Synthesis of 3-Benzoyl-4-styryl-2-pyrazolines and Their Oxidation to the Corresponding Pyrazoles

Diana C. G. A. Pinto,[a] Artur M. S. Silva,*[a] Albert Lévai,[b] José A. S. Cavaleiro,[a] Tamás Patonay,[b] and José Elguero[c]

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The 3-benzoyl-4-styryl-2-pyrazolines **2a–g** were prepared from the regioselective 1,3-dipolar cycloaddition reactions of (*E,E*)-cinnamylideneacetophenones **1a–g** and diazomethane. The new compounds 3-(2-benzofuranyl)-4-styryl-2-pyrazolines **(5c,d)** were also obtained as by-products in some cases. The oxidation of the 3-benzoyl-4-styryl-2-pyrazolines **2a–g** into 3(5)-benzoyl-4-styrylpyrazoles **3a–g** is also reported. Configurational and conformational features of all compounds were established by NMR spectroscopy.

Introduction

Pyrazoles and their reduced forms pyrazolines are well-known nitrogen-containing heterocyclic compounds and various procedures have been developed for their syntheses.[1,2] As a result, a wide variety of pyrazoles and pyrazolines have hitherto been described in the literature.[1,3,4] One of the most common synthetic procedures used for the preparation of pyrazolines is based on the cycloaddition of diazoalkanes to carbon−carbon double bonds.[5] Pyrazoles can also be prepared by other methods,[1,2] including the oxidation of pyrazolines by reagents such as lead dioxide, mercuric oxide, bromine, potassium permanganate, chromium oxide, silver nitrate, manganese dioxide, lead tetraacetate, potassium hexacyanoferrate(III), *N*-bromosuccinimide and chloranil.[6]

The reaction of α,β-unsaturated ketones with diazomethane is a frequently used procedure for the synthesis of pyrazolines. The first example for this 1,3-dipolar cycloaddition was published by Azzarello as early as 1906 when he described the synthesis of 3-acetyl-4-phenyl-2-pyrazoline by the reaction of benzalacetone with diazomethane in anhydrous ether.[7] Unfortunately, later on, numerous conflicting data were described for the synthesis of pyrazolines by the reaction of α,β-enones with diazomethane.[5] For this reason, it appeared expedient to reinvestigate this cycloaddition of a wide variety of α,β-unsaturated ketones. Our experimental results unambiguously revealed that the reaction of chalcones[8] and related α,β-unsaturated ketones[9] with diazomethane affords 2-pyrazolines as the only isolable products, where the methylene moiety of the diazomethane is connected to the β-carbon atom of each of the starting α,β-enones. We have also succeeded in the synthesis of 2-pyrazolines as major products by the reaction of 2-styrylchromones with diazomethane.[10] In this paper we report the synthesis of 3-benzoyl-4-styryl-2-pyrazolines **2a−g** by the reaction of the (*E,E*)-cinnamylideneacetophenones **1a−g** with diazomethane and the conversion of these 2-pyrazolines into the 3(5)-benzoyl-4-styrylpyrazoles **3a−g**.

Cizolirtine, (±)-5-[α-(2-dimethylaminoethoxy)benzyl]-1-methylpyrazole (E-3710), is a potent analgesic obtained as a racemic mixture from the reduction of the appropriate 3-benzoylpyrazole.[11] This points out the potential application of 3-benzoylpyrazole derivatives in the preparation of cizolirtine analogues for further biological evaluation. Hence it would be advantageous if they were made available by simple and easy synthetic transformations. We present here our results on the synthesis of the 3(5)-benzoyl-4-styrylpyrazoles **3a−g**.

Results and Discussion

Synthesis

The (*E,E*)-cinnamylideneacetophenones **1a−g** were prepared in good yields from the base-catalysed aldol reaction of cinnamaldehydes and the appropriate acetophenones (Scheme 1). These cinnamylideneacetophenones **1a−g** were treated with diazomethane, at room temperature or in the refrigerator, in dichloromethane solutions; the progress of the reactions were monitored by thin-layer chromatography until complete consumption of the starting materials. After evaporation of the organic solvents and recrystallisation from ethanol or methanol, the 3-benzoyl-4-styryl-2-pyrazolines **2a−g** were obtained in satisfactory to good yields

[a] Department of Chemistry, University of Aveiro,
3810-193 Aveiro, Portugal
Fax: (internat.) + 351-234/370-084
E-mail: arturs@dq.ua.pt
[b] Department of Organic Chemistry, University of Debrecen,
H-4010 Debrecen, Hungary
Fax: (internat.) + 36-52/310-936
E-mail: alevai@tigris.klte.hu
[c] Instituto de Química Médica,
c/ Juan de la Cierva 3, 28006 Madrid, Spain
Fax: (internat.) + 34-1/564-4853

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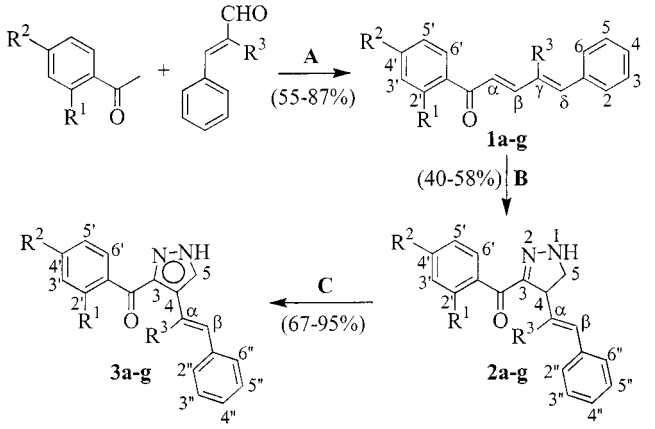
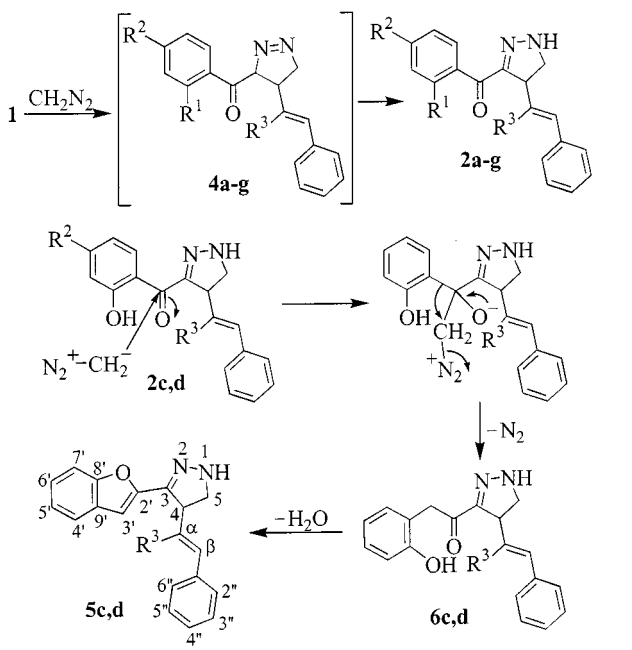


	R^1	R^2	R^3
1-3a	H	H	H
1-3b	H	H	CH_3
1-3c	OH	H	H
1-3d	OH	H	CH_3
1-3e	H	CH_3	H
1-3f	H	OCH_3	H
1-3g	H	F	H

Scheme 1. Synthesis of cinnamylideneacetophenones **1a−g**, 3-aroyl-4-styryl-2-pyrazolines **2a−g** and 3(5)-aroyl-4-styrylpyrazoles **3a−g** (**A**: $NaOH/H_2O$, MeOH; **B**: CH_2N_2, CH_2Cl_2/diethyl ether; **C**: Chloranil, toluene)

(Scheme 1). A thin layer chromatographic analysis of the mother liquors still revealed the presence of more **2a−g**, and, in the case of 2′-hydroxycinnamylideneacetophenones **1c,d** as starting materials, small amounts of 3-(2-benzofuranyl)-4-styryl-2-pyrazolines **5c,d** were also obtained (Scheme 2).

The obtained results indicate that these 1,3-dipolar cycloaddition reactions of cinnamylideneacetophenones **1a−g** with diazomethane may give rise 1-pyrazolines **4a−g**, which then isomerize into the isolable products **2a−g** (Scheme 2). Similar isomerisations of 1-pyrazolines into their appropriate 2-pyrazoline isomers have already been observed in the course of the reactions of α,β-enones with diazomethane.[8−10,12] It is worth mentioning that **2a−g** can be detected in the reaction mixtures by monitoring the progress of each reaction by thin layer chromatography and, therefore, are not the result of an improper isolation and/or purification of the 1-pyrazolines **4a−g** formed in the above-mentioned cycloaddition reactions.



Scheme 2. Proposed mechanism for the synthesis of 3-aroyl-4-styryl-2-pyrazolines **2a−g** and 3-(2-benzofuranyl)-4-styryl-2-pyrazolines **5c,d**

The formation of **4a−g** from the 1,3-dipolar cycloaddition reactions of **1a−g** with diazomethane indicates that this transformation is completely regioselective. Their formation results from the reaction between the $C_\alpha=C_\beta$ double bond of **1a−g** with diazomethane. The other possible cycloadducts, obtained from the reaction between the $C_\gamma=C_\delta$ double bond of **1a−g** with diazomethane, were not observed.

The formation of 3-(2-benzofuranyl)-4-styryl-2-pyrazolines **5c,d** can be explained by taking into consideration the insertion of a methylene group[13] between the carbonyl and the 2-hydroxyphenyl groups only in the case of 2-pyrazolines **2c,d**, leading to the formation of compounds **6c,d**. The intramolecular reaction of the hydroxyl group to the carbonyl carbon and a subsequent water elimination from the obtained hemiacetal leads to the formation of the benzofuran ring (Scheme 2).

The 3(5)-benzoyl-4-styrylpyrazoles **3a−g** were obtained by the oxidation of 3-benzoyl-4-styryl-2-pyrazolines **2a−g** with an excess of chloranil in refluxing toluene (Scheme 1) until the consumption of starting material, as monitored by thin-layer chromatography. After evaporation of the solvent and purification by column chromatography the 3(5)-benzoyl-4-styrylpyrazoles **3a−g** were obtained in good yields.

NMR Spectroscopy

The most noticeable feature of the structural characterisation of cinnamylideneacetophenones **1a−g** is the assignment of the proton resonances of their α,β,γ,δ-unsaturated moiety, which was made by a careful analysis of its ^1H and 2D COSY NMR spectra. From the values of the vicinal coupling constants ($^3J_{H_\alpha\text{-}H_\beta} \approx 15$ Hz) it was possible to establish the *trans* configuration of these two protons. As the resonances for the γ and δ protons of the cinnamylideneacetophenones **1a,e-g** appear as a multiplet, it was not possible to establish the stereochemistry of the double bonds $C_\gamma=C_\delta$. However, one can postulate a *trans* configuration for these double bonds by taking into consideration the vicinal coupling constants ($^3J_{H_\alpha\text{-}H_\beta} \approx 16$ Hz) found in the case of the 3-benzoyl-4-styryl-2-pyrazolines **2a,e-g** and the 3(5)-benzoyl-4-styrylpyrazoles **3a,e-g**.

The total stereochemistry of the **1a,e-g** was based on the NOE cross peaks found in their 2D NOESY experiments. The close proximity between α-H and 2′,6′-H and also between β-H and δ-H together with the absence of NOE cross peaks for α-H and β-H allowed us to establish the stereo-

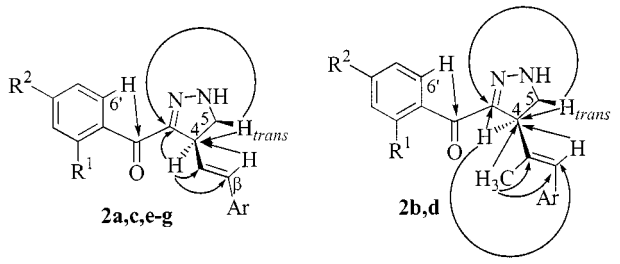


Figure 1. Important connectivities found in the HMBC spectra of 3-aroyl-4-styryl-2-pyrazolines **2a−g**

chemistry of the α,β,γ,δ-unsaturated moiety of compounds **1a,e-g** as *trans-(s-trans)-trans*, as shown in Scheme 1. The stereochemistry of the α,β,γ,δ-unsaturated moiety of compound γ-substituted **1b** was also established from the results of its 2D NOESY spectrum. The close proximity between α-H and γ-CH_3 and 2′,6′-H and also between β-H and δ-H is only compatible with the *trans-(s-trans)-trans* stereochemistry of **1b** as shown in Scheme 1. The stereochemistry of compounds **1c,d** was also established as *trans-(s-trans)-trans* in our previous work.[14,15]

A detailed analysis of ^{1}H, ^{13}C and 2D COSY, HETCOR and HMBC NMR spectra of compounds **2a−g** revealed the presence of a 2-pyrazoline ring, where the NH resonance appear as a broad singlet at δ = 6.35−6.69. The resonance of the two inequivalent methylene protons[16] ($\delta_{H\text{-}5trans}$ = 3.64−3.69 and $\delta_{H\text{-}5cis}$ = 3.81−3.93) and of the methynic proton ($\delta_{H\text{-}4}$ = 4.25−4.39) indicate that a 3,4-disubstituted 2-pyrazoline compound was present. The connectivities found in the HMBC spectra of compounds **2a−g** (Figure 1) gave unequivocal support for the structure of these 2-pyrazolines, where the methylene group of diazomethane is bonded to the β position of the starting materials **1a−g**.

The NOE cross peaks (4-H → β-H and α-H, for **2a,c,e-g**, or α-CH_3, for **2b,d**; H-5_{trans} → β-H and α-H, for **2a,c,e-g**, or α-CH_3, for **2b,d**) observed in the NOESY spectra of **2a−g** give unequivocal support for the structure of these compounds and indicate that there is free rotation around the C4−C_α bond. The absence of NOE cross peaks between the resonances of β-H and α-H, for **2a,c,e-g**, or α-CH_3, for **2b,d**, confirms the *trans* stereochemistry of these double bonds C_α=C_β.

The NMR spectroscopic data of the 4-styryl-2-pyrazoline moieties of **5c,d** are similar to those of **2a−g**, giving the same correlations in the NOESY and HMBC spectra. However, the resonance of the vinylic proton ($\delta_{3'\text{-}H}$ = 7.02−7.06) and carbon ($\delta_{C\text{-}3'}$ = 103.4−103.5) atoms and the connectivities of 3′-H with C-2′ (δ = 183.6), C-8′ and C-9′ (δ = 147.0−147.2), and also C-3 (δ = 147.7−147.8), that were found in the HMBC spectra of **5c,d**, unequivocally support the presence of a benzofuran ring.

The annular tautomerism of 3(5)-benzoylpyrazoles has not been studied previously.[17] There are two cases to consider, those of the most compounds reported here, **3a,b,e-g**, and those of the compounds with an *ortho*-hydroxy group on the benzoyl substituent, **3c,d**. In the first case, two tautomers **I** and **II** (Figure 2) can be written and all previous experience indicates that the 3-benzoyl one **(I)** should be the most stable.[17] The possible existence of a hydrogen bond that would stabilise the 5-benzoyl tautomer **IIb** does not appear to be sufficient to overcome the electron-withdrawing effect of the benzoyl group, maybe because it forms a small pseudo-five-membered ring. For instance, the related 3(5)-ethoxycarbonylpyrazoles exist in solution and in the solid state as their 3-ethoxycarbonyl tautomers.[18]

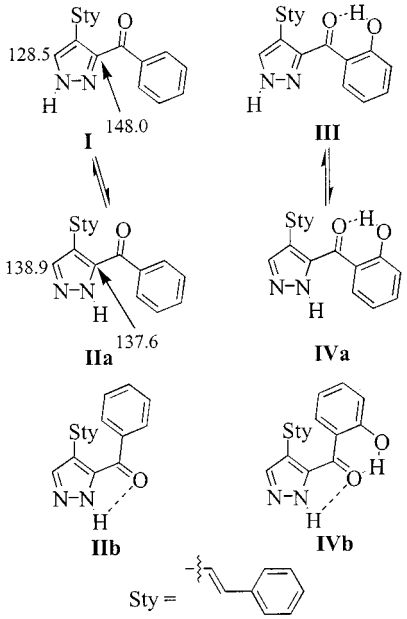


Figure 2. Possible intramolecular hydrogen bonds in pyrazoles **3a−g**; ^{13}C chemical shifts calculated using an additive model

Compounds **3a−g** in [D_6]DMSO present a deshielded broad singlet at δ = 13.5−13.7 due to the NH resonance. This shift is similar to that observed for 3-ethoxycarbonylpyrazoles (δ = 13.1−14.2).[18,19] In the ^{13}C NMR spectra, the tautomeric carbons C-3 and C-5 (see Experimental Section) appear at about δ = 128 (C−H) and δ = 146 (C-benzoyl). Considering that in pyrazole itself in [D_6]DMSO at low temperature (no prototropy) C-3 and C-5 appear at δ = 138.9 and δ = 128.5 ppm, respectively,[4] and that the effect of a benzoyl substituent in benzenes (C_{ipso}) is δ = 9.1,[20] it seems that **I** must represent the tautomer present in DMSO solution (see Figure 2).

The case of compounds **3c** and **3d** is, in principle, a little more complex due to the O−H···O=C hydrogen bond. The observation of two signals at δ = 127.5 and δ = 146 in the ^{13}C NMR of both compounds, in [D_6]DMSO, clearly indicates that here also the 3-aroyl tautomer **III** is present in these conditions. Therefore, the signals in the ^{1}H NMR spectrum at δ = 13.6 and 11.5 belong to the NH associated with the solvent and to the OH forming an intramolecular hydrogen bond (IMHB) with the carbonyl oxygen, respectively.

The ^{13}C CPMAS NMR spectra of compounds **3a** and **3c** have been recorded (see Experimental Section). The presence of signals at δ = 144.4 and δ = 129.0 in **3a** and at δ = 145.4 and δ = 128.2 in **3c** proves conclusively that these

compounds exist in the solid state as the 3-aroyl tautomers **I** and **III**.

The assignment of the carbon resonances of the pyrazole moiety was based on the connectivities (NH → C-3, C-4 and C-5; 5-H → C-3 and C-4; β-H → C-4) found in the HMBC spectra of **3a−g**. The connectivities of the pyrazolic NH proton and those of the OH with C-1′, C-2′ and C-3′, in the case of compounds **3c,d**, also gave unequivocal support for the assignments of these two proton resonances.

In summary, we established a new synthetic route for 3(5)-benzoyl-4-styrylpyrazoles **3a−g**. Firstly, the regioselective 1,3-dipolar cycloaddition reactions of (*E,E*)-cinnamylideneacetophenones **1a−g** with diazomethane afforded new 3-benzoyl-4-styryl-2-pyrazolines **2a−g**. The oxidation of these 2-pyrazoline derivatives with chloranil gave pyrazoles **3a−g**. We have also demonstrated that the obtained 3(5)-benzoyl-4-styrylpyrazoles **3a−g** exist in solution and in the solid state as their 3-benzoyl-4-styrylpyrazoles tautomers **I** and **III**.

Experimental Section

General Remarks: Melting points (uncorrected): Reichert Thermovar apparatus fitted with a microscope. − FT NMR: Bruker AMX 300 spectrometer (300.13 and 75.47 MHz, for ^1H and ^{13}C, respectively); $CDCl_3$ as solvent except for 3-benzoyl-4-styrylpyrazoles which were recorded in [D_6]DMSO, TMS as internal reference, chemical shifts (δ) in ppm, coupling constants (*J*) in Hz. Unequivocal ^1H assignments were made with the aid of 2D-COSY ($^1H/^1H$) and NOESY spectra (phase-sensitive experiment, mixing time of 800 ms), while ^{13}C assignments were made on the basis of 2D-HETCOR ($^1H/^{13}C$, delay for the one bond *J* C/H couplings was optimised at 156 Hz) and HMBC (delays for one bond and long-range *J* C/H couplings were optimised for 145 and 7 Hz, respectively) experiments. All the 2D spectra were acquired using the standard Bruker supplied microprograms. ^{13}C CPMAS NMR spectra was recorded at 100.62 MHz on a Bruker MSL 400 spectrometer with the following conditions: 5 s of recycle delay, 4 ms of time contact, 90° pulse of 5 μs and AQ of 41 ms. − Electron impact (EI, 70 eV) and fast atom bombardment (with 3-nitrobenzyl alcohol as a matrix) MS: VG Autospec Q and M spectrometers. − Elemental Analysis: Microanalytical laboratories at the Department of Organic Chemistry of the University of Debrecen and in the University of Aveiro. − Preparative thin-layer chromatography: Merck or Riedel silica gel 60 DGF_{254}. − Column chromatography: Merck silica gel 60, 70−230 mesh.

General Procedure for the Synthesis of Cinnamylideneacetophenones 1a−g: To a methanolic solution (30 mL) of the appropriate acetophenone (5.0 mmol) was slowly added an aqueous solution of sodium hydroxide (60%, 25 mL). After cooling the solution to room temperature, the appropriate cinnamaldehyde (6.0 mmol) was added. The mixture was stirred at room temperature for 20 h, then it was poured into water (100 mL), ice (100 g) and hydrochloric acid (pH adjusted to ca. 5). The obtained solid was removed by filtration, dissolved in chloroform (150 mL) and washed with an aqueous solution of sodium hydrogen carbonate (5%, 2 × 100 mL). The organic layer was collected, dried over anhydrous sodium sulfate and the solution evaporated to dryness. The residue was purified by silica gel column chromatography with dichloromethane as eluent. Finally, the cinnamylideneacetophenones **1a−g** were recrystallised from ethanol.

(*E,E*)-Cinnamylideneacetophenone (1a): Yield 81%. − M.p. 102−103 °C (recrystallisation from ethanol, ref.[21] 100 °C). − ^1H NMR: δ = 7.01−7.04 (m, 2 H, γ,δ-H), 7.09 (d, *J* = 14.8 Hz, 1 H, α-H), 7.29−7.40 (m, 3 H, 3,4,5-H), 7.46−7.52 (m, 4 H, 2,6,3′,5′-H), 7.57 (dd, *J* = 7.9 and 1.5 Hz, 1 H, 4′-H), 7.57−7.65 (m, 1 H, β-H), 7.98 (dd, *J* = 8.3 and 1.5 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 125.3 (C-α), 126.9 (C-γ), 127.2 (C-2,6), 128.3 (C-2′,6′), 128.5 (C-3′,5′), 128.8 (C-3,5), 129.2 (C-4), 132.6 (C-4′), 136.0 (C-1), 138.1 (C-1′), 141.9 (C-δ), 144.8 (C-β), 190.5 (C=O). − EI-MS: *m/z* (%) = 234 (100) [$M^{+\bullet}$], 233 (47), 215 (16), 205 (18), 191 (11), 157 (46), 128 (65), 127 (29), 115 (14), 105 (47), 91 (24), 77 (63).

(*E,E*)-γ-Methylcinnamylideneacetophenone (1b): Yield 79%. − M.p. 70−71 °C (recrystallisation from ethanol). − ^1H NMR: δ = 2.17 (s, 3 H, γ-CH_3), 6.97 (s broad, 1 H, δ-H), 7.06 (d, *J* = 15.3 Hz, 1 H, α-H), 7.28−7.33 (m, 1 H, 4-H), 7.37−7.41 (m, 4 H, 2,3,5,6-H), 7.49 (dd, *J* = 7.7 and 7.1 Hz, 2 H, 3′,5′-H), 7.57 (tt, *J* = 7.1 and 1.6 Hz, 1 H, 4′-H), 7.64 (d, *J* = 15.3 Hz, 1 H, β-H), 7.99 (dd, *J* = 7.7 and 1.6 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 13.9 (γ-CH_3), 121.5 (C-α), 127.6 (C-4), 128.3 (C-2,6), 128.4 (C-2′,6′), 128.5 (C-3′,5′), 129.5 (C-3,5), 132.6 (C-4′), 134.6 (C-γ), 136.7 (C-1), 138.4 (C-1′), 140.5 (C-δ), 150.2 (C-β), 190.8 (C=O). − EI-MS: *m/z* (%) = 248 (100) [$M^{+\bullet}$], 233 (70), 205 (16), 171 (47), 143 (46), 128 (50), 115 (25), 105 (47), 91 (15), 77 (56). − $C_{18}H_{16}O$ (248.3): calcd. C 87.06, H 6.49; found C 87.14, H 6.54.

(*E,E*)-2′-Hydroxycinnamylideneacetophenone (1c) and (*E,E*)-2′-Hydroxy-γ-methylcinnamylideneacetophenone (1d): These compounds were obtained as previously reported.[14,15]

(*E,E*)-4′-Methylcinnamylideneacetophenone (1e): Yield 55%. − M.p. 91−92 °C (recrystallisation from ethanol). − ^1H NMR: δ = 2.42 (s, 3 H, 4′-CH_3), 6.96−7.04 (m, 2 H, γ,δ-H), 7.10 (d, *J* = 14.9 Hz, 1 H, α-H), 7.25−7.40 (m, 3 H, 3,4,5-H), 7.28 (d, *J* = 8.1 Hz, 2 H, 3′,5′-H), 7.49 (dd, *J* = 7.9 and 1.2 Hz, 2 H, 2,6-H), 7.55−7.64 (m, 1 H, β-H), 7.89 (d, *J* = 8.1 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 21.6 (4′-CH_3), 125.4 (C-α), 127.0 (C-γ), 127.2 (C-3′,5′), 128.5 (C-2′,6′), 128.8 (C-2,6), 129.1 (C-4), 129.2 (C-3,5), 135.6 (C-1′), 136.1 (C-1), 141.6 (C-δ), 143.4 (C-4′), 144.4 (C-β), 189.9 (C=O). − EI-MS: *m/z* (%) = 248 (100) [$M^{+\bullet}$], 247 (47), 233 (18), 219 (15), 215 (15), 205 (30), 171 (51), 157 (20), 128 (65), 127 (28), 119 (78), 115 (15), 105 (21), 91 (60), 77 (16), 65 (20). − $C_{18}H_{16}O$ (248.3): calcd. C 87.06, H 6.49; found C 87.21, H 6.44.

(*E,E*)-4′-Methoxycinnamylideneacetophenone (1f): Yield 63%. − M.p. 77−78 °C (recrystallisation from ethanol). − ^1H NMR: δ = 3.88 (s, 3 H, 4′-OCH_3), 6.97 (d, *J* = 8.9 Hz, 2 H, 3′,5′-H), 6.98−7.05 (m, 2 H, γ,δ-H), 7.11 (d, *J* = 15.1 Hz, 1 H, α-H), 7.31−7.40 (m, 3 H, 3,4,5-H), 7.50 (dd, *J* = 8.0 and 1.3 Hz, 2 H, 2,6-H), 7.56−7.64 (m, 1 H, β-H), 8.00 (d, *J* = 8.9 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 55.5 (4′-OCH_3), 113.8 (C-3′,5′), 125.2 (C-α), 127.0 (C-γ), 127.2 (C-2,6), 128.8 (C-3,5), 129.1 (C-4), 130.7 (C-2′,6′), 131.1 (C-1′), 136.2 (C-1), 141.4 (C-δ), 144.0 (C-β), 163.3 (C-4′), 188.7 (C=O). − EI-MS: *m/z* (%) = 264 (100) [$M^{+\bullet}$], 263 (28), 235 (16), 205 (10), 187 (21), 135 (44), 128 (25), 92 (11), 77 (16). − $C_{18}H_{16}O_2$ (264.3): calcd. C 81.79, H 6.10; found C 81.94, H 6.07.

(*E,E*)-4′-Fluorocinnamylideneacetophenone (1g): Yield 70%. − M.p. 98−99 °C (recrystallisation from ethanol). − ^1H NMR: δ = 6.99−7.05 (m, 2 H, γ,δ-H), 7.06 (d, *J* = 14.9 Hz, 1 H, α-H), 7.15 (dd, *J* = 8.7 Hz and J_{HF} = 8.6 Hz, 2 H, 3′,5′-H), 7.32−7.40 (m, 3 H, 3,4,5-H), 7.49 (dd, *J* = 8.0 and 1.5 Hz, 2 H, 2,6-H), 7.56−7.65 (m, 1 H, β-H), 8.01 (dd, *J* = 8.7 Hz and J_{HF} = 5.5 Hz, 2 H, 2′,6′-

H). − ^{13}C NMR: δ = 115.6 (d, J_{CF} = 21.0 Hz, C-3′,5′), 124.8 (C-α), 126.7 (C-γ), 127.3 (C-2,6), 128.8 (C-3,5), 129.3 (C-4), 130.9 (d, J_{CF} = 9.0 Hz, C-2′,6′), 134.5 (d, J_{CF} = 3.0 Hz, C-1′), 136.0 (C-1), 142.2 (C-δ), 145.0 (C-β), 165.5 (d, J_{CF} = 252.1 Hz, C-4′), 188.7 (C=O). − EI-MS: *m/z* (%) = 252 (100) [$M^{+\bullet}$], 251 (46), 233 (15), 223 (13), 209 (10), 175 (41), 157 (16), 149 (13), 146 (16), 128 (56), 127 (27), 123 (63), 115 (12), 109 (17), 102 (10), 95 (39), 91 (22), 77 (13). − $C_{17}H_{13}FO$ (252.3): calcd. C 80.93, H 5.19; found C 80.78, H 5.21.

General Procedure for the Synthesis of 3-Benzoyl-4-styryl-2-pyrazolines (2a−d): A solution of the appropriate (*E,E*)-cinnamylideneacetophenone **1a−d** (2 mmol) in a 1:1 mixture of dichloromethane and diethyl ether (100 mL) was saturated with diazomethane[22] and allowed to stand at room temperature until the consumption of the starting material was completed. The solution was evaporated to dryness in each case and the residue recrystallised from ethanol yielding, after filtration, 3-benzoyl-4-styryl-2-pyrazolines **2a−d**. The preparative thin layer chromatographic analysis of each mother liquor, with dichloromethane as eluent, gave more **2a−d** and, in some cases, 3-(2-benzofuranyl)-4-styryl-2-pyrazolines **5c,d**.

3-Benzoyl-4-styryl-2-pyrazoline (2a): Yield 52%. − M.p. 125−126 °C (recrystallisation from ethanol). − ^{1}H NMR: δ = 3.69 (dd, *J* = 10.2 and 5.9 Hz, 1 H, H-5$_{trans}$), 3.86 (ddd, *J* = 10.8, 10.2 and 1.9 Hz, 1 H, H-5$_{cis}$), 4.27−4.35 (m, 1 H, 4-H), 6.32 (dd, *J* = 15.9 and 7.8 Hz, 1 H, α-H), 6.40 (s broad, 1 H, NH), 6.60 (d, *J* = 15.9 Hz, 1 H, β-H), 7.20 (t, *J* = 7.0 Hz, 1 H, 4′′-H), 7.28 (t, *J* = 7.0 Hz, 2 H, 3′′,5′′-H), 7.35 (d, *J* = 7.0 Hz, 2 H, 2′′,6′′-H), 7.43 (t, *J* = 7.4 Hz, 2 H, 3′,5′-H), 7.52 (t, *J* = 7.4 Hz, 1 H, 4′-H), 8.09 (d, *J* = 7.4 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 45.8 (C-4), 55.0 (C-5), 126.2 (C-α), 126.3 (C-2′′,6′′), 127.5 (C-4′′), 128.0 (C-3′,5′), 128.4 (C-3′′,5′′), 129.9 (C-2′,6′), 131.7 (C-β), 132.3 (C-4′), 136.8 (C-1′′), 137.4 (C-1′), 151.4 (C-3), 187.4 (C=O). − EI-MS: *m/z* (%) = 276 (25) [$M^{+\bullet}$], 275 (11), 197 (8), 185 (20), 171 (51), 144 (17), 129 (13), 115 (25), 105 (100), 77 (68), 51 (22). − $C_{18}H_{16}N_2O$ (276.3): calcd. C 78.24, H 5.84, N 10.14; found C 78.01, H 5.62, N 9.87.

3-Benzoyl-4-(α-methylstyryl)-2-pyrazoline (2b): Yield 48%. − Yellow oil. − ^{1}H NMR: δ = 1.92 (d, *J* = 3.0 Hz, 3 H, α-CH$_3$), 3.67 (dd, *J* = 11.2 and 6.2 Hz, 1 H, H-5$_{trans}$), 3.92 (ddd, *J* = 11.8, 11.2 and 2.0 Hz, 1 H, H-5$_{cis}$), 4.28 (dd, *J* = 11.8 and 6.2 Hz, 1 H, 4-H), 6.41 (s broad, 1 H, NH), 6.45 (s, 1 H, β-H), 7.16−7.32 (m, 5 H, 2′′,3′′,4′′,5′′,6′′-H), 7.44 (tt, *J* = 7.1 and 1.5 Hz, 2 H, 3′,5′-H), 7.53 (tt, *J* = 7.1 and 1.9 Hz, 1 H, 4′-H), 8.09 (d broad, *J* = 7.1 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 15.9 (α-CH$_3$), 52.4 (C-4), 54.8 (C-5), 126.3 (C-4′′), 127.0 (C-β), 128.0 (C-2′′,6′′ and C-3′,5′), 128.9 (C-3′′,5′′), 129.8 (C-2′,6′), 132.0 (C-4′), 136.1 (C-α), 137.5 and 137.6 (C-1′ and C-1′′), 151.2 (C-3), 187.6 (C=O). − EI-MS: *m/z* (%) = 290 (4) [$M^{+\bullet}$], 288 (10), 199 (7), 188 (12), 185 (44), 156 (6), 129 (12), 122 (43), 115 (9), 105 (100), 77 (54). − EI-HRMS ($C_{19}H_{18}N_2O$ [$M^{+\bullet}$]): calcd. 290.1419; found 290.1405.

3-(2-Hydroxybenzoyl)-4-styryl-2-pyrazoline (2c): Yield 58%. − M.p. 152−153 °C (recrystallisation from ethanol). − ^{1}H NMR: δ = 3.69 (dd, *J* = 9.9 and 6.1 Hz, 1 H, H-5$_{trans}$), 3.89 (ddd, *J* = 11.9, 9.9 and 2.1 Hz, 1 H, H-5$_{cis}$), 4.31−4.39 (m, 1 H, 4-H), 6.28 (dd, *J* = 15.9 and 8.1 Hz, 1 H, α-H), 6.51 (s broad, 1 H, NH), 6.59 (d, *J* = 15.9 Hz, 1 H, β-H), 6.89 (ddd, *J* = 8.0, 7.6 and 1.0 Hz, 1 H, 5′-H), 6.97 (dd, *J* = 8.1 and 1.0 Hz, 1 H, 3′-H), 7.21−7.37 (m, 5 H, 2′′,3′′,4′′,5′′,6′′-H), 7.44 (ddd, *J* = 8.1, 7.6 and 1.5 Hz, 1 H, 4′-H), 8.63 (dd, *J* = 8.0 and 1.5 Hz, 1 H, 6′-H), 12.29 (s, 1 H, OH-2′). − ^{13}C NMR: δ = 46.1 (C-4), 54.8 (C-5), 118.0 (C-3′), 118.6 (C-5′), 119.3 (C-1′), 126.1 (C-α), 126.3 (C-2′′,6′′), 127.6 (C-4′′), 128.5 (C-3′′,5′′), 131.9 (C-β), 132.9 (C-6′), 135.7 (C-4′), 136.6 (C-1′′), 151.0 (C-3), 163.0 (C-2′), 190.1 (C=O). − EI-MS: *m/z* (%) = 292 (52) [$M^{+\bullet}$], 248 (11), 201 (16), 197 (17), 171 (28), 162 (18), 144 (30), 130 (36), 121 (100), 115 (28), 104 (10), 93 (27), 77 (13), 65 (35). − $C_{18}H_{16}N_2O_2{\cdot}CH_2Cl_2$ (377.3): calcd. C 60.49, H 4.81, N 7.43; found C 60.44, H 4.90, N 7.59.

3-(2-Hydroxybenzoyl)-4-(α-methylstyryl)-2-pyrazoline (2d): Yield 48%. − M.p. 145−147 °C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.90 (s, 3 H, α-CH$_3$), 3.67 (dd, *J* = 10.4 and 6.4 Hz, 1 H, H-5$_{trans}$), 3.93 (dd, *J* = 12.3 and 10.4 Hz, 1 H, H-5$_{cis}$), 4.32 (dd, *J*= 12.3 and 6.4 Hz, 1 H, 4-H), 6.42 (s broad, 1 H, β-H), 6.69 (s broad, 1 H, NH), 6.89 (ddd, *J* = 7.9, 7.6 and 1.1 Hz, 1 H, 5′-H), 6.97 (dd, *J* = 8.0 and 1.1 Hz, 1 H, 3′-H), 7.16−7.33 (m, 5 H, 2′′,3′′,4′′,5′′,6′′-H), 7.45 (ddd, *J* = 8.0, 7.6 and 1.7 Hz, 1 H, 4′-H), 8.62 (dd, *J* = 7.9 and 1.7 Hz, 1 H, 6′-H), 12.32 (s, 1 H, OH-2′). − ^{13}C NMR: δ = 15.8 (α-CH$_3$), 52.7 (C-4), 54.5 (C-5), 118.0 (C-3′), 118.6 (C-5′), 119.3 (C-1′), 126.4 (C-4′′), 127.2 (C-β), 128.1 (C-2′′,6′′), 128.8 (C-3′′,5′′), 132.9 (C-6′), 135.7 (C-4′), 135.9 (C-α), 137.4 (C-1′′), 150.6 (C-3), 162.9 (C-2′), 190.3 (C=O). − EI-MS: *m/z* (%) = 306 (17) [$M^{+\bullet}$], 288 (10), 215 (17), 185 (67), 175 (26), 158 (36), 155 (28), 144 (33), 129 (35), 121 (100), 115 (27), 95 (31), 93 (28), 77 (11), 65 (33). − $C_{19}H_{18}N_2O_2$ (306.4): calcd. C 74.49, H 5.92, N 9.14; found C 74.54, H 5.90, N 8.69.

3-(2-Benzofuranyl)-4-styryl-2-pyrazoline (5c): Yield 2%. − Yellow oil. − ^{1}H NMR: δ = 3.74 (dd, *J* = 10.7 and 6.3 Hz, 1 H, H-5$_{trans}$), 3.94 (dd, *J* = 11.4 and 10.7 Hz, 1 H, H-5$_{cis}$), 4.11−4.20 (m, 1 H, 4-H), 6.21 (dd, *J* = 16.0 and 7.7 Hz, 1 H, α-H), 6.52 (d, *J* = 16.0 Hz, 1 H, β-H), 6.76−6.88 (m, 5 H, NH and 4′,5′,6′,7′-H), 7.02 (s, 1 H, H-3′), 7.18−7.34 (m, 5 H, 2′′,3′′,4′′,5′′,6′′-H). − ^{13}C NMR: δ = 44.2 (C-4), 55.5 (C-5), 103.4 (C-3′), 108.6 (C-5′,7′), 121.8 (C-4′,6′), 125.4 (C-α), 126.4 (C-2′′,6′′), 127.7 (C-4′′), 128.5 (C-3′′,5′′), 132.1 (C-β), 136.5 (C-1′′), 147.0 and 147.1 (C-8′ and C-9′), 147.8 (C-3), 183.6 (C-2′). − EI-MS: *m/z* (%) = 288 (1) [$M^{+\bullet}$], 279 (4), 199 (6), 167 (5), 149 (7), 121 (100), 115 (5), 77 (3), 65 (7). − EI-HRMS ($C_{19}H_{16}N_2O$ [$M^{+\bullet}$]): calcd. 288.1263; found 288.1276.

3-(2-Benzofuranyl)-4-(α-methylstyryl)-2-pyrazoline (5d): Yield 10%. − Yellow oil. − ^{1}H NMR: δ = 1.83 (s, 1 H, α-CH$_3$), 3.73 (dd, *J* = 10.6 and 6.2 Hz, 1 H, H-5$_{trans}$), 3.99 (dd, *J* = 12.5 and 10.6 Hz, 1 H, H-5$_{cis}$), 4.12 (dd, *J* = 12.5 and 6.2 Hz, 1 H, 4-H), 6.38 (s, 1 H, β-H), 6.77 (s broad, 1 H, NH), 6.80−6.88 (m, 4 H, 4′,5′,6′,7′-H), 7.06 (s, 1 H, 3′-H), 7.16−7.32 (m, 5 H, 2′′,3′′,4′′,5′′,6′′-H). − ^{13}C NMR: δ = 15.5 (α-CH$_3$), 50.9 (C-4), 55.3 (C-5), 103.5 (C-3′), 108.6 and 108.7 (C-5′ and C-7′), 121.8 (C-4′,6′), 135.1 (C-α), 128.9 (C-2′′,6′′), 126.5 (C-4′′), 128.0 (C-3′′,5′′), 127.6 (C-β), 137.4 (C-1′′), 147.1 and 147.2 (C-8′ and C-9′), 147.7 (C-3), 183.6 (C-2′). − EI-MS: *m/z* (%) = 302 (7) [$M^{+\bullet}$], 300 (12), 295 (8), 213 (7), 122 (9), 121 (100), 95 (5), 91 (3), 65 (5). − EI-HRMS ($C_{20}H_{18}N_2O$ [$M^{+\bullet}$]): calcd. 302.1419, found 302.1429.

Synthesis of 3-Benzoyl-4-styryl-2-pyrazolines 2e−g: A solution of the appropriate (*E,E*)-cinnamylideneacetophenone **2e−g** (5 mmol) in dichloromethane (50 mL) was saturated with diazomethane[22] and allowed to stand in a refrigerator for 48 h. Then the solvent was evaporated under reduced pressure and the residue recrystallised from methanol, giving 3-benzoyl-4-styryl-2-pyrazolines **2e−g**.

3-(4-Methylbenzoyl)-4-styryl-2-pyrazoline (2e): Yield 52%. − M.p. 126−127 °C (recrystallisation from methanol). − ^{1}H NMR: δ = 2.39 (s, 3 H, 4′-CH$_3$), 3.65 (dd, *J* = 10.2 and 5.9 Hz, 1 H, H-5$_{trans}$), 3.82 (dd, *J* = 10.6 and 10.2 Hz, 1 H, H-5$_{cis}$), 4.25−4.33 (m, 1 H, 4-H), 6.31 (dd, *J* = 15.9 and 7.8 Hz, 1 H, α-H), 6.39 (s broad, 1 H, NH), 6.58 (d, *J* = 15.9 Hz, 1 H, β-H), 7.17−7.29 (m, 3 H,

3′′,4′′,5′′-H), 7.23 (d, J = 8.3 Hz, 2 H, 3′,5′-H), 7.35 (d, J = 7.8 Hz, 2 H, 2′′,6′′-H), 8.02 (d, J = 8.3 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 21.6 (4′-CH_3), 45.9 (C-4), 54.9 (C-5), 126.3 (C-α and C-2′′,6′′), 127.4 (C-4′′), 128.4 (C-3′,5′), 128.7 (C-3′′,5′′), 130.0 (C-2′,6′), 131.6 (C-β), 134.7 (C-1′), 136.8 (C-1′′), 143.0 (C-4′), 151.6 (C-3), 187.1 (C=O). − EI-MS: m/z (%) = 290 (25) [$M^{+\bullet}$], 291 (11), 199 (18), 171 (48), 144 (14), 130 (10), 119 (100), 115 (17), 104 (20), 91 (56), 83 (20), 65 (22). − $C_{19}H_{18}N_2O$ (290.4): calcd. C 78.59, H 6.25, N 9.65; found C 78.51, H 6.28, N 9.67.

3-(4-Methoxylbenzoyl)-4-styryl-2-pyrazoline (2f): Yield 40%. − M.p. 137−138 °C (recrystallisation from methanol). − ^{1}H NMR: δ = 3.64 (dd, J = 9.5 and 5.9 Hz, 1 H, H-5$_{trans}$), 3.81 (dd, J = 10.6 and 9.5 Hz, 1 H, H-5$_{cis}$), 3.84 (s, 3 H, 4′-OCH_3), 4.26−4.34 (m, 1 H, 4-H), 6.31 (dd, J = 15.9 and 7.8 Hz, 1 H, α-H), 6.35 (s broad, 1 H, NH), 6.58 (d, J = 15.9 Hz, 1 H, β-H), 6.92 (d, J = 8.7 Hz, 2 H, 3′,5′-H), 7.19 (t, J = 7.1 Hz, 1 H, 4′′-H), 7.27 (t, J = 7.1 Hz, 2 H, 3′′,5′′-H), 7.34 (d, J = 7.1 Hz, 2 H, 2′′,6′′-H), 8.18 (d, J = 8.7 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 46.2 (C-4), 54.8 (C-5), 55.4 (4′-OCH_3), 113.3 (C-3′,5′), 126.3 (C-α and C-2′′,6′′), 127.5 (C-4′′), 128.4 (C-3′′,5′′), 131.6 (C-1′and C-β), 132.3 (C-2′,6′), 136.8 (C-1′′), 151.9 (C-3), 163.1 (C-4′), 185.8 (C=O). − EI-MS: m/z (%) = 306 (43) [$M^{+\bullet}$], 305 (18), 304 (12), 215 (16), 197 (23), 171 (34), 135 (100), 115 (14), 109 (12), 92 (19), 77 (24). − $C_{19}H_{18}N_2O_2$ (306.4): calcd. C 74.49, H 5.92, N 9.14; found C 74.42, H 5.89, N 9.18.

3-(4-Fluorobenzoyl)-4-styryl-2-pyrazoline (2g): Yield 51%. − M.p. 128−129 °C (recrystallisation from methanol). − ^{1}H NMR: δ = 3.67 (dd, J = 10.3 and 5.8 Hz, 1 H, H-5$_{trans}$), 3.84 (dd, J = 10.7 and 10.3 Hz, 1 H, H-5$_{cis}$), 4.25−4.33 (m, 1 H, 4-H), 6.30 (dd, J = 15.9 and 7.8 Hz, 1 H, α-H), 6.45 (s broad, 1 H, NH), 6.58 (d, 1H, J = 15.9 Hz, β-H), 7.09 (dd, J = 8.8 Hz and J_{HF} = 7.0 Hz, 2 H, 3′,5′-H), 7.17−7.22 (m, 1 H, 4′′-H), 7.27 (t, 2 H, J = 7.2 Hz, 3′′,5′′-H), 7.35 (d, J = 7.2 Hz, 2 H, 2′′,6′′-H), 8.18 (dd, J = 8.8 Hz and J_{HF} = 5.6 Hz, 2 H, 2′,6′-H). − ^{13}C NMR: δ = 45.9 (C-4), 55.0 (C-5), 115.1. (d, J_{CF} = 21.9 Hz, C-3′,5′), 126.1 (C-α), 126.3 (C-2′′,6′′), 127.6 (C-4′′), 128.5 (C-3′′,5′′), 131.7 (C-β), 132.6 (d, J_{CF} = 9.8 Hz, C-2′,6′), 133.6 (d, J_{CF} = 2.3 Hz, C-1′), 136.7 (C-1′′), 151.3 (C-3), 165.3 (d, J_{CF} = 253.6 Hz, C-4′), 185.6 (C=O). − EI-MS: m/z (%) = 294 (20) [$M^{+\bullet}$], 293 (11), 292 (21), 203 (15), 171 (39), 144 (10), 129 (10), 123 (100), 115 (23), 104 (21), 95 (58), 83 (26), 75 (11). − $C_{18}H_{15}FN_2O$ (294.3): calcd. C 73.45, H 5.14, N 9.52; found C 73.49, H 5.11, N 9.57.

General Procedure for the Synthesis of 3(5)-Benzoyl-4-styrylpyrazoles (3a−g): To a solution of the appropriate 3-benzoyl-4-styryl-2-pyrazoline **2a−g** (1 mmol) in toluene (50 mL) was added chloranil (3.0 mmol, 738 mg). The mixture was heated at reflux under nitrogen until the consumption of the starting material was completed. The solution was then evaporated to dryness and, in each case, the residue was purified by column chromatography. With dichloromethane as eluent the excess of chloranil was removed, whereas with acetone as eluent the expected 3(5)-benzoyl-4-styrylpyrazoles **3a−g** were collected. These compounds were, in each case, recrystallised from cyclohexane.

3(5)-Benzoyl-4-styrylpyrazole (3a): Yield 78%. − M.p. 186−187 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = 7.13 (d, J = 16.6 Hz, 1 H, β-H), 7.26 (t, J = 7.6 Hz, 1 H, 4′′-H), 7.38 (t, J = 7.6 Hz, 2 H, 3′′,5′′-H), 7.50 (d, J = 7.6 Hz, 2 H, 2′′,6′′-H), 7.54 (t, J = 7.6 Hz, 2 H, 3′,5′-H), 7.60 (d, J = 16.6 Hz, 1 H, α-H), 7.65 (t, J = 7.6 Hz, 1 H, 4′-H), 8.09 (d, J = 7.6 Hz, 2 H, 2′,6′-H), 8.41 (s, 1 H, 5-H), 13.68 (s broad, 1 H, NH). − ^{13}C NMR: δ = 119.2 (C-α), 122.4 (C-4), 126.0 (C-2′′,6′′), 127.5 (C-5,4′′), 128.1 (C-3′,5′), 128.8 (C-3′′,5′′), 129.1 (C-β), 130.2 (C-2′,6′), 132.5 (C-4′), 137.3 (C-1′), 138.0 (C-1′′), 145.9 (C-3), 189.4 (C=O). − ^{13}C CPMAS NMR: δ = 119.5 (C-α), 123.5 (C-4), 127.0 (C-2′′,6′′, C-3′,5′, C-4′′, C-5), 129.0 (C-β, C-3′′,5′′), 130.8 (C-2′,6′, C-4′), 137.8 (C-1′, C-1′′), 144.4 (C-3), 191.9 (C=O). − EI-MS m/z (%) = 274 (100) [$M^{+\bullet}$], 273 (32), 257 (7), 245 (14), 218 (6), 197 (27), 183 (8), 169 (23), 140 (9), 115 (24), 105 (34), 91 (7), 77 (48), 51 (14). − $C_{18}H_{14}N_2O$ (274.3): calcd. C 78.81, H 5.14, N 10.21; found C 78.83, H 5.17, N 9.89.

3(5)-Benzoyl-4-(α-methylstyryl)pyrazole (3b): Yield 71%. − Yellow oil. − ^{1}H NMR: δ = 2.10 (d, J = 1.2 Hz, 3 H, α-CH_3), 6.59 (s broad, 1 H, β-H), 7.19−7.27 (m, 3 H, 2′′,4′′,6′′-H), 7.35 (t, J = 7.5 Hz, 2 H, 3′′,5′′-H), 7.52 (dd, J = 8.1 and 7.3 Hz, 2 H, 3′,5′-H), 7.63 (dt, J = 7.3 and 1.5 Hz, 1 H, 4′-H), 7.96 (dd, J = 8.1 and 1.5 Hz, 2 H, 2′,6′-H), 8.07 (d, J = 1.3 Hz, 1 H, 5-H), 13.51 (s broad, 1H, NH). − ^{13}C NMR: δ = 18.9 (α-CH_3), 126.4 (C-4′′), 127.5 (C-4,α), 128.2 (C-3′,3′′,5′,5′′), 128.6 (C-5), 128.8 (C-2′′,6′′), 129.3 (C-β), 130.0 (C-2′,6′), 132.8 (C-4′), 137.5 (C-1′), 137.8 (C-1′′), 146.2 (C-3), 190.0 (C=O). − EI-MS m/z (%) = 288 (100) [$M^{+\bullet}$], 287 (18), 273 (42), 259 (8), 245 (6), 211 (33), 197 (23), 183 (38), 168 (12), 154 (7), 140 (7), 128 (14), 115 (18), 105 (38), 91 (12), 77 (50), 51 (14). − EI-HRMS ($C_{19}H_{16}N_2O$ [$M^{+\bullet}$]): calcd. 288.1263; found 288.1266.

3(5)-(2-Hydroxybenzoyl)-4-styrylpyrazole (3c): Yield 86%. − M.p. 183−184 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = 6.92−7.00 (m, 2 H, 3′,5′-H), 7.12 (d, J = 16.5 Hz, 1 H, β-H), 7.37 (dd, J = 7.4 and 7.7 Hz, 2 H, 3′′,5′′-H), 7.47−7.52 (m, 3 H, 2′′, 4′′,6′′-H), 7.25 (dd, J = 7.3 and 7.0 Hz, 1 H, 4′-H), 7.53 (d, J = 16.5 Hz, 1 H, α-H), 8.17 (d, J = 7.8 Hz, 1 H, 6′-H), 8.41 (s, 1 H, 5-H), 11.51 (s broad, 1 H, 2′-OH), 13.72 (s broad, 1 H, NH). − ^{13}C NMR: δ = 117.2 (C-3′), 118.7 (C-5′), 119.0 (C-α), 122.3 (C-4), 122.4 (C-1′), 126.0 (C-2′′,6′′), 127.45 (C-4′′), 127.50 (C-5), 128.8 (C-3′′,5′′), 129.2 (C-β), 132.7 (C-6′), 134.8 (C-4′), 137.3 (C-1′′), 146.1 (C-3), 160.3 (C-2′), 192.8 (C=O). − ^{13}C CPMAS NMR: δ = 116.6 (C-3′), 118.4 (C-5′), 119.6 (C-α), 122.3 (C-1′, C-4), 125.4 (C-2′′,6′′, C-4′′, C-5), 128.2 (C-β, C-3′′,5′′), 134.1 (C-6′), 136.4 (C-1′′, C-4′), 145.4 (C-3), 160.7 (C-2′), 193.6 (C=O). − EI-MS m/z (%) = 290 (100) [$M^{+\bullet}$], 289 (21), 273 (19), 261 (15), 245 (8), 213 (20), 199 (34), 185 (10), 170 (34), 140 (10), 121 (37), 115 (29), 93 (14), 77 (10), 65 (38). − $C_{18}H_{14}N_2O_2$ (290.3): calcd. C 74.47, H 4.86, N 9.65; found C 74.17, H 4.87, N 10.02.

3(5)-(2-Hydroxybenzoyl)-4-(α-methylstyryl)pyrazole (3d): Yield 95%. − M.p. 124−125 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = δ 2.10 (d, J = 1.1 Hz, 3 H, α-CH_3), 6.57 (s broad, 1 H, β-H), 6.94 (dd, J = 8.0 and 7.5 Hz, 1 H, 5′-H), 6.98 (d, J = 8.5 Hz, 1 H, 3′-H), 7.18−7.27 (m, 5 H, 3′′,4′′,5′′-H), 7.34 (d, J = 7.4 Hz, 2 H, 2′′,6′′-H), 7.52 (ddd, J = 8.0, 7.5 and 1.5 Hz, 1 H, 4′-H), 7.89 (dd, J = 8.0 and 1.5 Hz, 1 H, 6′-H), 8.08 (s, 1 H, 5-H), 11.52 (s broad, 1 H, OH-2′), 13.55 (s broad, 1 H, NH). − ^{13}C NMR: δ = 18.9 (α-CH_3), 117.3 (C-3′), 118.8 (C-5′), 121.8 (C-1′), 126.4 (C-4′′), 127.2 (C-α), 127.5 (C-5), 128.2 (C-3′′,5′′), 128.6 (C-4), 128.7 (C-2′′,6′′), 129.0 (C-β), 133.1 (C-6′), 135.5 (C-4′), 137.4 (C-1′′), 146.0 (C-3), 160.8 (C-2′), 194.3 (C=O). − EI-MS m/z (%) = 304 (55) [$M^{+\bullet}$], 286 (33), 227 (15), 213 (36), 197 (14), 183 (27), 169 (16), 155 (22), 153 (20), 141 (20), 127 (28), 121 (36), 113 (33), 105 (10), 99 (36), 91 (13), 85 (59), 71 (79), 57 (100). − EI-HRMS ($C_{19}H_{16}N_2O_2$ [$M^{+\bullet}$]): calcd. 304.1212, found 304.1213.

3(5)-(4-Methylbenzoyl)-4-styrylpyrazole (3e): Yield 71%. − M.p. 155−156 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = 2.38 (s, 3 H, 4′-CH_3), 7.13 (d, J = 15.8 Hz, 1 H, β-H), 7.24 (t, J = 6.6 Hz, 1 H, 4′′-H), 7.33 (d, J = 6.6 Hz, 2 H, 3′,5′-H), 7.36 (dd,

J = 7.5 and 6.6 Hz, 2 H, 3′′,5′′-H), 7.48 (d, J = 7.5 Hz, 2 H, 2′′,6′′-H), 7.59 (d, J = 15.8 Hz, 1 H, α-H), 8.03 (d, J = 6.6 Hz, 2 H, 2′,6′-H), 8.38 (s, 1 H, 5-H), 13.68 (s broad, 1 H, NH). − ^{13}C NMR: δ = 21.2 (4′-CH_3), 119.2 (C-α), 122.3 (C-4), 126.0 (C-2′′,6′′), 127.4 (C-4′′,5), 128.78 and 128.81 (C-3′,5′ and C-3′′,5′′), 129.0 (C-β), 130.4 (C-2′,6′), 135.3 (C-1′), 137.4 (C-1′′), 143.0 (C-4′), 146.1 (C-3), 188.8 (C=O). − EI-MS m/z (%) = 288 (100) [$M^{+\bullet}$], 287 (25), 273 (34), 259 (12), 211 (24), 197 (12), 169 (15), 140 (10), 119 (44), 115 (28), 91 (54), 65 (24). − $C_{19}H_{16}N_2O$ (288.3): calcd. C 79.14, H 5.59, N 9.72; found C 78.84, H 5.65, N 9.40.

3(5)-(4-Methoxybenzoyl)-4-styrylpyrazole (3f): Yield 78%. − M.p. 162−164 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = 3.85 (s, 3 H, 4′-OCH_3), 7.07 (d, J = 8.8 Hz, 2 H, 3′,5′-H), 7.10 (d, J = 16.6 Hz, 1 H, β-H), 7.24 (t, J = 7.3 Hz, 1 H, 4′′-H), 7.37 (dd, J = 7.6 and 7.3 Hz, 2 H, 3′′,5′′-H), 7.48 (d, J = 7.6 Hz, 2 H, 2′′,6′′-H), 7.57 (d, J = 16.6 Hz, 1 H, α-H), 8.18 (d, J = 8.8 Hz, 2 H, 2′,6′-H), 8.39 (s, 1 H, 5-H), 13.62 (s broad, 1 H, NH). − ^{13}C NMR: δ = 55.5 (4′-OCH_3), 113.5 (C-3′,5′), 119.4 (C-α), 122.1 (C-4), 126.0 (C-2′′,6′′), 127.3 (C-5), 127.4 (C-4′′), 128.7 (C-β), 128.8 (C-3′′,5′′), 130.4 (C-1′), 132.7 (C-2′,6′), 137.4 (C-1′′), 146.3 (C-3), 162.9 (C-4′), 187.6 (C=O). − EI-MS m/z (%) = 304 (100) [$M^{+\bullet}$], 303 (26), 273 (19), 227 (21), 140 (12), 135 (59), 115 (35), 107 (12), 92 (35), 77 (39), 64 (16). − $C_{19}H_{16}N_2O_2$ (304.3): calcd. C 74.98, H 5.30, N 9.20; found C 74.72, H 5.33, N 8.90.

3(5)-(4-Fluorobenzoyl)-4-styrylpyrazole (3g): Yield 67%. − M.p. 213−214 °C (recrystallisation from cyclohexane). − ^{1}H NMR: δ = 7.13 (d, J = 16.5 Hz, 1 H, β-H), 7.25 (t, J = 7.2 Hz, 1 H, 4′′-H), 7.35−7.40 (m, 4 H, 3′,3′′,5′,5′′-H), 7.49 (d, J = 7.5 Hz, 2 H, 2′′,6′′-H), 7.60 (d, J = 16.5 Hz, 1 H, α-H), 8.19−8.23 (m, 2 H, 2′,6′-H), 8.41 (s, 1 H, 5-H), 13.72 (s broad, 1 H, NH). − ^{13}C NMR: δ = 115.2 (d, J_{CF} = 21.9 Hz, C-3′,5′), 119.1 (C-α), 122.5 (C-4), 126.0 (C-2′′,6′′), 127.5 (C-4′′,5), 128.8 (C-3′′,5′′), 129.2 (C-β), 133.1 (d, J_{CF} = 9.1 Hz, C-2′,6′,), 134.4 (d, J_{CF} = 2.3 Hz, C-1′), 137.3 (C-1′′), 145.7 (C-3), 164.7 (d, J_{CF} = 251.2 Hz, C-4′), 187.6 (C=O). − EI-MS m/z (%) = 292 (100) [$M^{+\bullet}$], 291 (31), 263 (13), 215 (26), 169 (23), 140 (10), 123 (50), 115 (30), 95 (55), 75 (19). − $C_{18}H_{14}FN_2O$ (292.3): calcd. C 73.96, H 4.48, N 9.58; found C 73.96, H 4.37, N 9.26.

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