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Synthetic Studies on the Flavone Derivatives. XIII.[1] Synthesis of Flavones with Tetramethoxyl Groups in Ring B

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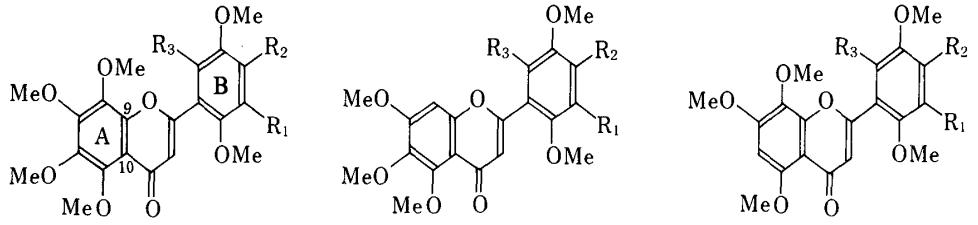
2′,3′,4′,5,5′,6,7,8-Octamethoxy- (Ia) and 2′,3′,4′,5,5′,6,7-heptamethoxyflavone (IIa) and their position isomers substituted with tetramethoxyl groups in ring B were synthesized to confirm the structures of agehoustin A and agehoustin B isolated from *Ageratum houstonianum*. The characteristics of the synthesized flavones were investigated by spectroscopic methods.

Keywords——2′,3′,4′,5,5′,6,7,8-octamethoxyflavone; 2′,3′,4′,5,5′,6,7-heptamethoxyflavone; 2′,3′,4′,5,5′,7,8-heptamethoxyflavone; tetramethoxyl flavone in ring B; agehoustin A; agehoustin B; ^{13}C-NMR

Two new highly oxygenated flavones, octa-substituted and hepta-substituted flavones, isolated from *Ageratum houstonianum* (Asteraceae), were established by spectroscopic and degradative evidence to be 2′,3′,4′,5,5′,6,7,8-octamethoxyflavone (Ia) and 2′,3′,4′,5,5′,6,7-heptamethoxyflavone (IIa), respectively. The former was named agehoustin A, and the latter, agehoustin B.[2] Flavones tetra-oxygenated in ring B are very rare as naturally occurring flavones. To the best of our knowledge, only a hepta-oxygenated flavone, 2′,3′,6,7-tetramethoxy-4′,5,6′-trihydroxyflavone, isolated from *Notholaena aschenborniana*, has been reported previously.[3,4]



I II III

a : R_1=R_2=OMe, R_3=H
b : R_2=R_3=OMe, R_1=H
c : R_1=R_3=OMe, R_2=H

Chart 1

In synthetic and biogenetic cyclizations,[5] β-diketones possessing oxygen at C-2′ tend to yield two kinds of flavones arising from the two equivalent reactive directions towards ring A and ring B. A flavone having a methoxyl group at C-2′ was treated with hydrogen iodide in an attempt at demethylation, but gave another flavone which had a different substitution pattern from that of the parent flavone.[6] This rearrangement resulted from recyclization of the β-diketone which occurred spontaneously during demethylation (the Wassely–Moser rearrangement in a broad sense). Thus, the flavone substituted at C-2′,3′,4′,5′- (a) is converted to one

substituted at C-6,7,8, and similarly, C-2′,3′,4′,6′- (b) is converted to C-5,6,7 or C-5,7,8, and C-2′,3′,5′,6′ (c) is converted to C-5,6,8. The substitution patterns of ring A, hence, are considered to be closely related to those of ring B. To investigate the structures of highly oxygenated flavones, agehoustins A and B and their position isomers were synthesized. The structural differences of these flavones are described in terms of spectral properties in this paper.

A starting material for the ring B moiety of agehoustins A and B, 2,3,4,5-tetramethoxybenzaldehyde (IV), which had been prepared from phloroglucinol in five steps in 50% yield,[7] was prepared in a different way as follows; 3,4-dimethoxy-5-hydroxybromobenzene[8] was subjected to the Elbs oxidation to afford 2,5-dihydroxy-3,4-dimethoxybromobenzene, and the bromine was converted to an aldehyde group in two steps in a manner similar to that described in previous papers[5,8] to give IV (total yield; 35%). The aldehyde IV was condensed with 2-hydroxy-3,4,5,6-tetramethoxyacetophenone (V) [obtained from 4′,5,6,7,8-pentamethoxyflavone (ponkanetin) by alkaline degradation], 2-hydroxy-4,5,6-trimethoxyacetophenone (VI) and 2-hydroxy-3,4,6-trimethoxyacetophenone (VII) to give the chalcones, 2′-hydroxy-2,3,3′,4,4′,5,5′,6′-octamethoxy- (VIIIa), 2′-hydroxy-2,3,4,4′,5,5′,6′-heptamethoxy- (IXa) and 2′-hydroxy-2,3,3′,4,4′,5,6′-heptamethoxychalcone (Xa), respectively. These chalcones were converted by treatment with H_3PO_4 in ethanol to the corresponding flavanones (VIII′a, IX′a and X′a), which were oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to Ia, IIa and 2′,3′,4′,5,5′,7,8-heptamethoxyflavone (IIIa), respectively. By direct comparison (mixed mp, co-thin layer chromatography (TLC) and proton nuclear magnetic resonance (^{1}H-NMR)) of synthesized Ia and IIa with the natural flavones isolated from *A. houstonianum*, agehoustins A and B were confirmed to be 2′,3′,4′,5,6′,6,7,8-octamethoxyflavone (Ia) and 2′,3′,4′,5,5′,6,7-heptamethoxyflavone (IIa). On the other hand, flavones substituted with methoxyl groups at C-2′,3′,4′ and 6′ were synthesized as follows: the ring B moiety of these flavones, 2,3,4,6-tetramethoxybenzaldehyde (XI), was prepared by the Vilsmeier reaction of 1,2,3,5-tetramethoxybenzene (XI: mp 86—87 °C) (lit.[9] mp 87—88 °C). The aldehyde XI was condensed with V, VI and VII to give the chalcones, 2′-hydroxy-2,3,3′,4,4′,5′,6,6′-octamethoxy- (VIIIb), 2′-hydroxy-2,3,4,4′,5′,6,6′-heptamethoxy- (IXb), and 2′-hydroxy-2,3,3′,4,4′,6,6′-heptamethoxychalcone (Xb), respectively. Direct oxidation of these chalcones with DDQ[10] gave the corresponding flavones (Ib, IIb and IIIb). The other flavones, isomers of agehoustins A and B, substituted with methoxyl groups at C-2′,3′,5′ and 6′ were synthesized *via* β-diketones. 2,3,5,6-Tetramethoxybenzoic acid (XII) was obtained by alkaline hydrolysis of 1-cyano-2,3,5,6-tetramethoxybenzene.[11] The acetophenones (V, VI and VII) were esterified with the benzoic acid XII in the presence of trifluoroacetic anhydride in dry benzene to give the esters, 2-(2′,3′,5′,6′-tetramethoxybenzoyloxy)-3,4,5,6-tetramethoxy- (VIIIc), 2-(2′,3′,5′,6′-tetramethoxybenzoyloxy)-4,5,6-trimethoxy- (IXc) and 2-(2′,3′,5′,6′-tetramethoxybenzoyloxy)-3,4,6-trimethoxyacetophenone (Xc), respectively. The esters were subjected to the Baker–Venkataraman rearrangement to give the β-diketones (VIII′c, IX′c and X′c), which were converted to the corresponding flavones (Ic, IIc and IIIc) on treatment with sulfuric acid in acetic acid.

The structural characteristics of the flavones thus obtained were investigated by means of ultraviolet (UV), mass and nuclear magnetic resonance (NMR) spectroscopies. In their UV spectra there were no marked differences among the position isomers (see Experimental). In the mass spectrum (MS), the major fragmentation pathways for the synthesized flavones were as illustrated in Chart 2. The $M^+ - 45$ ion is produced by loss of three methyl radicals from the parent fragment, shown as the *p*-quinone form in ring B (2). In the case of 5,6,7-trioxygenated flavones (II type), the base peak is the $M^+ - 15$ ion due to the predominance of the fragment shown as (1), whereas in 5,7,8-trioxygenated flavones (III type), the base peak is the parent peak (9).[12] On the other hand, a 5,6,8-trioxygenated flavone characteristically has

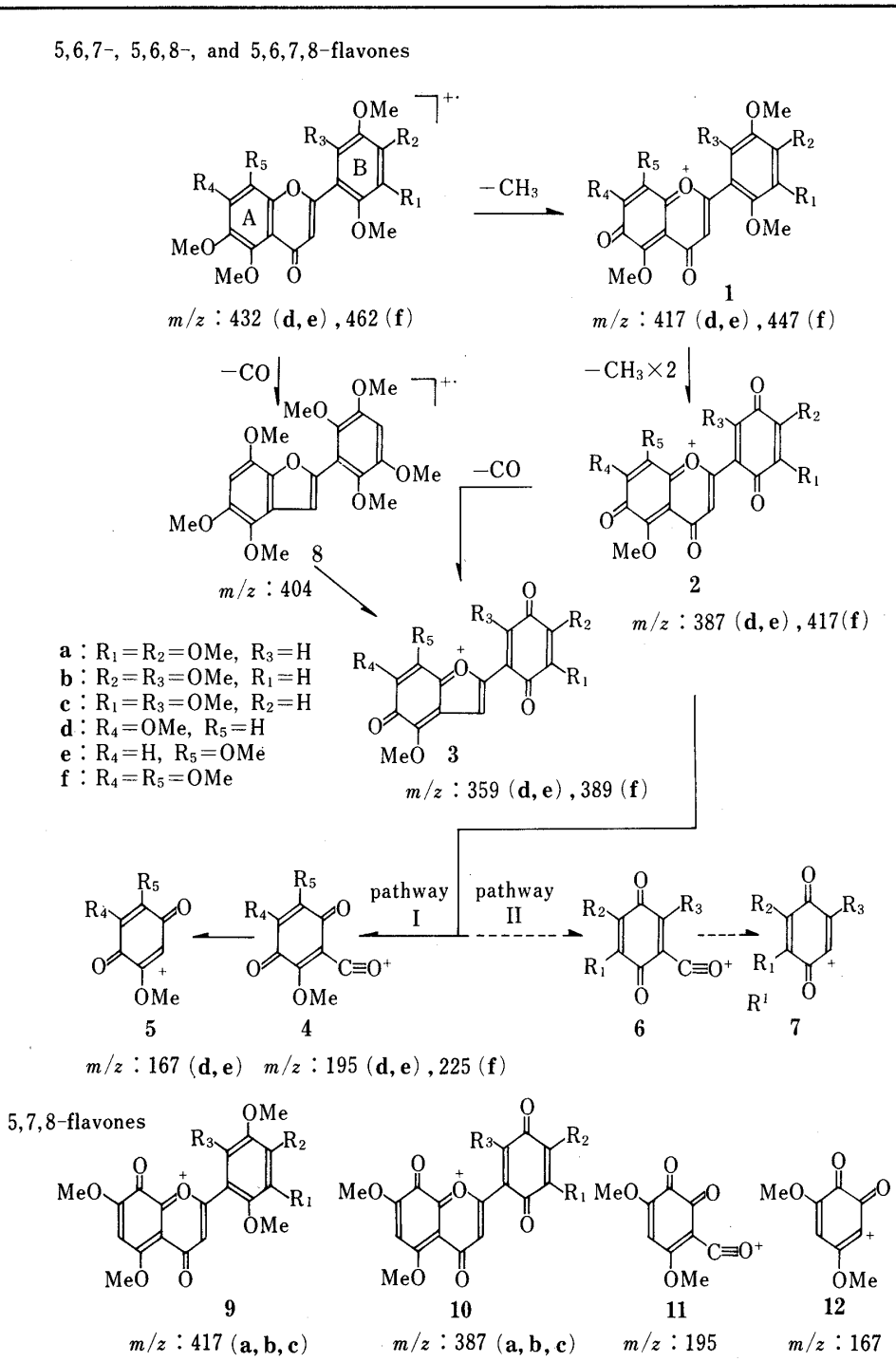


Chart 2

the fragment shown as (8), formed by loss of CO. The fragmentation pathways for the flavones with tetramethoxyl groups in ring A (I type) are similar to those of II type flavones. The fragments shown as (4) and (5), or (6) and (7) are produced by pathway I or pathway II. The flavones of I type do not show the fragments (6) and (7), so pathway II does not operate in these flavones. In the ^{1}H-NMR spectra, the chemical shift of the proton at C-3 was influenced by the methoxyl groups at C-2′ and C-6′, which caused an upfield shift by *ca.* 0.5 ppm as compared with flavones having only the methoxyl group at C-2′ (Fig. 1). A similar shift was also observed in the signal of the proton at C-3 of skullcapflavone II (2′,5-dihydroxy-6,6′,7,8-tetramethoxyflavone) (6.63 ppm in $CDCl_3$,[5] 6.32 ppm in dimethyl sulfoxide (DMSO)-d_6[13]). An upfield shift of the proton at C-3 due to the steric effects, therefore,

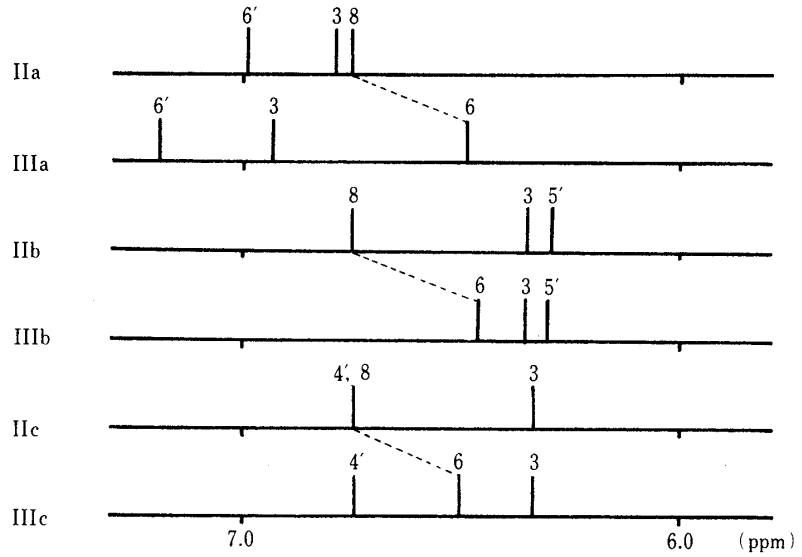


Fig. 1. Correlation of the Aromatic Proton Signals of IIa, IIIa, IIb, IIIb, IIc and IIIc in the ^{1}H-NMR Spectra

TABLE I. ^{13}C-NMR Chemical Shifts of Flavones with Tetramethoxyl Groups in Ring B[a)]

	Ia	Ib	Ic	IIa	IIb	IIc	IIIa	IIIb	IIIc
2	159.0	158.1	158.1	159.1	157.4	158.9	158.0	156.3	157.4
3	112.1	115.3	114.7	112.5	115.2	114.8	112.3	115.5	114.8
4	177.7	177.3	176.9	177.2	176.9	176.9	177.7	177.8	177.1
5	144.1	143.8	144.1	154.7	155.2	155.3	151.8	152.8	152.4
6	137.9	138.0	138.1	140.4	140.0	140.4	92.6	92.5	92.6
7	151.5	151.0	151.3	157.7	157.7	157.7	156.3	156.3	156.2
8	137.9	138.0	138.1	96.2	96.2	96.4	130.5	130.8	130.5
9	148.3	148.2	148.3	152.5	152.6	152.7	156.1	156.2	156.1
10	114.7	115.0	114.7	112.5	112.8	112.8	106.0	109.2	108.9
1′	119.8	109.1	101.9	120.2	109.0	102.0	119.7	109.2	108.9
2′	147.4	154.1	141.0	147.0	153.9	141.0	147.2	154.2	140.7
3′	145.8	136.2	149.1	145.7	136.0	149.1	145.4	136.3	148.9
4′	149.5	155.8	115.0	149.5	155.6	114.8	149.2	155.7	112.9
5′	147.8	92.4	149.1	147.6	92.4	149.1	147.4	92.8	148.9
6′	106.1	152.9	141.0	106.6	152.6	141.0	106.0	153.0	140.7
OCH_3	62.2 (5) 61.8 (8) 61.7 (6, 7) 61.3 (2′, 3′, 4′) 56.2 (5′)	62.1 (5) 61.8 (2′, 8) 61.0 (6, 7, 3′) 56.1 (4′, 6′)	62.2 (5) 62.0 (8) 61.7 (6, 7, 2′, 6′) 56.7 (3′, 5′)	62.2 (5) 61.5 (6) 61.3 (2′, 3′, 4′) 56.6 (5′) 56.3 (7)	62.0 (5) 61.4 (2′) 61.3 (6) 60.9 (3′) 56.0 (7, 4′, 6′)	62.2 (5) 61.7 (2′, 6′) 61.6 (6) 56.8 (3′, 5′) 56.3 (7)	61.2 (8) 61.1 (2′, 3′) 61.0 (4′) 56.4 (5′) 56.1 (5) 56.0 (7)	61.7 (8) 61.4 (2′) 61.0 (3′) 56.7 (4′) 56.3 (6′) 56.2 (5, 7)	61.4 (8) 61.2 (2′, 6′) 56.4 (3′, 5′) 56.1 (5, 7)

a) All spectra were measured in $CDCl_3$.

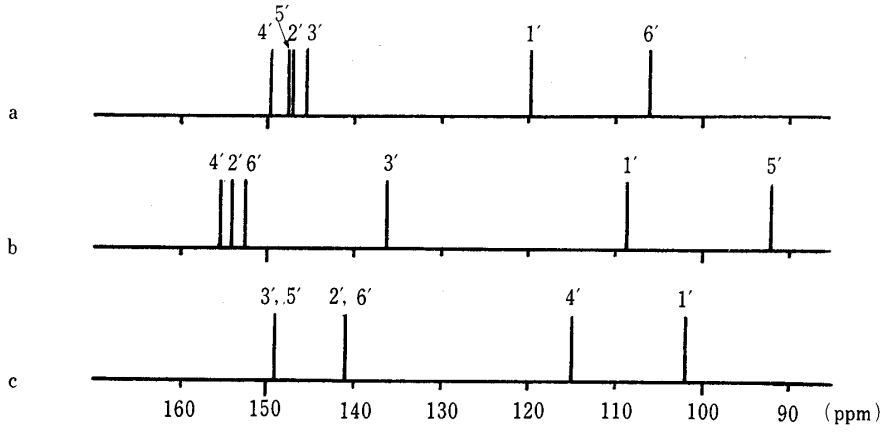


Fig. 2. Correlation of the ^{13}C-NMR Signals of Ring B of 2′,3′,4′,5′- (a), 2′,3′,4′,6′- (b) and 2′,3′,5′,6′-Tetramethoxyflavone (c)

is generally observed in flavones having methoxyl and/or hydroxyl groups at C-2′ and C-6′. The chemical shifts of the ring B protons of these highly oxygenated flavones were similar to those of flavones having methoxyl groups in ring B (H-6′, 7.20 ppm; H-4′, 6.74 ppm; H-5′, 6.30 ppm). On the other hand, the chemical shifts of the ring A protons agreed well the results reported by Hennick *et al.*[14] In their ^{13}C-NMR spectra, all carbons were assigned by calculations based on the extensive additivity rules previously reported.[15] For instance, the chemical shifts of carbons in ring B of 2′,3′,4′,6′-tetramethoxyflavones (Ib, IIb and IIIb) were obtained by calculation on the basis of 2′,3′,4′-trimethoxy- or 2′,4′,6′-trimethoxyflavone[15] as follows: 105 (1′), 153 (2′), 133 (3′), 157 (4′), 91 (5′) and 150 (6′) ppm. These values were consistent with the observed values. The differences of chemical shifts of the carbons of ring B are illustrated in Fig. 2. The chemical shift of the carbon at C-3 reflects the substitution pattern at C-2′ and C-6′ (2′,6′-dimethoxyl, *ca.* 115 ppm; 2′-methoxyl, *ca.* 112 ppm; no methoxyl, *ca.* 105 ppm[15]). The chemical shifts of methoxyl groups were dependent on their locations. The ^{13}C-NMR spectra of these flavones provided valuable information about their structures.

Experimental[16]

Flavone synthesis *via* chalcone or β-diketone was described in detail in the previous paper.[1]

Synthesis of 2,3,4,5-Tetramethoxybenzaldehyde (IV)——A solution of 3,4-dimethoxy-5-hydroxybromobenzene[8] (6.0 g, 26 mmol) in 10% NaOH (50 g) was added dropwise to 300 ml of a solution of $K_2S_2O_8$ (7.1 g) with stirring for 3 h at 20 °C. The mixture was left overnight in an ice bath and acidified to pH 5—6 with HCl. The unreacted starting material was removed by extraction with AcOEt, and the aq. solution was further acidified to pH 2, and then heat for 2 h on a water bath after addition of Na_2SO_3 (5 g). The cooled solution was extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated under reduced pressure and the residue was chromatographed on silica gel (solvent; $CHCl_3$) to give 2,5-dihydroxy-3,4-dimethoxybromobenzene (2.5 g) as a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 3.94, 3.95 (3H, each s, OCH_3), 5.90 (2H, br s, 2 × OH), 6.86 (1H, s, H-6). Methylation of the diphenol (1.5 g, 6 mmol) with dimethyl sulfate (1.52 g, 12 mmol) and K_2CO_3 (5 g) in acetone (50 ml) gave 2,3,4,5-tetramethoxybromobenzene (1.2 g) as a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 3.83, 3.88 (3H, each s, OCH_3), 3.95 (6H, s, 2 × OCH_3), 6.84 (1H, s, H-6). The bromine of this product was replaced by an aldehyde group[5,8] to yield IV as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 3.90, 3.95, 3.98, 4.00 (3H, each s, OCH_3), 7.11 (1H, s, H-6), 10.27 (1H, s, CHO).

Synthesis of 2,3,5,6-Tetramethoxybenzoic Acid (XII)——A solution of 1-cyano-2,3,5,6-tetramethoxybenzene[11] (1.5 g, 6.7 mmol) in 30% KOH (50 ml) was treated with 30% H_2O_2 solution (20 ml) with stirring. The mixture was boiled under reflux for 3 h. The cooled solution was acidified with HCl, and crude crystals of XII (1.7 g) were precipitated, mp 206—208 °C (MeOH), colorless needles. IR ν_{max}^{KBr} cm^{-1}: 1720 (CO). MS *m/z*: 242 (M^+).

2′,3′,4′,5,5′,6,7,8-Octamethoxyflavone (Ia)——2′-Hydroxy-2,3,3′,4,4′,5,5′,6′-octamethoxychalcone (VIIIa): mp 59—60 °C (EtOH), red prisms. ^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s, OCH_3), 3.93 (12H, s, 4 × OCH_3), 3.98 (6H, s,

2×OCH_3), 4.11 (3H, s, OCH_3), 6.93 (1H, s, H-6), 7.85 (1H, d, J=15.0 Hz, H-β), 8.15 (1H, d, J=15.0 Hz, H-α), 13.19 (1H, s, OH). 2′,3′,4′,5,5′,6,7,8-Octamethoxyflavanone (VIII′a): a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 2.85 (1H, d, J=5.3 Hz, H-3 *cis*), 2.91 (1H, d, J=10.5 Hz, H-3 *trans*), 3.88 (12H, s, 4×OCH_3), 3.93 (6H, s, 2×OCH_3), 3.95, 4.08 (3H, each s, OCH_3), 5.70 (1H, dd, J=10.5, 5.3 Hz, H-2), 6.90 (1H, s, H-6′). 2′,3′,4′,5,5′,6,7,8-Octamethoxyflavone (Ia) (agehoustin A): mp 114—115 °C (AcOEt–C_6H_{14}), colorless needles (lit.[2] mp 116—117 °C). ^{1}H-NMR ($CDCl_3$) δ: 3.94 (6H, s, 2×OCH_3), 3.99 (9H, s, 3×OCH_3), 4.01 (6H, s, 2×OCH_3), 4.13 (3H, s, OCH_3), 6.95 (1H, s, H-3), 7.19 (1H, s, H-6′). IR ν_{max}^{KBr} cm^{-1}: 1640, 1580, 1560. UV λ_{max}^{MeOH} nm: 250 sh, 270, 321. MS m/z (rel. int.): 462 (36), 447 (100), 417 (16), 389 (4), 225 (7), 216 (4), 197 (9).

2′,3′,4′,5,5′,6,7-Heptamethoxyflavone (IIa)——2′-Hydroxy-2,3,4,4′,5,5′,6′-heptamethoxychalcone (IXa): mp 83—84 °C (EtOH), orange-yellow needles. ^{1}H-NMR ($CDCl_3$) δ: 3.85 (3H, s, OCH_3), 3.93 (9H, s, 3×OCH_3), 3.98 (9H, s, 3×OCH_3), 6.30 (1H, s, H-3′), 6.93 (1H, s, H-6). IR ν_{max}^{KBr} cm^{-1}: 3400, 1630, 1610. MS m/z: 434 (M^+), 403 (100%). 2′,3′,4′,5,5′,6,7-Heptamethoxyflavanone (IX′a): mp 120—122 °C (EtOH), colorless prisms. ^{1}H-NMR ($CDCl_3$) δ: 2.84 (1H, d, J=4.8 Hz, H-3 *cis*), 2.91 (1H, d, J=12.0 Hz, H-3 *trans*), 3.85,3.88, 3.94, 3.96, 3.99 (3H, each s, OCH_3), 3.91 (6H, s, 2×OCH_3), 5.74 (1H, dd, J=12.0, 4.8 Hz, H-2), 6.39 (1H, s, H-8), 6.85 (1H, s, H-6′). 2′,3′,4′,5,5′,6,7-Heptamethoxyflavone (IIa) (agehoustin B): mp 98—99 °C (AcOEt–C_6H_{14}), colorless needles (lit.[2] mp 85—86 °C). ^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s, OCH_3), 3.94 (6H, s, 2×OCH_3), 3.98 (3H, s, OCH_3), 3.99 (6H, s, 2×OCH_3), 4.02 (3H, s, OCH_3), 6.75 (1H, s, H-8), 6.79 (1H, s, H-3), 6.99 (1H, s, H-6′). IR ν_{max}^{KBr} cm^{-1}: 1643, 1630, 1603. UV λ_{max}^{MeOH} nm (log ε): 239 sh (4.4), 267 sh (4.3), 312 (4.4). MS m/z (rel. int.): 432 (M^+) (28), 418 (26), 417 (100), 401 (7), 387 (29), 373 (5), 371 (5), 369 (5), 301 (3), 245 (3), 223 (2), 207 (7), 201 (9), 195 (10), 187 (7), 185 (5), 180 (6), 167 (11), 158 (6), 144 (7).

2′,3′,4′,5,5′,7,8-Heptamethoxyflavone (IIIa)——2′-Hydroxy-2,3,3′,4,4′,5,6′-heptamethoxychalcone (Xa): mp 117—118 °C (EtOH), a yellow powder. ^{1}H-NMR ($CDCl_3$) δ: 3.88 (3H, s, OCH_3), 3.93 (6H, s, 2×OCH_3), 3.98 (12H, s, 4×OCH_3), 6.05 (1H, s, H-5′), 6.91 (1H, s, H-6), 7.80, 8.13 (2H, each d, J=15.0 Hz, Hβ, Hα), 13.99 (1H, s, OH). 2′,3′,4′,5,5′,7,8-Heptamethoxyflavanone (X′a): a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 2.89 (1H, d, J=5.3 Hz, H-3 *cis*), 2.93 (1H, d, J=11.3 Hz, H-3 *trans*), 3.81 (3H, s, OCH_3), 3.88 (6H, br s, 2×OCH_3), 3.93 (3H, s, OCH_3), 3.94 (6H, s, 2×OCH_3), 3.96 (3H, s, OCH_3), 5.73 (1H, dd, J=11.3, 5.3 Hz, H-2), 6.18 (1H, s, H-6), 6.90 (1H, s, H-6′). 2′,3′,4′,5,5′,7,8-Heptamethoxyflavone (IIIa): mp 159—161 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.93 (3H, s, OCH_3), 3.94 (6H, s, 2×OCH_3), 3.98 (3H, s, OCH_3), 4.00 (6H, s, 2×OCH_3), 4.09 (3H, s, OCH_3), 6.49 (1H, s, H-6), 6.93 (1H, s, H-3), 7.19 (1H, s, H-6′). UV λ_{max}^{MeOH} nm: 261 sh, 270, 293 sh, 337. MS m/z (rel. int.): 432 (M^+) (100), 417 (93), 404 (10), 401 (5), 387 (5), 373 (5), 222 (2), 207 (2), 201 (2), 195 (12), 187 (3), 181 (2), 179 (2), 167 (17).

2′,3′,4′,5,6,6′,7,8-Octamethoxyflavone (Ib)——2′-Hydroxy-2,3,3′,4,4′,5′,6,6′-octamethoxychalcone (VIIIb): mp 113—114 °C (EtOH), red prisms. ^{1}H-NMR ($CDCl_3$) δ: 3.85, 3.88, 3.91, 3.93, 3.95, 3.96, 3.99, 4.01 (3H, each s, OCH_3), 6.43 (1H, s, H-5), 7.10, 7.42 (1H, each s, J=15.0 Hz, Hβ, Hα), 13.49 (1H, s, OH). IR ν_{max}^{KBr} cm^{-1}: 1618, 1600, 1540. 2′,3′,4′,5,6,6′,7,8-Octamethoxyflavone (Ib): a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 3.85, 3.88 (3H, each s, OCH_3), 3.95 (6H, s, 2×OCH_3), 3.98 (9H, s, 3×OCH_3), 4.11 (3H, s, OCH_3), 6.33 (1H, s, H-5′), 6.38 (1H, s, H-3). UV λ_{max}^{MeOH} nm: 257, 317. MS m/z (rel. int.): 462 (41), 447 (100), 417 (33), 389 (7), 225 (8), 216 (5), 207 (9), 197 (8).

2′,3′,4′,5,6,6′,7-Heptamethoxyflavone (IIb)——2′-Hydroxy-2,3,4,4′,5′,6,6′-heptamethoxychalcone (IXb): mp 130—132 °C (EtOH), an orange powder. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (6H, s, 2×OCH_3), 3.90 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 3.95 (6H, s, 2×OCH_3), 3.96 (3H, s, OCH_3), 6.30, 6.33 (1H, each s, H-5,3′), 8.12, 8.45 (1H, each d, J=15.0 Hz, Hβ, Hα), 13.95 (1H, s, OH). IR ν_{max}^{KBr} cm^{-1}: 3420, 1610, 1605, 1540. MS m/z: 434 (M^+), 403 (100%), 2′,3′,4′,5,6,6′,7-Heptamethoxyflavone (IIb): mp 149—151 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.81, 3.86, 3.90, 3.93, 3.94, 3.95, 4.01 (3H, each s, OCH_3), 6.29 (1H, s, H-5′), 6.35 (1H, s, H-3), 6.75 (1H, s, H-8). IR ν_{max}^{KBr} cm^{-1}: 1650, 1600. UV λ_{max}^{MeOH} nm (log ε): 259 (4.5), 308 (4.5). MS m/z (red. int.): 432 (M^+) (23), 418 (22), 417 (100), 387 (23), 207 (15), 195 (17), 188 (17), 187 (10), 173 (20), 167 (13).

2′,3′,4′,5,6′,7,8-Heptamethoxyflavone (IIIb)——2′-Hydroxy-2,3,3′,4,4′,6,6′-heptamethoxychalcone (Xb): mp 137—138 °C (EtOH), orange-yellow prisms. ^{1}H-NMR ($CDCl_3$) δ: 3.85 (6H, s, 2×OCH_3), 3.90, 3.94 (3H, each s, OCH_3), 3.96 (9H, s, 3×OCH_3), 6.04 (1H, s, H-5′), 6.33 (1H, s, H-5), 8.05, 8.41 (1H, each d, J=15.0 Hz, Hβ, Hα), 13.20 (1H, s, OH). IR ν_{max}^{KBr} cm^{-1}: 3400, 1620, 1598. MS m/z: 434 (M^+), 403 (100%). 2′,3′,4′,5,6′,7,8-Heptamethoxyflavone (IIIb): mp 166—167 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.80, 3.85, 3.86, 3.93, 3.96 (3H, each s, OCH_3), 4.01 (6H, s, 2×OCH_3), 6.30 (1H, s, H-5′), 6.35 (1H, s, H-3), 6.46 (1H, s, H-6). IR ν_{max}^{KBr} cm^{-1}: 1650, 1600. UV λ_{max}^{MeOH} nm: 255 sh, 260, 295 sh, 327. MS m/z (rel. int.): 432 (M^+) (100), 417 (89), 404 (11), 387 (9), 373 (3), 222 (3), 216 (3), 201 (3), 195 (14), 187 (6), 181 (3), 179 (6), 167 (17).

2′,3′,5,5′,6,6′,7,8-Octamethoxyflavone (Ic)——2-(2′,3′,5′,6′-Tetramethoxybenzoyloxy)-,3,4,5,6-tetramethoxyacetophenone (VIIIc): mp 126—128 °C (EtOH), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, s, $COCH_3$), 6.69 (1H, s, H-4′). 2-Hydroxy-2′,3,3′,4,5,5′,6,6′-octamethoxydibenzoylmethane (VIII′c): a yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 6.65 (1H, s, H-4′), 6.92 (2H, s, $COCH_2CO$), 12.95 (1H, s, OH). 2′,3′,5,5′,6,6′,7,8-Octamethoxyflavone (Ic): mp 118—120 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.83 (6H, s, 2×OCH_3), 3.93 (9H, s, 3×OCH_3), 3.99, 4.01, 4.13 (3H, each s, OCH_3), 6.43 (1H, s, H-3), 6.75 (1H, s, H-4′). IR ν_{max}^{KBr} cm^{-1}: 1650, 1638, 1600. UV λ_{max}^{MeOH} nm: 258, 292 sh, 318 sh. MS m/z (rel. int.): 462 (M^+) (37), 447 (100), 417 (13), 389 (5), 225 (9), 216 (4), 207 (8), 197 (15).

2′,3′,5,5′,6,6′,7-Heptamethoxyflavone (IIc)——2-(2′,3′,5′,6′-Tetramethoxybenzoyloxy)-4,5,6-trimethoxyacetophenone (IXc): mp 106—107 °C (EtOH), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 2.53 (3H, s, $COCH_3$), 3.89 (15H, s, $5\times OCH_3$), 3.95 (6H, s, $2\times OCH_3$), 6.60 (1H, s, H-3), 6.68 (1H, s, H-4′). 2-Hydroxy-2′,3′,4,5,5′,6,6′-heptamethoxydibenzoylmethane (IX′c): a yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 3.75, 3.81 (3H, each s, OCH_3), 3.88 (12H, s, $4\times OCH_3$), 3.93 (3H, s, OCH_3), 6.28, 6.65 (1H, each s, H-3,4′), 6.90 (2H, s, $COCH_2CO$), 13.20 (1H, s, OH). 2′,3′,5,5′,6,6′,7-Heptamethoxyflavone (IIc): mp 149—150 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.79 (6H, s, $2\times OCH_3$), 3.94 (12H, s, $4\times OCH_3$), 4.04 (3H, s, OCH_3), 6.33 (1H, s, H-3), 6.74 (2H, s, H-8 and H-4′). IR ν_{max}^{KBr} cm^{-1}: 1650, 1610. UV λ_{max}^{MeOH} nm: 257 sh, 295. MS *m/z* (rel. int.): 432 (M^+) (36), 417 (100), 404 (1), 387 (49), 373 (2), 371 (3), 222 (1), 207 (6), 201 (13), 195 (9), 187 (7), 179 (7), 167 (20), 164 (9).

2′,3′,5,5′,6′,7,8-Heptamethoxyflavone (IIIc)——2-(2′,3′,5′,6′-Tetramethoxybenzoyloxy)-3,4,6-trimethoxyacetophenone (Xc): mp 157—159 °C (EtOH), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 2.54 (3H, $COCH_3$), 3.89 (3H, s, OCH_3), 3.90 (15H, s, $5\times OCH_3$), 3.98 (3H, s, OCH_3), 6.50 (1H, s, H-5), 6.68 (1H, s, H-4′). 2-Hydroxy-2′,3,3′,4,5′,6,6′-heptamethoxydibenzoylmethane (X′c): mp 131—133 °C (EtOH), a pale yellow powder. ^{1}H-NMR ($CDCl_3$) δ: 3.83, 3.85, 3.93 (6H, each s, $2\times OCH_3$), 3.96 (3H, s, OCH_3), 6.01, 6.65 (1H, each s, H-5, 4′), 6.88 (2H, s, $COCH_2CO$), 13.58 (1H, s, OH). 2′,3′,5,5′,6′,7,8-Heptamethoxyflavone (IIIc): mp 173—174 °C (AcOEt–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 3.80 (6H, s, $2\times OCH_3$), 3.85 (3H, s, OCH_3), 3.93 (6H, s, $2\times OCH_3$), 4.05 (6H, s, $2\times OCH_3$), 6.32 (1H, s, H-3), 6.50 (1H, s, H-6), 6.74 (1H, s, H-4′). IR ν_{max}^{KBr} cm^{-1}: 1660, 1630, 1600. UV λ_{max}^{MeOH} nm: 260, 297 sh, 321. MS *m/z* (rel. int.): 432 (M^+) (100), 417 (79), 403 (14), 402 (21), 387 (31), 373 (7), 359 (10), 242 (17), 227 (10), 226 (7), 212 (7), 211 (10), 201 (12), 195 (14), 181 (5), 179 (7), 167 (31).

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References and Notes

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