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# Synthesis, Characterization and Antimicrobial Analysis Of Various Substituted 6-(3-(5-Bromothiophen-2-Yl)-1-Phenyl-1H-Pyrazol-4-Yl)-4-(2-Hydroxyphenyl) Pyrimidine-2(1H)-Thiones

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## ABSTRACT

The title compounds thiopyrimidines 3(a-h) have been synthesized from chromones 1(a-h) by refluxing thiourea 2 with potassium hydroxide. The structures of all newly synthesized compounds have been confirmed by IR, $^1$H NMR and Mass spectral data. The synthesized compounds have been screened for their antimicrobial activity. Some of the compounds show moderate antimicrobial activity as compared to the reference drugs Ciprofloxacin and Fluconazole.

**Keywords:** Chromones, Pyrazolopyrimidines, Antimicrobial Activity

## I. INTRODUCTION

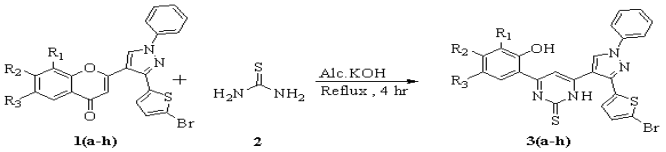
Pyrimidine derivatives are important among different heterocyclic compounds, due anti- antiviral, anti-inflammatory, neoplastic and antibiotic in addition to other microbial activities[1]. In nucleic acids, uric acid, purines, several vitamins, few marine microorganisms and coenzymes the pyrimidine ring system is present. Many synthetic members of pyrimidine are important as synthetic drugs and chemotherapeutic agents. Their remarkable biological activities attracted consideration to the chemistry of nitrogen heterocycles[2,3] Many novel drugs are planned using the small 5-acetyl pyrimidine-2, 4, 6-(1*H*, 3*H*, 5*H*)-trione moiety as a preliminary building block in the synthesis. Directly 5-acylbarbiturates are applied in pharmaceutical and other industry[4].Synthetic heterocyclic compounds, like furan, pyrrole, thiophene, pyrrolidine, piperidine, thiazole and pyridine having significant application and many are important intermediates in preparation[5]. Fused pyrimidines attracted much attention due to biological activities. This is obvious from publications where the pyrimidine ring is fused to various heterocycles such as purines, pteridines, pyridopyrimidines, quinazolines, triazolo pyrimidines, pyrazolopyrimidines, pyrimidoazepines and furopyrimidines. Work of well-known chemists like Riedel, Bischler, Gabriel, Niementowski and Bogert recognized for major progress in this field[6]. Many simple fused pyrimidines such as purines and pteridines are biologically active by themselves[7, 8] or are necessary constituents of very essential naturally occurring substances. Some pteridine derivatives are as anti-leukemic drugs[9], or potassium-conserving diuretics[10]. Moreover, several quinazoline alkaloids exhibit hypnotic[11, 12], bronchodilatory[13], and antimalarial activity [14, 15].

Many cardio circulatory syndromes such as deep vein thrombosis (DVT), myocardial infarction (MI) or unstable angina (UA) is one of the utmost significant causes of death worldwide. The importance of fused pyrimidines as antithrombotic and antiplatelet drugs has been definitely recognized by medical trials. Thus, extra investigation of pyrimidine chemistry seems to be worthwhile[16]. Pyrimidine derivatives show antibacterial[17, 18], antihyperlipidemic[19] anti-cancer[20] antihypertensive[21] and anti-HIV activities[22].

## II. MATERIALS AND METHODS

All the chemicals required for the synthesis of the compounds were obtained from Sigma Aldrich and SD Fine chemicals. Melting points were recorded in open capillaries and are uncorrected. $^1$H NMR spectra were recorded on Varian 400 MHz spectrophotometer in $CDCl_3$, DMSO-$d_6$ and TMS as an internal standard. The infra-red spectra were recorded as potassium bromide disk using Schimadzu-FT-IR Spectrophotometer. Mass spectra were recorded on Micromass mass spectrophotometer. The purity of the synthesized compounds was checked by TLC silica gel coated plates obtained from Merck as stationary phase and solvent mixture of ethyl acetate/hexane (20:80) as mobile phase. General procedure for the synthesis of 4-(5-bromo-2-hydroxyphenyl)-6-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl) pyrimidine-2(1*H*)-thione (3g): To a mixture of Comp. 1 (0.00078 mmole) and KOH (0.05 mmole) in ethanol (10 ml), thiourea 2 (0.0025 mmole) was added and reaction mixture was refluxed for four hr. After completion of the reaction (monitored by TLC), reaction mass was cooled to the room temperature and poured on crushed ice, and acidified with conc. HCl to get yellow solid. The solid was filtered off and recrystallized from ethanol to afford 3(a-h) pure solid. The physical data of the compounds 3(a-h) were recorded in Table I. Their structures have been confirmed by $^1$H NMR, Mass and IR spectra.

IR (3g) (cm$^{-1}$): 1258 (C-Br), 1478(C=C), 1559 (C=S), 3371(N-H), 3827(O-H);$^1$H NMR (3g) (DMSO) δ ppm: 6.905 (s, 1H, N-H), 7.157-7.602 (m, 10H, Ar-H), 7.801(s, 1H, Ar-H), 8.713(s, 1H, Pyrazole-H), 12.953 (s, 1H, Ar-OH); ES-MS (3g) (m/z): 585.1(M+1), 587(M+3), 589.1(M+5).




1(a-h) 2 3(a-h)

**Scheme 1**

**Table 1**. Physical data of compounds 3(a-h)

| Comp. | $R_1$ | $R_2$ | $R_3$ | M.P. (°C) | Yield (%) |
|---|---|---|---|---|---|
| **3a** | H | H | H | 130-132 | 62 |
| **3b** | H | H | $CH_3$ | 180-182 | 72 |
| **3c** | H | H | Cl | 136-138 | 64 |
| **3d** | Cl | H | Cl | 176-178 | 70 |
| **3e** | H | H | F | 190-192 | 70 |
| **3f** | H | $CH_3$ | Cl | 188-190 | 68 |
| **3g** | H | H | Br | 140-142 | 68 |
| **3h** | $CH_3$ | H | $CH_3$ | 184-186 | 64 |

## III. RESULTS AND DISCUSSION

The thiopyrimidine derivatives were synthesized successfully in moderate to good yields. The newly synthesized compounds were identified on the basis of melting point range, IR, $^1$H NMR, Mass spectral analysis. All the newly synthesized derivatives were screened for antimicrobial activity using disc diffusion method.

Antimicrobial activity: Compounds 3(a-h) were screened for their in vitro antimicrobial activity against Escherichia coli (ATCC 25922), Pseudomonas aeruginosa (ATCC 27853), Staphylococcus aureus (ATCC 25923), Staphylococcus albus, Klebsiella pnuemoniae using Ciprofloxacin as a reference standard drug by paper disc diffusion method. Antifungal activity was evaluated against Candida sp. using Fluconazole as standard drug. All the tests were evaluated at 100 µg/ml concentration. The culture media was Muller Hinton agar. The zone of inhibition was measured in mm after 24 hr of incubation at 37°C. DMSO is used as control. Microbial data for corresponding compounds is summarized in Table 2.

**Table 2**. Antimicrobial Analysis Data

| Sr. No. | Compound No. | Inhibition Zone Diameter (mm) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Candida sp. | S. aureus | S.albus | Klebsiella pnuemoniae | E. coli | Pseudomonas sp. |
| 1. | 3a | 2 | - | 5 | 7 | 8 | 3 |
| 2. | 3b | 4 | 8 | 8 | 4 | 10 | 8 |
| 3. | 3c | 5 | 9 | 5 | 6 | 7 | 4 |
| 4. | 3d | 3 | 7 | 8 | 6 | 7 | 2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 5. | 3e | 5 | 10 | 5 | 6 | 6 | 3 |
| 6. | 3f | 2 | 8 | 4 | 5 | 8 | 5 |
| 7. | 3g | 7 | 6 | 7 | 10 | 7 | - |
| 8. | 3h | 4 | 8 | 4 | 5 | 7 | - |
| 9. | Control | 8 | 3 | 3 | 4 | 6 | 10 |
| 10. | Ciprofloxacin | --- | 20 | 22 | 22 | 21 | 23 |
| 11. | Fluconazole | 23 | --- | --- | --- | --- | --- |

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