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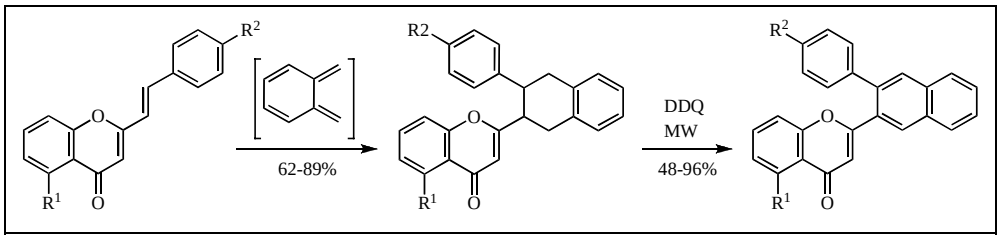

The Diels-Alder reaction of 5-hydroxy-2-styrylchromones with *ortho*-benzoquinodimethane, generated "*in situ*" by thermal extrusion of sulfur dioxide from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide, leads to 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)-5-hydroxychromones. These cycloadducts were dehydrogenated with DDQ, using classical thermal reflux conditions and microwave irradiation, affording the corresponding 2-(3-arylnaphth-2-yl)-5-hydroxychromones in high yields (48-96%).

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INTRODUCTION

Chromones (4*H*-benzo[*b*]pyran-4-ones) are an important class of heterocyclic compounds widely distributed in the plant kingdom, where they participate in several biological functions [1,2]. Natural and synthetic derivatives are known to possess biocidal, pharmacological and antioxidant activities [1,2]. Flavones (2-phenylchromones) are the major constituents of this class of natural compounds and therefore the most known and studied ones. These compounds, widely occurring in plants, are present in human diet in significant amounts [3]. The study of the biological properties of flavones have shown that these compounds present a broad spectrum of pharmacological activities in mammalian cell systems, namely inhibiting the proliferation of cancer and tumour cells or acting as antioxidants due to their ability to chelate metal ions and to scavenge free radicals. Some of these compounds are already marketed as drugs [4-14]. This type of compounds also presents antibacterial, antifungal and antiviral activities [4,15-18].

Although 2-styrylchromones are the rarest group of natural chromones, only two natural 2-styrylchromones are known [19,20], they exhibit potent *in vitro* cytotoxic activities against human leukemia cells, and some of their synthetic derivatives have been shown to possess anti-allergic, antiviral, anti-tumour and antioxidant activities [19-27].

The presence of a 5-hydroxyl group in 2-(phenyl or styryl)chromones seems to be very important for observing biological activity, especially pharmacological and antioxidant properties, since this feature is present in many chromones that have displayed those biological properties [4,12,22,24].

5,6- and 7,8-Benzoflavone derivatives (also known as α- and β-naphthoflavones) are well-studied compounds due to their important biological activities, namely the ability to attenuate benzodiazepine dependence [28], to prevent chronic alcoholism, nicotine and cannabinoid-induced azospermia, sterility and decrease libido [29-32] and to activate the cystic fibrosis transmembrane conductance regulator [33]. These compounds also display anxiolitic [34], phytotoxic [35] and moderate anti-tumour activities [36]. Two naturally occurring naphthaflavones are used in traditional medicine to cure the above-referred diseases [35,37].

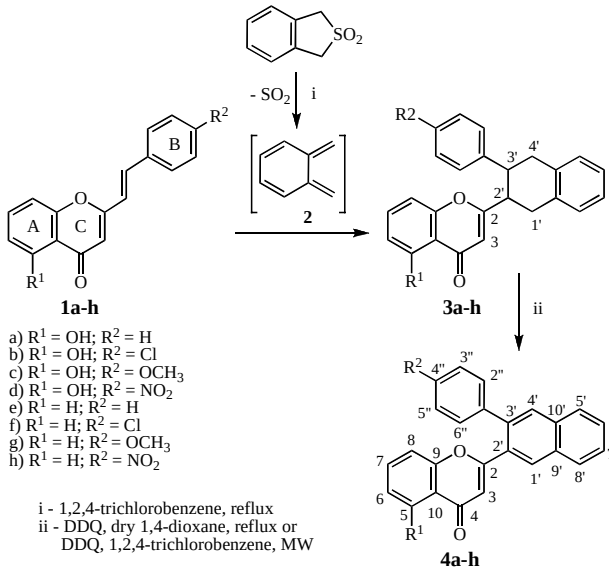
There are several references to the synthesis of A-ring benzannulated flavone compounds (5,6- and 7,8-benzoflavones) starting from the appropriate 1-acetyl-2-naphthols or 2-acetyl-1-naphthols and aroyl halides [38]. However, the synthesis of B-ring benzannulated flavone derivatives remains unexplored. In this communication, an extension of a previous work [39], we describe not only the synthesis of 2-(2-naphthyl)chromone derivatives having a 5-hydroxyl group but also an efficient method for the dehydrogenation of the Diels-Alder cycloadducts.

RESULTS AND DISCUSSION

The tetrahydronaphthylchromones **3a-d** were obtained from the Diels-Alder reaction of (*E*)-5-hydroxy-2-styryl-chromones **1a-d** with an excess of *ortho*-benzoquino-dimethane **2**, a very reactive diene generated *in situ* by thermal extrusion of sulfur dioxide from 1,3-dihydro-benzo[*c*]thiophene 2,2-dioxide in refluxing 1,2,4-trichlorobenzene [40]. In order to study the reactivity of (*E*)-5-hydroxy-2-styrylchromones **1a-d** in this type of cycloaddition reaction and to compare the results with those of unsubstituted A-ring 2-styrylchromones **1e-h** [41], the referred reaction conditions were used for all these compounds (Table 1). The obtained results show that the presence of electron-donor groups in B-ring of

(*E*)-2-styrylchromones **1c**,**g** decreases their reactivity as dienophiles. With these compounds, the cycloadducts **3c,g** are obtained in lower yield (62-63%), when compared to the other cycloadducts (76-89%), and a relatively higher amount of the starting material is recovered (20-24%). Since the Cα=Cβ double bond of 2-styrylchromones is conjugated with the carbonyl group through the C2=C3 double bond, these compounds are expected to be good dienophiles. In addition, the presence of neutral and electron-withdrawing substituents should increase the reactivity of those compounds. In fact, the cycloadducts formed from **1a,b,d-f,h** were obtained in good yields and almost no starting materials were recovered. In contrast, the reactivity of compounds **1c,g** (bearing electron-donor groups) is lower, as those groups increase the energy of LUMO of the reactive double bond of the dienophile.

In order to improve the efficiency of the Diels-Alder reaction of 5-hydroxy-2-styrylchromones **3a-d** with **2**, we decided to use aluminum chloride as catalyst [42-44]. It was expected that it could form a chelate with the 5-hydroxy and carbonyl oxygen atoms and make the styryl double bond more reactive. However, the Diels-Alder reaction of 5-hydroxy-2-styrylchromone **3a** with *ortho*-benzoquinodimethane in the presence of aluminum chloride (one molar equivalent), under the conditions described above, afforded **4a** in only 65% yield after 10



hours reaction time and complete disappearance of **3a**. With this new methodology the expected cycloadduct **4a** was formed in a short reaction time but with a lower yield. Because of that, we decided not to use aluminum chloride in the Diels-Alder reaction with the other styrylchromones.

The preparation of 2-(3-arylnaphth-2-yl)chromones **4e-g** in our previous work was achieved by benzylic bromination of 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)chromones **3e-g** with NBS, in the presence of benzoyl peroxide, followed by dehydrobromination of the resulting derivatives by treatment with triethylamine [39]. Although this method afforded the 2-(3-arylnaphth-2-yl)chromones **4e-g** in good yields, it involved a two-step reaction and a difficult purification process due to the presence of brominated side-products. This method is not suitable for the dehydrogenation of chromones **3a-d** since the presence of a 5-hydroxyl group in the A-ring should promote the bromination of this ring [45]. In order to establish a successful dehydrogenation method, the cycloadduct **3a** was submitted to dehydrogenation using quinones and different reaction conditions. In the first attempt, compound **3a** was treated with an excess of *p*-chloranil in refluxing toluene, for a week, but all the starting material was recovered. The reaction was repeated using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing toluene for 4 days. In this case the 2-(3-phenylnaphth-2-yl)-5-hydroxychromone **4a** was obtained in low yield (13%) and 63% of starting compound **3a** was recovered. The dehydrogenation of **3a** was also attempted with manganese dioxide (20 equiv) in refluxing chlorobenzene. In this case **4a** was obtained in 11% yield and 49% of **3a** was recovered. Because none of these results were satisfactory, we decided to use 1,4-dioxane as solvent, since it has been successfully used in dehydrogenation reactions [44,46]. In that way, cycloadduct **3a** was treated with DDQ in refluxing dry 1,4-dioxane for 24 hours. This reaction afforded the expected 2-(3-phenylnaphth-2-yl)-5-hydroxychromone **4a** in 87% yield. This methodology was then used for the dehydrogenation of the other cycloadducts **3b-h**. Surprisingly, only chromones **4a,e,g** were obtained in good yields (Table 2). In order to circumvent this problem, we used *p*-toluenesulfonic acid (PTSA) as catalyst in these dehydrogenation reactions [47-49]. In spite of chromones **4b** and **4h** could be obtained by this method, but only in moderate yields (39% for **4b**; 20% for **4h**, Table 2), we were not able to dehydrogenate cycloadducts **3d** and **3f**, even after several attempts.

In the last years, microwave radiation has been used as an alternative to conventional heating for introducing energy into organic reactions [50-55]. Recently, we described the use of microwave irradiation to promote the oxidation of some hydroaromatic compounds [56]. We decided then to perform the dehydrogenation of cycloadducts **3a-h** under similar conditions. In that way, a mixture of a chromone **3** and DDQ (3 equiv) (under conventional heating conditions 5 equiv were used) in 1,2,4-trichlorobenzene was submitted to microwave radiation for 36 minutes at a maximum power of 800 W; the microwave heating program allowed the temperature to rise from ambient temperature to 170 ºC in 6 minutes and to keep the reaction at that temperature for more 30 minutes. Under these experimental conditions, the 2-(3-

arylnaphth-2-yl)chromones **4a-h** were obtained in good yields (Table 2) and in shorter reaction times.

Table 1

Synthesis of Tetrahydronaphthylchromones **3a-h**

Compounds	Substituents	Yield (%) of cycloadducts **3a-h**	Recovered (%) 2-styrylchromones
3a	R^1 = OH, R^2 = H	76	9
3b	R^1 = OH, R^2 = Cl	76	5
3c	R^1 = OH, R^2 = OMe	63	20
3d	R^1 = OH, R^2 = NO_2	79	0
3e	R^1 = R^2 = H	89	0
3f	R^1 = H, R^2 = Cl	76	3
3g	R^1 = H, R^2 = OMe	62	24
3h	R^1 = H, R^2 = NO_2	80	0

Table 2

Dehydrogenation of Cycloadducts **3a-h**

Product	R^1	R^2	Yield (%)	
			Conventional heating	Microwave irradiation
4a	OH	H	87	92
4b	OH	Cl	--- (39)*	91
4c	OH	OCH_3	50	83
4d	OH	NO_2	---	48
4e	H	H	81	95
4f	H	Cl	---	93
4g	H	OCH_3	88	96
4h	H	NO_2	--- (20)*	81

** Dehydrogenation in the presence of catalytic amounts of PTSA.*

Nuclear Magnetic Resonance Spectroscopy. The main features of the ^{1}H NMR spectra of 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)chromones **3a-h** are the resonances of the six aliphatic protons H-1', H-2', H-3' and H-4', which appear as multiplets at δ 3.06-3.62 ppm, and that of H-3 appearing as singlet at δ 5.99-6.09 ppm. In the case of 5-hydroxy-2-[3-(4-nitrophenyl)-1,2,3,4-tetrahydronaphth-2-yl]chromone **3d** and 2-[3-(4-nitrophenyl)-1,2,3,4-tetrahydronaphth-2-yl]chromone **3h** the aliphatic region is better resolved. The proton resonance of H-3' is observed as an isolated multiplet at higher frequency values (δ 3.52-3.62 ppm) due to the mesomeric deshielding effect of the 4''-nitro group. The ^{1}H NMR spectra of 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)chromones **3a-d** also present the typical resonance of the 5-OH proton at high frequency values, appearing as a singlet at δ 12.30-12.49 ppm, due to intramolecular hydrogen bond with the carbonyl group.

The most relevant resonances in the ^{13}C NMR spectra of the tetrahydronaphth-2-ylchromones **3a-h** correspond to the aliphatic carbons C-1', C-2', C-3' and C-4' appearing at δ 34.4-46.7 ppm. It is also important to notice the carbon resonances of C-3 (δ 109.2-110.8 ppm), C-2 (δ 169.1-171.9 ppm) and C-4 (δ 183.0-183.3 ppm for **3a-d** and δ 177.8-178.1 ppm for **3e-h**). The assignments of carbon resonances of these compounds were made by analyses of their HSQC and HMBC spectra (Figure 1 shows some of the main long-range connectivities found in the HMBC spectra).

In the ^{1}H NMR spectra of 2-(3-arylnaphth-2-yl)chromones **4a-h** there are no signals in the aliphatic region; the distinctive singlets at δ 8.17-8.28 and δ 7.87-7.96 ppm are attributed to the resonances of protons H-1' and H-4', respectively. The unequivocal assignment of these proton resonances was based on the connectivities found in the HMBC spectra, namely in that of H-1' and C-2 and of H-4' with C-1'' (Figure 1). The connectivities found in HSQC and HMBC spectra allowed the assignment of all carbon resonance in the ^{13}C NMR spectra of compounds **4a-h**.

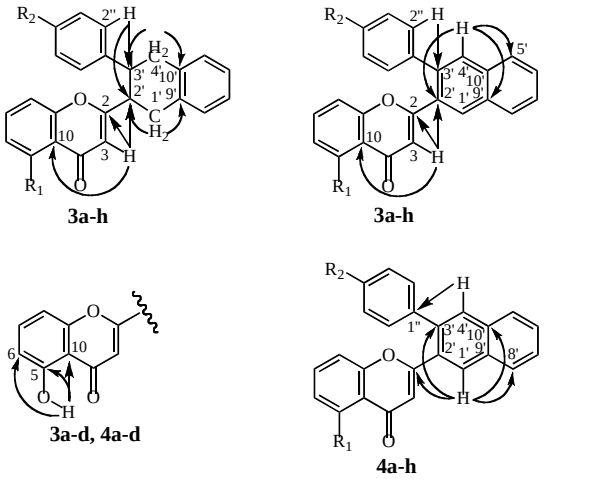


Figure 1. Main connectivities on the HMBC spectra of naphthylchromones **3a-h** and **4a-h**.

EXPERIMENTAL

Melting points were measured in a Reichert Thermovar apparatus fitted with a microscope and are uncorrected. NMR spectra were recorded on a Bruker Avance 300 spectrometer (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C), in $CDCl_3$ as solvent. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) in Hz. The internal standard was TMS. Unequivocal ^{13}C assignments were made with the aid of 2D *g*HSQC and *g*HMBC experiments (delays for one bond and long-range *J* C/H couplings were optimized for 145 and 7 Hz,

respectively). Electron impact (EI, 70 eV) MS were recorded on VG AutoSpec Q and M spectrometers. Elemental analyses were obtained with a CHNS 932 Leco analyser (University of Aveiro) or with a Carlo Erba 1108 analyzer (University of Vigo). Preparative thin-layer chromatography was performed with Merck silica gel 60 DGF_{254}. Column chromatography was performed with Merck silica gel 60, 70-230 mesh. All other chemicals and solvents used were obtained from commercial sources and used as received or dried using standard procedures. Microwave assisted synthesis was carried out in an Ethos SYNTH Microwave (Milestone Inc.) apparatus.

2-Styrylchromones 1a-h. Prepared as described in the literature [57].

1,3-Dihydrobenzo[*c*]thiophene 2,2-Dioxide. Prepared according to literature procedure [40].

Synthesis of 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)chromones 3a-h. A solution of an appropriate 2-styrylchromone **1a-h** (1.5 mmol) and 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (336 mg, 2 mmol) in 1,2,4-trichlorobenzene (10 mL), under nitrogen atmosphere, was refluxed for 10 h. Then more 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (84 mg, 0.5 mmol) was added and the reflux maintained for 14 hours. After cooling to room temperature, the reaction mixture was purified by column chromatography on silica gel. Elution with light petroleum removed 1,2,4-trichlorobenzene, while elution with a 7:3 mixture of dichloromethane:light petroleum afforded the cycloadducts 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)]chromones **3a-h** in good yields.

5-Hydroxy-2-(3-phenyl-1,2,3,4-tetrahydronaphth-2-yl)-chromone (3a). Yield: 387 mg (70%); mp 138-140 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.22-3.44 (m, 6 H, 2 x H-1', H-2', H-3', 2 x H-4'), 6.06 (s, 1 H, H-3), 6.78 (br d, 1 H, *J* 8.3 Hz, H-6), 6.88 (br d, 1 H, *J* = 8.3 Hz, H-8), 7.18-7.32 (m, 9 H, H-5',6',7',8', 3'-C_6H_5), 7.52 (t, 1 H, *J* = 8.3 Hz, H-7), 12.49 (s, 1H, 5-O*H*). ^{13}C NMR: δ = 34.5 (C-1'), 37.8 (C-4'), 44.0 (C-3'), 46.4 (C-2'), 106.6 (C-8), 109.2 (C-3), 110.4 (C-10), 111.1 (C-6), 126.2 and 126.4 (C-6' and C-7'), 127.0 (C-4''), 127.1 (C-3'',5''), 128.6 (C-5',8'), 128.7 (C-2'',6''), 133.9 (C-9'), 135.0 (C-7), 135.3 (C-10'), 142.5 (C-1''), 156.5 (C-9), 160.6 (C-5), 171.7 (C-2), 183.2 (C-4). EI-MS: *m/z* relative intensity 368 ($M^{+\bullet}$, 100), 277 (37), 263 (13), 252 (12), 193 (24), 178 (13), 149 (5), 137 (16), 115 (23), 104 (27), 91 (21), 71 (12), 57 (15). *Anal.* calcd. for $C_{25}H_{20}O_3$: C 81.14, H 5.48. Found C 81.50, H 5.47%.

2-[3-(4-Chlorophenyl)-1,2,3,4-tetrahydronaphth-2-yl]-5-hydroxychromone (3b). Yield: 435 mg (72%); mp 118-120 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.18-3.30 (m, 5 H, 2 x H-1', H-2', 2 x H-4'), 3.31-3.44 (m, 1 H, H-3'), 5.99 (s, 1 H, H-3), 6.73 (dd, 1 H, *J* = 8.3 and 0.6 Hz, H-6), 6.80 (dd, 1 H, *J* = 8.4 and 0.6 Hz, H-8), 7.11-7.25 (m, 4 H, H-5',6',7',8'), 7.12 (d, 2 H, *J* = 8.4 Hz, H-2'',6''), 7.19 (d, 2 H, *J* = 8.4 Hz, H-3'',5''), 7.46 (dd, 1 H, *J* = 8.3 and 8.4 Hz, H-7), 12.39 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 34.5 (C-1'), 37.7 (C-4'), 43.4 (C-3'), 46.2 (C-2'), 106.5 (C-8), 109.2 (C-3), 110.4 (C-10), 111.3 (C-6), 126.4 and 126.5 (C-6' and C-7'), 128.5 (C-2'',6''), 128.58 and 128.64 (C-5' and C-8'), 128.9 (C-3'',5''), 132.6 (C-4''), 133.7 (C-10'), 134.9 (C-9'), 135.1 (C-7), 141.0 (C-1''), 156.4 (C-9), 160.6 (C-5), 171.2 (C-2), 183.1 (C-4). EI-MS: *m/z* relative intensity 402 ($M^{+\bullet}$, 100), 368 (2), 297 (6), 286 (7), 277 (40), 263 (7), 227 (23), 202 (7), 192 (19), 176 (9), 165 (5), 149 (10), 137 (20), 125 (20), 115 (22), 104 (45), 91 (8), 78 (12). EI-HRMS: calcd. for $C_{25}H_{19}ClO_3$ 402.1023; found 402.1032.

5-Hydroxy-2-[3-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphth-2-yl]chromone (3c). Yield: 376 mg (63%); mp 164-166 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.12-3.24 (m, 4 H, H-1', H-2', 2 x H-4'), 3.30-3.40 (m, 2 H, H-3', H-1'), 3.73 (s, 3 H, 4''-OCH_3), 5.99 (s, 1 H, H-3), 6.73 (dd, 1 H, *J* = 8.2 and 0.8 Hz, H-6), 6.75 (d, 2 H, *J* = 8.7 Hz, H-3'',5''), 6.82 (dd, 1 H, *J* = 8.4 and 0.8 Hz, H-8), 7.10 (d, 2 H, *J* = 8.7 Hz, H-2'',6''), 7.13-7.21 (m, 4 H, H-5',6',7',8'), 7.47 (dd, 1 H, *J* = 8.2 and 8.4 Hz, H-7), 12.43 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 34.6 (C-1'), 38.0 (C-4'), 43.1 (C-3'), 46.7 (C-2'), 106.6 (C-8), 109.3 (C-3), 110.5 (C-10), 111.1 (C-6), 114.1 (C-3'',5''), 126.2 and 126.4 (C-6' and C-7'), 128.1 (C-2'',6''), 128.6 and 129.0 (C-5' and C-8'), 134.0 and 134.5 (C-9' and C-10'), 135.0 (C-7), 135.5 (C-1''), 156.6 (C-9), 158.3 (C-4''), 160.6 (C-5), 171.9 (C-2), 183.3 (C-4). EI-MS: *m/z* relative intensity 398 ($M^{+\bullet}$, 100), 293 (3), 277 (2), 223 (24), 137 (3), 121 (85), 115 (13), 104 (9), 91 (2). *Anal.* calcd. for $C_{26}H_{22}O_4$: C 78.37, H 5.57. Found C 78.25, H 5.56%.

5-Hydroxy-2-[3-(4-nitrophenyl)-1,2,3,4-tetrahydronaphth-2-yl]chromone (3d). Yield: 490 mg (79%); mp 195-197 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.18 (dd, 1 H, *J* = 12.2 and 5.5 Hz, H-1'), 3.27 (dd, 1 H, *J* = 12.2 and 3.4 Hz, H-1'), 3.10-3.41 (m, 3 H, 2 x H-4', H-2'), 3.52-3.62 (m, 1 H, H-3'), 6.01 (s, 1 H, H-3), 6.74 (dd, 1 H, *J* = 8.3 and 0.6 Hz, H-6), 6.80 (d br, 1 H, *J* = 8.2 Hz, H-8), 7.13-7.26 (m, 4 H, H-5',6',7',8'), 7.39 (d, 2 H, *J* = 8.7 Hz, H-2'',6''), 7.47 (dd, 1 H, *J* = 8.3 and 8.2 Hz, H-7), 8.11 (d, 2 H, *J* = 8.7 Hz, H-3'',5''), 12.30 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 34.4 (C-1'), 37.4 (C-4'), 44.0 (C-3'), 46.0 (C-2'), 106.4 (C-8), 109.3 (C-3), 110.4 (C-10), 111.6 (C-6), 124.1 (C-3'',5''), 126.7 (C-6',7'), 128.1 (C-2'',6''), 128.3 and 128.7 (C-5' and C-8'), 133.5 (C-10'), 134.3 (C-9'), 135.3 (C-7), 147.0 (C-4''), 150.2 (C-1''), 156.4 (C-9), 160.7 (C-5), 170.5 (C-2), 183.0 (C-4). EI-MS m/z relative intensity 413 ($M^{+\bullet}$, 100), 277 (25), 192 (10), 137 (14), 115 (9), 104 (44), 78 (7). EI-HRMS: calcd. for $C_{25}H_{19}NO_5$ 413.1263; Found 413.1269.

2-(3-Phenyl-1,2,3,4-tetrahydronaphth-2-yl)chromone (3e). Yield: 467 mg (89%); mp 141-143 ºC (from cyclohexane/dichloromethane) (lit. mp [39]: 143-145 ºC).

2-[3-(4-Chlorophenyl)-1,2,3,4-tetrahydronaphth-2-yl]-chromone (3f). Yield: 531 mg (92%); mp 163-165 ºC (from cyclohexane/dichloromethane) (lit. mp [39]: 162-164 ºC).

2-[3-(4-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-2-yl]-chromone (3g). Yield: 354 mg (62%); mp 169-171 ºC (from cyclohexane/dichloromethane) (lit. mp [39]: 169-171 ºC).

2-[3-(4-Nitrophenyl)-1,2,3,4-tetrahydronaphth-2-yl]-chromone (3h). Yield: 477 mg (80%); mp 195-197 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.14-3.37 (m, 5 H, 2 x H-1', H-2', 2 x H-4'), 3.54-3.59 (m, 1 H, H-3'), 6.09 (s, 1 H, H-3), 7.13-7.24 (m, 4 H, H-5',6',7',8'), 7.33-7.36 (m, 1 H, H-6), 7.36 (dd, 1 H, *J* = 8.1 and 0.7 Hz, H-8), 7.39 (d, 2 H, *J* = 9.0 Hz, H-2'',6''), 7.63 (dt, 1 H, *J* = 8.1 and 1.6 Hz, H-7), 8.06-8.09 (m, 1 H, H-5), 8.08 (d, 2 H, *J* = 9.0 Hz, H-3'',5''). ^{13}C NMR: δ = 34.4 (C-4'), 37.5 (C-1'), 44.0 (C-3'), 45.9 (C-2'), 110.8 (C-3), 117.4 (C-8), 123.6 (C-10), 124.0 (C-3'',5''), 125.2 (C-6), 125.7 (C-5), 126.6 (C-5',8'), 128.2 (C-2'',6''), 128.6 and 128.7 (C-6' and C-7'), 133.7 (C-7), 133.8 (C-10'), 134.4 (C-9'), 146.9 (C-4''), 150.5 (C-1''), 156.1 (C-9), 169.1 (C-2), 177.8 (C-4). EI-MS: *m/z* relative intensity 397 ($M^{+\bullet}$, 3), 281 (13), 261 (100), 238 (4), 192 (9), 160 (5), 141 (6), 121 (13), 116 (21), 104 (43), 92 (3), 78 (7). *Anal.* calcd. for $C_{25}H_{19}NO_4$: C 75.55, H 4.82, N 3.52. Found C 75.42, H 4.87, N 3.51%.

Synthesis of 2-(3-arylnaphth-2-yl)chromones 4a-h. General procedure.

Method A: A mixture of the appropriate 2-(3-aryl-1,2,3,4-tetrahydronaphth-2-yl)chromone **3a-h** (1 mmol) and DDQ (1.14 g, 5 mmol) in dry 1,4-dioxane (10 mL) was refluxed for 24 hours under nitrogen atmosphere. In the case of **3b** and **3h** *p*-toluenesulfonic acid monohydrate (0.1 mg, 0.1 mmol) was also added. After the reflux, the solvent was evaporated and the mixture was dissolved in chloroform and washed with a diluted $NaHCO_3$ solution. The organic phase was concentrated and purified by silica gel thin-layer chromatography using dichloromethane as eluent. The following 2-(3-arylnaphth-2-yl)chromones were obtained in good yields: **4a**, 87%; **4e**, 81%; **4g**, 88%.

Method B: Each 2-[3-(4-chlorophenyl)-1,2,3,4-tetrahydronaphth-2-yl]chromone **3a-h** (1 mmol), DDQ (0.68 mg, 3 mmol), in 1,2,4-trichlorobenzene (5 mL), in a two neck round bottom flask, with magnetic stirring and an optic fiber temperature control and a reflux condenser, was heated with the following microwave program: first step: 6 minutes, ramp to 170 ºC, maximum power of 800 W; second step: 30 minutes, temperature at 170 ºC, maximum power 800 W. After cooling to room temperature, the reaction mixture was separated by a column chromatography on silica gel. Elution with light petroleum removed 1,2,4-trichlorobenzene while elution with dichloromethane afforded the 2-(3-arylnaphth-2-yl)chromones **4a-h** in good yields: **4a**, 92%; **4b**, 91%; **4c**, 83, **4d**, 48%; **4e**, 95%; **4f**, 93%; **4g**, 96%; **4h**, 81%.

5-Hydroxy-2-(3-phenylnaphth-2-yl)chromone (4a). mp 182-184 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 6.44 (dd, 1 H, *J* = 8.4 and 0.7 Hz, H-8), 6.46 (s, 1 H, H-3), 6.75 (dd, 1 H, *J* = 8.2 and 0.7 Hz, H-6), 7.28-7.42 (m, 5 H, H-2",3",4",5",6"), 7.40 (dd, 1 H, *J* = 8.4 and 8.2 Hz, H-7), 7.61 (dd, 1 H, *J* = 7.5 and 1.4 Hz, H-6' or H-7'), 7.63 (dd, 1 H, *J* = 7.1 and 1.7 Hz, H-6' or H-7'), 7.93 (br d, 1 H, *J* = 7.1 Hz, H-5' or H-8'), 7.94 (s, 1 H, H-4'), 7.98 (dd, 1 H, *J* = 7.5 and 1.7 Hz, H-5' or H-8'), 8.24 (s, 1 H, H-1'), 12.51 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 106.8 (C-8), 110.6 (C-10), 110.7 (C-3), 111.2 (C-6), 127.1 (C-7'), 127.4 (C-4"), 127.9 (C-5'), 128.4 (C-8'), 128.4 (C-6'), 128.47 (C-3",5"), 128.55 (C-2",6"), 129.5 (C-2'), 130.2 (C-4'), 130.4 (C-1'), 131.8 (C-9'), 134.2 (C-10'), 135.2 (C-7), 138.1 (C-3'), 140.5 (C-1"), 156.4 (C-9), 160.6 (C-5), 167.0 (C-2), 183.3 (C-4). EI-MS: *m/z* relative intensity 364 ($M^{+\bullet}$, 70), 347 (11), 289 (5), 238 (13), 228 (100), 215 (11), 202 (11), 182 (6), 147 (6), 118 (9), 108 (16), 91 (8), 83 (21). Anal. calcd. for $C_{25}H_{16}O_3$: C 82.40, H 4.43.Found C 82.19, H 4.44%.

2-[3-(4-Chlorophenyl)naphth-2-yl]-5-hydroxychromone (4b). mp 174-176 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 6.46 (s, 1 H, H-3), 6.47 (dd, 1 H, *J* = 8.4 and 0.9 Hz, H-8), 6.77 (dd, 1 H, *J* = 8.4 and 0.7 Hz, H-6), 7.33 (s, 5 H, H-2",3",5",6"), 7.43 (t, 1 H, *J* = 8.4 Hz, H-7), 7.58-7.67 (m, 2 H, H-7' and H-6'), 7.89 (s, 1 H, H-4'), 7.90-7.99 (m, 2 H, H-5' and H-8'), 8.21 (s, 1 H, H-1'), 12.48 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 106.7 (C-8), 110.6 (C-10), 110.7 (C-3), 111.4 (C-6), 127.4 (C-7'), 127.9 (C-5'), 128.4 (C-8'), 128.6 (C-6'), 128.7 (C-2",6"), 129.2 (C-2'), 129.8 (C-3",5"), 130.2 (C-4'), 130.6 (C-1'), 131.9 (C-9'), 133.5 (C-4"), 134.1 (C-10'), 135.4 (C-7), 136.7 (C-1"), 139.0 (C-3'), 156.3 (C-9), 160.6 (C-5), 166.7 (C-2), 183.2 (C-4). EI-MS: *m/z* relative intensity 398 ($M^{+\bullet}$, 100), 381 (18), 362 (9), 334 (10), 289 (9), 277 (18), 262 (95), 226 (52), 182 (32), 137 (17), 108 (17). EI-HRMS: calcd. for $C_{25}H_{15}ClO_3$ 398.0710; found 398.0712.

5-Hydroxy-2-[3-(4-methoxyphenyl)naphth-2-yl]chromone (4c). mp 196-198 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 3.81 (s, 3 H, 4"-OCH_3), 6.41 (s, 1 H, H-3), 6.56 (dd, 1 H, *J* = 8.4 and 0.8 Hz, H-8), 6.77 (dd, 1 H, *J* = 8.2 and 0.8 Hz, H-6), 6.89 (d, 2 H, *J* = 8.8 Hz, H-3",5"), 7.32 (d, 2 H, *J* = 8.8 Hz, H-2",6"), 7.43 (dd, 1 H, *J* = 8.4 and 8.2 Hz, H-7), 7.57-7.63 (m, 2 H, H-7' and H-6'), 7.90 (s, 1 H, H-4'), 7.90-7.98 (m, 2 H, H-5' and H-8'), 8.21 (s, 1 H, H-1'), 12.54 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 106.9 (C-8), 110.6 (C-10), 110.8 (C-3), 111.2 (C-6), 114.0 (C-3",5"), 127.0 (C-7'), 127.8 (C-5'), 128.3 (C-6'), 128.4 (C-8'), 129.6 (C-2'), 129.7 (C-2",6"), 130.1 (C-4'), 130.4 (C-1'), 131.6 (C-9'), 132.7 (C-1"), 134.3 (C-10'), 135.3 (C-7), 137.7 (C-3'), 156.5 (C-9), 159.0 (C-4"), 160.6 (C-5), 167.2 (C-2), 183.3 (C-4). EI-MS: *m/z* relative intensity 394 ($M^{+\bullet}$, 100), 377 (14), 350 (8), 258 (70), 243 (9), 223 (7), 215 (43), 197 (11), 189 (10), 137 (11), 121 (25), 108 (10). EI-HRMS: calcd. for $C_{26}H_{18}O_4$ 394.1205; found: 394.1205.

5-Hydroxy-2-[3-(4-nitrophenyl)naphth-2-yl]chromone (4d). mp 231-233 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 6.35 (dd, 1 H, *J* = 8.4 and 0.6 Hz, H-8), 6.56 (s, 1 H, H-3), 6.77 (dd, 1 H, *J* = 8.2 and 0.6 Hz, H-6), 7.40 (dd, 1 H, *J* = 8.4 and 8.2 Hz, H-7), 7.59 (d, 2 H, *J* = 8.8 Hz, H-2",6"), 7.64-7.72 (m, 2 H, H-7' and H-6'), 7.95 (s, 1 H, H-4'), 7.97-8.03 (m, 2 H, H-5' and H-8'), 8.24 (d, 2 H, *J* = 8.8 Hz, H-3",5"), 8.27 (s, 1 H, H-1'), 12.41 (s, 1 H, 5-O*H*). ^{13}C NMR: δ = 106.4 (C-8), 110.5 (C-10), 110.7 (C-3), 111.7 (C-6), 123.7 (C-3",5"), 128.0 (C-7'), 128.1 (C-5'), 128.5 (C-8'), 128.8 (C-2'), 128.9 (C-6'), 129.4 (C-2",6"), 130.6 (C-4'), 131.0 (C-1'), 132.3 (C-9'), 134.0 (C-10'), 135.5 (C-3'), 135.6 (C-7), 147.0 (C-4"), 147.5 (C-1"), 156.1 (C-9), 160.7 (C-5), 166.1 (C-2), 183.1 (C-4). EI-MS: m/z relative intensity 409 ($M^{+\bullet}$, 100), 391 (10), 362 (11), 273 (29), 226 (27), 215 (9), 108 (21), 92 (7). EI-HRMS: calcd. for $C_{25}H_{15}NO_5$ 409.0950; found 409.0938.

2-(3-Phenylnaphth-2-yl)chromone (4e). mp 147-149 ºC (from cyclohexane/ dichloromethane) (lit. mp [39]: 145-147 ºC).

2-[3-(4-Chlorophenyl)naphth-2-yl]chromone (4f). mp 160-162 ºC (from cyclohexane/ dichloromethane) (lit. mp [39]: 159-161 ºC). Anal. Calcd. For $C_{25}H_{15}ClO_2$: C 78.43, H 3.95. Found: C 78.20, H 3.94%

2-[3-(4-Methoxyphenyl)naphth-2-yl]chromone (4g). mp 115-117 ºC (from cyclohexane/dichloromethane). Anal. Calcd. For $C_{26}H_{18}O_3$: C 82.52, H 4.79. Found: C 82.79, H 4.79%.

2-[3-(4-Nitrophenyl)naphth-2-yl]chromone (4h). mp 236-238 ºC (from cyclohexane/dichloromethane). ^{1}H NMR: δ = 6.65 (s, 1 H, H-3), 6.90 (d, 1 H, *J* = 8.1 Hz, H-8), 7.38 (ddd, 1 H, *J* = 7.7, 7.6 and 0.8 Hz, H-6), 7.55 (ddd, 1 H, *J* = 8.1, 7.6 and 1.8 Hz, H-7), 7.61 (d, 2 H, *J* = 8.8 Hz, H-2",6"), 7.63-7.69 (m, 2 H, H-6' and H-7'), 7.96 (s, 1 H, H-4'), 7.96-8.03 (m, 2 H, H-5', H-8'), 8.19 (dd, 1 H, *J* = 7.7 and 1.8 Hz, H-5), 8.22 (d, 2 H, *J* = 8.8 Hz, H-3",5"), 8.28 (s, 1 H, H-1') ^{13}C NMR: δ = 112.3 (C-3), 117.4 (C-8), 123.6 (C-10), 123.7 (C-3", 5"), 125.5 (C-6), 125.7 (C-5), 127.9 (C-7'), 128.1 (C-5'), 128.5 (C-8'), 128.7 (C-6'), 129.4 (C-2", 6"), 129.4 (C-2'), 130.5 (C-4'), 130.8 (C-1'), 132.4 (C-9'), 133.9 (C-10'), 134.0 (C-7), 135.6 (C-3'), 146.9 (C-4"), 147.7 (C-1"), 156.0 (C-9), 165.0 (C-2), 178.0 (C-4). EI-MS: m/z relative intensity 393 ($M^{+\bullet}$, 100), 376 (17), 346 (13), 318 (12), 289 (14), 276 (23), 261 (15), 226 (33), 121 (15), 92 (18). EI-HRMS: calcd. for $C_{25}H_{15}NO_4$ 393.1001; found 393.0990.

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