Darzens Reaction of 2-Bromo-4,6-dimethoxy-3(2*H*)-benzofuranone with Aromatic Aldehydes to Form Flavonoids

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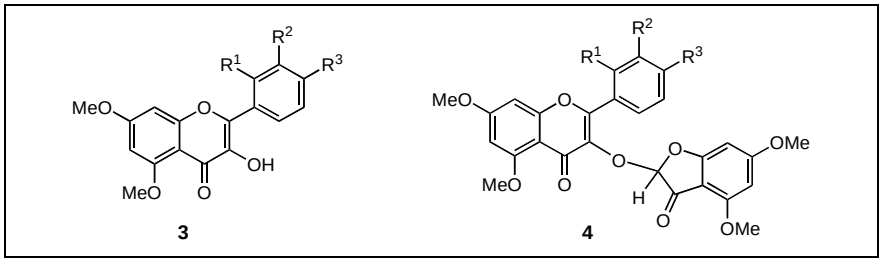

The applicability of 2-bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (**1**) to produce flavonoid-derived epoxides in the course of the Darzens reaction with aldehydes was investigated. However, instead of the epoxides, flavonols **3** and, in certain cases, benzofuranyl-substituted flavonols **4** were isolated. The generation of **3** is assumed due to a ring expansion of the initially formed epoxides. These flavonols can react with **1** to produce the unexpected 1:2 adducts **4** as minor products. The structure of the hexamethoxy derivative **4b** (R^1 = H, R^2 = R^3 = OMe) was confirmed by X-ray crystallographic analysis.

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INTRODUCTION

Flavonoids are polyphenolic plant constituents that are widely distributed in the plant kingdom and possess a variety of biological activities [1]. The antimicrobial [2], antiprotozoal [3], antiviral [4], antiinflammatory [5], and antitumor activity [6] of several flavonoids has been described. Flavonoids are known to act as vascular antioxidants [7] and modulators of P-glycoprotein-mediated multidrug resistance [8].

Alphitonin (**IV**) and taxifolin (**II**) share the substitution pattern (R = R' = OH, R" = 3,4-$(OH)_2$) with quercetin (**I**), a flavonol whose glycosides are highly abundant dietary flavonoids. The auronol alphitonin has been identified as a metabolite of the quercetin degradation by the anaerobic human intestinal bacterium *Eubacterium ramulus* [9]. To prepare auronols of type **IV**, the epoxide **III** (R = R' = R" = H) was successfully transformed with H_2 in the presence of Pd/C in toluene at –25 to –20° to obtain **IV** (R = R' = R" = H), the prototype of naturally occurring auronols [10]. In a further attempt, we planned to prepare the tetramethoxy substituted epoxide **III** (R = R' = OMe, R" = 3,4-$(OMe)_2$). It was intended to reduce this compound to the protected auronol **IV** (R = R' = OMe, R" = 3,4-$(OMe)_2$), which should then be deprotected to alphitonin **IV** (R = R' = OH, R" = 3,4-$(OH)_2$).

In contrast to the oxidation of 2-benzylidenebenzofuran-3(2*H*)-one, which easily afforded the unsubstituted **III** upon treatment with H_2O_2 and Triton B (benzyl trimethylammonium hydroxide) [10,11], the preparation of the tetramethoxy substituted epoxide **III** (R = R' = OMe, R" = 3,4-$(OMe)_2$) turned out to be difficult.

The corresponding 4,6-dimethoxy-2-(3,4-dimethoxybenzylidene)benzofuran-3(2*H*)-one [12] failed to react with H_2O_2 and Triton B in dioxane at room temperature. Treatment with *meta*-chloroperbenzoic acid in boiling toluene resulted in a product mixture that still contained starting material. Even the reaction of 4,6-dimethoxy-2-(3,4-dimethoxybenzylidene)benzofuran-3(2*H*)-one with dimethyldioxirane [13] in methylene chloride/acetone under argon atmosphere at room temperature led to an incomplete conversion, and the desired **III** (R = R' = OMe, R" = 3,4-$(OMe)_2$) was not obtained.

Herein we report a further approach to synthesize flavonoid-derived epoxides **III** by means of the Darzens condensation.

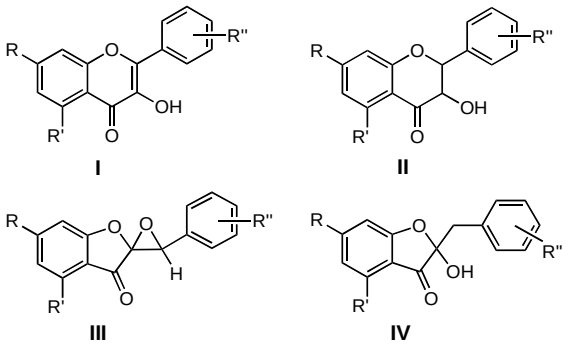


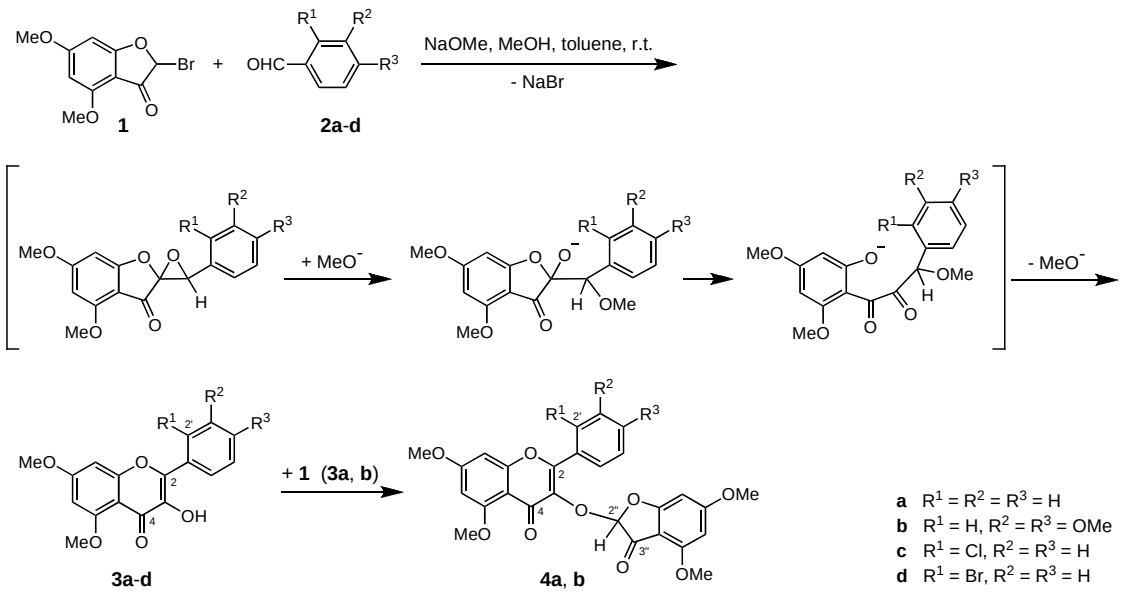
Figure 1

RESULTS AND DISCUSSION

The Darzens reaction of aldehydes or ketones with α-halo carbonyl compounds furnishes α,β-epoxy carbonyl compounds in the course of an intramolecular S_N2 mechanism [14]. This powerful C-C bond forming process was also applied to the preparation of two flavonoid-derived epoxides. Brady *et al.* [11] have reacted 2-bromo-6-methoxy-3(2*H*)-benzofuranone with 2-nitrobenzaldehyde to obtain an epoxide **III** (R = OMe, R' = H, R'' = 2-NO_2) in 89% yield of the crude product. By using benzaldehyde, the corresponding epoxide **III** (R = OMe, R' = R'' = H) was isolated in traces.

In order to find a synthetic access to tetramethoxy substituted epoxides **III** (R = R' = OMe, R'' = 3,4-$(OMe)_2$) as potential precursors to alphitonin, we have performed the Darzens reaction of 2-bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (**1**) with 3,4-dimethoxybenzaldehyde (**2b**) (Scheme 1).

Scheme 1



Compound **1** [15] was prepared by bromination of 4,6-dimethoxy-3(2*H*)-benzofuranone [12,16] with phenyltrimethyl ammoniumbromide dibromide [17] in tetrahydrofuran.

When performing the reaction of equimolar amounts of **1** and **2b** in toluene/methanol in the presence of one equivalent sodium methoxide at room temperature, a precipitate was formed after addition of the sodium methoxide solution. The insoluble material was isolated and contained an organic compound besides sodium bromide. Unexpectedly, this organic product was composed of two units derived from **1** and one unit derived from **2b**, as it could be concluded from NMR and mass spectroscopic data. The structure for the 2:1 adduct was unambiguously assigned as **4b** on the basis of X-ray crystallographic analysis.

Similarly, the analogous adduct **4a** was obtained in the reaction of **1** with benzaldehyde **2a**. Compounds **4**, however, were not the main products of these Darzens reactions. After the separation of the 2:1 adducts **4**, other products were achieved from the reaction solutions and their structures were elucidated as flavonols **3a** and **3b**, respectively. The corresponding flavonols **3c** and **3d** were isolated as the only organic products when **1** was reacted with the 2-halobenzaldehydes **2c** and **2d**, respectively.

It is known, that the epoxide oxygen of α,β-epoxy ketones can be displaced by nucleophilic attack either the α-position or, more frequently, at the β-position [11]. Thus, the generation of flavonols **3** could be envisaged by a possible mechanism shown in Scheme 1.

It involves the initial epoxide ring closure, attack of methoxide at the β-carbon prior to the opening of the furanone ring and subsequent recyclization to the 6-membered pyranone ring. Flavonol formation from aurone epoxides in the presence of hydroxide ions has already been observed by Brady *et al.* [11]. The authors have considered an alternative mechanism of an α-attack with the opening of the furanone ring prior the epoxide cleavage.

Once generated, flavonols **3** could be converted in the course of a nucleophilic substitution with a second bromobenzofuranone **1** to produce the 1:2 adducts **4**. Their isolation, however, was impaired since partial decomposition was observed after the treatment with water to remove sodium bromide, and they were therefore purified by recrystallization.

MS fragmentation data showed a cleavage at the C(3)-O bond of **4a** and **4b** to form the characteristic fragment (M^+ - $C_{10}H_8O_4$). Key signals in the nmr spectra of **4** were the resonances of the 2´´-protons at 6.23, 6.28 ppm, respectively. The corresponding ^{13}C nmr signals for C-2´´ were found at 98.65, 98.45 ppm, respectively. The ^{13}C chemical shifts of the carbonyl groups were also in agreement with the structures **4**. Whereas the signals of C-3´´ appeared at 188.20, 188.41 ppm, respectively, those of the α,ß-unsaturated, α-hydroxy ketone carbon C-4 were shifted upfield to 171.45, 171.28 ppm, respectively. As expected, the C-4 signals of the flavonols **3a**-**d** were in the same range of 171-172 ppm. ^{13}C nmr data of **3a** were in agreement with those reported from Pelter *et al.* [18].

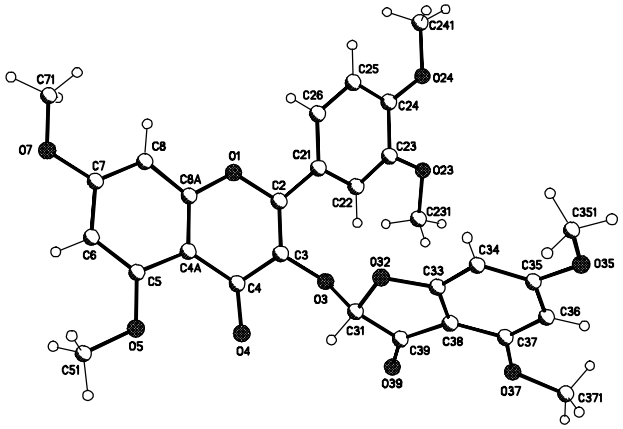


Figure 2. Molecular structure of **4b** as determined by X-ray crystallographic analysis and the numbering.

Table 1
Crystal data and structure refinement for **4b**

Empirical formula	$C_{29}H_{26}O_{11}$
Formula weight	550.50
Temperature	123(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/n$ (No.14)
Unit cell dimensions	a = 9.9913(2) Å α = 90°
	b = 13.4375(3) Å β = 98.797(1)°
	c = 19.4220(5) Å γ = 90°
Volume	2576.89(10) $Å^3$
Z, Calculated density	4, 1.419 Mg/m^3
Absorption coefficient	0.110 mm^{-1}
F(000)	1152
Crystal size	0.20 × 0.08 × 0.04 mm
Diffractometer	Nonius KappaCCD
θ range for data collection	3.03° - 25.03°
Limiting indices	-10 ≤ h ≤ 11, -15 ≤ k ≤15, -23 ≤ l ≤ 19
Reflections collected / unique	16437 / 4522 [R(int) = 0.0383]
Reflections with I > 2σ(*I*)	2880
Completeness to θ = 25.03	99.6%
Absorption correction	none
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4522 / 0 / 367
Goodness-of-fit on F^2	0.952
Final R indices [I > 2σ(*I*)]	R_1 = 0.0480, wR_2 = 0.1223
R indices (all data)	R_1 = 0.0827, wR_2 = 0.1343
Largest diff. peak and hole	0.455 and -0.238 e $Å^{-3}$

Table 2
Weak hydrogen bonds for **4b** [Å] and [°]

D-H...A	D-H	H...A	D...A	<(DHA)
C(351)-H(35C)...O(4)#1	0.98	2.36	3.055(4)	127.2
C(231)-H(23B)...O(4)#2	0.98	2.58	3.550(3)	169.7
C(371)-H(37B)...O(7)#2	0.98	2.51	3.437(3)	157.9
C(371)-H(37C)...O(23)#3	0.98	2.64	3.561(3)	157.0
C(371)-H(37C)...O(24)#3	0.98	2.53	3.335(3)	138.8
C(351)-H(35B)...O(35)#4	0.98	2. 59	3.454(4)	146.4
C(51)-H(51C)...O(39)#5	0.98	2.44	3.227(4)	137.1
C(351)-H(35A)...O(39)#6	0.98	2.60	3.190(4)	118.9

Symmetry transformations used to generate equivalent atoms:
#1: *x*-1, *y*, *z*; #2: *x*-1/2, -*y*+1/2, *z*-1/2; #3: -*x*+1/2, *y*-1/2, -*z*+1/2;
#4: -*x*, -*y*, -*z*+1; #5: *x*+1/2, -*y*+1/2, *z*+1/2; #6: -*x*+1, -*y*, -*z*+1

The structure of **4b** was confirmed by X-ray analysis (Figure 2). All three units of the molecule are planar. The mean deviations are 0.009 Å (benzopyranone), 0.004 Å (phenyl), and 0.032 Å (benzofuranone). The latter ring adopts a slight envelope conformation with C31 being 0.065 Å above the plane. In all substructures, oxygen and carbon atoms of the methoxy groups are in plane. Dihedral angles between the planes are as follows, benzopyran and benzofuran 69°, benzopyran and phenyl 26°, benzofuran and phenyl 60°. Hydrogen bond parameters are listed in Table 2. Only weak hydrogen bonds were observed, all of them are intermolecular. Two carbonyl oxygen atoms (O4, O39) are acceptors of bifurcated hydrogen bonds, connecting three independent molecules. C371 acts as a bifurcated donor to the oxygens of the dimethoxyphenyl group (O23, O24) of one molecule.

EXPERIMENTAL

Melting points were obtained on a Rapido Boetius apparatus and are uncorrected. ^1H nmr spectra were recorded on a Bruker Avance spectrometer at 500 MHz. ^{13}C nmr spectra were recorded on a Bruker Avance spectrometer at 125 MHz. Mass spectra (EI, 70 eV) were measured on a MS-50 A.E.I. spectrometer. Thin-layer chromatography was carried out using aluminum sheets coated with silica gel 60 F_{254} (Merck). 4,6-Dimethoxy-3(2*H*)-benzofuranone was prepared as reported [8b, 12].

2-Bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (**1**). A mixture of 4.85 g (0.025 mole) of 4,6-dimethoxy-3(2*H*)-benzofuranone and 175 mL of dry tetrahydrofuran was heated 40°. A solution of 9.40 g (0.025 mol) phenyltrimethyl ammonium-bromide dibromide in 65 mL of dry tetrahydrofuran was added dropwise over 30 minutes and the mixture was stirred for additional 75 minutes at 40° and kept at room temperature for 20 minutes. The insoluble material was removed by suction filtration und the filtrate was evaporated. The residue was recrystallized from toluene and the precipitate was dissolved in acetone. After addition of 150 mg of charcoal, the mixture was stirred at room temperature for 30 minutes and filtrated. The filtrate was evaporated to dryness to obtain a light brown solid. 4.52 g (66%). mp 139-142°, ref [15] 143-145°; ^1H nmr (DMSO-

d_6): δ 3.82, 3.84 (each s, 3H, CH_3), 5.43 (s, 1H, 2-H), 6.14, 6.25 ppm (each d, 1H, 5-H, 7-H, J = 1.7 Hz); ^{13}C nmr (DMSO-d_6) δ 56.06, 56.41 (CH_3), 89.48 (C-2), 92.76, 98.48 (C-5, C-7), 102.51 (C-3a), 159.04, 170.13, 173.34 (C-4, C-6, C-7a), 192.48 ppm (C-3).

Reaction of 2-Bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (1) with benzaldehyde (2a). Compound **1** (983 mg, 3.60 mmol) was dissolved upon heating in dry toluene (35 mL) and subsequently cooled to room temperature. Benzaldehyde (382 mg, 3.60 mmol) was added, followed by an equimolar amount of sodium methoxide in methanolic solution, prepared from dry methanol (3.0 mL) and sodium (83 mg). The reaction mixture was stirred for 45 minutes at room temperature and a precipitate was isolated by suction filtration and dried (110 mg). The precipitate was suspended in water (20 mL), filtered off and dried (71 mg). The material was recrystallized from toluene/DMF (3:1) to obtain pure **4a** (35 mg, 2%) as pale yellow crystals. The filtrate that was obtained by the suction filtration after 45 minutes was stirred for further 135 minutes. It was filtrated and the filtrate was cooled (8°) for 7 days. The precipitate formed was isolated by suction filtration to furnish pure **3a** (412 mg, 38%) as brown crystals.

3-Hydroxy-5,7-dimethoxy-2-phenyl-4*H*-1-benzopyran-4-one (3a). mp 170-173°, ref [19] 172-174°; ^{1}H nmr (DMSO-d_6): δ 3.86, 3.89 (each s, 3H, CH_3), 6.47, 6.82 (each d, 1H, 6-H, 8-H, J = 2.3 Hz), 7.45 (tt, 1H, 4´-H, J = 1.3, 7.6 Hz), 7.51-7.56 (m, 2H, 3´-H, 5´-H), 8.16-8.19 (m, 2H, 2´-H, 6´-H), 9.02 ppm (s, 1H, OH); ^{13}C nmr (DMSO-d_6) δ 56.12, 56.35 (CH_3), 92.96, 95.87 (C-6, C-8), 106.49 (C-4a), 127.10 (C-2´, C-6´), 128.63 (C-3´, C-5´), 129.49 (C-4´), 131.35 (C-1´), 138.94 (C-3), 141.44 (C-2), 158.37 (C-8a), 160.35, 164.04 (C-5, C-7), 171.38 ppm (C-4).

3-(4,6-Dimethoxy-3-oxo-2,3-dihydrobenzofuran-2-yloxy)-5,7-dimethoxy-2-phenyl-4*H*-1-benzopyran-4-one (4a). mp 213-217°; ^{1}H nmr (DMSO-d_6): δ 3.79, 3.84, 3.87, 3.90 (each s, 3H, CH_3), 6.09, 6.18 (each d, 1H, 5´´-H, 7´´-H, J = 1.9 Hz), 6.23 (s, 1H, 2´´-H), 6.55, 6.84 (each d, 1H, 6-H, 8-H, J = 2.2 Hz), 7.36-7.41 (m, 3H, phenyl protons), 7.85-7.87 ppm (m, 2H, phenyl protons); ^{13}C nmr (DMSO-d_6) δ 56.24, 56.40, 56.53 (CH_3), 89.77, 93.30 (C-5´´, C-7´´), 93.60, 96.49 (C-6, C-8), 98.65 (C-2´´), 102.12 (C-3a´´), 108.73 (C-4a), 128.34 (C-2´, C-6´), 128.42 (C-3´,C-5´), 130.05 (C-4´), 130.69 (C-1´), 136.18 (C-3), 153.63 (C-2), 158.53 (C-8a), 159.24, 170.27, 173.60 (C-4´´, C-6´´, C-7a´´), 160.63, 164.32 (C-5, C-7), 171.45 (C-4), 188.20 ppm (C-3´´); ms: m/z 490 (95%, M^+), 298 (79%, M^+-$C_{10}H_8O_4$), 282 (100%, M^+-$C_{10}H_8O_5$), 269 (48%, M^+-$C_{11}H_9O_5$).

Reaction of 2-Bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (1) with 3,4-dimethoxybenzaldehyde (2b). Compound **1** (983 mg, 3.60 mmol) was dissolved upon heating in dry toluene (35 mL) and subsequently cooled to room temperature. 3,4-Dimethoxybenzaldehyde (598 mg, 3.60 mmol) was added, followed by an equimolar amount of sodium methoxide in methanolic solution, prepared from dry methanol (3.0 mL) and sodium (83 mg). A bright precipitate was formed in the orange reaction mixture. The suspension was stirred for 45 minutes at room temperature and the precipitate was collected by filtration, dried and washed with water (20 mL) and dried. The material (94 mg) was recrystallized from toluene/DMF (3:1) to obtain a pure product **4b** (44 mg, 2%) as a yellow solid. The filtrate that was obtained from the suction filtration after 45 minutes was stirred for further 19 hours and evaporated to dryness. The residue was recrystallized from toluene to furnish **3b** (99 mg, 8%) as a brown solid.

2-(3,4-Dimethoxyphenyl)-3-hydroxy-5,7-dimethoxy-4*H*-1-benzopyran-4-one (3b). mp 189-193°, ref [20] 184-186°; ^{1}H nmr (DMSO-d_6): δ 3.83, 3.84, 3.85, 3.90 (each s, 3H, CH_3), 6.47 (d, 1H, 6-H or 8-H, J = 0.9 Hz), 6.83 (bs, 1H, 6-H or 8-H), 7.12 (d, 1H, 5´-H, J = 8.5 Hz), 7.75 (bs, 1H, 2´-H), 7.79 (dd, 1H, 6´-H, J = 1.3, 8.5 Hz), 8.84 ppm (s, 1H, OH); ^{13}C nmr (DMSO-d_6) δ 55.74, 55.86, 56.13, 56.32 (CH_3), 93.05, 95.83 (C-6, C-8), 106.40 (C-4a), 110.73, 111.75 (C-5´,C-2´), 120.86 (C-6´), 123.75 (C-1´), 138.02 (C-3), 141.81 (C-2), 148.63, 150.10 (C-3´, C-4´), 158.20 (C-8a), 160.26, 163.87 (C-5, C-7), 171.14 ppm (C-4).

3-(4,6-Dimethoxy-3-oxo-2,3-dihydrobenzofuran-2-yloxy)-2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-1-benzopyran-4-one (4b). mp 214-219°; ^{1}H nmr (DMSO-d_6): δ 3.50, 3.77, 3.78, 3.85, 3.86, 3.91 (each s, 3H, CH_3), 6.10, 6.19 (each d, 1H, 5´´-H, 7´´-H, J = 1.6 Hz), 6.28 (s, 1H, 2´´-H), 6.53, 6.84 (each d, 1H, 6-H, 8-H, J = 2.1 Hz), 6.98 (d, 1H, 5´-H, J = 8.5 Hz), 7.44 (d, 1H, 2´-H, J = 2.2 Hz), 7.53 ppm (dd, 1H, 6´-H, J = 2.2, 8.5 Hz); ^{13}C nmr (DMSO-d_6) δ 55.01, 55.70, 56.23, 56.29, 56.35, 56.50 (CH_3), 89.88, 93.31 (C-5´´, C-7´´), 93.65, 96.38 (C-6, C-8), 98.45 (C-2´´), 101.91 (C-3a´´), 108.38 (C-4a), 111.37, 111.69 (C-2´, C-5´), 121.64 (C-6´), 122.19 (C-1´), 135.39 (C-3), 148.13, 150.91 (C-3´, C-4´), 153.26 (C-2), 158.35 (C-8a), 159.30, 170.31, 173.60 (C-4´´, C-6´´ ,C-7a´´), 160.54, 164.18 (C-5, C-7), 171.28 (C-4), 188.41 ppm (C-3´´); ms: m/z 550 (29%, M^+), 358 (77%, M^+-$C_{10}H_8O_4$), 329 (100%, M^+-$C_{11}H_9O_5$).

2-(2-Chlorophenyl)-3-hydroxy-5,7-dimethoxy-4*H*-1-benzopyran-4-one (3c). Upon heating, 2-bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (**1**) (492 mg, 1.80 mmol) was dissolved in dry toluene (20 mL) and subsequently cooled to room temperature. 2-Chlorobenzaldehyde (**2c**) (253 mg, 1.80 mmol) was added, followed by an equimolar amount sodium methoxide in a methanolic solution, prepared from dry methanol (3.0 mL) and sodium (41 mg). The orange-green suspension was stirred for 100 minutes and a colorless precipitate was removed by filtration (143 mg). The filtrate was evaporated to dryness and the residue was recrystallized from toluene to obtain **3c** as brown crystals (267 mg, 45%), mp 190-194°C; ^{1}H nmr (DMSO-d_6): δ 3.85, 3.87 (each s, 3H, CH_3), 6.49, 6.64 (each d, 3H, 6-H, 8-H, J = 2.2 Hz), 7.48, 7.54 (each dt, 1H, 4´-H, 5´-H, J = 1.6, 7.4 Hz), 7.62 (dd, 1H, 3´-H or 6´-H, J = 1.3, 8.0 Hz), 7.64 (dd, 1H, 3´-H or 6´-H, J = 1.9, 7.6 Hz), 8.69 ppm (s, 1H, OH); ^{13}C nmr (DMSO-d_6) δ 56.11, 56.42 (CH_3), 92.88, 95.96 (C-6, C-8), 107.27 (C-4a), 127.30 (C-5´), 129.85, 131.75, 132.09 (C-3´, C-4´, C-6´), 130.06 (C-1´), 132.92 (C-2´), 139.26 (C-3), 142.25 (C-2), 158.81 (C-8a), 160.35, 164.04 (C-5, C-7), 171.35 ppm (C-4). *Anal.* Calcd. for $C_{17}H_{13}ClO_5$: C, 61.37; H, 3.94. Found: C, 61.22; H, 4.01.

2-(2-Bromophenyl)-3-hydroxy-5,7-dimethoxy-4*H*-1-benzopyran-4-one (3d). Following the aforementioned procedure, 2-bromo-4,6-dimethoxy-3(2*H*)-benzofuranone (**1**) (492 mg, 1.80 mmol) was reacted with 2-bromobenzaldehyde (**2d**) (333 mg, 1.80 mmol) to obtain **3d** as brown crystals (260 mg, 38%), mp 187-190° (toluene); ^{1}H nmr (DMSO-d_6): δ 3.85, 3.87 (each s, 3H, CH_3), 6.49, 6.64 (each d, 1H, 6-H, 8-H, J = 2.4 Hz), 7.45, 7.52 (each dt, 1H, 4´-H, 5´-H, J = 1.6, 7.6 Hz), 7.62 (dd, 1H, 6´-H, J = 1.6, 7.6 Hz), 7.79 (dd, 1H, 3´-H, J = 1.0, 8.2 Hz), 8.69 ppm (s, 1H, OH); ^{13}C nmr (DMSO-d_6): δ 56.11, 56.42 (CH_3), 92.89, 95.95 (C-6, C-8), 107.31 (C-4a), 122.85 (C-2´), 127.81 (C-5´), 131.88, 132.23, 132.95 (C-3´, C-4´, C-6´), 132.11 (C-1´), 138.99 (C-3), 143.58 (C-2), 158.76 (C-8a), 160.57, 163.94 (C-5, C-7), 171.43 ppm (C-4).

Anal. Calcd. for $C_{17}H_{13}BrO_5$: C, 54.13; H, 3.47. Found: C, 54.33; H, 3.66.

X-ray crystal structure analysis. Appropriate crystals of **4b** were obtained by recrystallization from toluene/DMF (3:1). Crystal data, the data collection procedure and structure determination for compound **4b** are given in Table 1. The following programs were used to solve and refine the structure, SHELXS97 [21], SHELXL97 [22]. SHELXTL [23] was used for molecular graphics, and DIAMOND [24] and SHELXL97 for preparing material for publication. The details of the structure analysis have been deposited at the Cambridge Crystallographic Data Centre with the number CCDC-665667. These data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1233-336033; e-mail: deposit@ccdc.cam.ac.uk; internet: http://www.ccdc.cam.ac.uk).

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