Chapter 5

Microwave assisted synthesis of 3-(coumarin-3-yl)-furo[3,2-c] coumarins and 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines
Microwave assisted synthesis of 3-(coumarin-3-yl)-furo[3,2-c]coumarins and 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines

The work presented in this chapter deals with microwave assisted synthesis of various 3-(coumarin-3-yl)-furo[3,2-c]coumarins and 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines. The synthesis of various 3-(coumarin-3-yl)-furo[3,2-c]coumarins has been carried out by reacting various 4-hydroxy coumarins with 3-(ω-bromoacetyl) coumarins under MWI. The synthesis of 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines has been carried out by reacting various 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones (coumarin chalcones) with hydrazine hydrate in acetic acid or propionic acid under MWI. The structures of all the compounds synthesized have been supported by analytical and spectral data.

5.1 Introduction

Microwave assisted organic synthesis has revolutionized organic syntheses. Compounds can be synthesized within a very short time, a fraction of a time required by classical thermal methods. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes.

During the last decade, microwave heating has become a convenient and widely used tool in organic synthesis. In the past few decades, especially when heating was necessary, oil baths and heating jackets were the main equipments used. These traditional heating techniques are slow and time-consuming, and sometimes can lead to overheating and decomposition of the substrates and products. To this end, microwave irradiation (MWI) has not only dramatically accelerated organic reactions and reduced reaction time from days or
hours to minutes, but also improved yields and selectivity.\textsuperscript{1-3} Microwave technologies have found especially extensive application in medicinal chemistry and pharmaceuticals in the field of drug discovery. The demand for new chemical compounds is continuously growing in medicinal chemistry, thereby promoting the development of new technologies, which are designed for fast synthesis of large number of compounds. Acceleration of chemical reactions by microwave irradiation enables both the intensification of already existing methods and the development of new processes in medicinal chemistry.

Synthesis of heterocycles is one of the most widely used area in the microwave chemistry. Furthermore, heterocycles are among the most frequently encountered scaffolds in drugs and pharmaceutically relevant substances. Because of the drug like character and considerable range of structural diversity, large collections or libraries of diverse heterocycles are routinely employed in high-throughput screening at early stages of drug discovery programs. Due to potential of automatization, microwave technology has become one of the most suitable methods for synthesis of large heterocycle libraries. Moreover, microwave heating has emerged as a powerful technique to promote a variety of chemical reactions.\textsuperscript{4-6} Microwave reactions under solvent-free conditions are attractive in offering reduced pollution with simplicity in processing and handling.\textsuperscript{7-8} The recent introduction of single-mode technology\textsuperscript{9} assures safe and reproducible experimental procedures and microwave synthesis has gained acceptance and popularity among the synthetic chemist community. The growing number of publications in microwave-assisted syntheses includes virtually all types of chemical reactions such as additions, substitutions, eliminations, hydrolysis, hydrogenation, cyclization, aromatization, fragmentations etc.\textsuperscript{10-15} The prominence of coumarins in natural products and biologically active molecules has promoted considerable efforts toward their synthesis. As a “prevailed” scaffold, furocoumarin shows
interesting biological properties, presumably related to the natural defense of plants against fungal attack. It is inherently photosensitive and found to have therapeutic uses. Many furocoumarins are recorded to have phototoxic effects to insects, fungi, viruses and bacteria.

Furocoumarins having furan ring fused to benzene ring of coumarin, like psoralen, xanthotoxin have interesting therapeutic properties. Furocoumarins with furan ring fused to the lactone ring of coumarin are also naturally occurring and they also possess variety of physiological activities. Coumestrol (3,9-dihydroxy benzofuro[3,2-c]coumarin) is a naturally occurring furocoumarin known for its estrogenic properties. Owing to the natural occurrence and varied biological activities, the synthesis of furocoumarins has remained a subject of an active interest and extensive work on furocoumarins has been carried out by various workers. Recently, synthesis, natural occurrence and biological activity of furocoumarins have been reviewed by L Santana et al.

Considering the importance of furocoumarins earlier a variety of furocoumarin derivatives were synthesized in our laboratory. In continuation of our interest in synthesizing furocoumarin derivatives, recently various 3-(coumarin-3-yl)furo[3,2-c]coumarin derivatives have been synthesized in our laboratory. These compounds have been synthesized by the reaction of various 4-hydroxy coumarins with 3-(ω-bromoacetyl) coumarins in the presence of ammonium acetate and acetic acid through classical thermal method. The synthesis of these compounds is outlined in scheme 1.

\[
\text{Scheme 1}
\]
As earlier mentioned, the microwave assisted synthesis enhances the reaction rate as well as improves the yield of the product by decreasing the formation of byproducts, many researchers have resynthesized variety of compounds using microwave irradiation and studied the yields, reaction time period etc. with respect to earlier conventional method results. Many coumarin derivatives have also been resynthesized using microwave irradiation and dramatical reduction in time period and improvement in yields has been observed\textsuperscript{29-31}. Looking to these encouraging reports, it was thought worthwhile to resynthesize these 3-(coumarin-3-yl)-furo[3,2-c] coumarins under microwave irradiation and to study the effect on yield, reaction time etc. with respect to earlier conventional method used.

5.2 Present work

As discussed in the introduction, in the present work various 3-(coumarin-3-yl)furo[3,2-c] coumarins have been resynthesized. The compounds have been synthesized by reacting 4-hydroxy coumarins with 3-(ω-bromoacetyl) coumarins in the presence of ammonium acetate and acetic acid using microwave irradiation (Scheme 2). The yield and reaction time observed in the present synthesis have been compared with those observed using earlier classical thermal method.

\begin{center}
\textbf{Scheme 2}
\end{center}

5.2.1 Synthesis of 3-(coumarin-3-yl)-furo [3,2-c] coumarins (3a-l)

Various 4-hydroxy coumarins (1a-d) were reacted with 3-(ω-bromoacetyl)coumarins (2a-c) in the presence of ammonium acetate and acetic acid using microwave irradiation (Scheme 3).
The reaction of 4-hydroxy coumarins (1a-d) with 3-(ω-bromoacetyl) coumarins (2a-c) proceeded smoothly and gave products 3-(coumarin-3-yl)-furo[3,2-c]coumarins (3a-l) in excellent yield i.e. 73-86%. Earlier by conventional thermal method these compounds were obtained in 53-80% yield. In addition to yield there is a drastic

**Scheme 3**
reduction in the reaction time also. In the present synthesis, the formation of compounds (3a-l) took place within 4-7 minutes while it took 16 hours in earlier synthesis.

The formation of (3a-l) follows a well known Feist-Benary synthesis mechanism\textsuperscript{32,33}.

The structures of all the compounds (3a-l) were confirmed by analytical and spectral data.

Thus the condensation of 4-hydroxy coumarin (1a) with 3-(ω-bromoacetyl) coumarin (2a) in the presence of ammonium acetate and acetic acid proceeded smoothly within 4 minutes and gave the expected product (3a) as a white solid in 80% yield.

The IR spectrum of compound 3a (Fig 1) showed a strong band at 1725 cm\(^{-1}\), which is due to carbonyl stretching of δ-lactone ring present in coumarin moiety. The band observed at 1627 cm\(^{-1}\) is due to aromatic C=C stretching vibrations. A band observed at 1126 cm\(^{-1}\) is due to C-O-C stretching of furan moiety. A band observed at 3061 cm\(^{-1}\) is due to aromatic C-H stretching.

The PMR spectrum of compound 3a (Fig 2) showed the multiplet integrating for eight protons between 7.35-8.01 δ. This is due to eight aromatic protons. A singlet appeared at 8.79 δ for one proton is due to C\(_2\)-H proton of furan ring. A singlet appeared at 9.39 δ for one proton is due to C\(_4\)-H of coumarin ring.

The \(^{13}\)C spectrum of compound 3a (Fig 3) showed signals at 108.01, 112.38, 116.27, 117.01, 118.90, 119.30, 121.27, 124.71, 124.78, 128.96, 131.37, 131.88, 142.85, 146.43, 152.60, 152.86, 158.52, 158.82, 159.60 and 159.78 δ corresponding to twenty different types of carbon atoms present in the compound. The DEPT-90 spectrum of compound 3a (Fig 4) showed signals at 116.27, 117.01, 121.27, 124.71, 124.78, 128.96, 131.37, 131.88, 142.85 and 146.43 δ, which are due to ten tertiary carbon atoms.

The mass spectrum of compound 3a (Fig 5) showed M+ peak at 330(100%) (m/z %) along with some other fragments peaks at 302
(26%), 246(16%), 218(18%), 189(29%), 151(9%), 126(9%), 109(5%), 94(10%), 81(4%) etc.

The IR and NMR data for the other compounds (3b-l) are given below.

**Compound 3b**

<table>
<thead>
<tr>
<th>Property</th>
<th>Data</th>
</tr>
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<tbody>
<tr>
<td>IR (cm(^{-1}))</td>
<td>(\nu_{\text{max}}) 1730 (C=O stretching of (\delta)-lactone of coumarin), 1605 and 3060 (aromatic C=C and C-H stretching), 1115 (C-O-C stretching of furan ring)</td>
</tr>
<tr>
<td>PMR ((\delta), ppm)</td>
<td>2.50 (3H, singlet, CH(_3)), 7.35-7.76 (7H, multiplet, aromatic protons), 8.78 (1H, singlet, C(_2)-H of furan ring), 9.40 (1H, singlet, C(_4)-H of coumarin ring)</td>
</tr>
<tr>
<td>(^{13})C-NMR ((\delta), ppm)</td>
<td>21.06(CH(_3)), 107.99(C), 112.12(C), 116.31(CH), 116.78(CH), 117.14(C), 118.91(C), 119.38(C), 120.91(CH), 124.75(CH), 129.05(CH), 131.88(CH), 132.53(CH), 134.71(C), 142.91(CH), 146.39(CH), 150.87(C), 152.94(C), 158.78(C), 159.01(C), 159.96(C)</td>
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</tbody>
</table>

**Compound 3c**

<table>
<thead>
<tr>
<th>Property</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (cm(^{-1}))</td>
<td>(\nu_{\text{max}}) 1730 (C=O stretching of (\delta)-lactone of coumarin), 1590 and 3050 (aromatic C=C and C-H stretching), 1115 (C-O-C stretching of furan ring)</td>
</tr>
<tr>
<td>PMR ((\delta), ppm)</td>
<td>2.56 (3H, singlet, CH(_3)), 7.30-7.83 (7H, multiplet, aromatic protons), 8.78 (1H, singlet, C(_2)-H of furan ring), 9.41 (1H, singlet, C(_4)-H of coumarin ring)</td>
</tr>
<tr>
<td>(^{13})C-NMR ((\delta), ppm)</td>
<td>15.95(CH(_3)), 107.84(C), 112.08(C), 116.27(CH), 117.10(C), 118.83(C), 118.88(CH), 119.36(C), 124.38(CH), 124.71(CH), 126.59(C), 128.88(CH), 131.81(CH), 132.65(CH), 142.80(CH), 146.35(CH), 151.05(C), 152.86(C), 158.59(C), 159.31(C), 159.89(C)</td>
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**Compound 3d**

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<th>Property</th>
<th>Data</th>
</tr>
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<tbody>
<tr>
<td>IR (cm(^{-1}))</td>
<td>(\nu_{\text{max}}) 1730 (C=O stretching of (\delta)-lactone of coumarin), 1615 and 3055 (aromatic C=C and C-H stretching), 1125 (C-O-C stretching of furan ring)</td>
</tr>
<tr>
<td>Compound 3e</td>
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<tr>
<td><strong>PMR</strong>&lt;br&gt;(δ, ppm)&lt;br&gt;(Fig 10)</td>
<td>7.37-7.96 (7H, multiplet, aromatic protons), 8.81 (1H, singlet, C2-H of furan ring), 9.34 (1H, singlet, C4-H of coumarin ring)</td>
</tr>
<tr>
<td><strong>13C-NMR</strong>&lt;br&gt;(δ, ppm)&lt;br&gt;(Fig 11)</td>
<td>108.76(C), 113.49(C), 116.46(CH), 116.84(C), 118.54(CH), 119.11(C), 119.30(C), 120.75(CH), 124.85(CH), 129.08(CH), 130.41(C), 131.42(CH), 132.11(CH), 143.03(CH), 147.01(CH), 150.92(C), 152.94(C), 157.49(C), 157.99(C), 159.82(C)</td>
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<tr>
<td><strong>13C-NMR</strong>&lt;br&gt;(δ, ppm)&lt;br&gt;(Fig 13)</td>
<td>56.38(OCH3), 110.31(C), 110.93(C), 112.33(C), 113.10(C), 114.11(CH), 116.04(C), 116.82(C), 117.17(CH), 119.99(C), 120.53(CH), 121.42(CH), 125.10(CH), 125.30(CH), 131.76(CH), 144.04(CH), 146.67(CH), 152.44(C), 153.76(C), 158.79(C), 160.72(C)</td>
</tr>
</tbody>
</table>
**Compound 3g**

**IR (cm⁻¹)**  
ν\(_{\text{max}}\) 1730 (C=O stretching of δ-lactone of coumarin), 1595 and 3040 (aromatic C=C and C-H stretching), 1120 (C-O-C stretching of furan ring)

**PMR (δ, ppm) (Fig 16)**  
2.53 (3H, singlet, CH₃), 4.02 (3H, singlet, OCH₃), 7.15-7.86 (6H, multiplet, aromatic protons), 8.71 (1H, singlet, C₂-H of furan ring), 9.30 (1H, singlet, C₄-H of coumarin ring)

**¹³C-NMR (δ, ppm) (Fig 17)**  
15.57(CH₃), 56.39(OCH₃), 107.28(C), 111.90(C), 113.13(C), 114.30(CH), 115.97(C), 116.59(C), 118.08(C), 119.07(CH), 119.91(C), 120.54(CH), 125.18(CH), 125.39(CH), 126.92(C), 133.30(CH), 142.00(C), 144.40(CH), 146.67(CH), 150.74(C), 157.90(C), 160.07(C)

**Compound 3h**

**IR (cm⁻¹)**  
ν\(_{\text{max}}\) 1725 (C=O stretching of δ-lactone of coumarin), 1605 and 3065 (aromatic C=C and C-H stretching), 1100 (C-O-C stretching of furan ring)

**PMR (δ, ppm) (Fig 18)**  
4.02 (3H, singlet, OCH₃), 7.15-7.97 (6H, multiplet, aromatic protons), 8.79 (1H, singlet, C₂-H of furan ring), 9.30 (1H, singlet, C₄-H of coumarin ring)

**¹³C-NMR (δ, ppm) (Fig 19)**  
56.34(OCH₃), 113.19(C), 113.34(C), 113.56(C), 114.13(CH), 114.92(C), 116.64(C), 118.62(CH), 119.84(C), 120.03(C), 120.48(CH), 120.89(CH), 125.11(CH), 127.14(C), 130.79(C), 131.72(CH), 134.25(C), 143.96(CH), 147.02(CH), 159.20(C), 159.84(C)

**Compound 3i**

**IR (cm⁻¹)**  
ν\(_{\text{max}}\) 1730 (C=O stretching of δ-lactone of coumarin), 1590 and 3050 (aromatic C=C and C-H stretching), 1115 (C-O-C stretching of furan ring)

**PMR (δ, ppm) (Fig 20)**  
7.41-8.62 (10H, multiplet, aromatic protons), 8.94 (1H, singlet, C₂-H of furan ring), 10.56 (1H, singlet, C₄-H of coumarin ring)
This text contains data on 

\begin{tabular}{ll}
\textbf{Compound 3j} & \\
IR (cm\textsuperscript{-1}) & \quad \nu_{\text{max}} 1735 (C=O stretching of \(\delta\)-lactone of coumarin), 1600 and 3060 (aromatic C=C and C-H stretching), 1115 (C-O-C stretching of furan ring) \\
PMR (\(\delta\), ppm) & 2.51 (3H, singlet, CH\textsubscript{3}), 7.42-8.53 (9H, multiplet, aromatic protons), 8.86 (1H, singlet, C\textsubscript{2}-H of furan ring), 10.47 (1H, singlet, C\textsubscript{4}-H of coumarin ring) \\
\textbf{Compound 3k} & \\
IR (cm\textsuperscript{-1}) & \quad \nu_{\text{max}} 1730 (C=O stretching of \(\delta\)-lactone of coumarin), 1590 and 3050 (aromatic C=C and C-H stretching), 1115 (C-O-C stretching of furan ring) \\
PMR (\(\delta\), ppm) & 2.55 (3H, singlet, CH\textsubscript{3}), 7.27-8.51 (9H, multiplet, aromatic protons), 8.84 (1H, singlet, C\textsubscript{2}-H of furan ring), 10.47 (1H, singlet, C\textsubscript{4}-H of coumarin ring) \\
\end{tabular}
Compound 3l

IR (cm\(^{-1}\))

\(\nu_{\text{max}}\) 1735 (C=O stretching of \(\delta\)-lactone of coumarin), 1590 and 3060 (aromatic C=C and C-H stretching), 1110 (C-O-C stretching of furan ring)

PMR (\(\delta\), ppm) (Fig 26)

7.47-8.52 (9H, multiplet, aromatic protons), 8.89 (1H, singlet, C\(_2\)-H of furan ring), 10.43 (1H, singlet, C\(_4\)-H of coumarin ring)

\(^{13}\)C-NMR (\(\delta\), ppm) (Fig 27)

110.89(C), 113.04(C), 113.20(C), 113.94(C), 115.87 (CH), 116.09(C), 118.53(CH), 118.62(C), 118.72(CH), 120.90 (CH), 122.26(CH), 126.70(CH), 128.94(CH), 129.02(C), 130.59(C), 131.09(C), 131.89(CH), 134.31 (CH), 140.47 (CH), 146.98(CH), 150.61(C), 152.23(C), 159.59(C), 161.26(C)
**Fig 1** IR spectrum of compound 3a

**Fig 2** PMR spectrum of compound 3a
Fig 3  $^{13}$C NMR spectrum of compound 3a

Fig 4  DEPT-90 spectrum of compound 3a
Fig 5  Mass spectrum of compound 3a
Fig 6  PMR spectrum of compound 3b

Fig 7  $^{13}$C NMR spectrum of compound 3b
Fig 8  PMR spectrum of compound 3c

Fig 9  $^{13}$C NMR spectrum of compound 3c
Fig 10  PMR spectrum of compound 3d

Fig 11  $^{13}$C NMR spectrum of compound 3d
Fig 12  PMR spectrum of compound 3e

Fig 13  $^{13}$C NMR spectrum of compound 3e
Fig 14  PMR spectrum of compound 3f

Fig 15  $^{13}$C NMR spectrum of compound 3f
Fig 16  PMR spectrum of compound 3g

Fig 17  $^{13}$C NMR spectrum of compound 3g
Fig 18  PMR spectrum of compound 3h

Fig 19  $^{13}$C NMR spectrum of compound 3h
Fig 20  PMR spectrum of compound 3i

Fig 21  $^{13}$C NMR spectrum of compound 3i
Fig 22  PMR spectrum of compound 3j

Fig 23  $^{13}$C NMR spectrum of compound 3j
Fig 24  PMR spectrum of compound 3k

Fig 25  $^{13}$C NMR spectrum of compound 3k
Fig 26  PMR spectrum of compound 3l

Fig 27  $^{13}$C NMR spectrum of compound 3l
5.2.2 Coumarin substituted pyrazolines

Pyrazolines are important nitrogen containing five membered heterocyclic compounds. Several pyrazoline derivatives showed considerable biological activities, e.g. antimicrobial, central nervous system and immuno-suppressive activities. Considering the importance of pyrazolines and with a view to incorporating this heterocycle in coumarin moiety, Brahmbhatt et al. had synthesized various 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines by reacting 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones(coumarin chalcones) with hydrazine hydrate in acetic acid or propionic acid using conventional thermal method. The work is outlined in scheme 4.

![Scheme 4](image)

The success obtained in resynthesizing 3-(coumarin-3-yl)-furo[3,2c]coumarins (3a-l) (Scheme 3) using microwave irradiation, prompted author to resynthesize above mentioned coumarin substituted pyrazolines also using microwave irradiation. Therefore in the present work various 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines have been synthesized by reacting 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones(coumarin chalcones) with hydrazine hydrate in acetic acid or propionic acid using microwave irradiation.

5.2.3 Synthesis of 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines (5a-j)

The reaction of appropriate 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones(coumarin chalcones) (4a-e) with hydrazine hydrate in acetic acid or propionic acid under microwave irradiation gave expected 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines (5a-j) in 78-86% yield (Scheme 5).
The formation of (5a-j) was observed very fast (4-7 minutes) and with good yields (78-86%) compared to the earlier conventional thermal method\textsuperscript{37} were by formation of the products took place in 3 hours and yields were 67-80%.

The structures of all the compounds (5a-j) were confirmed by analytical and spectral data.

Thus the microwave irradiation of 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-one (coumarin chalcone) (4a) with hydrazine hydrate
in the presence acetic acid proceeded smoothly within 5 minutes and gave the expected product (5a) as a yellow solid in 78% yield.

The IR spectrum of 5a (Fig 28) showed strong bands at 1720 and 1662 cm\(^{-1}\) which are due to carbonyl stretching of \(\delta\)-lactone ring present in coumarin nucleus and carbonyl of \(-\text{N-CO-CH}_3\) group respectively. The bands observed at 1605 and 1566 cm\(^{-1}\) are due to aromatic C=C and C=N stretching vibrations respectively. A sharp and intense band observed at 765 cm\(^{-1}\) is due to C-H out of plane bending vibrations for mono substituted phenyl ring. The band observed at 3060 cm\(^{-1}\) is due to aromatic C-H stretching vibrations.

The PMR spectrum of compound 5a (Fig 29 and 30) showed a signal at 2.46 \(\delta\) integrating for three protons. This is due to methyl group \(-\text{N-CO-CH}_3\). A doublet of doublet centered at 3.43 \(\delta\) (\(J = 19.0\) and 4.8 Hz) integrating for one proton, is due to \(\text{C}_4\)-H\(_{\text{trans}}\). A doublet of doublet centered at 3.98 \(\delta\) (\(J = 19.0\) and 12.0 Hz) integrating for one proton, is due to \(\text{C}_4\)-H\(_{\text{cis}}\). A doublet of doublet centered at 5.61 \(\delta\) (\(J = 12.0\) and 4.8 Hz) integrating for one proton, is due to proton attached at \(\text{C}_5\). Nine aromatic protons were observed between 7.21-7.64 \(\delta\) as a multiplet. The \(\text{C}_4\)'-H of coumarin ring appeared as a singlet at 8.45 \(\delta\).

The \(^{13}\text{C}\) NMR spectrum of compound 5a (Fig 31) showed signals at 21.93, 44.33, 60.47, 116.66, 118.82, 119.72, 124.97, 125.51, 127.70, 128.80, 128.88, 132.86, 140.92, 141.45, 150.86, 154.15, 159.14 and 168.94 \(\delta\) corresponding to eighteen different type of carbon atoms present in the compound. The signal appeared at 21.93 \(\delta\) is due to carbon of methyl group \(-\text{N-CO-CH}_3\). The most downfield signal appeared at 168.94 \(\delta\) can be assigned to the carbonyl carbon of \(-\text{N-CO-CH}_3\) group of pyrazoline nucleus. The DEPT-135 spectrum (Fig 32) showed signals at 21.93\(-\text{N-CO-CH}_3\), 44.33(\text{CH}_3), and also signals at 60.47, 116.66, 124.97, 125.51, 127.70, 128.80, 128.88, 132.86 and 140.92 \(\delta\) corresponding to nine different type of non equivalent tertiary carbon atoms present in the compound.
The mass spectrum of compound 5a (Fig 33) showed M+ peak at 332(55%) (m/z %) along with some other fragments peaks at 333 (11%), 289(78%), 255(74%), 213(100%), 187(32%), 115(54%), 77(36%), 57(52%), 55(43%), 43(98%) etc. The appearance of molecular ion peak at 332 mass unit supports the structure of compound 5a.

The IR and NMR data for other compounds (5b-j) are given below.

**Compound 5b**

| IR $(\text{cm}^{-1})$ | $\nu_{\text{max}}$ 1725 and 1665 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1610 and 1570 (aromatic C=C and C=N stretching), 825 (C-H bending vibration of p-disubstituted benzene ring), 3050 (aromatic C-H stretching) |
| PMR $(\delta, \text{ppm})$ (Fig 34) | 2.32 (3H, singlet, CH$_3$), 2.44 (3H, singlet, -N-CO-CH$_3$), 3.42 (1H, doublet of a doublet, $J = 18.8$ and 4.8 Hz, C$_4$-H$_{\text{trans}}$), 3.96 (1H, doublet of a doublet, $J = 18.8$ and 12.0 Hz, C$_4$-H$_{\text{cis}}$), 5.58 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$-H), 7.11-7.64 (8H, multiplet, aromatic protons), 8.45 (1H, singlet, C$_4$'-H of coumarin ring) |
| $^{13}$C-NMR $(\delta, \text{ppm})$ (Fig 35) | 21.09(CH$_3$), 21.98(CH$_3$), 44.28(CH$_2$), 60.26(CH), 116.67(CH), 118.85(C), 119.84(C), 124.94(CH), 125.50(CH), 128.77(CH), 129.52(CH), 132.79(CH), 137.36(C), 138.60(C), 140.79(CH), 150.72(C), 154.14(C), 159.15(C), 168.85(C) |

**Compound 5c**

| IR $(\text{cm}^{-1})$ | $\nu_{\text{max}}$ 1720 and 1670 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1600 and 1565 (aromatic C=C and C=N stretching), 830 (C-H bending vibration of p-disubstituted benzene ring), 3040 (aromatic C-H stretching) |
PMR ($\delta$, ppm) (Fig 36)

2.45 (3H, singlet, -N-CO-CH$_3$), 3.44 (1H, doublet of a doublet, $J = 19.2$ and 4.8 Hz, C$_4$-H$_{trans}$), 3.79 (3H, singlet, OCH$_3$), 3.95 (1H, doublet of a doublet, $J = 19.2$ and 12.0 Hz, C$_4$-H$_{cis}$), 5.57 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$-H), 6.85-7.65 (8H, multiplet, aromatic protons), 8.45 (1H, singlet, C$_4'$-H of coumarin ring)

$^{13}$C-NMR ($\delta$, ppm) (Fig 37)

21.97(CH$_3$), 44.19(CH$_2$), 55.28(OCH$_3$), 59.98(CH), 114.24(CH), 116.68(CH), 118.85(C), 119.83(C), 124.95(CH), 126.93(CH), 128.77(CH), 132.82(CH), 133.72(C), 140.81(CH), 150.83(C), 154.16(C), 159.09(C), 159.17(C), 168.91(C)

**Compound 5d**

IR (cm$^{-1}$) $\nu_{max}$ 1720 and 1665 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1600 and 1560 (aromatic C=C and C=N stretching), 835 (C-H bending vibration of 1,2,4-trisubstituted benzene ring), 3050 (aromatic C-H stretching)

PMR ($\delta$, ppm) (Fig 38)

2.45 (3H, singlet, -N-CO-CH$_3$), 3.47 (1H, doublet of a doublet, $J = 19.2$ and 4.8 Hz, C$_4$-H$_{trans}$), 3.86-3.98 (7H, multiplet, 2 x OCH$_3$ + C$_4$-H$_{cis}$), 5.56 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$-H), 6.76-7.65 (7H, multiplet, aromatic protons), 8.45 (1H, singlet, C$_4'$-H of coumarin ring)

$^{13}$C-NMR ($\delta$, ppm) (Fig 39)

21.98(CH$_3$), 44.21(CH$_2$), 55.95(OCH$_3$), 60.24(CH), 109.32(CH), 111.49(CH), 116.69(CH), 117.59(CH), 118.83(C), 119.90(C) 124.97(CH), 128.78(CH), 132.87(CH), 134.13(C), 140.87(CH), 148.60(C), 149.28(C), 150.89(C), 154.16(C), 159.24(C) 168.98(C)

**Compound 5e**

IR (ln cm$^{-1}$) $\nu_{max}$ 1730 and 1675 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in
pyrazoline nucleus respectively), 1605 and 1565 (aromatic C=C and C=N stretching), 830 (C-H bending vibration of p-disubstituted benzene ring), 3050 (aromatic C-H stretching)

PMR (δ, ppm) (Fig 40)

2.44 (3H, singlet, -N-CO-CH₃), 3.43 (1H, doublet of a doublet, J = 18.8 and 4.4 Hz, C₄-Htrans), 3.97 (1H, doublet of a doublet, J = 18.8 and 12.0 Hz, C₄-Hcis), 5.58 (1H, doublet of a doublet, J = 12.0 and 4.4 Hz, C₅-H), 7.16-7.65 (8H, multiplet, aromatic protons), 8.46 (1H, singlet, C₄'-H of coumarin ring)

¹³C-NMR (δ, ppm) (Fig 41)

21.94(CH₃), 44.16(CH₂), 59.89(CH), 116.70(CH), 118.78(C), 119.55(C), 125.01(CH), 127.09(CH), 128.82(CH), 129.04(CH), 132.96(CH), 133.49(C), 140.01(C), 141.02(CH), 150.67(C), 154.17(C), 159.17(C), 168.92(C)

**Compound 5f**

IR (in cm⁻¹) \( \nu_{\text{max}} \) 1725 and 1670 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH₃ group present in pyrazoline nucleus respectively), 1600 and 1570 (aromatic C=C and C=N stretching), 770 (C-H bending vibration of mono substituted benzene ring), 3030 (aromatic C-H stretching)

PMR (δ, ppm) (Fig 42)

1.22 (3H, triplet, J = 7.6 Hz, -CH₂CH₃), 2.85 (2H, quartet, J = 7.6 Hz, -CH₂CH₃), 3.42 (1H, doublet of a doublet, J = 19.0 and 4.8 Hz, C₄-Htrans), 3.97 (1H, doublet of a doublet, J = 19.0 and 12.0 Hz, C₄-Hcis), 5.60 (1H, doublet of a doublet, J = 12.0 and 4.8 Hz, C₅-H), 7.21-7.64 (9H, multiplet, aromatic protons), 8.44 (1H, singlet, C₄'-H of coumarin ring)

¹³C-NMR (δ, ppm) (Fig 43)

8.95(CH₃), 27.56(CH₂), 44.08(CH₂), 60.60(CH), 116.67(CH), 118.86(C), 119.89(C), 124.94(CH), 125.53(CH), 127.65(CH), 128.75(CH), 128.87(CH),
Compound 5g

IR (In cm$^{-1}$) $\nu_{\text{max}}$ 1735 and 1660 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1600 and 1560 (aromatic C=C and C=N stretching), 820 (C-H bending vibration of p-disubstituted benzene ring), 3020 (aromatic C-H stretching)

PMR ($\delta$, ppm) (Fig 44) 1.21 (3H, triplet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 2.32 (3H, singlet, CH$_3$), 2.83 (2H, quartet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 3.40 (1H, doublet of a doublet, $J = 18.8$ and 4.8 Hz, C$_4$-H$_{\text{trans}}$), 3.94 (1H, doublet of a doublet, $J = 18.8$ and 12.0 Hz, C$_4$-H$_{\text{cis}}$), 5.55 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$-H), 7.10-7.64 (8H, multiplet, aromatic protons), 8.43 (1H, singlet, C$_4$'-H of coumarin ring)

$^{13}$C-NMR ($\delta$, ppm) (Fig 45) 8.94(CH$_3$), 21.09(CH$_3$), 27.56(CH$_2$), 44.05(CH$_2$), 60.42(CH), 116.66(CH), 118.88(C), 119.95(C), 124.92(CH), 125.51(CH), 128.74(CH), 129.52(CH), 132.74(CH), 137.30(C), 138.81(C), 140.65(CH), 150.44(C), 154.12(C), 159.15(C), 172.29(C)

Compound 5h

IR (In cm$^{-1}$) $\nu_{\text{max}}$ 1730 and 1675 (C=O stretching of $\delta$-lactone of coumarin nucleus and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1605 and 1565 (aromatic C=C and C=N stretching), 830 (C-H bending vibration of p-disubstituted benzene ring), 3040 (aromatic C-H stretching)

PMR ($\delta$, ppm) (Fig 46) 1.21 (3H, triplet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 2.82 (2H, quartet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 3.42 (1H, doublet of a doublet, $J = 18.8$ and 4.4 Hz, C$_4$-H$_{\text{trans}}$), 3.79 (3H, singlet, OCH$_3$), 3.94 (1H, doublet of a doublet, $J = 18.8$ and 12.0 Hz, C$_4$-
H\textsubscript{cis}, 5.55 (1H, doublet of a doublet, \(J = 12.0\) and 4.4 Hz, C\textsubscript{5}-H), 6.85-7.64 (8H, multiplet, aromatic protons), 8.43 (1H, singlet, C\textsubscript{4}-H of coumarin ring)

\textbf{Compound 5i}

\textbf{IR (cm\textsuperscript{-1})} 
\(v_{\text{max}}\) 1725 and 1665 (C=O stretching of \(\delta\)-lactone of coumarin and carbonyl of -N-CO-CH\textsubscript{3} group present in pyrazoline nucleus respectively), 1610 and 1565 (aromatic C=C and C=N stretching), 830 (C-H bending vibration of 1,2,4-trisubstituted benzene ring), 3030 (aromatic C-H stretching)

\textbf{PMR (\(\delta\), ppm)} (Fig 48)
1.22 (3H, triplet, \(J = 7.6\) Hz, -CH\textsubscript{2}CH\textsubscript{3}), 2.83 (2H, quartet, \(J = 7.6\) Hz, -CH\textsubscript{2}CH\textsubscript{3}), 3.44 (1H, doublet of a doublet, \(J = 19.2\) and 4.8 Hz, C\textsubscript{4}-H\textsubscript{trans}), 3.80-3.95 (7H, multiplet, 2 x OCH\textsubscript{3} + C\textsubscript{4}-H\textsubscript{cis}), 5.54 (1H, doublet of a doublet, \(J = 12.0\) and 4.8 Hz, C\textsubscript{5}-H), 6.75-7.63 (7H, multiplet, aromatic protons), 8.42 (1H, singlet, C\textsubscript{4}-H of coumarin ring)

\textbf{13C-NMR (\(\delta\), ppm)} (Fig 49)
9.03(CH\textsubscript{3}), 27.62(CH\textsubscript{2}), 44.02(CH\textsubscript{2}), 55.93(OCH\textsubscript{3}), 60.38(CH), 109.24(CH), 111.53(CH), 116.66(CH), 117.61(CH), 118.83(C), 119.88(C), 124.96(CH), 128.76(CH), 132.82(CH), 134.37(C), 140.76(CH), 148.53(C), 149.25(C), 150.59(C), 154.12(C), 159.18(C), 172.45(C)

\textbf{Compound 5j}

\textbf{IR (cm\textsuperscript{-1})} 
\(v_{\text{max}}\) 1730 and 1670 (C=O stretching of \(\delta\)-lactone of coumarin and carbonyl of -N-CO-CH\textsubscript{3} group present in pyrazoline nucleus respectively), 1605 and 1560 (aromatic C=C and C=N stretching), 830 (C-H bending vibration of
p-disubstituted benzene ring), 3060 (aromatic C-H stretching)

PMR ($\delta$, ppm) (Fig 50)

1.20 (3H, triplet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 2.82 (2H, quartet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 3.38 (1H, doublet of a doublet, $J = 19.2$ and $4.8$ Hz, C$_4$-H$_{\text{trans}}$), 3.95 (1H, doublet of a doublet, $J = 19.2$ and $12.0$ Hz, C$_4$-H$_{\text{cis}}$), 5.54 (1H, doublet of a doublet, $J = 12.0$ and $4.8$ Hz, C$_5$-H), 7.15-7.63 (8H, multiplet, aromatic protons), 8.44 (1H, singlet, C$_4'$-H of coumarin ring)

$^{13}$C-NMR ($\delta$, ppm) (Fig 51)

8.90(CH$_3$), 27.54(CH$_2$), 43.93(CH$_2$), 60.03(CH), 116.66(CH), 118.80(C), 119.63(C), 125.00(CH), 127.10(CH), 128.81(CH), 129.03(CH), 132.91(CH), 133.40(C), 140.25(C), 140.92(CH), 150.40(C), 154.13(C), 159.17(C), 172.37(C)

In case of the compounds 5d and 5i the number of carbon signals in $^{13}$C NMR spectra are less than expected by one signal. This may be due to identical chemical shifts of certain carbons which may appear at same position.
Fig 28  IR spectrum of compound 5a

Fig 29  Expanded region of compound 5a
Fig 30  PMR spectrum of compound 5a

Fig 31  $^{13}$C spectrum of compound 5a
**Fig 32** DEPT-135 spectrum of compound 5a

**Fig 33** Mass spectrum of compound 5a
Fig 34  PMR spectrum of compound 5b

Fig 35  $^{13}$C spectrum of compound 5b
**Fig 36** PMR spectrum of compound 5c

**Fig 37** $^{13}$C spectrum of compound 5c
**Fig 38** PMR spectrum of compound 5d

**Fig 39** $^{13}$C spectrum of compound 5d
Fig 40  PMR spectrum of compound 5e

Fig 41  $^{13}$C spectrum of compound 5e
**Fig 42** PMR spectrum of compound 5f

**Fig 43** $^{13}$C spectrum of compound 5f
Fig 44  PMR spectrum of compound 5g

Fig 45  $^{13}$C spectrum of compound 5g
Fig 46  PMR spectrum of compound 5h

Fig 47  $^{13}$C spectrum of compound 5h
**Fig 48** PMR spectrum of compound 5i

**Fig 49** $^{13}$C spectrum of compound 5i
Fig 50  PMR spectrum of compound 5j

Fig 51  $^{13}$C spectrum of compound 5j
5.3 Experimental

For the preparation of compounds (3a-l), the 4-hydroxy coumarins used were (1a-d). Out of these four derivatives the preparation of three derivatives (1a, 1b and 1d) is already described in section 2 of chapter 1. The preparation of 8-methyl-4-hydroxy coumarin (1c) is given here in section 5.3.1. The condensing components used were 3-(ω-bromoacetyl) coumarins (2a-c) whose preparation is already described in section 1 of chapter 1.

For the preparation of compounds (5a-j), the 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones (coumarin chalcones) used were (4a-e). Here also the preparation of 4a-c is already given in chapter 3. The preparation of 4d and 4e is given here in section 5.3.3.

The microwave reactions were carried out on Raga’s electromagnetic system.

5.3.1 Preparation of 8-methyl-4-hydroxy coumarin (1c)

\[
\text{CH}_3\text{OH} + \text{H}_2\text{C} \text{ COOH} \xrightarrow{\text{ZnCl}_2, \text{POCl}_3} \text{CH}_3\text{O} \text{ COO} \text{ H}
\]

In a 500 mL round bottom flask attached with a reflux condenser and gas absorption trap, a mixture of appropriate phenol (0.2 mol), malonic acid (0.2 mol), anhydrous zinc chloride (0.6 mol) and phosphorous oxychloride (0.4 mol) was heated with stirring at 60-65°C for 35 hours. The yellow colored mixture was cooled and decomposed with water and left overnight. The resulting crude 4-hydroxy coumarin was filtered out, washed with water and dried. This crude product was purified by dissolving it in 10% sodium bicarbonate solution, filtering and reprecipitating by adding dilute HCl solution. The product was separated out as a yellowish-white solid. This was filtered out, washed with water, dried and recrystallized from ethanol.

Yield: 53%, mp 222°C (lit. 38 mp 223°C)
5.3.2 Preparation of 3-(coumarin-3-yl)-furo[3,2-c]coumarins (3a-l)

The following general procedure was used.

To a mixture of appropriate 4-hydroxy coumarin (1a-d) (0.002 mol) and 3-(ω-bromoacetyl) coumarin (2a-c) (0.002 mol) in glacial acetic acid (4 mL) was added ammonium acetate (0.01 mol) at room temperature. The reaction mixture was stirred at room temperature for 10 minutes and then irradiated for 4-7 minutes in microwave at 280 W (40%) power. The reaction mixture was poured into water (50 mL) and then extracted with chloroform (3 x 25 mL). The chloroform extract was washed with 5% sodium bicarbonate solution (2 x 20 mL). It was then washed with water and dried over anhydrous sodium sulphate. Distillation of chloroform resulted in a gummy residue, which was subjected to column chromatography using silica gel and hexane-chloroform (7:3) as an eluent to afford the compounds (3a-l). The compounds thus obtained were recrystallized from chloroform-hexane.

**Compound 3a:** \( R = R_1 = R_2 = R_3 = R_4 = H \)

Yield = 74%  
Yield  = 74%  
mp 250-252°C  
Molecular Formula: C_{20}H_{10}O_{5}  

Analysis  
% C  
% H  

Found  
72.55  
2.95  

Calculated  
72.73  
3.05  

**Compound 3b:** \( R = CH_3, R_1 = R_2 = R_3 = R_4 = H \)

Yield = 86%  
Yield  = 86%  
mp 248-250°C  
Molecular Formula: C_{21}H_{12}O_{5}  

Analysis  
% C  
% H  

Found  
73.36  
3.59  

Calculated  
73.25  
3.51
**Compound 3c:**  $R_1 = CH_3, R = R_2 = R_3 = R_4 = H$

Yield = 77%  
mp 282-284°C  
Molecular Formula: $C_{21}H_{12}O_5$

Analysis  
% C  % H

Found 73.15 3.43  
Calculated 73.25 3.51

**Compound 3d:**  $R = Cl, R_1 = R_2 = R_3 = R_4 = H$

Yield = 81 %  
mp 278-280 °C  
Molecular Formula: $C_{20}H_9ClO_5$

Analysis  
% C  % H

Found 65.92 2.58  
Calculated 65.86 2.49

**Compound 3e:**  $R_2 = OCH_3, R = R_1 = R_3 = R_4 = H$

Yield = 74%  
mp 285-287°C  
Molecular Formula: $C_{21}H_{12}O_6$

Analysis  
% C  % H

Found 69.88 3.28  
Calculated 70.00 3.36

**Compound 3f:**  $R = CH_3, R_2 = OCH_3, R_1 = R_3 = R_4 = H$

Yield = 73%  
mp >300°C  
Molecular Formula: $C_{22}H_{14}O_6$

Analysis  
% C  % H

Found 70.72 3.87  
Calculated 70.59 3.77

**Compound 3g:**  $R_1 = CH_3, R_2 = OCH_3, R = R_3 = R_4 = H$

Yield = 77%  
mp 265-267°C  
Molecular Formula: $C_{22}H_{14}O_6$

Analysis  
% C  % H

Found 70.67 3.88  
Calculated 70.59 3.77

**Compound 3h:**  $R = Cl, R_2 = OCH_3, R_1 = R_3 = R_4 = H$

Yield = 79%  
mp >300°C  
Molecular Formula: $C_{21}H_{11}ClO_6$

Analysis  
% C  % H

Found 64.06 3.01  
Calculated 63.89 2.81

**Compound 3i:**  $R = R_1 = R_2 = H, R_3 + R_4 = benzo$

Yield = 80%  
mp 298-299°C  
Molecular Formula: $C_{24}H_{12}O_5$
Chapter 5

Microwave assisted synthesis

Analysis % C % H
Found 75.88 3.27
Calculated 75.79 3.18

**Compound 3j:** R = CH₃, R₁ = R₂ = H, R₃ + R₄ = benzo
Yield = 77%  mp >300˚C  Molecular Formula: C₂₅H₁₄O₅
Analysis % C % H
Found 76.24 3.68
Calculated 76.14 3.58

**Compound 3k:** R₁ = CH₃, R = R₂ = H, R₃ + R₄ = benzo
Yield = 78%  mp >300˚C  Molecular Formula: C₂₅H₁₄O₅
Analysis % C % H
Found 76.22 3.67
Calculated 76.14 3.58

**Compound 3l:** R = Cl, R₁ = R₂ = H, R₃ + R₄ = benzo
Yield = 74%  mp >300˚C  Molecular Formula: C₂₄H₁₁ClO₅
Analysis % C % H
Found 69.55 2.74
Calculated 69.49 2.67
**Table 1:** Comparison of yield and reaction time of present microwave irradiation method with earlier conventional method.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Present microwave irradiation method</th>
<th>Earlier conventional method**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reaction Time (minutes)</td>
<td>% Yield</td>
</tr>
<tr>
<td>3a</td>
<td>4</td>
<td>74</td>
</tr>
<tr>
<td>3b</td>
<td>5</td>
<td>86</td>
</tr>
<tr>
<td>3c</td>
<td>4</td>
<td>77</td>
</tr>
<tr>
<td>3d</td>
<td>4</td>
<td>81</td>
</tr>
<tr>
<td>3e</td>
<td>5</td>
<td>74</td>
</tr>
<tr>
<td>3f</td>
<td>4</td>
<td>73</td>
</tr>
<tr>
<td>3g</td>
<td>5</td>
<td>77</td>
</tr>
<tr>
<td>3h</td>
<td>6</td>
<td>79</td>
</tr>
<tr>
<td>3i</td>
<td>7</td>
<td>80</td>
</tr>
<tr>
<td>3j</td>
<td>5</td>
<td>77</td>
</tr>
<tr>
<td>3k</td>
<td>7</td>
<td>78</td>
</tr>
<tr>
<td>3l</td>
<td>6</td>
<td>74</td>
</tr>
</tbody>
</table>

** indicates the time and yield for earlier synthesized compounds (3a-l) by conventional method.28.
5.3.3 Preparation of 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-ones (coumarin chalcones) (4a-e)

In a 100 mL round bottom flask, an appropriate 3-acetyl coumarin (0.01 mol) and aromatic aldehydes (0.015 mol) were taken in 50 mL of ethanol. Catalytic amount of piperidine (1.0 mL) was added and the reaction mixture was stirred for 10 minutes at room temperature. The mixture was then refluxed on waterbath for 4 hours. It was allowed to cool to room temperature. A solid product separated out was filtered off, washed with cold ethanol and dried. It was recrystallized from ethanol.

**Compound 4d:** \( R_1 = R_2 = \text{OCH}_3 \); Yield: 55%, mp 191-192°C (lit.\(^{39}\) mp 190-192°C)

**Compound 4e:** \( R_1 = \text{H}, R_2 = \text{Cl} \); Yield: 66%, mp 159-160°C (lit.\(^{40}\) mp 160°C)

5.3.4 Preparation of 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines (5a-j)

The following general procedure was used.

A mixture of appropriate 1-[2(H)-1-benzopyran-3-yl]-3-aryl-prop-2-en-1-one (coumarin chalcone) (4a-f) (0.005 mol), hydrazine hydrate (0.015 mol) in a acetic acid or propionic acid (8 mL) were
stirred at room temperature for 5 minutes and then irradiated for 4-7 minutes in microwave at 240 W (35%) power. The reaction mixture was then poured in to water (50 mL), whereby a solid product was separated out, which was filtered out, washed with water and recrystallized from methanol to afford 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines (5a-j).

**Compound 5a:** $R = CH_3$, $R_1 = R_2 = H$;
Yield = 78%  
mp 225-226°C  
Molecular Formula: C$_{20}$H$_{16}$N$_2$O$_3$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
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<tbody>
<tr>
<td>Found</td>
<td>72.17</td>
<td>4.94</td>
<td>8.54</td>
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<tr>
<td>Calculated</td>
<td>72.28</td>
<td>4.85</td>
<td>8.43</td>
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**Compound 5b:** $R = R_2 = CH_3$, $R_1 = H$;
Yield = 80%  
mp 201-202°C  
Molecular Formula: C$_{21}$H$_{18}$N$_2$O$_3$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
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<tr>
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<td>72.70</td>
<td>5.12</td>
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<tr>
<td>Calculated</td>
<td>72.82</td>
<td>5.24</td>
<td>8.09</td>
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</table>

**Compound 5c:** $R = CH_3$, $R_1 = H$, $R_2 = OCH_3$;
Yield = 82%  
mp 198-199°C  
Molecular Formula: C$_{21}$H$_{18}$N$_2$O$_4$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>69.69</td>
<td>5.12</td>
<td>7.64</td>
</tr>
<tr>
<td>Calculated</td>
<td>69.60</td>
<td>5.01</td>
<td>7.73</td>
</tr>
</tbody>
</table>

**Compound 5d:** $R = CH_3$, $R_1 = R_2 = OCH_3$;
Yield = 81%  
mp 175°C  
Molecular Formula: C$_{22}$H$_{20}$N$_2$O$_5$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
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<tbody>
<tr>
<td>Found</td>
<td>67.22</td>
<td>5.06</td>
<td>7.22</td>
</tr>
<tr>
<td>Calculated</td>
<td>67.34</td>
<td>5.14</td>
<td>7.14</td>
</tr>
</tbody>
</table>

**Compound 5e:** $R = CH_3$, $R_1 = H$, $R_2 = Cl$;
Yield = 86%  
mp 207-208°C  
Molecular Formula: C$_{20}$H$_{15}$ClN$_2$O$_3$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>65.41</td>
<td>4.00</td>
<td>7.56</td>
</tr>
<tr>
<td>Calculated</td>
<td>65.49</td>
<td>4.12</td>
<td>7.64</td>
</tr>
</tbody>
</table>
**Compound 5f:** \( R = \text{CH}_2\text{CH}_3, \ R_1 = R_2 = \text{H}; \)

Yield = 85%  
mp 222-223°C  
Molecular Formula: \( \text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
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<tbody>
<tr>
<td>Found</td>
<td>72.75</td>
<td>5.36</td>
<td>8.00</td>
</tr>
<tr>
<td>Calculated</td>
<td>72.82</td>
<td>5.24</td>
<td>8.09</td>
</tr>
</tbody>
</table>

**Compound 5g:** \( R = \text{CH}_2\text{CH}_3, \ R_1 = \text{H}, \ R_2 = \text{CH}_3; \)

Yield = 81%  
mp 182-183°C  
Molecular Formula: \( \text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.28</td>
<td>5.49</td>
<td>7.68</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.32</td>
<td>5.59</td>
<td>7.77</td>
</tr>
</tbody>
</table>

**Compound 5h:** \( R = \text{CH}_2\text{CH}_3, \ R_1 = \text{H}, \ R_2 = \text{OCH}_3; \)

Yield = 82%  
mp 185-186°C  
Molecular Formula: \( \text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_4 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>70.10</td>
<td>5.27</td>
<td>7.35</td>
</tr>
<tr>
<td>Calculated</td>
<td>70.20</td>
<td>5.36</td>
<td>7.44</td>
</tr>
</tbody>
</table>

**Compound 5i:** \( R = \text{CH}_2\text{CH}_3, \ R_1 = R_2 = \text{OCH}_3; \)

Yield = 79%  
mp 165°C  
Molecular Formula: \( \text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_5 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>67.88</td>
<td>5.39</td>
<td>6.94</td>
</tr>
<tr>
<td>Calculated</td>
<td>67.97</td>
<td>5.46</td>
<td>6.89</td>
</tr>
</tbody>
</table>

**Compound 5j:** \( R = \text{CH}_2\text{CH}_3, \ R_1 = \text{H}, \ R_2 = \text{Cl}; \)

Yield = 84%  
mp 190-191°C  
Molecular Formula: \( \text{C}_{21}\text{H}_{17}\text{ClN}_2\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>66.14</td>
<td>4.59</td>
<td>7.25</td>
</tr>
<tr>
<td>Calculated</td>
<td>66.23</td>
<td>4.50</td>
<td>7.36</td>
</tr>
</tbody>
</table>
Table 2: Comparison of yield and reaction time of present microwave irradiation method with earlier conventional method.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Present microwave irradiation method</th>
<th>Earlier conventional method**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reaction Time (minutes)</td>
<td>% Yield</td>
</tr>
<tr>
<td>5a</td>
<td>5</td>
<td>78</td>
</tr>
<tr>
<td>5b</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>5c</td>
<td>6</td>
<td>82</td>
</tr>
<tr>
<td>5d</td>
<td>4</td>
<td>81</td>
</tr>
<tr>
<td>5e</td>
<td>7</td>
<td>86</td>
</tr>
<tr>
<td>5f</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>5g</td>
<td>5</td>
<td>81</td>
</tr>
<tr>
<td>5h</td>
<td>7</td>
<td>82</td>
</tr>
<tr>
<td>5i</td>
<td>6</td>
<td>79</td>
</tr>
<tr>
<td>5j</td>
<td>6</td>
<td>84</td>
</tr>
</tbody>
</table>

** indicates the time and yield for earlier synthesized compounds by conventional method\(^{37}\).
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