Studies of the Selective *O*-Alkylation and Dealkylation of Flavonoids. XVIII.[1] A Convenient Method for Synthesizing 3,5,6,7-Tetrahydroxyflavones

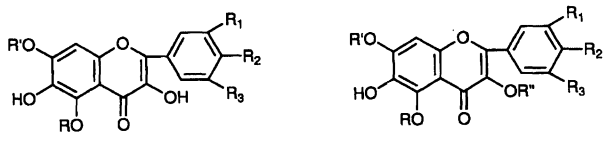
Tokunaru Horie,* Takashi Kobayashi, Yasuhiko Kawamura, Isao Yoshida, Hideaki Tominaga, and Kazuyo Yamashita

Department of Chemical Science and Technology, Faculty of Engineering, The University of Tokushima, Minamijosanjima-cho, Tokushima 770

(Received February 7, 1995)

In the demethylation of 6-hydroxy-3,4′,7-trimethoxy-5-(tosyloxy)flavone with anhydrous aluminum bromide, the 5-tosyloxyl group was eliminated with bromination to give 8-bromo-3,6,7-trihydroxy-4′-methoxyflavone as the main product. When anhydrous aluminum chloride was used in the demethylation of the acetate, the 5-tosyloxyl group was cleaved prior to the demethylation to give 5,6,7-trihydroxy-3,4′-dimethoxyflavone. Demethylation of 6-hydroxy-4′,5,7-trimethoxy-3-(tosyloxy)flavone and its acetate with the bromide or chloride afforded the 5,6,7-trihydroxyflavone without the cleavage of the 3-tosyloxyl group, but was not suitable for the general synthesis of the 3,5,6,7-tetrahydroxyflavones because of the difficulty in removing the protecting group. Consequently, it was found that the direct demethylation of 3,6-dihydroxy-5,7-dimethoxyflavones with anhydrous aluminum chloride–sodium iodide in acetonitrile was the most useful general method for synthesizing 3,5,6,7-tetrahydroxyflavones. Additionally, the reported structures of two natural flavones were revised.

In previous papers,[2,3] we reported that 5,6,7-trihydroxy-3-methoxyflavones (**2**) and 3,5,6-trihydroxy-7-methoxyflavones (**3**) were conveniently synthesized from 6-hydroxy-3,5,7-trimethoxyflavones (**4**) by selective demethylation. The result suggests that 3,5,6,7-tetrahydroxyflavones (**1**) can also be synthesized from **4** or 3,6-dihydroxy-5,7-dimethoxyflavones (**5**) by a similar method (Chart 1). The flavones **1** with no methoxyl group on the B ring are easily synthesized by the total demethylation of their methyl ethers,[4,5] but no synthetic method of **1** with methoxyl groups has been established and the general properties are not always clear. Thus the selective demethylation of the derivatives of **4** and **5** was examined. The demethylation of 6-hydroxy-3,4′,7-trimethoxy-5-(tosyloxy)flavone (**6b**) and its acetate (**A6b**) with anhydrous aluminum bromide or chloride in acetonitrile was accompanied by the cleavage or elimination of the tosyloxyl group and the desired product **8b** (the 5-tosylate of **1b**) was not obtained. In contrast, the 3-tosylate of **5b** (**7b**) and its acetate (**A7b**) were smoothly demethylated to the 3-tosylate (**9b**), but the hydrolysis of the tosyloxyl group was difficult. Consequently, it was found that the flavones **1** could be synthesized conveniently from **5** by direct demethylation with anhydrous aluminum chloride–sodium iodide in acetonitrile. In this paper, we report a convenient method for synthesizing the flavones **1** and these characterizations, and we revise the identification of some natural flavones.



1 R=R′=H
3 R=H, R′=Me
5 R=R′=Me
8 R=Ts, R′=H

2 R=R′=H, R″=Me
4 R=R′=R″=Me
6 R=Ts, R′=R″=Me
7 R=R′=Me, R″=Ts
9 R=R′=H, R″=Ts

a R_1=R_2=R_3=H **b** R_1=R_3=H, R_2=OMe **c** R_1=R_2=OMe, R_3=H
d R_1=R_2=R_3=OMe **e** R_1=R_3=H, R_2=OH **f** R_1=OMe, R_2=OH, R_3=H
g R_1=OH, R_2=OMe, R_3=H **h** R_1=R_2=OH, R_3=H

Chart 1.

Results and Discussion

In demethylation of flavones with anhydrous aluminum chloride or bromide in acetonitrile, the methoxyl group adjacent to the carbonyl or hydroxyl group was more easily cleaved than the other methoxyl groups.[2,6] The 3- or 5-methoxyl group in the flavones with the 5- or 3-hydroxyl group was also selectively cleaved with

the bromide via the corresponding tosylates.[3,7] Such results suggest that the 3,5,6,7-trihydroxyflavones (**1**) can be synthesized by the demethylation of 6-hydroxy-3,7-dimethoxy-5-(tosyloxy)flavones (**6**) or 6-hydroxy-5,7-dimethoxy-3-(tosyloxy)flavones (**7**). The 5-(tosyloxy)flavones **6** were easily synthesized from 6-hydroxy-3,5,7-trimethoxyflavones (**4**).[3] Although the flavones **7** may be also derived from 3,6-dihydroxy-5,7-dimethoxyflavones (**5**), the synthesis of 3-hydroxyflavones such as **5** is generally more difficult than that of the corresponding 3-methoxyflavones.[8,9] Recently, as a convenient method for synthesizing 3-hydroxyflavones, Adam et al.[10] have reported the direct oxidation of flavones with dimethyldioxirane. The method seems to be suitable for the synthesis of polyhydroxyflavones with the 3-hydroxy group. Therefore, the flavones **5** and **7b** were synthesized as shown in Scheme 1.

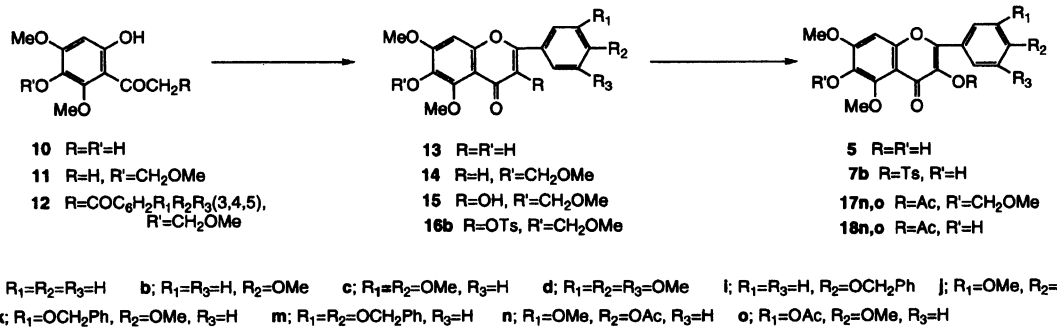
The crude mono(methoxymethyl) ether (**11**)[11] derived from 3′,6′-dihydroxy-2′,4′-dimethoxyacetophenone (**10**) was converted into the substituted benzoates and then transformed to the diketone derivatives (**12**) with potassium hydroxide in pyridine. The diketones (**12**) were cyclized with a small amount of sulfuric acid in acetic acid to give 6-hydroxy-5,7-dimethoxyflavones (**13**). The methoxymethyl ethers (**14**) derived from **13** were oxidized with dimethyldioxirane to give the corresponding 3-hydroxyflavones (**15**), which were easily hydrolyzed to the 3,6-dihydroxyflavones (**5**). 6-Hydroxy-4′,5,7-trimethoxy-3-(tosyloxy)flavone (**7b**) was synthesized from **15b** via the 3-tosylate **16b**. 3-Acetoxy-6-hydroxy-5,7-dimethoxyflavones **18n** and **18o** were also synthesized from **15** via **17**.

The demethylation of 6-acetoxy-3,7-dimethoxy-5-(tosyloxy)flavone (**A6b**)[3] with 30% (w/v) anhydrous aluminum chloride in acetonitrile was accompanied by the cleavage of the 5-tosyloxyl group to give 5,6,7-trihydroxy-3,4′-dimethoxyflavone (**2b**)[2] in high yield. In contrast, the demethylation of the hydroxyflavone **6b** with 10% (w/v) anhydrous aluminum bromide in acetonitrile was accompanied by the elimination of the 5-tosyloxyl group to give a 8-bromoflavone (**19b**) and a small amount of nonbrominated flavone (**20b**). The ^{1}H NMR spectrum for the acetate of **20b** (**A20b**) exhibits three singlets for acetoxyl groups, a singlet for methoxyl group, and two singlets at $\delta=8.02$ and 7.52 for the aromatic protons in the A ring. The results show that the structure of **20b** is 3,6,7-trihydroxy-4′-methoxyflavone. This structure was confirmed by an unambiguous synthesis from 2′,4′,5′-trihydroxyacetophenone. The MS spectra for **19b** exhibit two parent peaks at m/z 380 and 378, and the ^{1}H NMR spectral pattern for its acetate (**A19b**) is superimposable on that for **A20b** except for the C-8 proton signal at $\delta=7.52$, suggesting that the structure of **19b** is 8-bromo-3,6,7-trihydroxy-4′-methoxyflavone. This result suggests that the demethylation of the 5-tosylates proceeds as shown in Scheme 2 and the desired 3,6,7-trihydroxy-5-(tosyloxy)-flavones (**8**) are not synthesized by the demethylation of **6** and their acetates (**A6**): The cleavage of the 5-tosyloxyl group proceeds prior to the demethylation when anhydrous aluminum chloride is used; the elimination of the 5-tosyloxyl group, accompanied by bromination, proceeds after the demethylation when anhydrous aluminum bromide is used.

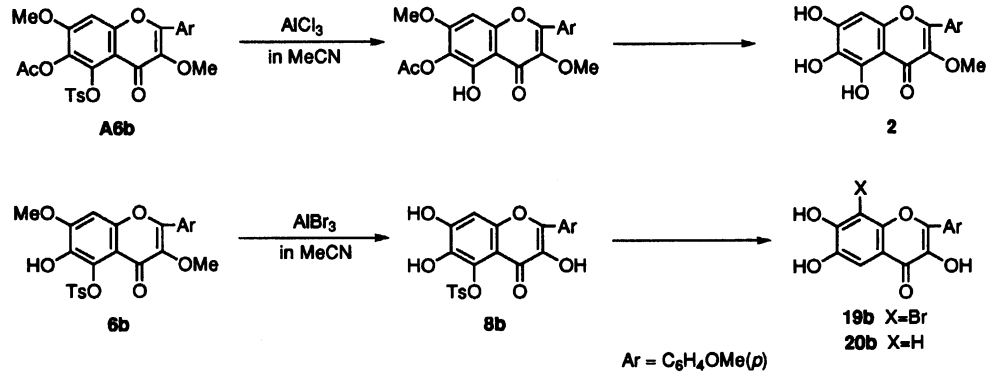
On the other hand, the demethylation of the 3-(tosyloxy)flavones (**7b**) and its acetate (**A7b**) proceeded smoothly without the elimination or cleavage of the 3-tosyloxyl group to give quantitatively 5,6,7-trihydroxy-4′-methoxyflavone (**9b**). The 3-tosyloxyl group in **9b** was hydrolyzed with potassium carbonate in methanol by protection of the 6- and 7-hydroxyl groups with a methoxymethyl group to give the crude 3,5-dihydroxyflavones (**21b**) (Scheme 3). The deprotection of the methoxymethyl groups in **21b** with hydrochloric acid in acetic acid was not achieved because of the dimerization of **1b** with formaldehyde formed by the hydrolysis. Although the side reaction decreased when acetone was used as a solvent, the purification is difficult and the method was not suitable for the synthesis of **1**. Therefore, the direct demethylation of the 3-hydroxyflavones **3b** and **5b** was examined. We found the following result.

That is, the demethylation of **3b**[3] with 10% (w/v) anhydrous aluminum bromide in acetonitrile proceeded smoothly to give the flavone **1b**, but the ratio of **1b** to **3b** reached about 80% after 16—24 h and then the reaction ceased. The flavone **1b** was also obtained in high yield by the demethylation of the acetate of **3b** (**A3b**) with 30% (w/v) anhydrous aluminum chloride in acetonitrile at 70 °C for 48 h. The result suggests that the 5- and 7-methoxyl groups in **5** can also be simultaneously cleaved to give the desired flavone **1**, in contrast to the demethylation of the 3-methoxyflavones **4** and their acetates (**A4**).[2] Actually, the demethylation of **5b** and its acetate (**A5b**) proceeded similarly to that of **3b** and **A3b**.

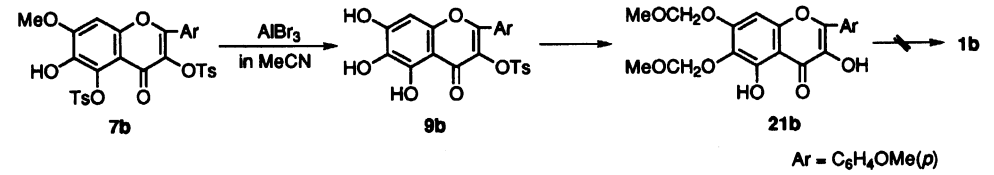
The demethylation pathway can be explained analogously to the cases of the 3-methoxyflavones **4** and 6-hydroxy-5,7-dimethoxyflavones and their acetates in our previous papers[2,6] as shown in Scheme 4. In the demethylation of the 3,6-dihydroxyflavone **5**, the two cyclic aluminum complexes **A** and **B** are formed by paths a and b and then the 5-methoxyl group in the complexes is cleaved by the participation of the 4-carbonyl oxygen atom to give more stable aluminum complexes, **C** and **D**, since the complexes **A** and **B** with five-membered rings are less stable than complexes with six-membered rings such as **C** and **D**: The 3-methoxyl group in the stable aluminum complexes **C′** and **D′**, which are formed in the demethylation of **4**, is not cleaved.[2] The 7-methoxyl group in complex **C** is easily cleaved to give complex **E**, but that in **D** is not cleaved because the 6-hydroxyl group is protected with an acetimidoyl group. Such reasoning suggests that when alu-



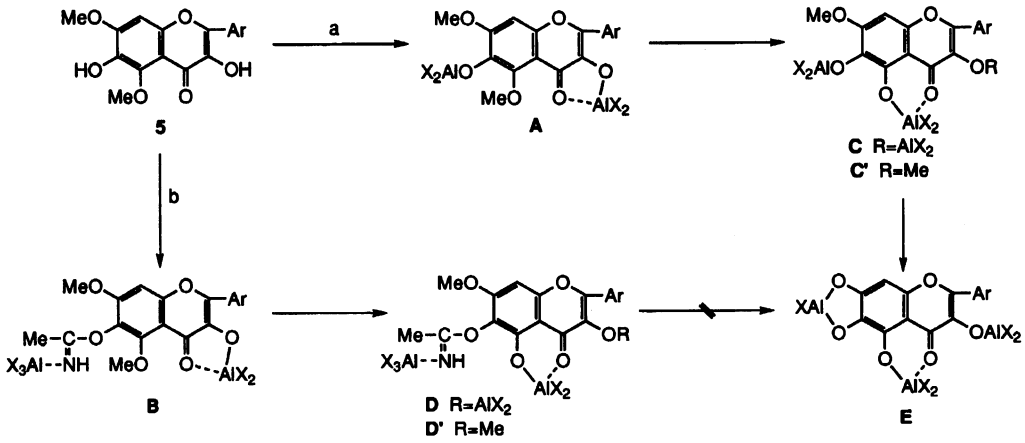
Scheme 1.



Scheme 2.



Scheme 3.



Scheme 4.

minum halides with a softer base than bromine atom, such as aluminum iodide, are used in the demethylation of **5**, the path a is more accelerated than the bromide and the flavones **1** are predominantly produced under more mild conditions.

Recently, Akiyama et al.[12] have reported that the demethylation of inositol derivatives with anhydrous aluminum chloride–sodium iodide is greatly promoted by participation of a vicinal hydroxyl group. Based on our results in the demethylation of 2′-methoxyacetophenones,[13] one of the reasons is considered to be that the formation of an aluminum–oxygen bond is accel-

erated by generating new reagents such as $AlCl_2I$ or $AlClI_2$ by exchange reaction of the halide ions. That finding suggests that the combined system could accelerate remarkably the cleavage of the methoxyl group adjacent to the carbonyl or hydroxyl group on the flavone and acetophenone skeletons. In order to demonstrate the demethylating ability of the reagent, the demethylation of 2′,4′-dimethoxyacetophenone with three reagents was additionally examined; the result is shown in Fig. 1. The cleavage of the 2′-methoxyl group with anhydrous aluminum chloride–sodium iodide proceeded much more rapidly than that with anhydrous aluminum bromide and was completed within 10 min.

This result suggests that the 5- and 7-methoxyl groups in **5** can be simultaneously cleaved by the reagent to give the desired flavones **1**. Actually, the demethylation of **5b** with anhydrous aluminum chloride–sodium iodide in acetonitrile at 30 °C was completed within 5 h to give quantitatively the flavone **1b**. On the other hand, the demethylation of **1c** and **1d** with two or three methoxyl groups produced an appreciable amount of the further demethylated products of **1c** or **1d** under the conditions, since the cleavage of the 4′-methoxyl group was accelerated with increasing the number of neighboring methoxyl groups.[6,14] The cleavage of these methoxyl groups, however, was slower than that of the 7-methoxyl group and was suppressed by shortening the reaction time: the flavones **1c** and **1d** were obtained in high yields from the respective demethylated products of **5c** (1 h) and **5d** (0.5 h) by removing a small amount of **3c** or **3d** by preparative HPLC (see Table 6). Although the methoxyl group adjacent to a hydroxyl group on the B ring in **1f** or **1g** was also easily cleaved, the cleavage was suppressed by the protection of the hydroxyl group with an acetyl group and the flavones **1f** and **1g** were quantitatively obtained

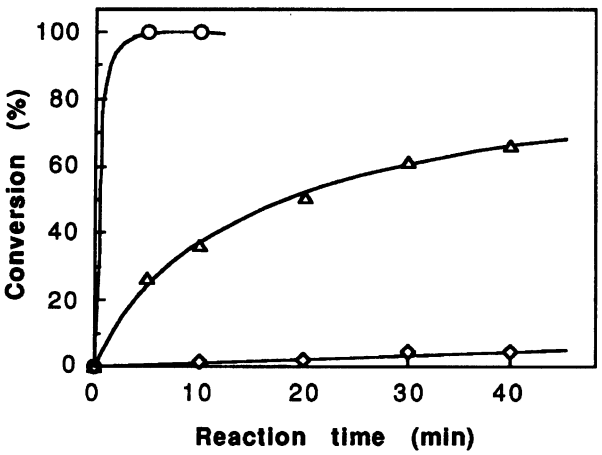


Fig. 1. Time conversion of the demethylation of 2′,4′-dimethoxyacetophenone (50 mg) at 0 °C. —○—, 5%(w/v) $AlCl_3$–MeCN (5 ml) containg NaI (280 mg), —△—, 5%(w/v) $AlBr_3$–MeCN (5 ml), —◇—, 5%(w/v) $AlCl_3$–MeCN (5 ml).

by the demethylation of **18n** and **18o** (reaction time, 5 h). The demethylation was useful as a general method for synthesizing **1**. The flavones (**1a**, **1e**, and **1h**) with no methoxyl group were synthesized more conveniently than was possible when the methods described in the previous papers were used.[4,5]

Characterization of the 3, 5, 6, 7-Tetrahydroxyflavones (1) and Identification of Natural Flavones. The ^1H NMR data for the 3,5,6,7-tetrahydroxyflavones (**1**) and their acetates (**A1**) are shown in Table 1. The C-8 proton signals in **1** (in DMSO-d_6) and their acetates **A1** (in $CDCl_3$) appear in the ranges of $\delta=6.49$ to 6.62 and of $\delta=7.48$ to 7.51, respectively; these ranges are similar to those in the 5,6,7-trihydroxyflavones such as **2** and their acetates.[2,6] Furthermore, the chemical shifts of the aromatic protons on the B ring in **1** and **A1** agree with those in the corresponding 3,5,6-trihydroxyflavones **3** and their acetates[3] within 0.1 ppm. The ^{13}C NMR data for the flavones **1** fully support the assigned structure and the carbon signals, except for the carbons at 6-, 7-, 8-, and 10-positions, are superimposable with those for the corresponding 3,5,6-trihydroxy-7-methoxyflavones (**3**):[3] The carbon signals at the 6-, 7-, 10-positions are observed at the slightly higher fields ($\delta=0.7$—1.0) and that at the 8-position is observed at 2.5 ppm lower field (Table 2).

The UV spectra for **1** comprise band II at 260—270 nm and band I at 360—375 nm, which is 15—20 nm longer than that for the corresponding 7-methyl ether of **1** (**3**).[3] These bands are characteristically shifted upon addition of aluminum chloride or sodium acetate (Table 3). The absorption patterns of **1** bearing the same oxygenated pattern on the B ring, however, are similar to each other (**1b** and **1e**; **1c**, **1f**, **1g**, and **1h**). These phenomena are similar to those for the flavones **2**[2] and **3**[3] and the characteristic shift attributed to the 7- and 4′-hydroxyl group is also not observed. Especially, the band I for the 7-methyl ethers **3** shifts bathochromically by 30—40 nm upon addition of sodium acetate, but the shift range of that for **1** is smaller (7—13 nm) in spite of the existence of a free hydroxyl group at the 7-position. The results suggest that the structural elucidation of natural flavones using the UV method must be carried out with scrupulous care.

In a study of the flavonoid excretion in the genus *Ostrya*, Wollenweber[15] had reported that the structure of one flavonoid component seemed to be 6-hydroxykaempferol 4′-methyl ether (**1b**) on the basis of the chromatographic and UV spectroscopic behaviors, but the identification was not possible because there was no explanation of the UV data. A natural flavone glucoside was also isolated from *Chrysanthemum coronarium* by Harborne et al.[16] The structure of the aglycone was proposed as quercetagetin 3′-methyl ether (**1f**) on the basis of the spectral and chemical evidence. The UV and MS data for the aglycone are similar to those for

Table 1. ^{1}H NMR Data for 3,5,6,7-Tetrahydroxyflavones (**1**) in DMSO-d_6 and Their Acetates (**A1**) in $CDCl_3$[a)]

Compd	Arom. H						OMe	OH or OAc
	C_8–H	$C_{3'}$–H	$C_{5'}$–H	$C_{4'}$–H	$C_{2'}$–H	$C_{6'}$–H		
1a	6.56s	7.55t(2H)		7.50t	8.15d(2H)		—	12.13s
1b	6.55s	7.11d(2H)		—	8.13d(2H)		3.84s	12.21s
1c	6.58s	—	7.13d	—	7.74d′	7.80dd	3.84s(6H)	12.20s
1d	6.62s	—	—	—	7.48s(2H)		3.76s 3.87s(6H)	12.14s
1e	6.53s	6.92d(2H)		—	8.03d(2H)		—	12.20 s
1f	6.56s	—	6.93d	—	7.74d′	7.68dd	3.89s	12.23s
1g	6.51s	—	7.08d	—	7.66d′	7.65dd	3.84s	12.21s
1h	6.49s	—	6.88d	—	7.67d′	7.53dd	—	12.27s
A1a	7.49s	7.50—7.55m(3H)			7.80dd(2H)		—	2.30s 2.34s 2.35s 2.44s
A1b	7.48s	7.01d(2H)		—	7.79d(2H)		3.89s	2.32s 2.33s 2.34s 2.43s
A1c	7.49s	—	6.97d	—	7.35d′	7.47dd	3.94s 3.96s	2.32(6H) 2.34s 2.35s
A1d	7.51s	—	—	—	7.04s(2H)		3.90s(6H) 3.93s	2.32s 2.34s 2.35s 2.44s
A1e	7.48s	7.26d(2H)		—	7.84d(2H)		—	2.32s 2.34s 2.35s(6H) 2.43s
A1f	7.48s	—	7.17d	—	7.38d′	7.41dd	3.89s	2.31s 2.34s 2.35s(6H) 2.44s
A1g	7.48s	—	7.07d	—	7.55d′	7.22dd	3.91s	2.32s 2.33s 2.34s 2.35s 2.43s
A1h	7.48s	—	7.35d	—	7.68d′	7.71dd	—	2.34s(9H) 2.35s(6H) 2.43s

a) s, Singlet; d, doublet (J=8.5—9.0 Hz); d′, doublet (J=2.0—2.5 Hz); dd, double doublet (J=9.0, 2.0 Hz); t, triplet (J=7.5 Hz); m, multiplet.

Table 2. ^{13}C NMR Data for 3,5,6,7-Tetrahydroxyflavones (**1**) in DMSO-d_6

Compd	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**
C_2	145.74	146.01	145.90	145.68	146.56	146.40	147.16	146.52
C_3	136.54	135.55	135.68	136.25	135.15	135.31	135.61	135.20
C_4	176.19	175.93	175.86	176.00	175.80	175.89	175.84	175.73
C_5	145.50	145.79	145.74	145.37	145.77	145.76	145.76	145.77
C_6	128.58	128.51	128.49	128.55	128.46	128.45	128.47	128.42
C_7	153.89	153.62	153.62	153.82	153.49	153.53	153.58	153.47
C_8	93.36	93.32	93.42	93.56	93.25	93.38	93.18	93.10
C_9	149.05	148.85	148.81	148.86	148.75	148.75	148.77	148.70
C_{10}	103.46	103.33	103.27	103.33	103.25	103.24	103.25	103.20
$C_{1'}$	131.09	123.43	123.46	126.37	121.82	122.15	123.57	122.09
$C_{2'}$	127.43	129.21	110.75	105.36	129.35	111.59	114.48	114.92
$C_{6'}$			121.25			121.56	119.59	119.81
$C_{4'}$	129.74	160.31	150.18	138.97	158.98	147.27	149.14	147.46
$C_{3'}$	128.42	113.92	148.26	152.61	115.32	148.59	146.07	144.93
$C_{5'}$			111.39			115.43	111.70	115.47
OMe	—	55.25	55.50	60.11	—	55.67	55.50	—
				55.94(2C)				

Table 3. UV Data for 3,5,6,7-Tetrahydroxyflavones (**1**)[a)]

Compd	λ_{max}/nm (log ε)								
	EtOH			EtOH–$AlCl_3$			EtOH–NaOAc		
1a		275 (4.27)	368sh (4.09)	259 (4.12)	284 (4.22)	378(4.25)	259 (4.23)	283sh (4.14)	375 (4.18)
1b	259sh (4.13)	276 (4.24)	363 (4.25)		283 (4.17)	387 (4.36)		275 (4.24)	376 (4.25)
1c	260 (4.17)	276sh (4.17)	368 (4.27)		266 (4.18)	392 (4.36)	261sh (4.17)	277 (4.17)	378 (4.25)
1d		278 (4.18)	370 (4.21)		282sh (4.13)	390 (4.32)	265sh (4.13)	282 (4.15)	379 (4.18)
1e		274 (4.24)	369 (4.27)		279 (4.20)	390 (4.39)		282 (4.21)	376 (4.25)
1f	261 (4.13)	275sh (4.10)	371 (4.18)		267 (4.16)	397 (4.29)		305 (4.09)	383 (3.87)
1g	262 (4.19)	275sh (4.17)	370 (4.25)		267 (4.22)	395 (4.35)		278sh (4.16)	379 (4.20)
1h	260 (4.18)	274sh (4.12)	373 (4.25)		270 (4.20)	403 (4.35)		305 (4.17)	385 (3.94)

a) sh, Shoulder.

the synthetic **1f**. This supports the conclusion that the structure is correct (Table 4).

Kaouadji et al.[17] had reported that a flavone was isolated along with alkylated flavonols from *Platanus*

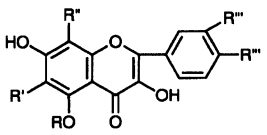
Table 4. Comparisons of the Three Natural Flavones with the Synthetic and Isomeric Flavones

	Synthetic	Natural	Isomeric
	3,4′,5,6,7-Pentahydroxy-3′-methoxyflavone (**1f**)[16]		
UV:λ_{max}/nm	(EtOH) 261 275sh 371	(EtOH) 257 277 366	
EIMS:*m*/*z*	(70 eV) 332(M^+, 100) 317(7)	332(M^+, 100) 317(5)	
(rel intensity)	303(7) 289(3) 261(4)	303 289 274	
	3,5,6,7-Tetrahydroxyflavone (**1a**)[17]		**22a**[19,a]
UV:λ_{max}/nm	(EtOH) 275 368sh	(MeOH) 270 355	(EtOH) 283 318sh 382
Acetate	**A1a**		**A22a**
^{1}H NMR in $CDCl_3$	7.49s 7.50—7.55m 7.80dd	7.00s 7.52m(3H) 7.75dd(2H)	6.99s 7.48—7.53m(3H) 7.74dd
	2.30s 2.34s 2.35s 2.44s	2.31s 2.36s 2.39s 2.47s	2.31s 2.35s 2.38s 2.43s
	3,3′,4′,6,7-Pentahydroxy-5-methoxyflavone (**23h**)[20]		**3h**[3]
Mp/°C	239—241	234—236	228—229
UV:λ_{max}/nm	(EtOH) 262 332sh 373	(EtOH) 260 355	(EtOH) 260 275sh 363
+$AlCl_3$	250 275 420	270 395	270 285sh 393
+NaOAc	265 332sh 368	250 285 400	283 390
Acetate	**A23h**		**A3h**
Mp/°C	118—119	215—216	206.5—207.5
^{1}H NMR in $CDCl_3$	7.29s 7.36d 7.75d′ 7.72dd	6.94 7.42 7.69(2H)	6.92s 7.35d 7.67d′ 7.70dd
	3.96s 2.34s(9H) 2.37s(6H)	3.94 2.33—2.43(15H)	3.95s 2.33s 2.34s(9H) 2.43s

a) Synthesized in our laboratory.

acerifolia. The structure was found to be 6-hydroxygalangin (**1a**), a new natural product, on the basis of the ^{1}H NMR for the acetate. In the ^{1}H NMR study of the acetate, the singlet at δ=7.00 has been assigned as the C-8 proton signal, but does not correspond to the signals for the 5,6,7-triacetoxyflavones. In the ^{1}H NMR for the 5,7-diacetoxy-6- and 8-methoxyflavones in $CDCl_3$, the C-8 proton signals are generally observed at ca. 0.4 ppm lower field than the corresponding C-6 protons.[18] That suggests that the structure of the natural flavone is 3,5,7,8-tetrahydroxyflavone[19] (**22a**), an isomer of **1a** (Chart 2). Although the UV data are different from those for **22a**, the ^{1}H NMR data for the natural flavone acetate are fully consistent with those for the flavone acetate **A22a** synthesized as shown in Table 4. The result shows that the structure of the natural one is **22a**.

Bhardwaji et al.[20] had reported that the structure of a flavone (allopatuletin) isolated from *Tagetes patula* was to be quercetagetin 5-methyl ether (3,3′,4′,6,7-pentahydroxy-5-methoxyflavone) (**23h**) on the basis of the spectral data for the flavone and its derivatives. In the ^{1}H NMR for the acetate in $CDCl_3$, the signal at δ=6.94 assigned to the C-8 proton does not correspond to the C-8 proton signals in 5,6,7-trioxygenated flavones



22a R=R'=R'''=H, R"=OH
23h R=Me, R'=R'''=OH, R"=H

Chart 2.

with 7-acetoxy group such as 5,7-diacetoxy-6-methoxyflavones[18] (δ=ca. 7.2), but rather matches with those in 5,6-diacetoxy-7-methoxyflavones (δ=ca. 6.9).[3] Such a result shows that the structure of the natural flavone is to be 3,3′,4′,5,6-pentahydroxy-7-methoxyflavone (**3h**), an isomer of **23h**. Therefore, the flavone **23h** was synthesized from 3,3′,4′,6,7-pentabenzyl ether derived from **1h** by the methylation and following debenzylation, then the natural flavone was compared with **23h** and **3h**. As shown in Table 4, the ^{1}H NMR and UV data for the natural one are not consistent with those for the proposed flavone **23h** and its acetate (**A23h**), but correspond well with those for the isomeric ones, **3h** and its acetate (**A3h**).[3] Consequently, the structure of the natural flavone, allopatuletin, was revealed to be quercetagetin 7-methyl ether (**3h**) which was recently isolated from *Balsamorhiza sagittata* by Bohm et al.[21]

Experimental

All melting points were determined in glass capillaries and are uncorrected. ^{1}H NMR (at 400 MHz) and ^{13}C NMR (at 100.4 MHz) spectra were recorded on a JEOL EX 400 NMR spectrometer, using tetramethylsilane as internal standard, and chemical shifts are given in δ values. UV and MS spectra were recorded on a Hitachi 124 spectrophotometer in EtOH and on a Shimadzu QP 1000 spectrometer, respectively. The high performance liquid chromatography (HPLC) was carried out with a Hitachi 635 instrument, using a column (2.1×500 mm) packed with Hitachi gel No. 3011, MeOH (0.5 ml min^{-1}) as an eluent, and a UV monitor at 340 nm. For the separation of demethylated products, a column (20×600 mm) packed with Hitachi gel No. 3019 using methanol as an eluent was employed. Column chromatography was carried out on Kiesel-gel 60 (70—230 mesh; Merck). Elemental

analyses were performed with a Yanaco CHN corder Model MT-5. The values of all crystalline compounds in this paper were within 0.3% of theoretical values.

6-Hydroxy-5,7-dimethoxyflavones (13). The flavones **13** were synthesized from 3′, 6′-dihydroxy-2′,4′-dimethoxyacetophenone (**10**) by a similar method to that described in a previous paper.[11] The crude methoxymethyl ether **11** which was obtained from **10** (5.0 g; 24 mmol) by methoxymethylation with $MeOCH_2Cl$ and diisopropylethylamine in CH_2Cl_2 was benzoylated with a substituted benzoyl chloride (45 mmol) in pyridine (30 ml) at 50—60 °C for 1—1.5 h to give a crude benzoate which contained an appreciable amount of the benzoic anhydride. To a solution of the dried benzoate in pyridine (30 ml), a freshly powdered KOH (12.0 g) was added, the mixture was stirred at 80 °C for 1—2 h and poured into a mixture of ice and HCl. The separated oily materials were extracted with EtOAc, washed with aq K_2CO_3, dried over Na_2SO_4, and then concentrated. The residue was recrystallized to give diketone derivative **12** (Table 5).

A solution of the diketone **12** (7.0 mmol) in HOAc (15—25 ml) was warmed with a few drops of conc H_2SO_4 at 60 °C for 5—10 min, diluted with H_2O, and then allowed to stand in a refrigerator. The separated precipitate was collected and recrystallized to give **13** (Table 5).

5,7-Dimethoxy-6-(methoxymethoxy)flavones (14). A mixture of the flavone **13** (5 mmol), $MeOCH_2Cl$ (2.0 ml), and *N*,*N*-diisopropylethylamine (6.6 ml) in CH_2Cl_2 (30—50 ml) was stirred at room temperature until the starting material disappeared. The mixture was washed with cooled 2—3% aq HCl, aq $NaHCO_3$, H_2O, and then concentrated. The residue was recrystallized to give **14** (Table 5).

3-Hydroxy-5,7-dimethoxy-6-(methoxymethoxy)-flavones (15). To a cold solution of the flavone **14** (5.0 mmol) in CH_2Cl_2 (10—20 ml), a cold solution of dimethyldioxirane[10] in Me_2CO (concn, 0.09—0.14 mol dm^{-3}; 80—120 ml; 7—17 mmol) was added. The mixture was stirred at 0 °C for 2—3 h and allowed to stand in a refrigerator overnight. Then the solvent was evaporated under reduced pressure. A solution of the residue in CH_2Cl_2 (15—20 ml) was stirred with TsOH (ca. 100 mg) at 0 °C for 0.5 h, washed with aq $NaHCO_3$, dried over Na_2SO_4, and concentrated. The residue was recrystallized to give **15** with no hydroxyl group on the B ring. The flavones (**15f,g**) with hydroxyl groups on the B ring were synthesized by the hydrogenolysis of the flavones **15j,k** with 10% Pd–C in EtOAc–MeOH (1 : 1) (Table 5).

3,6-Dihydroxy-5,7-dimethoxyflavones (5a—h). To a solution of the flavone (**15**) (2—3 mmol) in HOAc (15—25 ml), a few drops of concd HCl were added with stirring. The mixture was stirred at room temperature for 0.5 h and then it was diluted with H_2O. The separated precipitate was collected and recrystallized to give **5** (Table 5).

6-Hydroxy-4′,5,7-trimethoxy-3-(tosyloxy)flavone (7b) and Its Isomer (6b). A mixture of **15b** (770 mg; 2.0 mmol), TsCl (540 mg; 2.8 mmol), and anhydrous K_2CO_3 in Me_2CO (40 ml) was refluxed with stirring until the starting material disappeared. After K_2CO_3 was filtered off, the filtrate was concentrated and the residue was recrystallized from $CHCl_3$–MeOH to give a tosylate **16b**: Mp 165—166 °C; yield, 1.05 g (98%); $C_{27}H_{26}O_{10}S$. The tosylate **16b** was hydrolyzed with HCl in AcOH to give quantitatively **7b**; mp 221—222 °C (from $CHCl_3$—MeOH); $C_{25}H_{22}O_9S$. The acetate (**A7b**): Mp 199—200 °C (from $CHCl_3$—MeOH); $C_{27}H_{24}O_{10}S$.

6-Hydroxy-3,7-dimethoxy-5-tosyloxyflavone (**6b**) (mp 189—190 °C, from $CHCl_3$–Et_2O; $C_{25}H_{22}O_9S$) was synthesized from its acetate (**A6b**)[3] by hydrolysis with HCl in MeOH.

3-Acetoxy-6-hydroxy-5,7-dimethoxyflavones (18n and 18o). To a solution of **15f** or **15g** (500 mg) in pyridine (4 ml), acetic anhydride (1.2 ml) was added. The mixture was allowed to stand at room temperature overnight and then diluted with ice cooled H_2O. The separated precipitate was collected and recrystallized from MeOH to give an acetate **17**: **17n**; mp 155—156 °C; yield, 530 mg (88%); $C_{24}H_{24}O_{11}$: **17o**; mp 144—145 °C; yield, 490 mg (81%); $C_{24}H_{24}O_{11}$. The acetates were hydrolyzed by the method described in the synthesis of 5 to give **18**: **18n**; mp 197—198 °C (MeOH); yield, 89%; $C_{22}H_{20}O_{10}$: **18o**; mp 157—158 °C (MeOH–Et_2O); yield, 81%; $C_{22}H_{20}O_{10}$.

Demethylation of the 5-(Tosyloxy)flavones (6b and A6b) and 3-(Tosyloxy)flavones (7b and A7b) with Anhydrous Aluminum Chloride or Bromide in Acetonitrile. The flavone **A6b** (430 mg; 0.8 mmol) was dissolved in a solution of anhydrous $AlCl_3$ (4.0 g; 30 mmol) in MeCN (13.5 ml) and this was heated at 70 °C for 48 h. The mixture was poured into ca. 3% aq HCl, warmed at 60—70 °C for 20—30 min, and then allowed to stand in a refrigerator. The separated precipitate was collected and recrystallized from aq MeOH to give **2b**:[2] Yield, 220 mg (84%). The flavone **A7b** (400 mg) was demethylated by the same method to give the 3-tosyloxyflavone **9b**: Mp 203—204 °C ($CHCl_3$–MeOH); yield, 337 mg (90%); $C_{23}H_{18}O_9S$. The flavone **9b** was also obtained from **7b** in 86% yield by the demethylation with 10% (w/v) anhydrous $AlBr_3$ in MeCN at 70 °C for 10 h.

The flavone **6b** (400 mg; 0.8 mmol) was dissolved in a solution of anhydrous $AlBr_3$ (2.0 g; 7.5 mmol) in MeCN (20 ml) and heated at 70 °C for 48 h. The reaction mixture was treated with ca. 3% aq HCl to give a demethylated product. After the product was acetylated with hot acetic anhydride–pyridine, the acetate was chromatographed on a silica-gel column with $CHCl_3$–EtOAc (5 : 1) as an eluent to give **A19b** and **A20b**.

A19b: Mp 224—225 °C ($CHCl_3$–MeOH); yield, 270 mg (67%); $C_{22}H_{17}O_9Br$; ^{1}H NMR ($CDCl_3$) δ=8.03 (1H, s, C_5–H), 7.05 (2H, d, J=8.5 Hz, $C_{3',5'}$–H), 7.98 (2H, d, J=8.5 Hz, $C_{2',6'}$–H), 3.90 (3H, s, OMe), 2.34, 2.38, 2.42 (each 3H, s, OAc).

A20b: Mp 179—180 °C ($CHCl_3$–MeOH); yield, 27 mg (8%); $C_{22}H_{18}O_9$; ^{1}H NMR ($CDCl_3$) δ=8.03 (1H, s, C_5–H), 7.52 (1H, s, C_8–H), 7.02 (2H, d, J=8.5 Hz, $C_{3',5'}$–H), 7.83 (2H, d, J=8.5 Hz, $C_{2',6'}$–H), 3.90 (3H, s, OMe), 2.34, 2.34, 2.42 (each 3H, s, OAc).

The acetates were hydrolyzed to **19b** and **20b** with 16% aq HCl–MeOH (1 : 10).

19b: Mp 253—255 °C (aq DMF); $C_{16}H_{11}O_6Br \cdot 1/2H_2O$; ^{1}H NMR (DMSO) δ=7.37 (1H, s, C_5–H), 7.15 (2H, d, J=8.5 Hz, $C_{3',5'}$–H), 8.23 (2H, d, J=8.5 Hz, $C_{2',6'}$–H), 3.85 (3H, s, OMe), 9.32 (1H, s, OH), 10.62 (2H, s, OH); MS (20 eV) m/z (rel intensity) 380, 378 (M^+; each 100), 300 (16), 248, 246 (21 and 23).

20b: Mp 289—291 °C (aq DMF); $C_{16}H_{12}O_6$; ^{1}H NMR

Table 5. 3,5,6,7-Tetrahydroxyflavone Derivatives (**5** and **15**), 6′-Hydroxy-2′,4′-dimethoxy-3′-methoxymethoxy-α-aroylacetophenones (**12**), and 6-Hydroxy-5,7-dimethoxyflavone Derivatives (**13** and **14**)

Compd	Mp °C	Recystn. solvent	Yield %	Formula	Compd	Mp °C	Recystn. solvent	Yield %	Formula
5a	187—188	MeOH–H_2O	90	$C_{11}H_{14}O_6$	**12a**	101—102	MeOH	54	$C_{19}H_{20}O_7$
5b	174—176	MeOH	91	$C_{18}H_{16}O_7$	**12b**	107—109	$CHCl_3$–MeOH	65	$C_{20}H_{22}O_8$
5c	126—127	MeOH	95	$C_{19}H_{18}O_8$	**12c**	122—124	$CHCl_3$–MeOH	72	$C_{21}H_{24}O_9$
5d	223—224	MeOH	91	$C_{20}H_{20}O_9$	**12d**	115—117	MeOH	57	$C_{22}H_{26}O_{10}$
5e	282—284	MeOH	68	$C_{17}H_{14}O_7$	**12i**	101—103	$CHCl_3$–MeOH	47	$C_{26}H_{26}O_8$
5f	245—246	MeOH	83	$C_{18}H_{16}O_8$	**12j**	114—116	$CHCl_3$–MeOH	85	$C_{27}H_{28}O_9$
5g	105—106	MeOH–H_2O	88	$C_{18}H_{16}O_8$	**12k**	118—120	$CHCl_3$–MeOH	63	$C_{27}H_{28}O_9$
5h	259—261	MeOH–H_2O	91	$C_{17}H_{14}O_8 \cdot H_2O$	**12m**[11]	98—100	EtOAc–MeOH	70	$C_{33}H_{32}O_9$
5i	113—115	MeOH	86	$C_{24}H_{20}O_7$	**14a**	118—118.5	MeOH–Et_2O	85	$C_{19}H_{18}O_6$
5j	150—151	$CHCl_3$–MeOH	86	$C_{25}H_{22}O_8$	**14b**	117—119	MeOH	95	$C_{20}H_{20}O_7$
5k	175—177	$CHCl_3$–MeOH	84	$C_{25}H_{22}O_8$	**14c**	135—137	MeOH	97	$C_{21}H_{22}O_8$
5m	138—139	MeOH–Hexane	89	$C_{31}H_{26}O_8$	**14d**	143—145	MeOH	87	$C_{22}H_{24}O_9$
					14i	125—127	MeOH	88	$C_{26}H_{24}O_7$
15a	144—145	$CHCl_3$–MeOH	52	$C_{19}H_{18}O_7$	**14j**	103—105	MeOH	97	$C_{27}H_{26}O_8$
15b	136—137	$CHCl_3$–MeOH	75	$C_{20}H_{20}O_8$	**14k**	122—123	$CHCl_3$–MeOH	96	$C_{27}H_{26}O_8$
15c	160—161	MeOH	60	$C_{21}H_{22}O_9$	**14m**	68—70	MeOH	93	$C_{33}H_{30}O_8$
15d	164—165	$CHCl_3$–MeOH	48	$C_{22}H_{24}O_{10}$	**13a**[22]	206—207	MeOH–Et_2O	88	$C_{17}H_{14}O_5$
15f	142—143	MeOH	90	$C_{20}H_{20}O_9$	**13b**[23]	217—218	MeOH	89	$C_{18}H_{16}O_6$
15g	182—183	$CHCl_3$–MeOH	98	$C_{20}H_{20}O_9$	**13c**[24]	228—230	MeOH	98	$C_{19}H_{18}O_7$
15i	136—137	$CHCl_3$–MeOH	85	$C_{26}H_{24}O_8$	**13d**[23]	203—205	MeOH	83	$C_{20}H_{20}O_8$
15j	150—151	$CHCl_3$–MeOH	72	$C_{27}H_{26}O_9$	**13i**	71—73	MeOH	98	$C_{24}H_{20}O_6$
15k	147—148	$CHCl_3$–MeOH	67	$C_{27}H_{26}O_9$	**13j**	100—102	MeOH	96	$C_{25}H_{22}O_7$
15m	149—150	$CHCl_3$–MeOH	74	$C_{33}H_{30}O_9$	**13k**	197—198	$CHCl_3$–MeOH	89	$C_{25}H_{22}O_7$
					13m[11]	174—176	MeOH	94	$C_{31}H_{26}O_7$

Table 6. 3,5,6,7-Tetrahydroxyflavones (**1**) and Their Acetates (**A1**)

Compd	Mp °C	Recystn. solvent	Yield %	Formula	Found (%) C	Found (%) H	Calcd (%) C	Calcd (%) H
1a[4]	242—243	MeOH–H_2O	94	$C_{15}H_{10}O_6$	59.96	3.95	60.10	3.87
1b	222—223	Me_2CO–H_2O	93	$C_{16}H_{12}O_7$	58.21	4.22	58.27	4.13
1c	212—213	MeOH–H_2O	83	$C_{17}H_{14}O_8$	59.06	4.35	58.96	4.07
1d	179—180, 189—190	Me_2CO–H_2O	83	$C_{18}H_{16}O_9$	54.34	4.78	54.60	4.75
1e[4,5]	>280	MeOH–H_2O	81	$C_{15}H_{10}O_7$	59.37	3.55	59.61	3.33
1f	246—247	MeOH–H_2O	97	$C_{16}H_{12}O_8 \cdot H_2O$	55.14	4.10	55.43	3.95
1g	199—200, 254—256	MeOH–H_2O	93	$C_{16}H_{12}O_8$	57.62	3.88	57.84	3.64
1h[4]	>280	MeOH–H_2O	81	$C_{15}H_{10}O_8$	52.22	4.00	52.18	3.79
A1a[4]	183—185	$CHCl_3$–MeOH	85	$C_{23}H_{18}O_{10}$	61.00	4.07	60.80	3.99
A1b	200—200.5	$CHCl_3$–MeOH	83	$C_{24}H_{20}O_{11}$	59.47	4.18	59.51	4.16
A1c	182—183	MeOH	81	$C_{25}H_{22}O_{12}$	58.14	4.19	58.37	4.31
A1d	196—198	$CHCl_3$–MeOH	81	$C_{26}H_{24}O_{13}$	57.10	4.23	57.36	4.44
A1e[4,5]	235—236	MeOH	70	$C_{25}H_{20}O_{12}$	58.40	4.09	58.60	3.93
A1f	197—199	MeOH	80	$C_{26}H_{22}O_{13}$	57.79	4.02	57.57	4.09
A1g	214—216	$CHCl_3$–MeOH	92	$C_{26}H_{22}O_{13}$	57.36	4.09	57.57	4.09
A1h[4]	187—189	$CHCl_3$–MeOH	83	$C_{27}H_{22}O_{14}$	56.63	3.95	56.85	3.89

(DMSO) δ=7.31 (1H, s, C_5–H), 6.97 (1H, s, C_8–H), 7.10 (2H, d, J=8.5 Hz, $C_{3',5'}$–H), 8.12 (2H, d, J=8.5 Hz, $C_{2',6'}$–H), 3.84 (3H, s, OMe), 9.01, 9.74, 10.42 (each 1H, s, OH).

The compound **20b** as an authentic sample was also synthesized from 2′,4′,5′-trihydroxyacetophenone by using the oxidation with dimethyldioxirane by Adam et al.,[10] via the following compounds: 4′,5′-bis(benzyloxy)-2′-hydroxyacetophenone (mp 97—99 °C; $C_{22}H_{20}O_4$), 4′,5′-bis(benzyloxy)-2′-hydroxy-2-(*p*-methoxybenzoyl)acetophenone (mp 126—128 °C; $C_{30}H_{26}O_6$), 6,7-bis(benzyloxy)-4′-methoxyflavone (mp 180—182 °C; $C_{30}H_{24}O_5$), and 6,7-bis(benzyloxy)-3-hydroxy-4′-methoxyflavone (mp 199—201 °C; $C_{30}H_{24}O_6$). The synthesized flavone was identical with the compound **20b** obtained from the demethylated product.

Hydrolysis of the 3-(Tosyloxy)flavone (9b). The flavone **9b** (520 mg) was methoxymethylated with $MeOCH_2Cl$ (0.3 ml) and diisopropylethylamine (1.5 ml) in CH_2Cl_2 (30 ml) at room temperature for 30—40 min to give a crude methoxymethyl ether. A mixture of the ether and K_2CO_3 (1.8 g) in MeOH (40 ml) was refluxed with stirring

for 1 h and then acidified with dil HCl. After the methanol was distilled off, the separated precipitate was collected and recrystallized from $CHCl_3$–MeOH to give **21b**: Mp 159—160 °C; yield, 335 mg (75%); $C_{20}H_{20}O_9$.

To a solution of **21b** (250 mg) in Me_2CO (20 ml), concd HCl (1 ml) was added, and the mixture was stirred at room temperature for 30—40 min. This mixture was diluted with H_2O and then concentrated under reduced pressure. The separated precipitate was converted into an acetate and purified by recrystallization to give **A1b**: Yield, 225 mg (75%).

Demethylation of 2′,4′-Dimethoxyacetophenone with Anhydrous Aluminum Chloride, Bromide, or Chloride–Sodium Iodide in Acetonitrile. In a test tube (18 i.d. ×150 mm) fitted with a calcium chloride tube, the acetophenone (50 mg) was dissolved in the demethylating reagent and the solution was heated at a definite temperature in a thermostat-controlled oil bath. A small amount of the reaction mixture (0.1—0.2 ml) was removed at intervals, diluted with 2—3% aq HCl, heated at 60—70 °C for 20—30 min, and extracted with EtOAc. The extract was directly analyzed by gas chromatography[13] [column, Silicone OV-101 (GL Science Co., Ltd.)] and the yield of the products was calculated from the chromatogram (Fig. 1).

Demethylation of 3,6-Dihydroxy-5,7-dimethoxyflavones (5a—e and 5h) and 3-Acetoxy-6-hydroxy-5,7-dimethoxyflavones (18n and 18o) with Anhydrous Aluminum Chloride–Sodium Iodide in Acetonitrile. Ten percent (w/v) solution of anhydrous $AlCl_3$ in MeCN (20 ml; 15 mmol) was stirred with dried NaI (2.3 g; 15 mmol) for 30 min. To the solution, the flavone **5** or **18** (1.5 mmol) (**5e**, 1.0 mmol; **5h**, 0.75 mmol) was dissolved with stirring and the solution was warmed at 30 °C for 5 h (**5c**, 1 h; **5d**, 0.5 h). The mixture from **5** was diluted with ca. 3% aq HCl, warmed with Na_2SO_3 (0.4—0.6 g) at 60—70 °C for 20—30 min. The separated precipitate was collected and purified by recrystallization or preparative HPLC (**1c** and **1d**) to give **1**. The reaction mixture from **18** was diluted with a mixture of ca. 6% aq HCl (10—15 ml) and Na_2SO_3 (0.5 g) in MeOH (40—50 ml), and refluxed for 2—3 h. After the mixture was diluted with H_2O, the solvent was evaporated under reduced pressure. The separated precipitate was collected and recrystallized to give **1e** and **1f** (Table 6).

The flavones **1** were changed to the corresponding acetates (**A1**) by hot acetic anhydride-pyridine method (Table 6).

Synthesis of 3,3′,4′,6,7-Pentahydroxy-5-methoxyflavone (23h). A mixture of **1h** (200 mg), $PhCH_2Cl$ (0.75 ml), and dried K_2CO_3 (2.1 g) in DMF (5 ml) was heated at 150 °C for 10 min. Then this mixture was diluted with H_2O and the excess $PhCH_2Cl$ was removed by steam distillation. The separated precipitate was collected and recrystallized from $CHCl_3$–MeOH to give the hexabenzyl ether: Mp 161—162 °C; yield, 430 mg (80%); $C_{57}H_{46}O_8$. To a cooled suspension of the ether (250 mg) in MeCN, 2% (w/v) anhydrous $AlCl_3$ in MeCN (5.8 ml) was added, and the mixture was stirred at 0 °C for 30 min. The mixture was diluted with ca. 2% aq HCl and warmed at 60—70 °C for 20 min. The separated precipitate was collected and recrystallized from $CHCl_3$–MeOH to give 3,3′,4′,6,7-pentakis(benzyloxy)-5-hydroxyflavone: Mp 149—150 °C; yield, 143 mg (64%); $C_{50}H_{40}O_8$. The flavone (136 mg) was methylated with Me_2SO_4 and dried K_2CO_3 in Me_2CO to give 3,3′,4′,6,7-pentakis(benzyloxy)-5-methoxyflavone: Mp 124—125 °C (from $CHCl_3$–MeOH); yield, 120 mg (86%); $C_{51}H_{42}O_8$. The flavone (110 mg) was hydrogenolyzed with 10% Pd–C in EtOAc–MeOH (1 : 1) and the product was recrystallized from aq MeOH to give **23h**: Mp 239—241 °C; yield, 40 mg (83%); [Found: C, 52.04; H, 4.15%. Calcd for $C_{16}H_{12}O_8$: C, 52.18; H, 4.38%.].

Pentaacetate **A23h**: Mp 118—119 °C; [Found: C, 57.76; H, 4.38%. Calcd for $C_{26}H_{22}O_{13}$: C, 57.57; H, 4.09%.].

References

1) Part XVII: T. Horie, Y. Kawamura, H. Yamamoto, T. Kitou, and K. Yamashita, *Phytochemistry*, in press (1995).

2) T. Horie, H. Tominaga, I. Yoshida, and Y. Kawamura, *Bull. Chem. Soc. Jpn.*, **66**, 877 (1993).

3) H. Tominaga and T. Horie, *Bull. Chem. Soc. Jpn.*, **66**, 2668 (1993).

4) L. R. Row and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, **23A**, 23 (1946); *Chem. Abstr.*, **40**, 5050 (1946).

5) H. Wagner, L. Hörhammer, G. Hitzler, and L. Farkas, *Chem. Ber.*, **99**, 2430 (1966).

6) T. Horie, H. Tominaga, Y. Kawamura, and T. Yamada, *J. Org. Chem.*, **57**, 3343 (1992).

7) T. Horie, M. Tsukayama, Y. Kawamura, M. Seno, and S. Yamamoto, *Bull. Chem. Soc. Jpn.*, **61**, 441 (1988).

8) H. Wagner and L. Farkas, "The Flavonoids," ed by J. B. Harborne, T. S. Mabry, and H. Mabry, Chapman and Hall, London (1975), pp. 141—50.

9) T. Horie, M. Tsukayama, Y. Kawamura, and S. Yamamoto, *Chem. Pharm. Bull.*, **35**, 4465 (1987).

10) W. Adam, D. Golsch, L. Hadjiarapoglou, and T. Patonai, *J. Org. Chem.*, **56**, 7292 (1991).

11) T. Horie, M. Tsukayama, H. Kourai, Y. Nakayama, and M. Nakayama, *Chem. Pharm. Bull.*, **34**, 30 (1986).

12) T. Akiyama, N. Takechi, H. Shima, and S. Ozaki, *Chem. Lett.*, **1990**, 1881.

13) Y. Kawamura, H. Takatsuki, F. Torii, and T. Horie, *Bull. Chem. Soc. Jpn.*, **67**, 511 (1994).

14) T. Horie, H. Kourai, and N. Fujita, *Bull. Chem. Soc. Jpn.*, **56**, 3773 (1983).

15) E. Wollenweber, *Z. Pflanzenphysiol.*, **74**, 415 (1975).

16) J. B. Harborne, V. H. Heywood, and N. A. M. Saleh, *Phytochemistry*, **9**, 2011 (1970).

17) M. Kaouadji, S. Chiron, J. Garcia, F. Thomasson, M. Tissut, and P. Ravanel, *Phytochemistry*, **31**, 2131 (1992).

18) T. Horie, *J. Sci. Hiroshima Univ. A-II*, **33**, 221 (1969).

19) K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, **25A**, 417 (1947); *Chem. Abstr.*, **43**, 636 (1949).

20) D. K. Bhardwaj, M. S. Bisht, S. C. Uain, C. K. Mehta, and G. C. Sharma, *Phytochemistry*, **19**, 713 (1980).

21) B. A. Bohm and J. B. Choy, *Biochem. Syst. Ecol.*, **15**, 541 (1987).

22) V. D. N. Sastri and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, **23A**, 273 (1946).

23) T. Horie, *Nippon Kagaku-Kaishi*, **1978**, 748.

24) K. Fukui, M. Nakayama, T. Matsui, M. Masumura, and T. Horie, *Nippon Kagaku-Zasshi*, **90**, 1270 (1969).