Supporting Information

Access to pyrrolo[2,1-a]isoindolediones from oxime acetates and ninhydrin via Cu(I)-mediated domino annulations

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1. General Information:

All the reactions were carried out in oven-dried glassware. Column chromatography was performed on silica gel (60−120 mesh) using hexane and ethyl acetate as eluents. Evaporation of solvents was done under reduced pressure at temperatures less than 40 °C. ^{1}H NMR spectra were recorded at 300, 400 and 500 MHz and ^{13}C NMR at 75 and 100 MHz. For ^{1}H NMR, $CDCl_3$ (δ = 7.26) and DMSO-d^6 (δ = 2.50) was used as an internal standard and the values are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t= triplet, q = quartet, m = multiplet, brs = broadsinglet, dt = doublet of triplet), and the coupling constants in Hz. For ^{13}C NMR $CDCl_3$ (δ = 77.16) and DMSO-d^6 (δ = 39.52) were used as an internal standards and spectra were obtained with complete proton decoupling. Melting points were measured on micro melting point apparatus. The precursors, oxime acetate was prepared according to reported procedures. Commercially available Ninhydrin, Copper(I)bromide, DMSO were used without further purification.

2. Synthesis of starting materials:

2.1. Synthesis of oxime acetate was done by following the procedure (A):[1]

To a solution of aromatic ketones (2 mmol) in C_2H_5OH/H_2O (v/v = 1:1) was added, hydroxylamine hydrochloride (2.2 mmol), NaOAc (3 mmol) in one portion, and the reaction mixture were stirred at 100°C for 6-8 h. Upon completion of the reaction as indicated by TLC, the reaction mixture was diluted with water, extracted with ethyl acetate and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give oximes.

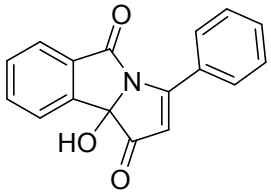
General procedure for synthesis aromatic ketoxime acetates: The mixture of aromatic ketoxime (2.0 mmol), anhydride (4.0 mmol, 2.0 equiv.) was stirred at 100°C for 3h. Upon completion of the reaction as indicated by TLC, the reaction mixture was diluted with ethyl

acetate (25 mL), washed with H_2O (20 mL). After that, neutralization was done with $NaHCO_3$, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The crude residue was purified by column chromatography using silica gel with hexane and ethyl acetate as the eluent to afford aromatic ketoxime acetates.

3. General procedures for the synthesis of 9b-hydroxy-1*H*-pyrrolo[2,1-a]isoindoledione derivatives (B):

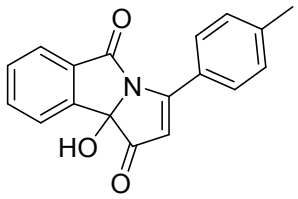
In a round bottle flask, a mixture of Oxime acetate **1** (1 mmol), Ninhydrin **2** (1 mmol), CuBr (0.3 mmol) was stirred in 2 mL DMSO at 100 °C (oil bath) for 4 h. After completion of the reaction, the mixture was diluted with water and extracted with EtOAc (4 × 15 mL), and the extract was washed with brine, dried over Na_2SO_4, and evaporated; the crude product was purified by column chromatography on silica gel(eluent: EtOAc/hexanes) to afford the product **3**. Characterization data for the new compounds are given below

4. Spectral data of 9b-hydroxy-1*H*-pyrrolo[2,1-a]isoindoledione derivatives

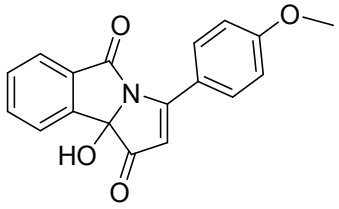


9b-hydroxy-3-phenyl-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9bH)-dione (3a) :According to general procedure B, 1a (177 mg, 1 mmol) gave 3a (222 mg, 80%) as a yellow solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p. 181-182 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.06 (s, 1H), 7.95-7.92 (m, 2H), 7.88-7.81 (m, 2H), 7.76-7.61 (m, 3H), 7.56 (t, *J* = 7.5 Hz, 2H), 6.46 (s, 1H); ^{13}C NMR

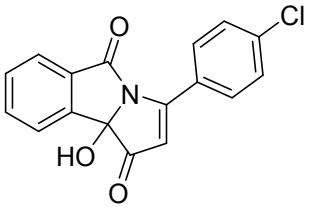
(100 MHz, DMSO) δ 195.8, 169.8, 167.7, 142.7, 135.2, 132.6, 131.29, 130.9, 129.9 129.6, 128.3, 124.4, 124.3, 112.3, 91.3; MS (EI) *m/z* 157 $[M+1]^+$; HRMS (ESI) calcd for $C_{17}H_{11}NO_3[M+H]^+$ 278.0817, found 278.0824.



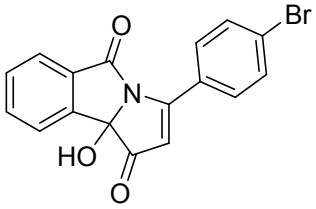
9b-hydroxy-3-(p-tolyl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9bH)-dione) (3b) : According to general procedure B, 1b (191 mg, 1 mmol) gave 3b (248 mg, 85%) as a brown solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p. 198-199 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* =7.5 Hz, 1H), 7.79-7.72 (m, 4H), 7.62-7.57 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.02 (s, 1H), 2.46 (s, 3H).); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 172.4, 168.1, 144.4, 142.3, 135.4, 131.5, 131.5, 130.1, 129.3, 127.0, 125.3, 124.3, 110.4, 90.9, 22.0; HRMS (ESI) calcd for C18H13NO3$[M+H]^+$ 292.0974, found 292.0983.



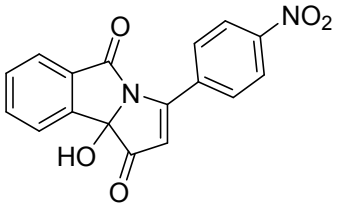
9b-hydroxy-3-(4-methoxyphenyl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3c) : According to general procedure B, 1c (207 mg, 1 mmol) gave 3c (271 mg, 88%) as a pale yellow solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p. 189-190 ºC; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO) δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.75-7.71 (m, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.32 (s, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.97 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$+DMSO) δ 195.3, 170.1, 167.8, 162.8, 142.7, 134.2, 131.4, 131.0, 130.3, 124.0, 123.8, 121.8, 113.2, 109.0, 91.0, 55.0; HRMS (ESI) calcd for $C_{18}H_{13}NO_4[M+Na]^+$ 330.0742, found 330.0744.



3-(4-chlorophenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3d) : According to general procedure B, 1d (211 mg, 1 mmol) gave 3d (218 mg, 70%) as yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 212-213 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.10 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 2H), 7.89-7.79 (m, 2H), 7.74 (d, *J* = 7.3 Hz, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 6.50 (s, 1H).); ^{13}C NMR (100 MHz, DMSO) δ 195.8, 168.4, 167.9, 142.7, 137.3, 135.3, 131.3, 130.9, 128.7, 128.4, 124.5, 124.3, 112.7, 91.3; HRMS (ESI) calcd for $C_{17}H_{10}ClNO_3[M+H]^+$ 312.0427, found 312.0440.

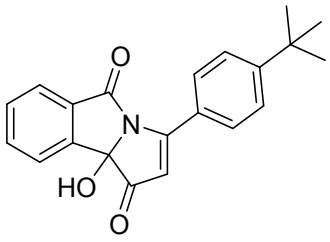


3-(4-bromophenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3e) : According to general procedure B, 1e (256 mg, 1 mmol) gave 3e (232 mg, 65%) as yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 231-232 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.09 (s, 1H), 7.91 – 7.83 (m, 3H), 7.82-7.77 (m, 3H), 7.71 (dd, *J* = 7.2, 6.1 Hz, 2H), 6.53 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 195.8, 168.5, 167.9, 142.7, 135.3, 131.4, 131.3, 129.1, 126.3, 124.5, 124.3, 112.8, 91.2; HRMS (ESI) calcd for $C_{17}H_{10}{}^{79}BrNO_3[M+H]^+$ 355.9922, found 355.9921; HRMS (ESI) calcd for $C_{17}H_{10}{}^{81}BrNO_3[M+H]^+$ 357.9902, found 357.9903

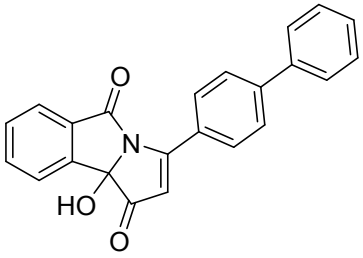


9b-hydroxy-3-(4-nitrophenyl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3f) : According to general procedure B, 1f (222mg, 1 mmol) gave 3f (187 mg, 58%) as a pale yellow solid. R_f =

0.4 (EtOAc/hexanes, 3:7); m.p. 253-254 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.39 (d, *J* = 8.7 Hz, 2H), 8.22-8.11 (m, 3H), 7.95-7.79 (m, 2H), 7.76-7.68 (m, 2H), 6.70 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 196.0, 168.0, 167.0, 149.3, 142.6, 135.9, 135.4, 131.4, 130.8, 130.7, 124.6, 124.3, 123.3, 115.3, 91.2; HRMS (ESI) calcd for $C_{17}H_{10}N_2O_3[M+H]^+$ 323.0668, found 323.0679.

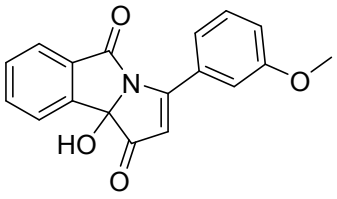


3-(4-(*tert*-butyl)phenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3g) : According to general procedure B, 1g (233 mg, 1 mmol) gave 3g (250 mg, 75%) as a brown solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p. 281-282 ºC; ^{1}H NMR (300 MHz, DMSO) δ 7.95 (d, *J* = 5.2 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.84-7.81 (m, 1H), 7.74-7.66 (m, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 1H), 6.39 (s, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ 195.7, 169.8, 167.8, 155.9, 142.8, 135.2, 131.3, 131.0, 129.6, 127.2, 125.2, 124.5, 124.3, 111.6, 91.3, 34.9, 30.8; HRMS (ESI) calcd for $C_{21}H_{19}NO_3[M+H]^+$ 334.1443, found 334.1447.

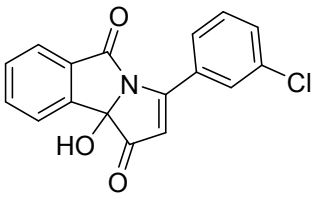


3-([1,1'-biphenyl]-4-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3h) : According to general procedure B, 1h (253 mg, 1 mmol) gave 3h (255 mg, 72%) as a yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 235-236 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.08 (s, 1H), 8.04 (d, *J* = 8.3 Hz, 2H), 7.90-7.79 (m, 6H), 7.77-7.71 (m, 2H), 7.53 (t, *J* = 7.3 Hz, 2H), 7.46 (d, *J* = 7.2 Hz, 1H), 6.53 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 195.8, 169.3, 167.9,

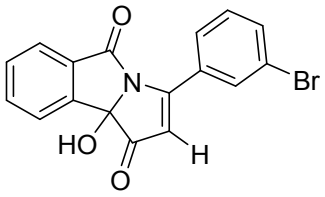
144.0, 142.8, 138.8, 135.2, 131.3, 131.0, 130.4, 129.1, 128.9, 128.4, 126.9, 126.4, 124.5, 124.3, 112.2, 91.3; HRMS (ESI) calcd for $C_{23}H_{15}NO_3[M+H]^+$ 354.1130, found 354.1135.



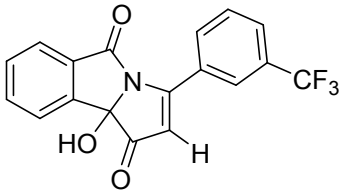
9b-hydroxy-3-(3-methoxphenyl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3i) : According to general procedure B, 1i (207 mg, 1 mmol) gave 3i (231 mg, 75%) as a yellow solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p.194-195 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.04 (s, 1H), 7.90-7.79 (m, 2H), 7.77-7.66 (m, 2H), 7.55-7.44 (m, 3H), 7.24-7.19 (m, 1H), 6.50 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 195.9, 169.7, 167.7, 158.9, 142.7, 135.2, 131.3, 131.2, 131.0, 129.4, 124.5, 124.3, 122.1, 118.5, 114.5, 112.7, 91.3, 55.4; HRMS (ESI) calcd for $C_{18}H_{13}N_2O_4[M+Na]^+$ 330.0742, found 330.0746.



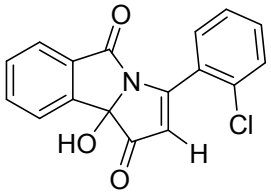
3-(3-chlorophenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3j) : According to general procedure B, 1J (211 mg, 1 mmol) gave 3J (193 mg, 62%) as a pale yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p.161-162 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.10 (s, 1H), 7.96 (s, 1H), 7.93-7.80 (m, 3H), 7.77-7.66 (m, 3H), 7.60 (t, *J* = 7.9 Hz, 1H), 6.59 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 195.9, 167.99,167.95, 142.6, 135.3, 133.1, 132.1, 131.9, 131.3, 130.9, 130.2, 128.9, 128.2, 124.5, 124.3, 113.5, 91.2; HRMS (ESI) calcd for $C_{17}H_{10}ClNO_3[M+H]^+$ 312.0427, found 312.0437.



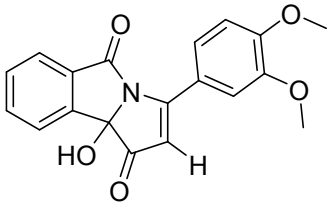
3-(3-bromophenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3k) : According to general procedure B, 1k (256 mg, 1 mmol) gave 3k (218 mg, 61%) as a yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 155-156 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.09 (s, 2H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.90-7.80 (m, 3H), 7.77-7.67 (m, 2H), 7.53 (t, *J* = 7.9 Hz, 1H), 6.58 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ 195.8, 167.8, 142.6, 135.3, 135.0, 132.1 131.7, 131.3, 130.9, 130.4, 128.5, 124.5, 124.3, 121.5 113.5, 91.2; HRMS (ESI) calcd for $C_{17}H_{10}{}^{79}BrNO_3[M+H]^+$ 355.9922, found 355.9906; HRMS (ESI) calcd for $C_{17}H_{10}{}^{81}BrNO_3[M+H]^+$ 355.9902, found 357.9903.



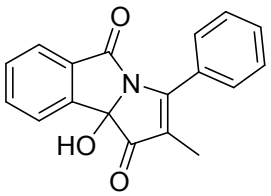
9b-hydroxy-3-(3-(trifluoromethyl)phenyl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3l) : According to general procedure B, 1l (245 mg, 1 mmol) gave 3l (190 mg, 55%) as a brown solid. R_f = 0.4 (EtOAc/hexanes, 2:8); m.p. 217-218 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.24-8.22 (m, 2H), 8.11 (s, 1H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.91-7.79 (m, 3H), 7.77-7.66 (m, 2H), 6.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 196.2, 168.3, 168.1, 142.8, 135.6, 133.5, 131.6, 131.07, 131.02, 129.8, 129.5 129.1, 126.2, 126.1, 124.8, 124.5, 124.1 (q, *J* = 184.8 Hz)113.9, 91.4; ^{19}F NMR(300 MHz, DMSO) δ -56.55 (s, CF_3); HRMS (ESI) calcd for $C_{18}H_{10}F_3NO_3[M+H]^+$ 346.0691, found 346.0699.



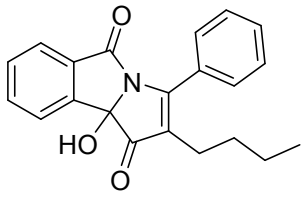
3-(2-chlorophenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3m) : According to general procedure B, 1m (211 mg, 1 mmol) gave 3m (187 mg, 60%) as a yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 97-98 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.12 (s, 1H), 7.87-7.80 (m, 2H), 7.70 (t, *J* = 7.3 Hz, 3H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 6.27 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 195.9, 167.1, 166.7, 142.5, 135.3, 132.7, 132.5, 131.8, 131.3, 131.0, 130.3, 129.6, 127.1, 124.4, 124.3, 115.05, 90.0; HRMS (ESI) calcd for $C_{17}H_{10}ClNO_3[M+H]^+$ 312.0427, found 312.0429.



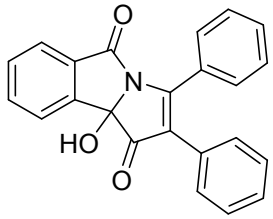
3-(3,4-dimethoxyphenyl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3n) : According to general procedure B, 1n (237 mg, 1 mmol) gave 3n (260 mg, 77%) as a white solid. R_f = 0.2 (EtOAc/hexanes, 3:7); m.p.225-226 ºC; ^{1}H NMR (400 MHz, DMSO) δ 7.99 (s, 1H), 7.89-7.77 (m, 2H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.71-7.65 (m, 1H), 7.60 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 6.41 (s, 1H), 3.88 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 195.4, 169.7, 167.9, 152.9, 148.2, 143.0, 135.2, 131.3, 131.0, 124.5, 124.4, 124.3, 122.2, 112.6, 111.0, 110.5, 91.6, 55.89, 55.80; HRMS (ESI) calcd for $C_{19}H_{15}NO_5[M+H]^+$ 338.1028, found 338.1033.



9b-hydroxy-2-methyl-3-phenyl-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3o) :According to general procedure B, 1o (191 mg, 1 mmol) gave 3o (222 mg, 76%) as a yellow solid. R_f = 0.3 (EtOAc/hexanes, 3:7); m.p. 193-194 ºC; ^{1}H NMR (400 MHz, DMSO) δ 7.94 (s, 1H), 7.85-7.83 (m, 2H), 7.79-7.75 (m, 2H), 7.69-7.66 (m, 2H), 7.60-7.57 (m, 3H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 196.8, 168.3, 163.1, 142.8, 135.1, 131.3, 131.27,131.24, 131.0, 129.6, 128.3, 124.41, 120.6, 89.5, 8.3; HRMS (ESI) calcd for $C_{18}H_{13}NO_3[M+H]^+$ 292.0974, found 292.0979.

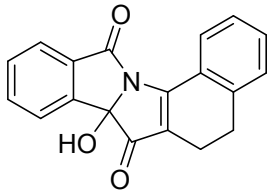


2-butyl-9b-hydroxy-3-phenyl-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3p) : According to general procedure B, 1p (233 mg, 1 mmol) gave 3p (234 mg, 70%) as a pale yellow solid. R_f = 0.4 (EtOAc/hexanes, 1:9); m.p.129-130 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.01 (s, 1H), 7.86-7.79 (m, 2H), 7.72-7.62 (m, 4H), 7.61-7.54 (m, 3H), 2.37-2.16 (m, 2H), 1.42-1.32 (m, 2H), 1.27 - 1.17 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 197.0, 168.5, 163.6, 142.9, 135.3, 131.5, 131.39, 131.37, 131.2, 129.2, 128.6, 125.0, 124.6, 124.5, 89.3, 30.1, 22.2, 22.1, 13.7; HRMS (ESI) calcd for $C_{21}H_{19}NO_3[M+H]^+$ 334.1486, found 334.1490.

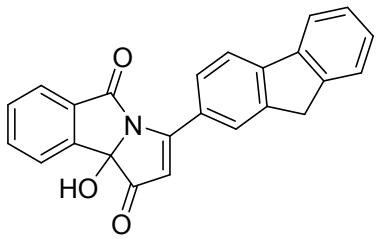


9b-hydroxy-2,3-diphenyl-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3q) : According to general procedure B, 1q (253 mg, 1 mmol) gave 3q (259 mg, 73%) as a yellow solid. R_f = 0.4 (EtOAc/hexanes, 3:7); m.p. 233-234 ºC; ^{1}H NMR (300 MHz, DMSO) δ 8.17 (s, 1H), 7.90-7.89 (m, 2H), 7.73-7.70 (m, 2H), 7.52-7.50 (m, 3H), 7.43-7.38 (m, 2H), 7.31 (d, *J* = 7.4 Hz, 3H), 7.17-7.12 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ 194.4, 169.2, 167.8, 163.8, 142.6, 135.2,

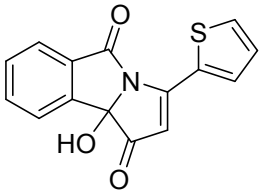
134.3, 131.4, 131.3, 130.1, 128.9, 128.2, 128.0, 127.5, 124.4, 124.3, 123.8, 122.9, 89.8; HRMS (ESI) calcd for $C_{23}H_{15}NO_3[M+H]^+$ 354.1130, found 354.1137.



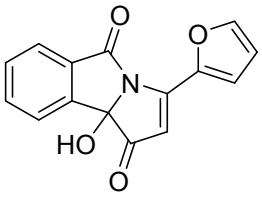
7a-hydroxy-5,6-dihydro-7*H*-benzo[*g*]isoindolo[2,1-*a*]indole-7,12(7a*H*)-dione (3r) : According to general procedure B, 1r (203 mg, 1 mmol) gave 3r (197 mg, 65%) as a yellow solid. R_f = 0.2 (EtOAc/hexanes, 3:7); m.p. 193-194 ºC; ^{1}H NMR (300 MHz, DMSO) δ 7.96 (d, *J* = 8.8 Hz, 2H), 7.88-7.81 (m, 2H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.73-7.66 (m, 1H), 7.51 (dt, *J* = 7.4, 3.8 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 2.97-2.85 (m, 2H), 2.63 -2.53 (m, 1H), 2.39-2.28 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.4, 168.8, 163.6, 143.4, 140.6, 135.6, 132.9, 131.8, 131.2, 129.0, 128.6, 127.4, 126.8, 125.0, 124.6, 122.5, 92.3, 27.5, 17.1; HRMS (ESI) calcd for $C_{19}H_{13}NO_3[M+H]^+$ 304.0974, found 304.0973.



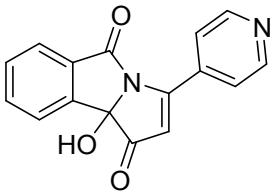
3-(9*H*-fluoren-2-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3s) : According to general procedure B, 1s (265 mg, 1 mmol) gave 3s (249 mg, 68%) as a yellow solid . R_f = 0.4 (EtOAc/hexanes, 3:7); ^{1}H NMR (400 MHz, DMSO) δ 8.16 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 6.6 Hz, 2H), 8.00 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.89-7.83 (m, 2H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.73-7.65 (m, 2H), 7.50-7.41 (m, 2H), 6.51 (s, 1H), 4.05 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 195.8, 170.3, 168.0, 145.7, 144.4, 142.9, 140.1, 135.3, 131.4, 131.1, 129.1, 128.3, 127.2, 126.5, 125.5, 124.6, 124.4, 121.2, 119.9, 111.8, 91.5,36.5; HRMS (ESI) calcd for $C_{24}H_{15}NO_3[M+H]^+$ 366.1130, found 366.1135.



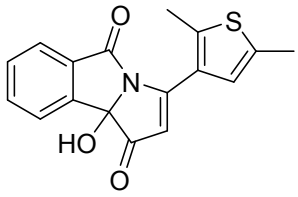
9b-hydroxy-3-(thiophen-2-yl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3t) : According to general procedure B, 1t (183 mg, 1 mmol) gave 3t (196 mg, 69%) as a yellow solid; Rf = 0.2 (EtOAc/hexanes, 3:7); m.p. 211-212 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.13 (br d, *J* = 4.5 Hz, 1H), 8.05-8.00 (m, 2H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.81-7.76 (m, 2H), 7.70 (t, *J* = 7.3 Hz, 1H), 7.36 -7.32 (m, 1H), 6.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.9, 167.8, 162.5, 142.92, 135.3, 134.8, 134.7, 132.5, 131.2, 130.7, 128.6, 124.6, 124.3, 110.1, 91.5 ; HRMS (ESI) calcd for $C_{15}H_9NO_3S[M+H]^+$ 284.0381, found 284.0380.



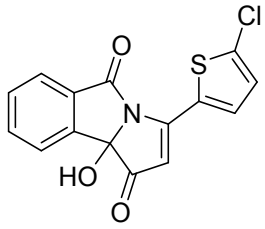
3-(furan-2-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3u) : According to general procedure B, 1u (167 mg, 1 mmol) gave 3u (190 mg, 71%) as a colourless solid. Rf = 0.2 (EtOAc/hexanes, 2:8); m.p. 189-190 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.16 (d, *J* = 1.1 Hz, 1H), 8.00 (s, 1H), 7.87-7.84 (m, 1H), 7.80-7.78 (m, 2H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 3.6 Hz, 1H), 6.90 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.16 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.7, 167.6, 156.9, 148.9, 145.0, 143.0, 135.2, 131.3, 130.7, 124.6, 124.3, 121.6, 113.6, 108.4, 91.0; HRMS (ESI) calcd for $C_{15}H_9NO_4[M+H]^+$ 268.0610, found 268.0611.



9b-hydroxy-3-(pyridin-4-yl)-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3v) : According to general procedure B, 1v (178 mg, 1 mmol) gave 3v (181 mg, 65%) as a yellow solid. Rf = 0.2 (EtOAc/hexanes, 4:6); m.p. 241-242 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.81 (d, *J* = 5.5 Hz, 2H), 8.16 (s, 1H), 7.91-7.81 (m, 4H), 7.77-7.66 (m, 2H), 6.71 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 196.1, 167.9, 167.2, 149.9, 142.5, 137.1, 135.4, 131.4, 130.9, 124.6, 124.3, 122.8, 115.3, 91.1; HRMS (ESI) calcd for $C_{16}H_{10}N_2O_3$[M+H]$^+$ 279.0770, found 279.0775.

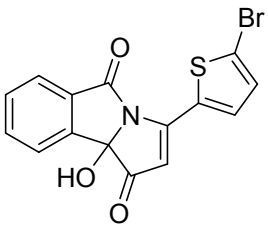


3-(2,5-dimethylthiophen-3-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3w) :According to general procedure B, 1w (211 mg, 1 mmol) gave 3w (224 mg, 72%) as a grey solid . Rf = 0.2 (EtOAc/hexanes, 3:7); m.p. 245-246 ºC; ^{1}H NMR (500 MHz, DMSO) δ 7.95 (s, 1H), 7.86-7.83 (m, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.69-7.66 (m, 1H), 7.01 (d, *J* = 0.6 Hz, 1H), 6.00 (s, 1H), 2.61 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 195.5, 167.4, 163.9, 144.1, 142.7, 135.5, 135.1, 131.2, 130.9, 128.0, 127.1, 124.4, 124.3, 111.3, 90.5, 14.7, 14.5; HRMS (ESI) calcd for $C_{17}H_{13}NO_3S$[M+H]$^+$ 312.0694, found 312.0712.

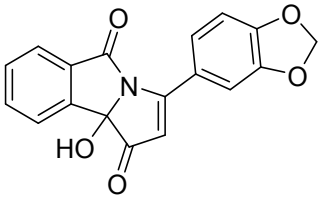


3-(5-chlorothiophen-2-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3x) : According to general procedure B, 1x (217 mg, 1 mmol) gave 3x (213 mg, 67%) as a yellow solid . Rf = 0.2 (EtOAc/hexanes, 2:8); m.p.199-200 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.06 (s, 1H), 7.93 (d, *J* = 4.1 Hz, 1H), 7.89-7.82 (m, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 4.1 Hz, 1H), 6.40 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.9, 168.0, 161.0,

142.8, 136.6, 135.4, 134.5, 131.3,131.2, 130.5, 128.6, 124.6, 124.3, 110.6, 91.5; HRMS (ESI) calcd for $C_{15}H_8ClNO_3S[M+H]^+$ 317.9987, found 317.9991.



3-(5-bromothiophen-2-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3y) : According to general procedure B, 1y (260 mg, 1 mmol) gave 3y (252 mg, 70%) as a pale yellow solid . Rf = 0.4 (EtOAc/hexanes, 2:8); m.p.229-230 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.05 (s, 1H), 7.88-7.84 (m, 2H), 7.80-7.77 (m, 2H), 7.72-7.68 (m, 1H), 7.50 (d, *J* = 4.1 Hz, 1H), 6.40 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.9, 168.0, 160.9, 142.88, 135.4, 135.2, 133.9, 132.0, 131.3, 130.5, 124.6, 124.3, 120.8, 110.6, 91.5; HRMS (ESI) calcd for $C_{15}H_8{}^{79}BrNO_3S[M+H]^+$ 361.9453, found 361.9439; HRMS (ESI) calcd for $C_{15}H_8{}^{81}BrNO_3S[M+H]^+$ 361.9432, found 361.9467.



3-(benzo[*d*][1,3]dioxol-5-yl)-9b-hydroxy-1*H*-pyrrolo[2,1-*a*]isoindole-1,5(9b*H*)-dione) (3z) : According to general procedure B, 1z (221 mg, 1 mmol) gave 3z (232 mg, 73%) as A brown solid . Rf = 0.2 (EtOAc/hexanes, 3:7); m.p.151-152 ºC; ^{1}H NMR (400 MHz, DMSO) δ 8.02 (s, 1H), 7.88-7.82 (m, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.71-7.65 (m, 1H), 7.56 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.46 (d, *J* = 1.7 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.36 (s, 1H), 6.17 (s, 2H); ^{13}C NMR (100 MHz, DMSO) δ 195.5, 169.4, 167.9, 151.3, 147.51, 142.9, 135.3,

131.3, 130.9, 126.1, 124.5, 124.3, 123.8, 110.9, 109.1, 108.2, 102.2, 91.6; HRMS (ESI) calcd for $C_{18}H_{11}NO_5$ $[M+H]^+$ 322.0715, found 322.0722.

5. X-ray Crystallography.

X-ray data for KA533 was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. O bound H atom was located in difference Fourier maps and its positions and isotropic displacement parameters were refined. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H or $1.2U_{eq}(C)$ for other H atoms].

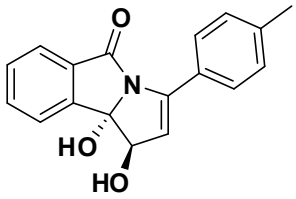
Crystal structure determination of 3d:

Crystal Data for $C_{17}H_{10}NO_3Cl$ (M =311.73 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 16.2453(4) Å, b = 8.9674(2) Å, c = 9.7074(2) Å, β = 93.2014(10)°, V = 1411.95(6) Å^3, Z = 4, T = 294.15 K, μ(Mo Kα) = 0.282 mm^{-1}, *Dcalc* = 1.4663 g/cm^3, 15624 reflections measured (5.02° ≤ 2Θ ≤ 61.06°), 4283 unique (R_{int} = 0.0345, R_{sigma} = 0.0403) which were used in all calculations. The final R_1 was 0.0620 (I>=2u(I)) and wR_2 was 0.1448 (all data). CCDC 1954828 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1. Bruker (2016). APEX3, SAINT and SADABS. Bruker AXS, Inc., Madison, Wisconsin, USA.
2. Sheldrick G. M. (2015) Acta Crystallogr C71: 3-8

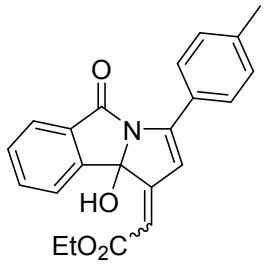
6. Synthetic application of 3b

Synthesis of compound 4:



1,9b-dihydroxy-3-(*p*-tolyl)-1,9-dihydro-5*H*-pyrrolo[2,1-*a*]isoindol-5-one (±4) : Compound 3b (0.5 mmol, 1 equiv) was dissolved in methanol (3 ml) and cooled to 0 °C, sodium borohydride was added and allow to stire for 1 hour after the complete consumption of starting material (monitored by TLC) then solvent was evaporated in vacuo and water (2mL) was added. The product was extracted with ethyl acetate (5 mL X 3) and the combine organic layer was washed with brine (10 mL) and solvent was evaporated under reduce pressure to get **4** (122 mg, 84 %) as yellow colour solid. m.p.203-204 ºC; ^{1}H NMR (400 MHz, DMSO) δ 7.74-7.65 (m, 3H), 7.60-7.55 (m, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 6.96 (s, 1H), 5.96 (d, *J* = 1.8 Hz, 1H), 5.67 (d, *J* = 7.8 Hz, 1H), 4.88 (dd, *J* = 7.8, 1.5 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 166.9, 147.1, 139.7, 138.1, 133.2, 132.1, 129.9, 128.5, 126.7, 123.5, 123.4, 121.0, 98.7, 76.1, 20.9; HRMS (ESI) calcd for $C_{18}H_{15}NO_3$ $[M+Na]^+$ 316.0950, found 316.0953.

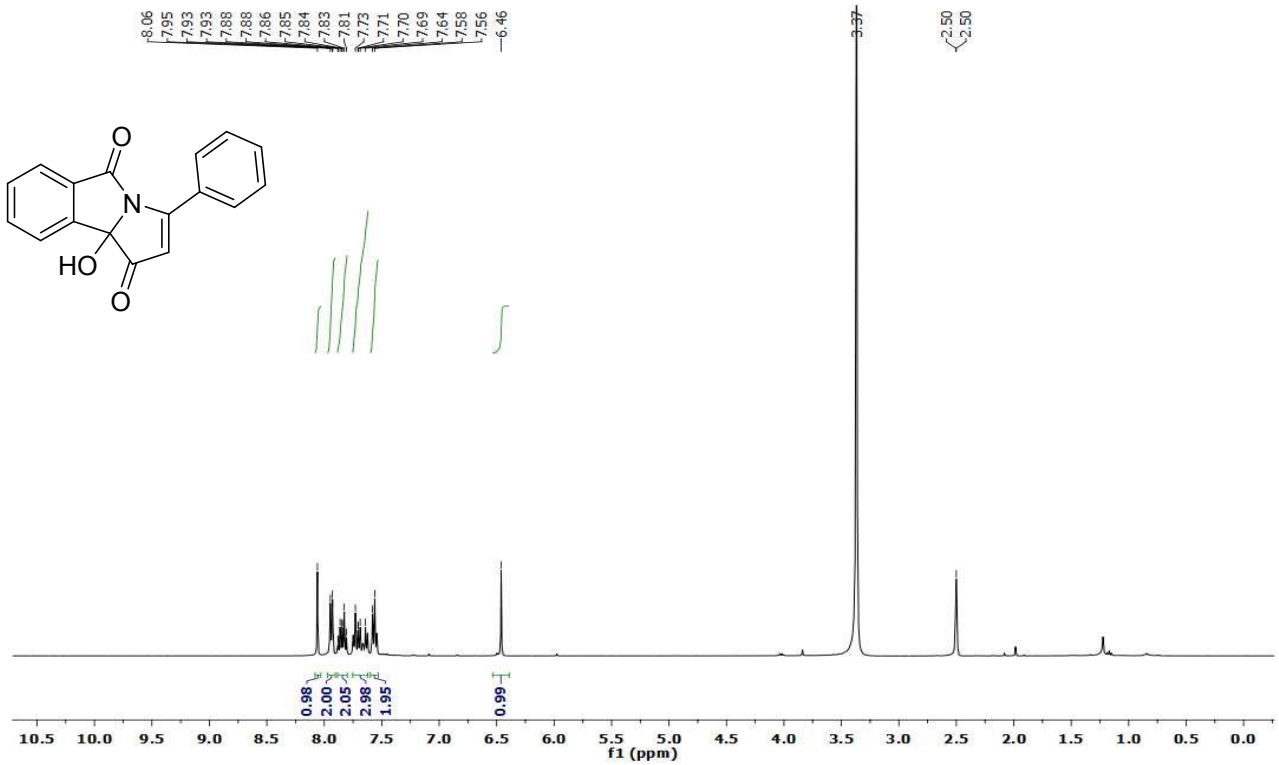
Synthesis of compound 5:



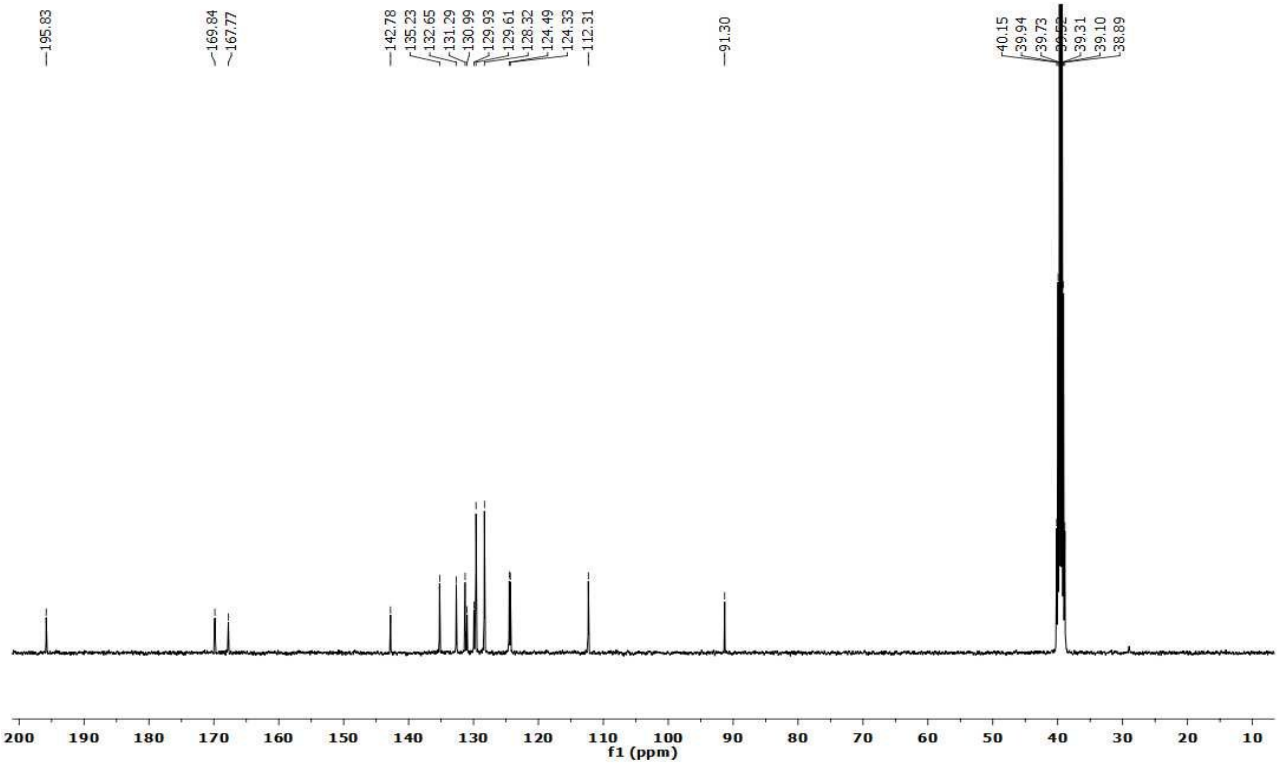
Ethyl-2-(9b-hydroxy-5-oxo-3-(p-tolyl)-5,9b-dihydro-1H-pyrrolo[2,1-*a*]isoindol-1-ylidene)acetate (5): Compound 3b (0.5 mmol) and Ethyl (Triphenylphosphoranylidene)acetate (0.6 mmol) were dissolved in toluene (3 ml) and reflux for 48 hours. After the completion of the reaction solvent was evaporated under reduced pressure and crude residue was purified by silica

gel column chromatography to yield compound **5** (139 mg, 77%). m.p.289-290 ºC;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.70 (m, 5H), 7.56 (t, *J* = 7.5, 1H), 7.24 (m, 3H), 6.06 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.98, 166.63, 156.17, 153.88, 144.91, 141.70, 134.77, 132.30, 131.12, 129.16, 129.01, 127.88, 125.48, 123.19, 111.41, 110.66, 97.01, 60.53, 21.81, 14.48.; HRMS (ESI) calcd for $C_{22}H_{19}NO_4$ $[M+Na]^+$ 384.1212, found 384.1216.

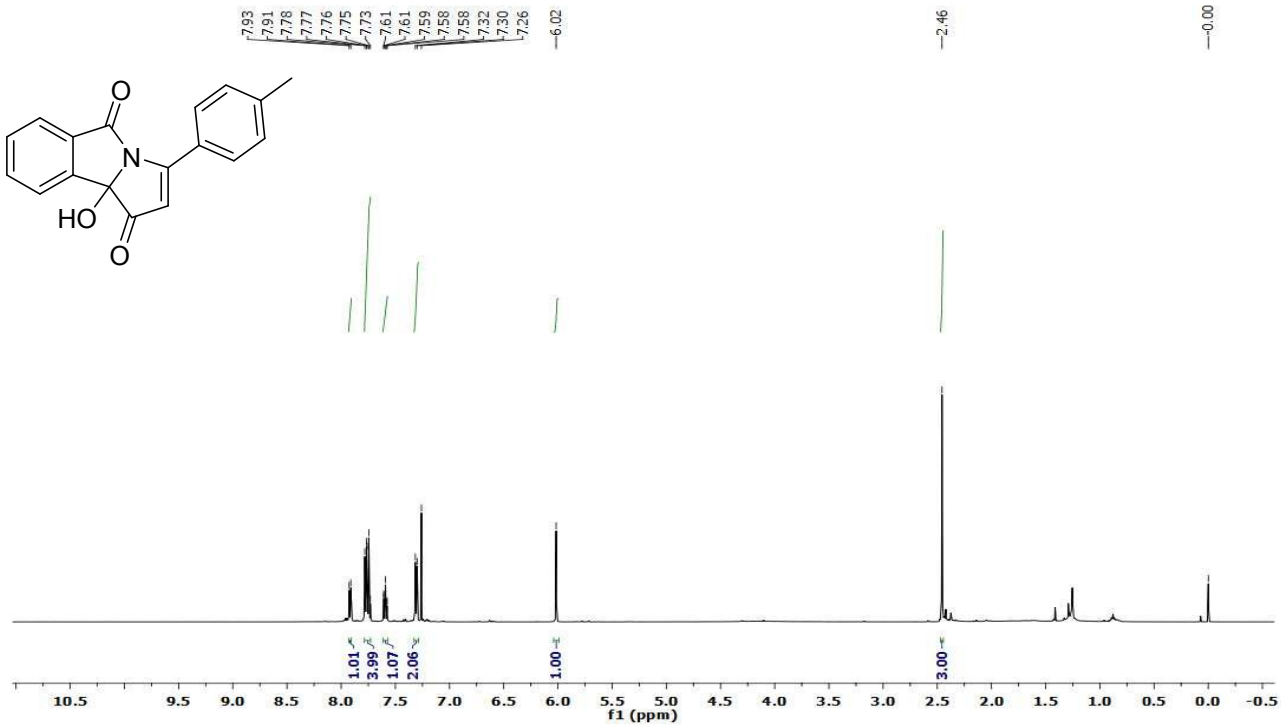
7. ^{1}H and ^{13}C NMR spectra



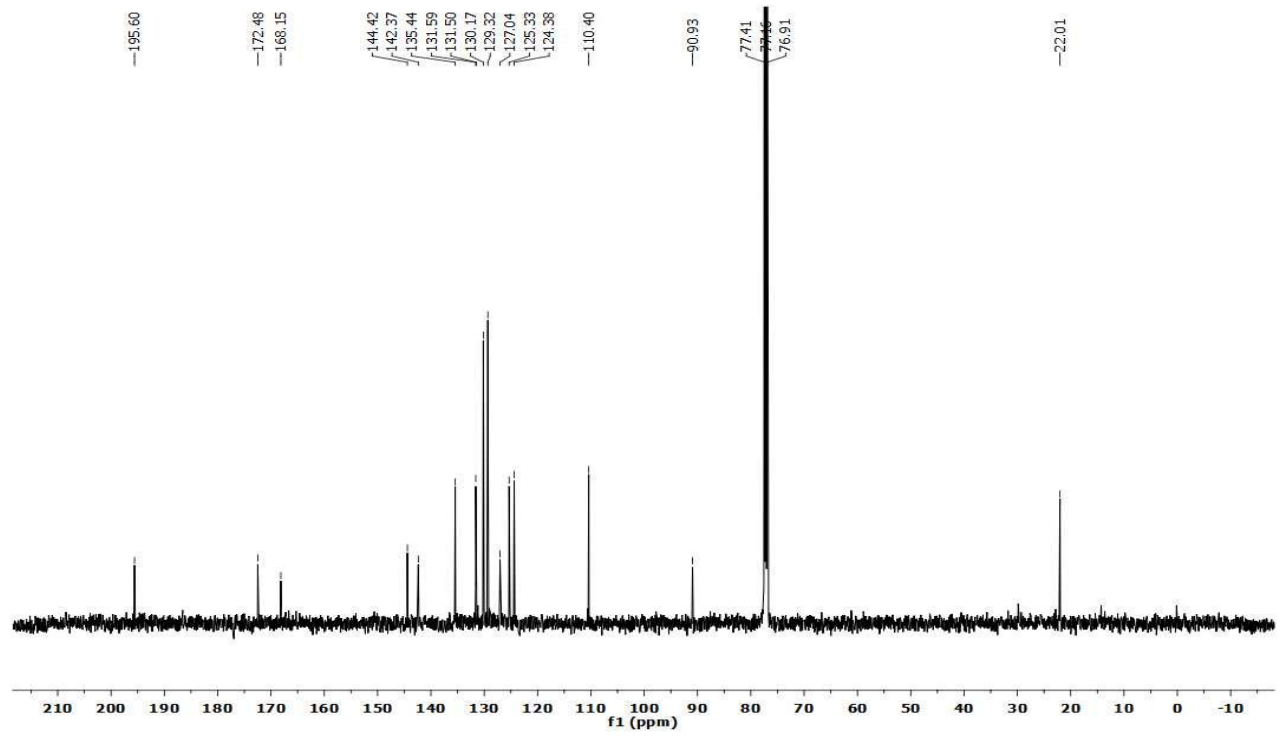
^{1}H-NMR spectrum of **3a** (400 MHz, DMSO-d^{6})



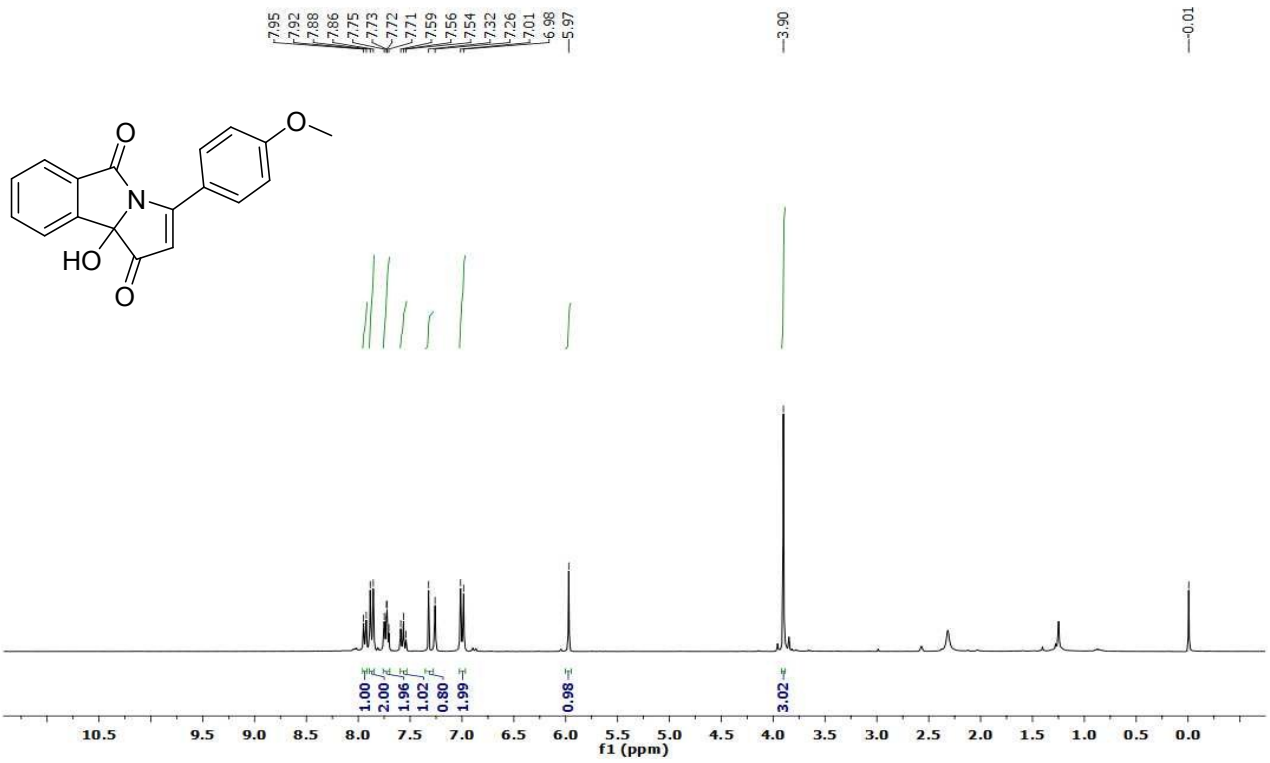
^{13}C-NMR spectrum of **3a** (100 MHz, DMSO-d^{6})



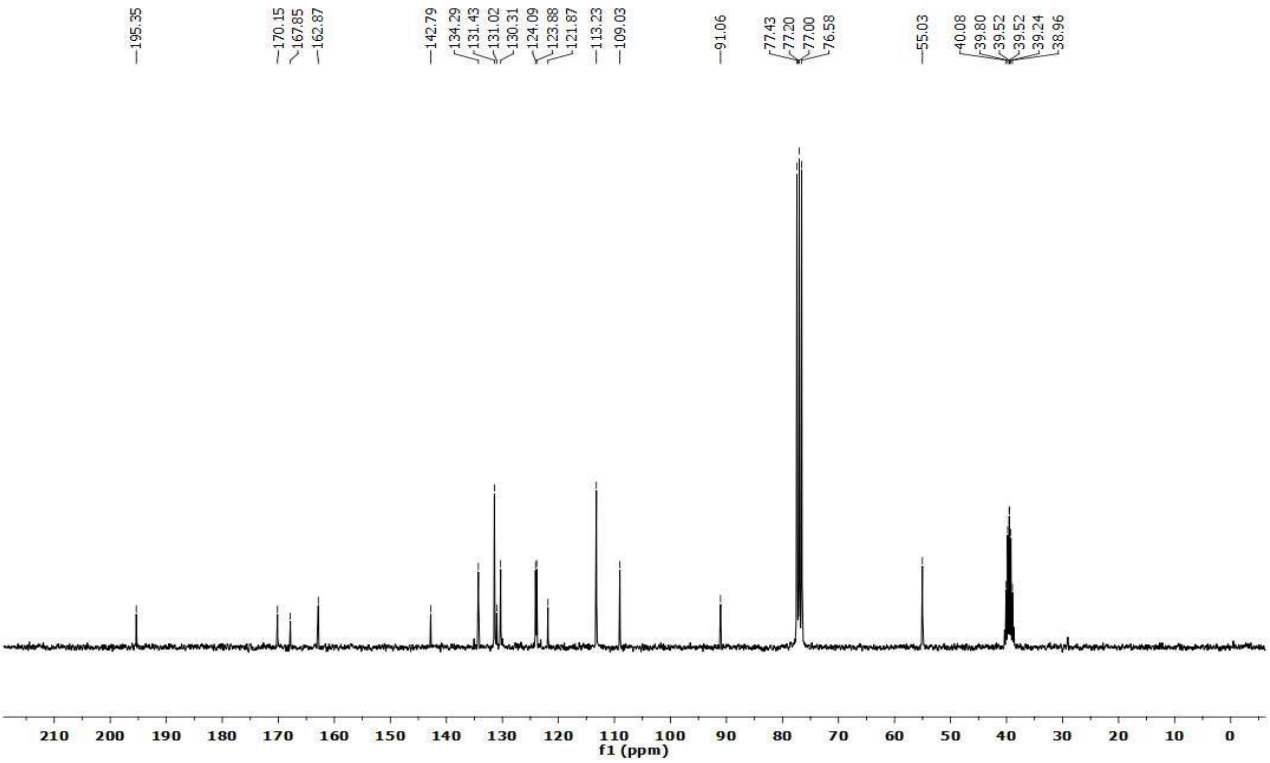
^{1}H-NMR spectrum of **3b** (500 MHz, $CDCl_3$)



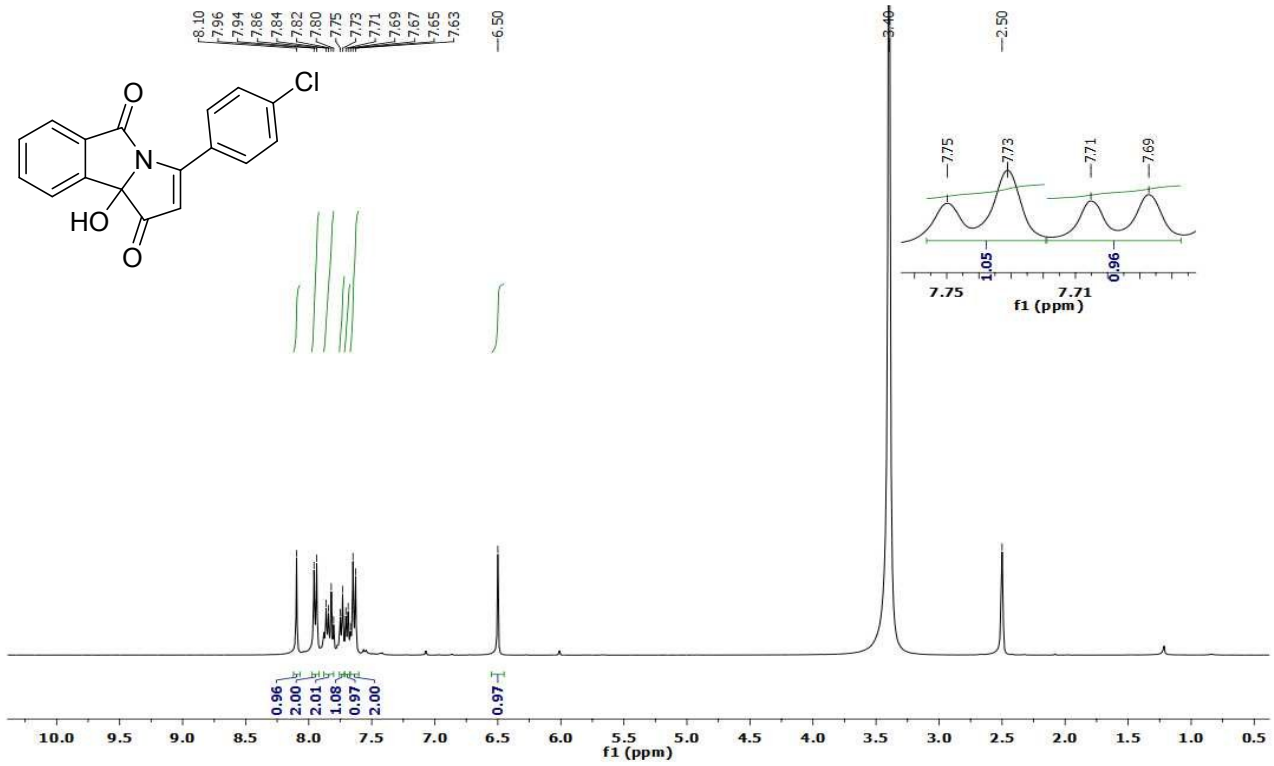
^{13}C-NMR spectrum of **3b** (100 MHz, $CDCl_3$)



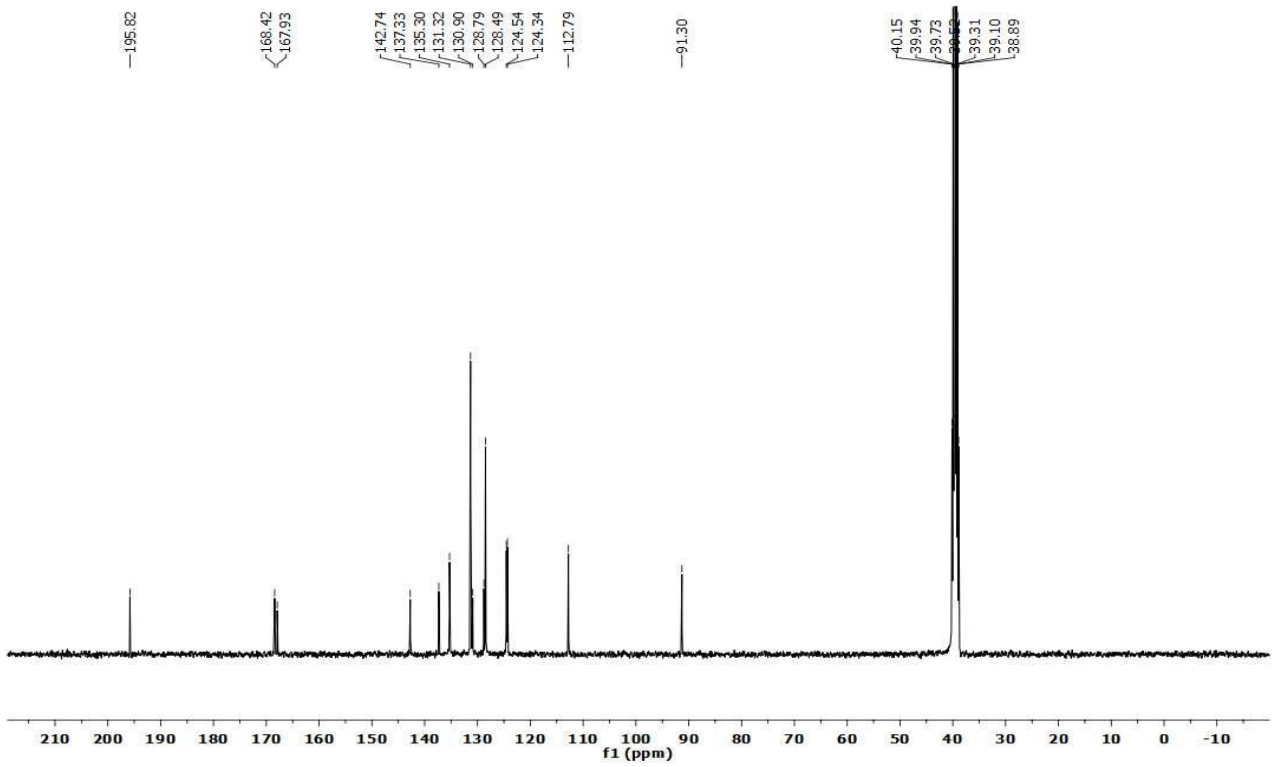
^{1}H-NMR spectrum of **3c** (300 MHz, $CDCl_3$+DMSO-d^6)



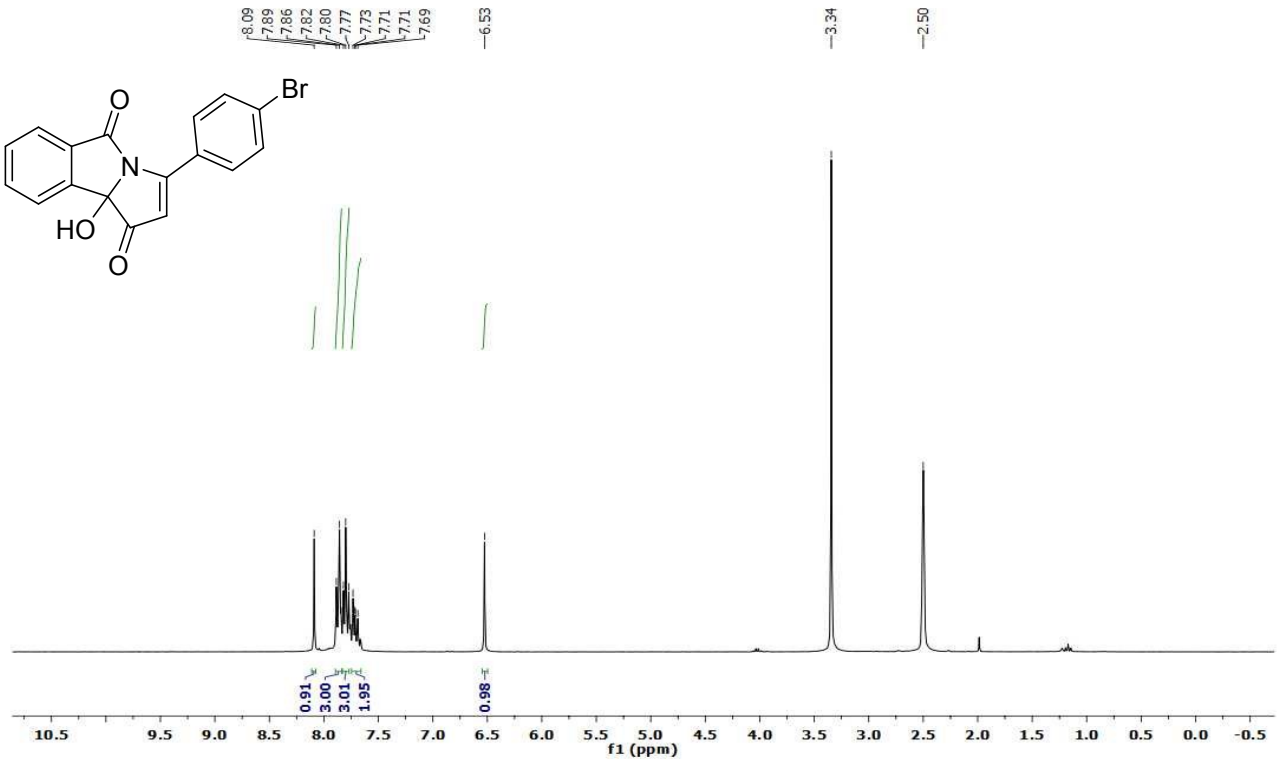
^{13}C-NMR spectrum of **3c** (75 MHz, $CDCl_3$+DMSO-d^6)



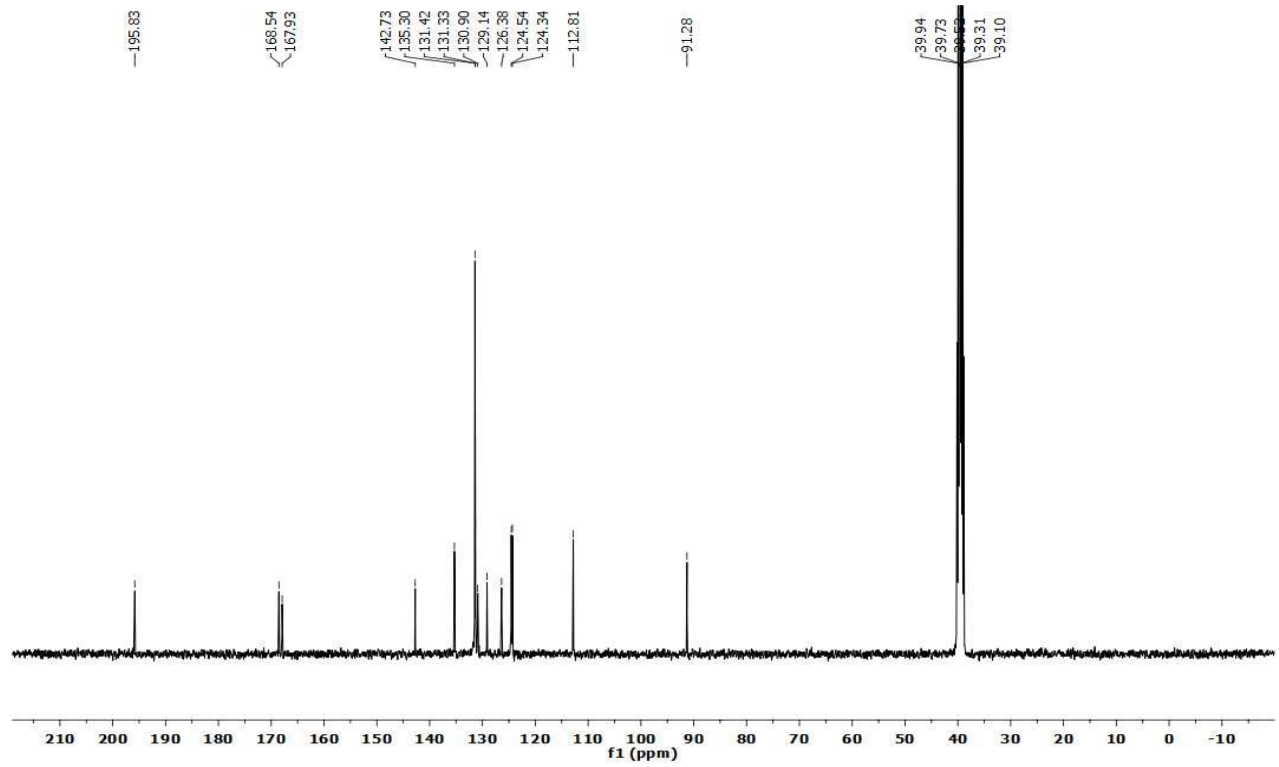
^{1}H-NMR spectrum of **3d** (400 MHz, DMSO-d^{6})



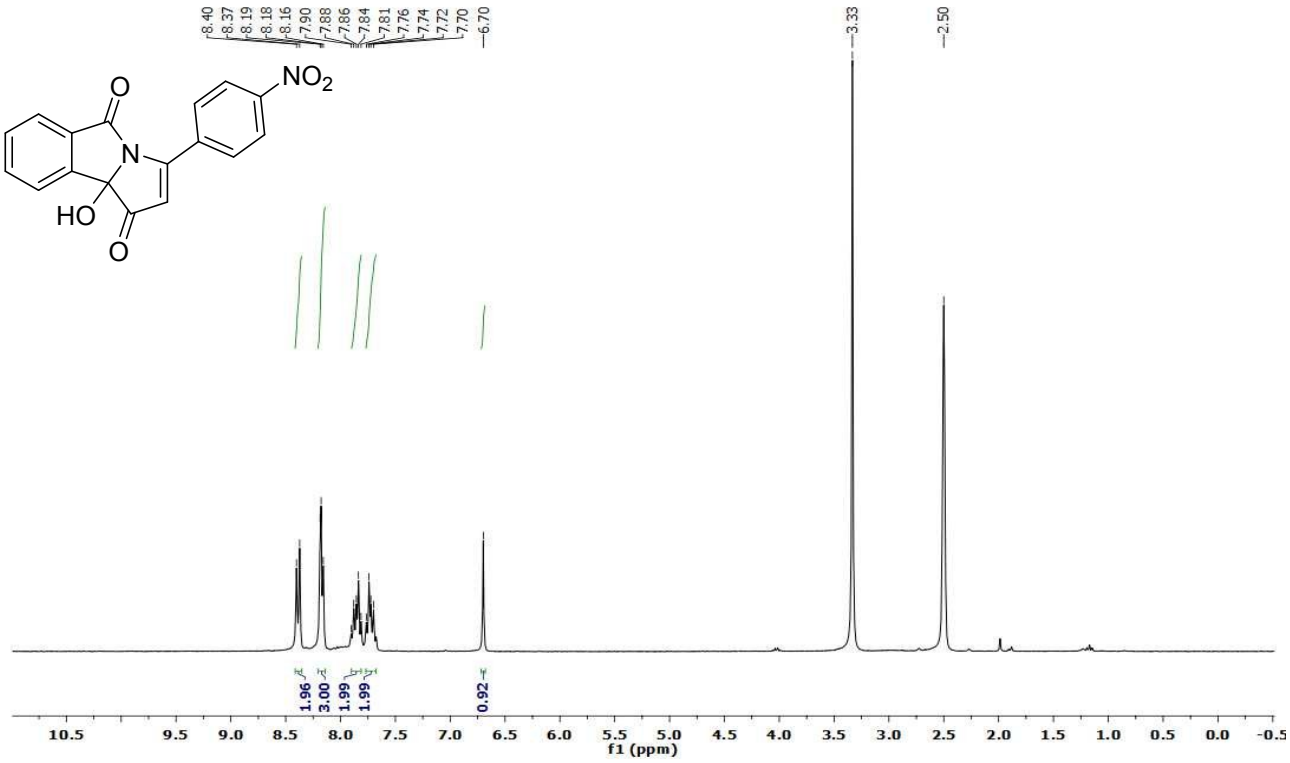
^{13}C-NMR spectrum of **3d** (100 MHz, DMSO-d^{6})



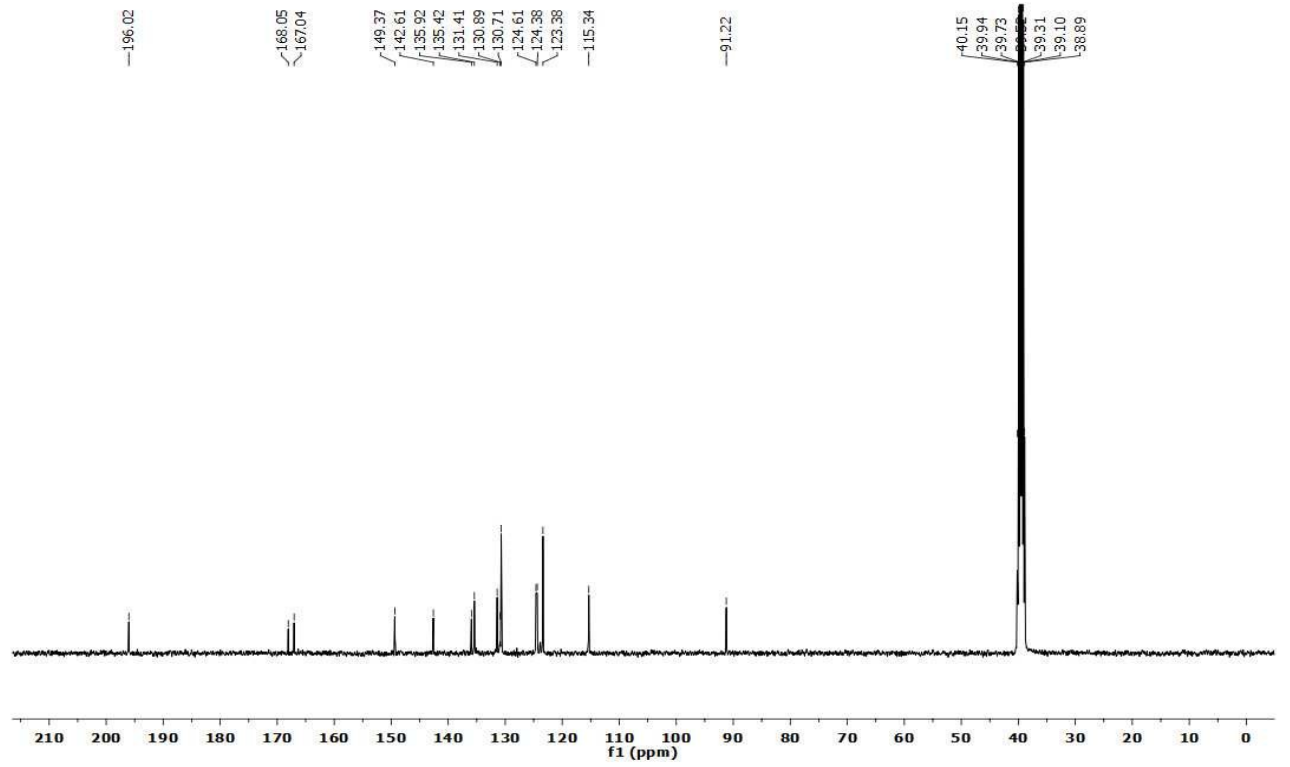
^{1}H-NMR spectrum of **3e** (300 MHz, DMSO-d^{6})



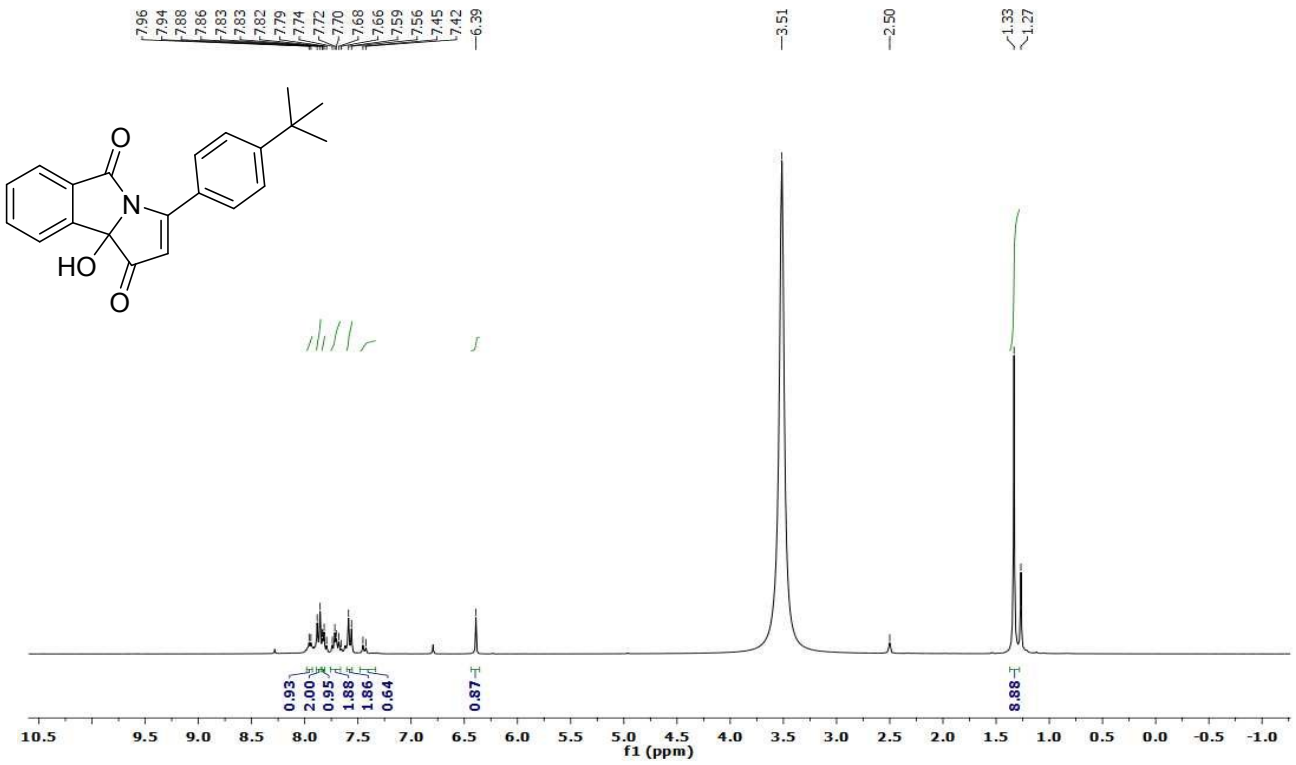
^{13}C-NMR spectrum of **3e** (100 MHz, DMSO-d^{6})



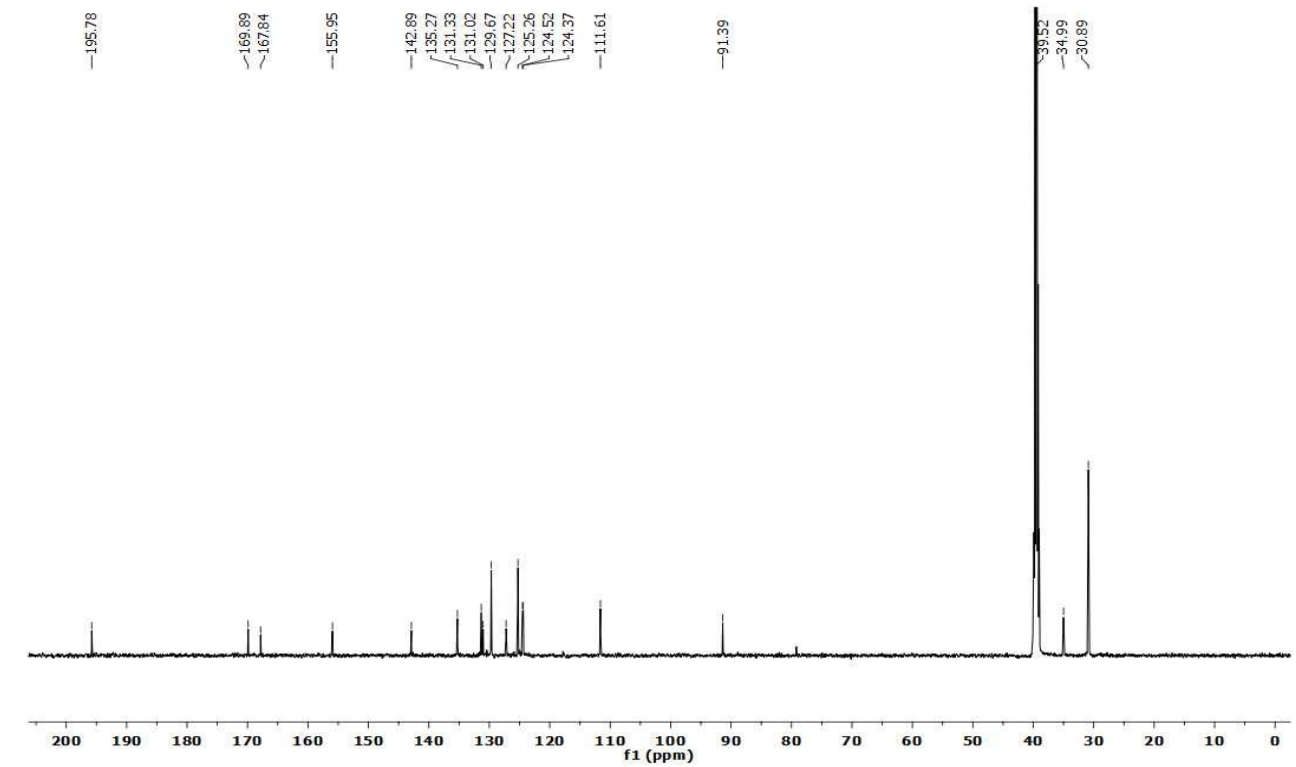
^{1}H-NMR spectrum of **3f** (300 MHz, DMSO-d^{6})



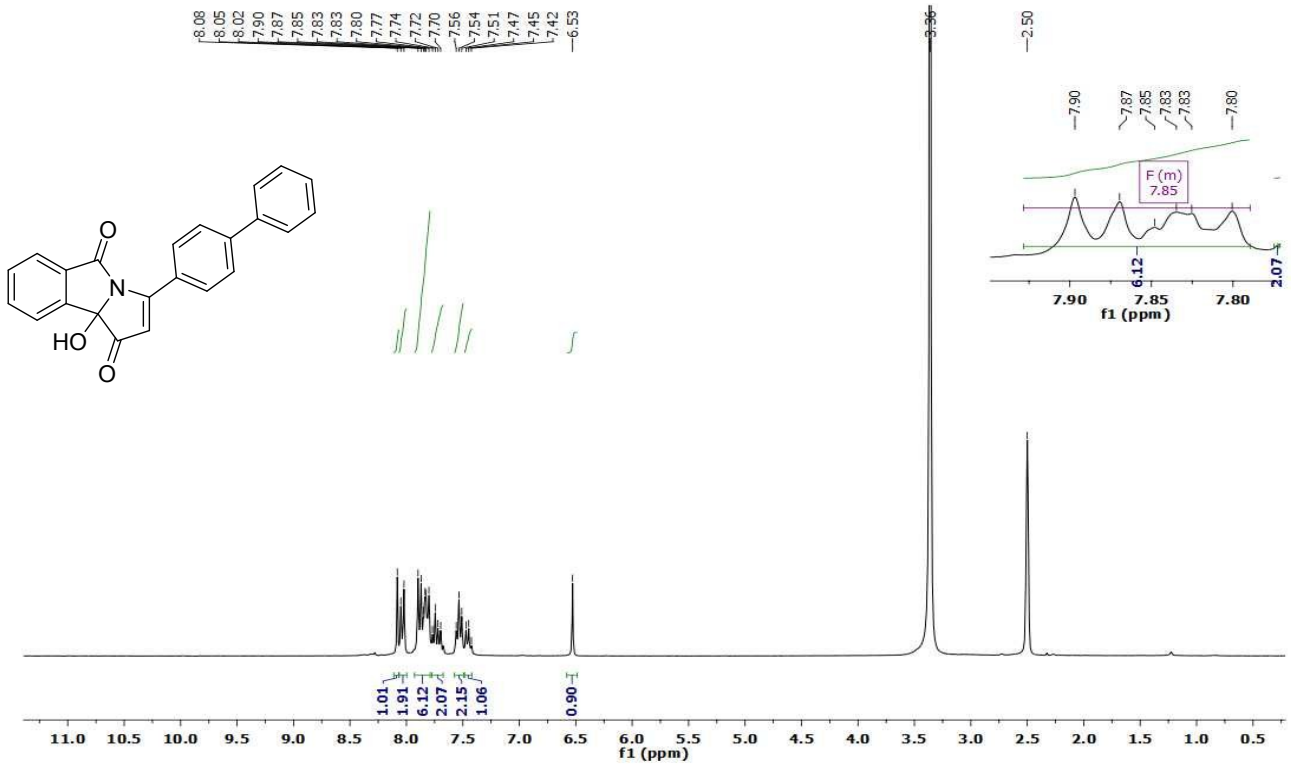
^{13}C-NMR spectrum of **3f** (100 MHz, DMSO-d^{6})



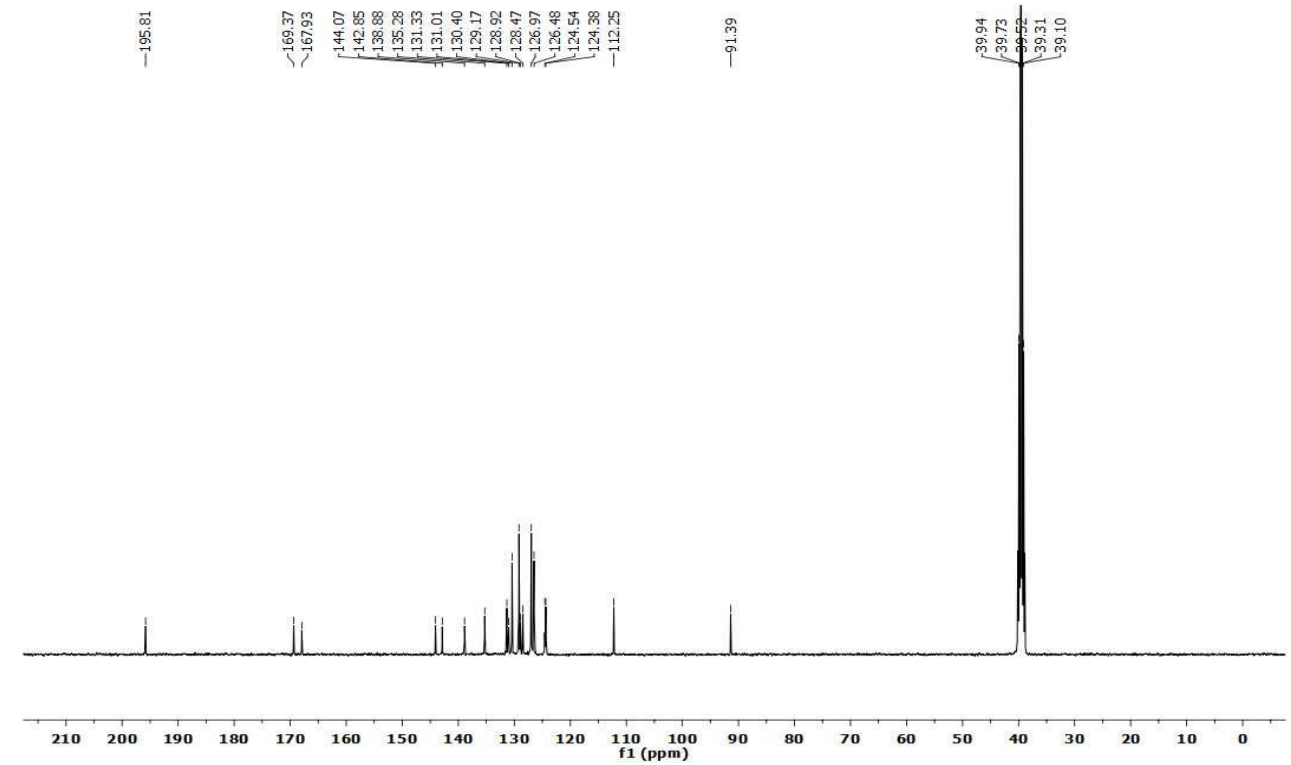
^{1}H-NMR spectrum of **3g** (300 MHz, DMSO-d^{6})



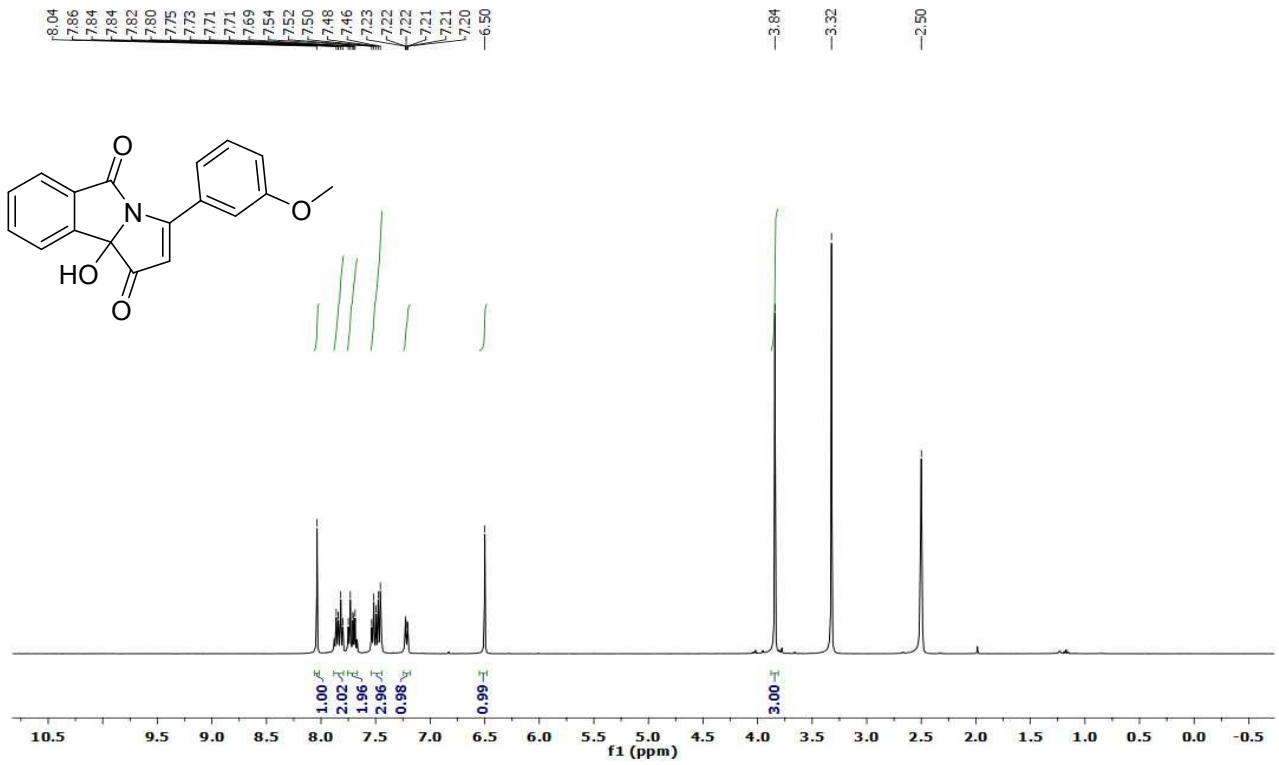
^{13}C-NMR spectrum of **3g** (100 MHz, DMSO-d^{6})



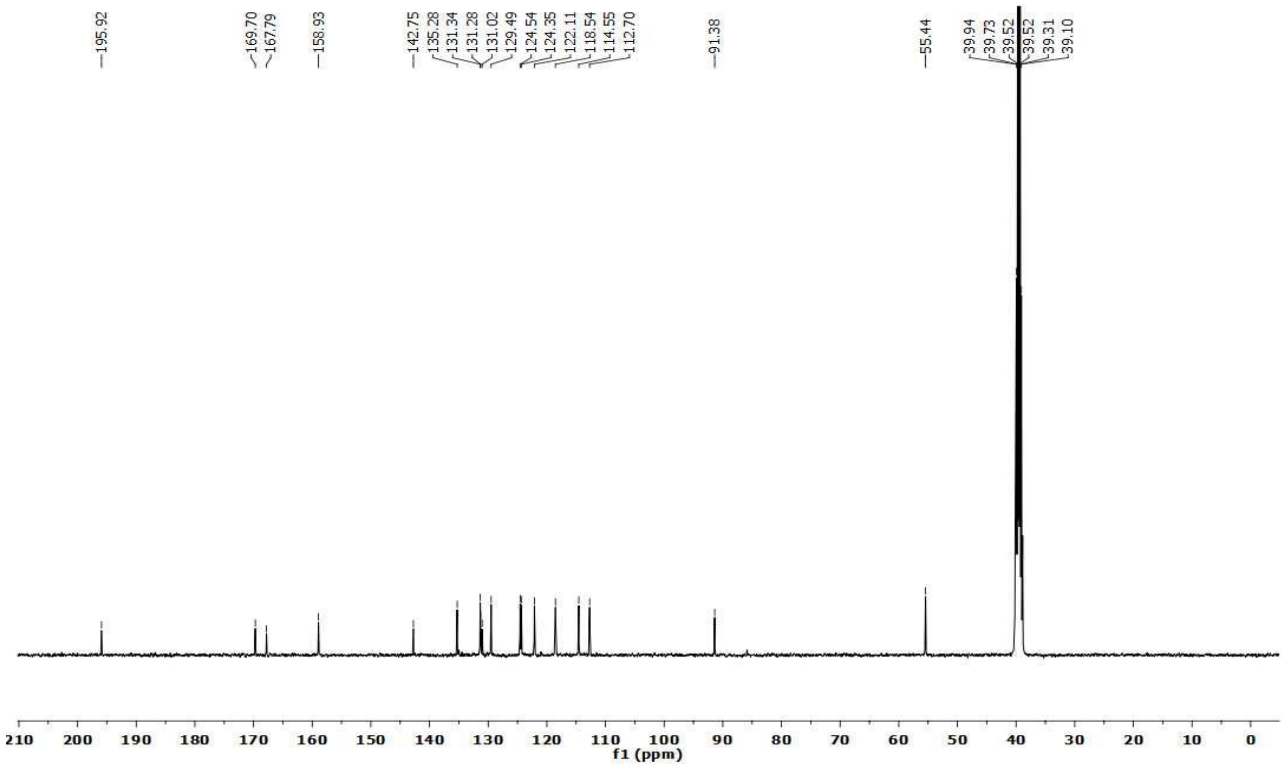
^{1}H-NMR spectrum of **3h** (300 MHz, DMSO-d^{6})



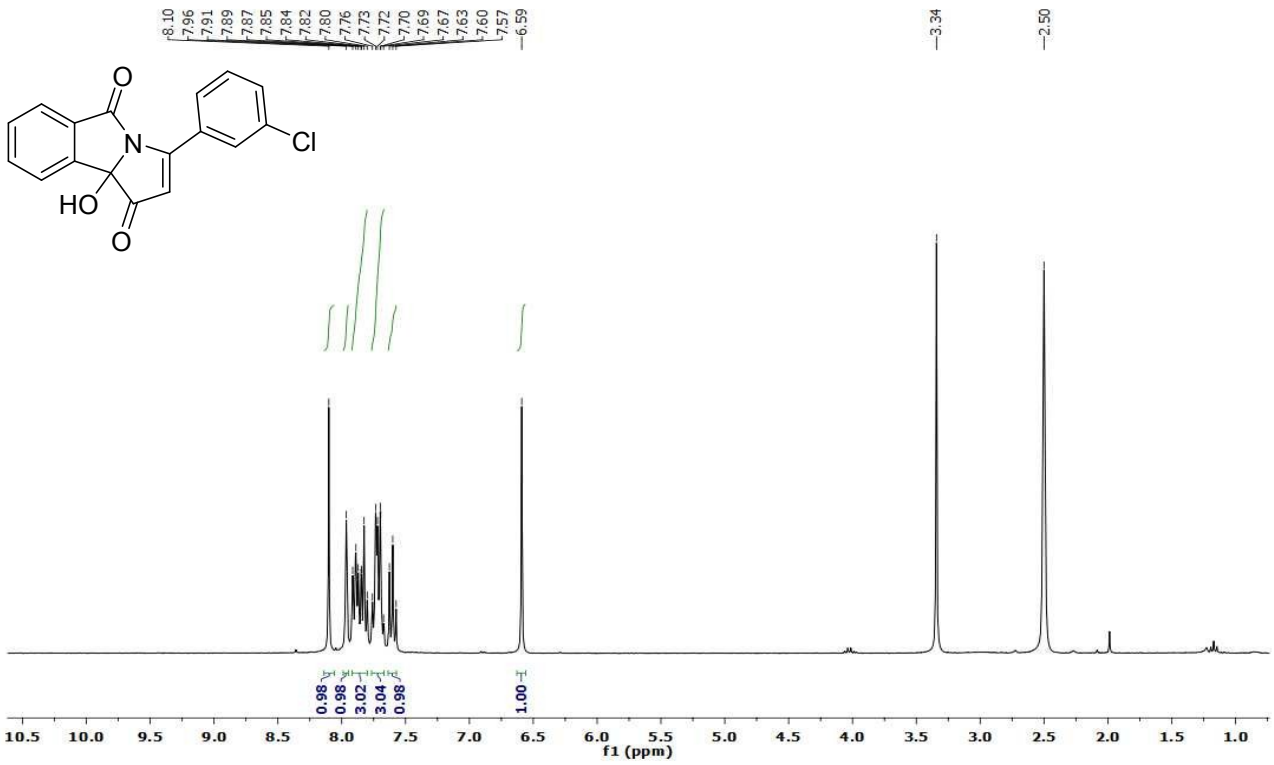
^{13}C-NMR spectrum of **3h** (100 MHz, DMSO-d^{6})



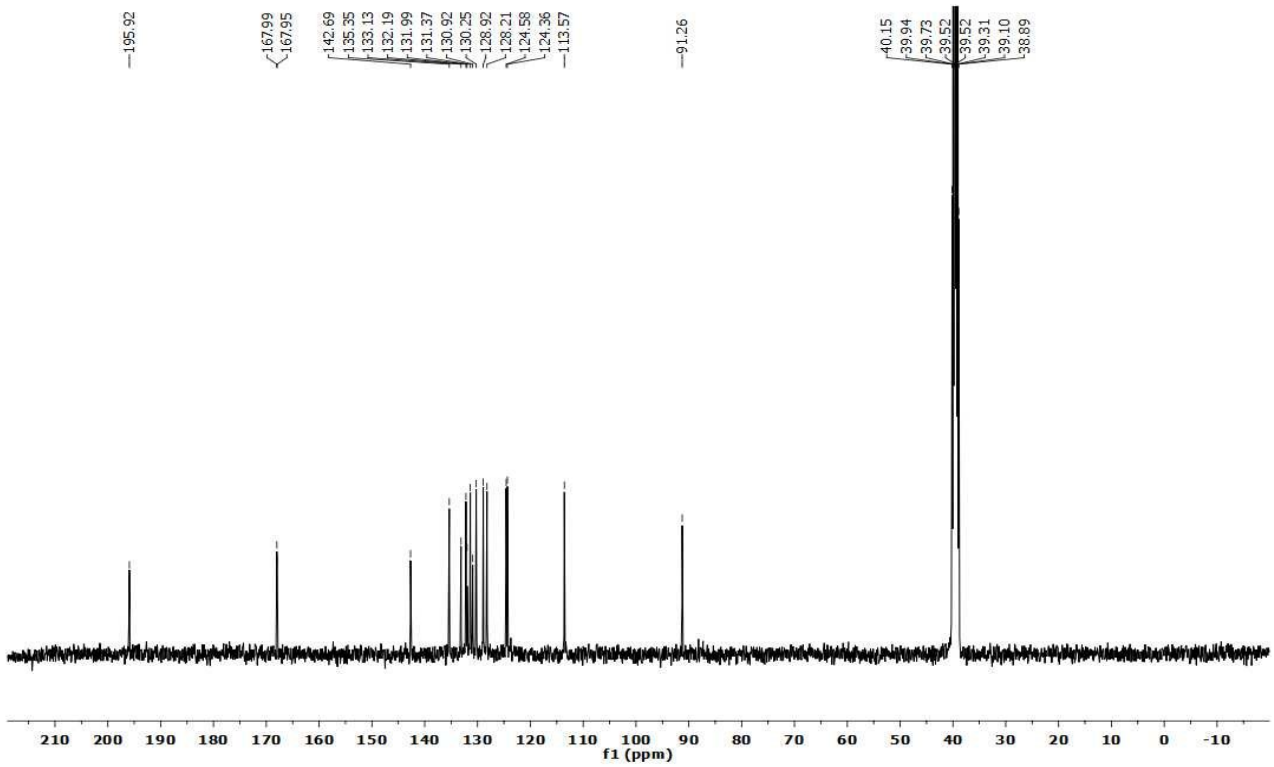
^{1}H-NMR spectrum of **3i** (400 MHz, DMSO-d^{6})



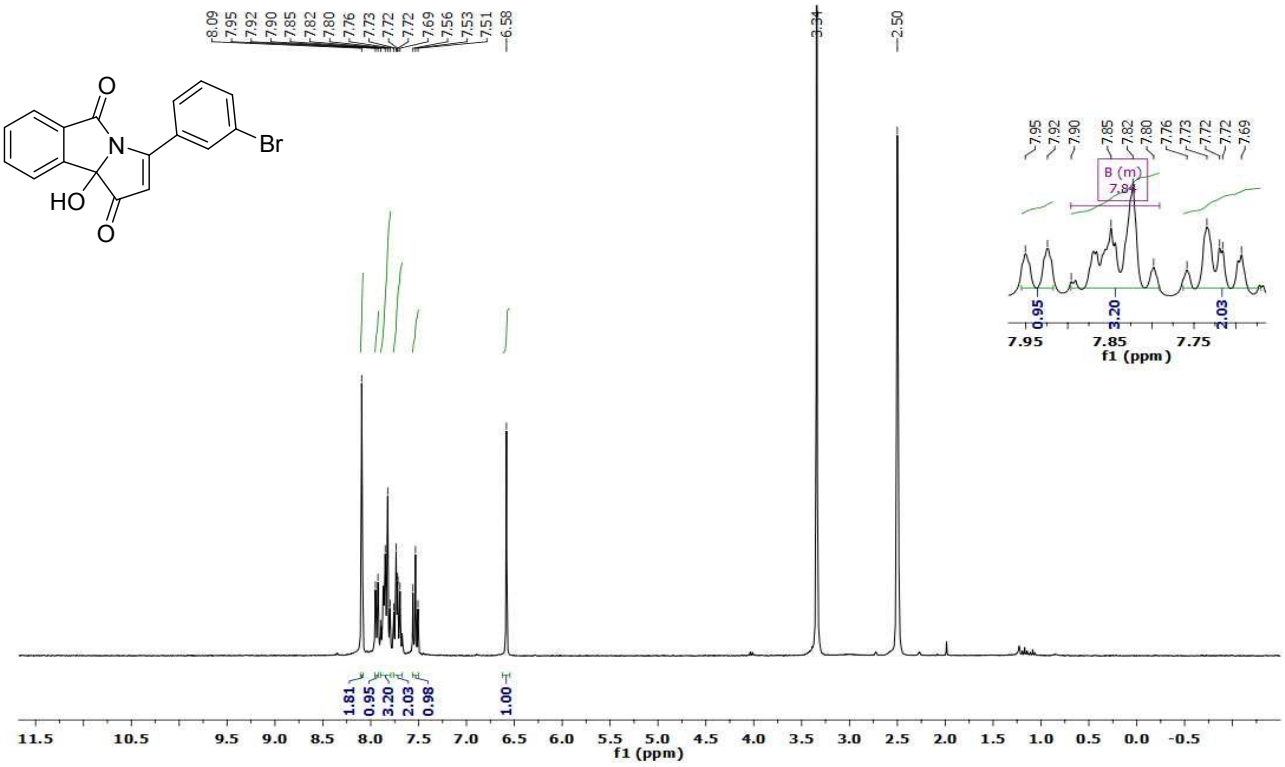
^{13}C-NMR spectrum of **3i** (100 MHz, DMSO-d^{6})



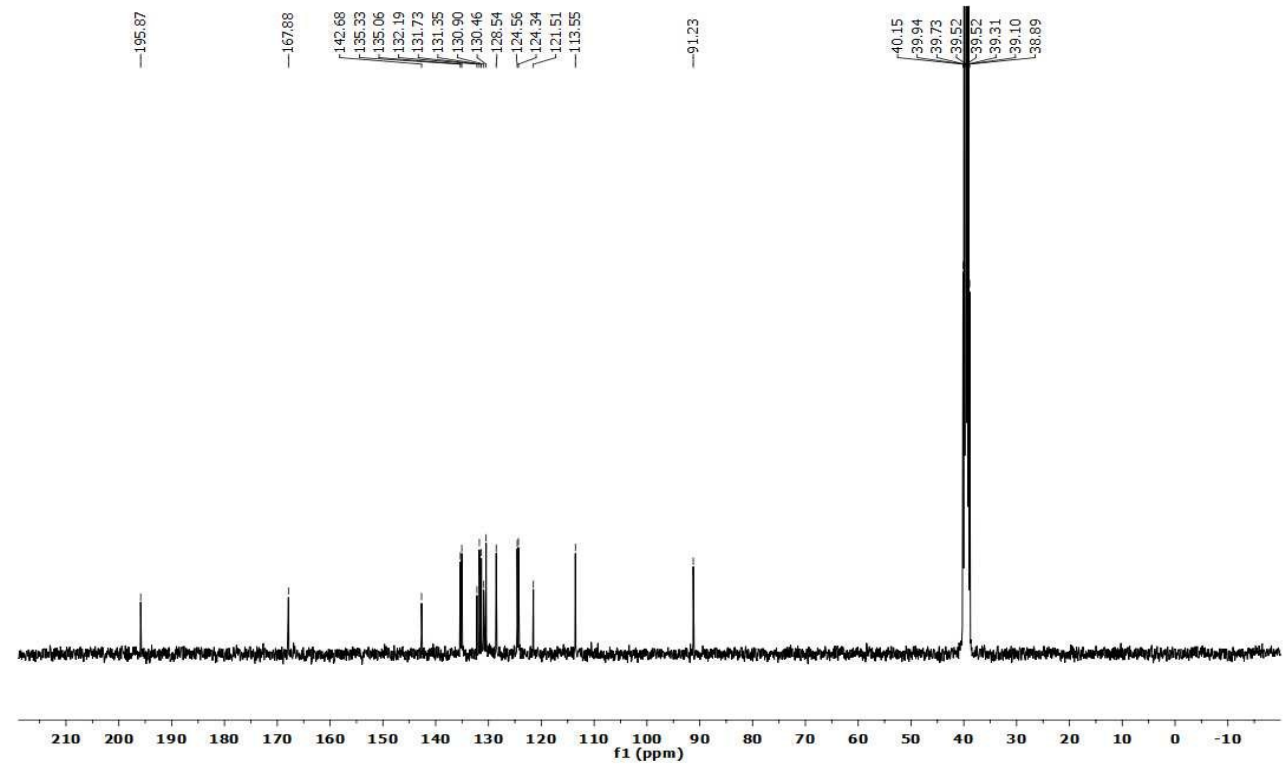
^{1}H-NMR spectrum of **3j** (300 MHz, DMSO-d^{6})



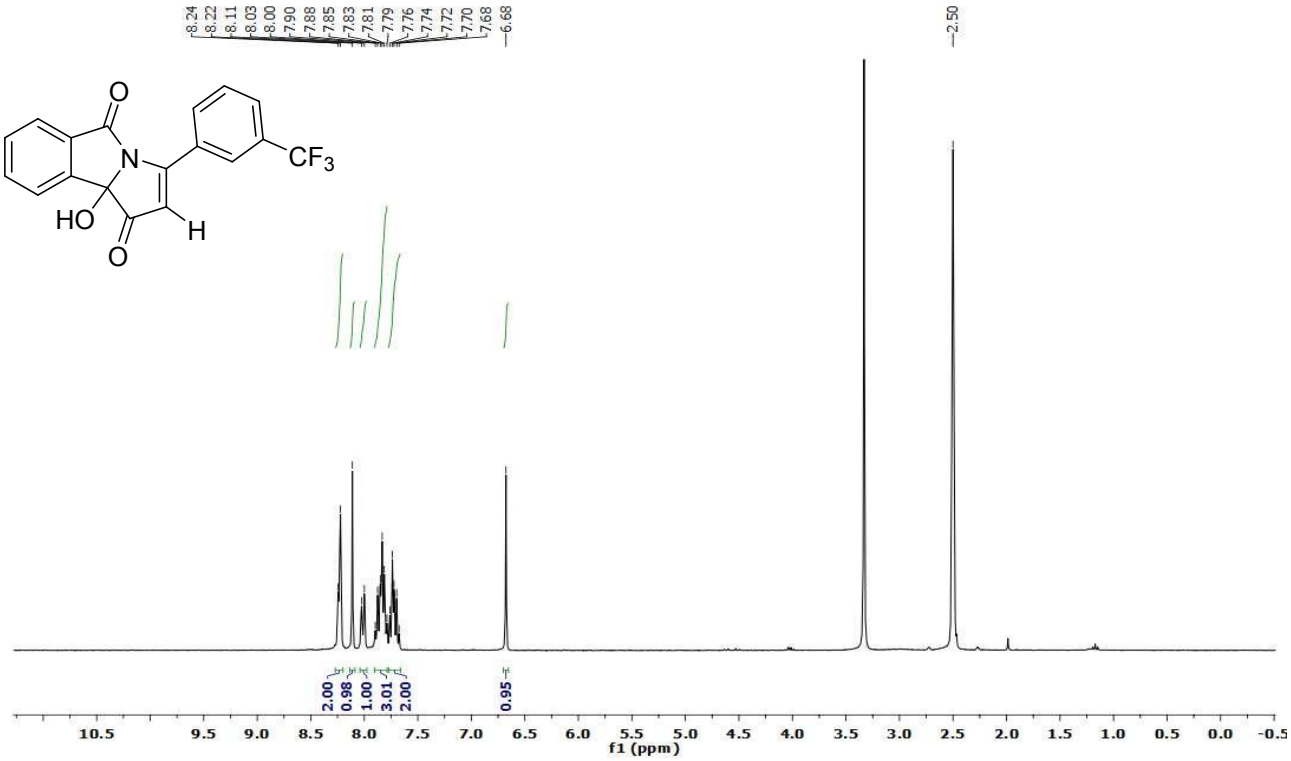
^{13}C-NMR spectrum of **3j** (100 MHz, DMSO-d^{6})



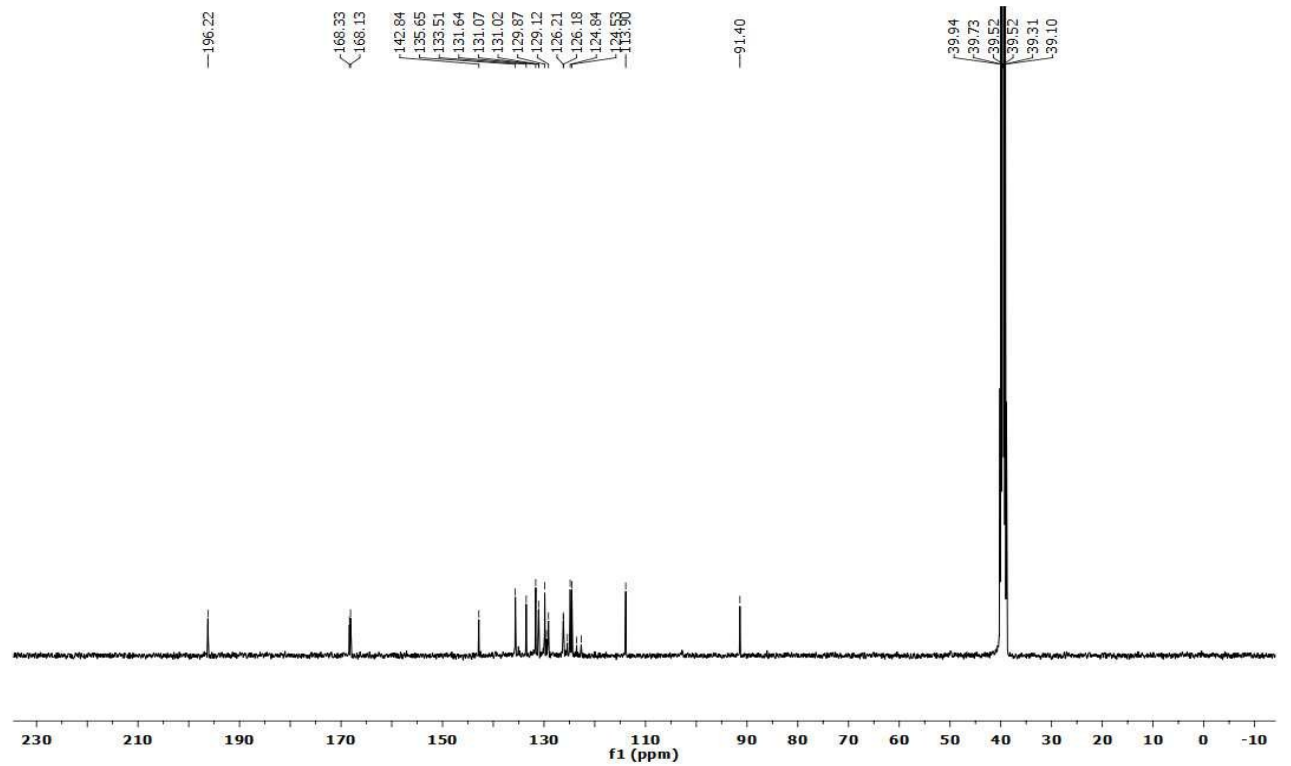
^{1}H-NMR spectrum of **3k** (300 MHz, DMSO-d^{6})



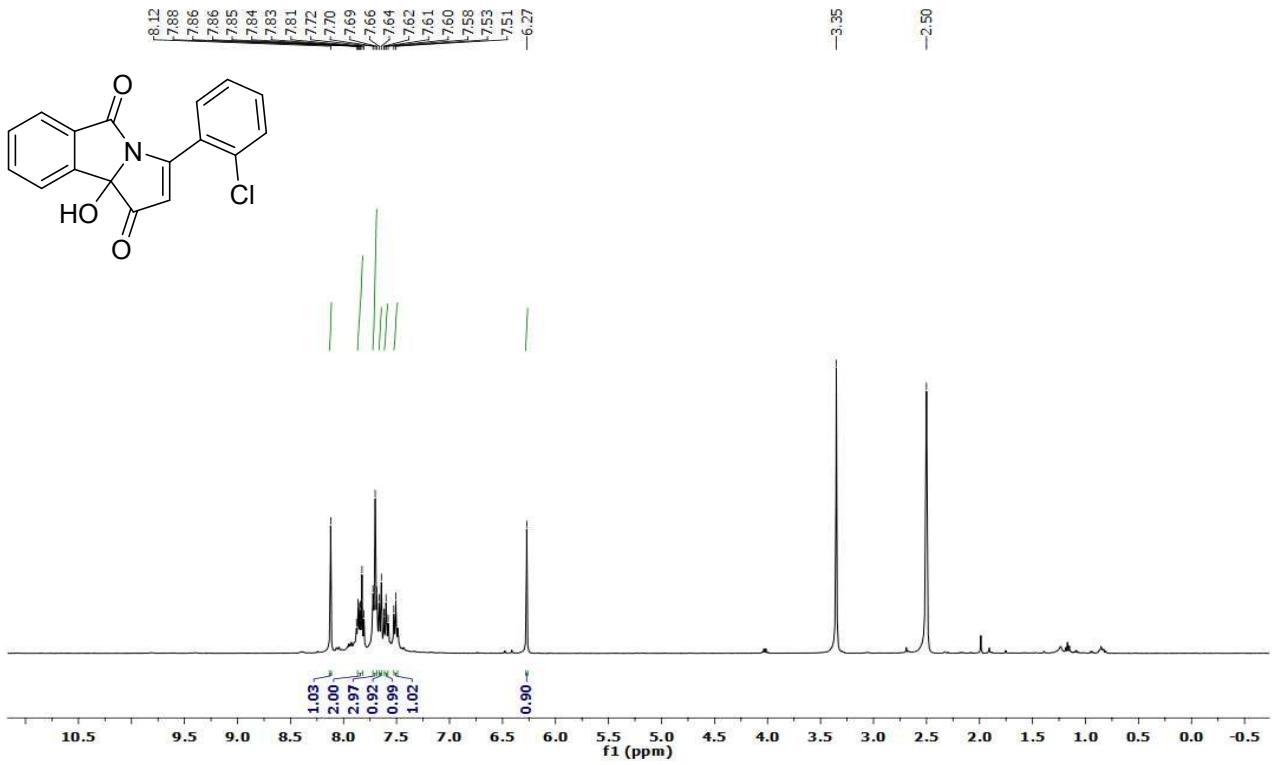
^{13}C-NMR spectrum of **3k** (100 MHz, DMSO-d^{6})



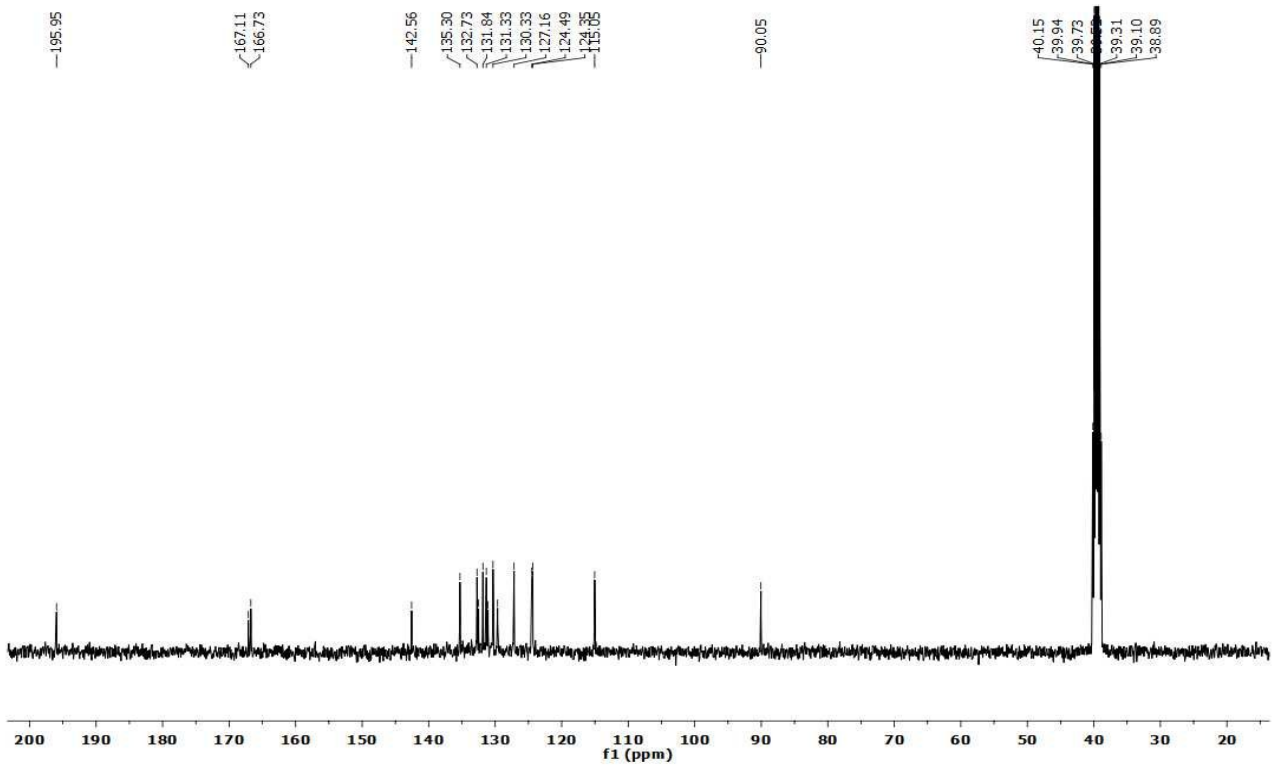
^{1}H-NMR spectrum of **3l** (300 MHz, DMSO-d^{6})



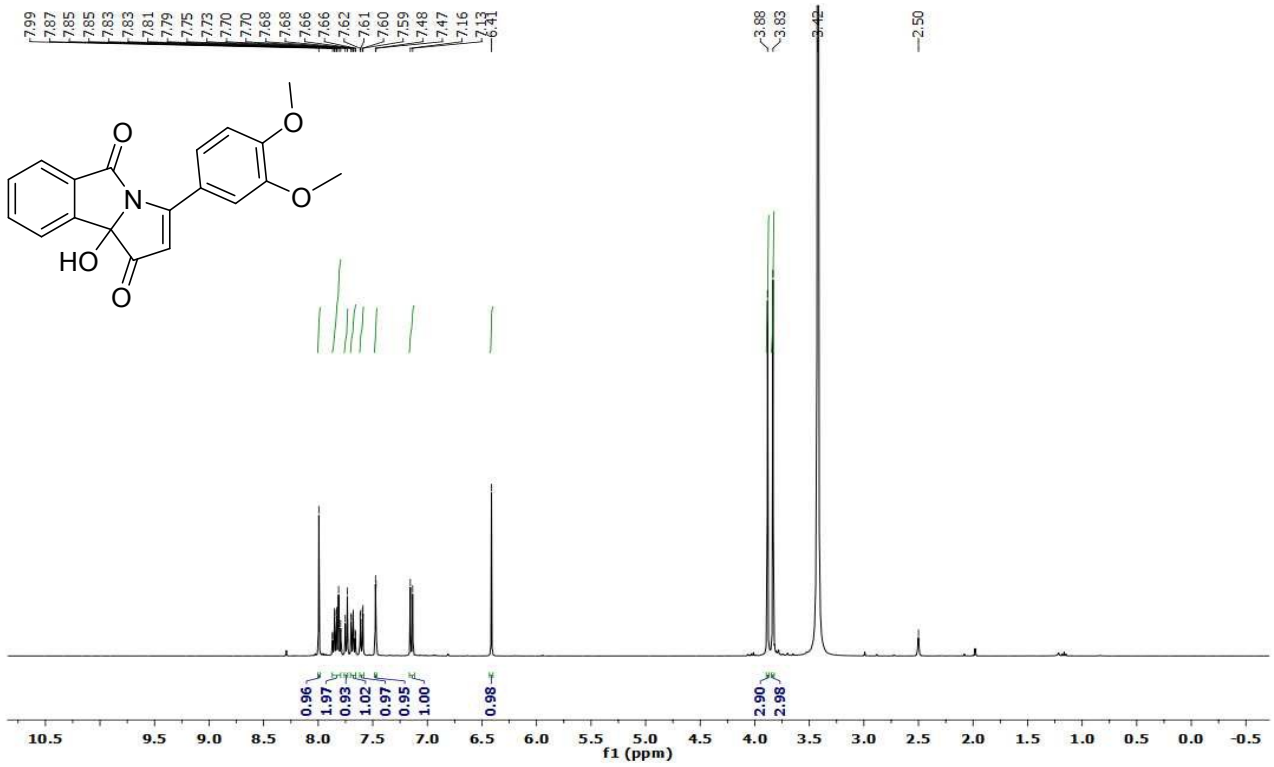
^{13}C-NMR spectrum of **3l** (100 MHz, DMSO-d^{6})



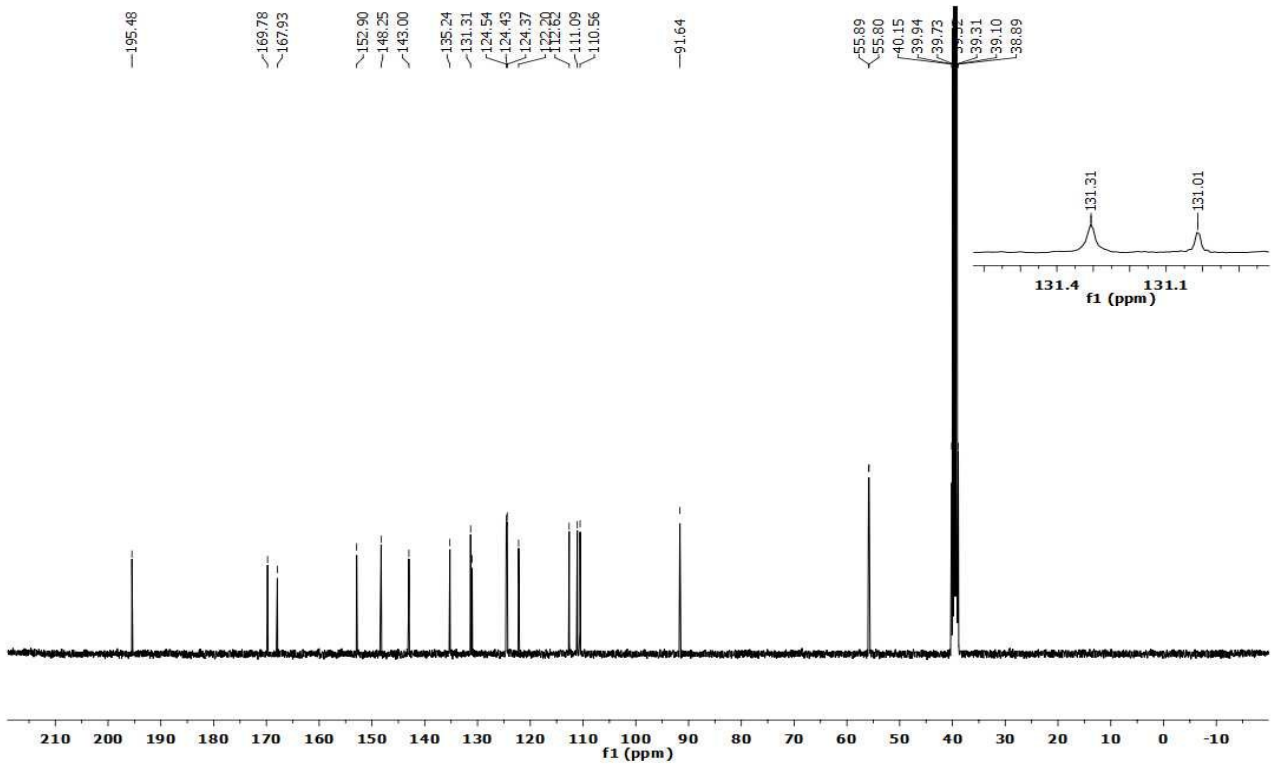
^{1}H-NMR spectrum of **3m** (400 MHz, DMSO-d^{6})



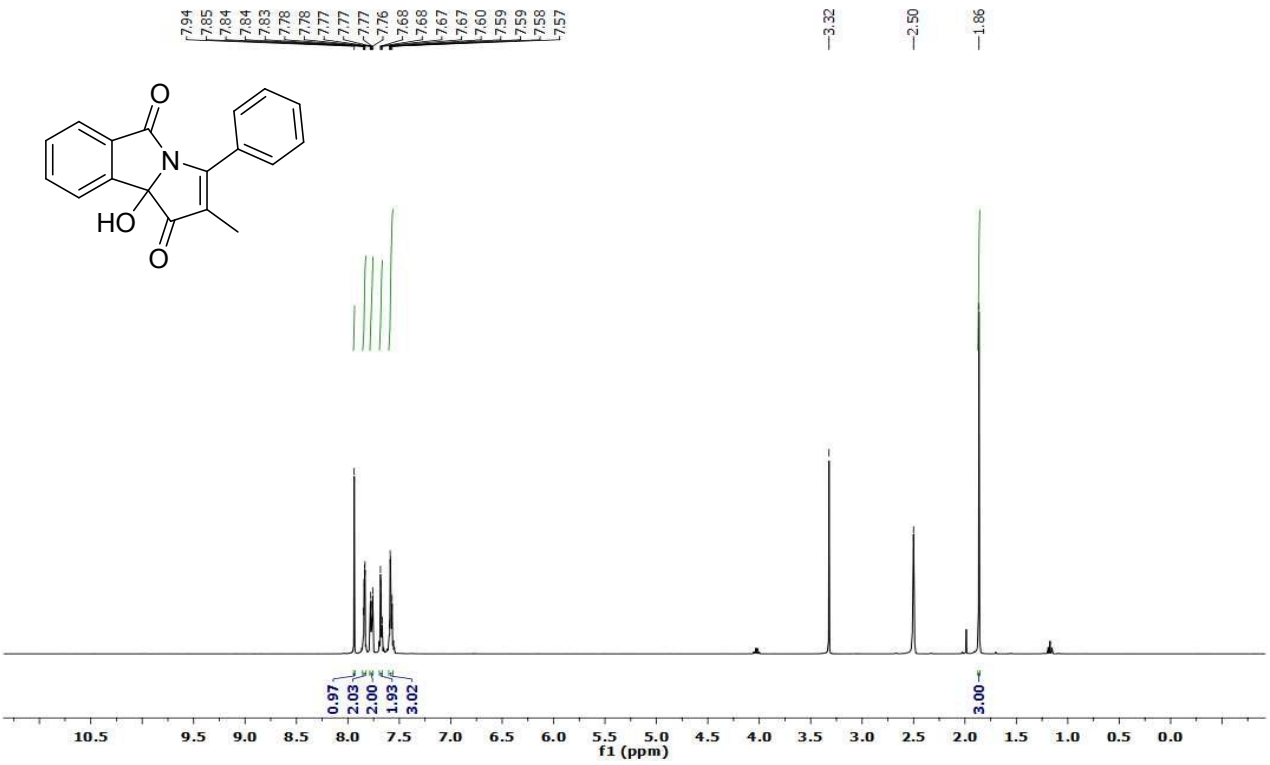
^{13}C-NMR spectrum of **3m** (100 MHz, DMSO-d^{6})



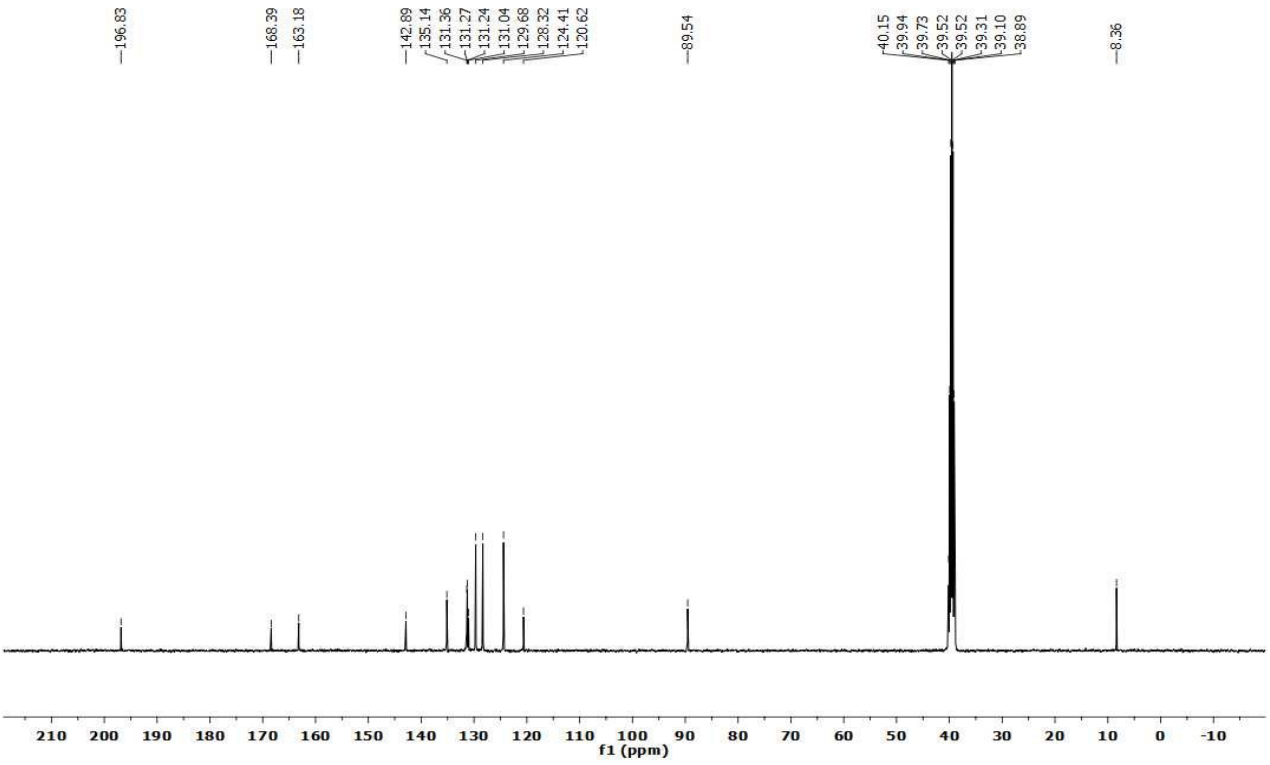
^{1}H-NMR spectrum of **3n** (400 MHz, DMSO-d^{6})



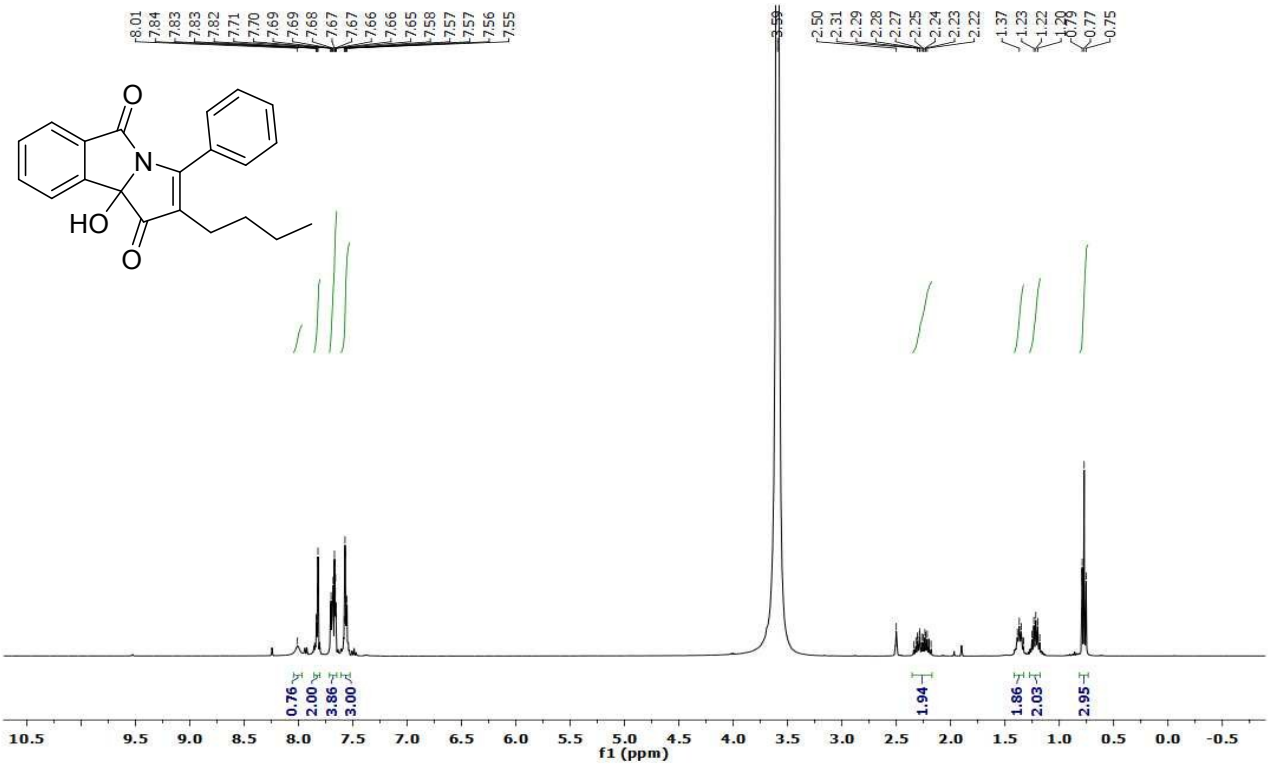
^{13}C-NMR spectrum of **3n** (100 MHz, DMSO-d^{6})



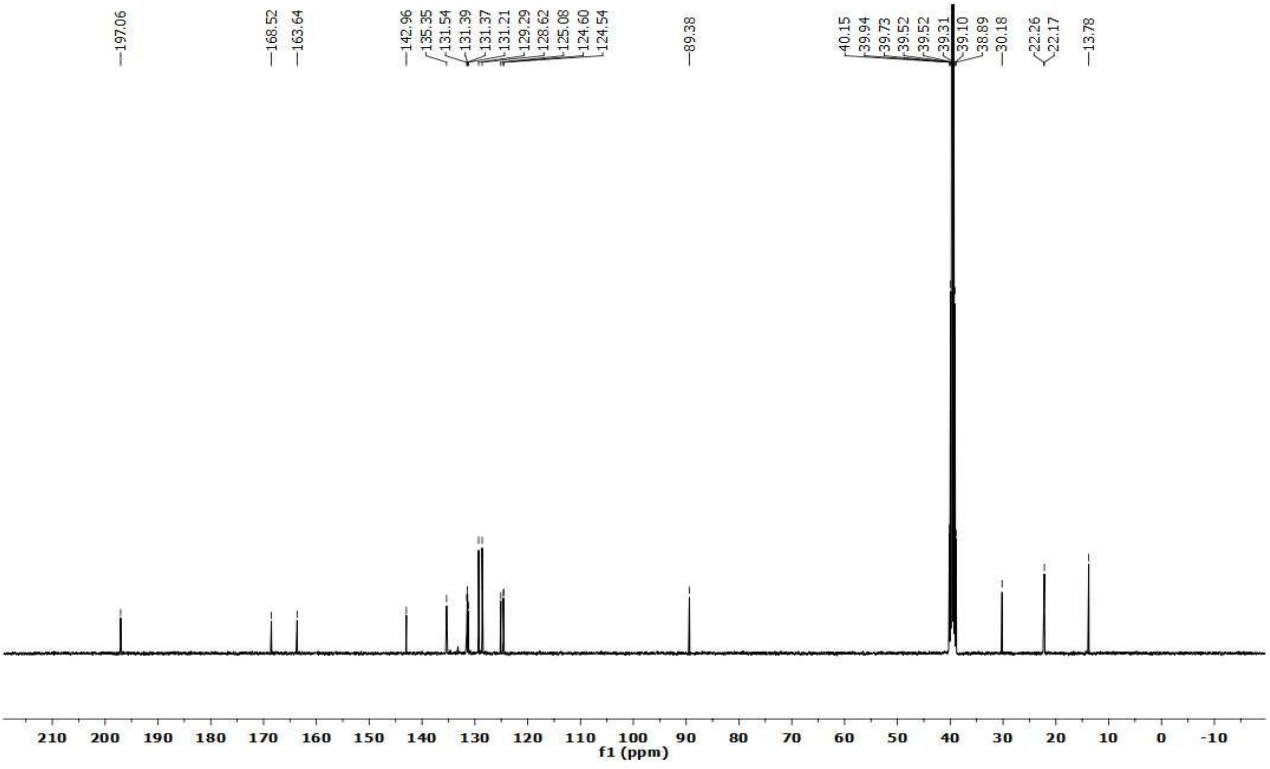
^{1}H-NMR spectrum of **3o** (400 MHz, DMSO-d^{6})



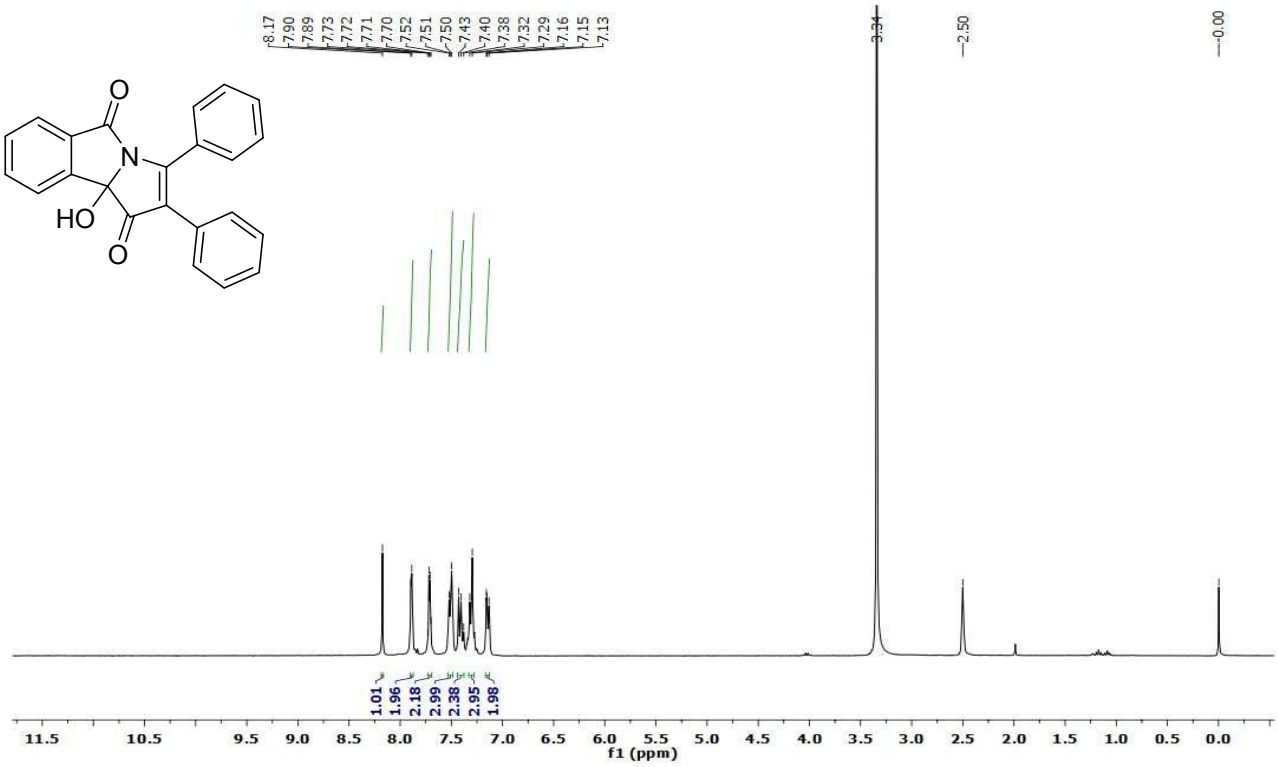
^{13}C-NMR spectrum of **3o** (100 MHz, DMSO-d^{6})



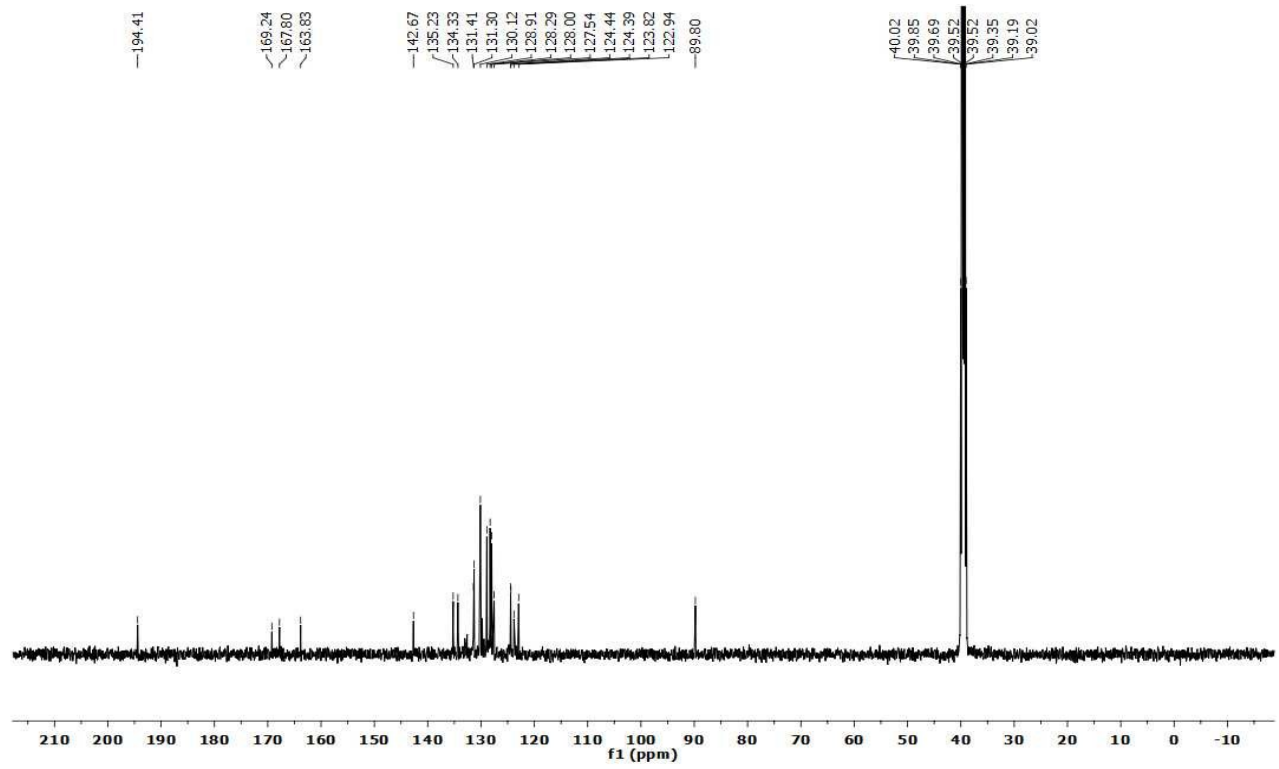
^{1}H-NMR spectrum of **3p** (400 MHz, DMSO-d^{6})



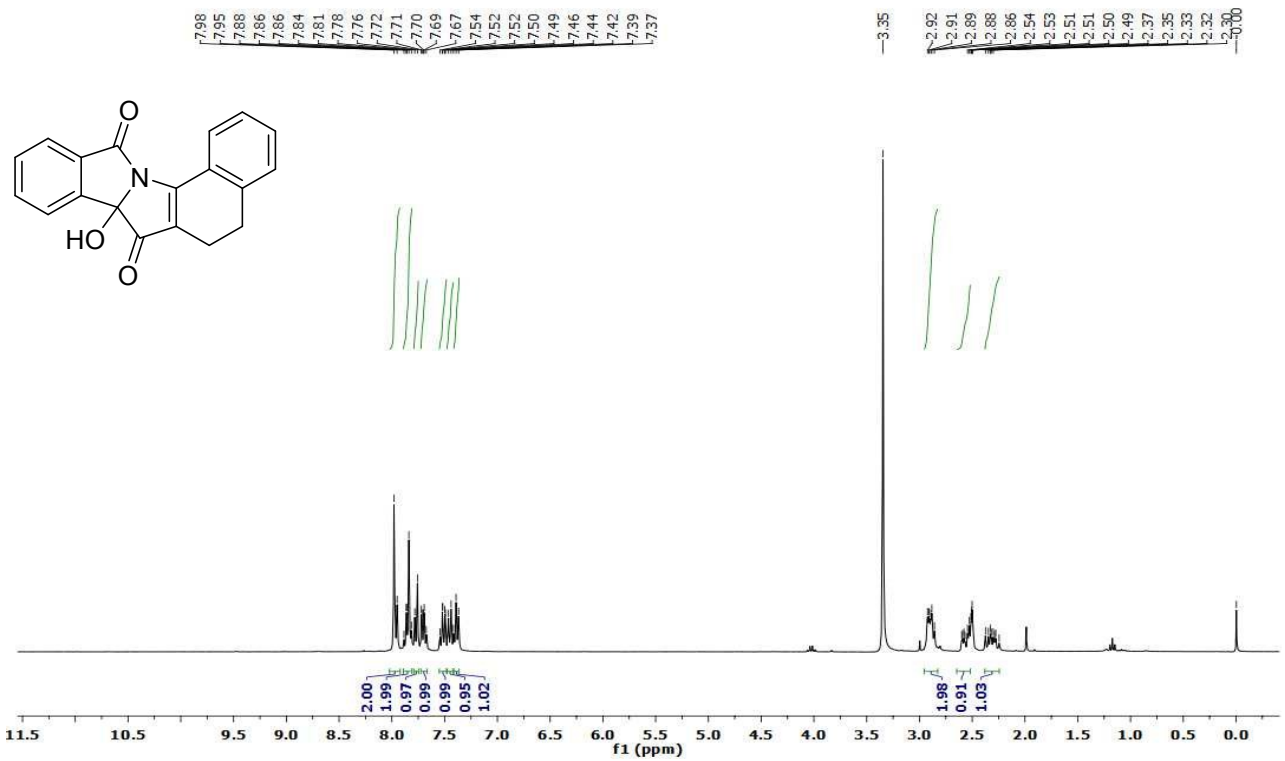
^{13}C-NMR spectrum of **3p** (100 MHz, DMSO-d^{6})



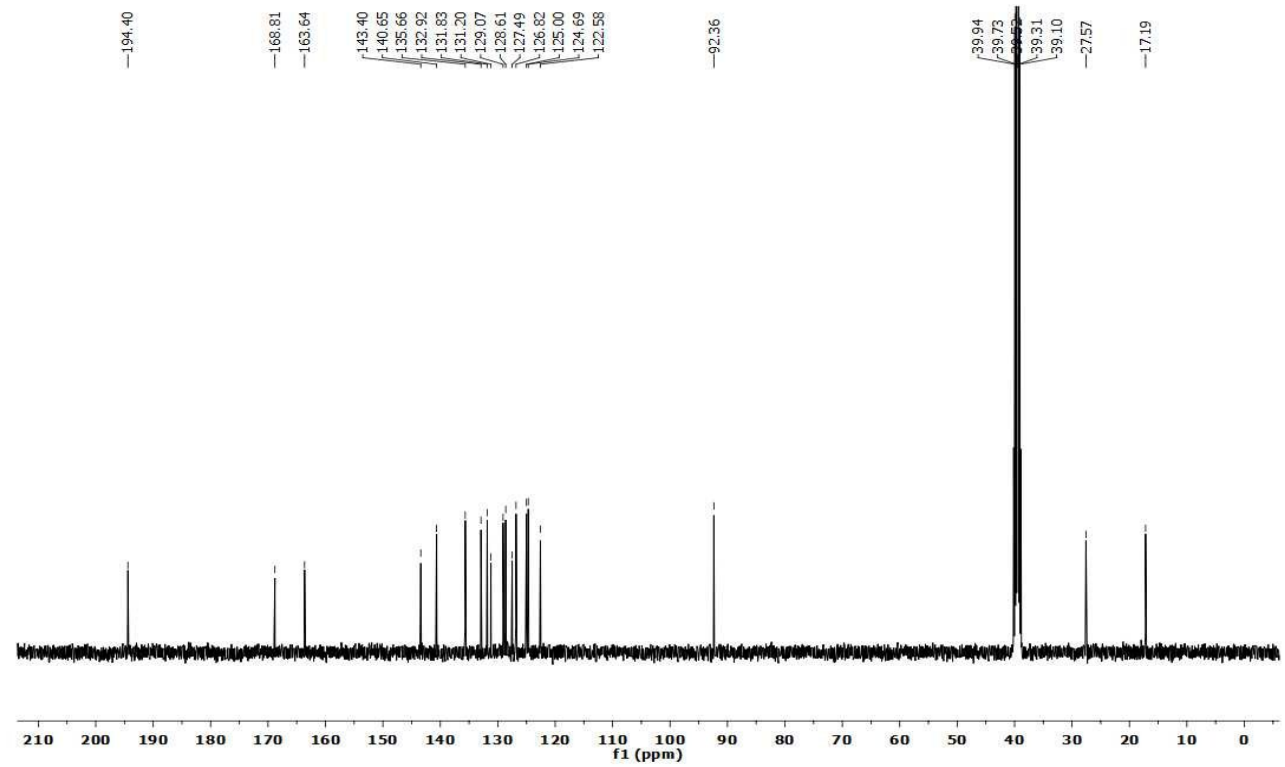
^{1}H-NMR spectrum of **3q** (300 MHz, DMSO-d^{6})



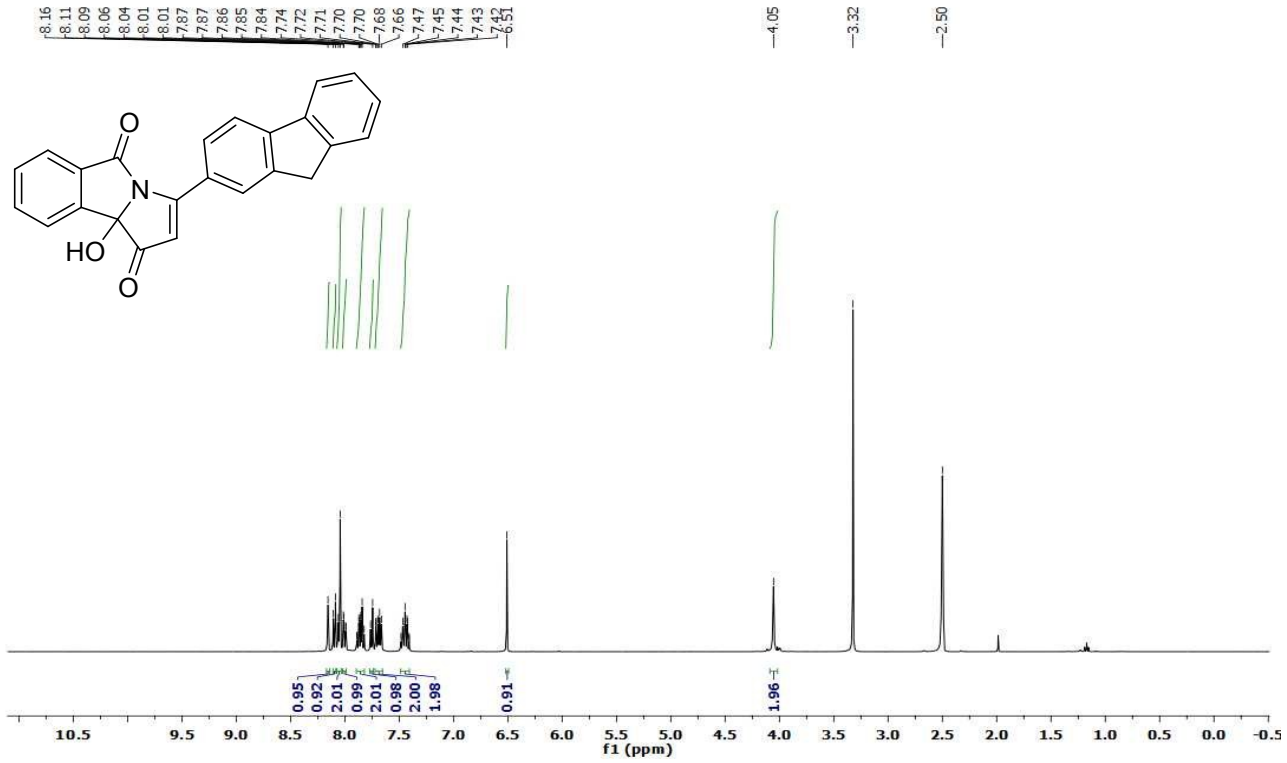
^{13}C-NMR spectrum of **3q** (100 MHz, DMSO-d^{6})



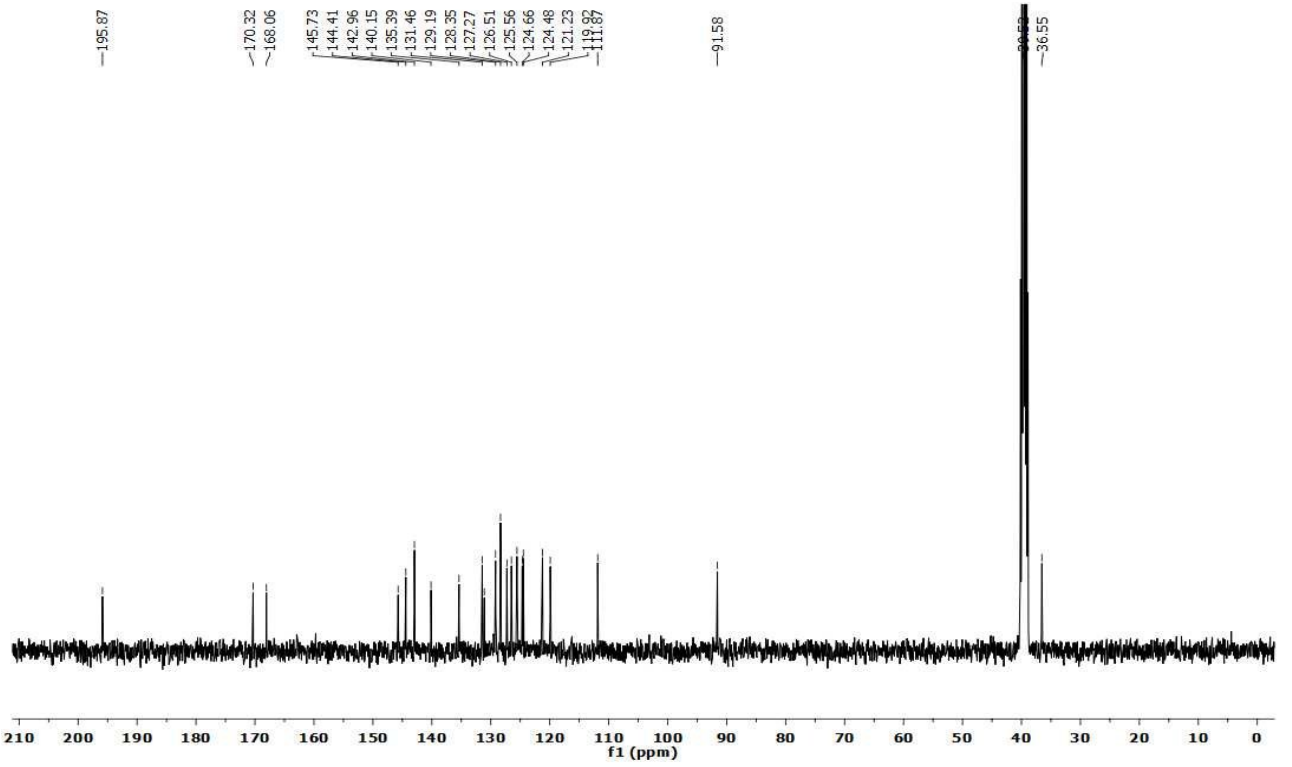
^{1}H-NMR spectrum of **3r** (300 MHz, DMSO-d^{6})



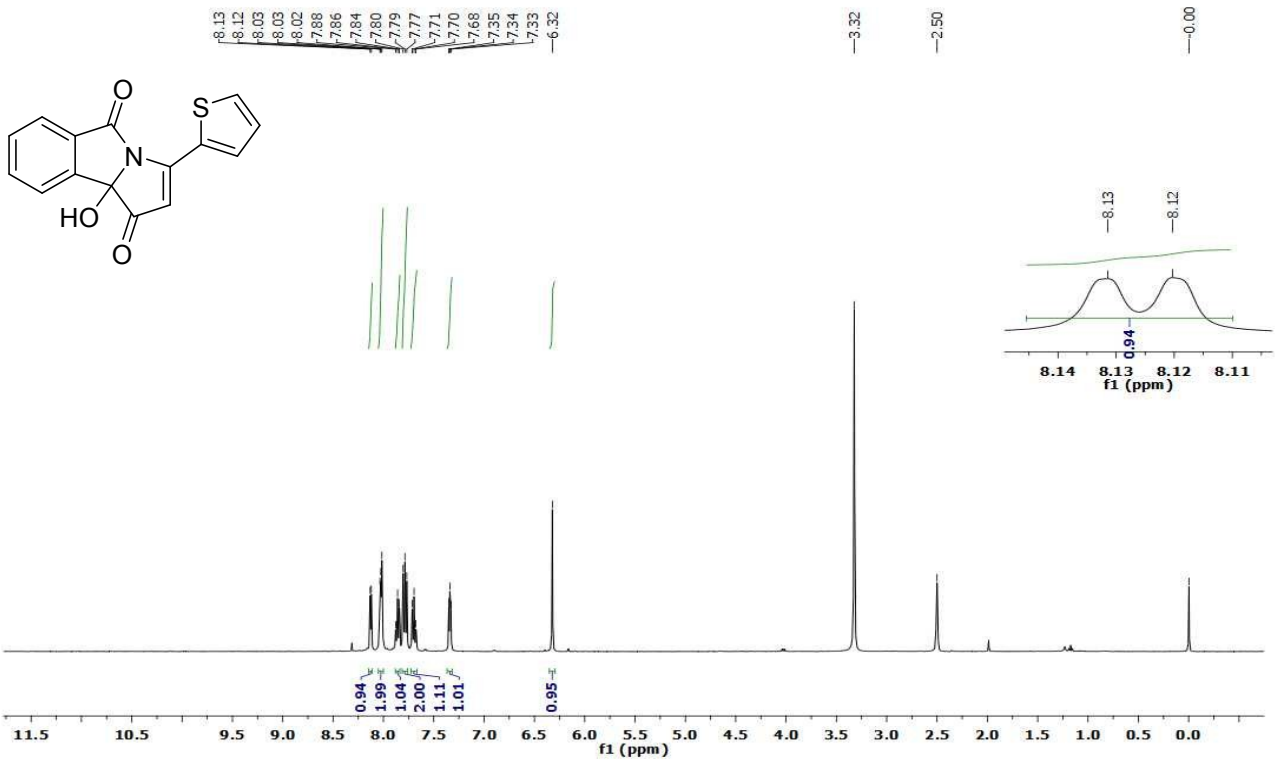
^{13}C-NMR spectrum of **3r** (100 MHz, DMSO-d^{6})



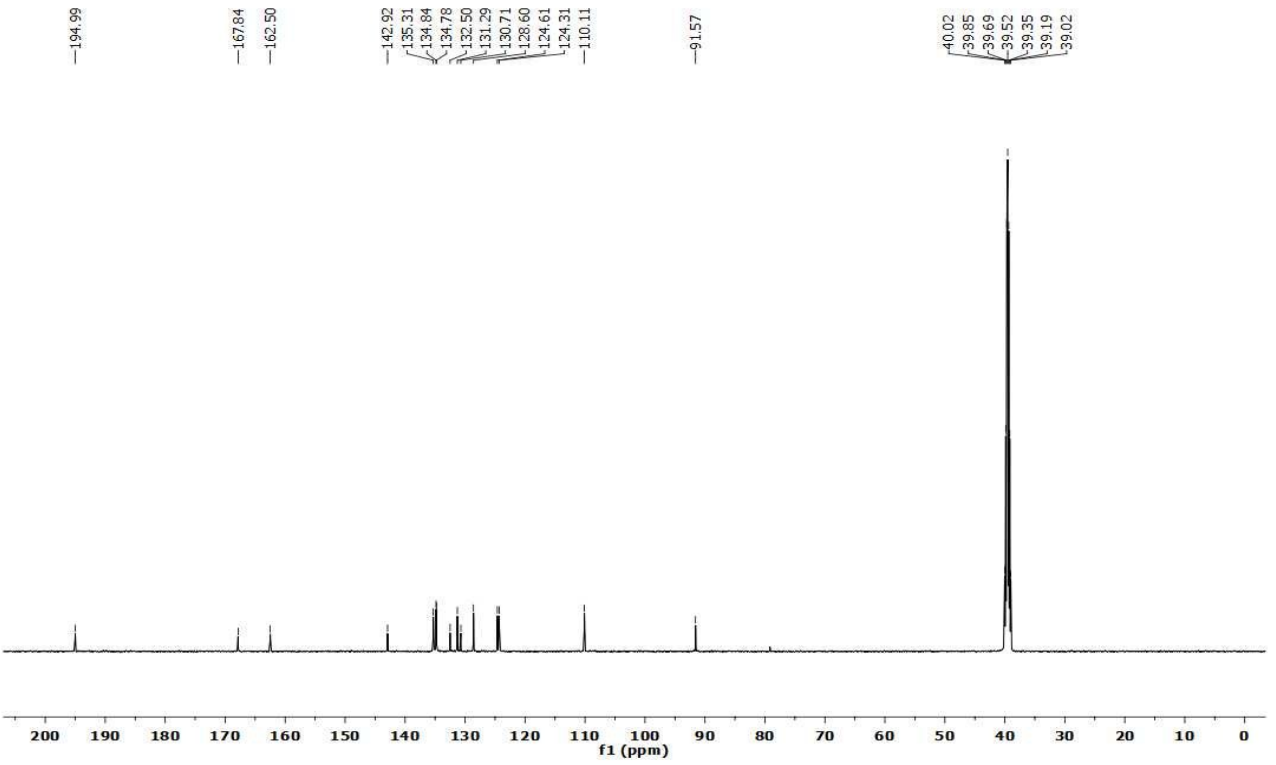
^{1}H-NMR spectrum of **3s** (400 MHz, DMSO-d^{6})



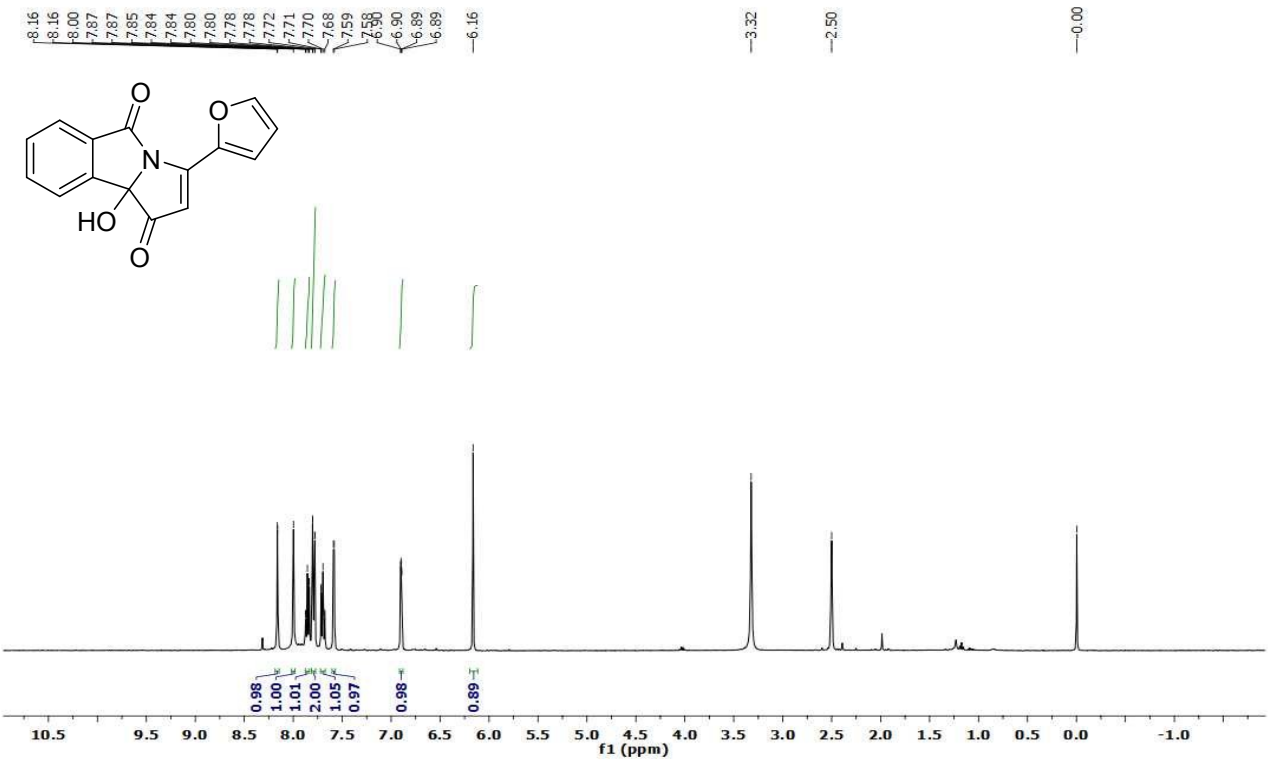
^{13}C-NMR spectrum of **3s** (100 MHz, DMSO-d^{6})



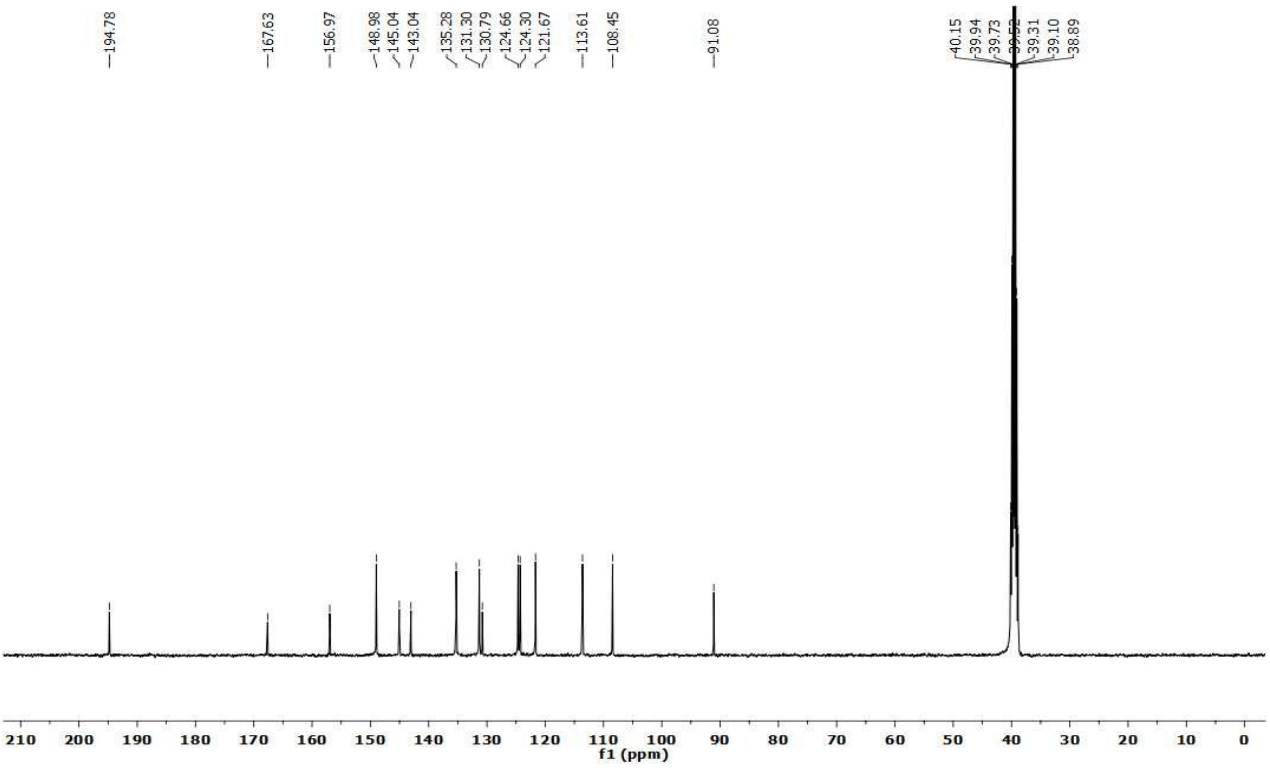
^{1}H-NMR spectrum of **3t** (400 MHz, DMSO-d^{6})



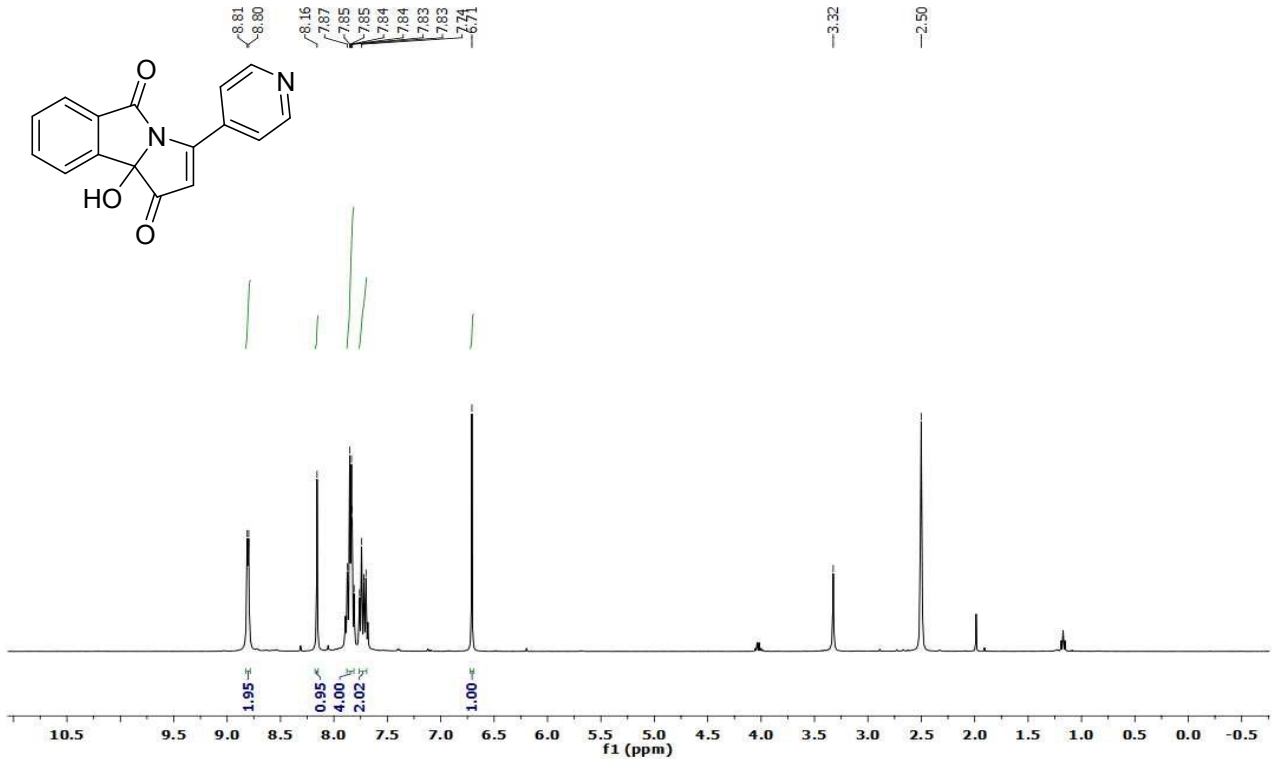
^{13}C-NMR spectrum of **3t** (100 MHz, DMSO-d^{6})



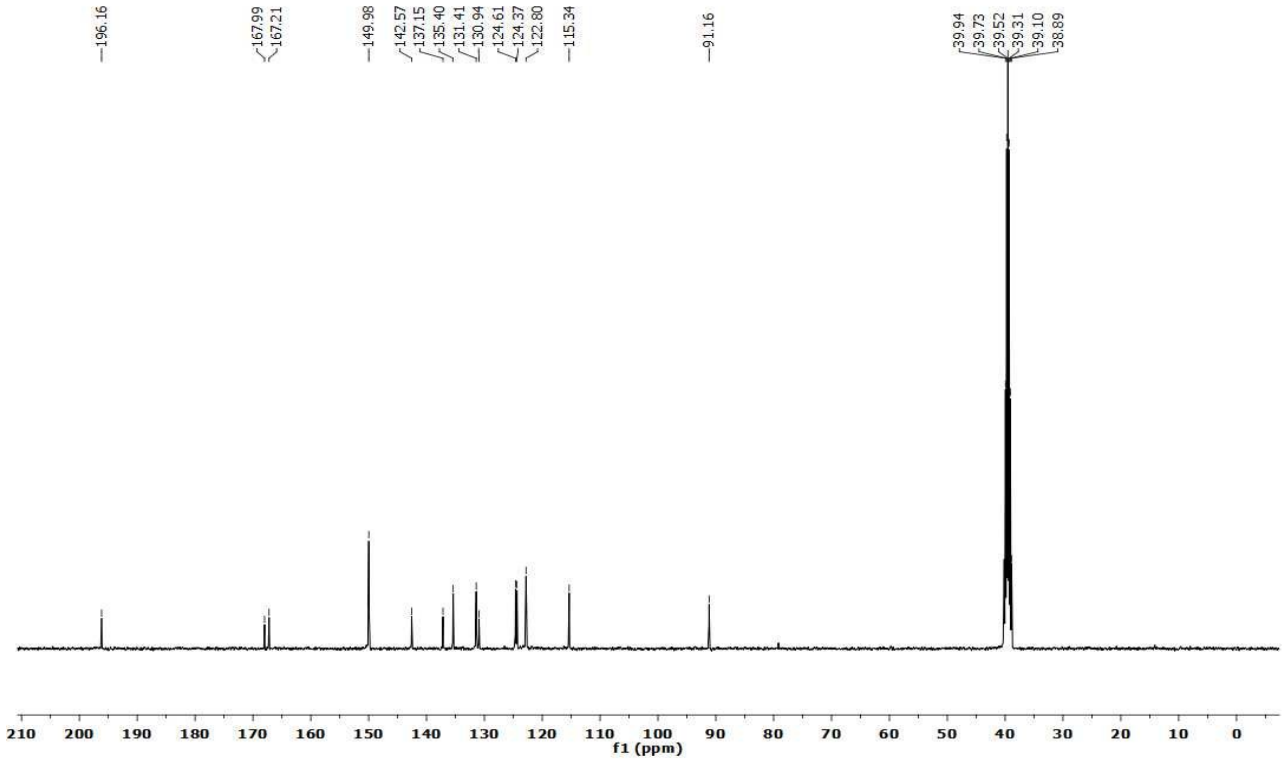
^{1}H-NMR spectrum of **3u** (400 MHz, DMSO-d^{6})



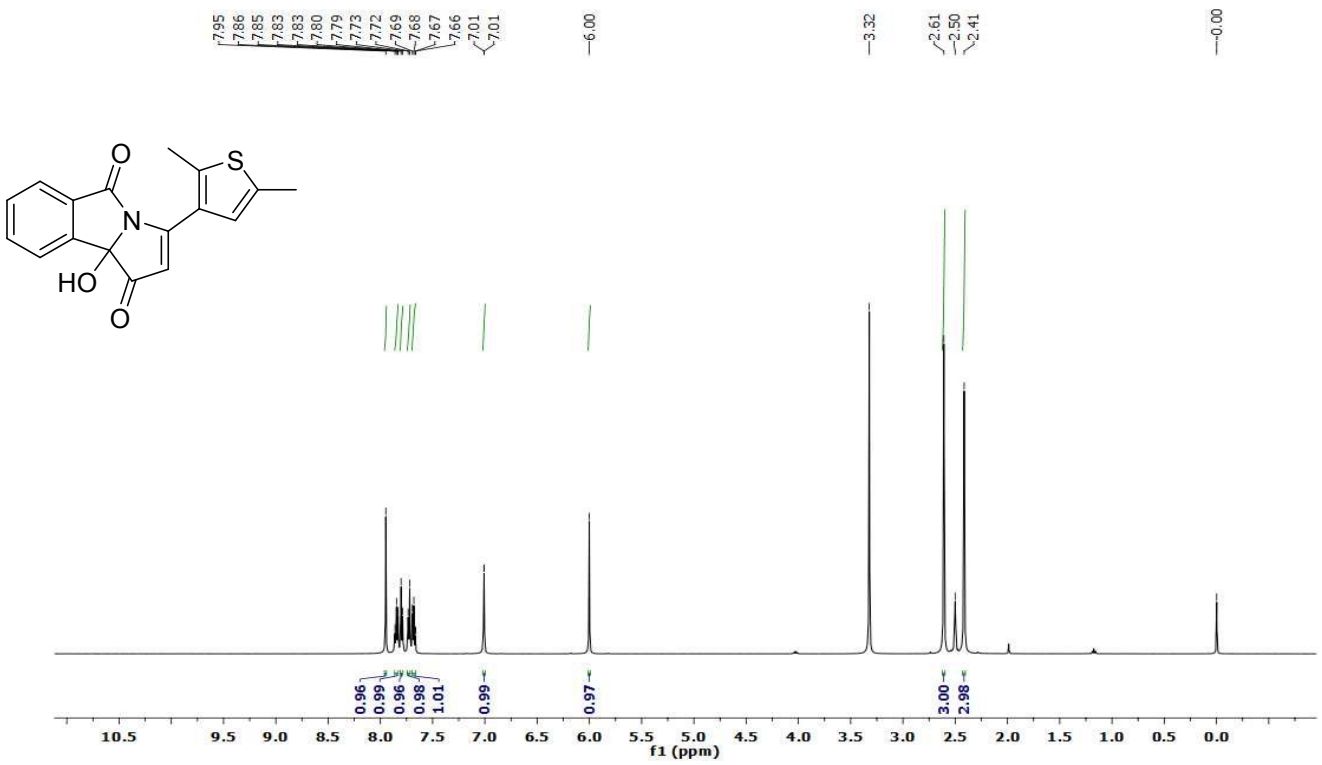
^{13}C-NMR spectrum of **3u** (100 MHz, DMSO-d^{6})



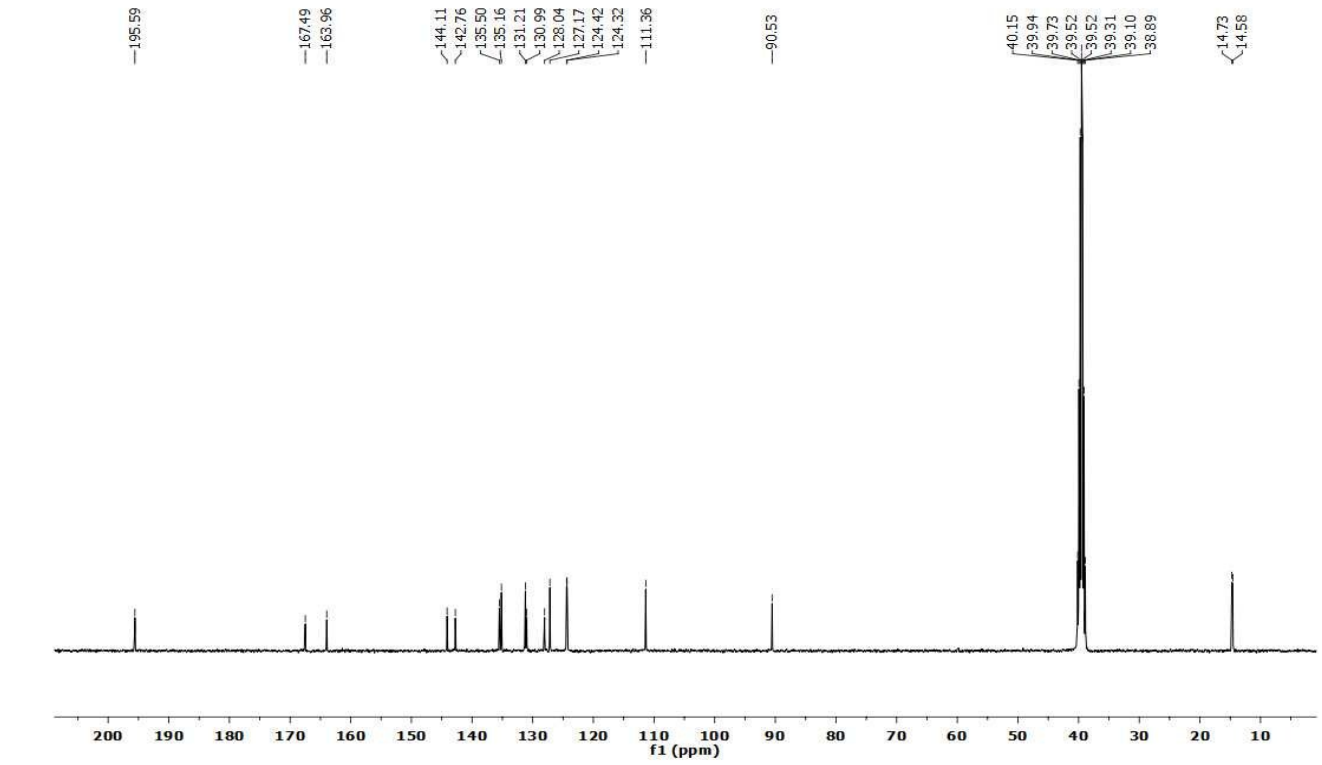
^{1}H-NMR spectrum of **3v** (400 MHz, DMSO-d^{6})



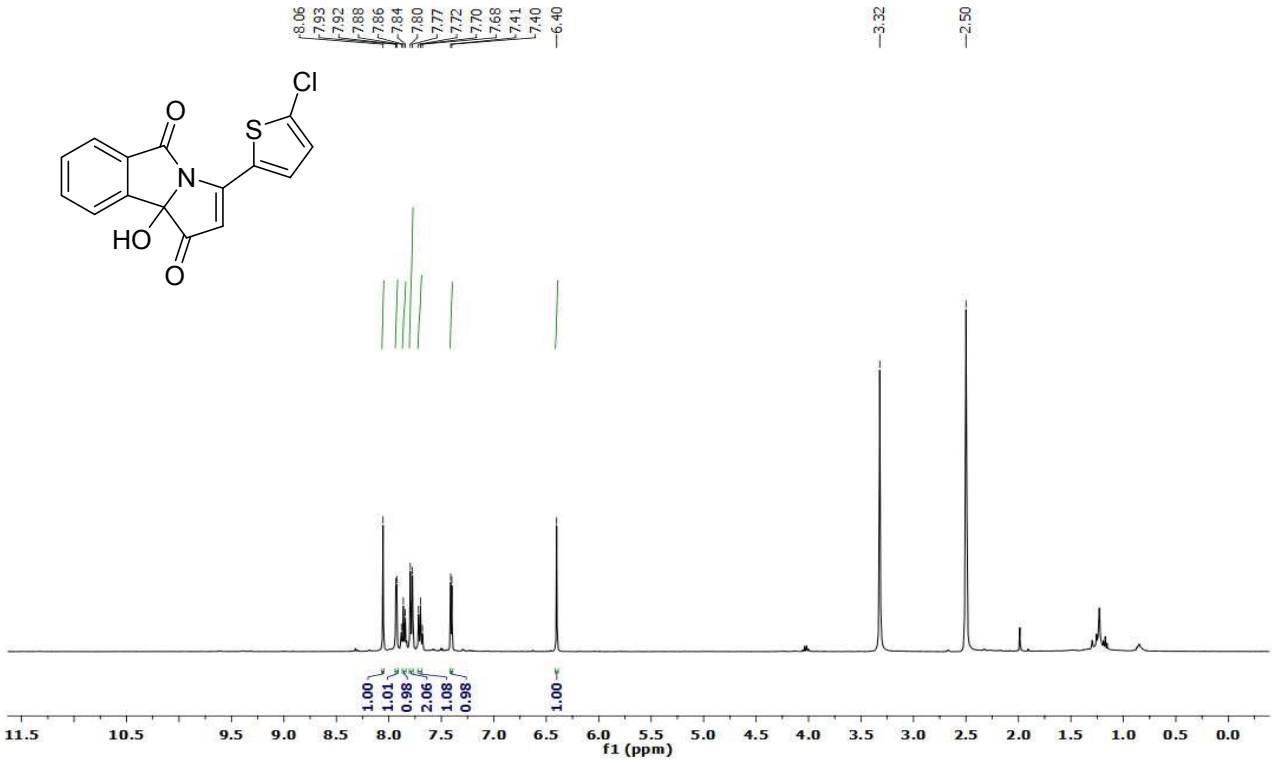
^{13}C-NMR spectrum of **3v** (100 MHz, DMSO-d^{6})



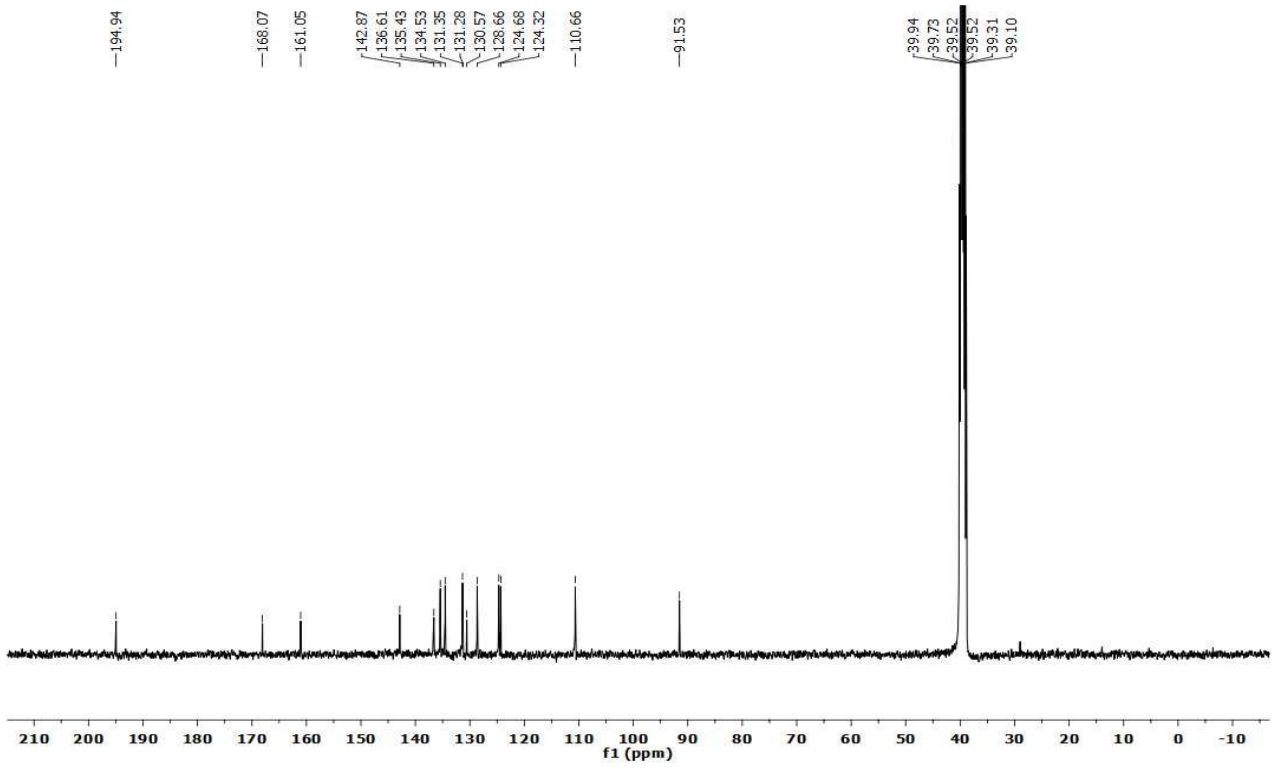
^{1}H-NMR spectrum of **3w** (500 MHz, DMSO-d^{6})



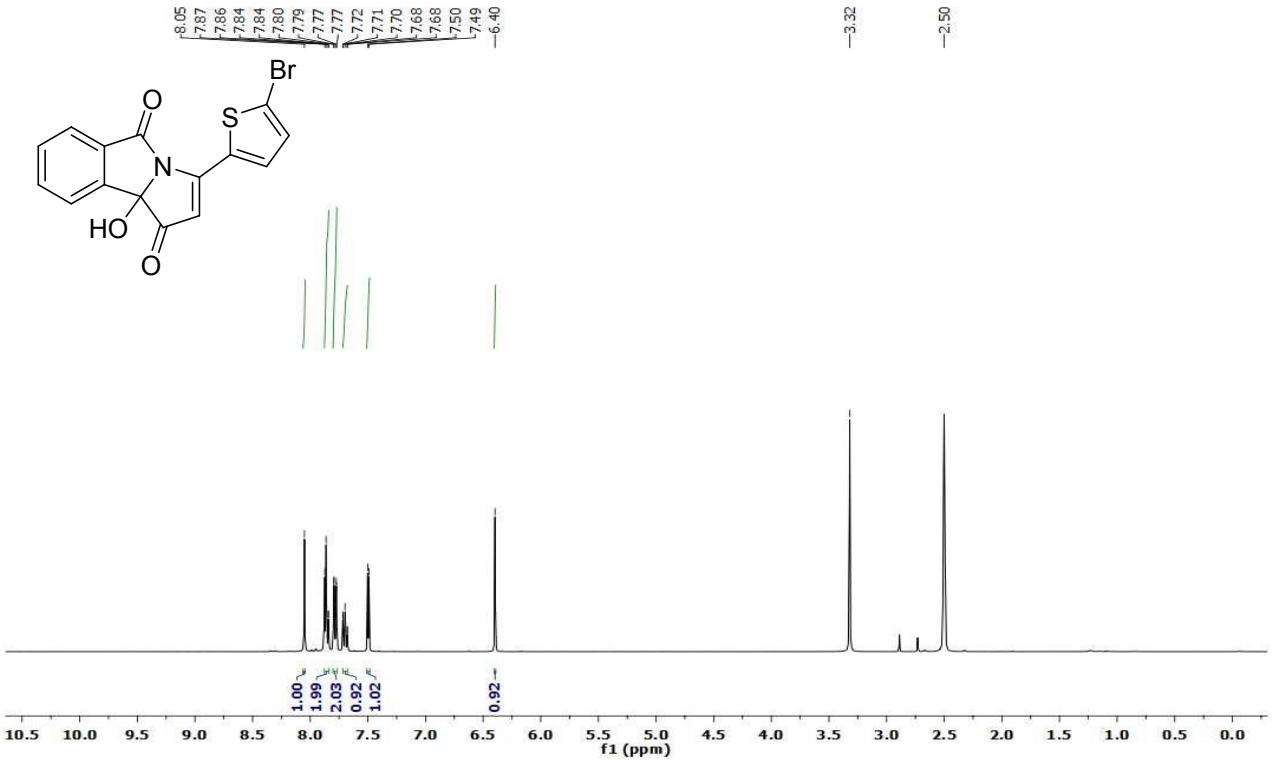
^{13}C-NMR spectrum of **3w** (100 MHz, DMSO-d^{6})



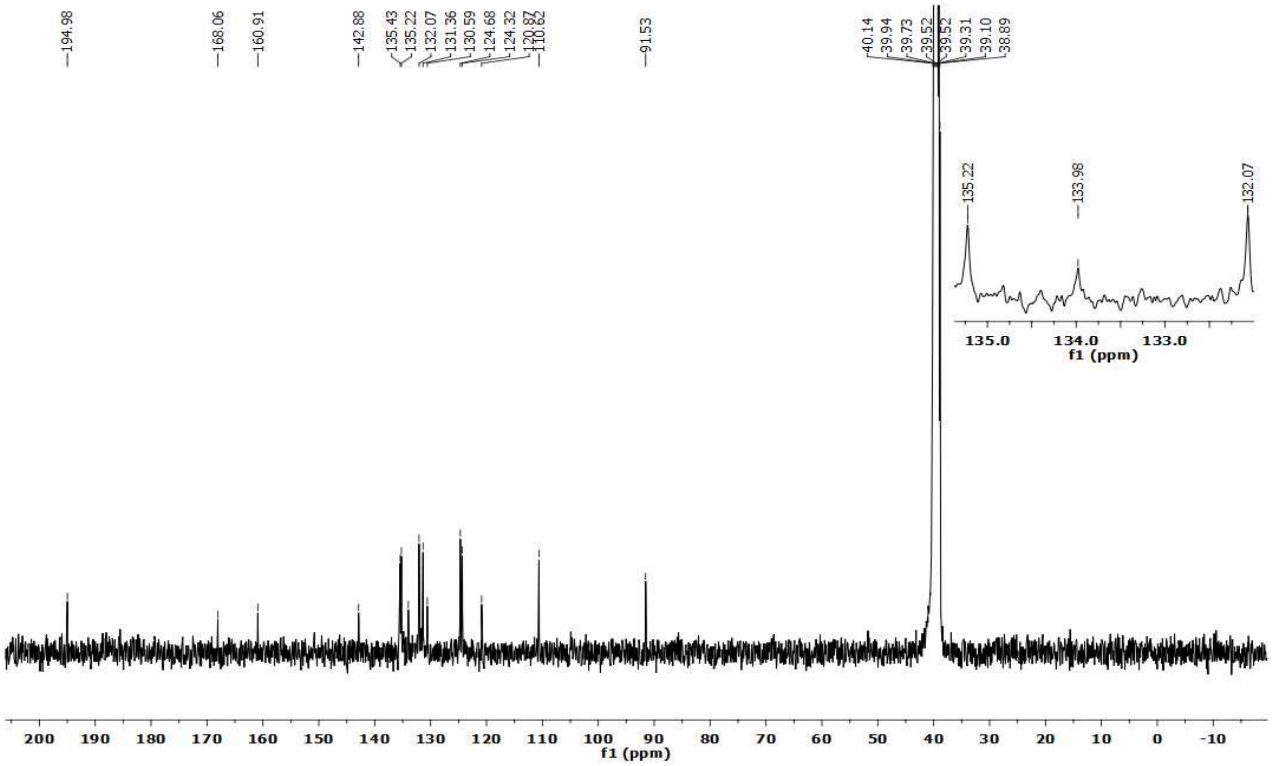
^{1}H-NMR spectrum of **3x** (400 MHz, DMSO-d^{6})



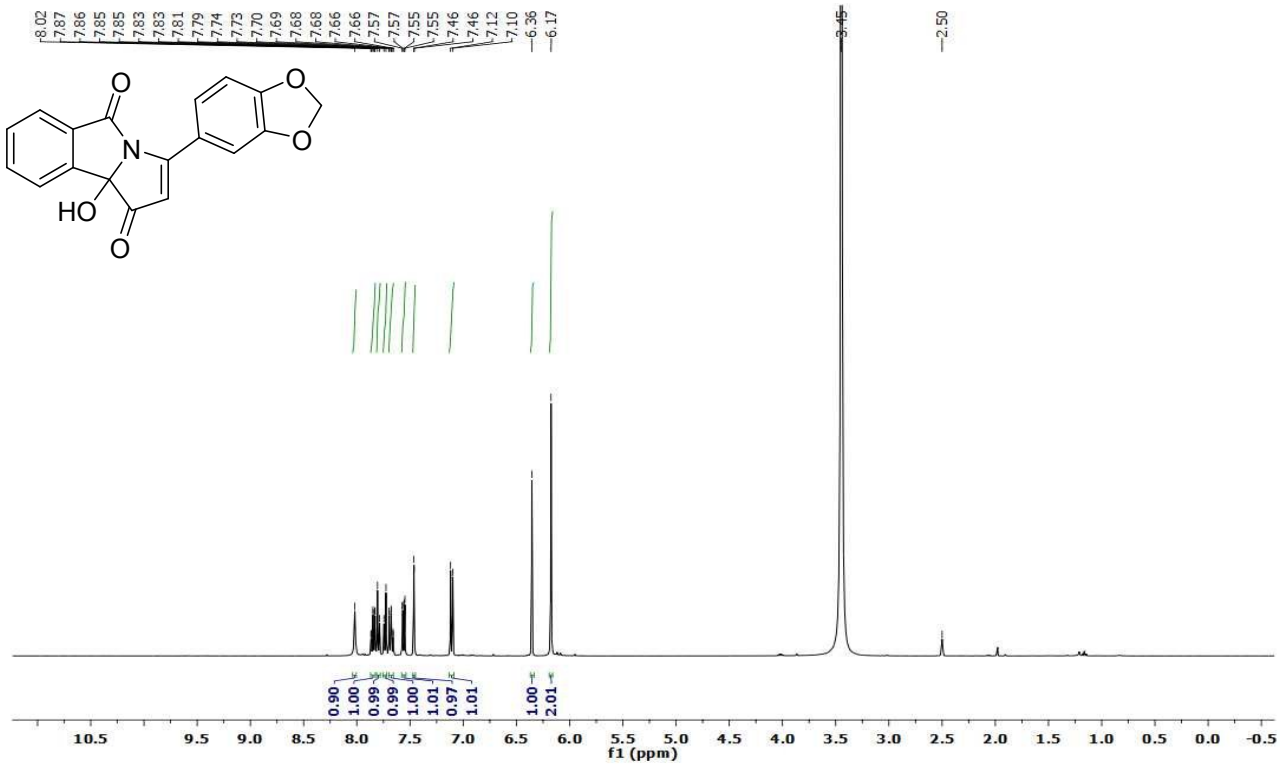
^{13}C-NMR spectrum of **3x** (100 MHz, DMSO-d^{6})



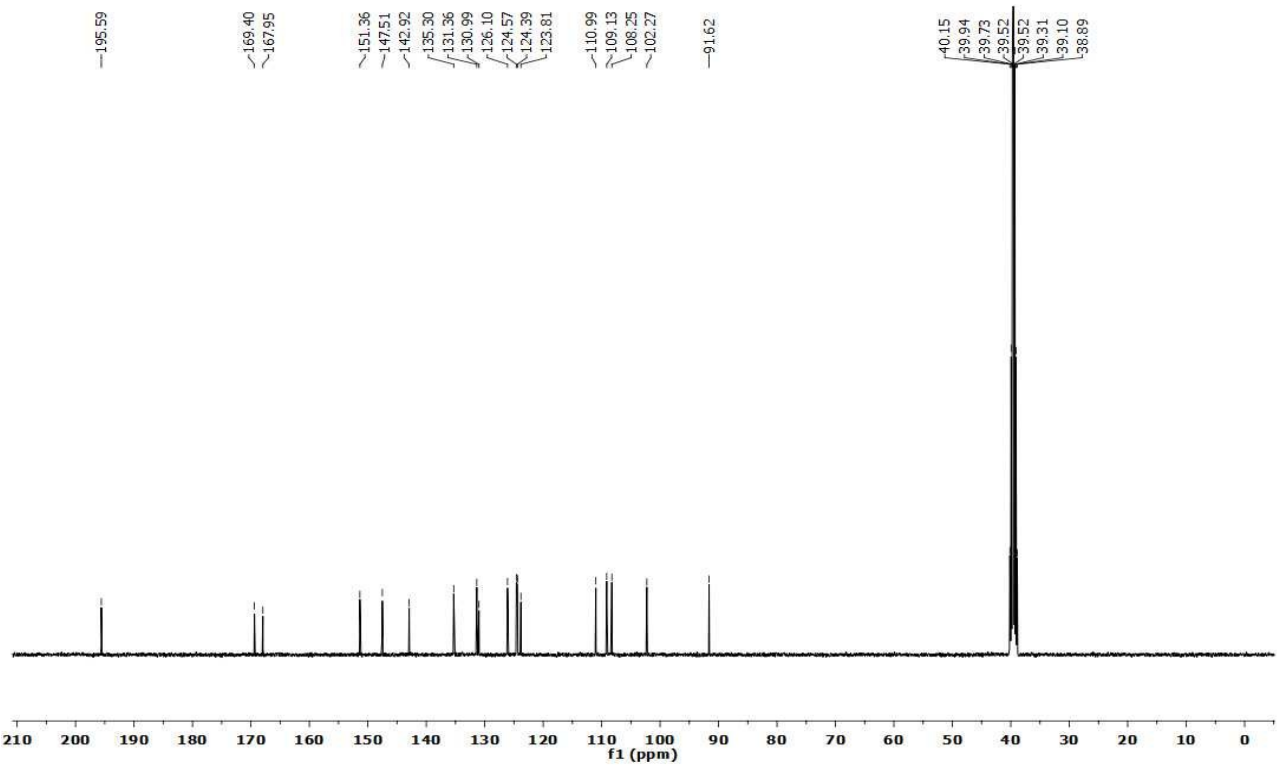
^{1}H-NMR spectrum of **3y** (400 MHz, DMSO-d^{6})



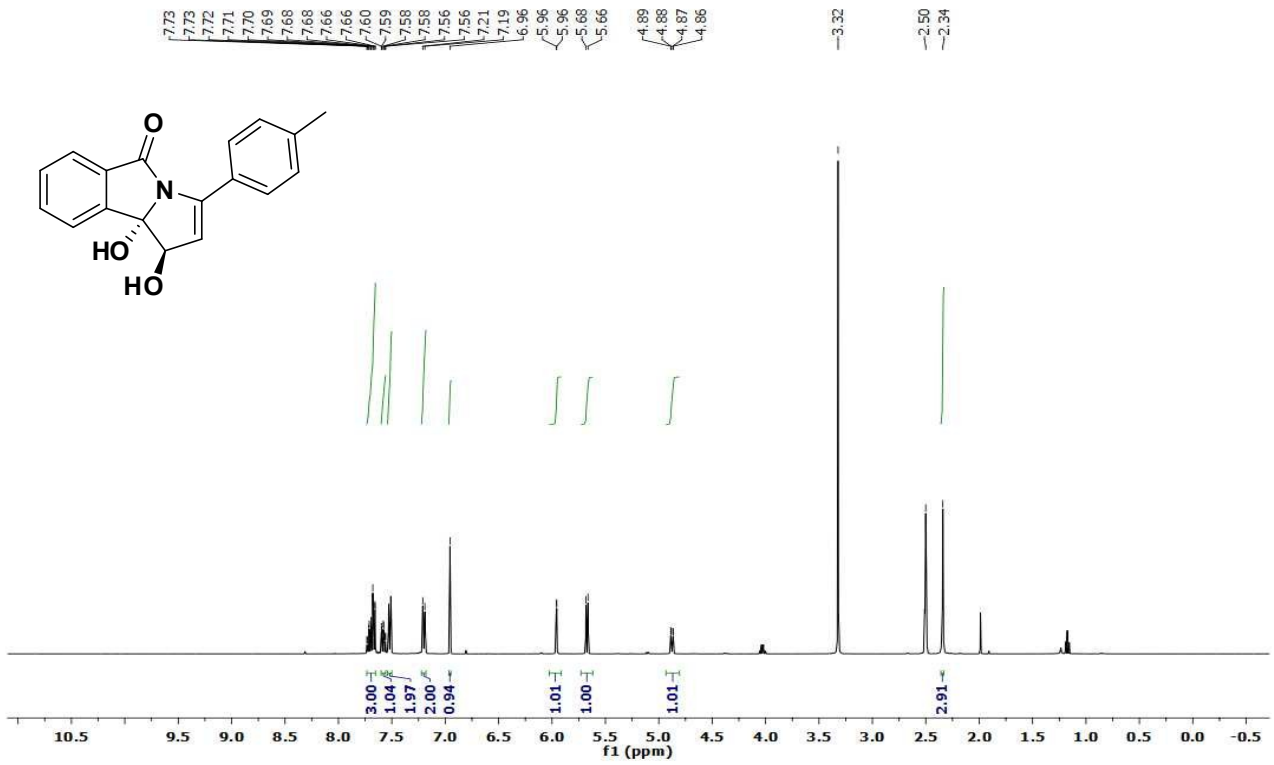
^{13}C-NMR spectrum of **3y** (100 MHz, DMSO-d^{6})



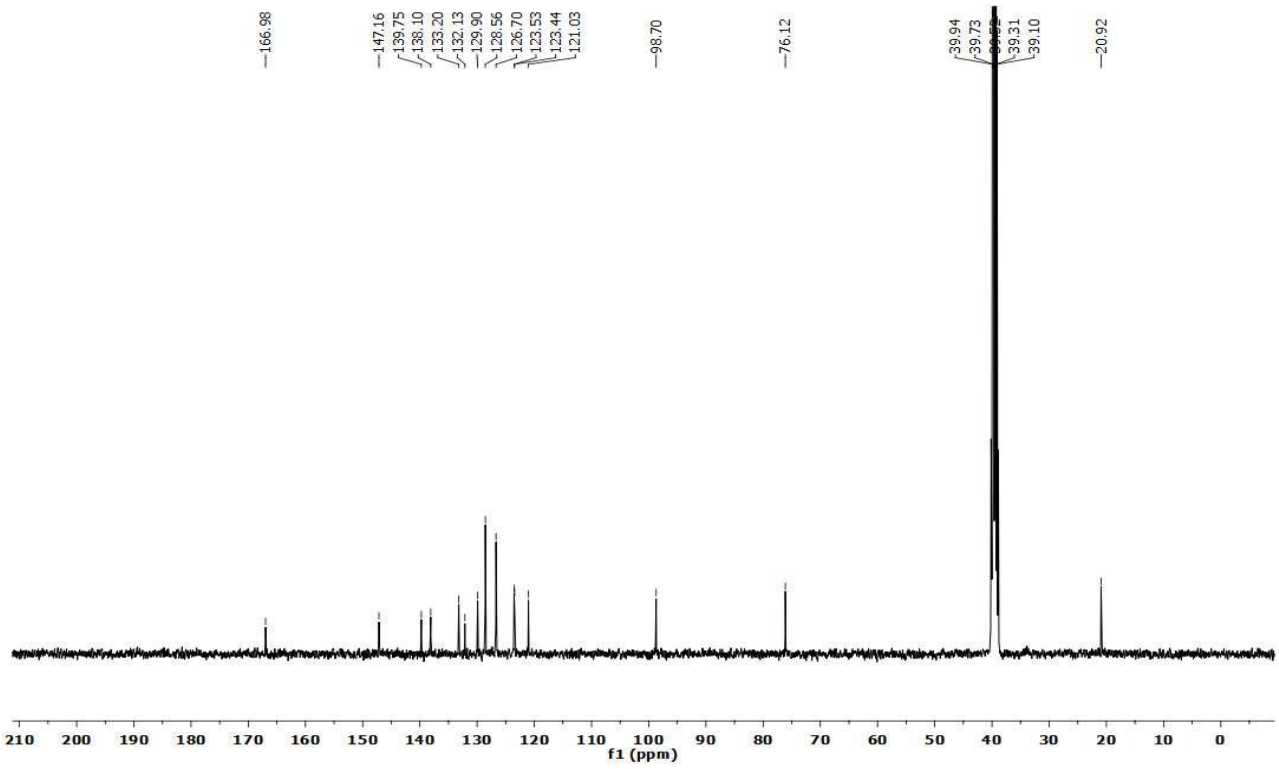
^{1}H-NMR spectrum of **3z** (400 MHz, DMSO-d^{6})



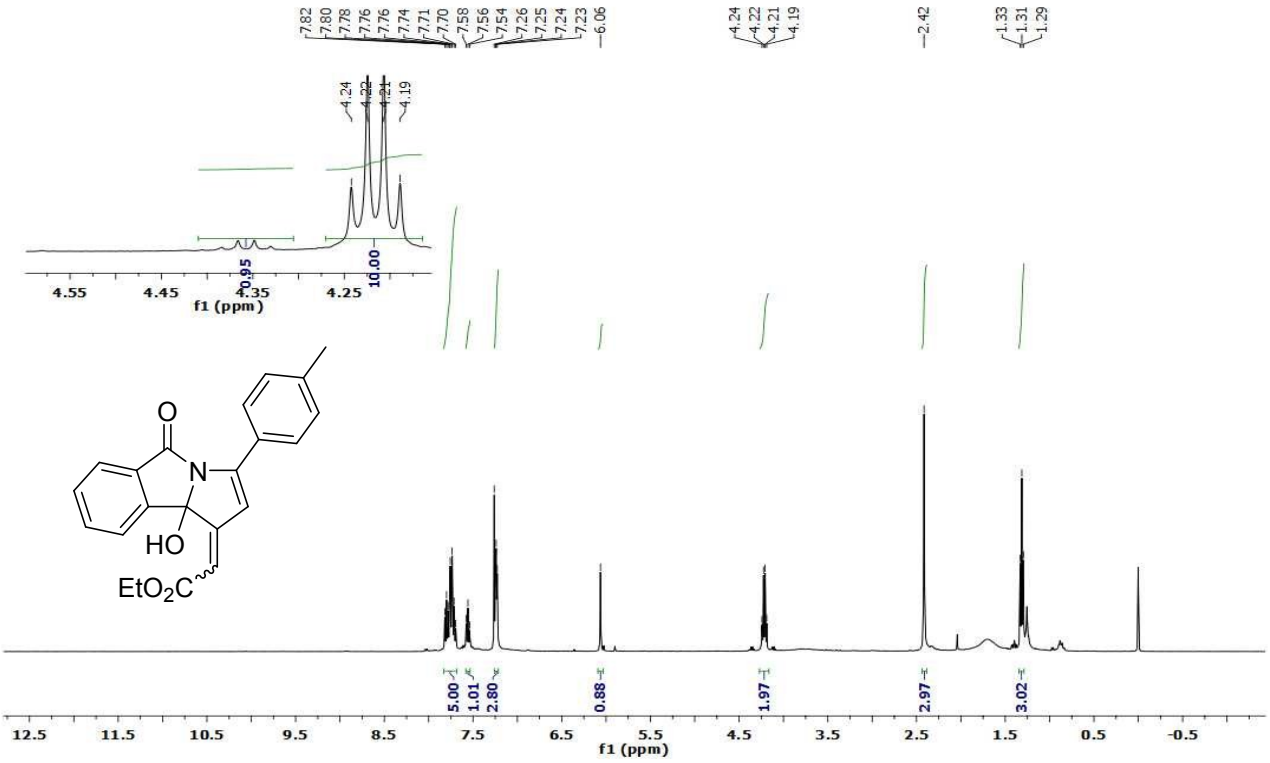
^{13}C-NMR spectrum of **3z** (100 MHz, DMSO-d^{6})



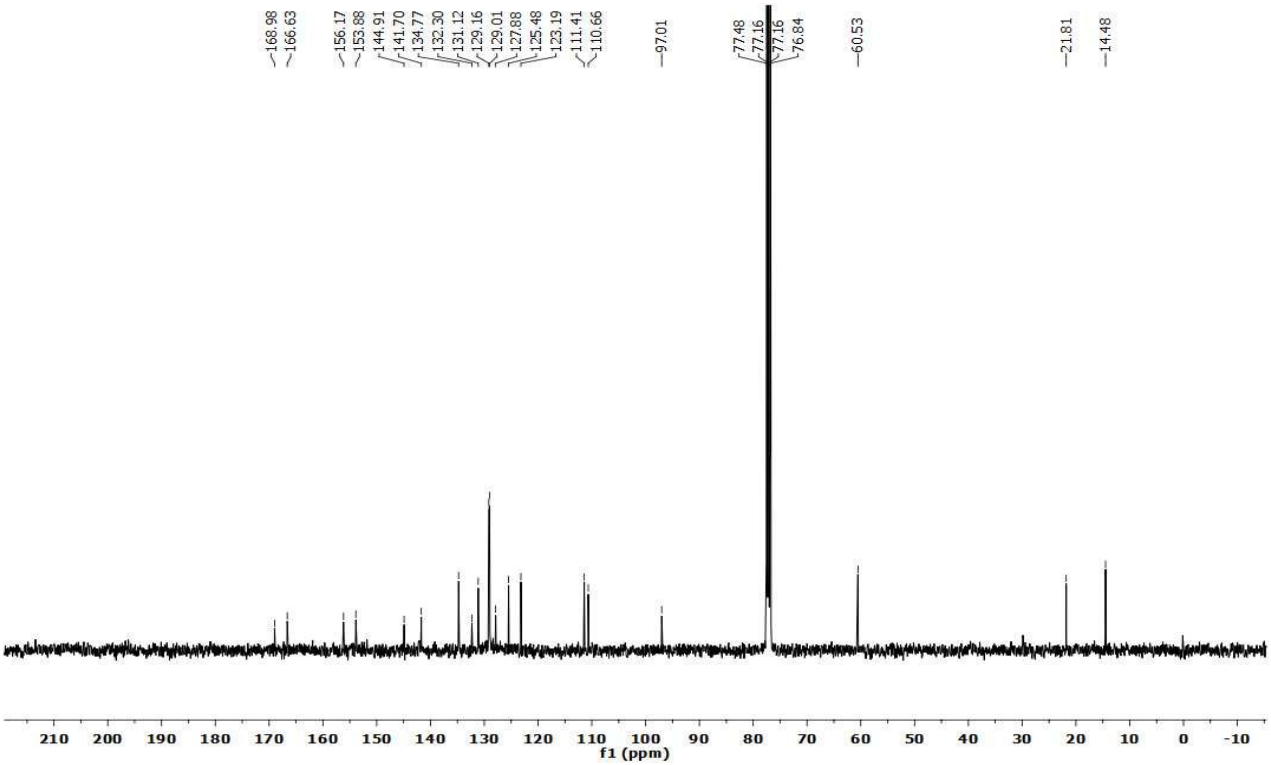
^{1}H-NMR spectrum of **4** (400 MHz, DMSO-d^{6})



^{13}C-NMR spectrum of **4** (100 MHz, DMSO-d^{6})

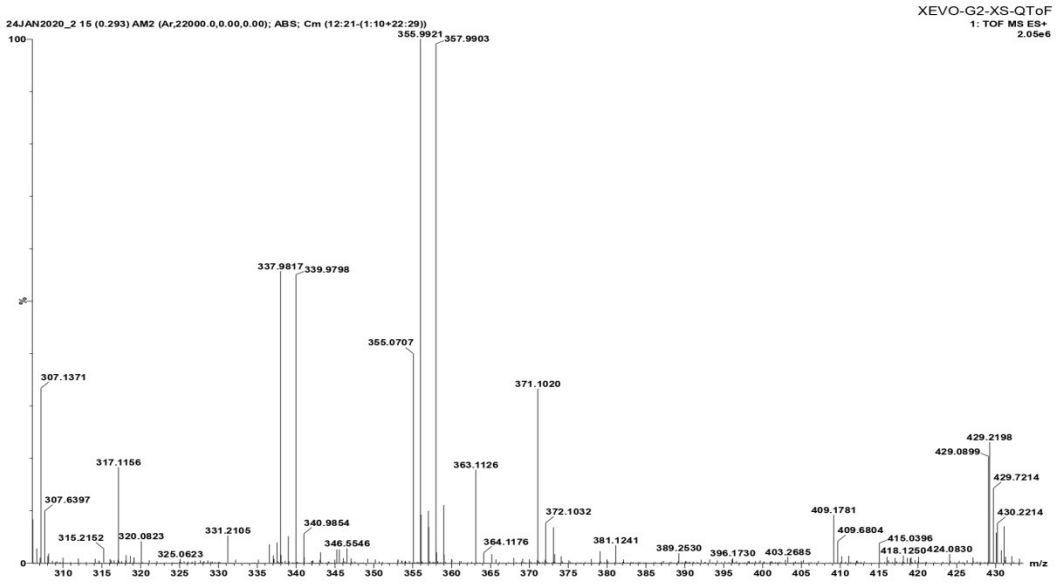


^{1}H-NMR spectrum of **5** (400 MHz, $CDCl_3$)

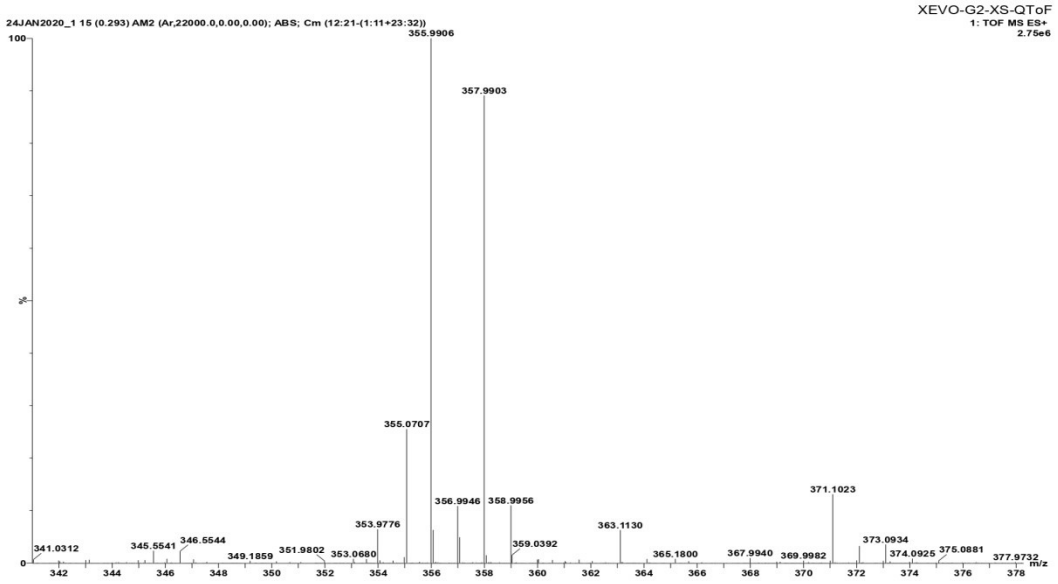


^{13}C-NMR spectrum of **5** (100 MHz, $CDCl_3$)

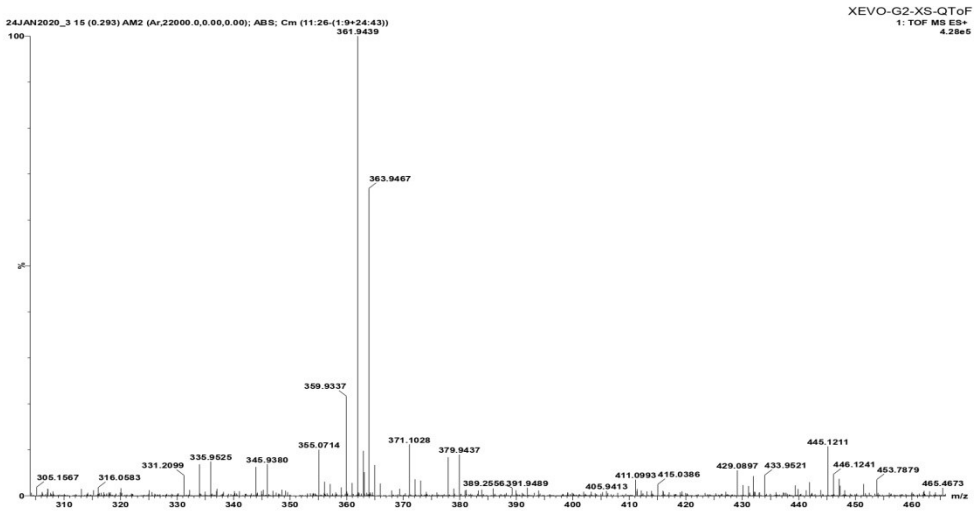
8. HRMS spectra of bromo compounds



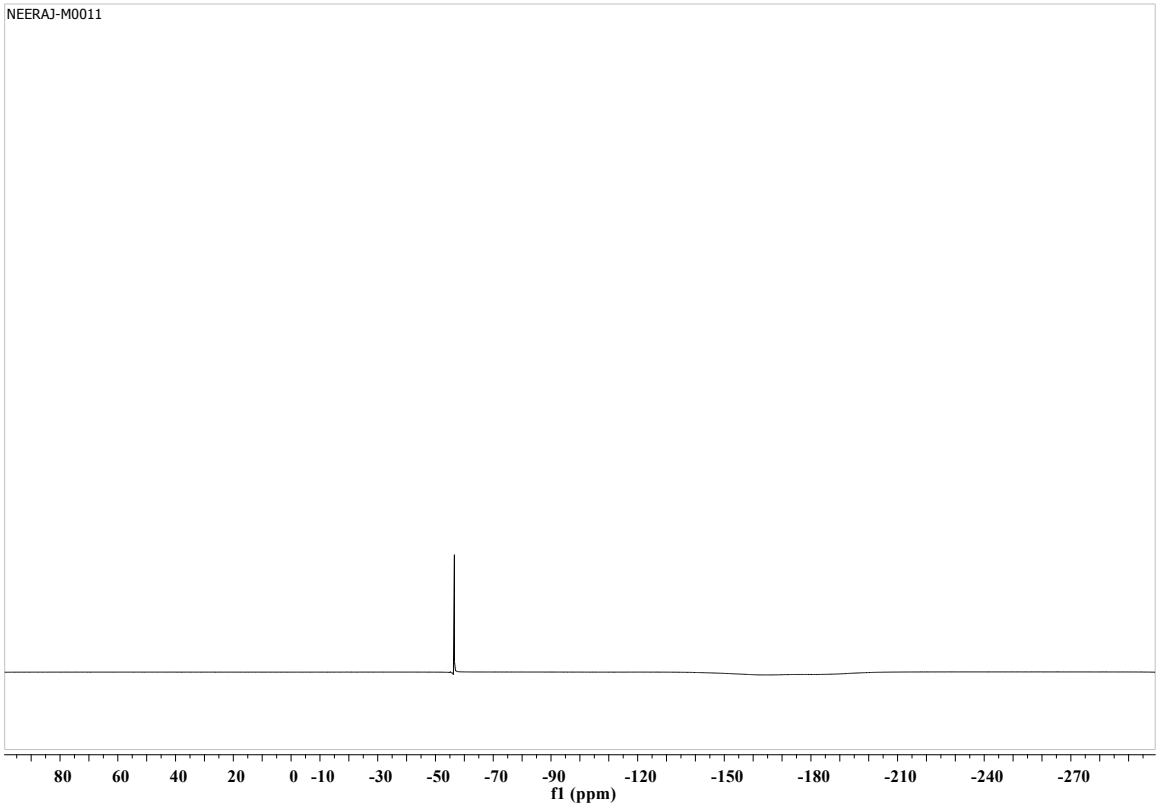
HRMS of compound 3e



HRMS of compound 3k



HRMS of compound 3y



19F NMR spectrum of **3l** (300 MHZ, DMSO)

9. Reference :

1) Z. Zhu, X. Tang, J. Li, X. Li, W. Wu, G. Deng and H. Jiang, *Chem Comm*., 2017, **53**, 3228.