Synthesis and antimicrobial activity of some new chalcones and flavones containing substituted naphthalene moiety

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Abstract

Seven new chalcones and flavones containing substituted naphthalene nucleus in their structure were synthesized and the structures of these compounds were confirmed by spectral data. The newly synthesized compounds were screened for antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*.

Keywords: Halohydroxy substituted acetophenones, substituted naphthaldehydes, 2’-hydroxychalcones, flavones, antibacterial activity.

Introduction

The flavoniods have been reported to possess a wide range of biological activities such as antimicrobial [1-4], anticancer [5], antioxidant [6], antinociceptive [7], anti-inflammatory [8,9], antihypertensive[10] and antifeedant[11]. In view of these observations and in continuation of our work on biologically active chalcones and their heterocycles [12], we have been planned to synthesize the some new flavones (IIa-h) from chalcones (Ia-h) and also studied their antibacterial activity against *Escherichia coli* (E. coli) and *Staphylococcus aureus* (S. aureus) using Tetracycline as a standard drug.
Materials and Methods

Melting points were determined in open glass capillaries and were found uncorrected. The purity of the compounds was checked by TLC. The IR spectra of all compounds were recorded on perkin-Elmer-1420 spectrometer and \(^1\)NMR spectra (CDCl\(_3\)) on a varian 300 MHz spectrometer using TMS as internal standard (δ ppm).

**Synthesis of 1-(2’-hydroxy-5’-chlorophenyl)-3-(4-bromo naphtha-1-yl)-2-propen-1-one (Id).**
2-hydroxy-5-chloroacetophenone (1.70gm: 0.01mol) and 4-bromo-naphthalene-1-carbaldehyde (2.35gm: 0.01mol) were dissolved in ethanol (25ml), under stirring aqueous KOH solution (10%, 10ml) was added dropwise. The reaction mixture was stirred at room temperature and kept at 55 °C for 14 hr. It was then diluted with water and acidified with Conc. HCl. The solid obtained was filtered, washed with cold water and crystallised from glacial acetic acid.

IR νmax (KBr): 3200 (-OH), 1625 (C=O), 1590, 1486 (Ring C=C), 1055 (C-O) cm\(^{-1}\).

Similarly other compounds of the series were prepared by same method. Physical constant and analytical data of compounds (Ia-h) are recorded in table-1.

**Table:-1 Physical, analytical and antibacterial activity of chalcones and flavones**

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R’</th>
<th>R''</th>
<th>M.P. (°C)</th>
<th>Molecular Formula</th>
<th>Halogen analysis % found (required)</th>
<th>Antimicrobial activity %</th>
<th>Zone of Inhibition in mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia)</td>
<td>2-OH</td>
<td>4-Br</td>
<td>160</td>
<td>C(<em>{19})H(</em>{13})O(_2)Br</td>
<td>02.26 (02.40)</td>
<td>04</td>
<td>09</td>
</tr>
<tr>
<td>Ib)</td>
<td>5-Br</td>
<td>4-Br</td>
<td>122</td>
<td>C(<em>{19})H(</em>{13})O(_2)Br</td>
<td>37.13 (37.00)</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Ic)</td>
<td>3, 5-Cl</td>
<td>4-Br</td>
<td>179</td>
<td>C(<em>{19})H(</em>{13})O(_2)BrCl</td>
<td>35.78 (35.50)</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Id)</td>
<td>5-Cl</td>
<td>4-Br</td>
<td>151</td>
<td>C(<em>{19})H(</em>{13})O(_2)BrCl</td>
<td>29.80 (29.71)</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Ie)</td>
<td>3-1, 5-CH(_3)</td>
<td>2-OCH(_3)</td>
<td>102</td>
<td>C(<em>{21})H(</em>{17})O(_3)Cl</td>
<td>10.27 (10.00)</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>If)</td>
<td>3-1, 5-Cl</td>
<td>2-OCH(_3)</td>
<td>112</td>
<td>C(<em>{20})H(</em>{17})O(_3)ClII</td>
<td>34.22 (35.00)</td>
<td>14</td>
<td>18</td>
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<tr>
<td>Ig)</td>
<td>3-1, 4-CH(_3), 5-Cl</td>
<td>2-OCH(_3)</td>
<td>142</td>
<td>C(<em>{21})H(</em>{17})O(_3)ClII</td>
<td>33.34 (34.00)</td>
<td>14</td>
<td>09</td>
</tr>
<tr>
<td>Ih)</td>
<td>3-Br, 5-CH(_3)</td>
<td>2-OCH(_3)</td>
<td>137</td>
<td>C(<em>{21})H(</em>{17})O(_3)Br</td>
<td>02.15 (02.02)</td>
<td>02</td>
<td>--</td>
</tr>
<tr>
<td>Ila)</td>
<td>---------</td>
<td>4-Br</td>
<td>210</td>
<td>C(<em>{19})H(</em>{13})O(_2)Br</td>
<td>02.10 (02.21)</td>
<td>08</td>
<td>03</td>
</tr>
<tr>
<td>IIb)</td>
<td>6-Br</td>
<td>4-Br</td>
<td>245</td>
<td>C(<em>{19})H(</em>{13})O(_2)Br</td>
<td>37.83 (38.00)</td>
<td>04</td>
<td>08</td>
</tr>
<tr>
<td>IIc)</td>
<td>6-8-Cl</td>
<td>4-Br</td>
<td>190</td>
<td>C(<em>{19})H(</em>{13})O(_2)ClBr</td>
<td>34.36 (34.01)</td>
<td>14</td>
<td>19</td>
</tr>
<tr>
<td>IIId)</td>
<td>6-Cl</td>
<td>4-Br</td>
<td>255</td>
<td>C(<em>{19})H(</em>{13})O(_2)BrCl</td>
<td>28.20 (28.21)</td>
<td>11</td>
<td>03</td>
</tr>
<tr>
<td>IIe)</td>
<td>8-I, 6-CH(_3)</td>
<td>2-OCH(_3)</td>
<td>205</td>
<td>C(<em>{21})H(</em>{17})O(_3)I</td>
<td>28.35 (28.69)</td>
<td>04</td>
<td>07</td>
</tr>
<tr>
<td>IIf)</td>
<td>8-1, 6-Cl</td>
<td>2-OCH(_3)</td>
<td>201</td>
<td>C(<em>{20})H(</em>{17})O(_3)ClI</td>
<td>35.40 (35.10)</td>
<td>18</td>
<td>29</td>
</tr>
<tr>
<td>IIg)</td>
<td>8-1, 7-CH(_3), 6-Cl</td>
<td>2-OCH(_3)</td>
<td>195</td>
<td>C(<em>{23})H(</em>{17})O(_3)ClII</td>
<td>33.88 (34.09)</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>IIh)</td>
<td>8-Br, 6-CH(_3)</td>
<td>2-OCH(_3)</td>
<td>222</td>
<td>C(<em>{21})H(</em>{17})O(_3)Br</td>
<td>1.87 (02.01)</td>
<td>09</td>
<td>00</td>
</tr>
</tbody>
</table>

2-(4-Bromonaphthalen-1-yl)-6-chloro-chromen-4-one (IID): 1-(2’-hydroxy-5’-chlorophenyl)-3-(4-bromo naphtha-1-yl)-2-propen-1-one (2.67gm: 0.01mol) dissolved in DMSO (10ml), iodine (0.127gm) was added and mixture was refluxed for 1 hr. On
cooling up to 20 °C; solid separated. Separated solid obtained was filtered, washed with cold water and crystallised from dioxane.

IR $\nu_{\text{max}}$ (KBr): 1642 (C=O), 1580, 1475 (Ring C=C) cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 6.71 (s, 1H, COCH), $\delta$ 7.25-8.73 (m, 9H, Ar-H); Similarly other compounds of the series were prepared. Physical and analytical data of the compounds (IIa-h) recorded in table-1.

**Scheme- I**

**Results and Discussion**

In present work chalcones were prepared by Claisen-Schmidt condensation of Substituted 2-hydroxy acetophenones and substituted naphthaldehyde. The IR spectra of chalcones (Ia-h) showed absorption band in the region of 1625-1645 cm$^{-1}$ (C=O) and 3090-3210 cm$^{-1}$ (2'-OH). The $^1$H NMR spectra further supported for their structure and showed doublet at near $\delta$ 6.89 and another doublet at $\delta$ 7.65 due to -CH=CH- (olefinic protons) and also showed singlet in the region 12.20-13.15 due to ortho hydroxyl group.

Further chalcones (Ia-h) were converted to the corresponding flavones (IIa-h) by oxidative cyclisation of chalcones. All these flavones didn't gave violet colouration with ferric chloride solution and pink colouration with concentrated sulphuric acid. The IR spectra of flavones showed absence of band in the region 3090-3210 cm$^{-1}$ (2'-OH). The $^1$H NMR spectra showed
singlet at $\delta$ 6.89-7.10 due to –COCH proton and absence of singlet in the region 12.20-13.15 due to proton of ortho hydroxyl group.

All the newly synthesized compounds were evaluated for \textit{in vitro} antibacterial activity. The results are showed in Table-1. It has been observed that compounds \textbf{Ic, Id, If, IIC} and \textbf{IIf} indicated better activity than Standard Tetracycline. The remaining compounds were less active than the reference drug.

\textbf{Antibacterial activity}

All these chalcones and flavones were screened for their antibacterial activity against \textit{Escherichia coli} and \textit{Staphylococcus aureus} by disc diffusion method [13], using tetracycline antibiotic for comparison of activity. Compounds and tetracycline 100 $\mu$g/ml were dissolved in 5 \% aqueous DMF and used.

It was found that the compounds with chloro substituents have shown remarkable inhibition against \textit{E. coli} and \textit{S. aureus}.

\textbf{Conclusion}

In summary, we have synthesized some new 2’-hydroxychalcones by claisen-schmidt condensation and converted them into flavones. The antibacterial study show that compounds \textbf{Ic}, \textbf{Id, If, IIC} and \textbf{IIf} showed better zone of inhibition than standard antibiotic Tetracycline.

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\textbf{References}