Supplementary Information

Design, Synthesis, Pharmacological Evaluation and Molecular Docking Studies of Substituted Oxadiazolyl-2-Oxoindolinylidene Propane Hydrazide Derivatives

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General methods for synthesis of substituted ethyl benzoates (**16-30**)[1]

To a solution of substituted benzoic acid (**1-15**) (0.246 mol) in dry ethanol (2.5 mol), concentrated sulphuric acid (0.5 mL) was added. The reaction mixture was refluxed for 8 h. Excess of ethanol was distilled off and the content was allowed to cool. The residue was poured into separating funnel containing 60 mL of water. Carbon-tetrachloride (5-10 mL) was added to obtain sharp separation of aqueous and ester layer. Ester layer was washed with sodium hydrogen carbonate solution. The esters (**16-30**) were collected and recrystallised from ethanol, since the compounds are very well known and characterised, we have done their preliminary investigations only to confirm the formation of these compounds. Details of which is mentioned as below.

Ethyl benzoate (**16**)

Yield: 5.8 g (58%); b.p. 208-210 ºC; R_f 0.53 (chloroform).

Ethyl 4-hydroxybenzoate (**17**)

Yield: 7.3 g (73%); m.p. 114-116 ºC; R_f 0.57 (chloroform).

Ethyl 4-methylbenzoate (**18**)

Yield: 8.2 g (82%), b.p. 230-232 ºC; R_f 0.67 (chloroform).

Ethyl 3-nitrobenzoate (**19**)

Yield: 6.9 g (69%); m.p. 40-44 ºC; R_f 0.68 (chloroform).

Ethyl 2,3-dimethoxybenzoate (**20**)

Yield: 7.6 g (76%); m.p. 180-182 ºC; R_f 0.68 (chloroform).

Ethyl 4-chlorobenzoate (**21**)

Yield: 4.5 g (45%); b.p. 240-242 ºC; R_f 0.68 (chloroform).

Ethyl 4-nitrobenzoate (**22**)

Yield: 7.1 g (71%); m.p. 60-62 ºC; R_f 0.76 (chloroform).

Ethyl 4-acetylbenzoate (**23**)

Yield: 7.4 g (74%); m.p. 58-60 ºC; R_f 0.57 (chloroform).

Ethyl 4-fluorobenzoate (**24**)

Yield: 8.1 g (81%); b.p. 212-214 ºC; R_f 0.76 (chloroform).

Ethyl 2-chlorobenzoate (**25**)

Yield: 7.3 g (73%); b.p. 240-242 ºC; R_f 0.76 (chloroform).

Ethyl 2-nitrobenzoate (**26**)

Yield: 7.5 g (75%); b.p. 106-108 ºC; R_f 0.66 (chloroform).

Ethyl 3-chlorobenzoate (**27**)

Yield: 7.5 g (75%); b.p. 124-26 ºC; R_f 0.62 (chloroform).

Ethyl 2-fluorobenzoate (**28**)

Yield: 7.5 g (75%); b.p. 118-120 ºC; R_f 0.61 (chloroform).

Ethyl 4-bromobenzoate (**29**)

Yield: 7.5 g (75%); b.p. 134-136 ºC; R_f 0.54 (chloroform).

Ethyl 3-bromobenzoate (**30**)

Yield: 7.5 g (75%); b.p. 131-133 ºC; R_f 0.66 (chloroform), m.p. 26-30 ºC.

General methods for synthesis of substituted aryl acid hydrazides (**31-45**)[2]

The substituted ethyl benzoates (**16**-**30**) (0.01 mol) dissolved in dry ethanol (25 mL), hydrazine hydrate (99%, 0.01 mol) was added and the mixture was refluxed for 6 h. The reaction mixture was cooled and the solid obtained was filtered and recrystallized from dilute ethanol. Since these compounds are very well known and characterised, we have done their preliminary investigations only to confirm the formation of these compounds. Details of which is mentioned as below.

Benzoic acid hydrazide (**31**)

Yield: 3.87 g (77%); m.p. 110-112 ºC; R_f 0.76 (chloroform).

4-hydroxybenzoic acid hydrazide (**32**)

Yield: 5.18 g (71%); m.p. 264-266 ºC; R_f 0.72 (chloroform).

4-Methylbenzoic acid hydrazide (**33**)

Yield: 5.67 g (70%); m.p. 114-116 ºC; R_f 0.68 (chloroform).

3-Nitrobenzoic acid hydrazide (**34**)

Yield: 4.69 g (69%); m.p. 158-160 ºC; R_f 0.54 (chloroform).

2,3-Dimethoxybenzoic acid hydrazide (**35**)

Yield: 5.55 g (74%); m.p. 76-78 ºC; R_f 0.65 (chloroform).

4-Chlorobenzoic acid hydrazide (**36**)

Yield: 3.12 g (71%); m.p. 162-164 ºC; R_f 0.65 (chloroform).

4-Nitrobenzoic acid hydrazide (**37**)

Yield: 5.25 g (70%); m.p. 218-220 ºC; R_f 0.63 (chloroform).

4-Acetylbenzoic acid hydrazide (**38**)

Yield: 5.69 g (73%); m.p. 206-208 ºC; R_f 0.77 (chloroform).

4-Fluorobenzoic acid hydrazide (**39**)

Yield: 6.8 g (85%); m.p. 164-166 ºC; R_f 0.69 (chloroform).

2-Chlorobenzoic acid hydrazide (**40**)

Yield: 6.2 g (82%); m.p. 120-122 ºC; R_f 0.69 (chloroform).

2-Nitrobenzoic acid hydrazide (**41**)

Yield: 4.8 g (65%); m.p. 122-124 ºC; R_f 0.69 (chloroform).

3-Chlorobenzoic acid hydrazide (**42**)

Yield: 5.8 g (75%); m.p. 154-156 ºC; R_f 0.69 (chloroform).

2-Fluorobenzoic acid hydrazide (**43**)

Yield: 6.4 g (83%); m.p. 77-79 ºC; R_f 0.69 (chloroform).

4-Bromobenzoic acid hydrazide (**44**)

Yield: 7.2 g (92%); m.p. 168-170 ºC; R_f 0.69 (chloroform).

3-Bromobenzoic acid hydrazide (**45**)

Yield: 6.3 g (81%); m.p. 158-160 ºC; R_f 0.69 (chloroform).

^{1}H NMR and ^{13}C NMR spectra of selected compounds

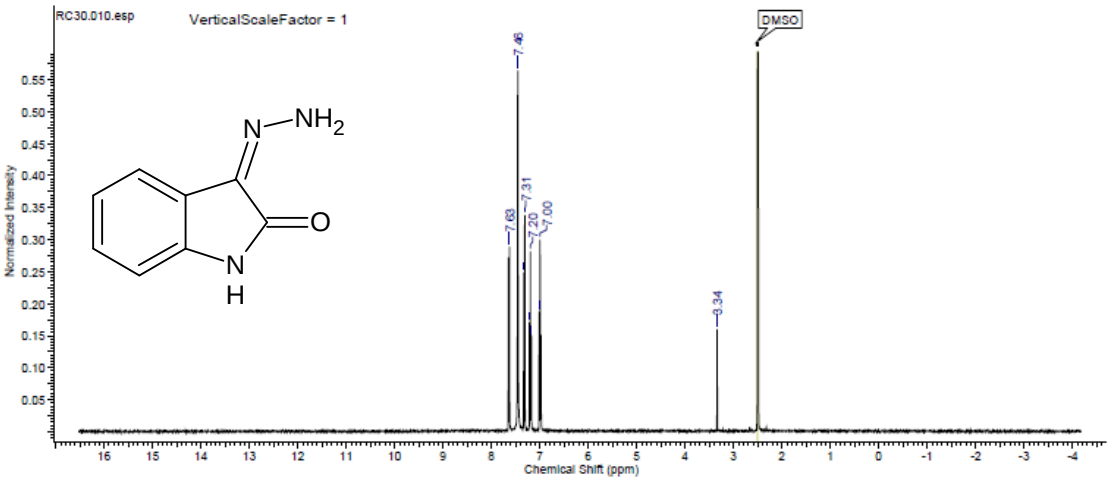

Figure S1. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-hydrazinylidene-1,3-dihydro-2*H*-indol-2-one (**47**).

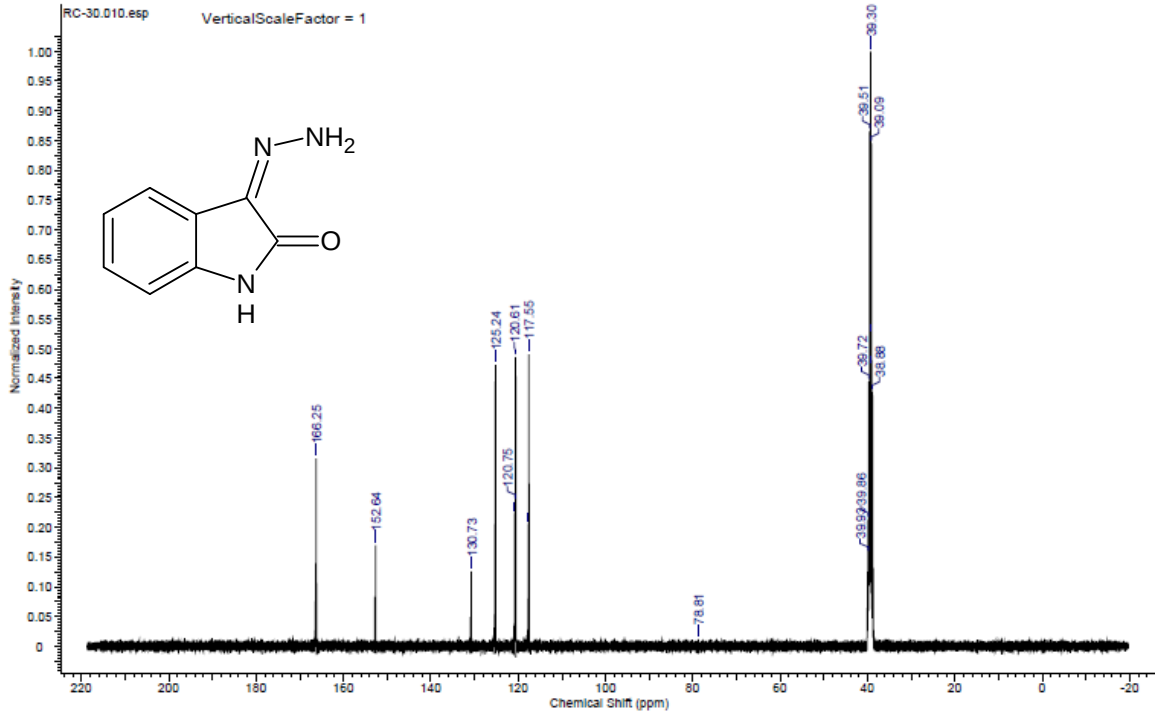

Figure S2. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-hydrazinylidene-1,3-dihydro-2*H*-indol-2-one (**47**).

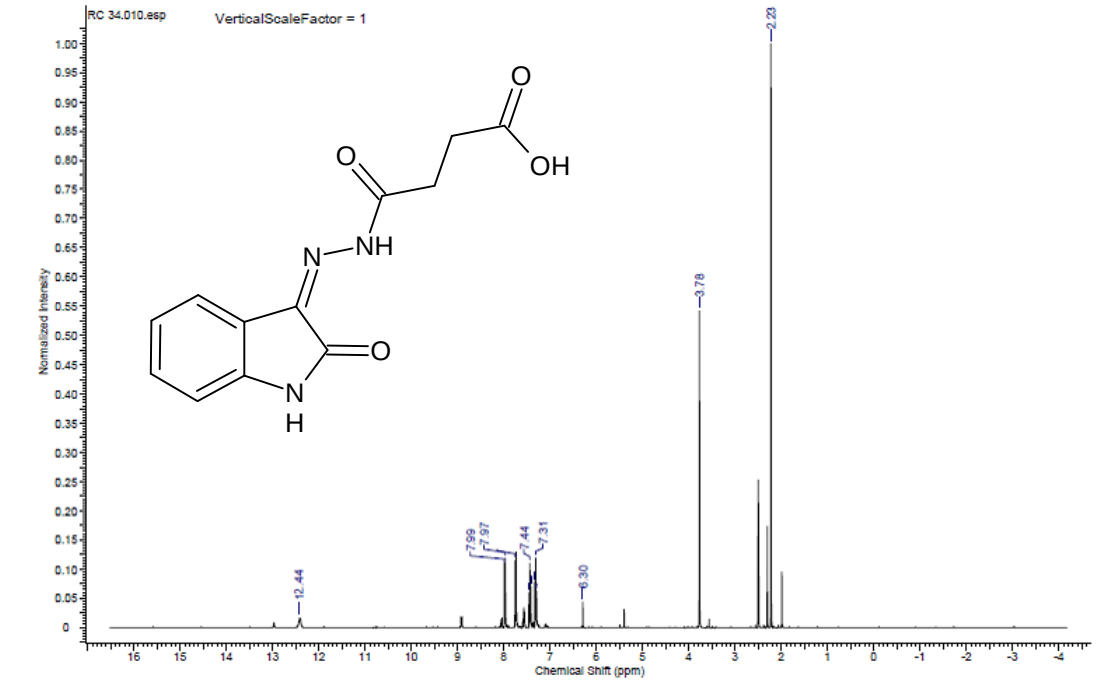

Figure S3. ^{1}H NMR spectrum (400 MHz, DMSO) of 4-oxo-4-[2-(2-oxo-1,2-dihydro-3*H*-indol-3-ylidene)-hydrazinyl] butanoic acid (**48**).

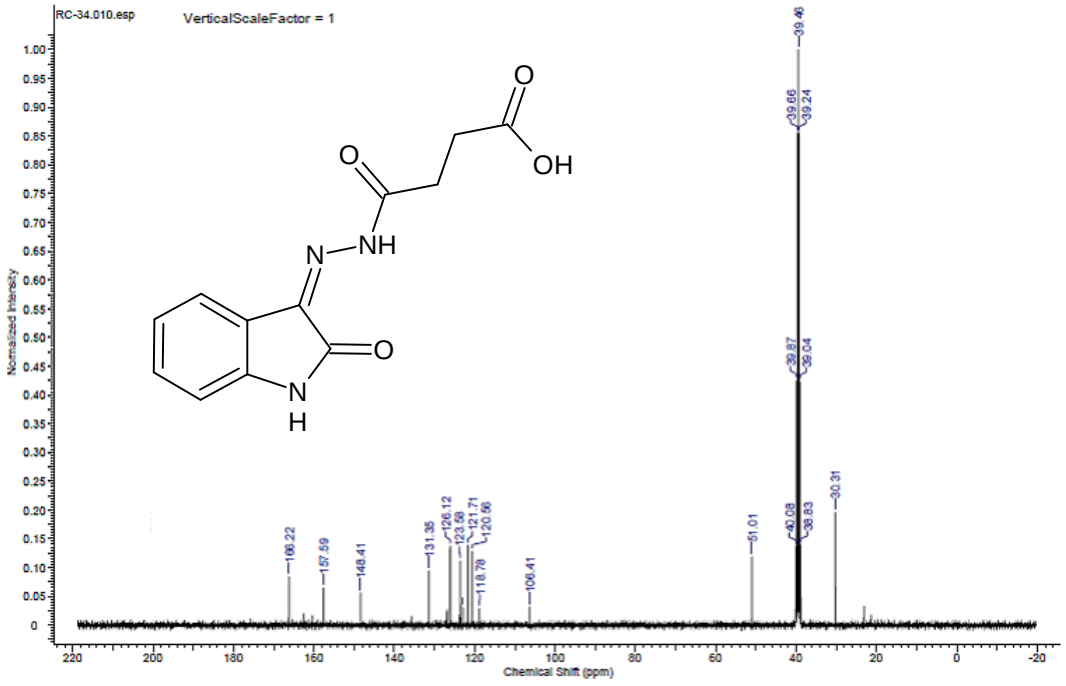

Figure S4. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 4-oxo-4-[2-(2-oxo-1,2-dihydro-3*H*-indol-3-ylidene)-hydrazinyl] butanoic acid (**48**).

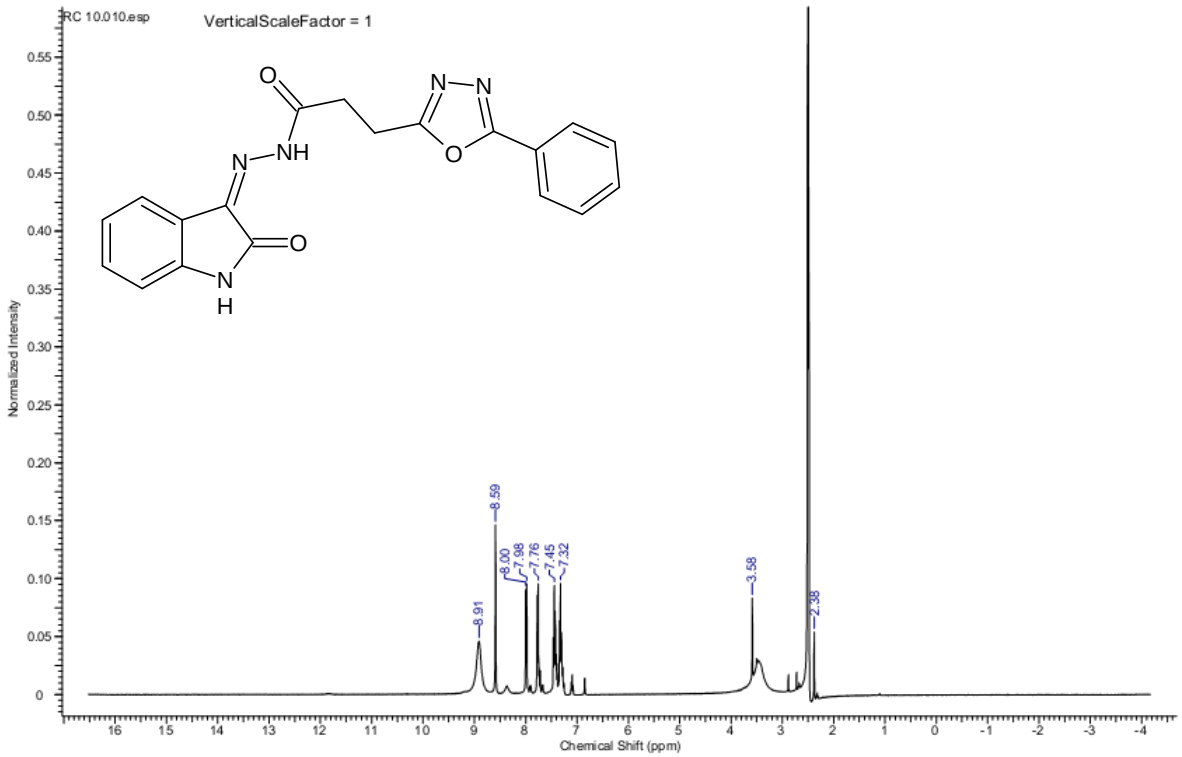

Figure S5. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-(5-phenyl-1,3,4-oxadiazol-2-yl)-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**49**).

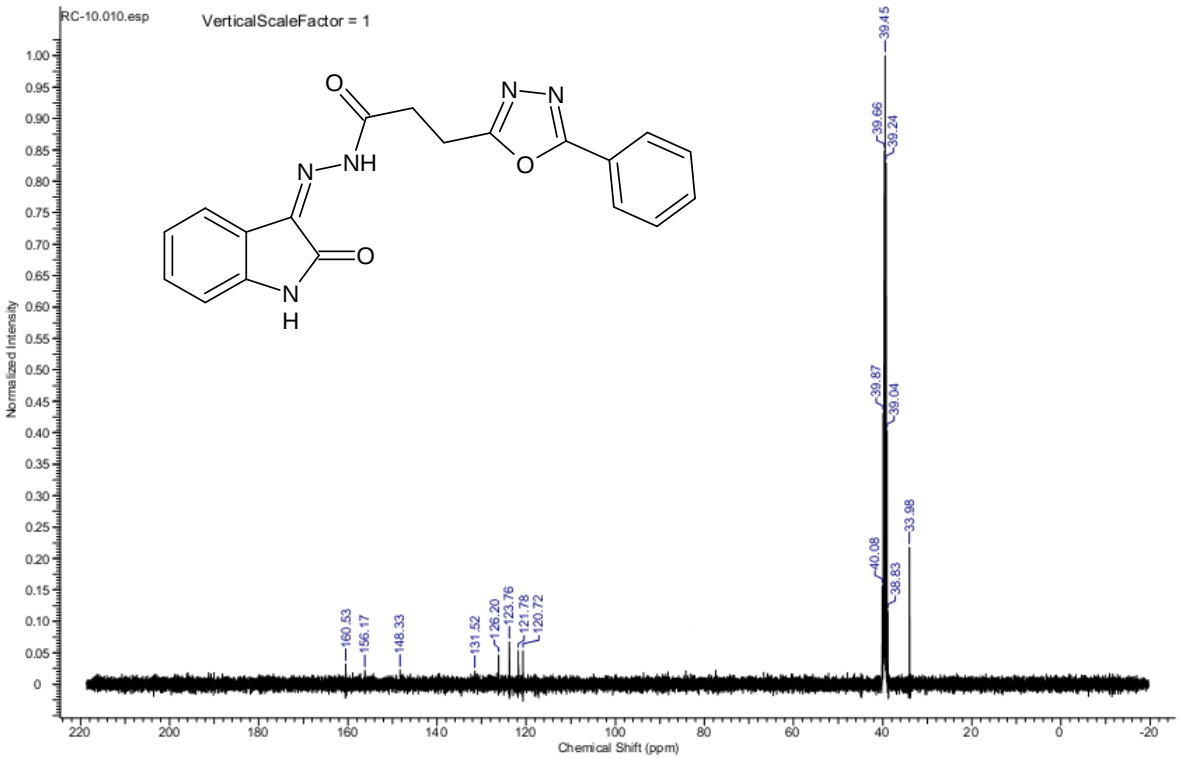

Figure S6. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-(5-phenyl-1,3,4-oxadiazol-2-yl)-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**49**).

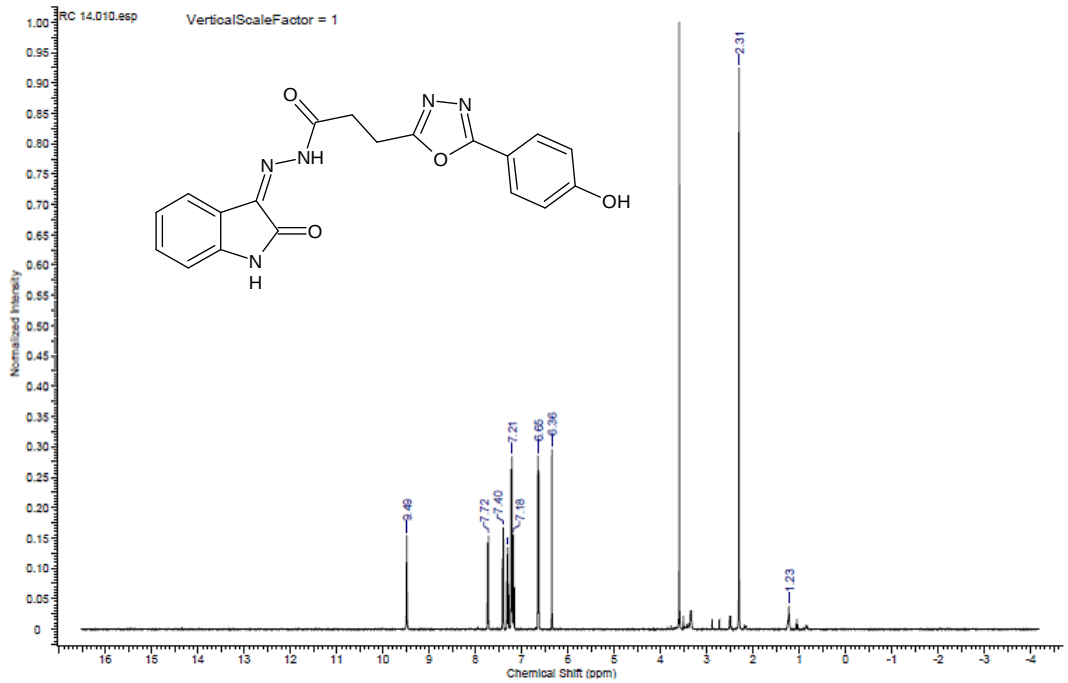

Figure S7. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**50**).

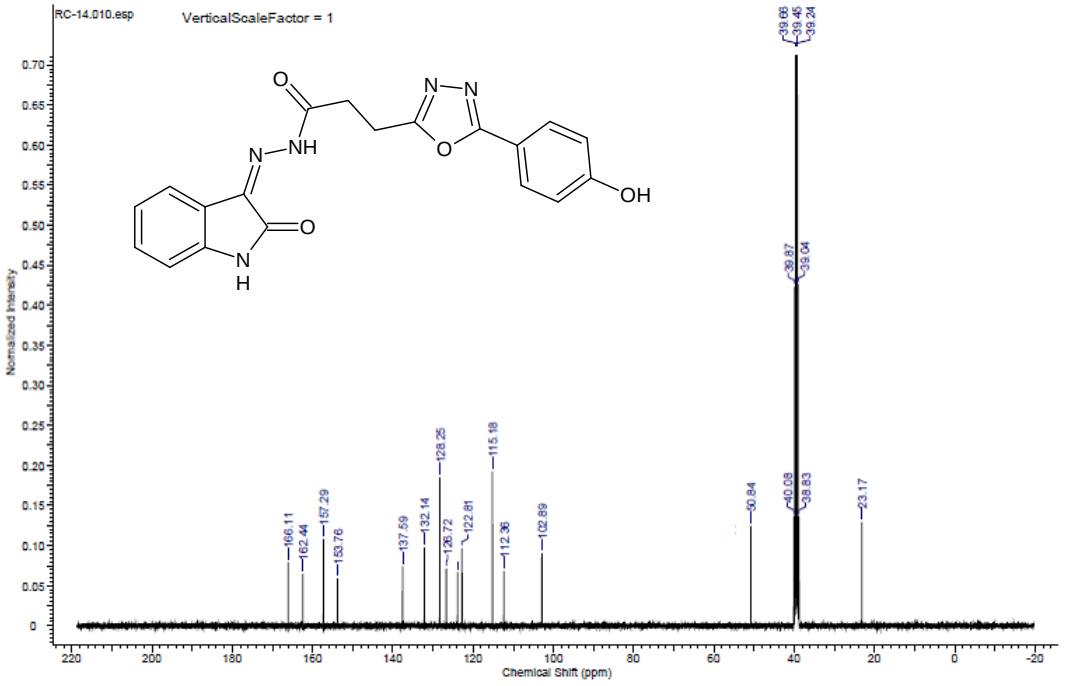

Figure S8. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**50**).

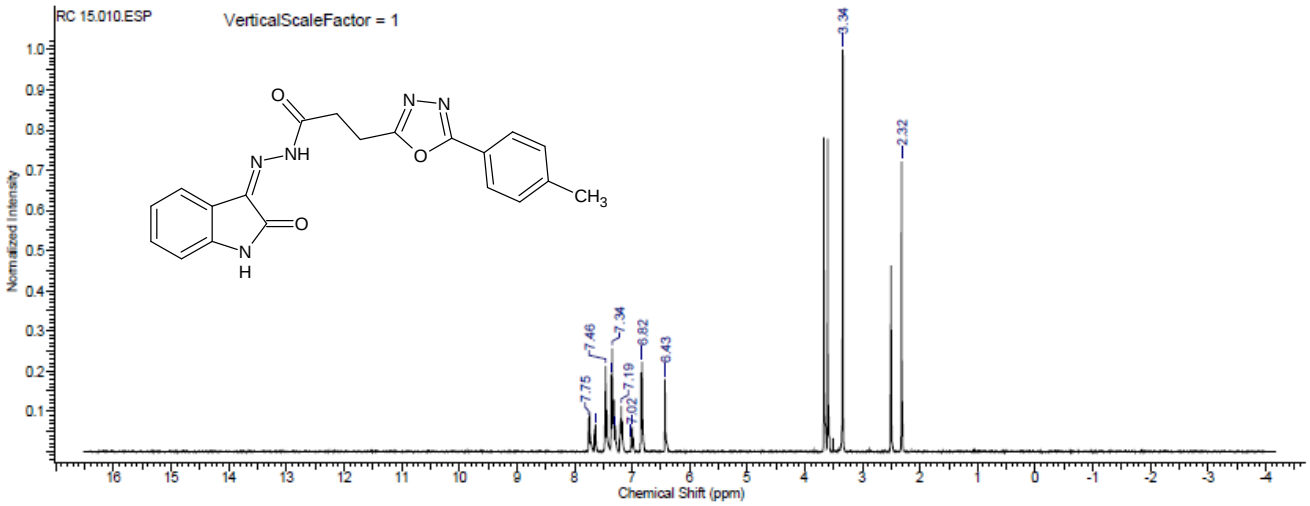

Figure S9. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**51**).

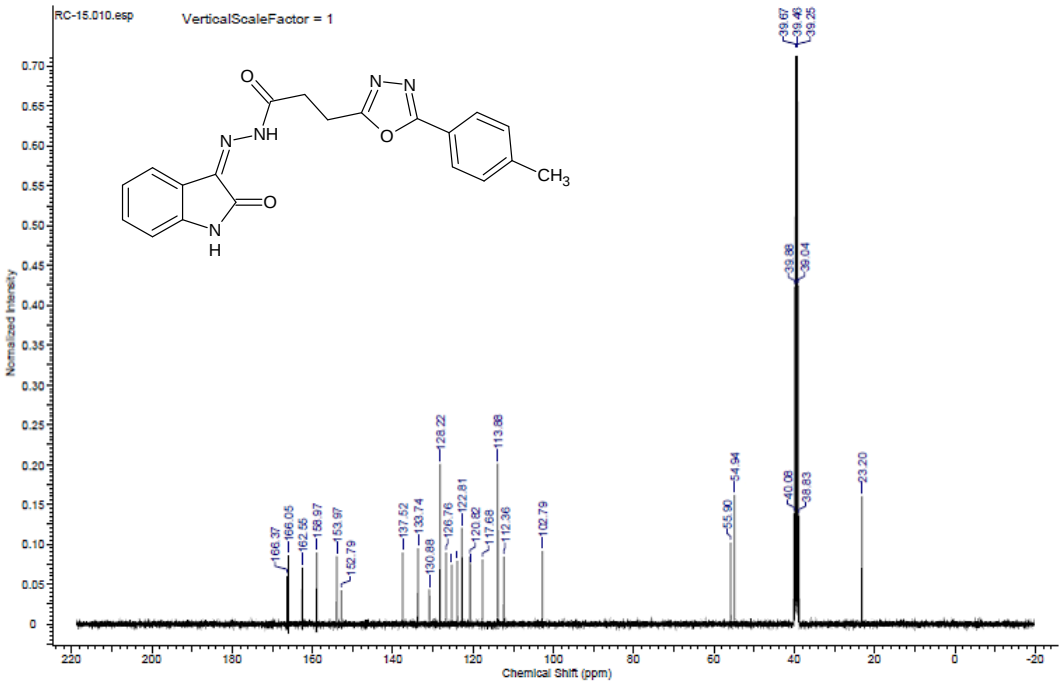

Figure S10. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**51**).

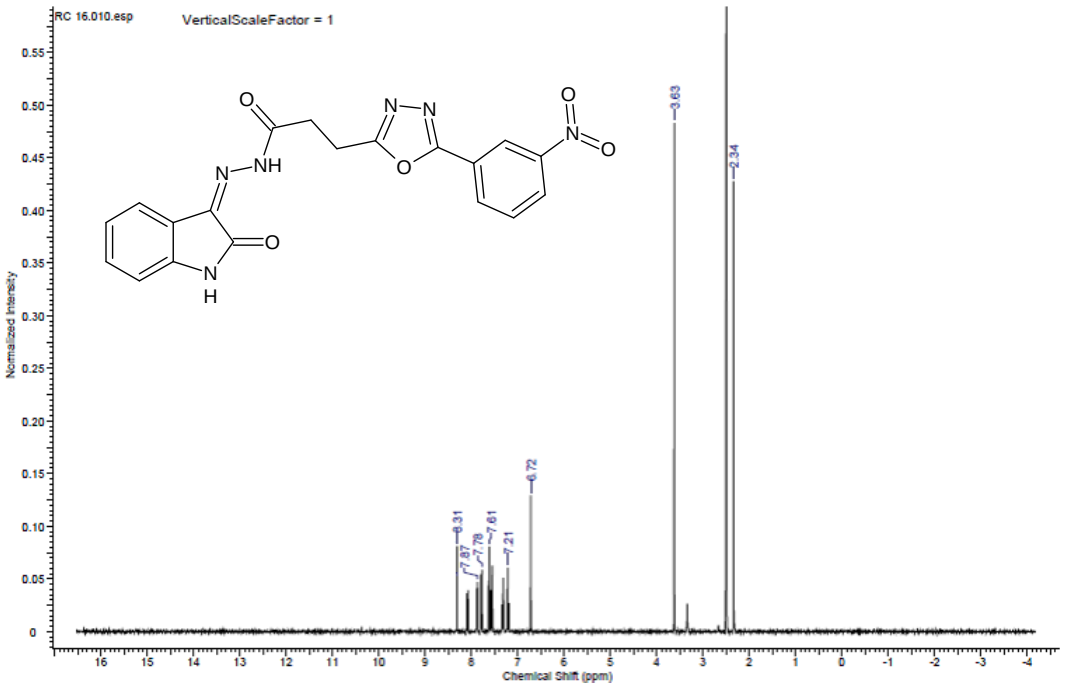

Figure S11. [1]H NMR spectrum (400 MHz, DMSO) of 3-[5-(3-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**52**).

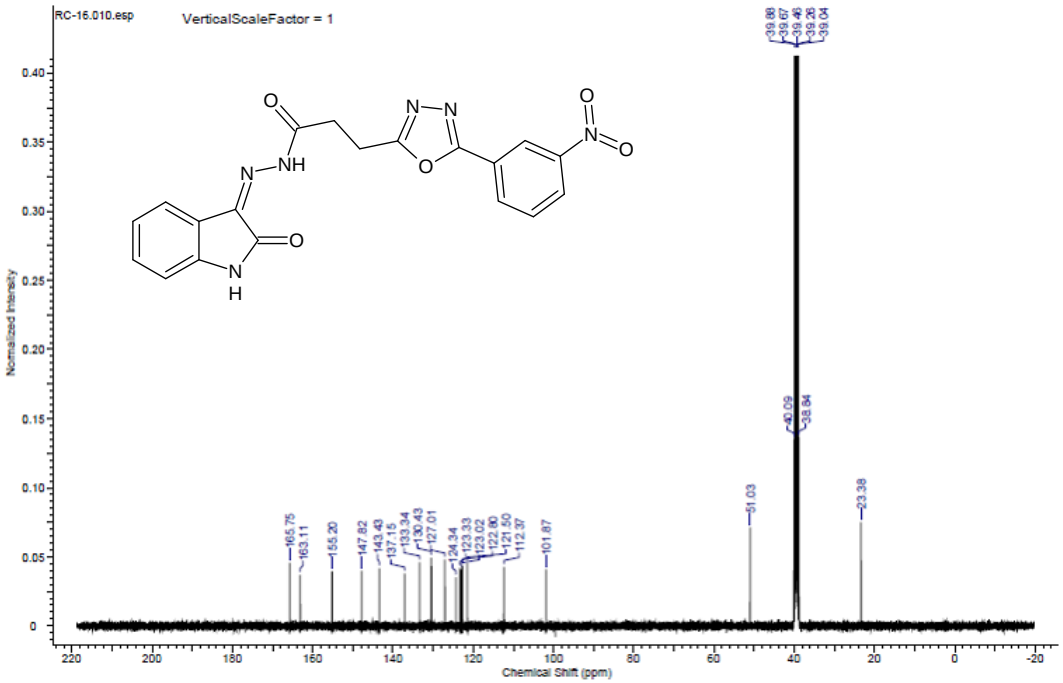

Figure S12. [13]C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(3-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**52**).

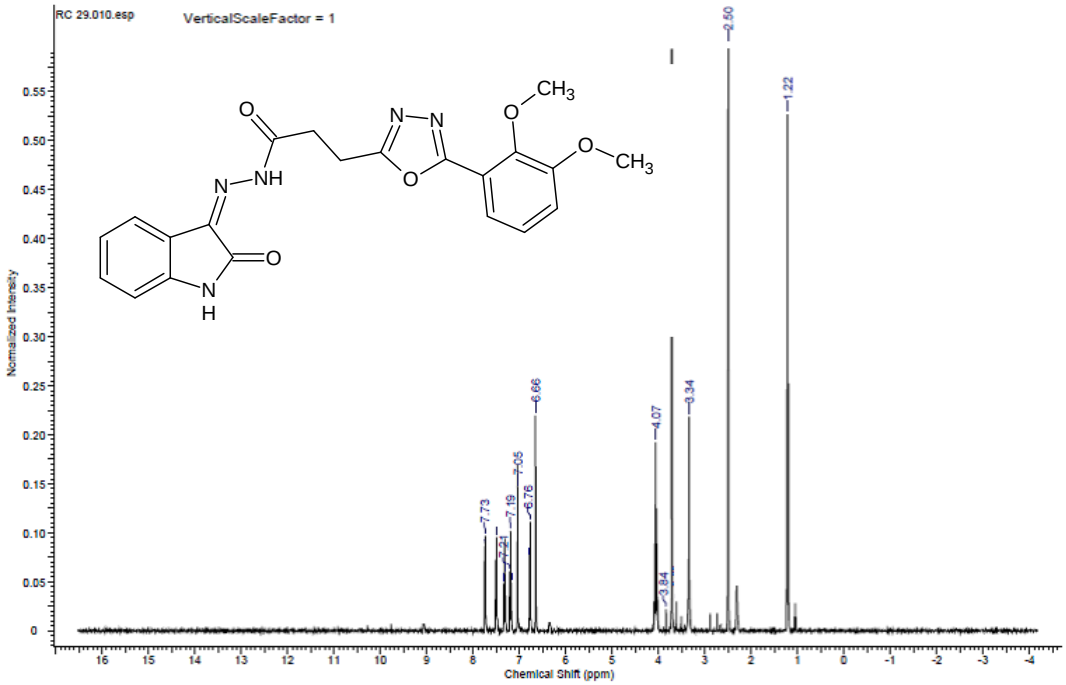

Figure S13. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(2,3-dimethoxyphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**53**).

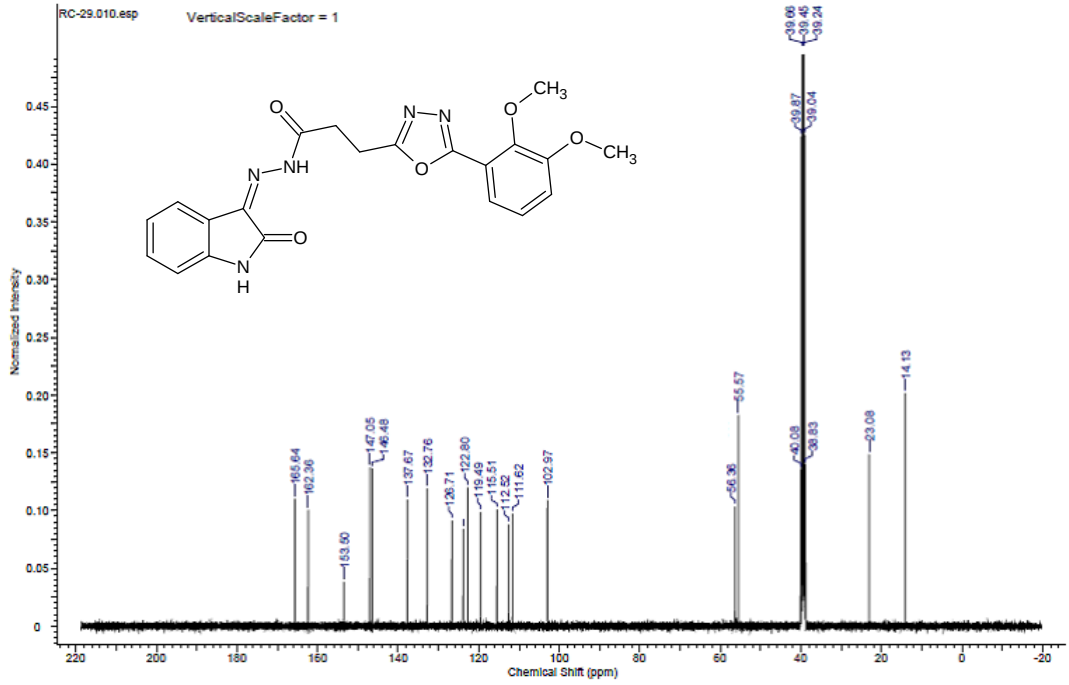

Figure S14. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(2,3-dimethoxyphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**53**).

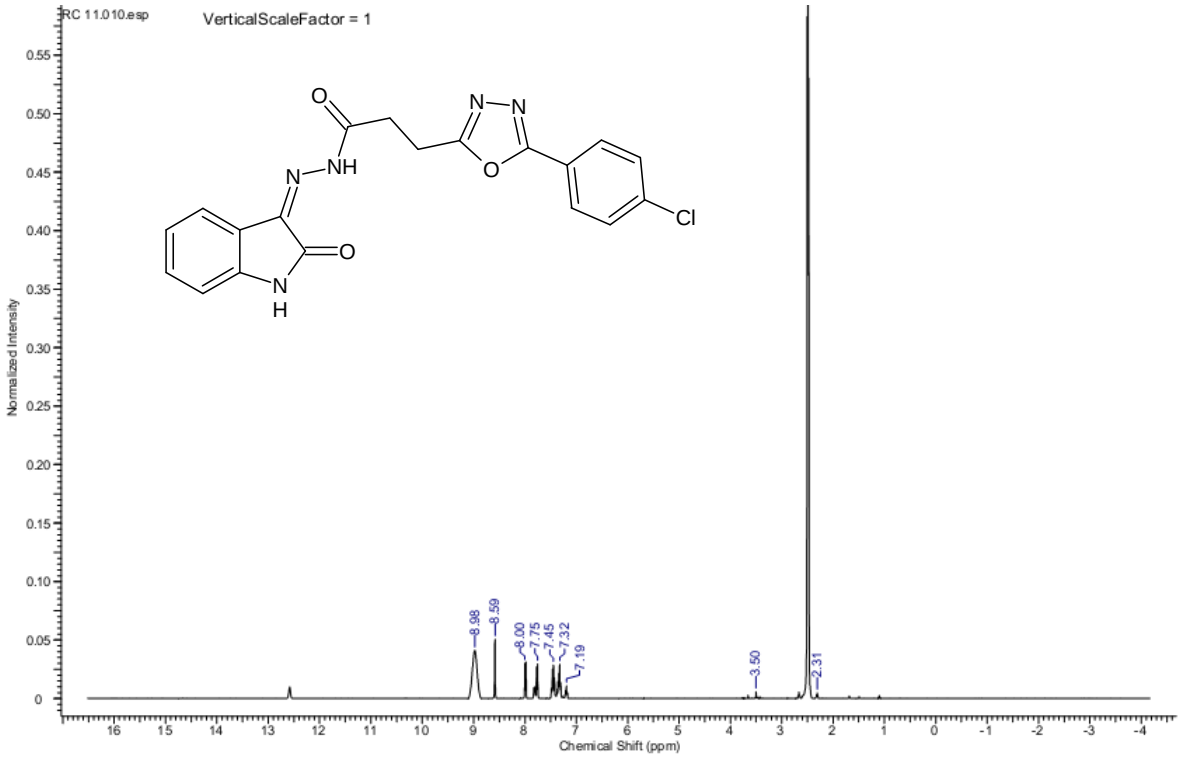

Figure S15. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**54**).

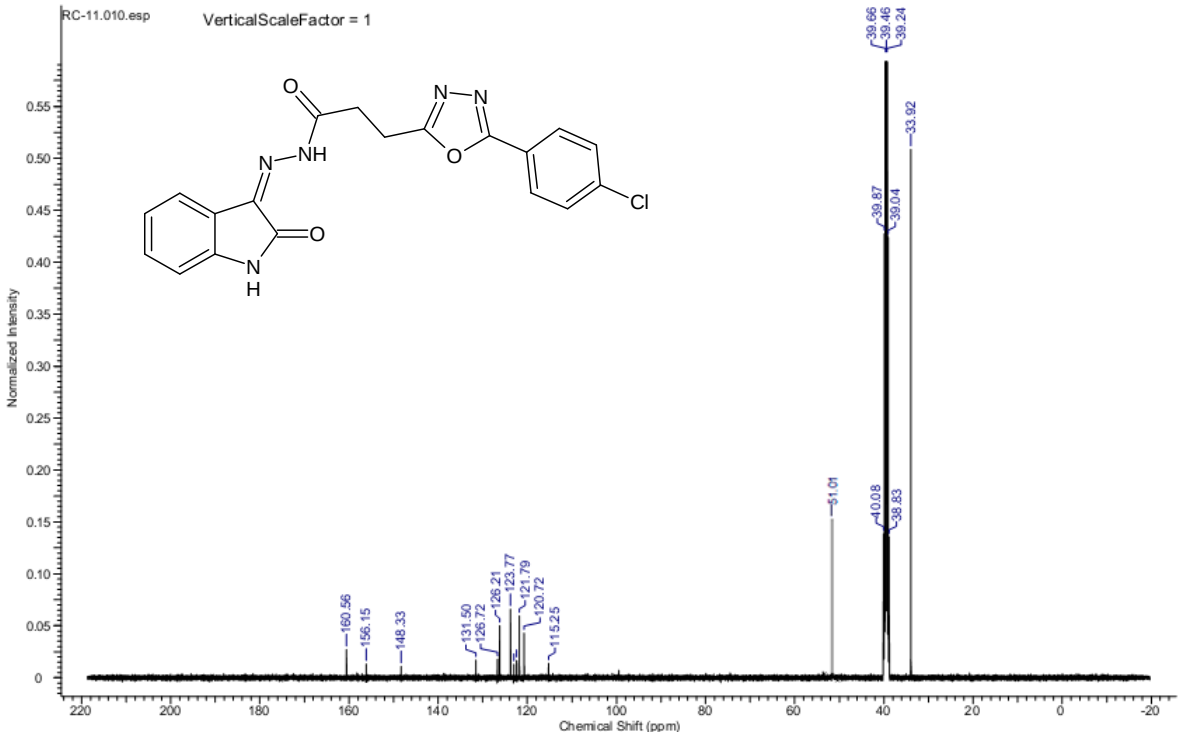

Figure S16. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**54**).

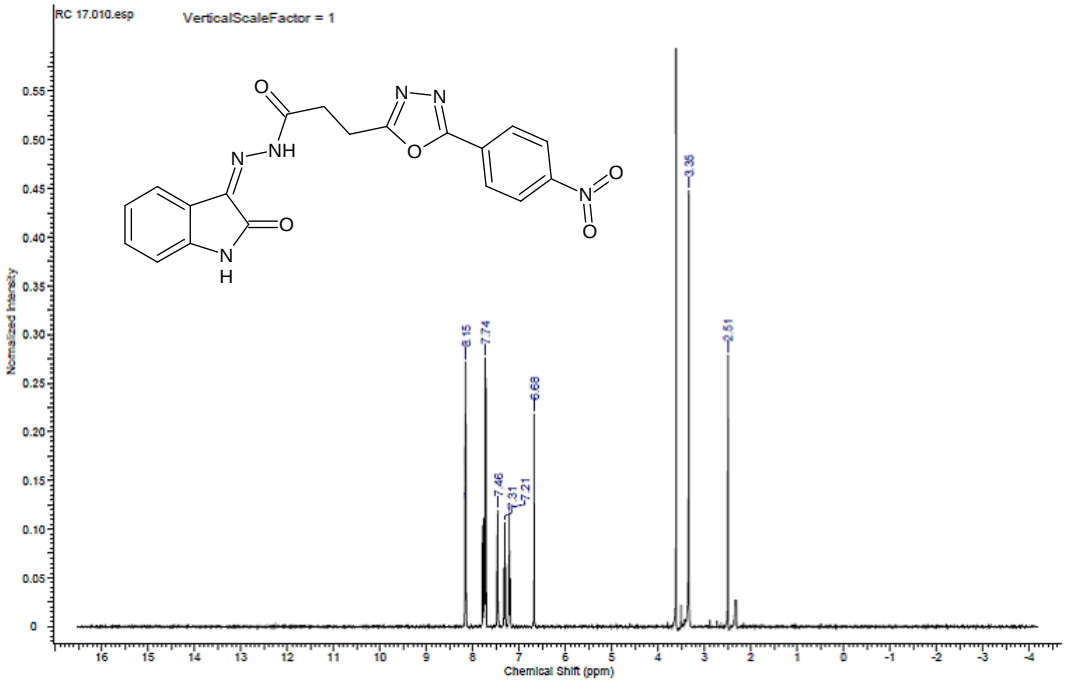

Figure S17. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**55**).

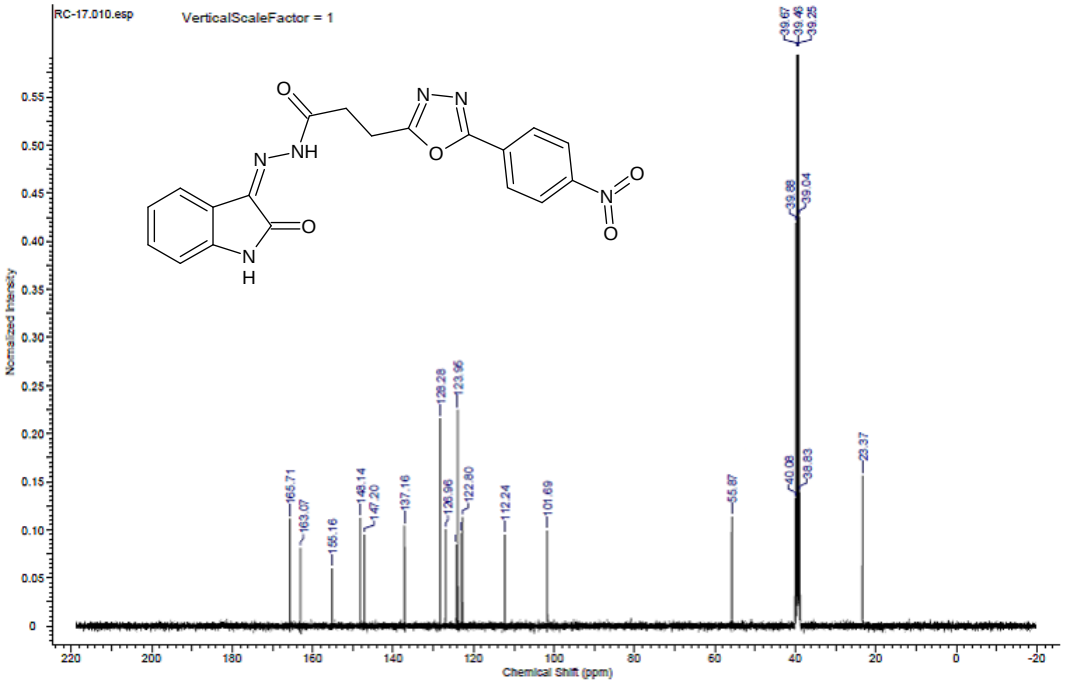

Figure S18. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**55**).

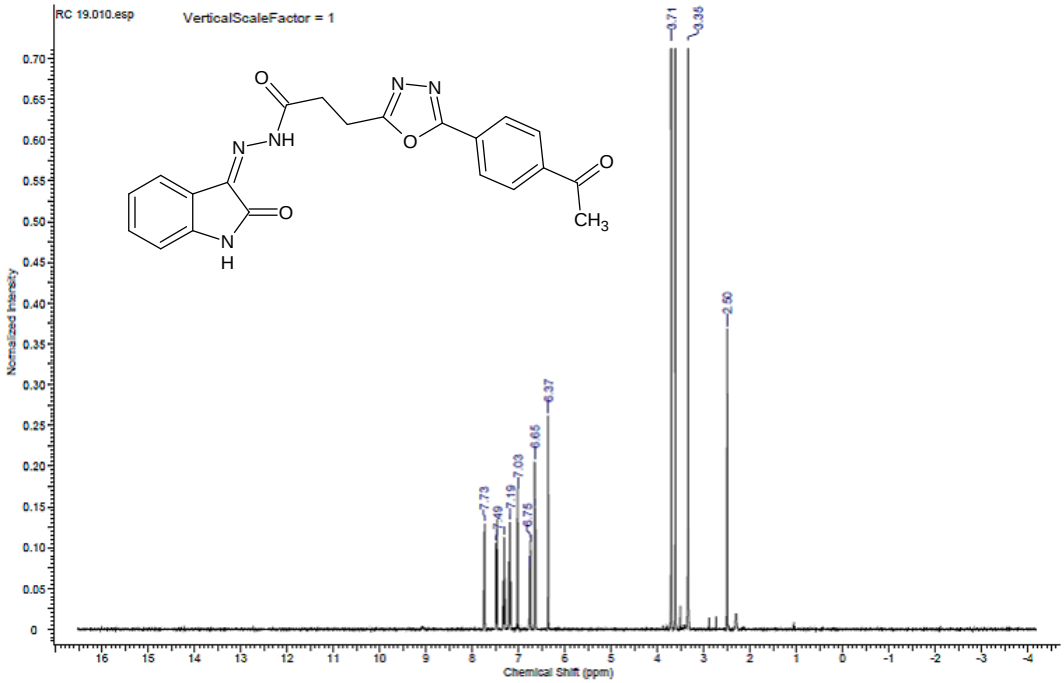

Figure S19. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-acetylphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**56**).

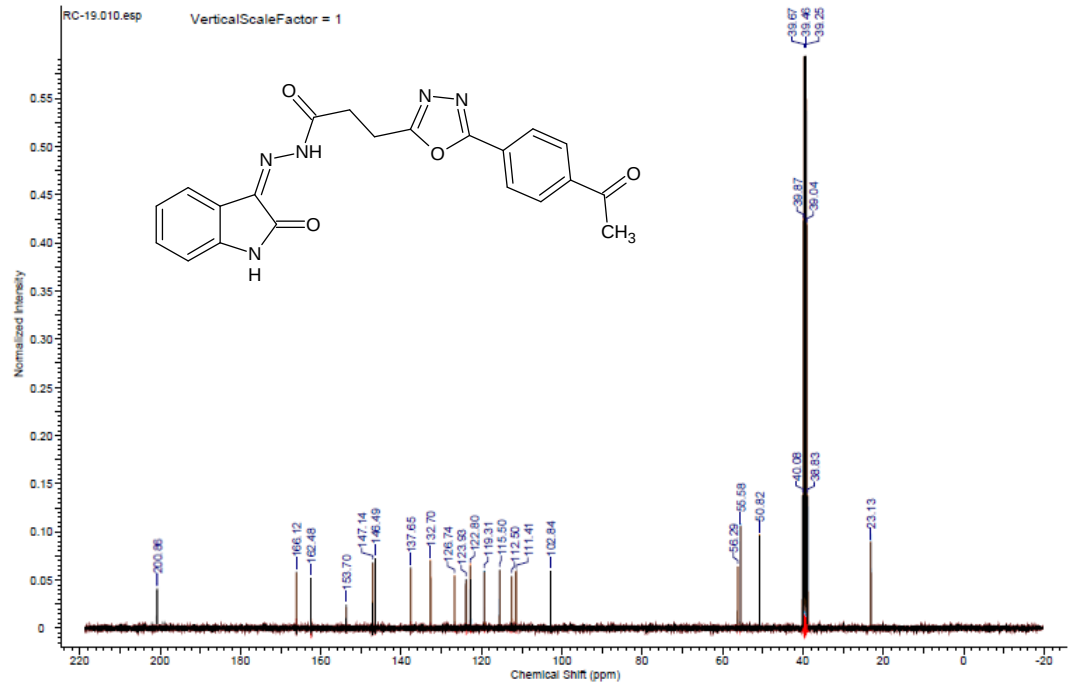

Figure S20. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-acetylphenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**56**).

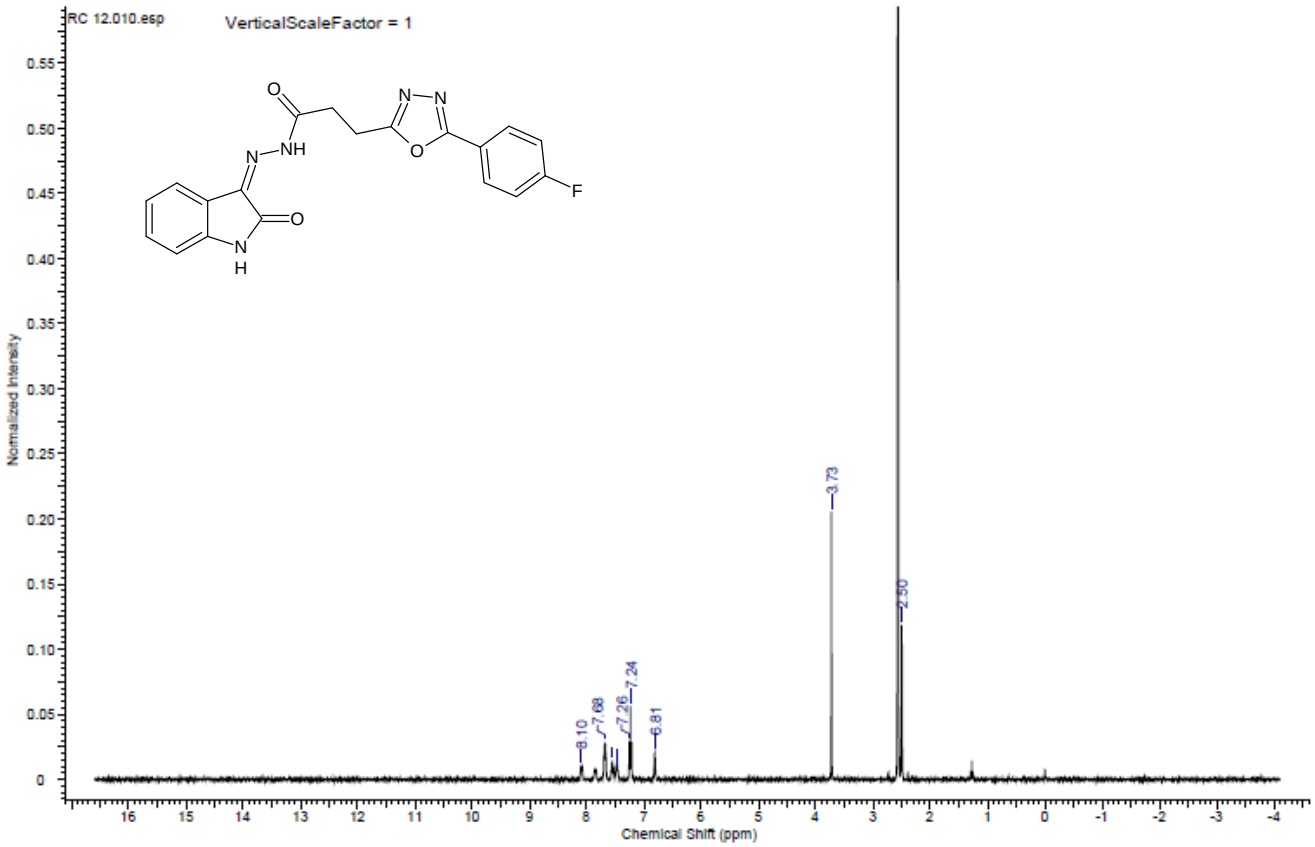

Figure S21. ^{1}H NMR spectrum (400 MHz, DMSO) of 3-[5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**57**).

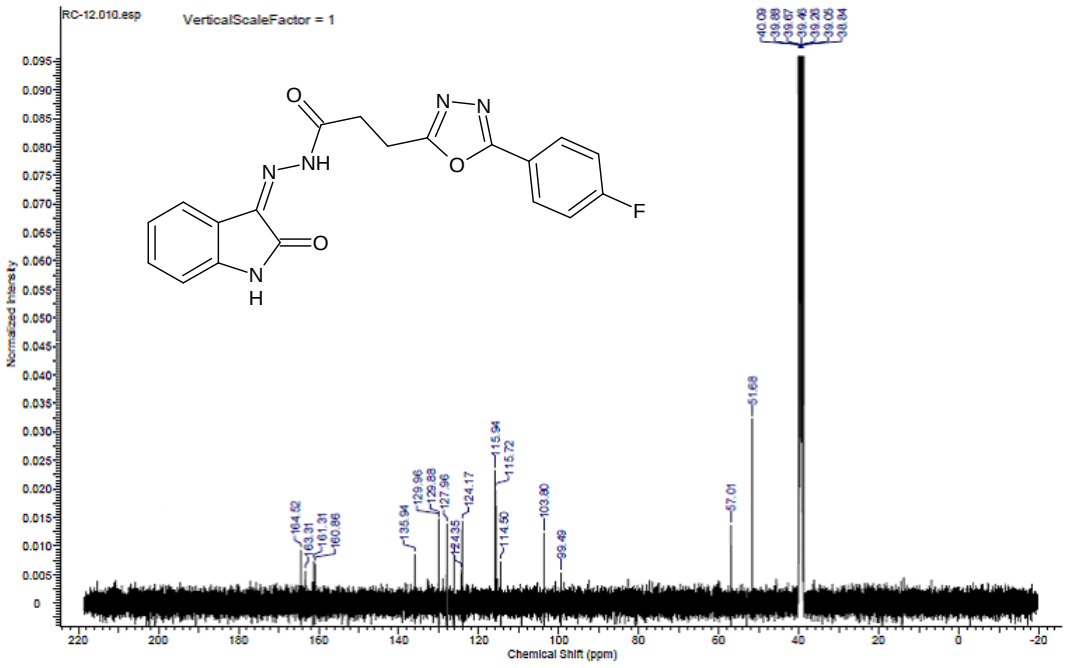

Figure S22. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**57**).

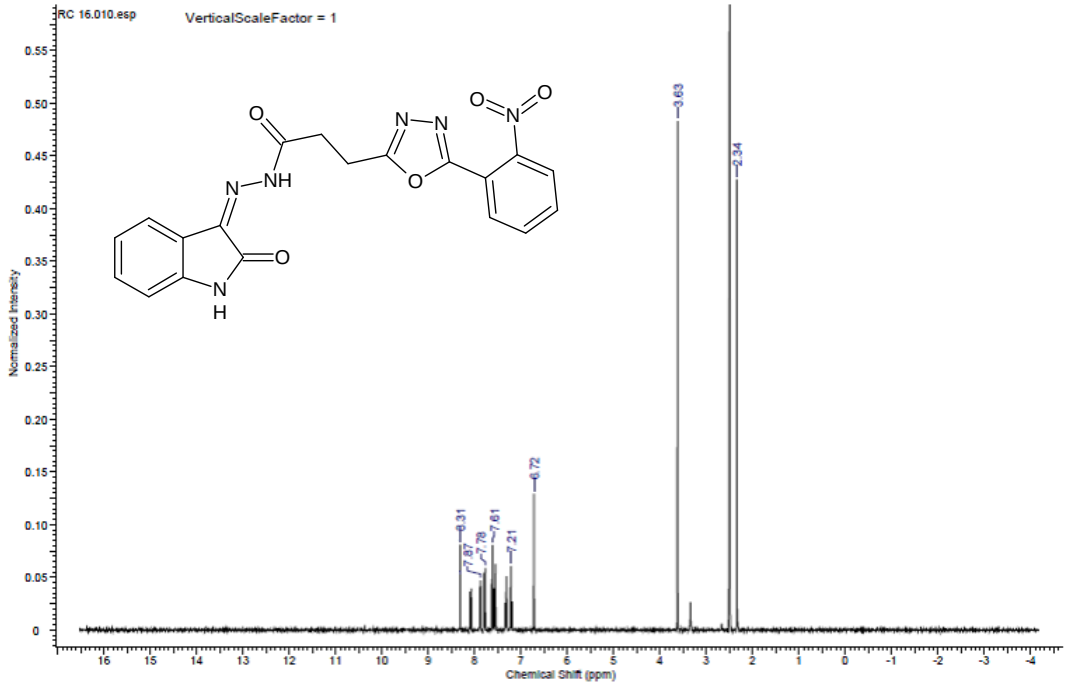

Figure S23. [1]H NMR spectrum (400 MHz, DMSO) of 3-[5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**59**).

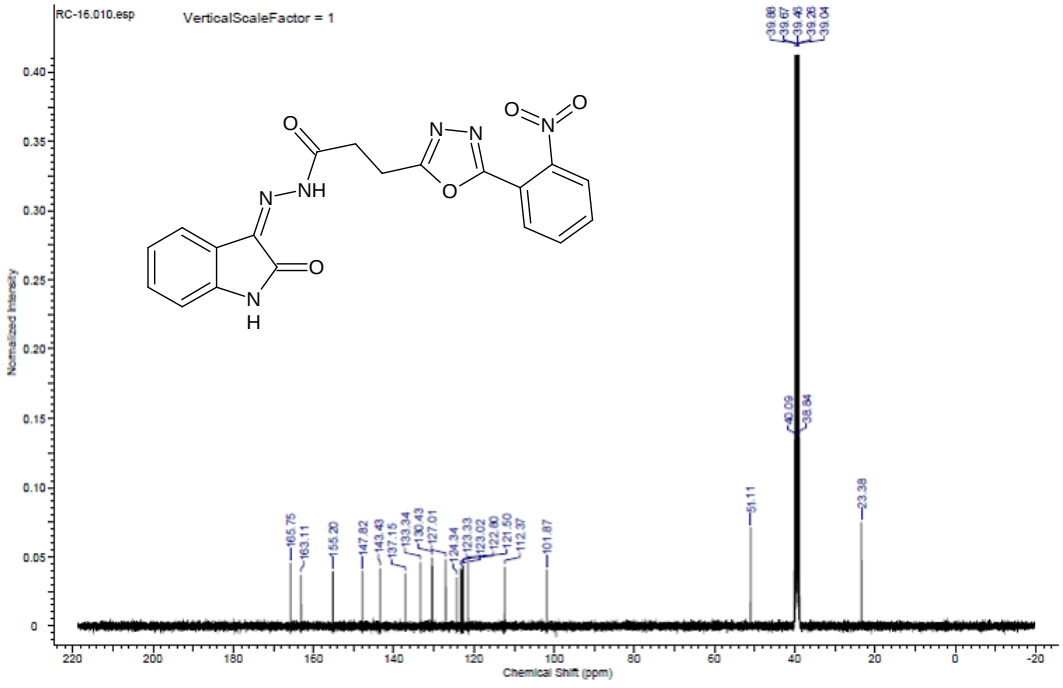

Figure S24. [13]C NMR spectrum (100 MHz, DMSO-d_6) of 3-[5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl]-*N*'-[2-oxo-1,2-dihydro-3*H*-indol-3-ylidene]propane hydrazide (**59**).

References

1. Chikhale, R.; Thorat, S.; Pant, A.; Jadhav, A.; Thatimala, K. C.; Bansode, R.; Bhargavi, G.; Karodia, N.; Rajasekharan, M. V.; Paradkar, A.; Khedekar, P.; *Bioorg. Med. Chem.* **2015**, *23*, 6689.
2. Furniss, B.; Hannaford, A. H.; Smith, P. W. G.; Tatchell, A. R.; *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longman: Harlow, 1998.