

Supplementary file

Synthesis, characterization and biological evaluation of fused thiazolo[3,2-*a*]pyrimidine derivatives

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X-ray crystallography

Diffraction quality crystals of **8e** were chosen and the single crystal X-ray diffraction data were collected on a CCD detector-based diffractometer-SMART APEX from Bruker-Nonius AXS using Mo-K α radiation ($\lambda = 1.54184 \text{ \AA}$) at 273(2) K. The lattice parameters were determined from least-squares analysis, and reflection data were integrated using the program SHELXTL. The structure was solved by direct methods using SHELXS-2013 and refined by full-matrix least squares on F^2 with anisotropic displacement parameters for non-H atoms, using SHELXL-2013. The positions of all aromatic and aliphatic C–H and O–H hydrogen atoms were calculated geometrically, and a riding model was used in the refinement. All the N–H hydrogen's were refined from difference Fourier maps. The software used to prepare material for publication was Mercury 2.3 (Build RC4), ORTEP-3 and X-Seed.

Single crystal X-ray diffraction analysis of compound **8e** was carried out on a crystal obtained from the reaction mixture. The compound was crystallizes in the triclinic space group $P-1$ with one completely protonated **8e**, one partially protonated **8e**, one Br⁻, one partially proton transferred HBr and three molecules of acetic acid in the asymmetric unit. The two **8e** molecules crystallized in the asymmetric unit are two conformational isomers. The two phenyl groups of two **8e** molecules are not essentially coplanar with the thiazole rings (N1-C2-C15-C20 = -126.79° and N3-C30-C43-C44 = -101.36°). The two CH₂ groups on the two quinazoline moieties of **8e** are not oriented in a similar fashion (Torsion angles: C10-C5-C4-C12 = -40.47° and C38-C33-C32-C40 = 24.24°). The two HBr molecules are crystallized along with the two **8e** molecules in the crystal structure. One of the HBr molecules transfer the proton completely to one **8e** molecule to pyrimidine nitrogen (N2) and the other HBr molecule partially transfers the proton to pyrimidine nitrogen (N4) of second **8e** molecule. Among the three acetic acid molecules, two are forming carboxylic acid dimer synthon with O–H \cdots O hydrogen bonds. The third molecule of acetic acid interacting with the

inversion related **8e** molecules *via* C–H...O hydrogen bonding. The overall structure is a one dimensional tape like structure. Further, the crystal structure is stabilized by weak N–H...Br and C–H...O interactions. The absolute configuration at chiral centre (C3 in the crystal structure) of the molecule is ‘S’. A summary of the crystallographic data and structure refinement details are given in Table 4. The geometrical parameters of hydrogen bonds are listed in Table 5. The ORTEP representation of the molecular structure of **8e** is shown in Figure 2 (main document), and the packing diagram is given in Figure 4.

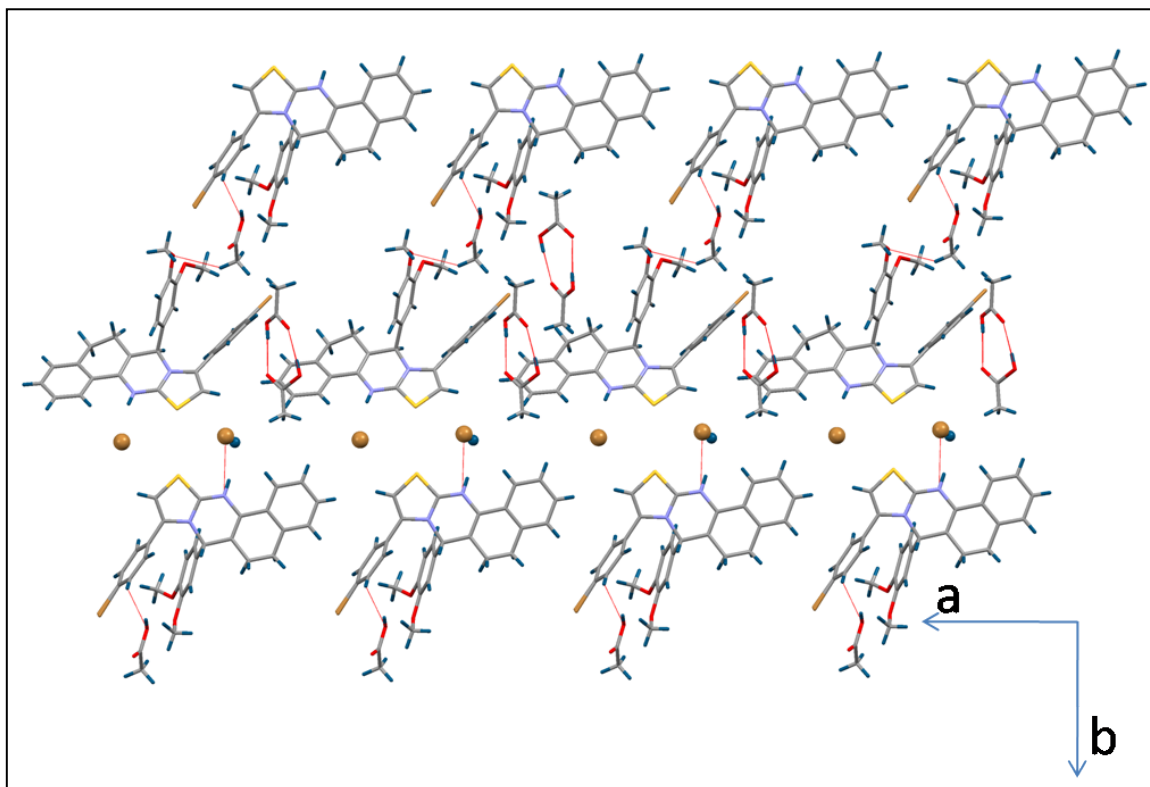


Figure 4. Packing diagram of compound **8e**.

Table 4. Crystallographic and experimental data of **8e**.

	8e
Empirical formula	C ₆₂ H ₆₁ Br ₄ N ₄ O ₁₀ S ₂
Formula weight	1408.29
Temperature (K)	273(2)
Wavelength (Å)	1.54184
Crystal system, Space group	Triclinic, <i>P</i> -1
Unit cell parameters (Å, °)	$a = 12.9000(12)$ $b = 14.6334(14)$ $c = 16.9440(16)$ $\alpha = 87.112(2)$ $\beta = 84.698(2)$ $\gamma = 74.154(2)$
Volume (Å ³)	3062.8(5)
<i>Z</i>	4
Crystal size (mm ³)	0.38 x 0.34 x 0.22
<i>D</i> _{calc} (g/m ³)	1.527
<i>F</i> (0 0 0)	1428.1
Absorption coefficient (mm ⁻¹)	2.776
θ range for data collection (°)	1.447-26.079
Index ranges	$-15 \leq h \leq 15$ $-18 \leq k \leq 18$ $-20 \leq l \leq 20$
Reflections collected	27220
Independent reflections	7611 [R(int) = 0.0580]
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data / restraints / parameters	11939 / 0 / 773
Final R indices (<i>I</i> > 2σ(<i>I</i>))	R ₁ = 0.0454, wR ₂ = 0.1059
R indices (all data)	R ₁ = 0.0845, wR ₂ = 0.1218
Goodness-of-fit on <i>F</i> ²	1.016

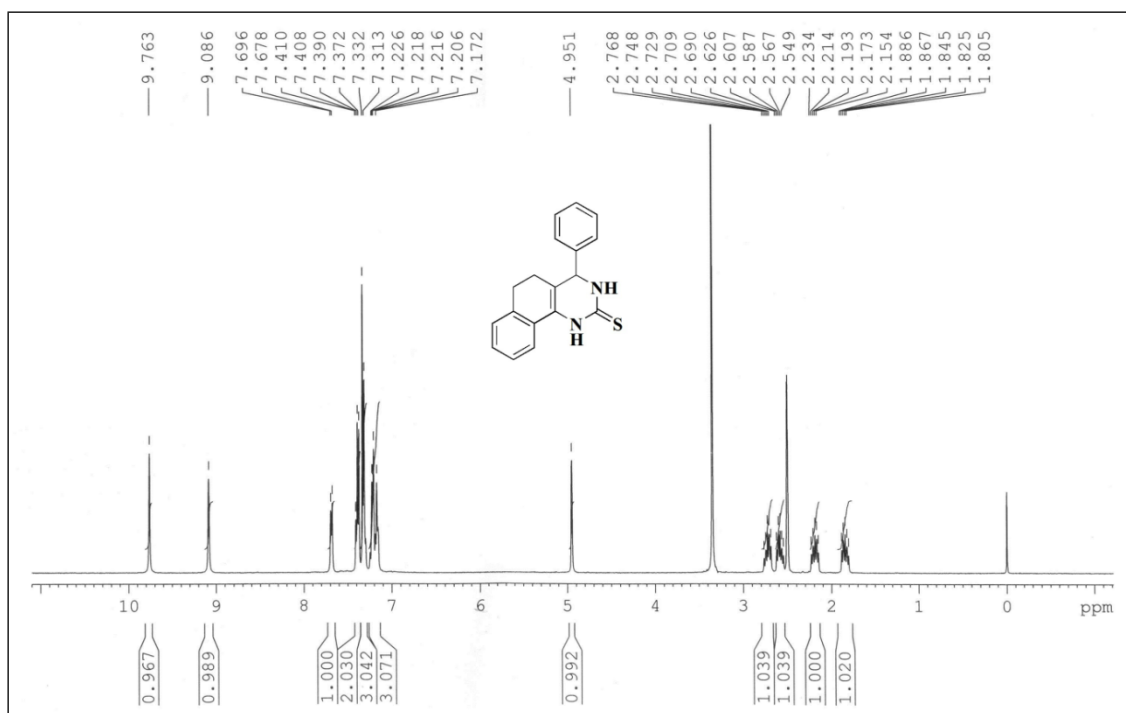
Table 5. Geometrical parameters of hydrogen bonds in **8e**.

D–H···A^a	D–A (Å)	H···A (Å)	D–H···A (°)
N(2)–H(2)···Br(4)	3.353(3)	2.36	167
N(4)–H(62A)···Br(3)	3.211(3)	2.26	156
O(6)–H(63)···Br(4)	3.317(4)	2.37	162
O(10)–H(64)···O(7)	2.773(17)	1.89	148
O(8)–H(65)···O(9)	2.859(9)	1.88	171
O(8)–H(65)···O(10)	3.507(13)	2.72	137
C(5)–H(5A)···S(2)	3.544(4)	2.75	130
C(9)–H(9)···Br(4)	3.799(5)	2.74	166
C(22)–H(22)···O(5)	3.454(6)	2.37	179
C(32)–H(32B)···O(3)	3.721(5)	2.78	146
C(32)–H(32B)···O(4A)	3.427(6)	2.66	127
C(45)–H(45)···O(1)	3.495(6)	2.70	130
C(47)–H(47)···Br(4)	3.894(4)	3.10	131
C(47)–H(47)···O(6)	3.282(5)	2.49	129
C(61)–H(61A)···O(5)	3.545(10)	2.62	143

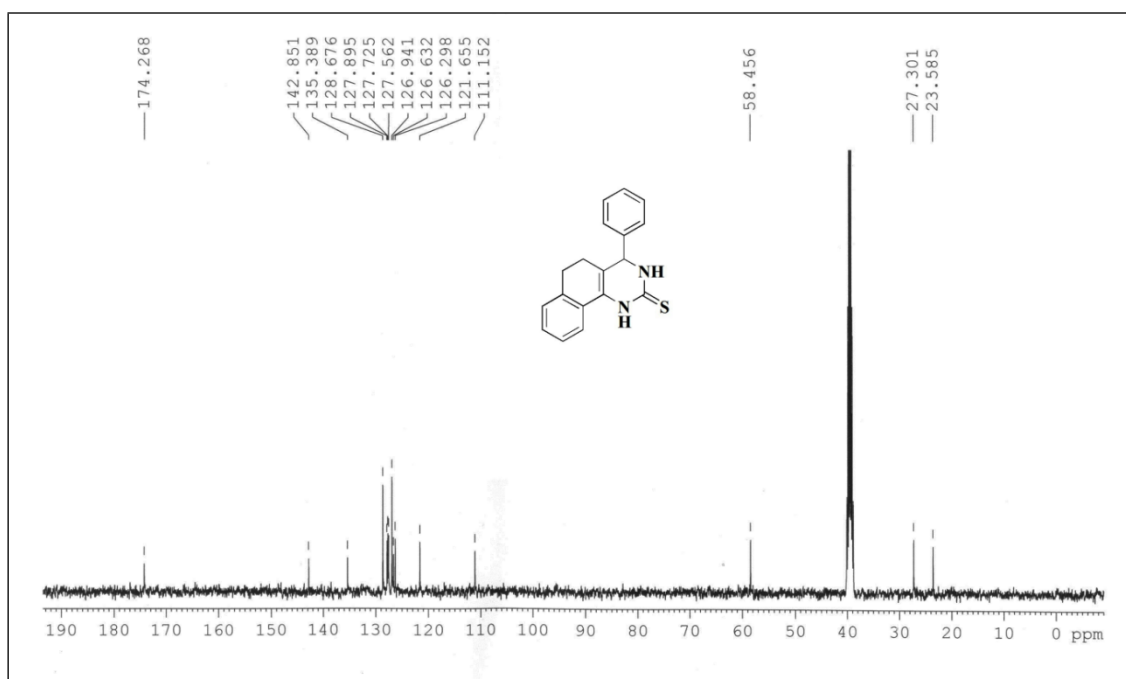
^a All of the C–H, N–H and O–H bonds are neutron normalized to 1.083, 1.009 and 0.983 Å respectively.

Spectra

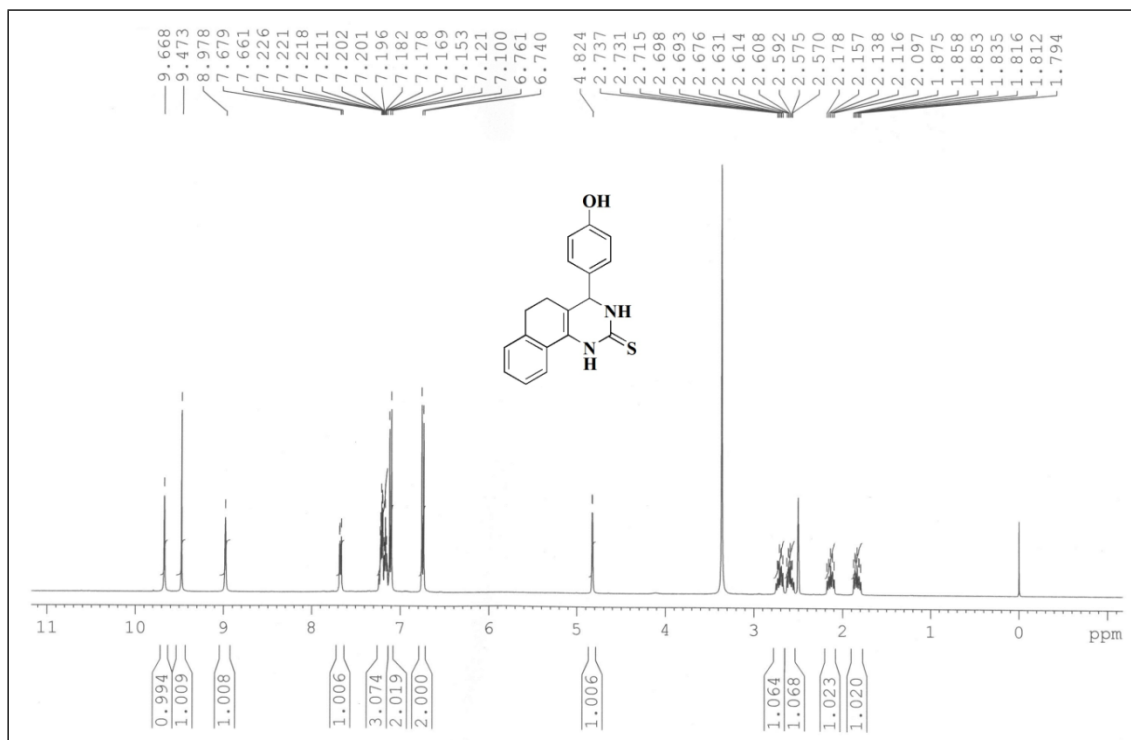
Compound 4a: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



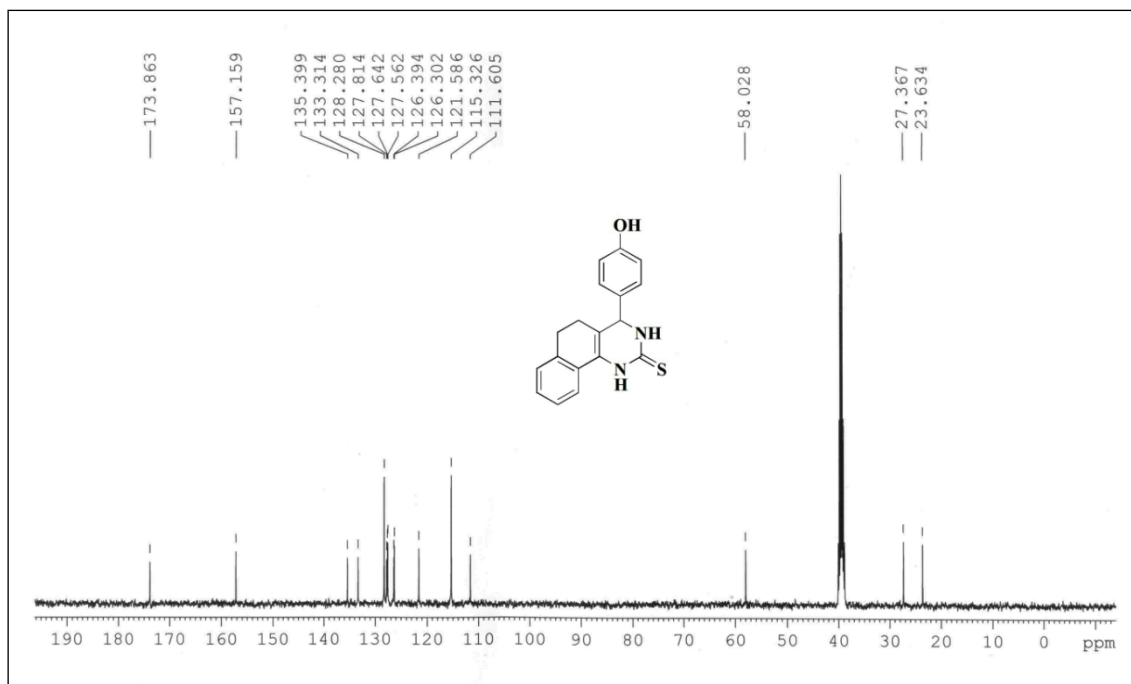
Compound 4a: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



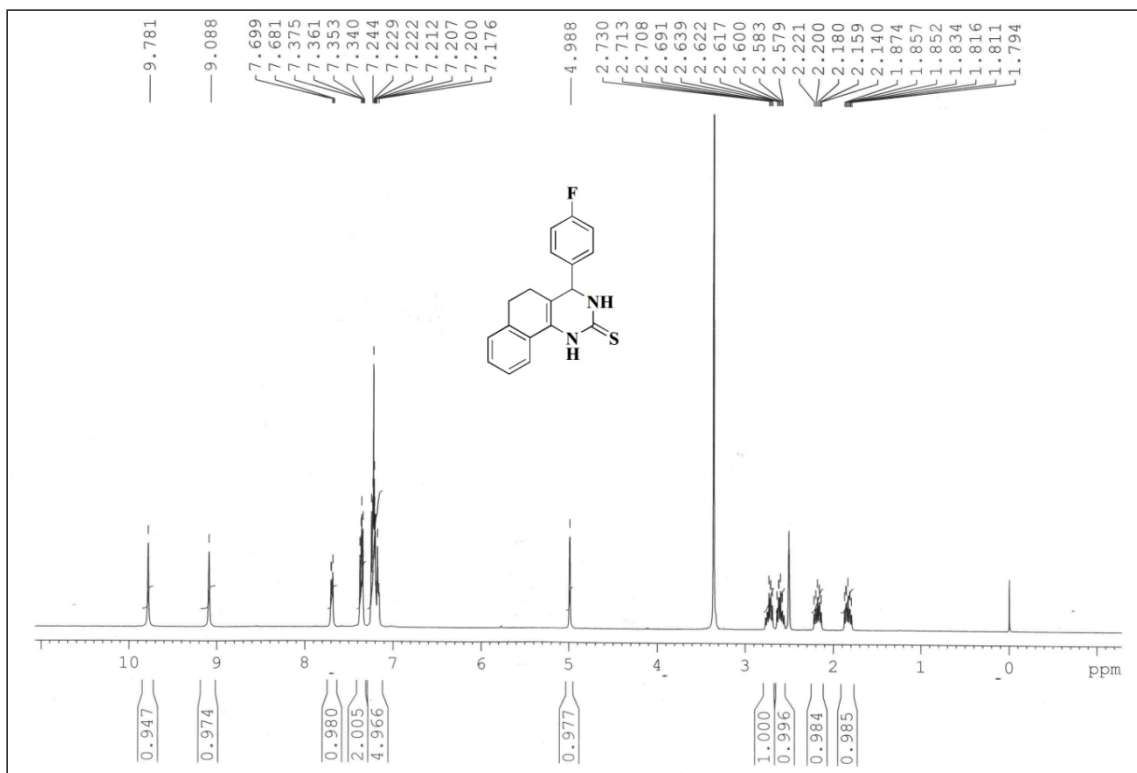
Compound 4b: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



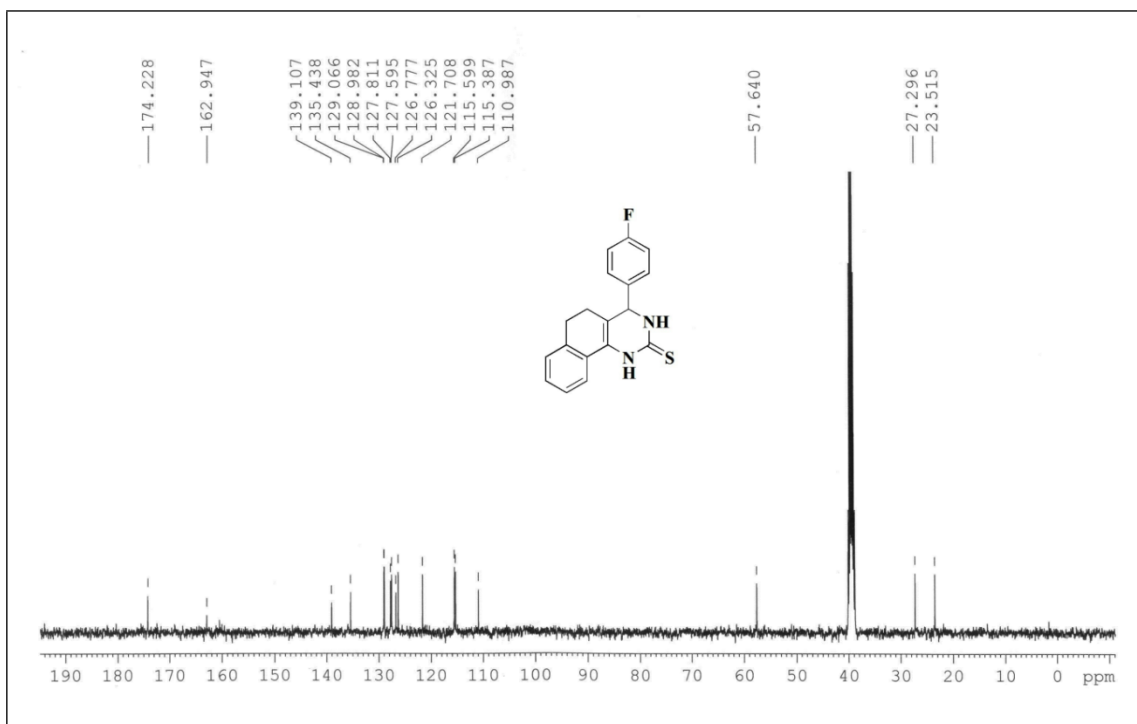
Compound 4b: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



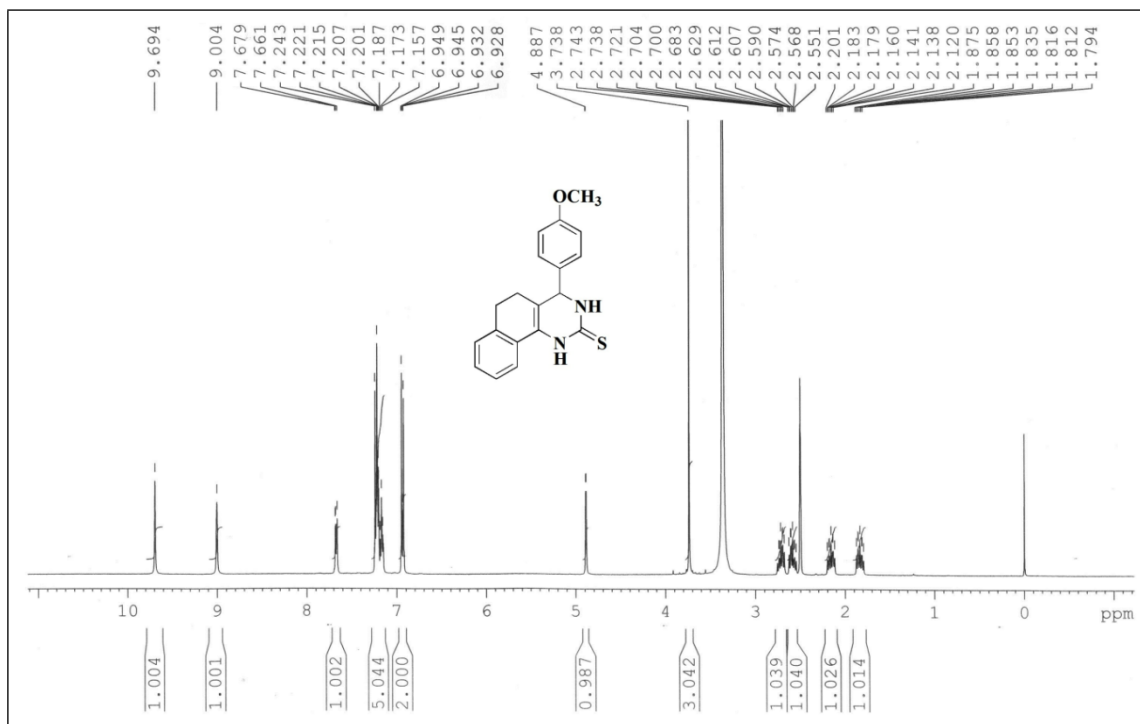
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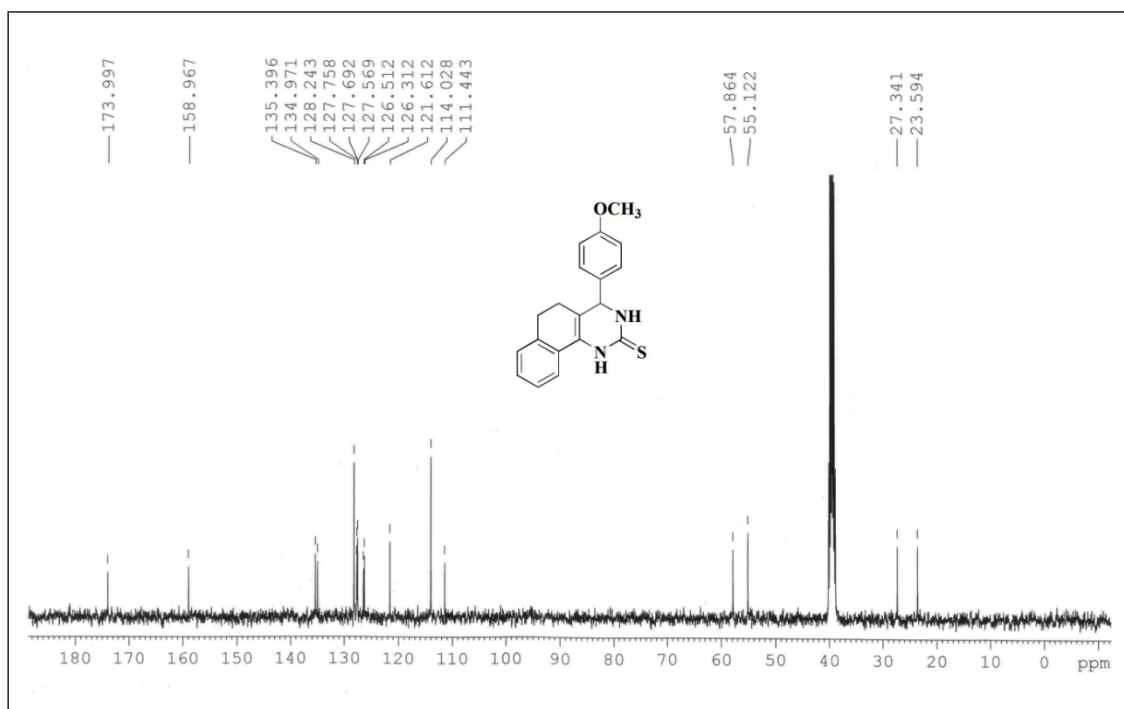
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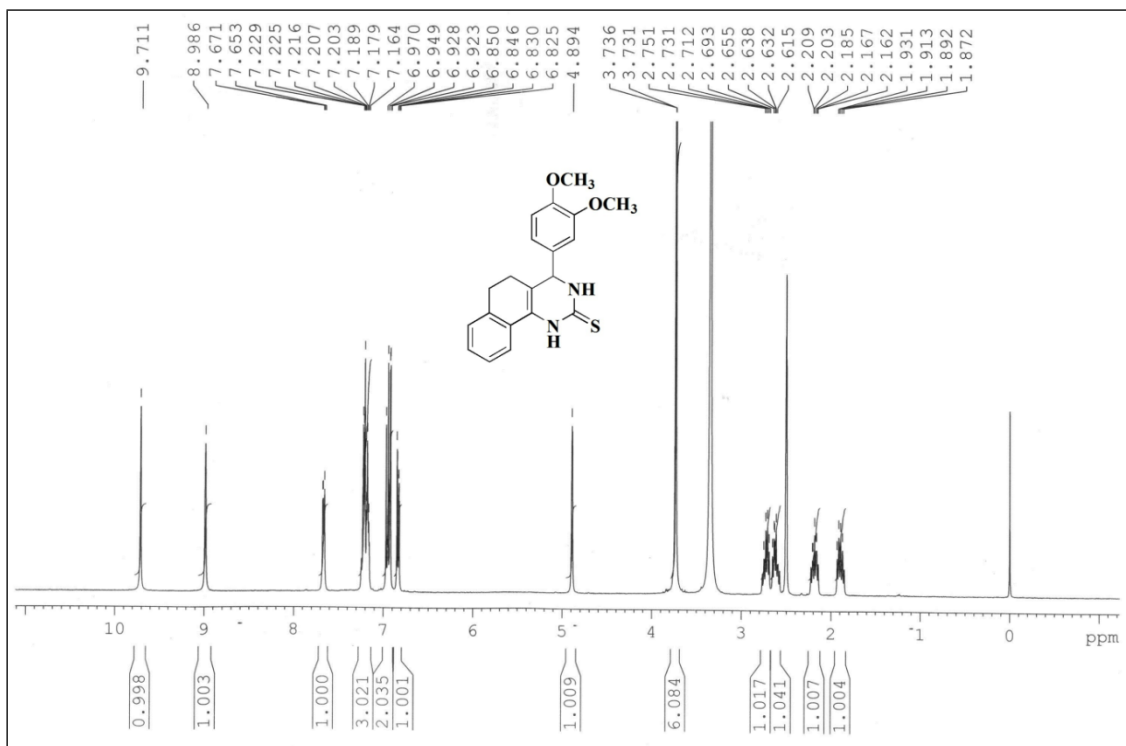
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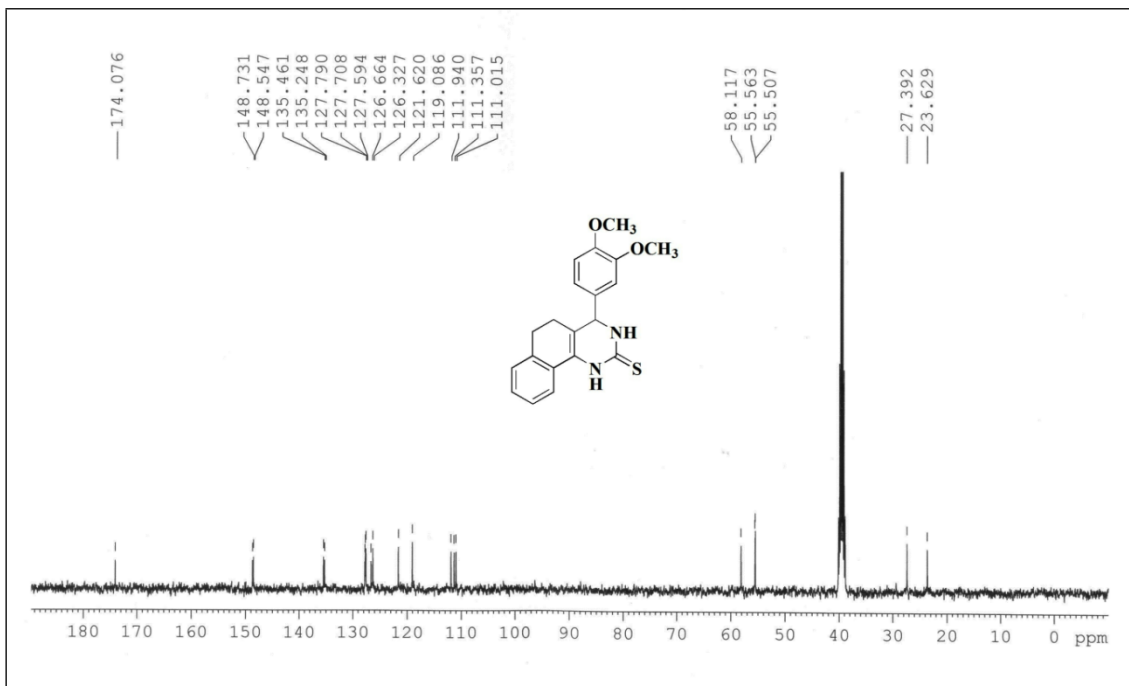
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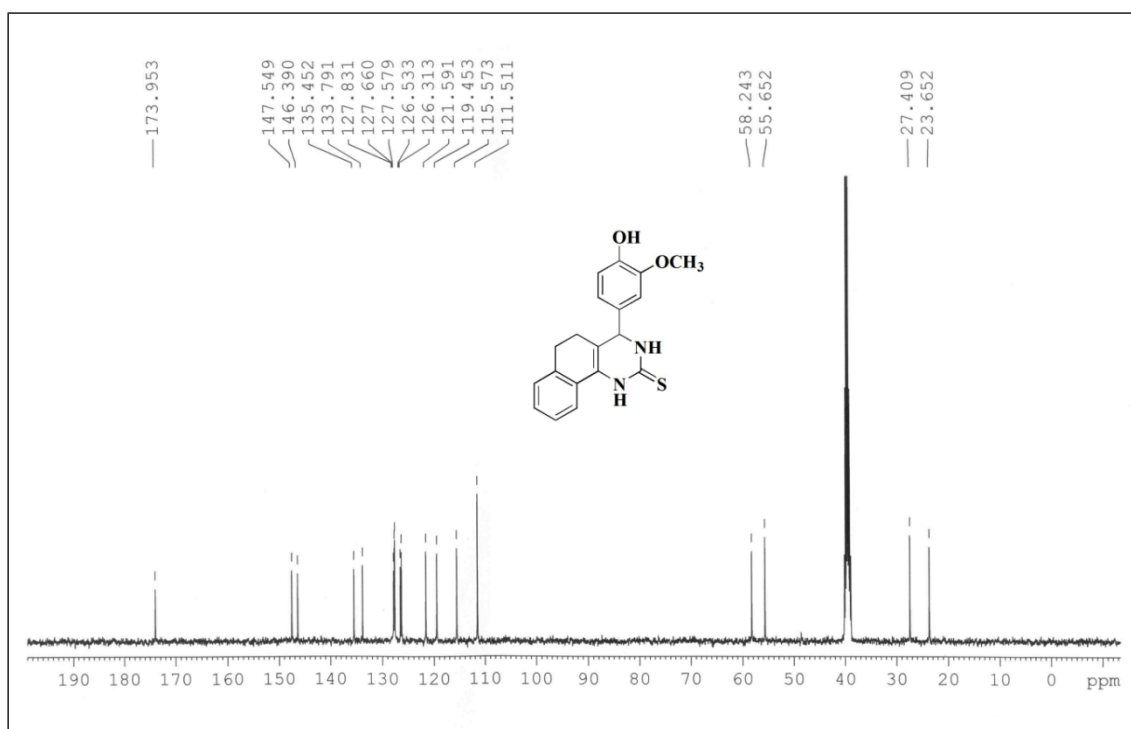
Compound 4e: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



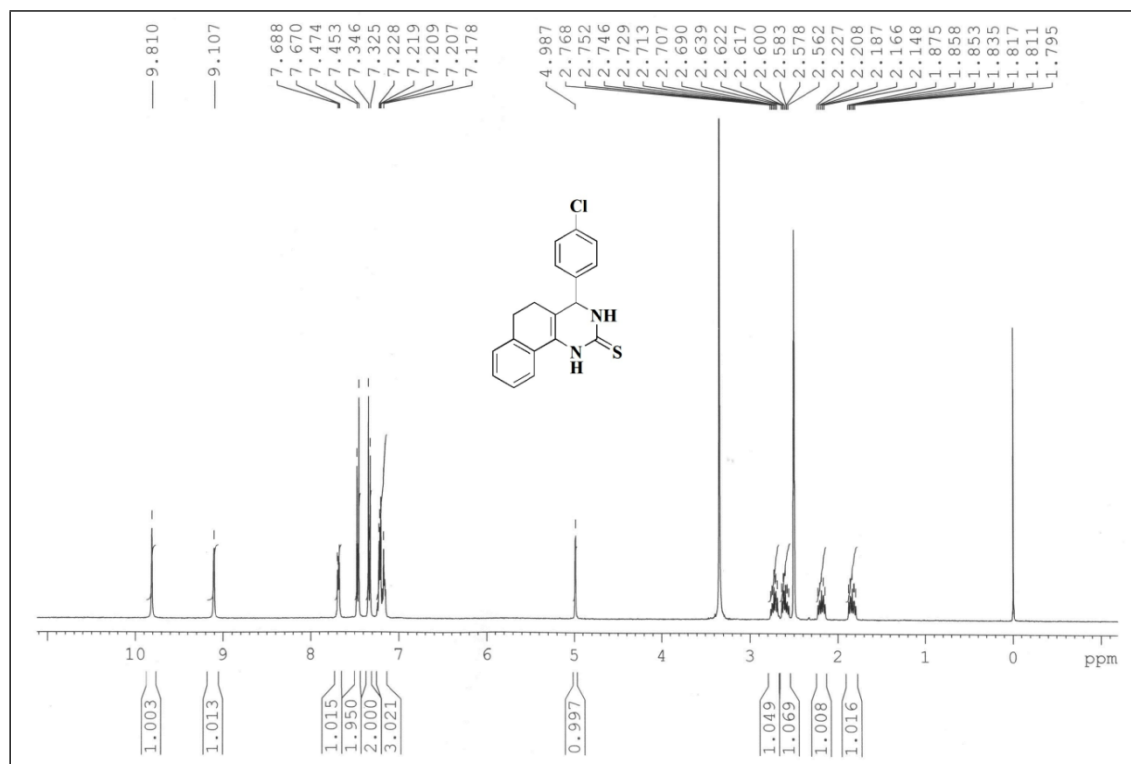
Compound 4e: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



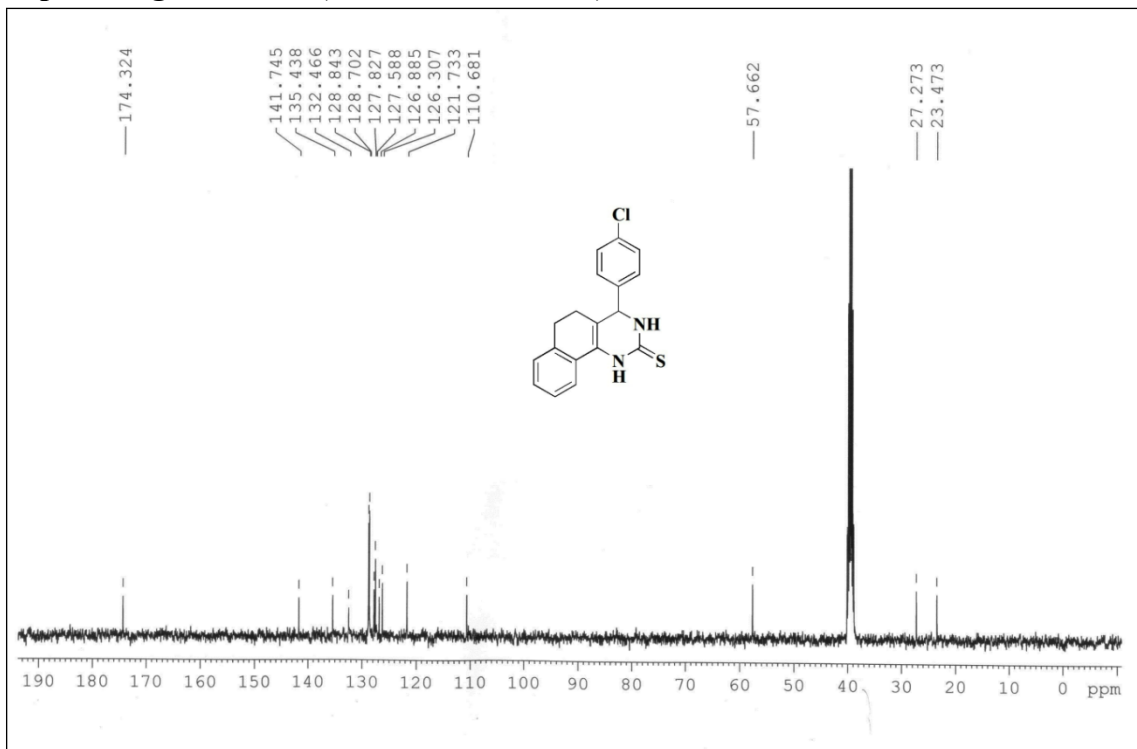
Compound 4f: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



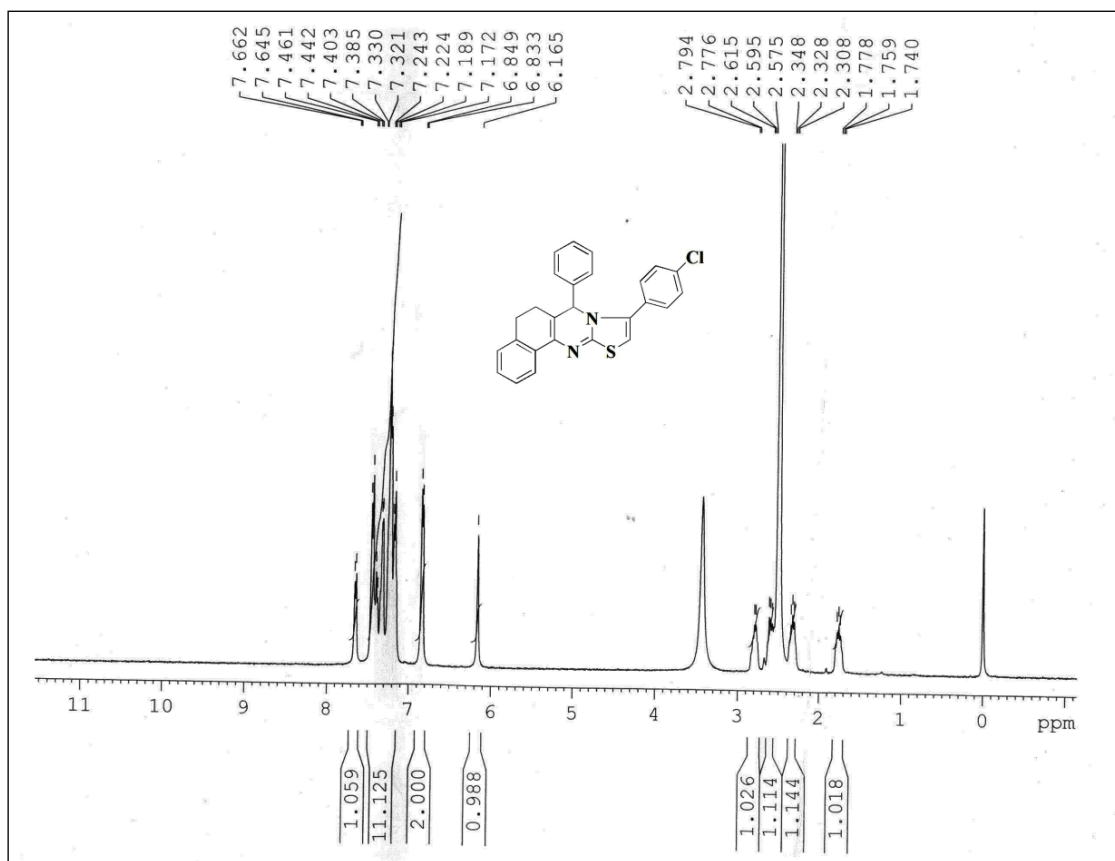
Compound 4g: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



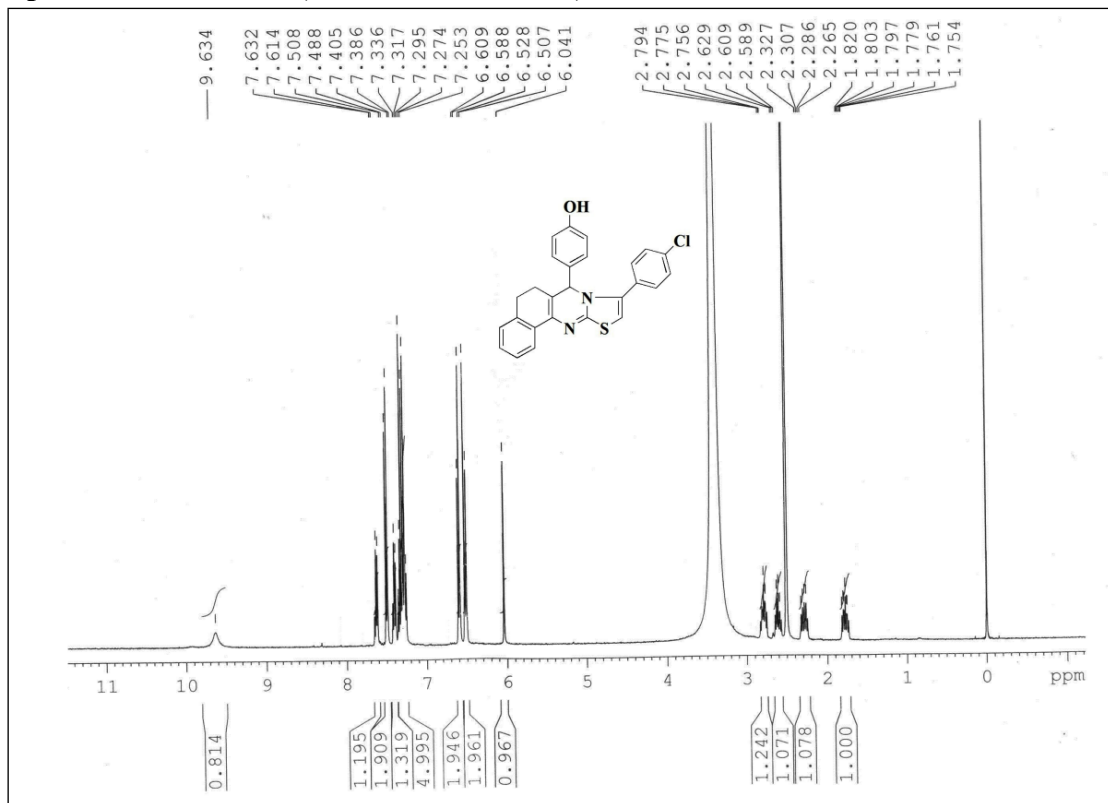
Compound 4g: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



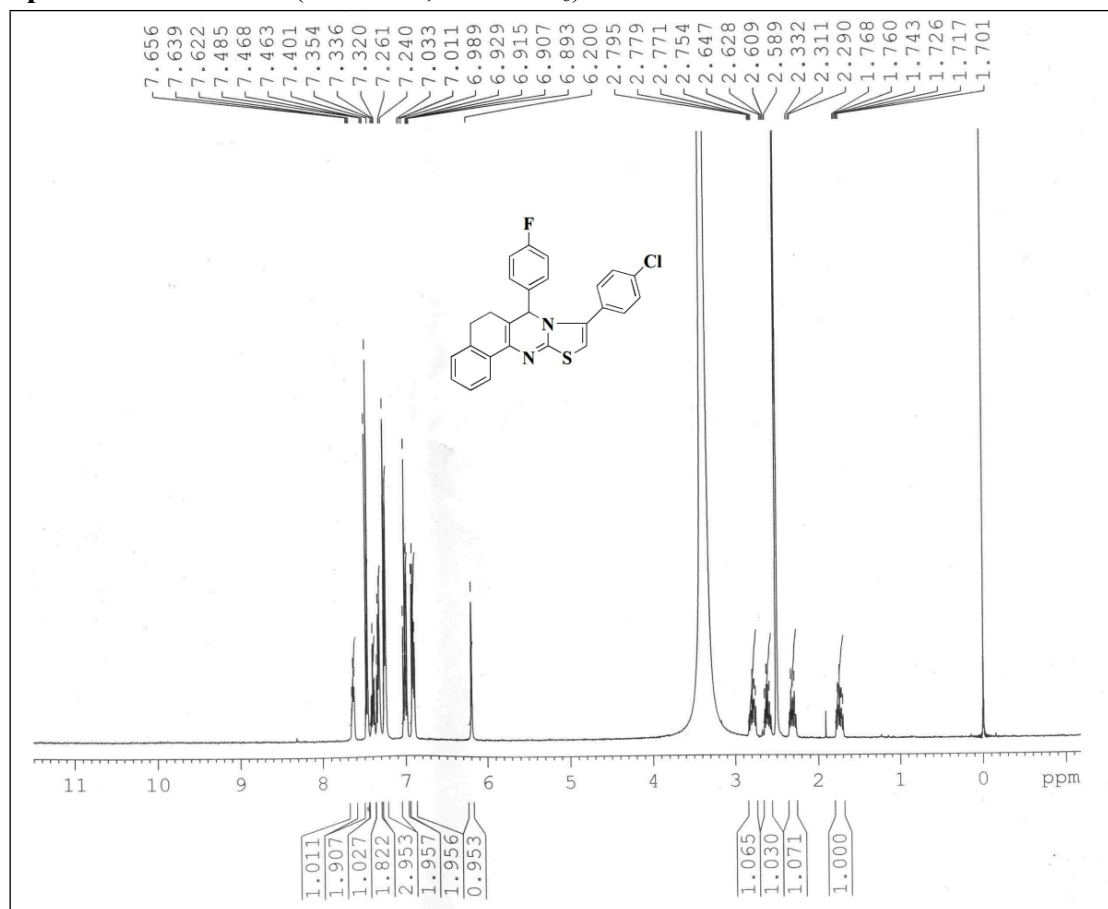
Compound 7a: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



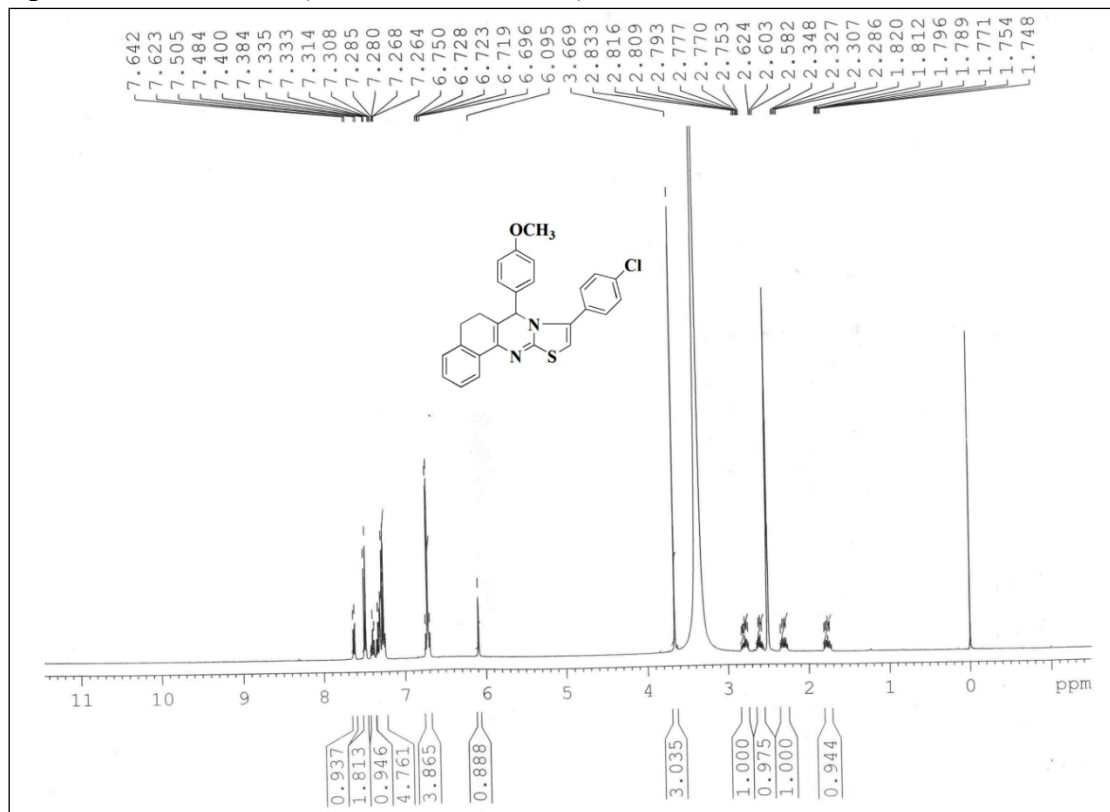
Compound 7b: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



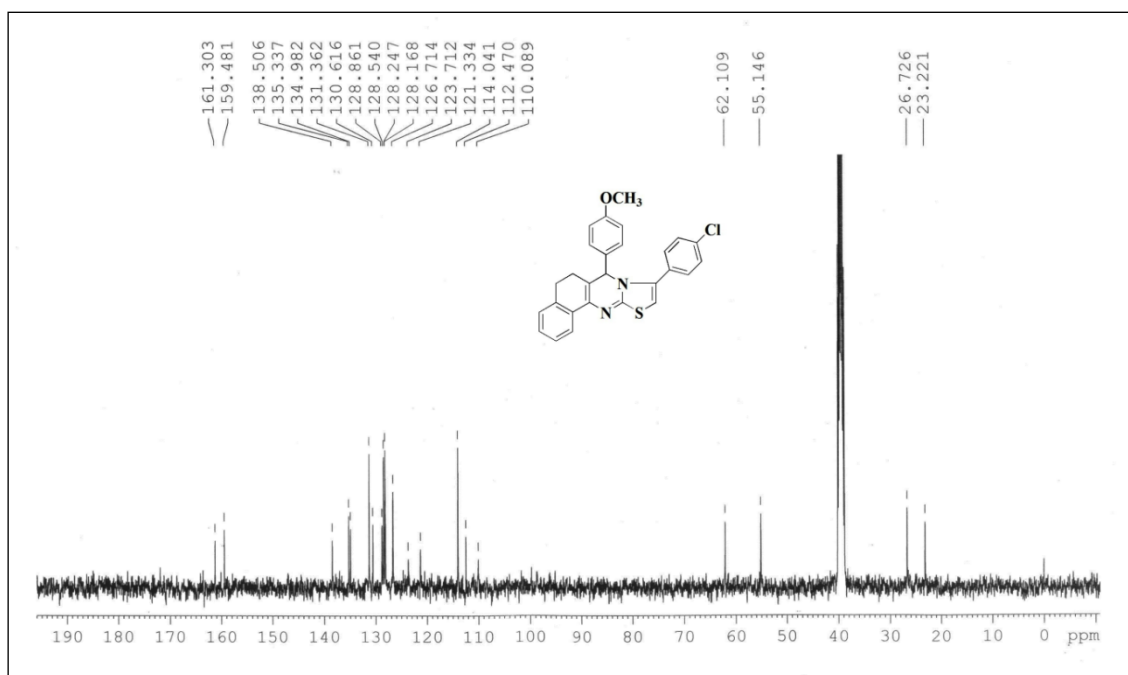
Compound 7c: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



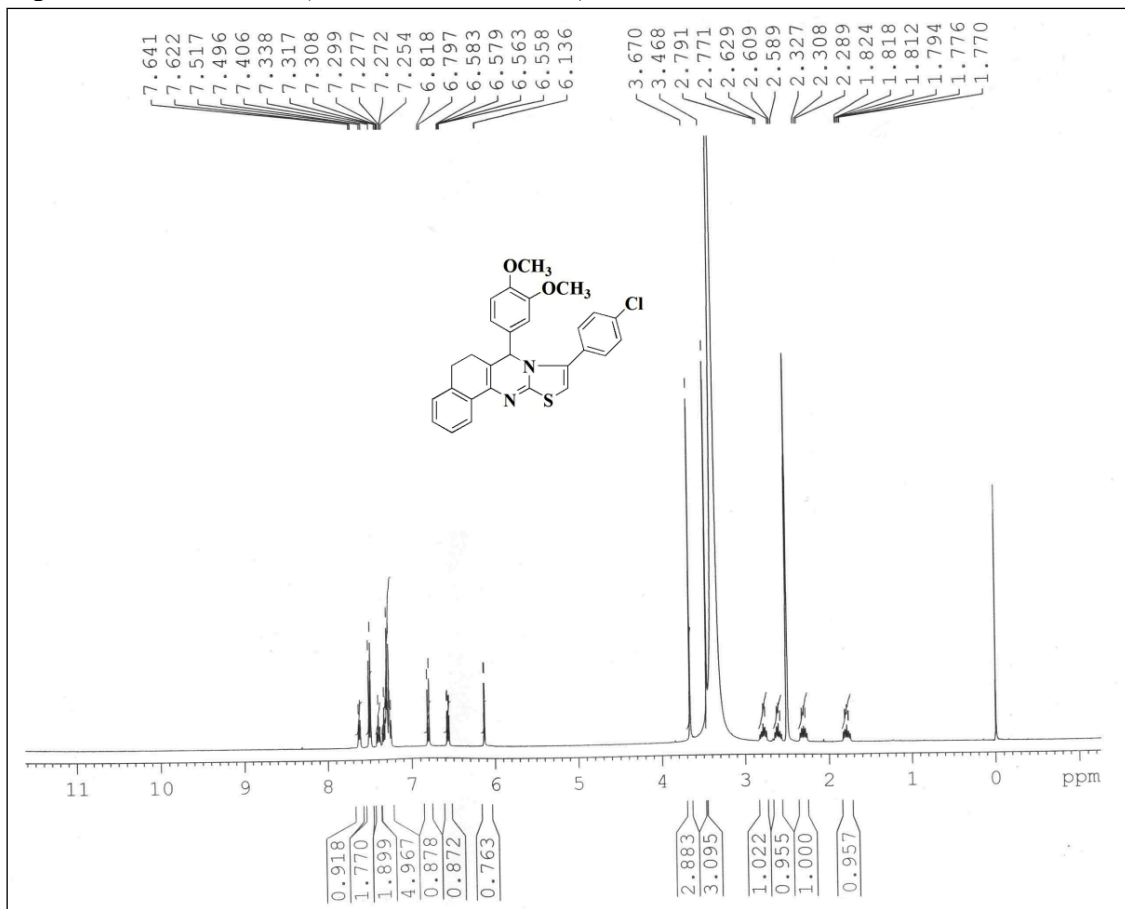
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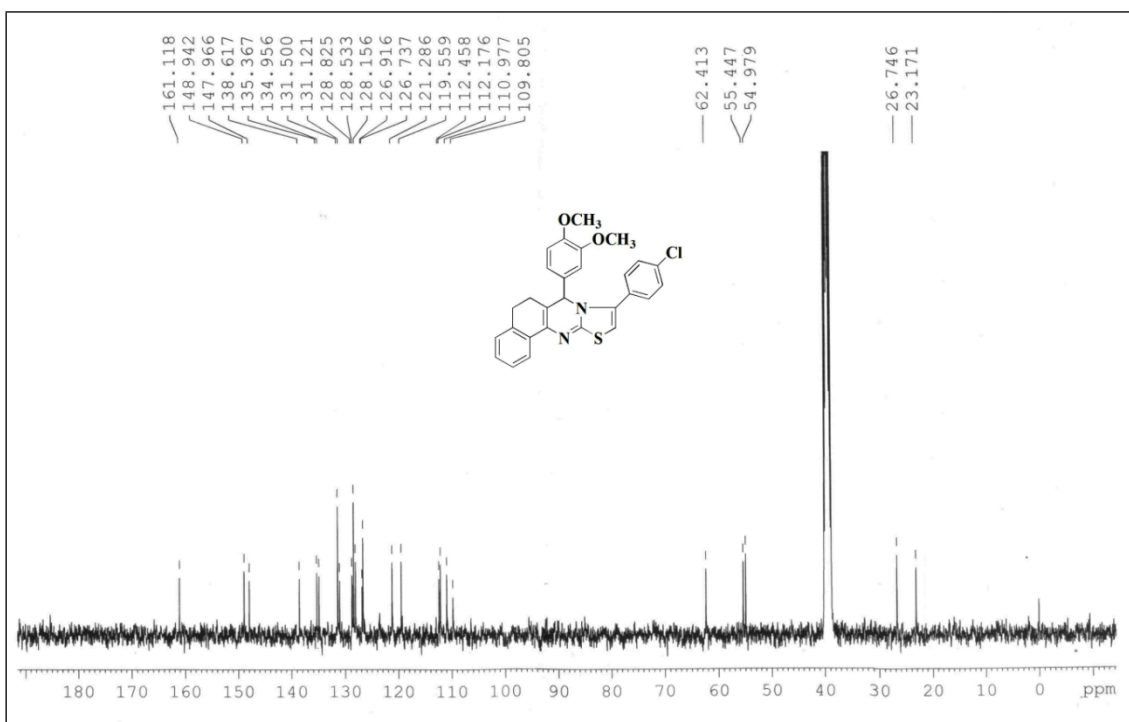
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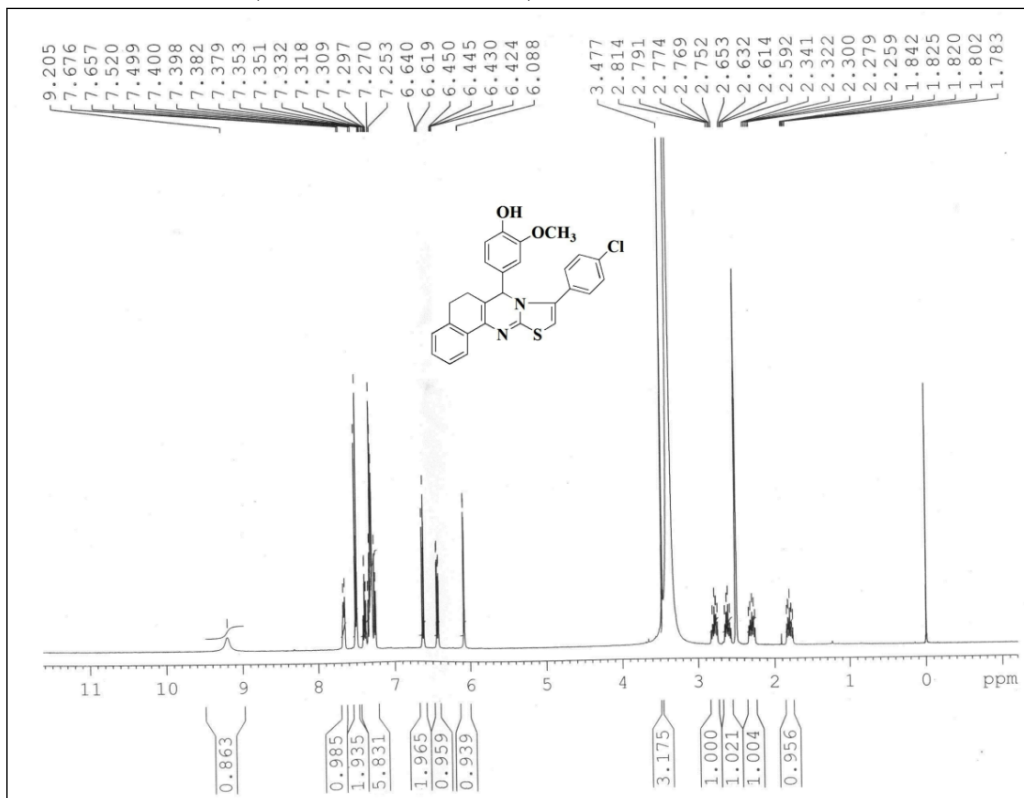
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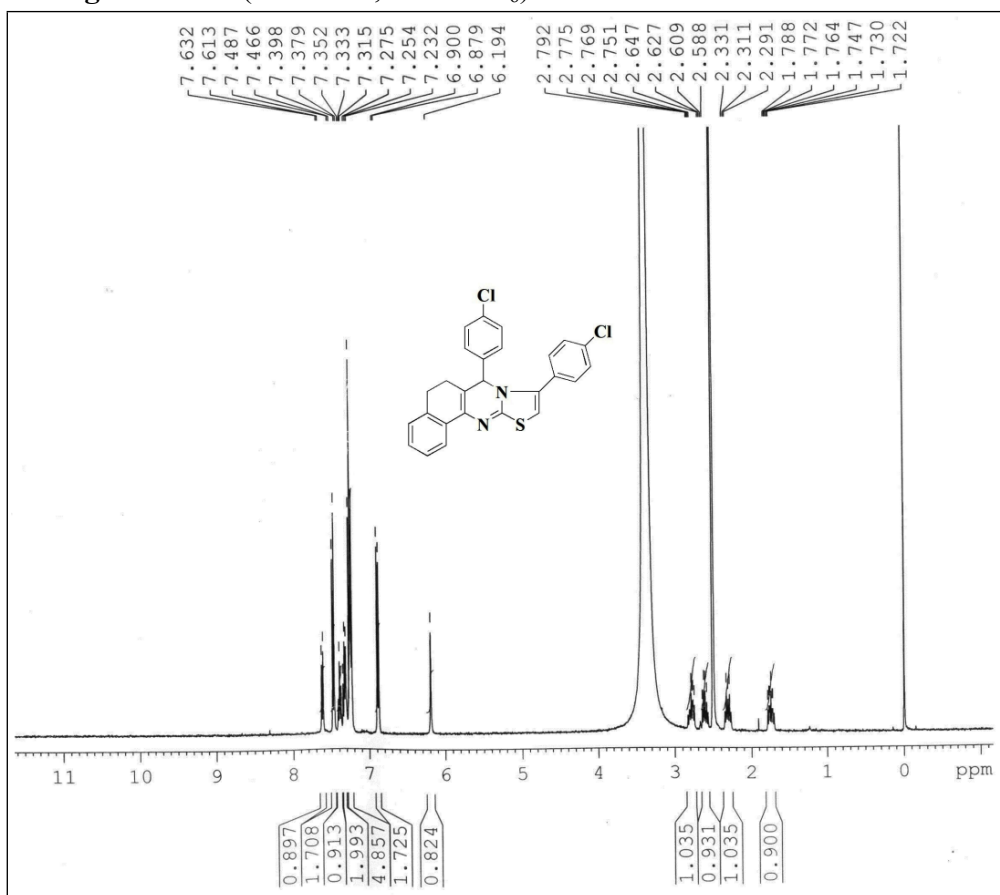
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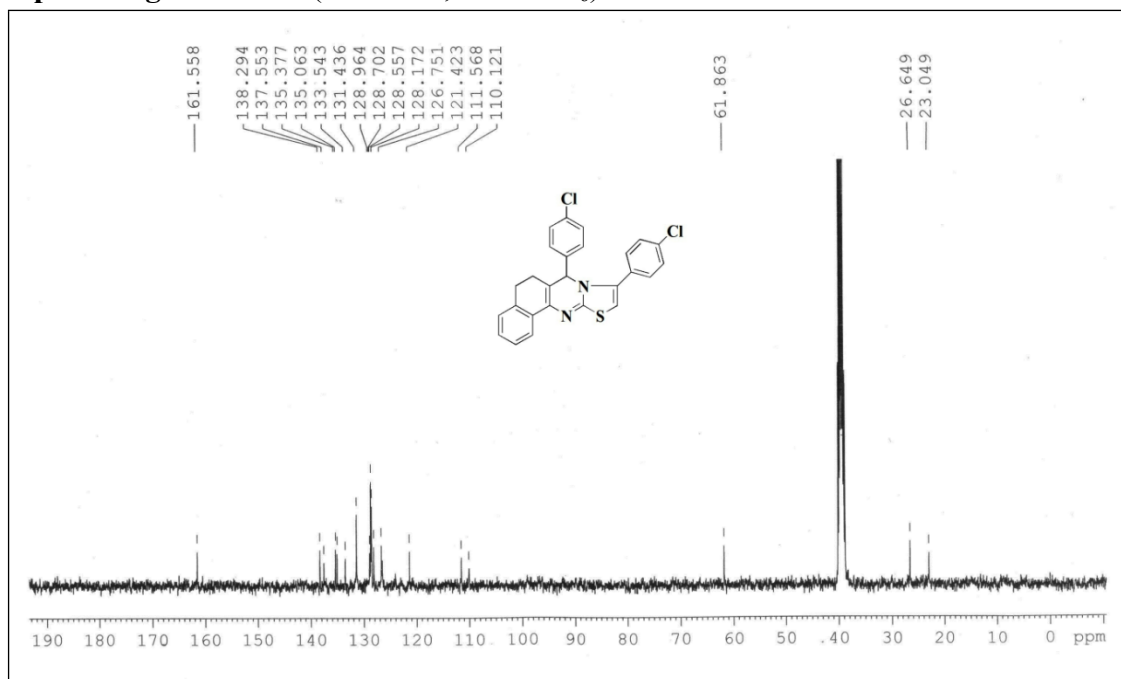
Compound 7f: ^1H NMR (400 MHz, $\text{DMSO}-d_6$)



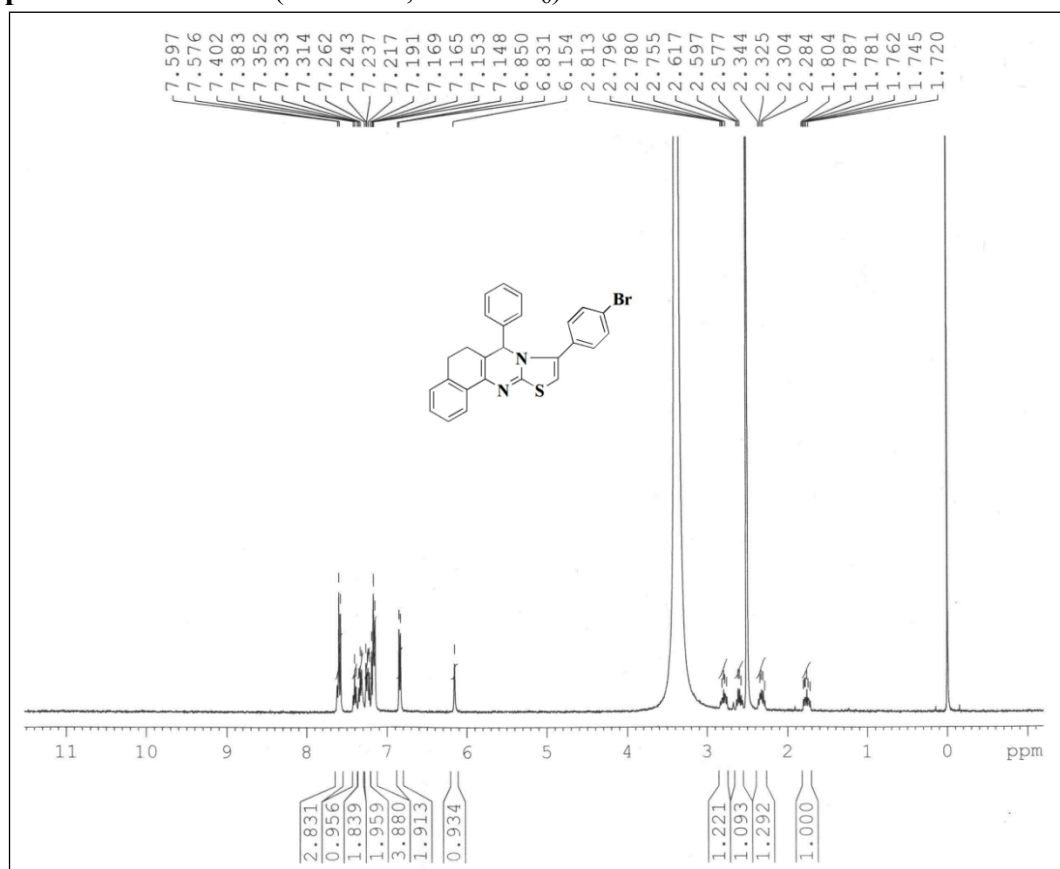
Compound 7g: ^1H NMR (400 MHz, $\text{DMSO}-d_6$)



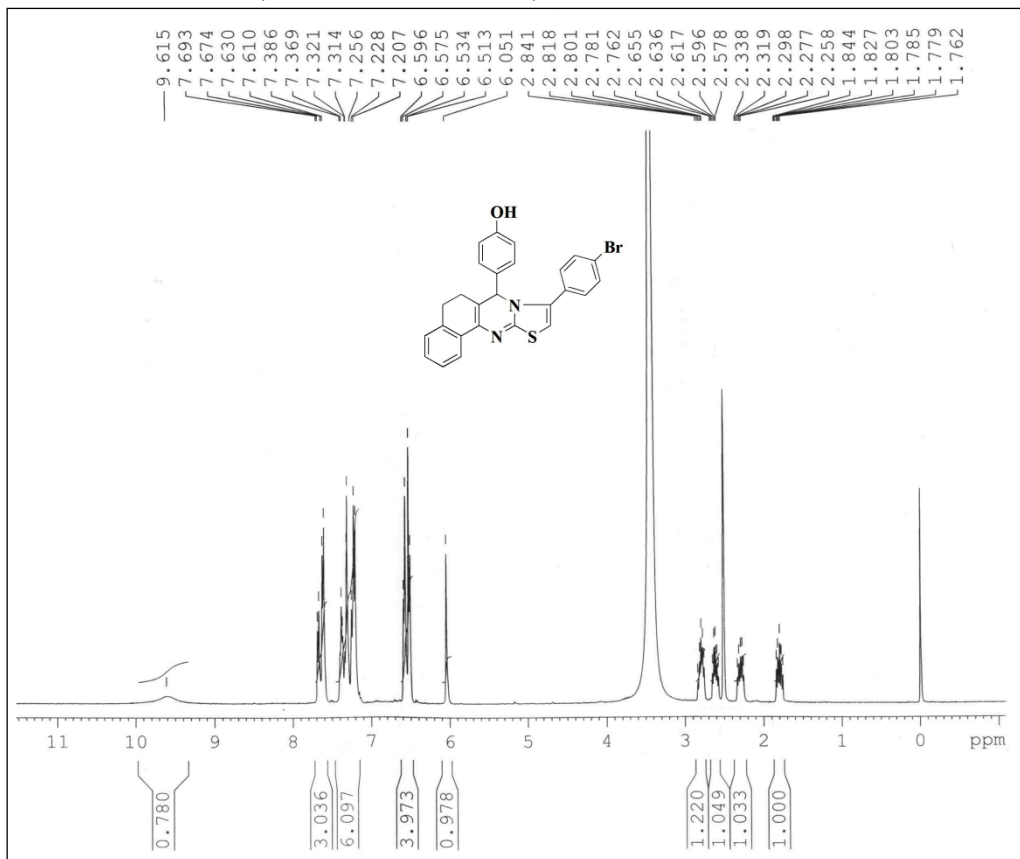
Compound 7g: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



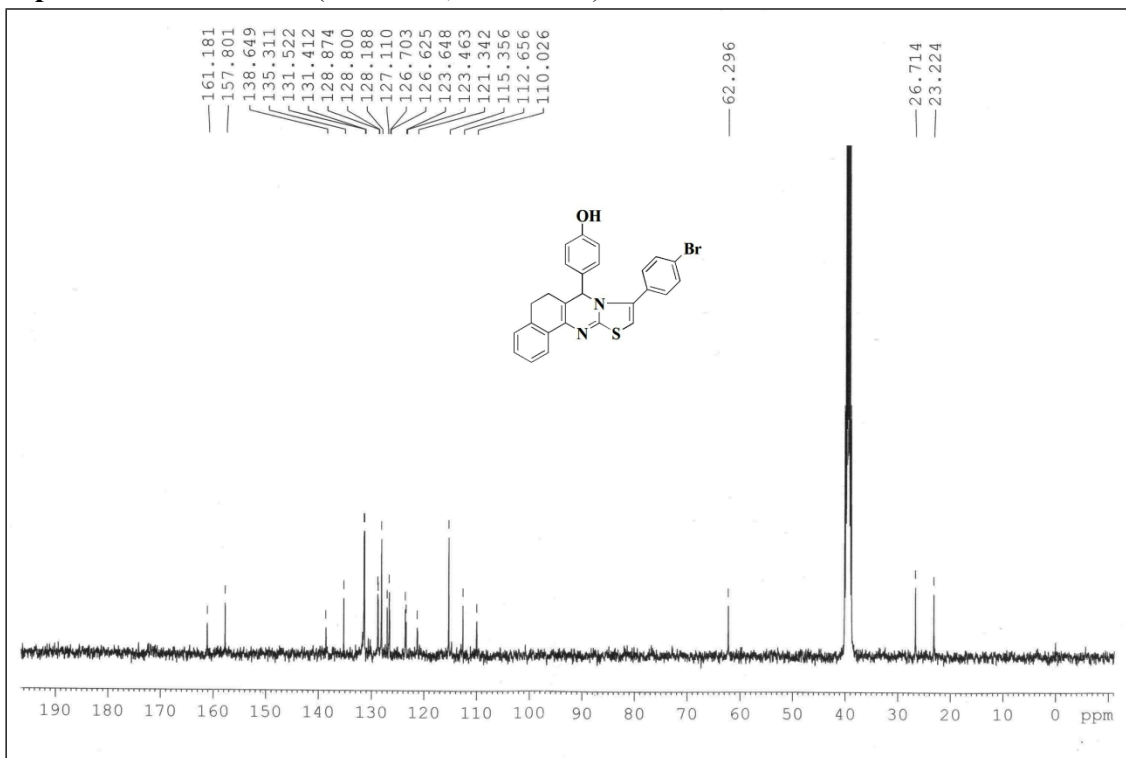
Compound 8a: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



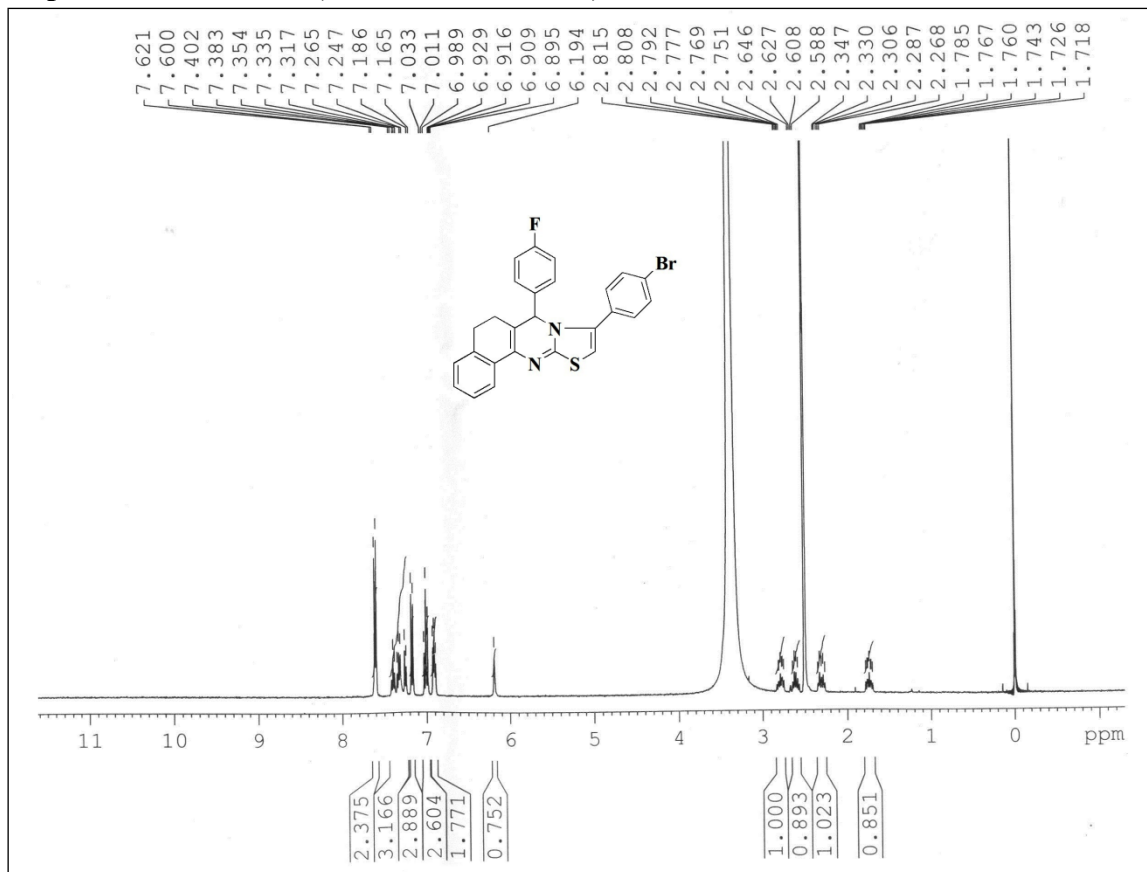
Compound 8b: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



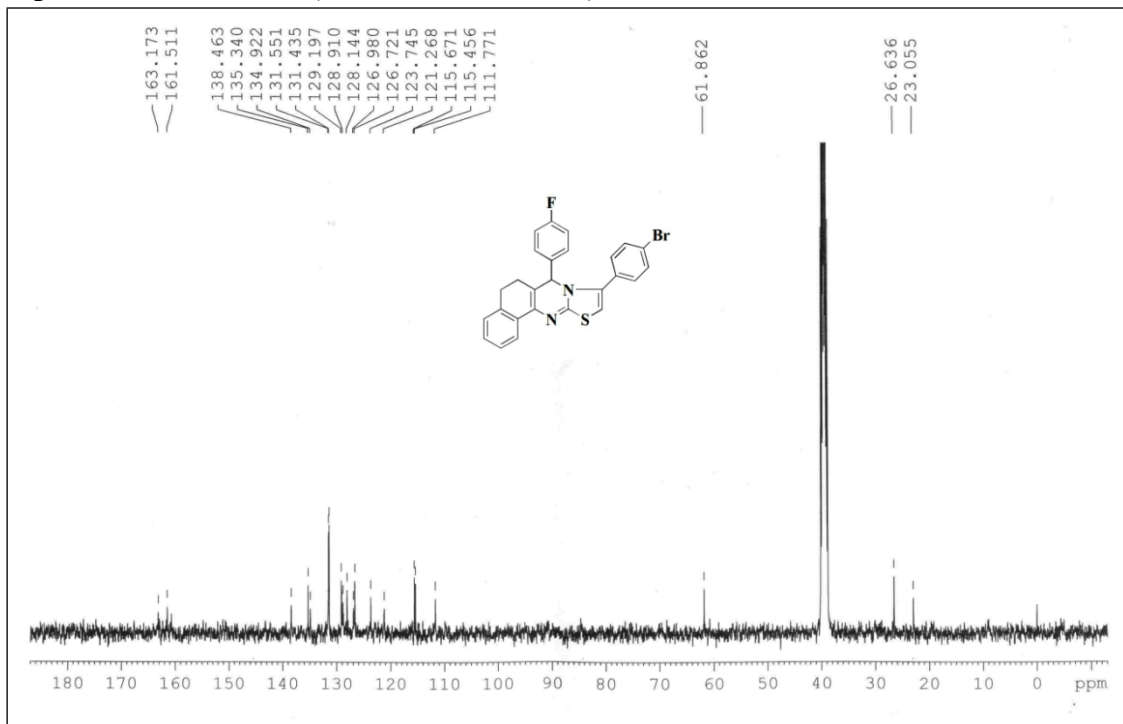
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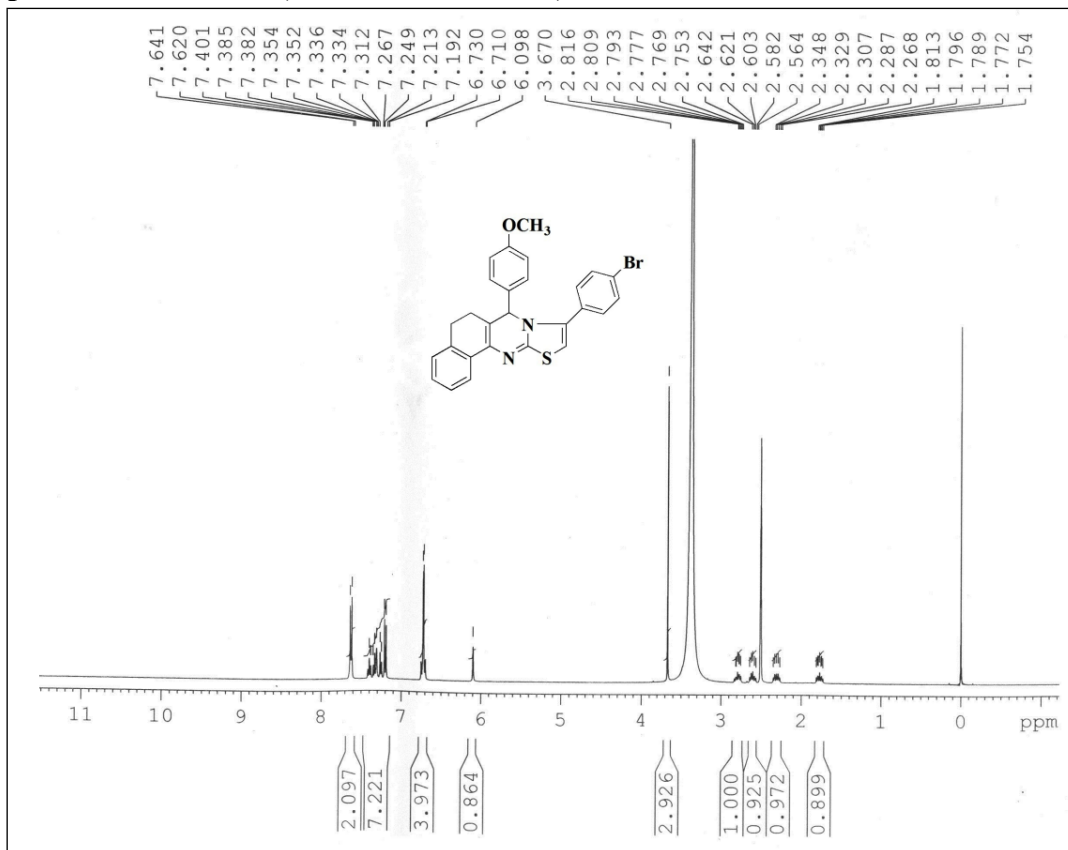
Compound 8c: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



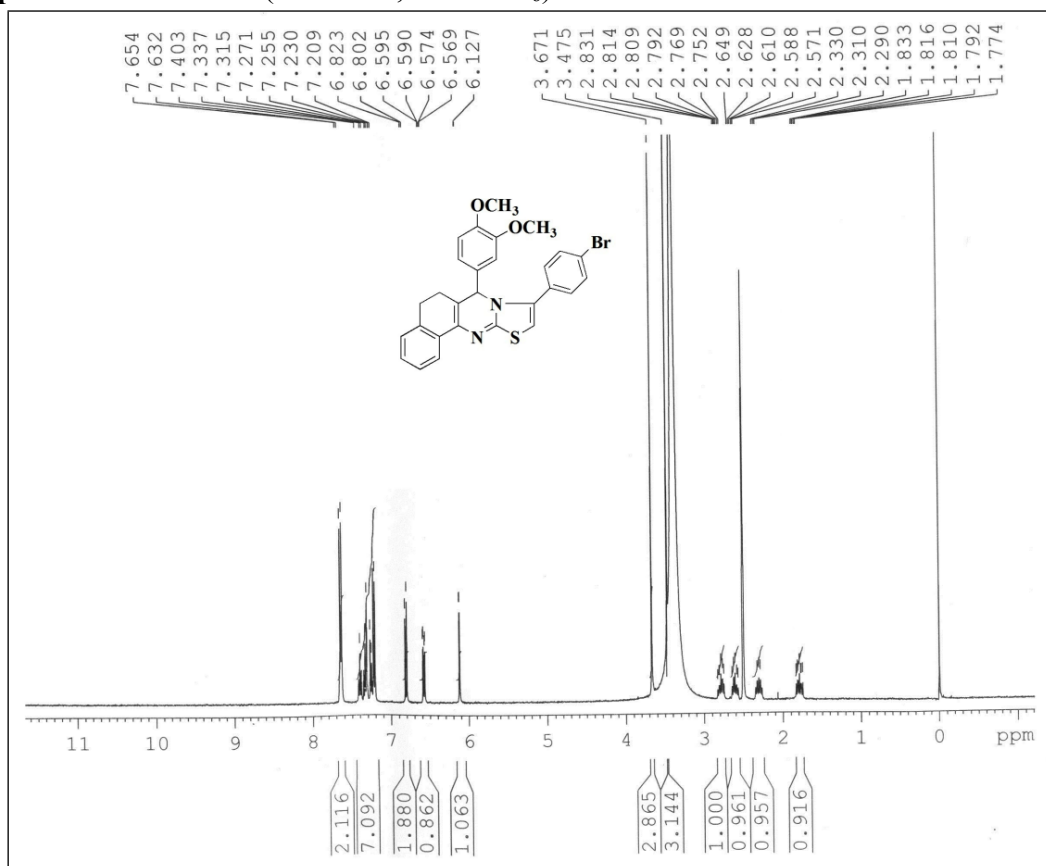
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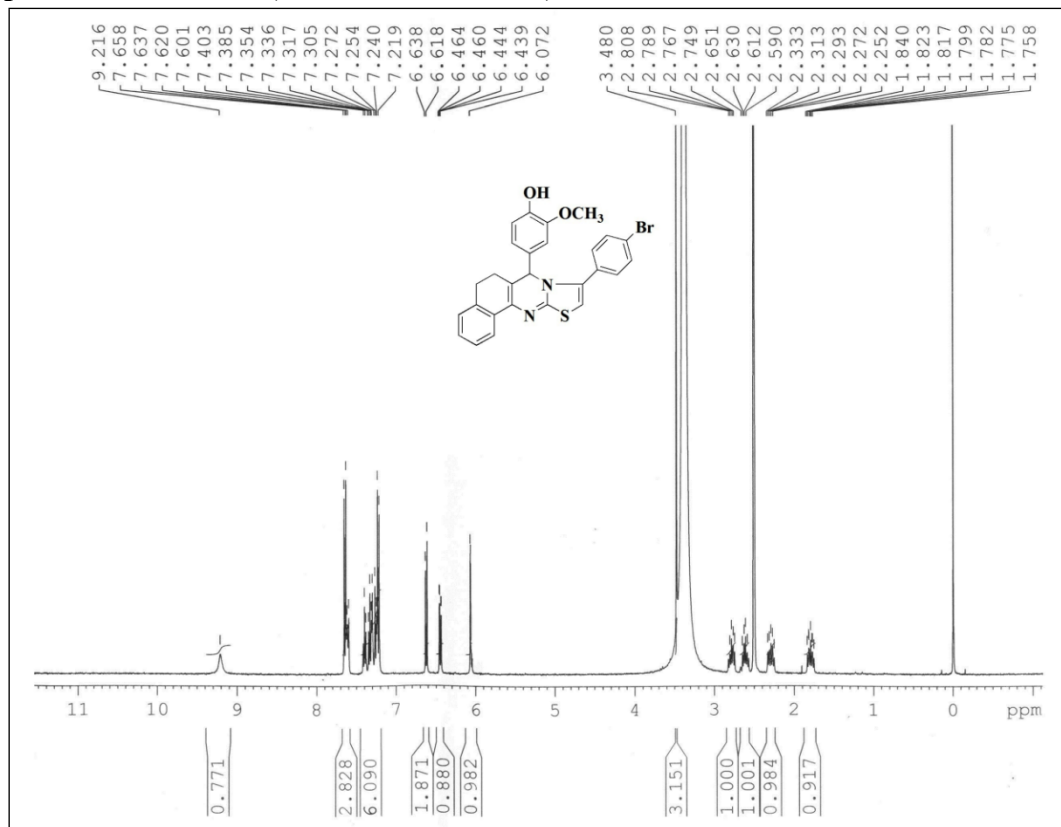
Compound 8d: ^1H NMR (400 MHz, $\text{DMSO}-d_6$)



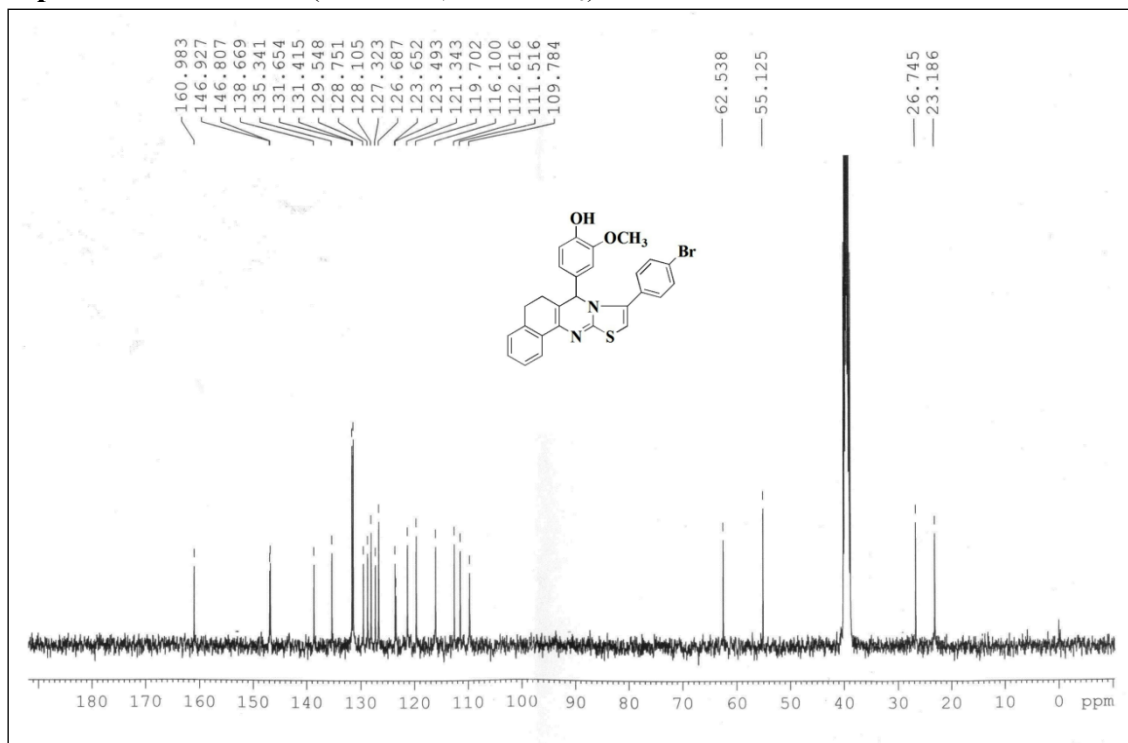
Compound 8e: ^1H NMR (400 MHz, $\text{DMSO}-d_6$)



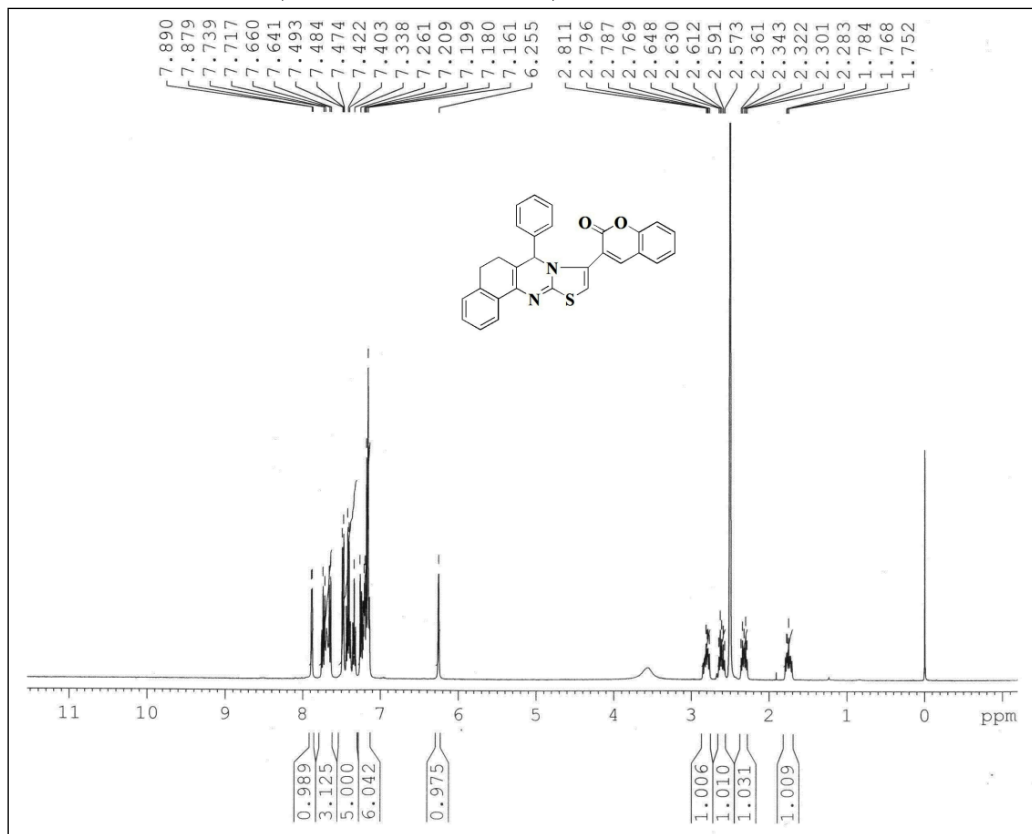
Compound 8f: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



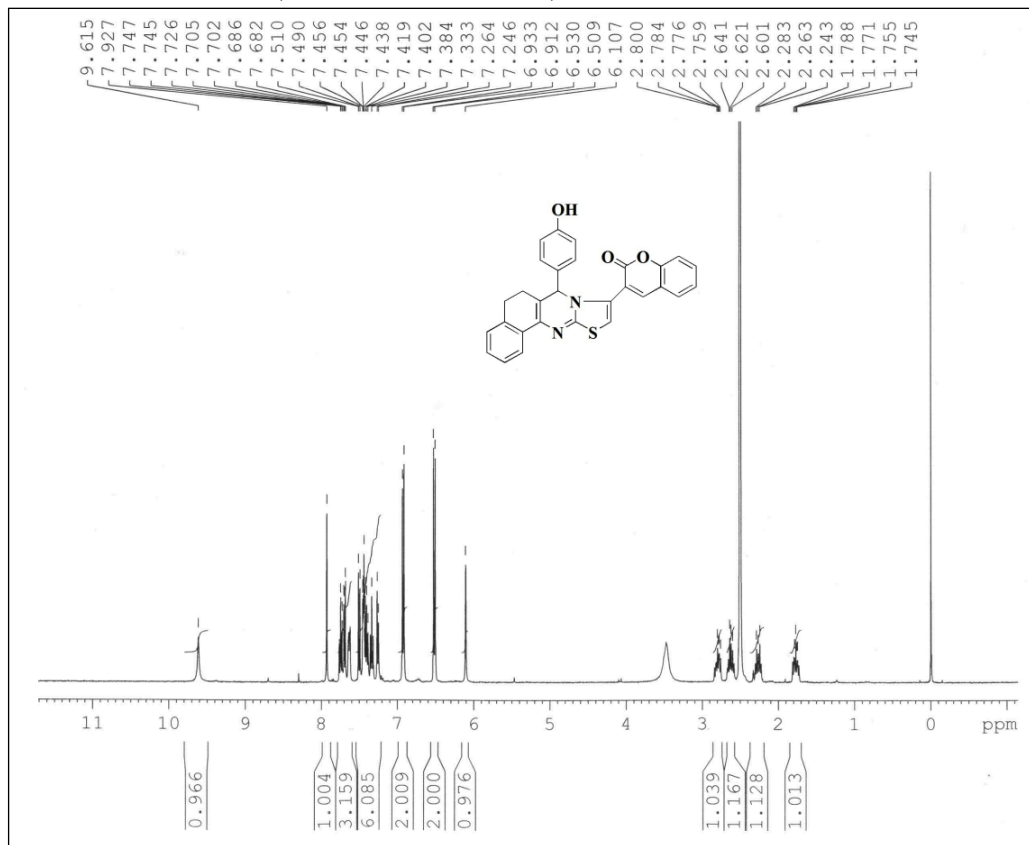
Compound 8f: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



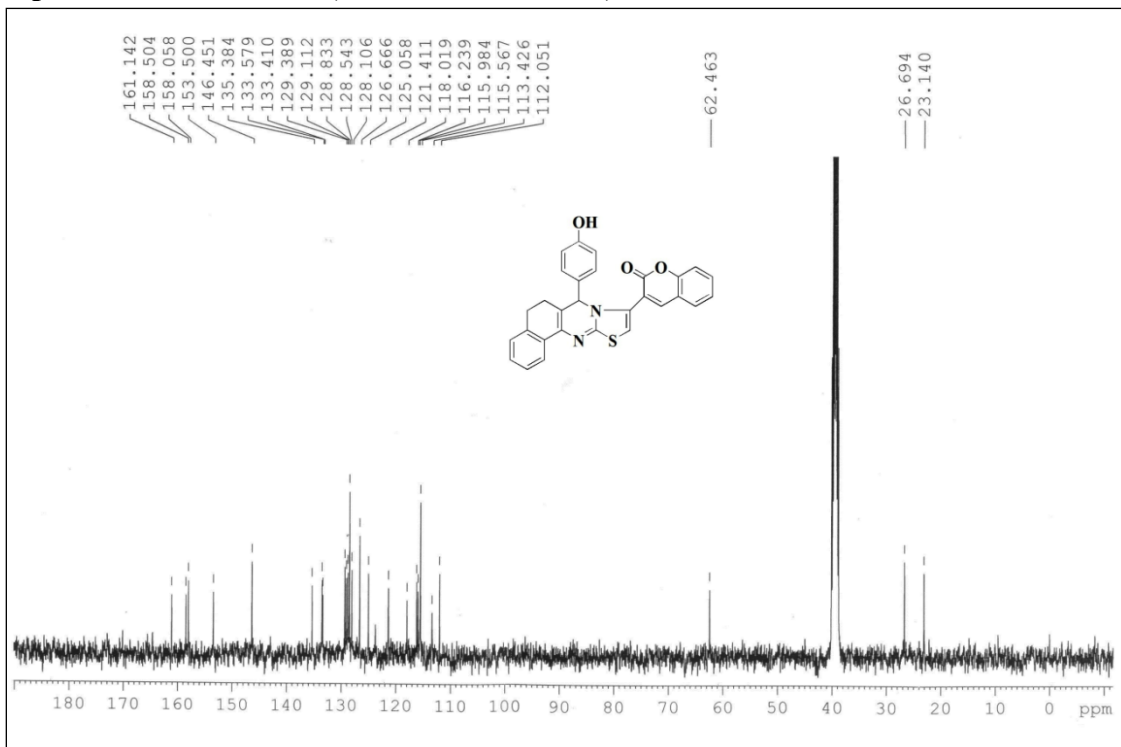
Compound 11a: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



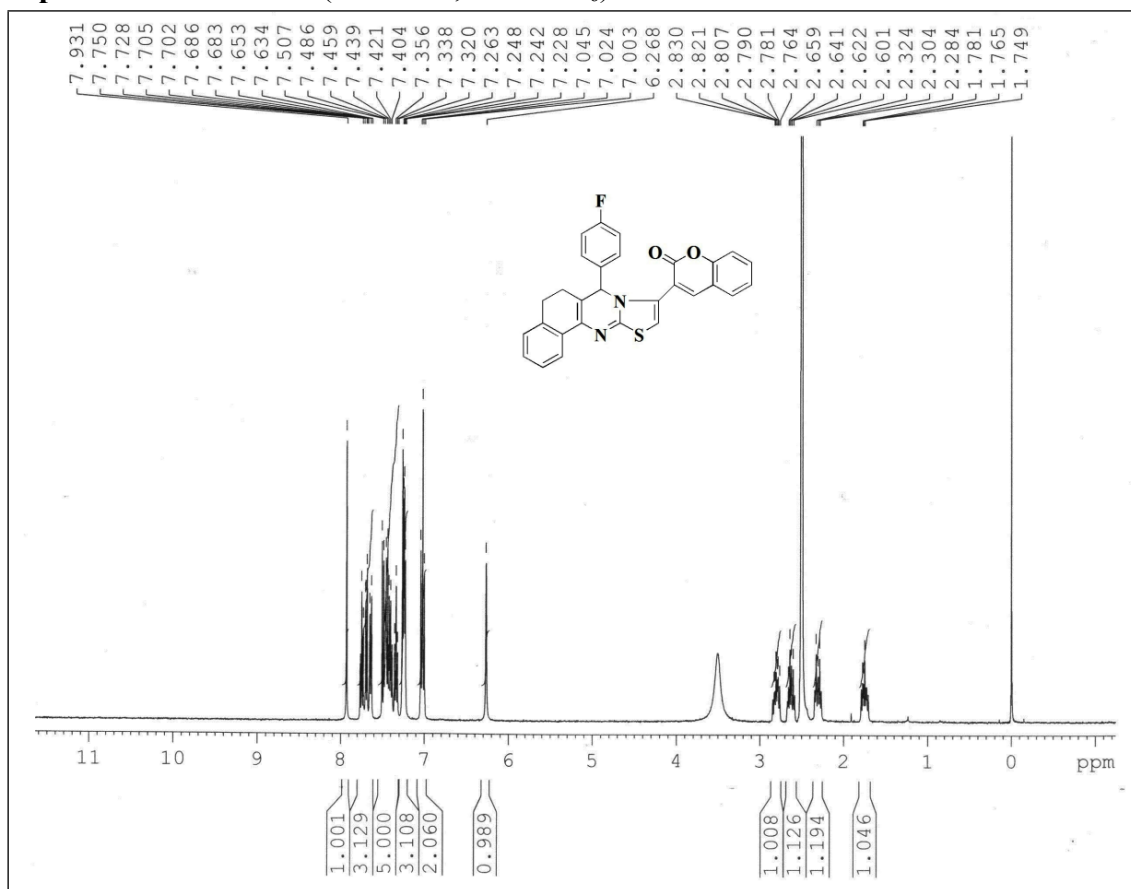
Compound 11b: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



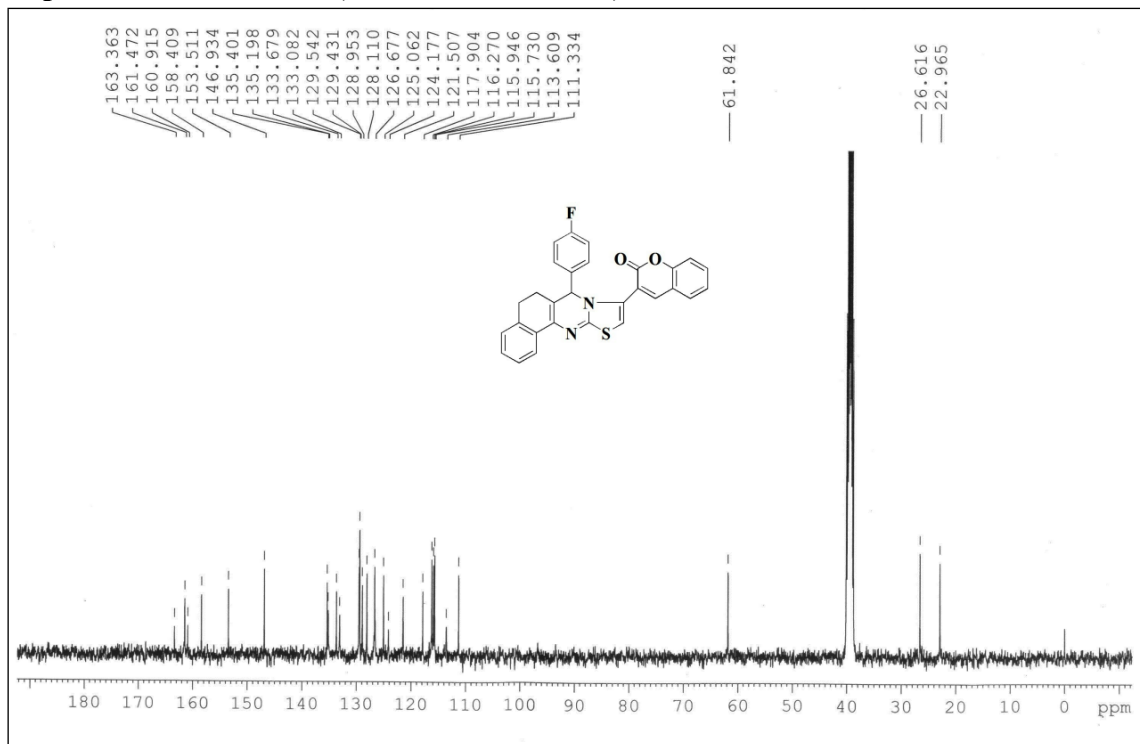
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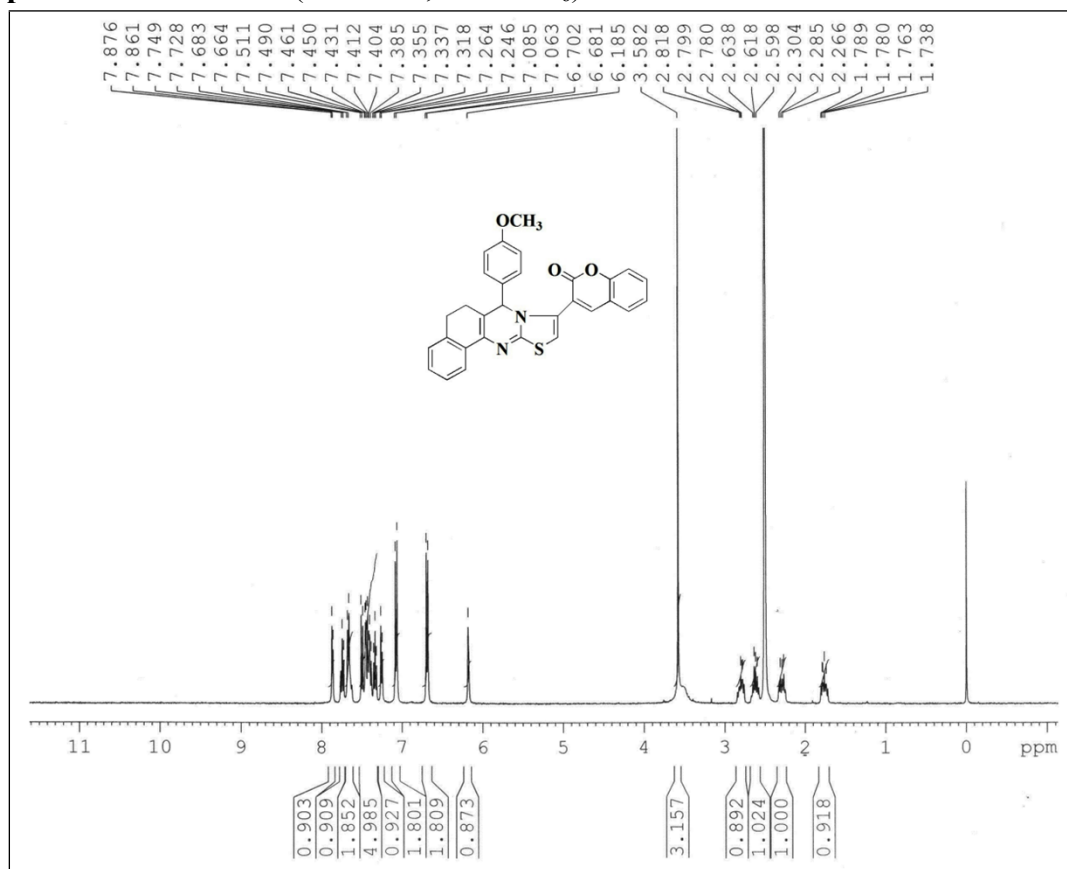
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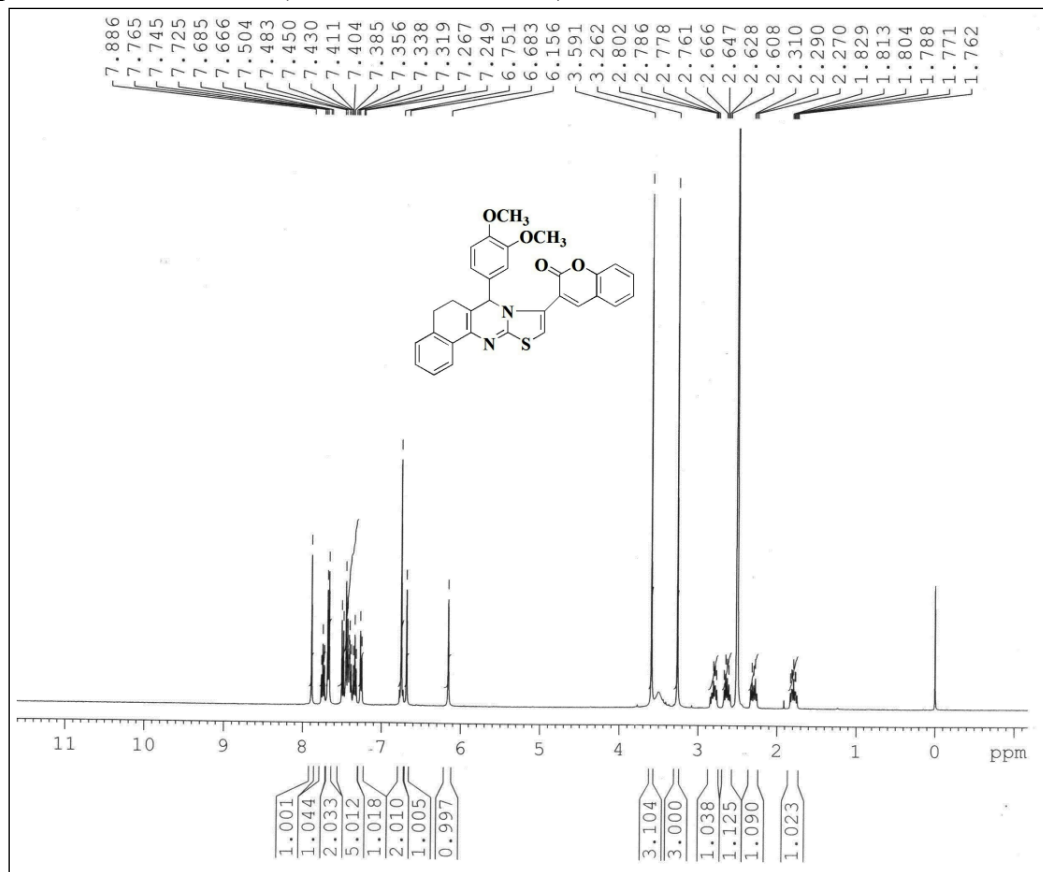
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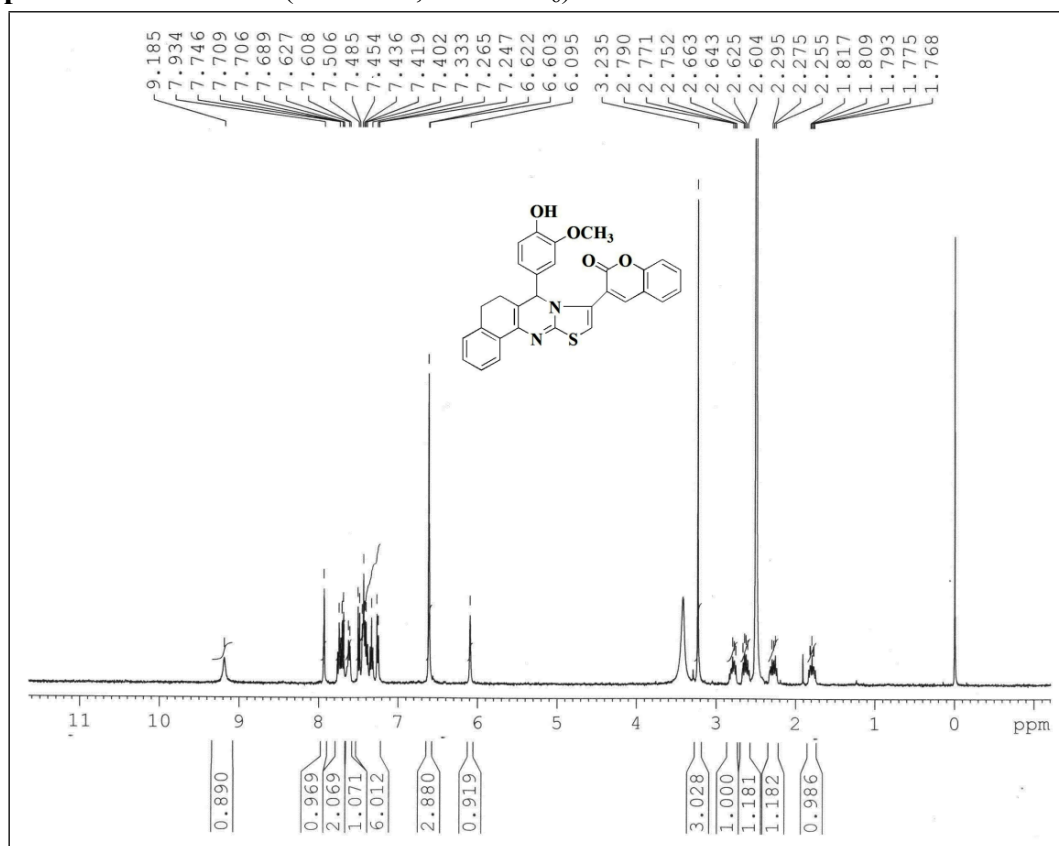
Compound 11d: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



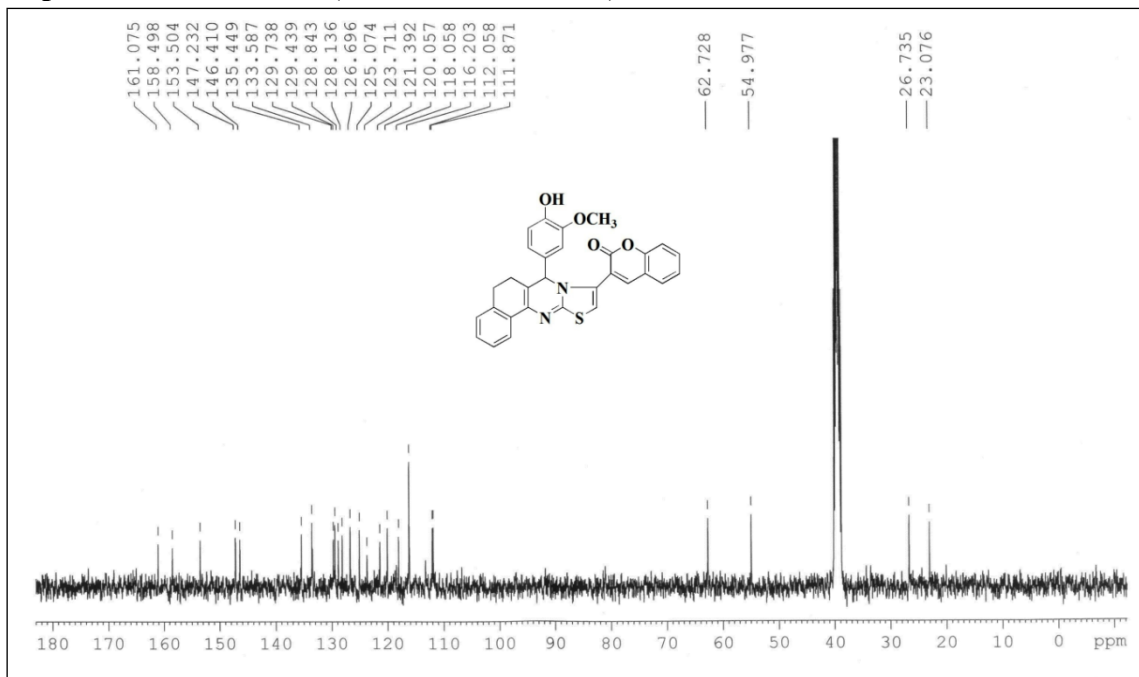
Compound 11e: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



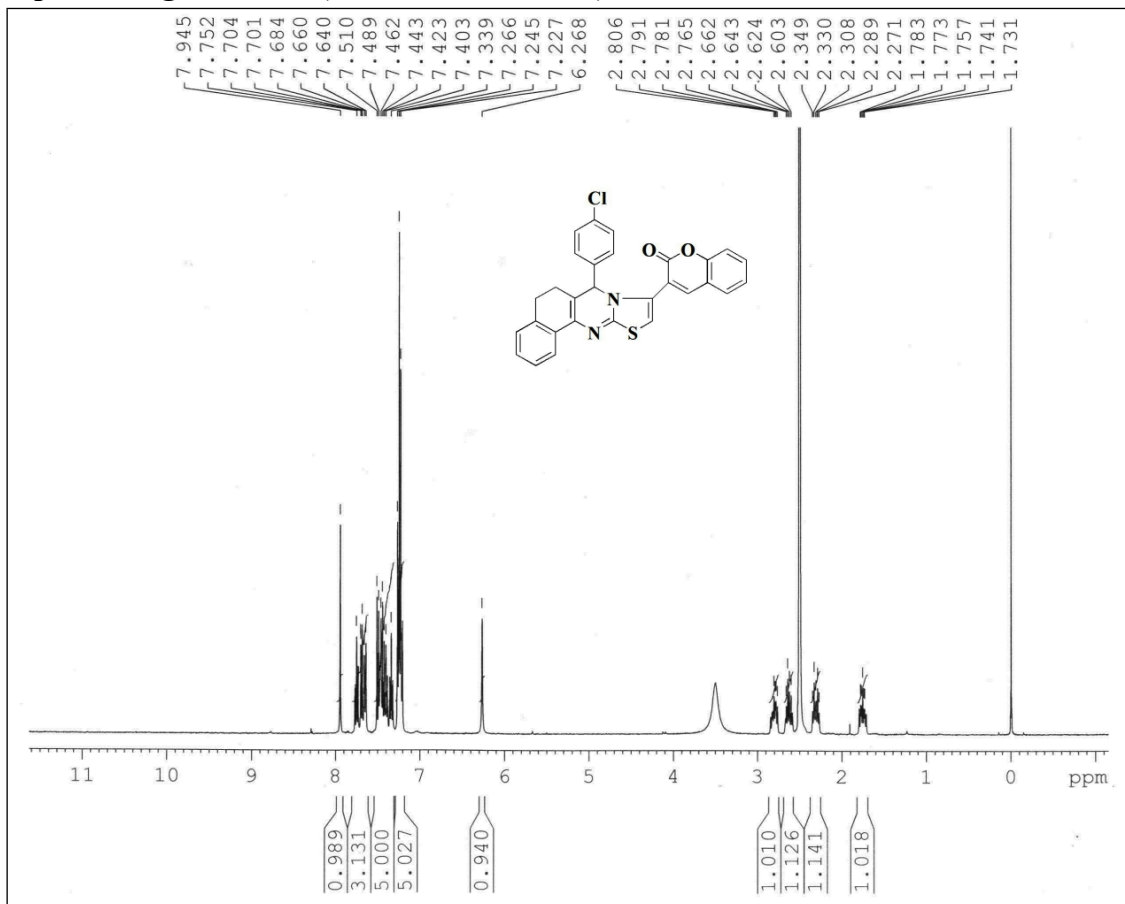
Compound 11f: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



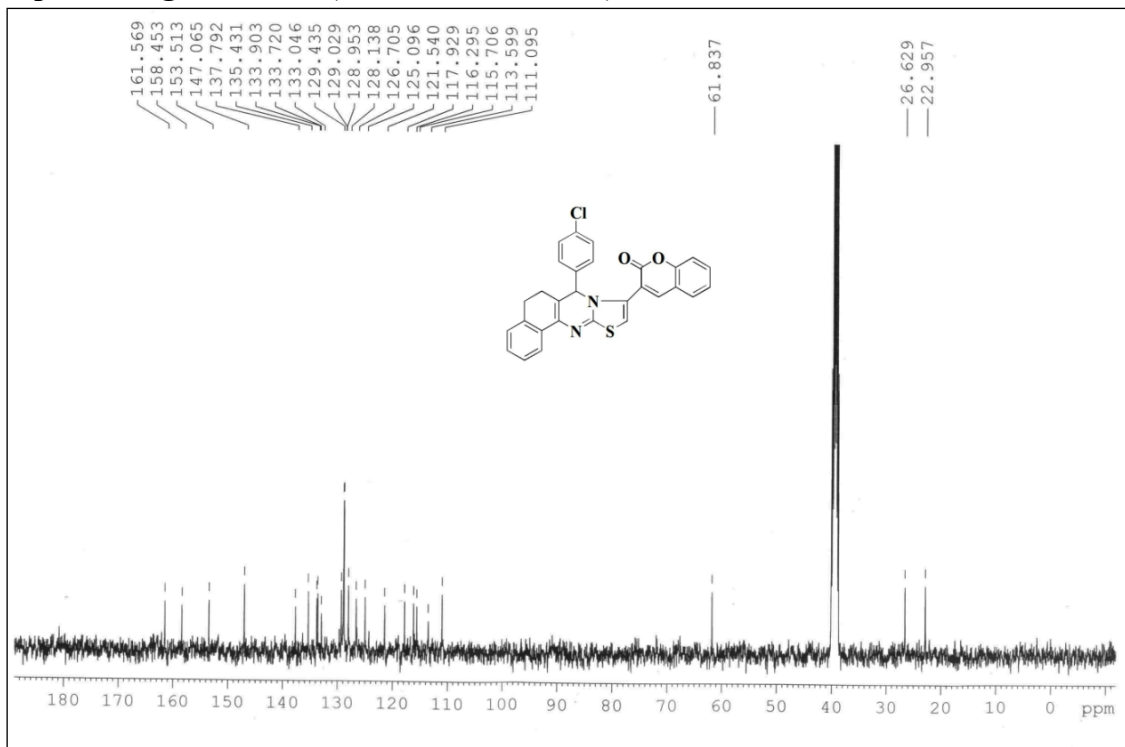
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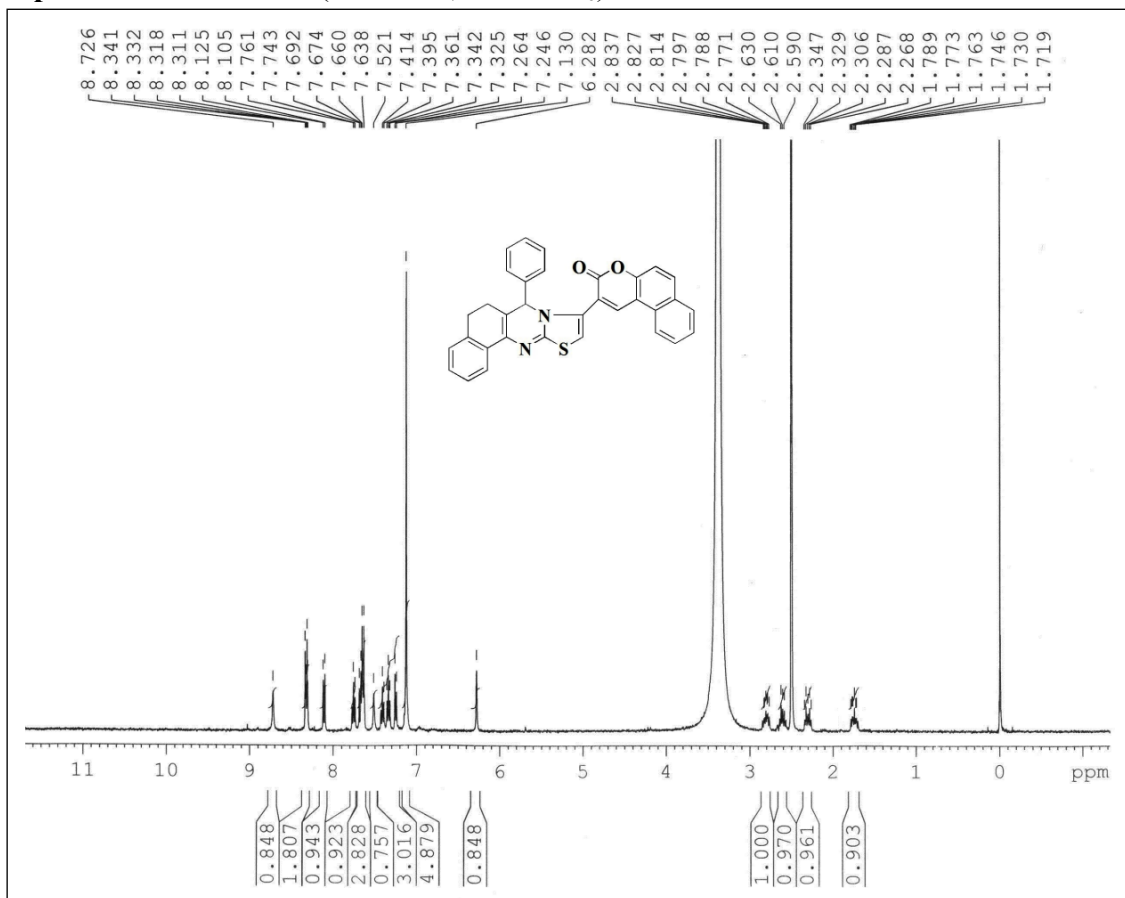
Compound 11g: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



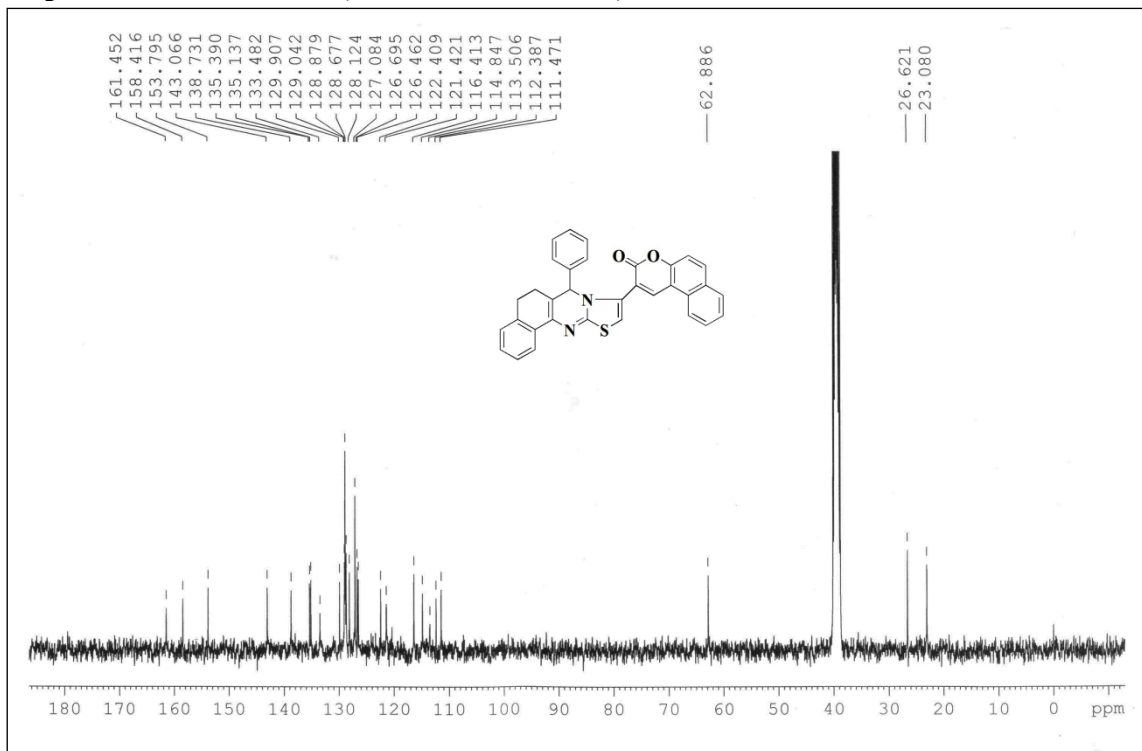
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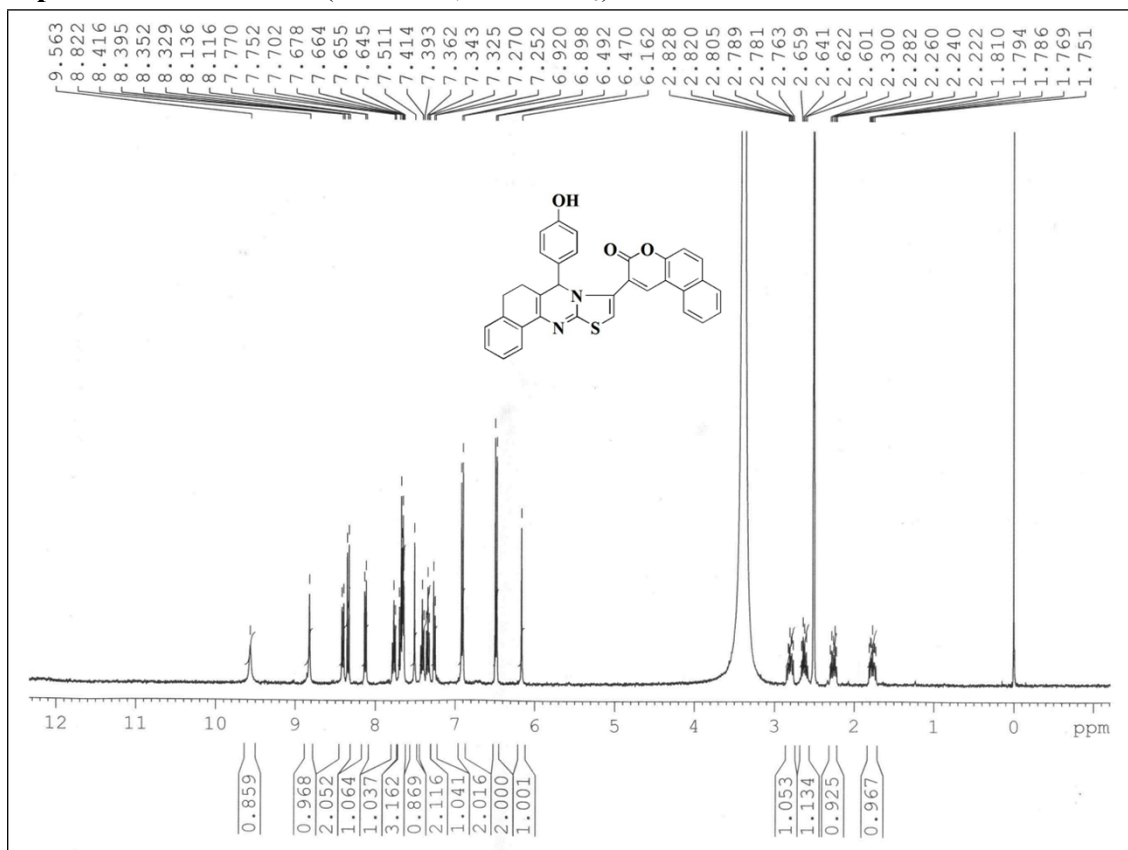
Compound 12a: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



Compound 12a: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)



Compound 12b: ^1H NMR (400 MHz, $\text{DMSO-}d_6$)



Compound 12b: ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)

