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New Benzo[*b*]xanthones from Diels-Alder Reactions of Chromone-3-carboxaldehydes with *ortho*-Benzoquinodimethanes

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Summary. New benzo[*b*]xanthone derivatives, having substituents in the A and D rings, were prepared from cycloaddition reactions of chromone-3-carboxaldehydes with *ortho*-benzoquinodimethanes, generated *in situ* from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide, followed by oxidation of the obtained diastereomeric adducts. The structure of all compounds was fully established by 1D and 2D NMR, MS, and elemental analysis. The stereochemistry of the obtained diastereomeric cycloadducts was established by N*O*ESY experiments.

Keywords. Benzo[*b*]xanthones; *ortho*-Benzoquinodimethanes; Cycloadditions; Oxidations; NMR Spectroscopy.

Introduction

Xanthones constitute an important family of polyphenolic heterocyclic compounds widely occurring in nature [1]. The great interest in these compounds is due to their abundance in nature and also to their important biological properties [2]. Benzo[*b*] xanthones form a class of xanthones with a scarce natural occurrence. The first natural derivative was bikaverin **I**, a red pigment with significant and specific antiprotozoal and cytotoxic activities [3]. The benzo[*b*]xanthone skeleton was also found in a small family of microbial natural products, the polycyclic xanthone antibiotics (*e.g.* **II**), which showed important antibacterial, antifungal, and cytotoxic activities [4]. Certain synthetic benzo[*b*]xanthones are used in the treatment of a series of human diseases [5].

Despite the important biological applications of benzo[*b*]xanthones, synthetic strategies leading to these compounds have not been widely explored. Some of the first reports on the synthesis of these compounds have used appropriate *ortho*-hydroxynaphthoic acid derivatives as starting materials, including the heating of

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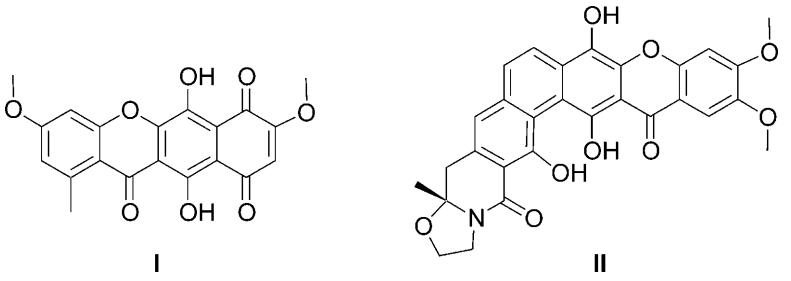


Fig. 1. Structures **I** and **II**

ortho-hydroxyarylnaphthoates, pyrolysis of *ortho*-hydroxynaphthoic acids and *ortho*-hydroxyarylnaphthoates [6], heating mixtures of 1- or 2-naphthol with phenyl *ortho*-hydroxybenzoates [7], and condensation of *ortho*-hydroxynaphthoic acid with phloroglucinol [8]. Thermal condensation of 2-naphthol with appropriate β-ketoesters [9], photochemical reactions of substituted 3-aroylchromones [10] and of 2-benzyl- and 2-benzhydryl-3-benzoylchromones [11], and decomposition of *ortho*-carboxynaphthalenediazonium tetrafluoroborates in the presence of phenols [12] have been other studied transformations giving rise to a limited number of benzo[*b*]xanthones. 11-Hydroxybenzo[*b*]xanthones were synthesised by thermal decomposition of an appropriate ketoylide [13] and some derivatives have also been synthesized through an efficient *Claisen* type condensation of appropriate *ortho*-hydroxyacetophenone enolate ions with dimethyl homophthalates [14]. The benzo[*b*]xanthone skeleton was also obtained by [4 + 2] cycloaddition reactions of a benzochromone-3-carboxaldehyde with *Danishefsky*'s diene [15], by coupling salts of 1-naphthol with appropriate 2-iodobenzoic acids [16], or by nucleophilic addition of aryl lithiates to dithiane-protected γ-benzopyrone-fused cyclobutenediones [17].

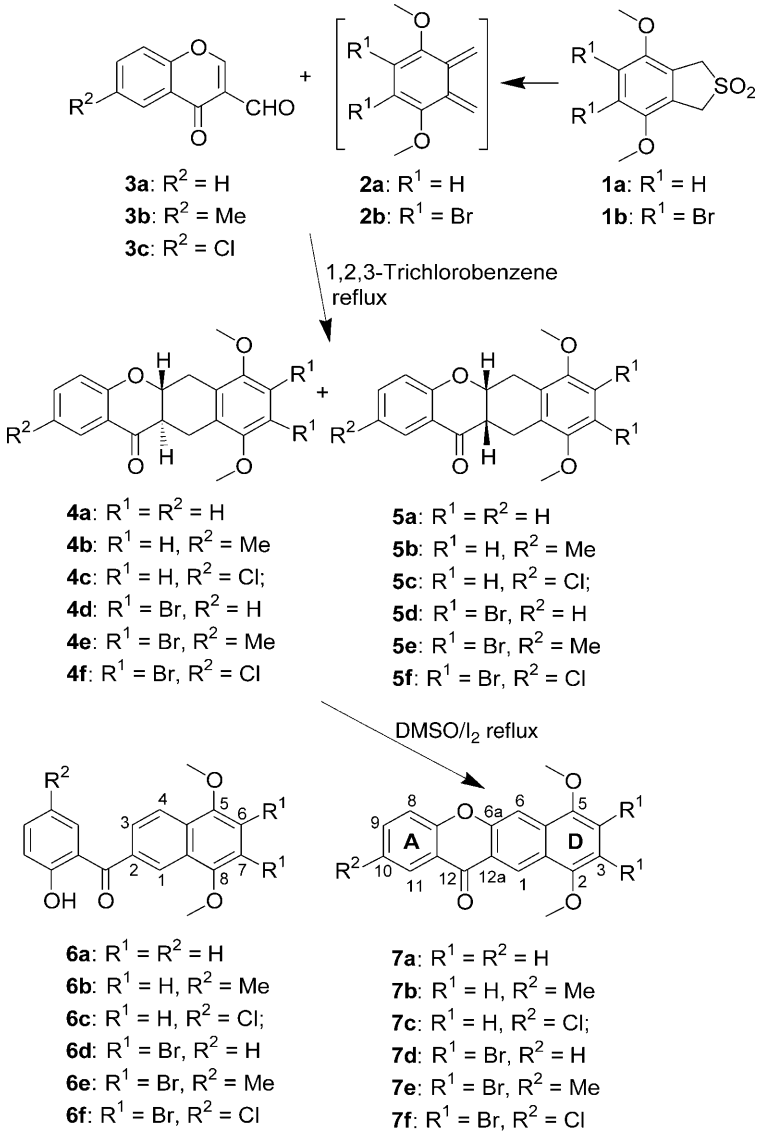
All these synthetic methods came up as the result of studies on the behaviour of starting materials or the desire to synthesise a particular benzo[*b*]xanthone derivative. A few specific synthetic methods were also developed for the synthesis of bikaverin [3] and of the polycyclic xanthone antibiotics [18].

In a previous paper we reported an efficient new route to the benzo[*b*]xanthones' system, by cycloaddition reactions of chromone-3-carboxaldehydes with the *ortho*-benzoquinodimethane, followed by oxidation of the adducts [19]. Ten benzo[*b*] xanthone derivatives bearing A ring substituents were, thus, synthesized. In order to prepare other benzo[*b*]xanthones for further studies on the structure pharmacological activity relationship and to investigate the synthetic scope of our method, we have studied the *Diels-Alder* reactions of other *ortho*-benzoquinodimethanes **2a** and **2b** with chromone-3-carboxaldehydes **3a**–**3c**. As a result, we describe here the synthesis of novel benzo[*b*]xanthones bearing substituents in the A and D rings.

Results and Discussion

Synthesis

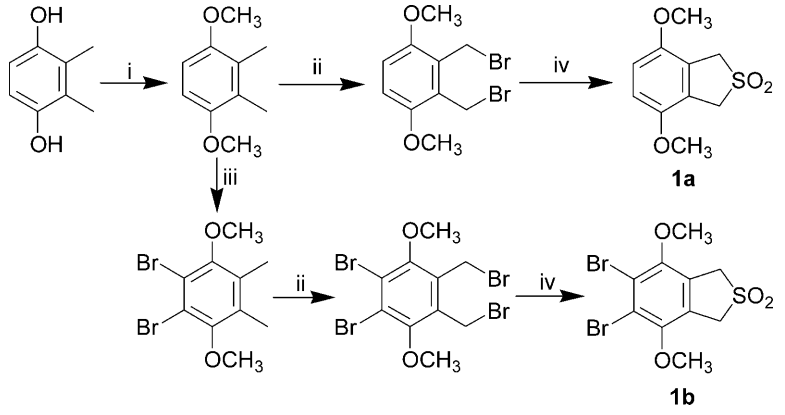
Our experiments considered the *Diels-Alder* reactions of chromone-3-carboxaldehydes **3a**–**3c** with *ortho*-benzoquinodimethanes **2a** and **2b**, formed *in situ* by



Scheme 1

thermal extrusion of sulfur dioxide from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxides **1a** and **1b** (Scheme 1). Compounds **1a** and **1b** were synthesized by the method described by *Cava et al.* [20] from the appropriate α,α'-dibromo-*ortho*-xylene derivatives, which were prepared by reactions sequences reported in literature [21] (Scheme 2). To our knowledge, sulfone **1b** was synthesized for the first time.

The *Diels-Alder* reactions of chromone-3-carboxaldehydes **3a**–**3c** with *ortho*-benzoquinodimethanes **2a** and **2b** gave rise to the expected adduct, a β-ketoaldehyde which was prone to deformylation under the reaction conditions, yielding a mixture of diastereomers **4a**–**4f** and **5a**–**5f** in good overall yields (88–93%), which were separated by thin layer chromatography [19]. In some cases small amounts of **6** were also isolated. (2-Hydroxyphenyl)-2-naphthylketones **6a**, **6c**–**6e** can be formed by pyran ring opening during an oxidation process. Oxidation of adducts



Scheme 2. i) Dimethyl sulphate, K_2CO_3, acetone, reflux; ii) NBS, AIBN, CCl_4, reflux; iii) Br_2, $CHCl_3$, room temp.; iv) 1) $Na_2SO_3 \cdot 9H_2O$, ethanol, reflux; 2) Oxone, aluminium oxide grade I, $CHCl_3$, reflux

4a–**4f** and **5a**–**5f** with dimethyl sulfoxide in the presence of catalytic amounts of iodine gave the new benzo[*b*]xanthones **7a**–**7f** in good yields (88–94%). These are all substituted in their A and D rings. Thus, the synthetic procedure can be considered of general applicability for such derivatives.

NMR Spectroscopy

The most important features of the ^{1}H and ^{13}C NMR spectra of the benzotetrahydroxanthones **4a**–**4f** and **5a**–**5f** are the resonances appearing in their aliphatic region. The signals that immediately indicate the presence of the *trans* **4a**–**4f** or the *cis* **5a**–**5f** cycloadducts are those of H-6a and H-12a and, particularly, the coupling between them. In the case of compounds **5a**–**5f** H-6a appears as narrow multiplet ($\delta = 4.89$–4.97 ppm) whereas in the case of **4a**–**4f** they appear as double doublet of doublets ($\delta = 4.49$–4.54 ppm). The coupling constants, $^3J_{\mathrm{H6a-H12a}} = 13.1$–$13.4$ Hz in the latter cases, indicate the *trans* configuration of these two protons for **4a**–**4f**. The coupling constants, $^3J_{\mathrm{H6a-H12a}} = 2$–$3$ Hz, measured from the signal of H-12a of compounds **5a**–**5f** support a *cis* configuration of these protons. This configuration was confirmed by the close proximity of H-6a and H-12a found in the N*O*ESY spectra of adducts **5a**–**5f**.

The resonances of C-6 ($\delta = 27.5$–31.2 ppm) and C-6a ($\delta = 73.7$–77.8 ppm) appear at higher frequency values than those of C-1 ($\delta = 20.6$–23.6 ppm) and C-12a ($\delta = 43.9$–45.3 ppm) due to the inductive deshielding effect of the oxygen atom of the heterocyclic ring.

The resonances of all other protons and carbons of compounds **4a**–**f** and **5a**–**f** were assigned by COSY, HSQC, HMBC, and N*O*ESY spectra.

In the ^{1}H NMR spectra of (2-hydroxyphenyl)-2-naphthylketones **6a**, **6c**–**6e** one can conclude on the presence of the hydroxyl group ($\delta = 11.82$–12.12 ppm) involved in a hydrogen bond with the carbonyl group ($\delta = 200.8$–201.8 ppm), the absence of aliphatic resonances, and the presence of a 1,3,4-unsubstituted phenyl ring that support the structure of ketones **6a**, **6c**–**6e** as depicted in Scheme 1. The higher frequency values of H-1 ($\delta = 8.39$–8.56 ppm) and H-4

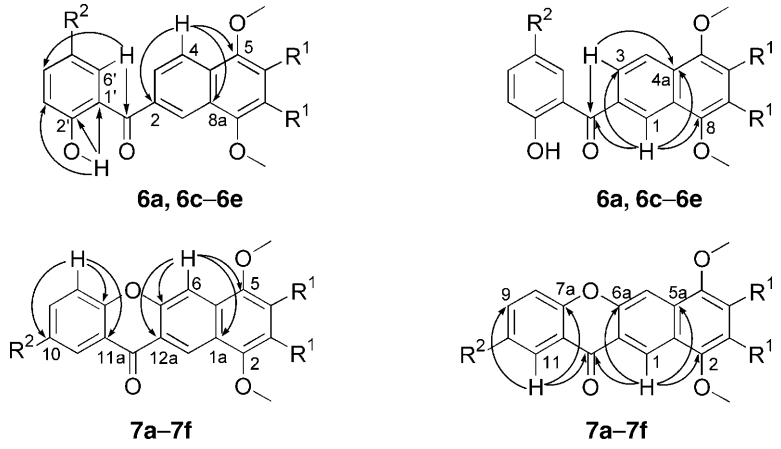


Fig. 2. Important correlations found in the HMBC spectra of compounds **6a, 6c–6e** and **7a–7f**

($\delta = 8.23$–8.34 ppm) resonances relative to those of H-3 ($\delta = 7.76$–7.86 ppm) are due to the through space deshielding effect of the 5- and 8-methoxy groups.

The most deshielded protons of compounds **7a–7f** are H-1 ($\delta = 9.12$–9.28 ppm), H-11 ($\delta = 8.11$–8.38 ppm), and H-6 ($\delta = 8.10$–8.29 ppm. The higher frequency value of H-1 resonance is due to the mesomeric and anisotropic deshielding effect of the carbonyl group and also of the through space effect of the 2-methoxy group. H-11 only experienced the mesomeric and anisotropic deshielding effect of the carbonyl group whereas H-6 only suffered the through space effect of the 5-methoxy group.

The correlations found in the HMBC spectra of compounds **6a**, **6c–6e** and **7a–7f** allowed the unequivocal assignment of all carbons (Fig. 2 shows the most important correlations).

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 $CDCl_3$, if not stated otherwise, on Bruker AMX 300 and DRX 300 spectrometers operating at 300.13 and 75.47 MHz; the chemical shifts are expressed in δ (ppm) values relative to *TMS* as internal reference and the coupling constants (*J*) are given in Hz. ^{1}H Assignments were made using 2D COSY and N*O*ESY (mixing time of 800 ms) experiments, whereas ^{13}C assignments were made using 2D *g*HSQC and *g*HMBC experiments (long range C/H coupling constants were optimised to 4 and 7 Hz). Mass spectra (EI, 70 eV) were measured on VG Autospec Q an M mass spectrometers. Elemental analyses were obtained on a LECO 932 CHN analyser; these values were in accordance with the calculated ones, as well as the high resolution MS. Preparative thin layer chromatography was carried out on Riedel silica gel 60 DGF_{254} and column chromatography on Merck silica gel 60, 70–230 mesh.

5,6-Dibromo-4,7-dimethoxy-1,3-dihydrobenzo[c]thiophene 2,2-dioxide (**1b**, $C_{10}H_{10}Br_2O_4$)

A mixture of 2.0 g of 2,3-dimethyl-1,4-dihydroxybenzene (14.47 mmol), 3 cm^3 of dimethyl sulfate (14.47 mmol), and 13.2 g of K_2CO_3 (95.5 mmol) in 100 cm^3 of acetone was refluxed for 24 h. After this period K_2CO_3 was filtered off and washed with 20 cm^3 of acetone. The solvent was evaporated and the residue was purified by column chromatography using a mixture of light petroleum:$CH_2Cl_2 = 1{:}1$.

After solvent evaporation and recrystallisation from ethanol, 2.2 g of 2,3-dimethyl-1,4-dimethoxybenzene (92%; mp 76–77°C; ref. [22] 78–79°C) was obtained.

A mixture of 1.8 g of 2,3-dimethyl-1,4-dimethoxybenzene (10.8 mmol) and 1.1 cm^3 of Br_2 (21.4 mmol) in 40 cm^3 of $CHCl_3$ was stirred at room temp. and protected from daylight for 2 h. After this period the solvent was evaporated and the residue was recrystallised from ethanol giving 2.4 g of 5,6-dibromo-2,3-dimethyl-1,4-dimethoxybenzene (72%; mp 117–118°C; ref. [23] 117–119°C).

A mixture of 2.0 g of *N*-bromosuccinimide (11.2 mmol), 180.6 mg of 2,2′-azobisisobutyronitrile (1.1 mmol), and 1.7 g of 5,6-dibromo-2,3-dimethyl-1,4-dimethoxybenzene (5.2 mmol) in 100 cm^3 of CCl_4 was refluxed for 2 h. After this period the solvent was evaporated and recrystallisation of the residue ethanol/H_2O gave 1.9 g of 5,6-dibromo-2,3-di(bromomethyl)-1,4-dimethoxybenzene (76%; mp 115–116°C; ref. [24] 104–105°C).

A solution of 1.2 g of $Na_2SO_3 \cdot 9H_2O$ (5.0 mmol) and 1.6 g of 5,6-dibromo-2,3-di(bromomethyl)-1,4-dimethoxybenzene (3.3 mmol) in ethanol was refluxed for 17 h. After this period the formed NaCl was filtered off and the filtrate was concentrated. Water (50 cm^3) was added to the reaction mixture and this was extracted with 3 × 50 cm^3 of cyclohexane. The solvent was evaporated and the residue was recrystallised from ethanol giving 0.8 g of 5,6-dibromo-4,7-dimethoxy-1,3-dihydrobenzo[*c*]thiophene (69%). Mp 148–150°C; ^{1}H NMR: $\delta = 3.81$ (s, 2 OCH_3), 4.26 (s, 2 H-1,3) ppm; ^{13}C NMR: $\delta = 35.7$ (C-1,3), 60.3 (2 OCH_3), 119.5 (C-5,6), 135.9 (C-3a,7a), 150.4 (C-4,7) ppm; MS: m/z (%) = 358 (5), 357 (13), 356 ($M^{+\bullet}$, ^{81}Br, 64), 355 (30), 354 (100), 353 (31), 352 ($M^{+\bullet}$, ^{79}Br, 63), 351 (13), 341 (12), 339 (21), 337 (13), 325 (26), 324 (11), 323 (42), 321 (26), 259 (10), 245 (13), 243 (17), 242 (20), 240 (15), 232 (14), 231 (16), 230 (16), 229 (20), 217 (10), 215 (12), 179 (15), 151 (17), 149 (11), 133 (14), 131 (16), 121 (12), 111 (24), 108 (12).

A mixture of 1.06 g of 5,6-dibromo-4,7-dimethoxy-1,3-dihydrobenzo[*c*]thiophene (3 mmol), 5.54 g of oxone (9 mmol), and 3 g of aluminium oxide (grade I) in 100 cm^3 of $CHCl_3$ was refluxed for 4 h. After this period the solids were filtered off and washed with 50 cm^3 of $CHCl_3$ and 50 cm^3 of acetone. The solvents were evaporated and the residue was crystallised from ethanol giving 1.13 g of 5,6-dibromo-4,7-dimethoxy-1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide **1b** (98%). Mp 198–199°C; ^{1}H NMR: $\delta = 3.84$ (s, 2 OCH_3), 4.37 (s, 2 H-1,3) ppm; ^{13}C NMR: $\delta = 54.8$ (C-1,3), 60.9 (2 OCH_3), 121.9 (C-5,6), 125.7 (C-3a,7a), 151.4 (C-4,7) ppm; MS: m/z (%) = 389 (3), 388 ($M^{+\bullet}$, ^{81}Br, 26), 387 (7), 386 (42), 385 (3), 384 ($M^{+\bullet}$, ^{79}Br, 25), 325 (10), 324 (60), 323 (20), 322 (100), 321 (12), 320 (61), 309 (30), 308 (9), 307 (50), 305 (31), 292 (7), 279 (11), 213 (7), 200 (9), 198 (11), 185 (21), 183 (22), 170 (12), 157 (14), 155 (15), 133 (19), 131 (21), 119 (7), 104 (8), 91 (14).

Diels-Alder reactions of chromone-3-carboxaldehydes **3a–3c** *with ortho-benzoquinodimethanes* **2a** *and* **2b**: *Synthesis of benzo[b]-1,6,6a,12a-tetrahydroxanthones* **4a–4f** *and* **5a–5f**

A mixture of 1.15 mmol of chromone-3-carboxaldehydes **3a–3c** and 1.26 mmol of the appropriate 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide **1a** and **1b** in 5 cm^3 of 1,2,4-trichlorobenzene was refluxed under N_2 for 12 h in the case of **1a** and 24 h in the case of **1b**. After cooling the solvent was removed by column chromatography (silica gel, light petroleum as eluent) and then the cycloadducts were eluted with CH_2Cl_2. The solvent was evaporated and the residue was separated by preparative thin layer chromatography using an appropriate mixture of solvents (with polarities ranging from light petroleum to $CHCl_3$). Each of the cycloadducts **4a–4f** and **5a–5f** was crystallised from ethanol. In some cases (2-hydroxyphenyl)-2-naphthylketones **6a**, **6c–6e** were also obtained as by-products.

trans-2,5-Dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone (**4a**, $C_{19}H_{18}O_4$)

Yield: 199.7 mg (56%); mp 206–209°C; ^{1}H NMR: $\delta = 2.59$ (ddd, $J = 18.1$, 11.5, 1.6 Hz, H-1), 2.86 (ddd, $J = 13.4$, 11.5, 5.8 Hz, H-12a), 2.92 (ddd, $J = 15.9$, 10.3, 1.6 Hz, H-6), 3.54 (dd, $J = 15.9$, 5.9 Hz, H-6), 3.60 (dd, $J = 18.1$, 5.8 Hz, H-1), 3.80 and 3.79 (2s, 2 OCH_3), 4.51 (ddd, $J = 13.4$, 10.3, 5.9 Hz, H-6a), 6.67 (s, H-3,4), 7.02 (d, $J = 8.4$ Hz, H-8), 7.03 (ddd, $J = 8.0$, 7.1, 0.9 Hz, H-10), 7.50 (ddd, $J = 8.4$,

7.1, 1.7 Hz, H-9), 7.94 (dd, $J = 8.0$, 1.7 Hz, H-11) ppm; ^{13}C NMR: $\delta = 22.9$ (C-1), 30.5 (C-6), 45.2 (C-12a), 55.5 and 55.6 (2 OCH_3), 77.4 (C-6a), 107.5 (C-3,4), 117.8 (C-8), 120.7 (C-11a), 121.3 (C-10), 123.1 (C-1a), 124.3 (C-5a), 127.2 (C-11), 135.9 (C-9), 151.0 and 151.3 (C-2,5), 161.2 (C-7a), 193.7 (C-12) ppm; MS: m/z (%) = 311 ($(M+1)^+$, 26), 310 ($M^{+\bullet}$, 100), 309 (10), 291 (11), 279 (25), 277 (18), 261 (37), 190 (11), 189 (22), 175 (10), 160 (11), 159 (12), 151 (18), 121 (48), 120 (9), 115 (15), 92 (12), 77 (6).

cis-2,5-Dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone (**5a**, $C_{19}H_{18}O_4$)

Yield: 121.3 mg (34%); mp 155–157°C; ^{1}H NMR: $\delta = 2.74$ (dd, $J = 16.4$, 10.7 Hz, H-1), 2.86 (ddd, $J = 10.7$, 5.6, 2.2 Hz, H-12a), 2.93 (dd, $J = 18.4$, 4.2 Hz, H-6), 3.03 (dd, $J = 16.4$, 5.6 Hz, H-1), 3.29 (dd, $J = 18.4$, 3.2 Hz, H-6), 3.74 and 3.80 (s, 2 OCH_3), 4.93–4.97 (m, H-6a), 6.64 (AB, $J = 9.1$ Hz, H-3 or H-4), 6.67 (AB, $J = 9.1$ Hz, H-4 or H-3), 6.93 (d, $J = 8.4$ Hz, H-8), 7.01 (ddd, $J = 8.4$, 7.0, 1.6 Hz, H-9), 7.45 (ddd, $J = 7.9$, 7.0, 0.9 Hz, H-10), 7.92 (dd, $J = 7.9$, 1.6 Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.7$ (C-1), 27.6 (C-6), 43.9 (C-12a), 55.5 and 55.6 (2 OCH_3), 74.3 (C-6a), 107.2 and 107.3 (C-3,4), 118.0 (C-8), 119.3 (C-11a), 121.4 (C-10), 122.0 (C-1a), 124.2 (C-5a), 127.5 (C-11), 135.9 (C-9), 151.0 and 151.4 (C-2,5), 160.9 (C-7a), 195.2 (C-12) ppm; MS: m/z (%) = 311 ($(M+1)^+$, 30), 310 ($M^{+\bullet}$, 100), 309 (9), 291 (10), 279 (20), 277 (17), 261 (30), 190 (15), 189 (27), 175 (16), 160 (11), 159 (12), 151 (14), 149 (11), 121 (32), 120 (8), 115 (14), 92 (11), 77 (5).

trans-2,5-Dimethoxy-10-methylbenzo[b]-1,6,6a,12a-tetrahydroxanthone (**4b**, $C_{20}H_{20}O_4$)

Yield: 208.7 mg (56%); mp 199–201°C; ^{1}H NMR: $\delta = 2.32$ (s, CH_3), 2.59 (dd, $J = 18.3$, 11.7 Hz, H-1), 2.84 (ddd, $J = 13.3$, 11.7, 5.8 Hz, H-12a), 2.91 (dd, $J = 17.0$, 10.3 Hz, H-6), 3.53 (dd, $J = 17.0$, 6.0 Hz, H-6), 3.60 (dd, $J = 18.3$, 5.8 Hz, H-1), 3.80 and 3.81 (2s, 2 OCH_3), 4.49 (ddd, $J = 13.3$, 10.3, 6.0 Hz, H-6a), 6.67 (s, H-3, 4), 6.92 (d, $J = 8.4$ Hz, H-8), 7.31 (dd, $J = 8.4$, 2.0 Hz, H-9), 7.73 (d, $J = 2.0$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.4$ (CH_3), 22.9 (C-1), 30.5 (C-6), 45.3 (C-12a), 55.6 and 55.7 (2 OCH_3), 77.4 (C-6a), 107.5 (C-3,4), 117.6 (C-8), 120.4 (C-11a), 123.2 (C-1a), 124.4 (C-5a), 126.7 (C-11), 130.7 (C-10), 136.9 (C-9), 151.0 and 151.3 (C-2,5), 159.3 (C-7a), 193.9 (C-12) ppm; MS: m/z (%) = 325 ($(M+1)^+$, 31), 324 ($M^{+\bullet}$, 100), 323 (11), 305 (14), 293 (12), 291 (20), 275 (39), 190 (15), 189 (22), 175 (10), 174 (13), 159 (9), 151 (11), 135 (44), 115 (13), 106 (6), 77 (9).

cis-2,5-Dimethoxy-10-methylbenzo[b]-1,6,6a,12a-tetrahydroxanthone (**5b**, $C_{20}H_{20}O_4$)

Yield: 134.2 mg (36%); mp 164–165°C; ^{1}H NMR: $\delta = 1.60$ (s, CH_3), 2.72 (dd, $J = 16.1$, 11.0 Hz, H-1), 2.83 (ddd, $J = 11.0$, 5.4, 2.2 Hz, H-12a), 2.91 (dd, $J = 18.7$, 4.7 Hz, H-6), 3.03 (dd, $J = 16.1$, 5.4 Hz, H-1), 3.28 (dd, $J = 18.7$, 3.0 Hz, H-6), 3.74 and 3.80 (2s, 2 OCH_3), 4.89–4.93 (m, H-6a), 6.64 (AB, $J = 9.0$ Hz, H-3 or H-4), 6.67 (AB, $J = 9.0$ Hz, H-4 or H-3), 6.84 (d, $J = 8.4$ Hz, H-8), 7.27 (dd, $J = 8.4$, 2.2 Hz, H-9), 7.71 (d, $J = 2.2$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.4$ (CH_3), 20.7 (C-1), 27.6 (C-6), 43.9 (C-12a), 55.5 and 55.6 (2 OCH_3), 74.2 (C-6a), 107.2 and 107.3 (C-3,4), 117.7 (C-8), 118.9 (C-11a), 122.0 (C-1a), 124.3 (C-5a), 127.0 (C-11), 130.8 (C-10), 136.9 (C-9), 150.9 and 151.4 (C-2,5), 159.0 (C-7a), 195.5 (C-12) ppm; MS: m/z (%) = 325 ($(M+1)^+$, 32), 324 ($M^{+\bullet}$, 100), 323 (9), 305 (14), 293 (18), 291 (20), 275 (34), 190 (25), 189 (38), 175 (15), 174 (14), 164 (15), 159 (13), 151 (11), 149 (12), 135 (47), 115 (19), 77 (16).

trans-2,5-Dimethoxy-10-chlorobenzo[b]-1,6,6a,12a-tetrahydroxanthone (**4c**, $C_{19}H_{17}ClO_4$)

Yield: 221.9 mg (56%); mp 209–211°C; ^{1}H NMR: $\delta = 2.56$ (dd, $J = 18.1$, 11.5 Hz, H-1), 2.85 (ddd, $J = 13.5$, 11.5, 5.8 Hz, H-12a), 2.92 (dd, $J = 16.5$, 10.3 Hz, H-6), 3.54 (dd, $J = 16.5$, 5.9 Hz, H-6), 3.60 (dd, $J = 18.1$, 5.8 Hz, H-1), 3.80 and 3.81 (2s, 2 OCH_3), 4.52 (ddd, $J = 13.5$, 10.3, 5.9 Hz, H-6a), 6.68

(s, H-3,4), 6.98 (d, $J = 8.8$ Hz, H-8), 7.43 (dd, $J = 8.8$, 2.6 Hz, H-9), 7.89 (d, $J = 2.6$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 22.8$ (C-1), 30.4 (C-6), 45.1 (C-12a), 55.6 and 55.7 (2 OCH_3), 77.8 (C-6a), 107.6 (C-3, 4), 119.6 (C-8), 121.5 (C-11a), 122.9 (C-1a), 124.1 (C-5a), 126.5 (C-11), 126.8 (C-10), 135.7 (C-9), 151.0 and 151.3 (C-2,5), 159.7 (C-7a), 192.7 (C-12) ppm; MS: m/z (%) = 347 (12), 346 ($M^{+\bullet}$, ^{37}Cl, 45), 345 (32), 344 ($M^{+\bullet}$, ^{35}Cl, 100), 343 (10), 342 (9), 340 (16), 329 (9), 327 (13), 325 (25), 315 (9), 313 (30), 311 (24), 297 (19), 296 (15), 295 (41), 190 (21), 189 (51), 175 (17), 174 (16), 173 (12), 161 (8), 159 (17), 158 (13), 157 (21), 156 (8), 155 (48), 151 (35), 144 (7), 131 (10), 128 (8), 127 (9), 126 (11), 121, (12), 115 (25), 103 (9), 91 (10), 77 (14).

cis-2,5-Dimethoxy-10-chlorobenzo[b]-1,6,6a,12a-tetrahydroxanthone (**5c**, $C_{19}H_{17}ClO_4$)

Yield: 142.7 mg (36%); mp 194–196°C; ^{1}H NMR: $\delta = 2.71$ (dd, $J = 16.7$, 10.7 Hz, H-1), 2.87 (ddd, $J = 10.7$, 6.2, 2.5 Hz, H-12a), 2.93 (dd, $J = 19.0$, 4.6 Hz, H-6), 3.02 (dd, $J = 16.7$, 6.2 Hz, H-1), 3.28 (dd, $J = 19.0$, 3.2 Hz, H-6), 3.75 and 3.80 (2s, 2 OCH_3), 4.93–4.96 (m, H-6a), 6.64 (AB, $J = 9.2$ Hz, H-3 or H-4), 6.68 (AB, $J = 9.2$ Hz, H-4 or H-3), 6.90 (d, $J = 8.9$ Hz, H-8), 7.39 (dd, $J = 8.9$, 2.6 Hz, H-9), 7.87 (d, $J = 2.6$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.6$ (C-1), 27.5 (C-6), 43.6 (C-12a), 55.5 and 55.6 (2 OCH_3), 74.7 (C-6a), 107.3 (C-3,4), 119.7 (C-8), 120.2 (C-11a), 121.8 (C-1a), 123.9 (C-5a), 126.8 (C-11), 126.9 (C-10), 135.7 (C-9), 151.0 (C-2), 151.3 (C-5), 159.4 (C-7a), 194.0 (C-12) ppm; MS: m/z (%) = 347 (7), 346 ($M^{+\bullet}$, ^{37}Cl, 35), 345 (23), 344 ($M^{+\bullet}$, ^{35}Cl, 100), 325 (5), 313 (13), 311 (10), 297 (8), 295 (22), 190 (15), 189 (47), 175 (13), 174 (11), 164 (10), 159 (11), 158 (9), 157 (9), 155 (25), 151 (14), 149 (13), 121 (7), 115 (15), 103 (6), 91 (9), 83 (12), 77 (9).

trans-3,4-Dibromo-2,5-dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone (**4d**, $C_{19}H_{16}Br_2O_4$)

Yield 269.0 mg (50%); mp 187–189°C; ^{1}H NMR: $\delta = 2.71$ (dd, $J = 18.2$, 12.0 Hz, H-1), 2.91 (dd, $J = 13.2$, 12.0, 5.5 Hz, H-12a), 3.05 (ddd, $J = 17.0$, 10.4, 1.2 Hz, H-6), 3.62 (dd, $J = 17.0$, 5.8 Hz, H-6), 3.66 (dd, $J = 18.2$, 5.5 Hz, H-1), 3.85 and 3.86 (2s, 2 OCH_3), 4.54 (ddd, $J = 13.2$, 10.4, 5.8 Hz, H-6a), 7.04 (d, $J = 8.3$ Hz, H-8), 7.05–7.10 (m, H-10), 7.53 (ddd, $J = 8.3$, 7.0, 1.7 Hz, H-9), 7.95 (dd, $J = 7.8$, 1.7 Hz, H-11) ppm; ^{13}C NMR: $\delta = 23.5$ (C-1), 31.2 (C-6), 45.1 (C-12a), 60.1 and 60.2 (2 OCH_3), 76.7 (C-6a), 117.8 (C-8), 118.9 (C-3,4), 120.6 (C-11a), 121.7 (C-10), 127.3 (C-11), 128.3 (C-5a), 129.4 (C-1a), 136.2 (C-9), 152.4 and 152.6 (C-2,5), 160.9 (C-7a), 192.8 (C-12) ppm; MS: m/z (%) = 471 (8), 470 ($M^{+\bullet}$, ^{81}Br, 36), 469 (19), 468 (60), 467 (14), 466 ($M^{+\bullet}$, ^{79}Br, 36), 453 (7), 451 (8), 449 (7), 439 (16), 438 (7), 437 (33), 436 (6), 435 (27), 426 (9), 425 (8), 424 (33), 423 (10), 422 (29), 421 (12), 420 (8), 419 (19), 393 (16), 391 (18), 375 (11), 373 (9), 309 (7), 253 (9), 225 (7), 207 (8), 188 (14), 173 (9), 160 (24), 159 (15), 145 (11), 122 (13), 121 (100), 120 (17), 115 (16), 114 (9), 105 (12), 102 (14), 93 (12), 92 (31), 77 (16), 76 (10).

cis-3,4-Dibromo-2,5-dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone (**5d**, $C_{19}H_{16}Br_2O_4$)

Yield: 231.4 mg (43%); mp 158–160°C; ^{1}H NMR: $\delta = 2.80$–2.88 (m, H-1, 12a), 3.03 (dd, $J = 18.6$, 4.9 Hz, H-6), 3.02–3.14 (m, H-1), 3.34 (dd, $J = 18.6$, 3.6 Hz, H-6), 3.76 and 3.84 (2s, 2 OCH_3), 4.95 (bs, H-6a), 6.97 (d, $J = 8.0$ Hz, H-8), 7.07 (dd, $J = 7.7$, 7.6 Hz, H-10), 7.51 (dd, $J = 8.0$, 7.6 Hz, H-9), 7.93 (d, $J = 7.7$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 21.3$ (C-1), 28.3 (C-6), 43.7 (C-12a), 60.1 and 60.2 (2 OCH_3), 73.8 (C-6a), 118.0 (C-8), 118.8 (C-3,4), 119.1 (C-11a), 121.8 (C-10), 127.5 (C-1a), 127.6 (C-11), 129.3 (C-5a), 136.3 (C-9), 152.3 and 152.7 (C-2,5), 160.6 (C-7a), 194.2 (C-12) ppm; MS: m/z (%) = 471 (13), 470 ($M^{+\bullet}$, ^{81}Br, 53), 469 (27), 468 (87), 467 (18), 466 ($M^{+\bullet}$, ^{79}Br, 53), 451 (6), 439 (11), 437 (26), 435 (21), 426 (16), 425 (14), 424 (51), 423 (13), 422 (43), 412 (11), 419 (16), 393 (13), 391 (17), 390 (10), 388 (9), 375 (11), 348 (7), 307 (9), 263 (8), 253 (9), 207 (8), 1898 (15), 173 (10), 160 (19), 150 (10), 145 (10), 129 (7), 122 (12), 121 (100), 115 (12), 104 (10), 102 (10), 92 (21), 85 (17), 83 (25).

trans-3,4-Dibromo-2,5-dimethoxy-10-methylbenzo[b]-1,6,6a,12a-tetrahydroxanthone
(**4e**, $C_{20}H_{18}Br_2O_4$)

Yield: 310.3 mg (56%); mp 179–181°C; ^{1}H NMR: $\delta = 2.33$ (s, CH_3), 2.69 (dd, $J = 17.8$, 11.6 Hz, H-1), 2.87 (ddd, $J = 13.1$, 11.6, 5.5 Hz, H-12a), 3.03 (ddd, $J = 16.5$, 10.3, 0.8 Hz, H-6), 3.60 (dd, $J = 16.5$, 5.8 Hz, H-6), 3.66 (dd, $J = 17.8$, 5.5 Hz, H-1), 3.83 and 3.84 (2s, 2 OCH_3), 4.49 (ddd, $J = 13.1$, 10.3, 5.8 Hz, H-6a), 6.93 (d, $J = 8.4$ Hz, H-8), 7.34 (dd, $J = 8.4$, 2.1 Hz, H-9), 7.73 (d, $J = 2.1$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.4$ (CH_3), 23.6 (C-1), 31.2 (C-6), 45.1 (C-12a), 60.1 and 60.2 (2 OCH_3), 76.7 (C-6a), 117.5 (C-8), 119.1 (C-3,4), 120.2 (C-11a), 126.8 (C-11), 128.4 and 129.5 (C-1a,5a), 131.2 (C-10), 137.3 (C-9), 152.4 and 152.6 (C-2,5), 159.0 (C-7a), 193.0 (C-12) ppm; MS: m/z (%) = 485 (11), 484 ($M^{+\bullet}$, ^{81}Br, 48), 483 (26), 482 (88), 481 (20), 480 ($M^{+\bullet}$, ^{79}Br, 52), 467 (11), 466 (9), 465 (15), 464 (16), 463 (13), 453 (22), 452 (12), 451 (49), 450 (9), 449 (39), 435 (16), 434 (12), 433 (28), 432 (7), 431 (14), 348 (7), 254 (8), 237 (8), 188 (9), 174 (18), 173 (16), 145 (8), 135 (100), 134 (20), 115 (10), 105 (13), 78 (12), 77 (13).

cis-3,4-Dibromo-2,5-dimethoxy-10-methylbenzo[b]-1,6,6a,12a-tetrahydroxanthone
(**5e**, $C_{20}H_{18}Br_2O_4$)

Yield: 177.4 mg (32%); mp 160–162°C; ^{1}H NMR: $\delta = 2.33$ (s, CH_3), 2.77–2.88 (m, H-1, 12a), 3.03 (dd, $J = 18.6$, 4.5 Hz, H-6), 3.01–3.13 (m, H-1), 3.33 (dd, $J = 18.6$, 3.2 Hz, H-6), 3.75 and 3.83 (2s, 2 OCH_3), 4.90–4.93 (m, H-6a), 6.87 (d, $J = 8.4$ Hz, H-8), 7.32 (dd, $J = 8.4$, 2.4 Hz, H-9), 7.73 (d, $J = 2.4$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 20.4$ (CH_3), 21.4 (C-1), 28.4 (C-6), 43.7 (C-12a), 60.08 and 60.13 (2 OCH_3), 73.7 (C-6a), 117.8 (C-8), 118.72 and 118.77 (C-11a,3,4), 127.1 (C-11), 127.5 and 129.4 (C-1a,5a), 131.4 (C-10), 137.4 (C-9), 152.3 and 152.7 (C-2,5), 158.7 (C-7a), 194.5 (C-12) ppm; MS: m/z (%) = 485 (14), 484 ($M^{+\bullet}$, ^{81}Br, 61), 483 (32), 482 (100), 481 (21), 480 ($M^{+\bullet}$, ^{79}Br, 60), 465 (8), 463 (8), 453 (12), 451 (28), 449 (24), 435 (11), 433 (19), 341 (10), 404 (21), 402 (22), 348 (16), 346 (11), 333 (7), 307 (8), 253 (10), 252 (9), 251 (10), 188 (15), 174 (16), 173 (17), 145 (9), 136 (12), 135 (96), 134 (19), 115 (11), 107 (9), 106 (12), 105 (15), 82 (12), 80 (12), 78 (19), 77 (20).

trans-3,4-Dibromo-10-chloro-2,5-dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone
(**4f**, $C_{19}H_{15}Br_2ClO_4$)

Yield: 312.0 mg (54%); mp 226–227°C; ^{1}H NMR: $\delta = 2.70$ (ddd, $J = 18.2$, 11.5, 1.1 Hz, H-1), 2.89 (ddd, $J = 13.3$, 11.5, 5.6 Hz, H-12a), 3.04 (ddd, $J = 17.0$, 10.4, 1.1 Hz, H-6), 3.61 (dd, $J = 17.0$, 5.9 Hz, H-6), 3.67 (dd, $J = 18.2$, 5.6 Hz, H-1), 3.83 and 3.84 (2s, 2 OCH_3), 4.53 (ddd, $J = 13.3$, 10.4, 5.9 Hz, H-6a), 7.00 (d, $J = 8.8$ Hz, H-8), 7.47 (dd, $J = 8.8$, 2.6 Hz, H-9), 7.89 (d, $J = 2.6$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 23.4$ (C-1), 31.0 (C-6), 44.9 (C-12a), 60.14 and 60.19 (2 OCH_3), 76.95 (C-6a), 119.0 and 119.3 (C-3,4), 119.5 (C-8), 121.3 (C-11a), 126.5 (C-11), 127.3 (C-10), 128.0 (C-1a), 129.2 (C-5a), 136.1 (C-9), 152.35 and 152.57 (C-2,5), 159.3 (C-7a), 191.7 (C-12) ppm; MS: m/z (%) = 506 ($M^{+\bullet}$, ^{81}Br, ^{37}Cl, 17), 505 (18), 504 (74), 503 (27), 502 (100), 501 (16), 500 ($M^{+\bullet}$, ^{79}Br, ^{35}Cl, 50), 487 (8), 485 (9), 483 (7), 473 (28), 471 (45), 469 (33), 455 (20), 454 (11), 453 (27), 451 (12), 405 (7), 348 (6), 309 (10), 307 (6), 268 (13), 266 (13), 253 (11), 250 (10), 250 (13), 239 (8), 237 (9), 204 (10), 188 (11), 173 (8), 157 (39), 156 (12), 155 (76), 154 (21), 126 (16), 115 (10).

cis-3,4-Dibromo-10-chloro-2,5-dimethoxybenzo[b]-1,6,6a,12a-tetrahydroxanthone
(**5f**, $C_{19}H_{15}Br_2ClO_4$)

Yield: 202.3 mg (35%); mp 188–190°C; ^{1}H NMR: $\delta = 2.80$ (dd, $J = 15.8$, 10.6 Hz, H-1), 2.90 (ddd, $J = 10.6$, 5.2, 2.3 Hz, H-12a), 3.04 (dd, $J = 18.8$, 5.0 Hz, H-6), 3.07 (dd, $J = 15.8$, 5.2 Hz, H-1), 3,33 (dd, $J = 18.8$, 3.4 Hz, H-6), 3.76 and 3.83 (2s, 2 OCH_3), 4.93–4.97 (m, H-6a), 6.93 (d, $J = 8.8$ Hz, H-8), 7.44 (dd, $J = 8.8$, 2.6 Hz, H-9), 7.89 (d, $J = 2.6$ Hz, H-11) ppm; ^{13}C NMR: $\delta = 21.2$ (C-1), 28.2 (C-6),

43.4 (C-12a), 60.1 (2 OCH_3), 74.1 (C-6a), 118.9 (C-3,4), 119.7 (C-8), 120.0 (C-11a), 126.9 (C-11), 127.2 and 127.4 (C-1a,10), 129.0 (C-5a), 136.1 (C-9), 152.3 and 152.7 (C-2,5), 159.0 (C-7a), 193.0 (C-12) ppm; MS: m/z (%) = 506 ($M^{+\bullet}$, ^{81}Br, ^{37}Cl, 16), 505 (16), 504 (76), 503 (25), 502 (100), 501 (13), 500 ($M^{+\bullet}$, ^{79}Br, ^{35}Cl, 48), 475 (15), 473 (26), 471 (19), 457 (13), 455 (18), 348 (7), 309 (9), 307 (10), 268 (16), 266 (17), 254 (10), 253 (12), 252 (12), 251 (13), 237 (8), 188 (12), 173 (7), 157 (24), 156 (8), 155 (61), 154 (9), 126 (14), 115 (10), 102 (9), 77 (6).

(2-Hydroxyphenyl)(5,8-dimethoxynaphth-2-yl)ketone (**6a**, $C_{19}H_{16}O_4$)

Yield: 17.8 mg (5%); ^1H NMR: δ = 3.96 and 4.00 (2s, 2 OCH_3), 6.78 (d, J = 8.4 Hz, H-7), 6.84 (d, J = 8.4 Hz, H-6), 6.90 (ddd, J = 8.0, 7.2, 1.0 Hz, H-5′), 7.10 (dd, J = 8.4, 1.0 Hz, H-3′), 7.53 (ddd, J = 8.4, 7.2, 1.6 Hz, H-4′), 7.68 (dd, J = 8.0, 1.6 Hz, H-6′), 7.79 (dd, J = 8.7, 1.7 Hz, H-3), 8.33 (d, J = 8.7 Hz, H-4), 8.56 (d, J = 1.7 Hz, H-1), 12.12 (s, 2′-OH) ppm; ^{13}C NMR: δ = 55.7 and 55.8 (2 OCH_3), 104.2 (C-7), 105.7 (C-6), 118.3 (C-3′), 118.7 (C-5′), 119.4 (C-1′), 122.4 (C-4), 124.6 (C-1), 125.1 (C-3), 125.3 (C-8a), 127.6 (C-4a), 133.8 (C-6′), 134.8 (C-2), 136.2 (C-4′), 149.2 (C-5), 150.1 (C-8), 163.2 (C-2′), 201.8 (CO) ppm; MS: m/z (%) = 309 ($(M+1)^+$, 35), 308 ($M^{+\bullet}$, 100), 294 (21), 293 (68), 284 (14), 278 (20), 277 (10), 262 (5), 256 (16), 234 (8), 222 (7), 221 (7), 204 (7), 185 (17), 173 (7), 157 (14), 154 (9), 146 (8), 129 (10), 121 (35), 118 (14), 101 (10), 99 (9), 93 (11), 85 (15), 71 (19), 65 (15).

(5-Chloro-2-hydroxyphenyl)(5,8-dimethoxynaphth-2-yl)ketone (**6c**, $C_{19}H_{15}ClO_4$)

Yield: 15.9 mg (4%); ^1H NMR: δ = 3.97 and 4.00 (2s, 2 OCH_3), 6.79 (d, J = 8.4 Hz, H-7), 6.86 (d, J = 8.4 Hz, H-6), 7.06 (d, J = 8.9 Hz, H-3′), 7.47 (dd, J = 8.9, 2.6 Hz, H-4′), 7.63 (d, J = 2.6 Hz, H-6′), 7.76 (dd, J = 8.7, 1.7 Hz, H-3), 8.34 (d, J = 8.7 Hz, H-4), 8.55 (d, J = 1.7 Hz, H-1), 11.98 (s, 2′-OH) ppm; ^{13}C NMR: δ = 55.8 and 55.9 (2 OCH_3), 104.4 (C-7), 106.1 (C-6), 120.0 (C-3′), 120.1 (C-1′), 122.6 (C-4), 123.4 (C-5′), 124.7 (C-1), 125.0 (C-3), 125.2 (C-8a), 127.7 (C-4a), 132.7 (C-6′), 134.2 (C-2), 136.0 (C-4′), 149.2 (C-5), 150.2 (C-8), 161.6 (C-2′), 200.8 (CO) ppm; MS: m/z (%) = 345 (13), 344 ($M^{+\bullet}$, ^{37}Cl, 44), 343 (27), 342 ($M^{+\bullet}$, ^{35}Cl, 100), 330 (8), 329 (25), 328 (17), 327 (56), 314 (11), 313 (11), 312 (25), 204 (10), 189 (7), 188 (10), 185 (13), 173 (9), 157 (20), 156 (8), 155 (24), 129 (13), 127 (9), 114 (7), 101 (14), 99 (9).

(2-Hydroxyphenyl)(6,7-dibromo-5,8-dimethoxynaphth-2-yl)ketone (**6d**, $C_{19}H_{14}Br_2O_4$)

Yield 21.6 mg (4%); ^1H NMR: δ = 3.99 and 4.02 (2s, 2 OCH_3), 6.91 (dd, J = 7.9, 7.4 Hz, H-5′), 7.13 (d, J = 8.2 Hz, H-3′), 7.56 (ddd, J = 8.2, 7.9, 1.4 Hz, H-4′), 7.61 (dd, J = 7.4, 1.4 Hz, H-6′), 7.86 (dd, J = 8.6, 1.5 Hz, H-3), 8.23 (d, J = 8.6 Hz, H-4), 8.40 (bs, H-1), 12,00 (s, 2′-OH) ppm; ^{13}C NMR: δ = 61.7 and 61.9 (2 OCH_3), 117.7 (C-7), 118.6 (C-3′), 118.9 (C-5′), 119.0 (C-1′), 119.1 (C-6), 123.4 (C-4), 124.9 (C-1), 126.8 (C-3), 127.1 (C-8a), 129.3 (C-4a), 133.4 (C-6′), 136.4 (C-2), 136.7 (C-4′), 151.1 (C-5), 151.9 (C-8), 163.3 (C-2′), 200.9 (CO) ppm; MS: m/z (%) = 469 (18), 468 ($M^{+\bullet}$, ^{81}Br, 55), 467 (29), 466 (93), 465 (19), 464 ($M^{+\bullet}$, ^{79}Br, 54), 454 (8), 453 (31), 452 (15), 451 (52), 450 (9), 449 (31), 436 (11), 424 (10), 422 (27), 420 (22), 409 (5), 407 (17), 405 (13), 388 (8), 357 (29), 355 (30), 343 (15), 329 (18), 327 (18), 311 (8), 291 (10), 289 (12), 236 (10), 234 (11), 220 (11), 218 (11), 163 (12), 122 (15), 121 (100), 93 (27), 65 (32).

(2-Hydroxy-5-methylphenyl)(6,7-dibromo-5,8-dimethoxynaphth-2-yl)ketone (**6e**, $C_{20}H_{16}Br_2O_4$)

Yield: 19.4 mg (3.5%); ^1H NMR: δ = 2.25 (s, CH_3) 3.99 and 4.03 (2 s, 2 OCH_3), 7.04 (d, J = 9.0 Hz, H-3′), 7.37–7.39 (m, H-4′,6′), 7.86 (dd, J = 8.7, 1.6 Hz, H-3), 8.24 (d, J = 8.7 Hz, H-4), 8.39 (d, J = 1.6 Hz, H-1), 11.82 (s, 2′-OH) ppm; ^{13}C NMR: δ = 20.4 (CH_3), 61.6 and 61.8 (2 OCH_3), 117.6

(C-7), 118.3 (C-1′), 118.7 (C-3′), 119.0 (C-6), 123.4 (C-4), 124.8 (C-1), 126.8 (C-3), 127.1 (C-8a), 128.0 (C-5′), 129.2 (C-4a), 133.0 (C-6′), 136.5 (C-2), 137.7 (C-4′), 151.0 (C-5), 151.8 (C-8), 161.2 (C-2′), 200.8 (CO) ppm; MS: m/z (%) = 482 ($M^{+\bullet}$, ^{81}Br, 14), 481 (6), 480 (29), 479 (4), 478 ($M^{+\bullet}$, ^{79}Br, 13), 467 (5), 465 (11), 463 (5), 284 (7), 256 (13), 212 (14), 211 (17), 197 (33), 191 (9), 183 (12), 169 (34), 155 (44), 154 (17), 153 (24), 149 (22), 141 (35), 135 (20), 127 (66), 126 (31), 125 (42), 118 (19), 113 (87), 112 (45), 111 (80), 99 (100), 98 (20), 97 (58).

Synthesis of 2,5-dimethoxybenzo[b]xanthones **7a–7f**

A mixture of 0.4 mmol of **4** and **5** and 10.2 mg of I_2 (0.04 mmol) in 5 cm^3 of DMSO was refluxed for 2 h. After cooling the reaction mixture was poured into ice and H_2O. A small amount of $Na_2S_2O_3$ was added and the reaction mixture was stirred for some minutes. The obtained yellow solid was filtered off, washed with H_2O, dissolved in $CHCl_3$, and washed with H_2O. The solvent was evaporated and the residue crystallised from ethanol yielding **7a–7f**.

2,5-Dimethoxybenzo[b]xanthone (**7a**, $C_{19}H_{14}O_4$)

Yield: 115.1 mg (94%); mp 235–236°C; ^{1}H NMR: δ = 3.99 and 4.00 (2s, 2 OCH_3), 6.62 (d, J = 8.3 Hz, H-3), 6.79 (d, J = 8.3 Hz, H-4), 7.36 (ddd, J = 7.9, 7.0, 0.9 Hz, H-10), 7.50 (dd, J = 8.4, 0.9 Hz, H-8), 7.74 (dd, J = 8.4, 7.0, 1.6 Hz, H-9), 8.21 (s, H-6), 8.38 (dd, J = 7.9, 1.6 Hz, H-11), 9.28 (s, H-1) ppm; ^{13}C NMR: δ = 55.6 and 55.8 (2 OCH_3), 101.7 (C-3), 106.0 (C-4), 108.6 (C-6), 117.9 (C-8), 120.8 (C-12a), 121.3 (C-11a), 123.0 (C-1a), 123.1 (C-1), 123.3 (C-10), 127.0 (C-11), 130.2 (C-5a), 135.1 (C-9), 148.4 (C-5), 150.8 (C-2), 152.7 (C-6a), 156.7 (C-7a), 177.9 (C-12) ppm; MS: m/z (%) = 307 ($(M+1)^+$, 30), 306 ($M^{+\bullet}$, 99), 292 (31), 291 (100), 276 (10), 263 (13), 248 (24), 222 (9), 220 (17), 194 (16), 192 (8), 163 (9), 153 (11), 138 (9).

2,5-Dimethoxy-10-methylbenzo[b]xanthone (**7b**, $C_{20}H_{16}O_4$)

Yield: 119.1 mg (93%); mp 217–219°C; ^{1}H NMR: δ = 2.46 (s, CH_3), 3.97 and 3.99 (2s, 2 OCH_3), 6.60 (d, J = 8.3 Hz, H-3), 6.76 (d, J = 8.3 Hz, H-4), 7.38 (d, J = 8.6 Hz, H-8), 7.52 (dd, J = 8.6, 2.1 Hz, H-9), 8.14 (d, J = 2.1 Hz, H-11), 8.17 (s, H-6), 9.25 (s, H-1) ppm; ^{13}C NMR: δ = 20.8 (CH_3), 55.6 and 55.8 (2 OCH_3), 101.6 (C-3), 105.9 (C-4), 108.6 (C-6), 117.6 (C-8), 120.8 and 120.9 (C-11a,12a), 123.0 and 123.1 (C-1a,1), 126.3 (C-11), 130.2 (C-5a), 133.1 (C-10), 136.3 (C-9), 148.4 (C-5), 150.8 (C-2), 152.8 (C-6a), 154.9 (C-7a), 178.0 (C-12) ppm; MS: m/z (%) = 321($(M+1)^+$, 31), 320 ($M^{+\bullet}$, 100), 306 (29), 305 (95), 290 (21), 289 (11), 277 (8), 262 (15), 261 (9), 234 (7), 208 (10), 160 (8).

10-Chloro-2,5-dimethoxybenzo[b]xanthone (**7c**, $C_{19}H_{13}ClO_4$)

Yield: 121.3 mg (89%); mp >274°C; ^{1}H NMR ($CDCl_3$ + *TFA*): δ = 4.03 and 4.04 (2s, 2 OCH_3), 6.73 (d, J = 8.3 Hz, H-3), 6.94 (d, J = 8.3 Hz, H-4), 7.55 (d, J = 9.0 Hz, H-8), 7.78 (dd, J = 9.0, 2.5 Hz, H-9), 8.29 (s, H-6), 8.32 (d, J = 2.5 Hz, H-11), 9.23 (s, H-1) ppm; ^{13}C NMR ($CDCl_3$ + *TFA*): δ = 55.9 and 56.1 (2 OCH_3), 102.7 (C-3), 107.6 (C-4), 109.2 (C-6), 119.2 (C-12a), 119.9 (C-8), 121.1 (C-11a), 123.4 (C-1a), 123.7 (C-1), 126.2 (C-11), 129.7 (C-10), 130.9 (C-5a), 136.5 (C-9), 148.3 (C-5), 150.8 (C-2), 152.4 (C-6a), 155.5 (C-7a), 178.7 (C-12) ppm; MS: m/z (%) = 343 (13), 342 ($M^{+\bullet}$, ^{37}Cl, 47), 341 (31), 340 ($M^{+\bullet}$, ^{35}Cl, 100), 328 (12), 327 (44), 326 (29), 325 (93), 312 (6), 310 (16), 297 (11), 284 (9), 282 (23), 256 (13), 254 (15), 228 (19), 170 (12), 162 (14), 137 (6).

3,4-Dibromo-2,5-dimethoxybenzo[b]xanthone (**7d**, $C_{19}H_{12}Br_2O_4$)

Yield: 170.8 mg (92%); mp 247–248°C; ^{1}H NMR: δ = 4.05 (s, 5-OCH_3), 4.09 (s, 2-OCH_3), 7.41 (ddd, J = 8.0, 7.3, 0.8 Hz, H-10), 7.53 (dd, J = 8.4, 0.8 Hz, H-8), 7.79 (ddd, J = 8.4, 7.3, 1.6 Hz, H-9), 8.15

(s, H-6), 8.38 (dd, $J = 8.0$, 1.6 Hz, H-11), 9.16 (s, H-1) ppm; ^{13}C NMR: $\delta = 61.4$ (5-OCH_3), 62.1 (2-OCH_3), 109.7 (C-6), 115.4 (C-3), 117.9 (C-8), 120.1 (C-11a), 121.1 (C-12a), 122.2 (C-4), 123.9 (C-10), 124.2 (C-1), 124.6 (C-1a), 127.1 (C-11), 131.4 (C-5a), 135.7 (C-9), 150.2 (C-5), 152.5 (C-2), 153.5 (C-6a), 156.6 (C-7a), 177.4 (C-12) ppm; MS: m/z (%) = 467 (10), 466 (49), 465 (20), 464 (100), 463 (10), 462 ($M^{+\bullet}$, ^{79}Br, 50), 452 (7), 451 (35), 450 (14), 449 (72), 448 (8), 447 (35), 355 (28), 353 (29), 326 (13), 324 (13), 299 (5), 297 (5), 231 (5), 190 (10), 162 (11).

3,4-Dibromo-2,5-dimethoxy-10-methylbenzo[b]xanthone (**7e**, $C_{20}H_{14}Br_2O_4$)

Yield: 179.8 mg (94%); mp 257–258°C; ^{1}H NMR: $\delta = 2.48$ (s, CH_3), 4.04 (s, 5-OCH_3), 4.08 (s, 2-OCH_3), 7.40 (d, $J = 8.6$ Hz, H-8), 7.57 (dd, $J = 8.6$, 2.5 Hz, H-9), 8.10 (s, H-6), 8.11 (d, $J = 2.5$ Hz, H-11), 9.12 (s, H-1) ppm; ^{13}C NMR: $\delta = 20.8$ (CH_3), 61.3 (5-OCH_3), 62.1 (2-OCH_3), 109.6 (C-6), 115.2 (C-3), 117.6 (C-8), 119.9 (C-4), 120.7 (C-11a), 122.2 (C-12a), 124.1 (C-1), 124.5 (C-1a), 126.3 (C-11), 131.4 (C-5a), 133.7 (C-10), 136.9 (C-9), 150.2 (C-5), 152.5 (C-2), 153.5 (C-6a), 154.7 (C-7a), 177.4 (C-12) ppm; MS: m/z (%) = 481 (10), 480 (52), 479 (22), 478 (100), 477 (11), 476 ($M^{+\bullet}$, ^{79}Br, 52), 466 (7), 465 (35), 464 (14), 463 (69), 462 (8), 461 (36), 369 (27), 367 (27), 341 (14), 339 (14), 303 (7), 245 (7), 204 (14), 176 (9), 85 (36), 83 (55).

3,4-Dibromo-10-chloro-2,5-dimethoxybenzo[b]xanthone (**7f**, $C_{19}H_{11}Br_2ClO_4$)

Yield: 181.5 mg (91%); mp 269–270°C; ^{1}H NMR: $\delta = 4.05$ (s, 5-OCH_3), 4.08 (s, 2-OCH_3), 7.48 (d, $J = 8.9$ Hz, H-8), 7.71 (dd, $J = 8.9$, 2.6 Hz, H-9), 8.14 (s, H-6), 8.31 (d, $J = 2.6$ Hz, H-11), 9.13 (s, H-1) ppm; ^{13}C NMR: $\delta = 61.4$ (5-OCH_3), 62.1 (2-OCH_3), 109.8 (C-6), 115.8 (C-3), 119.7 (C-8), 120.5 (C-4), 121.7 (C-12a), 121.9 (C-11a), 124.4 (C-1), 124.7 (C-1a), 126.3 (C-11), 129.7 (C-10), 131.5 (C-5a), 135.7 (C-9), 150.2 (C-5), 152.5 (C-6a), 153.2 (C-2), 154.9 (C-7a), 176.3 (C-12) ppm; MS: m/z (%) = 502 (15), 501 (15), 500 (72), 499 (20), 498 (100), 497 (10), 496 ($M^{+\bullet}$, ^{79}Br, 43), 487 (10), 486 (10), 485 (49), 484 (14), 483 (70), 482 (7), 481 (30), 391 (8), 390 (7), 389 (34), 387 (25), 361 (15), 359 (11), 333 (7), 241 (6), 224 (8), 193 (8), 180 (8), 98 (6).

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