Microwave assisted synthesis of pyrazole pyrazoline substituted coumarins

The work incorporated in this chapter is on microwave assisted synthesis of various pyrazole pyrazoline substituted coumarins. The synthesis of various 3-[1-acetyl/propionyl-5-(1,3-diaryl-1H-pyrazol-4-yl)-4,5-dihydro-1H-pyrazol-3-yl]coumarins and 3-[5-(1,3-diaryl-1H-pyrazol-4-yl)-1-aryl-4,5-dihydro-1H-pyrazol-3-yl]coumarins have been carried out by reacting various 3-[3-(1,3-diaryl-1H-pyrazol-4-yl)acroyl] coumarins (coumarin chalcones) with hydrazine hydrate in acetic acid or propionic acid and phenyl hydrazine derivatives in acetic acid respectively 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 areas 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 thorough put screening at early stages of drug discovery programs. Due to potential 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.\(^4\)\(^-\)\(^6\) Microwave reactions under solvent-free conditions are attractive in offering reduced pollution with simplicity in processing and handling.\(^7\)\(^-\)\(^8\) The recent introduction of single-mode technology\(^9\) 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.\(^{10\text{-}15}\)

Pyrazoles are well-known and important nitrogen containing heterocyclic compounds, and various methods have been developed for their synthesis\(^{16}\). Due to the interesting biological activity of substituted pyrazoles, considerable attention has been focused on this class of compounds.
Pyrazole derivatives have been found to possess antimicrobial\textsuperscript{17}, analgesic\textsuperscript{18}, immunosuppressive\textsuperscript{19}, anticancer\textsuperscript{20}, antidiabetic\textsuperscript{21}, and anti-inflammatory\textsuperscript{22} activity.

V Rajeswar Rao et al\textsuperscript{23} had synthesized various coumarinoyl substituted 3,5-dimethylpyrazoles by reacting 3-(2-bromoacetyl) coumarins with acetylacetone and hydrazine hydrate in ethanol.

![Chemical reaction involving pyrazole and coumarin](image)

Pyrazolines are also important nitrogen containing five membered heterocyclic compounds. Several pyrazoline derivatives showed considerable biological activities, e.g. antimicrobial\textsuperscript{24}, central nervous system\textsuperscript{25} and immuno-suppressive activities\textsuperscript{26}. Many pyrazoline derivatives have been reported to possess potent anti-inflammatory activity\textsuperscript{27-28}. Considering the bioactivities of both the coumarins and the pyrazolines, researchers have synthesized certain pyrazoline substituted coumarins. The work on pyrazoline substituted coumarins reported in literature is summarized in the following paragraphs.

Albert Levai et al\textsuperscript{29} had synthesized various 1-acetyl/propionyl-5-aryl-3-(3-coumarinyl)-2-pyrazolines and 5-aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines by reacting 1-[2\{H\}-1-benzopyran-2-one-3-yl]-3-aryl-prop-2-en-1-ones (coumarin chalcones) with hydrazine hydrate in refluxing acetic acid or propionic acid and phenyl hydrazine in refluxing pyridine respectively.
A H Mandour et al\textsuperscript{30} had synthesized 5-aryl-3-(3-coumarinyl)-1\textsubscript{H}-pyrazolines and 5-aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines by reacting 3-cinnamoyl coumarin derivatives with hydrazine hydrate and phenyl hydrazine in refluxing ethanol respectively.

M Bhalla et al\textsuperscript{31} had synthesized 1-acetyl-5-aryl-3-(7-hydroxy-4-methyl-2(\textsubscript{H})-1-benzopyran-2-one-8-yl)-2-pyrazolines by reacting 8-cinnamoyl coumarin derivatives with hydrazine hydrate/acetic acid in refluxing ethanol. The compounds were screened for anti-inflammatory activity against the carrageenin-induced rat's paw oedema in albino rats.
Considering the importance of pyrazoline substituted coumarins, some pyrazoline substituted coumarins were synthesized from our laboratory\textsuperscript{32} using microwave irradiation. In continuation of our work in synthesizing newer pyrazoline substituted coumarins, in the present work various pyrazole pyrazoline substituted coumarins have been synthesized using microwave irradiation.

5.2 Present work

As discussed in introduction, various 3-[1-acetyl/propionyl-5-(1,3-diaryl-1\textit{H}-pyrazol-4-yl)-4,5-dihydro-1\textit{H}-pyrazol-3-yl]coumarins (2a-h) and 3-[5-(1,3-diaryl-1\textit{H}-pyrazol-4-yl)-1-aryl-4,5-dihydro-1\textit{H}-pyrazol-3-yl]coumarins (4a-l) have been synthesized using microwave irradiation.

5.2.1 Synthesis of 3-[1-acetyl/propionyl-5-(1,3-diaryl-1\textit{H}-pyrazol-4-yl)-4,5-dihydro-1\textit{H}-pyrazol-3-yl]coumarins (5a-h)

The synthesis of 3-[1-acetyl/propionyl-5-(1,3-diaryl-1\textit{H}-pyrazol-4-yl)-4,5-dihydro-1\textit{H}-pyrazol-3-yl]coumarins (2a-h) have been carried out by reacting various 3-[3-(1,3-diaryl-1\textit{H}-pyrazol-4-yl)acryloyl]coumarin (1a-d) with hydrazine hydrate and acetic/propionic acid under MWI for 4 minutes (Scheme 1).
The formation of (2a-h) was observed very fast (4 minutes) and with good yields (79-88%).

The structures of all the compounds (2a-h) were confirmed by analytical and spectral data.

Thus the microwave irradiation of 3-[3-(1,3-diphenyl-1H-pyrazol-4-yl)acryloyl]coumarin (coumarin chalcone) (1a) with hydrazine hydrate in the presence of acetic acid proceeded smoothly and gave the expected product (2a) as a yellowish solid in 83% yield.

The IR spectrum of 2a (Fig 1) showed strong bands at 1734 and 1657 cm\(^{-1}\) which are due to carbonyl stretching of \(\delta\)-lactone ring present in coumarin nucleus and carbonyl of -N-CO-CH\(_3\) group respectively. The bands observed at 1606 and 1503 cm\(^{-1}\) are due to aromatic C=C and C=N stretching vibrations respectively. The sharp bands observed at 697 and 757 cm\(^{-1}\) are due to C-H out of plane bending vibrations for mono substituted benzene ring. The compound showed bands at 2930 and 3053 cm\(^{-1}\), which are due to aliphatic C-H stretching of pyrazoline ring and aromatic C-H stretching vibrations respectively.

The PMR spectrum of compound 2a (Fig 2 and 3) showed a signal at 2.45 \(\delta\) integrating for three protons. This is due to methyl
group (-N-CO-CH$_3$). A doublet of doublet centered at 3.36 δ ($J = 18.8$ and $4.8 \text{ Hz}$) integrating for one proton, is due to C$_4'$-H$_{\text{trans}}$. A doublet of doublet centered at 3.89 δ ($J = 18.8$ and $12.0 \text{ Hz}$) integrating for one proton, is due to C$_4'$-H$_{\text{cis}}$. A doublet of doublet centered at 5.86 δ ($J = 12.0$ and $4.8 \text{ Hz}$) integrating for one proton, is due to proton attached at C$_5'$. Fifteen aromatic protons were observed between 7.26-7.83 δ as a multiplet. The C$_4$-H of coumarin ring appeared as a singlet at 8.31 δ.

The $^{13}$C NMR spectrum of compound 2a (Fig 4) showed signals at 22.10, 44.02, 52.75, 116.70, 118.77, 119.16, 119.66, 122.43, 124.98, 125.79, 126.49, 128.13, 128.51, 128.63, 128.72, 129.31, 132.92, 139.89, 140.89, 150.61, 150.98, 154.12, 158.98, 163.79 and 168.98 δ corresponding to twenty five different type of carbon atoms present in the compound. The signal appeared at 22.10 δ is due to carbon of methyl group (-N-CO-CH$_3$). The signals appeared at 44.02 and 52.75 δ are due to C$_4'$ and C$_5'$ respectively. The signal appeared at 163.79 δ can be assigned to the carbonyl carbon of the δ-lactone ring of coumarin. The most downfield signal appeared at 168.98 δ can be assigned to the carbonyl carbon of -N-CO-CH$_3$ group present in pyrazoline nucleus. The DEPT-135 spectrum of compound 2a (Fig 5) showed inverted signal at 44.03 δ, which further confirms that this signal is for C$_4'$ carbon. The upward signals at 22.13 and 52.73 δ confirm that these signals are due to carbon of methyl group (-N-CO-CH$_3$) and C$_5'$ respectively. The signals appeared at 116.70, 119.16, 122.43, 124.98, 125.79, 126.49, 128.13, 128.51, 128.63, 129.31, 132.92 and 140.89 δ correspond to twelve non equivalent tertiary carbon atoms present in the compound.

The mass spectrum of compound 2a (Fig 6) showed M$^+$ peak at 474(40%) (m/z %) alongwith some other fragments peaks at 431 (100%), 245(18%), 220(77%), 187(16%), 115(23%), 104(17%), 77(65%), 43(69%) etc. The appearance of molecular ion peak at 474 mass unit supports the structure of compound 5a.
The IR and NMR data for other compounds (2b-h) are given below.

**Compound 2b**

IR
- $v_{\text{max}}$ 1722 and 1650 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1610 and 1510 (aromatic C=C and C=N stretchings), 695 and 750 (C-H bending vibrations of mono substituted benzene ring), 865 (C-H bending vibration of p-disubstituted benzene ring), 2927 (aliphatic C-H stretching), 3055 (aromatic C-H stretching).

PMR
- 2.32 (3H, singlet, CH$_3$), 2.45 (3H, singlet, -N-CO-CH$_3$), 3.33 (1H, doublet of a doublet, $J = 18.8$ and 4.8 Hz, C$_4$'-H$_{\text{trans}}$), 3.86 (1H, doublet of a doublet, $J = 18.8$ and 12.0 Hz, C$_4$'-H$_{\text{cis}}$), 5.85 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$'-H), 7.21-7.81 (14H, multiplet, aromatic protons), 8.29 (1H, singlet, C-H).

$^{13}$C-NMR
- 21.21(CH$_3$), 22.07(-N-CO-CH$_3$), 43.85(CH$_2$), 52.73(CH), 116.69(CH), 118.74(C), 119.10(CH), 119.62(C), 122.26(C), 124.95(CH), 125.78(CH), 126.37(CH), 128.52(CH), 128.70(CH), 129.20(CH), 129.28(CH), 130.29(C), 132.86(CH), 137.91(C), 139.89(C), 140.87(CH), 150.65(C), 151.08(C), 154.09(C), 158.94(CO of coumarin), 168.96(-N-CO-CH$_3$).

**Compound 2c**

IR
- $v_{\text{max}}$ 1730 and 1648 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1600 and 1521 (aromatic C=C and C=N stretchings), 688 and 759 (C-H bending vibrations of mono substituted benzene ring), 2940 (aliphatic C-H stretching), 3041 (aromatic C-H stretching).
PMR  
(δ, ppm) 2.44 (3H, singlet, -N-CO-CH₃), 3.36 (1H, doublet of a doublet, J = 18.8 and 4.4 Hz, C₄'-Hₜranₜ), 3.90 (1H, doublet of a doublet, J = 18.8 and 12.0 Hz, C₄'-Hₜ₪₢), 3.99 (3H, singlet, OCH₃), 5.84 (1H, doublet of a doublet, J = 12.0 and 4.4 Hz, C₅'-H), 7.13-7.83 (14H, multiplet, aromatic protons), 8.29 (1H, singlet, C₄-H).

13C-NMR  
(δ, ppm) 22.07(-N-CO-CH₃), 44.04(CH₂), 52.74(CH), 56.32(OCH₃), 114.62(CH), 119.15(CH), 119.38(C), 119.85(C), 120.02(CH), 122.45(C), 124.82(CH), 125.77(CH), 126.45(CH), 128.12(CH), 128.52(C), 128.63(CH), 129.29(CH), 133.18(C), 139.88(C), 141.10(CH), 147.11(C), 150.63(C), 150.99(CO of coumarin), 168.96(-N-CO-CH₃).

**Compound 2d**

IR  
(ν, cm⁻¹)  
ν max 1728 and 1659 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH₃ group present in pyrazoline nucleus respectively), 1598 and 1501 (aromatic C=C and C=N stretchings), 687 and 748 (C-H bending vibrations of mono substituted benzene ring), 859 (C-H bending vibration of p-disubstituted benzene ring), 2929 (aliphatic C-H stretching), 3047 (aromatic C-H stretching).

PMR  
(δ, ppm) 2.32 (3H, singlet, CH₃), 2.44 (3H, singlet, -N-CO-CH₃), 3.33 (1H, doublet of a doublet, J = 18.8 and 4.4 Hz, C₄'-Hₜranₜ), 3.88 (1H, doublet of a doublet, J = 18.8 and 12.0 Hz, C₄'-Hₜ₪₢), 3.99 (3H, singlet, OCH₃), 5.83 (1H, doublet of a doublet, J = 12.0 and 4.4 Hz, C₅'-H), 7.13-7.81 (13H, multiplet, aromatic protons), 8.26 (1H, singlet, C₄-H).

13C-NMR  
(δ, ppm) 21.21(CH₃), 22.07(-N-CO-CH₃), 43.91(CH₂), 52.74(CH), 56.32(OCH₃), 114.59(CH), 119.10(CH), 119.38(C), 119.85(C), 120.01(CH), 122.33(C), 124.81(C), 125.74(CH), 126.34(CH), 128.53(CH), 129.20(CH), 129.27(CH), 130.30(CH), 137.88(C), 139.91(C), 141.05(CH), 143.76(CH), 147.09(C), 151.07(C), 158.44(CO of coumarin), 168.91(-N-CO-CH₃).
Compound 2e

IR $\nu_{\text{max}}$ 1734 and 1655 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1603 and 1503 (aromatic C=C and C=N stretchings), 699 and 755 (C-H bending vibrations of mono substituted benzene ring), 2938 (aliphatic C-H stretching), 3049 (aromatic C-H stretching).

PMR 1.23 (3H, triplet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 2.87 (2H, quartet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 3.54 (1H, doublet of a doublet, $J = 19.2$ and 4.4 Hz, C$_4$'-H$_{\text{trans}}$), 3.97 (1H, doublet of a doublet, $J = 19.2$ and 12.0 Hz, C$_4$'-H$_{\text{cis}}$), 5.85 (1H, doublet of a doublet, $J = 12.0$ and 4.4 Hz, C$_5$'-H), 7.46-8.22 (15H, multiplet, aromatic protons), 8.45 (1H, singlet, C$_4$-H).

$^{13}$C-NMR 9.03(CH$_3$), 27.22(CH$_2$), 44.37(CH$_3$), 51.97(CH), 110.05(C), 112.90(C), 115.75(CH), 117.28(C), 118.37(CH), 118.57(CH), 118.57(CH), 121.74(C), 122.17(C), 122.93(C), 124.39(CH), 124.39(CH), 126.46(CH), 128.88(CH), 129.28(CH), 129.91(CH), 130.36(CH), 133.19(CH), 137.98(CH), 144.71(CH), 148.31(C), 152.47(C), 153.83(CO of coumarin), 176.09(-N-CO-CH$_3$).

Compound 2f

IR $\nu_{\text{max}}$ 1738 and 1646 (C=O stretching of $\delta$-lactone of coumarin and carbonyl of -N-CO-CH$_3$ group present in pyrazoline nucleus respectively), 1612 and 1525 (aromatic C=C and C=N stretchings), 690 and 743 (C-H bending vibrations of mono substituted benzene ring), 856 (C-H bending vibration of p-disubstituted benzene ring), 2922 (aliphatic C-H stretching), 3053 (aromatic C-H stretching).

PMR 1.25 (3H, triplet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 2.31 (3H, singlet, CH$_3$), 2.84 (2H, quartet, $J = 7.6$ Hz, -CH$_2$CH$_3$), 3.32 (1H, doublet of a doublet, $J = 18.8$ and 4.8 Hz, C$_4$'-H$_{\text{trans}}$), 3.84 (1H, doublet of a doublet, $J = 18.8$ and 12.0 Hz, C$_4$'-H$_{\text{cis}}$), 5.84 (1H, doublet of a doublet, $J = 12.0$ and 4.8 Hz, C$_5$'-
H), 7.21-7.81 (14H, multiplet, aromatic protons), 8.28 (1H, singlet, C-4-H).

\(^{13}\)C-NMR (δ, ppm) (Fig 16)
8.99(CH\(_3\)), 21.20(CH\(_3\)), 27.67(CH\(_2\)), 43.63(CH\(_2\)), 52.79(CH), 116.68(CH), 118.78(CH), 119.09(CH), 122.47(C), 124.93(CH), 125.71(CH), 126.34(C), 128.56(CH), 128.66(CH), 129.19(CH), 129.27(CH), 130.33(C), 132.79(CH), 137.88(C), 139.92(C), 140.71(CH), 150.75(C), 154.08(CO of coumarin), 172.36(-N-CO-CH\(_3\)).

**Compound 2g**

**IR** (ν\(_{\text{max}}\) in cm\(^{-1}\))
ν\(_{\text{max}}\) 1727 and 1643 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH\(_3\) group present in pyrazoline nucleus respectively), 1601 and 1513 (aromatic C=C and C=N stretchings), 684 and 747 (C-H bending vibrations of mono substituted benzene ring), 2931 (aliphatic C-H stretching), 3059 (aromatic C-H stretching).

**PMR** (δ, ppm) (Fig 17)
1.24 (3H, triplet, J = 6.8 Hz, -CH\(_2\)CH\(_3\)), 2.83 (2H, quartet, J = 6.8 Hz, -CH\(_2\)CH\(_3\)), 3.34 (1H, doublet of a doublet, J = 18.8 and 4.8 Hz, C\(_4\)'-H\(_{\text{trans}}\)), 3.86 (1H, doublet of a doublet, J = 18.8 and 12.0 Hz, C\(_4\)'-H\(_{\text{cis}}\)), 3.98 (3H, singlet, OCH\(_3\)), 5.82 (1H, doublet of a doublet, J = 12.0 and 4.8 Hz, C\(_5\)'-H), 7.12-7.82 (14H, multiplet, aromatic protons), 8.27 (1H, singlet, C-4-H).

\(^{13}\)C-NMR (δ, ppm) (Fig 18)
8.86(CH\(_3\)), 27.66(CH\(_2\)), 44.07(CH\(_2\)), 52.82(CH), 56.32(OCH\(_3\)), 114.40(CH), 114.75(C), 119.12(C), 119.38(CH), 119.90(CH), 122.65(CH), 125.72(CH), 126.57(CH), 128.14(CH), 128.64(CH), 129.30(CH), 133.18(C), 139.87(C), 140.97(CH), 143.73(CH), 147.07(C), 150.65(C), 150.73(C), 158.49(CO of coumarin), 172.42(-N-CO-CH\(_3\)).

**Compound 2h**

**IR** (ν\(_{\text{max}}\) in cm\(^{-1}\))
ν\(_{\text{max}}\) 1729 and 1655 (C=O stretching of δ-lactone of coumarin and carbonyl of -N-CO-CH\(_3\) group present in pyrazoline nucleus respectively), 1611 and 1515 (aromatic
C=C and C=N stretchings), 689 and 754 (C-H bending vibrations of mono substituted benzene ring), 867 (C-H bending vibration of p-disubstituted benzene ring), 2935 (aliphatic C-H stretching), 3043 (aromatic C-H stretching).

**(1H, doublet of a doublet, J = 18.8 and 4.8 Hz, C_4′-H_{trans}), 3.86 (1H, doublet of a doublet, J = 18.8 and 12.0 Hz, C_4′-H_{cis}), 3.99 (3H, singlet, OCH_3), 5.82 (1H, doublet of a doublet, J = 12.0 and 4.8 Hz, C_5′-H), 7.13-7.81 (13H, multiplet, aromatic protons), 8.25 (1H, singlet, C_4-H).**

In case of the compounds 2c, 2d, 2f and 2g, the number of non-equivalent carbon signals in $^{13}$C NMR spectra is less than expected (in case of compound 2d, one signal, in compounds 2c and 2g, two signals and in compound 2f, three signals). This may be due to identical chemical shifts of certain carbons which may appear at same position.
**Fig 1**  IR spectrum of compound 2a

**Fig 2**  PMR spectrum of compound 2a
Fig 3  Expanded PMR (2.0-6.0 δ) of compound 2a

Fig 4  $^{13}$C NMR spectrum of compound 2a
**Fig 5**  DEPT-135 spectrum of compound 2a

**Fig 6**  Mass spectrum of compound 2a
Fig 7  PMR spectrum of compound 2b

Fig 8  $^{13}$C NMR spectrum of compound 2b
Fig 9  PMR spectrum of compound 2c

Fig 10  $^{13}$C NMR spectrum of compound 2c
Fig 11  PMR spectrum of compound 2d

Fig 12  $^{13}$C NMR spectrum of compound 2d
**Fig 13** PMR spectrum of compound 2e

**Fig 14** $^{13}$C NMR spectrum of compound 2e
**Fig 15**  PMR spectrum of compound 2f

**Fig 16**  $^{13}$C NMR spectrum of compound 2f
Fig 17  PMR spectrum of compound 2g

Fig 18  $^{13}$C NMR spectrum of compound 2g
Fig 19  PMR spectrum of compound 2h

Fig 20  $^{13}$C NMR spectrum of compound 2h
5.2.2 Synthesis of 3-[5-(1,3-diaryl-1H-pyrazol-4-yl)-1-aryl-4,5-dihydro-1H-pyrazol-3-yl]coumarins (4a-l)

The synthesis of 3-[5-(1,3-diaryl-1H-pyrazol-4-yl)-1-aryl-4,5-dihydro-1H-pyrazol-3-yl]coumarins (4a-l) have been carried out by reacting various 3-[3-(1,3-diaryl-1H-pyrazol-4-yl)acryloyl]coumarins (1a-d) with appropriate phenyl hydrazine (3a-c) in the presence of acetic acid under MWI for 6 minutes (Scheme 3).

![Scheme 3](image)

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The formation of (4a-l) was observed very fast (6 minutes) and with good yields (77-85%).

The structures of all the compounds (4a-l) were confirmed by analytical and spectral data.

Thus the microwave irradiation of 3-[3-(1,3-diphenyl-1H-pyrazol-4-yl)acryloyl]coumarin (coumarin chalcone) (1a) with phenyl hydrazine (3a) in the presence acetic acid proceeded smoothly and gave the expected product (4a) as a red colored solid in 80% yield.

The IR spectrum of 4a (Fig 21) showed strong band at 1729 cm\(^{-1}\) which is due to carbonyl stretching of δ-lactone ring present in coumarin nucleus. The bands observed at 1598 and 1499 cm\(^{-1}\) are...
due to aromatic C=C and C=N stretching vibrations respectively. The sharp and intense bands observed at 692 and 751 cm\(^{-1}\) are due to C-H out of plane bending vibrations for mono substituted phenyl ring. The bands observed at 2934 and 3061 cm\(^{-1}\) are due to aliphatic C-H stretching of pyrazoline ring and aromatic C-H stretching vibrations respectively.

The PMR spectrum of compound 4a (Fig 22 and 23) showed a doublet of doublet centered at 3.55 \(\delta\) \((J = 18.0\) and \(6.8\) Hz\) integrating for one proton, is due to \(\text{C}_4\)\(^{\prime}\)-H\(_{\text{trans}}\). A doublet of doublet centered at 4.13 \(\delta\) \((J = 18.0\) and \(12.4\) Hz\) integrating for one proton, is due to \(\text{C}_4\)\(^{\prime}\)-H\(_{\text{cis}}\). A doublet of doublet centered at 5.56 \(\delta\) \((J = 12.4\) and \(6.8\) Hz\) integrating for one proton, is due to proton attached at \(\text{C}_5\)\(^{\prime}\). Twenty aromatic protons were observed between 6.86-7.94 \(\delta\) as a multiplet. The \(\text{C}_4\)-H of coumarin ring appeared as a singlet at 8.38 \(\delta\).

The \(^{13}\)C NMR spectrum of compound 4a (Fig 24) showed signals at 44.57, 56.06, 110.38, 113.19, 114.23, 116.05, 116.80, 118.91, 119.15, 121.58, 121.88, 123.35, 125.73, 128.59, 129.63, 130.22, 130.97, 131.26, 131.58, 132.06, 132.89, 134.15, 135.52, 140.81, 142.97, 153.08 and 160.19 \(\delta\) corresponding to twenty seven different type of carbon atoms present in the compound. The signals appeared at 44.57 and 56.06 \(\delta\) are due to \(\text{C}_4\)\(^{\prime}\) and \(\text{C}_5\)\(^{\prime}\) respectively. The signal appeared at 160.19 \(\delta\) can be assigned to the carbonyl carbon of the \(\delta\)-lactone ring of coumarin. The DEPT-135 spectrum of compound 4a (Fig 25) showed inverted signal at 44.57 \(\delta\), which further confirms that this signal is for \(\text{C}_4\)\(^{\prime}\) carbon. The upward signal at 56.06 \(\delta\) confirms that it is due to \(\text{C}_5\)\(^{\prime}\). The signals appeared at 113.19, 114.23, 116.05, 118.91, 119.15, 121.58, 121.88, 123.35, 125.73, 128.59, 129.63, 131.26, 131.58, 134.15 and 135.52 \(\delta\) correspond to fifteen non equivalent tertiary carbon atoms present in the compound.

The mass spectrum of compound 4a (Fig 26) showed \(M^+\) peak at 507(100%) (m/z %) along with some other fragments peaks at 473(8%), 416(10%), 289(22%), 91(28%), 77(36%), 64(8%), 44(9%) etc.
appearance of molecular ion peak at 507 mass unit supports the structure of compound 4a.

The IR and NMR data for other compounds (4b-l) are given below.

**Compound 4b**

| IR (cm⁻¹) | νmax 1730 (C=O stretching of δ-lactone of coumarin), 1600 and 1500 (aromatic C=C and C=N stretchings), 690 and 750 (C-H bending vibrations of mono substituted benzene ring), 870 (C-H bending vibrations of p-disubstituted benzene ring), 2920 (aliphatic C-H stretching), 3063 (aromatic C-H stretching). |
| PMR (δ, ppm) (Fig 27) | 2.45 (3H, singlet, CH₃), 3.54 (1H, doublet of a doublet, J = 18.0 and 6.8 Hz, C₄'-Htrans), 4.14 (1H, doublet of a doublet, J = 18.0 and 12.4 Hz, C₄'-Hcis), 5.56 (1H, doublet of a doublet, J = 12.4 and 6.8 Hz, C₅'-H), 6.84-7.76 (19H, multiplet, aromatic protons), 8.38 (1H, singlet, C₄-H). |
| ¹³C-NMR (δ, ppm) (Fig 28) | 21.33(CH₃), 44.72(CH₂), 57.01(CH), 113.87(CH), 116.48(CH), 118.92(CH), 119.47(C), 120.10(CH), 120.87(C), 122.47(C), 124.74(CH), 126.04(CH), 126.38(CH), 127.96(CH), 128.18(CH), 129.07(CH), 129.28(CH), 129.53(CH), 130.03(C), 131.60(CH), 137.80(CH), 138.17(C), 139.81(C), 143.27(C), 143.80(C), 150.26(C), 153.58(C), 159.60(CO of coumarin). |

**Compound 4c**

| IR (cm⁻¹) | νmax 1740 (C=O stretching of δ-lactone of coumarin), 1591 and 1496 (aromatic C=C and C=N stretchings), 695 and 770 (C-H bending vibrations of mono substituted benzene ring), 2927 (aliphatic C-H stretching), 3055 (aromatic C-H stretching). |
| PMR (δ, ppm) (Fig 29) | 3.57 (1H, doublet of a doublet, J = 18.4 and 7.2 Hz, C₄'-Htrans), 4.02 (3H, singlet, OCH₃), 4.17 (1H, doublet of a doublet, J = 18.4 and 12.4 Hz, C₄'-Hcis), 5.56 (1H, doublet
of a doublet, \(J = 12.4\) and \(7.2\) Hz, \(C_5'-H\), 6.83-7.83 (19H, multiplet, aromatic protons), 8.38 (1H, singlet, \(C_4-H\)).

\(\text{\(^{13}\)C-NMR (\(\delta\), ppm) (Fig 30)\)}

\[\begin{align*}
44.84(\text{CH}_2), & \quad 56.31(\text{OCH}_3), & \quad 57.00(\text{CH}), & \quad 113.54(\text{CH}), \\
113.86(\text{CH}), & \quad 118.96(\text{CH}), & \quad 119.47(\text{C}), & \quad 119.70(\text{CH}), \\
120.10(\text{C}), & \quad 122.47(\text{C}), & \quad 124.58(\text{CH}), & \quad 126.14(\text{CH}), \\
126.47(\text{CH}), & \quad 128.09(\text{CH}), & \quad 128.33(\text{CH}), & \quad 128.84(\text{CH}), \\
129.07(\text{CH}), & \quad 129.30(\text{CH}), & \quad 130.03(\text{C}), & \quad 131.60(\text{CH}), \\
137.80(\text{C}), & \quad 138.03(\text{CH}), & \quad 139.81(\text{C}), & \quad 143.27(\text{C}), \\
143.80(\text{C}), & \quad 150.26(\text{C}), & \quad 153.58(\text{C}), & \quad 159.60(\text{C of coumarin}).
\end{align*}\]

\textbf{Compound 4d}

\(\text{IR (cm}^{-1}\) \(v_{\text{max}}\) 1720 (C=O stretching of \(\delta\)-lactone of coumarin), 1596 and 1493 (aromatic C=C and C=N stretchings), 694 and 740 (C-H bending vibrations of mono substituted benzene ring), 864 (C-H bending vibrations of p-disubstituted benzene ring), 2929 (aliphatic C-H stretching), 3047 (aromatic C-H stretching).

\(\text{PMR (\(\delta\), ppm) (Fig 31)}\)

\[\begin{align*}
2.45 (3\text{H, singlet, CH}_3), & \quad 3.55 (1\text{H, doublet of a doublet, }J = 18.0\) and \(6.8\) Hz, \(C_4'\)-H\text{\_trans}), \\
4.00 (3\text{H, singlet, OCH}_3), & \quad 4.16 (1\text{H, doublet of a doublet, }J = 18.0\) and \(12.4\) Hz, \(C_4'\)-H\text{\_cis}), \\
5.55 (1\text{H, doublet of a doublet, }J = 12.4\) and \(6.8\) Hz, \(C_5'\)-H), & \quad 6.83-7.76 (18H, multiplet, aromatic protons), \\
8.37 (1\text{H, singlet, C}_4-H). & \quad \text{8.37 (1H, singlet, C}_4-H).\n\end{align*}\]

\(\text{\(^{13}\)C-NMR (\(\delta\), ppm) (Fig 32)\)}

\[\begin{align*}
21.63(\text{CH}_3), & \quad 44.57(\text{CH}_2), & \quad 56.36(\text{OCH}_3), & \quad 57.06(\text{CH}), \\
110.38(\text{C}), & \quad 113.19(\text{CH}), & \quad 114.23(\text{CH}), & \quad 116.05(\text{CH}), \\
116.80(\text{C}), & \quad 118.91(\text{CH}), & \quad 119.15(\text{CH}), & \quad 121.58(\text{CH}), \\
121.88(\text{CH}), & \quad 123.35(\text{CH}), & \quad 125.73(\text{CH}), & \quad 128.59(\text{CH}), \\
129.63(\text{CH}), & \quad 130.22(\text{C}), & \quad 130.97(\text{C}), & \quad 131.26(\text{C}), \\
132.06(\text{C}), & \quad 132.89(\text{C}), & \quad 134.15(\text{CH}), & \quad 135.52(\text{C}), \\
140.81(\text{C}), & \quad 142.97(\text{C}), & \quad 153.08(\text{C}), & \quad 160.19 (\text{CO of coumarin}).
\end{align*}\]

\textbf{Compound 4e}

\(\text{IR (cm}^{-1}\) \(v_{\text{max}}\) 1726 (C=O stretching of \(\delta\)-lactone of coumarin), 1591 and 1497 (aromatic C=C and C=N stretchings), 690 and
750 (C-H bending vibrations of mono substituted benzene ring), 880 (C-H bending vibrations of p-disubstituted benzene ring), 2932 (aliphatic C-H stretching), 3051 (aromatic C-H stretching).

PMR (δ, ppm) (Fig 33)

3.55 (1H, doublet of a doublet, J = 18.0 and 7.2 Hz, C₄'-Htrans), 4.15 (1H, doublet of a doublet, J = 18.0 and 12.4 Hz, C₄'-Hcis), 5.50 (1H, doublet of a doublet, J = 12.4 and 7.2 Hz, C₅'-H), 6.90-7.79 (19H, multiplet, aromatic protons), 8.35 (1H, singlet, C₄-H).

13C-NMR (δ, ppm) (Fig 34, 34a and 34b)

44.89(CH₂), 57.48(CH), doublet centered at 115.07 (C₂" & C₆"), 3J_C-F = 7.0 Hz), doublet centered at 115.64 (C₃" & C₅"), 2J_C-F = 22.0 Hz), 116.50(CH), 118.95(C), 119.40(C), 120.70(CH), 122.31(CH), 124.79(CH), 126.13(CH), 126.58(CH), 128.10(CH), 128.21(CH), 128.41(CH), 128.87(C), 129.36(CH), 131.71(CH), 132.83(CH), 137.93(C), 139.72(C), 140.43(C), 143.44(C), 150.32(C), 153.58(C), doublet centered at 157.40 (C₄", 1J_C-F = 237.0 Hz), 159.56(CO of coumarin).

**Compound 4f**

IR (cm⁻¹)

νmax 1733 (C=O stretching of δ-lactone of coumarin), 1589 and 1490 (aromatic C=C and C=N stretchings), 699 and 743 (C-H bending vibrations of mono substituted benzene ring), 868 (C-H bending vibrations of p-disubstituted benzene ring), 2928 (aliphatic C-H stretching), 3070 (aromatic C-H stretching).

PMR (δ, ppm) (Fig 35)

2.45 (3H, singlet, CH₃), 3.54 (1H, doublet of a doublet, J = 17.6 and 7.2 Hz, C₄'-Htrans), 4.15 (1H, doublet of a doublet, J = 17.6 and 12.4 Hz, C₄'-Hcis), 5.49 (1H, doublet of a doublet, J = 12.4 and 7.2 Hz, C₅'-H), 6.89-7.77 (18H, multiplet, aromatic protons), 8.35 (1H, singlet, C₄-H).

13C-NMR (APT) (δ, ppm)

21.34(CH₃), 44.85(CH₂), 57.50(CH), doublet centered at 115.03 (C₂" & C₆"), 3J_C-F = 7.0 Hz), doublet centered at 115.63 (C₃" & C₅"), 2J_C-F = 22.0 Hz), 116.50(CH),
(Fig 36) 118.91(CH), 119.40(C), 120.74(C), 122.16(C), 124.78(CH), 126.02(CH), 126.48(CH), 127.95(CH), 128.19(CH), 128.34(CH), 129.56(CH), 129.92(C), 131.69(CH), 137.89(CH), 138.26(C), 139.75(C), 140.40(C), 143.43(C), 150.57(C), 153.57(C), doublet centered at 157.37 (C₄″, ¹J_C-F = 237.0 Hz), 159.56(CO of coumarin).

**Compound 4g**

IR \(\text{v}_{\text{max}}\) 1736 (C=O stretching of δ-lactone of coumarin), 1586 and 1493 (aromatic C=C and C=N stretchings), 700 and 760 (C-H bending vibrations of mono substituted benzene ring), 861 (C-H bending vibrations of p-disubstituted benzene ring), 2940 (aliphatic C-H stretching), 3060 (aromatic C-H stretching).

PMR \(\delta, \text{ppm}\)

3.56 (1H, doublet of a doublet, \(J = 18.0 \text{ and } 7.2 \text{ Hz}\), C₄′-H\text{trans}), 3.99 (3H, singlet, OCH₃), 4.17 (1H, doublet of a doublet, \(J = 18.0 \text{ and } 12.4 \text{ Hz}\), C₄′-H\text{cis}), 5.49 (1H, doublet of a doublet, \(J = 12.4 \text{ and } 7.2 \text{ Hz}\), C₅′-H), 6.89-7.78 (18H, multiplet, aromatic protons), 8.35 (1H, singlet, C₄-H).

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

44.93(CH₂), 56.27(OCH₃), 57.51(CH), 113.57(CH), doublet centered at 115.04 (C₂″ & C₆″, \(^3\)J_C-F = 7.0 Hz), doublet centered at 115.62 (C₃″ & C₅″, \(^2\)J_C-F = 22.0 Hz), 118.95(CH), 119.67(CH), 120.04(C), 120.94(C), 122.33(C), 124.62(CH), 126.12(CH), 126.56(CH), 128.09(CH), 128.39(CH), 128.86(CH), 129.35(CH), 132.80(CH), 138.11(CH), 139.73(C), 140.43(C), 143.21(C), 143.48(CH), 147.00(C), 150.33(C), doublet centered at 157.38 (C₄″, ¹J_C-F = 237.0 Hz), 159.04(CO of coumarin).

**Compound 4h**

IR \(\text{v}_{\text{max}}\) 1730 (C=O stretching of δ-lactone of coumarin), 1593 and 1499 (aromatic C=C and C=N stretchings), 705 and 755 (C-H bending vibrations of mono substituted benzene ring), 876 (C-H bending vibrations of p-disubstituted benzene ring), 2931 (aliphatic C-H stretching), 3053 (aromatic C-H stretching).
PMR ($\delta$, ppm)  
(Fig 39)

2.45 (3H, singlet, CH$_3$), 3.55 (1H, doublet of a doublet, $J = 18.0$ and 7.2 Hz, C$_4$'-H$_{\text{trans}}$), 3.99 (3H, singlet, OCH$_3$), 4.16 (1H, doublet of a doublet, $J = 18.0$ and 12.4 Hz, C$_4$'-H$_{\text{cis}}$), 5.48 (1H, doublet of a doublet, $J = 12.4$ and 7.2 Hz, C$_5$'-H), 6.89-7.77 (17H, multiplet, aromatic protons), 8.34 (1H, singlet, C$_4$-H).

$^{13}$C-NMR ($\delta$, ppm)  
(Fig 40)

21.32(CH$_3$), 44.89(CH$_2$), 56.28(OCH$_3$), 57.56(CH), 113.60(CH), doublet centered at 115.05 (C$_2''$ & C$_6''$, $^3J_{C-F} = 7.0$ Hz), doublet centered at 115.60 (C$_3''$ & C$_5''$, $^2J_{C-F} = 22.0$ Hz), 118.92(CH), 119.68(CH), 120.07(C), 120.99(C), 122.21(C), 124.60(CH), 126.02(CH), 126.45(CH), 127.98(CH), 129.32(CH), 129.54(CH), 129.93(C), 138.04(CH), 138.24(C), 139.79(C), 140.46(C), 143.24(C), 143.48(C), 147.02(C), 150.40(C), doublet centered at 157.38 (C$_4''$, $^1J_{C-F} = 237.0$ Hz), 159.02(CO of coumarin).

Compound 4i

IR (cm$^{-1}$)  

$\nu_{\text{max}}$ 1710 (C=O stretching of $\delta$-lactone of coumarin), 1603 and 1490 (aromatic C=C and C=N stretchings), 691 and 747 (C-H bending vibrations of mono substituted benzene ring), 860 (C-H bending vibrations of p-disubstituted benzene ring), 2933 (aliphatic C-H stretching), 3073 (aromatic C-H stretching).

PMR ($\delta$, ppm)  
(Fig 41)

3.57 (1H, doublet of a doublet, $J = 18.0$ and 6.8 Hz, C$_4$'-H$_{\text{trans}}$), 4.15 (1H, doublet of a doublet, $J = 18.0$ and 12.4 Hz, C$_4$'-H$_{\text{cis}}$), 5.53 (1H, doublet of a doublet, $J = 12.4$ and 6.8 Hz, C$_5$'-H), 7.00-7.79 (19H, multiplet, aromatic protons), 8.37 (1H, singlet, C$_4$-H).

$^{13}$C-NMR (APT) ($\delta$, ppm)  
(Fig 42)

44.88(CH$_2$), 56.87(CH), 114.96(CH), 116.53(CH), 118.98(CH), 119.34(C), 120.57(C), 122.08(C), 124.82(CH), 124.94(C), 126.03(CH), 126.62(CH), 128.08(CH), 128.26(CH), 128.44(CH), 128.89(CH), 128.98(CH), 129.35(CH), 131.83(CH), 132.75(C), 138.20(CH), 139.68(C), 142.26(C), 143.46(C), 150.27(C), 153.62(C), 159.53(CO of coumarin).
**Compound 4j**

**IR (cm⁻¹)**

\[ \nu_{\text{max}} \] 1729 (C=O stretching of δ-lactone of coumarin), 1596 and 1497 (aromatic C=C and C=N stretchings), 686 and 755 (C-H bending vibrations of mono substituted benzene ring), 855 (C-H bending vibrations of p-disubstituted benzene ring), 2920 (aliphatic C-H stretching), 3052 (aromatic C-H stretching).

**PMR (δ, ppm) (Fig 43)**

2.45 (3H, singlet, CH₃), 3.56 (1H, doublet of a doublet, \( J = 18.0 \) and \( 6.4 \) Hz, \( C_4'\)-H\text{trans})), 4.14 (1H, doublet of a doublet, \( J = 18.0 \) and \( 12.4 \) Hz, \( C_4'\)-H\text{cis})), 5.52 (1H, doublet of a doublet, \( J = 12.4 \) and \( 6.4 \) Hz, \( C_5'\)-H), 7.00-7.73 (18H, multiplet, aromatic protons), 8.36 (1H, singlet, C₄-H).

**13C-NMR (APT) (δ, ppm) (Fig 44)**

21.34(CH₃), 44.84(CH₂), 56.89(CH), 114.96(CH), 116.52(CH), 118.94(CH), 119.35(C), 120.60(C), 121.93(C), 124.81(CH), 124.89(C), 125.92(CH), 126.51(CH), 127.95(CH), 128.24(CH), 128.97(CH), 129.33(CH), 129.58(CH), 129.86(C), 131.81(CH), 138.15(CH), 138.30(C), 139.72(C), 142.26(C), 143.86(C), 150.32(C), 153.61(C), 159.52(CO of coumarin).

**Compound 4k**

**IR (cm⁻¹)**

\[ \nu_{\text{max}} \] 1735 (C=O stretching of δ-lactone of coumarin), 1595 and 1495 (aromatic C=C and C=N stretchings), 695 and 765 (C-H bending vibrations of mono substituted benzene ring), 876 (C-H bending vibrations of p-disubstituted benzene ring), 2934 (aliphatic C-H stretching), 3065 (aromatic C-H stretching).

**PMR (δ, ppm) (Fig 45)**

3.58 (1H, doublet of a doublet, \( J = 18.0 \) and \( 6.8 \) Hz, \( C_4'\)-H\text{trans})), 3.98 (3H, singlet, OCH₃), 4.16 (1H, doublet of a doublet, \( J = 18.0 \) and \( 12.4 \) Hz, \( C_4'\)-H\text{cis})), 5.51 (1H, doublet of a doublet, \( J = 12.4 \) and \( 6.8 \) Hz, \( C_5'\)-H), 6.99-7.76 (18H, multiplet, aromatic protons), 8.34 (1H, singlet, C₄-H).

**13C-NMR (APT)**

44.92(CH₂), 56.27(OCH₃), 56.88(CH), 113.66(CH),
(δ, ppm)(Fig 46) 114.95(CH), 118.97(CH), 119.71(CH), 119.98(C), 120.79(C), 122.11(C), 124.65(CH), 124.89(C), 126.04(CH), 126.59(CH), 128.09(CH), 128.42(CH), 128.88(CH), 128.96(CH), 129.35(C), 132.75(CH), 138.37(CH), 139.69(C), 142.26(C), 143.24(C), 143.88(C), 147.00(C), 150.27(C), 159.02(CO of coumarin).

**Compound 4l**

**IR (cm**^-1)**

ν\textsubscript{max} 1725 (C=O stretching of δ-lactone of coumarin), 1589 and 1488 (aromatic C=C and C=N stretchings), 696 and 759 (C-H bending vibrations of mono substituted benzene ring), 869 (C-H bending vibrations of p-disubstituted benzene ring), 2921 (aliphatic C-H stretching), 3048 (aromatic C-H stretching).

**PMR (δ, ppm)(Fig 47)**

2.45 (3H, singlet, CH\textsubscript{3}), 3.57 (1H, doublet of a doublet, J = 18.0 and 6.8 Hz, C\textsubscript{4}'-H\textsub{trans}), 3.99 (3H, singlet, OCH\textsubscript{3}), 4.15 (1H, doublet of a doublet, J = 18.0 and 12.4 Hz, C\textsubscript{4}'-H\textsub{cis}), 5.51 (1H, doublet of a doublet, J = 12.4 and 6.8 Hz, C\textsubscript{5}'-H), 6.99-7.74 (17H, multiplet, aromatic protons), 8.34 (1H, singlet, C\textsubscript{4}-H).

**\textsuperscript{13}C-NMR (APT)(δ, ppm)(Fig 48)**

21.34(CH\textsubscript{3}), 44.87(CH\textsubscript{2}), 56.26(OCH\textsubscript{3}), 56.90(CH), 113.64(CH), 114.95(CH), 118.93(CH), 119.70(CH), 119.99(C), 120.83(C), 122.97(C), 124.64(CH), 124.84(C), 125.93(CH), 126.48(CH), 127.96(CH), 128.95(CH), 129.32(CH), 129.57(CH), 129.88(C), 138.28(C), 138.31(CH), 139.73(C), 142.27(C), 143.23(C), 143.88(C), 146.99(C), 150.32(C), 158.98(CO of coumarin).

In \textsuperscript{13}C spectra of compounds 4e-h, the three sets of carbon i.e, C\textsubscript{2}”, C\textsubscript{3}” and C\textsubscript{4}” appear as doublets due to the \textsuperscript{3}J\textsubscript{C-F}, \textsuperscript{2}J\textsubscript{C-F}, \textsuperscript{1}J\textsubscript{C-F} couplings respectively. In figure 34a and 34b expanded \textsuperscript{13}C spectra, these doublets are shown for compound 4e.
**Fig 21** IR spectrum of compound 4a

**Fig 22** PMR spectrum of compound 4a
**Fig 23** Expanded PMR (2.0-6.0 δ) of compound 4a

**Fig 24** $^{13}$C NMR spectrum of compound 4a
**Fig 25** DEPT-135 spectrum of compound 4a

**Fig 26** Mass spectrum of compound 4a
Fig 27  PMR spectrum of compound 4b

Fig 28  $^{13}$C NMR spectrum of compound 4b
**Fig 29**  PMR spectrum of compound 4c

**Fig 30**  $^{13}$C NMR spectrum of compound 4c
**Fig 31** PMR spectrum of compound 4d

**Fig 32** $^{13}$C NMR spectrum of compound 4d
Fig 33  PMR spectrum of compound 4e

Fig 34  $^{13}$C NMR spectrum of compound 4e
Fig 34a  Expanded $^{13}$C NMR (114.5-116.5 δ) of compound 4e

Fig 34b  Expanded $^{13}$C NMR (154.0-160.0 δ) of compound 4e
Fig 35  PMR spectrum of compound 4f

Fig 36  APT spectrum of compound 4f
**Fig 37** PMR spectrum of compound 4g

**Fig 38** APT spectrum of compound 4g
Fig 39  PMR spectrum of compound 4h

Fig 40  \textsuperscript{13}C NMR spectrum of compound 4h
Fig 41  PMR spectrum of compound 4i

Fig 42  APT spectrum of compound 4i
Fig 43  PMR spectrum of compound 4j

Fig 44  APT spectrum of compound 4j
**Fig 45** PMR spectrum of compound 4k

**Fig 46** APT spectrum of compound 4k
Fig 47  PMR spectrum of compound 41

Fig 48  APT spectrum of compound 41
5.3 Experimental

The microwave reactions were carried out on Raga’s electromagnetic system. The starting material 3-acetyl coumarins were prepared as described in chapter 2.

5.3.1 Preparation of 1-phenyl-3-aryl-1H-pyrazole-4-carbaldehydes

The following general procedure was used.

In a 100 mL round bottom flask a mixture of acetophenone (0.01 mol), phenyl hydrazine (0.01 mol) and ethanol (5 mL) containing 1-2 drops of glacial acetic acid was warmed on the steam cone for 15 minutes. The separated phenyl hydrazone was filtered off, washed with cold ethanol (5 mL) and dried. It was recrystallized from ethanol.

The freshly prepared acetophenone phenyl hydrazone (0.06 mol) was taken in a 250 mL three necked round bottom flask fitted with addition funnel and guard tube in anhydrous dimethyl formamide (DMF) (0.6 mol) and the reaction mixture was cooled to 0°C with stirring. In this well stirred reaction mixture, phosphorous oxychloride (POCl₃) (0.18 mol) was added dropwise during one hour. After addition was completed, the reaction mixture was further stirred at 0°C for one hour. The reaction mixture was then heated at 65-70°C for two hours. It was then poured into crushed ice (200 g) and left overnight in refrigerator, during which a solid product was separated out which was filtered off, washed with sodium carbonate (5%, 3 x 30 mL) and water. It was then dried and recrystallized from ethanol.

**Compound a**: R = H; Yield: 95%, mp 139°C (lit.₃₃ mp 140°C)

**Compound b**: R = CH₃; Yield: 93%, mp 162°C (lit.₃₃ mp 164°C)
5.3.2 Preparation of 3-[3-(1,3-diaryl-1H-pyrazol-4-yl)acryloyl]coumarins (1a-d)

In a 100 mL round bottom flask, an appropriate 3-acetyl coumarin (0.01 mol) and appropriate pyrazole aldehyde (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 2a:** \( R = R_1 = H; \)
Yield: 86%, mp 234°C

<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>77.64</td>
<td>4.29</td>
<td>6.62</td>
</tr>
<tr>
<td>Calculated</td>
<td>77.50</td>
<td>4.34</td>
<td>6.69</td>
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IR \( \nu_{\text{max}} \) 1720 (C=O stretching of \( \delta \)-lactone of coumarin), 1659 (\( \alpha,\beta \) unsaturated carbonyl group), 1605 and 1535 (aromatic C=C and C=N stretchings), 687 and 756 (C-H bending vibrations of mono substituted benzene ring), 3063 (aromatic C-H stretching)

PMR 7.35-8.01 (16H, multiplet, fourteen aromatic protons + two olefinic proton), 8.47 (1H, singlet, proton of pyrazole ring), 8.60 (1H, singlet, \( C_4 \)-H of coumarin)

**Compound 2b:** \( R = H, \ R_1 = CH_3; \)
Yield: 81%, mp 208°C

<table>
<thead>
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<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
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<tr>
<td>Found</td>
<td>77.88</td>
<td>4.62</td>
<td>6.51</td>
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<tr>
<td>Calculated</td>
<td>77.76</td>
<td>4.66</td>
<td>6.48</td>
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IR (cm\(^{-1}\)) \(\nu_{\text{max}}\) 1705 (C=O stretching of \(\delta\)-lactone of coumarin), 1659 (\(\alpha,\beta\) unsaturated carbonyl group), 1605 and 1528 (aromatic C=C and C=N stretchings), 820 (C-H bending vibrations of \textit{para} disubstituted benzene ring), 679 and 764 (C-H bending vibrations of mono substituted benzene ring), 2921 (aliphatic C-H stretching), 3024 (aromatic C-H stretching)

PMR (\(\delta\), ppm) 2.45 (3H, singlet, CH\(_3\)), 7.32-8.01 (15H, multiplet, thirteen aromatic protons + two olefinic proton), 8.46 (1H, singlet, proton of pyrazole ring), 8.60 (1H, singlet, C\(_4\)-H of coumarin)

**Compound 2c**: R = OCH\(_3\), R\(_1\) = H;

Yield: 89%, mp 220°C \hspace{1cm} Molecular Formula: C\(_{28}\)H\(_{20}\)N\(_2\)O\(_4\)

<table>
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<th>% N</th>
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<tr>
<td>Found</td>
<td>75.16</td>
<td>4.62</td>
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<td>Calculated</td>
<td>74.99</td>
<td>4.50</td>
<td>6.25</td>
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IR (cm\(^{-1}\)) \(\nu_{\text{max}}\) 1720 (C=O stretching of \(\delta\)-lactone of coumarin), 1661 (\(\alpha,\beta\) unsaturated carbonyl group), 1610 and 1535 (aromatic C=C and C=N stretchings), 687 and 780 (C-H bending vibrations of mono substituted benzene ring), 2933 (aliphatic C-H stretching), 3046 (aromatic C-H stretching)

PMR (\(\delta\), ppm) 4.02 (3H, singlet, OCH\(_3\)), 7.19-8.01 (15H, multiplet, thirteen aromatic protons + two olefinic proton), 8.48 (1H, singlet, proton of pyrazole ring), 8.58 (1H, singlet, C\(_4\)-H of coumarin)

**Compound 2d**: R = OCH\(_3\), R\(_1\) = CH\(_3\);

Yield: 91%, mp 160°C \hspace{1cm} Molecular Formula: C\(_{29}\)H\(_{22}\)N\(_2\)O\(_4\)

<table>
<thead>
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<th>% C</th>
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<th>% N</th>
</tr>
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<tbody>
<tr>
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<td>75.18</td>
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<tr>
<td>Calculated</td>
<td>75.31</td>
<td>4.79</td>
<td>6.06</td>
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</table>

IR (cm\(^{-1}\)) \(\nu_{\text{max}}\) 1728 (C=O stretching of \(\delta\)-lactone of coumarin), 1651 (\(\alpha,\beta\) unsaturated carbonyl group), 1605 and 1574
(aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of \textit{para} disubstituted benzene ring), 680 and 779 (C-H bending vibrations of mono substituted benzene ring), 2925 (aliphatic C-H stretching), 3056 (aromatic C-H stretching)

PMR ($\delta$, ppm)

2.45 (3H, singlet, CH$_3$), 4.02 (3H, singlet, OCH$_3$), 7.19-8.01 (14H, multiplet, twelve aromatic protons + two olefinic proton), 8.46 (1H, singlet, proton of pyrazole ring), 8.58 (1H, singlet, C$_4$-H of coumarin)

5.3.3 Preparation of 3-[1-acetyl/propionyl-5-(1,3-diaryl-1H pyrazol-4-y1)-4,5-dihydro-1H-pyrazol-3-yl]coumarins (2a-h)

The following general procedure was used.

A mixture of an appropriate 3-[3-(1,3-diaryl-1H-pyrazol-4-y1) acryloyl]coumarin (coumarin chalcone) (1a-d) (0.003 mol), hydrazine hydrate (0.009 mol) in acetic acid or propionic acid (8 mL) were stirred at room temperature for 15 minutes and then irradiated for 4 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 3-[1-acetyl/propionyl-5-(1,3-diaryl-1H-pyrazol-4-y1)-4,5-dihydro-1H-pyrazol-3-y1]coumarins (2a-h).

\textbf{Compound 2a}: R = R$_1$ = H, R$_2$ = CH$_3$;

Yield = 83\% \hspace{1em} mp 274°C \hspace{1em} Molecular Formula: C$_{29}$H$_{22}$N$_4$O$_3$ \hspace{1em} O

\begin{tabular}{lccc}
 & \% C & \% H & \% N \\
Analysis & 73.54 & 4.60 & 11.83 \\
Found & 73.40 & 4.67 & 11.81 \\
Calculated & & & \\
\end{tabular}
**Compound 2b:** \( R = H, R_1 = R_2 = \text{CH}_3; \)

Yield = 87%  
mp 262°C  
Molecular Formula: \( \text{C}_{30}\text{H}_{24}\text{N}_4\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.66</td>
<td>5.00</td>
<td>11.45</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.76</td>
<td>4.95</td>
<td>11.47</td>
</tr>
</tbody>
</table>

**Compound 2c:** \( R = \text{OCH}_3, R_1 = H, R_2 = \text{CH}_3; \)

Yield = 79%  
mp 224°C  
Molecular Formula: \( \text{C}_{30}\text{H}_{24}\text{N}_4\text{O}_4 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>71.30</td>
<td>4.73</td>
<td>11.13</td>
</tr>
<tr>
<td>Calculated</td>
<td>71.42</td>
<td>4.79</td>
<td>11.10</td>
</tr>
</tbody>
</table>

**Compound 2d:** \( R = \text{OCH}_3, R_1 = R_2 = \text{CH}_3; \)

Yield = 82%  
mp 246°C  
Molecular Formula: \( \text{C}_{31}\text{H}_{26}\text{N}_4\text{O}_4 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>71.66</td>
<td>5.11</td>
<td>10.83</td>
</tr>
<tr>
<td>Calculated</td>
<td>71.80</td>
<td>5.05</td>
<td>10.80</td>
</tr>
</tbody>
</table>

**Compound 2e:** \( R = R_1 = H, R_2 = \text{CH}_2\text{CH}_3; \)

Yield = 88%  
mp 278°C  
Molecular Formula: \( \text{C}_{30}\text{H}_{24}\text{N}_4\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.87</td>
<td>4.90</td>
<td>11.44</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.76</td>
<td>4.95</td>
<td>11.47</td>
</tr>
</tbody>
</table>

**Compound 2f:** \( R = H, R_1 = \text{CH}_3, R_2 = \text{CH}_2\text{CH}_3; \)

Yield = 80%  
mp 258°C  
Molecular Formula: \( \text{C}_{31}\text{H}_{26}\text{N}_4\text{O}_3 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.95</td>
<td>5.17</td>
<td>11.11</td>
</tr>
<tr>
<td>Calculated</td>
<td>74.09</td>
<td>5.21</td>
<td>11.15</td>
</tr>
</tbody>
</table>

**Compound 2g:** \( R = \text{OCH}_3, R_1 = H, R_2 = \text{CH}_2\text{CH}_3; \)

Yield = 85%  
mp 242°C  
Molecular Formula: \( \text{C}_{31}\text{H}_{26}\text{N}_4\text{O}_4 \)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>71.91</td>
<td>5.10</td>
<td>10.76</td>
</tr>
<tr>
<td>Calculated</td>
<td>71.80</td>
<td>5.05</td>
<td>10.80</td>
</tr>
</tbody>
</table>

**Compound 2h:** \( R = \text{OCH}_3, R_1 = \text{CH}_3, R_2 = \text{CH}_2\text{CH}_3; \)

Yield = 81%  
mp 240°C  
Molecular Formula: \( \text{C}_{32}\text{H}_{28}\text{N}_4\text{O}_4 \)
5.3.4 Preparation of 3-[5-(1,3-diaryl-1H-pyrazol-4-yl)-1-aryl-4,5-dihydro-1H-pyrazol-3-yl]coumarins (4a-l)

The following general procedure was used.

A mixture of an appropriate 3-[3-(1,3-diaryl-1H-pyrazol-4-yl)acryloyl]coumarin (coumarin chalcone) (1a-d) (0.003 mol) and an appropriate phenyl hydrazine (0.009 mol) in acetic acid (8 mL) were stirred at room temperature for 15 minutes and then irradiated for 6 minutes in microwave at 240 W (35%) power. The reaction mixture was then poured in to the crushed ice. The solid product was separated out, which was filtered out, washed with water and recrystallized from methanol to afford 3-[5-(1,3-diaryl-1H-pyrazol-4-yl)-1-aryl-4,5-dihydro-1H-pyrazol-3-yl]coumarins (4a-l).

**Compound 4a:** R = R<sub>1</sub> = R<sub>2</sub> = H;

Yield = 80%  \[ mp \text{ 216}^\circ\text{C} \]

Molecular Formula: C<sub>33</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>

Analysis % C % H % N

Found 78.04 4.71 11.05
Calculated 77.93 4.76 11.02

**Compound 4b:** R<sub>1</sub> = CH<sub>3</sub>, R = R<sub>2</sub> = H;

Yield = 84%  \[ mp \text{ 238}^\circ\text{C} \]

Molecular Formula: C<sub>34</sub>H<sub>26</sub>N<sub>4</sub>O<sub>2</sub>

Analysis % C % H % N

Found 78.01 5.07 10.69
Calculated 78.14 5.01 10.72
**Compound 4c**: R = OCH$_3$, R$_1$ = R$_2$ = H;  
Yield = 77%  mp 226°C  Molecular Formula: C$_{34}$H$_{26}$N$_4$O$_3$  
Analysis  % C  % H  % N  
Found  75.68  4.82  10.42  
Calculated  75.82  4.87  10.40

**Compound 4d**: R = OCH$_3$, R$_1$ = CH$_3$, R$_2$ = H;  
Yield = 79%  mp 244°C  Molecular Formula: C$_{35}$H$_{28}$N$_4$O$_3$  
Analysis  % C  % H  % N  
Found  76.19  5.16  10.18  
Calculated  76.07  5.11  10.14

**Compound 4e**: R = R$_1$ = H, R$_2$ = F;  
Yield = 85%  mp 216°C  Molecular Formula: C$_{33}$H$_{23}$FN$_4$O$_2$  
Analysis  % C  % H  % N  
Found  75.13  4.46  10.67  
Calculated  75.27  4.40  10.64

**Compound 4f**: R = H, R$_1$ = CH$_3$, R$_2$ = F;  
Yield = 80%  mp 218°C  Molecular Formula: C$_{34}$H$_{25}$FN$_4$O$_2$  
Analysis  % C  % H  % N  
Found  75.40  4.61  10.33  
Calculated  75.54  4.66  10.36

**Compound 4g**: R = OCH$_3$, R$_1$ = H, R$_2$ = F;  
Yield = 82%  mp 240°C  Molecular Formula: C$_{34}$H$_{25}$FN$_4$O$_3$  
Analysis  % C  % H  % N  
Found  73.49  4.59  10.10  
Calculated  73.37  4.53  10.07

**Compound 4h**: R = OCH$_3$, R$_1$ = CH$_3$, R$_2$ = F;  
Yield = 83%  mp 162°C  Molecular Formula: C$_{35}$H$_{27}$FN$_4$O$_3$  
Analysis  % C  % H  % N  
Found  73.51  4.72  9.86  
Calculated  73.67  4.77  9.82

**Compound 4i**: R = R$_1$ = H, R$_2$ = Cl;  
Yield = 85%  mp 170°C  Molecular Formula: C$_{33}$H$_{23}$ClN$_4$O$_2$
Analysis  % C     % H     % N
Found     72.87    4.32    10.33
Calculated 72.99    4.27    10.32

**Compound 4j**: R = H, R₁ = CH₃, R₂ = Cl;
Yield = 79%     mp 236°C    Molecular Formula: C₃₄H₂₅ClN₄O₂
Analysis  % C     % H     % N
Found     73.43    4.46    10.03
Calculated 73.31    4.52    10.06

**Compound 4k**: R = OCH₃, R₁ = H, R₂ = Cl;
Yield = 83%     mp 242°C    Molecular Formula: C₃₄H₂₅ClN₄O₃
Analysis  % C     % H     % N
Found     71.39    4.34    9.75
Calculated 71.26    4.40    9.78

**Compound 4l**: R = OCH₃, R₁ = CH₃, R₂ = Cl;
Yield = 81%     mp 250°C    Molecular Formula: C₃₅H₂₇ClN₄O₃
Analysis  % C     % H     % N
Found     71.47    4.69    9.55
Calculated 71.61    4.64    9.54
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