Synthesis and Biological Evaluation of 2-((2-Chlorophenyl) (6,7-Dihydrothieno [3,2-
c]Pyridin-5(4H)-YL)Methyl)-4-Methylthiazole-5-Carboxylic Acid Derivatives

Joga Sree Ram Babu*1, K. Sudhakar Babu1, T. Ravisankar2, J. Latha3

1. Department of Chemistry, Sri Krishnadevaraya University, Ananthapuramu, India.
2. Department of Research and Development Virchow labs, Hyderabad, India.
3. Department of Bio-technology, Sri Krishnadevaraya University, Ananthapuramu, India.

ABSTRACT
During the course of our investigation in the field of carboxylic acid antithrombotic agents, we have identified and synthesized 2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylic acid derivatives (5a-k), with good in vivo activity. These findings prompted us to prepare new 2-((2-chlorophenyl)(6,7-dihydrothieno [3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylic acid derivatives (5a-k),were synthesized by reaction of 2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylic acid with substituted halo anilines by using thionyl chloride and hydroxy benzotriazole in presence of triethylamine in Dichloromethane obtained the tile compounds. All the newly synthesized compounds were characterized by spectral methods. The title compounds were screened for in vitro antibacterial activity. Most of the compounds show moderate to good antimicrobial activity.

Keywords: Anti-bacterial activity, ethyl-2-chloro acetoacetate, thienopyridine, thiazole carboxylic acid, HOBt-SOCl2, antifungal activity

INTRODUCTION
Thienopyridines (4,5,6,7-tetrahydro thieno[3,2-c]pyridines) and their derivatives are important heterocyclic compounds that are widely distributed in nature. Many of the compounds containing tetrahydrothienopyridine skeleton are reported as antibacterial [1] non-peptide GPIIb/IIIa antagonists [2] platelet aggregators and antithrombotic agents[3]. The incorporation of benzylic or substituted benzylic groups on the nitrogen of the thienopyridine ring can bring an extensive modification in the biological activities of parent compound. Among the substitutions occurred at nitrogen of the thienopyridine moiety[4], the increased effect in the biological activity of the parent moiety affects the good antithrombotic activity in Ticlopidine and with more increased activity in Clopidogrel. Later on, the studies proved that the Prasugrel to be more efficient drug candidate than the existing Clopidogrel by making the structural modifications to the parent thienopyridine moiety. Hence, different substitutions at nitrogen of the biological activity of the new chemical entities (NCEs). Thiazole and their derivatives have attracted continuing interest over the years because of their varied biological activities. [5]1,3-Thiazole nucleus containing compounds have exhibited a broad range of biological activities. [6-15]. Thiazole is five membered unsaturated heterocyclic moiety containing sulphur and nitrogen atoms as the main heterocyclic constituents. In continuation of our work towards the synthesis of new heterocyclic moieties on the phenyl system along with tetrahydrothieno pyridine nucleus in its structure we explored to introduce the thiazole ring system on the second position of phenyl system. For this strategy, we are keen to use the one of the known intermediates for the functionalization of the thiazole mother skeleton. we found 2-
(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetonitrile(1) as an important intermediate for the preparation of thiazole moiety. For instance, the introduction of thiazole ring into the molecule of 2-(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetonitrile 1 and also some of the derivatives of this substrate might afford the promising metabolically stable analogs. The nitrile function of compound 1 was transformed into thioamide(2) followed by ring construction using commercially available ethyl-2-chloro acetoacetate under reagent free conditions affords the thiazole skeleton ethyl 2-((2-chlorophenyl)(6,7-)
dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylate(3).

Thus we had targeted the synthesis of 2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylic acid 4 and acid amide derivatives with an objective to study their biological activity. With this aim, we started to prepare the required pharmacophore using the known intermediates, 2-(2-chlorophenyl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetonitrile are the synthesis for the preparation of compounds (5a-5k)

![Thieno pyridine acetonitrile](image)

**Thieno pyridine acetonitrile**

1

**MATERIAL AND METHODS**

All solvents used were of commercial grade purchased from a qualified vendor. Melting point range reported was uncorrected and taken on a Polmon melting apparatus. The FT-IR spectra were recorded in the solid state as KBr dispersion using a Perkin-Elmer 1650 FT-IR spectrophotometer. Thin layer chromatography was performed on Merck precoated silicagel 60F254 plates using UV light as visualizing agent. 1H NMR and 13C NMR spectra were recorded on 400 and 100 MHz Gemini Varian spectrometer using CDCl3 as solvent and tetramethylsilane as an internal standard. The mass spectra were recorded on an Agilent 6310 Ion Trap.

**Synthesis of 2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxamidine(2)**

To a solution of the compound 1 (10.0 g, 0.024 moles) in Dimethyl form amide (100.0 mL), was added NaSH.H2O (4.5 g, 0.071 moles) the reaction mixture was for stirred over night at ambient temperature. The progress of the reaction mixture monitored using TLC. It was poured into water (200.0mL). The product was filtered and washed the solid with water (20.0 m) to remove the impurities. The obtained compound 2

**Thiazole 5-carboxylic acid containing thienopyridine**

The wet material suspended in water (50.0 mL) and adjusted to the 7–8 pH using dilute 1% aq. HCl solution to afford the title compound 2 as a cream colored solid. The wet compound was dried under reduced pressure at 25-30°C for 4.5 h. yield 80%, mp: 205–210°C, IR (KBr) cm−1; 1620 (C=O), 3371(NH2), 1HNMR (400 MHz CDCl3) 1.27 (t, 3H, CH3), 1.72 (s, 2H, NH2), δ 2.65-2.89 (m, 4H, 2 x CH2), δ 3.60 (s, 2H, CH2), δ 3.96 (s, 1H, CH), δ 6.71-7.5 (6H, ArH). 13C NMR (100 MHz, CDCl3): δ, 50.85, 53.12, 73, 125.22, 127.82, 128.16, 128.88, 129.98, 130.01, 130.82, 132.11, 133.32, 135.91, 138.05, 202.5. MS(m/z):323(M+1)

**Synthesis of 2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxamidine (3)**

To a solution of the compound 2(10.0 g, 0.033 moles) in ethanol (100.0 mL), was added 2-chloro ethyl acetoacetate (22.0 mL, 0.156moles)(4.5 g, 0.071 moles) the
reaction mixture was for stirred over night at 50-60°C the progress of the reaction mixture monitored using TLC. Reaction mixture is heterogeneous throughout the reaction time cycle. The product was filtered and washed the solid with chilled ethanol (20.0 mL). The wet material was recrystallized from ethanol and dried the compound at 50-60°C under reduced pressure for 3-4 h. The obtained compound 3 yield 80%, mp: 105–110 °C, IR (KBr) cm⁻¹: 1710 (C=O) 1HNMR (400 MHz CDCl₃) : δ 2.35 (s, 3H, CH₃), 2.73–2.85 (m, 4H, 2 x CH), 3.63 (s, 2H, CH₂), 5.2 (s, 1H, CH), 6.78–7.5 (6H, ArH).¹³C NMR (100 MHz, CDCl₃): δ 15.42, 17.41, 25.63, 50.85, 53.12, 60.04, 61.86, 125.22, 127.82, 129.16, 129.88, 129.98, 130.01, 130.05, 133.32, 133.61, 139.61, 139.75, 159.42, 167.14, 168.16. MS (m/z): 433 (M⁺1).

**Synthesis of 2[(2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl]-4-methylthiazole-5-carboxylic acid (4)**

To a solution of the compound 3 (10.0 g, 0.024 moles) in acetonitrile (50.0 mL), was added KOH powder (2.0 g, 0.037 moles) the reaction mixture was for reflux and maintained for 5-6 h. The progress of the reaction mixture monitored using TLC. It was cooled to 25–30 °C. The product was filtered and washed the solid with acetonitrile (10.0 mL) to remove the impurities. The obtained product is in the form of potassium salt of compound 4. The potassium salt is dissolved in water (50.0 mL) and adjusted to the 4–5 pH using 5% acetic acid to afford the title product 4 as crude material. Recrystallized in acetonitrile (25.0 mL) affords compound 4 as white solid material. Off white solid, yield 80%, mp: 205–210 °C, IR (KBr) cm⁻¹: 1698 (C=O), 3600 (OH), ¹HNMR (400 MHz CDCl₃) : δ 2.35 (s, 3H, CH₃), 2.78–2.91 (m, 4H, 2 x CH), 3.60 (s, 2H, CH₂), 5.1 (s, 1H, CH), 6.78–8.12 (6H, ArH).¹³C NMR (100 MHz, CDCl₃): δ 12.42, 25.63, 50.85, 53.12, 60.22, 125.22, 127.82, 129.16, 129.88, 129.98, 130.01, 130.05, 133.32, 133.61, 139.61, 139.75, 159.42, 167.14, 169.16. MS (m/z): 405 (M⁺1).

**Synthesis of title compounds (5a-k2)**

To a solution of the compound 4 (10.0 g, 0.01 moles) in dichloromethane (50.0 mL) and was added HOBT (0.31 g, 0.002 moles) under nitrogen atmosphere. It was cooled the reaction mixture to -5°C to 0°C and was added TEA (0.42 g, 0.004 moles) slowly into the reaction mixture at below -5°C. Then thionyl chloride added into the reaction mixture over a period of 30–40 minutes under nitrogen atmosphere at below -5°C. After completion of addition, the temperature was raised slowly to 10–15°C and maintained the reaction mixture at the same temperature for 2 h. Then water (5.0 mL) was added into the reaction mixture and stirred for 5 minutes and separated the organic layer (active ester layer). Charged the active ester layer into the RBF and substituted aniline (0.23 g, 0.002 moles) was taken into DCM (10.0 mL) and added the solution slowly over period of 30–40 minutes at 10–15°C. After completion of the addition the temperature of the reaction mixture was raised to 25–30 °C and maintained for 10–12 h at the same temperature. Progress of the reaction was monitored by using TLC, after completion of the reaction water (10.0 mL) was added into the reaction mixture, stirred for 10–15 minutes. Separated the organic layer and the organic layer was washed with 10% K₂CO₃ solution (5 mL) followed by water (5 mL) washing. Organic layer was dried over anhydrous sodium sulphate and solvent was removed completely under reduced pressure. Co-distillation of the solvent with diisopropyl ether (2 x 10 mL) followed by isolation in diisopropyl ether (5 mL) affords the title compound 5a quantitatively. Pale brown solid, yield 70%, mp: 156–159 °C, IR (KBr)(cm⁻¹): 1718 (C=O), 3400 (NH₂).¹HNMR (400 MHz, CDCl₃) : δ 2.35 (s, 3H, CH₃), 2.78–2.80 (m, 4H, 2 x CH₂), 3.53 (s, 2H, CH₂), 4.9 (s, 1H, CH), NH₂ 8.5 (s, 2H) 6.70–7.69 (6H, ArH).¹³C NMR (100 MHz, CDCl₃): δ 12.62, 25.63, 50.58, 55.14, 116.2, 124.82, 127.28, 129.10, 129.38, 129.65, 130.00, 130.28, 132.01, 133.19, 137.52, 138.05, 159.24, 161.91, 166.76. MS (m/z): 404 (M⁺1).

Employing the similar procedure as mentioned for 5a the remaining amides (5b-
k) were prepared in quantitatively.

2-{4-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-ylmethyl)-phenyl-2-yl]-4-methylthiazole-5-carboxylic Acid phenyl amide (5b)

Pale yellow solid, yield 75%, mp: 120–123°C, IR (KBr) (cm⁻¹): 1660 (C=O), 3350 (NH) ¹HNMR (400 MHz, CDC₁₃): δ 2.41 (s, 3H, CH₃), 2.83–2.91 (m, 4H, 2 x CH₂, pyridine ring), 3.61 (s, 2H, CH₂allylic pyridine ring), 5.0 (s, 1H, CH), NH-7.5 (s,1H),6.61–7.8 (11H, ArH).¹³C NMR (100 MHz, CDC₁₃): δ 15.33, 25.4, 50.70, 53.09, 56, 114, 120.31, 124.85, 125.31, 127.40, 128.11, 129.32, 129.78, 129.97, 129.88, 130.02, 130.85, 131.75, 133.33, 133.70, 137.28, 137.41, 160.04, 162.9, 166.7 (m/z): 514. (M⁺).

2-{(2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl}-N-(2,3dichlorophenyl)-4-methylthiazole-5-carboxamide (5f)

Off white solid, yield 62%, mp: 150–153 °C, IR (KBr) (cm⁻¹): 1638 (C=O),825 (C-Cl)¹HNMR (400 MHz, , CDC₁₃): δ 2.41 (s, 3H, CH₃), 2.83–2.91 (m, 4H, 2 x CH₂, pyridine ring), 3.61 (s, 2H, CH₂allylic pyridine ring), 5.0 (s, 1H, CH), NH-7.6 (s,1H) 6.61–7.8 (10H, ArH).¹³C NMR (100 MHz, CDC₁₃): δ 15.33, 25.42, 50.70, 53.09, 56, 114, 120.31, 124.85, 125.31, 127.40, 128.11, 129.32, 129.78, 129.97, 129.88, 130.02, 130.85, 131.75, 133.33, 133.70, 137.28, 137.41, 160.04, 162.9, 166.7 (m/z): 514. (M⁺).
3451(NH), 769 (C-F) \text{^1}HNMR (400 MHz, CDCl\textsubscript{3}): δ 2.41 (s, 3H, CH\textsubscript{3}), 2.78-2.91 (m, 4H, 2 x CH\textsubscript{2}, pyridine ring), 3.61 (s, 2H,CH\textsubscript{2}allylic pyridine ring), 5.0 (s, 1H, CH), NH-7.5 (s,1H), 6.7-7.8 (11H, ArH).\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 15.33, 25.42, 50.70, 53.09, 56, 119, 120.31, 124.85, 125.31, 127.40, 128.11, 128.84, 129.79, 130.02, 130.38, 131.75, 133.33, 133.70, 137.41, 143.14, 157, 160.04, 162.9, 166.66. MS (m/z): 498 (M+1).

2-((2-chlorophenyl)(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-N-(4-fluorophenyl)-4-methylthiazole-5-carboxamide (5i)

Off white solid, yield 70%, mp: 146 °C, IR (KBr) (cm\textsuperscript{-1}): 1635 (C=O), 3418 (NH), 794 (C=O). \textsuperscript{1}HNMR (400 MHz, CDCl\textsubscript{3}): δ 2.41 (s, 3H, CH\textsubscript{3}), 2.83-2.91 (m, 4H, 2 x CH\textsubscript{2}, pyridine ring), 3.61 (s, 2H,CH\textsubscript{2}allylic pyridine ring), 5.0 (s, 1H, CH), NH-7.6 (s,1H) 6.61-7.7 (11H, ArH).\textsuperscript{13}C NMR(100 MHz, CDCl\textsubscript{3}): δ 15.33, 25.42, 50.70, 53.09, 56, 116, 120.31, 124.85, 125.31, 127.40, 128.11, 128.84, 129.42, 129.79, 129.88, 130.02, 130.38, 131.75, 133.33, 133.70, 137.28, 160.04, 163.9, 164.2, 166.66. MS (m/z): 498.1 (M+).
using commercially available ethyl-2-chloro acetoacetate under reagent free conditions affords the thiazole skeleton ethyl 2-[(2-chlorophenyl)](6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl)-4-methylthiazole-5-carboxylate (3).

The compound 3 appeared in the $^1$H NMR spectrum (400 MHz, CDCl$_3$), the signals observed at $\delta 1.25$ as triplet which is due to CH$_3$ of ester moiety of thiazole ring (t, $J=7.2$ Hz, 3H, CH$_3$), asinglet appeared at $\delta 2.69$ is due to the CH$_3$ of thiazole ring (s, 3H, CH$_3$), adjacent methylene protons displayed between $\delta$ 2.73-2.85 (m, 4H, 2 x CH$_2$). Another singlet proton appeared at $\delta$ 3.6 is allylic CH$_2$ of thienopyridine ring and another singlet appeared at $\delta$ 5.2 is due to benzylic CH. A quartet appeared at $\delta$ 4.23 (q, $J=7.2$ Hz, 2H, OCH$_2$) is due to the ester CH$_2$ protons. In the $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum the signals observed at $\delta$ 15.42 are signals of CH$_3$ of thiazole ring, 17.41 (CH$_3$ ester), 25.63 (CH$_2$ pyridine ring), 50.81 (CH$_2$ allylic), 53.12 (CH$_2$ pyridine ring), 61.04 (benzylic CH), 61.86 (CH$_2$ ester), the compound 3 which is upon saponification gives 2-[[2-chlorophenyl][6,7-dihydrothieno[3,2-c]pyridin-5-ylmethyl]-2-yl]-4-methyl-thiazole-5-carboxylic acid (4). The compound (4) in the $^1$H NMR (400 MHz, CDCl$_3$) spectrum the signals observed at $\delta$ 2.35 (3H, CH$_3$) is due to the methyl protons of the thiazole ring system. Two adjacent methylene protons displayed between $\delta$ 2.78-2.91 (m, 4H, 2 x CH$_2$). Two singlet protons appeared at $\delta$ 3.60 (s, 2H, CH$_2$) and $\delta$ 5.1 (s, 1H, CH). In the $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum the signals observed at $\delta$ 15.32 are signals of CH$_3$ of thiazole ring, 25.36 (CH$_2$ pyridine ring), 50.85 (CH$_2$, allylic), 53.12 (CH$_2$ pyridine ring), 51 (benzylic CH).

Finally the acid function further converted into amide (5a-k) as per the synthetic path way the synthesis of target molecules using the commercially available, economically cheap starting materials to give different 2-[(2-chlorophenyl)](6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)methyl]-4-methylthiazole-5-carboxylic acid (5a-k).

The compound 5a in the $^1$H NMR (400 MHz, CDCl$_3$) spectrum, the signals observed at $\delta$ 2.35 (s, 3H, CH$_3$) is due to the methyl protons of the thiazole ring system. Two adjacent methylene protons displayed between $\delta$ 2.78-2.93 (m, 4H, 2 x CH$_2$). Two singlet protons appeared at 3.50 (s, 2H, CH$_2$) and $\delta$ 5.1 (s, 1H, CH) are due to the methylene protons of the pyridine ring and benzylic protons respectively. Aromatic protons resonated between $\delta$ 6.79-7.69 (6H, ArH). In the $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum, the signals observed at $\delta$ 15.42 are signals of CH$_3$ of thiazole ring, 25.63 (CH$_2$ pyridine ring), 50.68 (CH$_2$, allylic), 53.14 (CH$_2$ pyridine ring).

**Scheme 1: Synthesis of title compounds thiazole-5-carboxylic acid amides (5a-5K)**

R$_1$=substituted halo anilines

Where R=H, phenyl, 2-chloro phenyl, 3-chloro phenyl, 4-chloro phenyl, 2,3-dichloro phenyl, 3,4-dichloro phenyl, 2-fluoro phenyl, 4-fluoro phenyl, 2,5-difluoro phenyl, 2,3,4-trifluoro phenyl

---

Joga Sree Ram Babu et.al, IJPRR 2016;5(7):14
BIOLOGICAL ACTIVITY
Antimicrobial Activity
All the newly prepared compounds (5a–k) were screened for the antibacterial activities done by the paper disc method. Organisms used: Escherichia coli and K. pneumonia (Gram-negative), Staphylococcus aureus and B. subtilis (gram-positive). To evaluate the activity of the synthesized compounds, the zone of inhibition was determined. The in vitro antimicrobial screening results of tested compounds are listed in (Table 1 and 2).

The antibacterial screening data showed that almost all the compounds 5a–k is active and showing moderate to good antibacterial activity. among the screened compounds 5c, 5f, 5i and 5k in which respectively showed high activity against all the micro-organism employed. The activities of these compounds are almost equal to the standards the remaining compounds showed moderate to good antibacterial activity.

Table 1: Antibacterial screening results of the compounds 5a−5k (Zone diameter of growth inhibition in mm)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conc. µg/ml</th>
<th>S. aureus</th>
<th>B. subtilis</th>
<th>E. coli</th>
<th>K. Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>100</td>
<td>200</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>5a</td>
<td></td>
<td>26</td>
<td>30</td>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>5b</td>
<td></td>
<td>24</td>
<td>27</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>5c</td>
<td></td>
<td>33</td>
<td>36</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>5d</td>
<td></td>
<td>23</td>
<td>20</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>5e</td>
<td></td>
<td>14</td>
<td>15</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>5f</td>
<td></td>
<td>36</td>
<td>39</td>
<td>34</td>
<td>37</td>
</tr>
<tr>
<td>5g</td>
<td></td>
<td>23</td>
<td>25</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>5h</td>
<td></td>
<td>23</td>
<td>32</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>5i</td>
<td></td>
<td>32</td>
<td>34</td>
<td>33</td>
<td>30</td>
</tr>
<tr>
<td>5j</td>
<td></td>
<td>20</td>
<td>22</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>5k</td>
<td></td>
<td>38</td>
<td>43</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td></td>
<td>35</td>
<td>39</td>
<td>38</td>
<td>41</td>
</tr>
</tbody>
</table>

Table 2: Antifungal screening results of the compounds 5a−5k (Zone diameter of growth inhibition in mm)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conc. µg/ml</th>
<th>F. solani</th>
<th>C. lunata</th>
<th>A. niger</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>100</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>5a</td>
<td></td>
<td>16</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>5b</td>
<td></td>
<td>19</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>5c</td>
<td></td>
<td>17</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>5d</td>
<td></td>
<td>9</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>5e</td>
<td></td>
<td>24</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>5f</td>
<td></td>
<td>25</td>
<td>21</td>
<td>34</td>
</tr>
<tr>
<td>5g</td>
<td></td>
<td>17</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>5h</td>
<td></td>
<td>17</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>5i</td>
<td></td>
<td>23</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>5j</td>
<td></td>
<td>16</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>5k</td>
<td></td>
<td>21</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td>38</td>
<td>42</td>
<td>38</td>
</tr>
</tbody>
</table>

The result of antifungal activity revealed that all the tested compounds show moderate to good antifungal activity as compared to the standard drug ketoconazole. Compound 5e (R =4-chloro), and 5i (R =4-fluoro –) exhibited good activities against all the fungal species. However compounds 5e, is inactive against
bacterial strain but showed good antifungal activity. Thus, it is concluded that compounds with $R = 2$-chloro, 2,3 dichloro, 4-fluoro and 2,3,5 trifluoro show good to excellent antibacterial activity.

**CONCLUSION**

We have successfully synthesized eleven new thiazole-5-carboxylic acid amide derivatives (5a–k) via (2) in good yields. The structures of all the compounds were confirmed by their spectral data. All the newly synthesized compounds were screened for their MIC and zone of inhibition against four strains of bacteria. Amongst the compounds screened, most of the compounds 5c, 5f, 5i, 5k have shown moderate to good antibacterial activity. The antimicrobial activity results make them interesting lead molecules for further synthetic and biological evaluation. Further studies are in progress to acquire more information regarding structure activity relationship.

**ACKNOWLEDGEMENT**

I am very thankful to S.K. University authorities for providing such an environment for doing better research very much. It’s my pleasure to express my thanks to Department of Chemistry and Prof. K. SudhakarBabu giving an opportunity to do research.

**REFERENCES**


