Synthesis of bipyridyl substituted coumarins

The work incorporated in this chapter is on synthesis of various bipyridyl substituted coumarins. The compounds have been synthesized by the reaction of 3-coumarinoyl methyl pyridinium salts with 3-aryl-1-(pyridin-3-yl)prop-2-en-1-ones and 3-aryl-1-(pyridin-4-yl)prop-2-en-1-ones under Krohnke’s reaction condition. The structures of all the compounds synthesized have been supported by analytical and spectral data.

2.1 Introduction

The survey of the literature reveals that a very large number of coumarin derivatives containing heterocyclic moieties are used in drugs and dyes. A large number of coumarin derivatives having heterocyclic moieties like benzimidazole, triazole, diazole, thia diazole, oxadiazole, quinazoline, diazine etc. as substituent groups either in the lactone ring or in the benzene ring of coumarin are used as dyes or fluorescent whitening agents\(^1\)-\(^7\). Similarly, variety of coumarin derivatives having nucleus like pyridine, indole, imidazole, thiazole, and triazole as substituent groups possess important biological activities\(^8\)-\(^10\). Thus, incorporation of another heterocyclic moiety in coumarin nucleus as substituent component or fused component changes the properties of parent coumarins and converts them into more useful derivatives.

Among the heterocyclic substituted coumarins, pyridyl coumarins have a special importance due to their diverse physiological actions. A number of coumarin derivatives having pyridine substituted mainly at 3- or 4- position of the coumarin possess CNS depressant activity. R B Moffett\(^{11}\)-\(^{13}\) synthesized number of 3-pyridyl and 4-pyridyl coumarins using modified Pechmann, Knoevenagel and Perkin reactions of pyridine acetic acid or pyridoyl acetic acid with substituted phenols and salicylaldehydes.

Moffett tested the synthesized pyridyl coumarin derivatives for various physiological activities. Most of them showed a central
nervous system depression property\textsuperscript{11}. 3-(3-Pyridyl)coumarin inhibited monoamine oxidase (MAO) \textit{in vitro} and hence was considered as possible stimulant. 6-Bromo-3-(2-pyridyl) and 6-bromo-3-(3-pyridyl) coumarins were found to be antifungal agents \textit{in vitro}\textsuperscript{12}. Certain derivatives of these class of compounds were also found to be useful UV screening agents and as optical brightening agents for textile. When certain pyridyl derivatives having \(-\text{NH}_2\) function in the benzene ring were reacted with fluosilicic acid, they formed amine-fluosilicate salts which were found to be effective as moth-proofing agents\textsuperscript{13}.

\textit{Srenivasulu et al}\textsuperscript{14} have synthesized some 3-(3-pyridyl)coumarin derivatives. The compounds were synthesized by reacting substituted salicylaldehyde/o-hydroxy acetophenone with 3-pyridine acetic acid or its sodium salt under \textit{Perkin} reaction conditions. These compounds were reported to have fish toxicity and bactericidal activities. \textit{Bragg} and \textit{Wibberely}\textsuperscript{15} have synthesized 3-(2-pyridyl) and 3-(4-pyridyl) coumarins using \textit{Knoevenagel} reaction, in which salicylaldehyde was treated with ethyl-2-pyridyl acetate or ethyl-4-pyridyl acetate in the presence of piperidine. \textit{R M Mohareb et al}\textsuperscript{16} have synthesized 3-(2-pyridyl)coumarin with substituents in pyridine nucleus. Some selected biologically active pyridyl substituted coumarins are shown in chart 1.
Considering the importance of pyridyl substituted coumarins, earlier a lot of work was carried out on the synthesis of pyridyl substituted coumarins and large number of variety of pyridyl substituted coumarin derivatives were synthesized from our laboratory. Thus, synthesis of some 3-(4,6-diaryl-pyridin-2-yl)coumarins (A)\textsuperscript{17}, 3-(6-aryl-
pyridin-2-yl)coumarins (B)\textsuperscript{18}, 3-(4-styryl-6-aryl-pyridin-2-yl)coumarins (C)\textsuperscript{19}, 3-(4-aryl-6-styryl-pyridin-2-yl)coumarins (D)\textsuperscript{19}, 3-phenyl-4-methyl-6-(4,6-diaryl-pyridin-2-yl)coumarins (E)\textsuperscript{20} and 3-phenyl-4-methyl-6-(6-styryl-4-aryl-pyridin-2-yl)coumarins (F)\textsuperscript{21} have been reported from our laboratory (Chart 2).

\begin{center}
\begin{tabular}{ccc}
\includegraphics[width=0.3\textwidth]{chart2a} & \includegraphics[width=0.3\textwidth]{chart2b} \\
(A) & (B) \\
\includegraphics[width=0.3\textwidth]{chart2c} & \includegraphics[width=0.3\textwidth]{chart2d} \\
(C) & (D) \\
\includegraphics[width=0.3\textwidth]{chart2e} & \includegraphics[width=0.3\textwidth]{chart2f} \\
(E) & (F) \\
\end{tabular}
\end{center}

**Chart 2**

All the above compounds in chart 2 were synthesized using Krohnke’s pyridine synthesis\textsuperscript{22-23}.

In Krohnke’s pyridine synthesis, an aroylmethyl pyridinium salt (I) is reacted with $\alpha,\beta$-unsaturated ketone (II) in the presence of ammonium acetate and acetic acid to give 2,4,6-trisubstituted pyridine (III) (Scheme 1).
Krohnke’s Pyridine Synthesis

\[
\begin{align*}
\text{(I)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{NH}_2 \quad \text{OAc} \quad \text{AcOH} \\
\text{(II)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{Ar}'' \quad \text{H} \\
\text{(III)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{Ar}''
\end{align*}
\]

Reaction Mechanism:

1,5-Dionylpyridinium salt intermediate

\[
\begin{align*}
\text{(I)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{Ar}'' \quad \text{H} \\
\text{(II)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{H}_2\text{N} \quad \text{H} \\
\text{(III)} & \quad \text{Ar}^+ \quad \text{Br}^- \quad \text{Ar} \quad \text{CO} \quad \text{H}_2\text{O}
\end{align*}
\]

Scheme 1

In place of aroylmethyl pyridinium salt (I), an appropriate 3- or 6-coumarinoyl methyl pyridinium salt was used for the synthesis of 3- or 6-pyridyl coumarins shown in chart 2.
2.1.1 Bipyridines

Bipyridines are molecules which results when two pyridine nuclei are connected by a carbon-carbon single bond. Bipyridines can be of two types, (1) symmetric bipyridines (A-C) and (2) asymmetric bipyridines (D-F) as shown in chart 3.

Chart 3

Large number of bipyridines and substituted bipyridines are widely used in the complexation of inorganic metal ions. Their use as ligands in coordination and supramolecular chemistry is also reported in literature. The transition metal complexes of bipyridines are reported to have important applications like photocatalysis, chemosensors and luminescent probes for biomolecular systems. In addition to their use as ligands in metal complexes, the bipyridines are also reported to have other interesting applications. Some of the bipyridines are used as building blocks for the construction of efficient molecular and macromolecular nonlinear optical (NLO) chromophores. Certain bipyridines are also reported to have important medicinal applications, e.g. 5-aryl-2,2′-bipyridines are reported to
have a strong fungicidal activity against different plant diseases\textsuperscript{29}. Certain bipyridine derivatives are used as cardiotonic drugs\textsuperscript{30}.

Thus, considering the importance of above bipyridine derivatives and in continuation of our interest in synthesizing newer modified pyridyl substituted coumarin derivatives, it was thought worthwhile to incorporate bipyridine nucleus in coumarin moiety as a substituent group and therefore in the present work, synthesis of various 3-(4-aryl-2,3'-bipyridin-6-yl)coumarins and 3-(4-aryl-2,4'-bipyridin-6-yl)coumarins have been carried out.

2.2 Present work

In the present work, various 3-(4-aryl-2,3'-bipyridin-6-yl)coumarins (A) and 3-(4-aryl-2,4'-bipyridin-6-yl)coumarins (B) have been synthesized using Krohnke’s pyridine synthesis.

![Chemical structures](image)

### 2.2.1 Synthesis of 3-(4-aryl-2,3'-bipyridin-6-yl)coumarins (3a-i)

The synthesis of 3-(4-aryl-2,3'-bipyridin-6-yl)coumarins (3a-i) have been carried out by reacting 3-coumarinoyl methyl pyridinium salts (1a-c) with 3-aryl-1-(pyridin-3-yl)prop-2-en-1-ones (2a-c) in the presence of ammonium acetate in refluxing acetic acid (Scheme 2).

The starting material 3-coumarinoyl methyl pyridinium salts (1a-c) were prepared by the reaction of appropriate 3-(ω-bromoacetyl) coumarin with pyridine in refluxing toluene. The 3-(ω-bromoacetyl) coumarins were in turn prepared by the reaction of appropriate 3-acetyl coumarin with bromine in acetic acid. The 3-acetylpyridine chalcones (2a-c) were prepared by reacting 3-acetylpyridine with various benzaldehydes in the presence of NaOH in ethanol.
The condensation of 3-coumarinoyl methyl pyridinium salts (1a-c) with 3-aryl-1-(pyridin-3-yl)prop-2-en-1-ones (2a-c) under Krohnke's reaction condition proceeded smoothly and gave the expected products (3a-i) in 53-67% yield. The detailed mechanism for the formation of compounds (3a-i) is shown in scheme 3.

Scheme 2
The condensation of 3-coumarinoyl methyl pyridinium salts (1a-c) with 3-aryl-1-(pyridin-3-yl)prop-2-en-1-ones (2a-c) under Krohnke’s reaction condition proceeded smoothly and gave the expected products (3a-i) in 53-67% yield. The detailed mechanism for the formation of compounds (3a-i) is shown in scheme 3.
The structures of all the compounds (3a-i) were confirmed by analytical and spectral data.

Thus, the reaction of 3-coumarinoyl methyl pyridinium salt (1a) with 3-(p-tolyl)-1-(pyridin-3-yl)prop-2-en-1-one (2a) in the presence of ammonium acetate in refluxing acetic acid gave a compound (3a) as a white colored solid product in 57% yield.
The IR spectrum of 3a (Fig 1) showed a strong band at 1725 cm\(^{-1}\) which is due to carbonyl stretching of \(\delta\)-lactone ring present in coumarin nucleus. The bands observed at 1595 and 1454 cm\(^{-1}\) are due to aromatic C=C and C=N stretching vibrations respectively. The sharp and intense band observed at 816 cm\(^{-1}\) is due to C-H out of plane bending vibrations for para disubstituted benzene ring. A band appeared at 2919 cm\(^{-1}\) is due to aliphatic C-H stretching vibrations. The band observed at 3037 cm\(^{-1}\) is due to aromatic C-H stretching vibrations.

The \(^1\)H NMR spectrum of compound 3a (in CDCl\(_3\)) (Fig 2) showed a singlet at 2.44 \(\delta\) integrating for three protons, which is due to methyl protons. Total fifteen protons were observed in the region 7.32-9.43 \(\delta\). A poorly resolved doublet observed at 9.43 \(\delta\) (1H) is due to proton at C\(_{2''}\). The singlet observed at 8.96 \(\delta\) (1H) is due to proton at C\(_{4}\) of coumarin ring. The remaining thirteen aromatic protons appeared as a multiplet between 7.32-8.72 \(\delta\).

The \(^{13}\)C NMR spectrum of compound 3a (in CDCl\(_3\)) (Fig 3) showed signals at 21.28, 116.38, 117.92, 119.49, 121.30, 124.07, 124.68, 124.94, 127.10, 129.03, 129.91, 132.33, 134.99, 135.55, 139.63, 142.90, 147.18, 148.38, 148.46, 150.38, 151.87, 153.84, 153.99 and 160.23 \(\delta\). Thus, total twenty four carbon signals are seen. The compound is having twenty four types of non equivalent carbon atoms and hence expected number of signals is observed. The signal appeared at 21.28 \(\delta\) is due to methyl carbon. The most downfield signal appeared at 160.23 \(\delta\) can be assigned to the carbonyl carbon of the \(\delta\)-lactone ring of coumarin. The DEPT-135 spectrum of compound 3a (in CDCl\(_3\)) (Fig 4) showed signals at 21.28, 116.37, 117.91, 121.29, 124.06, 124.67, 127.09, 129.05, 129.91, 132.34, 135.57, 142.91, 147.18 and 148.46 \(\delta\). The signal at 21.28 \(\delta\) is due to methyl carbon. The signals appeared at 116.37, 117.91, 121.29, 124.06, 124.67, 127.09, 129.05, 129.91, 132.34, 135.57, 142.91, 147.18 and 148.46 \(\delta\) are due to thirteen tertiary carbons.

The mass spectrum of compound 3a (Fig 5) showed M\(^+\) peak at 390(26%) (m/z %) alongwith some other fragments peaks at 362(8%), 97(3%), 73(6%), 69(20%), 55(19%), 44(100%), etc. The appearance of
molecular ion peak at 390 mass unit supports the structure of compound 3a.

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

**Compound 3b**

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

\(v_{\text{max}}\) 1737 (C=O stretching of \(\delta\)-lactone of coumarin), 1609 and 1454 (aromatic C=C and C=N stretchings), 827 (C-H bending vibrations of p-disubstituted benzene ring), 2969 (aliphatic C-H stretching), 3049 (aromatic C-H stretching)

\(^1\)H NMR (\(\delta\), ppm) (CDCl\(_3\)) (Fig 6)

3.90 (3H, singlet, OCH\(_3\)), 7.05-8.75 (13H, multiplet, aromatic protons), 8.97 (1H, singlet, proton at C\(_4\) of coumarin ring), 9.48 (1H, poorly resolved doublet, proton at C\(_2\)"")

\(^13\)C NMR (\(\delta\), ppm) (CDCl\(_3\)) (Fig 7)

55.45(OCH\(_3\)), 114.71(CH), 116.39(CH), 117.55(CH), 119.49(C), 121.12(CH), 123.21(C), 124.25(CH), 124.65(CH), 124.93(C), 128.50(CH), 129.07(CH), 130.11(C), 132.36(CH), 136.17(CH), 142.91(CH), 146.53(CH), 147.64(CH), 150.13(C), 152.02(C), 153.51(C), 154.05(C), 160.23(CO of coumarin), 160.94(C)

**Compound 3c**

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

\(v_{\text{max}}\) 1725 (C=O stretching of \(\delta\)-lactone of coumarin), 1602 and 1458 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of p-disubstituted benzene ring), 2914 (aliphatic C-H stretching), 3043 (aromatic C-H stretching)

\(^1\)H NMR (\(\delta\), ppm) (CDCl\(_3\)) (Fig 8)

7.37-8.75 (13H, multiplet, aromatic protons), 9.04 (1H, singlet, proton at C\(_4\) of coumarin ring), 9.43 (1H, poorly resolved doublet, proton at C\(_2\)"")

\(^13\)C NMR (\(\delta\), ppm) (CDCl\(_3\)) (Fig 9)

116.46(CH), 117.98(CH), 119.50(C), 121.11(CH), 123.71(CH), 124.74(CH), 124.86(C), 128.06(CH), 129.06(CH), 129.44(CH), 132.46(CH), 134.65(CH), 134.84(C), 135.67(C), 136.62(C),
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143.11(CH), 148.28(CH), 149.28(C), 149.87(CH), 152.06(C), 154.07(C), 154.74(C), 160.32(CO of coumarin)

**Compound 3d**

**IR (cm⁻¹)**

ν_max 1720 (C=O stretching of δ-lactone of coumarin), 1603 and 1479 (aromatic C=C and C=N stretchings), 801 (C-H bending vibrations of p-disubstituted benzene ring), 2932 (aliphatic C-H stretching), 3027 (aromatic C-H stretching)

**¹H NMR (δ, ppm) (CDCl₃) (Fig 10)**

2.46 (3H, singlet, CH₃), 4.03 (3H, singlet, OCH₃), 7.15-8.76 (12H, multiplet, aromatic protons), 8.99 (1H, singlet, proton at C₄ of coumarin ring), 9.42 (1H, poorly resolved doublet, proton at C₂")

**¹³C NMR (δ, ppm) (CDCl₃) (Fig 11)**

55.41(OCH₃), 56.30(OCH₃), 114.09(CH), 114.60(CH), 117.52(CH), 120.16(C), 120.42(CH), 120.86(CH), 123.83(CH), 124.44(CH), 125.16(C), 128.48(CH), 130.24(C), 135.14(CH), 135.33(C), 142.96(CH), 143.69(C), 146.94(C), 147.62(CH), 148.92(CH), 149.90(C), 151.76(C), 154.03(C), 159.68(CO of coumarin), 160.81(C)

**Compound 3e**

**IR (cm⁻¹)**

ν_max 1729 (C=O stretching of δ-lactone of coumarin), 1604 and 1480 (aromatic C=C and C=N stretchings), 821 (C-H bending vibrations of p-disubstituted benzene ring), 2929 (aliphatic C-H stretching), 3035 (aromatic C-H stretching)

**¹H NMR (δ, ppm) (CDCl₃) (Fig 12)**

3.90 and 4.03 (6H, two singlets, 2 x OCH₃), 7.05-8.76 (12H, multiplet, aromatic protons), 8.95 (1H, singlet, proton at C₄ of coumarin ring), 9.47 (1H, poorly resolved doublet, proton at C₂")

**¹³C NMR (δ, ppm) (CDCl₃) (Fig 13)**

55.41(OCH₃), 56.30(OCH₃), 114.09(CH), 114.60(CH), 117.52(CH), 120.16(C), 120.42(CH), 120.86(CH), 123.83(CH), 124.44(CH), 125.16(C), 128.48(CH), 130.24(C), 135.14(CH), 135.33(C), 142.96(CH), 143.69(C), 146.94(C), 147.62(CH), 148.92(CH), 149.90(C), 151.76(C), 154.03(C), 159.68(CO of coumarin), 160.81(C)
Compound 3f

IR (cm$^{-1}$)

$\nu_{\text{max}}$ 1710 (C=O stretching of $\delta$-lactone of coumarin), 1606 and 1479 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of p-disubstituted benzene ring), 2927 (aliphatic C-H stretching), 3050 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (DMSO-$d_6$+TFA-$d_1$) (Fig 14)

3.92 (3H, singlet, OCH$_3$), 7.29-9.07 (12H, multiplet, aromatic protons), 9.52 (1H, singlet, proton at C$_4$ of coumarin ring), 9.85 (1H, poorly resolved doublet, proton at C$_2''$)

$^{13}$C NMR ($\delta$, ppm) (DMSO-$d_6$+TFA-$d_1$) (Fig 15)

56.40(OCH$_3$), 110.95(C), 113.80(C), 115.31(C), 116.65(CH), 118.48(C), 119.50(C), 120.71(CH), 122.83(C), 123.12(CH), 123.48(CH), 128.33(CH), 129.20(CH), 129.53(CH), 132.50(CH), 135.97(CH), 143.77(CH), 144.16(C), 144.81(C), 147.68(CH), 148.89(CH), 150.33(C), 152.26(C), 159.60(CO of coumarin)

Compound 3g

IR (cm$^{-1}$)

$\nu_{\text{max}}$ 1726 (C=O stretching of $\delta$-lactone of coumarin), 1592 and 1465 (aromatic C=C and C=N stretchings), 822 (C-H bending vibrations of p-disubstituted benzene ring), 2923 (aliphatic C-H stretching), 3062 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (CDCl$_3$) (Fig 16)

2.46 (3H, singlet, CH$_3$), 7.35-8.88 (15H, multiplet, aromatic protons), 9.58 (1H, singlet, proton at C$_4$ of coumarin ring), 9.75 (1H, poorly resolved doublet, proton at C$_2''$)

$^{13}$C NMR ($\delta$, ppm) (CDCl$_3$) (Fig 17)

21.29(CH$_3$), 113.71(C), 116.49(CH), 117.82(CH), 121.45(CH), 121.90(CH), 123.36(C), 124.47(CH), 126.27(CH), 127.10(CH), 128.67(CH), 129.04(CH), 129.52(C), 129.94(CH), 130.33(C), 133.93(CH), 134.89(C), 136.48(CH), 138.54(CH), 139.73(C), 146.28(CH), 147.34(CH), 150.55(C), 152.21(C), 153.28(C), 153.97(C), 160.26(CO of coumarin)
**Compound 3h**

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

\(\nu_{\text{max}}\) 1725 (C=O stretching of \(\delta\)-lactone of coumarin), 1573 and 1463 (aromatic C=C and C=N stretchings), 816 (C-H bending vibrations of p-disubstituted benzene ring), 2934 (aliphatic C-H stretching), 3034 (aromatic C-H stretching)

*\(^1\)H NMR (\(\delta, \text{ ppm}\)) (DMSO-\(d_6\)+TFA-\(d_1\)) (Fig 18)*

3.87 (3H, singlet, OCH\(_3\)), 7.12-9.60 (15H, multiplet, aromatic protons), 9.77 (1H, singlet, proton at C\(_4\) of coumarin ring), 9.93 (1H, poorly resolved doublet, proton at C\(_2\)"")

*\(^{13}\)C NMR (\(\delta, \text{ ppm}\)) (CDCl\(_3\)+TFA-\(d_1\)) (Fig 19)*

55.45(OCH\(_3\)), 109.93(C), 112.74(C), 115.55(C), 115.94(CH), 118.39(C), 119.76(CH), 121.22(CH), 121.73(C), 125.55(C), 128.35(CH), 128.88(CH), 129.92(CH), 130.21(CH), 130.72(CH), 131.16(C), 131.91(C), 140.76(CH), 141.38(CH), 143.22(CH), 143.81(CH), 144.54(CH), 145.73(CH), 148.43(CH), 151.46(C), 153.26(C), 155.85(C), 159.64(CO of coumarin)

**Compound 3i**

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

\(\nu_{\text{max}}\) 1725 (C=O stretching of \(\delta\)-lactone of coumarin), 1595 and 1458 (aromatic C=C and C=N stretchings), 822 (C-H bending vibrations of p-disubstituted benzene ring), 2914 (aliphatic C-H stretching), 3036 (aromatic C-H stretching)

*\(^1\)H NMR (\(\delta, \text{ ppm}\)) (CDCl\(_3\)) (Fig 20)*

7.52-8.84 (15H, multiplet, aromatic protons), 9.51 (1H, singlet, proton at C\(_4\) of coumarin ring), 9.86 (1H, poorly resolved doublet, proton at C\(_2\)"")

*\(^{13}\)C NMR (\(\delta, \text{ ppm}\)) (CDCl\(_3\)) (Fig 21)*

113.79(C), 116.56(CH), 117.85(CH), 121.00(CH), 121.91(CH), 123.36(C), 123.73(CH), 126.30(CH), 128.58(CH), 128.67(CH), 129.12(CH), 129.42(CH), 129.59(C), 130.40(C), 133.99(CH), 134.51(CH), 135.64(C), 136.62(C), 138.72(CH), 148.51(CH), 149.29(C), 150.02(CH), 152.23(C), 154.05(C), 154.78(C), 156.60(C), 160.40(CO of coumarin)
In case of the compounds 3d and 3g, the number of non-equivalent carbon signals observed is one less than expected. This may be due to identical chemical shifts of certain carbons which may appear at same position.
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Fig 1  IR spectrum of compound 3a

Fig 2  $^1$H NMR spectrum of compound 3a
Fig 3  $^{13}$C NMR spectrum of compound 3a

Fig 4  DEPT-135 spectrum of compound 3a
Fig 5  Mass spectrum of compound 3a
Fig 6  $^1$H NMR spectrum of compound 3b

Fig 7  $^{13}$C NMR spectrum of compound 3b
**Fig 8** $^1$H NMR spectrum of compound 3c

**Fig 9** $^{13}$C NMR spectrum of compound 3c
**Fig 10** $^1$H NMR spectrum of compound 3d

**Fig 11** $^{13}$C NMR spectrum of compound 3d
**Fig 12** $^1H$ NMR spectrum of compound 3e

**Fig 13** $^{13}C$ NMR spectrum of compound 3e
Fig 14  $^1$H NMR spectrum of compound 3f

Fig 15  $^{13}$C NMR spectrum of compound 3f
Fig 16 $^1$H NMR spectrum of compound 3g

Fig 17 $^{13}$C NMR spectrum of compound 3g
Fig 18  $^1$H NMR spectrum of compound 3h

Fig 19  $^{13}$C NMR spectrum of compound 3h
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**Fig 20**  $^1$H NMR spectrum of compound 3i

**Fig 21**  $^{13}$C NMR spectrum of compound 3i
2.2.2 Synthesis of 3-(4-aryl-2,4′-bipyridin-6-yl)coumarins (5a-i)

The synthesis of 3-(4-aryl-2,4′-bipyridin-6-yl)coumarins (5a-i) have been carried out by reacting 3-coumarinoyl methyl pyridinium salts (1a-c) with 3-aryl-1-(pyridin-4-yl)prop-2-en-1-ones (4a-c) in the presence of ammonium acetate in refluxing acetic acid (Scheme 4).

The 4-acetylpyridine chalcones (4a-c) were prepared by reacting 4-acetylpyridine with various benzaldehydes in the presence of NaOH in ethanol.

![Scheme 4]

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The condensation of 3-coumarinoyl methyl pyridinium salts (1a-c) with 3-aryl-1-(pyridin-4-yl)prop-2-en-1-ones (4a-c) under Krohnke’s reaction condition proceeded smoothly and gave the expected products (5a-i) in 50-68% yield.

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

Thus, the reaction of 3-coumarinoyl methyl pyridinium salt (1a) with 3-(p-tolyl)-1-(pyridin-4-yl)prop-2-en-1-one (4a) in the presence of ammonium acetate in refluxing acetic acid gave a compound (5a) as a white colored solid product in 65% yield.

The IR spectrum of 5a (Fig 22) showed a strong band at 1734 cm$^{-1}$ which is due to carbonyl stretching of $\delta$-lactone ring present in coumarin nucleus. The bands observed at 1591 and 1454 cm$^{-1}$ are due to aromatic $\text{C}=\text{C}$ and $\text{C}=\text{N}$ stretching vibrations respectively. The sharp and intense band observed at 811 cm$^{-1}$ is due to C-H out of plane bending vibrations for para disubstituted benzene ring. A band appeared at 2958 cm$^{-1}$ is due to aliphatic C-H stretching vibrations. The band observed at 3030 cm$^{-1}$ is due to aromatic C-H stretching vibrations.

The $^1\text{H}$ NMR spectrum of compound 5a (in CDCl$_3$) (Fig 23) showed a singlet at 2.47 $\delta$ integrating for three protons, which is due to methyl protons. Total fifteen protons were observed in the region 7.36-8.96 $\delta$. The most downfield signal observed at 8.96 $\delta$ (1H) as a singlet is due to proton at $\text{C}_4$ of coumarin ring. The remaining fourteen aromatic protons appeared as a multiplet between 7.36-8.89 $\delta$.

The $^{13}\text{C}$ NMR spectrum of compound 5a (in CDCl$_3$) (Fig 24) showed signals at 21.28, 116.39, 118.21, 119.44, 121.44, 121.99, 124.66, 124.92, 127.06, 129.01, 129.91, 132.36, 134.90, 139.66, 142.88, 146.98, 149.83, 150.36, 151.87, 154.00, 154.10 and 160.20 $\delta$. Thus, total twenty two carbon signals are seen. The compound is having twenty two types of non equivalent carbon atoms and hence expected number of signals is observed. The signal appeared at 21.28 $\delta$ is due to methyl carbon. The most downfield signal appeared at 160.20 $\delta$ can be assigned to the carbonyl carbon of the $\delta$-lactone ring of coumarin. The DEPT-135 spectrum of compound 5a (in CDCl$_3$)
(Fig 25) showed signals at 21.28, 116.39, 118.21, 121.38, 121.97, 124.65, 127.06, 129.00, 129.91, 132.36, 142.88 and 149.88 δ. The signal at 21.28 δ is due to methyl carbon. The signals appeared at 116.39, 118.21, 121.38, 121.97, 124.65, 127.06, 129.00, 129.91, 132.36, 142.88 and 149.88 δ are due to eleven tertiary carbons.

The mass spectrum of compound 5a (Fig 26) showed M+ peak at 390(13%) (m/z %) along with some other fragments peaks at 341(26%), 295(8%), 289(18%), 207(16%), 176(9%), 148(21%), 139(5%), 115(8%), 105(23%), 91(55%), 73(100%), 61(60%), 55(45%), etc. The appearance of molecular ion peak at 390 mass unit supports the structure of compound 5a.

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

**Compound 5b**

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

\( \nu_{\text{max}} \) 1731 (C=O stretching of δ-lactone of coumarin), 1594 and 1455 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of p-disubstituted benzene ring), 2972 (aliphatic C-H stretching), 3037 (aromatic C-H stretching)

**\(^1\)H NMR (δ, ppm) (CDCl\(_3\)) (Fig 27)**

3.91 (3H, singlet, OCH\(_3\)), 7.07-8.87 (14H, multiplet, aromatic protons), 8.96 (1H, singlet, proton at C\(_4\) of coumarin ring)

**\(^13\)C NMR (δ, ppm) (CDCl\(_3\)) (Fig 28)**

55.43(OCH\(_3\)), 114.67(CH), 116.41(CH), 117.98(CH), 119.45(C), 121.62(CH), 121.85(CH), 124.67(CH), 124.92(C), 128.47(CH), 129.01(CH), 130.00(C), 132.39(CH), 142.91(CH), 147.86(C), 148.97(CH), 150.05(C), 151.97(C), 153.73(C), 154.03(C), 160.20(CO of coumarin), 160.94(C)

**Compound 5c**

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

\( \nu_{\text{max}} \) 1725 (C=O stretching of δ-lactone of coumarin), 1602 and 1458 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of p-disubstituted benzene ring), 2920 (aliphatic C-H stretching), 3037 (aromatic C-H stretching)
$^1$H NMR ($\delta$, ppm) (CDCl$_3$) (Fig 29)
7.37-8.82 (14H, multiplet, aromatic protons), 9.02 (1H, singlet, proton at C$_4$ of coumarin ring)

$^{13}$C NMR ($\delta$, ppm) (CDCl$_3$) (Fig 30)
116.49(CH), 118.26(CH), 119.44(C), 121.25(CH), 121.98(CH), 123.27(C), 124.75(C), 124.81(CH), 128.58(CH), 129.05(CH), 129.47(CH), 132.54(CH), 135.75(C), 136.48(C), 143.16(CH), 149.35(C), 150.32(CH), 152.14(C), 154.08(C), 154.77(C), 160.35(CO of coumarin)

**Compound 5d**

IR (cm$^{-1}$)
$\nu_{max}$ 1705 (C=O stretching of $\delta$-lactone of coumarin), 1593 and 1478 (aromatic C=C and C=N stretchings), 820 (C-H bending vibrations of p-disubstituted benzene ring), 2941 (aliphatic C-H stretching), 3029 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (CDCl$_3$) (Fig 31)
2.46 (3H, singlet, CH$_3$), 4.04 (3H, singlet, OCH$_3$), 7.17-8.85 (13H, multiplet, aromatic protons), 8.93 (1H, singlet, proton at C$_4$ of coumarin ring)

$^{13}$C NMR ($\delta$, ppm) (CDCl$_3$+TFA-d$_1$) (Fig 32)
21.32(CH$_3$), 56.43(OCH$_3$), 110.52(C), 113.36(CH), 115.78(CH), 116.18(C), 119.04(C), 119.60(C), 120.87(CH), 121.88(C), 124.14(CH), 124.87(CH), 125.72(CH), 127.34(CH) 130.44(CH), 141.82(C), 142.28(CH), 143.51(C), 146.02(CH), 146.99(C), 148.94(C), 151.96(C), 161.19(CO of coumarin)

**Compound 5e**

IR (cm$^{-1}$)
$\nu_{max}$ 1731 (C=O stretching of $\delta$-lactone of coumarin), 1591 and 1480 (aromatic C=C and C=N stretchings), 826 (C-H bending vibrations of p-disubstituted benzene ring), 2935 (aliphatic C-H stretching), 3020 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (CDCl$_3$) (Fig 33)
3.91 and 4.04 (6H, two singlets, 2 x OCH$_3$), 7.06-8.85 (13H, multiplet, aromatic protons), 8.93 (1H, singlet, proton at C$_4$ of coumarin)
coumarin ring)

$^{13}$C NMR ($\delta$, ppm) ($CDCl_3$+TFA-$d_1$) (Fig 34)

55.57(OCH$_3$), 56.45(OCH$_3$), 113.46(C), 115.29(CH), 116.32(CH),
119.47(C), 120.25(C), 120.49(CH), 121.00(CH), 122.96(CH),
124.45(C), 124.88(CH), 125.95(CH), 127.39(C), 129.14(CH),
142.39(CH), 143.54(C), 146.53(CH), 147.06(C), 147.92(C), 151.11(C),
161.42(CO of coumarin), 162.60(C)

**Compound 5f**

IR ($cm^{-1}$)

$\nu_{max}$ 1710 (C=O stretching of $\delta$-lactone of coumarin), 1606 and 1479
(aromatic C=C and C=N stretchings), 818 (C-H bending vibrations of
p-disubstituted benzene ring), 2941 (aliphatic C-H stretching), 3028
(aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) ($DMSO-d_6$+TFA-$d_1$) (Fig 35)

3.91 (3H, singlet, OCH$_3$), 7.27-9.04 (14H, multiplet, aromatic protons
+ proton at C$_4$)

$^{13}$C NMR ($\delta$, ppm) ($DMSO-d_6$+TFA-$d_1$) (Fig 36)

56.12(OCH$_3$), 110.94(C), 113.74(CH), 116.66(C), 119.52(CH),
119.93(CH), 123.18(CH), 124.53(CH), 124.92(CH), 129.19(CH),
129.52(CH), 135.44(C), 135.68(C), 142.32(CH), 144.03(CH),
146.71(C), 148.98(C), 150.96(C), 152.81(C), 154.35(C), 156.74(C),
159.54(CO of coumarin)

**Compound 5g**

IR ($cm^{-1}$)

$\nu_{max}$ 1729 (C=O stretching of $\delta$-lactone of coumarin), 1594 and 1464
(aromatic C=C and C=N stretchings), 813 (C-H bending vibrations of
p-disubstituted benzene ring), 2918 (aliphatic C-H stretching), 3024
(aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) ($CDCl_3$) (Fig 37)

2.47 (3H, singlet, CH$_3$), 7.35-8.88 (16H, multiplet, aromatic protons),
9.76 (1H, singlet, proton at C$_4$ of coumarin ring)

$^{13}$C NMR ($\delta$, ppm) ($CDCl_3$) (Fig 38)

21.29(CH$_3$), 113.77(CH), 116.59(CH), 118.37(CH), 121.62(CH),
121.68(CH), 121.82(C), 122.23(CH), 123.61(C), 126.29(CH),
127.14(CH), 128.61(CH), 129.16(CH), 129.59(C), 130.01(CH), 130.42(C), 134.00(C), 134.96(CH), 138.65(CH), 139.73(C), 149.34(C), 150.62(C), 152.32(C), 152.89(C), 154.08(C), 160.29(CO of coumarin)

**Compound 5h**

IR (cm$^{-1}$)

$\nu_{\text{max}}$ 1727 (C=O stretching of $\delta$-lactone of coumarin), 1596 and 1465 (aromatic C=C and C=N stretchings), 821 (C-H bending vibrations of p-disubstituted benzene ring), 2938 (aliphatic C-H stretching), 3031 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (DMSO-d$_6$+TFA-d$_1$) (Fig 39)

3.84 (3H, singlet, OCH$_3$), 7.10-9.12 (16H, multiplet, aromatic protons), 9.68 (1H, singlet, proton at C$_4$ of coumarin ring)

$^{13}$C NMR ($\delta$, ppm) (DMSO-d$_6$+TFA-d$_1$) (Fig 40)

55.65(OCH$_3$), 111.04(C), 113.59(C), 113.91(CH), 115.06(CH), 116.76(CH), 118.24(CH), 119.63(CH), 122.78(CH), 124.78(CH), 126.70(CH), 129.00(CH), 129.45(CH), 130.33(C), 130.45(C), 134.75(CH), 139.08(CH), 142.58(CH), 149.80(C), 151.13(C), 151.88(C), 153.05(C), 154.10(C), 154.58(C), 159.83(CO of coumarin), 161.30(C)

**Compound 5i**

IR (cm$^{-1}$)

$\nu_{\text{max}}$ 1725 (C=O stretching of $\delta$-lactone of coumarin), 1595 and 1458 (aromatic C=C and C=N stretchings), 822 (C-H bending vibrations of p-disubstituted benzene ring), 2925 (aliphatic C-H stretching), 3043 (aromatic C-H stretching)

$^1$H NMR ($\delta$, ppm) (DMSO-d$_6$) (Fig 41)

7.62-8.81 (16H, multiplet, aromatic protons), 9.69 (1H, singlet, proton at C$_4$ of coumarin ring)

$^{13}$C NMR ($\delta$, ppm) (CDCl$_3$+TFA-d$_1$) (Fig 42)

109.99(C), 112.82(C), 114.04(C), 115.65(CH), 118.47(C), 121.31(CH), 121.94(CH), 123.09(CH), 125.72(CH), 128.47(CH), 128.90(C), 129.19(CH), 130.03(CH), 130.64(CH), 130.89(CH), 131.07(C), 131.58(C), 141.05(C), 141.24(CH), 143.52(CH), 144.93(CH), 147.82(C), 149.38(C), 156.08(C), 159.16(CO of coumarin)
Chapter 2                                                                 Bipyridyl substituted coumarins

Fig 22  IR spectrum of compound 5a

Fig 23  $^1$H NMR spectrum of compound 5a
Fig 24  $^{13}$C NMR spectrum of compound 5a

Fig 25  DEPT-135 spectrum of compound 5a
Fig 26  Mass spectrum of compound 5a
Fig 27  $^1$H NMR spectrum of compound 5b

Fig 28  $^{13}$C NMR spectrum of compound 5b
**Fig 29** $^1$H NMR spectrum of compound 5c

**Fig 30** $^{13}$C NMR spectrum of compound 5c
Fig 31  $^1$H NMR spectrum of compound 5d

Fig 32  $^{13}$C NMR spectrum of compound 5d
Fig 33 $^1$H NMR spectrum of compound 5e

Fig 34 $^{13}$C NMR spectrum of compound 5e
Chapter 2  
Bipyridyl substituted coumarins

**Fig 35** $^1$H NMR spectrum of compound 5f

![H NMR spectrum of compound 5f](image)

**Fig 36** $^{13}$C NMR spectrum of compound 5f

![C NMR spectrum of compound 5f](image)
Fig 37 $^1$H NMR spectrum of compound 5g

Fig 38 $^{13}$C NMR spectrum of compound 5g
Chapter 2  
Bipyridyl substituted coumarins

Fig 39  $^1$H NMR spectrum of compound 5h

Fig 40  $^{13}$C NMR spectrum of compound 5h
Fig 41  $^1$H NMR spectrum of compound 5i

Fig 42  $^{13}$C NMR spectrum of compound 5i
2.3  Experimental

2.3.1 Preparation of 3-acetyl coumarins

In a 100 mL round bottom flask, a mixture of appropriate salicylaldehyde (0.01 mol), ethyl acetoacetate (0.01 mol) and 3-4 drops of piperidine was stirred for 10 minutes at room temperature. It was then heated for 30 minutes in water bath. On cooling, a yellow solid product was obtained, which was filtered out and washed with cold ether. It was recrystallized from chloroform-hexane.

**Compound a:** \( R = R_1 = R_2 = H \), Yield: 97%, mp 119°C (lit.\(^{31}\) mp 120°C)

**Compound b:** \( R = \text{OCH}_3, R_1 = R_2 = H \), Yield: 95%, mp 171°C (lit.\(^{31}\) mp 174°C)

**Compound c:** \( R = H, R_1 + R_2 = \text{benzo} \), Yield: 86%, mp 185°C (lit.\(^{32}\) mp 186°C)

2.3.2 Preparation of 3-(ω-bromoacetyl)coumarins

In a 100 mL three necked flask, a solution of appropriate 3-acetyl coumarin (0.01 mol) in glacial acetic acid (20 mL) was taken. To this bromine (0.01 mol) in glacial acetic acid (10 mL) was added with stirring during 30 minutes at room temperature. The reaction mixture was stirred at room temperature for 3 hours. It was then poured into ice cold water and the solid obtained was filtered out. It was washed with water and dried. The product was recrystallized from chloroform.

**Compound a:** \( R = R_1 = R_2 = H \), Yield: 83%, mp 162°C (lit.\(^{33}\) mp165°C)
**Compound b:** \( R = \text{OCH}_3, R_1 = R_2 = \text{H} \), Yield: 80%, mp 201°C (lit.\(^{34}\) mp 206°C)

**Compound c:** \( R = \text{H}, R_1 + R_2 = \text{benzo} \), Yield: 84%, mp 199-201°C (lit.\(^{35}\) mp 198-200°C)

### 2.3.3 Preparation of 3-coumarinoyl methyl pyridinium salts (1a-c)

![Chemical Reaction Diagram]

In a 100 mL round bottom flask fitted with a reflux condenser, a solution of appropriate 3-(ω-bromoacetyl) coumarin (0.01 mol) in dry toluene (30 mL) was taken and pyridine (0.01 mol) was added. The reaction mixture was refluxed in an oil bath for 2 hours. It was then allowed to come to room temperature and was left for 4 to 5 hours. The pyridinium salt was separated out which was filtered out and washed with hot toluene and dried. It was recrystallized from acetic acid.

**Compound 1a:** \( R = R_1 = R_2 = \text{H} \), Yield: 93%, mp 218°C (dec.) (lit.\(^{33}\) mp 220°C (dec.))

**Compound 1b:** \( R = \text{OCH}_3, R_1 = R_2 = \text{H} \), Yield: 91%, mp 250°C (dec.) (lit.\(^{34}\) mp 250°C (dec.))

**Compound 1c:** \( R = \text{H}, R_1 + R_2 = \text{benzo} \), Yield: 84%, mp 179-180°C (dec.) [lit.\(^{35}\) mp 180°C (dec.)]

### 2.3.4 Preparation of 3-aryl-1-(pyridin-3-yl)prop-2-en-1-ones (2a-c) and 3-aryl-1-(pyridin-4-yl)prop-2-en-1-ones (4a-c)

![Chemical Reaction Diagram]
In a 100 mL three necked flask equipped with a thermometer and magnetic needle, an aqueous 10% sodium hydroxide solution (25 ml) and ethanol (20 ml) were added with stirring and the mixture was cooled to 0-10°C in an ice bath. An appropriate aromatic aldehyde (0.02 mol) was introduced in one portion. Then 3-acetyl pyridine or 4-acetylpyridine (0.02 mol) was added in small portions over a period of 10 minutes. The mixture was stirred for three hours at 10°C under stirring. The resulting solid was isolated by filtration and was washed with cold ethanol. The solid was then dried and recrystallized from ethanol to give yellow crystals.

**Compound 2a:** \( R_3 = \text{CH}_3 \), Yield: 84%, mp 101°C

Analysis

- % C
- % H
- %N

Found (C_{15}H_{13}NO) 80.44 5.78 6.37

Calculated 80.69 5.87 6.27

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

\( \nu_{\text{max}} \) 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 802 (C-H bending vibration of p-disubstituted benzene ring), 3032 (aromatic C-H stretching)

**\(^1\)H NMR (\( \delta \), ppm) (CDCl\(_3\))**

- 2.42 (3H, singlet, CH\(_3\)), 7.25-8.82 (9H, multiplet, aromatic protons except proton at C\(_2\) of pyridine ring + two olefinic protons at C\(_2\) and C\(_3\)), 9.25 (1H, poorly resolved doublet, proton at C\(_2\) of pyridine ring)

**Compound 2b:** \( R_3 = \text{OCH}_3 \), Yield: 82%, mp 96°C

Analysis

- % C
- % H
- %N

Found (C_{15}H_{13}NO\(_2\)) 75.13 5.41 5.77

Calculated 75.30 5.48 5.85

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

\( \nu_{\text{max}} \) 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3040 (aromatic C-H stretching)
$^{1}$H NMR ($\delta$, ppm) (CDCl$_3$)

3.89 (3H, singlet, OCH$_3$), 6.96-8.82 (9H, multiplet, aromatic protons except protons at C$_2$ of pyridine ring + two olefinic protons at C$_2$ and C$_3$), 9.24 (1H, poorly resolved doublet, proton at C$_2$ of pyridine ring)

**Compound 2c**: $R_3$ = Cl, Yield: 77%, mp 134°C

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<th>% C</th>
<th>% H</th>
<th>% N</th>
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<td>68.80</td>
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$\nu_{\text{max}}$ 1659 (C=O stretching), 1589 and 1489 (aromatic C=C and C=N stretching), 802 (C-H bending vibration of p-disubstituted benzene ring), 3086 (aromatic C-H stretching)

$^{1}$H NMR ($\delta$, ppm) (CDCl$_3$)

7.42-8.84 (9H, multiplet, aromatic protons except protons at C$_2$ of pyridine ring + two olefinic protons at C$_2$ and C$_3$), 9.24 (1H, poorly resolved doublet, proton at C$_2$ of pyridine ring)

**Compound 4a**: $R_3$ = CH$_3$, Yield: 85%, mp 132°C

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<td>80.69</td>
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$\nu_{\text{max}}$ 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3032 (aromatic C-H stretching)

$^{1}$H NMR ($\delta$, ppm) (CDCl$_3$)

2.41 (3H, singlet, CH$_3$), 7.24-7.84 (8H, multiplet, aromatic protons except protons at C$_2$ and C$_6$ of pyridine ring + two olefinic protons at C$_2$ and C$_3$), 8.85 (2H, apparently doublet, protons at C$_2$ and C$_6$ of pyridine ring)

**Compound 4b**: $R_3$ = OCH$_3$, Yield: 80%, mp 115°C

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<td>Found</td>
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<td>75.30</td>
<td>5.48</td>
<td>5.85</td>
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$\nu_{\text{max}}$ 1660 (C=O stretching), 1590 and 1510 (aromatic C=C and C=N stretching)
stretches), 810 (C-H bending vibration of p-disubstituted benzene ring), 3053 (aromatic C-H stretching)

1H NMR (δ, ppm) (CDCl3)
3.89 (3H, singlet, OCH₃), 6.96-7.84 (8H, multiplet, aromatic protons except protons at C₂ and C₆ of pyridine ring + two olefinic protons at C₂ and C₃), 8.84 (2H, apparently doublet, protons at C₂ and C₆ of pyridine ring)

**Compound 4c**: R₃ = Cl, Yield: 75%, mp 139°C

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<td>Found (C₁₄H₁₀ClNO)</td>
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<td>69.00</td>
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IR (cm⁻¹)
νmax 1660 (C=O stretching), 1600 and 1490 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3034 (aromatic C-H stretching)

1H NMR (δ, ppm) (CDCl₃)
7.43-7.82 (8H, multiplet, aromatic protons except protons at C₂ and C₆ of pyridine ring + two olefinic protons at C₂ and C₃), 8.86 (2H, apparently doublet, protons at C₂ and C₆ of pyridine ring)

### 2.3.5 Preparation of 3-(4-aryl-2,3′-bipyridin-6-yl)coumarins (3a-i)

The following general procedure was used.

In a 100 mL three necked round bottom flask equipped with a dropping funnel, condenser, guard tube and magnetic needle, an appropriate 3-coumarinoyl methyl pyridinium salt (1a-c) (0.003 mol) in glacial acetic acid (15mL) was taken. To this ammonium acetate (0.03 mol) was added with stirring at room temperature. Then a solution of an appropriate 3-aryl-1-(pyridin-3-yl)prop-2-en-1-one (2a-
c) (0.003 mol) in glacial acetic acid (15 mL) was added with stirring at room temperature during 15 minutes. The reaction mixture was further stirred for 1 hour at room temperature and then refluxed for 8 hours at 140°C. It was then allowed to come to room temperature and was poured into ice-cold water (75 mL). A crude solid obtained was extracted with chloroform (3 x 30 mL). The organic layer was washed with 5% sodium bicarbonate solution (3 x 20 mL), water (2 x 20 mL) and dried over anhydrous sodium sulfate. The removal of chloroform under reduced pressure gave crude material which was subjected to column chromatography using silica gel and ethyl acetate-petroleum ether (60-80) (1:4) as an eluent to give 3-(4-aryl-2,3′-bipyridin-6-yl)coumarins (3a-i) as white colored solid. The compounds were recrystallized from chloroform-hexane.

**Compound 3a:**  R = R1 = R2 = H, R3 = CH3;
Yield = 57%  
mp 174-176°C  
Molecular Formula: C26H18N2O2

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<td>79.98</td>
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**Compound 3b:**  R = R1 = R2 = H, R3 = OCH3;
Yield = 66%  
mp 183-185°C  
Molecular Formula: C26H18N2O3

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<td>76.83</td>
<td>4.46</td>
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**Compound 3c:**  R = R1 = R2 = H, R3 = Cl;
Yield = 60%  
mp 188-190°C  
Molecular Formula: C25H15ClN2O2

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>72.83</td>
<td>3.58</td>
<td>6.91</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.08</td>
<td>3.68</td>
<td>6.82</td>
</tr>
</tbody>
</table>

**Compound 3d:**  R = OCH3, R1 = R2 = H, R3 = CH3;
Yield = 53%  
mp 208-210°C  
Molecular Formula: C27H20N2O3

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
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<tr>
<td>Found</td>
<td>77.37</td>
<td>4.71</td>
<td>6.59</td>
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<td>Calculated</td>
<td>77.13</td>
<td>4.79</td>
<td>6.66</td>
</tr>
</tbody>
</table>

**Compound 3e:**  R = OCH3, R1 = R2 = H, R3 = OCH3;
Yield = 67%  
mp 200-202°C  
Molecular Formula: C27H20N2O4
Analysis % C % H % N
Found 74.02 4.53 6.34
Calculated 74.30 4.62 6.42

**Compound 3f**: R = OCH$_3$, R$_1$ = R$_2$ = H, R$_3$ = Cl;
Yield = 59% mp 264-266°C Molecular Formula: C$_{26}$H$_{17}$ClN$_2$O$_3$

Analysis % C % H % N
Found 70.52 3.95 6.41
calculated 70.83 3.89 6.35

**Compound 3g**: R = H, R$_1$ + R$_2$ = Benzo, R$_3$ = CH$_3$;
Yield = 65% mp 228-230°C Molecular Formula: C$_{30}$H$_{20}$N$_2$O$_2$

Analysis % C % H % N
Found 81.66 4.52 6.29
calculated 81.80 4.58 6.36

**Compound 3h**: R = H, , R$_1$ + R$_2$ = Benzo, R$_3$ = OCH$_3$;
Yield = 66% mp 241-243°C Molecular Formula: C$_{30}$H$_{20}$N$_2$O$_3$

Analysis % C % H % N
Found 78.72 4.34 6.05
calculated 78.93 4.42 6.14

**Compound 3i**: R = H, R$_1$ + R$_2$ = Benzo, R$_3$ = Cl;
Yield = 64% mp 263-265°C Molecular Formula: C$_{29}$H$_{17}$ClN$_2$O$_2$

Analysis % C % H % N
Found 75.79 3.67 6.00
calculated 75.57 3.72 6.08

2.3.6 Preparation of 3-(4-aryl-2,4′-bipyridin-6-yl)coumarins (5a-i)

The following general procedure was used.

In a 100 mL three necked round bottom flask equipped with a dropping funnel, condenser, guard tube and magnetic needle, an
appropriate 3-coumarinoyl methyl pyridinium salt (1a-c) (0.003 mol) in glacial acetic acid (15 mL) was taken. To this ammonium acetate (0.03 mol) was added with stirring at room temperature. Then a solution of an appropriate 3-aryl-1-(pyridin-4-yl)prop-2-en-1-one (4a-c) (0.003 mol) in glacial acetic acid (15 mL) was added with stirring at room temperature during 15 minutes. The reaction mixture was further stirred for 1 hour at room temperature and then refluxed for 8 hours at 140°C. It was then allowed to come to room temperature and was poured into ice-cold water (75 mL). A crude solid obtained was extracted with chloroform (3 x 30 mL). The organic layer was washed with 5% sodium bicarbonate solution (3 x 20 mL), water (2 x 20 mL) and dried over anhydrous sodium sulfate. The removal of chloroform under reduced pressure gave crude material which was subjected to column chromatography using silica gel and ethyl acetate-petroleum ether (60-80) (1:4) as an eluent to give 3-(4-aryl-2,4'-bipyridin-6-yl)coumarins (5a-i) as white colored solid. The compounds were recrystallized from chloroform-hexane.

**Compound 5a:**  
\[ \text{R} = \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{CH}_3; \]  
Yield = 65%  
mp 198-200°C  
Molecular Formula: \( \text{C}_{26}\text{H}_{18}\text{N}_2\text{O}_2 \)  
\begin{align*}  
\text{Analysis} & : & \% \text{C} & : & \% \text{H} & : & \% \text{N} \\
\text{Found} & : & 79.70 & : & 4.58 & : & 7.10 \\
\text{Calculated} & : & 79.98 & : & 4.65 & : & 7.17 \\
\end{align*}

**Compound 5b:**  
\[ \text{R} = \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{OCH}_3; \]  
Yield = 67%  
mp 192-194°C  
Molecular Formula: \( \text{C}_{26}\text{H}_{18}\text{N}_2\text{O}_3 \)  
\begin{align*}  
\text{Analysis} & : & \% \text{C} & : & \% \text{H} & : & \% \text{N} \\
\text{Found} & : & 76.59 & : & 4.52 & : & 6.98 \\
\text{Calculated} & : & 76.83 & : & 4.46 & : & 6.89 \\
\end{align*}

**Compound 5c:**  
\[ \text{R} = \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{Cl}; \]  
Yield = 62%  
mp 231-233°C  
Molecular Formula: \( \text{C}_{25}\text{H}_{15}\text{ClN}_2\text{O}_2 \)  
\begin{align*}  
\text{Analysis} & : & \% \text{C} & : & \% \text{H} & : & \% \text{N} \\
\text{Found} & : & 72.78 & : & 3.59 & : & 6.73 \\
\text{Calculated} & : & 73.08 & : & 3.68 & : & 6.82 \\
\end{align*}

**Compound 5d:**  
\[ \text{R} = \text{OCH}_3, \text{R}_1 = \text{R}_2 = \text{H}, \text{R}_3 = \text{CH}_3; \]  
Yield = 50%  
mp 224-226°C  
Molecular Formula: \( \text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_3 \)  
\begin{align*}  
\text{Analysis} & : & \% \text{C} & : & \% \text{H} & : & \% \text{N} \\
\end{align*}
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<th>Compound</th>
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<th>R₃</th>
<th>Yield</th>
<th>mp (°C)</th>
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<th>Found %</th>
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<td>H</td>
<td>OCH₃</td>
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