Supporting Information

From Botanical Waste to Biocatalyst: *Kigelia pinnata* Flowers Derived CQDs for Triazolidine-3-thione Synthesis and Their In-Silico Evaluation

Sunita Teli[1], Shivani Soni[1], Nisarg Rana[2], Anu Manhas[2], Shikha Agarwal[1]*

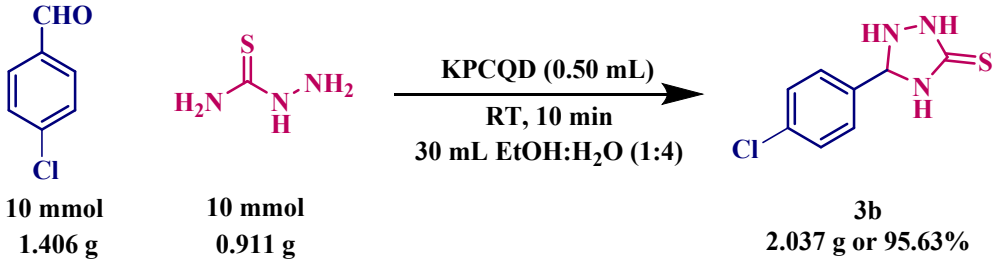
[1]*Synthetic Organic Chemistry Laboratory, Department of Chemistry, Mohanlal Sukhadia University, Udaipur-313001, Rajasthan, India*

[2]*Department of Chemistry, School of Energy Technology, Pandit Deendayal Energy University, Gandhinagar, 382426, India*

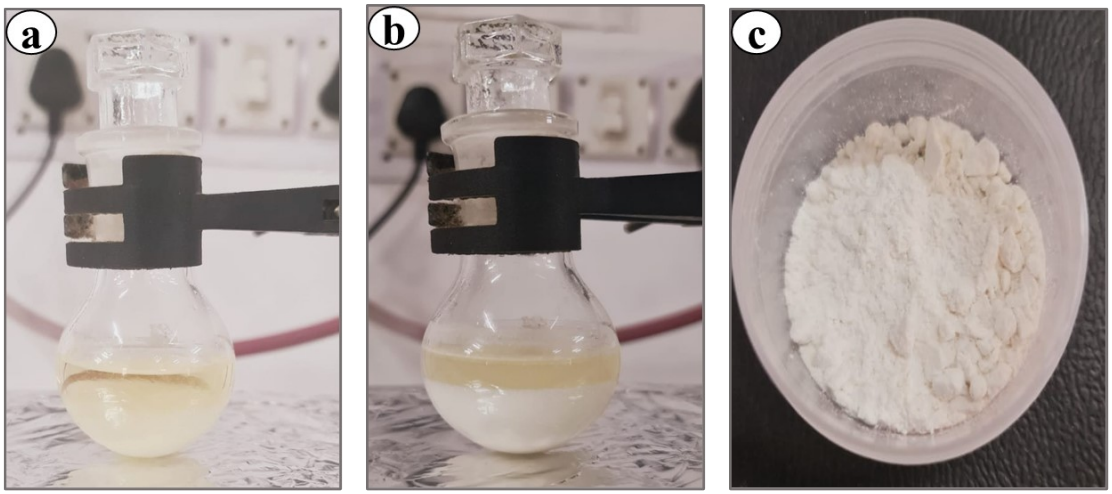
Table of Contents

1. Gram scale synthesis

To evaluate the potential for large-scale synthesis, the reaction was carried out under gram-scale conditions using the previously optimized protocol. For this, equimolar amounts of reactants: thiosemicarbazide (10 mmol, 0.911 g) and 4-chlorobenzaldehyde (10 mmol, 1.406 g) were reacted at RT in the presence of 0.50 mL of KP-CQDs and 30 mL of an ethanol:water (1:4) mixture as the solvent. The reaction was reached at completion within 10 min, as confirmed by TLC analysis. The product precipitated as white solid out of the solution and readily separated from the catalyst and solvent via simple filtration. The residue was washed thoroughly with water to isolate the final product (**3b**). The product was obtained in excellent yield; 2.037 g or 95.63%, thereby demonstrating the scalability and efficiency of this green, catalyst-assisted method (**scheme S1** and **figure S1**).



Scheme S1. Gram-scale production of 5-(4-chlorophenyl)-1,2,4-triazolidine-3-thione (**3b**).



FigureS1. Gram scale production of compound 3b: (a) reaction mixture before stirring (b) reaction mixture after completion of reaction (c) final dried product.

2. Reusability of KP-CQDs

The KP-CQDs demonstrated excellent activity across six reuse cycles, but a noticeable change in the catalyst's color was observed during repeated use- from dark brown to a lighter brown tone (**figureS2 a and b**). Despite this visual change, the catalyst maintained its characteristic green emission under UV light (**figureS2c**), suggesting its preserved optical and catalytic characters.

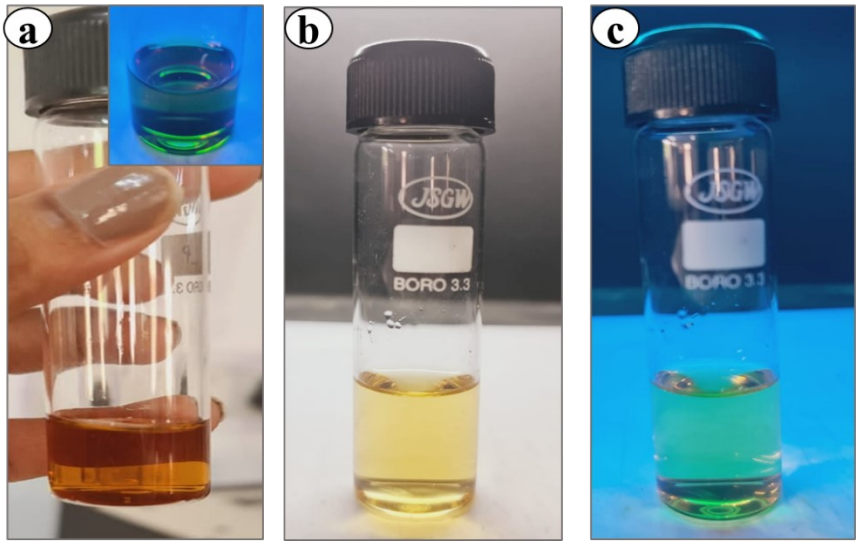


Figure S2. Change in the colour of KP-CQDs during reusability: (a) Fresh KP-CQDs in daylight; inset shows fluorescence behavior under UV light (b) KP-CQDs after six cycles in daylight (c) Reused KP-CQDs in UV-light.

3. Green chemistry metrics

In contemporary synthetic chemistry, the adoption of green chemistry principles has gained significant importance, driven by the need for environmentally sustainable, safe, and resource-efficient processes[1]. The concept of green metrics involves the quantitative evaluation and optimization of chemical reactions to minimize the use and generation of hazardous substances, reduce energy consumption, and improve the overall environmental impact of the synthesis[2, 3]. In this study, green metrics were calculated for all synthesized derivatives based on established

parameters, and the results are summarized in **Table S1**. For compound **3a**, detailed green chemistry calculations are given below-

I. Eco-score (E-score):

An ideal Eco-score value is 100, with the Eco-scale ranging from 0 to 100, categorized as follows: > 75, excellent; > 50, acceptable; and < 50, inadequate.

E-score has been calculated for the reaction by evaluating the following six parameters-

S. No.	Parameter	Values	Penalty points
1	Yield	(100-96.87)/ 2	1.565
2	Price of the reaction components	Inexpensive	0
3	Safety (Reactant)*	5+5 = 10	10
4	Technical setup	Common setup	0
5	Temperature/ Time	Room temp./ < 1h	1
6	Workup and purification	Basic workup	0
	Total penalty points		12.565
***Based on the hazard warning symbols.**			

*Eco-Score = 100 – the sum of individual penalties.

= 100 – 12.565

= 88.435 (>75, excellent synthesis).

II. Atom-economy (AE):

AE = MW of product ÷ Σ (MW of stoichiometric reactants) × 100

= 224.24 ÷ 242.25 × 100

= 0.9257 × 100

= 92.57 %

III. Reaction mass efficiency (RME):

RME = Mass of product /Σ (Mass of stoichiometric reactants) × 100

= 217.22 /242.25 × 100

= 0.89667 × 100

= 89.67%

Higher RME value means cleanness of the reaction.

IV. Environmental factor (E-factor):

E-factor = Mass of waste ÷ Mass of product

[Where; mass of waste = total mass of raw materials - total mass of the product]

= 242.25 -217.22

= 25.03

E-factor = 25.03 ÷ 217.22

= 0.1152

V. Process mass intensity (PMI):

PMI = Σ (Mass of stoichiometric reactants + solvent) / Mass of product

= (242.25 + 3)/217.22

= 245.25/217.22

= 1.129

{Ideal value of PMI = E-factor + 1}

Table S1. Green chemistry metrics data (E-factor, AE, RME, PMI and E-score) for all the synthesized compounds.

S.NO	***Code***	***E-factor***	***AE (%)***	***RME (%)***	***PMI***	***E-score***
1	3a	0.115	92.57	89.67	1.129	88.44
2	3b	0.125	92.22	88.90	1.139	88.20
3	3c	0.211	92.72	82.59	1.225	84.54
4	3d	0.217	92.75	82.16	1.232	84.29
5	3e	0.357	90.38	73.71	1.378	80.78
6	3f	0.188	93.41	84.15	1.201	85.05
7	3g	0.157	93.78	86.40	1.169	86.07
8	3h	0.237	93.00	80.84	1.251	83.46
9	3i	0.256	88.62	79.65	1.267	84.94

Our method demonstrated excellent green chemistry metrics, including high atom economy (88.62-93.78%), an impressive eco-score (80.78-88.44%), and efficient reaction mass performance (73.71-89.67%). Additionally, the process exhibited a favorable process mass intensity (1.129-1.378) and a low environmental factor (E-factor ≤ 0.357), highlighting the overall sustainability and minimal waste generation of the reaction system.

4. Yield and concentration of KP-CQDs

The **yield (%)** and **concentration (mg/mL)** were calculated using the following equations:

Yield (%) = {Mass of dried KP-CQDs obtained (g) / Mass of biomass used (g)} × 100

[Mass of dried KP-CQDs = Final beaker weight – Initial beaker weight]

= 49.023 - 47.928

= 1.095 g or 1095 mg

Yield (%) = (1.095 g / 4.000 g) × 100

= **27.375**%

Concentration (mg/mL) = Mass of dried KP-CQDs (mg) / Volume of KP-CQDs solution (mL)

= 1095 mg / 62 mL

= **17.661** mg/mL

The yield of the KP-CQDs was found **27.375**% and the concentration was found **17.661** mg/mL.

5. Synthesis of 1,2,4-triazolidine compounds

5.1. Materials and methods

All chemicals used in this study were procured from reliable commercial suppliers, including Avra, BLD-Pharma, Sigma-Aldrich, SRL and Merck and were employed without further purification. TECHINSTRO Teflon-lined hydrothermal autoclave (capacity-150 mL) was used for hydrothermal process. Filtration of the catalyst was performed using a Merck MCE 0.45 µm, 47 mm diameter filter membrane. Reaction progress was monitored using thin-layer chromatography (TLC) performed on silica gel 60 RP-18 F254S plates and visualized under a 3 NOS UV cabinet. HRTEM and SAED analyses were conducted using an FEI Technai G2 F30 microscope operated at 300 kV. XRD analysis of was performed using a Rigaku Ultima IV diffractometer with CuKα radiation (λ = 0.1541 nm). FT-IR spectra were recorded on a Bruker FT-IR spectrometer. EDX analysis was carried out using a Hitachi SU8010 system (Japan). UV-Visible spectrum was obtained using a JASCO V-750 spectrophotometer, while fluorescence emission spectrum was recorded on a JASCO FP-8850 fluorometer. Melting points of the synthesized compounds were determined using a digital melting point apparatus and are reported without correction. ^{1}H,^{13}C, and ^{19}F NMR spectra were acquired on a JEOL JNM-ECZ400S/L1 spectrometer operating at 400, 100, and 376 MHz, respectively, using DMSO-d_6 as the solvent and

tetramethylsilane (TMS) as the internal reference. HRMS analyses were performed using a Xevo G2-XS QToF mass spectrometer (LC-MS/MS) coupled with an Acquity H-Class PLUS UPLC system.

5.2. General synthetic procedure

A mixture of substituted aldehyde (1 mmol), and thiosemicarbazide (1 mmol) was stirred with KP-CQDs (0.50 mL) in 3 ml of ethanol:water combination (1:4) at RT. The reaction progress was monitored by TLC (hexane-ethyl acetate, 7:3). Upon completion, the precipitated product was separated by simple filtration, and thoroughly washed with water, and dried in an oven at 60 °C. The catalyst + solvent mixture (found as filtrate) was reused directly in subsequent reactions without any purification step.

For the synthesis of **3i**, the starting material ratios were adjusted:

Synthesis of **3i**: Terphthaldehyde (0.5 mmol) was reacted with thiosemicarbazide (1.0 mmol) to produce a bis-triazolidine product.

5.3. Spectroscopic data of the synthesized compounds

5.3.1. 5-(4-nitrophenyl)-1,2,4-triazolidine-3-thione (*3a*)

Shiny yellow powder; 97% yield; M.P. 221-224 °C[4]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.69 (s, 1H, NH), 8.39 (s, 1H, NH), 8.25 (s, 1H, NH), 8.18 (d, J = 9.2 Hz, 2H, Ar-H), 8.08 – 8.06 (m, 2H, Ar-H), 8.04 (s, 1H, CH). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.93, 148.07, 141.27, 140.03, 128.70, 124.33. $C_8H_8N_4O_2S$ [m/z] 224.0368.

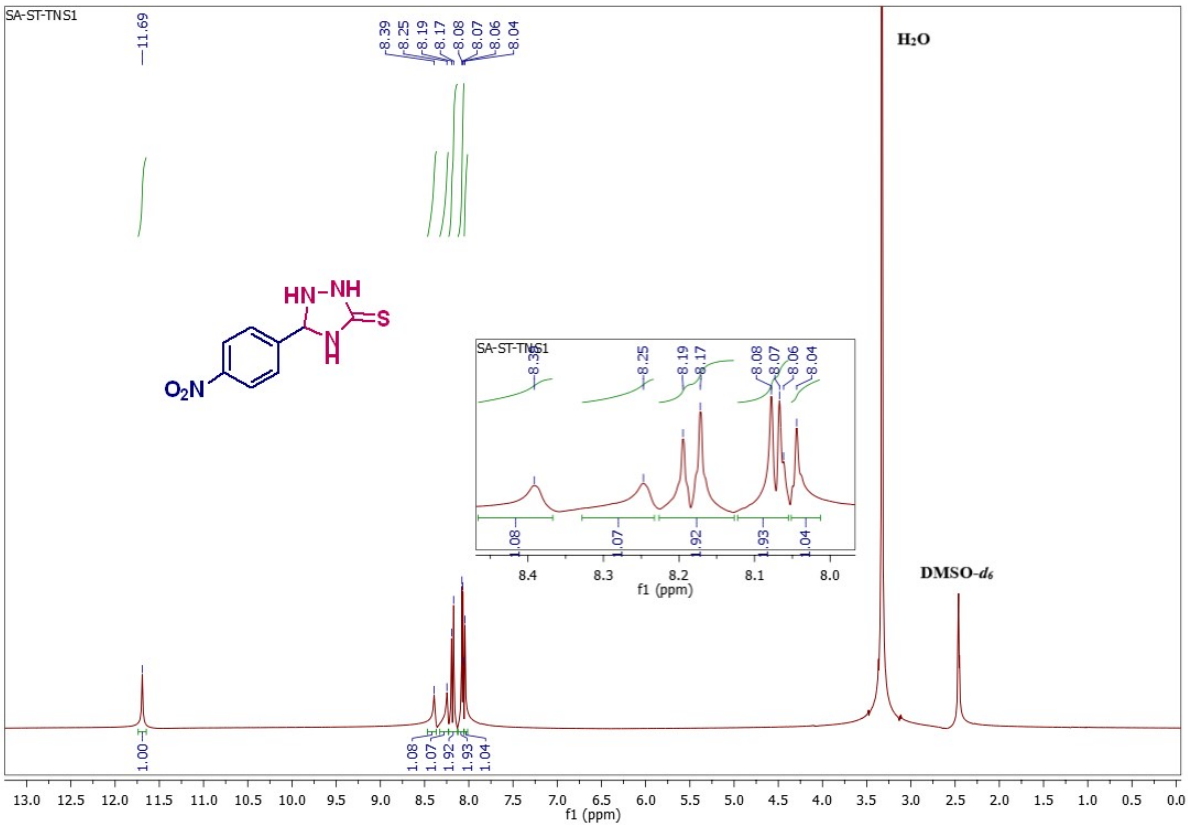


Figure S3. ^{1}H NMR spectrum of 3a.

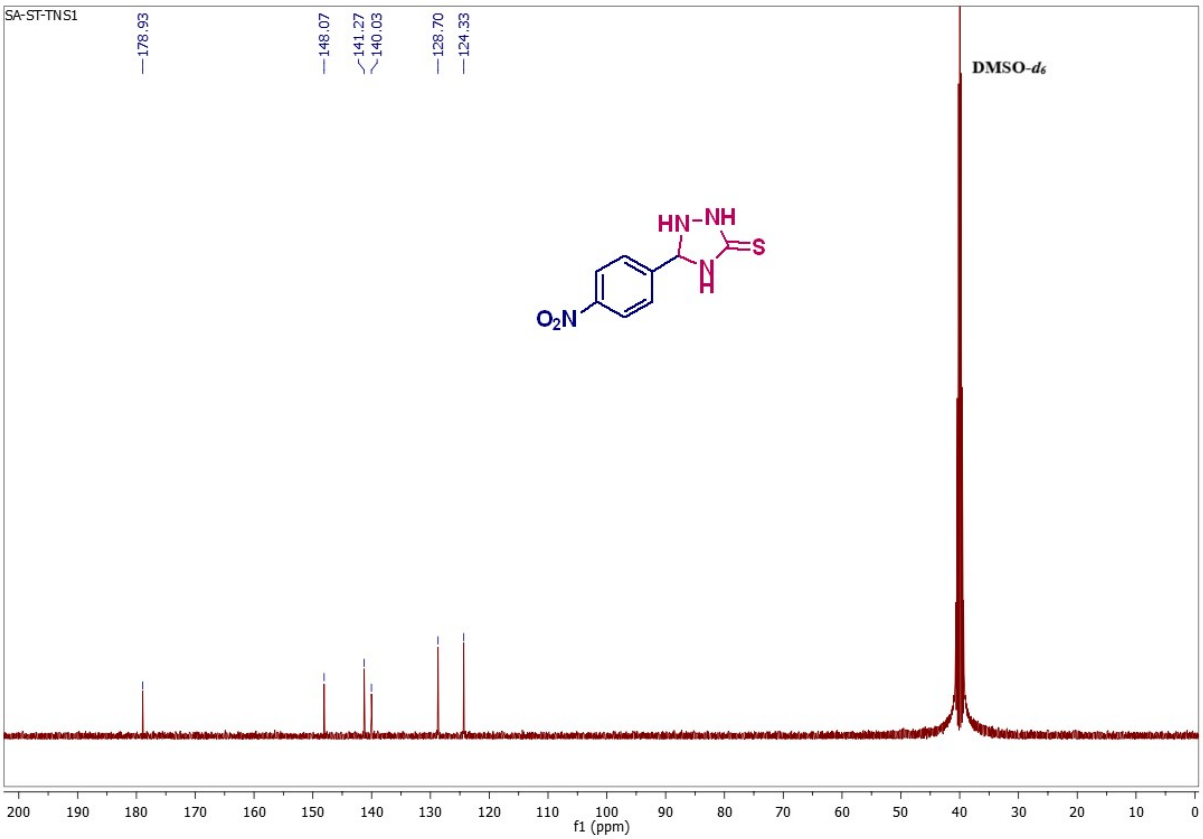


Figure S4. ^{13}C NMR spectrum of 3a.

5.3.2. 5-(4-chlorophenyl)-1,2,4-triazolidine-3-thione (*3b*)

White powder; 96% yield; M.P. 204-206 °C[5]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.46 (s, 1H, NH), 8.22 (s, 1H, NH), 8.05 (s, 1H, NH), 7.98 (s, 1H, CH), 7.81 – 7.79 (m, 2H, Ar-H), 7.42 – 7.40 (m, 2H, Ar-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.54, 141.33, 134.74, 133.71, 129.48, 129.22. $C_8H_8ClN_3S$ [m/z] 213.0127.

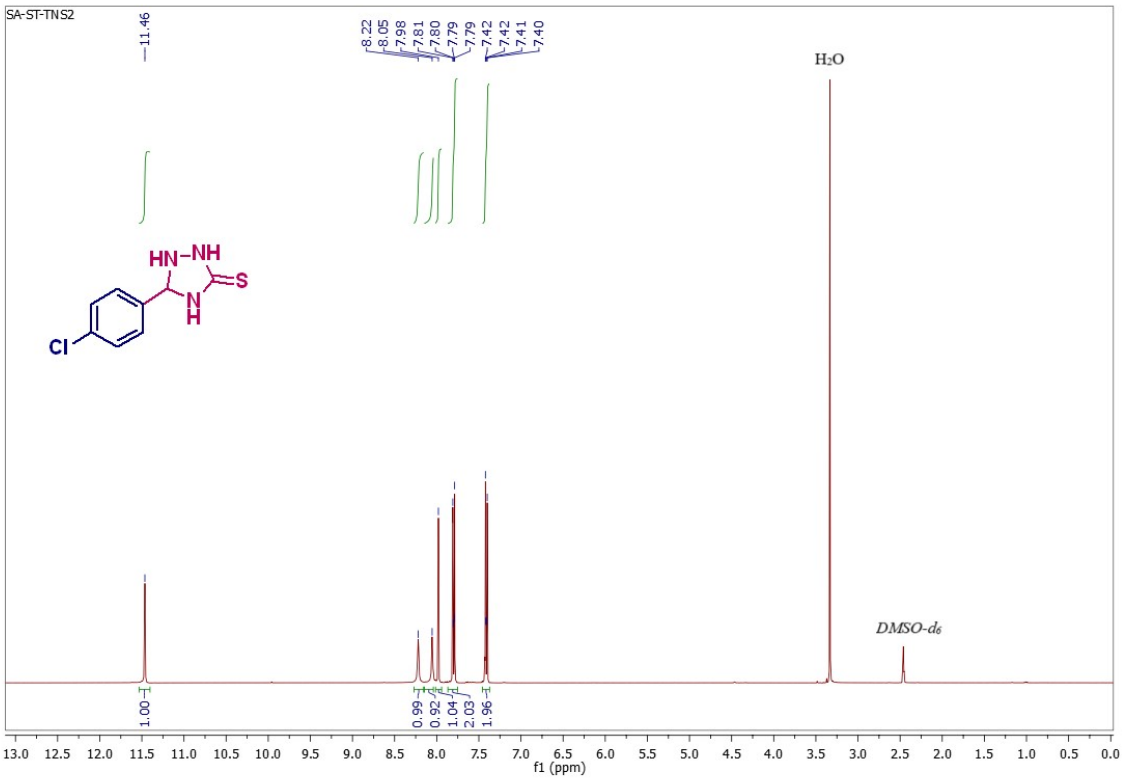


Figure S5. ^{1}H NMR spectrum of 3b.

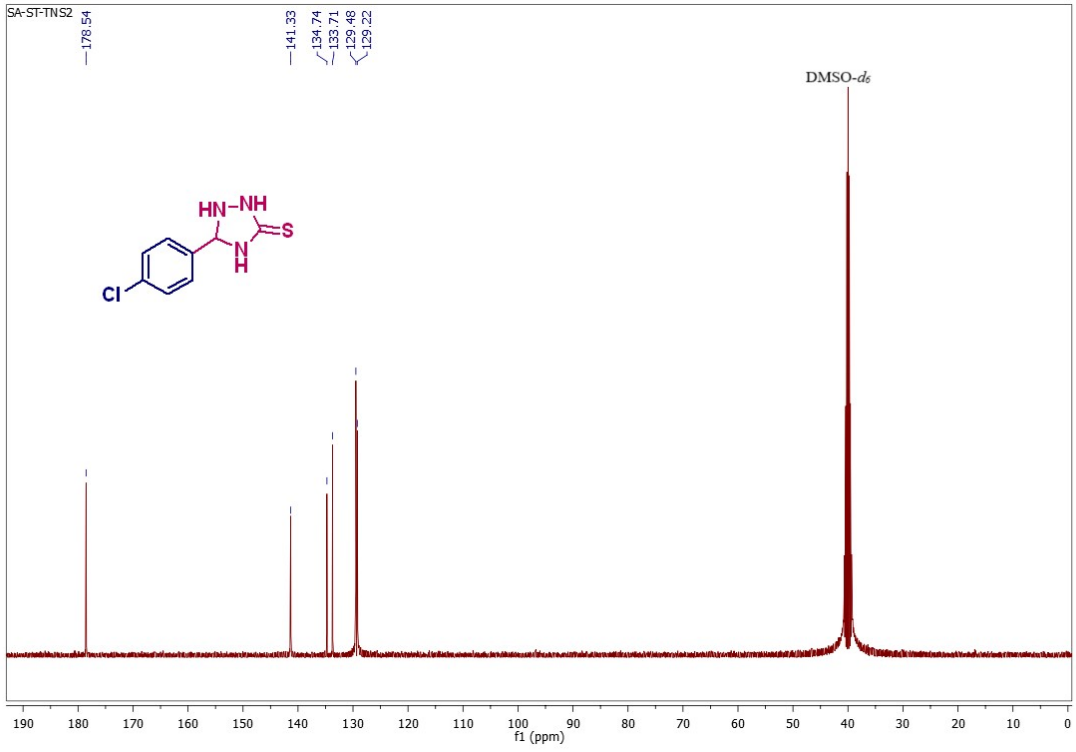


Figure S6. ^{13}C NMR spectrum of 3b.

5.3.3. 5-(naphthalen-1-yl)-1,2,4-triazolidine-3-thione (*3c*)

Off-white fluffy powder; 89% yield; M.P. 209-211 °C[6]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.45 (s, 1H, NH), 8.88 (s, 1H, CH), 8.32 - 8.29 (m, 2H, NH), 8.19 (dd, J = 7.3, 0.8 Hz, 1H, Ar-H), 7.97 – 7.95 (m, 3H, Ar-H), 7.63 – 7.59 (m, 1H, Ar-H), 7.56 – 7.51 (m, 2H, Ar-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.35, 141.44, 133.91, 130.99, 130.76, 129.76, 129.37, 127.79, 126.68, 126.28, 126.11, 123.36. $C_{12}H_{11}N_3S$ [m/z] 229.0674.

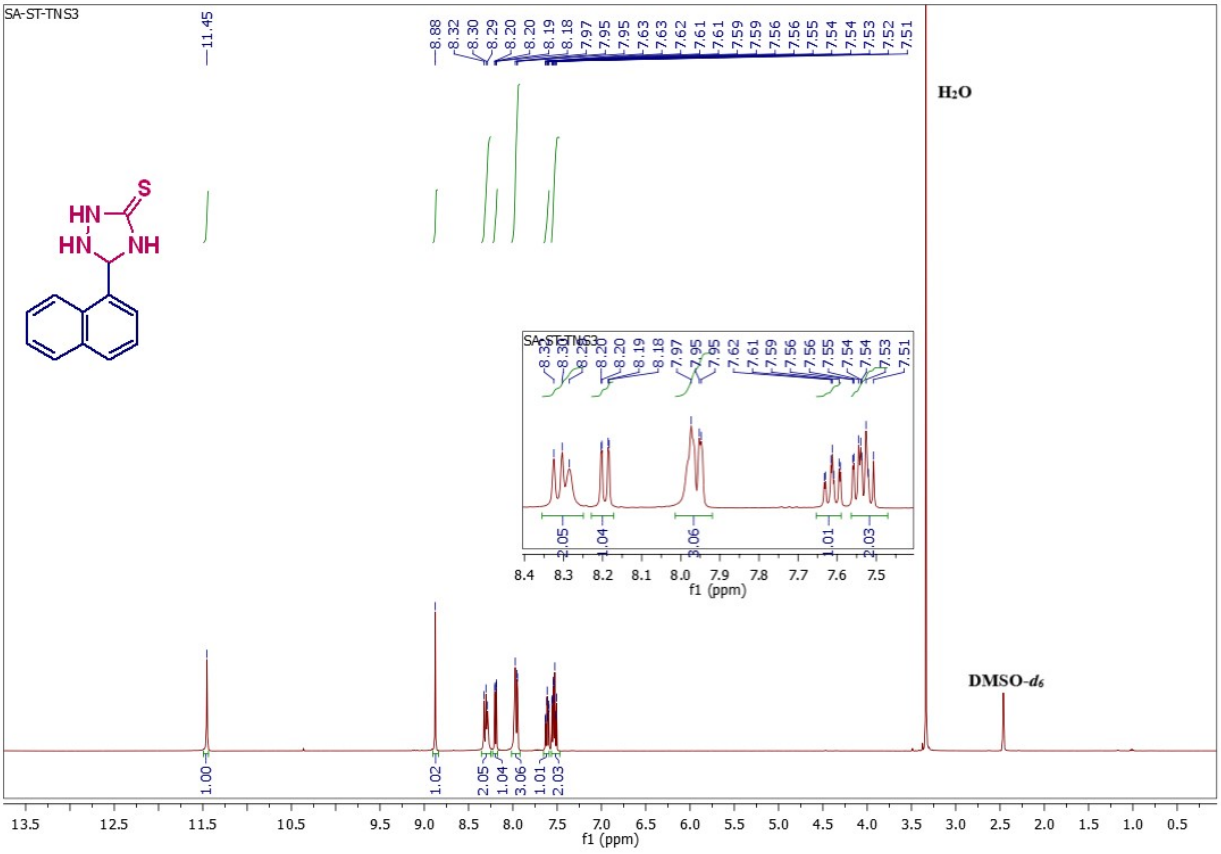


Figure S7. ^{1}H NMR spectrum of 3c.

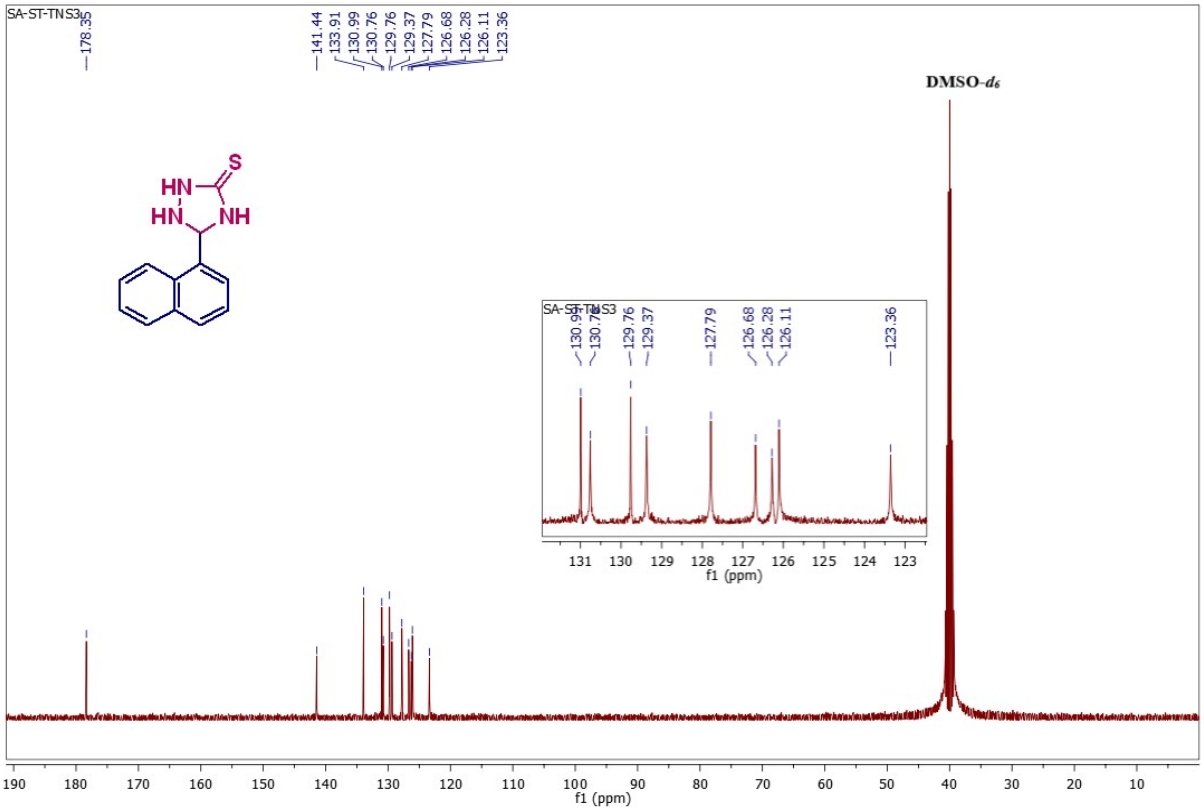


Figure S8. ^{13}C NMR spectrum of 3c.

5.3.4. 5-(quinolin-4-yl)-1,2,4-triazolidine-3-thione (*3d*)

Off-white powder; 89% yield; M.P. 232-235 °C^{new}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.66 (s, 1H, NH), 8.89 (d, J = 4.6 Hz, 1H, Ar-H), 8.84 (s, 1H, CH), 8.45 (s, 1H, NH), 8.25 (d, J = 8.3 Hz, 1H, Ar-H), 8.19 (s, 1H, NH), 8.14 (d, J = 4.6 Hz, 1H, Ar-H), 8.04 (d, J = 8.3 Hz, 1H, Ar-H), 7.79 – 7.75 (m, 1H, Ar-H), 7.69 – 7.65 (m, 1H, Ar-H),). ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.00, 150.64, 148.90, 138.31, 137.82, 130.37, 130.07, 127.93, 125.58, 123.52, 118.46. HRMS for $C_{11}H_{10}N_4S$ (M+H$^+$); calculated: 231.0660 and found: 231.0705.

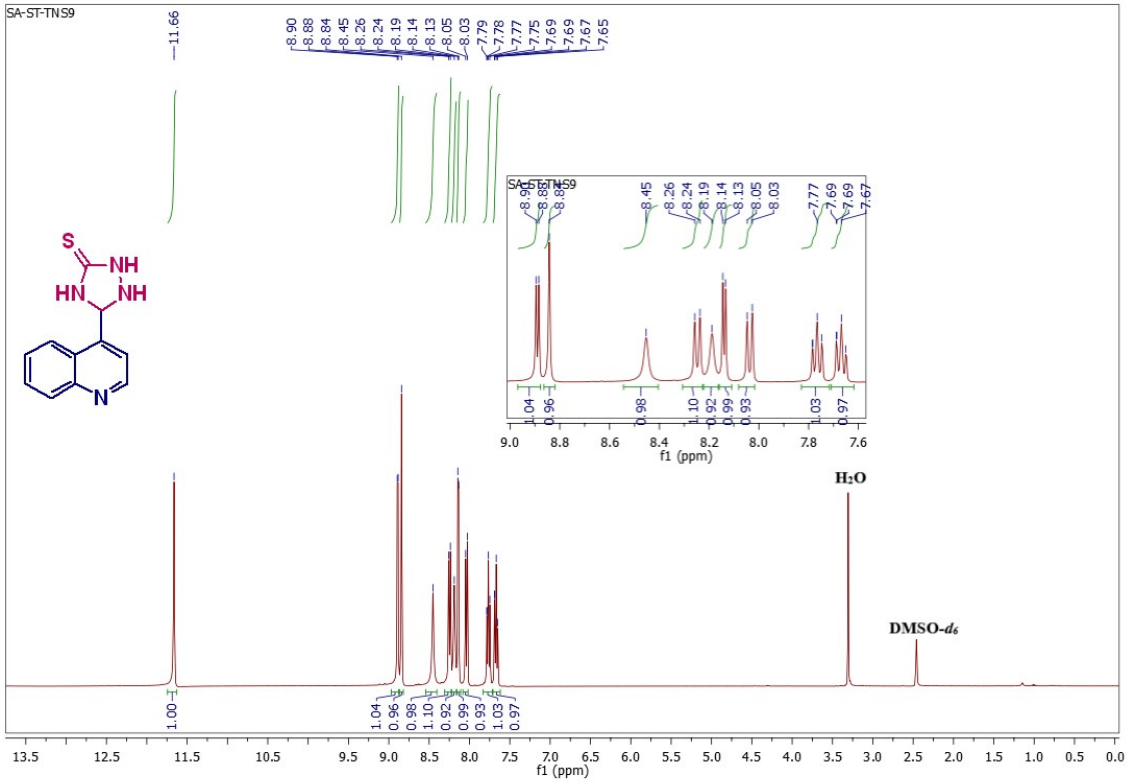


Figure S9. ^{1}H NMR spectrum of 3d.

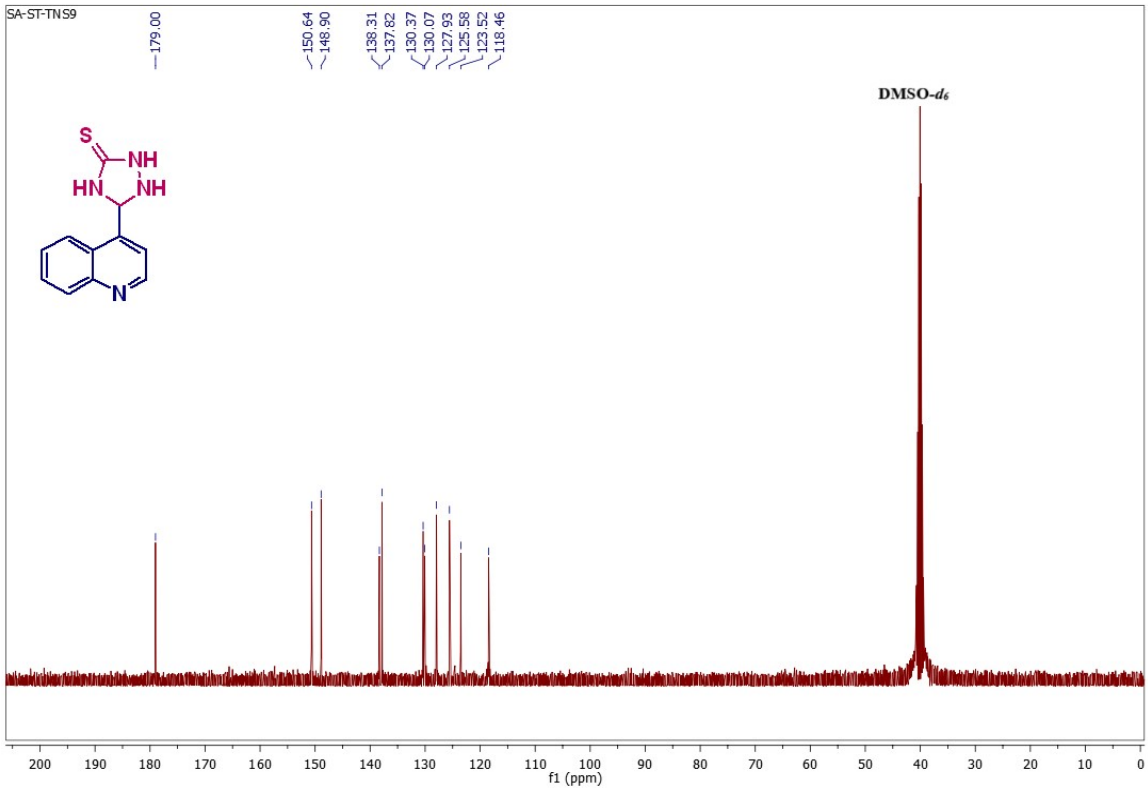


Figure S10. ^{13}C NMR spectrum of 3d.

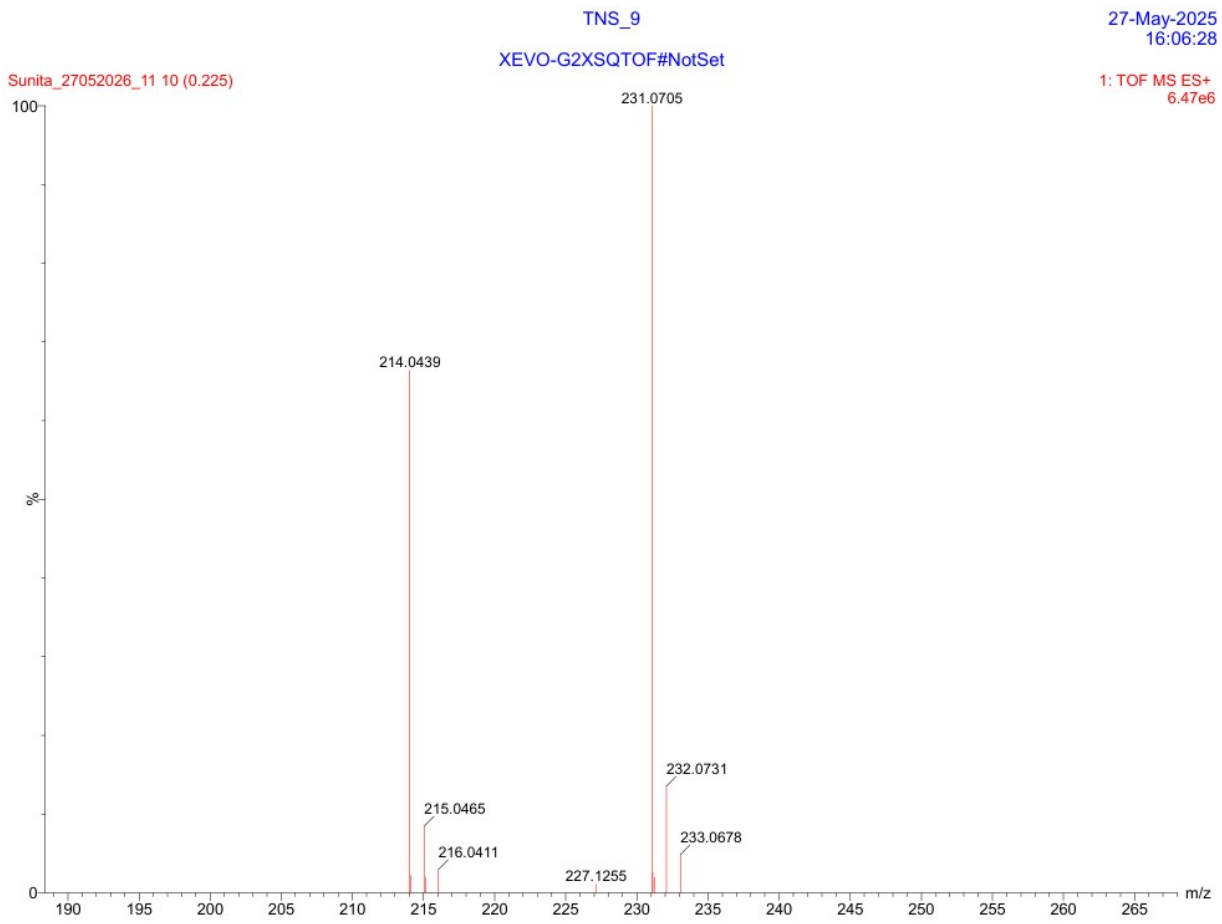


Figure S11. HRMS spectrum of 3d.

5.3.5. 5-(1*H*-imidazol-4-yl)-1,2,4-triazolidine-3-thione (*3e*)

Shiny beige powder; 82% yield; M.P. 190-193 °C[new]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.45 (s, 1H, NH of imidazole), 11.36 (s, 1H, NH), 8.14 (s, 1H, NH), 7.90 (s, 2H, Ar-H), 7.76 (s, 1H, CH), 7.26 (br, 1H, NH). HRMS for $C_5H_7N_5S$ ($M+H^+$); calculated: 170.0456 and found: 170.0500.

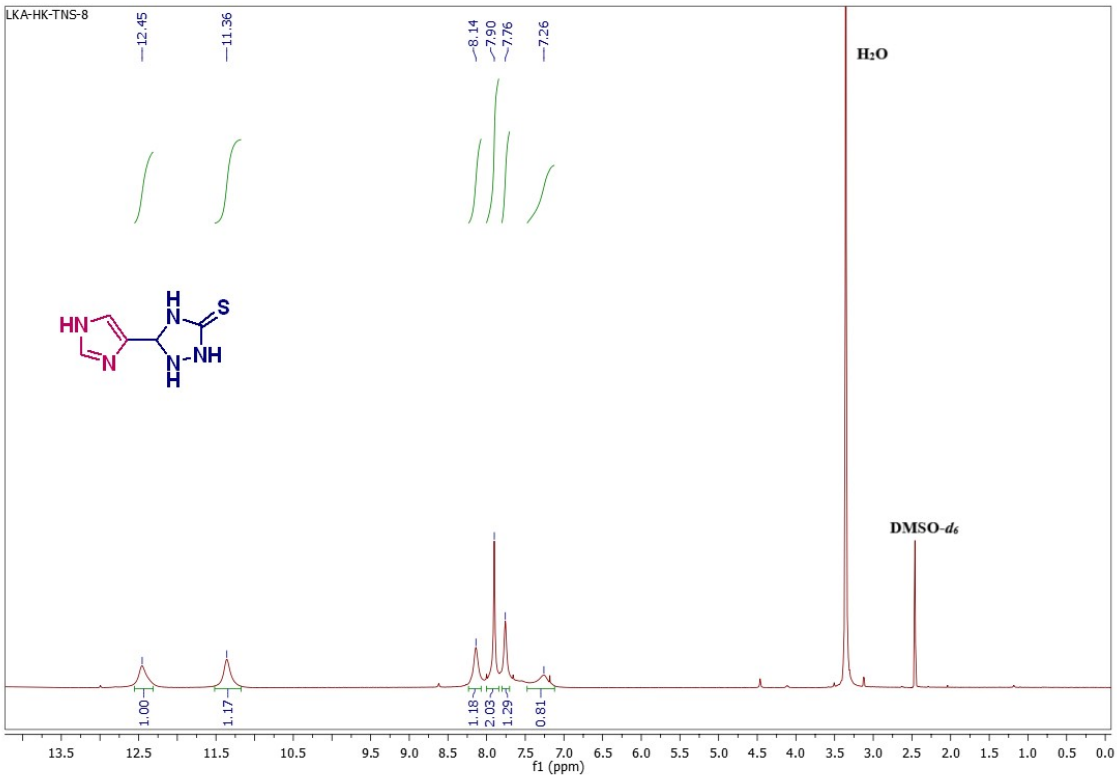


Figure S12. ^{1}H NMR spectrum of 3e.

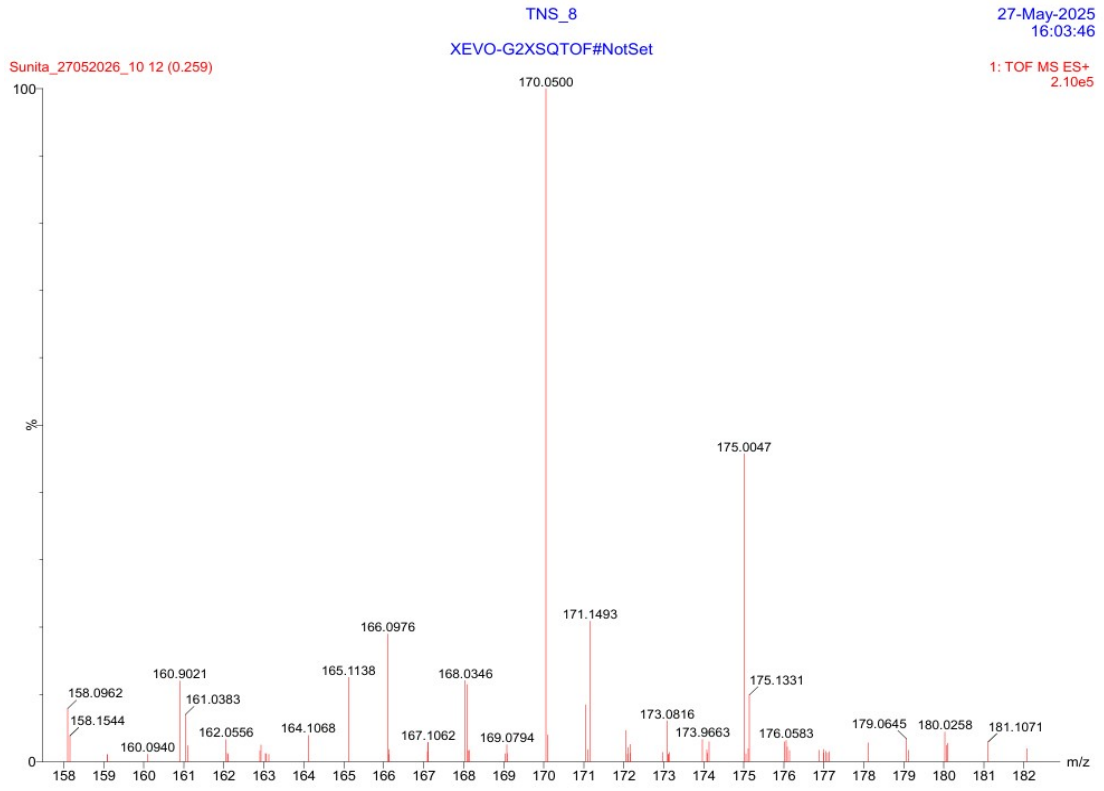


Figure S13. HRMS spectrum of 3e.

5.3.6. 5-(4-hydroxy-3,5-dimethoxyphenyl)-1,2,4-triazolidine-3-thione (*3f*)

Fluffy white powder; 90% yield; M.P. 136-139 °C[new]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.30 (s, 1H, NH), 8.80 (br, 1H, OH), 8.12 (s, 1H, NH), 7.98 (s, 1H, NH), 7.87 (s, 1H, CH), 7.00 (s, 2H, Ar-H), 3.76 (s, 6H, OCH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.83, 148.56, 143.41, 138.12, 124.87, 105.32, 56.60. HRMS for $C_{10}H_{13}N_3O_3S$ ($M+H^+$); calculated: 256.0711 and found: 256.0757.

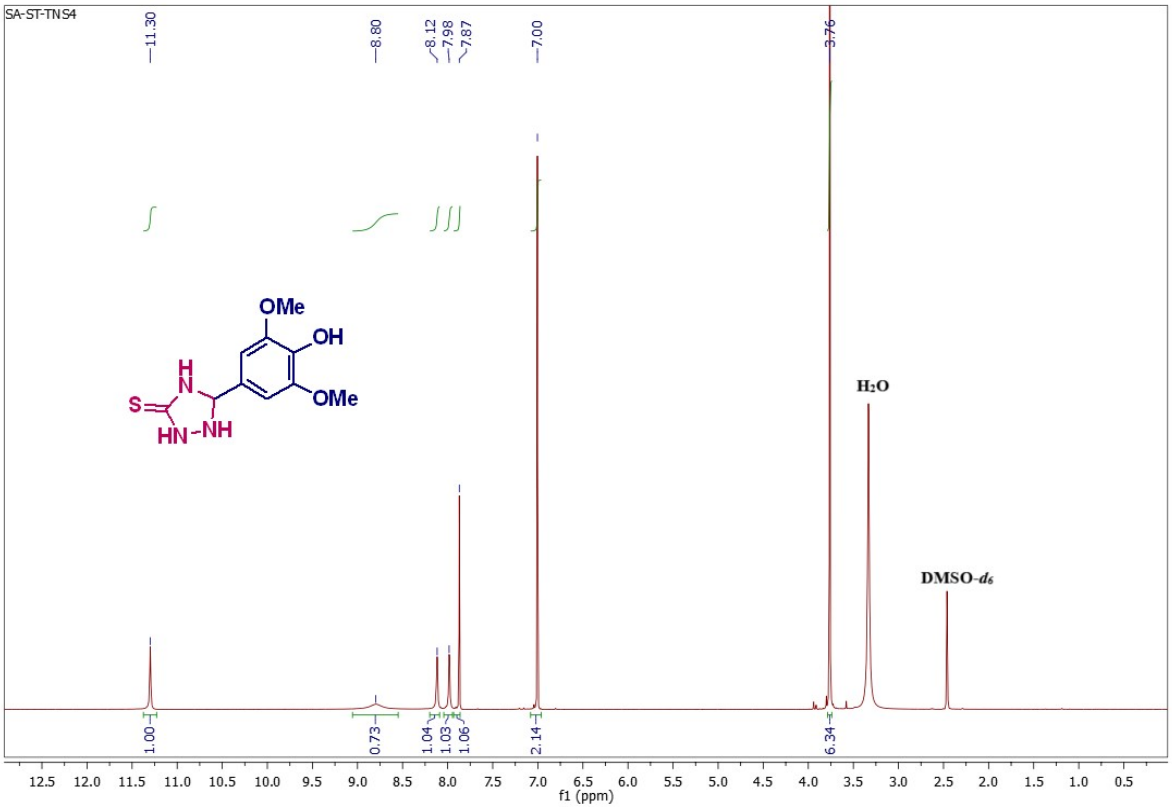


Figure S14. ^{1}H NMR spectrum of 3f.

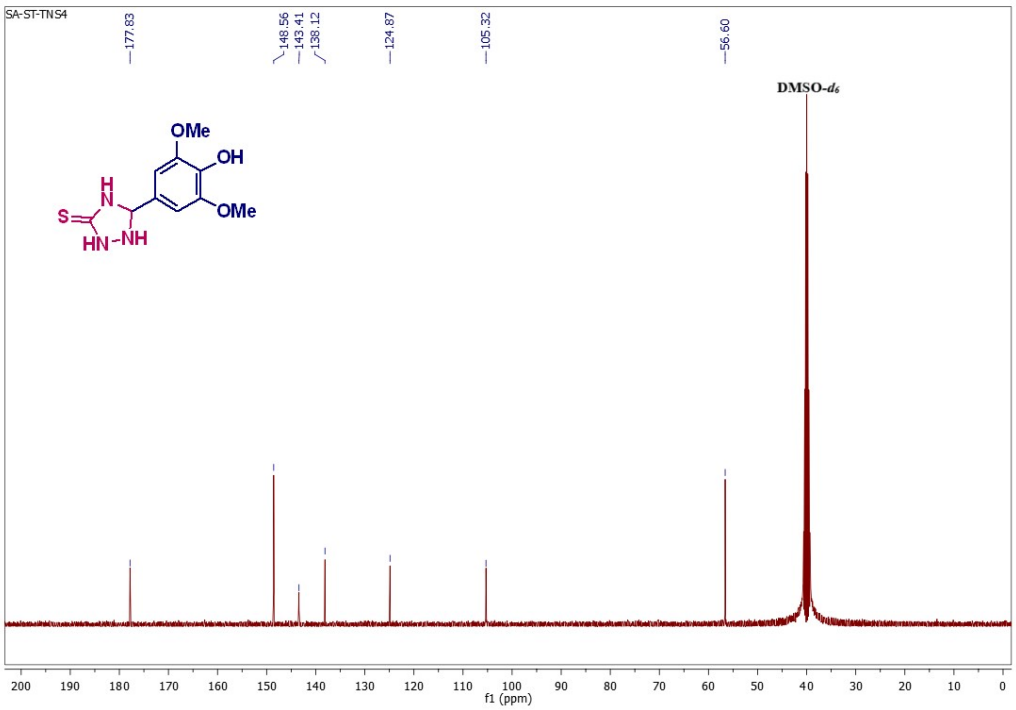


Figure S15. ^{13}C NMR spectrum of 3f.

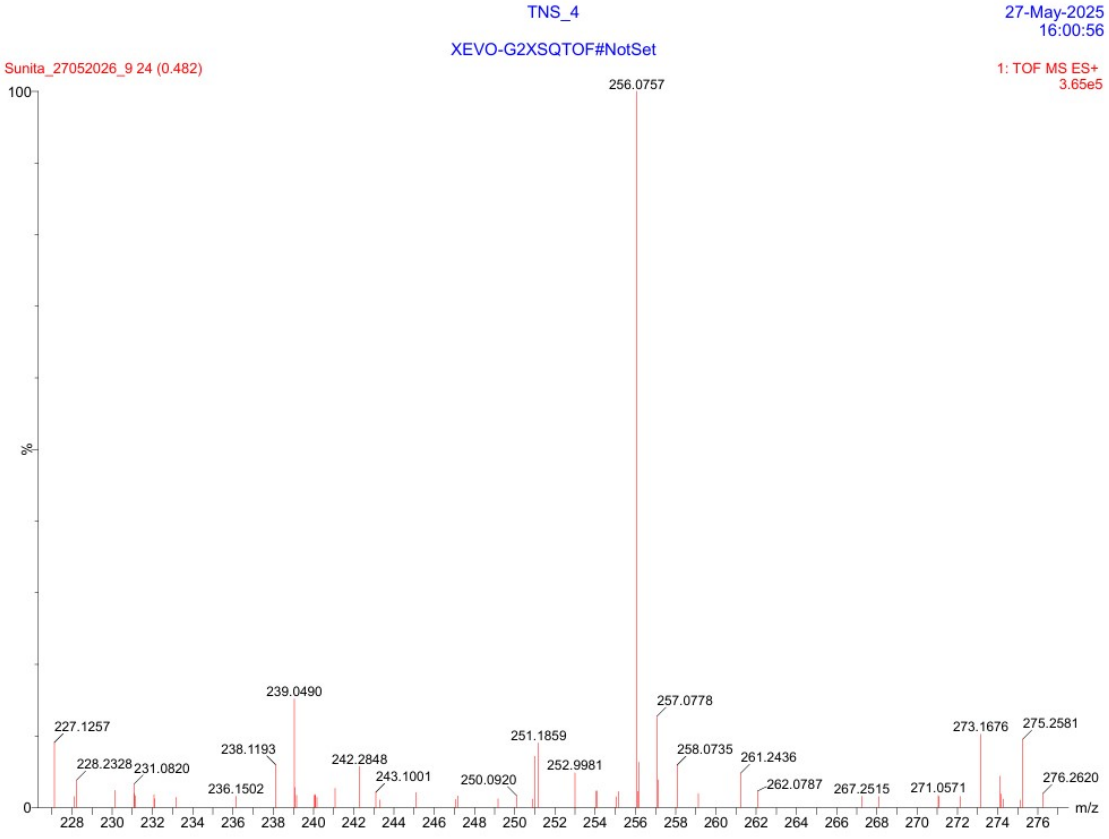


Figure S16. HRMS spectrum of 3f.

5.3.7. 5-(3-phenoxyphenyl)-1,2,4-triazolidine-3-thione (*3g*)

White fluffy powder; 92% yield; M.P. 201-203 °C[6]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.44 (s, 1H, NH), 8.19 (s, 1H, NH), 8.05 (s, 1H, NH), 7.98 (s, 1H, CH), 7.58 – 7.57 (m, 1H, Ar-H), 7.49 (dd, J = 6.7, 1.1 Hz, 1H, Ar-H), 7.39 – 7.33 (m, 3H, Ar-H), 7.11 – 7.07 (m, 1H, Ar-H), 6.97 – 6.94 (m, 3H, Ar-H),). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.52, 157.27 (d, J = 7.9 Hz), 141.94, 136.91, 130.85, 130.61, 123.83 (d, J = 13.4 Hz), 120.70, 118.77, 117.81. $C_{14}H_{13}N_3OS$ [m/z] 271.0779.

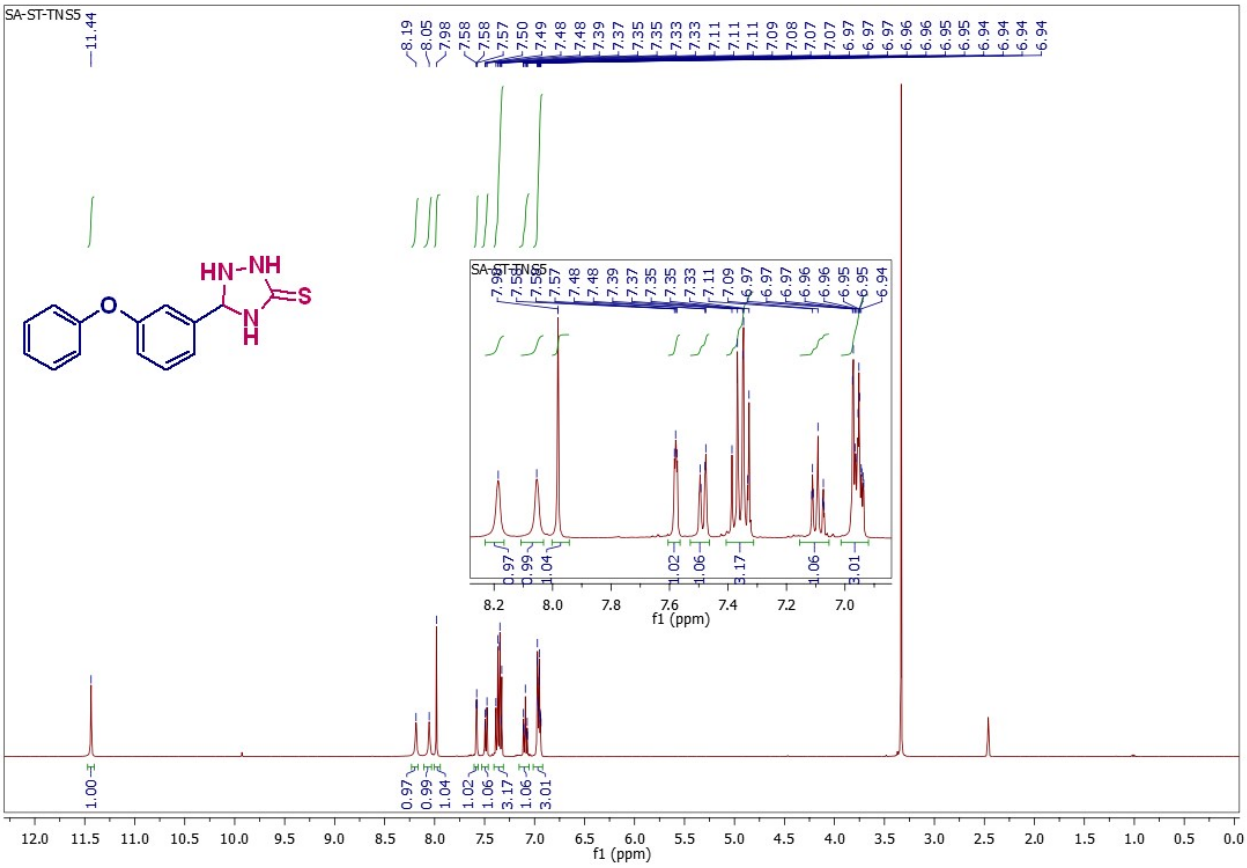


Figure S17. ^{1}H NMR spectrum of 3g.

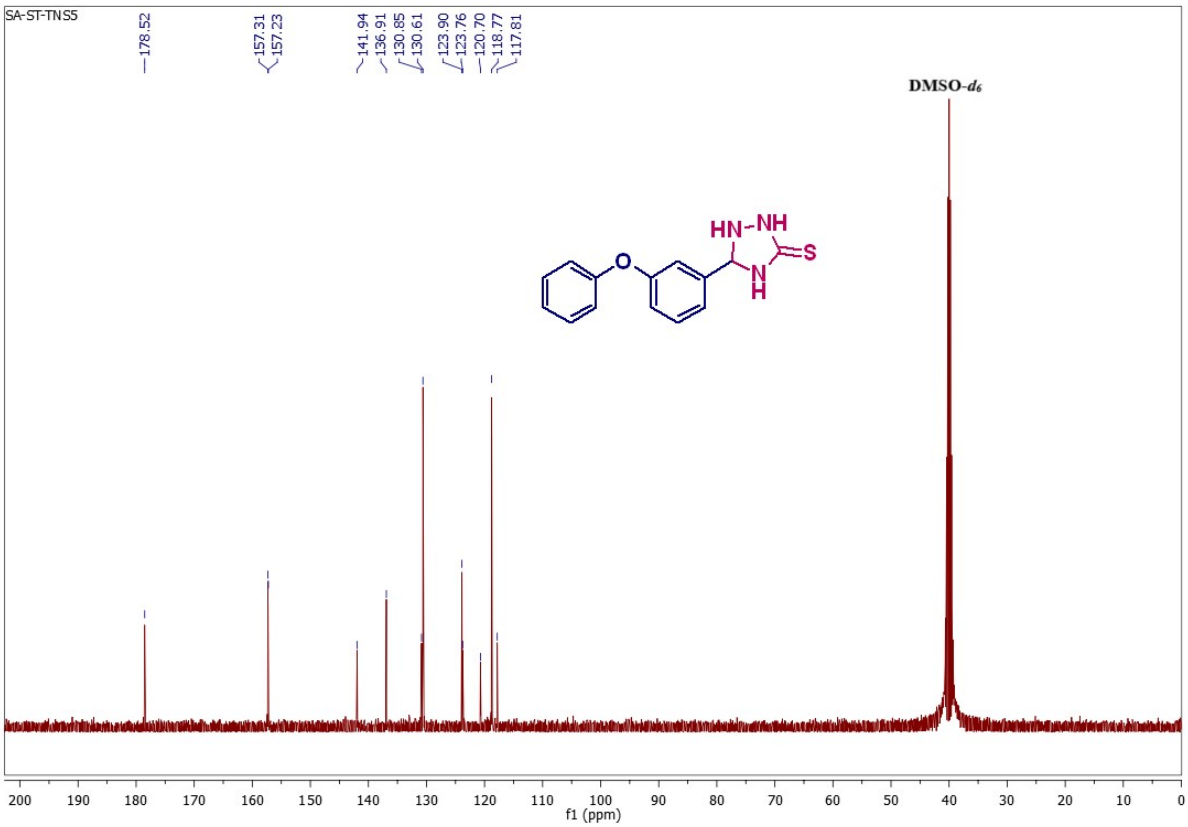


Figure S18. ^{13}C NMR spectrum of 3g.

5.3.8. 5-(3-ethoxy-4-hydroxyphenyl)-1,2,4-triazolidine-3-thione (*3h*)

White powder; 87% yield; M.P. 172-175 °C[6]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.22 (s, 1H, NH), 9.36 (s, 1H, OH), 8.08 (s, 1H, NH), 7.93 (s, 1H, NH), 7.87 (s, 1H, CH), 7.42 (d, J = 1.8 Hz, 1H, Ar-H), 6.97 (dd, J = 8.2, 1.8 Hz, 1H, Ar-H), 6.74 (d, J = 8.1 Hz, 1H, Ar-H), 4.03 (q, J = 7.0 Hz, 2H, CH_2), 1.30 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.81, 149.50, 147.76, 143.43, 126.07, 122.87, 115.73, 110.84, 64.37, 15.24. $C_{10}H_{13}N_3O_2S$ [m/z] 239.0728.

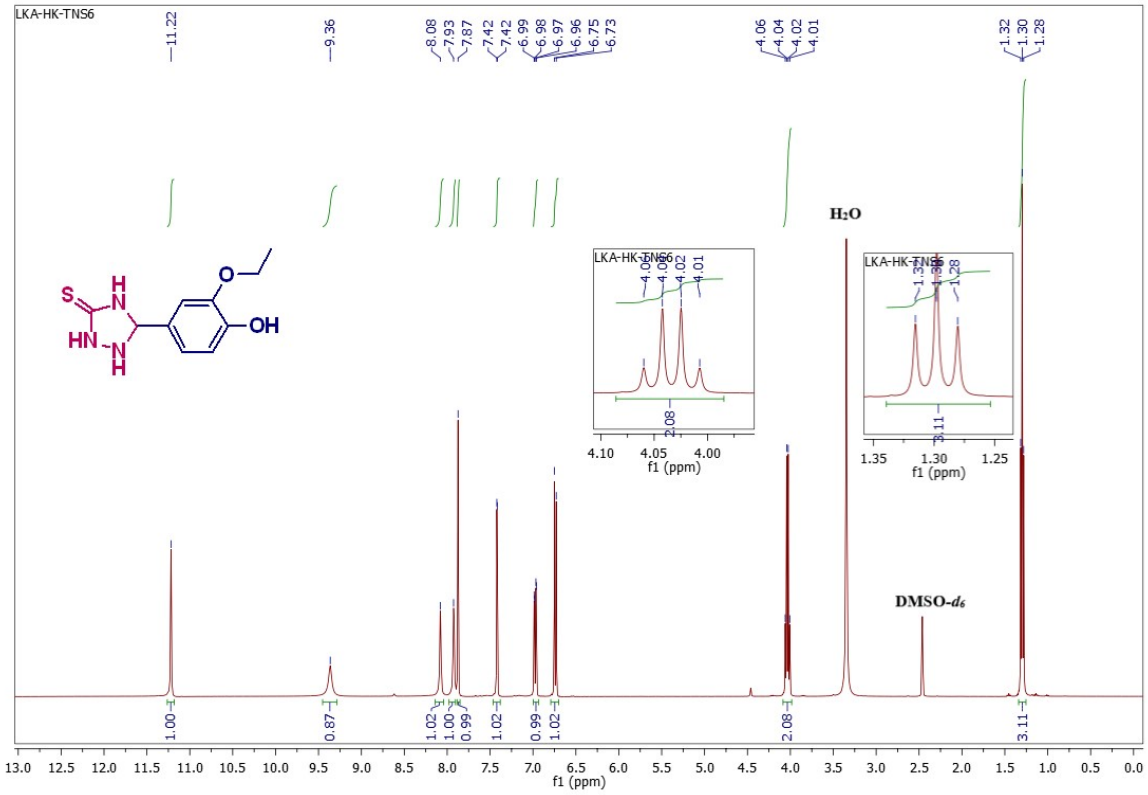


Figure S19. ^{1}H NMR spectrum of 3h.

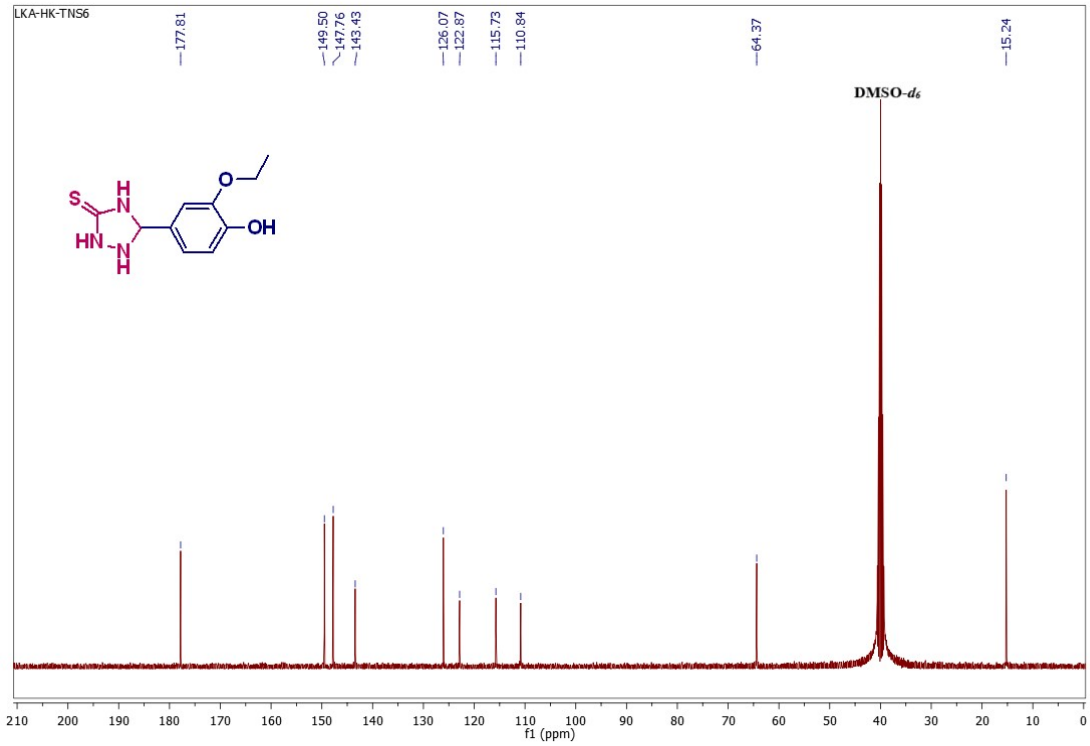


Figure S20. ^{13}C NMR spectrum of 3h.

5.3.9. 5,5'-(1,4-phenylene)bis(1,2,4-triazolidine-3-thione) (*3i*)

White fluffy powder; 90% yield; M.P. 202-204 °C[5]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.44 (s, 2H, NH), 8.19 (s, 2H, NH), 8.01 (d, J = 5.3 Hz, 2H of NH + 2H of CH), 7.77 (s, 4H, Ar-H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.54, 142.16, 135.92, 128.04. $C_{10}H_{12}N_6S_2$ [m/z] 280.0565.

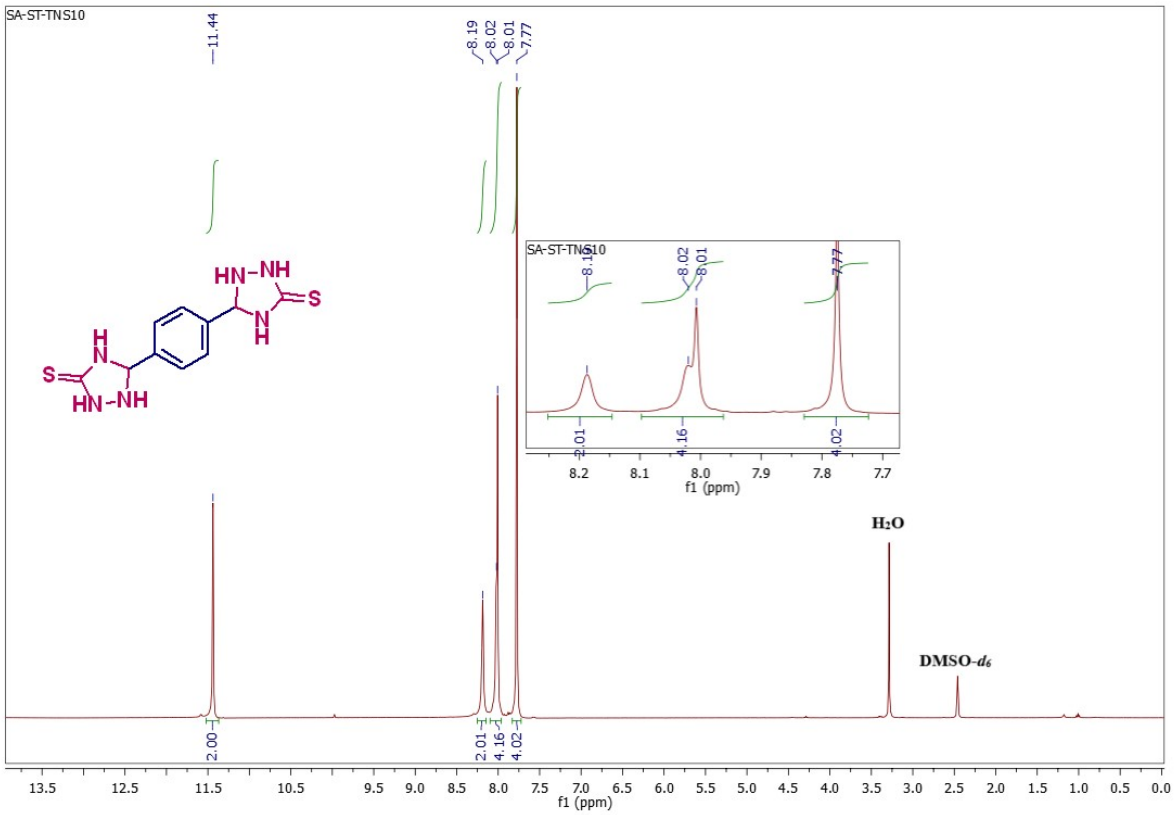


Figure S21. ^{1}H NMR spectrum of 3i.

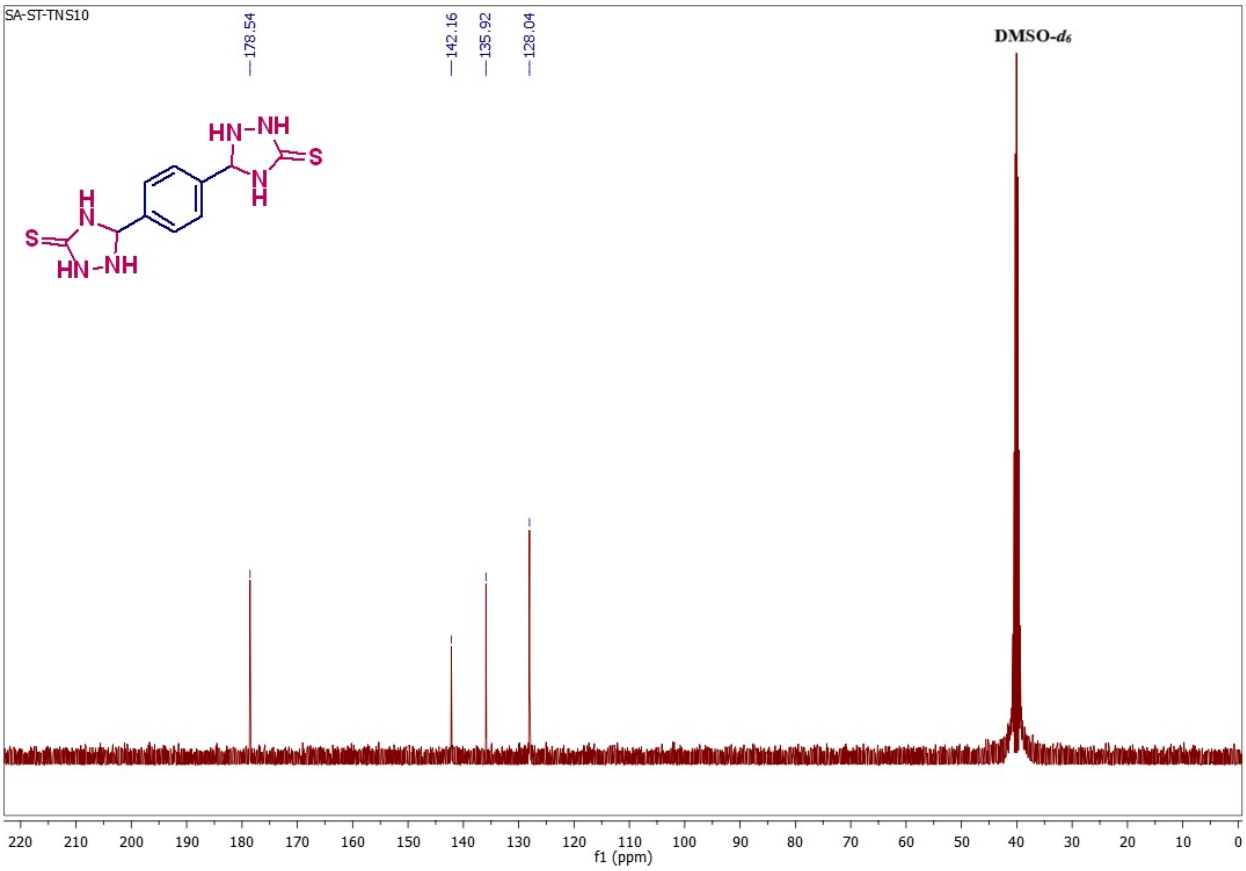


Figure S22. ^{13}C NMR spectrum of 3i.

6. Molecular docking

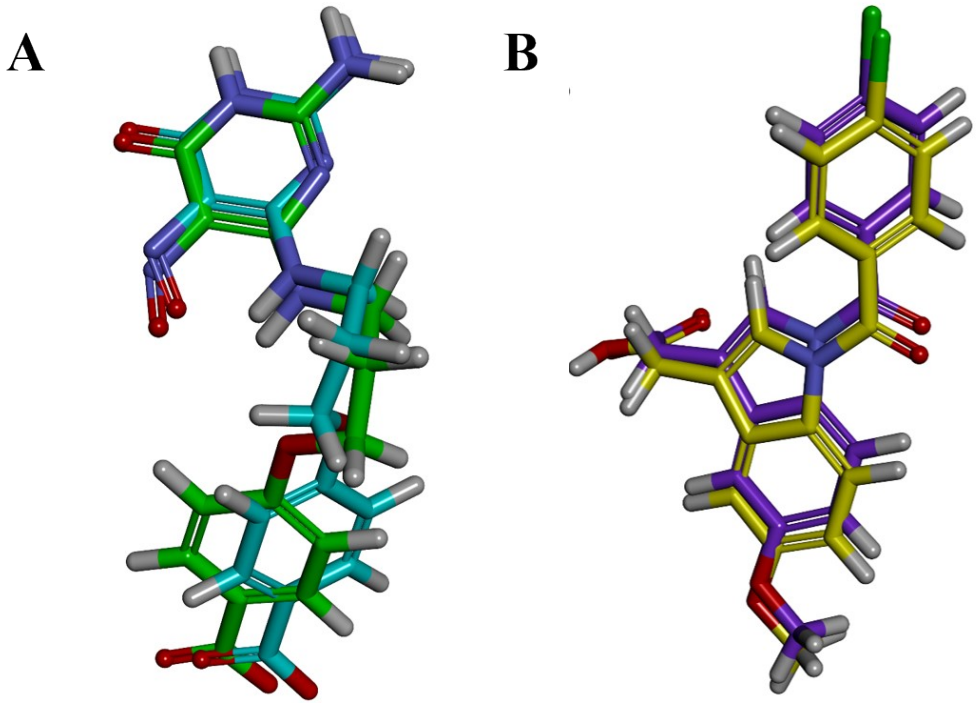


Figure S23. Superimposed pose of (A) Co-crystalized B54 (green), and redocked pose (cyan), (B) Co-crystalized pose of 511 (purple), and redocked pose (yellow).

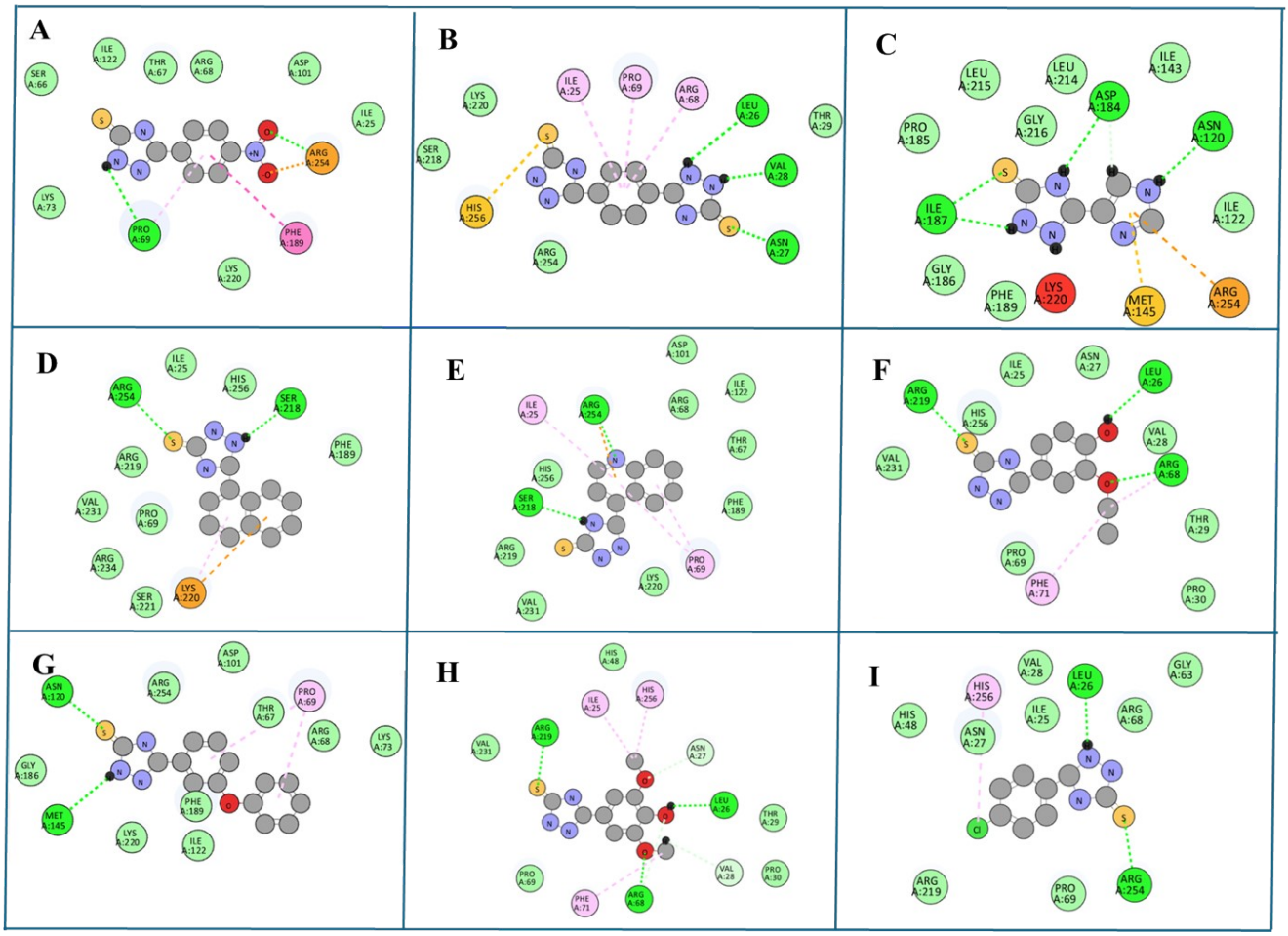
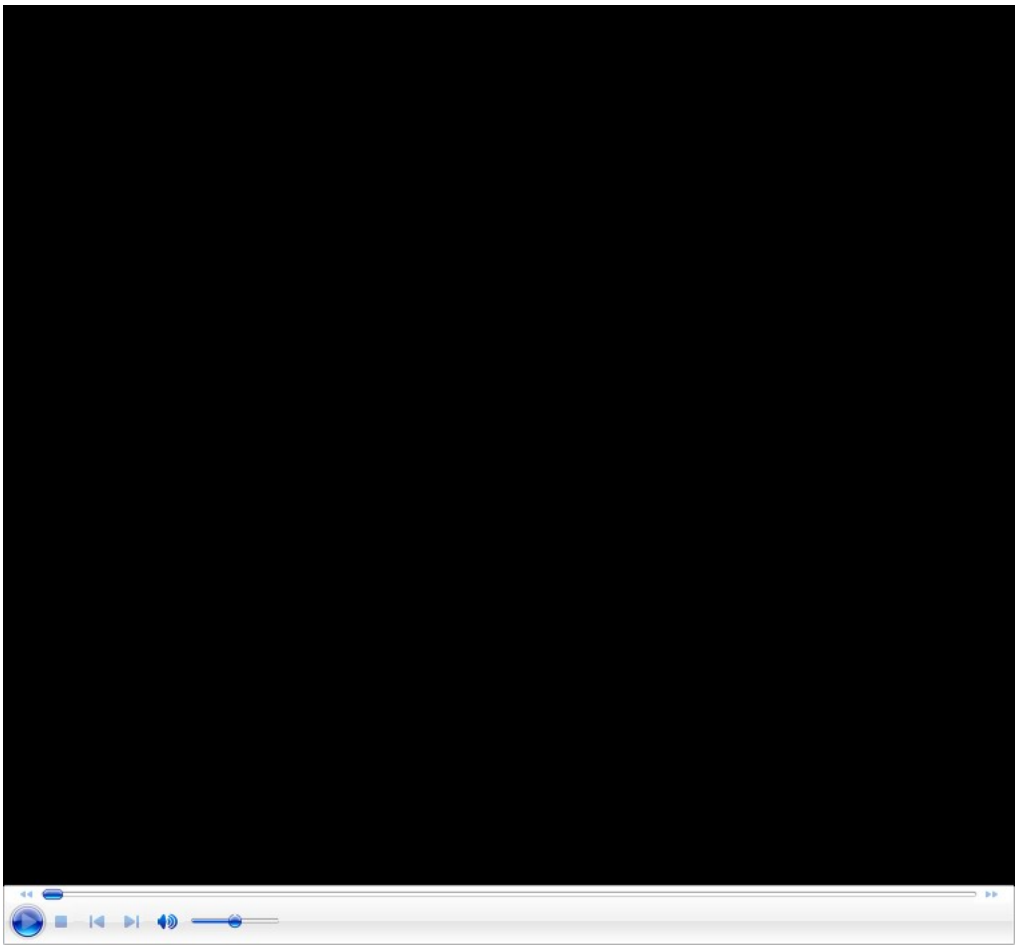


Figure S24. 2D representation of 3H23 docked with all selected molecules. (A) 3H23-3a, (B) 3H23-3i, (C) 3H23-3e, (D) 3H23-3c, (E) 3H23-3d, (F) 3H23-3h, (G) 3H23-3g, (H) 3H23-3f, (I) 3H23-3b.



Video 1. 3D representation of 3H23 docked with 9 selected molecules.

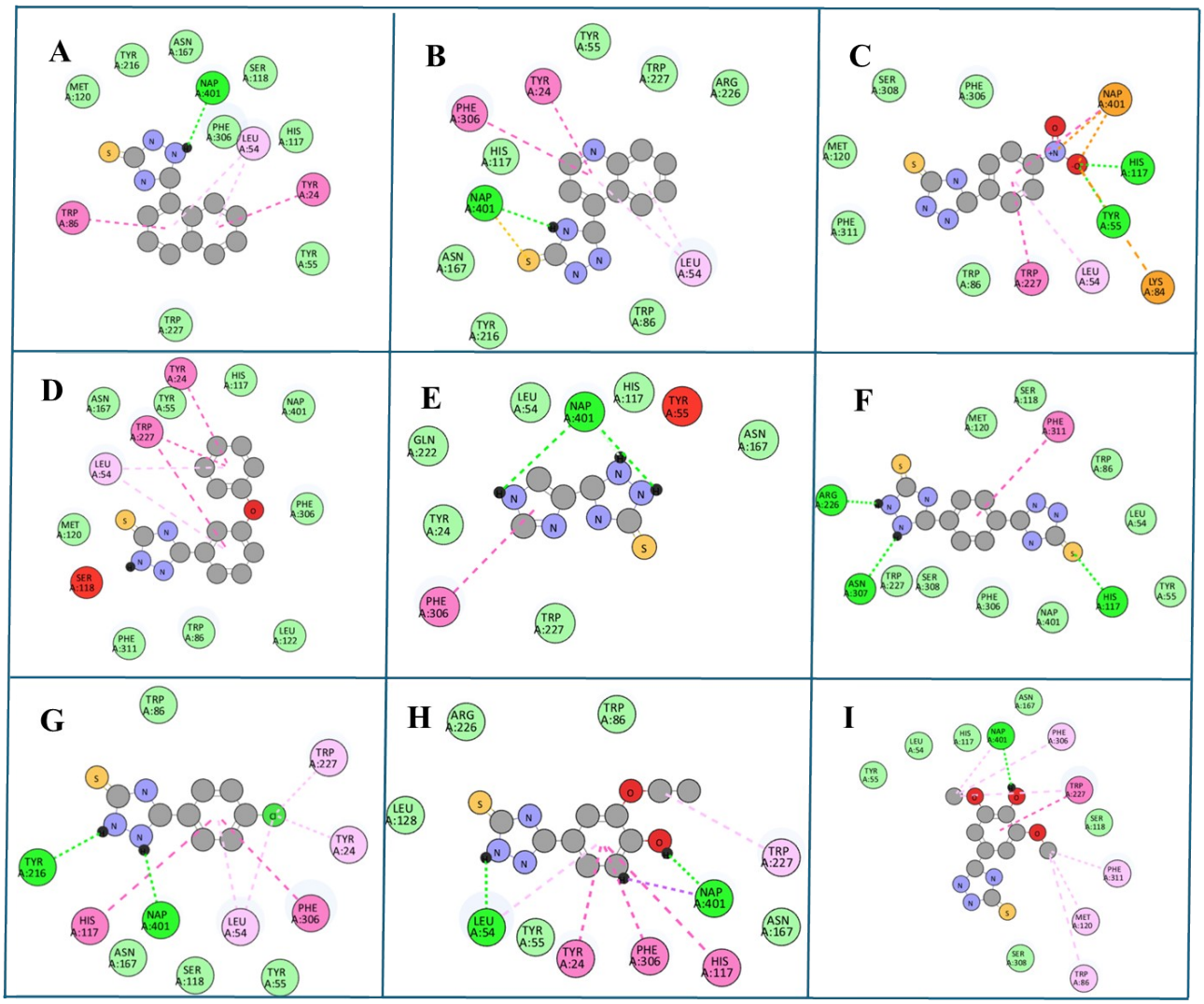


Figure S25. 2D representation of 4DBW docked with 9 selected molecules. (A) 4DBW-3c, (B) 4DBW-3d, (C) 4DBW-3a, (D) 4DBW-3g, (E) 4DBW-3e, (F) 4DBW-3i, (G) 4DBW-3b, (H) 4DBW-3f, (I) 4DBW-3h.

Video 2. 3D representation of 4DBW docked with 9 selected molecules.

7. ADMET parameters

Table S2. List of the ADMET parameters and their acceptable range.

Pharmacokinetic properties	Parameter	Acceptable range	Notes
Absorption	Molecular Weight	≤ 500	-
	TPSA	≤ 140 Å^2	Indicates better oral bioavailability
	Lipinski rule	Accept	-
	Caco-2	> -5	Indicates intestinal permeability.
	HIA	> 0.85	Closer to 1 is better.
Distribution	BBB	> 0.5	For CNS drugs: higher values

			preferred.
	PPB	< 0.9	>0.9 indicates high binding, may reduce free drug availability.
Metabolism	CYP2B6_inhibitor	< 0.5	To reduce metabolic drug-drug interactions.
	HLM	> 0.2	Indicates good metabolic stability.
Excretion	CLr	≤ 0.7	High renal clearance may decrease the drug's half-life.
	T50	> -0.3	Log-transformed, but longer half-life preferred.
Toxicity	Neurotoxicity	> -2.5	Less neurotoxic is better.
	DILI	< 0.7	Closer to 0 = safer profile.

References

1. Soni, S.; Teli, P.; Sahiba, N.; Teli, S.; Agarwal, S., Exploring the synthetic potential of a gC 3 N 4· SO 3 H ionic liquid catalyst for one-pot synthesis of 1, 1-dihomoarylmethane scaffolds via Knoevenagel–Michael reaction. *RSC advances* **2023,** *13* (19), 13337-13353.
2. Teli, S.; Soni, S.; Manhas, A.; Jha, P. C.; Agarwal, D. K.; Agarwal, S., Meglumine-catalyzed eco-friendly synthesis of pyrazolo [3, 4-b] pyridines: exploring their potential against inflammation and arthritis using in silico studies. *Research on Chemical Intermediates* **2025,** *51* (2), 789-809.
3. Sheldon, R. A., Metrics of green chemistry and sustainability: past, present, and future. *ACS Sustainable Chemistry & Engineering* **2018,** *6* (1), 32-48.
4. Teli, P.; Soni, S.; Teli, S.; Agarwal, S., Unveiling the catalytic potency of a novel hydrazone-linked covalent organic framework for the highly efficient one-pot synthesis of 1, 2, 4-triazolidine-3-thiones. *Nanoscale Advances* **2024,** *6* (22), 5568-5578.
5. Masram, L. B.; Salim, S. S.; Barkule, A. B.; Gadkari, Y. U.; Telvekar, V. N., An efficient and expeditious synthesis of 1, 2, 4-triazolidine-3-thiones using meglumine as a reusable catalyst in water. *Journal of Chemical Sciences* **2022,** *134* (3), 94.

6. Dutta, A.; Abha Saikia, R.; Jyoti Thakur, A., A Mechanistic Approach to Liquid-Assisted Mechanochemical Synthesis of 5-Aryl/Spiro-[1, 2, 4]-triazolidine-3-thiones. *European Journal of Organic Chemistry* **2022,** *2022* (34), e202101472.