Supporting Information

Green, Practical & Scalable Approach towards Synthesis of Valuable α-Keto Amides Using Metal-free catalyst under Solvent-free conditions

Shubham R. Bankar[a,b], Sambhaji S. Ghadge[a,b], Vrushali H. Jadhav[a,b]*

[a]Division of Catalysis & Inorganic Chemistry, CSIR-National Chemical Laboratory, Dr. Homi-Bhabha Road, Pashan, Pune 411008, India

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Experimental section

General methods

All reagents and solvents were obtained from commercial sources and used as it is unless otherwise stated. Column chromatography was performed on silica gel (230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. High-resolution mass spectra (HRMS) were recorded using electron spray ionization (ESI) with a time-off-flight mass analyzer. NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, td = triplet of doublet, m = multiplet), coupling constants (Hz), and integration.

Preparation of GCM Catalyst:

Glucose carbonaceous material (GCM) catalyst was prepared by simple hydrothermal carbonisation method in a teflon lined stainless-steel hydrothermal autoclave. In typical procedure, D-glucose (25 g) was primarily dissolved in 50 mL of deionised water (DI) to form homogeneous solution and placed in 150mL autoclave, autoclave was then sealed and kept in a muffle furnace for 10 h at 180 ℃. The temperature of the muffle furnace was set at 5 °C/min and reached 180 ° C in 40 min. After 10 h, the autoclave was cooled to room temperature, and the resultant precipitate (glucose-derived carbonaceous material (GCM)) was separated by filtration, cleaned with DI water and ethanol (EtOH), and dried for 12 h at 100 °C in a vacuum oven, to give black solid denoted as GCM.

Catalyst characterization:

GCM catalyst was characterized using relevant analysis such as Infra-Red FTIR (Perkin Elmer, Spectrum 400, USA), Powder X-ray diffraction (P-XRD) (Rigaku MiniFlex 600)

Power: 100-240 VAC 1ϕ 15A 50/60 Hz, Energy Dispersive X-ray analysis (EDAX) and Field Emission Scanning Electron Microscopy (FE-SEM) (FEI, NOVA NANOSEM 450, USA), High Resolution Transmission Electron Microscopy HR-TEM (Jeol JEM F200), Solid-state Cross-Polarization Magic Angle Spinning Carbon-13 Nuclear Magnetic Resonance ^{13}C CP-MAS (Jeol ECX 400), Thermogravimetric analysis TGA (Diamond - TG/DTA), X-ray Photo Electron Spectroscopy XPS (Thermo K-Alpha) & Brunauer-Emmett-Teller BET (Quantachrome Boynton Beach, FL 33, 426, USA) techniques.

General Procedure for the Synthesis of α-Ketoamides:

Method-I: Using Phenyl glyoxal and amine

In general procedure synthesis of α-keto amide from phenyl glyoxal (100 mg, 0.7 mmol) & piperidine (0.073 mL, 0.7 mmol), 10 wt% GCM were taken in a round bottom flask, stirred & heated at a given time & temperature under non-inert conditions. After completion of reaction was observed from TLC (thin layer chromatography), catalyst was filtered off and water was added to the reaction mixture and the reaction mixture was extracted in ethyl acetate and the organic layer was evaporated on rota-vac & the crude product was purified using 10-20% EtOAc/Pet-ether column chromatography. The product was then analysed by ^{1}H NMR, ^{13}C & DEPT NMR, HRMS analysis.

Method-II: Using 2-hydroxyacetophenone and amine

In general procedure synthesis of α-keto amide from 2-hydroxyacetophenone (100 mg, 0.7 mmol) & piperidine (0.072 mL, 0.7 mmol), 10 wt% GCM were taken in a round bottom flask, stirred & heated for given time & temperature under non-inert conditions. After completion of the reaction was observed from TLC (thin layer chromatography), catalyst was filtered off and water was added to the reaction mixture and the reaction mixture was extracted in ethyl acetate and the organic layer was evaporated on rota-vac & the crude product were purified using 10-20% EtOAc/ Pet-ether column chromatography. The product was then analyzed by ^{1}H NMR, ^{13}C & DEPT NMR, HRMS analysis.

Synthesis of Anti-HIV agent: 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)- ethane-1,2-dione (1d)

Step-I: Synthesis of 2-naphthalen-2-yl-2-oxoacetaldehyde (6b)

A 2-acetonaphthone (500 mg, 2.9 mmol) was heated with I_2 (189 mg, 1.5 mmol) in DMSO (6 ml) at 95 ℃ temperature in a 50 ml round bottom flask & stirred for 4h under non-inert conditions. When the reaction was completed (monitored by TLC), the excess iodine from the reaction mixture was quenched by using 10% sodium thiosulfate ($Na_2S_2O_3.5H_2O$) solution. Next, the reaction mixture was filtered using ordinary filter paper and the volume of the reaction mixture reduced to half on rota-vac and was purified by silica gel column chromatography using 15% EtOAc/ Pet-ether as an eluent to obtain pale yellow solid (382 mg, 6b).

Step-II: Synthesis of 1-benzoyl piperazine (7c)

A 9-BBN (600 mg, 3.7 mmol) was added to a solution of piperazine (222 mg, 3.7 mmol), in dry THF (10ml). After stirring for 1h at room temperature, benzoyl chloride (0.4 ml, 3.5 mmol) was added and stirred for a further 2h at room temperature under inert (N_2) condition. The reaction mixture was quenched with H_2O, the aqueous layer was extracted with EtOAc (2 x 100 ml), and the organic layer dried over Na_2SO_4. Extracted layer evaporate on rota-vac afforded a residue that was purified by silica gel column chromatography using 15% EtOAc/Pet-ether as an eluent to give a transparent solid (480 mg, 7c).

Step- III: Synthesis of 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)- ethane-1,2-dione (IV)

Synthesis of Anti-HIV agent (IV) from 2-naphthalen-2-yl-2-oxoacetaldehyde (100 mg, 0.5 mmol, 6b) & 1-benzoyl piperazine (103 mg, 0.5 mmol, 7c), 10 wt% GCM were taken in a 50 ml round bottom flask and stirred in an oil bath at 50℃ under non-inert conditions. After 8h starting was completely consumed was observed from TLC (thin layer chromatography), catalyst was filtered off and water was added to the reaction mixture and the reaction mixture was extracted in ethyl acetate and the organic layer was evaporated on rota-vac & the crude product was purified using silica gel column chromatography using 20% EtOAc/Pet-ether to give a colorless solid (153 mg, IV).

All product obtained was then analyzed by ^1H NMR (400MHz, $CDCl_3$ solvent), ^{13}C & DEPT (100 MHz, $CDCl_3$ solvent) NMR, and HRMS analysis.

Characterization of Products

1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3a): Light yellow solid (93% yield). Synthesized following the general procedure from phenyl glyoxal (100 mg, 0.7 mmol) &

piperidine (0.073 mL, 0.7 mmol).^{1}H NMR (400 MHz, $CDCl_3$): 7.94 (d, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H) ppm, 3.70 (bs, 2H), 3.28 (t, *J* = 5Hz, 2H), 1.69 (bs, 4H), 1.54 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.9, 165.4, 134.6, 133.2, 129.5, 129.0, 47.0, 42.1, 26.2, 25.4, 24.3 ppm; HRMS (ESI) calcd. for $C_{13}H_{16}O_2N$: 218.1176 $[M+1]^+$; Found: 218.1181.

1-morpholino-2-phenylethane-1,2-dione (3b): Yellow wax (86% yield). Synthesized following the general procedure from Phenyl glyoxal (100 mg, 0.7 mmol) & morpholine (0.064 mL, 0.7 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.95 (d, *J* = 7.3 Hz, 2H), 7.66 (t, *J* = 7.65 Hz, 1H), 7.52 t, *J* = 7.52 Hz, 2H), 3.79 (s, 4H), 3.65 (t, *J* = 5 Hz, 2H), 3.38 (t, *J* = 5 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.1, 165.1, 134.9, 133.0, 129.7, 129.1, 66.7, 66.6, 46.2, 41.6 ppm; HRMS (ESI) calcd. for $C_{12}H_{14}O_3N$: 220.0968 $[M+1]^+$; Found: 220.0974.

1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3c): Yellow wax (91% yield). Synthesized following the general procedure from Phenyl glyoxal (100 mg, 0.7 mmol) & pyrrolidine (0.061 mL, 0.7 mmol). ^{1}H NMR (400MHz, $CDCl_3$): 7.98 (d, *J* = 7.4 Hz, 2H), 7.62 (t, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 2H), 3.65 (t, *J* = 6.2 Hz, 2H), 3.42 (t, *J* = 6.5 Hz, 2H), 1.98-1.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 191.5, 164.9, 134.6, 132.9, 129.9, 128.9, 46.7, 45.2, 25.9, 24.0 ppm; HRMS (ESI) calcd. for $C_{12}H_{14}O_2N$: 204.1019 $[M+1]^+$; Found: 204.1023.

1-(4-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3d): Yellow liquid (83% yield). Synthesized following the general procedure from Phenyl glyoxal (100 mg, 0.7 mmol) & 4-methylpiperidine (0.038 mL, 0.7 mmol). ^{1}H NMR (400MHz, $CDCl_3$): 7.94 (d, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.4 Hz ,1H), 7.50 (t, *J* = 7.6 Hz, 2H), 4.60-4.64 (m, 1H), 3.50-3.54 (m, 1H), 3.05 (td, *J* = 12.9, 2.8 Hz, 1H), 2.79 (td, *J* = 12.8, 3.1 Hz, 1H), 1.77- 1.81 (m, 1H), 1.62 (d, *J* = 13.6 Hz, 2H), 1.12-1.16 (m, 2H), 0.97 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 165.8, 164.8, 132.0 (s), 126.3, 114.3 (s), 46.3, 41.4, 34.3, 31.0, 29.7, 21.6 ppm; HRMS (ESI) calcd. for $C_{14}H_{18}O_2N$: 232.1332 $[M+1]^+$; Found: 232.1339.

1-(3-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3e): Colourless liquid (79% yield). Synthesized following the general procedure from Phenyl glyoxal (100 mg, 0.7 mmol) & 3-methylpiperidine (0.038 mL, 0.7 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.94 (d, J = 7.8 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 4.50 (t, *J* = 10.8 Hz, 1H), 3.39-3.49 (m, 1H), 2.66-2.83 (m, 1H), 2.48 (t, *J* =10.8 Hz, 1H), 1.86 (d, *J* = 10.6 Hz, 1H), 1.61-1.65 (m, 2H), 1.13-1.24 (m, 1H), 0.98-0.99 (d, *J* = 6.6 Hz, 2H), 0.87 (d, *J* = 6.6 Hz, 1H), 0.79-0.80 (d,

J = 0.74 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 165.7, 164.8, 132.0 (s), 126.3, 114.3 (s), 53.6, 48.3, 41.5, 32.8, 31.0, 19.0 ppm; HRMS (ESI) calcd. for $C_{14}H_{18}O_2N$: 232.1332 $[M+1]^+$; Found: 232.1340.

1-(4-bromopiperidine-1-yl)-2-phenylethane-1,2-dione 2(3f): White solid (86% yield), Synthesized following the general procedure from Phenyl glyoxal (100 mg, 0.7 mmol) & 4-bromopiperidine (0.11 mL, 0.7 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.94 (t, *J* = 7.8 Hz, 2H), 7.64 (bs, 1H), 7.51 (bs, 2H), 5.74-5.92 (m, 2H), 4.22 (bs, *J* = 2.3Hz, 1H), 3.84 (m, 2H), 3.43 (t, *J* = 5.6 Hz, 1H), 2.31 (s, 1H), 2.09-2.16 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.4, 166.0, 134.7, 133.2, 129.6 (s), 129.0 (s), 48.2, 42.9, 41.0, 38.1, 25.4 ppm; HRMS (ESI) calcd. for $C_{13}H_{15}O_2NBr$: 296.0281 $[M+1]^+$; Found: 296.0284.

1-(4-methoxypiperidine-1-yl)-2-phenylethane-1,2-dione (3g): Transparent liquid (85% yield). Synthesized following the general procedure from phenyl glyoxal (100 mg, 0.7 mmol) & piperidine (0.079 mL, 0.7 mmol). ^{1}H NMR (400MHz, $CDCl_3$): 7.93 (d, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.50 (d, *J* = 7.7 Hz, 2H), 3.87-3.93 (m, 1H), 3.61-3.67 (m, 1H), 3.47-3.53 (m, 2H), 3.35 (s, 3H), 3.16-3.22 (m, 1H), 1.91-1.97 (m, 1H), 1.71- 1.84 (m, 2H), 1.56-1.64 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.7, 165.4, 134.7 (s), 133.1, 129.5, 129.0 (s), 74.7, 55.8, 42.9, 38.1, 30.7, 29.7 ppm; HRMS (ESI) calcd. for $C_{14}H_{18}O_3N$: 248.1281 $[M+1]^+$; Found: 248.1275.

1-(4-Benzoyl-1-piperazinyl)-2-phenylethane-1,2-dione (3h): White solid (69% yield). Synthesized following the general procedure from phenyl glyoxal (100 mg, 0.7 mmol) & 1-benzoyl piperazine (141 mg, 0.7 mmol). ^{1}H NMR (400MHz, $CDCl_3$): 7.89 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.35 (s, 5H), 3.73 (bs, 5H), 3.34 (bs, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.9, 170.7, 165.6, 135.1, 134.8, 132.9, 130.2, 129.7 (d), 129.1 (d), 128.7 (s), 127.0 (s), 41.4, 37.1, 31.9, 27.0 ppm; HRMS (ESI) calcd. for $C_{19}H_{19}O_3N_2$: 323.1390 $[M+1]^+$; Found: 323.1389.

1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3i): Yellow oil (74% yield). Synthesized following the general procedure from 4-bromophenyl glyoxal (100 mg, 0.4 mmol) & piperidine (0.046 mL, 0.4 mmol). ^{1}H NMR (400MHz, $CDCl_3$): 7.81 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 3.69 (bs, 2H), 3.27 (t, *J* = 6.2 Hz, 2H), 1.68-1.70 (m, 4H), 1.53-1.56 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.5, 165.4, 134.6 (s), 133.2, 129.5 (s),

129.0, 47.0, 42.1, 26.2, 25.4, 24.3 ppm; HRMS (ESI) calcd. for $C_{13}H_{15}O_2NBr$: 296.0281 $[M+1]^+$; Found: 296.0284.

1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3j): Yellow liquid (73% yield). Synthesized following the general procedure from 4-bromophenyl glyoxal (100 mg, 0.4 mmol) & pyrrolidine (0.028 mL, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.87 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 3.64 (t, *J* = 3.58 Hz, 2H), 3.43 (t, *J* = 6.3 Hz, 2H), 1.93-1.98 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.9, 165.4, 134.6, 133.2, 129.5 (s), 129.0 (s), 47.0, 42.1, 26.2, 25.4 ppm; HRMS (ESI) calcd. for $C_{12}H_{13}O_2NBr$: 282.0128 $[M+1]^+$; Found: 282.0128.

1-(4-bromophenyl)-2-(4-methylpiperidine-1-yl)ethane-1,2-dione (3k): Colourless liquid (71% yield). Synthesized following the general procedure from 4-bromophenyl glyoxal (100 mg, 0.4 mmol) & 4-methylpiperidine (0.045 mL, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.80 (d, *J* = 8 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 4.6 (d, *J* = 13.3 Hz, 1H), 3.5 (d, *J* = 12.6 Hz, 1H), 3.05 (t, *J* = 12.5 Hz, 1H), 2.78 (t, *J* = 13.1 Hz, 1H), 1.79 (d, *J* = 12.4 Hz, 1H), 1.56-1.61 (m, 4H), 0.97 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 189.8, 164.0, 131.5 (s), 131.2, 130.1 (s), 129.2, 45.4, 40.7, 32.7, 30.1, 28.8, 20.7 ppm; HRMS (ESI) calcd. for $C_{14}H_{17}O_2NBr$: 310.0437 $[M+1]^+$; Found: 310.0439.

1-(4-bromophenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3l): Transparent liquid (70% yield). Synthesized following the general procedure from 4-bromophenyl glyoxal (100 mg, 0.4 mmol) & 3-methylpiperidine (0.045 mL, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.80 (d, *J* = 8.1 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 4.43 (t, *J* = 12.7 Hz, 1H), 3.37-3.46 (m, 1H), 2.66- 2.84 (m, 1H), 2.48 (t, *J* = 11.8 Hz, 1H), 1.85-1.88 (d, *J* = 12.6 Hz, 1H), 1.55 (s, 4H), 0.98 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 165.7, 164.8, 132.0 (s), 126.3, 114.3(s), 53.3, 48.3, 46.5, 41.5, 31.6, 31.0 ppm; HRMS (ESI) calcd. for $C_{14}H_{17}O_2NBr$: 310.0437 $[M+1]^+$; Found: 310.0440.

1-(4-bromophenyl)-2-(4-methoxypiperidine-1-yl)ethane-1,2-dione (3m): White solid (73% yield). Synthesized following the general procedure from 4-bromophenylglyoxal (100 mg, 0.4 mmol) & 4-methoxy piperidine (0.050 mL, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.80 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 3.83- 3.89 (m, 1H), 3.63-3.69 (m, 1H), 3.45-3.53 (m, 2H), 3.35 (s, 3H), 3.15-3.21 (m, 1H), 1.88-1.95 (m, 1H), 1.71-1.83 (m, 2H), 1.57-1.65 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.5, 164.9, 132.4, 131.9, 130.9,

130.2, 74.5, 55.9, 42.9, 38.1, 30.8, 29.8 ppm; HRMS (ESI) calcd. for $C_{14}H_{17}O_3NBr$: 326.0386 $[M+1]^+$; Found: 326.0381.

1-(4-methoxyphenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3n): Yellow wax (77% yield), Synthesized following the general procedure from 4-methoxyphenyl glyoxal (100 mg, 0.5 mmol) & piperidine (0.054 mL, 0.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.90 (d, *J* = 8 Hz, 2H), 6.96 (d, *J* = 8 Hz, 2H), 3.88 (s, 3H), 3.68 (bs, 2H), 3.27 (t, *J* = 5.38 Hz, 2H), 1.68 (bs, 4H), 1.53 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 171.1, 164.7, 132.0 (s), 126.4, 114.3 (s), 60.4, 55.6, 47.0, 42.1, 26.2, 24.4 ppm; HRMS (ESI) calcd. for $C_{14}H_{18}O_3N$: 248.1281 $[M+1]^+$; Found: 248.1281.

1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3o): Transparent liquid (76% yield). Synthesized following the general procedure from 4-methoxyphenyl glyoxal (100 mg, 0.5 mmol) & piperidine (0.045 mL, 0.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.94 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.41 (t, *J* = 6.2 Hz, 2H), 1.90-1.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 190.2, 165.3, 164.7, 132.3 (s), 126.0, 114.2 (s), 55.6, 46.7, 45.2, 29.7, 25.9 ppm; HRMS (ESI) calcd. for $C_{13}H_{16}O_3N$: 234.1125 $[M+1]^+$; Found: 234.1126.

1-(4-methoxyphenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3p): Yellow liquid (78% yield). Synthesized following the general procedure from 4-methoxyphenyl glyoxal (100 mg, 0.5 mmol) & 4- methylpiperidine (0.053ml, 0.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.90 (d, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 4.61 (d, *J* = 11.6 Hz, 1H), 3.88 (s, 3H), 3.52 (d, *J* = 11.9 Hz, 1H), 3.03 (t, *J* = 12.9 Hz, 1H), 2.77 (t, *J* = 12.8 Hz, 1H), 1.77 (d, *J* = 13.4 Hz, 1H), 1.59-1.66 (m, 2H), 1.12 (d, *J* = 1.07 Hz, 2H), 0.96 (d, *J* = 6.3 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 165.8, 164.8, 132.0 (s), 126.3, 114.3 (s), 55.6, 46.3, 41.4, 34.3, 33.6, 31.0, 21.6 ppm; HRMS (ESI) calcd. for $C_{15}H_{20}O_3N$: 262.1438 $[M+1]^+$; Found: 262.1438.

1-(4-methoxyphenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3q): White solid (75% yield). Synthesized following the general procedure from 4-methoxyphenyl glyoxal (100 mg, 0.5 mmol) & 3- methylpiperidine (0.053ml, 0.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): 7.90 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 4.49 (t, *J* = 13.6 Hz, 1H), 3.87 (s, 3H), 3.40-3.49 (m, 1H), 2.64- 2.81 (m, 1H), 2.46 (t, *J* = 12.1 Hz, 1H), 1.8 (d, *J* = 12.9 Hz, 1H), 1.56- 1.64 (m, 2H), 1.17 (d, *J* = 12.3 Hz, 1H), 0.96 (d, *J* = 6.5 Hz, 2H), 0.79 (d, *J* = 6.6 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 165.7, 164.8, 132.0 (s), 126.3, 114.3 (s), 55.6, 53.3, 48.3, 41.5, 32.8, 31.6, 19.0 ppm; HRMS (ESI) calcd. for $C_{15}H_{20}O_3N$: 262.1438 $[M+1]^+$; Found: 262.1438.

2-naphthalen-2-yl-2-oxoacetaldehyde (6b): Pale yellow solid (71% yield), Synthesized following the general procedure from 2-acetonaphthone (500 mg, 2.9 mmol), I_2 (189 mg, 1. mmol) & DMSO (6 ml). ^1H NMR (400 MHz, $CDCl_3$): 9.75 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 1H), 8.06 (d, *J* = 6.8 Hz, 1H), 8.00 (d, *J* = 4.8 Hz, 3H), 7.65 (d, *J* = 7.65 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 192.7, 189.9, 136.7, 134.2, 132.9, 132.3, 130.0, 129.4, 128.6, 127.8, 127.0, 124.3 ppm; HRMS (ESI) calcd. for $C_{12}H_9O_2$: 185.0597 $[M+1]^+$; Found: 185.0598.

1-benzoyl piperazine (7c): Transparent solid (70%). Synthesized following the general procedure from piperazine (222 mg, 3.7 mmol), 9-BBN (600 mg, 3.7 mmol) & benzoyl chloride (0.4 ml, 3.5 mmol). ^1H NMR (400 MHz, $CDCl_3$): 7.38 (s, 5H), 3.75 (bs, 2H), 3.40 (bs, 2H), 2.82 (bs, 4H), 2.53 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 170.4, 135.8, 129.6, 128.5 (s), 127.0 (s), 48.9, 45.9, 35.9, 29.6 ppm; HRMS (ESI) calcd. for $C_{11}H_{15}ON2$: 191.1179 $[M+1]^+$; Found: 191.1181.

1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)- ethane-1,2-dione (IV): Colorless solid (76%). Synthesized following the general procedure from 2-naphthalen-2-yl-2-oxoacetaldehyde (100 mg, 0.5 mmol, 6b) & 1-benzoyl piperazine (103 mg, 0.5 mmol, 7c). ^1H NMR (400 MHz, $CDCl_3$): 8.45 (s, 1H), 7.93-8.02 (m, 3H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 7 Hz, 1H), 7.58 (t, J = 7 Hz, 1H), 7.40 (s, 5H), 3.85 (bs, 5H), 3.43 (bs, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 191.0, 170.7, 165.7, 136.5, 134.8, 134.3, 133.1, 132.4, 130.3, 129.9, 129.6, 129.2, 128.7 (s), 128.0, 127.3, 127.0 (s), 123.5, 46.0(br), 41.5(br) ppm; HRMS (ESI) calcd. for $C_{23}H_{21}O_3N_2$: 373.1547 $[M+1]^+$; Found: 373.1544.

^{1}H NMR:

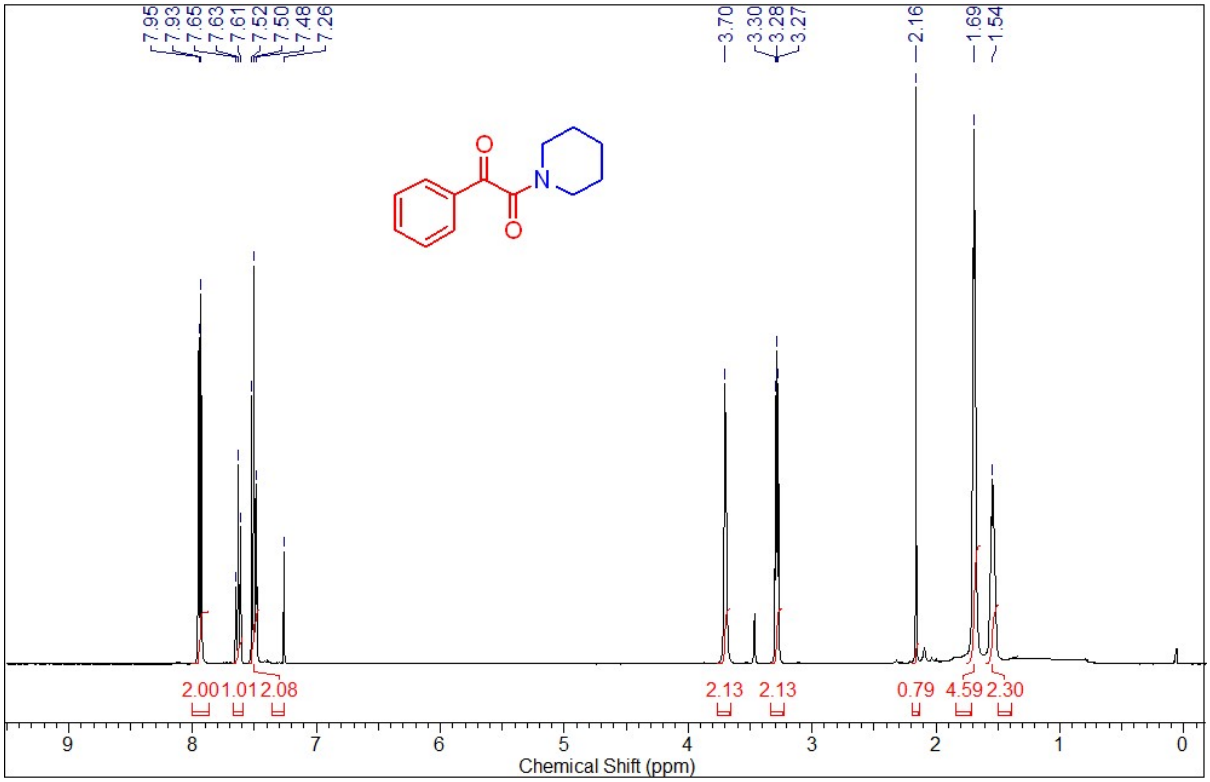


Fig 1:^{1}H NMR (400 MHz, $CDCl_3$) of 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3a)

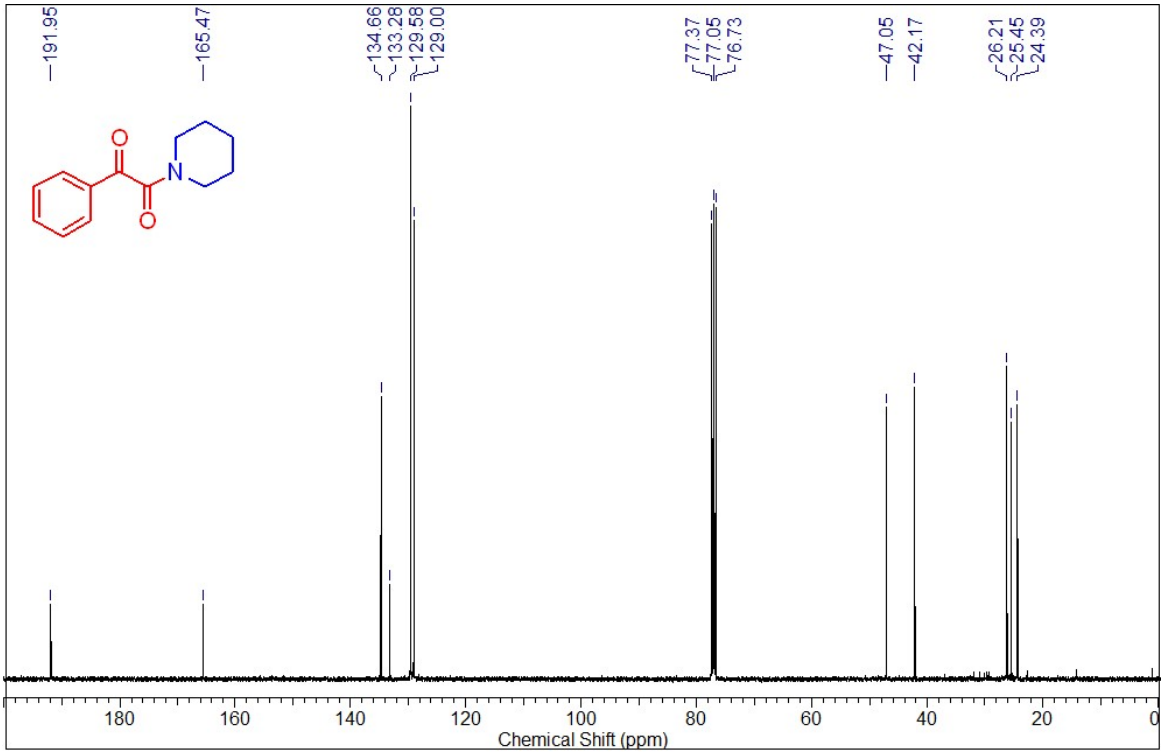


Fig 2: ^{13}C (100 MHz, $CDCl_3$) of 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3a)

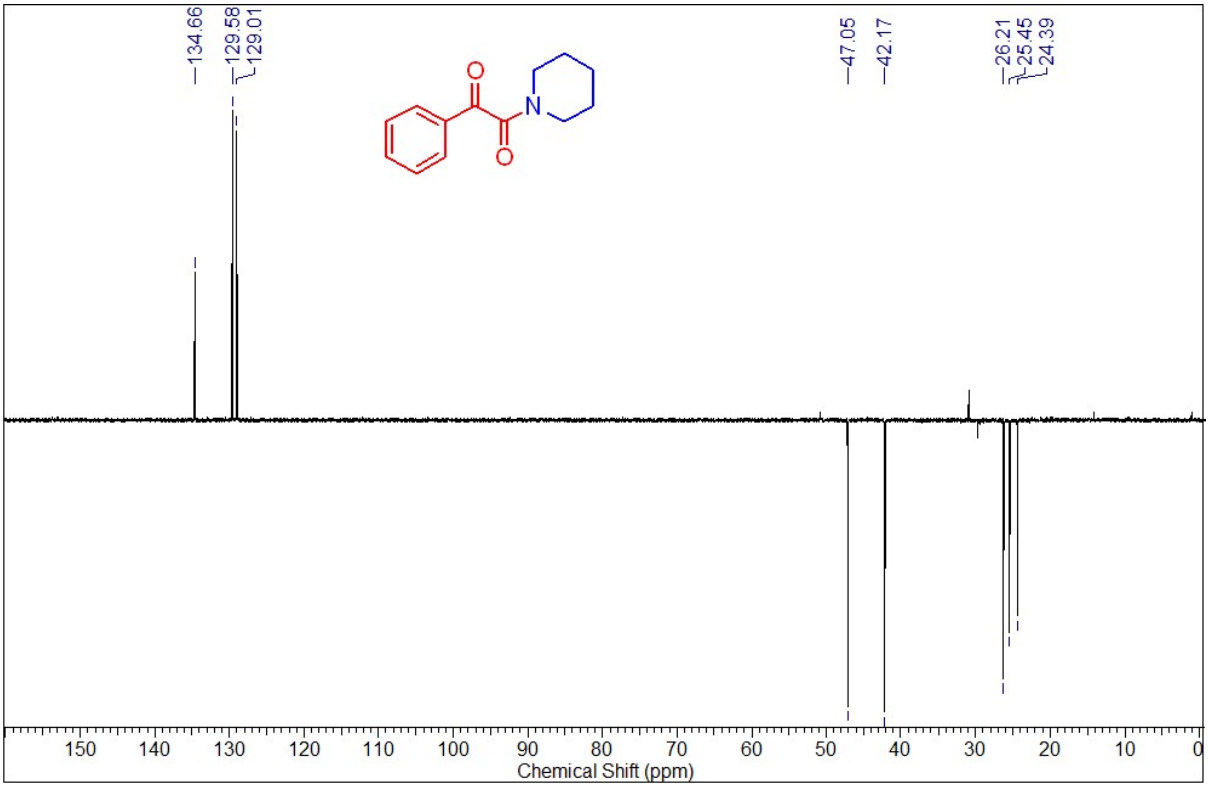


Fig 3: DEPT (100 MHz, $CDCl_3$) of 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3a)

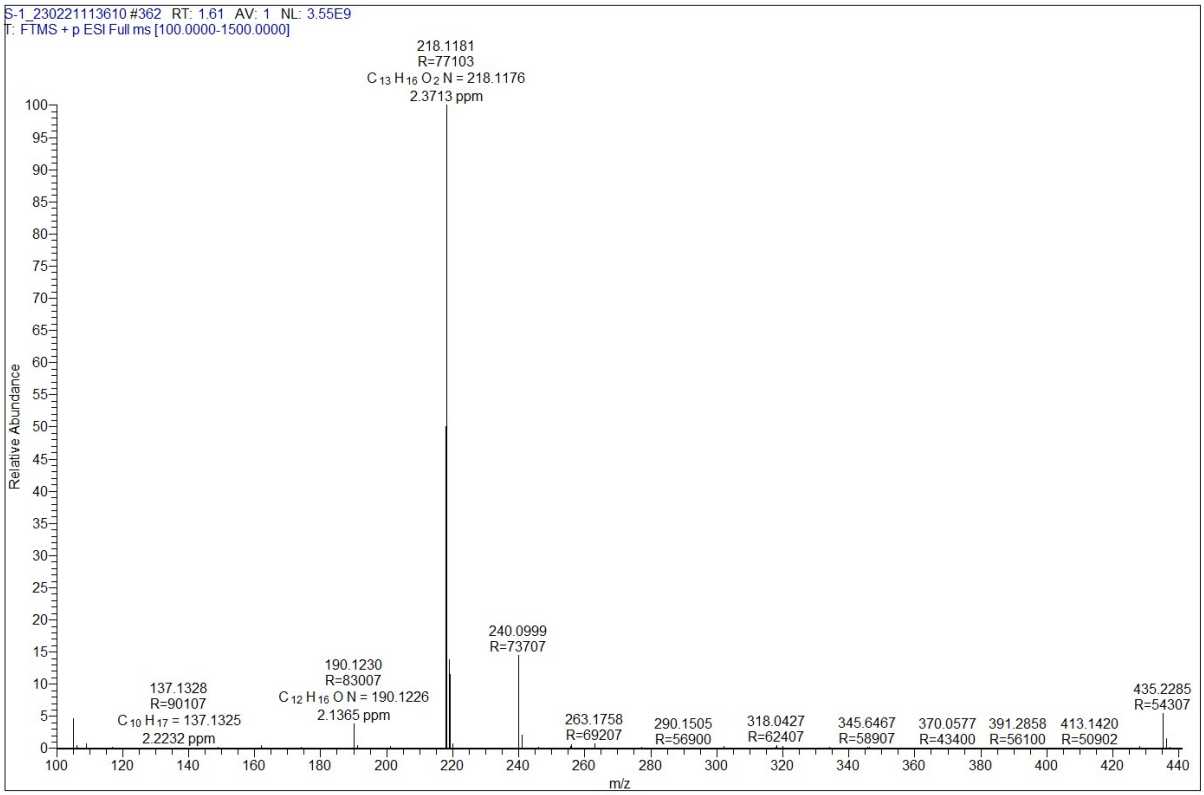


Fig 4: HRMS of 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione (3a)

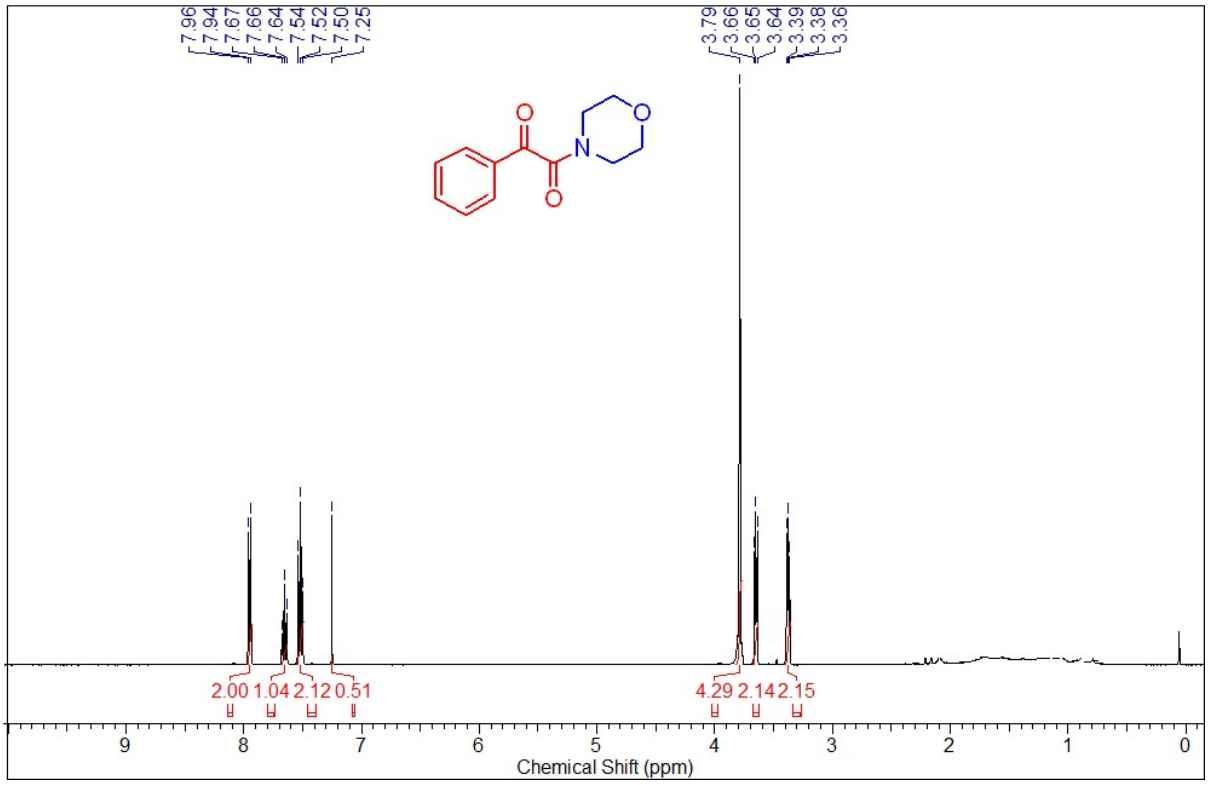


Fig 5:^{1}H NMR (400 MHz, $CDCl_3$) of 1-morpholino-2-phenylethane-1,2-dione (3b)

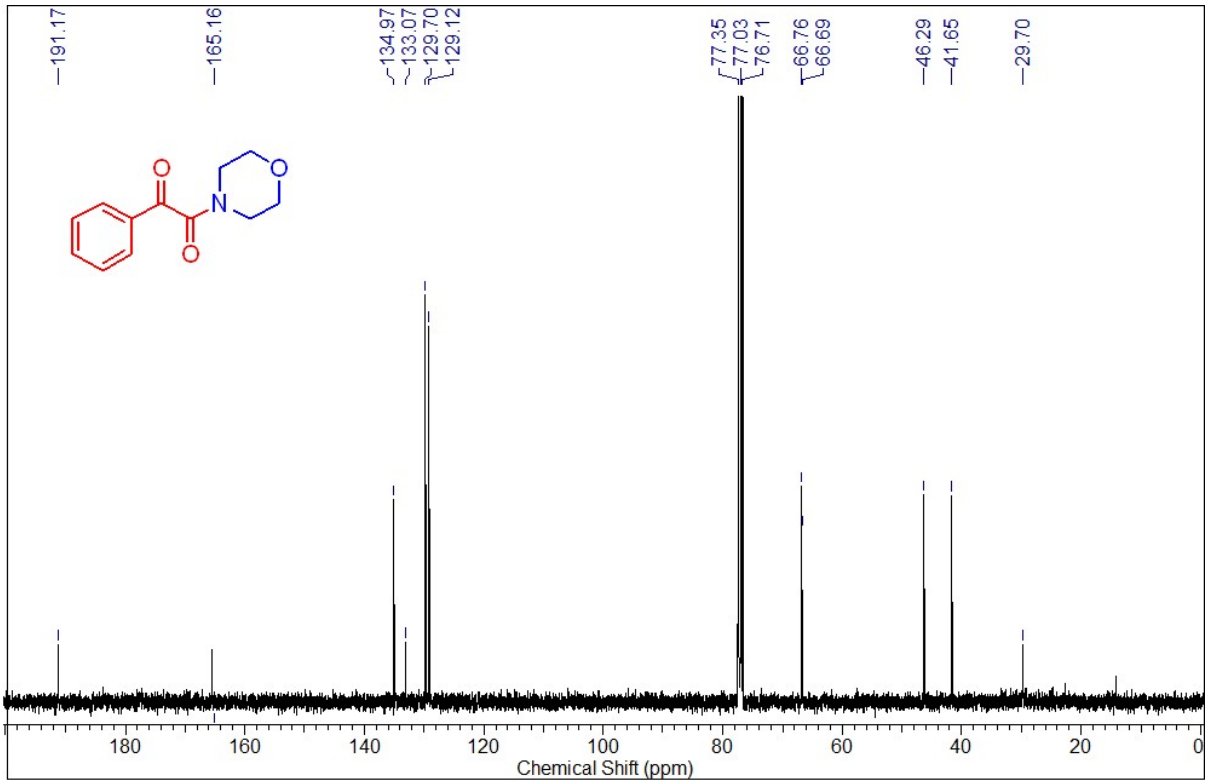


Fig 6: ^{13}C (100 MHz, $CDCl_3$) of 1-morpholino-2-phenylethane-1,2-dione (3b)

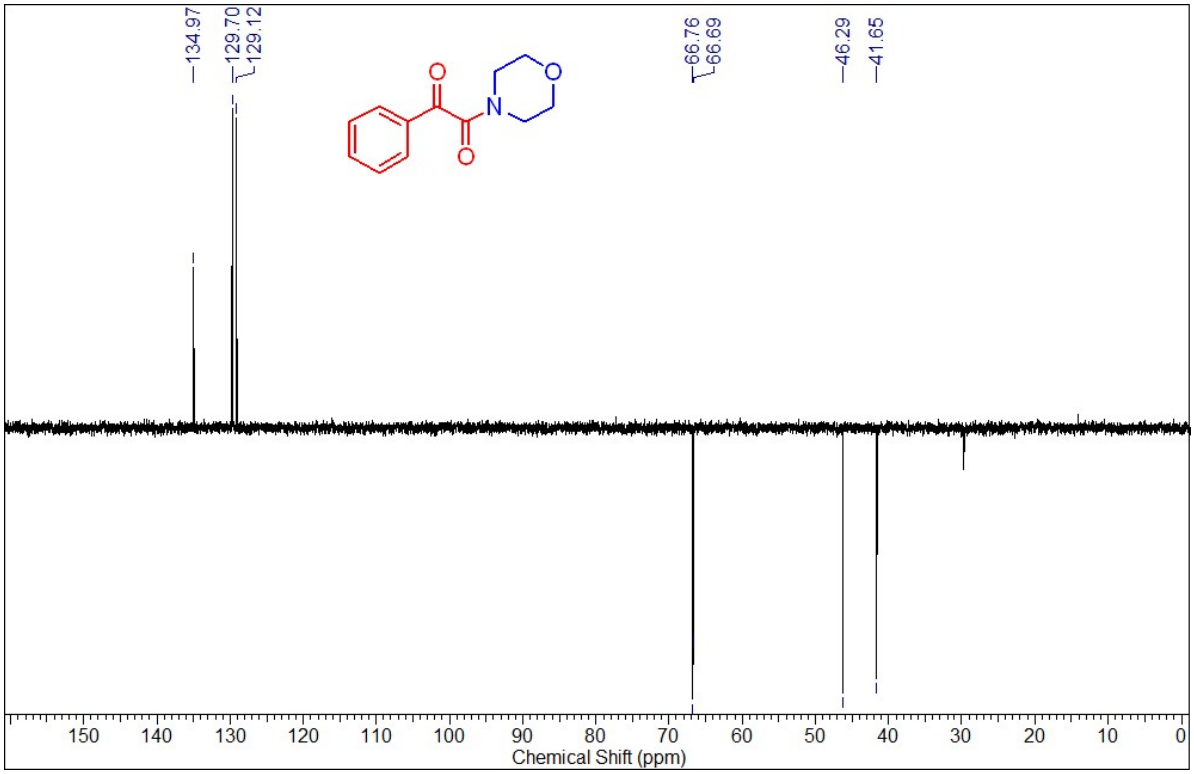


Fig 7: DEPT (100 MHz, $CDCl_3$) of 1-morpholino-2-phenylethane-1,2-dione (3b)

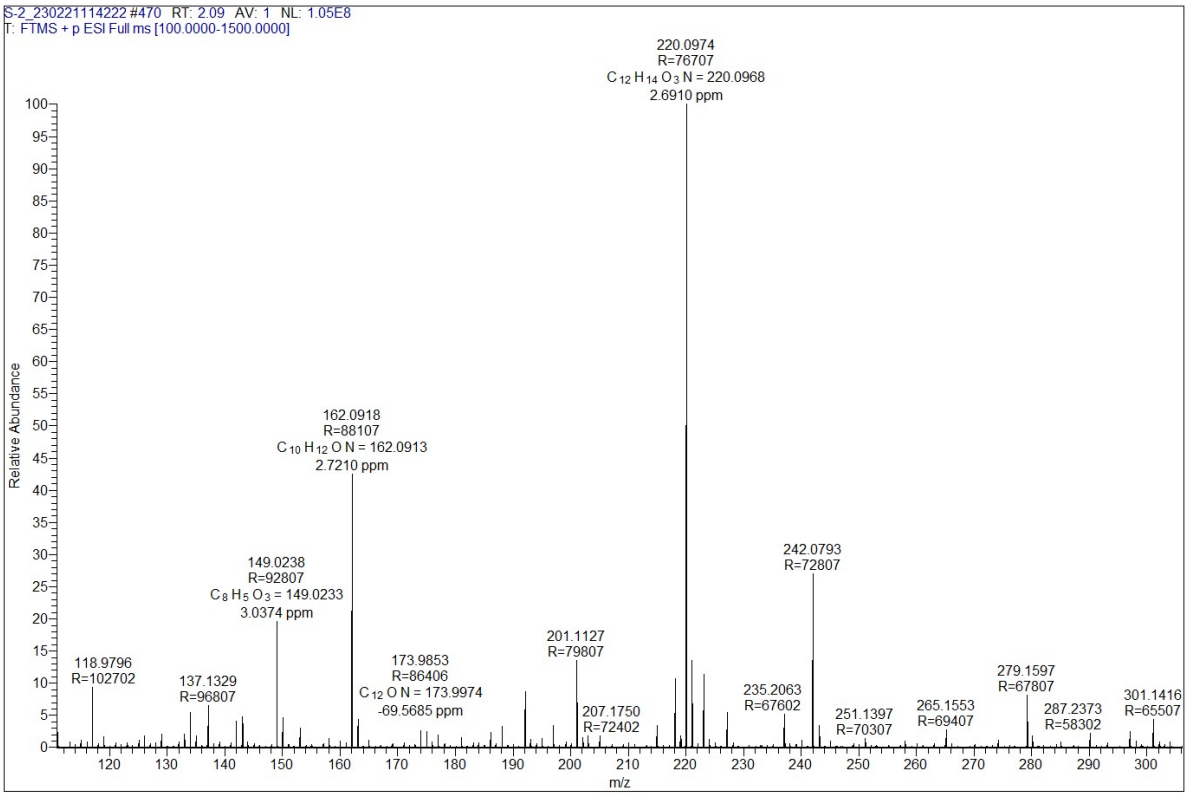


Fig 8: HRMS of 1-morpholino-2-phenylethane-1,2-dione (3b)

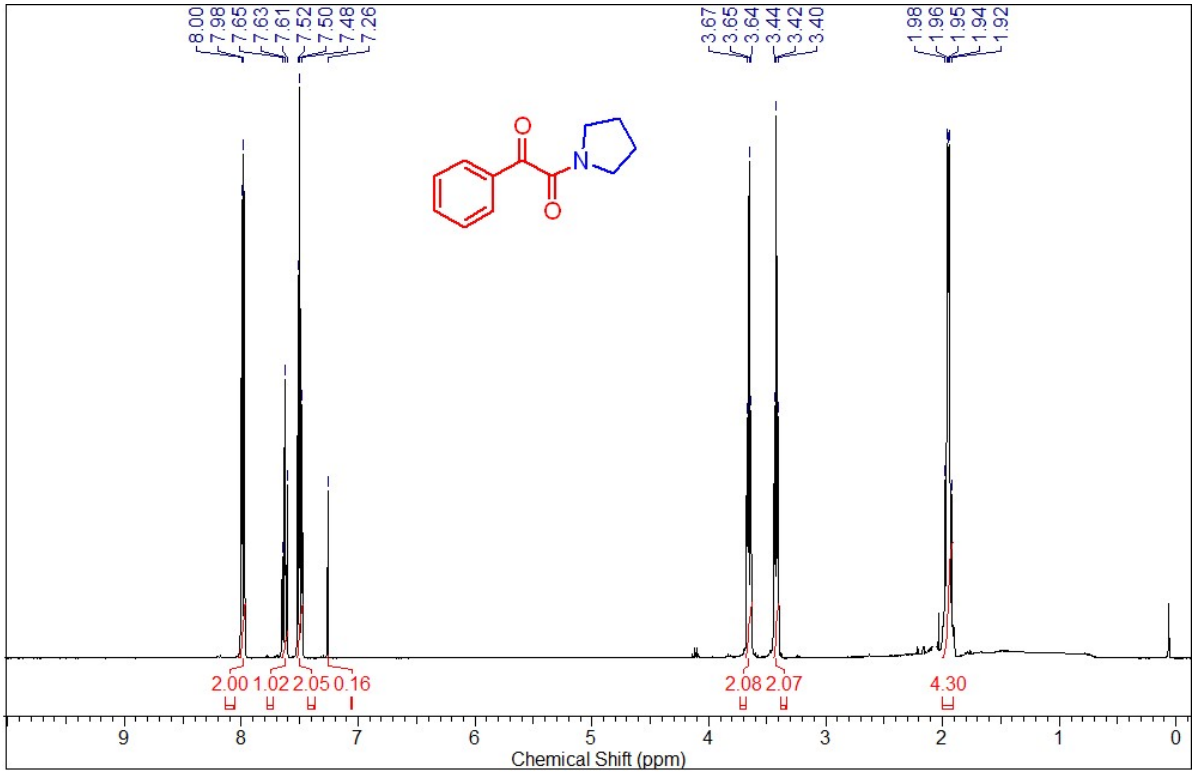


Fig 9: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3c)

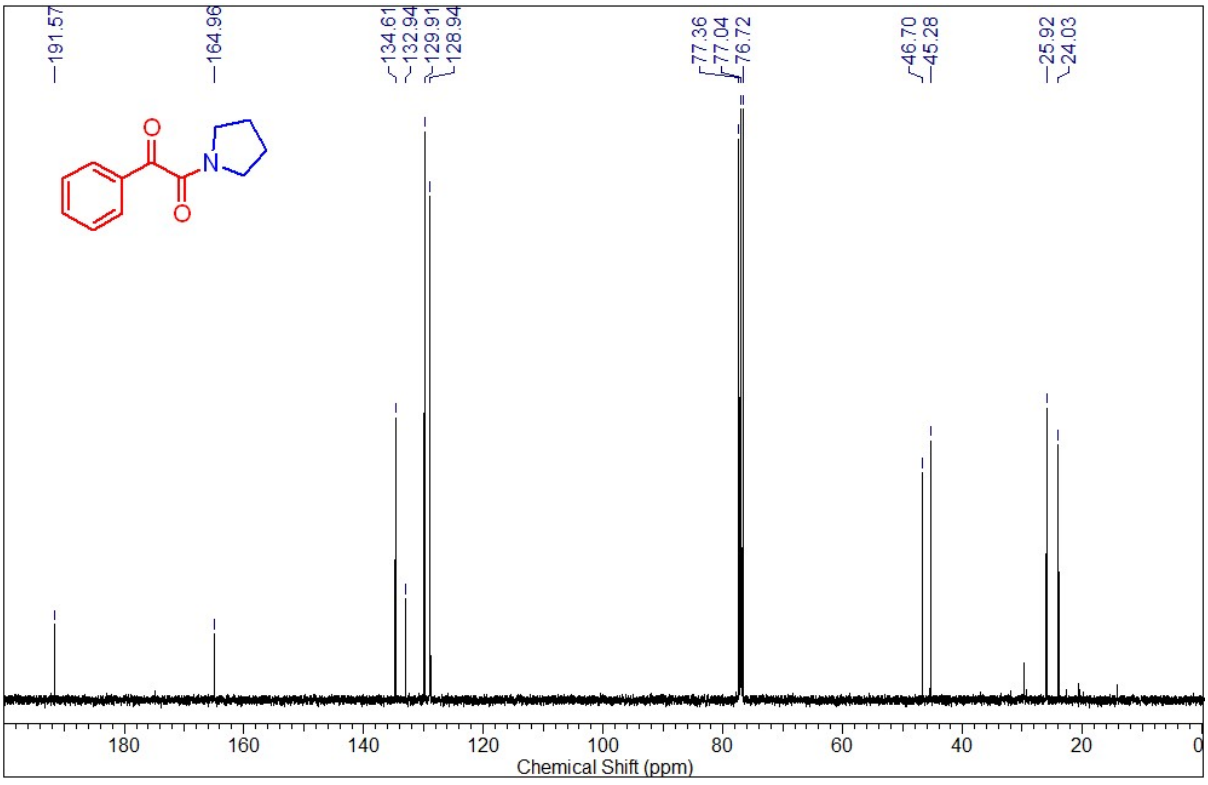


Fig 10: ^{13}C (100 MHz, $CDCl_3$) of 1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3c)

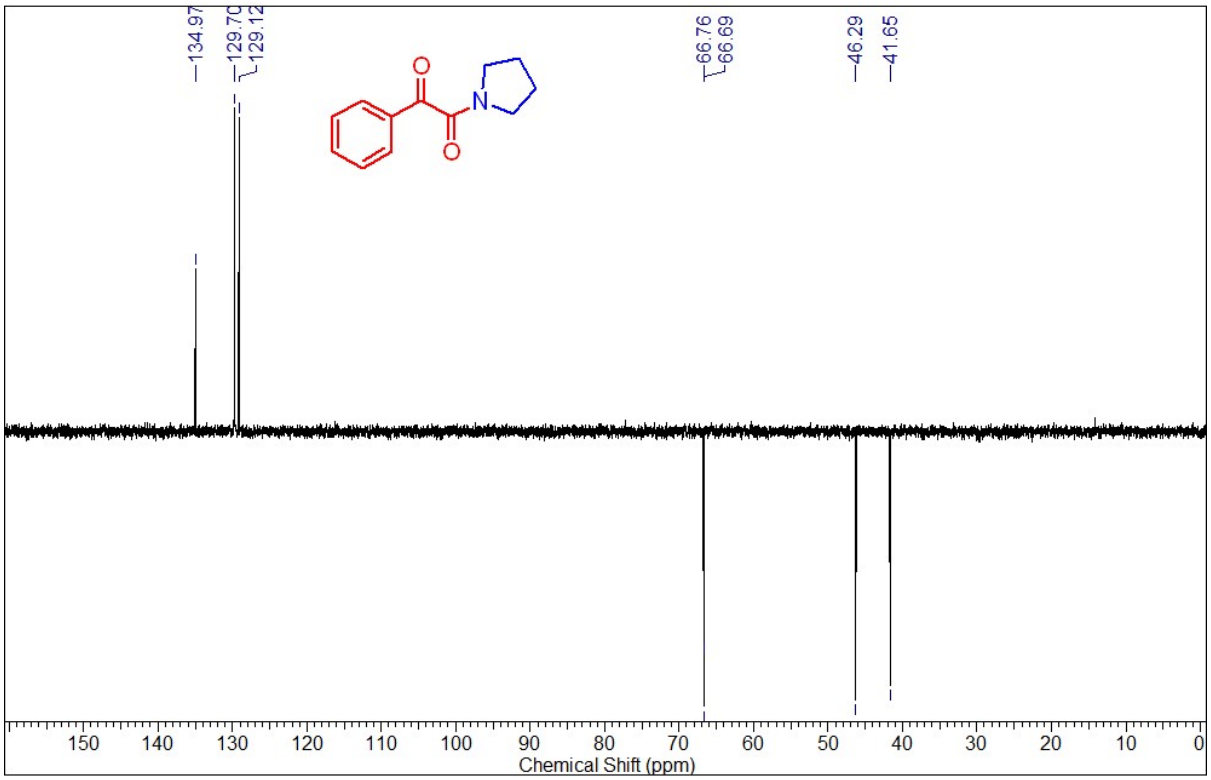


Fig 11: DEPT (100 MHz, $CDCl_3$) of 1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3c)

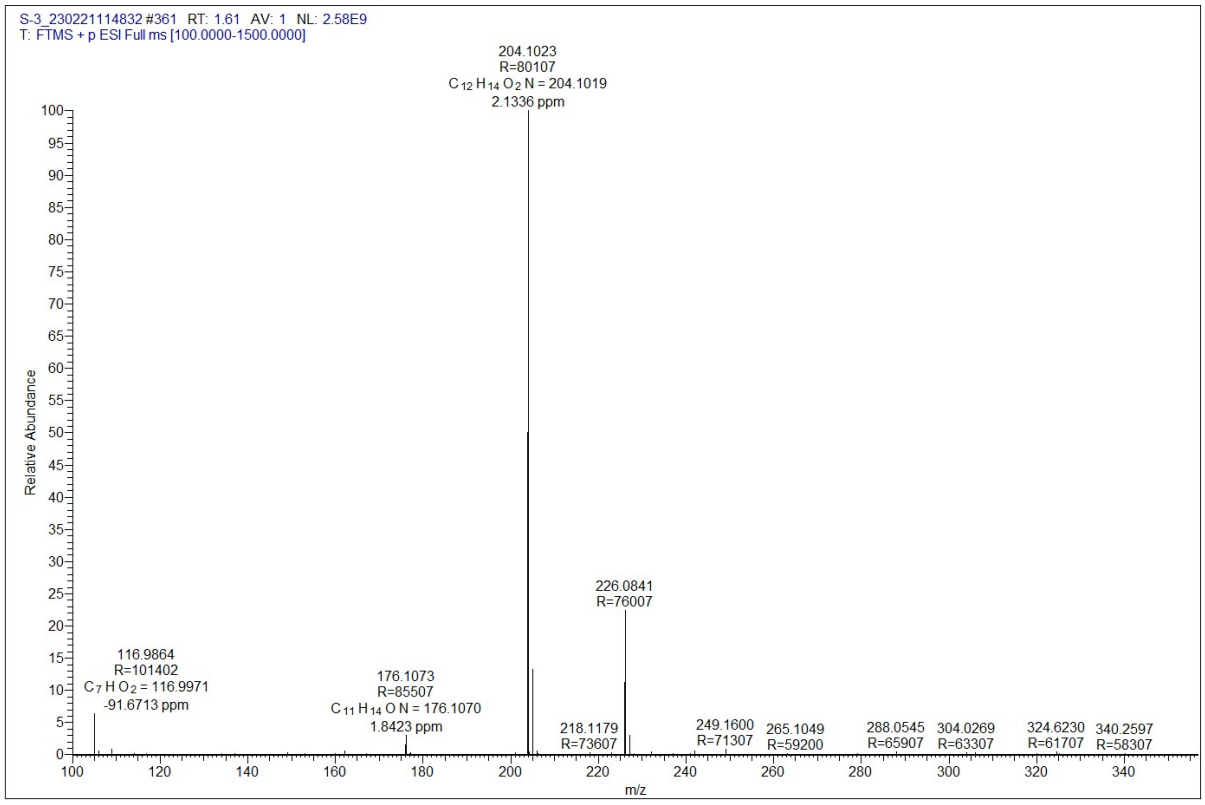


Fig 12: HRMS of 1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3c)

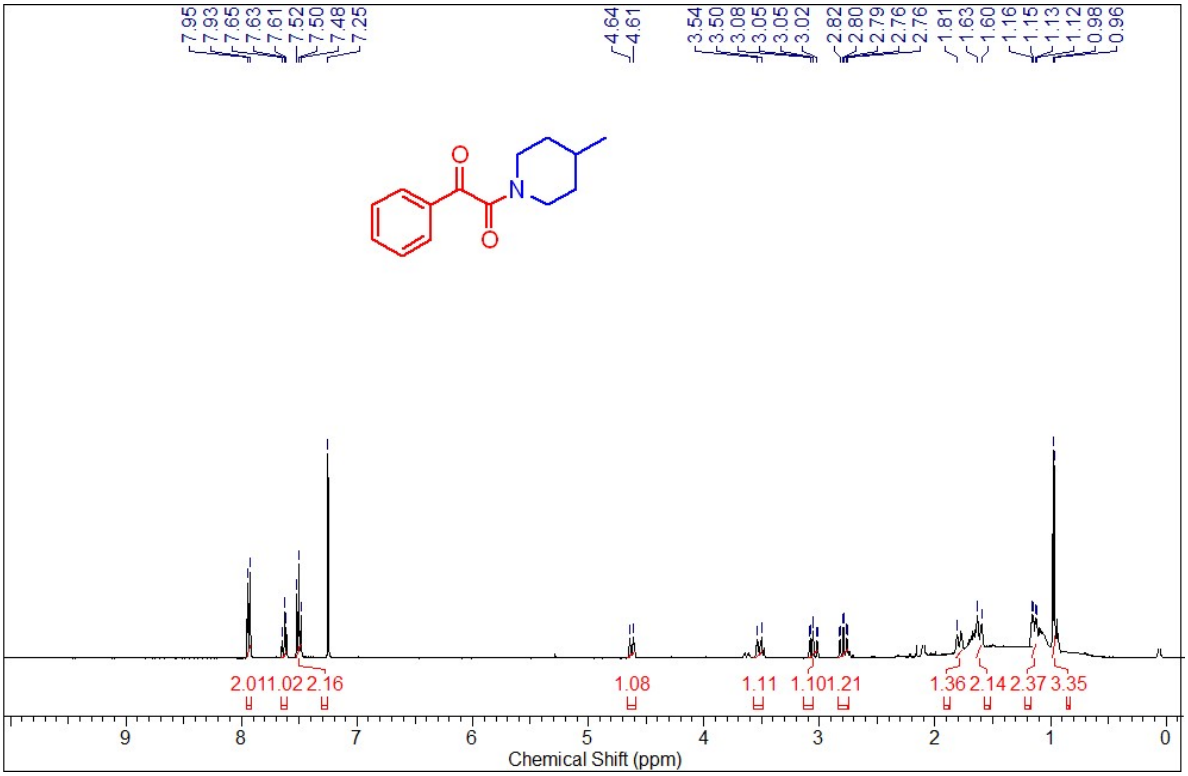


Fig 13: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3d)

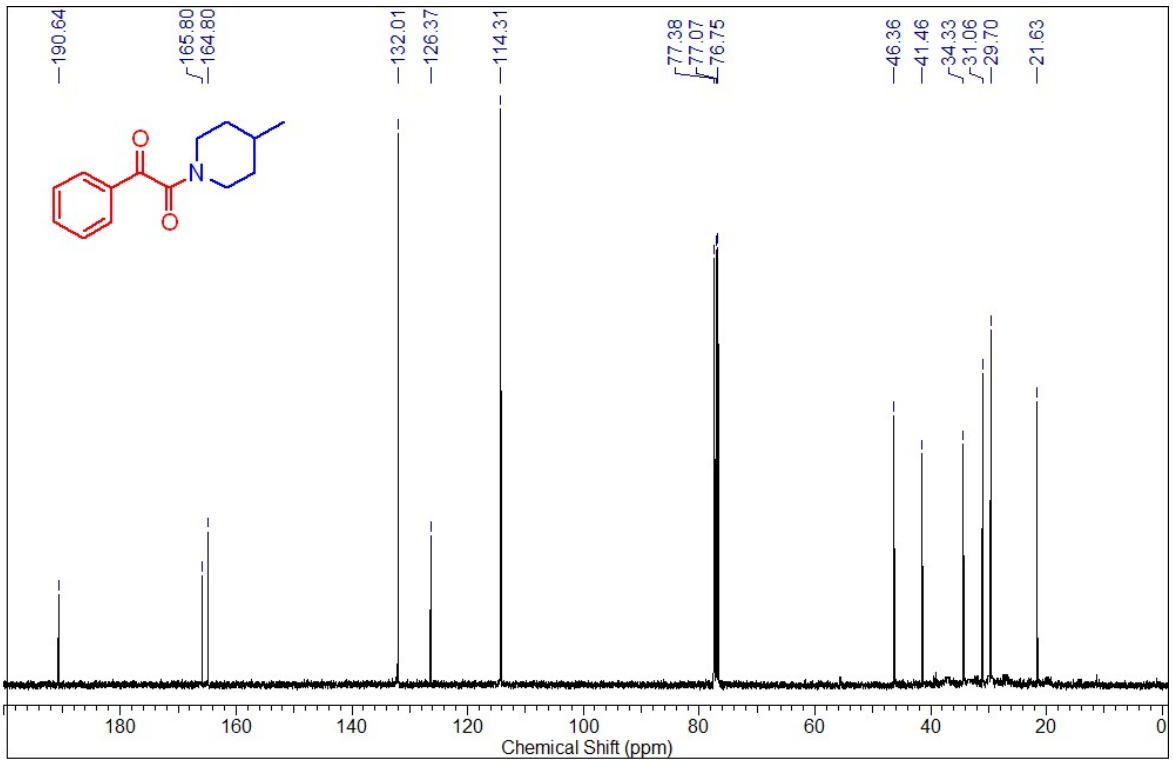


Fig 14: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3d)

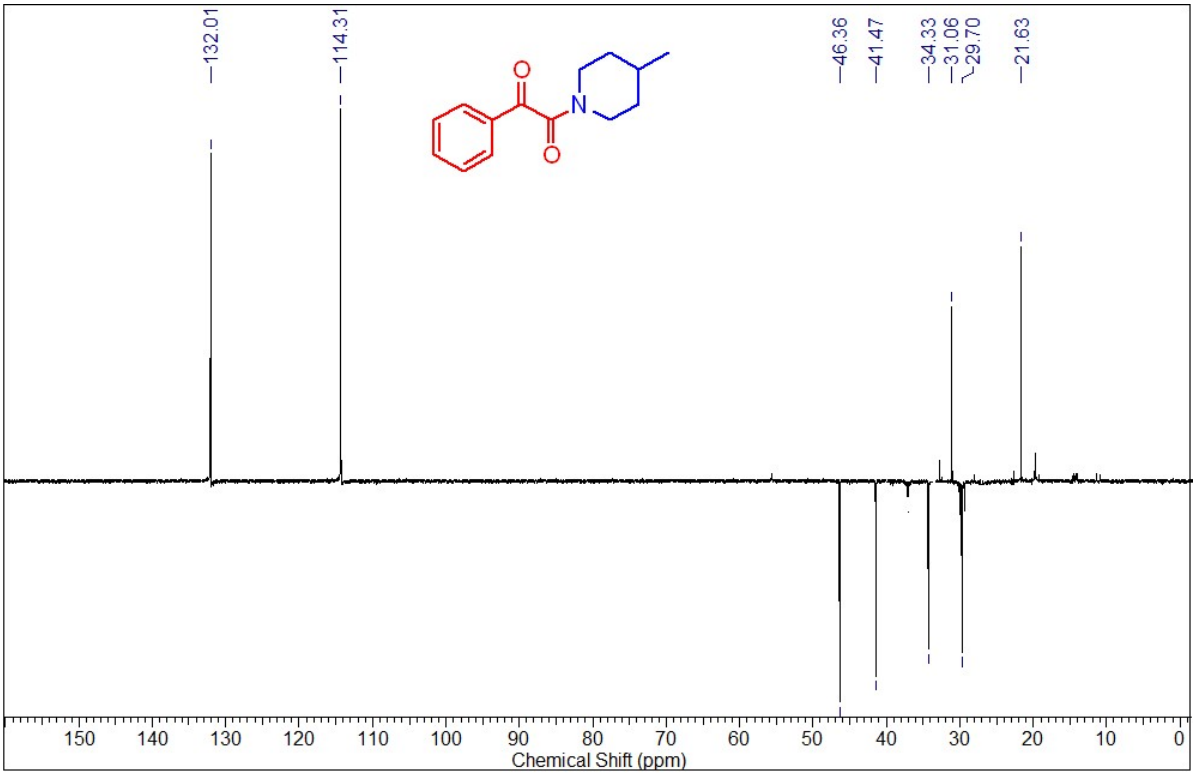


Fig 15: DEPT (100 MHz, $CDCl_3$) of 1-(4-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3d)

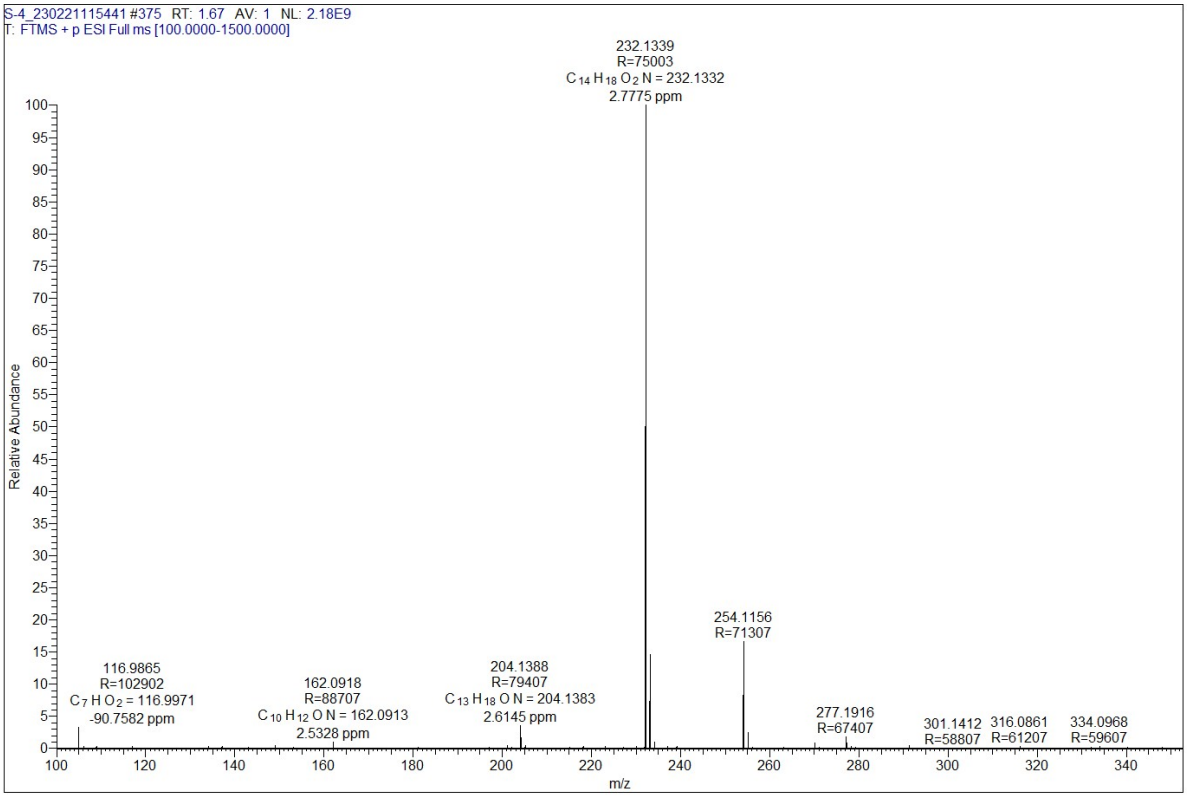


Fig 16: HRMS of 1-(4-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3d)

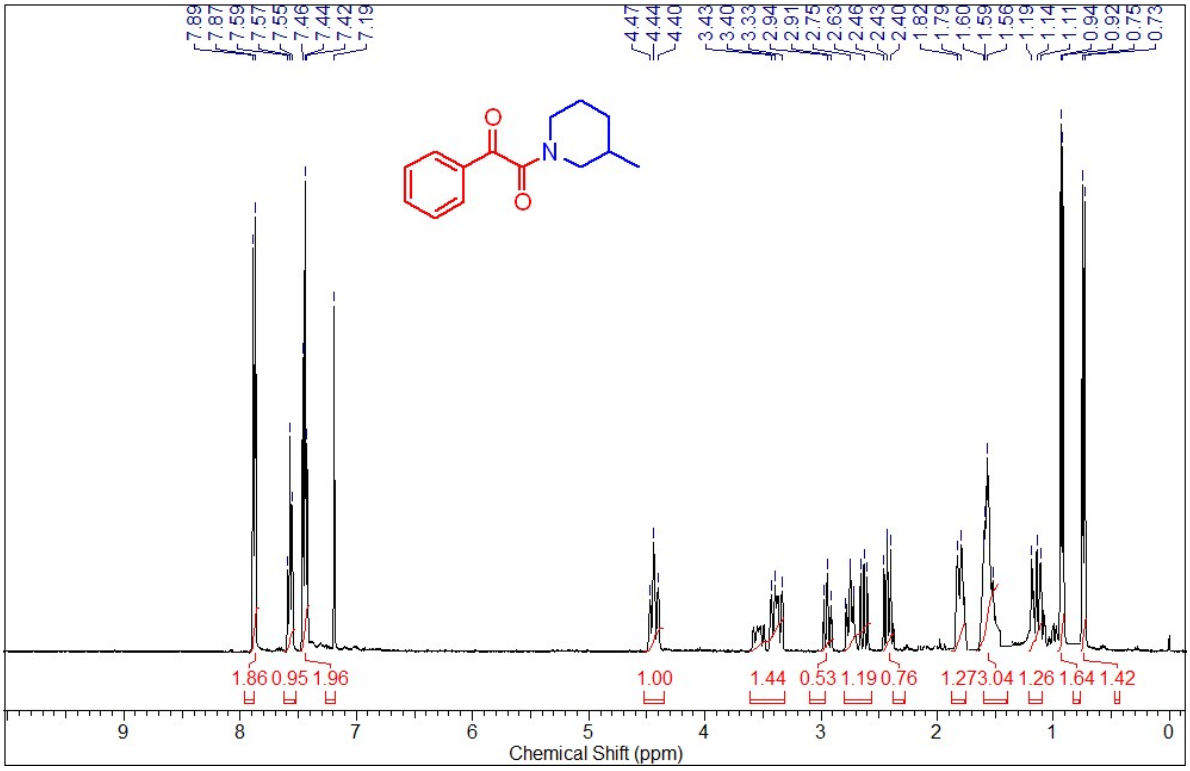


Fig 17: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(3-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3e)

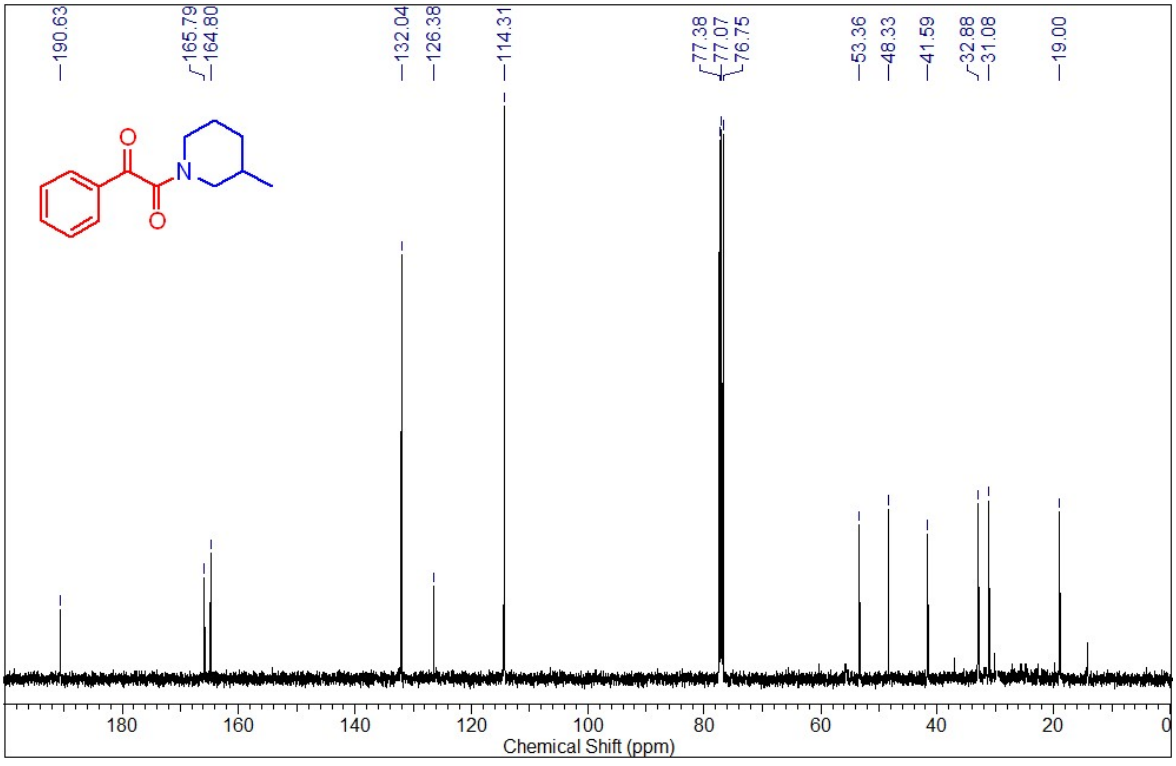


Fig 18: ^{13}C (100 MHz, $CDCl_3$) of 1-(3-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3e)

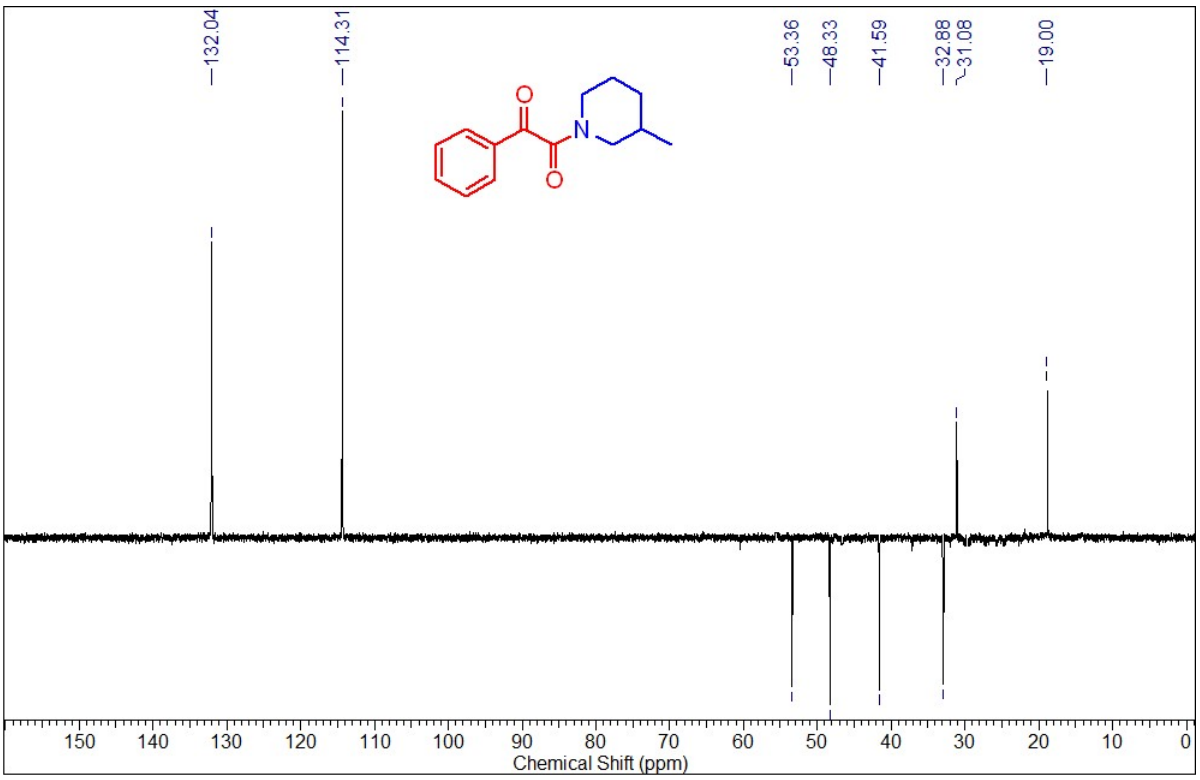


Fig 19: DEPT (100 MHz, $CDCl_3$) of 1-(3-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3e)

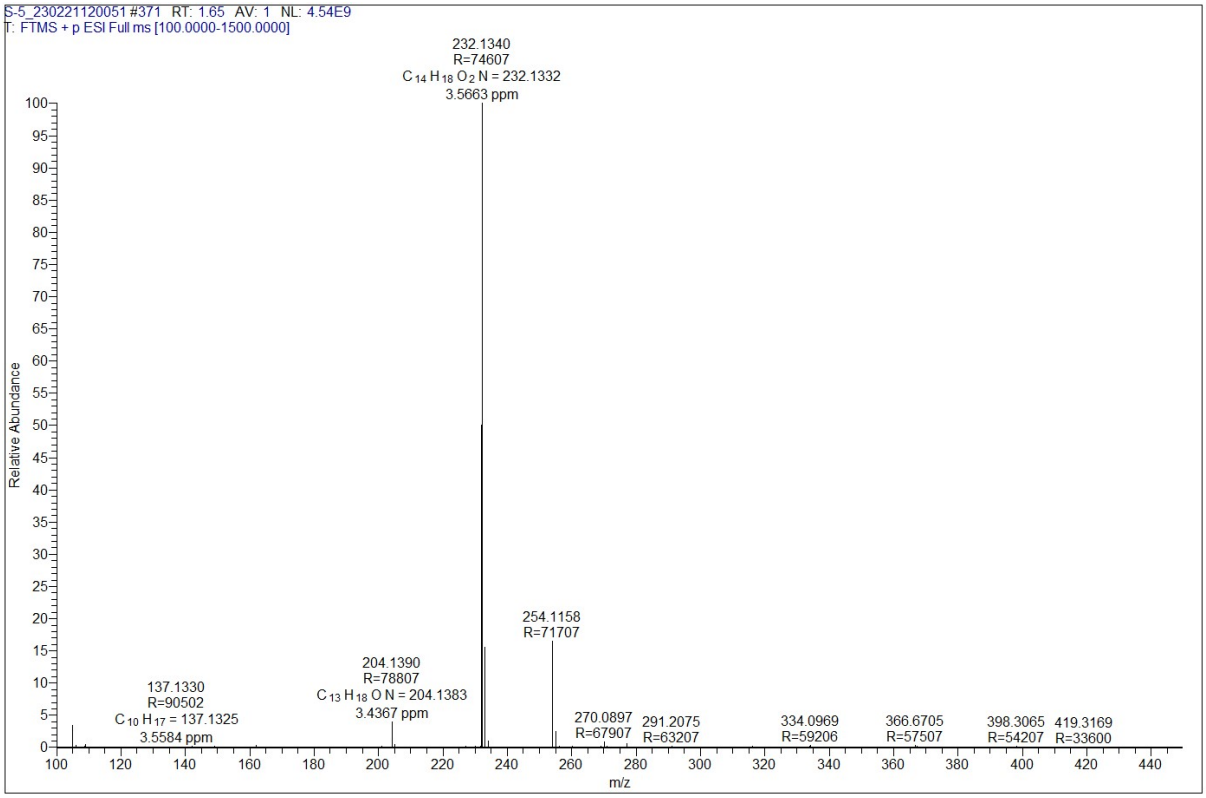


Fig 20: HRMS of 1-(3-methylpiperidine-1-yl)-2-phenylethane-1,2-dione (3e)

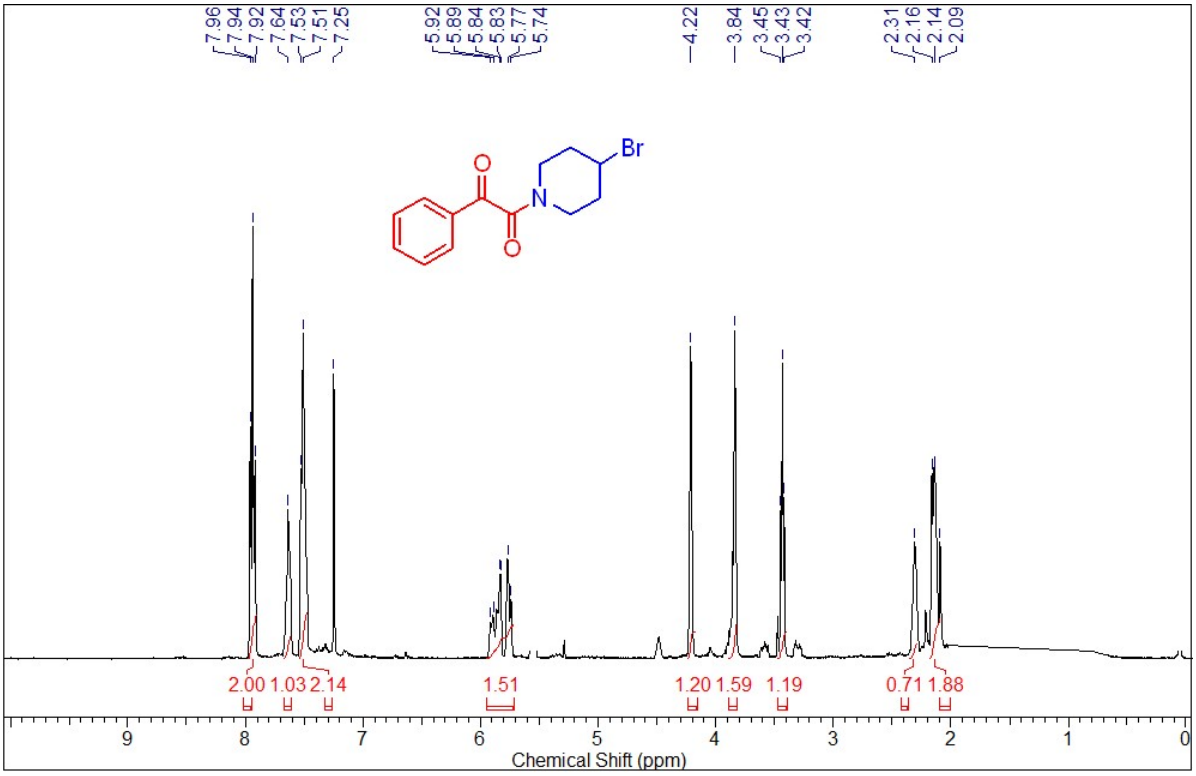


Fig 21: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromopiperidine-1-yl)-2-phenylethane-1,2-dione(3f)

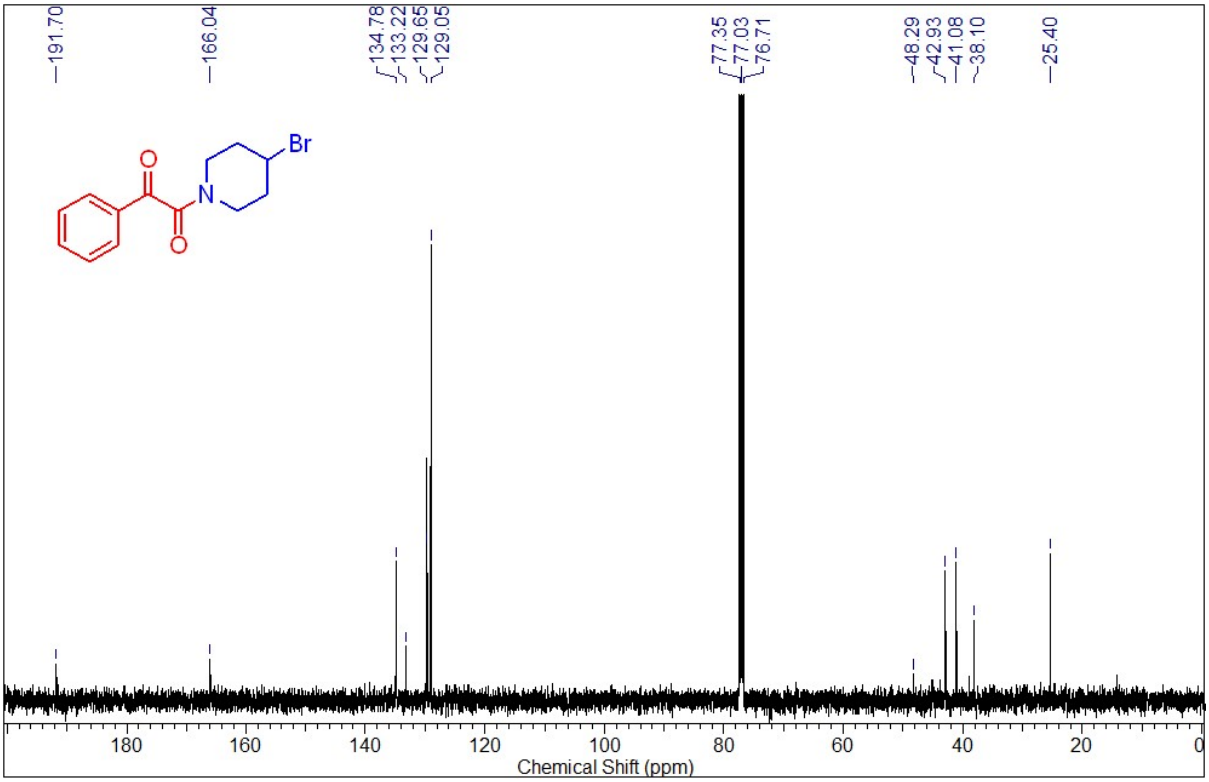


Fig 22: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromopiperidine-1-yl)-2-phenylethane-1,2-dione (3f)

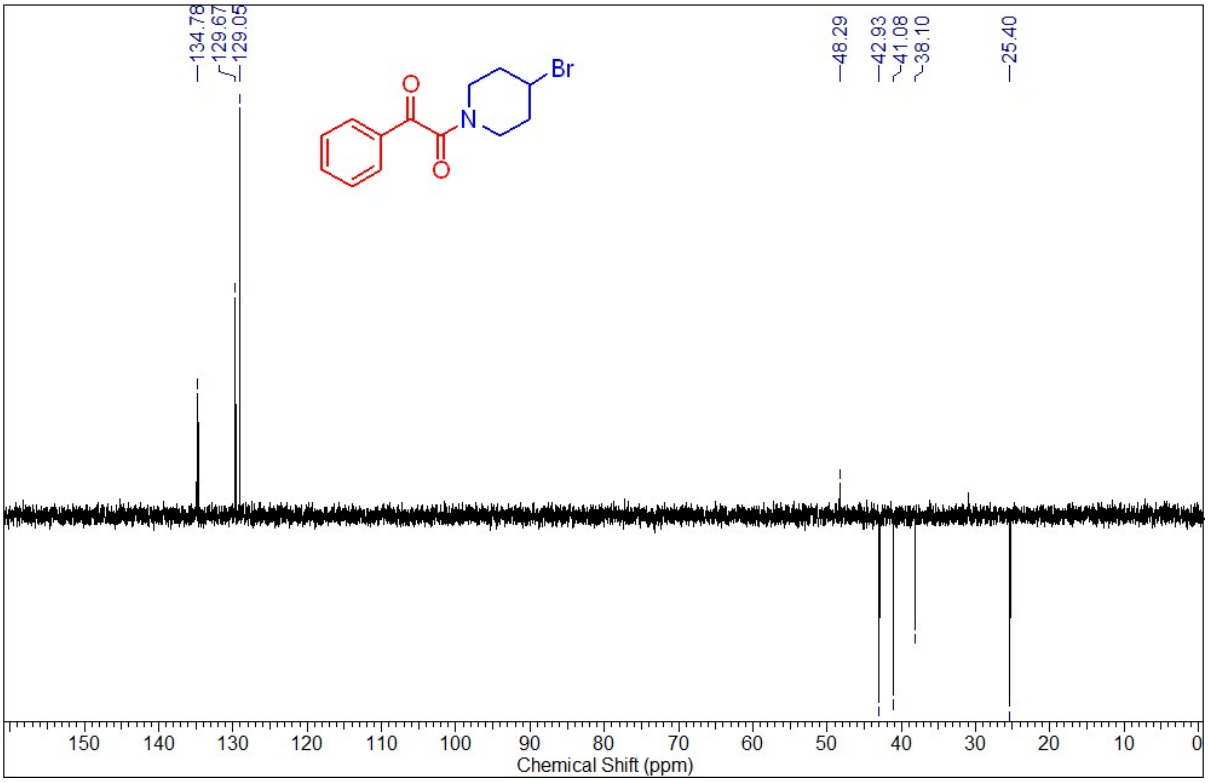


Fig 23: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromopiperidine-1-yl)-2-phenylethane-1,2-dione (3f)

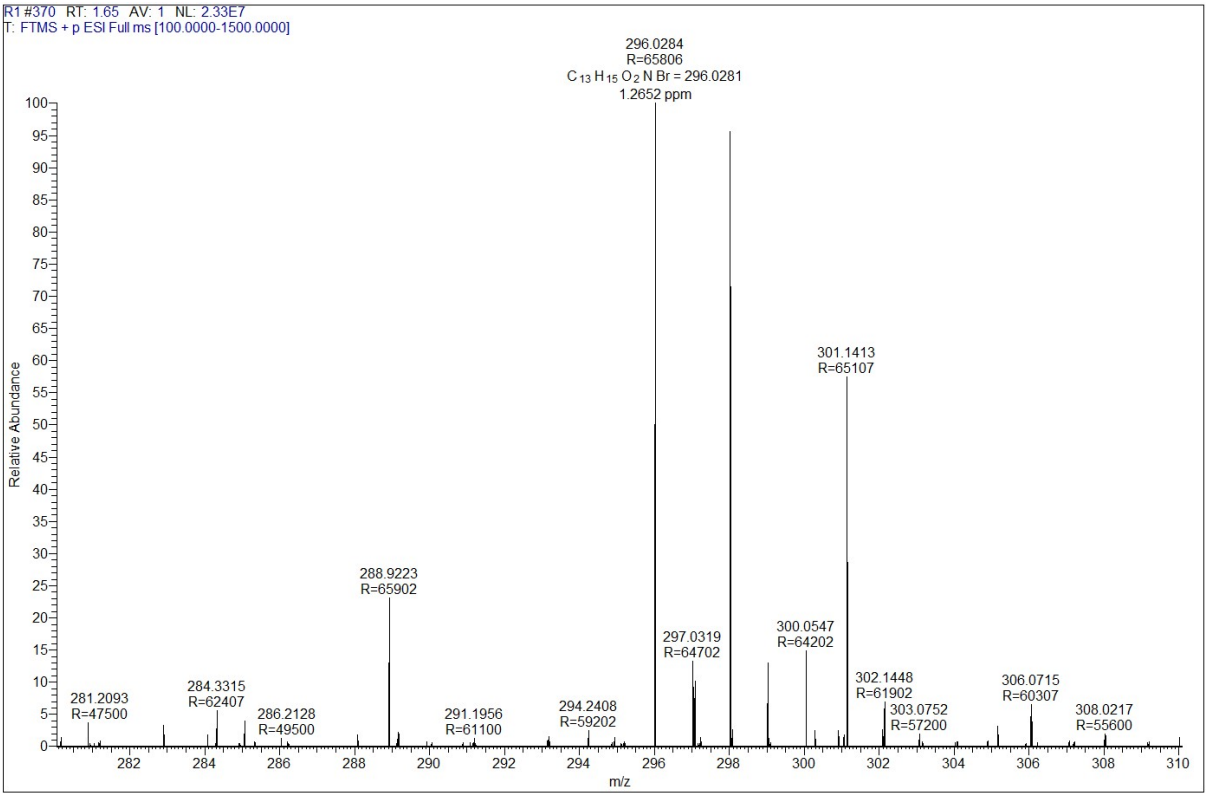


Fig 24: HRMS of 1-(4-bromopiperidine-1-yl)-2-phenylethane-1,2-dione (3f)

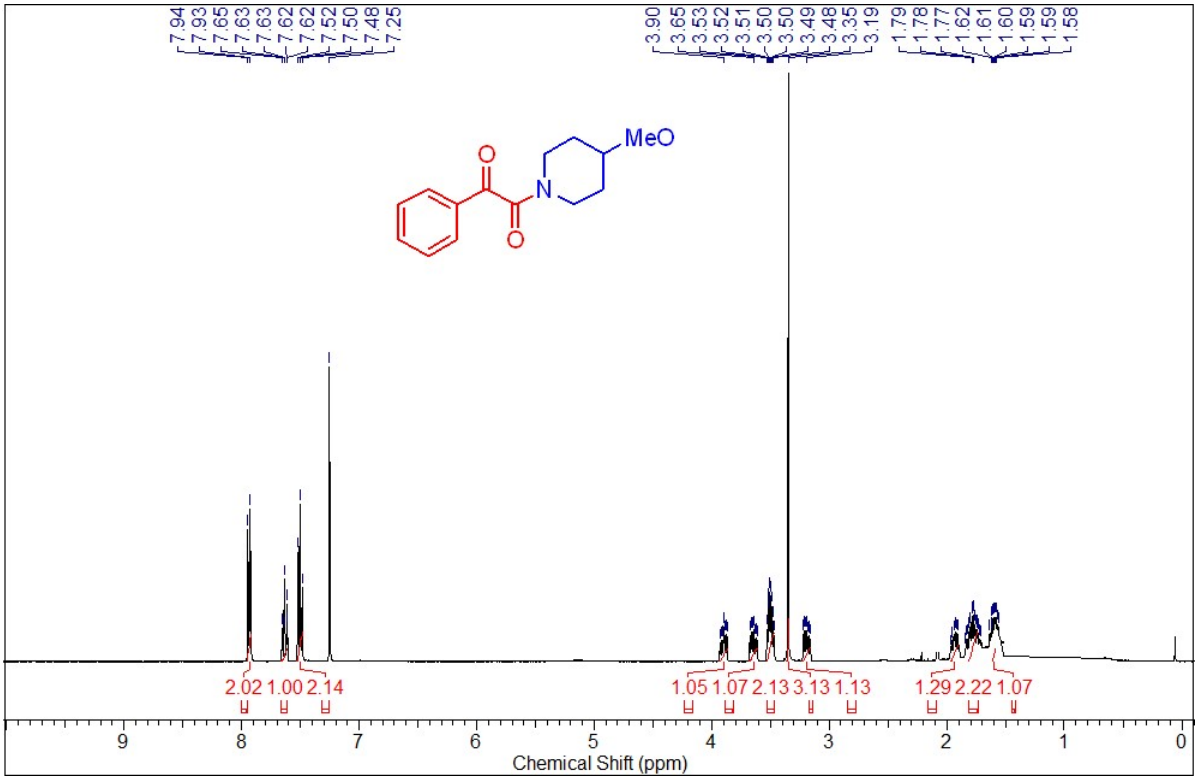


Fig 25: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methoxypiperidine-1-yl)-2-phenylethane-1,2-dione (3g)

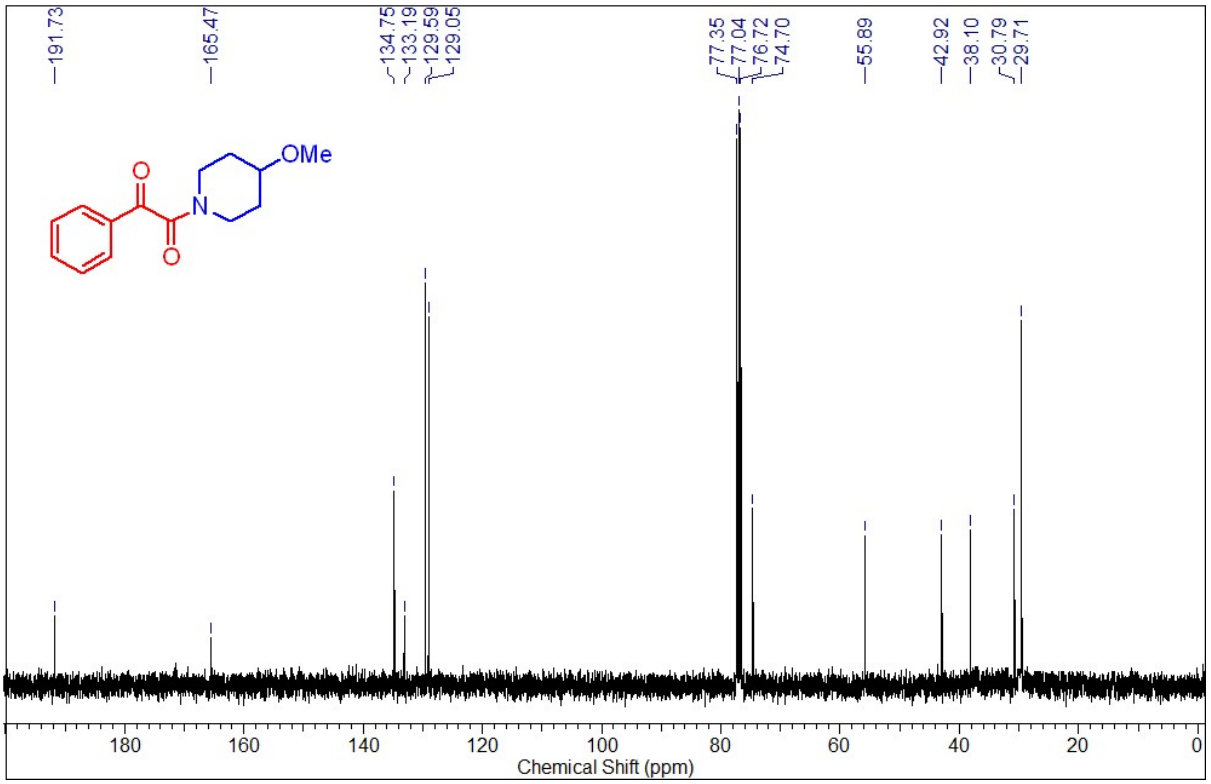


Fig 26: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methoxypiperidine-1-yl)-2-phenylethane-1,2-dione (3g)

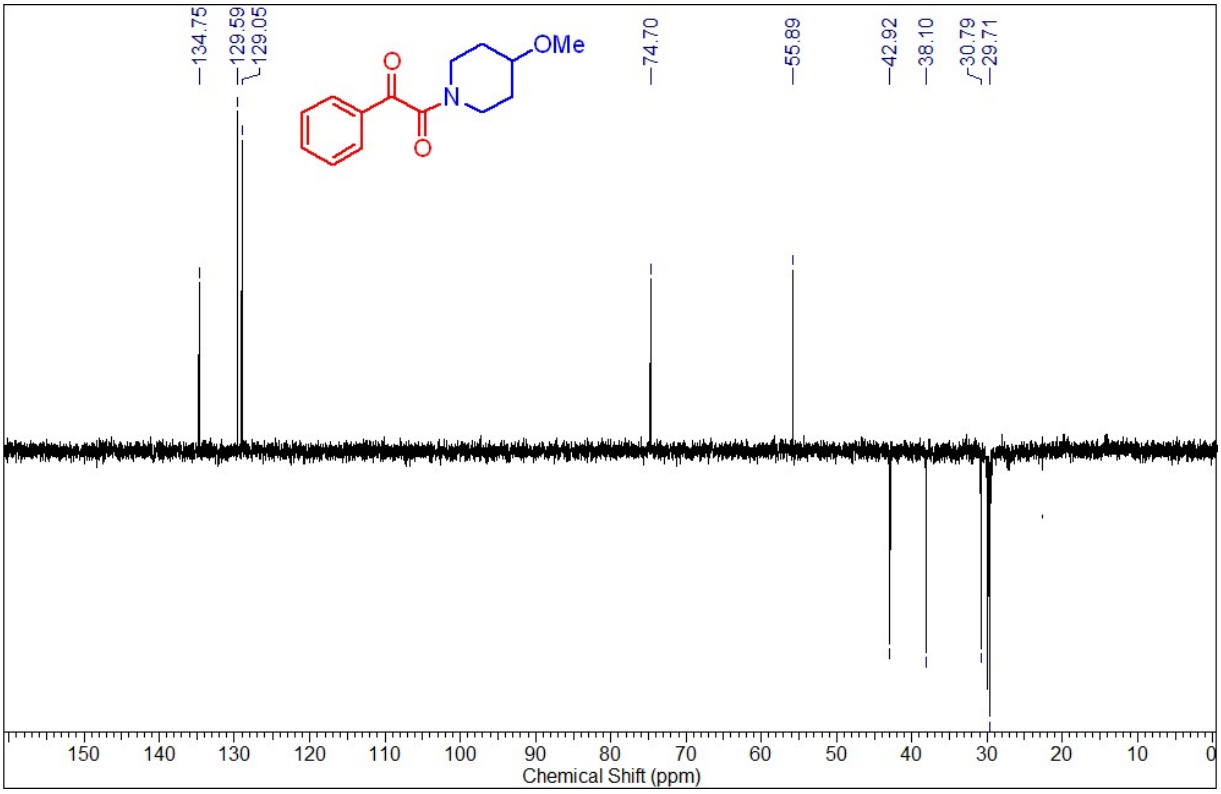


Fig 27: DEPT (100 MHz, $CDCl_3$) of 1-(4-methoxypiperidine-1-yl)-2-phenylethane-1,2-dione (3g)

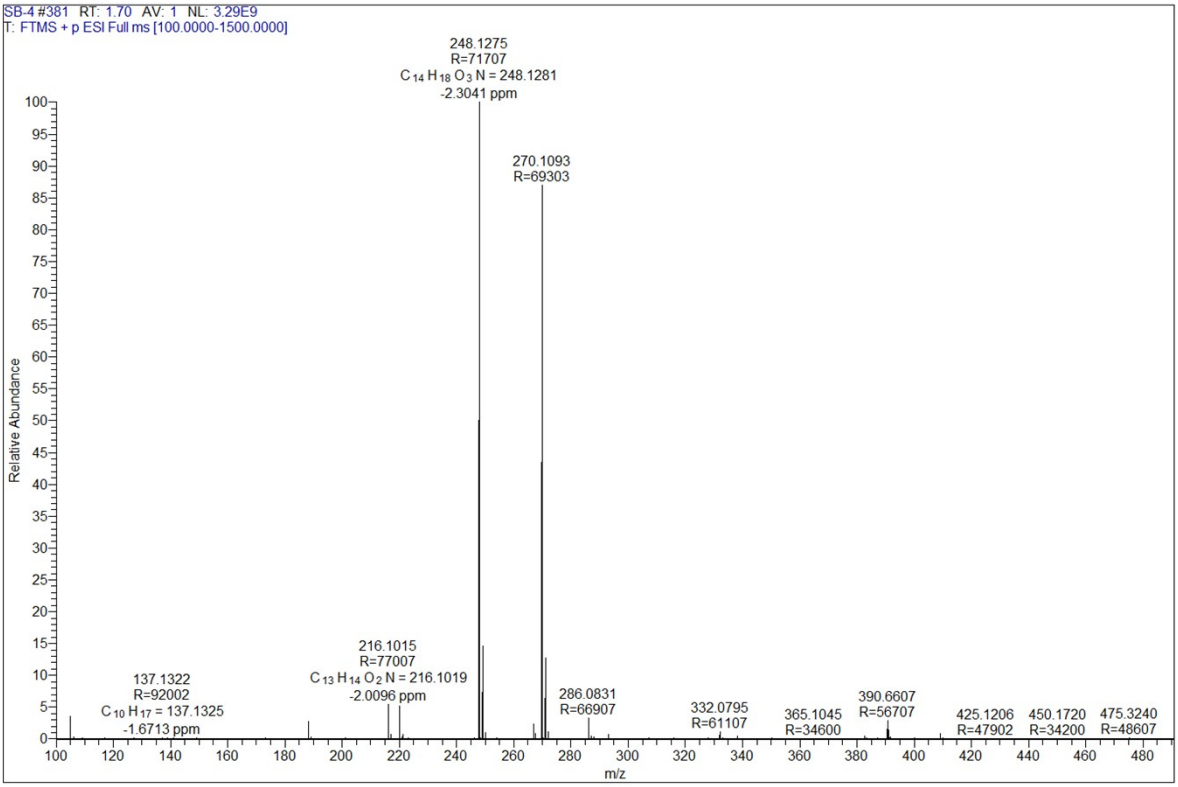


Fig 28: HRMS of 1-(4-methoxypiperidine-1-yl)-2-phenylethane-1,2-dione (3g)

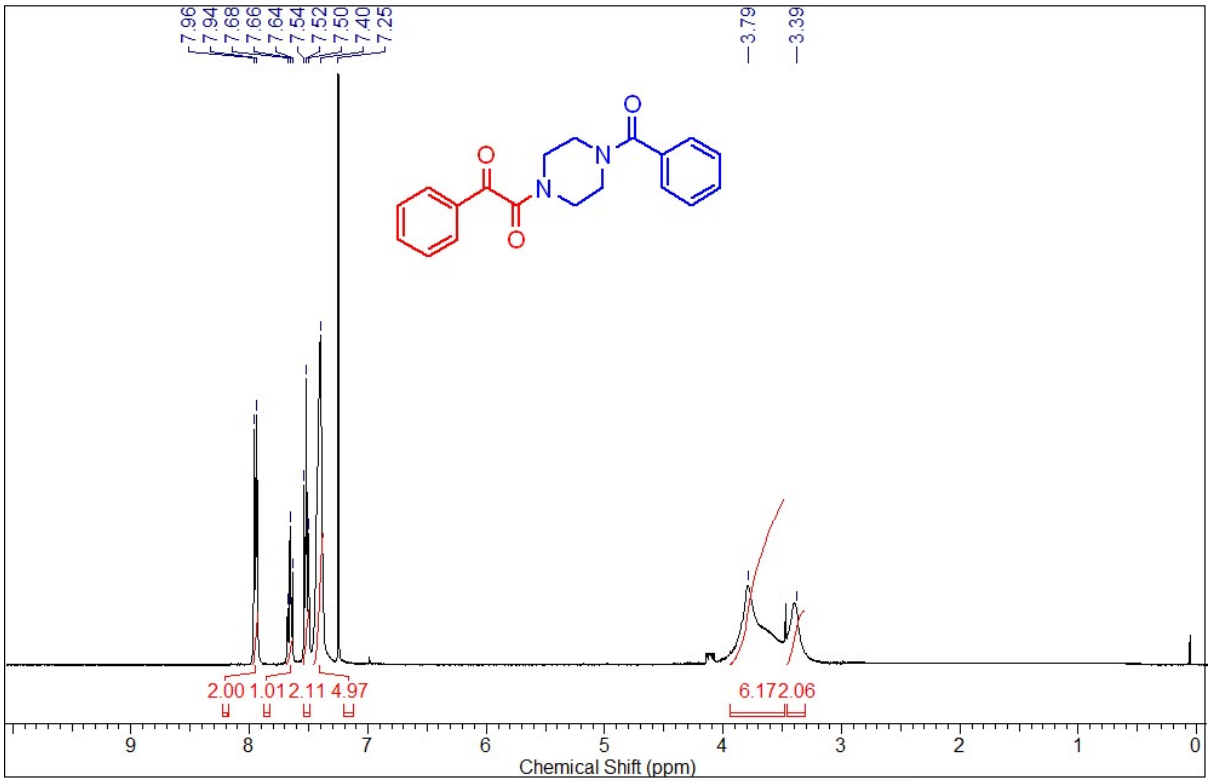


Fig 29: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-phenylethane-1,2-dione (3h)

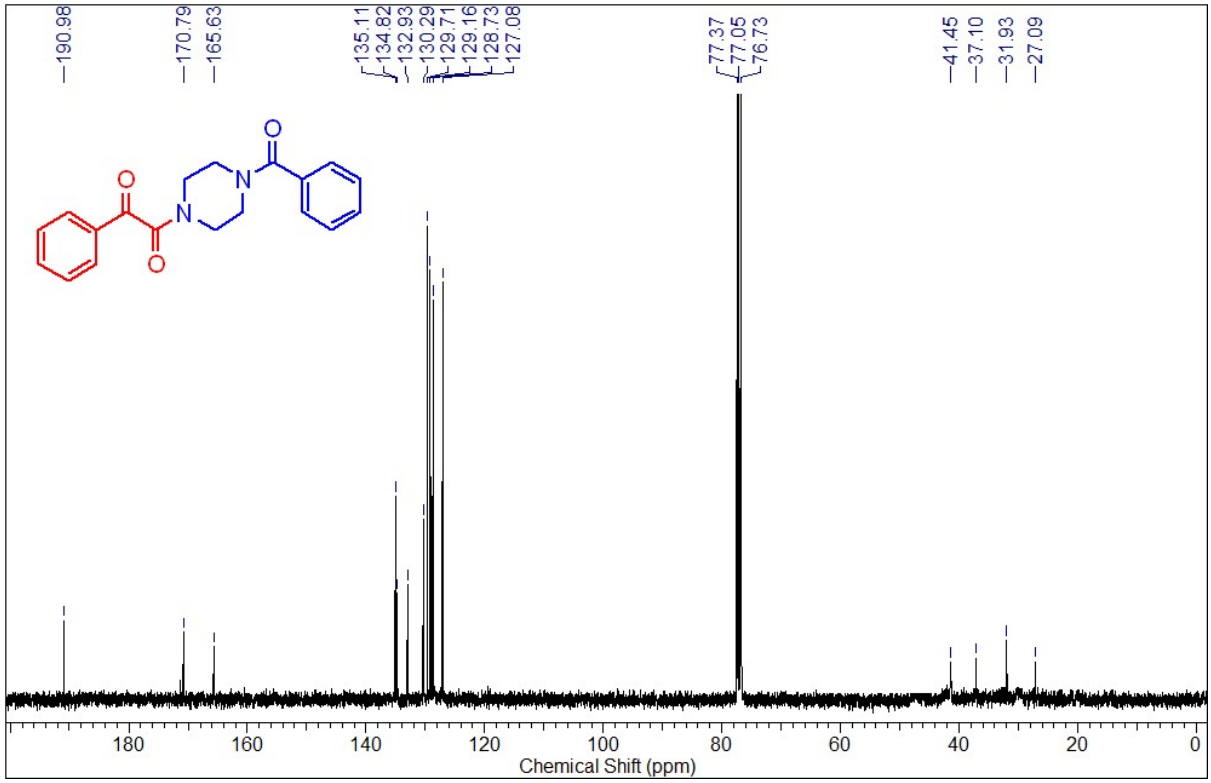


Fig 30: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-phenylethane-1,2-dione (3h)

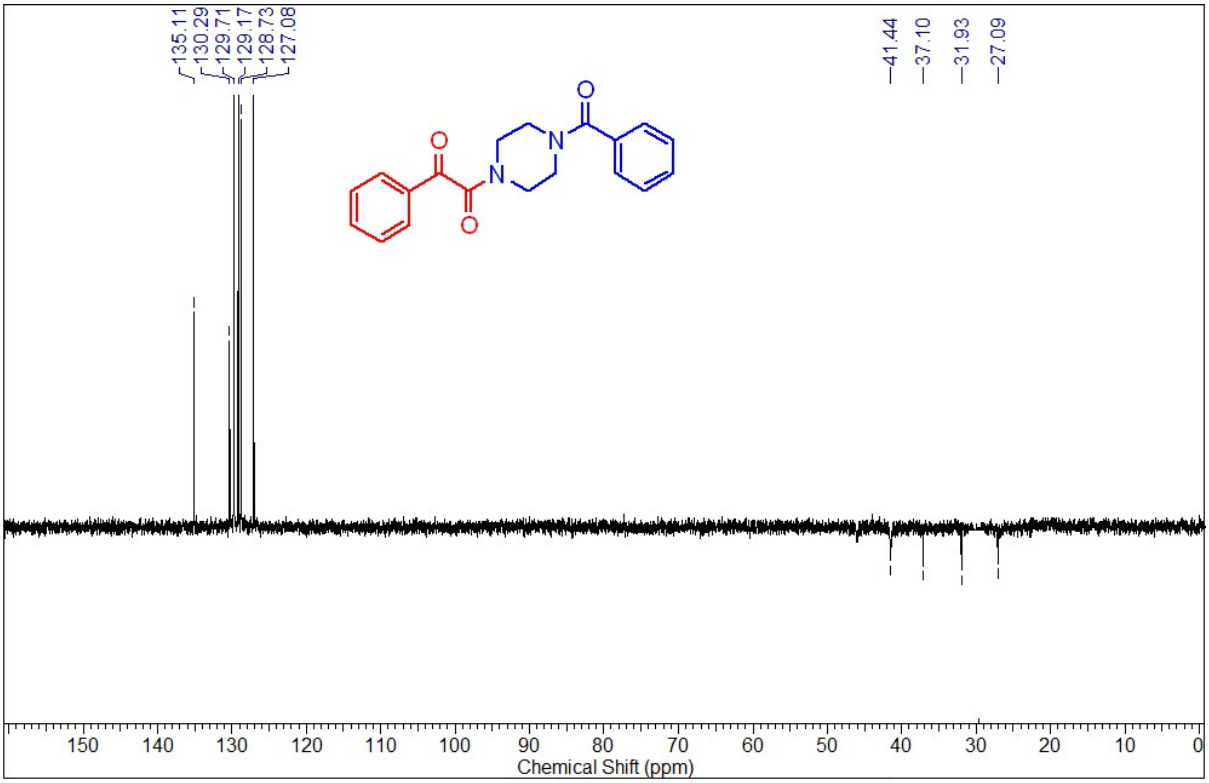


Fig 31: DEPT (100 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-phenylethane-1,2-dione (3h)

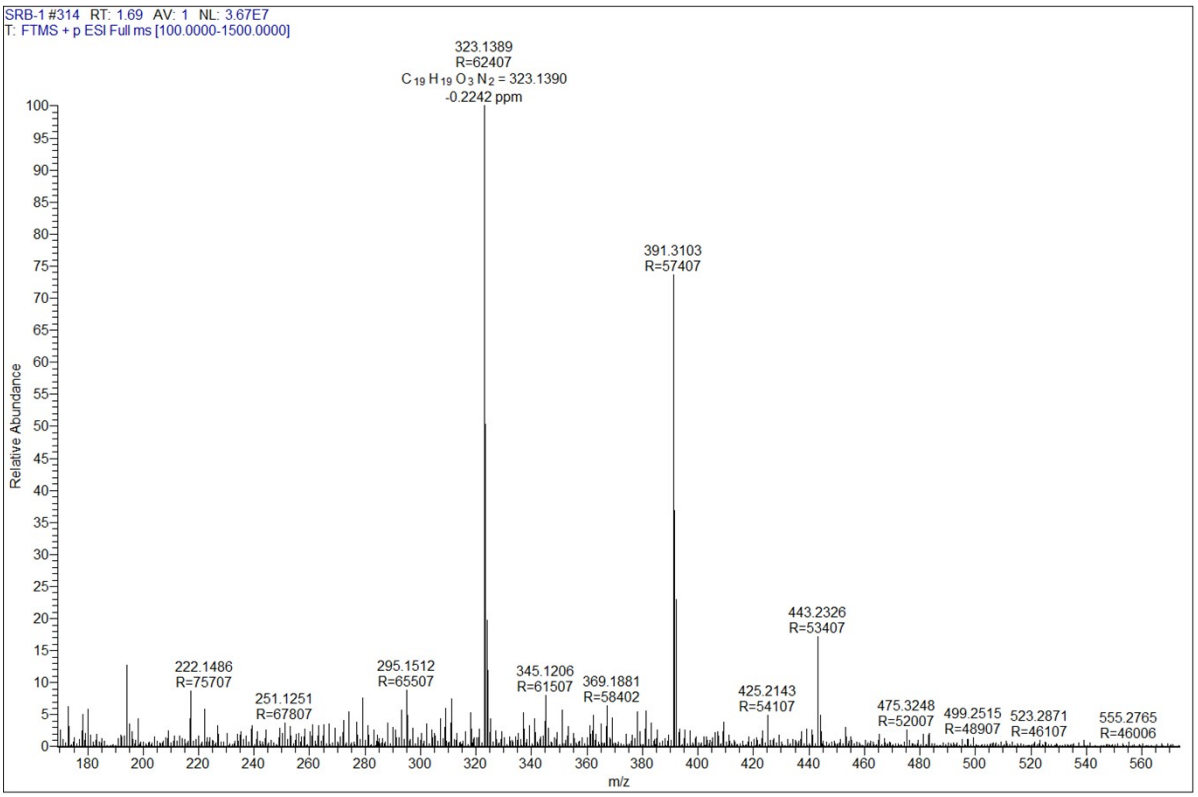


Fig 32: HRMS of 1-(4-Benzoyl-1-piperazinyl)-2-phenylethane-1,2-dione (3h)

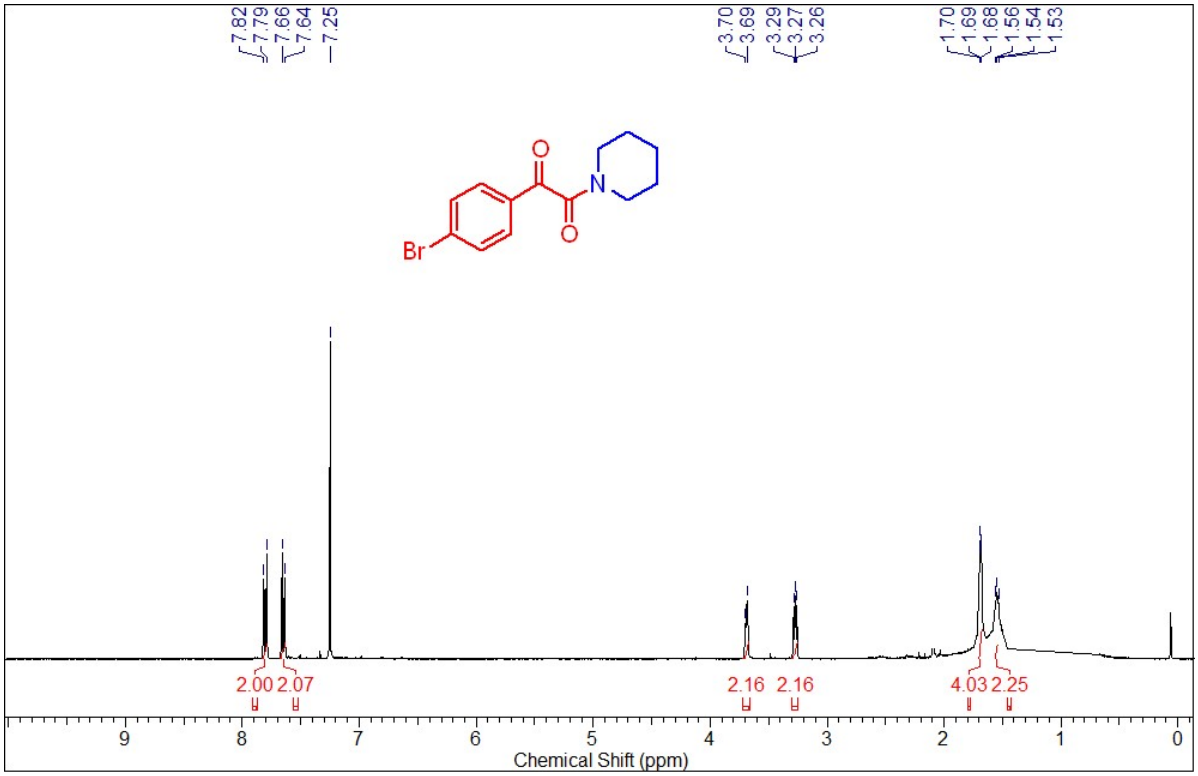


Fig 33: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3i)

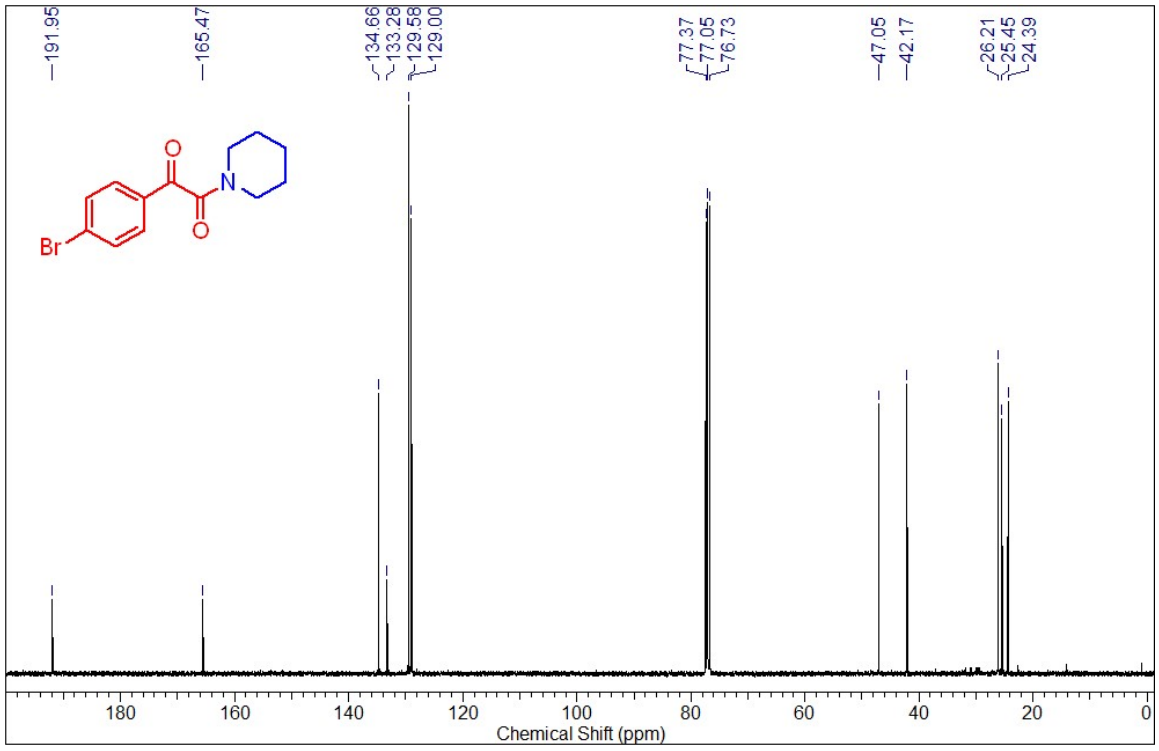


Fig 34: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3i)

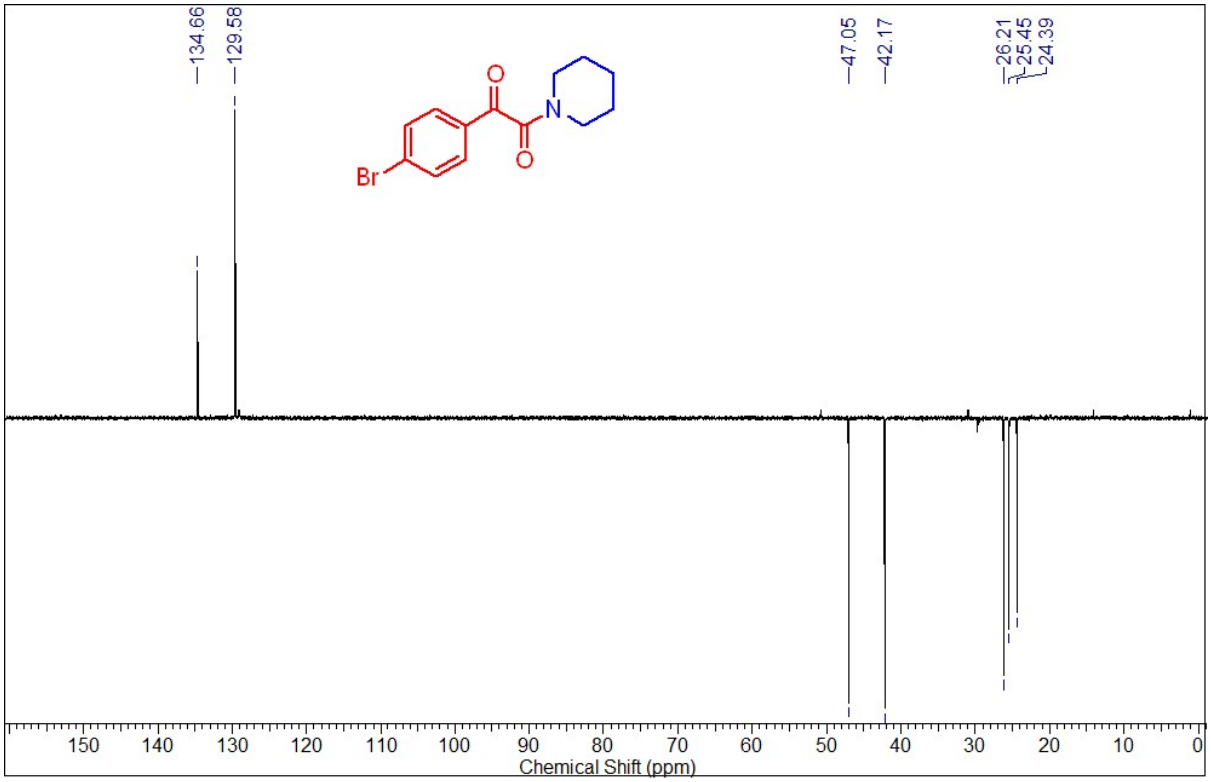


Fig 35: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3i)

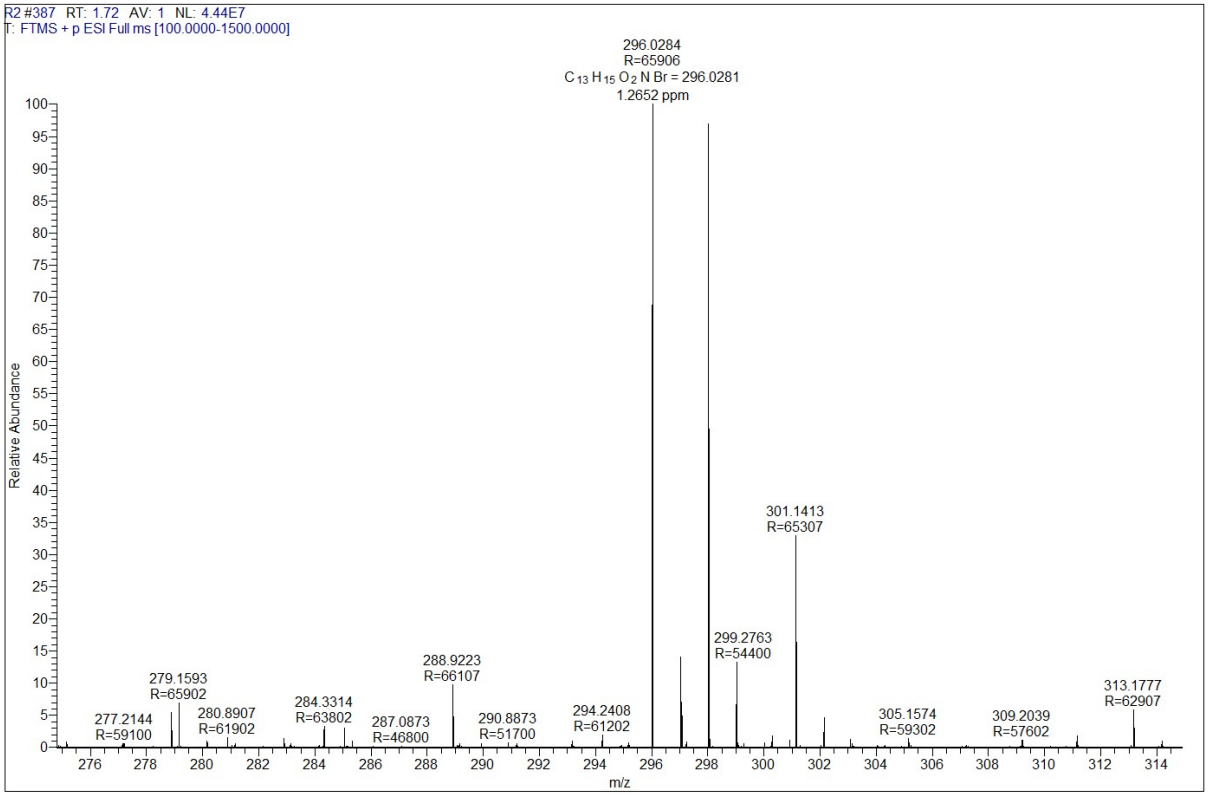


Fig 36: HRMS of 1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3i)

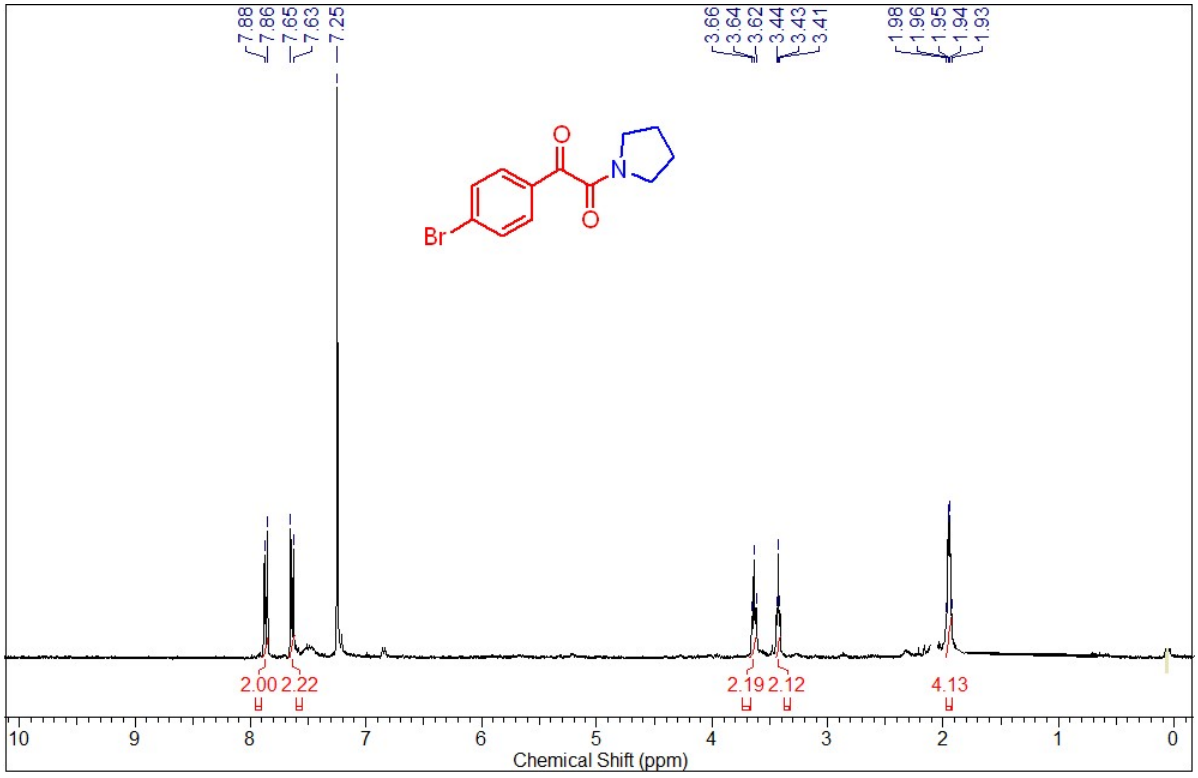


Fig 37: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione(3j)

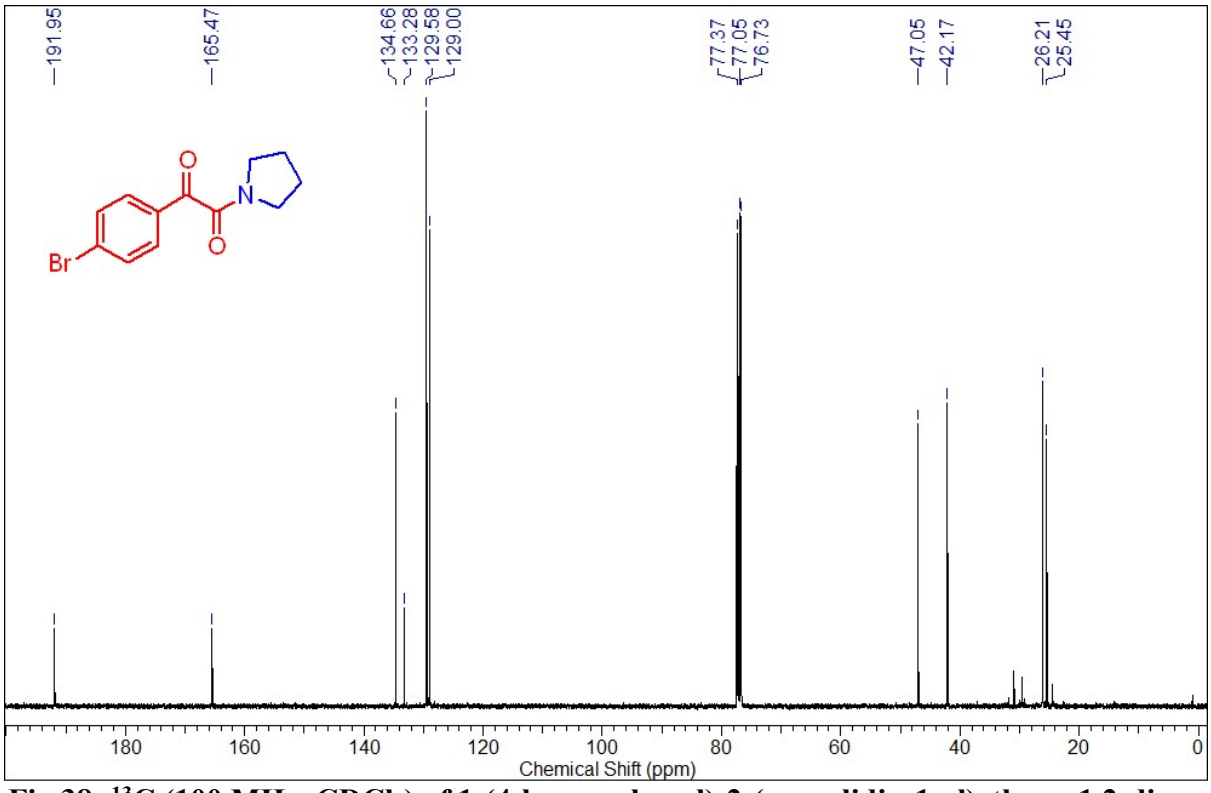


Fig 38: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3j)

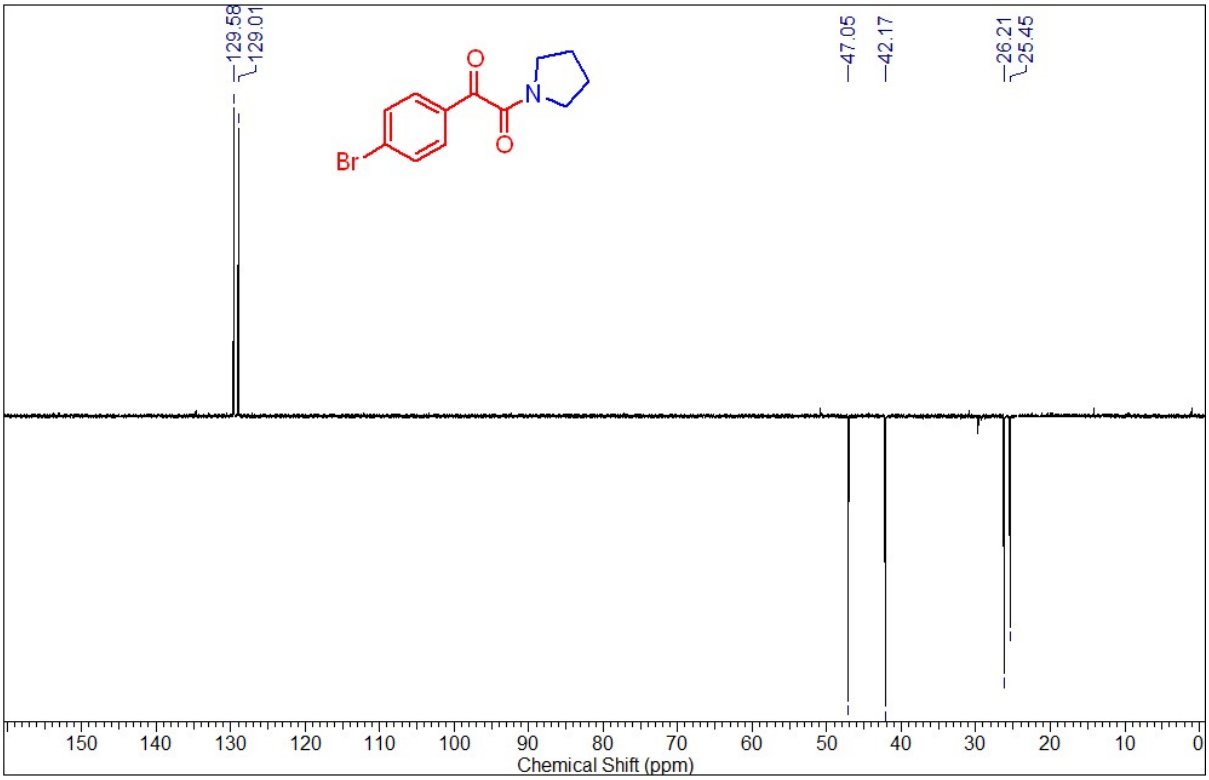


Fig 39: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3j)

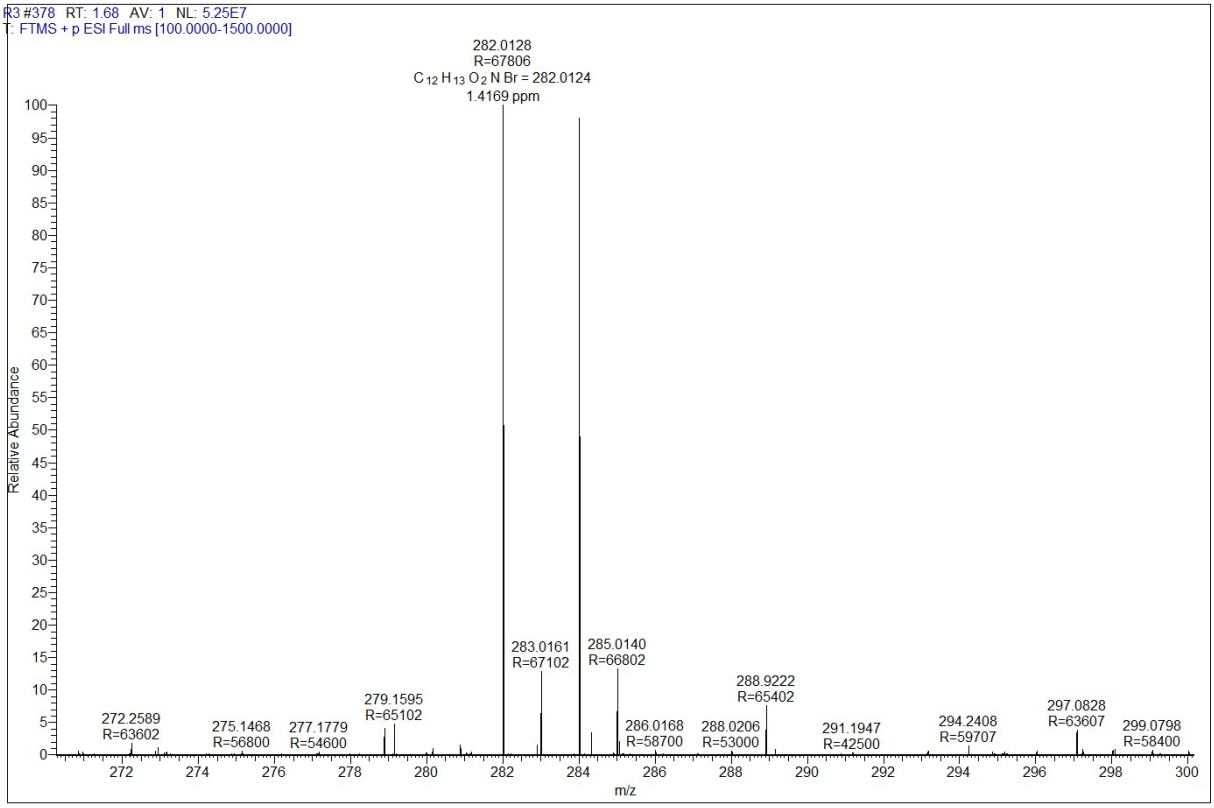


Fig 40: HRMS of 1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3j)

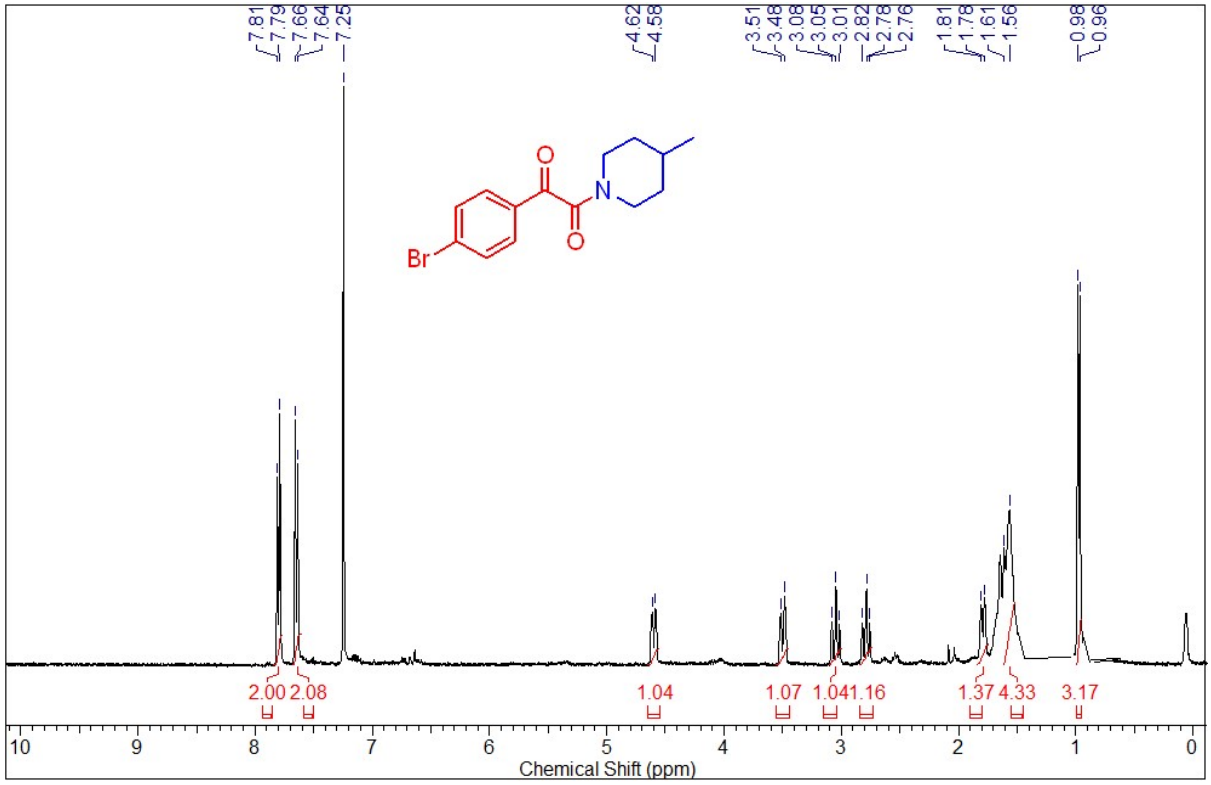


Fig 41: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3k)

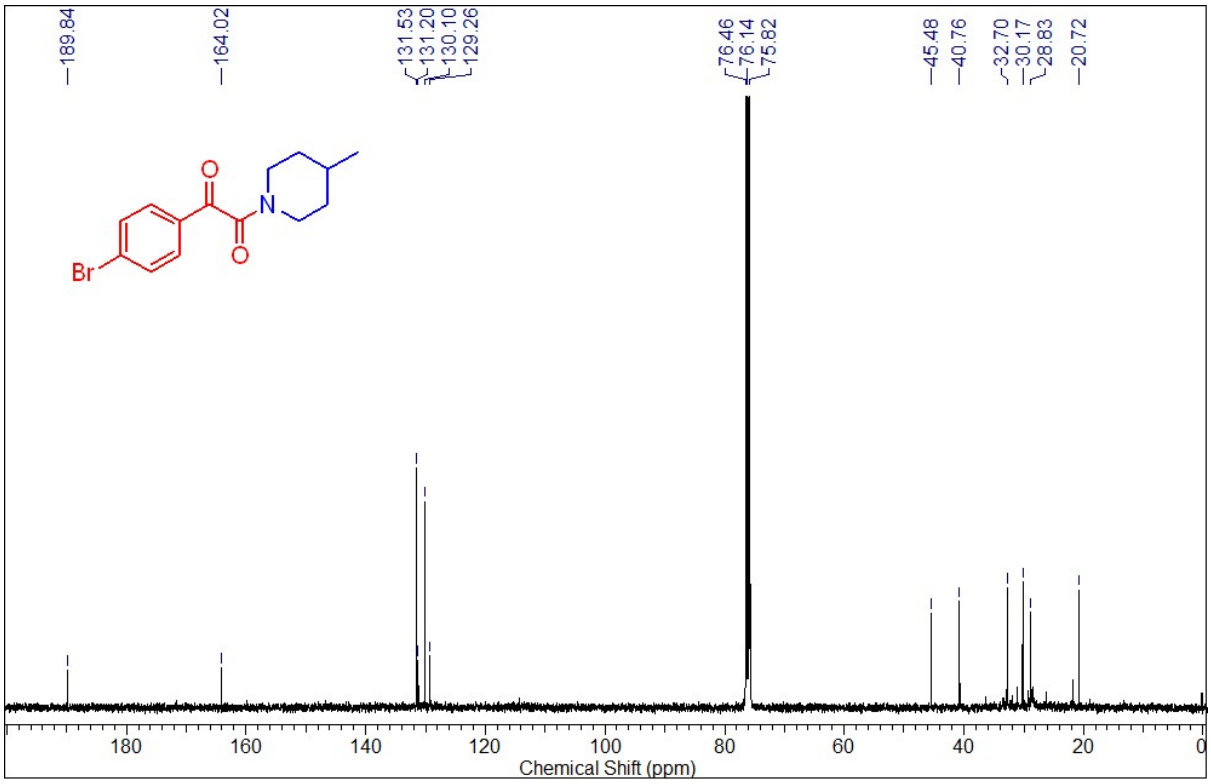


Fig 42: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3k)

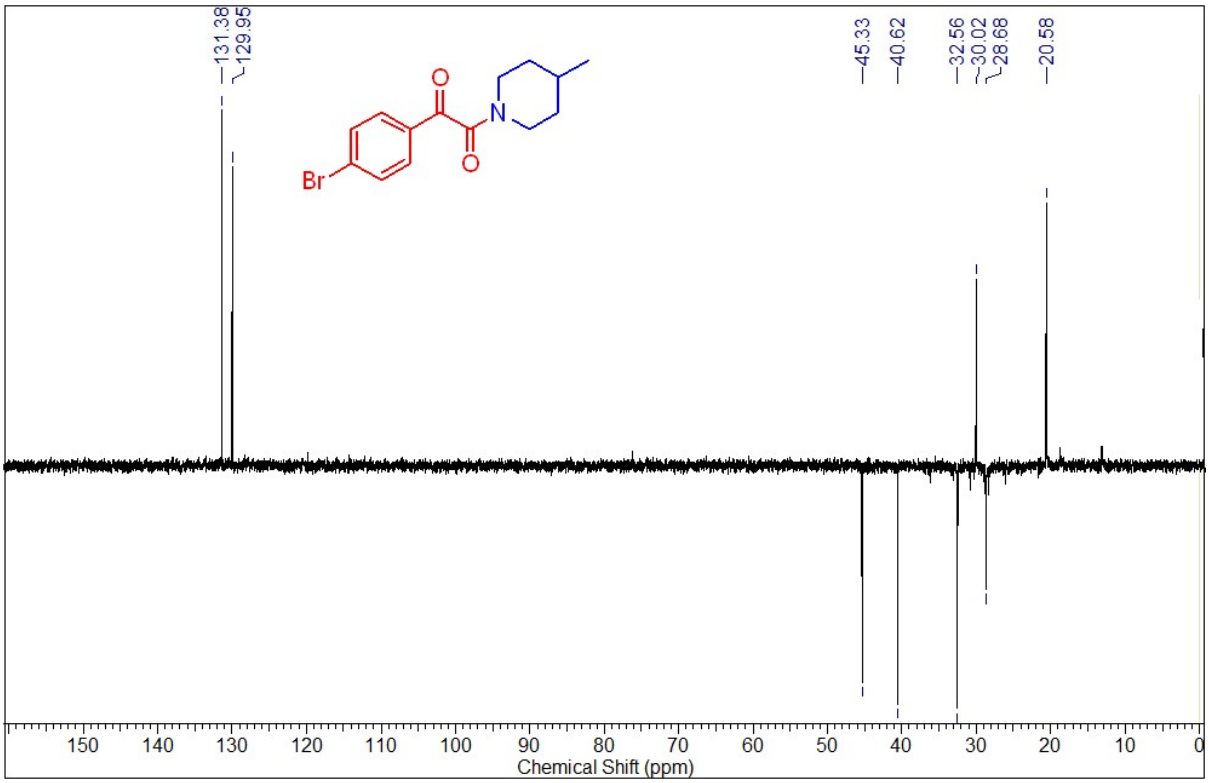


Fig 43: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3k)

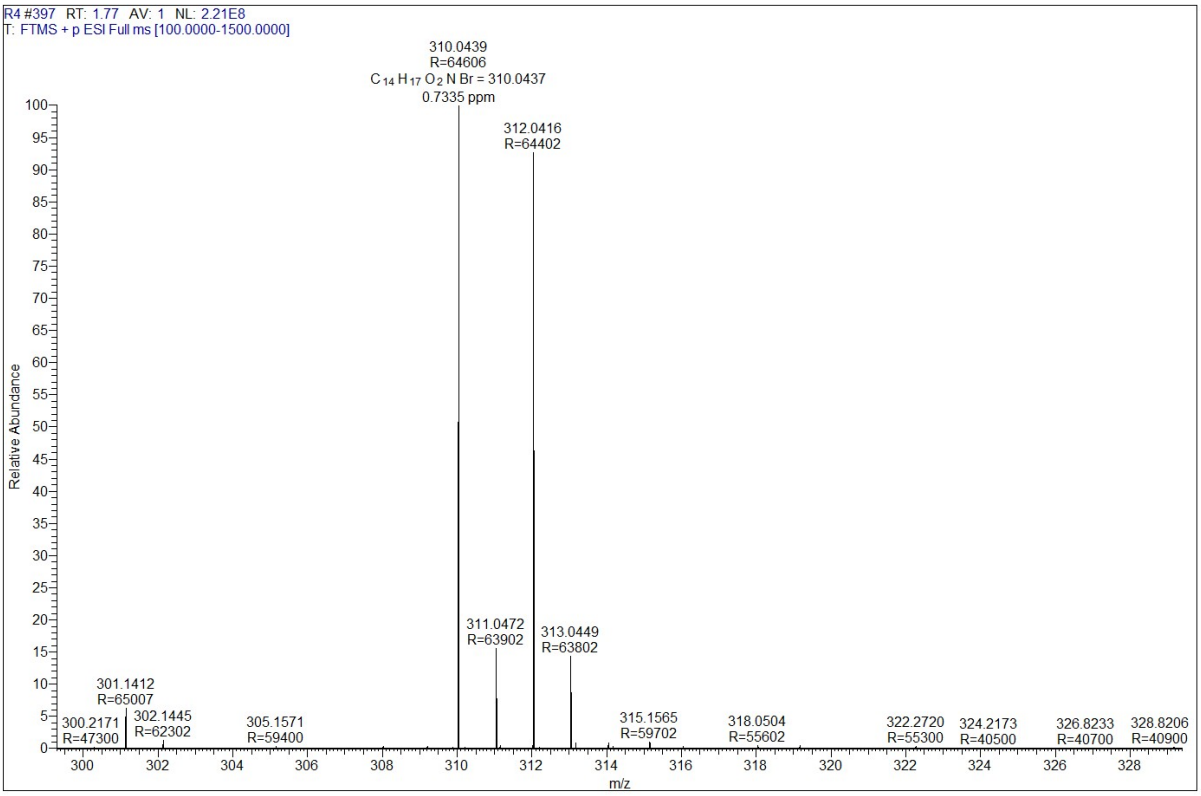


Fig 44: HRMS of 1-(4-bromophenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3k)

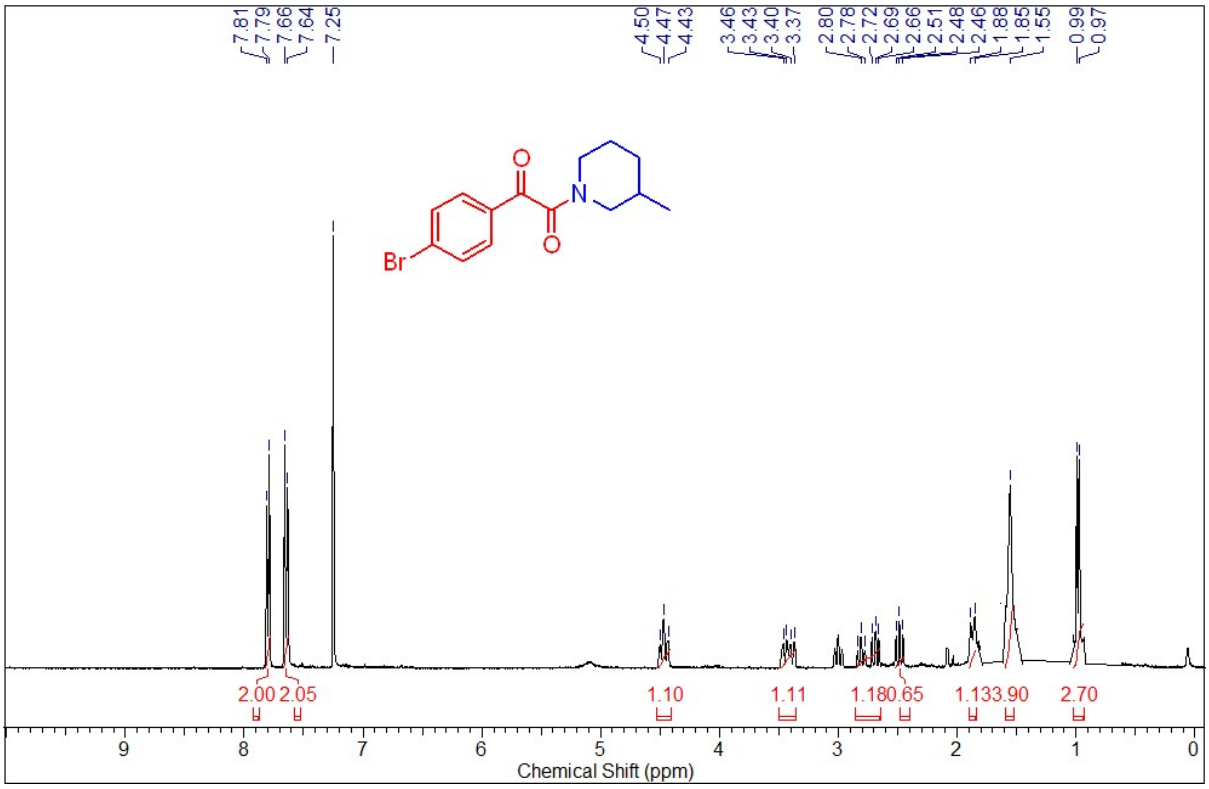


Fig 45: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3l)

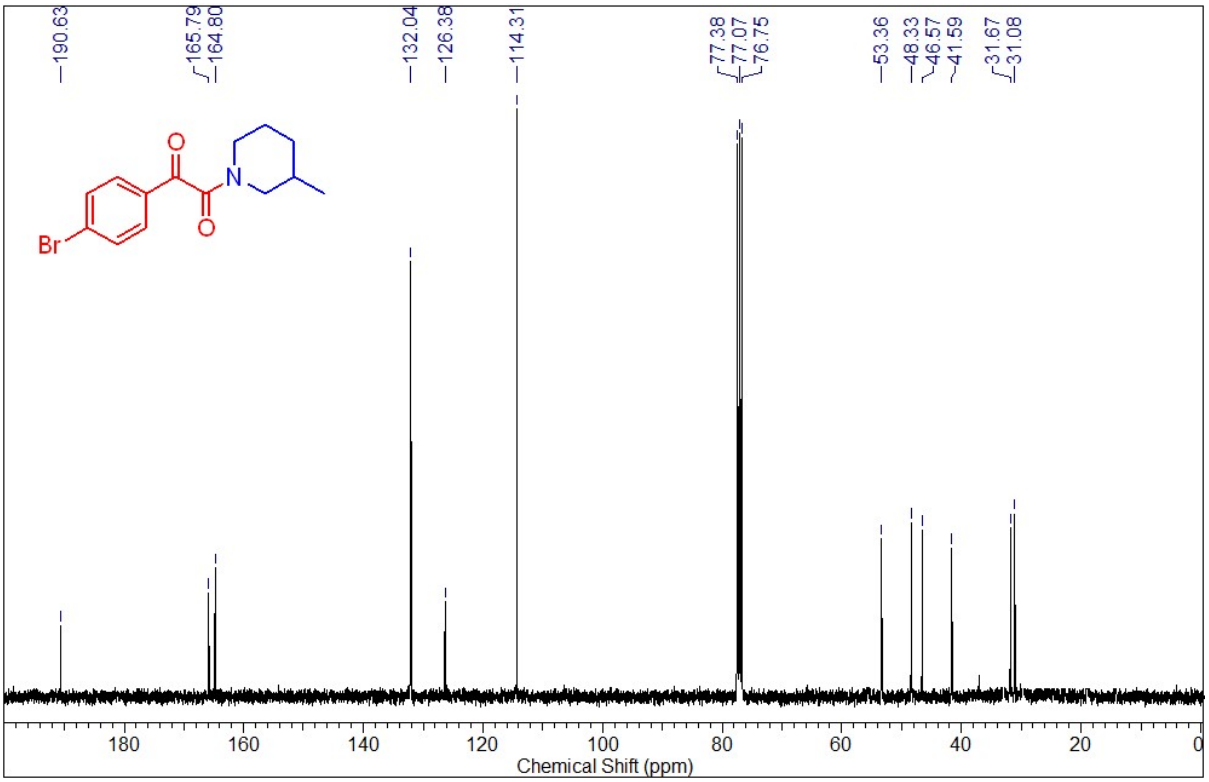


Fig 46: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3l)

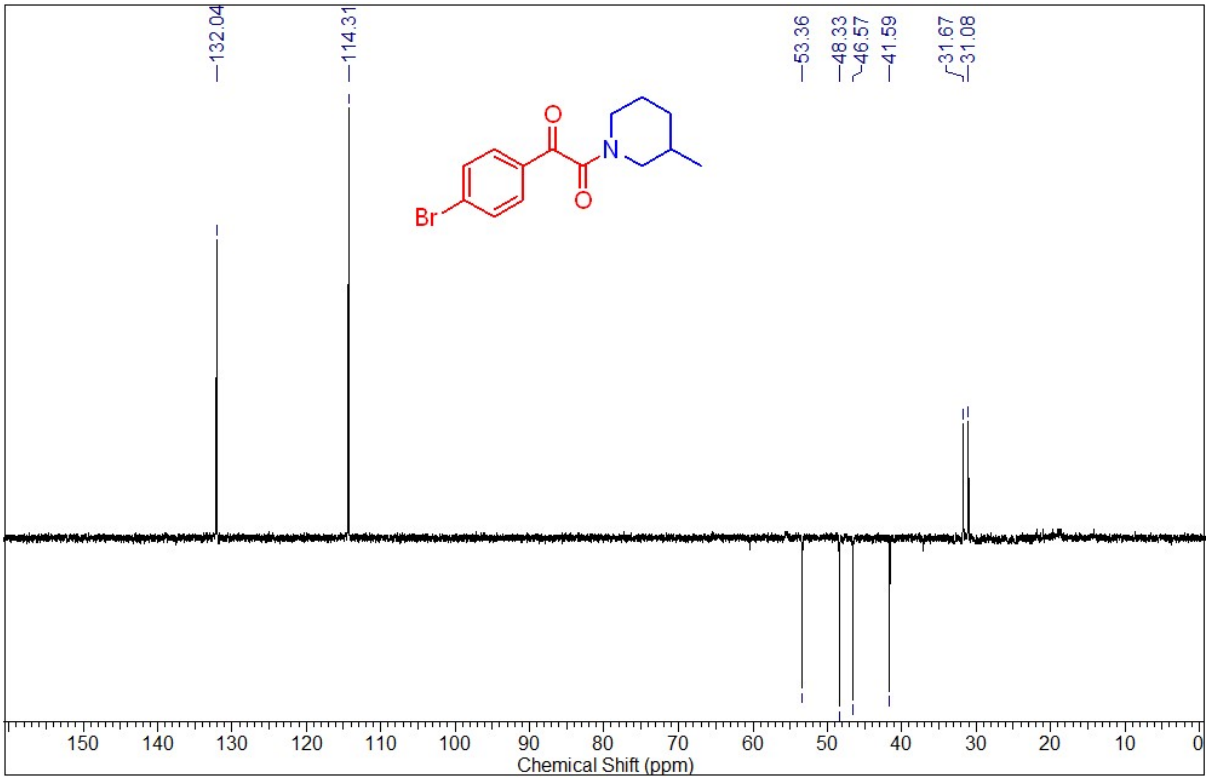


Fig 47: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3l)

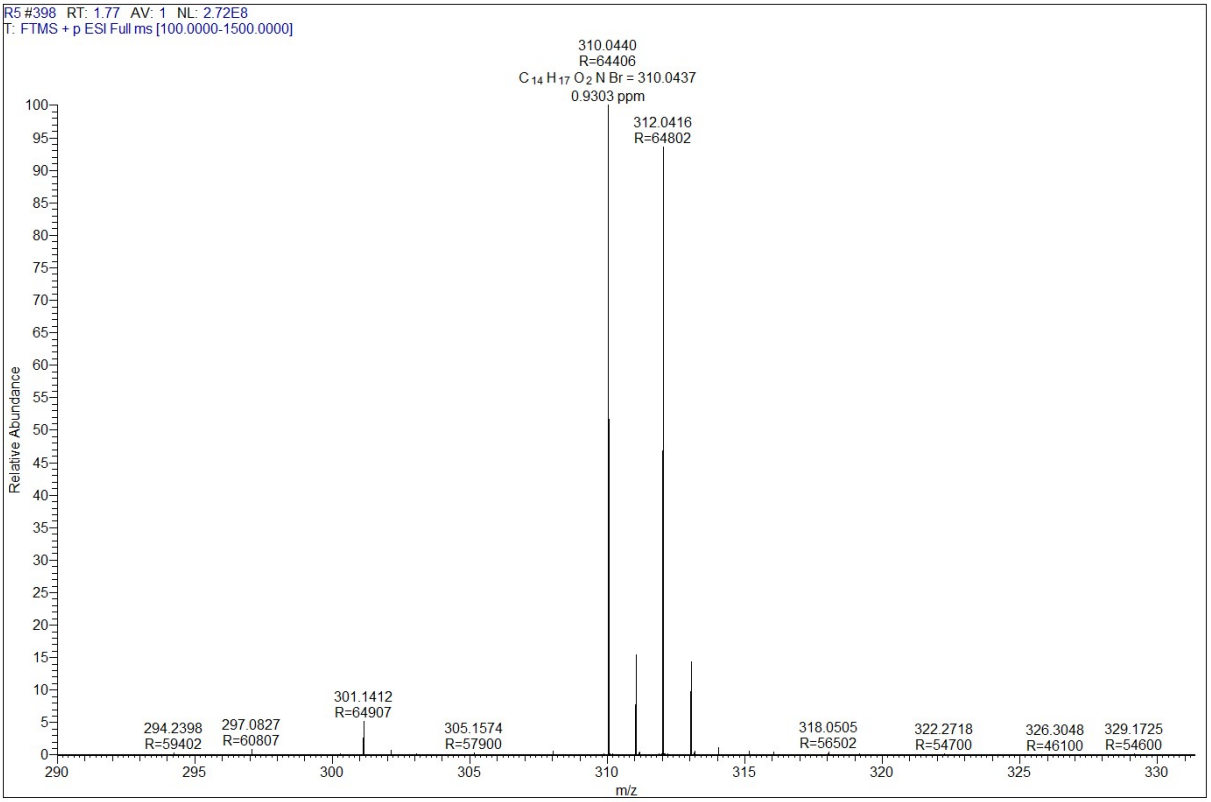


Fig 48: HRMS of 1-(4-bromophenyl)-2-(3-methylpiperidine-1-yl)ethane-1,2-dione (3l)

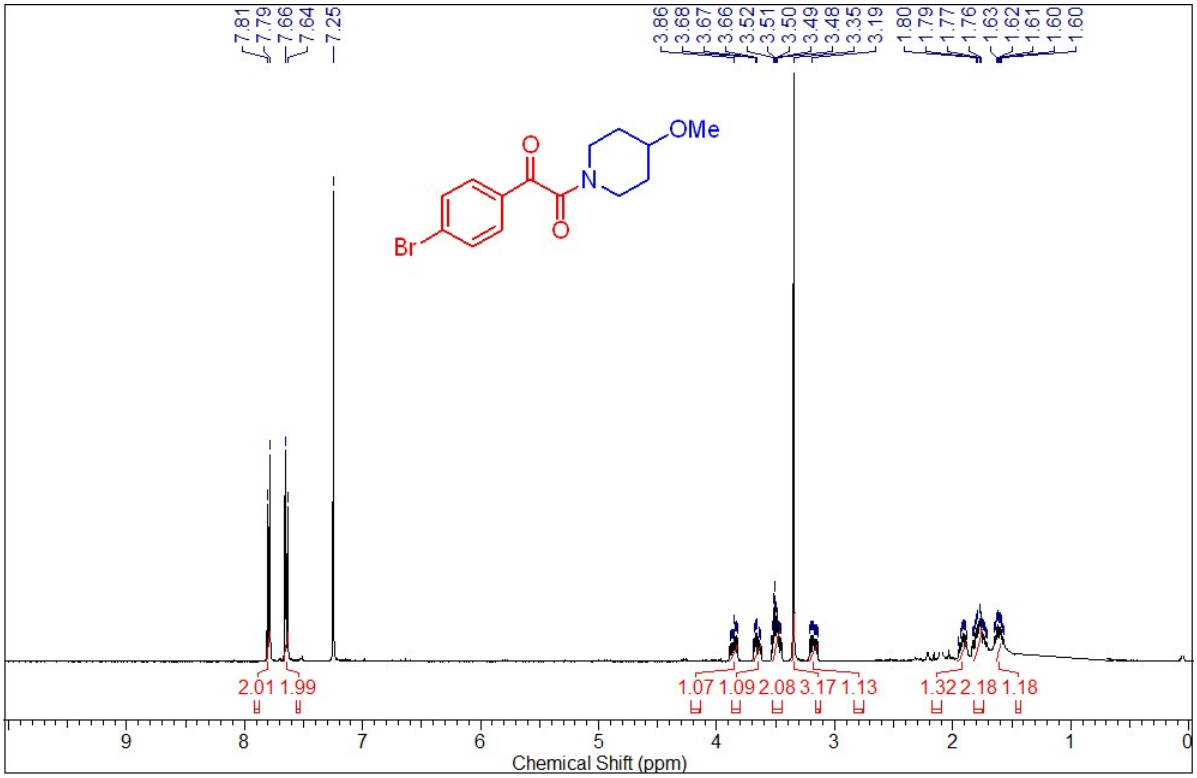


Fig 49: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methoxypiperidine-1-yl)ethane-1,2-dione (3m)

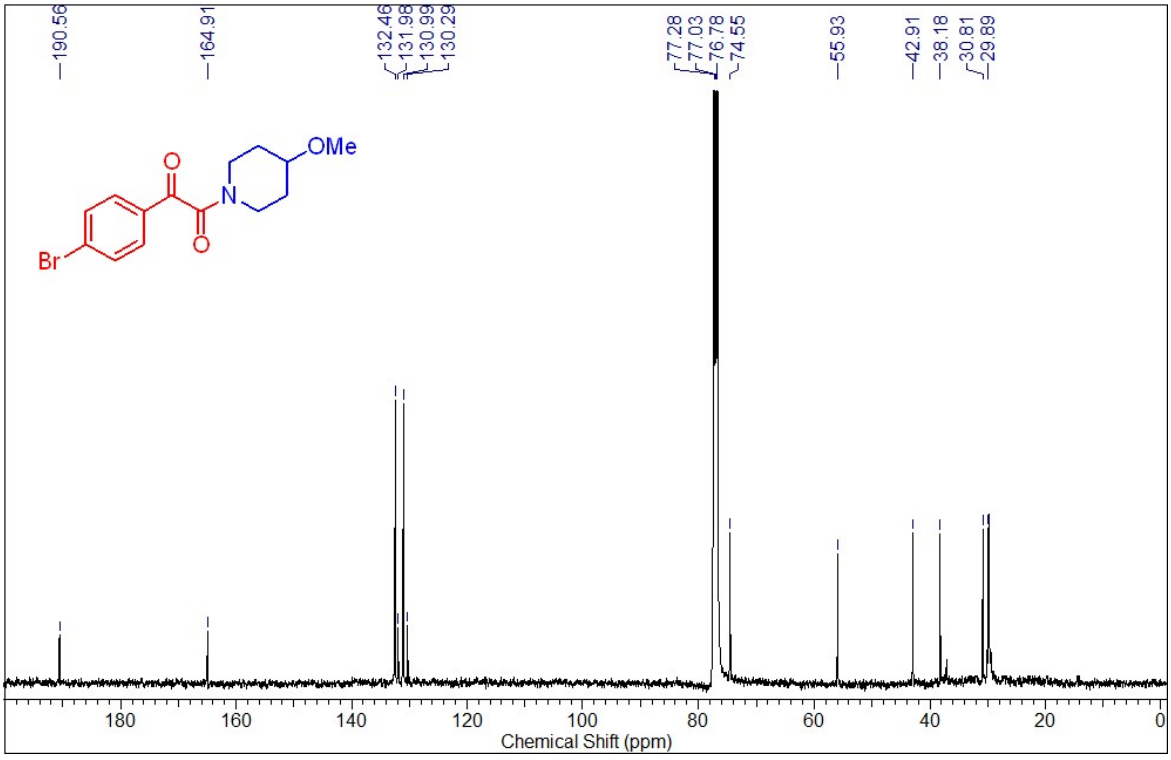


Fig 50: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methoxypiperidine-1-yl)ethane-1,2-dione (3m)

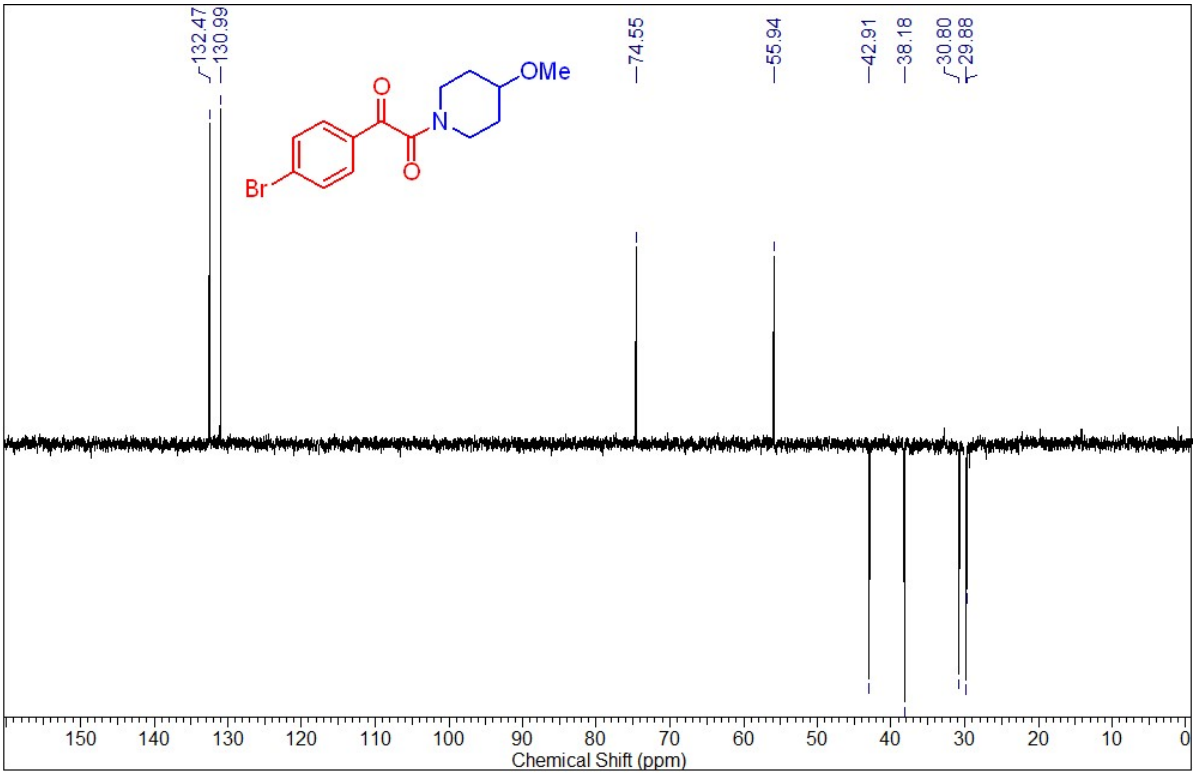


Fig 51: DEPT (100 MHz, $CDCl_3$) of 1-(4-bromophenyl)-2-(4-methoxypiperidine-1-yl)ethane-1,2-dione (3m)

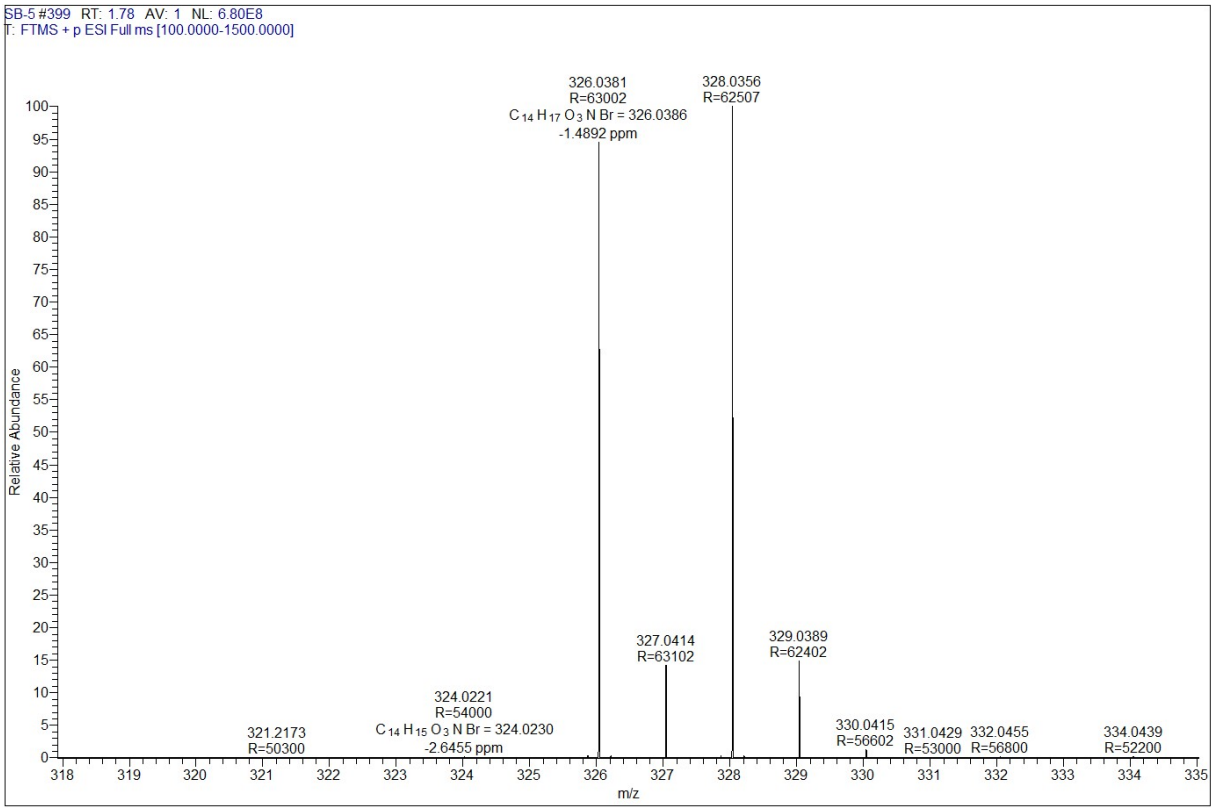


Fig 52: HRMS of 1-(4-bromophenyl)-2-(4-methoxypiperidine-1-yl)ethane-1,2-dione (3m)

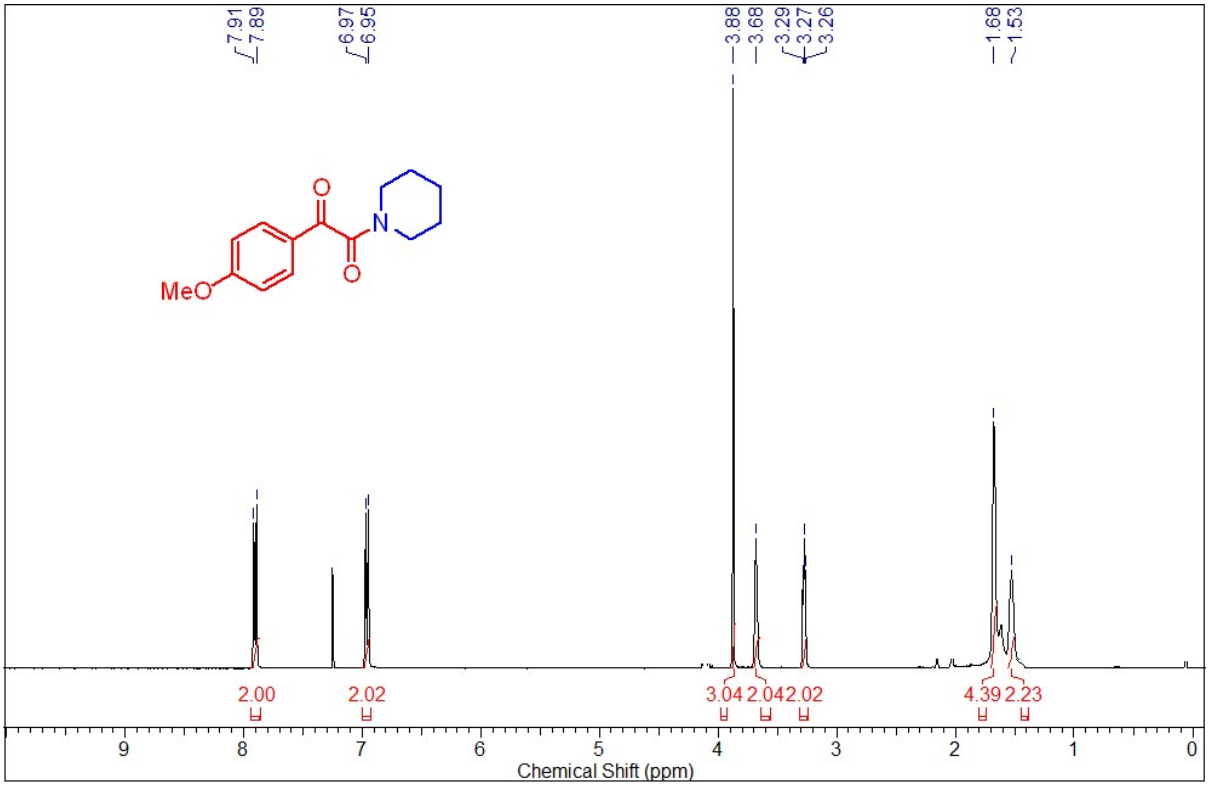


Fig 53: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione (3n)

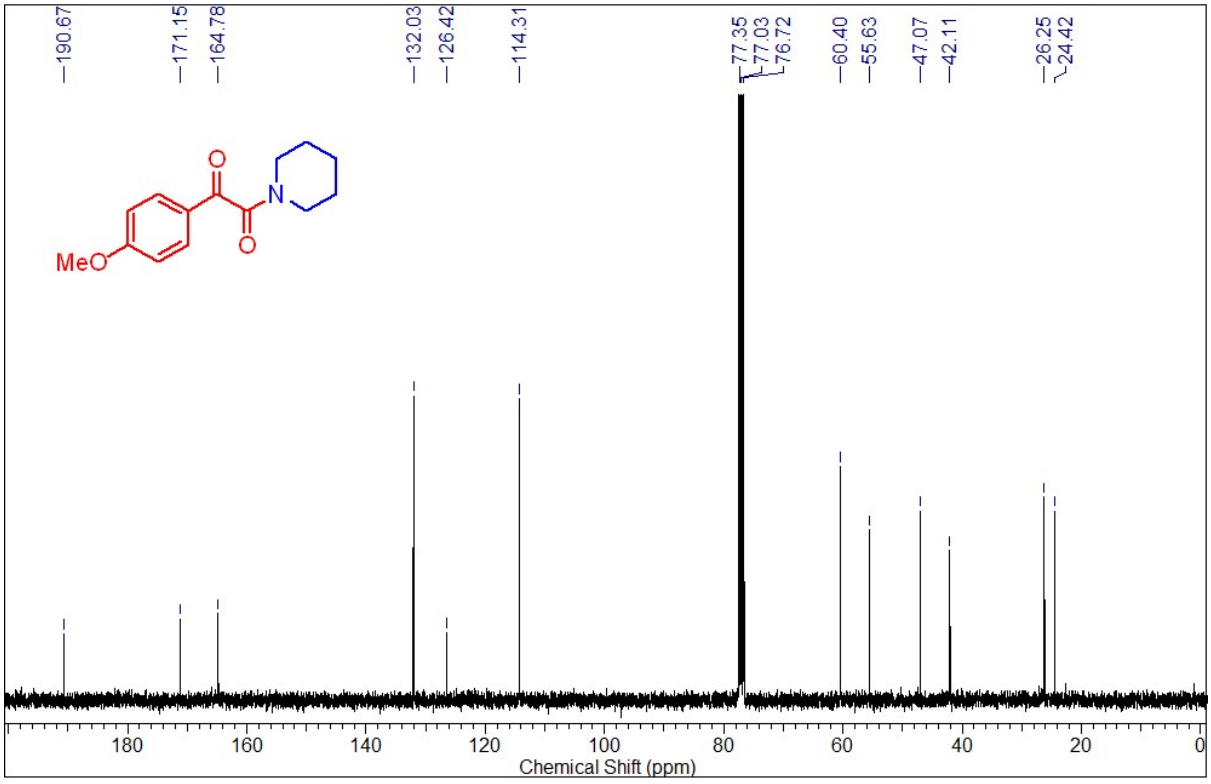


Fig 54: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(piperidin-1-yl) ethane 1,2-dione (3n)

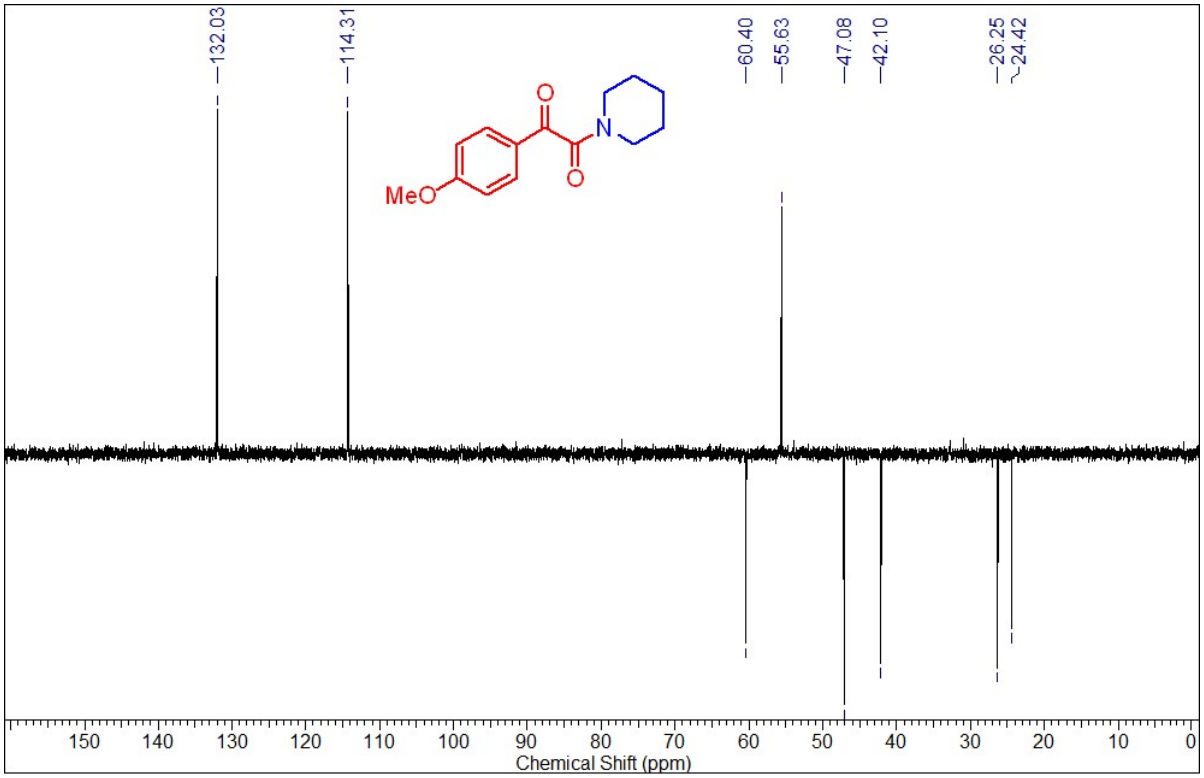


Fig 55: DEPT (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(piperidin-1-yl) ethane 1,2-dione (3n)

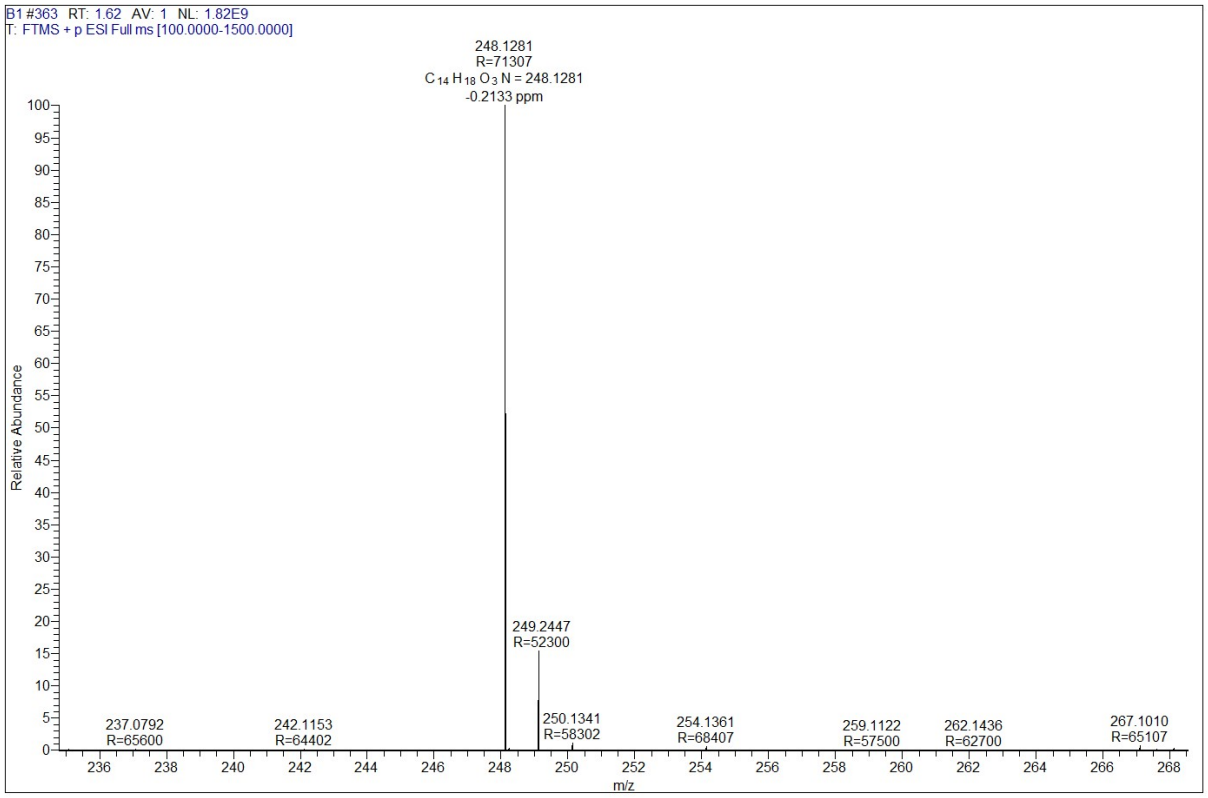


Fig 56: HRMS of 1-(4-methoxyphenyl)-2-(piperidin-1-yl)ethane 1,2-dione (3n)

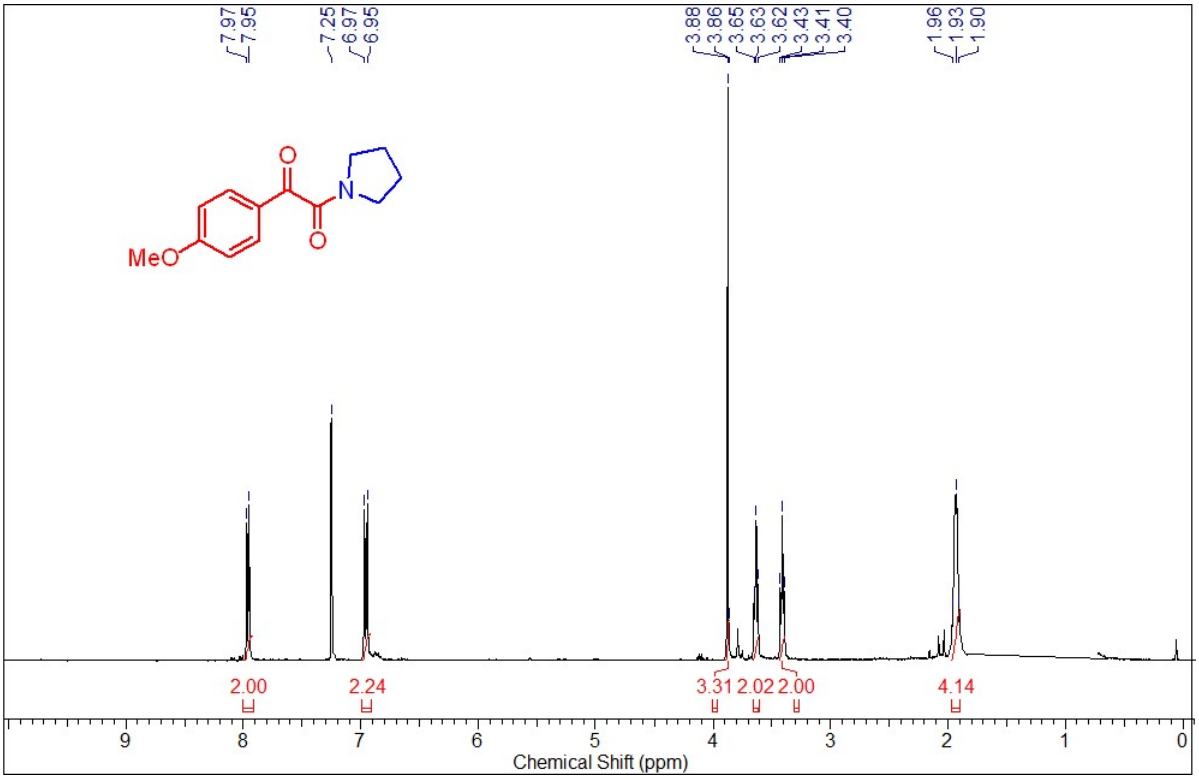


Fig 57: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3o)

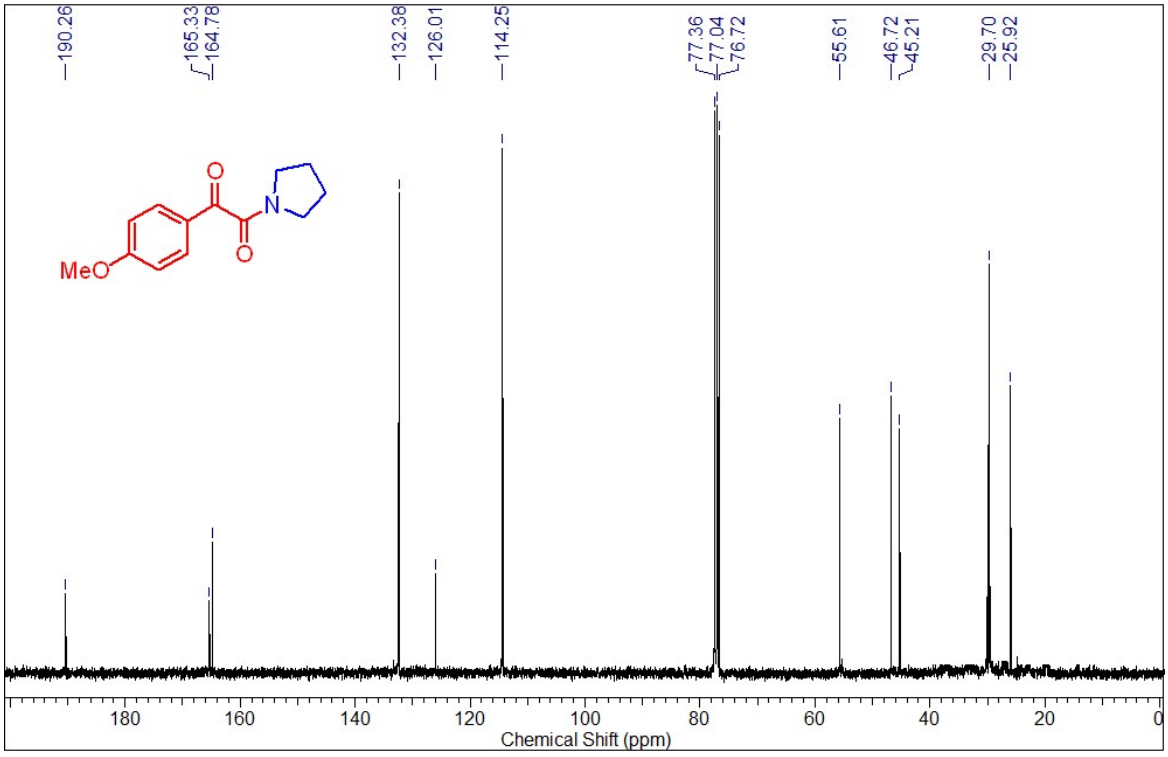


Fig 58: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3o)

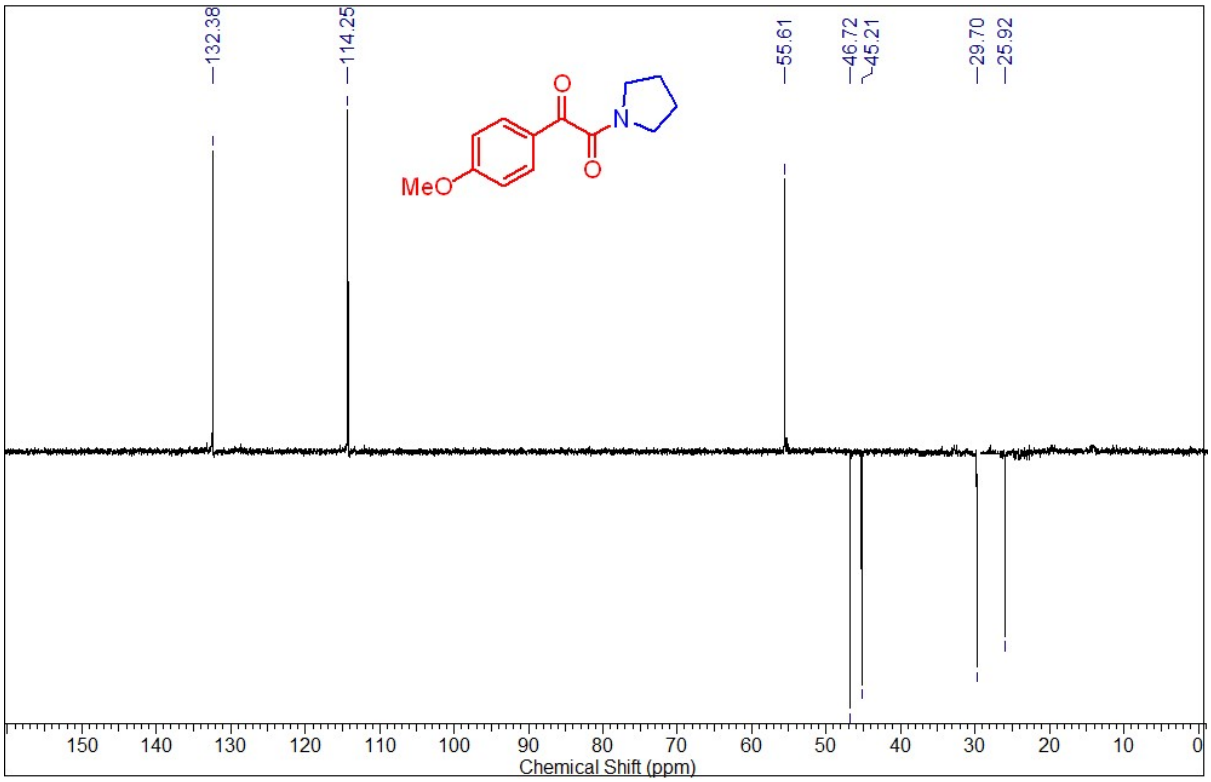


Fig 59: DEPT (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3o)

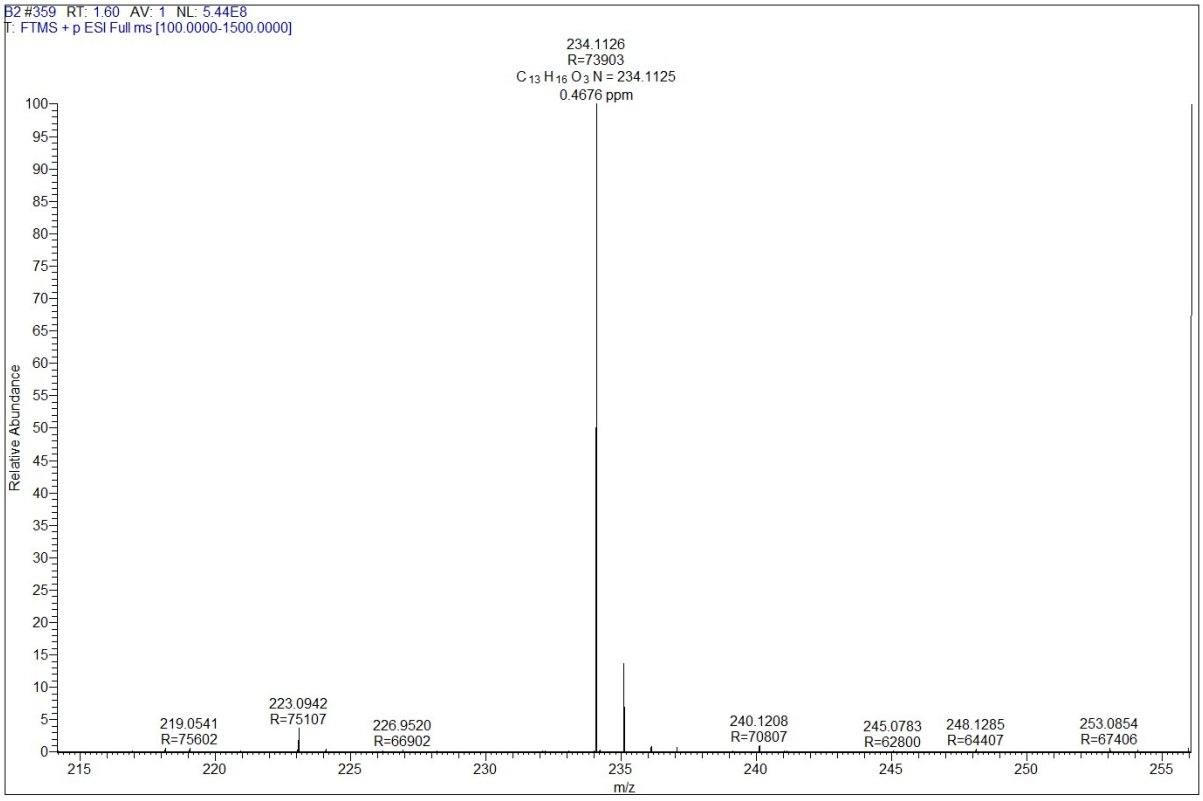


Fig 60: HRMS of 1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dion (3o)

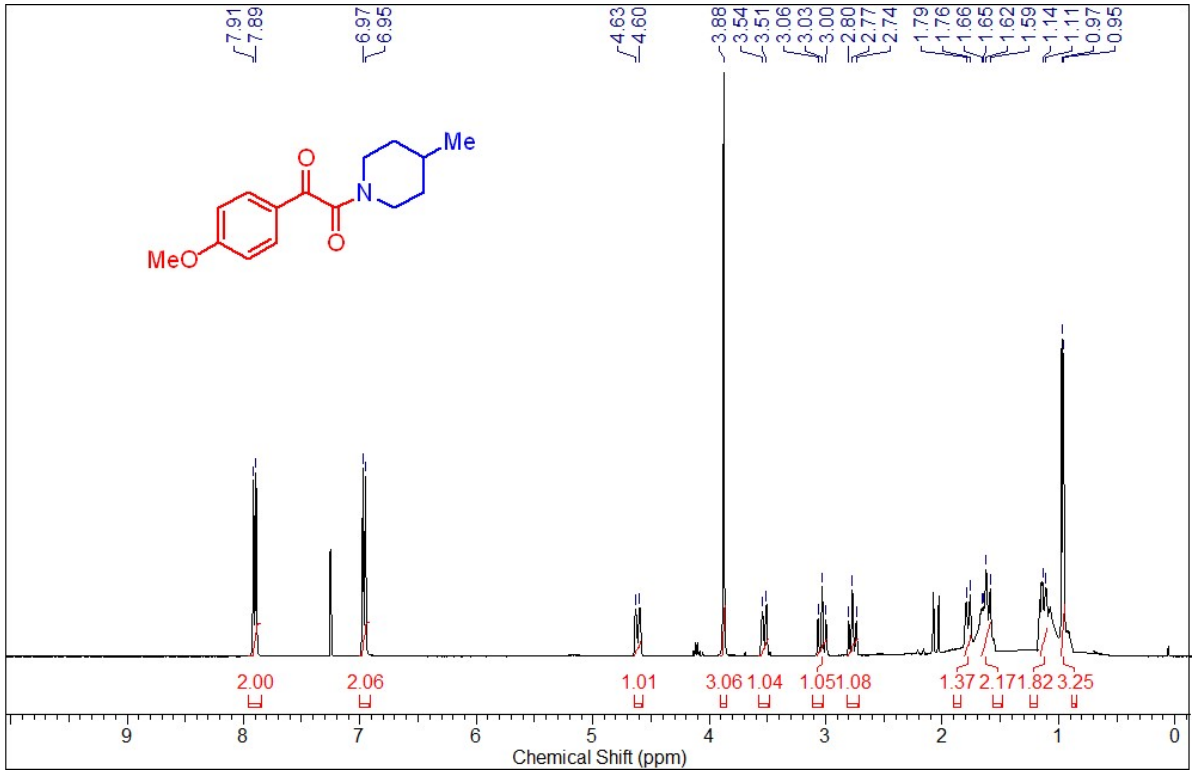


Fig 61: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3p)

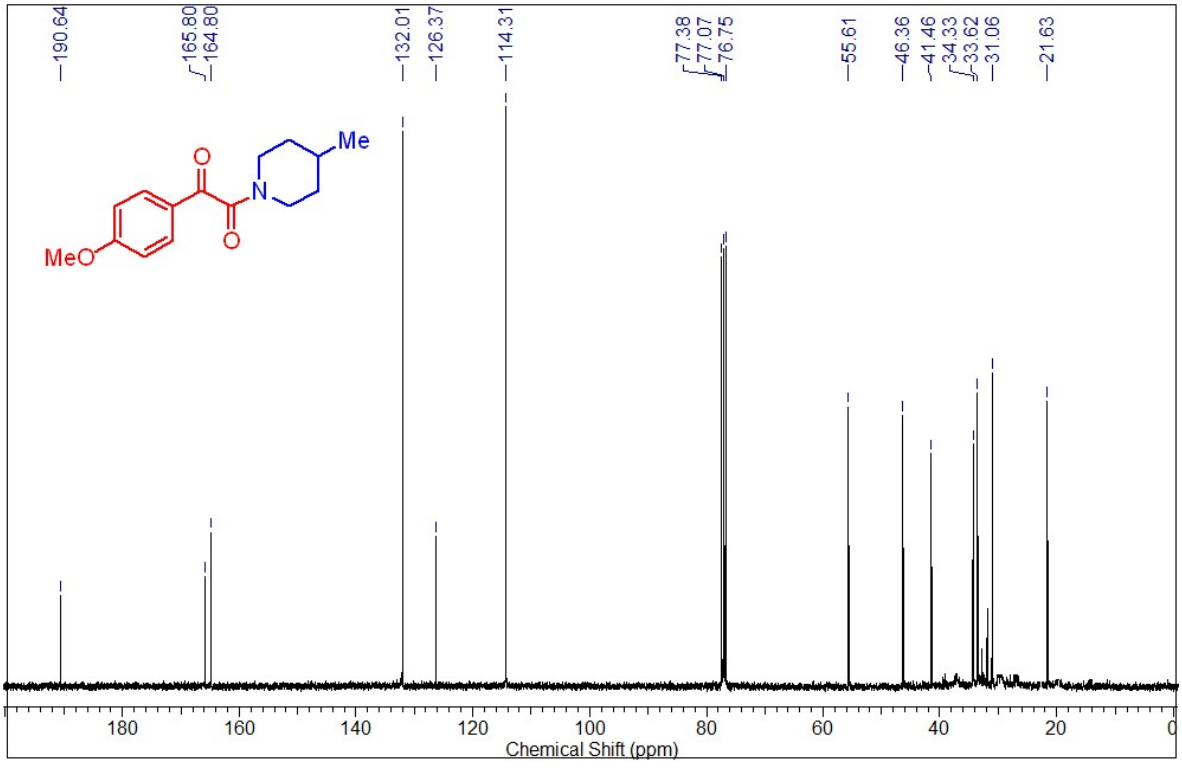


Fig 62: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3p)

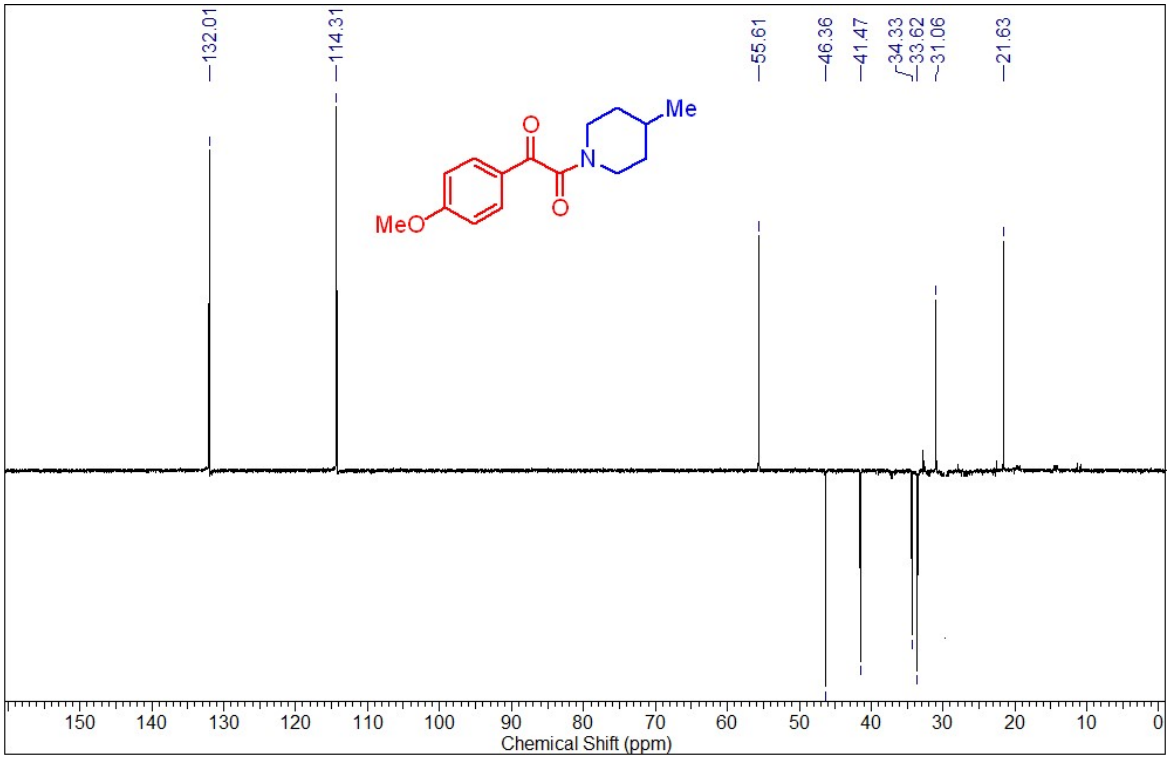


Fig 63: DEPT (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3p)

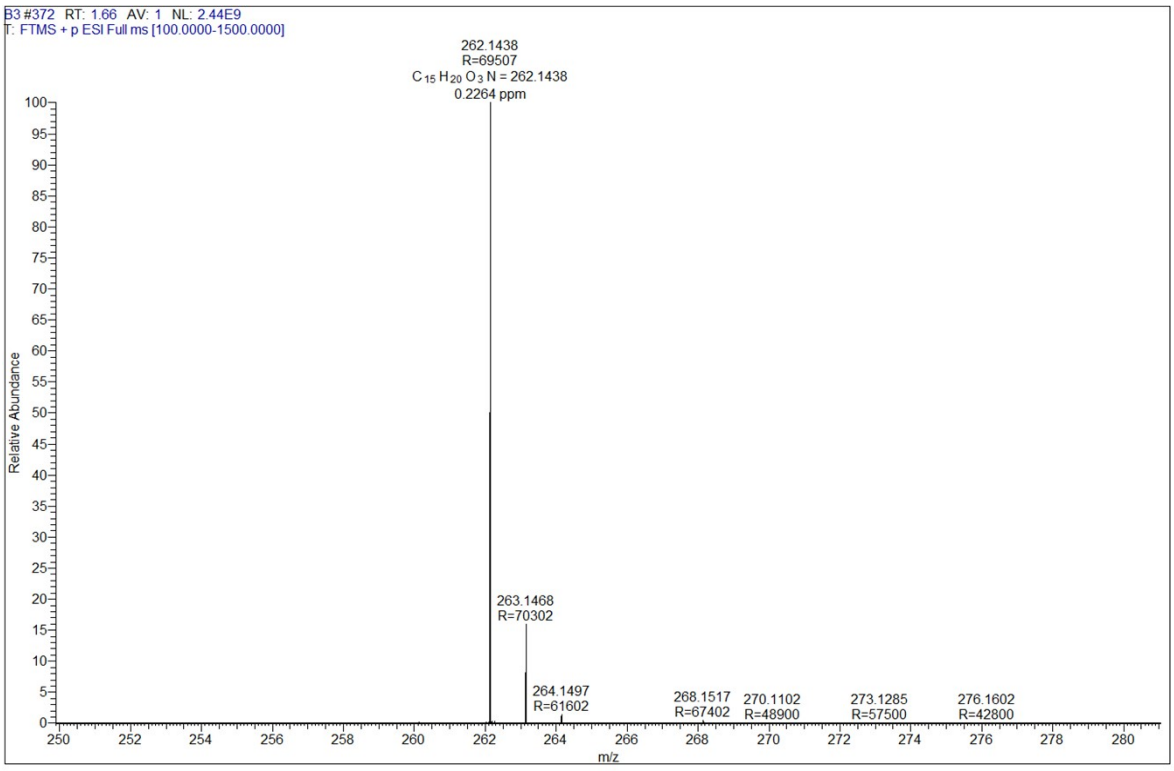


Fig 64: HRMS of 1-(4-methoxyphenyl)-2-(4-methylpiperidine-1-yl) ethane-1,2-dione (3p)

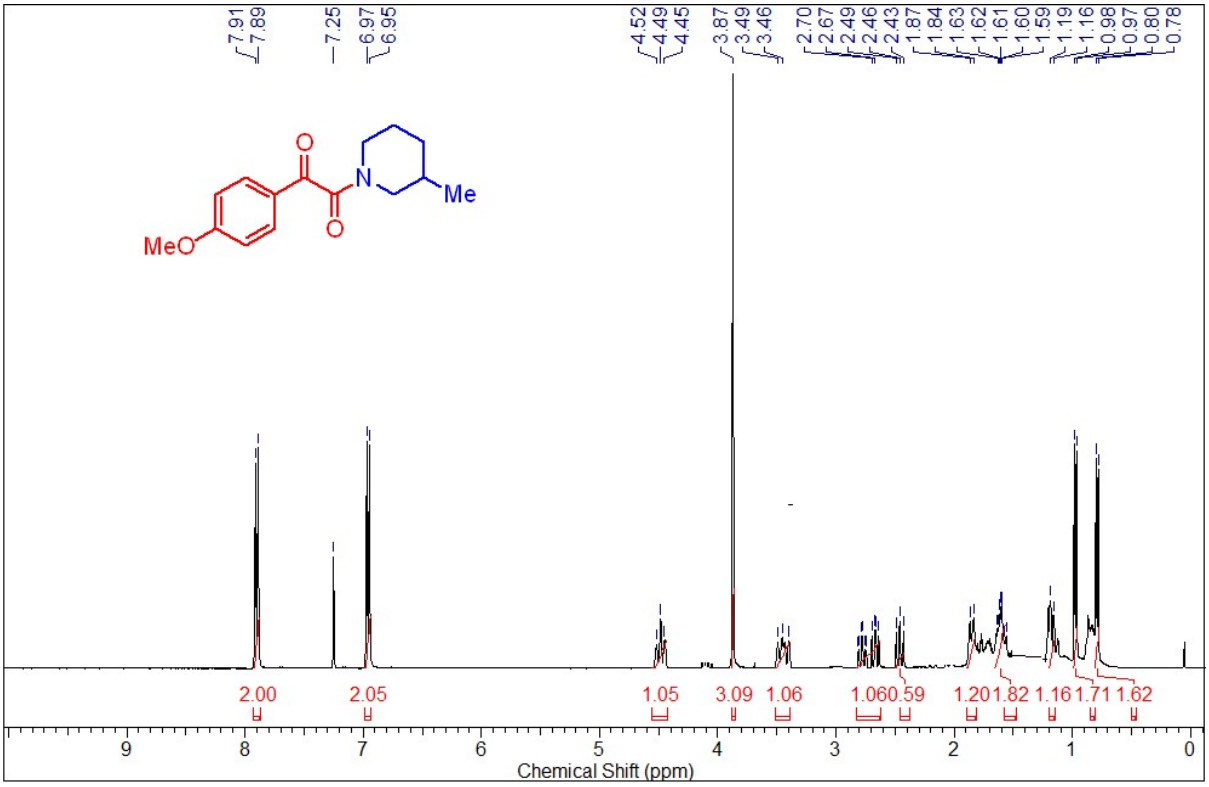


Fig 65: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(3-methylpiperidine-1-yl) ethane-1,2-dione (3q)

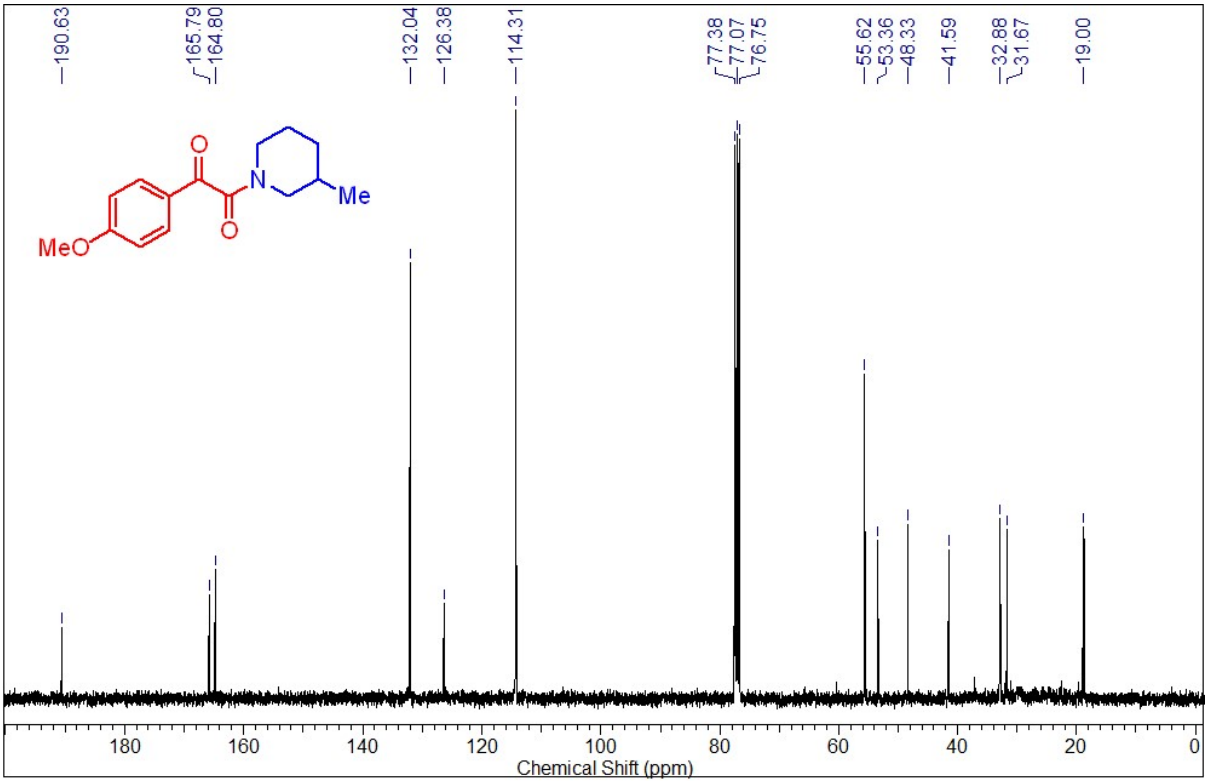


Fig 66: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(3-methylpiperidine-1-yl) ethane-1,2-dione (3q)

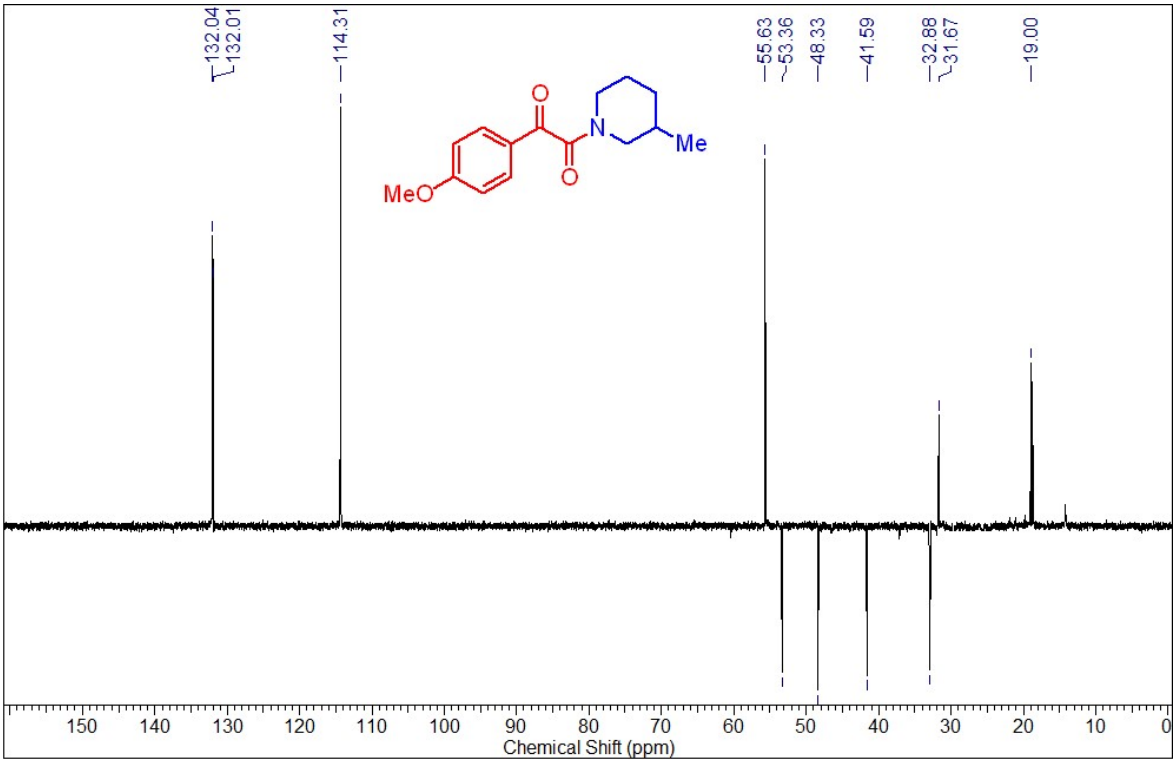


Fig 67: DEPT (100 MHz, $CDCl_3$) of 1-(4-methoxyphenyl)-2-(3-methylpiperidine-1-yl) ethane-1,2-dione (3q)

Fig 68: HRMS of 1-(4-methoxyphenyl)-2-(3-methylpiperidine-1-yl) ethane-1,2-dione (3q)

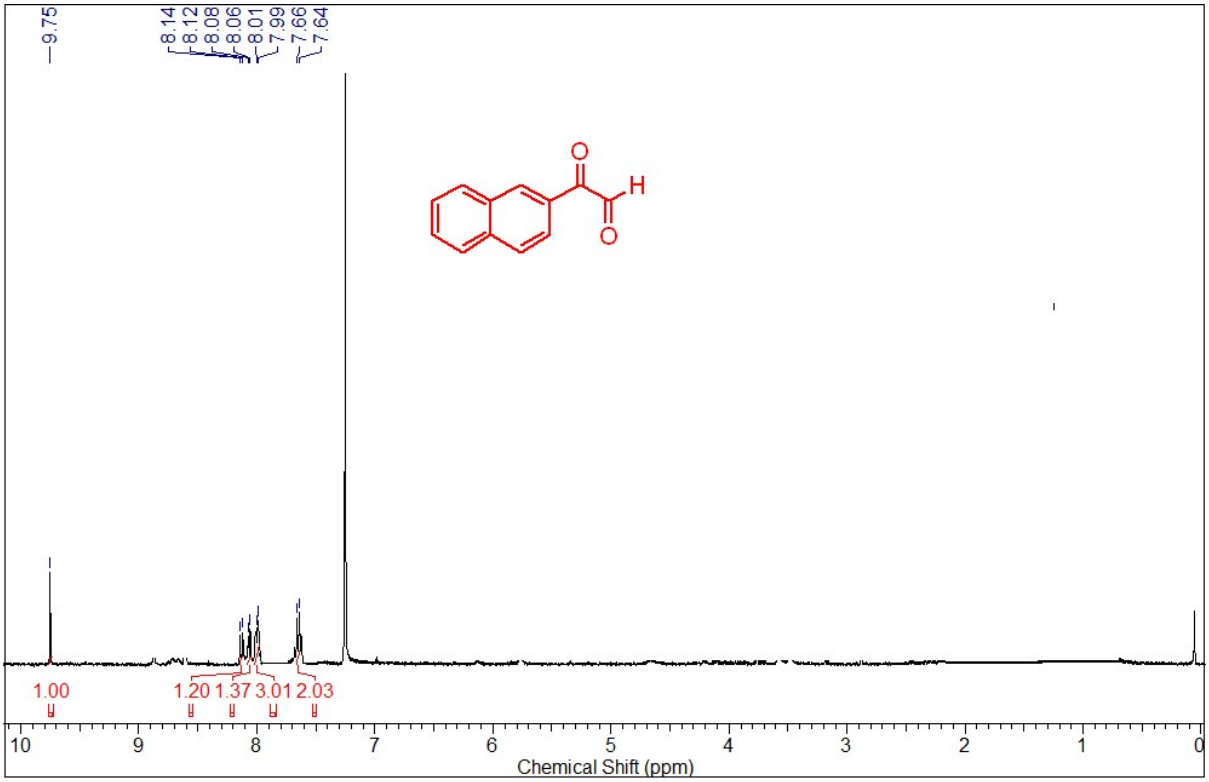


Fig 69: ^{1}H NMR (400 MHz, $CDCl_3$) of 2-naphthalen-2-yl-2-oxoacetaldehyde (6b)

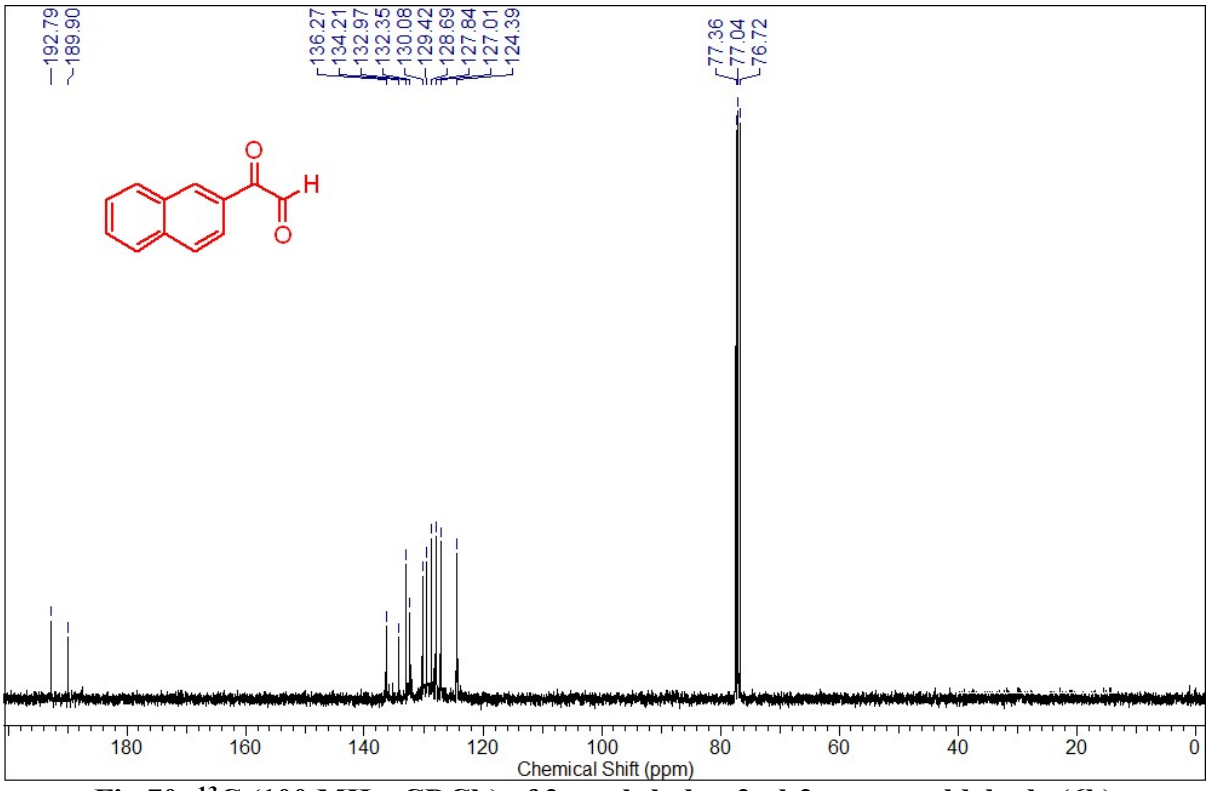


Fig 70: ^{13}C (100 MHz, $CDCl_3$) of 2-naphthalen-2-yl-2-oxoacetaldehyde (6b)

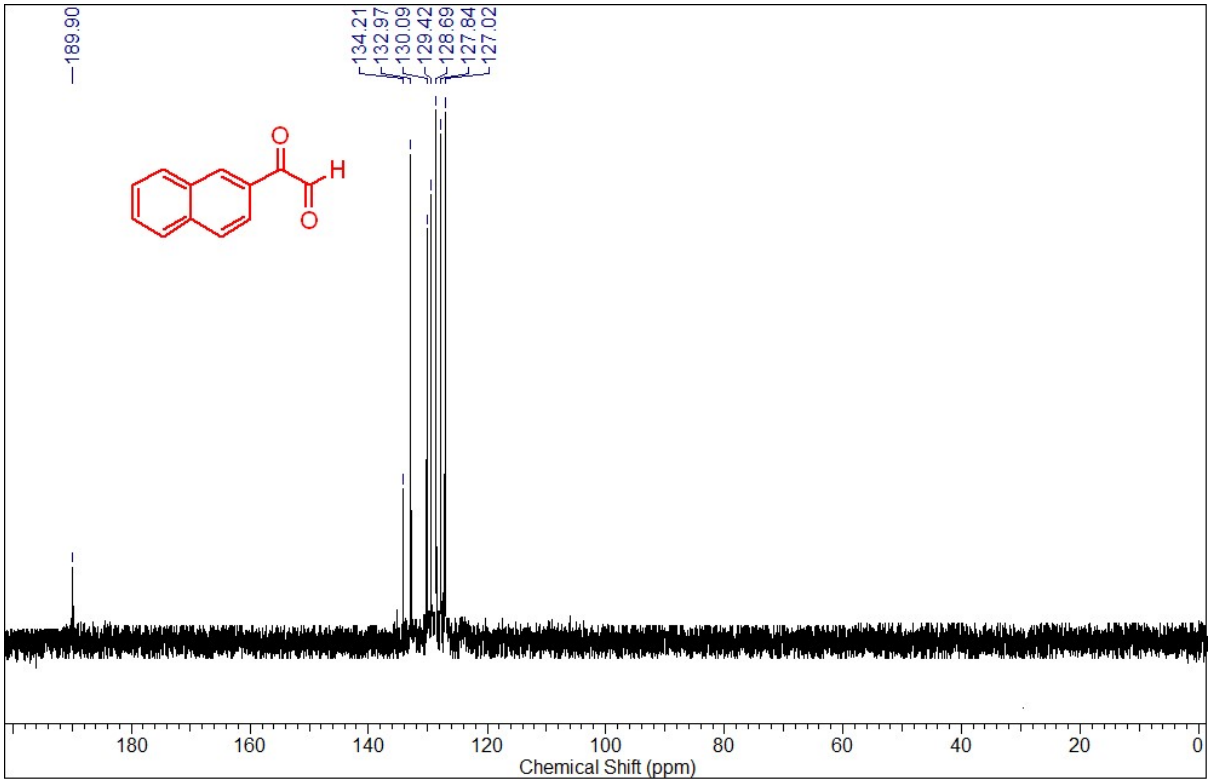


Fig 71: DEPT (100 MHz, $CDCl_3$) of 2-naphthalen-2-yl-2-oxoacetaldehyde (6b)

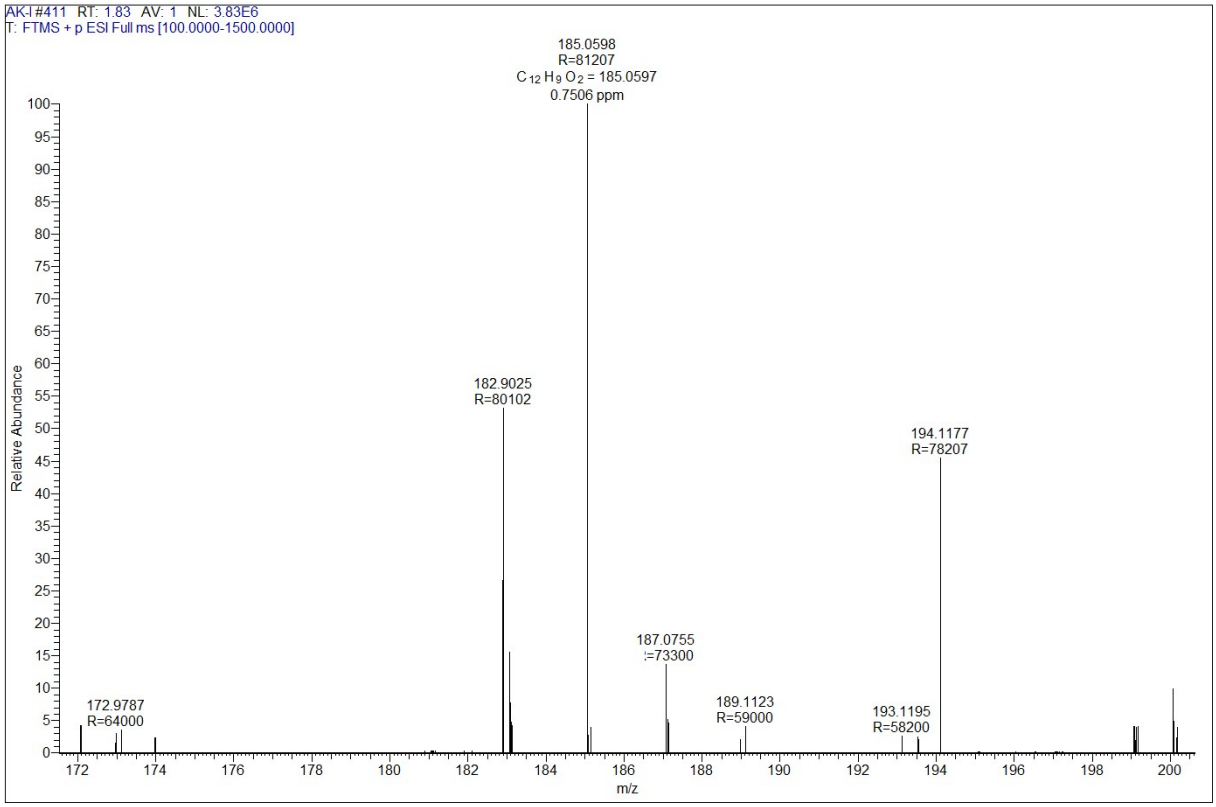


Fig 72: HRMS of 2-naphthalen-2-yl-2-oxoacetaldehyde (6b)

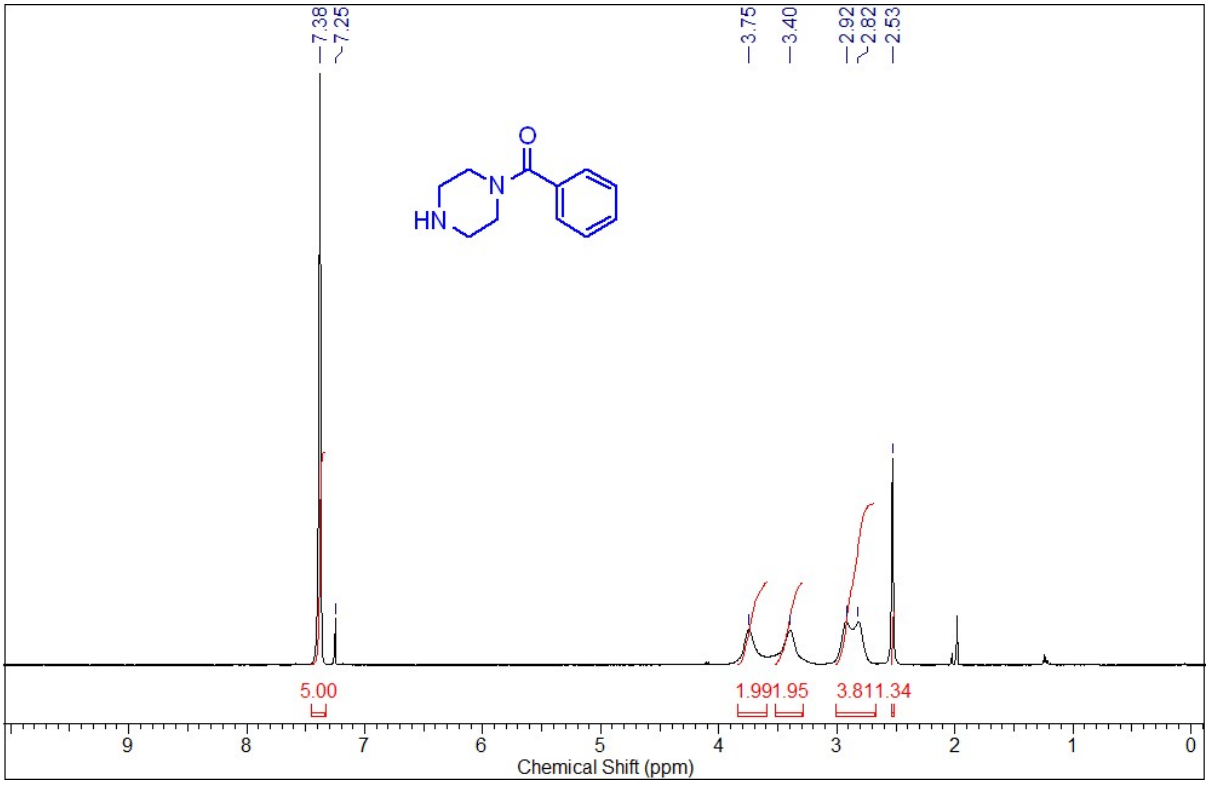


Fig 73: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-benzoyl piperazine

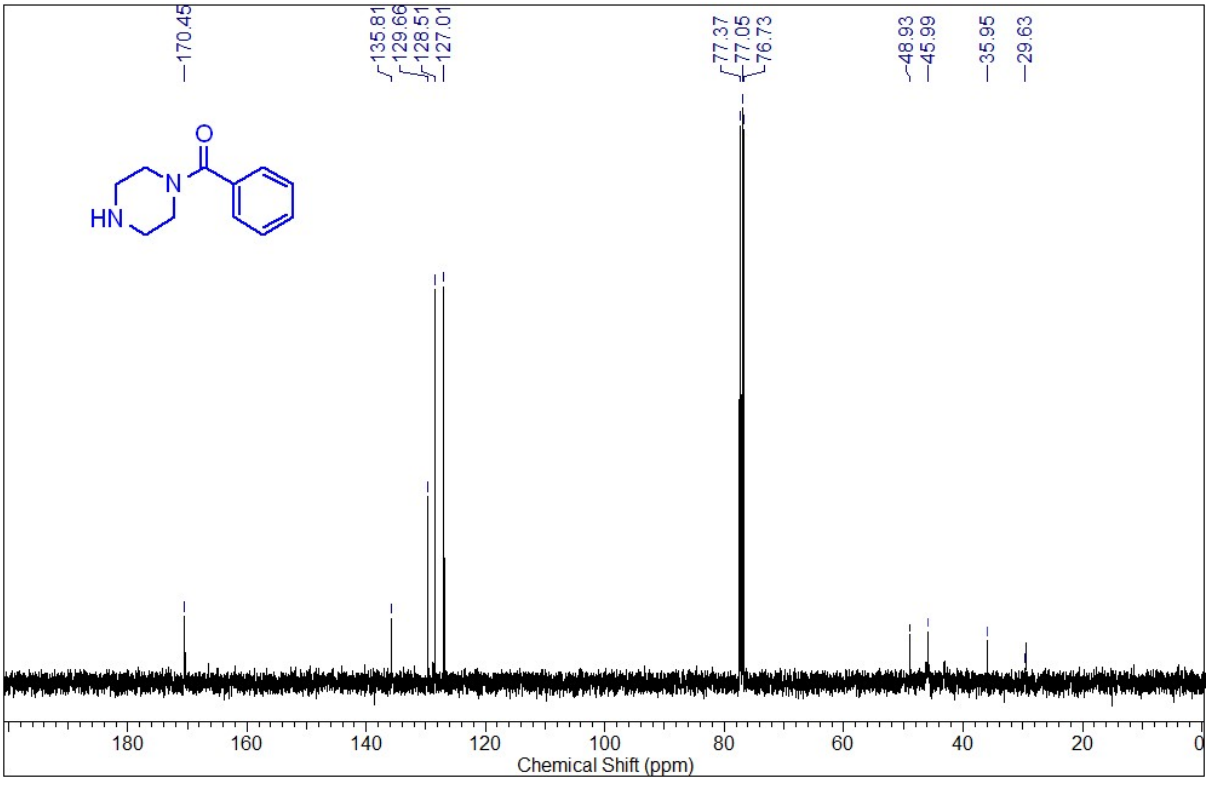


Fig 74: ^{13}C (100 MHz, $CDCl_3$) of 1-benzoyl piperazine (7c)

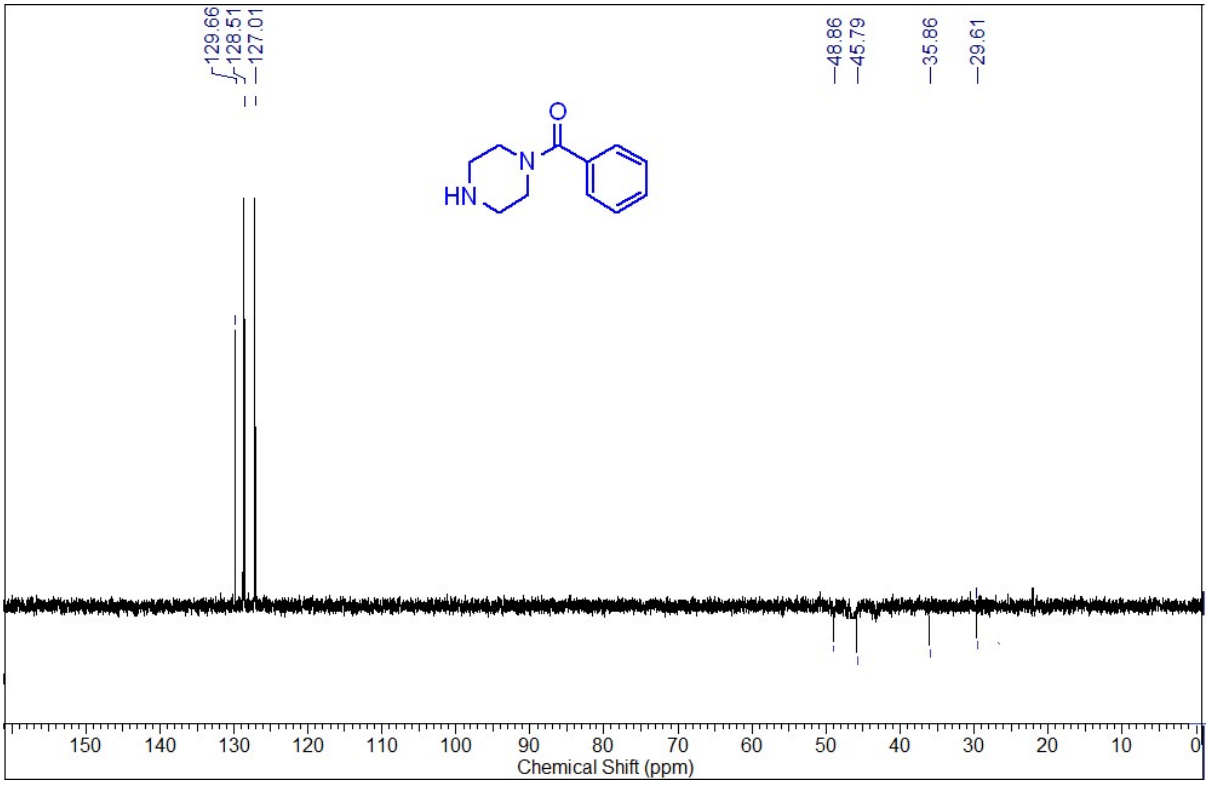


Fig 75: DEPT (100 MHz, $CDCl_3$) of 1-benzoyl piperazine (7c)

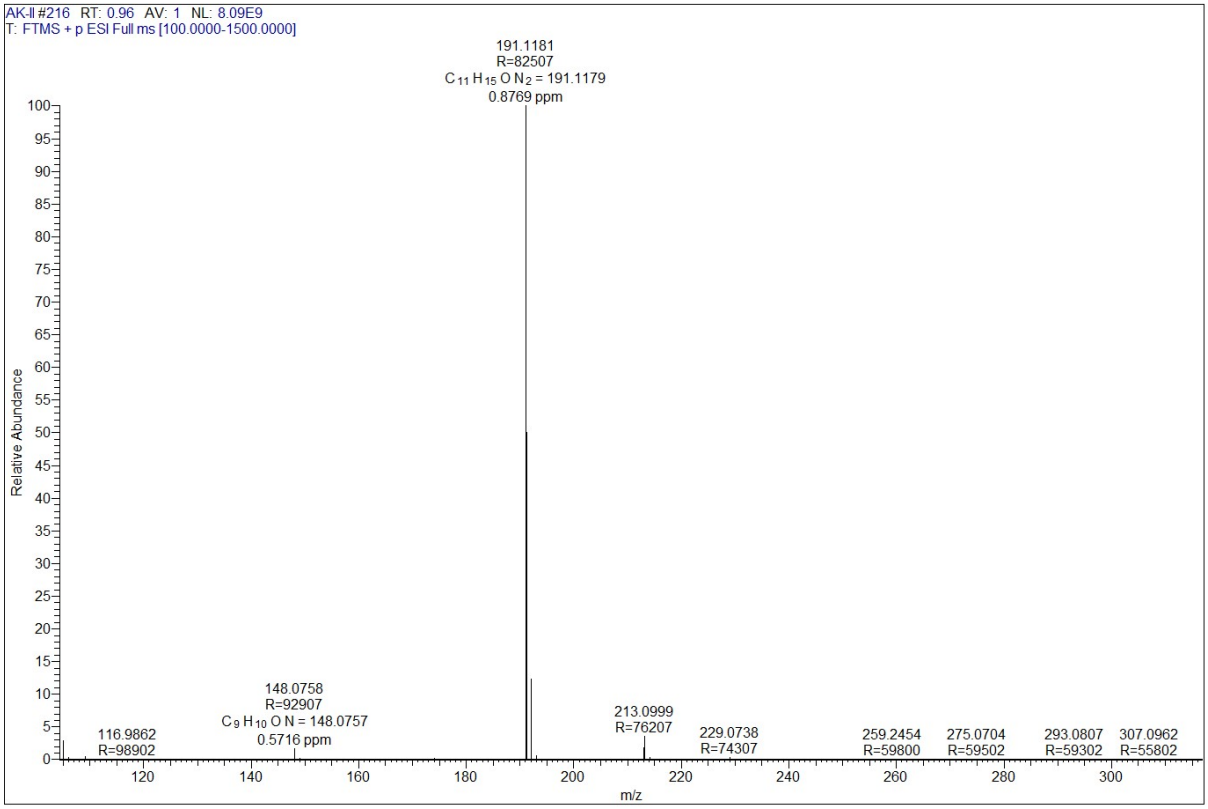


Fig 76: HRMS of 1-benzoyl piperazine (7c)

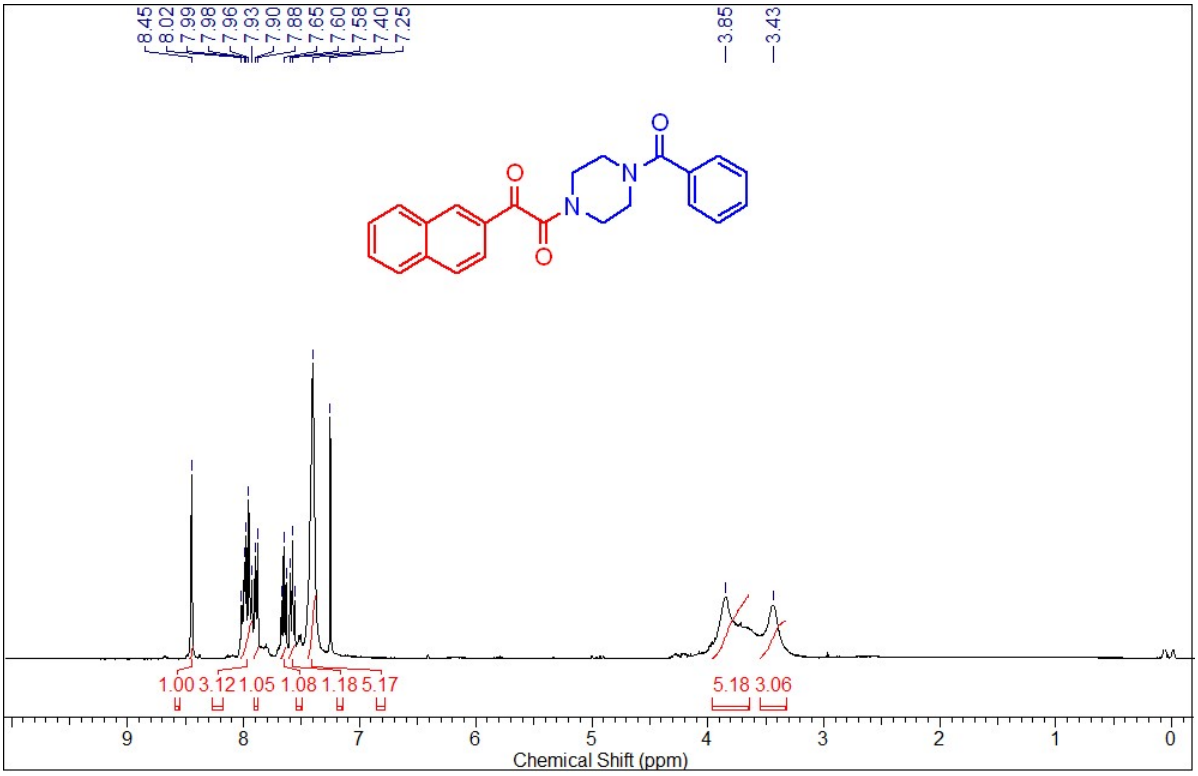


Fig 77: ^{1}H NMR (400 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl) ethane-1,2-dione (IV)

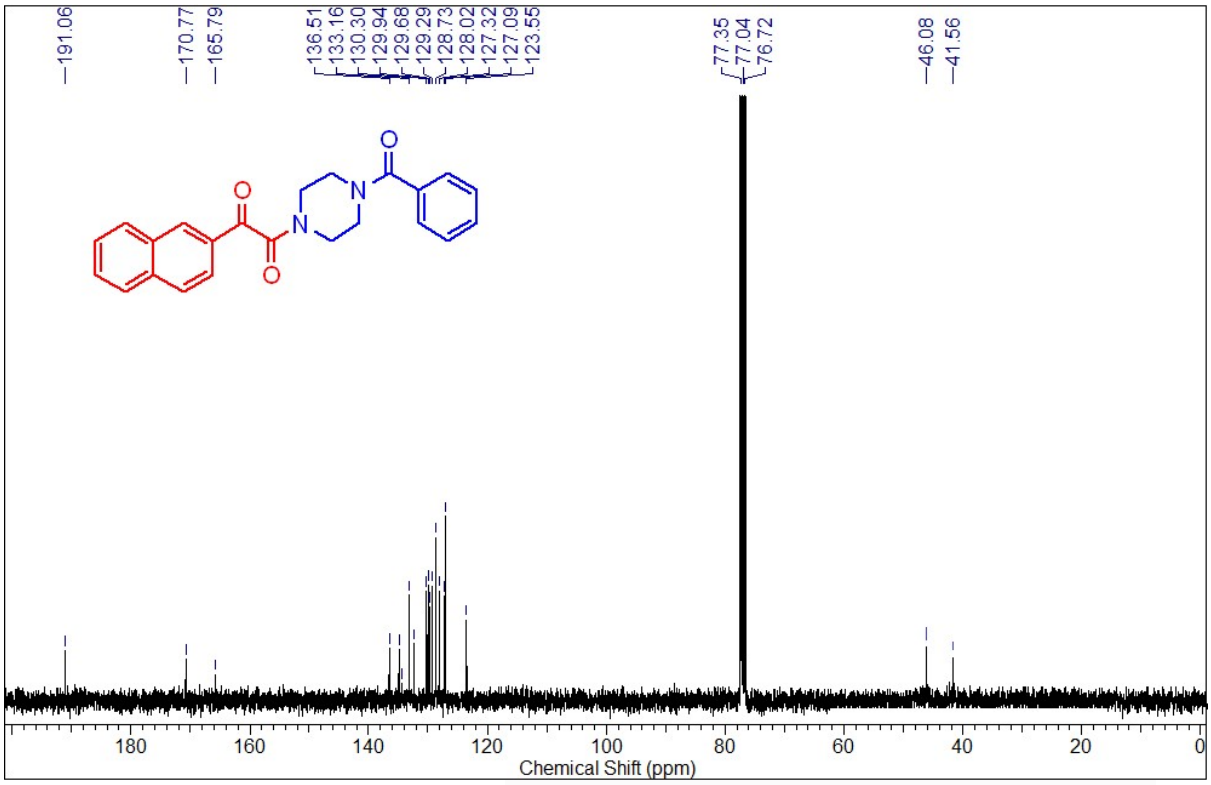


Fig 78: ^{13}C (100 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)-ethane-1,2-dione (IV)

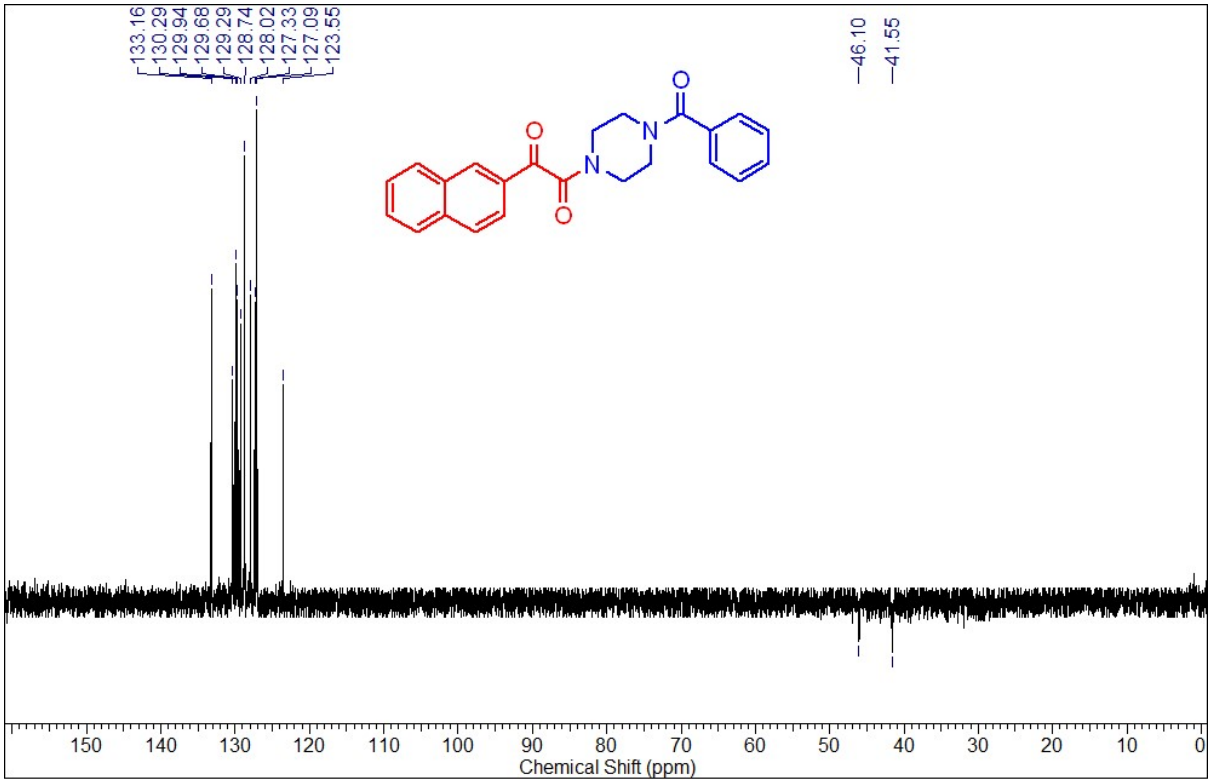


Fig 79: DEPT (100 MHz, $CDCl_3$) of 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)-ethane-1,2-dione (IV)

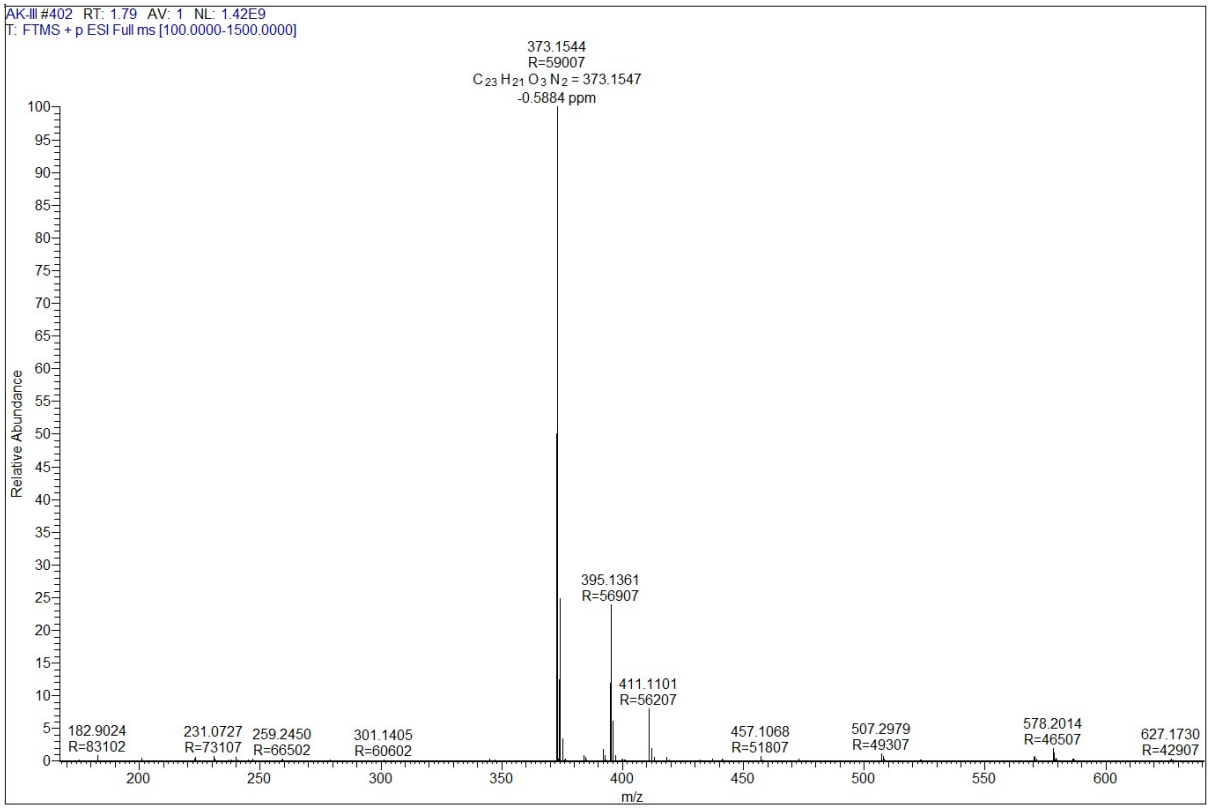
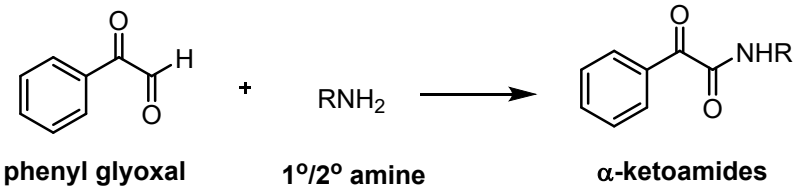


Fig 80: HRMS of 1-(4-Benzoyl-1-piperazinyl)-2-(2-naphthalenyl)- ethane-1,2-dione (IV)

Table S1: Reaction of phenyl glyoxal with amines using GCM



phenyl glyoxal **1°/2° amine** **α-ketoamides**

entry	substrate	catalyst (wt%)	solvent	Base (equiv)	temp (°C)	Yield
1	n-propyl amine	10	neat	-	50	Substrate unconsumed
2	di-isopropyl amine	10	neat	-	50	Substrate unconsumed
3	diethyl amine	10	neat	-	50	Substrate unconsumed
4	aniline	10	neat	-	50	Substrate unconsumed
5	aniline	10	CH_3CN	DABCO (2.0)	80	traces of impurities
6	aniline	10	CH_3CN	KOH (2.0)	80	traces of impurities
7	aniline	20	Toluene	-	80	Substrate unconsumed
8	aniline	20	DMSO	-	100	Substrate unconsumed

Reaction conditions: Phenyl glyoxal (1 mmol), amine (1 mmol), GCM catalyst.

Table S2: Reaction of phenyl glyoxal with amines using model catalyst

entry	catalyst	yield (%)[b]
1	1-pyrene carboxylic acid	65
2	pyrene	9
3	Benzoic acid	trace

[a]**Reaction conditions:** Phenyl glyoxal (1 mmol), piperidine (1 mmol), catalyst (10 wt%), neat, 50°C,[b]Isolatedyield.