SUPPORTING INFORMATION

Development of Naphthalimide hydrazide derivatives as potent antibacterial agents against Carbapenem-resistant *A. baumannii*

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1. Experimental section

1.1 General methods

All the reagents and solvents were obtained from commercial suppliers and were used without further purification. Analytical thin layer chromatography (TLC) was performed on MERCK precoated silica gel 60-F254 (0.5 mm) aluminum plates. Visualization of the spots on TLC plates was achieved by UV light. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 500 MHz by making a solution of samples in the DMSO-d_6 as solvent using tetramethylsilane (TMS) as the internal standard. Chemical shifts for ^{1}H and ^{13}C NMR are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constant (*J*) values are reported in hertz (Hz). HRMS were determined with Agilent QTOF mass spectrometer 6540 series instrument. Wherever required, column chromatography was performed using silica gel (60-120). The reactions are carried under positive nitrogen pressure using freshly distilled solvents wherever anhydrous conditions are required. All evaporation of solvents was carried out under reduced pressure using a rotary evaporator below 45 °C. The melting point of compounds was determined with an electrothermal digital melting point apparatus IA9100 and is uncorrected. The names of all the compounds given in the experimental section were taken from ChemDraw Professional, Version 20.0.

1.2 General experimental procedure for the synthesis of intermediate 3a, 3b, 7 and 10a-c

To the solution of 1,8-naphthalic anhydride or substituted naphthalic anhydride (1 mmol) in DMF, amino acid (1.2 mmol) was added and allowed to reflux for 12h. After the completion of the reaction as monitored by TLC, the reaction mixture was poured into ice-cold water. The precipitate obtained was subjected to vacuum filtration to give pure product.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanoic acid (3a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.3 Hz, 2H), 8.23 (d, *J* = 8.2 Hz, 2H), 7.76 (t, *J* = 7.7 Hz, 2H), 4.50 (t, *J* = 7.7 Hz, 2H), 2.77 (t, *J* = 7.7 Hz, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 163.9, 134.1,

131.6, 131.2, 128.1, 126.9, 122.4, 36.2, 32.6. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{15}H_{12}NO_4$ 270.0761; found 270.0764.

3-(6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanoic acid (3b)

^{1}H NMR (500 MHz, DMSO) δ 12.43 (s, 1H), 8.55 (ddd, *J* = 13.2, 7.9, 1.1 Hz, 2H), 8.32 (d, *J* = 7.9 Hz, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.00 (dd, *J* = 8.5, 7.3 Hz, 1H), 4.27 – 4.21 (m, 2H), 2.64 – 2.55 (m, 2H). ^{13}C NMR (125 MHz, DMSO) δ 172.9, 163.2, 163.2, 133.1, 132.0, 131.8, 131.4, 130.2, 129.6, 129.3, 128.7, 123.2, 122.4, 44.9, 36.3, 32.6.

2-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanoic acid (7)

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.97 (s, 1H), 8.50 – 8.43 (m, 4H), 7.87 (t, *J* = 7.8 Hz, 2H), 7.17 – 7.13 (m, 2H), 7.13 – 7.07 (m, 2H), 7.06 – 7.00 (m, 1H), 5.89 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.57 (dd, *J* = 14.0, 5.4 Hz, 1H), 3.39 (dd, *J* = 14.1, 10.1 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.2, 163.5, 138.4, 135.3, 131.7, 131.7, 129.4, 128.6, 127.9, 127.7, 126.7, 121.7, 54.5, 34.7.

2-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetic acid (*10a*)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 – 8.56 (m, 2H), 8.27 – 8.21 (m, 2H), 7.77 (dt, *J* = 8.2, 6.9 Hz, 2H), 4.93 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 163.7, 134.3, 131.6, 131.4, 128.2, 126.9, 122.2, 77.5, 77.3, 77.0, 41.3. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{14}H_{10}NO_4$ 256.0604; found 256.0610.

***4-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)butanoic acid* (10b)**

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (dd, *J* = 18.9, 7.8 Hz, 4H), 7.83 (t, *J* = 7.7 Hz, 2H), 4.07 (t, *J* = 7.0 Hz, 2H), 2.28 (t, *J* = 7.3 Hz, 2H), 1.88 (p, *J* = 7.2 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 174.9, 163.8, 134.6, 131.6, 131.0, 127.7, 127.5, 122.4, 39.6, 32.2, 23.6.

6-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanoic acid (*10c*)

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.00 (s, 1H), 8.50 (dd, *J* = 7.3, 1.2 Hz, 2H), 8.46 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.87 (dd, *J* = 8.3, 7.2 Hz, 2H), 4.04 (dd, *J* = 8.3, 6.6 Hz, 2H), 2.22 (t, *J* = 7.4 Hz, 2H), 1.68 –

1.60 (m, 2H), 1.56 (p, *J* = 7.5 Hz, 2H), 1.40 – 1.30 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 174.9, 163.8, 134.7, 131.7, 131.2, 127.8, 127.7, 122.5, 40.0, 34.0, 27.7, 26.5, 24.7.

1.3 General experimental procedure for the synthesis of 5a-s, 8a-d and 11a-e

To the solution of acid (1 mmol) in DMF, HATU (1 mmol) was added and allowed to stir at room temperature for 10 min. Then, amine (1.2 mmol) and DIPEA (3 mmol) was added and allowed to stir at room temperature. After the completion of the reaction as monitored by TLC, the reaction mixture was poured into ice-cold water. The precipitate obtained was subjected to vacuum filtration followed by purification using column chromatography.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylpropanehydrazide (5a)

Off white solid; yield 75%; mp 240-242°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.72 (d, *J* = 3.0 Hz, 1H), 8.52 (d, *J* = 7.3 Hz, 2H), 8.48 (d, *J* = 8.2 Hz, 2H), 7.90 (t, *J* = 7.7 Hz, 2H), 7.65 (d, *J* = 2.8 Hz, 1H), 7.04 (t, *J* = 7.8 Hz, 2H), 6.66 (t, *J* = 6.5 Hz, 4H), 4.33 (t, *J* = 7.5 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.2, 163.8, 149.7, 134.8, 131.8, 131.2, 129.0, 127.9, 127.7, 122.6, 118.8, 112.5, 36.7, 32.2. HRMS (ESI): *m/z* calculated for $[M+H^]^+$ $C_{21}H_{18}N_3O_3^+$ 360.1343; found 360.1327.

N'-(4-cyanophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5b)

Off white solid; yield 72%; mp 266-268°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.58 (s, 1H), 8.51 (dd, *J* = 20.1, 7.8 Hz, 4H), 7.90 (t, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 6.74 – 6.69 (m, 2H), 4.34 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4, 163.8, 153.2, 134.8, 133.7, 131.8, 131.2, 127.9, 127.7, 122.6, 120.5, 112.1, 99.2, 36.6, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{22}H_{17}N_4O_3$ 385.1295; found 385.1288.

N'-(4-chlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5c)

White solid; yield 76%; mp 246-248°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (d, *J* = 2.9 Hz, 1H), 8.51 (ddd, *J* = 18.0, 7.7, 1.1 Hz, 4H), 7.92 – 7.86 (m, 3H), 7.08 – 7.03 (m, 2H), 6.67 – 6.61 (m, 2H), 4.32 (t, *J* = 7.5 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 148.7, 134.8, 131.8, 131.2, 128.8, 127.7, 122.6, 122.1, 114.0, 36.7, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}ClN_3O_3^+$ 394.0953; found 394.0942.

N'-(4-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5d)

Off white solid; yield 70%; mp 228-230°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.84 – 9.74 (m, 1H), 8.52 (d, *J* = 7.2 Hz, 2H), 8.48 (d, *J* = 8.2 Hz, 2H), 7.92 – 7.87 (m, 3H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.64 – 6.56 (m, 2H), 4.32 (t, *J* = 7.5 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H).^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 149.1, 134.8, 131.8, 131.7, 131.2, 127.9, 127.7, 122.6, 114.5, 109.6, 36.7, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}BrN_3O_3^+$ 438.0448; found 438.0432.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-fluorophenyl)propanehydrazide (5e)

Pinkish solid; yield 75%; mp 240-242°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.76 (d, *J* = 3.2 Hz, 1H), 8.52 (d, *J* = 7.2 Hz, 2H), 8.48 (d, *J* = 8.2 Hz, 2H), 7.90 (t, *J* = 7.7 Hz, 2H), 7.65 (d, *J* = 2.9 Hz, 1H), 6.88 (t, *J* = 8.9 Hz, 2H), 6.66 (ddt, *J* = 7.2, 4.8, 2.9 Hz, 3H), 4.32 (t, *J* = 7.5 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 157.1, 155.3, 146.2, 134.8, 131.8, 131.2, 127.9, 127.7, 122.6, 115.5, 115.4, 113.7, 113.7, 36.7, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}FN_3O_3$ 378.1248; found 378.1235.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(3-fluorophenyl)propanehydrazide (5f)

Off white solid; yield 76%; mp 230-233°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (d, *J* = 2.7 Hz, 1H), 8.50 (dd, *J* = 19.5, 7.7 Hz, 4H), 7.99 (s, 1H), 7.89 (t, *J* = 7.7 Hz, 2H), 7.06 (q, *J* = 7.6 Hz, 1H), 6.53 – 6.47 (m, 1H), 6.47 – 6.38 (m, 2H), 4.33 (t, *J* = 7.4 Hz, 2H), 2.62 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4, 164.6, 163.8, 162.7, 152.0, 151.9, 134.8, 131.8, 131.2, 130.7, 130.6, 127.7, 122.6, 108.5, 104.9, 104.8, 99.1, 98.9, 36.7, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}FN_3O_3$ 378.1248; found 378.1236.

N'-(3,5-difluorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5g)

Off white solid; yield 78%; mp 252-255°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.85 (s, 1H), 8.48 (dt, *J* = 19.8, 9.4 Hz, 4H), 8.28 (s, 1H), 7.88 (q, *J* = 10.0 Hz, 2H), 6.40 (t, *J* = 9.4 Hz, 1H), 6.30 (d, *J* = 9.6 Hz, 2H), 4.33 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.5, 164.7, 164.6, 163.8, 162.8, 162.7, 152.8, 134.8, 131.8, 131.2, 127.9, 127.7, 122.6, 95.2, 95.0, 93.5,

93.2, 93.0, 36.6, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{16}F_2N_3O_3$ 396.1154; found 396.1146.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(p-tolyl)propanehydrazide (5h)

Off white solid; yield 72%; mp 238-240°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.53 (d, *J* = 3.3 Hz, 1H), 8.53 (d, *J* = 7.3 Hz, 2H), 8.46 (d, *J* = 8.1 Hz, 2H), 7.88 (q, *J* = 6.6 Hz, 2H), 7.21 (d, *J* = 3.0 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 2H), 6.64 – 6.59 (m, 2H), 4.36 (t, *J* = 7.4 Hz, 2H), 2.63 (t, *J* = 7.4 Hz, 2H), 2.17 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.1, 163.8, 147.4, 134.8, 131.8, 131.2, 129.5, 127.9, 127.7, 127.6, 127.4, 122.6, 112.8, 36.7, 32.2, 20.6. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{22}H_{20}N_3O_3$ 374.1499; found 374.1491.

N'-(2-chlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5i)

White solid; yield 74%; mp 241-243°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (d, *J* = 2.1 Hz, 1H), 8.53 (d, *J* = 7.2 Hz, 2H), 8.49 (d, *J* = 8.2 Hz, 2H), 7.90 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 2.2 Hz, 1H), 7.26 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.99 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.72 (td, *J* = 7.6, 2.3 Hz, 2H), 4.34 (t, *J* = 7.5 Hz, 2H), 2.65 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 145.0, 134.8, 131.8, 131.2, 129.5, 128.1, 127.9, 127.7, 122.6, 119.9, 117.5, 113.3, 36.7, 32.1. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}ClN_3O_3$ 394.0953; found 394.0943.

N'-(2-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5j)

White solid; yield 77%; mp 238-240°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.53 (dd, *J* = 7.3, 1.1 Hz, 2H), 8.49 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.92 – 7.87 (m, 2H), 7.42 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.13 (s, 1H), 7.07 – 7.02 (m, 1H), 6.72 – 6.63 (m, 2H), 4.34 (t, *J* = 7.5 Hz, 2H), 2.64 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.9, 146.0, 134.7, 132.7, 131.9, 131.1, 128.6, 128.0, 127.6, 122.8, 120.8, 114.0, 36.7, 32.5. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}BrN_3O$ 438.0448; found 438.0435.

N'-(3-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5k)

Off white solid; yield 76%; mp 252-254°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.80 (d, J = 2.7 Hz, 1H), 8.53 (d, J = 7.3 Hz, 2H), 8.48 (d, J = 8.2 Hz, 3H), 7.98 (d, J = 2.6 Hz, 1H), 7.90 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.9 Hz, 1H), 6.85 – 6.79 (m, 2H), 6.65 (d, J = 8.2 Hz, 1H), 4.33 (t, J = 7.5 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 151.4, 134.7, 131.9, 131.1, 130.9, 128.0, 127.6, 122.7, 122.5, 121.3, 115.1, 111.7, 36.7, 32.5. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}BrN_3O_3$ 438.0448; found 438.0435.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-nitrophenyl)propanehydrazide (5l)

Brown solid; yield 72%; mp 270-272°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.89 (s, 1H), 8.78 (s, 1H), 8.54 (d, J = 7.2 Hz, 2H), 8.52 – 8.45 (m, 2H), 7.96 (d, J = 8.8 Hz, 2H), 7.90 (t, J = 7.7 Hz, 2H), 6.77 – 6.72 (m, 2H), 4.40 (t, J = 7.3 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.8, 155.2, 138.4, 134.9, 131.8, 131.2, 127.9, 127.7, 126.2, 122.6, 111.0, 36.6, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{17}N_4O_5$ 405.1193; found 405.1185.

N'-(3,5-dichlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5m)

White solid; yield 75%; mp 251-252°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.87 (s, 1H), 8.52 (dd, J = 7.3, 1.2 Hz, 2H), 8.48 (dd, J = 8.3, 1.2 Hz, 2H), 8.28 (s, 1H), 7.89 (dd, J = 8.2, 7.2 Hz, 2H), 6.79 (t, J = 1.8 Hz, 1H), 6.66 (dd, J = 3.2, 1.8 Hz, 2H), 4.36 – 4.31 (m, 2H), 2.63 (t, J = 7.3 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.5, 163.8, 152.2, 134.8, 131.8, 131.2, 127.9, 127.7, 122.6, 117.5, 110.6, 36.6, 32.3. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{16}Cl_2N_3O_3$ 428.0563; found 428.0551.

N'-(2,4-dichlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5n)

White solid; yield 80%; mp 239-241°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 (s, 1H), 8.54 – 8.50 (m, 2H), 8.50 – 8.45 (m, 2H), 7.90 (t, J = 7.7 Hz, 2H), 7.59 (s, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.05 (dd, J = 8.7, 2.4 Hz, 1H), 6.71 (dd, J = 8.8, 3.3 Hz, 1H), 4.33 (t, J = 7.5 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.4, 163.8, 144.3, 134.8, 131.8, 131.2, 128.8, 128.0, 127.9, 127.7, 122.6, 122.3, 117.9, 114.3, 36.6, 32.1. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{16}Cl_2N_3O_3$ 428.0563; found 428.0552.

3-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-methoxyphenyl)propanehydrazide (5o)

Light brown solid; yield 76%; mp 207-210°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.70 (s, 1H), 8.51 (d, J = 7.3 Hz, 2H), 8.48 (d, J = 8.3 Hz, 2H), 7.89 (t, J = 7.7 Hz, 2H), 7.34 (d, J = 3.1 Hz, 1H), 6.63 (t, J = 7.3 Hz, 4H), 4.32 (t, J = 7.5 Hz, 2H), 3.63 (s, 3H), 2.59 (t, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.1, 163.8, 153.0, 143.5, 134.8, 131.8, 131.2, 127.9, 127.7, 122.6, 114.5, 114.0, 55.7, 36.8, 32.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{22}H_{20}N_3O_4$ 390.1448; found 390.1431.

N'-(2,4-dimethylphenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (5p)

White solid; yield 78%; mp 224-226°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.74 (d, J = 3.1 Hz, 1H), 8.52 (d, J = 7.2 Hz, 2H), 8.48 (d, J = 8.3 Hz, 2H), 7.90 (t, J = 7.8 Hz, 2H), 6.85 (d, J = 3.0 Hz, 1H), 6.79 (s, 1H), 6.62 (d, J = 8.1 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 4.33 (t, J = 7.6 Hz, 2H), 2.63 (t, J = 7.7 Hz, 2H), 2.13 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.0, 163.8, 144.7, 134.8, 131.8, 131.2, 127.9, 127.7, 127.5, 127.0, 122.6, 122.3, 111.7, 36.7, 32.1, 20.5, 17.6. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{23}H_{22}N_3O_3$ 388.1656; found 388.1641.

3-(6-Bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-chlorophenyl)propanehydrazide (5q)

Yellow solid; yield 75%; mp 222-225°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.64 – 8.56 (m, 1H), 8.37 (d, J = 7.9 Hz, 1H), 8.26 (d, J = 8.2 Hz, 1H), 8.04 (t, J = 8.0 Hz, 1H), 7.87 (s, 1H), 7.07 (d, J = 8.2 Hz, 1H), 6.66 (d, J = 8.2 Hz, 2H), 4.31 (t, J = 7.4 Hz, 2H), 2.61 (t, J = 7.6 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.2, 133.1, 132.1, 131.8, 131.4, 130.3, 129.6, 129.3, 128.8, 123.3, 122.5, 114.0, 36.8, 32.1. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{16}BrClN_3O_3$ 472.0058; found 472.0036.

3-(6-Bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-bromophenyl)propanehydrazide (5r)

Yellow solid; yield 70%; mp 235-236°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (d, J = 2.9 Hz, 1H), 8.58 (dd, J = 12.1, 7.9 Hz, 2H), 8.35 (d, J = 7.9 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 8.02 (t, J = 7.9 Hz,

1H), 7.89 (s, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.61 (d, *J* = 8.1 Hz, 2H), 4.30 (t, *J* = 7.5 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H).^{13}C NMR (125 MHz, DMSO-d_6) δ 170.2, 163.3, 163.2, 149.1, 133.1, 132.1, 131.9, 131.7, 131.5, 130.3, 129.6, 129.3, 128.8, 123.3, 122.5, 114.5, 114.0, 109.6, 36.8, 32.0. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{16}Br_2N_3O_3$ 515.9553; found 515.9529.

3-(6-Bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-cyanophenyl)propanehydrazide (5s)

Yellow solid; yield 74%; mp 246-248°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.63 – 8.52 (m, 3H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 2H), 4.32 (t, *J* = 7.3 Hz, 2H), 2.63 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.3, 163.3, 153.2, 133.8, 133.2, 132.1, 131.9, 131.5, 130.3, 129.7, 129.3, 128.8, 123.3, 122.5, 120.5, 112.1, 99.2, 36.8, 32.1. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{22}H_{16}BrN_4O_3$ 463.0400; found 463.0377.

2-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N',3-diphenylpropanehydrazide (8a)

White solid; yield 80%; mp 189-191°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.91 – 9.87 (m, 1H), 8.49 – 8.43 (m, 4H), 7.86 (t, *J* = 7.8 Hz, 2H), 7.66 (s, 1H), 7.18 – 7.08 (m, 4H), 7.07 (t, *J* = 7.5 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 5.92 (dd, *J* = 10.3, 5.3 Hz, 1H), 3.68 (dd, *J* = 14.1, 5.3 Hz, 1H), 3.42 (dd, *J* = 14.0, 10.3 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 168.9, 164.0, 149.9, 138.5, 134.7, 131.7, 131.1, 129.5, 129.0, 128.5, 128.0, 127.7, 126.7, 122.8, 118.8, 112.8, 54.7, 34.3. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{27}H_{22}N_3O_3$ 436.1656; found 436.1640.

N'-(4-bromophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide (8b)

White solid; yield 83%; mp 225-226°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 – 9.92 (m, 1H), 8.46 (d, *J* = 8.1 Hz, 4H), 7.91 (d, *J* = 2.1 Hz, 1H), 7.86 (t, *J* = 7.8 Hz, 2H), 7.31 – 7.24 (m, 2H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 2H), 7.03 – 6.95 (m, 1H), 6.72 (dd, *J* = 9.0, 2.4 Hz, 2H), 5.91 (dd, *J* = 10.3, 5.3 Hz, 1H), 3.66 (dd, *J* = 13.9, 5.3 Hz, 1H), 3.40 (dd, *J* = 13.9, 10.3 Hz, 1H). ^{13}C NMR (125

MHz, DMSO-d_6) δ 169.0, 164.0, 149.3, 138.4, 134.8, 131.6, 131.2, 129.5, 128.5, 128.0, 127.7, 126.7, 122.8, 114.8, 109.6, 54.6, 34.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{27}H_{21}BrN_3O_3$ 514.0761; found 514.0740.

N'-(4-cyanophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide (8c)

Off white solid; yield 80%; mp 235-237°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.07 (d, *J* = 2.7 Hz, 1H), 8.61 (s, 1H), 8.47 (t, *J* = 6.0 Hz, 4H), 7.87 (t, *J* = 7.7 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 7.5 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 2H), 7.00 (t, *J* = 7.2 Hz, 1H), 6.82 (dd, *J* = 8.8, 2.4 Hz, 2H), 5.96 (dd, *J* = 10.2, 5.3 Hz, 1H), 3.67 (dd, *J* = 14.0, 5.3 Hz, 1H), 3.40 (dd, *J* = 13.9, 10.2 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.1, 164.1, 153.5, 138.2, 134.9, 133.7, 131.7, 131.2, 129.5, 128.5, 128.0, 127.7, 126.7, 122.7, 120.6, 112.3, 99.2, 54.5, 34.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{28}H_{21}N_4O_3$ 461.1608; found 461.1591.

N'-(4-chlorophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide(8d)

White solid; yield 85%; mp 185-187°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.94 (d, *J* = 2.7 Hz, 1H), 8.46 (d, *J* = 8.1 Hz, 4H), 7.87 (dd, *J* = 14.6, 7.0 Hz, 3H), 7.20 – 6.97 (m, 7H), 6.76 (d, *J* = 8.2 Hz, 2H), 5.92 (dd, *J* = 10.2, 5.3 Hz, 1H), 3.66 (dd, *J* = 14.1, 5.3 Hz, 1H), 3.40 (dd, *J* = 13.9, 10.3 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.0, 164.0, 148.9, 138.4, 134.8, 131.6, 131.1, 129.5, 128.8, 128.5, 128.0, 127.7, 126.7, 122.8, 122.1, 114.2, 54.6, 34.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{27}H_{21}ClN_3O_3$ 470.1266; found 470.1252.

N'-(4-cyanophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetohydrazide (11a)

Off white solid; yield 72%; mp 279-280°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.28 – 10.23 (m, 1H), 8.70 (d, *J* = 1.8 Hz, 1H), 8.55 (d, *J* = 7.2 Hz, 2H), 8.51 (d, *J* = 8.2 Hz, 2H), 7.91 (t, *J* = 7.8 Hz, 2H), 7.60 – 7.55 (m, 2H), 6.81 (dd, *J* = 8.7, 2.3 Hz, 2H), 4.81 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 167.6, 163.9, 153.2, 135.1, 133.9, 131.8, 131.4, 128.0, 127.8, 122.4, 120.5, 112.2, 99.5, 42.0. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{21}H_{15}N_4O_3$ 371.1139; found 371.1126.

4-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylbutanehydrazide (11b)

White solid; yield 75%; mp 268-270°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.60 (s, 1H), 8.52 (d, J = 7.3 Hz, 2H), 8.47 (d, J = 8.3 Hz, 2H), 7.88 (q, J = 8.6 Hz, 2H), 7.66 (s, 1H), 7.12 (t, J = 7.7 Hz, 2H), 6.69 (dd, J = 15.1, 7.4 Hz, 3H), 4.12 (t, J = 7.3 Hz, 2H), 2.29 (d, J = 7.8 Hz, 2H), 1.96 (q, J = 7.9 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.9, 164.0, 149.8, 134.7, 131.8, 131.2, 129.4, 129.1, 127.9, 127.7, 122.6, 118.8, 112.5, 39.9, 31.7, 24.4. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{22}H_{20}N_3O_3$ 374.1499; found 374.1485.

N'-(4-cyanophenyl)-4-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)butanehydrazide (11c)

White solid; yield 78%; mp 275-277°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.80 (s, 1H), 8.58 (s, 1H), 8.53 (d, J = 7.3 Hz, 2H), 8.48 (d, J = 8.4 Hz, 2H), 7.89 (t, J = 7.9 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 4.13 (t, J = 7.0 Hz, 2H), 2.31 (t, J = 7.7 Hz, 2H), 1.96 (p, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.0, 164.0, 153.4, 134.8, 133.8, 131.8, 131.2, 127.9, 127.7, 122.6, 120.6, 112.1, 99.1, 31.5, 24.1. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{23}H_{19}N_4O_3$ 399.1452; found 399.1437.

6-(1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylhexanehydrazide (11d)

White solid; yield 75%; mp 230-232°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.58 (s, 1H), 8.62 – 8.33 (m, 4H), 7.89 (s, 2H), 7.66 (s, 1H), 7.10 (s, 2H), 6.68 (s, 3H), 4.07 (s, 2H), 2.22 (d, J = 36.7 Hz, 2H), 1.65 (d, J = 32.6 Hz, 4H), 1.39 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.4, 163.9, 150.0, 134.8, 131.8, 131.2, 129.1, 127.8, 127.7, 122.5, 118.8, 112.5, 33.6, 27.8, 26.7, 25.4. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{24}H_{24}N_3O_3$ 402.1812; found 402.1797.

N'-(4-cyanophenyl)-6-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanehydrazide (11e)

White solid; yield 80%; mp 220-222°C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (s, 1H), 8.58 (s, 1H), 8.55 – 8.37 (m, 4H), 7.88 (d, J = 8.1 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 6.72 (d, J = 8.4 Hz, 2H), 4.07 (q, J = 6.6 Hz, 2H), 2.21 (t, J = 7.4 Hz, 2H), 1.64 (m, 4H), 1.38 (p, J = 7.9 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.5, 163.9, 153.5, 134.8, 134.8, 133.8, 131.8, 131.2, 127.8, 127.7, 122.5, 120.5,

112.0, 99.1, 40.1, 33.5, 27.8, 27.7, 26.6, 26.5, 25.2. HRMS (ESI): *m/z* calculated for $[M+H]^+$ $C_{25}H_{23}N_4O_3$ 427.1765; found 427.1757.

1.4Bacterial strains and media

The bacterial pathogen panel comprises *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Klebsiella pneumoniae* BAA-1705, *Acinetobacter baumannii* BAA 1605 and *Pseudomonas aeruginosa* ATCC 27853. These strains are typically cultured on Mueller-Hinton Agar (MHA). A single colony was picked from MHA plate, inoculated in Mueller-Hinton cation supplemented broth II (CA-MHB), and incubated overnight at 37^{o}C while shaking for 18-24 h to get the starter culture. MtbH37Rv ATCC 27294 was cultured in Middlebrook 7H9 (Difco, Becton, NJ, U.S.A.) media supplemented with 10% (v/v) A.D.C. (Bovine Serum Albumin, Dextrose, NaCl), 0.2% (v/v) glycerol and 0.05% (v/v) Tween-80 (ADC-Tween-80).

1.4.1Antibiotic susceptibility testing against bacterial pathogen panel

Antibiotic susceptibility testing of newly synthesized compounds was conducted according to conventional CLSI criteria to ascertain the Minimum Inhibitory Concentration (MIC) [22,23]. MIC is defined as the lowest concentration at which there is complete inhibition of growth appears. Bacterial cultures were grown in Mueller-Hinton cation-enriched broth (CA-MHB). Theoptical density (OD_{600}) of the cultures was measured and they were subsequently diluted to ~ 10^6 cfu/mL. This inoculum was then kept in a microtitre plate with wells containing varying concentrations of the test substance ranging from 64-0.5 µg/mL. The cells with medium (without compound and cells) and Levofloxacin as a reference standard serve as controls. Following incubation at 37°C for 16-18 hours, MIC values were determined based on the absence or presence of visible growth. MIC determinations were conducted independently three times for each compound, using duplicate samples each time.

1.4.2Cell cytotoxicity assay

Using the MTT assay, the newly synthesized active compounds were assessed for cell toxicity against Vero cells [24]. ~10^3 cells per well were seeded in a 96-well plate and incubated at 37 °C

with 5% CO2. After 24 hours, compounds ranging from 5 to 100 mg/L were added and incubated for 72 hours at 37 °C in a 5% CO_2 environment. Following the incubation period, each well received 5 mg/L MTT and was then incubated for an additional 4 hours at 37 C. Subsequently, the medium was discarded and the formazan crystals were solubilized with 0.1 mL DMSO. The Optical density was measured at 540 nm to determine the CC_{50}. The CC_{50} value is the lowest concentration of a compound that reduces cell viability by 50%. Doxorubicin was used as positive control and each experiment was repeated in triplicate.

1.4.3. Time kill study

The bactericidal activity was assessed by the time-kill method [25]. *Acinetobacter baumannii* BAA 1605 cells were diluted up to ~10^6 cfu/mL and treated with compound for concentrations corresponding to 1x and 10x of MIC of compound **5d** and Tobramycin in MHB in triplicate and incubated at 37 ^oC. 100 mL samples were collected after time intervals of 0 h, 1 h, 6 h and 24 h and serially diluted in PBS and plated on TSA followed by incubation at 37 ^oC for 18-20 h. Kill curves were constructed by counting the colonies from plates and plotting the cfu/mL of surviving bacteria at each time point in the presence and absence of the compound [26].

1.4.4. Synergy screen

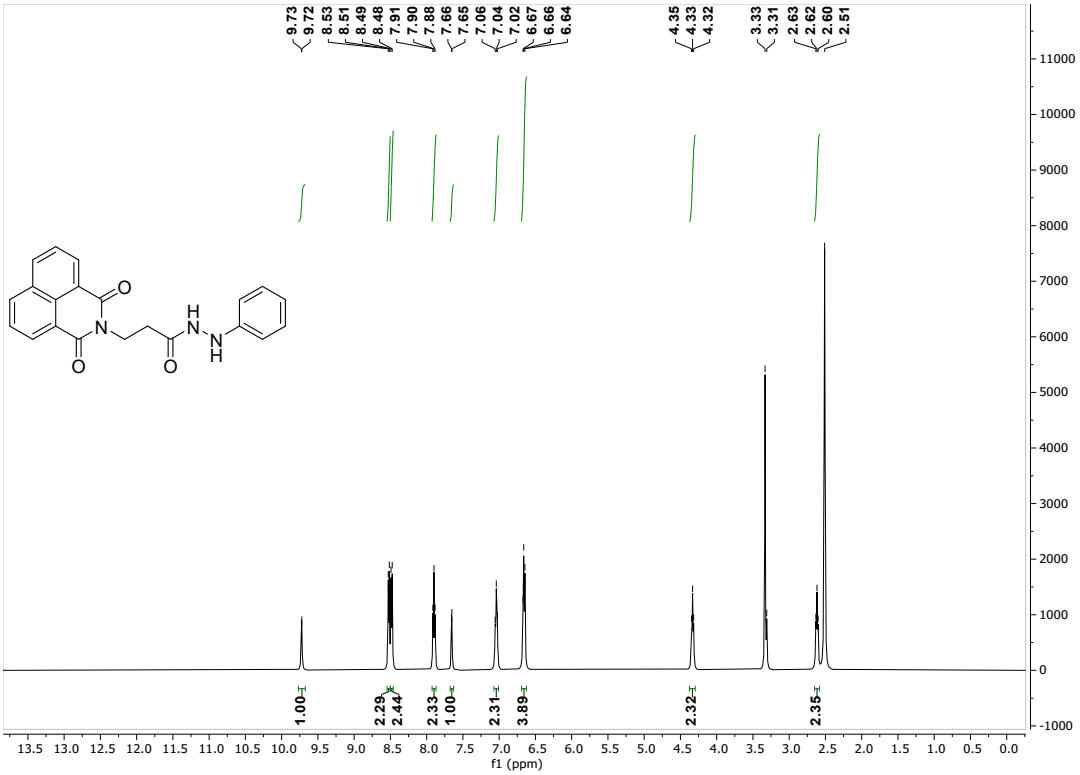
Checkerboard method was used to determine synergy between compound **5d** and the antibiotics that included Amikacin, Levofloxacin, Minocycline, Polymyxin B, Rifampicin, Tobramycin[27,28]. According to CLSI guidelines, stock solution of each drug and serial two-fold dilutions of each drug to at least double the MIC were freshly prepared prior to testing. The compounds were serially diluted along the ordinate, ranging from 0.03 to 4 μg/mL, while the antibiotics were serially diluted as shown along the abscissa, ranging from 0.03 to 64 μg/mL in 96 well microtiter plate. An inoculum ~10^6 CFU/mL was prepared and inoculated with 100 mL of a bacterial inoculum and plates were incubated at 37 ^0C for 24 h under aerobic conditions. The combination is considered synergistic when the FIC is <0.5, indifferent when the FIC is > 0.5 to 4 and antagonistic when the FIC is > 4 [29].

Table ST1. ADME profile predicted by QikProp

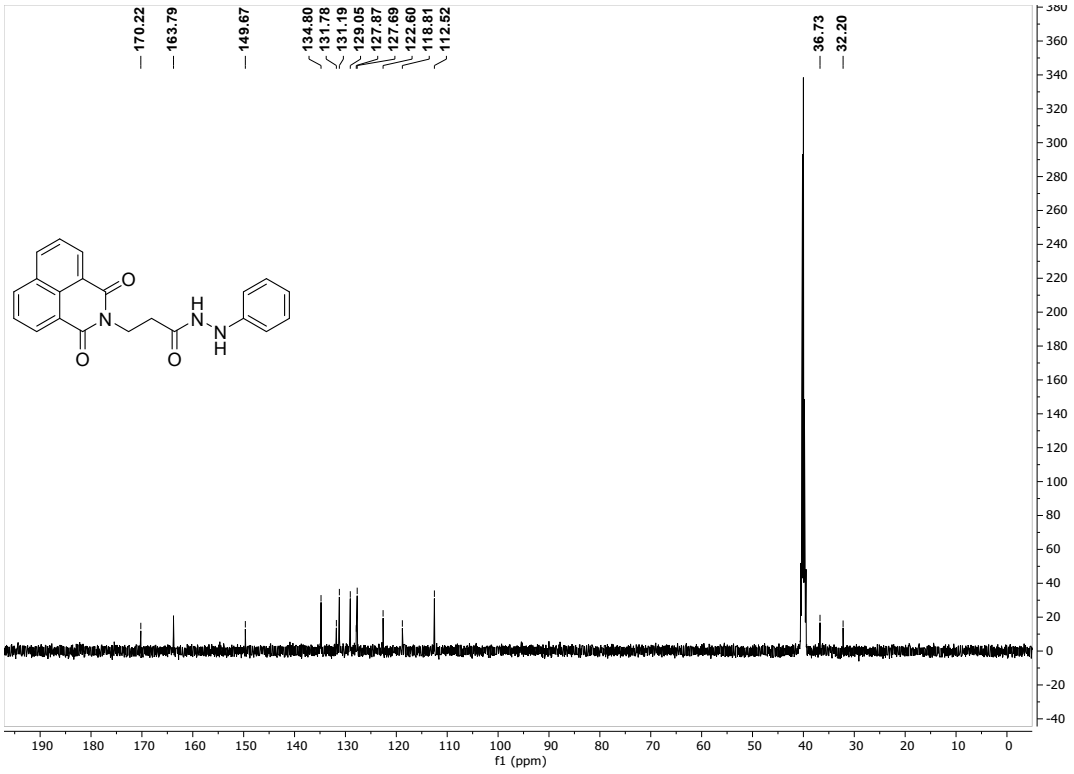
S.no	ADME parameters	Range or recommended values	Compound **5d**
1	Rule of five (Number of violations of Lipinski's rule of five)	Maximum is 4	0
2	PSA (Van der Waals surface area of polar nitrogen and oxygen atoms)	7.0-200.0	104.356
3	SASA (Total solvent accessible surface area in square angstroms)	300-1000	798.178
4	Molecular Weight	0-500	438.28
5	Dipole moment	1.0-12.5	8.903
6	Donor H.B.	0-6	2
7	Acceptor H.B.	2-20	6.5
8	QPlogKhsa (Prediction of binding to human serum albumin)	-1.5-1.5	0.33
9	QPlogPo/w (Predicted octanol/water partition coefficient	-2.0-6.5	3.616
10	QPpolrz (Predicted polarizability in cubic angstroms)	13.0-70.0	42.107
11	QPlogBB (Predicted brain/ blood partition coefficient)	-3.0-1.2	-1.146
12	QPlogKp (Predicted skin permeability)	-8.0--1.0	-2.364
13	QPlogHERG (Predicted IC50 value for blockage of HERG K+ channels)	Concern below -5	-4.6
14	QPPCaco (Predicted apparent Caco-2 cell permeability in nm/sec)	<25 is poor, >500 is great	377.835
15	P.O.A. (Predicted human oral absorption on 0–100% scale)	<25% is poor, >80% is high	94.24

4. ^{1}H NMR, ^{13}C NMR and HRMS spectra

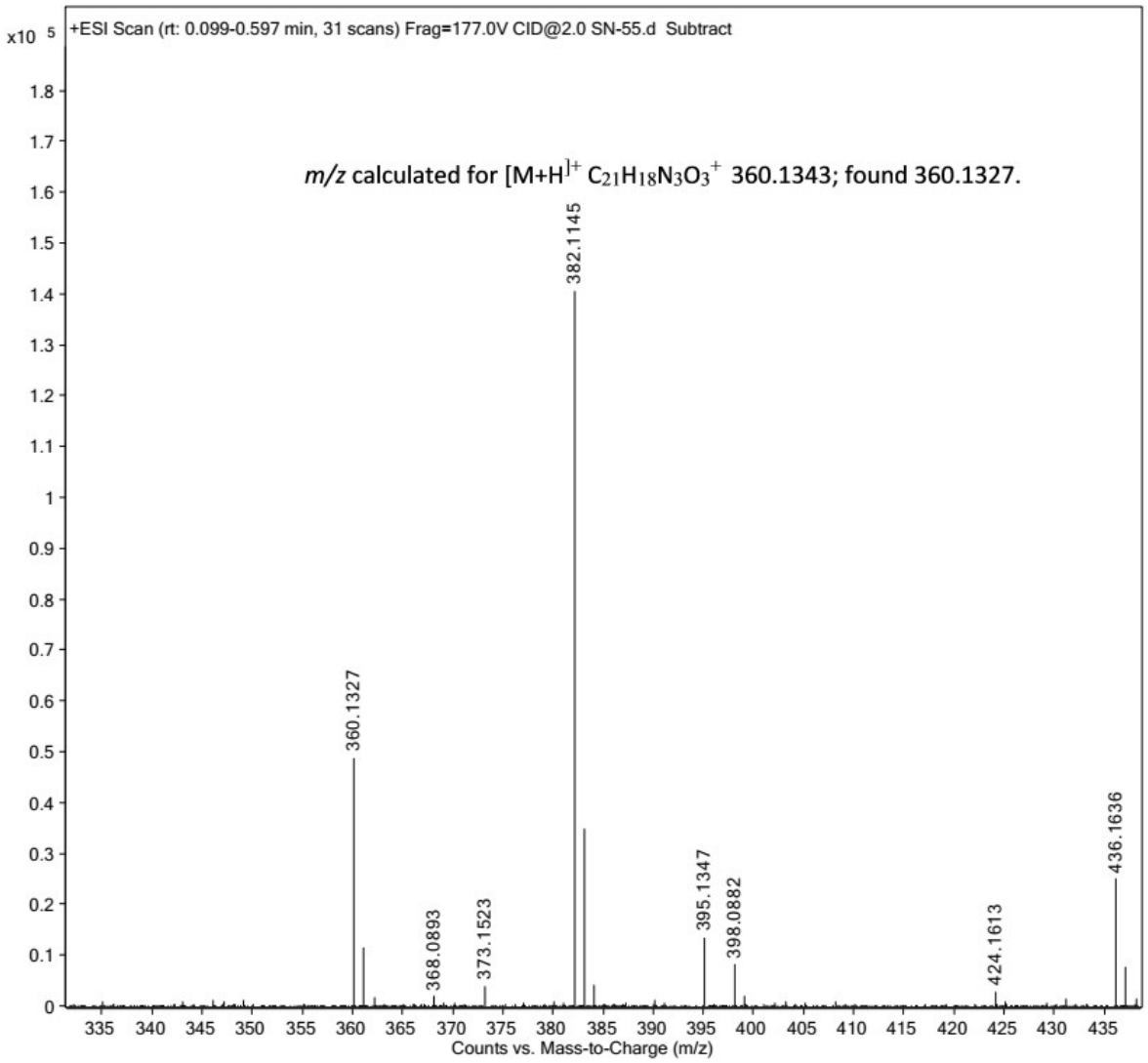
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylpropanehydrazide (**5a**)*



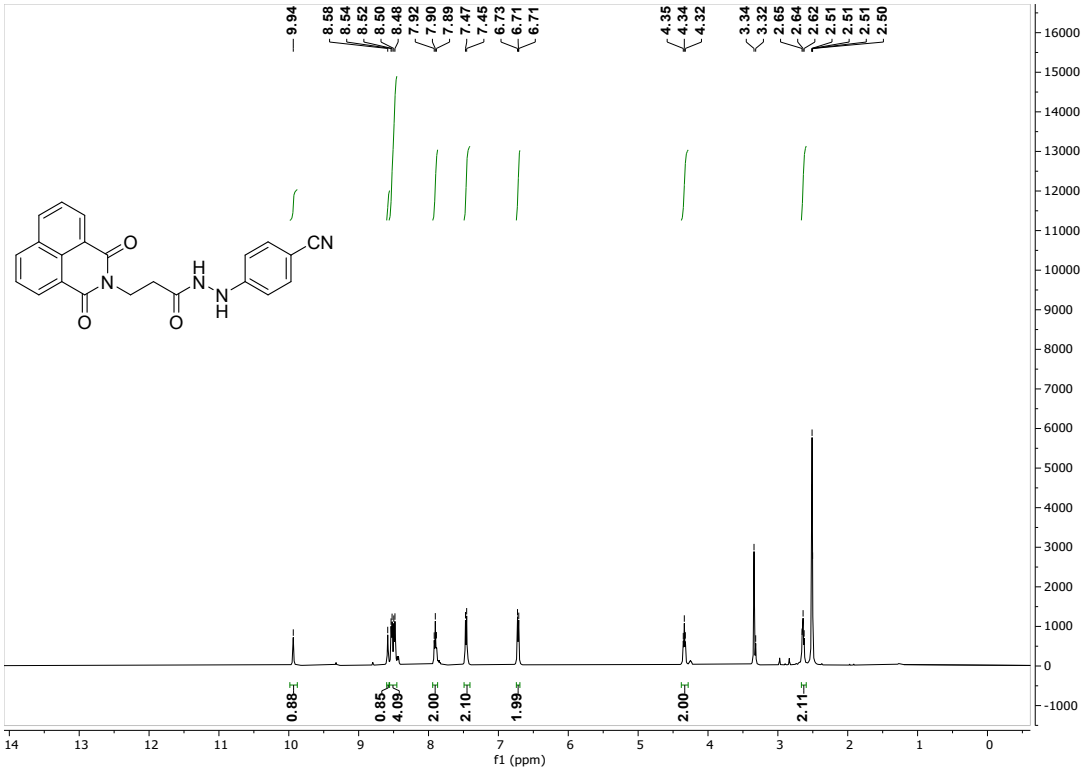
^{1}H NMR spectrum of compound **5a**, DMSO-d_6, 500MHz



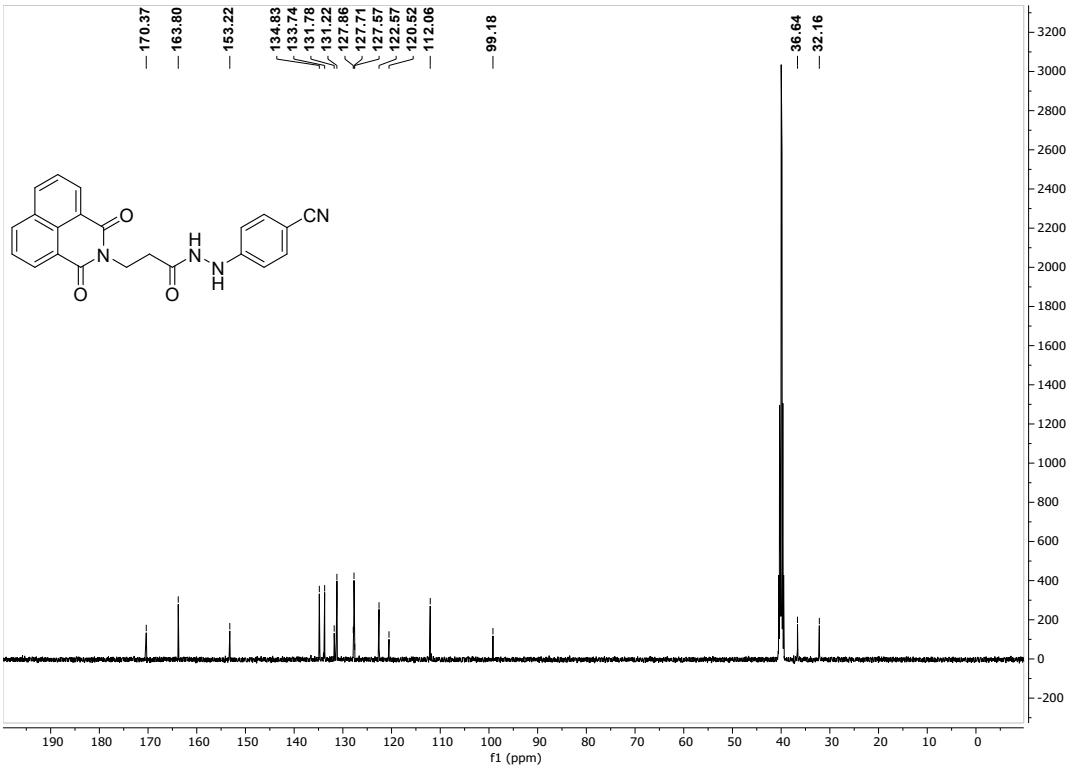
^{13}C NMR spectrum of compound **5a**, DMSO-d_6, 125MHz


+ESI Scan (rt: 0.099-0.597 min, 31 scans) Frag=177.0V CID@2.0 SN-55.d Subtract
x10 5
m/z calculated for [M+H]+ C21H18N3O3+ 360.1343; found 360.1327.
382.1145
360.1327
368.0893
373.1523
395.1347
398.0882
424.1613
436.1636
Counts vs. Mass-to-Charge (m/z)

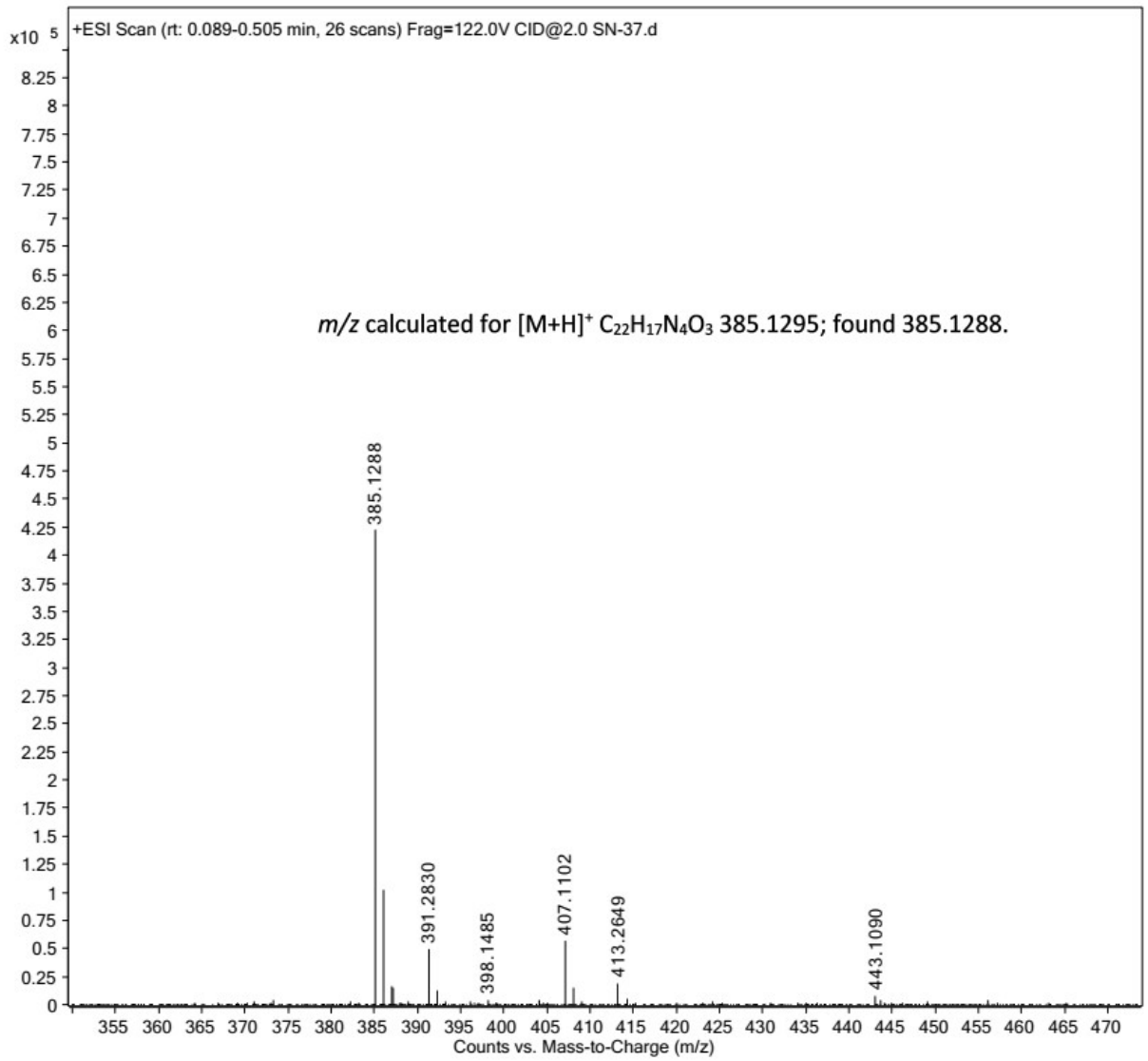
*N'-(4-cyanophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5b**)*



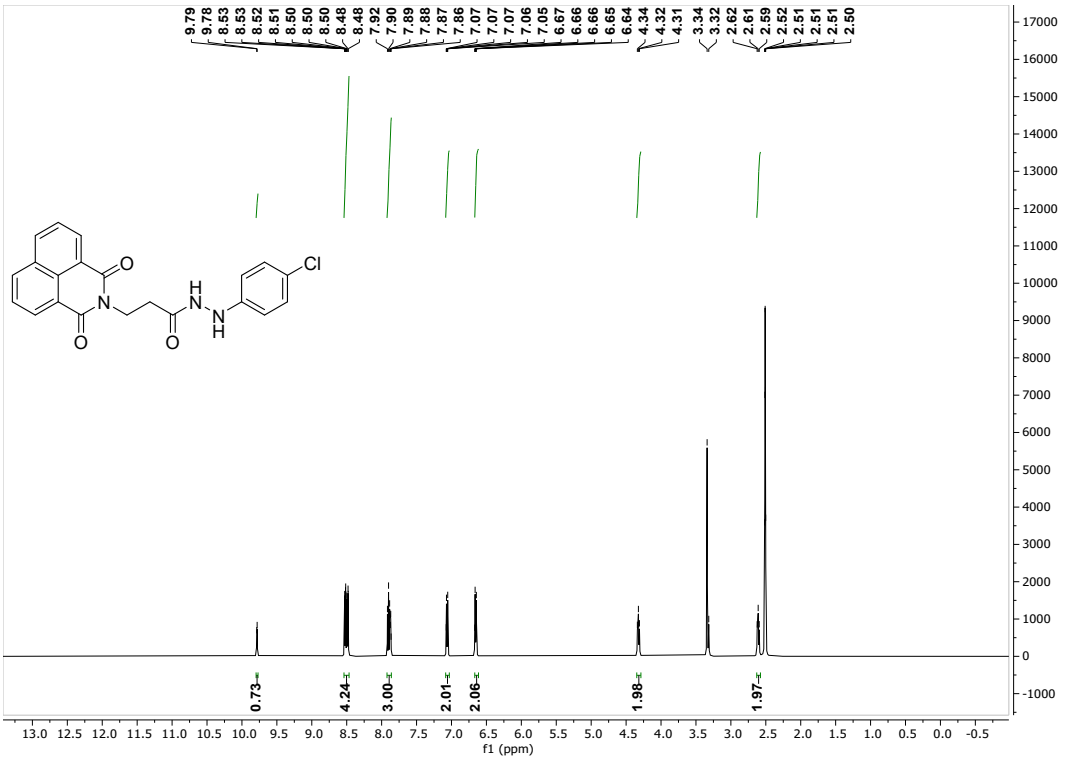
^{1}H NMR spectrum of compound **5b**, DMSO-d_6, 500MHz



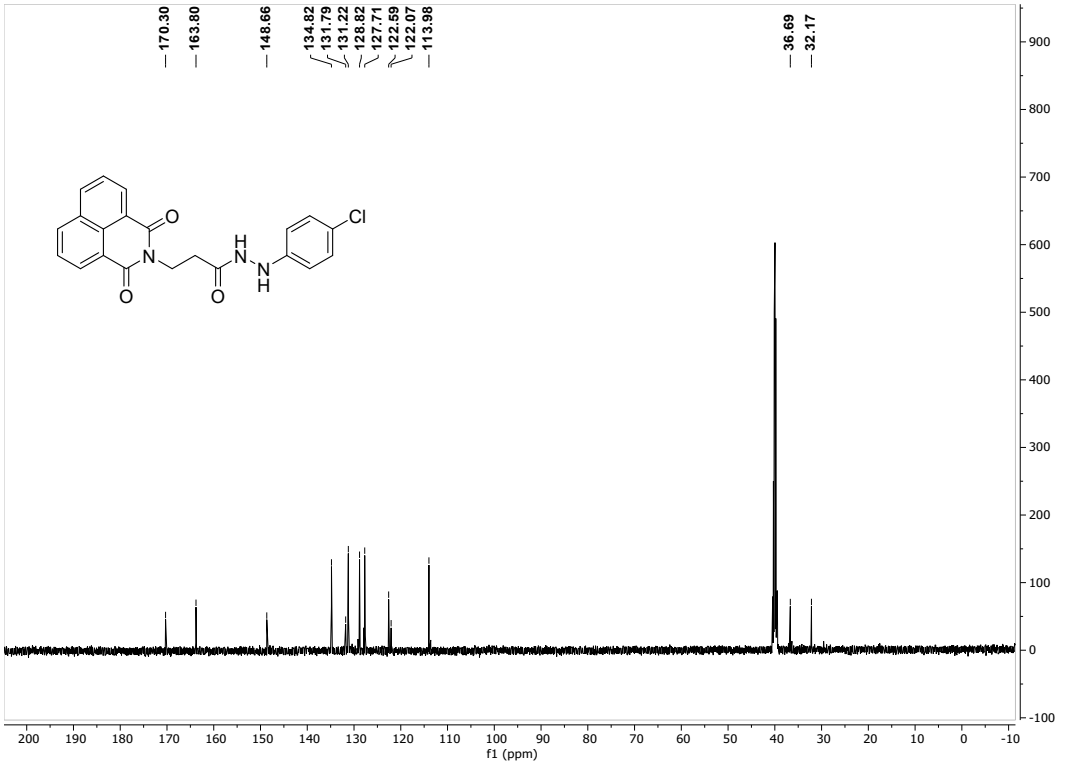
^{13}C NMR spectrum of compound **5b**, DMSO-d_6, 125MHz



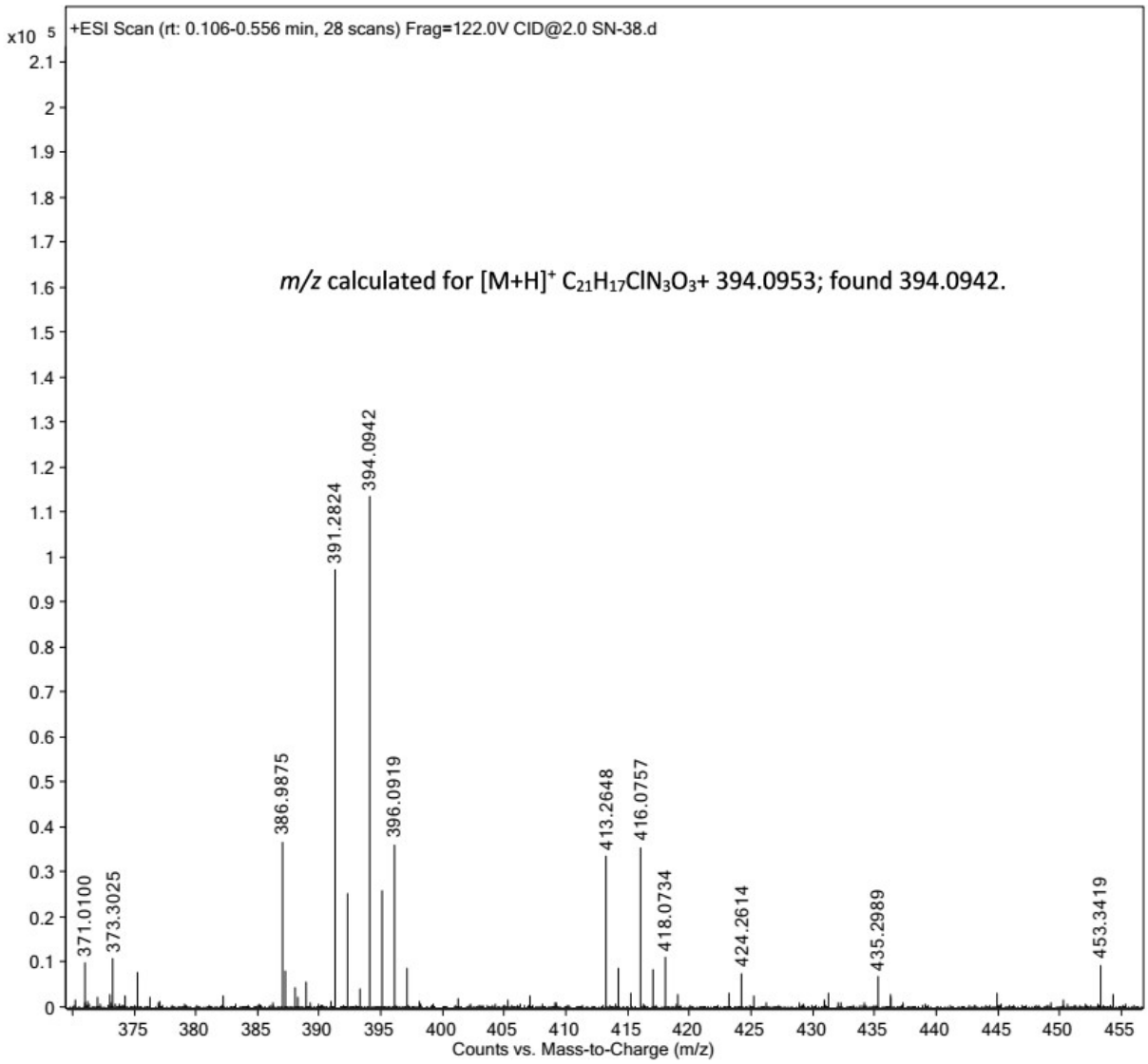
*N'-(4-chlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5c**)*



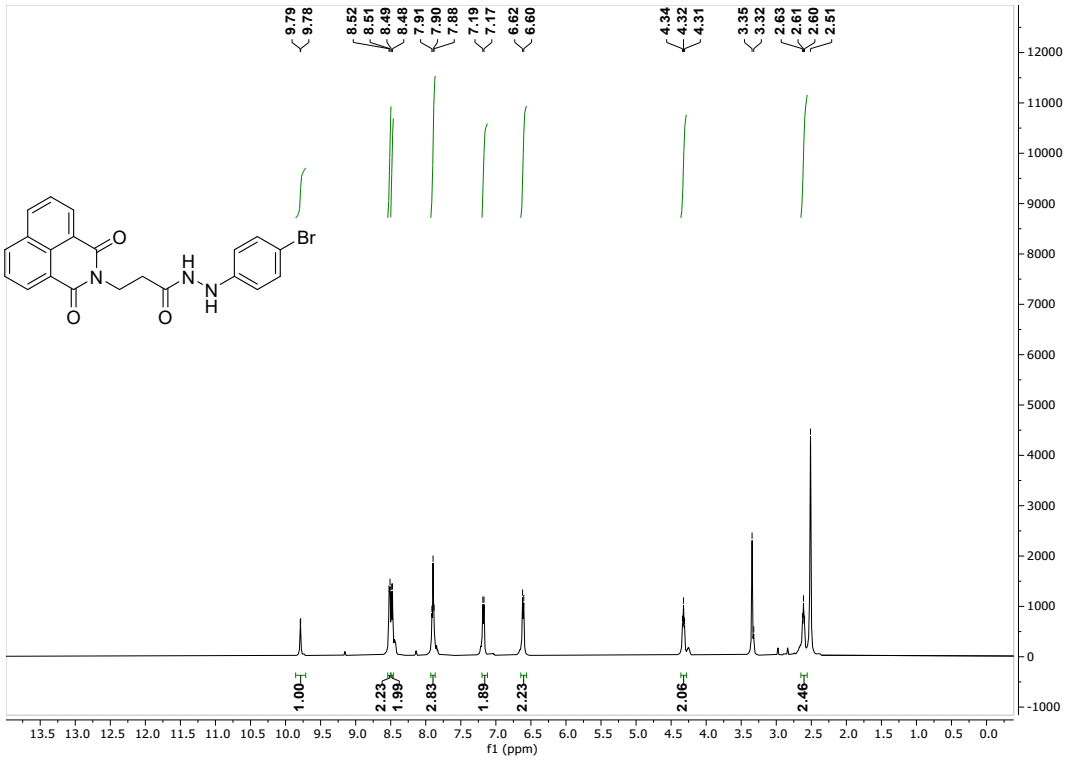
^{1}H NMR spectrum of compound **5c**, DMSO-d_6, 500MHz



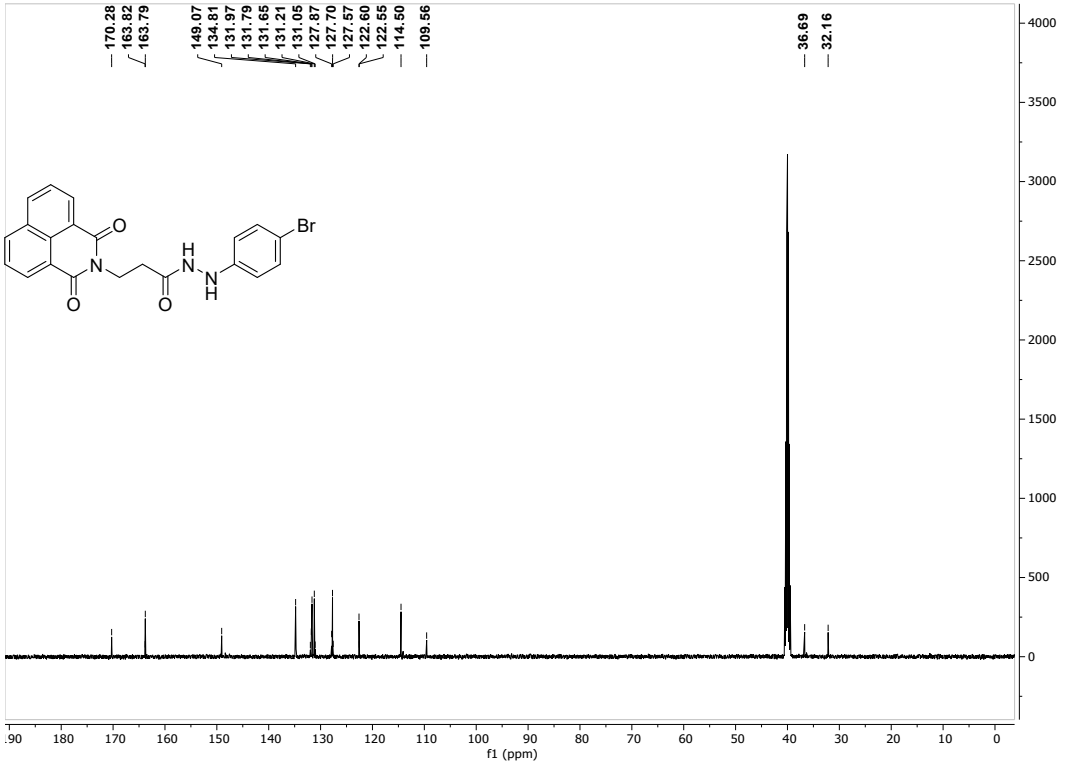
^{13}C NMR spectrum of compound **5c**, DMSO-d_6, 125MHz



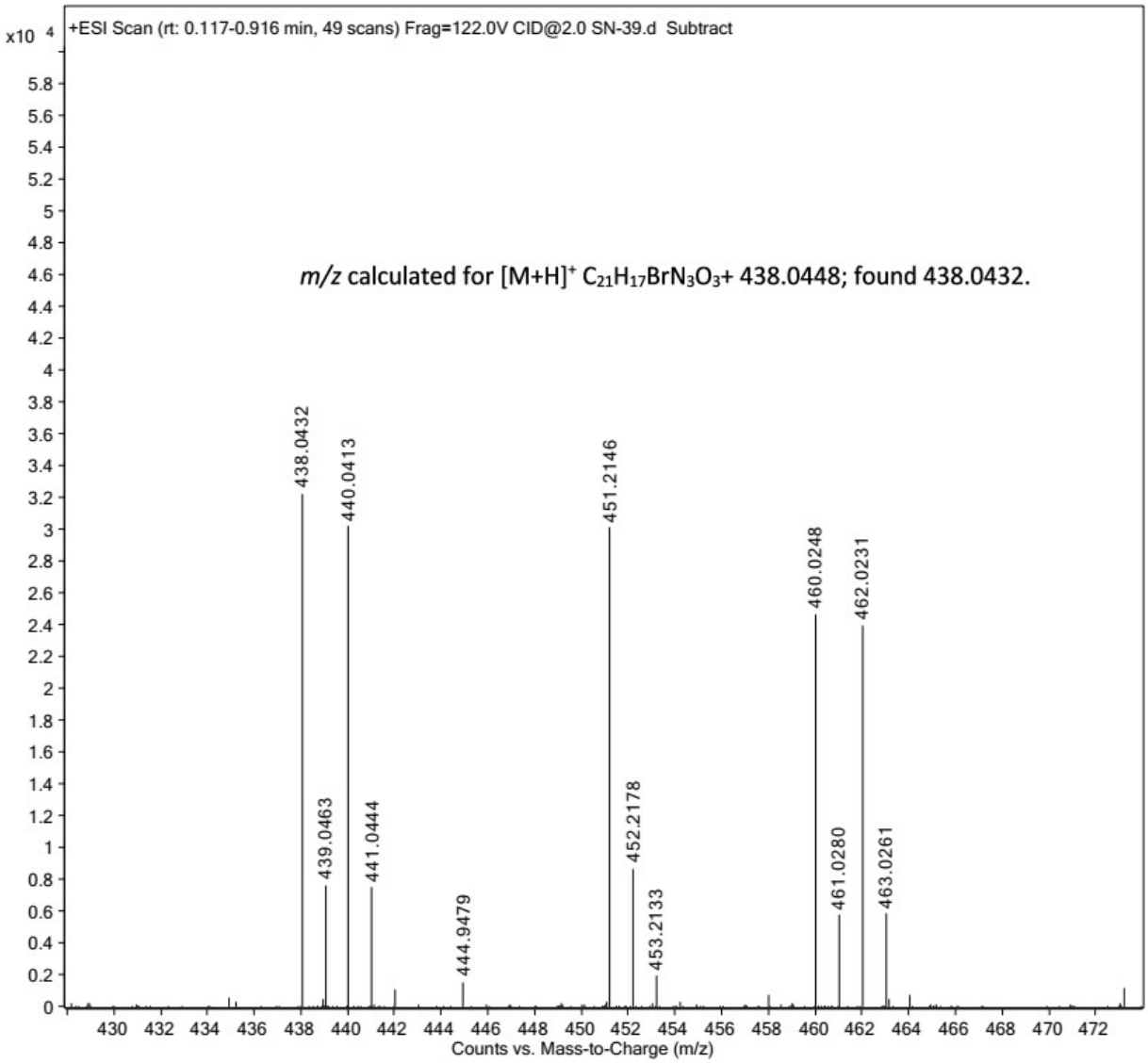
*N'-(4-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5d**)*



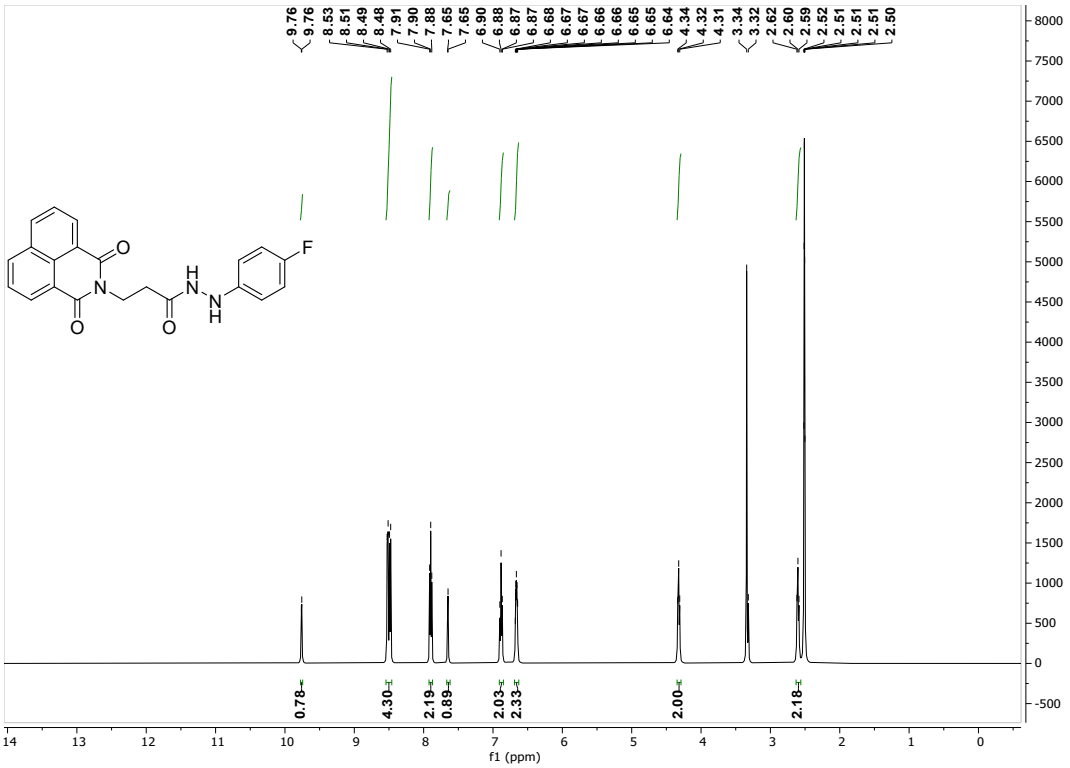
^{1}H NMR spectrum of compound **5d**, DMSO-d_6, 500MHz



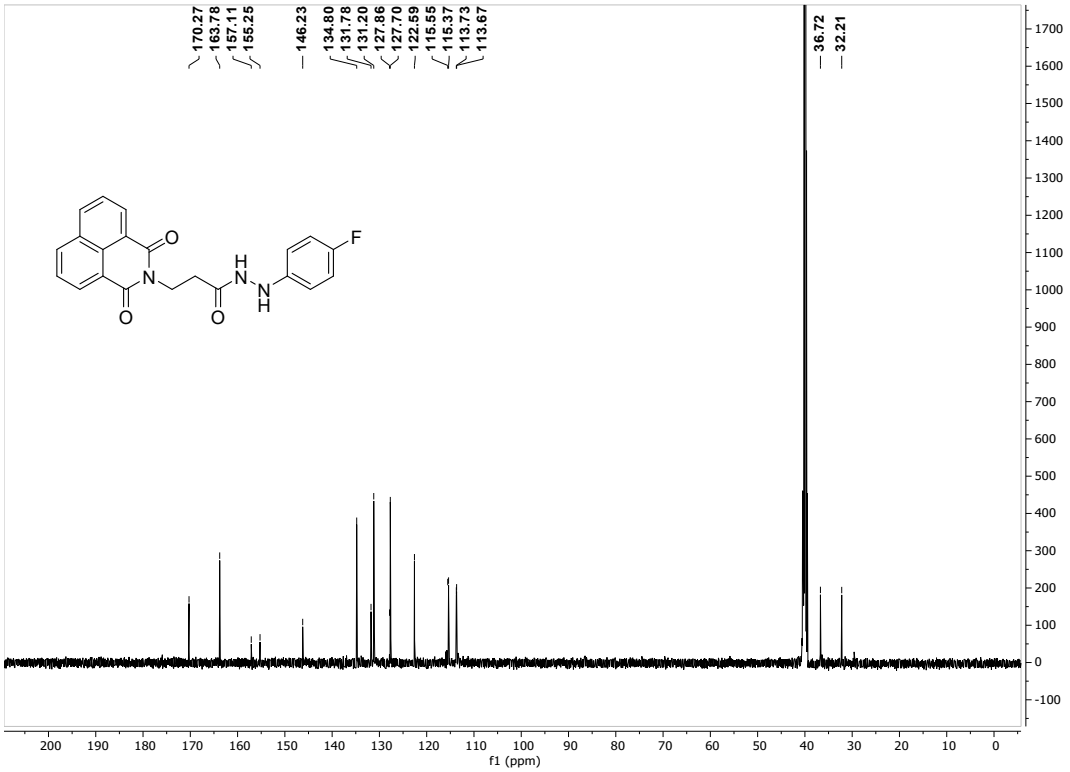
^{13}C NMR spectrum of compound **5d**, DMSO-d_6, 125MHz



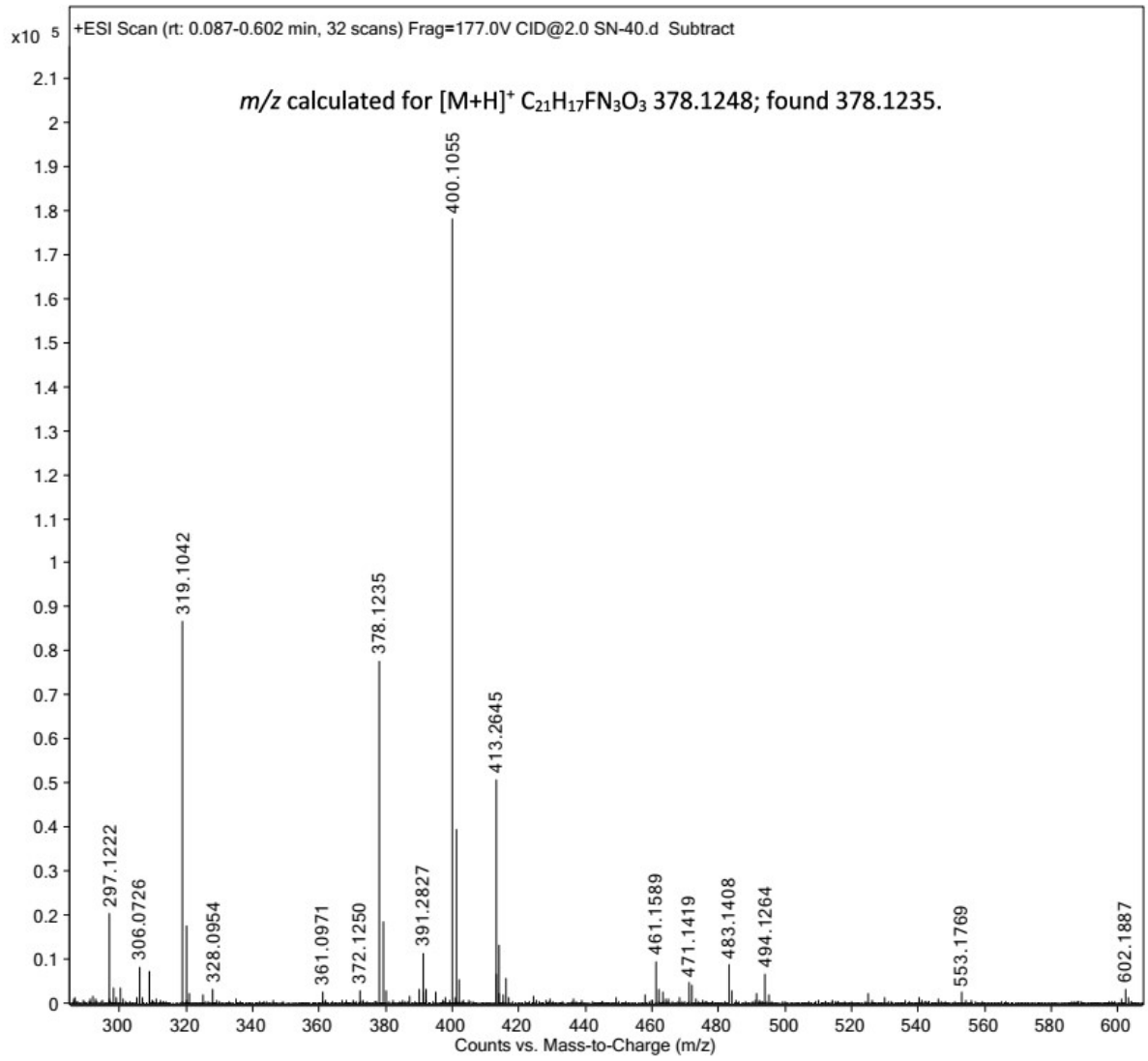
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-fluorophenyl)propanehydrazide (**5e**)*



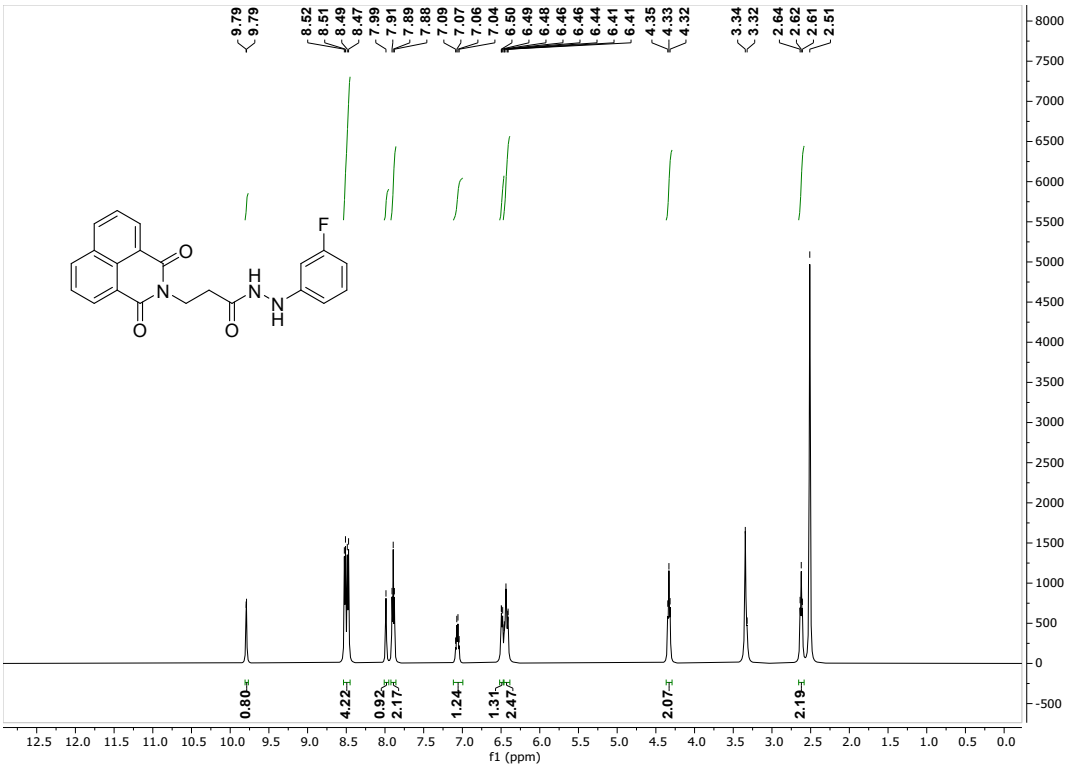
^{1}H NMR spectrum of compound **5e**, DMSO-d_6, 500MHz



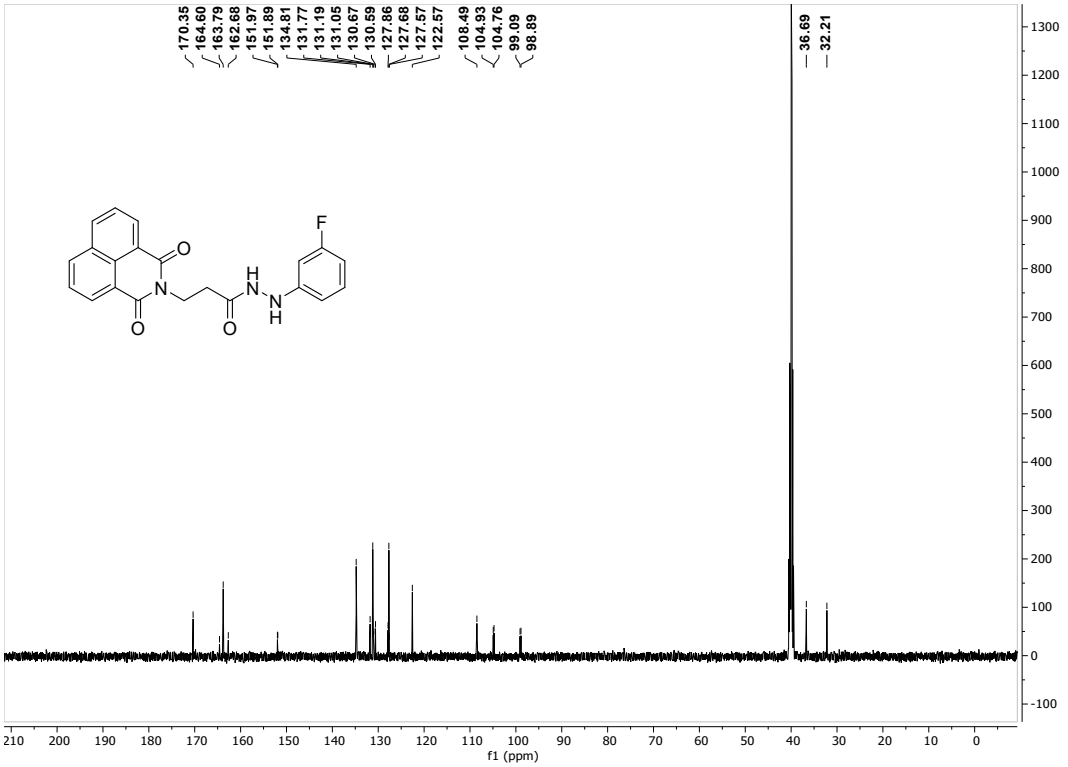
^{13}C NMR spectrum of compound **5e**, DMSO-d_6, 125MHz



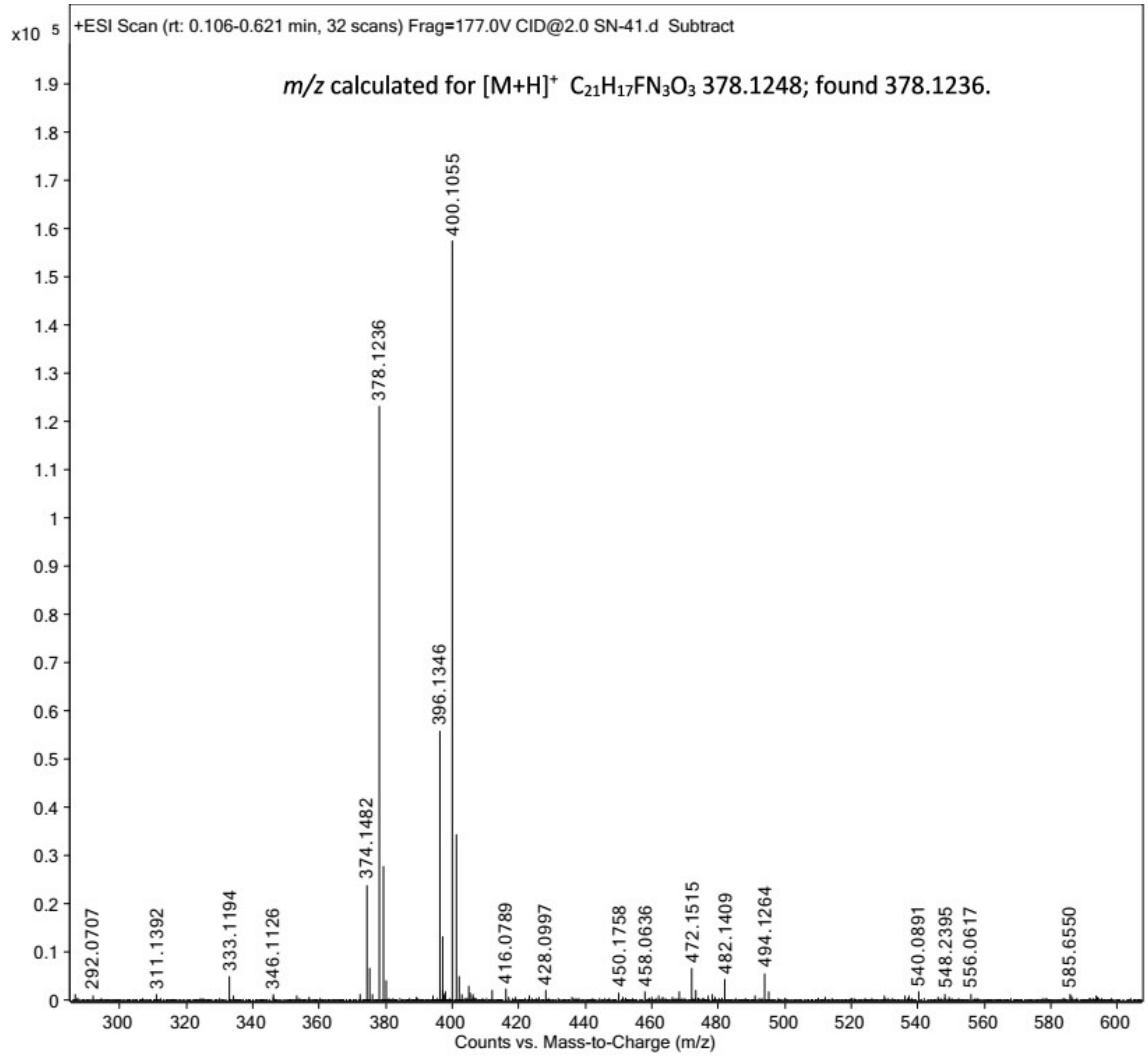
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(3-fluorophenyl)propanehydrazide (**5f**)*



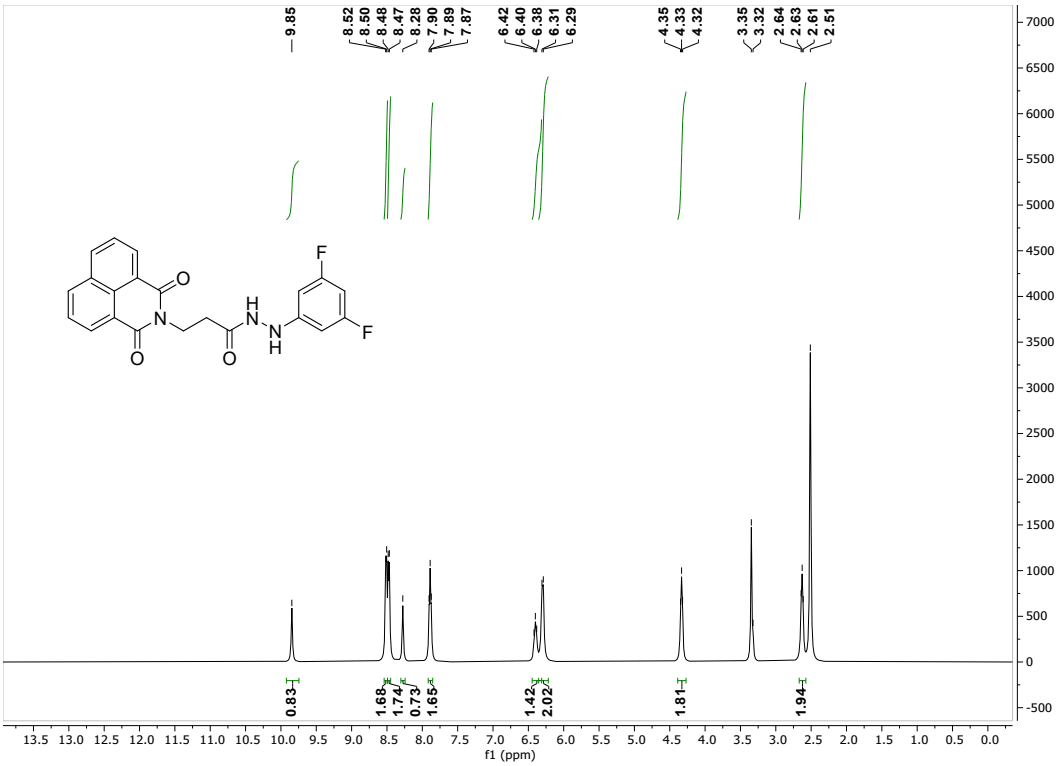
^{1}H NMR spectrum of compound **5f**, DMSO-d_6, 500MHz



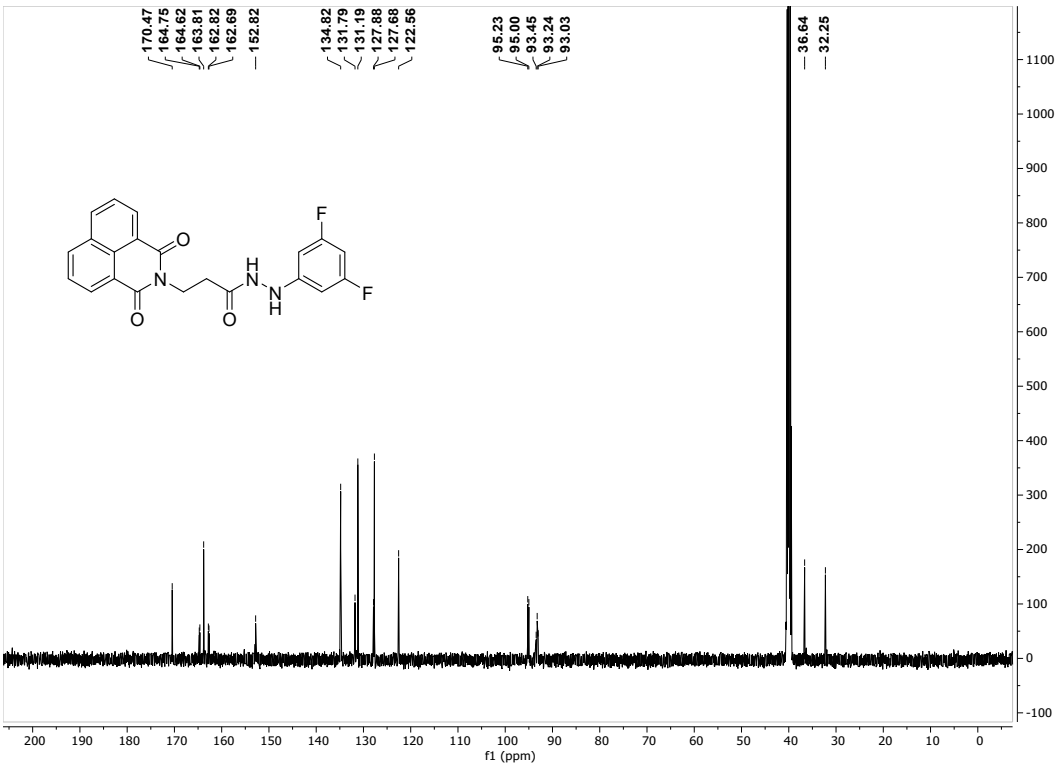
^{13}C NMR spectrum of compound **5f**, DMSO-d_6, 125MHz



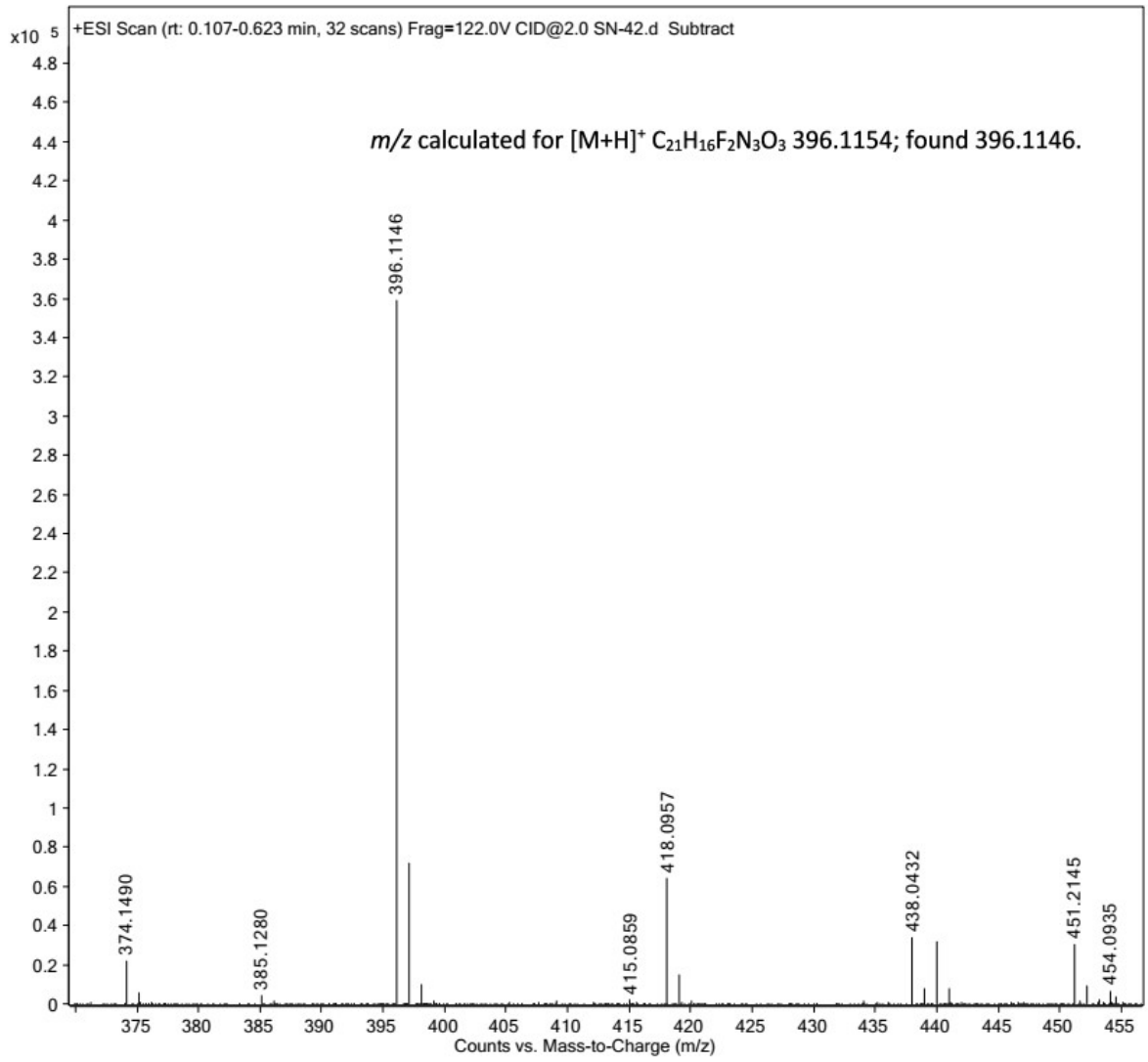
*N'-(3,5-difluorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5g**)*



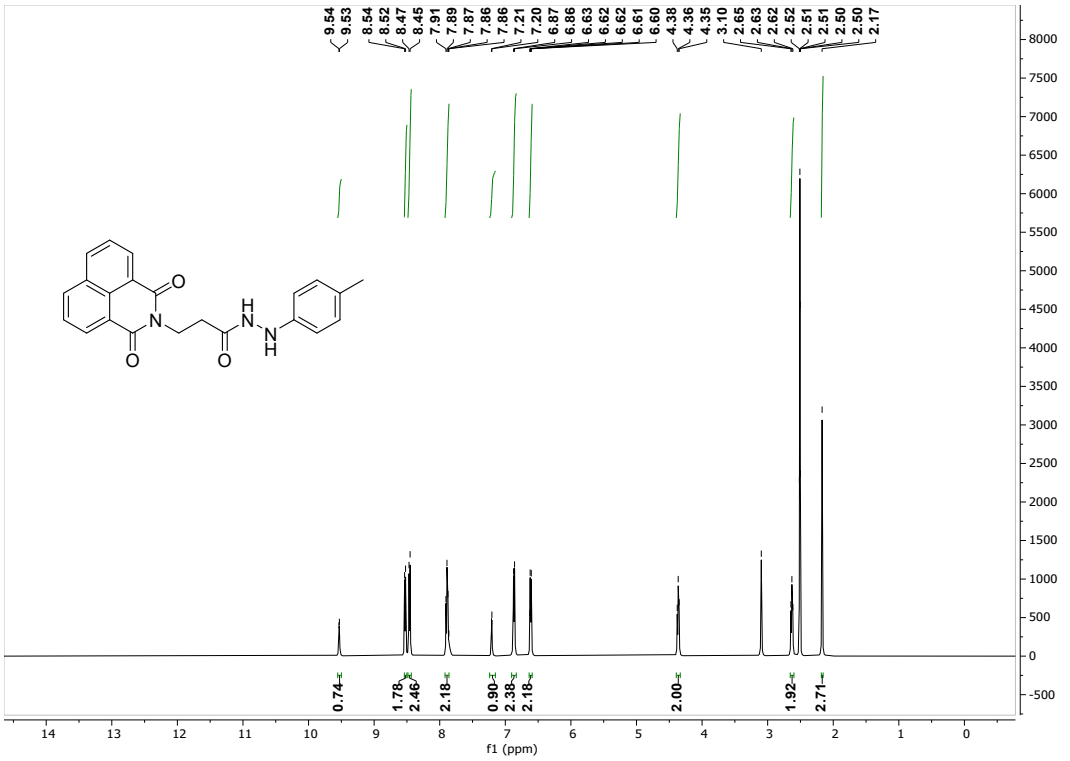
^{1}H NMR spectrum of compound **5g**, DMSO-d_6, 500MHz



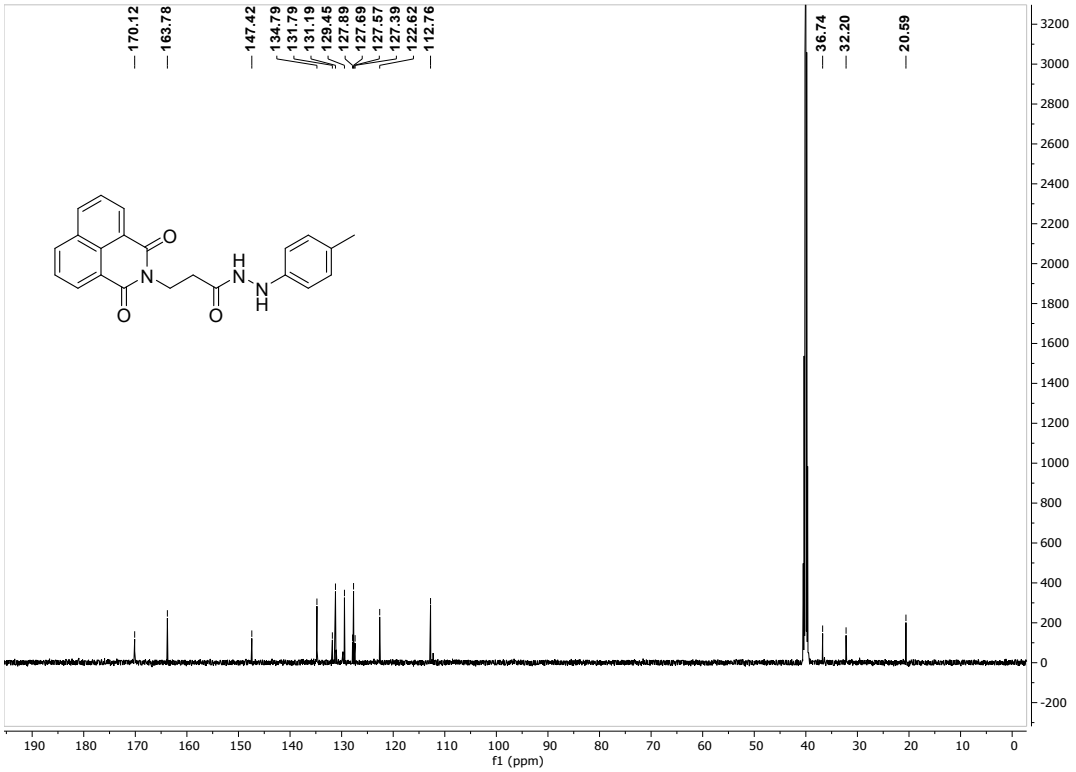
^{13}C NMR spectrum of compound **5g**, DMSO-d_6, 125MHz



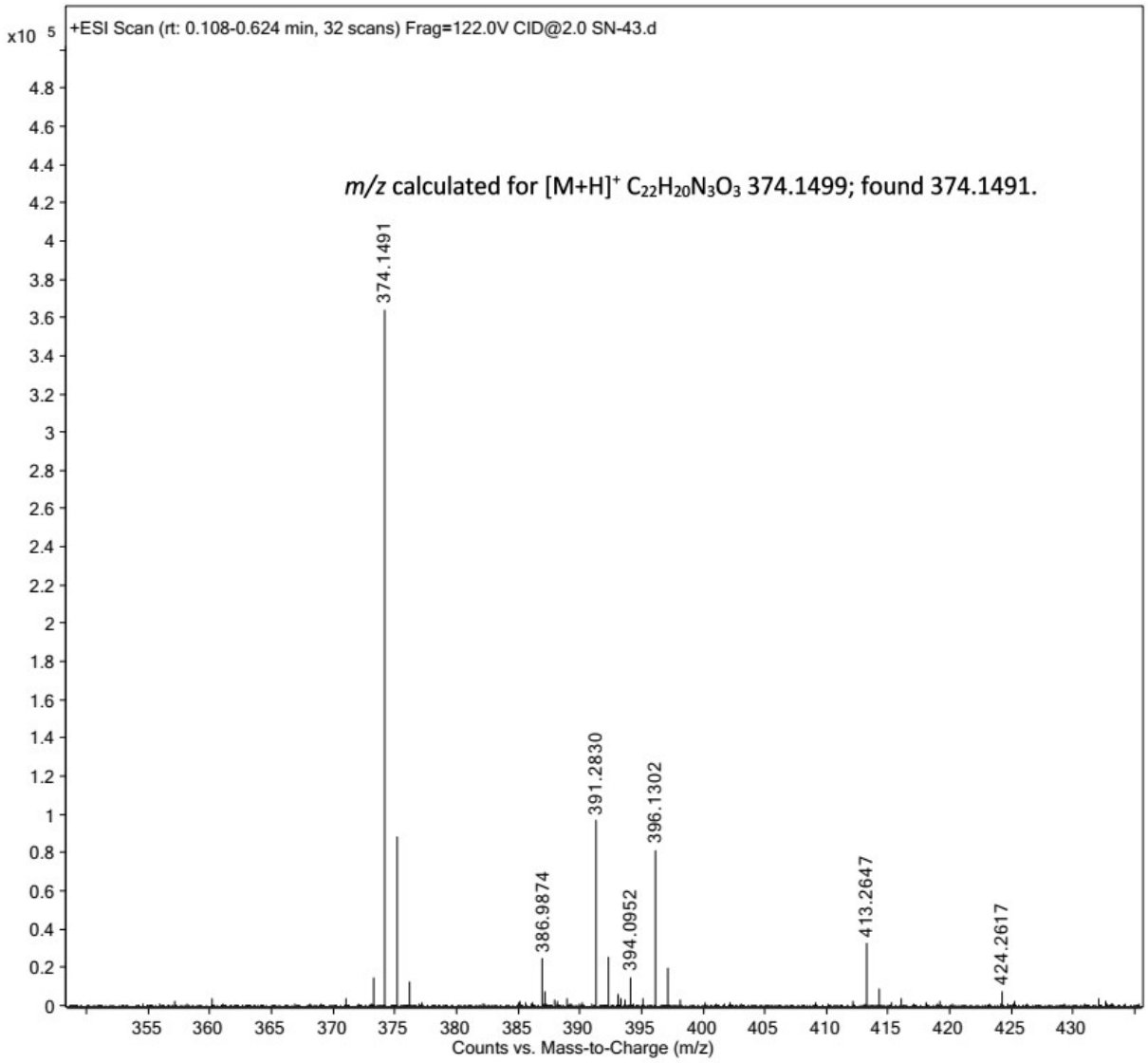
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(p-tolyl)propanehydrazide (**5h**)*



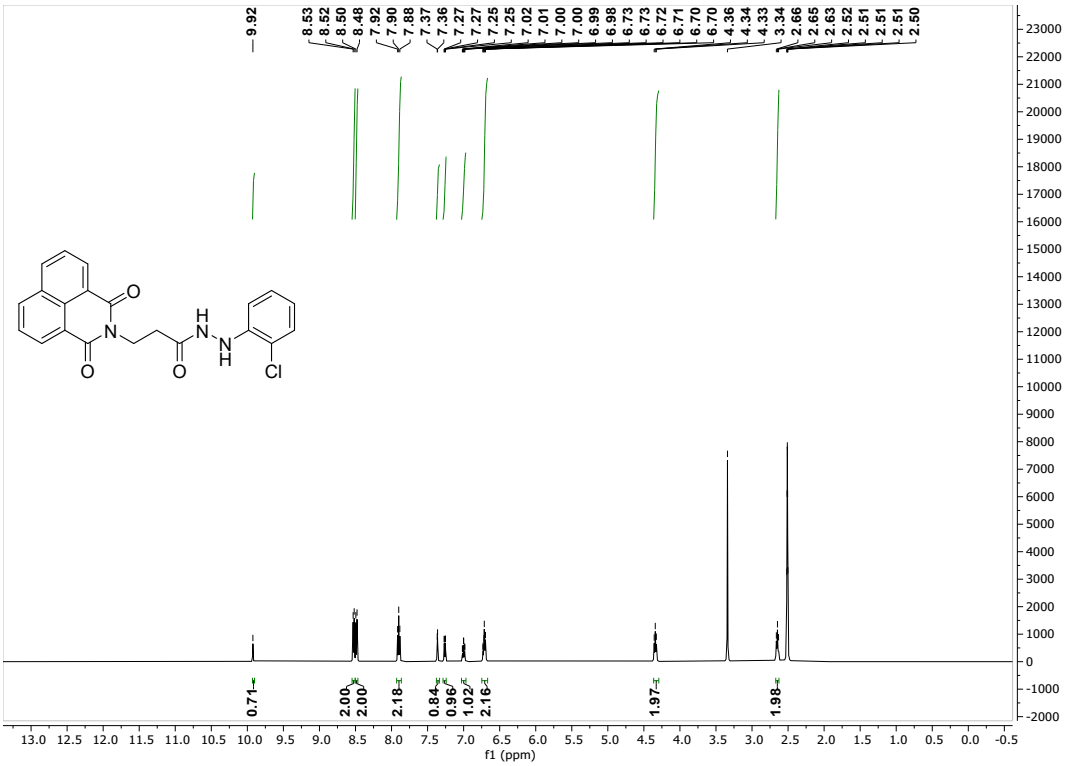
^{1}H NMR spectrum of compound **5h**, DMSO-d_6, 500MHz



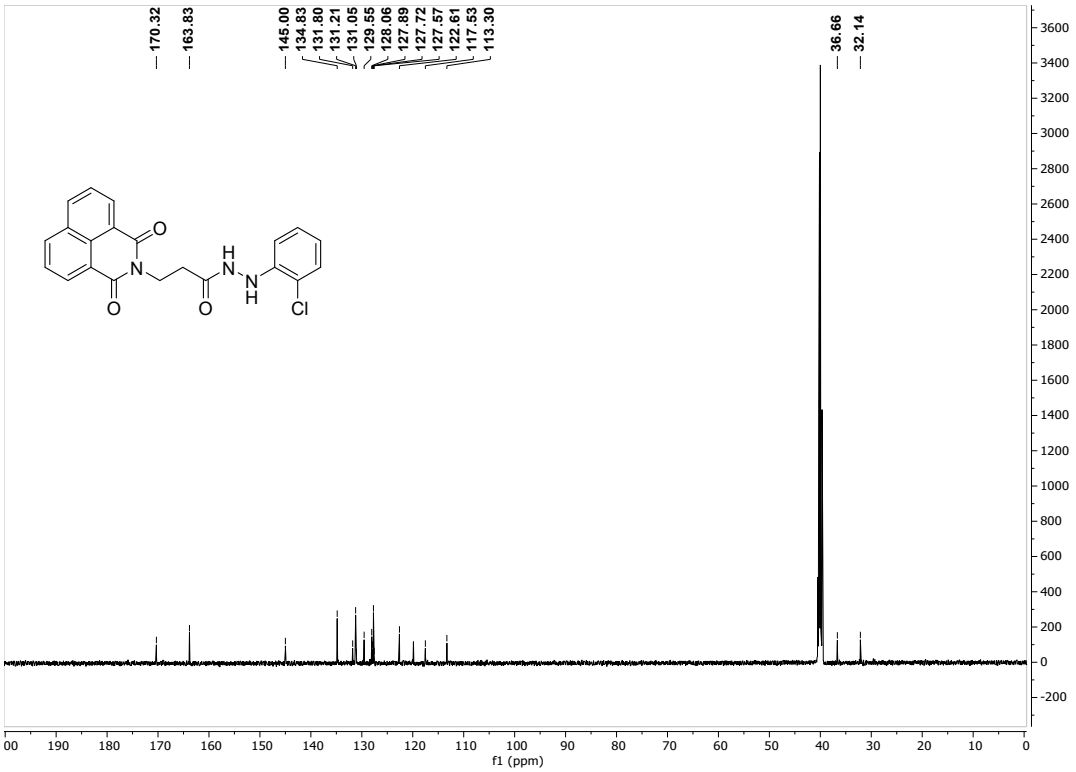
^{13}C NMR spectrum of compound **5h**, DMSO-d_6, 125MHz



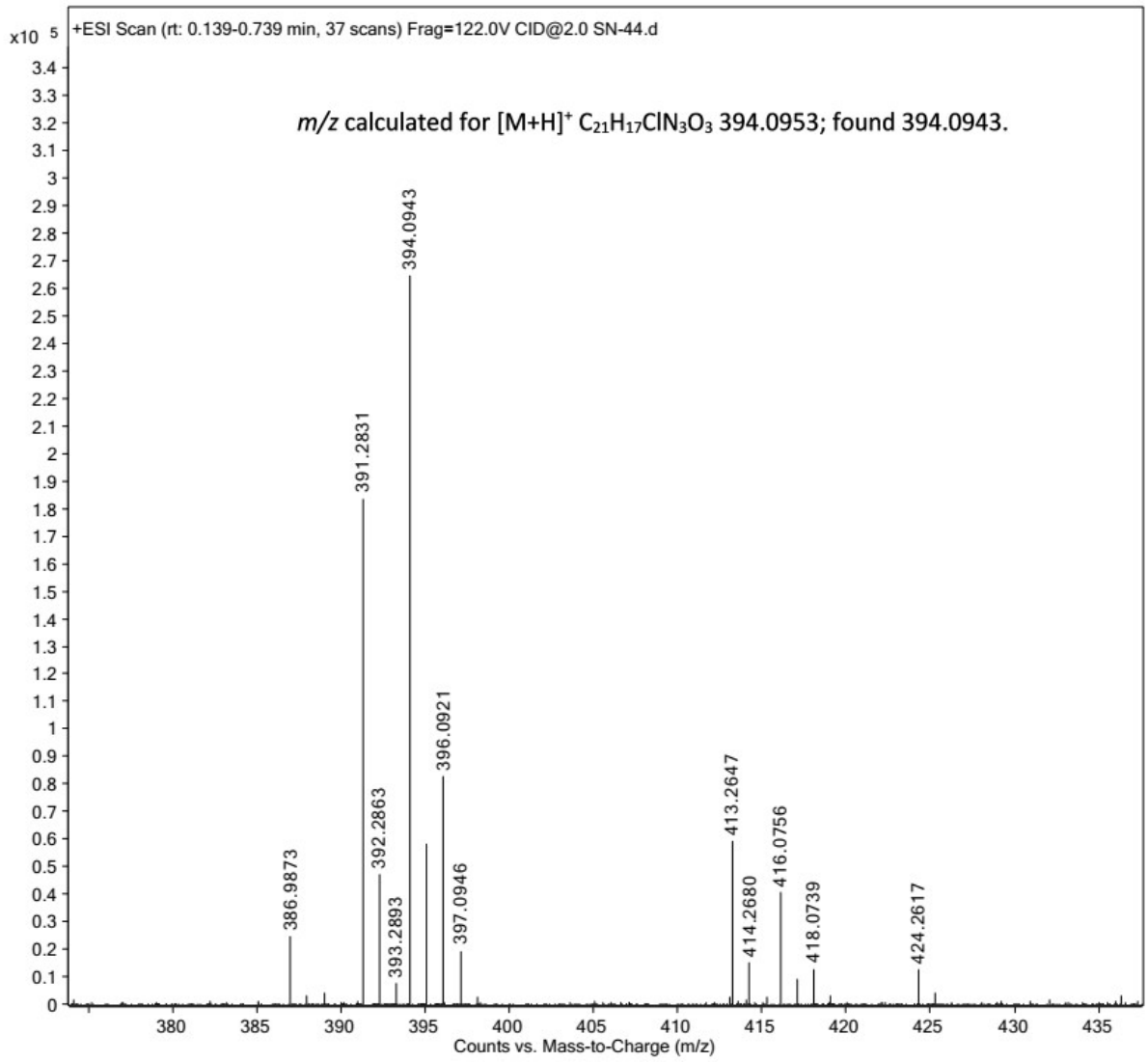
*N'-(2-chlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5i**)*



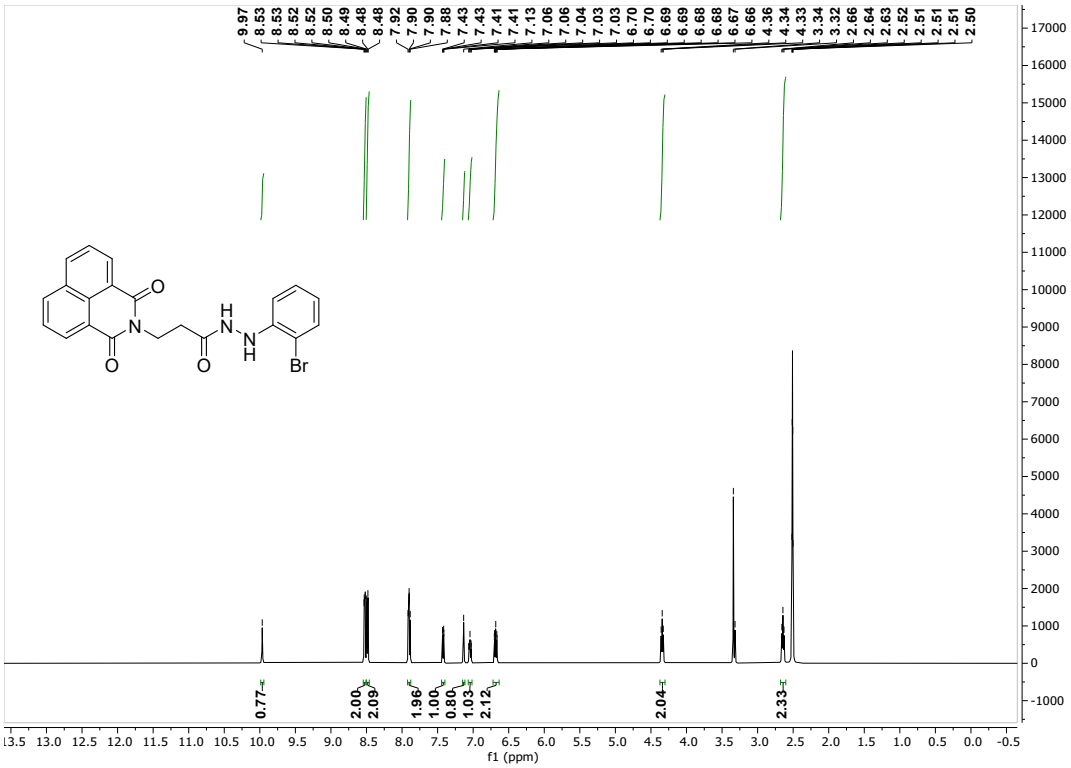
^{1}H NMR spectrum of compound **5i**, DMSO-d_6, 500MHz



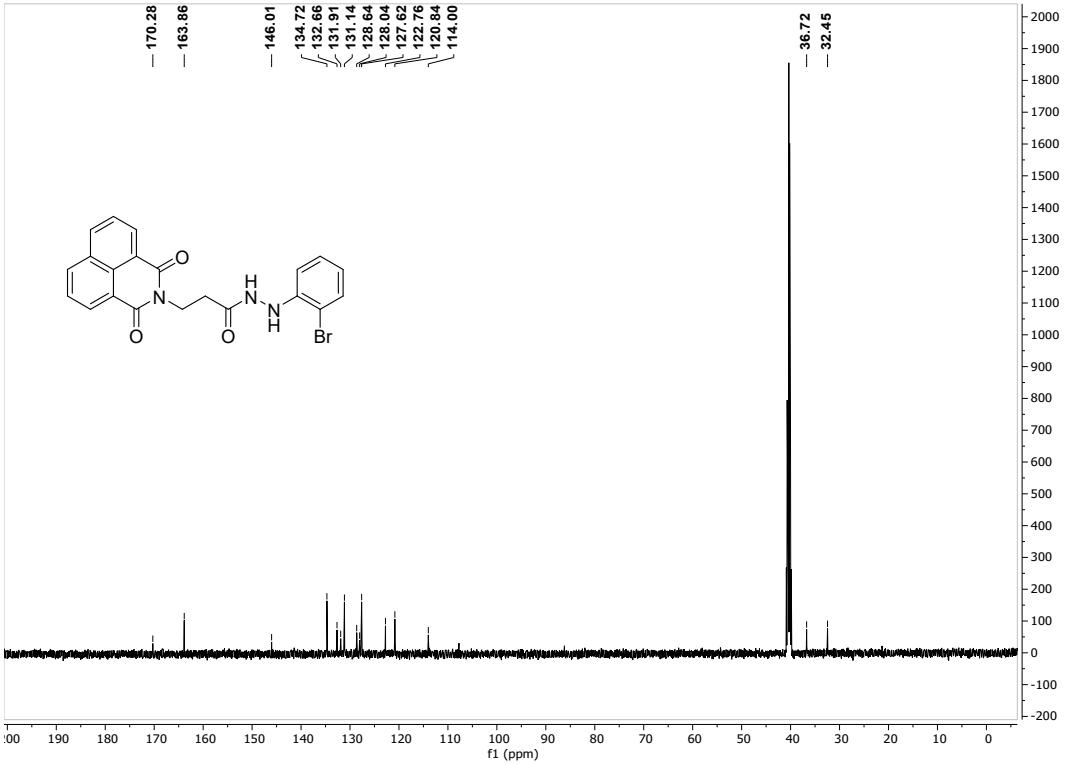
^{13}C NMR spectrum of compound **5i**, DMSO-d_6, 125MHz



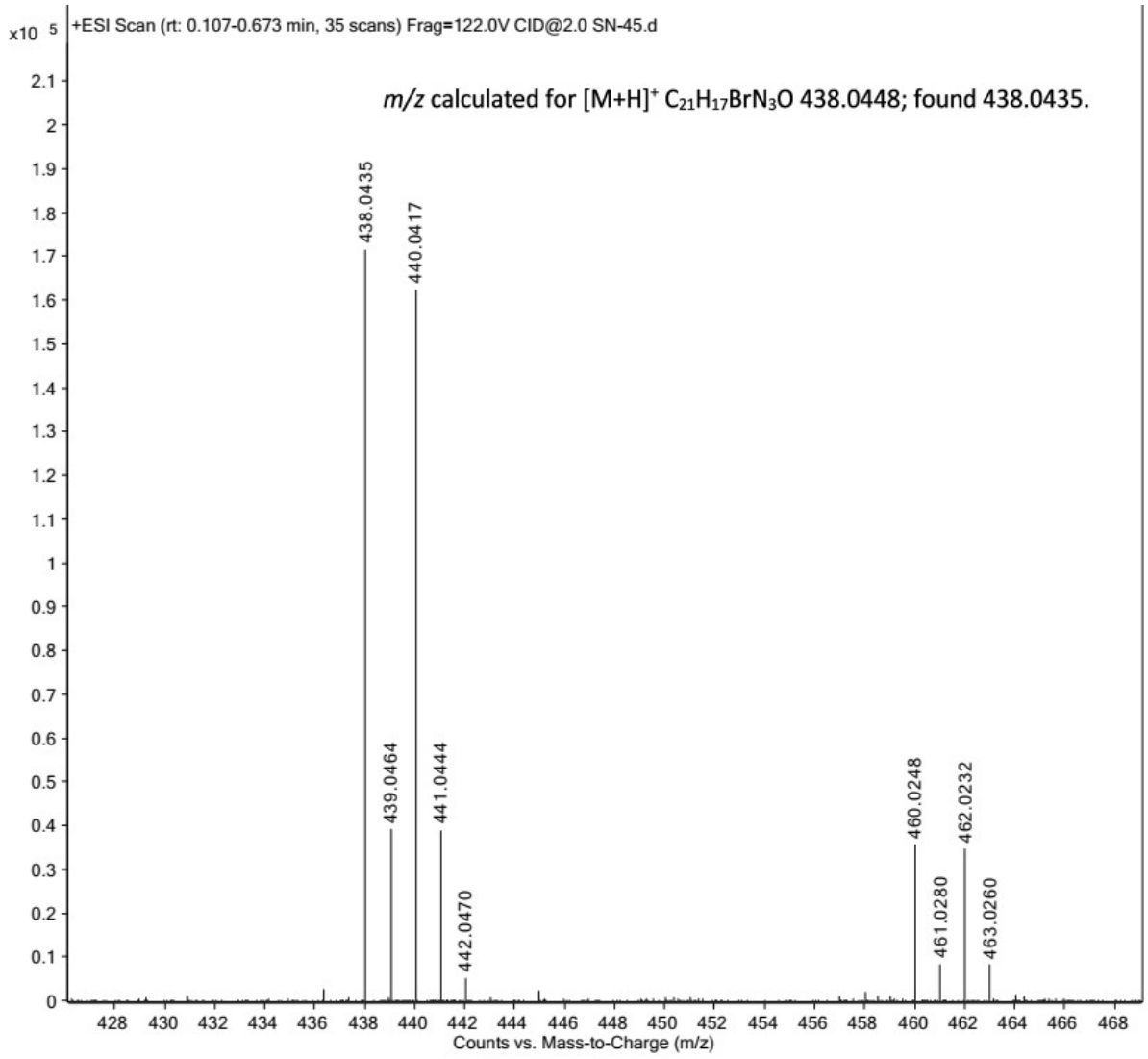
*N'-(2-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5j**)*



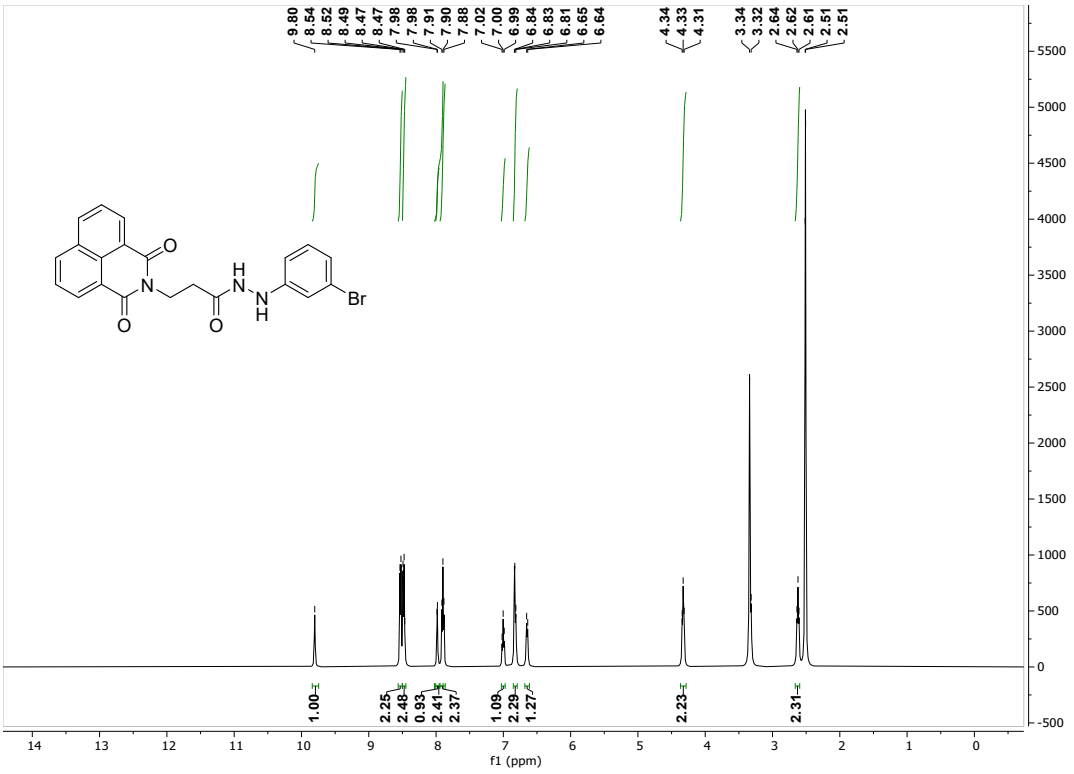
^{1}H NMR spectrum of compound **5j**, DMSO-d_6, 500MHz



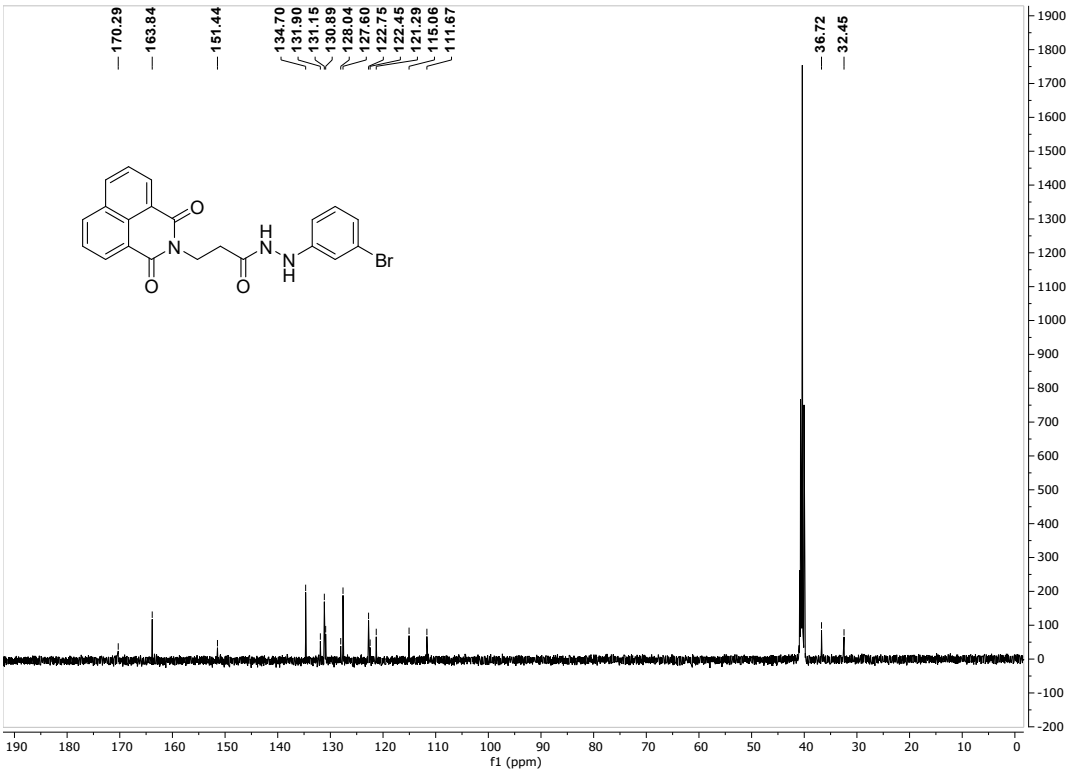
^{13}C NMR spectrum of compound **5j**, DMSO-d_6, 125MHz



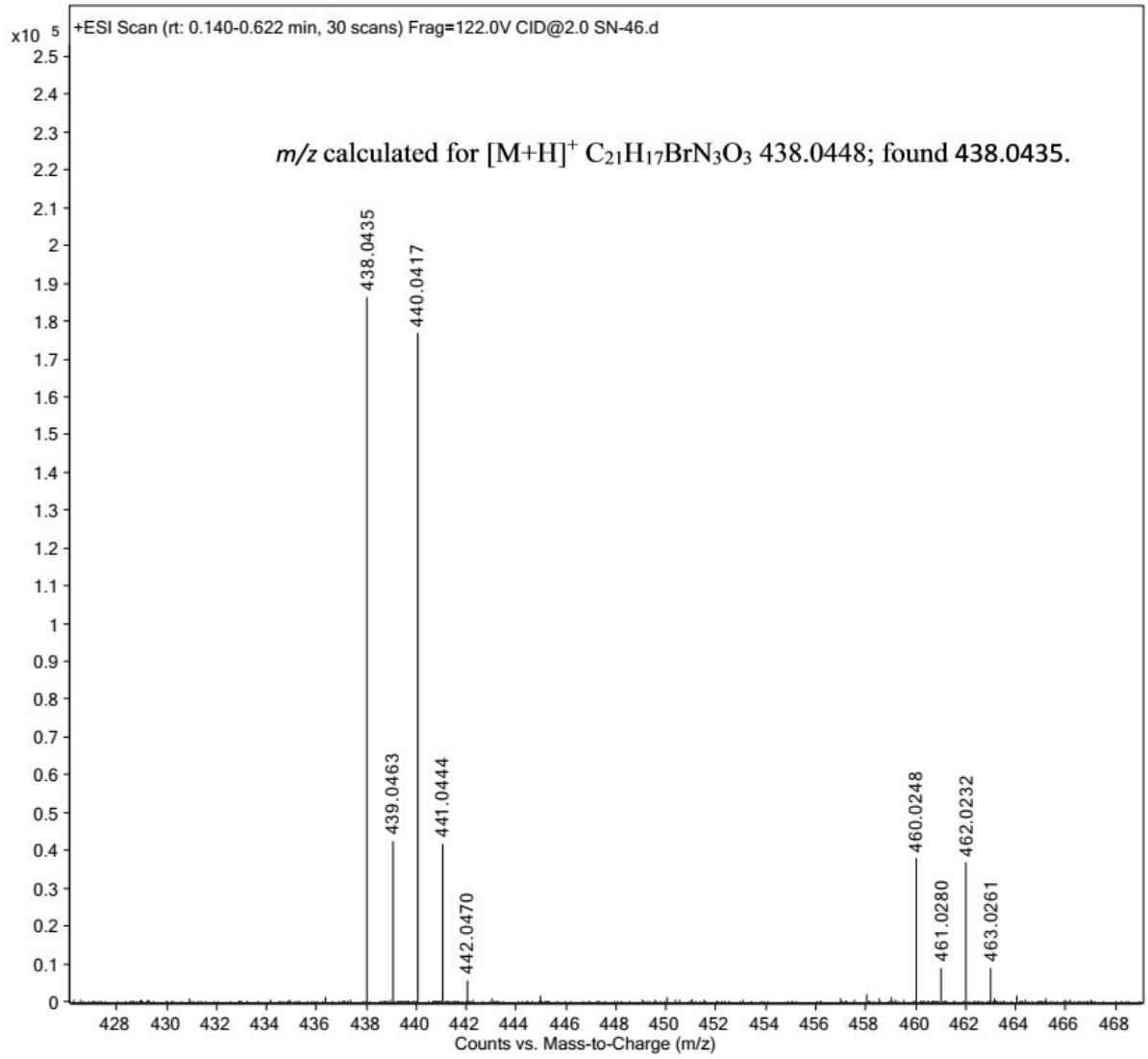
*N'-(3-bromophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5k**)*



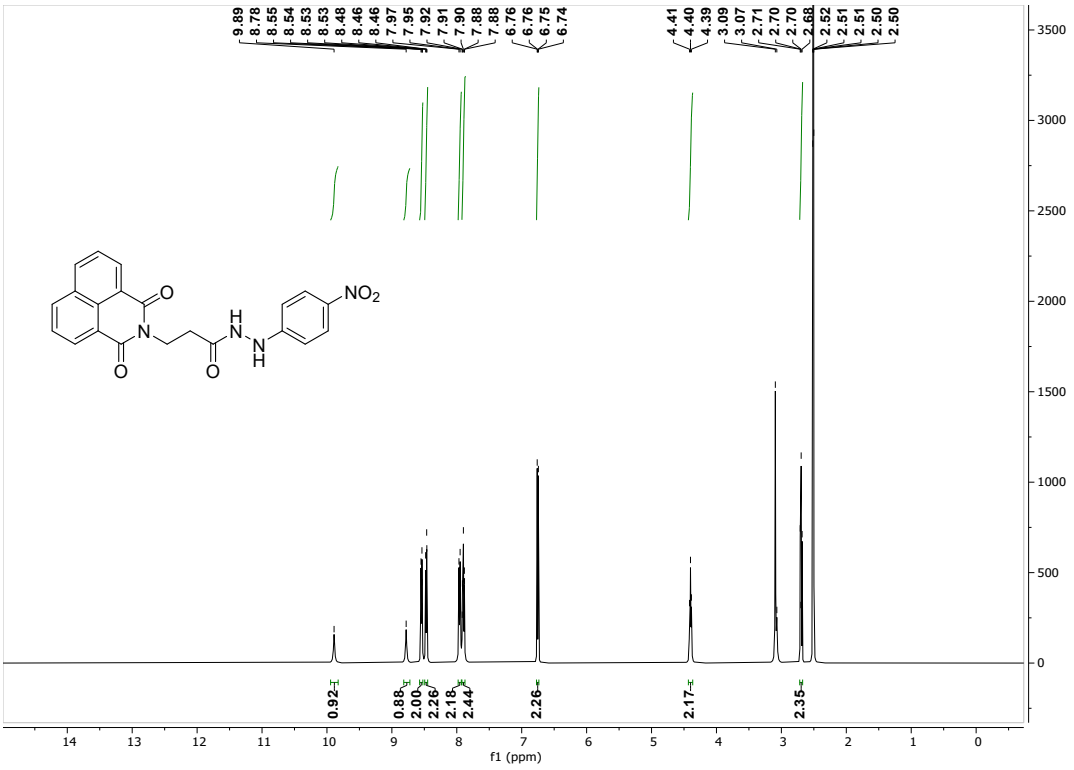
^{1}H NMR spectrum of compound **5k**, DMSO-d_6, 500MHz



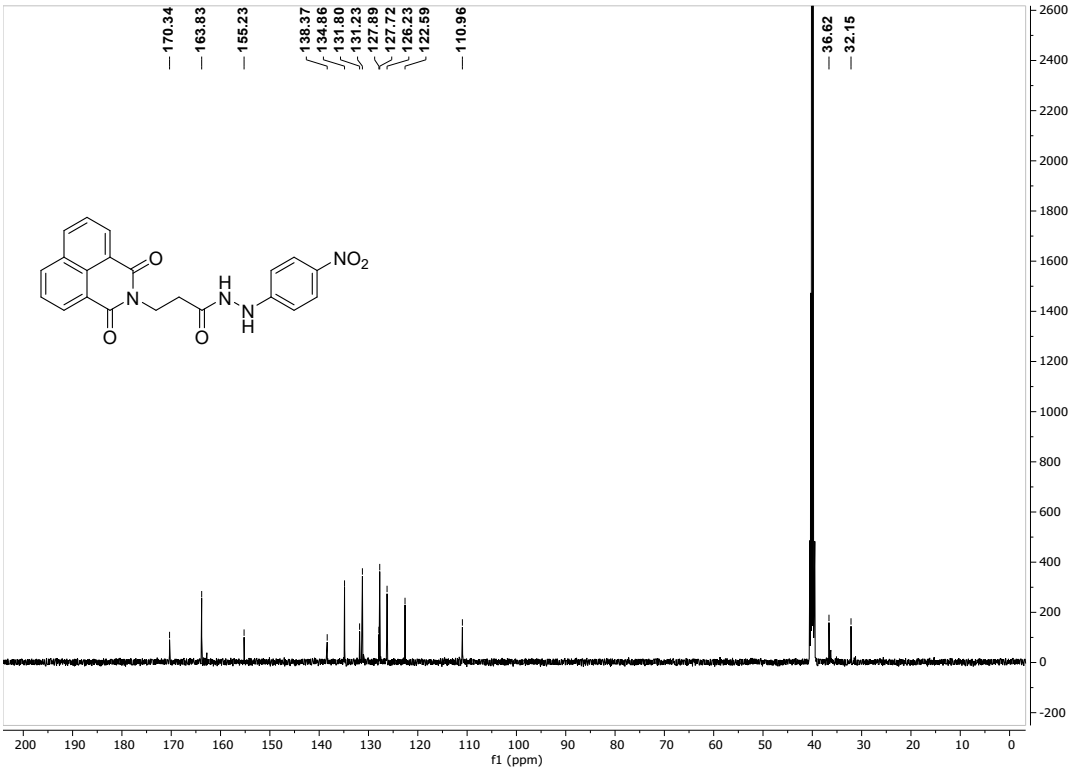
^{13}C NMR spectrum of compound **5k**, DMSO-d_6, 125MHz



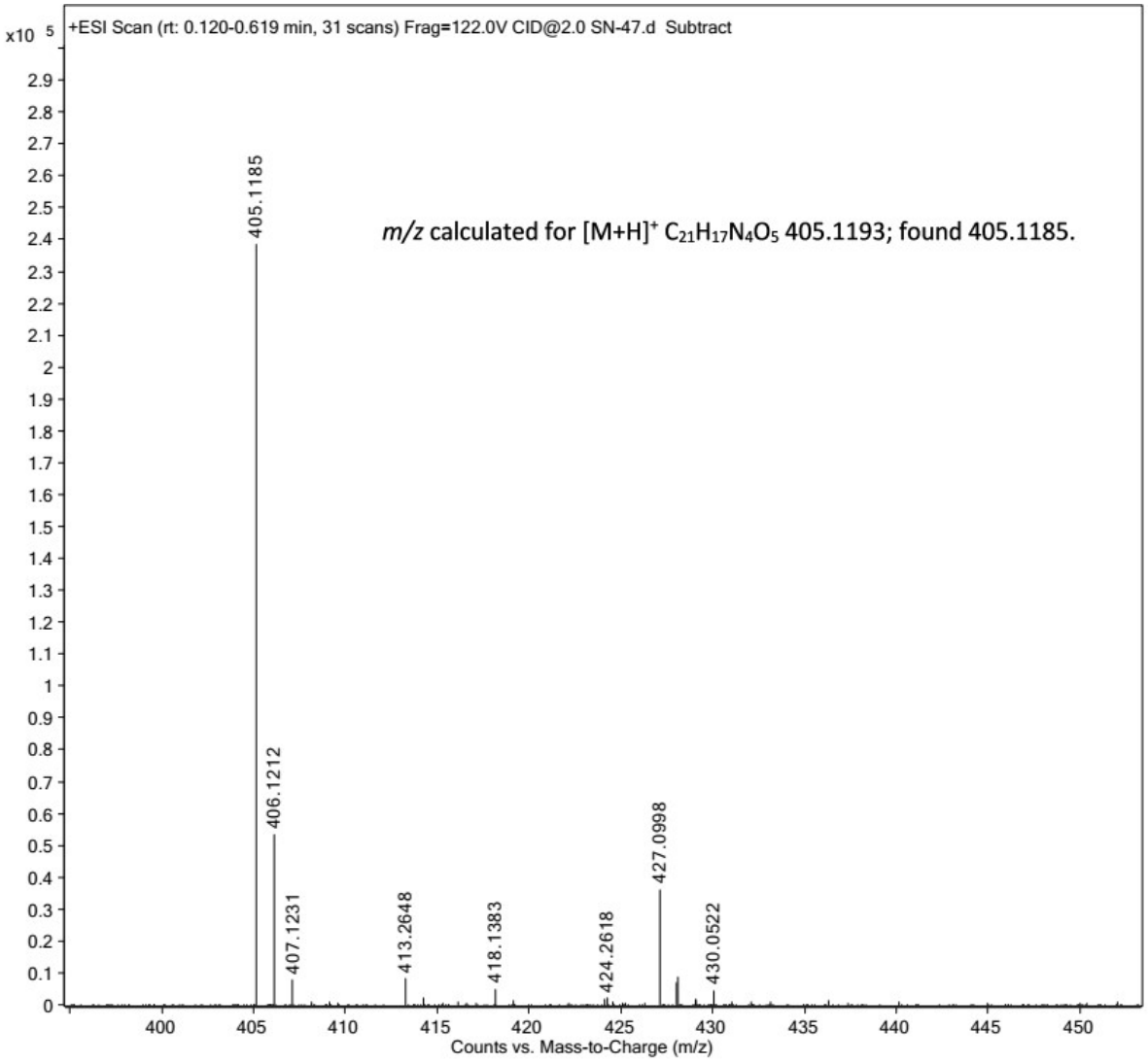
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-nitrophenyl)propanehydrazide (**5l**)*



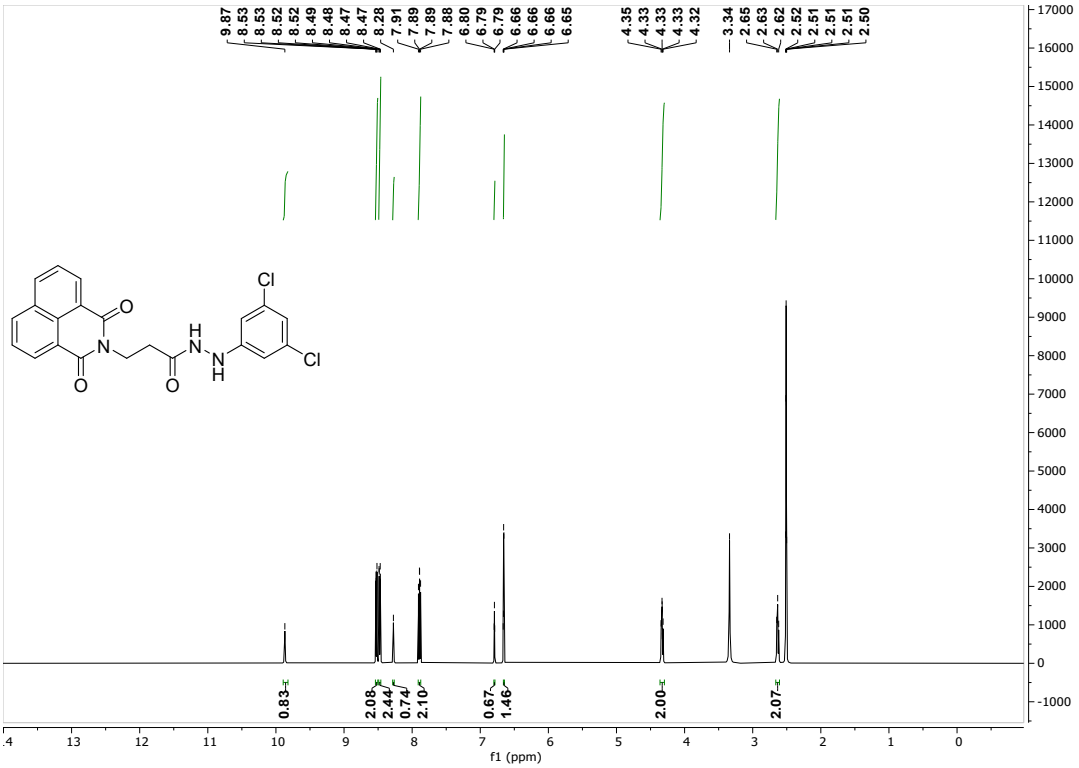
^{1}H NMR spectrum of compound **5l**, DMSO-d_6, 500MHz



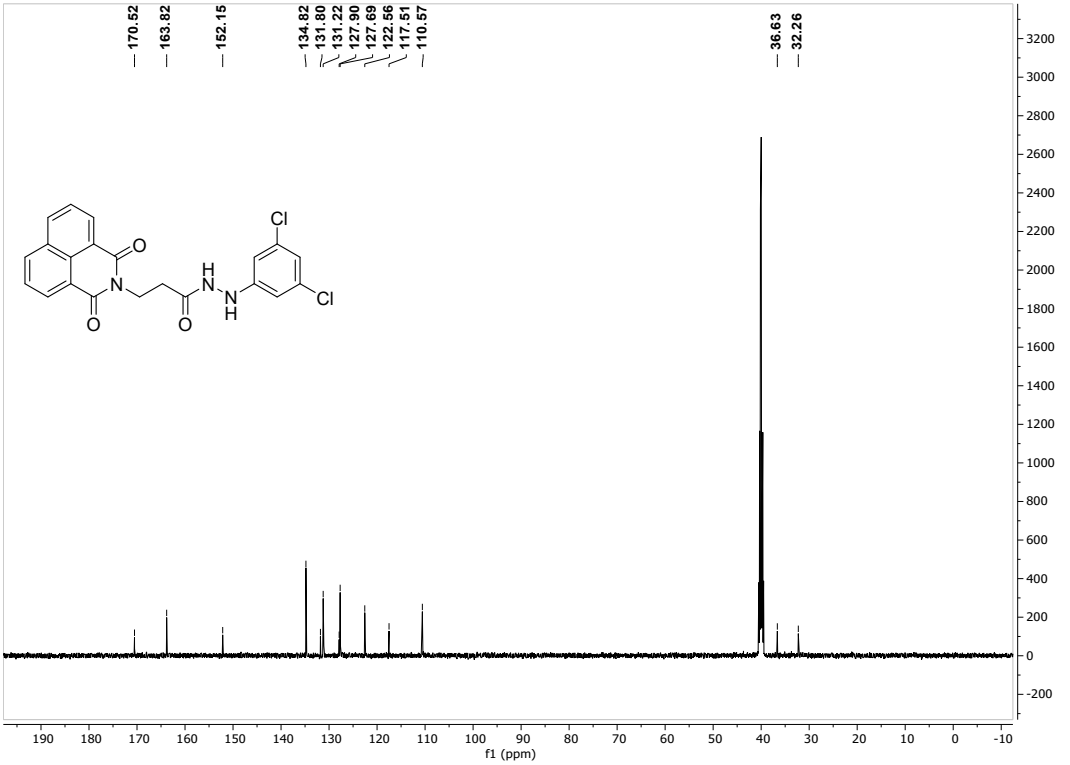
^{13}C NMR spectrum of compound **5l**, DMSO-d_6, 125MHz



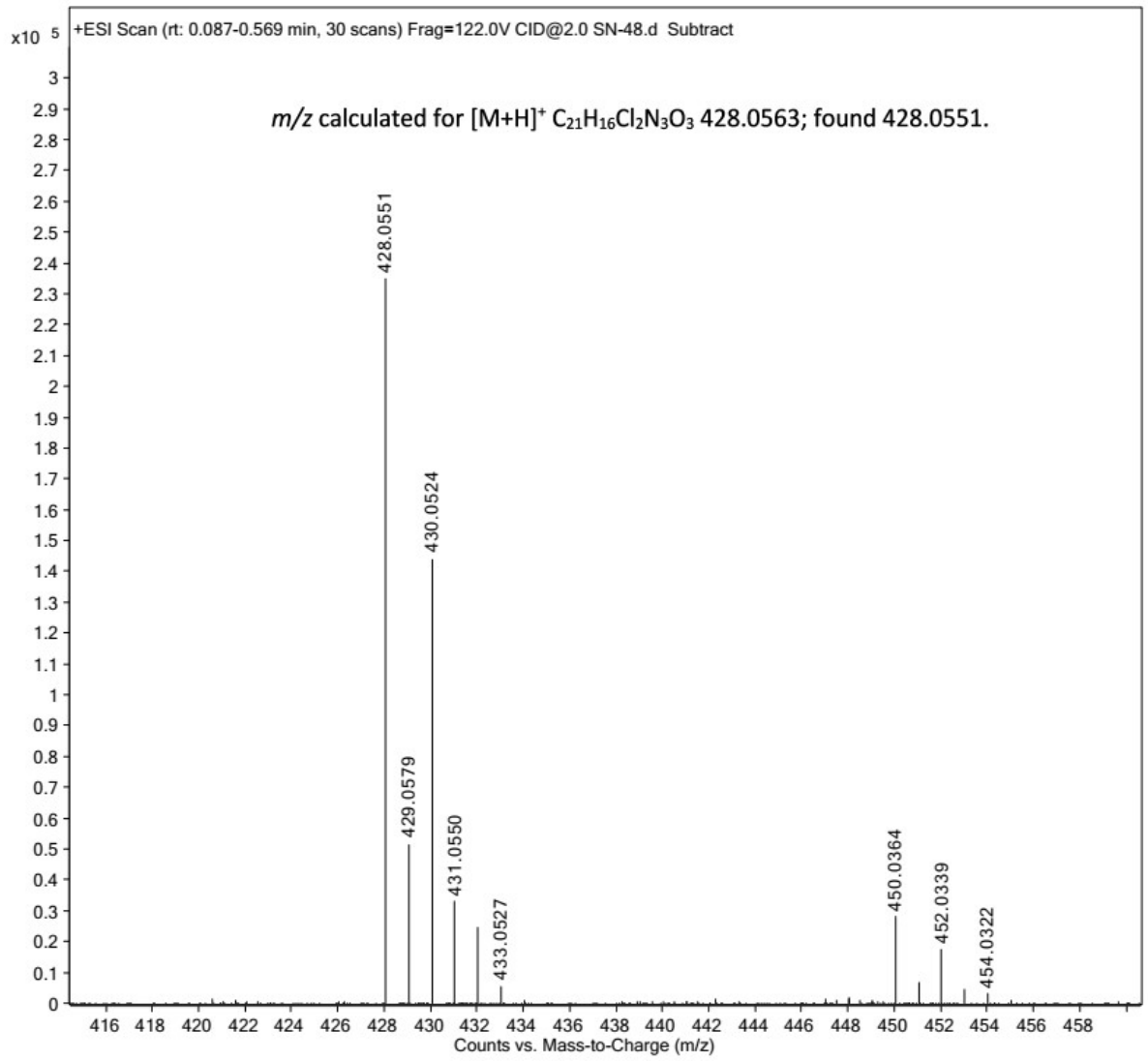
*N'-(3,5-dichlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5m**)*



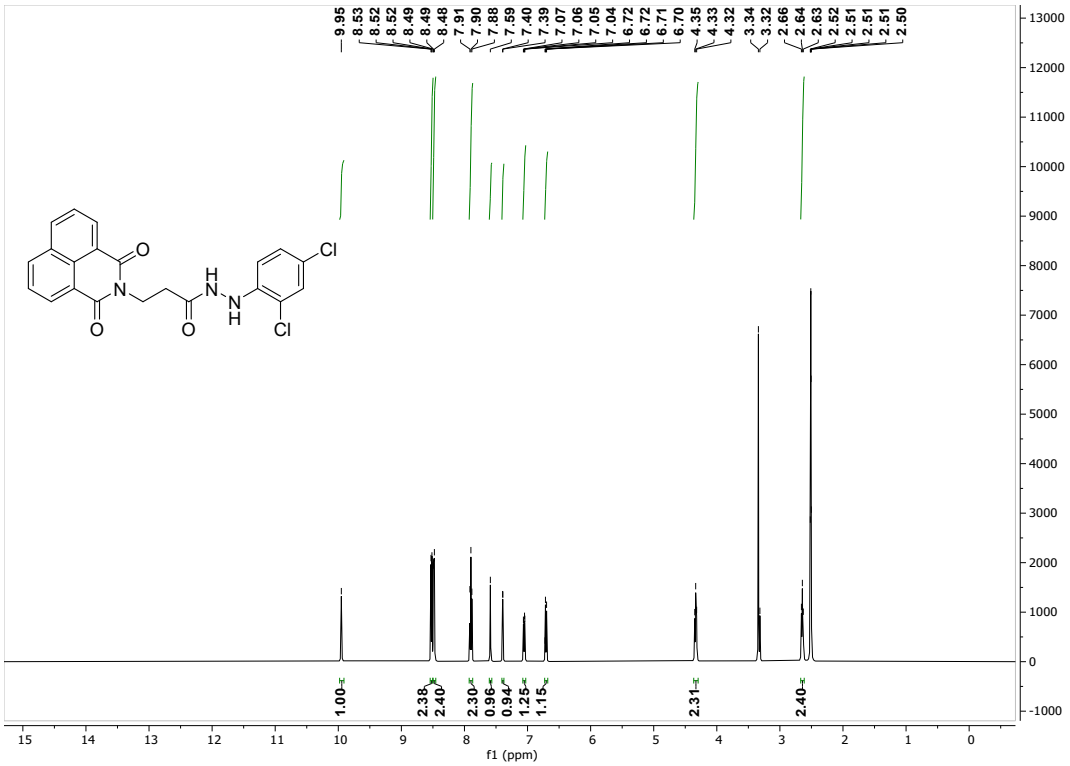
^{1}H NMR spectrum of compound **5m**, DMSO-d_6, 500MHz



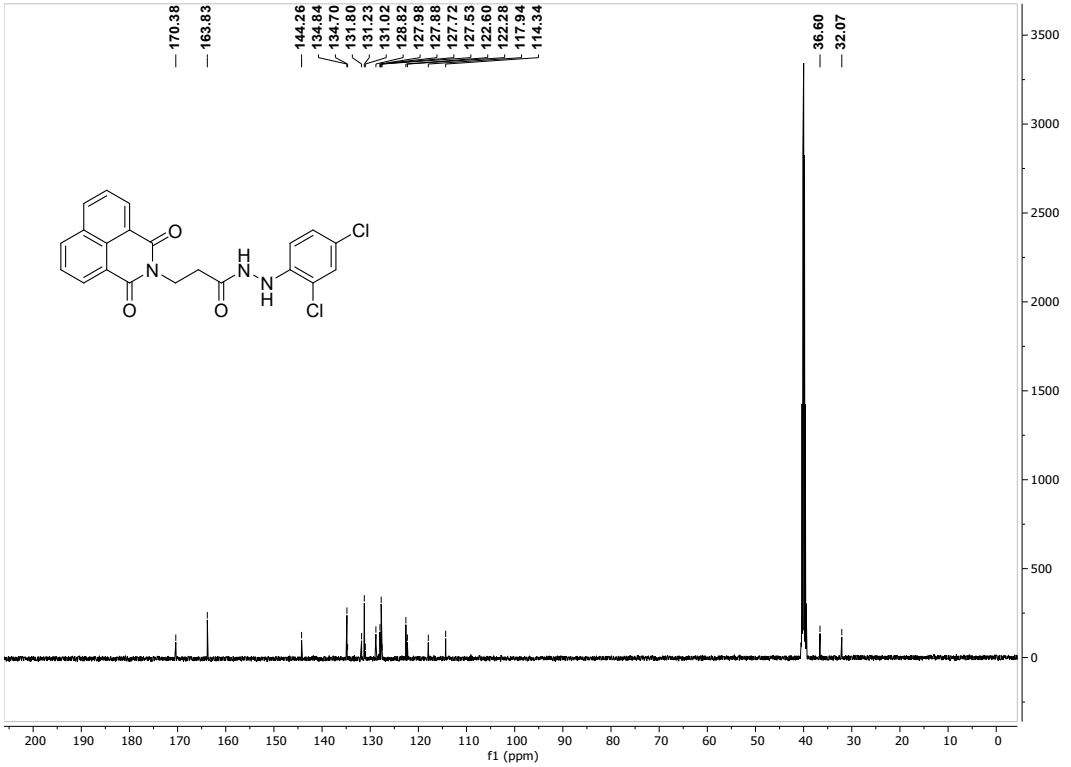
^{13}C NMR spectrum of compound **5m**, DMSO-d_6, 125MHz



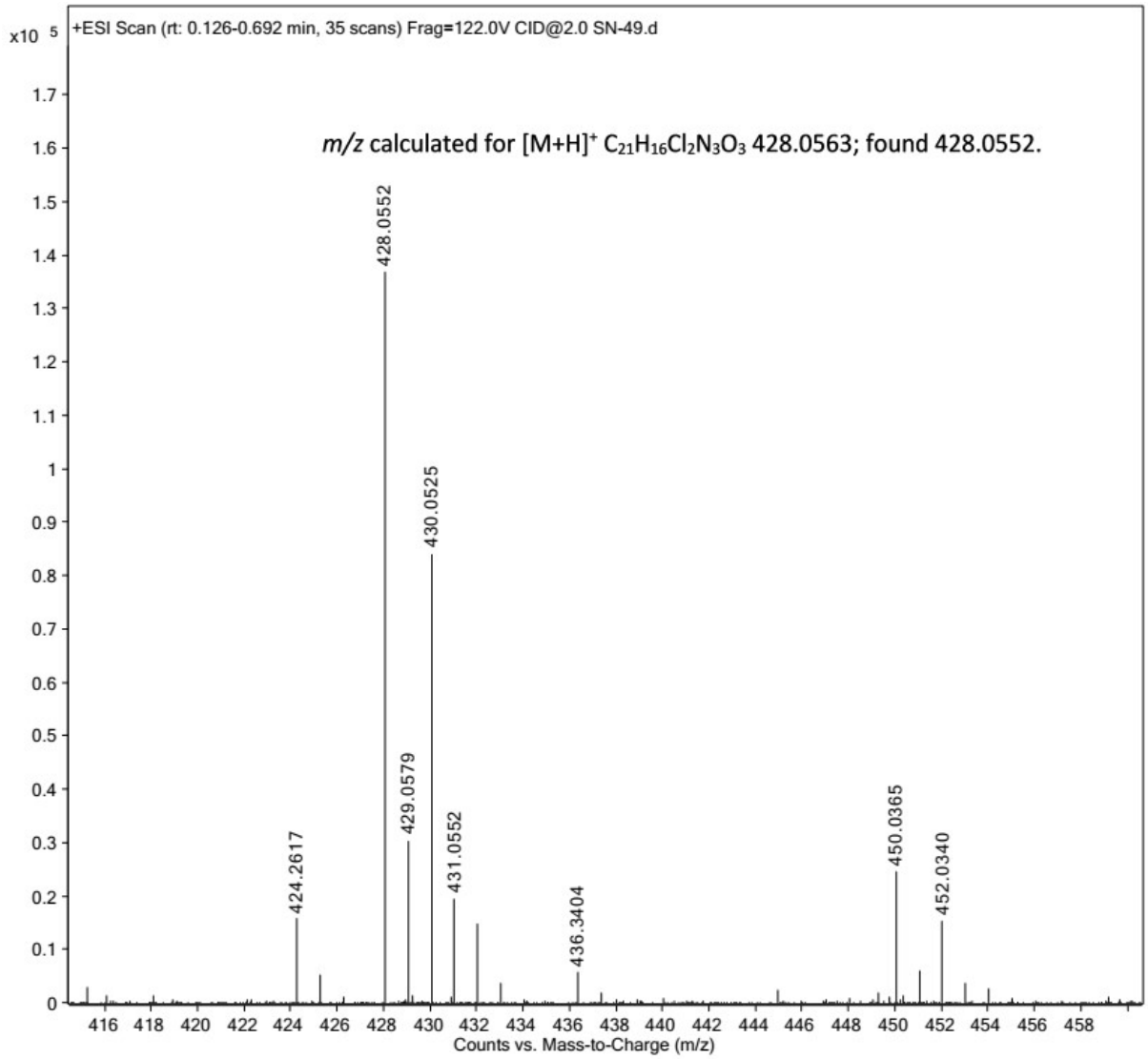
*N'-(2,4-dichlorophenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5n**)*



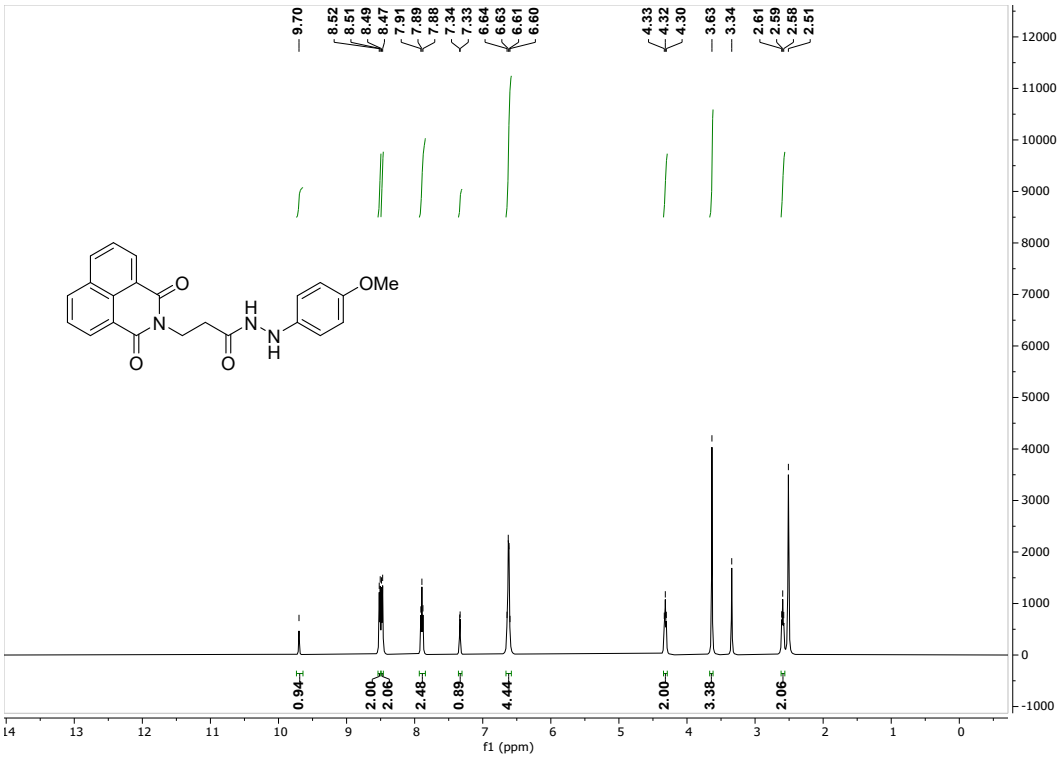
^{1}H NMR spectrum of compound **5n**, DMSO-d_6, 500MHz



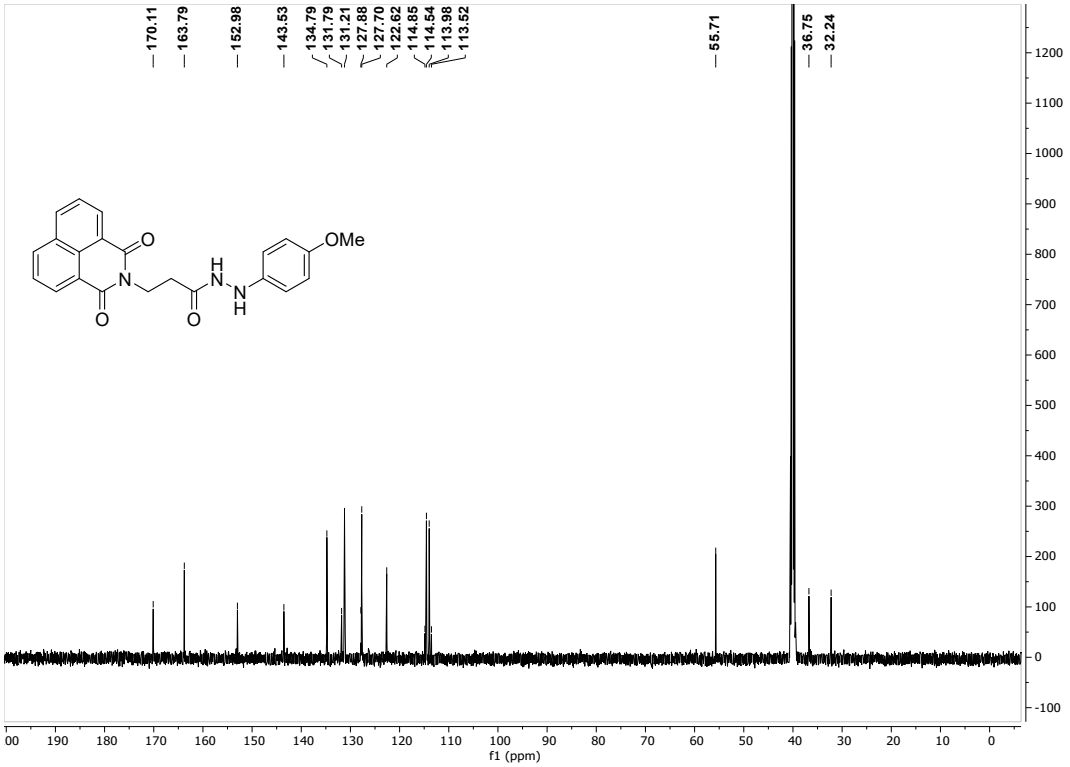
^{13}C NMR spectrum of compound **5n**, DMSO-d_6, 125MHz



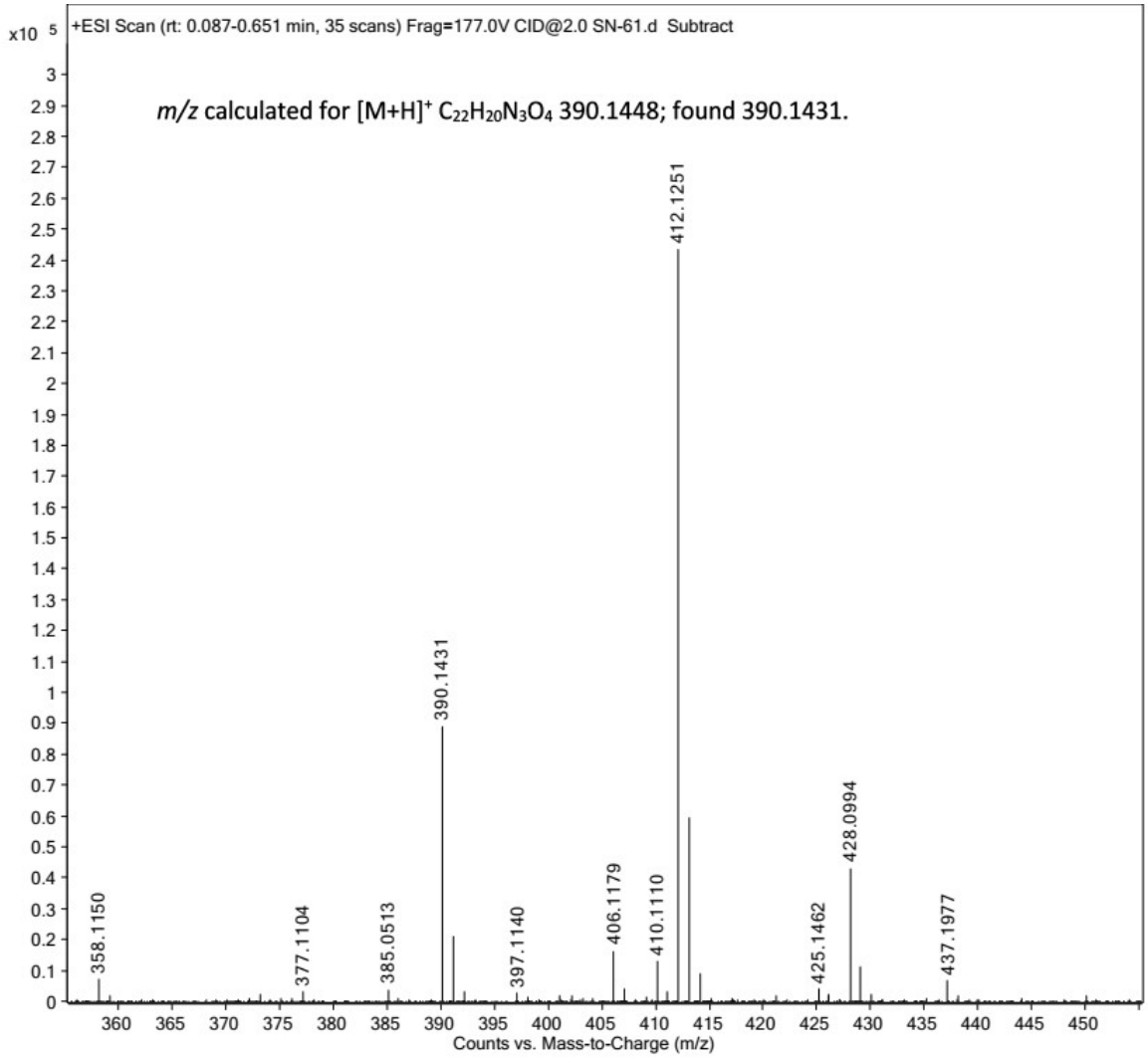
*3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-methoxyphenyl)propanehydrazide (**5o**)*



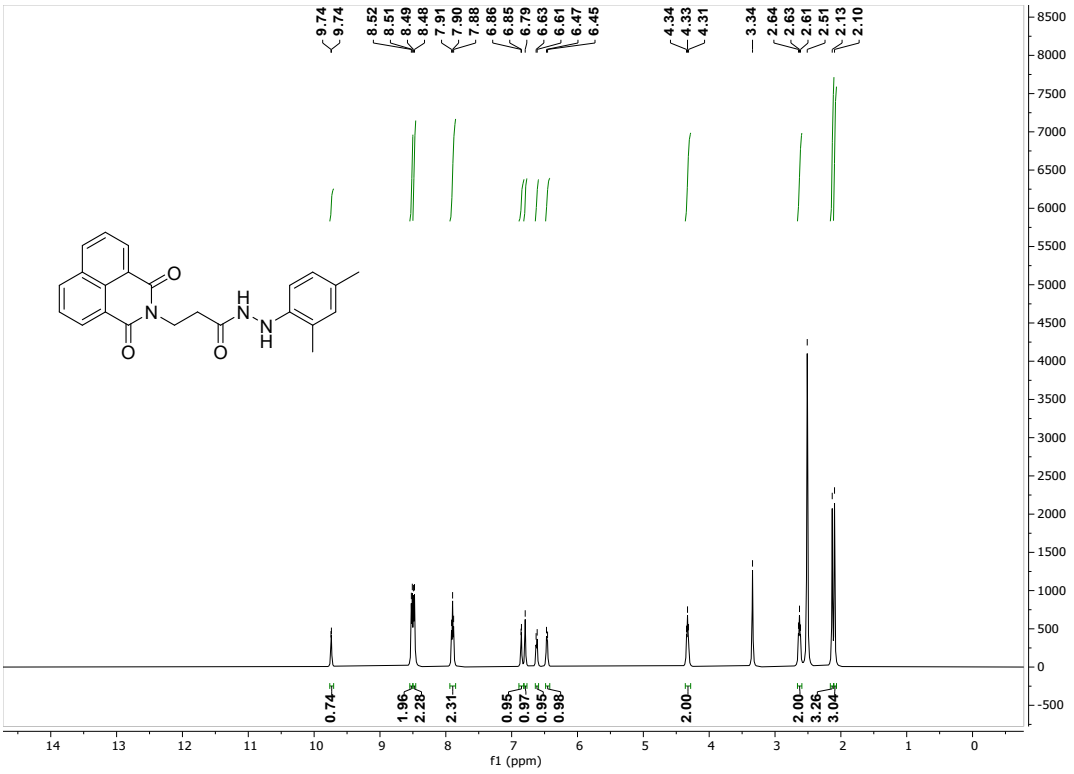
^{1}H NMR spectrum of compound **5o**, DMSO-d_6, 500MHz



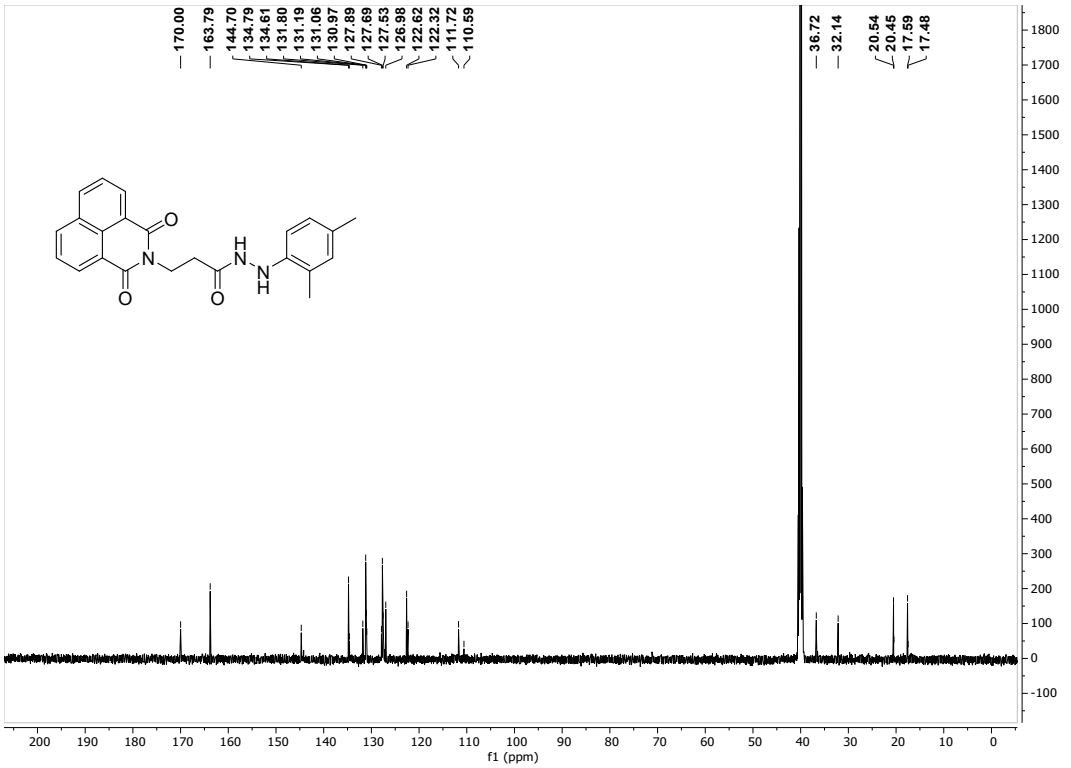
^{13}C NMR spectrum of compound **5o**, DMSO-d_6, 125MHz



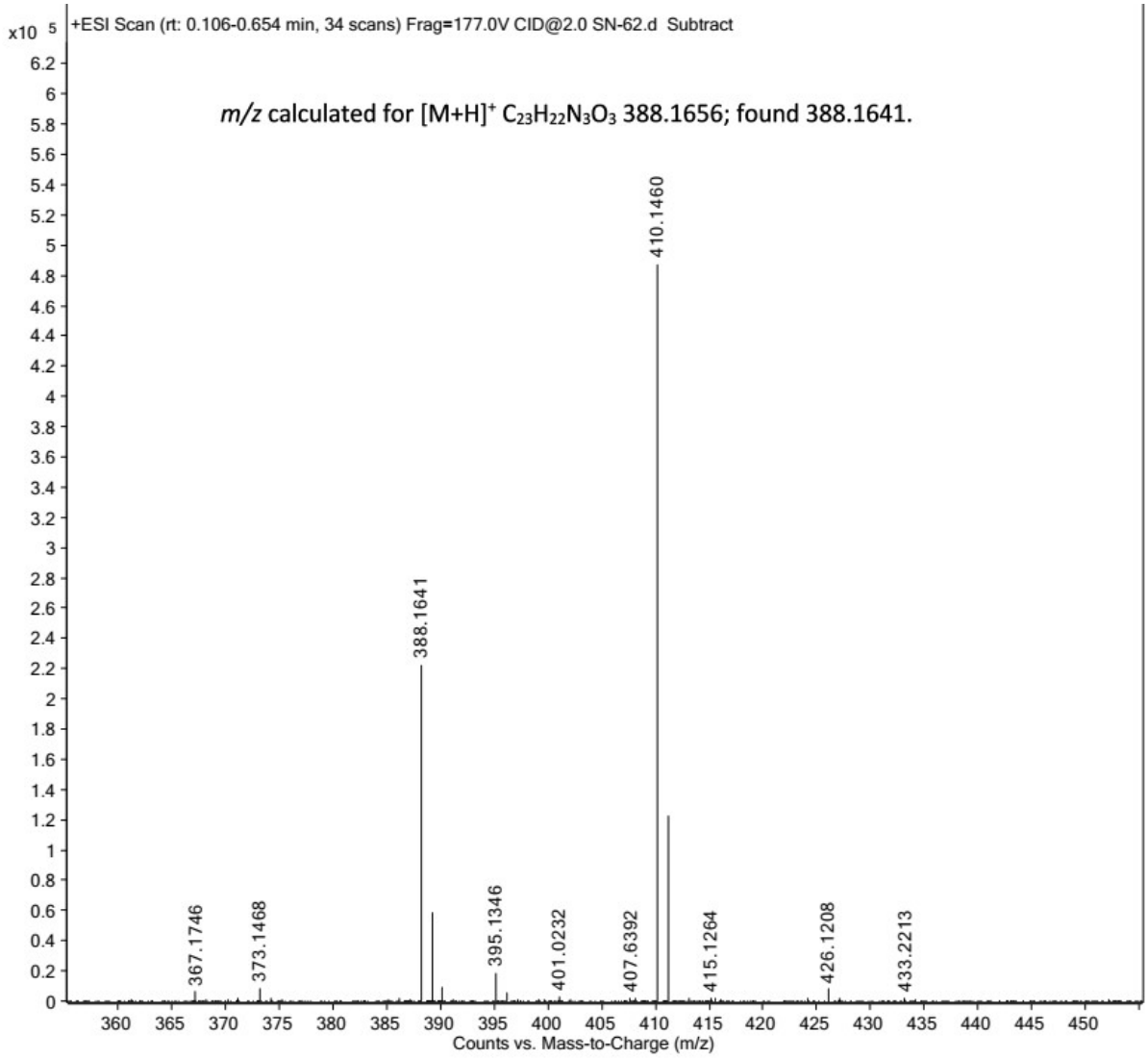
*N'-(2,4-dimethylphenyl)-3-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)propanehydrazide (**5p**)*



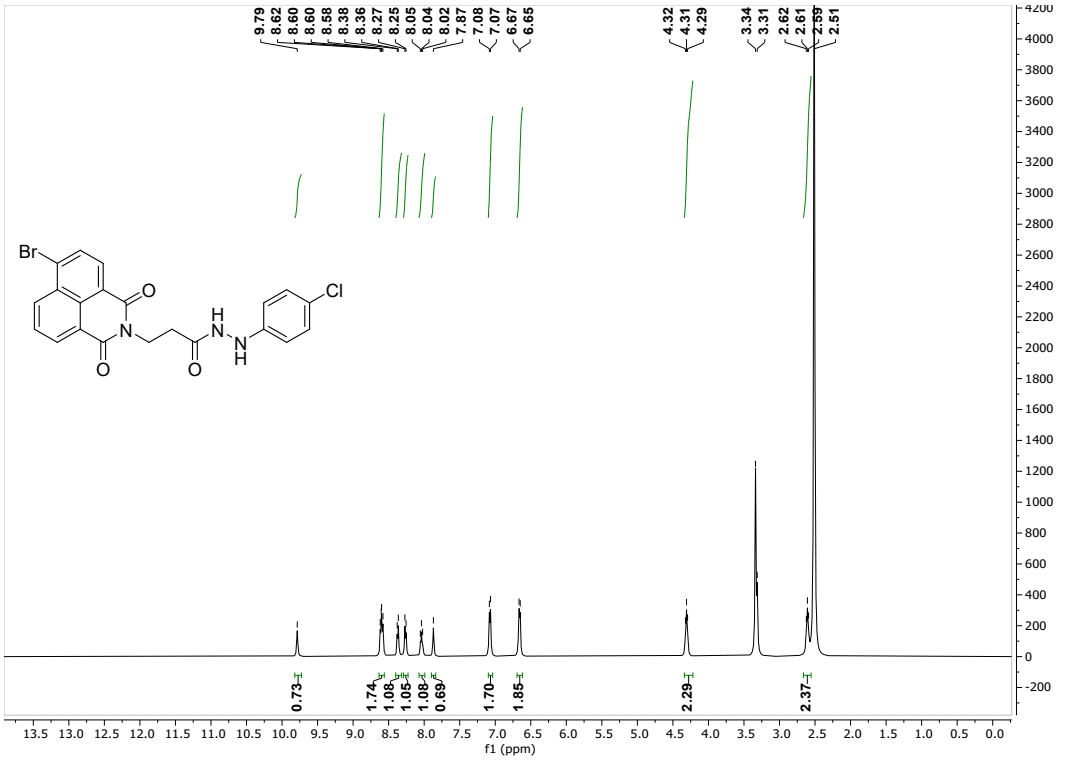
^{1}H NMR spectrum of compound **5p**, DMSO-d_6, 500MHz



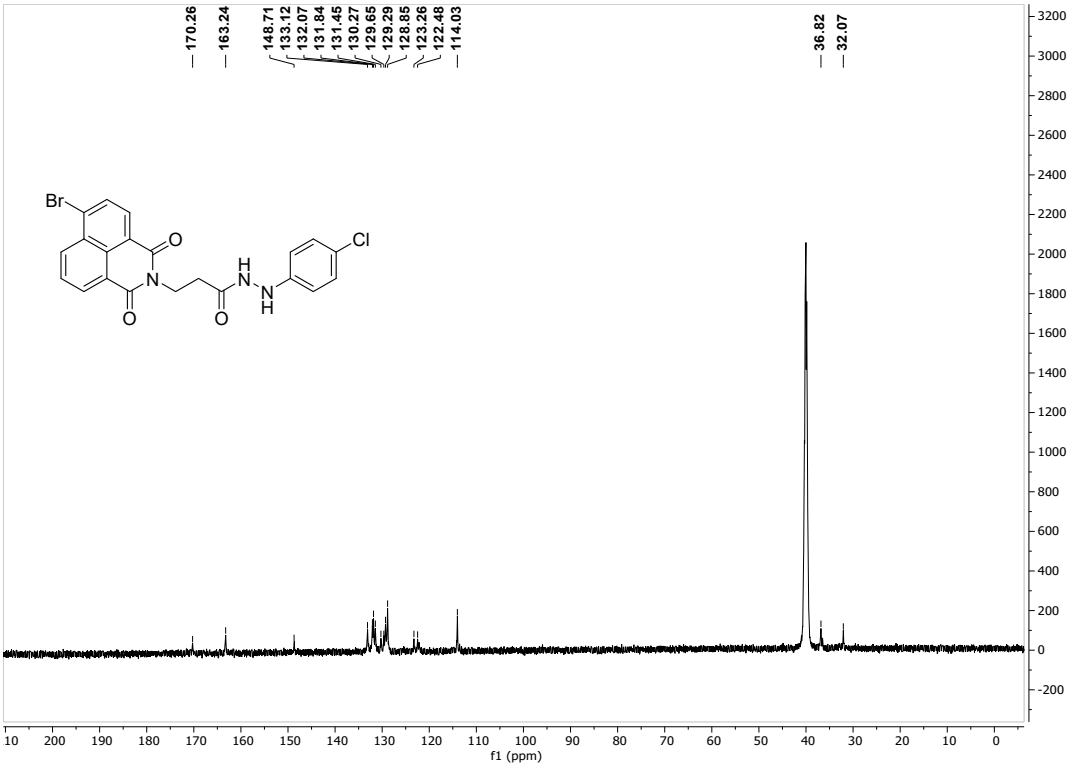
^{13}C NMR spectrum of compound **5p**, DMSO-d_6, 125MHz



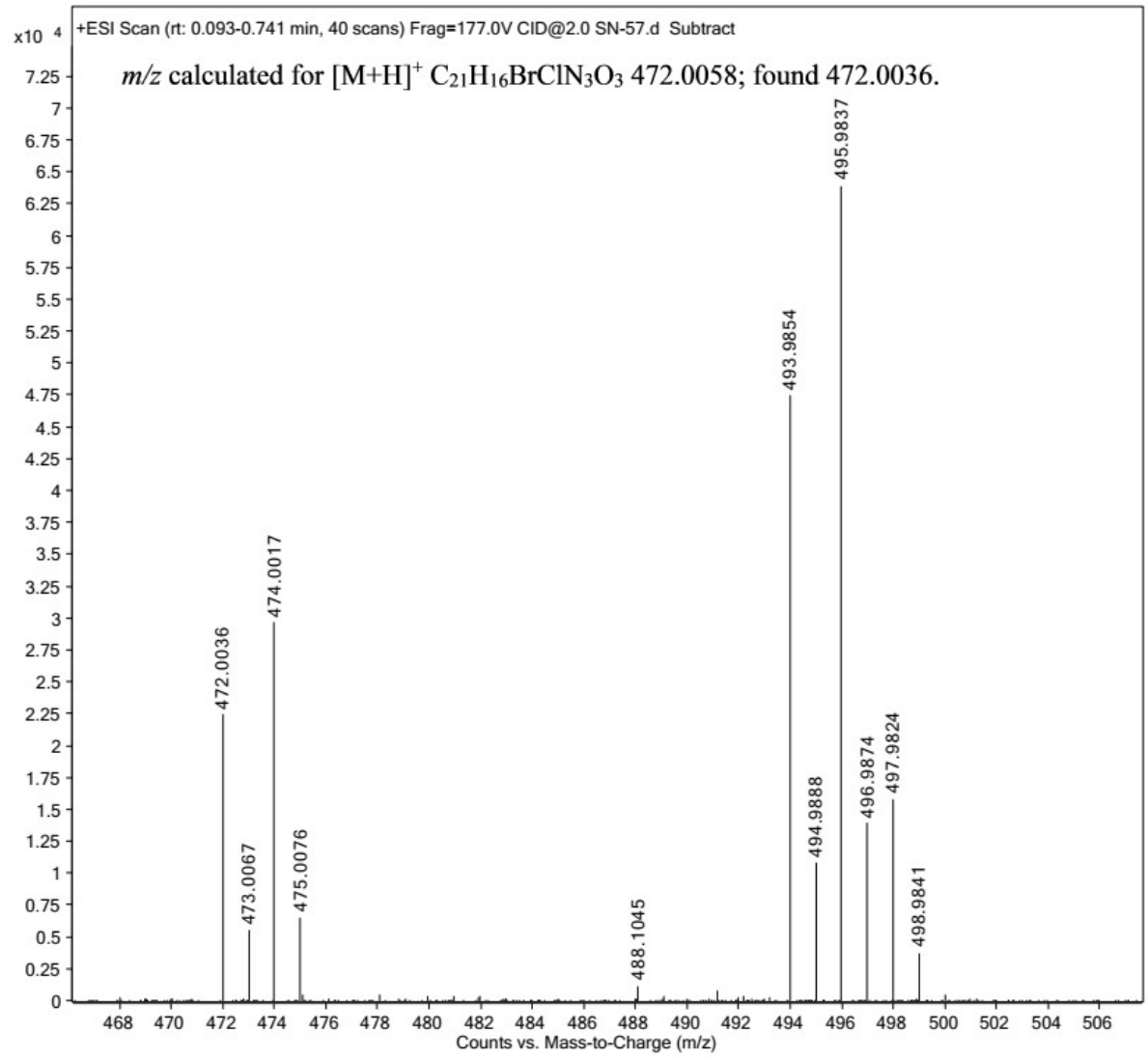
3-(6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-chlorophenyl)propanehydrazide ***(5q)***



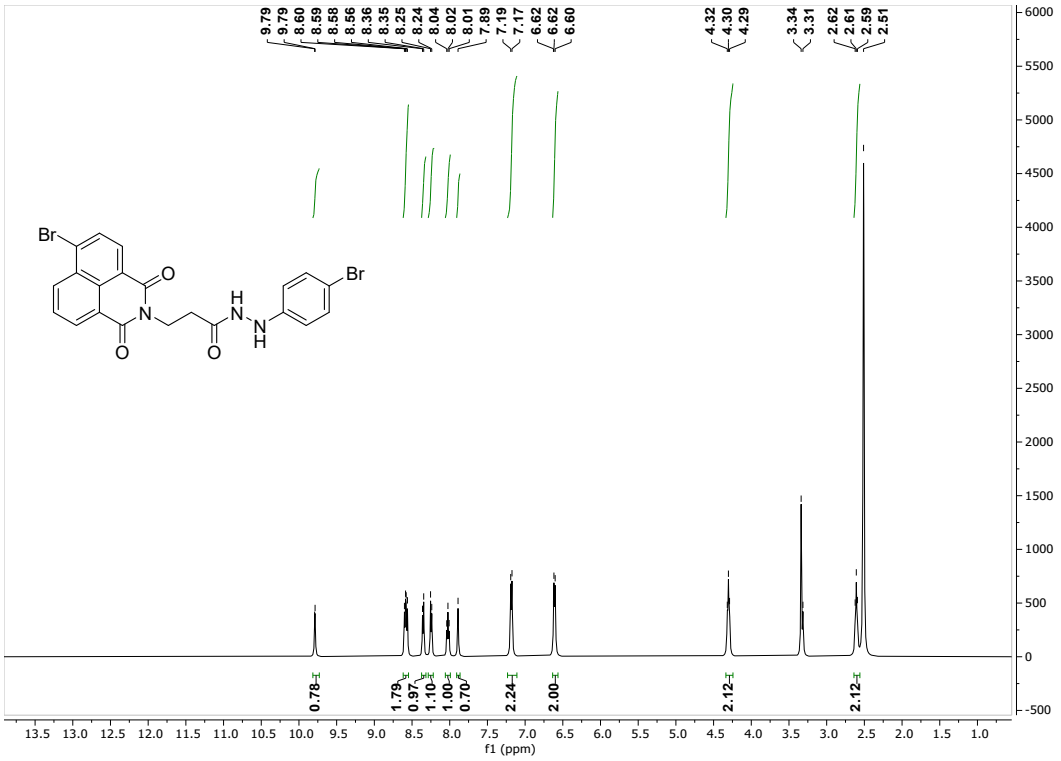
^{1}H NMR spectrum of compound **5q**, DMSO-d_6, 500MHz



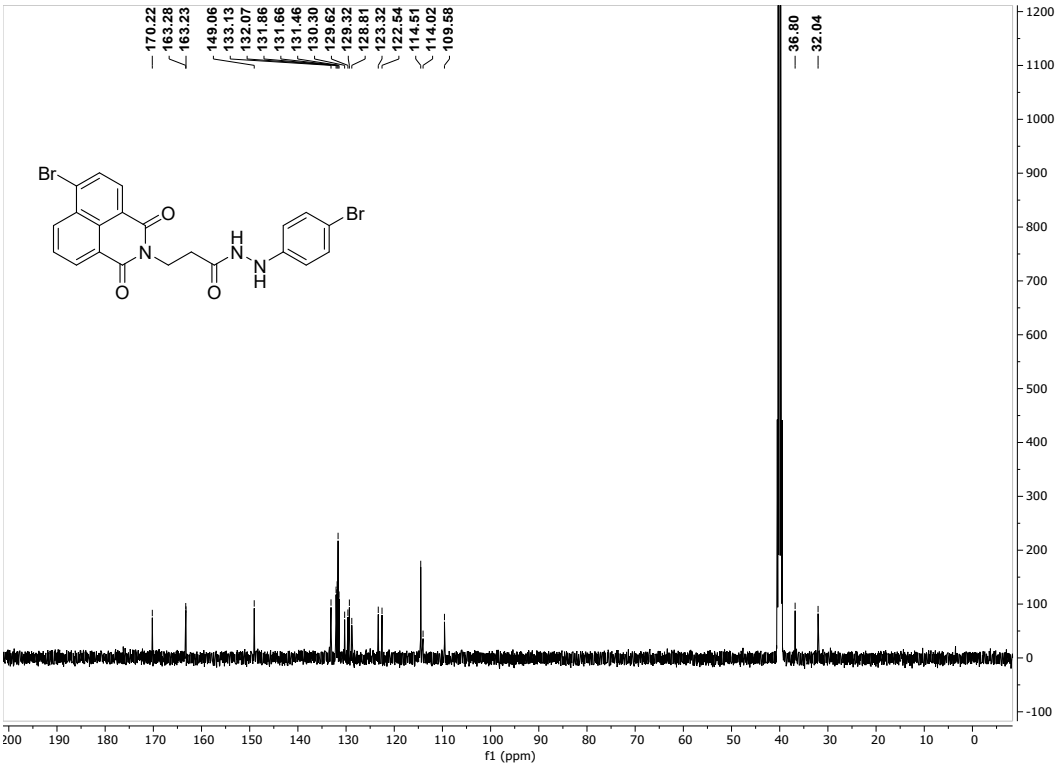
^{13}C NMR spectrum of compound **5s**, DMSO-d_6, 125MHz



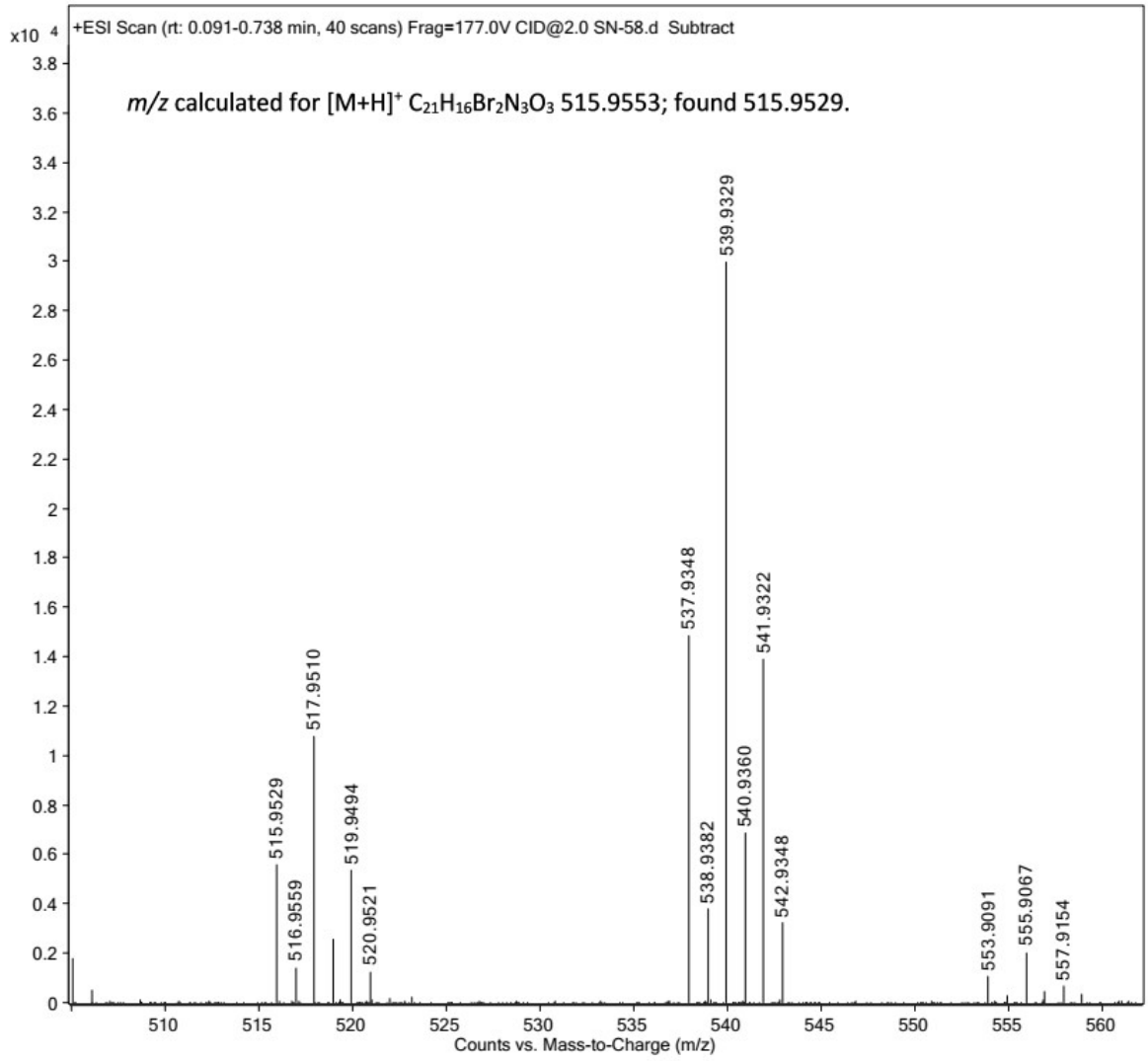
*3-(6-bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-(4-bromophenyl)propanehydrazide (**5r**)*

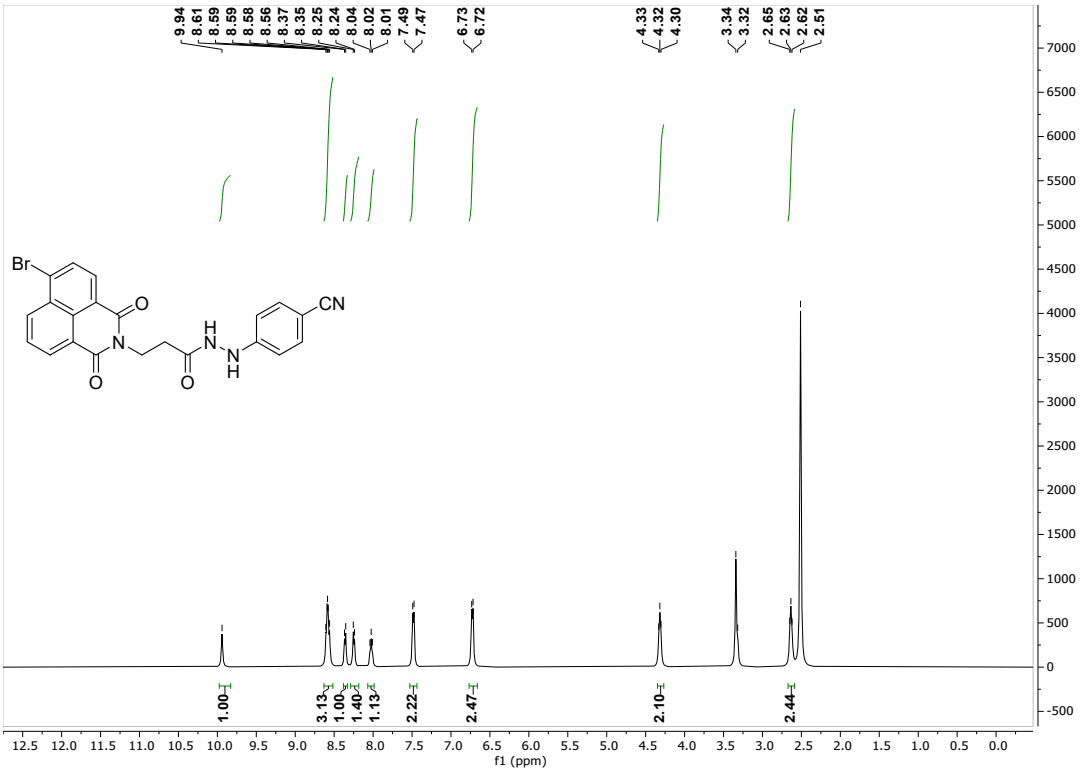


^{1}H NMR spectrum of compound **5r**, DMSO-d_6, 500MHz

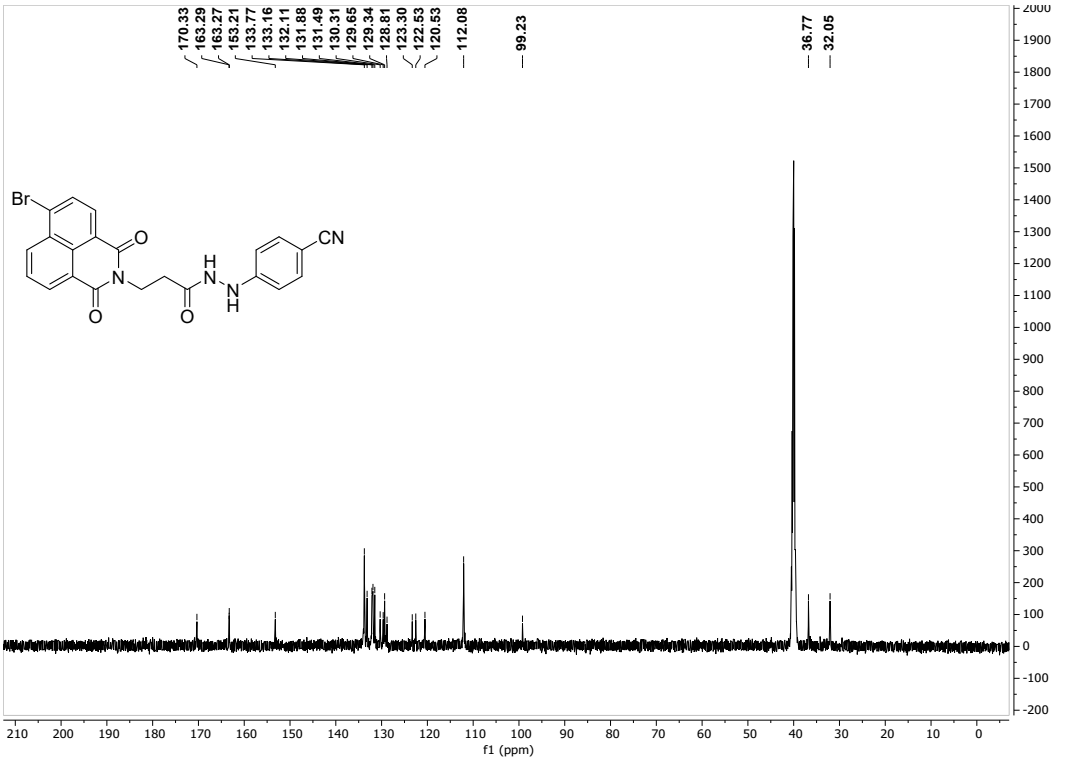


^{13}C NMR spectrum of compound **5r**, DMSO-d_6, 125MHz

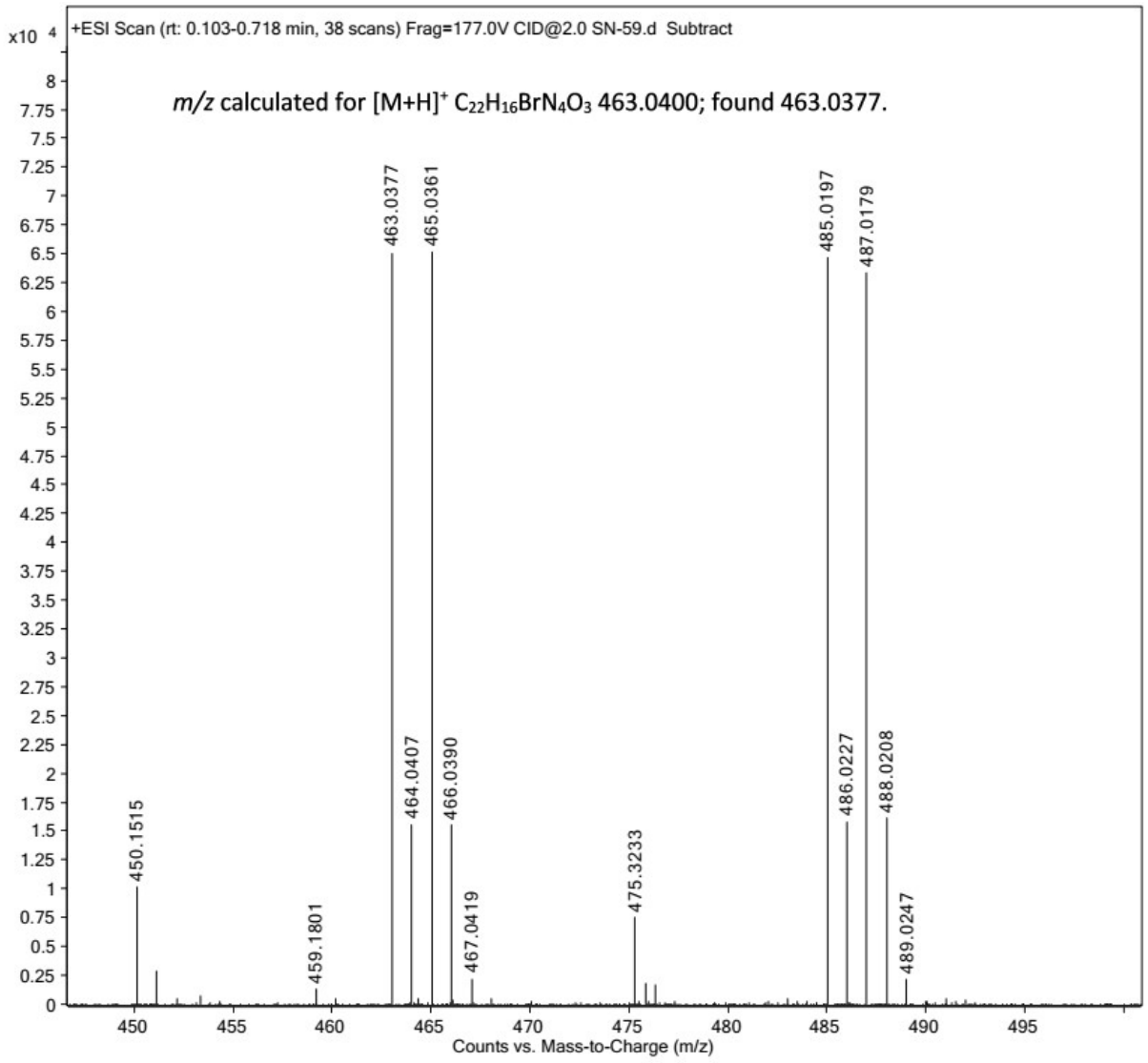

+ESI Scan (rt: 0.091-0.738 min, 40 scans) Frag=177.0V CID@2.0 SN-58.d Subtract
x10 4
m/z calculated for [M+H]+ C21H16Br2N3O3 515.9553; found 515.9529.
539.9329
537.9348
541.9322
517.9510
515.9529
519.9494
540.9360
538.9382
542.9348
516.9559
520.9521
553.9091
555.9067
557.9154
Counts vs. Mass-to-Charge (m/z)

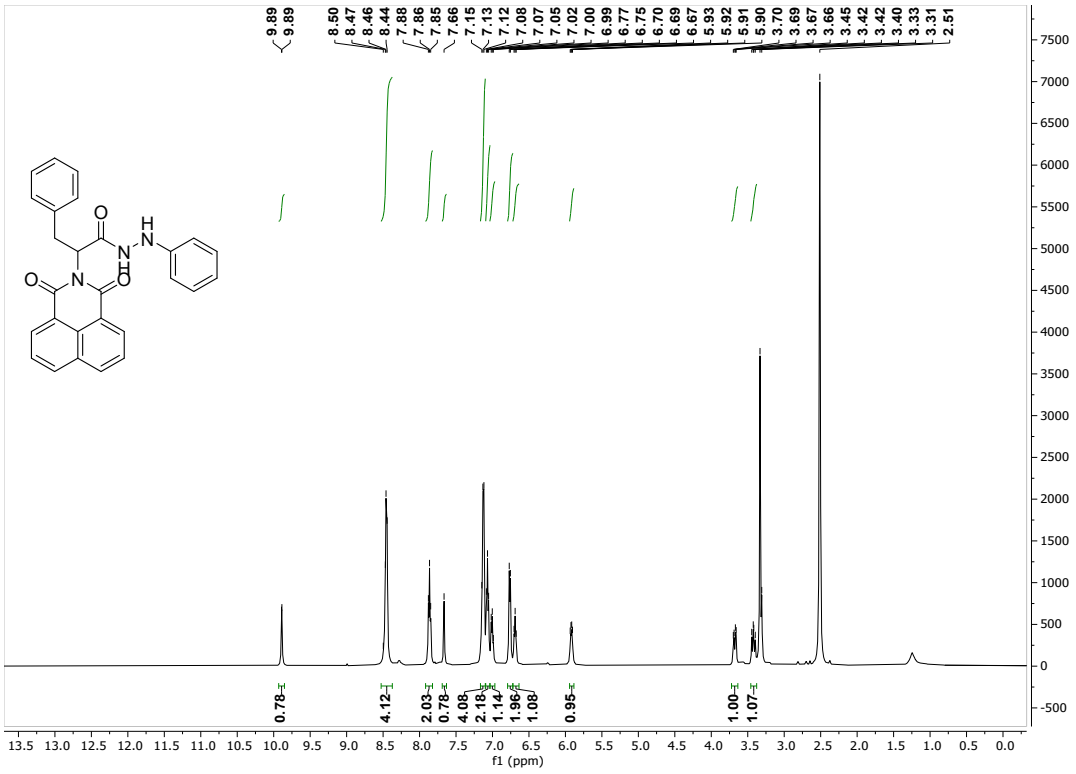


^{1}H NMR spectrum of compound **5s**, DMSO-d_6, 500MHz

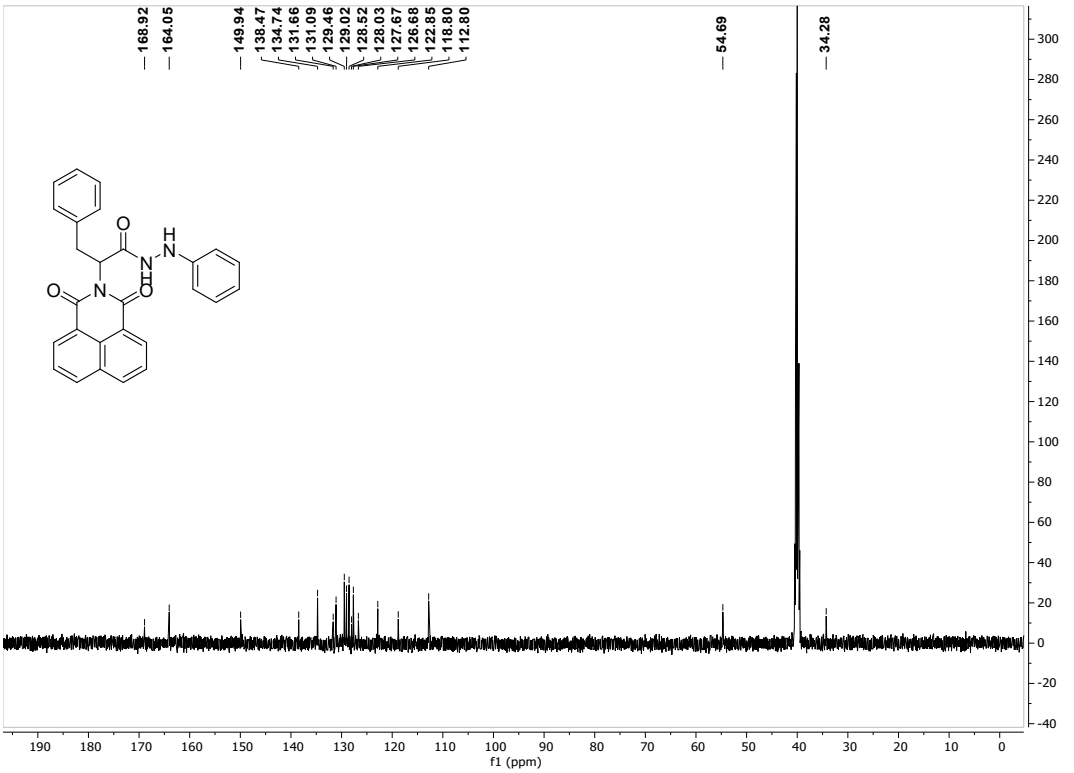


^{13}C NMR spectrum of compound **5s**, DMSO-d_6, 125MHz

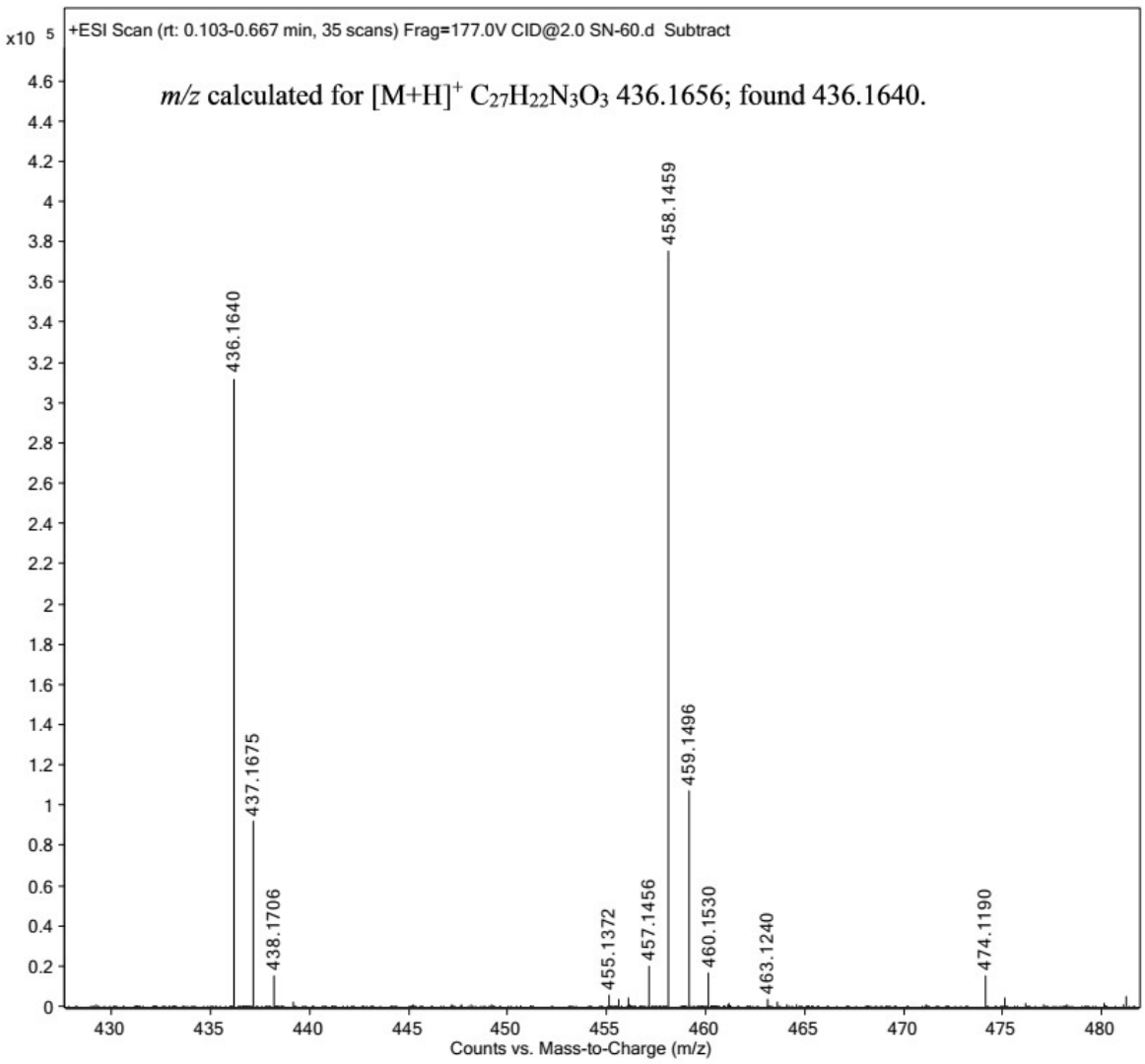

+ESI Scan (rt: 0.103-0.718 min, 38 scans) Frag=177.0V CID@2.0 SN-59.d Subtract
x10 4
m/z calculated for [M+H]+ C22H16BrN4O3 463.0400; found 463.0377.
463.0377
465.0361
485.0197
487.0179
450.1515
459.1801
464.0407
466.0390
467.0419
475.3233
486.0227
488.0208
489.0247
Counts vs. Mass-to-Charge (m/z)



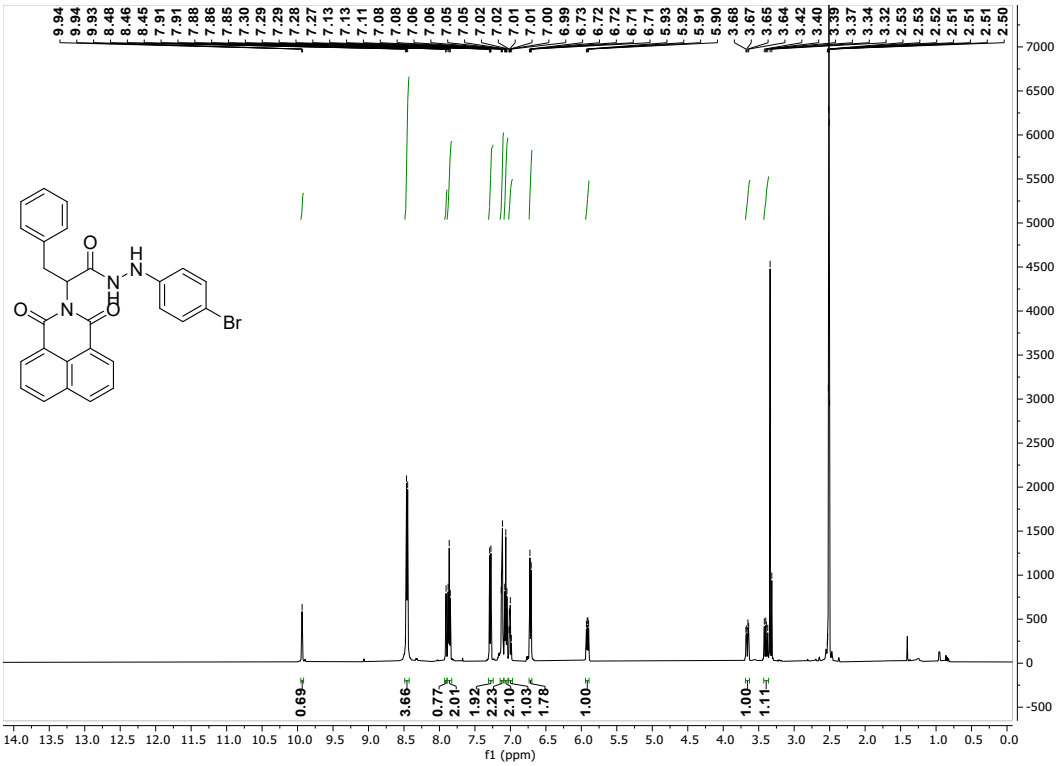
^{1}H NMR spectrum of compound **8a**, DMSO-d_6, 500MHz



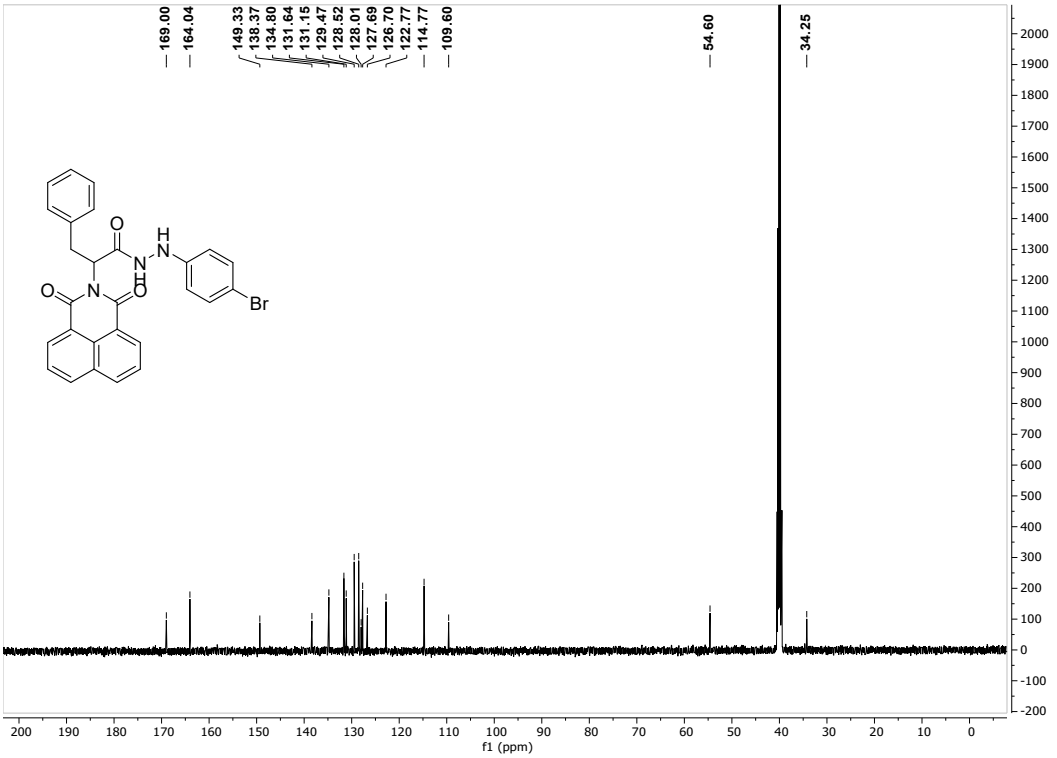
^{13}C NMR spectrum of compound **8a**, DMSO-d_6, 125MHz



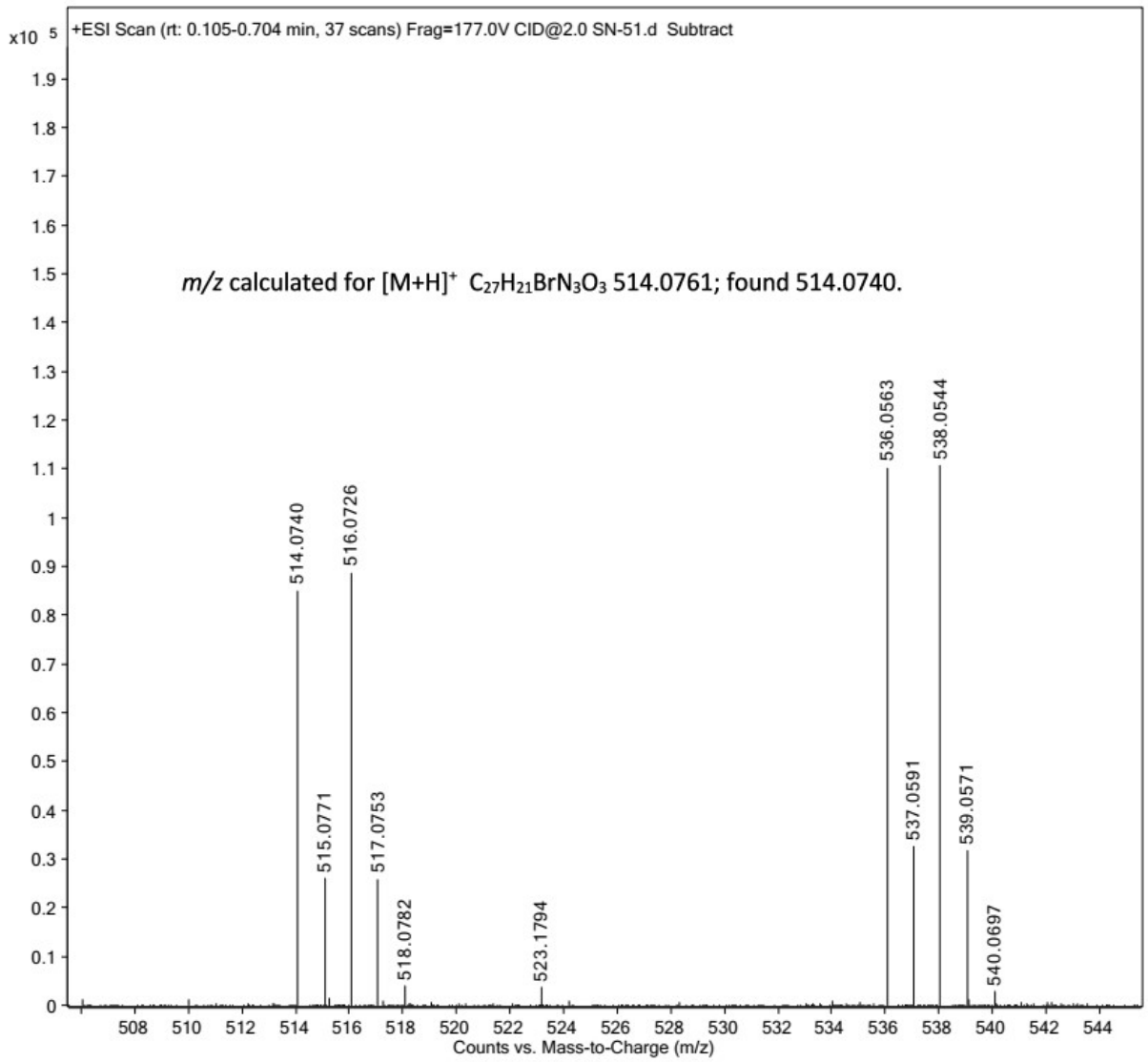
N'-(4-bromophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide ***(8b)***



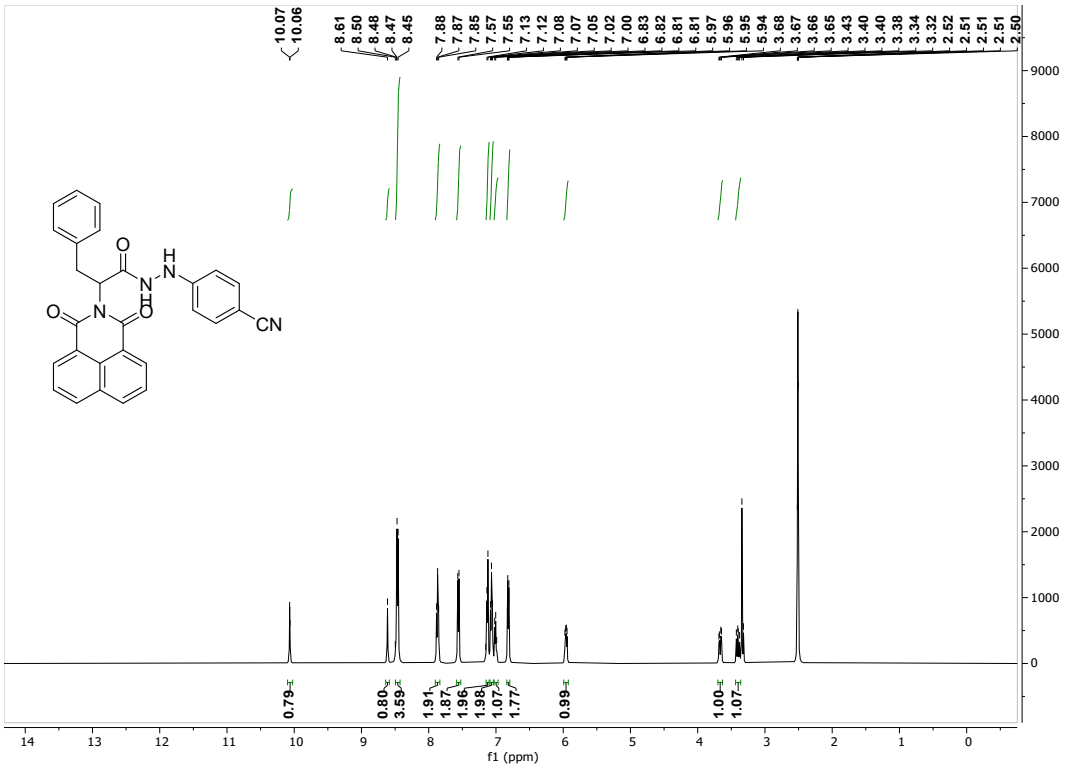
^{1}H NMR spectrum of compound **8b**, DMSO-d_6, 500MHz



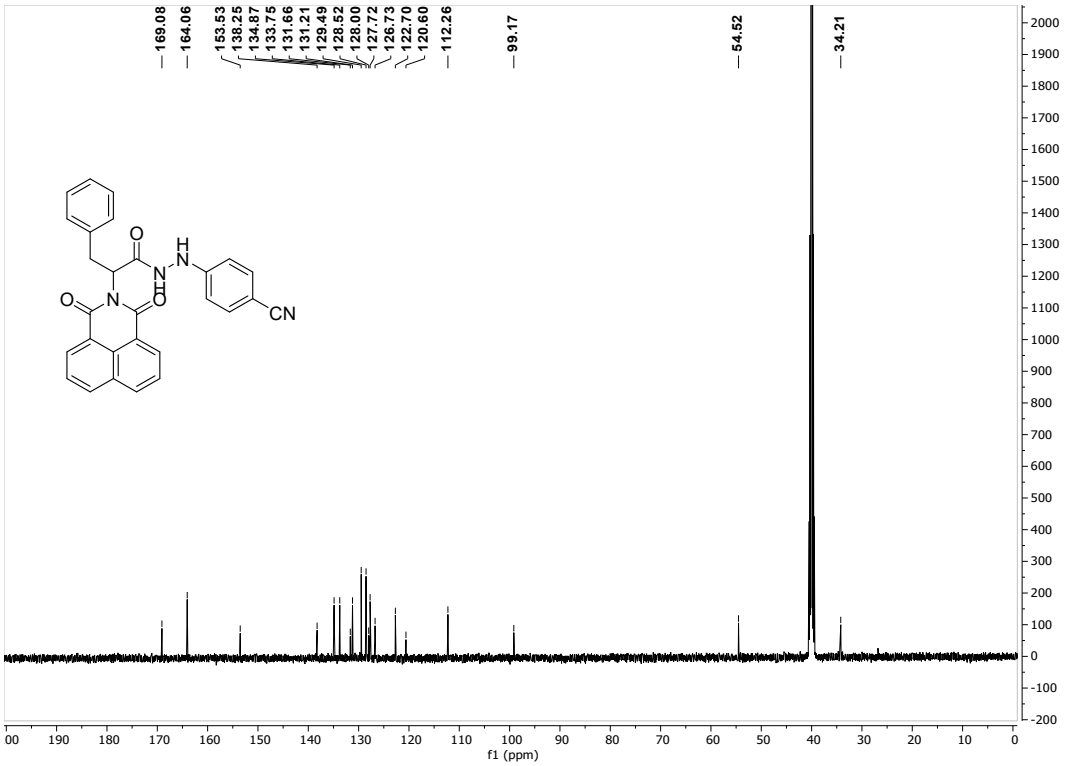
^{13}C NMR spectrum of compound **8b**, DMSO-d_6, 125MHz



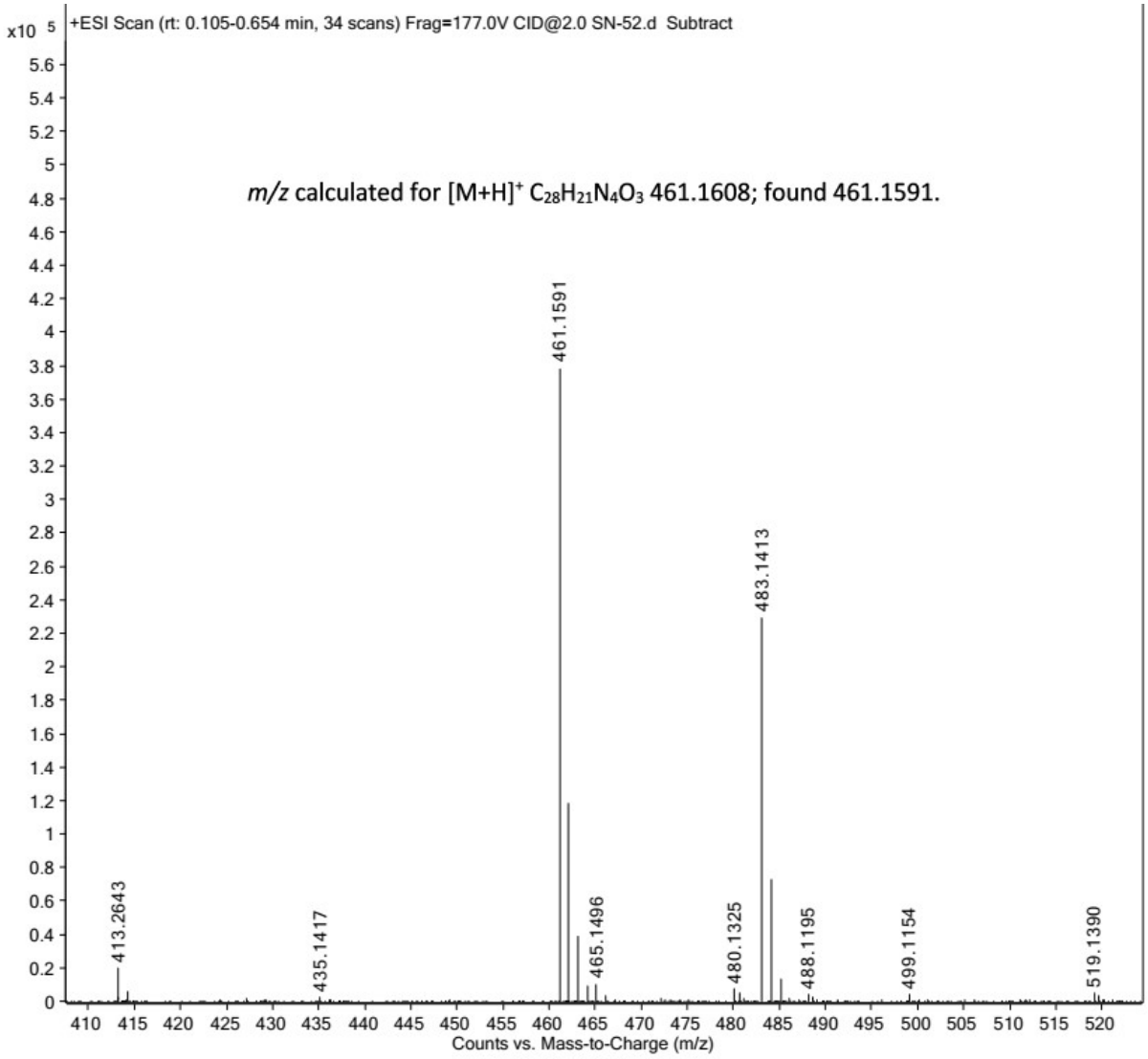
N'-(4-cyanophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide ***(8c)***



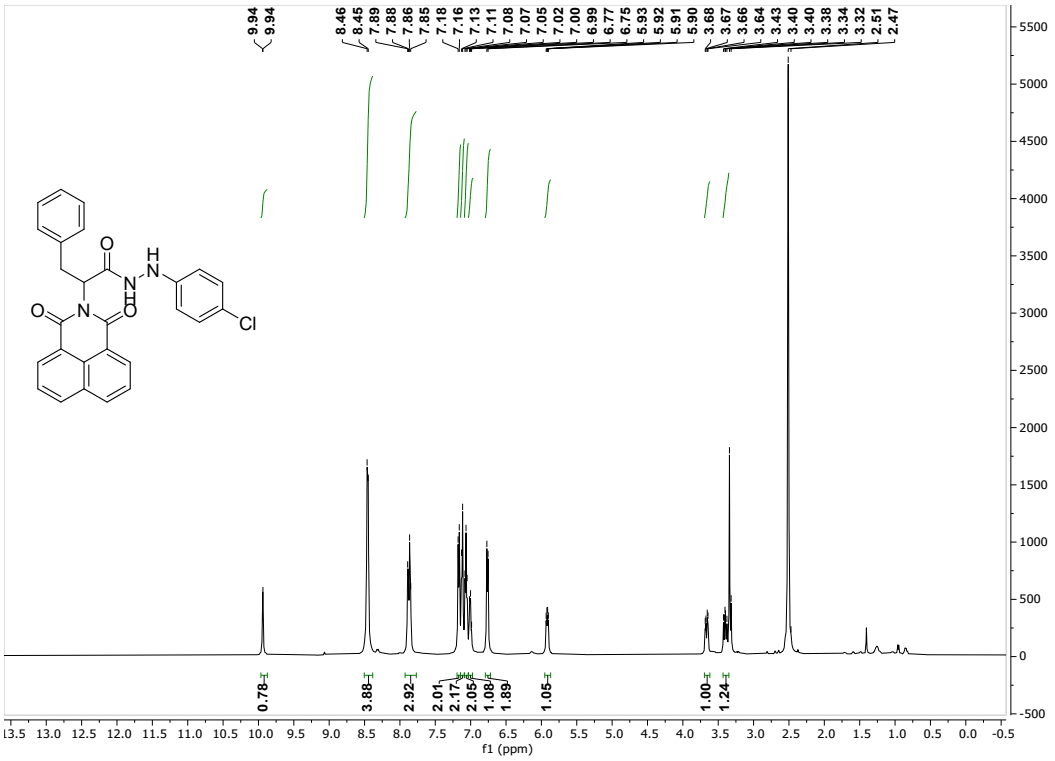
^{1}H NMR spectrum of compound **8c**, DMSO-d_6, 500MHz



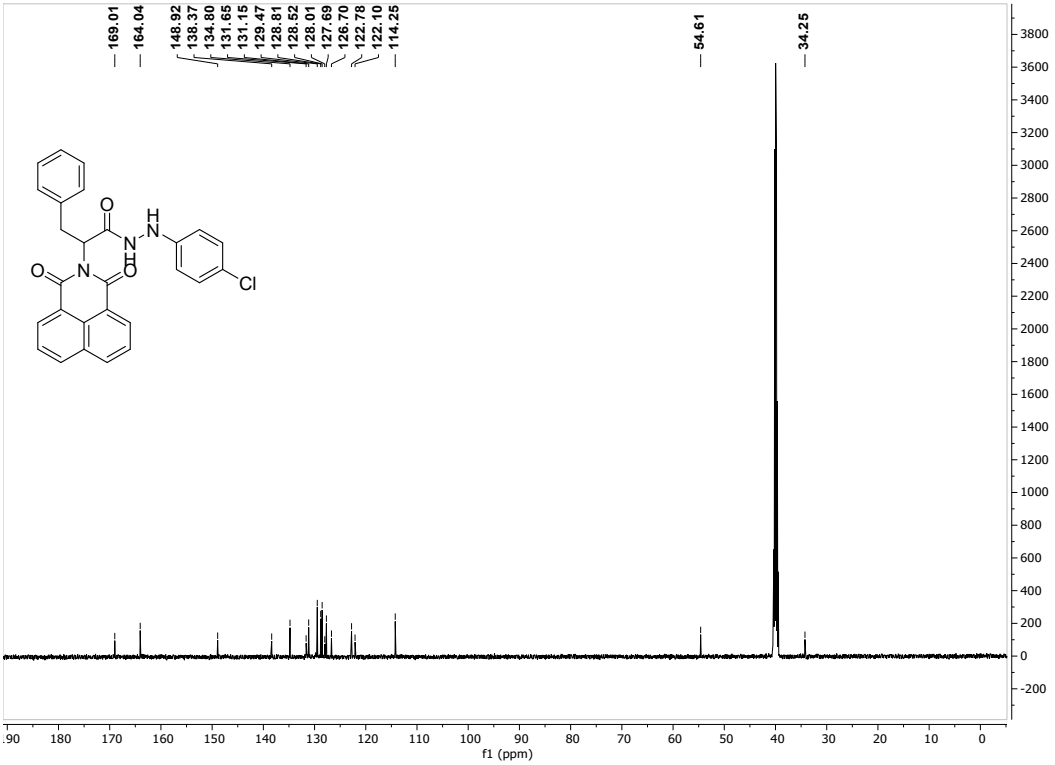
^{13}C NMR spectrum of compound **8c**, DMSO-d_6, 125MHz



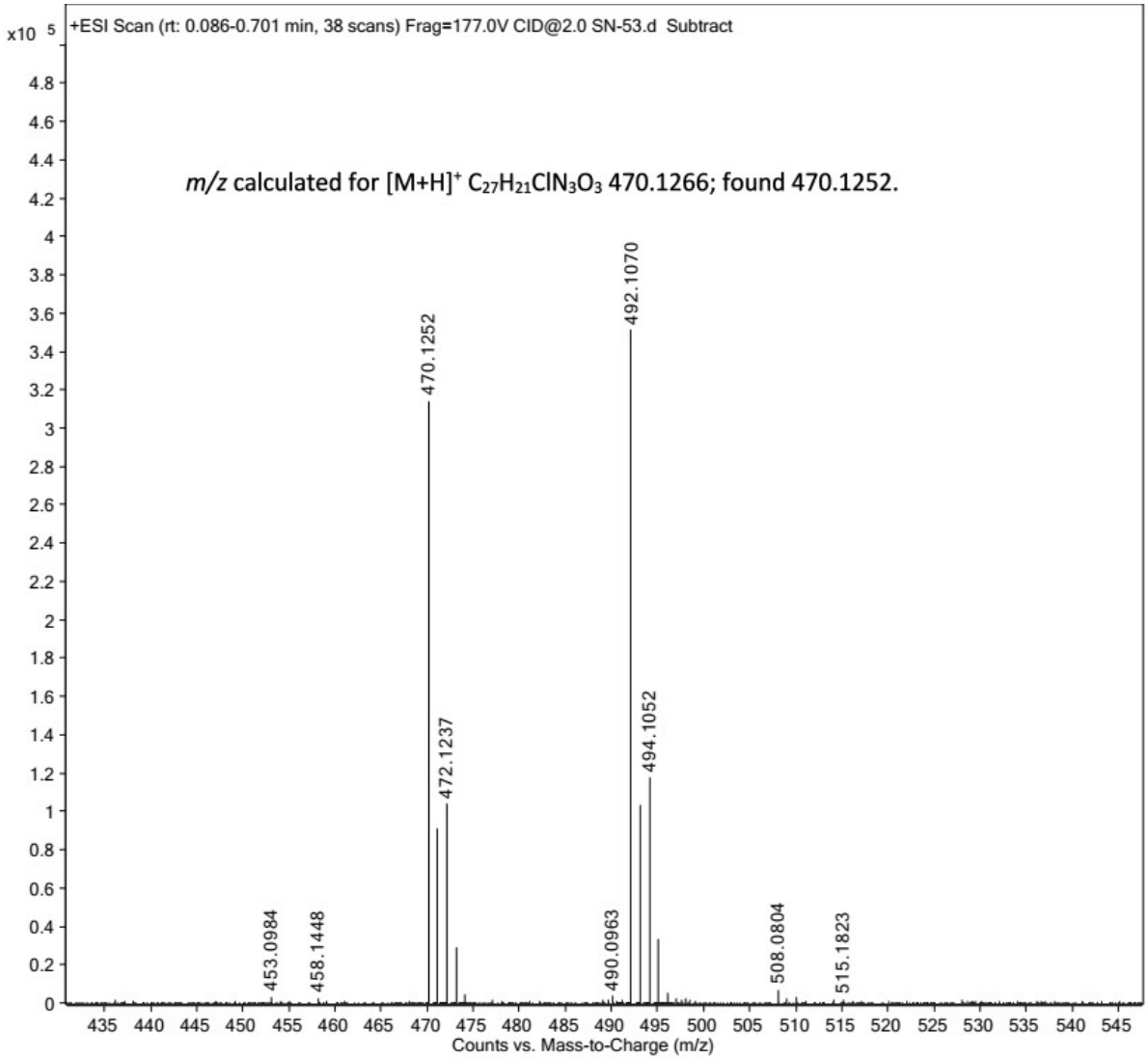
N'-(4-chlorophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-3-phenylpropanehydrazide ***(8d)***



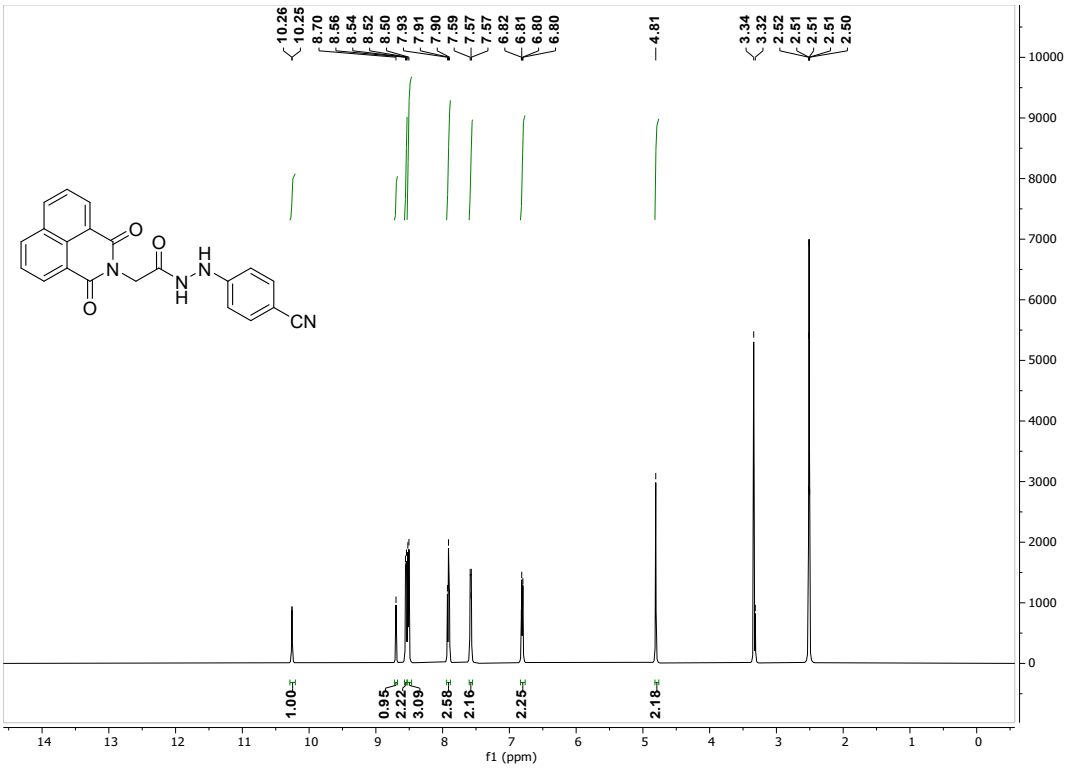
^{1}H NMR spectrum of compound **8d**, DMSO-d_6, 500MHz



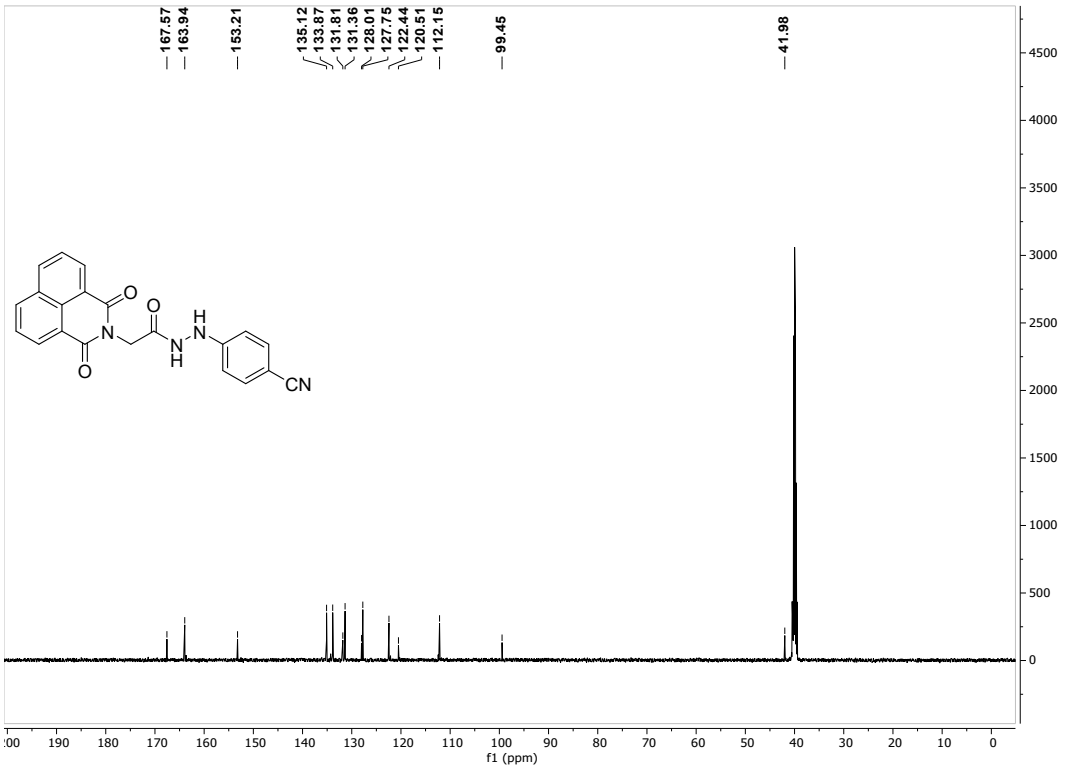
^{13}C NMR spectrum of compound **8d**, DMSO-d_6, 125MHz



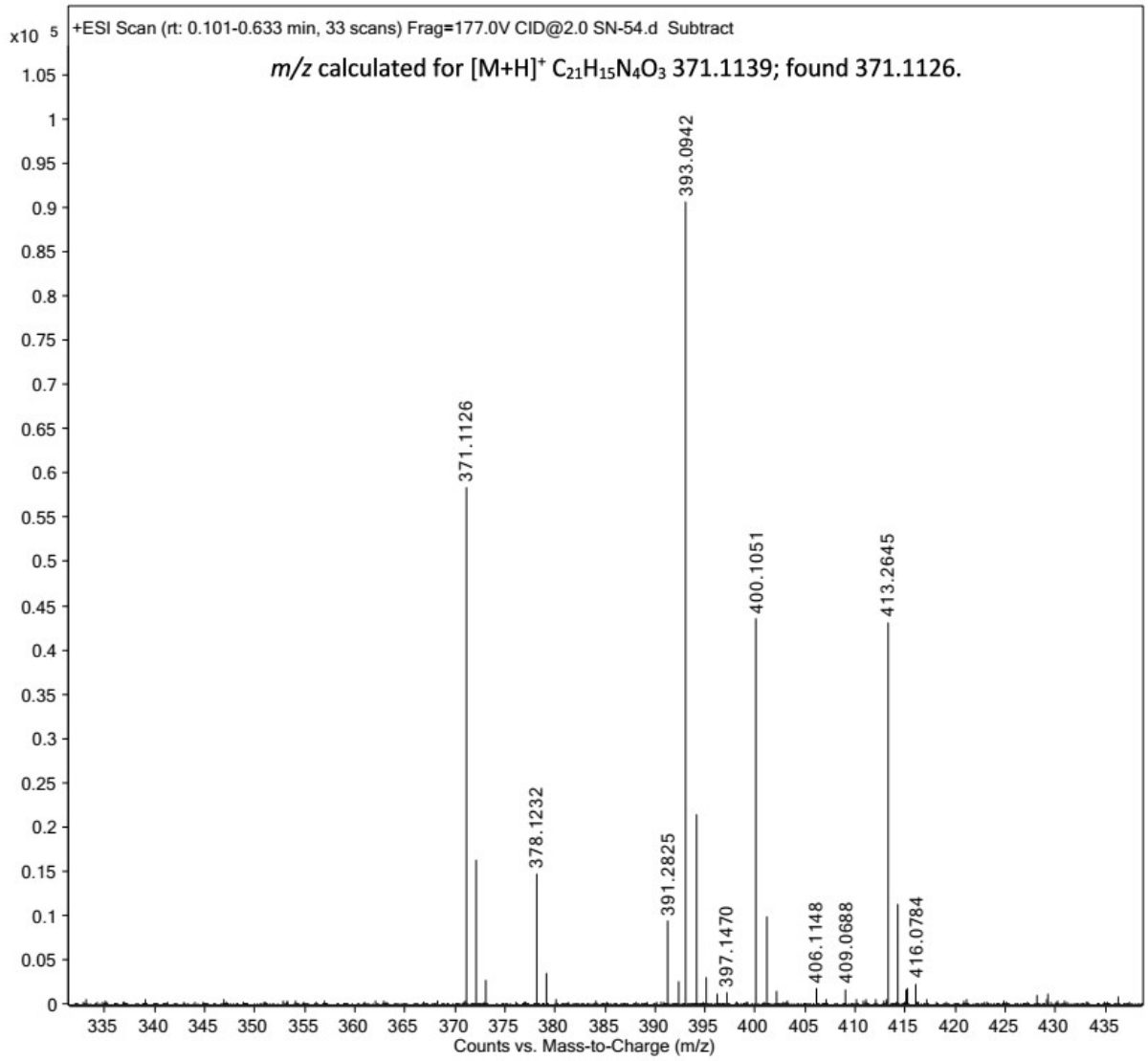
*N'-(4-cyanophenyl)-2-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)acetohydrazide (**11a**)*



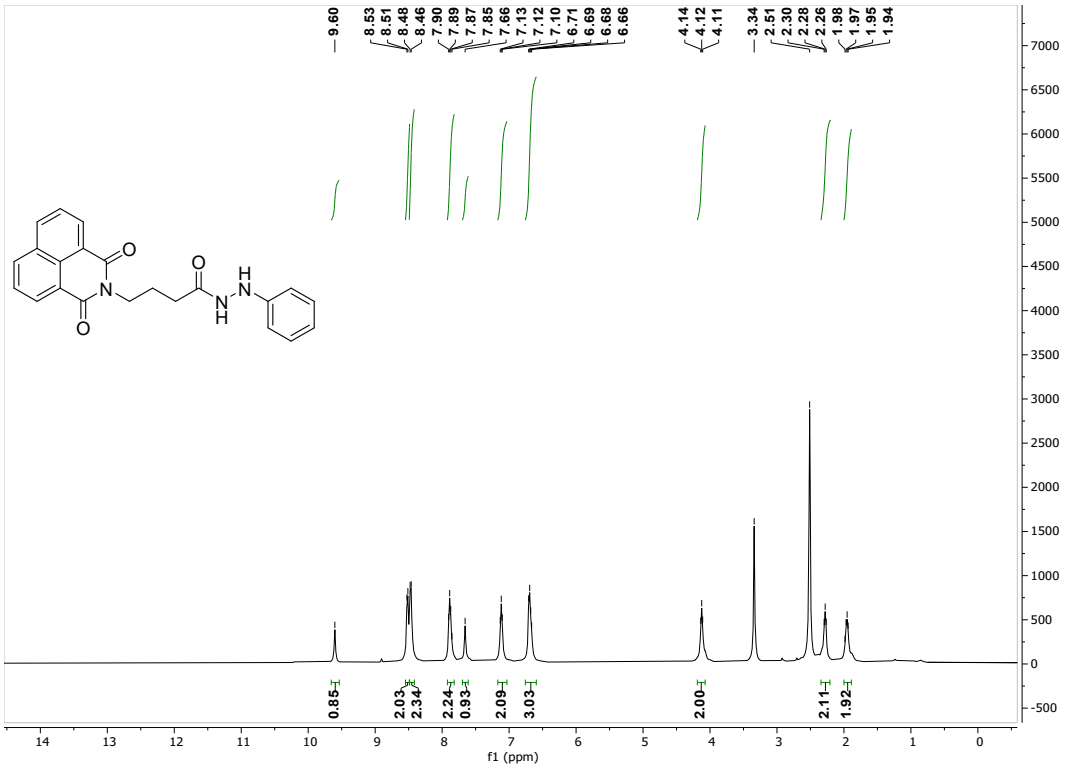
^{1}H NMR spectrum of compound **11a**, DMSO-d_6, 500MHz



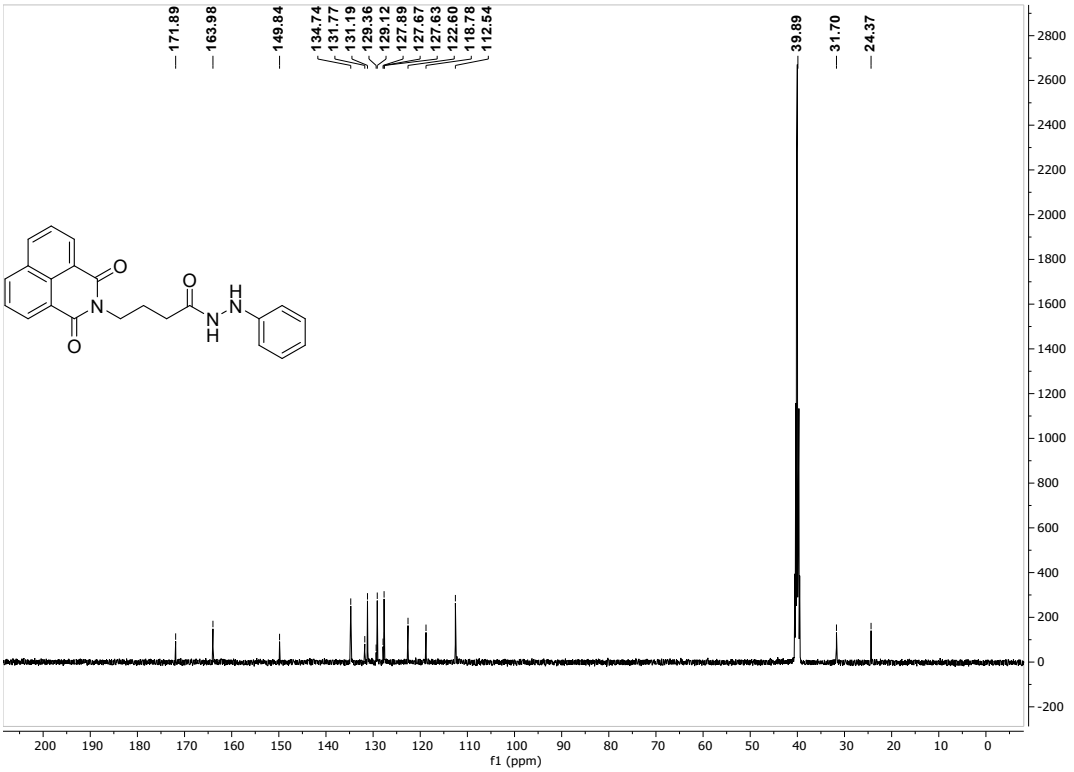
^{13}C NMR spectrum of compound **11a**, DMSO-d_6, 125MHz



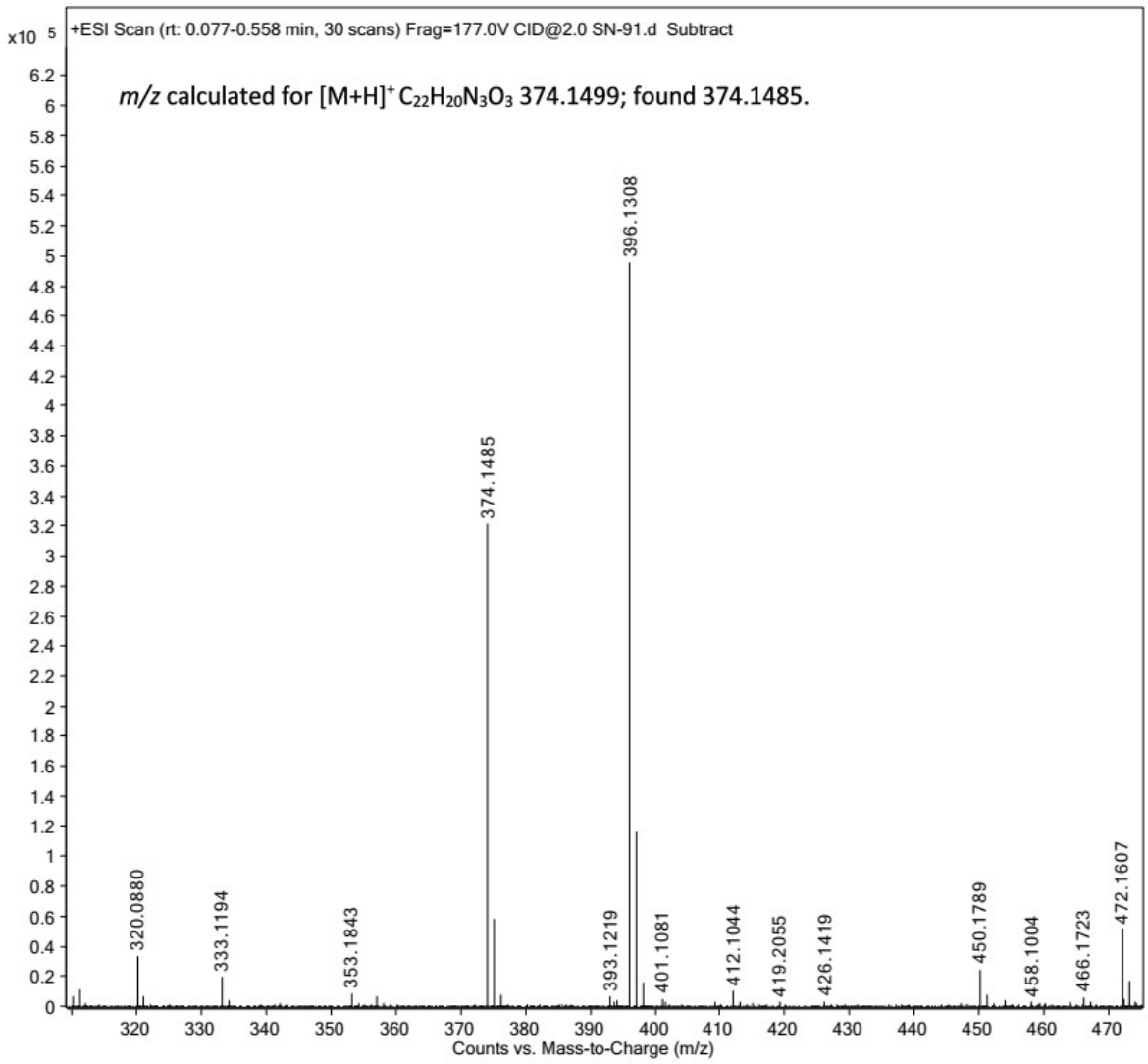
*4-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylbutanehydrazide (**11b**)*



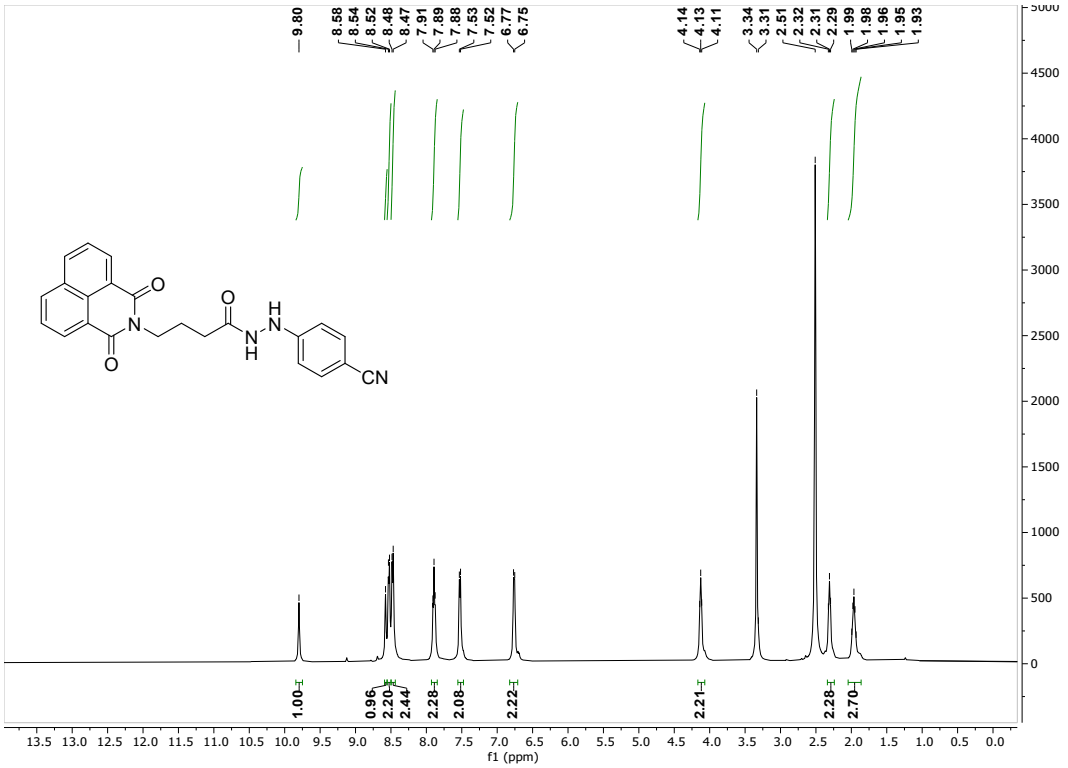
^{1}H NMR spectrum of compound **11b**, DMSO-d_6, 500MHz



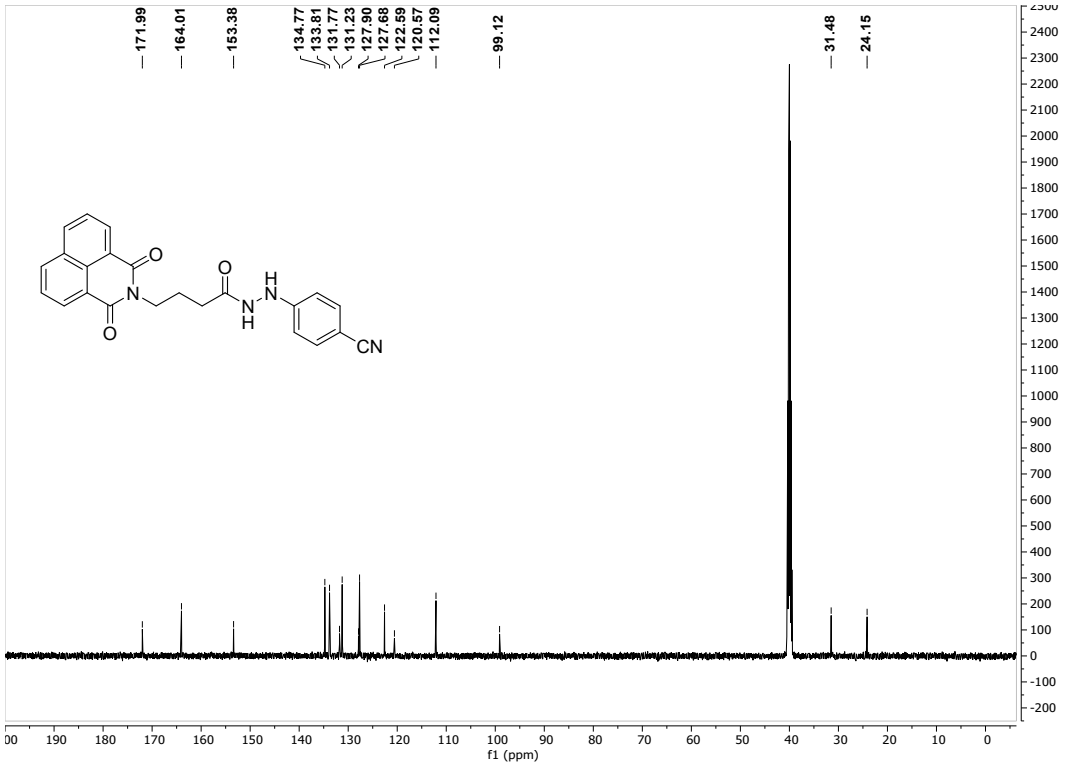
^{13}C NMR spectrum of compound **11b**, DMSO-d_6, 125MHz



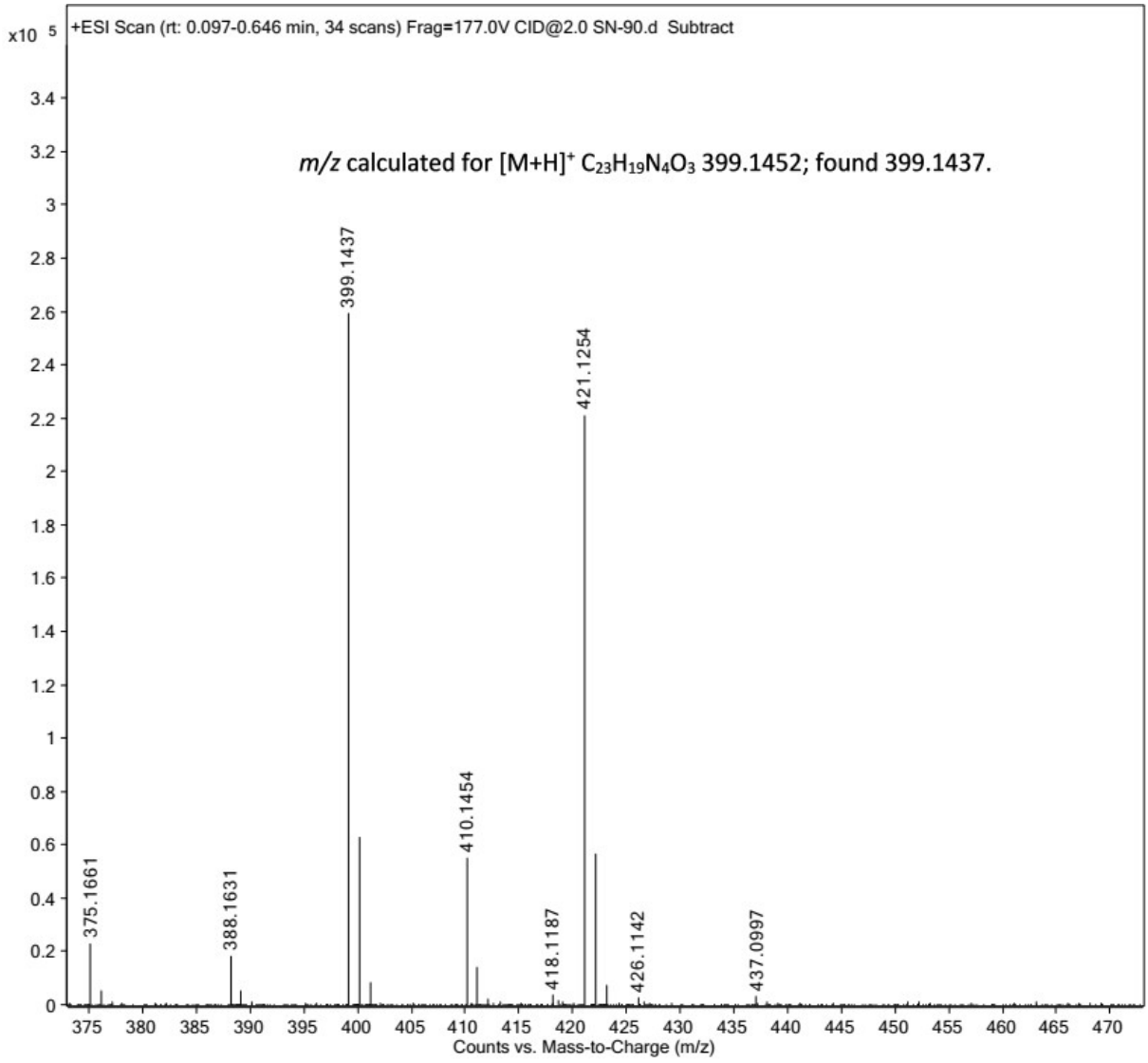
*N'-(4-cyanophenyl)-4-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)butanehydrazide (**11c**)*



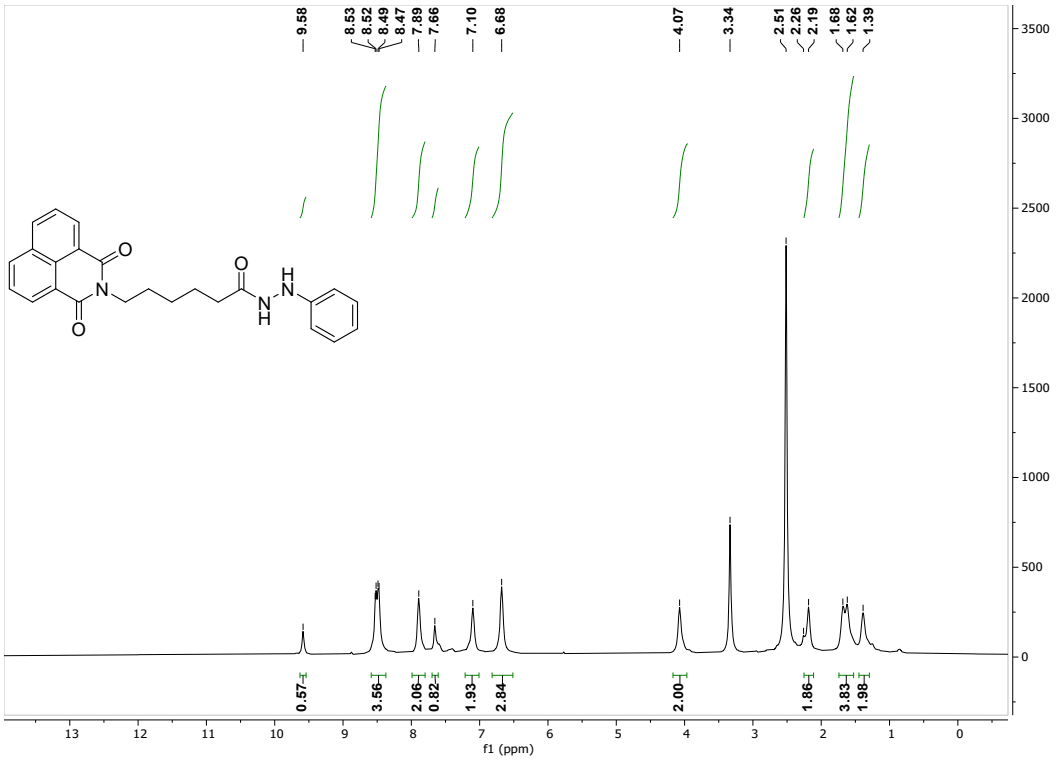
^{1}H NMR spectrum of compound **11c**, DMSO-d_6, 500MHz



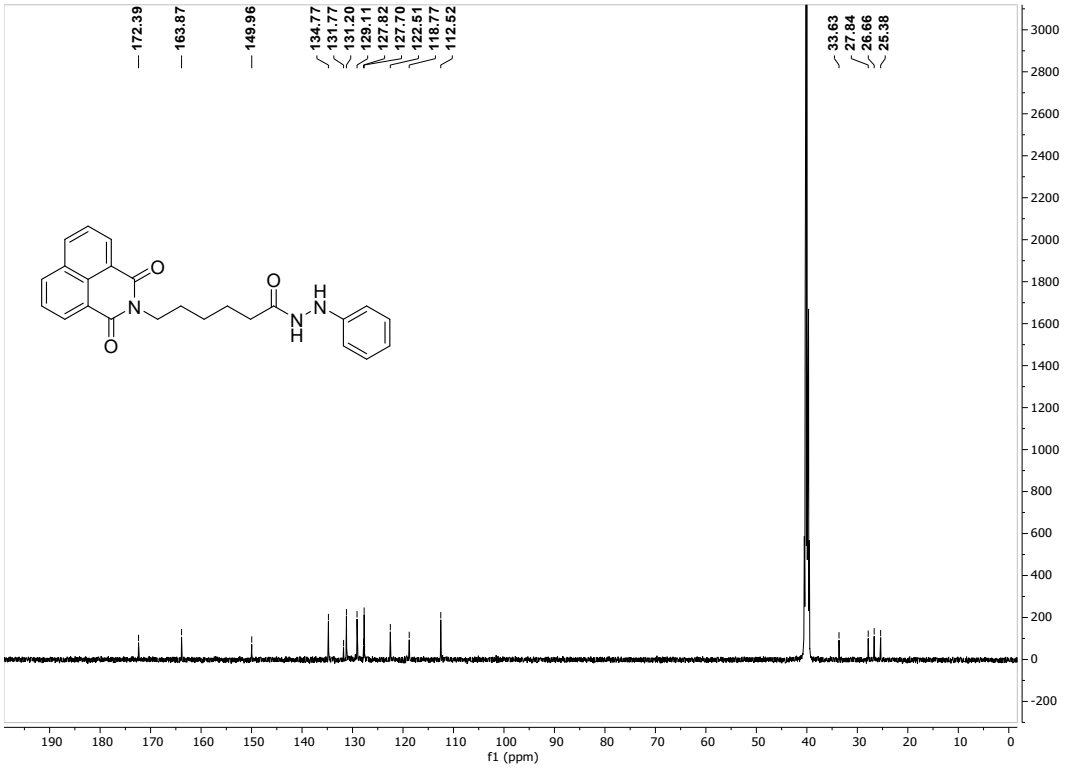
^{13}C NMR spectrum of compound **11c**, DMSO-d_6, 125MHz



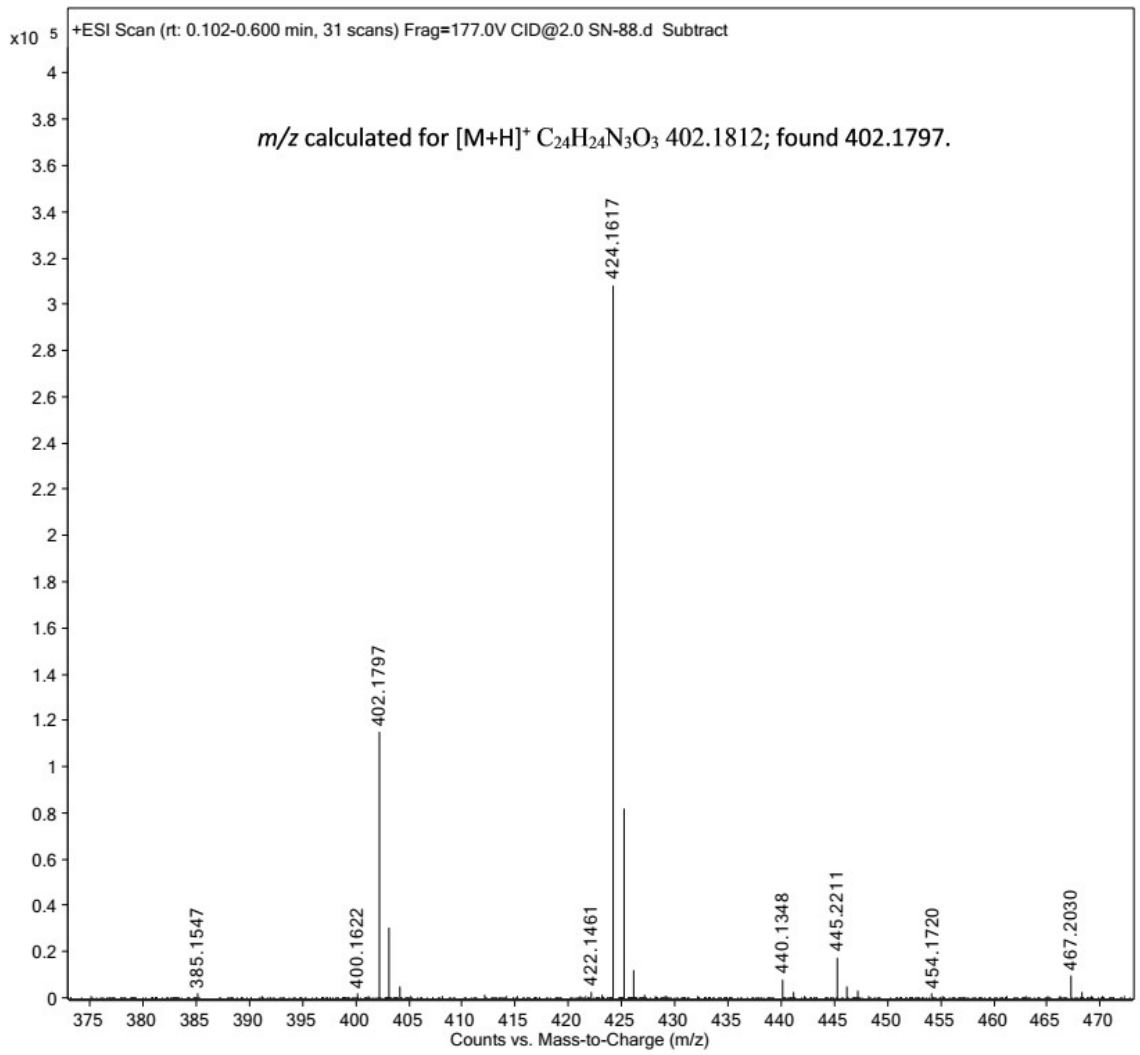
*6-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)-N'-phenylhexanehydrazide (**11d**)*



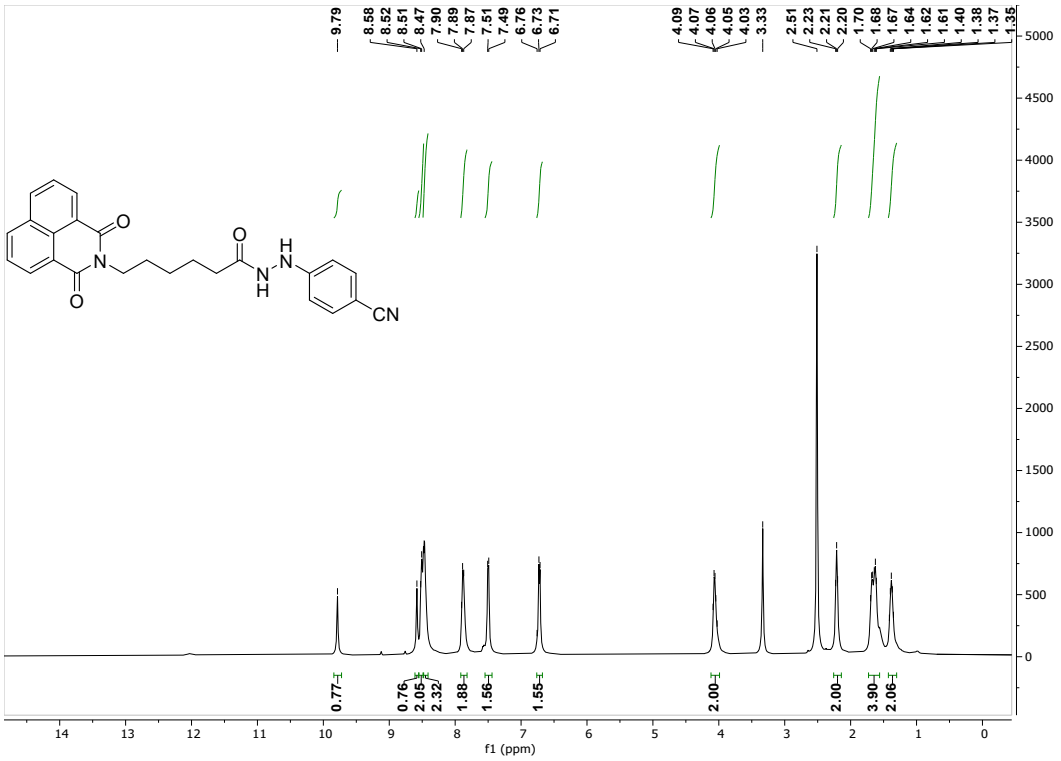
^{1}H NMR spectrum of compound **11d**, DMSO-d_6, 500MHz



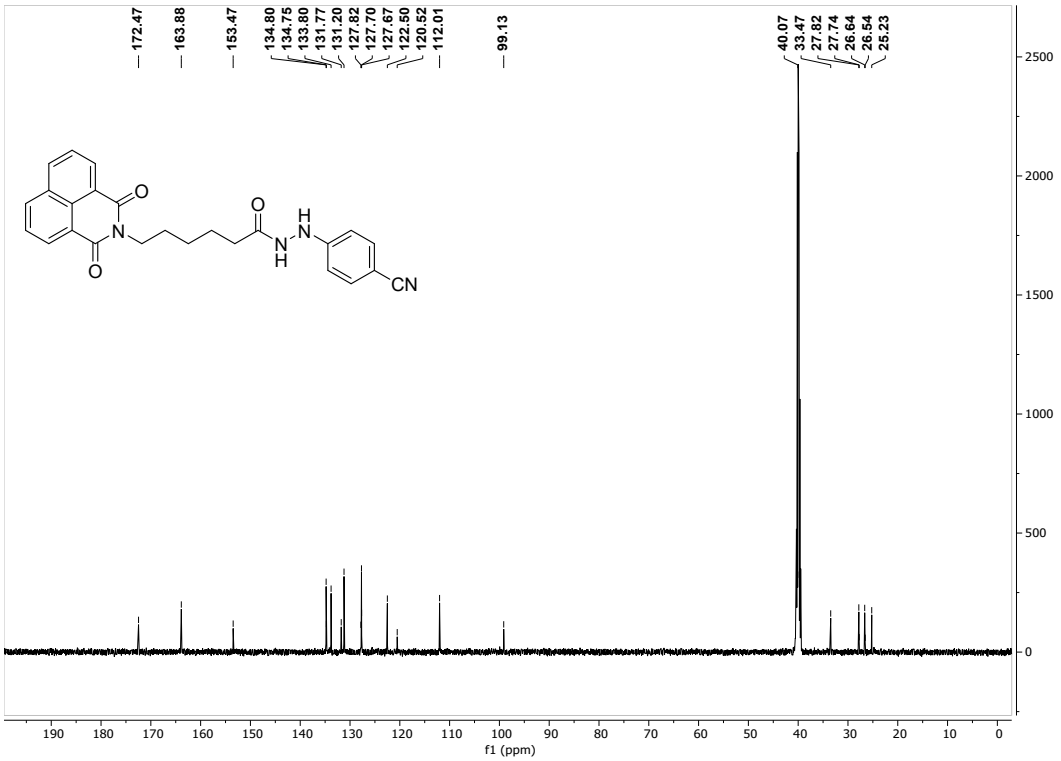
^{13}C NMR spectrum of compound **11d**, DMSO-d_6, 125MHz



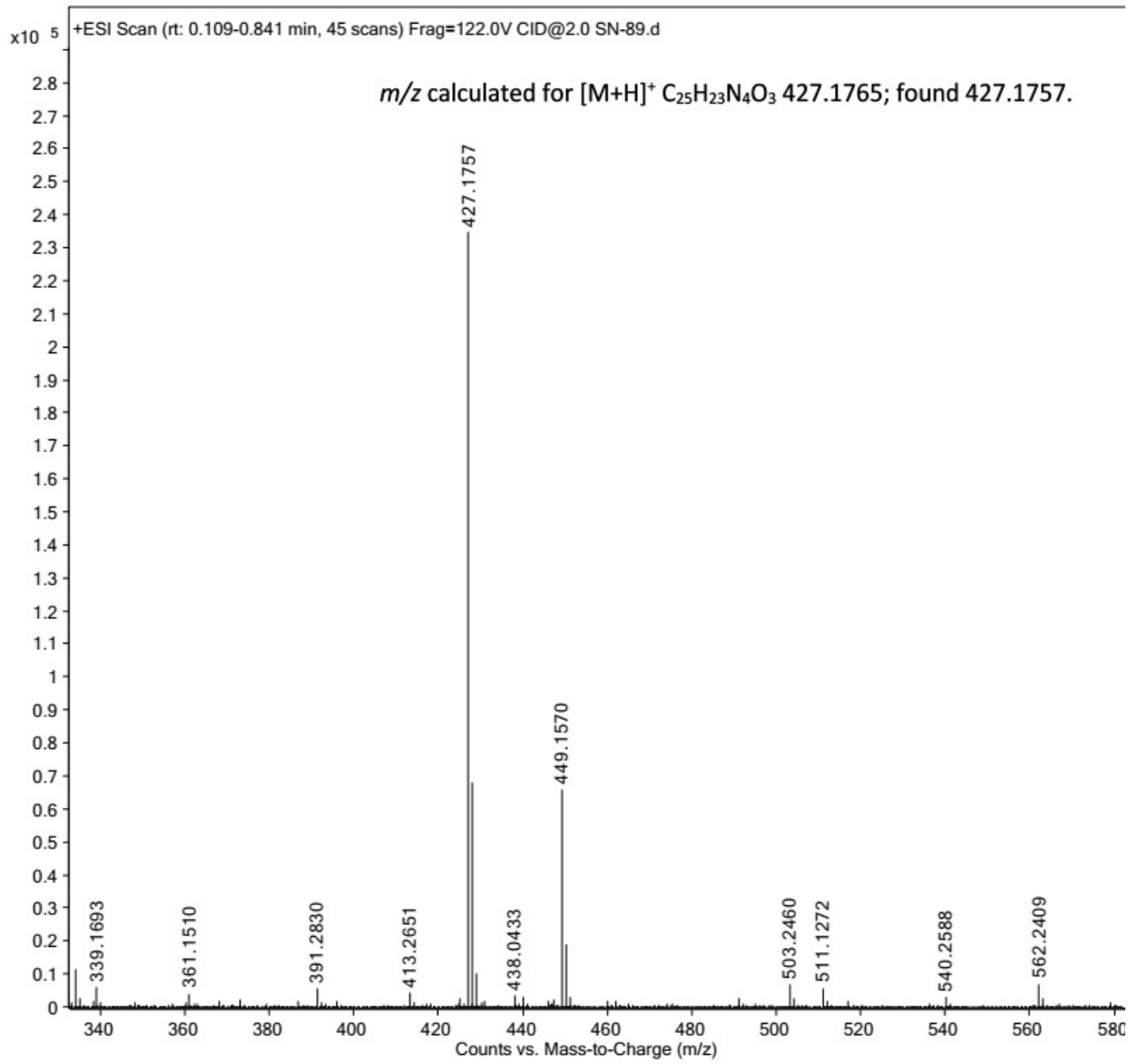
*N'-(4-cyanophenyl)-6-(1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)hexanehydrazide (**11e**)*



^{1}H NMR spectrum of compound **11e**, DMSO-d_6, 500MHz



^{13}C NMR spectrum of compound **11e**, DMSO-d_6, 125MHz


+ESI Scan (rt: 0.109-0.841 min, 45 scans) Frag=122.0V CID@2.0 SN-89.d
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m/z calculated for [M+H]+ C25H23N4O3 427.1765; found 427.1757.
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449.1570
339.1693
361.1510
391.2830
413.2651
438.0433
503.2460
511.1272
540.2588
562.2409
Counts vs. Mass-to-Charge (m/z)