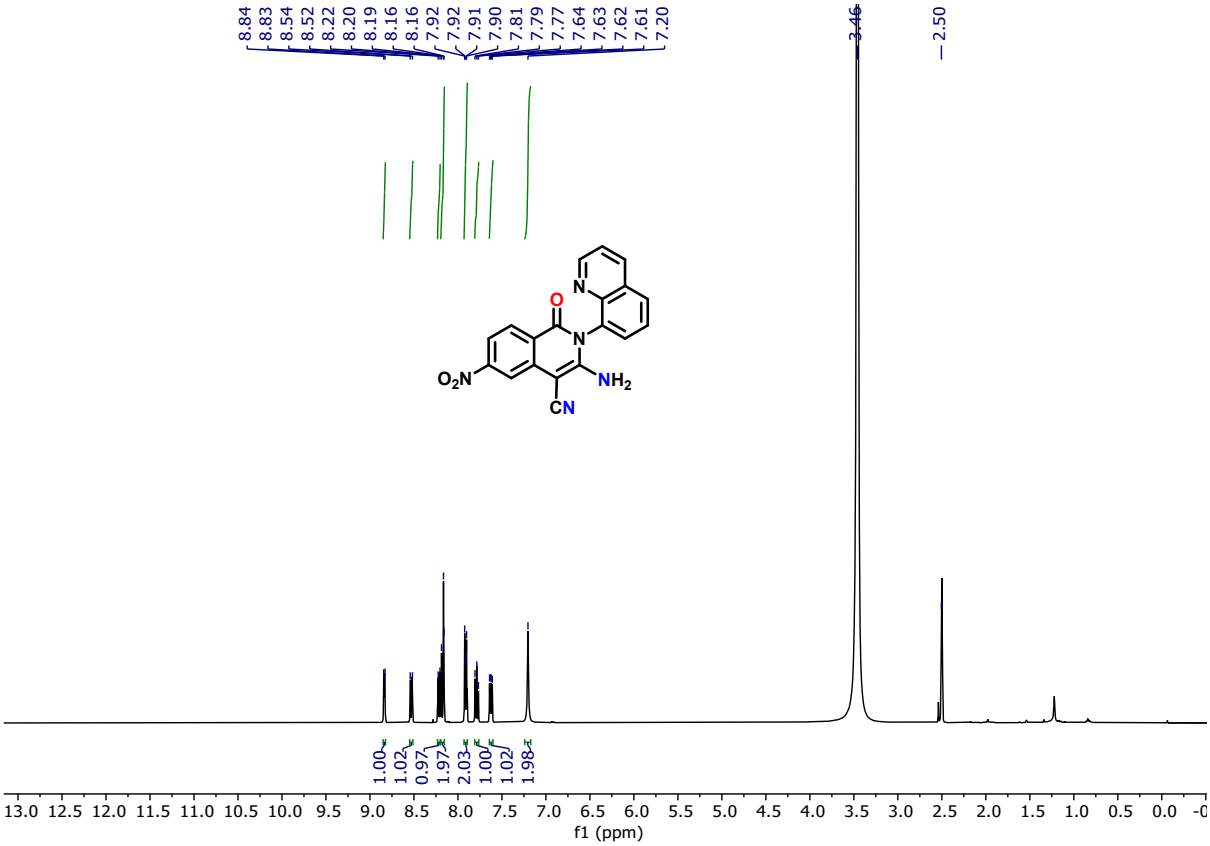


Figure S75. ^{1}H NMR (300 MHz) spectrum of **4fd** in DMSO-d_6.

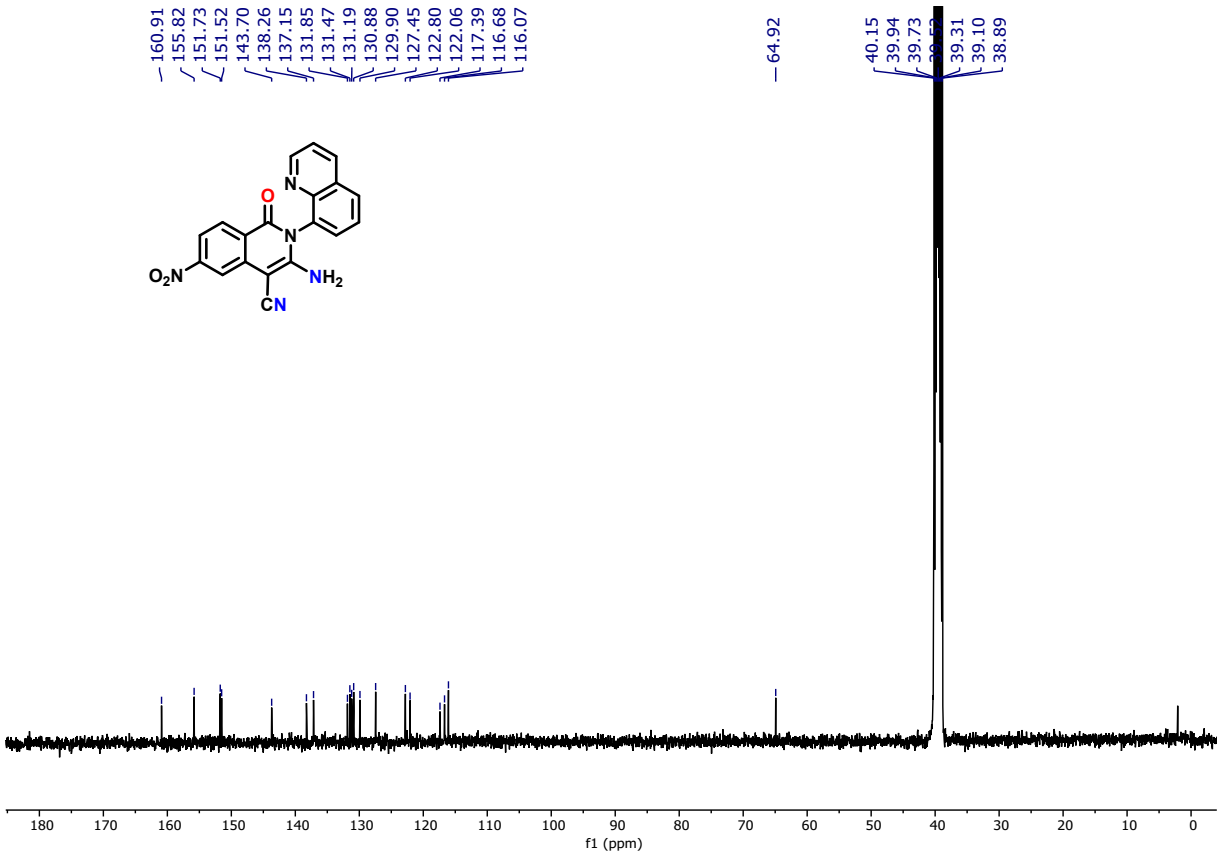


Figure S76. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4fd** in DMSO-d_6.

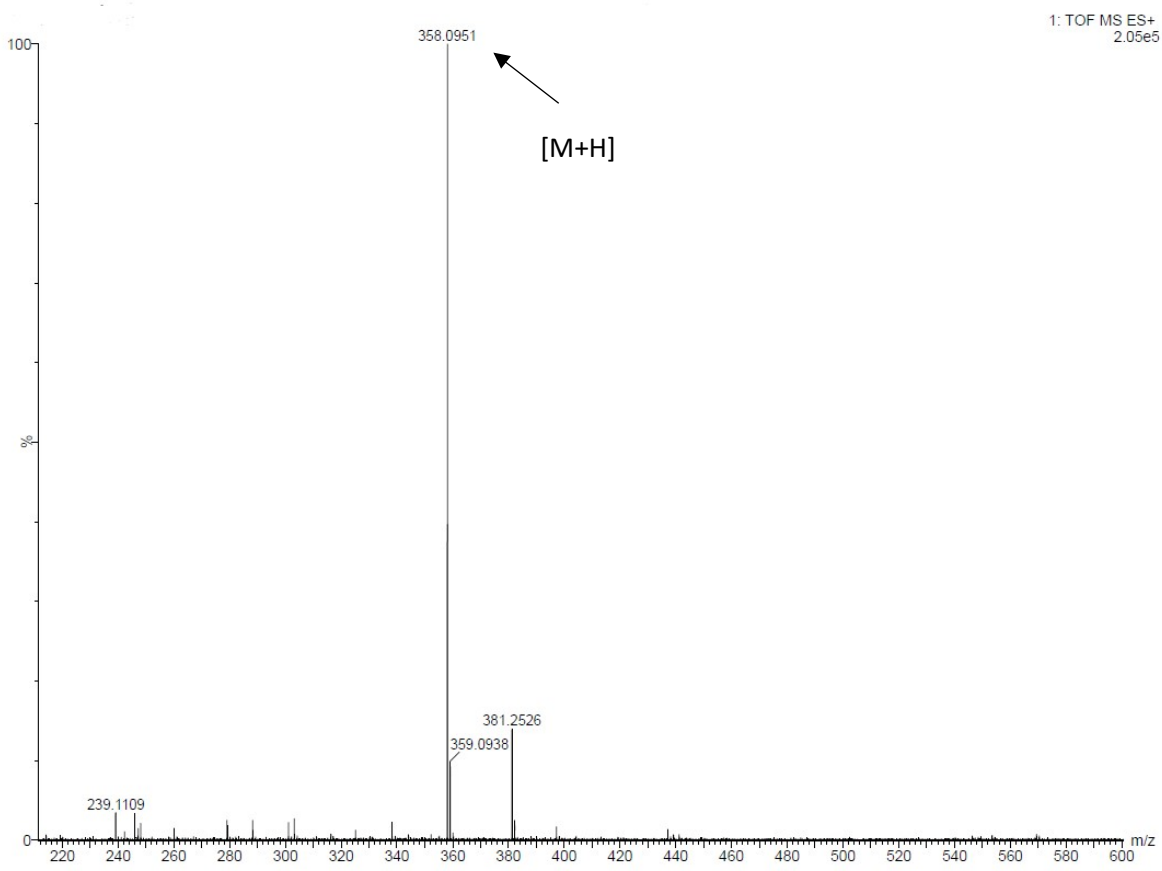


Figure S77. HRMS of compound **4fd**.

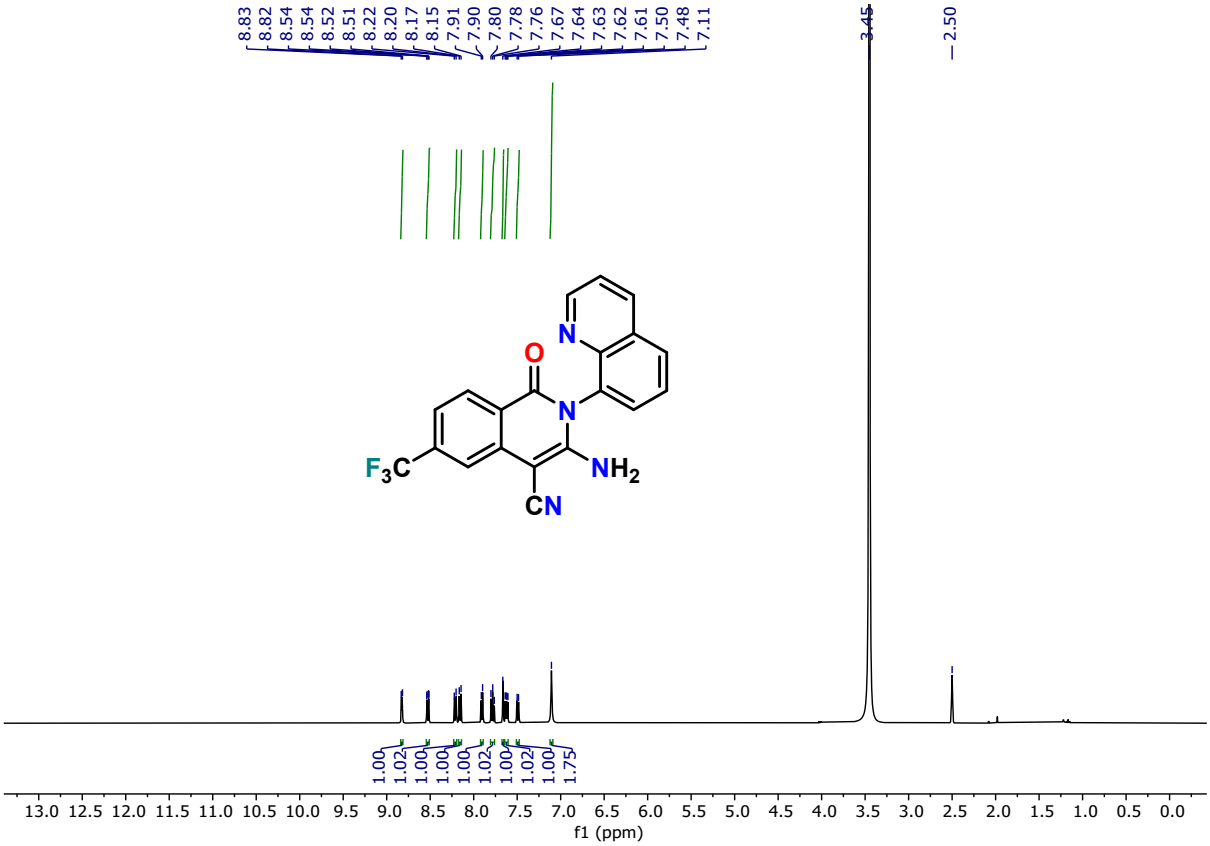


Figure S78. ^{1}H NMR (300 MHz) spectrum of **4hd** in DMSO-d_6.

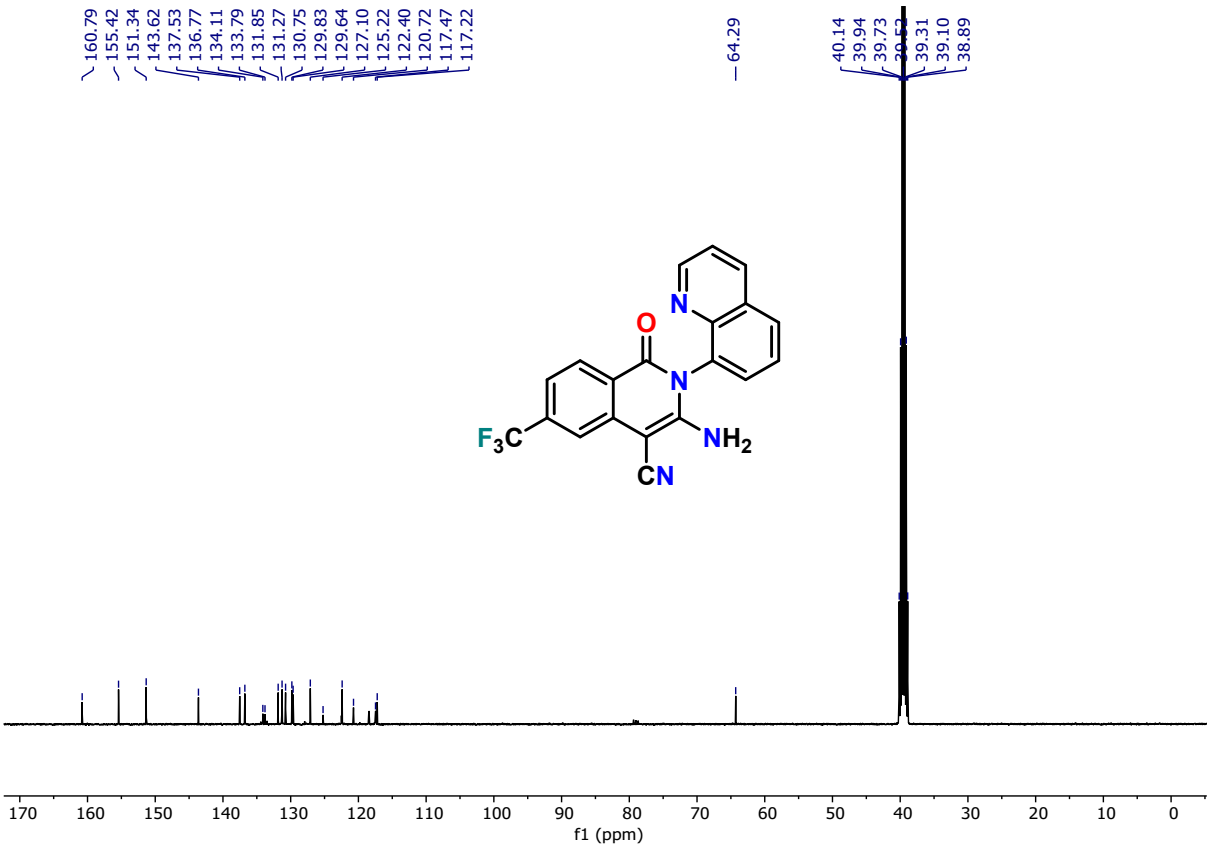


Figure S79. ^{13}C NMR (100 MHz) spectrum of **4hd** in DMSO-d_6.

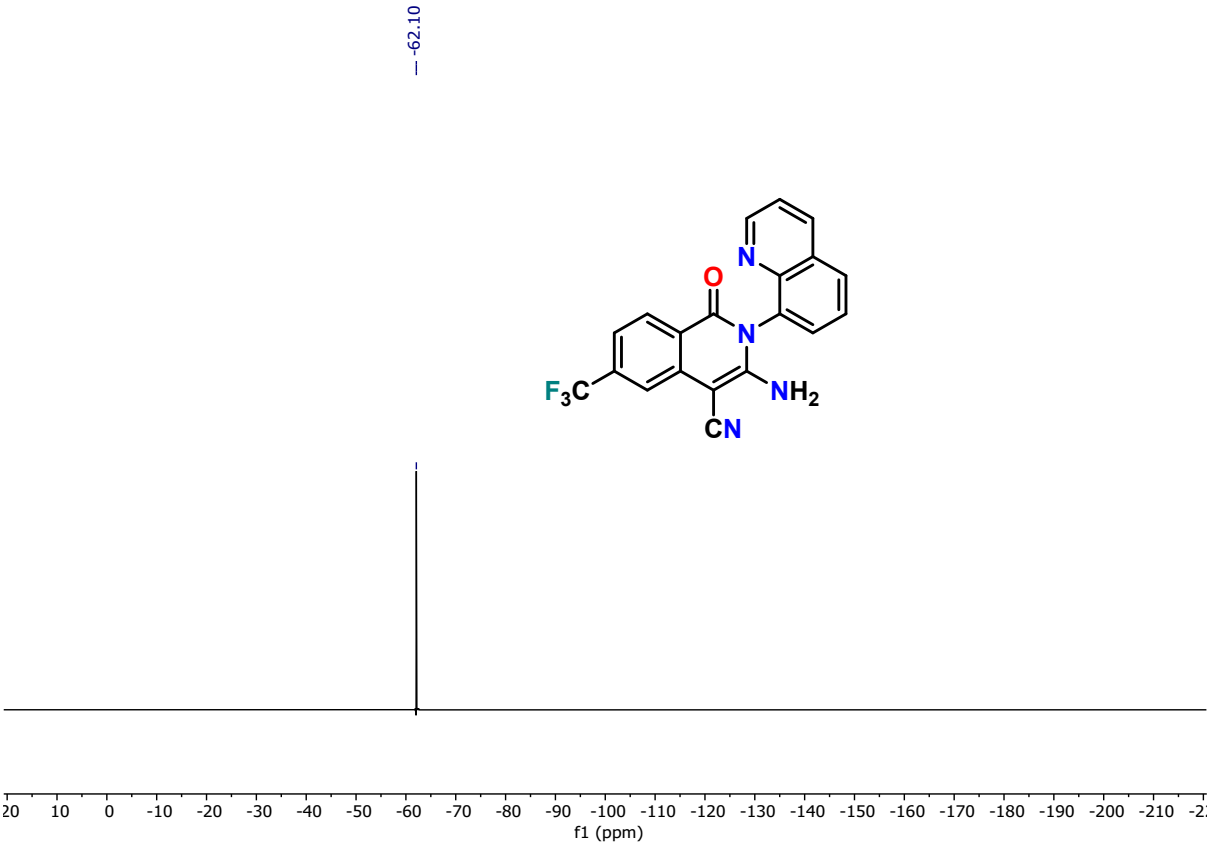


Figure S80. ^{19}F NMR (282 MHz) spectrum of **4hd** in DMSO-d_6.

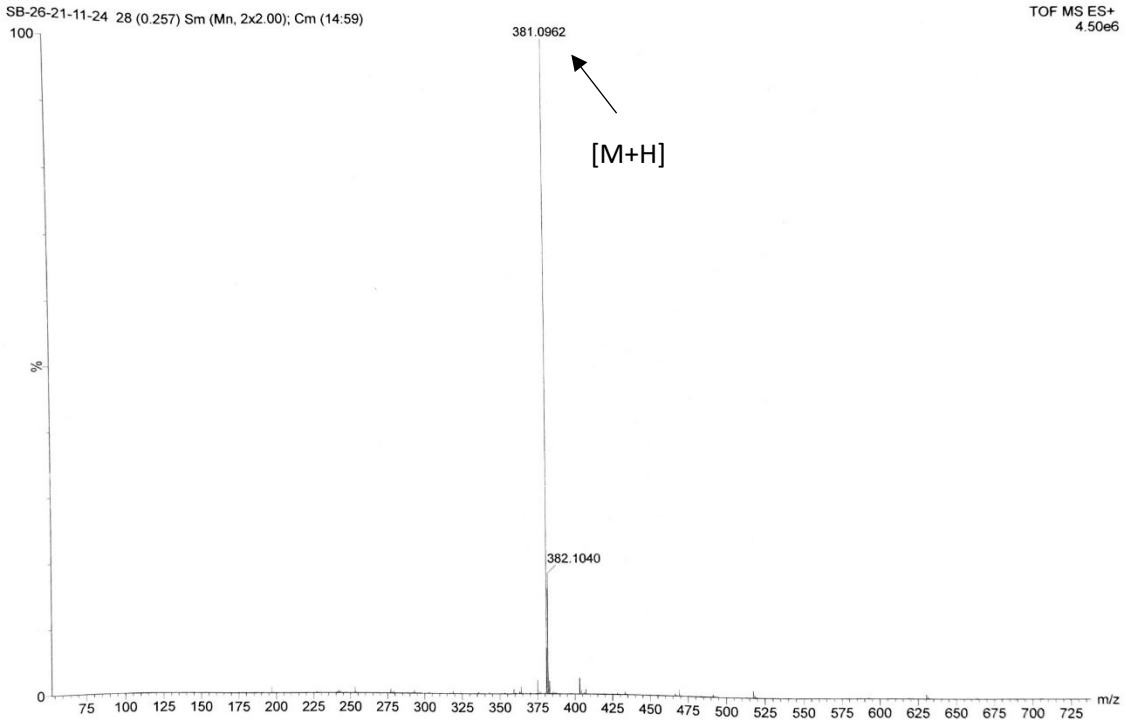


Figure S81: HRMS of compound **4hd**.

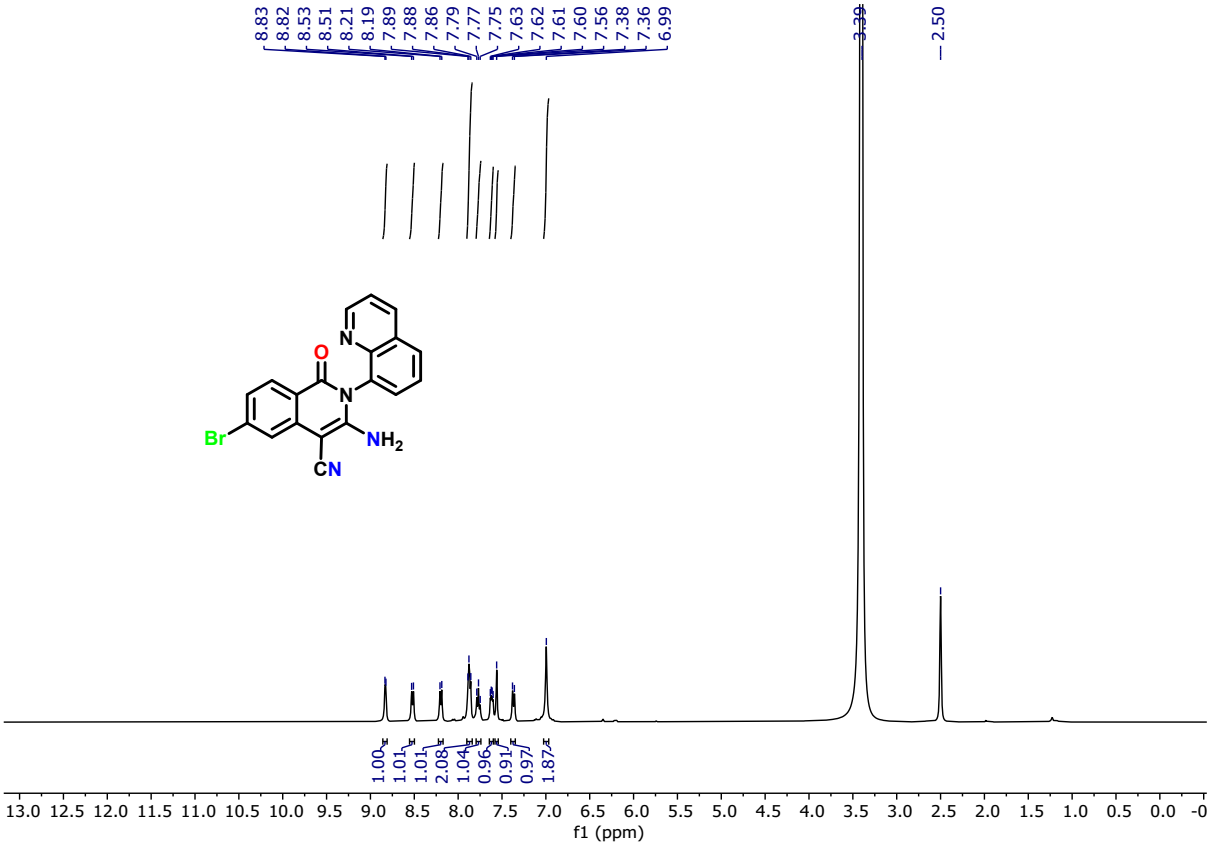


Figure S82. ^{1}H NMR (300 MHz) spectrum of **4id** in DMSO-d_6.

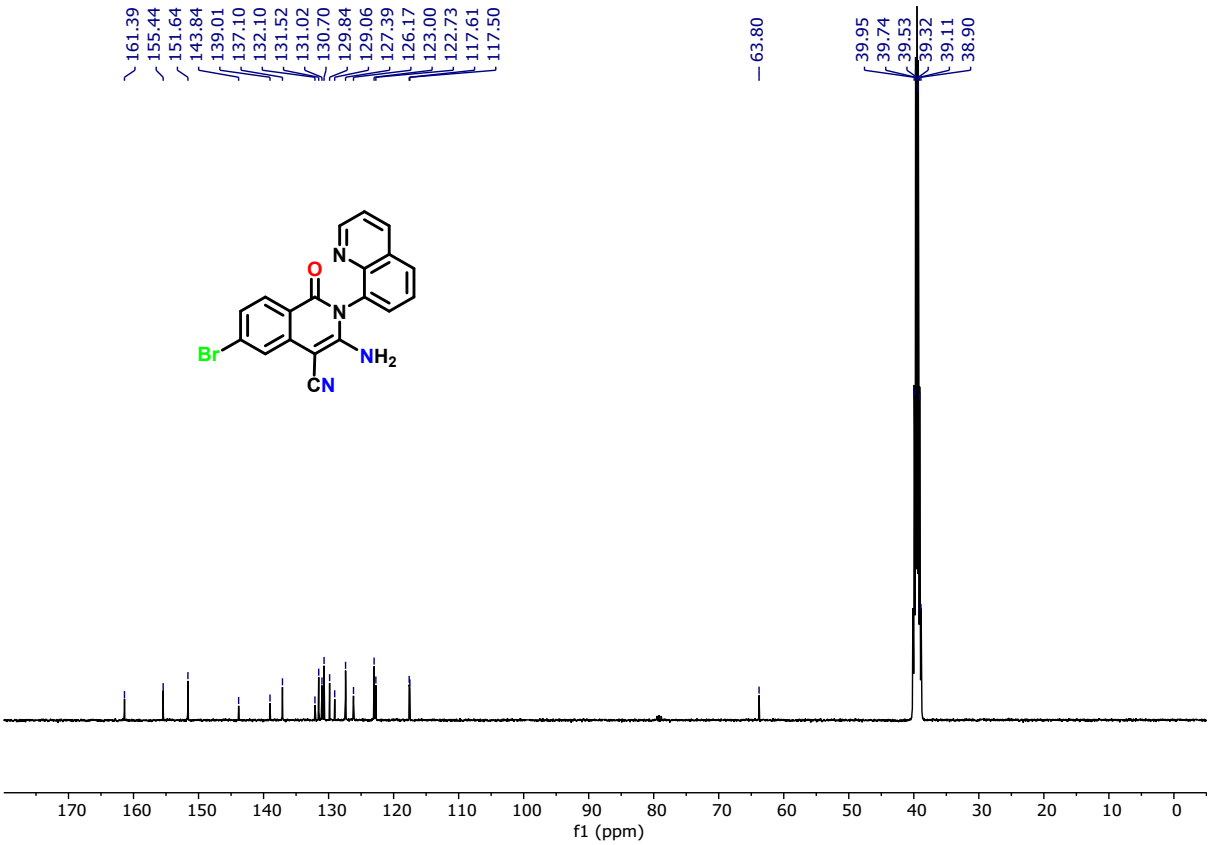


Figure S83. $^{13}C\{^{1}H\}$ NMR (100 MHz) spectrum of **4id** in DMSO-d_6.

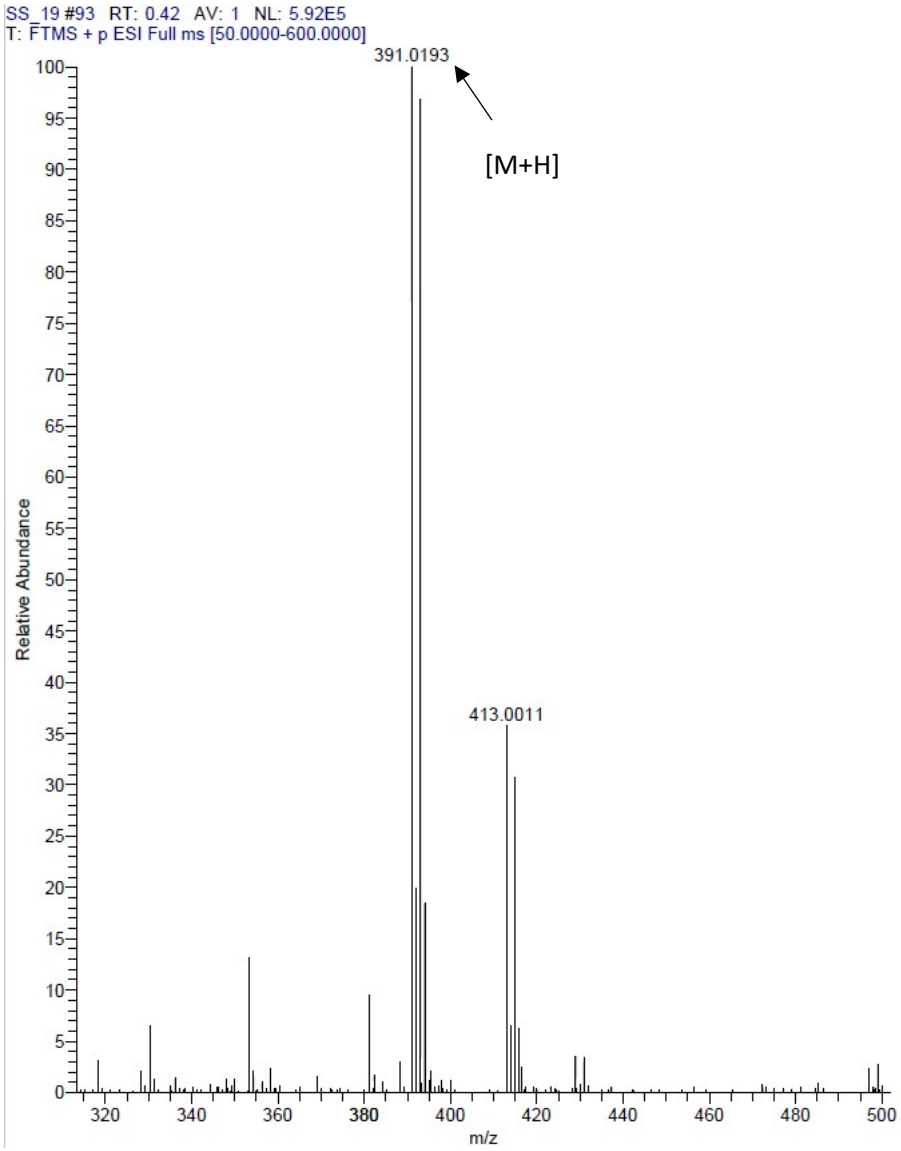


Figure S84: HRMS of compound **4id**.

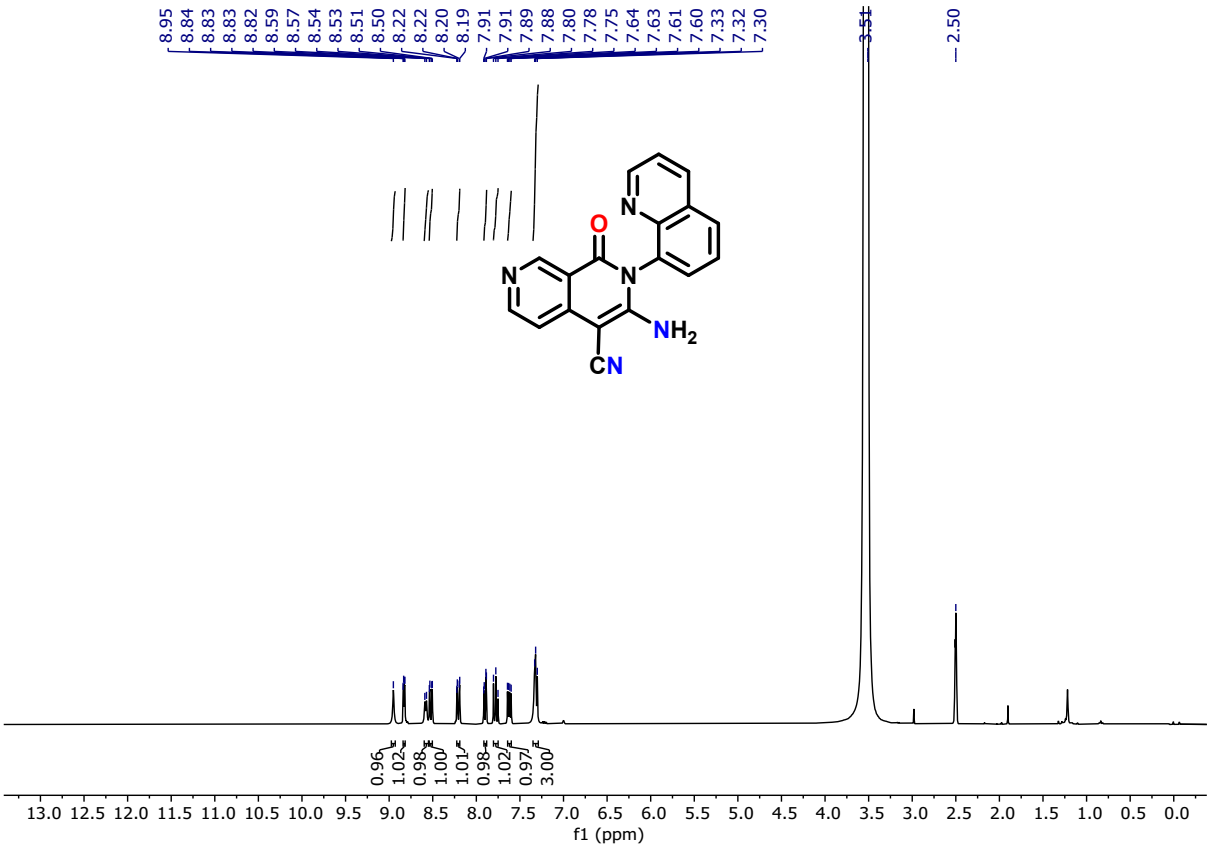


Figure S85. ^{1}H NMR (300 MHz) spectrum of **4ld** in DMSO-d_6.

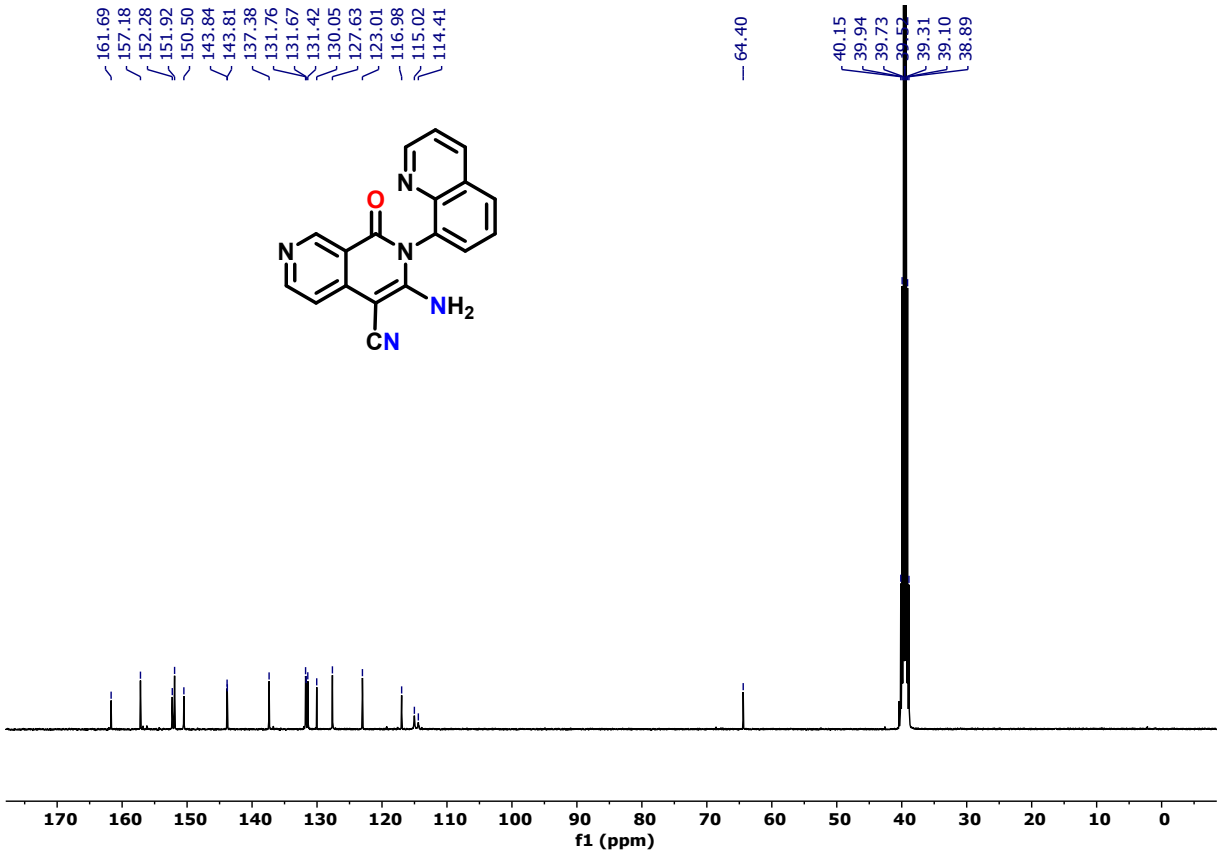


Figure S86. ^{13}C NMR (100 MHz) spectrum of **4ld** in DMSO-d_6.

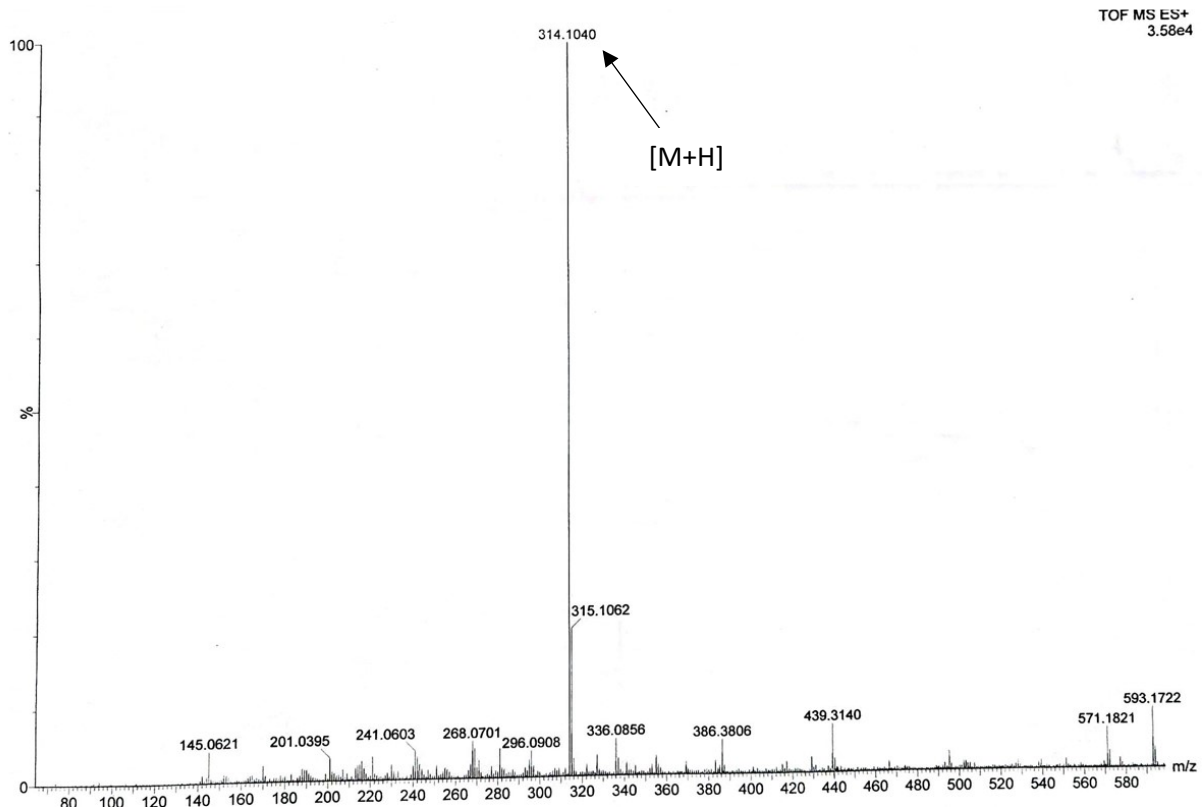


Figure S87. HRMS of compound **4ld**.

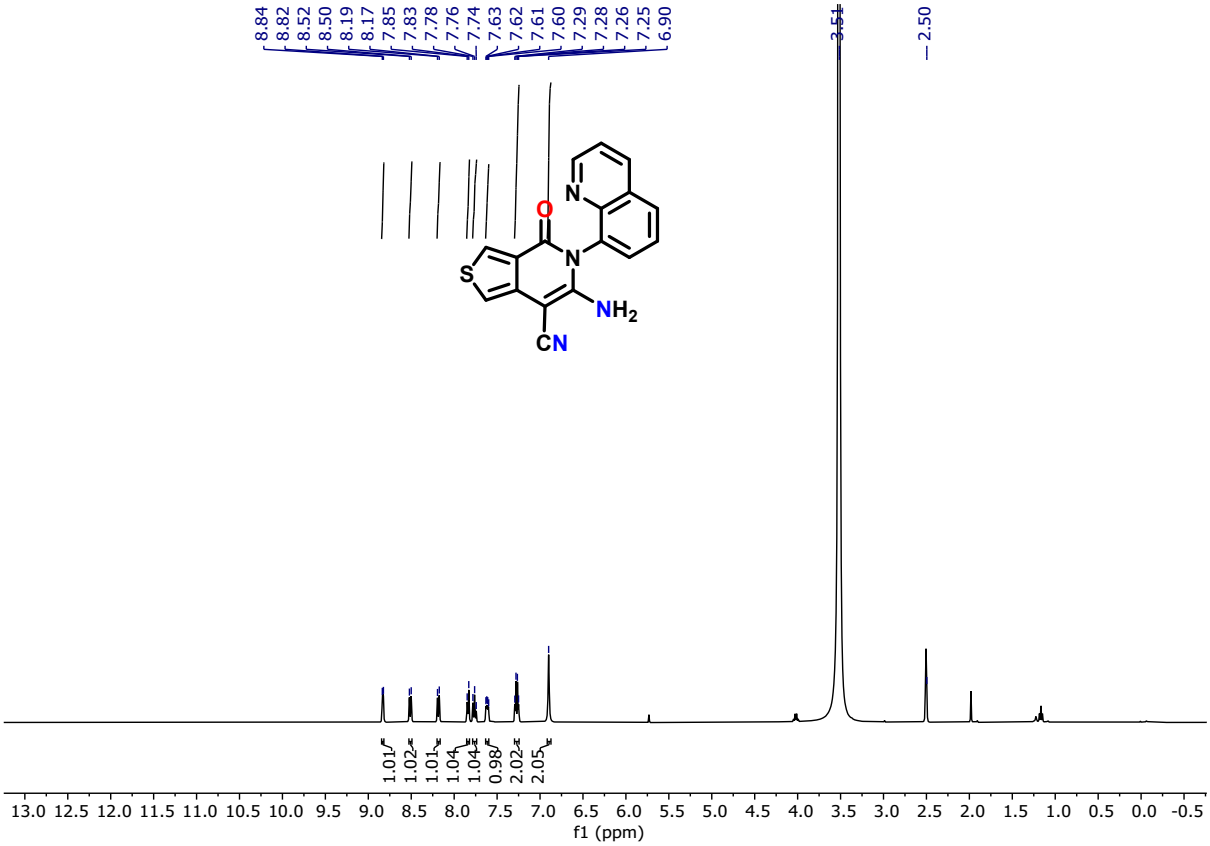


Figure S88. ^{1}H NMR (300 MHz) spectrum of **4md** in DMSO-d_6.

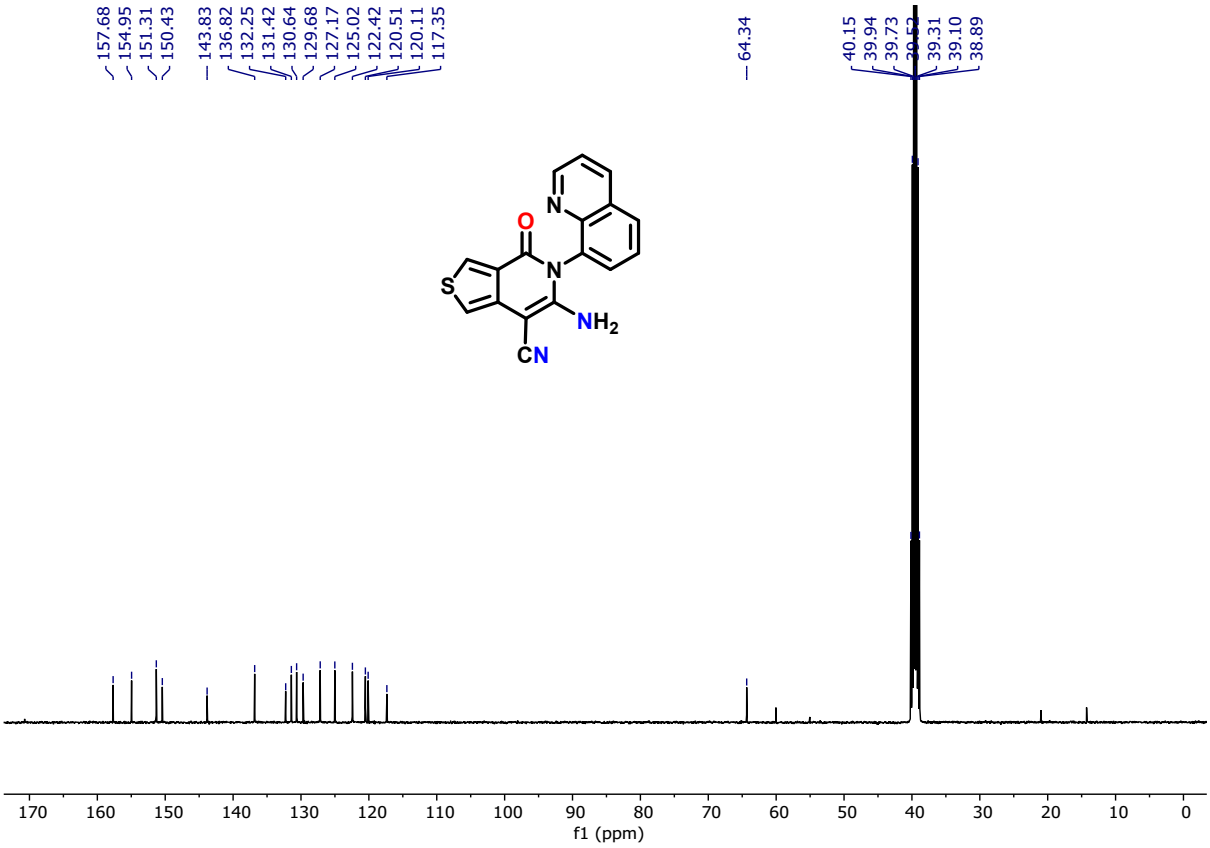


Figure S89. ^{13}C NMR (100 MHz) spectrum of **4md** in DMSO-d_6.

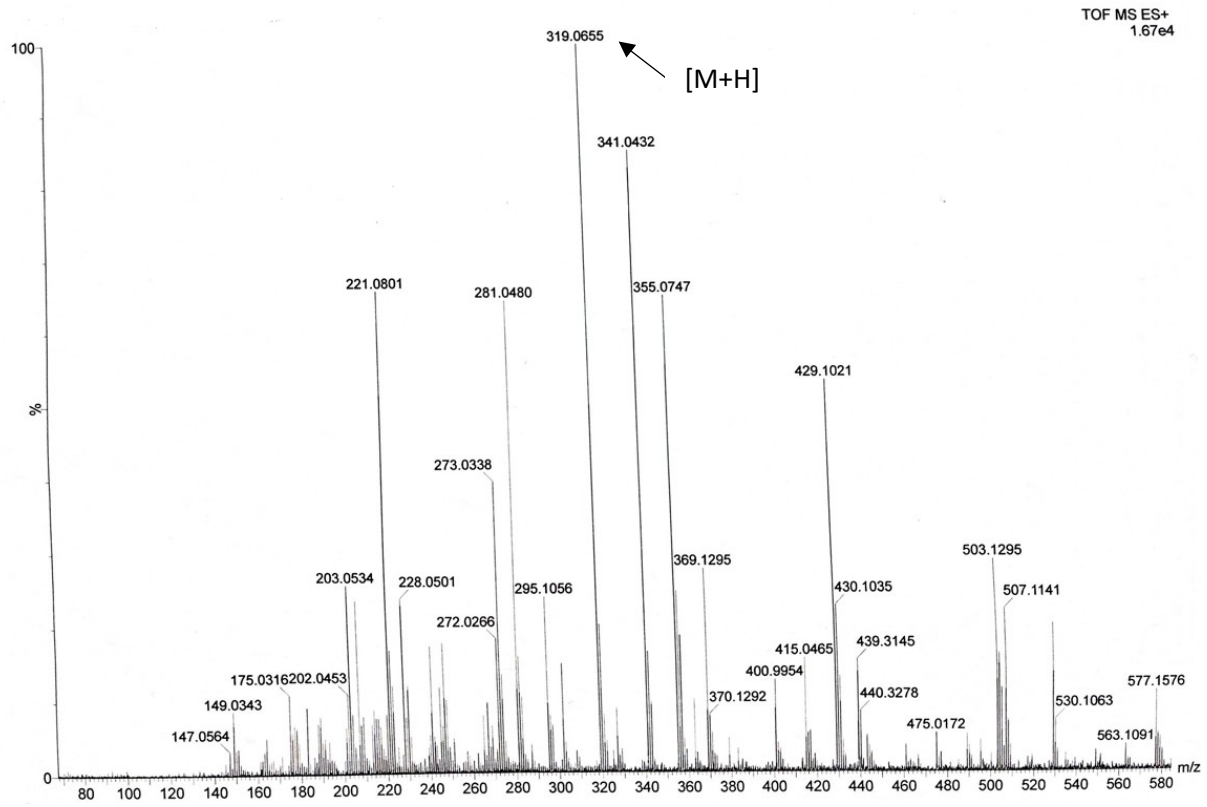


Figure S90: HRMS of compound **4md**.

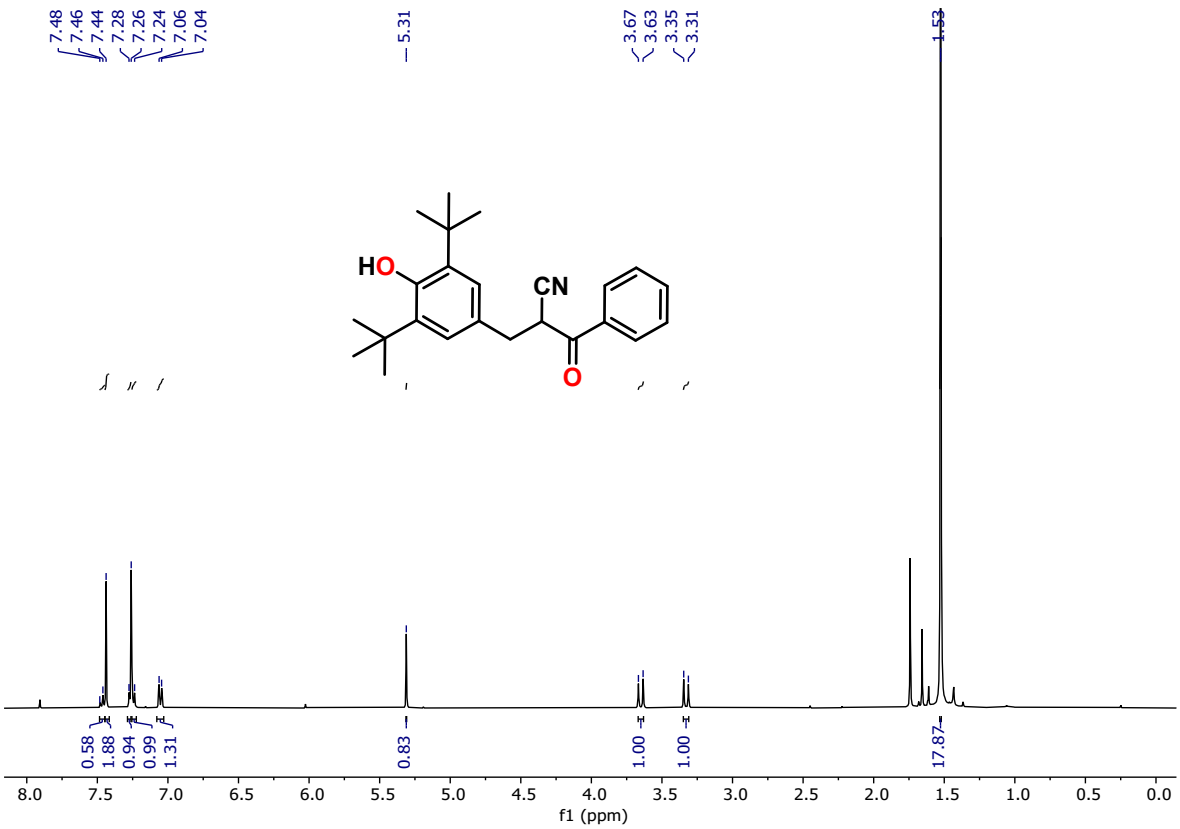


Figure S91. ^{1}H NMR (300 MHz) spectrum of **5** in $CDCl_3$.

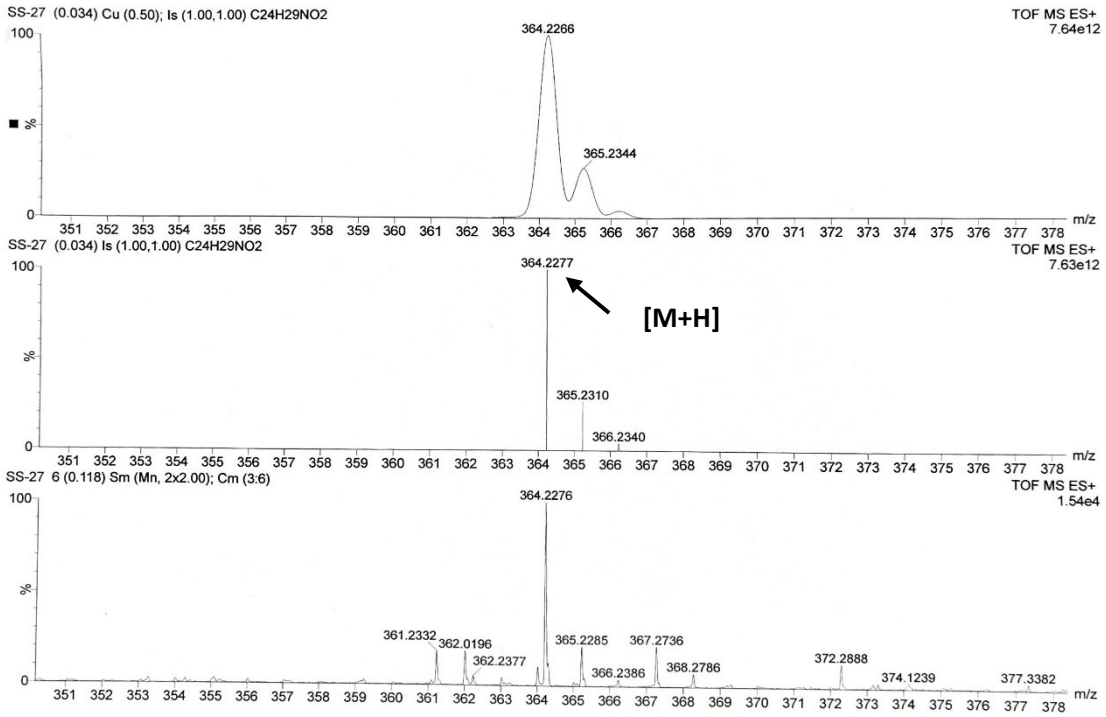


Figure S92: HRMS of compound BHT radical adduct **5**.

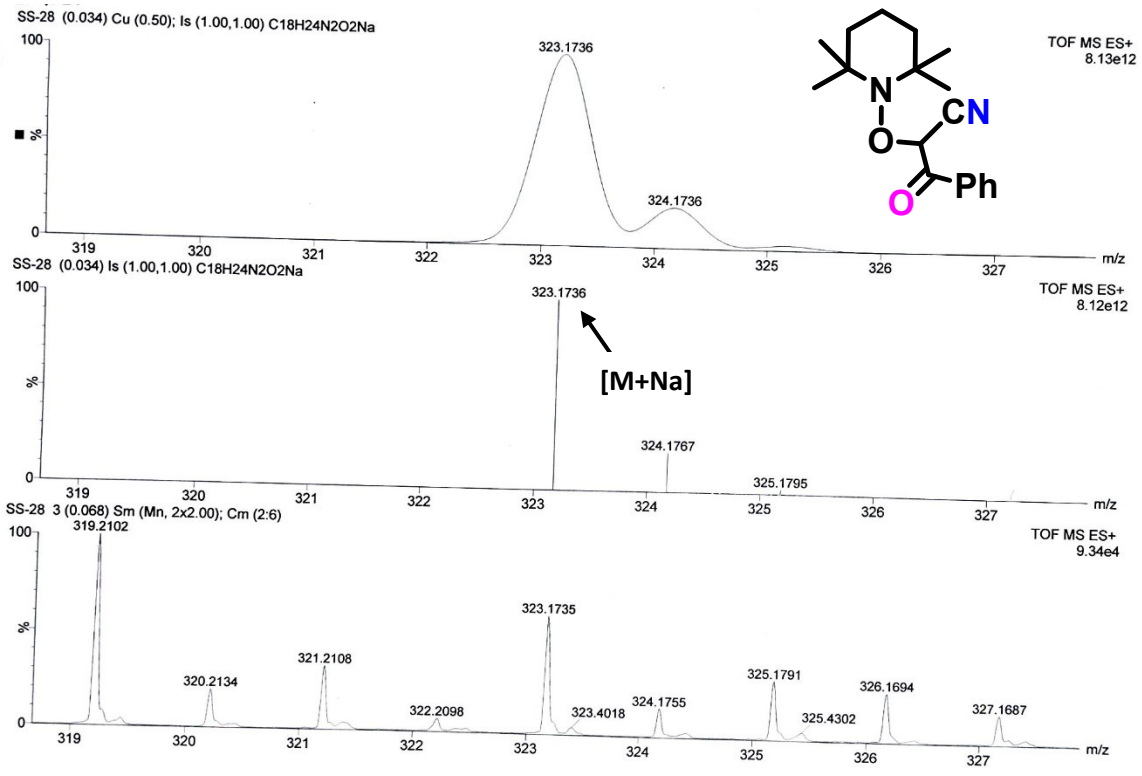


Figure S93. HRMS of TEMPO radical adduct **6**.

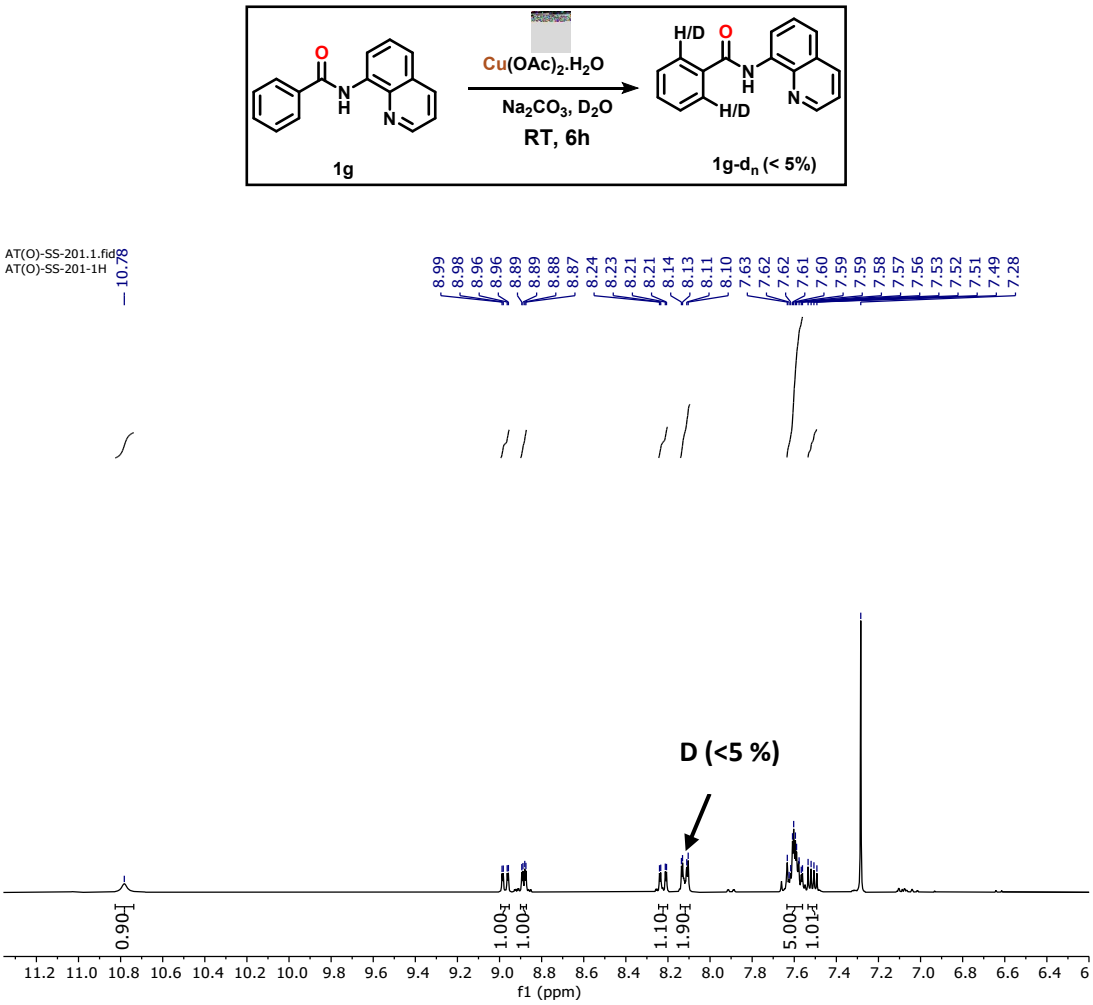


Figure S94. ^{1}H NMR of mixture of **1g** and **1g-d$_n$**.

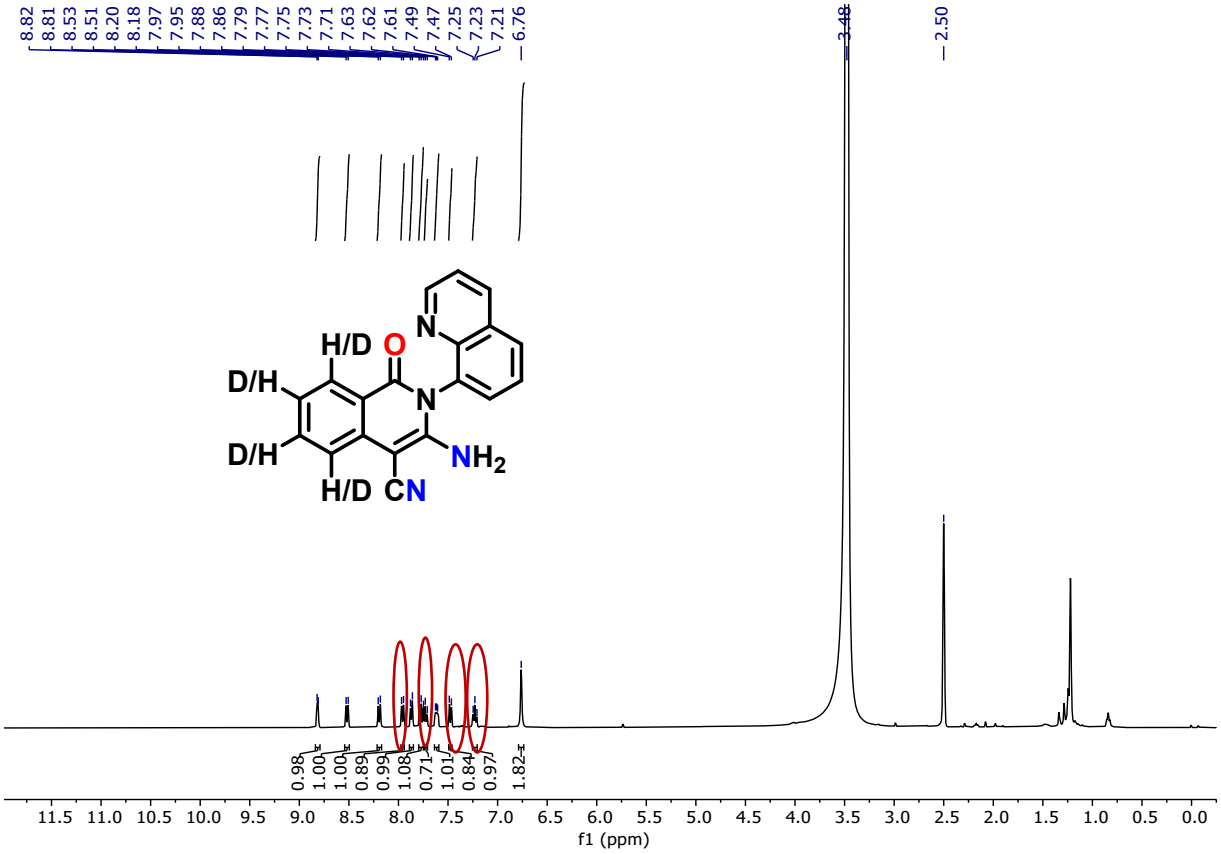


Figure S95. ^{1}H (300 MHz) NMR of mixture of compound **4g** and **[D]-4g**.

There are 3.41H instead of 4H, so the difference is (4 - 3.41) = 0.59.

Therefore k_H = 3.41 and k_D = 0.59

k_H/k_D = 3.41/0.59

= 5.77

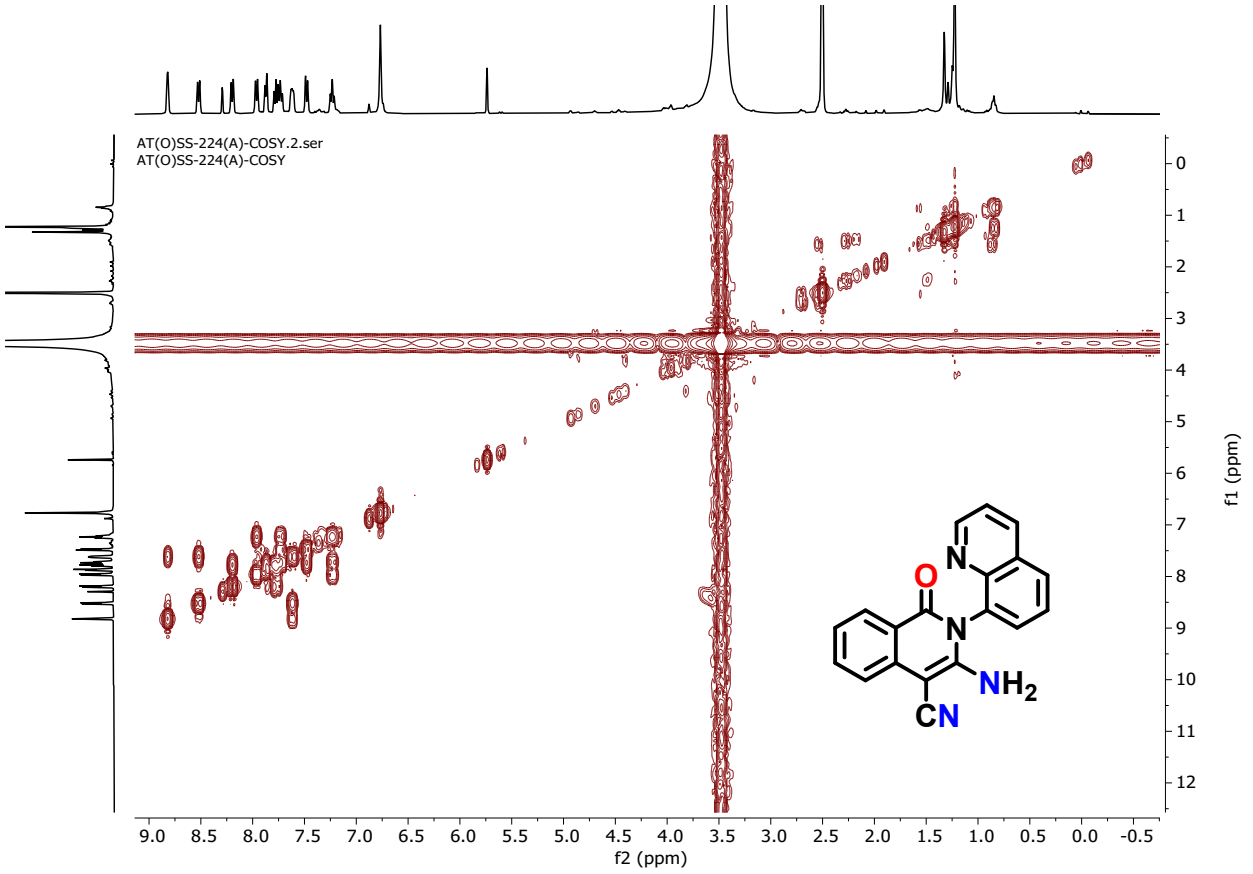


Figure S96. COSY (300 MHz) NMR of compound **4g**.

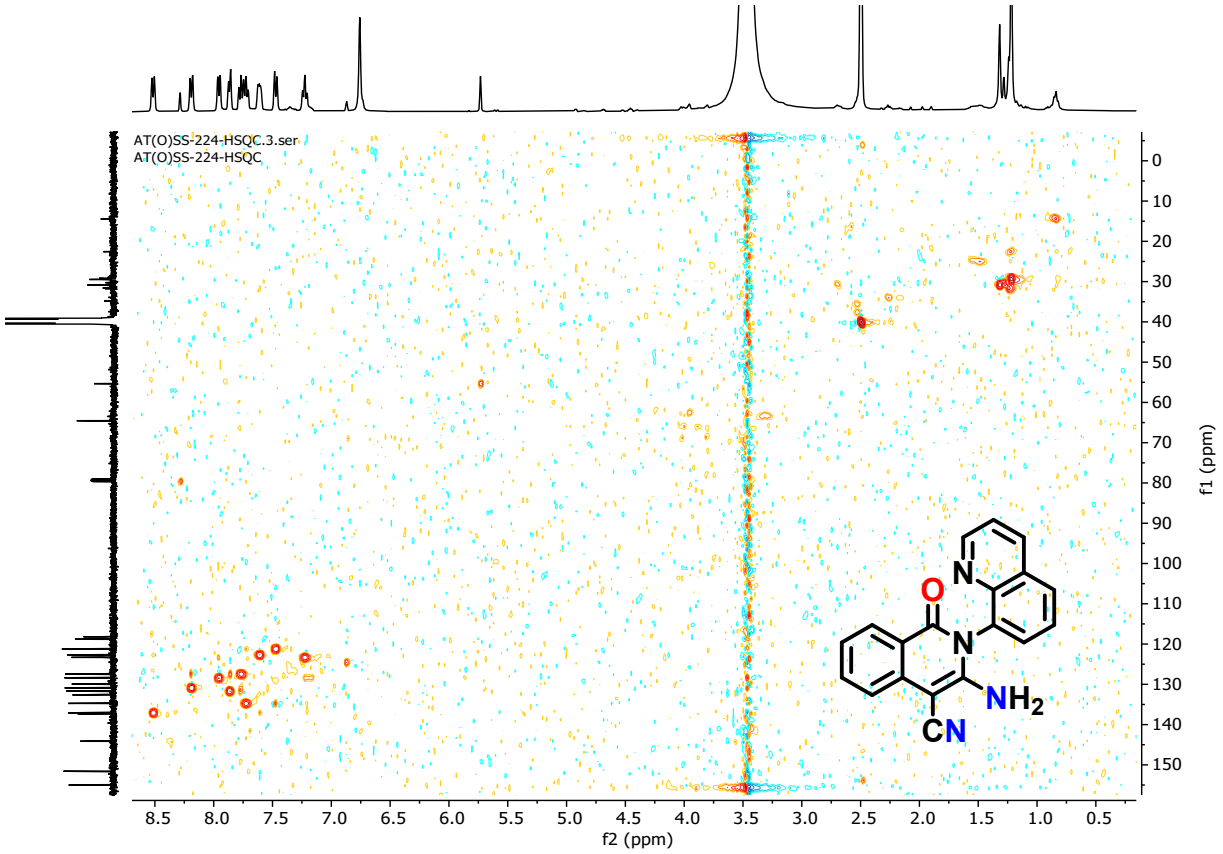
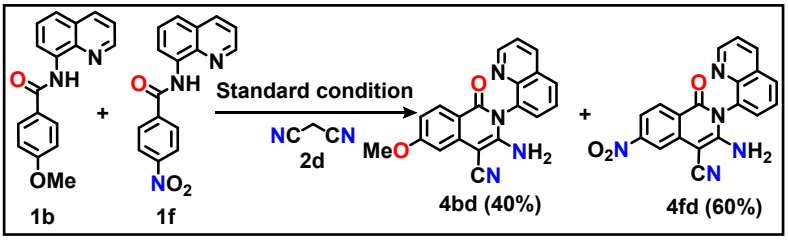


Figure S97. HSQC (300 MHz) NMR of compound **4g**.



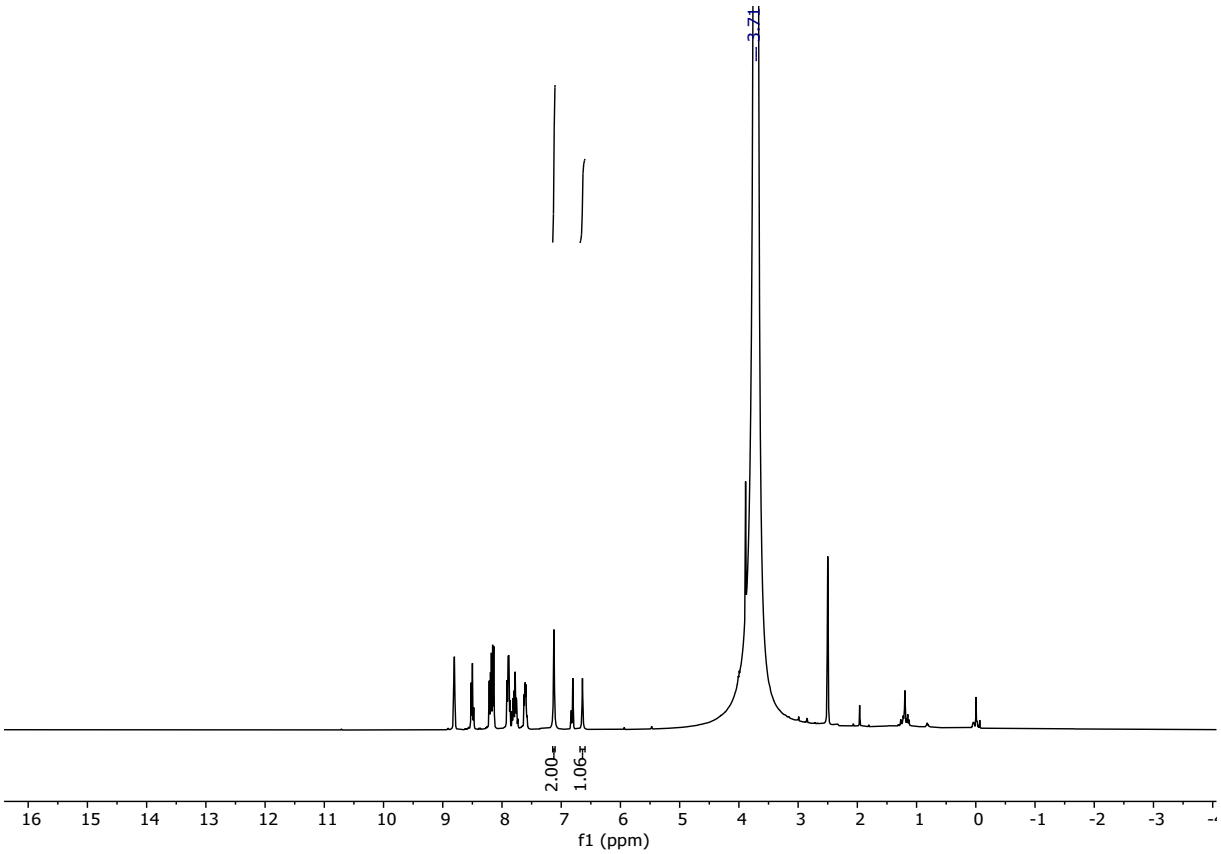


Figure S98. ^{1}H NMR of the competitive reaction between **1b** and **1f**.

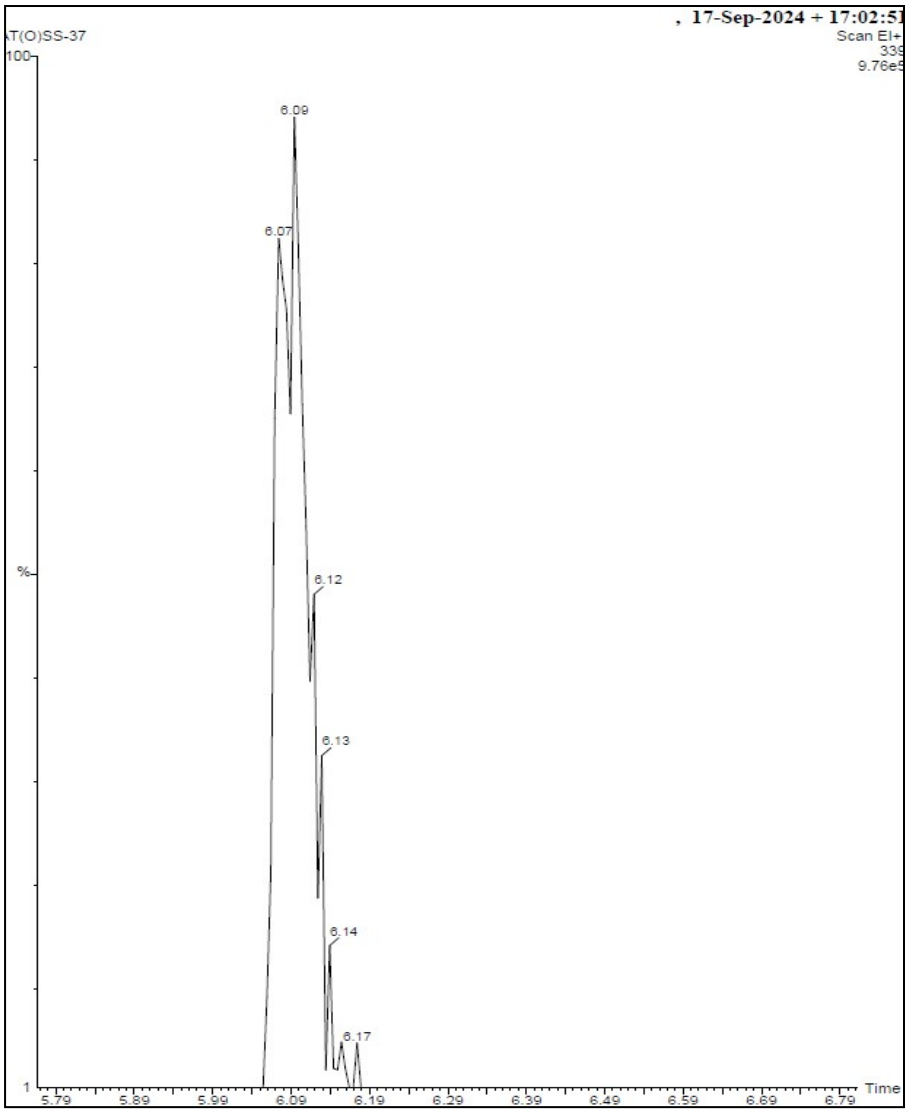


Figure S99. GC of intermediate **B**.

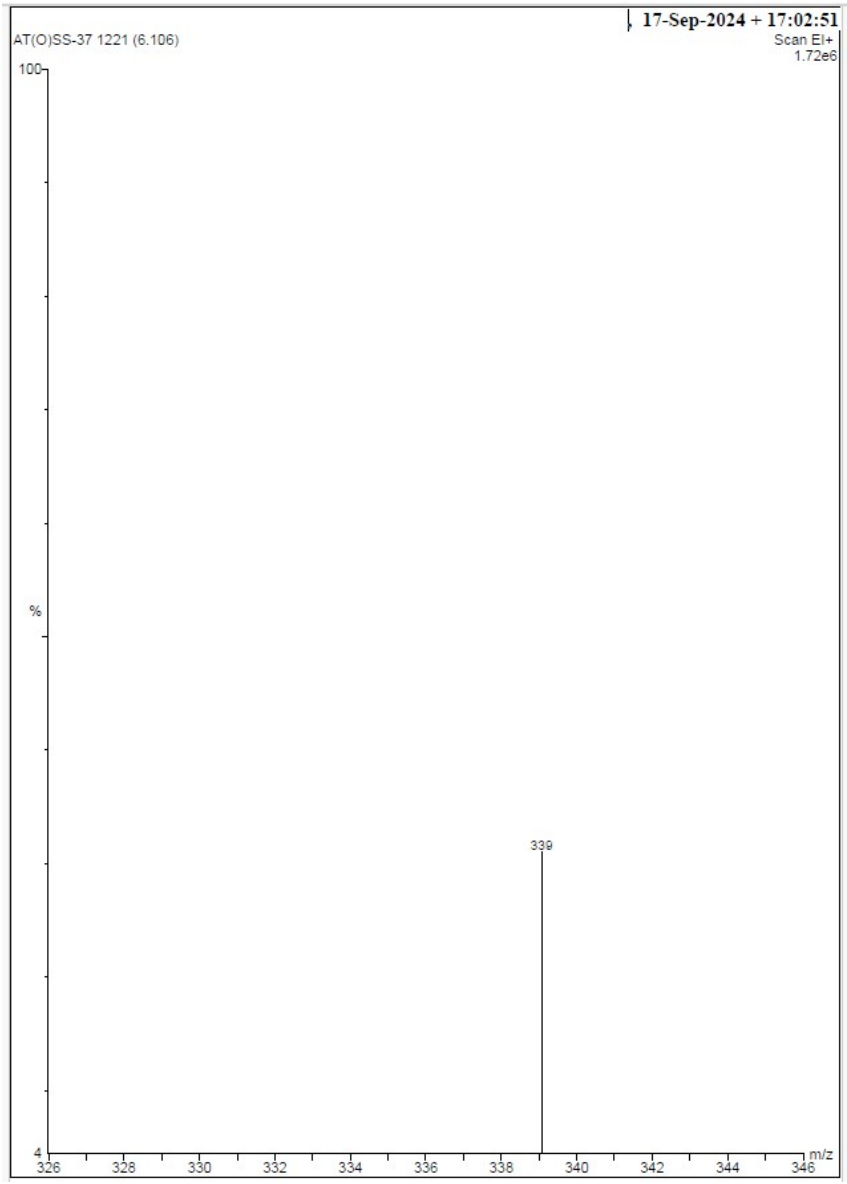


Figure S100. GCMS of intermediate **B**.

Data File: D:\GC DATA\AT\AT-SS-3.rslt\AT-SS-3.dat
Method: D:\GC 8860\Method\gas 080822.met
Acquired: 28-04-2025 17:09:25 (GMT +05:30)
Printed: 28-04-2025 19:32:34 (GMT +05:30)

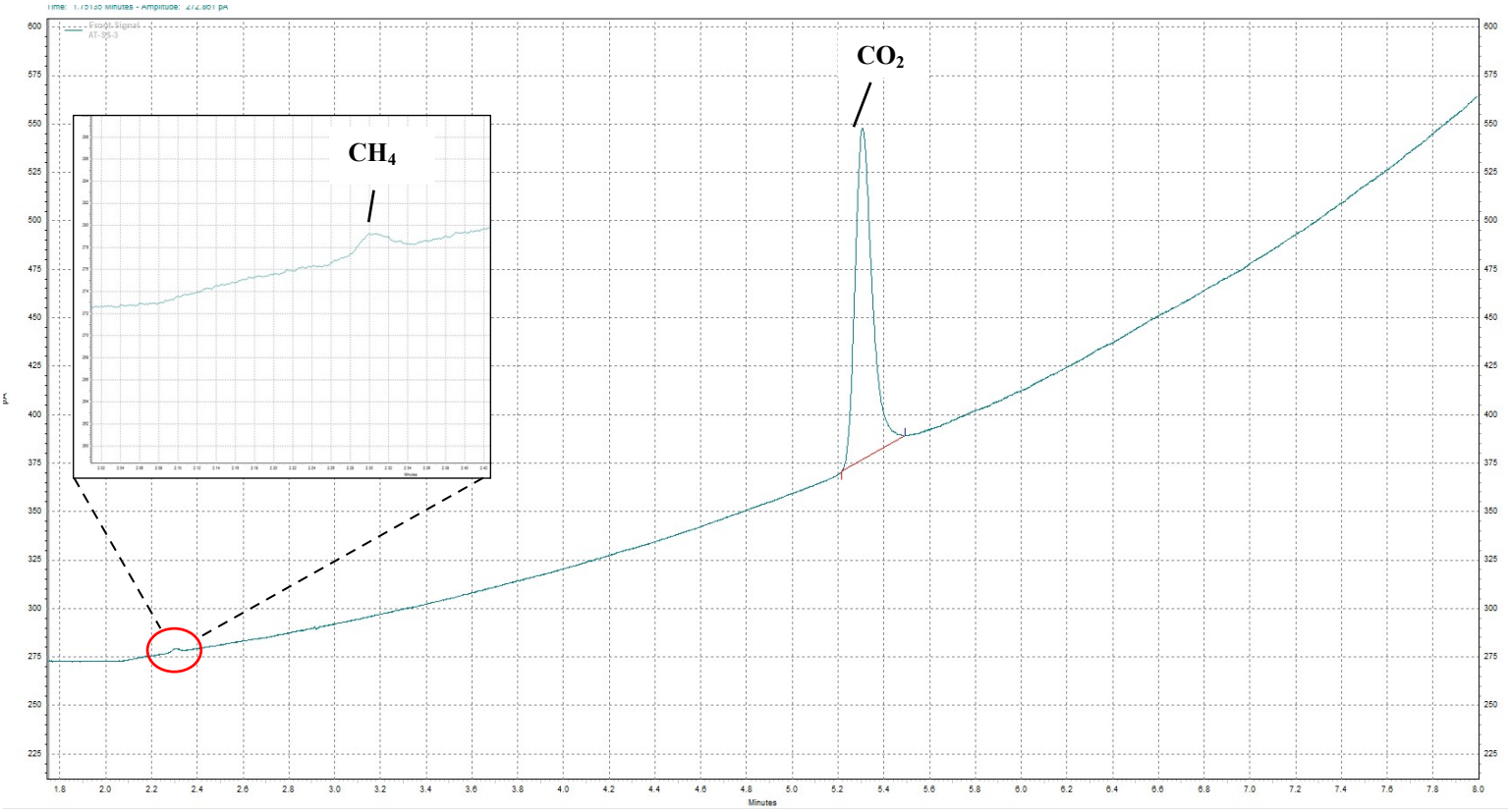


Figure S101. GC for the detection of CO_2 and CH_4 liberated in the LMCT process.

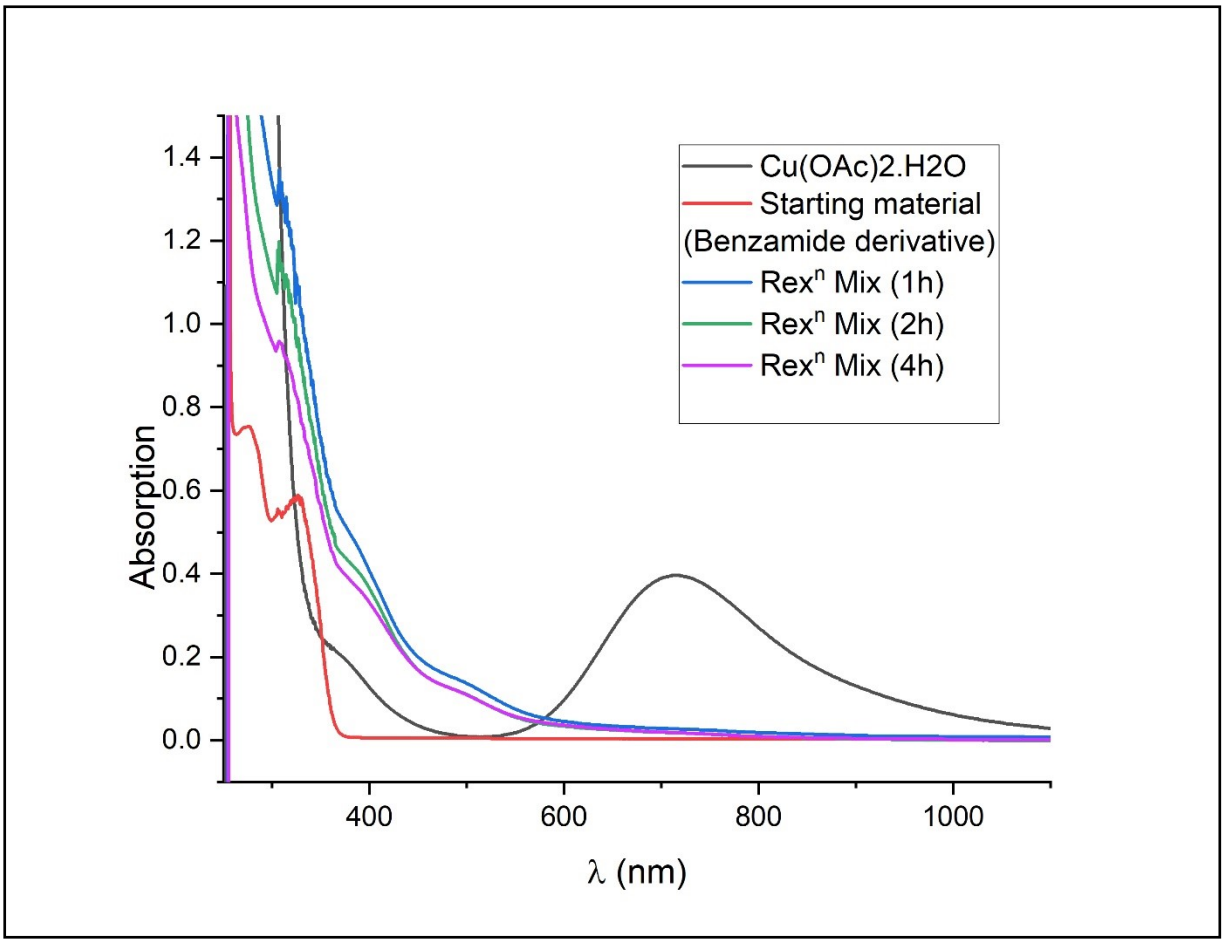


Figure S102. UV-vis spectra of $Cu(OAc)_2 \cdot H_2O$, starting material, and reaction mixture with different time intervals in DMSO solvent.

According to the literature[4] report, we found that in the case of Cu(III) complexes, the absorption band arises from 300 nm to 390 nm) whereas in the case of Cu(II) complexes, the absorption band arises from 430-460 nm. Upon reaction under standard conditions in DMSO two absorption bands appeared at 398 nm and 498 nm so we can speculate that in the reaction copper formed the chelate complex with both oxidation states Cu^{3+} and Cu^{2+} respectively.

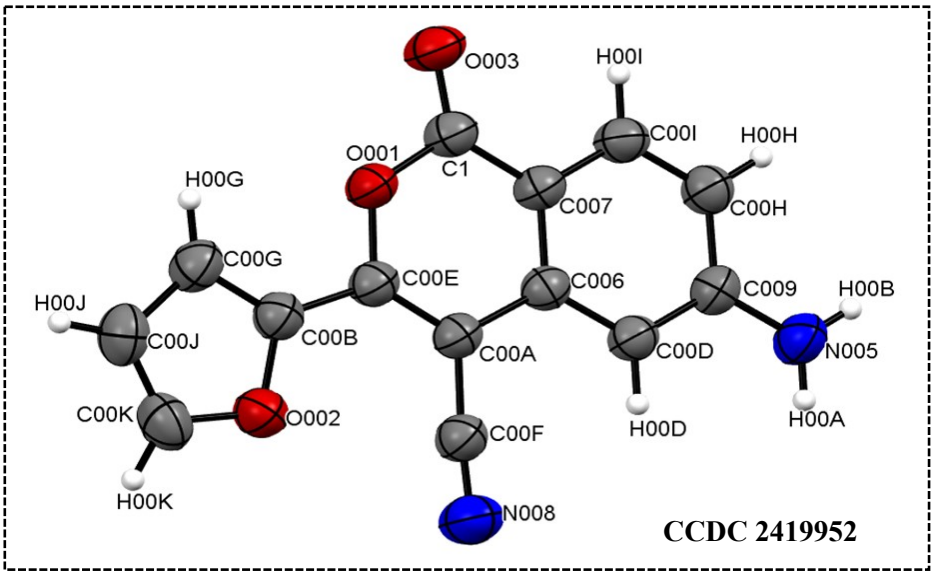


Figure S103. ORTEP representation of the molecular structure of **3db** with thermal ellipsoids drawn at the 50% probability level. Crystallization solvents (water molecules) are omitted for clarity. Selected bond lengths (Å) and angles (deg) for **3db**: C1-O003 1.210(3), O001-C1 1.391(3), O001 C00E 1.365(3), C00B-C00E 1.439(3), O002-C00B 1.367(3), N008-C00F 1.143(3), N005-C009 1.353(3), O003-C1-O001 114.29(19), O003-C1-C007 128.6(2), C00E-O001-C1 122.99(16), C00B-O002-C00K 105.70(19), N008-C00F-C00A 174.7(3), N005-C009-C00D 120.7(2), N005-C009-C00H 120.6(2).

Table S3. Crystallographic details of compound **3db**.

Empirical formula	$C_{2.43}H_{1.57}N_{0.35}O_{0.61}$
Formula weight	45.43
Crystal system	monoclinic
Space group	*C2/c*
a [Å]	a=19.198(12)
b [Å]	b=7.335(5)
c [Å]	c=16.724(1)
α [°]	90
β [°]	95.816(2)
γ [°]	90
volume [Å^3]	2343.0(3)

Z	46
F(000)	1080.0
μ MoK$_\alpha$ [mm^{-1}]	0.109
Temperature [K]	273.15
R_{int}	0.0656
Range of h, k, l	–24/24, –9/9, –21/21
$\theta_{min/max}$ (°)	2.45/27.04
GOF on F^2	1.168
Final R indices [I > 2σ(I)]	$R1$ = 0.0581 $wR2$ = 0.2101
R indices [all data]	$R1$ = 0.0928 $wR2$ = 0.2107

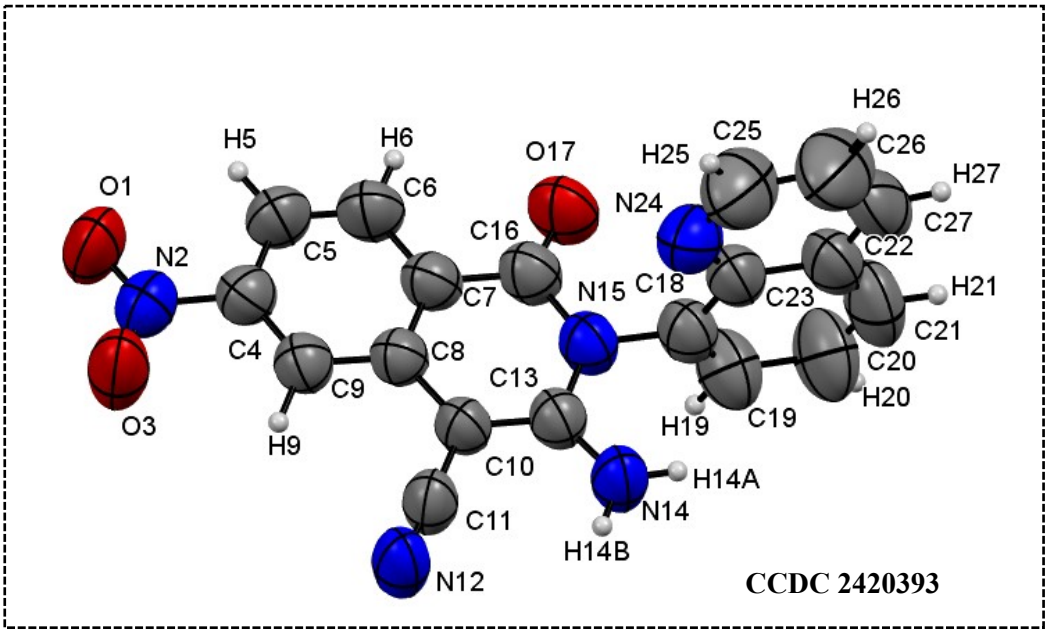


Figure S104. ORTEP representation of the molecular structure of **4fd** with thermal ellipsoids drawn at the 50% probability level. Crystallization solvents (DMSO) are omitted for clarity. Selected bond lengths (Å) and angles (deg) for **4fd**: O1-N2 1.219(5), N2-C4 1.470(6), N12-C11 1.145(5), C11-C10 1.406(5), C13-C10 1.399(5), N15-C13 1.390(5), N15-C16 1.399(5), C16-O17 1.225(4), C7-C16 1.466(6), N24-C23 1.357(6), N24-C25 1.314(7), O3-N2-O1 122.1(4), O3-N2-C4 119.1(4), O1-N2-C4 118.8(4), N14-C13-N15 118.4(3), N15-C13-C10 118.3(4), N15-C16-C7 116.8(3), N24-C23-C22 123.5(4).

Table S4. Crystallographic details of compound **4fd**.

Empirical formula	$C_{21}H_{17}N_5O_4S$
Formula weight	435.46
Crystal size (mm)	0.34 X 0.25 X 0.25
Crystal system	triclinic
Space group	P-1
a [Å]	a=7.580(6)
b [Å]	b=8.795(7)
c [Å]	c=15.937(12)
α [°]	94.493(3)
β [°]	102.417(2)
γ [°]	97.971(3)
volume [Å^3]	1021.26(14)
Z	2
F(000)	452.0
μ MoK$_\alpha$ [mm^{-1}]	0.198
Temperature [K]	273.15
R_{int}	0.0559
Range of h, k, l	–9/9, –11/11 –20/20
GOF on F^2	1.573
Final R indices [I > 2σ(I)]	$R1$ = 0.1231 $wR2$ = 0.3678
R indices [all data]	$R1$ = 0.1775 $wR2$ = 0.4441