Synthesis and Antimicrobial Study of Some New Chlorosubstituted 4-Aroyl Pyrazolines

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Abstract: Chlorosubstituted heterocycles containing five members nitrogen ring have a very broad spectrum of antifungal, antibacterial and growth promoting hormonal activities. We therefore, synthesized some new chlorosubstituted 4-aroyl pyrazolines (2a-d) by the interactions of chlorosubstituted 3-aroyl flavones and 3-Aroyl Chromones with phenyl hydrazine hydrochloride and dioxane containing few drops of piperidine. The newly synthesized chlorosubstituted 4-aroyl pyrazolines were evaluated for their antimicrobial activity against E. coli, S. aureus, P. aeruginosa, P. vulgaris by disc diffusion method. The results obtained were very encouraging.

Keywords: 4-aroyl pyrazolines, E. coli, S. aureus, P. aeruginosa, P. vulgaris.

Introduction:

Some new chlorosubstituted 4-Aroylpyrazolines (2a-d) were synthesised by condensation of chlorosubstituted 3-aroyl flavones (1a-d) with phenyl hydrazine hydrochloride in DMSO medium containing a little piperidine. The structure of the comps (2a-d) were established by elemental analysis, chemical properties & spectral data.

Pyrazoline ring has fairly accessible properties and hence attracted much attention in the fast developing area of synthetic heterocyclic chemistry. It has been reported that the heterocyclic compounds containing Pyrazoline ring shows broad spectrum of biological activity. It has been revealed that substituent in the Phenyl ring enhances their antibacterial activity. It was considered worthwhile to synthesize the new chlorosubstituted 4-aroyl hydrazolines to screen them for antimicrobial activity.

The newly synthesized chlorosubstituted pyrazolines were assayed for their antimicrobial activity on E. coli, S. aureus, P. aeruginosa, P. vulgaris.
Experimental:

A) Synthesis of Chlorosubstituted Pyrazolines:

A mixture of 3-aroylflavanone (0.01 mol) and phenyl hydrazine hydrochloride (0.02 mol) in dioxane (20 ml) containing a few drops of piperidine was refluxed for 2.5 hours. After cooling, the reaction mixture was acidified with dil. HCl (1:1). The solid product thus obtained crystallized from ethanol-acetic acid mixture to get 4-aroyl pyrazolines. It gives no coloration with neutral FeCl₃ solution and dissolve in NaOH indicating thereby the presence of free phenolic –OH group.

Scheme:

Where,

R : a = C₆H₅, b = 

R₁: a = C₆H₅, b = 

i) 2a = C₆H₅COCl, 10% NaOH
   2b = COONH₄, Dry pyridine, POCl₃

ii) KOH, Pyridine

iii) Benzaldehyde, Piperidine, Furfuraldehyde, Piperidine

iv) PhNHNH₂.HCl + DMSO + Piperidine.
Table 1: Physical and Analytical Characterization of Data of Newly Synthesized Compounds

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Mol. Formula</th>
<th>Mol. Wt.</th>
<th>R</th>
<th>Rf</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
<th>Found (Calcd.)</th>
<th>Rf</th>
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<tbody>
<tr>
<td>2a</td>
<td>C₈H₆Cl₂O₂</td>
<td>205</td>
<td></td>
<td></td>
<td>70</td>
<td>53</td>
<td></td>
<td></td>
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<tr>
<td>3a</td>
<td>C₁₅H₁₀O₄Cl₂</td>
<td>308</td>
<td>-C₆H₅</td>
<td></td>
<td>75</td>
<td>65</td>
<td>58.16</td>
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</tr>
<tr>
<td>3b</td>
<td>C₁₃H₁₆O₄Cl₂</td>
<td>299</td>
<td></td>
<td></td>
<td>67</td>
<td>98</td>
<td>52.17</td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td>C₁₅H₁₀O₄Cl₂</td>
<td>338</td>
<td>-C₆H₅</td>
<td></td>
<td>75</td>
<td>112</td>
<td>58.19</td>
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<tr>
<td>4b</td>
<td>C₁₃H₁₆O₄Cl₂</td>
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<td></td>
<td></td>
<td>80</td>
<td>117</td>
<td>56.50</td>
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<tr>
<td>5a</td>
<td>C₂₀H₁₂O₄Cl₂</td>
<td>387</td>
<td>-C₆H₅</td>
<td></td>
<td>80</td>
<td>165</td>
<td>61.98</td>
<td>0.46</td>
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<tr>
<td>5b</td>
<td>C₁₅H₁₀O₅Cl₂</td>
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<td></td>
<td>85</td>
<td>156</td>
<td>64.00</td>
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<tr>
<td>5c</td>
<td>C₂₂H₁₄O₅Cl₂</td>
<td>397</td>
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<td>-C₆H₅</td>
<td>70</td>
<td>160</td>
<td>65.11</td>
<td>0.59</td>
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<tr>
<td>5d</td>
<td>C₂₀H₁₂O₄Cl₂</td>
<td>387</td>
<td></td>
<td></td>
<td>75</td>
<td>175</td>
<td>64.50</td>
<td>0.66</td>
</tr>
<tr>
<td>6a</td>
<td>C₂₆H₁₈O₃N₂Cl₂</td>
<td>505</td>
<td>-C₆H₅</td>
<td>-C₆H₅</td>
<td>80</td>
<td>80</td>
<td>64.12</td>
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<tr>
<td>6b</td>
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<td></td>
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<td>174</td>
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<tr>
<td>6c</td>
<td>C₂₈H₂₀O₂N₂Cl₂</td>
<td>515</td>
<td>-C₆H₅</td>
<td>-C₆H₅</td>
<td>60</td>
<td>155</td>
<td>55.11</td>
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<tr>
<td>6d</td>
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<td>505</td>
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<td></td>
<td>75</td>
<td>155</td>
<td>64.00</td>
<td>5.11</td>
</tr>
</tbody>
</table>

The spectral analysis of compounds 5a and 6a are given below:

(5a): IR (cm⁻¹): 1660 (>C=O), 1600 (>C=O), 1265 (C=O), 923 (2’ furyl), 820 (C=Cl); PMR (δppm): 5.20 (d 1H CH₆–CH), 5.39 (d 1H CH–CH₂), 6.22 – 7.95 (m 10H Ar – H)

(6a): IR (cm⁻¹): 3450 (O = H), 1600 (>C=O), 1560 (>C=O), 1250 (>C=O), 925 (2’ furyl), 795 (C=Cl); PMR (δppm): 5.10 (d 1H CH₆–CH), 5.43 (d 1H CH–CH₂), 6.75 – 8.19 (m 15H Ar – H), 9.5 (s 1H Ar – OH).

Discussion

The punch discs of 6.25 mm diameter of Whatman filter paper no. 1 were prepared and dispensed in the batches of 100 each in screw capped bottles. These were sterilized by dry heat at 140°C for 60 minutes. The solution of 0.01 mol dilution of test compound was prepared in diaxone solvent separately. The discs were soaked, assuming that each disc will contain approximately 0.01 mol of the test solution.

The culture media for pathogens was prepared by using following compositions for one liter distilled water:

- Peptone : 5.0 gm/liter
- Sodium chloride : 5.0 gm/liter
- Beef extract : 1.5 gm/liter
Yeast extract : 1.5 gm/liter
Agar : 15.0 gm/liter
pH (approximately) : 7.4 ± 0.2

The culture medium was thus prepared was sterilized in autoclave at 15 lbs/inch pressure and at 121°C. After sterilization, it was cooled down to about 50°C and poured into pre-sterilized petriplates of 8.5 mm in diameter each and allowed to solidify the nutrient agar medium of about 14 mm depth the petriplates were kept with nutrient broth at 37°C for 4 hours in an incubator.

The culture of pathogens was inculcated separately in petriplates on the surface nutrient agar broth uniformly with all septic precautions. The plates were dried again for 30 minutes and without further delay the discs soaked in the test compound were applied at adequate spacing 2 cm or more apart to the surface of culture medium with help of sterilized forceps. The discs were pressed gently to ensure their full contact with the medium. The control was run using plane solvent for aseptic conditions. The plates were kept in inculcator at 37°C for about 18-24 hours. Soon after the incubation period is over, the degree of sensitivity to the test compounds was determined by measuring the visible clean area of growth free zone (zones of inhibition) produced by diffusion of antibiotics into medium from the discs by Calipers in M.M. The results obtained are tabulated in Table 2.

Table 2: Antibacterial Activity Data of 4-Aroyl Pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>E. coli</th>
<th>S. aureus</th>
<th>P. aeruginosa</th>
<th>P. vulgaris</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>11</td>
<td>12</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>6b</td>
<td>14</td>
<td>15</td>
<td>13</td>
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<tr>
<td>6c</td>
<td>09</td>
<td>09</td>
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<td>11</td>
</tr>
<tr>
<td>6d</td>
<td>12</td>
<td>10</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>

Result:

It was noticed that almost all these compounds shown remarkable inhibitory activity. The compound 6a, 6b and 6d show remarkable activity against all organisms than 6b. It may be due to the presence of furol-oxy group in the nucleus. However, the compound 6c showed moderate activity against the organism.

Acknowledgement:

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References:


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