Chapter - II

SYNTHESIS OF 2-HYDROXY-3-H/SUBSTITUTED-5-METHYL-α-BROMOACETOPHENONES AND 2-(2'/4'-H/SUBSTITUTED)BENZYLIDENE-5-METHYL-7-H/SUBSTITUTED COUMARAN-3-ONES
Abstract -

Interaction of 2-hydroxy-5-methylacetophenone (I) with bromine in acetic acid have been investigated in different reaction conditions and also (I) was first nitrated with nitrating mixture, followed by bromination to obtain 2-hydroxy-3-H/substituted-5-methyl-α-bromoacetophenones (III), (IV) and (VI) respectively. The products thus obtained were further cyclized by condensing with various aromatic aldehydes in alkaline alcoholic medium to synthesize 2-(2'/4'-H/substituted)benzylidene-5-methyl-7-H/substituted coumaran-3-ones (VIII-Xa-f). The compounds synthesised in these reactions were characterised on the basis of conventional elemental analysis, chemical characteristics and IR and NMR spectral studies.

Introduction -

Organic chemistry of acetophenone, its compounds and coumaran-3-ones with special reference to their applications in pharmaceutical, medicinal, industrial and biological sciences¹⁻¹⁴ have been briefly reviewed (General Introduction, Page 2 to 11). As 2-hydroxy-5-methyl acetophenone contains phenolic –OH and acetyl group in the same molecule, so it was thought interesting to use it as an intermediate in the synthesis of highly reactive methylene compounds. Hence interactions of 2-hydroxy-5-methylacetophenone have been carried out with bromine in acetic acid in two different reaction conditions to isolate 2-hydroxy-5-methyl-α-bromoacetophenone (III) and 2-hydroxy-3-bromo-5-methyl-α-bromoacetophene (IV). 2-Hydroxy-5-methylacetophenone (I) was further nitrated with nitric acid (conc.) in presence of sulphuric acid (conc.) to obtain nitroacetophenone which on further bromination in acetic acid yielded2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) (Scheme-1).
In view of the utility of these compounds in various fields and as a part of research work, presently being undertaken in this laboratory in the synthesis of newer type of benzenoids and heterocyclic compounds, it appeared sufficiently fascinating to investigate the reactions of 2-hydroxy-5-methyl-α-bromoacetophenone (III), 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone (IV), 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) with various aldehydes in alkaline alcoholic medium to provide alternative and somewhat direct and easy route for the synthesis of coumaran-3-ones also named as aurones (Scheme-2).
Scheme - 2

The present investigation deals with suitable method for the synthesis of yet new series of 2-hydroxy-3-H/substituted-5-methyl-α-bromoacetophenone and 2-(2'/4'-H/substituted)benzylidene-5-methyl-7-H/substituted coumaran-3-ones, which are hitherto unknown. With the above aims and objectives the present syntheses were carried out.

This chapter is divided into 2 sections, Section-A and Section-B.
Results and Discussion -

Section - A

Synthesis of 2-hydroxy-3H/substituted-5-methyl-α-bromoacetophenones

(i) Reaction of 2-hydroxy-5-methylacetophenone and bromine in hot condition:

Synthesis of 2-hydroxy-5-methyl-α-bromoacetophenone (III)

2-Hydroxy-5-methyl-α-bromoacetophenone (III) was synthesised by refluxing 2-hydroxy-5-methylacetophenone (I) and bromine in acetic acid (II) for 15 minutes. The reaction mixture was poured in ice cold water, brownish white crystals were separated out which were washed several times with cold water and recrystallized with aqueous acetic acid, yield 87%, mp 52°C. The reaction of the formation of (III) is depicted below.

Properties of (III):

1. It is brownish white, lachrymal, crystalline solid, mp 52°C.
2. It contains carbon, hydrogen and bromine elements.
3. It gives deep violet colouration with aqueous ferric chloride indicating the presence of phenolic –OH group.
4. The Rf value was found to be 0.32 in dioxane solvent on silica gel-G plate with layer thickness of 0.3 mm.
5. **Elemental analysis**:

<table>
<thead>
<tr>
<th>Elements</th>
<th>%Found</th>
<th>%Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>46.81</td>
<td>47.16</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>3.82</td>
<td>3.93</td>
</tr>
<tr>
<td>Bromine</td>
<td>34.77</td>
<td>34.90</td>
</tr>
</tbody>
</table>

6. From analytical data the molecular formula was found to be $\text{C}_x\text{H}_y\text{O}_z\text{Br}$.

7. **IR Spectrum** : The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 1. The important absorption can be correlated as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm$^{-1}$)</th>
<th>Assignment</th>
<th>Absorption expected (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3422</td>
<td>H-bonded phenolic $\text{–OH}$ stretching</td>
<td>3500-3000$^{17,18}$</td>
</tr>
<tr>
<td>1636</td>
<td>$\text{&gt;C=O}$ stretching in o-hydroxy aryl ketone</td>
<td>1676-1635$^{19-21}$</td>
</tr>
<tr>
<td>669</td>
<td>Aliphatic $\text{C–Br}$ stretching</td>
<td>667$^{22-24}$</td>
</tr>
</tbody>
</table>

The carbonyl stretching was observed at 1636 cm$^{-1}$. The lower value of $\nu$ may be due to intramolecular hydrogen bonding.

8. **PMR** : The PMR spectrum was carried out in CDCl$_3$+ DMSO-$d_6$ solvent with TMS as an internal standard and reproduced on PMR-Sheet 1.

This spectrum$^{15,16,25-30}$ distinctly displayed the signals due to Ar–OH protons at $\delta$ 11.50 ppm, Ar-H protons at $\delta$ 6.85-7.63 ppm, $\text{–CH}_2$– protons $\delta$ 4.40 ppm, and $\text{–CH}_3$ protons at $\delta$ 2.35 ppm.

The signals at $\delta$ 1.25-1.45 are due to moisture in CDCl$_3$/DMSO-$d_6$. 

S. S. Aswale, Ph.D. Thesis ... 61
All the above observations confirm the structure of compound (III) as 2-hydroxy-5-methyl-α-bromoacetophenone.

(III)

ii) Reaction of 2-hydroxy-5-methylacetophenone and bromine in ice cold condition:

Synthesis of 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone (IV):

Interaction of 2-hydroxy-5-methylacetophenone (I) and bromine in acetic acid (II) was carried out in ice cold (0-5°C) condition to yield 2-hydroxy-3-bromo-5-methylacetophenone (Ia). The product was then refluxed with bromine in acetic acid which on further pouring in ice-cold water yielded 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone (IV), yield 84%, mp 136°C.
Properties of (IV):

1. It is pale yellowish, crystalline solid, mp 136°C.
2. It contains carbon, hydrogen and bromine elements.
3. It gives violet colouration with aqueous ferric chloride indicating the presence of phenolic -OH group.
4. The Rf value was found to be 0.31.
5. Elemental analysis:

<table>
<thead>
<tr>
<th>Elements</th>
<th>%Found</th>
<th>%Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>34.79</td>
<td>35.06</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>2.25</td>
<td>2.58</td>
</tr>
<tr>
<td>Bromine</td>
<td>51.52</td>
<td>51.90</td>
</tr>
</tbody>
</table>

6. From analytical data the molecular formula was found to be C₉H₅O₂Br₂.
7. IR Spectrum: The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 2. The important absorption can be correlated as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm⁻¹)</th>
<th>Assignment</th>
<th>Absorption expected (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3403</td>
<td>H-bonded phenolic -OH stretching</td>
<td>3500-3000⁻¹⁷,¹⁸</td>
</tr>
<tr>
<td>1645</td>
<td>&gt;C=O stretching in o-hydroxy aryl ketone</td>
<td>1676-1635⁻¹⁹,²¹</td>
</tr>
<tr>
<td>663</td>
<td>Aliphatic C–Br stretching</td>
<td>650²²,²⁴</td>
</tr>
<tr>
<td>713</td>
<td>Aromatic C–Br stretching</td>
<td>711³¹, 740³²</td>
</tr>
</tbody>
</table>

The carbonyl stretching was observed at 1645 cm⁻¹. The lower value of ν may be due to intramolecular hydrogen bonding.
8. **PMR**: The PMR spectrum was carried out in CDCl₃ + DMSO-d₆ solvent with TMS as an internal standard and reproduced on PMR-Sheet 2.

This spectrum distinctively displayed the signals due to Ar–OH protons at δ 11.79 ppm, Ar–H protons at δ 6.71-7.66 ppm, –CH₂– protons δ 4.40 ppm, and –CH₃ protons at δ 2.34 ppm.

The signals at δ 1.25-1.45 are due to moisture in CDCl₃/DMSO-d₆.

All the above observations confirm the structure of compound (IV) as 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone.

![Chemical Structure](IV)

iii) **Synthesis of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI):**

Interaction of 2-hydroxy-5-methylacetophenone (I) and HNO₃ (conc.) in presence of H₂SO₄ (conc.) (V) was carried out at 0-5°C to obtain 2-hydroxy-3-nitro-5-methylacetophenone (Ib) which on further refluxing with bromine in acetic acid (II) yielded 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) on pouring in ice cold water, yield 82%, mp 88°C.

![Chemical Reaction](chemical_reaction)
Properties of (VI):

1. It is golden brown coloured crystalline solid, mp 88°C.
2. It contains carbon, hydrogen, nitrogen and bromine as elements.
3. It gives purple colouration with aqueous ferric chloride indicating the presence of phenolic –OH group.
4. It gives diazotization test after reduction by Zn dust and HCl, showing the presence of –NO₂ group.
5. The Rf value was found to be 0.31 for dioxane as solvent on silica gel-G plate with layer thickness 0.3 mm.
6. **Elemental analysis:**

<table>
<thead>
<tr>
<th>Elements</th>
<th>% Found</th>
<th>% Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>39.25</td>
<td>39.42</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>2.75</td>
<td>2.92</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>4.87</td>
<td>5.01</td>
</tr>
<tr>
<td>Bromine</td>
<td>29.01</td>
<td>29.20</td>
</tr>
</tbody>
</table>

7. From analytical data the molecular formula was found to be C₉H₈O₂NBr.
8. **IR Spectrum:** The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 3. The important absorption can be correlated as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm⁻¹)</th>
<th>Assignment</th>
<th>Absorption expected (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3404</td>
<td>H-bonded phenolic –OH stretching</td>
<td>3500-3000¹⁷,¹⁸</td>
</tr>
<tr>
<td>1652</td>
<td>&gt;C=O stretching in o-hydroxy aryl ketone</td>
<td>1655-1635¹⁹-²¹</td>
</tr>
<tr>
<td>663</td>
<td>Aliphatic C–Br stretching</td>
<td>650²²-²⁴</td>
</tr>
<tr>
<td>1530</td>
<td>Ar–NO₂ asymmetric stretching</td>
<td>1550-1490³³-³⁵</td>
</tr>
<tr>
<td>1356</td>
<td>Ar–NO₂ symmetric stretching</td>
<td>1355-1315³³-³⁵</td>
</tr>
</tbody>
</table>
9. **PMR**: The PMR spectrum was carried out in CDCl$_3$ + DMSO-$d_6$ solvent with TMS as internal standard and reproduced on PMR-Sheet 3.

This spectrum$^{15,16,25-30}$ distinctly displayed the signals due to Ar-OH protons at $\delta$ 12.44 ppm, Ar-H protons at $\delta$ 7.25-8.09 ppm, $-CH_2$ protons $\delta$ 4.55 ppm, and $-CH_3$ protons at $\delta$ 2.40 ppm.

The signals at $\delta$ 1.25-1.45 are due to moisture in CDCl$_3$/DMSO-$d_6$.

All the above observations confirm the structure of compound (VI) as 2-hydroxy-3-nitro-5-methyl-$\alpha$-bromoacetophenone.

\[
\begin{align*}
\text{NO}_2 & \\
\text{H}_3\text{C} & \\
\text{OH} & \\
\text{C} - \text{CH}_2 - \text{Br} & \\
\text{O} & \\
\end{align*}
\]

(VI)

Section - B:

**Synthesis of 2-(2/4'-H/substituted)benzylidene-5-methyl-7-H/substituted coumaran-3-ones**

i) **Synthesis of 2-benzylidene-5-methylcoumaran-3-ones (VIIa)**:

Reaction mixture of 2-hydroxy-5-methyl-$\alpha$-bromoacetophenone (III) and benzaldehyde (VIIa) in ethanol medium was refluxed upto just boiling. To it 40% NaOH solution was added in hot condition, the solution acquired red colour. It was kept for 24 hrs at room conditions. A thick syrupy liquid was obtained. It was poured in aqueous HCl (1:1) to produce middle buff coloured crystals, yield 82%, mp 112°C.

\[
\begin{align*}
\text{H}_3\text{C} & \\
\text{OH} & \\
\text{C} - \text{CH}_2 - \text{Br} & \\
\text{O} & \\
\end{align*}
\]

(III)

\[
\begin{align*}
\text{H} & \\
\text{C} & \\
\text{O} & \\
\text{CH} & \\
\text{C} & \\
\text{C} & \\
\end{align*}
\]

(VIIa)

\[
\begin{align*}
\text{H}_3\text{C} & \\
\text{OH} & \\
\text{C} - \text{CH}_2 - \text{Br} & \\
\text{O} & \\
\end{align*}
\]

(VIIIa)
Properties of (VIIIa):

1. It is middle buff coloured crystalline solid, mp 112°C.
2. It contains carbon and hydrogen as elements.
3. It gives yellow colouration after addition of aqueous ferric chloride solution which clearly indicates that the phenolic hydroxy group is absent and involved into cyclization.
4. The Rf value was found to be 0.31 for dioxane as solvent.
5. **Elemental analysis:**

<table>
<thead>
<tr>
<th>Elements</th>
<th>% Found</th>
<th>% Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>81.21</td>
<td>81.36</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>4.94</td>
<td>5.08</td>
</tr>
</tbody>
</table>

6. From analytical data the molecular formula was found to be $C_{16}H_{12}O_2$.

7. **IR Spectrum**: The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 4. The important absorption can be correlated as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm$^{-1}$)</th>
<th>Assignment</th>
<th>Absorption expected (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1715</td>
<td>C=O stretching in 5 membered ring</td>
<td>1745$^{16}$</td>
</tr>
<tr>
<td>1286</td>
<td>C–O–C stretching in 5 membered ring</td>
<td>1205-1253$^{37}$</td>
</tr>
</tbody>
</table>

IR spectrum indicates the cyclization by:

p) Absence of band in the range 3600-3200 cm$^{-1}$ for phenolic –OH group.

q) Increase in frequency of carbonyl group from 1636 to 1715 cm$^{-1}$.

r) The appearance of band at 1286 for C–O–C stretching.
8. **PMR**: The PMR spectrum was carried out in CDCl$_3$ + DMSO-$d_6$ solvent with TMS as an internal standard and reproduced on PMR-Sheet 4.

This spectrum\textsuperscript{15,16,25-30} distinctly displayed the signals due to Ar–H protons at $\delta$ 6.57-7.86 ppm, –CH protons at $\delta$ 4.48 ppm and –CH$_3$ protons $\delta$ 2.24 ppm.

The signals at $\delta$ 1.25-1.45 are due to moisture in CDCl$_3$/DMSO-$d_6$.

From all the above observations, compound (VIIa) may be assigned the structure as 2-benzylidene-5-methylcoumaran-3-one.

![Structure of VIIa]

Similarly, (VIIb-f) were synthesized by the above method and are enlisted in Table-1.

**Table - 1**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compd.</th>
<th>Aldehyde</th>
<th>2-(2′/4′-H/ substi- tuted) benzylidene-5-methylcoumaran-3-ones</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(VIIb)</td>
<td>Salicylaldehyde (VIIb)</td>
<td>2-(2′-hydroxy) benzylidene-5-methylcoumaran-3-one</td>
<td>85</td>
<td>205</td>
<td>PO Red</td>
</tr>
<tr>
<td>2.</td>
<td>(VIIc)</td>
<td>Anisaldehyde (VIIc)</td>
<td>2-(4′-methoxy) benzylidene-5-methylcoumaran-3-one</td>
<td>82</td>
<td>96</td>
<td>Sand stone</td>
</tr>
<tr>
<td>3.</td>
<td>(VIIId)</td>
<td>p-Chlorobenzaldehyde (VIIId)</td>
<td>2-(4′-chloro) benzylidene-5-methylcoumaran-3-one</td>
<td>78</td>
<td>144</td>
<td>Brick red</td>
</tr>
<tr>
<td>4.</td>
<td>(VIIe)</td>
<td>p-Nitrobenzaldehyde (VIIe)</td>
<td>2-(4′-nitro) benzylidene-5-methylcoumaran-3-one</td>
<td>81</td>
<td>80</td>
<td>Noble red</td>
</tr>
<tr>
<td>5.</td>
<td>(VIIIf)</td>
<td>p-N-dimethylamino benzaldehyde (VIIIf)</td>
<td>2-(4′-N-dimethylamino) benzylidene-5-methylcoumaran-3-one</td>
<td>84</td>
<td>94</td>
<td>Crimson red</td>
</tr>
</tbody>
</table>

*Gave satisfactory results of C, H, N and Cl elemental analysis.
ii) Synthesis of 2-benzylidene-5-methyl-7-bromocoumaran-3-ones (IXa):

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone (IV) and benzaldehyde (VIIa) in ethanol medium was refluxed up to just boiling. To it 40% NaOH solution was added in hot condition, the red coloured solution was obtained. It was kept for 24 hrs at room conditions. A thick syrupy liquid was obtained. It was poured in aqueous HCl (1:1) to yield candy coloured product, yield 80%, mp 115°C.

![Chemical Structures](image)

Properties of (IXa):

1. It is candy coloured crystalline compound, mp 115°C.
2. It contains carbon, hydrogen and bromine as elements.
3. It gives yellow colouration after addition of aqueous ferric chloride solution which clearly indicates that the phenolic hydroxy group is absent and involved into cyclization.
4. The Rf value was found to be 0.32 for dioxane as solvent.
5. Elemental analysis:

<table>
<thead>
<tr>
<th>Elements</th>
<th>% Found</th>
<th>% Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>60.88</td>
<td>60.95</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>3.37</td>
<td>3.49</td>
</tr>
<tr>
<td>Bromine</td>
<td>25.31</td>
<td>25.40</td>
</tr>
</tbody>
</table>

S. S. Aswale, Ph.D. Thesis ... 69
6. From analytical data the molecular formula was found to be $\text{C}_{16}\text{H}_{11}\text{O}_{2}\text{Br}$.

7. **IR Spectrum**: The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 5. The important absorption can be correlated as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm$^{-1}$)</th>
<th>Assignment</th>
<th>Absorption expected (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1726</td>
<td>C=O stretching in 5 membered ring</td>
<td>1745$^{36}$</td>
</tr>
<tr>
<td>1244</td>
<td>C−O-C stretching in 5 membered ring</td>
<td>1205-1253$^{37}$</td>
</tr>
<tr>
<td>706</td>
<td>Aromatic C−Br stretching</td>
<td>711$^{31}$</td>
</tr>
</tbody>
</table>

IR spectrum indicates the cyclization by:

p) Absence of band in the range 3600-3200 cm$^{-1}$ for phenolic −OH group.

q) Increase in frequency of carbonyl group from 1645 to 1726 cm$^{-1}$.

r) The appearance of band at 1244 cm$^{-1}$ for C−O−C stretching.

8. **PMR**: The PMR spectrum was carried out in CDCl$_3$+ DMSO-$d_6$ solvent with TMS as internal standard and reproduced on PMR-Sheet No. 5.

This spectrum$^{15,16,25-30}$ distinctly displayed the signals due to Ar−H protons at $\delta$ 7.18-8.58 ppm, −CH protons at $\delta$ 4.50 ppm and −CH$_3$ protons $\delta$ 2.41 ppm.

The signals at $\delta$ 1.25-1.45 are due to moisture in CDCl$_3$/DMSO-$d_6$.

From all the above observations, compound (IXa) may be assigned the structure as 2-benzylidene-5-methyl-7-bromocoumaran-3-one.

![Structure of IXa](image)
Similarly, (IXb-f) were synthesized by the above method and are enlisted in Table-2.

### Table - 2*

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compd.</th>
<th>Aldehyde</th>
<th>2-(2/4'-H/substituted) benzylidene-5-methyl-7-bromocoumaran-3-ones</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(IXb)</td>
<td>Salicylaldehyde (VIIb)</td>
<td>2-(2'-hydroxy) benzylidene-5-methyl-7-bromocoumaran-3-one</td>
<td>78</td>
<td>135</td>
<td>Golden brown</td>
</tr>
<tr>
<td>2.</td>
<td>(IXc)</td>
<td>Anisaldehyde (VIIc)</td>
<td>2-(4'-methoxy) benzylidene-5-methyl-7-bromocoumaran-3-one</td>
<td>76</td>
<td>132</td>
<td>Middle buff</td>
</tr>
<tr>
<td>3.</td>
<td>(IXd)</td>
<td>p-Chlorobenzaldehyde (VIIId)</td>
<td>2-(4'-chloro) benzylidene-5-methyl-7-bromocoumaran-3-one</td>
<td>81</td>
<td>164</td>
<td>Pinkish brown</td>
</tr>
<tr>
<td>4.</td>
<td>(IXe)</td>
<td>p-Nitrobenzaldehyde (VIIe)</td>
<td>2-(4'-nitro) benzylidene-5-methyl-7-bromocoumaran-3-one</td>
<td>75</td>
<td>98</td>
<td>Orange</td>
</tr>
<tr>
<td>5.</td>
<td>(IXf)</td>
<td>p-N-dimethylamino benzaldehyde (VIIi)</td>
<td>2-(4'-N-dimethylamino) benzylidene-5-methyl-7-bromocoumaran-3-one</td>
<td>83</td>
<td>92</td>
<td>Brown</td>
</tr>
</tbody>
</table>

*Gave satisfactory results of C, H, N, Br elemental analysis.

### iii) Synthesis of 2-benzylidene-5-methyl-7-nitrocoumaran-3-ones (Xa):

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) and benzaldehyde (VIIa) in ethanol medium was refluxed upto just boiling. To it 40% NaOH solution was added. It was kept for 24 hrs at room conditions. A thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1) to yield red coloured product, yield 68%, mp 145°C.

![Diagram](image-url)
Properties of (Xa):

1. It is red coloured crystalline compound, mp 145°C.
2. It contains carbon, hydrogen and nitrogen as elements.
3. It gives yellow colouration after addition of aqueous ferric chloride solution which clearly indicates that the phenolic hydroxy group is absent and involved into cyclization.
4. The Rf value was found to be 0.30 for dioxane as solvent on silica gel-G plate with layer of thickness 0.3 mm.
5. It gives diazotization test after reduction by zinc dust and HCl, showing the presence of $-\text{NO}_2$ group.
6. **Elemental analysis:**

<table>
<thead>
<tr>
<th>Elements</th>
<th>% Found</th>
<th>% Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>67.77</td>
<td>68.33</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>4.68</td>
<td>4.91</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>4.44</td>
<td>4.98</td>
</tr>
</tbody>
</table>

7. From analytical data the molecular formula was found to be $\text{C}_{16}\text{H}_{11}\text{NO}_4$.
8. **IR Spectrum:** The IR spectrum was carried out in KBr pellets and is reproduced on IR-Sheet 6. The important absorption band can be correlated\textsuperscript{15-24,31-37} as follows.

<table>
<thead>
<tr>
<th>Absorption observed (cm$^{-1}$)</th>
<th>Assignment</th>
<th>Absorption expected (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1694</td>
<td>C=O stretching in 5 membered ring</td>
<td>1745\textsuperscript{36}</td>
</tr>
<tr>
<td>1267</td>
<td>C–O–C stretching in 5 membered ring</td>
<td>1205-1253\textsuperscript{37}</td>
</tr>
<tr>
<td>1532</td>
<td>Ar–NO$_2$ asymmetric stretching</td>
<td>1550-1490\textsuperscript{33-35}</td>
</tr>
<tr>
<td>1346</td>
<td>Ar–NO$_2$ symmetric stretching</td>
<td>1355-1315\textsuperscript{33-35}</td>
</tr>
</tbody>
</table>
IR spectrum indicates the cyclization by -

p) Absence of band in the range 3600-3200 cm\(^{-1}\) for phenolic \(-\text{OH}\) group.
q) Increase in frequency of carbonyl group from 1652 to 1698 cm\(^{-1}\).
r) The appearance of band at 1260 cm\(^{-1}\) for C-\(\text{O}-\text{C}\) stretching.

9. **PMR**: The PMR spectrum was carried out in CDCl\(_3\) + DMSO-\(d_6\) solvent with TMS as internal standard and reproduced on PMR-Sheet 6.

This spectrum\(^{15,16,25-30}\) distinctly displayed the signals due to Ar-\(\text{H}\) protons at \(\delta\) 6.90-8.12 ppm, \(-\text{CH}\) protons at \(\delta\) 4.60 ppm and \(-\text{CH}_3\) protons \(\delta\) 2.45 ppm.

The signals at \(\delta\) 1.25-1.45 are due to moisture in CDCl\(_3\)/DMSO-\(d_6\).

From all the above observations, compound (Xa) may be assigned the structure as 2-benzylidene-5-methyl-7-nitrocoumaran-3-one.

![Structure of (Xa)](image)

Similarly, (Xb-f) were synthesized by the above method and are enlisted in Table-3.

### Table - 3*

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compd</th>
<th>Aldehyde</th>
<th>2-(2'/4'-H/substituted) benzylidene-5-methyl-7-nitrocoumaran-3-ones</th>
<th>Yield (%)</th>
<th>mp (°C)</th>
<th>Colour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(Xb)</td>
<td>Salicylaldehyde (VIIb)</td>
<td>2-(2'-hydroxy) benzylidene-5-methyl-7-nitrocoumaran-3-one</td>
<td>64</td>
<td>160</td>
<td>Reddish brown</td>
</tr>
<tr>
<td>2.</td>
<td>(Xc)</td>
<td>Anisaldehyde (VIIc)</td>
<td>2-(4'-methoxy) benzylidene-5-methyl-7-nitrocoumaran-3-one</td>
<td>67</td>
<td>168</td>
<td>Brown</td>
</tr>
<tr>
<td>3.</td>
<td>(Xd)</td>
<td>p-Chlorobenzaldehyde (VIId)</td>
<td>2-(4'-chloro) benzylidene-5-methyl-7-nitrocoumaran-3-one</td>
<td>70</td>
<td>182</td>
<td>Golden brown</td>
</tr>
<tr>
<td>4.</td>
<td>(Xe)</td>
<td>p-Nitrobenzaldehyde (VIIe)</td>
<td>2-(4'-nitro) benzylidene-5-methyl-7-nitrocoumaran-3-one</td>
<td>62</td>
<td>112</td>
<td>Leaf brown</td>
</tr>
<tr>
<td>5.</td>
<td>(Xf)</td>
<td>p-N,N-dimethylanobenzaldehyde (VIIf)</td>
<td>2-(4'-N,N-dimethylamino) benzylidene-5-methyl-7-nitrocoumaran-3-one</td>
<td>69</td>
<td>118</td>
<td>Coffee brown</td>
</tr>
</tbody>
</table>

*Gave satisfactory results of C, H, N and Cl elemental analysis.
Experimental - 

The melting points of all the synthesised compounds were recorded using hot paraffin bath and are uncorrected. The carbon and hydrogen analysis was carried out on Carlo-Ebra-1106 analyser, nitrogen estimation was carried out on Colman-N-analyser-29. IR spectra were recorded on Perkin Elmer spectrometer in the range 4000-400 cm$^{-1}$ in KBr pellets. PMR spectra were recorded on Bruker AC-300F spectrometer using CDCl$_3$ and DMSO-$d_6$ as solvent with TMS as internal standard. The purity of the compounds was checked on Silica Gel-G plates by TLC with layer thickness of 0.30 mm. All chemicals used were of AR grade (India make) which were used to synthesise $\alpha$-bromo-acetophenones and coumaran-3-ones. 2-Hydroxy-5-methylacetophenone has been prepared by known described method.

Preparation of 2-hydroxy-5-methylacetophenone (I):

Reaction mixture of p-cresol (1 M, 100 ml), acetic anhydride (1 M, 120 ml) and fused sodium acetate (8.2 g) was refluxed for 2 hrs. The reaction mixture was cooled and poured in water at room conditions with constant stirring to obtain heterogenous liquid system. Organic layer was separated out and washed several times with water and distilled at 205°C in an oil bath to isolate p-cresylacetate. This p-cresylacetate (1 M, 100 ml) was further refluxed with anhydrous AlCl$_3$ (260 g) in Kjeldahl's flask at 120°C in an oil bath for 1.5 hrs to yield thick sticky liquid which was poured in ice-cold water containing conc. HCl (2 ml) to obtain a white solid. It was filtered and crystallized by aqueous acetic acid, yield 82%, mp 58°C.
Experiment No. 1:

Synthesis of 2-hydroxy-5-methyl-α-bromoacetophenone (III):

A reaction mixture of 2-hydroxy-5-methylacetophenone (I) (0.1M, 15 g) and acetic acid (150 ml) was refluxed on gentle Bunsen burner directly. During refluxing a solution of bromine in acetic acid [70 ml, (25%, 6.4 ml bromine in 93.6 ml acetic acid)] was added dropwise in the reaction mixture. After complete addition of the brominating mixture it was cooled and poured in an ice-cold water, the brownish white crystals were separated out. It was washed several times with cold-water and recrystallized with aqueous acetic acid, yield 87%, mp 52°C.

Experiment No. 2:

Synthesis of 2-hydroxy-3-bromo-5-methyl-α-bromoacetophenone (IV):

2-Hydroxy-5-methylacetophenone (I) (0.1 M, 15 g) was dissolved in acetic acid (150 ml) at 0-5°C. To this cold solution, bromine in acetic acid [70 ml, (25%, 6.4 ml bromine in 93.6 ml acetic acid)] was added dropwise and it was kept for 15 minutes, maintaining the same temperature. Then the reaction mixture was poured in ice-cold water, pale yellow coloured crystals were separated out. It was recrystallized from aqueous acetic acid, yield 75%, mp 90°C. On characterization it was found to be 2-hydroxy-3-bromo-5-methylacetophenone (Ia). A reaction mixture of (Ia) (0.1 M, 22.9g) in acetic acid (150 ml) was further refluxed. During refluxing a solution of bromine in acetic acid [70 ml, (25%, 6.4 ml bromine in 93.6 ml acetic acid)] was added dropwise. After complete addition the reaction mixture was cooled and poured in an ice-cold water, pale cream colour shiny crystals were obtained and recrystallised from aqueous acetic acid, yield 84%, mp 136°C.
Experiment No. 3 :

Synthesis of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) :

2-Hydroxy-5-methylacetophenone (I) (0.1 M, 15 g) was dissolved in acetic acid (150 ml) containing acetic anhydride (5 ml) at 0-5°C. To this a cold nitrating mixture (V) [50 ml, (3:2, 30 ml conc. HNO₃ + 20 ml conc. H₂SO₄)] was added dropwise with constant stirring and maintaining the temperature at 0-5°C, shiny needle shape yellow colour crystals separated out. It was kept for 15 minutes at same temperature. After filtration, crystals were washed several times with distilled water. It was recrystallized from aqueous acetic acid, yield 80%, mp 120°C. On characterization it was found to be 2-hydroxy-3-nitro-5-methylacetophenone (Ib). A reaction mixture of (Ia) (0.1 M, 19.5 g) in acetic acid (150 ml) was refluxed. During refluxing a solution of bromine in acetic acid (70 ml) was added dropwise. The reaction mixture was cooled and poured in ice-cold water, shiny golden brown colour crystals were obtained and recrystallized from aqueous acetic acid, yield 82%, mp 88°C.

Experiment No. 4 :

Synthesis of 2-benzylidene-5-methylcoumaran-3-one (VIIa) :

Reaction mixture of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g), benzaldehyde (VIIa) (0.01 M, 1 ml) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions. A thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce middle buff coloured crystals. It was recrystallized with aqueous alcohol, yield 82%, mp 112°C.
Experiment No. 5 :

Synthesis of 2-(2'-hydroxy)benzylidene-5-methylcoumaran-3-one (VIIIb):

Interaction of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g) and salicylaldehyde (VIIb) (0.01 M, 1.2 ml) was carried out in ethanol medium (15 ml) up to just boiling. To this reaction mixture 40% NaOH solution (5 ml) was added in hot condition with constant stirring. The solution acquired red colour. It was kept for 24 hrs at room conditions to obtain a thick syrupy liquid. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce maroon coloured product. It was crystallized with aqueous alcohol, yield 85%, mp 205°C.

Experiment No. 6 :

Synthesis of 2-(4'-methoxy)benzylidene-5-methylcoumaran-3-one (VIIIc):

Reaction mixture of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g), anisaldehyde (VIIc) (0.01 M, 1.2 ml) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, to obtain thick syrupy liquid. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce sandstone coloured product. It was crystallized with aqueous alcohol, yield 82%, mp 96°C.

Experiment No. 7 :

Synthesis of 2-(4'-chloro)benzylidene-5-methylcoumaran-3-one (VIIIId):

Reaction mixture of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g), p-chlorobenzaldehyde (VIIId) (0.01 M, 1.41 g) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid
was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce brick red coloured product. It was crystallized with aqueous alcohol, yield 78%, mp 144°C.

Experiment No. 8:

Synthesis of 2-(4'-nitro)benzylidene-5-methylcoumaran-3-one (VIIe):

Reaction mixture of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g), p-nitrobenzaldehyde (VIIe) (0.01 M, 1.51 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce red coloured product. It was crystallized with aqueous alcohol, yield 81%, m.p. 80°C.

Experiment No. 9:

Synthesis of 2-(4'-N-dimethylamino)benzylidene-5-methylcoumaran-3-one (VIIIf):

Reaction mixture of 2-hydroxy-5-methyl-α-bromoacetophenone (III) (0.01 M, 2.28 g), p-N-dimethylaminobenzaldehyde (VIIIf) (0.01 M, 1.5 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce crimson red coloured product. It was crystallized with aqueous alcohol, yield 84%, mp 94°C.
Experiment No. 10:

Synthesis of 2-benzylidene-5-methyl-7-bromocoumaran-3-one (IXa):

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-\(\alpha\)-bromoacetophenone (IV) (0.01 M, 3.07 g), benzaldehyde (VIlia) (0.01 M, 1 ml) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce candy leaf brown coloured product. It was crystallized with aqueous alcohol, yield 80%, mp 115°C.

Experiment No. 11:

Synthesis of 2-(2'-hydroxy)benzylidene-5-methyl-7-bromocoumaran-3-one (IXb):

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-\(\alpha\)-bromoacetophenone (IV) (0.01 M, 3.07 g), salicylaldehyde (Villb) (0.01 M, 1.2 ml) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce golden brown coloured product. It was crystallized with aqueous alcohol, yield 78%, mp 135°C.

Experiment No. 12:

Synthesis of 2-(4'-methoxy)benzylidene-5-methyl-7-bromocoumaran-3-one (IXc):

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-\(\alpha\)-bromoacetophenone (IV) (0.01 M, 3.07 g), anisaldehyde (VIlle) (0.01 M, 1.2 ml) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was
added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce middle buff coloured product. It was crystallized with aqueous alcohol, yield 76%, mp 132°C.

Experiment No. 13:

**Synthesis of 2-(4'-chloro)benzylidene-5-methyl-7-bromocoumaran-3-one (IXd):**

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-α-bromoaceto-phenone (IV) (0.01 M, 3.07 g), p-chlorobenzaldehyde (VIIId) (0.01 M, 1.41 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce pinkish brown coloured product. It was crystallized with aqueous alcohol, yield 81%, mp 164°C.

Experiment No. 14:

**Synthesis of 2-(4'-nitro)benzylidene-5-methyl-7-bromocoumaran-3-one (IXe):**

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-α-bromoaceto-phenone (IV) (0.01 M, 3.07 g), p-nitrobenzaldehyde (VIIe) (0.01 M, 1.51 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce orange coloured product. It was crystallized with aqueous alcohol, yield 75%, mp 98°C.

S. S. Aswale, Ph.D. Thesis... 80
Experiment No. 15:

Synthesis of 2-(4'-N-dimethylamino)benzylidene-5-methyl-7-bromo-coumaran-3-one (IXf):

Reaction mixture of 2-hydroxy-3-bromo-5-methyl-α-bromoaceto-phenone (IV) (0.01 M, 3.07 g) p-N-dimethylaminobenzaldehyde (VIIf) (0.01 M, 1.5 g) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce brown coloured product. It was crystallized with aqueous alcohol, yield 83%, mp 92°C.

Experiment No. 16:

Synthesis of 2-benzylidene-5-methyl-7-nitrocoumaran-3-one (Xa):

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoaceto-phenone (VI) (0.01 M, 2.74 g), benzaldehyde (VIIa) (0.01 M, 1 ml) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce red coloured product. It was crystallized with aqueous alcohol, yield 68%, mp 145°C.

Experiment No. 17:

Synthesis of 2-(2'-hydroxy)benzylidene-5-methyl-7-nitrocoumaran-3-one (Xb):

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoaceto-phenone (VI) (0.01 M, 2.74 g), salicylaldehyde (VIIb) (0.01 M, 1.2 ml) and ethanol (15 ml) was refluxed up to just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution
acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce reddish brown coloured product. It was crystallized with aqueous alcohol, yield 64%, mp 160°C.

Experiment No. 18:

**Synthesis of 2-(4'-methoxy)benzylidene-5-methyl-7-nitrocoumaran-3-one (Xc):**

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) (0.01 M, 2.74 g), anisaldehyde (VIIc) (0.01 M, 1.2 ml) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce brown coloured product. It was crystallized with aqueous alcohol, yield 67%, mp 168°C.

Experiment No. 19:

**Synthesis of 2-(4'-chloro)benzylidene-5-methyl-7-nitrocoumaran-3-one (Xd):**

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) (0.01 M, 2.74 g), p-chlorobenzaldehyde (VIIIc) (0.01 M, 1.41 g) and ethanol medium (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce golden brown coloured product. It was crystallized with aqueous alcohol, yield 70%, mp 182°C.
Experiment No. 20:

Synthesis of 2-(4'-nitro)benzylidene-5-methyl-7-nitrocoumaran-3-one (Xe):

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) (0.01 M, 2.74 g), p-nitrobenzaldehyde (VIIe) (0.01 M, 1.51 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce leaf brown coloured product. It was crystallized with aqueous alcohol, yield 62%, mp 112°C.

Experiment No. 21:

Synthesis of 2-(4'-N-dimethylamino)benzylidene-5-methyl-7-nitrocoumaran-3-one (Xf):

Reaction mixture of 2-hydroxy-3-nitro-5-methyl-α-bromoacetophenone (VI) (0.01 M, 2.74 g), p-N-dimethylaminobenzaldehyde (VIIf) (0.01 M, 1.5 g) and ethanol (15 ml) was refluxed upto just boiling. To this 40% NaOH solution (5 ml) was added in hot condition with constant stirring, then the solution acquired red colour. It was kept for 24 hrs at room conditions, when a thick syrupy liquid was obtained. This liquid was poured in aqueous HCl (1:1 molar ratio, 100 ml) to produce coffee brown coloured product. It was crystallized with aqueous alcohol, yield 69%, mp 118°C.
REFERENCES


