A New Synthesis of 5-Arylbenzo[*c*]xanthones from Photoinduced Electrocyclisation and Oxidation of (*E*)-3-Styrylflavones

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Abstract: A new synthetic route to 5-arylbenzo[*c*]xanthones is established. This was accomplished by use the Heck reaction of 3-bromoflavones with styrene derivatives, leading to (*E*)-3-styrylflavones with total diastereoselectivity. This transformation was greatly improved under microwave irradiation. The one-pot, photoinduced electrocyclisation of (*E*)-3-styrylflavones and further in situ oxidation of the cycloadduct leads to 5-arylbenzo[*c*]xanthones.

Key words: microwave irradiation, Heck reaction, photocyclisation, oxidation

The xanthone ring system is a structural motif present in natural products and prevalent in higher plant families such as *Guttiferae* and *Gentianaceae*.[1] Both natural and synthetic derivatives are often endowed with interesting pharmacological properties, such as anti-inflammatory,[2] antitumour[3] and antioxidant activity.[4] To the best of our knowledge, benzo[*c*]xanthones and 3-styrylflavones are not found in natural sources and their syntheses are scarce.[5] On the other hand, related compounds, such as benzo[*a*] and benzo[*b*]xanthones exhibit appealing pharmacological properties. For instance, antibacterial and fungicidal activities,[6] α-glucosidase inhibition[7] and cytotoxicity against L1210 cells[8] have been described.

Following our research interests in the synthesis of 3-styrylchromone[9] and benzoxanthone derivatives,[5d,10] along with the fact that new synthetic routes towards these compounds are of significance in both synthetic and medicinal chemistry, a program aimed at the synthesis of (*E*)-3-styrylflavones **4a**–**g** and their photoinduced electrocyclisation and oxidation into 5-arylbenzo[*c*]xanthones **5a**–**h** was set up (Scheme 1). One important transformation in this synthetic route is the Heck reaction of 3-bromoflavones **2a**–**f** with styrene derivatives **3a** and **3b**. The Heck reaction is widely used in synthetic chemistry as it is one of the most noteworthy methodologies for carbon–carbon bond formation,[11] however, it has rarely been used in the field of oxygen heterocycles.[9b,12] Photoinduced reactions have played important roles in building diverse organic frameworks that are otherwise difficult to make.[13] In our case, the photoinduced electrocyclisation of (*E*)-3-styrylflavones **4a**–**g** plays a key role in the new synthetic procedure.

Initially, we studied the synthesis of 3-bromoflavones **2a**–**f** by treating 3-aryl-1-(2-hydroxyphenyl)propan-1,3-diones **1a**–**f** with phenyltrimethylammonium tribromide (PTT),[12] in a one-pot method in which bromination and cyclisation occurred leading to the formation of 3-bromochromones in moderate yields.[14] However, in this work, the expected bromo-derivatives were obtained in only modest yields, with the highest being obtained with 3-bromo-4-methylflavone[15] (**2b**; 45%) and the lowest with 3-bromo-3,4-dimethoxyflavone (**2f**; 32%). Since our results were not satisfactory, mostly because the corresponding non-brominated flavones were obtained as by-products, we investigated other methodologies. The direct bromination of flavones using pyridinium bromide perbromide[16] or *N*-bromosuccinimide,[17] and also microwave irradiation,[18] were attempted, but in all cases the results were unsatisfactory, with the desired 3-bromo-flavones being obtained in poor yields (up to 20%).[19]

These results, together with the fact that the first method involves fewer reaction steps and can be applied to derivatives bearing either electron-donating or electron-withdrawing groups, meant that the initial approach was used to obtain 3-bromoflavones **2a**–**f**. The most important features in the NMR spectra of 3-bromoflavones **2a**–**f** are: (i) the resonances of the deshielded aromatic protons H-5 and H-7 at δ = 8.29–8.31 and 7.72–7.78 ppm, due to the mesomeric (both protons) and anisotropic (H-5) deshielding effect of the carbonyl group; (ii) the absence of the typical H-3 signal of flavones, which generally appears as a singlet at δ = 6–7 ppm; and (iii) the resonances of C-3 and C-4 carbon atoms appearing at, respectively, δ = 108.6–110.8 and 172.6–173.3 ppm.

The next step in our strategy was the Heck reaction[9b,12,20] of 3-bromoflavones **2a**–**f** with styrene **3a**. A study to find the optimal reaction conditions (palladium catalysts, solvent, reaction time and heating conditions) was carried out (Table 1). Attempts were made to take advantage of the beneficial effects of microwave (MW) irradiation in synthesis,[21] and using the Jeffery reaction conditions,[22] since they are reported to improve the yields of the Heck reaction; however, (*E*)-3-styrylflavone **4a** was only obtained in poor yields (Table 1, entries 1–4). Lowering the MW irradiation power allowed **4a** to be obtained in good yields (Table 1, entry 5). Changing the palladium source

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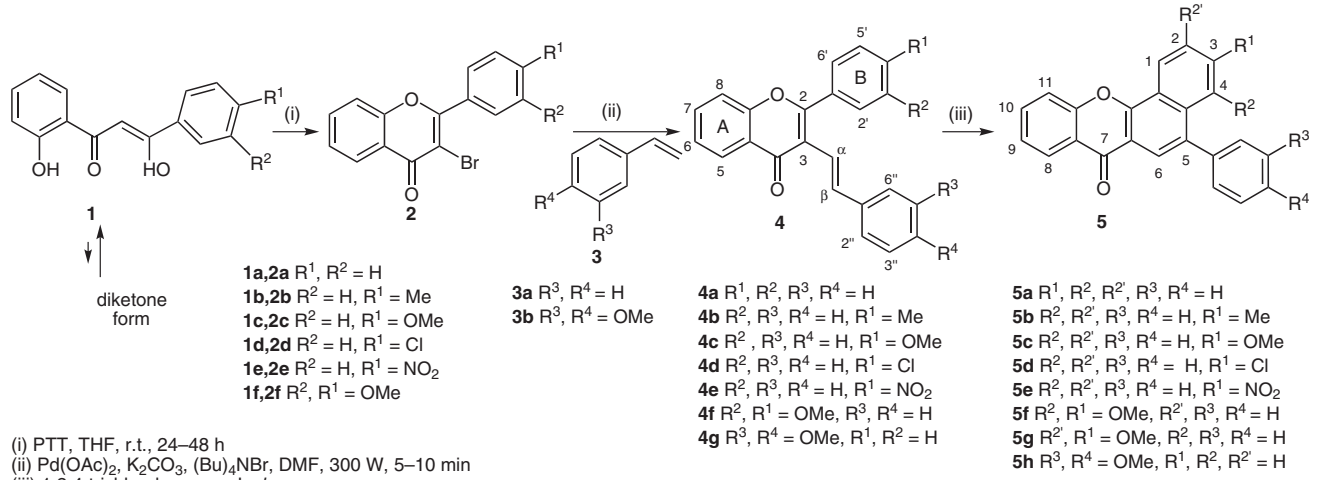


(i) PTT, THF, r.t., 24–48 h
(ii) $Pd(OAc)_2$, K_2CO_3, $(Bu)_4NBr$, DMF, 300 W, 5–10 min
(iii) 1,2,4-trichlorobenzene, I_2, *hν*

Scheme 1

did not improve our results (Table 1, entries 6 and 7), nor did using classical heating conditions (Table 1, entry 8). In the latter case, the reaction time was clearly too long (3 h) compared with the reaction time under MW irradiation (10 min).

The Heck/Jeffery reaction conditions were extended to the reaction of 3-bromoflavones **2b–f** with styrene **3a**,[23] and the corresponding (*E*)-3-styrylflavone derivatives **4b–f** were obtained in moderate to good yields (46%). The reaction of 3-bromoflavone (**2a**) with 3,4-dimethoxystyrene (**3b**) also yielded the expected (*E*)-3-styrylflavone **4g**[24] in good yield (63%).

The main features in the ^{1}H NMR spectra of (*E*)-3-styrylflavones are the resonances of H-α and H-β, which appear as two doublets at δ = 6.72–6.88 and 7.95–8.04 ppm, respectively. The coupling constant for these protons (*J* ~17 Hz) indicates a *trans* configuration for this vinylic system. The higher frequency values of H-β resonances are due to the anisotropic deshielding effect of the carbonyl group. The depicted 3-styryl group conformation was also confirmed by NOESY experiments in which NOE correlations between H-α and H-2′,6′ were observed. The ^{13}C NMR spectroscopic assignments were possible due to HSQC and HMBC experiments, and the most noticeable carbon resonances appeared at δ = 177.1–177.6 ppm (C-4), and at δ = 118.3–120.4 and 133.9–136.3 ppm, due to the vinylic C-α and C-β, respectively.

Following our interest in thermal electrocyclisations,[12,25] (*E*)-3-styrylflavones **4a–g** were heated at reflux in 1,2,4-trichlorobenzene, however, all attempts to cyclise the compounds failed, even when iodine[26] was used as catalyst or microwave radiation as heating source (Table 2, entries 1–4). Knowing that photoinduced electrocyclisations can be a successful methodology,[5c] a chloroform solution of (*E*)-3-styrylflavone **4a** was irradiated with a halogen white-light projector; under these conditions, the desired 5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5a**)[27] was obtained, albeit in poor yield (Table 2, entry 5). Some starting material **4a** was recovered (50%) and the by-product, 5-phenyl-5*H*-benzo[*c*]xanthen-7(6*H*)-one (**6a**)[28] was also obtained (8%; Scheme 2). The most important features in the ^{1}H NMR spectrum of **6a** are the double doublets at δ = 3.24, 3.33 and 4.32 ppm, assigned respectively to the resonances of H-6_{cis}, H-6_{trans}, and H-5. In the ^{13}C

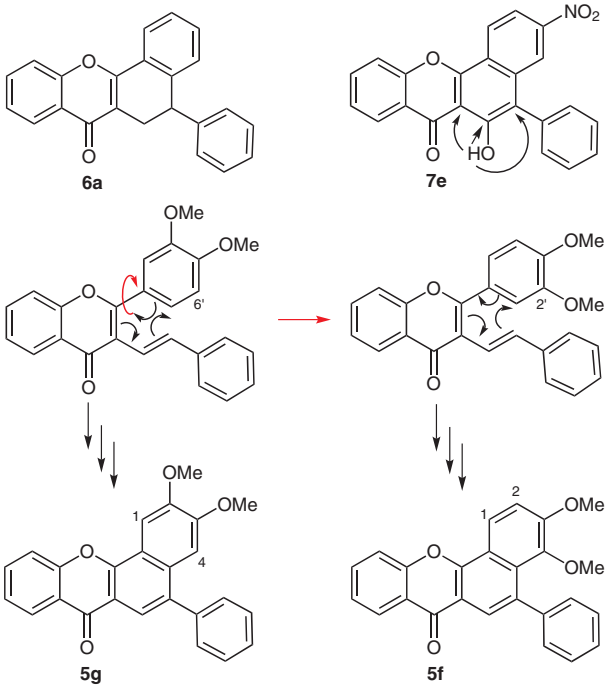
Table 1 Synthesis of (*E*)-3-Styrylflavone **4a**

Entry	Reagents	Solvent	Heating	Time (min)	Yield **4a** (%)[a]
1	$Pd(OAc)_2$, K_2CO_3, KCl, TBAB, DABCO	NMP	400 W (MW)	15	35
2	$Pd(OAc)_2$, K_2CO_3, TBAB	DMF	400 W (MW)	10	40
3	$Pd(OAc)_2$, K_2CO_3, NBu_4HSO_4	DMF	400 W (MW)	10	–
4	$Pd(OAc)_2$, K_2CO_3, TBAB	NMP	400 W (MW)	10	25
5	$Pd(OAc)_2$, K_2CO_3, TBAB	DMF	300 W (MW)	10	72
6	$PdCl_2(PPh_3)_2$, K_2CO_3, TBAB	DMF	300 W (MW)	10	40
7	$Pd(Ph_3)_4$, K_2CO_3, TBAB	DMF	300 W (MW)	10	37
8	$Pd(OAc)_2$, K_2CO_3, TBAB	DMF	150 °C	1–3 h	45

[a] Maximum yield obtained.

NMR spectrum, the aliphatic resonances of C-6 and C-5 at δ = 27.2 and 43.1 ppm, respectively, and the carbonyl carbon at δ = 177.2 ppm should be highlighted. The most noticeable signal from the ^{1}H NMR spectrum of benzo[*c*]xanthen-7-one (**5a**) is the singlet at δ = 8.24 ppm assigned to H-6, which resonates at high frequency values due to the carbonyl anisotropic deshielding effect.

Since the previous procedures in the synthesis of benzo[*c*]xanthen-7-one **5a** did not give satisfactory results, an attempt using daylight in the presence or absence of iodine was carried out, but, once again, the desired product was obtained in only poor yield (Table 2, entries 6 and 7). These results, together with the fact that the use of a mercury lamp seems to be a good method for a photocyclization process to give a dihydrobenzo[*c*]xanthone,[5a] led us to use a high pressure mercury UV lamp. This procedure led us to develop a new synthetic route for 5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5a**)[29] (Table 2, entry 8). We then successfully extended this method to the other derivatives, except for 3-nitro-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5e**), which was obtained in low yield.[29] This low yield can be explained by the formation of 6-hydroxy-3-nitro-5-phenyl-7*H*-benzo[*c*]xanthen-7-one[30] (**7e**; 54%, Scheme 2). The ^{1}H NMR spectrum of **7e** shows, in addition to the benzo[*c*]xanthone protons, a singlet at δ = 12.71 ppm due to a hydroxyl group proton involved in a hydrogen bond with a carbonyl group. This data, the disappearance of the typical H-6 singlet of 5-aryl-benzo[*c*]xanthone **5a**, and the HMBC connectivities unequivocally prove the structure of **7e** (Scheme 2).



Scheme 2 Structures of 5-phenyl-5*H*-benzo[*c*]xanthen-7(6*H*)-one (**6a**), 6-hydroxy-3-nitro-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**7e**) and formation of 3,4-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5f**) and 2,3-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5g**)

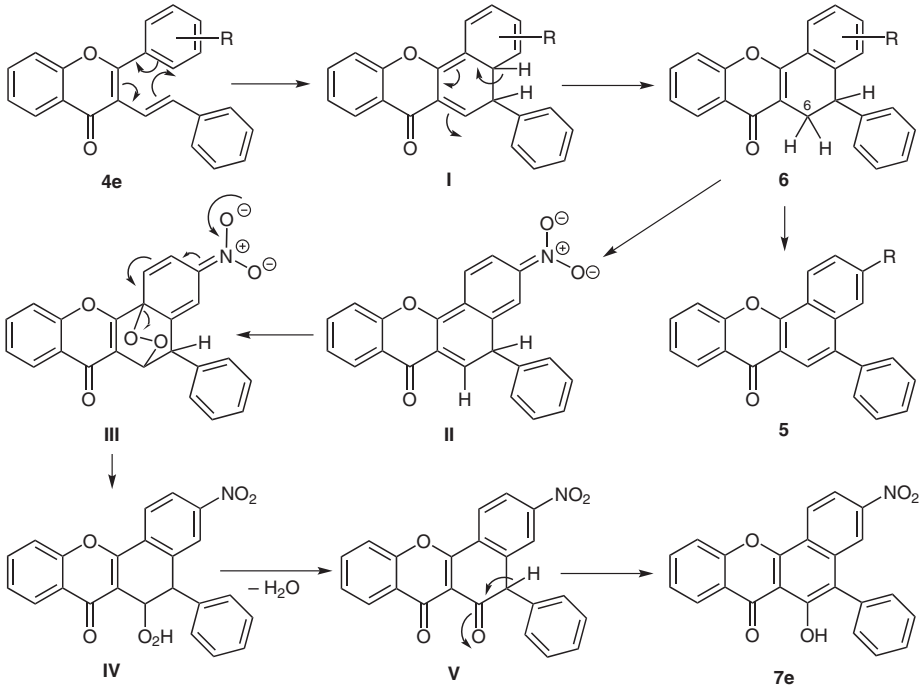
Table 2 Synthesis of 5-Arylbenzo[*c*]xanthone **5a**

Entry	Conditions[a]	Heating	Time (d)	Yield **6a** (%)[b]	Yield **5a** (%)
1	TCB	230 °C	3	–	–
2	TCB, I_2	230 °C	3	–	–
3	TCB, I_2	230 °C	7	–	–
4	TCB, I_2	400 W	45 min	–	–
5	$CHCl_3$	500 W[c]	7	8	15[b]
6	$CHCl_3$	r.t.	7	15	14[b]
7	TCB, I_2	r.t.	5	10	17[b]
8	TCB, I_2, hυ	400 W		–	70[d]

[a] TCB = 1,2,4-trichlorobenzene.
[b] Maximum yield obtained.
[c] Halogen white light projector;
[d] Average yield.

The appearance of this 6-hydroxyl group can be envisaged from the reaction mechanism (Scheme 3). After electrocyclisation and rearomatisation of **I**, the intermediate **6** can be directly oxidised to compounds **5**; this is the main pathway for derivatives having electron-donating R substituents (e.g., **4b**). In the case of strong electron-withdrawing groups (R = NO_2; **4e**), the loss of the acidic methylenic H-6 proton generates diene **II**, which may react with singlet oxygen leading to the formation of cycloadduct **III** (Scheme 3). The latter can rearrange to hydroperoxide **IV**, which can dehydrate, as reported by others authors in similar circumstances,[31] to give a ketone that undergoes a keto-enol tautomerism to afford a completely aromatised 3-nitro-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**7e**). To confirm this idea, reactions of **4b** and **4e** were repeated in the presence of methylene blue, which is a known singlet oxygen sensitiser.[31] Under these conditions, **4e** was only transformed into **5e** and the yield of xanthone **7e** improved to 86%, confirming the involvement of singlet oxygen in the unexpected formation of **7e**.

Photoinduced electrocyclisation and oxidation processes of (*E*)-3,4-dimethoxy-3-styrylflavone (**4f**) yielded two isomers, 3,4-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5f**) and 2,3-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (**5g**), with the latter being formed as the major product. The free rotation of the (*E*)-3,4-dimethoxy-3-styrylflavone B ring allowed two possible sites for electrocyclisation, C-2′ or C-6′. Probably due to some steric hindrance between the 3′-OMe group and the styryl group, the cyclisation at C-6′ is favourable (Scheme 2). Unequivocal proof for the proposed structures was mainly based on the ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum of compound **5f**[32] shows, in addition to the phenylxanthone moiety protons, two doublets at δ = 7.49 and 8.60 ppm (*J* = 9.2 Hz), due to the resonance of H-2 and H-1, respectively. In the case of **5g**,[33] the ^{1}H NMR spectrum shows, in addition to the phenylxanthone moiety protons,



Scheme 3

two singlets at δ = 7.34 and 8.01 ppm, due to the resonance of protons H-4 and H-1, respectively. The higher frequency values of the H-1 resonances in both cases can be attributed to the through-space deshielding effect of the heterocyclic oxygen atom.

In conclusion, a successful methodology for the synthesis of (*E*)-3-styrylflavones using microwave irradiation to perform the Heck reaction of 3-bromoflavones with styrene has been developed. The beneficial effects of microwave irradiation were a reduction in reaction time (from more than 1 h to 10 min or less), and an improvement in product yield (from 45 to 73%). Photoinduced electrocyclisation and oxidation processes undergone by (*E*)-3-styrylflavones with a high-pressure mercury lamp led to a new synthetic route to 5-arylbenzo[*c*]xanthones in moderate yields.

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(14) **Optimised procedure for the synthesis of 3-bromoflavones 2a–f**: Phenyltrimethylammonium tribromide (0.94 g, 2.45 mmol) was added to an anhydrous THF (30 mL)

solution of the appropriate 3-aryl-1-(2-hydroxyphenyl)-propan-1,3-dione **1a–f** (1.63 mmol). The reaction mixture was stirred at room temperature for 24–48 h. After that period, the reaction mixture was poured into a mixture of ice (10 g) and water (30 mL), stirred for 30 min, and extracted with chloroform (3 × 20 mL). The combined extracts were dried over sodium sulfate and evaporated to dryness. The obtained residue was purified by TLC (CH_2Cl_2–light petroleum, 9:1). After solvent evaporation, the obtained residue was recrystallised from ethanol giving 3-bromoflavones **2a–f** [**2a**: 196 mg (40%); **2b**: 226 mg (44%); **2c**: 343 mg (45%); **2d**: 230 mg (42%); **2e**: 237 mg (42%); **2f**: 188 mg (32%)]

(15) **3-Bromo-4-methylflavone (2b)**: Yellow solid; mp 146–148 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.47 (s, 3 H, 4′-CH_3), 7.34 (d, *J* = 8.2 Hz, 2 H, H-3′,5′), 7.44 (br dd, *J* = 7.1, 8.3 Hz, 1 H, H-6), 7.51 (br d, *J* = 8.3 Hz, 1 H, H-8), 7.72 (ddd, *J* = 1.7, 7.1, 8.1 Hz, 1 H, H-7), 7.78 (d, *J* = 8.2 Hz, 2 H, H-2′,6′), 8.31 (dd, *J* = 1.7, 8.3 Hz, 1 H, H-5). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 21.6 (4′-CH_3), 108.9 (C-3), 117.8 (C-8), 121.8 (C-10), 125.6 (C-6), 126.5 (C-5), 129.0 (C-3′,5′), 129.3 (C-2′,6′), 133.7 (C-1′), 134.1 (C-7), 141.7 (C-4′), 155.6 (C-9), 162.1 (C-2), 173.2 (C-4). MS (ESI$^+$): *m/z* (%) = 315 (100) ([M + H]$^+$, ^{79}Br), 317 (90) ([M + H]$^+$, ^{81}Br), 337 (87) ([M + Na]$^+$, ^{79}Br), 339 (83) ([M + Na]$^+$, ^{81}Br). Anal. Calcd for $C_{16}H_{11}O_2Br$ (315.16): C, 60.98; H, 3.52. Found: C, 60.88; H, 3.52

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(23) **Optimised procedure for the synthesis of 3-styrylflavones 4a–g**: A mixture of the appropriate 3-bromoflavone **2a–f** (0.296 mmol), anhydrous K_2CO_3 (123 mg, 0.888 mmol), tetrabutylammonium bromide (TBAB; 238 mg, 0.740 mmol), palladium acetate (9.97 mg, 0.044 mmol) and styrene **3a** (0.170 mL, 1.48 mmol) in DMF (6 mL), was poured into a two-necked flask equipped with a magnetic stirring bar, fibre-optic temperature control, and reflux condenser and placed under a nitrogen atmosphere. The mixture was then irradiated in an Ethos SYNTH microwave (Milestone Inc.) at constant power of 300 W from 5–10 min. After that period, the reaction mixture was poured into a mixture of ice (1 g) and water (10 mL) and extracted with diethyl ether (3 × 10 mL). The organic layer was evaporated to dryness and the obtained residue was taken in ethyl acetate (10 mL) and washed with water (2 × 10 mL). The organic layer was dried with anhydrous sodium sulfate, evaporated and purified by column chromatography ($CHCl_3$–acetone, 9.6:0.4). After solvent evaporation, the obtained residue was recrystallised from ethanol to give 3-styrylflavones **4a–g** [**4a**: 67 mg (70%); **4b**: 68 mg (68%); **4c**: 73 mg (70%); **4d**: 66 mg (62%); **4e**: 55 mg (50%); **4f**: 51 mg (45%)]. The reaction of 3-bromoflavone **2a** (0.296 mmol) with styrene **3b** (1.48 mmol), under the same reaction conditions, yielded 3-(3,4-dimethoxystyryl)flavone **4g** (72 mg, 63%)

(24) **(*E*)-3-(3,4-Dimethoxystyryl)flavone (4g):** Yellow solid; mp 158–160 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, 4″-OCH_3), 3.88 (s, 3 H, 3″-OCH_3), 6.72 (d, *J* = 16.2 Hz, 1 H, H-α), 6.82 (d, *J* = 8.1 Hz, 1 H, H-5″), 6.93 (d, *J* = 1.6 Hz, 1 H, H-2″), 6.95 (d, *J* = 9.2 Hz, 1 H, H-6″), 7.44 (ddd, *J* = 1.7, 7.1, 8.3 Hz, 1 H, H-6), 7.51 (dd, *J* = 1.7, 8.3 Hz, 1 H, H-8), 7.53–7.58 (m, 3 H, H-3′,4′,5′), 7.69 (ddd, *J* = 1.7, 7.1, 8.3 Hz, 1 H, H-7), 7.76–7.79 (m, 2 H, H-2′,6′), 7.95 (d, *J* = 16.2 Hz, 1 H, H-β), 8.33 (dd, *J* = 1.7, 8.3 Hz, 1 H, H-5). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 55.8 (4″-OCH_3), 55.9 (3″-OCH_3), 109.3 (C-2″), 111.2 (C-5″), 117.8 (C-3), 117.9 (C-8), 118.3 (C-α), 119.3 (C-6″), 123.5 (C-10), 125.1 (C-6), 126.3 (C-5), 128.4 (C-3′,5′), 129.9 (C-2′,6′), 130.6 (C-4′), 131.3 (C-1″), 133.3 (C-1′), 133.4 (C-7), 134.1 (C-β), 148.8 (C-3″), 148.9 (C-4″), 155.4 (C-9), 162.5 (C-2), 177.6 (C-4). MS (ESI$^+$): *m/z* (%) = 385 (100) [M + H]$^+$, 407 (20) [M + Na]$^+$. Anal. Calcd for $C_{25}H_{20}O_4$ (384.42): C, 78.11; H, 5.24. Found: C, 78.15; H, 5.31

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(27) **5-Phenyl-7*H*-benzo[*c*]xanthen-7-one (5a)**: Mp 197–198 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.47 (br dd, *J* = 7.0, 8.0 Hz, 1 H, H-9), 7.47–7.50 (m, 1 H, H-4′), 7.52–7.54 (m, 4 H, H-2′,3′,5′,6′), 7.67 (ddd, *J* = 1.5, 6.2, 8.0 Hz, 1 H, H-3), 7.74 (ddd, *J* = 1.5, 6.2, 8.0 Hz, 1 H, H-2), 7.75 (br d, *J* = 8.0 Hz, 1 H, H-11), 7.81 (ddd, *J* = 1.3, 7.0, 8.0 Hz, 1 H, H-10), 8.02 (dd, *J* = 1.5, 8.0 Hz, 1 H, H-4), 8.24 (s, 1 H, H-6), 8.44 (dd, *J* = 1.3, 8.0 Hz, 1 H, H-8), 8.81 (dd, *J* = 1.5, 8.0 Hz, 1 H, H-1). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 117.1 (C-6a), 118.1 (C-11), 121.9 (C-6), 122.5 (C-7a), 123.1 (C-1), 124.4 (C-12b), 124.5 (C-9), 126.6 (C-2), 126.7 (C-4), 126.8 (C-8), 127.6 (C-4′), 128.4 (C-2′,6′), 129.6 (C-3), 130.1 (C-3′,5′), 132.1 (C-10), 133.7 (C-4a), 134.4 (C-5), 136.6 (C-1′), 155.8 (C-12a), 168.4 (C-11a), 177.2 (C-7). MS (ESI$^+$): *m/z* (%) = 323 (100) [M + H]$^+$, 345 (22) [M + Na]$^+$. MS (EI$^+$): *m/z* calcd for $C_{23}H_{14}O_2$: 322.0994; found: 322.0995

(28) **5-Phenyl-5*H*-benzo[*c*]xanthen-7(6*H*)-one (6a)**: ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.24 (dd, *J* = 9.0, 16.5 Hz, 1 H, H-6_{cis}), 3.33 (dd, *J* = 7.3, 16.5 Hz, 1 H, H-6_{trans}), 4.32 (dd, *J* = 7.3, 9.0 Hz, 1 H, H-5), 7.06 (dd, *J* = 7.6 Hz, 1 H, H-2), 7.18–7.23 (m, 2 H, H- 3′,5′), 7.23–7.26 (m, 1 H, H-4), 7.27–7.32 (m, 2 H, H-2′,6′), 7.38- 7.49 (m, 3 H, H-9,3,4′), 7.59 (dd, *J* = 1.4, 8.3 Hz, 1 H, H-11), 7.69 (ddd, *J* = 1.4, 7.0, 8.3 Hz, 1 H, H-10), 8.09 (dd, *J* = 1.8, 7.6 Hz, 1 H, H-1), 8.24 (dd, *J* = 1.4, 8.3 Hz, 1 H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 27.2 (C-6), 43.1 (C-5), 115.4 (C-6a), 117.9 (C-11), 123.6 (C-7a), 124.0 (C-1), 125.9 (C-8), 126.8 (C-4), 127.3 (C-4′), 128.2 (C-3′,5′), 128.47 (C-12b), 128.5 (C-2′,6′), 128.7 (C-2), 131.4 (C-3), 133.3 (C-10), 141.7 (C-1′), 142.7 (C-4a), 155.6 (C-11a), 157.4 (C-12a), 177.2 (C-7). MS (EI$^+$): *m/z* calcd for $C_{23}H_{16}O_2$: 324.1150; found: 324.1147

(29) **Optimised procedure for the synthesis of 5-phenyl-7*H*-benzo[*c*]xanthen-7-ones 5a–h**: A mixture of the appropriate 3-styrylflavone **4a–g** (0.15 mmol) and a catalytic amount of I_2 (10% mol) in 1,2,4-trichlorobenzene (20 mL), was poured into a three-necked flask equipped with a magnetic stirring bar, reflux condenser and a high-pressure mercury UV lamp with 400 W power. The mixture was then irradiated from 2 to 6 days. After that period, the reaction mixture was poured into a silica gel column and eluted with light petroleum to remove the excess of iodine and 1,2,4-

trichlorobenzene. Upon changing the eluent to ethyl acetate–light petroleum (1:9 or 3:7), 5-phenyl-7*H*-benzo[*c*]xanthen-7-ones were obtained, which were recrystallised from ethanol **5a**–**h** [**5a**: 50 mg (70%); **5b**: 22 mg (45%); **5c**: 50 mg (73%); **5d**: 35 mg (74%); **5e**: 15 mg (30%); **5f**: 11 mg (20%); **5g**: 23 mg (40%); **5h**: 35 mg (60%)]

(30) **Physical data of 6-hydroxy-3-nitro-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (7e):** ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 7.46 (br d, *J* = 8.4 Hz, 2 H, H-3′,5′), 7.52–7.56 (m, 1 H, H-4′), 7.53–7.59 (m, 1 H, H-9), 7.56–7.62 (m, 2 H, H-2′,6′), 7.79 (br d, *J* = 8.3 Hz, 1 H, H-11), 7.93 (ddd, *J* = 1.4, 7.0, 8.3 Hz, 1 H, H-10), 8.20 (dd, *J* = 2.2, 9.2 Hz, 1 H, H-2), 8.41 (dd, *J* = 1.4, 8.3 Hz, 1 H, H-8), 8.51 (d, *J* = 2.2 Hz, 1 H, H-4), 8.77 (d, *J* = 9.2 Hz, 1 H, H-1), 12.71 (s, 1 H, 6-OH). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 109.5 (C-6a), 116.9 (C-2), 118.2 (C-11), 119.5 (C-5), 120.3 (C-12b), 121.3 (C-7a), 121.4 (C-4), 125.0 (C-1), 125.5 (C-9), 126.2 (C-8), 128.3 (C-4′), 128.9 (C-2′,6′), 131.0 (C-3′,5′), 133.3 (C-1′), 136.1 (C-10), 136.6 (C-4a), 148.7 (C-3), 153.0 (C-12a), 154.3 (C-6), 155.7 (C-11a), 182.0 (C-7) ppm. MS (EI$^+$): *m*/*z* calcd for $C_{23}H_{13}O_5N$ 383.0794; found: 383.0791

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(32) **Physical data of 3,4-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (5f):** ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.18 (s, 3 H, 4-OCH_3), 4.03 (s, 3 H, 3-OCH_3), 7.34–7.46 (m, 6 H, H-9,2′,3′,4′,5′,6′), 7.49 (d, *J* = 9.2 Hz, 1 H, H-2), 7.72 (d, *J* = 8.3 Hz, 1 H, H-11), 7.79 (ddd, *J* = 1.5, 7.0, 8.3 Hz, 1 H, H-10), 8.04 (s, 1 H, H-6), 8.41 (dd, *J* = 1.5, 8.3 Hz, 1 H, H-8), 8.60 (d, *J* = 9.2 Hz, 1 H, H-1). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 56.4 (4-OCH_3), 60.6 (3-OCH_3), 110.1 (C-6a), 114.0 (C-2), 118.0 (C-11), 120.1 (C-1), 122.6 (C-7a), 124.4 (C-9), 124.8 (C-6), 126.3 (C-4′), 126.6 (C-8), 126.9 (C-2′,6′), 129.2 (C-3′,5′), 130.4 (C-4a), 130.8 (C-5), 134.2 (C-10), 141.4 (C-12a), 144.6 (C-4), 155.1 (C-3), 156.7 (C-11a), 178.9 (C-7). MS (EI$^+$): *m*/*z* calcd for $C_{25}H_{18}O_4$: 382.1205; found: 382.1207

(33) **Physical data of 2,3-dimethoxy-5-phenyl-7*H*-benzo[*c*]xanthen-7-one (5g):** ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, 3-OCH_3), 4.18 (s, 3 H, 2-OCH_3), 7.34 (s, 1 H, H-4), 7.45 (br dd, *J* = 7.0, 8.2 Hz, 1 H, H-9), 7.46–7.49 (m, 1 H, H-4′), 7.50–7.58 (m, 4 H, H-2′,3′,5′,6′), 7.75 (dd, *J* = 1.7, 8.2 Hz, 1 H, H-11), 7.79 (ddd, *J* = 1.7, 7.0, 8.2 Hz, 1 H, H-10), 8.01 (s, 1 H, H-1), 8.13 (s, 1 H, H-6), 8.45 (dd, *J* = 1.7, 8.2 Hz, 1 H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 55.9 (3-OCH_3), 56.2 (2-OCH_3), 102.0 (C-4), 105.9 (C-1), 116.4 (C-6a), 118.0 (C-11), 119.2 (C-12b), 120.7 (C-6), 122.4 (C-1′), 124.2 (C-9), 126.5 (C-7a), 126.7 (C-8), 127.6 (C-4′), 128.5 (C-2′,6′), 129.9 (C-3′,5′), 131.4 (C-4a), 134.1 (C-5), 135.3 (C-10), 139.9 (C-12a), 149.8 (C-2), 151.9 (C-3), 155.8 (C-11a), 176.9 (C-7). MS (EI$^+$): *m*/*z* calcd for $C_{25}H_{18}O_4$: 382.1205; found: 382.1207

