Taiwaniaflavone and its Derivatives: a New Series of Biflavones from *Taiwania cryptomerioides* Hayata

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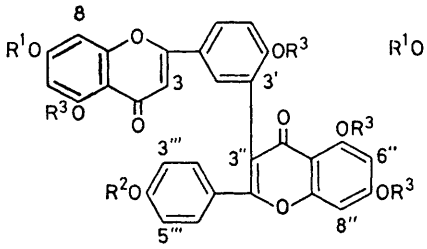
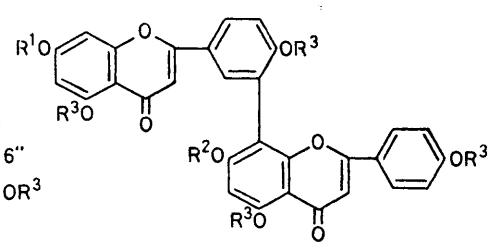
Taiwaniaflavone (3,3′-linked biapigenin) (1) and its methyl ethers [(2) and (3)] isolated from the leaves of *Taiwania cryptomerioides* Hayata (Taxodiaceae) have been identified on the basis of spectral data and by synthesis of taiwaniaflavone methyl ethers [(5) and (29)]. Five known biflavones [(7), (8), (9), (10), and (11)] have also been isolated from the same plant.

Taiwania cryptomerioides Hayata (Taxodiaceae) is a conifer found in Formosa (Taiwan), China, and North Burma and resembles cryptomeria in habit. Hinokiflavone (9) has been reported [1] to be the only biflavone constituent from the leaf extracts in addition to a sesquiterpene [2] and lignans.[3] In our study, extraction of the plant leaves with acetone gave a new type of biflavone, which we have named taiwaniaflavone.

A mixture of biflavones obtained from the leaves gave three fractions (TC-I, TC-II, and TC-III) by p.l.c. and after methylation [4] with dimethyl sulphate these fractions showed the presence of hexa-*O*-methylamentoflavone (4), penta-*O*-methylhinokiflavone (6), and a new compound, hexa-*O*-methyltaiwaniaflavone (5). The three fractions were, therefore, subjected to countercurrent distribution to give taiwaniaflavone (1) and amentoflavone (7) [5] from TC-I, 7-*O*-methyltaiwanaflavone (2), sequoiaflavone (8),[6] and hinokiflavone (9) [5] from TC-II, and 4‴,7-di-*O*-methyltaiwaniaflavone (3), 7,7″-di-*O*-methylamentoflavone (10),[7] and isocryptomerin (11) [8] from TC-III.

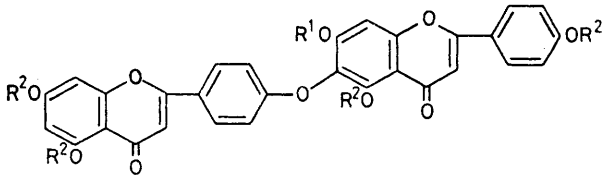
On methylation with dimethyl sulphate taiwaniaflavone (1) and its mono- and di-methyl ethers [(2) and (3)] gave the same hexamethyl ether (5), which showed an intense molecular ion peak of composition $C_{36}H_{20}O_{10}$. On acetylation they gave taiwaniaflavone hexa-acetate





(1) $R^1 = R^2 = R^3 = H$
(2) $R^1 = Me$, $R^2 = R^3 = H$
(3) $R^1 = R^2 = Me$, $R^3 = H$
(5) $R^1 = R^2 = R^3 = Me$
(12) $R^1 = R^2 = R^3 = Ac$
(13) $R^1 = Me$, $R^2 = R^3 = Ac$
(14) $R^1 = R^2 = Me$, $R^3 = Ac$

(4) $R^1 = R^2 = R^3 = Me$
(7) $R^1 = R^2 = R^3 = H$
(8) $R^1 = Me$, $R^2 = R^3 = H$
(10) $R^1 = R^2 = Me$, $R^3 = H$



(6) $R^1 = R^2 = Me$
(9) $R^1 = R^2 = H$
(11) $R^1 = Me$, $R^2 = H$

(12), 7-*O*-methyltaiwaniaflavone penta-acetate (**13**), and 4‴,7-di-*O*-methyltaiwaniaflavone tetra-acetate (**14**), respectively. The ^{1}H n.m.r. data (see Table) of the

TABLE

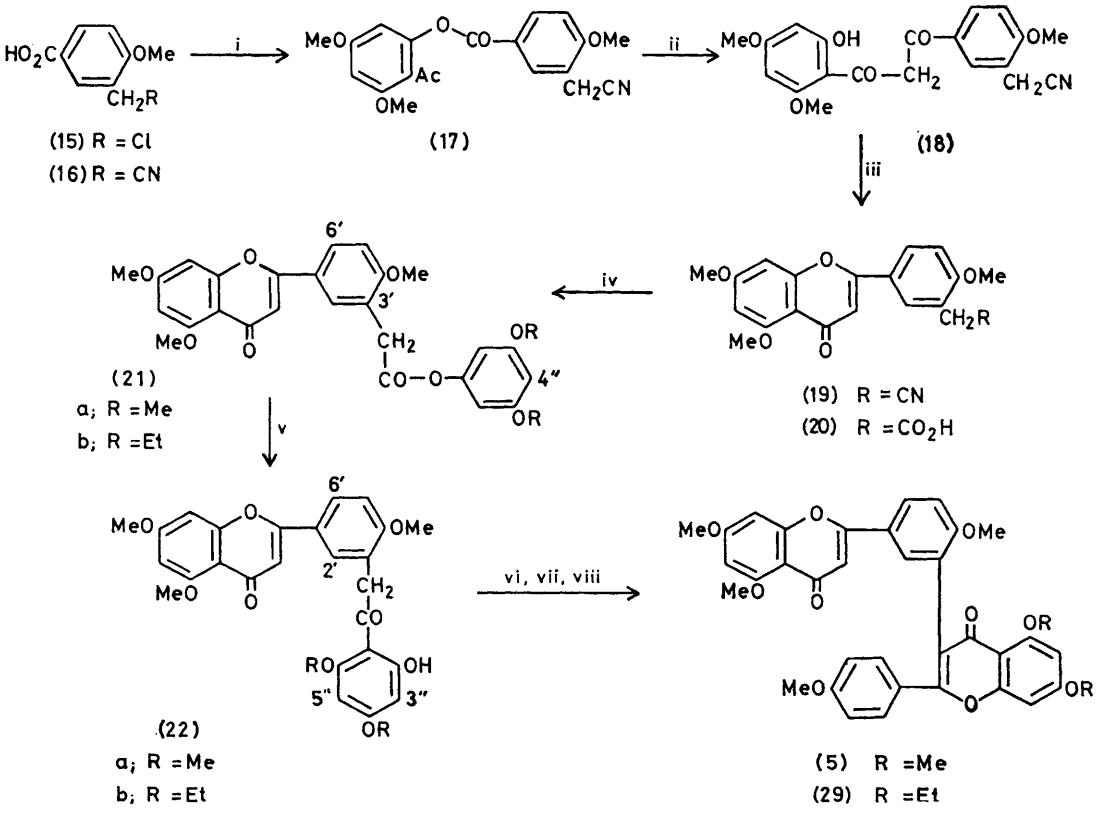
^{1}H N.m.r. data (δ values) of taiwaniaflavone derivatives

Protons		Compounds (5)	(12)	(13)	(14)
H-6	d	6.31	6.82	6.55	6.55
-6″	d	6.36	6.89	6.85	6.84
-8	d	6.51	7.25	6.73	6.74
-8″	d	6.54	7.34	7.30	7.31
-3	s	6.53	6.50	6.33	6.33
-2′	d	7.71	7.47	7.43	7.46
-6′	q	7.78	7.84	7.79	7.82
-5′	d	6.92	7.32	7.35	7.34
-2‴ and 6‴	d	7.36	7.45	7.42	7.38
-3‴ and 5‴	d	6.75	7.06	7.03	6.74
OMe	s	3.65		3.85	3.74
		3.75			3.85
		3.86			
		3.91 (9 H)			
OAc	s		2.18	2.15	2.15
			2.24	2.22	2.33
			2.33	2.33	2.36
			2.36	2.35	2.38
			2.38	2.37	
			2.40		

hexamethyl ether (**5**) and the hexa-acetate (**12**) are quite similar to those of 3,3′-linked biapigenin, which has already been reported [9] as one of the oxidative coupling products of apigenin with alkaline potassium ferricyanide. The structure of taiwaniaflavone was, therefore, deduced to be the first naturally occurring example of a 3,3′-linked biapigenin.

Further confirmation of the structure of taiwaniaflavone was made by a stepwise synthesis of the hexamethyl ether (**5**) as shown in Scheme 1. Starting from 3-chloromethyl-4-methoxybenzoic acid (**15**), tri-*O*-methylapigenin-3′-ylacetic acid (**20**) was prepared. The acid (**15**) was obtained by chloromethylation [10] of *p*-anisic acid and converted into (**16**) by cyanation.[10] The diketone (**18**) was obtained by a Baker–Venkataraman rearrangement (B.V. rearrangement) of the 2-acetyl-3,5-dimethoxyphenol ester (**17**) of (**16**). Subsequent ring closure of (**18**) followed by hydrolysis gave the acid (**20**). Esterification [11] of (**20**) and Fries rearrangement of the ester (**21a**) gave a ketoflavone (**22a**). The B.V. rearrangement of the *p*-anisoyl ester of (**22a**) followed by ring closure of the product gave a hexa-*O*-methylbiflavone, m.p. 264—265 °C, which was identified with the hexamethyl ether (**5**) of natural taiwaniaflavone.

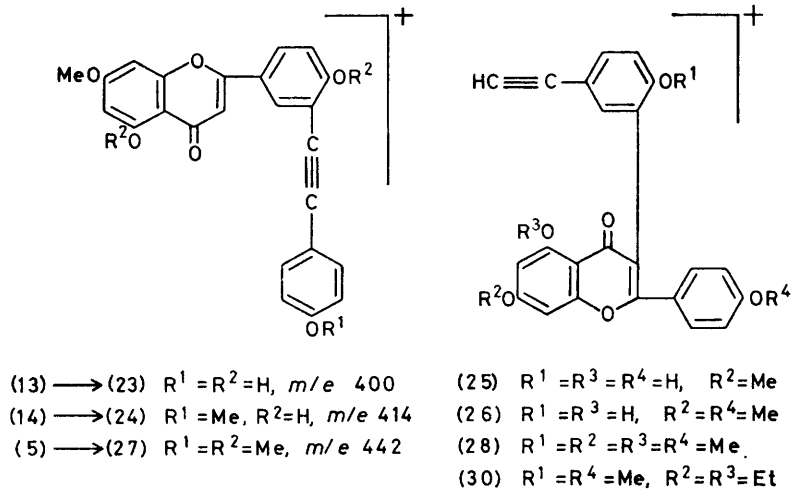
In a comparison of the δ-values (Table) of the four doublet signals due to H-6, -6″, -8, and -8″ of the two acetates [(**12**) and (**13**)], it was found that the two signals at δ 6.55 and 6.73 of (**13**) showed considerable upfield shifts compared with those (δ 6.82 and 7.25) of (**12**). These shifts suggest the presence of a 7- or 7″-*O*-methyl group in (**13**). Similarly, the doublet at δ 6.74 due

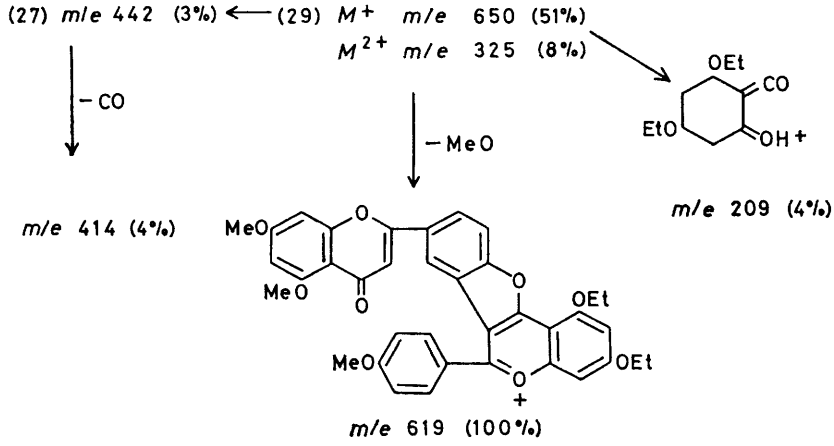


SCHEME 1 Synthetic route of taiwaniaflavone methyl ethers. *Reagents and conditions:* i, 2-acetyl-3,5-dimethoxyphenol; ii, KOH, B.V. rearrangement; iii, conc. H_2SO_4; iv, 3,5-diethoxy- or 3,5-dimethoxy-phenol; v, $AlCl_3$; vi, *p*-anisoyl chloride; vii, B.V. rearrangement; viii, ring closure

to H-3''' and -5''' of (14) suggests the presence of a 4'''-methoxy-group in (14). Thus the monomethyl ether is identified as 7- or 7''-*O*-methyltaiwaniaflavone and the dimethyl ether as 4''',7- or 4''',7''-di-*O*-methyltaiwaniaflavone.

In order to determine the position of the remaining B, 5'',7''-di-*O*-ethyl-4',4''',5,7-tetra-*O*-methyltaiwaniaflavone (29) was synthesized using 3,5-diethoxyphenol instead of 3,5-dimethoxyphenol (see Scheme 1). The mass spectrum of (29) showed an ion peak at *m/e* 442 (27), which is identical with that from (5) and almost no signal was observed at *m/e* 470, for which a Type B





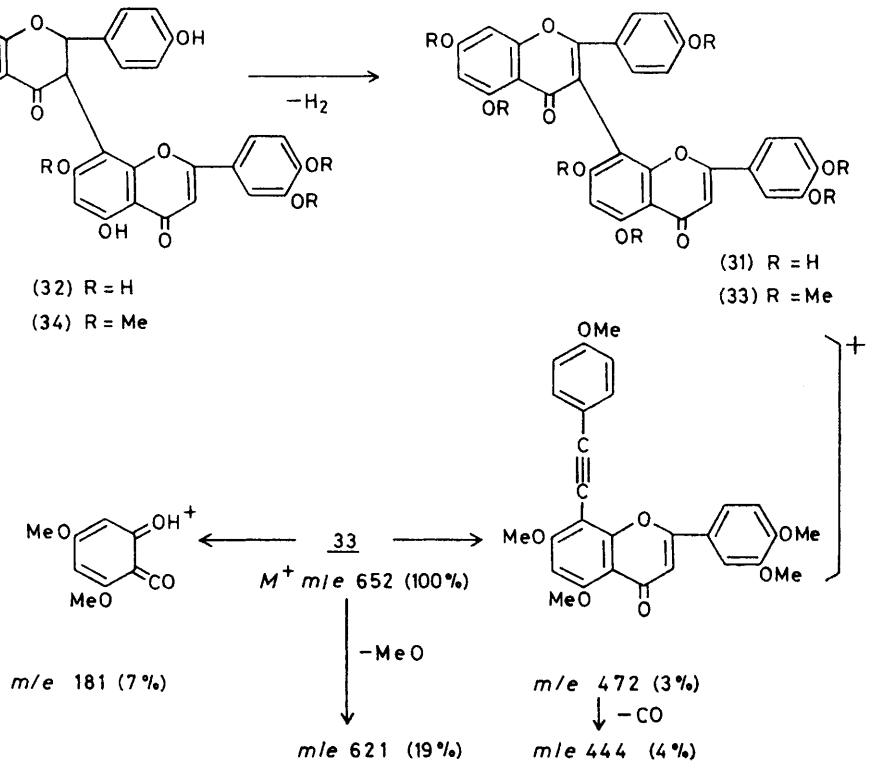
SCHEME 2 Mass fragmentation of taiwaniaflavone derivatives

methoxy-group the mass spectra of the two acetates [(13) and (14)] were examined. Compound (13) gave an intense fragment ion peak at *m/e* 400 (base peak) and (14) gave a similar peak at *m/e* 414. The structures of these fragments can be deduced as shown in Scheme 2: (23) is derived from (13) and (24) from (14) (Type A fission). However, another fragmentation pattern to give (25) and (26) (Type B fission) is also possible for the same ion peaks at *m/e* 400 and 414 respectively.

These two fragmentation patterns, A and B can be considered also for the methyl ether (5): (27) (Type A) and (28) (Type B) for the ion peak at *m/e* 442 from (5). In order to distinguish between the patterns A and fission product (30) is assignable (Scheme 2). The two ions, *m/e* 442 and 209 from (29) are fragments formed by a retro-Diels-Alder reaction. These observations support Type A fission as a mass fragmentation pattern in the taiwaniaflavone nucleus. Accordingly, formulae (23) and (24) are more preferable than (25) and (26) for the fragment ions from the two acetates. Therefore, the structures of the two natural methyl ethers [(2) and (3)] are deduced as 7-*O*-methyl- and 4''',7-di-*O*-methyltaiwaniaflavone respectively.

Saharanflavone (31) has been reported [12] as a dehydrogenation product of fukugetin (32) [13] (= morelloflavone) and constitutes another example of biflavones which have

an interflavone linkage at the 3-position. In mass spectral studies [14] of hepta-*O*-methylsaharanflavone (**33**) an intense molecular ion peak at *m/e* 652 was observed along with some fragment ion peaks (see Scheme 3). They correspond well to those of (**29**) (Scheme 2). A similar fragment ion (*m/e* **474**) has been reported [13] also in the mass spectrum of hepta-*O*-methylfukugetin and a very intense fragment ion (*m/e* **446**) was reported [15] in the mass spectrum of tetra-*O*-methylmorelloflavone (**34**). These evidences are all in good accord with the mass fragmentation pattern of taiwaniaflavone, supporting that the Type A fission is more preferable than Type B.



SCHEME 3 Mass fragmentation of hepta-*O*-methylsaharanflavone

It seems to be remarkable that one of the phenolic oxidative coupling products of apigenin was isolated from natural source as taiwaniaflavone. The formation of biflavonoids is generally explained [16] by oxidative coupling of two chalcone units followed by modification of the central C_3-units. However, isolation of taiwaniaflavone and its methyl ethers suggests that apigenin itself may be considered as a precursor of natural biflavones in a biosynthetic pathway.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded with a JEOL PS-100 instrument using tetramethylsilane as internal reference in $CDCl_3$ solutions. Mass spectra were obtained from a JEOL OISG double-focusing high-resolution instrument. T.l.c. analysis was carried out by using silica gel G according to Stahl (Merck) and a solvent system, benzene–pyridine–formic acid (**36** : 9 : 5; BPF) or toluene–ethyl formate–formic acid (5 : 4 : 1; TEFF). Counter-current distribution (c.c.d.) was performed with an apparatus equipped with 300 tubes of 10 ml moving and 10 ml stationary layers.

Extraction of Biflavones.—Dried and powdered leaves (1 kg) of *T. cryptomerioides* Hayata collected in Taiwan were completely exhausted with light petroleum (b.p. 40—60 °C) and then with benzene. The treated leaves were dried and again extracted with boiling acetone until the extract was almost colourless. The combined acetone extracts were concentrated *in vacuo* to give a dark viscous mass, which was extracted successively with boiling light petroleum, benzene, and $CHCl_3$ until the solvent in each case was almost colourless. The residue was then treated with boiling water. The water-insoluble mass was dissolved in EtOH and the filtrate was dried under reduced pressure to give a residue (5 g), which responded to the usual colour tests for flavonoids. The dried extracts were dissolved in dry acetone (50 ml) and placed on a column of silica gel (150 g) with light petroleum. Elution was carried out with the following solvents successively, giving the materials shown in parentheses: (i) light petroleum (greenish gummy mass), (ii) benzene (waxy product), (iii) $CHCl_3$ (oily product), (iv) acetone–benzene, 7 : 3 (brownish green solid, 2 g), and (v) acetone (dark brown mass, 0.2 g). Fractions (iv) and (v) gave positive colour tests for flavonoids. These two fractions were combined (2.2 g), dissolved in dry pyridine (50 ml) and separated into three fractions by p.l.c. (BPF): TC-I (0.4 g) from band I (R_F 0.15), TC-II (0.5 g) from band II (R_F 0.37), and TC-III (0.5 g) from band III (R_F 0.62).

Methylation of the Fractions.—TC-I (0.2 g) was methylated with Me_2SO_4 and K_2CO_3 in boiling dry acetone and the methylated product showed two spots (TEFF, R_F 0.40

and 0.37). On a p.l.c. separation (BPF) colourless needles (30 mg, from EtOH), m.p. 225—226 °C were obtained from the lower band and identified with hexa-*O*-methylamentoflavone (4) (mixed m.p. and ^{1}H n.m.r.).

Hexa-O-*methyltaiwaniaflavone* (5). The upper band yielded colourless rods (35 mg) (MeOH), m.p. 264—265 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 266 (4.68) and 325 nm (4.61), $\nu_{max.}^{(KBr)}$ 1 625, 1 600, 1 480, 1 450, 1 400, 1 330, 1 250, 1 200, 1 155, 1 110, 1 050, 830, and 810 cm^{-1}; *m/e* (%) 622.182 2 (31) (M^+, $C_{36}H_{30}O_{10}$ requires 622.183 8), 608 (10), 593 (39), 592 (100), 577 (4), 561 (5), 545 (5), 442 (2), 427 (2), 411 (2), 311 (M^{2+}, 4), 232 (4) and 181 (4), ^{1}H n.m.r. data are given in the Table (Found: C, 69.35; H, 4.9. $C_{36}H_{30}O_{10}$ requires C, 69.44; H, 4.86%). Similarly, TC-II was methylated and the product was found to be a mixture of three methyl ethers, identified with (4), (5), and (6) (t.l.c., mixed m.p. and ^{1}H n.m.r.). TC-III was also methylated to give a mixture of the same three compounds (4), (5), and (6).

Taiwaniaflavone (1).—TC-I (150 mg) was subjected to c.c.d. between a borate buffer (pH 9.6) and methyl ethyl ketone (MEK). After 555 transfers the following two fractions were collected: TC-Ia (60 mg) from tubes Nos. 161—215 and TC-Ib (30 mg) from tubes nos. 220—260. On recrystallization from MEK–$CHCl_3$ TC-Ia gave pale yellow crystals (43 mg), m.p. >315 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 269 (4.60) and 340 nm (4.50), $\nu_{max.}^{(KBr)}$ 1 644, 1 604, 1 490, 1 350, 1 270, 1 250, 1 162, 1 033, 1 020, 940, and 825 cm^{-1} (Found: C, 67.01; H, 3.28. $C_{30}H_{18}O_{10}$ requires C, 66.92; H, 3.37%).

The hexa-acetate (12). Acetylation of (1) with Ac_2O and NaOAc for 30 min at 120 °C gave a solid which crystallized as needles, m.p. 193—195 °C (MeOH–$CHCl_3$), $\lambda_{max.}^{(EtOH)}$ (log ε) 256 (4.51) and 303 nm (4.44); *m/e* (%) 706 (8), 664 (27), 622 (44), 580 (42), 538 (27), 428 (19), 386 (100), 234 (19), and 153 (25); ^{1}H n.m.r. data are given in the Table (Found: C, 63.65; H, 3.9. $C_{42}H_{30}O_{16}$ requires: C, 63.80; H, 3.82%).

Amentoflavone (7).—TC-Ib was crystallized from MeOH as pale yellow crystals, whose acetate, m.p. 231—232 °C, was identified with an authentic sample of hexa-*O*-acetylamentoflavone (mixed m.p. and ^{1}H n.m.r.).

7-O-*Methyltaiwaniaflavone* (2).—TC-II (120 mg) was subjected to c.c.d. between a borate buffer of pH 9.8 and MEK. After 80 transfers TC-IIa (25 mg) from tubes no. 16—30, TC-IIb (40 mg) from no. 51—66, and TC-IIc (30 mg) from no. 71—80 were collected. TC-IIc was crystallized from MeOH to give yellow prisms (20 mg), m.p. 285—287 °C

The penta-acetate (13). This had m.p. 160—162 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 262 (4.59) and 309 nm (4.52); $\nu_{max.}^{(KBr)}$ 1 775, 1 635, 1 432, 1 370, 1 280, 1 195, 1 160, 1 040, 905 and 840 cm^{-1}; *m/e* (%) 594 (19), 552 (50), 401 (49), 400 (100), 355 (31), 281 (32), 167 (53), and 153 (30); ^{1}H n.m.r. data are given in the Table (Found: C, 64.7; H, 4.05. $C_{41}H_{30}O_{15}$ requires C, 64.56; H, 3.96%).

Sequoiaflavone (8) and *Hinokiflavone* (9).—TC-IIa was acetylated to give an acetate (EtOAc), m.p. 225—226 °C, which was identified with penta-*O*-acetylhinokiflavone (i.r. and ^{1}H n.m.r.). TC-IIb was crystallized from MeOH to give pale yellow crystals, whose acetate, m.p. 245—247 °C, was identified with an authentic sample of penta-*O*-acetylsequoiaflavone (mixed m.p. and ^{1}H n.m.r.).

4‴,7-*Di*-O-*methyltaiwaniaflavone* (3).—TC-III (130 mg) was subjected to c.c.d. between a borate buffer of pH 9.8 and MEK. After 200 transfers the following were collected, TC-IIIa (20 mg) from tubes nos. 21—45; TC-IIIb (35 mg) from nos. 61—90; and TC-IIIc (25 mg) from nos. 101—130. TC-IIIc was crystallized from MeOH to give yellow crystals (22 mg), m.p. 285—288 °C; $\lambda_{max.}^{(EtOH)}$ (log ε) 271 (4.62) and 342 nm (4.53); $\nu_{max.}^{(KBr)}$ 1 650, 1 602, 1 494, 1 352, 1 250, 1 155, 1 031, and 827 cm^{-1}.

The tetra-acetate (14). This had m.p. 168—169 °C (EtOAc), *m/e* (%) 650 (4), 608 (36), 567 (31), 566 (78), 414 (100), 399 (8), 385 (5), 371 (4), 167 (6), and 153 (3); ^{1}H n.m.r. data are given in the Table (Found: C, 65.55; H, 4.25. $C_{40}H_{30}O_{14}$ requires: C, 65.39; H, 4.12%).

7,7″-*Di*-O-*methylamentoflavone* (10) *and Isocryptomerin* (11).—TC-IIIa on crystallization from MeOH gave pale yellow prisms (10 mg), whose acetate, m.p. 209—210 °C (EtOAc) was identified with an authentic sample of tetra-*O*-acetylisocryptomerin (mixed m.p. and ^{1}H n.m.r.). TC-IIIb gave pale yellow prisms (MeOH), m.p. above 315 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 271 (4.49) and 340 nm (4.49), which was identified with 7,7″-di-*O*-methylamentoflavone [7] obtained from the leaves of *Araucaria excelsa* by mixed m.p. of the acetate, m.p. 176—178 °C and by comparison of the ^{1}H n.m.r. spectrum of the acetate.

3-*Chloromethyl*-4-*methoxybenzoic Acid* (15).— A formaldehyde solution (37%; 60 ml) mixed with *p*-anisic acid (10 g) and anhydrous $ZnCl_2$ (15 g) was treated with a vigorous stream of dry HCl at 70 °C for 7 h and then allowed to stand overnight at room temperature. The reaction mixture was poured into water to yield a precipitate, which was collected, washed with water, dried, and crystallized from benzene to give the acid (15) as needles (12.5 g, 95%), m.p. 178—179 °C, δ 3.93 (3 H, s), 4.62 (2 H, s), 6.94 (1 H, d, *J* 9 Hz), 8.12 (1 H, d, *J* 2 Hz) and 8.08 (1 H, q, *J* 2 and 9 Hz) (Found: C, 53.95; H, 4.55; Cl, 17.35. $C_9H_9ClO_3$ requires C, 53.9; H, 4.5; Cl, 17.70%).

3-*Cyanomethyl*-4-*methoxybenzoic Acid* (16).—The acid (15) (1 g) was added in portion to a stirred mixture of finely powdered NaCN (0.5 g) and Me_2SO (10 ml) until the latter had dissolved. The mixture was then set aside overnight after which it was poured into ice–water and acidified with hydrocholic acid to yield a precipitate. This was filtered off, washed with water, and crystallized from benzene to give the acid (16) (0.83 g, 87%), m.p. 214—216 °C, δ 3.68 (2 H, s), 3.93 (3 H, s), 6.95 (1 H, d, *J* 9 Hz), 8.08 (1 H, d, *J* 2 Hz) and, 8.09 (1 H, q, *J* 2 and 9 Hz) (Found: C, 63.15; H, 4.7; N, 6.5. $C_{10}H_9O_3N$ requires C, 62.82; H, 4.75; N, 7.33%).

2-*Acetyl*-3,5-*dimethoxyphenyl* 3-*Cyanomethyl*-4-*methoxybenzoate* (17).—$SOCl_2$ (25 ml) was added dropwise to a solution of the acid (16) (5.0 g) in $CHCl_3$ (100 ml) and the mixture was then refluxed for 1 h. Excess of $SOCl_2$ was distilled off under reduced pressure and a solution of 2-acetyl-3,5-dimethoxyphenol (4.5 g) in anhydrous pyridine (40 ml) was slowly added. After being kept at 60 °C for 1 h on a water-bath, pyridine was distilled off under reduced pressure. The residue was dissolved in $CHCl_3$, washed with diluted hydrochloric acid, water, 10% Na_2CO_3, and water successively, and then dried (Na_2SO_4). On evaporation of $CHCl_3$ followed by recrystallizations from benzene, the ester (17) was obtained as prisms (7.0 g, 73%), m.p. 176—177 °C, δ 2.46 (3 H, s), 3.70 (2 H, s), 3.82, 3.85, 3.95 (3 H, s, each), 6.3—6.4 (2 H, m), 6.97 (1 H, d, *J* 9 Hz), 8.10 (1 H, d, *J* 2 Hz), and 8.13 (1 H, q, *J* 2 and 9 Hz) (Found: C, 65.3; H, 5.2; N, 3.5. $C_{20}H_{19}NO_6$ requires: C, 65.03; H, 5.19; N, 3.79%).

2-(3-*Cyanomethyl*-4-*methoxybenzoylacetyl*)-3,5-*dimethoxyphenol* (18).—A mixture of the ester (17) (5.9 g), powdered KOH (3.8 g), and anhydrous pyridine (20 ml) was kept at 80 °C for 5 min with occasional stirring. After addition of ice–water the reaction mixture was acidified with dilute hydrochloric acid and extracted with $CHCl_3$. The com-

bined $CHCl_3$ layer was washed with water, dried ($MgSO_4$) and evaporated to give the phenol (18) as yellow needles (5.7 g) from acetic acid, m.p. 182.5—183 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 292 nm (4.33); $\nu_{max.}^{(KBr)}$ 1 596, 1 566, 1 496, 1 480, 1 397, 1 290 1 250, 1 215, 1 156, 1 110, 1 083, 1 034, 867, 818, and 756 cm^{-1}; δ 3.73 (2 H, s), 3.82, 3.92, 3.94 (3 H, s, each), 5.98 (1 H d, *J* 2.5 Hz), 6.10 (1 H, d, *J* 2.5 Hz), 6.97 (1 H, d, *J* 9 Hz), 7.38 (1 H, s), and 7.90—8.00 (2 H, m) (Found: C, 64.75; H, 5.1; N, 3.5. $C_{20}H_{19}NO_6$ requires C, 65.03; H, 5.19; N, 3.79%).

3′-*Cyanomethyl*-4′,5,7-*trimethoxyflavone* (19).—A mixture (10 g) of conc. H_2SO_4 and AcOH (1 : 4, w/w) was added to the phenol (18) (4.2 g) dissolved in hot AcOH (40 ml). The solution was kept at 80 °C for 20 min and then poured into ice–water (200 ml) to yield a yellow precipitate, which was collected, washed with water and then EtOH, and dried (1.4 g). The flavone (19) was obtained as crystals from dimethylformamide, m.p. 267—268 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 268 (4.36) and 324 nm (4.39); $\nu_{max.}^{(KBr)}$ 1 632, 1 600, 1 568, 1 503, 1 480, 1 455, 1 418, 1 340, 1 290, 1 254, 1 200, 1 156, 1 125, 1 100, 825, and 816 cm^{-1}; δ 3.72 (2 H, s), 3.89 (3 H, s), 3.92 (6 H, s), 6.59 (1 H, s), 6.35, 6.55 (1 H, d, *J* 2 Hz, each), 6.98 (1 H, d, *J* 9 Hz), 7.86 (1 H, d, *J* 2 Hz), and 7.82 (1 H, q, *J* 2 and 9 Hz) (Found: C, 68.0; H, 4.85; N, 3.75. $C_{20}H_{17}NO_5$ requires C, 68.37; H, 4.88; N, 3.99%).

4′,5,7-*Trimethoxyflavone*-3′-*ylacetic Acid* (20).—The flavone (19) (1.32 g) was added to a mixture (11 g) of conc. H_2SO_4, AcOH, and water (2 : 2 : 1) and kept for 1.5 h in an oil-bath at 105 °C. After being cooled the mixture was poured into water (80 ml) to yield a precipitate, which was collected, washed with water, and dried (1.1 g). Recrystallization from MeOH–dimethylformamide gave needles, m.p. 285—287 °C (Found: C, 64.25; H, 4.95. $C_{20}H_{18}O_7$ requires C, 64.86; H, 4.90%).

3″,5″-*Dimethoxyphenyl* 4′,5,7-*Trimethoxyflavone*-3′-*ylacetate* (21a).— A mixture of the acid (20) (2.5 g), 3,5-dimethoxyphenol (1.06 g), triphenylphosphine (2.03 g), CCl_4 (1.6 g), Et_3N (1.04 g), and ethanol-free $CHCl_3$ (15 ml) were refluxed for 1 h on a water-bath. After filtration of the reaction mixture the brownish filtrate was evaporated to a syrup, which afforded the ester (21a) through column chromatography on silica gel with $CHCl_3$ as eluant. The ester (21a) was crystallized from MeOH to yield prisms (1.4 g, 41%), m.p. 178—180 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 268 (4.36) and 328 nm (4.41); $\nu_{max.}^{(KBr)}$ 1 765, 1 636, 1 600, 1 497, 1 470, 1 450, 1 420, 1 346, 1 252, 1 200, 1 140, 1 120, 1 100, 1 050, 840, 815, and 795 cm^{-1}; δ 3.72 (6 H, s), 3.88 (5 H, s), 3.92 (6 H, s), 6.58 (1 H, s), 6.24 (2 H, d, 2″- and 6″-H), 6.25 (1 H, d, 4″-H), 6.34 (1 H, d, 6-H), 6.54 (1 H, d, 8-H), 7.80 (1 H, d, 2′-H), 6.98 (1 H, d, 5′-H), and 7.81 (1 H, q, 6′-H) (Found: C, 66.2; H, 5.15. $C_{28}H_{26}O_9$ requires C, 66.39; H, 5.17%).

3′-(2″-*Hydroxy*-4″,6″-*dimethoxybenzoylmethyl*)-4′,5,7-*trimethoxyflavone* (22a).—The ester (21a) (1.1 g) was dissolved in dry nitromethane (20 ml), to which anhydrous $AlCl_3$ (1.2 g) was added and the mixture was kept for 48 h in an ice-box; cracked ice (3 g) and diluted HCl (2 ml) were then added to it. The mixture was steam-distilled to remove nitromethane and the residue was filtered off. The water-insoluble part was dissolved in $CHCl_3$ and washed with 5% aqueous K_2CO_3 to remove the acid (20), and then with water. The $CHCl_3$ solution was dried ($MgSO_4$) and purified chromatographically using a silica-gel column and $CHCl_3$. The product was obtained as needles (0.52 g, 47%) from MeOH, m.p. 203—203.5 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 268 (4.42), 292 (4.52), and 328 nm (4.50); $\nu_{max.}^{(KBr)}$ 1 636, 1 602, 1 575, 1 455, 1 418, 1 345, 1 250, 1 210, 1 155, 1 050, 1 030, and 812 cm^{-1}; δ 3.80, 3.82, 3.91 (3 H, s, each), 3.87 (6 H, s), 4.35 (2 H, s), 6.58 (1 H, s), 5.95, 6.07 (1 H, d, each, 3″- and 5″-H), 6.33 (1 H, d, 6-H), 6.53 (1 H, d, 8-H), 7.65 (1 H, d, 2′-H), 6.98 (1 H, d, 5′-H), and 7.80 (1 H, q, 6′-H) (Found: C, 65.9; H, 5.15. $C_{28}H_{26}O_9$ requires C, 66.39; H, 5.17%).

Hexa-O-*methyltaiwaniaflavone* (5).—A solution of the flavone (22a) (1 83 g) in anhydrous pyridine (12 ml) was added dropwise to 4-methoxybenzoyl chloride (0.7 g) and the mixture was kept at 60 °C for 1 h. Pyridine was distilled off under reduced pressure and the residue was dissolved in $CHCl_3$. The solution was washed with dilute HCl, water, 10% Na_2CO_3, and water successively, and then dried (Na_2SO_4) and evaporated. The residue was chromatographically purified using silica gel and $CHCl_3$ to give an ester (0.27 g), which was mixed with anhydrous pyridine (5 ml) and powdered KOH (0.2 g), and kept at 90 °C for 6 min and then at 100 °C for 2 min in an oil-bath. After cooling of the mixture ice was added to it, and the whole extracted with $CHCl_3$. The $CHCl_3$ layer was washed with dilute HCl and water, dried (Na_2SO_4), and evaporated. The residue was dissolved in hot AcOH (5 ml) and a mixture (2 g) of conc. H_2SO_4 and AcOH (1 : 4 w/w) was added to the AcOH solution. The mixture was kept at 85 °C for 20 min and poured into ice–water to give a precipitate, which was collected, washed with water, and purified chromatographically using silica gel and $CHCl_3$. Prisms (14 mg) from MeOH, m.p. 264—265 °C, were obtained and identified with the hexamethyl ether of natural taiwaniaflavone by mixed m.p. and comparison of spectral data (i.r. and ^1H n.m.r.).

3″,5″-*Diethoxyphenyl* 4′,5,7-*Trimethoxyflavone*-3′-*ylacetate* (21b).— A mixture of the acid (20) (1.53 g), 3,5-diethoxyphenol (0.67 g), triphenylphosphine (1.05 g), CCl_4 (0.93 g), Et_3N (0.6 g), and ethanol-free $CHCl_3$ (8 ml) were refluxed for 1 h. $CHCl_3$ (10 ml) was added to the mixture which was then filtered whilst hot. The filtrate was evaporated and purified chromatographically through a silica column using Et_2O and then $CHCl_3$ as eluants. The ester (21b) was obtained from a $CHCl_3$ fraction as prisms (0.64 g) from MeOH, m.p. 196—198° C, $\lambda_{max.}^{(EtOH)}$ (log ε) 268 (4.41) and 328 nm (4.47); $\nu_{max.}^{(KBr)}$ 1 752, 1 636, 1 600, 1 458, 1 340, 1 295, 1 252, 1 194, 1 126, 1 055, 924, 834, 825, and 798 cm^{-1}, δ 1.35 (6 H, t), 3.85—4.04 (9 H, OMe and 6 H, CH_2), 6.65 (1 H, s, 3), 6.22 (2 H, d, 2″- and 6″-H), 6.28 (1 H, d, 4″-H), 6.36, 6.55 (1 H, each d, 6-H and 8-H), 7.80 (1 H, d, 2′-H), 6.97 (1 H, d, 5′-H), and 7.81 (1 H, q, 6′-H).

3′-(2″-*Hydroxy*-4″,6″-*diethoxybenzoylmethyl*)-4′,5,7-*trimethoxyflavone* (22b).—(21b) (0.70 g) was treated in an identical fashion to that described for the conversion of (21a) into (22a). Needles (0.45 g, 64%) were obtained from MeOH, m.p. 203—206 °C, $\lambda_{max.}^{(EtOH)}$ (log ε) 268 (4.44), 293 (4.54), and 328 nm (4.51); $\nu_{max.}^{(KBr)}$ 1 635, 1 602, 1 575, 1 422, 1 345, 1 250, 1 210, 1 175, 1 155, 1 050, 1 030, 828, and 812 cm^{-1}; δ 1.44, 1.51 (3 H, t, each), 3.85, 3.89, 3.93 (OMe each), 3.93—4.16 (4 H, two q), 4.40 (2 H, s), 6.57 (1 H, s, 3-H), 6.04 (1 H, d, 3″-H), 5.93 (1 H, d, 5″-H), 6.33, 6.53, 7.66, 6.97 (1 H, d, each), and 7.83 (1 H, q, 6′-H).

5″,7″-*Di*-O-*ethyl*-4′,4‴,5,7-*tetra*-O-*methyltaiwaniaflavone* (29).—A solution of the flavone (22b) (0.115 g) in anhydrous pyridine (4 ml) was added dropwise to 4-methoxybenzoyl chloride (0.15 g) and the mixture kept at 80 °C for 1.5 h. It was then treated in the same way as described in the preparation of (5) from (22a) to give prisms (10 mg) from AcOEt, m.p. 288—290 °C *m/e* (%) 650 (M^+, 51), 635 (68), 619 (100), 605 (31), 591 (12), 577 (7), 561 (6), 544 (7), 442 (3),

427 (5), 325 (M^{2+}, 8), 311 (6) and 209 (4), δ 1.45, 1.48 (3 H, t, each), 3.60, 3.73, 3.86, 3.90 (3 H, s, each, OMe), 3.98—4.20 (4 H, two q), 6.60 (1 H, s), 6.34, 6.36, 6.50, 6.54 (1 H, d, each, 6-, 6″-, 8-, and 8″-H), 6.74 (2 H, d, 3‴- and 5‴-H), 6.90 (1 H, d, 5′-H), 7.36 (2 H, d, 2‴- and 6‴-H), 7.77 (1 H, d, 2′-H), and 7.80 (1 H, q, 6′-H) (Found: C, 69.95; H, 5.15. $C_{38}H_{34}O_{10}$ requires C, 70.14; H, 5.27%).

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