Supporting information

Efficient synthesis of novel *N*-substituted 2-carboxy-4-quinolones via lithium bis(trimethylsilyl)amide (LiHMDS)-induced *in situ* cyclocondensation reaction

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Content

1. General information

All the reagents and solvents (analytical grade) were procured from Sigma-Aldrich, USA. Reactions were monitored by thin-layer chromatographic analysis on precoated Merck silica gel 60 F_{254} TLC aluminum sheets. Infrared spectra were recorded on Agilent Cary 630 FT-IR spectrometer; wave numbers are given in cm^{-1}. ^{1}H and ^{13}C NMR spectra were obtained on Bruker Spectrospin DPX-300 spectrometer at 300 MHz and 75 MHz, respectively or a Bruker Avance II 400 spectrometer at 400 MHz. ^{1}H and ^{13}C NMR chemical shifts (δ) values are reported in parts per million (ppm) relative to residual solvent $CDCl_3$, δ 7.26 and 77.16; DMSO-d_6, δ 2.54 and 39.5, respectively with tetramethylsilane (TMS) as an internal standard. Splitting patterns are designated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) or brs (broad) and coupling constants (*J*) are expressed in Hertz (Hz). Mass spectra were recorded on Agilent RRLC MS 6320 ion trap spectrometer fitted with an electrospray ionization (ESI) interface or Waters ZQ Single Quadrupole Detector (SQD) electron spray ionization mass spectrometer. Ultra-performance liquid chromatography was performed on API 2000 triple quadrupole detector (TQD) mass spectrometer (UPLC-MS/MS). Melting points were recorded on a digital Buchi melting point apparatus (M-560) and are uncorrected. Purification of the compounds was carried out by flash column chromatography (silica gel, 230-400 mesh size, Merck, Germany) with the indicated solvent.

2. General synthetic procedures and characterization data of all products

2.1. General procedure for reductive amination (3a-j) (Representative example 3a)

Method A: To a solution of 1-ethyl-1*H*-pyrazole-4-carboxaldehyde **1a** (1.2 g, 9.6 mmol, 1.0 eq) in DCE (22 ml) was added 2′-aminoacetophenone, **2** (1.3 g, 9.6 mmol, l.0 eq). The reaction mixture was stirred at room temperature for 30 min. Sodium triacetoxyborohydride [$Na(OAc)_3BH$] (4.051 g, 19.2 mmol, 2.0 eq) was added to the reaction mixture followed by acetic acid (0.576 g, 9.6 mmol, 1.0 eq) and the stirring was continued further at room temperature for 16 hr. The reaction was quenched with aqueous solution of sodium bicarbonate (50 mL) and the product was extracted with dichloromethane (3×50 mL). The combined organic phase was washed with brine (50 mL), dried over anhyd. sodium sulphate and concentrated

under *vacuo*. The crude obtained was purified by column chromatography eluted by a solution of ethyl acetate:hexane (2:8) to yield pure secondary amine **3a**.[1]

Method B: To a solution of 1-ethyl-1*H*-pyrazole-4-carboxaldehyde **1a** (1.2 g, 9.6 mmol, 1.0 eq) in methanol (22 ml) was added 2′-aminoacetophenone, **2** (1.3 g, 9.6 mmol, l.0 eq). The reaction mixture was stirred at room temperature for 30 min. Sodium cyanoborohydride [$NaCNBH_3$] (1.2 g, 19.2 mmol, 2.0 eq) and acetic acid (0.576 g, 9.6 mmol,1.0 eq) was added to the reaction mixture and the stirring was continued further at room temperature for 16 hr. The reaction mixture was concentrated under *vacuo* and aqueous solution of sodium bicarbonate (50 mL) was added to the residue. The product was extracted with dichloromethane (3×50 mL) and the combined organic layers were washed with brine (50 mL), dried over anhyd. sodium sulphate and concentrated. The crude product was purified by column chromatography eluted by ethyl acetate:hexane (2:8) to yield pure secondary amine **3a**.[2]

Method C: 1-Ethyl-1*H*-pyrazole-4-carboxaldehyde **1a** (1.2 g, 9.6 mmol, 1.0 eq) was dissolved in THF (20 mL) and to this solution were added 2′-aminoacetophenone, **2** (1.3 g, 9.6 mmol, l.0 eq) and dibutyltindichloride (0.583 g, 1.92 mmol, 0.2 eq). After stirring for 20 min, phenyl silane (1.036 g, 9.6 mmol, 1.0 eq) was added and the reaction mixture was stirred further at room temperature for 16 hr. After completion of the reaction the reaction mixture was diluted with water and the compound was extracted with ethyl acetate. The combined organic layers were washed with brine solution, dried over anhyd. sodium sulphate and concentrated under *vacuo*. The product was purified by column chromatography eluted with ethyl acetate: hexane (2:8) to yield pure product **3a** in quantitative yield.[3]

1-((2-((1-ethyl-1*H*-pyrazol-4-yl)methyl)amino)phenyl)ethanone (3a)

Yellow oil, yield: 76%, R_f = 0.60 (Ethyl acetate/ hexane, 40:60), ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.86 (s, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.71 (s, 1H), 7.41-7.37 (m, 2H), 6.84 (d, J = 8.5 Hz, 1H,), 6.61 (t, J = 7.3 Hz, 1H), 4.24 (d, J = 4.9 Hz, 2H) 4.09 (q, J = 7.2 Hz, 2H), 2.50 (s. 3H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.36, 148.62, 136.23,

134.54, 129.67, 125.82, 120.64, 118.03, 114.25, 111.82, 54.59, 39.02, 28.95, 15.43. ESI-MS (*m/z*): 244.14 $[M+H]^+$.

1-((2-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)amino)phenyl) ethanone (3b)

Yellow solid, yield: 87%, R_f = 0.50 (Ethyl acetate/ hexane, 40:60), mp 112-114 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.91 (m, 2H), 8.57-8.54 (m, 2H), 8.12 (d, J = 8.3 Hz, 1H), 7.86-7.79 (m, 3H), 7.49-7.46 (m, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 8.9 Hz, 2H), 6.89 (d, J = 8.5 Hz, 1H), 6.66 (t, J = 6.9 Hz, 1H), 4.50 (s, 2H), 3.81 (s, 3H), 3.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.06, 158.48, 150.29, 148.94, 148.71, 147.68, 135.19, 134.93, 133.57, 132.79, 129.26, 127.82, 123.54, 120.80, 118.43, 118.03, 114.85, 114.55, 111.89, 55.59, 38.02, 27.95. ESI-MS (*m/z*): 399.0 $[M+H]^+$.

1-((2-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)amino)phenyl)ethanone (3c)

Light yellow oil, yield: 84%, R_f = 0.54 (Ethyl acetate/ hexane, 40:60), ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.95 (s, 1H), 8.93 (s, 1H), 7.89-7.84 (m, 3H), 7.75 (d, J = 7.2 Hz, 2H), 7.52 (t, J = 7.9 Hz, 2H), 7.47-7.37 (m, 4H), 7.33 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 6.65 (t, J = 7.5 Hz, 1H), 4.48 (s, 2H), 2.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 199.89, 150.45, 148.78, 140.19, 134.94, 133.64, 130.79, 129.53, 128.45, 128.12, 127.62, 126.81, 123.23, 120.61, 118.37, 118.01, 115.85, 113.58, 37.02, 28.95. ESI-MS (*m/z*): 368.1 $[M+H]^+$.

1-((2-((5-bromopyridin-2-yl)methyl)amino)phenyl)ethanone (3d)

Light yellow solid, yield: 61%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 88-90 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 9.36 (s, 1H), 8.58-8.51 (m, 2H), 7.80 (d, J = 7.8 Hz, 2H), 7.34-7.27 (m, 1H), 6.67 (t, J = 7.5 Hz, 1H), 6.55 (d, J = 8.7 Hz, 1H), 4.48 (d, 2H, J = 6.0 Hz, CH_2), 2.62 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.76, 155.69, 152.24, 149.67,

145.23, 136.03, 129.78, 129.47, 125.45, 118.54, 115.93, 113.62, 111.92, 46.82, 28.78. ESI-MS (*m/z*): 305.1 $[M+H]^+$, 307.0 $[(M+2)+H]^+$.

1-((2-((4-chloropyridin-2-yl)methyl)amino)phenyl)ethanone (3e)

Light yellow solid, yield: 67%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 78-81 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 9.41 (s, 1H), 8.54 (s, 1H), 7.86 (d, J = 7.5 Hz, 1H), 7.44 (s, 2H), 7.35 (t, J = 7.4 Hz, 1H), 6.68-6.61 (m, 2H), 4.58 (d, J = 5.3 Hz, 2H), 2.57 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.21, 160.71, 150.40, 145.06, 135.14, 132.81, 122.59, 121.30, 118.29, 115.04, 112.09, 48.28, 28.00. ESI-MS (*m/z*): 261.2 $[M+H]^+$.

1-(2-(4-(1*H*-pyrazol-1-yl)benzylamino)phenyl)ethanone (3f)

Off-white solid, yield: 98%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 141-143 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 9.34 (s, 1H), 7.88 (s, 1H), 7.77 (d, J = 7.9 Hz, 1H), 7.70 (s. 1H), 7.64 (d, J = 8.4 Hz, 2H),7.41 (d, J = 8.3 Hz, 2H), 7.28 (t, J = 7.8 Hz, 1H), 6.63-6.59 (m, 2H), 6.44 (s, 1H), 4.49 (d, J = 5.6 Hz, 2H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.15, 150.73, 141.03, 139.29, 137.08, 135.06, 132.77, 127.99, 126.74, 119.53, 117.97, 114.64, 112.20, 107.56, 46.19, 28.03. ESI-MS (*m/z*): 292.1 $[M+H]^+$.

1-(2-(4-(trifluoromethyl)benzylamino)phenyl)ethanone (3g)

Light yellow solid, yield: 98%, R_f = 0.54 (Ethyl acetate/ hexane, 40:60), mp 83-85 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 9.39 (s, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 7.8 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.31-7.25 (m, 1H), 6.63 (t, J = 7.5 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 4.52 (d, J = 5.7 Hz, 2H), 2.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.24, 150.58, 143.04, 135.09, 132.82, 129.68, 127.13, 125.66, 122.38, 118.11, 114.90, 112.05, 46.29, 27.99. ESI-MS (*m/z*): 294.1 $[M+H]^+$.

1-(2-(4-(trifluoromethoxy)benzylamino)phenyl)ethanone (3h)

Light yellow solid, yield: 93%, R_f = 0.74 (Ethyl acetate/ hexane, 40:60), mp 70-73 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 9.33 (s, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.37-7.25 (m, 3H), 7.17 (d, *J* = 8.1 Hz, 2H), 6.65-6.58 (m, 2H), 4.46 (d, *J* = 5.7 Hz, 2H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.16, 150.65, 148.31, 137.52, 135.09, 132.79, 128.29, 121.22, 118.02, 114.76, 112.04, 46.01, 27.98. ESI-MS (*m/z*): 255.1, 283.3, 311.4.

1-((2-(furan-2-ylmethyl)amino)phenyl)ethanone (3i)

Light yellow solid, yield: 95%, R_f = 0.64 (Ethyl acetate/ hexane, 40:60), mp 76-78 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 9.19 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.37-7.32 (m, 2H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.31-6.22 (m, 2H), 4.42 (d, *J* = 5.4 Hz, 2H), 2.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 200.98, 152.12, 150.52, 141.95, 135.00, 132.70, 118.05, 114.70, 111.84, 110.34, 106.87, 40.09, 27.94. ESI-MS (*m/z*): 234.4.

1-((2-((2-bromo-3-fluoropyridin-4-yl)methyl)amino)phenyl)ethanone (3j)

Off-white solid, yield: 98%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 90-92 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 9.39 (s, 1H), 8.09 (d, *J* = 4.8 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.35-7.29 (m, 1H), 7.20 (t, *J* = 4.9 Hz, 1H), 6.69 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 8.7 Hz, 1H), 4.59 (d, *J* = 6.0 Hz, 2H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 201.48, 155.72, 152.29, 149.93, 145.59, 137.03, 135.28, 132.96, 129.78, 122.57, 118.48, 115.68, 111.62, 39.82, 28.04. ESI-MS (*m/z*): 323.1 $[M+H]^+$, 325.1 $[(M+2)+H]^+$.

2.2. General procedure for the synthesis of *N*-substituted ethyl 4-oxo-1,4-dihydroquinoline-2-carboxylate (4a-j) (Representative example 4a)

To the solution of LiHMDS (1M solution in THF) (10 mL, 10 mmol, 2.5 eq), kept at -60 °C, was added a solution of secondary amine (**3a-d, f-j**) (1.0 g, 4.1 mmol, 1.0 eq) in THF (20 ml) and the reaction mixture was stirred for 30 min. Then a solution of diethyl oxalate (1.5 g, 10 mmol, 2.5 eq) in THF (5mL) was added drop wise over a period of 20 min at -60 °C. The reaction mixture was then refluxed for 16 hr. The reaction was cooled and quenched with saturated solution of

NH_4Cl (50 mL) and the compound was extracted with ethyl acetate (3×20 mL). The combined organic layers were washed with brine, dried over anhyd. sodium sulphate and concentrated under *vacuo*. The crude product was purified by column chromatography eluted with ethyl acetate: hexane (4:6) to yield pure product.

Ethyl 1-((1-ethyl-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4a)

Light brown solid, yield: 45%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 87-89 °C. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.17 (d, J = 7.8 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.68 (s, 1H), 7.44-7.40 (m, 2H), 6.39 (s, 1H), 5.36 (s, 2H), 4.41 (q, J = 7.1 Hz, 2H), 4.04 (q, J = 7.2 Hz, 2H), 1.31-1.23 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 179.02, 164.26, 153.78, 144.47, 140.25, 135.38, 129.98, 127.61, 126.89, 118.04, 116.94, 114.55, 112.10, 63.28, 53.58, 43.28, 14.45, 13.82. ESI-MS (*m/z*): 326.1 $[M+H]^+$.

Ethyl 1-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4b)

Yellow solid, yield: 44%, R_f = 0.30 (Ethyl acetate/ hexane, 40:60), mp 164-166 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.94 (s, 1H), 8.62 (s, 1H), 8.19-8.12 (m, 3H), 7.73-7.66 (m, 4H), 7.52-7.49 (m, 1H), 7. 41 (m, 1H), 6.99 (d, J = 8.9 Hz, 2H), 6.44 (s, 1H), 5.67 (s, 2H), 4.20-4.19 (m, 2H), 3.76 (s, 3H), 1.09 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 178.10, 163.66, 158.71, 149.14, 148.38, 146.47, 143.65, 141.05, 135.46, 133.34, 133.10, 128.98, 127.72, 127.38, 126.89, 124.45, 123.89, 120.73, 117.04, 116.57, 114.55, 113.10, 63.14, 55.58, 45.28, 13.93. ESI-MS (*m/z*): 481.0 $[M+H]^+$.

Ethyl 1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4c)

Off-white solid, yield: 69%, R_f = 0.54 (Ethyl acetate/ hexane, 40:60), mp 150-152 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.20-8.18 (m, 2H), 7.82-7.76 (m, 4H), 7.71-7.67 (m, 1H),

7.62-7.60 (m, 1H), 7.52-7.48 (m, 2H), 7.46-7.39 (m, 4H), 7.29-7.25 (m, 1H), 6.45 (s, 1H), 5.64 (s, 2H), 4.19 (q, J = 7.1 Hz, 2H), 1.09 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 178.10, 163.78, 150.42, 143.92, 141.01, 139.59, 133.22, 132.51, 129.40, 128.96, 128.62, 128.03, 127.36, 126.78, 124.35, 118.97, 116.93, 116.82, 112.78, 63.11, 45.52, 13.94. ESI-MS (*m/z*): 450.6 $[M+H]^+$.

Ethyl 1-((5-bromopyridin-2-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4d)

Brown solid, yield: 69%, R_f = 0.54 (Ethyl acetate/ hexane, 40:60), mp 140-142 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.63 (s, 1H), 8.40 (s, 1H), 8.21 (d, J = 7.2 Hz, 1H), 7.85 (s, 1H), 7.72 (t, J = 7.3 Hz, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.44 (t, J = 7.3 Hz, 1H), 6.54 (s, 1H), 5.61 (s, 2H), 4.31 (q, J = 7.0 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 180.10, 164.58, 154.78, 150.42, 145.29, 143.81, 135.69, 132.76, 130.51, 128.66, 120.35, 117.97, 116.93, 114.82, 112.78, 63.11, 54.52, 13.90. ESI-MS (*m/z*): 388.46 $[M+H]^+$.

Ethyl 1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4f)

Creamish solid, yield: 69%, R_f = 0.44 (Ethyl acetate/ hexane, 40:60), mp 214-216 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.64 (s, 1H), 8.56 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H), 7.71 (d, J = 8.4 Hz, 3H), 7.56 (t, J = 7.1 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.32-7.25 (m, 3H), 6.47 (s, 1H), 5.43 (s, 2H), 4.42 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 174.42, 165.67, 149.65, 141.45, 140.27, 139.00, 132.65, 132.28, 129.26, 127.95, 127.29, 126.69, 125.27, 119.82, 116.49, 111.35, 108.05, 60.99, 56.93, 14.46. ESI-MS (*m/z*): 374.5 $[M+H]^+$.

Ethyl 1-(4-(trifluoromethyl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4g)

Brown solid, yield: 53%, R_f = 0.34 (Ethyl acetate/ hexane, 40:60), mp 108-110 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.44 (d, J = 8.1 Hz, 1H), 7.68-7.55 (m, 3H), 7.39 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 9.0 Hz, 3H), 6.80 (s, 1H), 5.57 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.2

Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 178.18, 163.51, 143.86, 141.31, 140.17, 133.40, 130.37, 127.38, 126.93, 126.23, 126.03, 125.68, 124.51, 116.76, 113.33, 63.13, 52.62, 13.83. ESI-MS (*m/z*): 374.2 $[M-H]^-$, 376.3 $[M+H]^+$.

Ethyl 1-(4-(trifluoromethoxy)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4h)

Light Yellow solid, yield: 59%, R_f = 0.54 (Ethyl acetate/ hexane, 40:60), mp 76-78 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.44 (d, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.42-7.33 (m, 2H), 7.26-7.19 (m, 4H), 6.77 (s, 1H), 5.52 (s, 2H), 4.40-4.31 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 179.23, 164.21, 158.81, 154.26, 144.86, 135.47, 133.26, 130.62, 128.76, 127.23, 122.51, 118.97, 116.76, 115.34, 114.89, 64.13, 51.62, 14.21. ESI-MS (*m/z*): 392.1 $[M+H]^+$.

Ethyl 1-(furan-2-ylmethyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4i)

Brown solid, yield: 53%, R_f = 0.34 (Ethyl acetate/ hexane, 40:60), mp 71-73 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.43 (d, *J* = 7.8 Hz, 1H), 7.71-7.69 (m, 2H), 7.49-7.35 (m, 2H), 6.73 (s, 1H), 6.31-6.27 (m, 2H), 5.58 (s, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 178.13, 163.78, 149.05, 143.36, 142.61, 141.28, 133.09, 127.39, 126.81, 124.28, 116.48, 113.40, 110.71, 109.00, 62.99, 44.78, 13.97. ESI-MS (*m/z*): 302.1.

Ethyl 1-((2-bromo-3-fluoropyridin-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4j)

Light brown, yield: 54%, R_f = 0.34 (Ethyl acetate/ hexane, 40:60), mp 210-212 °C, ^{1}H NMR (300 MHz, $CDCl_3$) (δ, ppm): 8.44 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 4.8 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 6.89-6.83 (m, 2H), 5.57 (s, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 178.17,

163.23, 154.63, 151.20, 145.81, 142.97, 141.16, 134.38, 133.84, 130.11, 127.29, 124.86, 121.93, 115.95, 114.36, 63.36, 47.02, 13.88. ESI-MS (*m/z*): 403.1 $[M-H]^-$, 405.2 $[M+H]^+$.

General procedure for the hydrolysis of *N*-substituted ethyl 4-oxo-1,4-dihydroquinoline-2-carboxylate (5a-j) (Representative hydrolysis of 4a)

The compound **4a** (0.2 g, 0.61 mmol, 1.0 eq) was dissolved in THF (6 mL) and water (2 mL) mixture. To this solution $LiOH.H_2O$ (0.056 g, 1.35 mmol, 2.2 eq) was added and the reaction mixture was stirred for 4 hr at room temperature. After completion of the reaction, it was concentrated under *vacuo*. The residue was dissolved in water (50 mL) and acidified with 1N HCl up to pH-2~3. The compound was extracted with ethyl acetate (3×50 mL) and the combined organic layer was washed with brine (50 mL), dried over anhyd. sodium sulphate and concentrated under *vacuo* to afford 0.040 g (22 %) off white solid compound **5a**.[4]

1-((1-ethyl-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5a)

Light yellow solid, yield: 22%, R_f = 0.44 (Methanol/ DCM, 10:90), mp 182-184 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.17 (d, J = 7.5 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.77-7.69 (m, 2H), 7.42 (m, 2H), 6.34 (s, 1H), 5.43 (s, 2H), 4.05-4.00 (m, 2H), 1.28 (t, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 180.14, 165.47, 152.39, 143.51, 140.27, 135.78, 131.28, 128.56, 125.72, 119.45, 117.95, 113.42, 112.54, 54.76, 43.34, 14.78. ESI-MS (*m/z*): 298.2 $[M+H]^+$.

1-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5b)

Yellow solid, yield: 63%, R_f = 0.1 (Methanol/ DCM, 10:90), mp 164-166 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.98 (s, 1H), 8.65 (s, 1H), 8.19-8.16 (m, 2H), 8.06 (s, 1H), 7.76-7.52 (m, 5H), 7.38 (t, J = 7.4 Hz, 1H), 6.98 (d, J = 9.0 Hz, 2H), 6.40 (s, 1H), 5.72 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 177.14, 165.39, 158.29, 149.39, 148.58, 146.52,

144.51, 141.19, 135.51, 133.23, 129.06, 128.34, 127.19, 125.96, 124.25, 120.38, 118.45, 114.95, 110.54, 55.86, 43.16. ESI-MS (*m/z*): 451.4 $[M-H]^-$, 453.3 $[M+H]^+$.

1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5c)

Light brown solid, yield: 74%, R_f = 0.44 (Methanol/ DCM, 10:90), mp 177-179 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.19 (d, J = 8.4 Hz, 2H), 8.12 (s, 1H), 7.80-7.74 (m, 2H), 7.63 (t, J = 7.3 Hz, 2H), 7.55-7.36 (m, 7H), 7.27 (t, J = 7.2 Hz, 1H), 6.43 (s, 1H), 5.69 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 178.54, 164.49, 152.29, 150.39, 145.26, 140.19, 135.23, 133.27, 130.72, 129.42, 128.46, 127.36, 126.64, 125.96, 123.78, 120.67, 118.45, 117.56, 114.95, 112.96, 42.16. ESI-MS (*m/z*): 420.5 $[M-H]^-$, 422.5 $[M+H]^+$.

1-((5-bromopyridin-2-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5d)

Light brown solid, yield: 74%, R_f = 0.44 (Methanol/ DCM, 10:90), mp 171-173 °C, ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.62 (s, 1H), 8.41 (s, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.87 (s, 1H), 7.69 (t, J = 7.9 Hz, 1H), 7.59 (d, J = 8.7 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 6.49 (s, 1H), 5.64 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 177.04, 165.20, 149.71, 147.02, 146.76, 140.94, 137.13, 135.37, 133.75, 127.14, 126.17, 124.74, 120.58, 118.16, 110.90, 50.19.ESI-MS (*m/z*): 357.1 $[M-H]^-$, 361.2 $[(M+2)+H]^+$.

1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5f)

Off-white solid, yield: 64%, R_f = 0.34 (Methanol/ DCM, 40:60), mp 278-280 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 15.14 (s, 1H), 9.32 (s, 1H), 8.44-8.39 (m, 2H), 7.89-7.81 (m, 4H), 7.72 (s, 1H), 7.62 (t, J = 6.9 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 6.52 (s, 1H), 5.91 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 178.48, 166.50, 150.68, 141.58, 139.91, 139.84,

134.63, 133.59, 128.49, 128.23, 126.82, 126.45, 126.26, 119.27, 119.08, 108.42, 56.46. ESI-MS (*m/z*): 346.2 $[M+H]^+$.

1-(4-(trifluoromethyl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5g)

Off-white solid, yield: 86%, R_f = 0.44 (Methanol/ DCM, 10:90), mp 210-212 °C. ^{1}H NMR (300 MHz, DMSO) (δ, ppm): 8.24 (m, 1H, Ar-H), 7.72-7.42 (m, 6H, Ar-H), 6.50 (s, 1H, Ar-H), 5.75 (s, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) (δ, ppm): 176.96, 165.28, 147.61, 142.12, 140.97, 133.55, 128.18, 127.54, 127.40, 126.09, 124.62, 118.29, 110.39, 52.18. ESI-MS (*m/z*): 348.2 $[M+H]^+$.

1-(4-(trifluoromethoxy)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5h)

Off-white solid, yield: 63%, R_f = 0.1 Methanol/ DCM, 10:90), mp 173-175 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.29-8.27 (m, 1H), 7.75-7.65 (m, 3H), 7.48-7.39 (m, 4H), 6.55 (s, 1H), 5.74 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 176.89, 165.31, 147.90, 147.44, 140.92, 136.59, 133.53, 128.57, 127.18, 126.07, 124.64, 121.72, 118.38, 110.32, 51.81. ESI-MS (*m/z*): 364.2 $[M+H]^+$.

1-(furan-2-ylmethyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5i)

Off-white solid, yield: 88%, R_f = 0.44 (Methanol/ DCM, 10:90), mp 179-180 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.19 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 9.0 Hz, 1H), 7.79 (t, J = 7.8 Hz, 1H), 7.62-7.60 (m, 1H), 7.45 (t, J = 7.5 Hz, 1H, Ar-), 6.46-6.41 (m, 3H), 5.76 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 176.87, 165.44, 149.72, 146.49, 145.18, 143.59, 141.03, 133.44, 127.08, 125.98, 124.66, 118.26, 111.17, 109.64, 44.49. ESI-MS (*m/z*): 270.2 $[M+H]^+$.

1-((2-bromo-3-fluoropyridin-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5j)

Light yellow solid, yield: 81%, R_f = 0.1 (Methanol/ DCM, 10:90), mp 173-175 °C, ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 8.22 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 4.8 Hz, 1H), 7.74-7.54 (m, 2H), 7.44 (t, J = 7.5 Hz, 1H), 6.92 (t, J = 5.1 Hz, 1H), 6.53 (s, 1H), 5.75 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 177.28, 164.97, 147.35, 146.50, 141.32, 136.36, 136.18, 133.85, 129.24, 126.93, 126.13, 124.73, 123.23, 117.92, 111.35, 47.32. ESI-MS (*m/z*): 377.2 $[M+H]^+$.

3. References

1. A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff and R. D. Shah, *J. Org. Chem.*,1996, **61**, 3849-3862.

2. R. F. Borch, M. D. Bernstein and H. D. Durst, *J. Am. Chem. Soc*., 1971, **93**, 2897-2904.

3. R. Apodaca, and W. Xiao, *Org. Lett*., 2001, **3**, 1745-1748.

4. B. Chen, H. F. Yin, Z. S. Wang, J. H. Xu, L. Q. Fan and J. Zhao, *Adv. Synth. Catal.*, 2009, **351**, 2959-2966.

4. Spectroscopic data of representative compounds

4.1. 1-(2-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1H-pyrazol-4-yl)methyl)aminophenyl)ethanone (3b)

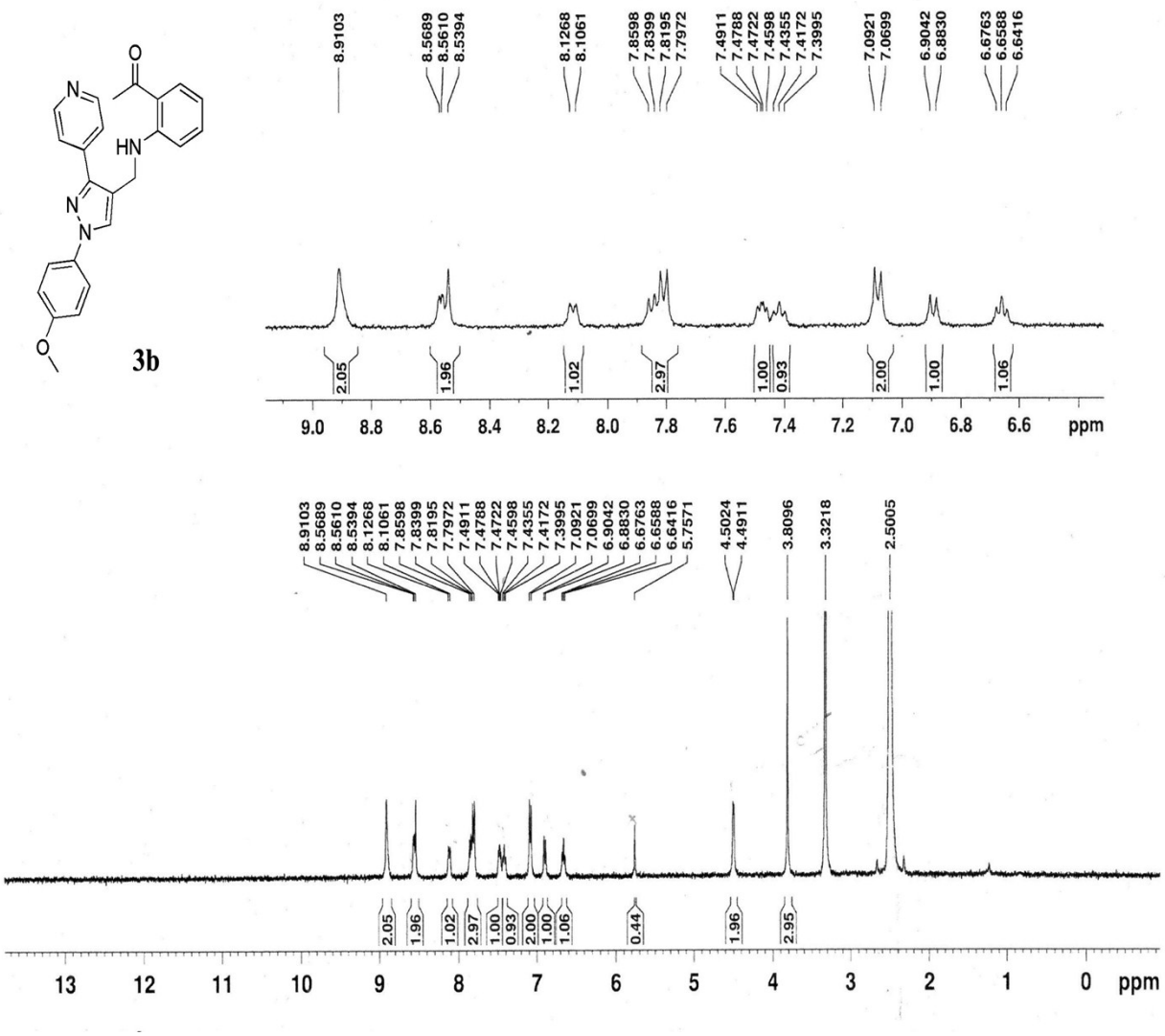


Fig. S1. ^{1}H NMR spectrum

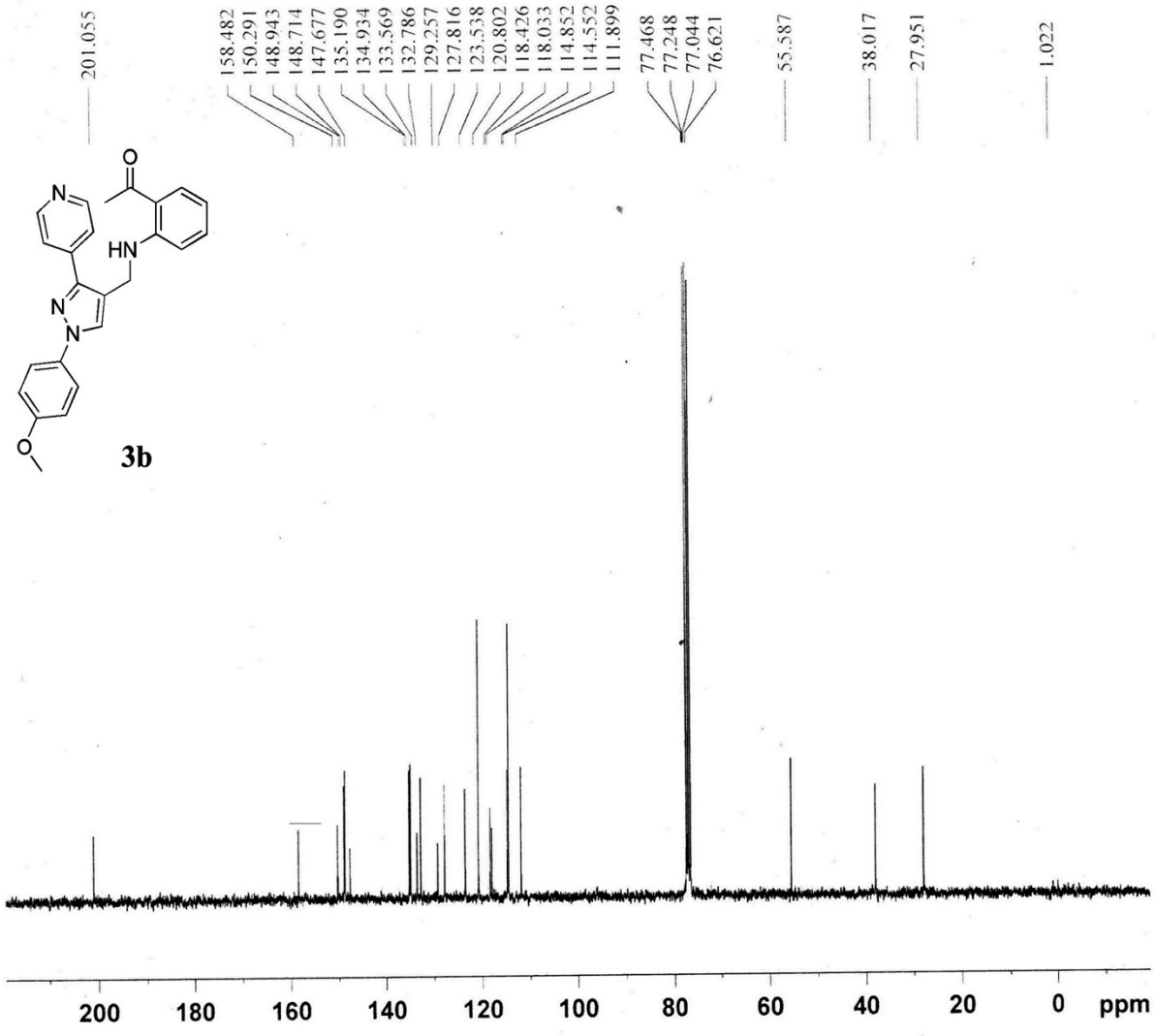


Fig. S2: ^{13}C NMR spectrum

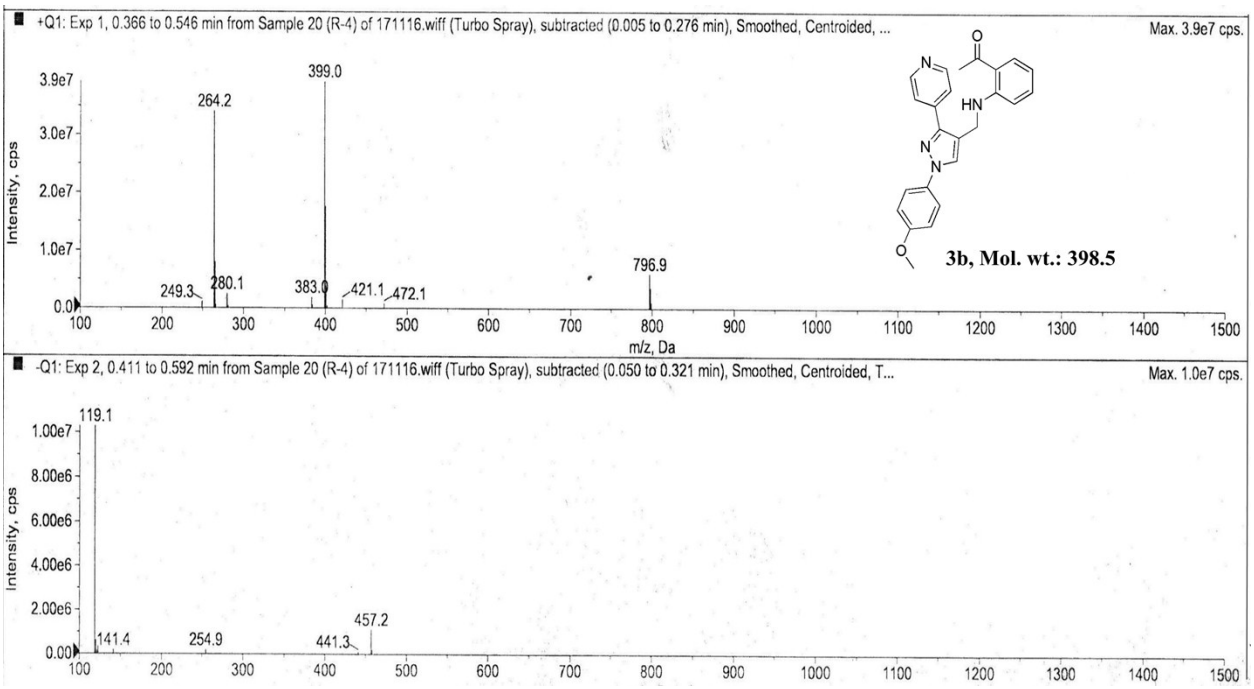


Fig. S3: ESI-MS spectrum

4.2. Ethyl 1-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1H-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydro quinoline -2-carboxylate (4b)

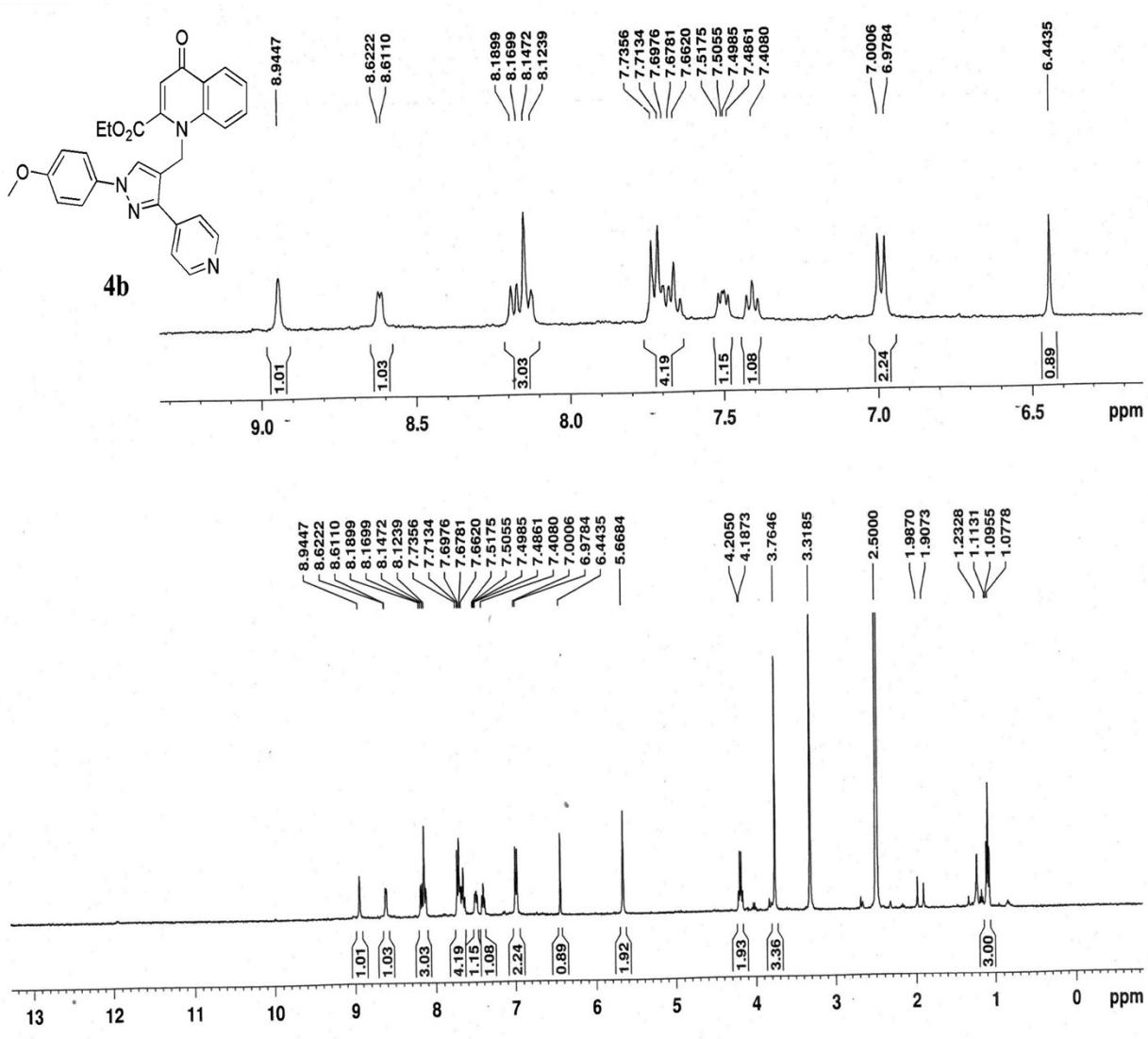


Fig. S4. ^{1}H NMR spectrum

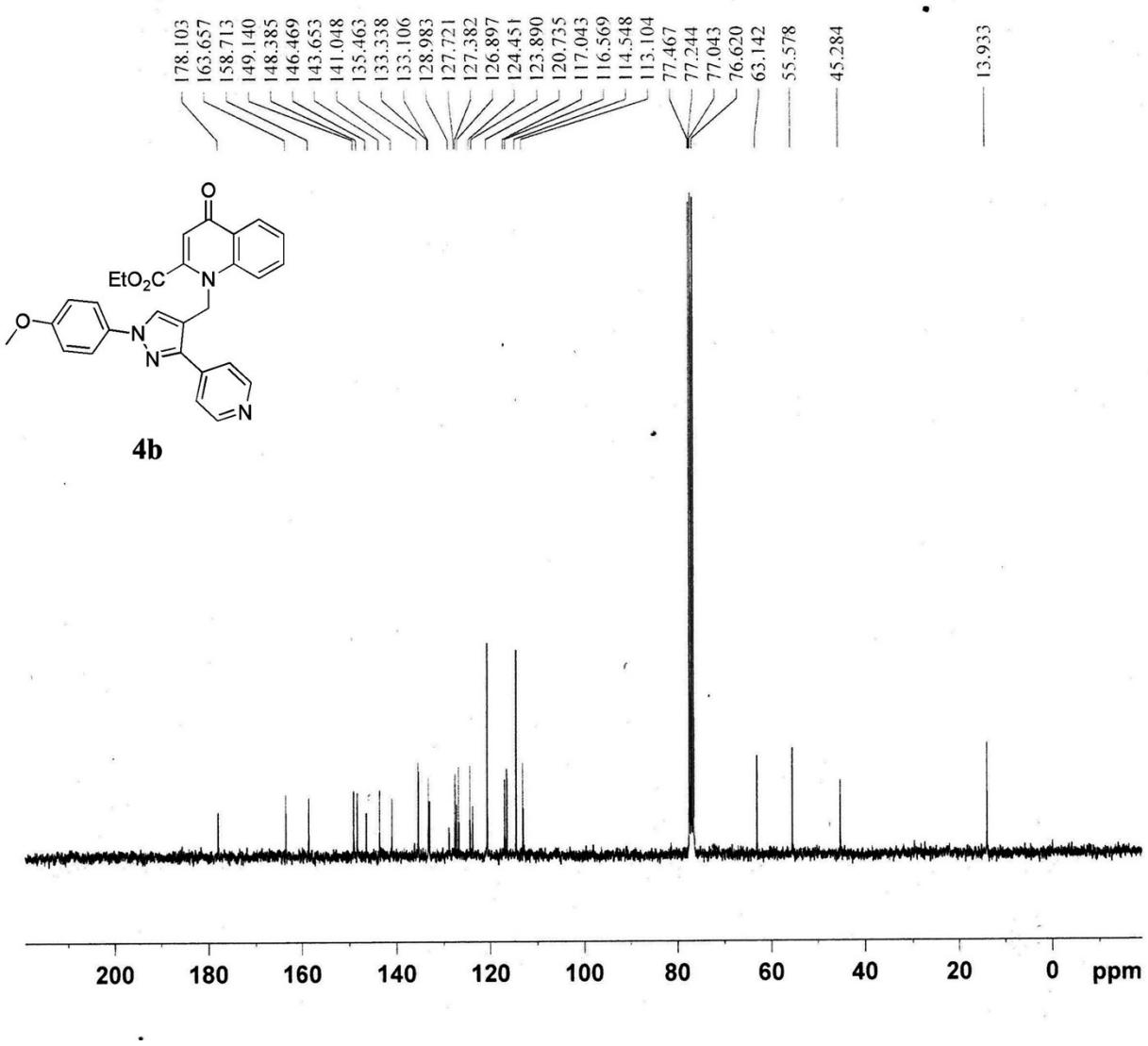


Fig. S5: ^{13}C NMR spectrum

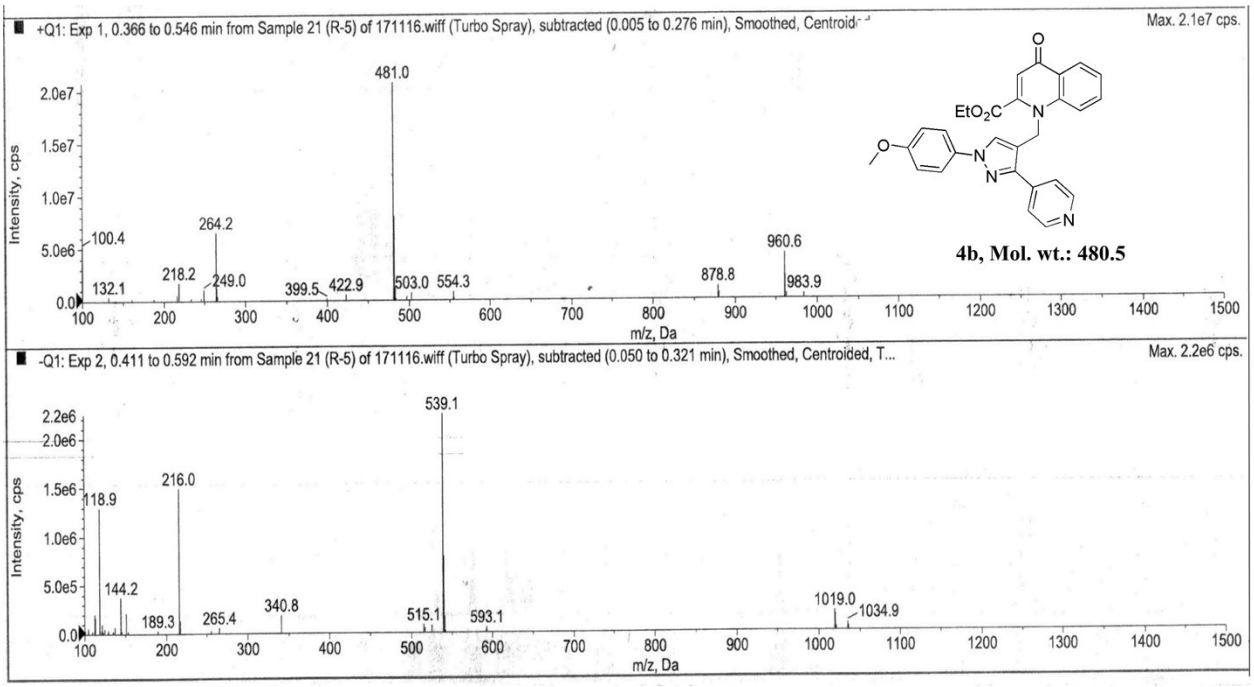


Fig. S6: ESI-MS spectrum

4.3. 1-((1-(4-methoxyphenyl)-3-(pyridin-4-yl)-1H-pyrazol-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5b)

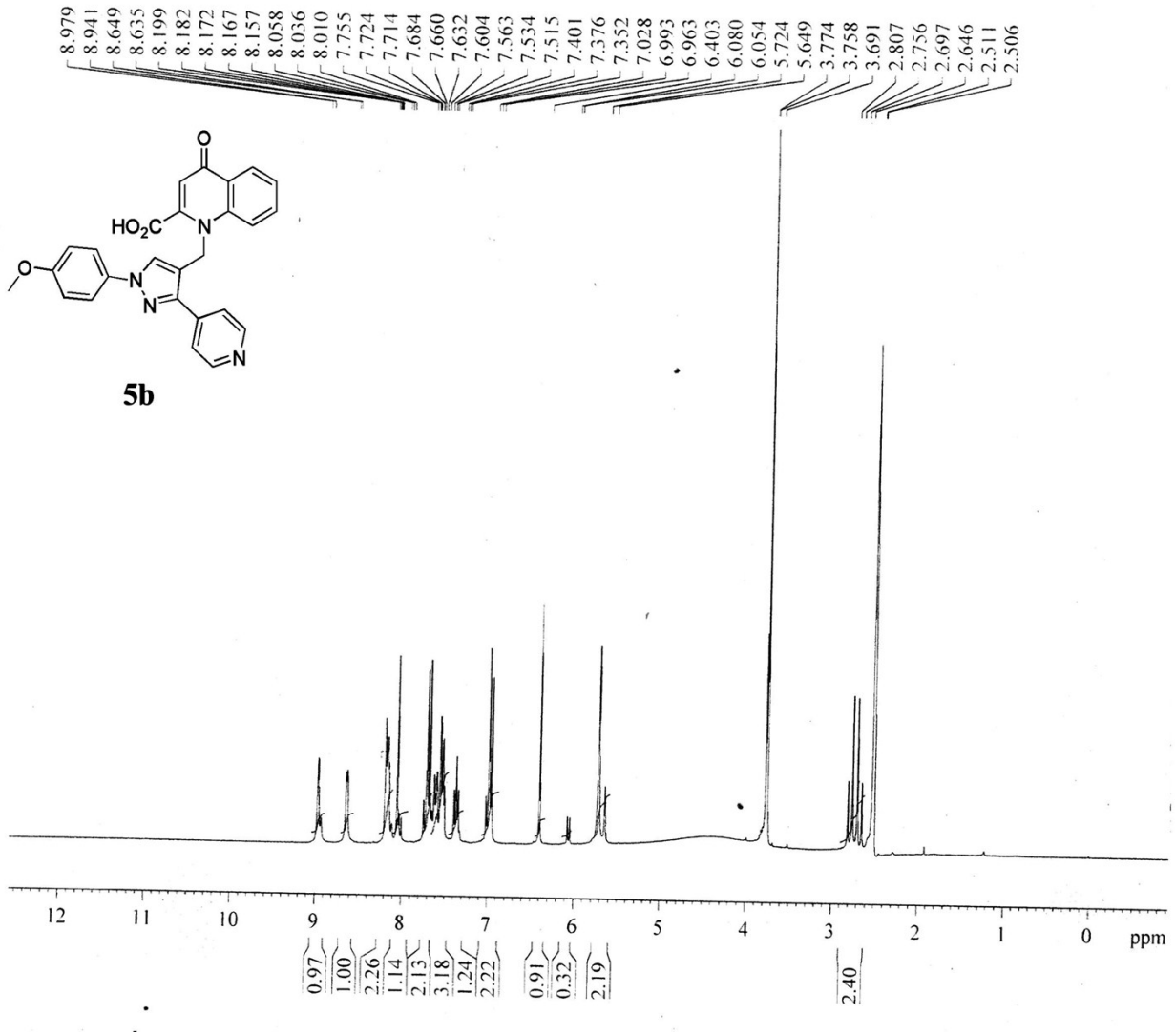


Fig. S7. ^{1}H NMR spectrum

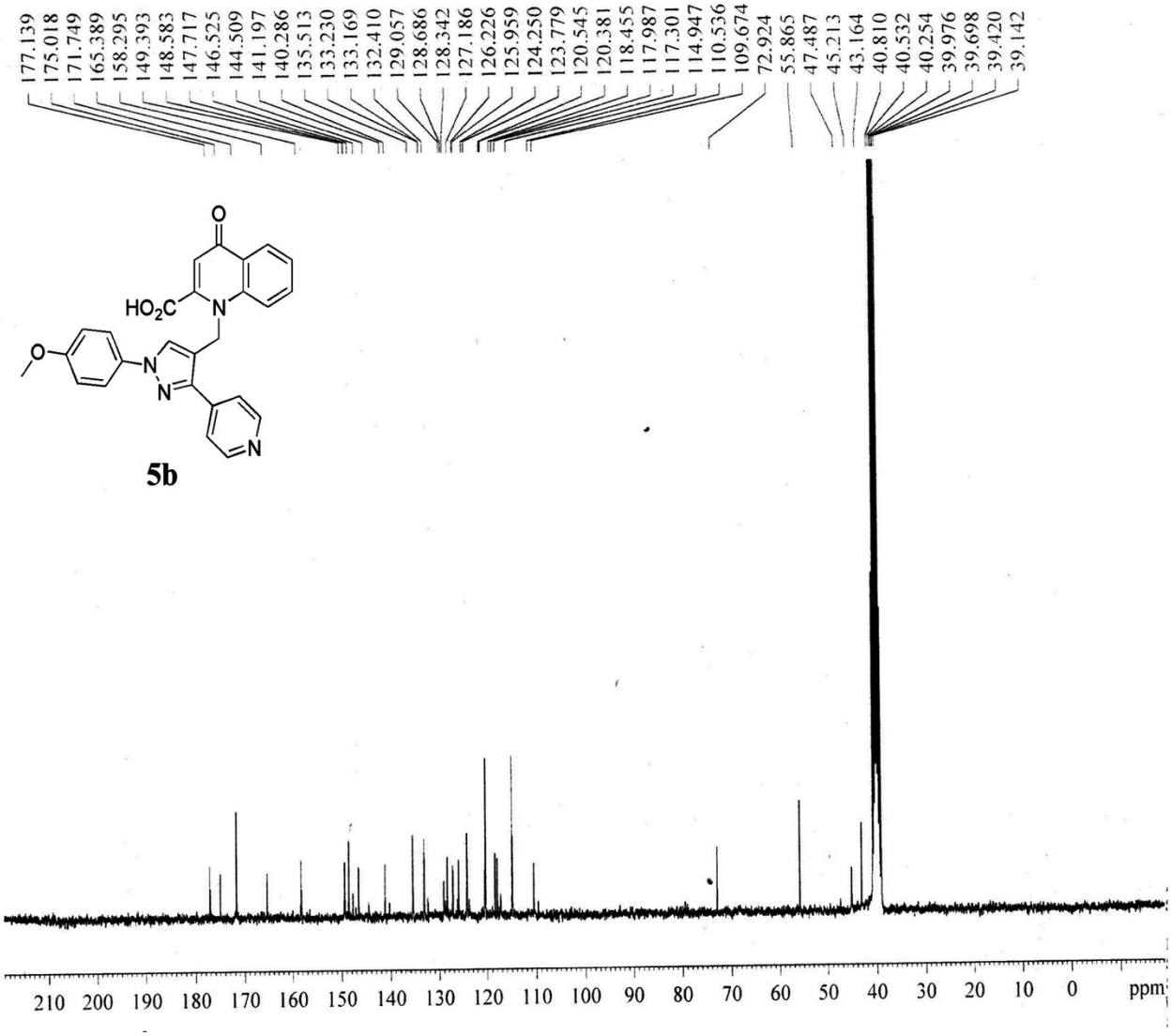


Fig. S8. ^{13}C NMR spectrum

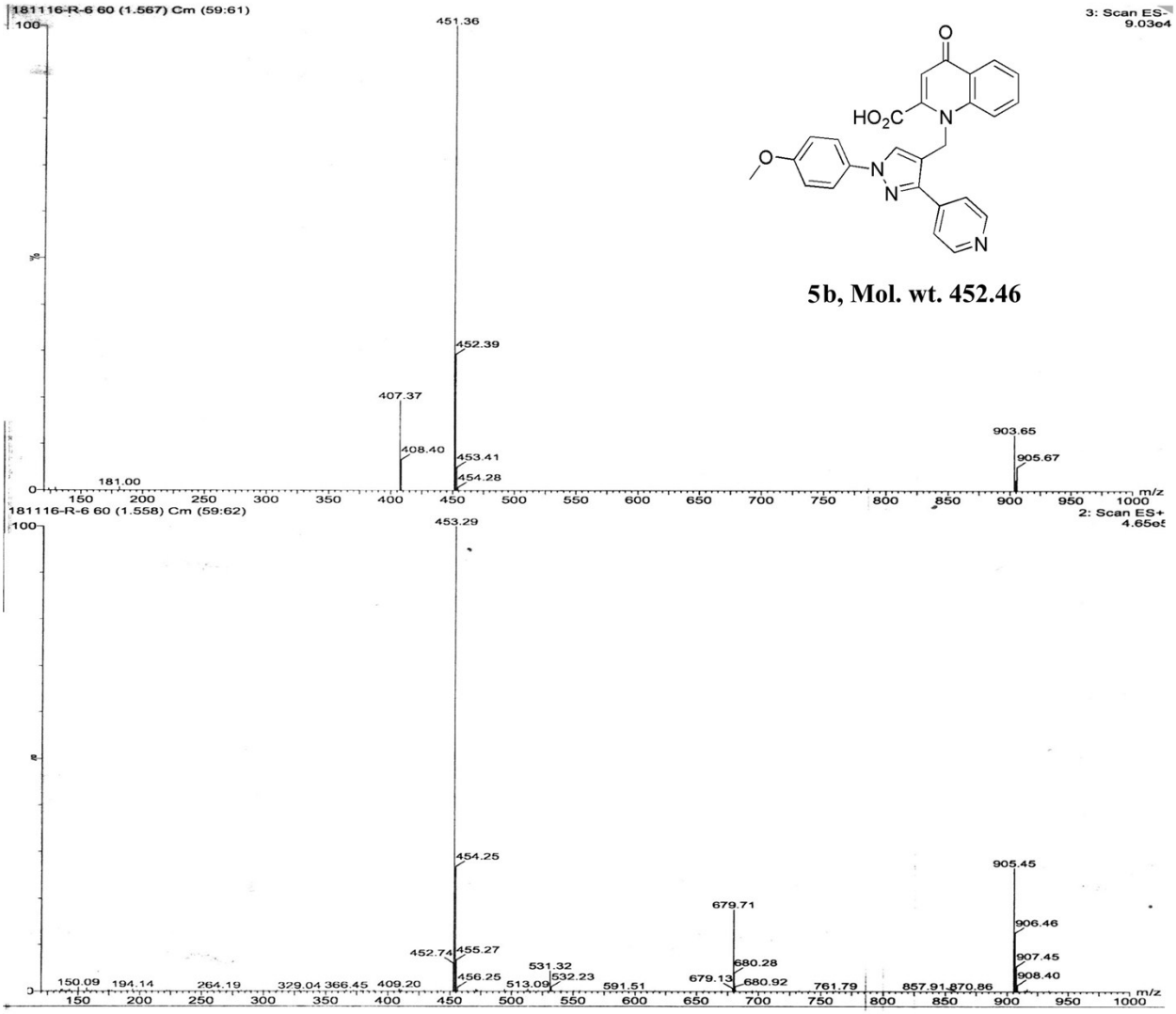


Fig. S9: ESI-MS spectrum

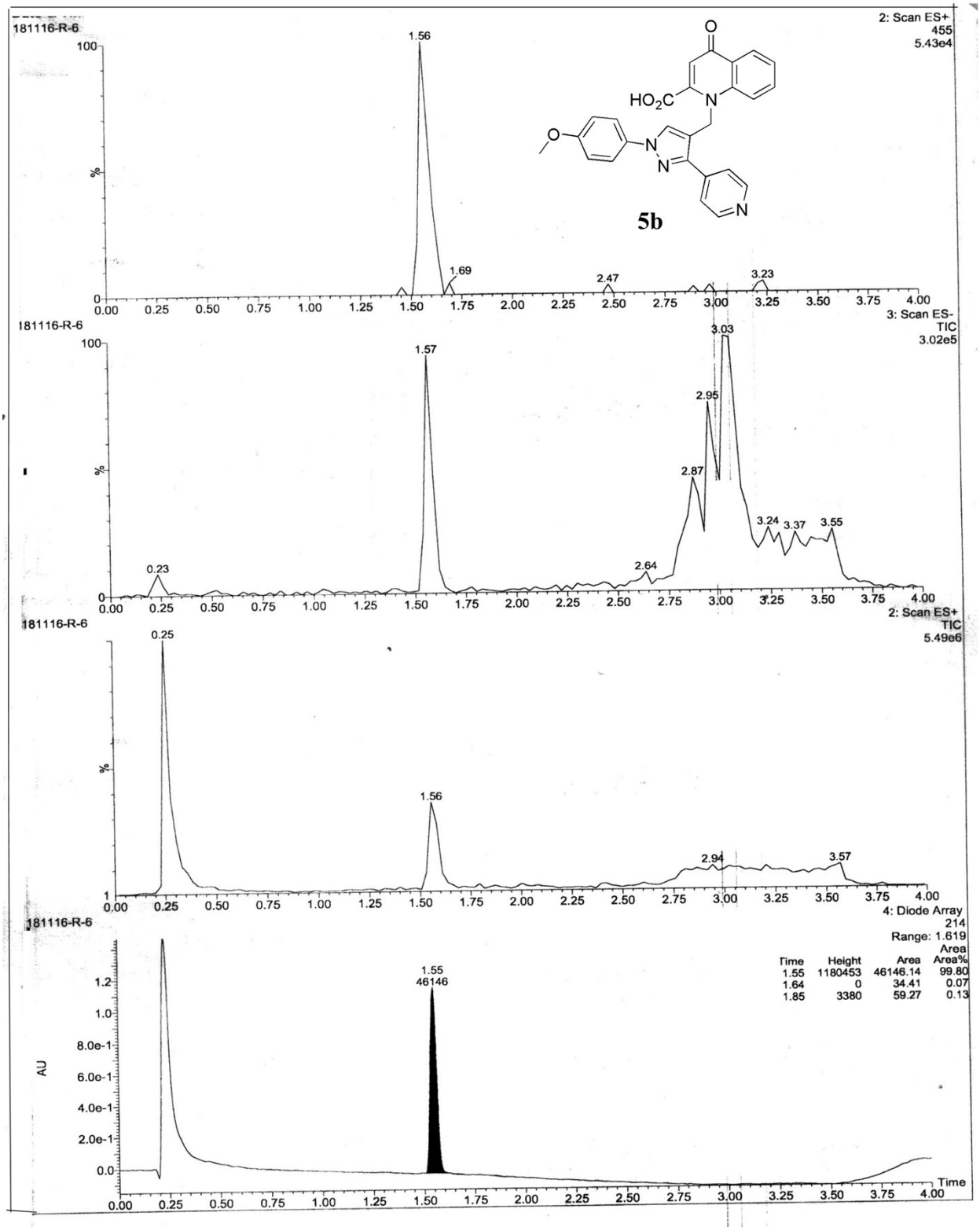


Fig. S10: HPLC spectrum

4.4. 1-(2-(4-(1*H*-pyrazol-1-yl)benzylamino)phenyl)ethanone (3f)

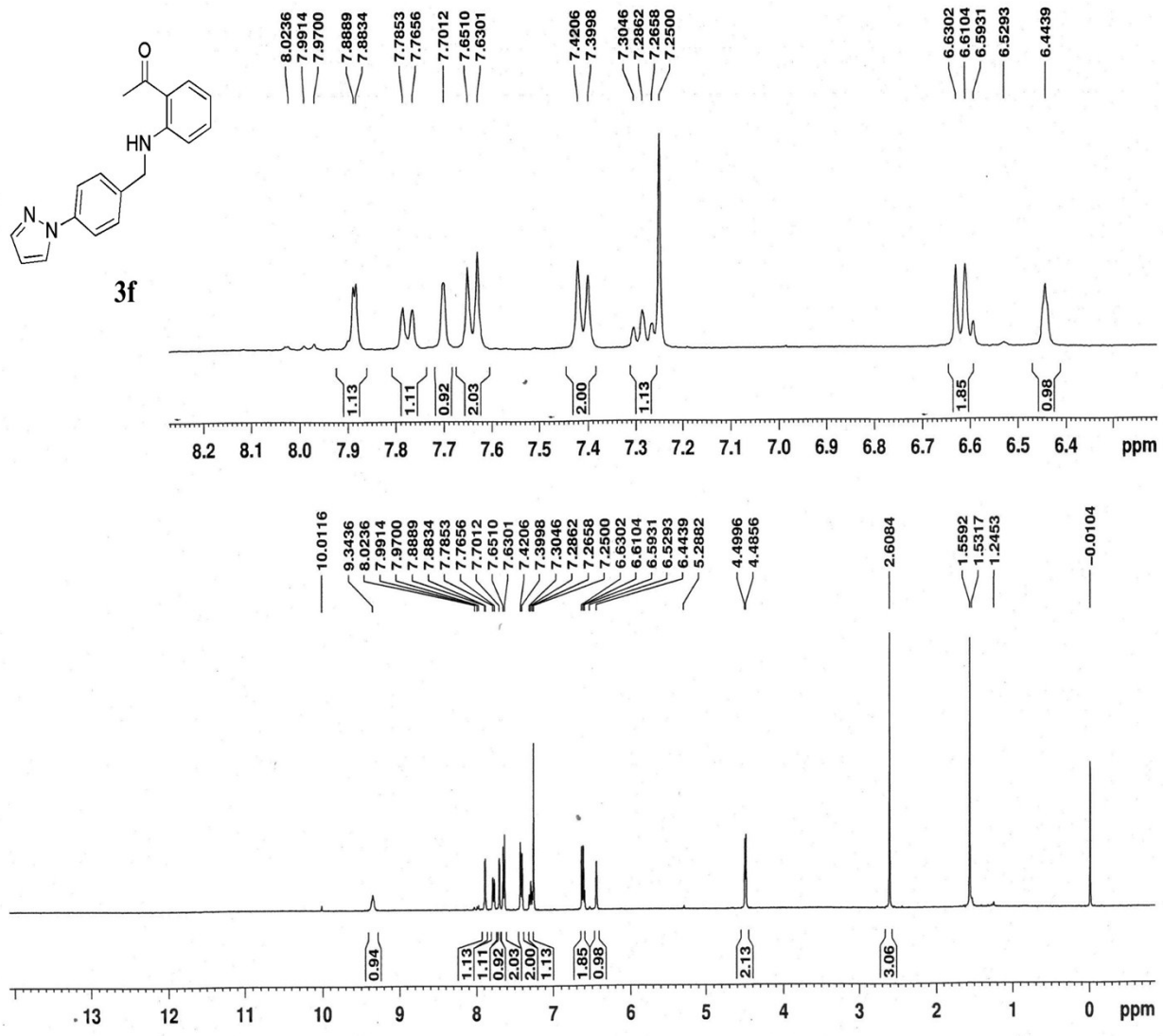


Fig. S11. ^{1}H NMR spectrum

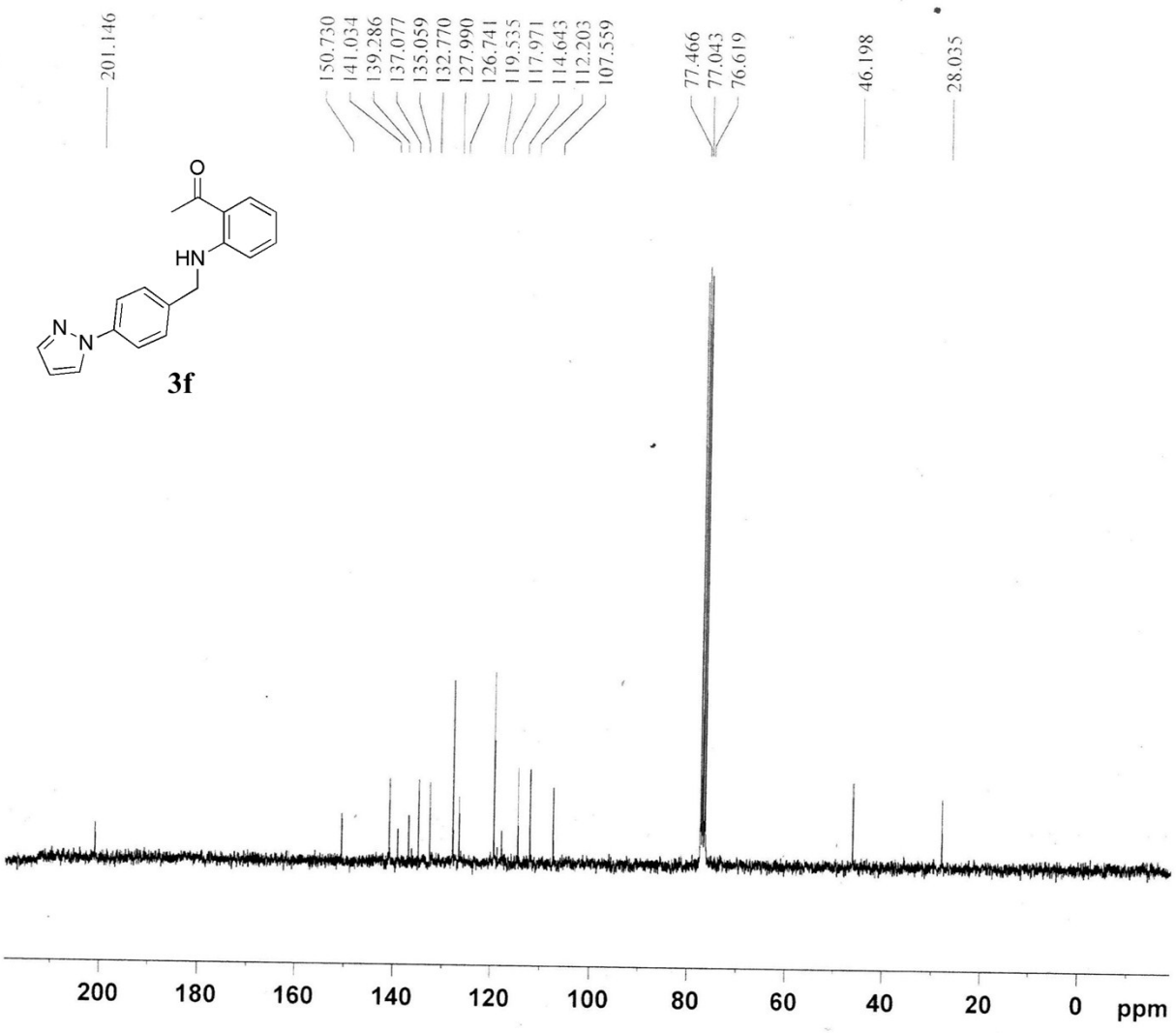


Fig. S12. ^{13}C NMR spectrum

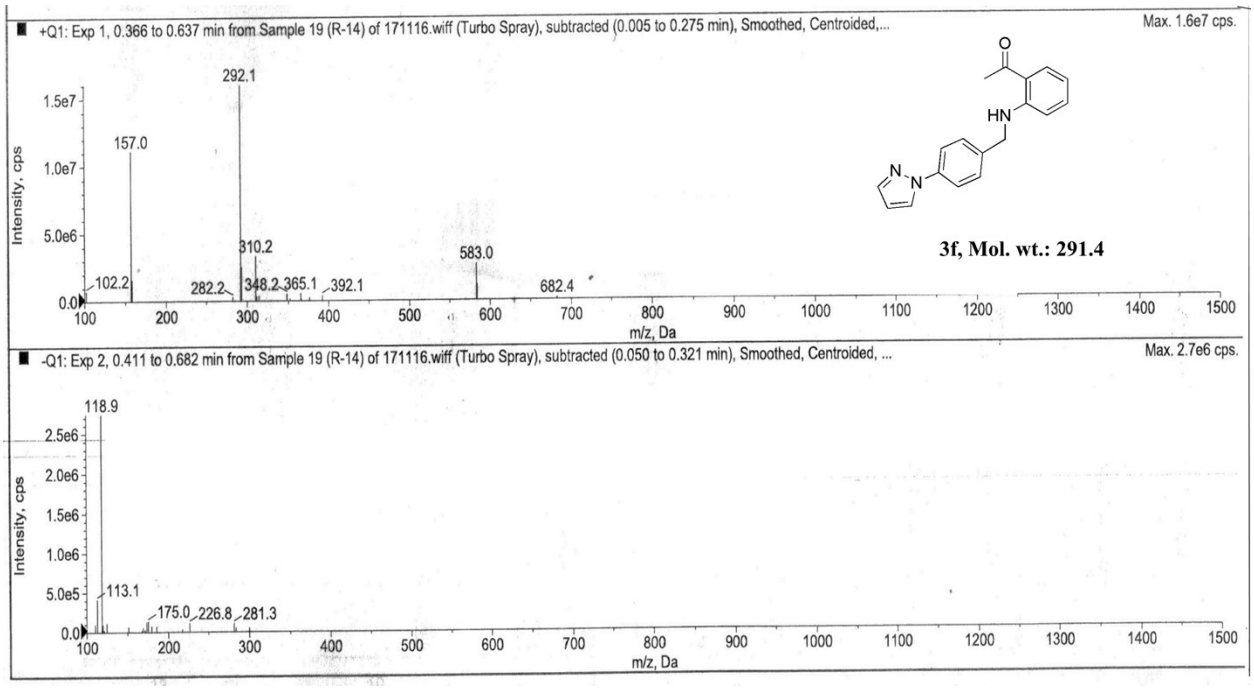


Fig. S13: ESI-MS spectrum

4.5. Ethyl 1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4f)

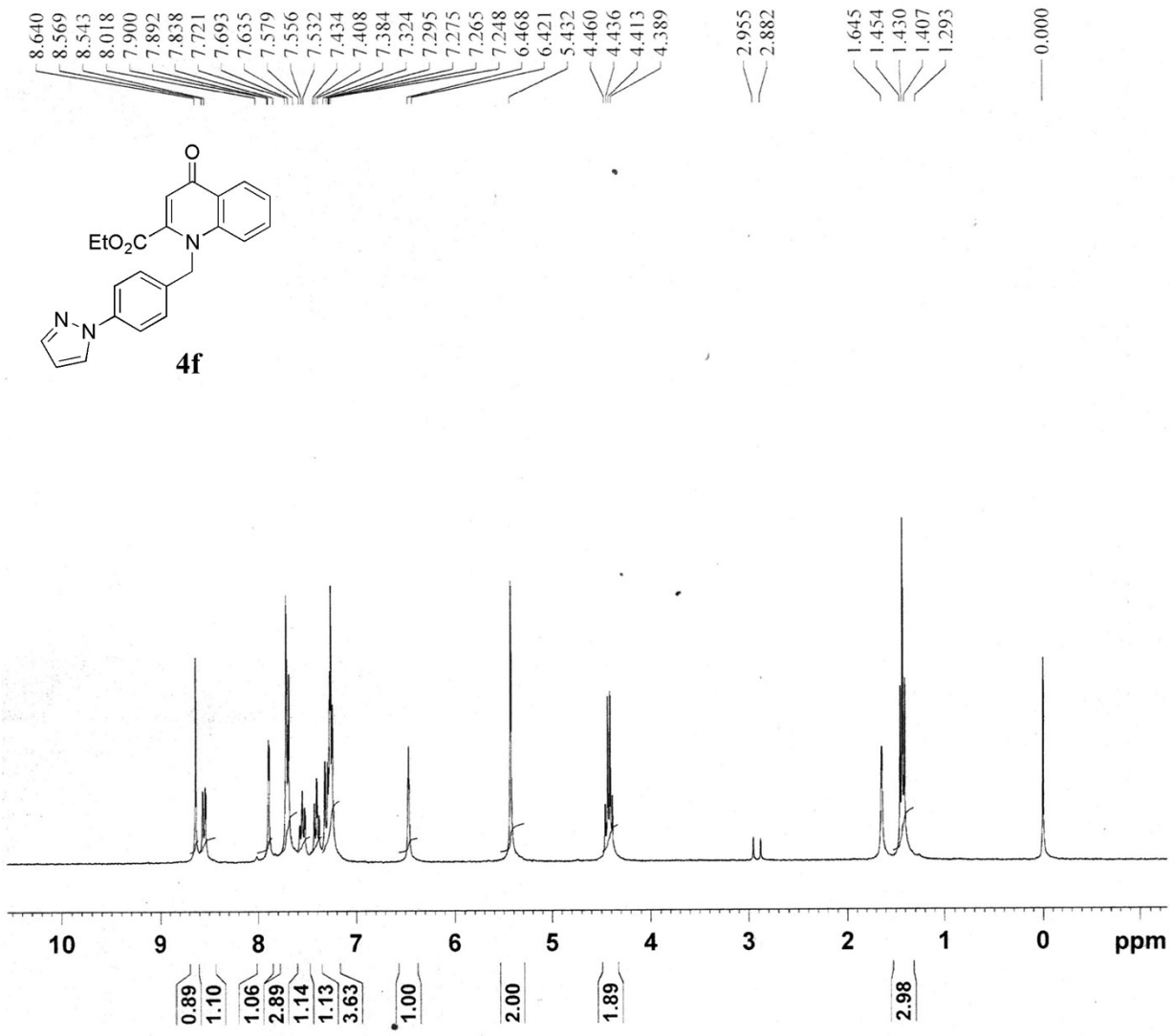


Fig. S14. ^{1}H NMR spectrum

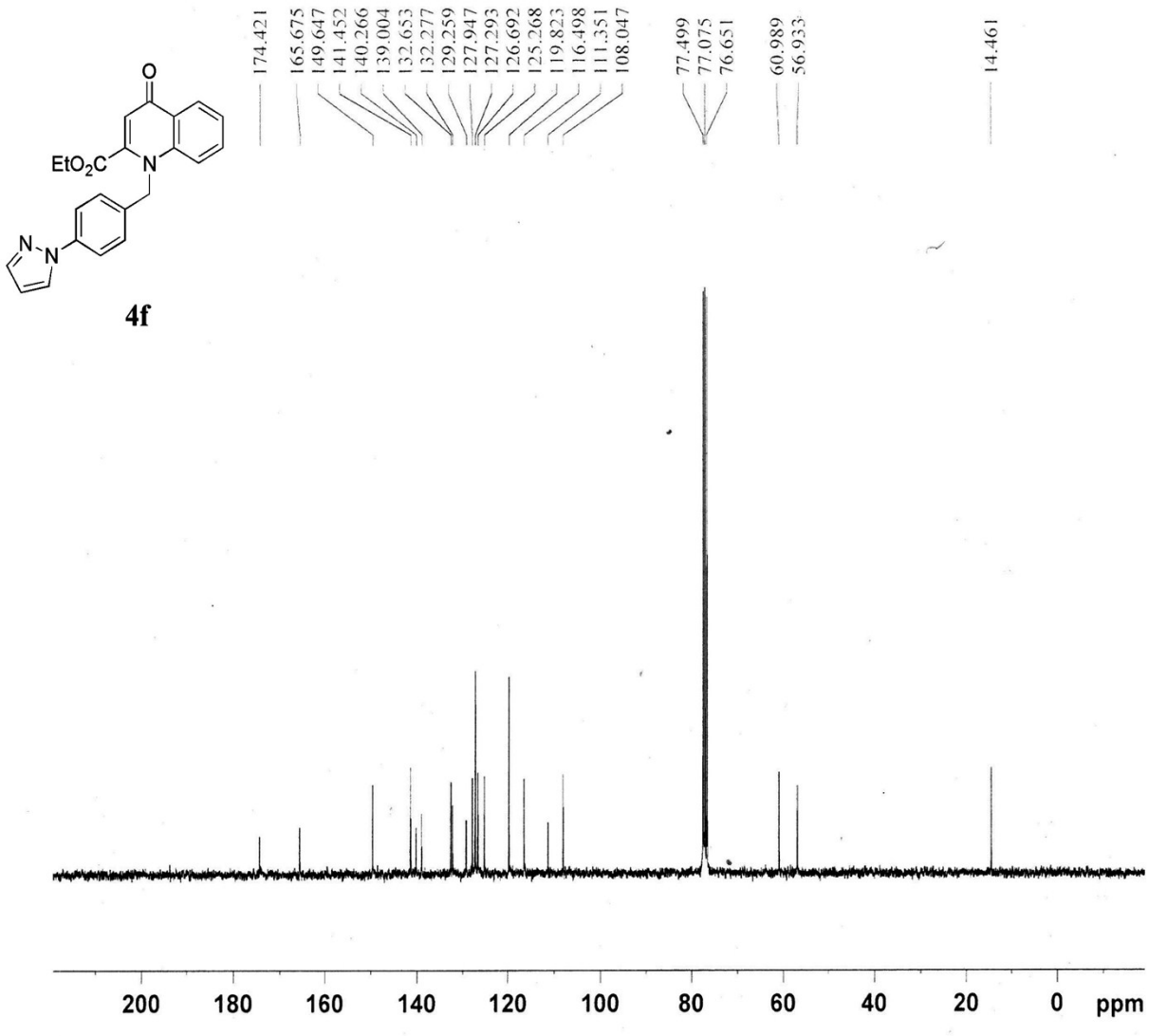


Fig. S15. ^{13}C NMR spectrum

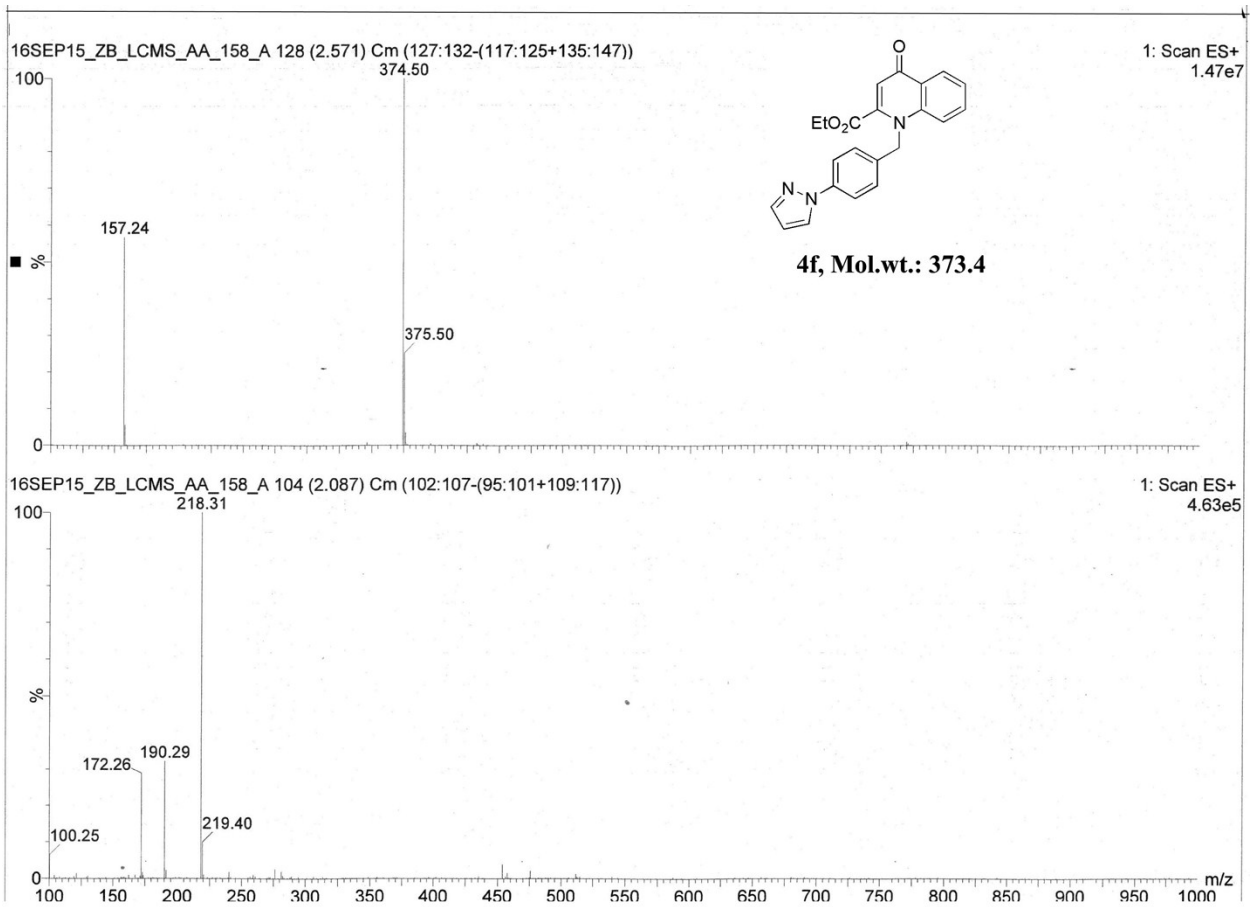


Fig. S16. ESI-MS spectrum

4.6. 1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5f)

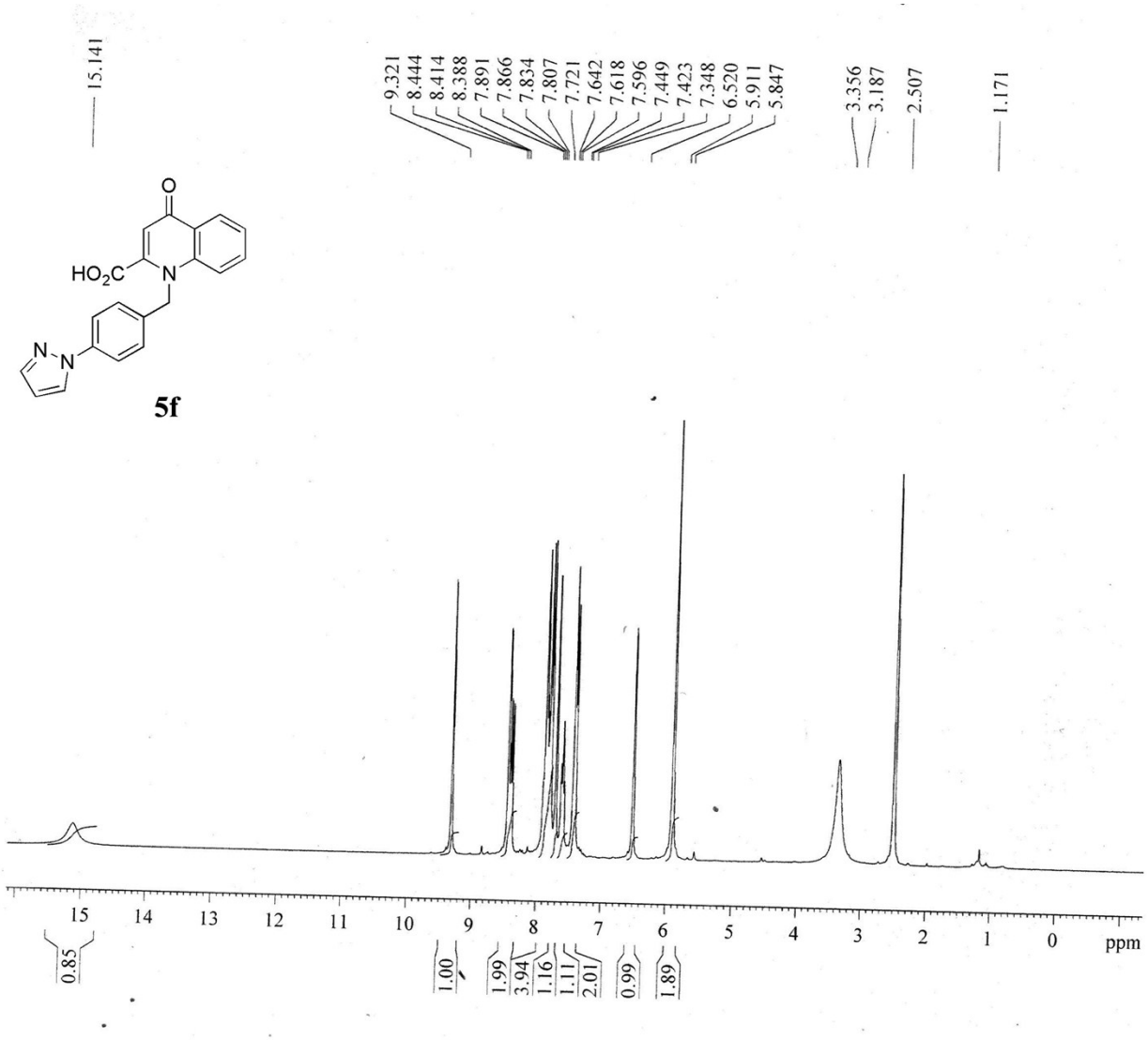


Fig. S17. ^{1}H NMR spectrum

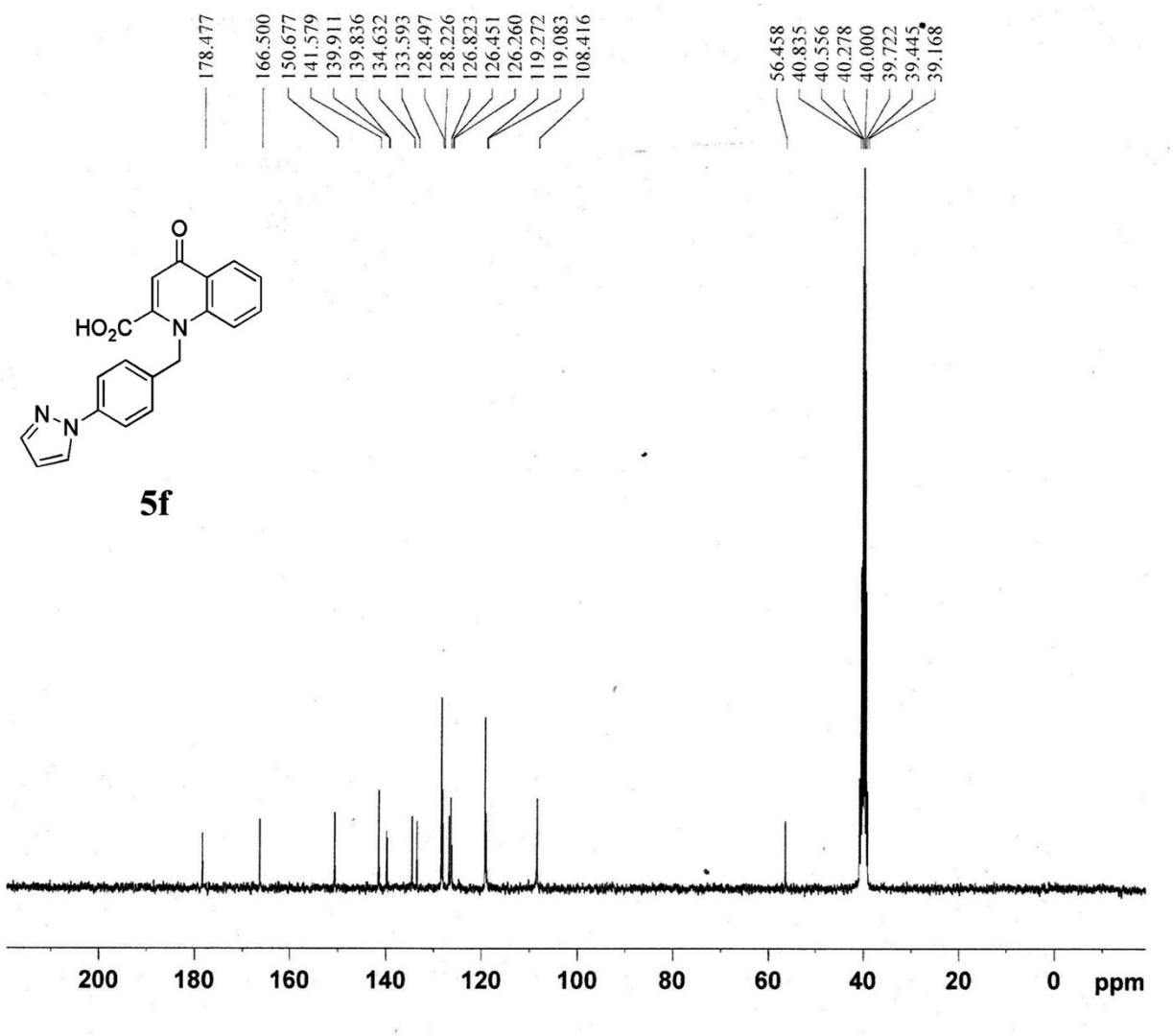


Fig. S18. ^{13}C NMR spectrum

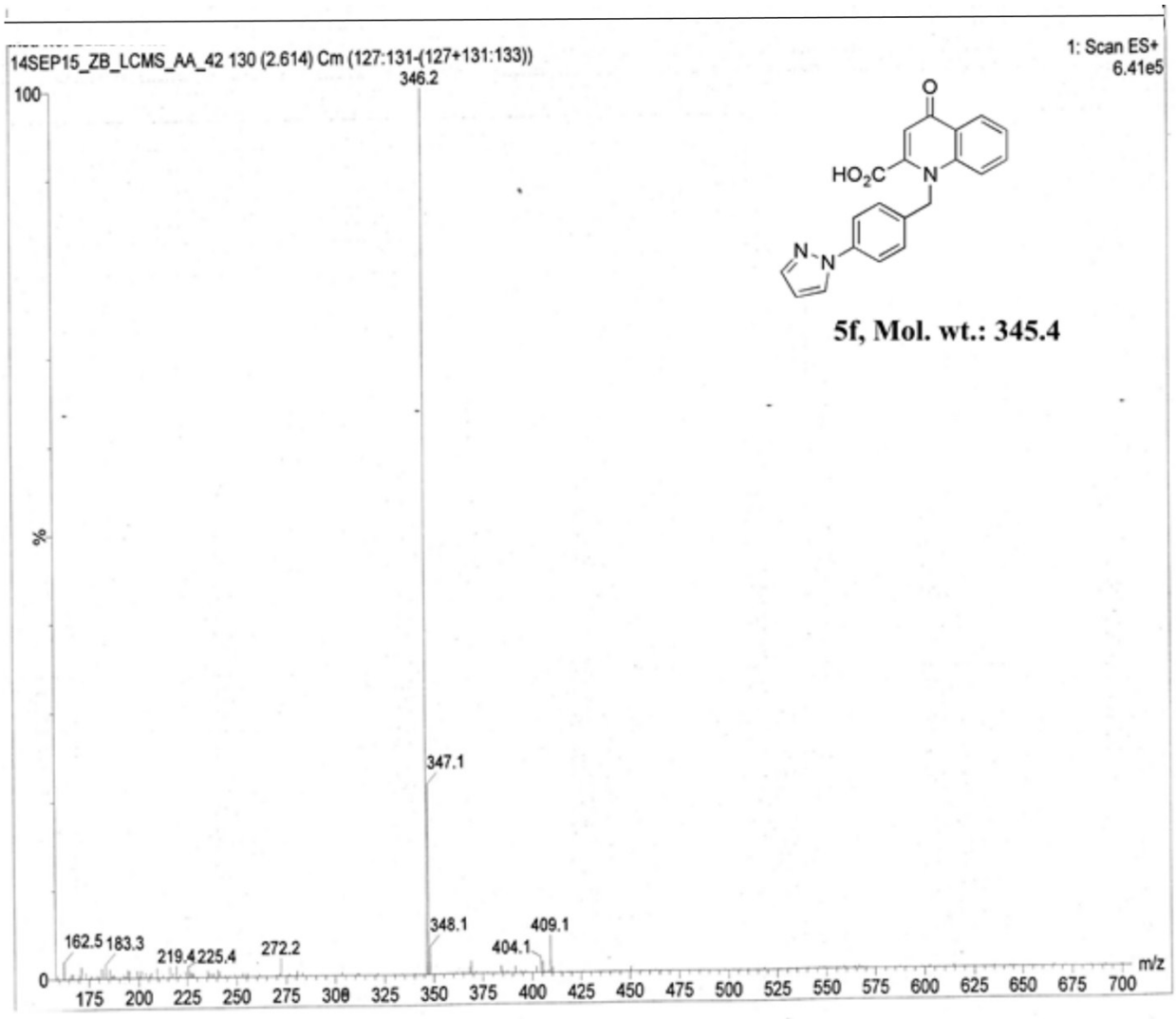


Fig. S19. ESI-MS spectrum

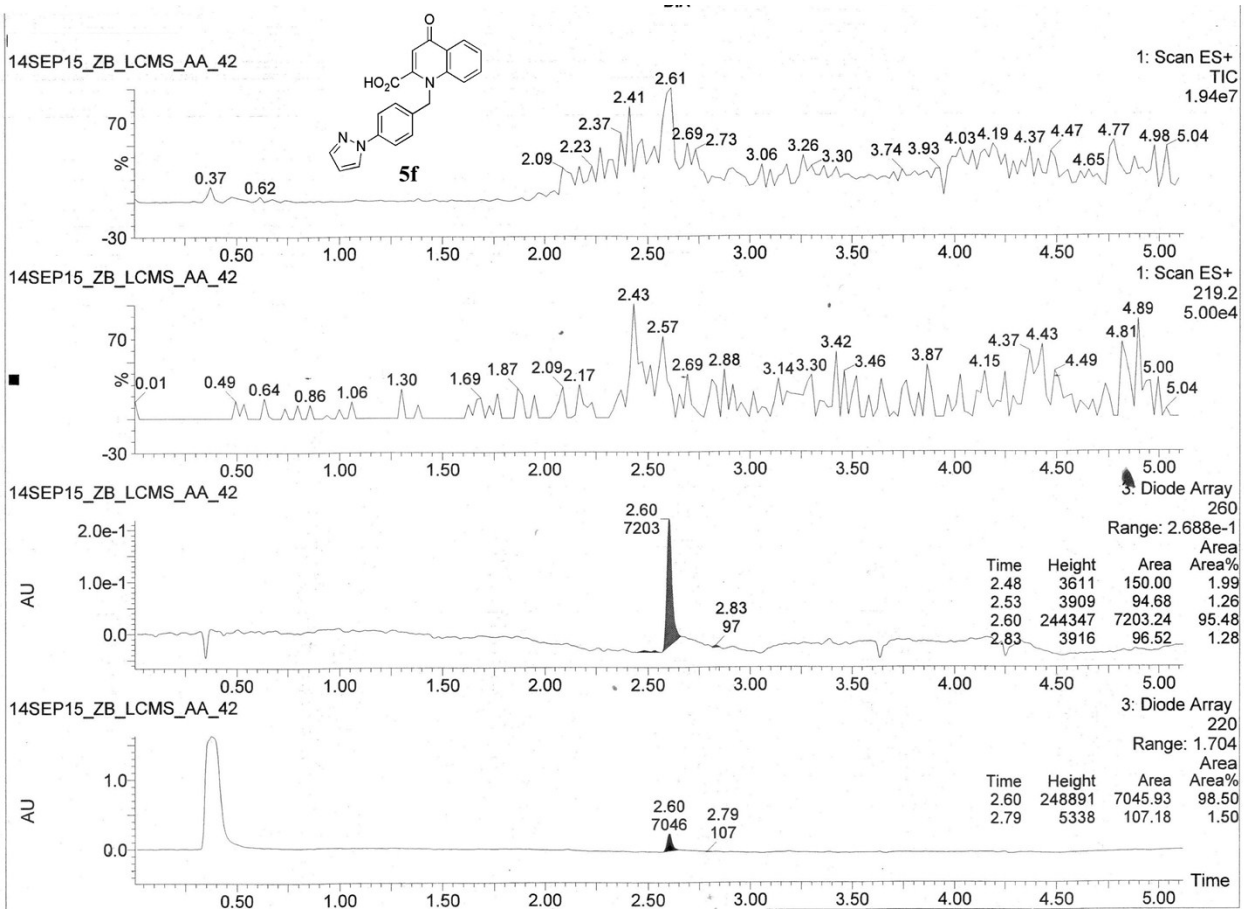


Fig. S20. HPLC spectrum

4.7. 1-(2-(4-(trifluoromethyl)benzylamino)phenyl)ethanone (3g)

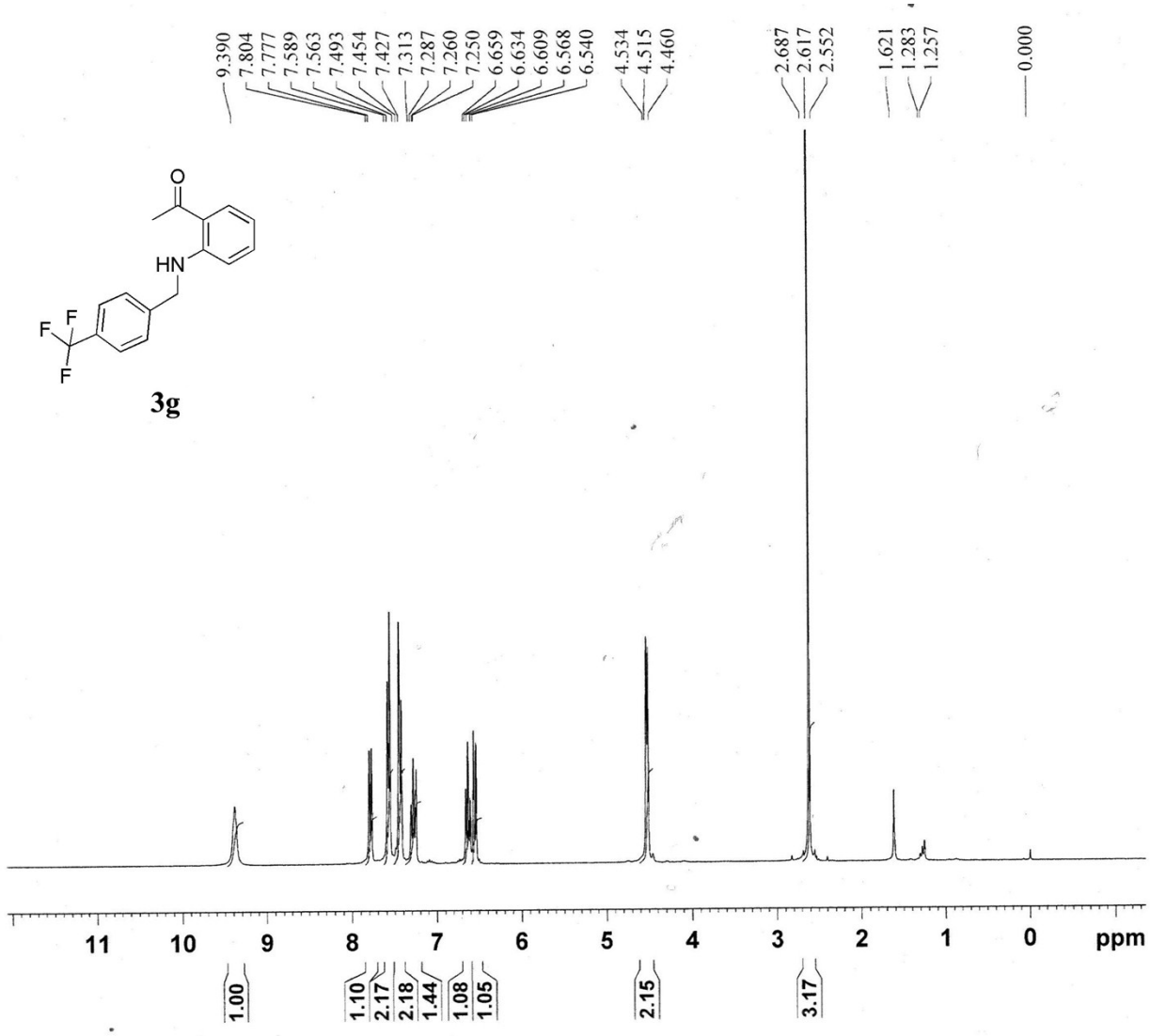


Fig. S21. ^{1}H NMR spectrum

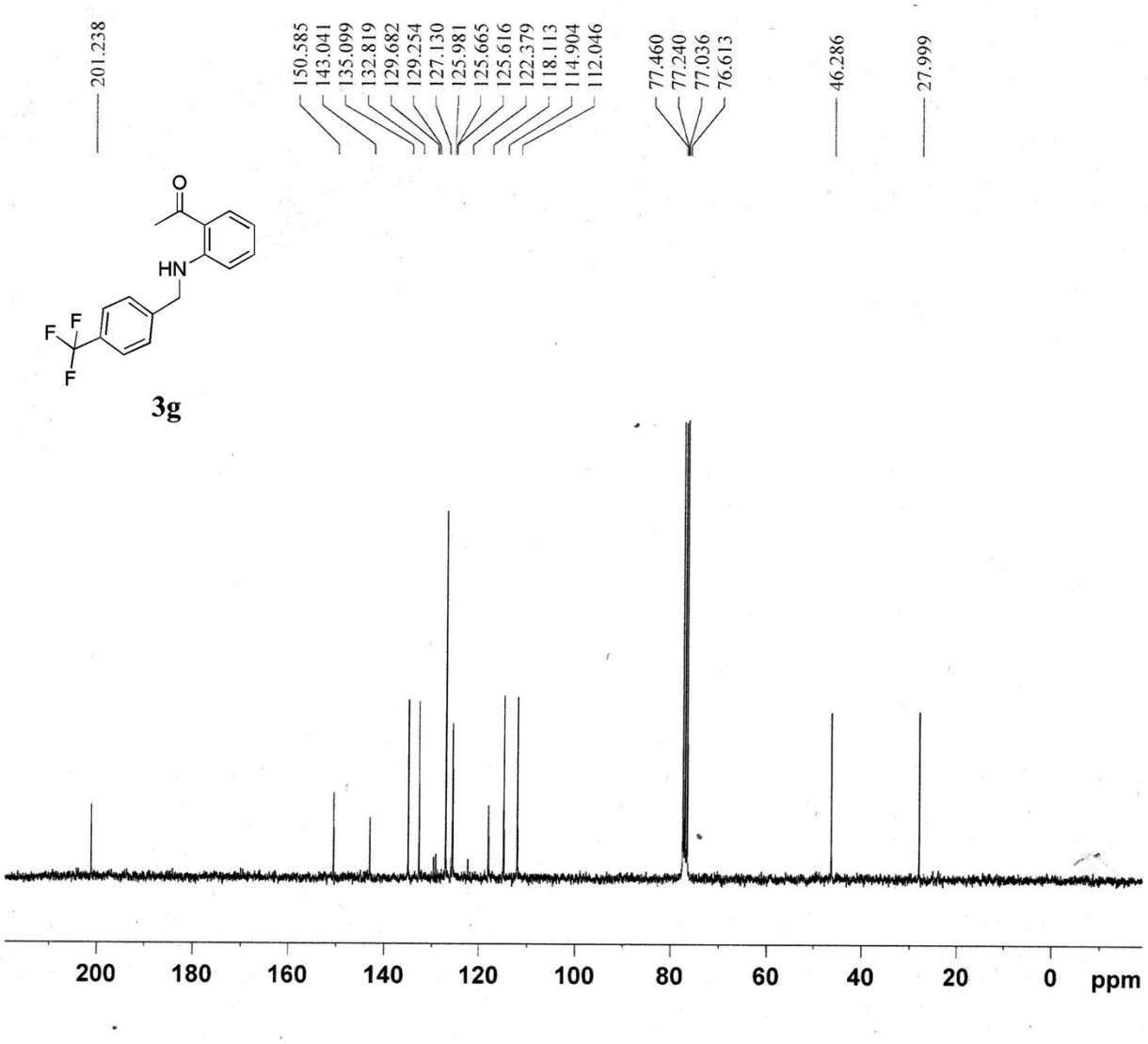
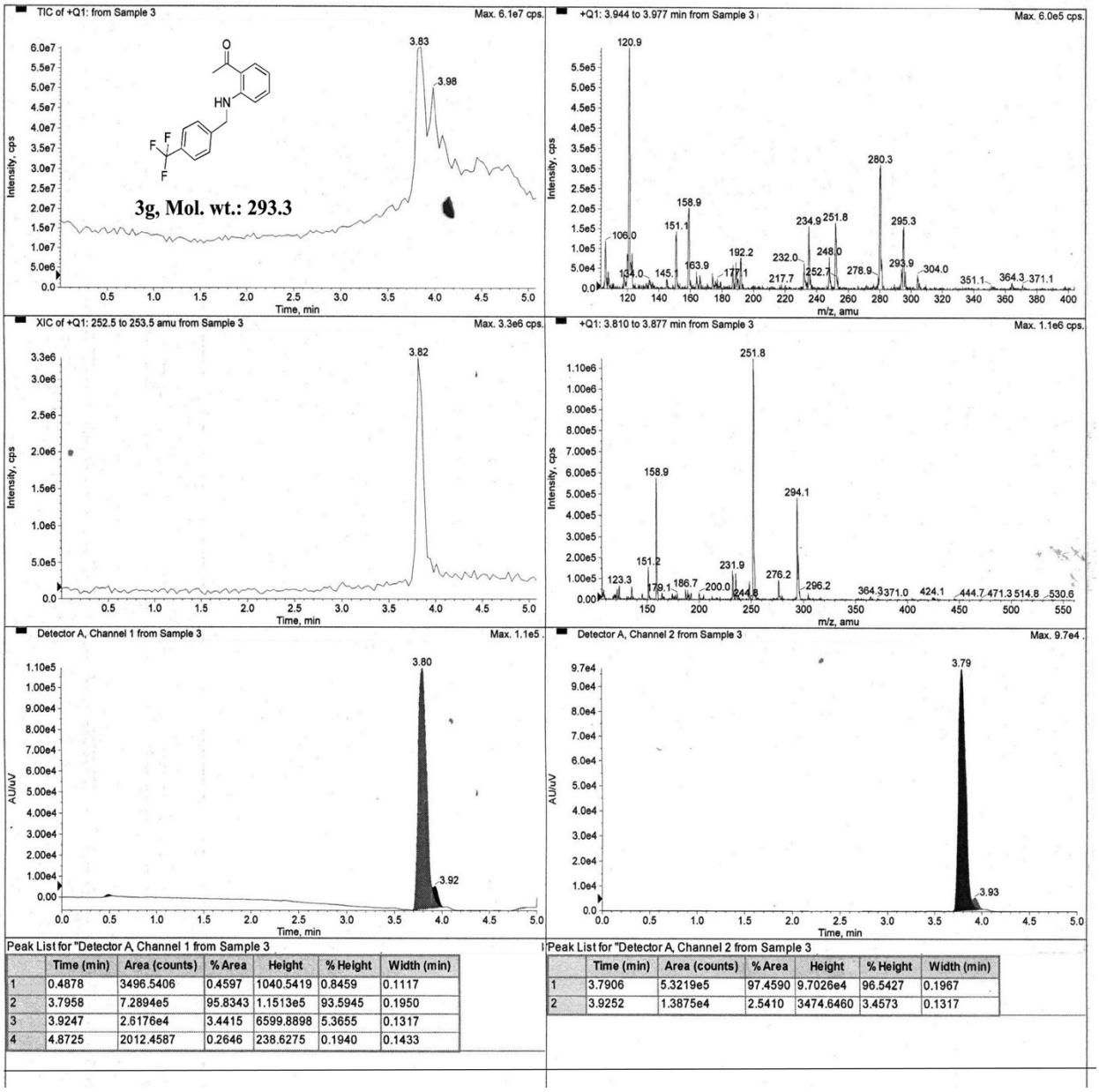


Fig. S22. ^{13}C NMR spectrum



Peak List for "Detector A, Channel 1 from Sample 3

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	0.4878	3496.5406	0.4597	1040.5419	0.8459	0.1117
2	3.7958	7.2894e5	95.8343	1.1513e5	93.5945	0.1950
3	3.9247	2.6176e4	3.4415	6599.8898	5.3655	0.1317
4	4.8725	2012.4587	0.2646	238.6275	0.1940	0.1433

Peak List for "Detector A, Channel 2 from Sample 3

	Time (min)	Area (counts)	% Area	Height	% Height	Width (min)
1	3.7906	5.3219e5	97.4590	9.7026e4	96.5427	0.1967
2	3.9252	1.3875e4	2.5410	3474.6460	3.4573	0.1317

Fig. S23. Mass spectrum

4.8. Ethyl 1-(4-(trifluoromethyl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4g)

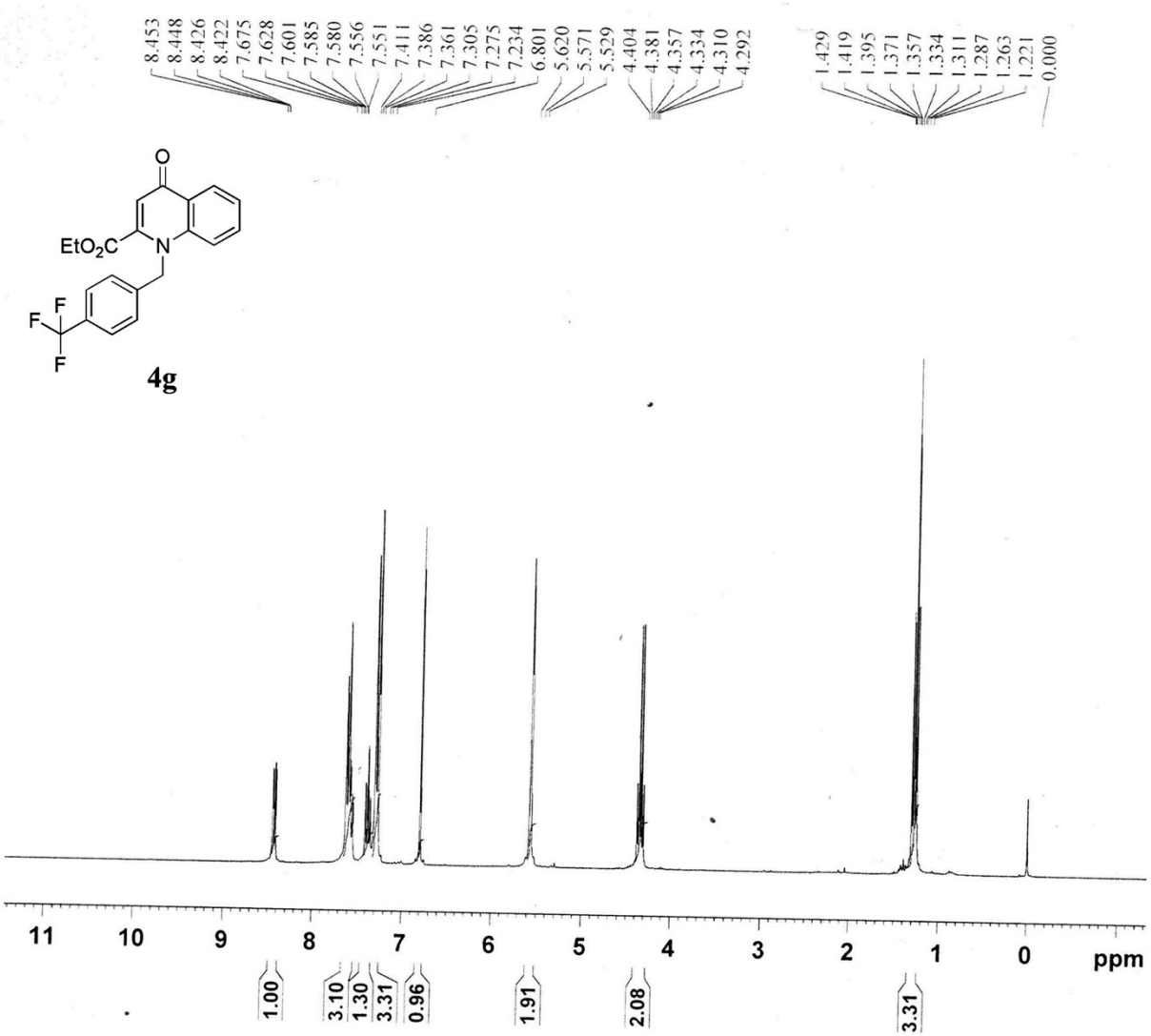


Fig. S24. ^{1}H NMR spectrum

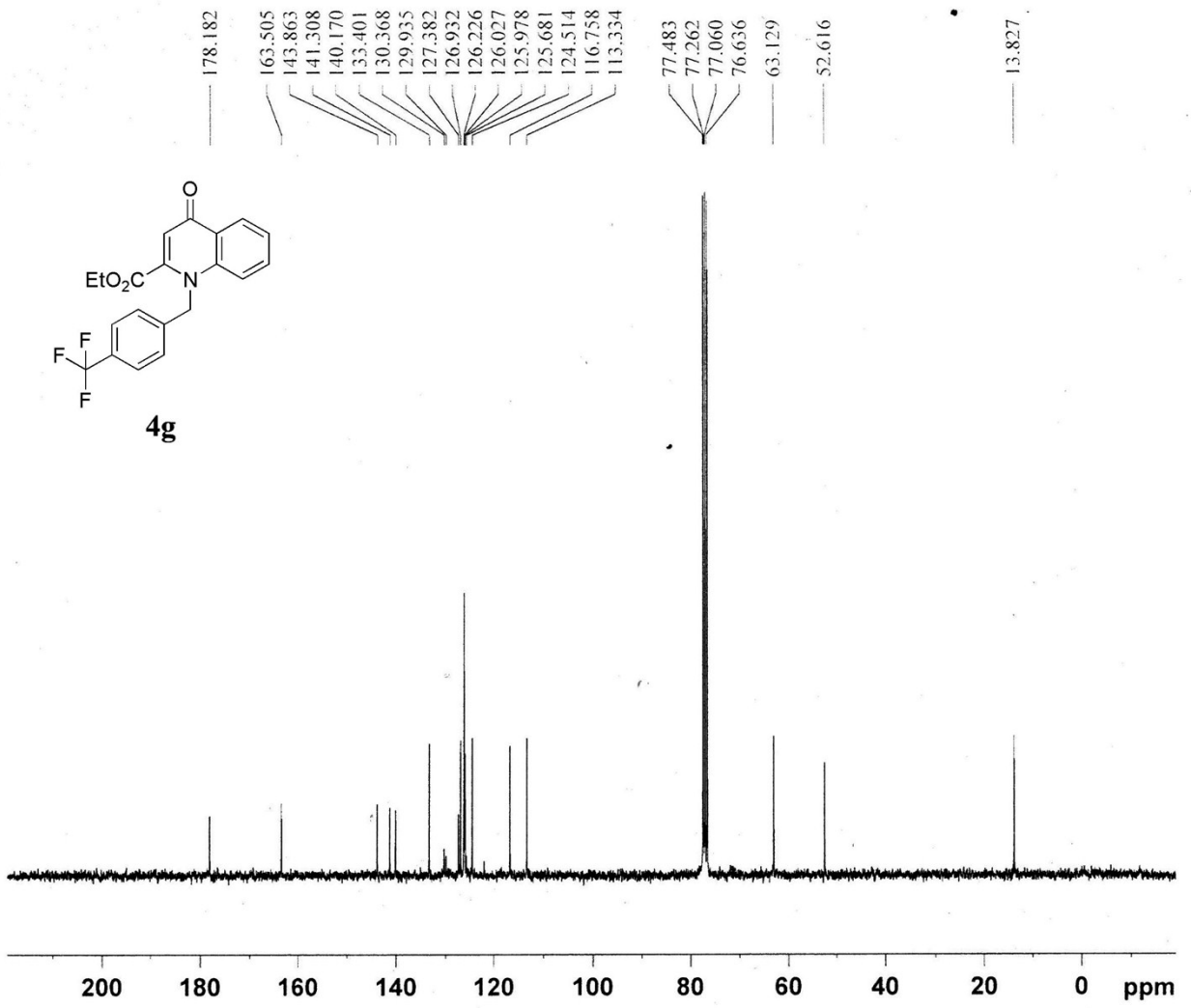


Fig. S25. ^{13}C NMR spectrum

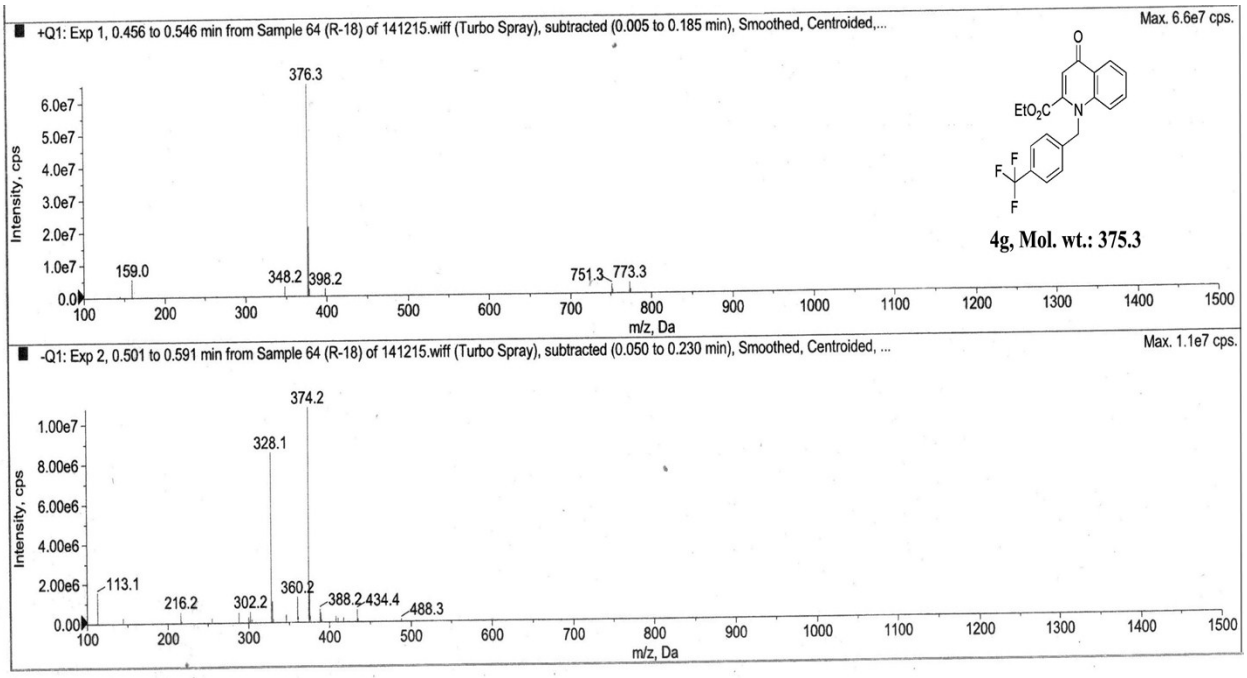


Fig. S26. ESI-MS spectrum

4.9. 1-(4-(trifluoromethyl)benzyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5g)

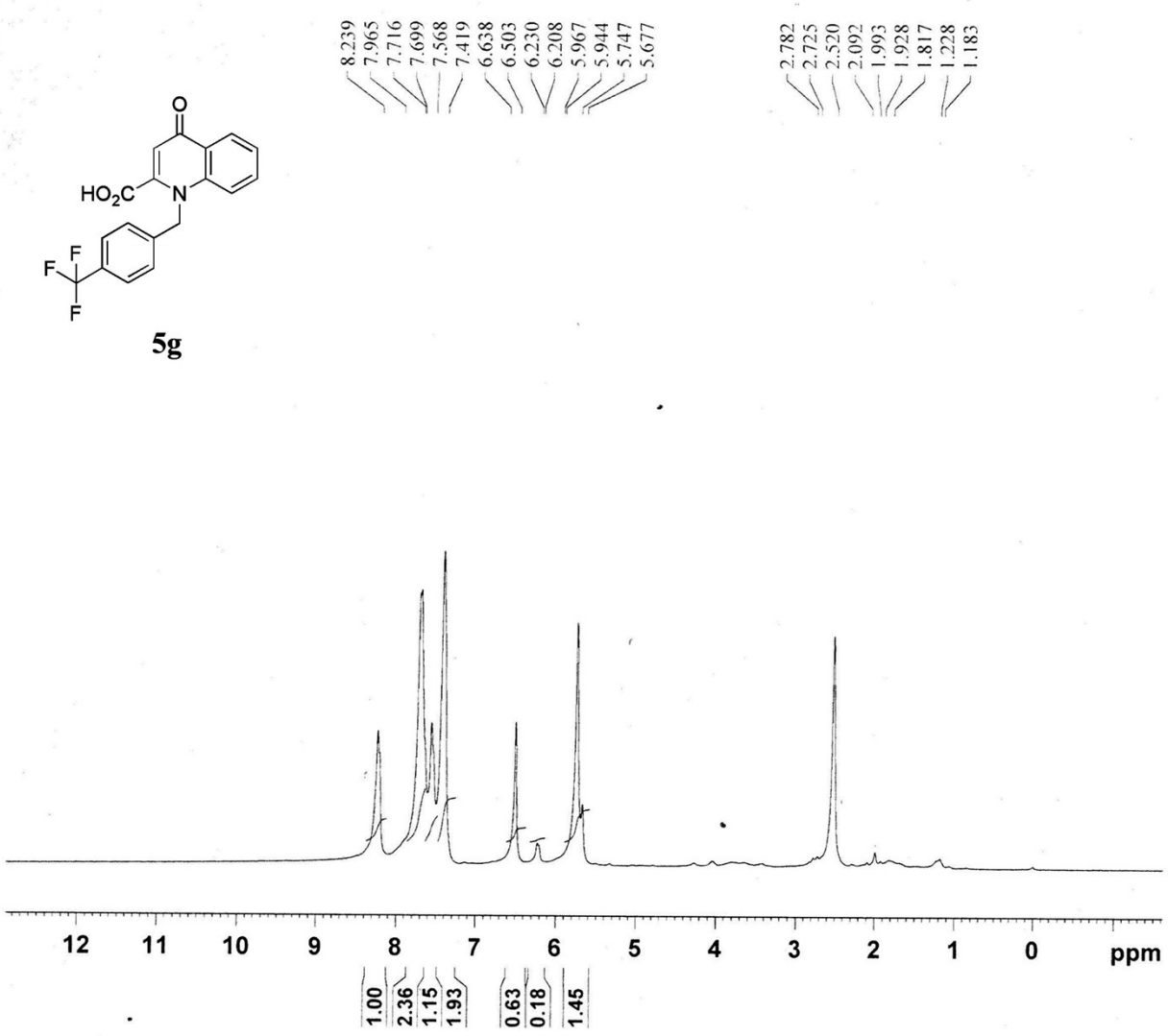


Fig. S27. ^{1}H NMR spectrum

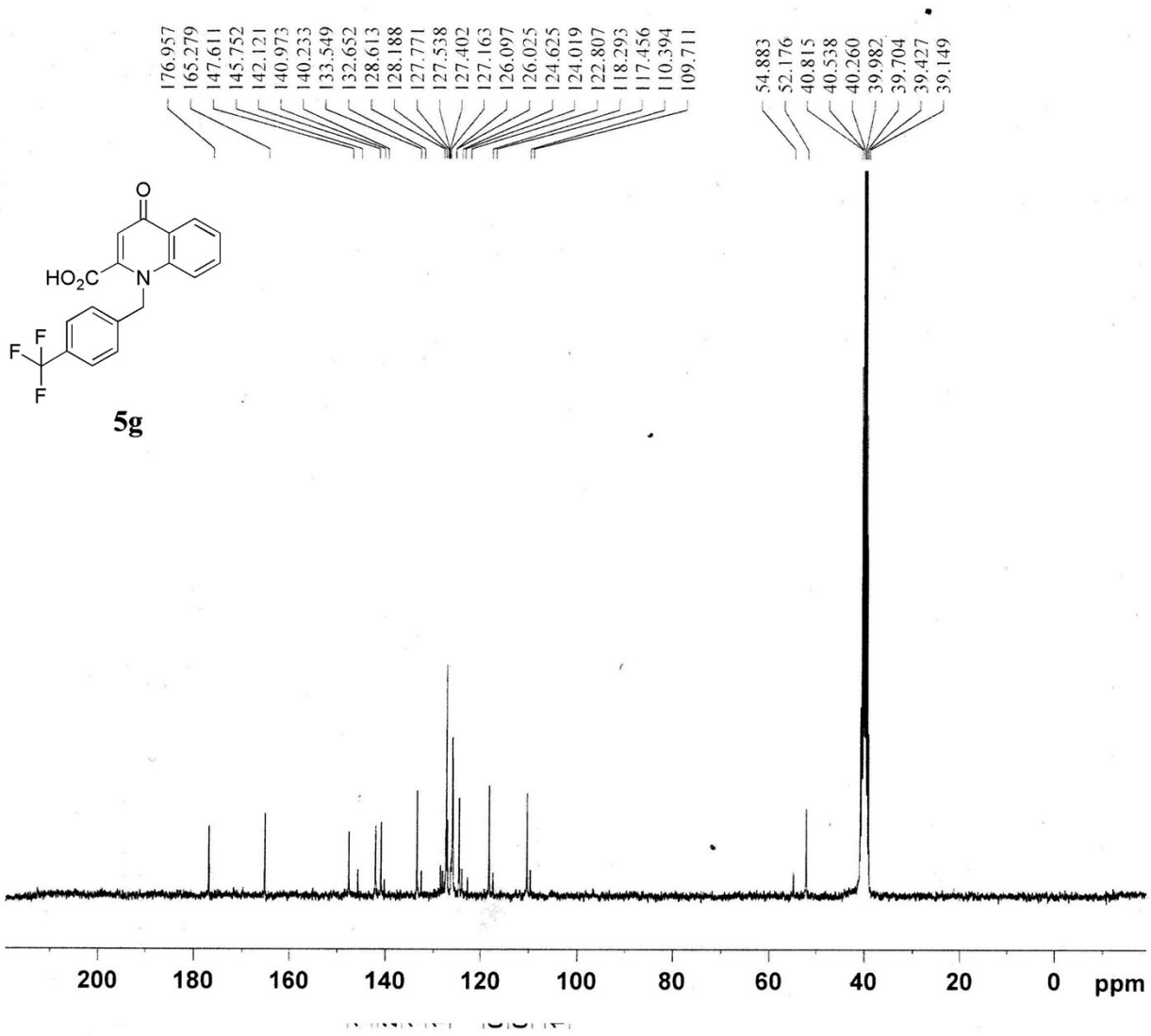


Fig. S28. ^{13}C NMR spectrum

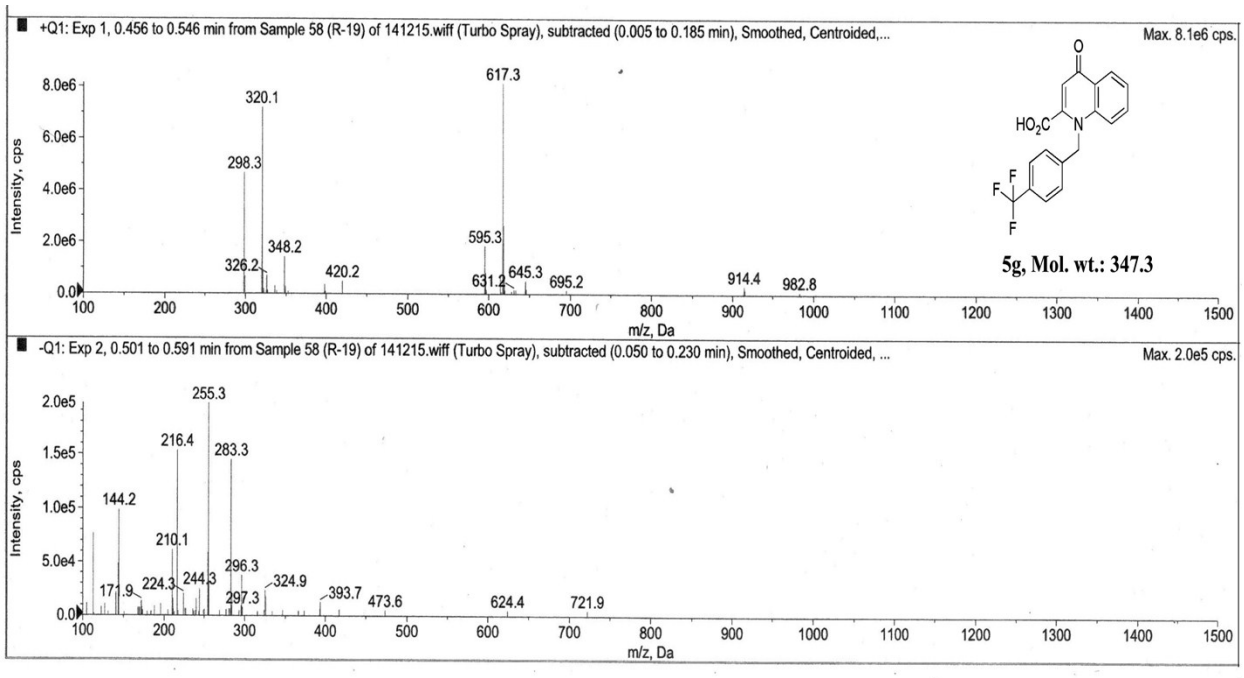


Fig. S29. ESI-MS spectrum

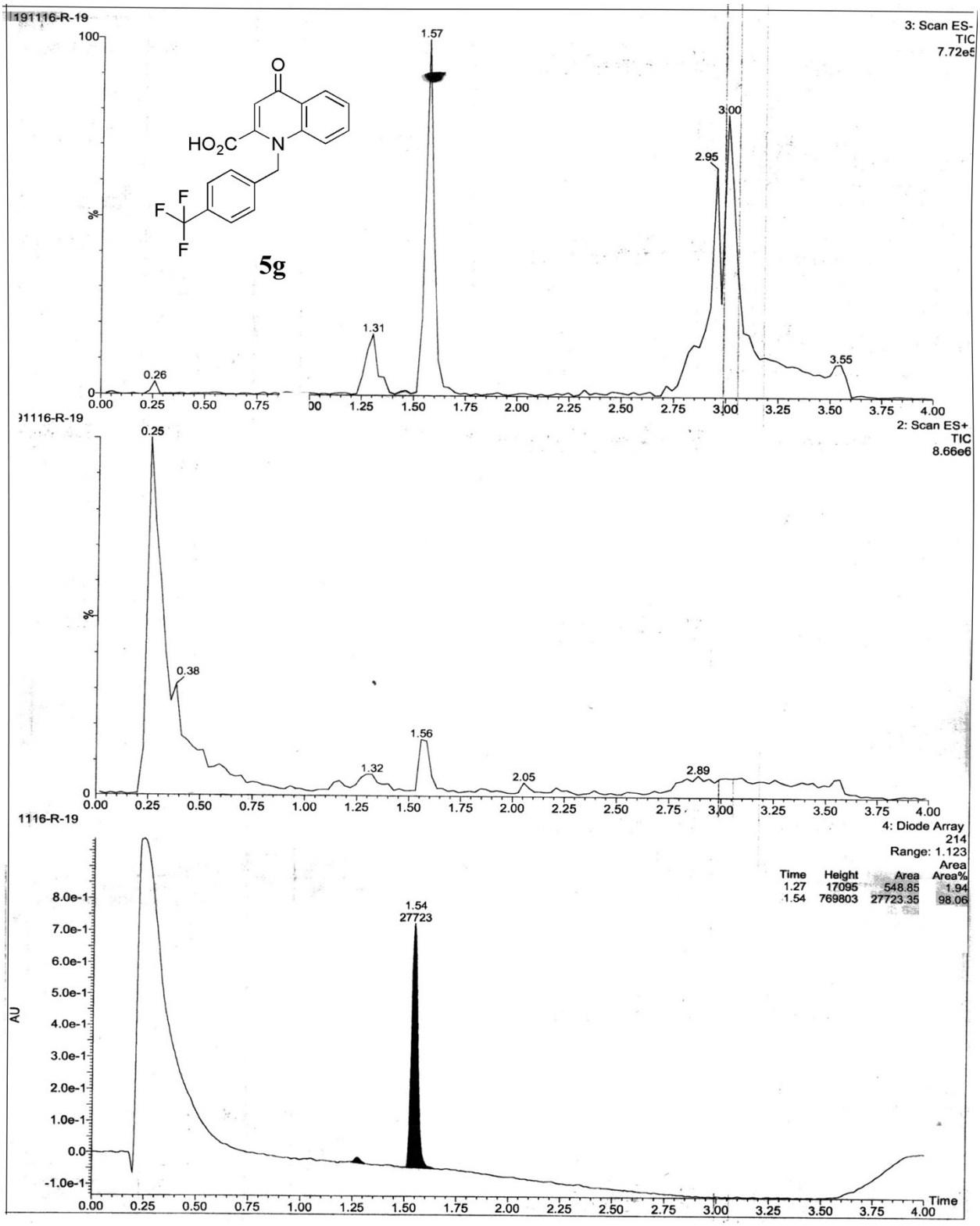


Fig. S30. HPLC spectrum

4.10. 1-((2-(furan-2-ylmethyl)amino)phenyl)ethanone (3i)

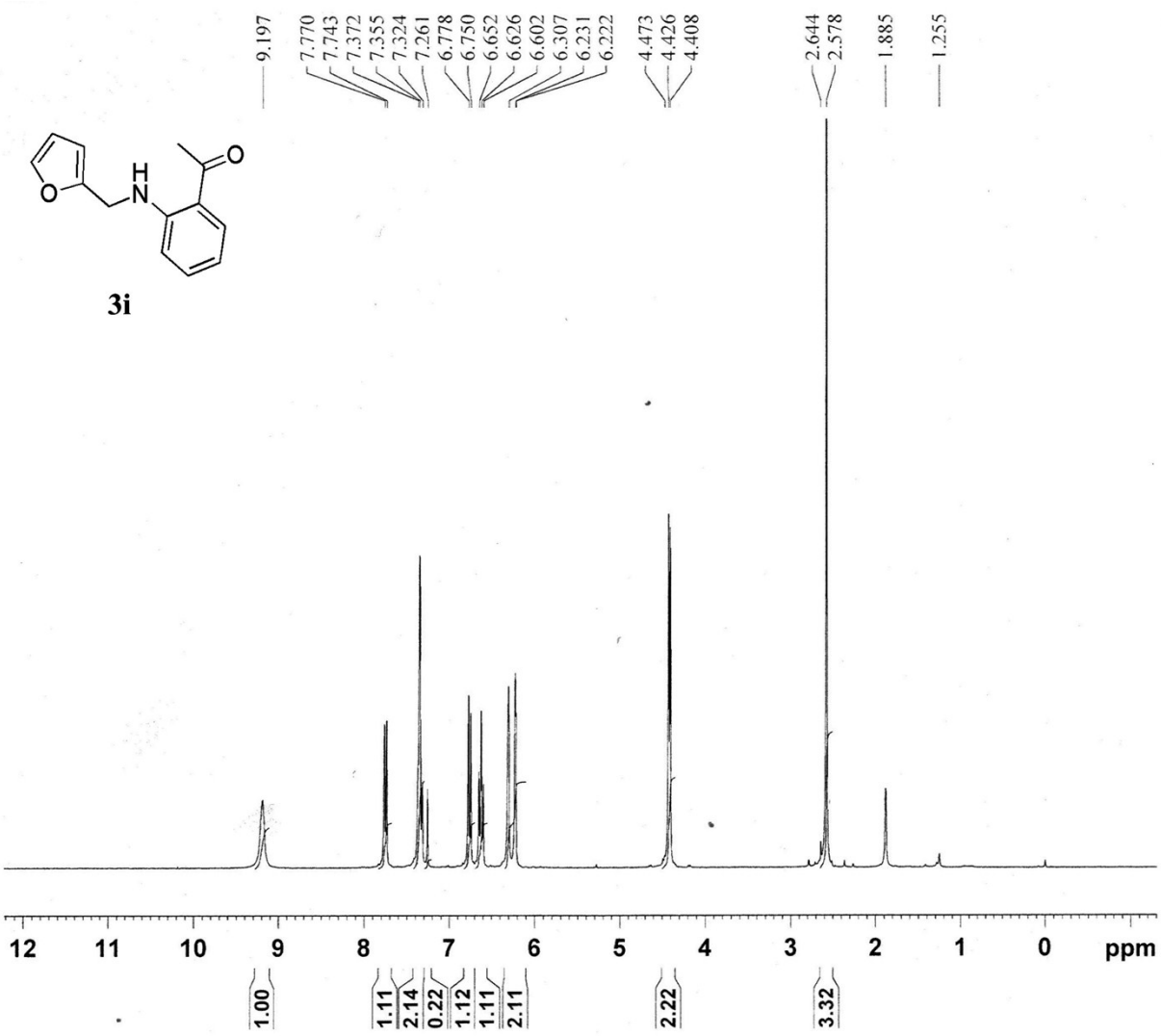


Fig. S31. ^{1}H NMR spectrum

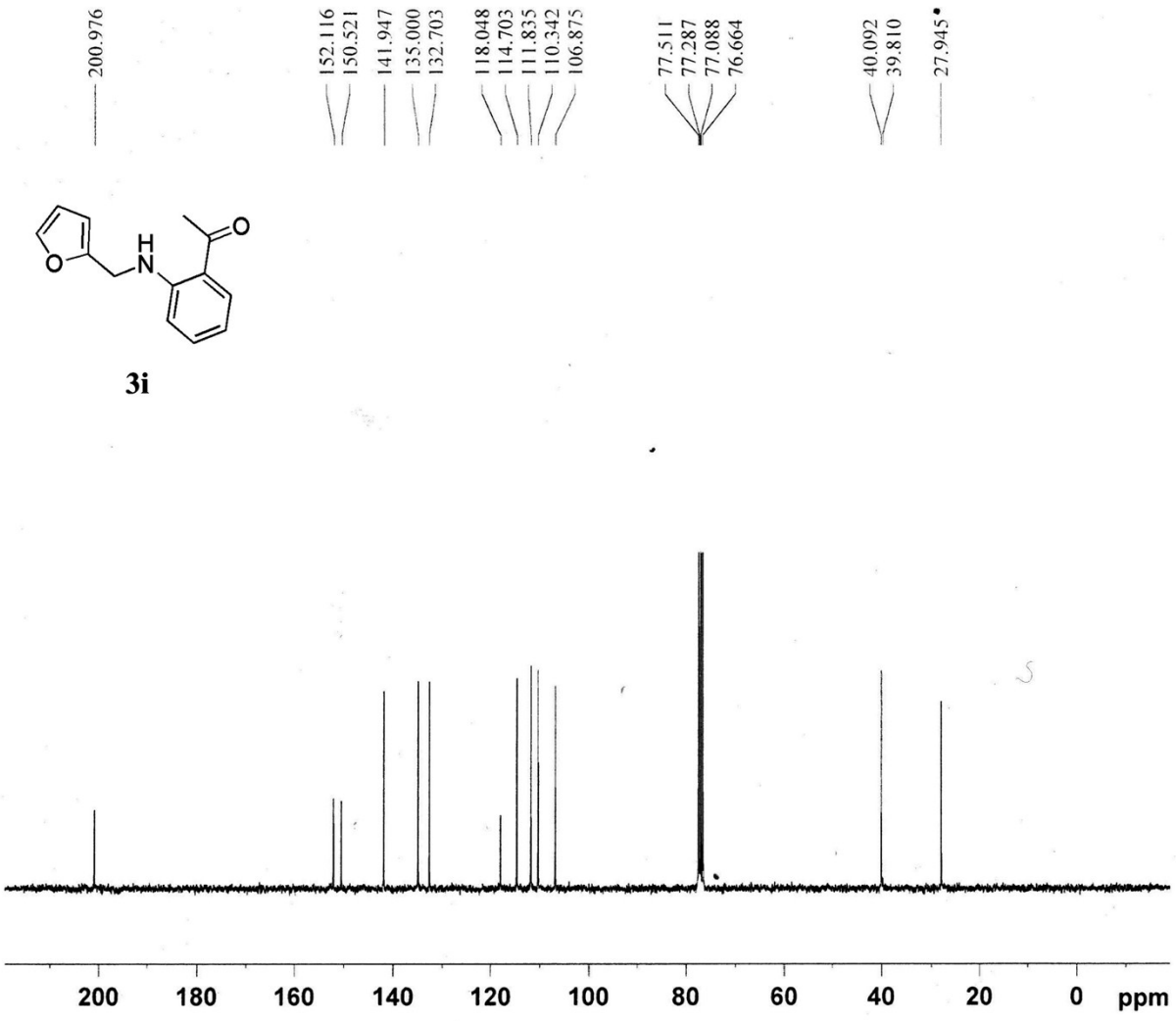


Fig. S32. ^{13}C NMR spectrum

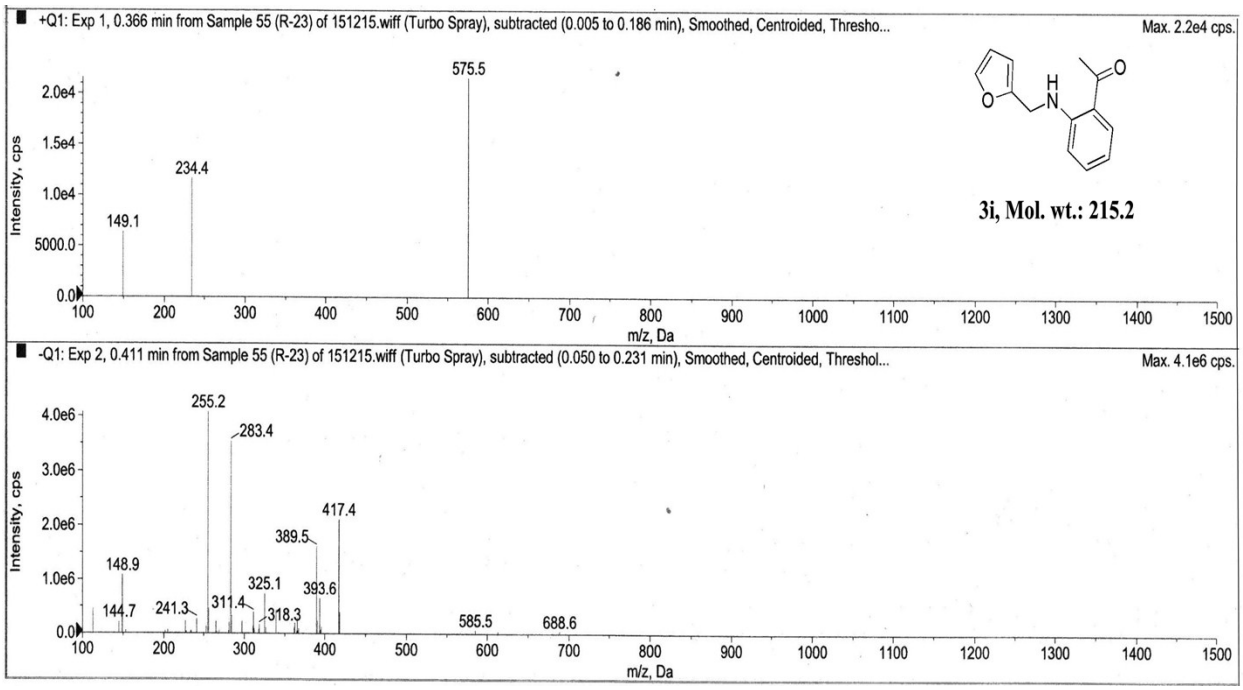


Fig. S33. ESI-MS spectrum

4.11. Ethyl 1-(furan-2-ylmethyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4i)

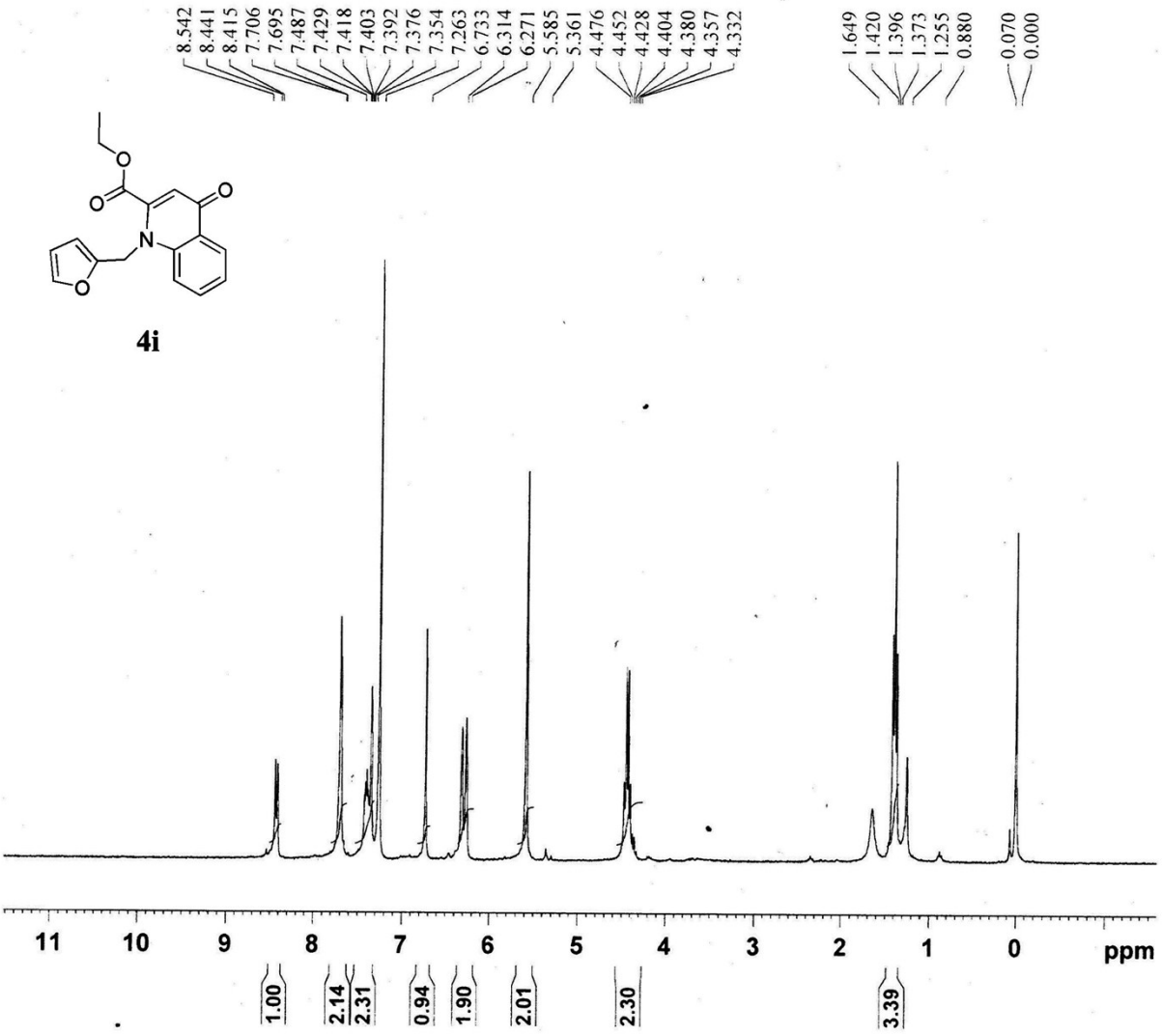


Fig. S34. ^{1}H NMR spectrum

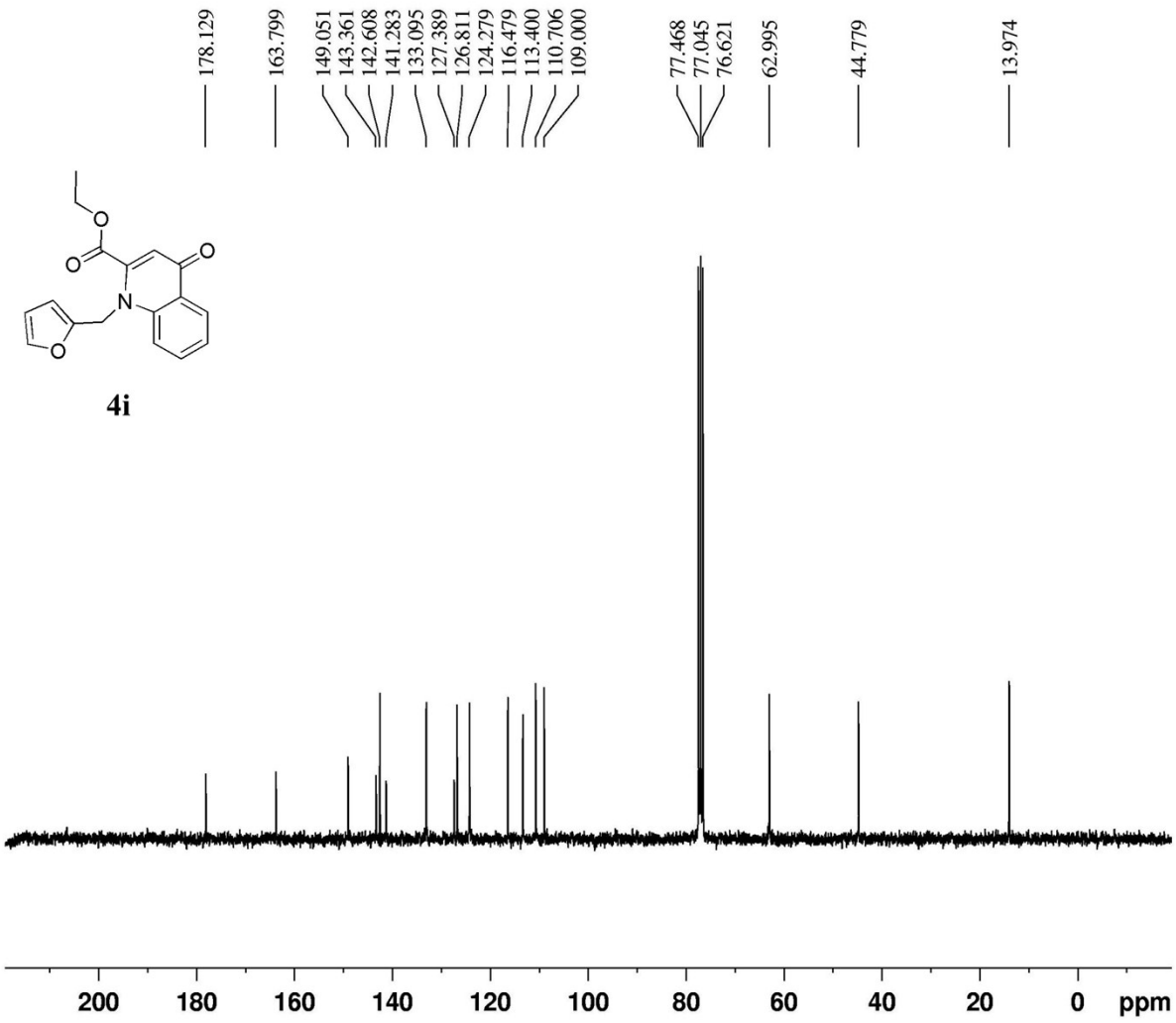


Fig. S35. ^{13}C NMR spectrum

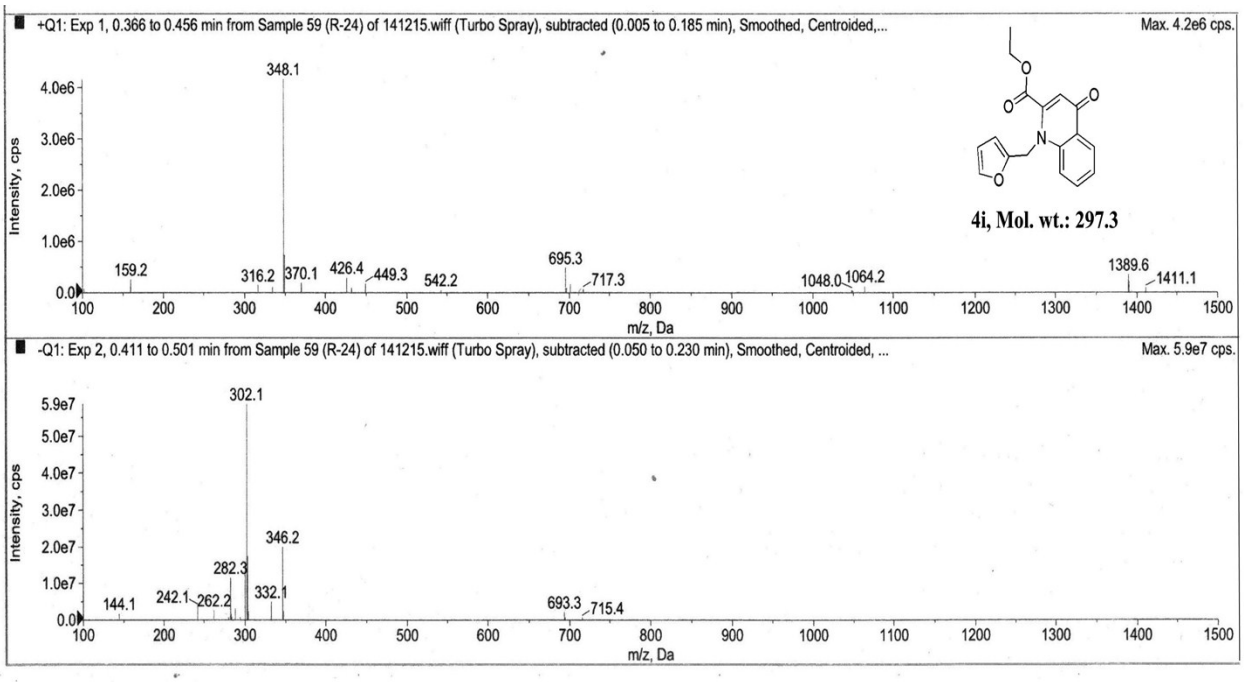


Fig. S36. ESI-MS spectrum

4.12. 1-(furan-2-ylmethyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5i)

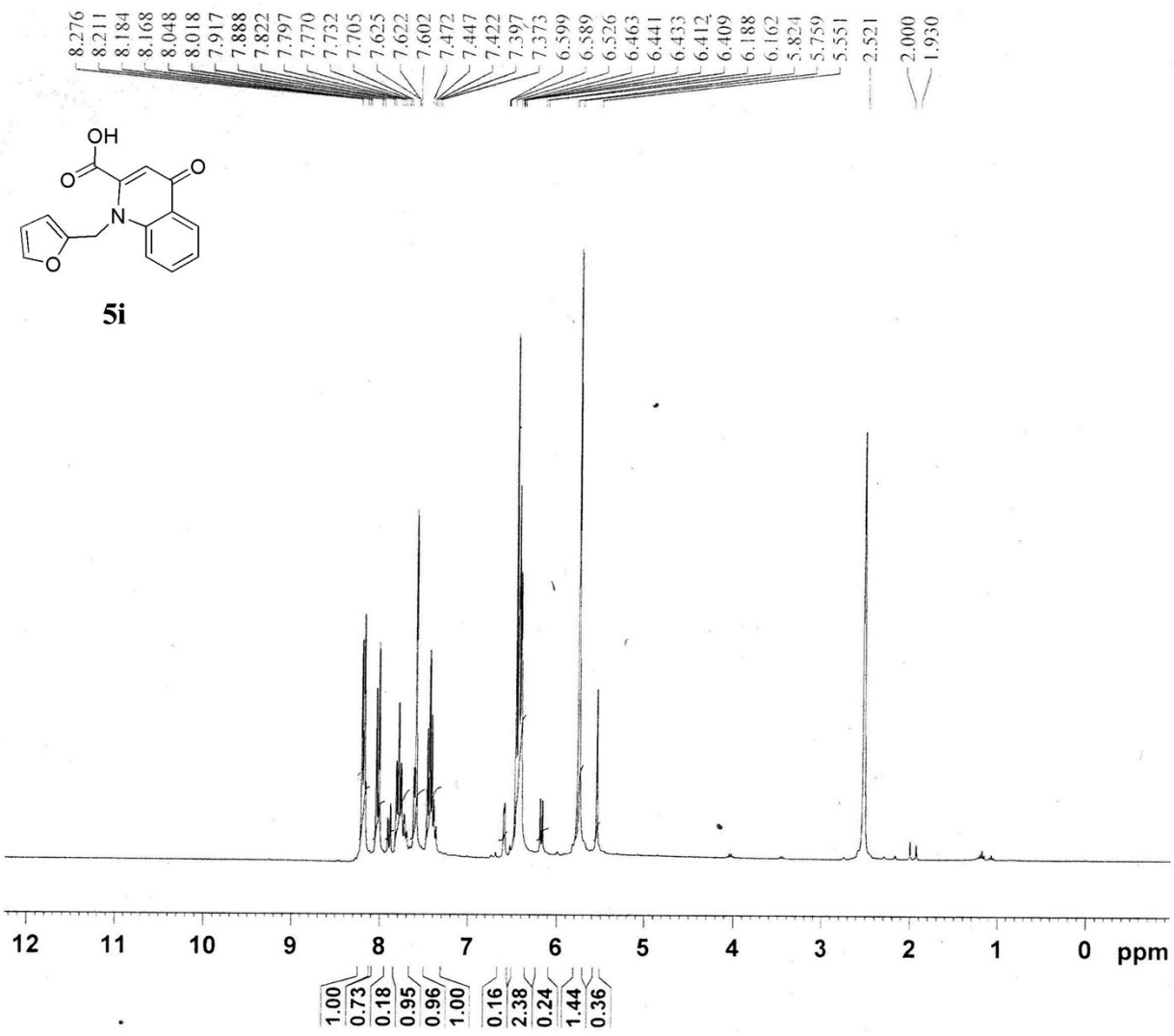


Fig. S37. ^{1}H NMR spectrum

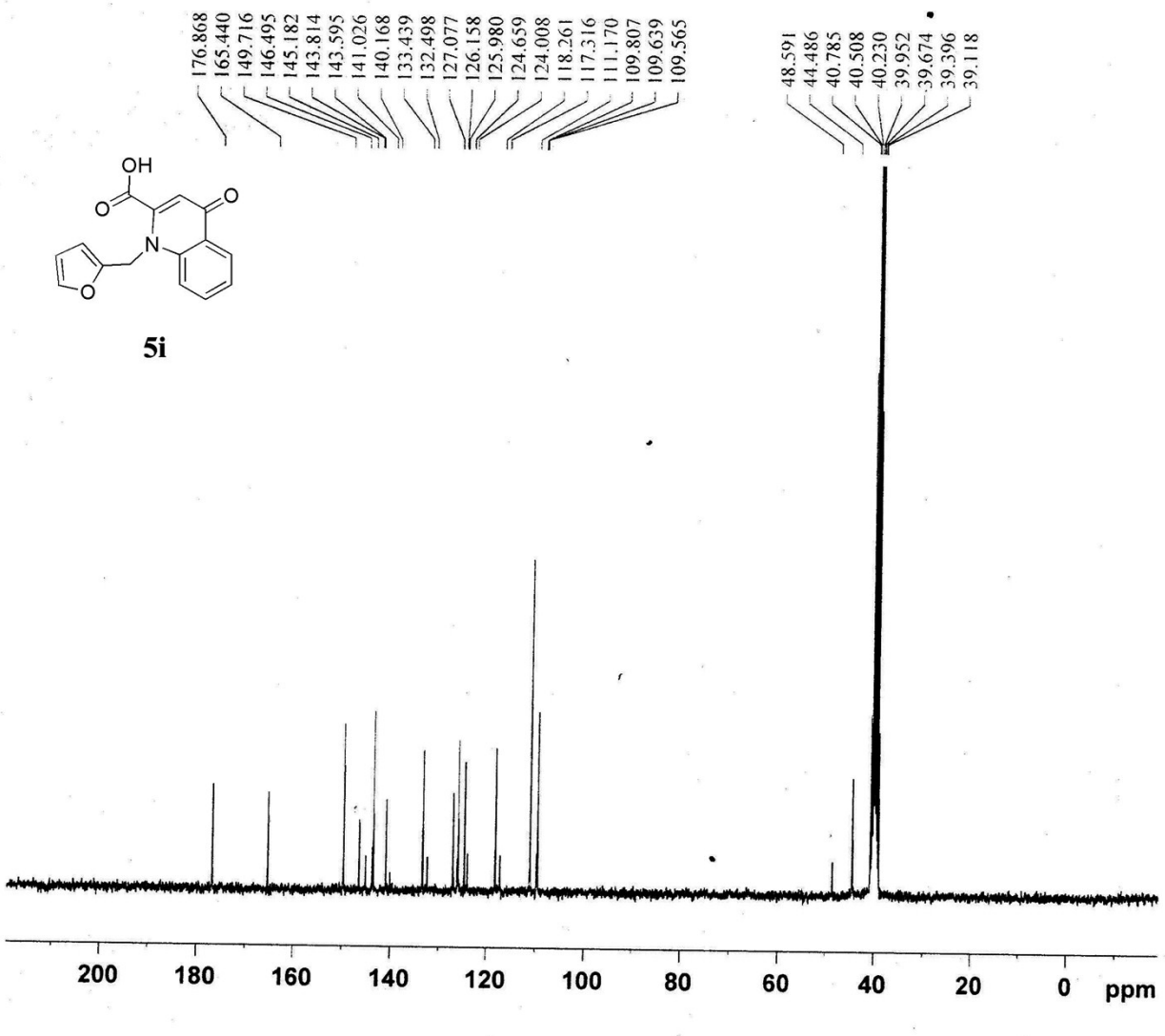


Fig. S38. ^{13}C NMR spectrum

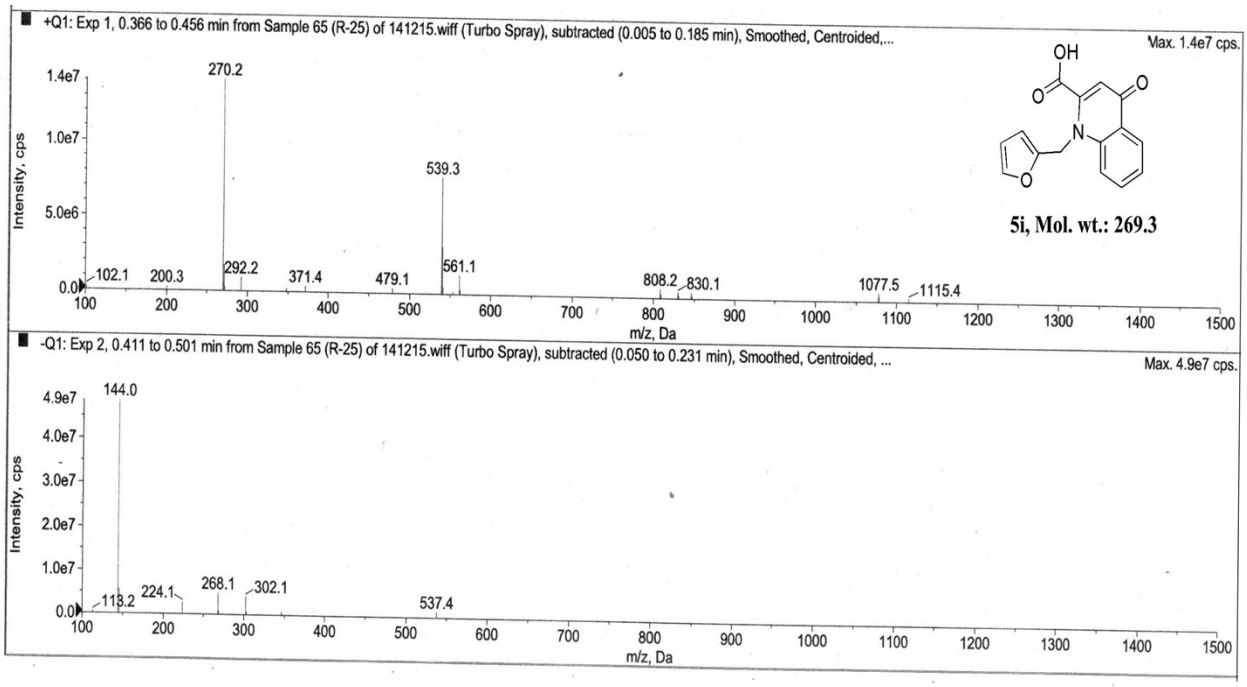


Fig. S39. ESI-MS spectrum

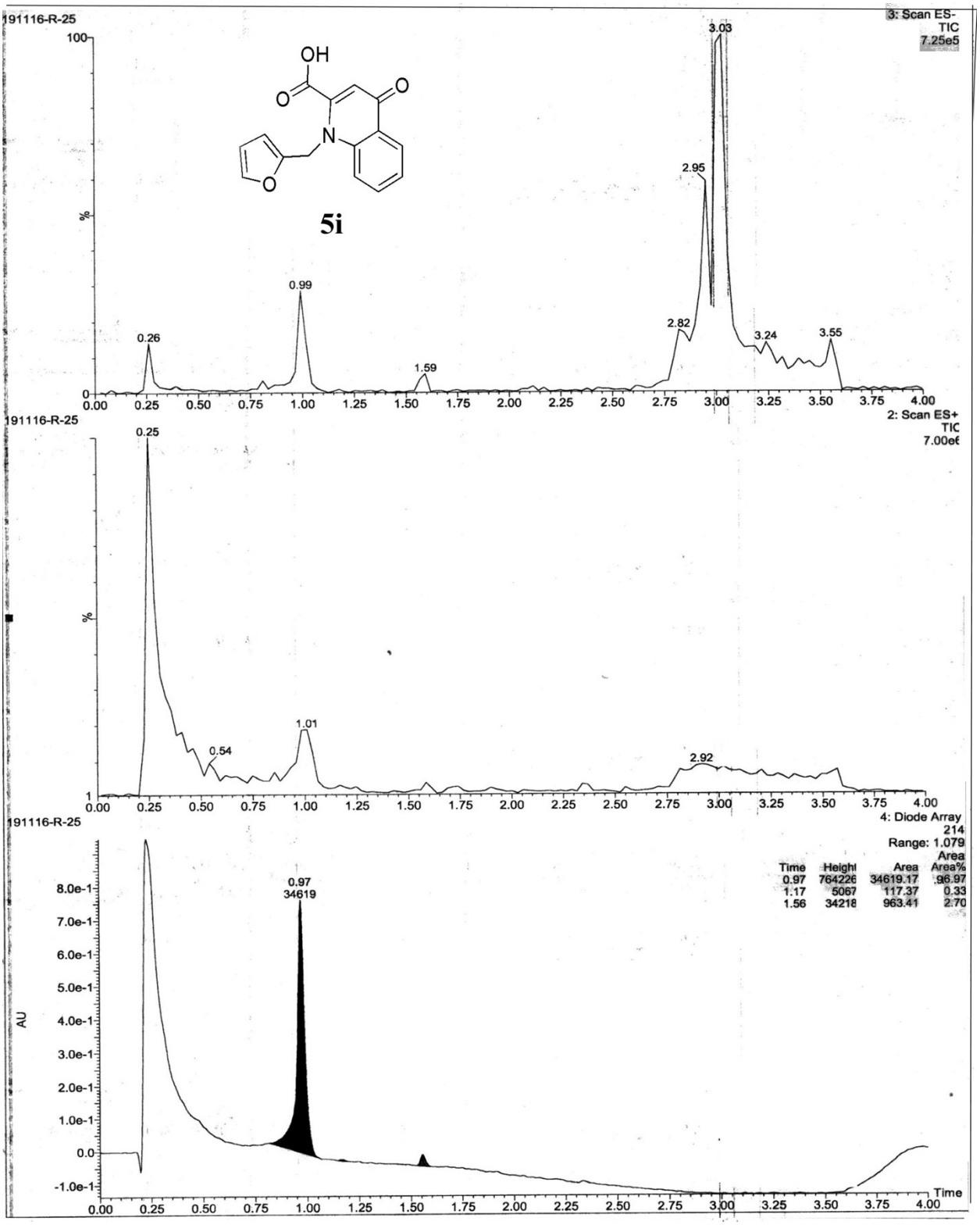


Fig. S40. HPLC spectrum

4.13. 1-((2-((2-bromo-3-fluoropyridin-4-yl)methyl)amino)phenyl)ethanone (3j)

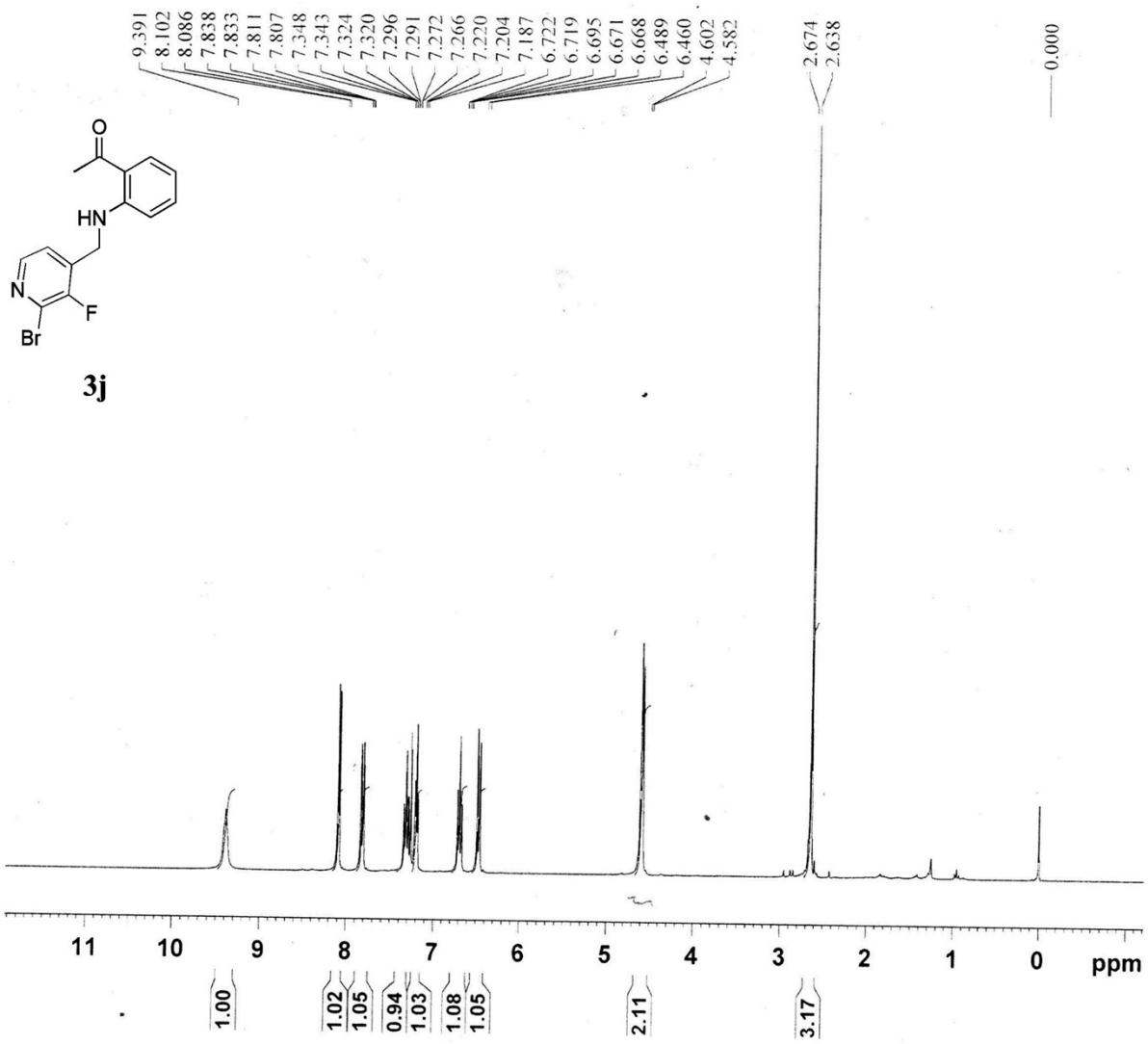


Fig. S41. ^{1}H NMR spectrum

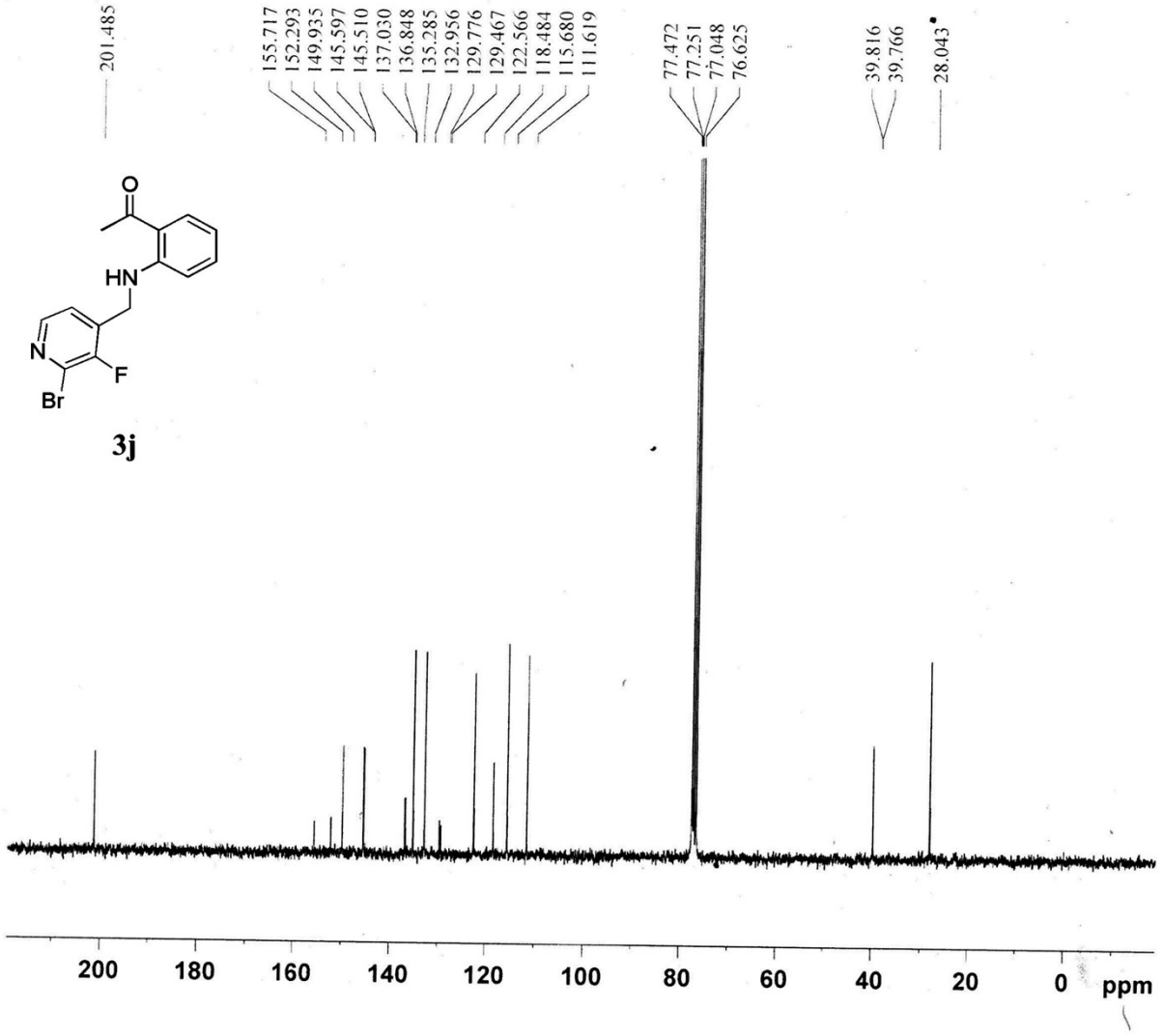


Fig. S42. ^{13}C NMR spectrum

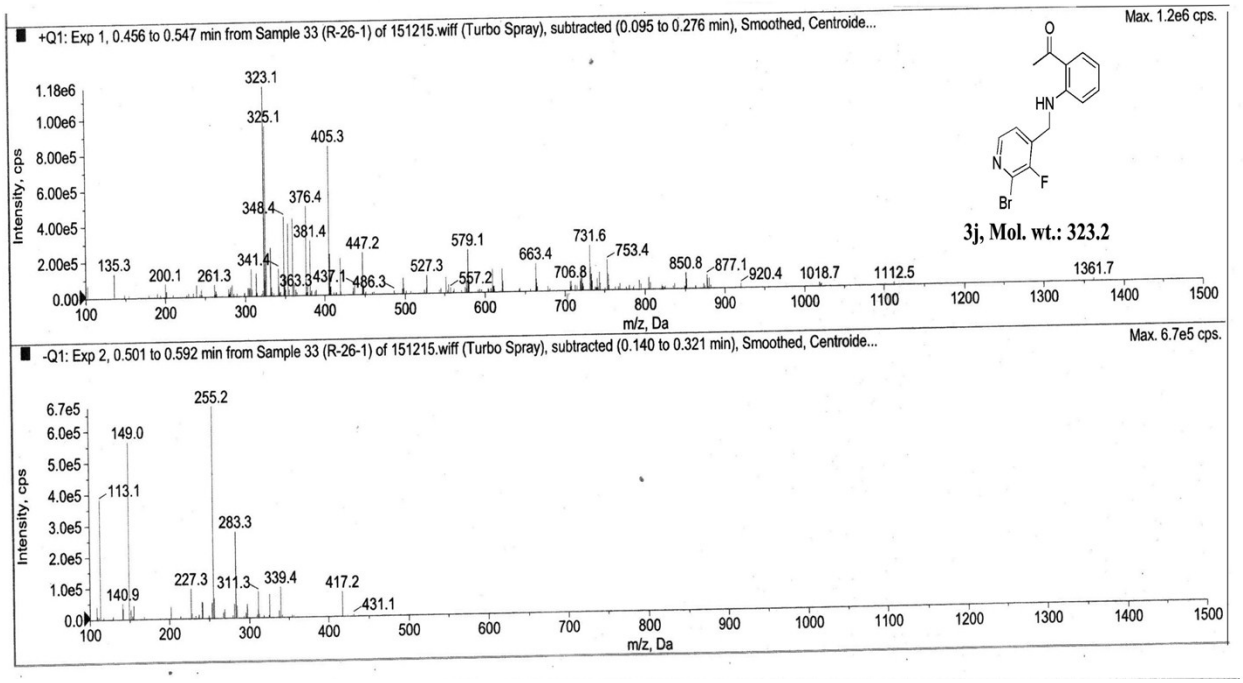


Fig. S43. ESI-MS spectrum

4.14. Ethyl 1-((2-bromo-3-fluoropyridin-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylate (4j)

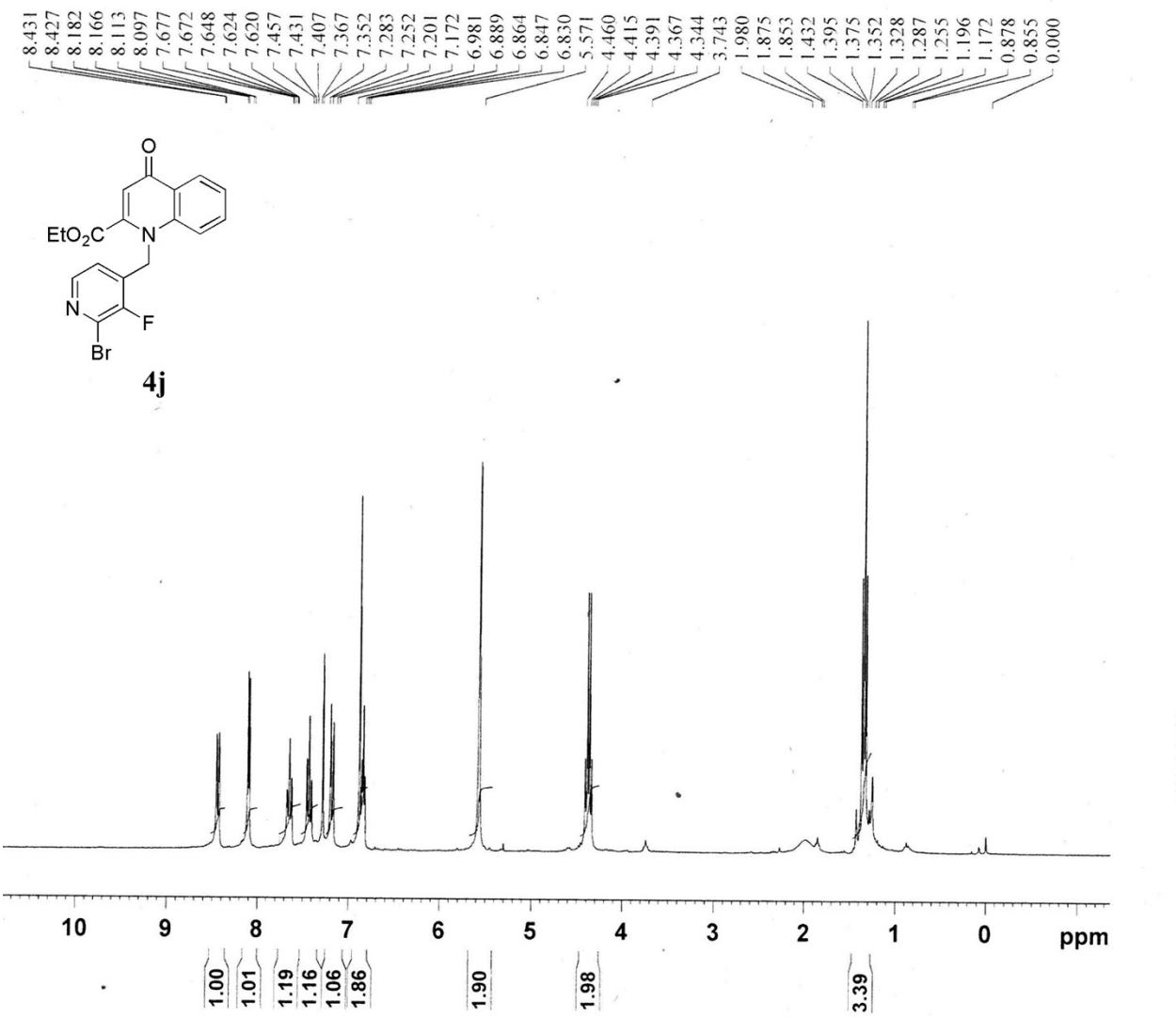


Fig. S44. ^{1}H NMR spectrum

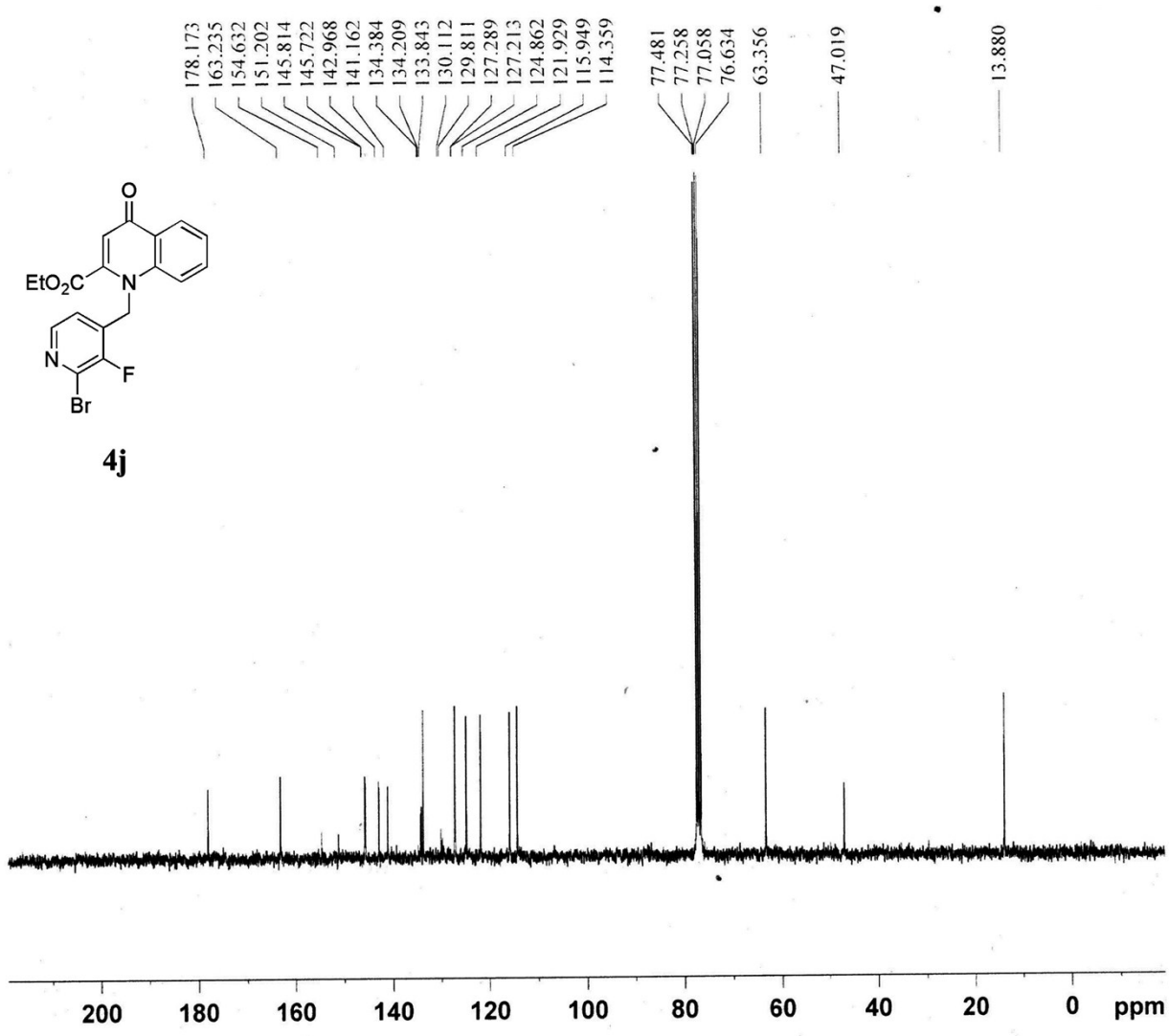


Fig. S45. ^{13}C NMR spectrum

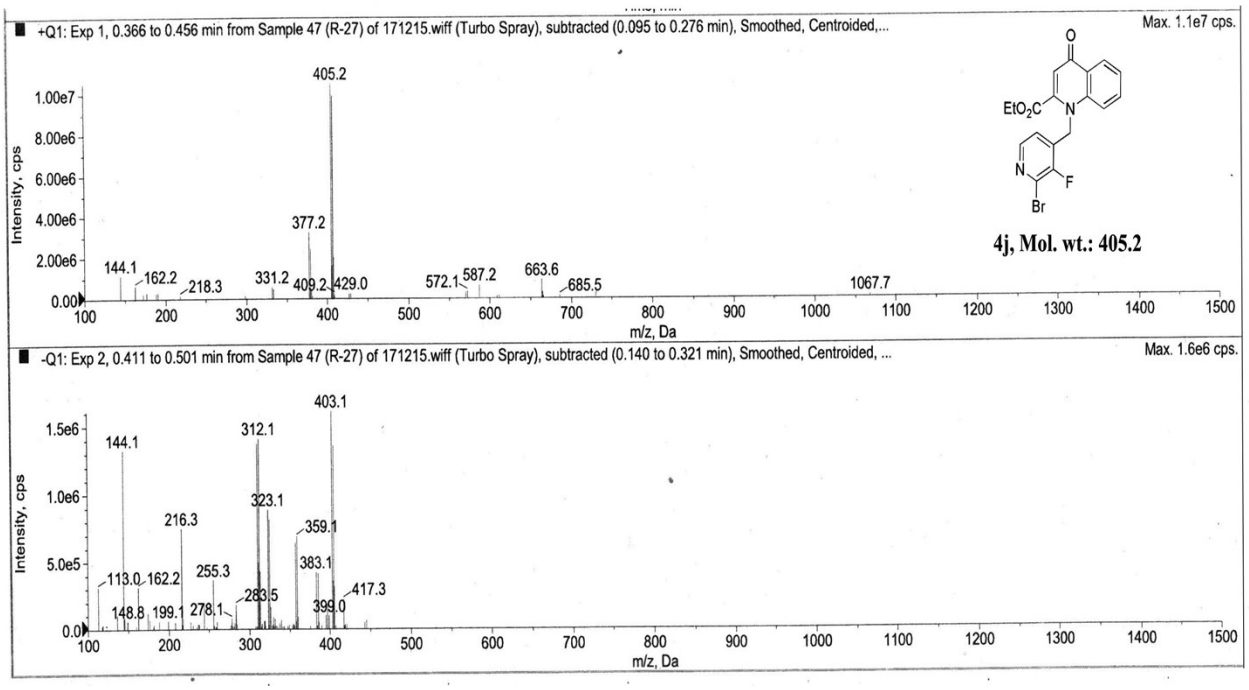


Fig. S46. ESI-MS spectrum

4.15. 1-((2-bromo-3-fluoropyridin-4-yl)methyl)-4-oxo-1,4-dihydroquinoline-2-carboxylic acid (5j)

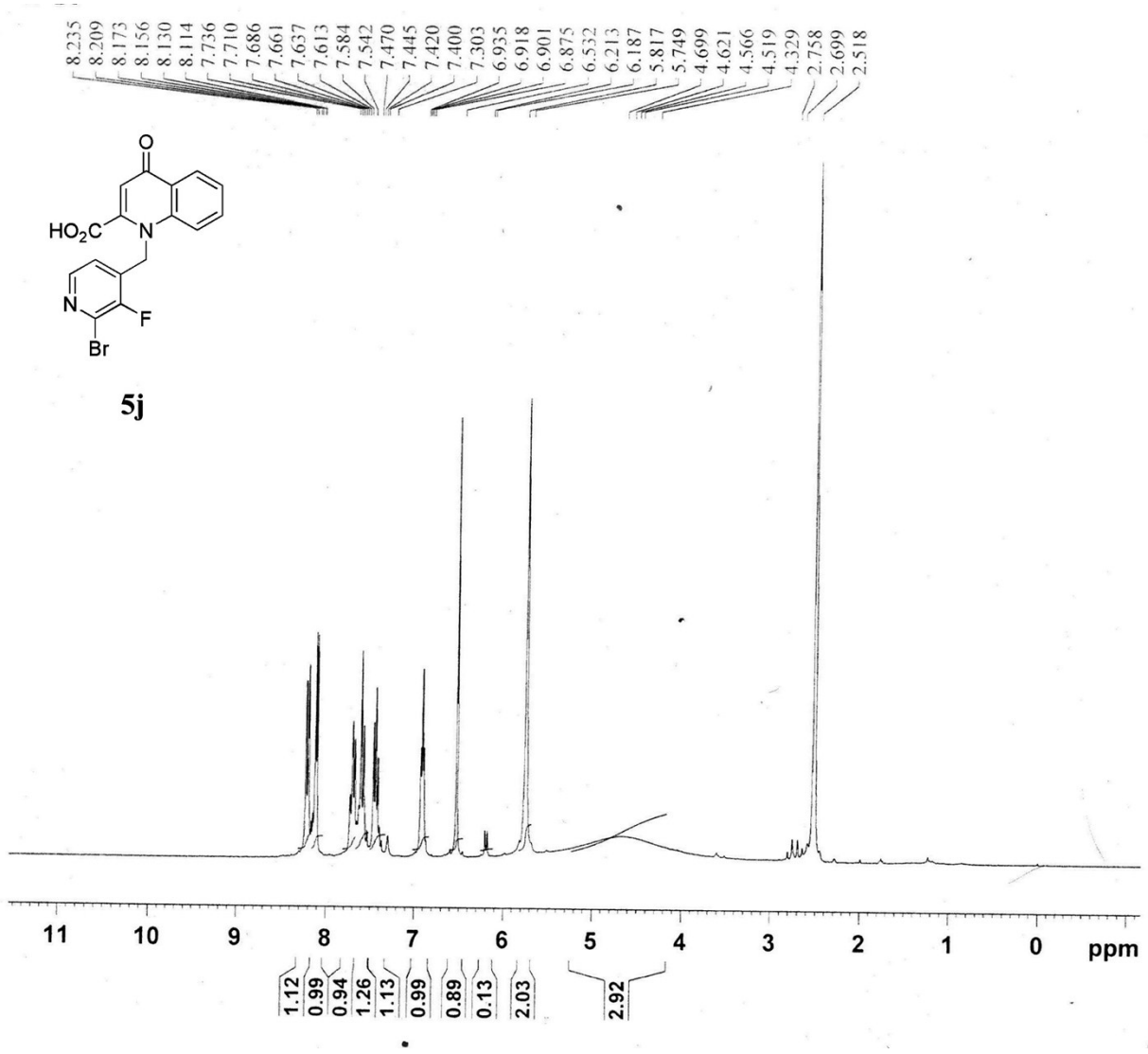


Fig. S47. ^{1}H NMR spectrum

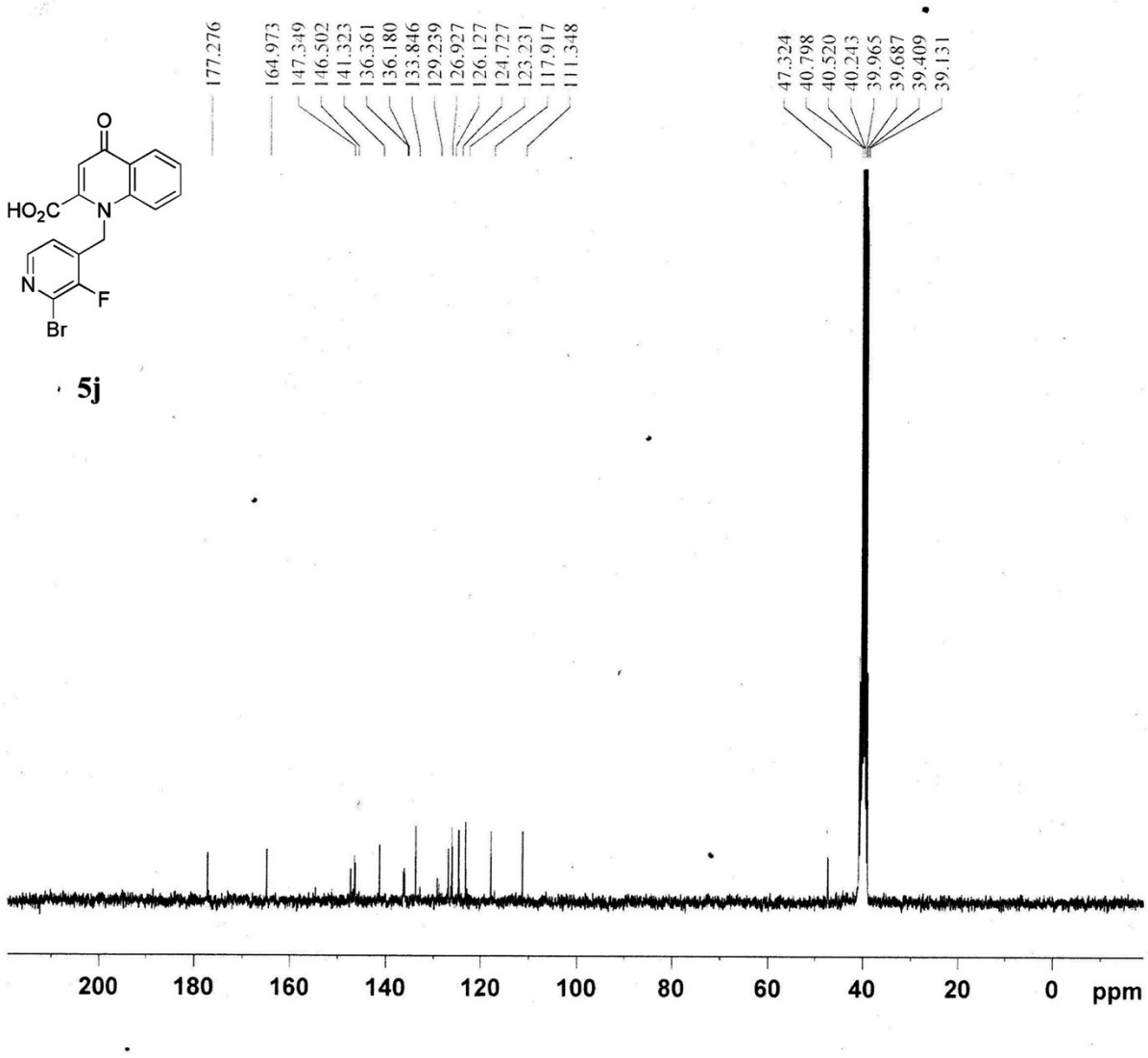


Fig. S48. ^{13}C NMR spectrum

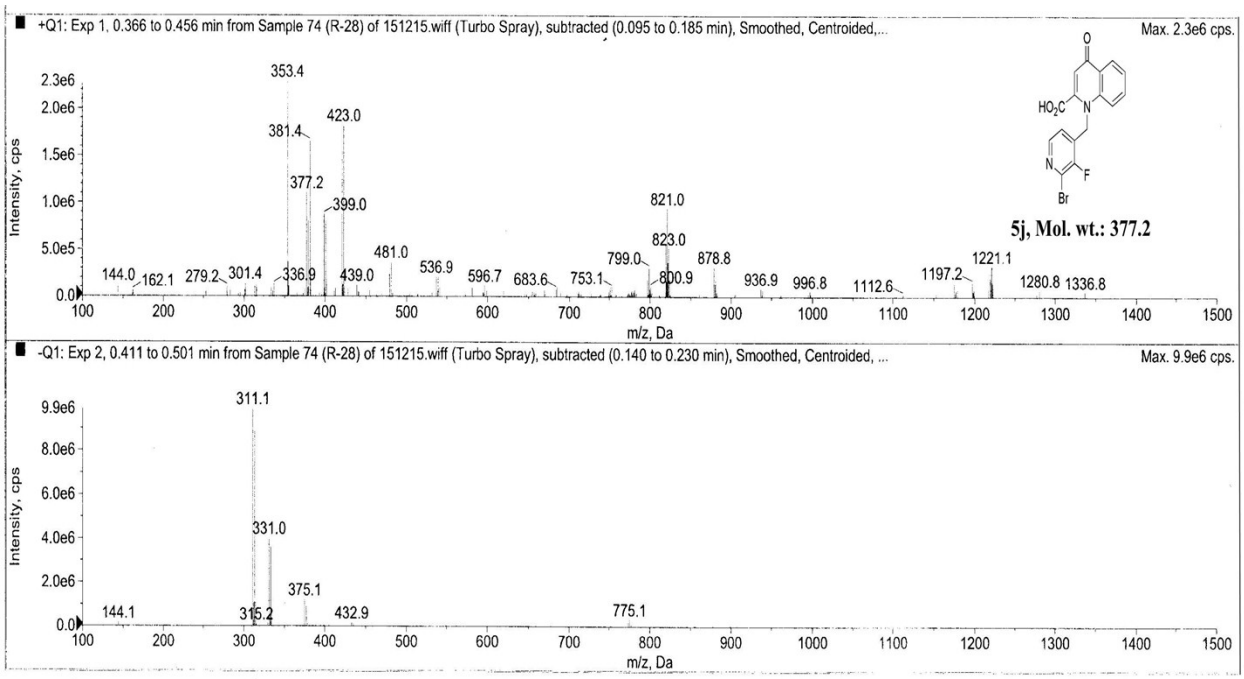


Fig. S49. ESI-MS spectrum

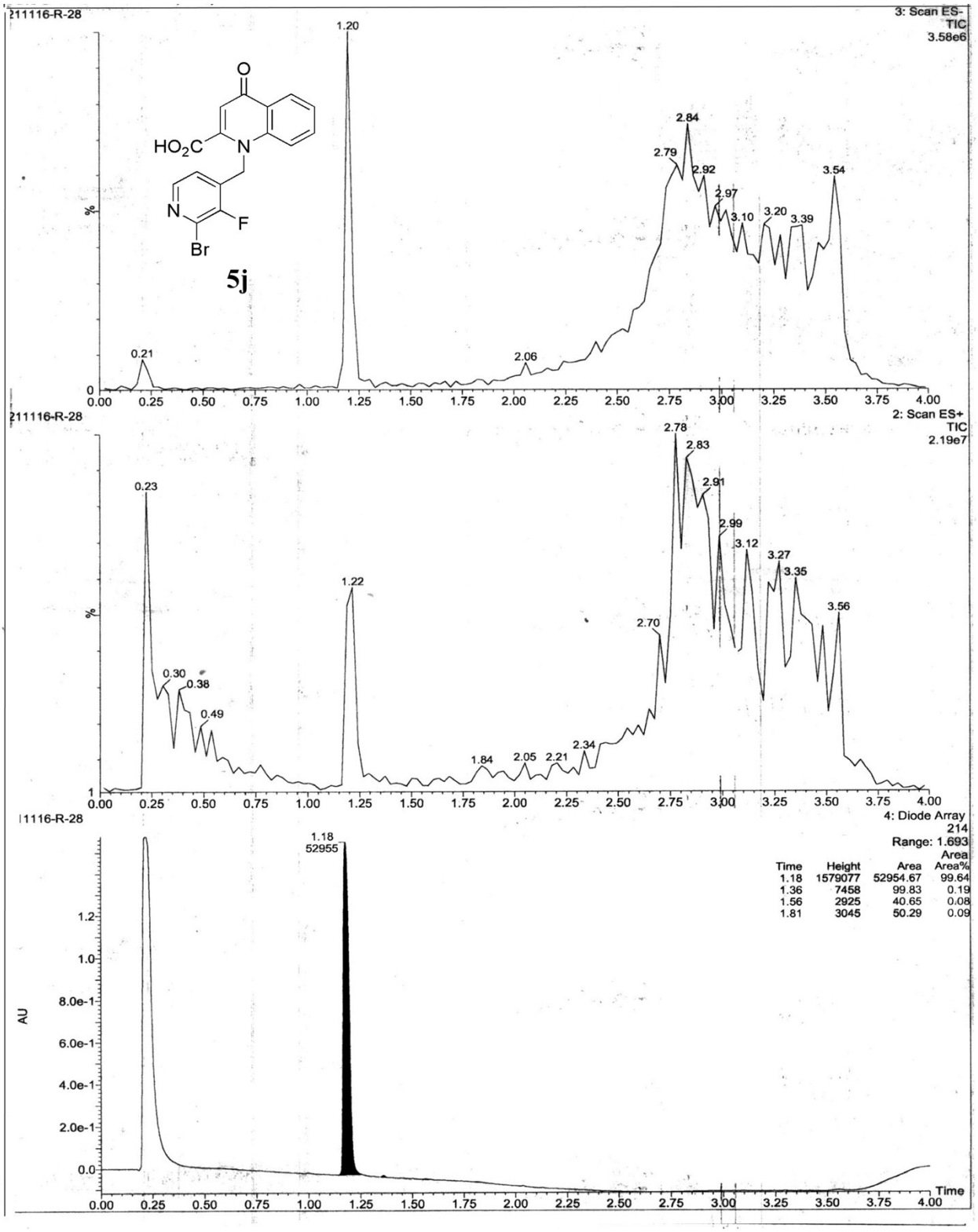


Fig. S50. HPLC spectrum

5. X-ray crystallographic data

The structures of **3c** and **3e** were determined by the X-ray diffraction technique. The suitable crystals of these compounds were obtained by the slow evaporation of mixed solvent system of ethanol and ethyl acetate and crystallized in P-1 and P21/n space groups, respectively. ORTEP diagram of compounds with ellipsoids drawn at 30% probability level along with their atomic numbering schemes is shown in Figure S5.1 and 5.3. Crystal structure of **3c** consist of three planar six membered rings connected with a five membered pyrazole ring. The planar six membered ring make angles of 25.5°, 17.4° and 88.1° respectively with the five member ring. Unit cell of **3c** contains two molecules of similar conformations which are interacted through aromatic π...π interactions (Figure 5.2). Intramolecular N-H...O hydrogen bonding and intermolecular C-H...π interactions also play critical roles in stabilizing the crystal structure.

Crystal structure analysis of compound **3e** shows that both the six membered rings connected through linker, are planar and also lie in the same plane (angle between the planes is 1.29º). Crystal packing diagram of **3e** shows four molecules in the unit cell forming dimer through C-H...O hydrogen bonding interactions (Figure 5.4). Intramolecular N-H...O hydrogen bonding interactions is also demonstrated by (I) in the crystal state. Several other non covalent interactions are also exhibited by the crystal packing. C7-H7A...Cg(2)(d(H...π) = 2.65Å, C-H...π = 149°); C10-Cl1...Cg(1)(d(Cl...π) = 3.605Å, C-Cl...π = 101.9°, symmetry position x, 1+y, z); C10-Cl1...Cg(2)(d(Cl...π) = 3.466Å, C-Cl...π = 155.5°, symmetry position ½+x, 3/2-y, ½+z) and C13-O1...Cg(1)(d(O...π) = 3.553Å, C-O...π = 91.0°, symmetry position x, -1+y, z) hydrogen bondings are also observed in the crystal structure.

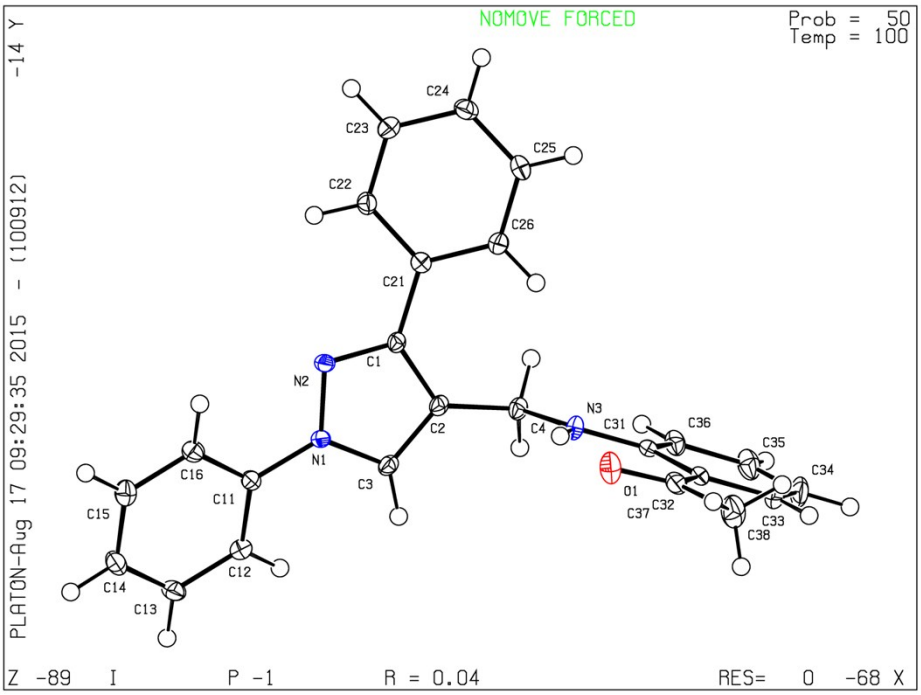


Figure 5.1: Crystal structure of compound 3c

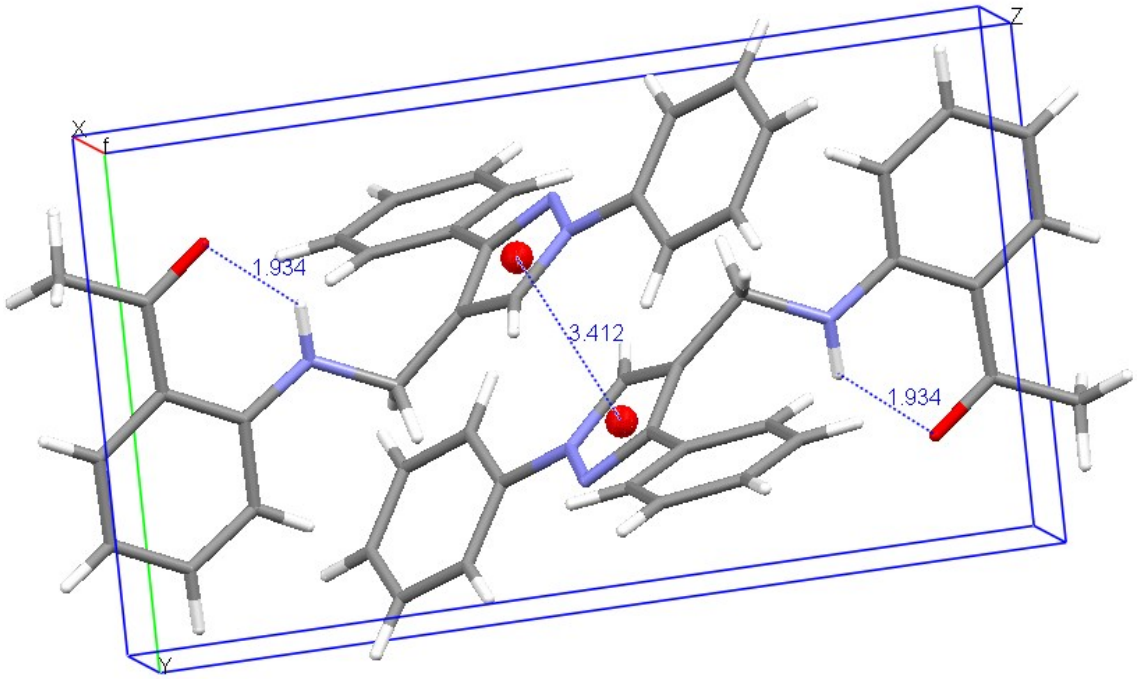


Figure 5.2: Unit cell in the crystal packing of compound **3c** (Hydrogen bonding is shown by dotted lines)

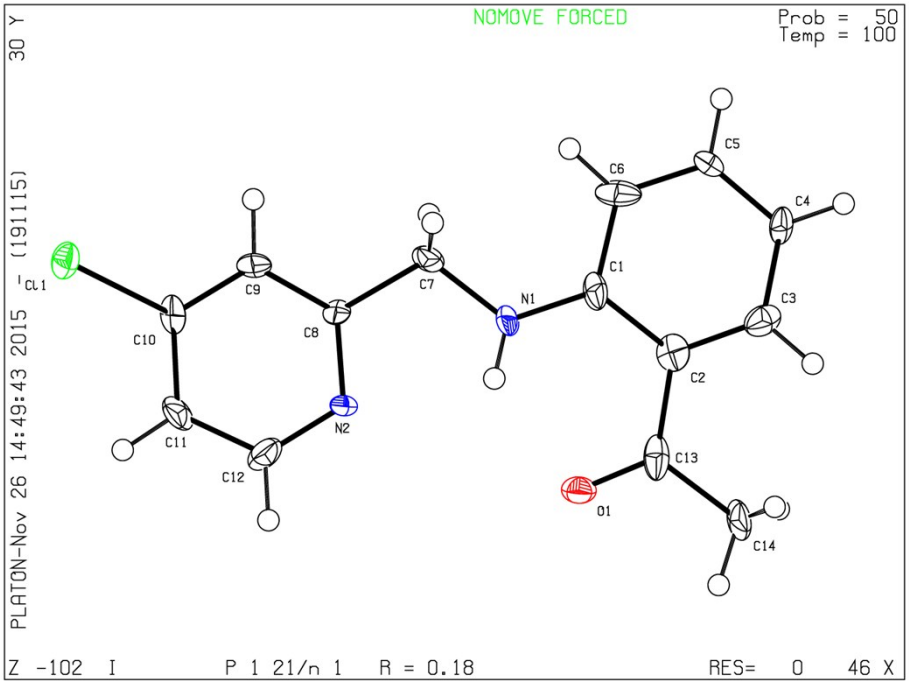


Figure 5.3: Crystal structure of compound 3e

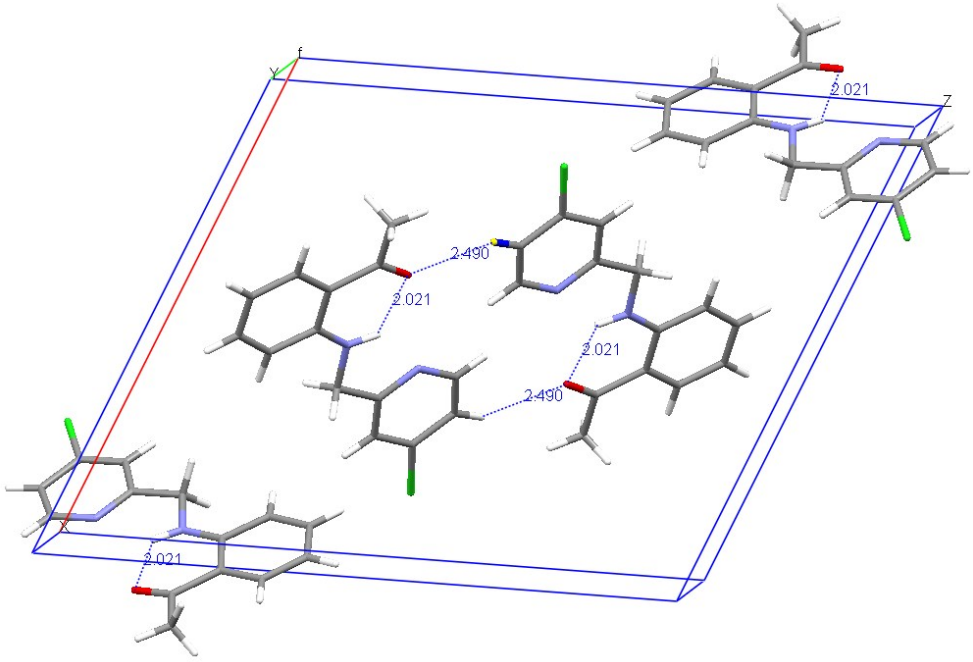


Figure 5.4: Unit cell in the crystal packing of compound **3e** (Hydrogen bonding is shown by dotted lines)

Table 5.1. Sample and crystal data for 3c and 3e.

	3c	**3e**
Chemical formula	$C_{24}H_{21}N_3O$	$C_{14}H_{13}ClN_2O$
Formula weight	367.44 g/mol	260.71 g/mol
Temperature	100(2) K	100(2) K
Wavelength	0.71073 Å	1.54178 Å
Crystal size	0.181 × 0.370 × 0.381 mm	0.032 × 0.047 × 0.469 mm
Crystal habit	colorless prism	colorless needle
Crystal system	triclinic	monoclinic
Space group	P -1	P1 2_1/n1
Unit cell dimensions	a = 8.5010(4) Å b = 8.6149(4) Å c = 13.9713(6) Å α = 91.269(2)° β = 94.756(2)° γ = 114.531(2)°	a = 14.5288(10) Å b = 5.2501(4) Å c = 17.6225(12) Å α = 90° β = 113.257(4)° γ = 90°
Volume	925.82(7) $Å^3$	1234.98(16) $Å^3$
Z	2	4
Density (calculated)	1.318 g/cm^3	1.402 g/cm^3
Absorption coefficient	0.082 mm^{-1}	2.642 mm^{-1}
F(000)	388	544

Table 5.2. Data collection and structure refinement for 3c and 3e**.**

	3c	3e
Theta range for data collection	2.60 to 27.10°	3.36 to 64.37°
Index ranges	-10<=h<=10, -11<=k<=11, -17<=l<=17	-16<=h<=16, -6<=k<=6, -20<=l<=20
Reflections collected	16565	9359
Independent reflections	4057 [R(int) = 0.0492]	2017 [R(int) = 0.1326]
Coverage of independent reflections	99.6%	97.9%
Absorption correction	multi-scan	multi-scan
Max. and min. transmission	0.9850 and 0.9690	0.9200 and 0.3700
Structure solution technique	direct methods	direct methods
Structure solution program	SHELXL-2014 (Sheldrick, 2014)	SHELXL-2014 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2	Full-matrix least -squares on F^2

Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4057 / 0 / 258	2017 / 1 / 167
Goodness-of-fit on F^2	1.055	1.328
Final R indices	3425 data; I>2σ (I) R1 = 0.0427, wR2 = 0.1031	1686 data; I>2σ (I) R1 = 0.1800, wR2 = 0.3342
	all data R1 = 0.0529, wR2 = 0.1095	all data R1 = 0.2002, wR2 = 0.3428
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0492P)^2+0.3840P]$ where $P=(F_o^2+2F_c^2)/3$	$w=1/[\sigma^2(F_o^2)+(0.0001P)^2+30.4509P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.275 and -0.307 eÅ^{-3}	0.492 and -0.545 eÅ^{-3}
R.M.S. deviation from mean	0.051 eÅ^{-3}	0.130 eÅ^{-3}

5.3. X-ray crystallographic data of compound **3c**

Table 5.3.1. Bond lengths (Å)

N1-C3	1.3592(16)	N1-N2	1.3622(14)
N1-C11	1.4240(16)	N2-C1	1.3411(16)
N3-C31	1.3653(16)	N3-C4	1.4612(15)
N3-H1	0.899(18)	O1-C37	1.2370(16)
C1-C2	1.4249(17)	C1-C21	1.4697(17)
C2-C3	1.3685(18)	C2-C4	1.4989(17)
C3-H3	0.95	C4-H4A	0.99
C4-H4B	0.99	C11-C16	1.3916(18)
C11-C12	1.3922(18)	C12-C13	1.3884(19)
C12-H12	0.95	C13-C14	1.389(2)
C13-H13	0.95	C14-C15	1.3881(19)
C14-H14	0.95	C15-C16	1.3915(18)
C15-H15	0.95	C16-H16	0.95
C21-C26	1.4026(17)	C21-C22	1.4027(17)
C22-C23	1.3846(18)	C22-H22	0.95
C23-C24	1.3972(18)	C23-H23	0.95
C24-C25	1.3910(19)	C24-H24	0.95
C25-C26	1.3871(18)	C25-H25	0.95
C26-H26	0.95	C31-C36	1.4113(18)
C31-C32	1.4312(18)	C32-C33	1.4085(18)

C32-C37	1.4731(19)	C33-C34	1.379(2)
C33-H33	0.95	C34-C35	1.394(2)
C34-H34	0.95	C35-C36	1.3802(19)
C35-H35	0.95	C36-H36	0.95
C37-C38	1.5135(18)	C38-H38A	0.98
C38-H38B	0.98	C38-H38C	0.98

Table 5.3.2. Bond angles (°)

C3-N1-N2	111.72(10)	C3-N1-C11	127.43(11)
N2-N1-C11	120.82(10)	C1-N2-N1	104.83(10)
C31-N3-C4	122.49(11)	C31-N3-H1	116.1(10)
C4-N3-H1	120.2(11)	N2-C1-C2	111.16(11)
N2-C1-C21	119.90(11)	C2-C1-C21	128.92(11)
C3-C2-C1	104.48(11)	C3-C2-C4	124.89(11)
C1-C2-C4	130.40(11)	N1-C3-C2	107.81(11)
N1-C3-H3	126.1	C2-C3-H3	126.1
N3-C4-C2	111.27(10)	N3-C4-H4A	109.4
C2-C4-H4A	109.4	N3-C4-H4B	109.4
C2-C4-H4B	109.4	H4A-C4-H4B	108.0
C16-C11-C12	120.52(12)	C16-C11-N1	119.92(11)
C12-C11-N1	119.56(11)	C13-C12-C11	119.37(12)
C13-C12-H12	120.3	C11-C12-H12	120.3
C12-C13-C14	120.69(12)	C12-C13-H13	119.7
C14-C13-H13	119.7	C15-C14-C13	119.42(12)
C15-C14-H14	120.3	C13-C14-H14	120.3
C14-C15-C16	120.66(12)	C14-C15-H15	119.7
C16-C15-H15	119.7	C15-C16-C11	119.28(12)
C15-C16-H16	120.4	C11-C16-H16	120.4
C26-C21-C22	118.41(12)	C26-C21-C1	121.50(11)
C22-C21-C1	120.09(11)	C23-C22-C21	120.81(12)
C23-C22-H22	119.6	C21-C22-H22	119.6
C22-C23-C24	120.23(12)	C22-C23-H23	119.9
C24-C23-H23	119.9	C25-C24-C23	119.45(12)
C25-C24-H24	120.3	C23-C24-H24	120.3
C26-C25-C24	120.38(12)	C26-C25-H25	119.8
C24-C25-H25	119.8	C25-C26-C21	120.69(12)
C25-C26-H26	119.7	C21-C26-H26	119.7
N3-C31-C36	120.37(11)	N3-C31-C32	121.16(12)
C36-C31-C32	118.47(11)	C33-C32-C31	118.10(12)
C33-C32-C37	120.27(12)	C31-C32-C37	121.63(11)

C34-C33-C32	122.59(13)	C34-C33-H33	118.7
C32-C33-H33	118.7	C33-C34-C35	118.75(12)
C33-C34-H34	120.6	C35-C34-H34	120.6
C36-C35-C34	120.95(13)	C36-C35-H35	119.5
C34-C35-H35	119.5	C35-C36-C31	121.13(12)
C35-C36-H36	119.4	C31-C36-H36	119.4
O1-C37-C32	122.27(12)	O1-C37-C38	118.15(13)
C32-C37-C38	119.57(12)	C37-C38-H38A	109.5
C37-C38-H38B	109.5	H38A-C38-H38B	109.5
C37-C38-H38C	109.5	H38A-C38-H38C	109.5
H38B-C38-H38C	109.5		

Table 5.3.3. Torsion angles (°)

C3-N1-N2-C1	-0.07(13)	C11-N1-N2-C1	-178.04(10)
N1-N2-C1-C2	0.31(13)	N1-N2-C1-C21	178.58(10)
N2-C1-C2-C3	-0.43(14)	C21-C1-C2-C3	-178.51(12)
N2-C1-C2-C4	174.22(12)	C21-C1-C2-C4	-3.9(2)
N2-N1-C3-C2	-0.20(14)	C11-N1-C3-C2	177.60(11)
C1-C2-C3-N1	0.37(14)	C4-C2-C3-N1	-174.66(11)
C31-N3-C4-C2	167.44(11)	C3-C2-C4-N3	-93.27(14)
C1-C2-C4-N3	93.05(15)	C3-N1-C11-C16	164.00(12)
N2-N1-C11-C16	-18.37(17)	C3-N1-C11-C12	-16.74(19)
N2-N1-C11-C12	160.88(11)	C16-C11-C12-C13	-2.24(19)
N1-C11-C12-C13	178.50(11)	C11-C12-C13-C14	1.0(2)
C12-C13-C14-C15	1.3(2)	C13-C14-C15-C16	-2.3(2)
C14-C15-C16-C11	1.0(2)	C12-C11-C16-C15	1.24(19)
N1-C11-C16-C15	-179.51(11)	N2-C1-C21-C26	155.09(12)
C2-C1-C21-C26	-27.0(2)	N2-C1-C21-C22	-24.78(18)
C2-C1-C21-C22	153.16(13)	C26-C21-C22-C23	0.16(19)
C1-C21-C22-C23	-179.97(12)	C21-C22-C23-C24	0.8(2)
C22-C23-C24-C25	-0.9(2)	C23-C24-C25-C26	-0.1(2)
C24-C25-C26-C21	1.1(2)	C22-C21-C26-C25	-1.11(19)
C1-C21-C26-C25	179.02(12)	C4-N3-C31-C36	7.48(18)
C4-N3-C31-C32	-172.06(11)	N3-C31-C32-C33	179.06(11)
C36-C31-C32-C33	-0.48(18)	N3-C31-C32-C37	-0.38(18)
C36-C31-C32-C37	-179.93(11)	C31-C32-C33-C34	0.0(2)
C37-C32-C33-C34	179.44(13)	C32-C33-C34-C35	0.3(2)
C33-C34-C35-C36	-0.1(2)	C34-C35-C36-C31	-0.4(2)
N3-C31-C36-C35	-178.84(12)	C32-C31-C36-C35	0.71(19)
C33-C32-C37-O1	-177.34(13)	C31-C32-C37-O1	2.1(2)

C33-C32-C37-C38	1.59(19)	C31-C32-C37-C38	-178.99(12)

Table 5.3.4. Hydrogen bond distances (Å) and angles (°)

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
N3-H1···O1	0.899(18)	1.934(17)	2.6518(15)	135.6(14)

5.4. X-ray crystallographic data of compound **3e**

Table 5.4.1. Bond lengths (Å)

Cl1-C10	1.733(12)	N1-C1	1.333(15)
N1-C7	1.450(15)	N1-H1	0.86(2)
N2-C12	1.332(16)	N2-C8	1.346(14)
O1-C13	1.213(15)	C1-C2	1.425(17)
C1-C6	1.445(17)	C2-C3	1.364(18)
C2-C13	1.527(18)	C3-C4	1.392(16)
C3-H3	0.95	C4-C5	1.370(17)
C4-H4	0.95	C5-C6	1.364(18)
C5-H5	0.95	C6-H6	0.95
C7-C8	1.518(16)	C7-H7A	0.99
C7-H7B	0.99	C8-C9	1.366(16)
C9-C10	1.361(17)	C9-H9	0.95
C10-C11	1.422(17)	C11-C12	1.382(18)
C11-H11	0.95	C12-H12	0.95
C13-C14	1.490(18)	C14-H14A	0.98
C14-H14B	0.98	C14-H14C	0.98

Table 5.4.2. Bond angles (°)

C1-N1-C7	123.4(10)	C1-N1-H1	121.(10)
C7-N1-H1	114.(9)	C12-N2-C8	117.3(11)
N1-C1-C2	123.2(11)	N1-C1-C6	121.7(12)
C2-C1-C6	115.1(11)	C3-C2-C1	121.9(12)
C3-C2-C13	118.9(11)	C1-C2-C13	119.2(11)
C2-C3-C4	120.9(12)	C2-C3-H3	119.5
C4-C3-H3	119.5	C5-C4-C3	119.3(11)
C5-C4-H4	120.4	C3-C4-H4	120.4
C6-C5-C4	121.5(12)	C6-C5-H5	119.3
C4-C5-H5	119.3	C5-C6-C1	121.3(12)
C5-C6-H6	119.4	C1-C6-H6	119.4

N1-C7-C8	111.7(9)	N1-C7-H7A	109.3
C8-C7-H7A	109.3	N1-C7-H7B	109.3
C8-C7-H7B	109.3	H7A-C7-H7B	107.9
N2-C8-C9	123.7(11)	N2-C8-C7	116.1(10)
C9-C8-C7	120.1(10)	C10-C9-C8	119.3(11)
C10-C9-H9	120.4	C8-C9-H9	120.4
C9-C10-C11	118.6(11)	C9-C10-Cl1	122.2(10)
C11-C10-Cl1	119.2(9)	C12-C11-C10	117.7(11)
C12-C11-H11	121.2	C10-C11-H11	121.2
N2-C12-C11	123.4(11)	N2-C12-H12	118.3
C11-C12-H12	118.3	O1-C13-C14	120.3(12)
O1-C13-C2	121.6(12)	C14-C13-C2	118.0(11)
C13-C14-H14A	109.5	C13-C14-H14B	109.5
H14A-C14-H14B	109.5	C13-C14-H14C	109.5
H14A-C14-H14C	109.5	H14B-C14-H14C	109.5

Table 5.4.3. Torsion angles (°)

C7-N1-C1-C2	174.5(12)	C7-N1-C1-C6	-5.9(18)
N1-C1-C2-C3	179.0(12)	C6-C1-C2-C3	-0.6(18)
N1-C1-C2-C13	-2.6(18)	C6-C1-C2-C13	177.9(11)
C1-C2-C3-C4	-0.1(19)	C13-C2-C3-C4	-178.6(11)
C2-C3-C4-C5	1.0(19)	C3-C4-C5-C6	-1.(2)
C4-C5-C6-C1	0.(2)	N1-C1-C6-C5	-179.0(12)
C2-C1-C6-C5	0.6(18)	C1-N1-C7-C8	-177.8(10)
C12-N2-C8-C9	-0.2(18)	C12-N2-C8-C7	179.8(11)
N1-C7-C8-N2	4.1(15)	N1-C7-C8-C9	-175.9(10)
N2-C8-C9-C10	0.7(18)	C7-C8-C9-C10	-179.3(11)
C8-C9-C10-C11	-2.1(17)	C8-C9-C10-Cl1	177.7(9)
C9-C10-C11-C12	2.9(18)	Cl1-C10-C11-C12	-176.9(10)
C8-N2-C12-C11	1.1(19)	C10-C11-C12-N2	-2.(2)
C3-C2-C13-O1	-175.6(12)	C1-C2-C13-O1	5.9(18)
C3-C2-C13-C14	1.0(17)	C1-C2-C13-C14	-177.6(11)

Table 5.4.4. Hydrogen bond distances (Å) and angles (°)

	Donor-H	**Acceptor-H**	**Donor-Acceptor**	**Angle**
N1-H1···N2	0.86(2)	2.20(13)	2.652(13)	113.(11)
N1-H1···O1	0.86(2)	2.02(11)	2.642(13)	129.(12)
C11-H11···O1	0.95	2.49	3.163(15)	127.9