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TETRAHEDRON

Synthesis and Molecular Structure of 3-(2-Benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles. Reaction of 2-Styrylchromones and Hydrazine Hydrate

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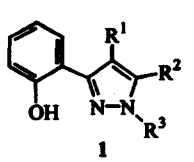
Abstract: 3-(2-Benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a-e** were prepared from the reaction of 2-styrylchromones and hydrazine hydrate. 3-(2-Benzyloxy-6-hydroxyphenyl)-5-(2-phenylethyl)-pyrazoles **8a,d,e** and 3-(2-benzyloxy-β,6-dihydroxystyryl)-5-aryl-2-pyrazolines **9a-e** were also obtained as by-products. The crystal and molecular structure of two 3-(2-benzyloxy-6-hydroxyphenyl)-5-styryl-pyrazoles **7a,b** have been determined by X-Ray analysis. Although the substitution of an hydrogen by a methyl group on the double bond of the styryl moiety seems to be a minor perturbation, it produces drastic changes in the crystal packing where only one conformer is present. The OH group is involved as donor of an intramolecular hydrogen bond and the NH group is responsible for the formation of chains via intermolecular hydrogen bonds. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Pyrazoles are widely studied five-membered heterocyclic compounds and their syntheses have been extensively studied.[1] Such studies have been stimulated by some promising pharmacological, agrochemical and analytical applications.[1] For instance, in recent years the use of *o*-hydroxyphenylpyrazoles as ultraviolet stabilisers,[2] as analytical reagents in the complexation of transition metal ions[3] and also as analgesic agents and platelet aggregation inhibitors[4] have been described.

These applications and our interest on the preparation and molecular structure determination of *o*-hydroxy-phenylpyrazoles,[5] prompted us to devote our attention to a new type of these derivatives, the 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles. These compounds were obtained by the reaction of 2-styrylchromones and hydrazine hydrate.[6] The reaction of hydrazine hydrate with chromone, 2-methyl- and 2-phenylchromone was firstly studied in the 1940s and 1950s. The research groups involved in these studies agreed that the reaction products were 5(3)-*o*-hydroxyphenylpyrazoles **1a-c** and **2a-c** and not the hydrazones of the chromones as previously believed.[7] In 1986, Takagi *et al.*[4] studied the reaction of 3-nitro-2-methylchromone with hydrazine hydrate and methylhydrazine and established that the products obtained were 3-*o*-hydroxyphenylpyrazoles **1d,e**.



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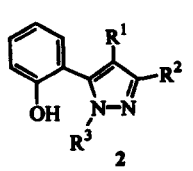
a) $R^1 = R^2 = R^3 = H$
b) $R^1 = R^3 = H$, $R^2 = CH_3$
c) $R^1 = R^3 = H$, $R^3 = C_6H_5$
d) $R^1 = NO_2$, $R^2 = CH_3$, $R^3 = H$
e) $R^1 = NO_2$, $R^2 = R^3 = CH_3$



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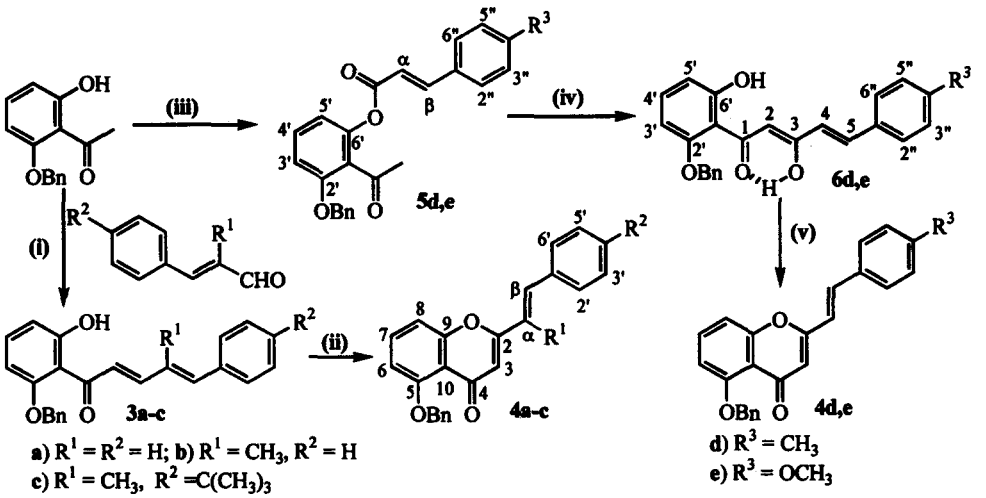
RESULTS AND DISCUSSION

Chemistry

2-Styrylchromone derivatives. 5-Benzyloxy-2-styrylchromones **4a-e** were prepared in good overall yields by two different methods, depending on the available starting materials (Scheme 1). 2-Styrylchromones **4a-c** were prepared by oxidative cyclization of the 2'-benzyloxy-6'-hydroxycinnamylideneacetophenones **3a-c**, obtained by base-catalysed aldol reaction of cinnamaldehydes and 2'-benzyloxy-6'-hydroxyacetophenone, with a catalytic amount of iodine in DMSO at reflux, for 30 min.[8] 2-Styrylchromones **4d,e** were prepared by a modification of the Baker-Venkataraman procedure.[9] This method involves the cinnamoylation of the 2'-benzyloxy-6'-hydroxyacetophenone, the intramolecular Claisen condensation of 2'-benzyloxy-6'-cinnamoyloxyacetophenones **5d,e** and the cyclodehydration of 5-aryl-1-(2-benzyloxy-6-hydroxyphenyl)-3-hydroxy-2,4-penten-1-ones **6d,e** into chromones **4d,e** (Scheme 1).

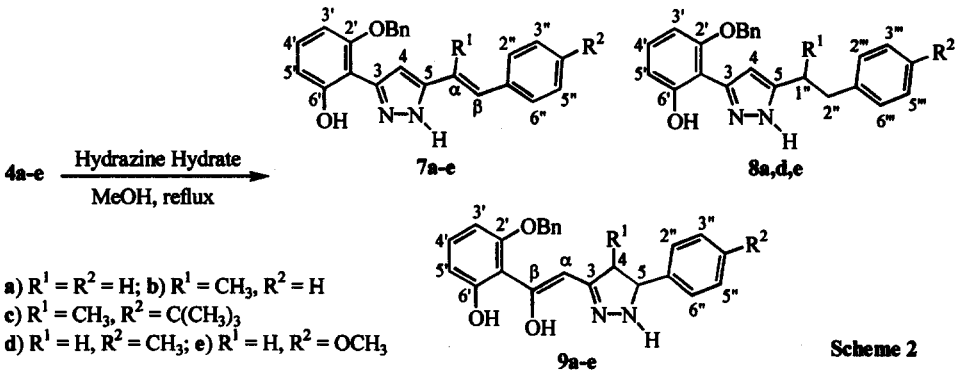


Scheme 1: (i) $NaOH/H_2O$, MeOH, room temp. (67-83%); (ii) $DMSO/I_2$, reflux (78-93%); (iii) R^3-C_6H_4-CH=CH-CO_2H, $POCl_3$, pyridine, 60°C (82-89%); (iv) NaH, THF, reflux (70-73%); (v) $DMSO/I_2$, 100°C (57-60%)

Pyrazole derivatives. Reactions of 5-benzyloxy-2-styrylchromones **4a-e** with an excess of hydrazine hydrate, in methanol at reflux, gave 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a-e** in moderate yields (41-70%). The chromatographic analysis of the crystallisation mother liquors of the pyrazoles **7a-e** still revealed the presence of **7a-e** and small amounts of 3-(2-benzyloxy-6-hydroxyphenyl)-5-(2-phenylethyl)pyrazoles **8a,d,e** and 3-(2-benzyloxy-β,6-dihydroxystyryl)-5-aryl-2-pyrazolines **9a-e** (Scheme 2).

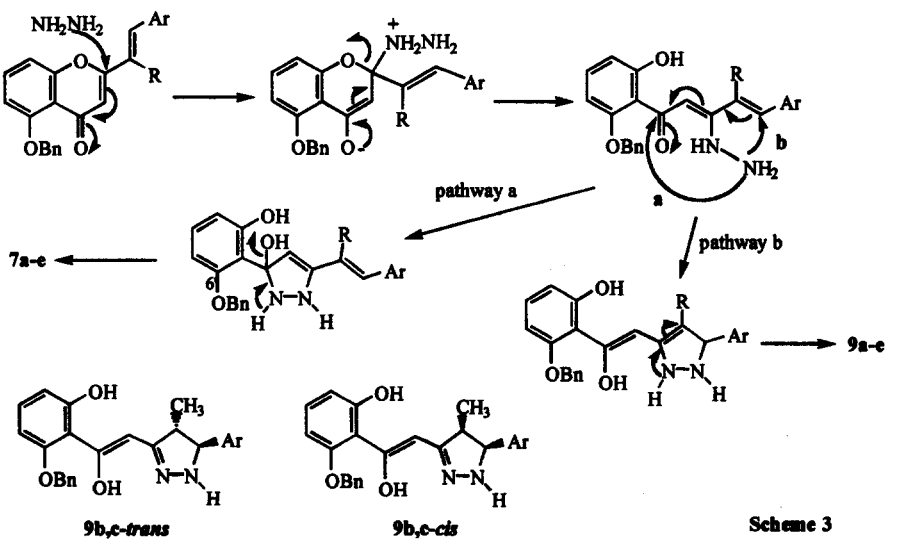
The quantities of the by-products **8a,d,e** increased when the amount of hydrazine hydrate was greater and/or the refluxing time was longer than that necessary for the disappearance of the starting chromones **4a,d,e**. These results indicate that under the reaction conditions, the 3-(2-benzyloxy-6-hydroxyphenyl)-5-(2-phenylethyl)pyrazoles **8a,d,e** were obtained by reduction of 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a,d,e**. It is known that diazene (N_2H_2), formed by oxidation of hydrazine, is an alkene reducting agent.[10] In the case of

3-(2-benzyloxy-6-hydroxyphenyl)-5-α-methylstyrylpyrazoles **7b,c** there was no reduction of their Cα=Cβ double bonds. These results agree with reported studies which indicate that the reactivity of a double bond decreases as the degree of its alkyl substitution increases.[11]



Scheme 2

The formation of 3-(2-benzyloxy-β,6-dihydroxystyryl)-5-aryl-2-pyrazolines **9a-e** can be explained taking into consideration the reaction mechanism of the reaction between chromones and hydrazines (Scheme 3).[4,12] After nucleophilic attack at C-2 of the 2-styrylchromone and subsequent ring opening, there are two possible intramolecular reactions: i) the reaction of the hydrazine and the carbonyl group, leading to the formation of 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a-e** (pathway **a** Scheme 3); and ii) the conjugate addition of the hydrazine to C-γ of the α,β,γ,δ-unsaturated system, giving 3-(2-benzyloxy-β,6-hydroxystyryl)-5-aryl-2-pyrazolines **9a-e** (pathway **b** Scheme 3). In the case of 2-pyrazolines **9b,c** a mixture of diastereomers, *cis* and *trans*, was obtained[13] (Scheme 3). Their separation by thin-layer chromatography was not successful, even after several attempts.



Scheme 3

NMR Spectroscopy

2-Styrylchromones and intermediate compounds. The most important features of the ^{1}H NMR spectra of 5-aryl-1-(2-benzyloxy-6-hydroxyphenyl)-3-hydroxy-2,4-penten-1-ones **6d,e** are the resonances at δ 6.83 (H-2), 12.91-12.93 (6'-O*H*) and 14.69-14.77 ppm (3-O*H*). These data indicate that these compounds exist only in the enolic form presented in Scheme 1.

In the structural characterisation of 2-styrylchromones **4a-e**, it is important to report from their ^{1}H NMR spectra the singlets at δ 5.26-5.30 and 6.20-6.43 ppm, corresponding to the resonances of benzylic C*H*$_2$ and H-3, respectively. In these spectra, the resonances assigned to H-β (δ 7.49-7.63 ppm) and C-β (δ 133.0-136.2 ppm) appeared at higher frequency values than that of H-α (δ 6.60-6.68 ppm) and C-α (δ 117.7-128.0 ppm), due to the mesomeric deshielding effect of the carbonyl group.

The values of the vinylic coupling constants (^3J ~16 Hz) in the case of compounds **4a,d,e**, **5d,e** and **6d,e**, indicate the *trans* configuration for this vinylic moiety. On the other hand, the stereochemistry of 2-styryl-chromones **4a-e** was established using NOESY experiments. NOE cross peaks were observed between H-α (**4a,d,e**) or α-CH$_3$ (**4b,c**) and H-3 and H-2',6', thus demonstrating the *trans* configuration of these compounds as depicted in Scheme 1.

Pyrazole derivatives. In the ^{1}H NMR spectra of 3-(2-benzyloxy-6-hydroxyphenyl)-5-substituted pyrazoles **7a-e** and **8a,d,e** there are two deshielded broad singlets at δ 9.65-10.22 and 11.79-12.02 ppm, which are due to the N*H* and 6'-O*H* resonances. The high frequency value of the hydroxylic proton is due to the intramolecular hydrogen bond with N2 (see the tautomer represented in Scheme 2).

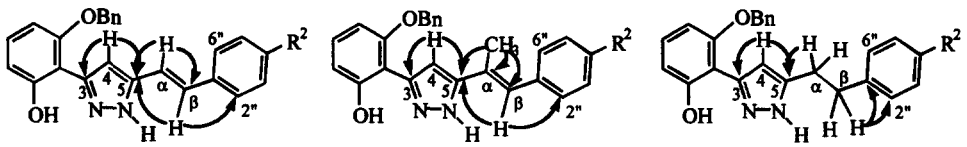
The stereochemistry of the 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7b-e** was established using 2D NOESY experiments. NOE cross peaks were observed between α-CH$_3$ (**7b,c**) or H-α (**7d,e**) and H-4 and H-2",6" and also between H-β and H-4 and H-2",6". These results allowed us to conclude that the Cα=Cβ double bonds have a *trans* configuration and also that there is a free rotation around the C5-Cα bond. In the case of 5-benzyloxy-2-styrylchromone **7a**, the configuration of their double bond was assumed and not established because the H-α and H-β resonances appears as a singlet.

The connectivities found in the HMBC spectra of pyrazoles **7a-e** and **8a,d,e** (Fig. 1) allowed the unequivocal assignments of their C-3 and C-5 carbon resonances and, at the same time, one can conclude that in these cases there is no prototropy.

The presence of a 2-pyrazoline ring in compounds **9a-e** was based on the NMR results. In the case of compounds **9a,d,e** the resonances of a methylene group [4-CH$_2$, δ 2.98-3.02 (dd), 3.06-3.08 (dd) and 34.9-36.4 ppm] and a methynic group [5-CH, δ 4.58-4.95 (dd) and 73.2-73.7 ppm] were observed. However, the connectivities found in the HMBC spectra and the NOE cross peaks observed in the NOESY spectra (Fig. 2), gave unequivocal support for the structure of compounds **9a,d,e**.

Compounds **9b** and **9c** appear as mixtures of diastereomers;[13] their *cis/trans* proportion(38/62 for **9b** and 28/72 for **9c**) was determined using the integral intensity of the H-5 resonance. The separations of these

diastereomers were not successful and they were characterised from the mixture. In the NOESY spectra of these mixtures, NOE cross peaks were observed between 4-CH_3 (δ 1.08-1.10 ppm) and H-4, H-5 and H-α for diastereomers **9b,c**-*trans* and between 4-CH_3 (δ 0.99-1.00 ppm) and H-4, H-α and H-2",6" for diastereomers **9b,c**-*cis*.



7a,d,e **7b,c** **8a,d,e**

Fig. 1. Important Connectivities Found in the HMBC Spectra of Pyrazoles **7a-e** and **8a,d,e**

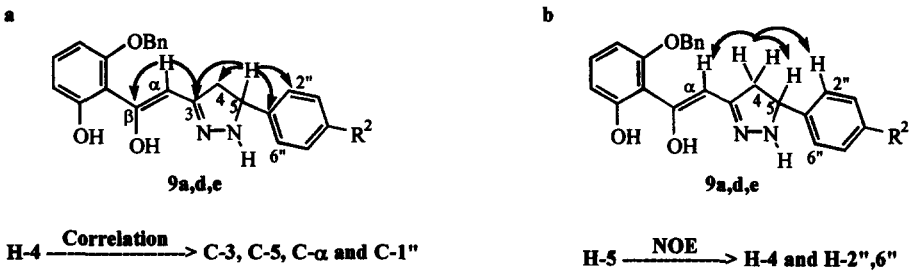


Fig. 2 a) Important Connectivities Found in the HMBC Spectra of Compounds **9a,d,e**

b) Important NOE cross peaks observed in the NOESY spectra of compounds **9,a,d,e**

X-ray Crystallographic Study. The crystal structure of 3-(2-benzyloxy-6-hydroxyphenyl)-5-styryl-pyrazoles **7a,b** with the atomic numbering are displayed in Fig. 3. The presence of a methyl group at the α-carbon of the styryl moiety (C21) has little influence on the molecular structure, although drastic changes appear in the crystal since only one conformer is present in the structure of **7b**. Both compounds display a similar pattern of bond distances and angles, either to each other or when compared with the previously reported 3,5-bis(2-hydroxyphenyl)pyrazole.[5] Both **7a** or **7b** present an (*E*) configuration around the double bond (C21-C22) and slight, but not significant, differences in the twist of the phenyl rings (Table 1).

Table 1. Selected torsions (°)

	(7a)	(7b)		(7a)	(7b)
N1-C5-C21-C22	174.3(2)	170.9(3)	C3-C6-C11-O13	-2.7(3)	-3.1(5)
C5-C21-C22-C23	179.7(3)	-178.7(3)	C6-C11-O13-C14	165.5(2)	165.8(3)
C21-C22-C23-C28	12.8(5)	28.4(6)	C11-O13-C14-C15	-175.1(2)	-168.1(3)
N2-C3-C6-C7	12.8(3)	-2.9(5)	O13-C14-C15-C20	67.6(3)	75.7(5)

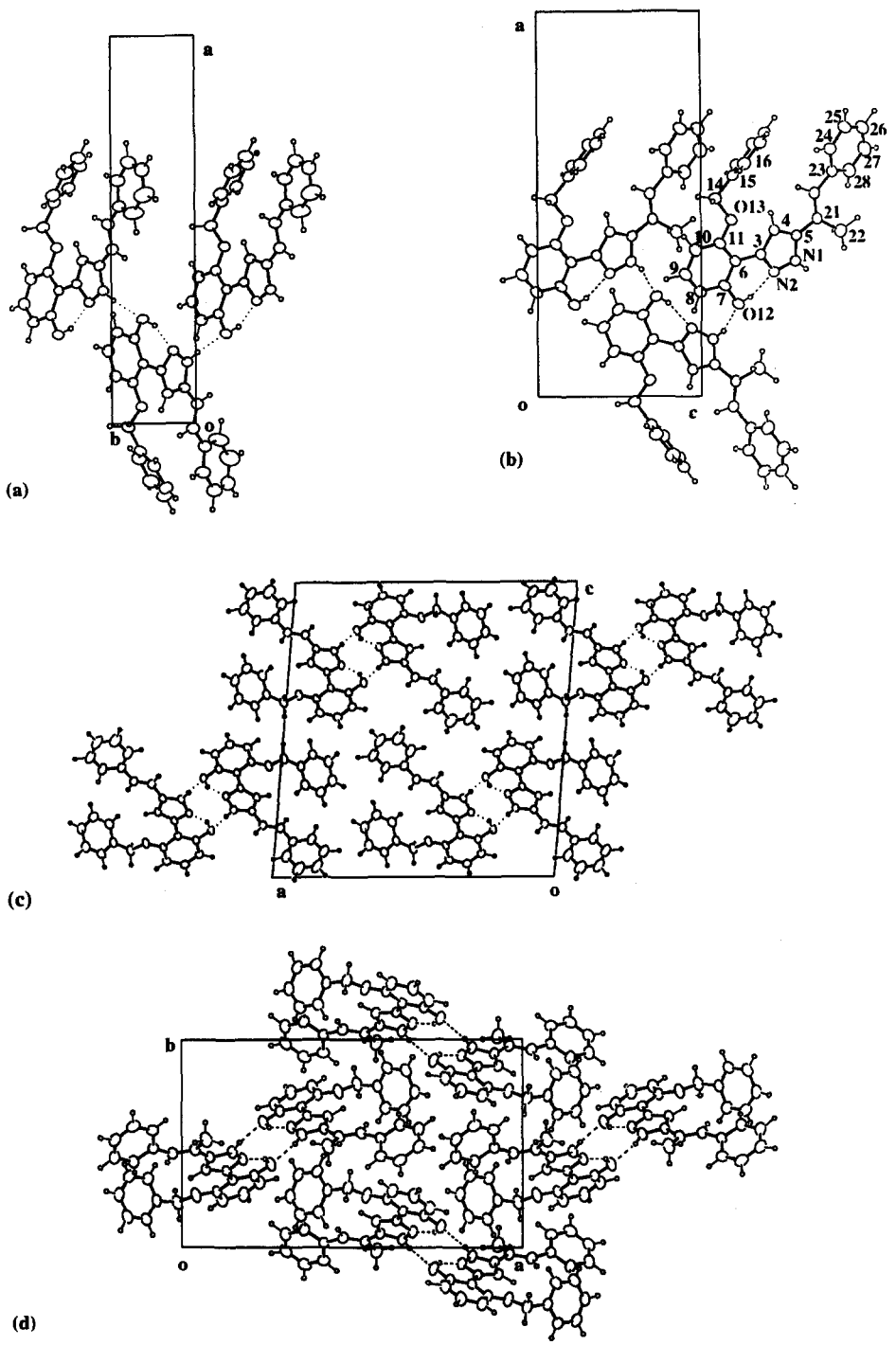


Fig. 3.- Secondary structure in chains of compounds **7a** (a) and **7b** (b). View of the crystal structures showing the packing of the chains in **7a** (c) and in **7b** (d).

At the crystal packing level, the hydroxyl groups in **7a** and **7b** act as donors of intramolecular hydrogen bonds (O12-H12···N2) [0.94(4), 2.586(2), 1.74(4) Å, 148(3)° and 0.77(5), 2.520(4), 1.82(5) Å, 151(5)°]. They present a secondary structure in chains that differs in the way in which the N-H group joins molecules (N1-H1···O12) [0.91(3), 3.038(3), 2.13(3) Å, 171(3)° and 0.87(5), 2.839(4), 2.00(5) Å, 160(4)°], that is, two-fold plus a unit cell translation (1/2-x, -1+y, 1/2-z) and two-fold screw axis (3/2-x, -y, -1/2+z), respectively (Fig. 3a and 3b). The hydrogen bonding interactions, as measured by the O···N distances, are stronger in compound **7b**. In **7a**, the crystal is built up of centrosymmetrically related chains whereas in **7b**, the chains are related by two-fold screw axes (Fig. 3c and 3d), linked in both structures by van der Waals interactions.[14] The efficiency in the packing of these chains is higher in **7a** than **7b** as reflected by the density of both compounds (1.28 vs 1.22 g/cm^3). In all the studied 3-(2-hydroxyphenyl)pyrazole derivatives[2,5,15] the phenyl ring is almost coplanar with the pyrazole moiety and the OH group is engaged in intramolecular hydrogen bonds to the nitrogen lone pair of the pyrazole [O···N distances, O-H···N angles and N2-C3-C6-C7 torsion angles in the 2.579(3)-2.606(3) Å, 145(4)-151(4)° and 0.1(3)-4.7(3)° ranges, respectively].

EXPERIMENTAL SECTION

General. Melting points were determined on a Reichert Thermovar apparatus fitted with a microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in deuteriochloroform solutions (*ca.* 0.3%, unless otherwise stated), 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 TMS as internal reference. ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using HETCOR and HMBC (delays for long-range *J* C/H couplings were optimised for 7 Hz) experiments. Electron impact mass spectra were obtained at 70 eV electron impact ionisation using a VG Autospec Q mass spectrometer. Infrared spectra were recorded on a Fourier transform Matson Polaris spectrometer using potassium bromide pellets. Elemental analyses were carried out in the Microanalytical laboratory of the Department of Chemistry, University of Coimbra, and on a LECO 932 CHN analyser in Aveiro. Preparative thin layer chromatography was carried out on silica gel plates (Merck or 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 were obtained from commercial sources and used as received or dried using standard procedures.

X-ray Analysis. **7a**: $C_{24}H_{20}N_2O_2$, monoclinic, P2/n, a = 20.4488(12), b = 4.4115(1), c = 21.2930(16) Å, 94.850(5)°, V = 1914.0(2) Å^3, Z = 4, R and Rw = 0.048, 0.059 (for 2602 observed reflections for 334 variables). **7b**: $C_{25}H_{22}N_2O_2$, orthorhombic, P2$_1$2$_1$2$_1$, a = 20.0219(9), b = 12.1456(4), c = 8.5506(2) Å, V = 2079.3(1) Å^3, Z = 4, R and Rw = 0.045, 0.067 (for 1877 observed reflections for 351 variables). The structures were solved by direct methods (SIR92)[16] and refined by least-squares procedures on Fobs. All hydrogens were obtained from difference Fourier synthesis and included and refined isotropically in the last cycles. The absolute structure (conformational enantiomers) was established according to the Flack parameters[17] 0.33(88). The scattering factors were taken from the International Tables for X-Ray Crystallography.[18] The calculations were carried out with XTAL,[19] PESOS[20] and PARST[21] sets of programs running on a DEC3000-300X workstation.

Syntheses

2'-Benzyloxy-6'-hydroxycinnamylideneacetophenones 3a-c were prepared as previously reported.[22]

5-Benzyloxy-2-styrylchromones 4a-c

Iodine (6.1 mg, 0.024 mmol) was added to a solution of the appropriate 2'-benzyloxy-6'-hydroxy-cinnamylideneacetophenone **3a-c** (0.6 mmol) in DMSO (5 mL). The mixture was refluxed for 30 minutes; then it was poured into ice and water. The resulting solid was removed by filtration. The solid was dissolved in chloroform (10 mL) and purified by silica gel column chromatography, using dichloromethane as eluent. The solvent was evaporated to dryness and the residue was crystallised from ethanol giving the 2-styrylchromones **4a-c**.

5-Benzyloxy-2-styrylchromone 4a (197.5 mg, 93 %) displayed spectroscopic and analytical data identical to those previously reported.[23]

5-Benzyloxy-2-α-methylstyrylchromone 4b (176.6 mg, 80%): mp 121-123 °C (white needles). IR ν_{max} 1650, 1601, 1477, 1447 cm^{-1}. ^1H NMR δ 2.19 (s, 3H, α-CH_3), 5.30 (s, 2H, 5-OCH_2C$_6$H$_5$), 6.43 (s, 1H, H-3), 6.83 (d, 1H, *J* 8.4 Hz, H-6), 7.10 (d, 1H, *J* 8.4 Hz, H-8), 7.28-7.46 (m, 8H, H-2',3',4',5',6' and H-3,4,5 of 5-OCH$_2$C$_6$*H*$_5$), 7.51 (t, 1H, *J* 8.4 Hz, H-7), 7.62 (d, 2H, *J* 6.8 Hz, H-2,6 of 5-OCH$_2$C$_6$*H*$_5$), 7.63 (s, 1H, H-β). ^{13}C NMR δ 14.1 (α-*C*H$_3$), 70.8 (5-O*C*H$_2$C$_6$H$_5$), 108.3 (C-6), 109.9 (C-3), 110.4 (C-8), 114.9 (C-10), 126.6 (C-2,6 of 5-OCH$_2$*C*$_6$H$_5$), 127.6 (C-4 of 5-OCH$_2$*C*$_6$H$_5$), 128.0 (C-α), 128.3 (C-4'), 128.4 (C-2',6'), 128.6 (C-3,5 of 5-OCH$_2$*C*$_6$H$_5$), 129.5 (C-3',5'), 133.1 (C-β), 133.6 (C-7), 136.2 (C-1'), 136.6 (C-1 of 5-OCH$_2$*C*$_6$H$_5$), 158.1 (C-9), 158.5 (C-5), 162.1 (C-2), 178.5 (C-4). EI MS m/z (rel. int.) 368 ($M^{+\bullet}$, 90), 367 (17), 291 (12), 262 (46), 261 (30), 247 (20), 245 (22), 142 (12), 141 (13), 115 (14), 91 (100), 65 (18). Anal. Calcd. for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.55; H, 5.61%.

5-Benzyloxy-4'-*tert*-butyl-2-α-methylstyrylchromone 4c (198.4 mg, 78%): mp 140-141 °C (white needles). IR ν_{max} 2959, 1645, 1606, 1596, 1478, 1448 cm^{-1}. ^1H NMR δ 1.36 [s, 9H, 4'-C(C*H*$_3$)$_3$], 2.20 (s, 3H, α-C*H*$_3$), 5.30 (s, 2H, 5-OC*H*$_2$C$_6$H$_5$), 6.42 (s, 1H, H-3), 6.83 (d, 1H, *J* 8.4 Hz, H-6), 7.10 (d, 1H, *J* 8.4 Hz, H-8), 7.30 (t, 1H, *J* 6.7 Hz, H-4 of 5-OCH$_2$C$_6$*H*$_5$), 7.38 (t, 2H, *J* 6.7 Hz, H-3,5 of 5-OCH$_2$C$_6$*H*$_5$), 7.39 (d, 2H, *J* 8.1 Hz, H-2',6'), 7.45 (d, 2H, *J* 8.1 Hz, H-3',5'), 7.50 (t, 1H, *J* 8.4 Hz, H-7), 7.59 (s, 1H, H-β), 7.63 (d, 2H, *J* 6.7 Hz, H-2,6 of 5-OCH$_2$C$_6$*H*$_5$). ^{13}C NMR δ 14.2 (α-*C*H$_3$), 31.2 [4'-C(*C*H$_3$)$_3$], 34.7 [4'-*C*(CH$_3$)$_3$], 70.8 (5-O*C*H$_2$C$_6$H$_5$), 108.2 (C-6), 109.8 (C-3), 110.4 (C-8), 114.9 (C-10), 125.4 (C-3',5'), 126.6 (C-2,6 of 5-OCH$_2$*C*$_6$H$_5$), 127.5 (C-α), 127.6 (C-4 of 5-OCH$_2$*C*$_6$H$_5$), 128.5 (C-3,5 of 5-OCH$_2$*C*$_6$H$_5$), 129.4 (C-2',6'), 133.0 (C-β), 133.3 (C-1'), 133.5 (C-7), 136.6 (C-1 of 5-OCH$_2$*C*$_6$H$_5$), 151.2 (C-4'), 158.1 (C-9), 158.4 (C-5), 162.3 (C-2), 178.5 (C-4). EI MS m/z (rel. int.) 424 ($M^{+\bullet}$, 100), 423 (27), 347 (18), 318 (47), 317 (15), 303 (58), 301 (17), 261 (27), 121 (14), 91 (100), 65 (20), 57 (30). Anal. Calcd. for $C_{29}H_{28}O_3$: C, 82.05; H, 6.65. Found: C, 82.10; H, 6.58%.

2'-Benzyloxy-6'-cinnamoyloxyacetophenones 5d,e

The appropriate cinnamic acid (10.8 mmol) and phosphoryl chloride (1.00 mL, 10.8 mmol) were added to a solution of 2'-benzyloxy-6'-hydroxyacetophenone (1.3 g, 5.4 mmol) in dry pyridine (50 mL). The solution was heated at 60 °C for 12 h; after that period it was poured into ice and water, and the p*H* adjusted to 4-5 with hydrochloric acid. The obtained solid was removed by filtration, dissolved in chloroform (15 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 crystallised from ethanol giving the 2'-benzyloxy-6'-cinnamoyloxyacetophenones **5d,e**.

2'-Benzyloxy-6'-(4-methylcinnamoyloxy)acetophenone 5d (1.71 g, 82 %): mp 87-88 °C (white needles). IR ν_{max} 1744, 1695, 1635, 1602, 1577, 1456 cm^{-1}. ^1H NMR δ 2.38 (s, 3H, 4"-C*H*$_3$), 2.52 (s, 3H, 2-C*H*$_3$), 5.13 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.53 (d, 1H, *J* 16.0 Hz, H-α), 6.82 (dd, 1H, *J* 8.2 and 0.6 Hz, H-5'), 6.89 (d, 1H, *J* 8.3 Hz, H-3'), 7.21 (d, 2H, *J* 8.0 Hz, H-3",5"), 7.32-7.40 (m, 6H, H-4' and 2'-OCH$_2$C$_6$*H*$_5$), 7.46 (d, 2H, *J* 8.0 Hz, H-2",6"), 7.81 (d, 1H, *J* 16.0 Hz, H-β). ^{13}C NMR δ 21.5 (4"-*C*H$_3$), 31.8 (2-*C*H$_3$), 70.8 (2'-OCH$_2$C$_6$H$_5$), 109.9 (C-3'), 115.4 (C-5' and C-α), 125.0 (C-1'), 127.3 (C-2,6 of 2'-OCH$_2$*C*$_6$H$_5$), 128.2 (C-4 of 2'-OCH$_2$*C*$_6$H$_5$), 128.4 (C-2",6"), 128.7 (C-3,5 of 2'-OCH$_2$*C*$_6$H$_5$), 129.7 (C-3",5"), 130.9 (C-4'), 131.3 (C-1"), 136.0 (C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 141.3 (C-4"), 147.2 (C-6'), 147.7 (C-β), 156.4 (C-2'), 165.3 (C=O), 200.6 (C-1). EI MS m/z (rel. int.) 386 ($M^{+\bullet}$, 5), 145 (100), 117 (19), 115 (18), 91 (36), 65 (12). Anal. Calcd. for $C_{25}H_{22}O_4$: C, 77.70; H, 5.74. Found: C, 77.67; H, 5.45%.

2'-Benzyloxy-6'-(4-methoxycinnamoyloxy)acetophenone 5e (1.93 g, 89 %): mp 73-74 °C (white needles). IR ν_{max} 1724, 1693, 1626, 1603, 1573, 1512, 1453, 1423 cm^{-1}. ^1H NMR δ 2.52 (s, 3H, 2-CH_3), 3.85 (s, 3H, 4"-OCH_3), 5.13 (s, 2H, 2'-OC$H_2C_6H_5$), 6.44 (d, 1H, *J* 15.9 Hz, H-α), 6.81 (d, 1H, *J* 8.1 Hz, H-5'), 6.89 (d, 1H, *J* 8.3 Hz, H-3'), 6.92 (d, 2H, *J* 8.8 Hz, H-3",5"), 7.32-7.40 (m, 6H, H-4' and 2'-OCH$_2C_6H_5$), 7.52 (d, 2H, *J* 8.8 Hz, H-2",6"), 7.79 (d, 1H, *J* 15.9 Hz, H-β). ^{13}C NMR δ 31.8 (2-CH_3), 55.4 (4"-OCH$_3$), 70.8 (2'-OCH$_2C_6H_5$), 109.9 (C-3'), 113.9 (C-α), 114.4 (C-3",5"), 115.5 (C-5'), 125.0 (C-1'), 126.8 (C-1"), 127.3 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.2 (C-4 of 2'-OCH$_2C_6H_5$), 128.6 (C-3,5 of 2'-OCH$_2C_6H_5$), 130.1 (C-2",6"), 130.8 (C-4'), 136.0 (C-1 of 2'-OCH$_2C_6H_5$), 146.9 (C-β), 147.8 (C-6'), 156.4 (C-2'), 161.8 (C-4"), 165.4 (C=O), 200.7 (C-1). EI MS m/z (rel. int.) 402 ($M^{+\bullet}$, 9), 161 (100), 133 (20), 91 (27), 65 (7). Anal. Calcd. for $C_{25}H_{22}O_5$: C, 74.61; H, 5.51. Found: C, 74.74; H, 5.26%.

5-Aryl-1-(2-benzyloxy-6-hydroxyphenyl)-3-hydroxy-2,4-penten-1-ones 6d,e

Sodium hydride (180 mg, 7.5 mmol) was added to a solution of the appropriate 2'-benzyloxy-6'-cinnamoyloxy-acetophenone **5d,e** (5.0 mmol) in dry THF (80 mL). The mixture was refluxed under nitrogen for 3 h. Then it was poured into ice and water, and the p*H* adjusted to 5-6 with hydrochloric acid. The obtained solid was removed by filtration and recrystallised from ethanol giving the 5-aryl-1-(2-benzyloxy-6-hydroxyphenyl)-3-hydroxy-2,4-penten-1-ones **6d,e**.

1-(2-Benzyloxy-6-hydroxyphenyl)-5-(4-methylphenyl)-3-hydroxy-2,4-penten-1-one 6d (1.35 g, 70 %): mp 107-108 °C (yellow needles). IR ν_{max} 1626, 1594, 1453 cm^{-1}. ^1H NMR δ 2.39 (s, 3H, 4"-CH_3), 5.15 (s, 2H, 2'-OC$H_2C_6H_5$), 6.13 (d, 1H, *J* 15.8 Hz, H-4), 6.50 (d, 1H, *J* 8.3 Hz, H-5'), 6.62 (d, 1H, *J* 8.3 Hz, H-3'), 6.85 (s, 1H, H-2), 7.20 (d, 2H, *J* 8.1 Hz, H-3",5"), 7.32 (t, 1H, *J* 8.3 Hz, H-4'), 7.34 (d, 2H, *J* 8.1 Hz, H-2",6"), 7.42-7.54 (m, 6H, H-5 and 2'-OCH$_2C_6H_5$), 12.91 (s, 1H, 6'-O*H*), 14.69 (d, 1H, *J* 0.9 Hz, 3-O*H*). ^{13}C NMR δ 21.5 (4"-CH_3), 71.2 (2'-OCH$_2C_6H_5$), 102.8 (C-3'), 103.8 (C-2), 110.6 (C-1'), 111.4 (C-5'), 121.8 (C-4), 127.8 (C-2",6"), 128.1 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.4 (C-4 of 2'-OCH$_2C_6H_5$), 128.7 (C-3,5 of 2'-OCH$_2C_6H_5$), 129.6 (C-3",5"), 132.4 (C-1"), 135.1 (C-4'), 136.1 (C-1 of 2'-OCH$_2C_6H_5$), 138.9 (C-5), 140.2 (C-4"), 159.4 (C-6'), 164.3 (C-2'), 174.6 (C-3), 194.8 (C-1). EI MS m/z (rel. int.) 386 ($M^{+\bullet}$, 18), 368 (22), 295 (19), 279 (13), 226 (23), 208 (19), 193 (13), 145 (67), 137 (21), 117 (20), 115 (19), 91 (100), 65 (19). Anal. Calcd. for $C_{25}H_{22}O_4.H_2O$: C, 74.24; H, 5.98. Found: C, 74.61; H, 5.86 %.

1-(2-Benzyloxy-6-hydroxyphenyl)-5-(4-methoxyphenyl)-3-hydroxy-2,4-penten-1-one 6e (1.47 g, 73 %): mp 143-144 °C; (yellow needles). IR ν_{max} 1629, 1604, 1577, 1564, 1510, 1473, 1462, 1444, 1419 cm^{-1}. ^1H NMR δ 3.86 (s, 3H, 4"-OCH_3), 5.15 (s, 2H, 2'-OC$H_2C_6H_5$), 6.05 (d, 1H, *J* 15.8 Hz H-4), 6.49 (d, 1H, *J* 8.3 Hz, H-5'), 6.61 (d, 1H, *J* 8.3 Hz, H-3'), 6.83 (s, 1H, H-2), 6.92 (d, 2H, *J* 8.7 Hz, H-3",5"), 7.32 (t, 1H, *J* 8.3 Hz, H-4'), 7.39 (d, 2H, *J* 8.7 Hz, H-2",6"), 7.42-7.54 (m, 6H, H-5 and 2'-OCH$_2C_6H_5$), 12.93 (s, 1H, 6'-O*H*), 14.77 (s, 1H, 3-O*H*). ^{13}C NMR δ 55.4 (4"-OCH$_3$), 71.2 (2'-OCH$_2C_6H_5$), 102.8 (C-3'), 103.5 (C-2), 110.6 (C-1'), 111.4 (C-5'), 114.3 (C-3",5"), 120.4 (C-4), 127.9 (C-1"), 128.1 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.3 (C-4 of 2'-OCH$_2C_6H_5$), 128.7 (C-3,5 of 2'-OCH$_2C_6H_5$), 129.5 (C-2",6"), 135.0 (C-4'), 136.1 (C-1 of 2'-OCH$_2C_6H_5$), 138.7 (C-5), 159.5 (C-6'), 161.1 (C-4"), 164.3 (C-2'), 175.0 (C-3), 194.5 (C-1); EI MS m/z (rel. int.) 402 ($M^{+\bullet}$, 11), 384 (13), 311 (15), 226 (17), 224 (21), 161 (81), 137 (15), 133 (19), 121 (12), 91 (100), 65 (18). Anal. Calcd. for $C_{25}H_{22}O_5$: C, 74.61; H, 5.51. Found: C, 74.51; H, 5.49%.

5-Benzyloxy-2-styrylchromones 4d,e

Iodine (12 mg, 0.047 mmol) was added to a solution of the appropriated 5-aryl-1-(2-benzyloxy-6-hydroxy-phenyl)-3-hydroxy-2,4-penten-1-one **6d,e** (1.0 mmol) in DMSO (20 mL). The mixture was heated at 100 °C for 24 h. Then it was poured into ice and water, and the obtained solid was removed by filtration. The solid was dissolved in chloroform (15 mL) and purified by silica gel column chromatography, using dichloromethane as eluent. The solvent was evaporated to dryness and the residue was crystallised from ethanol giving the 5-benzyloxy-2-styrylchromones **4d,e**.

5-Benzyloxy-4'-methyl-2-styrylchromone 4d (209.8 mg, 57 %): mp 167-168 °C (white needles). IR ν_{max} 1639, 1601, 1476, 1448 cm^{-1}. ^1H NMR δ 3.02 (s, 3H, 4'-CH_3), 5.26 (s, 2H, 5-OC$H_2C_6H_5$), 6.21 (s, 1H, H-3),

6.68 (d, 1H, *J* 16.0 Hz, H-α), 6.81 (d, 1H, *J* 8.4 Hz, H-6), 7.09 (d, 1H, *J* 8.4 Hz, H-8), 7.21 (d, 2H, *J* 8.1 Hz, H-3',5'), 7.26-7.43 (m, 3H, H-3,4,5 of 5-$OCH_2C_6H_5$), 7.46 (d, 2H, *J* 8.1 Hz, H-2',6'), 7.49 (t, 1H, *J* 8.4 Hz, H-7), 7.50 (d, 1H, *J* 16.0 Hz, H-β), 7.63 (d, 2H, *J* 7.3 Hz, H-2,6 of 5-$OCH_2C_6H_5$,). ^{13}C NMR δ 21.4 (4'-CH_3), 70.7 (5-$OCH_2C_6H_5$), 108.2 (C-6), 110.3 (C-8), 111.9 (C-3), 115.1 (C-10), 118.9 (C-α), 126.5 (C-2,6 of 5-$OCH_2C_6H_5$), 127.5 (C-2',6' and C-4 of 5-$OCH_2C_6H_5$), 128.6 (C-3,5 of 5-$OCH_2C_6H_5$), 129.6 (C-3',5'), 132.2 (C-1'), 133.5 (C-7), 136.2 (C-β), 136.5 (C-1 of 5-$OCH_2C_6H_5$), 140.0 (C-4'), 158.0 (C-9), 158.4 (C-5), 159.7 (C-2), 178.2 (C-4). EI MS m/z (rel. int.) 368 ($M^{+\bullet}$, 83), 367 (28), 291 (24), 278 (16), 277(15), 262 (52), 261 (45), 247 (31), 245 (33), 142 (33), 141 (26), 115 (22), 91 (100), 65 (27). Anal. Calcd. for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.23; H, 5.49%.

5-Benzyloxy-4'-methoxy-2-styrylchromone 4e (230.4 mg, 60 %): mp 174-175 °C (white needles). IR ν_{max} 1647, 1601, 1513, 1476, 1447 cm^{-1}. ^{1}H NMR δ 3.85 (s, 3H, 4'-OCH_3), 5.27 (s, 2H, 5-$OCH_2C_6H_5$), 6.20 (s, 1H, H-3), 6.60 (d, 1H, *J* 16.0 Hz, H-α), 6.82 (d, 1H, *J* 8.4 Hz, H-6), 7.09 (d, 1H, *J* 8.4 Hz, H-8), 6.93 (d, 2H, *J* 8.8 Hz, H-3',5'), 7.30 (t, 1H, *J* 7.3 Hz, H-4 of 5-$OCH_2C_6H_5$), 7.40 (t, 2H, *J* 7.3 Hz, H-3,5 of 5-$OCH_2C_6H_5$), 7.49 (d, 1H, *J* 16.0 Hz, H-β), 7.50 (t, 1H, *J* 8.4 Hz, H-7), 7.52 (d, 2H, *J* 8.8 Hz, H-2',6'), 7.64 (d, 2H, *J* 7.3 Hz, H-2,6 of 5-$OCH_2C_6H_5$). ^{13}C NMR δ 55.4 (4'-OCH_3), 70.8 (5-$OCH_2C_6H_5$), 108.2 (C-6), 110.3 (C-8), 111.6 (C-3), 114.4 (C-3',5'), 115.2 (C-10), 117.7 (C-α), 126.5 (C-2,6 of 5-$OCH_2C_6H_5$), 127.5 (C-4 of 5-$OCH_2C_6H_5$), 127.8 (C-1'), 128.5 (C-3,5 of 5-$OCH_2C_6H_5$), 129.1 (C-2',6'), 133.4 (C-7), 135.9 (C-β), 136.6 (C-1 of 5-$OCH_2C_6H_5$), 158.0 (C-9), 158.5 (C-5), 159.9 (C-2), 160.9 (C-4'), 178.1 (C-4). EI MS m/z (rel. int.) 384 ($M^{+\bullet}$, 100), 383 (28), 367 (10), 307 (18), 278 (61), 277 (53), 265 (21), 261 (26), 247 (11), 158 (28), 115 (24), 91 (100), 65 (22). Anal. Calcd. for $C_{25}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.49; H, 5.23%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles 7a-e

To a methanolic solution (50 mL) of the appropriate 5-benzyloxy-2-styrylchromone **4a-e** (1.0 mmol) was added hydrazine hydrate (0.2 mL, 4.1 mmol). The mixture was refluxed for 24 h, under nitrogen. Then the solution was evaporated to dryness, the residue was taken up in chloroform (50 ml), washed with water and purified by silica gel column chromatography, using chloroform as eluent. The residue was crystallised from cyclohexane giving the 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a-e**. The preparative thin-layer chromatographic analysis of each mother liquor, using dichloromethane as eluent, gave other quantities of 3-(2-benzyloxy-6-hydroxyphenyl)-5-styrylpyrazoles **7a-e** (R_f 0.88), 3-(2-benzyloxy-6-hydroxy-phenyl)-5-(2-phenylethyl)pyrazoles **8a,d,e** (R_f 0.39) and 3-(2-benzyloxy-β,6-dihydroxystyryl)-5-aryl-2-pyrazolines **9a-e** (R_f 0.11).

3-(2-Benzyloxy-6-hydroxyphenyl)-5-styrylpyrazole 7a (150.9 mg, 41 %): mp 88-90 °C (white needles). IR ν_{max} 3271, 1615, 1592, 1557, 1449, 1440 cm^{-1}. ^{1}H NMR δ 5.20 (s, 2H, 2'-$OCH_2C_6H_5$), 6.59 (d, 1H, *J* 8.2 Hz, H-3'), 6.72 (d, 1H, *J* 8.2 Hz, H-5'), 6.89 (s, 2H, H-α,β,), 7.16 (s, 1H, H-4), 7.16 (t, 1H, *J* 8.2 Hz, H-4'), 7.27-7.48 (m, 8H, H-2",3",4",5",6" and H-3,4,5 of 2'-$OCH_2C_6H_5$), 7.54 (d, 2H, *J* 7.9 Hz, H-2,6 of 2'-$OCH_2C_6H_5$), 10.04 (s broad, 1H, N*H*), 11.79 (s broad, 1H, 6'-O*H*). ^{13}C NMR δ 70.7 (2'-$OCH_2C_6H_5$), 103.1 (C-3'), 105.0 (C-4), 106.5 (C-1'), 110.4 (C-5'), 114.5 (C-α), 126.6 (C-2",6"), 128.0 (C-2,6 of 2'-$OCH_2C_6H_5$), 128.2 (C-4 of 2'-$OCH_2C_6H_5$), 128.5 (C-4"), 128.6 (C-3,5 of 2'-$OCH_2C_6H_5$), 128.8 (C-3",5"), 129.0 (C-4'), 131.7 (C-1"), 136.9 (C-1 of 2'-$OCH_2C_6H_5$), 137.8 (C-β), 141.0 (C-5), 149.6 (C-3), 157.2 (C-2'), 158.0 (C-6'). EI MS m/z (rel. int.) 368 ($M^{+\bullet}$, 100), 367 (40), 351 (12), 291 (37), 277 (17), 264 (14), 262 (14), 249 (21), 238 (10), 219 (14), 218 (13), 162 (7), 115 (10), 103 (6), 91 (93), 77 (7), 65 (13). Anal. Calcd. for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. Found: C, 77.99; H, 5.75; N, 7.41%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-α-methylstyrylpyrazole 7b (252.1 mg, 66%): mp 171-172 °C (white needles). IR ν_{max} 3237, 1622, 1586, 1553, 1451 cm^{-1}. ^{1}H NMR δ 2.13 (d, 3H, *J* 1.2 Hz, α-C*H*3), 5.17 (s, 2H, 2'-$OCH_2C_6H_5$), 6.60 (d, 1H, *J* 8.2 Hz, H-3'), 6.73 (d, 1H, *J* 8.2 Hz, H-5'), 6.85 (s, 1H, H-β), 7.13 (s, 1H, H-4), 7.17 (t, 1H, *J* 8.2 Hz, H-4'), 7.30 (t, 1H, *J* 6.2 Hz, H-4"), 7.33 (t, 2H, *J* 6.2 Hz, H-3",5"), 7.37-7.44 (m, 5H, H-2",6" and H-3,4,5 of 2'-$OCH_2C_6H_5$), 7.53 (d, 2H, *J* 6.8 Hz, H-2,6 of 2'-$OCH_2C_6H_5$), 10.20 (s broad, 1H, N*H*), 11.83 (s broad, 1H, 6'-O*H*). ^{13}C NMR δ 15.9 (α-CH_3), 70.9 (2'-$OCH_2C_6H_5$), 103.0 (C-3'), 105.0 (C-4), 106.6 (C-1'), 110.3 (C-5'), 125.4 (C-α), 127.2 (C-4"), 127.3 (C-β), 128.1 (C-2,4,6 of 2'-$OCH_2C_6H_5$), 128.3 (C-2",6"),

128.6 (C-3,5 of 2'-$OCH_2C_6H_5$), 128.9 (C-4'), 129.2 (C-3",5"), 136.5 (C-1"), 136.8 (C-1 of 2'-$OCH_2C_6H_5$), 144.9 (C-5), 149.7 (C-3), 157.2 (C-2'), 158.0 (C-6'). EI MS m/z (rel. int.) 382 ($M^{+\bullet}$, 85), 381 (50), 365 (9), 305 (36), 291 (25), 290 (11), 276 (13), 263 (22), 233 (9), 218 (5), 128 (8), 117 (8), 115 (17), 91 (100), 77 (6), 65 (20), 51 (6). Anal. Calcd. for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.78; H, 5.47; N, 6.99%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-(4-*tert*-butyl-α-methylstyryl)pyrazole 7c (306.6 mg, 70 %): mp 162-163 °C (white needles). IR ν_{max} 3337, 2961, 1624, 1591, 1548, 1452, 1408 cm^{-1}. ^1H NMR δ 1.34 [s, 9H, 4"-C(CH_3)$_3$], 2.13 (d, 3H, *J* 1.3 Hz, α-CH_3), 5.16 (s, 2H, 2'-$OCH_2C_6H_5$), 6.59 (dd, 1H, *J* 8.3 and 0.9 Hz, H-3'), 6.73 (dd, 1H, *J* 8.3 and 0.9 Hz, H-5'), 6.82 (s broad, 1H, H-β), 7.10 (s, 1H, H-4), 7.16 (t, 1H, *J* 8.3 Hz, H-4'), 7.25 (d, 2H, *J* 9.2 Hz, H-2",6"), 7.35-7.43 (m, 5H, H-3",5" and H-3,4,5 of 2'-$OCH_2C_6H_5$), 7.52 (d, 2H, *J* 8.0 Hz, H-2,6 of 2'-$OCH_2C_6H_5$), 10.22 (s broad, 1H, N*H*), 11.95 (s, 1H, 6'-O*H*). ^{13}C NMR δ 16.0 (α-CH_3), 31.3 [4"-C(CH_3)$_3$], 34.6 [4"-*C*(CH_3)$_3$], 70.9 (2'-$OCH_2C_6H_5$), 103.0 (C-3'), 104.8 (C-4), 106.7 (C-1'), 110.3 (C-5'), 124.8 (C-α), 125.3 (C-3",5"), 127.1 (C-β), 128.1 (C-2,4,6 of 2'-$OCH_2C_6H_5$), 128.6 (C-3,5 of 2'-$OCH_2C_6H_5$), 128.9 (C-4'), 129.0 (C-2",6"), 133.7 (C-1"), 136.8 (C-1 of 2'-$OCH_2C_6H_5$), 145.1 (C-5), 149.7 (C-3), 150.3 (C-4"), 157.2 (C-2'), 158.0 (C-6'). EI MS m/z (rel. int.) 438 ($M^{+\bullet}$, 100), 437 (420), 423 (16), 421 (13), 398 (22), 381 (13), 361 (17), 348 (20), 332 (18), 319 (19), 305 (21), 291 (22), 263 (15), 232 (18), 147 (9), 115 (10), 91 (66), 65 (17), 57 (19). Anal. Calcd. for $C_{29}H_{30}N_2O_2$: C, 79.42; H, 6.90; N, 6.39. Found: C, 79.57; H, 6.48; N, 6.30%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-(4-methylstyryl)pyrazole 7d (225.4 mg, 59 %): mp 153-155 °C (white needles). IR ν_{max} 3269, 1617, 1588, 1558, 1453, 1439 cm^{-1}. ^1H NMR δ 2.36 (s, 3H, 4"-CH_3), 5.19 (s, 2H, 2'-$OCH_2C_6H_5$), 6.58 (dd, 1H, *J* 8.1 and 0.9 Hz, H-3'), 6.73 (dd, 1H, *J* 8.1 and 0.9 Hz, H-5'), 6.83 (AB, 1H, *J* 16.5 Hz, H-α), 6.85 (AB, 1H, *J* 16.5 Hz, H-β), 7.14 (s, 1H, H-4), 7.16 (t, 1H, *J* 8.1 Hz, H-4'), 7.17 (d, 2H, *J* 8.0 Hz, H-3",5"), 7.31 (d, 2H, *J* 8.0 Hz, H-2",6"), 7.39-7.47 (m, 3H, H-3,4,5 of 2'-$OCH_2C_6H_5$), 7.53 (d, 2H, *J* 7.8 Hz, H-2,6 of 2'-$OCH_2C_6H_5$), 10.12 (s broad, 1H, N*H*), 11.85 (s broad, 1H, 6'-O*H*); ^{13}C NMR δ 21.3 (4"-CH_3), 70.9 (2'-$OCH_2C_6H_5$), 103.2 (C-3'), 104.7 (C-4), 106.6 (C-1'), 110.4 (C-5'), 113.6 (C-α), 126.5 (C-3",5"), 128.0 (C-2,6 of 2'-$OCH_2C_6H_5$), 128.1 (C-4 of 2'-$OCH_2C_6H_5$), 128.6 (C-3,5 of 2'-$OCH_2C_6H_5$), 129.0 (C-4'), 129.5 (C-2",6"), 131.6 (C-1"), 133.3 (C-4"), 136.9 (C-1 of 2'-$OCH_2C_6H_5$), 138.5 (C-β), 141.2 (C-5), 150.0 (C-3), 157.2 (C-2'), 158.0 (C-6'). EI MS m/z (rel. int.) 382 ($M^{+\bullet}$, 15), 381 (5), 291 (5), 263 (15), 115 (6), 91 (100), 65 (18). Anal. Calcd. for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.33. Found: C, 78.44; H, 6.11; N, 7.60%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-(4-methoxystyryl)pyrazole 7e (246.8 mg, 62 %): mp 142-143 °C (white needles). IR ν_{max} 3312, 1607, 1587, 1540, 1512, 1477, 1462, 1453 cm^{-1}. ^1H NMR δ 3.82 (s, 3H, 4"-OCH_3), 5.18 (s, 2H, 2'-$OCH_2C_6H_5$), 6.58 (dd, 1H, *J* 8.2 and 0.9 Hz, H-3'), 6.73 (dd, 1H, *J* 8.2 and 0.9 Hz, H-5'), 6.72 (AB, 1H, *J* 16.4 Hz, H-α), 6.83 (AB, 1H, *J* 16.4 Hz, H-β), 6.89 (d, 2H, *J* 8.8 Hz, H-3",5"), 7.12 (s, 1H, H-4), 7.15 (t, 1H, *J* 8.2 Hz, H-4'), 7.34 (d, 2H, *J* 8.8 Hz, H-2",6"), 7.39-7.47 (m, 3H, H-3,4,5 of 2'-$OCH_2C_6H_5$), 7.53 (d, 2H, *J* 7.9 Hz, H-2,6 of 2'-$OCH_2C_6H_5$), 10.10 (s broad, 1H, N*H*), 11.88 (s broad, 1H, 6'-O*H*). ^{13}C NMR δ 55.4 (4"-OCH_3), 71.0 (2'-$OCH_2C_6H_5$), 103.3 (C-3'), 104.7 (C-4), 106.8 (C-1'), 110.5 (C-5'), 112.5 (C-α), 114.4 (C-3",5"), 127.9 (C-2,6 of 2'-$OCH_2C_6H_5$), 128.0 (C-2",6"), 128.1 (C-4 of 2'-$OCH_2C_6H_5$), 128.6 (C-3,5 of 2'-$OCH_2C_6H_5$), 129.0 (C-4' and C-1"), 131.4 (C-β), 137.1 (C-1 of 2'-$OCH_2C_6H_5$), 141.4 (C-5), 149.9 (C-3), 157.4 (C-2'), 158.1 (C-6'), 160.0 (C-4"). EI MS m/z (rel. int.) 398 ($M^{+\bullet}$, 29), 397 (9), 291 (6), 279 (12), 121 (6), 91 (100), 77 (6), 65 (17). Anal. Calcd. for $C_{25}H_{22}N_2O_3$: C, 75.36; H, 5.57; N, 7.19. Found: C, 75.16; H, 5.51; N, 7.19%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-(2-phenylethyl)pyrazole 8a (29.6 mg, 8 %): mp 94-96 °C (white powder). IR ν_{max} 3292, 2860, 1615, 1591, 1562, 1479, 1443 cm^{-1}. ^1H NMR δ 2.85-2.97 (m, 4H, 2 x H-1",2"), 5.16 (s, 2H, 2'-$OCH_2C_6H_5$), 6.55 (d, 1H, *J* 8.4 Hz, H-3'), 6.69 (d, 1H, *J* 8.1 Hz, H-5'), 6.81 (s, 1H, H-4), 7.19-7.50 (m, 11H, H-4', H-2,3,4,5,6 of 2'-$OCH_2C_6H_5$ and of 2"-C_6H_5), 9.65 (s broad , 1H, N*H*), 11.90 (s broad, 1H, 6'-O*H*). ^{13}C NMR δ 27.3 (C-1"), 35.0 (C-2"), 70.8 (2'-$OCH_2C_6H_5$), 103.1 (C-3'), 105.6 (C-4), 106.8 (C-1'), 110.3 (C-5'), 126.5 (C-4 of 2"-C_6H_5), 127.8 (C-2,6 of 2'-$OCH_2C_6H_5$), 128.0 (C-4 of 2'-$OCH_2C_6H_5$), 128.3 (C-2,6 of 2"-C_6H_5), 128.6 (C-3,5 of 2'-$OCH_2C_6H_5$ and of 2"-C_6H_5), 128.7 (C-4'), 137.0 (C-1 of 2'-$OCH_2C_6H_5$),

140.4 (C-1 of 2"-C_6H_5), 142.5 (C-5), 149.4 (C-3), 157.1 (C-2'), 158.0 (C-6'). EI MS m/z (rel. int.) 370 ($M^{+\bullet}$, 84), 369 (27), 353 (18),293 (32), 279 (45), 265 (29), 251 (23), 189 (8), 173 (12), 160 (15), 117 (18), 105 (14), 91 (100), 77 (8), 65 (19). Anal. Calcd. for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.93; H, 5.68; N, 7.47%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-[2-(4-methylphenyl)ethyl]pyrazole 8d (15.4 mg, 4 %): mp 106-107 °C (white powder). IR ν_{max} 3305, 2917, 2859, 1617, 1590, 1563, 1514, 1481, 1444 cm^{-1}. ^1H NMR δ 2.30 (s, 3H, 4'''-CH_3), 2.80-2.90 (m, 4H, 2 x H-1",2"), 5.14 (s, 2H, 2'-OC$H_2C_6H_5$), 6.54 (d, 1H, *J* 8.1 Hz, H-3'), 6.69 (d, 1H, *J* 8.1 Hz, H-5'), 6.80 (s, 1H, H-4), 6.99 (d, 2H, *J* 7.8 Hz, H-2''',6'''), 7.08 (d, 2H, *J* 7.8 Hz, H-3''',5'''), 7.11 (t, 1H, *J* 8.1 Hz, H-4'), 7.33-7.42 (m, 3H, H-3,4,5 of 2'-OCH$_2C_6H_5$), 7.47 (d, 2H, *J* 6.9 Hz, H-2,6 of 2'-OCH$_2C_6H_5$,), 9.80 (s broad , 1H, N*H*), 11.95 (s broad , 1H, 6'-O*H*). ^{13}C NMR δ 21.0 (4'''-CH_3), 27.3 (C-1"), 34.4 (C-2"), 70.7 (2'-OCH$_2C_6H_5$), 103.1 (C-3'), 105.6 (C-4), 106.9 (C-1'), 110.2 (C-5'), 127.7 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.0 (C-4 of 2'-OCH$_2C_6H_5$), 128.2 (C-3,5 of 2"-C_6H_5), 128.5 (C-2,6 of 2"-C_6H_5), 128.7 (C-4'), 129.3 (C-3,5 of 2'-OCH$_2C_6H_5$), 135.9 (C-4 of 2"-C_6H_5), 136.9 (C-1 of 2'-OCH$_2C_6H_5$), 137.4 (C-1 of 2"-C_6H_5), 142.7 (C-5), 149.2 (C-3), 157.1 (C-2'), 157.9 (C-6'). EI MS m/z (rel. int.) 384 ($M^{+\bullet}$, 100), 383 (34), 367 (18), 307 (28), 293 (25), 279 (38), 265 (45), 189 (7), 173 (8), 160 (14), 131 (20), 119 (8), 105 (41), 91 (86), 77 (15), 65 (19). Anal. Calcd. for $C_{25}H_{24}N_2O_2$: C, 78.10; H, 6.29; N, 7.29. Found: C, 77.96; H, 5.97; N, 7.01%.

3-(2-Benzyloxy-6-hydroxyphenyl)-5-[2-(4-methoxyphenyl)ethyl]pyrazole 8e (12.0 mg, 3 %): mp 101-103 °C (white powder). IR ν_{max} 3368, 2917, 2841, 1616, 1591, 1560, 1514, 1483, 1449 cm^{-1}. ^1H NMR δ 3.75 (s, 3H, 4'''-OCH_3), 2.75-2.88 (m, 4H, 2 x H-1",2"), 5.14 (s, 2H, 2'-OC$H_2C_6H_5$), 6.54 (d, 1H, *J* 8.4 Hz, H-3'), 6.69 (d, 1H, *J* 8.1 Hz, H-5'), 6.79 (s, 1H, H-4), 6.80 (d, 2H, *J* 8.4 Hz, H-3''',5'''), 7.00 (d, 2H, *J* 8.4 Hz, H-2''',6'''), 7.11 (dd, 1H, *J* 8.4 and 8.1 Hz, H-4'), 7.33-7.41 (m, 3H, H-3,4,5 of 2'-OCH$_2C_6H_5$), 7.46 (d, 2H, *J* 6.6 Hz, H-2,6 of 2'-OCH$_2C_6H_5$), 9.85 (s broad , 1H, N*H*), 12.02 (s broad, 1H, 6'-O*H*). ^{13}C NMR δ 27.4 (C-1"), 34.0 (C-2"), 55.2 (4'''-OCH$_3$), 70.7 (2'-OCH$_2C_6H_5$), 103.1 (C-3'), 105.6 (C-4), 106.9 (C-1'), 110.2 (C-5'), 113.9 (C-3,5 of 2"-C_6H_5), 127.7 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.0 (C-4 of 2'-OCH$_2C_6H_5$), 128.5 (C-3,5 of 2'-OCH$_2C_6H_5$), 128.6 (C-4'), 129.2 (C-2,6 of 2"-C_6H_5), 132.5 (C-1 of 2"-C_6H_5), 136.9 (C-1 of 2'-OCH$_2C_6H_5$), 142.7 (C-5), 149.1 (C-3), 157.1 (C-2'), 157.8 (C-6') 158.0 (C-4 of 2"-C_6H_5). EI MS m/z (rel. int.) 400 ($M^{+\bullet}$, 100), 399(26), 383 (15), 323 (20), 309 (29), 296 (18), 281 (25), 279 (23), 265 (20), 211 (16), 121 (62), 91 (53), 77 (12), 65 (29). Anal. Calcd. for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00. Found: C, 74.64; H, 5.84; N, 6.72%.

3-(2-Benzyloxy-β,6-dihydroxystyryl)-5-phenyl-2-pyrazoline 9a (57.9 mg, 15 %): Colourless oil. IR ν_{max} 3447, 3402, 1620, 1591, 1554, 1455 cm^{-1}. ^1H NMR δ 3.00 (dd, 1H, *J* 15.3 and 4.5 Hz, H-4$_{trans}$), 3.07 (dd, 1H, *J* 15.3 and 7.9 Hz, H-4$_{cis}$), 4.95 (dd, 1H, *J* 7.9 and 4.5 Hz, H-5), 5.15 (s, 2H, 2'-OC$H_2C_6H_5$), 6.54 (dd, 1H, *J* 8.3 and 0.8 Hz, H-3'), 6.69 (dd, 1H, *J* 8.3 and 0.8 Hz, H-5'), 6.78 (s, 1H, H-α), 7.11 (t, 1H, *J* 8.3 Hz, H-4'), 7.30-7.46 (m, 10H, H-2",3",4",5",6" and 2'-OCH$_2C_6H_5$). ^{13}C NMR δ 34.9 (C-4), 70.7 (2'-OCH$_2C_6H_5$), 73.7 (C-5), 103.1 (C-3'), 106.5 (C-α), 106.8 (C-1'), 110.3 (C-5'), 125.6 (C-2",6"), 127.7 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.0 (C-4"), 128.2 (C-4 of 2'-OCH$_2C_6H_5$), 128.5 (C-3,5 of 2'-OCH$_2C_6H_5$), 128.6 (C-4'), 128.7 (C-3",5"), 137.0 (C-1 of 2'-OCH$_2C_6H_5$), 140.1 (C-3), 143.1 (C-1"), 148.8 (C-β), 157.1 (C-2'), 158.1 (C-6'). EI MS m/z (rel. int.) 386 ($M^{+\bullet}$, 19), 368 (10), 367 (9), 296 (8), 291 (6), 280 (11), 277 (25), 265 (6), 249 (10), 189 (8), 105 (17), 91 (100), 77 (25), 65 (17), 51 (9). HRMS (EI) m/z calcd. $C_{24}H_{22}N_2O3$: 386.1630. Found: 386.1622.

3-(2-Benzyloxy-β,6-dihydroxystyryl)-4-methyl-5-phenyl-2-pyrazoline 9b (16.0 mg, 4 %) [colourless oil, mixture of the two possible diastereomers: *cis* and *trans*][13]

9b-*trans*: ^1H NMR δ 1.08 (d, 3H, *J* 7.2 Hz, 4-CH_3), 3.29 (m, 1H, H-4), 4.85 (d, 1H, *J* 4.5 Hz, H-5), 5.09 (s, 2H, 2'-OC$H_2C_6H_5$), 6.54 (d, 1H, *J* 8.3 Hz, H-3'), 6.67 (s, 1H, H-α), 6.70 (d, 1H, *J* 8.3 Hz, H-5'), 7.05-7.08 (m, 2H, H-2",6"), 7.12 (t, 1H, *J* 8.3 Hz, H-4'), 7.25-7.38 (m, 8H, H-3",4",5" and 2'-OCH$_2C_6H_5$). ^{13}C NMR δ 14.2 (4-CH_3), 37.5 (C-4), 70.8 (2'-OCH$_2C_6H_5$), 77.5 (C-5), 103.1 (C-3'), 105.9 (C-α), 107.0 (C-1'), 110.3 (C-5'), 126.5 (C-2",6"), 127.7 (C-2,6 of 2'-OCH$_2C_6H_5$), 128.1 (C-4 of 2'-OCH$_2C_6H_5$), 128.3 (C-3",5"), 128.5 (C-3,5 of 2'-OCH$_2C_6H_5$), 128.6 (C-4'), 128.7 (C-4"), 136.9 (C-1 of 2'-OCH$_2C_6H_5$), 140.9 (C-1"), 144.7 (C-3), 148.4 (C-β), 157.1 (C-2'), 157.9 (C-6').

9b-*cis*: ^1H NMR δ 0.99 (d, 3H, *J* 7.4 Hz, 4-CH_3), 3.11 (quintet, 1H, *J* 7.4 Hz, H-4,), 4.55 (d, 1H, *J* 7.4 Hz, H-5,), 5.13 (s, 2H, 2'-OC$H_2C_6H_5$), 6.56 (d, 1H, *J* 8.3 Hz, H-3'), 6.70 (d, 1H, *J* 8.3 Hz, H-5'), 6.80 (s, 1H, H-α),

7.12 (t, 1H, *J* 8.3 Hz, H-4'), 7.25-7.38 (m, 8H, H-2",3",4",5",6" and H-3,4,5 of 2'-OCH$_2$C$_6$*H*$_5$), 7.45-7.48 (m, 2H, H-2,6 of 2'-OCH$_2$C$_6$*H*$_5$). ^{13}C NMR δ 16.2 (4-*C*H$_3$), 38.2 (C-4), 70.8 (2'-O*C*H$_2$C$_6$H$_5$), 78.9 (C-5), 103.0 (C-3'), 105.3 (C-α), 107.0 (C-1'), 110.3 (C-5'), 126.5 (C-2",6"), 127.9 (C-2,6 of 2'-OCH$_2$*C*$_6$H$_5$), 128.0 (C-4 of 2'-OCH$_2$*C*$_6$H$_5$), 128.3 (C-3",5"), 128.5 (C-3,5 of 2'-OCH$_2$*C*$_6$H$_5$), 128.6 (C-4'), 128.7 (C-4"), 136.9 (C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 142.3 (C-1"), 145.5 (C-3), 148.4 (C-β), 157.1 (C-2'), 158.0 (C-6').

IR ν_{max} 3406, 3288, 1619, 1591, 1562, 1492, 1452 cm^{-1}. EI MS m/z (rel. int.) 400 ($M^{+\bullet}$, 73), 382 (27), 381 (14), 310 (15), 305 (13), 294 (37), 292 (35), 291 (28), 277 (15), 265 (26), 263 (16), 203 (54), 173 (17), 105 (21), 91 (100), 77 (30), 65 (19), 51 (13). HRMS (EI) m/z calcd. $C_{25}H_{24}N_2O3$: 400.1787. Found: 400.1784.

3-(2-Benzyloxy-β,6-dihydroxystyryl)-4-methyl-5-(4-*tert*-butylphenyl)-2-pyrazoline 9c (18.3 mg, 4%) [colourless oil, mixture of the two possible diastereomers: *cis* and *trans*][13]

9c-*trans*: ^{1}H NMR δ 1.10 (d, 3H, *J* 7.2 Hz, 4-C*H*$_3$), 1.28 [s, 9H, 4"-C(C*H*$_3$)$_3$], 3.32 (m, 1H, H-4), 4.87 (d, 1H, *J* 4.5 Hz, H-5), 5.10 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.56 (d, 1H, *J* 7.8 Hz, H-3'), 6.70 (s, 1H, H-α), 6.71 (d, 1H, *J* 7.8 Hz, H-5'), 7.01 (d, 2H, *J* 8.1 Hz, H-2",6"), 7.14 (t, 1H, *J* 7.8 Hz, H-4'), 7.21-7.49 (m, 7H, H-3",5" and 2'-OCH$_2$C$_6$*H*$_5$). ^{13}C NMR δ 14.2 (4-*C*H$_3$), 31.3 [4"-C(*C*H$_3$)$_3$], 34.5 [4"-*C*(CH$_3$)$_3$], 37.3 (C-4), 70.9 (2'-O*C*H$_2$C$_6$H$_5$), 77.5 (C-5), 103.1 (C-3'), 105.9 (C-α), 107.1 (C-1'), 110.4 (C-5'), 125.3 (C-3",5"), 126.3 (C-2",6"), 127.7 (C-2,6 of 2'-OCH$_2$*C*$_6$H$_5$), 127.9 (C-4 of 2'-OCH$_2$*C*$_6$H$_5$), 128.4 (C-3,5 of 2'-OCH$_2$*C*$_6$H$_5$), 128.6 (C-4'), 136.9 (C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 137.9 (C-1"), 144.8 (C-3), 148.5 (C-β), 151.2 (C-4"), 157.1 (C-6'), 158.0 (C-2').

9c-*cis*: ^{1}H NMR δ 1.00 (d, 3H, *J* 7.6 Hz, 4-C*H*$_3$,), 1.32 [s, 9H, 4"-C(C*H*$_3$)$_3$], 3.13 (quintet, 1H, *J* 7.6 Hz, H-4), 4.56 (d, 1H, *J* 7.6 Hz, H-5), 5.14 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.57 (d, 1H, *J* 7.8 Hz, H-3'), 6.71 (d, 1H, *J* 7.8 Hz, H-5'), 6.82 (s, 1H, H-α), 7.14 (t, 1H, *J* 7.8 Hz, H-4'), 7.21-7.49 (m, 9H, H-2",3",5",6" and 2'-OCH$_2$C$_6$*H*$_5$). ^{13}C NMR δ 16.2 (4-*C*H$_3$), 31.3 [4"-C(*C*H$_3$)$_3$], 34.6 [4"-*C*(CH$_3$)$_3$], 38.0 (C-4), 70.9 (2'-O*C*H$_2$C$_6$H$_5$), 78.8 (C-5), 102.9 (C-3'), 105.3 (C-α), 107.1 (C-1'), 110.4 (C-5'), 125.6 (C-3",5"), 126.3 (C-2",6"), 127.9 (C-2,6 of 2'-OCH$_2$*C*$_6$H$_5$), 128.0 (C-3,4,5 of 2'-OCH$_2$*C*$_6$H$_5$), 128.6 (C-4'), 136.9 (C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 139.3 (C-1"), 145.7 (C-3), 148.5 (C-β), 151.5 (C-4"), 157.1 (C-6'), 158.1 (C-2'). HRMS (EI) m/z calcd. $C_{29}H_{32}N_2O3$: 456.2413. Found: 456.2398.

IR ν_{max} 3396, 3283, 2922, 1618, 1591, 1514, 1451 cm^{-1}. EI MS m/z (rel. int.) 456 ($M^{+\bullet}$, 53), 438 (39), 381 (15), 367 (13), 308 (15), 294 (49), 291 (26), 277 (13), 265 (25), 203 (49), 173 (13), 161 (18), 118 (13), 91 (100), 71 (15), 57 (57).

3-(2-Benzyloxy-β,6-dihydroxystyryl)-5-(4-methylphenyl)-2-pyrazoline 9d (28.0 mg, 7 %): Colourless oil. IR ν_{max} 3414, 3275, 2962, 1619, 1591, 1560, 1453 cm^{-1}. ^{1}H NMR δ 2.35 (s, 3H, 4"-C*H*$_3$), 2.98 (dd, 1H, *J* 15.5 and 4.0 Hz, H-4$_{trans}$), 3.06 (dd, 1H, *J* 15.5 and 8.3 Hz, H-4$_{cis}$), 4.92 (dd, 1H, *J* 8.3 and 4.0 Hz, H-5), 5.16 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.54 (d, 1H, *J* 8.2 Hz, H-3'), 6.70 (d, 1H, *J* 8.2 Hz, H-5'), 6.78 (s, 1H, H-α), 7.12 (t, 1H, *J* 8.2 Hz, H-4'), 7.17 (d, 2H, *J* 8.0 Hz, H-3",5"), 7.23 (d, 2H, *J* 8.0 Hz, H-2",6"), 7.32-7.40 (m, 3H, H-3,4,5 of 2'-OCH$_2$C$_6$*H*$_5$), 7.45 (d, 2H, *J* 6.6 Hz, H-2,6 of 2'-OCH$_2$C$_6$*H*$_5$), 10.40 and 11.98 (2s, 1H, 6'-O*H* and β-O*H*). ^{13}C NMR δ 21.2 (4"-*C*H$_3$), 34.9 (C-4), 70.7 (2'-OCH$_2$C$_6$H$_5$), 73.7 (C-5), 103.1 (C-3'), 106.6 (C-α), 106.9 (C-1'), 110.4 (C-5'), 125.6 (C-2",6"), 127.7 (C-2,6 of 2'-OCH$_2$*C*$_6$H$_5$), 128.0 (C-4 of 2'-OCH$_2$*C*$_6$H$_5$), 128.6 (C-3,5 of 2'-OCH$_2$*C*$_6$H$_5$), 128.7 (C-4'), 129.5 (C-3",5"), 137.0 (C-1 of 2'-OCH$_2$*C*$_6$H$_5$), 138.1 (C-4"), 140.2 (C-3 and C-1"), 148.8 (C-β), 157.1 (C-2'), 158.1 (C-6'). EI MS m/z (rel. int.) 400 ($M^{+\bullet}$, 47), 382 (45), 381 (38), 367 (15), 305 (21), 291 (60), 280 (49), 277 (40), 263 (39), 189 (39), 160 (14), 121 (20), 105 (13), 91 (100), 77 (26), 65 (26), 51 (10). HRMS (EI) m/z calcd. $C_{25}H_{24}N_2O3$: 400.1787. Found: 400.1781.

3-(2-Benzyloxy-β,6-dihydroxystyryl)-5-(4-methoxyphenyl)-2-pyrazoline 9e (41.6 mg, 10 %): Colourless oil. IR ν_{max} 3439, 3196, 3150, 1612, 1591, 1565, 1511, 1478, 1453, 1443 cm^{-1}. ^{1}H NMR (acetone-d$_6$) δ 3.02 (dd, 1H, *J* 14.7 and 5.8 Hz, H-4$_{trans}$), 3.08 (dd, 1H, *J* 14.7 and 7.3 Hz, H-4$_{cis}$), 3.75 (s, 3H, 4"-OC*H*$_3$), 4.58 (d, 1H, *J* 3.9 Hz, N*H*), 4.92 (m, 1H, H-5), 5.22 (s, 2H, 2'-OC*H*$_2$C$_6$H$_5$), 6.54 (dd, 1H, *J* 8.2 and 0.8 Hz, H-5'), 6.63 (dd, 1H, *J* 8.2 and 0.8 Hz, H-3'), 6.84 (s, 1H, H-α), 6.85 (d, 2H, *J* 8.9 Hz, H-3",5"), 7.07 (t, 1H, *J* 8.2 Hz, H-4'), 7.26 (d, 2H, *J* 8.9 Hz, H-2",6"), 7.35 (t, 1H, *J* 7.0 Hz, H-4 of 2'-OCH$_2$C$_6$*H*$_5$), 7.43 (t, 2H, *J* 7.0 Hz, H-3,5 of 2'-OCH$_2$C$_6$*H*$_5$), 7.54 (d, 2H, *J* 7.0 Hz, H-2,6 of 2'-OCH$_2$C$_6$*H*$_5$), 12.06 and 12.18 (2s, 1H, 6'-O*H* and β-O*H*). ^{13}C NMR (acetone-d$_6$) δ 36.4 (C-4), 55.4 (4"-OCH$_3$), 71.1 (2'-OC*H*$_2$C$_6$H$_5$), 73.2 (C-5), 103.9 (C-3'), 107.2 (C-α),

107.9 (C-1'), 110.7 (C-5'), 114.2 (C-3",5"), 127.9 (C-2",6"), 128.6 (C-2,6 of 2'-$OCH_2C_6H_5$), 128.7 (C-4 of 2'-$OCH_2C_6H_5$), 129.1 (C-4'), 129.3 (C-3,5 of 2'-$OCH_2C_6H_5$), 137.6 (C-1"), 138.3 (C-1 of 2'-$OCH_2C_6H_5$), 141.5 (C-3), 149.5 (C-β), 157.9 (C-2'), 159.2 (C-6'), 159.8 (C-4"). EI MS m/z (rel. int.) 416 ($M^{+\bullet}$, 32), 398 (61), 397 (35),321 (14),307 (100), 292 (10), 280 (61), 279 (47), 277 (24), 263 (12), 189 (49),160 (14), 137 (35), 135 (31), 121 (26), 109 (17), 91 (91), 77 (30), 65 (27), 51 (10). HRMS (EI) m/z calcd. $C_{25}H_{24}N_2O4$: 416.1736. Found: 416.1725.

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REFERENCES AND NOTES

1. Elguero, J. in *Comprehensive Heterocyclic Chemistry II* (Katritzky, A. R.; Rees, C. W.; Scriven, E. F., Eds.), Pergamon, Oxford, 1996, Vol. 3, p. 1.
2. Catalán, J.; Fabero, F.; Claramunt, R. M.; Santa María, M. D.; Foces-Foces, M. C.; Cano, F. H.; Martínez-Ripoll, M.; Elguero, J.; Sastre, R. *J. Am. Chem. Soc.* **1992**, *114*, 5039.
3. Ahmad, R.; Ahmad, N.; Zia-Ul-Haq, M., Wahid, A. *J. Chem. Soc. Pak.* **1996**, *18*, 38.
4. Takagi, K.; Tanaka, M.; Murakami, Y.; Morita, H. and Aotsuka, T. *Eur. J. Med. Chem. - Chim. Ther.* **1986**, *21*, 65.
5. Silva, A. M. S.; Almeida, L. M. P. M.; Cavaleiro, J. A. S.; Foces-Foces, C.; Llamas-Saiz, A. L.; Fontenas, C.; Jagerovic, N.; Elguero J. *Tetrahedron* **1997**, *53*, 11645.
6. Pinto, D. C. G. A.; Silva, A. M. S.; Cavaleiro, J. A. S. *Heterocycl. Commun.* **1996**, *3*, 433.
7. a) Koenigs, E.; Freund, J. *Ber.* **1947**, *80*, 143; b) Baker, W.; Harborne, J. B.; Ollis, W. D. *J. Chem. Soc.* **1952**, 1303; c) Schönberg, A.; Sidky, M. M. *J. Am. Chem. Soc.* **1953**, *75*, 5128.
8. a) Silva, A. M. S.; Pinto, D. C. G. A.; Cavaleiro J. A. S. *Tetrahedron Lett.* **1994**, *35*, 5899; b) Pinto, D. C. G. A.; Silva, A. M. S.; Cavaleiro, J. A. S. *J. Heterocycl. Chem.* **1996**, *33*, 1887.
9. a) Baker, W. *J. Chem. Soc.* **1933**, 1381; b) Mahal, H. S.; Venkataraman, K. *J. Chem. Soc.* **1934**, 1767.
10. a) Miller, C. E. *J. Chem. Soc.* **1965**, *42*, 254; b) Pasto, D. J.; Chipman, D. M. *J. Am. Chem. Soc.* **1979**, *101*, 2290.
11. Garbisch Jr., E. W.; Schildcrout, S. M.; Patterson, D. B.; Aprecher, C. M. *J. Am. Chem. Soc.* **1965**, *87*, 2932.
12. Chila, V. P.; Aitmambetov, A.; Usmailov, U.; Grishko, L. G. *Khim. Prirodnych Soedin* **1993**, 629.
13. Although the described 5-aryl-3-(2-benzyloxy-β,6-dihydroxystyryl)-4-methyl-2-pyrazolines **9d,e**-*cis* and *trans* are racemates, only one enantiomer is illustrated.
14. Vainshtein, B. K.; Fridkin, V. M.; Indenbom, V. L., *Modern Crystallography II*; Springer-Verlag: New York, 1982, pp. 87.
15. Allen, F. H.; Davies, J. E.; Galloy, Johnson, O.; Kennard, O.; Macrae, C. F.; Mitchell, E. M.; Mitchell, J. F.; Smith, J. M.; Watson, D. G. *J. Chem. Info. Comput. Sci.* **1991**, *31*, 187.
16. Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G.; SIR92 *J. Appl. Cryst.* **1994**, *27*, 435.
17. Flack, H. D. *Acta Cryst. Sect.* **1983**, *A39*, 876.
18. *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1974.
19. Hall, S. R.; Flack, H. D.; Stewart, J. M. *Xtal3.2*, Ed. Univ. Western Australia: Lamb-Perth, 1994.
20. Martínez-Ripoll, J. M.; Cano, F. H. *PESOS*, Unpublished Program.
21. Nardelli, M. *Comput Chem.* **1993**, *7*, 95.
22. Silva, A. M. S.; Pinto, D. C. G. A.; Tavares, H. R.; Cavaleiro, J. A. S.; Jimeno, M. L.; Elguero, J. *Eur. J. Org. Chem.* **1998**, 2031.
23. Pinto, D. C. G. A.; Silva, A. M. S.; Cavaleiro, J. A. S. *J. Heterocycl. Chem.* **1996**, *33*, 1887.