Novel (*E*)- and (*Z*)-2-Styrylchromones from (*E,E*)-2′-Hydroxycinnamylideneacetophenones – Xanthones from Daylight Photooxidative Cyclization of (*E*)-2-Styrylchromones

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The oxidative cyclization of (*E,E*)-2′-hydroxycinnamylideneacetophenones **1a–e**, and (*E,E*)-2′-benzyloxy-6′-hydroxycinnamylideneacetophenones **1i–l** with DMSO/iodine, gave (*E*)-2-styrylchromones **3a–e**,**i–l**. However, in the case of (*E,E*)-γ-alkyl-2′-hydroxycinnamylideneacetophenones **1f–h**, (*E*)- and (*Z*)-2-styrylchromones **3f–h** and **4f–h** were obtained. The stereochemistry of the (*E,E*)-cinnamylideneacetophenones **1** and (*E*)- and (*Z*)-2-styrylchromones **3** and **4** was established by NOE experiments. The induced daylight photooxidative cyclization of some (*E*)-2-styrylchromones **3a**,**f–h** gave 12*H*-benzo[*a*]xanthene-12-ones **6a**,**f–h**.

Introduction

Chromones are one of the most widely distributed classes of natural compounds occurring in the plant kingdom.[1][2] Both natural and synthetic derivatives are known to present important biological functions, namely as potential agrochemicals,[3][4] new drugs,[1][5][6] or antioxidants.[7][8]

2-Phenylchromones, also known as flavones, are the major constituents of this class of compounds and are responsible for a great variety of biological activities.[5][6][9] However, other groups of chromones are scarce in nature. For example, for the newest group of 2-styrylchromones, only two natural derivatives have been found during the last decade, and they have shown potent in vitro cytotoxicity against human leukaemia cells.[10][11] Prior to the isolation of these natural 2-styrylchromones, studies have been already carried out on numerous synthetic derivatives,[12] which have also shown promising anti-tumour and anti-allergic activities.[13][14]

The reagent system DMSO/iodine has been used by us in the synthesis of 2-(phenyl and styryl)chromones since 1991.[15][16] At the same time that we have published our first paper on this subject,[15] an Indian group have also applied this reagent system for the synthesis of other 2-styrylchromones derivatives,[17] both put forward the stereochemistry of the vinylic system of 2-styrylchromones as being (*E*).

In this publication the syntheses of several new (*E*)- and (*Z*)-2-styrylchromone derivatives **3a−l**, **4f−h**, and **5m**,**n** are reported. The synthesis of the (*Z*) isomers are reported by the first time. Our results indicate that such chromones unsubstituted in the vinylic system are formed only as (*E*) species, whereas in the case of 5-unsubstituted-2-α-alkylstyrylchromones both (*E*) and (*Z*) isomers were formed, the (*E*) being present in higher proportions.

Our studies have been extended to the daylight photooxidative cyclization of some (*E*)-2-styrylchromones.[18] This photocyclodehydrogenation let us prepare some new xanthone derivatives in acceptable yields (50−60%), which are an improvement on some literature data (1−31%).[19][20] This transformation of (*E*)-2-styrylchromones **3a**,**f−h** into xanthones **6a**,**f−h** was followed by ^{1}H NMR, and allowed us to conclude that it involves the (*E*)-to-(*Z*) photoisomerization followed by electrocyclic and oxidative processes.

Results and Discussion

Syntheses

2′-Hydroxycinnamylideneacetophenones **1a**,**f−h** and 2′-benzyloxy-6′-hydroxycinnamylideneacetophenones **1i−l** were synthesised by base-catalysed aldol reaction of cinnamaldehydes and 2′-hydroxyacetophenone or 2′-benzyloxy-6′-hydroxyacetophenone, respectively, in methanol. By the other hand, 2′-hydroxycinnamylideneacetophenones **1b−e** were obtained as minor products in the synthesis of 2′-hydroxychalcones **2b−e**, when the base-catalysed aldol reactions were carried out in ethanol.[15] The formation of compounds **1b−e**, with two extra carbon atoms in its structure, can be envisaged through the formation of acetaldehyde by the Oppenauer oxidation of solvent ethanol, under the al-

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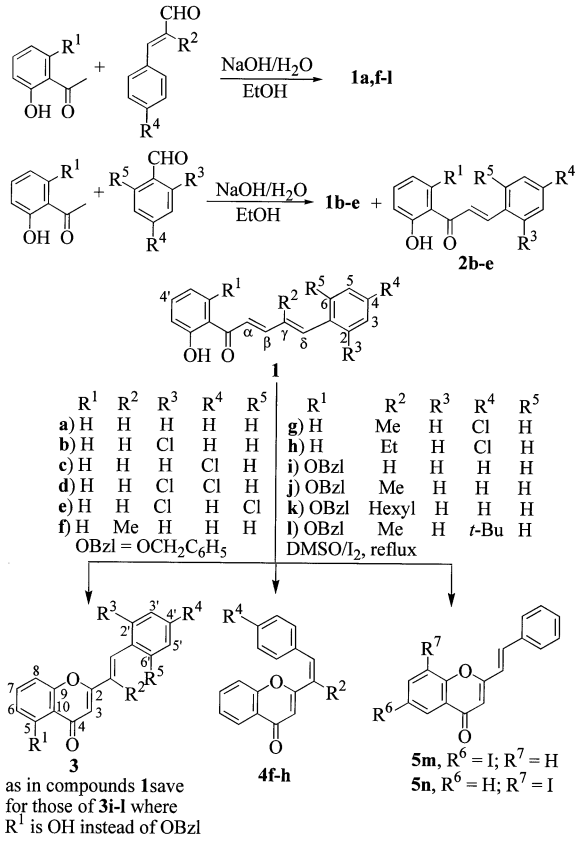
kaline conditions used in these reactions, followed by condensations with benzaldehydes and of the resultant products, cinnamaldehydes, with 2′-hydroxyacetophenone. In order to reinforce this process, we have carried out two different experiments: i) the addition of acetaldehyde to the reactional mixture of 2′-hydroxyacetophenone and 4-chlorobenzaldehyde increased the yield of 4-chloro-2′-hydroxycinnamylideneacetophenone (**1c**) from 15 to 30%; and ii) base-catalysed aldol reaction of 2′-hydroxyacetophenone and 4-chlorobenzaldehyde in 1-propanol yielded the expected 4-chloro-2′-hydroxychalcone (**2c**) and 4-chloro-2′-hydroxy-γ-methylcinnamylideneacetophenones (**1g**).

The syntheses of 2-styrylchromones **3** were carried out by treatment of 2′-hydroxycinnamylideneacetophenones **1a−h** and 2′-benzyloxy-6′-hydroxycinnamylideneacetophenones **1i−l** with a catalytic amount of iodine in DMSO at reflux, for half an hour or two hours, respectively (Scheme 1).[15][21] The synthesis of 2-styrylchromones **3i−l** involves, in one step, the oxidative cyclizations of reagents **1i−l** and also the debenzylation of the 5-substituent of the formed chromones **3i−l**, whereas in the other cases only oxidative cyclizations were involved.

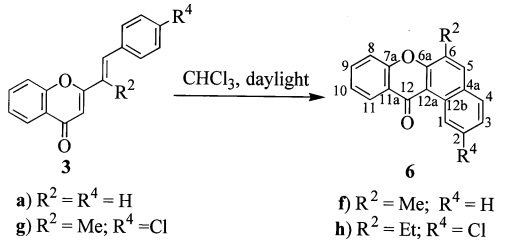
In the oxidative cyclizations of 2′-hydroxycinnamylideneacetophenones **1a−e**, unsubstituted in the vinylic moiety, only the isomers (*E*)-2-styrylchromones **3a−e** were obtained, whereas in the case of 2′-hydroxy-γ-alkylcinnamylideneacetophenones **1f−h** both isomers (*E*)-2-α-alkylstyrylchromones **3f-h** and (*Z*)-2-α-alkylstyrylchromones **4f−h** were formed, (*E*) being obtained in higher proportions. In order to be sure that only isomer (*E*) was present in the case of chromones **3a−e**, the chromatographic (TLC) analysis of the mother liquors of 2-styrylchromone (**3a**) still revealed the presence of another quantity of chromone **3a** and small amounts of 6-iodo-2-styrylchromone (**5m**) and 8-iodo-2-styrylchromone (**5n**) (Scheme 1). The formation of these latter compounds involves cyclization of the reagent **1a**, catalysed by the iodine/DMSO mixture, as well as an electrophilic substitution process at the most activated aromatic positions. In the synthesis of 5-hydroxy-2-styrylchromones **3i−l**, both substituted or unsubstituted in the vinylic system, only the (*E*) isomer was obtained.

In order to understand the appearance of both (*E*) and (*Z*) isomers in the synthesis of some 2-styrylchromone derivatives, chloroform solutions of (*E*)-2-α-alkylstyrylchromones **3f−h** were exposed to daylight and their evolution followed by ^{1}H NMR during several days. The analysis of the obtained ^{1}H-NMR spectra allowed us to conclude that the first transformation occurred in those solutions was the (*E*)-to-(*Z*) isomerization. Other transformations, electrocyclic and oxidative processes, have occurred leading to the formation of 12*H*-benzo[*a*]xanthene-12-ones **6f−h** (Scheme 2).[18] Similar transformations were also possible with the unsubstituted (*E*)-2-styrylchromone (**3a**), however in this case a longer period of time was necessary. Chloroform solutions of (*E*)-2-α-alkylstyrylchromones **3f−h** remain unaltered if they are kept in the dark, at room temperature or at reflux. These results seem to indicate that the (*E*)-to-(*Z*) isomerization is a photochemical process and is facilitated by the presence of α-substituents.

Scheme 1



Scheme 2



Nuclear Magnetic Resonance Spectroscopy

From the ^{1}H-NMR spectra and 2D-COSY experiments, all the proton resonances of compounds **1a−l** have been assigned. For compounds unsubstituted in the α,β,γ,δ-unsaturated moiety, due to second-order effects of its ^{1}H NMR, it was necessary to determine the coupling constants by computer simulation of this ABCD spin system.[22] The obtained results ($^3J_{H\alpha\text{-}H\beta}$ = 14.7 Hz; $^3J_{H\beta\text{-}H\gamma}$ = 11.3 Hz; $^3J_{H\gamma\text{-}H\delta}$ = 15.6 Hz) are similar to those of compound **1d**, the unique compound where its experimental determination was possible, and allowed us to established the stereochemistry of the two double bonds as *trans*. However, the stereochemistry of the all-α,β,γ,δ-unsaturated moieties of **1a−e** was established by NOE experiments. In the case of 2,4-dichloro-2′-hydroxycinnamylideneacetophenone (**1d**), a

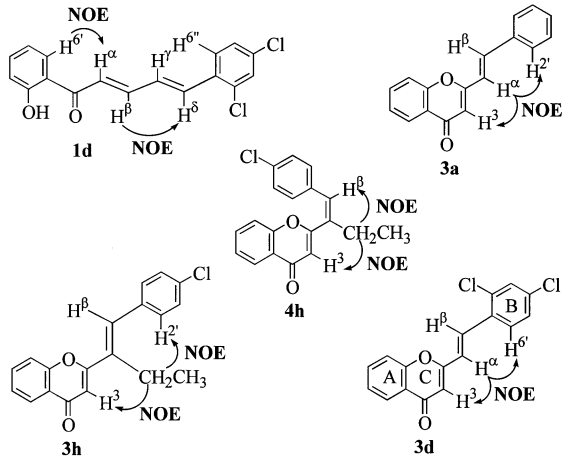
close proximity between 6′-H and α-H and also between β-H and δ-H have been found (Figure 1), thus allowing us to establish the stereochemistry of the compounds **1a−e** as *trans(s-trans)-trans* as shown in Scheme 1. The stereochemistry of γ-substituted compounds **1f−h** was also established as *trans(s-trans)-trans* in our previous work.[23]

The analysis of the ^{1}H-NMR spectra of 2′-hydroxycinnamylideneacetophenones **1a−e** revealed that in the case of compounds **1b**, **d**, **e** there is a shift to higher frequency values in the δ-H resonance compared with those of the 2-unsubstituted derivatives **1a**, **c**. This effect can be explained by the steric interaction between δ-H and the 2-chloro substituent,[24][25] and is also responsible for the shift to lower frequency values of the C-δ resonance.

The stereochemistry of all types of 2-styrylchromones was established by NOE experiments and allowed us to discuss some conformational aspects. The coupling constant value of $^3J_{H\alpha\text{-}H\beta} \approx 16$ Hz indicates a *trans* configuration of the Cα=Cβ double bond of 2-styrylchromones unsubstituted in the vinylic system. However, NOE experiments of 2-styrylchromone (**3a**), where a close proximity between α-H and 3-H and 2′,6′-H was found, unequivocally prove that only the (*E*) isomer is present (Figure 1). In the case of 2′,4′-dichloro-2-styrylchromone (**3d**), NOE experiments indicate a close proximity between α-H and 3-H and 6′-H, whereas upon irradiation of β-H no effect was observed. These results allowed us to consider the (*E*) stereochemistry of its Cα=Cβ double bond and also to establish the conformation of the B ring of compound **3d** (Figure 1).

4′-Chloro-2-α-ethylstyrylchromones were used for the establishment of the stereochemistry of Cα=Cβ double bonds of α-substituted chromones. In the case of compound **3h**, NOE experiments indicate a close proximity between α-CH_2 and 3-H and 2′,6′-H, whereas in the case of the other stereoisomer **4h** a close proximity between α-CH_2 and 3-H and β-H was found (Figure 1). These results allowed us to unequivocally establish the Cα=Cβ double bond stereochemistry of 4′-chloro-2-α-ethylstyrylchromones **3h** and **4h** as being (*E*) and (*Z*), respectively. The stereochemistry of these double bonds was also established by NOE experiments in the case of 2-α-methylstyrylchromones **3f** and **4f**.[18]

Figure 1. NOE observed for 2,4-dichloro-2′-hydroxycinamylideneacetophenone (**1d**) and the 2-styrylchromones **3a**, **d**, **h** and **4h**



In (*E*)-2-styrylchromones **3b**, **d**, **e** there is a steric interaction between β-H and the 2′-chloro substituent,[24][25] which is responsible for the shifts to lower and higher frequency values of the C-β and β-H resonances, respectively, compared to those of 2′-unsubstituted derivatives **3a**, **c**.

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Experimental Section

General: Melting points (uncorrected): Reichert Thermovar apparatus fitted with a microscope. − ^{1}H and ^{13}C NMR: Varian Gemini and Bruker AMX 300 spectrometers, at 199.975, 300.13 and 50.289, 75.47 MHz, respectively, $CDCl_3$ as solvent, TMS as internal reference, chemical shifts (δ) in ppm, coupling constants (*J*) in Hertz [Hz]. − 2D COSY and HETCOR experiments: Bruker standard microprograms. − Homonuclear NOE difference experiments: 2 s for the irradiation time and 4 s for the relaxation delay. − Electron impact (EI, 70 eV) MS: VG Autospec Q mass spectrometer. − Elemental analysis: Microanalytical Laboratory of the Chemistry Department, University of Liverpool, U. K., and University of Coimbra, Portugal. − Preparative thin layer chromatography: Riedel silica gel 60 DGF_{254}. − Column chromatography: Merck silica gel 60, 70−230 mesh. − The unequivocal ^{1}H assignments were made using 2D-COSY, while ^{13}C assignments were made using 2D-HETCOR experiments as well as one-dimensional selective INEPT[26] (long-range C/H coupling constants were optimized to 7 Hz).

(E,E)-2′-Hydroxycinnamylideneacetophenone (**1a**): To a methanolic solution (160 ml) of 2′-hydroxyacetophenone (4.0 ml, 33.0 mmol), was added a 60% aqueous solution of sodium hydroxide (160 ml). After cooling the solution to room temperature, cinnamaldehyde (37.0 mmol) was added and the reaction mixture stirred, for 20 h. The reaction mixture was poured into ice/hydrochloric acid (pH adjusted to ca. 2). The obtained solid was removed by filtration, taken up in chloroform (150 ml) and washed with a solution of hydrogen carbonate (2 × 100 ml) and water (100 ml). The organic layer was collected, dried (sodium sulfate), and the solvent evaporated to dryness. The obtained residue was dissolved in dichloromethane (100 ml) and purified by silica gel column chromatography, using dichloromethane as eluent. The solvent was evaporated and the residue crystallised from ethanol yielding 7.2 g of **1a** (87%), yellow crystals, m.p. 154−156°C (recrystallisation from ethanol; ref.[17] 154−155°C). − ^{1}H NMR: δ = 6.92 (ddd, *J* = 7.8, 7.6 and 1.1 Hz, 1 H, 5′-H), 7.01 (dd, *J* = 8.1 and 1.1 Hz, 1 H, 3′-H), 7.05−7.07 (m, 2 H, γ,δ-H), 7.22 (d, *J* = 14.7 Hz, 1 H, α-H), 7.34−7.42 (m, 3 H, 3,4,5-H), 7.49 (ddd, *J* = 8.1, 7.6 and 1.4 Hz, 1 H, 4′-H), 7.52 (dd, *J* = 7.8 and 1.7 Hz, 2 H, 2,6-H), 7.67−7.76 (m, 1 H, β-H), 7.85 (dd, *J* = 7.8 and 1.4 Hz, 1 H, 6′-H), 12.88 (s, 1 H, 2′-O*H*). − ^{13}C NMR: δ = 118.6 (C-3′), 118.8 (C-5′), 120.0 (C-1′), 123.5 (C-α), 126.7 (C-γ), 127.4 (C-2,6), 128.9 (C-3,5), 129.4 (C-4), 129.5 (C-6′), 135.9 (C-1), 136.2 (C-4′), 142.9 (C-δ), 145.4 (C-β), 163.5 (C-2′), 194.0 (C=O). − MS (EI); *m/z* (%): 250 ($M^{+\bullet}$, 100), 249 (43), 173 (30), 157 (8), 147 (18), 130 (23), 129 (30), 128 (36), 121 (47), 93 (14). − $C_{17}H_{14}O_2$ (250.3): calcd. C 81.58, H 5.64; found C 81.49, H 5.63.

(E,E)-2′-Hydroxycinnamylideneacetophenones **1b−e**: To a solution of the 2′-hydroxyacetophenone (4.0 ml, 33.0 mmol) in ethanol

(160 ml) was added a 60% aqueous solution of sodium hydroxide (160 ml). After cooling the solution to room temperature, the appropriate benzaldehyde (66 mmol) was added and the reaction mixture stirred for 5 h. The reaction mixture was poured into ice/hydrochloric acid (pH adjusted to ca. 2). The obtained solid was removed by filtration, taken up in chloroform (150 ml) and washed with a solution of hydrogen carbonate (2 × 100 ml) and water (100 ml). The organic layer was collected, dried (sodium sulfate) and the solvent evaporated. The obtained residue, in each case, was dissolved in dichloromethane (100 ml) and chromatographed on preparative thin layer chromatography plates, eluting several times with a mixture of dichloromethane/light petroleum ether (2:8). Two spots with very close R_f values were obtained. The high R_f value was seen to be (*E*,*E*)-2′-hydroxycinnamylideneacetophenones **1b−e**, whereas that of the lower R_f value was constituted by the corresponding (*E*)-2′-hydroxychalcones **2b−e**. Finally, all the compounds were crystallised from ethanol. The obtained yields are given in Table 1.

Table 1. Yields of **1b−e** and **2b−e**

2′-Hydroxycinnamylidene-acetophenones		2′-Hydroxychalcones	
1b	10%	**2b**	80%
1c	15%	**2c**	70%
1d	17%	**2d**	71%
1e	10%	**2e**	76%

(E,E)-2-Chloro-2′-hydroxycinnamylideneacetophenone (**1b**): M.p. 140−142°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.93 (ddd, *J* = 8.2, 7.5 and 0.7 Hz, 1 H, 5′-H), 6.98 (dd, *J* = 6.9 and 0.7 Hz, 1 H, 3′-H), 7.02−7.10 (m, 1 H, γ-H), 7.25 (d, *J* = 14.9 Hz, 1 H, α-H), 7.26−7.30 (m, 2 H, 4,5-H), 7.42 (d, *J* = 9.4 Hz, 1 H, 6-H), 7.49 (ddd, *J* = 7.5, 6.9 and 1.2 Hz, 1 H, 4′-H), 7.50 (d, *J* = 15.6 Hz, 1 H, δ-H), 7.66 (d, *J* = 6.9 Hz, 1 H, 3-H), 7.75 (m, 1 H, β-H), 7.84 (dd, *J* = 8.2 and 1.2 Hz, 1 H, 6′-H), 12.81 (s, 1 H, 2′-O*H*). − ^{13}C NMR: δ = 118.7 (C-3′), 118.8 (C-5′), 120.0 (C-1′), 124.5 (C-α), 126.9 (C-γ), 127.0 (C-5), 129.5 (C-6′), 130.0 (C-6), 130.2 (C-3), 130.2 (C-4), 134.0 (C-2), 134.4 (C-1), 136.4 (C-4′), 138.3 (C-δ), 145.1 (C-β), 163.7 (C-2′), 193.7 (C=O). − MS (EI); *m*/*z* (%): 284 ($M^{+\bullet}$, 100), 283 (29), 249 (32), 191 (7), 173 (35), 147 (27), 129 (32), 128 (35), 121 (48), 93 (16). − $C_{17}H_{13}ClO_2$ (284.7): calcd. C 71.71, H 4.60; found C 71.80, H 4.58.

(E,E)-4-Chloro-2′-hydroxycinnamylideneacetophenone (**1c**): M.p. 181−183°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.92 (ddd, *J* = 8.1, 7.4 and 1.2 Hz, 1 H, 5′-H), 7.01 (dd, *J* = 8.0 and 1.2 Hz, 1 H, 3′-H), 6.99−7.02 (m, 2 H, γ,δ-H), 7.22 (d, *J* = 14.7 Hz, 1 H, α-H), 7.35 (d, *J* = 8.7 Hz, 2 H, 2,6-H), 7.44 (d, *J* = 8.7 Hz, 2 H, 3,5-H), 7.49 (ddd, *J* = 8.0, 7.4 and 1.6 Hz, 1 H, 4′-H), 7.62−7.75 (m, 1 H, β-H), 7.83 (dd, *J* = 8.1 and 1.6 Hz, 1 H, 6′-H), 12.83 (s, 1 H, 2′-O*H*). − ^{13}C NMR: δ = 118.7 (C-3′), 118.9 (C-5′), 120.0 (C-1′), 124.0 (C-α), 127.3 (C-γ), 128.6 (C-3,5), 129.2 (C-2,6), 129.5 (C-6′), 134.5 (C-1), 135.3 (C-4), 136.3 (C-4′), 141.3 (C-δ), 145.0 (C-β), 163.7 (C-2′), 193.6 (C=O). − MS (EI); *m*/*z* (%): 284 ($M^{+\bullet}$, 100), 283 (34), 249 (20), 191 (6), 173 (25), 147 (16), 129 (32), 128 (31), 127 (25), 121 (25), 93 (14). − $C_{17}H_{13}ClO_2$ (284.7): calcd. C 71.71, H 4.60; found C 71.77, H 4.57.

(E,E)-2,4-Dichloro-2′-hydroxycinnamylideneacetophenone (**1d**): M.p. 225−227°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.93 (ddd, *J* = 7.9, 7.7, and 1.0 Hz, 1 H, 5′-H), 7.01 (dd, *J* = 11.3 and 15.1 Hz, 1 H, γ-H), 7.02 (dd, *J* = 8.2 and 1.0 Hz, 1 H, 3′-H), 7.26 (d, *J* = 14.9 Hz, 1 H, α-H), 7.27 (d, *J* = 8.5 Hz, 1 H, 5-H), 7.41 (d, *J* = 15.1 Hz, 1 H, δ-H), 7.43 (s broad, 1 H, 3-H), 7.50 (ddd, *J* = 8.2, 7.7 and 1.1 Hz, 1 H, 4′-H), 7.60 (d, *J* = 8.5 Hz, 1 H, 6-H), 7.73 (dd, *J* = 11.3 and 14.9 Hz, 1 H, β-H), 7.83 (dd, *J* = 7.9 and 1.1 Hz, 1 H, 6′-H), 12.77 (s, 1 H, 2′-O*H*). − ^{13}C NMR: δ = 118.7 (C-3′), 118.9 (C-5′), 119.9 (C-1′), 124.9 (C-α), 127.5 (C-5), 127.6 (C-γ), 129.3 (C-3), 129.5 (C-6′), 130.6 (C-6), 132.6 (C-1), 134.8 (C-2), 135.4 (C-4), 136.5 (C-4′), 136.9 (C-δ), 144.7 (C-β), 163.6 (C-2′), 193.5 (C=O). − MS (EI); *m*/*z* (%): 318 ($M^{+\bullet}$, 100), 317 (22), 283 (18), 225 (5), 173 (26), 162 (33), 147 (28), 127 (26), 121 (58), 93 (17). − $C_{17}H_{12}Cl_2O_2$ (319.2): calcd. C 63.97, H 3.79; found C 63.65, H 3.77.

(E,E)-2,6-Dichloro-2′-hydroxycinnamylideneacetophenone (**1e**): M.p. 142−144°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.92 (ddd, *J* = 8.0, 7.6 and 1.0 Hz, 1 H, 5′-H), 7.02 (dd, *J* = 8.1 and 1.0 Hz, 1 H, 3′-H), 7.12−7.20 (m, 2 H, γ,δ-H), 7.26 (d, *J* = 14.9 Hz, 1 H, α-H), 7.19 (t, *J* = 7.6 Hz, 1 H, 4-H), 7.36 (d, *J* = 7.6 Hz, 2 H, 3,5-H), 7.49 (ddd, *J* = 8.0, 7.6 and 1.5 Hz, 1 H, 4′-H), 7.66−7.78 (m, 1 H, β-H), 7.85 (dd, *J* = 8.0 and 1.5 Hz, 1 H, 6′-H), 12.77 (s, 1 H, 2′-O*H*). − ^{13}C NMR. δ = 118.6 (C-3′), 118.9 (C-5′), 119.9 (C-1′), 125.3 (C-α), 128.9 (C-3,5), 129.2 (C-γ), 129.6 (C-6′), 133.0 (C-1), 134.8 (C-2,6), 134.9 (C-4), 135.9 (C-δ), 136.4 (C-4′), 144.8 (C-β), 163.6 (C-2′), 193.7 (C=O). − MS (EI), *m*/*z* (%): 318 ($M^{+\bullet}$, 100), 317 (60), 283 (56), 225 (10), 173 (72), 162 (72), 147 (72), 127 (66), 121 (79), 93 (46). − $C_{17}H_{12}Cl_2O_2$ (319.2): calcd. C 63.97, H 3.79; found C 64.05, H 3.75.

(E)-2′-Hydroxychalcones **2b−e** were shown to possess spectroscopic and analytical data identical to those previously reported.[27]

(E,E)-2′-Hydroxy-γ-methylcinnamylideneacetophenone (**1f**), *(E,E)-4-chloro-2′-hydroxy-γ-methylcinnamylideneacetophenone* (**1g**), and *(E,E)-4-chloro-γ-ethyl-2′-hydroxycinnamylideneacetophenone* (**1h**) were obtained and characterised as previously reported.[23]

(E,E)-2′-Benzyloxy-6′-hydroxycinnamylideneacetophenones **1i−l**: To a methanolic solution (24 ml) of 2′-benzyloxy-6′-hydroxyacetophenone (1.2 g, 5.0 mmol), was added a 60% aqueous solution of sodium hydroxide (24 ml). After cooling the solution to room temperature, the appropriate cinnamaldehyde (7.5 mmol) was added and the reaction mixture stirred, for 20 h. The reaction mixture was poured into ice/hydrochloric acid (pH adjusted to ca. 2). The obtained solid was removed by filtration, dissolved in chloroform (100 ml), and washed with a solution of sodium hydrogen carbonate (2 × 100 ml) and water (100 ml). The organic layer was collected, the solvent evaporated and the residue purified by silica gel column chromatography, using dichloromethane as eluent. The solvent was evaporated and the residue was crystallised from ethanol giving (*E,E*)-2′-benzyloxy-6′-hydroxycinnamylideneacetophenones **1i−l**.

(E,E)-2′-Benzyloxy-6′-hydroxycinnamylideneacetophenone (**1i**) was shown to possess spectroscopic and analytical data identical to those previously reported.[16]

(E,E)-2′-Benzyloxy-6′-hydroxy-γ-methylcinnamylideneacetophenone (**1j**): 78%; m.p. 85−88°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.55 (s, 3 H, γ-CH_3), 5.10 (s, 2 H, 2′-OCH_2C$_6$H$_5$), 6.53 (d, *J* = 8.2 Hz, 1 H, 3′-H), 6.64 (d, *J* = 8.4 Hz, 1 H, 5′-H), 6.87 (s, 1 H, δ-H), 7.38 (d, *J* = 15.4 Hz, 1 H, α-H), 7.28−7.49 (m, 11 H, 2,3,4′,4,5,6-H and 2′-OCH$_2$C$_6$*H*$_5$), 7.59 (d, *J* = 15.4 Hz, 1 H, β-H), 13.44 (s, 1 H, 6′-O*H*). − ^{13}C NMR: δ = 13.3 (γ-CH_3), 71.3 (2′-OCH_2C$_6$H$_5$), 102.3 (C-3′), 111.3 (C-5′), 112.0 (C-1′), 127.4 (C-α), 127.7 (C-4 of 2′-OCH$_2$C$_6$H$_5$), 128.3 (C-2,6), 128.5 (C-2,6 of 2′- OCH$_2$C$_6$H$_5$), 128.6 (C-4), 128.8 (C-3,5 of 2′-OCH$_2$C$_6$H$_5$), 129.5 (C-3,5), 135.3 (C-γ), 135.7 (C-1), 135.8 (C-4′), 136.9 (C-1 of 2′-OCH$_2$C$_6$H$_5$), 140.0 (C-δ), 148.9 (C-β), 160.1 (C-6′), 165.2 (C-2′), 194.7 (C=O). − MS (EI); *m*/*z* (%): 370 ($M^{+\bullet}$,

74), 355 (7), 293 (5), 279 (65), 264 (11), 261 (13), 253 (17), 251 (20), 227 (13), 171 (19), 163 (8), 143 (15), 142 (20), 141 (18), 137 (65), 129 (90), 128 (17), 127 (10), 115 (23), 91 (100). − $C_{25}H_{22}O_3$ (370.5): calcd. C 81.06, H 5.99; found C 81.14, H 5.98.

(E,E)-2′-Benzyloxy-γ-hexyl-6′-hydroxycinnamylideneacetophenone (**1k**): 85%; m.p. 71−73°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 0.82 (t, *J* = 7.0 Hz, 3 H, C*H*$_3$), 1.09−1.39 [m, 8 H, γ-CH$_2$(C*H*$_2$)$_4$CH$_3$], 2.13 [m, 2 H, γ-C*H*$_2$(CH$_2$)$_4$CH$_3$], 5.17 (s, 2 H, 2′-OC*H*$_2$C$_6$H$_5$), 6.49 (d, *J* = 8.3 Hz, 1 H, 3′-H), 6.64 (d, *J* = 8.4 Hz, 1 H, 5′-H), 6.86 (s, 1 H, δ-H), 7.43 (d, *J* = 15.3 Hz, 1 H, α-H), 7.28−7.44 (m, 11 H, 2,3,4′,4,5,6-H and 2′-OCH$_2$C$_6$*H*$_5$), 7.55 (d, *J* = 15.3 Hz, 1 H, β-H), 13.25 (s, 1 H, 6′-O*H*). − ^{13}C NMR: δ = 14.0 (*C*H$_3$), 22.6, 27.1, 28.7, 29.4 and 31.5 [*C*H$_2$(*C*H$_2$)$_4$CH$_3$], 71.1 (2′-O*C*H$_2$C$_6$H$_5$), 102.8 (C-3′), 111.2 (C-5′), 112.4 (C-1′), 127.0 (C-α), 127.6 (C-2,6 of 2′-OCH$_2$*C*$_6$H$_5$), 127.8 (C-4 of 2′-OCH$_2$*C*$_6$H$_5$), 128.3 (C-4), 128.4 (C-2,6), 128.8 (C-3,5 of 2′-OCH$_2$*C*$_6$H$_5$), 129.2 (C-3,5), 135.6 (C-4′), 135.9 (C-1), 136.8 (C-1 of 2′-OCH$_2$*C*$_6$H$_5$), 139.8 (C-δ), 140.3 (C-γ), 148.4 (C-β), 160.0 (C-6′), 164.9 (C-2′), 194.8 (C=O). − MS (EI) *m/z* (%): 440 (M$^{+\bullet}$, 35), 355 (9), 349 (35), 253 (11), 227 (11), 199 (17), 163 (5), 137 (40), 129 (28), 128 (7), 115 (9), 91 (100). − $C_{30}H_{32}O_3$ (440.6): calcd. C 81.78, H 7.32; found C 81.97, H 7.34.

(E,E)-2′-Benzyloxy-4-tert-butyl-6′-hydroxy-γ-methylcinnamylideneacetophenone (**1l**): 67%; m.p. 123−126°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.33 [s, 9 H, 4-C(C*H*$_3$)$_3$], 1.57 (d, *J* = 1.1 Hz, 3 H, γ-C*H*$_3$), 5.10 (s, 2 H, 2′-OC*H*$_2$C$_6$H$_5$), 6.52 (dd, *J* = 8.2 and 0.9 Hz, 1 H, 3′-H); 6.60 (dd, *J* = 8.4 and 0.9 Hz, 1 H, 5′-H), 6.85 (s, 1 H, δ-H), 7.26 (d, *J* = 7.4 Hz, 1 H, 2,6-H), 7.38 (d, *J* = 15.5 Hz, 1 H, α-H), 7.33−7.42 (m, 6 H, 4′,3,5-H and 3,4,5-H of 2′-OCH$_2$C$_6$*H*$_5$), 7.47 (m, 2 H, 2,6-H of 2′-OCH$_2$C$_6$*H*$_5$); 7.60 (d, *J* = 15.5 Hz, 1 H, β-H), 13.46 (s, 1 H, 6′-O*H*). − ^{13}C NMR: δ = 13.4 (γ-*C*H$_3$), 31.2 [4-C(*C*H$_3$)$_3$], 34.7 [4-*C*(CH$_3$)$_3$], 71.3 (2′-O*C*H$_2$C$_6$H$_5$), 102.3 (C-3′), 111.2 (C-5′), 112.0 (C-1′), 125.3 (C-3,5), 126.9 (C-α), 128.4 (C-2,6 of 2′-OCH$_2$*C*$_6$H$_5$), 128.5 (C-4 of 2′-OCH$_2$*C*$_6$H$_5$), 128.7 (C-3,5 of 2′-OCH$_2$*C*$_6$H$_5$), 129.4 (C-2,6), 134.1 (C-1), 134.7 (C-γ), 135.6 (C-1 of 2′-OCH$_2$*C*$_6$H$_5$), 135.7 (C-4′), 140.1 (C-δ), 149.3 (C-β), 151.0 (C-4), 160.1 (C-6′), 165.1 (C-2′), 194.6 (C=O). − MS (EI); *m/z* (%): 426 (M$^{+\bullet}$, 58); 411 (4), 397 (2), 369 (2), 335 (19), 320 (7), 279 (38), 251 (8), 227 (16), 185 (15), 170 (16), 155 (6), 142 (5), 141 (7), 137 (46), 129 (37), 128 (9), 115 (7), 91 (100). − $C_{29}H_{30}O_3$ (426.6): calcd. C 81.66, H 7.09; found C 81.54, H 7.33.

2-Styrylchromones **3a−h**, **4f−h**, **5m**,**n**: Iodine (0.16 mmol, 40 mg) was added to a solution of the appropriate (*E,E*)-2′-hydroxycinnamylideneacetophenone **1a−h** (2 mmol) in DMSO (10 ml). The mixture was refluxed for 30 min, then poured into ice and water. The obtained solid was removed by filtration, taken up in chloroform (150 ml) and washed with a 20% aqueous solution of thiosulfate (2 × 150 ml). The organic layer was collected, dried (anhydrous sodium sulfate) and the solvent evaporated. The residue was purified by column chromatography, using chloroform as eluent.

When 2′-hydroxycinnamylideneacetophenones **1a-e** were used as starting materials, the obtained residues were crystallised in ethanol and the (*E*)-2-styrylchromones **3a−e** obtained in good yield (85−99%). The TLC analysis of the mother liquors of (*E*)-2-styrylchromone (**3a**) have revealed the presence of still another quantity of this chromone **3a** and small amounts of (*E*)-6-iodo-2-styrylchromone (**5m**) (4%) and of (*E*)-8-iodo-2-styrylchromone (**5n**) (4%).

When 2′-hydroxycinnamylideneacetophenones **1f−h** were used as starting materials, the obtained residues were purified by preparative thin layer chromatography, using a mixture of dichloromethane/light petroleum ether (2:8) as eluent. After several elutions, two close spots were obtained in each case, that of higher R_f value was constituted by (*Z*)-2-styrylchromones **4f−h** whereas that of lower R_f value by (*E*)-2-styrylchromones **3f−h**.

(E)-2-Styrylchromone (**3a**): 85%; m.p. 131−133°C (recrystallisation from ethanol, ref.[17] 133−134°C). − ^{1}H NMR: δ = 6.36 (s, 1 H, 3-H), 6.79 (d, *J* = 16.0 Hz, 1 H, α-H), 7.42 (dd, *J* = 7.9 and 7.4 Hz, 1 H, 6-H), 7.36−7.48 (m, 3 H, 3′,4′,5′-H), 7.53 (dd, *J* = 8.2 and 1.0 Hz, 1 H, 8-H), 7.58 (dd, *J* = 7.7 and 1.7 Hz, 2 H, 2′,6′-H), 7.61 (d, *J* = 16.0 Hz, 1 H, β-H), 7.68 (ddd, *J* = 8.2, 7.9 and 1.7 Hz, 1 H, 7-H), 8.20 (dd, *J* = 7.9 and 1.7 Hz, 1 H, 5-H). − ^{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* (%): 248 (M$^{+\bullet}$, 87), 247 (100), 231 (64), 219 (18), 218 (11), 155 (27), 128 (82), 127 (32), 121 (26), 120 (14), 102 (24), 92 (45).

(E)-2′-Chloro-2-styrylchromone (**3b**): 92%; m.p. 179−182°C (recrystallisation from ethanol, ref.[28] 191°C). − ^{1}H NMR: δ = 6.37 (s, 1 H, 3-H), 6.79 (d, *J* = 16.1 Hz, 1 H, α-H), 7.29−7.48 (m, 3 H, 4′,5′,6′-H), 7.40 (ddd, *J* = 7.7, 7.6 and 1.2 Hz, 1 H, 6-H), 7.57 (dd, *J* = 8.1 and 1.2 Hz, 1 H, 8-H), 7.70 (dd, *J* = 9.4 and 3.3 Hz, 1 H, 3′-H), 7.70 (ddd, *J* = 8.1, 7.6 and 1.7 Hz, 1 H, 7-H), 8.03 (d, *J* = 16.1 Hz, 1 H, β-H), 8.20 (dd, *J* = 7.7 and 1.7 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 111.3 (C-3), 118.0 (C-8), 122.8 (C-α), 124.1 (C-10), 125.1 (C-6), 125.7 (C-5), 127.2 (C-6′), 127.2 (C-5′), 130.2 (C-3′), 130.6 (C-4′), 132.8 (C-β), 133.3 (C-2′), 133.8 (C-7), 134.7 (C-1′), 156.0 (C-9), 161.3 (C-2), 178.4 (C-4). − MS (EI); *m/z* (%): 282 (M$^{+\bullet}$, 91), 281 (89), 265 (54), 247 (100), 218 (30), 162 (43), 127 (52), 126 (24), 121 (35), 120 (27), 109 (36), 92 (63). − $C_{17}H_{11}ClO_2 \cdot 1/4\ H_2O$ (287.3): calcd. C 71.09, H 4.03; found C 71.04, H 3.78.

(E)-4′-Chloro-2-styrylchromone (**3c**); 93%; m.p. 181−183°C (recrystallisation from ethanol, ref.[28] 226°C). − ^{1}H NMR: δ = 6.26 (s, 1 H, 3-H), 6.69 (d, *J* = 15.9 Hz, 1 H, α-H), 7.32 (d, *J* = 8.6 Hz, 2 H, 3′,5′-H), 7.33 (ddd, *J* = 7.8, 7.2 and 1.1 Hz, 1 H, 6-H), 7.45 (dd, *J* = 8.1 and 1.1 Hz, 1 H, 8-H), 7.45 (d, *J* = 8.6 Hz, 2 H, 2′,6′-H), 7.49 (d, *J* = 15.9 Hz, 1 H, β-H), 7.62 (ddd, *J* = 8.1, 7.2 and 1.7 Hz, 1 H, 7-H), 8.13 (dd, *J* = 7.8 and 1.7 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 111.0 (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′), 129.3 (C-3′,5′), 133.5 (C-1′), 133.8 (C-7), 135.4 (C-β), 135.7 (C-4′), 156.0 (C-9), 161.3 (C-2), 178.4 (C-4). − MS (EI); *m/z* (%): 282 (M$^{+\bullet}$, 86), 281 (100), 265 (63), 247 (41), 218 (22), 189 (29), 162 (41), 127 (40), 126 (19), 109 (32), 92 (27). − $C_{17}H_{11}ClO_2$ (282.7): calcd. C 72.22, H 3.92; found C 71.90, H 3.89.

(E)-2′,4′-Dichloro-2-styrylchromone (**3d**): 95%; m.p. 221−223°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.36 (s, 1 H, 3-H), 6.76 (d, *J* = 16.0 Hz, 1 H, α-H), 7.30 (dd, *J* = 8.7 and 2.1 Hz, 1 H, 5′-H), 7.40 (ddd, *J* = 8.3, 6.5 and 1.2 Hz, 1 H, 6-H), 7.46 (d, *J* = 2.1 Hz, 1 H, 3′-H), 7.55 (ddd, *J* = 8.2, 1.2 and 0.4 Hz, 1 H, 8-H), 7.63 (dd, *J* = 8.3 and 6.5 Hz, 1 H, 6′-H), 7.69 (ddd, *J* = 8.2, 6.5 and 1.6 Hz, 1 H, 7-H), 7.92 (d, *J* = 16.0 Hz, 1 H, β-H), 8.19 (ddd, *J* = 8.3, 1.6 and 0.4 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 111.5 (C-3), 118.0 (C-8), 123.2 (C-α), 124.2 (C-10), 125.2 (C-6), 125.7 (C-5), 127.7 (C-5′), 127.9 (C-6′), 130.1 (C-3′), 131.5 (C-1′), 131.5 (C-β), 133.9 (C-7), 135.2 (C-2′), 135.9 (C-4′), 156.0 (C-9), 163.8 (C-2), 178.4 (C-4). − MS (EI); *m/z* (%): 316 (M$^{+\bullet}$, 91), 315 (98), 299 (55), 281 (100), 246 (20), 223 (13), 218 (47), 196 (30), 189 (22), 161 (24), 126 (52), 121 (48), 120 (45), 109 (22), 92 (84). − $C_{17}H_{10}Cl_2O_2$ (317.2): calcd. C 64.38, H 3.18; found C 64.36, H 3.16.

(E)-2′,6′-Dichloro-2-styrylchromone (**3e**): 97%; m.p. 180−183°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.39 (s, 1 H, 3-

H), 6.97 (d, J = 16.5 Hz, 1 H, α-H), 7.21 (d, J = 8.0 Hz, 1 H, 4′-H), 7.40 (d, J = 8.0 Hz, 2 H, 3′,5′-H), 7.41 (dd, J = 8.4 and 7.8 Hz, 1 H, 6-H), 7.57 (d, J = 8.1 Hz, 1 H, 8-H), 7.71 (d, J = 16.5 Hz, 1 H, β-H), 7.71 (ddd, J = 8.4, 8.1 and 1.6 Hz, 1 H, 7-H), 8.21 (dd, J = 7.8 and 1.6 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 111.7 (C-3), 118.1 (C-8), 124.1 (C-10), 125.2 (C-6), 125.7 (C-5), 128.8 (C-α), 128.9 (C-3′,5′), 129.7 (C-4′), 130.6 (C-3′,5′), 132.5 (C-1′), 134.0 (C-7), 134.9 (C-β), 156.1 (C-9), 160.8 (C-2), 178.5 (C-4). − MS (EI); *m/z* (%): 316 ($M^{+\bullet}$, 24), 281 (100), 246 (12), 218 (17), 189 (9), 161 (7), 126 (15), 120 (11), 92 (30). − $C_{17}H_{10}Cl_2O_2$ (317.2): calcd. C 64.38, H 3.18; found C 64.27, H 3.16.

2-α-Methylstyrylchromone (96%)

(E)-2-α-Methylstyrylchromone (**3f**): 85%; m.p. 117−119°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 2.19 (s, 3 H, CH_3), 6.51 (s, 1 H, 3-H), 7.31−7.42 (m, 5 H, 2′,3′,4′,5′,6′-H), 7.37 (dd, J = 7.9 and 7.3 Hz, 1 H, 6-H), 7.51 (d, J = 8.5 Hz, 1 H, 8-H), 7.66 (s broad, 1 H, β-H), 7.66 (ddd, J = 8.5, 7.3 and 1.5 Hz, 1 H, 7-H), 8.19 (dd, J = 7.9 and 1.5 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 14.1 (*C*H_3), 108.1 (C-3), 117.8 (C-8), 123.6 (C-10), 124.9 (C-6), 125.5 (C-5), 128.4 (C-α), 128.1 (C-4′), 128.4 (C-3′,5′), 129.5 (C-2′,6′), 133.7 (C-7), 133.8 (C-β), 136.0 (C-1′), 155.9 (C-9), 164.3 (C-2), 178.7 (C-4). − MS (EI); *m/z* (%): 262 ($M^{+\bullet}$, 78), 261 (100), 247 (80), 246 (80), 245 (94), 218 (26), 191 (30), 169 (22), 142 (56), 141 (68), 121 (27), 120 (10), 115 (57), 92 (38). − $C_{18}H_{14}O_2$ (262.3): calcd. C 82.42, H 5.38; found C 82.69, H 5.41.

(Z)-2-α-Methylstyrylchromone (**4f**): 11%; transparent oil. − ^{1}H NMR: δ = 2.23 (d, J = 1.5 Hz, 3 H, CH_3), 6.27 (s broad, 1 H, 3-H), 6.86 (q, J = 1.5 Hz, 1 H, β-H), 7.00 (dd, J = 8.1 and 1.2 Hz, 1 H, 8-H), 7.15−7.24 (m, 5 H, 2′,3′,4′,5′,6′-H), 7.34 (dt, J = 7.7 and 1.2 Hz, 1 H, 6-H), 7.55 (ddd, J = 8.1, 7.7 and 1.6 Hz, 1 H, 7-H), 8.15 (dd, J = 7.7 and 1.6 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 22.6 (*C*H_3), 111.0 (C-3), 117.9 (C-8), 123.9 (C-10), 125.0 (C-6), 125.4 (C-5), 127.6 (C-4′), 128.1 (C-3′,5′), 128.4 (C-2′,6′), 128.9 (C-α), 133.6 (C-7), 135.2 (C-β), 136.6 (C-1′), 155.9 (C-9), 165.1 (C-2), 178.3 (C-4). − MS (EI); *m/z* (%): 262 ($M^{+\bullet}$, 60), spectrum similar to that of the (*E*) isomer.

4′-Chloro-2-α-methylstyrylchromone (93%)

(E)-4′-Chloro-2-α-methylstyrylchromone (**3g**): 78%; m.p. 107−108°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 2.17 (d, J = 1.3 Hz, 3 H, CH_3,), 6.50 (s, 1 H, 3-H), 7.34 (d, J = 8.7 Hz, 2 H, 3′,5′-H), 7.39 (d, J = 8.7 Hz, 2 H, 2′,6′-H), 7.38 (ddd, J = 8.0, 7.7 and 0.9 Hz, 1 H, 6-H), 7.51 (dd, J = 8.1 and 0.9 Hz, 1 H, 8-H), 7.59 (s broad, 1 H, β-H), 7.67 (ddd, J = 8.1, 7.7 and 1.6 Hz, 1 H, 7-H), 8.18 (dd, J = 8.0 and 1.6 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 14.1 (*C*H_3), 108.3 (C-3), 117.8 (C-8), 123.5 (C-10), 124.9 (C-6), 125.5 (C-5), 128.6 (C-2′,6′), 129.0 (C-α), 130.8 (C-3′,5′), 132.4 (C-β), 133.8 (C-7), 133.8 (C-1′), 134.4 (C-4′), 155.9 (C-9), 163.9 (C-2), 178.7 (C-4). − MS (EI); *m/z* (%): 296 ($M^{+\bullet}$, 84), 295 (94), 281 (98), 279 (100), 278 (91), 261 (33), 243 (35), 228 (33), 218 (38), 203 (30), 176 (45), 175 (33), 141 (50), 139 (40), 121 (37), 120 (48), 115 (51), 92 (58). − $C_{18}H_{13}ClO_2$ (296.8): calcd. C 72.85, H 4.42, found C 72.78; H 4.40.

(Z)-4′-Chloro-2-α-methylstyrylchromone (**4g**): 15%; transparent oil. − ^{1}H NMR: δ = 2.24 (d, J = 1.6 Hz, 3 H, CH_3), 6.28 (s, 1 H, 3-H), 6.79 (s broad, 1 H, β-H), 7.11 (d, J = 8.5 Hz, 2 H, 3′,5′-H), 7.22 (d, J = 8.5 Hz, 2 H, 2′,6′-H), 7.06 (dd, J = 8.1 and 1.0 Hz, 1 H, 8-H), 7.38 (ddd, J = 7.9, 7.6 and 1.0 Hz, 1 H, 6-H), 7.60 (ddd, J = 8.1, 7.6 and 1.8 Hz, 1 H, 7-H), 8.16 (dd, J = 7.9 and 1.8 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 22.7 (*C*H_3), 111.2 (C-3), 117.9 (C-8), 123.9 (C-10), 125.2 (C-6), 125.6 (C-5), 128.4 (C-2′,6′), 129.7 (C-α), 129.8 (C-3′,5′), 133.8 (C-1′), 133.9 (C-7), 135.0 (C-4′), 135.0 (C-β), 156.0 (C-9), 164.7 (C-2), 178.3 (C-4). − MS (EI); *m/z* (%): 296 ($M^{+\bullet}$, 63), spectrum similar to that of the (*E*) isomer.

4′-Chloro-2-α-ethylstyrylchromone (91%)

(E)-4′-Chloro-2-α-ethylstyrylchromone (**3h**): 76%; m.p. 116−117°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.25 (t, J = 7.5 Hz, 3 H, CH_3), 2.64 (q, J = 7.5 Hz, 2 H, CH_2), 6.56 (s, 1 H, 3-H), 7.34 (d, J = 8.6 Hz, 2 H, 3′,5′-H), 7.41 (d, J = 8.6 Hz, 2 H, 2′,6′-H), 7.41 (ddd, J = 8.0, 7.7 and 0.8 Hz, 1 H, 6-H), 7.52 (s broad, 1 H, β-H), 7.53 (dd, J = 8.1 and 0.8 Hz, 1 H, 8-H), 7.70 (ddd, J = 8.1, 7.7 and 1.7 Hz, 1 H, 7-H), 8.21 (dd, J = 8.0 and 1.7 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 13.8 (*C*H_3), 20.5 (*C*H_2), 108.4 (C-3), 117.9 (C-8), 123.6 (C-10), 125.0 (C-6), 125.5 (C-5), 128.7 (C-2′,6′), 130.3 (C-3′,5′), 132.1 (C-β), 133.8 (C-7), 134.0 (C-1′), 134.4 (C-4′), 135.7 (C-α), 156.1 (C-9), 163.5 (C-2), 178.7 (C-4). − MS (EI); *m/z* (%): 310 ($M^{+\bullet}$, 51), 309 (60), 295 (63), 293 (75), 281 (100), 277 (49), 246 (15), 218 (25), 190 (16), 175 (22), 121 (29), 92 (29). − $C_{19}H_{15}ClO_2$ (310.8): calcd. C 73.43, H 4.86; found C 73.42, H 4.85.

(Z)-4′-Chloro-2-α-ethylstyrylchromone (**4h**): 15%; transparent oil. − ^{1}H NMR: δ = 1.20 (t, J = 7.4 Hz, 3 H, CH_3), 2.58 (dq, J = 7.4 and 1.4 Hz, 2 H, CH_2), 6.24 (s, 1 H, 3-H), 6.72 (s broad, 1 H, β-H), 7.10 (d, J = 8.6 Hz, 2 H, 3′,5′-H), 7.20 (d, J = 8.6 Hz, 1 H, 2′,6′-H), 7.20 (dd, J = 8.3 and 1.0 Hz, 1 H, 8-H), 7.39 (ddd, J = 8.0, 7.7 and 1.0 Hz, 1 H, 6-H), 7.63 (ddd, J = 8.3, 7.7 and 1.7 Hz, 1 H, 7-H), 8.18 (dd, J = 8.0 and 1.7 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 13.0 (*C*H_3), 29.6 (*C*H_2), 111.8 (C-3), 118.0 (C-8), 124.0 (C-10), 125.3 (C-6), 125.6 (C-5), 128.5 (C-2′,6′), 129.8 (C-3′,5′), 133.5 (C-1′), 133.8 (C-7), 134.7 (C-β), 134.7 (C-4′), 136.3 (C-α), 156.3 (C-9), 164.9 (C-2), 178.1 (C-4). − MS (EI); *m/z* (%): 310 ($M^{+\bullet}$, 57), spectrum similar to that of the (*E*) isomer.

(E)-6-Iodo-2-styrylchromone (**5m**): 4%: m.p. 168−170°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.33 (s, 1 H, 3-H), 6.76 (d, J = 15.9 Hz, 1 H, α-H), 7.39−7.46 (m, 3 H, 3′,4′,5′-H), 7.58 (dd, J = 6.2 and 2.2 Hz, 2 H, 2′,6′-H), 7.29 (d, J = 8.8 Hz, 1 H, 8-H), 7.59 (d, J = 15.9 Hz, 1 H, β-H), 7.92 (dd, J = 8.8 and 2.2 Hz, 1 H, 7-H), 8.50 (d, J = 2.2 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 88.8 (C-6), 110.6 (C-3), 119.8 (C-α), 119.9 (C-8), 125.7 (C-10), 127.7 (C-2′,6′), 129.0 (C-3′,5′), 130.1 (C-4′), 134.6 (C-5), 134.8 (C-1′), 137.5 (C-β), 142.2 (C-7), 155.4 (C-9), 162.0 (C-2), 176.8 (C-4). − MS (EI); *m/z* (%): 374 ($M^{+\bullet}$, 100), 373 (77), 357 (45), 247 (12), 246 (23), 218 (17), 189 (19), 155 (20), 128 (92), 127 (22), 102 (18), 91 (12). − $C_{17}H_{11}IO_2$ (374.2): calcd. C 54.55, H 2.96; found C 54.66, H 2.95.

(E)-8-Iodo-2-styrylchromone (**5n**): 4%; m.p. 223−225°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 6.36 (s, 1 H, 3-H), 6.79 (d, J = 16.0 Hz, 1 H, α-H), 7.40−7.44 (m, 3 H, 3′,4′,5′-H), 7.62 (dd, J = 8.5 and 1.9 Hz, 2 H, 2′,6′-H), 7.16 (t, J = 7.8 Hz, 1 H, 6-H), 7.84 (d, J = 16.0 Hz, 1 H, β-H), 8.12 (dd, J = 7.8 and 1.5 Hz, 1 H, 7-H), 8.17 (dd, J = 7.8 and 1.5 Hz, 1 H, 5-H). − ^{13}C NMR: δ = 85.0 (C-8), 110.3 (C-3), 119.7 (C-α), 124.8 (C-10), 126.2 (C-5), 126.5 (C-6), 127.9 (C-2′,6′), 129.0 (C-3′,5′), 130.1 (C-4′), 135.0 (C-1′), 138.9 (C-β), 143.5 (C-7), 162.2 (C-2), 165.1 (C-9), 178.0 (C-4). − MS (EI); *m/z* (%): 374 ($M^{+\bullet}$, 100), 373 (82), 357 (44), 247 (12), 246 (23), 218 (16), 189 (14), 155 (25), 128 (70), 127 (18), 102 (11), 91 (14). − $C_{17}H_{11}IO_2$ (374.2): calcd. C 54.55, H 2.96; found C 54.53, H 2.85.

(E)-2-Styrylchromones **3i−l**: Iodine (6.1 mg, 0.024 mmol) was added to a solution of the appropriate (*E,E*)-2′-benzyloxy-6′-hydroxycinnamilidenoacetophenone (0.6 mmol) in DMSO (5 ml). The mixture was refluxed for 2 h, poured into ice and water, and the obtained solid 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 and the residue was crystallized from ethanol, yielding the expected (*E*)-2-styrylchromones **3i−l**.

(E)-5-Hydroxy-2-styrylchromone (**3i**) was shown to possess spectroscopic and analytical data identical to those previously reported.[16]

(*E*)-*5-Hydroxy-2-α-methylstyrylchromone* (**3j**): 68%; m.p. 118−120°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 2.19 (s, 3 H, α-CH_3), 6.41 (s, 1 H, 3-H), 6.78 (d, *J* = 8.3 Hz, 1 H, 6-H), 6.94 (d, *J* = 8.2 Hz, 1 H, 8-H), 7.41 (m, 5 H, 2′,3′,4′,5′,6′-H), 7.52 (dd, *J* = 8.3 and 8.2 Hz, 1 H, 7-H), 7.66 (s, 1 H, β-H), 12.57 (s, 1 H, 5-O*H*). − ^{13}C NMR: δ = 14.2 (*C*H$_3$), 106.7 (C-8), 106.9 (C-3), 110.6 (C-10), 111.1 (C-6), 128.0 (C-α), 128.4 (C-4′), 128.5 (C-2′,6′), 129.6 (C-3′,5′), 134.8 (C-β), 135.4 (C-7), 135.9 (C-1′), 156.2 (C-9), 160.7 (C-5), 165.5 (C-2), 183.9 (C-4). − MS (EI); *m/z* (%): 278 (M$^{+\bullet}$, 100), 277 (55), 263 (70), 261 (53), 260 (39), 234 (6), 232 (5), 169 (8), 142 (63), 141 (45), 137 (18), 136 (17), 128 (9), 115 (34), 108 (30), 91 (11). − $C_{18}H_{14}O_3$ (278.3): calcd. C 77.68, H 5.07; found C 77.10, H 5.19.

(E)-5-Hydroxy-2-α-hexylstyrylchromone (**3k**): 76%; yellow oil. − ^{1}H NMR: δ = 0.87 (t, *J* = 6.7 Hz, 3 H, CH_3), 1.25-1.65 [m, 8 H, α-CH$_2$(CH_2)$_4$CH$_3$], 2.61 [t, *J* = 8.2 Hz, 2 H, α-CH_2(CH$_2$)$_4$CH$_3$], 6.45 (s, 1 H, 3-H), 6.80 (d, *J* = 8.2 Hz, 1 H, 6-H), 6.96 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.36−7.47 (m, 5 H, 2′,3′,4′,5′,6′-H), 7.54 (dd, *J* = 8.4 and 8.2 Hz, 1 H, 7-H), 7.58 (s, 1 H, β-H), 12.59 (s, 1 H, 5-O*H*). − ^{13}C NMR: δ = 14.1 (*C*H$_3$), 22.6, 27.5, 29.2, 29.4, 31.4 [α-*C*H$_2$(*C*H$_2$)$_4$CH$_3$], 106.8 (C-8), 106.9 (C-3), 110.7 (C-10), 111.2 (C-6), 128.4 (C-4′), 128.6 (C-2′,6′), 129.2 (C-3′,5′), 133.8 (C-α), 134.7 (C-β), 135.4 (C-7), 135.9 (C-1′), 156.4 (C-9), 160.7 (C-5), 165.6 (C-2), 184.0 (C-4). − MS (EI); *m/z* (%): 348 (M$^{+\bullet}$, 73), 347 (19), 331 (28), 330 (18), 287 (11), 277 (14), 273 (10), 263 (100), 260 (15), 247 (6), 212 (6), 142 (14), 141 (26), 137 (28), 136 (6), 128 (9), 115 (22), 108 (12), 91 (15).

(E)-4′-tert-Butyl-5-hydroxy-2-α-methylstyrylchromone (**3l**): 72%; m.p. 135−136°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.35 [s, 9 H, 4′-C(CH_3)$_3$], 2.21 (s, 3 H, α-CH_3), 6.41 (s, 1 H, 3-H), 6.77 (dd, *J* = 8.3 and 0.8 Hz, 1 H, 6-H), 6.94 (dd, *J* = 8.4 and 0.8 Hz, 1 H, 8-H), 7.38 (d, *J* = 8.4 Hz, 2 H, 2′,6′-H), 7.45 (d, *J* = 8.4 Hz, 2 H, 3′,5′-H), 7.51 (dd, *J* = 8.4 and 8.3 Hz, 1 H, 7-H), 7.64 (s, 1 H, β-H), 12.60 (s, 1 H, 5-O*H*). − ^{13}C NMR: δ = 14.2 (α-*C*H$_3$), 31.2 [4′-C(*C*H$_3$)$_3$], 34.7 [4′-*C*(CH$_3$)$_3$], 106.5 (C-8), 106.8 (C-3), 110.6 (C-10), 111.0 (C-6), 125.4 (C-3′,5′), 127.2 (C-α), 129.6 (C-2′,6′), 132.9 (C-1′), 134.7 (C-β), 135.3 (C-7), 151.7 (C-4′), 156.1 (C-9), 160.6 (C-5), 165.8 (C-2), 183.9 (C-4). − MS (EI); *m/z* (%): 334 (M$^{+\bullet}$, 59), 333 (11), 319 (100), 317 (39), 316 (27), 301 (6), 294 (57), 279 (40), 277 (45), 263 (13), 251 (9), 198 (13), 183 (27), 165 (8), 160 (16), 155 (16), 153 (7), 146 (25), 142 (10), 141 (10), 137 (43), 128 (13), 115 (17), 108 (16), 91 (7). − $C_{22}H_{22}O_3$ (334.4): calcd. C 79.02, H 6.63; found C 78.90, H 6.79.

12H-Benzo[a]xanthene-12-ones **6a**,**f−h**: Chloroform solutions (30 ml) of (*E*)-2-styrylchromones **3a**,**f−h** (1 mmol), at room temperature, were exposed to daylight during several days (30−50 d). During that period more chloroform was added several times in order to maintain a constant volume in each case. After consumption of the starting material, controlled by TLC and ^{1}H NMR, the solvent was evaporated. The residue was purified by silica gel column chromatography, using a mixture of light petroleum ether/dichloromethane (2:8) as eluent. Finally, the residue, obtained by solvent evaporation, was crystallised from ethanol, giving the xanthones **6a**,**f−h**.

12H-Benzo[a]xanthene-12-one (**6a**): 40%; m.p. 135−137°C (recrystallisation from ethanol, ref.[20] 144−145°C). − ^{1}H NMR: δ = 7.44 (dd, *J* = 7.7 and 7.5 Hz, 1 H, 10-H), 7.53−7.56 (m, 2 H, 6,8-H), 7.59 (dd, *J* = 8.2 and 7.6 Hz, 1 H, 3-H), 7.73 (dd, *J* = 8.4 and 7.5 Hz, 1 H, 9-H), 7.78 (ddd, *J* = 8.4, 7.6 and 1.4 Hz, 1 H, 2-H), 7.89 (d, *J* = 8.2 Hz, 1 H, 4-H), 8.12 (d, *J* = 9.0 Hz, 1 H, 5-H), 8.44 (dd, *J* = 7.7 and 1.4 Hz, 1 H, 11-H), 10.09 (d, *J* = 8.4 Hz, 1 H, 1-H). − ^{13}C NMR. δ = 114.6 (C-11a), 117.5 (C-6), 118.0 (C-8), 123.6 (C-12a), 124.3 (C-10), 126.1 (C-3), 126.7 (C-11), 127.0 (C-1), 128.4 (C-4), 129.6 (C-2), 130.1 (C-4a), 131.1 (C-12b), 133.9 (C-9), 136.7 (C-5), 154.7 (C-7a), 157.6 (C-6a), 178.5 (C-4). − MS (EI); *m/z* (%): 246 (M$^{+\bullet}$, 100), 218 (41), 189 (42), 163 (10), 123 (7), 114 (9), 109 (13), 95 (14).

6-Methyl-12H-benzo[a]xanthene-12-one (**6f**): 56%; m.p. 134−137°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 2.67 (d, *J* = 0.9 Hz, 3 H, CH_3), 7.45 (ddd, *J* = 7.8, 7.5 and 1.1 Hz, 1 H, 10-H), 7.55 (ddd, *J* = 7.7, 7.6 and 0.9 Hz, 1 H, 3-H), 7.59 (dd, *J* = 8.1 and 1.1 Hz, 1 H, 8-H), 7.72 (ddd, *J* = 8.1, 7.6 and 1.2 Hz, 1 H, 2-H), 7.74 (ddd, *J* = 8.1, 7.5 and 2.1 Hz, 1 H, 9-H), 7.82 (dd, *J* = 7.7 and 1.2 Hz, 1 H, 4-H), 7.96 (s broad, 1 H, 5-H), 8.44 (dd, *J* = 7.8 and 1.2 Hz, 1 H, 11-H), 10.05 (dd, *J* = 8.1 and 0.9 Hz, 1 H, 1-H). − ^{13}C NMR: δ = 16.9 (*C*H$_3$), 114.4 (C-12a), 117.6 (C-8), 123.4 (C-11a), 124.3 (C-10), 126.1 (C-3), 126.6 (C-1), 126.7 (C-12b), 126.7 (C-11), 127.5 (C-4), 128.5 (C-2), 129.9 (C-4a), 130.1 (C-6), 133.8 (C-9), 136.1 (C-5), 154.5 (C-7a), 156.8 (C-6a), 178.8 (C-12). − MS (EI); *m/z* (%): 260 (M$^{+\bullet}$, 100), 259 (22), 232 (14), 231 (24), 203 (7), 202 (17), 139 (5), 130 (6), 101 (8), 91 (8). − $C_{18}H_{12}O_2$ (260.3): calcd. C 83.06, H 4.65; found C 82.79, H 4.59.

2-Chloro-6-methyl-12H-benzo[a]xanthene-12-one (**6g**): 52%; m.p. 223−226°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 2.67 (d, *J* = 0.9 Hz, 3 H, CH_3), 7.47 (ddd, *J* = 7.9, 7.7 and 0.9 Hz, 1 H, 10-H), 7.51 (dd, *J* = 8.6 and 2.1 Hz, 1 H, 3-H), 7.60 (ddd, *J* = 8.1, 0.9 and 0.4 Hz, 1 H, 8-H), 7.73 (d, *J* = 8.6 Hz, 1 H, 4-H), 7.76 (ddd, *J* = 8.1, 7.7 and 1.6 Hz, 1 H, 9-H), 7.92 (s broad, 1 H, 5-H), 8.42 (dd, *J* = 7.9 and 1.6 Hz, 1 H, 11-H), 10.12 (d, *J* = 2.1 Hz, 1 H, 1-H). − ^{13}C NMR: δ = 16.9 (*C*H$_3$), 113.7 (C-12a), 117.6 (C-8), 123.2 (C-11a), 124.6 (C-10), 126.0 (C-1), 126.9 (C-3), 126.6 (C-11), 127.1 (C-6), 128.1 (C-4a), 128.7 (C-4), 130.7 (C-12b), 134.1 (C-9), 134.9 (C-2), 135.6 (C-5), 154.5 (C-7a), 157.2 (C-6a), 178.5 (C-12). − MS (EI); *m/z* (%): 294 (M$^{+\bullet}$, 100), 259 (41), 231 (14), 202 (23), 129 (20), 101 (13). − $C_{18}H_{11}ClO_2$ (294.7): calcd. C 73.35, H 3.76; found C 73.64, H 3.85.

2-Chloro-6-ethyl-12H-benzo[a]xanthene-12-one (**6h**): 50%; m.p. 153−155°C (recrystallisation from ethanol). − ^{1}H NMR: δ = 1.42 (t, *J* = 7.5 Hz, 3 H, CH_3), 3.04 (q, *J* = 7.5 Hz, 3 H, CH_2), 7.44 (ddd, *J* = 8.0, 7.6 and 1.1 Hz, 1 H, 10-H), 7.46 (dd, *J* = 8.4 and 2.1 Hz, 1 H, 3-H), 7.54 (dd, *J* = 8.0 and 1.1 Hz, 1 H, 8-H), 7.69 (d, *J* = 8.4 Hz, 1 H, 4-H), 7.73 (ddd, *J* = 8.0, 7.6 and 1.5 Hz, 1 H, 9-H), 7.85 (s broad, 1 H, 5-H), 8.38 (ddd, *J* = 8.0, 1.5 and 0.3 Hz, 1 H, 11-H), 10.07 (d, *J* = 2.1 Hz, 1 H, 1-H). − ^{13}C NMR: δ = 13.6 (*C*H$_3$), 23.5 (*C*H$_2$), 113.5 (C-12a), 117.5 (C-8), 123.1 (C-11a), 124.5 (C-10), 125.9 (C-1), 126.5 (C-11), 126.8 (C-3), 128.1 (C-4a), 128.9 (C-4), 130.5 (C-12b), 132.6 (C-6), 133.9 (C-5), 134.0 (C-9), 134.8 (C-2), 154.4 (C-7a), 156.8 (C-6a), 178.4 (C-12). − MS (EI); *m/z* (%): 308 (M$^{+\bullet}$, 100), 295 (44), 293 (88), 279 (15), 273 (15), 265 (20), 258 (9), 229 (9), 202 (14), 200 (9), 129 (12), 101 (7), 100 (7). − $C_{19}H_{13}ClO_2.H_2O$ (326.9): calcd. C 72.85, H 4.34; found C 72.55, H 4.23.

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