Uncatalyzed Reaction of Phenols and Naphthols with Methyl Cinnamates. A Simple Synthesis of 4-Arylchroman-2-ones and 1-Arylbenzo[*f*]chroman-3-ones

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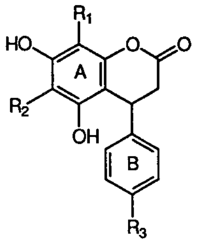
4-Arylchroman-2-ones and 1-arylbenzo[*f*]chroman-3-ones can be prepared in moderate to good yields by reaction of phenols or *β*-naphthols with *p*-substituted methyl cinnamates in *o*-xylene under reflux.

The 4-arylchroman-2-one system (cf. **1**) is of synthetic interest because it is present in a number of natural molecules, such as 4-aryl-3,4-dihydrocoumarins (neoflavonoids),[1,2] complex flavonoids,[3] e.g. calomelanols B (**1a**) and C (**1b**),[4] and 1-arylbenzo[*f*]chroman-3-ones.[5]

Although the preparation of specific 4-arylchroman-2-ones has been accomplished in different ways,[2,6,7] the general approach based on the condensation of phenols with cinnamic acids (or alkyl cinnamates), as well as the cyclization of phenyl cinnamates, has been exploited in strong acidic media only.[8] Due to the drastic conditions used, a variety of different products (i.e. cinnamates, chalcones, flavanones, and indanones) were found to be formed, besides chroman-2-ones, depending on the structures of the reacting molecules and the nature of the catalyst employed.

We report here that moderate to good yields of chroman-2-ones can be obtained by heating methyl (*E*)-cinnamates and phenols or *β*-naphthols in *o*-xylene under reflux without any added catalyst (Scheme 1). As an application of this preparative method, a two-step synthesis of calomelanol C (**1b**) was achieved from phloroglucinol (21 % overall yield). It should be pointed out that the only published syntheses of natural 5,7-dihydroxy-8-(3-phenylpropionyl)neoflavanones were accomplished from phloroacetophenone in five steps (compound **1d**, ca. 3 % overall yield),[7] or seven steps [calomelanol B (**1a**), yields not indicated].[4]



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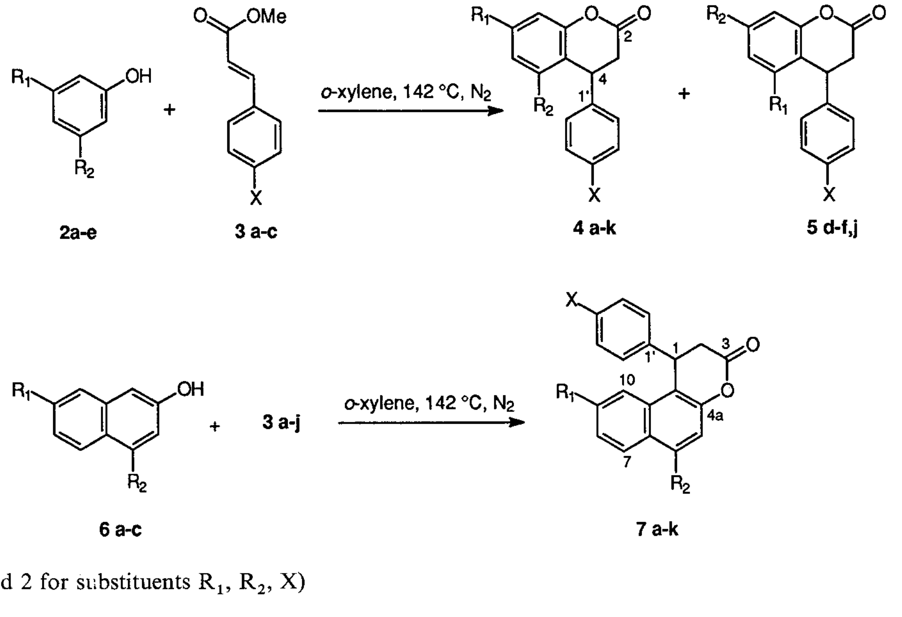
a R_1 = 4-OH-C_6H_4-$(CH_2)_2$-CO- R_2 = R_3 = H
b R_1 = C_6H_5-$(CH_2)_2$-CO- R_2 = H R_3 = OH
c R_1 = H R_2 = C_6H_5-$(CH_2)_2$-CO- R_3 = OH
d R_1 = C_6H_5-$(CH_2)_2$-CO- R_2 = R_3 = H

The general procedure described below was used for preparing the 4-arylchroman-2-ones **4**/**5** and the 1-arylbenzo[*f*]chroman-3-ones **7** listed in Tables 1 and 2, respectively. The structure of each product, whose physical and spectral data are reported in Table 3, was confirmed, when necessary, by ^{1}H NOE, ^{1}H- ^{1}H COSY and HETCOR experiments.



Scheme 1 (see Tables 1 and 2 for substituents R_1, R_2, X)

Table 1. Condensation of Phenols **2a–e** with Methyl Cinnamates **3a–c**

Entry	Reagents	R_1	R_2	X	Product	Reaction time [h]	Isolated Yield [%][a]
1	**2a/3a**	OH	H	OH	**4a**	11	52
2	**2a/3b**	OH	H	OMe	**4b**	10	55
3	**2a/3c**	OH	H	NMe_2	**4c**	5	60
4	**2b/3a**	OH	Me	OH	**4d (5d)**[b]	10	32 (8)
5	**2b/3b**	OH	Me	OMe	**4e (5e)**[b]	14	21 (13)
6	**2b/3c**	OH	Me	NMe_2	**4f (5f)**	7	75 (2.5:1)[c]
7	**2c/3a**	OH	OH	OH	**4g**	2	90
8	**2c/3b**	OH	OH	OMe	**4h**	3	61
9	**2c/3c**	OH	OH	NMe_2	**4i**	1	70
10	**2d/3a**	OH	OMe	OH	**4j (5j)**	13	76 (2:1)[d]
11	**2e/3a**	OMe	OMe	OH	**4k**	13	61

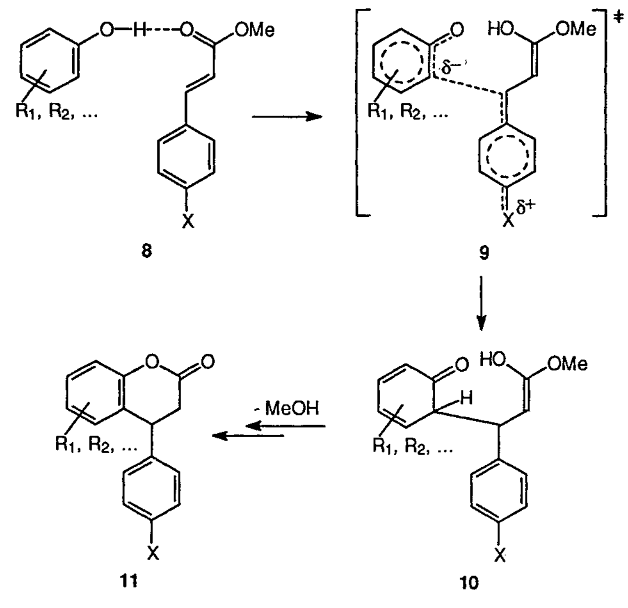
[a] Isolated yield of pure product. [b] Separation of the two isomers was performed by repeated flash chromatography. [c] Yield refers to the isomeric mixture. Regioisomer ratio determined by ^{1}H NMR analysis. [d] Unresolved mixture of the two isomers.

The solvent of choice for the condensation reaction appears to be *o*-xylene, in that no reaction was found to occur either in amphiprotic (e.g. H_2O at 100°C) or in dipolar aprotic solvents (e.g. nitrobenzene, 1,3-dimethoxybenzene, dimethylsulfoxide at 140–150°C).[9] The reaction temperature and the substrate concentration are also critical. Thus, lowering the temperature and/or increasing the solvent/reagents ratio caused the reaction rate to drop steeply. On the other hand, on increasing the reaction temperature, e.g. by using a higher-boiling apolar solvent like mesitylene, no advantage was apparent because of a more pronounced formation of phenolic byproducts.

As concerns the reactivity of the phenolic substrate it must be noted that neither phenol nor α-naphthol gave rise to the corresponding chromanone even if the counterpart was the highly reactive methyl (*E*)-*p*-coumarate (**3a**). In addition, β-naphthol (**6a**), resorcinol (**2a**) and naphthoresorcinol (**6b**) furnished one product, while a mixture of the two regioisomers (**4** and **5**) resulted from reactions of orcinol (**2b**) and phloroglucinol monomethyl ether (**2d**) (entries 4–6 and 10 of Table 1).

From a mechanistic point of view, it seems reasonable to assume the protonation of the ester function, followed by or with the concomitant formation of the C—C bond, as an early event in the process (Scheme 2). The involvement of H-bonded molecular complexes as depicted in **8** is supported by the the fact that the reaction between the nucleophilic phenol and the electrophilic center of the α,β-unsaturated ester is precluded in solvents acting as hydrogen-bond acceptors.[9] Analogous H-bonded associations have been invoked to explain the uncatalyzed phenol–formaldehyde reaction in nonpolar aprotic solvents.[10]

That the mechanism outlined in Scheme 2 may occur, at least when X is an electron-donor group, is strongly suggested by inspection of Table 2 which shows higher yields and shorter reaction times for methyl cinnamates bearing the NMe_2 or OH or OMe substituent in the *para* position. Similar effects have been reported in the case of addition



Scheme 2

of CN^- to 1,1-diaryl-2-nitroethylenes[11] and of amines to β-nitrostyrenes,[12] when these substrates were *para*-substituted with a OMe or NMe_2 group. The pronounced positive deviation from the Hammet plot was interpreted in terms of the ability of the electron-donor substituents to stabilize a radicaloid[11] or a cationoid center at the benzylic carbon. In the latter case a transition state similar to **9** was proposed.[12] It must also be considered that no intramolecular cyclization was observed when (*E*)-3-(*p*-methoxycinnamoyloxy)-1-naphthol[5] was kept under the reaction conditions employed for preparing chromanones according to Scheme 1.

Calomelanol C (**1b**), the first complex flavonoid possessing an oxygen function in the B ring,[4] was synthesized as follows. 3-Phenyl-1-(2,4,6-trihydroxyphenyl)propan-1-one[13] was condensed with methyl *p*-coumarate according to the general procedure. The two isomeric chroman-

Table 2. Condensation of Hydroxynaphthalenes **6a**–**c** with Methyl Cinnamates **3a**–**j**

Entry	Reagents	R^1	R^2	X	Product	Reaction time [h]	Isolated Yield [%][a]
1	**6a/3a**	H	H	OH	**7a**	17	35
2	**6b/3b**	H	OH	OMe	**7b**	9	60
3	**6c/3a**	OH	H	OH	**7c**	6	75
4	**6c/3b**	OH	H	OMe	**7d**	8	60
5	**6c/3c**	OH	H	NMe_2	**7e**	8	83
6	**6c/3d**	OH	H	Me	**7f**	14	31
7	**6c/3e**	OH	H	H	**7g**	15	43
8	**6c/3f**	OH	H	F	**7h**	9	50
9	**6c/3g**	OH	H	Cl	**7i**	14	60
10	**6c/3h**	OH	H	Br	**7j**	14	56
11	**6c/3i**	OH	H	CF_3	**7k**	11	34
12	**6c/3j**	OH	H	NO_2		no reaction	

[a] Isolated yield of pure product.

ones formed in approximately 2:1 ratio were identified, after separation through column chromatography, by means of their 2D two- and three-bond C–H correlation spectra. In the spectrum of the most abundant compound (50% isolated yield) the aromatic proton of the ring A ($\delta = 6.29$) caused a cross-peak with the carbon at $\delta = 156.70$ (C-8a) (which in turn gave a cross-peak with H-4 at $\delta = 4.48$), thus allowing structure **1c** to be assigned to this regioisomer. The other isomer (**1b**, 25% isolated yield) exhibited correlations between the aromatic proton at $\delta = 6.27$ and both phenolic carbons of the same ring, i.e. at $\delta = 160.14$ (C-5) and 162.55 (C-7). Compound **1b** was found to be identical with calomelanol C by comparison of its spectroscopic data with those reported for the natural product.[4]

Melting points (Büchi apparatus) are uncorrected. Microanalyses were obtained with a Perkin-Elmer 240 Elemental Analyzer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 300 and on a Bruker AC 200 spectrometer in DMSO-d_6, using the solvent signal as internal standard ($\delta_H = 2.50$, $\delta_C = 39.50$). Silica gel (Merck, 40–63 μm) was used for flash chromatography. Analytical TLC was performed on silica gel 60 F_{254} aluminum sheet (0.2-mm thickness, Merck) using the following eluents: A, CH_2Cl_2-EtOAc (3:1); B, Et_2O-hexane (1:1); C, $CHCl_3$-EtOAc (5:1); D, CH_2Cl_2-EtOAc (5:1); E, Et_2O-hexane (2:1); F, CH_2Cl_2-EtOAc (1:1); G, $CHCl_3$-EtOAc (5:3).

All reagents were of commercial quality or purified prior to use by standard methods. Methyl cinnamates **3a**–**j** were prepared by esterification of the corresponding acids with $MeOH/H_2SO_4$. Cinnamic acid, *p*-coumaric acid, and *p*-methoxy-, *p*-trifluoromethyl- and *p*-nitrocinnamic acid were commercially available. The other cinnamic acids were synthesized by condensation of the corresponding aldehydes with malonic acid in pyridine solution in the presence of piperidine.[14] Partial methylation of phloroglucinol (**2c**) to give mono- (**2d**) and dimethyl ether (**2e**) was carried out by treatment with Me_2SO_4/K_2CO_3.

General Procedure:

The mixture of the appropriate reagents, i.e. the phenol (2.5 mmol) and the methyl cinnamate (2.0 mmol) in anhydrous *o*-xylene (1 mL), was heated under reflux (142 °C) in N_2 atmosphere until complete disappearance of the ester. The reaction progress was monitored by TLC (eluent systems as reported in Table 3 for each product). After removing the solvent under reduced pressure, the residue was dissolved in MeOH, adsorbed on sea sand until completely dried, and flash-chromatographed on silica gel using the same eluent system as for TLC. Purity of the isolated product was checked by TLC, elemental analysis, ^1H and ^{13}C NMR.

Calomelanol C (1b):

3-Phenyl-1-(2,4,6-trihydroxyphenyl)propan-1-one (650 mg, 2.5 mmol), obtained by reaction of phloroglucinol with 3-phenylpropionitrile and $ZnCl_2$[13] in 86% yield, was treated with methyl *p*-hydroxycinnamate (**3a**) (360 mg, 2 mmol) in *o*-xylene (1 mL) according to the above procedure (reaction time, 2 h). Purification by flash chromatography (eluent A) afforded, in elution order, compounds **1c** (390 mg) and **1b** (195 mg) which were shown to be pure by TLC.

1b: $R_f = 0.39$ (eluent A); mp 221–224 °C.

^1H NMR (300.13 MHz, DMSO-d_6): $\delta = 2.87$ (br d, $J = 15.9$ Hz, 1 H, H-3a), 2.97 (app t, $<J> = 7.2$ Hz, 2 H, H_2-3″), 3.23 (dd, $J = 15.9$, 6.3 Hz, 1 H, H-3b), 3.38 (app t, $<J> = 7.2$ Hz, 2 H, H_2-2″), 4.45 (br d, $J = 6.3$ Hz, 1 H, H-4), 6.27 (s, 1 H, H-6), 6.70 (d, $J = 8.1$ Hz, 2 H, H-3′, H-5′), 6.93 (d, $J = 8.1$ Hz, 2 H, H-2′, H-6′), 7.19–7.30 (m, 5 H, aromatic), 9.24 (s, 1 H, 4′-OH), 10.90 (s, 1 H, 5-OH), 12.81 (s, 1 H, 7-OH).

^{13}C NMR (75.47 MHz, DMSO-d_6): $\delta = 29.91$ (C-3″), 32.63 (C-4), 36.33 (C-3), 44.95 (C-2″), 98.59 (C-6), 104.56 (C-8), 105.19 (C-4a), 115.29 (C-3′, C-5′), 125.67 (C-7″), 127.41 (C-2′, C-6′), 128.13 (C-5″, C-6″, C-8″, C-9″), 131.24 (C-1′), 141.00 (C-4″), 152.82 (C-8a), 156.13 (C-4′), 160.14 (C-5), 162.55 (C-7), 166.52 (C-2), 203.02 (C-1″).

$C_{24}H_{20}O_6$ (404.4)	calc. found	C 71.28 71.07	H 4.98 5.05

^{13}C NMR signals in acetone-d_6 were found to be coincident with those reported for calomelanol C.[4]

1c: $R_f = 0.63$ (eluent A); mp 203–205 °C.

^1H NMR (300.13 MHz, DMSO-d_6): $\delta = 2.89$ (br d, $J = 15.8$ Hz, 1 H, H-3a), 2.97 (app t, $<J> = 7.6$ Hz, 2 H, H_2-3″), 3.22 (dd, $J = 15.8$, 6.8 Hz, 1 H, H-3b), 3.45 (app t, $<J> = 7.6$ Hz, 2 H, H_2-2″), 4.48 (br d, $J = 6.8$ Hz, 1 H, H-4), 6.29 (s, 1 H, H-8), 6.73 (d, $J = 8.2$ Hz, 2 H, H-3′, H-5′), 6.94 (d, $J = 8.2$ Hz, 2 H, H-2′, H-6′), 7.19–7.30 (m, 5 H, aromatic), 9.25 (s, 1 H), 11.28 (s, 1 H) and 13.84 (s, 1 H) (5-OH, 7-OH and 4′-OH).

^{13}C NMR (75.47 MHz, DMSO-d_6): $\delta = 29.84$ (C-3″), 32.74 (C-4), 36.90 (C-3), 45.28 (C-2″), 94.96 (C-8), 104.23 (C-4a), 106.81 (C-6), 115.40 (C-3′, C-5′), 125.70 (C-7″), 127.36 (C-2′, C-6′), 128.17 (C-5″, C-6″, C-8″, C-9″), 131.69 (C-1′), 141.24 (C-4″), 156.24 (C-4′), 156.70 (C-8a), 106.87 (C-7), 161.57 (C-5), 166.77 (C-2), 205.64 (C-1″).

$C_{24}H_{20}O_6$ (404.4)	calc. found	C 71.28 71.05	H 4.98 5.10

Table 3. Chromanones **4a–i**, **k**, **5d–f**, and **7a–k** Prepared

Product[a]	R_f (eluent)[b]	mp (°C) (solvent for crystallization)	^{1}H NMR (DMSO-d_6) δ, J (Hz)	^{13}C NMR (DMSO-d_6) δ
4a	0.31 (B)	140–143 (petroleum ether –CH_2Cl_2)	2.95 (dd, J = 15.8, 6.2, 1H, H-3a), 3.07 (dd, J = 15.8, 6.2, 1H, H-3b), 4.26 (app t, $<J>$ = 6.2, 1H, H-4), 6.53 (d, J = 2.5, 1H, H-8), 6.56 (dd, J = 8.4, 2.5, 1H, H-6), 6.73 (d, J = 8.5, 2H, H-3', H-5'), 6.85 (d, J = 8.4, 1H, H-5), 6.95 (d, J = 8.5, 2H, H-2', H-6'), 9.29 (s, 1H) and 9.65 (s, 1H) (7-OH, 4'-OH)	36.80, 37.92, 103.14, 111.45, 115.31, 116.61, 127.43, 128.01, 128.72, 151.75, 156.14, 157.34, 167.60
4b	0.55 (C)	169–171 (hexane–EtOAc)	2.99 (dd, J = 15.7, 6.4, 1H, H-3a), 3.09 (dd, J = 15.7, 5.9, 1H, H-3b), 3.32 (s, 3H, OCH_3), 4.33 (app t, $<J>$ = 6.2, 1H, H-4), 6.53 (d, J = 2.6, 1H, H-8), 6.56 (dd, J = 8.1, 2.6, 1H, H-6), 6.85 (d, J = 8.1, 1H, H-5), 6.91 (d, J = 8.6, 2H, H-3', H-5'), 6.91 (d, J = 8.6, 2H, H-3', H-5'), 7.08 (d, J = 8.6, 2H, H-2', H-6'), 9.71 (s, 1H, 7-OH)	36.78, 37.93, 54.96, 103.23, 111.54, 114.08, 116.45, 128.18, 128.76, 133.55, 151.84, 157.47, 158.16, 167.58
4c	0.23 (C)	172–173 (hexane–EtOAc)	2.86 (s, 6H, $N(CH_3)_2$), 2.92 (dd, J = 15.9, 6.2, 1H, H-3a), 3.04 (dd, J = 15.9, 6.2, 1H, H-3b), 4.22 (app t, $<J>$ = 6.2, 1H, H-4), 6.49 (d, J = 2.3, 1H, H-8), 6.53 (dd, J = 8.1, 2.3, 1H, H-6), 6.67 (d, J = 8.7, 2H, H-3', H-5'), 6.84 (d, J = 8.1, 1H, H-5), 6.95 (d, J = 8.7, 2H, H-2', H-6'), 9.55 (s, 1H, 7-OH)	36.89, 37.84, 40.02, 103.15, 111.46, 112.56, 116.85, 127.58, 128.80, 128.91, 149.37, 151.80, 157.34, 167,80
4d	0.34 (D)	203–206 (hexane–EtOAc)	2.04 (s, 3H, CH_3), 2.77 (dd, J = 15.7, 1.8, 1H, H-3a), 3.16 (dd, J = 15.7, 6.3, 1H, H-3b), 4.31 (br d, J = 6.3, 1H, H-4), 6.39 (d, J = 2.3, 1H, H-8), 6.48 (d, J = 2.3, 1H, H-6), 6.67 (d, J = 8.6, 2H, H-3', H-5'), 6.82 (d, J = 8.6, 2H, H-2', H-6'), 9.26 (s, 1H) and 9.58 (s, 1H) (7-OH, 4'-OH); relevant NOE associations (% intensity enhancement) from H-4 to 5-CH_3 (5.7), from 5-CH_3 to H-4 (10.9) and to H-6 (11.7)	18.39, 35.79, 38.74, 101.21, 113.31, 114.41, 115.56, 127.69, 131.57, 137.34, 152.42, 156.24, 157.10, 167.55
4e	0.43 (E)	151 (hexane–EtOAc)	2.04 (s, 3H, CH_3), 2.79 (br d, J = 15.7, 1H, H-3a), 3.20 (dd, J = 15.7, 6.4, 1H, H-3b), 3.70 (s, 3H, OCH_3), 4.37 (br d, J = 6.4, 1H, H-4), 6.40 (d, J = 1.9, 1H, H-6), 6.48 (d, J = 1.9, 1H, H-8), 6.84 (d, J = 8.7, 2H, H-3', H-5'), 6.94 (d, J = 8.7, 2H, H-2', H-6'), 9.64 (s, 1H, 7-OH); relevant NOE associations (% intensity enhancement) from H-4 to 5-CH_3 (3.2), from 5-CH_3 to H-4 (12.8) and to H-6 (13.7)	18.13, 35.58, 37.57, 54, 84, 101.06, 113.14, 114.07, 127.53, 133.15, 137.13, 152.27, 156.99, 158.01, 167.17
4f	0.31 (C)		(in mixture with **5f**) 2.07 (s, 3H, CH_3), 2.79 (dd, J = 15.7, 1.7, 1H, H-3a), 2.85 (s, 6H, $N(CH_3)_2$), 3.17 (dd, J = 15.7, 6.4, 1H, H-3b), 4.31 (br d, J = 6.4, 1H, H-4), 6.41 (d, J = 2.1, 1H, H-8), 6.49 (d, J = 2.1, 1H, H-6), 6.65 (d, J = 8.7, 2H, H-3', H-5'), 6.85 (d, J = 8.7, 2H, H-2', H-6'), 9.52 (s, 1H, 7-OH); relevant NOE associations (% intensity enhancement) from H-4 to 5-CH_3 (2.1), from 5-CH_3 to H-4 (9.6) and to H-6 (9.1)	
4g	0.31 (F)	261–264 (hexane–EtOAc) Lit.[15] 260–270	2.76 (br d, J = 15.7, 1H, H-3a), 3.11 (dd, J = 15.7, 6.6, 1H, H-3b), 4.33 (br d, J = 6.6, 1H, H-4), 6.00 (s, 1H) and 6.16 (s, 1H) (H-6, H-8), 6.65 (d, J = 8.3, 2H, H-3', H-5'), 6.85 (d, J = 8.3, 2H, H-2', H-6'), 9.24 (s, 1H) and 9.67 (s, 1H) (5-OH, 7-OH, 4'-OH)	32.85, 37.18, 94.61, 98.71, 103.61, 115.12, 127.36, 132.40, 152.73, 155.13, 155.88, 157.57, 167.71
4h	0.31 (G)	147–148 (hexane–EtOAc)	2.79 (br d, J = 15.8, 1H, H-3a), 3.15 (dd, J = 15.8, 6.5, 1H, H-3b), 3.69 (s, 3H, OCH_3), 4.38 (br d, J = 6.5, 1H, H-4), 6.01 (d, J = 2.2, 1H) and 6.17 (d, J = 2.2, 1H) (H-6, H-8), 6.73 (d, J = 8.7, 2H, H-3', H-5'), 6.98 (d, J = 8.7, 2H, H-2', H-6'), 9.52 (s, 1H) and 9.71 (s, 1H) (5-OH, 7-OH)	32.92, 37.25, 55.02, 94.66, 98.70, 103.39, 113.95, 127.62, 134.27, 147.54, 152.87, 155.83, 157.78, 167.88
4i	0.12 (E)	175–178 (hexane–EtOAc)	2.79 (br d, J = 15.5, 1H, H-3a), 2.84 (s, 6H, $N(CH_3)_2$), 3.11 (dd, J = 15.5, 6.6, 1H, H-3b), 4.36 (br d, J = 6.6, 1H, H-4), 6.03 (d, J = 1.9, 1H) and 6.19 (d, J = 1.9, 1H) (H-6, H-8), 6.64 (d, J = 8.6, 2H, H-3', H-5'), 6.90 (d, J = 8.6, 2H, H-2', H-6'), 9.41 (s, 1H) and 9.57 (s, 1H) (5-OH, 7-OH)	32.71, 37.18, 40.02, 94.07, 98.70, 103.78, 112.48, 126.93, 129.69, 149.19, 152.72, 155.12, 157.48, 167.79
4k	0.21 (E)	202–204 (hexane–EtOAc)	2.79 (dd, J = 15.8, 1.2, 1H, H-3a), 3.17 (dd, J = 15.8, 6.5, 1H, H-3b), 3.73 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.39 (br d, J = 6.5, 1H, H-4), 6.39 (d, J = 2.2, 1H) and 6.43 (d, J = 2.2, 1H) (H-6, H-8), 6.65 (d, J = 8.5, 2H, H-3', H-5'), 6.83 (d, J = 8.5, 2H, H-2', H-6'), 9.27 (s, 1H, 4'-OH)	32.80, 36.90, 55.57, 55.75, 94.05, 94.88, 106.26, 115.25, 127.26, 131.78, 152.52, 156.03, 156.97, 160.07, 167.30

Table 3. (continued)

Product[a]	R_f (eluent)[b]	mp (°C) (solvent for crystallization)	^{1}H NMR (DMSO-d_6) δ, *J* (Hz)	^{13}C NMR (DMSO-d_6) δ
5d	0.40 (D)	198–200 (hexane–EtOAc)	2.25 (s, 3 H, CH_3), 2.82 (br d, *J* = 15.8, 1 H, H-3a), 3.12 (dd, *J* = 15.8, 6.6, 1 H, H-3b), 4.44 (br d, *J* = 6.6, 1 H, H-4), 6.42 (s, 1 H) and 6.50 (s, 1 H) (H-6, H-8), 6.68 (d, *J* = 8.6, 2 H, H-3', H-5'), 6.88 (d, *J* = 8.6, 2 H, H-2', H-6'), 9.09 (s, 1 H) and 9.56 (s, 1 H) (5-OH, 4'-OH)	20.78, 33.03, 36.96, 107.59, 109.90, 111.80, 115.22, 127.48, 131.84, 138.25, 152.21, 154.41, 156.02, 167.73
5e	0.29 (E)	140 (hexane–EtOAc)	2.24 (s, 3 H, CH_3), 2.82 (dd, *J* = 15.4, 1.5, 1 H, H-3a), 3.17 (dd, *J* = 15.4, 6.4, 1 H, H-3b), 3.69 (s, 3 H, OCH_3), 4.46 (br d, *J* = 6.4, 1 H, H-4), 6.44 (s, 1 H, H-8), 6.49 (s, 1 H, H-6), 6.83 (d, *J* = 8.7, 2 H, H-3', H-5'), 6.98 (d, *J* = 8.7, 2 H, H-2', H-6'), 9.77 (s, 1 H, 5-OH)	20.79, 33.01, 36.84, 54.92, 107.60, 109.66, 111.79, 113.94, 127.55, 133.59, 138.38, 152.19, 154.41, 157.96, 167.65
5f	0.31 (C)		(in mixture with **4f**) 2.25 (s, 3 H, CH_3), 2.79 (dd, *J* = 15.7, 1.7, 1 H, H-3a), 2.84 (s, 6 H, $N(CH_3)_2$), 3.13 (dd, *J* = 15.7, 6.6, 1 H, H-3b), 4.44 (br d, *J* = 6.6, 1 H, H-4), 6.44 (br s, 1 H) and 6.51 (br s, 1 H) (H-6, H-8), 6.64 (d, *J* = 8.7, 2 H, H-3', H-5'), 6.91 (d, *J* = 8.7, 2 H, H-2', H-6'), 9.63 (s, 1 H, 5-OH)	
7a	0.18 (E)	227–230 (Et_2O–hexane)	2.96 (br d, *J* = 15.8, 1 H, H-2a), 3.44 (dd, *J* = 15.8, 6.7, 1 H, H-2b), 5.05 (br d, *J* = 6.7, 1 H, H-1), 6.68 (d, *J* = 8.4, 2 H, H-3', H-5'), 6.94 (d, *J* = 8.4, H-2', H-6'), 7.41 (d, *J* = 8.8, 1 H), 7.49 (app t, <*J*> = 6.9, 1 H), 7.55 (app t, <*J*> = 6.9, 1 H), 7.90 (d, *J* = 8.1, 1 H) and 7.96–8.02 (m, 2 H) (aromatic), 9.30 (s, 1 H, 4'-OH)	35.41, 37.13, 115.49, 117.07, 118.51, 123.10, 124.87, 127.04, 127.57, 128.33, 129.22, 130.43, 131.33, 133.78, 149.05, 156.25, 167.10
7b	0.53 (C)	see ref. 5	see ref. 5	see ref. 5
7c	0.26 (E)	136 ($CHCl_3$)	2.92 (dd, *J* = 15.1, 1.2, 1 H, H-2a), 3.39 (dd, *J* = 15.1, 6.6, 1 H, H-2b), 4.80 (dd, *J* = 6.6, 1.2, 1 H, H-1), 6.70 (d, *J* = 8.3, 2 H, H-3', H-5'), 6.92 (d, *J* = 8.3, 2 H, H-2', H-6'), 7.05 (br d, *J* = 8.8, 1 H, H-8), 7.07 (s, 1 H, H-10), 7.14 (d, *J* = 8.8, 1 H, H-5), 7.81 (d, *J* = 8.8, 1 H), 7.84 (d, *J* = 8.8, 1 H) (H-6, H-7), 9.27 (s, 1 H, 4'-OH), 9.79 (s, 1 H, 9-OH)	35.97, 37.66, 105.23, 113.77, 115.76, 116.74, 117.58, 125.26, 127.90, 129.25, 130.31, 131.51, 132.60, 149.77, 156.54, 167.57
7d	0.52 (G)	174–176 (Et_2O–hexane)	2.94 (br d, *J* = 15.9, 1 H, H-2a), 3.42 (dd, *J* = 15.9, 6.7, 1 H, H-2b), 3.71 (s, 3 H, OCH_3), 4.87 (br d, *J* = 6.7, 1 H, H-1), 6.85 (d, *J* = 8.7, 2 H, H-3', H-5'), 7.00–7.04 (m, 4 H, aromatic), 7.15 (d, *J* = 8.8, 1 H, H-5), 7.79 (d, *J* = 8.8, 1 H) and 7.84 (d, *J* = 8.8, 1 H) (H-6, H-7), 9.85 (s, 1 H, 9-OH)	35.68, 37.26, 54.87, 104.94, 113.48, 114.24, 116.27, 117.33, 125.02, 127.70, 129.06, 130.03, 132.34, 133.02, 149.56, 156.47, 158.31, 167.12
7e	0.31 (G)	217–221 (Et_2O–hexane)	2.83 (s, 6 H, $N(CH_3)_2$), 2.92 (br d,, *J* = 15.7, 1 H, H-2a), 3.65 (dd, *J* = 15.7, 7.1, 1 H, H-2b), 4.78 (br d, *J* = 7.1, 1 H, H-1), 6.65 (d, *J* = 8.7, 2 H, H-3', H-5'), 6.93 (d, *J* = 8.7, 2 H, H-2', H-6'), 7.03 (dd, *J* = 2.4, 1 H, H-8), 7.08 (d, *J* = 2.4, 1 H, H-10), 7.14 (d, *J* = 8.7, 1 H, H-5), 7.80 (d, *J* = 8.8, 1 H, H-7), 7.84 (d, *J* = 8.8, 1 H, H-6), 9.79 (s, 1 H, 9-OH)	35.68, 37.42, 39.88, 105.07, 112.68, 113.50, 116.70, 117.31, 125.04, 127.17, 128.39, 128.89, 130.02, 132.41, 149.45, 156.42, 167.35
7f	0.43 (G)	189–191 (Et_2O–hexane)	2.25 (s, 3 H, CH_3), 2.94 (br d, *J* = 16.0, 1 H, H-2a), 3.44 (dd, *J* = 16.0, 6.9, 1 H, H-2b), 4.88 (br d, *J* = 6.9, 1 H, H-1), 7.00–7.06 (m, 4 H) and 7.10–7.17 (m, 3 H) (aromatic), 7.82 (d, *J* = 8.6, 1 H) and 7.86 (d, *J* = 8.9, 1 H) (H-6, H-7), 9.79 (s, 1 H, 9-OH)	20.46, 36.21, 37.30, 105.01, 113.64, 116.21, 117.48, 125.11, 126.67, 129.27, 129.50, 130.25, 132.45, 136.32, 138.34, 149.77, 156.59, 167.34
7g	0.43 (C)	194–197 (Et_2O–hexane)	2.98 (dd, *J* = 15.9, 1.3, 1 H, H-2a), 3.47 (dd, *J* = 15.9, 7.2, 1 H, H-2b), 4.94 (dd, *J* = 7.2, 1.3, 1 H, H-1), 7.03–7.08 (m, 2 H), 7.13–7.18 (m, 3 H) and 7.24–7.35 (m, 3 H) (aromatic), 7.82 (d, *J* = 8.7, 1 H) and 7.87 (d, *J* = 8.9, 1 H) (H-6 and H-7), 9.85 (s, 1 H, 9-OH)	36.43, 37.03, 104.85, 113.41, 115.86, 117.31, 124.99, 126.85, 128.68, 129.10, 129.97, 132.32, 141.17, 149.66, 156.46, 166.89
7h	0.38 (C)	163–165 (Et_2O–hexane)	2.98 (br d, *J* = 16.0, 1 H, H-2a), 3.47 (dd, *J* = 16.0, 7.1, 1 H, H-2b), 4.96 (br d, *J* = 7.1, 1 H, H-1), 7.03–7.08 (m, 2 H), 7.11–7.19 (m, 5 H) (aromatic), 7.83 (d, *J* = 8.9, 1 H) and 7.88 (d, *J* = 8.8, 1 H) (H-6, H-7), 9.87 (s, 1 H, 9-OH)	
7i	0.38 (C)	167–170 (Et_2O–hexane)	2.97 (br d, *J* = 15.8, 1 H, H-2a), 3.48 (dd, *J* = 15.8, 7.0, 1 H, H-2b), 4.96 (br d, *J* = 7.0, 1 H, H-1), 7.04–7.07 (m, 2 H, H-8, H-10), 7.15 (d, *J* = 8.5, 2 H, H-2', H-6'), 7.16 (d, *J* = 8.9, 1 H, H-5), 7.39 (d, *J* = 8.5, 2 H, H-3', H-5'), 7.83 (d, *J* = 9.4, 1 H) and 7.88 (d, *J* = 8.9, 1 H) (H-6, H-7), 9.83 (s, 1 H, 9-OH)	35.84, 36.96, 104.85, 113.61, 115.53, 117.54, 125.11, 128.69, 128.86, 129.50, 130.25, 131.81, 132.33, 140.25, 149.82, 156.70, 167.00
7j	0.52 (C)	193–196 (Et_2O–hexane)	2.97 (br d, *J* = 16.3, 1 H, H-2a), 3.48 (dd, *J* = 16.3, 7.0, 1 H, H-2b), 4.94 (br d, *J* = 7.0, 1 H, H-1), 7.03–7.07 (m, 2 H, H-8, H-10), 7.09 (d, *J* = 8.4, 2 H, H-2', H-6'), 7.16 (d, *J* = 8.8, 1 H, H-5), 7.52 (d, *J* = 8.4, 2 H, H-3', H-5'), 7.83 (d, *J* = 8.8, 1 H) and 7.88 (d, *J* = 8.9, 1 H) (H-6, H-7), 9.84 (s, 1 H, 9-OH)	35.87, 36.89, 104.84, 113.61, 115.46, 117.62, 120.26, 125.10, 129.04, 129.50, 130.25, 131.81, 132.33, 140.71, 149.82, 156.67, 167.00

Table 3. (continued)

Product[a]	R_f (eluent)[b]	mp (°C) (solvent for crystallization)	^{1}H NMR (DMSO-d_6) δ, J (Hz)	^{13}C NMR (DMSO-d_6) δ
7k	0.38 (C)	178–180 (Et_2O–hexane)	3.02 (dd, J = 16.0, 1.4, 1 H, H-2a), 3.54 (dd, J = 16.0, 7.2, 1 H, H-2b), 5.08 (dd, J = 7.2, 1.4, 1 H, H-1), 7.04–7.08 (m, 2 H, H-8 and H-10), 7.18 (d, J = 8.8, 1 H, H-5), 7.37 (d, J = 8.1, 2 H, H-2', H-6'), 7.7 (d, J = 8.1, 2 H, H-3', H-5'), 7.84 (d, J = 9.3, 1 H) and 7.90 (d, J = 8.8, 1 H) (H-6, H-7), 9.83 (s, 1 H, 9-OH)	36.17, 36.69, 104.72, 113.56, 115.08, 117.49, 125.05, 125.79, 127.65, 129.60, 130.22, 132.27, 146.00, 149.85, 156.66, 166.82

[a] All compounds gave satisfactory elemental analyses (C ± 0.31), (H ± 0.22).

[b] See Experimental Section for eluents.

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