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Research Article

STEPWISE SYNTHESIS AND CHARACTERIZATION OF NEWLY SYNTHESIZED 1,2,4-TRIAZOLE DERIVATIVES

Kavitha Siddoju[1*] and Jagadeesh Kumar Ega[2]

Department of Chemistry, CDC (Autonomous),
Kakatiya Univerisity, Warangal, Telangana, India.

ABSTRACT

In this paper we would like to discuss the efficient synthesis of pyrazin fused N-(3-Mercapto-5-Aryl-[1,2,4]triazol-4-yl)-amide (5a-m and 6a-r) from4-Amino-5-Aryl-4H-[1,2,4]triazole-3-thiols(4a-b) through N-acylaton under dry dioxane, R^1COCl, reflux, 10 h by a sequential manner probably the steps are mentioned in Scheme-1 ,Table-1,2. The structures of the compounds were elucidated by spectral (IR,^{1}HNMR, ^{13}CNMR and MS) analysis. The reactions are easy to conduct, under mild conditions, and form amide substituted triazole derivatives with excellent yields.

Keywords: Pyrazins,1,2,4-Triazoles, N-acylaton.

1. INTRODUCTION

Substituted 1,2,4-triazoles and their derivatives are key skeletons of many biologically active molecules[1-3] and they exhibit wide applications in pesticides, medicines, functional materials, and organocatalysts. In the last few decades, the chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. For example, a large number of 1,2,4-triazole-containing ring system have been incorporated into a wide variety of therapeutically interesting drugs[4-5] containing the 1,2,4-triazole group such as Voriconazole , Triazolam , Alprazolam and Fosfluconazole .

The mercapto- and thione-substituted 1,2,4-triazole ring systems have been well studied and so far a variety of biological properties have been reported for a large number of their derivatives, such as antibacterial, antifungal[6], antitubercular anticancer[7], diuretic[8] and hypoglycemic[9] activities.

Prakash and Sharma[10] reported that the reaction of α,α-dibromoacetophenones with 4-amino-5-mercapto-3-methyl-5-triazole in alcohol as a solvent under reflux conditions furnished the 7*H*-7-alkoxy-6-aryl-3-methyl-s-triazolo[3,4-*b*][1,3,4]thiadi-azines.Triazoles are an efficient hetero cyclic compounds exhibiting potent biological activity[11-13] .

2. MATERIAL AND METHODS

Melting points were determined on a Cintex melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a BRUKER Spectrometer (400 MHz). ^{13}C NMR spectra were recorded on100MHz. Chemical shifts were reported in parts per million using tetramethylsilane as an internal standard and were given in δ units. The solvent for NMR spectra was DMSO. Infrared spectra were taken on SHIMADZU-FTIR-8400 Spectrophotometer instrument in the frequency range of 4000-400 cm^{-1} by KBr powder method. The Mass spectra were recorded by MS-SHIMADZU-QP2010. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60F254 (Merck) plates using UV light for detection. Common reagent grade chemicals are either commercially available and were used without further purification.

General procedure for the preparation of carboxylic acid methyl esters (3a-b)

To the solution of carboxylic acid (0.01mole) in methanol (10mL), catalytic amount of sulphuric acid was added and refluxed for 4h. The reaction completion was monitored by TLC using hexane: ethyl acetate (9:1) as mobile phase. The solvent was removed under reduced pressure. The product obtained was purified by column chromatography using hexane: ethyl acetate (9:1) as mobile phase.

3. RESULTS AND DISCUSSION

General procedure for the preparation of carboxylic acid hydrazide (1a-b)

To the solution of ester (0.01mole) in methanol (10mL), hydrazine hydrate (0.05mole) (99%) was added and refluxed for 9h. The reaction was monitored by using TLC using hexane: ethyl acetate (9:1) as mobile phase. The solvent was removed under reduced pressure and the product obtained was treated with 4-5 mL of ice cold water. The solid obtained was filtered under vacuum and dried. The product obtained was purified by column chromatography using hexane: ethyl acetate (9:1) as mobile phase.

General procedure for the preparation of 5-Aryl-[1,3,4]oxadiazole-2-thiol (1a-b)

To the solution of acid hydrazide (0.01mole) in methanol (10mL), (0.02mole) triethylamine and (0.02mole) carbon disulphide were added and refluxed for 10h. The progress of the reaction was monitored by TLC using hexane: ethyl acetate (8:2) as mobile phase. The solvent was removed under reduced pressure and the product obtained was dissolved in 100 mL of cold water and acidified with concentrated HCl to pH 6-7. The precipitate obtained was filtered, washed with cold water and dried. The product was purified by column chromatography using hexane: ethyl acetate (8:2) as mobile phase.

General procedure for the preparation of 4-Amino-5-Aryl-4H-[1,2,4]triazole-3-thiol (4a-b)

To the solution of the oxadiazole (0.01mole) in absolute ethanol, hydrazine hydrate 99% (0.01mole) was added and refluxed for 12h. The progress of the reaction was monitored by TLC using hexane: ethyl acetate (7:3) as mobile phase. At the end, the solvent was removed under reduced pressure. The concentrated product was added to 100 mL of cold water and acidified with concentrated HCl to pH 5. The product obtained was filtered, washed with water and dried. Purification was done by column chromatography using hexane: ethyl acetate (7:3) as mobile phase.

General procedure for the preparation of N-(3-Mercapto-5-Aryl-[1,2,4]triazol-4-yl)-amide (5a-m and 6a-r)

To a solution of amino triazole (0.001mole) in dry dioxane, (0.0012 moles) acid chloride was added drop wise with stirring. After the addition, the reaction mixture was refluxed for 10h and monitored by TLC using chloroform: methanol (9:1) as mobile phase. The solvent was removed under reduced pressure and the product was purified by column chromatography using chloroform: methanol (9:1) as mobile phase.

Spectral data and characterization

4-Amino-5-pyrazin-2-yl-4H-[1,2,4]triazole-3-thiol (4a)

FTIR (KBr, cm^{-1}): 3458 (N-H, str.), 3197 (C-H, str.), 2698 (S-H, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.96 (s, 2H), 8.29 (dd, *J*=2.4 Hz and 1.6 Hz, 1H), 8.81 (d, *J*=2.4 Hz, 1H), 9.26 (d, *J*=1.6 Hz, 1H), 14.19 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 141.48, 144.96, 145.05, 146.34, 146.91, 166.81. GCMS (EI, *m/z*) 194 $(M)^+$.

4-Amino-5-(5-methyl-pyrazin-2-yl)-4H-[1,2,4]triazole-3-thiol(4b)

FTIR(KBr,cm^{-1}): 3458 (N-H, str.), 3115 (C-H, str.), 2372 (S-H, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.48 (s, 3H), 5.96 (s, 2H), 8.70 (d, *J*=1.2 Hz, 1H), 9.12 (d, *J*=1.6 Hz, 1H), 14.13 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.78, 138.56, 143.84, 144.49, 147.03, 155.68, 166.57. GCMS (EI, *m/z*) 208 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-acetamide (5a)

FTIR (KBr, cm^{-1}): 3345 (N-H, str.), 3041 (Ar-H, str.), 1691 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.99 (s,3H), 8.77 (d, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.80 (d, *J*= 2.4 Hz, 1H), 9.10 (d, *J*= 1.6 Hz, 1H),
11.46 (s, 1H), 14.39 (s, 1H); GCMS (EI, *m/z*) 236 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-propionamide (5b)

FTIR (KBr, cm^{-1}): 3407 (N-H, str.), 3047(Ar-H, str.), 2771 (S-H, str.), 1741 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.00 (t, *J*= 7.2 Hz, 3H), 2.67- 2.72 (m, 2H), 8.80 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.68 (d, *J*= 2.4 Hz, 1H), 9.26 (d, *J*= 1.6 Hz, 1H), 11.46 (s, 1H), 14.81 (s, 1H); GCMS (EI, *m/z*) 250 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-butyramide (5c)

FTIR (KBr, cm^{-1}): 3319 (N-H, str.), 3095 (Ar-H, str.), 2368 (S-H, str.), 1741 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.82 (t, *J*= 7.2 Hz, 3H), 1.47- 1.56 (m, 2H), 2.71 (dd, 2H), 8.80 (d, *J*= 2.4 Hz,1H), 8.67 (d, *J*= 1.6 Hz, 1H), 9.26 (s, 1H), 11.44 (s, 1H), 14.79 (s, 1H); GCMS (EI, *m/z*) 264$(M)^+$.

Pentanoic acid (3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-amide (5d)

FTIR (KBr,cm^{-1}): 3341 (N-H, str.), 3167 (C-H, str.), 1712 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.857(t, *J*= 7.2Hz, 3H), 1.19- 1.28

(m, 2H), 1.45- 1.52 (m, 2H), 2.77 (t, *J*= 7.2 Hz, 2H), 8.74 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.79 (d, *J*= 2.4 Hz, 1H), 9.09 (d, *J*= 1.6 Hz, 1H), 11.44 (s, 1H), 14.37 (s, 1H); LCMS (ESI, *m/z*) 279.03 $(M+H)^+$.

Hexanoic acid (3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-amide (5e)

FTIR (KBr,cm^{-1}): 3300 (N-H, str.), 3163 (C-H, str.), 2956 (Ar-H, str.), 2605 (S-H, str.), 1714 (C=O, str.);^{1}H NMR (400 MHz, DMSO-d_6): δ 0.84 (t, *J*= 7.2Hz, 3H), 1.18- 1.27 (m, 4H), 1.46- 1.54 (m, 2H), 2.26 (t, *J*= 7.2 Hz, 2H), 8.74 (d, 1.6 Hz, 1H), 8.80 (d, *J*= 2.4 Hz, 1H), 9.09 (s, 1H), 11.44 (s, 1H), 14.38 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.29, 22.23, 24.74, 31.00, 33.41, 140.97, 143.99, 144.80, 146.69, 147.69, 169.37, 171.63. LCMS (ESI, *m/z*) 294.88 $(M+H)^+$.

Heptanoic acid (3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-amide (5f)

FTIR (KBr,cm^{-1}): 3348 (N-H, str.), 3153 (C-H, str.), 2956 (Ar-H, str.), 2370 (S-H, str.), 1680 (C=O, str.);^{1}H NMR (400 MHz, DMSO-d_6): δ 0.85 (t, *J*= 6.8 Hz, 3H), 1.51(t, *J*= 6.8 Hz, 2H), 1.21-1.24 (m, 6H), 2.26 (t, *J*= 7.2 Hz, 2H), 8.74 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.80 (d, *J*= 1.6 Hz, 1H), 9.09 (d, *J*= 1.6 Hz, 1H), 11.46 (s, 1H), 14.37 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.37, 22.42, 25.03, 29.50, 31.37, 33.47, 140.97, 143.99, 144.79, 146.69, 147.31, 169.38, 171.63. GCMS (EI, *m/z*) 306 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-2-methyl-benzamide (5g)

FTIR (KBr,cm^{-1}): 3390 (N-H, str.), 3032 (Ar-H, str.), 1707 (C=O, str.); ^{13}CNMR (100 MHz, DMSO-d_6): δ 19.56, 126.17, 128.21, 131.19, 133.45, 136.94, 141.00, 144.00, 144.81, 146.81, 147.13, 167.79, 169.62. GCMS (EI, *m/z*) 312 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-3-methoxy-benzamide(5h)

FTIR(KBr, cm^{-1}): 3385 (N-H, str.), 3099 (Ar-H, str.), 3034 (C-H, str.), 1685 (C=O, str.); ^{1}H NMR(400 MHz, DMSO-d_6): δ 3.81 (s, 3H), 7.19-7.22 (m, 1H), 7.42- 7.44 (m, 1H), 7.46- 7.50 (m,2H), 8.66- 8.67 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.76 (d, *J*= 2.4 Hz, 1H), 9.17 (d, *J*= 1.6 Hz,1H), 12.03 (s, 1H), 14.49 (s, 1H); GCMS (EI, *m/z*) 328 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-4-methoxy-benzamide (5i)

FTIR (KBr,cm^{-1}): 3338 (N-H, str.), 2960 (Ar-H, str.), 2681 (S-H, str.), 1693 (C=O, str.), 1290 (Assym.C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.81 (s, 3H), 7.04 (d, *J*= 8.8 Hz, 2H); 7.72 (d, *J*=8.8 Hz, 2H), 8.87- 8.88 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 9.00 (d, *J*= 2.4 Hz, 1H), 9.20 (d, *J*= 1.6 Hz, 1H), 12.29 (s, 1H), 14.09 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.87, 113.29, 119.05, 120.46, 130.46, 133.00, 140.92, 143.89, 144.90, 146.77, 147.25, 159.78, 165.52, 169.69. GCMS (EI, *m/z*) 328 $(M)^+$.

4-Fluoro-N-(3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-benzamide (5j)

FTIR (KBr, cm^{-1}): 3340 (N-H, str.), 3039 (Ar-H, str.), 2964 (C-H, str.), 2360 (S-H, str.), 1697 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.30-7.42 (m, 2H), 7.96- 8.00 (m, 2H), 8.64- 8.65 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.76 (d, *J*= 2.4 Hz, 1H), 9.177 (d, *J*= 1.6 Hz, 1H), 12.11 (s, 1H), 14.51 (s, 1H); GCMS (EI, *m/z*) 316 $(M)^+$.

4-Ethyl-N-(3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-benzamide(5k)

FTIR(KBr,cm^{-1}): 3068 (Ar-H, str.), 2960 (C-H, str.), 2682 (S-H, str.), 1691 (C=O, str.); ^{1}H NMR (400MHz, DMSO-d_6): δ 1.22 (t, *J*= 7.6 Hz, 3H), 2.65- 2.71 (dd, *J*= 15.2 Hz and 7.6 Hz, 2H), 7.39 (d, *J*= 8 Hz, 2H), 7.84 (d, *J*= 8 Hz, 2H), 8.65- 8.66 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.76 (d, *J*= 2.4 Hz, 1H), 9.16 (d, *J*= 1.6 Hz, 1H), 11.96 (s, 1H), 14.47 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 15.74, 28.62, 128.57, 129.15, 140.96, 143.89, 144.90, 145.15, 146.10, 146.73, 147.38, 149.50, 164.65, 165.64, 169.70. GCMS (EI, *m/z*) 326 $(M)^+$.

4-Ethoxy-N-(3-mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-benzamide (5l)

FTIR (KBr,cm^{-1}): 3347 (N-H, str.), 2989 (Ar-H, str.), 2466 (S-H, str.), 1691 (C=O, str.), 1269 (Assym.C-O-C, str.), 873; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.36 (t, *J*= 7.2 Hz and 14 Hz, 3H), 4.08-4.14 (dd, *J*= 7.2 Hz and 14 Hz, 2H), 7.06 (d, *J*= 8.8 Hz, 2H), 7.85- 7.88 (m, 2H), 8.64- 8.65 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.75 (d, *J*= 2.4 Hz, 1H), 9.14 (d, *J*= 1.6 Hz, 1H), 11.86 (s, 1H), 14.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.95, 63.82, 15.33, 117.09, 129.43, 143.09, 144.46, 144.53, 149.50, 150.93, 161.01, 162.56, 168.32. GCMS (EI, *m/z*) 342 $(M)^+$.

N-(3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazol-4-yl)-3,4-dimethoxy-benzamide (5m)

FTIR(KBr, cm^{-1}): 3080 (Ar-H, str.), 3034 (C-H, str.), 2364 (S-H, str.), 1680 (C=O, str.), 1253(Assym. C-O-C, str.), 1134 (Sym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.78-3.83 (m, 6H), 7.11 (d, *J*= 8.4 Hz, 1H), 7.45 (d, *J*= 2 Hz, 1H), 7.59 (dd, *J*= 8.4 Hz and 2 Hz, 1H), 8.65- 8.66 (dd, *J*= 2.4 Hz and 1.6 Hz, 1H), 8.76 (d, *J*= 2.4 Hz, 1H), 9.15 (d, *J*= 1.6 Hz, 1H), 11.88 (s, 1H), 14.46 (s, 1H); LCMS (ESI, *m/z*) 359.07 $(M+H)^+$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-acetamide (6a)
FTIR (KBr,cm^{-1}): 3223 (N-H, str.), 2956 (Ar-H, str.), 2368 (S-H, str.), 1722 (C=O, str.); ^{1}H NMR (400MHz, DMSO-d_6): δ 1.98 (s, 3H), 2.07 (s, 3H), 8.60 (d, *J*= 0.8 Hz, 1H), 8.94 (d, *J*= 1.2 Hz, 1H), 9.11 (d, *J*= 1.2 Hz, 1H), 11.42 (s, 1H), 14.73 (s, 1H); LCMS (ESI, *m/z*) 251.06 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-propionamide(6b)
FTIR(KBr, cm^{-1}): 2956 (Ar-H, str.), 2368 (S-H, str.), 1672 (C=O, str.), 1577 (C-C, str.); ^{1}H NMR(400 MHz, DMSO-d_6): δ 1.04 (t, *J*= 7.6 Hz, 2H), 2.24- 2.28 (q, *J*=7.6 Hz, 3H), 2.56 (s, 3H), 8.64 (d, *J*= 0.8 Hz, 1H), 8.95 (d, *J*= 1.2 Hz, 1H), 11.37 (s, 1H), 14.30 (s, 1H); LCMS (ESI, *m/z*) 265.08(M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-butyramide(6c)
FTIR(KBr, cm^{-1}): 2956 (Ar-H, str.), 2368 (S-H, str.), 1635 (C=O, str.), 1558 (C-C, str.); ^{1}H NMR(400 MHz, DMSO-d_6): δ 0.87 (t, *J*= 7.4Hz, 3H), 1.49- 1.56 (m, 2H), 2.24 (t, *J*= 7.2 Hz, 2H),2.56 (s, 3H), 8.63 (d, *J*= 1.2 Hz, 1H), 8.94 (d, *J*= 1.6 Hz, 1H), 11.40 (s, 1H), 14.30 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.90, 18.59, 21.76, 35.41, 138.11, 142.82, 144.37,147.51, 156.13, 169.23, 171.48. LCMS (ESI, *m/z*) 280.09 (M+H)$^{+}$.

Pentanoic acid [3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-amide (6d)
FTIR (KBr, cm^{-1}): 3340 (N-H, str.), 2972 (Ar-H, str.), 2823 (C-H, str.), 2368 (S-H, str.), 1710 (C=O, str.), 1521 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.85 (t, *J*= 7.4 Hz, 3H), 1.22-1.26 (m, 2H), 1.45- 1.52 (m, 2H), 2.26 (t, *J*= 7.2 Hz, 2H), 2.57 (s, 3H), 8.63 (d, *J*= 0.8 Hz, 1H), 8.93 (d, *J*= 1.2 Hz, 1H), 11.41 (s, 1H), 14.30 (s, 1H); LCMS (ESI, *m/z*) 294.82 (M+H)$^{+}$.

Hexanoic acid [3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-amide (6e)
FTIR (KBr, cm^{-1}): 3340 (S-H, str.), 3018 (Ar-H, str.), 2951 (Ar-H, str.), 2825 (C-H, str.), 2357 (S-H, str.), 1701 (C=O, str.), 1521 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.84 (t, *J*= 7 Hz, 3H), 1.25- 1.27 (m, 2H), 1.46- 1.53 (m, 4H), 2.25 (t, *J*= 7.4 Hz, 2H), 2.57 (s, 3H), 8.63 (d, *J*= 0.8 Hz, 1H), 8.93 (d, *J*= 1.6 Hz, 1H), 11.41 (s, 1H), 14.30 (s, 1H); LCMS (ESI, *m/z*) 307.13 (M+H)$^{+}$.

Heptanoic acid [3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-amide (6f)
FTIR (KBr, cm^{-1}): 3330 (N-H, str.), 3018 (Ar-H, str.), 2937 (C-H, str.),2357 (S-H, str.),1708 (C=O, str.), 1494 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.85 (t, *J*= 6.4 Hz, 3H),1.20-1.23 (m, 6H), 1.50 (t, *J*= 6.8 Hz, 2H), 2.25 (t, *J*= 7.4 Hz, 2H), 2.56 (s, 3H), 8.63 (d, *J*=0.8 Hz, 1H), 8.93 (d, *J*= 1.2 Hz, 1H), 11.41 (s, 1H), 14.29 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.35, 21.75, 22.44, 25.03, 28.48, 31.38, 33.47, 138.10, 142.87, 144.37, 147.61, 156.11, 169.23, 171.58. LCMS (*m/z*) 321.14 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-benzamide(6g)
FTIR(KBr, cm^{-1}): 3323 (N-H, str.), 3018 (Ar-H, str.), 2357 (S-H, str.), 1701 (C=O, str.), 1521 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.52 (s, 3H), 7.57 (t, *J*= 7.6 Hz, 2H), 7.64 (t, *J*= 7.2 Hz, 1H), 7.89- 7.91 (dd, *J*= 7.2 Hz and 5.2 Hz, 2H), 8.55 (d, *J*= 0.8 Hz, 1H), 9.02 (d, *J*=1.2 Hz, 1H), 12.04 (s, 1H), 14.42 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.73, 128.26, 129.21, 131.74, 133.15, 138.09, 142.75, 144.49, 147.53, 156.25, 165.72, 169.51. LCMS (+ESI, *m/z*) 313.08 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-2-methyl-benzamide (6h)
FTIR (KBr, cm^{-1}): 3340 (N-H, str.), 2972 (Ar-H, str.), 2357 (S-H, str.), 1701 (C=O, str.),1492 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.38 (s, 3H), 2.51 (s, 3H), 7.33- 7.34 (dd, *J*= 8.4 Hz and 2.4 Hz, 2H), 7.51- 7.53 (m, 1H), 7.82 (d, *J*= 8.4 Hz, 2H), 8.54 (d, *J*= 0.8 Hz, 1H), 9.00 (d, *J*= 1.6 Hz, 1H), 11.42 (s, 1H), 14.39 (s, 1H); LCMS (+ESI, *m/z*) 327.09 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-4-methyl-benzamide(6i)
FTIR (KBr, cm^{-1}): 3398 (N-H, str.), 2980 (Ar-H, str.), 2357 (S-H, str.), 1664 (C=O, str.),1494 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.38 (s, 3H), 2.51 (s, 3H), 7.36 (d, *J*= 8 Hz, 2H), 7.82 (d, *J*= 8.4 Hz, 2H), 8.54 (d, *J*= 0.8 Hz, 1H), 9.00 (d, *J*= 1.6 Hz, 1H), 11.42 (s, 1H), 14.39 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.58, 21.72, 128.30, 128.90, 129.71, 138.09, 142.74, 143.38, 144.48, 147.61, 156.23, 165.58, 169.54. LCMS (+ESI, *m/z*) 327.09 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-3-methoxy-benzamide (6j)
FTIR (KBr, cm^{-1}): 3234, 3018 (Ar-H, str.), 2850 (C-H, str.), 2366 (S-H, str.), 1662 (C=O,str.), 1467 (C-C, str.), 1261 (Assym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.52 (s, 3H), 3.81 (s, 3H), 7.19- 7.22 (m, 1H), 7.43- 7.50 (m, 3H), 8.56 (d, *J*= 0.8 Hz, 1H), 9.01 (d, *J*= 1.6 Hz, 1H), 12.01 (s, 1H), 14.50 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.73, 55.72, 113.29, 120.46, 130.44, 133.01, 138.05, 142.74, 144.50, 147.50, 156.28, 159.77, 165.45, 169.50. LCMS (+ESI, *m/z*) 343.09 (M+H)$^{+}$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-4-methoxy-benzamide (6k)

FTIR (KBr, cm^{-1}): 3340 (N-H, str.), 3018 (Ar-H, str.), 2980 (C-H, str.), 2357 (S-H, str.),1662 (C=O, str.), 1467 (C-C, str.), 1261(Sym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ2.55 (s, 3H), 3.83 (s, 3H), 7.06- 7.08 (dd, *J*= 12.4 Hz and 6.8 Hz, 3H), 7.87- 7.90 (dd, *J*=6.8 Hz and 2 Hz, 1H), 8.56 (d, *J*= 0.8 Hz, 1H), 9.01 (d, *J*= 1.6 Hz, 1H), 12.01 (s, 1H), 14.42 (s, 1H); LCMS (+ESI, *m/z*) 343.09 $(M+H)^+$.

2-Chloro-N-[3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-benzamide(6*l*)

FTIR (KBr, cm^{-1}): 3016 (Ar-H, str.), 2355 (S-H, str.), 1705 (C=O, str.); ^{1}H NMR (400 MHz,DMSO-d_6): δ 2.52 (s, 3H), 7.65 (dd, *J*= 6.8 Hz and 2 Hz, 1H), 7.94- 7.90 (m, 3H), 8.54 (d, *J*= 1.2 Hz, 1H), 9.02 (d, *J*= 1.2 Hz, 1H), 12.41 (s, 1H), 14.44 (s, 1H); LCMS (+ESI, *m/z*) 347.03 $(M+H)^+$.

4-Chloro-N-[3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-benzamide (6m)

FTIR (KBr, cm^{-1}): 3022 (Ar-H, str.), 2897 (C-H, str.), 2384 (S-H, str.), 1678 (C=O, str.), 1467 (C-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.60 (s, 3H), 7.33- 7.36 (m, 2H), 7.80-7.83 (m, 2H), 8.74 (d, *J*= 1.2 Hz, 1H), 9.03 (d, *J*= 1.2 Hz, 1H), 12.20 (s, 1H), 14.20 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.74, 129.22, 130.18, 131.62, 138.02, 130.48, 138.27, 142.74, 144.45, 147.33, 156.28, 164.86, 166.93, 169.45. LCMS (+ESI, *m/z*) 347.04 $(M+H)^+$.

4-Fluoro-N-[3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-benzamide (6n)

FTIR (KBr, cm^{-1}): 3022 (Ar-H, str.), 2899 (C-H, str.), 2368 (S-H, str.), 1678 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.63 (s, 3H), 7.36 (t, *J* = 8.8 Hz, 2H), 7.79- 7.83 (m, 2H), 8.74 (s, 1H), 9.03 (s, 1H), 12.20 (s, 1H), 14.20 (s, 1H); LCMS (+ESI, *m/z*) 331.21 $(M+H)^+$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-2-phenoxy-acetamide (6o)

FTIR (KBr, cm^{-1}): 3022 (Ar-H, str.), 2887 (C-H, str.), 2360 (S-H, str.), 1712 (C=O, str.),1284 (Assym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.62 (s, 3H), 5.05 (s, 2H),6.89- 6.94 (m, 3H), 7.20- 7.24 (m, 2H), 8.70 (d, *J* = 1.2 Hz, 1H), 9.08 (d, *J* = 1.6 Hz, 1H),12.07 (s, 1H), 14.05 (s, 1H); LCMS (+ESI, *m/z*) 343.09 $(M+H)^+$.

4-Ethyl-N-[3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-benzamide (6p)

FTIR (KBr, cm^{-1}): 3024 (Ar-H, str.), 2935 (C-H, str.), 2362 (S-H, str.), 1691 (C=O, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.22 (t, *J* = 7.6 Hz, 3H), 2.52 (s, 3H), 2.65- 2.71 (dd, *J* = 15.2 Hz and 7.6 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.84 (d, *J*= 8.4 Hz, 2H), 8.55 (d, *J* = 1.2 Hz,1H), 9.00 (d, *J* = 1.6 Hz, 1H), 11.93 (s, 1H), 14.40 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ15.76, 21.72, 28.62, 127.58, 128.01, 128.40, 128.56, 129.16, 129.90, 138.09, 142.74, 144.50, 147.63, 149.48, 156.23, 165.58, 169.54. LCMS (+ESI, *m/z*) 341.11 $(M+H)^+$.

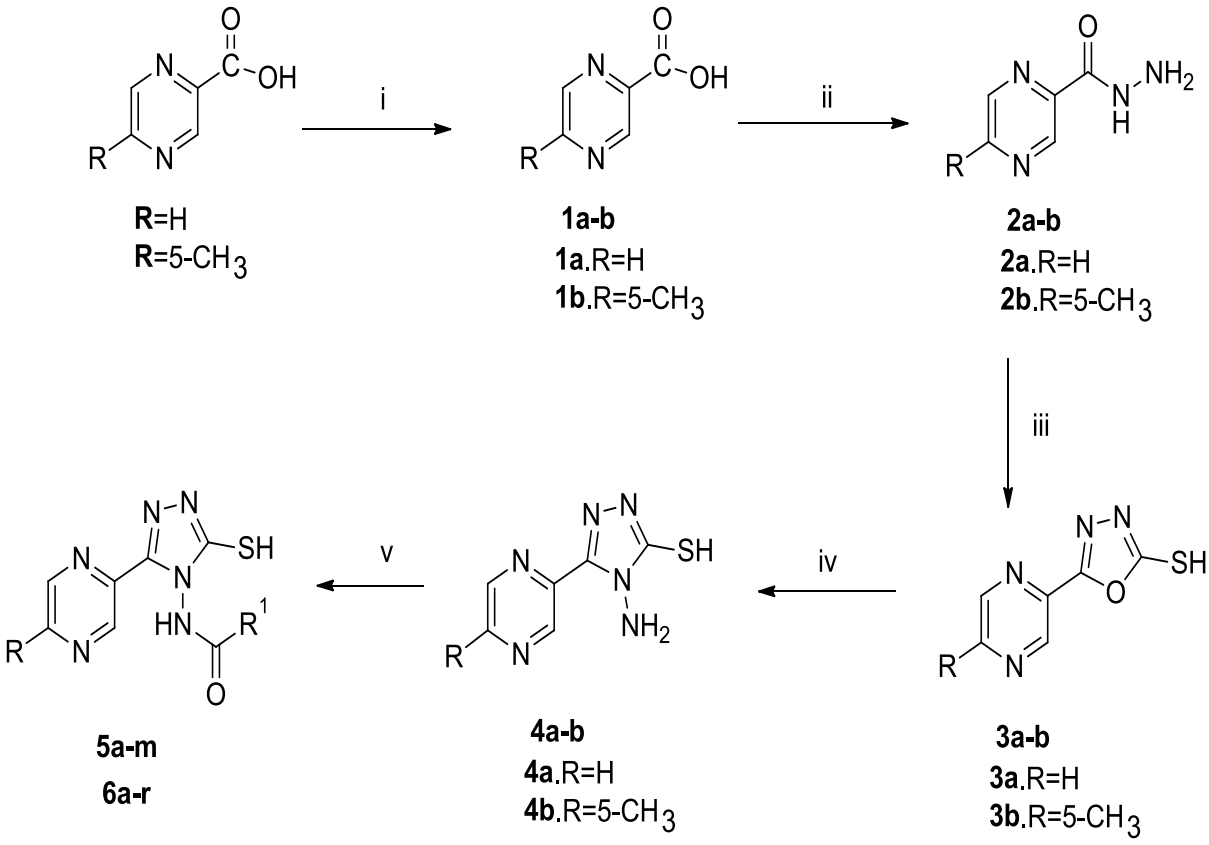
4-Ethoxy-N-[3-mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]benzamide(6q)

FTIR (KBr, cm^{-1}): 3305 (N-H, str.), 2989 (Ar-H, str.), 2937 (C-H, str.), 2366 (S-H, str.), 1683(C=O, str.), 1500 (C-C, str.), 1261 (Assym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.36 (t, *J* = 6.8 Hz, 3H), 2.51 (s, 3H), 4.07- 4.14 (m, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 7.85- 7.88 (m, 2H), 2H), 8.54 (d, *J* = 1.2 Hz, 1H), 8.99 (d, *J* = 1.6 Hz, 1H), 11.84 (s, 1H), 14.38 (s, 1H); LCMS (+ESI, *m/z*) 357.10 $(M+H)^+$.

N-[3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazol-4-yl]-3,4-dimethoxy-benzamide (6r)

FTIR (KBr, cm^{-1}): 3419 (N-H, str.), 3022 (Ar-H, str.), 2887 (C-H, str.), 2353 (S-H, str.),1695 (C=O, str.), 1469 (C-C, str.), 1192 (Sym. C-O-C, str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.52 (s, 3H), 3.82 (s, 3H), 3.83 (s, 3H), 7.46- 7.05 (m, 2H), 7.50-7.59 (m, 2H), 2H), 8.55 (d, *J* = 1.2 Hz, 1H), 9.00 (d, *J* = 1.6 Hz, 1H), 11.86 (s, 1H), 14.39 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.72, 56.10, 56.21, 121.36, 121.95, 123.66, 124.24, 142.75, 144.54, 147.75, 148.94, 152.15, 152.89, 156.22, 165.90, 169.57. LCMS (+ESI, *m/z*) 373.10 $(M+H)^+$.

REACTION SCHEME 1



5a. R= H, R^1= CH_3, **5b.** R= H, R^1= C_2H_5, **5c.** R= H, R^1= C_3H_7, **5d.** R= H, R^1= C_4H_9, **5e.** R= H, R^1= C_5H_{11} **5f.** R= H, R^1= C_6H_{13}, **5g.** R= H, R^1= 2-CH_3Ph, **5h.** R= H, R^1= 3-OCH_3Ph, **5i.** R= H, R ^{1}= 4-OCH_3Ph, **5j.** R= H, R^1= 4-F Ph, **5k.** R= H, R^1= 4-C_2H_5 Ph, **5l.** R= H, R^1= 4-OC_2H_5 Ph, **5m.** R= H, R^1= 3,4-OCH_3 Ph
6a. R= CH_3, R^1= CH_3, **6b.** R=CH_3, R^1= C_2H_5, **6c.** R=CH_3, R^1= C_3H_7, **6d.** R=CH_3, R^1= C_4H_9, **6e.** R=CH_3, R^1= C_5H_{11}, **6f.** R= CH_3, R^1= C_6H_{13}, **6g.** R= CH_3, R ^{1}= Ph, **6h.** R= CH_3, R ^{1}= 2-CH_3Ph, **6i.** R= CH_3, R^1= 4-CH_3Ph, **6j.** R= CH_3, R^1= 3-OCH_3Ph, **6k.** R= CH_3, R^1= 4-OCH_3Ph, **6l.** R= CH_3, R^1= 2-Cl Ph, **6m.** R= CH_3, R^1= 4-Cl Ph, **6n.** R= CH_3, R^1= 4-F Ph, **6o.**R= CH_3, R^1= -CH_2O Ph, **6p.** R= CH_3, R^1= 4-C_2H_5 Ph, **6q.** R= CH_3, R^1= 4-OC_2H_5 Ph, **6r.** R= CH_3, R^1= 3,4-OCH_3 Ph

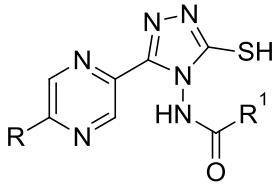
REAGENTS AND CONDITIONS
(i)MeOH, Conc.H_2SO_4 (Cat.,) reflux, 4h. (ii) $N_2H_4.2H_2O$, MeOH, reflux, 9h. (iii)CS_2, Et_3N ,MeOH, reflux.10 h. (iv) $N_2H_4.2H_2O$, EtOH, reflux, 12 h. (v) Dry Dioxane, R^1COCl, reflux, 10 h.

4. CONCLUSION

A step wise series of desired compounds 3-Mercapto-5-pyrazin-2-yl-[1,2,4]triazolyls, 3-Mercapto-5-(5-methyl-pyrazin-2-yl)-[1,2,4]triazolyl derivatives (**5a-m**) and (**6a-r**) successfully synthesized with high yields. The newly synthesized compounds were also screened for antimicrobial activity in future scope.

ACKNOWLEDGEMENT
Authors thank to Director, IICT-Hyderabad, India, for providing the spectral data.

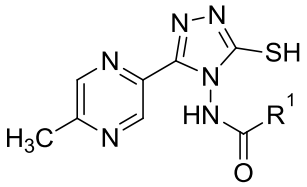
Table 1: Physical properties of synthesized compounds (5a-m)



5a-m

S.No.	Code	R	Mol. Wt.	M.P. (°C)	Yield (%)
1	5a	-CH_3	236	151-153	82
2	5b	-C_2H_5	251	161-162	85
3	5c	-C_3H_7	265	167-169	84
4	5d	-C_4H_9	279	172-174	87
5	5e	-C5H11	293	171-172	83
6	5f	-C_6H_{13}	306	172-175	86
7	5g	2-$CH_3C_6H_4$	312	183-184	85
8	5h	3-OCH_3 C_6H_4	328	250-252	90
9	5i	4-OCH_3 C_6H_4	328	256-258	68
10	5j	4-F C_6H_4	316	266-267	77
11	5k	4-C_2H_5 C_6H_4	326	245-246	85
12	5l	4-OC_2H_5 C_6H_4	342	258-260	82
13	5m	3,4-$(OCH_3)_2C_6H_3$	358	276-280	81

Table 2: Physical properties of synthesized compounds (6a-r)



6a-r

S.No.	Code	R1	Mol. Wt.	M.P. (°C)	Yield(%)
14	6a	-CH_3	250	165	87
15	6b	-C_2H_5	264	182	85
16	6c	-C_3H_7	278	198-200	81
17	6d	-C_4H_9	293	181	87
18	6e	-C_5H_{11}	306	168-170	85
19	6f	-C_6H_{13}	320	154-156	86
20	6g	-C_6H_5	312	220-225	84
21	6h	2-$CH_3C_6H_4$	326	255-256	90
22	6i	4-CH_3 C_6H_4	326	230-232	68
23	6j	3-OCH_3 C_6H_4	342	212-215	77
24	6k	4-OCH_3 C_6H_4	342	228-230	85
25	6l	2-Cl C_6H_4	346.5	250-252	82
26	6m	4-Cl C_6H_4	346.5	232-234	81
27	6n	4-F C_6H_4	330	230-232	88
28	6o	-$CH_2OC_6H_5$	342	194-196	85
29	6p	4-C_2H_5 C_6H_4	340	222-224	68
30	6q	4-OC_2H_5 C_6H_4	356	226-228	77
31	6r	3,4-$(OCH_3)_2C_6H_3$	372	230-232	85

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