Facile and regioselective synthesis of 4´, 7-dihydroxy-4-phenyl-chroman-2-ones

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Abstract

A highly effective, facile, one-pot regioselective synthesis of a series of 4´,7-dihydroxy-4-phenyl-chroman-2-ones is described. The mechanism involves a dienone-phenol rearrangement followed by a Michael type reaction.

Keywords: Chroman-2-ones, Michael addition, esterification, regioselective synthesis

Introduction

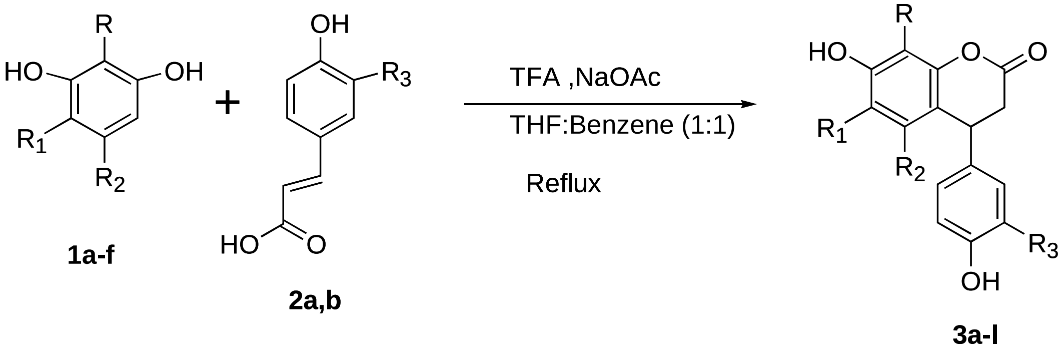
Tannins have attracted scientific interest because of their wide range of biological actions,[1] such as selective inhibition of HIV replication.[2] Chinese and Japanese medicines use tannin-containing plant extracts for the treatment of infections and disease.[3] The flavonoids 4′,7-dihydroxy-4-phenyl-chroman-2-ones, which are tannins found in woody plants, might be attractive candidates for new lead compounds for biological testing. However, they are minor constituents in these plants and, because of their high polarity, are difficult to isolate in significant amount. Thus, appropriate methods for their synthesis are desired. Recently, Kadota *et al.*[4] reported a facile and regioselective synthesis of phenylpropanoid-substituted flavan-3-ols by the reaction of caffeic acid and *p*-hydroxycinnamic acid with catechin and epicatechin in the presence of trifluoroacetic acid (TFA) and sodium acetate. The reaction was highly dependent on solvent used with THF or THF-benzene (1:1) giving the highest selectivity. Furthermore, acid derivatives lacking a 4-phenolic hydroxy group (*e.g.* *p*-methoxycinnanmic acid) decomposed under these conditions. A mechanism involving a dienone-phenol rearrangement followed by a Michael-type reaction[5] was proposed.

In another study, Speranza *et al.*[6] prepared another series of chroman-2-ones and chroman-3-ones by the reaction of methyl cinnamates and resorcinols in *o*-xylene under reflux. The yields of the chroman-2-ones were modest and many cases mixtures of regioisomers were obtained. Subsequently, Lee[7] prepared a series of 5,7-dihydroxy-4-phenylneoflavonoids by the

Montmorillonite K-10 catalysed reaction of phlorogucinol and cinnamyl chlorides. However, several of these flavonoids were not pure (as indicated by hplc) and in one case the other regioisomeric product, 7-hydroxy-4-(dihydropyhenyl)-chroman-2-one was obtained.

Results and Discussion

Using Kadota's conditions, we have found that 4-hydroxycinnamic acid (**2a**) and 3,4-dihydroxy-cinnamic acid (**2b**) reacted with several resorcinols (**1a-f**) regioselectively to give 4',7-dihydroxy-4-phenyl-chroman-2-ones (**3a-l**) using TFA and sodium acetate in THF-benzene (1:1) (Eq. 1).



1a-f

2a,b

3a-l

The results are listed in Table 1 and reveal important points. First, the reaction yields are highly dependent upon solvent. For example, the reaction **1a** with **2a** in THF-benzene (1:1) gave 4',7-dihydroxy-4-phenyl-chroman-2-one (**3a**) exclusively in 95% yield. However the use of THF (entry 2) or dioxane (entry 3) gave a mixture of **3a** and its 5-hydroxy isomer, while an inextractable tarry residue (entry 4) was obtained when the reaction of **1a** and **2a** was carried out in DMSO. The yields of the other products listed in Table 1 are produced as single products and with, few exceptions (54%, entry 8 and 60%, entry13), in excellent yields ranging from 85-99%. Compounds (**3b,d-l**) are new, while the yields of the known compounds (**3a,c**) listed in Table 1 are vastly superior to previously reported synthetic methods. For example, compound (**3c)** was obtained exclusively in 85% yield, whereas a mixture of **3c** and its 5-hydroxy regioisomers were obtained in low yields in a previous study.[6]

The products were identified on the basis of ^{1}H NMR and ^{13}C NMR spectroscopy. In addition, the structures of 4',7-dihydroxy-5-methyl-4-phenyl-chroman-2-one (**3c)** and 6-chloro-4'7-dihydroxy-3'-methoxy-4-phenyl-chroman-2-one (**3h**) were determined by single crystal X-ray crystallography; ORTEP drawings for **3c** and **3h** are shown in Figure 1 and Figure 2, respectively.

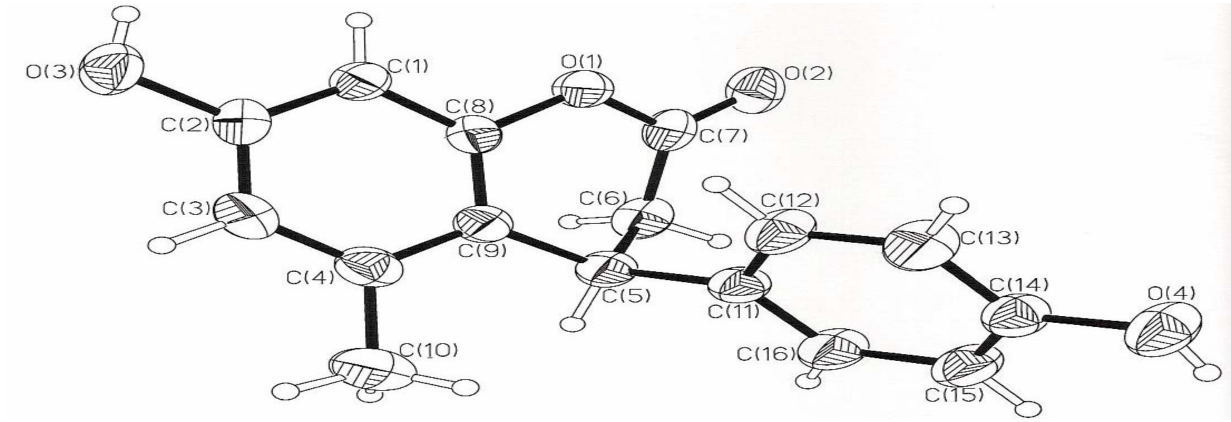
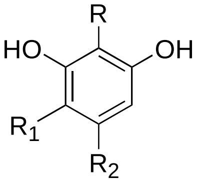
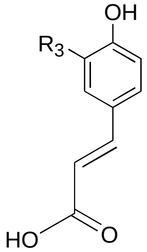
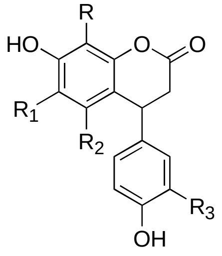


Figure 1. ORTEP of Compound (**3c**).

Table 1. Facile one-pot regioselective synthesis of 4',7-dihydroxy-4-phenyl-chroman-2-ones (**3a-l**) from resorcinols (**1a-f**) and hydroxyacids (**2a,b**)

Entry	 **1a-f**				 **2a,b**		Rx time[a] (h)	 **3a-l**					Yld (%)
	No.	R	R_1	R_2	No.	R_3		No	R	R_1	R_2	R_3	
1	**1a**	H	H	H	**2a**	H	12	**3a**	H	H	H	H	95
2	**1a**	H	H	H	**2a**	H	10[b]	**3a**	H	H	H	H	31
3	**1a**	H	H	H	**2a**	H	48[c]	**3a**[e]	H	H	H	H	16
4	**1a**	H	H	H	**2a**	H	20[d]	**3a**	H	H	H	H	<1
5	**1b**	H	Cl	H	**2a**	H	8	**3b**	H	Cl	H	H	99
6	**1c**	H	H	Me	**2a**	H	13	**3c**	H	H	Me	H	85
7	**1d**	H	Br	H	**2a**	H	10	**3d**	H	Br	H	H	86
8	**1e**	H	H	OMe	**2a**	H	16	**3e**	H	H	OMe	H	54
9	**1f**	Me	H	H	**2a**	H	10	**3f**	Me	H	H	H	89
10	**1a**	H	H	H	**2b**	OMe	12	**3g**	H	H	H	OMe	91
11	**1b**	H	Cl	H	**2b**	OMe	20	**3h**	H	Cl	H	OMe	94
12	**1c**	H	H	Me	**2b**	OMe	12	**3i**	H	H	Me	OMe	99
13	**1d**	H	Br	H	**2b**	OMe	10	**3j**	H	Br	H	OMe	60
14	**1e**	H	H	OMe	**2b**	OMe	7	**3k**	H	H	OMe	OMe	97
15	**1f**	Me	H	H	**2b**	OMe	14	**3l**	Me	H	H	OMe	93

[a] Unless indicated otherwise, THF-C_6H_6 solvent system was used. [b] THF. [c] dioxane.
[d] DMSO. [e] 5-hydroxy isomer also formed in about 10% yield as determined by ^{1}H NMR.

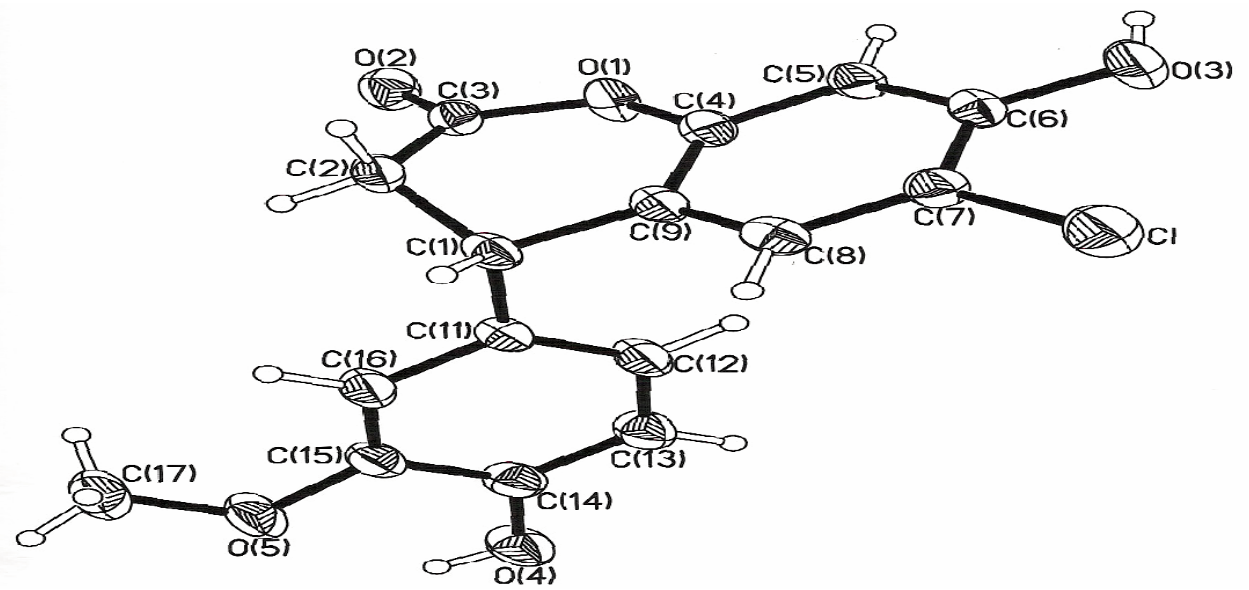
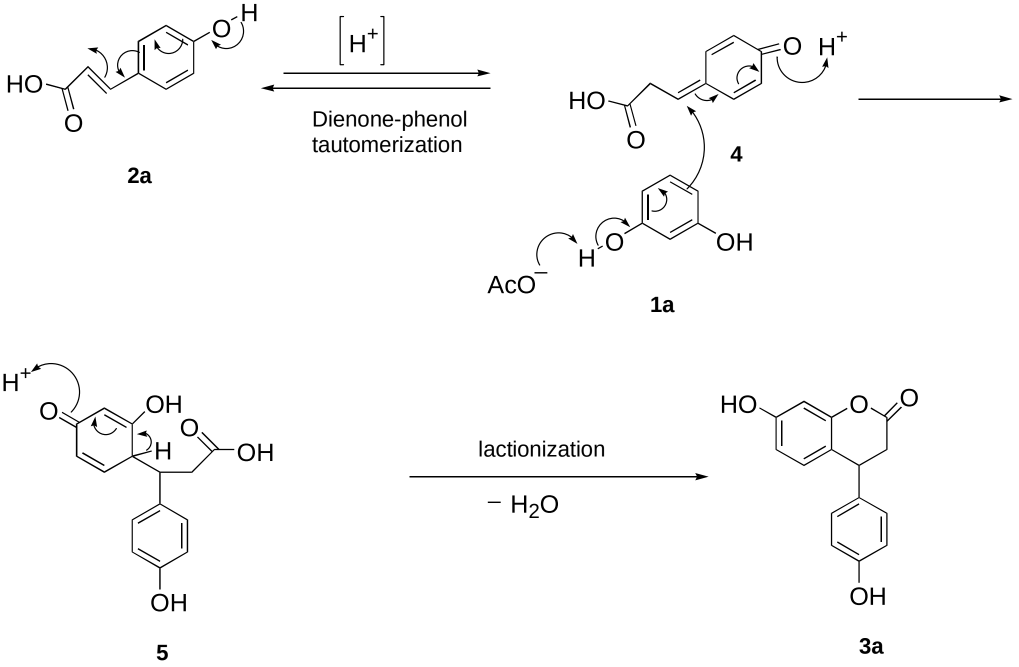


Figure 2. ORTEP for Compound (**3h**).

We subsequently found that cinnamic acid (**2c**) and p-methoxycinnamic acid (**2d**) failed to react with resorcinol **(1a**), indicating the importance of the 4-phenolic hydroxy group in these reactions. This fact coupled with our observation that the reactions of resorcinol (**1a)** with acids (**2a,b)** failed in the absence of TFA, even after prolonged treatment under similar conditions, are in agreement with Kadota's[4] proposed mechanism. Scheme 1 describes the salient features of this mechanism using the reaction of **1a** and **2a** as typical example.



Scheme 1

Thus, 4-hydroxycinnamic acid **2a** undergoes rearrangement in the presence of TFA to give the dienone (**4**).[8] This rearrangement is assisted by the resonance effect of the 4-phenolic hydroxy group. Dienone (**4**), acting as a Michael acceptor, then undergoes addition at its electron-deficient β-position of **4** by the C-5 position of resorcinol (**1a**) to give adduct (**5**). Adduct (**5**) then ring closes by lactonization to provide the product (**3a**).

In conclusion, we have described a facile, one-step procedure for construction of 4',7-dihydroxy-4-phenyl-chroman-2-ones. Biological activities of the synthesized compounds are now under investigation and will be reported elsewhere.

Experimental Section

General Procedures. Melting points were taken on a Mel-Temp capillary apparatus and are uncorrected with respect to stem correction. IR spectra were recorded on a Nicolet Magna-IRTM 550 FTIR spectrophoto-meter. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AVANCE DRX-400 Multinuclear NMR spectrometer. Chemical shifts are reported in reference to TMS as internal standard. The glassware was heated in an oven at 125 ºC prior to use. Elemental analysis were obtained from SMU Analytical Services Laboratories. HRMS analyses were provided by the Washington University Mass Spectrometry Resource, an NIH Research Resource (Grant No. P41RR0954).

General procedure using the synthesis of 3a as typical example

A mixture of resorcinol (**1a**, 200 mg, 1.81 mmol), p-hydroxycinnamic acid (**2a**, 200 mg, 1.21 mmol) and 1 equiv of NaOAc (143 mg, 1.81 mmol) was dissolved in THF: benzene(1:1) (10 mL) under an Ar atmosphere. To the solution, 6 equiv of TFA (0.83 mL, 10.9 mmol) was added, and the mixture was refluxed with stirring. The progress of reaction was continuously monitored by checking the disappearance of the resorcinol spot on TLC every hour. The reaction was then quenched by adding saturated sodium bicarbonate solution (10mL) and the mixture was extracted with ethyl acetate (3 X 30 mL). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography using ethyl acetate: hexane (3:7) as eluent to afford the lactonization product (**3a**). Compounds (**3b-l)** were synthesized according this procedure and the spectral data of **3a-l** are as follows.

4',7-Dihydroxy-4-phenyl-chroman-2-one (3a). Colorless solid, mp 147-148 °C (lit.[6] 140-143 °C). ^{1}H NMR (400MHz, DMSO-d_6): δ 2.94 (dd, *J* = 15.8 , 6.3 Hz, 1H, H-3_a), 3.05 (dd, *J* = 15.8, 5.9Hz, 1H, H-3_b), 4.24 (t, *J* = 5.8Hz, 1H, H-4), 6.50 (d, *J* = 2.5 Hz, 1H, H-8), 6.53 (dd *J* = 8.7Hz, 2.5 Hz, 1H, H-6), 6.70 (d, *J* = 7.9Hz, 2H, H-3', H-5'), 6.83 (d, *J* = 8.0Hz, 1H, H-5), 6.92 (d, *J* = 7.9Hz, 2H, H-2', H-6'), 9.35 (bs, 7-OH), 9.71 (bs, 4'-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.81 (C-4), 38.83 (C-3), 104.12 (C-8), 112.45 (C-6), 116.31 (C-3',C-5'), 117.62 C-4a), 129.09 (C-2', C-4'), 129.80 (C-5), 132.73 (C-1'), 152.76 (C-7), 157.16 (C-8a), 158.34 (C-4'), 168.76 (C=O).

6-Chloro-4´,7-dihydroxy-4-phenyl-chroman-2-one (3b). Colorless needles, mp 197-197.5 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.97 (dd, *J* = 15.8, 6.5Hz, 1H, H-3$_a$), 3.06 (dd, *J* = 15.8, 6.5Hz, 1H, 3$_b$), 4.28 (d, *J* = 6.0Hz, 1H, H-4), 6.71 (s, 1H, H-8), 6.72 (d, *J* = 8.4Hz, 2H, H-3',H-5'), 6.94 (d, *J* = 8.1Hz, 2H, H2',H-6'), 6.97 (s, 1H, H-5), 9.42 (bs, 7-OH), 10.56 (bs, 4'-OH) ; ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 37.29(C-4), 38.57(C-3), 105.46(C-8), 116.05(C-3',C-5'), 116.42(C-6), 119.22(C-2',C-6'), 129.12(C-4a), 129.52(C-5), 132.09(C-1'), 151.20(C-8a), 153.75(C-4'), 157.30(C-7), 168.36(C=O); Anal. Calcd for $C_{15}H_{11}Cl\ O_4$: C, 61.98; H, 3.81. Found: C, 62.29; H, 3.94.

4´,7-Dihydroxy-5-methyl-4-phenyl-chroman-2-one (3c). Colorless needles, mp 211-212 °C (lit.^{6} 203-206 °C). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.03 (s, 5-CH$_3$), 2.76 (dd, *J* = 15.8, 6.5Hz, 1H, H-3a), 3.17 (dd, *J* = 15.6, 6.7Hz, 1H, H-3b), 4.30 (d, *J* = 6.0Hz, 1H, H-4), 6.39 (s, 1H, H-8), 6.47 (s, 1H, H-6), 6.66 (d, *J* = 8.0Hz, 2H, H-3',H-5'), 6.81 (d, *J* = 8.1Hz, 2H, H-2',H-6'), 9.34 (s, 7-OH), 9.65 (s, 4'-OH); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 19.29(5-CH$_3$), 36.59(C-4), 38.73(C-3), 102.03(C-8), 114.12(C-6), 115.26(C-3',C-5'), 116.39(C-4a), 128.58(C-2',C-6'), 132.39(C-1'), 138.24(C-5), 153.27(C-7), 157.12(C-8a), 157.97(C-4'), 168.54(C=O).

6-Bromo-4´,7-dihydroxy-4-phenyl-chroman-2-one (3d). Colorless solid, mp 193-194 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.96 (dd, *J* = 15.8, 6.6 Hz, 1H, H-3$_a$), 3.04 (dd, *J* = 15.8, 5.9Hz, 1H, H-3$_b$), 4.28 (d, *J* = 6.0Hz, 1H, H-4), 6.69 (s, 1H, H-8), 6.72 (d, 8.4Hz, 2H, H-3',H-5'), 6.93 (d, *J* = 8.4Hz, 2H, H-2',H-6'), 7.10 (s, 1H, H-5), 9.38 (s, 7-OH), 10.57 (s, 4'-OH); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 37.32(C-4), 38.54(C-3), 105.09(C-6), 115.19(C-8), 116.43(C-3',C-5'), 119.80(C-2',C-6'), 129.12(C-4a), 132.12(C-5), 132.41(C-1'), 151.87(C-8a), 154.76(C-4'), 157.32(C-7), 168.33(C=O). Anal. Calcd for $C_{15}H_{11}BrO_4$: C, 53.76; H, 3.31. Found: C, 53.98; H, 3.40.

4´,7-Dihydroxy-5-methoxy-4-phenyl-chroman-2-one (3e). Colorless solid, mp 240-241.5 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.76 (dd, *J* = 15.7, 6.5Hz, 1H, H-3$_a$), 3.14 (dd, *J* = 15.7, 6.8Hz, 1H. H-3$_b$), 3.33 (s, 5-OCH$_3$), 4.35 (d, *J* = 6.6Hz, 1H, H-4), 6.16 (d, *J* = 1.8Hz, 1H, H-8), 6.27 (s, 1H, H-6), 6.64 (dd, *J* = 8.4, 3.2Hz, 2H, H-3'H-5'), 6.82 (dd, *J* = 8.4, 3.0Hz, 2H, H-2',H-6'), 9.30 (s, 7-OH), 9.81 (s, 4'-OH); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 33.74(C-4), 38.18(C-3), 56.51(5-OCH$_3$), 96.31(C-6), 96.57(C-8), 105.36(C-4a), 116.21(C-3',C-5'), 128.38(C-2',C-6'), 133.02(C-1'), 153.45(C-4'), 157.00(C-8a), 157.94(C-7), 159.13(C-5), 168.65(C=O). Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.13; H, 4.93. Found: C, 66.98; H, 5.06.

4´,7-Dihydroxy-8-methyl-4-phenyl-chroman-2-one (3f). Colorless solid, mp 211-212 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.07 (s, 8-CH$_3$), 2.97 (dd, *J* = 15.8, 6.4Hz, 1H, H-3$_a$), 3.00 (dd, *J* = 15.8, 6.5Hz, 1H. H-3$_b$), 4.22 (d, *J* = 6.2Hz 1H, H-4), 6.57 (d, *J* = 8.3Hz 1H, H-6), 6.65 (d, *J* = 8.2Hz 2H, H-3',H-5'), 6.73(d, *J* = 8.4Hz, 1H, H-5), 6.91 (d, *J* = 8.4Hz, 2H, H-2',H-6'), 9.34 (s, 7-OH), 9.59 (s, 4'-OH); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 9.32(8-CH$_3$), 37.67(C-4), 39.19(C-3), 111.35(C-8), 112.50(C-6), 116.26(C-3',C-5'), 117.69(C-5), 126.11(C-4a), 129.09(C-2',C-6'), 132.79(C-1'), 150.97(C-4'), 156.13(C-8a), 157.11(C-7), 168.86(C=O); HRMS (*m/z*): Calcd for $C_{16}H_{14}O_4$: 270.0892. Found: 270.0888.

4´,7-Dihydroxy-3´-methoxy-4-phenyl-chroman-2-one (3g). Colorless solid, mp 210-211 °C.^{1}H NMR (400 MHz, DMSO-d_6): δ 2.35 (dd, *J* = 15.7,6.3Hz, 1H, H-3$_a$), 3.02 (dd, *J* = 15.8, 6.2Hz, 1H. H-3$_b$), 3.71 (s, 3’-OCH$_3$), 4.24 (d, *J* = 6.1Hz, 1H, H-4), 6.44 (dd, *J* = 8.0, *J* = 1.9Hz, 1H, H-6), 6.50 (d, *J* = 2.2Hz, 1H, H-8), 6.53 (d, *J* = 8.2 Hz, 1H, H-5), 6.69 (d, *J* = 8.0 Hz, 1H, H-5’), 6.83 (d, *J* = 8.2Hz, 2H, H-2’,H-6’), 8.92 (s, 7-OH), 9.72 (s, 4’-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.75(C-4), 39.23(C-3), 56.46(3’-OCH$_3$), 104.31(C-8), 112.46(C-6), 112.52(C-2’), 116.36(C-5’), 117.61(C-6’), 120.25(C-4a), 129.80(C-5), 133.35(C-1’), 146.43(C-4’), 148.61(C-3’), 152.76(C-8), 158.35(C-7), 168.82(C=O); HRMS (*m/z*): Calcd for $C_{16}H_{14}O_5$: 286.0841. Found: 286.0852.

6-Chloro-4´,7-dihydroxy-3´-methoxy-4-phenyl-chroman-2-one (3h). Colorless solid, mp 211-212 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.96 (dd, *J* = 15.8,6.4Hz, 1H, H-3$_a$), 3.12 (dd, *J* = 15.7, 6.5Hz, 1H. H-3$_b$), 3.72 (s, 3’-OCH$_3$), 4.28 (d, *J* = 6.2Hz, 1H, H-4), 6.45 (d, *J* = 2.5, Hz, 1H, H-8), 6.71 (d, *J* = 8.5Hz, 2H, H-2’,H-6’), 6.80 (s, 1H, H-5), 6.97 (d, *J* = 8.1Hz, 1H, H-5’), 8.96 (bs, 7-OH), 10.56 (bs, 4’-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.25(C-4), 39.01(C-3), 56.52(3’-OCH$_3$), 105.44(C-8), 112.55(C-2’), 116.07(C-5’), 116.46(C-6), 119.24(C-6’), 120.24(C-4a), 129.52(C-5), 132.72(C-1’), 146.59(C-4’), 148.68(C-3’), 151.19(C-8a), 153.72(C-7), 168.39(C=O); HRMS (*m/z*): Calcd for $C_{16}H_{13}ClO_5$: 320.0451. Found: 320.0461.

4´,7-Dihydroxy-3´-methoxy-5-methyl-4-phenyl-chroman-2-one (3i). Colorless solid, mp 182-183 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.05 (s, 5-CH$_3$), 2.82 (dd, *J* = 15.8,6.8Hz, 1H, H$_a$), 3.17 (dd, *J* = 15.7, 6.8Hz, 1H, H$_b$), 3.70 (s, 3’-OCH$_3$), 4.31 (d, *J* = 6.2Hz, 1H, H-4), 6.39 (s, 1H, H-8), 6.47 (s, 1H, H-6), 6.63 (d, *J* = 8.0Hz, 2H, H-2’,H-6’), 6.72 (s, 1H, H-5’), 8.89 (bs, 7-OH), 9.64 (bs, 4’OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 19.30 (5-CH$_3$), 37.03(C-4), 38.72(C-3), 56.43(3’-OCH$_3$), 102.06(C-8), 112.15(C-6), 114.17(C-2’), 115.17(C-5’), 116.44(C-6’), 119.43(C-4a), 133.17(C-1’), 138.35(C-5), 146.43(C-4’), 148.66(C-3’), 153.35(C-8a), 158.01(C-7), 168.57(C=O); HRMS (*m/z*): calcd for $C_{17}H_{16}O_5$: 300.0998. Found: 300.0995

6-Bromo-4´,7-dihydroxy-3´-methoxy-4-phenyl-chroman-2-one (3j). Colorless solid, mp 209-210 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.04 (dd, *J* = 15.8,6.8Hz, 1H, H-3$_a$), 3.16 (dd, *J* = 15.7, 6.6Hz, 1H. H-3$_b$), 3.72 (s, 3’-OCH$_3$), 4.29 (d, *J* = 6.5 Hz, 1H, H-4), 6.45 (d, *J* =7.8, Hz, 1H, H-5’), 6.71 (d, *J* = 8.1Hz, 2H, H-2’,H-6’), 6.80 (s, 1H, H-8), 7.11 (s, 1H, H-5), 8.96 (bs, 7-OH), 10.59 (bs, 4’-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.28(C-4), 38.97(C-3), 56.51(3’-OCH$_3$), 105.10(C-6), 105.17(C-8), 112.54(C-2’), 116.48(C-5’), 119.79(C-6’), 120.25(C-4a), 132.41(C-5), 132.76(C-1’), 146.59(C-4’), 148.68(C-3’), 150.97(C-8a), 154.76(C-7), 168.37(C=O); HRMS (*m/z*): Calcd for $C_{16}H_{13}BrO_5$: 363.9946. Found: 363.9941.

4´,7-Dihydroxy-3´,5-dimethoxy-4-phenyl-chroman-2-one (3k). Colorless solid, mp 221-222 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.83 (dd, *J* = 15.8, 6.7Hz, 1H, H$_a$), 3.13 (dd, *J* = 15.8 Hz, 6.9Hz, 1H, H-$_b$), 3.70 (s, 5-OCH$_3$, 3’-OCH$_3$), 4.37 (d, *J* = 6.0Hz, 1H, H-4), 6.17 (s, 1H, H-8), 6.28 (d, *J* = 4.2Hz, 2H, H-2’,H-6’), 6.62 (s, 1H, H-6), 6.73 (d, *J* = 8.4Hz, 1H, H-5’), 8.87 (bs, 7-OH), 9.81 (bs, 4’-OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 34.07(C-4), 38.09(C-3), 56.42(5-OCH$_3$), 56.51(3’-OCH$_3$), 96.34(C-6), 96.57(C-8), 105.29(C-4a), 112.10(C-2’), 116.21(C-5’), 119.08(C-6’), 133.76(C-1’), 146.29(C-4’), 148.52(C-3’), 153.49(C-8a), 157.98(C-7), 159.14(C-5), 168.71(C=O); HRMS (*m/z*): Calcd for $C_{17}H_{16}O_6$: 316.0947. Found: 316.0944.

4´,7-Dihydroxy-3´-methoxy-8-methyl-4-phenyl-chroman-2-one (3l). Colorless solid, mp 162-163 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.06 (s, 8-CH$_3$), 3.01 (dd, *J* = 15.8,6.3Hz, 1H, H-3a), 3.19 (dd, *J* = 15.7, 6.8Hz, 1H. H-3b), 3.71 (s, 3’-OCH$_3$), 4.22 (d, *J* = 5.9Hz, 1H, H-4), 6.43 (d, *J* = 8.0 Hz, 1H, H-6), 6.57 (d, *J* = 8.3Hz, 1H, H-5), 6.67 (d, *J* = 8.1Hz, 2H, H-2’,H-6’), 6.78 (d, *J* = 8.3Hz, 1H, H-5’), 8.89 (bs, 7-OH), 9.58 (bs, 4’-OH); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 9.32(8-CH$_3$), 37.60(C-4), 39.60(C-3), 56.48(3’-OCH$_3$), 111.37(C-6), 112.49(C-2’), 112.60(C-5’), 116.33(C-8), 117.72(C-6’), 120.30(C-5), 126.10(C-4a), 133.39(C-1’), 146.39(C-4’), 148.58(C-3’), 150.97(C-8a), 156.13(C-7), 168.91(C=O); HRMS (*m/z*): Calcd for $C_{17}H_{16}O_5$: 300.0998. Found: 300.0996.

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