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SHORT COMMUNICATION

# Synthesis, characterization and biological property of 3-(5-bromothiophen-2-yl)-6-phenyl-1,7a-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole derivatives

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**ABSTRACT**

A library of novel 3-(5-bromothiophen-2-yl)-6-phenyl-1,7a-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole were synthesized in excellent yields via domino one-pot two component reactions of 4-amino-3-(5-bromothiophen-2-yl)-4,5-dihydro-1H-1,2,4-triazole-5-thiol and benzoic acid derivatives respectively. A triazolo-thiadiazole system may be viewed as a cyclic analogue of two very important components - thiosemicarbazide and biguanide which often display diverse biological activities. The significant advantages of this reaction include one-pot process, simple work-up procedure, excellent yields and no column chromatographic purification. All intermediates and final compounds were confirmed by $^{1}H$ NMR, $^{13}C$ NMR, Mass Spectroscopy methods and IR analysis.

***Keywords*:** triazole, thiadiazole, antibacterial

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## 1. INTRODUCTION

1,3,4-thiadiazoles exhibit a wide spectrum of biological activities, possibly due to the presence of toxophoric >N-C-S- moiety. A triazolo-thiadiazole system may be viewed as a cyclic analogue of two very important components - thiosemicarbazide and biguanide which often display diverse biological activities.

The earliest use of thiadiazoles has been in the field of pharmaceuticals as antibacterial with similar properties to those of sulphonamide drugs. They exhibit a broad spectrum of interesting pharmacological properties like antipanosomal, antibacterial, anticoccoidal, fungicidal, herbicidal, insecticidal, hypoglycemic, diuretic, anti-inflammatory, antiviral, antiacetylcholine, antitubercular, tranquillizer and sedative [1-3]. Fused triazolo-thiadiazoles display an array of biological activities as shown below.

4-Amino-1,2,4-triazole is used as an intermediate for the synthesis of antifungal agents such as fluconazole and other organic compounds. Because of its purity and its chemical structure, 4-amino-1,2,4 triazole is used to increase the selectivity of the desired active isomers and thus obtain excellent yields. Triazoles are veterinary products (especially thanks to the anti-fungal properties of these Triazoles) also triazoles are used for Photographic products.

Triazole is a five-membered heterocycles containing three nitrogens in the ring and its derivatives have biological activities such as antiviral, antibacterial.

## 2. EXPERIMENTAL PROCEDURE

### A: General introduction

For all these conversions, progress of reaction was carried out on TLC plate silica gel $GF^{254}$ and the melting points were recorded by open capillary method. Mass spectra were recorded on Shimadzu GCMS-QP-2010 model using Direct Injection Probe technique. $^{1}H$ NMR was determined in $CDCl_3$/DMSO solution on a Bruker AVANCE II 400 MHz.

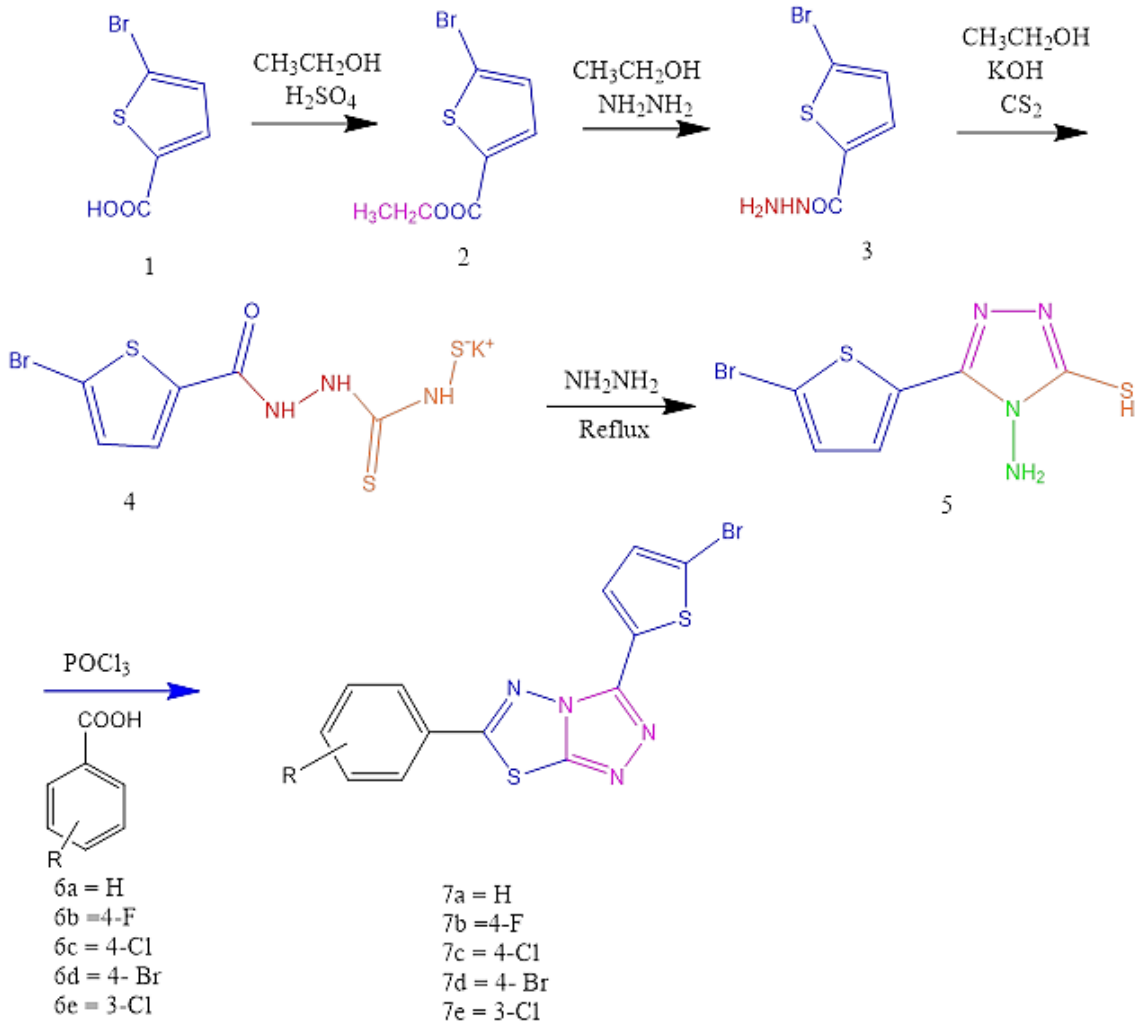
### B: General method of synthesis

Scheme 1. Rout of synthesis for compounds 4a-d.

## 3. ANTIBACTERIAL ACTIVITY

The antibacterial activity of 3-(5-bromothiophen-2-yl)-6-phenyl-1,7a-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (7b,d,e) was appraised against *E. coli*, *P. aeruginosa*, *Kl. Pneumoniae, S. aureus, P. marneffei* (anti-fungal bacteria) using Furacin and ltraconozoleas standard drugs.

Minimum bacterial inhibitory concentration (MIC) values were resolved by Broth dilution technique. Dimethyl sulfoxide was used as diluent. MIC values of the appraised compounds are recorded in (Table 1). Majority of the prepared compounds displayed less activity than standard drug Furacin and ltraconozole against *E. coli, P. aeruginosa, Kl. pneumoniae, S. aureus, P. marneffei.*




**Scheme 1.** Rout of synthesis for compounds 4a-d.

**Table 1.** Antibacterial / fungal activity table [microgramme/ml]

| MINIMAL INHIBITION CONCENTRATION | | | | | | |
|---|---|---|---|---|---|---|
| Sr. No | Code | *E. coli* | *P. aeruginosa* | *KL. pneumoniae* | *S. aureus* | *P. marneffei* |
| | | MTCC 443 | MTCC 1688 | MTCC 109 | MTCC 96 | WILD STAIN |
| 1 | 4a | 25 | 50 | 100 | 50 | 500 |
| 2 | 4b | 12.5 | 25 | 25 | 100 | 100 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | 4c | 50 | 50 | 100 | 25 | 250 |
| 4 | 4d | 100 | 25 | 50 | 50 | 100 |
| 5 | 4e | 25 | 50 | 100 | 25 | 50 |
| 6 | Furacin | 25 | 25 | 50 | 50 | - |
| 7 | Itraconozole | - | - | - | - | 100 |

## 4. EXPERIMENTAL SECTION

### General procedure for the synthesis of 3-(5-bromothiophen-2-yl)-6-phenyl[1,2,4]triazolo [3,4-b][1,3,4]thiadiazole derivatives (7a-e)

An equimolar mixture (0.10 mol) of intermediate -5 and aromatic acids in phosphorus oxychloride (10 mL) was refluxed for 5 h. The reaction mixture was cooled to room temperature and then gradually poured onto crushed ice with stirring. The mixture was allowed to stand overnight and the solid separated out was filtered, treated with dilute sodium bicarbonate solution and washed thoroughly with cold water. The compound so obtained was dried and recrystallized from ethanol.

### 3-(5-bromothiophen-2-yl)-6-phenyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (7a)

Molecular Weight: 363 (8a); White coloured, Yield: 82% m.p: 182-184 ºC, $^{1}$H NMR: (400 MHz, $CDCl_3$-d), δ 7.77 (s, 1H), 7.76 – 7.63 (m, 2H), 7.51 (s, 1H), 7.50 – 7.43 (m, 2H), 7.38 (s, 1H). $^{13}$C NMR (100 MHz) δ 160.60 (s), 154.25 (s), 151.37 (s), 140.07 (s), 133.76 (s), 131.70 (s), 129.82 (s), 129.13 – 128.92 (m), 127.29 (s), 125.79 – 125.57 (m), 119.14 (s). LC mass m/z: 363 (M.F: $C_{13}H_7BrN_4S_2$).

### 3-(5-bromothiophen-2-yl)-6-(4-fluorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (7b)

White coloured, Yield: 77% compound, m.p: 173-175 ºC, $^{1}$H NMR (400 MHz, Chloroform) δ 7.67 (t, J = 5.1 Hz, 3H), 7.43 (s, 1H), 7.24 – 7.17 (m, 2H). $^{13}$C NMR (100 MHz) δ 166.62 (s), 160.60 (s), 154.25 (s), 151.37 (s), 140.07 (s), 129.82 (s), 129.39 (s), 129.11 – 128.44 (m), 127.29 (s), 119.14 (s), 117.20 – 114.92 (m).LC mass m/z: 381 (M.F: $C_{13}H_6FBrN_4S_2$)

### 3-(5-bromothiophen-2-yl)-6-(4-chlorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (7c)

White coloured, Yield: 85% m.p: 181-184 ºC, $^{1}$H NMR: (400 MHz) δ 7.75 – 7.56 (m, 4H), 7.55 – 7.38 (m, 2H). $^{13}$C NMR (125 MHz, Common NMR Solvents), δ 160.60 (s), 154.25 (s), 151.37 (s), 140.07 (s), 136.46 (s), 133.82 (s), 129.82 (s), 129.31 – 128.92 (m), 127.46 – 127.18 (m), 119.14 (s). LC mass m/z: 398 (M.F $C_{13}H_6ClBrN_4S_2$)

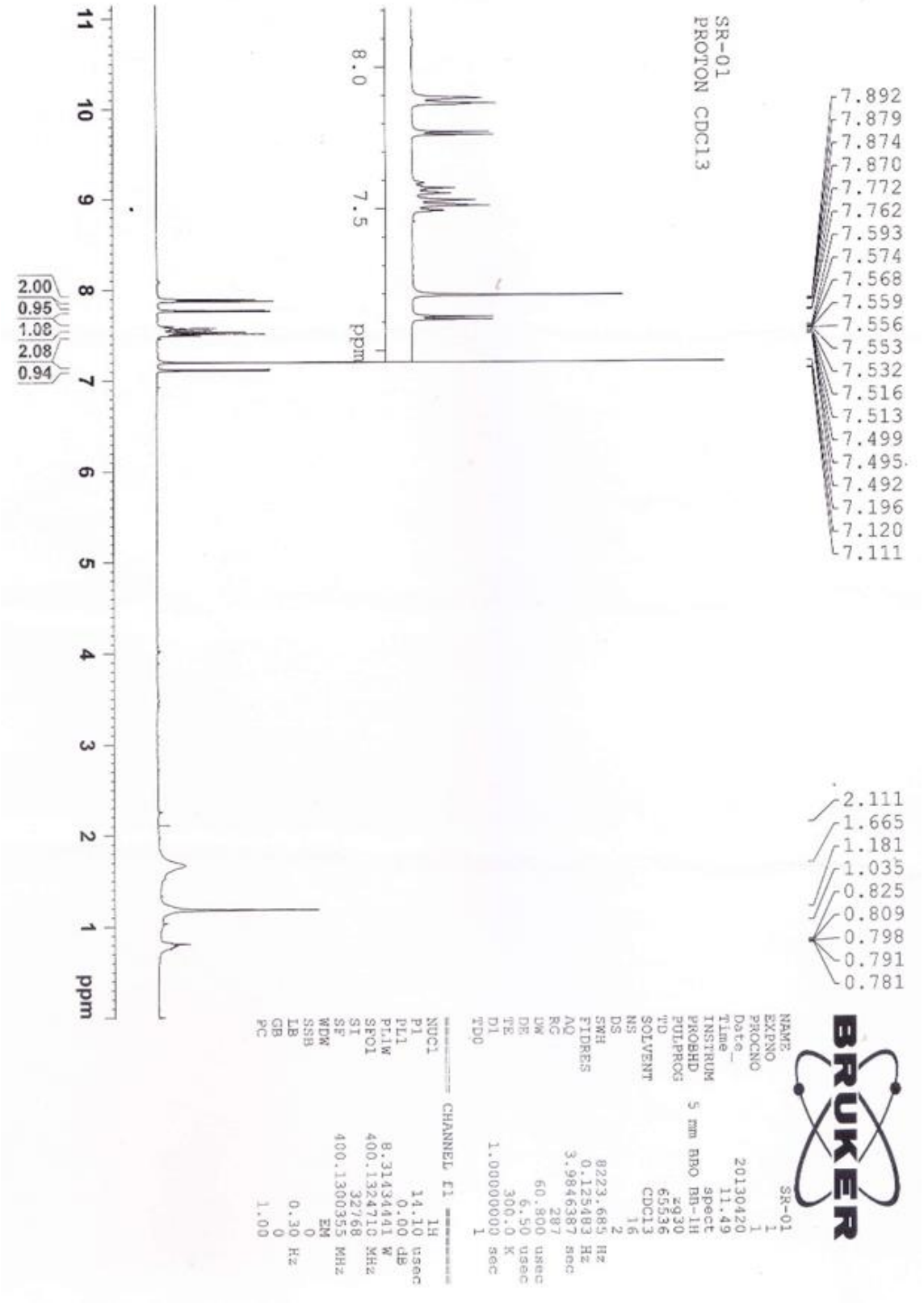



**Fig. 1.** NMR Spectra

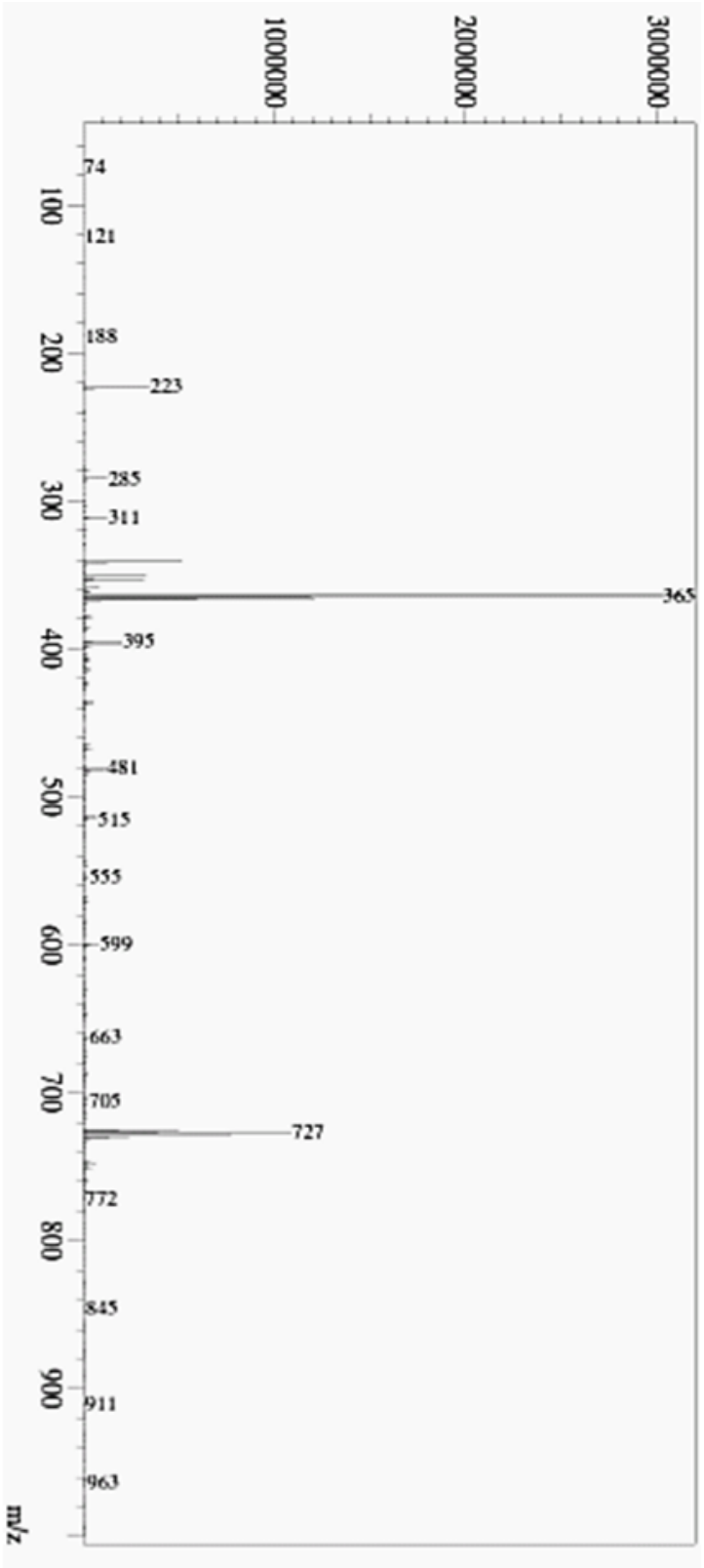



**Fig. 2. Mass Spectra**

## 5. CONCLUSIONS

A series of five new triazolo-thiadiazoles were obtained by cyclo-condensation reaction of triazoles with substituted Aromatic acids using phosphorous oxychloride as cyclizing agent. The compounds were characterized by various spectral techniques 3-(5-bromothiophen-2-yl)-6-phenyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole derivatives were found to show Biological property of antibacterial and anti-fungal activity.

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