Synthesis of 3-Aryl-5-styryl-2-pyrazolines by the Reaction of (*E,E*)-Cinnamylideneacetophenones with Hydrazines and their Oxidation into Pyrazoles

Albert Lévai* and Tamás Patonay

Department of Organic Chemistry, University of Debrecen, P.O.Box 20, H-4010 Debrecen, Hungary

Artur M. S. Silva, Diana C. G. A. Pinto and José A. S. Cavaleiro

Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal

Received December 14, 2001

Dedicated to Professor Dr. András Messmer on the occasion of his 80th birthday.

New 3-aryl-5-styryl-2-pyrazolines have been synthesized by the reaction of (*E,E*)-cinnamylideneacetophenones with hydrazines. These 2-pyrazolines have also been converted into the corresponding pyrazoles by oxidation with chloranil. Structures of all new compounds have been elucidated by elemental analysis, mass spectrometry, ir and nmr spectroscopic measurements.

J. Heterocyclic Chem., **39**, 751 (2002).

Introduction.

Pyrazoles and pyrazolines are important nitrogen-containing five-membered heterocyclic compounds and various methods have been developed for their syntheses [1-3]. As a result, a wide variety of pyrazoles and pyrazolines have hitherto been reported in the literature [1-4].

The first example for a pyrazoline formation in the reaction of an α,β-enone with a hydrazine derivative was published by Fischer and Knövenagel in the late nineteenth century. In their experiment, acrolein and phenylhydrazine were allowed to react and 1-phenyl-2-pyrazoline was obtained [5]. After this pioneering study, the reaction of α,β-unsaturated aldehydes and ketones with hydrazines became one of the most popular procedures for the synthesis of 2-pyrazolines [6-17]. Synthesis of tricyclic 2-pyrazolines by reaction of the exocyclic α,β-unsaturated ketones and hydrazines has also been achieved in several laboratories [18-31]. Special representatives of the 2-pyrazolines are their styryl derivatives prepared from different starting materials. 3-Styryl-2-pyrazolines were synthesized by the reaction of diarylideneacetones with hydrazines [32-34]. Such 2-pyrazolines have also been obtained as by-products on the reaction of 2-styrylchromones with hydrazine hydrate [35]. However, very few representatives of 5-styryl-2-pyrazolines have hitherto been described in the literature. Reaction of cinnamylideneacetophenones with phenylhydrazine afforded 3-aryl-1-phenyl-5-styryl-2-pyrazolines [36-38]. As another example, Huisgen *et al*. [39] synthesized 1,3-diphenyl-5-styryl-2-pyrazoline by the cycloaddition of *trans*-1-phenyl-1,3-butadiene with (α-chlorobenzylidene)phenylhydrazine in the presence of triethylamine.

Pyrazoles can be prepared by several procedures [1-3] including the oxidation of pyrazolines by using various oxidizing agents, *viz.* mercuric oxide, lead dioxide, chromium oxide, manganese dioxide, potassium permanganate, silver nitrate, lead tetraacetate, bromine, *N*-bromosuccinimide, potassium hexacyanoferrate(III) and chloranil [40,41].

Since 2-pyrazolines and pyrazoles bearing an unsaturated side-chain have hitherto received less attention, although they may have an important role in drug research, it appeared expedient to find simple and convenient procedures for their preparation. Herein we report the synthesis of 3-aryl-5-styryl-2-pyrazolines and their oxidation into the corresponding pyrazoles.

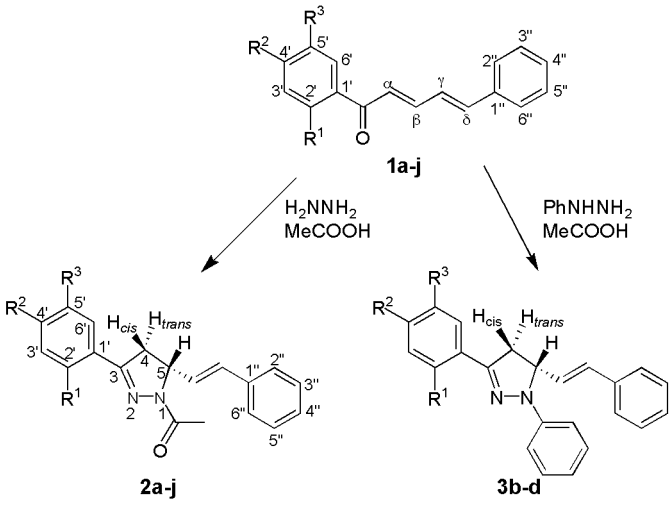
Results and Discussion.

Synthesis.

Previously we have worked out a convenient procedure for the synthesis of 3-benzoyl-4-styryl-2-pyrazolines by the 1,3-dipolar cycloaddition of (*E,E*)-cinnamylideneacetophenones with diazomethane [42]. As a continuation, synthesis of 3-aryl-5-styryl-2-pyrazolines has been scheduled by the reaction of these α,β,γ,δ-unsaturated ketones with hydrazines.

In one series of our experiments, (*E,E*)-cinnamylideneacetophenones **1a-j** were allowed to react with hydrazine hydrate in hot acetic acid to provide 1-acetyl-3-aryl-5-styryl-2-pyrazolines **2a-j** as sole isolable products (Scheme 1). No other pyrazoline type compound could be detected in the crude reaction products. It was found that the initially formed pyrazoline was completely *N*-acetylated under these reaction conditions in each case. *N*-Acetyl-3-aryl-2-pyrazolines **2a-j** proved to be stable substances that can be stored and utilized for further chemical transformations.

In our present study, (*E,E*)-cinnamylideneacetophenones **1b-d** have also reacted with phenylhydrazine in boiling acetic acid to afford 3-aryl-1-phenyl-5-styryl-2-pyrazolines **3b-d** (Scheme 1). Our results prove that this simple procedure can be advantageously utilized for the synthesis of 3-aryl-5-styryl-2-pyrazolines.



a: R^1=R^2=R^3=H; b: R^1=R^3=H, R^2=Me; c: R^1=R^3=H, R^2=OMe; d: R^1=R^3=H, R^2=F; e: R^1=R^3=H, R^2=Cl; f: R^1=R^3=H, R^2=Br; g: R^1=OH, R^2=R^3=H; h: R^1=OH, R^2=Me, R^3=H; i: R^1=OH, R^2=H, R^3=F; j: R^1=OH, R^2=H, R^3=Cl

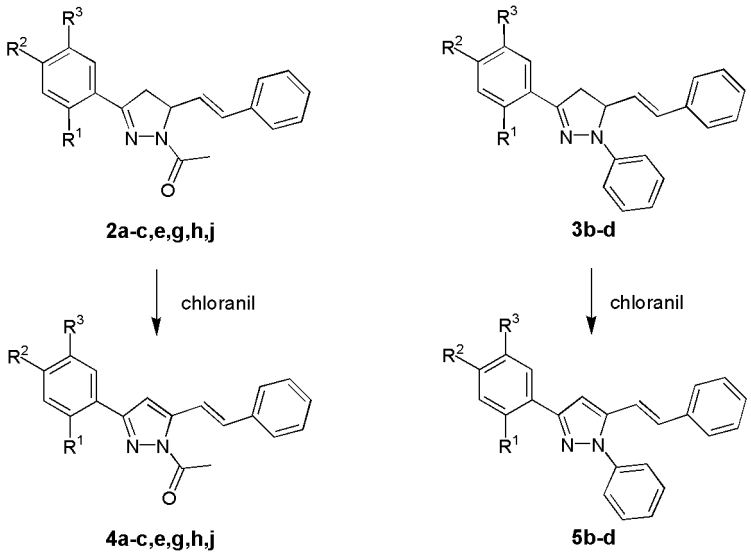
The oxidation of pyrazolines is a versatile procedure for the preparation of pyrazoles. In our previous study, chloranil was found to be the oxidant of choice for the conversion of 3-benzoyl-4-styryl-2-pyrazolines into the corresponding pyrazoles [42]. For this reason, 3-aryl-5-styryl-2-pyrazolines **2a-c,e,g,h,j** and **3b-d** were allowed to react with chloranil in hot toluene until the complete consumption of the starting material, as monitored by thin-layer chromatography. After removal of the solvent, the residue was subjected to column chromatography to obtain 3-aryl-5-styrylpyrazoles **4a-c,e,g,h,j** and **5b-d** in good (65-89%) yields (Scheme 2). On the basis of our previous [42] and present results, it can be concluded that the chloranil is equally a good oxidant for the conversion of both 4-styryl-2-pyrazolines and 5-styryl-2-pyrazolines into the corresponding pyrazoles. Structures of all new pyrazolines and pyrazoles synthesized in the course of our present study have been elucidated by elemental analyses, mass spectrometry, ir and nmr spectroscopic measurements.

Nuclear Magnetic Resonance Spectroscopy.

A detailed analysis of the aliphatic region in the ^{1}H and ^{13}C nmr spectra of compounds **2a-j**, with the aid of the COSY and HSQC spectra, revealed the presence of a methylene group (δ_H 3.08-3.23 and 3.49-3.63 ppm; δ_C 39.2-39.7 ppm) and a methine group (δ_H 5.20-5.29 ppm; δ_C 56.3-58.1 ppm). These data and the connectivities of these protons, found in the HMBC spectra (Table 1), with the carbon resonances at δ 146.6-156.6 ppm (C-3) supported the presence of a 2-pyrazoline ring. The presence of an acetyl group in the structure of **2a-j** was indicated by the resonances of a methyl group (δ_H 2.35-2.42 ppm; δ_C 22.0-22.1 ppm) and a carbonyl group (δ_C 167.8-169.0 ppm) and by the connectivity between them found in the corresponding HMBC spectra.

Another important feature in the ^{1}H nmr spectra of 1-acetyl-2-pyrazolines **2a-j** is the resonances of their vinylic protons ($\delta_{H\text{-}\alpha}$ 6.17-6.20 ppm; $\delta_{H\text{-}\beta}$ 6.58-6.64 ppm). The coupling constants $^3J_{H\alpha\text{-}H\beta}$ = 15.8-15.9 Hz indicate *trans* configurations for such double bonds. The NOESY spectra of compounds **2a-j** revealed intense NOE cross peaks between the resonances of H-α and H-β with those of H-4_{trans}, H-5 and H-2",6" (Table 2), suggesting in each case a free rotation around the C5-Cα bond. The assignments of H-4_{trans}, H-4_{cis}, and H-5 and their relative stereochemistry was mainly based in the data obtained from the NOESY spectra of **2a-j** (Table 2).

The assignments of the quaternary carbons of 1-acetyl-3-aryl-5-styryl-2-pyrazolines **2a-j** were based on the con-



nectivities found in their HMBC spectra (Table 1). In the case of compounds **2g-j** the connectivities of the most deshielded proton (2'-OH, δ 10.03-10.25 ppm), due to the intramolecular hydrogen bond with the *N*-2 of the 2-pyrazoline ring, allowed the assignment of C-1', C-2' and C-3'.

The ^{1}H and ^{13}C nmr spectra of compounds **3b-d** are very similar to those of 2-pyrazolines **2a-j**. The main differences are the absence of the proton and carbon resonances of the acetyl group and the presence of those of an *N*-phenyl ring. The comparison of the 2-pyrazoline ring carbon resonances of 1-acetyl-2-pyrazolines **2a-j** with those of 1-phenyl-2-pyrazolines **3b-d** shows a great deshielding effect on C-5 (Δδ = +5 to +6 ppm) and a high shielding effect on C-3 (Δδ ~ -6 to –9 ppm), due to the replacement of the acetyl group by the phenyl ring on *N*-1.

The main connectivities found in the HMBC spectra of compounds **3b-d** and the NOE cross peaks observed in their NOESY spectra are also similar to those of 2-pyrazolines **2a-j** (Tables 1 and 2).

Table 1

Main Connectivities Found in the HMBC Spectra of 3-Aryl-1-substituted-5-styryl-2-pyrazolines **2a-j** and **3b, c**

Protons	Long-range Correlated Carbons
2 x H-4, H-5, H-2',6'	C-3
2 x H-4, H-α, H-β	C-5
H-3",5", H-α, H-β	C-1"
CH_3	C=O
*For **2b** and **3b***; 4'-CH_3	C-3',5', C-4'
*For **2c** and **3c***; 4'-OCH_3	C-4'
*For **2g-j***; 2'-OH	C-1', C-2', C-3'
*For **2h***; 4'-CH_3	C-3', C-4', C-5'

Table 2

Main Results Obtained from the NOESY spectra of 3-Aryl-1-substituted-5-styryl-2-pyrazolines **2a-j** and **3b**

Protons	NOE cross peaks with
H-4$_{cis}$	H-4$_{trans}$, H-5, H-2',6'
H-4$_{trans}$	H-4$_{cis}$, H-α, H-β, H-2',6'
H-5	H-4$_{cis}$, H-α, H-β
H-α, H-β	H-5, H-4$_{trans}$, H-2",6"

The ^{1}H and ^{13}C nmr spectra of 3-aryl-1-substituted-5-styrylpyrazoles **4a-c,e,g,h,j** and **5b-d** are similar to those of the corresponding 3-aryl-1-substituted-5-styryl-2-pyrazolines **2a-c,e,g,h,j** and **3b-d**, except for the resonances of the pyrazole ring: i) H-4 (δ 6.86-7.07 ppm); ii) C-4 (δ 100.6-104.6 ppm); and iii) C-3 (δ 151.3-153.9 ppm) and C-5 (δ 142.4-146.3 ppm). The assignment of C-4 was based on the correlation found in the HSQC spectra with H-4, whereas the assignments of the C-3 and C-5 the connectivities found in the HMBC spectra (H-4 → C-3 and C-5; H-α → C-4 and C-1"; H-β → C-5 and C-2",6"; H-2',6' or H-6' → C-3) have been considered.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H and ^{13}C nmr spectra were recorded in diluted deuteriochloroform solutions (*ca*. 0.3%) on a Bruker DRX 300 spectrometer, at 300.13 and 75.47 MHz, respectively; the chemical shifts are expressed in δ (ppm) values relative to tetramethylsilane as internal reference and the coupling constants *J* are expressed in Hz. Unequivocal ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using 2D *g*HSQC and *g*HMBC experiments (long range C/H coupling constants were optimised to 7 Hz). Ir spectra were obtained in KBr pellets on a MATTSON 7000 FTIR spectrometer. EI-ms spectra were recorded with a VG Trio-2 apparatus. Elemental analyses were performed with a Carlo Erba 1106 EA instrument. TLC was carried out on Kieselgel 60 F_{254} (Merck) layer with hexane-acetone (7:3 v/v) as a solvent. The starting materials **1a-j** were synthesized according to known procedures [37,42-47].

Synthesis of 1-Acetyl-3-aryl-5-styryl-2-pyrazolines **2a-j** by the Reaction of (*E*,*E*)-Cinnamylideneacetophenones **1a-j** with Hydrazine.

General Procedure.

A mixture of the appropriate (*E*,*E*)-cinnamylideneacetophenones **1a-j** (5.0 mmoles), hydrazine hydrate (50.0 mmoles) and acetic acid (60 ml) was refluxed for 3 hours, then poured into water. The precipitate was isolated by filtration, washed with water and recrystallised from methanol to afford 1-acetyl-3-aryl-5-styryl-2-pyrazolines **2a-j** (Scheme 1).

1-Acetyl-3-phenyl-5-styryl-2-pyrazoline (**2a**).

This compound was obtained as white needles in 41% yield, mp 131-132°; ir: ν 1662, 1598, 1334, 1143, 956, 878, 772, 757, 699, 635, 578 cm^{-1}; ^{1}H nmr: δ 2.42 (s, 3 H, CH_3), 3.11 (dd, *J* 4.6 and 17.5 Hz, 1 H, H-4$_{trans}$), 3.53 (dd, *J* 11.3 and 17.5 Hz, 1 H, H-4$_{cis}$), 5.27 (ddd, *J* 4.5, 6.8 and 11.3 Hz, 1 H, H-5), 6.20 (dd, *J* 6.8 and 15.9 Hz, 1 H, H-α), 6.59 (d, *J* 15.9 Hz, 1 H, H-β), 7.18-7.30 (m, 3 H, H-3",4",5"), 7.36 (d, *J* 7.7 Hz, 2 H, H-2",6"), 7.41-7.45 (m, 3 H, H-3',4',5'), 7.73-7.76 (m, 2 H, H-2',6'); ^{13}C nmr: δ 22.0 (*C*H_3), 39.3 (C-4), 57.9 (C-5), 126.4 (C-2',6'), 126.5 (C-1' and C-2",6"), 127.0 (C-α), 127.8 (C-4"), 128.4 (C-3",5"), 128.7 (C-3',5'), 130.2 (C-4'), 131.3 (C-β), 136.1 (C-1"), 154.1 (C-3), 169.0 (C=O).

Anal. Calcd. for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.64. Found: C, 78.53; H, 6.21; N, 9.68.

1-Acetyl-3-(4-methylphenyl)-5-styryl-2-pyrazoline (**2b**).

This compound was isolated as white crystals in 52% yield, mp 134-135°; ir: ν 1657, 1594, 1491, 1448, 1429, 1330, 955, 820, 751, 697, 624 cm^{-1}; ^{1}H nmr: δ 2.39 (s, 3 H, 4'-CH_3), 2.41 (s, 3 H, CH_3), 3.08 (dd, *J* 4.5 and 17.5 Hz, 1 H, H-4$_{trans}$), 3.50 (dd, *J* 11.3 and 17.5 Hz, 1 H, H-4$_{cis}$), 5.26 (ddd, *J* 4.5, 6.8 and 11.3 Hz, 1 H, H-5), 6.20 (dd, *J* 6.8 and 15.9 Hz, 1 H, H-α), 6.59 (d, *J* 15.9 Hz, 1 H, H-β), 7.17-7.30 (m, 5 H, H-3',3",4",5',5"), 7.35 (d, *J* 7.7 Hz, 2 H, H-2",6"), 7.63 (d, *J* 8.2 Hz, 2 H, H-2',6'); ^{13}C nmr: δ

21.4 (4'-*C*H$_3$), 22.0 (*C*H$_3$), 39.3 (C-4), 57.7 (C-5), 126.4 (C-2',6'), 126.5 (C-2",6"), 127.1 (C-α), 127.7 (C-4"), 128.4 (C-3",5"), 128.6 (C-1'), 129.4 (C-3',5'), 131.2 (C-β), 136.1 (C-1"), 140.6 (C-4'), 154.2 (C-3), 168.9 (C=O).

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.19. Found: C, 78.86; H, 6.65; N, 9.15.

1-Acetyl-3-(4-methoxyphenyl)-5-styryl-2-pyrazoline (**2c**).

This substance was prepared as white plates in 56% yield, mp 110-111°; ir: ν 1646, 1611, 1521, 1362, 1311, 1256, 1178, 1034, 977, 839, 804, 750, 699, 629, 570 cm^{-1}; ^{1}H nmr: δ 2.41 (s, 3 H, C*H*$_3$), 3.07 (dd, *J* 4.5 and 17.4 Hz, 1 H, H-4$_{trans}$), 3.49 (dd, *J* 11.2 and 17.4 Hz, 1 H, H-4$_{cis}$), 3.84 (s, 3 H, 4'-OC*H*$_3$), 5.25 (ddd, *J* 4.5, 6.7 and 11.2 Hz, 1 H, H-5), 6.20 (dd, *J* 6.7 and 15.9 Hz, 1 H, H-α), 6.58 (d, *J* 15.9 Hz, 1 H, H-β), 6.93 (d, *J* 8.7 Hz, 2 H, H-3',5'), 7.17-7.29 (m, 3 H, H-3",4",5"), 7.35 (d, *J* 7.1 Hz, 2 H, H-2",6"), 7.68 (d, *J* 8.7 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 22.0 (*C*H$_3$), 39.4 (C-4), 55.4 (4'-O*C*H$_3$), 57.8 (C-5), 114.1 (C-3',5'), 124.0 (C-1'), 126.6 (C-2",6"), 127.2 (C-α), 127.7 (C-4"), 128.1 (C-2',6'), 128.4 (C-3",5"), 131.2 (C-β), 136.2 (C-1"), 154.0 (C-3), 161.3 (C-4'), 168.8 (C=O).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.93; H, 6.26; N, 8.70.

1-Acetyl-3-(4-fluorophenyl)-5-styryl-2-pyrazoline (**2d**).

This substance was obtained as white needles in 63% yield, mp 142-143°; ir: ν 1659, 1606, 1449, 1414, 1320, 1219, 1156, 980, 913, 832, 744, 697, 623 cm^{-1}; ^{1}H nmr: δ 2.41 (s, 3 H, C*H*$_3$), 3.08 (dd, *J* 4.6 and 17.5 Hz, 1 H, H-4$_{trans}$), 3.52 (dd, *J* 11.3 and 17.5 Hz, 1 H, H-4$_{cis}$), 5.28 (ddd, *J* 4.6, 6.8 and 11.3 Hz, 1 H, H-5), 6.20 (dd, *J* 6.8 and 15.9 Hz, 1 H, H-α), 6.59 (d, *J* 15.9 Hz, 1 H, H-β), 7.12 (dd, J_{HH} 8.8 and J_{HF} 8.7 Hz, 2 H, H-3',5'), 7.18-7.30 (m, 3 H, H-3",4",5"), 7.36 (dd, *J* 1.4 and 7.1 Hz, 2 H, H-2",6"), 7.73 (dd, J_{HH} 8.8 and J_{HF} 5.4 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 22.0 (*C*H$_3$), 39.3 (C-4), 58.0 (C-5), 115.8 (d, J_{CF} 22.0 Hz, C-3',5'), 126.5 (C-2",6"), 126.9 (C-α), 127.7 (d, J_{CF} 3.2 Hz, C-1'), 127.8 (C-4"), 128.42 (C-3",5"), 128.43 (d, J_{CF} 8.5 Hz, C-2',6'), 131.4 (C-β), 136.0 (C-1"), 153.0 (C-3), 163.8 (d, J_{CF} 251.0 Hz, C-4'), 169.0 (C=O).

Anal. Calcd. for $C_{19}H_{17}FN_2O$: C, 74.01; H, 5.56; N, 9.08. Found: C, 74.08; H, 5.53; N, 9.04.

1-Acetyl-3-(4-chlorophenyl)-5-styryl-2-pyrazoline (**2e**).

This compound was prepared as white plates in 45% yield, mp 168-169°; ir: ν 1658, 1592, 1447, 1415, 1320, 1089, 976, 832, 742, 699, 637 cm^{-1}; ^{1}H nmr: δ 2.41 (s, 3 H, C*H*$_3$), 3.08 (dd, *J* 4.5 and 17.5 Hz, 1 H, H-4$_{trans}$), 3.52 (dd, *J* 11.4 and 17.5 Hz, 1 H, H-4$_{cis}$), 5.29 (ddd, *J* 4.6, 6.9 and 11.4 Hz, 1 H, H-5), 6.20 (dd, *J* 6.9 and 15.9 Hz, 1 H, H-α), 6.59 (d, *J* 15.9 Hz, 1 H, H-β), 7.21-7.31 (m, 3 H, H-3",4",5"), 7.36 (d, *J* 7.8 Hz, 2 H, H-2",6"), 7.40 (d, *J* 8.6 Hz, 2 H, H-3',5'), 7.67 (d, *J* 8.6 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 22.0 (*C*H$_3$), 39.2 (C-4), 58.1 (C-5), 126.6 (C-2",6"), 126.8 (C-α), 127.7 (C-2',6'), 127.9 (C-4"), 128.5 (C-3",5"), 129.0 (C-3',5'), 129.9 (C-1'), 131.5 (C-β), 136.0 and 136.2 (C-1" and C-4'), 152.9 (C-3), 169.1 (C=O).

Anal. Calcd. for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.31; H, 5.26; N, 8.65.

1-Acetyl-3-(4-bromophenyl)-5-styryl-2-pyrazoline (**2f**).

This substance was obtained as white crystals in 54% yield, mp 148-149°; ir: ν 1662, 1596, 1447, 1415, 1393, 1358, 1319, 1011, 972, 820, 746, 691, 641, 629 cm^{-1}; ^{1}H nmr: δ 2.41 (s, 3 H, C*H*$_3$), 3.08 (dd, *J* 5.1 and 17.5 Hz, 1 H, H-4$_{trans}$), 3.51 (dd, *J* 11.3 and 17.5 Hz, 1 H, H-4$_{cis}$), 5.28 (ddd, *J* 5.1, 6.8 and 11.3 Hz, 1 H, H-5), 6.20 (dd, *J* 6.8 and 15.9 Hz, 1 H, H-α), 6.59 (d, *J* 15.9 Hz, 1 H, H-β), 7.19-7.30 (m, 3 H, H-3",4",5"), 7.36 (d, *J* 7.1 Hz, 2 H, H-2",6"), 7.55 (d, *J* 8.7 Hz, 2 H, H-3',5'), 7.60 (d, *J* 8.7 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 22.1 (*C*H$_3$), 39.2 (C-4), 58.1 (C-5), 124.6 (C-1'), 126.6 (C-2",6"), 126.8 (C-α), 127.9 (C-4"), 128.0 (C-2',6'), 128.5 (C-3",5"), 130.4 (C-4'), 131.6 (C-β), 131.9 (C-3',5'), 136.1 (C-1"), 153.1 (C-3), 169.1 (C=O).

Anal. Calcd. for $C_{19}H_{17}BrN_2O$: C, 61.79; H, 4.64; N, 7.58. Found: C, 61.84; H, 4.61; N, 7.61.

1-Acetyl-3-(2-hydroxyphenyl)-5-styryl-2-pyrazoline (**2g**).

This compound was prepared as pale yellow crystals in 51% yield, mp 170-171°; ir: ν 1652, 1598, 1497, 1445, 1412, 1333, 1255, 1155, 1021, 972, 960, 889, 829, 680, 632 cm^{-1}; ^{1}H nmr: δ 2.38 (s, 3 H, C*H*$_3$), 3.23 (dd, *J* 4.6 and 17.7 Hz, 1 H, H-4$_{trans}$), 3.63 (dd, *J* 11.3 and 17.7 Hz, 1 H, H-4$_{cis}$), 5.24 (ddd, *J* 4.6, 6.9 and 11.3 Hz, 1 H, H-5), 6.18 (dd, *J* 6.9 and 15.8 Hz, 1 H, H-α), 6.63 (d, *J* 15.8 Hz, 1 H, H-β), 6.95 (dd, *J* 7.3 and 7.7 Hz, 1 H, H-5'), 7.05 (d, *J* 7.8 Hz, 1 H, H-3'), 7.20-7.38 (m, 7 H, H-2",3",4',4",5",6',6"), 10.25 (s, 1 H, 2'-OH); ^{13}C nmr: δ 22.2 (*C*H$_3$), 39.7 (C-4), 56.5 (C-5), 115.1 (C-1'), 117.0 (C-3'), 119.7 (C-5'), 126.2 (C-α), 126.6 (C-2",6"), 128.0 (C-4"), 128.4 (C-6'), 128.5 (C-3",5"), 132.1 and 132.2 (C-4' and C-β), 135.8 (C-1"), 156.6 (C-3), 157.5 (C-2'), 167.9 (C=O).

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.42; H, 5.95; N, 9.17.

1-Acetyl-3-(2-hydroxy-4-methylphenyl)-5-styryl-2-pyrazoline (**2h**).

This substance was obtained as pale yellow needles in 50% yield, mp 192-193°; ir: ν 1666, 1594, 1491, 1359, 1338, 1269, 1223, 1139, 1028, 960, 879, 811, 695, 627 cm^{-1}; ^{1}H nmr: δ 2.345 and 2.352 (2s, 2 x 3 H, 2 x C*H*$_3$), 3.18 (dd, *J* 4.5 and 17.6 Hz, 1 H, H-4$_{trans}$), 3.58 (dd, *J* 11.3 and 17.6 Hz, 1 H, H-4$_{cis}$), 5.20 (ddd, *J* 4.5, 7.0 and 11.3 Hz, 1 H, H-5), 6.16 (dd, *J* 7.0 and 15.8 Hz, 1 H, H-α), 6.61 (d, *J* 15.8 Hz, 1 H, H-β), 6.75 (dd, *J* 0.9 and 8.0 Hz, 1 H, H-5'), 6.86 (s br, 1 H, H-3'), 7.12 (d, *J* 8.0 Hz, 1 H, H-6'), 7.19-7.30 (m, 3 H, H-3",4",5"), 7.35 (dd, *J* 1.3 and 7.3 Hz, 2 H, H-2",6"), 10.18 (s, 1 H, 2'-OH); ^{13}C nmr: δ 21.5 (4'-*C*H$_3$), 22.1 (*C*H$_3$), 39.6 (C-4), 56.3 (C-5), 112.5 (C-1'), 117.3 (C-3'), 120.7 (C-5'), 126.3 (C-α), 126.5 (C-2",6"), 127.9 (C-6'), 128.1 (C-4"), 128.4 (C-3",5"), 131.9 (C-β), 135.8 (C-1"), 143.1 (C-4'), 156.5 (C-3), 157.4 (C-2'), 167.8 (C=O).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.91; H, 6.32; N, 8.78.

1-Acetyl-3-(5-fluoro-2-hydroxyphenyl)-5-styryl-2-pyrazoline (**2i**).

This compound was isolated as pale yellow crystals in 56% yield, mp 141-142°; ir: ν 1670, 1603, 1498, 1362, 1330, 1264, 1190, 956, 867, 835, 773, 757, 691, 664, 633 cm^{-1}; ^{1}H nmr: δ 2.38 (s, 3 H, C*H*$_3$), 3.19 (dd, *J* 4.6 and 17.7 Hz, 1 H, H-4$_{trans}$), 3.62 (dd, *J* 11.4 and 17.7 Hz, 1 H, H-4$_{cis}$), 5.27 (ddd, *J* 4.6, 7.0 and 11.4 Hz, 1 H, H-5), 6.18 (dd, *J* 7.0 and 15.9 Hz, 1 H, H-α), 6.64 (d, *J* 15.9 Hz, 1 H, H-β), 6.95 (dd, J_{HH} 2.9 and J_{HF} 8.9 Hz, 1 H, H-6'), 7.00 (dd, J_{HH} 9.0 and J_{HF} 4.7 Hz, 1 H, H-3'), 7.08 (ddd, J_{HH} 2.9 and 9.0 and J_{HF} 7.8 Hz, 1 H, H-4'), 7.21-7.33 (m, 3 H, H-3",4",5"), 7.37 (dd, *J* 1.5 and 8.2 Hz, 2 H, H-2",6"), 10.03 (s, 1 H, 2'-OH); ^{13}C nmr: δ 22.2 (*C*H$_3$), 39.6 (C-4), 56.7 (C-5), 113.9 (d,

J_{CF} 24.4 Hz, C-6'), 114.4 (d, J_{CF} 7.7 Hz, C-1'), 118.1 (d, J_{CF} 7.9 Hz, C-3'), 119.0 (d, J_{CF} 23.2 Hz, C-4'), 125.9 (C-α), 126.6 (C-2",6"), 128.1 (C-4"), 128.5 (C-3",5"), 132.4 (C-β), 135.7 (C-1"), 153.7 (C-2'), 155.8 (d, J_{CF} 237.7 Hz, C-5'), 155.5 (d, J_{CF} 2.9 Hz, C-3), 168.0 (C=O).

Anal. Calcd. for $C_{19}H_{17}FN_2O_2$: C, 70.36; H, 5.28; N, 8.63. Found: C, 70.31; H, 5.31; N, 8.66.

1-Acetyl-3-(5-chloro-2-hydroxyphenyl)-5-styryl-2-pyrazoline (**2j**).

This substance was prepared as pale yellow plates in 41% yield, mp 201-202°; ir: ν 1674, 1490, 1487, 1433, 1365, 1330, 1285, 1216, 1152, 1109, 1026, 956, 887, 841, 756, 696, 650, cm^{-1}; ^1H nmr: δ 2.36 (s, 3 H, CH_3), 3.19 (dd, *J* 4.7 and 17.7 Hz, 1 H, H-4$_{trans}$), 3.59 (dd, *J* 11.4 and 17.7 Hz, 1 H, H-4$_{cis}$), 5.24 (ddd, *J* 4.7, 6.9 and 11.4 Hz, 1 H, H-5), 6.17 (dd, *J* 6.9 and 15.8 Hz, 1 H, H-α), 6.62 (d, *J* 15.8 Hz, 1 H, H-β), 6.98 (d, *J* 8.8 Hz, 1 H, H-3'), 7.20 (d, *J* 2.5 Hz, 1 H, H-6'), 7.23-7.31 (m, 4 H, H-3",4',4",5"), 7.35 (dd, *J* 1.3 and 8.2 Hz, 2 H, H-2",6"), 10.20 (s, 1 H, 2'-OH); ^{13}C nmr: δ 22.1 (*C*H_3), 39.4 (C-4), 56.7 (C-5), 116.3 (C-1'), 118.4 (C-3'), 124.3 (C-5'), 125.9 (C-α), 126.6 (C-2",6"), 126.6 (C-6'), 128.0 (C-4"), 128.5 (C-3",5"), 131.8 (C-4'), 132.3 (C-β), 135.7 (C-1"), 155.3 (C-3), 156.0 (C-2'), 167.9 (C=O).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 5.03; N, 8.22. Found: C, 66.91; H, 5.05; N, 8.26.

Synthesis of 3-Aryl-1-phenyl-5-styryl-2-pyrazolines **3b-d** by the Reaction of (*E,E*)-Cinnamylideneacetophenones **1b-d** with Phenylhydrazine.

General Procedure.

A mixture of the appropriate (*E,E*)-cinnamylideneacetophenones **1b-d** (5.0 mmoles), phenylhydrazine (50.0 mmoles) and acetic acid (60 ml) was refluxed for 2 hours and then poured into water. The precipitate was isolated by filtration, washed with water and recrystallised from methanol to afford 3-aryl-1-phenyl-5-styryl-2-pyrazolines **3b-d** (Scheme 1).

3-(4-Methylphenyl)-1-phenyl-5-styryl-2-pyrazoline (**3b**).

This compound was isolated as yellow crystals in 54% yield, mp 114-115°; ir: ν 1602, 1500, 1397, 1322, 1132, 1069, 972, 820, 746, 690 cm^{-1}; ^1H nmr: δ 2.37 (s, 3 H, CH_3), 3.10 (dd, *J* 7.1 and 16.9 Hz, 1 H, H-4$_{trans}$), 3.61 (dd, *J* 11.7 and 16.9 Hz, 1 H, H-4$_{cis}$), 4.89 (ddd, *J* 7.1, 7.3 and 11.7 Hz, 1 H, H-5), 6.30 (dd, *J* 7.3 and 15.9 Hz, 1 H, H-α), 6.65 (d, *J* 15.9 Hz, 1 H, H-β), 6.79-6.85 (m, 1 H, H-4 of *N*-Ph), 7.19 (d, *J* 8.1 Hz, 2 H, H-3',5'), 7.22-7.37 (m, 9 H, H-2",3",4",5",6" and H-2,3,5,6 of *N*-Ph), 7.62 (d, *J* 8.1 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 21.4 (CH_3), 40.8 (C-4), 63.0 (C-5), 113.7 (C-2,6 of *N*-Ph), 119.1 (C-4 of *N*-Ph), 125.6 (C-2',6'), 126.5 (C-2",6"), 127.8 (C-4"), 128.6 and 128.9 (C-3",5" and C-3,5 of *N*-Ph), 129.2 (C-3',5'), 129.4 (C-α), 129.9 (C-1'), 131.5 (C-β), 136.2 (C-1"), 138.7 (C-4'), 145.5 (C-1 of *N*-Ph), 147.8 (C-3).

Anal. Calcd. for $C_{24}H_{22}N_2$: C, 85.17; H, 6.55; N, 8.27. Found: C, 85.11; H, 6.58; N, 8.23.

3-(4-Methoxyphenyl)-1-phenyl-5-styryl-2-pyrazoline (**3c**).

This substance was prepared as yellow needles 58% yield, mp 114-115°; ir: ν 1595, 1495, 1452, 1381, 1315, 1291, 1259, 1175, 831, 746, 689 cm^{-1}; ^1H nmr: δ 3.05 (dd, *J* 7.2 and 16.9 Hz, 1 H, H-4$_{trans}$), 3.55 (dd, *J* 11.6 and 16.9 Hz, 1 H, H-4$_{cis}$), 3.80 (s, 3 H, OCH_3), 4.83 (ddd, *J* 7.2, 7.3 and 11.6 Hz, 1 H, H-5), 6.27 (dd, *J* 7.3 and 15.9 Hz, 1 H, H-α), 6.62 (d, *J* 15.9 Hz, 1 H, H-β), 6.77-6.83 (m, 1 H, H-4 of *N*-Ph), 6.90 (d, *J* 8.8 Hz, 2 H, H-3',5'), 7.19-7.35 (m, 9 H, H-2",3",4",5",6" and H-2,3,5,6 of *N*-Ph), 7.65 (d, *J* 8.8 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 40.8 (C-4), 55.3 (O*C*H_3), 63.0 (C-5), 113.6 (C-2,6 of *N*-Ph), 113.9 (C-3',5'), 119.0 (C-4 of *N*-Ph), 125.5 (C-1'), 126.4 (C-2",6"), 127.1 (C-2',6'), 127.8 (C-4"), 128.5 and 128.9 (C-3",5" and C-3,5 of *N*-Ph), 129.4 (C-α), 131.4 (C-β), 136.2 (C-1"), 145.6 (C-1 of *N*-Ph), 147.6 (C-3), 160.0 (C-4').

Anal. Calcd. for $C_{24}H_{22}N_2O$: C, 81.33; H, 6.26; N, 7.90. Found: C, 81.39; H, 6.23; N, 7.94.

3-(4-Fluorophenyl)-1-phenyl-5-styryl-2-pyrazoline (**3d**).

This compound was isolated as yellow crystals in 52% yield, mp 110-111°; ir: ν 1602, 1502, 1382, 1224, 1156, 977, 842, 757, 696 cm^{-1}; ^1H nmr: δ 3.07 (dd, *J* 7.0 and 16.9 Hz, 1 H, H-4$_{trans}$), 3.57 (dd, *J* 11.7 and 16.9 Hz, 1 H, H-4$_{cis}$), 4.90 (ddd, *J* 7.0, 7.3 and 11.7 Hz, 1 H, H-5), 6.28 (dd, *J* 7.3 and 15.9 Hz, 1 H, H-α), 6.64 (d, *J* 15.9 Hz, 1 H, H-β), 6.80-6.86 (m, 1 H, H-4 of *N*-Ph), 7.07 (dd, J_{HH} 8.4 and J_{HF} 8.6 Hz, 2 H, H-3',5'), 7.23-7.36 (m, 9 H, H-2",3",4",5",6" and H-2,3,5,6 of *N*-Ph), 7.69 (dd, J_{HF} 5.5 and J_{HH} 8.4 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 40.7 (C-4), 63.1 (C-5), 113.7 (C-2,6 of *N*-Ph), 115.7 (d, *J* 21.9 Hz, C-3',5'), 119.3 (C-4 of *N*-Ph), 126.5 (C-2",6"), 127.4 (d, *J* 8.1 Hz, C-2',6'), 127.9 (C-4"), 128.6 and 128.9 (C-3",5" and C-3,5 of *N*-Ph), 129.0 (d, *J* 6.0 Hz, C-1'), 129.1 (C-α), 131.6 (C-β), 136.1 (C-1"), 145.2 (C-1 of *N*-Ph), 146.6 (C-3), 162.9 (d, *J* 248.8 Hz, C-4').

Anal. Calcd. for $C_{23}H_{19}FN_2$: C, 80.68; H, 5.59; N, 8.18. Found: C, 80.61; H, 5.61; N, 8.15.

Preparation of 1-Acetyl-3-aryl-5-styrylpyrazoles **4a-c,e,g,h,j** by the Oxidation of Compounds **2a-c,e,g,h,j** with Chloranil.

General Procedure.

To a solution of the appropriate 1-acetyl-3-aryl-5-styryl-2-pyrazolines **2a-c,e,g,h,j** (0.8 mmole) in toluene (45.0 ml) was added chloranil (2.0 mmoles). The mixture was refluxed under nitrogen until the consumption of the starting material was completed (70 to 80 hours, except for **2g,h,j** which needed 180 to 200 hours). The solution was then evaporated to dryness and, in each case, the residue was purified by column chromatography, using dichloromethane as eluent. The crude products 1-acetyl-3-aryl-5-styrylpyrazoles **4a-c,e,g,h,j** were recrystallised from methanol (Scheme 2).

1-Acetyl-3-phenyl-5-styrylpyrazole (**4a**).

This Compound was prepared as white crystals in 65 % yield, mp 105-107°; ir: ν 1732, 1557, 1462, 1442, 1364, 1302, 1289, 1218, 10681, 963, 941, 815, 759, 697, 684, 653 cm^{-1}; ^1H nmr: δ 2.78 (s, 3 H, CH_3), 6.96 (s, 1 H, H-4), 7.13 (d, *J* 16.7 Hz, 1 H, H-β), 7.25-7.47 (m, 6 H, H-3',4',5',3",4",5"), 7.53 (d, *J* 7.4 Hz, 2 H, H-2",6"), 7.88 (dd, *J* 1.7 and 8.1 Hz, 2 H, H-2',6'), 7.93 (d, *J* 16.7 Hz, 1 H, H-α); ^{13}C nmr: δ 23.9 (*C*H_3), 104.6 (C-4), 117.2 (C-α), 126.2 (C-2',6'), 127.0 (C-2",6"), 128.5 (C-4"), 128.7 (C-3',5' and C-3",5"), 129.1 (C-4'), 131.7 (C-1'), 133.9 (C-β), 136.3 (C-1"), 146.1 (C-5), 153.4 (C-3), 172.4 (C=O). EI-ms m/z (rel. int.) 288 ($M^{+\bullet}$, 60), 245 (100), 215 (15), 142 (15), 115 (20), 77 (8).

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.86; H, 5.82; N, 9.68.

1-Acetyl-3-(4-methylphenyl)-5-styrylpyrazole (**4b**).

This substance was obtained as white needles in 89 % yield, mp 114-115°; ir: ν 1735, 1553, 1443, 1392, 1370, 1339, 1321, 1300, 1281, 1219, 963, 942, 801, 749, 693, 654 cm^{-1}; ^1H nmr: δ 2.40 (s, 3 H, 4'-CH_3), 2.79 (s, 3 H, CH_3), 6.94 (s, 1 H, H-4), 7.13 (d, *J* 16.5

Hz, 1 H, H-β), 7.25 (d, *J* 7.7 Hz, 2H, H-3',5'), 7.26-7.32 (m, 1 H, H-4''), 7.37 (dd, *J* 7.0 and 7.6 Hz, 2 H, H-3'',5''), 7.53 (d, *J* 7.0 Hz, 2 H, H-2'',6''), 7.78 (d, *J* 7.7 Hz, 2H, H-2',6'), 7.93 (d, *J* 16.5 Hz, 1 H, H-α); ^{13}C nmr: δ 21.4 (4'-*C*H$_3$), 23.9 (*C*H$_3$), 104.6 (C-4), 126.1 (C-2',6'), 127.0 (C-2'',6''), 117.3 (C-α), 128.5 (C-4''), 128.7 (C-3'',5''), 128.9 (C-1'), 129.4 (C-3',5'), 133.8 (C-β), 136.4 (C-1''), 139.1 (C-4'), 146.0 (C-5), 153.5 (C-3), 172.4 (C=O). EI-ms m/z (rel. int.) 302 (M$^{+\bullet}$, 70), 259 (100), 215 (15), 142 (15), 115 (20), 91 (5).

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.49; H, 5.98; N, 9.28.

1-Acetyl-3-(4-methoxyphenyl)-5-styrylpyrazole (**4c**).

This compound was prepared as pale yellow crystals in 86 % yield, mp 125-127°; ir: ν 1743, 1682, 1618, 1570, 1523, 1434, 1394, 1367, 1292, 1250, 1112, 1028, 940, 836, 807, 754, 656 cm^{-1}; ^{1}H nmr: δ 2.77 (s, 3 H, C*H*$_3$), 3.83 (s, 3 H, 4'-OC*H*$_3$), 6.89 (s, 1 H, H-4), 6.96 (d, *J* 9.4 Hz, 2 H, H-3',5'), 7.11 (d, *J* 16.5 Hz, 1 H, H-β), 7.26-7.39 (m, 3 H, H-3'',4'',5''), 7.53 (d, *J* 7.7 Hz, 2 H, H-2'',6''), 7.81 (d, *J* 9.4 Hz, 2 H, H-2',6'), 7.92 (d, *J* 16.5 Hz, 1 H, H-α); ^{13}C nmr: δ 23.9 (*C*H$_3$), 55.3 (4'-O*C*H$_3$), 104.4 (C-4), 114.1 (C-3',5'), 117.3 (C-α), 124.3 (C-1'), 127.0 (C-2'',6''), 127.5 (C-2',6'), 128.5 (C-4''), 128.7 (C-3'',5''), 133.8 (C-β), 136.3 (C-1''), 146.0 (C-5), 153.2 (C-3), 160.3 (C-4'), 172.3 (C=O). EI-ms m/z (rel. int.) 318 (M$^{+\bullet}$, 86), 276 (100), 275 (85), 261 (12), 202 (11), 142 (8), 115 (14), 58 (6).

Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.09; H, 5.98; N, 8.87.

1-Acetyl-3-(4-chlorophenyl)-5-styrylpyrazole (**4e**).

This substance was obtained as yellow crystals in 67 % yield, mp 191-193°; ir: ν 1729, 1552, 1504, 1430, 1389, 1364, 1324, 1294, 1092, 1013, 964, 943, 802, 753, 694, 651 cm^{-1}; ^{1}H nmr: δ 2.80 (s, 3 H, C*H*$_3$), 6.96 (d, *J* 0.6 Hz, 1 H, H-4), 7.93 (dd, *J* 0.6 and 16.5 Hz, 1 H, H-α), 7.15 (d, *J* 16.5 Hz, 1 H, H-β), 7.32-7.39 (m, 3 H, H-3'',4'',5''), 7.55 (d, *J* 8.2 Hz, 2 H, H-2'',6''), 7.43 (d, *J* 8.7 Hz, 2 H, H-3',5'), 7.84 (d, *J* 8.7 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 23.9 (*C*H$_3$), 104.4 (C-4), 117.1 (C-α), 127.0 (C-2'',6''), 127.4 (C-2',6'), 128.7 (C-4''), 128.8 (C-3'',5''), 129.0 (C-3',5'), 130.2 (C-1'), 134.2 (C-β), 135.0 (C-4'), 136.2 (C-1''), 146.3 (C-5), 152.4 (C-3), 172.3 (C=O). EI-ms m/z (rel. int.) 322 (M$^{+\bullet}$, 67), 279 (100), 246 (11), 215 (27), 142 (25), 115 (29), 77 (7).

Anal. Calcd. for $C_{19}H_{15}ClN_2O$: C, 70.70; H, 4.68; N, 8.68. Found: C, 71.04; H, 4.74; N, 8.94.

1-Acetyl-3-(2-hydroxyphenyl)-5-styrylpyrazole (**4g**).

This compound was prepared as pale yellow crystals in 82 % yield, mp 119-120°; ir: ν 1743, 1622, 1546, 1459, 1364, 1344, 1331, 1322, 1293, 1199, 1160, 1039, 967, 801, 755, 687, 653 cm^{-1}; ^{1}H nmr: δ 2.78 (s, 3 H, C*H*$_3$), 7.07 (s, 1 H, H-4), 7.93 (d, *J* 16.5 Hz, 1 H, H-α), 7.23 (d, *J* 16.5 Hz, 1 H, H-β), 6.99 (ddd, *J* 1.0, 7.4 and 7.7 Hz, 1 H, H-5'), 7.07 (dd, *J* 1.0 and 8.2 Hz, 1 H, H-3'), 7.31-7.43 (m, 4 H, H-3'',4',4'',5''), 7.57 (d, *J* 6.9 Hz, 2 H, H-2'',6''), 7.64 (dd, *J* 1.6 and 7.7 Hz, 1 H, H-6'), 10.40 (s, 1 H, 2'-OH); ^{13}C nmr: δ 24.0 (*C*H$_3$), 104.1 (C-4), 114.8 (C-1'), 117.4 (C-3'), 119.7 (C-5'), 116.5 (C-α), 127.2 (C-2'',6''), 129.0 (C-4''), 127.4 (C-6'), 128.8 (C-3'',5''), 131.0 (C-4'), 135.6 (C-β), 136.0 (C-1''), 145.8 (C-5), 153.9 (C-3), 156.5 (C-2'), 170.8 (C=O). EI-ms m/z (rel. int.) 304 (M$^{+\bullet}$, 52), 262 (100), 261 (56), 202 (7), 142 (11), 115 (16), 77 (7).

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 74.87; H, 5.43; N, 9.18.

1-Acetyl-3-(2-hydroxy-4-methylphenyl)-5-styrylpyrazole (**4h**).

This compound was obtained as white needles in 80 % yield, mp 128-129°; ir: ν 1731, 1633, 1553, 1448, 1370, 1342, 1299, 1255, 1197, 960, 862, 787, 751, 693, 658, 640 cm^{-1}; ^{1}H nmr: δ 2.37 (s, 3 H, 4'-C*H*$_3$), 2.77 (s, 3 H, C*H*$_3$), 7.04 (s, 1 H, H-4), 7.92 (d, *J* 16.6 Hz, 1 H, H-α), 7.22 (d, *J* 16.6 Hz, 1 H, H-β), 6.80 (dd, *J* 1.0 and 7.9 Hz, 1 H, H-5'), 6.89 (s br, 1 H, H-3'), 7.52 (d, *J* 7.9 Hz, 1 H, H-6'), 7.34-7.43 (m, 3 H, H-3'',4'',5''), 7.57 (d, *J* 8.1 Hz, 2 H, H-2'',6''), 10.33 (s, 1 H, 2'-OH); ^{13}C nmr: δ 21.5 (4'-*C*H$_3$), 24.0 (*C*H$_3$), 104.0 (C-4), 112.2 (C-1'), 117.73 (C-3'), 120.7 (C-5'), 116.6 (C-α), 127.2 (C-6' and C-2'',6''), 129.9 (C-4''), 128.8 (C-3'',5''), 135.5 (C-β), 136.0 (C-1''), 141.6 (C-4'), 145.7 (C-5), 154.0 (C-3), 156.4 (C-2'), 170.8 (C=O). EI-ms m/z (rel. int.) 318 (M$^{+\bullet}$, 53), 276 (100), 275 (55), 202 (5), 142 (10), 115 (15), 77 (5).

Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.06; H, 5.93; N, 8.74.

1-Acetyl-3-(5-chloro-2-hydroxyphenyl)-5-styrylpyrazole (**4j**).

This substance was prepared as yellow crystals in 75 % yield, mp 168-170°; ir: ν 1735, 1694, 1679, 1569, 1467, 1364, 1289, 1111, 963, 831, 751, 717, 694, 657 cm^{-1}; ^{1}H nmr: δ 2.75 (s, 3 H, C*H*$_3$), 6.99 (d, *J* 8.8 Hz, 1 H, H-3'), 7.01 (s, 1 H, H-4), 7.21 (d, *J* 16.2 Hz, 1 H, H-β), 7.25 (dd, *J* 2.5 and 8.8 Hz, 1 H, H-4'), 7.33-7.43 (m, 3 H, H-3'',4'',5''), 7.55 (dd, *J* 7.1 Hz, 2 H, H-2'',6''), 7.57 (d, *J* 2.5 Hz, 1 H, H-6'), 7.90 (dd, *J* 0.6 and 16.2 Hz, 1 H, H-α), 10.34 (s, 1 H, 2'-OH); ^{13}C nmr: δ 24.0 (*C*H$_3$), 103.9 (C-4), 116.0 (C-1'), 116.1 (C-α), 118.8 (C-3'), 124.4 (C-5'), 126.8 (C-6'), 127.2 (C-2'',6''), 128.8 (C-3'',5''), 129.1 (C-4''), 130.6 (C-4'), 135.8 (C-1''), 135.9 (C-β), 146.0 (C-5), 152.6 (C-3), 155.1 (C-2'), 170.6 (C=O). EI-ms m/z (rel. int.) 338 (M$^{+\bullet}$, 43), 296 (100), 295 (48), 246 (28), 202 (11), 173 (16), 160 (17), 142 (11), 115 (18), 87 (24), 77 (7).

Anal. Calcd. for $C_{19}H_{15}ClN_2O_2$: C, 67.36; H, 4.46; N, 8.27. Found: C, 67.69; H, 4.86; N, 8.49.

Synthesis of 3-Aryl-1-phenyl-5-styrylpyrazoles **5b-d** by the Oxidation of 2-Pyrazolines **3b-d** with Chloranil.

General Procedure.

To a solution of the appropriate 3-aryl-1-phenyl-5-styryl-2-pyrazolines **3b-d** (0.6 mmole) in toluene (40.0 ml) was added chloranil (1.6 mmoles). The mixture was refluxed under nitrogen until the consumption of the starting material was completed (24 to 32 hours). The solution was then evaporated to dryness and, in each case, the residue was purified by column chromatography, using dichloromethane as eluent. The obtained 3-aryl-1-phenyl-5-styrylpyrazoles **5b-d** were recrystallised from methanol (Scheme 2).

3-(4-Methylphenyl)-1-phenyl-5-styrylpyrazole (**5b**).

This compound was obtained as brown powder in 84% yield, mp 156-157°; ir: ν 1598, 1548, 1519, 1501, 1454, 1410, 1312, 1202, 1018, 963, 885, 827, 801, 762, 749, 694, 570, 527 cm^{-1}; ^{1}H nmr: δ 2.39 (s, 3 H, CH_3), 6.90 (d, *J* 16.3 Hz, 1 H, H-α), 6.96 (s, 1 H, H-4), 7.15 (d, *J* 16.3 Hz, 1 H, H-β), 7.24 (d, *J* 8.0 Hz, 2 H, H-3',5'), 7.24-7.28 (m, 1 H, H-4''), 7.34 (dd, *J* 6.7 and 7.6 Hz, 2 H, H-3'',5''), 7.41-745 (m, 3 H, H-2'', 6'' and H-4 of *N*-Ph), 7.51 (dd, *J* 7.2 and 8.0 Hz, 2 H, H-3,5 of *N*-Ph), 7.57 (d, *J* 8.0 Hz, 2 H, H-2,6 of *N*-Ph), 7.81 (d, *J* 8.0 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 21.3 (CH_3), 101.0 (C-4), 115.7 (C-α), 125.6 (C-2,6 of *N*-Ph), 125.7 (C-2',6'), 126.7 (C-2'',6''), 128.0 (C-4 of *N*-Ph), 128.3 (C-4''),

128.8 (C-3",5"), 129.3 (C-3,5 of *N*-Ph), 129.4 (C-3',5'), 130.1 (C-1'), 132.1 (C-β), 136.4 (C-1"), 137.8 (C-4'), 139.5 (C-1 of *N*-Ph), 142.5 (C-5), 152.0 (C-3). EI-ms m/z (rel. int.) 336 ($M^{+\bullet}$, 100), 335 (56), 259 (17), 217 (13), 168 (5), 115 (8), 91 (10), 77 (14).

Anal. Calcd. for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33. Found: C, 85.97; H, 5.66; N, 8.32.

3-(4-Methoxyphenyl)-1-phenyl-5-styrylpyrazole (**5c**).

This substance was prepared as brown powder in 84% yield, mp 156-157°; ir: ν 1596, 1536, 1503, 1457, 1414, 1396, 1308, 1175, 1136, 1071, 952, 769, 703, 660, 520 cm^{-1}; ^1H nmr: δ 3.82 (s, 3 H, OCH_3), 6.88 (d, *J* 16.2 Hz, 1 H, H-α), 6.90 (s, 1 H, H-4), 6.95 (d, *J* 8.9 Hz, 2 H, H-3',5'), 7.13 (d, *J* 16.2 Hz, 1 H, H-β), 7.25-7.35 (m, 3 H, H-3",4",5"), 7.39-7.42 (m, 2 H, H-2",6"), 7.41-7.43 (m, 1 H, H-4 of *N*-Ph), 7.49 (dd, *J* 7.1 and 7.9 Hz, 2 H, H-3,5 of *N*-Ph), 7.55 (d, *J* 7.1 Hz, 2 H, H-2,6 of *N*-Ph), 7.84 (d, *J* 8.9 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 55.2 (OCH_3), 100.6 (C-4), 113.9 (C-3',5'), 115.5 (C-α), 125.4 (C-2,6 of *N*-Ph), 125.5 (C-1'), 126.6 (C-2",6"), 127.0 (C-2',6'), 127.9 (C-4 of *N*-Ph), 128.2 (C-4"), 128.7 (C-3",5"), 129.2 (C-3,5 of *N*-Ph), 132.0 (C-β), 136.3 (C-1"), 139.4 (C-1 of *N*-Ph), 142.4 (C-5), 151.7 (C-3), 159.5 (C-4'). EI-ms m/z (rel. int.) 352 ($M^{+\bullet}$, 100), 351 (40), 337 (13), 275 (11), 217 (8), 202 (6), 176 (6), 115 (8), 91 (7), 77 (19).

Anal. Calcd. for $C_{24}H_{20}N_2O$: C, 81.79; H, 5.72; N, 7.95. Found: C, 82.09; H, 5.85; N, 8.35.

3-(4-Fluorophenyl)-1-phenyl-5-styrylpyrazole (**5d**).

This compound was obtained as yellow powder in 85 % yield, mp 137-138°; ir: ν 1595, 1514, 1501, 1458, 1447, 1398, 1279, 1231, 1177, 1150, 1138, 955, 883, 841, 789, 696, 663, 584, 528 cm^{-1}; ^1H nmr: δ 6.89 (d, *J* 16.5 Hz, 1 H, H-α), 6.92 (s, 1 H, H-4), 7.11 (dd, J_{HH} 7.4 and J_{HF} 9.9 Hz, 2 H, H-3',5'), 7.14 (d, *J* 16.5 Hz, 1 H, H-β), 7.27-7.37 (m, 3 H, H-3",4",5"), 7.40-7.46 (m, 3 H, H-2",6" and H-4 of *N*-Ph), 7.49-7.58 (m, 4 H, H-2,3,5,6 of *N*-Ph), 7.87 (dd, J_{HF} 5.0 and J_{HH} 7.4 Hz, 2 H, H-2',6'); ^{13}C nmr: δ 100.9 (C-4), 115.5 (d, J 21.6 Hz, C-3',5' and C-α), 125.5 (C-2,6 of *N*-Ph), 126.6 (C-2",6"), 127.4 (d, J 8.1 Hz, C-2',6'), 128.0 (C-4 of *N*-Ph), 128.4 (C-4"), 128.8 (C-3",5"), 129.2 (d, J 3.4 Hz, C-1' and C-3,5 of *N*-Ph), 132.2 (C-β), 136.3 (C-1"), 139.4 (C-1 of *N*-Ph), 142.6 (C-5), 151.1 (C-3), 162.7 (d, *J* 246.6 Hz, C-4'). EI-ms m/z (rel. int.) 340 ($M^{+\bullet}$, 100), 339 (66), 263 (22), 217 (10), 170 (8), 142 (7), 115 (11), 91 (11), 77 (19).

Anal. Calcd. for $C_{23}H_{17}FN_2$: C, 81.16; H, 5.03; N, 8.23. Found: C, 80.82; H, 5.19; N, 8.34.

Acknowledgements.

Thanks are due to the Hungarian National Research Foundation (Grant No. OTKA T034123), University of Aveiro and "Fundação para a Ciência e Tecnologia", Portugal, and to the Hungarian-Portuguese Intergovernmental Science and Technology Cooperation Programme (Project No. P-2/01) for financial support. Technical assistance of Mrs. M. Nagy is highly appreciated.

REFERENCES AND NOTES

[1] Pyrazoles, Pirazolines, Pyrazolidines, Indazoles and Condensed Rings, K. H. Wiley, ed, in The Chemistry of Heterocyclic Compounds, Vol. **22**, A. Weissberger, ed, Interscience Publishers, New York, 1967, p 180.

[2] J. Elguero, in Comprehensive Heterocyclic Chemistry, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, Oxford, **5**, 167 (1984).

[3] Elguero, J. in Comprehensive Heterocyclic Chemistry II, A. R. Katritzky, C. W. Rees and E. F. Scriven, eds, Pergamon Press, Oxford, **3**, 1 (1996).

[4] A. Lévai, *Khim. Geterotsikl. Soedin.*, 747 (1997).

[5] E. Fischer and O. Knövenagel, *Ann. Chem.*, **239**, 194 (1887).

[6] L. C. Raiford and W. J. Peterson, *J. Org. Chem.*,**1**, 544 (1936).

[7] L. C. Raiford and G. V. Gundy, *J. Org. Chem.*, **3**, 265 (1938).

[8] W. Ried and G. Dankert, *Chem. Ber.*, **57**, 2707 (1957).

[9] R. H. Wiley, C. H. Jarboe, F. N. Hayes, E. Hansbury, J. T. Nielsen, P. X. Callahan and M. C. Sellars, *J. Org. Chem.*, **23**, 732 (1958).

[10] A. E. A. Sammour, *Tetrahedron*, **20**, 1067 (1964).

[11] J. L. Aubagnac, J. Elguero and R. Jacquier, *Bull. Soc. Chim. Fr.*, 3292 (1969).

[12] Y. A. Al-Farkh, F. H. Al-Hajjar, F. S. Al-Shamali and H. S. Hamoud, *Chem. Pharm. Bull.*, **27**, 257 (1979).

[13] T. C. Sharma, S. P. Pawar and N. J. Reddy, *Acta Chim. Hung.*, **112**, 159 (1983).

[14] S. P. Sachchar and A. K. Singh, *J. Indian Chem. Soc.*, **62**, 142 (1985).

[15] C. Gao and A. S. Hay, *Synth. Commun.*, **25**, 1877 (1995).

[16] A. S. R. Anjaneyulu, G. S. Rani, K. G. Annapurna, U. V. Mallavadhani and Y. L. N. Murthy, *Indian J. Chem.*, **34B**, 933 (1995).

[17] N. Mishriky, F. M. Asaad, Y. A. Ibrahim and A. S. Girgis, *Pharmazie*, **51**, 544 (1996).

[18] N. K. Sangwan and S. N. Rastogi, *Indian J. Chem.*, **20B**, 135 (1981).

[19] A. Lévai, Á. Szöllősy and G. Tóth, *J. Chem. Res. (S)*, 392 (1985).

[20] T. Lóránd, D. Szabó, A. Földesi, L. Párkányi, A. Kálmán and A. Neszmélyi, *J. Chem. Soc., Perkin Trans. 1*, 481 (1985).

[21] J. Kamecki, W. Perka and L. Pijewska, *Polish J. Chem.*, **59**, 285 (1985).

[22] N. R. El-Rayyes and A. Al-Jawhary, *J. Heterocyclic Chem.*, **23**, 135 (1986).

[23] N. K. Sangwan, *J. Chem. Res. (S)*, 22 (1987).

[24] N. R. El-Rayyes and N. H. Bahtiti, *J. Heterocyclic Chem.*, **26**, 209 (1989).

[25] G. Tóth, Á. Szöllősy, T. Lóránd, T. Kónya, D. Szabó, A. Földesi and A. Lévai, *J. Chem. Soc., Perkin Trans. 2*, 319 (1989).

[26] Á. Szöllősy, G. Tóth, T. Lóránd, T. Kónya, F. Aradi and A. Lévai, *J. Chem. Soc., Perkin Trans. 2*, 489 (1991).

[27] H. M. Faidallah and M. S. I. Makki, *J. Chin. Chem. Soc.*, **41**, 585 (1994).

[28] T. Lóránd, F. Aradi, Á. Szöllősy G. Tóth and T. Kónya, *Monatsh. Chem.*, **127**, 971 (1996).

[29] A. Lévai, *J. Heterocyclic. Chem.*, **35**, 13 (1998).

[30] A. Lévai, *Heterocyclic. Commun.*, **5**, 151 (1999).

[31] N. Mishriky, Y. A. Ibrahim, A. S. Girgis and N. G. Fawzy, *Pharmazie*, **54**, 738 (1999).

[32] F. Straus, *Ber. Dtsch. Chem. Ges.*, **51**, 1457 (1918).

[33] L. C. Raiford and R. H. Manley, *J. Org. Chem.*, **5**, 590 (1940).

[34] H. Ferres, M. S. Hamdam and W. R. Jackson, *J. Chem. Soc. (B)*, 1892 (1971).

[35] D. C. G. A. Pinto, A. M. S. Silva, J. A. S. Cavaleiro, C. Foces-Foces, A. L. Llamas-Saiz, N. Jagerovic and J. Elguero, *Tetrahedron*, **55**, 10187 (1999).

[36] E. E. Baroni, K. A. Kobyrzina and E. A. Anreesheb, *Zh. Obshch. Khim.*, **30**, 2002 (1960).

[37] J. Grimshaw and J. Trocha-Grimshaw, *J. Chem. Soc., Perkin Trans. 1,* 1383 (1974).

[38] D. Nauduri and G. B. S. Reddy, *Chem. Pharm. Bull.*, **46**, 1254 (1998).

[39] W. Fliege, R. Huisgen, W. Kolbeck and V. Weberndörfer, *Chem. Ber.,* **116**, 3438 (1983).

[40] W. Ried and R. Lantzsch, *Chem. Ber.*, **102**, 378 (1969).

[41] R. N. Butler, *Chem. Rev.*, **84**, 249 (1984).

[42] D. C. G. A. Pinto, A. M. S. Silva, A. Lévai, J. A. S. Cavaleiro, T. Patonay and J. Elguero, *Eur. J. Org. Chem.*, 2593 (2000).

[43] M. Scholtz and A. Wiedemeann, *Ber. Dtsch. Chem. Ges.*, **36**, 845 (1903).

[44] H. Bauer and E. Breit, *Ber. Dtsch. Chem. Ges.*, **39**, 1916 (1906).

[45] U. S. Cheema, K. G. Gulati and K. Venkataraman, *J. Chem. Soc.*, 925 (1932).

[46] E. T. Oganesyan, A. V. Simonyan and V. S. Cherevatyi, *Khim. Farm. Zh.*, **22**, 1104 (1988).

[47] A. Lévai, A. M. S. Silva, J. A. S. Cavaleiro, T. Patonay and V. L. M. Silva, *Eur. J. Org. Chem.*, 3213 (2001).