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SYNTHESIS AND CHARACTERIZATION OF NEW THIAZOLYL 1,3,4-OXADIAZOLE AND 1,2,4-TRIAZOLE DERIVATIVES

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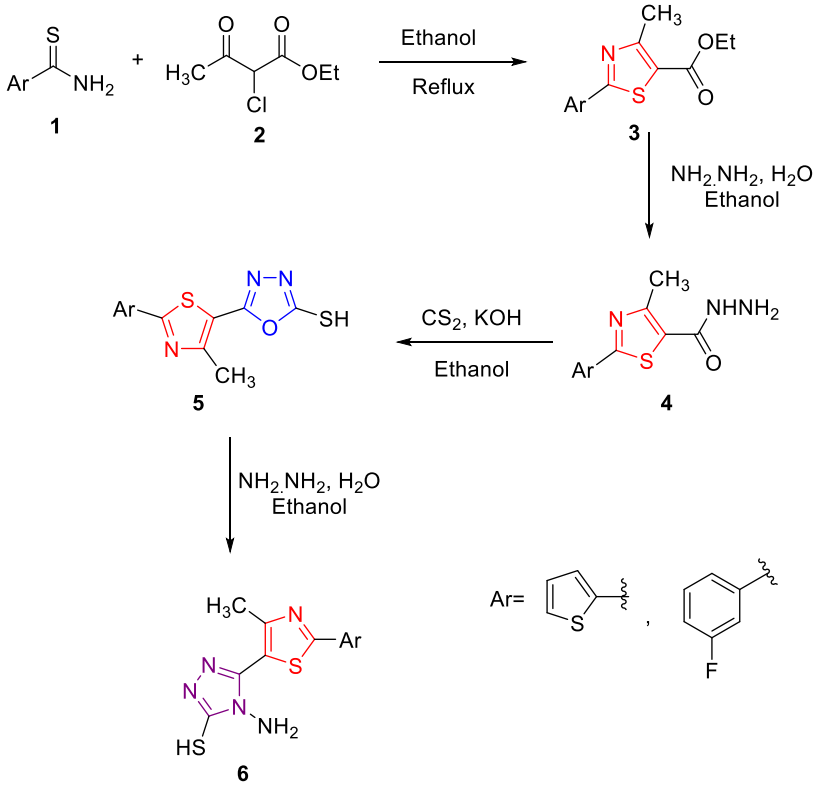
ABSTRACT
In the present study, we have synthesized new 5-(2-aryl-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiols **5** and 4-amino-5-(2-aryl-4-methylthiazol-5-yl)-4*H*-1,2,4-triazole-3-thiols **6**. All the newly synthesized compounds were characterized with the help of IR, ^{1}H NMR and Mass spectroscopic techniques.

KEYWORDS: 1,3,4-oxadiazole, 1,2,4-triazole, thiazole, thiophene

INTRODUCTION
Heterocyclic compounds have attracted a lot of interest because of their many important applications in biology and medicine. Heterocycles are also useful in a variety of disciplines, such as biology and pharmaceutical chemistry. The primary uses of heterocyclic compounds are in pharmaceuticals, agrochemicals, and veterinary products. 1,3,4-Oxadiazole-containing compounds possess various biological activities such as antibacterial[i], anticancer[ii], antimicrobial[iii], antitubercular[iv], insecticidal[v], anti-oxidant and anti-inflammatory[vi], analgesic[vii], fungicidal[viii], antidepressant[ix], *etc*. 1,2,4-Triazole containing compounds known to have various pharmacological applications such as, anti-bacterial[x], antileishmanial[xi], fungicidal[xii], anticancer[xiii], herbicidal[xiv], *etc*. Activities associated with heterocycles prompted us to synthesize thiazolyl 1,3,4-oxadiazole and 1,2,4-triazole derivatives.

RESULT AND DISCUSSION
We have synthesized 5-(2-aryl-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiols **5** from 2-aryl-4-methylthiazole-5-carbohydrazide **4** on reaction with carbon disulfide in KOH. The IR

spectrum of compound **5a** showed characteristic stretching frequency at 1608 cm^{-1} (C=N) and 1573 and 1489 cm^{-1} (C=C). ^{1}H NMR spectrum of compound **5a** showed characteristic peak of S-H proton at 14.50 δ ppm and methyl group attached to thiazole ring showed singlet at 2.69 δ ppm. For compound **5a**, mass spectrum showed $[M+H]^+$ at 294 Also, when 5-(2-aryl-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiols **5** on reaction with hydrazine hydrate gave 4-amino-5-(2-aryl-4-methylthiazol-5-yl)-4*H*-1,2,4-triazole-3-thiols **6**. The IR spectrum of compound **6a** showed characteristic stretching frequency at 3410 cm^{-1} for N-H protons. In the ^{1}H NMR spectrum of compound **6a**, two N-H protons showed singlet at 5.87 δ ppm and one S-H proton at 14.08 δ ppm. Also methyl group attached to thiazole ring showed singlet at 2.70 δ ppm. Mass spectrum of compound **6a** showed $[M+H]^+$ at 307.98.



Scheme-1: Synthesis of thiazolyl 1,3,4-oxadiazole and 1,2,4-triazole derivatives

EXPERIMENTAL

Physical constants of all synthesized compounds were determined in open capillary tubes in liquid paraffin bath and are uncorrected. The IR spectra were recorded on Shimadzu IR Affinity-1S FTIR spectrophotometer. The NMR spectra were recorded on Varian NMR 400 MHz spectrometer (Varian Inc., Switzerland) and chemical shifts are given in δ ppm relative to TMS using deuterated DMSO and deuterated chloroform as solvents. Mass spectra were recorded on Water's Acquity Ultra Performance TQ Detector Mass Spectrometer.

General Procedure for the synthesis of 5-(2-aryl-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiols 5

A solution of KOH (0.015 mole) in ethanol (5 mL) and CS_2 (20 mL) was mixed with acid hydrazide **4** (0.01 mole) and ethanol (50 mL). For nine hours, the reaction mixture was heated under reflux to 80 °C. The completion of the reaction was checked by TLC. Following the completion of the reaction, the excess ethanol was extracted using a vacuum, and the residual solution was acidified to a pH of 5 using diluted HCl (10%). The organic product was obtained through the filtration of a solid. Organic product was recrystallized using ethanol to obtain pure compound **5**.

5-(2-(3-Fluorophenyl)-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiol 5a:
m.p.: 244-246 °C; Yield: 66 %; IR: 1608 (C=N), 1573 (C=C), 1489 (C=C), 1276 (C-F) cm^{-1}; 1H NMR (400 MHz, DMSO-d_6) δ, ppm: 2.69 (s, 3H, thiazole-CH_3), 7.39-7.44 (m, 1H), 7.56-7.62 (m, 1H), 7.80-7.86 (m, 2H), 14.50 (s, 1H, S-H); MS: m/z: 294 $[M+H]^+$.
5-(4-Methyl-2-(thiophen-2-yl)thiazol-5-yl)-1,3,4-oxadiazole-2-thiol 5b:
m.p.: 258-260 °C; Yield: 62 %; IR: 1624 (C=N), 1546 (C=C), 1464 (C=C) cm^{-1}; 1H NMR (400 MHz, DMSO-d_6) δ, ppm: 2.63 (s, 3H, thiazole-CH_3), 7.22 (t, 1H, J = 4.4 Hz), 7.84 (d, 2H, J = 4.4 Hz), 14.50 (s, 1H, S-H); MS: m/z: 281.95 $[M+H]^+$.
General Procedure for the synthesis of 4-amino-5-(2-aryl-4-methylthiazol-5-yl)-4*H*-1,2,4-triazole-3-thiols 6:
After dissolving oxadiazole **5** (0.005 mole) in 50 mL of ethanol and adding hydrazine hydrate 64 % (15 mL), the reaction mixture was heated for eight hours at 80 °C under reflux on a water bath. The completion of the reaction was checked by TLC. After completion of the reaction, the reaction mixture was added to ice-cold water to obtain crude product. The product was recrystallized by using ethanol to obtain pure compound **6**.
4-Amino-5-(2-(3-fluorophenyl)-4-methylthiazol-5-yl)-4H-1,2,4-triazole-3-thiol 6a:
m.p.: 286-288 °C; Yield: 58 %; IR: 3410 (N-H), 1610 (C=N), 1571 (C=C), 1473 (C=C), 1276 (C-F) cm^{-1}; 1H NMR (400 MHz, DMSO-d_6) δ, ppm: 2.70 (s, 3H, thiazole-CH_3), 5.87 (s, 2H, NH_2), 7.38 (t, 1H, J = 8 Hz), 7.54-7.60 (m, 1H), 7.76-7.83 (m, 2H), 14.08 (s, 1H, S-H); MS: m/z: 307.98 $[M+H]^+$.
4-Amino-5-(4-methyl-2-(thiophen-2-yl)thiazol-5-yl)-4H-1,2,4-triazole-3-thiol 6b:
m.p.: 276-278 °C; Yield: 54 %; IR: 3372 (N-H), 1622 (C=N), 1564 (C=C), 1486 (C=C) cm^{-1}; 1H NMR (400 MHz, DMSO-d_6) δ, ppm: 2.64 (s, 3H, thiazole-CH_3), 5.76 (s, 2H, N-H_2), 7.25 (t, 1H, J = 4.4 Hz), 7.80 (d, 2H, J = 4.4 Hz), 14.20 (s, 1H, S-H); MS: m/z: 296 $[M+H]^+$.

CONCLUSION

Herein, we have synthesized new 5-(2-aryl-4-methylthiazol-5-yl)-1,3,4-oxadiazole-2-thiol **5** derivatives and 4-amino-5-(2-aryl-4-methylthiazol-5-yl)-4*H*-1,2,4-triazole-3-thiol **6** derivatives. All the synthesized compounds were characterized with the help of spectral techniques.

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