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Supplementary Information

Cytotoxicity and Leishmanicidal Activity of Isoniazid-Derived Hydrazones and 2-Pyrazineformamide Thiosemicarbazones

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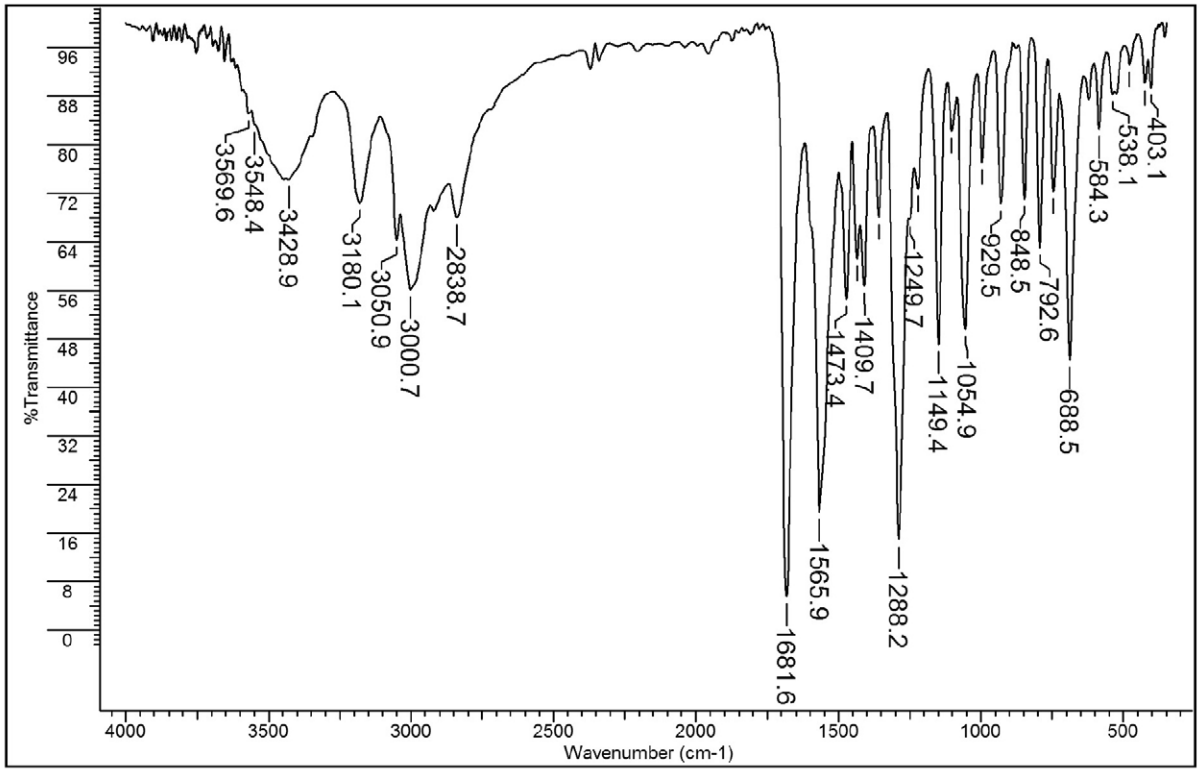

Figure S1. FTIR (KBr) spectrum of compound **1**.

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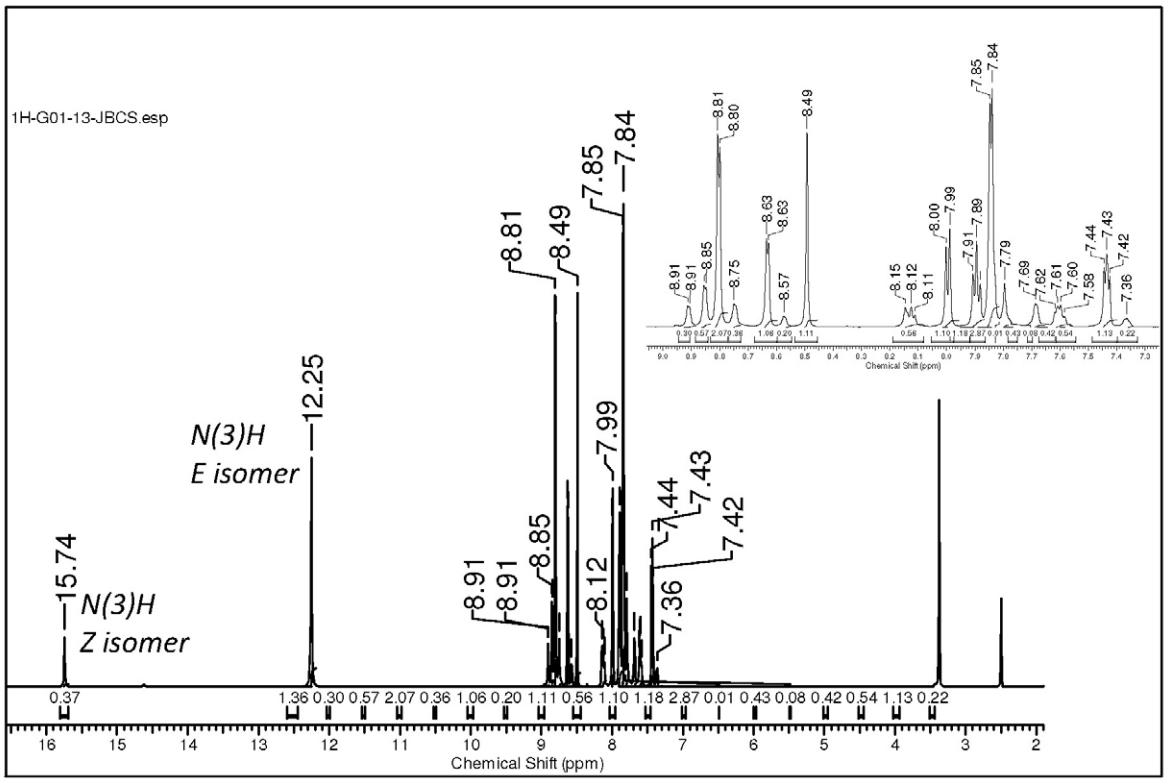


Figure S2. [1]H NMR spectrum (600 MHz, DMSO-d_6) of compound **1**.

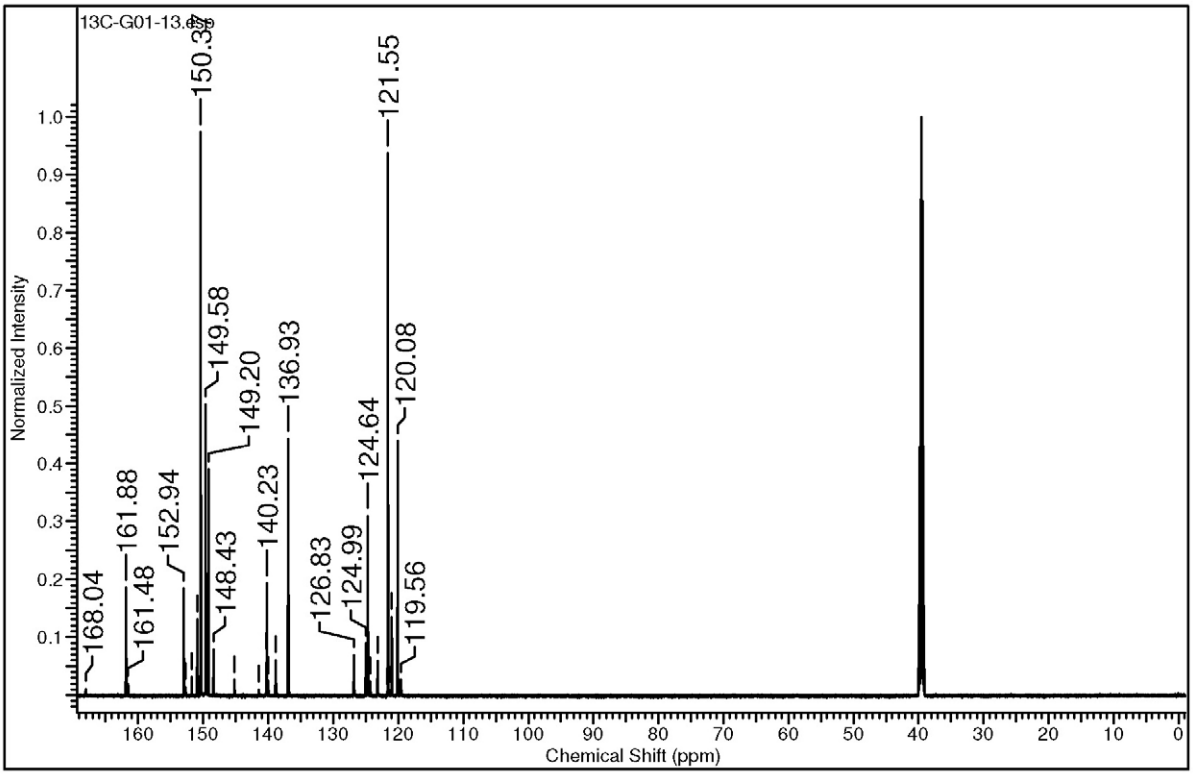


Figure S3. [13]C NMR spectrum (150 MHz, DMSO-d_6) of compound **1**.

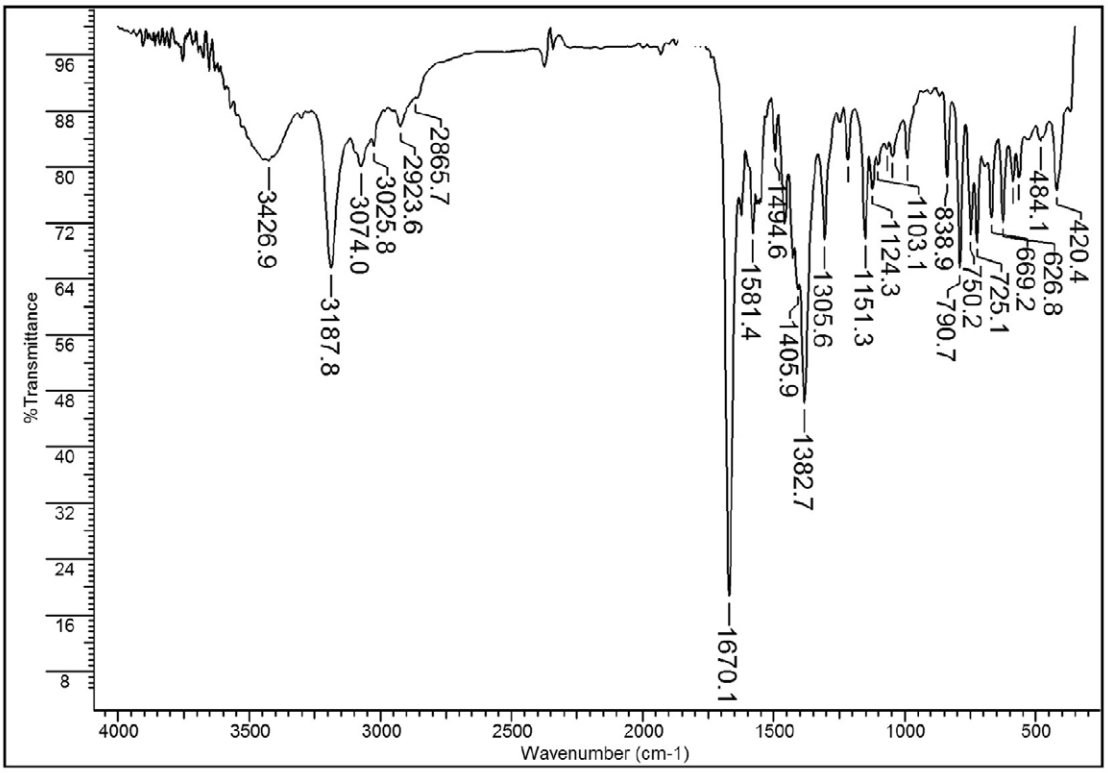


Figure S4. FTIR (KBr) spectrum of compound **2**.

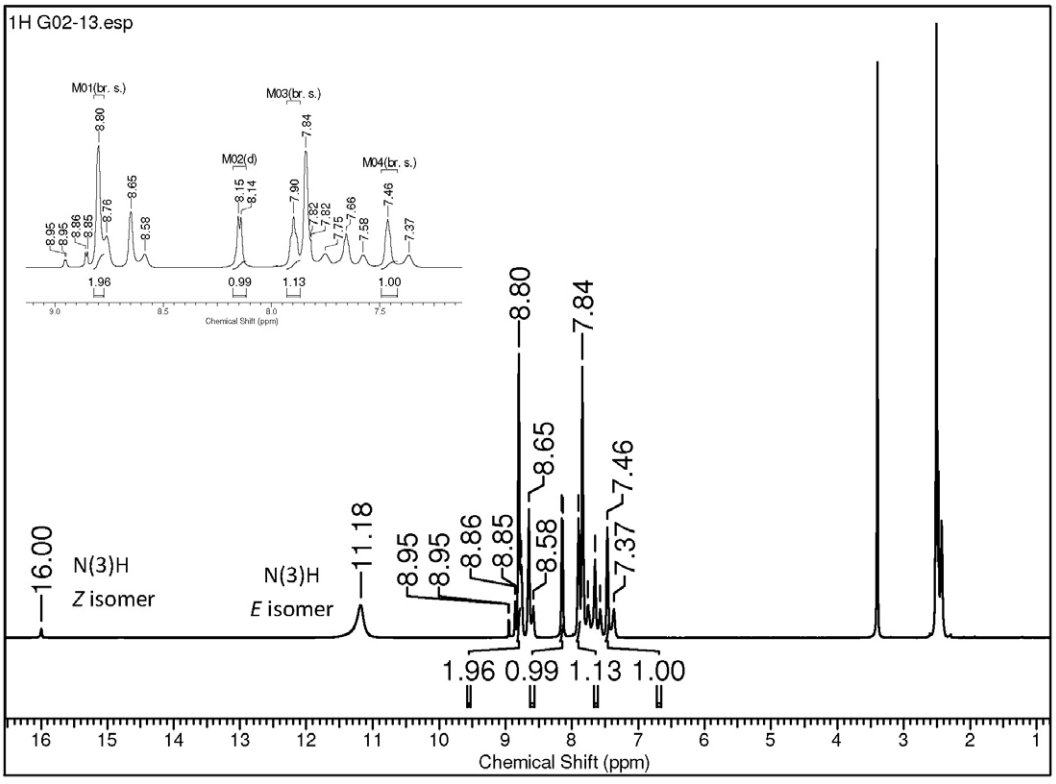


Figure S5. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of compound **2**.

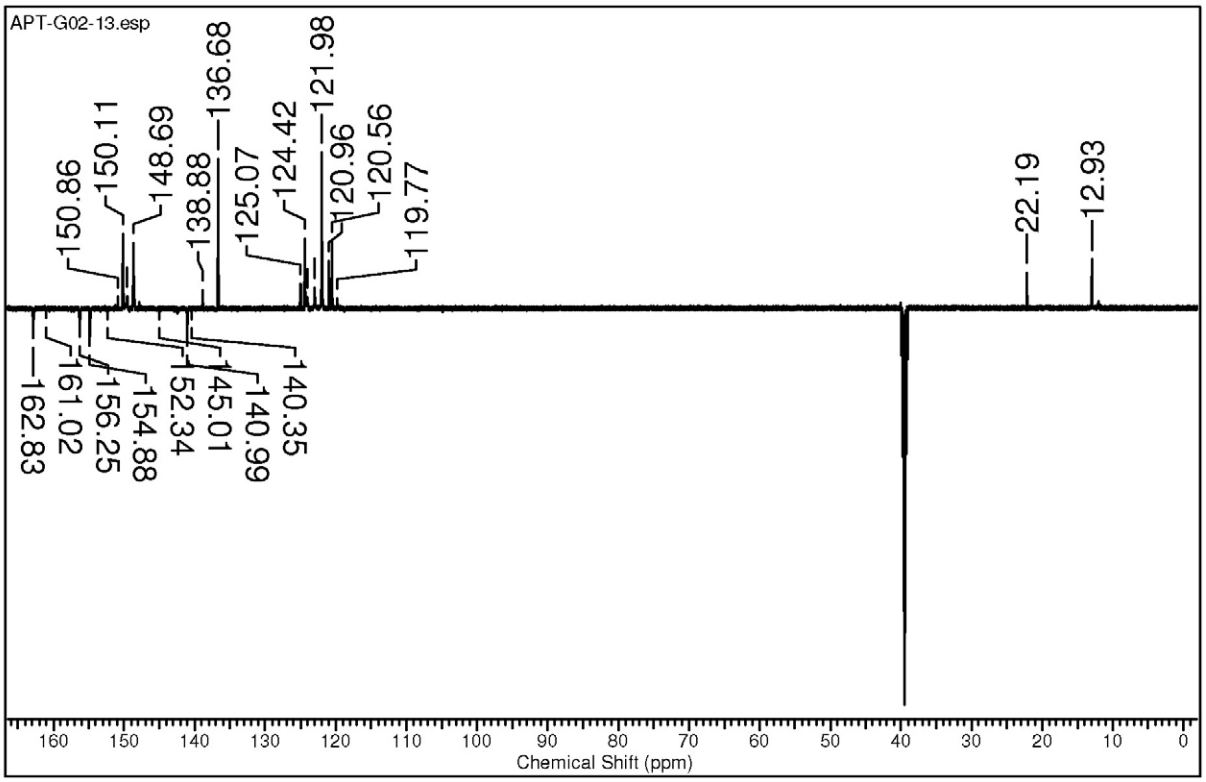


Figure S6. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of compound **2**.

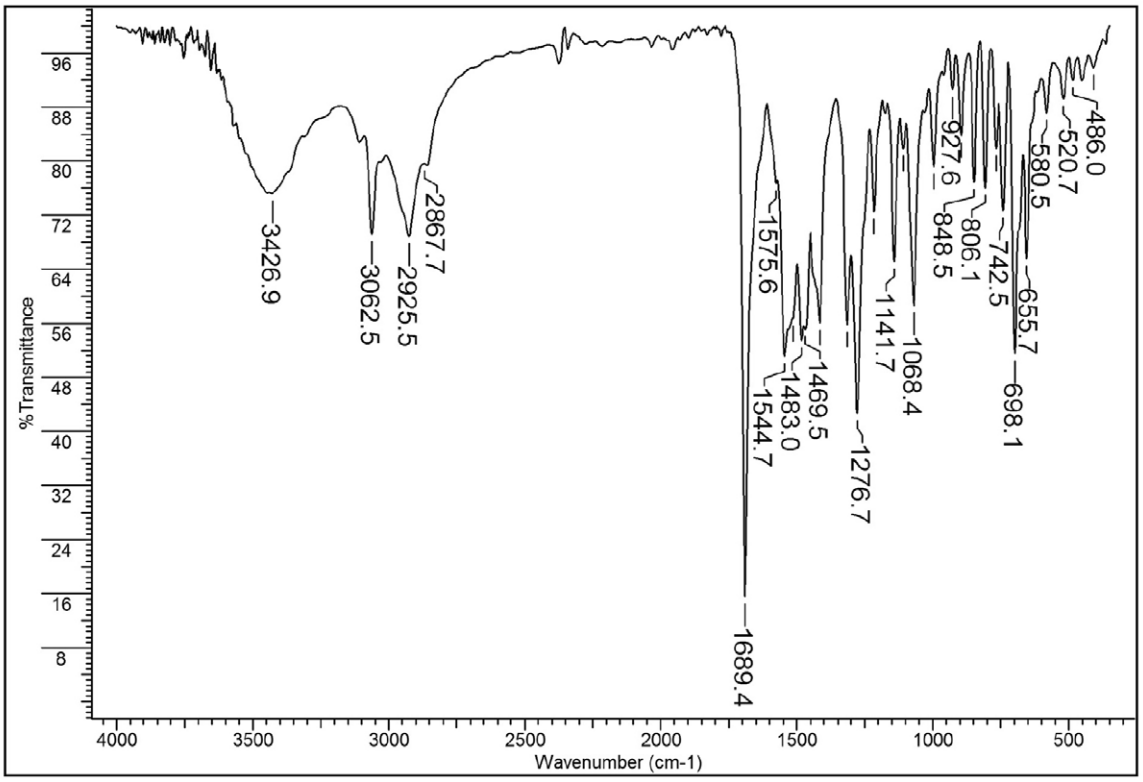


Figure S7. FTIR (KBr) spectrum of compound **3**.

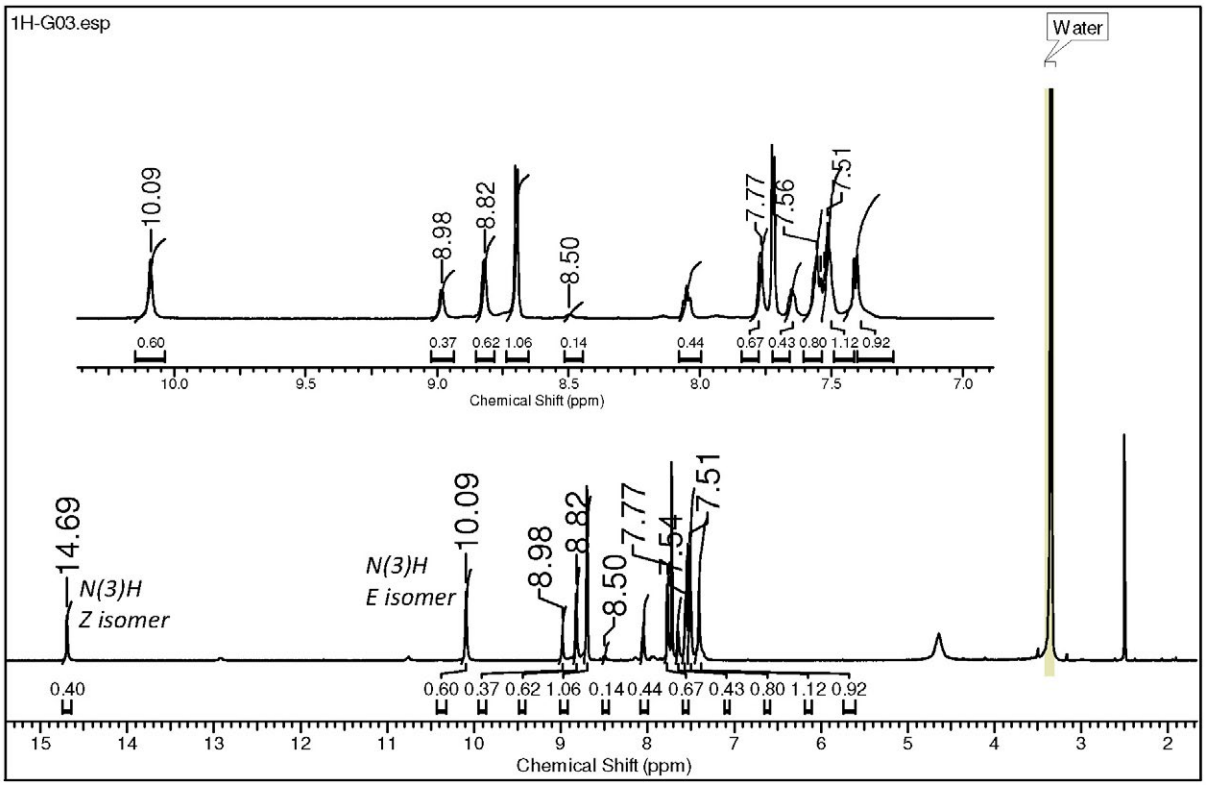


Figure S8. [1]H NMR spectrum (600 MHz, DMSO-d_6) of compound **3**.

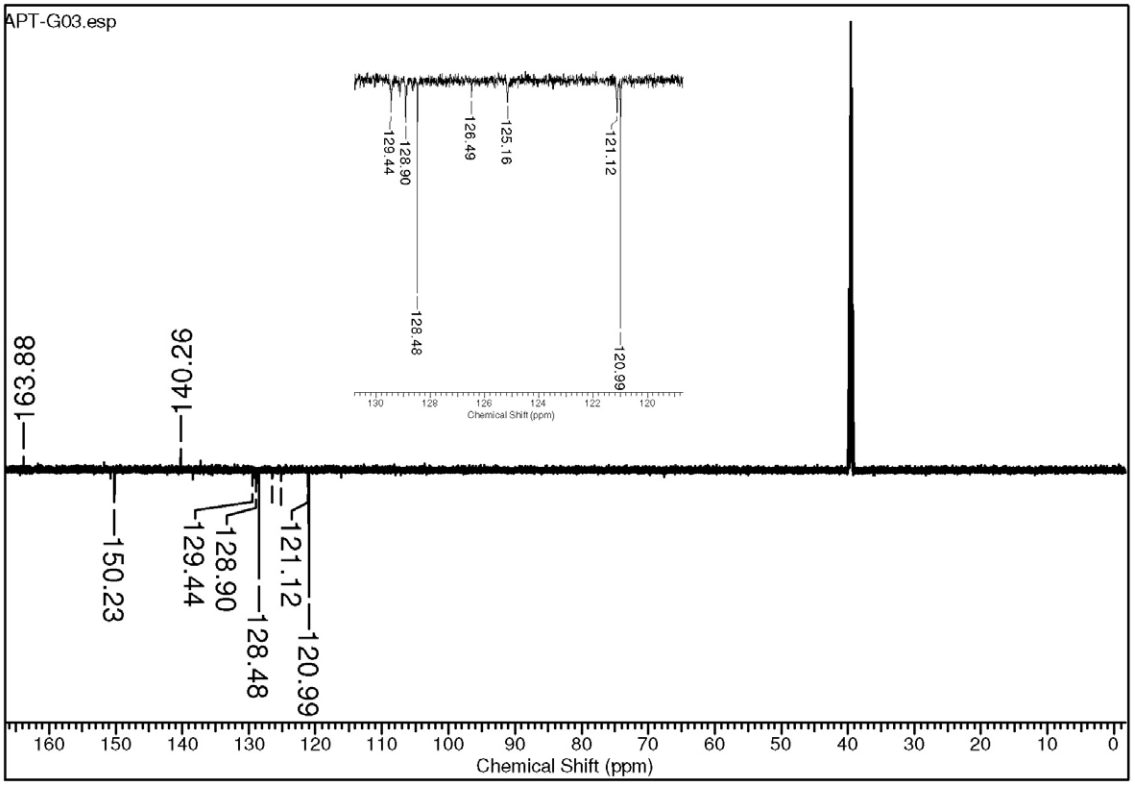


Figure S9. [13]C NMR spectrum (150 MHz, DMSO-d_6) of compound **3**.

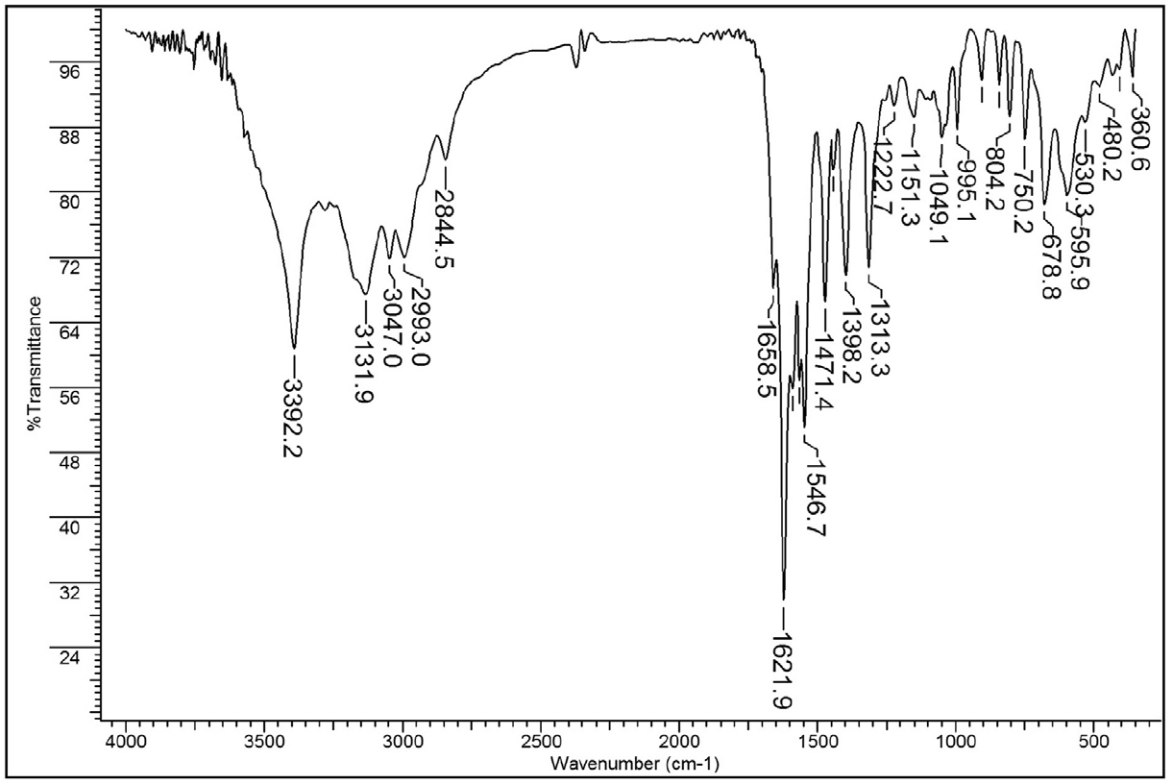


Figure S10. FTIR (KBr) spectrum of compound **4**.

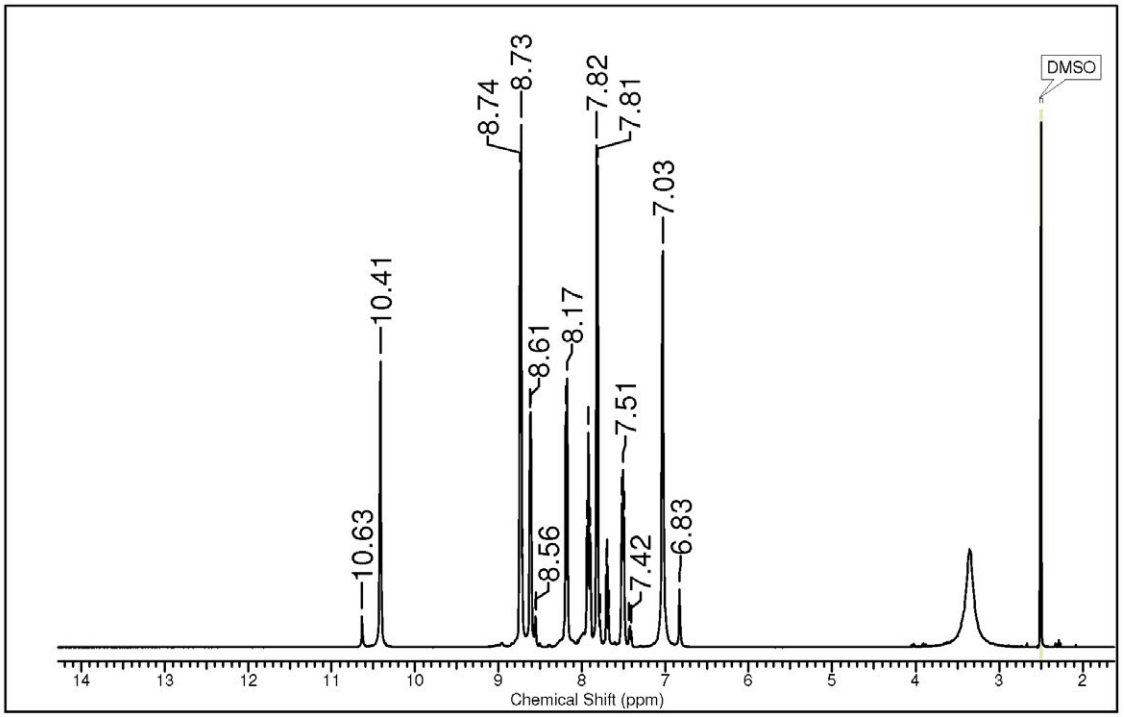


Figure S11. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **4**.

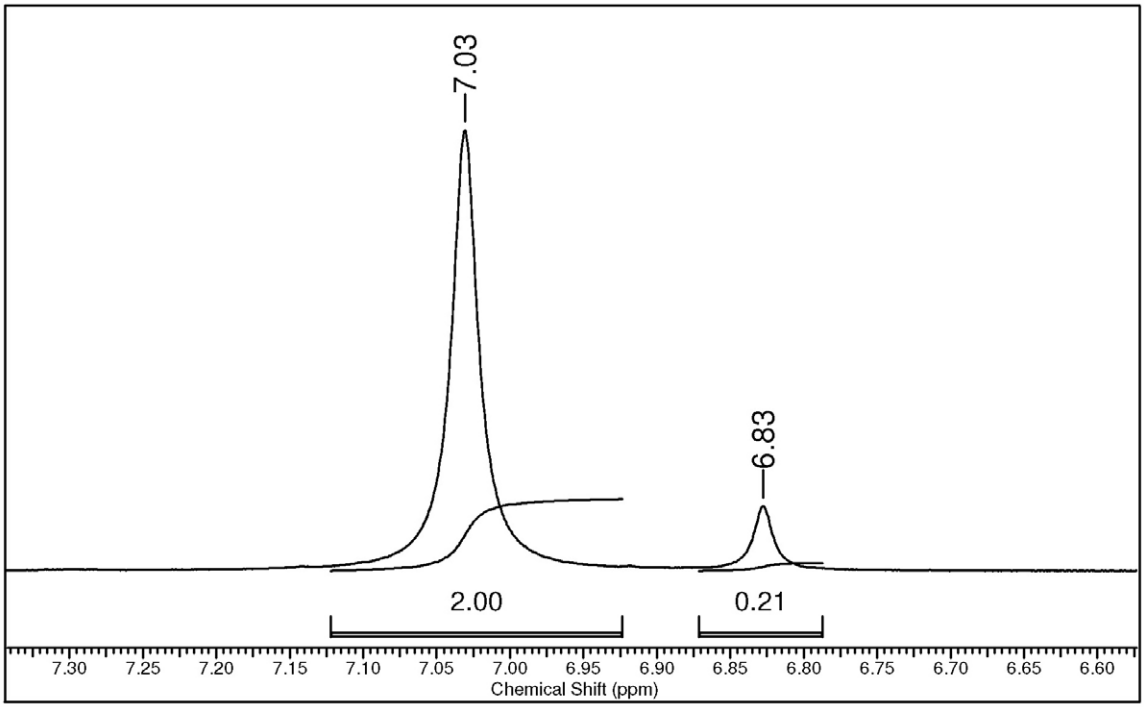


Figure S12. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **4** (6.60-7.30 ppm region).

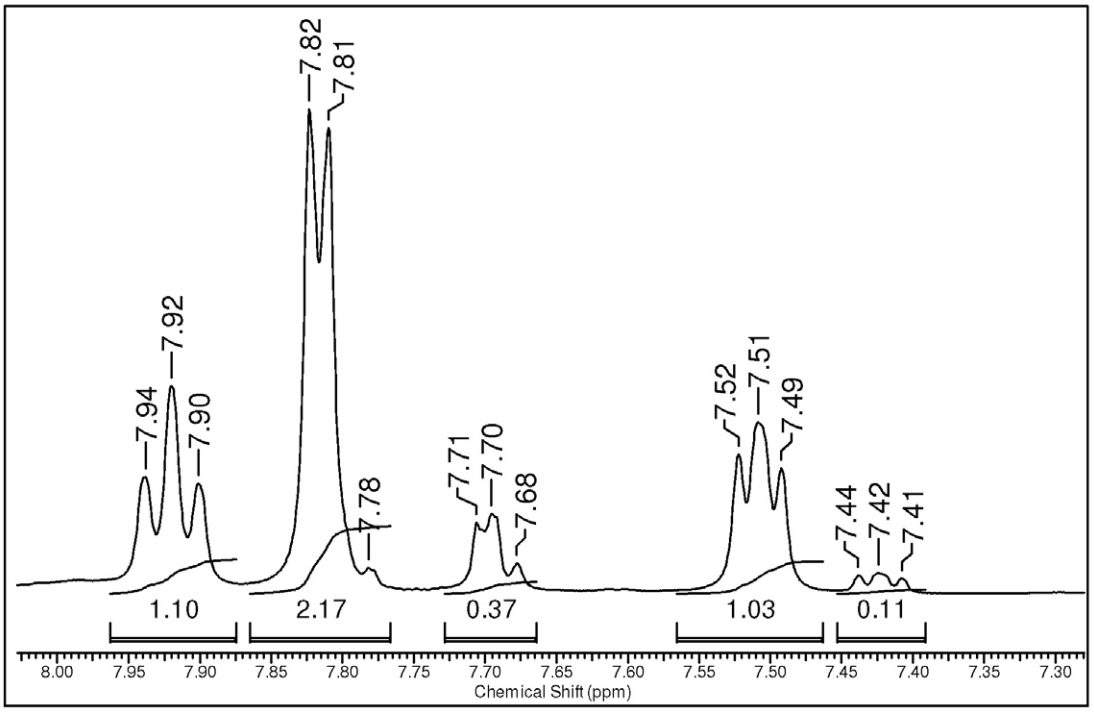


Figure S13. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of compound **4** (7.30-8.00 ppm region).

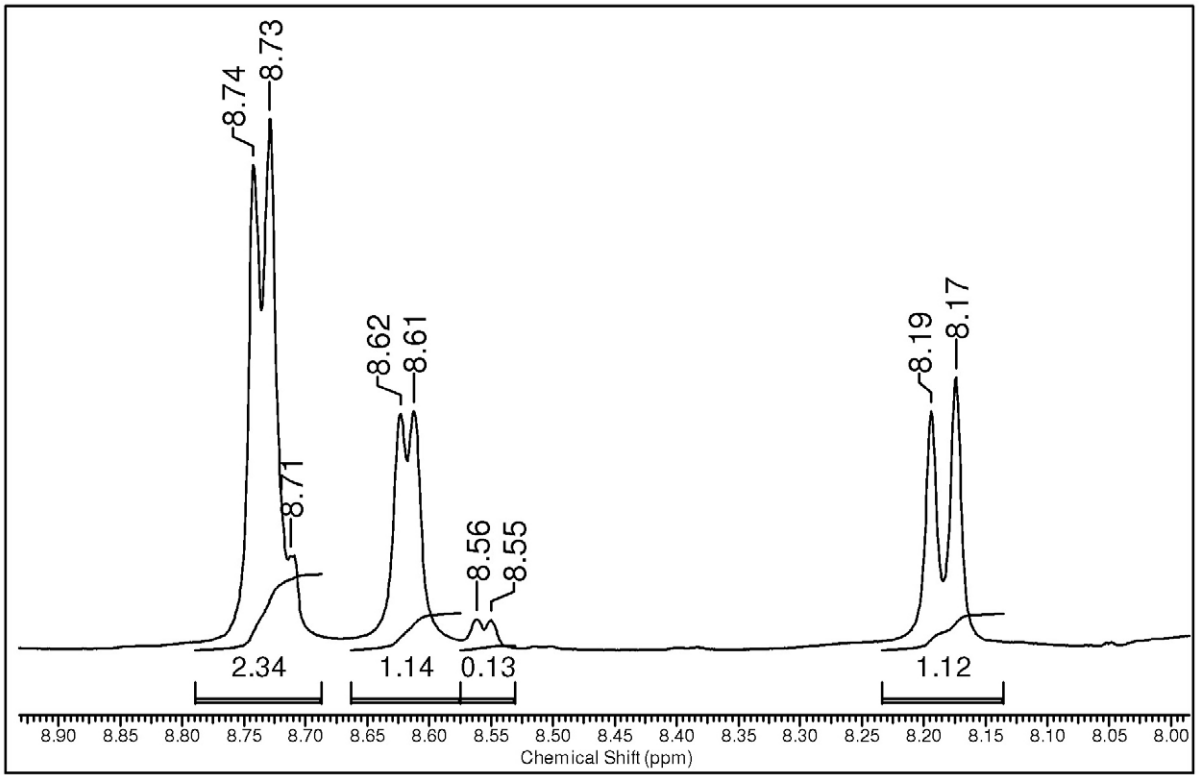


Figure S14. [1]H NMR spectrum (400 MHz, DMSO-d_6) of compound **4** (8.00-8.90 ppm region).

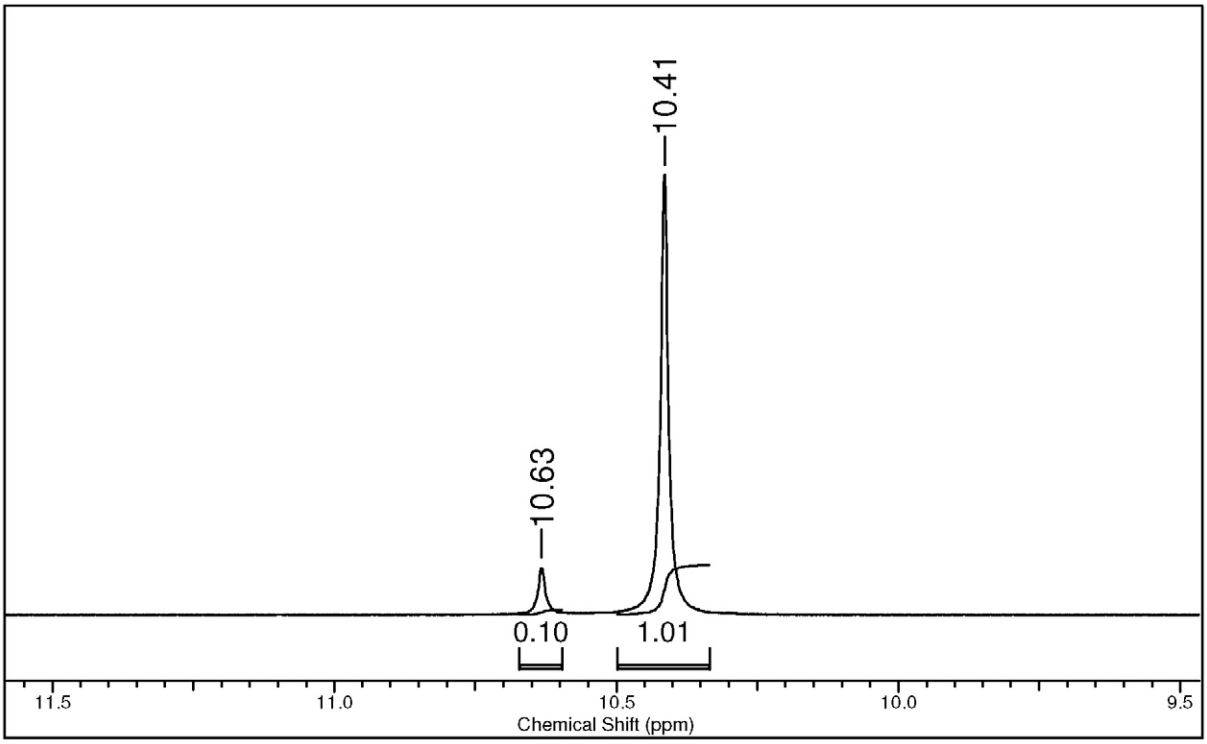


Figure S15. [1]H NMR spectrum (400 MHz, DMSO-d_6) of compound **4** (9.5-11.5 ppm region).

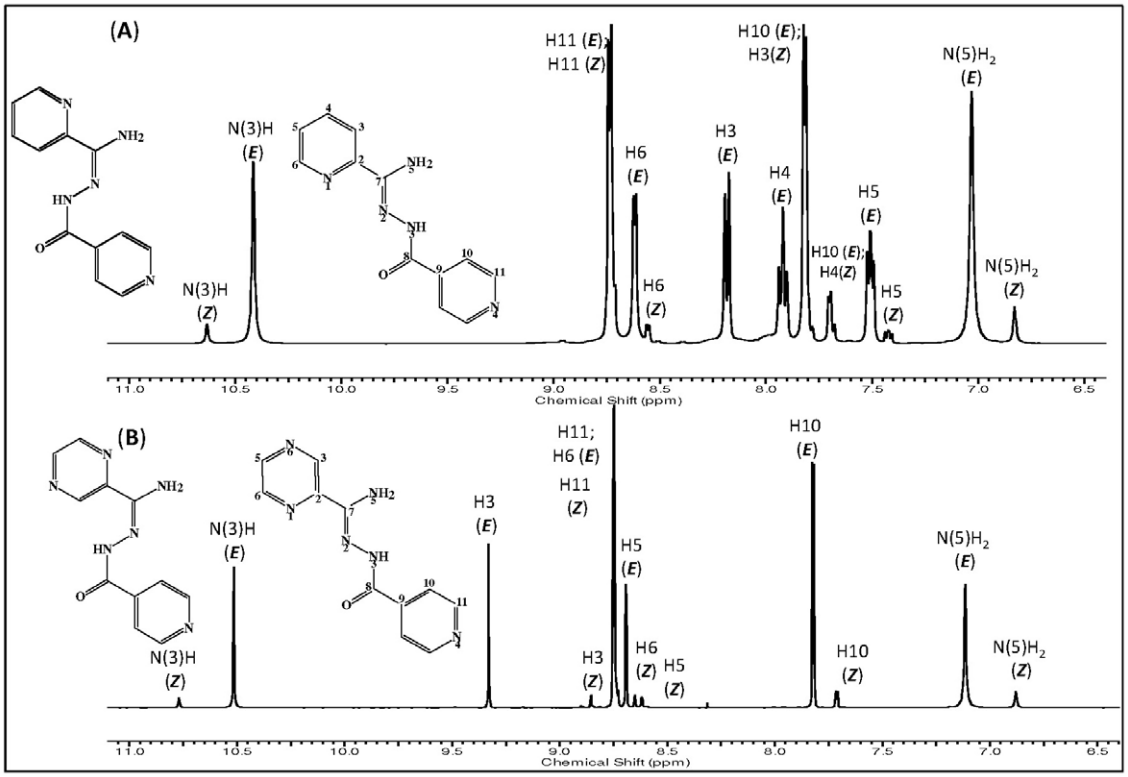


Figure S16. [1]H NMR spectra of **4** (A, 400 MHz) and **5** (B, 600 MHz) recorded in DMSO-d_6 (6.5-11.0 ppm region). In both cases, the data suggest the compounds exist as a mixture of *E* and *Z* isomers in solution. These isomers had previously been reported for compound **5**.[1]

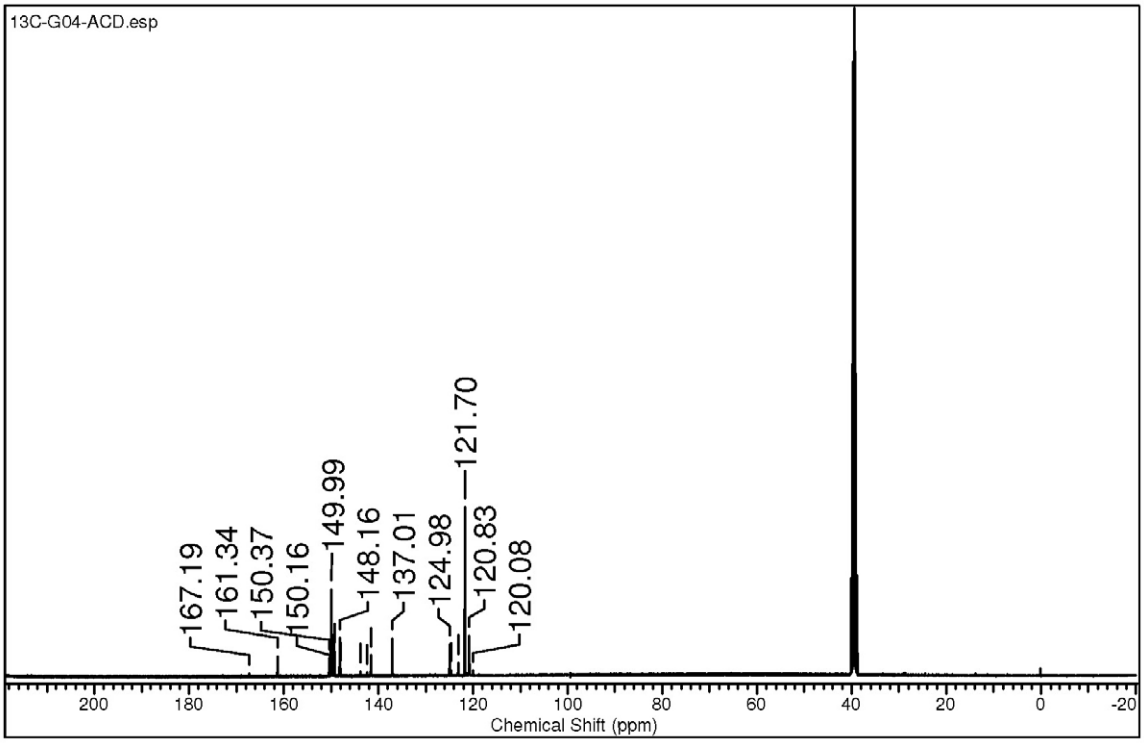


Figure S17. [13]C NMR spectrum (100 MHz, DMSO-d_6) of compound **4**.

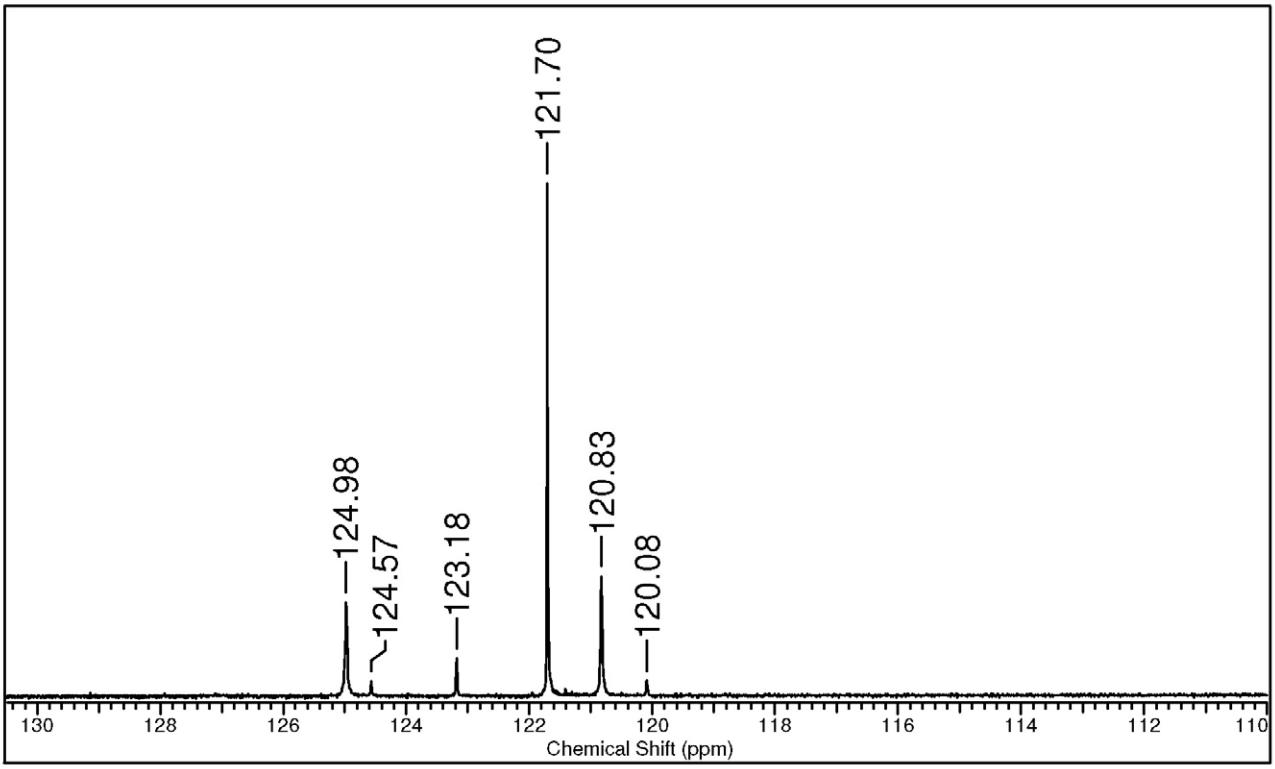


Figure S18. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **4** (110-130 ppm region).

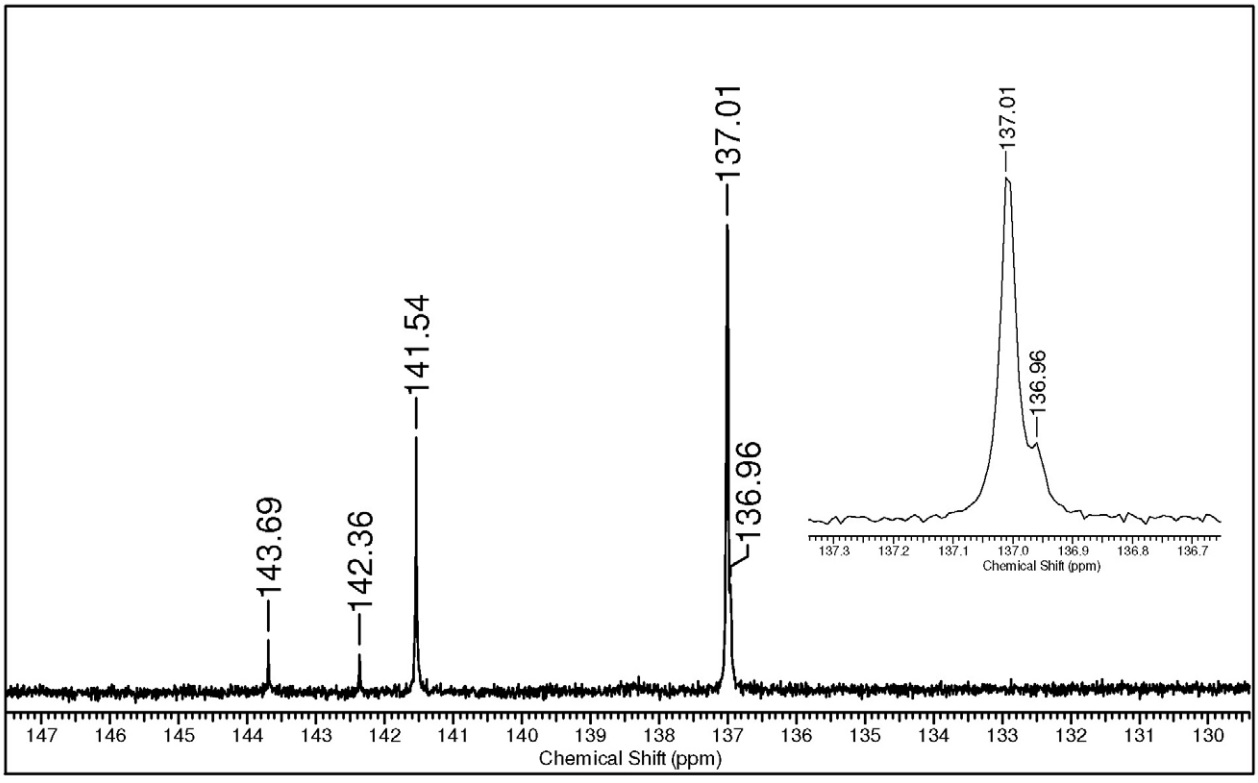


Figure S19. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **4** (130-147 ppm region).

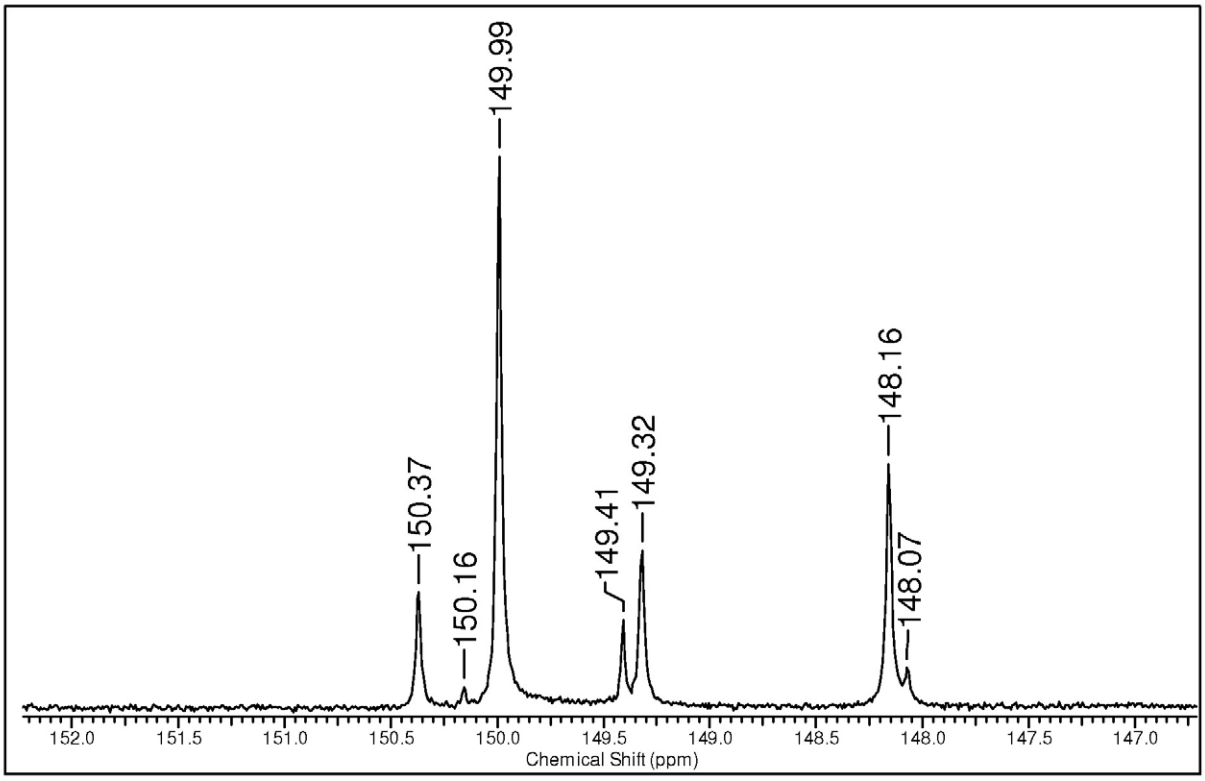


Figure S20. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **4** (147-152 ppm region).

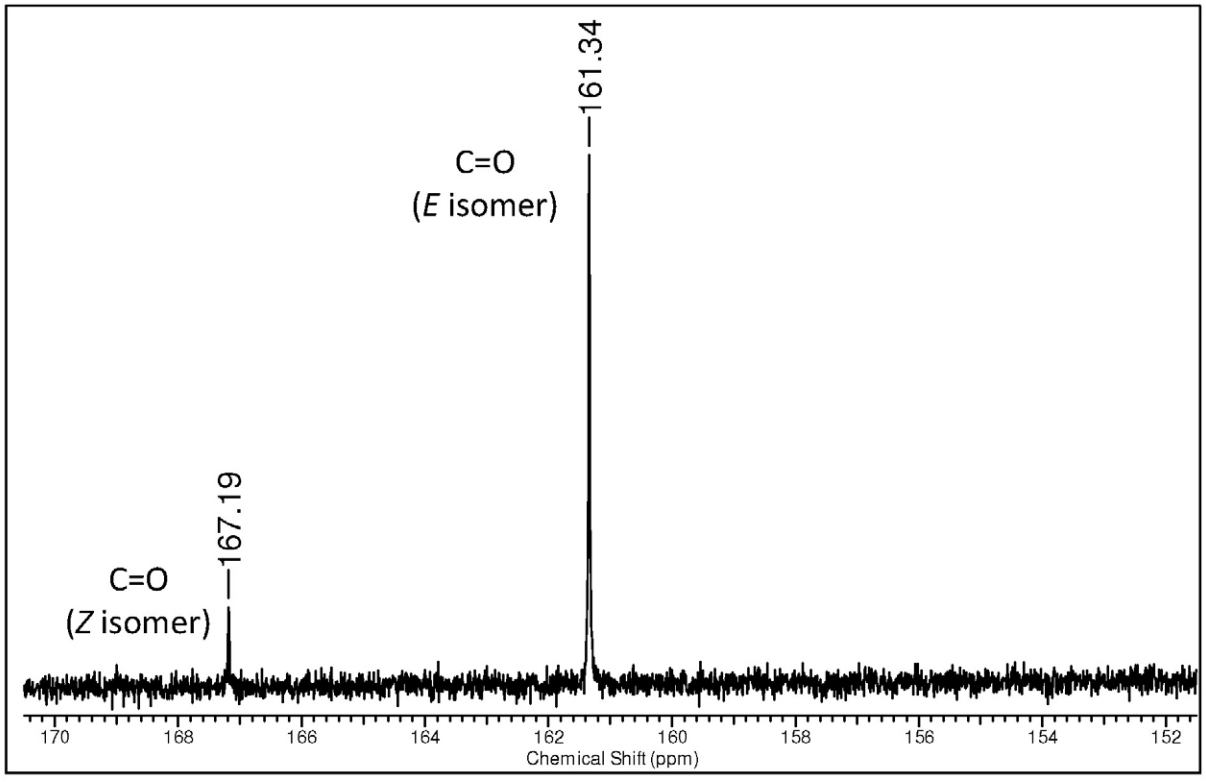


Figure S21. ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of compound **4** (152-170 ppm region).

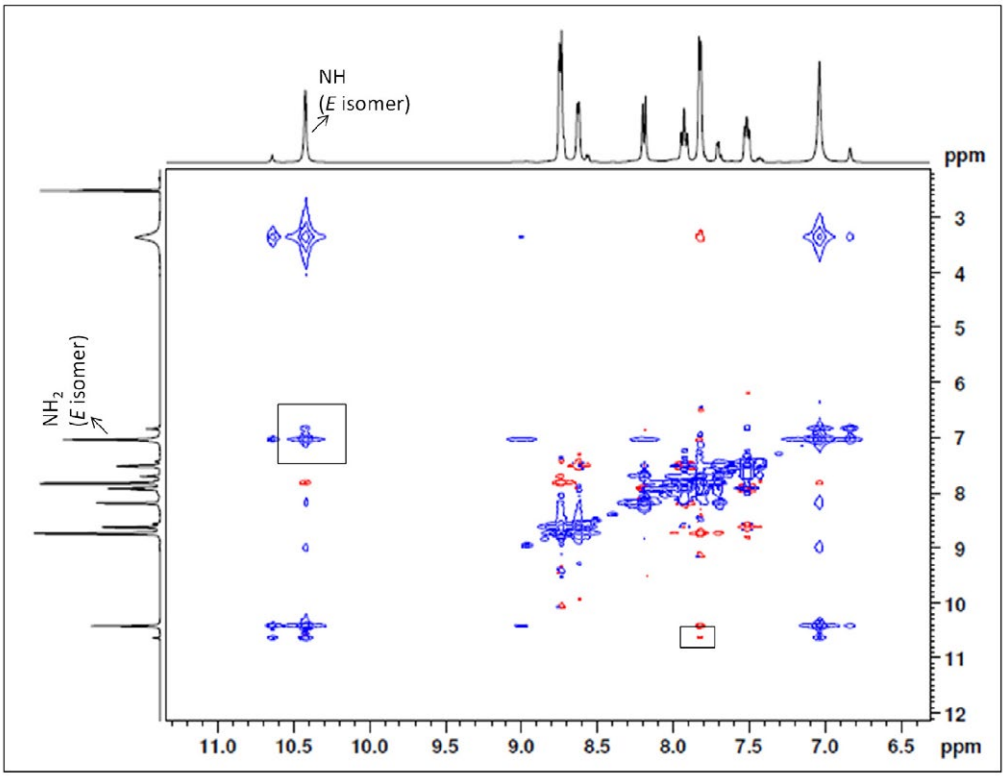


Figure S22. NOESY spectrum (400 MHz, DMSO-d_6) of compound **4**.

Compound Spectrum SmartFormula Report

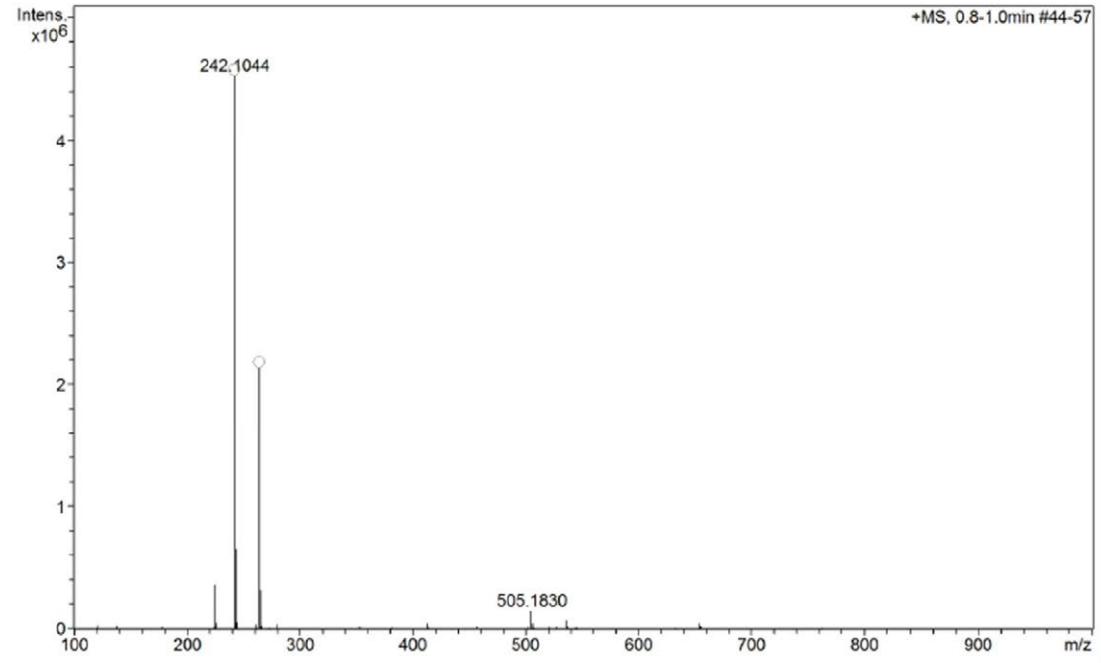
Analysis Info

Analysis Name	D:\Data\2015\SINTESE 2\71456 - G 05.d	Acquisition Date	8/31/2015 1:41:08 PM
Method	Tune_pos_Standard.m	Operator	BDAL@DE
Sample Name	71456 - G 05	Instrument	compact 8255754.10035
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	2000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-100 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Source
		Set Corona	0 nA	Set APCI Heater	0 °C

+MS, 0.8-1.0min #44-57



Meas. m/z	#	Ion Formula	m/z	err [ppm]	Mean err [ppm]	rdb	N-Rule	e⁻ Conf	mSigma	Std I	Std Mean m/z	Std I	VarNorm	Std m/z Diff	Std Comb Dev
242.104443	1	C12H12N5O	242.103636	-3.3	-3.3	9.5	ok	even	3.2	5.9	n.a.	n.a.	n.a.	n.a.	n.a.
	2	C11H16NO5	242.102299	-8.9	-8.2	4.5	ok	even	10.7	17.8	n.a.	n.a.	n.a.	n.a.	n.a.
	3	C9H16N5OS	242.107008	10.6	3.3	4.5	ok	even	26.2	42.8	n.a.	n.a.	n.a.	n.a.	n.a.
	4	C8H20NO5S	242.105670	5.1	-0.9	-0.5	ok	even	36.4	54.8	n.a.	n.a.	n.a.	n.a.	n.a.
264.086442	1	C12H11N5NaO	264.085581	-3.3	-3.0	9.5	ok	even	0.6	1.2	n.a.	n.a.	n.a.	n.a.	n.a.
	2	C11H15NNaO5	264.084243	-8.3	-7.4	4.5	ok	even	13.5	22.6	n.a.	n.a.	n.a.	n.a.	n.a.
	3	C9H15N5NaOS	264.088952	9.5	3.1	4.5	ok	even	27.8	43.9	n.a.	n.a.	n.a.	n.a.	n.a.
	4	C8H19NNaO5S	264.087614	4.4	-0.8	-0.5	ok	even	38.6	57.6	n.a.	n.a.	n.a.	n.a.	n.a.

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Figure S23. Mass spectrum (ESI-MS) of compound **4**.

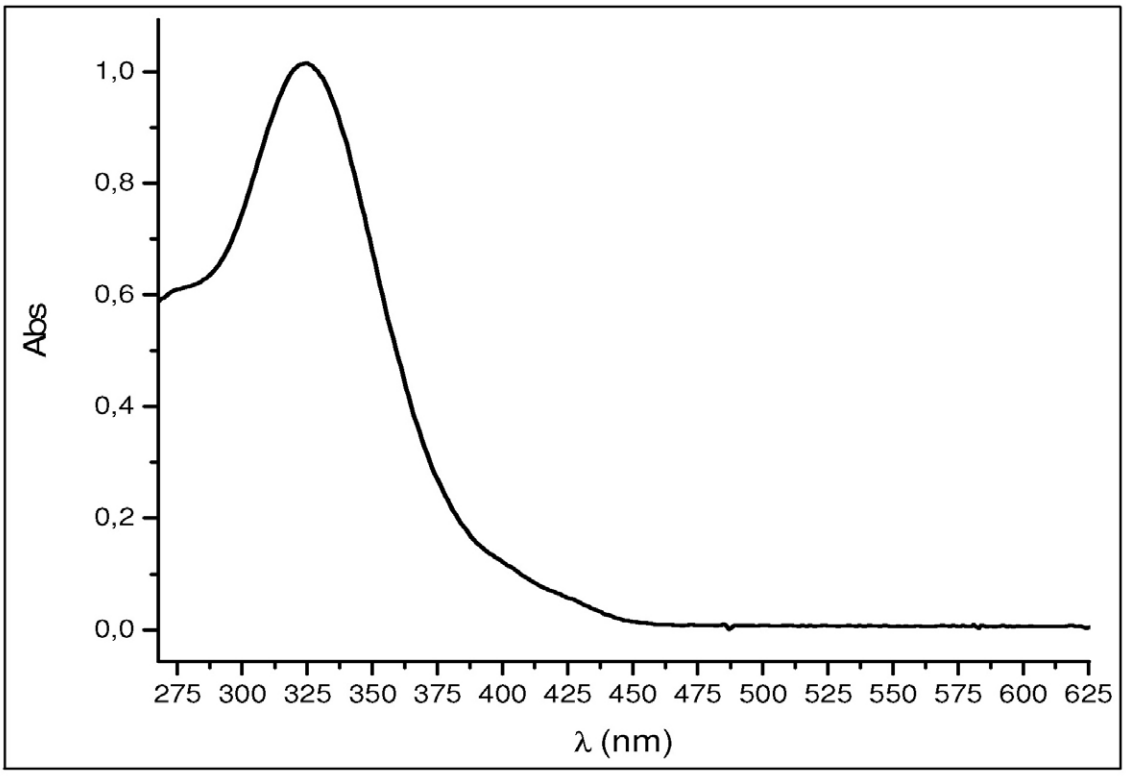


Figure S24. UV-Vis spectrum (DMSO) of compound **4**.

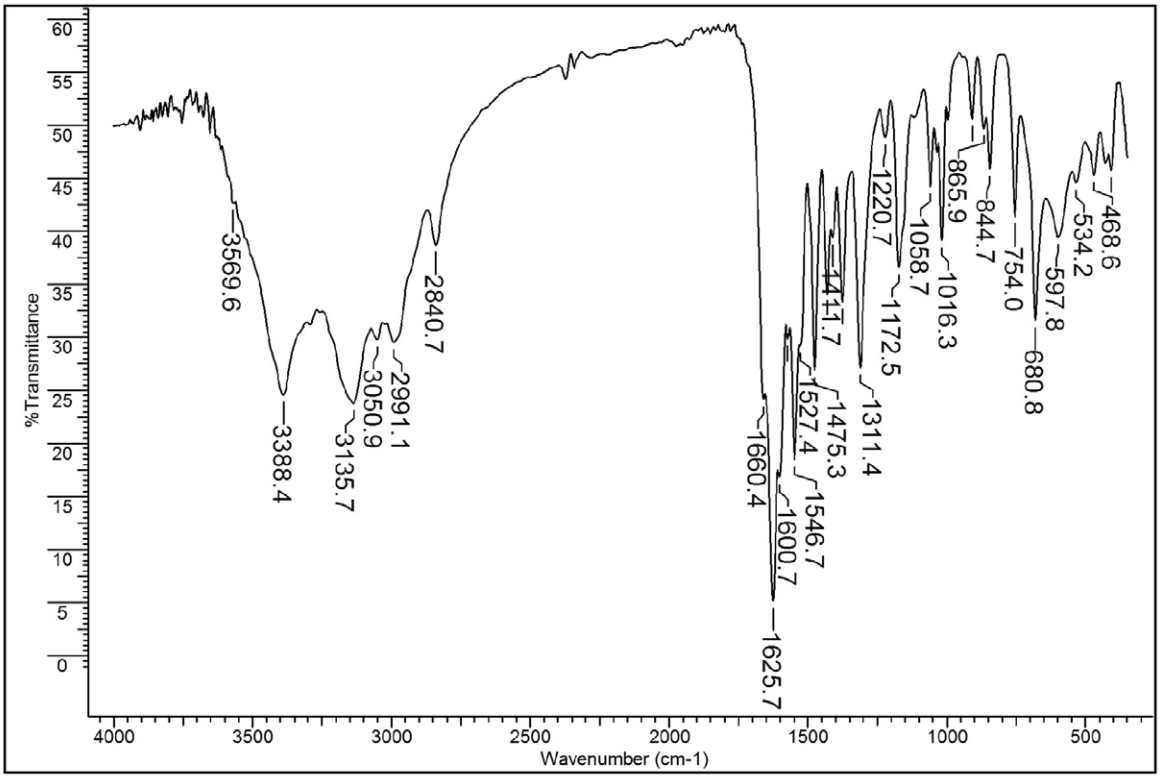


Figure S25. FTIR (KBr) spectrum of compound **5**.

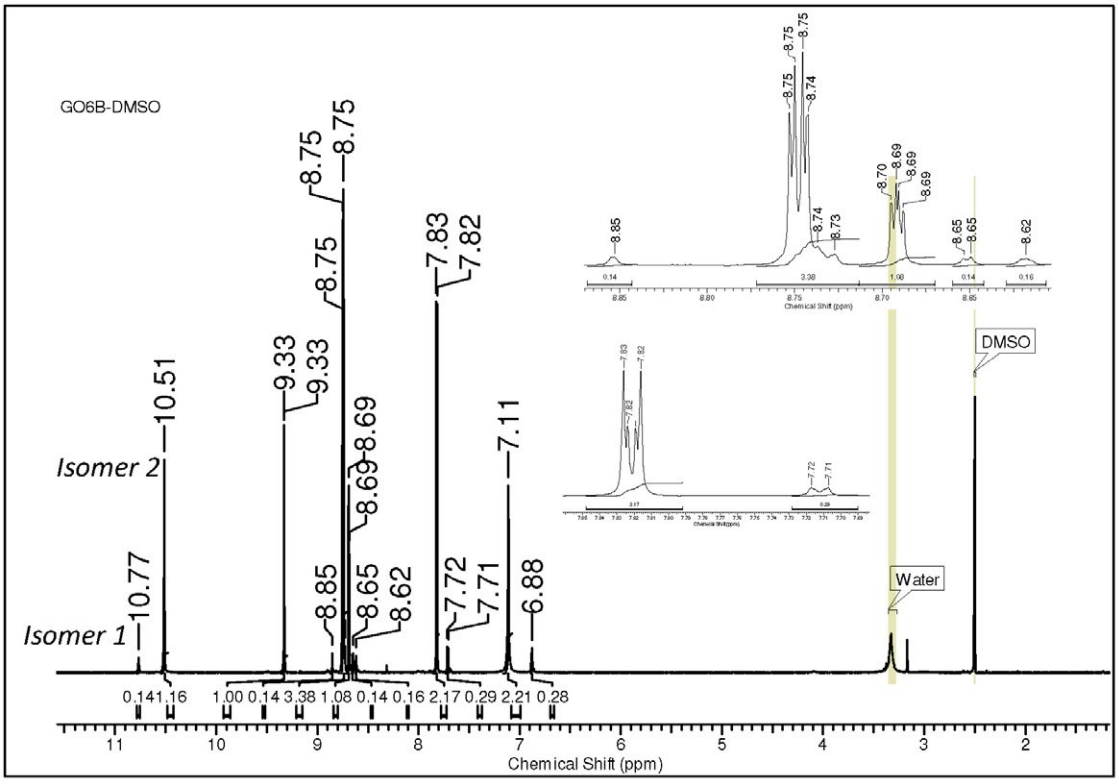


Figure S26. [1]H NMR spectrum (600 MHz, DMSO-d_6) of compound **5**.

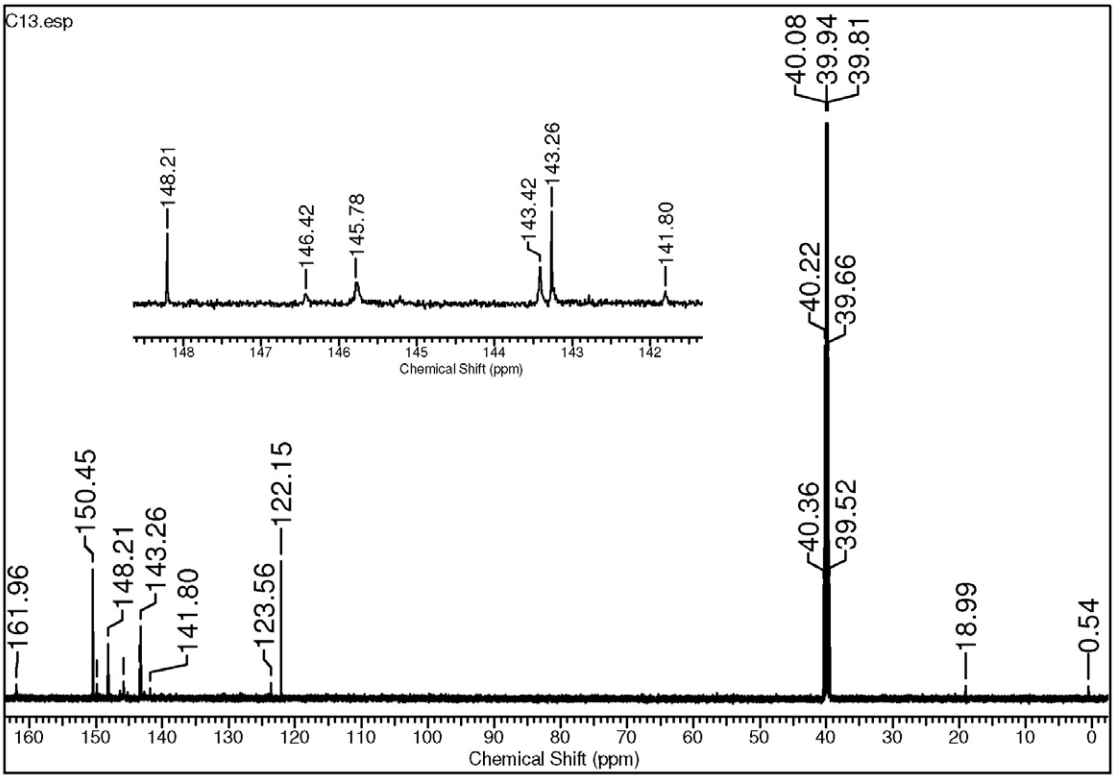


Figure S27. [13]C NMR spectrum (150 MHz, DMSO-d_6) of compound **5**.

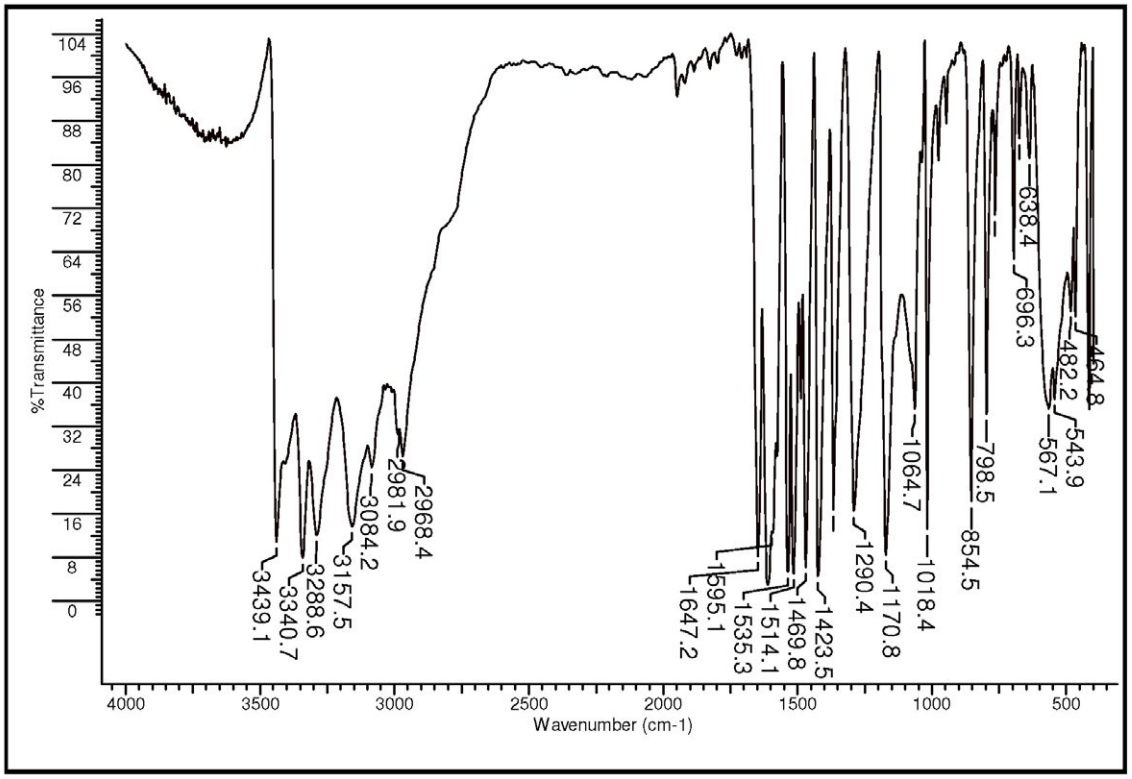


Figure S28. FTIR (KBr) spectrum of compound **6**.

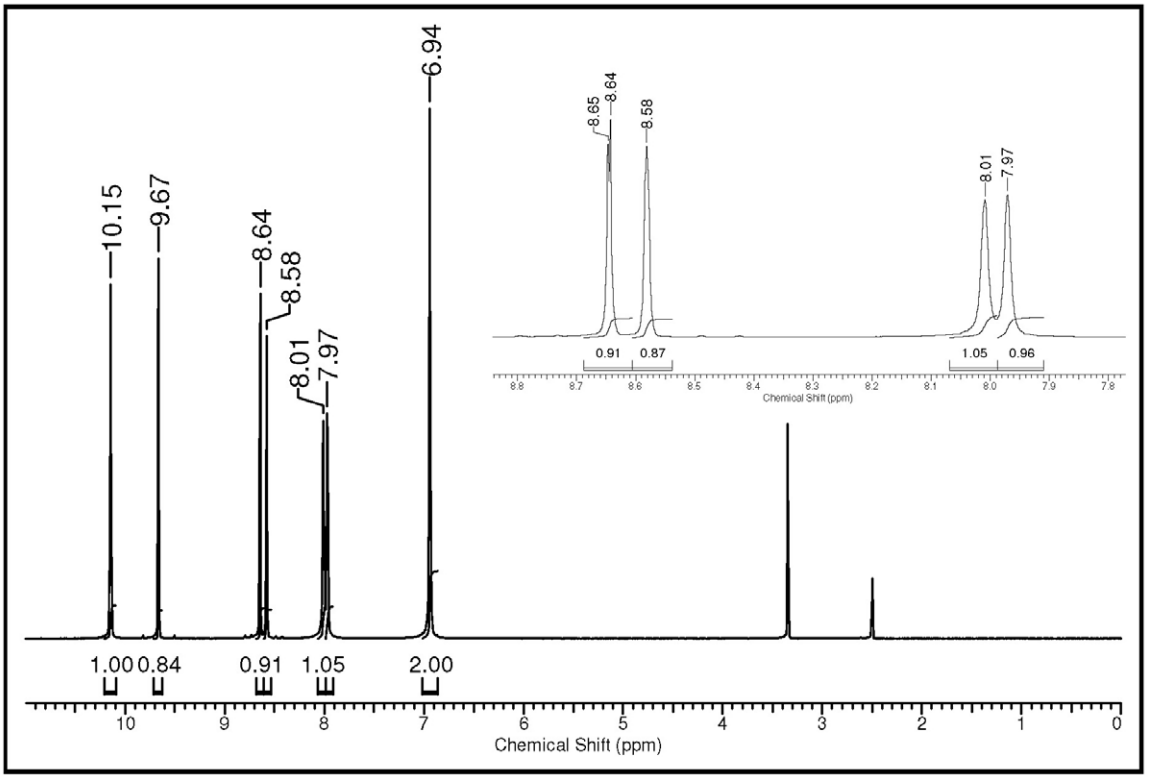


Figure S29. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of compound **6**.

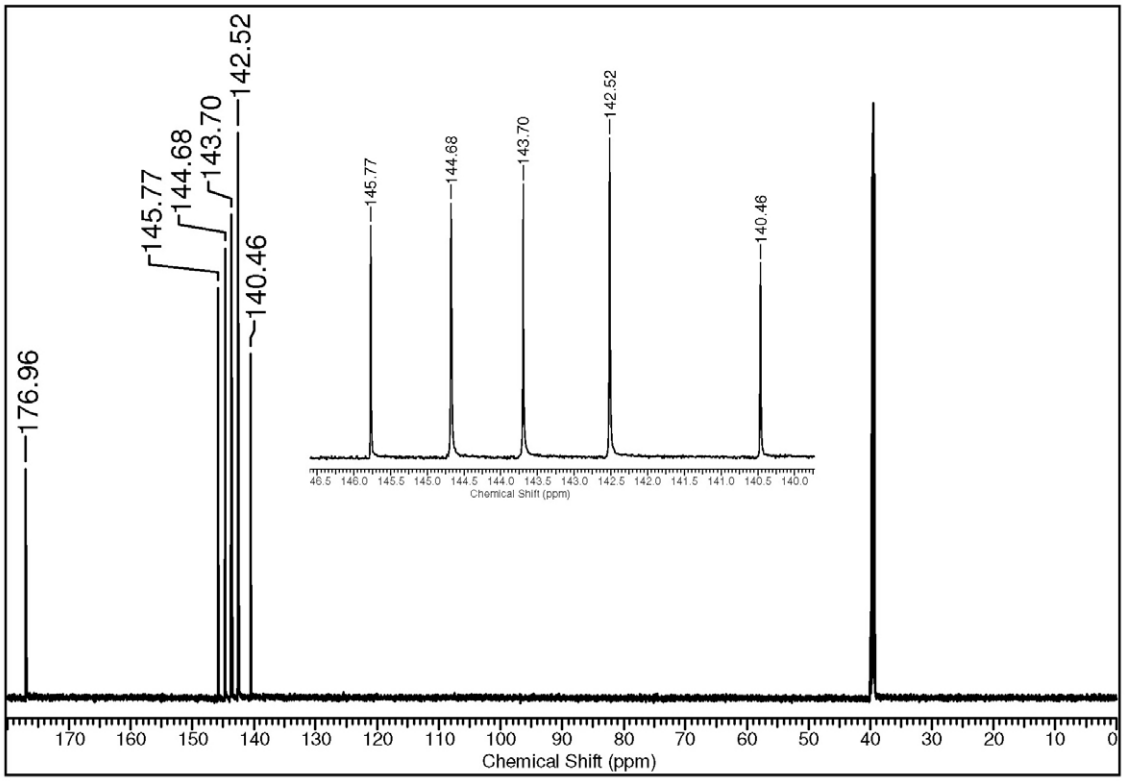


Figure S30. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of compound **6**.

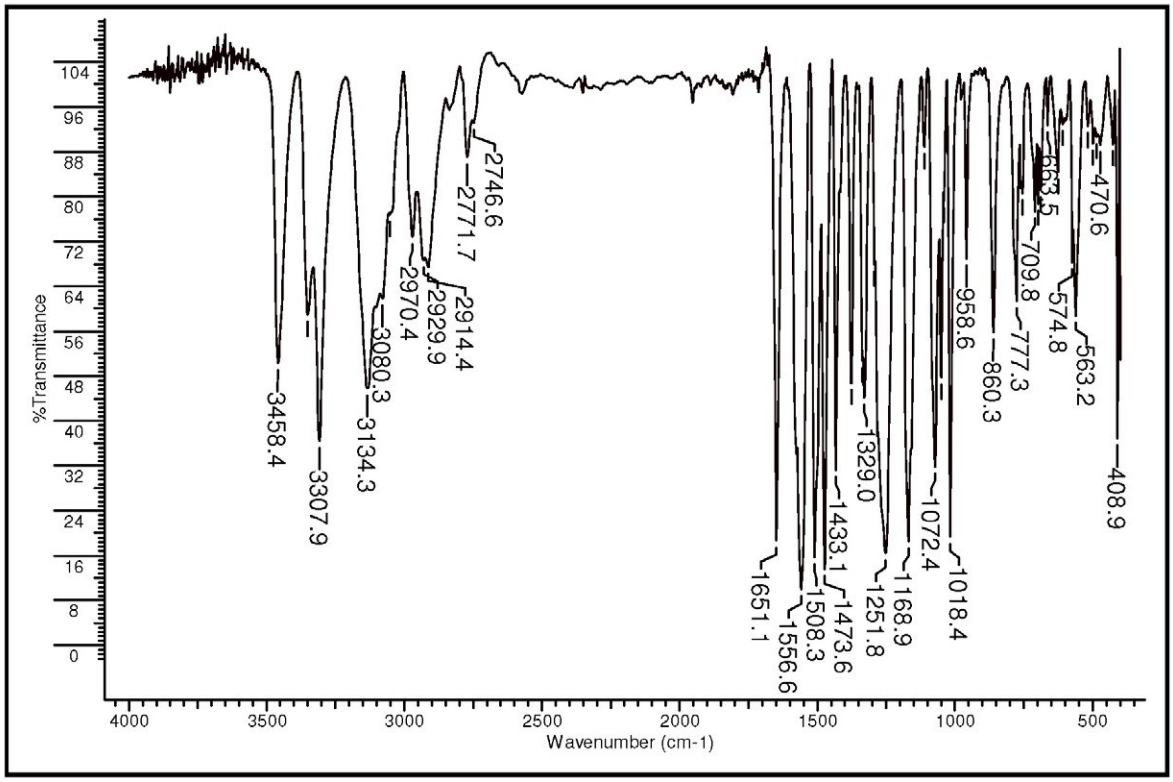


Figure S31. FTIR (KBr) spectrum of compound **7**.

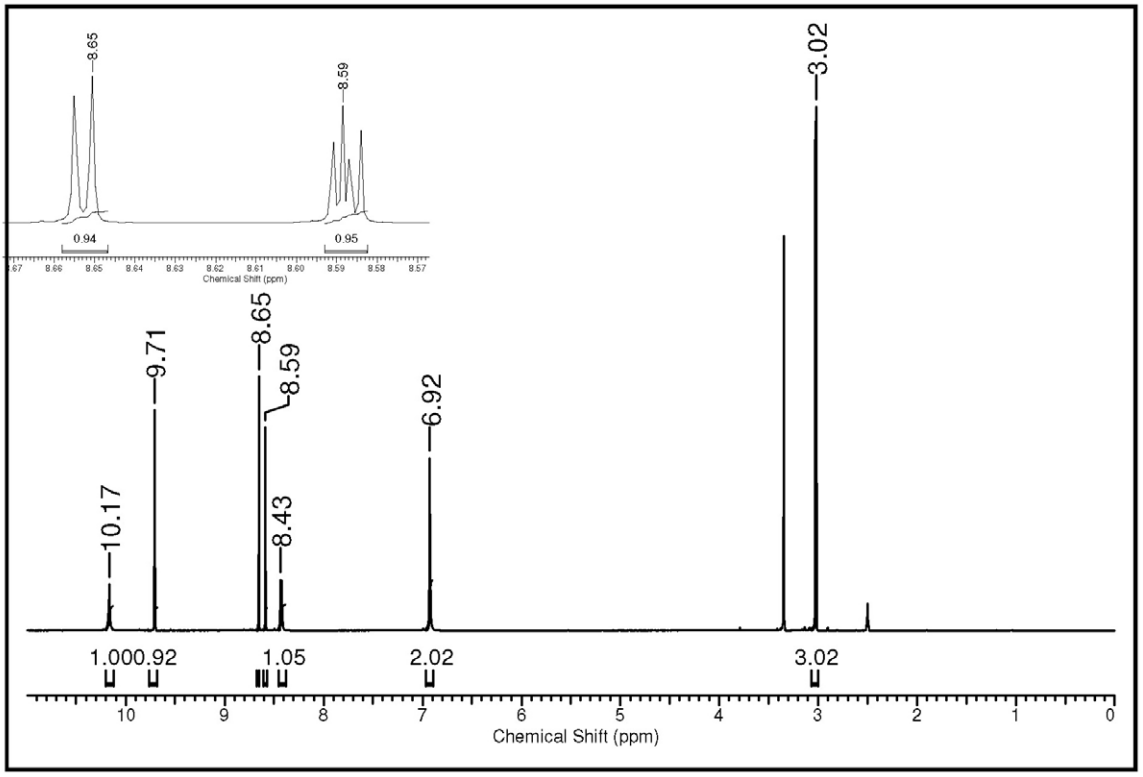


Figure S32. [1]H NMR spectrum (600 MHz, DMSO-d_6) of compound **7**.

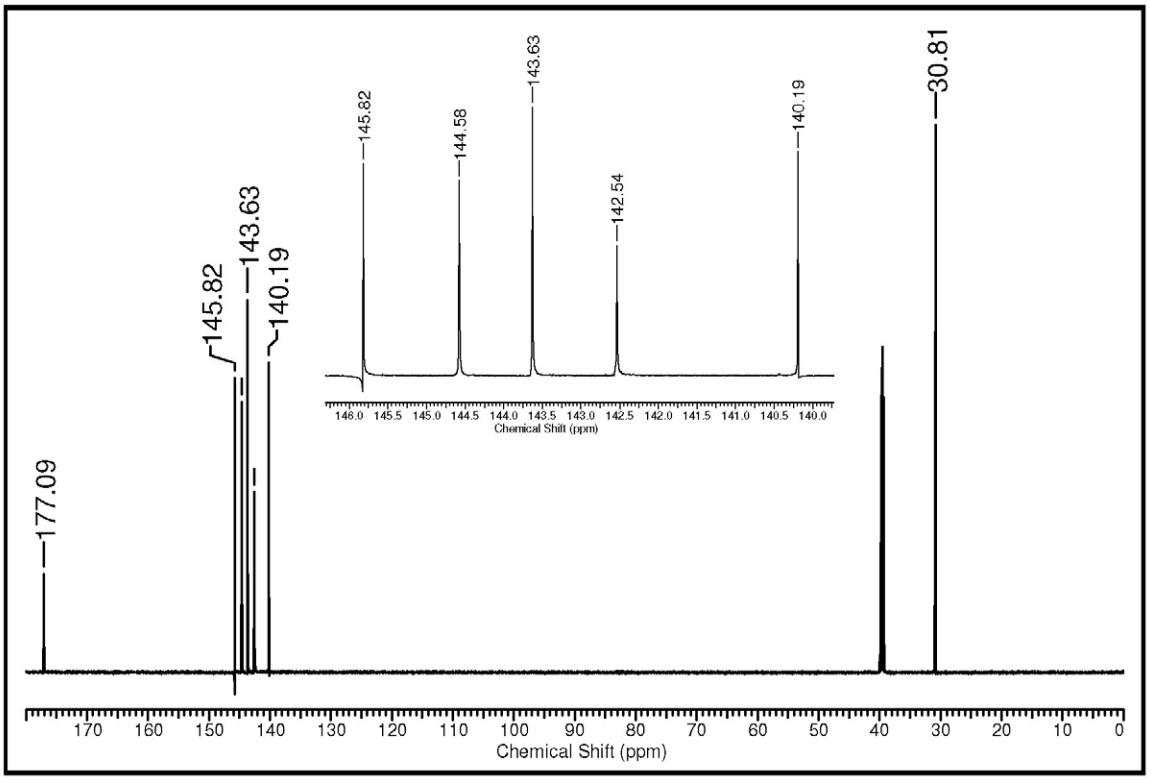


Figure S33. [13]C NMR spectrum (150 MHz, DMSO-d_6) of compound **7**.

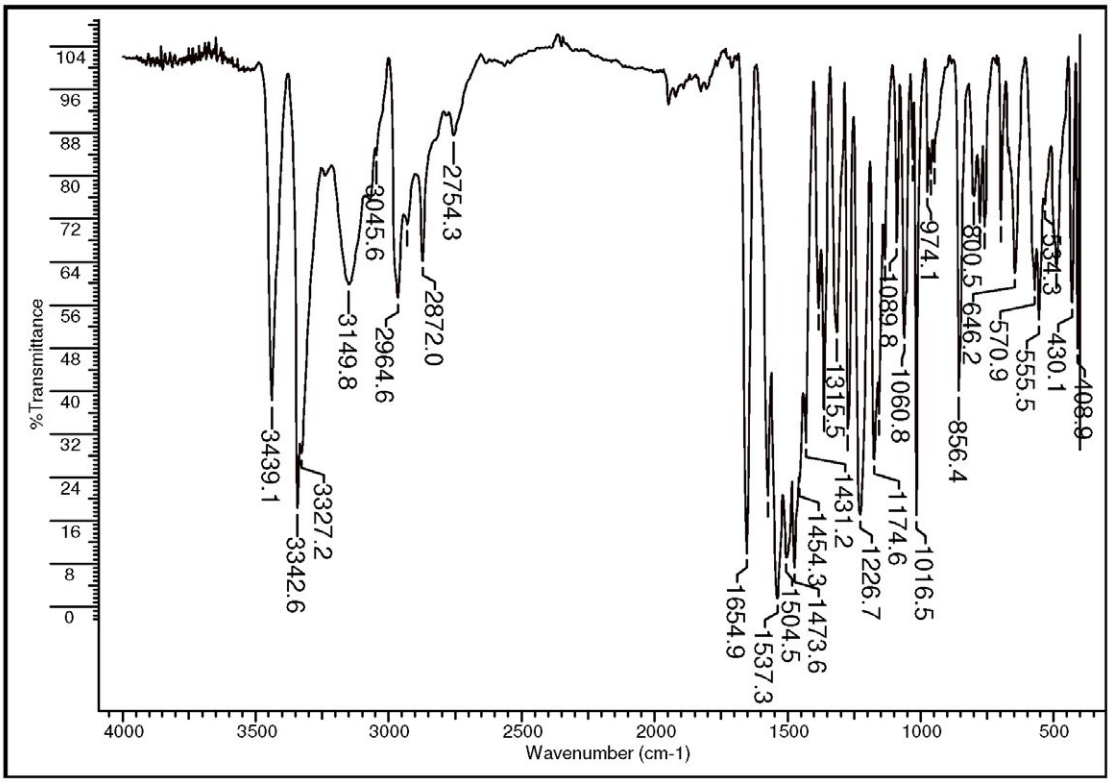


Figure S34. FTIR (KBr) spectrum of compound **8**.

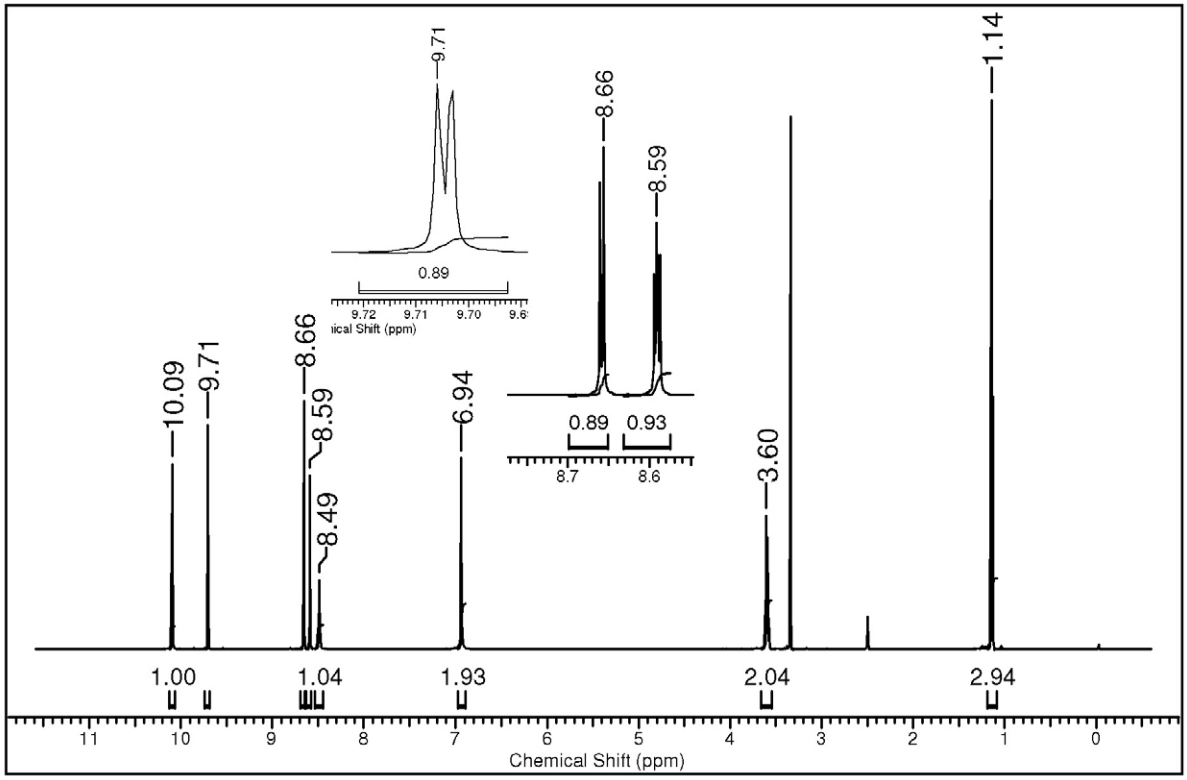


Figure S35. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of compound **8**.

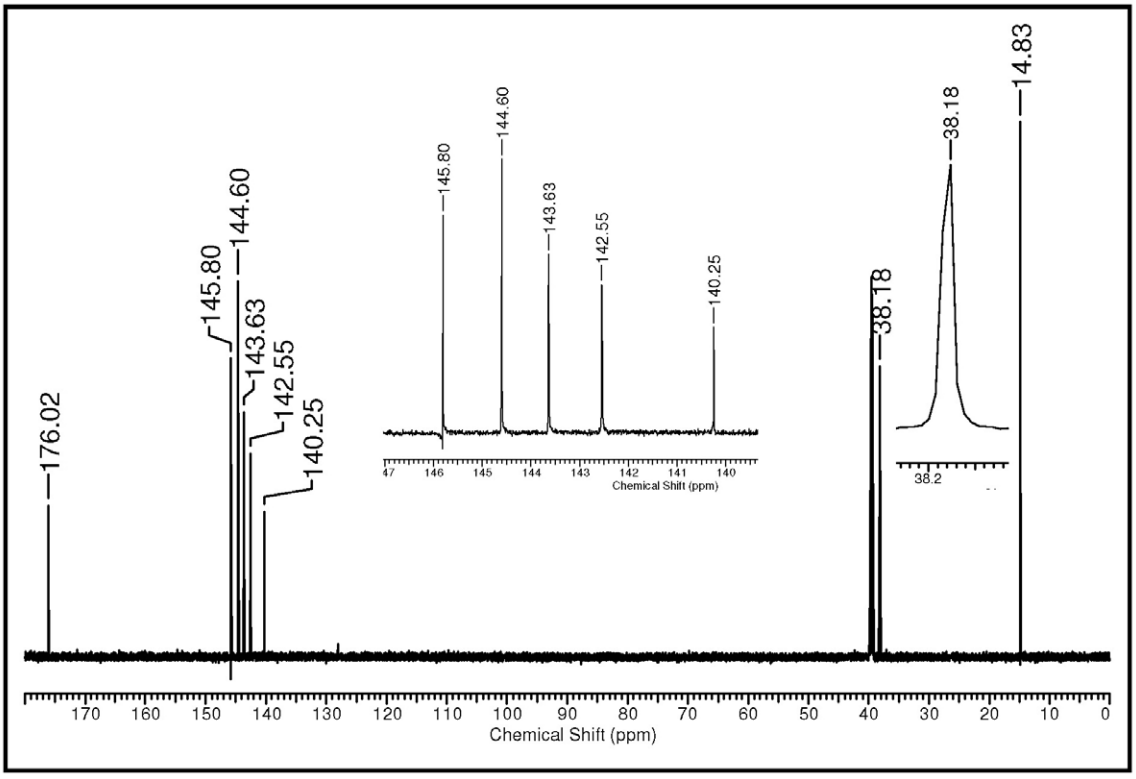
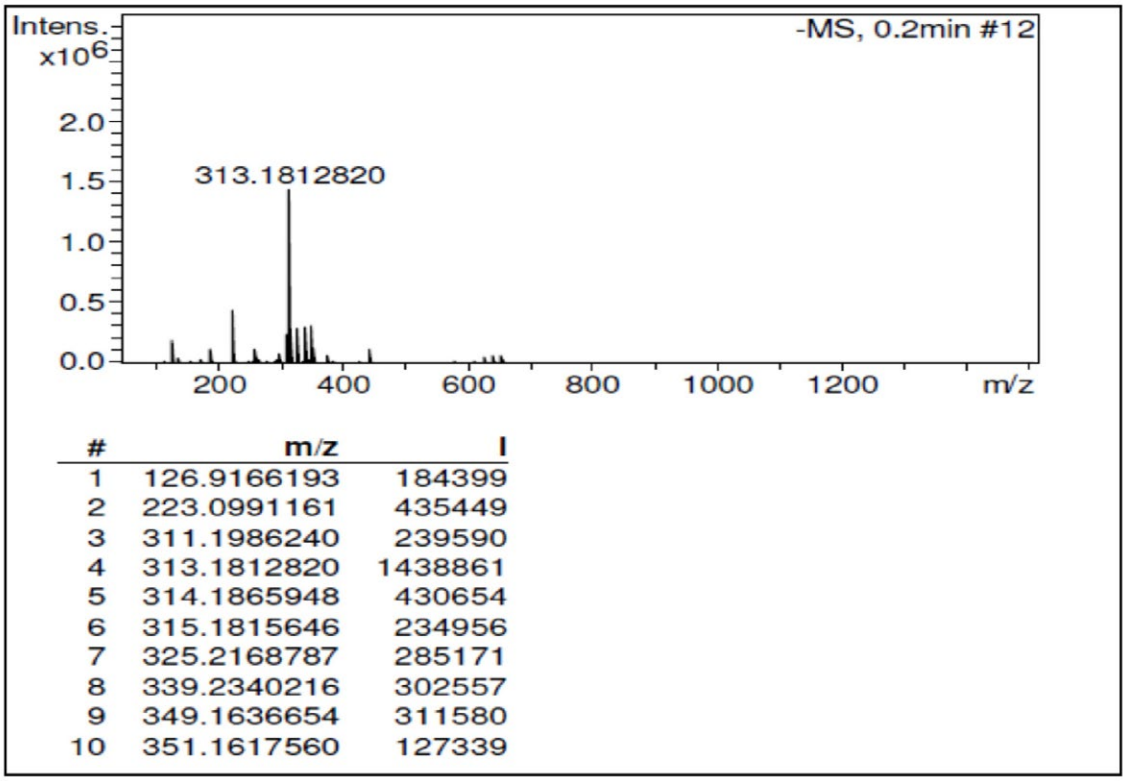


Figure S36. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of compound **8**.



#	m/z	I
1	126.9166193	184399
2	223.0991161	435449
3	311.1986240	239590
4	313.1812820	1438861
5	314.1865948	430654
6	315.1815646	234956
7	325.2168787	285171
8	339.2340216	302557
9	349.1636654	311580
10	351.1617560	127339

Figure S37. Mass spectrum (ESI-MS) of compound **8**.

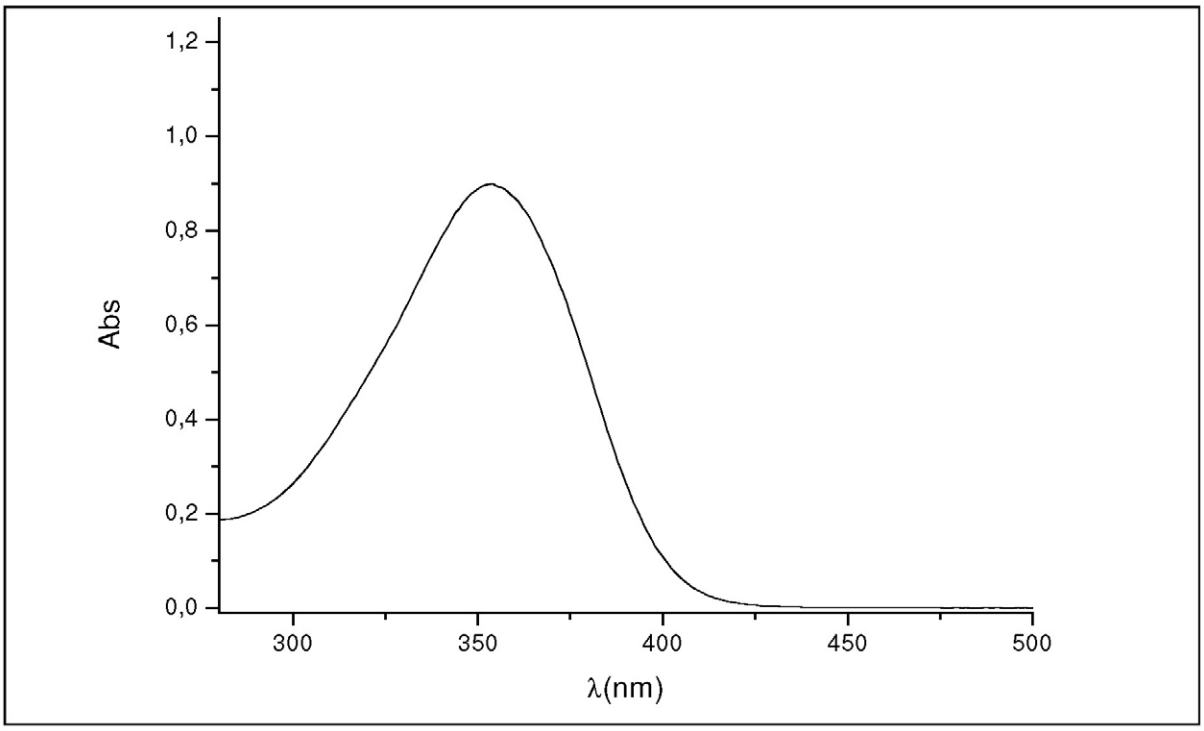


Figure S38. UV-Vis spectrum (DMF) of compound **8**.

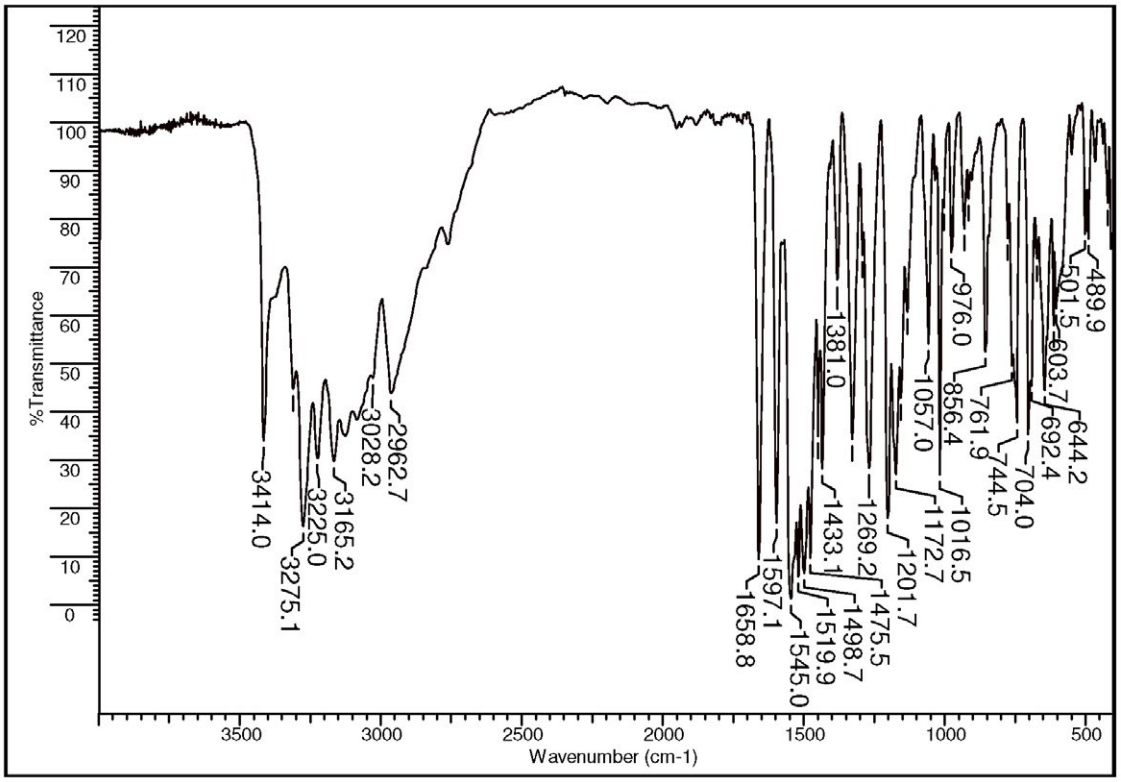


Figure S39. FTIR (KBr) spectrum of compound **9**.

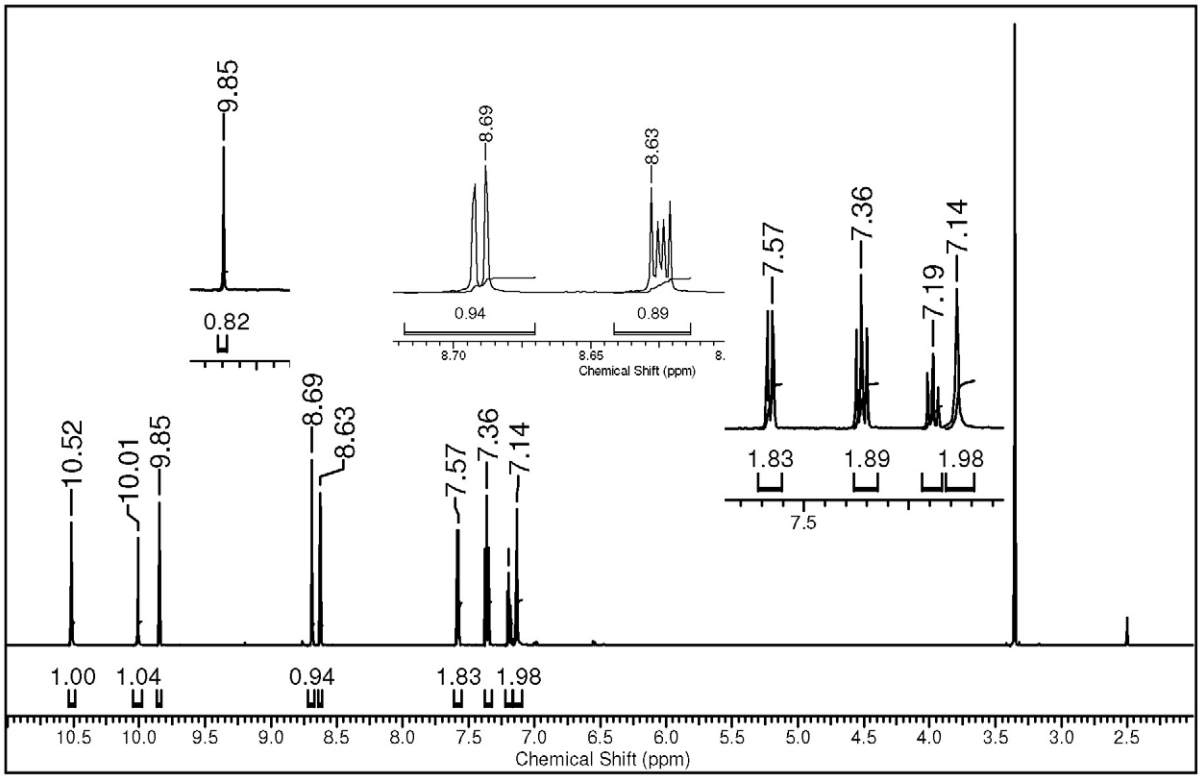


Figure S40. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of compound **9**.

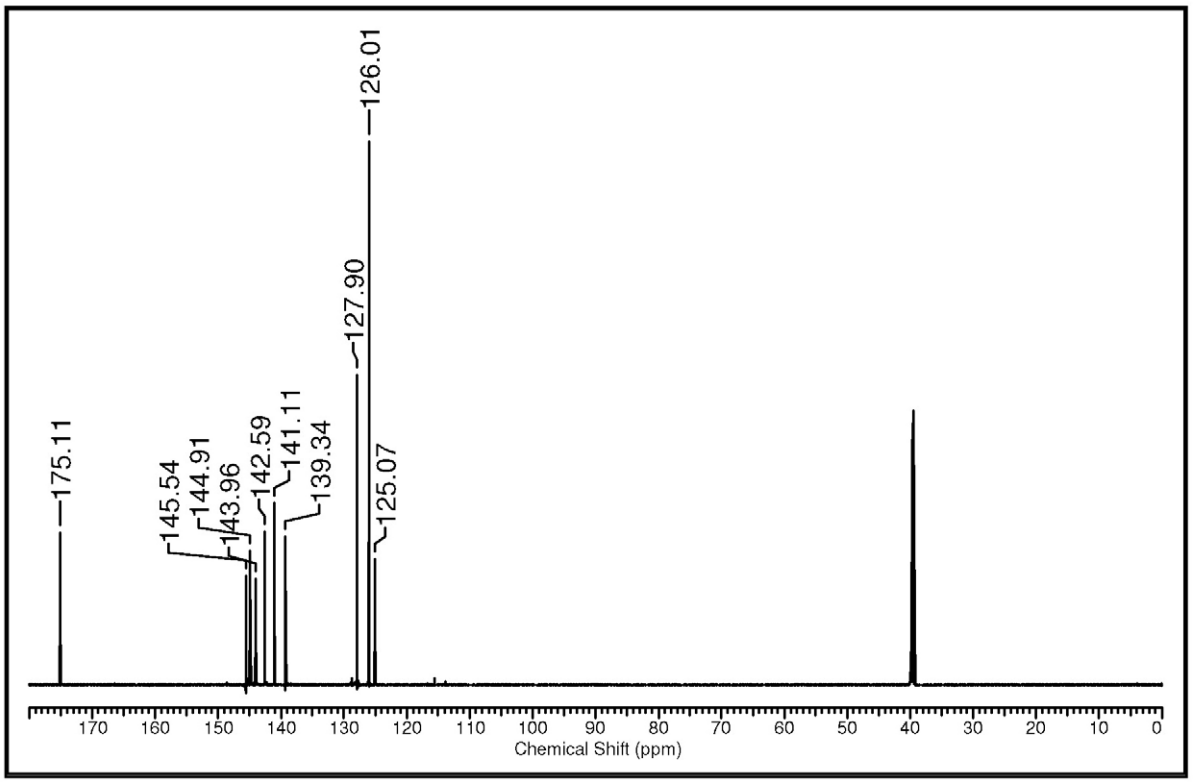
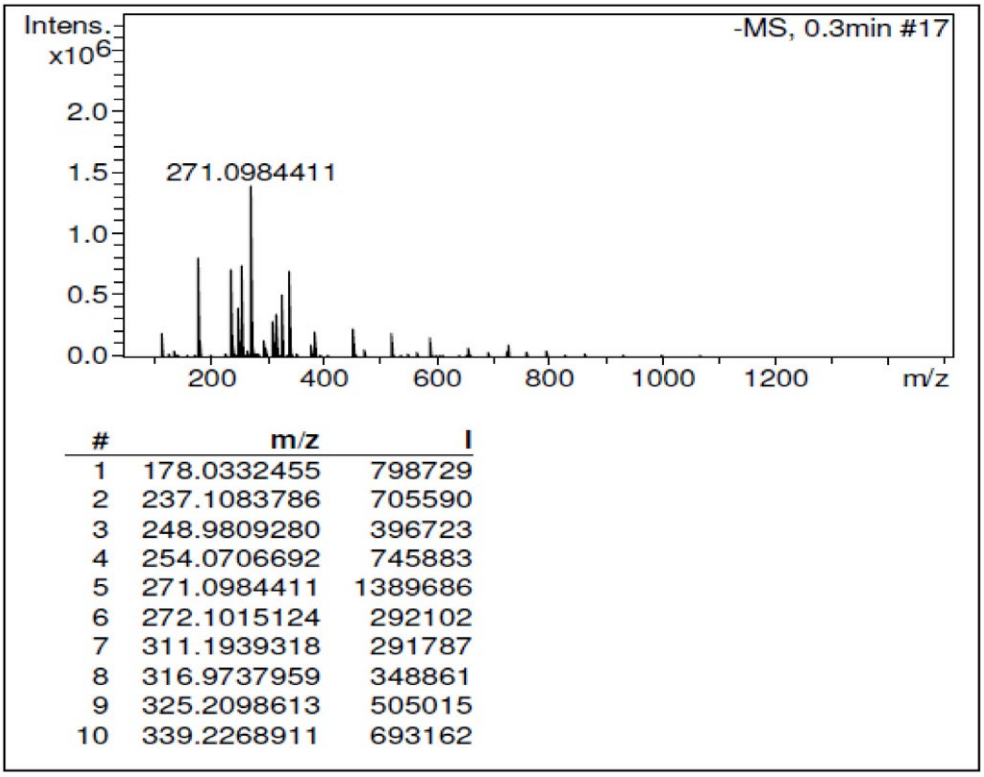


Figure S41. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of compound **9**.



#	m/z	I
1	178.0332455	798729
2	237.1083786	705590
3	248.9809280	396723
4	254.0706692	745883
5	271.0984411	1389686
6	272.1015124	292102
7	311.1939318	291787
8	316.9737959	348861
9	325.2098613	505015
10	339.2268911	693162

Figure S42. Mass spectrum (ESI-MS) of compound **9**.

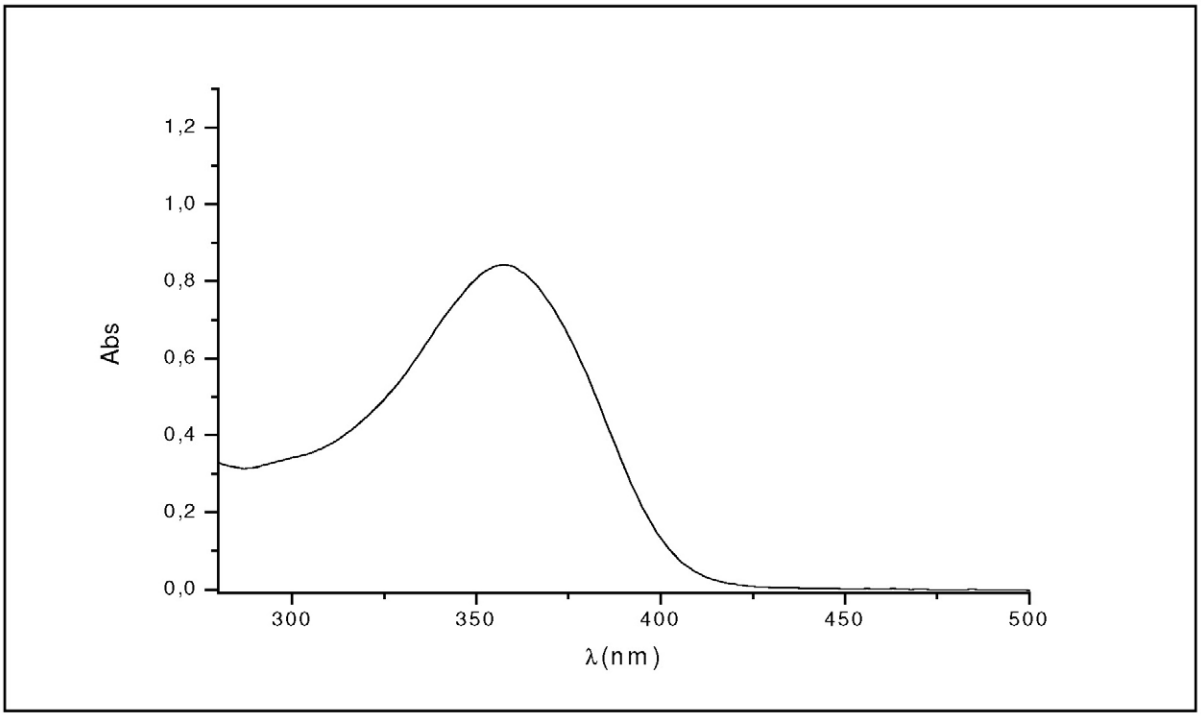


Figure S43. UV-Vis spectrum (DMF) of compound **9**.

Table S1. Crystallographic data of $[H_2PCIH]NO_3 \cdot H_2O$ (**1a**) and HPzAm4E (**8**)

Compound	$[H_2PCIH]NO_3 \cdot H_2O$ (**1a**)	HPzAm4E (**8**)
Empirical formula	$C_{12}H_{13}N_5O_5$	$C_8H_{12}N_6S$
Formula weight	307.27	224.30
Temperature / K	293.15	296.92
Crystal system	triclinic	monoclinic
Space group	P-1	$P2_1/n$
a[a] / Å	6.3407(4)	7.4889(3)
b[a] / Å	7.0760(6)	12.5626(5)
c[a] / Å	16.2140(12)	11.8649(4)
α[a] / degree	94.916(2)	90.00
β[a] / degree	99.164(2)	105.358(2)
γ[a] / degree	103.722(2)	90.00
Volume / Å^3	691.88(9)	1076.39(7)
Z[b]	2	4
ρ_{calc}[c] / (g cm^{-3})	1.475	1.384
μ[d] / mm^{-1}	0.118	0.278
F(000)[e]	320.0	472.0
Crystal size / mm^3	0.371 × 0.092 × 0.046	0.330 × 0.330 × 0.252
Radiation	Mo Kα (λ = 0.71073 Å)	Mo Kα (λ = 0.71073 Å)
2Θ range for data collection / degree	5.14 to 50.68	4.82 to 52.3
Index ranges	−7 ≤ h ≤ 7, −8 ≤ k ≤ 8, −19 ≤ l ≤ 19	−9 ≤ h ≤ 9, −15 ≤ k ≤ 15, −14 ≤ l ≤ 14
Reflections collected	22129	16447
Independent reflections	2533 [R_{int} = 0.0378, R_{sigma} = 0.0184]	2144 [R_{int} = 0.0341, R_{sigma} = 0.0175]
Data/restraints/parameters	2533/0/199	2144/3/143
Goodness-of-fit on F^2	1.032	1.094
Final R indexes [I >= 2σ (I)]	R_1 = 0.0454, wR_2 = 0.1088	R_1 = 0.0365, wR_2 = 0.0885
Final R indexes [all data]	R_1 = 0.0622, wR_2 = 0.1204	R_1 = 0.0478, wR_2 = 0.0972
Largest difference peak (hole) / (e Å^{-3})	0.29 (−0.24)	0.24 (−0.28)

[a]Lattice parameters; [b]number of atoms *per* unit cell; [c]calculated density; [d]absorption coefficient; [e]structure factor evaluated in the zeroth-order case h = k = l = 0.

Table S2. Selected bond distances for $[H_2PCIH]NO_3 \cdot H_2O$ (**1a**) and HPzAm4E (**8**) in comparison with HBPIH,[2] HPzAm4DH·H_2O[3] and HPzAm4M·$2H_2O$[3]

	Bond distance / Å		
	HBPIH (**3**)	$[H_2PCIH]NO_3 \cdot H_2O$ (**1a**)	
C2–C7	1.4904(15)	1.459(3)	
C7–N2	1.2961(1)	1.272(2)	
N2–N3	1.3678(1)	1.375(2)	
N3–C8	1.3601(1)	1.345(2)	
C8–C9	1.5053(1)	1.496(3)	
C8–O1	1.2156(1)	1.220(2)	
	HPzAm4DH·H_2O	HPzAm4M·$2H_2O$	HPzAm4E (**8**)
C2–C7	1.479(6)	1.484(3)	1.483(2)
C7–N2	1.289(5)	1.295(2)	1.283(2)
N2–N3	1.337(5)	1.380(2)	1.3889(19)
N3–C8	1.355(5)	1.350(3)	1.359(2)
C8–S1	1.690(5)	1.696(2)	1.6765(17)
C8–N4	1.316(6)	1.326(2)	1.323(2)
N4–C9	–	–	1.456(2)
C7–N5	1.335(6)	1.341(2)	1.359(2)

Table S3. Selected angles for $[H_2PCIH]NO_3 \cdot H_2O$ (**1a**) and HPzAm4E (**8**) in comparison with HBPIH,[2] $HPzAm4DH \cdot H_2O$[3] and $HPzAm4M \cdot 2H_2O$[3]

	Bond angle / degree		
	HBPIH	$[H_2PCIH]NO_3 \cdot H_2O$ (**1a**)	
N1–C2–C7	118.05(9)	114.18(17)	
C2–C7–N2	127.53(9)	121.57(18)	
C7–N2–N3	117.83(9)	115.20(16)	
N2–N3–C8	120.29(9)	118.86(15)	
N3–C8–O1	124.84(1)	124.51(19)	
N3–C8–C9	113.26(9)	115.26(16)	
	$HPzAm4DH \cdot H_2O$	$HPzAm4M \cdot 2H_2O$	HPzAm4E (**8**)
N1–C2–C7	118.6(4)	117.1(2)	116.79(15)
C2–C7–N2	113.8(4)	115.7(2)	116.54(14)
C7–N2–N3	119.0(4)	116.8(2)	117.19(14)
N2–N3–C8	117.4(4)	118.5(2)	116.93(14)
N3–C8–S1	120.6(4)	120.1(2)	120.73(13)
N3–C8–N4	115.3(5)	116.8(2)	115.62(15)
C8–N4–C9	–	–	125.40(16)

Table S4. Selected dihedral angles for $[H_2PCIH]NO_3 \cdot H_2O$ (**1a**) and HPzAm4E (**8**)

	Dihedral angle / degree	
	$[H_2PCIH]NO_3 \cdot H_2O$ (**1a**)	HPzAm4E (**8**)
N1–C2–C7–N2	178.83(18)	177.20(16)
C2–C7–N2–N3	179.73(17)	177.87(14)
C7–N2–N3–C8	178.14(18)	171.71(16)
N2–N3–C8–O1	–1.8(3)	–
N2–N3–C8–S1	–	173.94(12)

Table S5. Hydrogen bond distances and angles for $[H_2PCIH]NO_3 \cdot H_2O$ (**1a**) and HPzAm4E (**8**)

Compound	D–H···A	D–H / Å	H···A / Å	D···A / Å	D–H···A / degree
1a	N4–H4···O11[a]	0.86	2.07	2.872(3)	154
	N4–H4···O13[a]	0.86	2.09	2.835(3)	145
	N4–H4···N1[a]	0.86	2.46	3.308(3)	170
	N3–H3···O1W[b]	0.86	1.96	2.799(2)	166
	O1W–H1WA···N1[c]	0.93	2.03	2.917(2)	158
	O1W–H1WB···O1	0.90	2.04	2.859(2)	150
	O1W–H1WB···N2	0.90	2.54	3.220(2)	132
8	N4–H4···N2	0.86	2.15	2.564(2)	109
	N3–H3···N6[d]	0.86	2.34	3.119(2)	151
	N5–H5A···N1	0.85	2.28	2.692(2)	110(2)
	N5–H5B···S1[e]	0.85	2.70	3.364(2)	136(2)

Symmetry codes: [a]–x + 2, –y + 2, –z + 1; [b]x + 1, y, z; [c]–x + 1, –y + 2, –z (compound **1a**); [d]–x + 1/2, y – 1/2, –z + 3/2; [e]–x, –y + 1, –z + 1 (compound **8**).

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