Synthesis and Biological Evaluation of Novel Isopropyl 2-thiazolopyrimidine-6-carboxylate Derivatives


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ABSTRACT. In the present study, we have synthesized novel Isopropyl 2-(4-substitutedbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]-pyrimidine-6-carboxylate derivatives (6a-j). Elemental analysis, IR, 1H NMR and mass spectral data elucidated structure of newly synthesized compounds. The newly synthesized compounds were screened for anti-inflammatory and anti microbial studies. Their biological activity data of the 10 compounds indicates that two compounds posses potent anti-inflammatory and five have antimicrobial activities.

Key words: Isopropyl 2-thiazolopyrimidine-6-carboxylate, Anti-inflammatory, Antibacterial, Antifungal activities

INTRODUCTION

Heterocycles are ubiquitous to among pharmaceutical compounds.1 Pyrimidine moiety is an important class of N-containing heterocycles widely used as key building blocks for pharmaceutical agents. These compounds exhibit a wide spectrum of pharmacophore, as they act as bactericidal, fungicidal,2 analgesic,3 antioxidant,4 anti-hypertensive,5 antifilarial,6 and anti-tumor agents.7 Preclinical data from literature indicates the continuing research in polysubstituted pyrimidine as potential anti-tumor agents.8-10 Among these, thiouracils in particular are used as anti-inflammatory and virucidal agents.11 The biological and synthetic significance places this scaffold at a prestigious position in medicinal chemistry research.

The key role pyrimidines play in cellular processes has made them valuable leads for drug discovery. One important class of pyrimidines is 2-thiopyrimidine (2-TP) and its derivatives, which are also recognised as 2-mercaptopopyrimidine compounds.12 In 2-TP ring, sulfur atom serves as an interesting replacement for the existing oxygen atom bonded to C-2 in uridine base.13,14 Base on this approach, 2-TPs have attracted significant interest of synthetic-biochemists.15,16 A patent17 revealed the application of 2-TP derivatives in preparation of cardiotonic drugs. Pathak et al. have evaluated primary activity of 2-TP derivatives against Mycobacterium tuberculosis (Mtbb).18

One-step synthesis of 3,4-dihydropyrimidin-2(1H)-one by three-component condensation of aldehydes, ethyl acetacetate and urea in alcohol using strong mineral acid was first reported by Biginelli.19 These substances, popularly known as Biginelli compounds possess several pharmaceutical properties like anti-bacterial, anti-viral, anti-inflammatory, anti-hypertensive and anti-tumor agents.20 In continued quest of new antimicrobial, anti-inflammatory agents, we designed and synthesized novel Isopropyl 2-(4-substitutedbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate derivatives (6a-j) having substituted benzylthio groups. Structures of the products were characterized by IR, 1H-NMR and LC-MS mass spectrometry and elemental analysis. Their biological activity data of the 10 compounds indicates that two compounds posses’ potent anti-inflammatory and five have antimicrobial activities.

RESULTS AND DISCUSSION

All the synthesized compounds were obtained in good to high yields. Products were purified and characterized by various spectroscopic techniques. The IR spectra of compounds (6a-j) showed characteristic absorption bands at 2981-2969 cm−1, 1721-1706 cm−1, 1632-1606, 1568-1525 and 652-647 cm−1 corresponding to the C-H str, CO str, CN str, CC str and C-S str functions in the structures. Similarly the 1H NMR spectra showed peaks due to in the range of δ 1.24-1.30 for OCH-(CH3)2, δ 2.28-2.39 for Ar-CH3, δ 4.20-4.28 for -CH, δ 4.89-4.92 for OCH-(CH3)2, and δ 7.66-7.82 for -Ar-CH. The mass spectrum of all the compounds showed molecular ion peak at M+H, at M+2H corresponding to its
molecular formula, which confirmed its chemical structure. The IR, 1H NMR, mass spectra and elemental analysis showed the structure of various novel Isopropyl 2-(4-substitutedbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate derivatives (6a–j).

CHEMISTRY

The synthesis of titled compounds (6a–j) was carried out according to Scheme 1. Benzaldehyde 1 and isopropyl acetoacetate 2 in ethanol was refluxed with thiourea 3 using ethanol as solvent in basic conditions to yield 5-isopropoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-thione. It was synthesized by the multicomponent Biginelli reaction. The Biginilli compound 4 was treated with substituted aromatic aldehydes 5 in presence of anhydrous sodium acetate to afford the titled compounds (6a–j). The reaction sequences are outlined in Scheme 1.

**Table 1.** The anti-inflammatory activity of Isopropyl 2-thiazolopyrimidine-6-carboxylate (6a–j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Paw oedema thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30 m (X ± SE)</td>
</tr>
<tr>
<td>Control</td>
<td>–</td>
<td>1.5 ± 0.03</td>
</tr>
<tr>
<td>6a</td>
<td>Ph</td>
<td>1.3 ± 0.05</td>
</tr>
<tr>
<td>6b</td>
<td>4-Br-Ph</td>
<td>1.1 ± 0.03</td>
</tr>
<tr>
<td>6c</td>
<td>4-C6H5-Ph</td>
<td>1.2 ± 0.05</td>
</tr>
<tr>
<td>6d</td>
<td>4-CH3-Ph</td>
<td>1.2 ± 0.06</td>
</tr>
<tr>
<td>6e</td>
<td>4-OCH3-Ph</td>
<td>1.2 ± 0.03</td>
</tr>
<tr>
<td>6f</td>
<td>4-NO2-Ph</td>
<td>1.2 ± 0.03</td>
</tr>
<tr>
<td>6g</td>
<td>4-CH(CH3)3-Ph</td>
<td>1.2 ± 0.03</td>
</tr>
<tr>
<td>6h</td>
<td>4-Cl-Ph</td>
<td>1.4 ± 0.00</td>
</tr>
<tr>
<td>6i</td>
<td>4-CH(CH3)3-Ph</td>
<td>1.4 ± 0.00</td>
</tr>
<tr>
<td>6j</td>
<td>4-N(CH3)2-Ph</td>
<td>1.1 ± 0.03</td>
</tr>
<tr>
<td>Nimesulide</td>
<td>4-(CH3)3-Ph</td>
<td>1.1 ± 0.05</td>
</tr>
</tbody>
</table>

Data represent mean values ±SE of six mice per group and the percent changes versus 30, 60 and 120 m post-carrageenan injection. Data were analyzed using one-way ANOVA followed by Turkey–Krammer Multiple comparison test **p< 0.01. Percent oedema inhibition was calculated as regards saline control group. ** Significant difference from the control value at p< 0.01. SE=standard error The active compounds are marked in bold letters.

**PHARMACOLOGICAL STUDIES**

Anti-inflammatory activity

The results of tested compounds as well as reference standard were measured before administration of Carrageenan inflammation. After the Carrageenan inflammation was administered on rats, the effect was measured in the intervals of 30, 60 and 120 min. The percent oedema inhibition was calculated reference to saline control group, as depicted in Table 1. All the newly obtained compounds 6a–j were tested for anti-inflammatory activity. Compared to the standard, Nimesulide, bulk of the compounds exhibited moderate to good anti-inflammatory activity. The results revealed that, while 6b and 6f have shown potent anti-inflammatory activity, compounds 6a, 6g, 6j and Nimesulide
Table 2. Antibacterial activity of Isopropyl 2-thiazolopyrimidine-6-carboxylate (6a-j)

<table>
<thead>
<tr>
<th>Compound no</th>
<th>Staphylococcus aureus</th>
<th>Escherichia coli</th>
<th>Pseudomonas aeruginosa</th>
<th>Klebsiella pneumoniae</th>
<th>Streptococcus pyogenes</th>
</tr>
</thead>
<tbody>
<tr>
<td>6c</td>
<td>10 (12.5)</td>
<td>--</td>
<td>17 (6.25)</td>
<td>--</td>
<td>11 (6.25)</td>
</tr>
<tr>
<td>6d</td>
<td>8 (25)</td>
<td>23 (6.25)</td>
<td>9 (25)</td>
<td>--</td>
<td>8 (12.5)</td>
</tr>
<tr>
<td>6g</td>
<td>10 (12.5)</td>
<td>15 (25)</td>
<td>--</td>
<td>--</td>
<td>17 (12.5)</td>
</tr>
<tr>
<td>6h</td>
<td>12 (12.5)</td>
<td>21 (6.25)</td>
<td>--</td>
<td>--</td>
<td>8 (25)</td>
</tr>
</tbody>
</table>

--Indicates bacteria is resistant to the compounds at >100 µg/ml, MIC values are given in brackets. MIC (µg/ml)=minimum inhibitory concentration, ie. Lowest concentration to completely inhibit bacterial growth. Zone of inhibition in mm.

bCiprofloxacin was used as standard.

Table 3. Antifungal activity of Isopropyl 2-thiazolopyrimidine-6-carboxylate (6a-j)

<table>
<thead>
<tr>
<th>Compound no</th>
<th>Aspergillus fumigatus</th>
<th>Aspergillus flavus</th>
<th>Trichophyton mentagrophytes</th>
<th>Penicillium marneffei</th>
<th>Candida albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td>6b</td>
<td>8 (25)</td>
<td>--</td>
<td>12 (12.5)</td>
<td>--</td>
<td>17 (6.25)</td>
</tr>
<tr>
<td>6e</td>
<td>5 (25)</td>
<td>18 (6.25)</td>
<td>--</td>
<td>12 (12.5)</td>
<td>17 (6.25)</td>
</tr>
<tr>
<td>6g</td>
<td>11 (12.5)</td>
<td>12 (25)</td>
<td>--</td>
<td>--</td>
<td>14 (12.5)</td>
</tr>
<tr>
<td>6h</td>
<td>9 (25)</td>
<td>--</td>
<td>12 (12.5)</td>
<td>9 (25)</td>
<td>10 (12.5)</td>
</tr>
</tbody>
</table>

--Indicates fungus is resistant to the compounds at >100 mg/ml, MIC values are given in brackets. MIC (mg/ml)=minimum inhibitory concentration, ie. Lowest concentration to completely inhibit fungal growth. Zone of Inhibition in mm.

bAmphotericin was used as standard.

6c, 6d, 6e, 6g, 6h, 6i and 6j exhibited good anti-inflammatory activities. Examining the structure-activity relationship (SAR), the bromosubstituted (6b) and diaminomethyl substituted (6f) thiopyrimidines have shown potent anti-inflammatory activity. This has revealed a new path in the synthesis of new class of Isopropyl 2-(4-substitutedbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6a-j) derivatives.

Antibacterial activity

The newly synthesized compounds were screened for their antibacterial activity against Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pyogenes and Klebsiella pneumoniae (recultured) bacterial strains by disc diffusion method.22,23 The investigation of antibacterial screening data revealed that all the tested compounds showed moderate to good bacterial inhibition. The compounds 6a, 6b, 6e, 6f, 6i and 6j showed potent activity against all the bacterial strains in Table 2.

Antifungal studies

All the newly prepared compounds were screened for their antifungal activity against Aspergillus fumigatus, Candida albicans, Penicillium marneffei and Trichophyton mentagrophytes (recultured) in DMSO by serial plate dilution method.24,25 The antifungal screening data showed moderate to good activity. Compounds 6a, 6c, 6f, 6i and 6j emerged as potent active against all the fungal strains in Table 3.

EXPERIMENTAL

All reagents and solvents (Aldrich or Merck) were purchased and used without further purification. Melting
points were determined on a Fisher-Price melting point apparatus were uncorrected. Crude products were purified by column chromatography on silica gel of 60-120 mesh. IR spectra were obtained on a Perkin Elmer BX sired FT-IR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a Varian 300 MHz spectrometer for 1H NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. LC-MS Mass spectra were recorded on a MASPEC lo resolution mass spectrometer operating at 70 eV.

5-Isopropoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-thione(4)²¹

To a solution of isopropyl acetoacetate (1 mmol), aldehyde (1.1 mmol), triacetine (1.5 mmol), SrCl₂·6H₂O (1 mmol, 10 mol%) and EtOH (20 ml). The mixture was heated at 40 °C and the progress of the reaction was monitored by TLC. After completion of the reaction (about 3-5 h) the solution was cooled to room temperature and poured into crushed ice. The resultant solid product was collected and purified by column chromatography.

Isopropyl 2-(4-substitutedbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6 a-j)

A mixture of compound 4 (2 mmol), chloroacetic acid (2 mmol), sodium acetate anhydrous (2 g) in glacial acetic acid and acetic acid anhydride (40 mL, 3:1) was refluxed for 21 min., then equimolecular amount of the appropriate aromatic aldehydes were added. The reaction mixture was refluxed for 2 h, allowed to cool, poured onto cold water; the formed precipitate was filtered off, dried and crystallized from proper solvent to give the corresponding arylmethylene thiazolopyrimidine derivatives (6a-j) respectively.

Isopropyl 2-benzylidene-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6a)

Pale yellow solid; Yield 69%; mp 196-198 °C; IR (KBr, v cm⁻¹): 2976 (C-H), 1709 (C=O), 1625 (C=N), 1549 (C=C), 641 (C-S); 1H NMR (δ, DMSO-d₆): 1.24 (d, 6H, OCH₂(CH₃)₂), 2.35 (s, 3H, Ar-CH₃), 4.21 (d, 1H, -CH), 4.91 (m, 1H, OCH(CH₃)₂), 7.20-7.52 (m, 10H, Ar-H), 7.68 (s, 1H, Ar-CH); LCMS: (m/z) 419 [M+H]. Anal. Calcd. for C₂₈H₂₃N₂O₄S: C, 68.90; H, 5.30; N, 6.69. Found: C, 69.04; H, 5.24; N, 6.73.

Isopropyl 2-(4-bromobenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6b)

Yellow solid; Yield 63%; mp 215-216 °C; IR (KBr, v cm⁻¹): 2973 (C-H), 1710 (C=O), 1613 (C=N), 1528 (C=C), 754 (C-Br), 638 (C-S); 1H NMR (δ, DMSO-d₆): 1.30 (d, 6H, OCH(CH₃)₂), 2.39 (s, 3H, Ar-CH₃), 4.27 (d, 1H, -CH), 4.93 (m, 1H, OCH(CH₃)₂), 7.08-7.64 (m, 9H, Ar-H), 7.76 (s, 1H, Ar-CH); LCMS: (m/z) 496 [M⁺] & 498 [M+2H]. Anal. Calcd. for C₂₅H₂₂BrN₂O₄S: C, 57.94; H, 4.26; N, 5.64. Found: C, 57.91; H, 4.32; N, 5.70.

Isopropyl 2-(4-ethylbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6c)

Yellow solid; Yield 75%; mp 174-175 °C; IR (KBr, v cm⁻¹): 2969 (C-H), 1711 (C=O), 1609 (C=N), 1546 (C=C), 654 (C-S); 1H NMR (δ, DMSO-d₆): 1.18 (t, 3H, -ArCH₂CH₃), 1.26 (d, 6H, OCH₂(CH₃)₂), 2.34 (s, 3H, Ar-CH₃), 2.47 (q, 2H, -ArCH₂CH₃), 4.23 (d, 1H, -CH), 4.90 (m, 1H, OCH(CH₃)₂), 6.91-7.40 (m, 9H, Ar-H), 7.70 (s, 1H, Ar-CH); LCMS: (m/z) 447 [M⁺]. Anal. Calcd. for C₂₇H₂₄N₂O₄S: C, 69.93; H, 5.87; N, 6.29. Found: C, 70.02; H, 5.95; N, 6.21.

Isopropyl 2-(4-methylbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6d)

Pale yellow solid; Yield 65%; mp 223-224 °C; IR (KBr, v cm⁻¹): 2976 (C-H), 1710 (C=O), 1617 (C=N), 1544 (C=C), 648 (C-S); 1H NMR (δ, DMSO-d₆): 1.24 (d, 6H, OCH₂(CH₃)₂), 2.28-2.33 (m, 6H, -CH₂), 4.21 (d, 1H, -CH), 4.89 (m, 1H, OCH₂(CH₃)₂), 7.08-7.35 (m, 9H, Ar-H), 7.66 (s, 1H, Ar-CH); LCMS: (m/z) 433 [M+H]. Anal. Calcd. for C₂₇H₂₃N₂O₄S: C, 69.44; H, 5.59; N, 6.48. Found: C, 69.57; H, 5.53; N, 6.52.

Isopropyl 2-(4-methoxybenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6e)

Yellow solid; Yield 76%; mp 170-171 °C; IR (KBr, v cm⁻¹): 2980 (C-H), 1706 (C=O), 1606 (C=N), 1568 (C=C), 645 (C-S); 1H NMR (δ, DMSO-d₆): 1.30 (d, 6H, OCH₂(CH₃)₂), 2.38 (s, 3H, Ar-CH₃), 3.76 (s, 3H, -ArOCH₃), 4.26 (d, 1H, -CH), 4.92 (m, 1H, OCH₂(CH₃)₂), 6.84-7.36 (m, 9H, Ar-H), 7.80 (s, 1H, Ar-CH); LCMS: (m/z) 449 [M+H]. Anal. Calcd. for C₂₇H₂₃N₂O₅S: C, 66.95; H, 5.38; N, 6.26. Found: C, 67.04; H, 5.42; N, 6.33.

Isopropyl 2-(4-dimethylamino)benzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6f)

Yellow solid; Yield 82%; mp 210-212 °C; IR (KBr, v cm⁻¹): 2973 (C-H), 1718 (C=O), 1610 (C=N), 1538 (C=C), 642 (C-S); 1H NMR (δ, DMSO-d₆): 1.30 (d, 6H, OCH₂(CH₃)₂), 2.39 (s, 3H, Ar-CH₃), 2.94 (s, 6H, -ArN(CH₃)₂), 4.28 (d, 1H, -CH), 4.92 (m, 1H, OCH₂(CH₃)₂), 6.65-7.38 (m, 9H, Ar-H), 7.78 (s, 1H, Ar-CH); LCMS: (m/z) 462 [M+H]. Anal. Calcd. for C₂₉H₂₅N₃O₅S: C, 67.65; H, 5.90; N, 9.12. Found: C, 67.75; H, 5.97; N, 9.09.

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Isopropyl 2-(4-chlorobenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6g)

Yellow solid; Yield 80%; mp 252-253 °C; IR (KBr, υ cm⁻¹): 2981 (C=H), 1712 (C=O), 1628 (C=N), 1552 (C=C), 823 (C-Cl), 648 (C-S); ¹H NMR (δ, DMSO-d₆): 1.30 (d, 6H, OCH-(CH3)₂), 2.38 (s, 3H, Ar-CH3), 4.27 (d, 1H, -CH), 4.91 (m, 1H, OCH-(CH3)₂), 7.18-7.42 (m, 9H, Ar-H), 7.74 (s, 1H, Ar-CH); LCMS: (m/z) 453 [M+H].

Anal. Calcd. for C28H22ClN2O5S: C, 70.43; H, 6.13; N, 6.08. Found: C, 70.37; H, 6.18; N, 5.99.

Isopropyl 2-(4-isopropylbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6j)

Yellow solid; Yield 69%; mp 221-223 °C; IR (KBr, υ cm⁻¹): 2980 (C=H), 1720 (C=O), 1632 (C=N), 1555 (C=C), 650 (C-S); ¹H NMR (δ, DMSO-d₆): 1.30 (d, 6H, OCH-(CH3)₂), 2.38 (s, 3H, Ar-CH3), 4.28 (d, 1H, -CH), 4.93 (m, 1H, OCH-(CH3)₂), 7.10-7.43 (m, 9H, Ar-H), 7.82 (s, 1H, Ar-CH); LCMS: (m/z) 461 [M+H].


Isopropyl 2-(4-tert-butylbenzylidene)-5-methyl-3-oxo-7-phenyl-3,7-dihydro-2H-thiazolo[3,2-a]pyrimidine-6-carboxylate (6i)

Pale yellow solid; Yield 71%; mp 201-202 °C; IR (KBr, υ cm⁻¹): 2974 (C=H), 1713 (C=O), 1618 (C=N), 1538 (C=C), 647 (C-S); ¹H NMR (δ, DMSO-d₆): 1.26 (d, 6H, OCH-(CH3)₂), 2.33 (s, 3H, Ar-CH3), 2.64 (m, 1H, -ArCH(CH3)₂), 4.20 (d, 1H, -CH), 4.89 (m, 1H, OCH-(CH3)₂), 7.12-7.38 (m, 9H, Ar-H), 7.68 (s, 1H, Ar-CH); LCMS: (m/z) 475 [M+H].


Antifungal assay

Sabourauds agar media was prepared by dissolving 1 g peptone, 4 g D-glucose, and 2 g agar in 100 cm³ distilled water, and adjusting pH to 5.7 using buffer. Normal saline was used to make a suspension of spore of fungal strain for lawnning. A loop full of particular fungal strain was transferred to 3 cm³ saline to get a suspension of corresponding species. 20 cm² of agar media was poured in to each Petri dish. Excess of suspension was decanted and the plates were dried by placing in an incubator at 37 °C for 1 h.

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Using an agar punch, wells were made and each well was labeled. A control was also prepared in triplicate and maintained at 37 °C for 3-4 d. The inhibition zones in diameter were measured and compared with the controls. The Nutrient Broth, which contained logarithmic serially two fold diluted amount of test compound and controls was inoculated with approximately 1.6×10^8-6×10^9 c.f.u cm^{-1}. The cultures were incubated for 48 h at 35 °C and the growth was monitored. The lowest concentration (highest dilution) required to arrest the growth of fungus was regarded as minimum inhibitory concentrations (MIC). Amphotericin B was used as the standard drug. The diameter of zone of inhibition and minimum inhibitory concentration values are given in Table 3.

**CONCLUSION**

In conclusion, we have described simple and efficient protocol for the synthesis of novel Isopropyl 2-thiazolopyrimidine-6-carboxylate derivatives (6a-j) with good yields. All the synthesized compounds have been investigated for their anti-inflammatory, antibacterial and antifungal activities. With our newly synthesized compounds, it is evident that 6b and 6f have highest anti-inflammatory activity; 6a, 6b, 6e, 6f, 6i and 6j have antibacterial activity; and 6a, 6c, 6f, 6i and 6j have antifungal activity. Accordingly, these novel class of Isopropyl 2-thiazolopyrimidine-6-carboxylate derivatives reported from our laboratory emerge as a valuable lead series with great potential to be used as anti-inflammatory, antibacterial and antifungal agents, and as promising candidates for further efficiency evaluation.

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