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Flavonoids, 45 [1]. A General and Efficient Synthesis of Hydroxyflavones and -chromones[†]

Tamás Patonay*, Dénes Molnár, Zoltán Murányi

Department of Organic Chemistry, Kossuth Lajos University
H-4010 Debrecen, PO Box 20, Hungary

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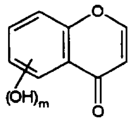
Summary – An efficient and versatile method for the synthesis of flavones hydroxylated in either ring A or B and of chromones hydroxylated in ring A is described. This approach is based on the acidic resin-promoted cyclodehydration and simultaneous deprotection of methoxymethoxylated 1-(2-hydroxyphenyl)propane-1,3-diones easily available by either the Baker-Venkataraman rearrangement or the Claisen condensation.

Amberlyst 15 / Baker-Venkataraman rearrangement / Claisen condensation / hydroxychromone / hydroxyflavone / methoxymethyl protection

Introduction

4*H*-1-Benzopyran-4-ones (chromones) and their 2-phenyl derivatives (flavones) and 3-phenyl derivatives (isoflavones) are widely investigated compounds because many of them occur in hydroxylated, methoxylated or glycosylated form in plants, while others possess considerable biological activity as either drugs for human or agents in the defensive system in plants (phytoalexins) [2, 3]. Recent results on their ability to inhibit retroviral enzymes such as reverse transcriptases and HIV-1 proteinase gave a new impetus for the study of hydroxylated chromones and flavones **1**,**2** [4].



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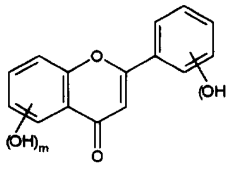

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Scheme 1

Although numerous methods have been developed for the synthesis of flavones, most of them have limitations or disadvantages in the case of hydroxyflavones. Dehydrogenation of flavanones or the isomeric 2′-hydroxychalcones with oxidants, such as SeO_2 [5], 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [6], palladium or platinum [7] or their salts [8], thallium(III)nitrate [9] and $NaIO_4$/dimethylsulfoxide (DMSO) [10], frequently gives a lower yield in the presence of hydroxy and/or alkoxy functions. Moreover the synthesis of the starting materials requires harsh conditions or leads to isomeric mixtures. Another approach widely used for the preparation of flavones utilizes dehydrohalogenation of 3-haloflavanones [11] or 2′-hydroxychalcone dibromides [12], but this method suffers from the competitive halogenation of the activated aromatic rings in the preparation of the starting compounds. Cyclization of 1,3-diarylprop-2-yn-1-ones [13, 14] is an excellent novel method, but it has not been reported for hydroxylated compounds. Preparation of flavones and chromones from 2′-hydroxyacetophenones *via* flavylium or chromylium perchlorates gives moderate yield in the presence of free hydroxy groups [15]. Another procedure available for the synthesis of flavones hydroxylated in ring A is the Allan-Robinson reaction [16] but the yields are often low and the major product isolated from the complex reaction mixture is the corresponding 3-aroylflavone derivative. A better method for the synthesis of ring A hydroxylated flavones and chromones based on an intramolecular Wittig reaction was developed by Le Floc'h *et al* [17]. The most common procedure to synthesize flavones and chromones is the cyclodehydration of 1-(2-hydroxyphenyl)propane-1,3-diones which are usually prepared by Baker-Venkataraman rearrangement [18]. Numerous modifications and versions have been reported for this approach [3, 4a, 19]. With the exception of using organometallic bases in the first aroylation step of the sequence [4a], the Baker-Venkataraman rearrangement is not applicable for the synthesis of flavones with free hydroxy groups. Indeed, a vast majority of

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[†] Dedicated to Prof Robert (Rob) V Hoffman on the occasion of his 50th birthday.

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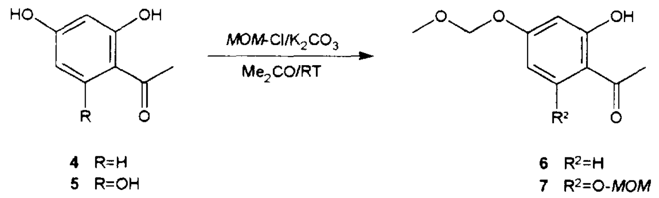
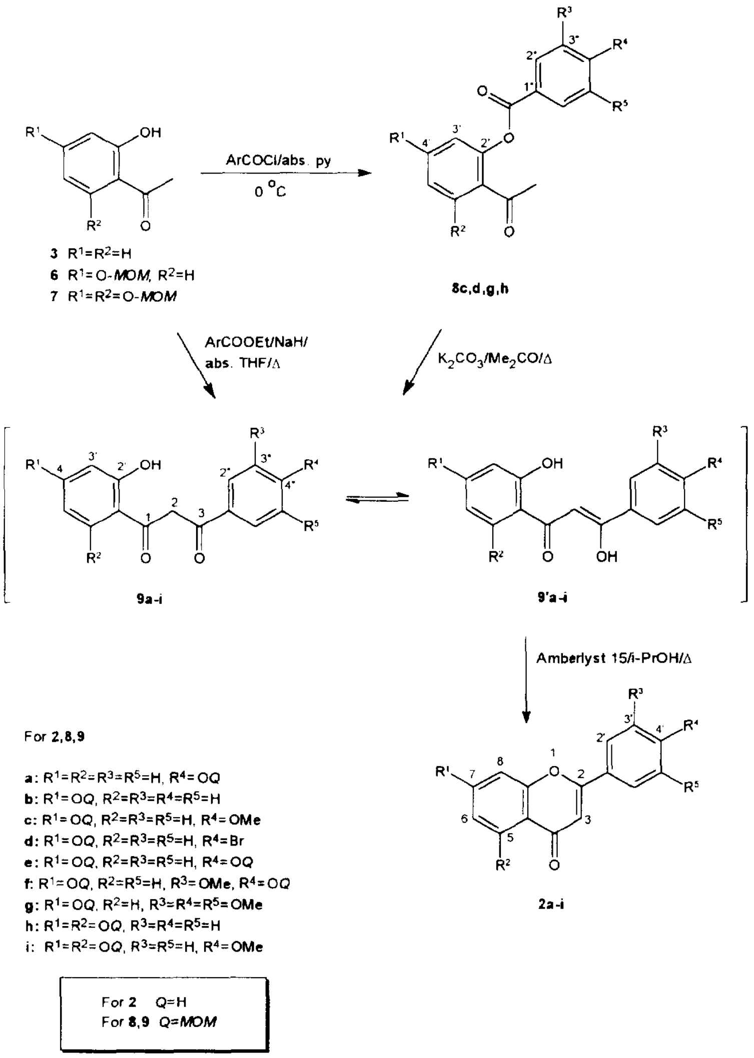


Scheme 2



Scheme 3

the publications utilized methoxy- and/or benzyloxy-protected substrates, but the cleavage of these protecting groups usually requires forced conditions and lacks regioselectivity [20]. Therefore, we decided to investigate the applicability of a more easily removable protecting group, namely the methoxymethyl function, in the β-diketone approach. This common protecting group [21] has rarely been used in the flavonoid chemistry; only a Japanese group has used it in the synthesis of phenolic 3-hydroxyflavanones [22].

We now wish to report an improved procedure for the synthesis of flavones hydroxylated in either ring A or B and of chromones hydroxylated in ring A. Our method is based on the acidic resin-promoted cyclodehydration and simultaneous deprotection of methoxymethylated 1-(2-hydroxyphenyl)propane-1,3-diones easily available by either the Baker-Venkataraman rearrangement or the Claisen condensation.

Table I. Synthesis of β-diketones **9**.

Entry	9	R^1	R^2	R^3	R^4	R^5	oxo/enol^a ($CDCl_3$)	Yield (%)^b [Procedure]
1	a	H	H	H	O-*MOM*	H	16:84	47 [B]
2	b	O-*MOM*	H	H	H	H	14:86	42 [B]
3	c	O-*MOM*	H	H	OMe	H	12:88	63 [B]
4								21 [A]^c
5	d	O-*MOM*	H	H	Br	H	13:87	50 [B]
6								32 [A]^c
7	e	O-*MOM*	H	H	O-*MOM*	H	23:77	35 [B]
8	f	O-*MOM*	H	OMe	O-*MOM*	H	33:67	33 [B]
9	g	O-*MOM*	H	OMe	OMe	OMe	28:72	28 [B]
10								21 [A]^c
11	h	O-*MOM*	O-*MOM*	H	H	H	55:45^d	48 [A]^c
12	i	O-*MOM*	O-*MOM*	H	OMe	H	70:30	54 [B]

^{a} Measured by ^{1}H NMR; ^{b} Yields refer to purified products; ^{c} Overall yield of aroylation and rearrangement steps based on the starting acetophenone; ^{d} DMSO-d_6.

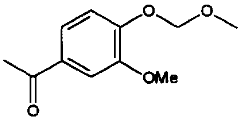
Results and discussion

The synthesis of the starting material acetophenones **6** and **7** is shown in scheme 2. The use of the weak base K_2CO_3 allowed regioselective methoxymethylation of the non-chelated hydroxyl(s) of acetophenones **4** and **5**.

The key compounds, (methoxymethoxy)-substituted 1-(2-hydroxyphenyl)-3-arylpropane-1,3-diones **9** (dibenzoylmethanes) were prepared using two procedures (scheme 3). First, we applied the "classical" Baker-Venkataraman approach. The 1-[(2-aroyloxy)phenyl]-3-arylpropane-1,3-diones **8c,d,g,h** were synthesized from the corresponding acetophenones **6, 7** upon treatment with aroyl chlorides in the presence of pyridine and were transformed to β-diketones **9c,d,g,h** in hot absolute acetone using anhydrous K_2CO_3 as base (table I, procedure A, entries 4, 6, 10, 11). Replacement of acetone with *N,N*-dimethylformamide (DMF), which has a higher boiling point, resulted in lower yields.

Procedure A, however, suffered from two limitations. First, the overall yields of the aroylation and rearrangement steps were relatively poor. Secondly, the range of B-ring substituents was limited to functions that are stable under both basic and acidic conditions as the preparation of most aroylating reagents requires acidic medium or generates acids as by-products. Our aim was to develop a flexible synthesis for all kinds of hydroxylated flavones to avoid the use of acid-stable protecting groups, which are difficult to remove and have led to problems in previous Baker-Venkataraman syntheses, and to eliminate the necessity of an extra exchange of the protecting groups in ring B. The obvious choice was therefore the use of methoxymethylated benzoic acid derivatives as precursors of hydroxylated ring B under basic conditions. Thus, we investigated the applicability of the Claisen condensation between 2′-hydroxyacetophenones **3**, **6** and **7** and esters of methoxymethoxylated benzoic acids for the preparation of β-diketones **9**. The Claisen condensation is widely used for the preparation of chromones [2], but it is a relatively rare approach for the construction of flavone skeleton [3, 19a]. According to our optimization studies the best yields could be achieved by addition of acetophenones **3**, **6** and **7** to the hot mixture of sodium hydride and ethyl (substituted) benzoate in absolute tetrahydrofuran (THF) under nitrogen atmosphere (table I, procedure B, entries 1-3, 5, 7-9, 12).

Comparison of yield data given in Table I clearly show the superiority of the Claisen method over the two-step Baker-Venkataraman approach. The yield of dibenzoylmethanes **9** in procedure B tends to decrease with the increasing number of the alkoxy substituents in ring B. An obvious reason for this phenomenon is the decreasing electrophilicity of the carbonyl center in the benzoate reagent. Another factor that lowers the yield is the retro-Claisen cleavage of product **9** in the strongly basic medium. This secondary reaction was verified by the isolation of acetophenone **10** from the reaction mixture of **9f**. The retro-Claisen reaction of β-diketones in the presence of hydroxocobalt(III) complexes has been reported [23].



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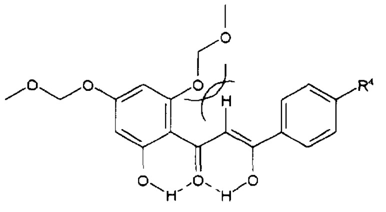
Scheme 4

In accordance with the previous data [19f,g, 24], β-diketones **9** without 6′-substituents predominantly exist in their enol form **9′** (scheme 3) and the oxo/enol ratio slightly shifts in favor of oxo tautomer with the increasing number of alkoxy functions in ring B (table I). Incorporation of a methoxymethoxy group in position 6′ results in a dramatic change. In the case of 1-[2-hydroxy-4,6-*bis*(methoxymethoxy)phenyl]-3-phenylpropane-1,3-dione **9h**, two desmotrops could be isolated by fractional crystallization and no enolization of oxo form **9h** was observed in $CDCl_3$ solution by ^{1}H NMR spectroscopy. Recently, 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylpropane-1,3-dione was reported to exist as a diketone in the solid form and to enolize very slowly in solution [24]. When **9h** was dissolved in DMSO-d_6 a relatively fast enolization occurred but a considerably higher oxo ratio was observed. Similarly, a strong shift into the oxo direction was found in the $CDCl_3$ solution of **9i** (table I). The preference of the oxo form in β-diketones **9** with 6′-substituent could be rationalized in terms of the steric interaction between the 6′-substituent and the propenone chain in the fully planar [24] enol form (scheme 5).



9'h,i

Scheme 5

Cyclodehydration and simultaneous deprotection of methoxymethylated dibenzoylmethanes **9a-i** synthesized by procedure A and/or B was accomplished in one step using Amberlyst 15 acidic cation-exchange resin in refluxing propan-2-ol solution to give hydroxyflavones **2a-i** in excellent yield (scheme 3, table II). The successful use of this resin for the preparation of methoxy-, methyl- or halo-substituted flavones has already been reported [25] but our work is the first demonstration of its application in a one-pot synthesis of hydroxyflavones. The developed method allows an easy synthesis of hydroxyflavones with a variety of substituents other than hydroxy functions, including naturally occurring compounds, such as pratol **2c**, geraldone **2f**, chrysin **2h** and acacetin **2i**.

Table II. Synthesis of flavones **2**.

2	R^1	R^2	R^3	R^4	R^5	Yield (%)^a
a	H	H	H	OH	H	83
b	OH	H	H	H	H	93
c	OH	H	H	OMe	H	94
d	OH	H	H	Br	H	94
e	OH	H	H	OH	H	87
f	OH	H	OMe	OH	H	96
g	OH	H	OMe	OMe	OMe	76
h	OH	OH	H	H	H	84
i	OH	OH	H	OMe	H	96

^{a} Yields refer to purified products.

The ease of this two-step access (Claisen condensation followed by treatment with Amberlyst 15) urged us to investigate the possible extension of our method for the synthesis of hydroxychromones. As data given in table III show, 1-[2-hydroxy-4-(methoxymethoxy)-phenyl]alkane-1,3-diones **11a-c** were obtained in good yield from acetophenone **6** and were smoothly converted into the corresponding 2-alkyl-7-hydroxychromones **1a-c** (scheme 6).

It is noteworthy that β-diketones **11** were found to exist in a triple equilibrium between the oxo **11**, the enol **11′** and the cyclic 2-hydroxychromanone **11″** forms in accordance with earlier reports [19g, 26]. Our data (table III), however, reveal a very marked substituent effect on the equilibrium. Any alkyl substituent attached to the C-3 decreases the electrophilicity of the carbonyl center and sterically hinders the cyclization making the cyclic form **11″** highly unfavored.

Table III. Synthesis of β-diketones **11** and hydroxychromones **1**.

	R	Yield (%)^a **11**	Ratio ($CDCl_3$)^b **11**:**11′**:**11″**	Yield (%)^a **1**
a	H	78	0:0:100	97
b	Me	67	28:52:18	82
c	Bu	60	37:59:4	84

In summary, Claisen condensation of methoxymethoxylated 2′-hydroxyacetophenones with carboxylic acid esters and the subsequent treatment of the 1,3-diketones formed with Amberlyst 15 resin offers an easy, general and efficient method for the synthesis of flavones with hydroxy groups in their ring A and/or B and of chromones hydroxylated in their ring A.

Experimental section

General

Mp's were determined on a Boetius hot-stage apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 16 PC FTIR instrument in KBr pellets unless otherwise specified. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded with a Bruker WP 200 SY instrument (internal standard TMS, δ = 0 ppm) in $CDCl_3$ solution unless otherwise stated. MS spectra were recorded with a VG 7035 GC-MS-DS system (EI, 70 eV). $MgSO_4$ was used as drying agent, column chromatography was performed on Kieselgel 60 (0.063-0.2 mm) (Reanal). Thin-layer chromatography was performed on Kieselgel 60 F_{254} (Alurolle) (Merck) using toluene/EtOAc (4:1) and hexane/Me_2CO (2:1) mixtures as developing systems.

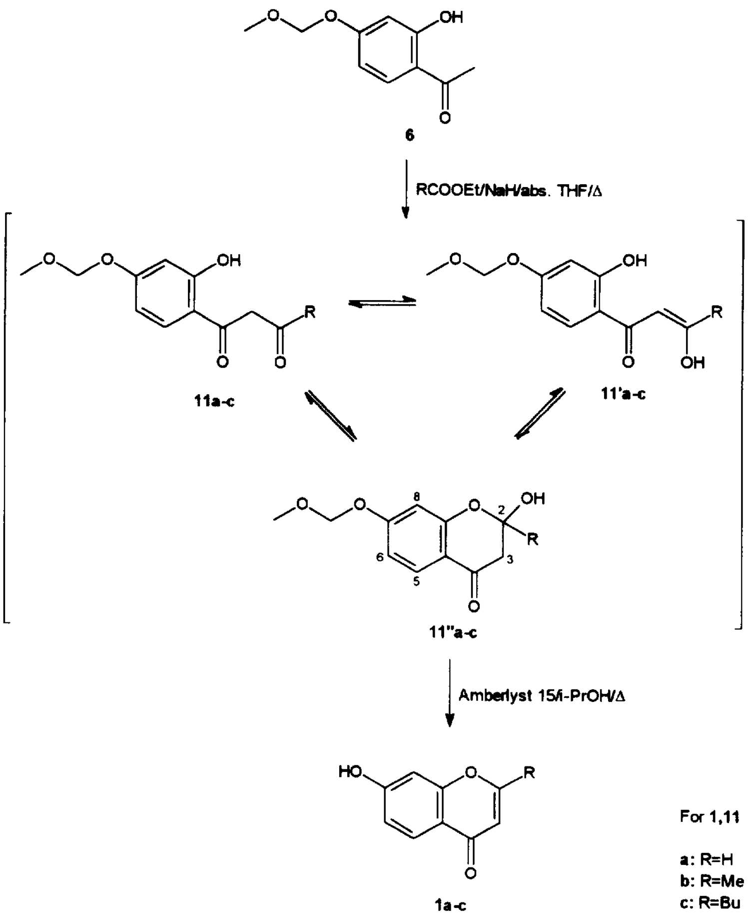
1-[2-Hydroxy-4-(methoxymethoxy)phenyl]ethanone **6**

Methoxymethyl chloride [27] (18.0 mL, 0.2 mol) was added dropwise to the stirred mixture of 1-(2,4-dihydroxyphenyl)ethanone **4** (16.0 g, 0.105 mol), anhydrous K_2CO_3 (35.0 g) and acetone (90 mL) at room temperature in 90 min. After 2.5 h stirring the mixture was filtered and washed with acetone, the filtrate was evaporated *in vacuo* and the residue was dissolved in CH_2Cl_2. The filtered salts were dissolved in water (250 mL), neutralized with diluted HCl and extracted with CH_2Cl_2. The combined CH_2Cl_2 layers were dried, the solvent was removed under reduced pressure and the oily residue was purified by column chromatography (hexane/EtOAc) (4:1) to give 13.35 g (65%) acetophenone **6**.

As an alternative, pure **6** could be isolated by vacuum distillation, bp : 138°C/3 mm Hg. Lit [28] bp : 110°C/0.15 mm Hg. CAUTION! Traces of acids or water in the residue may result in a violent decomposition of the material during distillation.

IR (neat) : 2 955, 2 824 (MeO), 1 630 (C=O), 1 367, 1 218 (C-O-C) cm^{-1}.

^1H NMR : 2.66 (s, 3H, 2-H), 3.59 (s, 3H, 4′-OCH_2OCH_3), 5.31 (s, 2H, 4′-OCH_2OCH_3), 6.65 (dd, J = 8.5 and



Scheme 6

2.5 Hz, 1H, 5'-H), 6.68 (d, J = 2.5 Hz, 1H, 3'-H), 7.75 (d, J = 8.5 Hz, 1H, 6'-H), 13.25 (s, 1H, 2'-OH).

1-[4,6-bis(Methoxymethoxy)-2-hydroxyphenyl] ethanone **7**

Reaction of 1-(2,4,6-trihydroxyphenyl)ethanone **5** (8.4 g, 49.96 mmol) and methoxymethyl chloride (20 mL, 0.222 mol) using the procedure and work-up given for **6** afforded 6.0 g (47%) pure **7**. Mp : 45-46.5°C (hexane).

IR : 1 664, 1 658 (C=O), 1 602, 1 382, 1 338, 1 209, 1 198 (C-O-C), 1 160, 939, 776 cm^{-1}.

^{1}H NMR : 2.67 (s, 3H, 2-H), 3.49, 3.53 (2 × s, 2 × 3H, 4',6'-OCH$_2$OC**H**$_3$), 5.18, 5.31 (2 × s, 2 × 2H, 4',6'-OC**H**$_2$OCH$_3$), 6.27 (overlapping doublets, 2H, 3',5'-H), 13.72 (s, 1H, 2'-OH).

Anal calc for $C_{12}H_{16}O_6$ (156.26) : C, 56.35; H, 6.29. Found : C, 56.48; H, 6.11.

Preparation of 2'-aroyloxy-(methoxymethoxy substituted) acetophenones **8**. *General procedure*

The hydroxyacetophenone **6** or **7** (20.40 mmol) was added to a cooled (0°C) solution of aroyl chloride (20.50 mmol) in absolute pyridine (20 mL) and allowed to stand for 24 h. The mixture was poured on crushed ice and the precipitation was filtered off and crystallized from methanol to give pure ester **8**.

- *2-Acetyl-5-(methoxymethoxy)]phenyl 4-methoxybenzoate* **8c**

Yield : 51%. Mp : 71-72°C.

IR : 2 970, 2 940, 2 843 (MeO), 1 732 (C=O, ester), 1 674 (C=O, ketone), 1 605, 1 512, 1 261br (C-O-C, ester + ether), 1 165, 1 126, 1 069, 995, 844, 764 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 2.50 (s, 3H, 2-H), 3.48 (s, 3H, 4'-OCH$_2$OC**H**$_3$), 3.94 (s, 3H, 4"-OMe), 5.37 (s, 2H, 4'-OC**H**$_2$OCH$_3$), 7.04 (d, J = 2.3 Hz, 1H, 3'-H), 7.13 (dd, J = 8.2 and 2.3 Hz, 1H, 5'-H), 7.20 (d, J = 7.9 Hz, 2H, 3",5"-H), 8.01 (d, J = 8.2 Hz, 1H, 6'-H), 8.13 (d, J = 7.9 Hz, 2H, 2",6"-H).

Anal calc for $C_{18}H_{18}O_6$ (330.34) : C, 65.45; H, 5.49. Found : C, 65.18; H, 5.59.

- *[2-Acetyl-5-(methoxymethoxy)]phenyl 4-bromobenzoate* **8d**

Yield : 75%. Mp : 98-100°C.

IR : 3 003, 2 938, 2 824 (MeO), 1 752 (C=O, ester), 1 672 (C=O, ketone), 1 612, 1 598, 1 361, 1 266, 1 250, 1 238, 1 209 (C-O-C, ester + ether), 1 157, 1 128, 1 068 (C-Br + C-O-C, ester), 1 011 (C-O-C, ether), 743 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 2.48 (s, 3H, 2-H), 3.42 (s, 3H, 4'-OCH$_2$OCH$_3$), 5.32 (s, 2H, 4'-OC**H**$_2$OCH$_3$), 7.04 (d, J = 2.4 Hz, 1H, 3'-H), 7.10 (dd, J = 8.2 and 2.4 Hz, 1H, 5'-H), 7.83 (d, J = 8.0 Hz, 2H, 3",5"-H), 8.01 (d, J =8.2 Hz, 1H, 6'-H), 8.04 (d, J = 8.0 Hz, 2H, 2",6"-H).

Anal calc for $C_{17}H_{17}BrO_5$ (379.21) : C, 53.85; H, 3.99; Br, 21.07. Found : C, 54.02; H, 4.13; Br, 21.00.

- *[2-Acetyl-5-(methoxymethoxy)]phenyl 3,4,5-trimethoxybenzoate* **8g**

Yield : 48%. Mp : 115-117°C.

IR : 2 961, 2 846 (MeO), 1 726 (C=O, ester), 1 682 (C=O, ketone), 1 592, 1 506, 1 417, 1 359, 1 258, 1 234, 1 211 (C-O-C, ester + ether), 1 169, 1 130, 1 061 (C-O-C, ester), 1 007 (C-O-C, ether) cm^{-1}.

^{1}H NMR (DMSO-d_6) : 2.48 (s, 3H, 2-H), 3.41 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 3.81 (s, 3H, 4″-OMe), 3.89 (s, 6H, 3″,5″-OMr), 5.32 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 7.01 (d, J = 2.1 Hz, 1H, 3′-H), 7.08 (dd, J = 8.1 and 2.1 Hz, 1H, 5′-H), 7.42 (s, 2H, 2″,6″-H), 7.98 (d, J = 8.2 Hz, 1H, 6′-H), 8.04 (d, J = 8.1 Hz, 2H, 2″,6″-H).

Anal calc for $C_{20}H_{22}O_8$ (390.39) : C, 61.53; H, 5.68. Found : C, 61.90; H, 5.65.

- *[2-Acetyl-4,6-bis(methoxymethoxy)]phenyl benzoate* **8h**

Yield : 89%. Mp : 72-73.5°C.

IR : 3 109, 2 975, 2 928, 2 843 (MeO), 1 751, 1 744 (C=O, ester), 1 700 (C=O, ketone), 1 621, 1 585, 1 484, 1 458, 1 445, 1 270, 1 252 (C-O-C, ester), 1 233, 1 224 (C-O-C, ether), 1 150, 1 088, 1 070, 1 042 (C-O-C, ester), 1 018, 1 005 (C-O-C, ether) cm^{-1}.

^{1}H NMR : 2.51 (s, 3H, 2-H), 3.48, 3.50 (2 × s, 2 × 3H, 4′,6′-OCH$_2$OC**H**$_3$), 5.19, 5.22 (2 × s, 2 × 2H, 4′,6′-OC**H**$_2$OCH$_3$), 6.62 (d, J = 1.9 Hz, 1H, 3′-H), 6.79 (d, J = 1.9 Hz, 1H, 5′-H), 7.49 (m, 2H, 3″,5″-H), 7.63 (m, 1H, 4″-H), 8.12 (dd, J = 8.0 and 2.1 Hz, 2H, 2″,6″-H).

Anal calc for $C_{19}H_{20}O_7$ (360.37) : C, 63.33; H, 5.59. Found : C, 63.09; H, 5.41.

Preparation of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones **9**. *General procedures*

Procedure A : A mixture of 2′-aroyloxyacetophenone **8** (15.00 mmol), anhydrous K_2CO_3 (18.5 g) and absolute acetone (45 mL) was stirred at reflux temperature for 22 h, and then poured into water and acidified with acetic acid. The precipitation was filtered off, washed with water and crystallized from methanol.

Procedure B : To a stirred suspension of sodium hydride (60% in mineral oil) (1.60 g, *ca* 40.00 mmol, rinsed with dry hexane prior to use) in absolute THF (10 mL), was added a solution of ethyl (substituted) benzoate [29] (25.00 mmol) in absolute THF (10 mL) under nitrogen. The mixture was stirred at reflux temperature and a solution of acetophenone **3**, **6** or **7** (10.00 mmol) in absolute THF (10 mL) was added dropwise in 30 min. After completion of the reaction (TLC monitoring) the mixture was poured into water (200 mL), neutralized with dilute HCl solution and extracted with CH_2Cl_2 (3 × 80 mL). The organic phase was washed with saturated $NaHCO_3$ solution, dried and evaporated. The crude products were purified by recrystallization from methanol or by column chromatography.

- *1-(2-Hydroxyphenyl)-3-[4-(methoxymethoxy) phenyl]propane-1,3-dione* **9a**

Procedure B. Reaction time : 2 h, yield : 47%. Mp : 79-82°C.

IR : 2 942, 2 854 (MeO), 1 606 (C=O), 1 584 (C=C-OH), 1 510, 1 490, 1 300, 1 240 (C-O-C), 1 174, 1 152, 1 080 (C-O-C), 998, 720 cm^{-1}.

^{1}H NMR : **9a** (oxo) : 3.48 (s, 3H, 4″-OCH$_2$OC**H**$_3$), 4.60 (s, 2H, 2-H), 5.25 (s, 2H, 4″-OC**H**$_2$OCH$_3$), 7.92 (dd, J = 8.6 and 1.8 Hz, 2H, 2″,6″-H), 11.98 (s, 1H, 2′-OH). **9′a** (enol) : 3.51 (s, 3H, 4″-OCH$_2$OC**H**$_3$), 5.26 (s, 2H, 4″-OC**H**$_2$OCH$_3$), 6.78 (s, 1H, 2-H), 7.99 (d, J = 9.3 Hz, 2H, 2″,6″-H), 12.14 (s, 1H, 2′-OH), 12.82 (s, 1H, 3-OH). Non-separable signals : 6.92 (m, 1H, 5′-H), 7.00 (m, 1H, 3′-H), 7.09-7.17 (m, 2H, 3″,5″-H), 7.47 (m, 1H, 4′-H), 7.78 (m, 1H, 6′-H). Oxo/enol ratio = 16:84 (on the basis of integrals of 2-H).

Anal calc for $C_{17}H_{16}O_5$ (300.31) : C, 67.93; H, 5.37. Found : C, 68.11; H, 5.51.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]-3-phenylpropane-1,3-dione* **9b**

Procedure B. Reaction time : 1.5 h, yield : 42%. Mp : 89-91°C.

IR : 2 958, 2 930, 2 900, 2 850, 2 828 (MeO), 1 610 (C=O), 1 568 (C=C-OH), 1 510, 1 490, 1 295, 1 242 (C-O-C), 1 160, 1 148, 1 078, 1 002 (C-O-C) cm^{-1}.

^{1}H NMR : **9b** (oxo) : 3.47 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 4.57 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 12.28 (s, 1H, 2′-OH). **9’b** (enol) : 3.49 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 5.22 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 6.72 (s, 1H, 2-H), 12.46 (s, 1H, 2′-OH), 13.15 (s, 1H, 3-OH). Non-separable signals : 6.58 (m, 1H, 5′-H), 6.64 (m, 1H, 3′-H), 7.44-7.58 (m, 3H, 3″,4″,5″-H), 7.72 (d, J = 8.5 Hz, 1H, 6′-H), 7.92 (m, 2H, 2″,6″-H). Oxo/enol ratio = 14:86 (on the basis of integrals of 2-H).

Anal calc for $C_{17}H_{16}O_5$ (300.31) : C, 67.93; H, 5.37. Found : C, 67.89; H, 5.12.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]-3-(4-methoxyphenyl)propane-1,3-dione* **9c**

Procedure A. Yield : 42%. Procedure B. Reaction time : 4.5 h, ethyl 4-methoxybenzoate was added neat, yield : 63%. Mp : 112-114°C.

IR : 2 958, 2 932, 2 836 (MeO), 1 604 (C=O), 1 568 (C=C-OH), 1 508, 1 440, 1 268, 1 240 (C-O-C), 1 214, 1 182, 1 144, 1 078, 1 002 (C-O-C), 785 cm^{-1}.

^{1}H NMR : **9c** (oxo) : 3.47 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 4.52 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 8.02 (d, J = 9.3 Hz, 2H, 2″,6″-H), 12.23 (s, 1H, 2′-OH). **9’c** (enol) : 3.50 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 5.23 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 6.67 (s, 1H, 2-H), 7.70 (d, J = 9.5 Hz, 2H, 2″,6″-H), 12.50 (s, 1H, 2′-OH), 12.97 (s, 1H, 3-OH). Non-separable signals : 3.90 (s, 3H, 4″-OMe), 6.57 (m, 1H, 5′-H), 6.62 (m, 1H, 3′-H), 6.98 (d, $J \sim$ 9.4 Hz, 2H, 3″,5″-H), 7.70 (d, J = 8.9 Hz, 1H, 6′-H). Oxo/enol ratio = 12:88 (on the basis of integrals of 2-H).

Anal calc for $C_{18}H_{18}O_6$ (330.34) : C, 65.45; H, 5.49. Found : C, 65.33; H, 5.82.

- *3-(4-Bromophenyl)-1-[2-hydroxy-4-(methoxymethoxy)phenyl]propane-1,3-dione* **9d**

Procedure A. Yield : 43%. Procedure B. Reaction time : 1.5 h, yield : 50%. Mp : 111-113°C.

IR : 2 948, 2 836 (MeO), 1 618 (C=O), 1 586, 1 568 (C=C-OH), 1 506, 1 448, 1 290, 1 242, 1 214 (C-O-C), 1 152, 1 078 (C-Br + C-O-C), 994, 930, 784 cm^{-1}.

^{1}H NMR : **9d** (oxo) : 3.48 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 4.54 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 7.89 (d, J = 9.2 Hz, 2H, 2″,6″-H), 12.23 (s, 1H, 2′-OH). **9’d** (enol) : 3.50 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 5.22 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 6.69 (s, 1H, 2-H), 7.79 (d, J = 9.2 Hz, 2H, 2″,6″-H), 12.40 (s, 1H, 2′-OH), 13.20 (s, 1H, 3-OH). Non-separable signals : 3.90 (s, 3H, 4″-OMe), 6.57 (m, 1H, 5′-H), 6.62 (m, 1H, 3′-H), 6.98 (d, $J \sim 9.4$ Hz, 2H, 3″,5″-H), 7.70 (d, $J = 8.9$ Hz, 1H, 6′-H). Oxo/enol ratio = 12:88 (on the basis of integrals of 2-H).

Anal calc for $C_{17}H_{15}BrO_5$ (379.21) : C, 53.85; H, 3.99; Br, 21.07. Found : C, 54.11; H, 4.05; Br, 21.34.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]-3-[4-(methoxymethoxy)phenyl]propane-1,3-dione* **9e**

Procedure B. Reaction time : 8 h, column chromatography (hexane/acetone 4:1), yield : 35%. Mp : 76-78°C (MeOH).

IR : 2 924, 2 854 (MeO), 1 606 (C=O), 1 570 (C=C-OH), 1 508, 1 442, 1 366, 1 340, 1 238, 1 206 (C-O-C), 1 178, 1 156, 1 076 (C-O-C), 990, 968, 948, 788 cm^{-1}.

^1H NMR : **9e** (oxo) : 3.45 (s, 3H, 4′-OCH_2OCH_3), 4.50 (s, 2H, 2-H), 5.19 (s, 2H, 4′-OCH_2OCH_3), 7.72 (d, $J = 8.8$ Hz, 1H, 6′-H), 7.99 (d, $J = 9.5$ Hz, 2H, 2″,6″-H), 12.32 (s, 1H, 2′-OH). **9′e** (enol) : 3.47 (s, 3H, 4′-OCH_2OCH_3), 5.20 (s, 2H, 4′-OCH_2OCH_3), 6.64 (s, 1H, 2-H), 7.68 (d, $J = 9.3$ Hz, 1H, 6′-H), 7.87 (d, $J = 9.2$ Hz, 2H, 2″,6″-H), 12.48 (s, 1H, 2′-OH), 13.02 (s, 1H, 3-OH). Non-separable signals : 3.49 (s, 3H, 4″-OCH_2OCH_3), 5.23 (s, 2H, 4″-OCH_2OCH_3), 6.52-6.62 (m, 2H, 3′,5′-H), 7.11 (overlapping doublets, 2H, 3″,5″-H). Oxo/enol ratio = 23:77 (on the basis of integrals of 2-H).

Anal calc for $C_{19}H_{20}O_7$ (360.37) : C, 63.33; H, 5.59. Found : C, 63.38; H, 5.79.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]-3-[3-methoxy-4-(methoxymethoxy)phenyl]propane-1,3-dione* **9f**

Procedure B. Reaction time : 8 h, column chromatography (hexane/acetone 4:1), yield : 33%. Mp : 96-98°C (MeOH).

IR : 2 968, 2 904, 2 840 (MeO), 1 604 (C=O), 1 580 (C=C-OH), 1 516, 1 446, 1 354, 1 246br (C-O-C), 1 200, 1 178, 1 154, 1 140, 1 080 (C-O-C), 992, 956, 786 cm^{-1}.

^1H NMR : **9f** (oxo) : 3.48 (s, 3H, 4′-OCH_2OCH_3), 3.53 (s, 3H, 4″-OCH_2OCH_3), 3.94 (s, 3H, 3″-OMe), 4.52 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OCH_2OCH_3), 7.25 (d, $J = 9.0$ Hz, 1H, 5″-H), 7.76 (d, $J = 8.9$ Hz, 1H, 6′-H), 12.31 (s, 1H, 2′-OH). **9′f** (enol) : 3.50 (s, 3H, 4′-OCH_2OCH_3), 3.55 (s, 3H, 4″-OCH_2OCH_3), 3.99 (s, 3H, 3″-OMe), 5.23 (s, 2H, 4′-OCH_2OCH_3), 6.67 (s, 1H, 2-H), 7.25 (d, $J = 9.0$ Hz, 1H, 5″-H), 7.70 (d, $J = 9.7$ Hz, 1H, 6′-H), 12.45 (s, 1H, 2′-OH), 12.92 (s, 1H, 3-OH). Non-separable signals : 5.32 (s, 2H, 4″-OCH_2OCH_3), 6.55-6.65 (m, 2H, 3′,5′-H), 7.48-7.61 (m, 2H, 2″,6″-H). Oxo/enol ratio = 33:67 (on the basis of integrals of 2-H).

Anal calc for $C_{20}H_{22}O_8$ (390.39) : C, 61.53; H, 5.68. Found : C, 61.39; H, 5.63.

- *1-[3-Methoxy-4-(methoxymethoxy)phenyl] ethanone* **10**

Product **10** was also isolated by column chromatography from the worked-up reaction mixture of **9f**.

Yield : 22% (on the basis of the starting material **6**). Mp : 44-47°C.

IR : 2 962, 2 932, 2 830 (MeO), 1 672 (C=O), 1 588, 1 510, 1 462, 1 416, 1 286, 1 272, 1 222, 1 202 (C-O-C), 1 172, 1 162, 1 140, 1 076 (C-O-C), 974, 814 cm^{-1}.

^1H NMR (DMSO-d_6) : 2.56 (s, 3H, 2-H), 3.45 (s, 3H, 4′-OCH_2OCH_3), 3.88 (s, 3H, 3′-OMe), 5.31 (s, 2H, 4′-OCH_2OCH_3), 7.18 (d, $J = 8.3$ Hz, 1H, 5′-H), 7.53 (s, 1H, 2′-H), 7.60 (d, $J = 8.3$ Hz, 1H, 6′-H).

^{13}C NMR (DMSO-d_6) : 178.20 (C-1), 150.27, 149.35 (C-3′, C-4′), 131.14 (C-1′), 122.59 (C-6′), 114.75, 110.83 (C-2′, C-5′), 94.44 (4′-OCH_2OCH_3), 55.87, 55.47 (4′-OCH_2OCH_3, 3′-OMe), 26.20 (C-2).

MS : 210 ($M^{+\cdot}$, 38%), 196 (3.5), 180 (18.5), 179 (6.5), 165 (24), 151 (12), 149 (6), 137 (5), 119 (11.5), 109 (4.5), 107 (4.5), 91 (10), 79 (16), 77 (10), 63 (11), 51 (22), 45 (100), 43 (66).

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]-3-(3,4,5-trimethoxyphenyl)propane-1,3-dione* **9g**

Procedure A. Yield : 44%. Procedure B. Reaction time : 6 h, yield : 28%. Mp : 89-91.5°C.

IR : 2 958, 2 934, 2 834 (MeO), 1 608 (C=O), 1 578 (C=C-OH), 1 504, 1 250 (C-O-C), 1 130, 1 076, 1 012 (C-O-C), 752 cm^{-1}.

^1H NMR : **9g** (oxo) : 3.48 (s, 3H, 4′-OCH_2OCH_3), 4.52 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OCH_2OCH_3), 7.80 (d, $J = 8.4$ Hz, 1H, 6′-H), 12.31 (s, 1H, 2′-OH). **9′g** (enol) : 3.50 (s, 3H, 4′-OCH_2OCH_3), 5.22 (s, 2H, 4′-OCH_2OCH_3), 6.63 (overlapping singlet and doublet, 2H, 2-H and 3′-H), 7.70 (d, $J = 8.5$ Hz, 1H, 6′-H), 12.45 (s, 1H, 2′-OH), 12.97 (s, 1H, 3-OH). Non-separable signals : 3.94 (s, 3H, 4″-OMe), 3.96 (s, 6H, 3″,5″-OMe), 6.60 (m, 1H, 5′-H), 7.25 (s, 2H, 2″,6″-H). Oxo/enol ratio = 28:72 (on the basis of integrals of 2-H).

Anal calc for $C_{20}H_{22}O_8$ (390.39) : C, 61.53; H, 5.68. Found : C, 61.71; H, 5.75.

- *1-[2-Hydroxy-4,6-bis(methoxymethoxy)phenyl]-3-phenylpropane-1,3-dione* **9h**

Procedure A. 7.11 mmol 7, 18 h reflux. Fractionated crystallization of the crude product from methanol resulted in 774 mg (30%) oxo desmotrop **9h** (as the less soluble isomer) and 613 mg (24%) enol desmotrop **9h′** (as the more soluble isomer).

9h. White crystals. Mp : 80-88°C (melts with yellow color).

IR : 2 918, 1 688, 1 634 (C=O), 1 605, 1 580, 1 342, 1 288, 1 218 (C-O-C), 1 159, 1 064, 1 024 (C-O-C), 919 cm^{-1}.

^1H NMR : 3.24 (s, 3H, 6′-OCH_2OCH_3), 3.47 (s, 3H, 4′-OCH_2OCH_3), 4.61 (s, 2H, 2-H), 4.85 (s, 2H, 6′-OCH_2OCH_3), 5.17 (s, 2H, 4′-OCH_2OCH_3), 6.23, 6.31 (2 × d, $J = 2.4$ Hz, 2 × 1H, 3′,5′-H), 7.52 (m, 2H, 3″,5″-H), 7.62 (m, 1H, 4″-H), 7.99 (dd, $J = 6.5$ and 1.8 Hz, 2H, 2″,6″-H), 13.50 (s, 1H, 2′-OH).

The ^1H NMR spectrum of **9h** taken in DMSO-d_6 showed an oxo-enol mixture with a ratio of 55:45.

Anal calc for $C_{19}H_{20}O_7$ (360.37) : C, 63.33; H, 5.59. Found : C, 63.21; H, 5.27.

9h′. Yellow crystals. Mp : 79-80.5°C.

IR : 3 176, 2 836, 2 822 (MeO), 1 596 (Ar and C=O), 1 565 (C=C-OH), 1 484, 1 474, 1 412, 1 321, 1 261, 1 209 (C-O-C), 1 159, 1 096, 1 054, 1 030 (C-O-C), 969, 925, 759 cm^{-1}.

^1H NMR : 3.49 (s, 3H, 4′-OCH_2OCH_3), 3.57 (s, 3H, 6′-OCH_2OCH_3), 5.19 (s, 2H, 4′-OCH_2OCH_3), 5.31 (s, 2H, 6′-OCH_2OCH_3), 6.26, 6.32 (2×d, $J = 2.0$ Hz, 2×1H, 3′,5′-H), 7.39 (s, 1H, 2-H), 7.50 (m, 3H, 3″,4″,5″-H), 7.89 (dd, $J = 8.7$ and 1.8 Hz, 2H, 2″,6″-H), 13.02, 13.07 (2×s, 2 × 1H, 3-OH and 2′-OH).

Anal calc for $C_{19}H_{20}O_7$ (360.37) : C, 63.33; H, 5.59. Found : C, 63.11; H, 5.57.

- *1-[2-Hydroxy-4,6-bis(methoxymethoxy)phenyl]-3-(4-methoxyphenyl)propane-1,3-dione* **9i**

Procedure B. Reaction time 4.5 h, yield : 54%. Mp : 89-91°C.

IR : 2 960, 2 842 (MeO), 1 598 (Ar and C=O), 1 570 (C=C-OH), 1 512, 1 260, 1 224 (C-O-C), 1 182, 1 156, 1 084, 1 056, 1 016 (C-O-C), 948, 826 cm^{-1}.

^{1}H NMR : **9i** (oxo) : 3.18 (s, 3H, 6′-OCH$_2$OC**H**$_3$), 3.48 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 3.90 (s, 3H, 4″-OMe), 4.57 (s, 2H, 2-H), 4.88 (s, 2H, 6′-OC**H**$_2$OCH$_3$), 5.18 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 7.98 (d, J = 8.5 Hz, 2H, 2″,6″-H), 13.52 (s, 1H, 2′-OH). **9′i** (enol) : 3.50 (s, 3H, 4′-OCH$_2$OC**H**$_3$), 3.57 (s, 3H, 6′-OCH$_2$OCH$_3$), 3.89 (s, 3H, 4″-OMe), 5.20 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 5.30 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 7.31 (s, 1H, 2-H), 7.88 (d, J = 9.5 Hz, 2H, 2″,6″-H), 12.79 (s, 1H, 2′-OH), 13.10 (s, 1H, 3-OH). Non-separable signals : 6.22 (m, 2H, 3′,5′-H), 7.00 (overlapping doublets, 2H, 3″,5″-H). Oxo/enol ratio = 28:72 (on the basis of integrals of 2-H).

Anal calc for $C_{20}H_{22}O_8$ (390.39) : C, 61.53; H, 5.68. Found : C, 61.61; H, 5.98.

Preparation of 1-[2-hydroxy-4-(methoxymethoxy)phenyl] alkane-1,3-diones **11**. *General procedure*

A solution of ethyl alkanoate (25.00 mmol) and 2′-hydroxy-4′-(methoxymethoxy)acetophenone **6** in absolute THF (5 mL) was added dropwise to the stirred suspension of sodium hydride (60% in mineral oil) (1.60 g, *ca* 40.00 mmol, rinsed with dry hexane prior to use) in absolute THF (5 mL) under nitrogen. The mixture was warmed up to reflux temperature and the reaction was monitored by TLC. After completion of the reaction the mixture was worked up as described for dibenzoylmethanes **9**. Pure diones **11** were obtained by recrystallization from hexane/absolute ethanol mixture.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]propane-1,3-dione* **11a**

Reaction time : 1.75 h, yield : 78%. Mp : 110-112°C.

IR : 3 390 (OH), 2 970, 2 914, 2 838 (MeO), 1 666 (C=O), 1 612, 1 574, 1 452, 1 442, 1 302, 1 252, 1 236 (C-O-C and C-OH), 1 090, 1 004 (C-O-C), 986, 952, 874 cm^{-1}.

^{1}H NMR : The compound exists entirely in 2-hydroxychromanone form **11a″**, numbering refers to this structure. **11a″** : 2.91 (AB qd, J_{AB} = 16.8 Hz, J_{AX} = 4.5 Hz, J_{BX} = 4.9 Hz, 2H, 3-H), 3.48 (s, 3H, 7-OCH$_2$OC**H**$_3$), 4.13 (br s, 1H, 2-OH), 5.20 (s, 2H, 7-OC**H**$_2$OCH$_3$), 5.85 (br coalesced m, 1H, 2-H), 6.62 (d, J = 2.3 Hz, 1H, 8-H), 7.39 (dd, J = 8.7 and 2.3 Hz, 1H, 6-H), 7.83 (d, J = 8.7 Hz, 1H, 5-H).

Anal calc for $C_{11}H_{12}O_5$ (224.22) : C, 58.93; H, 5.39. Found : C, 59.21; H, 5.61.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]butane-1,3-dione* **11b**

Reaction time : 2.75 h, yield : 67%. Mp : 101-104°C.

IR : 3 260 (OH), 2 980, 2 924, 2 826 (MeO), 1 662, 1 652 (C=O), 1 604, 1 580 (C=C-OH), 1 450, 1 322, 1 256, 1 226 (C-O-C and C-OH), 1 158, 1 122, 1 082, 996 cm^{-1}.

^{1}H NMR : **11b** (β-diketone) : 2.30 (s, 3H, 4-H), 4.03 (s, 2H, 2-H), 5.21 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 7.58 (d, J = 8.2 Hz, 1H, 6′-H), 12.31 (s, 1H, 2′-OH). **11b′** (enol) : 2.12 (s, 3H, 4-H), 5.20 (s, 2H, 4′-OC**H**$_2$OCH$_3$), 6.06 (s, 1H, 2-H), 7.56 (d, J = 8.8 Hz, 1H, 6′-H), 12.43 (s, 1H, 2′-OH), 13.71 (s, 1H, 3-OH). **11b″** (2-hydroxychromanone) : 1.74 (s, 3H, 2-Me), 2.88 (s, 2H, 3-H), 6.70 (dd, J = 9.3 and 2.1 Hz, 1H, 6-H), 7.85 (d, J = 9.3 Hz, 1H, 5-H). Non-separable signals : 3.48 (s, 3H, 4′/7-OCH$_2$OC**H**$_3$), 6.50-6.60 (m, 2H, 3′/8- and 5′-H). Ratio of isomers **11b**:**11b′**:**11b″** = 28:52:18.

Anal calc for $C_{12}H_{14}O_5$ (238.24) : C, 60.50; H, 5.92. Found : C, 60.41; H, 6.15.

- *1-[2-Hydroxy-4-(methoxymethoxy)phenyl]heptane-1,3-dione* **11c**

Reaction time : 6 h, yield : 60%. Mp : 46-48°C.

IR : 3 286 (OH), 2 956, 2 868, 1 654 (C=O), 1 608 (C=O), 1 578 (C=C-OH), 1 318, 1 250, 1 240 (C-O-C and C-OH), 1 158, 1 084, 994 cm^{-1}.

^{1}H NMR : **11c** (β-diketone) : 0.88 (t, J = 7.2 Hz, 3H, 7-H), 2.58 (t, J = 7.2 Hz, 2H, 4-H), 4.01 (s, 2H, 2-H), 7.59 (d, J = 8.8 Hz, 1H, 6′-H), 12.36 (s, 1H, 2′-OH). **11c′** (enol) : 0.95 (t, J = 7.2 Hz, 3H, 7-H), 2.34 (t, J = 7.3 Hz, 2H, 4-H), 6.05 (s, 1H, 2-H), 7.57 (d, J = 8.9 Hz, 1H, 6′-H), 12.45 (s, 1H, 2′-OH), 13.68 (s, 1H, 3-OH). **11c″** (2-hydroxychromanone) : 2.84 (AB q, 2H, 3-H), 6.70 (dd, J = 9.1 and 2.2 Hz, 1H, 6-H), 7.85 (d, J = 9.1 Hz, 1H, 5-H). Non-separable signals : 1.35 (m, 2H, 6-H), 1.62 (m, 2H, 5-H), 3.48 (s, 3H, 4′/7-OCH$_2$OC**H**$_3$), 5.20 (s, 2H, 4′-OCH$_2$OC**H**$_3$), 6.50-6.62 (m, 2H, 3′/8- and 5′-H). Ratio of isomers **11c**:**11c′**:**11c″** = 37:59:4.

Anal calc for $C_{15}H_{20}O_7$ (280.32) : C, 64.27; H, 7.19. Found : C, 64.59; H, 7.38.

Preparation of flavones **2** *and chromones* **1**. *General procedure*

A mixture of β-diketone **9** or **11** (3.00 mmol), Amberlyst 15 resin (0.75 g) and propan-2-ol (15 mL) was stirred at reflux temperature and the reaction was monitored by TLC. After completion the reaction DMF was added to the mixture to dissolve the precipitated flavone **2** (DMF addition was unnecessary in the case of chromones **1**). The resin was filtered off and washed with propan-2-ol, the filtrate was evaporated *in vacuo* and the residue was recrystallized from methanol.

- *4′-Hydroxyflavone* **2a**

Reaction time : 4.75 h, yield : 83%. Mp : 275-277°C. Lit [30] mp : 269-271°C.

IR : 3 140 br (OH), 3 070, 3 022, 1 630 (C=O), 1 598, 1 578, 1 564, 1 480, 1 464, 1 386 (flavone skeleton), 1 298, 1 264 (C-OH), 1 180, 836, 776 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.85 (s, 1H, 3-H), 6.95 (d, J = 7.8 Hz, 2H, 3′,5′-H), 7.47 (m, 1H, 6-H), 7.68-7.83 (m, 2H, 7,8-H), 7.96 (d, J = 7.8 Hz, 2H, 2′,6′-H), 8.02 (dd, J = 8.3 and 2.1 Hz, 1H, 5-H), 10.35 (br s, 1H, 4′-OH).

Anal calc for $C_{15}H_{10}O_3$ (238.25) : C, 75.62; H, 4.23. Found : C, 75.45; H, 4.48.

- *7-Hydroxyflavone* **2b**

Reaction time : 6.5 h, yield : 93%. Mp : 242-244°C. Lit [31] mp : 240°C.

IR : 3 178 br (OH), 1 626 (C=O), 1 582, 1 452, 1 380 (flavone skeleton), 1 248 (C-OH), 1 164, 846, 770, 688 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.94 (s, 1H, 3-H), 6.95 (d, J = 2.3 Hz, 1H, 8-H), 7.01 (dd, J = 8.1 Hz and 2.3 Hz, 1H, 6-H), 7.60 (m, 3H, 3′,4′,5′-H), 7.91 (d, J = 8.1 Hz, 1H, 5-H), 8.08 (m, 2H, 2′,6′-H), 10.86 (s, 1H, 7-OH).

Anal calc for $C_{15}H_{10}O_3$ (238.25) : C, 75.62; H, 4.23. Found : C, 75.31; H, 4.03.

- *7-Hydroxy-4′-methoxyflavone (Pratol)* **2c**

Reaction time : 12 h, yield : 94%. Mp : 268-270°C. Lit [32] mp : 264°C.

IR : 3 100 br (OH), 2 850 (MeO), 1 635 (C=O), 1 615, 1 586, 1 559, 1 519, 1 433, 1 390 (flavone skeleton), 1 257, 1 251 (C-O-C and C-OH), 1 182, 1 097, 1 030, 913, 838, 827 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 3.85 (s, 3H, 4′-MeO), 6.82 (s, 1H, 3-H), 6.92 (dd, J = 9.0 and 2.0 Hz, 1H, 6-H), 7.00 (d,

$J = 2.0$ Hz, 1H, 8-H), 7.10 (d, $J = 8.9$ Hz, 2H, 3′,5′-H), 7.88 (d, $J = 9.0$ Hz, 1H, 5-H), 8.02 (d, $J = 8.9$ Hz, 2H, 2′,6′-H), 10.80 (s, 1H, 7-OH).

Anal calc for $C_{16}H_{12}O_4$ (268.27) : C, 71.61; H, 4.51. Found : C, 71.33; H, 4.71.

• *4′-Bromo-7-hydroxyflavone* **2d**

Reaction time : 11 h, yield : 94%. Mp : 290-292°C (dec).

IR : 3 090 br (OH), 1 630 (C=O), 1 596, 1 579, 1 560, 1 492, 1 458, 1 412, 1 382 (flavone skeleton), 1 339, 1 250 (C-OH), 1 169, 1 098, 1 076 (C-Br), 1 010, 912, 824 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.92 (s, 1H, 3-H), 7.00 (m, 1H, 6,8-H), 7.78 (d, $J = 8.0$ Hz, 2H, 3′,5′-H), 7.90 (d, $J = 8.9$ Hz, 1H, 5-H), 8.01 (d, $J = 8.0$ Hz, 2H, 2′,6′-H), 10.85 (s, 1H, 7-OH).

Anal calc for $C_{15}H_9BrO_3$ (317.15) : C, 56.81; H, 2.86; Br, 25.20. Found : C, 56.97; H, 2.59; Br, 25.12.

• *7,4′-Dihydroxyflavone* **2e**

Reaction time : 3 h, yield : 87%. Mp : 324-328°C (dec). Lit [33] mp : 316°C.

IR : 3 208 br (OH), 1 630 (C=O), 1 604, 1 560, 1 504, 1 448, 1 384 (flavone skeleton), 1 270, 1 250, 1 236, 1 224 (C-OH), 1 180, 826 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.73 (s, 1H, 3-H), 6.95 (d, $J = 8.7$ Hz, 2H, 3′,5′-H), 6.89-6.98 (m, 2H, 6,8-H), 7.87 (d, $J = 9.4$ Hz, 1H, 5-H), 7.92 (d, $J = 8.7$ Hz, 2H, 2′,6′-H), 10.26 (br s, 1H, 4′-OH), 10.77 (br s, 1H, 7-OH).

Anal calc for $C_{15}H_{10}O_4$ (254.25) : C, 70.86; H, 3.96. Found : C, 71.47; H, 4.12.

• *7,4′-Dihydroxy-3′-methoxyflavone (Geraldone)* **2f**

Reaction time : 3.75 h, yield : 96%. Mp : 285-290°C (dec). Lit [34] mp : 293-294°C.

IR : ~3 100 br (OH), 3 062, 2 948, 2 830 (MeO), 1 624 (C=O), 1 606, 1 560, 1 512, 1 456, 1 432, 1 372 (flavone skeleton), 1 296, 1 272, 1 248, 1 236 (C-O-C and C-OH), 1 186, 1 150, 848, 818 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 3.89 (s, 3H, 3′-MeO), 6.81 (s, 1H, 3-H), 6.88-6.96 (m, 3H, 6,8,5′-H), 6.99 (d, $J = 2.1$ Hz, 1H, 8-H), 7.53 (m, 2H, 2′,6′-H), 7.86 (d, $J = 8.8$ Hz, 1H, 5-H), 9.85 (br s, 1H, 4′-OH), 10.73 (br s, 1H, 7-OH).

Anal calc for $C_{16}H_{12}O_5$ (284.27) : C, 67.60; H, 4.26. Found : C, 67.23; H, 4.46.

• *7-Hydroxy-3′,4′,5′-trimethoxyflavone* **2g**

Reaction time : 10 h, yield : 76%. Mp : 278-282°C (AcOH). Lit [35] mp : 279-280°C.

IR : 3 100 br (OH), 2 952, 2 846 (MeO), 1 648 (C=O), 1 596, 1 508, 1 466, 1 421, 1 389 (flavone skeleton), 1 345, 1 320, 1 260, 1 244 (C-O-C and C-OH), 1 179, 1 134, 1 002, 840, 818 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 3.77 (s, 3H, 4′-MeO), 3.92 (s, 6H, 3′,5′-MeO), 6.95 (dd, $J = 8.8$ and 1.8 Hz, 1H, 6-H), 7.00 (s, 1H, 3-H), 7.08 (d, $J = 1.8$ Hz, 1H, 8-H), 7.33 (s, 2H, 2′,6′-H), 7.90 (d, $J = 9.2$ Hz, 1H, 5-H), 10.73 (br s, 1H, 7-OH).

Anal calc for $C_{18}H_{16}O_6$ (328.32) : C, 65.85; H, 4.91. Found : C, 66.24; H, 5.25.

• *5,7-Dihydroxyflavone (Chrysin)* **2h**

Reaction time : 4.5 h, yield : 84%. Mp : 282-284°C. Lit [36] mp : 289-290°C.

IR : 1 659 (C=O), 1 620 (C=C), 1 584, 1 505, 1 457, 1 362 (flavone skeleton), 1 173, 840 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.23 (d, $J = 2.2$ Hz, 1H, H-6), 6.54 (d, $J = 2.2$ Hz, 1H, 8-H), 6.98 (s, 1H, 3-H), 7.60 (m, 3H, 3′,4′,5′-H), 8.08 (m, 2H, 2′,6′-H),10.93 (s, 1H, 7-OH), 12.84 (s, 1H, 5-OH).

Anal calc for $C_{15}H_{10}O_4$ (254.25) : C, 70.86; H, 3.96. Found : C, 70.97; H, 4.11.

• *5,7-Dihydroxy-4′-methoxyflavone (Acacetin)* **2i**

Reaction time : 4 h, yield : 96%. Mp : 262-264°C. Lit [32] mp : 261°C.

IR : 3 164 br (OH), 2 840 (MeO), 1 652 (C=O), 1 606, 1 584, 1 564, 1 508, 1 430, 1 366 (flavone skeleton), 1 300, 1 240 (C-O-C and C-OH), 1 186, 1 166, 1 032 (C-O-C), 826 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 3.87 (s, 3H, 4′-MeO), 6.21 (d, $J = 2.0$ Hz, 1H, 6-H), 6.52 (d, $J = 2.0$ Hz, 1H, 8-H), 6.88 (s, 1H, 3-H), 7.10 (d, $J = 9.0$ Hz, 2H, 3′,5′-H), 8.04 (d, $J = 9.0$ Hz, 2H, 2′,6′-H), 10.90 (s, 1H, 7-OH), 12.90 (s, 1H, 5-OH).

Anal calc for $C_{16}H_{12}O_5$ (284.25) : C, 67.60; H, 4.26. Found : C, 67.36; H, 4.26.

• *7-Hydroxychromone* **1a**

Reaction time : 4 h, yield : 97%. Mp : 219-222°C. Lit [37] mp : 221°C.

IR : 3 100 br (OH), 2 932, 1 628 (C=O and C=C), 1 560, 1 406 (chromone skeleton), 1 312, 1 268, 1 238 (C-OH), 1 042, 860, 842, 814 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 6.22 (d, $J = 6.1$ Hz, 1H, 3-H), 6.85 (d, $J = 2.2$ Hz, 1H, 8-H), 6.92 (dd, $J = 8.7$ and 2.2 Hz, 1H, 6-H), 7.88 (d, $J = 8.7$ Hz, 1H, 5-H), 8.15 (d, $J = 6.1$ Hz, 1H, 2-H), ~10.8 (very br s, 1H, 7-OH).

Anal calc for $C_9H_6O_3$ (162.15) : C, 66.67; H, 3.73. Found : C, 66.79; H, 3.91.

• *7-Hydroxy-2-methylchromone* **1b**

Reaction time : 9 h, yield : 82%. Mp : 253-257°C (dec). Lit [38] mp : 254-255°C.

IR : 3 104 br (OH), 2 940, 1 646 (C=O), 1 610 (C=C), 1 558, 1 508, 1 394 (chromone skeleton), 1 370, 1 346, 1 258, 1 234 (C-OH), 1 186, 1 096, 1 000, 836 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 2.33 (s, 3H, 2-Me), 6.10 (s, 1H, 3-H), 6.81 (d, $J = 1.9$ Hz, 1H, 8-H), 6.88 (dd, $J = 8.7$ and 1.9 Hz, 1H, 6-H), 7.83 (d, $J = 8.7$ Hz, 1H, 5-H). No signal for OH group was detected (too broad).

Anal calc for $C_{10}H_8O_3$ (176.17) : C, 68.17; H, 4.58. Found : C, 67.99; H, 4.65.

• *2-Butyl-7-hydroxychromone* **1c**

Reaction time : 7.5 h, yield : 84%. Mp : 117-120°C.

IR : 3 068 br (OH), 2 956, 2 934, 2 870, 1 628 (C=O and C=C), 1 568, 1 458, 1 424, 1 396 (chromone skeleton), 1 374, 1 348, 1 320, 1 268, 1 226 (C-OH), 1 172, 1 094, 986, 848 cm^{-1}.

^{1}H NMR (DMSO-d_6) : 0.94 (t, $J = 7.2$ Hz, 3H, 2-$(CH_2)_3$**CH_3**), 1.40 (m, 2H, 2-$(CH_2)_2$**CH_2**CH_3), 1.66 (m, 2H, 2-CH_2**CH_2**CH_2CH_3), 2.61 (t, $J = 7.4$ Hz, 2H, 2-**CH_2**$(CH_2)_2CH_3$), 6.19 (s, 1H, 3-H), 6.99 (d, $J = 1.9$ Hz, 1H, 8-H), 7.06 (dd, $J = 8.8$ and 1.9 Hz, 1H, 6-H), 8.08 (d, $J = 8.8$ Hz, 1H, 5-H), ~10.4 (very br s, 1H, 7-OH).

Anal calc for $C_{13}H_{14}O_3$ (218.25) : C, 71.54; H, 6.47. Found : C, 71.89; H, 6.78.

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