Synthesis of 4-Aryl-3-(2-chromonyl)-2-pyrazolines by the 1,3-Dipolar Cycloaddition of 2-Styrylchromones with Diazomethane

Diana C. G. A. Pinto, Artur M. S. Silva*, Lúcia M. P. M. Almeida, José A. S. Cavaleiro, Albert Lévai [a] and Tamás Patonay [a]

Department of Chemistry, University of Aveiro, 3810 Aveiro, Portugal
[a] Department of Organic Chemistry, Lajos Kossuth University, P. O. Box 20, H-4010 Debrecen, Hungary
Received October 8, 1997

The first reported 1,3-dipolar cycloaddition of 2-styrylchromones with diazomethane afforded 4-aryl-3-(2-chromonyl)-2-pyrazolines. However, 3-aryl-4-(2-chromonyl)-1-pyrazolines have been also found as minor products of this reaction. These two series of pyrazolines have been fully characterized.

J. Heterocyclic Chem., **35**, 217 (1998).

Introduction.

Pyrazolines are well known five-membered heterocyclic compounds and several procedures have been developed for their syntheses [1]. As a result, a wide variety of pyrazolines have hitherto been described in the literature. One of the most common synthetic methods is based on the cycloaddition of diazoalkanes to carbon-carbon double bonds. Although various diazoalkanes are available to prepare pyrazolines, diazomethane has been mainly used for this purpose. A pyrazoline type compound was first synthesised by Pechmann as early as 1894 from the reaction of diazomethane with dimethyl fumarate [2]. It has also turned out that Pechmann correctly anticipated the mechanism of that cycloaddition, *viz.* the primary product being a 1-pyrazoline, which in many cases is spontaneously isomerized into its thermodynamically more stable 2-pyrazoline isomer by a 1,3-H shift.

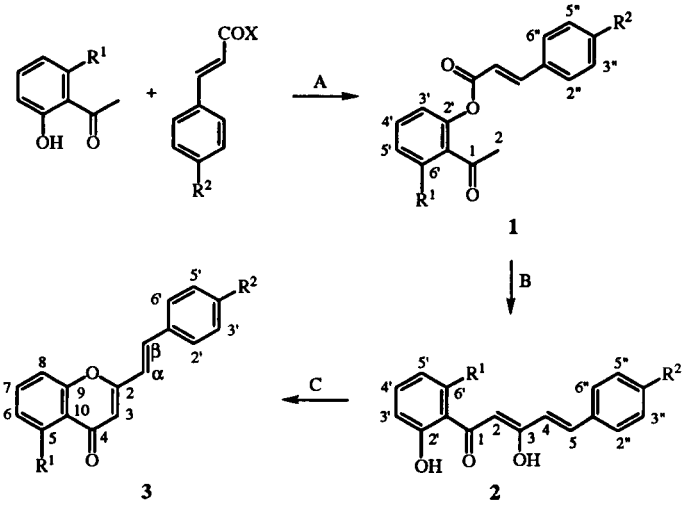
Probably the first example for the preparation of a pyrazoline by the reaction of an α,β-unsaturated ketone with a diazoalkane was published by Azzarello in 1906 [3]. Formation of 3-acetyl-4-phenyl-2-pyrazoline was observed in the reaction of benzalacetone with diazomethane in anhydrous ethyl ether. However, later on, many conflicting data were published concerning the synthesis of pyrazolines by the reaction of α,β-enones with diazoalkanes. This situation prompted us to reinvestigate this reaction with a wide variety of α,β-unsaturated ketones. Our experimental results unequivocally proved that the reaction of chalcones [4] and related α,β-unsaturated ketones [5,6] with diazomethane provides 2-pyrazolines as the sole 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 also have studied in detail the reaction of exocyclic α,β-unsaturated ketones with diazomethane [7-10]. It has been concluded that the 1-pyrazoline products are stable compounds, which can then be rearranged into their 2-pyrazoline isomers under acidic conditions [8,9]. As a continuation of these investigations, in this paper we report the reaction of 2-styrylchromones with diazomethane.

Results and Discussion.

Chemistry.

(*E*)-2-Styrylchromones **3** were prepared in good overall yields according to the three-step sequence, shown in Scheme 1 [11,12]. For this purpose, the 2'-cinnamoyloxyacetophenones **1a-e** were obtained from the reaction of the 2'-hydroxyacetophenone derivatives with the appropriate cinnamoyl chloride, commercially available in the case of **1a,e** or prepared *in situ* from cinnamic acids and phosphoryl chloride for **1b-d**. The rearrangement of compounds **1a-e** into 5-aryl-3-hydroxy-1-(2-hydroxyphenyl)-2,4-penten-1-ones **2a-e** was performed upon treatment with sodium hydride in dry tetrahydrofuran at reflux. Cyclization of these ketones **2a-e** into the desired (*E*)-2-styrylchromones **3a-e** was achieved with *p*-toluenesulfonic acid and by heating at 100° in dimethyl sulfoxide.

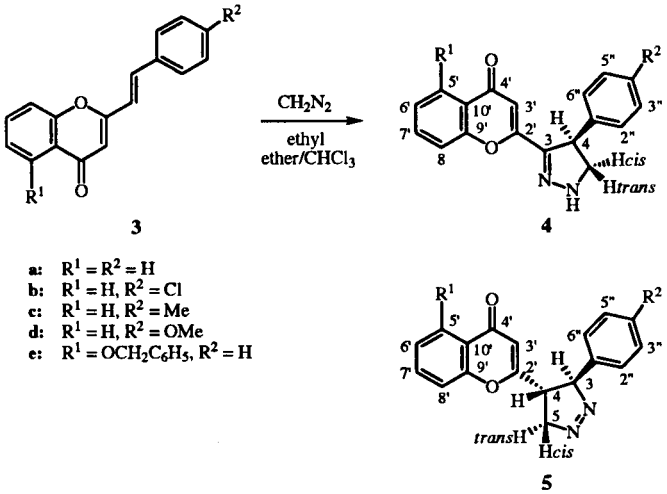
Scheme 1



a) $R^1 = R^2 = H$ b) $R^1 = H$, $R^2 = Cl$ c) $R^1 = H$, $R^2 = Me$
d) $R^1 = H$, $R^2 = OMe$ e) $R^1 = OCH_2C_6H_5$, $R^2 = H$
A - $R^2 = H$, X = Cl; py or $R^2 = Cl$, Me or OMe; X = OH; $POCl_3$, py
B - NaH, tetrahydrofuran
C - *p*-Toluenesulfonic acid, dimethyl sulfoxide

(*E*)-2-Styrylchromones **3a-e** were treated with diazomethane, at room temperature in a mixture of ethyl ether and chloroform. The progress of these reactions was monitored by thin-layer chromatography. New batches of diazomethane were added, as described in the Experimental, until consumption of the starting 2-styrylchromones **3a-e** was complete. After evaporation of the organic solvents and crystallisation from ethanol, the 4-aryl-3-(2-chromonyl)-2-pyrazolines **4a-e** have been obtained [13]. The thin layer chromatographic analysis of the mother liquors still have revealed the presence of other quantities of 4-aryl-3-(2-chromonyl)-2-pyrazolines **4a-e** and small amounts of 3-aryl-4-(2-chromonyl)-1-pyrazoline derivatives **5a-e** (Scheme 2) [13,14].

Scheme 2



3

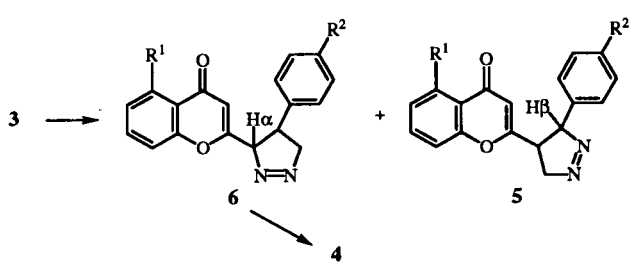
a: $R^1 = R^2 = H$
b: $R^1 = H, R^2 = Cl$
c: $R^1 = H, R^2 = Me$
d: $R^1 = H, R^2 = OMe$
e: $R^1 = OCH_2C_6H_5, R^2 = H$

4

5

The results obtained indicate that these 1,3-dipolar cycloadditions afford, in each case, the two possible regioisomers **5a-e** and **6a-e**. However, those **6a-e**, in which the methylene group is connected to the β carbon atom of the 2-styrylchromones, appear as the major products of these reactions, which then isomerize into the isolable products 4-aryl-3-(2-chromonyl)-2-pyrazolines **4a-e** (Scheme 3). Similar isomerations 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 [4-6,15]. The regioisomers **5a-e**, in which the methylene group is connected to the α carbon atom of the 2-styrylchromones, do not isomerize even after being submitted to preparative purification by thin layer chromatography. The isomerizations took place in the case of compounds **6a-e** because H_α protons are acidic whereas H_β of regioisomers **5a-e** are not. It is worth mentioning that 2-pyrazolines **4a-e** 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 1-pyrazolines formed on the above-mentioned cycloaddition. Our experimental results unequivocally prove that the 1,3-dipolar cycloaddition of 2-styrylchromones **3** and diazomethane provides 4-aryl-3-(2-chromonyl)-2-pyrazolines **4a-e**, after spontaneous isomerization of 1-pyrazolines **6**, as major products, with more than 90% regioselectivity according to the ^1H nmr determination of the composition of the crude reaction mixtures. This pronounced regioselectivity may originate from the fact that the β-carbon atom of the 2-styrylchromones **3** is much more electrophilic than the α carbon atom. However, the α-carbon atom should also have a weak positive charge to give rise to the formation of 1-pyrazolines **5** as minor cycloaddition products.

Scheme 3



Nuclear Magnetic Resonance Spectroscopy.

The most noticeable features of the ^1H and ^{13}C nmr spectra of 2'-cinnamoyloxyacetophenones **1a-e** are: i) the resonances of the 2-CH_3 proton and carbon atoms which appear, respectively, at δ 2.53-2.57 and 29.6-31.7 ppm; ii) the pair of doublets corresponding to the resonances of H_α and H_β protons; the corresponding coupling constants $J_{H\alpha\text{-}H\beta}$ ~ 16 Hz indicates the presence of a *trans* configuration of this double bond; iii) the resonances of the ester and ketone carbonyl groups which appear at δ 165.0-165.5 and 197.8-200.6 ppm, respectively.

In the ^1H nmr spectra of each one of 5-aryl-3-hydroxy-1-(2-hydroxyphenyl)-2,4-penten-1-ones **2a-e** it is possible to observe the presence of two signals, respectively, at 12.21-12.89 and 14.60-14.75 ppm, which are due to resonances of the protons involved in hydrogen bonds. One can conclude that these compounds **2a-e** exist in enolic forms, as shown in Scheme 1, and the former signals correspond to the resonances of the phenolic protons whereas the latter resonances are due to the 3-O*H* protons. From the values of the vicinal coupling constants $^3J_{H4\text{-}H5}$ it was possible to establish the *trans* configuration of these two protons. However, the stereochemistry of the other moiety of compounds **2a-e** was established by NOE experiments. Upon irradiation the H-2 resonance of 3-hydroxy-1-(2-hydroxyphenyl)-5-(4-methylphenyl)-2,4-penten-1-ones **2c**, NOE effects were observed on H-4 (6%) and H-6'

(22%), thus allow us to establish the stereochemistry of structures **2**, as shown in Scheme 1.

Based on our previous work [16] and on the $^3J_{H\alpha\text{-}H\beta}$ ~ 16 Hz it is possible to conclude that the vinylic moieties of 2-styrylchromones **3a-e** are in a *trans* configuration. However, only after NOE experiment with 4'-methyl-2-styrylchromone **3a** was it possible to conclude which one of the two possible isomers, taking into account the C_2-C_α isomerism, were present. In that case, upon irradiation the H-3 resonance, a NOE enhancement was observed on H-α (8%), and this is only compatible with structure **3**, as shown in Scheme 1.

A detailed analysis of the ^1H and the 2D COSY spectra of pyrazolines **4** revealed the presence of a 2-pyrazoline ring, where the N*H* resonance appears as a broad singlet at δ 6.31-6.43 ppm. However, in order to determine to which carbon, α or β, of the 2-styrylchromone is connected the methylene group of the diazomethane, one-dimensional selective INEPT experiments [17] were carried out on pyrazolines **4**. Upon irradiation of the H-3' resonance (δ 6.18-6.36 ppm), with a 7 Hz long-range J (C/H) coupling, enhancements on the signals of C-2' (δ 155.1-157.5 ppm), C-10' (δ 124.1 ppm for **4a-d** and δ 115.2 ppm for **4e**) and that at δ 146.1-146.7 ppm were observed. This latter resonance was assigned, in each case, to the C-3 carbon atom, an assignment supporting the structures of 2-pyrazolines **4** as shown in Scheme 2.

The assignments of the pyrazoline ring protons of compounds **4** were based on 2D NOESY experiments. In the case of 3-(2-chromonyl)-4-phenyl-2-pyrazolines **4a**, the results are the following:

H-3	-----NOE cross peaks with----→	H-3', H-2",6" and H-4 *cis*
H-4 *cis*	-----NOE cross peaks with----→	H-3 and H-4 *trans*
H-4 *trans*	-----NOE cross peaks with----→	H-2",6" and H-4 *cis*

A detailed analysis of ^1H, ^{13}C, 2D COSY and HETCOR spectra of pyrazolines **5** revealed the presence of a 1-pyrazoline ring. This conclusion was based on the presence of four protons coupled with each others, two methylenic and two methynic. The next step was to prove the presence of 1-pyrazolines **5** and not 1-pyrazolines **6**. This was done by using one-dimensional selective INEPT experiments [17] in the case of 4-(2-chromonyl)-3-(4-methoxyphenyl)-1-pyrazoline **5d** and with a long-range J (C/H) coupling optimized to 7 Hz:

Irradiated proton	Enhanced carbon resonances
H-3' (δ 6.14 ppm)	C-2' (δ 166.2 ppm), C-10' (δ 123.7 ppm) and C-4 (δ 46.3 ppm)
H-3 (δ 5.77 ppm)	C-2' (δ 166.2 ppm), C-1" (δ 129.0 ppm) and C-2",6" (δ 128.1 ppm)

These data are only compatible with the structure shown for 1-pyrazoline **5d**.

EXPERIMENTAL

Measurements.

Melting points are uncorrected and were determined on a Reichert Thermovar apparatus fitted with a microscope. The ^1H and ^{13}C nmr spectra were recorded in diluted deuteriochloroform solutions (*ca.* 0.3%) on a Bruker AMX 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. The ^1H assignments were made using 2D COSY and NOESY (2s for mixing time) experiments, while ^{13}C assignments were made using HETCOR experiments as well as one-dimensional selective INEPT [17] (long-range C/H coupling constants were optimized to 7 Hz). Mass spectra were obtained at 70 eV electron impact ionization using a VG Autospec Q mass spectrometer. Elemental analysis were carried out in the microanalytical laboratory at the Department of Organic Chemistry, Lajos Kossuth University of Debrecen and also in the Chemistry Department at the Coimbra University.

Preparative thin layer chromatography was carried out on silica gel plates (Riedel silica gel 60 DGF_{254}). Column chromatography was also performed on silica gel (Merck silica gel 60, 70-230 mesh). All other chemicals and solvents used herein were obtained from commercial sources and used as received or dried using standard procedures.

Synthesis.

Synthesis of 2'-Cinnamoyloxyacetophenones **1a-e**.

Method A.

Cinnamoyl chloride (2.4 g, 14.4 mmoles) was added to a solution of the appropriate 2'-hydroxyacetophenone (12.0 mmoles) in dry pyridine (30 ml). The solution was stirred at room temperature for 2 hours; after that period the solution was poured into ice and water, and the *p*H adjusted to 4 with hydrochloric acid. The solid obtained was removed by filtration, dissolved in dichloromethane (20 ml) and purified by silica gel column chromatography, using dichloromethane as the eluent. The solvent was evaporated in each case to dryness and the residue was crystallized from ethanol yielding the expected products **1a,e**.

2'-Cinnamoyloxyacetophenone **1a**.

This compound was obtained as white needles, in 94% yield, mp 68-69°; ^1H nmr: δ 2.56 (s, 3H, 2-C*H*$_3$), 6.68 (d, 1H, H-α, J = 16.0 Hz), 7.19 (dd, 1H, H-3', J = 8.0 and 1.1 Hz), 7.33 (dt, 1H, H-5', J = 7.7 and 1.1 Hz), 7.40-7.44 (m, 3H, H-3", 4", 5"), 7.55 (ddd, 1H, H-4', J = 8.0, 7.7 and 1.8 Hz), 7.59 (dd, 2H, H-2", 6", J = 6.0 and 2.3 Hz), 7.83 (dd, 1H, H-6', J = 7.7 and 1.8 Hz), 7.90 (d, 1H, H-β, J = 16.0 Hz); ^{13}C nmr: δ 29.7 (2-*C*H$_3$), 116.7 (C-α), 123.7 (C-3'), 126.0 (C-5'), 128.3 (C-2", 6"), 128.9 (C-3", 5"), 130.0 (C-6'), 131.2 (C-1'), 133.9 (C-1"), 133.2 (C-4'), 130.8 (C-4"), 147.3 (C-β), 149.0 (C-2'), 165.1 (C=O), 197.6 (C-1); ms: (EI) m/z (relative intensity) 266 ($M^{+\cdot}$, 19), 131 (100), 121 (12), 103 (71), 92 (13), 77 (50), 63 (16), 51 (21).

2'-Benzyloxy-6'-cinnamoyloxyacetophenone **1e**.

This compound was obtained as white needles in 89% yield, mp 86-87°; ^1H nmr: δ 2.53 (s, 3H, 2-C*H*$_3$), 5.11 (s, 2H, 6'-OC*H*$_2$C$_6$H$_5$), 6.58 (d, 1H, H-α, J = 16.0 Hz), 6.82 (d, 1H, H-3', J = 8.1 Hz), 6.89 (d, 1H, H-5', J = 8.4 Hz), 7.31-7.42 (m, 9H,

H-4', H-3", 4", 5" and 6'-$OCH_2C_6H_5$), 7.54-7.57 (m, 2H, H-2", 6"), 7.83 (d, 1H, H-β, J = 16.0 Hz); ^{13}C nmr: δ 31.7 (2-CH_3), 70.8 (6'-$OCH_2C_6H_5$), 109.9 (C-5'), 115.4 (C-3'), 116.5 (C-α), 124.9 (C-1'), 127.2 (C-2, 6 of 6'-$OCH_2C_6H_5$), 128.1 (C-4 of 6'-$OCH_2C_6H_5$), 128.3 (C-2", 6"), 128.6 (C-3, 5 of 6'-$OCH_2C_6H_5$), 129.1 (C-3", 5"), 130.7 (C-4"), 130.9 (C-4'), 133.9 (C-1"), 136.0 (C-1 of 6'-$OCH_2C_6H_5$), 147.1 (C-β), 147.6 (C-2'), 156.4 (C-6'), 165.0 (C=O), 200.6 (C-1); ms: (EI) m/z (relative intensity) 372 ($M^{+\cdot}$, 4), 241 (20), 224 (24), 131 (100), 103 (45), 91 (66), 77 (31), 65 (18), 51 (13).

Method B.

The appropriate cinnamic acid (14.4 mmoles) and phosphoryl chloride (3.3 ml, 35.4 mmoles) were added to a solution of 2'-hydroxyacetophenone (1.4 ml, 11.6 mmoles) in dry pyridine (30 ml). The solution was heated at 60° for 3 hours. After that period it was poured into ice and water, and the *p*H adjusted to 4 with hydrochloric acid. The solid obtained was removed by filtration, dissolved in dichloromethane (20 ml) and purified by silica gel column chromatography, using dichloromethane as eluent. The solvent was evaporated in each case to dryness and the residue was crystallized from ethanol to give the expected products **1b-d**.

2'-(4-Chlorocinnamoyloxy)acetophenone **1b**.

This compound was obtained as brown needles in 78% yield, mp 119-120°; ^1H nmr: δ 2.57 (s, 3H, 2-CH_3), 6.66 (d, 1H, H-α, J = 16.0 Hz), 7.19 (dd, 1H, H-3', J = 7.8 and 1.1 Hz), 7.35 (dt, 1H, H-5', J = 7.8 and 1.1 Hz), 7.40 (d, 2H, H-2", 6", J = 8.6 Hz), 7.54 (d, 2H, H-3", 5", J = 8.6 Hz), 7.57 (dt, 1H, H-4', J = 7.8 and 1.7 Hz), 7.84 (dd, 1H, H-6', J = 7.8 and 1.7 Hz), 7.85 (d, 1H, H-β, J = 16.0 Hz); ^{13}C nmr: δ 29.6 (2-CH_3), 117.3 (C-α), 123.7 (C-3'), 126.1 (C-5'), 129.3 (C-2", 6"), 129.6 (C-3", 5"), 130.2 (C-6'), 131.1 (C-1'), 132.5 (C-1"), 133.4 (C-4'), 136.8 (C-4"), 145.8 (C-β), 148.9 (C-2'), 165.0 (C=O), 197.8 (C-1); ms: (EI) m/z (relative intensity) [302 (5), 300 (12), $M^{+\cdot}$], 165 (100), 137 (29), 121 (7), 102 (29), 101 (29), 92 (12), 75 (16), 51 (13).

2'-(4-Methylcinnamoyloxy)acetophenone **1c**.

This compound was obtained as yellow needles in 80% yield, mp 93-94°; ^1H nmr: δ 2.39 (s, 3H, 4"-CH_3), 2.57 (s, 3H, 2-CH_3), 6.63 (d, 1H, H-α, J = 15.9 Hz), 7.19 (dd, 1H, H-3', J = 8.0 and 1.1 Hz), 7.23 (d, 2H, H-3", 5", J = 8.1 Hz), 7.34 (dt, 1H, H-5', J = 7.6 and 1.1 Hz), 7.50 (d, 2H, H-2", 6", J = 8.1 Hz), 7.56 (ddd, 1H, H-4', J = 8.0, 7.6 and 1.7 Hz), 7.83 (dd, 1H, H-6', J = 7.6 and 1.7 Hz), 7.88 (d, 1H, H-β, J = 15.9 Hz); ^{13}C nmr: δ 21.5 (4"-CH_3), 29.9 (2-CH_3), 115.6 (C-α), 123.8 (C-3'), 126.0 (C-5'), 128.4 (C-2", 6"), 129.7 (C-3", 5"), 130.1 (C-6'), 131.2 (C-1"), 131.4 (C-1'), 133.3 (C-4'), 141.4 (C-4"), 147.4 (C-β), 149.2 (C-2'), 165.4 (C=O), 197.8 (C-1); ms: (EI) m/z (relative intensity) 280 ($M^{+\cdot}$, 7), 145 (100), 117 (21), 115 (20), 102 (6), 91 (17), 65 (9).

2'-(4-Methoxycinnamoyloxy)acetophenone **1d**.

This compound was obtained as white needles in 83% yield, mp 103-105°; ^1H nmr: δ 2.57 (s, 3H, 2-CH_3), 3.86 (s, 3H, 4"-OCH_3), 6.54 (d, 1H, H-α, J = 15.9 Hz), 6.94 (d, 2H, H-3", 5", J = 8.8 Hz), 7.19 (dd, 1H, H-3', J = 8.2 and 1.0 Hz), 7.34 (dt, 1H, H-5', J = 7.5 and 1.0 Hz), 7.56 (ddd, 1H, H-4', J = 8.2, 7.5 and 1.7 Hz), 7.56 (d, 2H, H-2", 6", J = 8.8 Hz), 7.83 (dd, 1H, H-6', J = 7.5 and 1.7 Hz), 7.86 (d, 1H, H-β, J = 15.9 Hz); ^{13}C nmr: δ 29.9 (2-CH_3), 55.4 (4"-OCH_3), 114.1 (C-α), 114.4 (C-3", 5"), 123.8 (C-3'), 125.9 (C-5'), 126.7 (C-1"), 130.0 (C-6'), 130.2 (C-2", 6"), 131.5 (C-1'), 133.3 (C-4'), 147.1 (C-β), 149.3 (C-2'), 161.9 (C-4"), 165.5 (C=O), 197.9 (C-1); ms: (EI) m/z (relative intensity) 296 ($M^{+\cdot}$, 9), 161 (100), 133 (21), 118 (8), 103 (5), 92 (7), 77 (9), 63 (15), 51 (7).

General Procedure for the Synthesis of 5-Aryl-3-hydroxy-1-(2-hydroxyphenyl)-2, 4-penten-1-ones **2a-e**.

Sodium hydride (722 mg, 30.0 mmoles) was added to a solution of the appropriate 2'-cinnamoyloxyacetophenone **1a-e** (5.0 mmoles) in dry tetrahdrofuran (100 ml). The mixture was refluxed for 2 hours; after that period the solution was poured into ice and water, and the *p*H adjusted to 4 with hydrochloric acid. The solid obtained was removed by filtration, dissolved in dichloromethane (10 ml) and purified by silica gel column chromatography, using dichloromethane as the eluent. The solvent was evaporated in each case to dryness and the residue was crystallized from ethanol to give the expected products **2a-e**.

3-Hydroxy-1-(2-hydroxyphenyl)-5-phenyl-2, 4-penten-1-one **2a**.

This compound was obtained as yellow needles in 90% yield, mp 123-126° (lit 134° [18]); ^1H nmr: δ 6.32 (s, 1H, H-2), 6.59 (d, 1H, H-4, J = 15.8 Hz), 6.90 (t, 1H, H-5', J = 8.1 Hz), 6.99 (d, 1H, H-3', J = 8.1 Hz), 7.37-7.48 (m, 4H, H-4' and H-3", 4", 5"), 7.70 (d, 1H, H-6', J = 8.1 Hz), 7.54-7.57 (m, 2H, H-2", 6"), 7.65 (d, 1H, H-5, J = 15.8 Hz), 12.23 (s, 1H, 2'-O*H*), 14.65 (s, 1H, 3-O*H*); ^{13}C nmr: δ 97.0 (C-2), 118.7 (C-3'), 119.0 (C-1' and C-5'), 122.1 (C-4), 128.0 (C-2", 6"), 128.5 (C-6'), 129.0 (C-3", 5"), 130.1 (C-4"), 133.5 (C-1"), 135.8 (C-4'), 139.9 (C-5), 162.6 (C-2'), 174.4 (C-3), 196.0 (C-1); ms: (EI) m/z (relative intensity) 266 ($M^{+\cdot}$, 38), 247 (15), 231 (12), 189 (8), 163 (7), 145 (27), 144 (19), 131 (100), 121 (47), 115 (12), 103 (31), 91 (13), 77 (27), 65 (22), 51 (18).

5-(4-Chlorophenyl)-3-hydroxy-1-(2-hydroxyphenyl)-2, 4-penten-1-one **2b**.

This compound was obtained as yellow needles in 77% yield, mp 141-142°; ^1H nmr: δ 6.33 (s, 1H, H-2), 6.57 (d, 1H, H-4, J = 16.0 Hz), 6.91 (ddd, 1H, H-5', J = 7.9, 7.5 and 1.0 Hz), 7.00 (dd, 1H, H-3', J = 8.4 and 1.0 Hz), 7.38 (d, 2H, H-3", 5", J = 8.5 Hz), 7.70 (dd, 1H, H-6, J = 7.9 and 1.6 Hz), 7.50 (d, 2H, H-2", 6", J = 8.5 Hz), 7.61 (d, 1H, H-5, J = 16.0 Hz), 7.49 (ddd, 1H, H-4', J = 8.4, 7.5 and 1.6 Hz), 12.21 (s, 1H, 2'-O*H*), 14.60 (s, 1H, 3-O*H*); ^{13}C nmr: δ 97.2 (C-2), 118.8 (C-3'), 119.0 (C-1'), 119.1 (C-5'), 122.7 (C-4), 128.5 (C-6'), 129.1 (C-2", 6"), 129.2 (C-3", 5"), 133.5 (C-1"), 135.9 (C-4' and C-4"), 138.3 (C-5), 162.6 (C-2'), 173.9 (C-3), 196.1 (C-1); ms: (EI) m/z (relative intensity) [302 (7), 300 (23), $M^{+\cdot}$], 179 (8), 178 (8), 165 (100), 145 (8), 137 (22), 121 (89), 120 (14), 115 (23), 102 (26) 101 (28), 91 (13).

Anal. Calcd. for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36. Found: C, 68.20; H, 4.43.

3-Hydroxy-1-(2-hydroxyphenyl)-5-(4-methylpheny)-2, 4-penten-1-one **2c**.

This compound was obtained as yellow needles in 85% yield, mp 115-116°; ^1H nmr: δ 2.38 (s, 3H, 4"-CH_3), 6.30 (s, 1H, H-2), 6.55 (d, 1H, H-4, J = 15.8 Hz), 6.90 (ddd, 1H, H-5', J = 7.9, 7.7 and 1.0 Hz), 6.98 (dd, 1H, H-3', J = 8.1 and 1.0 Hz), 7.21 (d, 2H, H-3", 5", J = 8.1 Hz), 7.44 (ddd, 1H, H-4', J = 8.1, 7.7 and 1.5 Hz), 7.45 (d, 2H, H-2", 6", J = 8.1 Hz), 7.64 (d, 1H, H-5, J = 15.8 Hz), 7.69 (dd, 1H, H-6', J = 7.9 and 1.5 Hz), 12.27 (s, 1H, 2'-O*H*), 14.69 (s, 1H, 3-O*H*); ^{13}C nmr: δ 21.5 (4"-CH_3), 96.7 (C-2), 118.7 (C-3'), 119.0 (C-1' and C-5'), 121.0 (C-4), 128.0 (C-2", 6"), 128.4 (C-6'), 129.7 (C-3", 5"), 132.2 (C-1"), 135.7 (C-4'), 140.0 (C-5), 140.6 (C-4"),

162.5 (C-2'), 174.8 (C-3), 195.8 (C-1); ms: (EI) m/z (relative intensity) 280 ($M^{+\cdot}$, 46), 261 (17), 245 (16), 159 (35), 145 (100), 121 (41), 117 (25), 115 (26), 105 (11), 91 (23), 77 (11), 65 (19).

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%. Found C, 76.91; H, 5.85.

3-Hydroxy-1-(2-hydroxyphenyl)-5-(4-methoxypheny)-2, 4-penten-1-one **2d**.

This compound was obtained as yellow needles in 94% yield, mp 131-133° (lit 138° [18]); ^{1}H nmr: δ 3.84 (s, 3H, 4"-OC*H*$_3$), 6.27 (s, 1H, H-2), 6.46 (d, 1H, H-4, J = 15.7 Hz), 6.89 (ddd, 1H, H-5', J = 8.1, 7.6 and 1.0 Hz), 6.92 (d, 2H, H-3", 5", J = 8.8 Hz), 6.98 (dd, 1H, H-3', J = 7.6 and 1.0 Hz), 7.44 (dt, 1H, H-4', J = 7.6 and 1.6 Hz), 7.50 (d, 2H, H-2", 6", J = 8.8 Hz), 7.62 (d, 1H, H-5, J = 15.7 Hz), 7.68 (dd, 1H, H-6', J = 8.1 and 1.6 Hz), 12.28 (s, 1H, 2'-O*H*), 14.75 (s, 1H, 3-O*H*); ^{13}C nmr: δ 55.4 (4"-O*C*H$_3$), 96.4 (C-2), 114.4 (C-3", 5"), 118.7 (C-3'), 118.9 (C-5'), 119.1 (C-1'), 119.6 (C-4), 127.7 (C-1"), 128.4 (C-6'), 129.7 (C-2", 6"), 135.6 (C-4'), 139.7 (C-5), 161.3 (C-4"), 162.5 (C-2'), 175.1 (C-3), 195.5 (C-1); ms: (EI) m/z (relative intensity) 296 ($M^{+\cdot}$, 25), 278 (9), 261 (5), 175 (12), 161 (100), 133 (18), 121 (24), 92 (6), 77 (7), 65 (13), 51 (7).

3-Hydroxy-1-(2-benzyloxy-6-hydroxyphenyl)-5-phenyl-2, 4-penten-1-one **2e**.

This compound was obtained as yellow needles in 70% yield, mp 165-167°; ^{1}H nmr: δ 5.15 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.16 (dd, 1H, H-4, J = 16.0 and 1.2 Hz), 6.62 (dd, 1H, H-3', J = 8.3 and 1.0 Hz), 6.49 (dd, 1H, H-5', J = 8.3 and 1.0 Hz), 6.85 (s, 1H, H-2) 7.32 (t, 1H, H-4', J = 8.3 Hz), 7.48 (d, 1H, H-5, J = 16.0 Hz), 7.37-7.54 (m, 10H, H-2", 3", 4", 5", 6" and 2'-OCH$_2$C$_6$*H*$_5$), 12.89 (s, 1H, 6'-O*H*), 14.63 (d, 1H, 3-O*H*, J = 1.2 Hz); ^{13}C nmr: δ 71.2 (2'-O*C*H$_2$C$_6$H$_5$), 102.2 (C-2), 102.8 (C-3'), 110.6 (C-1'), 111.4 (C-5'), 122.8 (C-4), 127.8 (C-2", 6"), 128.1 (C-2, 6 of 2'-OCH$_2$*C*$_6$H$_5$), 128.4 (C-4 of 2'-OCH$_2$*C*$_6$H$_5$), 128.7 (C-3", 5"), 128.8 (C-3, 5 of 2'-OCH$_2$*C*$_6$H$_5$), 131.8 (C-4"), 135.2 (C-4'), 136.0 (C-1" and C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 138.8 (C-5), 159.5 (C-6'), 164.4 (C-2'), 174.1 (C-3), 195.0 (C-1); ms: (EI) m/z (relative intensity) 372 ($M^{+\cdot}$, 14), 354 (22), 281 (18), 226 (15), 223 (10), 194 (10), 137 (15), 131 (63), 103 (24), 91 (100), 77 (13), 65 (14).

Anal. Calcd. for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.33; H, 5.52.

General Procedure for the Synthesis of 2-Styrylchromones **3a-e**.

p-Toluenesulfonic acid (354 mg, 1.6 mmoles) was added to a solution of the appropriate 5-aryl-3-hydroxy-1-(2-hydroxyphenyl)-2, 4-penten-1-one **2a-e** (3.7 mmoles) in dimethyl sulfoxide (100 ml). The solution was heated, under nitrogen, at 100° for 2-3 hours. The disappearance of the starting material was monitored by tlc. The solution was poured into ice and water and the obtained solid removed by filtration. The solid was dissolved in dichloromethane (100 ml) and washed with water; the organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated in each case to dryness and the residue was crystallized from ethanol to give the expected products **3a-e**.

2-Styrylchromone **3a**.

This compound was obtained as white needles in 82% yield, mp 131-133° (lit 133-134° [12]); ^{1}H nmr: δ 6.36 (s, 1H, H-3), 6.79 (d, 1H, H-α, J = 16.0 Hz), 7.42 (dd, 1H, H-6, J = 7.9 and 7.4 Hz), 7.36-7.48 (m, 3H, H-3', 4', 5'), 7.53 (dd, 1H, H-8, J = 8.2 and 1.0 Hz), 7.58 (dd, 2H, H-2', 6', J = 7.7 and 1.7 Hz), 7.61 (d, 1H, H-β, J = 16.0 Hz), 7.68 (ddd, 1H, H-7, J = 8.2, 7.4 and 1.7 Hz), 8.20 (dd, 1H, H-5, J = 7.9 and 1.7 Hz); ^{13}C nmr: δ 110.6 (C-3), 117.9 (C-8), 120.2 (C-α), 124.0 (C-10), 125.1 (C-6), 125.7 (C-5), 127.7 (C-2', 6'), 129.0 (C-3', 5'), 129.9 (C-4'), 133.8 (C-7), 135.0 (C-1'), 137.1 (C-β), 156.0 (C-9), 161.9 (C-2), 178.5 (C-4); ms: (EI) m/z (relative intensity) 248 ($M^{+\cdot}$, 87), 247 (100), 231 (64), 219 (18), 218 (11), 155 (27), 128 (82), 127 (32), 121 (26), 120 (14), 102 (24), 92 (45).

4'-Chloro-2-styrylchromone **3b**.

This compound was obtained as yellow needles in 94% yield, mp 224-226°; ^{1}H nmr: δ 6.34 (s, 1H, H-3), 6.77 (d, 1H, H-α, J = 16.0 Hz), 7.40 (d, 2H, H-3', 5', J = 8.6 Hz), 7.42 (dd, 1H, H-6, J = 7.7 and 6.8 Hz), 7.53 (d, 2H, H-2', 6', J = 8.6 Hz), 7.55 (d, 1H, H-8, J = 7.0 Hz), 7.57 (d, 1H, H-β, J = 16.0 Hz), 7.69 (ddd, 1H, H-7, J = 7.0, 6.8 and 1.6 Hz), 8.20 (dd, 1H, H-5, J = 7.7 and 1.6 Hz); ^{13}C nmr: δ 110.9 (C-3), 117.8 (C-8), 120.8 (C-α), 124.1 (C-10), 125.1 (C-6), 125.7 (C-5), 128.8 (C-2', 6'), 129.2 (C-3', 5'), 133.5 (C-1'), 133.8 (C-7), 135.4 (C-β), 135.7 (C-4'), 155.9 (C-9), 161.3 (C-2), 178.4 (C-4); ms: (EI) m/z (relative intensity) [284 (59), 282 (89), $M^{+\cdot}$], 281 (100), 265 (67), 247 (48), 218 (35), 189 (47), 162 (55), 127 (67), 121 (45), 120 (33), 109 (44), 101 (21), 92 (69), 77 (26), 75 (31), 63 (47), 51 (23).

Anal. Calcd. for $C_{17}H_{11}ClO_2$: C, 72.22; H, 3.92. Found: C, 71.90; H, 3.89.

4'-Methyl-2-styrylchromone **3c**.

This compound was obtained as yellow needles in 90% yield, mp 159-160° (lit 164° [19]); ^{1}H nmr: δ 2.40 (s, 3H, 4'-C*H*$_3$), 6.32 (s, 1H, H-3), 6.76 (d, 1H, H-α, J = 16.0 Hz), 7.24 (d, 2H, H-3', 5', J = 8.1 Hz), 7.40 (ddd, 1H, H-6, J = 7.8, 7.7 and 0.9 Hz), 7.50 (d, 2H, H-2', 6', J = 8.1 Hz), 7.55 (dd, 1H, H-8, J = 8.0 and 0.9 Hz), 7.60 (d, 1H, H-β, J = 16.0 Hz), 7.69 (ddd, 1H, H-7, J = 8.0, 7.7 and 1.7 Hz), 8.20 (dd, 1H, H-5, J = 7.8 and 1.7 Hz); ^{13}C nmr: δ 21.5 (4'-*C*H$_3$), 110.3 (C-3), 117.8 (C-8), 119.2 (C-α), 124.1 (C-10), 124.9 (C-6), 125.6 (C-5), 127.7 (C-2', 6'), 129.7 (C-3', 5'), 132.2 (C-1'), 133.7 (C-7), 137.0 (C-β), 156.0 (C-9), 140.3 (C-4'), 162.0 (C-2), 178.5 (C-4); ms: (EI) m/z (relative intensity) 262 ($M^{+\cdot}$, 72), 261 (100), 247 (35), 245 (42), 218 (25), 189 (13), 169 (22), 142 (38), 141 (37), 121 (19), 115 (35), 109 (13), 92 (22), 63 (21).

4'-Methoxy-2-styrylchromone **3d**.

This compound was obtained as yellow needles in 88% yield, mp 137-138° (lit 139-140° [19]); ^{1}H nmr: δ 3.86 (s, 3H, 4'-OC*H*$_3$), 6.30 (s, 1H, H-3), 6.66 (d, 1H, H-α, J = 15.8 Hz), 6.95 (d, 2H, H-3', 5', J = 8.6 Hz), 7.39 (t, 1H, H-6, J = 7.7 Hz), 7.52 (d, 1H, H-8, J = 7.7 Hz), 7.54 (d, 2H, H-2', 6', J = 8.6 Hz),7.57 (d, 1H, H-β, J = 15.8 Hz), 7.67 (dt, 1H, H-7, J = 7.7 and 1.5 Hz), 8.20 (dd, 1H, H-5, J = 7.7 and 1.5 Hz); ^{13}C nmr: δ 55.4 (4'-O*C*H$_3$), 109.9 (C-3), 114.4 (C-3', 5'), 117.8 (C-α and C-8), 124.1 (C-10), 124.9 (C-6), 125.6 (C-5), 127.7 (C-1'), 129.3 (C-2', 6'), 133.6 (C-7), 136.6 (C-β), 156.0 (C-9), 161.1 (C-4'), 162.2 (C-2), 178.4 (C-4); ms: (EI) m/z (relative intensity) 278 ($M^{+\cdot}$, 100), 277 (69), 263 (16), 261 (47), 249 (16), 247 (14), 234 (14), 219 (12), 207 (14), 185 (14), 178 (17), 158 (44), 143 (12), 128 (10), 125 (12), 121 (11), 115 (28), 92 (14), 65 (10).

5-Benzyloxy-2-styrylchromone **3e**.

This compound was obtained as white needles in 61% yield, mp 179-181° (lit 179-181° [20]); ^{1}H nmr: δ 5.28 (s, 2H, 5-OC*H*$_2$C$_6$H$_5$), 6.24 (s, 1H, H-3), 6.74 (d, 1H, H-α, J = 16.0 Hz), 6.83 (d, 1H, H-6, J = 8.3 Hz), 7.11 (d, 1H, H-8, J = 8.3 Hz), 7.29 (t, 1H, H-4 of 5-OCH$_2$C$_6$*H*$_5$, J = 7.3 Hz), 7.37-7.44 (m, 5H, H-3',

4', 5' and H-3, 5 of 5-$OCH_2C_6H_5$), 7.51 (t, 1H, H-7, J = 8.3 Hz), 7.54 (d, 1H, H-β, J = 16.0 Hz), 7.57 (dd, 2H, H-2', 6', J = 7.7 and 1.4 Hz), 7.63 (d, 2H, H-2, 6 of 5-$OCH_2C_6H_5$, J = 7.3 Hz); ^{13}C nmr: δ 70.8 (5-$OCH_2C_6H_5$), 108.3 (C-6), 110.3 (C-8), 112.3 (C-3), 115.2 (C-10), 119.9 (C-α), 126.6 (C-2, 6 of 5-$OCH_2C_6H_5$), 127.5 (C-2', 6'), 127.6 (C-4 of 5-$OCH_2C_6H_5$), 128.5 (C-3, 5 of 5-$OCH_2C_6H_5$), 128.9 (C-3', 5'), 129.6 (C-4'), 133.5 (C-1'), 133.6 (C-7), 135.0 (C-1'), 136.2 (C-β), 136.6 (C-1 of 5-$OCH_2C_6H_5$), 158.0 (C-9), 158.5 (C-5), 159.5 (C-2), 178.1 (C-4); ms: (EI) m/z (relative intensity) 354 ($M^{+\cdot}$, 91), 353 (17), 277 (14), 264 (11), 248 (55), 247 (49), 231 (21), 218 (24), 91 (100), 65 (20).

General procedure for the Synthesis of 4-Aryl-3-(2-chromonyl)-2-pyrazolines **4a-e**.

A solution of the appropriate 2-styrylchromone **3a-e** (2.0 mmoles) in a 1:3 mixture of chloroform and diethyl ether (100 ml) was saturated (two times for **3b**, three for **3c** and four for **3a,d,e**) with diazomethane (**See Caution**) [21] and allowed to stand at room temperature until the consumption of the starting material as monitored by tlc was completed. The solvent was evaporated to dryness in each case and the residue was crystallized from ethanol yielding, after filtration, compounds **4a-e**. The composition of each mother liquor was analysed by preparative silica gel thin layer chromatography, yielding 3-(2-chromonyl)-4-aryl-2-pyrazolines **4a-e** (with higher R_f value) and of 4-(2-chromonyl)-3-aryl-1-pyrazolines **5a-e**. The overall yields are as follows: **4a**, 68%; **4b**, 73%; **4c**, 85%; **4d**, 92%; **4e**, 78% and **5a**, 0.5%; **5b**, 1%; **5c**, 2%; **5d**, 3%; **5e**, 5%.

3-(2-Chromonyl)-4-phenyl-2-pyrazoline **4a**.

This compound was obtained as yellow needles, mp 167-168°; ^1H nmr: δ 3.72 (dd, 1H, H-5 *cis*, J = 10.0 and 5.5 Hz), 4.14 (dd, 1H, H-5 *trans*, J = 11.4 and 10.0 Hz), 4.46 (dd, 1H, H-4, J = 11.4 and 5.5 Hz), 6.34 (s, 1H, H-3'), 6.40 (s broad, 1H, 1-N*H*), 7.23-7.37 (m, 6H, H-6' and 4-C_6H_5), 7.44 (d, 1H, H-8', J = 7.9 Hz), 7.62 (dt, 1H, H-7', J = 7.9 and 1.6 Hz), 8.11 (dd, 1H, H-5', J = 8.0 and 1.6 Hz); ^{13}C nmr: δ 49.5 (C-4), 58.3 (C-5), 109.7 (C-3'), 118.1 (C-8'), 124.1 (C-10'), 125.0 (C-6'), 125.5 (C-5'), 127.3 (C-2", 6"), 127.7 (C-4"), 129.2 (C-3", 5"), 133.8 (C-7'), 139.8 (C-1"), 146.4 (C-3), 156.1 (C-9'), 157.5 (C-2'), 178.0 (C-4'); ms: (EI) m/z (relative intensity) 290 ($M^{+\cdot}$, 100), 289 (27), 261 (44), 247 (13), 233 (9), 213 (10), 204 (12), 199 (23), 186 (9), 169 (16), 146 (18), 141 (39), 121 (40), 118 (26), 115 (19), 104 (76), 92 (26), 91 (35), 77 (19), 63 (24), 51 (16).

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.06; H, 4.72; N, 9.23.

3-(2-Chromonyl)-4-(4-chlorophenyl)-2-pyrazoline **4b**.

This compound was obtained as yellow needles, mp 168-170°; ^1H nmr: δ 3.70 (dd, 1H, H-5 *cis*, J = 10.0 and 5.1 Hz), 4.13 (ddd, 1H, H-5 *trans*, J = 11.4, 10.0 and 2.6 Hz), 4.45 (dd, 1H, H-4, J = 11.4 and 5.1 Hz), 6.36 (s, 1H, H-3'), 6.43 (s broad, 1H, 1-N*H*), 7.22 (d, 2H, H-2", 6", J = 8.4 Hz), 7.30 (d, 2H, H-3", 5", J = 8.4 Hz), 7.36 (t, 1H, H-6', J = 7.8 Hz), 7.43 (d, 1H, H-8', J = 7.8 Hz), 7.64 (dt, 1H, H-7', J = 7.8 and 1.5 Hz), 8.13 (dd, 1H, H-5', J = 7.8 and 1.5 Hz); ^{13}C nmr: δ 48.8 (C-4), 58.1 (C-5), 109.6 (C-3'), 118.0 (C-8'), 124.1 (C-10'), 125.2 (C-6'), 125.6 (C-5'), 128.6 (C-2", 6"), 129.4 (C-3", 5"), 133.6 (C-4"), 133.9 (C-7'), 138.2 (C-1"), 146.1 (C-3), 156.0 (C-9'), 157.3 (C-2'), 177.9 (C-4'); ms: (EI) m/z (relative intensity) [326 (44), 324 (100), $M^{+\cdot}$], 323 (11), 295 (25), 289 (7), 261 (7), 232 (24), 213 (8), 199 (28), 186 (8), 175 (17), 152 (11), 146 (14), 140 (18), 138 (25), 127 (19), 121 (38), 117 (11), 104 (17), 92 (42), 89 (67), 77 (11), 63 (39), 51 (20).

Anal. Calcd. for $C_{18}H_{13}ClN_2O_2$: C, 66.57; H, 4.04; N, 8.63. Found: C, 66.55; H, 4.12; N, 8.28.

3-(2-Chromonyl)-4-(4-methylphenyl)-2-pyrazoline **4c**.

This compound was obtained as yellow needles, mp 191-192°; ^1H nmr: δ 2.31 (s, 3H, 4"-CH_3), 3.70 (dd, 1H, H-5 *cis*, J = 10.0 and 5.6 Hz), 4.12 (dd, 1H, H-5 *trans*, J = 11.4 and 10.0 Hz), 4.43 (dd, 1H, H-4, J = 11.4 and 5.6 Hz), 6.31 (s, 2H, H-3' and 1-N*H*), 7.13 (AB, 2H, H-3", 5", J = 8.3 Hz), 7.16 (AB, 2H, H-2", 6", J = 8.3 Hz), 7.34 (dt, 1H, H-6', J = 7.5 and 1.0 Hz), 7.47 (d, 1H, H-8', J = 7.5 Hz), 7.63 (dt, 1H, H-7', J = 7.5 and 1.6 Hz), 8.11 (dd, 1H, H-5', J = 7.5 and 1.6 Hz); ^{13}C nmr: δ 21.1 (4"-CH_3), 49.2 (C-4), 58.3 (C-5), 109.9 (C-3'), 118.1 (C-8'), 124.1 (C-10'), 125.0 (C-6'), 125.5 (C-5'), 127.2 (C-2", 6"), 129.9 (C-3", 5"), 133.8 (C-7'), 136.7 (C-1"), 137.5 (C-4"), 146.6 (C-3), 156.1 (C-9'), 157.5 (C-2'), 178.1 (C-4'); ms: (EI) m/z (relative intensity) 304 ($M^{+\cdot}$, 100), 303 (19), 289 (13), 275 (35), 261 (12), 247 (7), 213 (7), 199 (7), 183 (12), 155 (27), 146 (10), 132 (12), 130 (12), 121 (24), 118 (30), 105 (27), 92 (16), 91 (16), 77 (17), 63 (15), 51 (7).

Anal. Calcd. for $C_{19}H_{16}N_2O_2 \cdot H_2O$: C, 70.79; H, 5.63; N, 8.69. Found: C, 71.04; H, 5.75; N, 8.44.

3-(2-Chromonyl)-4-(4-methoxyphenyl)-2-pyrazoline **4d**.

This compound was obtained as yellow needles, mp 149-150°; ^1H nmr: δ 3.68 (dd, 1H, H-5 *cis*, J = 10.0 and 5.5 Hz), 3.77 (s, 3H, 4"-OCH_3), 4.11 (dd, 1H, H-5 *trans*, J = 11.3 and 10.0 Hz), 4.42 (dd, 1H, H-4, J = 11.3 and 5.5 Hz), 6.33 (s, 1H, H-3'), 6.39 (s, 1H, 1-N*H*), 6.85 (d, 2H, H-3", 5", J = 8.6 Hz), 7.16 (d, 2H, H-2", 6", J = 8.6 Hz), 7.34 (t, 1H, H-6', J = 7.8 Hz), 7.46 (d, 1H, H-8', J = 7.8 Hz), 7.63 (t, 1H, H-7', J = 7.8 Hz), 8.12 (d, 1H, H-5', J = 7.8 Hz); ^{13}C nmr: δ 48.9 (C-4), 55.3 (4"-OCH_3), 58.3 (C-5), 109.8 (C-3'), 114.6 (C-3", 5"), 118.1 (C-8'), 124.1 (C-10'), 125.0 (C-6'), 125.5 (C-5'), 128.4 (C-2", 6"), 131.8 (C-1"), 133.8 (C-7'), 146.7 (C-3), 156.1 (C-9'), 157.5 (C-2'), 159.1 (C-4"), 178.1 (C-4'); ms: (EI) m/z (relative intensity) 320 ($M^{+\cdot}$, 68), 319 (21), 291 (51), 276 (29), 248 (12), 199 (13), 171 (16), 146 (54), 134 (79), 128 (11), 121 (100), 117 (9), 115 (11), 105 (14), 92 (47), 91 (67), 77 (50), 63 (39), 51 (22).

Anal. Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75. Found: C, 71.53; H, 5.21; N, 8.39.

3-(5-Benzyloxy-2-chromonyl)-4-phenyl-2-pyrazoline **4e**.

This compound was obtained as yellow needles, mp 213-215°; ^1H nmr: δ 3.68 (dd, 1H, H-5 *cis*, J = 10.2 and 5.6 Hz), 4.10 (dd, 1H, H-5 *trans*, J = 11.1 and 10.2 Hz), 4.42 (dd, 1H, H-4, J = 11.1 and 5.6 Hz), 5.22 (s, 2H, 5'-$OCH_2C_6H_5$), 6.18 (s, 1H, H-3'), 6.31 (s broad, 1H, 1-N*H*), 6.78 (d, 1H, H-6', J = 8.4 Hz), 7.08 (d, 1H, H-8', J = 8.4 Hz), 7.24-7.31 (m, 5H, 4-C_6H_5), 7.36 (t, 3H, H-3, 4, 5 of 5'-$OCH_2C_6H_5$, J = 6.2 Hz), 7.45 (t, 1H, H-7', J = 8.4 Hz), 7.58 (d, 2H, H-2, 6 of 5'-$OCH_2C_6H_5$, J = 6.2 Hz); ^{13}C nmr: δ 49.6 (C-4), 58.1 (C-5), 70.7 (5'-$OCH_2C_6H_5$), 108.2 (C-6'), 110.5 (C-8'), 111.7 (C-3'), 115.2 (C-10'), 126.5 (C-2, 6 of 5'-$OCH_2C_6H_5$), 127.3 (C-4"), 127.5 (C-2", 6"), 127.7 (C-4 of 5'-$OCH_2C_6H_5$), 128.5 (C-3, 5 of 5'-$OCH_2C_6H_5$), 129.2 (C-3", 5"), 133.7 (C-7'), 136.5 (C-1 of 5'-$OCH_2C_6H_5$), 139.7 (C-1"), 146.3 (C-3), 155.1 (C-2'), 158.1 (C-9'), 158.4 (C-5'), 177.6 (C-4'); ms: (EI) m/z (relative intensity) 396 ($M^{+\cdot}$, 52), 395 (10), 313 (10), 306 (15), 290 (25), 254 (12), 169 (64), 161 (22), 153 (16), 139 (13), 121 (12), 109 (39), 91 (100), 77 (14), 63 (15), 51 (14).

Anal. Calcd. for $C_{25}H_{20}N_2O_3$ C, 75.74; H, 5.09; N, 7.07%. Found: C, 75.67; H, 5.18; N, 6.65.

4-(2-Chromonyl)-3-phenyl-1-pyrazoline **5a**.

This compound was obtained as yellowish oil; ^{1}H nmr: δ 3.10 (dt, 1H, H-4, J = 9.5 and 7.1 Hz), 4.85 (ddd, 1H, H-5 *trans*, J = 17.9, 7.1 and 2.2 Hz), 5.17 (ddd, 1H, H-5 *cis*, J = 17.9, 9.5 and 2.2 Hz), 5.83 (dt, 1H, H-3, J = 7.1 and 2.2 Hz), 6.15 (s, 1H, H-3'), 7.17 (dd, 2H, H-2", 6", J = 7.5 and 1.7 Hz), 7.36-7.45 (m, 5H, H-6', 8' and H-3", 4", 5"), 7.69 (ddd, 1H, H-7', J = 8.1, 7.5 and 1.6 Hz), 8.18 (dd, 1H, H-5', J = 8.2 and 1.6 Hz); ^{13}C nmr: δ 46.1 (C-4), 80.7 (C-5), 95.6 (C-3), 110.9 (C-3'), 117.8 (C-8'), 123.7 (C-10'), 125.5 (C-6'), 125.8 (C-5'), 126.9 (C-2", 6"), 128.6 (C-4"), 129.3 (C-3", 5"), 134.0 (C-7'), 137.0 (C-1"), 156.3 (C-9'), 166.0 (C-2'), 177.6 (C-4'); ms: (EI) m/z (relative intensity) 290 ($M^{+\cdot}$, 94), 262 (65), 261 (72), 247 (32), 245 (26), 233 (15), 215 (8), 185 (21), 173 (32), 160 (17), 141 (63), 131 (30), 121 (100), 118 (41), 115 (51), 104 (40), 92 (55), 77 (65), 63 (48), 51 (40).

4-(2-Chromonyl)-3-(4-chlorophenyl)-1-pyrazoline **5b**.

This compound was obtained as yellowish oil; ^{1}H nmr: δ 3.04 (dt, 1H, H-4, J = 9.5 and 7.3 Hz), 4.84 (ddd, 1H, H-5 *trans*, J = 17.9, 7.3 and 2.3 Hz), 5.19 (ddd, 1H, H-5 *cis*, J = 17.9, 9.5 and 2.3 Hz), 5.78 (dt, 1H, H-3, J = 7.3 and 2.3 Hz), 6.15 (s, 1H, H-3'), 7.12 (d, 2H, H-2", 6", J = 8.4 Hz), 7.40 (d, 2H, H-3", 5", J = 8.4 Hz), 7.40 (d, 1H, H-8', J = 8.3 Hz), 7.43 (dd, 1H, H-6', J = 7.9 and 7.8 Hz), 7.69 (ddd, 1H, H-7', J = 8.3, 7.9 and 1.7 Hz), 8.19 (dd, 1H, H-5', J = 7.8 and 1.7 Hz); ^{13}C nmr: δ 46.3 (C-4), 80.9 (C-5), 94.6 (C-3), 111.0 (C-3'), 117.8 (C-8'), 123.7 (C-10'), 125.6 (C-6'), 125.9 (C-5'), 128.1 (C-2", 6"), 129.5 (C-3", 5"), 134.1 (C-7'), 135.5 (C-1"), 134.7 (C-4"), 156.2 (C-9'), 165.5 (C-2'), 177.5 (C-4'); ms: (EI) m/z (relative intensity) [326 (21), 324 (37), $M^{+\cdot}$], 296 (50), 295 (39), 281 (29), 279 (23), 267 (10), 261 (45), 231 (10), 218 (12), 203 (13), 185 (24), 176 (33), 175 (24), 171 (23), 160 (21), 149 (12), 141 (58), 125 (17), 121 (100), 115 (36), 101 (19), 92 (36), 89 (31), 77 (15), 63 (30), 51 (15).

4-(2-Chromonyl)-3-(4-methylphenyl)-1-pyrazoline **5c**.

This compound was obtained as yellowish oil; ^{1}H nmr: δ 2.37 (s, 3H, 4"-CH_3), 3.07 (dt, 1H, H-4, J = 9.5 and 7.0 Hz), 4.83 (ddd, 1H, H-5 *trans*, J = 17.9, 7.0 and 2.2 Hz), 5.15 (ddd, 1H, H-5 *cis*, J = 17.9, 9.5 and 2.2 Hz), 5.79 (dt, 1H, H-3, J = 7.0 and 2.2 Hz), 6.14 (s, 1H, H-3'), 7.05 (d, 2H, H-2", 6", J = 8.0 Hz), 7.21 (d, 2H, H-3", 5", J = 8.0 Hz), 7.40 (d, 1H, H-8', J = 8.4 Hz), 7.42 (ddd, 1H, H-6', J = 8.1, 7.2 and 0.9 Hz), 7.68 (ddd, 1H, H-7', J = 8.4, 7.2 and 1.7 Hz), 8.17 (dd, 1H, H-5', J = 8.1 and 1.7 Hz); ^{13}C nmr: δ 21.2 (4"-*C*H$_3$), 46.2 (C-4), 80.6 (C-5), 95.5 (C-3), 110.8 (C-3'), 117.9 (C-8'), 123.7 (C-10'), 125.5 (C-6'), 125.8 (C-5'), 126.7 (C-2", 6"), 129.9 (C-3", 5"), 134.0 (C-7' and C-1"), 138.5 (C-4"), 156.3 (C-9'), 166.3 (C-2'), 177.6 (C-4'); ms: (EI) m/z (relative intensity) 304 ($M^{+\cdot}$, 73), 276 (61), 261 (44), 247 (14), 196 (32), 182 (50), 161 (20), 155 (22), 147 (13), 141 (32), 131 (20), 121 (86), 119 (100), 115 (33), 105 (30), 92 (55), 91 (76), 77 (34), 63 (38), 51 (22).

4-(2-Chromonyl)-3-(4-methoxyphenyl)-1-pyrazoline **5d**.

This compound was obtained as yeellowish oil; ^{1}H nmr: δ 3.06 (dt, 1H, H-4, J = 9.5 and 7.1 Hz), 3.82 (s, 3H, 4"-OCH_3), 4.82 (ddd, 1H, H-5 *trans*, J = 17.8, 7.1 and 2.2 Hz), 5.11 (ddd, 1H, H-5 *cis*, J = 17.8, 9.5 and 2.2 Hz), 5.77 (dt, 1H, H-3, J = 7.1 and 2.2 Hz), 6.14 (s, 1H, H-3'), 6.93 (d, 2H, H-3", 5", J = 7.7 Hz), 7.09 (d, 2H, H-2", 6", J = 7.7 Hz), 7.40 (d, 1H, H-8', J = 8.3 Hz), 7.42 (t, 1H, H-6', J = 8.1 Hz), 7.68 (ddd, 1H, H-7', J = 8.3, 8.1 and 1.5 Hz), 8.18 (dd, 1H, H-5', J = 8.1 and 1.5 Hz); ^{13}C nmr: δ 46.3 (C-4), 55.4 (4"-O*C*H$_3$), 80.6 (C-5), 95.3 (C-3), 110.8 (C-3'), 114.6 (C-3", 5"), 117.8 (C-8'), 123.7 (C-10'), 125.5 (C-6'), 125.8 (C-5'), 128.1 (C-2", 6"), 129.0 (C-1"), 134.0 (C-7'), 156.3 (C-9'), 159.8 (C-4"), 166.2 (C-2'), 177.6 (C-4'); ms: (EI) m/z (relative intensity) 320 ($M^{+\cdot}$, 44), 292 (89), 291 (78), 277 (46), 261 (36), 199 (13), 184 (67), 172 (68), 171 (52), 157 (37), 147 (31), 141 (21), 132 (30), 129 (52), 128 (54), 121 (100), 115 (39), 103 (18), 102 (19), 92 (52), 91 (43), 77 (47), 63 (41), 51 (34).

4-(5-Benzyloxy-2-Chromonyl)-3-phenyl-1-pyrazoline **5e**.

This compound was obtained as yellowish oil; ^{1}H nmr: δ 3.03 (dt, 1H, H-4, J = 9.5 and 7.2 Hz), 4.81 (ddd, 1H, H-5 *trans*, J = 17.9, 7.2 and 2.2 Hz), 5.14 (ddd, 1H, H-5 *cis*, J = 17.9, 9.5 and 2.2 Hz), 5.28 (s, 2H, of 5'-OCH_2C$_6$H$_5$), 5.78 (dt, 1H, H-3, J = 7.2 and 2.2 Hz), 6.05 (s, 1H, H-3'), 6.85 (d, 1H, H-6', J = 8.3 Hz), 6.95 (d, 1H, H-8', J = 8.3 Hz), 7.17 (dd, 2H, H-2", 6", J = 7.6 and 1.7 Hz), 7.29 (t, 1H, H-4", J = 7.2 Hz), 7.37-7.41 (m, 5H, H-3", 5" and H-3, 4, 5 of 5'-OCH$_2$C$_6$*H*$_5$), 7.50 (t, 1H, H-7', J = 8.3 Hz), 7.59 (d, 2H, H-2, 6 of 5'-OCH$_2$C$_6$*H*$_5$, J = 7.3 Hz); ^{13}C nmr: δ 45.6 (C-4), 70.9 (5'-OCH$_2$C$_6$H$_5$), 80.5 (C-5), 95.3 (C-3), 108.8 (C-6'), 110.1 (C-8'), 112.4 (C-3'), 114.8 (C-10'), 126.6 (C-2, 6 of 5'-OCH$_2$C$_6$H$_5$), 126.8 (C-2", 6"), 127.7 (C-4"), 128.6 (C-3, 4, 5 of 5'-OCH$_2$C$_6$H$_5$), 129.3 (C-3", 5"), 133.7 (C-7'), 136.4 (C-1 of 5'-OCH$_2$C$_6$H$_5$), 137.1 (C-1"), 158.3 (C-9'), 158.6 (C-5'), 163.5 (C-2'), 177.2 (C-4'); ms: (EI) m/z (relative intensity) 396 ($M^{+\cdot}$, 20), 368 (40), 367 (11), 291 (11), 262 (32), 261 (17), 142 (14), 141 (14), 121 (26), 115 (18), 105 (14), 91 (100), 77 (22), 65 (49), 51 (24).

Acknowledgements.

Thanks are due to the University of Aveiro and JNICT, Lisbon, for funding the Research Unit No. 62/94 and also to the Portuguese-Hungarian Intergovernmental Science and Technology Cooperation Programme (Project No. 423/OMFB/SCIAE and P-2/96). One of us (L. M. P. M. A.) is also grateful to JNICT/PRAXIS XXI for the award of a grant (BTL/6303/95).

REFERENCES AND NOTES

* Author to whom correspondence should be addressed.

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

[2] H. Pechmann, *Ber.*, **27**, 1890 (1894).

[3] J. Azzarello, *Gazz. Chim. Ital.*, **36**, 50 (1906).

[4] A. L. Tókés, A. Szöllósy, G. Tóth, and A. Lévai, *Acta Chim. Hung.*, **112**, 335 (1983).

[5] A. Lévai, *Monatsh. Chem.*, **126**, 1245 (1995).

[6] A. Lévai, Z. Cziáky, J. Jekő and Z. Szabo, *Indian J. Chem.*, **35B**, 1091 (1996).

[7] G. Tóth, A. Szöllósy, A. Lévai and G. Kotovych, *J. Chem. Soc., Perkin Trans. 2*, 1895 (1986).

[8] G. Tóth, A. Lévai, and H. Duddeck, *Magn. Reson. Chem.*, **30**, 235 (1992).

[9] G. Tóth, A. Lévai, A. Szöllósy and H. Duddeck, *Tetrahedron*, **49**, 863 (1993).

[10] A. Lévai and G. Tóth, *Trends Heterocyclic Chemistry*, **4**, 89 (1995).

[11] W. A. Price, A. M. S. Silva and J. A. S. Cavaleiro, *Heterocycles*, **36**, 2601 (1993).

[12] J. K. Makrandi and V. Kumari, *Synth. Commun*, **19**, 1919 (1989).

[13] Although all chiral compounds described in this paper are racemates, owing to a better understanding of the stereochemistry, only one enantiomer is illustrated.

[14] The identification H-4 *trans* and H-4 *cis* in the case of 2-pyrazolines **4** is to show their stereochemistry relatively to H-3. However, in the case of 1-pyrazolines **5** H-5 *trans* and H-5 *cis* is to show their stereochemistry relatively to H-4.

[15] J. A. Alexandrova, N. A. Dorofeeva, A. V. Chernova and U. K. Khairullin, *Zh. Org. Khim.*, **14**, 1874 (1978).

[16] J. A. S. Cavaleiro, J. Elguero, M. L. Jimeno and A. M. S. Silva, *Chem. Letters*, 445 (1991).

[17] A. Bax, *J. Magn. Reson.*, **57**, 314 (1984).

[18] H. L. Gaggad, K. N. Wadodkar and B. J. Ghiya, *Indian J. Chem.*, **24B**, 1244 (1985).

[19] I. Yokoe, K. Higuchi, Y. Shirataki and M. Komatsu, *Chem. Pharm. Bull.*, **29**, 2670 (1981).

[20] D. C. G. A. Pinto, A. M. S. Silva and J. A. S. Cavaleiro, *J. Heterocyclic Chem.*, **33**, 1887 (1996).

[21] Diazomethane was bubbled through the flask containing the solution of each 2-styrylchromone **3a-e**. The saturation of this solution with diazomethane was complete when another flask, connected to the first one, containing ethyl ether became yellow. **Caution**. Diazomethane is a highly toxic, explosive gas. See: The Merck Index, Eleventh Edition, Published by Merck and Co., Inc., Rahway, NJ, USA, Compound No. 2983, 1989, p 473.