A convenient synthesis of new (*E*)-5-hydroxy-2-styrylchromones by modifications of the Baker–Venkataraman method

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Received (in Montpellier, France) 25th October 1999, Accepted 23rd November 1999

New 5-hydroxy-2-styrylchromones and 3-cinnamoyl-5-hydroxy-2-styrylchromones have been prepared by modifications of the Baker–Venkataraman method. All compounds were fully characterized using several 1D and 2D NMR techniques. The *E* stereochemistry of the double bonds of all the 5-hydroxy-2-styrylchromones and the conformational features of those substituted in the 2′ and 2″ positions were unambiguously established by NOE experiments.

Introduction

2-Styrylchromones are a small group of natural heterocyclic compounds. Only two natural 2-styrylchromones are known and they have been extracted from the blue-green algae *Chrysophaeum taylori*.[1] The pharmacological activity and potential medicinal uses of natural and synthetic 2-styrylchromones are already well known.[1–3] Natural derivatives have demonstrated cytotoxic activity against several leukaemia cells,[1] while those obtained by synthesis have exhibited anti-allergic, antitumour and anticancer properties.[2,3]

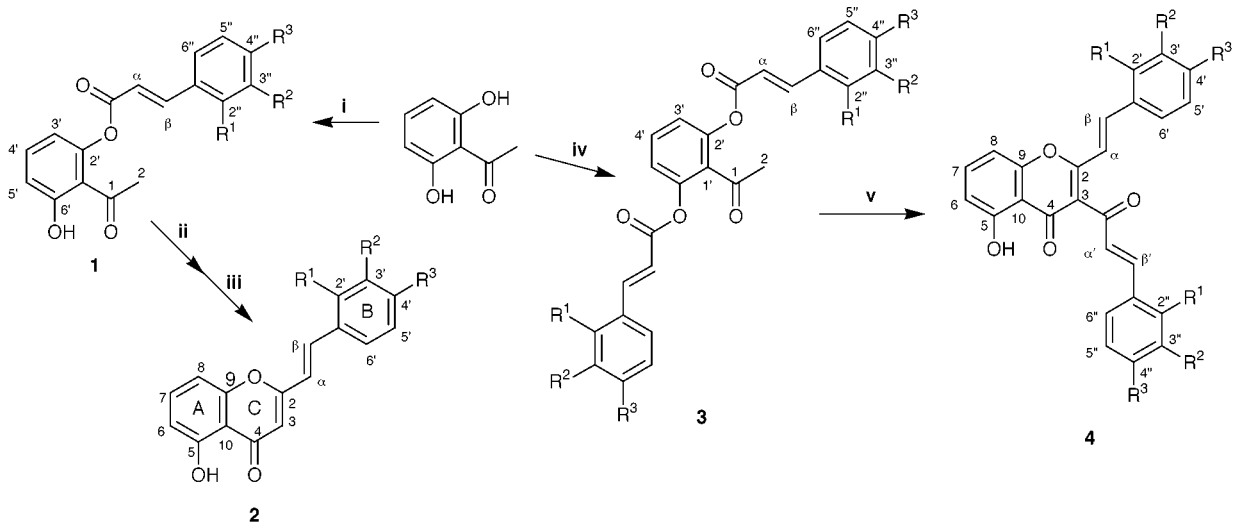
The 5-hydroxy-2-styrylchromone nucleus is present in the majority of the 2-styrylchromones that have shown important biological functions,[1,3] including the unique two natural derivatives. It is worth mentioning that in the case of its 2-phenylchromone analogues the same structural feature, *i.e.*, the presence of a 5-hydroxyl group, seems to be very important for observing biological activity, namely pharmacological and antioxidant properties.[4] Nevertheless, in spite of the potential uses of 5-hydroxy-2-(phenyl or styryl)chromones, the synthesis of 5-hydroxy-2-styrylchromone derivatives is too underdeveloped[3,5,6] for structure-activity relationship studies or/and exhaustive structural characterizations to be performed. In this context, it would be advantageous if certain 5-hydroxy-2-styrylchromone derivatives were available by simple and easy synthetic transformations. In our laboratory we have set up a programme to search for new 5-hydroxy-2-styrylchromones destined for further biological assessment and, at the same time, determine their conformational and configurational features. We report here the synthesis and structural characterization (including stereochemical and conformational aspects) of several 5-hydroxy-2-styrylchromone derivatives, **2a**–**i** and **4a**–**i**.

The most common method for the synthesis of 2-styrylchromone is the Baker–Venkataraman procedure.[7,8] This approach involves the *O*-acylation of a substituted *o*-hydroxyacetophenone with cinnamic acid derivatives, followed by a base-induced rearrangement of the formed *o*-cinnamoyloxyacetophenones to the corresponding 2-cinnamoyl-*o*-hydroxyacetophenones. The cyclodehydration of these compounds into 2-styrylchromones can be carried out using a sulfuric–glacial acetic acid mixture[9] and *p*-toluenesulfonic acid in benzene or DMSO.[10] All these procedures have been applied to the synthesis of 2-styrylchromones unsubstituted in the 5 position. Another related synthetic method consists in the modified Baker–Venkataraman procedure,[11] which involves the condensation of a substituted *o*-hydroxyacetophenone with cinnamoyl chloride in refluxing acetone containing anhydrous potassium carbonate. This procedure gives the corresponding 2-styrylchromones in one step. This method has been applied to the synthesis of 7-cinnamoyloxy- or 5,7-dicinnamoyloxy-2-styrylchromone derivatives starting from 2′,4′-dihydroxy-, 2′,4′,6′-trihydroxyacetophenones and related ketones and cinnamoyl chloride.[11] In continuation of our work on the synthesis of flavone derivatives[12] and in light of this literature analysis of the Baker–Venkataraman transformations, we examine the preparation of 5-hydroxy-2-styrylchromones with this method, in order to obtain 5-hydroxy-3-cinnamoyl-2-styrylchromones in a new way.

Results and discussion

Chemistry

5-Hydroxy-2-styrylchromones **2a**–**i** were prepared by the Baker–Venkataraman method[7,8] with some modifications of the experimental procedures (Scheme 1). Two methods were tried to perform the mono-*O*-cinnamoylation of 2′,6′-dihydroxyacetophenone. The first one consisted in the treatment of this acetophenone with the appropriate cinnamic acid derivatives in the presence of *N*,*N*-dicyclohexylcarbodiimide (DCC) and pyridine to yield the corresponding monocinnamoyl esters **1a**–**i** in yields of 30–40%. However, when DCC was used in the presence of a catalytic amount of 4-pyrrolidinopyridine, the 2′-cinnamoyloxy-6′-hydroxyacetophenones **1a**–**i** were obtained in much better yields (75–89%). Baker–Venkataraman rearrangement of **1a**–**i** with potassium hydroxide in DMSO, followed by the cyclodehydration of 2-cinnamoyl-2′,6′-dihydroxyacetophenone intermediates with an iodine–DMSO mixture,[13] led to the synthesis of **2a**–**i** in acceptable yields (35–45%). These results do not agree with those of Makrandi and Kumari,[10] who reported that the cyclodehydration of 2-cinnamoyl-2′-hydroxyacetophenones with the iodine–DMSO system provides a mixture of compounds. However, when *p*-



i 1 equiv. appropriate cinnamic acid, 1 equiv. DCC, 0.1 equiv. 4-pyrrolidinopyridine, CH_2Cl_2, room temp.
ii KOH (powder), DMSO, under nitrogen, room temp.
iii I_2–DMSO, 100 °C or *p*-toluenesulfonic acid–DMSO, 100 °C
iv 2 equiv. appropriate cinnamic acid, 2 equiv. DCC, 0.2 equiv. 4-pyrrolidinopyridine, CH_2Cl_2, room temp.
v K_2CO_3, dry pyridine, under nitrogen, 120 °C

a: $R^1 = R^2 = R^3 = H$
b: $R^1 = Cl$; $R^2 = R^3 = H$
c: $R^1 = OCH_3$; $R^2 = R^3 = H$
d: $R^1 = R^2 = H$; $R^3 = Cl$
e: $R^1 = R^2 = H$; $R^3 = CH_3$
f: $R^1 = R^2 = H$; $R^3 = OCH_3$
g: $R^1 = R^2 = H$; $R^3 = OBn$
h: $R^1 = R^3 = Cl$; $R^2 = H$
i: $R^1 = H$; $R^2 = R^3 = OBn$
$OBn = OCH_2C_6H_5$

Scheme 1 Synthesis of 5-hydroxy-2-styrylchromones **2a**–**i** and 3-cinnamoyl-5-hydroxy-2-styrylchromones **4a**–**i**.

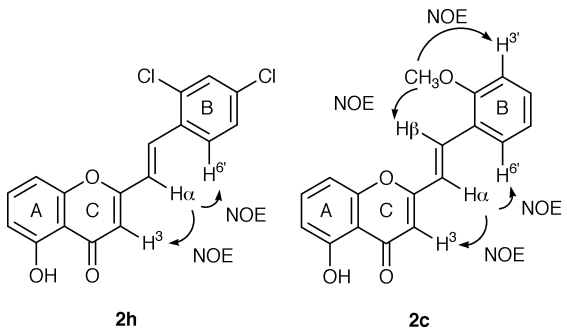
toluenesulfonic acid in DMSO was used in the cyclodehydration of 2-cinnamoyl-2′,6′-dihydroxyacetophenone intermediates, the desired **2a**–**i** were obtained in better yields (52–64%).

3-Cinnamoyl-5-hydroxy-2-styrylchromones **4a**–**i** were obtained by a modification of the Baker–Venkataraman method[14] (Scheme 1). 2′,6′-Dihydroxyacetophenone was first converted into the dicinnamoyl esters **3a**–**i**, by treatment with the appropriate cinnamic acid derivatives in the presence of DCC and 4-pyrrolidinopyridine. In the second step, treatment of 2′,6′-dicinnamoyloxyacetophenones **3a**–**i** with potassium carbonate in dry pyridine, under a nitrogen atmosphere, afforded **4a**–**i** in good yields (63–81%). The formation of the chromones **4a**–**i** involves the base-catalysed rearrangement of **3a**–**i** into 2,2-dicinnamoyl-2′,6′-dihydroxyacetophenone intermediates, which undergo *in situ* cyclodehydration to give the desired products **4a**–**i**. Similar transformations have already been reported for 2′,6′-dibenzoyloxyacetophenones.[15] Our modification of the Baker–Venkataraman method consists of a two-step procedure and constitutes a new method for the synthesis of **4a**–**i**. It is worth mentioning that our results do not agree with those of Reddy *et al.*, who reported that the condensation, by a modified Baker–Venkataraman procedure, of 2′,4′,6′-trihydroxyacetophenones and related ketones with cinnamoyl chloride derivatives gives the corresponding 2-styrylchromones in one step.[11]

Nuclear magnetic resonance spectroscopy

The main resonances in the ^1H and ^{13}C NMR spectra of 2′-cinnamoyloxy-6′-hydroxyacetophenones **1a**–**i** and 2′,6′-dicinnamoyloxyacetophenones **3a**–**i** are given in Table 1. The coupling constant values $^3J_{H\alpha\text{-}H\beta} = 15.8$–$16.1$ Hz indicate a *trans* configuration of the vinylic systems in these compounds. In compounds **1a**–**i** there is another important proton resonance, that of the 6′-O*H* group involved in a hydrogen bond with the C-1 carbonyl group.

The stereochemistry of 5-hydroxy-2-styrylchromones **2a**–**i** and 3-cinnamoyl-5-hydroxy-2-styrylchromones **4a**–**i** was established on the basis of NOE difference and NOESY experiments, which also allow us to discuss some conformational aspects. The coupling constant values $^3J_{H\alpha\text{-}H\beta} \approx 16$ Hz, and $^3J_{H\alpha'\text{-}H\beta'} \approx 16$ Hz for **4a**–**i**, indicate a *trans* configuration of these Cα=Cβ and Cα′=Cβ′ double bonds. In the case of 2′,4′-dichloro-5-hydroxy-2-styrylchromone **2h**, NOE experiments indicate a close proximity between H-α and H-3 and also H-6′, whereas, upon irradiation of H-β, no effect was observed (Fig. 1). These results allowed us to consider the *E* stereochemistry of the Cα=Cβ double bond and also to establish the conformation of the B ring of the chromone **2h** (as shown in Fig. 1 and Scheme 1). NOE experiments carried out with 5-hydroxy-2′-methoxy-2-styrylchromone **2c** (Fig. 1) also confirm the stereochemistry of the Cα=Cβ double bond in this type of chromone,[1,6,16] and the conformation of the B ring of 2′-substituted-2-styrylchromones.



2h **2c**

Fig. 1 NOE effects observed in 2′-substituted 5-hydroxy-2-styrylchromones **2c** and **2h**.

Table 1 Main ^1H and ^{13}C resonances of cinnamoyloxyacetophenones **1a**–**i** and **3a**–**i**

	6′-O*H*	H-2	H-α	H-β	C-2	C-1	*C*=O
1a–i	12.73–12.76	2.61–2.65	6.44–6.77	7.80–8.37	32.4–32.6	203.2–203.6	164.2–165.4
3a–i	—	2.49–2.54	6.37–6.71	7.74–8.30	31.2–31.4	198.5–199.0	164.0–165.3

Table 2 ^{1}H NMR data[a] of 5-hydroxy-2-styrylchromones **2a–i**

	2a	2b	2c	2d	2e	2f	2g	2h	2i
H-3	6.24	6.29	6.24	6.26	6.23	6.20	6.21	6.30	6.20
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
5-OH	12.60	12.54	12.66	12.56	12.64	12.67	12.66	12.51	12.66
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
H-6	6.79	6.81	6.78	6.80	6.78	6.78	6.78	6.82	6.78
	(dd; 8.3 and 0.8)	(dd; 8.4 and 0.8)	(dd; 8.3 and 0.8)	(d; 8.3)	(dd; 8.3 and 0.7)	(d; 8.6)	(dd; 8.3 and 0.8)	(dd; 8.3 and 0.7)	(d; 8.3)
H-7	7.52	7.55	7.51	7.54	7.53	7.52	7.52	7.56	7.51
	(t; 8.3)	(t; 8.4)	(t; 8.3)	(dd; 8.5 and 8.3)	(t; 8.3)	(t; 8.6)	(t; 8.3)	(t; 8.3)	(dd; 8.4 and 8.3)
H-8	6.96	7.00	6.98	6.96	6.96	6.94	6.95	7.00	6.94
	(dd; 8.3 and 0.8)	(dd; 8.4 and 0.8)	(dd; 8.3 and 0.8)	(d; 8.5)	(dd; 8.3 and 0.7)	(d; 8.6)	(dd; 8.3 and 0.8)	(dd; 8.3 and 0.7)	(d; 8.4)
H-α	6.75	6.76	6.86	6.74	6.72	6.62	6.63	6.75	6.54
	(d; 16.0)	(d; 16.0)	(d; 16.2)	(d; 16.1)	(d; 16.0)	(d; 15.8)	(d; 15.7)	(d; 16.0)	(d; 15.9)
H-β	7.61	8.04	7.92	7.58	7.60	7.57	7.58	7.96	7.50
	(d; 16.0)	(d; 16.0)	(d; 16.2)	(d; 16.1)	(d; 16.0)	(d; 15.8)	(d; 15.7)	(d; 16.0)	(d; 15.9)
H-2′	7.58			7.53	7.49	7.53	7.54		7.17
	(m)	—	—	(d; 8.5)	(d; 7.9)	(d; 8.6)	(d; 8.7)	—	(d; 2.0)
H-3′	7.42	7.70	6.95	7.40	7.23	6.94	7.02	7.49	—
	(m)	(m)	(d; 8.4)	(d; 8.5)	(d; 7.9)	(d; 8.6)	(d; 8.7)	(d; 2.1)	
H-4′	7.42	7.34	7.37	—	—	—	—	—	—
	(m)	(m)	(ddd; 8.4, 7.3 and 1.6)						
H-5′	7.42	7.34	7.00	7.40	7.23	6.94	7.02	7.32	6.95
	(m)	(m)	(dd; 7.7 and 7.3)	(d; 8.5)	(d; 7.9)	(d; 8.6)	(d; 8.7)	(dd; 8.5 and 2.1)	(d; 8.3)
H-6′	7.58	7.46	7.56	7.53	7.49	7.53	7.54	7.64	7.13
	(m)	(m)	(dd; 7.7 and 1.6)	(d; 8.5)	(d; 7.9)	(d; 8.6)	(d; 8.7)	(d; 8.5)	(dd; 8.3 and 2.0)

[a] ^{1}H chemical shifts of the substituents of some 2-styrylchromones: **2c** 3.94 (OCH_3, s); **2e** 2.40 (CH_3, s); **2f** 3.86 (OCH_3, s); **2g** 5.12 (OCH_2C$_6$H$_5$, s), 7.35–7.46 (OCH$_2$C$_6$$H_5$, m); **2i** 5.22 (2 × OCH_2C$_6$H$_5$, s), 7.31–7.50 (OCH$_2$C$_6$$H_5$, m).

Table 3 ^{13}C NMR chemical shifts[a] of 5-hydroxy-2-styrylchromones **2a–i**

	2a	2b	2c	2d	2e	2f	2g	2h	2i
C-2	162.8	162.4	163.6	162.4	163.1	163.3	163.3	162.0	163.2
C-3	109.0	109.6	108.6	109.3	108.7	108.2	108.3	109.9	108.4
C-4	183.6	183.6	183.6	183.5	183.6	183.5	183.5	183.6	183.5
C-5	160.8	160.8	160.8	160.8	160.8	160.8	160.8	160.8	160.8
C-6	111.3	111.4	111.2	111.4	111.3	111.2	111.2	111.5	111.3
C-7	135.3	135.5	135.2	135.4	135.3	135.2	135.2	135.6	135.2
C-8	106.8	107.0	107.0	106.8	106.8	106.8	106.8	107.0	106.8
C-9	156.2	156.2	156.2	156.1	156.2	156.2	156.2	156.1	156.2
C-10	110.9	111.0	111.0	111.0	111.0	110.9	110.9	111.0	110.9
C-α	119.5	122.0	120.1	120.1	118.5	117.1	117.3	122.4	117.6
C-β	138.0	133.8	133.5	136.5	138.1	137.7	137.7	132.5	137.8
C-1′	134.7	133.0	123.7	133.2	132.0	127.5	127.7	131.6	128.2
C-2′	127.8	134.8	158.1	128.9	127.8	129.5	128.7	135.3	113.4
C-3′	129.0	127.2	111.2	129.3	129.8	114.5	115.4	127.9	149.1
C-4′	130.2	130.9	131.4	136.0	140.7	161.3	160.5	136.2	151.0
C-5′	129.0	127.2	120.9	129.3	129.8	114.5	115.4	127.9	114.3
C-6′	127.8	130.3	128.5	128.9	127.8	129.5	128.7	130.1	122.7

[a] ^{13}C chemical shifts of the substituents of some 2-styrylchromones: **2c** 55.6 (OCH$_3$); **2e** 21.5 (CH$_3$); **2f** 55.4 (OCH$_3$); **2g** 70.1 (OCH$_2$C$_6$H$_5$), 127.5, 128.2, 129.5 and 136.3 (OCH$_2$$C_6H_5$); **2i** 70.9 and 71.4 (2 × OCH$_2$C$_6$H$_5$), 127.1, 127.2, 128.0, 128.6, 136.6 and 136.8 (2 × OCH$_2$$C_6H_5$).

The proximity between H-β and the 2′-substituents (OCH$_3$ or Cl) in **2b**, **2c** and **2h** can also be inferred from the shifts of the C-β (132.5–133.8 ppm) and H-β (7.92–8.04 ppm) resonances compared to those of the 2′-unsubstituted derivatives **2a**, **2d–g** and **2i** (C-β, 136.5–138.1 ppm; H-β, 7.50–7.61 ppm) (Tables 2 and 3), which are the consequence of a steric interaction between H-β and the 2′-substituent.[17]

In the substituted **4** compounds the same type of steric interaction between H-β and the 2′-substituent (and between H-β′ and the type 2″-substituent of **4b** or **4c**) can also be evidenced by comparison of the H-β (8.12–8.25 ppm), H-β′ (8.00–8.15 ppm), C-β (135.7–136.3 ppm) and C-β′ (139.9–140.7 ppm) chemical shifts, with those of the derivatives unsubstituted in the 2′- and 2″-positions, **4a**, **4d–g** and **4i** (H-β, 7.66–7.80 ppm; H-β′, 7.56–7.70 ppm; C-β, 139.6–140.8 ppm; C-β′, 142.9–145.1 ppm) (Tables 4 and 5). These results, together with the analysis of the NOESY spectrum of 3-cinnamoyl-5-hydroxy-2-styrylchromone **4a**, which does not show any NOE effect between H-α and H-α′, are only compatible with the structure shown for **4** in Scheme 1.

The unambiguous assignment of each AB spin system, corresponding to the resonances of H-α/H-β and H-α′/H-β′, of chromones **4a–i** was made on the basis of one-dimensional selective INEPT experiments.[18] On irradiation of the resonance assigned to H-β, enhancements of the C-2′, C-6′ and C-3 signals were observed, whereas, upon irradiation of the resonance ascribed to H-β′, enhancements were observed for the resonances of C-2″, C-6″ and C=O of the cinnamoyl group. The same experiment was used for the unambiguous assignment of the C-6, C-8, H-6 and H-8 resonances of chromones **2a–i** and **4a–i**. For instance, upon irradiation of the 5-OH resonance, enhancements of the signals of C-5, C-6 and C-10 were observed. These results, together with the analysis of the HETCOR experiments on chromones **2a–i** and **4a–i**, allowed

Table 4 ^{1}H NMR data[a] of 3-cinnamoyl-5-hydroxy-2-styrylchromones **4a–i**

	4a	4b	4c	4d	4e	4f	4g	4h	4i
5-OH	12.41 (s)	12.35 (s)	12.50 (s)	12.50 (s)	12.36 (s)	12.46 (s)	12.51 (s)	12.24 (s)	12.50 (s)
H-6	6.84 (d; 8.3)	6.86 (dd; 8.3 and 0.8)	6.82 (d; 8.2)	6.82 (dd; 8.3 and 0.8)	6.86 (dd; 8.3 and 0.7)	6.83 (d; 8.2)	6.83 (dd; 8.3 and 0.7)	6.86 (d; 8.3)	6.82 (dd; 8.3 and 0.6)
H-7	7.59 (m)	7.62 (t; 8.3)	7.59 (m)	7.55 (t; 8.3)	7.61 (t; 8.3)	7.58 (t; 8.2)	7.57 (t; 8.3)	7.60 (t; 8.3)	7.56 (t; 8.3)
H-8	7.03 (d; 8.4)	7.06 (dd; 8.3 and 0.8)	7.05 (d; 8.3)	7.00 (dd; 8.3 and 0.8)	7.02 (dd; 8.3 and 0.7)	7.01 (d; 8.2)	7.07 (dd; 8.3 and 0.8)	7.03 (d; 8.3)	6.98 (dd; 8.3 and 0.6)
H-α	7.17 (d; 15.9)	7.27 (d; 15.9)	7.20 (d; 16.0)	7.00 (d; 15.9)	7.19 (d; 15.9)	7.10 (d; 15.9)	7.00 (d; 15.8)	7.26 (d; 15.9)	6.89 (d; 16.3)
H-β	7.80 (d; 15.9)	8.25 (d; 15.9)	8.12 (d; 16.0)	7.74 (d; 15.9)	7.76 (d; 15.9)	7.77 (d; 15.9)	7.75 (d; 15.8)	8.14 (d; 15.9)	7.66 (d; 16.3)
H-2′	7.59 (m)	—	—	7.56 (d; 8.6)	7.53 (d; 8.4)	7.49 (d; 7.9)	7.57 (d; 8.5)	—	7.20 (d; 1.9)
H-3′	7.40 (m)	7.74 (m)	6.91 (d; 8.3)	6.98 (d; 8.6)	7.38 (d; 8.4)	7.20 (d; 7.9)	6.91 (d; 8.5)	7.45[b] (d; 2.1)	—
H-4′	7.40 (m)	7.33 (m)	7.37 (m)	—	—	—	—	—	—
H-5′	7.40 (m)	7.33 (m)	6.97 (t; 6.8)	6.98 (d; 8.6)	7.38 (d; 8.4)	7.20 (d; 7.9)	6.91 (d; 8.5)	7.26 (m)	6.91 (d; 8.1)
H-6′	7.59 (m)	7.43 (m)	7.59 (m)	7.56 (d; 8.6)	7.53 (d; 8.4)	7.49 (d; 7.9)	7.57 (d; 8.5)	7.65[c] (d, 8.3)	7.13 (m)
H-α′	7.24 (d; 16.0)	7.24 (d; 15.9)	7.28 (d; 16.2)	7.10 (d; 15.9)	7.24 (d; 16.0)	7.19 (d; 16.0)	7.11 (d; 15.9)	7.28 (d; 16.0)	7.02 (d; 15.9)
H-β′	7.70 (d; 16.0)	8.15 (d; 15.9)	8.00 (d; 16.2)	7.64 (d; 15.9)	7.66 (d; 16.0)	7.66 (d; 16.0)	7.65 (d; 15.9)	8.04 (d; 16.0)	7.56 (d; 15.9)
H-2″	7.59 (m)	—	—	7.56 (d; 8.6)	7.55 (d; 8.5)	7.49 (d; 7.9)	7.57 (d; 8.5)	—	7.13 (m)
H-3″	7.40 (m)	7.74 (m)	6.92 (d; 8.3)	6.98 (d; 8.6)	7.38 (d; 8.5)	7.20 (d; 7.9)	6.91 (d; 8.5)	7.47[b] (d; 2.1)	—
H-4″	7.40 (m)	7.33 (m)	7.37 (m)	—	—	—	—	—	—
H-5″	7.40 (m)	7.33 (m)	6.97 (t; 6.8)	6.98 (d; 8.6)	7.38 (d; 8.5)	7.20 (d; 7.9)	6.91 (d; 8.5)	7.26 (m)	6.91 (d; 8.1)
H-6″	7.59 (m)	7.43 (m)	7.59 (m)	7.56 (d; 8.6)	7.55 (d; 8.5)	7.49 (d; 7.9)	7.57 (d; 8.5)	7.67[c] (d, 8.3)	7.13 (m)

[a] ^{1}H chemical shifts of the substituents of some 3-cinnamoyl-2-styrylchromones: **4c** 3.86 and 3.91 (2 × OCH_3, 2s); **4e** 2.38 (2 × CH_3, s); **4f** 3.85 (2 × OCH_3, s); **4g** 5.10 (2 × OCH_2C$_6$H$_5$, s), 7.34–7.44 (2 × OCH$_2$C$_6$$H_5$, m); **4i** 5.18 and 5.20 (4 × OCH_2C$_6$H$_5$, 2s), 7.25–7.47 (4 × OCH$_2$C$_6$$H_5$, m). [b] and [c] Tentative assignment only; these two pairs may be interchanged.

Table 5 ^{13}C NMR chemical shifts[a] of 3-cinnamoyl-5-hydroxy-2-styrylchromones 4a–i

	4a	4b	4c	4d	4e	4f	4g	4h
C-2	162.5	162.8	162.6	162.7	162.7	162.6	162.7	162.5
C-3	120.8	121.0	120.8	120.3	120.8	120.6	120.3	120.3
C-4	181.7	181.9	181.7	181.6	181.8	181.7	181.6	181.5
C-5	161.0	161.0	161.0	160.9	161.1	161.0	161.0	161.0
C-6	111.9	112.1	111.7	111.7	112.1	111.8	111.7	111.7
C-7	136.0	135.8	135.7	135.8	136.2	135.9	135.8	135.8
C-8	106.9	107.1	107.0	106.7	106.8	106.8	106.8	106.8
C-9	155.3	155.3	156.5	155.4	155.3	155.4	155.4	155.3
C-10	110.5	110.6	110.6	110.5	110.5	110.5	110.5	110.4
C-α	117.4	119.9	118.0	115.1	118.0	116.4	115.0	115.3
C-β	140.8	136.3	135.7	140.3	139.6	140.8	140.4	140.5
C-1′	134.6	132.9	123.8	136.3	133.2	132.0	127.5	136.6[b]
C-2′	128.3	135.2	158.3	130.1	129.5	128.4	130.1	113.7
C-3′	129.0	127.2	111.2	115.3	129.4	129.8	114.5	149.0
C-4′	130.6	131.4	131.8	161.0	136.7	141.2	161.7	151.4
C-5′	129.0	128.0	120.9	115.3	129.4	129.8	114.5	114.0
C-6′	128.3	130.2	128.7	130.1	129.5	128.4	130.1	123.4
C=O	190.8	190.2	191.6	190.9	190.3	191.0	191.0	190.8
C-α′	127.1	129.1	127.9	125.3	127.4	126.4	125.2	125.5
C-β′	144.8	139.9	140.7	144.8	142.9	145.1	145.0	145.0
C-1″	134.4	132.7	123.4	136.3	132.9	131.7	127.2	136.8[b]
C-2″	128.8	136.8	158.9	130.6	129.9	128.8	130.7	114.0
C-3″	128.9	127.3	111.2	115.3	129.3	129.7	114.4	148.9
C-4″	130.9	131.5	132.2	161.1	136.8	141.5	162.0	151.6
C-5″	128.9	127.8	120.8	115.3	129.3	129.7	114.4	114.0
C-6″	128.8	130.3	129.4	130.6	129.9	128.8	130.7	124.0

[a] ^{13}C chemical shifts of the substituents of some 3-cinnamoyl-2-styrylchromones: **4c** 55.5 and 55.6 (2 × OCH_3); **4e** 21.6 (2 × CH_3); **4f** 55.4 (2 × OCH_3); **4g** 70.1 (2 × OCH_2C$_6$H$_5$), 127.5, 128.2, 128.7 and 136.3 (2 × OCH$_2$C$_6$$H_5$); **4i** 70.8, 70.9, 71.2 and 71.4 (4 × OCH_2C$_6$H$_5$), 127.1–128.6, 136.6 and 136.8 (4 × OCH$_2$C$_6$$H_5$). [b] These values may be interchanged.

us to assign H-8 (6.94–7.07 ppm) and C-6 (111.2–112.1 ppm) at higher frequency values than H-6 (6.78–6.86 ppm) and C-8 (106.7–107.1 ppm), respectively. (Tables 2–5).

Experimental

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 diluted deuteriochloroform solutions (*ca.* 0.3%) on a Bruker AMX 300 spectrometer, at 300.13 and 75.47 MHz, respectively; the chemical shifts are expressed in ppm values relative to tetramethylsilane (TMS) as internal reference. Unequivocal ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using HETCOR as well as one-dimensional selective INEPT[18] (long-range C–H coupling constants were optimized to 7 Hz). NOE experiments were performed using the NOE-difference technique, with an irradiation time of 4 s and a relaxation delay of 2 s. The electron impact (70 eV impact ionisation) and fast atom bombardment (nitrobenzyl alcohol as matrix) mass spectra were obtained on a VG Aupospec Q mass spectrometer. Elemental analyses were carried out using a Fisons Instruments EA 1108 CHNS analyser.

Column chromatography was performed on silica gel (Merck silica gel 60, 70–230 mesh). All chemicals and solvents were obtained from commercial sources and used as received, or dried using standard procedures.

Synthesis of 2′-cinnamoyloxy-6′-hydroxyacetophenones 1a–i

To a suspension of 2′,6′-dihydroxyacetophenone (0.5 g, 3.3 mmol) in dichloromethane (20 ml), the appropriate cinnamic acid (3.3 mmol), 4-pyrrolidinopyridine (49 mg, 0.33 mmol) and *N*,*N*-dicyclohexylcarbodiimide (0.7 g, 3.3 mmol) were added. The reaction mixture was stirred at room temperature for 30 min. The obtained dicyclohexylurea was filtered off and washed with dichloromethane (2 × 20 ml). The filtrate was evaporated to dryness and the residue purified by silica gel column chromatography (using a 7 : 3 mixture of dichloromethane–light petroleum). After evaporation of the solvents, the obtained residue was recrystallized in ethanol to give **1a–i**.

2′-Cinnamoyloxy-6′-hydroxyacetophenone 1a. Yield 75%, mp 110–111 °C. ^{1}H NMR: δ = 2.64 (s, 3 H, H-2), 6.67 (d, *J* 8.0 Hz, 1 H, H-3′), 6.68 (d, *J* 16.0 Hz, 1 H, H-α), 6.92 (d, *J* 8.5 Hz, 1 H, H-5′), 7.43–7.49 (m, 4 H, H-4′,3″,4″,5″), 7.60–7.64 (m, 2 H, H-2″,6″), 7.94 (d, *J* 16.0 Hz, 1 H, H-β), 12.75 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.5 (C-2), 114.0 (C-α), 114.6 (C-1′), 116.3 (C-3′,5′), 128.5 (C-2″,6″), 129.1 (C-3″,5″), 131.3 (C-4″), 133.7 (C-1″), 135.5 (C-4′), 148.3 (C-β), 151.4 (C-2′), 163.9 (C-6′), 164.9 (*C*=O), 203.4 (C-1). EI-MS: *m*/z (rel. int.) 282 (M$^{\cdot+}$, 12), 137 (6), 131 (100), 108 (7), 103 (53), 102 (14), 77 (41), 51 (18).

2′-(2-Chlorocinnamoyloxy)-6′-hydroxyacetophenone 1b. Yield 89%, mp 118–120 °C. ^{1}H NMR: δ = 2.65 (s, 3 H, H-2), 6.69 (dd, *J* 8.1 and 1.0 Hz, 1 H, H-3′), 6.67 (d, *J* 16.0 Hz, 1 H, H-α), 6.92 (dd, *J* 8.4 and 1.0 Hz, 1 H, H-5′), 7.35 (dt, *J* 7.8 and 1.9 Hz, 1 H, H-5″), 7.40 (dt, *J* 7.8 and 2.0 Hz, 1 H, H-4″), 7.47 (dd, *J* 8.4 and 8.1 Hz, 1 H, H-4′), 7.48 (d, *J* 7.8 Hz, 1 H, H-6″), 7.73 (dd, *J* 7.8 and 1.9 Hz, 1 H, H-3″), 8.37 (d, *J* 16.0 Hz, 1H, H-β), 12.76 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.6 (C-2), 114.0 (C-3′), 114.5 (C-1′), 116.4 (C-5′), 119.0 (C-α), 127.3 (C-5″), 127.9 (C-3″), 130.4 (C-6″), 131.9 (C-1″), 132.0 (C-4″), 135.4 (C-2″), 135.5 (C-4′), 143.9 (C-β), 151.3 (C-2′), 164.0 (C-6′), 164.4 (*C*=O), 203.3 (C-1). EI-MS: *m*/z (rel. int.) 316 (M$^{\cdot+}$, 11), 165 (100), 137 (37), 136 (9), 108 (10), 102 (27), 101 (41), 75 (24), 51 (17).

6′-Hydroxy-2′-(2-methoxycinnamoyloxy)acetophenone 1c. Yield 83%, mp 116–118 °C. ^{1}H NMR δ = 2.65 (s, 3 H, H-2), 3.93 (s, 3 H, OCH_3), 6.67 (dd, *J* 8.1 and 1.1 Hz, 1 H, H-3′), 6.77 (d, *J* 16.1 Hz, 1 H, H-α), 6.90 (dd, *J* 8.4 and 1.1 Hz, 1 H, H-5′), 6.97 (d, *J* 7.8 Hz, 1 H, H-3″), 7.02 (t, *J* 7.8 Hz, 1 H, H-5″), 7.43 (dt, *J* 7.8 and 1.6 Hz, 1 H, H-4″), 7.45 (dd, *J* 8.4 and 8.1 Hz, 1 H, H-4′), 7.59 (dd, *J* 7.8 and 1.6 Hz, 1 H, H-6″), 8.23 (d, *J* 16.1 Hz, 1 H, H-β), 12.75 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.5 (C-2), 55.6 (OCH_3), 111.3 (C-α), 114.1 (C-3″), 114.7 (C-1′), 116.1 (C-3′), 116.8 (C-5′), 120.9 (C-5″), 122.7 (C-1″), 129.5 (C-6″), 132.6 (C-4″), 135.5 (C-4′), 143.8 (C-β), 151.7 (C-2′), 158.8 (C-2″), 163.9(C-6′), 165.4 (*C*=O), 203.6 (C-1). EI-MS: *m*/z (rel. int.) 312 (M$^{\cdot+}$, 5), 161 (100), 152 (7), 146 (21), 137 (8), 131 (10), 123 (9), 118 (31), 108 (17), 105 (70), 103 (16), 102 (16), 90 (30), 89 (22), 77 (51), 51 (21).

2′-(4-Chlorocinnamoyloxy)-6′-hydroxyacetophenone 1d. Yield 84%, mp 124–127 °C. ^{1}H NMR: δ = 2.63 (s, 3 H, H-2), 6.65 (d, *J* 15.9 Hz, 1 H, H-α), 6.66 (d, *J* 8.4 Hz, 1 H, H-3′), 6.92 (d, *J* 8.1 Hz, 1 H, H-5′), 7.43 (d, *J* 8.5 Hz, 2 H, H-3″,5″), 7.46 (dd, *J* 8.4 and 8.1 Hz, 1 H, H-4′), 7.55 (d, *J* 8.5 Hz, 1 H, H-2″, 6″), 7.88 (d, *J* 15.9 Hz, 1 H, H-β), 12.73 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.4 (C-2), 113.9 (C-α), 114.6 (C-1′), 116.4 (C-3′), 116.9 (C-5′), 129.5 (C-3″,5″), 129.7 (C-2″,6″), 132.1 (C-1″), 135.5 (C-4′), 137.3 (C-4″), 146.8 (C-β), 151.3 (C-2′), 164.0 (C-6′), 164.7 (*C*=O), 203.3 (C-1). EI-MS: *m*/z (rel int.) 316 (M$^{\cdot+}$, 12), 165 (100), 137 (47), 136 (13), 123 (8), 108 (15), 102 (41), 101 (40), 75 (21).

6′-Hydroxy-2′-(4-methylcinnamoyloxy)acetophenone 1e. Yield 84%, mp 136–137 °C. ^{1}H NMR: δ = 2.41 (s, 3 H, 4″-CH_3), 2.63 (s, 3 H, H-2), 6.62 (d, *J* 15.8 Hz, 1 H, H-α), 6.66 (d, *J* 8.4 Hz, 1 H, H-3′), 6.90 (d, *J* 7.9 Hz, 1 H, H-5′), 7.25 (d, *J* 7.1 Hz, 1 H, H-3″,5″), 7.44 (dd, *J* 8.4 and 7.9 Hz, 1 H, H-4′), 7.51 (d, *J* 7.1 Hz, 1 H, H-2″,6″), 7.91 (d, *J* 15.8 Hz, 1 H, H-β), 12.75 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 21.6 (4″-*C*H$_3$), 32.4 (C-2), 114.0 (C-α), 114.6 (C-1′), 115.1 (C-3′), 116.2 (C-5′), 128.6 (C-2″, 6″), 129.9 (C-3″,5″), 131.0 (C-1″), 135.5 (C-4′), 142.0 (C-4″), 148.3 (C-β), 151.5 (C-2′), 163.9 (C-6′), 165.1 (*C*=O), 203.4 (C-1). EI-MS: *m*/z (rel. int.) 296 (M$^{\cdot+}$, 7), 145 (100), 117 (40), 116 (11), 115 (37), 91 (21), 65 (7).

6′-Hydroxy-2′-(4-methoxycinnamoyloxy)acetophenone 1f. Yield 79%, mp 115–117 °C. ^{1}H NMR: δ = 2.64 (s, 1 H, H-2), 3.87 (s, 3 H, OCH_3), 6.53 (d, *J* 15.9 Hz, 1 H, H-α), 6.66 (d, *J* 8.4 Hz, 1 H, H-3′), 6.90 (d, *J* 8.1 Hz, 1 H, H-5′), 6.96 (d, *J* 8.7 Hz, 2 H, H-3″,5″), 7.45 (dd, *J* 8.4 and 8.1 Hz, 1 H, H-4′), 7.57 (d, *J* 8.7 Hz, 1 H, H-2″,6″), 7.89 (d, *J* 15.9 Hz, 1 H, H-β), 12.75 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.5 (C-2), 55.5 (OCH_3), 113.6 (C-α), 114.1 (C-3′), 114.6 (C-3″,5″), 114.7 (C-1′), 116.2 (C-5′), 126.4 (C-1″), 130.4 (C-2″,6″), 135.5 (C-4′), 148.0 (C-β), 151.6 (C-2′), 162.2 (C-4″), 163.9 (C-6′), 165.3 (*C*=O), 203.5 (C-1). EI-MS: *m*/z (rel. int.) 312 (M$^{\cdot+}$, 1), 161 (100), 133 (25), 118 (10), 90 (10), 89 (9), 77 (9).

2′-(4-Benzyloxycinnamoyloxy)-6′-hydroxyacetophenone 1g. Yield 78%, mp 174–176 °C. ^{1}H NMR: δ = 2.63 (s, 3 H, H-2), 5.13 (s, 2 H, OCH_2C$_6$H$_5$), 6.53 (d, *J* 15.9 Hz, 1 H, H-α), 6.66 (dd, *J* 8.0 and 1.1 Hz, 1 H, H-3′), 6.90 (dd, *J* 8.5 and 1.1 Hz, 1 H, H-5′), 7.03 (d, *J* 8.8 Hz, 2 H, H-3″,5″), 7.35–7.47 (m, 6 H, H-4′ and OCH$_2$C$_6$*H*$_5$), 7.56 (d, *J* 8.8 Hz, 2 H, H-2″,6″), 7.88 (d, *J* 15.9 Hz, 1 H, H-β), 12.74 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.4 (C-2), 70.1 (OCH_2C$_6$H$_5$), 113.6 (C-α), 114.0 (C-3′), 114.6 (C-1′), 115.4 (C-3″,5″), 116.1 (C-5′), 126.6 (C-1″), 127.4 (C-2,6 of OCH$_2$*C*$_6$H$_5$), 128.2 (C-4 of OCH$_2$*C*$_6$H$_5$), 128.7 (C-3,5 of OCH$_2$*C*$_6$H$_5$), 130.3 (C-2″,6″), 135.5 (C-4′), 136.2 (C-1 of OCH$_2$*C*$_6$H$_5$), 147.9 (C-β), 151.5 (C-2′), 161.3 (C-4″), 163.8 (C-6′), 165.2 (*C*=O), 203.5 (C-1). EI-MS: *m*/z (rel. int.) 388 (M$^{\cdot+}$, 1), 370 (1), 237 (67), 146 (11), 118 (10), 91 (100), 65 (15).

2′(2,4-Dichlorocinnamoyloxy)-6′-hydroxyacetophenone 1h. Yield 75%, mp 140–142 °C. ^{1}H NMR: δ = 2.64 (s, 3 H, H-2), 6.65 (d, *J* 16.0 Hz, 1 H, H-α), 6.67 (dd, *J* 8.4 and 1.1 Hz, 1 H,

H-3′), 6.92 (dd, *J* 8.1 and 1.1 Hz, 1 H, H-5′), 7.33 (dd, *J* 8.4 and 2.1 Hz, 1 H, H-5″), 7.46 (dd, *J* 8.4 and 8.1 Hz, 1 H, H-4′), 7.50 (d, *J* 2.1 Hz, 1 H, H-3″), 7.66 (d, *J* 8.4 Hz, 1 H, H-6′), 8.28 (d, *J* 16.0 Hz, 1 H, H-β), 12.74 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.5 (C-2), 113.9 (C-3′), 114.5 (C-1′), 116.5 (C-5′), 119.4 (C-α), 127.8 (C-5″), 128.6 (C-3″), 130.3 (C-6″), 130.5 (C-1″), 135.5 (C-4′), 136.2 (C-2″), 137.4 (C-4″), 142.6 (C-β), 151.2 (C-2′), 164.0 (C-6′), 164.2 (*C*=O), 203.2 (C-1). EI-MS: *m*/*z* (rel. int.) 350 ($M^{\cdot+}$, 20), 199 (54), 171 (56), 164 (12), 152 (21), 137 (100), 136 (52), 135 (45), 123 (13), 109 (14), 108 (23), 101 (16), 100 (16), 99 (33), 77 (16), 75 (23), 74 (19), 51 (21).

2′(3,4-Dibenzyloxycinnamoyloxy)-6′-hydroxyacetophenone 1i. Yield 77%, mp 122–124 °C. ^{1}H NMR: δ = 2.61 (s, 3 H, H-2), 5.21 and 5.22 (s, 4 H, 3″,4″-OC*H*$_2$C$_6$H$_5$), 6.44 (d, *J* 15.9 Hz, 1 H, H-α), 6.64 (dd, *J* 8.0 and 1.1 Hz, 1 H, H-3′), 6.89 (dd, *J* 8.5 and 1.1 Hz, 1 H, H-5′), 6.95 (d, *J* 8.3 Hz, 1 H, H-5″), 7.15 (dd, *J* 8.3 and 2.0 Hz, 1 H, H-6″), 7.18 (d, *J* 2.0 Hz, 1 H, H-2″), 7.30–7.48 (m, 11 H, H-4′ and H-2,3,4,5,6 of 3″,4″-OCH$_2$C$_6$*H*$_5$), 7.80 (d, *J* 15.9 Hz, 1 H, H-β), 12.73 (s, 1 H, 6′-O*H*). ^{13}C NMR: δ = 32.4 (C-2), 70.8 and 71.4 (3″,4″-O*C*H$_2$C$_6$H$_5$), 113.9 (C-3′), 114.0 (C-5″,6″), 114.6 (C-1′), 116.2 (C-5′), 123.7 (C-α), 127.0 (C-2″), 127.1, 127.2, 127.3, 127.4, 128.0, 128.4 and 128.6 (C-1″ and C-2,3,4,5,6 of 3″,4″-OCH$_2$*C*$_6$H$_5$), 135.4 (C-4′), 136.4 and 136.7 (C-1 of 3″,4″-OCH$_2$*C*$_6$H$_5$), 148.0 (C-β), 149.0 (C-3″), 151.5 (C-2′), 151.8 (C-4″), 163.9 (C-6′), 165.1 (*C*=O), 203.4 (C-1). EI-MS: *m*/*z* (rel. int.) 494 ($M^{\cdot+}$, 1), 343 (66), 91 (100).

Synthesis of 2′,6′-dicinnamoyloxyacetophenones 3a–i

To a suspension of 2′,6′-dihydroxyacetophenone (0.76 g, 5.0 mmol) in dichloromethane (30 ml), the appropriate cinnamic acid (10 mmol), 4-pyrrolidinopyridine (148 mg, 1 mmol) and *N*,*N*-dicyclohexylcarbodiimide (2.1 g, 10 mmol) were added. The reaction mixture was stirred at room temperature for 30 min. The obtained dicyclohexylurea was filtered off and washed with dichloromethane (2 × 20 ml). The filtrate was evaporated to dryness and the residue purified by silica gel column chromatography (using an 8 : 2 mixture of dichloromethane–light petroleum). After evaporation of the solvents, the obtained residue was recrystallized in ethanol to provide **3a–i**.

2′,6′-Dicinnamoyloxyacetophenone 3a. Yield 77%, mp 140–142 °C. ^{1}H NMR: δ = 2.51 (s, 3 H, H-2), 6.61 (d, *J* 16.0 Hz, 2 H, 2 × H-α), 7.16 (d, *J* 8.2 Hz, 2 H, H-3′,5′), 7.40–7.46 (m, 6 H, 2 × H-3″,4″,5″), 7.50 (t, *J* 8.2 Hz, 1 H, H-4′), 7.57–7.61 (m, 4 H, 2 × H-2″,6″), 7.88 (d, *J* 16.0 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.3 (C-2), 116.2 (2 × C-α), 120.4 (C-3′,5′), 128.3 (C-1′), 128.5 (2 × C-2″,6″), 129.0 (2 × C-3″,5″), 130.8 (C-4′), 131.0 (2 × C-4″), 133.8 (2 × C-1″), 147.8 (2 × C-β and C-2′,6′), 164.7 (2 × *C*=O), 198.7 (C-1). EI-MS: *m*/*z* (rel. int.) 412 ($M^{\cdot+}$, 16), 131 (100), 103 (72), 102 (20), 77 (50), 51 (17). Anal. calcd. for C$_{26}$H$_{20}$O$_5$: C 75.72, H 4.89; found: C 75.52, H 4.79%.

2′,6′-Di(2-chlorocinnamoyloxy)acetophenone 3b. Yield 81%, mp 102–104 °C.^{1}H NMR: δ = 2.54 (s, 3 H, H-2), 6.61 (d, *J* 16.1 Hz, 2 H, 2 × H-α), 7.19 (dd, *J* = 8.2 Hz, 2 H, H-3′,5′), 7.32 (dt, *J* 7.4 and 1.6 Hz, 2 H, 2 × H-4″), 7.37 (dt, *J* 7.4 and 2.0 Hz, 2 H, 2 × H-5″), 7.46 (dd, *J* 7.4 and 1.6 Hz, 2 H, 2 × H-6″), 7.51 (t, *J* 8.2 Hz, 1 H, H-4′), 7.70 (dd, *J* = 7.4 and 2.0 Hz, 2 H, 2 × H-3″), 8.30 (d, *J* 16.1 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.4 (C-2), 118.9 (2 × C-α), 120.5 (C-3′,5′), 127.2 (2 × C-5″), 127.9 (2 × C-3″), 128.6 (C-1′), 130.3 (2 × C-6″), 130.8 (C-4′), 131.8 (2 × C-4″), 132.1 (2 × C-1″), 135.4 (2 × C-2″), 143.4 (2 × C-β), 147.7 (C-2′,6′), 164.2 (2 × *C*=O), 198.6 (C-1). EI-MS: *m*/*z* (rel. int.) 480 ($M^{\cdot+}$, 2), 445 (8), 316 (2), 301 (2), 273 (2), 165 (100), 137 (32), 102 (18), 101 (27), 75 (8). Anal. calcd. for C$_{26}$H$_{18}$Cl$_2$O$_5$: C 64.88, H 3.77; found: C 64.86, H, 3.76%.

2′,6′-Di(2-methoxycinnamoyloxy)acetophenone 3c. Yield 83%, mp 100–101 °C. ^{1}H NMR: δ = 2.52 (s, 3 H, H-2), 3.92 (s, 6 H, 2 × OC*H*$_3$), 6.71 (d, *J* 16.1 Hz, 2 H, 2 × H-α), 6.95 (d, *J* 7.8 Hz, 2 H, 2 × H-3″), 7.00 (t, *J* 7.8 Hz, 2 H, 2 × H-5″), 7.15 (d, *J* 8.2 Hz, 2 H, H-3′,5′), 7.40 (dt, *J* 7.8 and 1.6 Hz, 2 H, 2 × H-4″), 7.48 (t, *J* 8.2 Hz, 1 H, H-4′), 7.56 (dd, *J* 7.8 and 1.6 Hz, 2 H, 2 × H-6″), 8.17 (d, *J* 16.1 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.3 (C-2), 55.5 (2 × O*C*H$_3$), 111.2 (2 × C-3″), 116.8 (2 × C-α), 120.3 (C-3′,5′), 120.8 (2 × C-5″), 122.9 (2 × C-1″), 128.5 (C-1′), 129.6 (2 × C-6″), 130.7 (C-4′), 132.3 (2 × C-4″), 143.3 (2 × C-β), 147.9 (C-2′,6′), 158.7 (2 × C-2″), 165.3 (2 × *C*=O), 199.0 (C-1). EI-MS *m*/*z* (rel. int.) 472 ($M^{\cdot+}$, 2), 161 (100), 146 (6), 118 (12), 105 (15), 77 (8).

2′,6′-Di(4-chlorocinnamoyloxy)acetophenone 3d. Yield 76%, mp 165–166 °C. ^{1}H NMR: δ = 2.50 (s, 3 H, H-2), 6.57 (d, *J* 16.1 Hz, 2 H, 2 × H-α), 7.15 (d, *J* 8.2 Hz, 2 H, H-3′,5′) 7.40 (d, *J* 8.3 Hz, 4 H, 2 × H-3″,5″), 7.50 (t, *J* 8.2 Hz, 1 H, H-4′), 7.52 (d, *J* 8.3 Hz, 4 H, 2 × H-2″,6″), 7.82 (d, *J* 16.1 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.3 (C-2), 116.8 (2 × C-α), 120.4 (C-3′,5′), 128.2 (C-1′), 129.4 (2 × C-3″,5″), 129.6 (2 × C-2″,6″), 130.9 (C-4′), 132.3 (2 × C-1″), 137.0 (2 × C-4″), 146.3 (2 × C-β), 147.8 (C-2′,6′), 164.5 (2 × *C*=O), 198.6 (C-1). EI-MS: *m*/*z* (rel. int.) 480 ($M^{\cdot+}$, 1), 462 (13), 165 (100), 137 (26), 102 (19), 101 (19), 75 (7). Anal. calcd. for C$_{26}$H$_{18}$Cl$_2$O$_5$: C 64.88, H 3.77; found: C 64.86, H, 3.76%.

2′,6′-Di(4-methylcinnamoyloxy)acetophenone 3e. Yield 92%, mp 154–156 °C. ^{1}H NMR: δ = 2.40 (s, 6 H, 2 × 4″-C*H*$_3$), 2.51 (s, 3 H, H-2), 6.55 (d, *J* 15.9 Hz, 2 H, 2 × H-α), 7.15 (d, *J* 8.2 Hz, 2 H, H-3′,5′), 7.23 (d, *J* 8.1 Hz, 4 H, 2 × H-3″,5″), 7.48 (t, *J* 8.2 Hz, 1 H, H-4′), 7.48 (d, *J* 8.1 Hz, 4 H, 2 × H-2″,6″), 7.85 (d, *J* 15.9 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 21.6 (2 × 4″-*C*H$_3$), 31.3 (C-2), 115.1 (2 × C-α), 120.4 (C-3′,5′), 128.4 (C-1′), 128.5 (2 × C-2″,6″), 129.8 (2 × C-3″,5″), 130.7 (C-4′), 131.2 (2 × C-1″), 141.6 (2 × C-4″), 147.8 (2 × C-β and C-2′,6′), 164.9 (2 × *C*=O), 198.8 (C-1). EI-MS: *m*/*z* (rel. int.) 440 ($M^{\cdot+}$, 4), 422 (17), 145 (100), 117 (34), 116 (10), 115 (32), 91 (19), 65 (6). Anal. calcd. for C$_{28}$H$_{24}$O$_5$: C 76.35, H 5.49; found: C 76.50, H, 5.66%.

2′,6′-Di(4-methoxycinnamoyloxy)acetophenone 3f. Yield 82%, mp 157–158 °C. ^{1}H NMR: δ = 2.51 (s, 3 H, H-2), 3.86 (s, 6 H, 2 × OC*H*$_3$), 6.46 (d, *J* 15.9 Hz, 2 H, 2 × H-α), 6.93 (d, *J* 8.7 Hz, 4 H, 2 × H-3″,5″), 7.14 (d, *J* 8.2 Hz, 2 H, H-3′,5′), 7.47 (t, *J* 8.2 Hz, 1 H, H-4′), 7.54 (d, *J* 8.7 Hz, 4 H, 2 × H-2″,6″), 7.83 (d, *J* 15.9 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.3 (C-2), 55.4 (2 × O*C*H$_3$), 113.6 (2 × C-α), 114.5 (2 × C-3″,5″), 120.3 (C-3′,5′), 126.6 (2 × C-1″), 128.4 (C-1′), 130.3 (2 × C-2″,6″), 130.7 (C-4′), 147.5 (2 × C-β), 147.9 (C-2′,6′), 162.0 (2 × C-4″), 165.0 (2 × *C*=O), 198.9 (C-1). EI-MS: *m*/z (rel int.) 472 ($M^{\cdot+}$, 4), 384 (40), 302 (12), 259 (16), 203 (21), 176 (22), 161 (100), 134 (23), 133 (23), 121 (28), 98 (13), 77 (9), 55 (10).

2′,6′-Di(4-benzyloxycinnamoyloxy)acetophenone 3g. Yield 80%, mp 172–173 °C.^{1}H NMR δ = 2.50 (s, 3 H, H-2), 5.12 (s, 4 H, 2 × OC*H*$_2$C$_6$H$_5$), 6.46 (d, *J* 15.9 Hz, 2 H, 2 × H-α), 7.01 (d, *J* 8.8 Hz, 4 H, 2 × H-3″,5″), 7.14 (d, *J* 8.2 Hz, 2 H, H-3′,5′), 7.34–7.51 (m, 11 H, H-4′ and 10 H of 2 × OCH$_2$C$_6$*H*$_5$), 7.53 (d, *J* 8.8 Hz, 4 H, 2 × H-2″,6″), 7.82 (d, *J* 15.9 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.3 (C-2), 70.1 (2 × O*C*H$_2$C$_6$H$_5$), 113.7 (2 × C-α), 115.3 (2 × C-3″,5″), 120.3 (C-3′,5′), 126.9 (2 × C-1″), 127.5 (2 × C-2,6 of OCH$_2$*C*$_6$H$_5$), 128.2 (2 × C-4 of OCH$_2$*C*$_6$H$_5$), 128.4 (C-1′), 128.7 (2 × C-3,5 of OCH$_2$*C*$_6$H$_5$), 130.3 (2 × C-2″,6″), 130.6 (C-4′), 136.3 (2 × C-1 of OCH$_2$*C*$_6$H$_5$), 147.4 (2 × C-β), 147.9 (C-2′,6′), 161.1 (2 × C-4″), 165.0 (2 × *C*=O), 198.8 (C-1). EI-MS: *m*/*z* (rel. int.) 624 ($M^{\cdot+}$, 1), 335 (2), 282 (2), 237 (61), 146 (6), 137 (5), 118 (6), 91 (100), 83 (10), 65 (10).

2′,6′-Di(2,4-dichlorocinnamoyloxy)acetophenone 3h. Yield 90%, mp 138–140 °C. ^{1}H NMR: δ = 2.53 (s, 3 H, H-2), 6.59

(d, J 16.0 Hz, 2 H, 2 × H-α), 7.18 (d, J 8.2 Hz, 2 H, H-3′,5′), 7.32 (dd, J 8.5 and 1.9 Hz, 2 H, 2 × H-5″), 7.48 (d, J 1.9 Hz, 2 H, 2 × H-3″), 7.51 (t, J 8.2 Hz, 1 H, H-4′), 7.63 (d, J 8.5 Hz, 2 H, 2 × H-6″), 8.21 (d, J 16.0 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.4 (C-2), 119.2 (2 × C-α), 120.5 (C-3′,5′), 127.7 (2 × C-5″), 128.1 (C-1′), 128.6 (2 × C-3″), 130.2 (2 × C-6″), 130.6 (2 × C-1″), 130.9 (C-4′), 135.9 (2 × C-2″), 137.2 (2 × C-4″), 142.2 (2 × C-β), 147.7 (C-2′,6′), 164.0 (2 × *C*=O), 198.5 (C-1). EI-MS: *m*/*z* (rel. int.) 550 ($M^{\cdot+}$, 1), 350 (4), 199 (100), 181 (12), 171 (22), 136 (18), 135 (12), 99 (7).

2′,6′-Di(3,4-dibenzyloxycinnamoyloxy)acetophenone 3i. Yield 83%, mp 92–93 °C. ^{1}H NMR: δ = 2.49 (s, 3 H, H-2), 5.18 (s, 4 H, 2 × OCH_2C$_6$H$_5$), 6.37 (d, J 15.9 Hz, 2 H, 2 × H-α), 6.91 (d, J 8.4 Hz, 2 H, 2 × H-6″), 7.09 (dd, J 8.4 and 1.9 Hz, 2 H, 2 × H-5″), 7.11 (d, J 8.2 Hz, 2 H, H-3′,5′), 7.15 (d, J 1.9 Hz, 2 H, 2 × H-2″), 7.28–7.47 (m, 11 H, H-4′ and 2 × H-2,3,4,5,6 of OCH$_2$C$_6$*H*$_5$), 7.74 (d, J 15.9 Hz, 2 H, 2 × H-β). ^{13}C NMR: δ = 31.2 (C-2), 70.7 and 71.2 (2 × OCH_2C$_6$H$_5$), 113.8 and 113.9 (2 × C-2″,5″), 120.3 (C-3′,5′), 123.5 (2 × C-6″), 113.6 (2 × C-α), 127.1 and 127.2 (2 × C-2,6 of OCH$_2$*C*$_6$H$_5$), 127.1 and 128.5 (2 × C-4 of OCH$_2$*C*$_6$H$_5$), 127.9 and 128.5 (2 × C-3,5 of OCH$_2$*C*$_6$H$_5$), 128.3 (C-1′), 128.5 (2 × C-1″), 130.7 (C-4′), 136.5 and 136.7 (2 × C-1 of OCH$_2$*C*$_6$H$_5$), 147.5 (2 × C-β), 147.7 (C-2′,6′), 148.8 and 151.5 (2 × C-3″,4″), 164.8 (2 × *C*=O), 198.8 (C-1). FAB$^+$ − MS: *m*/*z* (rel. int.) 836 ($M^{\cdot+}$, 1), 343 (42), 251 (6), 181 (9), 135 (5), 107 (4), 105 (3), 91 (100), 77 (6).

Synthesis of 5-hydroxy-2-styrylchromones 2a–i

To a solution of the appropriate 2′-cinnamoyloxy-6′-hydroxyacetophenone **1a–i** (0.3 g, 1.3 mmol) in DMSO (20 ml), potassium hydroxide powder (281 mg, 5 mmol) was added. The reaction mixture was stirred under nitrogen for 4 h at room temperature and was then poured into a mixture of water, ice and hydrochloric acid (pH adjusted to 3). The obtained solid was removed by filtration, dissolved in chloroform (75 ml) and washed with a saturated solution of sodium hydrogen carbonate (3 × 50 ml). The organic layer was dried (anhydrous sodium sulfate), then evaporated to dryness. The obtained residue was used without further purification.

Method A. The obtained residue was dissolved in DMSO (15 ml) and iodine (6 mg, 24 μmol) was added. The mixture was heated (≈100 °C) under nitrogen for 1 h, then poured into water and ice. The obtained residue was taken up in chloroform (75 ml), washed with an aqueous saturated solution of sodium thiosulfate (3 × 50 ml) and again with a saturated solution of sodium hydrogen carbonate (3 × 50 ml). The organic layer was dried (anhydrous sodium sulfate), then evaporated to dryness. The obtained residue was purified by silica gel column chromatography (using dichloromethane as eluent). After removal of the solvent, the residue was recrystallized from ethanol to afford **2a–i**: yields **2a**, 35%; **2b**, 38%; **2c**, 42%; **2d**, 36%; **2e**, 40%; **2f**, 45%; **2g**, 44%; **2h**, 40% and **2i**, 45%.

Method B. The obtained residue was dissolved in DMSO (15 ml) and *p*-toluenesulfonic acid monohydrate (134.6 mg, 0.7 mmol) was added. The solution was heated (≈100 °C) under nitrogen for 2–3 h (the disappearance of the starting material was followed by TLC). The solution was poured into ice and water, and the obtained solid was removed by filtration. This solid was dissolved in dichloromethane (75 ml), then washed with water. The organic layer was dried (anhydrous sodium sulfate) and the solvent evaporated to dryness. The obtained residue was purified by silica gel column chromatography (using dichloromethane as eluent). After evaporation of the solvent, the residue was recrystallized from ethanol to yield **2a–i**: yield **2a**, 52%; **2b**, 55%; **2c**, 58%; **2d**, 53%; **2e**, 57%; **2f**, 63%; **2g**, 61%; **2h**, 56% and **2i**, 64%. The ^{1}H and ^{13}C NMR data for **2a–i** are given in Tables 2 and 3. 5-Hydroxy-2-styrylchromone **2a** was obtained as previously reported.[6]

2′-Chloro-5-hydroxy-2-styrylchromone 2b. Mp 176–178 °C. EI-MS *m*/z (rel. int.) 298 ($M^{\cdot+}$, 100), 297 (56), 280 (21), 263 (66), 234 (7), 189 (12), 178 (7), 162 (18), 136 (35), 127 (21), 126 (11), 108 (47), 83 (15), 77 (10), 63 (10), 51 (15). Anal. calcd. for $C_{17}H_{11}ClO_3$: C 68.35, H 3.71; found: C 68.35, H 3.61%.

5-Hydroxy-2′-methoxy-2-styrylchromone 2c. Mp 151–152 °C. EI-MS: *m*/z (rel. int.) 294 ($M^{\cdot+}$, 100), 293 (61), 279 (19), 278 (12), 276 (36), 263 (52), 158 (40), 137 (11), 115 (35), 108 (18), 91 (9), 89 (10), 77 (9), 63 (10), 58 (15), 51 (10). Anal. calcd. for $C_{18}H_{14}O_4$: C 73.46, H 4.80; found: C 73.55, H 5.07%.

4′-Chloro-5-hydroxy-2-styrylchromone 2d. Mp 204–206 °C. EI-MS: *m*/z (rel. int.) 298 ($M^{\cdot+}$, 100), 297 (74), 280 (45), 263 (34), 262 (13), 252 (9), 234 (10), 189 (15), 178 (8), 162 (26), 136 (44), 127 (28), 126 (13), 108 (46), 80 (11), 77 (9), 63 (9), 51 (11). Anal. calcd. for $C_{17}H_{11}ClO_3$: C 68.35, H 3.71; found: C 67.96, H 3.56%.

5-Hydroxy-4′-methyl-2-styrylchromone 2e. Mp 217–219 °C. EI-MS: *m*/z (rel. int.) 278 ($M^{\cdot+}$, 100), 277 (82), 263 (30), 260 (36), 234 (6), 142 (51), 141 (37), 137 (12), 136 (13), 115 (22), 108 (20), 91 (8), 63 (9), 51 (10). Anal. calcd. for $C_{18}H_{14}O_3$: C 77.68, H 5.07; found: C 77.96, H 5.36%.

5-Hydroxy-4′-methoxy-2-styrylchromone 2f. Mp 191–193 °C. EI-MS: *m*/z (rel. int.) 294 ($M^{\cdot+}$, 100), 293 (78), 279 (14), 276 (37), 263 (14), 250 (9), 158 (50), 133 (7), 115 (36), 108 (9), 89 (6), 63 (5), 51 (4). Anal. calcd. for $C_{18}H_{14}O_4$: C 73.44, H 4.80; found: C 73.55, H 4.90%.

4′-Benzyloxy-5-hydroxy-2-styrylchromone 2g. Mp 192–194 °C. EI-MS: *m*/z (rel. int.) 370 ($M^{\cdot+}$, 28), 279 (5), 251 (3), 165 (2), 115 (5), 108 (5), 91 (100), 83 (9), 65 (11). Anal. calcd. for $C_{24}H_{18}O_4$: C 77.82, H 4.90; found: C 77.55, H 4.85%.

2′,4′-Dichloro-5-hydroxy-2-styrylchromone 2h. Mp 208–209 °C. EI-MS: *m*/z (rel. int.) 332 ($M^{\cdot+}$, 100), 331 (56), 314 (25), 297 (57), 262 (27), 234 (17), 196 (11), 161 (12), 136 (51), 126 (22), 117 (13), 108 (78), 80 (16), 75 (13), 63 (11), 51 (15). Anal. calcd. for $C_{17}H_{10}Cl_2O_3$: C 61.29, H 3.02; found: C 61.43, H 3.01%.

3′,4′-Dibenzyloxy-5-hydroxy-2-styrylchomone 2i. Mp 176–177 °C. EI-MS: *m*/z (rel. int.) 476 ($M^{\cdot+}$, 16), 385 (11), 266 (3), 237 (3), 181 (4), 108 (4), 91 (100), 65 (16). Anal. calcd. for $C_{31}H_{24}O_5$: C 78.14, H 5.08; found: C 78.21, H 5.25%.

Synthesis of 3-cinnamoyl-5-hydroxy-2-styrylchromones 4a–i

To a solution of the appropriate 2′,6′-dicinnamoyloxyacetophenone **3a–i** (2.0 mmol) in pyridine (20 ml) was added potassium hydroxide powder (281 mg, 5 mmol). The reaction mixture was heated (≈120 °C) under nitrogen for 1 h and was then poured into a mixture of water, ice and hydrochloric acid (pH adjusted to 3). The obtained solid was removed by filtration, taken up in chloroform (75 ml), then washed with a saturated solution of sodium hydrogen carbonate (3 × 50 ml). The organic layer was dried (anhydrous sodium sulfate) and evaporated to dryness. The obtained residue was purified by silica gel column chromatography (using dichloromethane as eluent). After evaporation of the solvent, the residue was recrystallized in ethanol to afford **4a–i**. The ^{1}H and ^{13}C NMR data for **4a-i** are given in Tables 4 and 5.

3-Cinnamoyl-5-hydroxy-2-styrylchromone 4a. Yield (78%, mp 208–210 °C. EI-MS: *m*/z (rel. int.) 394 ($M^{\cdot+}$, 100), 393 (20), 376 (10), 365 (13), 317 (38), 315 (20), 303 (8), 289 (33), 275 (7), 263 (12), 180 (11), 155 (9), 137 (11), 131 (11), 127 (27), 103 (31),

91 (16), 77 (29), 51 (8). Anal. calcd. for $C_{26}H_{18}O_4$: C 79.17, H 4.60, found: C 79.09, H 4.64%.

2′-Chloro-3-(2-chlorocinnamoyl)-5-hydroxy-2-styrylchromone 4b. Yield 63%, mp 263–265 °C. EI-MS: *m*/z (rel. int.) 462 ($M^{\cdot+}$, 39), 427 (100), 424 (14), 399 (8), 351 (11), 315 (20), 291 (6), 263 (7), 246 (6), 218 (9), 205 (16), 189 (9), 171 (10), 161 (37), 153 (16), 137 (19), 126 (12), 125 (12), 109 (13), 101 (19), 91 (13), 69 (11), 55 (14). Anal. calcd. for $C_{26}H_{16}Cl_2O_4$: C 67.40, H 3.48; found: C 67.55, H 3.62%.

5-Hydroxy-2′-methoxy-3-(2-methoxycinnamoyl)-2-styrylchromone 4c. Yield 80%, mp 163–166 °C. EI-MS: *m*/z (rel. int.) 454 ($M^{\cdot+}$, 100), 436 (16), 423 (22), 347 (12), 345 (13), 335 (13), 333 (14), 319 (15), 318 (13), 315 (19), 303 (11), 240 (22), 227 (6), 161 (6), 137 (10), 121 (21), 118 (11), 105 (6), 91 (15), 77 (9). Anal. calcd. for $C_{28}H_{22}O_6$: C 74.00, H 4.88; found: C 73.92, H 4.92%.

4′-Chloro-3-(4-chlorocinnamoyl)-5-hydroxy-2-styrylchromone 4d. Yield 63%, mp 227–228 °C. EI-MS: *m*/z (rel. int.) 462 ($M^{\cdot+}$, 100), 461 (8), 427 (6), 351 (26), 349 (11), 325 (24), 323 (25), 315 (7), 297 (5), 248 (6), 226 (6), 189 (14), 165 (10), 161 (12), 137 (36), 136 (13), 126 (20), 125 (20), 108 (16), 102 (35), 101 (40), 75 (14). Anal. calcd. for $C_{26}H_{16}Cl_2O_4$: C 67.40, H 3.48; found: C 67.29, H 3.66%.

5-Hydroxy-4′-methyl-3-(4-methylcinnamoyl)-2-styrylchromone 4e. Yield 79%, mp 192–194 °C. EI-MS: *m*/z (rel. int.) 422 ($M^{\cdot+}$, 100), 421 (9), 407 (10), 404 (7), 393 (9), 331 (19), 329 (15), 319 (10), 315 (11), 303 (24), 277 (9), 208 (19), 141 (11), 115 (22), 105 (20), 91 (13). Anal. calcd. for $C_{28}H_{22}O_4$: C 79.60, H 5.25; found: C 79.56, H 5.35%.

5-Hydroxy-4′-methoxy-3-(4-methoxycinnamoyl)-2-styrylchromone 4f. Yield 81%, mp 206–209 °C. EI-MS: *m*/z (rel. int.) 454 ($M^{\cdot+}$, 94), 425 (8), 374 (6), 345 (15), 334 (10), 319 (22), 256 (6), 240 (100), 227 (19), 176 (9), 161 (11), 149 (25), 137 (13), 121 (52), 111 (16), 97 (27), 91 (79), 84 (51), 83 (78), 81 (28), 77 (32), 57 (64), 55 (65), 51 (18). Anal. calcd. for $C_{28}H_{22}O_4$: C 74.00, H 4.88; found: C 73.76, H 5.12%.

4′-Benzyloxy-3-(4-benzyloxycinnamoyl)-5-hydroxy-2-styrylchromone 4g. Yield 80%, mp 238–240 °C. EI-MS: *m*/z (rel. int.) 607 [$(M + H)^+$, 83], 549 (14), 523 (10), 397 (27), 369 (16), 307 (14), 237 (14), 154 (54), 136 (41), 123 (20), 107 (29), 91 (100). Anal. calcd. for $C_{40}H_{30}O_6 \cdot 1/2\ H_2O$: C 78.03, H 5.08; found: C 77.99, H 4.86%.

2′,4′-Dichloro-3-(2,4-dichlorocinnamoyl)-5-hydroxy-2-styrylchromone 4h. Yield 75%, mp 280–282 °C. EI-MS: *m*/z (rel. int.) 532 ($M^{\cdot+}$, 78), 497 (100), 467 (14), 385 (14), 359 (21), 349 (30), 223 (13), 199 (12), 171 (18), 161 (23), 137 (26), 136 (30), 108 (15), 99 (15). Anal. calcd. for $C_{26}H_{14}Cl_4O_4$: C 58.68, H 2.65; found: C 58.23, H 2.74%.

3′,4′-Dibenzyloxy-3-(3,4-dibenzyloxycinnamoyl)-5-hydroxy-2-styrylchromone 4i. Yield 80%, mp 171–172 °C. $FAB^+ - MS$: *m*/z (rel. int.) 819 [$(M + H)^+$, 15], 503 (10), 181 (8), 91 (100). Anal. calcd. for $C_{54}H_{42}O_8 \cdot 1/2\ H_2O$: C 78.34, H 5.24; found: C 78.11, H 5.03%.

Acknowledgements

We express our sincere thanks to Professor Robert A. W. Johnstone, University of Liverpool, UK for some microanalyses and to the University of Aveiro and to the former JNICT, Portugal, for funding. One of us (D. C. G. A. Pinto) is also grateful to the former JNICT for the award of a student grant.

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Paper a908539d