Synthesis of Pyrazolyl-2-pyrazolines by Treatment of 3-(3-Aryl-3-oxopropenyl)-chromen-4-ones with Hydrazine and Their Oxidation to Bis(pyrazoles)

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Dedicated to Professor Dr. Károly Lempert on the occasion of his 80th birthday

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The synthesis of several 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines **3a**–**3h** has been accomplished by treatment of the 3-(3-aryl-3-oxopropenyl)chromen-4-ones **1a**–**h** with hydrazine hydrate in hot acetic acid. The 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines **2a**–**2f** were also obtained as by-products. Oxidation of the 1-acetyl-4-pyrazolyl-2-pyrazolines **3a**–**3f** with DDQ gave the 3(5)-aryl-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]pyrazoles **5a**–**5f**. The oxidation of the 2-pyrazoline rings was accompanied by *N*-deacylation. The reaction mechanisms of both transformations are discussed, the first one being supported by experimental results. The structures of all new derivatives were established by NMR and the evidence of prototropic tautomerism is carefully discussed. Theoretical calculations of energies and of the ^{1}H and ^{13}C NMR chemical shifts of the possible tautomeric forms of 5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3(5)-(4-methoxyphenyl)pyrazole (**5c**), by B3LYP and GIAO, showed that compounds of this type probably exist as mixtures of two tautomers.

Introduction

The first representatives of 3-(3-aryl-3-oxopropenyl)chromen-4-ones **1** were described in the literature as early as 1976.[1] Although these chromones would appear to be convenient starting materials for the synthesis of a wide variety of heterocyclic ring systems, their chemical transformations have hitherto received relatively little attention, and for this reason we decided to study their utility for the preparation of nitrogen-containing heterocyclic compounds. In a first series of experiments, 4-aryl-2-(3-chromonyl)-2,3-dihydro-1,5-benzothiazepines were synthesized by treatment of compounds **1** with 2-aminothiophenol.[2] These 1,5-benzothiazepines gave 2,2-disubstituted 3-acetyl-2,3-dihydrobenzothiazoles under acetylating conditions.[2] Treatment with diazomethane provided 3-aroyl-4-(3-chromonyl)-2-pyrazolines,[3] similarly to chalcones and related α,β-unsaturated ketones.

In continuation of these studies[2,3] and of our previous work on the treatment of various chromone derivatives with hydrazines,[4] investigation of the reactivity of 3-(3-aryl-3-oxopropenyl)chromen-4-ones (**1**) towards hydrazines was carried out. Since compounds **1** possess two moieties, a 3-chromonyl group and an α,β-unsaturated ketone unit, prone to reaction with hydrazines, their planned chemical transformations seemed to be an especially challenging task.

It is well established that treatment of α,β-unsaturated ketones with hydrazines affords 3,5-disubstituted 2-pyrazolines.[5] If it is also true for treatment of 3-(3-aryl-3-oxopropenyl)chromen-4-ones with hydrazines, then the formation of 3-aryl-5-(3-chromonyl)-2-pyrazolines would be expected. It has also been known for decades that treatment of various chromone derivatives with hydrazines yields appropriately substituted pyrazoles.[4,6] In this paper, the reaction of compounds **1** with hydrazine hydrate and the structure elucidation of the products obtained in this transformation are described.

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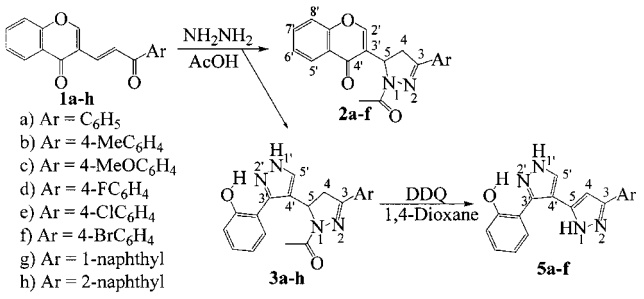
Results and Discussion

Chemistry

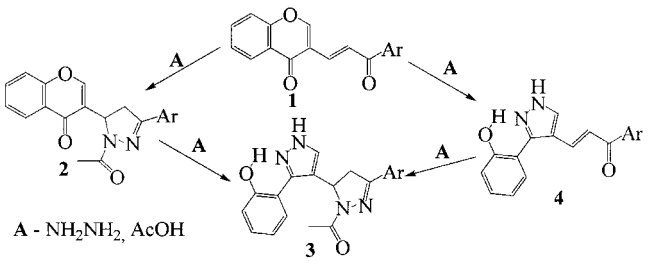
In the study described here, 3-(3-aryl-3-oxopropenyl)-chromen-4-ones (**1a**−**1h**) and hydrazine hydrate were allowed to react in hot acetic acid, giving the 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines **3a**−**3h** (63−75%). The 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines **2a**−**2f** (2−6%) were also obtained as by-products (Scheme 1). Compounds **2a**−**2f** and **3a**−**3f** were separated by column chromatography. In the cases of the starting materials **1g** and **1h**, a minor component was also detectable by thin-layer chromatography (TLC) in the crude reaction mixtures, but we failed to isolate these minor components by column chromatography. The structures of all these new compounds (**2a**−**2f** and **3a**−**2h**) were elucidated by elemental analyses and by combined use of various spectroscopic methods.



Scheme 1

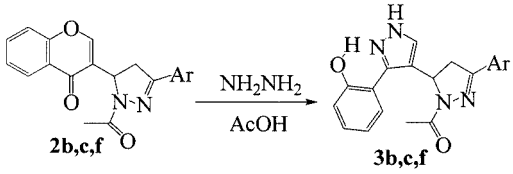
The elemental analyses and mass spectra unequivocally established the presence of two nitrogen atoms in the minor products **2a**−**2f** and four nitrogen atoms in the major products **3a**−**3h**. In the IR spectra (see Exp. Sect.) of compounds **2a**−**2f**, two C=O bands and one C=N band were assigned. The presence of NH, C=O and C=N bands in the IR spectra of substances **3a**−**3h** is consistent with pyrazolyl-2-pyrazoline structures. Structure elucidation of all new compounds was completed by NMR spectroscopy.

The pyrazolyl-2-pyrazolines **3a**−**3h** may be formed by reaction between the starting materials **1a**−**1h** and hydrazine in two different ways, as shown in Scheme 2. As a first step, the 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines **2** may be afforded, as in standard reactions between α,β-unsaturated ketones and hydrazines.[5] As another possibility, reaction between the 3-chromonyl group and hydrazine might precede the reaction of the α,β-unsaturated ketone moiety, yielding 3,4-disubstituted pyrazoles **4**. Both intermediates could then react with hydrazine to provide the pyrazolyl-2-pyrazolines **3a**−**3h** (Scheme 2).



Scheme 2

For differentiation between the two possible formation pathways of the pyrazolyl-2-pyrazolines **3a**−**3h** an important consideration was that the 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines **2a**−**2f** were isolated as minor components. The minor products **2b**, **2c** and **2f** gave the appropriate major products **3b**, **3c** and **3f** on treatment with hydrazine hydrate in hot acetic acid (Scheme 3). It should also be mentioned that the 3,4-disubstituted pyrazoles **4** shown in Scheme 2 as other possible intermediates could not be detected in the crude reaction mixtures (vide infra). In the crude reaction mixtures only one kind of minor component could be detected and in each case it was identified as the 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazoline (**2a**−**2f**).



Scheme 3

The first attempt to oxidise the pyrazolyl-2-pyrazolines **3a**−**3f** involved their treatment with chloranil in toluene or dry dioxane at reflux. This oxidant proved to be weak, since the pyrazolines **3a**−**3f** were not oxidized, and could be recovered, after several assays of different oxidation conditions [e.g., different quantities of chloranil (2.5 to 4 equiv.) and reaction times (3 to 8 days)]. As we had not obtained the expected oxidation products we changed the oxidant to DDQ. The oxidations of pyrazolines **3a**−**3f** with DDQ in toluene at reflux gave complex mixtures of compounds, but in dry dioxane the bispyrazoles **5a**−**5f** were obtained in fairly good yields (51−60%). The oxidation of 2-pyrazoline rings was accompanied by *N*-deacylation reactions. These results can be envisaged to proceed by the DDQ dehydrogenation mechanism.[7] In the present case one can postulate hydride transfer from the 5-positions of the 2-pyrazoline rings in **3a**−**3f**, followed by an acylium cation transfer, resulting in the formation of monoacetylated hydroquinone and the bispyrazoles **5a**−**5f**.

NMR Spectroscopy

The ^{1}H NMR spectra of the reaction mixtures of the 3-(3-aryl-3-oxopropenyl)chromen-4-ones **1a**−**1h** and hydrazine hydrate in [D$_6$]DMSO each showed four broad singlets at higher frequency values (at δ = 9.78−10.15, 10.40−10.58, 12.61−12.73, 12.95−13.04 ppm), and the resonances of the 2-pyrazoline rings also appear as very broad signals. After the addition of a few drops of trifluoroacetic acid (TFA) the signals became narrow and it was possible to identify the main compounds in these reaction mixtures

as the 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines **3a**−**3f**, together with the 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines **2a**−**2f** as by-products. These results indicate that compounds **3a**−**3f** exist in [D_6]DMSO solution as mixtures of tautomers, the described high-resonance singlets being due to the NH and OH resonances with the prototropic rate increasing after the addition of TFA.

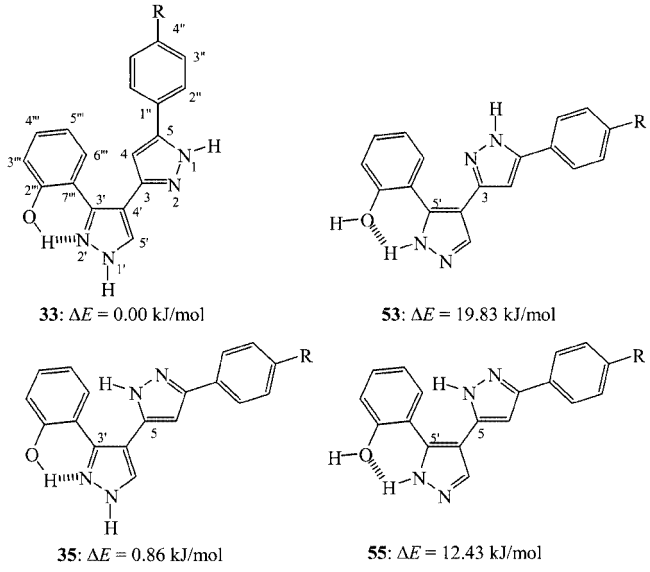
For the structural characterisation of compounds **3a**−**3f** it is important to report the presence of three double doublets in their ^{1}H NMR spectra ($CDCl_3$ + TFA), at δ_H = 3.08−3.15, 3.63−3.74 and 5.47−5.58 ppm, assigned to the resonances of 4-CH_2 and H-5 in the 2-pyrazoline rings. The resonances of the corresponding carbon atoms (δ_{CH2} = 41.5−42.5, $\delta_{C\text{-}5}$ = 52.1−52.7 ppm), assigned by analysis of their HSQC spectra, and the presence of acetyl groups (δ_H = 2.16−2.22 ppm and δ_C = 21.9−22.5 and 167.9−169.5 ppm) supported the presence of acetylated 2-pyrazoline rings. From the HMBC spectra of **3a**−**3f**, correlations between 4-CH_2, H-5, H-2′′,6′′ and C-3 (δ_C = 153.4−155.6 ppm) were established. These connectivities allowed the complete assignment of the pyrazoline rings, bearing aryl rings at their 3-positions and other substituents at their 5-positions.

The ^{1}H NMR spectra of compounds **3a**−**3f** also each presents a singlet at δ_H = 7.91−8.11 ppm, corresponding to the resonance of one proton, which correlates with the carbon at δ_C = 132.5−133.5 ppm in the HSQC spectra. In the HMBC spectra, these proton signals present connectivities with C-5 of the 2-pyrazoline ring and with two other carbons appearing at δ_C = 121.7−124.2 and 141.1−142.7 ppm. These data and the connectivities between H-6′′′ and the carbon appearing at δ_C = 141.1−142.7 ppm supported the 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazoline (**3a**−**3f**) structures and the assignment of their C-3′ and C-4′ carbon resonances. The structural identification of compounds **3g** and **3h** was similar to that described for **3a**−**3f**.

The most important features of the ^{1}H and ^{13}C NMR spectra of compounds **2a**−**2f** that allowed the establishment of their structures are: i) the resonances of the acetyl groups, δ_H = 2.27−2.29 ppm (singlet) and δ_C = 21.0−21.8 and 167.6−167.9 ppm, ii) resonances typical of H-2′′ and C-2′′ of the chromone nucleus, δ_H = 8.24−8.29 ppm (singlet) and δ_C = 154.4−154.8 ppm, iii) the resonances of the carbonyl groups of the chromone moieties, δ_C = 167.6−167.9 ppm, and iv) the signals characteristic of a 2-pyrazoline ring, as three double doublet signals at δ_H = 3.22−3.27, 3.70−3.75 and 5.39−5.43 ppm, corresponding to the resonances of 2 × H-4 and H-5. Some connectivities observed in their HMBC spectra (H-2′′ → C-5, C-3′′, C-4′′ and C-9′′; H-2′,6′ → C-3) supported the structures of the 1-acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines (**2a**−**2f**) and allowed the unequivocal assignment of some of their quaternary carbon resonances.

The ^{1}H NMR spectra of the 3(5)-aryl-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]pyrazoles (**5a**−**5f**) in [D_6]DMSO showed some broad singlets at higher frequency values (around 10 and 13 ppm) and the other resonances also appeared as very broad signals. After the addition of a few drops of trifluoroacetic acid (TFA) the signals of those spectra became narrow and it was possible to assign all proton and carbon resonances of these compounds (**5a**−**5f**).

The splitting of some signals in the ^{1}H NMR spectra of the bispyrazoles **5a**−**5f** indicates a prototropic tautomerism phenomenon. We carried out a more detailed ^{1}H and ^{13}C NMR study of compound **5c** (R = OCH_3), selected because of its reasonable solubility in pure [D_6]DMSO and its less complex ^{1}H NMR spectrum. We also carried out theoretical calculations of both energies and shieldings. The energies correspond to fully optimized geometries calculated at the B3LYP/6-311++G** level as well as to absolute shieldings (σ, ppm) obtained by the GIAO approximation using the same geometries on the parent compound **5a** (R = H). Compound **5c** could exist in four tautomeric forms corresponding to the two prototropic tautomers of each pyrazole (Scheme 4).



Scheme 4

The relative energies (absolute energy for **33**: −988.81751 Hartrees) show that the tautomerism of the first pyrazole ring should always be 3-substituted (i.e., the O−H···N hydrogen bond is preferred over the N−H···O one). These two tautomers, **33** and **35**, have very similar energies (less than 1 kJ/mol) and both should be present in solution.

The ^{1}H NMR spectrum (dilute solution: 5 mg in 0.5 mL) shows the well resolved signals of two compounds in a ratio of about 55:45. When the concentration of **5c** in [D_6]DMSO is increased (9 mg in 0.5 mL), the signals broaden but are still resolved. Finally (at 12 mg in 0.5 mL of [D_6]DMSO), the coalescence of all signals belonging to **33** and **35** is observed. This corresponds to the well known fact that the prototropic rate increases when the concentration increases.[8−10] To assign the signals to each tautomer (the 55:45 difference is difficult to use for some signals), we calculated the σ values of the different protons of tautomers **33** (45%) and **35** (55%). The results are reported in Table 1.

Table 1. Experimentally determined (**5c**, δ, ppm, [D_6]DMSO) and calculated (**5a**, σ, ppm) signals of tautomers **33** and **35** of compound **5c**

Signal	δ (**5c**, **33**)	σ (**5a**, **33**)	δ (**5c**, **35**)	σ (**5a**, **35**)
H-3′"	7.01	24.6103	7.01	24.7516
H-4′"	7.25	24.5694	7.25	24.5666
H-5′"	6.78	25.1315	6.78	25.1211
H-6′"	7.22	24.6454	7.25	24.5952
OH	13.02	21.8024	13.33	21.7711
NH-1′	10.10	22.8339	10.28	22.7655
H-5′	8.13	24.0408	7.85	24.2907
NH-1(or 2)	10.70	22.7372	9.90	22.8646
H-4	6.14	25.2166	6.36	25.0649

If only the CH protons are used and account is taken that the 3′′′ to 6′′′ signals have been estimated from 2D spectra, Equation (1) relating experiment and calculations is acceptable [Equation (1)].

$$\delta^1\text{H (ppm)} = (43 \pm 4) - (1.46 \pm 0.16)\,\sigma^1\text{H (ppm)},\ n = 12,\ r^2 = 0.90 \qquad (1)$$

The OH and both NH signals of **5c** disappear on addition of a drop of D_2O to the [D_6]DMSO solution, those in the 10 ppm zone more quickly than those in the 13 ppm zone. These last are the OH signals, protected from H/D exchange by the hydrogen bond. If the signals follow the order of the calculated σ, then the assignment in Table 1 should be correct.

Although compound **5c** was slightly soluble in [D_6]DMSO, its ^{13}C NMR spectrum was difficult to obtain (the reason why the solvent used in the Exp. Sect. is a mixture of [D_6]DMSO and TFA in a 99:1 ratio). The data reported in Table 2 are a compromise between the decoupled spectrum (considerable noise) and the HSQC experiment.

Table 2. Experimentally determined (**5c**, δ, ppm, [D_6]DMSO) and calculated (**5a**, σ, ppm) signals of tautomers **33** and **35** of compound **5c**

Signal	δ (**5c**, **33**)	σ (**5a**, **33**)	δ (**5c**, **35**)	σ (**5a**, **35**)
C-3	–	32.9632	160.0	24.0707
C-4	100.7	74.6200	98.7	77.2951
C-5	155.5	28.9739	137.3	42.5235
C-3′	158.8	26.4331	160.8	26.2206
C-4′	116.1	61.5873	–	66.8172
C-5′	137.6	49.8284	129.4	49.7409
C-1′"	118.0	61.0735	114.2	63.2599
C-2′"	–	17.7478	–	17.7149
C-3′"	116.2	60.4585	116.3	60.4585
C-4′"	131.1	47.4935	131.1	47.4935
C-5′"	118.9	61.7179	118.9	60.2312
C-6′"	129.8	48.8731	129.8	50.2525
C-1"	–	–	–	–
C-2"/6"	126.3	–	126.3	–
C-3"/5"	114.2	–	114.2	–
C-4"	–	–	–	–
OMe	55.1	–	55.1	–

With the exception of C-5′ of tautomer **33** (experimental 137.6, predicted 130.7 ppm) the remaining 19 points fitted to Equation (2).

$$\delta^{13}\text{C (ppm)} = (190 \pm 1) - (1.19 \pm 0.02)\,\sigma^{13}\text{C (ppm)},\ n = 19,\ r^2 = 0.995 \qquad (2)$$

In summary, the complex case of the double tautomerism of the bispyrazoles **5** has been solved by a combination of NMR spectroscopy and theoretical calculations.

If the ^{1}H and ^{13}C NMR spectra (in $CDCl_3$ + TFA) of the 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines **3a**−**3f** are compared with those of compounds **5a**−**5f**, the absence of the acetyl group and the oxidation of the 2-pyrazoline ring into another pyrazole ring can be deduced. The disappearance of the aliphatic region signals is observed, together with the appearance of the signals at δ_H = 6.50−6.52 ppm (as a singlet), and at δ_C = 101.5−103.2, 141.6−142.3 and 147.0−148.0 ppm (in the ^{13}C NMR spectra), attributed to the resonance of H-4, C-4, C-5 and C-3, respectively, in the formed pyrazole ring. Confirmation of these assignments was based on the connectivities found in the HMBC spectra of the 3(5)-aryl-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]pyrazoles (**5a**−**5f**) (H-2′′,6′′ → C-3; H-4 → C-3,C-5 and C-4′; H-5′ → C-3′,C-4′ and C-5).

Experimental Section

General Remarks: Melting points were measured in a Kofler hot-stage apparatus and are uncorrected. IR (KBr) spectra were recorded on Perkin−Elmer 16 PC and MATTSON 7000 FTIR spectrometers. Mass spectra were recorded on VG Trio-2 and VG Autospec Q instruments. Elemental analyses were obtained in a Carlo Erba 1106 apparatus. NMR spectra were recorded on a Bruker Avance 300 spectrometer (300.13 for ^{1}H and 75.47 MHz for ^{13}C), with $CDCl_3$ as a solvent, if not stated otherwise. Chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. The internal standard was TMS. ^{1}H assignments were made by 2D *g*COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made with the aid of 2D *g*HSQC and *g*HMBC (delays for one bond and long-range J C/H couplings were optimised for 145 and 7 Hz, respectively) experiments. Thin-layer chromatography (TLC) was performed with Merck silica gel (60 F_{254}) foils with 1,2-dichloroethane as eluent. The starting materials **1a**−**1h** were synthesized by known procedures.[1]

Computational Details: The structures of the molecules were initially optimized at the B3LYP/6-31G* computational level[11,12] in the GAUSSIAN98 package.[13] The conformations were confirmed to be minima by frequency calculations at the same computational level. Further optimization was carried out at the B3LYP/6-311++G**[14] level and the geometries obtained at this level were used to calculate the chemical shieldings by the GIAO method.[15]

Treatment of the 3-(3-Aryl-3-oxopropenyl)chromen-4-ones with Hydrazine Hydrate: A mixture of the appropriate starting material (**1a**−**1h**, 5.0 mmol), hydrazine hydrate (50.0 mmol) and acetic acid (30 mL) was heated at reflux for 3 h, and then poured into water.

The precipitate was filtered off, washed with water and dried. The minor products (**2a−2f**) and the major products (**3a−3h**) were separated by silica gel column chromatography with 1,2-dichloroethane as eluent and recrystallised from methanol.

Minor Products

1-Acetyl-5-(3-chromonyl)-3-phenyl-2-pyrazoline (2a): Yield 5%. M.p. 218−219 °C. IR (KBr): $\tilde{\nu}$ = 1662 (C=O), 1640 (C=O), 1607 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.29 (s, 3 H, CH_3), 3.27 (dd, J = 5.4, 17.8 Hz, 1 H, H-4$_{trans}$), 3.75 (dd, J = 12.2, 17.8 Hz, 1 H, H-4$_{cis}$), 5.43 (dd, J = 5.4, 12.2 Hz, 1 H, H-5), 7.46−7.53 (m, 4 H, H-6′′,3′,4′,5′), 7.67 (dd, J = 8.4, 0.8 Hz, 1 H, H-8′′), 7.77−7.85 (m, 3 H, H-7′′,2′,6′), 8.05 (dd, J = 8.0, 1.6 Hz, 1 H, H-5′′), 8.29 (s, 1 H, H-2) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.8 (*C*H$_3$), 39.1 (C-4), 53.7 (C-5), 118.4 (C-8′′), 122.3 (C-3′′), 123.5 (C-10′′), 124.9 (C-5′′), 125.6 (C-6′′), 126.6 (C-2′,6′), 128.8 (C-3′,5′), 130.2 (C-4′), 131.3 (C-1′), 134.3 (C-7′′), 154.6 (C-2′′), 155.1 (C-3), 155.7 (C-9′′), 167.8 (*C*OCH$_3$), 175.4 (C-4′′) ppm. MS: m/z = 332 [M$^+$]. $C_{20}H_{16}N_2O_3$ (332.3): calcd. C 72.28, H 4.85, N 8.42; found C 72.31, H 4.83, N 8.46.

1-Acetyl-5-(3-chromonyl)-3-(4-methylphenyl)-2-pyrazoline (2b): Yield 2%. M.p. 243−245 °C. IR (KBr): $\tilde{\nu}$ = 1658 (C=O), 1642 (C=O), 1610 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.28 (s, 3 H, CH_3), 2.36 (s, 3 H, 4′-CH_3), 3.24 (dd, J = 5.2, 17.8 Hz, 1 H, H-4$_{trans}$), 3.71 (dd, J = 12.2, 17.8 Hz, 1 H, H-4$_{cis}$), 5.40 (dd, J = 5.2, 12.2 Hz, 1 H, H-5), 7.29 (d, J = 7.9 Hz, 2 H, H-3′,5′), 7.50 (dd, J = 7.2, 7.6 Hz, 1 H, H-6′′), 7.67 (d, J = 7.8 Hz, 1 H, H-8′′), 7.67 (d, J = 7.9 Hz, 2 H, H-2′,6′), 7.82 (dd, J = 7.2, 7.8 Hz, 1 H, H-7′′), 8.04 (d, 1 H, J = 7.6 Hz, H-5′′), 8.27 (s, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.0 (4′-*C*H$_3$), 21.8 (*C*H$_3$), 39.2 (C-4), 53.6 (C-5), 118.4 (C-8′′), 122.3 (C-3′′), 123.5 (C-10′′), 124.9 (C-5′′), 125.6 (C-6′′), 126.6 (C-2′,6′), 128.6 (C-1′), 129.3 (C-3′,5′), 134.3 (C-7′′), 140.0 (C-4′), 154.5 (C-2′′), 155.0 (C-3), 155.7 (C-9′′), 167.7 (*C*OCH$_3$), 175.3 (C-4′′) ppm. MS: m/z = 346 [M$^+$]. $C_{21}H_{18}N_2O_3$ (346.3): calcd. C 72.82, H 5.24, N 8.08; found C 72.86, H 5.26, N 8.11.

1-Acetyl-5-(3-chromonyl)-3-(4-methoxyphenyl)-2-pyrazoline (2c): Yield 4%. M.p. 214−215 °C. IR (KBr): $\tilde{\nu}$= 1658 (C=O), 1640 (C=O), 1608 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.28 (s, 3 H, CH_3), 3.22 (dd, J = 5.2, 17.7 Hz, 1 H, H-4$_{trans}$), 3.70 (dd, J = 12.1, 17.7 Hz, 1 H, H-4$_{cis}$), 3.81 (s, 3 H, OCH_3), 5.39 (dd, J = 5.2, 12.1 Hz, 1 H, H-5), 7.02 (d, J = 8.4 Hz, 2 H, H-3′,5′), 7.50 (dd, J = 7.5, 7.8 Hz, 1 H, H-6′′), 7.65 (d, J = 8.2 Hz, 1 H, H-8′′), 7.71 (d, J = 8.4 Hz, 2 H, H-2′,6′), 7.81 (dd, J = 7.5, 8.2 Hz, 1 H, H-7′′), 8.04 (d, 1 H, J = 7.8 Hz, H-5′′), 8.24 (s, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.8 (*C*H$_3$), 39.2 (C-4), 53.5 (C-5), 55.4 (O*C*H$_3$), 114.2 (C-3′,5′), 118.4 (C-8′′), 122.3 (C-3′′), 123.5 (C-10′′), 123.8 (C-1′), 124.9 (C-5′′), 125.6 (C-6′′), 128.3 (C-2′,6′), 134.3 (C-7′′), 154.4 (C-2′′), 154.8 (C-3), 155.7 (C-9′′), 160.8 (C-4′), 167.6 (*C*OCH$_3$), 175.4 (C-4′′) ppm. MS: m/z = 362 [M$^+$]. $C_{21}H_{18}N_2O_4$ (362.4): calcd. C 69.60, H 5.01, N 7.73; found C 69.64, H 4.98, 7.77.

1-Acetyl-5-(3-chromonyl)-3-(4-fluorophenyl)-2-pyrazoline (2d): Yield 2%. M.p. 226−227 °C. IR (KBr): $\tilde{\nu}$ = 1658 (C=O), 1640 (C=O), 1608 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.28 (s, 3 H, CH_3), 3.27 (dd, J = 5.3, 17.8 Hz, 1 H, H-4$_{trans}$), 3.73 (dd, J = 12.2, 17.8 Hz, 1 H, H-4$_{cis}$), 5.42 (dd, J = 5.3, 12.2 Hz, 1 H, H-5), 7.32 (t, $J_{H,H}$ and $J_{H,F}$ = 8.9 Hz, 2 H, H-3′,5′), 7.50 (dd, J = 7.1, 8.0 Hz, 1 H, H-6′′), 7.67 (d, 1 H, J = 8.4 Hz, H-8′′), 7.79−7.85 (m, 3 H, H-7′′ and H-2′,6′), 8.04 (dd, 1 H, J = 1.6, 8.0 Hz, H-5′′), 8.29 (s, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.8 (*C*H$_3$), 39.1 (C-4), 53.8 (C-5), 115.8 (d, J = 22.0 Hz, C-3′,5′), 118.4 (C-8′′), 122.2 (C-3′′), 123.5 (C-10′′), 124.9 (C-5′′), 125.6 (C-6′′), 128.0 (d, J = 3.0 Hz, C-1′′), 128.9 (d, J = 8.5 Hz, C-2′,6′), 134.3 (C-7′′), 154.2 (C-3), 154.7 (C-2′′), 155.7 (C-9′′), 163.2 (d, J = 248.1 Hz, C-4′), 167.8 (*C*OCH$_3$), 175.3 (C-4′′) ppm. MS: m/z = 350 [M$^+$]. $C_{20}H_{15}FN_2O_3$ (350.3): calcd. C 68.56, H 4.32, N 7.99; found C 68.52, H 4.34, N 7.96.

1-Acetyl-3-(4-chlorophenyl)-5-(3-chromonyl)-2-pyrazoline (2e): Yield 4%. M.p. 200−201 °C. IR (KBr): $\tilde{\nu}$ = 1666 (C=O), 1644 (C=O), 1610 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.27 (s, 3 H, CH_3), 3.26 (dd, J = 5.3, 17.8 Hz, 1 H, H-4$_{trans}$), 3.71 (dd, J = 12.2, 17.8 Hz, 1 H, H-4$_{cis}$), 5.42 (dd, J = 5.3, 12.2 Hz, 1 H, H-5), 7.47−7.52 (m, 1 H, H-6′′), 7.54 (d, J = 8.5 Hz, 2 H, H-3′,5′), 7.65 (d, J = 8.3 Hz, 1 H, H-8′′), 7.78 (d, J = 8.5 Hz, 2 H, H-2′,6′), 7.79−7.83 (m, 1 H, H-7′′), 8.03 (d, 1 H, J = 7.7 Hz, H-5′′), 8.29 (s, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.8 (*C*H$_3$), 38.9 (C-4), 54.0 (C-5), 118.4 (C-8′′), 122.1 (C-3′′), 123.5 (C-10′′), 125.0 (C-5′′), 125.6 (C-6′′), 128.4 (C-2′,6′), 128.9 (C-3′,5′), 130.3 (C-1′), 134.4 (C-7′′), 134.7 (C-4′), 154.1 (C-3), 154.8 (C-2′′), 155.7 (C-9′′), 167.9 (*C*OCH$_3$), 175.4 (C-4′′) ppm. MS: m/z = 366 [M$^+$]. $C_{20}H_{15}ClN_2O_3$ (336.8): calcd. C 65.49, H 4.12, N 7.63; found C 65.45, H 4.14, N 7.66.

1-Acetyl-3-(4-bromophenyl)-5-(3-chromonyl)-2-pyrazoline (2f): Yield 6%. M.p. 206−207 °C. IR (KBr): $\tilde{\nu}$ = 1666 (C=O), 1644 (C=O), 1610 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 2.27 (s, 3 H, CH_3), 3.26 (dd, J = 5.4, 17.8 Hz, 1 H, H-4$_{trans}$), 3.71 (dd, J = 12.2, 17.8 Hz, 1 H, H-4$_{cis}$), 5.42 (dd, J = 5.4, 12.2 Hz, 1 H, H-5), 7.49 (ddd, J = 1.0, 7.5, 7.9 Hz, 1 H, H-6′′), 7.63−7.73 (m, 5 H, H-8′′,2′,3′,5′,6′), 7.81 (dt, J = 1.5, 7.9 Hz, 1 H, H-7′′), 8.03 (dd, 1 H, J = 1.5, 7.5 Hz, H-5′′), 8.29 (s, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 21.8 (*C*H$_3$), 38.9 (C-4), 54.0 (C-5), 118.4 (C-8′′), 122.1 (C-3′′), 123.5 (C-4′,10′′), 124.9 (C-5′′), 125.6 (C-6′′), 128.5 (C-2′,6′), 130.6 (C-1′), 131.7 (C-3′,5′), 134.3 (C-7′′), 154.2 (C-3), 154.7 (C-2′′), 155.7 (C-9′′), 167.9 (*C*OCH$_3$), 175.3 (C-4′′) ppm. MS: m/z = 411 [M$^+$]. $C_{20}H_{15}BrN_2O_3$ (411.2): calcd. C 58.41, H 3.68, N 6.81; found C 58.44, H 3.66, N 6.84.

Major Products

1-Acetyl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3-phenyl-2-pyrazoline (3a): Yield 75%. M.p. 248−249 °C. IR (KBr): $\tilde{\nu}$ = 3216 (NH), 1624 (C=O), 1594 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 2.16 (s, 3 H, CH_3), 3.14 (dd, J = 5.2, 17.9 Hz, 1 H, H-4$_{trans}$), 3.69 (dd, J = 11.9, 17.9 Hz, 1 H, H-4$_{cis}$), 5.51 (dd, J = 5.2, 11.9 Hz, 1 H, H-5), 6.83 (t, J = 7.5 Hz, 1 H, H-5′′′), 6.94 (d, J = 8.0 Hz, 1 H, H-3′′′), 7.22 (ddd, J = 1.4, 7.5, 8.0 Hz, 1 H, H-4′′′), 7.30−7.34 (m, 4 H, H-6′′′,3′′,4′′,5′′), 7.58−7.61 (m, 2 H, H-2′′,6′′), 8.11 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 22.4 (*C*H$_3$), 42.2 (C-4), 52.6 (C-5), 114.7 (C-1′′′), 117.4 (C-3′′′), 120.4 (C-5′′′), 123.9 (C-4′), 127.7 (C-2′′,6′′), 129.7 (C-3′′,5′′), 131.3 (C-4′′), 132.0 (C-6′′′), 132.4 (C-1′′), 132.9 (C-4′′′), 133.3 (C-5′), 142.4 (C-3′), 155.4 (C-3), 156.8 (C-2′′′), 169.3 (*C*OCH$_3$) ppm. MS: m/z = 346 [M$^+$]. $C_{20}H_{18}N_4O_2$ (346.3): calcd. C 69.35, H 5.24, N 16.17; found C 69.32, H 5.26, N 16.13.

1-Acetyl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3-(4-methylphenyl)-2-pyrazoline (3b): Yield 63%. M.p. 253−254 °C. IR (KBr): $\tilde{\nu}$ = 3216 (NH), 1640 (C=O), 1594 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 2.18 (s, 3 H, CH_3), 2.27 (s, 3 H, 4′′-CH_3), 3.13 (dd, J = 5.1, 17.8 Hz, 1 H, H-4$_{trans}$), 3.69 (dd, J = 11.9, 17.8 Hz, 1 H, H-4$_{cis}$), 5.51 (dd, J = 5.1, 11.9 Hz, 1 H, H-5), 6.86 (dd, J = 7.1, 7.6 Hz, 1 H, H-5′′′), 6.97 (d, J = 8.3 Hz, 1 H, H-3′′′), 7.17 (d, J = 8.1 Hz, 2 H, H-3′′,5′′), 7.26 (ddd, J = 1.6, 7.1, 8.3 Hz, 1 H, H-4′′′), 7.38 (dd, J = 1.6, 7.6 Hz, 1 H, H-6′′′), 7.52 (d, J = 8.1 Hz, 2 H, H-2′′,6′′), 8.11 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 21.5 (4′′-*C*H$_3$), 22.2 (*C*H$_3$), 42.0 (C-4), 52.2 (C-5), 114.6

(C-1′′′), 117.1 (C-3′′′), 120.1 (C-5′′′), 123.4 (C-4′), 127.4 (C-2′′,6′′), 129.3 (C-1′′), 130.0 (C-3′′,5′′), 131.7 (C-6′′′), 132.4 (C-4′′′), 133.0 (C-5′), 141.1 (C-4′′), 142.0 (C-3′), 155.1 (C-3), 156.5 (C-2′′′), 168.7 (*C*OCH$_3$) ppm. MS: *m*/*z* = 360 [M$^+$]. $C_{21}H_{20}N_4O_2$ (360.4): calcd. C 69.98, H 5.59, N 15.54; found C 69.99, H 5.57, N 15.52.

1-Acetyl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3-(4-methoxyphenyl)-4-pyrazoline (3c): Yield 71%. M.p. 235−237 °C. IR (KBr): $\tilde{\nu}$ = 3232 (NH), 1644 (C=O), 1608 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.13 (s, 3 H, CH_3), 3.08 (dd, *J* = 5.0, 17.7 Hz, 1 H, H-4$_{trans}$), 3.63 (dd, *J* = 11.7, 17.7 Hz, 1 H, H-4$_{cis}$), 3.69 (s, 3 H, OCH_3), 5.47 (dd, *J* = 5.0, 11.7 Hz, 1 H, H-5), 6.82 (t, *J* = 7.3 Hz, 1 H, H-5′′′), 6.85 (d, *J* = 8.7 Hz, 2 H, H-3′′,5′′), 6.94 (d, *J* = 7.9 Hz, 1 H, H-3′′′), 7.22 (dd, *J* = 7.3, 7.9 Hz, 1 H, H-4′′′), 7.30 (d, *J* = 7.3 Hz, 1 H, H-6′′′), 7.51 (d, *J* = 8.7 Hz, 2 H, H-2′′,6′′), 8.06 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 22.5 (*C*H$_3$), 42.5 (C-4), 52.7 (C-5), 56.2 (O*C*H$_3$), 114.7 (C-1′′′), 115.3 (C-3′′,5′′), 117.7 (C-3′′′), 120.7 (C-5′′′), 124.2 (C-4′), 125.1 (C-1′′), 129.6 (C-2′′,6′′), 132.3 (C-6′′′), 133.2 (C-4′′′), 133.5 (C-5′), 142.7 (C-3′), 155.6 (C-3), 157.1 (C-2′′′), 162.7 (C-4′′), 169.5 (*C*OCH$_3$) ppm. MS: *m*/*z* = 376 [M$^+$]. $C_{21}H_{20}N_4O_3$ (376.4): calcd. C 67.01, H 5.36, N 14.88; found C 66.96, H 5.38, N 14.84.

1-Acetyl-3-(4-fluorophenyl)-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazoline (3d): Yield 64%. M.p. 247−248 °C. IR (KBr): $\tilde{\nu}$ = 3204 (NH), 1636 (C=O), 1606 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.16 (s, 3 H, CH_3), 3.14 (dd, *J* = 5.0, 17.9 Hz, 1 H, H-4$_{trans}$), 3.69 (dd, *J* = 11.9, 17.9 Hz, 1 H, H-4$_{cis}$), 5.53 (dd, *J* = 5.0, 11.9 Hz, 1 H, H-5), 6.83 (t, *J* = 7.5 Hz, 1 H, H-5′′′), 6.93 (d, *J* = 8.1 Hz, 1 H, H-3′′′), 7.12 (t, $J_{H,H}$ = $J_{H,F}$ = 8.7 Hz, 2 H, H-3′′,5′′), 7.22 (dd, *J* = 7.5, 8.1 Hz, 1 H, H-4′′′), 7.32 (d, *J* = 7.5 Hz, 1 H, H-6′′′), 7.63 (dd, $J_{H,F}$ = 5.5 and $J_{H,H}$ = 8.7 Hz, 2 H, H-2′′,6′′), 8.09 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 22.2 (*C*H$_3$), 42.0 (C-4), 52.5 (C-5), 114.7 (C-1′′′), 116.5 (d, *J* = 22.0 Hz, C-3′′,5′′), 117.2 (C-3′′′), 120.2 (C-5′′′), 123.4 (C-4′), 128.7 (d, *J* = 3.1 Hz, C-1′′), 129.7 (d, *J* = 8.5 Hz, C-2′′,6′′), 131.8 (C-6′′′), 132.6 (C-4′′′), 133.2 (C-5′), 142.2 (C-3′), 154.4 (C-3), 156.6 (C-2′′′), 164.5 (d, *J* = 248.7 Hz, C-4′′), 169.0 (*C*OCH$_3$) ppm. MS: *m*/*z* = 364 [M$^+$]. $C_{20}H_{17}FN_4O_2$ (364.3): calcd. C 65.93, H 4.70, N 15.37; found C 65.97, H 4.18, N 15.41.

1-Acetyl-3-(4-chlorophenyl)-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazoline (3e): Yield 65%. M.p. 258−259 °C. IR (KBr): $\tilde{\nu}$ = 3224 (NH), 1640 (C=O), 1596 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.22 (s, 3 H, CH_3), 3.14 (dd, *J* = 4.9, 17.8 Hz, 1 H, H-4$_{trans}$), 3.74 (dd, *J* = 11.9, 17.8 Hz, 1 H, H-4$_{cis}$), 5.58 (dd, *J* = 4.9, 11.9 Hz, 1 H, H-5), 6.87 (t, *J* = 7.5 Hz, 1 H, H-5′′′), 6.94 (d, *J* = 8.0 Hz, 1 H, H-3′′′), 7.25 (ddd, *J* = 1.5, 7.5, 8.0 Hz, 1 H, H-4′′′), 7.39 (dd, *J* = 1.5, 7.5 Hz, 1 H, H-6′′′), 7.47 (d, 2 H, *J* = 8.6 Hz, H-3′′,5′′), 7.67 (d, 2 H, *J* = 8.6 Hz, H-2′′,6′′), 7.91 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 21.9 (*C*H$_3$), 41.5 (C-4), 52.1 (C-5), 115.6 (C-1′′′), 116.3 (C-3′′′), 119.4 (C-5′′′), 121.7 (C-4′), 128.5 (C-2′′,6′′), 129.0 (C-3′′,5′′), 130.4 (C-1′′), 130.8 (C-6′′′), 130.9 (C-4′′′), 132.5 (C-5′), 135.1 (C-4′′), 141.2 (C-3′), 153.4 (C-3), 155.6 (C-2′′′), 167.9 (*C*OCH$_3$) ppm. MS: *m*/*z* = 380 [M$^+$]. $C_{20}H_{17}ClN_4O_2$ (380.8): calcd. C 63.08, H 4.50, N 14.71; found C 63.04, H 4.54, N 14.73.

1-Acetyl-3-(4-bromophenyl)-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazoline (3f): Yield 70%. M.p. 262−263 °C. IR (KBr): $\tilde{\nu}$ = 3224 (NH), 1640 (C=O), 1592 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.17 (s, 3 H, CH_3), 3.15 (dd, *J* = 5.1, 17.9 Hz, 1 H, H-4$_{trans}$), 3.71 (dd, *J* = 12.0, 17.9 Hz, 1 H, H-4$_{cis}$), 5.55 (dd, *J* = 5.1, 12.0 Hz, 1 H, H-5), 6.85 (t, *J* = 7.5 Hz, 1 H, H-5′′′), 6.94 (d, *J* = 8.0 Hz, 1 H, H-3′′′), 7.24 (ddd, *J* = 1.4, 7.5, 8.0 Hz, 1 H, H-4′′′), 7.34 (dd, *J* = 1.4, 7.5 Hz, 1 H, H-6′′′), 7.55 (s, 4 H, H-2′′,3′′,5′′,6′′), 8.10 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 22.1 (*C*H$_3$), 41.6 (C-4), 52.4 (C-5), 114.7 (C-1′′′), 116.9 (C-3′′′), 120.0 (C-5′′′), 123.0 (C-4′), 124.4 (C-4′′), 129.1 (C-2′′,6′′), 131.2 (C-1′′), 131.5 (C-6′′′), 132.2 (C-4′′′), 132.4 (C-3′′,5′′), 133.1 (C-5′), 141.9 (C-3′), 154.1 (C-3), 156.3 (C-2′′′), 168.7 (*C*OCH$_3$) ppm. MS: *m*/*z* = 425 [M$^+$]. $C_{20}H_{17}BrN_4O_2$ (425.2): calcd. C 56.48, H 4.03, N 13.17; found C 56.44, H 4.04, N 13.14.

1-Acetyl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3-(1-naphthyl)-2-pyrazoline (3g): Yield 72%. M.p. 240−241 °C. IR (KBr): $\tilde{\nu}$ = 3216 (NH), 1644 (C=O), 1594 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.28 (s, 3 H, CH_3), 3.34 (dd, *J* = 5.1, 17.5 Hz, 1 H, H-4$_{trans}$), 3.97 (dd, *J* = 11.9, 17.5 Hz, 1 H, H-4$_{cis}$), 5.56 (dd, *J* = 5.1, 11.9 Hz, 1 H, H-5), 6.86 (t, *J* = 7.4 Hz, 1 H, H-5′′′), 6.94 (d, *J* = 7.9 Hz, 1 H, H-3′′′), 7.23 (dd, *J* = 7.4, 7.9 Hz, 1 H, H-4′′′), 7.41 (d, *J* = 7.4 Hz, 1 H, H-6′′′), 7.45−7.61 (m, 4 H, H-3′′, H-6′′, H-7′′ and H-8′′), 7.92−7.96 (m, 2 H, H-4′′ and H-5′′), 8.12 (s, 1 H, H-5′), 9.09 (d, *J* = 8.4 Hz, 1 H, H-2′′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 22.3 (*C*H$_3$), 44.3 (C-4), 51.1 (C-5), 115.0 (C-1′′′), 116.8 (C-3′′′), 119.8 (C-5′′′), 122.7 (C-4′), 125.7 and 128.0 (C-1′′, C-6′′ and C-7′′), 127.2 (C-2′′), 130.6 (C-10′′), 131.45 (C-4′′), 126.8 (C-3′′), 129.3 (C-5′′ and C-8′′), 131.35 (C-6′′′), 131.8 (C-4′′′), 132.9 (C-5′), 134.3 (C-9′′), 141.7 (C-3′), 155.2 (C-3), 156.1 (C-2′′′), 168.6 (*C*OCH$_3$) ppm. MS: *m*/*z* = 396 [M$^+$]. $C_{24}H_{20}N_4O_2$ (396.4): calcd. C 72.71, H 5.08, N 14.13; found C 72.76, H 5.05, N 14.09.

1-Acetyl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-3-(2-naphthyl)-2-pyrazoline (3h): Yield 69%. M.p. 261−262 °C. IR (KBr): $\tilde{\nu}$ = 3216 (NH), 1640 (C=O), 1588 (C=N) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO + TFA): δ = 2.18 (s, 3 H, CH_3), 3.27 (dd, *J* = 5.1, 17.8 Hz, 1 H, H-4$_{trans}$), 3.77 (dd, *J* = 11.9, 17.8 Hz, 1 H, H-4$_{cis}$), 5.55 (dd, *J* = 5.1, 11.9 Hz, 1 H, H-5), 6.82 (t, *J* = 7.4 Hz, 1 H, H-5′′′), 6.91 (d, *J* = 7.9 Hz, 1 H, H-3′′′), 7.19 (dd, *J* = 7.4, 7.9 Hz, 1 H, H-4′′′), 7.32 (d, *J* = 7.4 Hz, 1 H, H-6′′′), 7.41−7.46 (m, 2 H, H-5′′ and H-8′′), 7.78−7.88 (m, 4 H, H-3′′, H-4′′, H-6′′ and H-7′′), 7.89 (s, 1 H, H-1′′), 8.11 (s, 1 H, H-5′) ppm. NMR ([D$_6$]DMSO + TFA): δ = 22.4 (*C*H$_3$), 42.2 (C-4), 52.8 (C-5), 114.7 (C-1′′′), 117.5 (C-3′′′), 120.5 (C-5′′′), 124.0 (C-4′), 124.4 (C-3′′), 127.9 and 128.4 (C-1′′, C-5′′ and C-8′′), 128.9, 129.3 and 129.6 (C-4′′, C-6′′, C-7′′), 130.1 (C-2′′), 132.1 (C-6′′′), 133.0 (C-4′′′), 133.4 (C-5′), 134.1 (C-9′), 135.1 (C-10′′), 142.6 (C-3′), 155.6 (C-3), 156.9 (C-2′′′), 169.5 (*C*OCH$_3$) ppm. MS: *m*/*z* = 396 [M$^+$]. $C_{24}H_{20}N_4O_2$ (396.4): calcd. C 72.71, H 5.08, N 14.13; found C 72.67, H 5.09, N 14.18.

Transformation of the 1-Acetyl-3-aryl-5-(3-chromonyl)-2-pyrazolines 2b, 2c and 2f into the 1-Acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines 3b, 3c and 3f: A mixture of the appropriate 2-pyrazoline (**2b, 2c, 2f**, 1.0 mmol), hydrazine hydrate (0.5 mL, 10.0 mmol) and acetic acid (2.0 mL) was heated at reflux for 6 h, and then poured into water. The precipitate was separated by filtration, washed with water and dried to afford compounds **3b** (81%), **3c** (85%) and **3f** (79%). The substances prepared in this way were identical in every respect with those obtained as major products from treatment of **1b**, **1c** or **1f** with hydrazine hydrate.

Synthesis of the 3(5)-Aryl-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]pyrazoles 5a−5f: DDQ (159 mg, 0.7 mmol) was added to a solution of the appropriate 1-acetyl-3-aryl-5-[3-(2-hydroxyphenyl)pyrazol-4-yl]-2-pyrazolines **3a−3f** (0.7 mmol) in dry dioxane (30 mL). The mixture was heated at reflux under nitrogen until the consumption of the starting material was complete (≈10 hours). The solution was then evaporated to dryness and the residue was dissolved in chloroform (40 mL) and washed with a saturated aqueous solution

of potassium hydrogen carbonate (50 mL). The organic layer was collected and dried with anhydrous sodium sulfate, and the solvent was evaporated to dryness. The crude products were purified by flash chromatography on silica gel (SDS type 60 A C.C., 40−63 μm); with chloroform as eluent a mixture of three unidentified compounds was collected, while the bispyrazoles **5a**−**f** were eluted with a 1:1 mixture of chloroform/ethyl acetate.

5(3)-[3-(2-Hydroxyphenyl)pyrazol-4-yl]-3(5)-phenylpyrazole (5a): Yield 55% (116.3 mg). M.p. 218−219 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3434 (OH), 3234 (NH), 1613 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA; 500.13 MHz): δ = 6.55 (s, 1 H, H-4), 6.89 (t, J = 7.6 Hz, 1 H, H-5′′′), 7.00 (d, J = 8.0 Hz, 1 H, H-3′′′), 7.29 (dd, J = 7.6, 8.0 Hz, 1 H, H-4′′′), 7.34 (d, J = 7.6 Hz, 1 H, H-6′′′), 7.37 (t, J = 7.6 Hz, 1 H, H-4′′), 7.44 (t, J = 7.6 Hz, 2 H, H-3′′,5′′), 7.70 (d, J = 7.6 Hz, 2 H, H-2′′,6′′), 8.25 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA; 125.8 MHz): δ = 101.7 (C-4), 110.4 (C-4′), 116.8 (C-1′′′,3′′′), 119.7 (C-5′′′), 126.4 (C-2′′,6′′), 129.55 (C-4′′), 129.61 (C-3′′,5′′), 129.7 (C-1′′), 131.38 and 131.41) C-4′′′ and C-6′′′, 134.8 (C-5′), 141.6 (C-5), 142.1 (C-3′), 147.2 (C-3), 156.1 (C-2′′′) ppm. EI-MS: *m*/*z* (rel. int.) = 302 (62) [M$^{+\cdot}$], 285 (100), 182 (7), 171 (7), 151 (5), 115 (4). $C_{18}H_{14}N_4O$ (302.33): calcd. C 71.51, H 4.67, N 18.53; found C 71.61, H 4.65, N 18.56.

5(3)-[3-(2-Hydroxyphenyl)pyrazol-4-yl]-3(5)-(4-methylphenyl)-pyrazole (5b): Yield 60% (132.7 mg). M.p. 239−241 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3388 (OH), 3207 (NH), 1618 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 2.25 (s, 3 H, C*H*$_3$), 6.51 (s, 1 H, H-4), 6.84 (dd, J = 7.1, 7.8 Hz, 1 H, H-5′′′), 6.95 (d, J = 8.0 Hz, 1 H, H-3′′′), 7.20 (d, J = 8.0 Hz, 2 H, H-3′′,5′′), 7.22−7.26 (m, 1 H, H-4′′′), 7.27 (dd, J = 1.4, 7.8 Hz, 1 H, H-6′′′), 7.54 (d, J = 8.0 Hz, 2 H, H-2′′,6′′), 8.19 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 21.6 (*C*H$_3$), 102.6 (C-4), 109.9 (C-4′), 117.1 (C-1′′′), 117.7 (C-3′′′), 120.6 (C-5′′′), 125.8 (C-1′′), 127.5 (C-2′′,6′′), 131.0 (C-3′′,5′′), 132.1 (C-6′′′), 132.4 (C-4′′′), 135.9 (C-5′), 141.7 (C-4′′), 142.8 (C-5), 143.5 (C-3′), 148.0 (C-3), 156.8 (C-2′′′) ppm. EI-MS: *m*/*z* (rel. int.) = 316 (56) [M$^{+\cdot}$], 299 (100), 285 (6), 182 (6), 171 (7), 115 (6). $C_{19}H_{16}N_4O$ (316.36): calcd. C 72.13, H 5.10, N 17.71; found C 72.17, H 5.08, N 17.67.

5(3)-[3-(2-Hydroxyphenyl)pyrazol-4-yl]-3(5)-(4-methoxyphenyl)-pyrazole (5c): Yield 58% (134.8 mg). M.p. 240−242 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3462 (OH), 3241 (NH), 1624 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 3.75 (s, 3 H, OC*H*$_3$), 6.51 (s, 1 H, H-4), 6.87 (dt, J = 0.9, 7.6 Hz, 1 H, H-5′′′), 6.97 (dd, J = 0.9, 8.1 Hz, 1 H, H-3′′′), 7.01 (d, J = 8.9 Hz, 2 H, H-3′′,5′′), 7.27 (ddd, J = 1.6, 7.6, 8.1 Hz, 1 H, H-4′′′), 7.31 (dd, J = 1.6, 7.6 Hz, 1 H, H-6′′′), 7.64 (d, J = 8.9 Hz, 2 H, H-2′′,6′′), 8.19 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 55.8 (O*C*H$_3$), 101.5 (C-4), 109.2 (C-4′), 115.3 (C-3′′,5′′), 116.94 (C-1′′′), 116.99 (C-3′′′), 119.9 (C-5′′′), 120.6 (C-1′′), 128.5 (C-2′′,6′′), 131.5 (C-4′′′,6′′′), 135.5 (C-5′), 142.3 (C-5), 142.6 (C-3′), 147.2 (C-3), 156.1 (C-2′′′), 161.5 (C-4′′) ppm. EI-MS: *m*/*z* (rel. int.) = 332 (83) [M$^{+\cdot}$], 315 (100), 300 (4), 272 (4), 182 (7), 171 (9), 115 (4). $C_{19}H_{16}N_4O_2$ (332.36): calcd. C 68.66, H 4.85, N 16.86; found C 68.59, H 4.87, N 16.83.

3(5)-(4-Fluorophenyl)-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]-pyrazole (5d): Yield 51% (114.2 mg). M.p. 300−301 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3421 (OH), 3237 (NH), 1613 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 6.50 (s, 1 H, H-4), 6.84 (dd, J = 6.9, 7.5 Hz, 1 H, H-5′′′), 6.96 (d, J = 8.3 Hz, 1 H, H-3′′′), 7.16 (t, $J_{H,H}$ = 8.7 Hz and $J_{H,F}$ = 8.7 Hz, 2 H, H-3′′,5′′), 7.25 (ddd, J = 1.5, 6.9, 8.3 Hz, 1 H, H-4′′′), 7.26 (dd, J = 1.5, 7.5 Hz, 1 H, H-6′′′), 7.69 (dd, $J_{H,H}$ = 8.7 Hz and $J_{H,F}$ = 5.3 Hz, 2 H, H-2′′,6′′), 8.23 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 102.6 (C-4), 110.8 (C-4′), 116.9 (d, J = 18.2 Hz, C-3′′,5′′), 117.3 (C-1′′′), 117.6 (C-3′′′), 120.4 (C-5′′′), 126.1 (d, J = 2.9 Hz, C-1′′), 129.4 (d, J = 8.4 Hz, C-2′′,6′′), 132.0 (C-6′′′), 132.3 (C-4′′′), 135.4 (C-5′), 142.2 (C-5), 143.0 (C-3′), 147.1 (C-3), 156.7 (C-2′′′), 164.3 (d, J = 218.9 Hz, C-4′′) ppm. EI-MS: *m*/*z* (rel. int.) = 320 (62) [M$^{+\cdot}$], 303 (100), 219 (7), 182 (6), 171 (5), 160 (5), 122 (4). $C_{18}H_{13}FN_4O$ (320.32): calcd. C 67.49, H 4.09, N 17.49; found C 67.54, H 4.07, N 17.52.

3(5)-(4-Chlorophenyl)-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]-pyrazole (5e): Yield 54% (127.2 mg). M.p. 251−253 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$= 3454 (OH), 3236 (NH), 1624 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 6.52 (s, 1 H, H-4), 6.85 (dd, J = 7.3, 7.6 Hz, 1 H, H-5′′′), 6.98 (d, J = 8.1 Hz, 1 H, H-3′′′), 7.26 (ddd, J = 1.6, 7.3, 8.1 Hz, 1 H, H-4′′′), 7.30 (dd, J = 1.6, 7.6 Hz, 1 H, H-6′′′), 7.41 (d, J = 8.5 Hz, 2 H, H-3′′,5′′), 7.65 (d, J = 8.5 Hz, 2 H, H-2′′,6′′), 8.27 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 102.6 (C-4), 111.4 (C-4′), 116.6 (C-1′′′), 117.5 (C-3′′′), 120.3 (C-5′′′), 128.6 (C-2′′,6′′), 129.0 (C-1′′), 130.2 (C-3′′,5′′), 132.0 (C-6′′′), 132.3 (C-4′′′), 135.1 (C-5′), 135.4 (C-4′′), 141.8 (C-5), 142.8 (C-3′), 147.0 (C-3), 156.7 (C-2′′′) ppm. EI-MS: *m*/*z* (rel. int.) = 338 (M$^{+\cdot}$, ^{37}Cl, 25), 336 (M$^{+\cdot}$, ^{35}Cl, 61), 321 (35), 319 (100), 284 (5), 252 (8), 171 (11), 150 (27), 118 (10), 104 (12). $C_{18}H_{13}ClN_4O$ (336.77): calcd. C 64.19, H 3.89, N 16.64; found C 64.23, H 3.91, N 16.68.

3(5)-(4-Bromophenyl)-5(3)-[3-(2-hydroxyphenyl)pyrazol-4-yl]-pyrazole (5f): Yield 54% (144.0 mg). M.p. 253−254 °C (recrystallised from cyclohexane/ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3462 (OH), 3222 (NH), 1639 (C=N) cm^{-1}. ^1H NMR ([D$_6$]DMSO + TFA): δ = 6.50 (s, 1 H, H-4), 6.82 (t, J = 7.5 Hz, 1 H, H-5′′′), 6.95 (d, J = 7.9 Hz, 1 H, H-3′′′), 7.20−7.27 (m, 2 H, H-4′′′,6′′′), 7.51 (d, J = 8.9 Hz, 2 H, H-3′′,5′′), 7.55 (d, J = 8.9 Hz, 2 H, H-2′′,6′′), 8.23 (s, 1 H, H-5′) ppm. ^{13}C NMR ([D$_6$]DMSO + TFA): δ = 103.2 (C-4), 111.5 (C-4′), 116.7 (C-1′′′), 118.0 (C-3′′′), 120.8 (C-5′′′), 124.5 (C-4′′), 129.3 (C-2′′,6′′), 129.3 (C-1′′), 132.3 (C-6′′′), 132.9 (C-4′′′), 133.6 (C-3′′,5′′), 135.5 (C-5′), 142.3 (C-5), 143.5 (C-3′), 147.4 (C-3), 157.1 (C-2′′′) ppm. EI-MS: *m*/*z* (rel. int.) = 382 (M$^{+\cdot}$, ^{81}Br, 65), 380 (M$^{+\cdot}$, ^{79}Br, 64), 365 (99), 363 (100), 332 (13), 315 (18), 302 (8), 285 (19), 182 (14), 155 (6). $C_{18}H_{13}BrN_4O$ (381.23): calcd. C 56.71, H 3.44, N 14.70; found C 56.74, H 3.42, N 14.73.

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