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Synthetic Studies on the Flavone Derivatives. XII.^{1,2)} Synthesis of 2',3',5'- and 3',4',5'-Trioxxygenated Flavones

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Two unusual flavones, 5,5'-dihydroxy-2',3',6,7-tetramethoxyflavone (**1**) from *Gardenia cramerii* and 4',5-dihydroxy-3',5',6,7-tetramethoxyflavone (**6**) from *Artemisia mesatlantia*, and their position isomers were synthesized to investigate the structural correlation in terms of spectral data. The structure of the flavone from *G. cramerii* is discussed.

Keywords—5,5'-dihydroxy-2',3',6,7-tetramethoxyflavone; 2',5-dihydroxy-3',5',6,7-tetramethoxyflavone; 5-hydroxy-2',3',5',6,7-pentamethoxyflavone; 3',5-dihydroxy-4',5',6,7-tetramethoxyflavone; 4',5-dihydroxy-3',5',6,7-tetramethoxyflavone; 5-hydroxy-3',4',5',6,7-pentamethoxyflavone

As a continuation of our studies on the synthesis of flavones, we report in this paper the synthesis of new flavones hexa-oxygenated at C-2', -3', -5, -5', -6, -7 and C-3', -4', -5, -5', -6, -7. Flavones oxygenated at C-3', -4' and -5' are common among natural flavones tri-oxygenated in ring B, but flavones oxygenated at C-2' and -5' are not usual. The tri-oxygenated flavones with a hydroquinone moiety in ring B are classified into three types according to the position of the other O-functions, that is, 2',3',5'-[O]₃ (A), 2',4',5'-[O]₃ (B), and 2',3',6'-[O]₃ (C) (Chart 1). A few B type flavones have been found in nature.³⁾ On the other hand, A and C types are rare as naturally occurring flavones; the A type has been isolated from *Gardenia cramerii* and *G. fosbergii*,⁴⁾ and the C type from *Scutellaria baicalensis*.⁵⁾ A new flavone isolated from *G. cramerii* and deduced to be 5,5'-dihydroxy-2',3',6,7-tetramethoxyflavone (**1**), its isomer, 2',5-dihydroxy-3',5',6,7-tetramethoxyflavone

Chart 1

(2), and their monomethyl ether, 5-hydroxy-2',3',5',6,7-pentamethoxyflavone (3), were synthesized to investigate the relation between structure and spectral properties. Further, 3',5'-dihydroxy-4',5',6,7-tetramethoxyflavone (5) and 4',5'-dihydroxy-3',5',6,7-tetramethoxyflavone (6), which has recently been isolated from *Artemisia mesatlantica* by Bouzid *et al.*,⁶ were also prepared.

A convenient preparation of 2,3,5-trimethoxybenzaldehyde (8) and its carboxylic acid (9) had been previously reported by us.⁷ Compound 9 was partially demethylated with BCl_3 in CH_2Cl_2 ⁸ to 2-hydroxy-3,5-dimethoxybenzoic acid, which was benzylated then hydrolyzed to afford 2-benzyloxy-3,5-dimethoxybenzoic acid (10). The acid 10 was esterified with 2-hydroxy-4,5,6-trimethoxyacetophenone (11) to give 2-(2'-benzyloxy-3',5'-dimethoxybenzoyloxy)-4,5,6-trimethoxyacetophenone (12). The ester 12 was subjected to the Baker-Venkataraman rearrangement to afford the β -diketone (13), which was converted to 2'-benzyloxy-3',5,5',6,7-pentamethoxyflavone (14) in acetic acid containing a small amount of sulfuric acid. Catalytic hydrogenation with 10% Pd-C of 14 gave 2'-hydroxy-3',5,5',6,7-pentamethoxyflavone (15), mp 232—234°C, which was selectively demethylated at the methoxyl group at C-5 with BCl_3 ⁹ to furnish 2 (mp > 260°C). 5-Benzyloxy-2,3-dimethoxybenzaldehyde (16), as a starting material for the ring B moiety of 1, was prepared as follows: 1-bromo-5-hydroxy-2,3-dimethoxybenzene (17), which was obtained from bromoveratraldehyde by means of the Baeyer-Villiger reaction, was transformed to 5-hydroxy-2,3-dimethoxybenzaldehyde (18) by conversion of the bromine at C-1 into a nitrile, then into an aldehyde moiety in a manner similar to that described previously.⁷ Usual benzylation of 18 gave 16. Compounds 8 and 16 were each condensed with the acetophenone 11 in the presence of KOH in ethanol to give 2'-hydroxy-2,3,4',5',6'-hexamethoxychalcone (19) and 5-benzyloxy-2'-hydroxy-2,3,4',5',6'-pentamethoxychalcone (20), respectively. The chalcones, 19 and 20, were isomerized with H_3PO_4 to the corresponding flavanones (21 and 22), which were oxidized with DDQ in dry dioxane to the flavones 4 and 5'-benzyloxy-2',3',5,6,7-pentamethoxyflavone (23). Debenzylation of 23 by a method similar to that described above gave 5'-hydroxy-2',3',5,6,7-pentamethoxyflavone (24, mp 231—233°C). Partial demethylation of 24 and 4 with BCl_3 gave the desired flavones, 1 (mp 261°C, lit.⁴ mp 218°C) and 3 (mp 181—183°C, lit.⁴ mp 189—191°C). 3',5'-Dihydroxy-4',5',6,7-tetramethoxyflavone (5, mp 216°C (dec.)) was synthesized in the same way as 2 via 3-benzyloxy-2'-hydroxy-4,4',5,5',6'-pentamethoxychalcone after condensation of 11 with 3-benzyloxy-4,5-dimethoxybenzaldehyde prepared from *o*-vanillin by our new method.¹ The other flavone 4 was also prepared via 2-(4'-benzyloxy-3',5'-dimethoxybenzoyloxy)-4,5,6-trimethoxyacetophenone (25) and 4'-benzyloxy-2-hydroxy-3',4,5,5',6-pentamethoxydibenzoylmethane (26) after esterification of 11 with 4-benzyloxy-3,5-dimethoxybenzoic acid (syringic acid benzyl ether, mp 153—154°C) and application of the Baker-Venkataraman rearrangement. The β -diketone 26 gave 4'-hydroxy-3',5,5',6,7-pentamethoxyflavone (27) on treatment with sulfuric acid with simultaneous debenzylation. The flavone 27 was allowed to react with AlCl_3 in nitrobenzene to furnish 6 (mp 240—242°C, lit.⁶ mp 240—242°C). In a direct comparison (mixed mp, co-thin-layer chromatography (TLC) and infrared (IR)) of 6 with the flavone isolated from *Artemisia mesatlantica*, the flavone was confirmed to be 4',5'-dihydroxy-3',5',6,7-tetramethoxyflavone. Both 3'-hydroxy-4',5,5',6,7-pentamethoxyflavone (an intermediate of 5) and 27 were methylated to yield 3',4',5,5',6,7-hexamethoxyflavone (7), which was identical with the authentic flavone isolated from *Bauhinia championii*.¹⁰

Chemical shift due to ring B in the proton nuclear magnetic resonance (¹H-NMR) spectra of the flavones thus obtained are shown in Table I. The equivalent protons (H-2' and H-6') in 6 and 7 were observed as a singlet at 7.39 and 7.02 ppm in CDCl_3 ,^{10b} respectively, whereas in 5, they appeared as separate singlets at lower field than the H-3' and H-4' signals.

TABLE I. ^1H -NMR Chemical Shifts of the Ring B Moieties of the Flavones (1—6)

Chemical shifts (ppm)			
Reported flavone	6.9 ^{a)}	(1H, d, $J=2$ Hz, H-4')	7.2 ^{c)} (2H, s, H-4',6')
(ref. 4)	7.2	(1H, d, $J=2$ Hz, H-6')	
1	6.72 ^{b)}	(1H, d, $J=3.0$ Hz, H-4')	
	6.80	(1H, d, $J=3.0$ Hz, H-6')	
2	6.90 ^{c)}	(1H, d, $J=2.3$ Hz, H-4')	
	7.09	(1H, d, $J=2.3$ Hz, H-6')	
4	6.63 ^{a)}	(1H, d, $J=3.0$ Hz, H-4')	
	6.76	(1H, d, $J=3.0$ Hz, H-6')	
5	6.98 ^{b)}	(1H, d, $J=2.2$ Hz, H-2')	
	7.16	(1H, d, $J=2.2$ Hz, H-6')	
6	7.39 ^{c)}	(2H, s, H-2' and H-6')	

a) Measured in CDCl_3 . b) In $\text{CDCl}_3 + \text{DMSO}-d_6$. c) In $\text{DMSO}-d_6$.

TABLE II. UV Properties of 1, 2, 5 and 6 by the Use of Shift Reagents

Position of hydroxy group			Bathochromic shifts (nm)		
			AlCl_3	NaOMe	NaOAc
1	5'	Band I	+30	(dec.)	+3
		Band II	+6		-7
2	2'	Band I	+30	+84	0
		Band II	0	0	0
5	3'	Band I	+23	+45	0
		Band II	+12	+10	0
6	4'	Band I	+19	+73	+1
		Band II	0	-1	0

On the other hand, the protons (H-4' and H-6') in 2',3',5'-type flavones (1, 2 and 3) were observed as follows: one proton attributable to H-4' appeared at high field (>6.90 ppm), and the other (H-6') at slightly lower field, each as a doublet. Ultraviolet (UV) properties of the flavones (1, 2, 5 and 6) measured with the aid of shift reagents (AlCl_3 , NaOMe and NaOAc) are summarized in Table II. It is generally known that flavones possessing a 4'-hydroxyl group show a large bathochromic shift of Band I¹¹⁾ in the presence of NaOMe . A hydroxyl group at C-2' as in 2, however, caused a much larger bathochromic shift than one at C-4'. The λ_{max} positions of 5 (278 and 335 nm) are similar to those of the reported flavone (277 and 330 nm),⁴⁾ whereas the flavone 1 has λ_{max} at 282 and 322 nm. By comparison of the mp, ^1H -NMR and UV spectra of the reported flavone with those of 1 and 5, the flavone isolated from *G. cramerii* was concluded 3',5-dihydroxy-4',5',6,7-tetramethoxyflavone, not 5,5'-dihydroxy-2',3',6,7-tetramethoxyflavone. This conclusion is supported by the fact that the plant, *G. cramerii*, contained 5-hydroxy-3',4',5',6,7-pentamethoxyflavone and 3',5-dihydroxy-3,4',5',6,7-pentamethoxyflavone in addition to this new flavone.⁴⁾

Experimental¹²⁾

2-Benzoyloxy-3,5-dimethoxybenzoic Acid (10)—2,3,5-Trimethoxybenzoic acid⁷⁾ (4.2 g, 20 mmol) in CH_2Cl_2 (30 ml) was cooled at -70°C and treated with BCl_3 (2 ml) in CH_2Cl_2 (10 ml) at -70°C .⁹⁾ The solution was allowed to warm to room temperature, and then poured into water (100 ml). The mixture was extracted with AcOEt . After evaporation of the AcOEt extract, the residue was recrystallized from C_6H_6 to give 2-hydroxy-3,5-dimethoxybenzoic

acid as pale yellow rectangles, in 75% yield, mp 174–176 °C. $^1\text{H-NMR}$ ($\text{CDCl}_3 + \text{DMSO}-d_6$) δ : 3.77, 3.87 (3H, each s, OCH_3), 6.72 (1H, d, $J=3.0$ Hz, H-4), 6.89 (1H, d, $J=3.0$ Hz, H-6), 10.12, 11.10 (2H, each brs, OH and COOH). The phenolic carboxylic acid (2.0 g, 0.10 mol) was benzylated with benzyl chloride (2.8 g, 0.022 mol) and K_2CO_3 (4 g, 0.03 mol) in DMF (30 ml). The benzoate obtained was hydrolyzed in 1 N KOH ethanol solution (50 ml) to give **10** as colorless needles, mp 47–50 °C. $^1\text{H-NMR}$ (CCl_4) δ : 3.72, 3.80 (3H, each s, OCH_3), 5.0 (2H, s, OCH_2Ph), 6.57 (1H, d, $J=3.0$ Hz, H-4), 6.95 (1H, d, $J=3.0$ Hz, H-6), 7.16–7.32 (5H, m, Ph), 10.29 (1H, s, COOH).

2',5-Dihydroxy-3',5',6,7-tetramethoxyflavone (2)—The acid **10** (1.5 g, 5.2 mmol) and **11** (1.2 g, 5.2 mmol) were treated with trifluoroacetic anhydride (2 ml) in dry benzene (10 ml). The resulting solution was stirred at room temperature for 3 h. AcOEt (20 ml) was added and then the AcOEt layer was washed with water and evaporated under reduced pressure. The residue was chromatographed on silica gel (solvent: CHCl_3) to give **12** as a liquid in 77% yield. $^1\text{H-NMR}$ (CDCl_3) δ : 2.50 (3H, s, COCH_3), 3.79, 3.86, 3.89 (3H, each s, OCH_3), 3.98 (6H, s, $2 \times \text{OCH}_3$), 5.10 (2H, s, OCH_2Ph), 6.45 (1H, s, H-3), 6.75, 7.00 (1H, each d, $J=2.3$ Hz, H-4', 6'), 7.2–7.6 (5H, m, Ph). The ester **12** (1.0 g) was treated with powdered KOH (1.0 g) in pyridine (3 ml) at 100 °C for 20 min to give **13** in 85% yield. A solution of **13** (800 mg, 1.6 mmol) in acetic acid (5 ml) was added to acetic acid–sulfuric acid (10:1) solution (5 ml) and the mixture was stirred at room temperature for 1 h. The reactant was poured into water and the solution was extracted with AcOEt. The AcOEt extract was evaporated and the residue was recrystallized from EtOH to give **14**. Usual catalytic hydrogenation of **14** in AcOEt with 10% Pd–C gave **15** as pale yellow needles, mp 232–234 °C (EtOH). $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 3.83 (3H, s, OCH_3), 3.86 (6H, s, $2 \times \text{OCH}_3$), 3.93, 4.00 (3H, each s, OCH_3), 6.88, 7.08 (1H, each d, $J=2.3$ Hz, H-4', 6'), 7.04, 7.25 (1H, each s, H-3, 8). The flavone **15** (300 mg, 1.3 mmol) was partially demethylated with BCl_3 in the same manner as described above to give **2** in 69% yield as a light yellow powder, mp >260 °C (dec.) (EtOH). $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 3.78, 3.83, 3.91, 3.99 (3H, each s, OCH_3), 6.90 (1H, d, $J=2.3$ Hz, H-4'), 7.09 (1H, d, $J=2.3$ Hz, H-6'), 7.00, 7.13 (1H, each s, H-3, 8), 12.80 (1H, s, OH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3400, 1655, 1610, 1590. MS m/z (rel. int.): 374 (M^+) (100), 359 (71), 345 (17), 181 (17), 164 (11), 158 (12), 153 (26). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 268 sh, (4.7), 277 sh (4.5), 310 (4.3), 360 sh (4.0). $\lambda^+ \text{AlCl}_3$: 268 sh, 280, 294 sh, 335, 390. $\lambda^+ \text{AlCl}_3 + \text{HCl}$: 268 sh, 282, 295 sh, 334, 388. $\lambda^+ \text{MeONa}$: 268 sh, 278 sh, 325 sh, 444. $\lambda^+ \text{AcONa}$: 268 sh, 310, 360 sh.

5-Benzoyloxy-2,3-dimethoxybenzaldehyde (16)—Treatment of **17** with CuCN in DMF gave 1-cyano-5-hydroxy-2,3-dimethoxybenzene as colorless needles, mp 155–158 °C (C_6H_6). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2240. A mixture of the nitrile and Raney Ni in 70% HCOOH was boiled for 4 h to yield **18** as colorless needles, mp 129–131 °C (C_6H_{14} –AcOEt). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1668 (CHO). Benzylation of **18** (1.6 g, 8.8 mmol) with benzyl chloride (1.1 g, 9 mmol) and K_2CO_3 (2.5 g) in DMF (45 ml) gave **16** as a colorless oil. $^1\text{H-NMR}$ (CCl_4) δ : 6.67, 6.81 (1H, each d, $J=2.5$ Hz, H-4, 6), 10.22 (1H, s, CHO).

5-Hydroxy-2',3',5',6,7-pentamethoxyflavone (3)—A solution of **11** (1.5 g, 6.6 mmol) and **8** (1.3 g, 6.6 mmol) in 50 ml of 80% EtOH containing KOH (8 g) was stirred at room temperature overnight. The mixture was acidified with 20% HCl and then extracted with AcOEt. The extract was concentrated under reduced pressure, and the residue was recrystallized from MeOH to give 2.1 g of **19** as reddish-orange needles, mp 122–124 °C. $^1\text{H-NMR}$ (CDCl_3) δ : 6.25 (1H, s, H-3'), 6.52 (1H, d, $J=3.0$ Hz, H-4), 6.67 (1H, d, $J=3.0$ Hz, H-6), 7.82, 8.17 (1H, d, $J=15.6$ Hz, H β and α), 13.60 (1H, s, OH). A solution of **19** (2.1 g) in EtOH (100 ml) containing 16 g of 85% H_3PO_4 was boiled under reflux for 35 h, then extracted with water and AcOEt. The AcOEt extract was purified by column chromatography on silica gel, and 980 mg of **21** was obtained as colorless needles, mp 125–126 °C (C_6H_6 – C_6H_{14}). $^1\text{H-NMR}$ (CDCl_3) δ : 2.81 (1H, d, $J=5.7$ Hz, H-3 *cis*), 2.88 (1H, d, $J=10.5$ Hz, H-3 *trans*), 5.73 (1H, dd, $J=10.5, 5.7$ Hz, H-2). A solution of **21** (600 mg, 1.5 mmol) and DDQ (410 mg, 1.8 mmol) in dry dioxane (30 ml) was boiled for 8 h, then cooled. The reduced hydroquinone was removed by filtration, and the residue was recrystallized from C_6H_6 to obtain 480 mg of **4** as colorless needles, mp 140–142 °C (MeOH). $^1\text{H-NMR}$ (CDCl_3) δ : 3.80 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.89 (6H, s, $2 \times \text{OCH}_3$), 3.97 (6H, s, $2 \times \text{OCH}_3$), 6.63 (1H, d, $J=3.0$ Hz, H-4'), 6.76 (1H, d, $J=3.0$ Hz, H-6'), 6.77 (2H, s, H-3 and H-8). MS m/z (rel. int.): 402 (M^+) (35), 387 (100), 382 (11), 367 (29), 186 (17). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 266 (4.2), 310 (4.3). BCl_3 (0.5 ml) was added to a solution of CH_2Cl_2 (30 ml) containing **4** (200 mg) at –70 °C, and the mixture was left at room temperature for 1 h. The mixture was poured into water and extracted with AcOEt. The AcOEt extract was evaporated and the residue was purified by column chromatography to give **3** as yellow rectangles, mp 181–183 °C (AcOEt– C_6H_{14}). MS m/z (rel. int.): 388 (M^+) (22), 374 (100), 356 (23), 328 (16). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 278 (4.4), 322 (4.1). $\lambda^+ \text{AlCl}_3$: 288, 345. $\lambda^+ \text{AlCl}_3 + \text{HCl}$: 288, 340.

5,5'-Dihydroxy-2',3',6,7-tetramethoxyflavone (1)—The flavone **1** was prepared through the intermediates **20**, **22** and **24** in a manner similar to that described for **3**. 5-Benzoyloxy-2'-hydroxy-2,3,4',5',6'-pentamethoxychalcone (**20**): an orange-yellow oil. $^1\text{H-NMR}$ (CCl_4) δ : 6.15 (1H, s, H-3'), 6.63 (1H, d, $J=3.0$ Hz, H-4), 6.70 (1H, d, $J=3.0$ Hz, H-2), 7.81 (2H, brs, H- β and α), 12.27 (1H, s, OH). 5'-Benzoyloxy-2',3',5,6,7-pentamethoxyflavonone (**22**): mp 105–106 °C (C_6H_6 – C_6H_{14}), colorless needles. $^1\text{H-NMR}$ (CDCl_3) δ : 2.85 (1H, d, $J=6.0$ Hz, H-3 *cis*), 2.89 (1H, d, $J=10.8$ Hz, H-3 *trans*), 5.67 (1H, dd, $J=10.8, 6.0$ Hz, H-2), 6.37 (1H, s, H-8), 6.61 (1H, d, $J=3.0$ Hz, H-4'), 6.78 (1H, d, $J=3.0$ Hz, H-6'). 5'-Hydroxy-2',3',5,6,7-pentamethoxyflavone (**24**): mp 231–233 °C (EtOH), a colorless powder. MS m/z (rel. int.): 388 (M^+) (31), 373 (100), 357 (27), 167 (2). 5,5'-Dihydroxy-2',3',6,7-tetramethoxyflavone (**1**): mp 261 °C (AcOEt– C_6H_{14}), a yellow powder. $^1\text{H-NMR}$ ($\text{CDCl}_3 + \text{DMSO}-d_6$) δ : 3.79 (6H, s, $2 \times \text{OCH}_3$), 3.89 (6H, s, $2 \times \text{OCH}_3$), 6.58, 6.71 (1H, each s, H-3, 8), 6.72 (1H, d, $J=3.0$ Hz, H-4'), 6.80 (1H, d, $J=3.0$ Hz, H-6'), 12.58, 12.70.

(1H, each s, OH). MS m/z (rel. int.): 374 (M^+) (18), 360 (100), 346 (53), 342 (29), 331 (11), 314 (22). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3400, 2950, 2840, 1660, 1580, 1470. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 282 (4.2), 322 (4.1). $\lambda^{\text{+AlCl}_3}$: 288, 352. $\lambda^{\text{+AlCl}_3+\text{HCl}}$: 290, 344. $\lambda^{\text{+NaOAc}}$: 275, 325.

3',5-Dihydroxy-4',5',6,7-tetramethoxyflavone (5)—The flavone **5** was synthesized through the intermediates **28** and **29** in a manner similar to that described for **1**. 3'-Benzyloxy-4',5,5',6,7-pentamethoxyflavone (**28**): mp 179 °C (EtOH), colorless needles. $^1\text{H-NMR}$ (CDCl_3) δ : 6.60, 6.78 (1H, each s, H-3,8), 7.09, 7.16 (1H, each d, $J=2.3$ Hz, H-2',6'). 3'-Hydroxy-4',5,5',6,7-pentamethoxyflavone (**29**): mp 224–225 °C (EtOH), yellow prisms. $^1\text{H-NMR}$ (CDCl_3) δ : 3.96 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 4.03 (9H, s, $3 \times \text{OCH}_3$), 6.63, 6.82 (1H, each s, H-3,8), 6.96, 7.23 (1H, each d, $J=2.3$ Hz, H-2',6'). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 269, 320. 3',5-Dihydroxy-4',5',6,7-tetramethoxyflavone (**5**): mp 216 °C (dec.) (C_6H_6), pale yellow needles. $^1\text{H-NMR}$ ($\text{CDCl}_3 + \text{DMSO}-d_6$) δ : 3.93, 3.95, 3.99, 4.00 (3H, each s, OCH_3), 6.60 (2H, s, H-3 and H-8), 6.98, 7.16 (1H, each d, $J=2.2$ Hz, H-2',6'). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 278 (4.1), 335 (4.3). $\lambda^{\text{+AlCl}_3}$: 290, 300 sh, 358. $\lambda^{\text{+AlCl}_3+\text{HCl}}$: 290, 300 sh, 355. $\lambda^{\text{+MeONa}}$: 288, 297 sh, 380 sh. $\lambda^{\text{+AcONa}}$: 278, 355. MS m/z (rel. int.): 374 (M^+) (35), 360 (100), 346 (43). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3400, 1650, 1590.

4',5-Dihydroxy-3',5',6,7-tetramethoxyflavone (6)—The flavone **6** was synthesized through **25**, **26** and **27** in manner similar to that described for **2**. 2-(4'-Benzyloxy-3',5'-dimethoxybenzoyloxy)-4,5,6-trimethoxyacetophenone (**25**): mp 98–99 °C (MeOH), colorless needles. $^1\text{H-NMR}$ (CDCl_3) δ : 3.91 (3H, s, OCH_3), 3.96 (9H, s, $3 \times \text{OCH}_3$), 3.99 (3H, s, OCH_3), 5.15 (2H, s, OCH_2Ph), 6.60 (1H, s, H-3), 7.41 (2H, s, H-2' and H-6'), 7.38–7.52 (5H, m, Ph). 4'-Benzyloxy-2-hydroxy-3',4,5,5',6-pentamethoxydibenzoylmethane (**26**): mp 125–126 °C (MeOH), yellow prisms. $^1\text{H-NMR}$ (CDCl_3) δ : 3.85 (3H, s, OCH_3), 3.92 (9H, s, $3 \times \text{OCH}_3$), 5.14 (2H, s, OCH_2Ph), 6.32 (1H, s, H-3), 7.20 (2H, s, H-2' and H-6'), 7.38 (2H, s, COCH_2CO), 7.14–7.57 (5H, m, Ph), 12.82 (1H, s, OH). 4'-Hydroxy-3',5,5',6,7-pentamethoxyflavone (**27**): mp 210–211 °C (MeOH), pale yellow needles. $^1\text{H-NMR}$ (CDCl_3) δ : 3.95 (3H, s, OCH_3), 4.01 (12H, s, $4 \times \text{OCH}_3$), 6.61, 6.84 (1H, each s, H-3,8), 7.12 (2H, s, H-2' and H-6'). MS m/z (rel. int.): 388 (M^+) (29), 373 (20), 342 (9). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}_8$: C, 61.85; H, 5.19. Found: C, 61.61; H, 5.18; 4',5-Dihydroxy-3',5',6,7-tetramethoxyflavone (**6**): mp 240–242 °C (AcOEt), a yellow powder. $^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 3.79 (3H, s, OCH_3), 3.94 (6H, s, $2 \times \text{OCH}_3$), 3.99 (3H, s, OCH_3), 6.97, 7.03 (1H, each s, H-3,8), 7.39 (2H, s, H-2' and H-6'). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3150, 2970, 2930, 2840, 1650, 1605. MS m/z (rel. int.): 374 (M^+) (100), 359 (89), 345 (23), 331 (25), 328 (27). Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_8$: C, 60.96; H, 4.85. Found: C, 61.20; H, 4.87. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 269 sh (4.6), 278 sh (4.3), 349 (4.5). $\lambda^{\text{+AlCl}_3}$: 269 sh, 280 sh, 368. $\lambda^{\text{+AlCl}_3+\text{HCl}}$: 269 sh, 282, 372. $\lambda^{\text{+NaOMe}}$: 268 sh, 280 sh, 422. $\lambda^{\text{+AcONa}}$: 269 sh, 277 sh, 350.

Methylation of 27—The flavone **27** (190 mg, 0.49 mmol) was methylated with dimethyl sulfate (65 mg, 0.5 mmol) and K_2CO_3 (140 mg) in acetone to afford **7**, mp 113–114 °C (lit.^{10b} mp 114 °C). $^1\text{H-NMR}$ (CDCl_3) δ : 6.60, 6.81 (1H, each s, H-3,8), 7.03 (2H, s, H-2' and H-6').

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References and Notes

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