RASĀYAN *J. Chem.*
Vol. 18 | No. 3 |1362-1371| July-September | 2025
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

THE THIA-MICHAEL ADDITION REACTION: A SIMPLE AND EASY GREEN ONE-POT SYNTHESIS OF BIS 1,2,3-TRIAZOLYL *β*-MERCAPTO CARBONYL SPIN-OFFS

Murugesan Maheswari, Eswaran Baluchamy and Alagusundaram Ponnuswamy

School of Chemistry, Madurai Kamaraj University, Madurai-625021, (Tamil Nadu) India
✉Corresponding author: rmmaheswarim.phil@gmail.com

ABSTRCT

The present investigation deals with an efficient synthesis of a library of bis *β*-mercapto carbonyl triazole derivatives *via* a one-pot three-component solvent-free green protocol. Significance of the protocol has been realized due to its mild reaction conditions, cost effectiveness, quantitative yield of the product within a short reaction time, easy workup, and eco-friendliness. Water as the green solvent facilitates easy separation of pure products from the reaction medium without the need for chromatographic separation.

Keywords: Bis-1,2,3-Triazole, Thioether, Grinding, Solvent-Free Approach.

RASĀYAN *J. Chem.*, Vol. 18, No. 3, 2025

INTRODUCTION

Among the most effective and cost-effective methods for reactions involving the production of carbon-carbon and carbon-heteroatom bonds, Michael addition stands out. Oxo-Michael reactions,[1,2] aza-Michael reaction,[3,4,5,6] and the thia-Michael reaction[7,8] that have been used to synthesize various hybrid organic moieties. Thia-Michael's addition reaction is one of the valuable synthetic approaches towards diversified sulfur-containing organic scaffolds of medicinal importance. They exhibit numerous biological activities, such as anti-viral,[9] anti-inflammatory,[10] antioxidant,[11] antiproliferative,[12] antimicrobial,[13] antibacterial,[14] antifungal[15] anticancer,[16,] and antidiabetic.[17] In addition, the removal of the sulfur moiety allows for easy regeneration of the double bond, making the Thia-Michael addition to α, β-unsaturated carbonyl compounds a feasible technique for selectively protecting the C=C bond of conjugated enones. Hence, benzenethiol derivatives act as a fluorescent probe to differentiate toxic thiophenol derivatives from biologically important biothiols.[18] Over the decades, catalyst-free and solvent-free organic reactions have received much attention in synthetic organic chemistry.[19,20] Accordingly, many Organosulfur compounds have established their utility in pharmaceuticals and material science. Among them, aryl sulfides are privileged motifs found in many commercial drugs.[21] (Fig.-1).

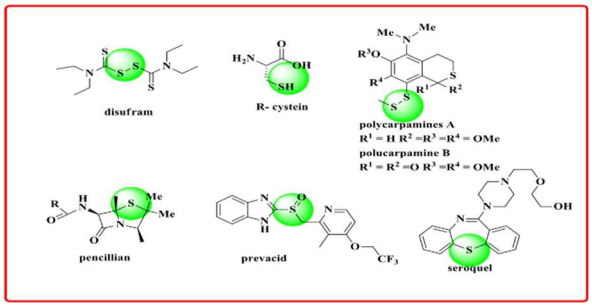


Fig.-1: Commercialized Therapeutic Drugs

In literature, Thia-Michael addition to electron-deficient olefins has been described in a number of methods, each with its own set of drawbacks, including a lengthy reaction time, high temperature, the use of halogenated and high-boiling solvents, the employment of metal catalysts, and moderate yields.

http://doi.org/10.31788/RJC.2025.1839315

Therefore, it is necessary to establish a clear, environmentally friendly, solvent-free, metal-free synthetic process for thia-Michael addition. Recently, hybrid molecules having more than one pharmacophore are gaining special attention in medicinal chemistry. The adaptable nature of the 1,2,3-triazole moiety proves its wide range of pharmacological activities, *viz*. antiproliferative,[22] antiviral,[23] antimicrobial,[24] antifungal,[25] anti-inflammatory.[26] However, triazole derivatives excellent solubility and stability increase their bioactivity in the biological system. By considering the medicinal importance of hybrid organic molecules, we planned to synthesize heterocycles consisting of green and efficient reagents, which, under very mild conditions, result in the formation of -*β*-mercapto carbonyl derivatives at room temperature *via* the one-pot protocol. We have successfully eliminated the need for costly solvents and catalysts, as well as complicated purification processes and multi-step procedures, by creating an effective solvent-free method for adding thiophenol to bis 1,2,3triazolyl linked *α, β*-unsaturated carbonyl compounds. Therefore, the current work reveals the synthesis of new bis 1,2,3-triazolyl-linked *β*-mercapto carbonyl derivatives using thia-Michael addition at room temperature without the use of a solvent.

EXPERIMENTAL

Materials and Methods

All the chemicals and reagents used for the synthesis were purchased from Avra Synthesis Pvt. Ltd. and Merck Pvt. Ltd., India. Melting points were analyzed using an open capillary tube. The structural analysis was done by NMR, FTIR, and mass spectrometry. ^{1}H, ^{13}C, and 2D NMR spectra were recorded using Bruker Advance spectrometer at 400 MHz for proton and 101 MHz for carbon-13 NMR. $CDCl_3$ solvent was used throughout the NMR experiment with TMS as internal reference. Chemical shift (δ) and coupling constants (J) were measured in terms of ppm and Hz, respectively. The terms s, d, t, dd, and m are abbreviated as singlet, doublet, triplet, doublet of doublet, and multiplet, respectively. ^{13}C NMR data and ^{1}H NMR data are reported with the solvent peak ($CDCl_3$=77.0 MHz, $CDCl_3$= δ 7.26) as the internal standard. Fourier transform infrared spectra were obtained from a Shimadzu IR Affinity-1 instrument. Mass spectra were recorded with a Q-Tof mass spectrometer. Elemental analyses of all the compounds were performed, which are in agreement with the calculated values within ±0.4%.

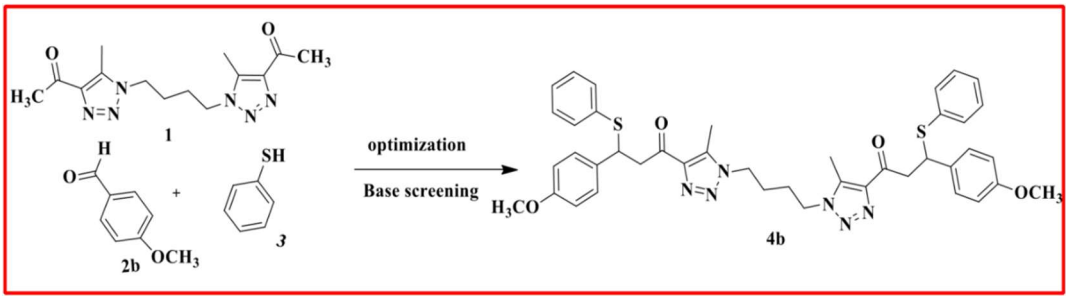
General Procedure

Synthesis of 1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1*H*1,2,3triazole-4,1-diyl)) diethanone (1)

A mixture of 1,4-dibromoazide (1 equiv), Acetyl acetone (2 equiv) was refluxed in the presence of potassium carbonate by using a suitable solvent. The completion of the reaction was monitored with the help of TLC, and then the crude product was separated with dichloromethane. The products were recrystallized from aqueous ethanol for further spectral analysis.

Synthesis of 1,1'-(1,1'-(butane-1,4-diyl)bis(5-methyl-1*H*1,2,3triazole-4,1-diyl))bis(3-aryl-3-(phenylthio)propan-1-one) hybrids (4a-m).

At the outset, a synthesis of 1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1*H*-1,2,3-triazole4,1diyl))bis(3-aryl-3-(phenylthio)propan-1-one) (4b) was attempted varying the bases (table 1)i.e. a mixture of bis 1,2,3-triazolyl ketone (1, 1.0 equiv), substituted aryl aldehyde (2 , 2equiv), thiophenol(3 , 2equiv) and base (1.5 equiv) was stirring well. TLC was used to track the reaction's completion. An excess of diluted sodium hydroxide aqueous solution was added to the reaction mixture.



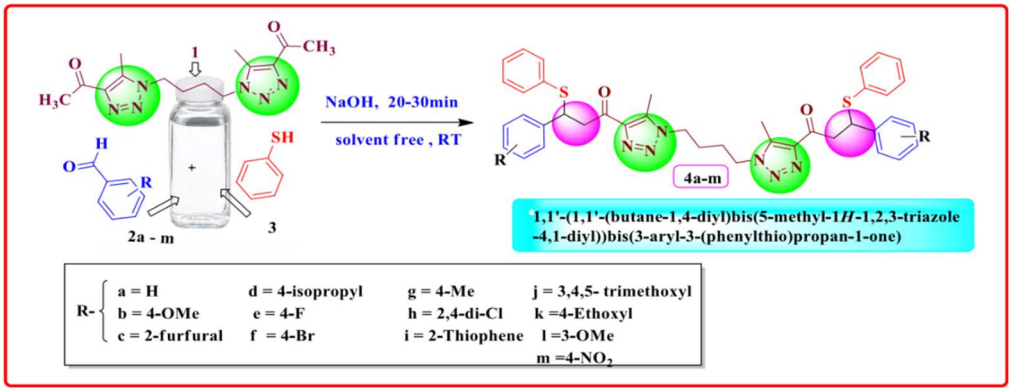
Scheme-1: Optimization for the Synthesis of 1,1'-(1,1'-(butane-1,4-diyl)bis(5-methyl-1*H*1,2,3triazole-4,1-diyl))bis(3-aryl-3-(phenylthio)propan-1-one) (4b)

The raw material was filtered and repeatedly cleaned with water. The water-soluble inorganic base, *viz,* sodium hydroxide, was noted to be the best, affording the product in good yield in a short reaction time.

Table-1: Optimization for the Synthesis of Compound (4b)

Entry	Base	Time (minutes)	Yield (%)
1	Et_3N	60	63
2	K_2CO_3	52	76
3	Na_2CO_3	45	75
4	KOH	40	88
5	NaOH	25	95
6	Pyridine	60	55

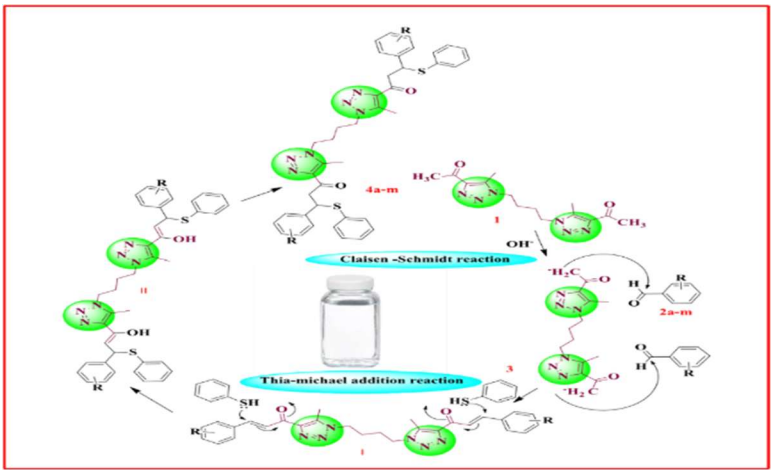
From Table-1, it is noted that the water-soluble inorganic base, *viz.,* sodium hydroxide, was noted to be the best, affording the product in good yield 95%) in a short reaction time (25 min).



Scheme-2: Synthesis of 1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1*H*-1,2,3-triazole-4,1-diyl))bis (3-aryl-3-(phenylthio) propan-1-one)

Reaction Mechanism

Plausible mechanism for the formation of 1,1'-(1,1'-(butane-1,4-diyl)bis(5-methyl-1*H*1,2,3triazole-4,1-diyl))bis(3-aryl-3-(phenylthio)propan-1-one) hybrids (4a-m) hybrids. It includes. 1) Base-catalyzed Claisen-Schmidt reaction – The base OH^- hits the proton in (1,4) bis 1,2,3- triazolyl ketone and followed by dehydration to form an intermediate (I) as (1,4) bis 1,2,3- triazolyl chalcone. 2) Thia-Michael addition reaction – lone pair of electrons on a sulfur atom in thiol hick the C=C double bond in (1,4) bis 1,2,3-triazolyl chalcone subsequently enol form of (1,4) bis 1,2,3triazolyl thiol hybrid (II) is formed, then the hybrid (II) undergoes keto-enol tautomerism to produce 1,1'(1,1'-(Butane-1,4-diyl)bis(5-methyl-1*H*-1,2,3-triazole-4,1-diyl))bis(3-aryl-3- (phenylthio)propan-1one) hybrids (4a-m).



Scheme-3: Mechanism of1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1*H*-1,2,3-triazole-4,1diyl))bis(3-aryl-3-(phenylthio)propan-1-one) hybrids (4a-m)

RESULTS AND DISCUSSION

Structural Assignment

A band at 688 cm^{-1} that corresponds to the C-S stretching vibration was visible in the FTIR spectra of a typical molecule, 4c. Furthermore, the carbonyl group's stretching frequency is the cause of another band seen at 1673 cm^{-1}. ESI-MS spectra of compound 4c reveals $[M+NH_4]^+$ at *m/z*=700.4373, which is in agreement with the calculated value. A multiplet between δ 7.22 and 7.50, which corresponds to eighteen aromatic protons, may be seen in the ^1H NMR spectra of a typical chemical 4b. At δ 4.27, aliphatic protons ($-NCH_2$) showed up as a triplet. The diastereotopic protons (Ha and Hb) are responsible for the two doublets of doublets seen at δ 3.67 and 3.85. The methyl groups belonging to triazole and the methoxy groups attached to phenyl rings, respectively, are responsible for the other two singlets at δ 2.48 and 3.75. The typical chemical 4b's C^{13} NMR signals were assigned using the H-HCOSY, C-H-COSY, and HMBC methods. The carbonyl and aliphatic two methylene carbons are represented by the signals at δ 193.2, 46.45, and 26.18, respectively. Furthermore, at δ 4.97, the chiral carbon displayed a triplet signal. At δ 45.73, the diastereotopic carbon showed a signal. Signals at δ 9.05 and 55.22 are produced by methyl groups linked to triazole and phenyl rings, respectively.

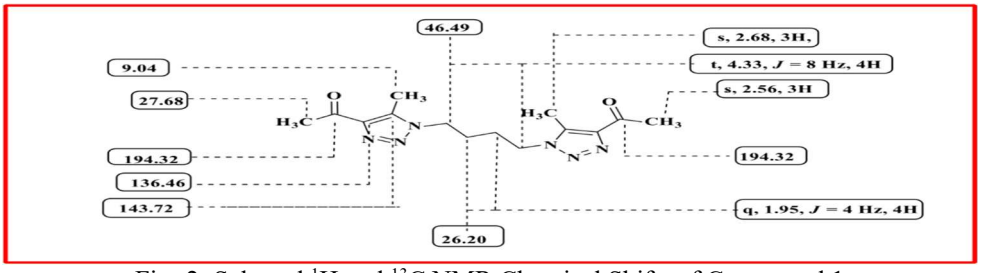


Fig.-2: Selected ^1H and ^{13}C NMR Chemical Shifts of Compound 1

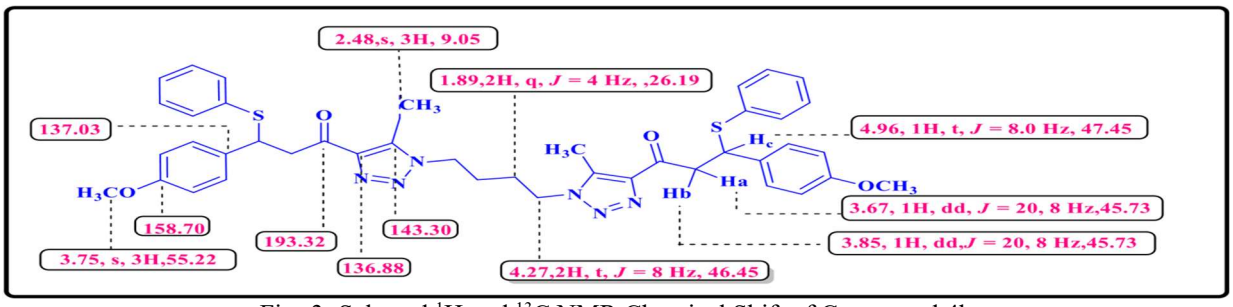


Fig.-3: Selected ^1H and ^{13}C NMR Chemical Shift of Compound 4b

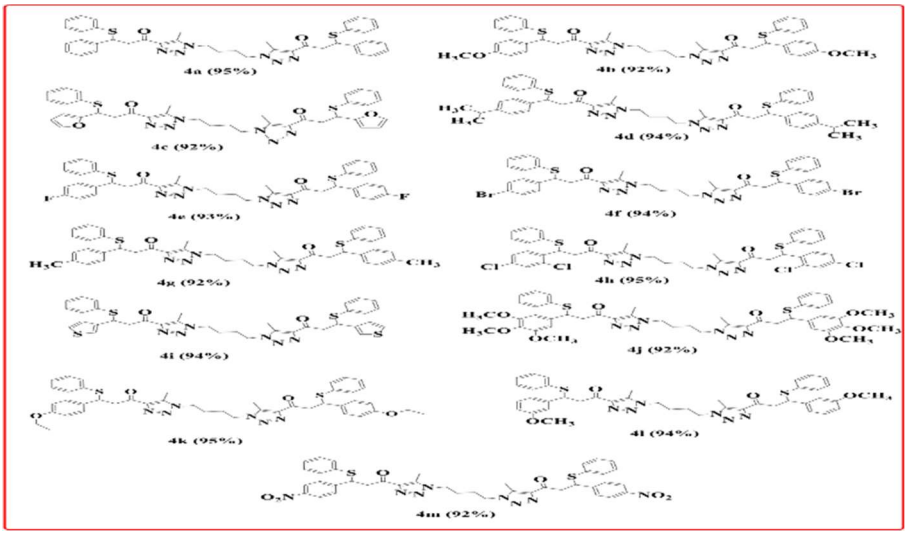


Fig.-4: Derivatives of 1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1*H*-1,2,3-triazole-4,1diyl))bis(3aryl-3-(phenylthio)propan-1-one) hybrids (4a-m)

Spectra of 1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1*H*-1,2,3-triazole-4,1-diyl)) diethanone (1)

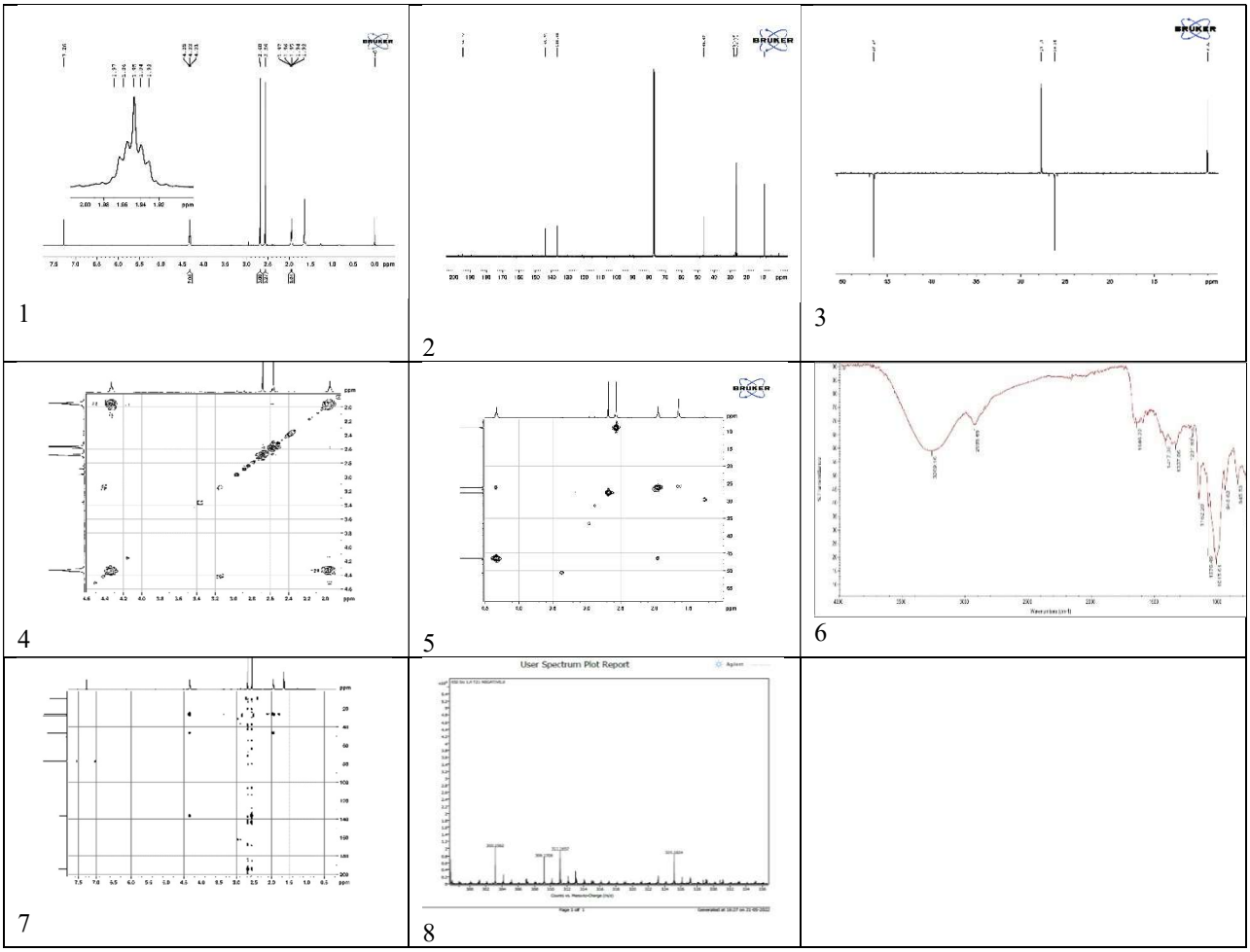
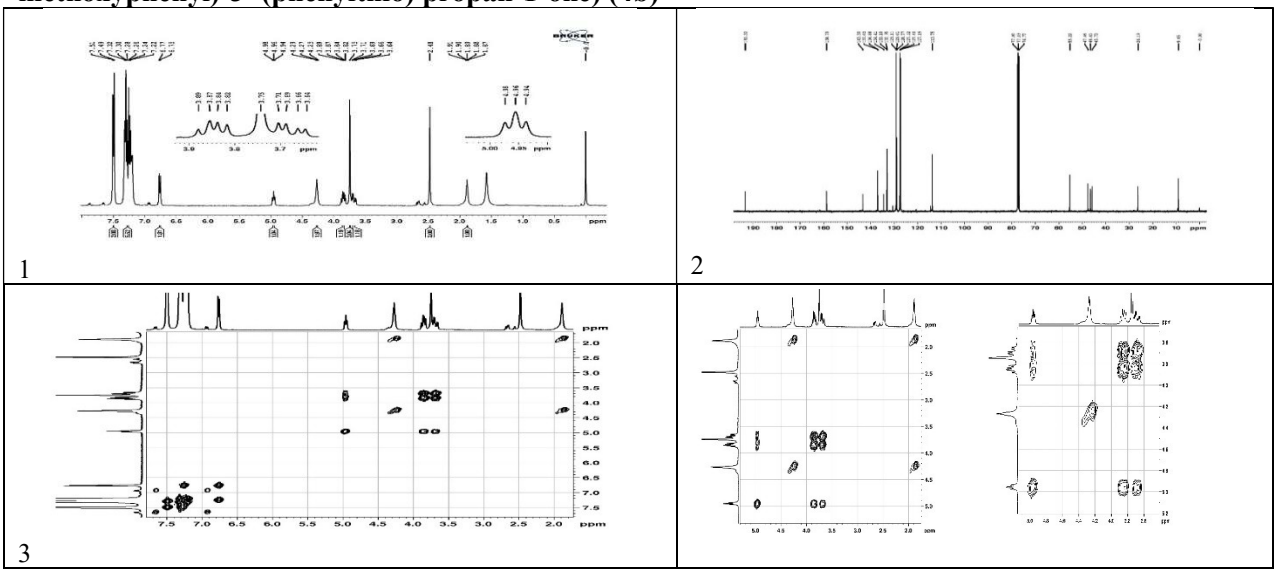


Fig.-5: (1) ^{1}H NMR (400 MHz, CDCl3), (2) ^{13}C NMR (101 MHz, CDCl3), (3) DEPT135, (4) H, H-COSY, (5) C, H-COSY, (6) IR, (7) HMBC, (8) ESI-MS

Spectra of 1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis (3-(4-methoxyphenyl)-3- (phenylthio) propan-1-one) (4b)



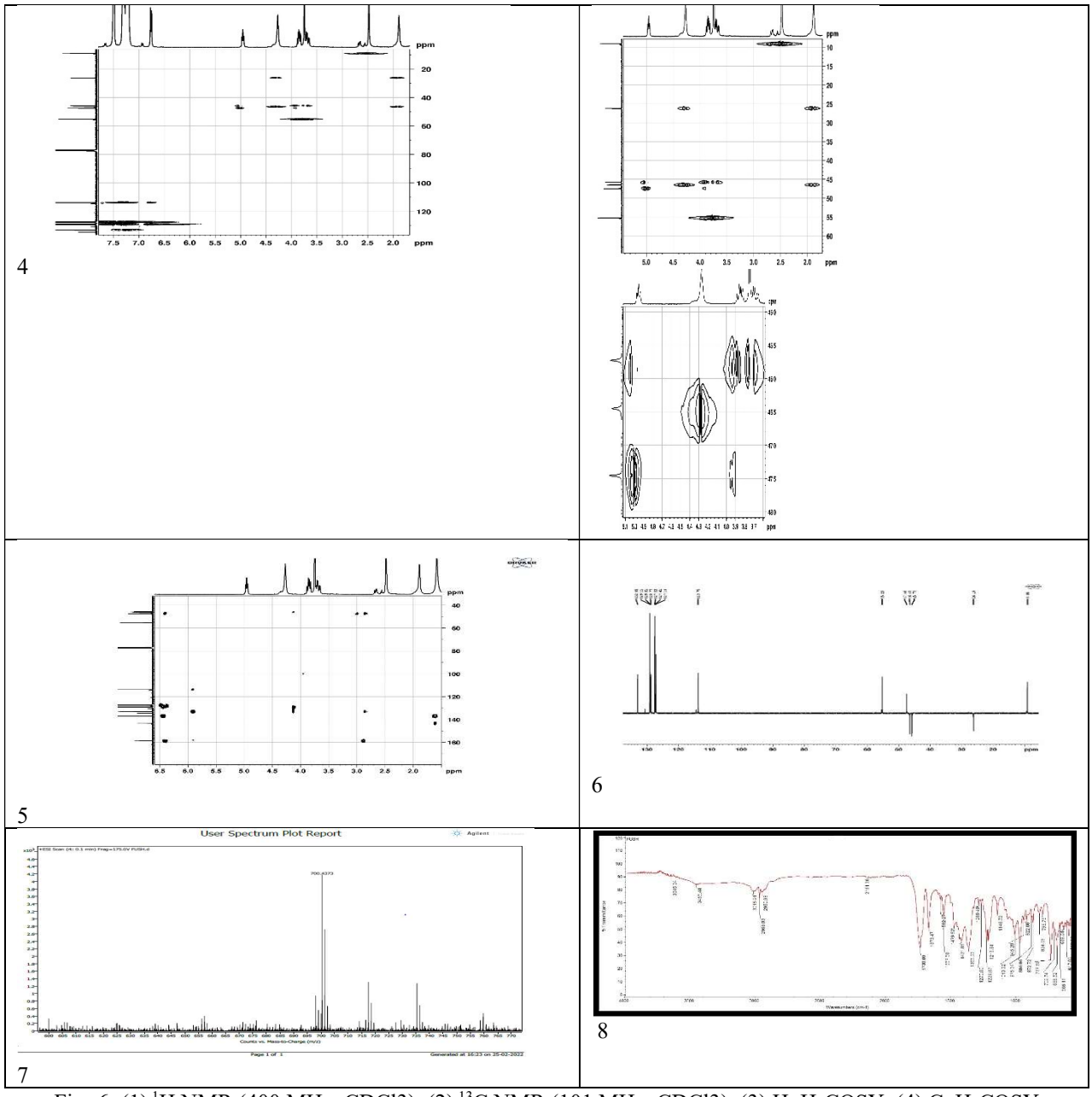


Fig.-6: (1) ^{1}H NMR (400 MHz, CDCl3), (2) ^{13}C NMR (101 MHz, CDCl3), (3) H, H-COSY, (4) C, H-COSY, (5) HMBC, (6) DEPT135, (7) ESI-MS, (8) IR

CONCLUSION

Bis 1,2,3-triazolyl beta-mercapto carbonyl derivatives have been synthesized in a high yield using a greener procedure using a one-pot multicomponent reaction at room temperature and an environmentally safe solvent.

Spectral Data of all Synthesized Organic Compounds

1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1diyl)) diethanone (1)

White solid; yield: 80%; m.p.98-100°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 (t, J =8.0 Hz, 4H), 2.68(s, 6H), 2.56 (s, 6H), 1.95 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.32, 143,72, 136.46, 46.49, 27.68, 26.20, 9.04. m/z of $[M-H]^-$: calculated 303.3574; found 303.1562. Anal. Calc. for $C_{14}H_{20}N_6O_2$: C, 55.25; H, 6.62; N, 27.61. Found: C, 55.18; H, 6.61; N, 27.63.

1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl)) bis(3-phenyl-3-(phenylthio) propan-1-one) (4a)
Yellow solid; yield: 95%; m.p.225-227°C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.17 (m, 20H), 4.97 (t, J = 8.0 Hz, 2H), 4.29 (t, J = 8.0 Hz, 4H), 3.86 (dd, J = 20.0, 8.0 Hz, 2H), 3.73 (dd, J = 20.0, 8.0 Hz, 2H), 2.667 (s, 6H), 1.90 (q, J = 4.0 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.70, 143.79, 141.26, 136.83, 134.51, 132.82, 130.72, 129.45, 127.97, 127.13, 122.91, 48.07, 46.80, 45.54, 25.93, 9.05. Anal. Calc. for $C_{40}H_{40}N_6O_2S_2$: C, 68.54; H, 5.75; N, 11.99; S, 9.15. Found: C, 68.46; H, 5.74; N, 11.97; S, 9.14.

1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis (3-(4-methoxyphenyl)-3-(phenylthio) propan-1-one) (4b)
Yellow solid; yield: 92%; m.p.220-222°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 4H), 7.32 – 7.22 (m, 10H), 6.76 (d, J = 8.0 Hz, 4H), 4.96 (t, J = 8.0 Hz, 2H), 4.27 (t, J = 8.0 Hz, 4H), 3.85 (dd, J = 20.0, 8.0 Hz, 2H), 3.75 (s, 6H), 3.67 (dd, J = 20.0, 8.0 Hz, 2H), 2.48 (s, 6H), 1.89 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.32, 158.70, 143.30, 137.03, 136.88, 134.41, 133.10, 132.95, 129.11, 129.01, 128.77, 127.52, 127.40, 127.19, 113.75, 55.22, 47.46, 46.45, 45.73, 26.19, 9.05. Anal. Calc. for-$C_{42}H_{44}N_6O_4S_2$:C, 66.29; H, 5.83; N, 11.04; S, 8.43. Found: C, 66.20; H, 5.84; N, 11.06; S, 8.42.

1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis(3-(furan-2-yl)-3-(phenylthio)propan-1-one) (4c)
Yellow solid; yield: 92%; m.p.232-234°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H), 7.32 – 7.24 (m, 10H), 6.20 (dd, J = 8.0, 4.0 Hz, 4H), 5.01 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.82 (dd, J = 16.0, 8.0 Hz, 2H), 3.73 (dd, J = 16.0, 8.0 Hz, 2H), 2.56 (s, 6H), 1.94 (q, J = 8.0 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.60, 153.49, 143.15, 141.89, 137.03, 134.03, 133.03, 128.75, 127.99, 110.22, 107.27, 46.51, 43.30, 41.22, 26.22, 9.05. m/z of $[M+NH_4]^+$: calculated 700.2197; found 700.4373. FTIR (υ, cm^{-1}): 1673.47(C=O), 688.52(C-S). Anal. Calc. for $C_{36}H_{36}N6O_4S_2$: C, 63.51; H, 5.33; N, 12.34; S, 9.42. Found: C, 63.44; H, 5.34; N, 12.36; S, 9.43.

1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis(3-(4-isopropylphenyl)-3-(phenylthio)propan-1-one) (4d)
Yellow solid; yield: 94%; m.p.229-231°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.20- 7.08 (m, 18H), 4.97 (t, J = 8.0 Hz, 2H), 4.29 (t, J = 8.0 Hz, 4H), 3.84 (dd, J = 20.0, 8.0 Hz, 2H), 3.72 (dd, J = 20.0, 8.0 Hz, 2H), 2.88-2.84 (m, 2H), 2.50 (s, 6H), 1.94 (q, J = 4.0 Hz, 4H), 1.20 (d, J = 8.0 Hz, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.33, 147.86, 143.30, 138.31, 136.83, 134.52, 132.83, 128.71, 127.72, 127.30, 127.04, 126.45, 47.90, 46.67, 45.68, 34.07, 26.17, 23.46, 9.14. Anal. Calc. for $C_{46}H_{52}N_6O_2S_2$: C, 70.37; H, 6.68; N, 10.70; S, 8.17. Found: C, 70.69; H, 6.67; N, 10.68; S, 8.16.

1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1H-1,2,3-triazole-4,1-diyl)bis(3-(4-fluorophenyl)-3(phenylthio) propan-1-one) (4e)
Yellow solid; yield: 93%; m.p.125-127°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 12.0 Hz, 4H), 7.26 – 7.10 (m, 10H), 6.87 (d, J = 8.0 Hz, 4H), 4.94 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.81 (dd, J = 8.0, 4.0 Hz, 2H), 3.71 (dd, J = 8.0, 4.0 Hz, 2H), 2.67 (s, 6H), 1.98 (q,, J = 4.0 Hz, 4H),^{13}C NMR (101 MHz, $CDCl_3$) δ 192.83, 143.96, 143.83, 142.40, 140.18, 136.24, 133.99, 133.96, 133.84, 132.62, 131.25, 130.16, 129.44, 129.10, 128.63, 127.96, 127.88, 127.78, 123.52, 121.17, 47.57, 46.48, 45.27, 26.16, 9.05. Anal. Calc. for $C_{40}H_{38}F_2N_6O_2S_2$ .C, 65.20; H, 5.20; N, 11.40; S, 8.70. Found: C, 65.12; H, 5.19; N, 11.38; S, 8.69.

1,1'-(1,1'-(Butane-1,4-diyl) bis (5-methyl-1H-1,2,3-triazole-4,1-diyl)) bis(3-(4-bromophenyl)3(phenylthio) propan-1-one) (4f)
Yellow solid; yield: 94%; m.p.223-225°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 12 Hz, 4H), 7.26 – 7.17 (m, 10H), 6.93 (d, J = 8.0 Hz, 4H), 4.90 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.83 (dd, J = 20.0, 8.0 Hz, 2H), 3.68 (dd, J = 20.0, 8.0 Hz, 2H), 2.67 s(s, 6H), 1.94 (q, J = 4.0 Hz, 4H),^{13}C NMR (101 MHz) δ 192.83, 143.96, 143.18, 142.24, 140.31, 136.99, 133.84, 133.62, 133.25, 132.16, 131.44, 130.10,

129.63, 129.07, 128.88, 127.78, 127.52, 127.17, 123.40, 121.04, 47.57, 46.48, 45.27, 26.16, 9.05. Anal. Calc. for $C_{40}H_{38}Br_2N_6O_2S_2$: C, 55.95; H, 4.46; N, 9.79; S, 7.47. Found: C, 55.88; H, 4.45; N, 9.81; S, 7.46.

1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis(3-(phenylthio)-3-(p-tolyl) propan-1-one) (4g)
Yellow solid; yield: 92%; m.p.235-237°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 4H), 7.24 – 7.14 (m, 10H), 6.77 (d, J = 8.0 Hz, 4H), 4.97 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.85 (dd, J = 20.0, 8.0 Hz, 2H), 3.73 (dd, J = 20.0, 8.0 Hz, 2H), 2.67 (s, 6H), 2.48 (s, 6H), 1.94 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.70, 143.79, 141.26, 136.83, 134.51, 132.82, 130.72, 129.45, 127.97, 127.13, 122.91, 48.07, 46.80, 45.54, 25.52, 21.52, 9.49. Anal. Calc. for $C_{42}H_{44}N_6O_2S_2$: C, 69.20; H, 6.08; N, 11.53; S, 8.80. Found: C, 69.12; H, 6.07; N, 11.50; S, 8.79.

1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl)) bis(3-(2,4-dichlorophenyl)3(phenylthiol) propan-1-one) (4h)
Yellow solid; yield: 95%; m.p.224-226°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 2H), 7.32 – 7.22 (m, 14H), 4.97 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.80 (dd, J = 8.0, 4.0 Hz, 2H), 3.76 (dd, J = 8.0, 4.0 Hz, 2H), 2.66 (s, 6H), 1.97 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.12, 157.07, 148.21, 143.58, 138.31, 136.83, 132.83, 130.70, 128.71, 127.72, 127.30, 126.45, 122.70, 115.96, 47.65, 46.59, 45.54, 26.35, 9.05. Anal. Calc. for $C_{40}H_{36}Cl_4N_6O_2S_2$: C, 57.28; H, 4.33; N, 10.02; S, 7.65. Found: C, 57.20; H, 4.34; N, 10.04; S, 7.64.

1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis(3-(phenylthio)-3- (thiophen-3-yl)propan-1-one) (4i)
Yellow solid; yield: 94%; m.p.242-244°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 2H)7.32 – 7.20 (m,10H), 6.77 (s, 4H), 4.87 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.77 (dd, J = 20.0, 8.0 Hz, 2H), 3.68 (dd, J = 20.0, 8.0 Hz, 2H), 2.67 (s, 6H), 1.98 (q, J = 4.0 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.60, 143.15, 141,89, 137.03, 134.03, 133.03, 129.07, 128.75, 127.99, 127.52, 127.17, 46.51, 43.30, 41.22, 26.22, 9.08, Anal. Calc. for $C_{36}H_{36}N_6O_2S_4$: C, 60.65; H, 5.09; N, 11.79; S, 17.99. Found: C, 60.57; H, 5.08; N, 11.77; S, 17.98.

1,1'-(1,1'-(Butane-1,4-diyl)bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis(3-(phenylthio)-3(3,4,5trimethoxyphenyl)propan-1-one) (4j)
Yellow solid; yield: 92%; m.p.229-231°C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 10H), 6.77 (s, 4H), 4.96 (t, J = 8.0 Hz, 2H), 4.27 (t, J = 8.0 Hz, 4H), 3.85 (dd, J = 20.0, 8.0 Hz, 2H), 3.75 (s, 18H), 3.68 (dd, J = 20.0, 8.0 Hz, 2H), 2.48 (s, 6H), 1.89 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.16, 143.71, 141.13, 136.89, 134.92, 134.18, 133.04, 130.54, 129.07, 128.90, 128.77, 128.74, 128.36, 127.90, 127.52, 127.47, 127.26, 122.84, 103.23, 59.89, 53.43, 48.01, 46.45, 45.55, 26.19, 9.04. Anal. Calc. for $C_{46}H_{52}N_6O_8S_2$: C, 62.71; H, 5.95; N, 9.54; S, 7.28. Found: C, 62.63; H, 5.94; N, 9.53; S, 7.27.

1,1'-(1,1'-(Butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl)) bis(3-(3-ethoxyphenyl)3(phenylthio) propan-1-one) (4k)
Yellow solid; yield: 95%; m.p.235-237°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.55 (m, 12H), 7.40 (s, 2H), 6.92 – 6.90 (m, 4H), 4.79 (t, J = 8.0 Hz, 2H), 4.36 (t, J = 8.0 Hz, 4H), 4.10 (m, 4H), 3.64 (dd, J = 20.0, 8.0 Hz, 2H), 3.26 (dd, J = 20.0, 8.0 Hz, 2H), 2.69 (s, 6H), 1.97 (q, J = 4.0 Hz 4H), 1.43 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 192.60, 143.15, 141.89, 137.03, 134.03, 133.03, 129.07, 128.75, 127.99, 127.52, 127.17, 122.75, 122.99, 64.51, 46.51, 43.30, 41.22, 26.22, 14.51, 9.08. Anal. Calc. for $C_{44}H_{48}N_6O_4S_2$: C, 66.98; H, 6.13; N, 10.65; S, 8.13. Found: C, 66.90; H, 6.12; N, 10.67; S, 8.12.

1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl))bis (3-(3-methoxyphenyl)3(phenylthio) propan-1-one) (4l)
Yellow solid; yield: 94%; m.p.225-227°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.20 (m, 10H), 7.00 (s, 4H) 6.66 – 6.60(m, 4H), 4.85 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.85 (dd, J = 20.0, 8.0 Hz, 2H), 3.70 (dd, J = 20.0, 8.0 Hz, 2H), 3.63 (s, 6H), 2.67 (s, 6H), 1.94 (q, J = 4.0 Hz, 4H),^{13}C NMR (101 MHz,

$CDCl_3$) δ 193.32, 158.30, 143.70, 137.03, 129.19, 128.10, 127.77, 127.52, 113.75, 55.45, 47.46, 46.45, 45.73, 26.19, 9.05. Anal. Calc. for $C_{42}H_{44}N_6O_4S_2$: C, 66.19; H, 5.83; N, 11.04; S, 8.43. Found: C, 66.28; H, 5.82; N, 11.03; S, 8.42.

1,1'-(1,1'-(butane-1,4-diyl) bis(5-methyl-1H-1,2,3-triazole-4,1-diyl)) bis (3-(4-nitrophenyl)3(phenylthio) propan-1-one(4m)

Yellow solid; yield: 92%; m.p.126-128°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 4H), 7.85 – 7.83 (m, 10H), 6.99 (d, J = 8.0 Hz, 4H), 4.95 (t, J = 8.0 Hz, 2H), 4.32 (t, J = 8.0 Hz, 4H), 3.94 (dd, J = 20.0, 8.0 Hz, 2H), 3.75 (dd, J = 20.0, 8.0 Hz, 2H), 2.56 (s, 6H), 1.98 (q, J = 4.0 Hz, 4H), ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.83, 143.18, 140.31, 136.99, 133.62, 133.25, 132.16, 131.44, 130.10, 129.63, 129.07, 128.88, 127.78, 127.52, 127.17, 123.40, 121.04, 47.57, 46.48, 45.27, 26.16, 9.05. Anal. Calc. for $C_{40}H_{38}N_8O_6S_2$: C, 60.74; H, 4.84; N, 14.17; S, 8.11. Found: C, 60.65; H, 4.83; N, 14.19; S, 8.10.

ACKNOWLEDGMENTS

The authors thank the Department of Science and Technology, New Delhi, India, for funds under the IRPHA program for the purchase of an NMR spectrometer.

CONFLICT OF INTERESTS

The authors declared that there is no conflict of interest in our manuscript.

AUTHOR CONTRIBUTIONS

The present work is related to *SDG-15: Life on Land*. All the authors contributed significantly to this manuscript, participated in reviewing/editing and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

Alagusundaram Ponnuswamy http://orcid.org/0000-0003-1564-2076
Mariappan Rajan http://orchid.org/0000-0001-9569-8744
Murugesan Maheswari http://orchid.org/0000-0001-9403-708X
Eswaran Baluchamy http://orcid.org/0009-0002-6851-3227

REFERENCES

1. J. Hu, D. Xu, , Q. Zhang, Y. Shang, M. Shi, Y. Huangfu, L. Liu, R.Liang, Y. Lai, Y.He, J. M. Gao, W. Xie, W, *RSC Advances,* **6(58),** 52583(2016), https://doi.org/10.1039/c6ra10399e
2. X. W. Du, L. M Stanley *Organic Letters,* **17(13),** 3276(2015), https://doi.org/10.1021/acs.orglett.5b01447
3. X. J. Zhou, J. Q. hao, X. M. Chen, J. R. Zhuo, Y. P. Zhang, Y. Z. Chen, X. M. Zhang, X.Y. Xu, W. C. Yuan, *Journal of Organic Chemistry,* **84(7),** 4381(2019), https://doi.org/10.1021/acs.joc.9b00401
4. Y. X . Song, D. M. Du, *Advanced Synthesis and Catalysis*, **363,** 4667(2021), https://doi.org/10.1002/adsc.202100624
5. A. Pellis, P. A. Hanson, J. W. Comerford, J. H. Clark, Farmer, T.J, *Polymer Chemistry*, **10(7)**, 843(2019), https://doi.org/10.1039/c8py01655k
6. R. W. Bates, W. Ko, V. Barát, *Royal Society of Chemistry*, **18**, 810(2020), https://doi.org/10.1039/c9ob02388g
7. P.A. Kharbanda, A. Sharma, *Asian Journal of Organic Chemistry*, **7**, **634**(2018), https://doi.org/10.1002/ajoc.201700609
8. N. Hayama, Y. Kobayashi, E. Sekimoto, A. Miyazaki, K. Inamoto, T. Kimachi, Takemoto, *Chemical Science,* **11(21)**, 5572(2020), https://doi.org/10.1039/d0sc01729a

9. O. I. Yarovaya, A. S. Sokolova, I. Y. Mainagashev, A. S.Volobueva, K. Lantseva, S. S. Borisevich, A. A. Shtro, V. V Zarubaev. N. F. Salakhutdinov, *Bioorganic and Medicinal Chemistry Letters*, **29(23)**, 126745**(**2019), https://doi.org/10.1016/j.bmcl.2019.126745
10. O. A. Nurkenov, M. K. Ibraev, I. A. Schepetkin, A. I. Khlebnikov, T. M. Seilkhanov, A. E Arinova and M. B. Isabaeva, *Russian Journal of General Chemistry*, **89(7)**, 1360(2019), https://doi.org/10.1134/S1070363219070028
11. M. Brancaccio, C. Mennitti, A. Cesaro, F. Fimiani, E. Moscarella, M. Caiazza, F. Gragnano, A. Ranieri, G . D'Alicandro, N. Tinto, C. Mazzaccara, B. Lombardo, R. Pero, G. Limongelli, G. Frisso, P. Calabrò, O. Scudiero, *International Journal of Environmental Research and Public Health*, **17(24),** 9424(2020), https://doi.org/10.3390/ijerph17249424
12. D. Bhattacherjee, A. Sufian, S. K. Mahato, S. Begum, K. Banerjee, S. De, H. K.Srivastava, K. P, Bhabak, *Chemical Communications*, **55(90)**, 13534(2019), https://doi.org/10.1039/c9cc05562b
13. N. Ahmed, N. K. Konduru, M. Owais, *Arabian Journal of Chemistry*, **12(8),** 1879(2019), https://doi.org/10.1016/j.arabjc.2014.12.008
14. M. Zhang, A. M. Prior, M. M. Maddox, W. J. Shen, K. E. Hevener, D. F. Bruhn, R. B. Lee,.; A. P. Singh, J. Reinicke, C. J. Simmons, J. G. Hurdle, R. E. Lee, D. Sun, *ACS Omega*, **3(12)**, 18343(2018), https://doi.org/10.1021/acsomega.8b03174
15. N. K. Konduru, S. Dey, M. Sajid, M. Owais, N. Ahmed, *European Journal of Medicinal Chemistry*, **59,** 23(2013), https://doi.org/10.1016/j.ejmech.2012.09.004
16. K. Xu, H. Yao, D. Fan, L. Zhou, S. Wei, *Carbohydrate Polymers*, **254,** 117286(2021), https://doi.org/10.1016/j.carbpol.2020.117286
17. S. Qamar, K. Hussain, N. I. Bukhari, S. Z. Siddique, Aziz-Ur-rehman, M. A. Abbasi, S. Parveen, A. Latif, A. Qamar, E. Ali, N. Shehzadi, M. Islam, S. Naheed, *Tropical Journal of Pharmaceutical Research*, **18(5),** 1095(2019), https://doi.org/10.4314/tjpr.v18i5.26
18. F. Li, C. H. Tian, Y. F. Du, B. X. Zhao, *Molecular and Biomolecular Spectroscopy*, **261,** 120058(2021), https://doi.org/10.1016/j.saa.2021.120058
19. S. T. Atkore, G. M. Bondle, V. T. Kamble, R. Varala, S. F. Adil, M. R. Hatshan, B. Shaik, *Journal of Saudi Chemical Society*, **25(12),** 101359(2021), https://doi.org/10.1016/j.jscs.2021.101359
20. X. Huang, J. Li, X. Li, J. Wang, Y. Peng, G. Song, *RSC Advances*, **9(45),** 26419(2019)
21. M. Feng, B. Tang, S. H. Liang, X. Jiang, *Current Topics in Medicinal Chemistry*, **16(11),** 1200(2016), https://doi.org/10.2174/1568026615666150915111741
22. J. A. Stefely, R. Palchaudhuri, P. A. Miller, R. J. Peterson, G. C. Moraski, P. J. Hergenrother, M. J. Miller, *Journal of Medicinal Chemistry*, **53(8),** 3389(2010), https://doi.org/10.1021/jm1000979
23. G. de Lourdes, M. Ferreira, L. C. S. Pinheiro, O. A. Santos-Filho, M. D. S. Peçanha, C. Q. Sacramento, V. Machado, V. F. Ferreira, T. M. L. Souza, N.Boechat, *Medicinal Chemistry Research*, **23(3),** 1501(2014), https://doi.org/10.1007/s00044-013-0762-6
24. P. López-Rojas, M. Janeczko, K. Kubiński, Á. Amesty, M. Masłyk, A. Estévez-Braun, *Molecules*, **23(1)**, 199(2018), https://doi.org/10.3390/molecules23010199
25. V. Kouznetsov, C. M. Meléndez Gómez, M. G. Derita, Svetaz, L. del Olmo, E. Zacchino, *Bioorganic and Medicinal Chemistry*, **20(21)**, 6506(2012), https://doi.org/10.1016/j.bmc.2012.08.036
26. K. K. Angajala, S. Vianala, R. Macha, M. Raghavender, M. K. Thupurani, P. J. Pathi, *Springerplus*, **5(1),** 423(2016), https://doi.org/10.1186/s40064-016-2052-5

[RJC-9315/2025]