Synthesis of 1-Substituted 5-Aryl-3-(3-coumarinyl)-2-pyrazolines by the Reaction of 3-Aryl-1-(3-coumarinyl)propen-1-ones with Hydrazines

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Dedicated to Professor Dr. Fritz Sauter on the occasion of his 75th birthday

1-Acetyl- and 1-propionyl-2-pyrazolines **11-27** have been synthesized by the reaction of (3-coumarinyl)chalcones **1-10** with hydrazine in hot acetic acid or propionic acid. While 5-aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines **28-35** have been prepared by the reaction of (3-coumarinyl)chalcones **1,3,5-10** with phenylhydrazine in hot pyridine. Structures of all new compounds have been elucidated by microanalyses, ^{1}H and ^{13}C nmr spectroscopies.

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Introduction.

Coumarins are natural oxygen heterocyclic compounds found in various plants [1-3]. Because of their well known bioactivities, *viz*. antibacterial and antifungal [4], anticoagulant [5,6], etc. activities, natural, semisynthetic and synthetic coumarins possess a prominent place in drug research. Their utility stimulated the development of new synthetic procedures for the preparation of coumarin type substances. Some of these compounds can be used as useful intermediates for the synthesis of valuable heterocyclic ring systems. Among others, the 3-cinnamoyl coumarins synthesized by the reaction of 3-acetyl coumarins with aromatic aldehydes [6-12] proved to be especially important. 3-Cinnamoyl coumarins have been used for the synthesis of pyridines [6], isoxazolines [12], 1,5-benzodiazepines [13] and 1,5-benzothiazepines [14,15] and other nitrogen-containing heterocyclic compounds.

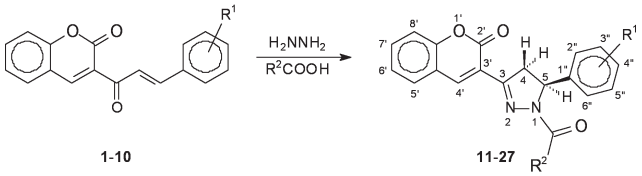
Pyrazolines are important nitrogen-containing five-membered heterocyclic compounds. Several pyrazoline derivatives were found to show considerable biological activities, *e.g*. antimicrobial [16], central nervous system [17] and immunosuppressive [18] activities. 2-Pyrazolines became the most frequently studied pyrazoline type compounds and various methods have been worked out for their synthesis [19-21]. Since the milestone work of Fischer and Knövenagel published in the late nineteenth century [22], the reaction of α,β-unsaturated aldehydes and ketones with hydrazines became a generally used simple and convenient procedure for the preparation of 2-pyrazolines [23-42]. As a consequence, numerous substituted 2-pyrazolines have been synthesized for various purposes. To continue our previous studies in this field [31-33,37,38,40-42], herein we describe the synthesis of 1-substituted 5-aryl-3-(3-coumarinyl)-2-pyrazolines by the reaction of (3-coumarinyl)-chalcones and hydrazines.

Results and Discussion.

As described in the introduction, both the coumarins and the 2-pyrazolines possess important bioactivities which render them useful substances in drug research. On this basis, it appeared expedient to synthesize new heterocyclic compounds bearing both a coumarinyl moiety and a 2-pyrazoline unit. Reaction of (3-coumarinyl)chalcones, as easily available α,β-unsaturated ketones, with hydrazines seemed to be a convenient route to fulfil this aim.

3-Aryl-1-(3-coumarinyl)propen-1-ones **1-10** were allowed to react with hydrazine hydrate in hot acetic acid or propionic acid to afford 1-acetyl-2-pyrazolines **11-20** and 1-propionyl-2-pyrazolines **21-27** in good yields (67-80%) (Scheme 1). Substitution pattern of the aromatic ring was almost without influence either on the course of the reaction or on the yields of the isolated products. It is worth mentioning that only one reaction product, *viz*. the 1-acylated-2-pyrazoline was detected or isolated under these reaction conditions. This outcome of the reaction is advantageous since the 1-acylated-2-pyrazolines are stable compounds, which can be used for biological trials without the risk of unwanted decompositions.

Scheme 1

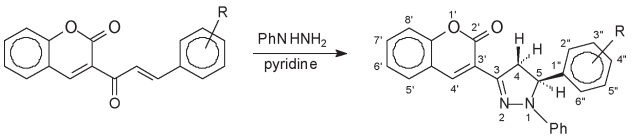


1-10 → **11-27**

1, **11**: R^1 = H, R^2 = Me
2, **12**: R^1 = 3-Me, R^2 = Me
3, **13**: R^1 = 4-Me, R^2 = Me
4, **14**: R^1 = 4-iPr, R^2 = Me
5, **15**: R^1 = 2-MeO, R^2 = Me
6, **16**: R^1 = 3-MeO, R^2 = Me
7, **17**: R^1 = 4-MeO, R^2 = Me
8, **18**: R^1 = 4-F, R^2 = Me
9, **19**: R^1 = 4-Cl, R^2 = Me
10, **20**: R^1 = 4-Br, R^2 = Me
1, **21**: R^1 = H, R^2 = Et
3, **22**: R^1 = 4-Me, R^2 = Et
4, **23**: R^1 = 4-iPr, R^2 = Et
7, **24**: R^1 = 4-MeO, R^2 = Et
8, **25**: R^1 = 4-F, R^2 = Et
9, **26**: R^1 = 4-Cl, R^2 = Et
10, **27**: R^1 = 4-Br, R^2 = Et

The reaction of (3-coumarinyl)chalcones with phenylhydrazine was carried out in hot acetic acid, leading to multicomponent reaction mixtures as shown by tlc monitoring. We have not tried to separate the products detected by tlc in the crude reaction mixtures. To overcome this difficulty, 3-aryl-1-(3-coumarinyl)propen-1-ones **1,3,5-10** were allowed to react with phenylhydrazine in hot pyridine as was the case with other α,β-unsaturated ketones [31,37,38,41] and 5-aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines **28-35** (Scheme 2) were obtained as sole isolable products in good yields (68-74%).

Scheme 2



1,3,5-10 **28-35**

1, **28**: R = H
3, **29**: R = 4-Me
5, **30**: R = 2-MeO
6, **31**: R = 3-MeO
7, **32**: R = 4-MeO
8, **33**: R = 4-F
9, **34**: R = 4-Cl
10, **35**: R = 4-Br

Structures of all new 1-substituted 2-pyrazolines **11-35** have been elucidated by elemental analyses, ^{1}H and ^{13}C nmr spectroscopic measurements. In the ^{1}H nmr spectra of substances **11-35**, the three protons attached to the C-4 and C-5 carbon atoms of the 2-pyrazoline unit gave an ABX spin system. Both the chemical shifts and the coupling constant values (*cf*. Experimental) unequivocally prove the 2-pyrazoline structure. In the ^{1}H nmr spectra of the 1-acetyl-2-pyrazolines **11-20** a singlet signal between 2.4 and 2.5 ppm refers to an N-acetyl group. While the triplet and the quartet signals of an N-propionyl moiety were assigned in the ^{1}H nmr spectra of 1-propionyl-2-pyrazolines **21-27**. In the ^{13}C nmr spectra of compounds **11-35**, the chemical shifts of carbon atoms C-3 (153-154 ppm), C-4 (43-45 ppm) and C-5 (59-64 ppm) corroborate the 2-pyrazoline structure deduced from the ^{1}H nmr data. ^{13}C nmr chemical shift values of the N-acetyl and N-propionyl groups have also been observed in the ^{13}C nmr spectra of compounds **11-20** and **21-27** (*cf.* Experimental).

In conclusion, we have synthesized new 1-substituted 5-aryl-3-(3-coumarinyl)-2-pyrazolines by the reaction of (3-coumarinyl)chalcones and hydrazines under simple and convenient reaction conditions. These new heterocyclic compounds may be beneficially used in drug reserach.

EXPERIMENTAL

Melting points were determined with a Koffler hot-stage apparatus and are uncorrected. ^{1}H and ^{13}C nmr spectra were recorded on a Varian Gemini 200 spectrometer at 200/50 MHz in $CDCl_3$ (internal standard TMS, δ = 0.0 ppm) at ambient temperature. Elemental analyses were measured in-house with a Carlo Erba instrument, model 1106 EA. The tlc was performed on Kieselgel 60 F_{254} (Merck) layer using toluene:ethyl acetate (4:1 v/v) or hexane:acetone (7:3 v/v) as eluents. Starting materials **1-10** were synthesized according to known procedures [6-12].

General Procedure for the Preparation of 1-Acetyl- (**11-20**) and 1-Propionyl-2-pyrazolines (**21-27**).

A mixture of (3-coumarinyl)chalcones (**1-10** or **1,3,4,7-10**, 5.0 mmoles), hydrazine hydrate (15.0 mmoles), acetic acid (25 ml) or propionic acid (25 ml) was refluxed for 3 hours, then poured into water. The precipitate was separated by filtration, washed with water and crystallized from methanol to obtain 2-pyrazolines **11-27** (Scheme 1).

1-Acetyl-3-(3-coumarinyl)-5-phenyl-2-pyrazoline (**11**).

This compound was obtained as white needles in 68% yield, mp 225-226°; ^{1}H nmr ($CDCl_3$): δ 2.43 (s, 3H, Me), 3.40 (dd, 1H, J = 4.8, 19.0 Hz, 4-H_{trans}), 3.96 (dd, 1H, J = 11.9, 19.0 Hz, 4-H_{cis}), 5.59 (dd, 1H, J = 4.8, 11.9 Hz, 5-H), 7.17-7.64 (m, 9 arom. H), 8.45 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.8, 44.2, 60.3, 116.7, 118.9, 119.8, 125.0, 125.6, 127.8, 128.8, 128.9, 132.9, 140.9, 141.6, 150.8, 154.3, 169.1.

Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.42. Found: C, 72.41; H, 4.89; N, 8.46.

1-Acetyl-3-(3-coumarinyl)-5-(3-methylphenyl)-2-pyrazoline (**12**).

This material was prepared as pale yellow needles in 72% yield, mp 191-192°; ^{1}H nmr ($CDCl_3$): δ 2.32 (s, 3H, Me), 2.43 (s, 3H, Me), 3.40 (dd, 1H, J = 4.8, 19.0 Hz, 4-H_{trans}), 3.97 (dd, 1H, J = 12.0, 19.0 Hz, 4-H_{cis}), 5.56 (dd, 1H, J = 4.8, 12.0 Hz, 5-H), 6.98-7.63 (m. 8 arom. H), 8.43 (s, 1H- 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.4, 21.9, 44.3, 60.4, 116.6, 118.8, 119.8, 122.4, 124.9, 126.1, 128.4, 128.7, 132.7, 138.5, 140.7, 141.5, 150.7, 154.1, 168.8.

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.08. Found: C, 72.91; H, 5.28; N, 8.15.

1-Acetyl-3-(3-coumarinyl)-5-(4-methylphenyl)-2-pyrazoline (**13**).

This substance was obtained as pale yellow needles in 67% yield, mp 200-201°; ^{1}H nmr ($CDCl_3$): δ 2.30 (s, 3H, Me), 2.43 (s, 3H, Me), 3.40 (dd, 1H, J = 4.7, 18.0 Hz, 4-H_{trans}), 3.95 (dd, 1H, J = 12.0, 18.0 Hz, 4-H_{cis}), 5.56 (dd, 1H, J = 4.7, 12.0 Hz, 5-H), 7.12-7.63 (m, 8 arom. H), 8.43 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 20.9, 21.8, 44.1, 60.2, 116.7, 118.9, 119.9, 125.1, 125.6, 128.9, 129.6, 132.9, 137.5, 138.8, 140.9, 150.8, 154.3, 160.1.

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.08. Found: C, 72.74; H, 5.19; N, 8.14.

1-Acetyl-3-(3-coumarinyl)-5-(4-isopropylphenyl)-2-pyrazoline (**14**).

This compound was isolated as white needles in 74% yield, mp 238-239°; ^{1}H nmr ($CDCl_3$): δ 1.22 (d, 6H, J = 6.9 Hz, $CH(CH_3)_2$), 2.42 (s, 3H, Me), 2.85 (m, 1H, $CH(CH_3)_2$), 3.41 (dd, 1H, 4.6, 18.8 Hz, 4-H_{trans}), 3.98 (dd, 1H, J = 11.7, 18.8 Hz, 4-H_{cis}), 5.59 (dd, 1H, J = 4.6, 11.7 Hz, 5-H), 7.16-7.62 (m, 8 arom. H), 8.44 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.8, 23.7, 33.6, 44.1, 60.1, 116.8, 118.9, 125.1, 125.4, 125.6, 127.0, 128.9, 132.9, 138.9, 140.9, 148.4, 151.0, 154.4, 169.1.

Anal. Calcd. for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48. Found: C, 73.90; H, 5.87; N, 7.54.

1-Acetyl-3-(3-coumarinyl)-5-(2-methoxyphenyl)-2-pyrazoline (**15**).

This substance was prepared as pale yellow plates in 71% yield, mp 118-119°; ^{1}H nmr ($CDCl_3$): δ 2.48 (s, 3H, Me), 3.25 (dd, 1H, J = 4.7, 18.9 Hz, 4-H_{trans}), 3.84 (s, 3H, MeO), 3.95 (dd, 1H, J = 11.6, 18.9 Hz, 4-H_{cis}), 5.82 (dd, 1H, J = 4.7, 11.6 Hz, 5-H), 6.96-7.62 (m, 8 arom. H), 8.41 (s, 1H- 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.8, 43.3, 55.3, 56.4, 111.0, 116.7, 119.0, 120.2, 125.0, 125.7, 128.8, 128.9, 129.0, 132.8, 140.7, 151.7, 154.3, 156.3, 169.1.

Anal. Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.71; H, 4.97; N, 7.76.

1-Acetyl-3-(3-coumarinyl)-5-(3-methoxyphenyl)-2-pyrazoline (**16**).

This material was obtained as pale yellow plates in 74% yield, mp 183-184°; ^{1}H nmr ($CDCl_3$): δ 2.34 (s, 3H, Me), 3.19 (dd, 1H, J = 4.2, 18.5, 4-H_{trans}), 3.73 (s, 3H, MeO), 3.89 (dd, 1H, J = 11.8, 18.5 Hz, 4-H_{cis}), 5.51 (dd, 1H, J = 4.7, 11.8 Hz, 5-H), 6.73-7.87 (m, 8 arom. H), 8.60 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.6, 43.8, 55.0, 59.3, 111.5, 112.5, 116.2, 117.5, 118.9, 119.3, 125.1, 129.5, 130.0, 133.2, 142.1, 144.1, 151.1, 153.7, 159.8, 167.9.

Anal. Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; 5.01; N, 7.73. Found: C, 69.51; H, 5.06; N, 7.69.

1-Acetyl-3-(3-coumarinyl)-5-(4-methoxyphenyl)-2-pyrazoline (**17**).

This compound was prepared as yellow needles in 69%, mp 199-200°; ^{1}H nmr ($CDCl_3$): δ 2.42 (s, 3H, Me), 3.41 (dd, 1H, J = 4.8, 19.0 Hz, 4-H_{trans}), 3.78 (3, 3H, MeO), 3.94 (dd, 1H, J = 11.9, 19.0 Hz, 4-H_{cis}), 5.54 (dd, 1H, J = 4.8, 11.9 Hz, 5-H), 6.83-7.62 (m, 8 arom. H), 8.45 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.8, 44.1, 55.2, 59.9, 114.3, 116.8, 118.9, 120.0, 125.1, 126.9, 127.1, 128.9, 132.9, 133.9, 140.9, 150.9, 154.4, 159.3, 169.1.

Anal. Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.68; H, 5.06; N, 7.68.

1-Acetyl-3-(3-coumarinyl)-5-(4-fluorophenyl)-2-pyrazoline (**18**).

This compound was prepared as yellow needles in 76% yield, mp 193-194°; ^{1}H nmr ($CDCl_3$): δ 2.43 (s, 3H, Me), 3.41 (dd, 1H, J = 4.9, 19.0 Hz, 4-H_{trans}), 3.97 (dd, 1H, J = 13.9, 19.0 Hz, 4-H_{cis}), 5.60 (dd, 1H, J = 4.9, 13.9 Hz, 5-H), 6.97-7.67 (m, 8 arom. H), 8.47 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.9, 44.2, 59.8, 115.4, 116.7, 118.8, 119.6, 124.9, 127.3, 128.8, 132.9, 137.3, 140.9, 150.6, 154.1, 168.8.

Anal. Calcd. for $C_{20}H_{15}FN_2O_3$: C, 68.56; H, 4.32; N, 7.99. Found: C, 68.64; H, 4.35; N, 8.06.

1-Acetyl-5-(4-chlorophenyl)-3-(3-coumarinyl)-2-pyrazoline (**19**).

This substance was isolated as yellow needles in 74% yield, mp 208-209°; ^{1}H nmr ($CDCl_3$): δ 2.42 (s, 3H, Me), 3.38 (dd, 1H, J = 5.1, 18.9 Hz, 4-H_{trans}), 3.96 (dd, 1H, J = 12.1, 18.9 Hz, 4-H_{cis}), 5.54 (dd, 1H, J = 5.1, 12.1 Hz, 5-H), 7.12-7.63 (m, 8 arom. H), 8.44 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.7, 44.0, 59.8, 116.7, 118.8, 119.6, 125.1, 127.2, 128.9, 129.1, 133.0, 133.6, 140.1, 141.1, 150.8, 154.5, 159.4, 169.1.

Anal. Calcd. for $C_{20}H_{15}Cl\ N_2O_3$: C, 65.49; H, 4.12; N, 7.63. Found: C, 65.58; H, 4.16; N, 7.67.

1-Acetyl-5-(4-bromophenyl)-3-(3-coumarinyl)-2-pyrazoline (**20**).

This compound was obtained as yellow plates in 74% yield, mp 227-228°; ^{1}H nmr ($CDCl_3$): δ 2.41 (s, 3H, Me), 3.39 (dd, 1H, J = 4.7, 18.8 Hz, 4-H_{trans}), 3.96 (dd, 1H, J = 11.7, 18.8 Hz, 4-H_{cis}), 5.52 (dd, 1H, J = 4.7, 11.7 Hz, 5-H), 7.08-7.67 (m, 8 arom. H), 8.42 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 21.7, 44.0, 59.9, 116.8, 118.9, 119.7, 121.7, 125.1, 125.4, 127.6, 128.9, 132.1, 132.7, 133.1, 1407, 141.2, 150.8, 154.4, 168.1.

Anal. Calcd. for $C_{20}H_{15}BrN_2O_3$: C, 58.41; H, 3.68; N, 6.81. Found: C, 58.47; H, 3.74; N, 6.86.

3-(3-Coumarinyl)-5-phenyl-1-propionyl-2-pyrazoline (**21**).

This compound was obtained as pale yellow needles in 80% yield, mp 221-222°; ^{1}H nmr ($CDCl_3$): δ 1.27 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.89 (dd, 2H, J = 7.5, 15.0 Hz, CH_2CH_3), 3.42 (dd, 1H, J = 4.9, 18.0 Hz, 4-H_{trans}), 3.98 (dd, 1H, J = 8.1, 18.0 Hz, 4-H_{cis}), 5.59 (dd, 1H, J = 4.9, 8.1 Hz, 5-H), 7.21-8.17 (m, 9 arom. H), 8.48 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 8.9, 27.6, 44.1, 60.6, 112.8, 116.7, 117.8, 118.9, 123.6, 125.5, 127.6, 128.4, 128.8, 130.9, 132.5, 140.7, 141.7, 150.4, 154.2, 172.3.

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.08. Found: C, 72.94; H, 5.29; N, 8.17.

3-(3-Coumarinyl)-5-(4-methylphenyl)-1-propionyl-2-pyrazoline (**22**).

This material was prepared as yellow needles in 68% yield, mp 183-184°; ^{1}H nmr ($CDCl_3$): δ 1.21 (t, 3H, J = 7.4 Hz, CH_2CH_3), 2.29 (s, 3H, Me), 2.80 (dd, 2H, J = 7.4, 14.8 Hz, CH_2CH_3), 3.40 (dd, 1H, J = 4.7, 18.9 Hz, 4-H_{trans}), 3.92 (dd, 1H, J = 12.0, 18.9 Hz, 4-H_{cis}), 5.54 (dd, 1H, J = 4.7, 12.0 Hz, 5-H), 7.08-7.60 (m, 8 arom. H), 8.39 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 8.9, 21.0, 27.5, 44.0, 60.4, 116.6, 118.8, 119.9, 125.5, 128.7, 132.7, 138.8, 140.6, 150.4, 154.1, 159.1, 172.2.

Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.46; H, 5.64; N, 7.68.

3-(3-Coumarinyl)-5-(4-isopropylphenyl)-1-propionyl-2-pyrazoline (**23**).

This substance was isolated as pale yellow plates in 67% yied, mp 137-138°; ^{1}H nmr ($CDCl_3$): δ 1.23 (m, 9H, CH_2CH_3, $CH(CH_3)_2$), 2.85 (m, 3H, CH_2CH_3, $CH(CH_3)_2$), 3.40 (dd, 1H, J = 4.7, 18.9 Hz, 4-H_{trans}), 3.93 (dd, 1H, J = 11.9, 18.9 Hz, 4-H_{cis}), 5.57 (dd, 1H, J = 4.7, 11.9 Hz, 5-H), 7.12-7.60 (m, 8 arom. H), 8.41 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 8.9, 23.9, 27.6, 33,7, 44.0, 60.3, 116.6, 118.9, 124.9, 125.5, 126.9, 128.7, 139,0, 140.6, 148.1, 150.5, 154.1, 159.1, 172.3.

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.21; H, 6.23; N, 7.21. Found: C, 74.13; H, 6.27; N, 7.34.

3-(3-Coumarinyl)-5-(4-methoxyphenyl)-1-propionyl-2-pyrazoline (**24**).

This compound was prepared as yellow needles in 71% yield, mp 184-185°; ^{1}H nmr ($CDCl_3$): δ 1.21 (t, 3H, J 7.5 Hz, CH_2CH_3), 2.81 (dd, 2H, J = 7.5, 15.0 Hz, CH_2CH_3), 3.41 (dd, 1H, J = 4.7, 19.0 Hz, 4-H_{trans}), 3.79 (dd, 1H, J = 12.0, 19.0 Hz, 4-H_{cis}), 5.54 (dd, 1H, J = 4.7, 12.0 Hz, 5-H), 6.82-7.61 (m, 8 arom. H), 8.39 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 8.9, 27.6, 43.9, 55.3, 60.1, 114.3, 116.7, 124.9, 126.9, 128.7, 132.7, 140.6, 150.6, 054.4, 172.4.

Anal. Calcd. for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.32; H, 5.31; N, 7.55.

3-(3-Coumarinyl)-5-(4-fluorophenyl)-1-propionyl-2-pyrazoline (**25**).

This substance was obtained as yellow plates in 69% yield, mp 161-162°; ^{1}H nmr ($CDCl_3$): δ 1.23 (t, 3H, J = 7.5 Hz, CH_2CH_3),

2.87 (dd, 2H, J = 7.5, 15.0, CH_2CH$_3$), 3.41 (dd, 1H, J = 4.9, 19.0 Hz, 4-H$_{trans}$), 3.98 (dd, 1H, J = 12.0, 19.0 Hz, 4-H$_{cis}$), 5.57 (dd, 1H, 4.9, 12.0 Hz, 5-H), 7.02-7.61 (m, 8 arom. H), 8.45 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 8.8, 27.5, 43.9, 59.9, 115.9, 116.8, 118.8, 119.7, 124.9, 127.3, 127.5, 128.7, 132.8, 137.5, 140.8, 150.3, 154.1, 159.1, 172.3.

Anal. Calcd. for $C_{21}H_{17}FN_2O_3$: C, 69.22; H, 4.70; N, 7.68. Found: C, 69.34; H, 4.65; N, 7.76.

5-(4-Chlorophenyl)-3-(3-coumarinyl)-1-propionyl-2-pyrazoline (**26**).

This material was isolated as yellow needles in 72% yield, mp 191-192°; ^{1}H nmr (CDCl$_3$): δ 1.21 (t, 3H, J = 7.5 Hz, CH$_2$CH_3), 2.82 (dd, 2H, J = 7.5, 15.0 Hz, CH_2CH$_3$), 3.39 (dd, 1H, J = 5.1, 18.9 Hz, 4-H$_{trans}$), 3.98 (dd, 1H, J = 12.1, 18.9 Hz, 4-H$_{cis}$), 5.56 (dd, 1H, J = 5.1, 12.1 Hz, 5-H), 7.16-7.62 (m, 8 arom. H), 8.43 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 8.9, 27.5, 43.9, 60.0, 116.7, 118.8, 119.7, 124.9, 127.1, 128.7, 129.0, 132.9, 133.4, 140.2, 150.3, 154.1, 159.2, 172.3.

Anal. Calcd. for $C_{21}H_{17}ClN_2O_3$: C, 66.23; H, 4.50; N, 7.35. Found: C, 66.31; H, 4.55; N, 7.26.

5-(4-Bromophenyl)-3-(3-coumarinyl)-1-propionyl-2-pyrazoline (**27**).

This compound was prepared as yellow plates in 74% yield, mp 217-218°; ^{1}H nmr (CDCl$_3$): δ 1.21 (t, 3H, J = 7.5 Hz, CH$_2$CH_3), 2.87 (dd, 2H, J = 7.5, 14.9 Hz, CH_2CH$_3$), 3.40 (dd, 1H, J = 5.1, 19.0 Hz, 4-H$_{trans}$), 3.98 (dd, 1H, J = 12.1, 19.0 Hz, 4-H$_{cis}$), 5.52 (dd, 1H, J = 5.1, 12.1 Hz, 5-H), 7.12-7.63 (m, 8 arom. H), 8.46 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 8.8, 27.5, 43.8, 60.0, 116.6, 118.8, 119.6, 121.5, 124.9, 128.7, 131.9, 132.8, 140.8, 150.3, 154.1, 159.1, 172.3.

Anal. Calcd. for $C_{21}H_{17}BrN_2O_3$: C, 59.31; H, 4.03; N, 6.58. Found: C, 59.41; H, 4.07; N, 6.67.

General Procedure for the Synthesis of 5-Aryl-3-(3-coumarinyl)-1-phenyl-2-pyrazolines (**28-35**)

A mixture of 3-(3-coumarinyl)chalcones (**1,3,5-10**, 5.0 mmoles), phenylhydrazine (20.0 mmoles) and pyridine (30 ml) was refluxed for 6 hours and then poured onto crushed ice. The precipitate was separated by filtration, washed with water and crystallized from methanol to afford compounds **28-35** (Scheme 2).

3-(3-Coumarinyl)-1,5-diphenyl-2-pyrazoline (**28**).

This compound was prepared as white needles in 71% yield, mp 181-182°; ^{1}H nmr (CDCl$_3$): δ 3.40 (dd, 1H, J = 7.3, 18.4 Hz, 4-H$_{trans}$), 4.11 (dd, 1H, J = 12.7, 18.4 Hz, 4-H$_{cis}$), 5.38 (dd, 1H, J = 7.3, 12.7 Hz, 5-H), 6.81-7.60 (m, 14 arom. H), 8.40 (s, 1H-4'-H); ^{13}C nmr (CDCl$_3$): δ 45.2, 64.9, 113.7, 116.4, 117.7, 119.5, 120.4, 124.7, 125.3, 127.6, 128.2, 129.2, 130.9, 131.4, 132.5, 137.5, 142.1, 144.0, 153.6, 159.6.

Anal. Clacd. for $C_{24}H_{18}N_2O_2$: C, 78.67; H, 4.95; N, 7.64. Found: C, 78.79; H, 4.89; N, 7.69.

3-(3-Coumarinyl)-5-(4-methylphenyl)-1-phenyl-2-pyrazoline (**29**).

This substance was obtained as yellow needles in 74% yield, mp 193-194°; ^{1}H nmr (CDCl$_3$): δ 2.31 (s, 3H, Me), 3.39 (dd, 1H, J = 7.2, 18.3 Hz, 4-H$_{trans}$), 4.11 (dd, 1H, J = 12.6, 18.3 Hz, 4-H$_{cis}$), 5.30 (dd, 1H, J = 7.2, 12.6 Hz, 5-H), 6.80-7.10 (m, 13 arom. H), 8.41 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 21.1, 45.3, 64.8, 109.1, 113.7, 116.5, 119.8, 124.7, 125.5, 125.7, 127.9, 128.3, 128.7, 129.1, 129.8, 131.5, 137.5, 17.8, 138.1, 153.6.

Anal. Calcd. for $C_{25}H_{20}N_2O_2$: C, 78.93; H, 5.29; N, 7.36. Found: C, 78.82; H, 5.35; N, 7.47.

3-(3-Coumarinyl)-5-(2-methoxyphenyl)-1-phenyl-2-pyrazoline (**30**).

This compound was prepared as yellow needles in 69% yield, mp 181-182°; ^{1}H nmr (CDCl$_3$): δ 3.29 (dd, 1H, J = 6.7, 18.4 Hz, 4-H$_{trans}$), 3.92 (s, 3H, MeO), 4.11 (dd, 1H, J = 12.6, 18.4 Hz, 4-H$_{cis}$), 5.70 (dd, 1H, 6.7, 12.6 Hz, 5-H), 6.79-7.60 (m, 13 arom. H), 8.39 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 29.7, 43.9, 59.1, 110.4, 111.2, 113.4, 116.4, 119.5, 120.7, 123.8, 124.5, 125.3, 126.3, 127.2, 128.2, 128.9, 130.6, 131.3, 137.3, 137.7, 141.2, 153.5.

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.74; H, 5.08; N, 7.06. Found: C, 75.63; H, 5.12; N, 6.98.

3-(3-Coumarinyl)-5-(3-methoxyphenyl)-1-phenyl-2-pyrazoline (**31**).

This material was isolated as yellow plates in 68% yield, mp 179-180°; ^{1}H nmr (CDCl$_3$): δ 3.40 (dd, 1H, J = 7.4, 18.4 Hz, 4-H$_{trans}$), 3.78 (s, 3H, MeO), 4.11 (dd, 1H, J = 12.7, 18.4 Hz, 4-H$_{cis}$), 5.31 (dd, 1H, J = 7.4, 12.7 Hz, 5-H), 6.80-7.68 (m, 13 arom. H), 8.41 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 45.2. 55.2, 64.9, 111.4, 112.8, 113.7, 116.4, 117.9, 119.5, 120.8, 123.6, 124.7, 125.2, 128.2, 128.9, 130.2, 131.5, 137.5, 143.0, 143.7, 144.1. 153.6, 160.2.

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.74; H, 5.08; N, 7.06. Found: 75.85; H, 5.02; N, 7.11.

3-(3-Coumarinyl)-5-(4-methoxyphenyl)-1-phenyl-2-pyrazoline (**32**).

This compound was prepared as yellow plates in 74% yield, mp 169-170°; ^{1}H nmr (CDCl$_3$): δ 3.36 (dd, 1H, J = 7.2, 18.4 Hz, 4-H$_{trans}$), 3.76 (s, 3H, MeO), 4.08 (dd, 1H, J = 12.6, 18.4 Hz, 4-H$_{cis}$), 5.30 (dd, 1H J = 7.2, 12.6, 5-H), 6.87-7.61 (m, 13 arom. H), 8.41 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 45.3, 55.3, 64.5, 113.7, 114.5, 116.4, 119.8, 124.7, 125.5, 126.9, 128.2, 128.9, 131.4, 134.2, 137.5, 142.8, 144.6, 153.1, 159.4.

Anal. Calcd. for $C_{25}H_{20}N_2O_3$: C, 75.74; H, 5.08; N, 7.06. Found: C, 75.82; H, 5.13; N, 7.14.

3-(3-Coumarinyl)-5-(4-fluorophenyl)-1-phenyl-2-pyrazoline (**33**).

This substance was isolated as yellow plates in 70% yield, mp 107-108°; ^{1}H nmr (CDCl$_3$): δ 3.39 (dd, 1H, J = 7.2, 18.4 Hz, 4-H$_{trans}$), 4.15 (dd, 1H, J = 12.6, 18.4 Hz, 4-H$_{cis}$), 5.36 (dd, 1H, J = 7.2, 12.6 Hz, 5-H), 6.82-7.58 (m, 13 arom. H), 8.44 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 45.3, 64.3, 113.7, 115.8, 116.3, 117.4, 119.5, 120.0, 120.7, 121.1, 124.7, 127.5, 128.2, 129.3, 131.6, 137.8, 138.5, 143.0, 153.6.

Anal. Calcd. for $C_{24}H_{17}FN_2O_2$: C, 74.98; H, 4.46; N, 7.28. Found: C, 74.87; H, 4.51; N, 7.36.

5-(4-Chlorophenyl)-3-(3-coumarinyl)-1-phenyl-2-pyrazoline (**34**).

This compound was obtained as yellow needles in 73% yield, mp 149-150°; ^{1}H nmr (CDCl$_3$): δ 3.39 (dd, 1H, J = 7.2, 18.4 Hz, 4-H$_{trans}$), 4.12 (dd, 1H, J = 12.7, 18.4 Hz, 4-H$_{cis}$), 5.31 (dd, 1H, J = 7.2, 12.7 Hz, 5-H), 6.89-7.58 (m, 13 arom. H), 8.41 (s, 1H, 4'-H); ^{13}C nmr (CDCl$_3$): δ 45.2, 64.3, 113.7, 116.5, 119.5, 120.1,

120.7, 124.7, 127.2, 128.2, 129.1, 129.3, 131.6, 133.4, 137.8, 140.6, 143.8, 153.6.

Anal. Calcd. for $C_{24}C_{17}ClN_2O_2$: C, 71.91; H, 4.28; N, 6.98. Found: C, 71.83; H, 4.33; N, 7.07.

5-(4-Bromophenyl)-3-(3-coumarinyl)-1-phenyl-2-pyrazoline (**35**).

This substance was prepared as yellow plates in 68% yield, mp 205-206°; ^{1}H nmr ($CDCl_3$): δ 3.38 (dd, 1H, J = 7.2, 18.4 Hz, 4-H_{trans}), 4.13 (dd, 1H, J = 12.7, 18.4 Hz, 4-H_{cis}), 5.34 (dd, 1H, J = 7.2, 12.7 Hz, 5-H), 6.88-8.12 (m, 13 arom. H), 8.40 (s, 1H, 4'-H); ^{13}C nmr ($CDCl_3$): δ 45.1, 64.4, 113.7, 116.5, 119.5, 120.1, 124.7, 127.6, 128.2, 129.1, 131.6, 132.3, 137.8, 141.1, 143.1, 143.7, 153.5.

Anal. Calcd. for $C_{24}H_{17}BrN_2O_2$: C, 64.73; H, 3.85; N, 6.29. Found: C, 64.84; H, 3.81; N, 6.40.

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