Supplementary file

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

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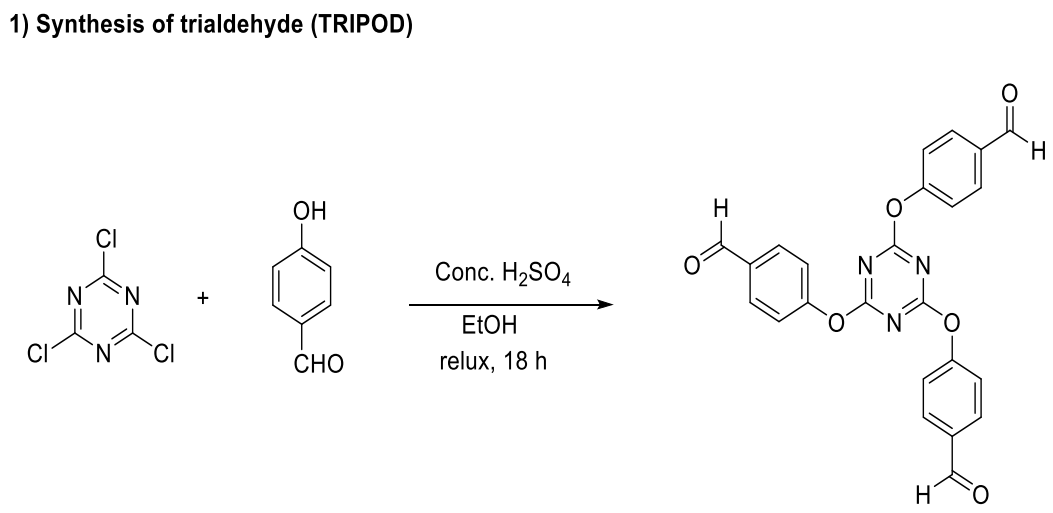
General remarks:

All the reagents and solvents were purchased from commercial suppliers and used without further purification unless otherwise noted. The COF was synthesized using an ultrasonic cleaner (Shumei KQ-100DB) with a power output of 100 W and a frequency of 40 KHz. Fourier transform infrared spectroscopy (FT-IR) was carried out with a Bruker Alpha FT-IR spectrometer. The samples for the IR study were prepared as KBr pellets. Scanning electron microscopy (SEM) was performed on a Hitachi (Japan), SU8010 series instrument. Transmission electron microscopy (TEM) was performed on a JEOL JEM-2100 plus instrument. Powder X-ray diffraction measurements were carried out with an X' Pert PROX system using monochromated Cu/Kα (λ = 0.1542 nm). The samples were spread on the square recess of an XRD sample holder as a thin layer. Nitrogen adsorption-desorption measurements were carried out using a *Quantachrome autosord IQ* automatic volumetric instrument. Before gas adsorption measurements, the as-prepared samples (~40 mg) were washed with anhydrous acetone through Soxhlet extraction for 6 h. The solvent was filtered and the samples were activated under vacuum at 120 °C for 8 h. Then the samples were used for gas adsorption-desorption measurements from 0 to 1 atm at 77 K. The Brunauer-Emmett-Teller (BET) method was utilized to calculate their specific surface areas. XPS was recorded on thermoscientific NEXA surface analyser, TGA and DTA recorded on Hitachi NEXTA STA300 device.

Preparation of 4,4′,4′′-[1,3,5-Triazine-2,4,6-triyltris(oxy)]tris-benzaldehyde (TRIPOD).

A reaction flask was prepared with cyanuric chloride (0.25 g, 1.35 mmol), 4-hydroxybenzaldehyde (0.51 g, 4.17 mmol), p-dioxane (20 mL), and Na_2CO_3 (0.50 g, 4.72 mmol). The mixture was stirred and refluxed under a nitrogen atmosphere for 18 hours. After refluxing, the mixture was concentrated under reduced pressure, and the resulting concentrate was added to cold water (10 mL). The formed precipitate was collected by filtration, rinsed with cold water (5 mL), and dried to yield the desired product (0.441 g, 74%)[1].

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 3H, 3CHO), 7.91 (d, J = 8.5 Hz, 6H, Ar-H), 7.31 (d, J = 8.6 Hz, 6H, Ar-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.80, 134.57, 131.45, 122.31.



Scheme 1: Synthesis of 4,4′,4′′-[1,3,5-Triazine-2,4,6-triyltris(oxy)]tris-benzaldehyde

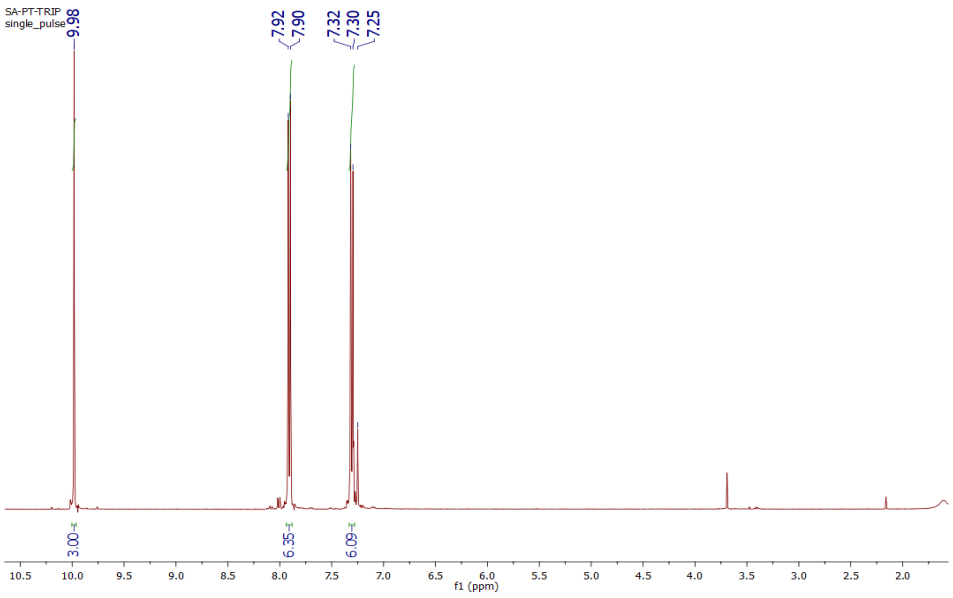


Figure S1: ^{1}H NMR spectra of 4,4′,4′′-[1,3,5-Triazine-2,4,6-triyltris(oxy)]tris-benzaldehyde

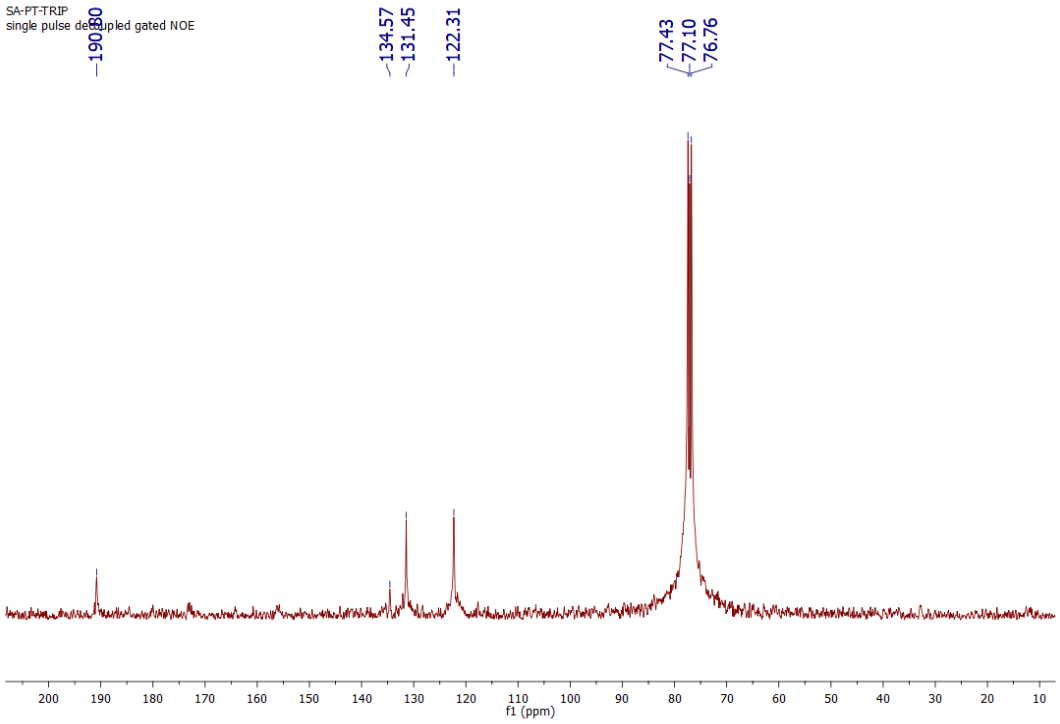


Figure S2: ^{13}C NMR spectra of 4,4′,4′′-[1,3,5-Triazine-2,4,6-triyltris(oxy)]tris-benzaldehyde

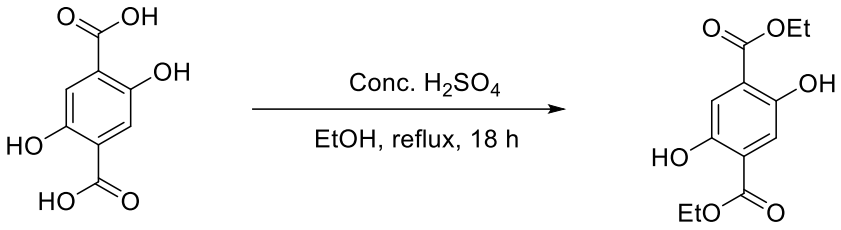
Synthesis of diethyl-2,5-dihydroxyterephthalate (DHTP)

A flask was charged with 2,5-dihydroxyterephthalic acid (0.75 g, 3.78 mmol) and dry ethanol (30 mL). To this mixture, 3 mL of concentrated sulfuric acid was added dropwise. The resulting mixture was refluxed for 18 hours until the solid fully dissolved. After

cooling to room temperature, 60 mL of deionized water was added. The precipitate formed was collected by filtration, thoroughly washed with deionized water, and then dried in an oven[2].

Yield: 0.80 g, 83.06%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 2H, 2OH), 7.46 (s, 2H, Ar-H), 4.40 (q, J = 7.3 Hz, 4H, $2CH_2$), 1.41 (t, J = 7.2 Hz, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.19, 152.98, 118.55, 117.78, 62.17, 14.17.

2) Synthesis of DHTP



Scheme 2 : Synthesis of diethyl-2,5-dihydroxyterephthalate

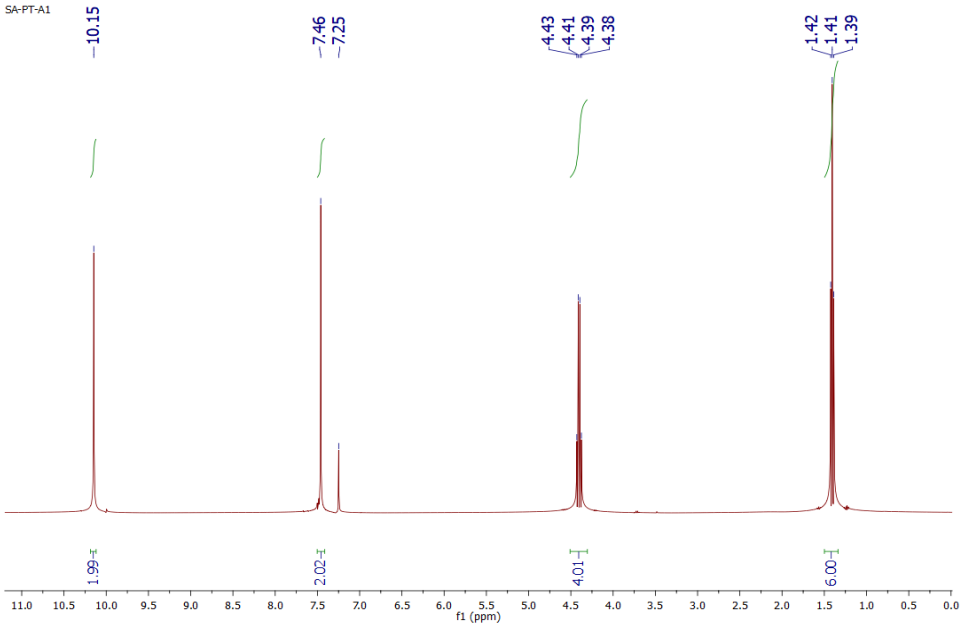


Figure S3: ^{1}H NMR spectra of diethyl-2,5-dihydroxyterephthalate

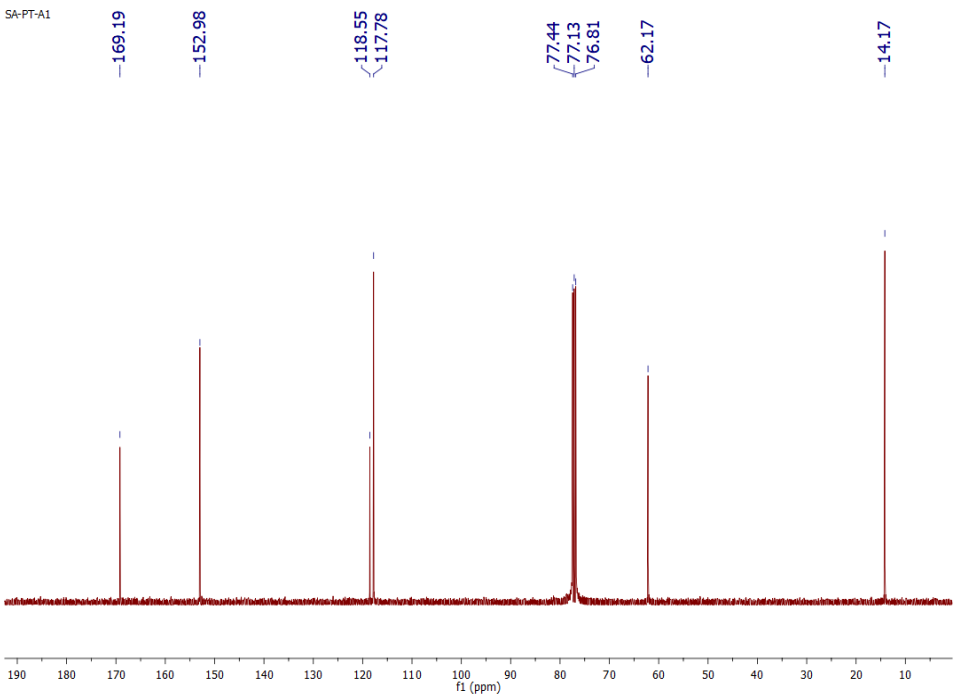


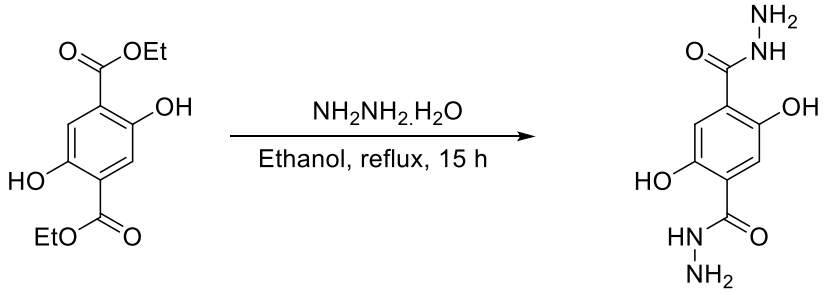
Figure S4: ^{13}C NMR spectra of diethyl-2,5-dihydroxyterephthalate

Synthesis of 2,5-dihydroxyterephthalohydrazide (DHTH)

A round-bottom flask was charged with diethyl-2,5-dihydroxyterephthalate (0.5 g, 1.96 mmol) and ethanol (20 mL). Hydrazine hydrate (2.5 mL, 51 mmol) was then added to the flask. The mixture was heated to 90 °C for 15 hours. After cooling to room temperature, a pale-yellow precipitate formed. The resulting crude product was collected by filtration, washed with ethanol three times, and dried under vacuum to yield the pure product[2].

Yield: 0.33 g, 74.5%. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 11.59 (s, 2H, 2OH), 10.03 (s. 2H, 2NH), 7.31 (s, 2H, Ar-H), 4.64 (s, 4H, 2NH$_2$). NMR (101 MHz, DMSO-d$_6$) δ 166.70, 150.94, 119.55, 115.46.

3) Synthesis of DHTH



Scheme 3: Synthesis of 2,5-dihydroxyterephthalohydrazide

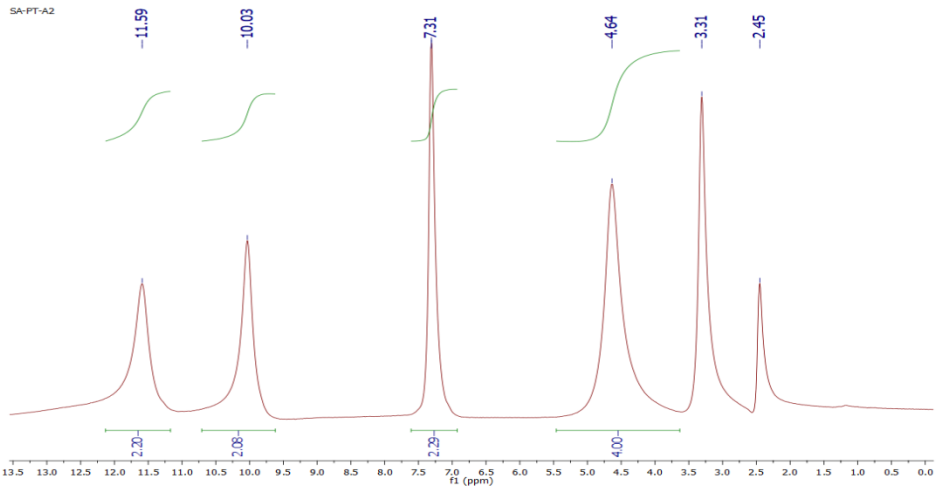


Figure S5: ^{1}H NMR spectra of 2,5-dihydroxyterephthalohydrazide

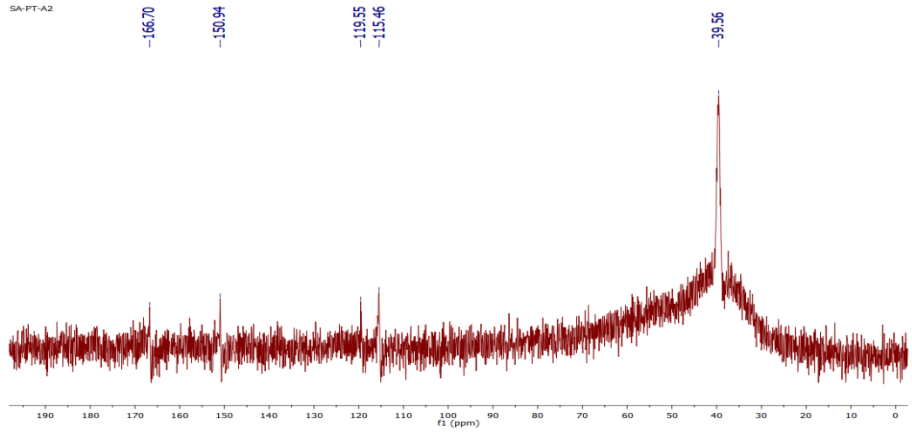
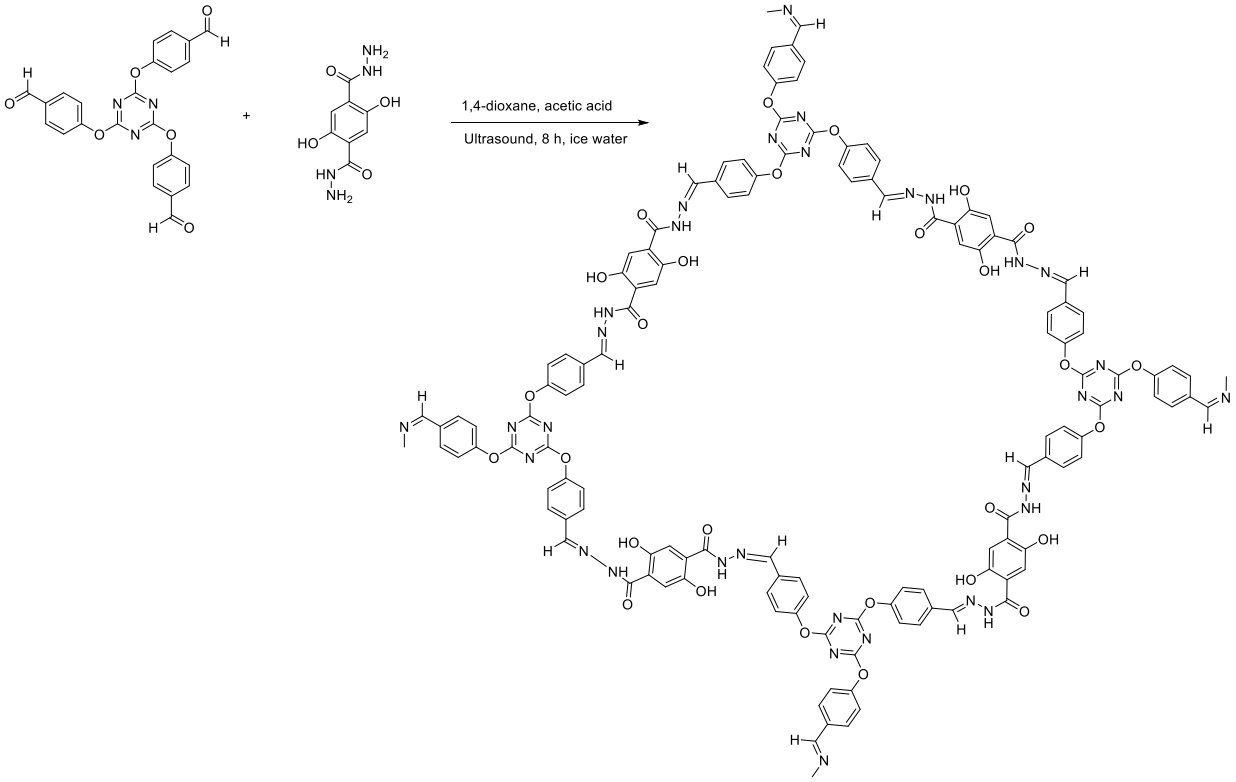


Figure S6: ^{13}C NMR spectra of 2,5-dihydroxyterephthalohydrazide

Preparation of COF:

A beaker containing 2,5-dihydroxyterephthalate (DHTH) (0.162 g, 0.72 mmol) and 4,4′,4″-[1,3,5-triazine-2,4,6-triyltris(oxy)]tris-benzaldehyde (TRIPOD) (0.112 mg, 0.48 mmol) was combined with a solution of 1,4-dioxane (12 mL) and 6.0 M aqueous acetic acid (2 mL). The mixture was then sonicated in an ice water bath for 8 hours. The resulting fluffy yellow solid, which swelled in the solvent system, was collected by filtration. The solid was sequentially washed three times with anhydrous dichloromethane, anhydrous acetone, and tetrahydrofuran, and then activated under vacuum at 120 °C for 8 hours to produce COF (0.28 g)[3].

4) Synthesis of COF



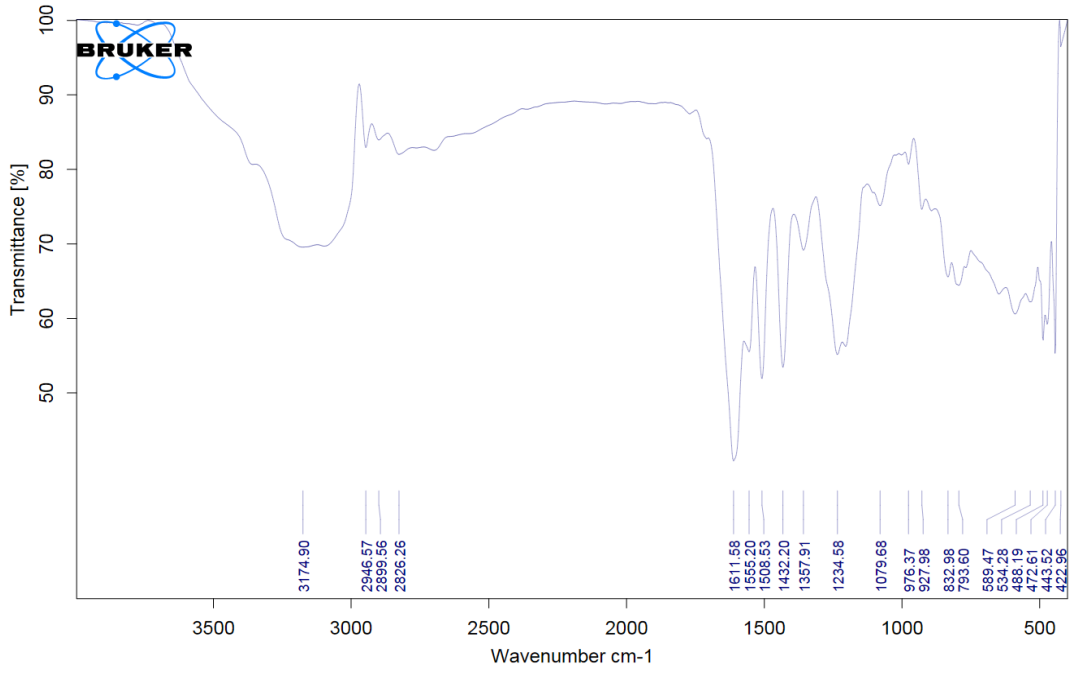


Figure S7: FT-IR spectrum of COF

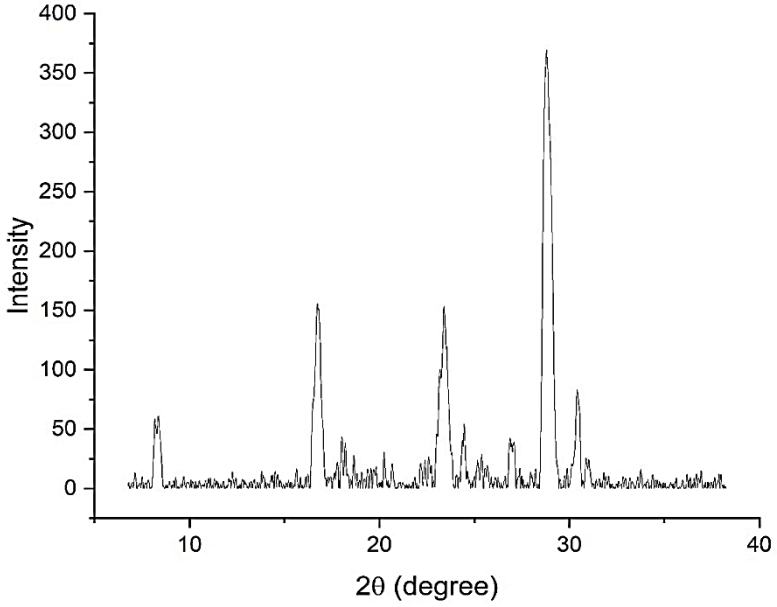


Figure S8: PXRD image of COF

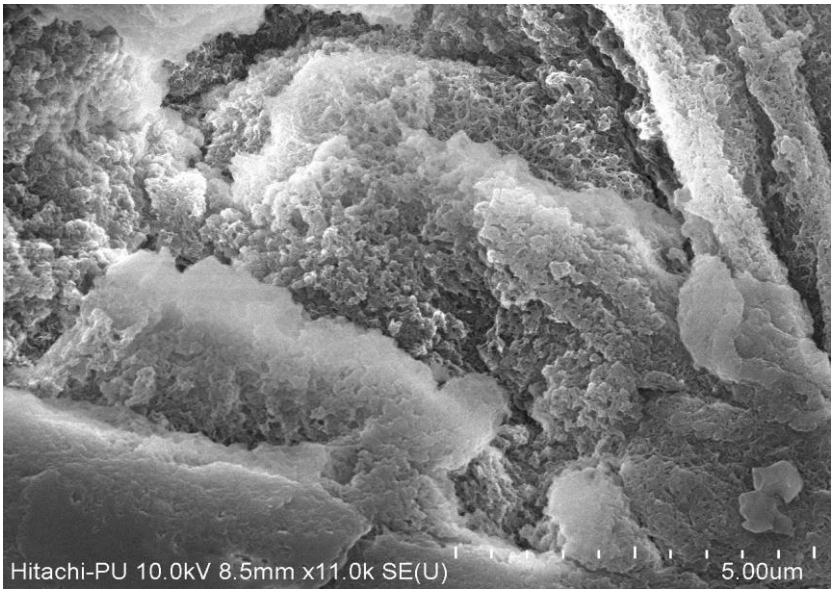


Figure S9: SEM image of COF

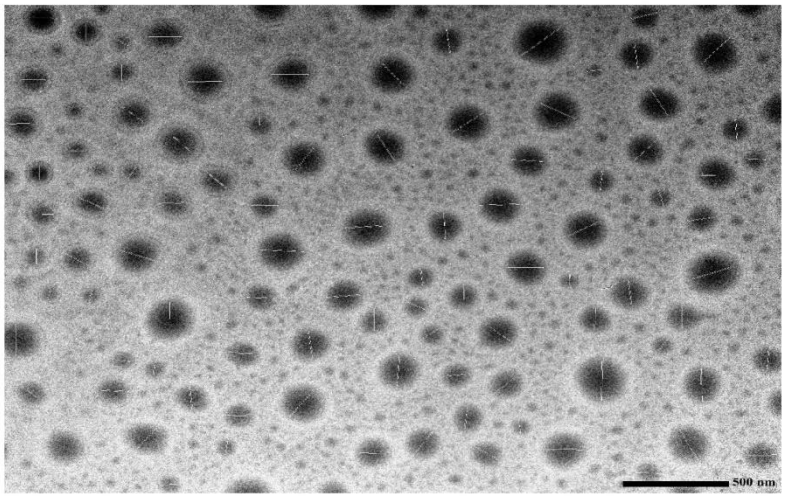


Figure S10: TEM image of COF

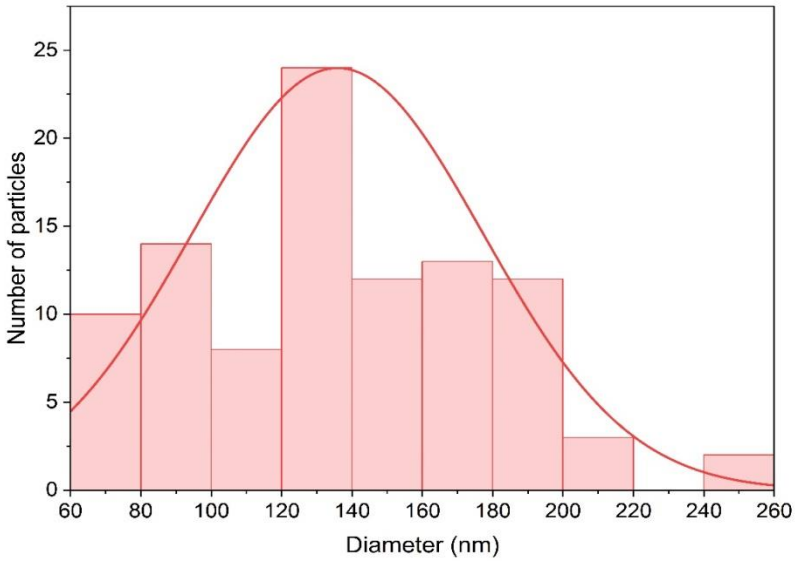


Figure S11: Histogram of particle size distribution of COF

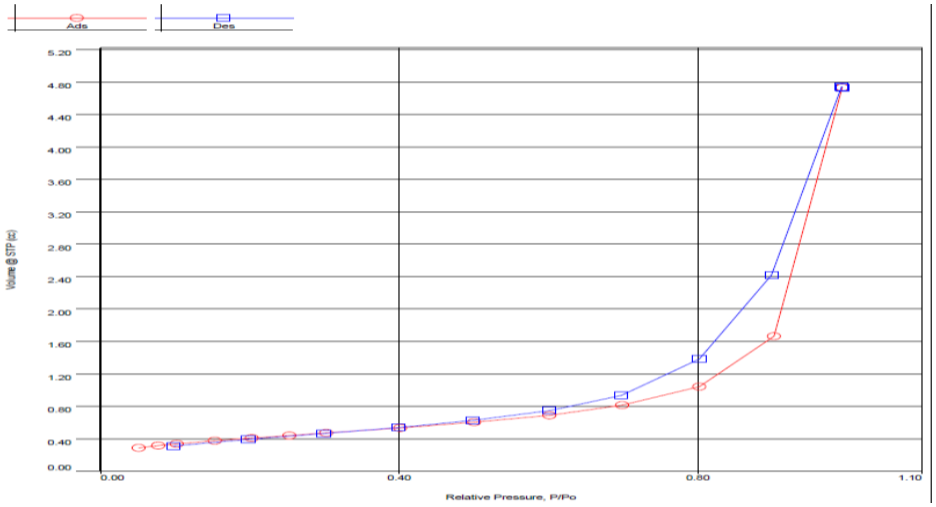
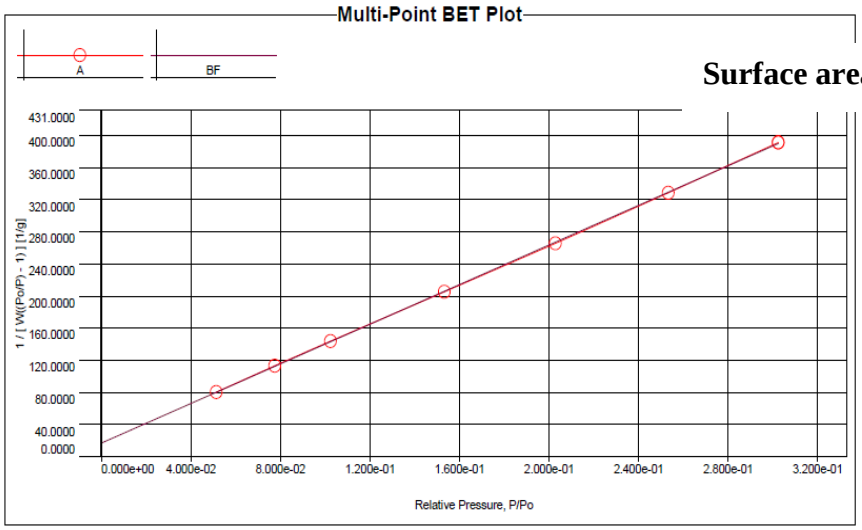
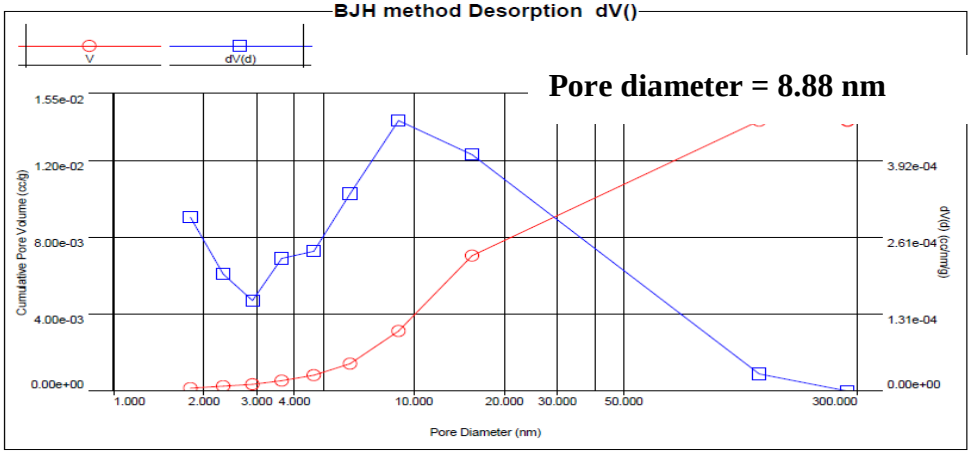


Figure S12: N_2 adsorption-desorption isotherms of COF



Surface area = 2.78 m^2/g

Figure S13: BET surface area plot for COF calculated from the adsorption data



Pore diameter = 8.88 nm

Figure S14: Average pore diameter calculation through BJH desorption method

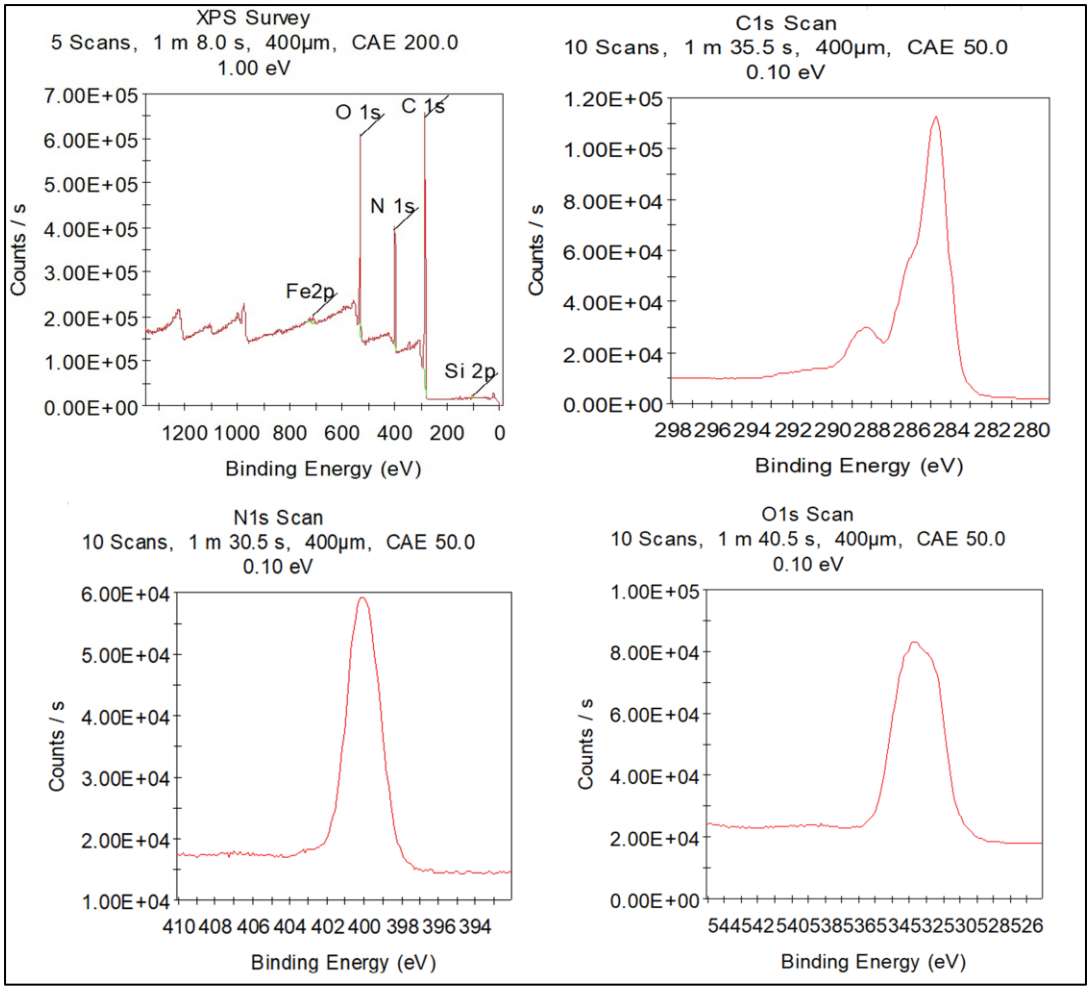


Figure S15: XPS study of COF

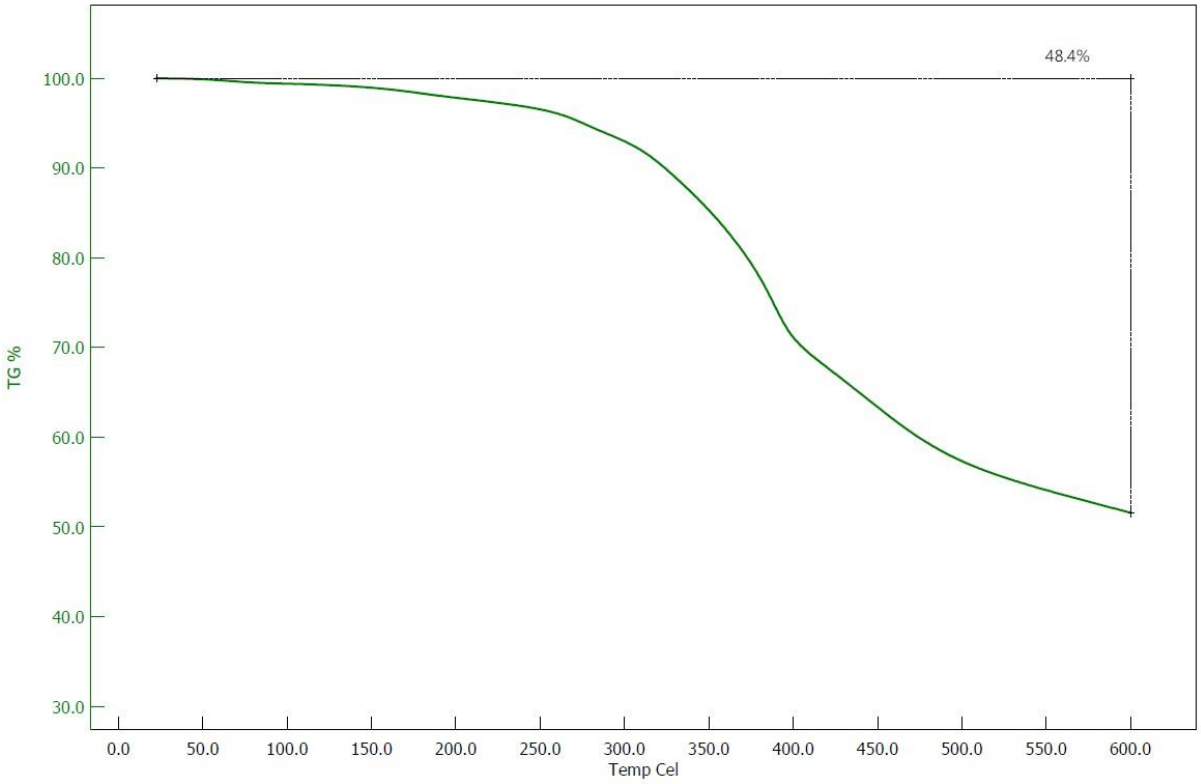


Figure S16: TGA curve of COF

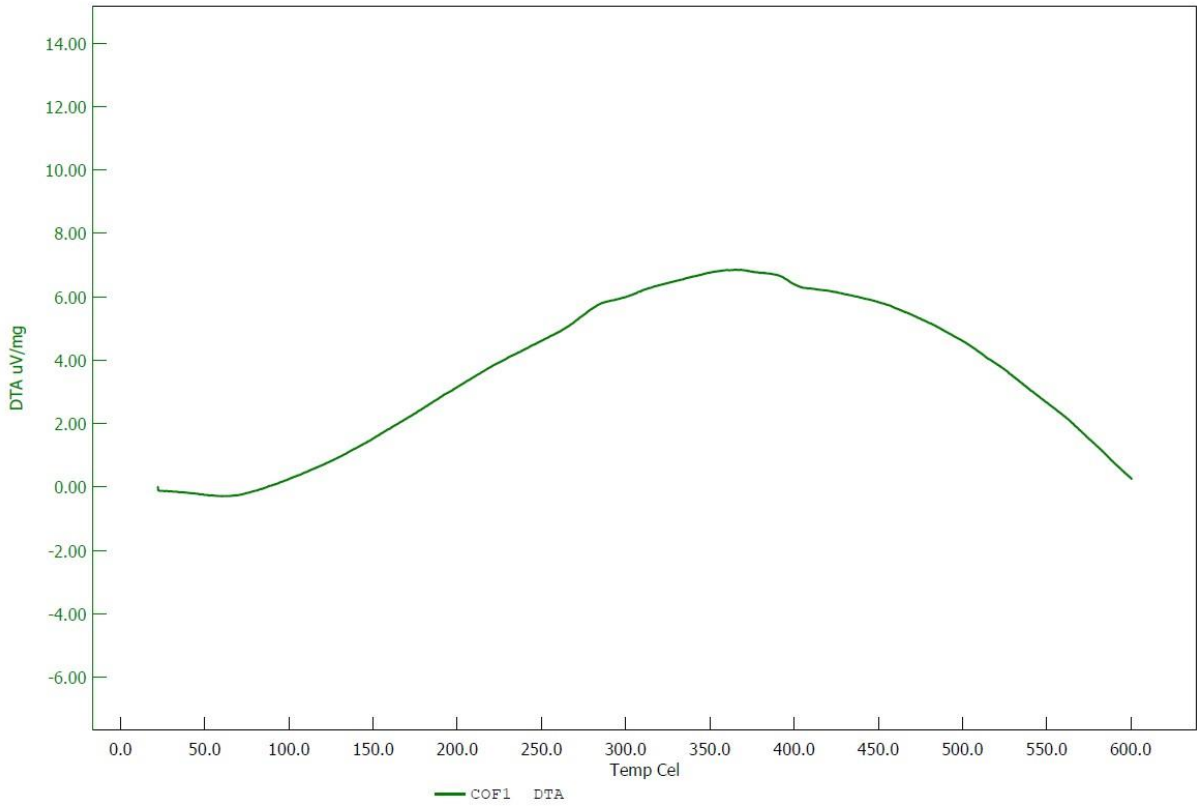


Figure S17: DTA curve of COF

General procedure for the synthesis of triazolidine-3-thione derivatives:

In a 100 mL round bottom flask, 10 mL of a water: ethanol mixture (1:2) was added to mixture of aromatic aldehyde or ketone (1.0 mmol), thiosemicarbazide (1.0 mmol), and COF (20 mg) at room temperature. The reaction progress was monitored using TLC. Upon completion, additional ethanol was added to dissolve the organic product, and the solid catalyst was separated by filtration. The final product was obtained by evaporating the ethanol under vacuum. The reaction products were characterized and confirmed using FT-IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectroscopy.

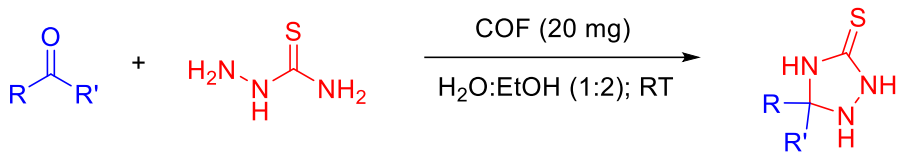
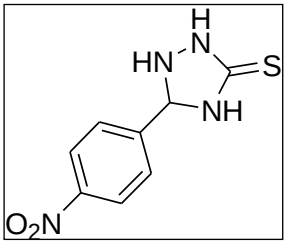


Figure S18: General reaction for synthesis of triazolidine-3-thione derivatives

Spectra of synthesized derivatives:

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



98% yield; m.p. 208-210 °C[4]; ^{1}H NMR (400 MHz, DMSO d_6): δ 11.70 (s, 1H, NH), 8.40 (s, 1H, NH), 8.25 (s, 1H, NH), 8.19 (s, 1H, Ar-H), 8.17 (s, 1H, Ar-H), 8.07 (d, *J* = 3.0 Hz, 2H, Ar-H), 8.05 (s, CH); ^{13}C NMR (101 MHz, DMSO d_6): δ 178.94, 148.08, 141.28, 140.02, 128.71, 124.33.

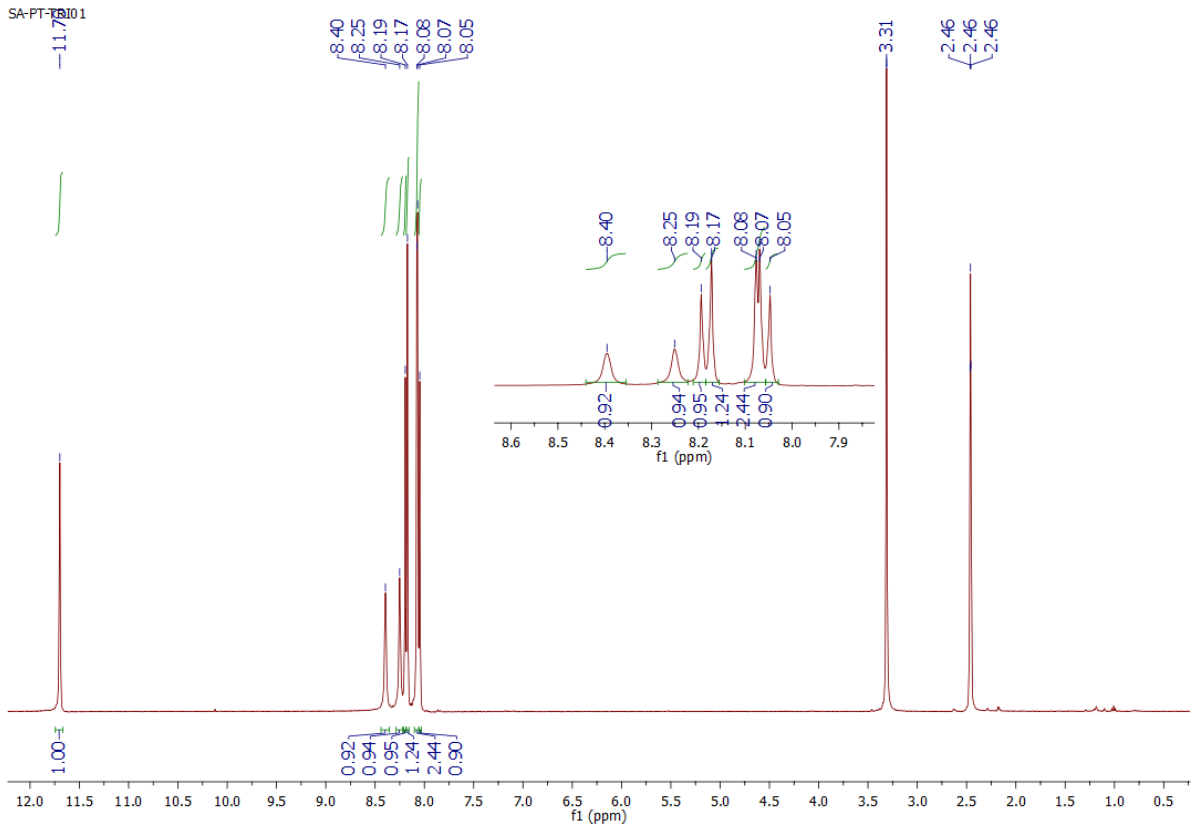


Figure S19: ^{1}H NMR of synthesized compound 3a

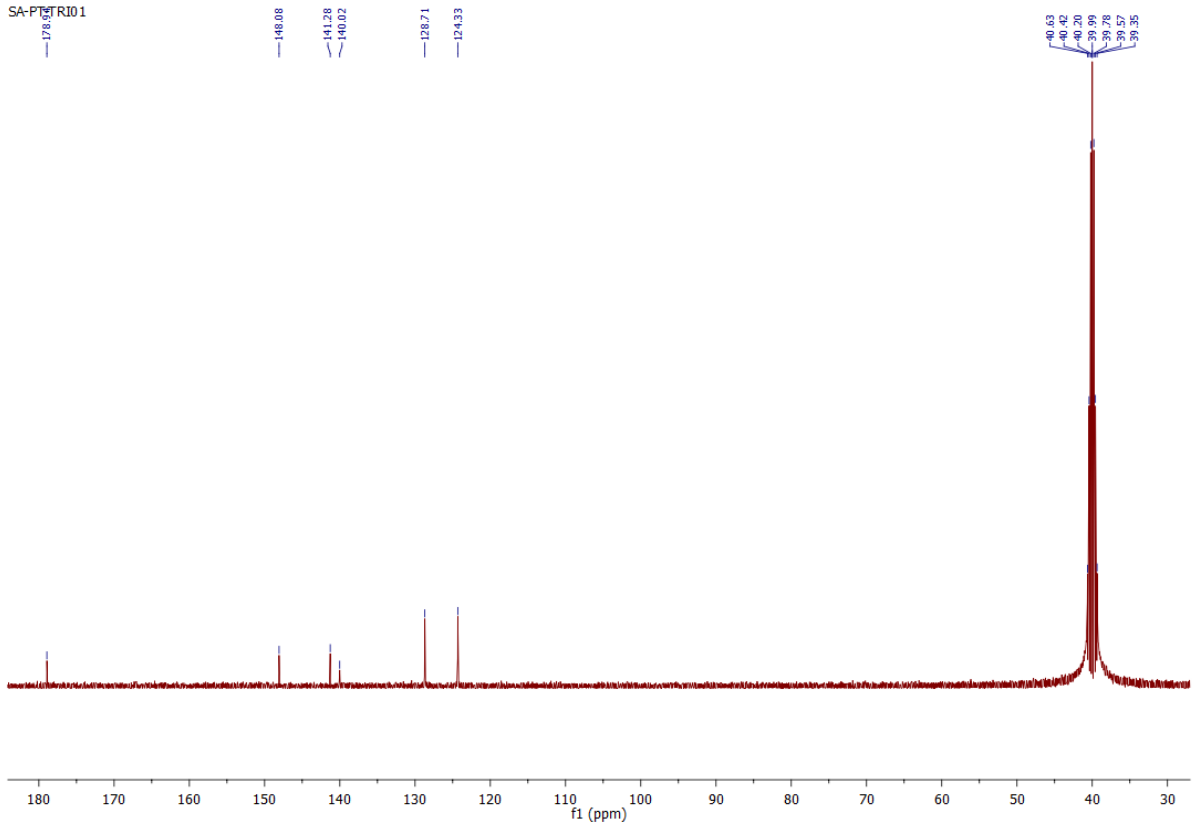
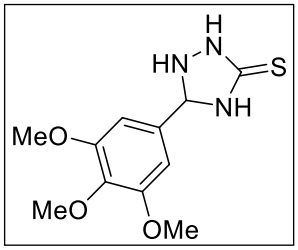


Figure S20: ^{13}C NMR of synthesized compound 3a

5-(3,4,5-trimethoxyphenyl)-1,2,4-triazolidine-3-thione **(3b)**:



95% yield; m.p. 215-217 °C; ^{1}H NMR (400 MHz, DMSO d_6): δ 11.29 (s, 1H, NH), 8.22 (s, 1H, Ar-H), 8.10 (s, 1H, NH), 7.88 (s, 1H, NH), 7.80 (d, J = 8.9 Hz, 1H, Ar-H), 6.81 (d, J = 9.0 Hz, 1H, CH), 3.79 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 3.71 (s, 3H, CH_3O); ^{13}C NMR (101 MHz, DMSO d_6): δ 178.00, 155.47, 153.21, 141.94, 138.73, 121.62, 120.84, 109.09, 62.36, 61.00, 56.52.

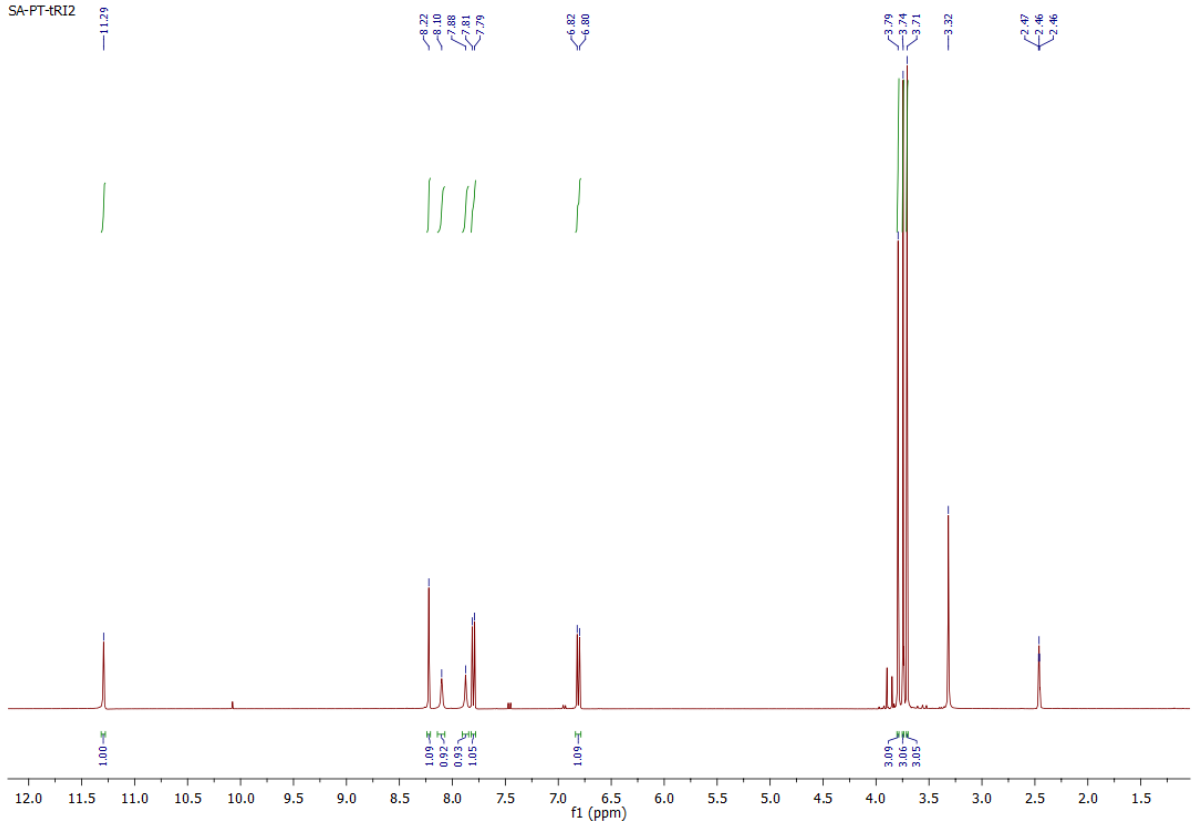


Figure S21: ^{1}H NMR of synthesized compound 3b

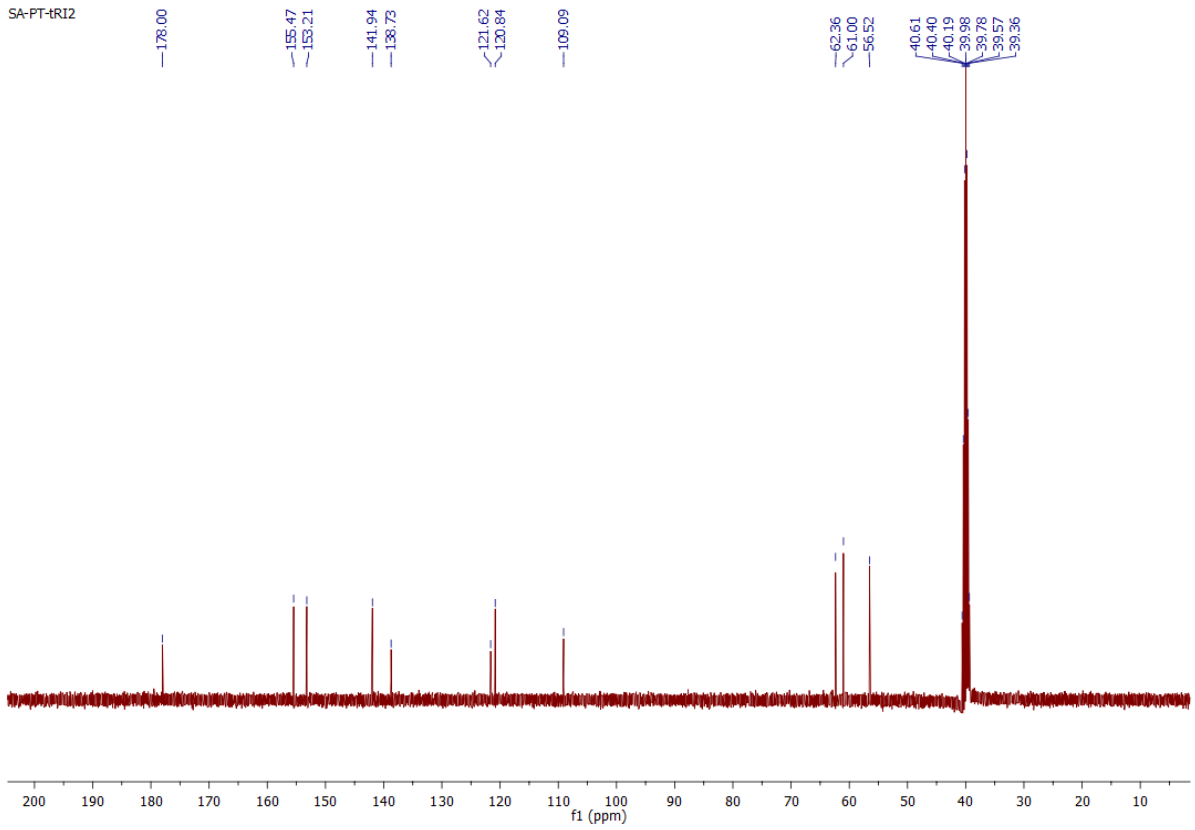
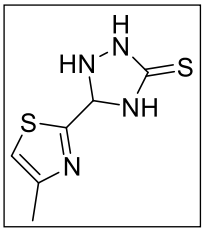


Figure S22: ^{13}C NMR of synthesized compound 3b

5-(4-methylthiazol-2-yl)-1,2,4-triazolidine-3-thione **(3c)**:



94% yield; m.p. 221-224 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.38 (s, 1H, NH), 9.00 (s, 1H, Ar-H), 8.31 (s, 1H, CH), 8.23 (s, 1H, NH), 7.60 (s, 1H, NH), 2.39 (s, 3H, CH_3 of thiazole ring). ^{13}C NMR (101 MHz, DMSO d_6) δ 177.98, 155.47, 154.72, 136.22, 127.82, 15.87.

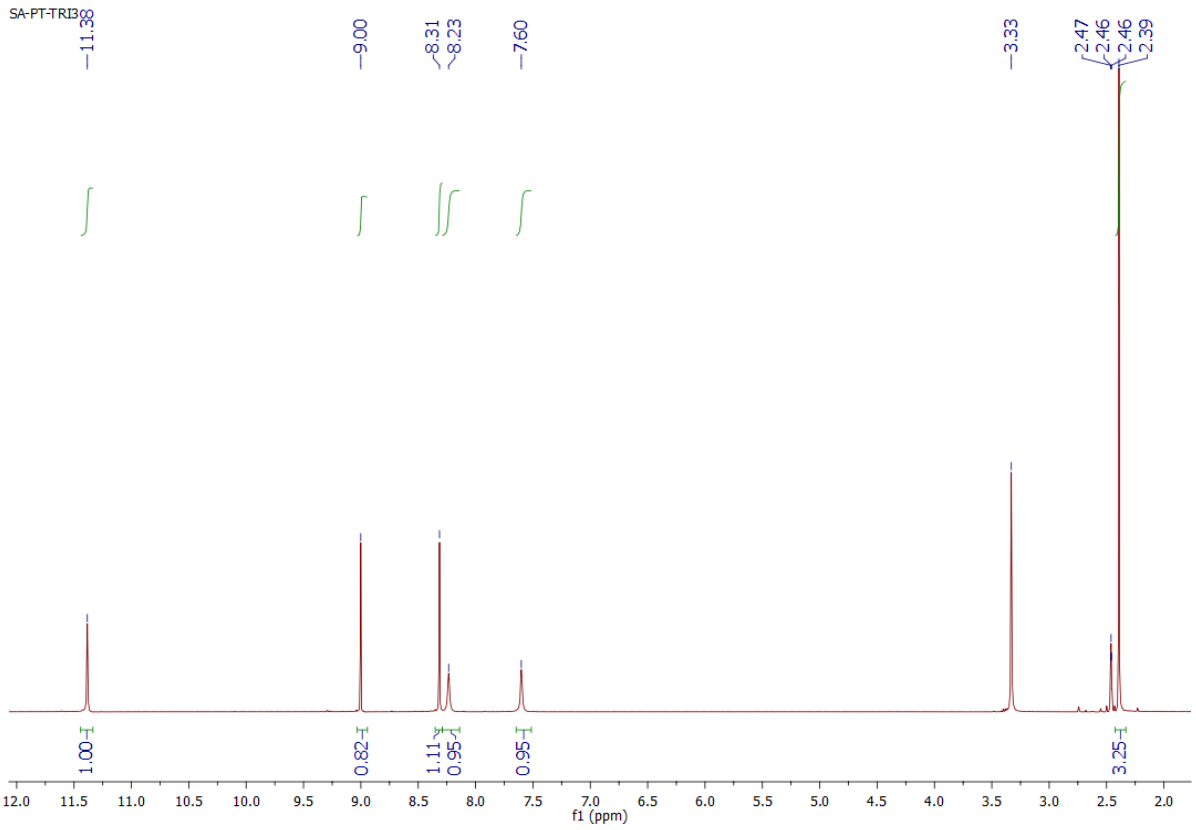


Figure S23: ^{1}H NMR of synthesized compound 3c

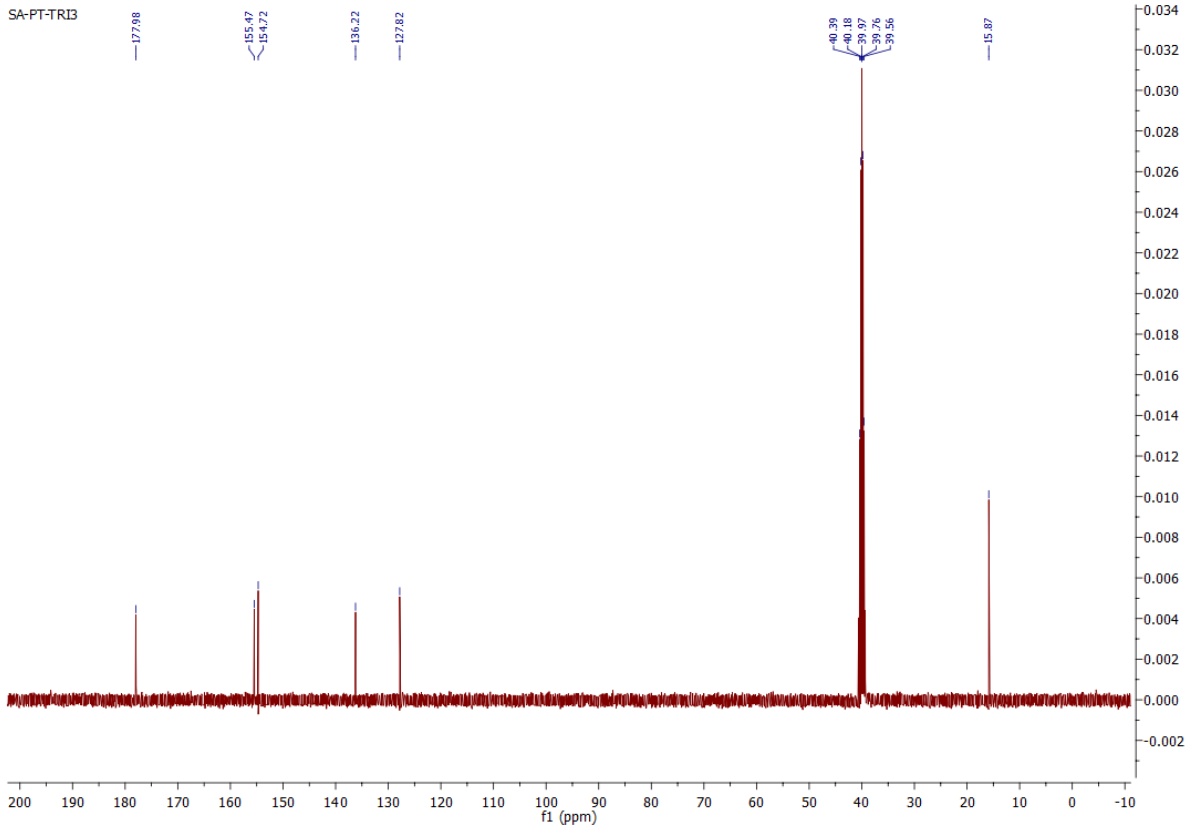
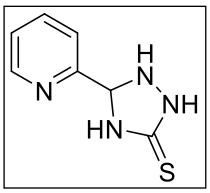


Figure S24: ^{13}C NMR of synthesized compound 3c

5-(pyridin-2-yl)-1,2,4-triazolidine-3-thione **(3d)**:



90% yield; m.p. 180-184 °C[4]; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.61 (s, 1H, NH), 8.52 – 8.50 (m, 1H, Ar-H), 8.33 (s, 1H, NH), 8.24 (d, J = 8.0 Hz, 1H, Ar-H), 8.15 (s, 1H, NH), 8.04 (s, 1H, CH), 7.81 – 7.74 (m, 1H, Ar-H), 7.34 – 7.31 (m, 1H, NH), ^{13}C NMR (101 MHz, DMSO d_6) δ 178.79, 153.82, 149.81, 143.00, 137.08, 124.64, 120.75.

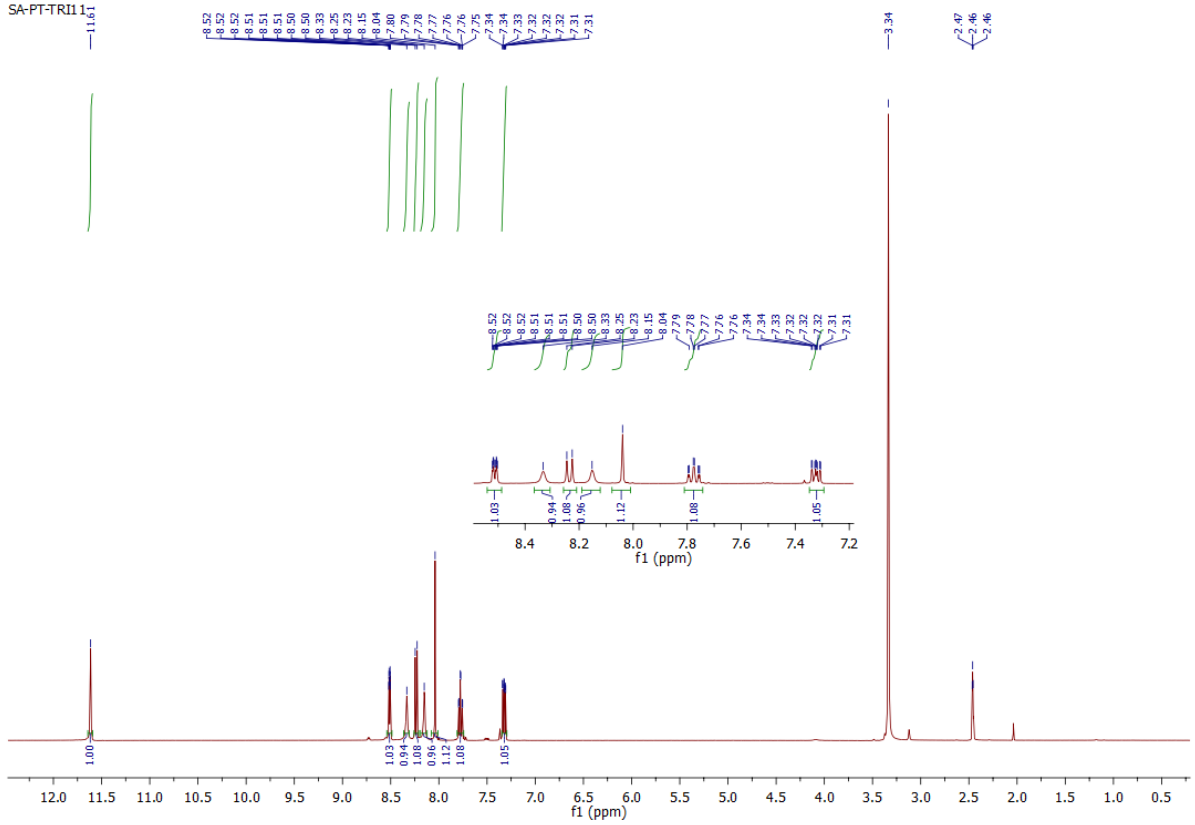


Figure S25: ^{1}H NMR of synthesized compound 3d

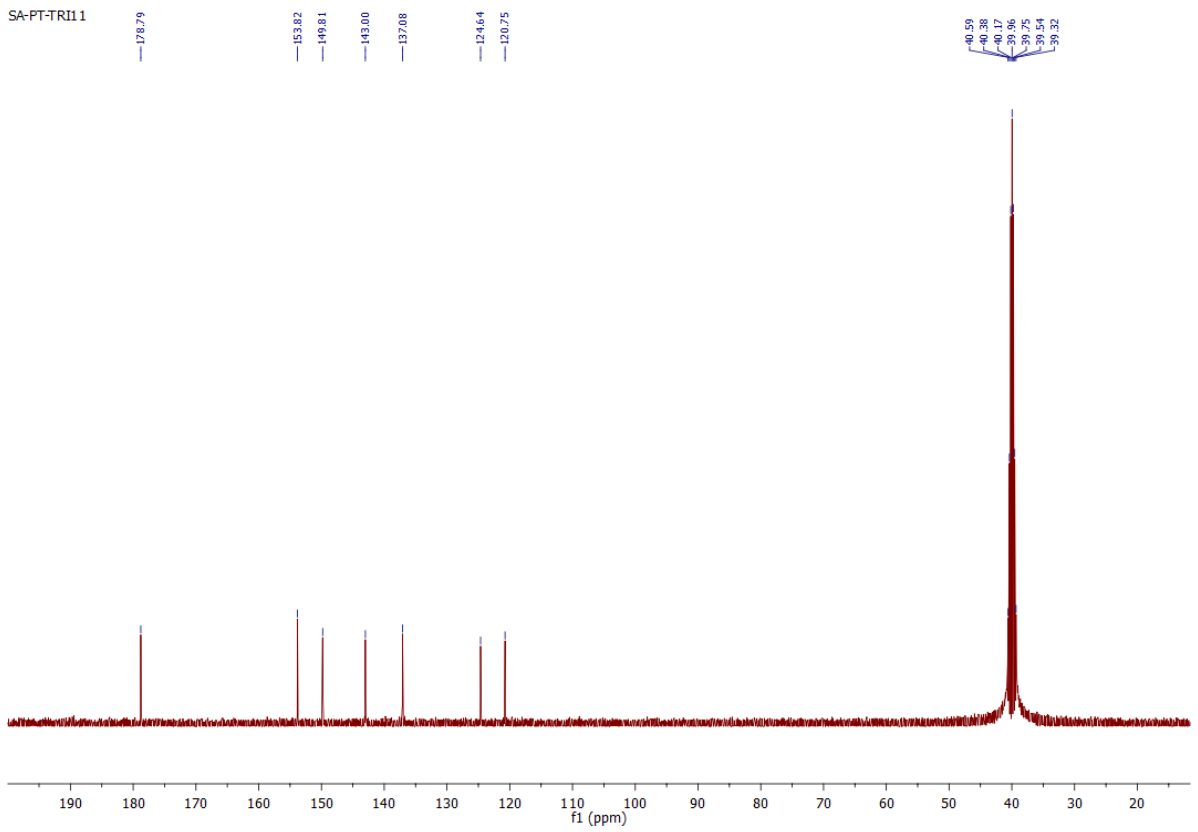
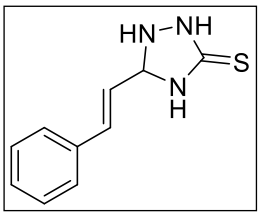


Figure S26: ^{13}C NMR of synthesized compound 3d

(E)-5-styryl-1,2,4-triazolidine-3-thione **(3e)**:



92% yield; m.p. 115-120 °C[5]; ^{1}H-NMR (400 MHz, DMSO d_6) δ 11.39 (s, 1H, NH), 8.18 (s, 1H, NH), 7.85 (d, J = 9.2 Hz, 1H, CH), 7.60 (s, 1H, NH), 7.51 (d, J = 7.3 Hz, 2H, Ar-H), 7.34 (t, J = 7.3 Hz, 2H, Ar-H), 7.29-7.26 (m, 1H, Ar-H), 6.98 (d, J = 16.3 Hz, 1H, CH (CH=CH)), 6.82 (dd, J = 16.2, 9.3 Hz, 1H, CH=CH); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.13, 145.21, 139.39, 136.39, 129.42, 129.38, 127.46, 125.56.

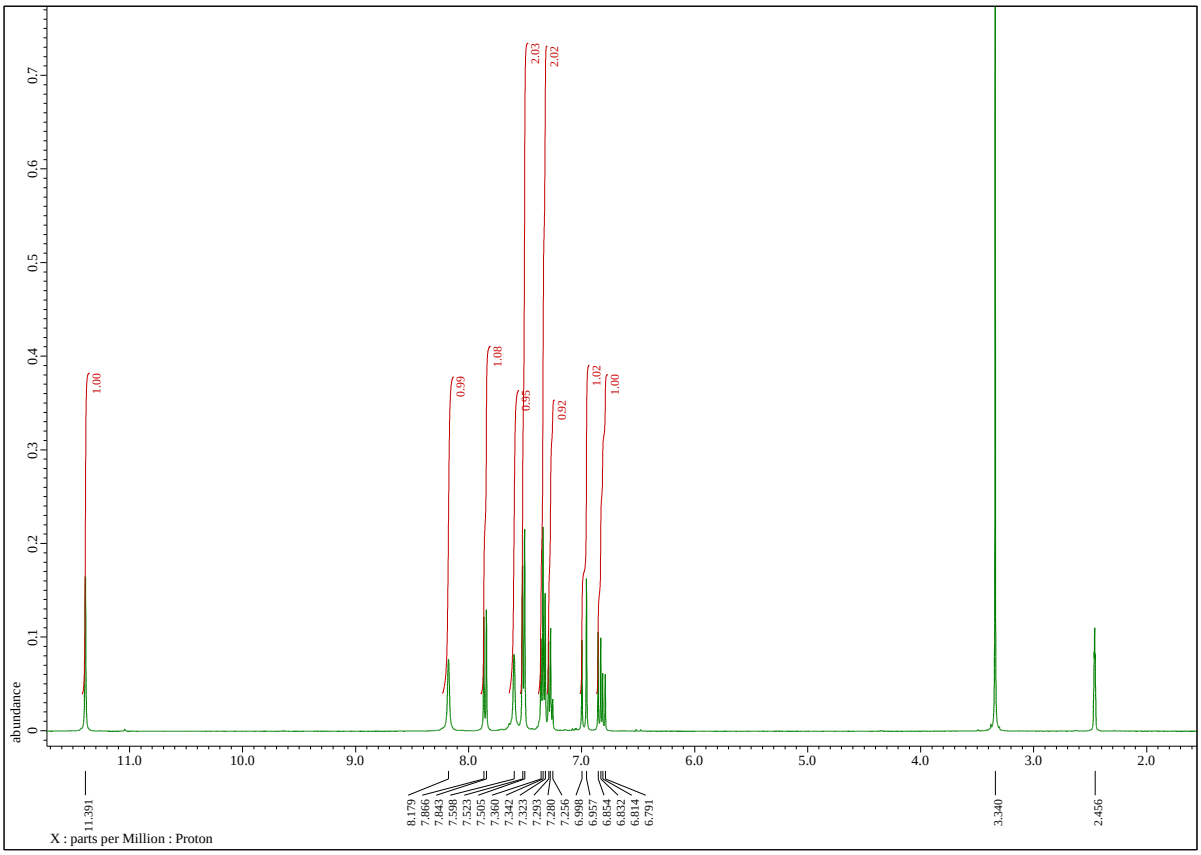


Figure S27: ^{1}H NMR of synthesized compound 3e

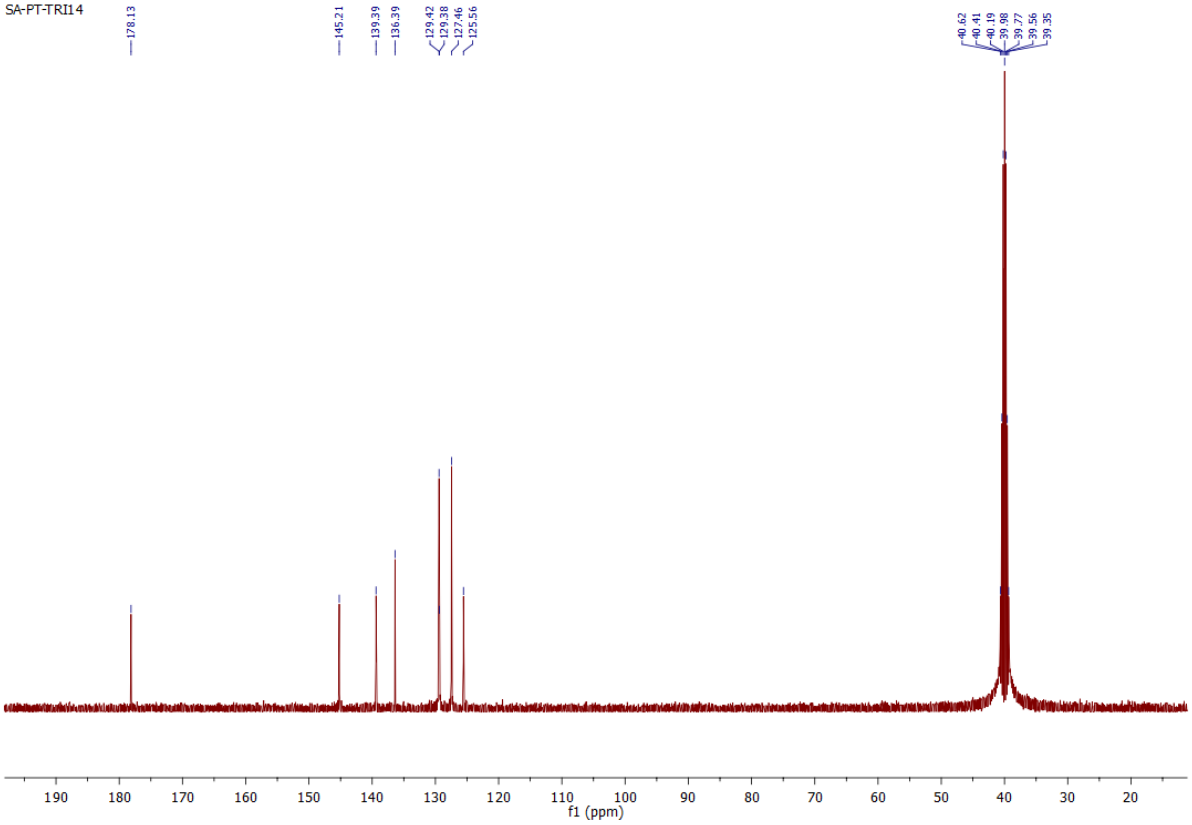
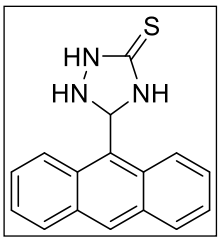


Figure S28: ^{13}C NMR of synthesized compound 3e

5-(anthracen-9-yl)-1,2,4-triazolidine-3-thione **(3f)**:



94% yield; m.p. 223-226 °C[6]; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.64 (s, 1H, NH), 9.29 (s, 1H, Ar-H), 8.66 (s, 1H, C-H), 8.56 – 8.49 (m, 2H, Ar-H), 8.33 (s, 1H, NH), 8.10 (d, J = 8.3 Hz, 2H, Ar-H), 7.72 (s, 1H, NH), 7.63 – 7.57 (m, 2H, Ar-H), 7.56 – 7.50 (m, 2H, Ar-H); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.48, 142.67, 131.38, 130.14, 129.98, 129.49, 127.86, 126.12, 125.49, 125.31.

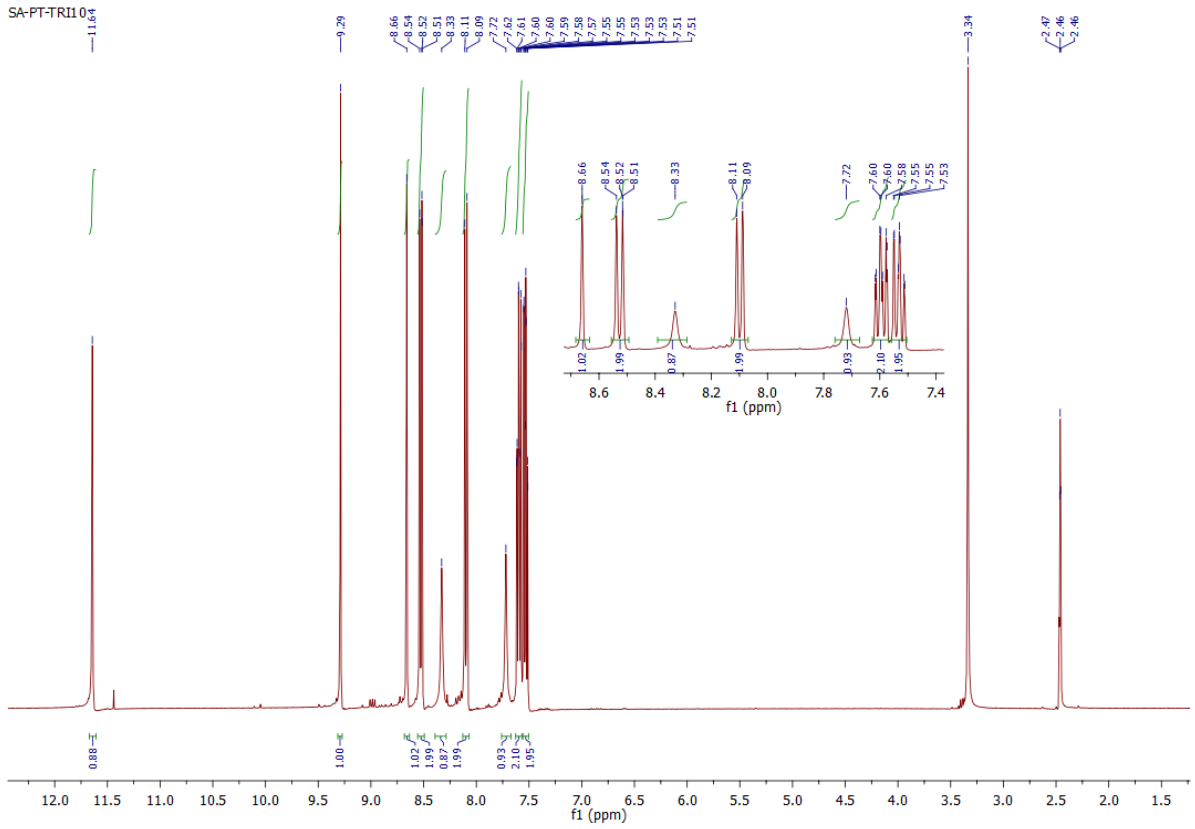


Figure S29: ^{1}H NMR of synthesized compound 3f

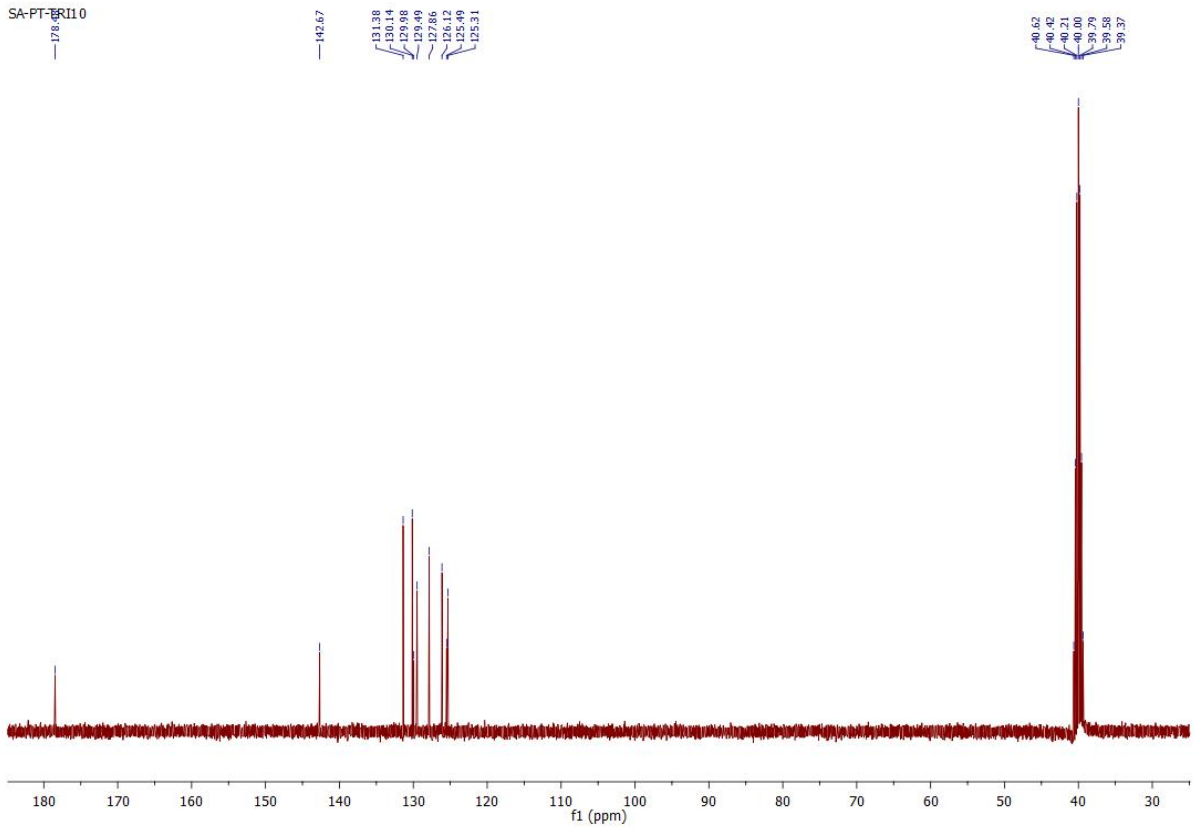
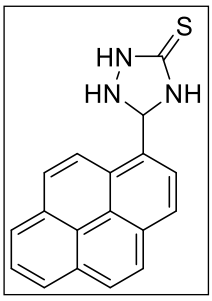


Figure S30: ^{13}C NMR of synthesized compound 3f

5-(pyren-1-yl)-1,2,4-triazolidine-3-thione **(3g)**:



90% yield; m.p. 255-259 °C[6]; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.56 (s, 1H, NH), 9.23 (s, 1H, NH), 8.86 (d, J = 8.2 Hz, 1H, Ar-H), 8.42 (d, J = 9.5 Hz, 1H, C-H), 8.35 (s, 1H, NH), 8.32 – 8.25 (m, 4H, Ar-H), 8.22 – 8.16 (m, 3H, Ar-H), 8.09 – 8.04 (m, 1H, Ar-H); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.33, 140.71, 132.31, 131.39, 130.65, 129.24, 129.21, 128.76, 127.98, 127.43, 127.11, 126.57, 126.24, 125.71, 124.72, 124.54, 124.35, 122.12.

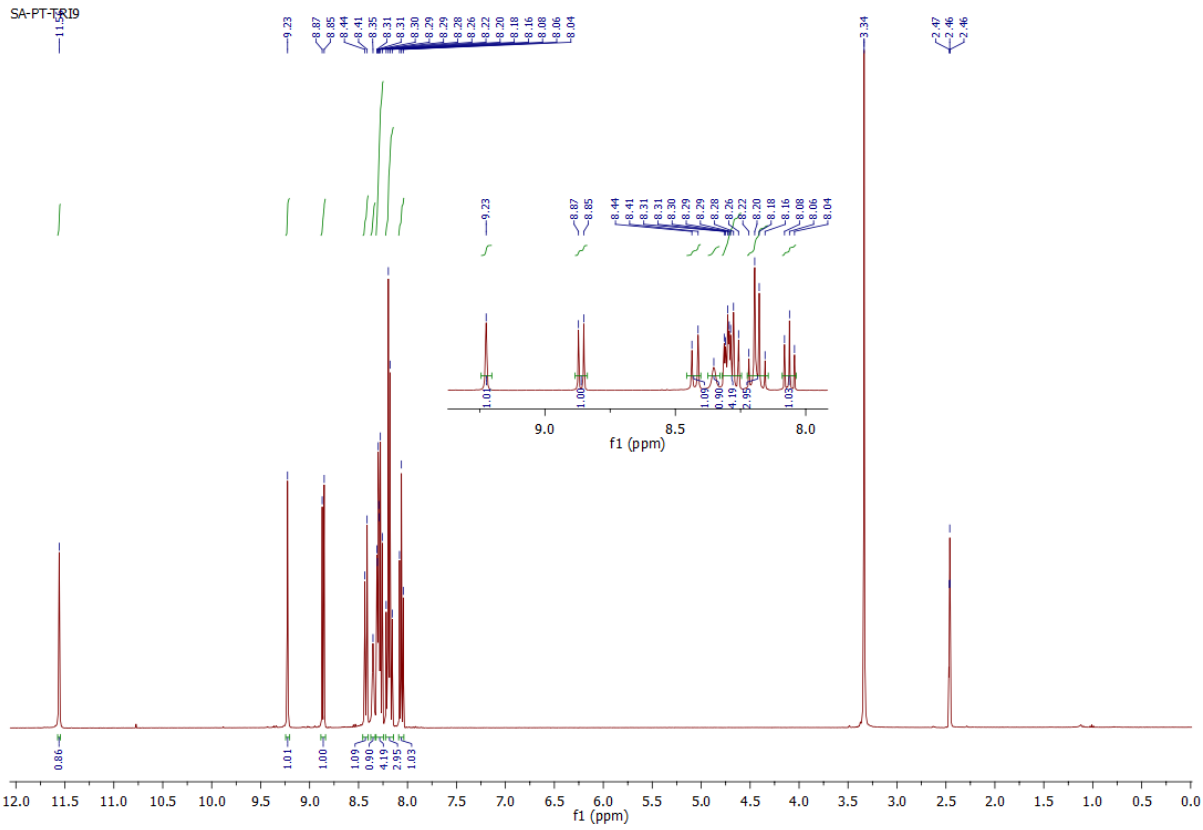


Figure S31: ^{1}H NMR of synthesized compound 3g

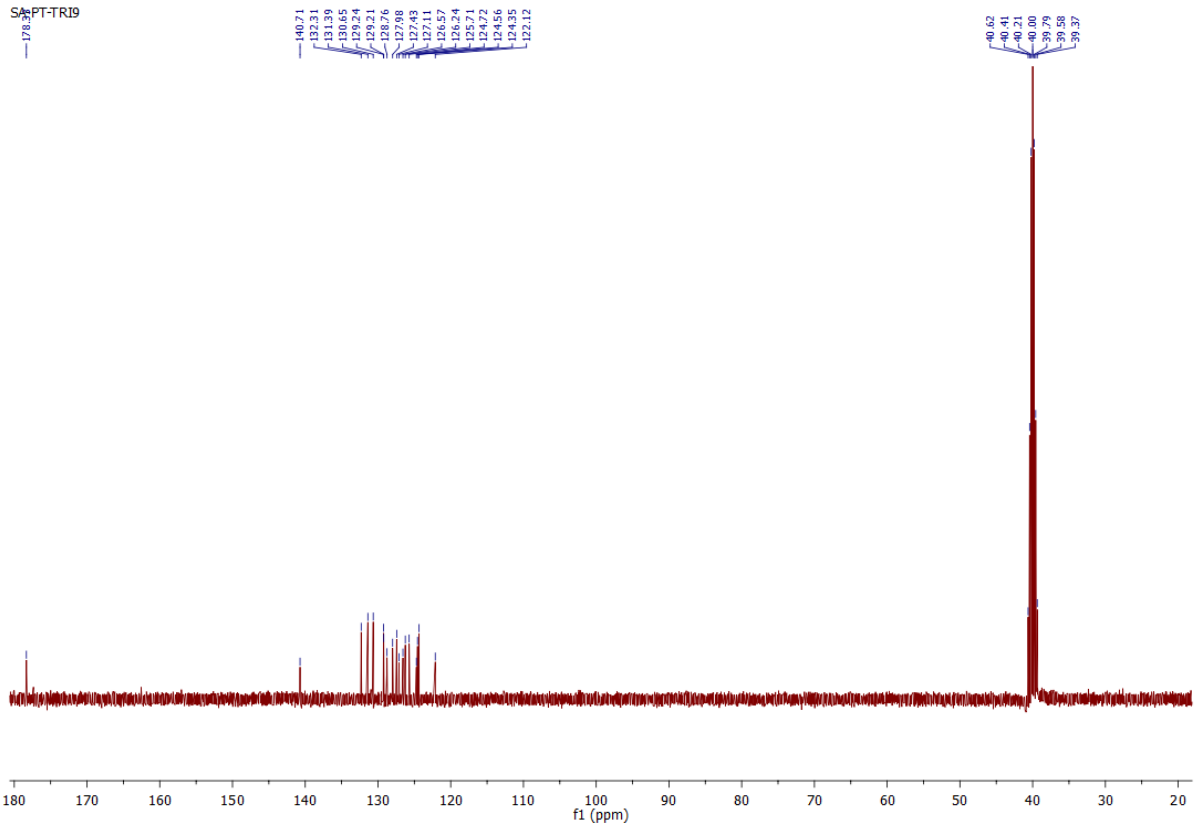
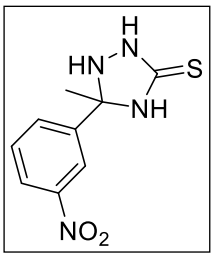


Figure S32: ^{13}C NMR of synthesized compound 3g

5-methyl-5-(3-nitrophenyl)-1,2,4-triazolidine-3-thione **(3h)**:



88% yield; m.p. 206-210 °C[7]; ^{1}H NMR (400 MHz, DMSO d_6) δ 10.40 (s, 1H, NH), 8.57 (t, J = 1.9 Hz, 1H, NH), 8.41 (s, 1H, NH), 8.39 (d, J = 0.9 Hz, 1H, Ar-H), 8.20 – 8.12 (m, 2H, Ar-H), 7.62 (t, J = 8.0 Hz, 1H, Ar-H), 2.32 (s, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO d_6) δ 179.64, 148.69, 146.09, 139.98, 133.51, 130.23, 124.14, 121.56, 14.61.

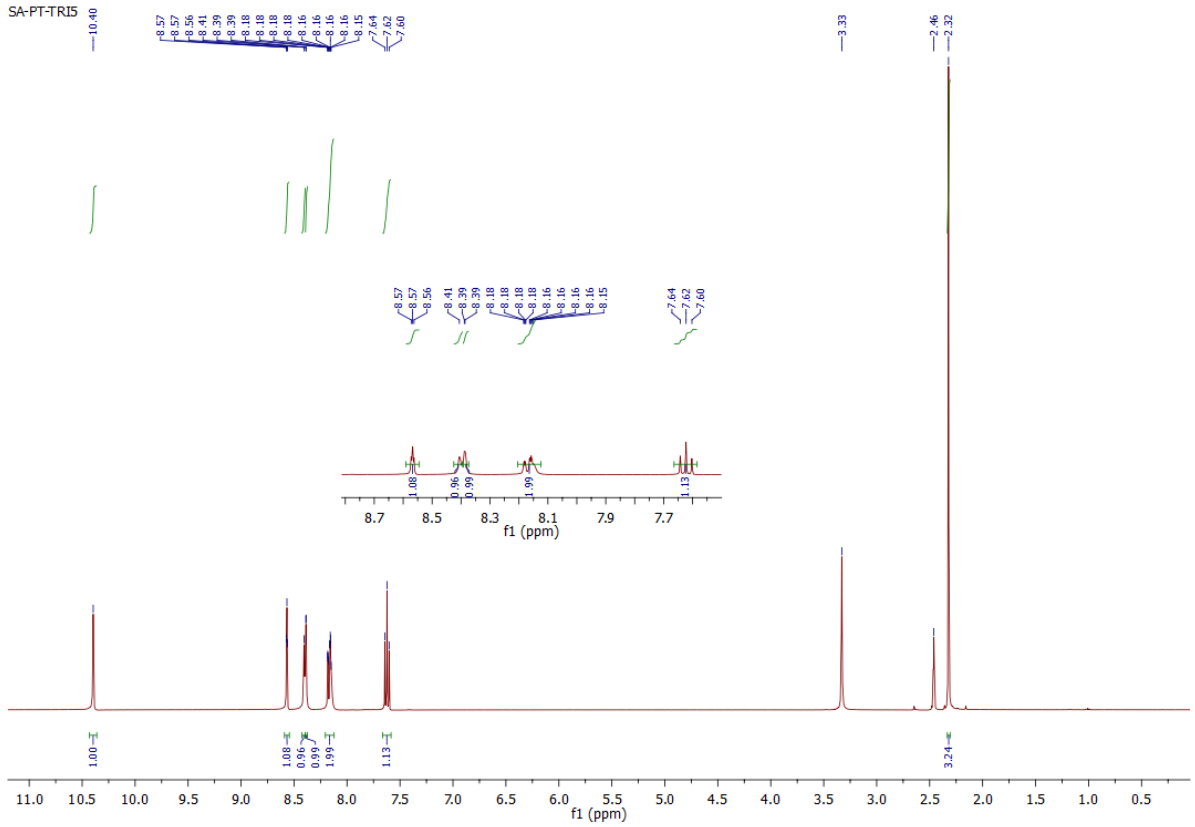


Figure S33: ^{1}H NMR of synthesized compound 3h

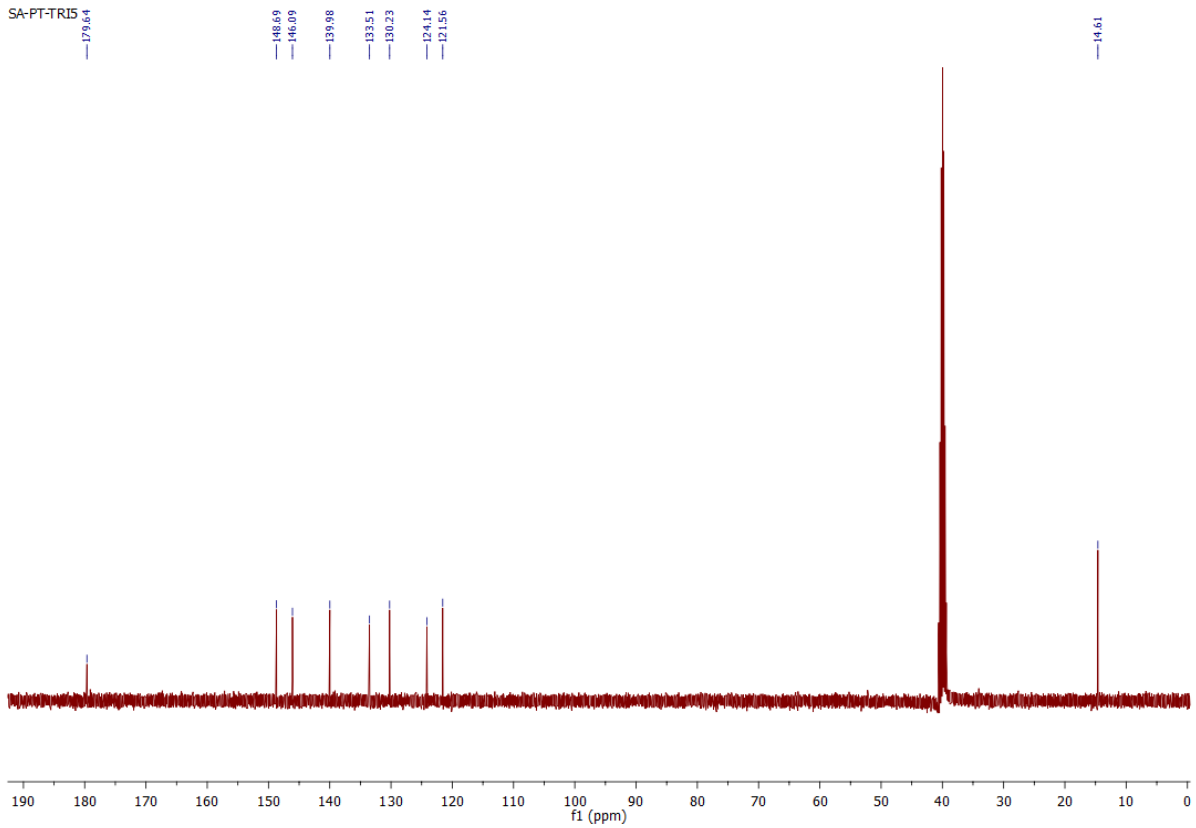
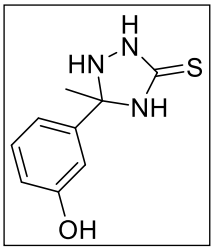


Figure S34: ^{13}C NMR of synthesized compound 3h

5-(3-hydroxyphenyl)-5-methyl-1,2,4-triazolidine-3-thione **(3i)**:



85% yield; m.p. 256-258 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1H-NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 1H, OH), 9.43 (s, 1H, NH), 8.26 (s, 1H, NH), 7.76 (s, 1H, NH), 7.30 (d, J = 8.3 Hz, 1H, Ar-H), 7.20 (d, J = 2.1 Hz, 1H, Ar-H), 7.13 (t, J = 8.0 Hz, 1H, Ar-H), 6.75 (d, J = 8.0 Hz, 1H, Ar-H), 2.21 (s, 3H, CH_3); NMR (101 MHz, DMSO-d_6) δ 179.34, 157.76, 148.57, 139.57, 129.73, 118.03, 116.78, 113.81, 14.73; LC-MS ($M+H^+$): 210.0747.

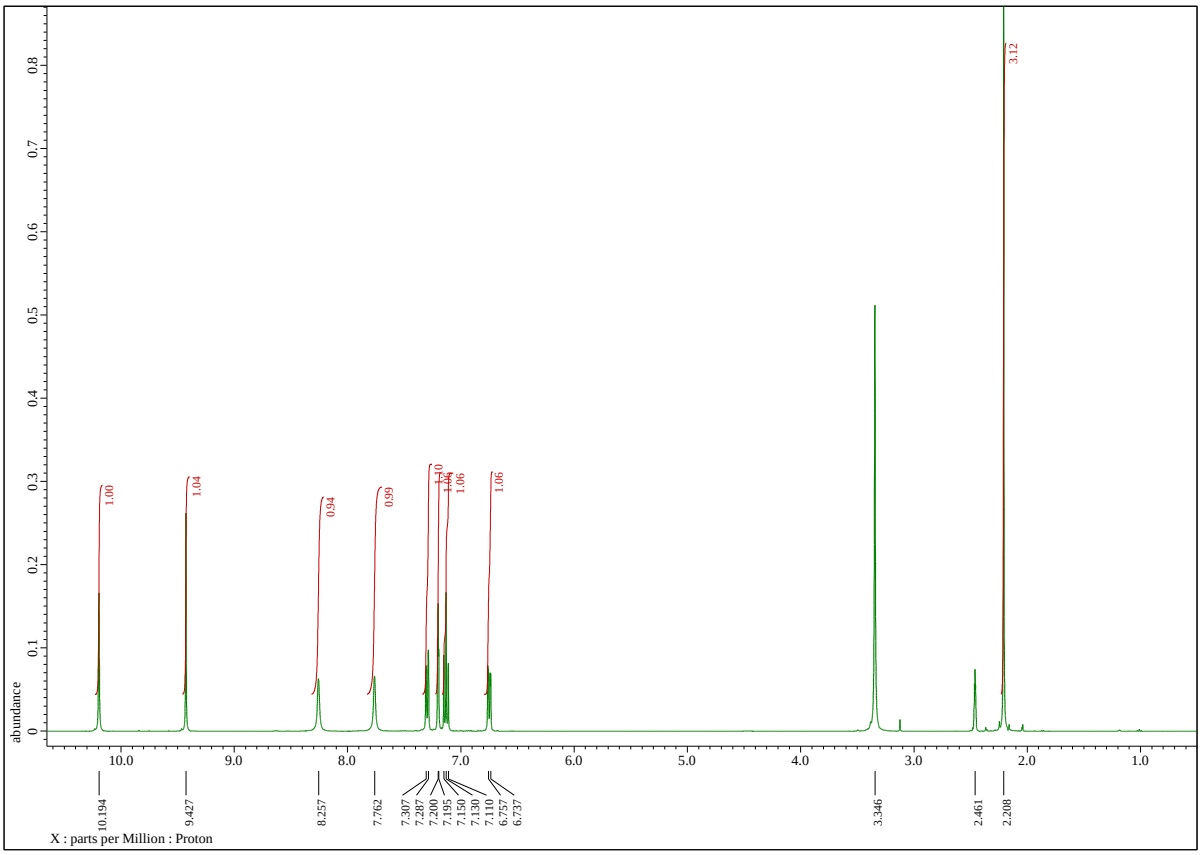


Figure S35: ^{1}H NMR of synthesized compound 3i

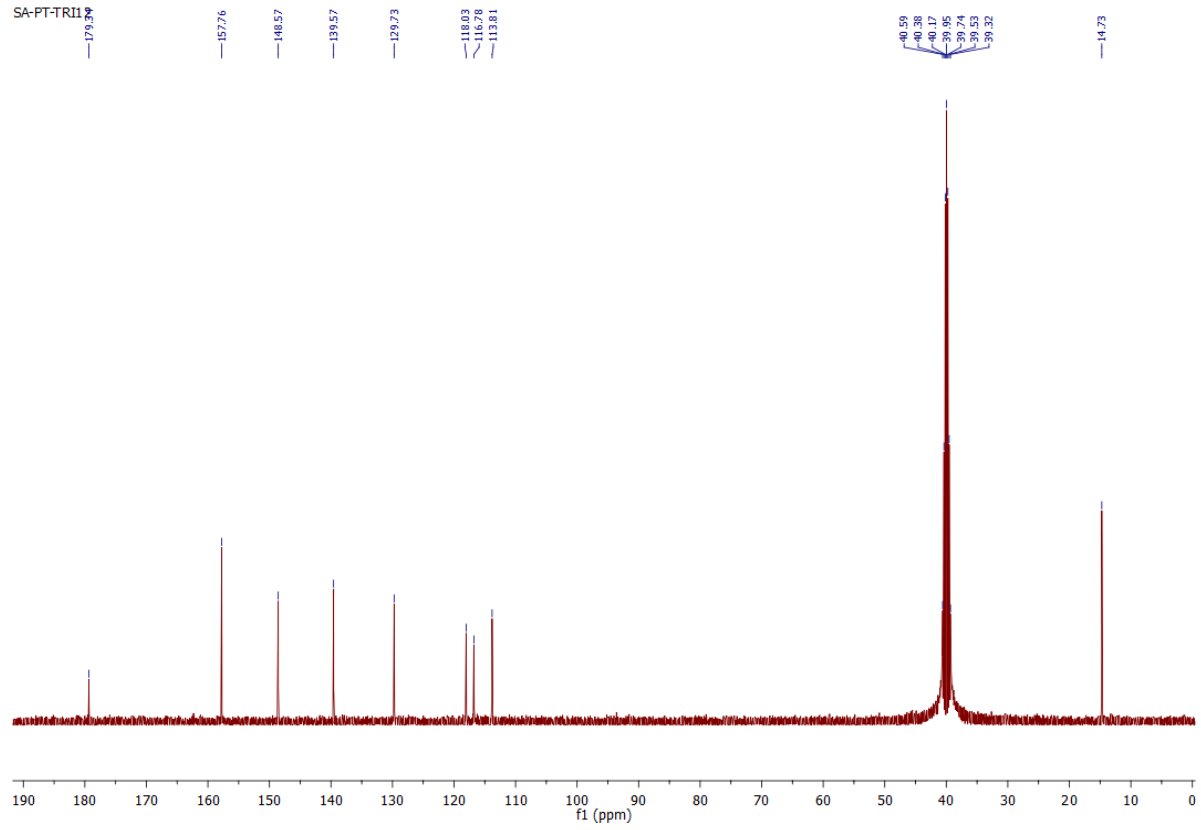


Figure S36: ^{13}C NMR of synthesized compound 3i

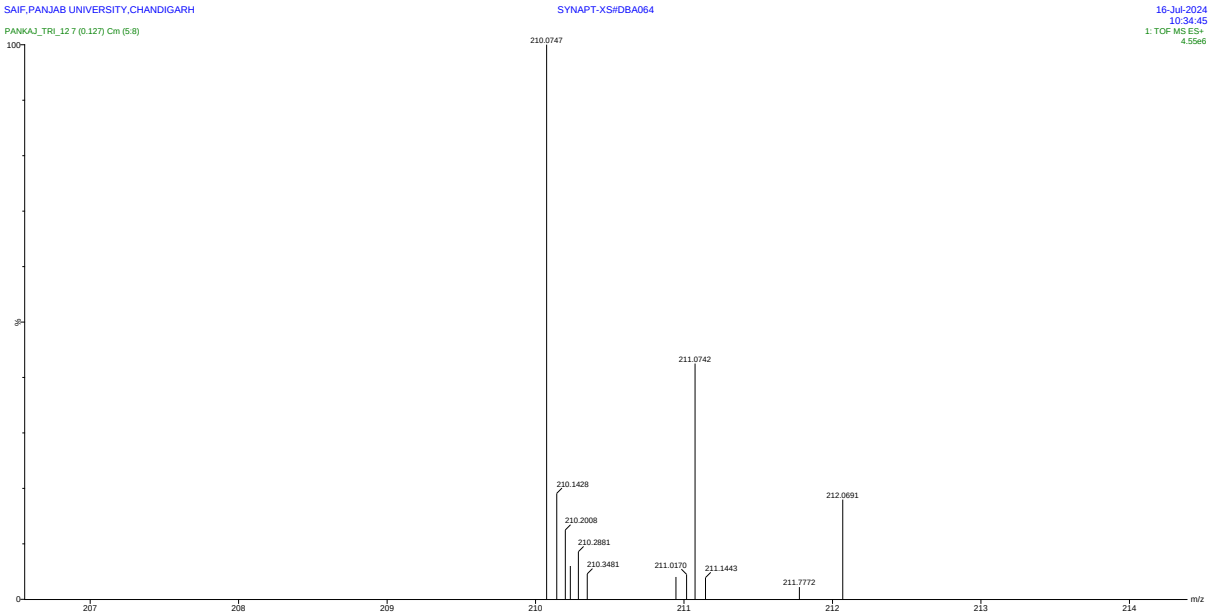
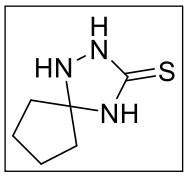


Figure S37: Mass spectra of synthesized compound 3i

1,2,4-triazaspiro[4.4]nonane-3-thione **(3j)**:



82% yield; m.p. 142-146 °C[8]; ^{1}H NMR (400 MHz, DMSO d_6) δ 9.81 (s, 1H, NH), 7.95 (s, 1H, NH), 7.45 (s, 1H, NH), 2.31 (t, J = 7.3 Hz, 2H, CH_2), 2.26 (t, J = 7.2 Hz, 2H, CH_2), 1.74 – 1.66 (m, 2H, CH_2), 1.65 – 1.58 (m, 2H, CH_2); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.61), 164.08, 33.59, 28.99, 25.09, 24.85.

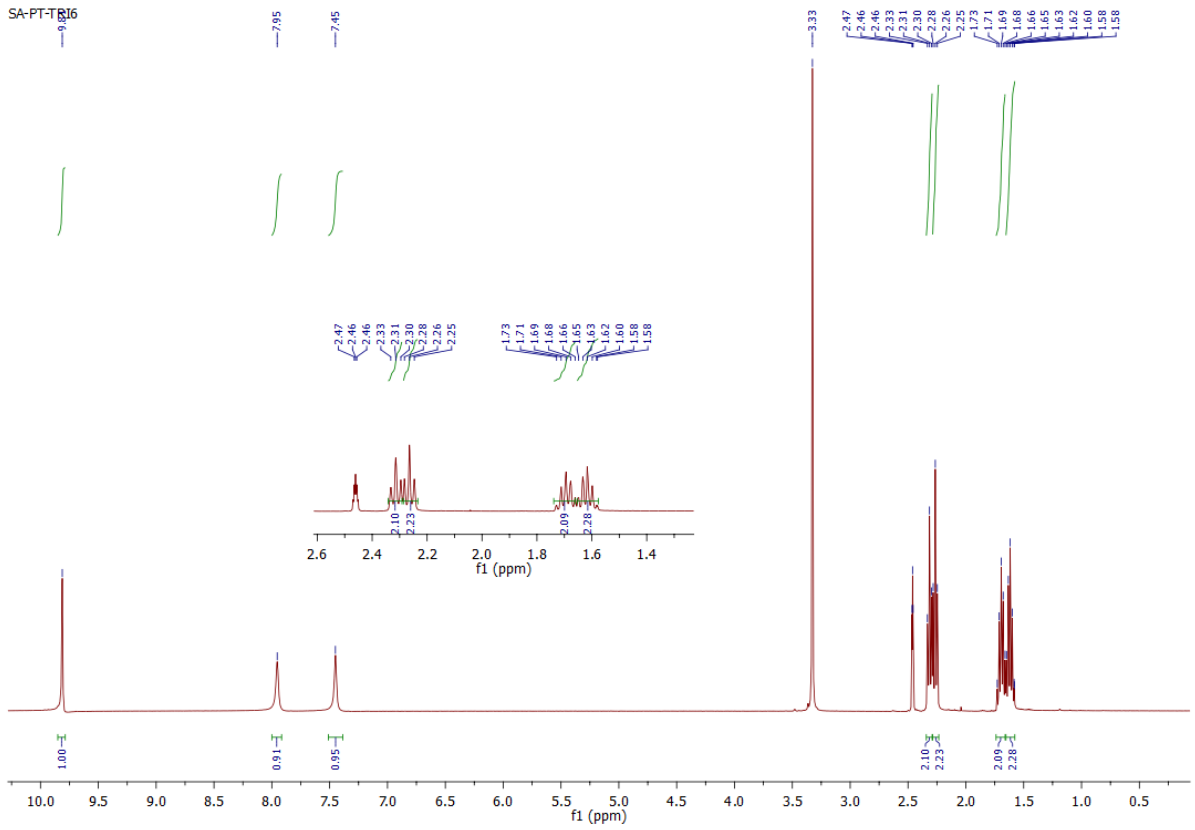


Figure S38: ^{1}H NMR of synthesized compound 3j

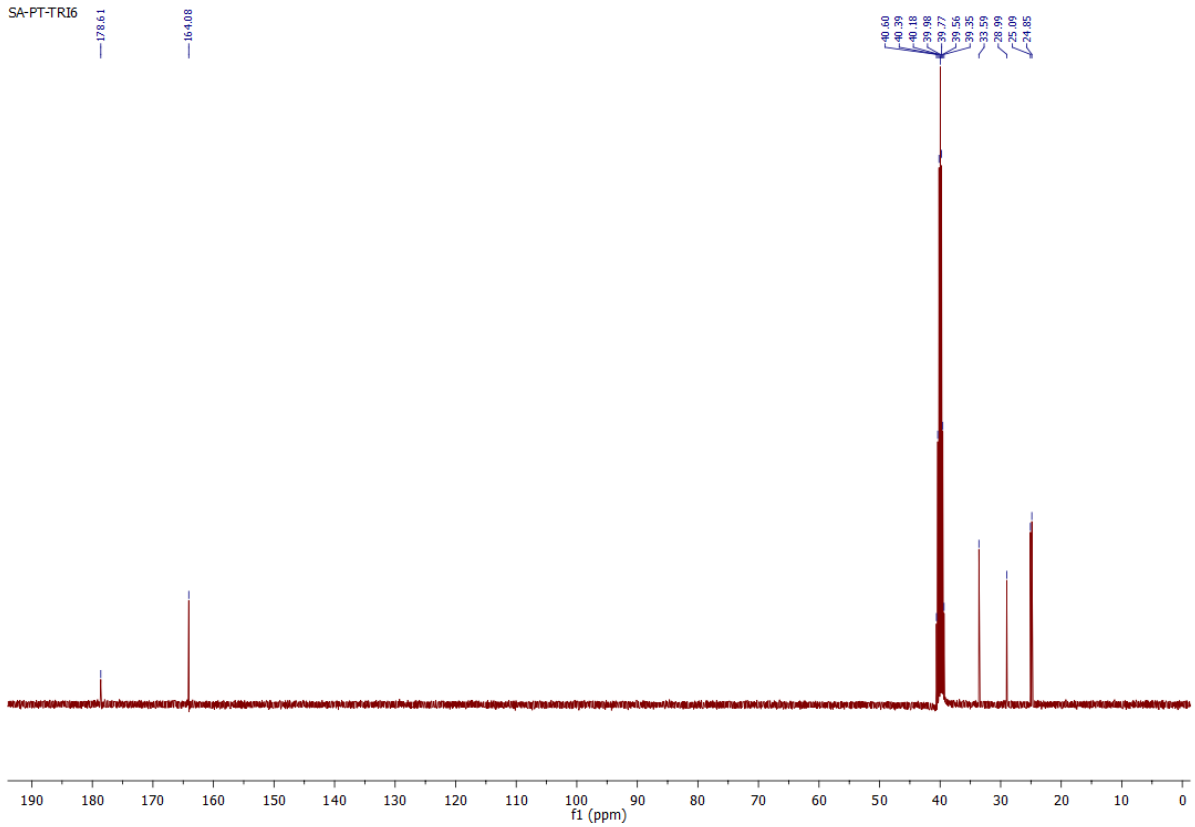
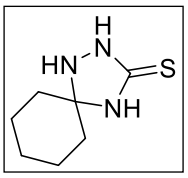


Figure S39: ^{13}C NMR of synthesized compound 3j

1,2,4-triazaspiro[4.5]decane-3-thione **(3k)**:



80% yield; m.p. 150-154 °C[8]; ^{1}H NMR (400 MHz, DMSO d_6) δ 10.14 (s, 1H, NH), 7.95 (s, 1H, NH), 7.49 (s, 1H, NH), 2.35 (s, 2H, CH_2), 2.22 – 2.02 (m, 2H, CH_2), 1.60 – 1.37 (m, 6H, CH_2); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.96, 157.46, 35.43, 27.73, 27.45, 26.26, 25.58.

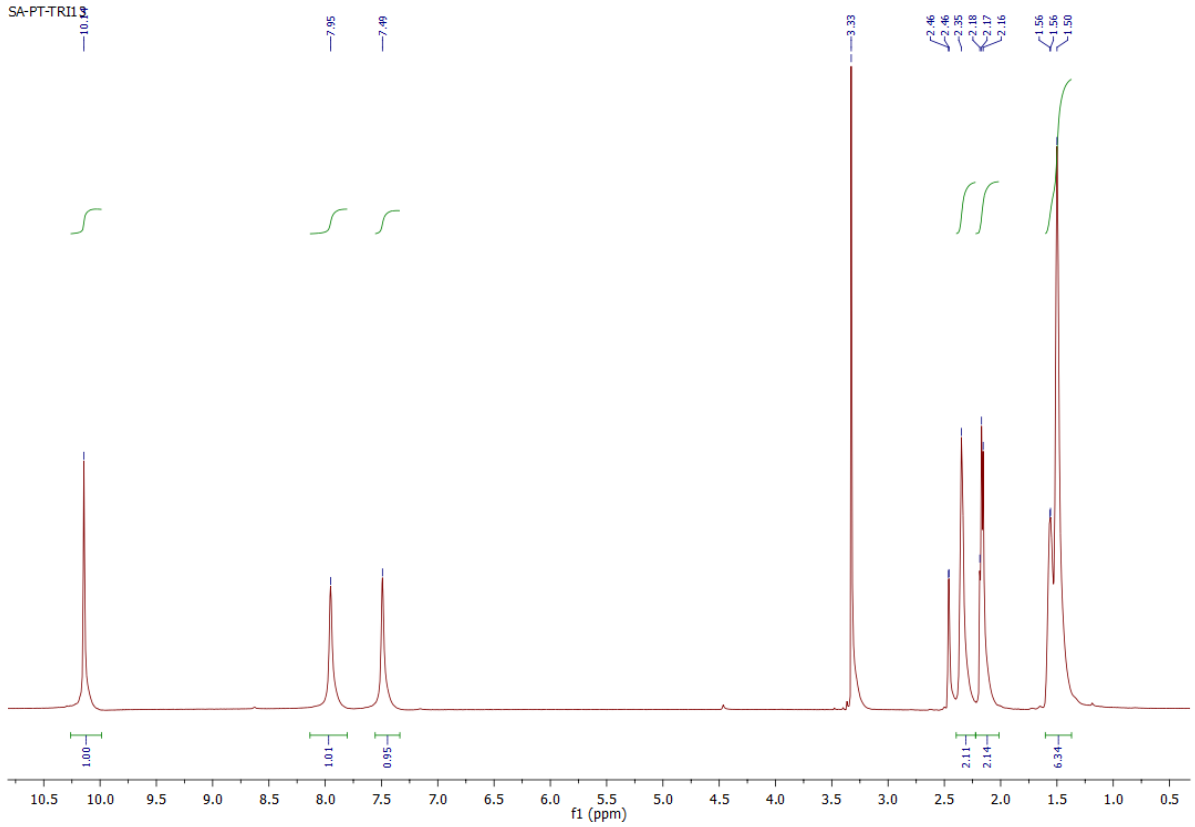


Figure S40: ^{1}H NMR of synthesized compound 3k

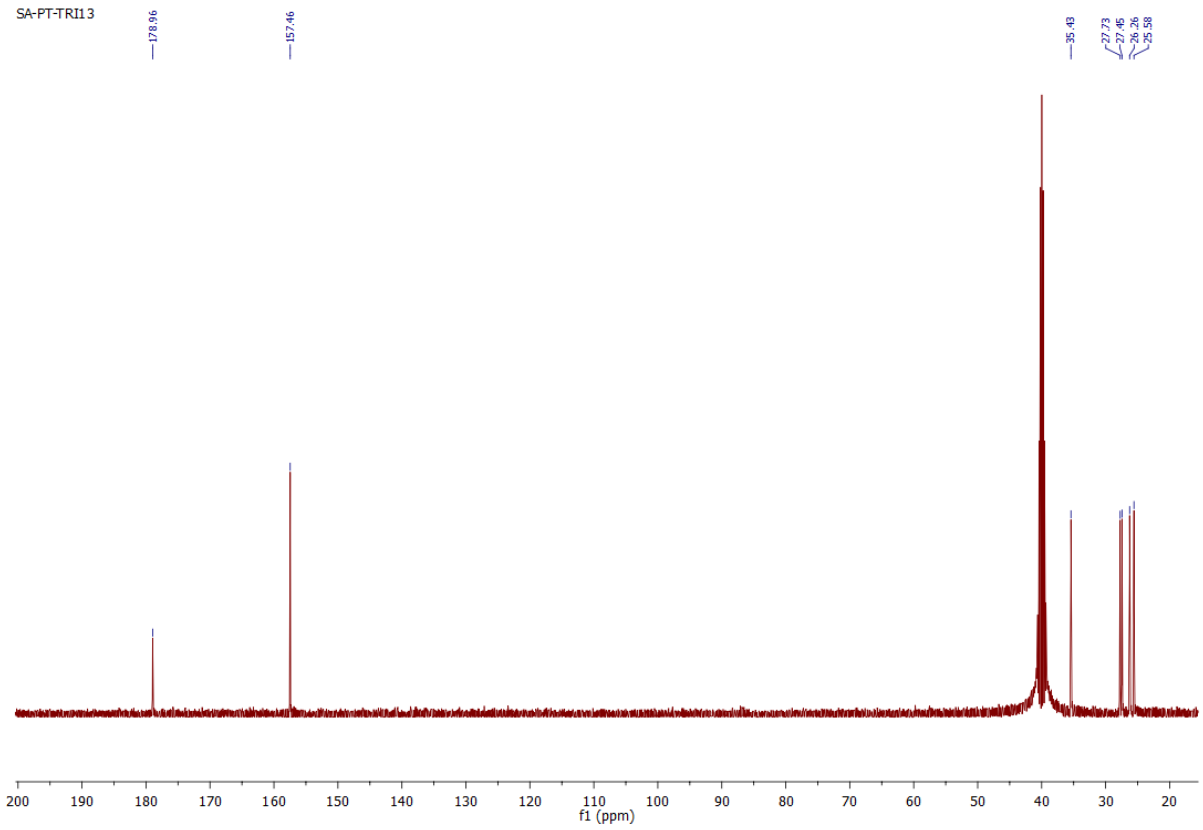
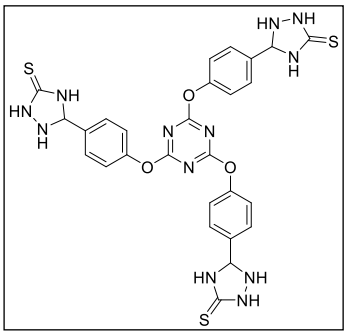


Figure S41: ^{13}C NMR of synthesized compound 3k

5,5',5''-(((1,3,5-triazine-2,4,6-triyl)tris(oxy))tris(benzene-4,1-diyl))tris(1,2,4-triazolidine-3-thione) **(10l)**:



92% yield; m.p. 431-435 °C; ^{1}H NMR (400 MHz, DMSO d_6) δ 11.46 (s, 3H, NH), 8.21 (s, 3H, NH), 8.03 (s, 3H, NH), 7.99 (s, 3H, CH), 7.84 (d, J = 8.8 Hz, 6H, Ar-H), 7.27 (d, J = 8.7 Hz, 6H, Ar-H); ^{13}C NMR (101 MHz, DMSO d_6) δ 178.44, 173.40, 152.78, 141.58, 132.69, 129.06, 122.19; HRMS ($M+H^+$): 661.1327.

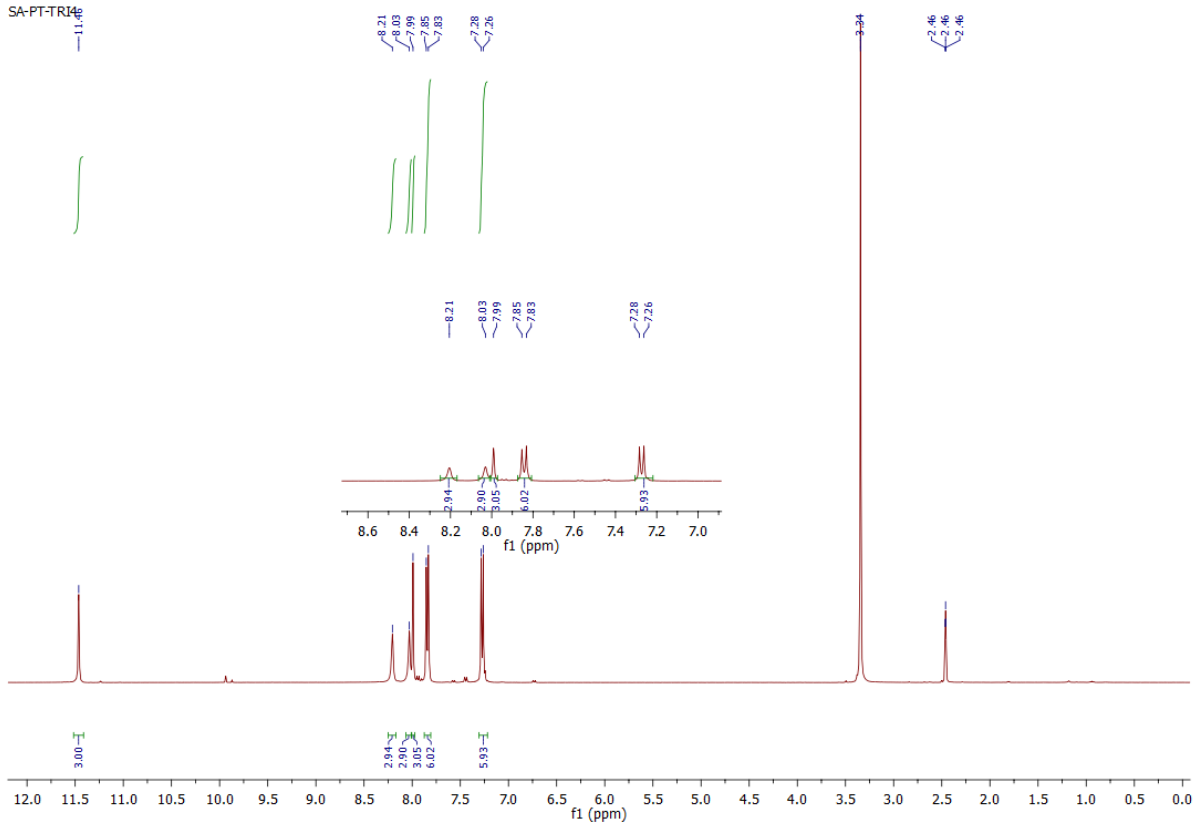


Figure S42: ^{1}H NMR of synthesized compound 3l

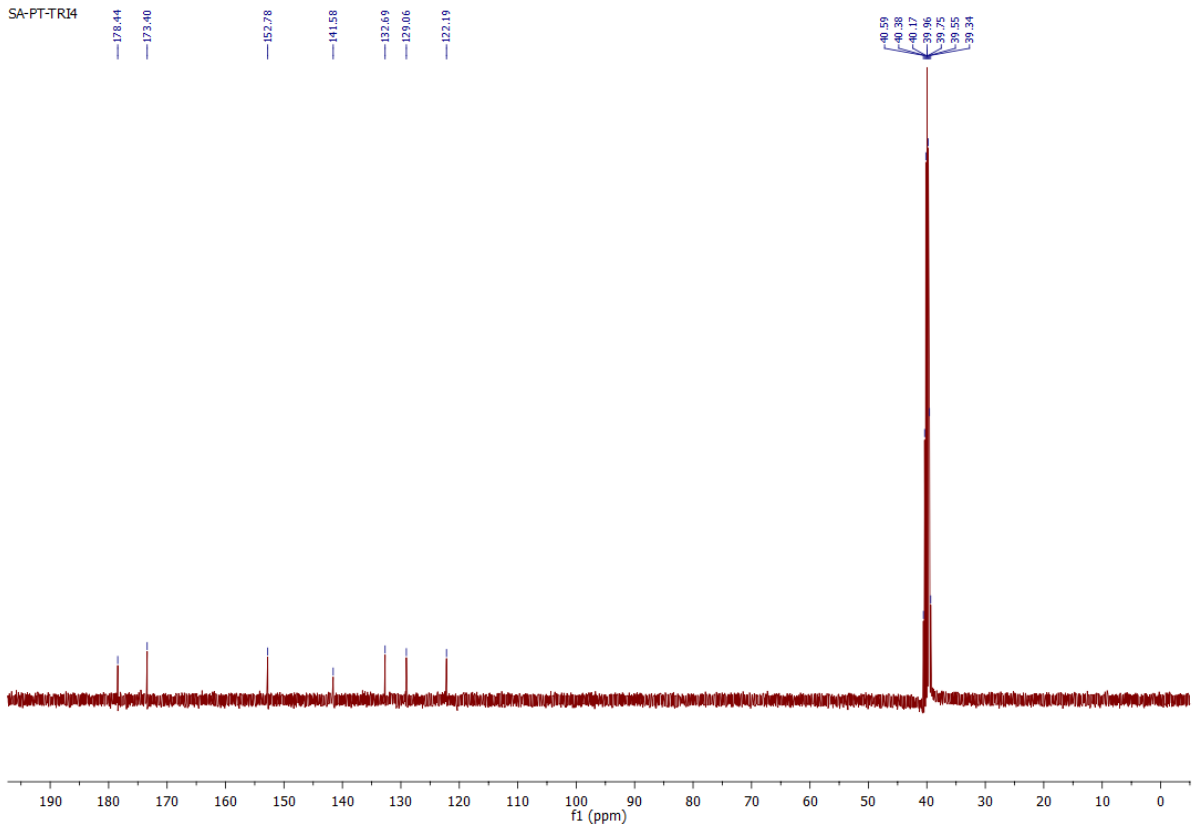


Figure S43: ^{13}C NMR of synthesized compound 3l

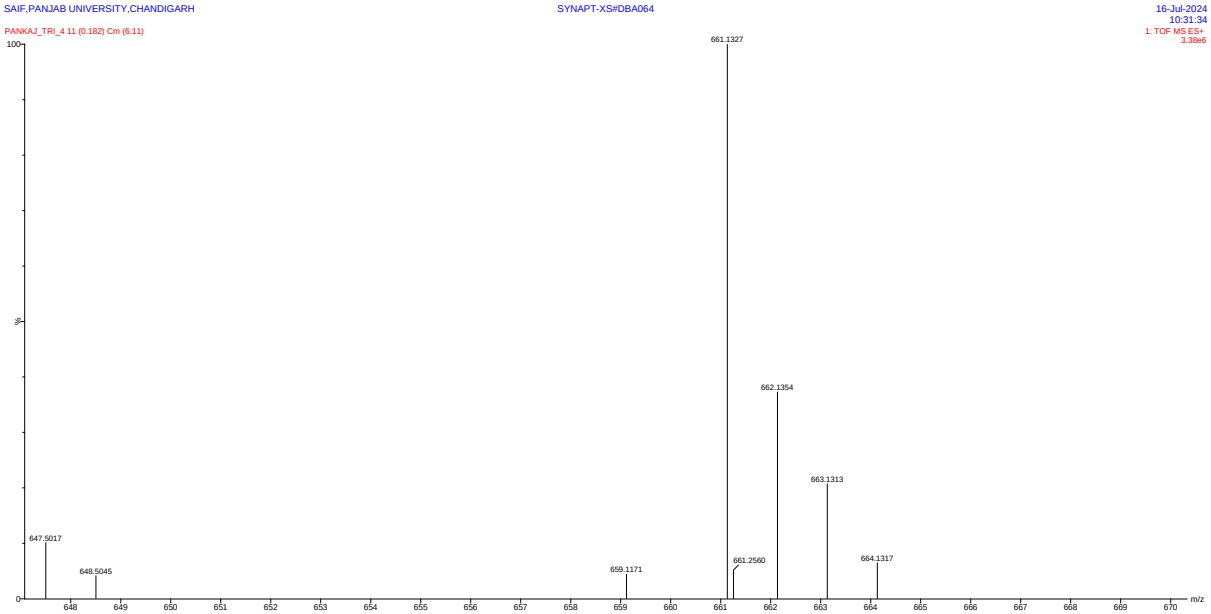


Figure S44: Mass spectra of synthesized compound 3l

References

1. Mikroyannidis, J. A.; Sharma, S.; Vijay, Y.; Sharma, G., Novel low band gap small molecule and phenylenevinylene copolymer with cyanovinylene 4-nitrophenyl segments: synthesis and application for efficient bulk heterojunction solar cells. *ACS Applied Materials & Interfaces* **2010,** *2* (1), 270-278.
2. Ahmed, L. R.; EL-Mahdy, A. F.; Pan, C.-T.; Kuo, S.-W., A water-soluble copper-immobilized covalent organic framework functioning as an "OFF–ON" fluorescent sensor for amino acids. *Materials Advances* **2021,** *2* (14), 4617-4629.
3. Gan, S.-X.; Jia, C.; Qi, Q.-Y.; Zhao, X., A facile and scalable synthetic method for covalent organic nanosheets: ultrasonic polycondensation and photocatalytic degradation of organic pollutants. *Chemical Science* **2022,** *13* (4), 1009-1015.
4. Pansambal, S.; Ghotekar, S.; Oza, R.; Deshmukh, K., Biosynthesis of CuO nanoparticles using aqueous extract of Ziziphus mauritiana L. leaves and their Catalytic performance for the 5-aryl-1, 2, 4-triazolidine-3-thione derivatives synthesis. *Int. J. Sci. Res. Sci. Technol* **2019,** *5* (4), 122-128.
5. Nami, N.; Lale Mohammadi, S., One-Pot Facile Synthesis of New 1, 2, 4-Triazolidine Derivatives Using Sodium Borohydride and Fe3O4 Magnetic Nanoparticles (MNPs). *International Journal of Nanoscience and Nanotechnology* **2017,** *13* (4), 347-357.
6. Mahajan, P. G.; Dige, N. C.; Vanjare, B. D.; Raza, H.; Hassan, M.; Seo, S.-Y.; Kim, C.-H.; Lee, K. H., Synthesis and biological evaluation of 1, 2, 4-triazolidine-3-thiones as potent acetylcholinesterase inhibitors: in vitro and in silico analysis through kinetics, chemoinformatics and computational approaches. *Molecular Diversity* **2020,** *24*, 1185-1203.
7. Patil, P. B.; Patil, J. D.; Korade, S. N.; Kshirsagar, S. D.; Govindwar, S. P.; Pore, D. M., An efficient synthesis of anti-microbial 1, 2, 4-triazole-3-thiones promoted by acidic ionic liquid. *Research on Chemical Intermediates* **2016,** *42*, 4171-4180.
8. Ramesh, R.; Lalitha, A., PEG-assisted two-component approach for the facile synthesis of 5-aryl-1, 2, 4-triazolidine-3-thiones under catalyst-free conditions. *RSC Advances* **2015,** *5* (63), 51188-51192.