Supporting Information

Facile Synthesis of Novel 3,4,5-Trisubstituted-1,2,4-triazin-6(1H)-ones via a Sequential Ugi-Smiles Type/Nucleophilic Substitution/Cyclization Reaction

Sorour Ramezanpour, *[a] Mohammad Nasim Rezaei, [a] Aref Vaezghaemi [a] and Frank Rominger [b]

[a] Department of Chemistry, K. N. Toosi University of Technology, P.O. Box 15875-4416 Tehran, Iran

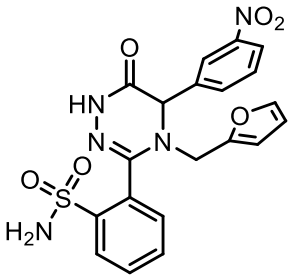
[b] Organisch-Chemisches Institut der Universitaet Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany

General Experimental Section: General information. Reagents and solvents were purchased from various commercial sources and were used directly without any further purification, unless otherwise stated. Column chromatography was performed using 63−200 mesh silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Chemical shifts were reported in parts per million (δ) using TMS, and coupling constants were expressed in Hertz. Melting points were recorded using an electrothermal capillary melting point apparatus and were uncorrected. MS spectra were recorded using mass spectra and were recorded on Mass-ESI spectrometer.

General Procedure for the Synthesis of 6a-i: To a solution of aldehyde **1a-c** (1 mmol) in EtOH (4 mL), amine **2a-e** (1 mmol), saccharin (1 mmol), and isocyanide **3a, b** (1 mmol) were added, respectively. The solution was stirred for 24 h at room temperature. The reaction progress was monitored by TLC using *n*-Hexane: EtOAc (1:1) as eluent. After completion of the reaction, solvent was removed under reduced pressure and subsequently dissolved in DMF (1 mL). hydrazine (3 equiv) was added to the mixture. The solution was stirred for 24 h at room temperature. The reaction progress was monitored by TLC using *n*-Hexane: EtOAc (1:1) as eluent. After the completion of the reaction, the desired product was extract through the addition of dichloromethane. The obtained sediment was filtered and dried and washed with methanol (1-2 mL) for ten minutes. The residue was filtered and dried. 2-phenylethylamine derivatives were purified by column chromatography using *n*-Hexane: EtOAc (1:1) as eluent.

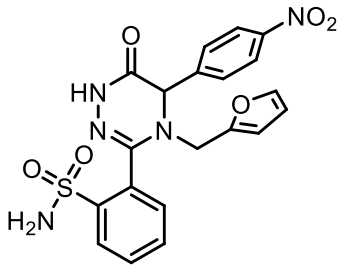
The Procedure for the Synthesis of 6a: To a solution of 3-nitrobenzaldehyde **1a** (151 mg, 05 mmol) in EtOH (4 mL), furfurylamine **2a** (97 mg, 1 mmol), saccharin **3** (183 mg, 1 mmol), and tert-Butyl isocyanide **4a** (0.115 mL, 1 mmol) were added, respectively. The solution was stirred for 24 h at room temperature. The reaction progress was monitored by TLC using *n*-Hexane: EtOAc (1:1) as eluent. After completion

of the reaction, solvent was removed under reduced pressure and subsequently dissolved in DMF (1 mL). hydrazine (0.145 mL, 3 equiv) was added to the mixture. The solution was stirred for 24 h at room temperature. The reaction progress was monitored by TLC using *n*-Hexane: EtOAc (1:1) as eluent. After the completion of the reaction, the desired product was extract through the addition of dichloromethane. The obtained sediment was filtered and dried and washed with methanol (1-2 mL) for ten minutes. The residue was filtered and dried.



2-(4-(furan-2-ylmethyl)-5-(3-nitrophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6a):

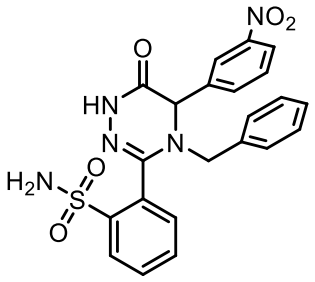
White powder; 319 mg (70%); mp 247-250 °C dec; IR (KBr, cm^{-1}) ν 1163.5, 1343, 1533, 1664, 2987, 3264; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 4.07 (*d*, 1H, *J* = 15.1Hz, CH_2), 4.21 (*d*, 1H, *J* =15.1 Hz, CH_2), 5.20 (*s*, 1H, H_{CH}), 6.18 (*s*, 2H, $H_{FurFuryl}$), 7.17 (*s*, 2H, NH_2), 7.30 (*s*, 1H, $H_{FurFuryl}$), 7.62- 7.65 (*m*, 2H, H_{Ar}), 7.67- 7.78 (*m*, 3H, H_{Ar}), 8.02- 8.04 (*m*, 2H, H_{Ar}), 8.15 (*d*, 1H, *J*= 7.7 Hz, H_{Ar}), 10.92 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 48.5, 60.9, 110.3, 110.5, 122.9, 127.7, 130.0, 130.2, 130.5, 130.9, 132.1, 142.7, 143.1, 147.6, 148.4, 159.3; MS ES^+ *m/z* 456.0 $(M+H)^+$, 933.0 $(2M+Na)^+$.



2-(4-(furan-2-ylmethyl)-5-(4-nitrophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6b):

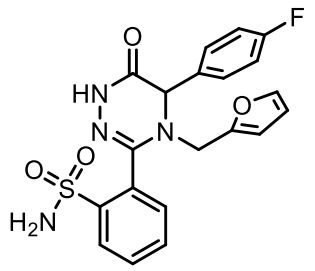
White powder; 346 mg (76%); mp 254-256 °C dec; IR (KBr, cm^{-1}) ν 1170, 1342, 1521, 1668, 3069, 3322; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 4.02- 4.22 (*m*, 2H, CH_2), 5.15 (*s*, 1H, CH), 6.18 (*brs*, 2H, $H_{FurFuryl}$), 7.15 (*s*, 2H, NH_2), 7.33 (*brs*, 1H, $H_{FurFuryl}$), 7.53 (*s*, 2H, H_{Ar}), 7.64 (*d*, 1H, *J* =7.3 Hz, H_{Ar}), 7.70-

7.76 (*m*, 2H, H_{Ar}), 8.03 (*d*, 1H, *J* =7.3 Hz, H_{Ar}), 8.19 (*d*, 2H, *J*=9.0 Hz, H_{Ar}), 10.90 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 48.6, 61.1, 110.4, 110.6, 123.6, 128.4, 130.0, 130.5, 131.1, 132.1, 142.6, 143.2, 145.5, 147.0, 148.3, 159.1; MS ES$^+$ *m/z* 456.0 $(M+H)^+$; Anal. Calcd for $C_{20}H_{17}N_5O_6S$: C, 52.74; H, 3.76; N, 15.38; S, 7.04. Found: C, 52.38; H, 3.73; N, 15.30; S, 7.05.



2-(4-benzyl-5-(3-nitrophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6c):

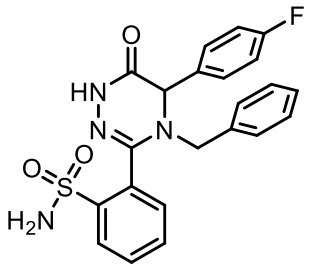
White powder; 316 mg (68%); mp 213-216 °C dec; IR (KBr, cm^{-1}) ν 1165, 1345, 1532, 1665, 3021, 3270; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.97- 4.00 (*m*, 1H, H_{CH2}), 4.16- 4.21 (*m*, 1H, H_{CH2}), 4.81 (*s*, 1H, CH), 7.23- 7.27 (*m*, 6H, H_{Ar} NH_2), 7.47 (*brs*, 1H, H_{Ar}), 7.69- 7.74 (*m*, 4H, H_{Ar}), 8.02- 8.05 (*m*, 2H, H_{Ar}), 8.21- 8.26 (*m*, 1H, H_{Ar}), 11.04 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 52.2, 61.7, 123.4, 127.9, 128.5, 129.8, 130.4, 130.7, 132.2, 134.7,147.6, 148.0, 159.3; MS ES$^+$ *m/z* 466.0 $(M+H)^+$, 931.1 $(2M+H)^+$.



2-(5-(4-fluorophenyl)-4-(furan-2-ylmethyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6d):

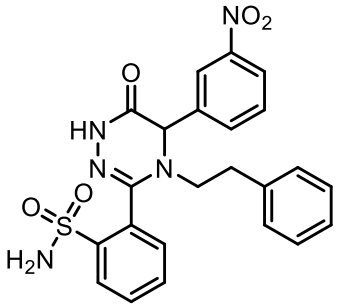
Yellow crystal; 278 mg (65%); mp 207-210 °C dec; IR (KBr, cm^{-1}) ν 1166, 1333, 1616, 1663, 3351; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.97- 4.10 (*m*, 2H, CH_2), 4.86 (s, 1H, -CH), 6.20- 6.27 (*m*, 2H, $H_{Furfury}$), 7.13- 7.19 (*m*, 4H, $H_{Ar,\ NH2,\ Furfuryl}$), 7.30- 7.33 (*m*, 2H, H_{Ar}), 7.44- 7.47 (*m*, 2H, H_{Ar}), 7.69- 7.88 (*m*, 4H, H_{Ar}), 10.81 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 48.5, 60.5, 110.1, 110.5, 115.4, 115.7 (*d*, $^2J_{CF}$= 21.75 Hz, CF), 120.9, 122.3, 122.4 (*d*, $^4J_{CF}$= 3.75 Hz, CF), 130.1, 130.2 (*d*, $^3J_{CF}$= 7.5 Hz,

CF), 130.4, 132.1, 132.6, 142.7, 160.1, 163.0 (*d*, $^{1}J_{CF}$= 218.4 Hz, CF); MS ES^{+} *m/z* 429.0 (M+H)$^{+}$; Anal. Calcd for $C_{20}H_{17}FN_4O_4S$: C, 56.07; H, 3.99; N, 13.08; S, 7.48. Found: C, 56.25; H, 4.08; N, 13.21; S, 7.49.



2-(4-benzyl-5-(4-fluorophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6e):

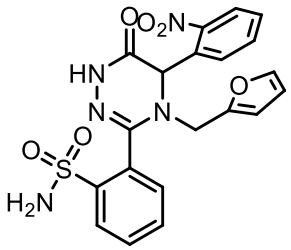
White powder; 263 mg (60%); mp °C dec; IR (KBr, cm^{-1}) ν 1173, 1342, 1607, 1673, 3060, 3332; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.85 (*d*, 1H, *J*= 14.2 Hz, H_{CH2}), 4.13 (*d*, 1H, *J*= 14.2 Hz, H_{CH2}), 4.47 (*s*, 1H, -CH), 7.17 (*s*, 2H, NH_2), 7.26- 7.34 (*m*, 9H, H_{Ar}), 7.69 (*t*, 2H, ^{4}J =5.1 Hz, H_{Ar}), 8.02 (*t*, 1H, ^{4}J= 5.1 Hz, H_{Ar}), 10.95 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 52.4, 62.2, 115.9, 116.3 (*d*, $^{2}J_{CF}$= 23.25 Hz, CF), 127.9, 128.0, 128.6, 128.7, 129.5, 129.9, 130.4, 130.6 (*d*, $^{3}J_{CF}$= 9.75 Hz, CF), 132.3, 133.9, 134.9, 146.1, 160.1, 160.6, 163.8 (*d*, $^{1}J_{CF}$= 243.6 Hz, CF); MS ES^{+} *m/z* 439.0 (M+H)$^{+}$, 899.1 (2M+Na)$^{+}$; Anal. Calcd for $C_{22}H_{19}FN_4O_3S$: C, 60.26; H, 4.37; N, 12.78; S, 7.31. Found: C, 60.31; H, 4.39; N, 12.74; S, 7.46.



2-(5-(3-nitrophenyl)-6-oxo-4-phenethyl-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6f):

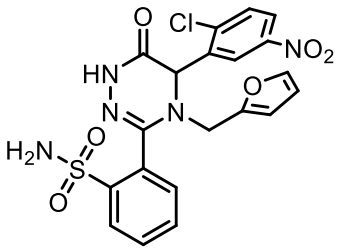
White powder; 326 mg (68%); mp 204-207 °C dec; IR (KBr, cm^{-1}) ν 1170, 1342, 1531, 1669, 3060, 3327; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.53- 2.60 (*m*, 1H, H_{CHN}), 2.71- 2.87 (*m*, 1H, H_{CHN}), 2.96- 3.17 (*m*, 2H, CH_2), 5.46 (*s*, 1H, CH), 6.81 (*d*, 2H, *J* =6.3 Hz, H_{Ar}), 7.09- 7.14 (*m*, 5H, H_{Ar} NH_2), 7.42 (*brs*, 1H, H_{Ar}), 7.68- 7.69 (*m*, 2H, H_{Ar}), 7.76 (*t*, 1H, *J* =7.5 Hz, H_{Ar}), 8.01- 8.03 (*m*, 2H, H_{Ar}), 8.25 (*d*, 1H, *J* =7.5

Hz, H_{Ar}), 8.35 (*brs*, 1H, H_{Ar}), 10.91 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 33.9, 60.6, 64.7, 123.4, 126.3, 128.4, 129.9, 130.4, 132.2, 138.1, 148.0, 159.6; MS ES$^+$ *m/z* 480.0 $(M+H)^+$, 959.0 $(2M+H)^+$; Anal. Calcd for $C_{23}H_{21}N_5O_5S$: C, 57.61; H, 4.41; N, 14.61; S, 6.69. Found: C, 58.01; H, 4.52; N, 14.70; S, 6.75.



2-(4-(furan-2-ylmethyl)-5-(2-nitrophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6g):

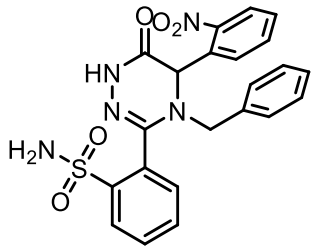
Yellow crystal; 232.27 mg (51%); m.p 229- 231 °C dec; IR (KBr, cm^{-1}) ν 732, 1163, 1361, 1524, 1671, 3275, 3366; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.91- 4.02 (*m*, 1H, H_{CH2}), 4.14- 4.20 (*m*, 1H, H_{CH2}), 5.85 (*s*, 1H, -CH), 6.03- 6.11 (*m*, 2H, $H_{Furfuryl}$), 7.19- 7.30 (*m*, 4H, $H_{NH2,\ Ar,\ Furfuryl}$), 7.53 (*t*, 1H, *J* = 7.8 Hz, H_{Ar}), 7.66- 7.78 (*m*, 4H, H_{Ar}), 7.89 (*d*, 1H, *J* = 8.0 Hz, H_{Ar}), 8.03 (*d*, 1H, *J* = 8 Hz, H_{Ar}), 10.82 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 46.3, 56.9, 109.9, 110.4, 124.7, 127.6, 129.4, 129.7, 130.2, 130.4, 132.1, 133.6, 143.1, 148.1, 158.9; MS ES$^+$ *m/z* 456.0 $(M+H)^+$; Anal. Calcd for $C_{20}H_{17}N_5O_6S$: C, 52.74; H, 3.76; N, 15.38; S, 7.04. Found: C, 52.38; H, 3.73; N, 15.30; S, 7.05.



2-(5-(2-chloro-5-nitrophenyl)-4-(furan-2-ylmethyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl) benzenesulfonamide (6h):

Grey solid; 333.11 mg (68%); m.p 199- 201 °C dec; IR (KBr, cm−1) ν 754, 1166, 1341, 1648, 3089, 3292; ^{1}H NMR (300 MHz, DMSO-d6) δ (ppm) 4.05- 4.19 (*m*, 2H, -CH2), 5.62 (*s*, 1H, -CH), 6.07- 6.10 (*m*, 2H, $H_{Furfuryl}$), 7.17- 7.20 (*m*, 3H, $H_{NH2,\ Furfuryl}$), 7.67- 7.77 (*m*, 4H, H_{Ar}), 8.03 (*d*, 1H, *J* = 7.5 Hz, H_{Ar}), 8.11 (*d*, 1H, *J* = 7.5 Hz, H_{Ar}), 8.22 (*brs*, 1H, H_{Ar}), 10.94 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 54.5, 60.0, 110.1, 110.3, 124.5, 125.1, 127.7, 130.3, 130.5, 131.1, 132.2, 135.3, 138.2, 142.7, 143.3,

145.6, 146.4, 148.3, 158.6; Anal. Calcd for $C_{20}H_{16}ClN_5O_6S$: C, 49.03; H, 3.29; N, 14.30; S, 6.55. Found: C, 48.95; H, 3.53; N, 14.24; S, 6.61.



2-(4-benzyl-5-(2-nitrophenyl)-6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)benzenesulfonamide (6i):

White solid; 233 mg (50%); m.p 205- 207 °C dec; IR (KBr, cm−1) ν 1165, 1345, 1532, 1665, 3021, 3270; ^{1}H NMR (300 MHz, DMSO-d6) δ (ppm) 3.91 (*d*, 1H, *J* = 14.2 Hz, H_{CH2}), 4.24 (*d*, 1H, *J* = 14.2 Hz, H_{CH2}), 5.53 (*s*, 1H, -CH), 7.17- 7.23 (*m*, 7H, $H_{NH2,\ Ar}$), 7.58- 7.63 (*m*, 3H, H_{Ar}), 7.70- 7.72 (*m*, 2H, H_{Ar}), 7.80 (*t*, 1H, *J* = 7.4 Hz, H_{Ar}), 7.93 (*d*, 1H, *J* = 7.9 Hz, H_{Ar}), 8.05 (*d*, 1H, *J* = 8.5 Hz, H_{Ar}), 10.94 (*s*, 1H, NH); ^{13}C NMR (75 MHz, DMSO- d_6) δ (ppm) 55.4, 67.3, 124.9, 127.91, 124.94, 128.0, 128.2, 128.4, 129.9, 130.5, 131.8, 132.3, 134.6, 137.4, 147.9, 158.9; Anal. Calcd for $C_{22}H_{19}N_5O_5S$: C, 56.77; H, 4.11; N, 15.05; S, 6.89. Found: C, 56.71; H, 4.09; N, 14.91; S, 6.90.

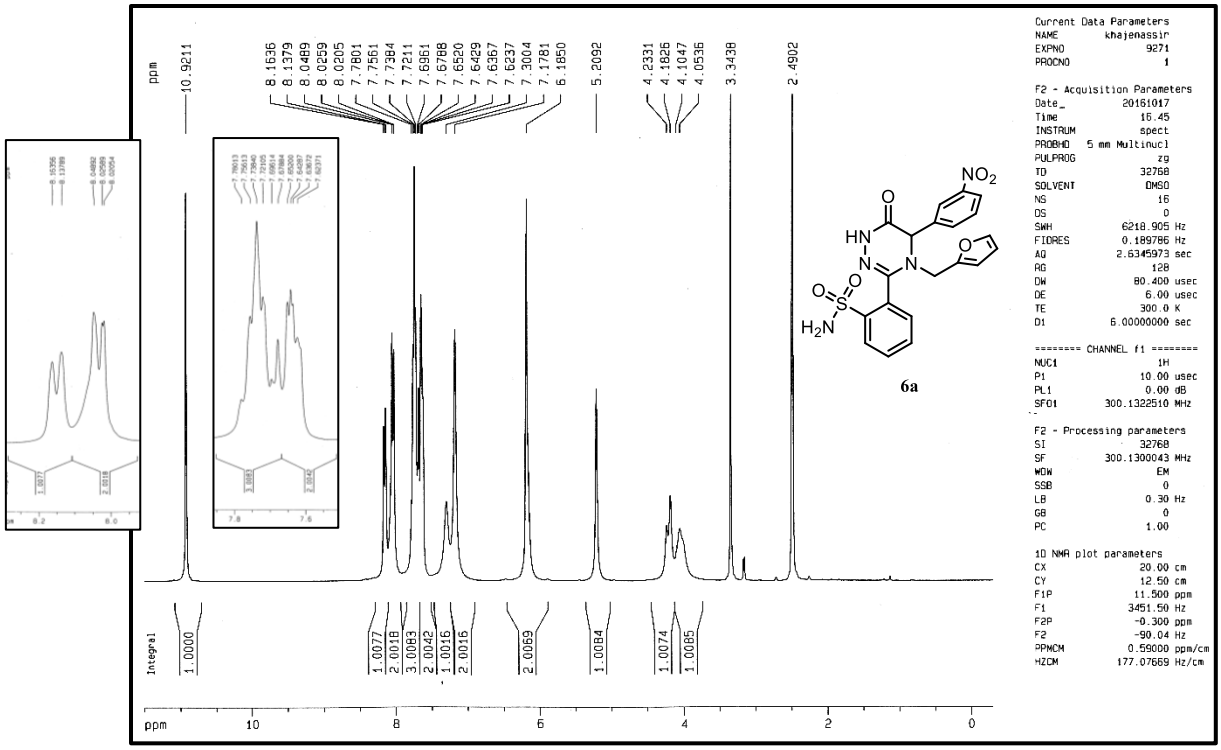


Figure S1. ^{1}H NMR spectrum of compound **6a** (300 MHz, DMSO).

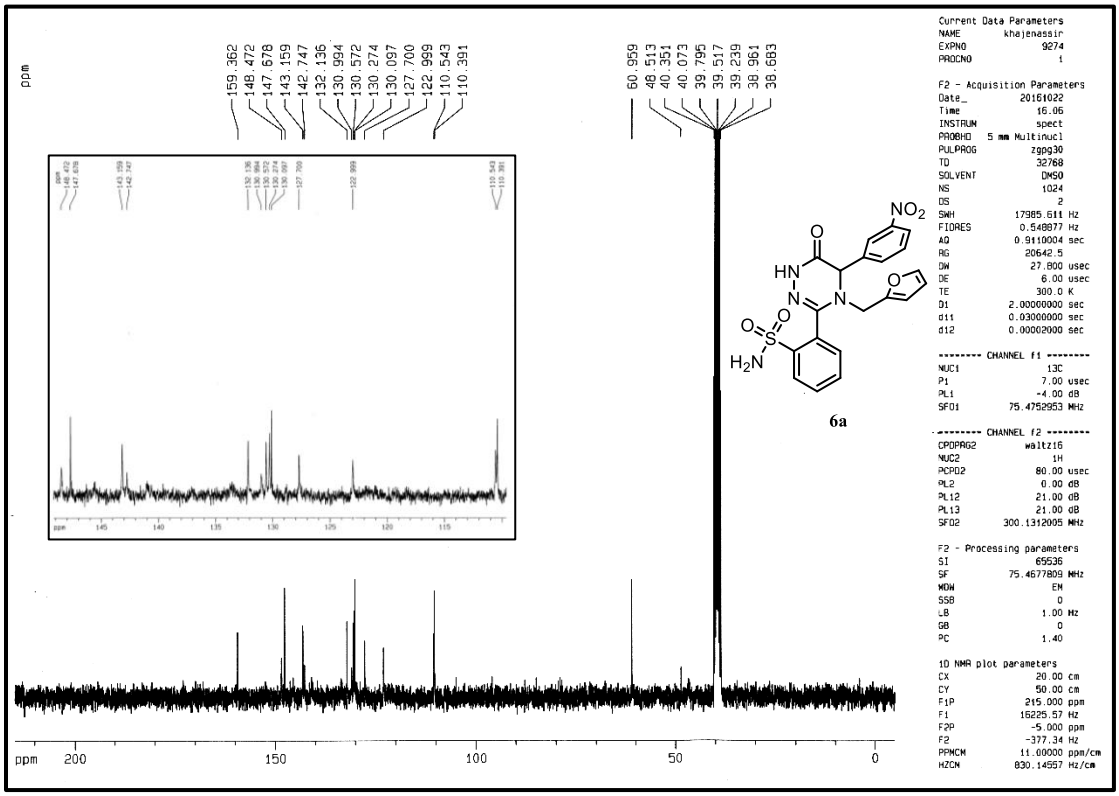


Figure S2. ^{13}C NMR spectrum of compound **6a** (75 MHz, DMSO).

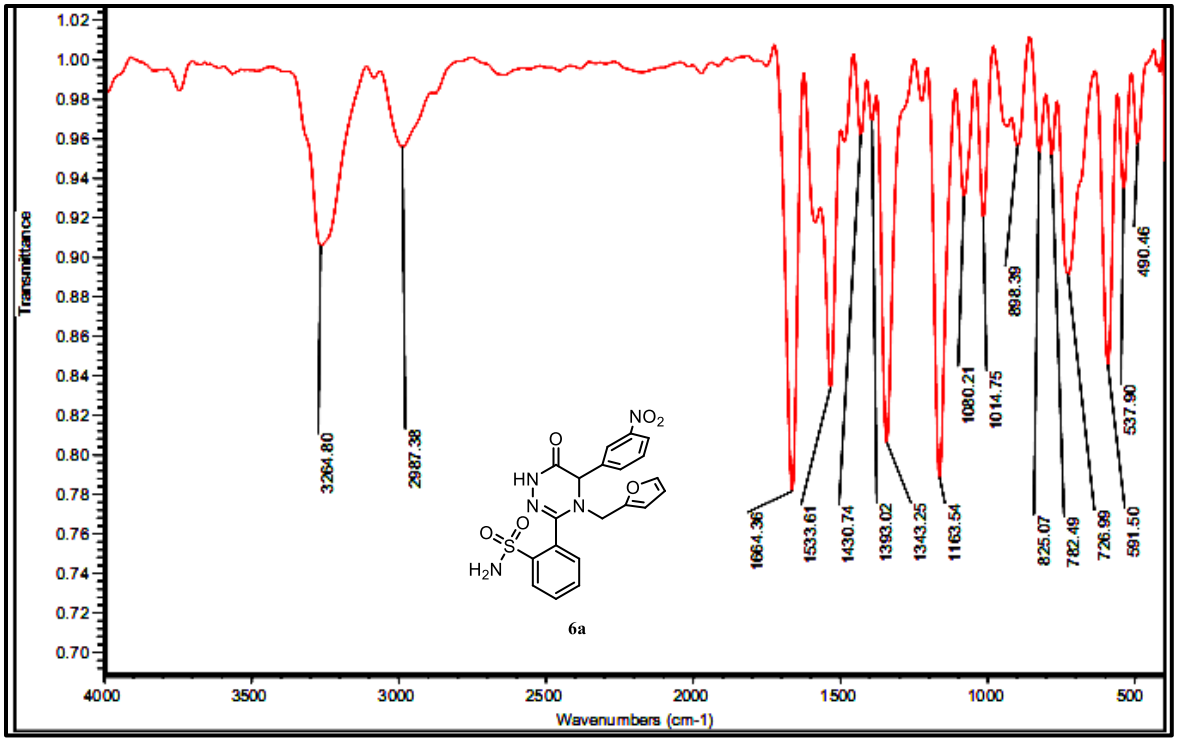


Figure S3. IR spectrum of compound **6a**.

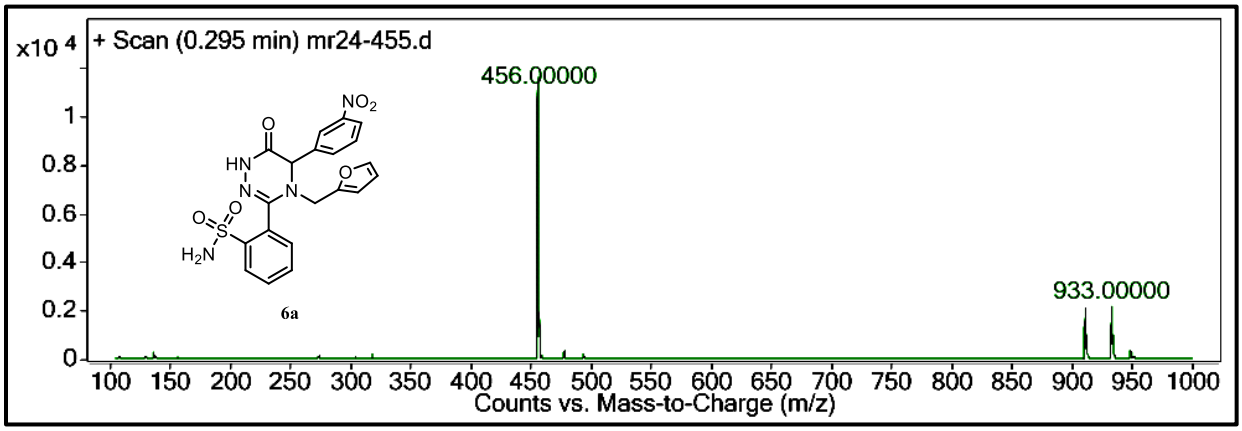


Figure S4. Mass spectrum of compound **6a**.

Crystallographic data for 6a:

Table S1: Crystal data and structure refinement for sba152.

Identification code	sba152
Empirical formula	$C_{20}H_{17}N_5O_6S$
Formula weight	455.45
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	orthorhombic
Space group	Pccn
Z	8
Unit cell dimensions	a = 17.4290(4) Å α =90 deg. b = 14.9664(4) Å β =90 deg. c = 15.2497(4) Å γ = 90 deg.
Volume	3977.88(17) $Å^3$
Density (calculated)	1.52 g/cm^3
Absorption coefficient	1.90 mm^{-1}
Crystal shape	little rod
Crystal size	0.130 x 0.120 x 0.050 mm^3
Crystal colour	colourless
Theta range for data collection	4.9 to 76.6 deg.
Index ranges	$-21 \le h \le 17$, $-18 \le k \le 14$, $-18 \le l \le 12$
Reflections collected	16394
Independent reflections	4055 (R(int) = 0.0372)
Observed reflections	3261 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.50 and 0.72
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4055 / 481 / 347
Goodness-of-fit on F^2	1.04
Final R indices (I>2sigma(I))	R1 = 0.037, wR2 = 0.090
Largest diff. peak and hole	0.28 and -0.35 $eÅ^{-3}$

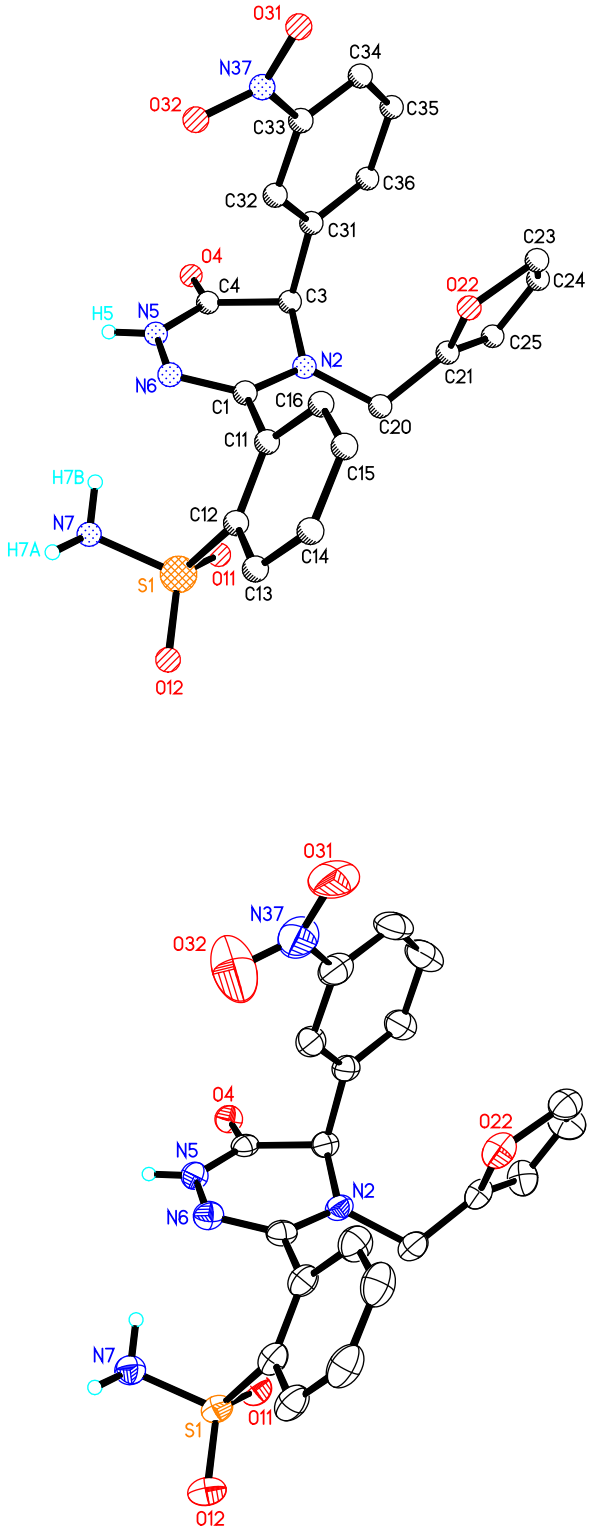


Figure S5. ORTEP structure of product **6a**; the ellipsoid probability level of each ORTEP diagram is 50%.

Experimental part:

sba152: colourless crystal (little rod), dimensions 0.130 x 0.120 x 0.050 mm^3, crystal system orthorhombic, space group Pccn, Z=8, a=17.4290(4) Å, b=14.9664(4) Å, c=15.2497(4) Å, alpha=90 deg, beta=90 deg, gamma=90 deg, V=3977.88(17) $Å^3$, rho=1.521 g/cm^3, T=100(2) K, $Theta_{max}$= 76.628 deg, radiation Mo Kalpha, lambda=1.54178 Å, 0.5 deg omega-scans with CCD area detector, covering the asymmetric unit in reciprocal space with a mean redundancy of 3.76and a completeness of 96.9% to a resolution of 0.79 Å, 16394 reflections measured, 4055 unique (R(int)=0.0372), 3261 observed ($I > 2\sigma(I)$), intensities were corrected for Lorentz and polarization effects, an empirical scaling and absorption correction was applied using STOE X-AREA Laue Analyzer based on the Laue symmetry of the reciprocal space, mu=1.90mm^{-1}, T_{min}=0.72, T_{max}=1.50, structure refined against F^2 with a Full-matrix least-squares algorithm using the SHELXL-2016/6 (Sheldrick, 2016) software [2], 347 parameters refined, hydrogen atoms were treated using appropriate riding models, except those at the nitrogen atoms, which were refined isotropically, goodness of fit 1.04 for observed reflections, final residual values R1(F)=0.037, $wR(F^2)$=0.090 for observed reflections, residual electron density -0.35 to 0.28 $eÅ^{-3}$. CCDC 1836444 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Lit. 1: (program SADABS 2014/5 for absorption correction)
G. M. Sheldrick, Bruker Analytical X-ray-Division, Madison, Wisconsin 2014

Lit. 2: (program SHELXL-2016/6 (Sheldrick, 2016) for structure refinement)
Acta Cryst. (2015). C71, 3-8

Lit. APEX, APEX2, SMART, SAINT, SAINT-Plus:
Bruker (2007). "Program name(s)". Bruker AXS Inc., Madison, Wisconsin, USA.

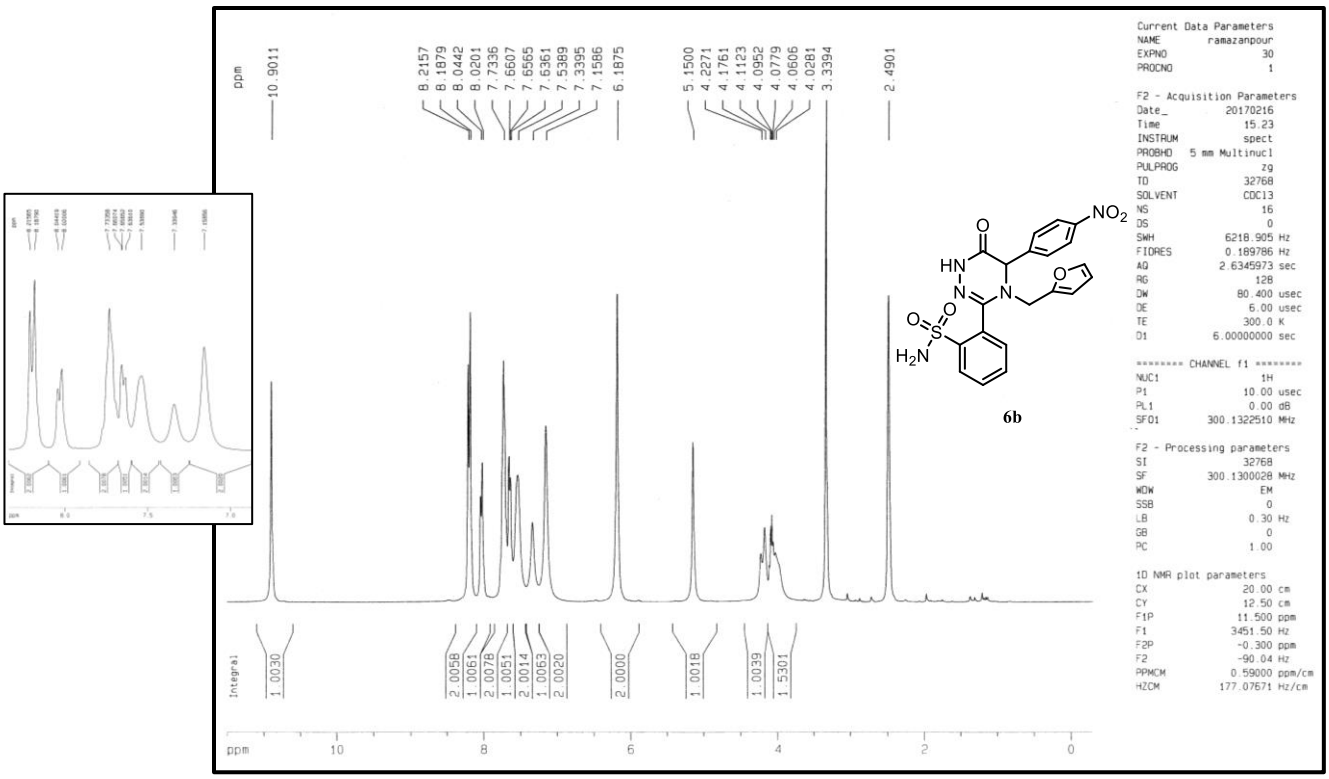


Figure S6. ^{1}H NMR spectrum of compound **6b** (300 MHz, $CDCl_3$).

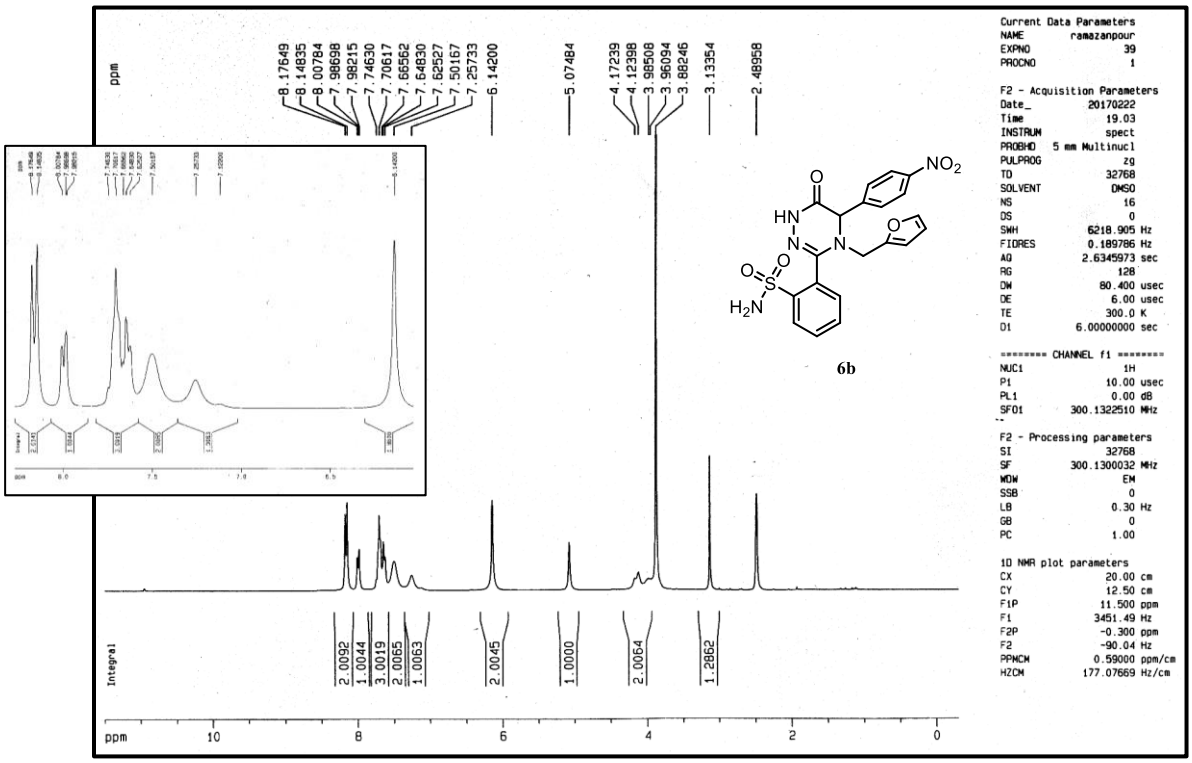


Figure S7. ^{1}H NMR spectrum of compound **6b** with D_2O (300 MHz, DMSO).

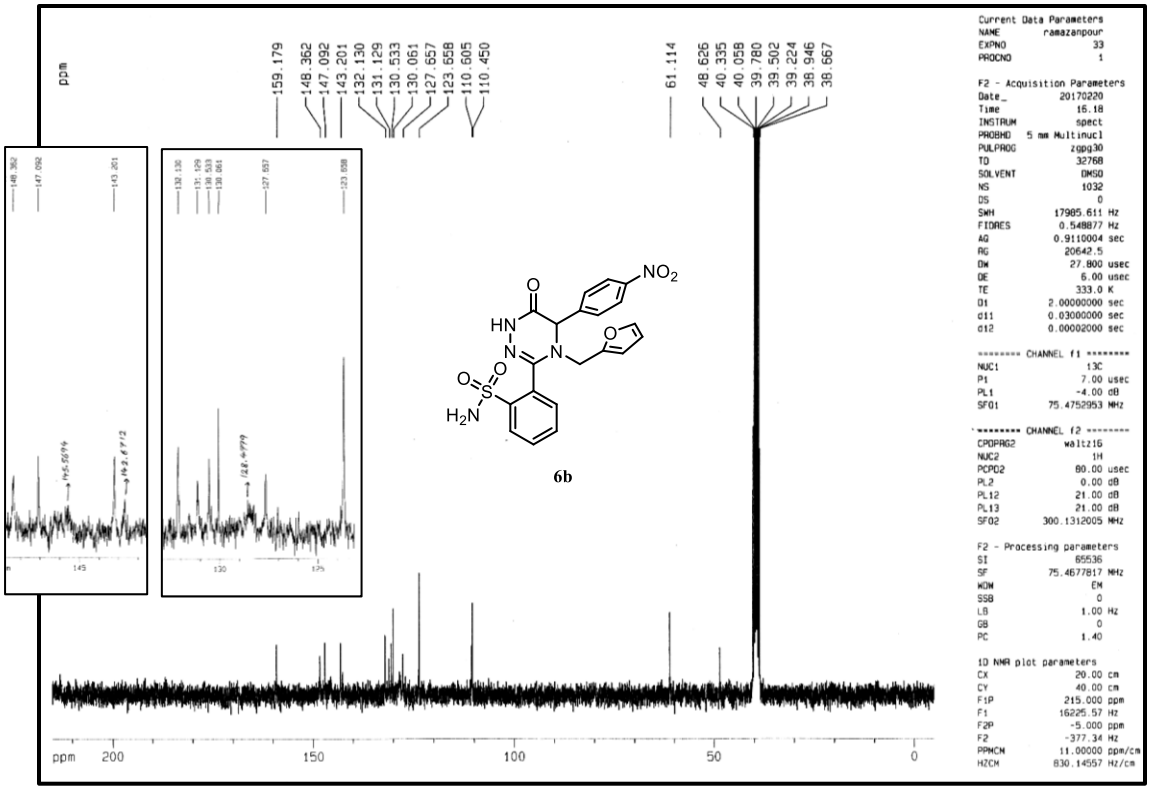


Figure S8. ^{13}C NMR spectrum of compound **6b** (75 MHz, DMSO).

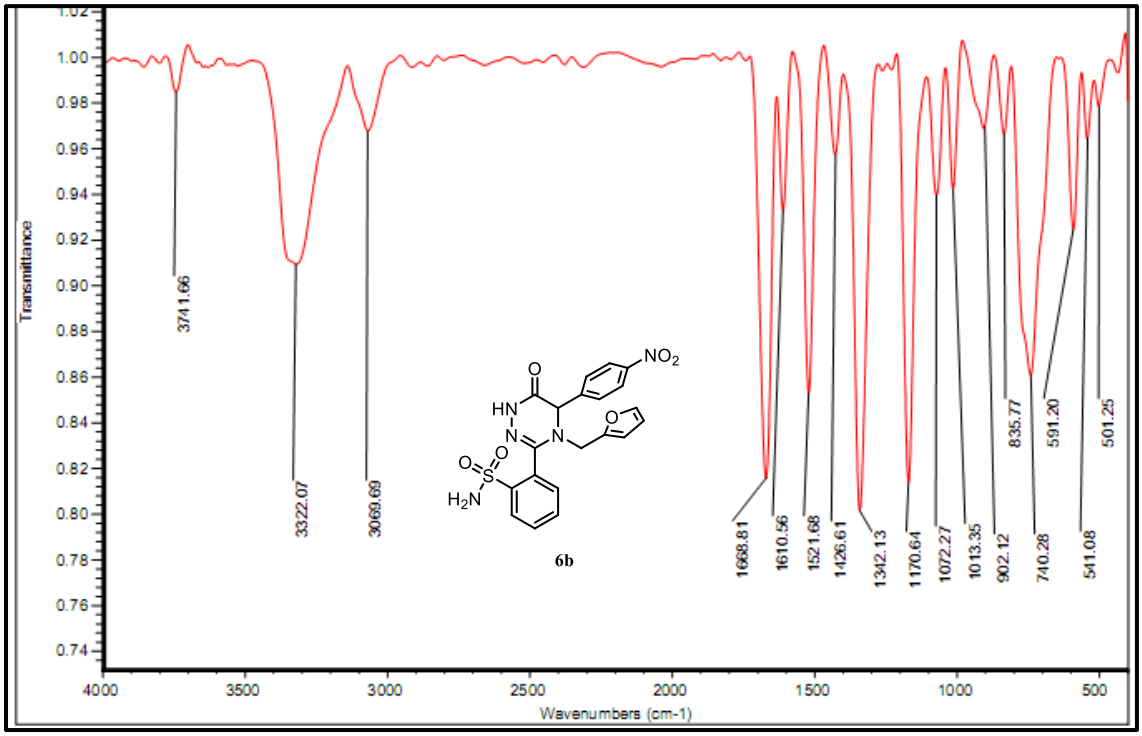


Figure S9. IR spectrum of compound **6b**.

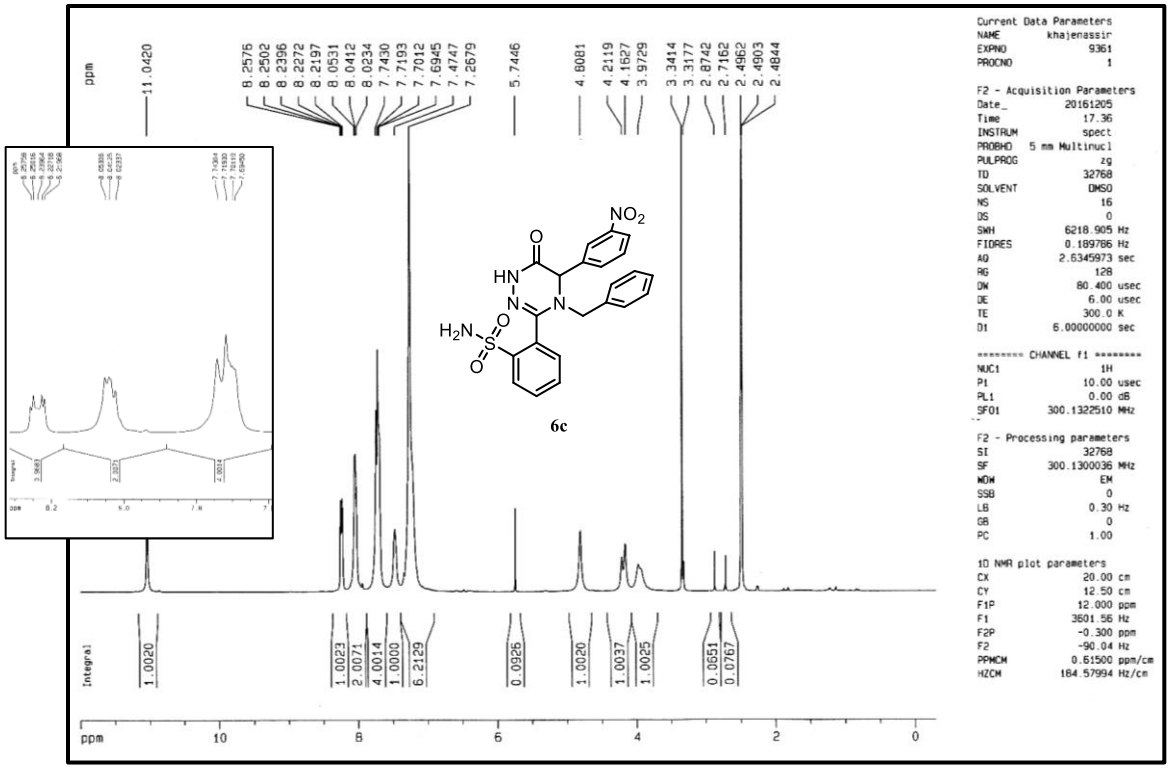


Figure S10. ^{1}H NMR spectrum of compound **6c** (300 MHz, DMSO).

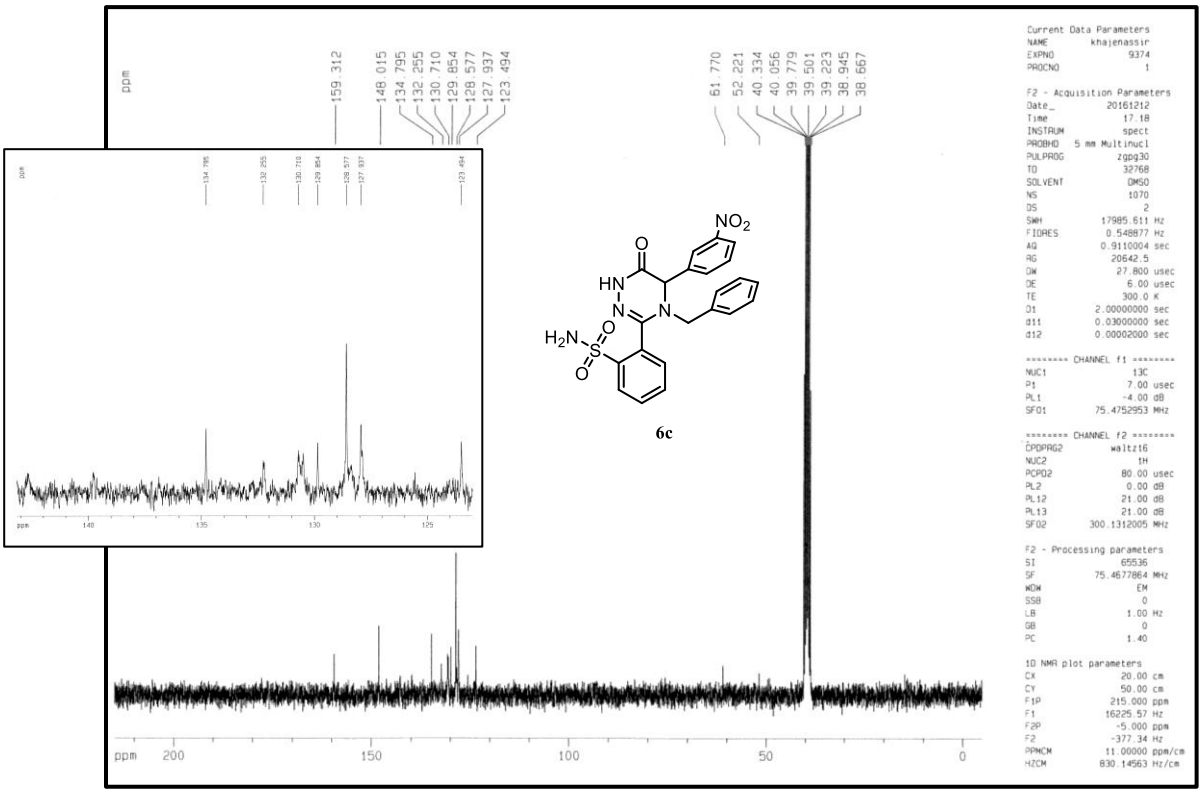


Figure S11. ^{13}C NMR spectrum of compound **6c** (75 MHz, DMSO).

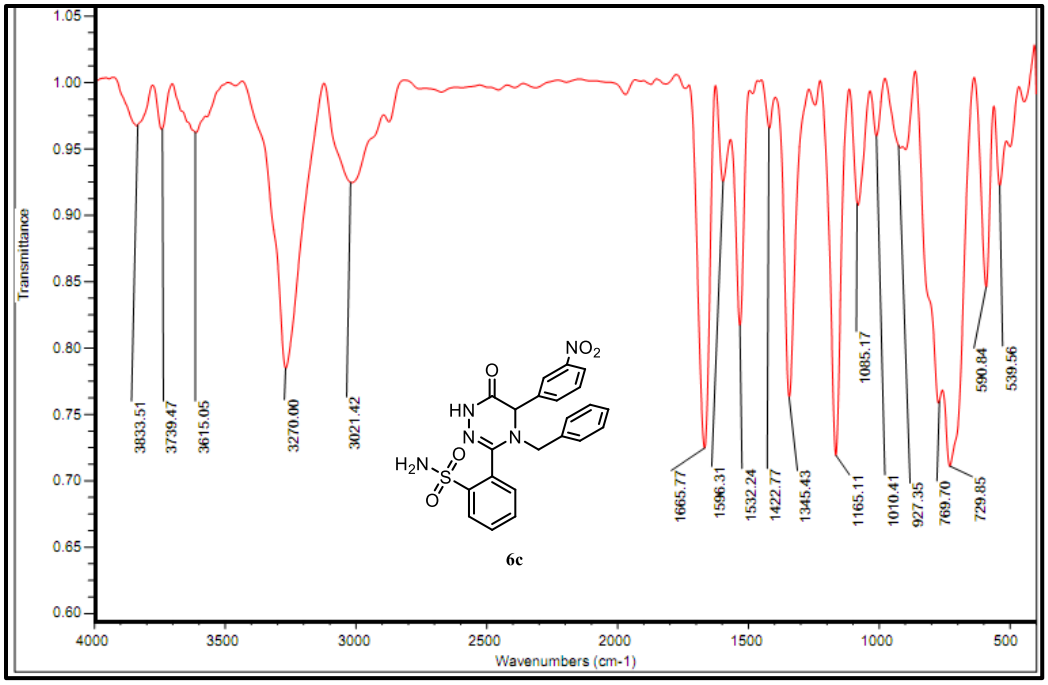


Figure S12. IR spectrum of compound **6c**.

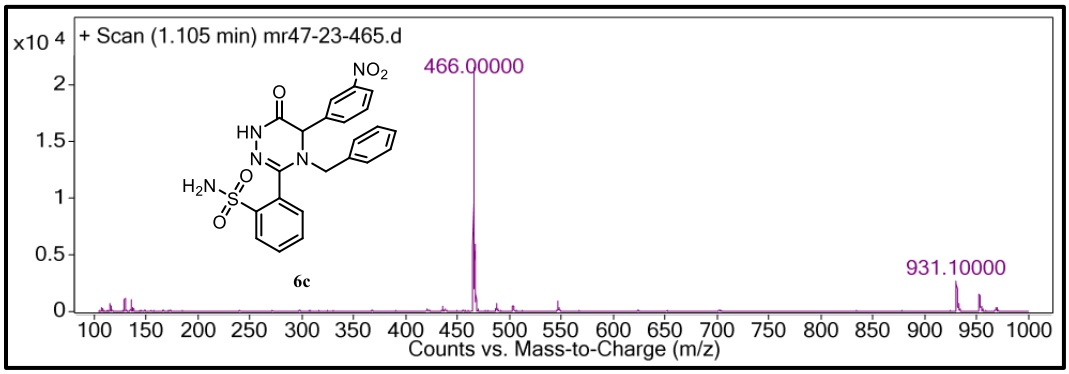


Figure S13. Mass spectrum of compound **6c**.

Crystallographic data for 6c:

Table S2: Crystal data and structure refinement for sba154.

Identification code	sba154
Empirical formula	$C_{22}H_{19}N_5O_5S$
Formula weight	465.48
Temperature	200(2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1/n$
Z	16
Unit cell dimensions	a = 15.5362(5) Å α =90 deg.
	b = 17.8907(5) Å β =90.3629(9) deg.
	c = 30.3195(8) Å γ = 90 deg.
Volume	8427.2(4) $Å^3$
Density (calculated)	1.47 g/cm^3
Absorption coefficient	0.20 mm^{-1}
Crystal shape	polyhedron
Crystal size	0.150 x 0.130 x 0.080 mm^3
Crystal colour	yellow
Theta range for data collection	1.3 to 25.0 deg.
Index ranges	$-18 \le h \le 18$, $-21 \le k \le 20$, $-34 \le l \le 36$
Reflections collected	53666
Independent reflections	14863 (R(int) = 0.0667)
Observed reflections	8565 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.96 and 0.89
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	14863 / 0 / 1221
Goodness-of-fit on F^2	1.00
Final R indices (I>2sigma(I))	R1 = 0.059, wR2 = 0.128
Largest diff. peak and hole	0.28 and -0.40 $eÅ^{-3}$

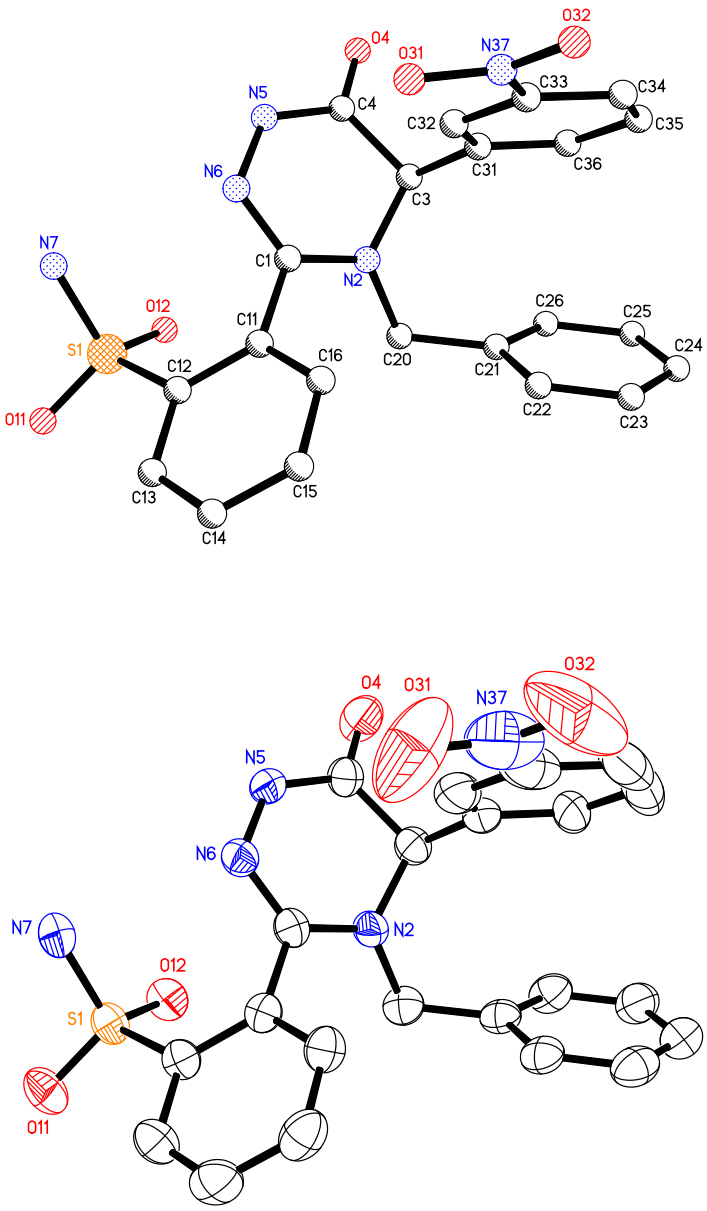


Figure S14. ORTEP structure of product **6c**; the ellipsoid probability level of ORTEP diagram is 50%.

Experimental part:

sba154: yellow crystal (polyhedron), dimensions 0.150 x 0.130 x 0.080 mm^3, crystal system monoclinic, space group $P2_1/n$, Z=16, a=15.5362(5) Å, b=17.8907(5) Å, c=30.3195(8) Å, alpha=90 deg, beta=90.3629(9) deg, gamma=90 deg, V=8427.2(4) $Å^3$, rho=1.468 g/cm^3, T=200(2) K, $Theta_{max}$= 25.049 deg, radiation Mo Kalpha, lambda=0.71073 Å, 0.5 deg omega-scans with CCD area detector, covering the asymmetric unit in reciprocal space with a mean redundancy of 3.55and a completeness of 99.6% to a resolution of 0.84 Å, 53666 reflections

measured, 14863 unique (R(int)=0.0667), 8565 observed ($I > 2\sigma(I)$), intensities were corrected for Lorentz and polarization effects, an empirical scaling and absorption correction was applied using SADABS[1] based on the Laue symmetry of the reciprocal space, mu=0.20mm^{-1}, T_{min}=0.89, T_{max}=0.96, structure refined against F^2 with a Full-matrix least-squares algorithm using the SHELXL-2016/6 (Sheldrick, 2016) software [2], 1221 parameters refined, hydrogen atoms were treated using appropriate riding models, except those at the NH_2 groups (N7), which were refined isotropically, goodness of fit 1.00 for observed reflections, final residual values R1(F)=0.059, wR(F^2)=0.128 for observed reflections, residual electron density -0.40 to 0.28 eÅ^{-3}. CCDC 1836446 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Lit. 1: (program SADABS 2014/5 for absorption correction)
G. M. Sheldrick, Bruker Analytical X-ray-Division, Madison, Wisconsin 2014

Lit. 2: (program SHELXL-2016/6 (Sheldrick, 2016) for structure refinement)
Acta Cryst. (2015). C71, 3-8

Lit. APEX, APEX2, SMART, SAINT, SAINT-Plus:
Bruker (2007). "Program name(s)". Bruker AXS Inc., Madison, Wisconsin, USA.

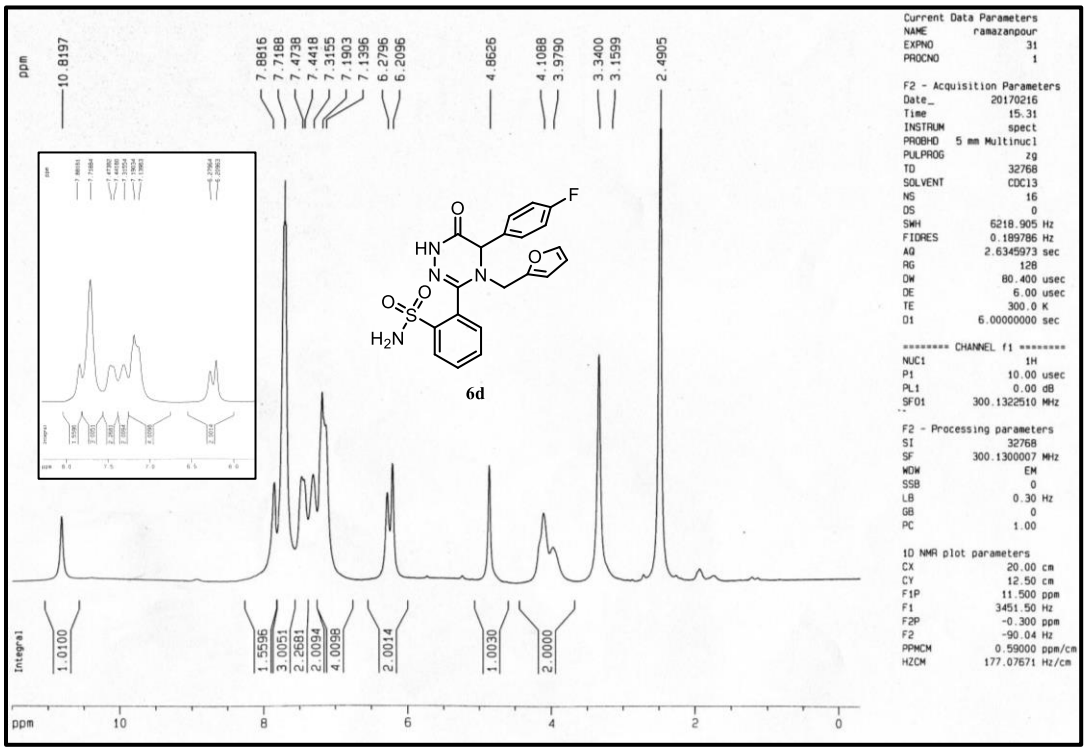


Figure S15. ^{1}H NMR spectrum of compound **6d** (300 MHz, $CDCl_3$).

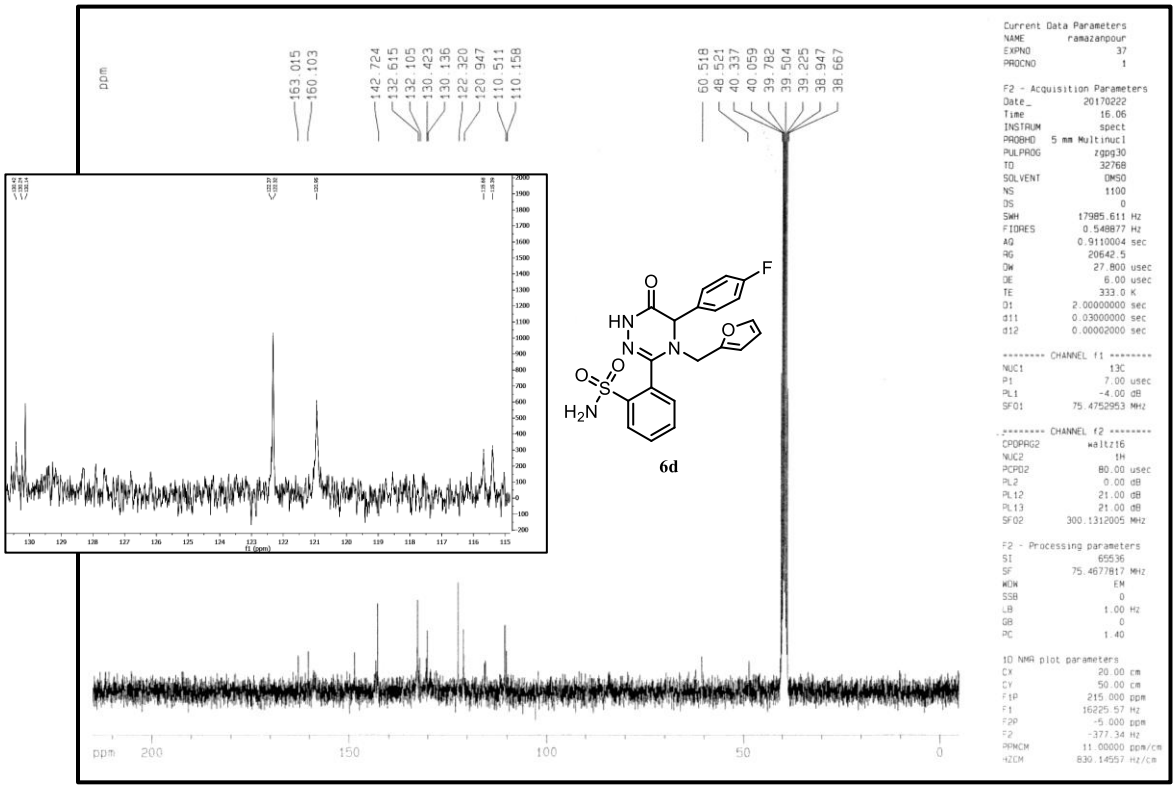


Figure S16. ^{13}C NMR spectrum of compound **6d** (75 MHz, DMSO).

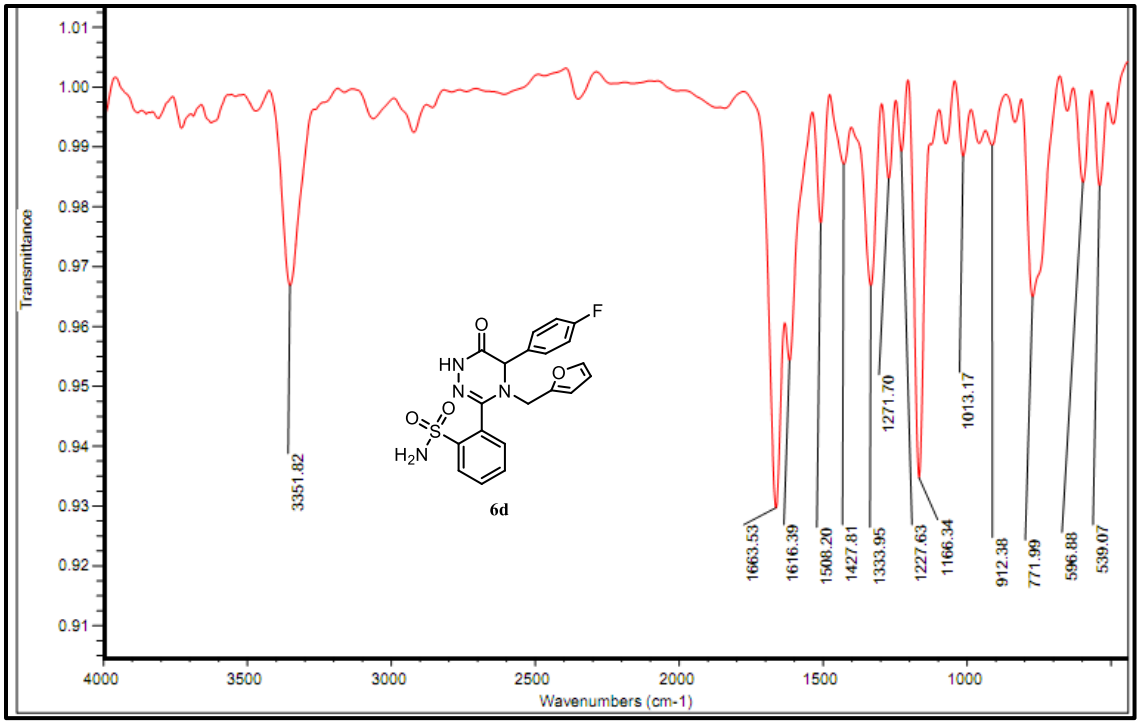


Figure S17. IR spectrum of compound **6d**.

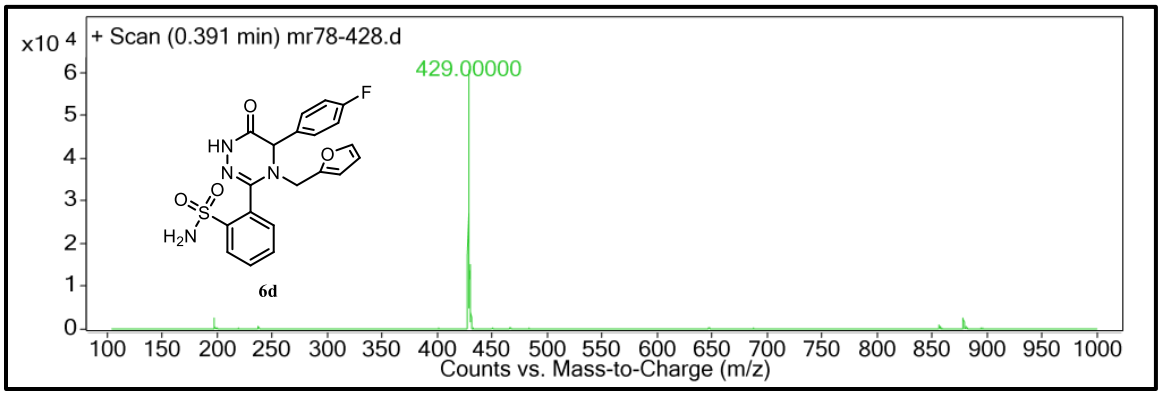


Figure S18. Mass spectrum of compound **6d**.

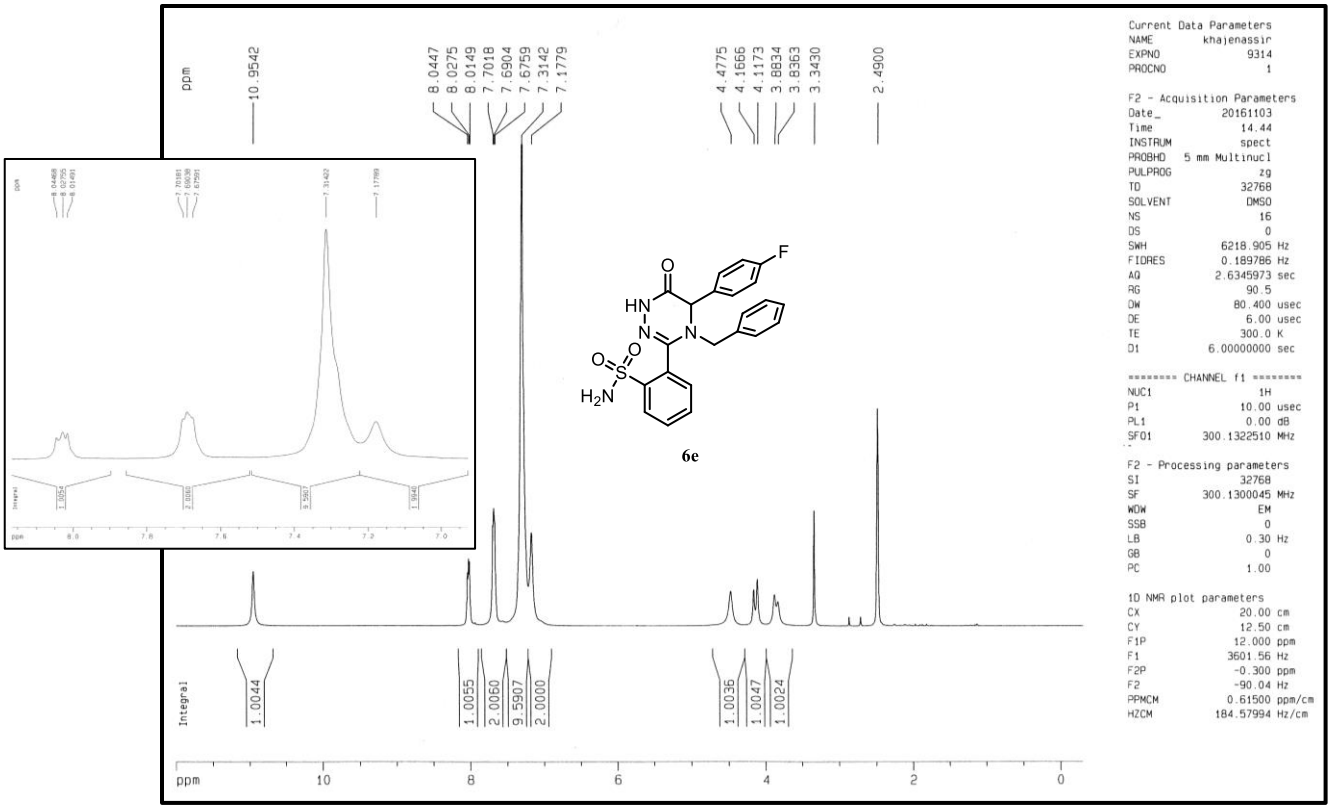


Figure S19. ^{1}H NMR spectrum of compound **6e** (300 MHz, DMSO).

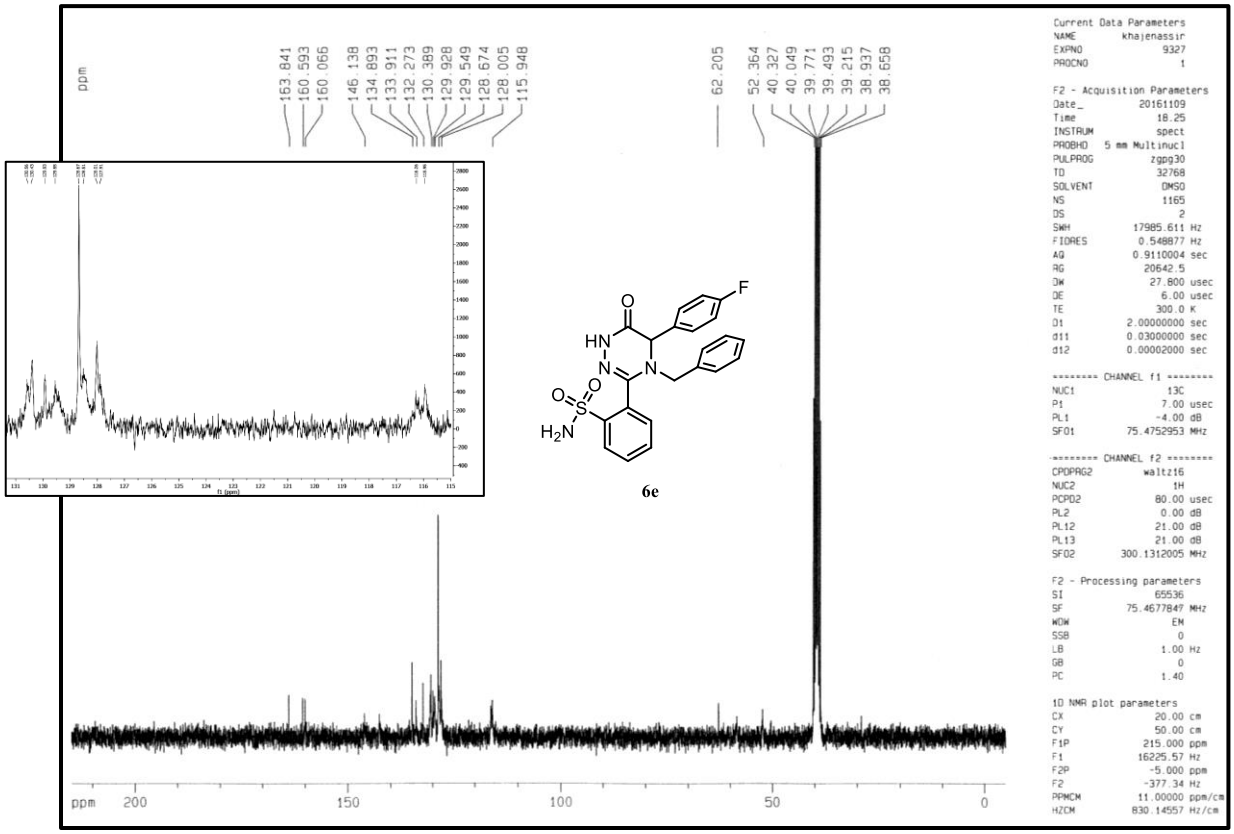


Figure S20. ^{13}C NMR spectrum of compound **6e** (75 MHz, DMSO).

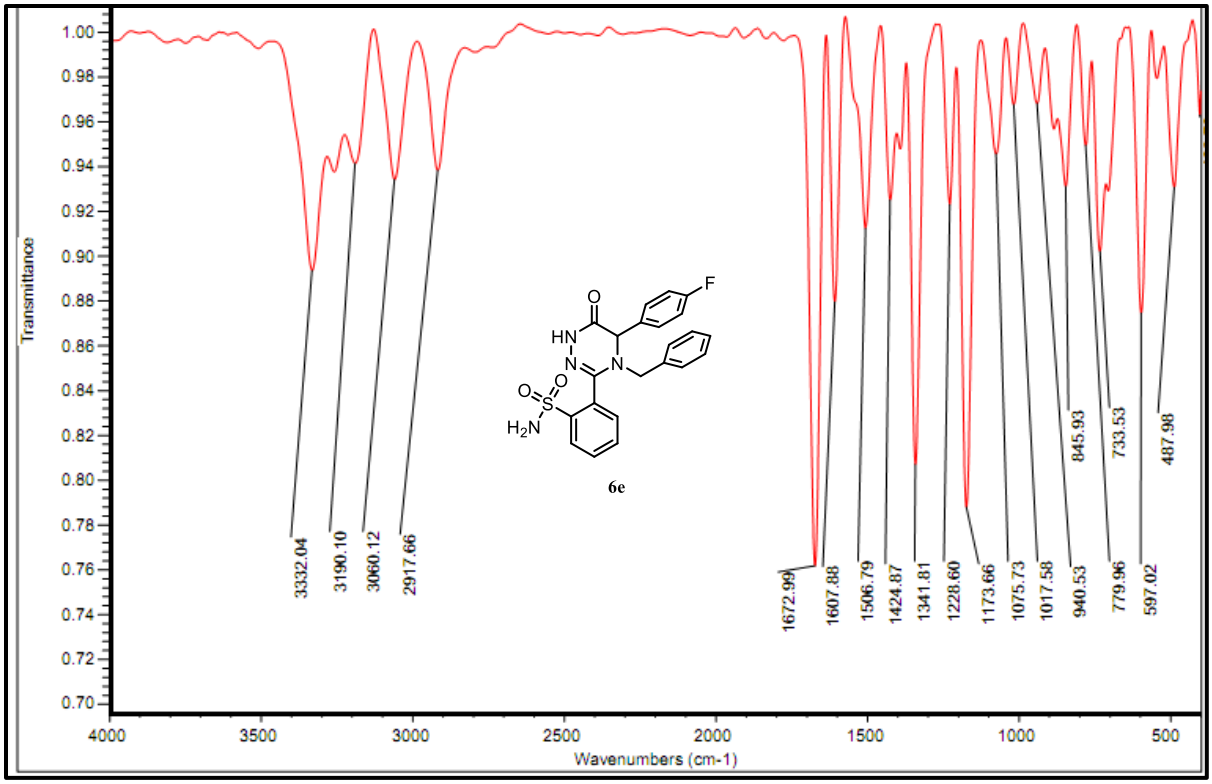


Figure S21. IR spectrum of compound **6e**.

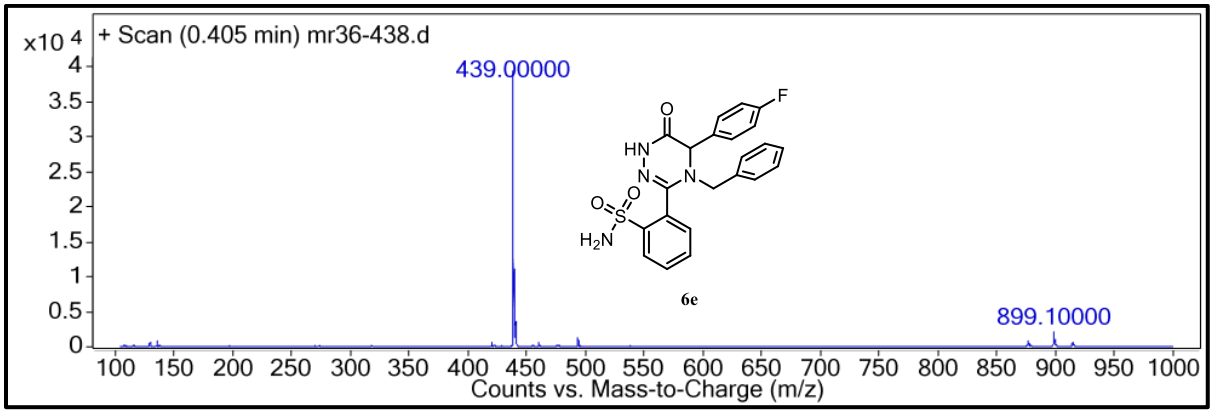


Figure S22. Mass spectrum of compound **6e**.

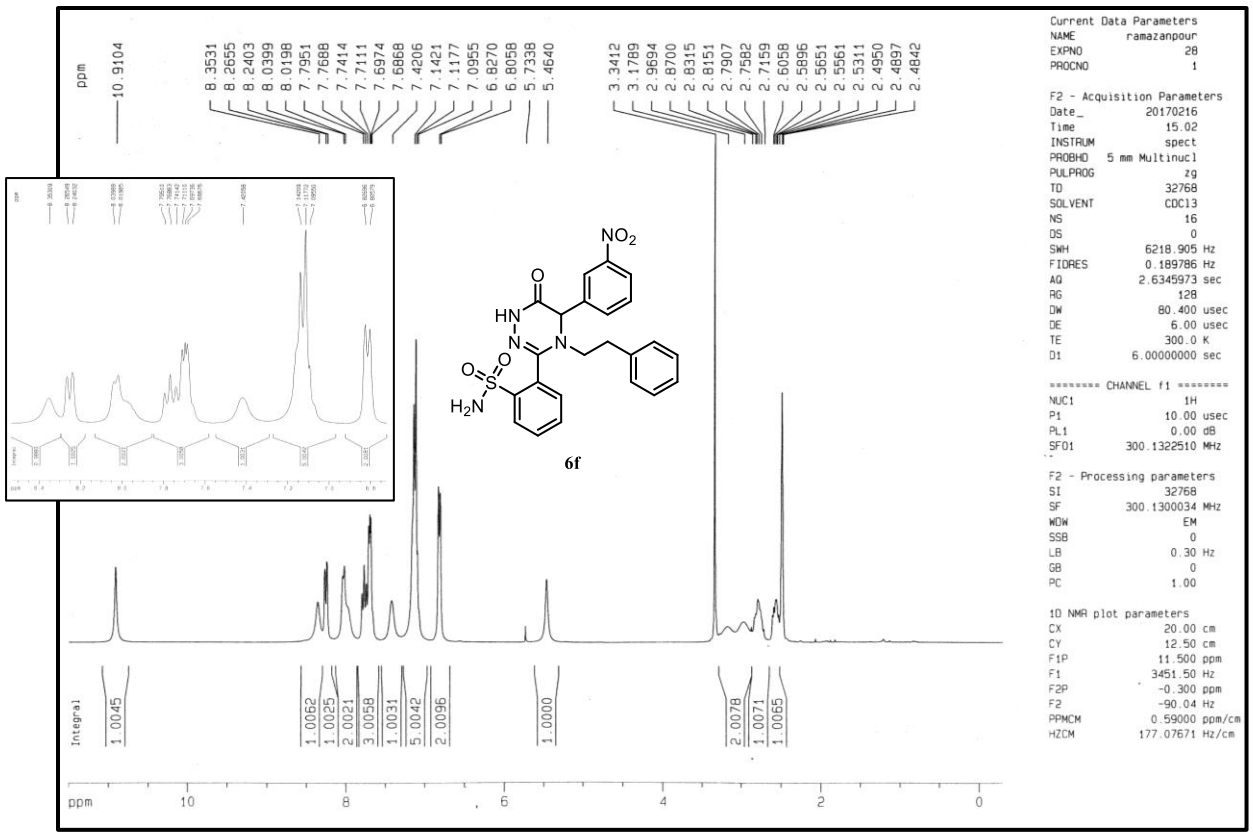


Figure S23. ^{1}H NMR spectrum of compound **6f** (300 MHz, $CDCl_3$).

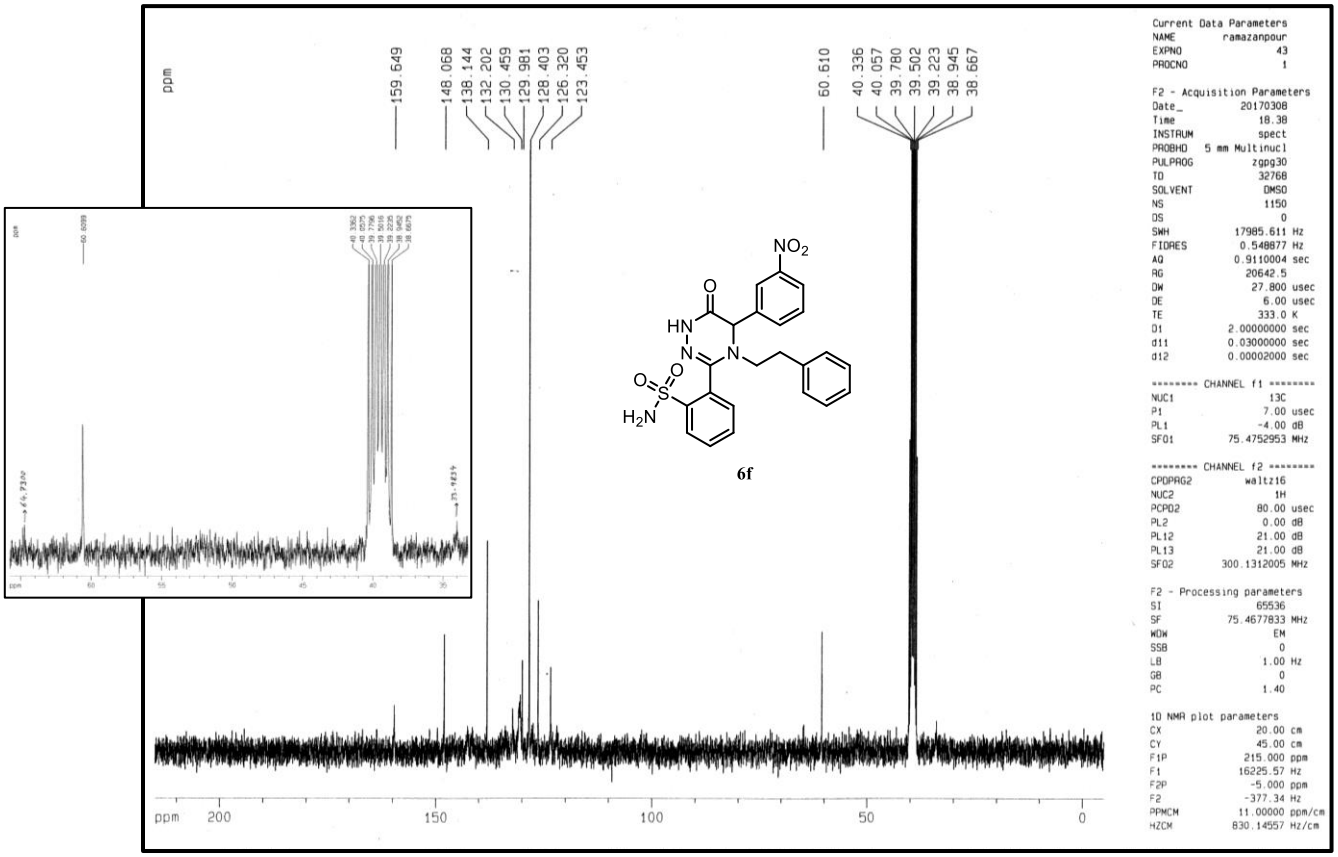


Figure S24. ^{13}C NMR spectrum of compound **6f** (75 MHz, DMSO).

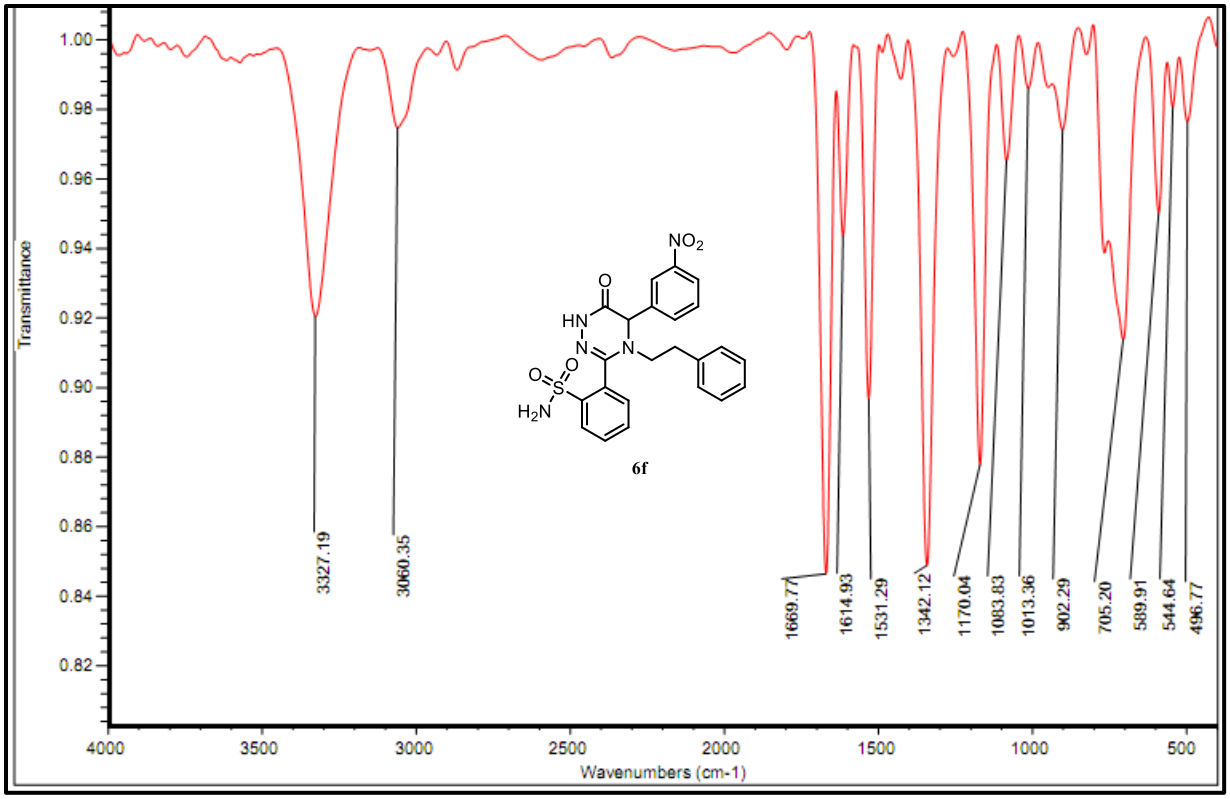


Figure S25. IR spectrum of compound **6f**.

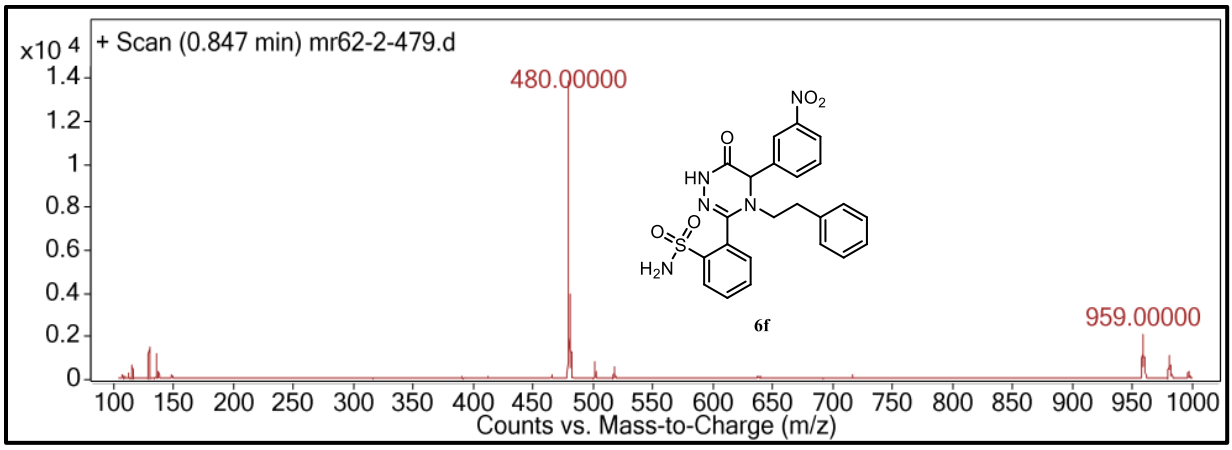


Figure S26. Mass spectrum of compound **6f**.

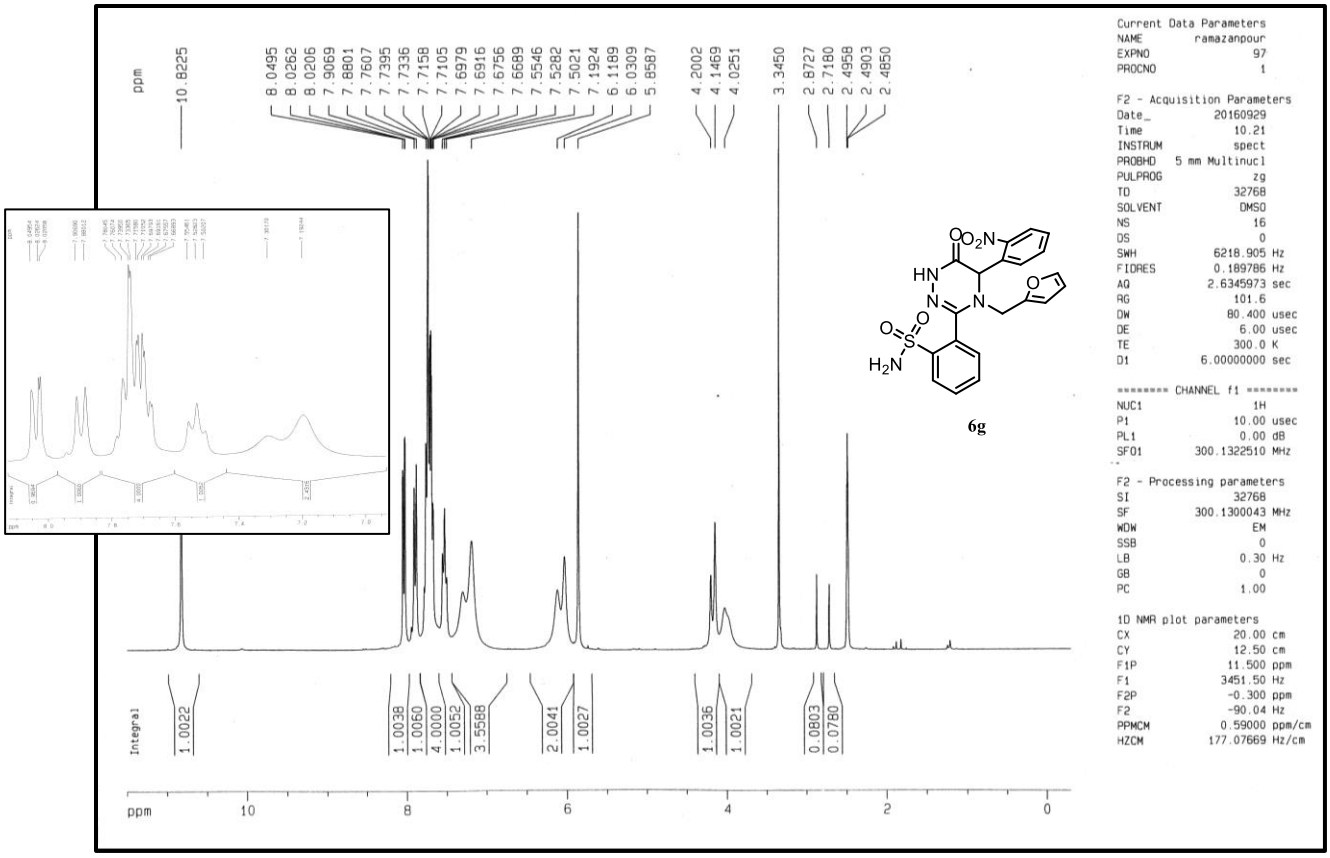


Figure S27. ^{1}H NMR spectrum of compound **6g** (300 MHz, DMSO).

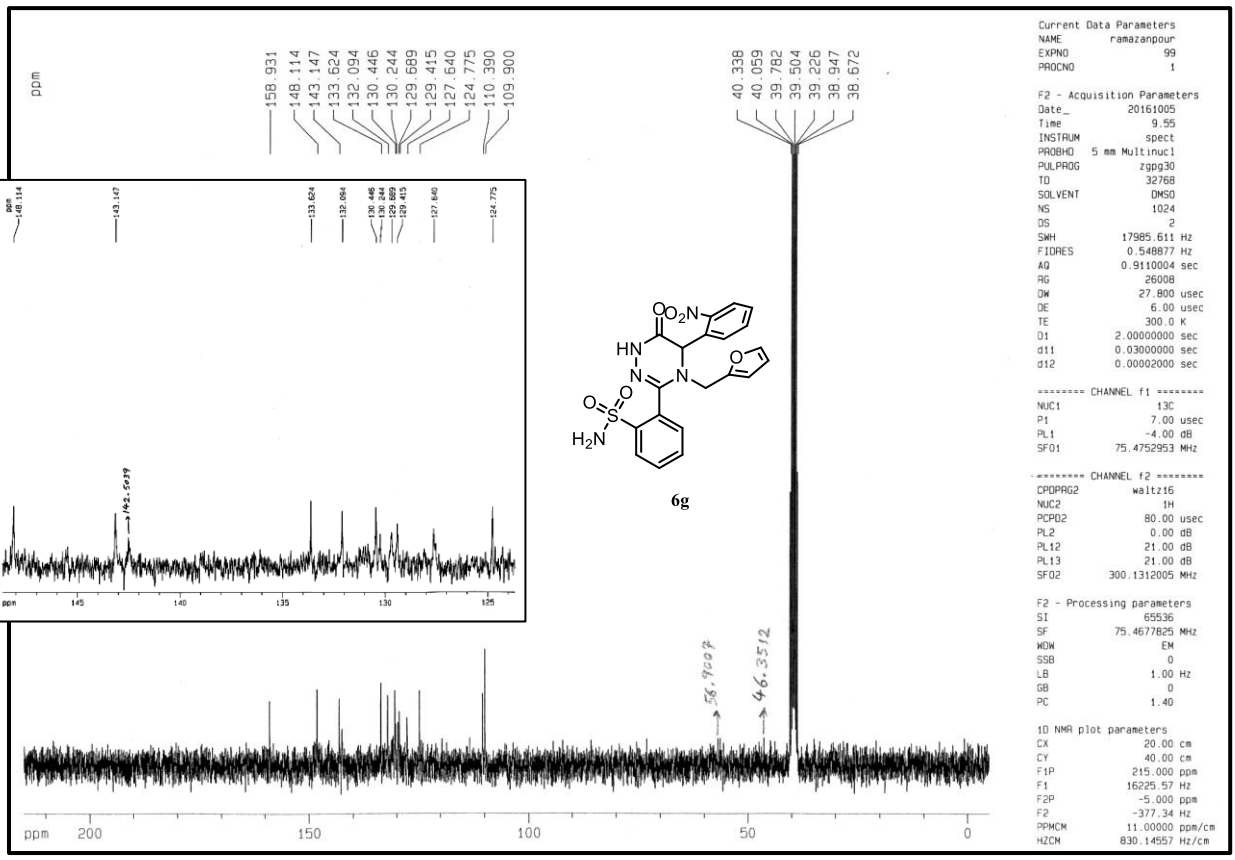


Figure S28. ^{13}C NMR spectrum of compound **6g** (75 MHz, DMSO).

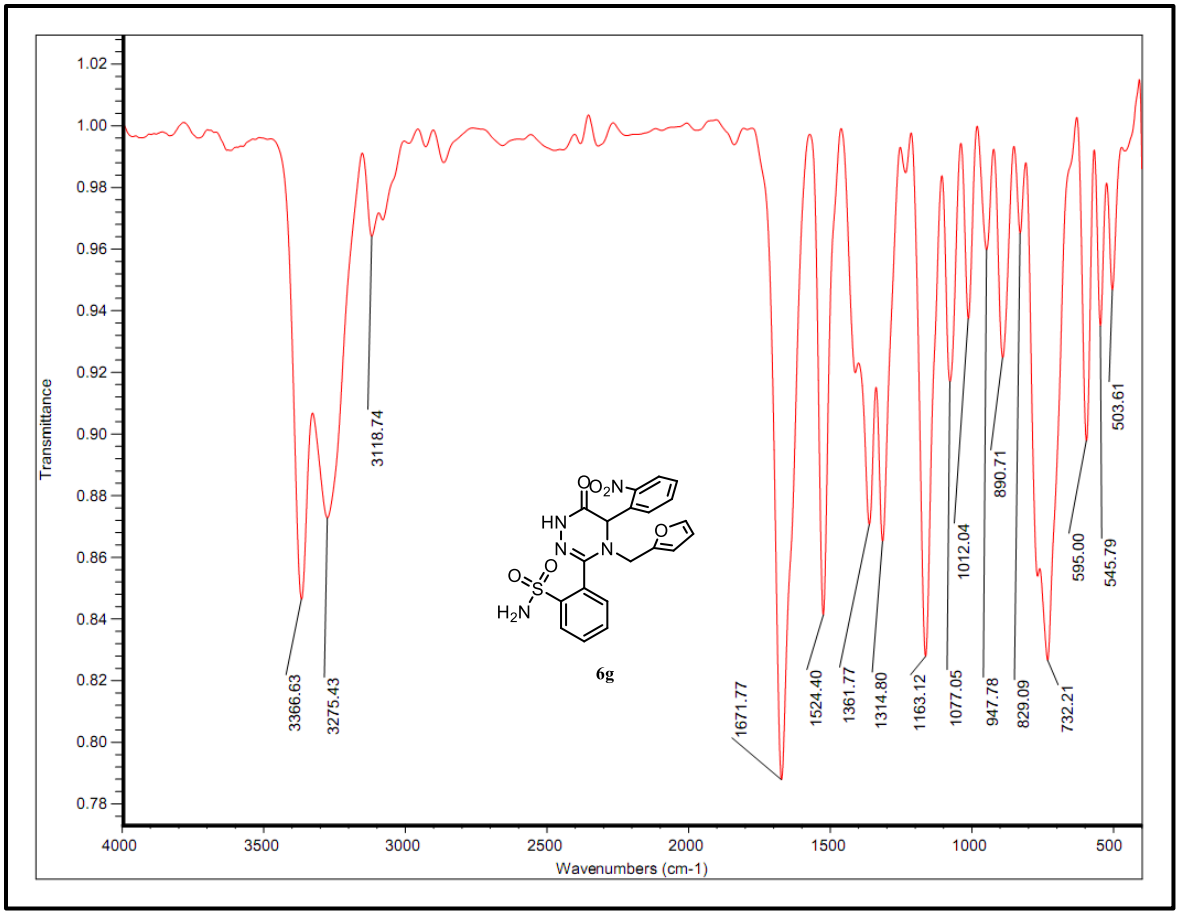


Figure S29. IR spectrum of compound **6g**.

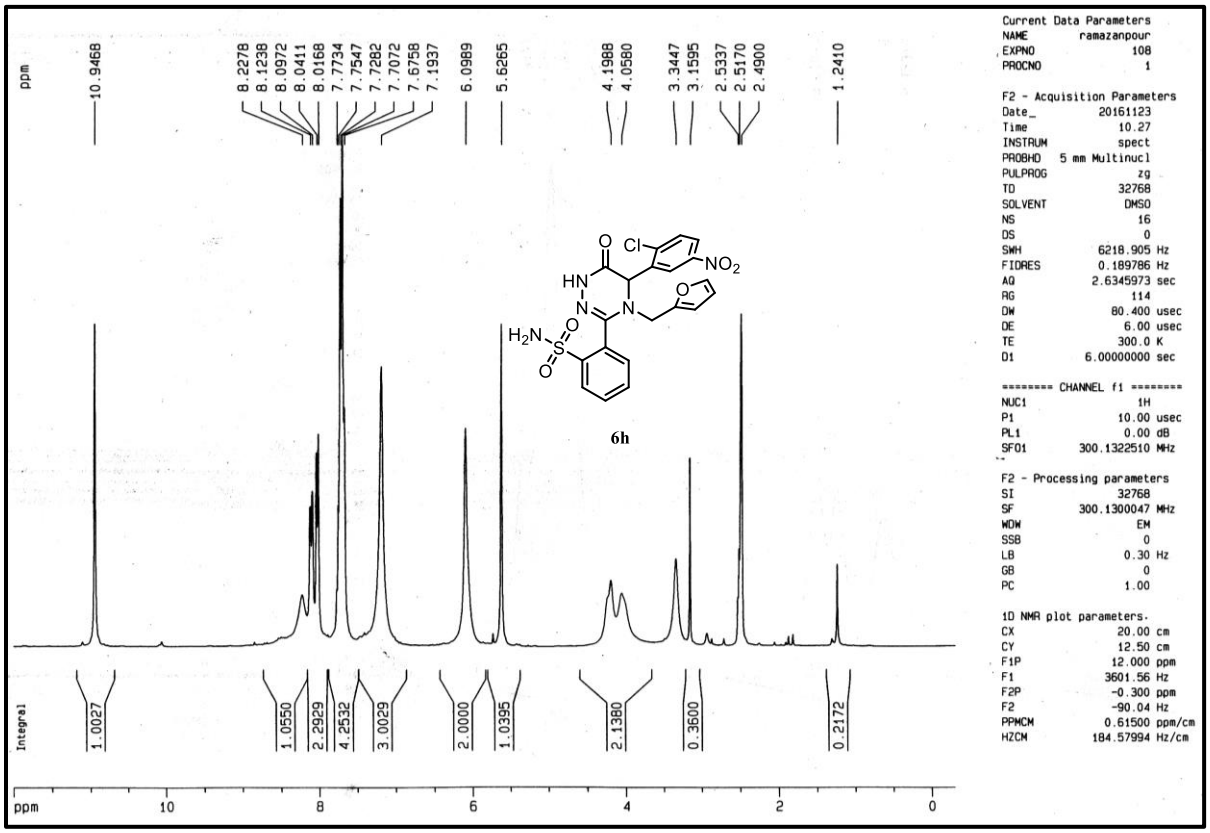


Figure S30. ^{1}H NMR spectrum of compound **6h** (300 MHz, DMSO).

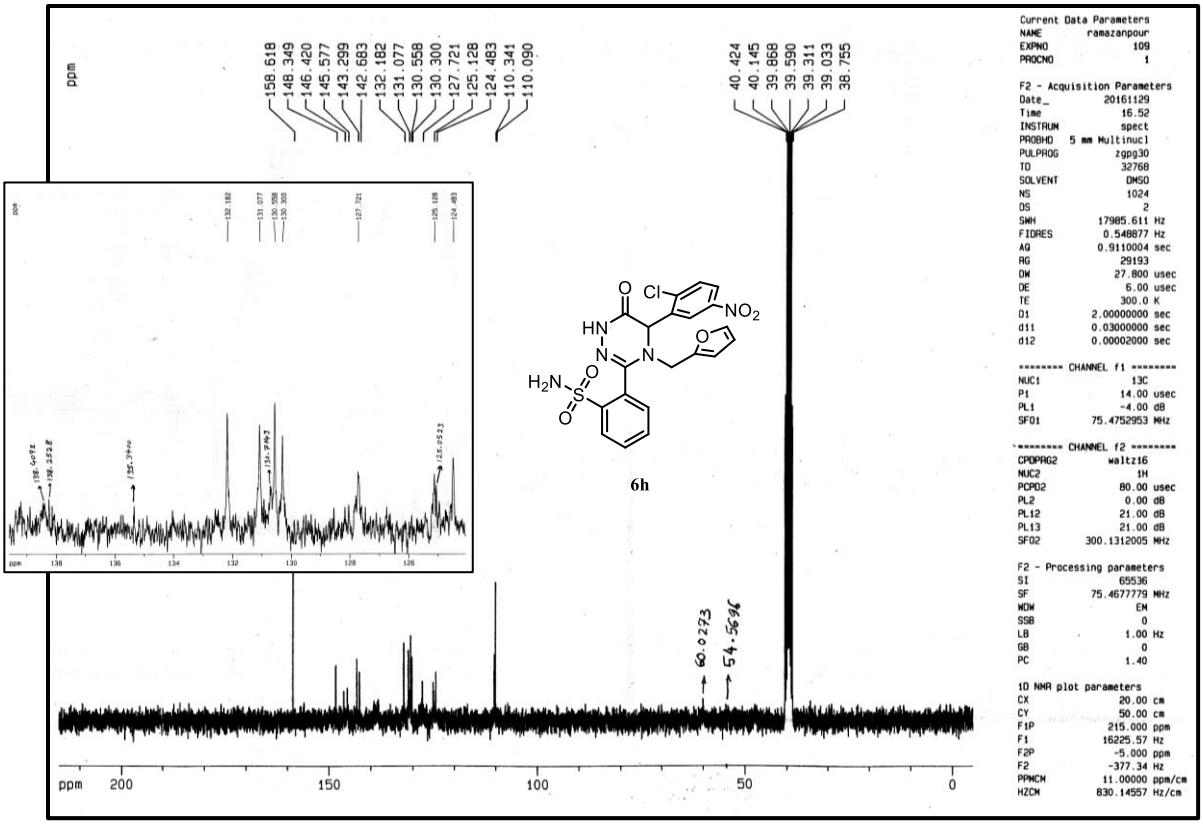


Figure S31. ^{13}C NMR spectrum of compound **6h** (75 MHz, DMSO).

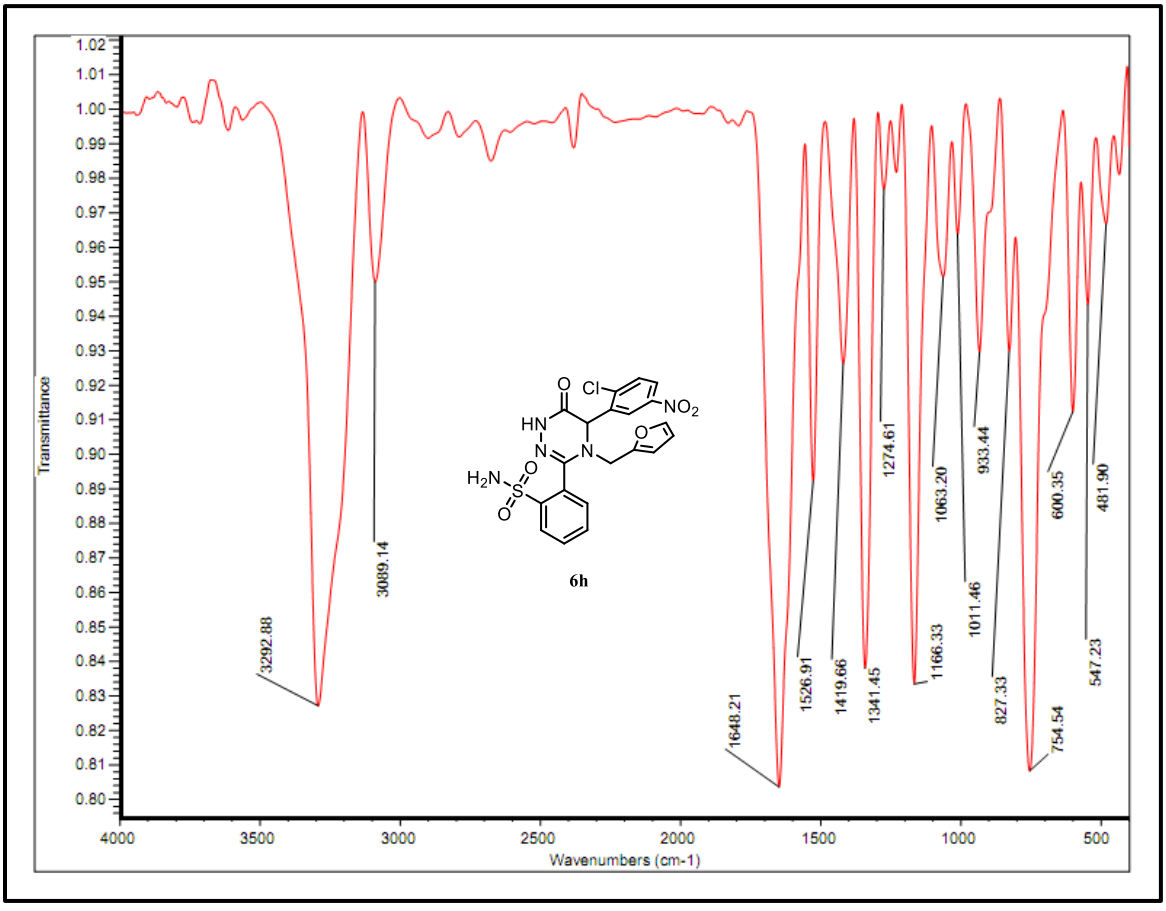


Figure S32. IR spectrum of compound **6h**.

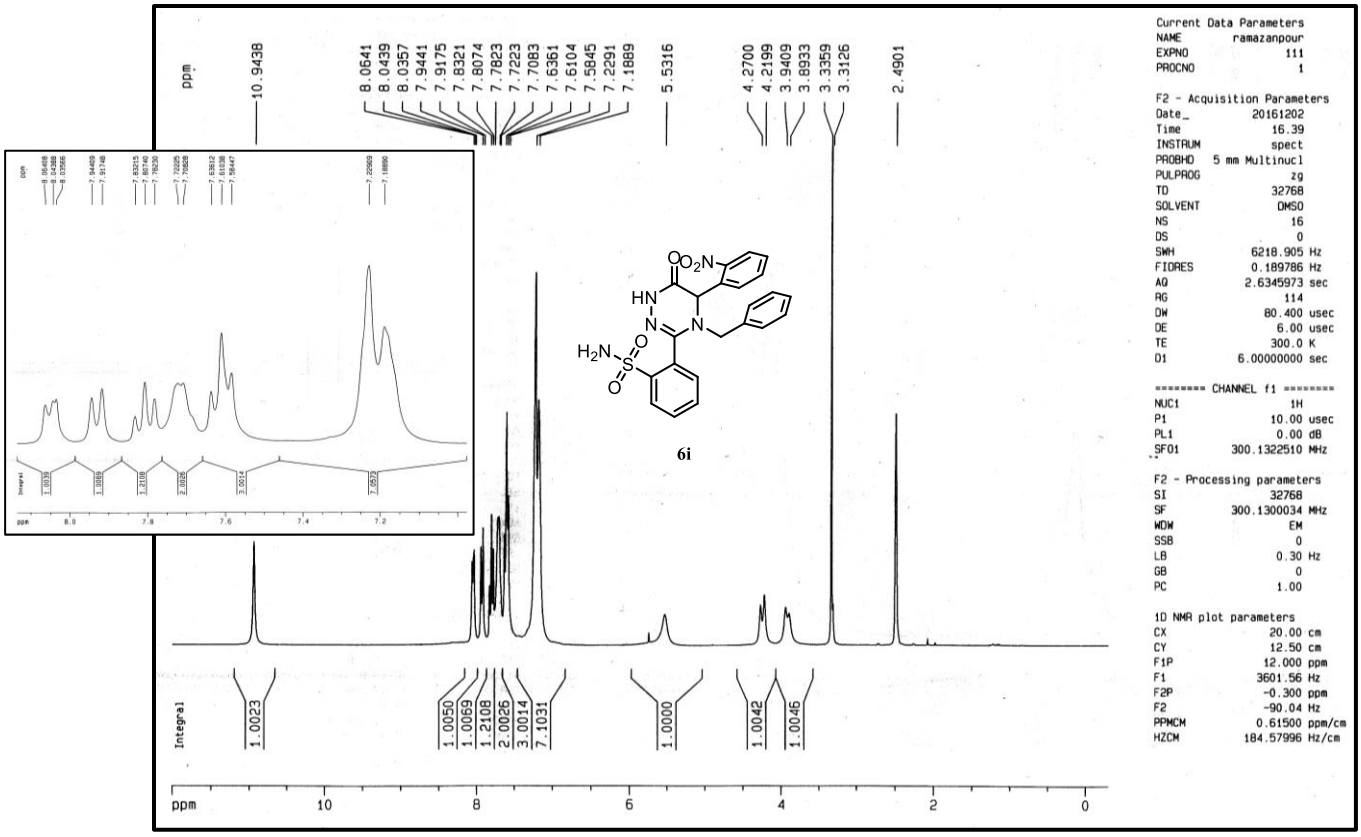


Figure S33. ^{1}H NMR spectrum of compound **6i** (300 MHz, DMSO).

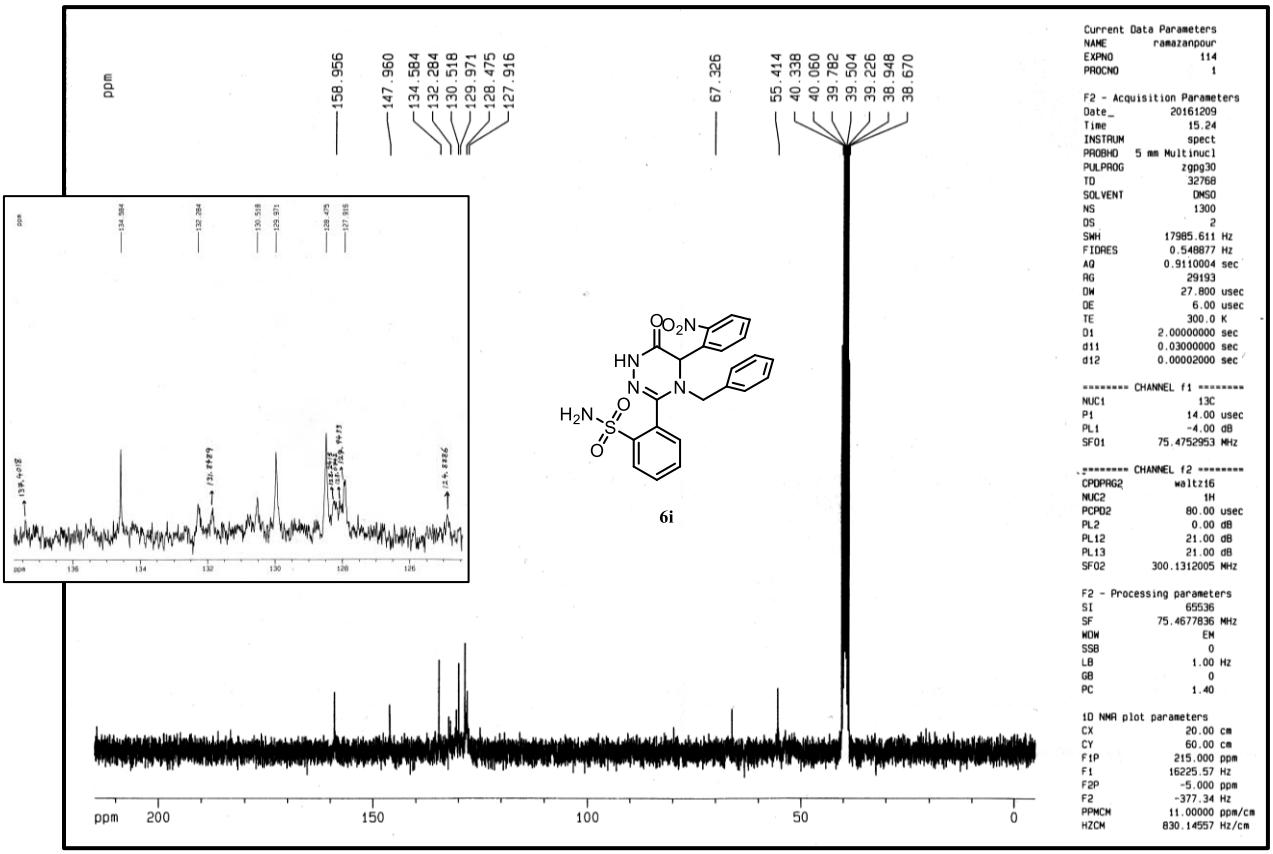


Figure S34. ^{13}C NMR spectrum of compound **6i** (75 MHz, DMSO).

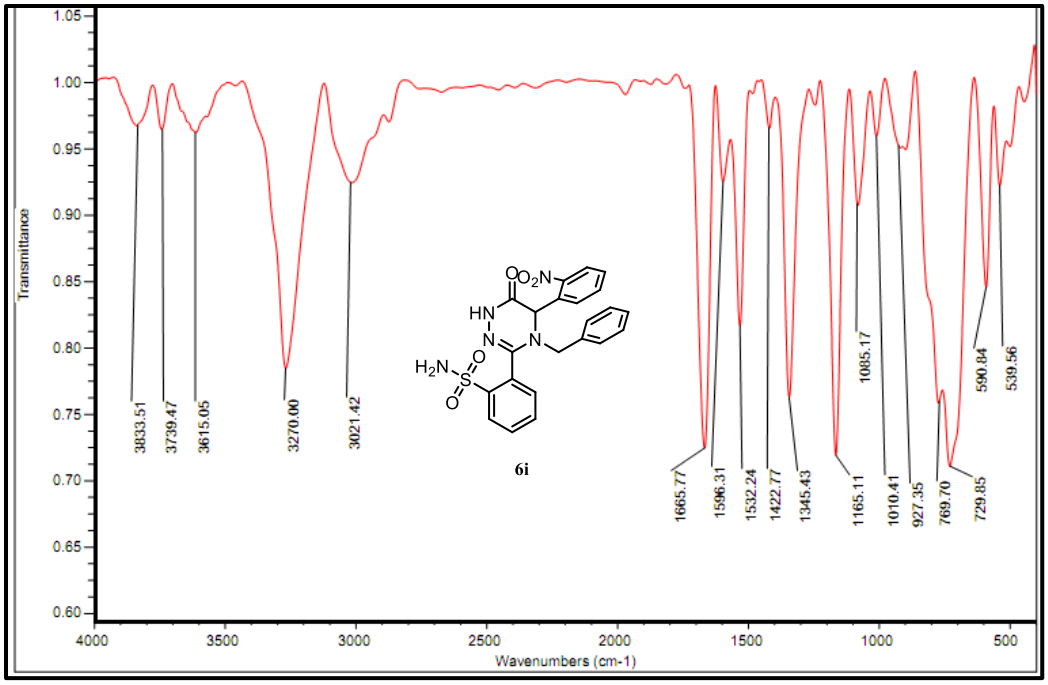


Figure S35. IR spectrum of compound **6i**.

Crystallographic data for 8a:

Table S3: Crystal data and structure refinement for sba153.

Identification code	sba153
Empirical formula	$C_{10}H_{11}N_3O_2S$
Formula weight	237.28
Temperature	200(2) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	Pnma
Z	4
Unit cell dimensions	a = 19.8951(11) Å α =90 deg. b = 6.7525(4) Å β =90 deg. c = 8.0436(4) Å γ = 90 deg.
Volume	1080.59(10) $Å^3$
Density (calculated)	1.46 g/cm^3
Absorption coefficient	0.29 mm^{-1}
Crystal shape	needle
Crystal size	0.320 x 0.050 x 0.050 mm^3
Crystal colour	colourless
Theta range for data collection	2.0 to 25.7 deg.
Index ranges	$-19 \le h \le 24$, $-8 \le k \le 8$, $-9 \le l \le 9$
Reflections collected	6871
Independent reflections	1122 (R(int) = 0.0451)
Observed reflections	919 ($I > 2\sigma(I)$)
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.96 and 0.84
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1122 / 0 / 99
Goodness-of-fit on F^2	1.05
Final R indices (I>2sigma(I))	R1 = 0.040, wR2 = 0.095
Largest diff. peak and hole	0.29 and -0.26 $eÅ^{-3}$

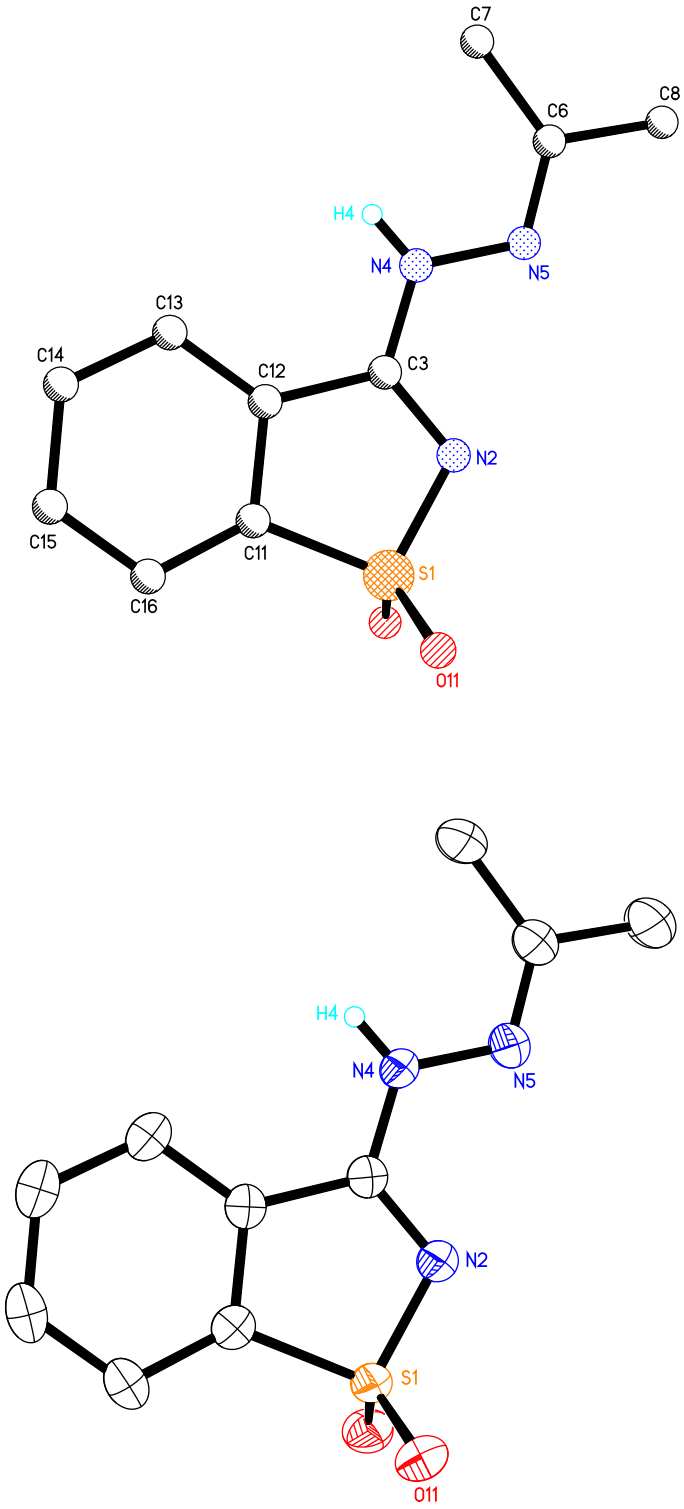


Figure S36. ORTEP structure of product **8a**; the ellipsoid probability level of ORTEP diagram is 50%.

Experimental part:

sba153: colourless crystal (needle), dimensions 0.320 x 0.050 x 0.050 mm^3, crystal system orthorhombic, space group Pnma, Z=4, a=19.8951(11) Å, b=6.7525(4) Å, c=8.0436(4) Å, alpha=90 deg, beta=90 deg, gamma=90 deg, V=1080.59(10) $Å^3$, rho=1.458 g/cm^3, T=200(2) K, $Theta_{max}$= 25.691 deg, radiation Mo Kalpha, lambda=0.71073 Å, 0.5 deg omega-scans with CCD area detector, covering the asymmetric unit in reciprocal space with a mean redundancy of 5.88and a completeness of 99.9% to a resolution of 0.82 Å, 6871 reflections measured, 1122 unique (R(int)=0.0451), 919 observed ($I > 2\sigma(I)$), intensities were corrected for Lorentz and polarization effects, an empirical scaling and absorption correction was applied using SADABS[1] based on the Laue symmetry of the reciprocal space, mu=0.29mm^{-1}, T_{min}=0.84, T_{max}=0.96, structure refined against F^2 with a Full-matrix least-squares algorithm using the SHELXL-2016/6 (Sheldrick, 2016) software [2], 99 parameters refined, hydrogen atoms were treated using appropriate riding models, except H4 at N4, which was refined isotropically, goodness of fit 1.05 for observed reflections, final residual values R1(F)=0.040, wR(F^2)=0.095 for observed reflections, residual electron density -0.26 to 0.29 e$Å^{-3}$. CCDC 1836445 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Lit. 1: (program SADABS 2014/5 for absorption correction)
G. M. Sheldrick, Bruker Analytical X-ray-Division, Madison, Wisconsin 2014

Lit. 2: (program SHELXL-2016/6 (Sheldrick, 2016) for structure refinement)
Acta Cryst. (2015). C71, 3-8

Lit. APEX, APEX2, SMART, SAINT, SAINT-Plus:
Bruker (2007). "Program name(s)". Bruker AXS Inc., Madison, Wisconsin, USA.