[Chem. Pharm. Bull. 32(4)1472—1476(1984)]

Synthetic Studies on Flavone Derivatives. XV. Isomerization of Chalcones into Flavanones in Methyl Cellosolve–Phosphoric Acid

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(Received August 12, 1983)

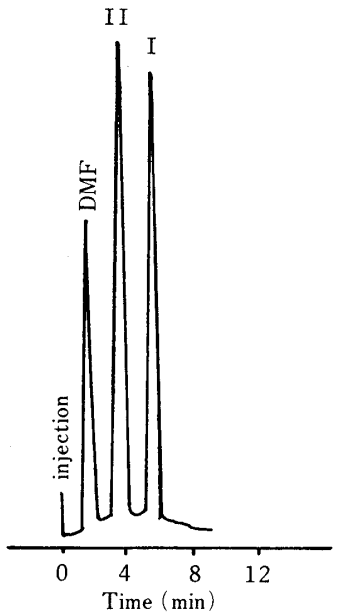
Isomerization of a chalcone having several benzyloxyl groups into a flavanone by the use of phosphoric acid in methyl cellosolve was investigated, and higher yields of flavanones were obtained with much shorter reaction times than in the conventional procedure. The reaction was applied to the synthesis of three flavanones, agestricins B, C and D, isolated from *Ageratum strictum*. A chalcone, agestricin A, was also prepared to confirm its structure.

Keywords——chalcone isomerization; flavanone synthesis; 3,4-dibenzyloxy-2′-hydroxy-4′-methoxychalcone; 3′,4′-dibenzyloxy-7-methoxyflavanone; 2′,5′-dihydroxy-4′,6′-dimethoxy-3,4-methylenedioxychalcone; 6-hydroxy-5,7-dimethoxy-3′,4′-methylenedioxyflavanone; 6-hydroxy-3′,4′,5,7-tetramethoxyflavanone; 4′,6-dihydroxy-3′,5,7-trimethoxyflavanone; 3′,6-dihydroxy-4′,5,7-trimethoxyflavanone

Flavanones, which are generally derived from chalcones, are believed to be biosynthetic precursors of flavones, and sometimes occur naturally themselves.[1] The most general method for flavanone synthesis is to heat the requisite chalcone either in the presence of an acid catalyst such as hydrochloric acid or phosphoric acid, or in the presence of a base catalyst. However, we have occasionally found that chalcones substituted with several benzyloxyl groups cannot be converted into the corresponding flavanones in the usual way. In this conversion, ethanol has frequently been employed as a solvent, but disadvantage of ethanol is that polybenzyloxy-substituted chalcones are poorly soluble. Cyclization of the chalcone into the flavanone might proceed in other solvents. After investigation of many polar solvents, methyl cellosolve (ethylene glycol monomethyl ether) and ethyl cellosolve (ethylene glycol monoethyl ether) were found to be effective. We describe in this paper an improved method which is widely applicable to the acid-catalyzed conversion of chalcones into flavanones.

As a preliminary study, the conversion of 3,4-dibenzyloxy-2′-hydroxy-4′-methoxychalcone (I) into 3′,4′-dibenzyloxy-7-methoxyflavanone (II) was examined by the use of phosphoric acid (PA) in ethanol, methyl cellosolve or ethyl cellosolve. In the case of methyl cellosolve, three concentrations of PA were examined. The conversion was followed periodically by high performance liquid chromatography, and the rate of isomerization was calculated from calibration curves prepared in advance. The results thus obtained are shown in Fig. 1. In methyl cellosolve and in ethyl cellosolve, the reactions rapidly attained equilibrium between I and II within 1 or 2 h. On the other hand, in ethanol the conversion was still proceeding even after 4 h. The higher concentration of PA (curve c) apparently resulted in more rapid conversion into the flavanone. An excess of PA (curve d), however, caused debenzylation of the chalcone.

In order to study the generality of the reaction, it was applied to the synthesis of other flavanones. The results of these experiments are shown in Table I. All conversions were carried out under the following conditions: chalcone (1 mmol) dissolved in methyl cellosolve (10 ml) containing 1 ml of 85% PA were boiled under reflux, and the ratios of chalcones and the



High-Performance Liquid Chromatogram of I and II

Column, Cosmosil $5C_{18}$ $4.6\phi \times 150$ mm.
Flow rate, 1 ml/min.
Solvent: 90% MeCN. Detector, UV 260 nm.

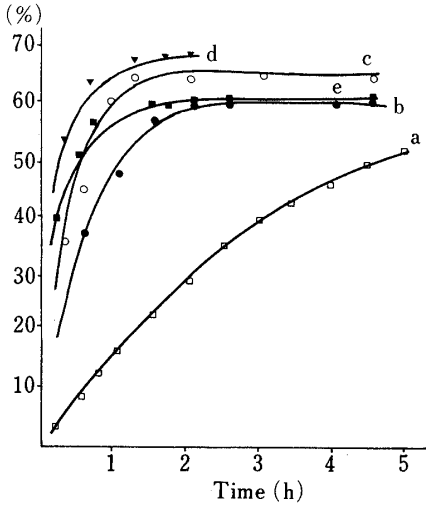
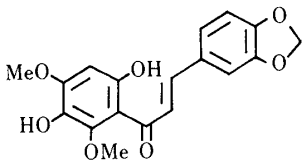


Fig. 1. Relationship between Conversion Ratio of Chalcone (I) into Flavanone (II) and Reaction Time

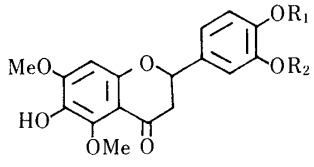
a, ethanol (10 ml) containing 2 ml of phosphoric acid (PA) (85%); b, methyl cellosolve (MC) (10 ml)+PA (1 ml); c, MC (10 ml)+PA (2 ml); d, MC (10 ml)+PA (3 ml); e, ethyl cellosolve (10 ml)+PA (1 ml).

TABLE I. Chalcone–Flavanone Isomerization Ratios in Methyl Cellosolve–Phosphoric Acid

	Chalcone (%)	Flavanone (%)	Reaction time (h)
2-Benzyloxy-2′-hydroxychalcone	50	50	2.5
5′-Benzyloxy-2′-hydroxychalcone	23	77	2.5
4,4′-Dibenzyloxy-2′-hydroxychalcone	49	51	2.5
4′,6′-Dibenzyloxy-2′-hydroxychalcone	44	56	2.5
2-Benzyloxy-2′-hydroxy-3′,4′,6′-trimethoxychalcone	65	35	2.5
4,4′,6′-Tribenzyloxy-2′-hydroxy-3-methoxychalcone	51	49	2.5
3,4,4′,6′-Tetrabenzyloxy-2′-hydroxychalcone	55	45	2.5



III



IV : $R_1=R_2=-CH_2-$
V : $R_1=R_2=Me$
VI : $R_1=H$, $R_2=Me$
VII : $R_1=Me$, $R_2=H$

Chart 1

produced flavanones were determined from the proton nuclear magnetic resonance (^{1}H-NMR) spectra by comparison of the integral values of α and β-protons of chalcones and C_3-protons of flavanones. The reaction was concluded to be widely useful for the conversion of chalcones substituted with polybenzyloxyl groups into flavanones. The reaction was further

applied to the preparation of some naturally occurring flavanones.

Four new flavonoids, 2′,5′-dihydroxy-4′,6′-dimethoxy-3,4-methylenedioxychalcone (III) and 6-hydroxy-5,7-dimethoxy-3′,4′-methylenedioxy- (IV), 6-hydroxy-3′,4′,5,7-tetramethoxy- (V), and 4′,6-dihydroxy-3′,5,7-trimethoxyflavanone (VI), isolated from aerial parts of *Ageratum strictum* by Quijano *et al.*,[2] were named agestricins A, B, C and D, respectively, and their structures were established on the basis of spectral data and chemical degradation. The 3′,6-dihydroxy-4′,5,7-trimethoxyflavanone VII was also prepared as an isomer of VI for comparison with these compounds. The starting material for the ring A moiety of these flavanones, 2,5-dihydroxy-4,6-dimethoxyacetophenone (VIII), was synthesized in the usual way.[3] Benzylation of VIII with benzyl chloride and K_2CO_3 in DMF gave 5-benzyloxy-2-hydroxy-4,6-dimethoxyacetophenone (IX).[4] Compound IX was condensed with piperonal, veratraldehyde, benzylvanillin or benzylisovanillin in the presence of KOH in ethanol to give 5′-benzyloxy-2′-hydroxy-4′,6′-dimethoxy-3,4-methylenedioxy- (X), 5′-benzyloxy-2′-hydroxy-3,4,4′,6′-tetramethoxy- (XI), 4,5′-dibenzyloxy-2′-hydroxy-3,4′,6′-trimethoxy- (XII) or 3,5′-dibenzyloxy-2′-hydroxy-4,4′,6′-trimethoxychalcone (XIII), respectively. The resulting chalcones could not be converted into the corresponding flavanones in the conventional way, so the improved method was applied to obtain 6-benzyloxy-5,7-dimethoxy-3′,4′-methylenedioxy- (XIV), 6-benzyloxy-3′,4′,5,7-tetramethoxy- (XV), 4′,6-dibenzyloxy-3′,5,7-trimethoxy- (XVI) and 3′,6-dibenzyloxy-4′,5,7-trimethoxyflavanone (XVII) in good yields. The flavanones thus obtained were subjected to catalytic hydrogenation with 10% Pd–C to afford IV, V, VI and VII, respectively. The flavanones thus prepared (IV, V, and VI) were shown to be identical with agestricins B, C and D by direct comparison (mixed mp, co-thin layer chromatography (TLC) and spectral data), and their structures were confirmed to be 6-hydroxy-5,7-dimethoxy-3′,4′-methylenedioxyflavanone, 6-hydroxy-3′,4′,5,7-tetramethoxyflavanone and 4′,6-dihydroxy-3′,5,7-trimethoxyflavanone. Preparation of III was accomplished by debenzylation of X according to the method described by Fuji *et al.*[5] A small

Table II. ^{13}C-NMR Chemical Shifts of IV, V, VI and VII

	IV	V	VI	VII
2	79.4	79.3	79.7	79.2
3	45.6	45.3	45.5	45.2
4	190.6	189.6	191.2	189.2
5	155.3	154.0	155.5	154.0
6	134.7	134.0	134.7	133.8
7	157.3	157.0	157.6	157.1
8	96.5	96.2	96.6	96.3
9	155.3	154.0	155.5	154.0
10	108.6	108.5	108.7	108.5
1′	132.8	131.3	130.6	131.8
2′	108.5	109.7	110.0	112.6
3′	148.2	149.4	147.8	146.0
4′	146.6	146.1	146.8	146.9
5′	106.9	111.3	115.4	110.8
6′	120.2	118.8	119.6	118.0
5-OMe	61.4	61.5	61.3	61.6
7-OMe	56.3	56.2	56.3	56.2
3′-OMe	—	56.0	56.1	—
4′-OMe	—	56.0	—	56.0
3′,4′-OCH_2O	101.5 *a)*	— *a)*	— *b)*	— *a)*

a) $CDCl_3$. *b)* $CDCl_3$–CD_3OD = 1 : 1.

amount of III was also obtained upon treatment of X with ethyl cellosolve containing 20% PA under reflux for 10 h. The chalcone III was identical with authentic agestricin A by the same criteria as described above.

Carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra of IV, V, VI and VII were measured and each signal was assigned in the following way. The skeletal carbons of ring B were assigned on the basis of those of 4′,5,7-trihydroxy-3′-methoxyflavanone (homoeriodictyol)[6] and 3′,5,7-trihydroxy-4′-methoxyflavanone (hesperetin),[6] whereas the chemical shifts of carbons of ring A were calculated by application of the extensive additivity rules previously reported.[7] All chemical shifts of these compounds were characteristic of the flavanone structures and reflected the differences of substituent patterns.

Experimental[8]

General Procedures for Isomerization of Chalcones into Flavanones——A solution of a chalcone (7 mmol) dissolved in methyl cellosolve (50 ml) containing 5 g of 85% phosphoric acid was boiled under reflux for 5 h. The mixture was extracted with water and AcOEt. The AcOEt extract was purified by column chromatography on silica gel to obtain the corresponding flavanone.

3,4-Dibenzyloxy-2′-hydroxy-4′-methoxychalcone (I)——Chalcone (I) was prepared by the conventional method of condensation of 2-hydroxy-4-methoxyacetophenone with 3,4-dibenzyloxybenzaldehyde as yellow needles, mp 121—123 °C (MeOH). ^{1}H-NMR ($CDCl_3$) δ: 3.79 (3H, s, OCH_3), 5.12 (4H, s, 2 × $OC\underline{H}_2Ph$), 6.33—7.82 (6H, m, H-2,5,6,3′,5′,6′), 7.28, 7.31 (5H, each s, Ph), 7.57 (2H, s, H-α and β). UV λ_{max}^{MeOH} nm (log ε): 248 (4.0), 260 (4.0), 315 sh (4.1), 377 (4.5).

3′,4′-Dibenzyloxy-7-methoxyflavanone (II)——According to the general procedure, the chalcone (I) was converted into II in 70% yield, mp 110—111 °C (C_6H_6–C_6H_{14}), colorless needles. ^{1}H-NMR ($CDCl_3$) δ: 2.75 (1H, d, J=5.5 Hz, H-3 *cis*), 2.86 (1H, d, J=10.6 Hz, H-3 *trans*), 3.71 (3H, s, OCH_3), 5.08 (4H, s, 2 × $OC\underline{H}_2Ph$), 5.23 (1H, dd, J=10.6, 5.5 Hz, H-2), 6.38—7.25 (5H, m, H-6,8,2′,5′,6′), 7.21 7.23 (5H, each s, Ph), 7.70 (1H, d, J=8.0 Hz, H-5). UV λ_{max}^{MeOH} nm (log ε): 234 (4.4), 276 (4.2), 313 (3.8).

2′,5′-Dihydroxy-4′,6′-dimethoxy-3,4-methylenedioxychalcone (Agestricin A) (III)——Condensation of IX (2.9 g, 10 mmol) with piperonal (1.5 g, 10 mmol) gave 5′-benzyloxy-2′-hydroxy-4′,6′-dimethoxy-3,4-methylenedioxychalcone (X) (3.8 g) as orange-yellow needles, mp 140—141 °C (MeOH). ^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 5.00 (2H, s, $OC\underline{H}_2Ph$), 6.04 (2H, s, OCH_2O), 6.32 (1H, s, H-3′), 6.80 (1H, d, J=8.7 Hz, H-5), 7.15 (1H, dd, J=8.7, 2.0 Hz, H-6), 7.30 (1H, d, J=2.0 Hz, H-2), 7.42 (5H, s, Ph), 7.48 (5H, s, Ph), 7.80 (2H, s, H-α and β), 13.70 (1H, OH). An EtSH solution of X was treated with 47% BF_3–ethyl ether (5 ml), and the mixture was left overnight at room temperature. The solution was poured into water (100 ml), and extracted with AcOEt. The AcOEt extract was washed with water and then concentrated. The residue was recrystallized from C_6H_6 to give III as red prisms, mp 188—189 °C (reported[2] mp 190—192 °C). ^{1}H-NMR ($CDCl_3$ + DMSO-d_6) δ: 3.89, 3.95 (3H, each s, OCH_3), 6.10 (2H, s, OCH_2O), 6.32 (1H, s, H-3′), 6.90 (1H, d, J=8.8 Hz, H-5), 7.17 (1H, d, J=1.5 Hz, H-2), 7.18 (1H, dd, J=8.8, 1.5 Hz, H-6), 7.78 (2H, s, H-α and β), 8.02 (1H, br s, OH), 13.28 (1H, s, OH). *Anal.* Calcd for $C_{18}H_{16}O_7$: C, 62.79: H, 4.68. Found: C, 62.55; H, 4.73. MS *m/z* (rel. int.): 344 (M^+) (25), 233 (5), 196 (100), 153 (23). UV λ_{max}^{MeOH} nm (log ε): 259 (4.1), 314 sh (4.1), 367 (4.3). IR ν_{max}^{KBr} cm^{-1}: 3350, 2975, 1620, 1600, 1550.

6-Hydroxy-5,7-dimethoxy-3′,4′-methylenedioxyflavanone (Agestricin B) (IV)——Isomerization of X, followed by debenzylation, gave IV as pale yellow prisms, mp 135—137 °C (reported[2] mp 136—137 °C). ^{1}H-NMR ($CDCl_3$) δ: 2.84 (1H, d, J=5.0 Hz, H-3 *cis*), 2.97 (1H, d, J=11.9 Hz, H-3 *trans*), 3.93 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 5.34 (1H, dd, J=11.9, 5.0 Hz, H-2), 6.01 (2H, s, OCH_2O), 6.39 (1H, s, H-8), 6.98—7.38 (3H, m, H-2′,5′,6′). MS *m/z* (rel. int.): 344 (M^+) (32), 223 (4), 196 (100), 181 (13), 153 (24), 148 (23). *Anal.* Calcd for $C_{18}H_{16}O_7$: C, 62.79; H, 4.68. Found: C, 63.00, H, 4.71. UV λ_{max}^{MeOH} nm (log ε): 238 (4.5), 281 (4.4), 342 (3.8). IR ν_{max}^{KBr} cm^{-1}: 3430, 2940, 1660, 1605, 1485.

6-Hydroxy-3′,4′,5,7-tetramethoxyflavanone (Agestricin C) (V)——Condensation of IX (1.2 g, 4.1 mmol) with veratraldehyde (0.7 g, 4.1 mmol) gave 5′-benzyloxy-2′-hydroxy-3,4,4′,6′-tetramethoxychalcone (XI) (1.6 g) as orange-yellow needles, mp 79—81 °C. ^{1}H-NMR ($CDCl_3$) δ: 3.90, 3.95 (3H, each s, OCH_3), 3.98 (6H, s, 2 × OCH_3), 5.00 (2H, s, $OC\underline{H}_2Ph$), 6.34 (1H, d, H-3′), 6.92 (1H, d, J=8.0 Hz, H-5), 7.20—7.48 (7H, m, H-2,6 and Ph), 7.85 (2H, s, H-α and β), 13.75 (1H, s, OH). The chalcone (XI) was converted to 6-benzyloxy-3′,4′,5,7-tetramethoxyflavanone (XV) by the general procedure as pale yellow needles, mp 113—115 °C (AcOEt–C_6H_{14}). ^{1}H-NMR ($CDCl_3$) δ: 2.85 (1H, d, J=4.8 Hz, H-3 *cis*), 2.97 (1H, d, J=12.0 Hz, H-3 *trans*), 3.84, 3.92 (3H, each s, OCH_3), 3.93 (6H, s, 2 × OCH_3), 4.98 (2H, s, $OC\underline{H}_2Ph$), 5.36 (1H, dd, J=12.0, 4.8 Hz, H-2), 6.35 (1H, s, H-8), 6.96—7.45 (8H, m, H-2′,4′,6′ and Ph). 6-Hydroxy-3′,4′,5,7-tetramethoxyflavanone (V): mp 156—157 °C (C_6H_6–C_6H_{14}), colorless needles (reported[2] mp 159—160 °C). ^{1}H-NMR ($CDCl_3$) δ: 2.87 (1H, d, J=5.0 Hz, H-3 *cis*), 2.93 (1H, d, J=11.8 Hz, H-3 *trans*), 3.94 (6H, s, 2 × OCH_3),

3.97 (6H, s, 2 × OCH_3), 5.57 (1H, dd, J = 11.8, 5.0 Hz, H-2), 6.40 (1H, s, H-8), 6.85—7.36 (3H, m, H-2′,5′,6′). MS m/z (rel. int.): 360 (M^+) (46), 356 (5), 282 (3), 213 (5), 196 (100), 181 (10), 164 (68). *Anal.* Calcd for $C_{19}H_{20}O_7$: C, 63.33; H, 5.59. Found: C, 63.18; H, 5.58. UV λ_{max}^{MeOH} nm (log ε): 237 (4.3), 280 (4.2), 345 (3.6). IR ν_{max}^{KBr} cm^{-1}: 3420, 2940, 2830, 1670, 1605, 1508, 1490.

4′,6-Dihydroxy-3′,5,7-trimethoxyflavanone (Agestricin D) (VI)——Condensation of IX (2.0 g, 6.9 mmol) with benzylvanillin (1.7 g, 6.9 mmol) gave 4,5′-dibenzyloxy-2′-hydroxy-3,4′,6-trimethoxychalcone (XII) (3.2 g) as orange-yellow needles, mp 115—116 °C (EtOH). ^{1}H-NMR ($CDCl_3$) δ: 3.88 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 5.00 (2H, s, $OC\underline{H}_2Ph$), 5.25 (2H, s, $OC\underline{H}_2Ph$), 6.32 (1H, s, H-3′), 6.92 (1H, d, J = 8.8 Hz, H-5), 7.25 (1H, dd, J = 8.8, 2.0 Hz, H-6), 7.36 (1H, d, J = 2.0 Hz, H-2), 7.42 (5H, br s, Ph), 7.46 (5H, br s, Ph), 7.84 (2H, s, H-α and β), 13.73 (1H, s, OH). The chalcone (XII) was converted by the general procedure to 4′,6-dibenzyloxy-3′,5,7-trimethoxyflavanone (XVI) as colorless needles, mp 125—126 °C (MeOH). ^{1}H-NMR ($CDCl_3$) δ: 2.84 (1H, d, J = 4.5 Hz, H-3 *cis*), 2.96 (1H, d, J = 12.0 Hz, H-3 *trans*), 3.82, 3.91, 3.93 (3H, each s, OCH_3), 4.96, 5.18 (2H, each s, $OC\underline{H}_2Ph$), 5.35 (1H, dd, J = 12.0, 4.5 Hz, H-2), 6.34 (1H, s, H-8), 6.90 (1H, d, J = 8.5 Hz, H-5′), 7.25—7.55 (2H, m, H-2′ and 6′), 7.38, 7.44 (5H, each s, Ph). 4′,6-Dihydroxy-3′,5,7-trimethoxyflavanone (VI): mp 173—174 °C. (C_6H_6–C_6H_{14}), colorless prisms (reported[2] mp 180—182 °C). ^{1}H-NMR ($CDCl_3$) δ: 2.76 (1H, d, J = 4.0 Hz, H-3 *cis*), 2.92 (1H, d, J = 12.1 Hz, H-3 *trans*), 3.82 (3H, s, OCH_3), 3.89 (6H, s, 2 × OCH_3), 5.33 (1H, dd, J = 12.1, 4.0 Hz, H-2), 6.41 (1H, s, H-8), 6.89—7.04 (3H, m, H-2′,5′,6′). MS m/z (rel. int.): 346 (M^+) (41), 223 (4), 197 (65), 196 (100), 181 (3), 156 (26), 150 (18). *Anal.* Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.20; H, 5.27. UV λ_{max}^{MeOH} nm (log ε): 237 (4.3), 280 (4.1), 345 (3.5). IR ν_{max}^{KBr} cm^{-1}: 3210, 2940, 2830, 1670, 1605, 1530, 1495.

3′,6-Dihydroxy-4′,5,7-trimethoxyflavanone (VII)——Condensation of IX (1.5 g, 5 mmol) with benzylisovanillin (1.3 g, 5 mmol) gave 3,5′-dibenzyloxy-2′-hydroxy-4,4′,6′-trimethoxychalcone (XIII) (2.3 g) as orange-yellow needles, mp 137—140 °C (MeOH). ^{1}H-NMR ($CDCl_3$) δ: 3.83, 3.88, 3.95 (3H, each s, OCH_3), 4.98, 5.23 (2H, each s, $OC\underline{H}_2Ph$), 6.29 (1H, s, H-3′), 6.92 (1H, d, J = 9.0 Hz, H-5), 7.18—7.38 (2H, m, H-2,6), 7.41, 7.45 (5H, each br s, Ph), 7.75 (2H, s, H-α and β), 13.75 (1H, s, OH). The chalcone (XIII) was converted by the general procedure to 3′,6-dibenzyloxy-4′,5,7-trimethoxyflavanone (XVII) as pale yellow needles, mp 129—130 °C (C_6H_6). ^{1}H-NMR ($CDCl_3$) δ: 2.80 (1H, d, J = 4.9 Hz, H-3 *cis*), 2.90 (1H, d, J = 12.0 Hz, H-3 *trans*), 3.84, 3.91, 3.95 (3H, each s, OCH_3), 5.00, 5.19 (2H, each s, $OC\underline{H}_2Ph$), 5.33 (1H, dd, J = 12.0, 4.9 Hz, H-2), 6.33 (1H, s, H-8), 6.99—7.56 (13H, H-2′,5′,6′ and 2 × Ph). 3′,6-Dihydroxy-4′,5,7-trimethoxyflavanone (VII): mp 117—118 °C (C_6H_6–C_6H_{14}), cololess needles. ^{1}H-NMR ($CDCl_3$) δ: 2.85 (1H, J = 5.0 Hz, H-3 *cis*), 2.95 (1H, d, J = 11.8 Hz, H-3 *trans*), 3.94 (6H, s, 2 × OCH_3), 3.98 (3H, s, OCH_3), 5.30 (1H, dd, J = 11.8, 5.0 Hz, H-2), 6.40 (1H, s, H-8), 6.91—7.31 (3H, m, H-2′,5′,6′). MS m/z (rel. int.): 346 (M^+) (37), 223 (6), 197 (49), 196 (100), 181 (14), 153 (29), 150 (17). *Anal.* Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24. Found: C, 62.33; H, 5.42. UV λ_{max}^{MeOH} nm (log ε): 237 (4.4), 280 (4.3), 344 (3.7). IR ν_{max}^{KBr} cm^{-1}: 3400, 2850, 1670, 1608, 1508, 1500.

Acknowledgement The authors are most grateful to Dr. L. Quijano, Instituto de Quimica, Universidad Nacional Autonoma de Mexico, for providing authentic samples of agestricins A, B, C and D.

References and Notes

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3) After oxidation of trimethylpyrogallol with nitric acid, reductive acetylation of the resulting quinone with sodium acetate and zinc powder in acetic anhydride gave 1,4-diacetoxy-2,6-dimethoxybenzene, which was subjected to the Fries rearrangement to afford VIII.
4) 5-Benzyloxy-2-hydroxy-4,6-dimethoxyacetophenone (IX): colorless liquid. ^{1}H-NMR (CCl_4) δ: 2.56 (3H, s, $COCH_3$), 3.75 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.84 (2H, s, $OC\underline{H}_2Ph$), 6.13 (1H, s, H-3), 7.29—7.38 (5H, m, Ph), 13.34 (1H, s, OH).
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8) Melting points were determined on a Büchi melting point apparatus, and are uncorrected. Ultraviolet (UV) spectra were taken on a Hitachi 323 spectrometer and mass spectra (MS) were obtained on a JEOL JMS-300 mass spectrometer at 70 eV. ^{1}H-NMR were taken on a Hitachi R-20B at 60 MHz and chemical shifts are given in δ values (ppm) with tetramethylsilane as an internal standard. ^{13}C-NMR spectra were obtained on a JEOL FX-60FT spectrometer operating at 25.15 MHz, spectral width 4000 Hz and 4096 data points. BW-820 MH (Fuji Devison Chemicals, Ltd.) was used for column chromatography.