Synthesis of some active and new E-2-(4-anisyl)-3-arylidene chromanone

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Received 8 August 2013; accepted (revised) 10 January 2015

A set of nine 3-arylidene chromanone have been synthesized by simple acid catalyzed condensation of appropriate 2-(4-anisyl) chromanone and substituted benzaldehyde using dry hydrogen chloride gas. Piperidine has been used as catalyst for the synthesis of 2-(4-anisyl)-3-arylidene chromanone. The structural assignments of the title compounds have been carried out using elemental analysis, IR and 1H NMR spectral studies.

Keywords: 2-(4-Anisyl) chromanone, substituted benzaldehyde, piperidine, dry hydrogen chloride

The E-arylidene chromanone have various biological activities1–7 and widely used as a precursor to synthesis of varied medicinal nuclei like 1,5-benzothiazepine8–10, etc. The basic structure of 3-aryldiene Chromanone have an extended conjugation at C-3 with carbonyl group (α,β unsaturation). The reaction of 3-arylidene chromanone with 5-substituted-2-aminothiophenol have been successfully carried out for the synthesis of 1,5 benzothiazepines9.

The synthesis of benzylidene chromanone has been reported in the literature in acidic11–12 and basic13–15 media. The synthesis of benzylidene Chromanone having 4-methoxy group in ring A and ring B has been reported in acidic medium11,11. The led to further synthesize a set of nine 3-aryldiene chromanone having 4-methoxy group in ring A and 4-chloro, 4-dimethylamino, 4-nitro, 4-bromo, 2-nitro, 4-hydroxy, 3-nitro, 3-chloro or 2-chloro group in ring B.

The later reaction was repeated in basic medium to obtain the desired product, m.p.136°C (reported11 m.p.89°C) equimolar was dissolved in dry ethanol and reacted with equimolar substituted benzaldehydes, the substituents being (i) p-dimethylamino benzaldehyde (ii) p-chlorobenzaldehyde (iii) p-nitrobenzaldehyde (iv) p-bromobenzaldehyde (v) o-chlorobenzaldehyde (vi) o-nitrobenzaldehyde (vii) p-hydroxybenzaldehyde (viii) m-chlorobenzaldehyde, (ix) m-nitrobenzaldehyde, by passing dry hydrogen chloride gas through the solution of the reaction mixture. The reaction mixture was kept for 24 hr at RT. The solid thus obtained, was crystallized from methanol to give corresponding 2-(4-anisyl)-3-(substitued arylidene) chromanone (Scheme I).

Spectral Studies

Homogeneity of the products was ascertained by thin layer chromatography and Rf values, m.p.’s were recorded. The final products were characterized on the basis of elemental and spectral analysis (Tables I, II and III).

The IR spectra of the products 3a–i indicated the completion of reaction and showed characteristic strong absorptions at 1730-1680 cm⁻¹ due to carbonyl stretching vibrations (C = O). The absorptions due to (C = C) was seen at 1610 cm⁻¹, vinyl C-H deformation vibrations at 870-850 cm⁻¹ (C=C-H) and skeletal vibrations of dihydro γ-pyrone ring at 1470, 1300, 1030 and 900 cm⁻¹ were observed. Besides aromatic and aliphatic CH stretching were observed at 3050 and 2950 cm⁻¹ respectively. The absorption at 785, 770 and 780 cm⁻¹ in compound 3g, 3h and 3b were indicative of the presence of ortho, meta and para chlorine, respectively and at 1550 and 1350 cm⁻¹ in 3c, 3f and 3l affirmed the presence of NO₂ group. The aliphatic C-H deformation vibrations at 1480, 1350 and 1300 cm⁻¹ were also seen. The absorption at 1230 cm⁻¹ represent the methoxy group in ring A.

The absorption at 750 cm⁻¹ in compound 3e indicate the presence of bromine and at 3410 cm⁻¹ in
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3d indicate the presence of OH group. The absorption pattern at around 810 cm\(^{-1}\) and 840 cm\(^{-1}\) were indicative of the ortho and para position in aromatic benzene ring, respectively and three peaks at around 690, 770 and 880 cm\(^{-1}\) were indicative of the meta position in aromatic benzene ring.

In the \(^1\)H NMR spectra, the absorption at \(\delta 8.10-7.4\) as a singlet may be assigned to vinyl proton, where as the absorption at \(\delta 6.1-5.88\) as a singlet may be assigned to C=H proton. Irrespective of the substituent group present in arylidene chromanone, these absorptions have been uniformly found in the spectra of all

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>m.p. (°C)</th>
<th>R_t (%)</th>
<th>Yield (Basic)</th>
<th>Molecular Formula (Mol. Wt.)</th>
<th>Elemental Analysis Found (Calcd) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>4-N(CH(_3))(_2)</td>
<td>180</td>
<td>0.81</td>
<td>75</td>
<td>C(<em>{25})H(</em>{23})O(_3)N (385)</td>
<td>78.04 5.20 12.32</td>
</tr>
<tr>
<td>3b</td>
<td>4-Cl</td>
<td>158</td>
<td>0.78</td>
<td>70</td>
<td>C(<em>{23})H(</em>{17})O(_3)Cl (376.50)</td>
<td>73.68 4.60 12.70</td>
</tr>
<tr>
<td>3c</td>
<td>4-NO(_2)</td>
<td>190</td>
<td>0.80</td>
<td>75</td>
<td>C(<em>{22})H(</em>{19})O(_5)N (387)</td>
<td>71.03 4.28 20.61</td>
</tr>
<tr>
<td>3d</td>
<td>4-OH</td>
<td>130</td>
<td>0.64</td>
<td>25</td>
<td>C(<em>{21})H(</em>{15})O(_4) (358)</td>
<td>77.03 4.95 17.82</td>
</tr>
<tr>
<td>3e</td>
<td>4-Br</td>
<td>153</td>
<td>0.57</td>
<td>68</td>
<td>C(<em>{22})H(</em>{15})O(_3)Br (421)</td>
<td>65.24 4.02 11.31</td>
</tr>
<tr>
<td>3f</td>
<td>2-NO(_2)</td>
<td>124</td>
<td>0.65</td>
<td>90</td>
<td>C(<em>{23})H(</em>{15})O(_3)N (387)</td>
<td>70.94 4.30 20.59</td>
</tr>
<tr>
<td>3g</td>
<td>2-Cl</td>
<td>145</td>
<td>0.60</td>
<td>26</td>
<td>C(<em>{22})H(</em>{17})O(_4)Cl (376.50)</td>
<td>73.54 4.62 12.72</td>
</tr>
<tr>
<td>3h</td>
<td>3-Cl</td>
<td>172</td>
<td>0.76</td>
<td>44</td>
<td>C(<em>{22})H(</em>{17})O(_3)Cl (376.50)</td>
<td>73.42 4.48 12.68</td>
</tr>
<tr>
<td>3i</td>
<td>3-NO(_2)</td>
<td>157</td>
<td>0.66</td>
<td>32</td>
<td>C(<em>{22})H(</em>{17})O(_3)N (387)</td>
<td>70.89 4.33 20.62</td>
</tr>
</tbody>
</table>

Compd 3a 3b 3c 3d 3e 3f 3g 3h 3i
R 4-N(CH\(_3\))\(_2\)-4-Cl-4-NO\(_2\)-4-OH 4-Br 2-NO\(_2\)-2-Cl 3-Cl 3-NO\(_2\)

Scheme I
compounds. The absorption due to such protons in arylidene chromanones have been found to be not affected by the presence of electron releasing or electron attracting substituents present in arylidene and phenyl groups of the 3-arylidene chromanone. The characterization of the cis-form (cis to the carbonyl group) and trans-structure have been reported\(^\text{13}\) to be distinct in the \(^1\)H NMR spectra of the arylidene chromanones. In the cis-form, vinyl proton absorbs much upfield i.e. at \(\delta\) 6.4 and the trans-form at downfield at around \(\delta\) 8.3. Vinyl proton in nine 3-arylidene chromanone are also absorbed downfield at around \(\delta\) 8.0.

It is further reported\(^\text{12,13}\) that the reaction of chromanone with aryl aldehydes mainly result into formation of the trans-forms.

All spectra showed the characteristic 3 proton signal (3H) at \(\delta\) 3.48 to 3.34 as singlet indicating the presence of methoxyl protons in the phenyl ring of the benzylidene chromanones. In the spectra of 3a, a 6H singlet at \(\delta\) 3.20 in addition to a 3H singlet at \(\delta\) 3.45 indicating the presence of N(CH\(_3\))\(_2\) and OCH\(_3\) groups respectively.

In the spectra of 3d, absorption at \(\delta\) 7.02 as a singlet indicating the presence of OH group. Besides, a doublet (\(J = 8\)Hz) at \(\delta\) 6.12 equivalent to two proton may be assigned to C\(_2\)-H and C\(_5\)-H protons. Another doublet (\(J = 8\)Hz) at \(\delta\) 6.46 equivalent to two proton may be assigned to C\(_2\)-H and C\(_6\)-H protons. Thus these two doublets downfield may be due to the four protons of the ring A. Thus, the detailed study of the spectra indicate that, the product in the trans form is the main product.
Experimental Section
All the melting points are uncorrected. Homogeneity of the compounds was checked by TLC on glass plate coated with silica gel G using solvent system, benzene: ethanol: aq. ammonia (7:2:1). The IR spectra were taken in KBr pellets on a Shimadzu FTIR spectrophotometer. $^1$H NMR spectra were recorded on a Jeol 90 MHz FT NMR spectrometer.

Synthesis of $E$-2-(4-methoxyphenyl)-3-(substituted benzylidene)flavanone 3c
Equimolar quantities of 4-methoxy chromanone 1 and 4-nitro benzaldehyde 2c were dissolved in ice-cold ethanol saturated with dry HCl gas. To this reaction mixture, dry HCl gas was passed with stirring in the solution till yellow colour persisted. The reaction mixture was kept for 24 hr at RT to separate the solid. The crude solid thus obtained was crystallized from methanol to afford the aryldiene chromanone 2-(4-methoxyphenyl)-3-(4-nitrobenzylidene) chromanone (3c, yellow crystals, m.p. 190°C, yield 75%). Similarly other compound 3a,b,d-i were prepared. It is reported$^{12}$ that $(E)$-3-arylidene chromanone was formed in 92-95%, this indicates that the main product is $(E)$-3-arylidene chromanone.

Acknowledgement
The authors wish to thank Dr. Ghanshyam Lal, Principal R. R. Govt. College, Alwar and Shri G. K. Sharma Head Department of Chemistry for providing necessary facilities. One of the authors (BSS) is grateful to UGC New Delhi for the award of a minor research project. Another author (VPB) is also grateful to UGC New Delhi for the award of RGNF fellowship. Authors also thank CDRI Lucknow for some of the analytical and spectral work.

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