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Studies of the Selective *O*-Alkylation and Dealkylation of Flavonoids. VIII.[1] Synthesis of Pedaliin

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3′,4′-Bis(benzyloxy)-6-hydroxy-5,7-dimethoxyflavone (**15**) was obtained from 6-hydroxy-2,4-dimethoxy-3-(methoxymethoxy)acetophenone (**13**) *via* 6′-hydroxy-2′,4′-dimethoxy-3′-methoxymethoxy-2-[3,4-bis(benzyloxy)benzoyl]acetophenone (**14**). The 5-methoxyl group of the acetate (**16**) of the flavone (**15**) was selectively split with about 5% (w/v) anhydrous aluminum chloride in acetonitrile to give 6-acetoxy-3′,4′-bis(benzyloxy)-5-hydroxy-7-methoxyflavone (**17**). The 5-hydroxyflavone (**17**) was converted into 3′,4′,5-tris(benzyloxy)-6-hydroxy-7-methoxyflavone (**20**) by benzylation and hydrolysis. Condensation of the 6-hydroxyflavone (**20**) with 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide, followed by hydrolysis of the resultant compound afforded the corresponding 6-*O*-β-D-glucoside (**22**), which was converted into 3′,4′,5,6-tetrahydroxy-7-methoxyflavone 6-*O*-β-D-glucoside (pedaliin) (**1**) by hydrogenolysis. The process should be useful as a general method for synthesizing 6-*O*-glucosides of 5,6-dihydroxy-7-methoxyflavones.

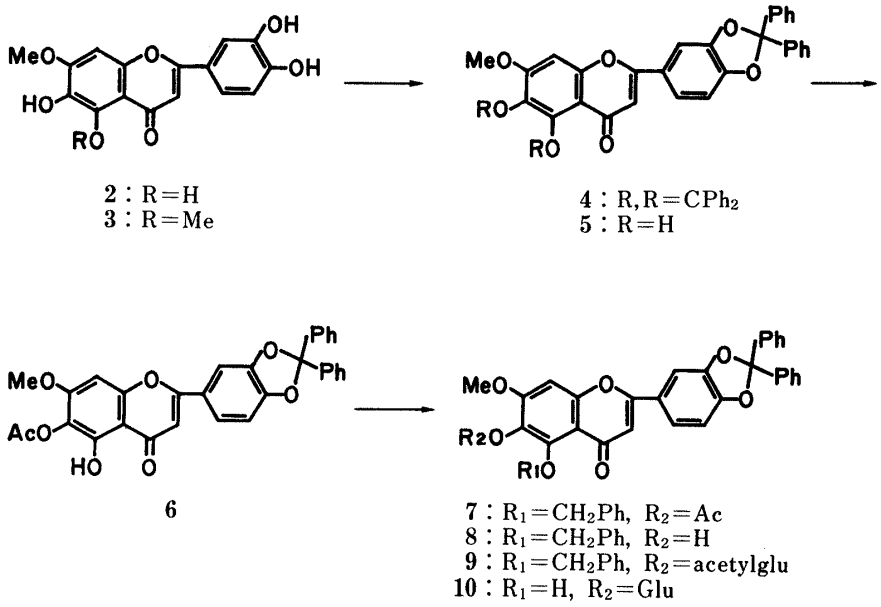
Keywords——flavone; selective demethylation; benzylation; pedaliin; 3′,4′-bis(benzyloxy)-6-hydroxy-5,7-dimethoxyflavone; 3′,4′,5-tris(benzyloxy)-6-hydroxy-7-methoxyflavone; 5,6-dihydroxy-7-methoxyflavone 6-*O*-glucoside

Pedaliin,[3] which was isolated from leaves of *Sesamun indicum*, was confirmed to be 3′,4′,5,6-tetrahydroxy-7-methoxyflavone 6-*O*-glucoside (**1**) on the basis of the synthesis of its aglycone (pedalitin) (**2**).[4,5] Two pedaliin analogs, 5,6-dihydroxy-4′,7-dimethoxyflavone and 4′,5,6-trihydroxy-3′,7-dimethoxyflavone 6-*O*-glucosides, were also isolated from natural sources.[6,7] On the other hand, in the synthesis of the glucosides of baicalein (5,6,7-trihydroxyflavone), Mezey-Vándor *et al.*[8] reported that baicalein 7-benzyl ether did not condense with 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide, but the 5,7-dibenzyl ether condensed with it in the usual way to give the acetylglucoside. The condensation of 5,6-dihydroxy-4′,7-dimethoxyflavone with the bromide also did not give any glucosides in our laboratory. The results suggest that the most important process in the synthesis of the glucosides is protection of the hydroxyl groups on the flavone skeleton. Therefore, we studied the selective protection of the 3′-, 4′-, and 5-hydroxyl groups in pedalitin (**2**), which has four hydroxyl groups, in order to establish a general method for synthesizing the 5,6-dihydroxy-7-methoxyflavone 6-*O*-glucosides and subsequently the synthesis of pedaliin (**1**).

Results and Discussion

Synthesis of 5-Benzyloxy-3′,4′-diphenylmethylenedioxy-6-hydroxy-7-methoxyflavone (8)

It can be presumed that the diphenylmethylenedioxyl group is an effective protecting group for the two vicinal hydroxyl groups[9] in the B ring of pedalitin (**2**). Therefore, the synthesis of **8** was attempted by the process shown in Chart 1.



2 : R=H
3 : R=Me

4 : R,R=CPh_2
5 : R=H

6

7 : R_1=CH_2Ph, R_2=Ac
8 : R_1=CH_2Ph, R_2=H
9 : R_1=CH_2Ph, R_2=acetylglu
10 : R_1=H, R_2=Glu

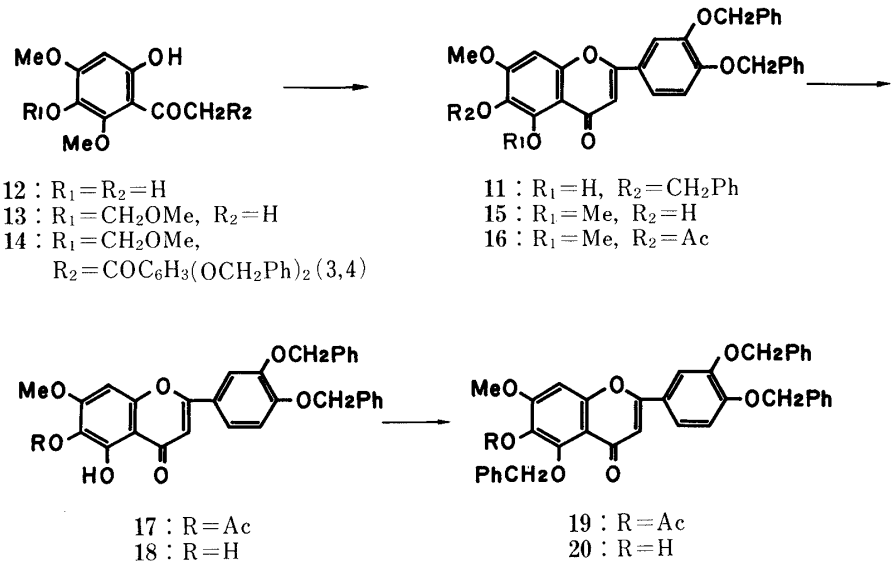
Chart 1

Pedalitin (**2**) or pedalitin 5-methyl ether (**3**)[5] was melted with α,α-dichlorodiphenylmethane to give 3′,4′:5,6-bis(diphenylmethylenedioxy)-7-methoxyflavone (**4**). The 5,6-diphenylmethylenedioxyl group in **4** was selectively split with aq. acetic acid to give 3′,4′-diphenylmethylenedioxy-5,6-dihydroxy-7-methoxyflavone (**5**). The partial acetylation of **5**, followed by benzylation of the resultant acetate afforded 6-acetoxy-5-benzyloxy-3′,4′-diphenylmethylenedioxy-7-methoxyflavone (**7**), which was converted into the corresponding 6-hydroxyflavone (**8**) by hydrolysis. Condensation of **8** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide in the presence of potassium hydroxide afforded the acetylglucoside (**9**). Hydrogenolysis with palladium on charcoal and hydrolysis of **9** afforded 5,6-dihydroxy-3′,4′-diphenylmethylenedioxy-7-methoxyflavone 6-*O*-glucoside (**10**) alone, but did not lead to pedaliin (**1**). The selective cleavage of the diphenylmethylenedioxyl group in **10** with dilute hydrochloric acid in methanol could not be achieved. This result indicates that a more efficient protecting group for the two vicinal hydroxyl groups is the benzyl group in the synthesis of flavone 6-*O*-glucosides.

Synthesis of 3′,4′,5-Tris(benzyloxy)-6-hydroxy-7-methoxyflavone (20)

The methoxyl groups in 4′,5,6,7-tetramethoxyflavone were split in the order of 5-, 6-, and 7-positions with anhydrous aluminum chloride in acetonitrile but in the order of 5-, 6-, and 4′-positions with hydroiodic acid in acetic acid.[10] These findings suggest that pedalitin 3′,4′-dibenzyl ether (**18**) might be prepared by the partial debenzylation of pedalitin 3′,4′,6-tribenzyl ether (**11**). Actually, the partial debenzylation of **11** with 5% (w/v) anhydrous aluminum chloride in acetonitrile at 50 °C afforded **18**, but the yield was low because of simultaneous cleavage of the benzyloxyl groups at the 3′- and 4′-positions. On the other hand, the 5-methoxyl group in the 5,6,7-trioxygenated flavones was rapidly split with anhydrous aluminum chloride in acetonitrile.[1] This result suggests that the 5-methoxyl group in 3′,4′-bis(benzyloxy)-6-hydroxy-5,7-dimethoxyflavone (**15**) and its acetate (**16**) could be selectively split to give the corresponding 5-hydroxyflavones (**18** and **17**), respectively. Though the flavone (**15**) has been synthesized from 3,6-dihydroxy-2,4-dimethoxyacetophenone (**12**) by Herz *et al.*,[11] the overall yield was low (about 15%). Therefore, the synthesis of 3′,4′,5-tris(benzyloxy)-6-hydroxy-7-methoxyflavone (**20**) was investigated as shown in Chart 2.

The 3-hydroxyl group in **12** was selectively methoxymethylated with methoxymethyl



12 : $R_1=R_2=H$
13 : $R_1=CH_2OMe$, $R_2=H$
14 : $R_1=CH_2OMe$, $R_2=COC_6H_3(OCH_2Ph)_2(3,4)$

11 : $R_1=H$, $R_2=CH_2Ph$
15 : $R_1=Me$, $R_2=H$
16 : $R_1=Me$, $R_2=Ac$

17 : R=Ac
18 : R=H

19 : R=Ac
20 : R=H

Chart 2

chloride and *N*,*N*-diisopropylethylamine in dichloromethane to give 6-hydroxy-2,4-dimethoxy-3-(methoxymethoxy)acetophenone (**13**). The crude 3,4-bis(benzyloxy)benzoate of **13** was converted into the diketone derivative (**14**) by means of the Baker–Venkataraman rearrangement with powdered potassium hydroxide in pyridine. Cyclization and demethoxymethylation of **14** with sulfuric acid in acetic acid gave **15** in good yield. The flavone **15** was also synthesized by cyclization of **14** with sodium acetate in acetic acid in low yield because of the formation of by-products. The 5-methoxyl group in the acetate (**16**) of **15** was selectively split with about 5% (w/v) anhydrous aluminum chloride in acetonitrile at 50 °C to give 6-acetoxy-3′,4′-bis(benzyloxy)-5-hydroxy-7-methoxyflavone (**17**) in good yield. Benzylation of **17** with benzyl chloride and potassium carbonate in acetone gave the corresponding benzyl ether (**19**), which was converted into the desired flavone (**20**), by hydrolysis with potassium hydroxide. The method should be available as a general synthesis of 5-benzyloxy-6-hydroxy-7-methoxyflavones. The proton nuclear magnetic resonance (^{1}H-NMR) and ultraviolet (UV)

Table I. ^{1}H-NMR Spectral Data for 3′,4′,5,6,7-Pentahydroxyflavone Derivatives in $CDCl_3$[a)]

Compd.	C_3-H	C_8-H	$C_{5'}$-H	OMe	OCH_2Ph	OAc	OH
4	6.50 s	6.59 s	6.89 d	3.94 s (3H)			
5	6.51 s	6.51 s	6.93 d	3.95 s (3H)			12.52 s
6	6.51 s	6.51 s	6.96 d	3.88 s (3H)		2.35 s (3H)	12.92 s
7	6.53 s	6.81 s	6.96 d	3.89 s (3H)	5.10 s (2H)	2.16 s (3H)	
8	6.57 s	6.83 s	6.98 d	3.97 s (3H)	5.19 s (2H)		5.77 br s
15	6.54 s	6.77 s	7.00 d	4.00 s (6H)	5.23 s (4H)		
16	6.50 s	6.75 s	6.98 d	3.91 s (6H)	5.21 s (4H)	2.34 s (3H)	
17	6.49 s	6.49 s	7.00 d	3.90 s (3H)	5.23 s (4H)	2.34 s (3H)	12.84 br s
18	6.50 s	6.52 s	7.00 d	3.99 s (3H)	5.22 s (4H)		12.54 s
19	6.48 s	6.77 s	6.98 d	3.90 s (3H)	5.09 s (2H) 5.20 s (4H)	2.16 s (3H)	
20	6.51 s	6.75 s	6.99 d	3.96 s (3H)	5.16 s (2H) 5.21 s (4H)		5.76 br s

a) The signals of the $C_{2'}$- and $C_{6'}$-protons overlapped with those of the benzyl aromatic protons: s, singlet; br s, broad singlet; d, doublet ($J=9$ Hz).

TABLE II. UV Spectral Data for 3′,4′,5,6,7-Pentahydroxyflavone Derivatives in Ethanol[a]

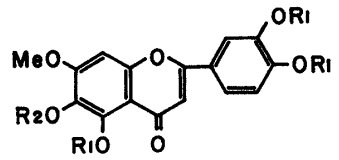
Compd.		λ_{max} nm (log ε)		
1		258 (4.16)	272 (4.17)	351 (4.32)
	($AlCl_3$)		279 (4.19)	378 (4.28)
	(NaOAc)	270 (4.18)	370 sh (4.10)	412 (4.19)
Nat.[3]		258 (4.17)	272 (4.19)	352 (4.31)
5		245 (4.30)	286 (4.25)	342 (4.44)
	($AlCl_3$)	252 (4.25)	296 (4.26)	364 (4.47)
6		276 (4.15)	285 sh (4.13)	342 (4.43)
	($AlCl_3$)	255 (4.26)	292 (4.21)	361 (4.42)
8		242 (4.40)	279 (4.22)	333 (4.50)
15			278 (4.26)	331 (4.46)
17		251 sh (4.26)	271 (4.22)	341 (4.41)
	($AlCl_3$)	259 (4.20)	282 (4.24)	355 (4.38)
18			286 (4.30)	340 (4.44)
	($AlCl_3$)		296 (4.33)	364 (4.47)
20			279 (4.28)	330 (4.48)

a) sh, shoulder.

spectral data of the compounds obtained here support fully those structures as shown in Tables I and II.

Synthesis and Identification of Pedaliin (1)

Condensation of the 6-hydroxyflavone (**20**) with 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide in the presence of potassium hydroxide in acetone afforded a mixture of the corresponding *O*-acetyl-α-D-glucoside (**21**) and the starting material (**20**). The mixture was hydrolyzed with aqueous potassium hydroxide and then separated into the glucoside (**22**) and **20** by silica-gel column chromatography. Hydrogenolysis of **22** with palladium on charcoal in methanol gave the desired flavone, 3′,4′,5,6-tetrahydroxy-7-methoxyflavone 6-*O*-β-D-glucoside (pedaliin) (**1**). The β-configuration of the glucose moiety in the synthetic 6-*O*-glucoside was supported by the fact that the *J* value of the anomeric proton in the ^{1}H-NMR spectrum of **1** was 7.3 Hz. The synthetic glucoside **1** was proved to be identical with the natural pigment on the basis of mixed melting point determination and UV and infrared (IR) spectral comparisons.



1: R_1 = H, R_2 = Glu
21: R_1 = CH_2Ph, R_2 = tetraacetylglu
22: R_1 = CH_2Ph, R_2 = Glu

Structure

Experimental

All the melting points were determined in glass capillaries and are uncorrected. ^{1}H-NMR spectra were measured with a Hitachi R-24 spectrometer (60 MHz), using tetramethylsilane as an internal standard, and chemical shifts are given in δ values. UV and IR spectra were taken on Hitachi 124 and Hitachi 215 spectrophotometers, respectively.

3′,4′:5,6-Bis(diphenylmethylenedioxy)-7-methoxyflavone (4)——(a) A mixture of pedalitin (**2**)[5] (1.06 g) and α,α-dichlorodiphenylmethane (1.6 ml) was melted at 230 °C for 5 min. The cooled mixture was dissolved in acetone, and then ether was added to the mixture. The precipitate was recrystallized from chloroform–methanol to give **4** (1.65 g, 76%) as colorless needles. mp 214—215.5 °C (sintered at 160—170 °C). *Anal.* Calcd for $C_{42}H_{28}O_7$: C, 78.25; H, 4.38.

Found: C, 77.97; H, 4.42.

(b) A mixture of pedalitin 5-methyl ether (**3**)[5] (1.0 g) and α,α-dichlorodiphenylmethane (1.6 ml) was melted under the same conditions to give **4** (1.56 g, 80%).

3′,4′-Diphenylmethylenedioxy-5,6-dihydroxy-7-methoxyflavone (5)——A mixture of **4** (1.5 g), acetic acid (10 ml), and water (1 ml) was refluxed for 10 min, and then water and ether were added to the mixture. The precipitate was recrystallized from ethyl methyl ketone–methanol to give **5** (0.87 g, 78%) as yellow needles. mp 125—126 °C (sintered at 213—214 °C and then crystallized). *Anal.* Calcd for $C_{29}H_{20}O_7 \cdot H_2O$: C, 69.87; H, 4.45. Found: C, 69.60; H, 4.62.

6-Acetoxy-3′,4′-diphenylmethylenedioxy-5-hydroxy-7-methoxyflavone (6)——The flavone **5** (0.5 g) was heated with acetic anhydride–pyridine (100 : 2, 5 ml) at 90 °C for 1—2 min, and then water was added to the mixture. The precipitate was washed with water and recrystallized from chloroform–ethyl acetate to give **6** (0.46 g, 86%) as pale yellow prisms. mp 245—246 °C. *Anal.* Calcd for $C_{31}H_{22}O_8$: C, 71.26; H, 4.24. Found: C, 71.10; H, 4.37.

6-Acetoxy-5-benzyloxy-3′,4′-diphenylmethylenedioxy-7-methoxyflavone (7)——A mixture of **6** (0.4 g), benzyl chloride (0.14 ml), potassium iodide (0.19 g), and potassium carbonate (1.2 g) in acetone (40 ml) was refluxed for 5 h with stirring. Water was added to the mixture, the solvent was evaporated under reduced pressure, and then the residue was allowed to stand for one day in a refrigerator. The precipitate was washed with methanol and then ether, and recrystallized from ethyl acetate to give **7** (0.28 g, 60%) as colorless needles. mp 218—220 °C. *Anal.* Calcd for $C_{38}H_{28}O_8$: C, 74.50; H, 4.61. Found: C, 74.49; H, 4.49.

5-Benzyloxy-3′,4′-diphenylmethylenedioxy-6-hydroxy-7-methoxyflavone (8)——The flavone **7** (300 mg) was added to methanol (30 ml) containing potassium hydroxide (150 ml) and stirred at 50 °C for 30 min. The solution was acidified with 0.2 ml of acetic acid. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate. The extracts were washed with aq. sodium carbonate and water, then concentrated under reduced pressure. The residue was recrystallized from ethyl acetate–ether to give **8** (240 mg, 86%) as pale yellow prisms. mp 178—180 °C. *Anal.* Calcd for $C_{36}H_{26}O_7$: C, 75.78; H, 4.59. Found: C, 75.66; H, 4.48.

3′,4′-Diphenylmethylenedioxy-5,6-dihydroxy-7-methoxyflavone 6-*O*-β-D-Glucoside (10)——To a solution of **8** (400 mg) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide (1.5 g) in aceton (20 ml) was added 2% potassium hydroxide solution (3.5 ml) and the mixture was allowed to stand in a refrigerator for 2 d. The mixture was concentrated under reduced pressure, diluted with water, and extracted with ethyl acetate. The extracts were chromatographed on a polyamide column using methanol. The acetylglucoside fraction was hydrogenolyzed over 10% palladium on charcoal (200 mg) in methanol (100 ml). The product was dissolved in methanol (15 ml) and 10% potassium hydroxide solution (5 ml) and then stirred at room temperature for 1 h. The mixture was acidified with 2% hydrochloric acid and the precipitate was recrystallized from methanol to give **10** (100 mg, 22%) as colorless needles. mp 187—189 °C. ^{1}H-NMR (400 MHz, in pyridine-d_5) δ: 6.95 (1H, s, C_3-H), 6.76 (1H, s, C_8-H), 7.67 (1H, d, J=1.7 Hz, $C_{2'}$-H), 7.15 (1H, d, J=8.2 Hz, $C_{5'}$-H), 7.56 (1H, dd, J=8.2, 1.7 Hz, $C_{6'}$-H), 3.83 (3H, s, OMe), 13.76 (1H, br s, C_5-OH); protons in the glucosyl moiety——6.04 (1H, d, J=6.9 Hz, C_1-H), 4.06 (1H, ddd, J=8.2, 4.7, 2.2 Hz, C_5-H), 4.49 (1H, dd, J=11.6, 2.2 Hz, C_6-H), 4.32—4.45 (4H, m, $C_{2,3,4, \text{and } 6}$-H); protons in the diphenylmethylenedioxyl moiety——7.77 (4H, d, J=6.9 Hz, $C_{2 \text{ and } 6}$-H), 7.43 (4H, t, J=6.9 Hz, $C_{3 \text{ and } 5}$-H), 7.38 (2H, t, J=6.9 Hz, C_4-H).

6′-Hydroxy-2′,4′-dimethoxy-3′-methoxymethoxy-2-[3,4-bis(benzyloxy)benzoyl]acetophenone (14)——Methoxymethyl chloride (5.7 ml) was added to a mixture of the acetophenone **12** (10 g) and *N*,*N*-diisopropylethylamine (11.5 ml) in dichloromethane (100 ml) with stirring. The mixture was allowed to stand at room temperature with stirring for 1 d. The solvent was evaporated and the residue was dissolved in ether. The ethereal solution was washed with dilute hydrochloric acid, aq. potassium carbonate, and water, then dried over sodium sulfate. The solvent was evaporated off to give **13** (about 12 g).

A solution of 3,4-bis(benzyloxy)benzoyl chloride (21.6 g) in dichloromethane (40 ml) was added to a solution of the crude **13** and *N*,*N*-diisopropylethylamine (15 ml) in dichloromethane (80 ml) with stirring, and then allowed to stand at room temperature with stirring overnight. The mixture was concentrated, diluted with water, and extracted with ether. The extracts were washed with dilute hydrochloric acid, aq. potassium carbonate, and water, then dried over sodium sulfate. The solvent was evaporated off to give the crude benzoate. A mixture of the benzoate and powdered potassium hydroxide (20 g) in pyridine (80 ml) was stirred at 50 °C for 5 h. The mixture was poured into a mixture of ice (500 g), hydrochloric acid (120 ml), and ethyl acetate (250 ml). The ethyl acetate layer was washed with water and aq. potassium carbonate, and concentrated under reduced pressure. The residue was recrystallized from ethyl acetate–methanol to give **14** (19 g, 70%) as yellow needles mp 99—100 °C. *Anal.* Calcd for $C_{33}H_{32}O_9$: C, 69.22; H, 5.63. Found: C, 69.17; H, 5.62.

3′,4′-Bis(benzyloxy)-6-hydroxy-5,7-dimethoxyflavone (15)——A solution of concentrated sulfuric acid (2 ml) in acetic acid (20 ml) was added to a solution of **14** (8.15 g) in acetic acid (15 ml). The mixture was vigorously stirred at 60 °C for 10 min and diluted with water. The precipitate was recrystallized from ethyl acetate–methanol to give **15** (6.82 g, 94%) as pale yellow prisms. mp 174—175 °C. *Anal.* Calcd for $C_{31}H_{26}O_7$: C, 72.93; H, 5.13. Found: C, 73.08; H, 5.10.

6-Acetoxy-3′,4′-bis(benzyloxy)-5,7-dimethoxyflavone (16)——The flavone **15** (6.22 g) was acetylated with hot acetic anhydride–pyridine (10 : 1, 20 ml). The acetate was recrystallized from ethyl acetate–methanol to give **16** (6.4 g,

95%) as colorless needles. mp 161—162 °C. *Anal.* Calcd for $C_{33}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.65; H, 5.07.

6-Acetoxy-3′,4′-bis(benzyloxy)-5-hydroxy-7-methoxyflavone (17)——The flavone **16** (6.2 g) was dissolved in acetonitrile (120 ml) containing anhydrous aluminum chloride (6 g) and heated at 50 °C for 90 min. The mixture was poured into a mixture of concentrated hydrochloric acid (25 ml) and ice-cold water (450 ml) and heated at 50—60 °C for 30 min. The mixture was concentrated under reduced pressure and the precipitate was recrystallized from chloroform–methanol to give **17** (4.85 g, 80%) as pale yellow needles. mp 173—174 °C. *Anal.* Calcd for $C_{32}H_{26}O_8$: C, 71.36; H, 4.87. Found: C, 71.30; H, 4.79.

The crystals recovered from the mother liquor were refluxed with 5% hydrochloric acid (10 ml) in methanol (80 ml) for 2 h, and the insoluble material was filtered off. The material obtained from the filtrate was recrystallized from chloroform–methanol to give 3′,4′-bis(benzyloxy)-5,6-dihydroxy-7-methoxyflavone (**18**) (0.26 g, 4.5%) as yellow needles. mp 150—152 °C. *Anal.* Calcd for $C_{30}H_{24}O_7$: C, 72.57; H, 4.87. Found: C, 72.62; H, 4.76.

6-Acetoxy-3′,4′,5-tris(benzyloxy)-7-methoxyflavone (19)——A mixture of **17** (3.47 g), benzyl chloride (1.2 ml), potassium iodide (1.64 g), and powdered potassium carbonate (9 g) in acetone (100 ml) was refluxed with stirring for 5 h. To the mixture was added water (300 ml) and the precipitate was recrystallized from chloroform–ethyl acetate to give **19** (3.0 g, 74%) as colorless needles. mp 93—95 °C. *Anal.* Calcd for $C_{39}H_{32}O_8$: C, 74.45; H, 5.02. Found: C, 74.51; H, 5.13.

6-Hydroxy-3′,4′,5-tris(benzyloxy)-7-methoxyflavone (20)——The flavone **19** (1.42 g) was stirred in methanol (50 ml) containing potassium hydroxide (0.7 g) at 50 °C for 1 h. After the mixture was acidified with acetic acid, the solvent was evaporated under reduced pressure, and then water and ether were added to the residue. The precipitate was recrystallized from ethyl acetate to give **20** (1.2 g, 91%) as colorless needles. mp 92—93 °C. *Anal.* Calcd for $C_{37}H_{30}O_7$: C, 75.75; H, 5.16. Found: C, 75.71; H, 5.04.

3′,4′,5,6-Tetrahydroxy-7-methoxyflavone 6-*O*-β-D-Glucoside (Pedaliin) (1)——To a solution of **20** (280 mg) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide (1 g) in acetone (40 ml) was added 2% potassium hydroxide solution (3 ml) and the solution was allowed to stand in a refrigerator for 1 d. After methanol (10 ml) and 10% potassium hydroxide (10 ml) were added to the solution, the mixture was stirred at room temperature for 0.5—1 h. The mixture was acidified with acetic acid, concentrated under reduced pressure, and extracted with ethyl acetate. The extracts were chromatographed on a silica-gel column (20 × 40 mm i.d.) with chloroform–ethyl acetate (2 : 1), followed by with ethyl methyl ketone saturated with water. From the eluate with chloroform–ethyl acetate, the starting material **20** (120 mg, 43%) was recovered. The oily glucoside **22** was obtained from the eluate with ethyl methyl ketone–water. The glucoside **22** was dissolved in methanol (40 ml) and shaken with 10% palladium on charcoal (150 mg) in a hydrogen atmosphere until the uptake of hydrogen ceased. After the catalyst was filtered off, the filtrate was concentrated and the residue was recrystallized from aq. methanol to give **1** (105 mg, 43%) as pale yellow needles. mp 263—265 °C (dec., sintered at 175—181 °C and then crystallized at 185—195 °C). ^{1}H-NMR (400 MHz, in pyridine-d_5) δ: 6.90 (1H, s, C_3-H), 6.59 (1H, s, C_8-H), 7.91 (1H, d, J=2.2 Hz, $C_{2'}$-H), 7.31 (1H, d, J=8.2 Hz, $C_{5'}$-H), 7.53 (1H, dd, J=8.2, 2.2 Hz, $C_{6'}$-H), 3.80 (3H, s, OMe), 13.93 (1H, s, C_5-OH); protons in the glucosyl moiety——6.02 (1H, d, J=7.3 Hz, C_1-H), 4.05 (1H, ddd, J=8.6, 5.2, 2.6 Hz, C_5-H), 4.49 (1H, dd, J=12.0, 2.6 Hz, C_6-H), 4.31—4.44 (4H, m, $C_{2,3,4,\text{and}\,6}$-H). *Anal.* Calcd for $C_{22}H_{22}O_{12}\cdot 2H_2O$: C, 51.36; H, 5.09. Found: C, 51.42; H, 5.07. The melting point was underpressed on admixture of the glucoside with the natural pigment.[3]

3′,4′,5-Tris(benzyloxy)-6-hydroxy-7-methoxyflavone 6-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucoside) (21)——The glucoside **22** was acetylated with acetic anhydride–pyridine (10 : 2) at room temperature for 1 d. The acetate was recrystallized from ethyl acetate–ether to give **21** as colorless needles. mp 100—101 °C. *Anal.* Calcd for $C_{51}H_{48}O_{16}$: C, 66.80; H, 5.28. Found: C, 66.89; H, 5.15.

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References and Notes

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