SYNTHESIS OF 4',5- AND 3',4',5-OXYGENATED PYRANOISOFLAVONES: ALPINUMISOFLAVONE AND RELATED COMPOUNDS, AND A REVISED STRUCTURE OF DERRONE

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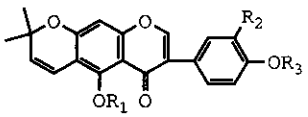
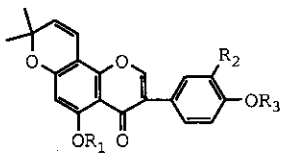
Abstract—Alpinumisoflavone (4',5-dihydroxy-2",2"-dimethylpyrano[5",6"-*g*]isoflavone) (1a) was synthesized by regioselective reduction of 7-(4-hydroxyphenyl)-2,3-dihydro-5-methoxy-2,2-dimethyl-4*H*,6*H*-benzo[1,2-*b*:5,4-*b'*]dipyran-4,6-dione (15a) with $NaBH_4$ and dehydration of the resultant alcohol, followed by demethylation with BCl_3. Its angular isomer (4',5-dihydroxy-2",2"-dimethylpyrano[6",5"-*h*]isoflavone) (2a) was synthesized from 3-(4-hydroxyphenyl)-8,9-dihydro-5-tosyloxy-8,8-dimethyl-4*H*,10*H*-benzo[1,2-*b*:3,4-*b'*]dipyran-4,10-dione (27a) in a similar manner.

In the previous papers, we have reported that 2',4',5- and 2',4',5,5'-oxygenated pyranoisoflavones can be prepared by an oxidative rearrangement of the corresponding pyronochalcones with thallium(III) nitrate (TTN).[1,2] This synthetic method has the following advantages: the easy conversion of pyronochalcones to pyronoisoflavones and the easy dealkylation of *o*-alkylpyranoisoflavones with BCl_3 to the hydroxypyranoisoflavones. As a further application of this simple methodology to the synthesis of 4',5- and 3',4',5-oxygenated pyranoisoflavones, we report here on the synthesis of new 3',5-dihydroxy-4'-methoxy-2",2"-dimethylpyrano[5",6"-*g*]isoflavone (1b),[3] alpinumisoflavone (1a),[3,4] and analogous compounds (1c and 2) and a revised structure of derrone.[5]

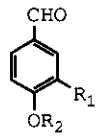
6-Acetyl-5-hydroxy-7-methoxy-2,2-dimethylchromanone (6)[1] was easily synthesized by demethylation of dimethyl ether (5) of 6-acetyl-5,7-dihyroxy-2,2-dimethylchromanone (3)[1] with $AlCl_3$, according to the selective demethylation of oxygenated acetophenones.[6] Condensation of chromanone (4)[3] or 6 with benzaldehydes (7) afforded the corresponding chalcones (8 or 20). The desired linear pyronoisoflavone (10a) was hardly obtained by the oxidative rearrangement of 2'-acetoxypyronochalcone (9a) with TTN and by the subsequent cyclization of the resultant compound with diluted HCl; instead a small amount of the aurone (11a) was obtained. The oxidation of 2'-hydroxypyronochalcone (8a) and 9a with TTN afforded a small amount of the coumaranone (12a) which was a precursor of 11a. These results suggest that cleavage of the 2'-acetoxy group in 9a and the subsequent cyclization to the α-position will



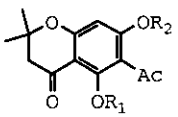
(1a) R_1=R_2=R_3=H
(1b) R_1=H, R_2=OH, R_3=Me
(1c) R_1=R_3=H, R_2=OMe
(17a) R_1=Me, R_2=R_3=H
(17b) R_1=R_3=Me, R_2=OH
(17c) R_1=Me, R_2=OMe, R_3=H
(18a) R_1=R_3=Ac, R_2=H
(18b) R_1=Ac, R_2=OAc, R_3=Me
(18c) R_1=R_3=Ac, R_2=OMe
(19a) R_1=R_3=Me, R_2=H
(19b) R_1=R_3=Me, R_2=OMe



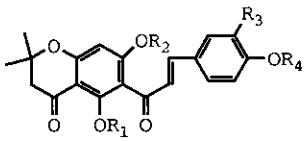
(2a) R_1=R_2=R_3=H
(2b) R_1=H, R_2=OH, R_3=Me
(2c) R_1=R_3=H, R_2=OMe
(24a) R_1=Me, R_2=H, R_3=CH_2Ph
(25a) R_1=Me, R_2=R_3=H
(29a) R_1=Ts, R_2=H, R_3=CH_2Ph
(29b) R_1=Ts, R_2=OCH_2Ph, R_3=Me
(29c) R_1=Ts, R_2=OMe, R_3=CH_2Ph
(30a) R_1=R_2=H, R_3=CH_2Ph
(30b) R_1=H, R_2=OCH_2Ph, R_3=Me
(30c) R_1=H, R_2=OMe, R_3=CH_2Ph
(31a) R_1=R_3=Ac, R_2=H
(31b) R_1=Ac, R_2=OAc, R_3=Me
(31c) R_1=R_3=Ac, R_2=OMe
(32a) R_1=R_3=Me, R_2=H
(32b) R_1=R_3=Me, R_2=OMe



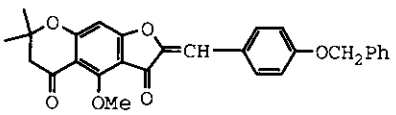
(7a) R_1=H, R_2=CH_2Ph
(7b) R_1=OCH_2Ph, R_2=Me
(7c) R_1=OMe, R_2=CH_2Ph



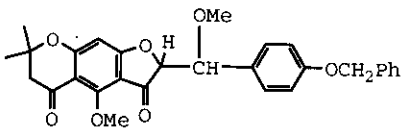
(3) R_1=R_2=H
(4) R_1=Me, R_2=H
(5) R_1=R_2=Me
(6) R_1=H, R_2=Me



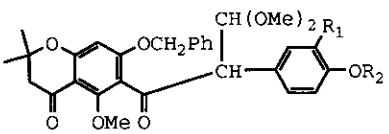
(8a) R_1=Me, R_2=R_3=H, R_4=CH_2Ph
(8b) R_1=Me, R_2=H, R_3=OCH_2Ph, R_4=Me
(8c) R_1=Me, R_2=H, R_3=OMe, R_4=CH_2Ph
(9a) R_1=Me, R_2=Ac, R_3=H, R_4=CH_2Ph
(13a) R_1=Me, R_2=R_4=CH_2Ph, R_3=H
(13b) R_1=R_4=Me, R_2=CH_2Ph, R_3=OCH_2Ph
(13c) R_1=Me, R_2=R_4=CH_2Ph, R_3=OMe
(20a) R_1=R_3=H, R_2=Me, R_4=CH_2Ph
(20b) R_1=H, R_2=R_4=Me, R_3=OCH_2Ph
(20c) R_1=H, R_2=Me, R_3=OMe, R_4=CH_2Ph
(21a) R_1=Ac, R_2=Me, R_3=H, R_4=CH_2Ph
(21b) R_1=Ac, R_2=R_4=Me, R_3=OCH_2Ph
(21c) R_1=Ac, R_2=Me, R_3=OMe, R_4=CH_2Ph



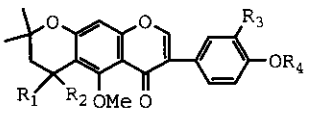
(11a)



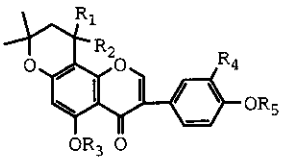
(12a)



(14a) R_1=H, R_2=CH_2Ph
(14b) R_1=OCH_2Ph, R_2=Me
(14c) R_1=OMe, R_2=CH_2Ph



(10a) R_1, R_2=O, R_3=H, R_4=CH_2Ph
(15a) R_1, R_2=O, R_3=R_4=H
(15b) R_1, R_2=O, R_3=OH, R_4=Me
(15c) R_1, R_2=O, R_3=OMe, R_4=H
(16a) R_1=R_3=R_4=H, R_2=OH
(16b) R_1=H, R_2=R_3=OH, R_4=Me
(16c) R_1=R_4=H, R_2=OH, R_3=OMe



(22a) R_1, R_2=O, R_3=Me, R_4=H, R_5=CH_2Ph
(22b) R_1, R_2=O, R_3=R_5=Me, R_4=OCH_2Ph
(22c) R_1, R_2=O, R_3=Me, R_4=OMe, R_5=CH_2Ph
(23a) R_1=R_4=H, R_2=OH, R_3=Me, R_5=CH_2Ph
(26a) R_1, R_2=O, R_3=R_4=H, R_5=CH_2Ph
(26b) R_1, R_2=O, R_3=H, R_4=OCH_2Ph, R_5=Me
(26c) R_1, R_2=O, R_3=H, R_4=OMe, R_5=CH_2Ph
(27a) R_1, R_2=O, R_3=Ts, R_4=H, R_5=CH_2Ph
(27b) R_1, R_2=O, R_3=Ts, R_4=OCH_2Ph, R_5=Me
(27c) R_1, R_2=O, R_3=Ts, R_4=OMe, R_5=CH_2Ph
(28a) R_1=R_4=H, R_2=OH, R_3=Ts, R_5=CH_2Ph
(28b) R_1=H, R_2=OH, R_3=Ts, R_4=OCH_2Ph, R_5=Me
(28c) R_1=H, R_2=OH, R_3=Ts, R_4=OMe, R_5=CH_2Ph

proceed more rapidly than the oxidative rearrangement of ring B to lead to 11a. The oxidation of 2'-benzyloxypyronochalcones (13) with TTN afforded easily the acetals (14), since cleavage of the 2'-benzyloxy group in 13 is difficult under the oxidation conditions.[7] Hydrogenolysis of 14 with palladium on charcoal, followed by cyclization of the resultant compounds with diluted HCl afforded the desired linear pyronoisoflavones (15). On the other hand, angular pyronoisoflavones (22) were easily synthesized by the oxidative rearrangement of 2'-acetoxypyronochalcones (21) with TTN. The regioselective reduction of the linear pyronoisoflavones (15) with $NaBH_4$, followed by dehydration of the resultant alcohols (16) gave the linear pyranoisoflavones (17) in good yields. Dealkylation of 17 with BCl_3 afforded the linear hydroxypyranoisoflavones (1) exclusively. However, dealkylation of the angular pyranoisoflavone (24a), which had been obtained from 22a, with BCl_3 did not afford the desired 4',5-dihydroxypyranoisoflavone (2a) and afforded 4'-hydroxy-5-methoxypyranoisoflavone (25a). Demethylation of 25a with $AlBr_3$ gave by-products, and 2a was not isolated. From this result, it is considered that the cleavage of the C_5-methoxy group in 24a is more difficult than that in the linear pyranoisoflavone (17a) because there is no substituent at the C_6-position adjacent to the C_5-methoxy group.[6] The angular pyronoisoflavones (22) stable to Lewis acids[1] were easily demethylated with $AlBr_3$ to give 5-hydroxypyronoisoflavones (26). The regioselective reduction of tosylates (27) of 26, followed by the dehydration of the resultant alcohols (28) gave the angular pyranoisoflavones (29). After hydrolysis of 29, debenzylation of the resultant compounds (30) with BCl_3 afforded the desired angular hydroxypyranoisoflavones (2) in good yields. Linear and angular pyranoisoflavones (1 and 2) were converted into the acetates (18 and 31) and dimethyl ethers (19 and 32), respectively. Properties of pyranoisoflavones obtained here were given in Tables I and II.

We have previously reported that ^1H nmr spectral data for 5-acetoxypyranoisoflavones and uv spectral data for 5-hydroxypyranoisoflavones can be used to distinguish clearly between linear and angular isomers.[8] For example, in the ^1H nmr spectra, acetylation of the 5-hydroxyl group in the linear pyranoisoflavones (1) causes marked downfield shifts ($\Delta\delta$ =0.36 $\sim$ 0.40) of the C_8-H signal and shifts ($\Delta\delta$ = 0.21$\sim$ 0.26) to higher field of the C_4"-H signal (18) (Table I). On the contrary, acetylation of the angular pyranoisoflavones (2) causes only slight downfield shifts ($\Delta\delta$ =0.20 $\sim$ 0.25) of the C_6-H signal and no shift to higher field of the C_4"-H signal (31). But a downfield shift of the C_4"-H signal (31) is caused only a little ($\Delta\delta$ =0.08 $\sim$ 0.13) by acetylation of 2 (Table I). The uv spectra of the angular pyranosoflavones (2), on addition of aluminum chloride, show a band II (240 $\sim$ 285 nm)[9] bathochromic shift of 8$\sim$ 16 nm and a new absorption maximum at a much longer wavelength (408 $\sim$ 415 nm), as shown in Table II. In the uv spectra of the linear isomers (1), on the contrary, no such characteristic bathochromic shift is observed. The uv spectra of the linear pyranoisoflavones (1) show an intense absorption maximum at a longer wavelength (283 $\sim$ 286 nm) than that (269$\sim$ 270 nm) of the angular

TABLE I. ^{1}H-Nmr(CDCl3) Spectral Data for Linear and Angular Synthetic (1, 18 and 2, 31) and Natural Pyranoisoflavones[a)]

Compd	Me x 2	C3"-H	C4"-H	C6-H	C8-H	C2-H	C2',6'-H	C3',5'-H	OH	OAc	OMe
1a	1.47s	5.62d	6.73d		6.34s	7.82s	7.38d'	6.87d'	5.09s(1H) 13.11s(1H)		
1b	1.43s	5.50d	6.62d		6.21s	7.68s	6.70 ~7.10m(3H)		5.60s(1H) 13.00s(1H)		3.83s(3H)
1c	1.44s	5.52d	6.62d		6.22s	7.69s	7.00 and 6.85s(3H)		5.61s(1H) 12.99s(1H)		3.85s(3H)
18a	1.49s	5.77d	6.49d		6.72s	7.78s	7.48d'	7.13d'		2.31s(3H) 2.45s(3H)	
18b	1.45s	5.65d	6.36d		6.57s	7.61s	6.84 ~7.40m(3H)			2.26s(3H) 2.40s(3H)	3.77s(3H)
18c	1.46s	5.67d	6.41d		6.62s	7.69s	7.03d'	6.92d'		2.28s(3H) 2.40s(3H)	3.69s(3H)
Natu. 1a	1.40s	5.53d	6.60d		6.23s	7.74s	7.25d'	6.80d'	13.20s(1H)		
1b	1.42s	5.53d	6.63d		6.22s	7.70s	7.03 ~6.85m(3H)		5.75s(1H) 13.00s(1H)		3.80s(3H)
18b	1.43s	5.70d	6.43d		6.63s	7.70s	7.13d" 7.27dd	6.91d'		2.27s(3H) 2.40s(3H)	3.77s(3H)
2a	1.48s	5.59d	6.68d	6.30s		7.89s	7.39d'	6.88d'	5.04s(1H) 12.90s(1H)		
2b	1.41s	5.61d	6.50d	6.15s		7.70s	6.80 ~6.95m(3H)		5.35s(1H) 12.76s(1H)		3.79s(3H)
2c	1.45s	5.48d	6.59d	6.18s		7.77s	6.84 ~7.02m(3H)		5.65s(1H) 12.77s(1H)		3.86s(3H)
31a	1.50s	5.70d	6.76d	6.50s		7.85s	7.48d'	7.14d'		2.31s(3H) 2.40s(3H)	
31b	1.49s	5.58d	6.63d	6.40s		7.72s	6.96 ~7.15m(3H)			2.26s(3H) 2.35s(3H)	3.78s(3H)
31c	1.48s	5.60d	6.67d	6.40s		7.74s	6.90 ~7.04m(3H)			2.29s(3H) 2.37s(3H)	3.80s(3H)
Natu. Derr-one	1.42s	5.56d	6.68d	6.27s		7.73s	7.29d'	6.77d'	13.80s(1H)		
Acet.	1.48s	5.8d	6.53d	6.73s		7.81s	7.51d'	7.18d'		2.30s(3H) 2.44s(3H)	

a) s, singlet; d, doublet (J=10 Hz); d', doublet (J=9 Hz); d", doublet (J=2 Hz); dd, double doublet (J=2 and 10 Hz); m, multiplet.

TABLE II. Uv Spectral Data for Linear and Angular Synthetic (1 and 2) and Natural Pyranoisoflavones[a)]

Linear form			Angular form		
Compd	λ_{max}nm(log ε)		Compd	λ_{max}nm(log ε)	
1a	(EtOH)	283(4.69)	2a	(EtOH)	270(4.66), 306(3.87), 355(3.46)
	($AlCl_3$)	283(4.69)		($AlCl_3$)	278(4.63), 327i(3.75), 408(3.39)
1b	(EtOH)	285(4.64)	2b	(EtOH)	269(4.66), 307sh(3.93), 358(3.51)
	($AlCl_3$)	285(4.64)		($AlCl_3$)	285(4.67), 323i(3.76), 415(3.45)
1c	(EtOH)	286(4.63)	2c	(EtOH)	270(4.66), 308sh(3.94), 358(3.49)
	($AlCl_3$)	287(4.61)		($AlCl_3$)	285(4.67), 323i(3.76), 413(3.45)
Natural Alpinum. 1a	(MeOH)	284(4.77)	Natural Derrone	(MeOH)	280, 359sh
	($AlCl_3$)	299(after 30min)		($AlCl_3$)	289, 365
3'-OH 5-OH 1b	(MeOH)	285(4.62)			
	($AlCl_3$	303(after 20min)			

a) sh, shoulder; i, inflection point.

isomers (2). On the basis of the syntheses and the ^{1}H nmr and uv spectral data described above, the physical properties of naturally occurring alpinumisoflavone and 3',5-dihydroxy-4'-methoxy-2",2"-dimethylpyrano[5",6"-*g*]isoflavone were fully consistent with those of the synthetic linear pyranoisoflavones (1a and 1b), respectively. The melting point of the synthetic pyranoisoflavone (1b) also was not depressed by admixture with natural product (1b). The physical properties of naturally occurring derrone, which had been proposed as the angular pyranoisoflavone (2a), and the acetate[5] were not consistent with those of the synthetic angular pyranoisoflavones (2a) and (31a) but consistent fully with those of the linear isomer (1a) and the acetate (18a). That is, in the ^{1}H nmr spectra of derrone and its acetate, the spectrum of the acetate shows a higher field shift ($\Delta\delta$ =0.15) of the C_4"-H signal and a marked downfield shift ($\Delta\delta$ =0.46) of the C_6-H signal (Table I). The uv spectrum of derrone shows an intense absorption maximum at 280 nm, and on addition of $AlCl_3$, the uv spectrum does not show a new absorption maximum at a much longer wavelength (more than 408 nm) (Table II). These facts were fairly consistent with the ^{1}H nmr chemical shifts and the uv spectra of the linear pyranoisoflavones (1a and 18a). The melting points of derrone and the acetate also are consistent with those of linear pyranoisoflavones (1a and 18a). Therefore, the structure of derrone must be revised as 4',5-dihydroxy-2",2"-dimethylpyrano[5",6"-*g*]isoflavone (alpinumisoflavone) (1a).

EXPERIMENTAL

All the melting points are uncorrected. The uv spectra were taken in ethanol on a Hitachi 124 spectrophotometer. The ^{1}H nmr spectra were measured with a Hitachi R-24B spectrometer (60 MHz), using tetramethylsilane as an internal standard (δ, ppm). Column chromatography and thin layer chromatography were carried out on Kieselgel 60 (70~230 mesh) and with Kieselgel 60 F-254 (Merck).

6-Acetyl-5-hydroxy-7-methoxy-2,2-dimethylchromanone (6): Chromanone (5) (45.66 g, 0.16 mol) was dissolved in a solution of 10%(w/v) anhydrous $AlCl_3$ in MeCN (650 ml) and the solution was stirred at 55℃ for 1 h, and then 10% HCl (100 ml) was added to the reaction mixture and stirred at 40℃ for 10 min. The reaction mixture was poured into water to give precipitates, which were recrystallized from MeOH-H_2O to give 6 as colorless needles (32.1 g, 74%), mp 117-119℃.[1]

5- and 7-Oxygenated 2,2-dimethyl-6-[1-oxo-3-(4- or 3,4-substituted phenyl)-2-propenyl]-4-chromanones (8 and 20): A mixture of chromanone (4) or (6) (3.8 mmol), benzaldehydes (7) (4.94 mmol) was refluxed with stirring in the presence of KOH (11.4 mmol) in EtOH (200 ml) for 2~3 h. After the reaction mixture was concentrated to *ca.* 100 ml under reduced pressure, HCl and water were added to the residue to give precipitates, which were recrystallized from $CHCl_3$-MeOH to give *8* or *20* as yellow needles in 61 ~ 91% yields.

8a: mp 173-175℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.46(6H, s, CH_3 x 2), 2.68(2H, s, $COCH_2$), 3.84 (3H, s, OCH_3), 5.06(2H, s, $C_6H_5\underline{CH_2}$), 6.20(1H, s, C_5'-H), 6.98(2H, d, J=9 Hz, $C_{3,5}$-H) 7.58(2H, d, J=9 Hz, $C_{2,6}$-H), 7.37(5H, s, $C_6\underline{H_5}CH_2$), 7.81(2H, s, CH=CH), 13.68(1H, s, OH). Anal. Calcd for $C_{28}H_{26}O_6$: C, 73.35; H, 5.72. Found: C, 73.24; H, 5.71.

8b: mp 151.5-153.5℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.45(6H, s, CH_3 x 2), 2.66(2H, s, $COCH_2$), 3.74(3H, s, OCH_3), 3.88(3H, s, OCH_3), 5.14(2H, s, $C_6H_5\underline{CH_2}$), 6.20(1H, s, C_5'-H), 6.73~7.34(3H, m, $C_{2,5,6}$-H), 7.35(5H, s, $C_6\underline{H_5}CH_2$), 7.69(2H, s, CH=CH), 13.70(1H, s, OH). Anal. Calcd for $C_{29}H_{28}O_7$: C, 71.30; H, 5.78. Found: C, 71.13; H, 5.63.

8c: mp 147-148℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.43(6H, s, CH_3 x 2), 2.65(2H, s, $COCH_2$), 3.70 and 3.89(each 3H, s, OCH_3), 5.12(2H, s, $C_6H_5\underline{CH_2}$), 6.20(1H, s, C_5'-H), 6.70~7.30(3H, m, $C_{2,5,6}$-H), 7.32(5H, s, $C_6\underline{H_5}CH_2$), 7.72(2H, s, CH=CH), 13.58(1H, s, OH). Anal. Calcd for $C_{29}H_{28}O_7$: C, 71.30; H, 5.78. Found: C, 71.26; H, 5.90.

20a: mp 142-143 ℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.48(6H, s, CH_3 x 2), 2.68(2H, s, $COCH_2$), 3.78 (3H, s, OCH_3), 5.03(2H, s, $C_6H_5\underline{CH_2}$), 5.97(1H, s, C_5'-H), 7.43 and 6.88(each 2H, d, J=9 Hz, $C_{2,6}$-H and $C_{3,5}$-H), 6.82 and 7.41(each 1H, d, J=16 Hz, CH=CH), 7.32(5H, s, $C_6\underline{H_5}CH_2$), 12.38(1H, s, OH). Anal. Calcd for $C_{28}H_{26}O_6$: C, 73.35; H, 5.72. Found: C, 73.08; H, 5.56.

20b: mp 164-165 ℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.45(6H, s, CH_3 x 2), 2.67(2H, s, $COCH_2$), 3.73 and 3.83(each 3H, s, OCH_3), 5.07(2H, s, $C_6H_5\underline{CH_2}$), 5.93(1H, s, C_5'-H), 6.61 ~ 7.40(5H, m, $C_{2,5,6}$-H and CH=CH), 7.30(5H, s, $C_6\underline{H_5}CH_2$), 12.31(1H, s, OH). Anal. Calcd for $C_{29}H_{28}O_7$: C, 71.30; H, 5.78. Found: C, 71.16; H, 5.88.

20c: mp 143-144 ℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.46(6H, s, CH_3 x 2), 2.66(2H, s, $COCH_2$), 3.76 and 3.85(each 3H, s, OCH_3), 5.09(2H, s, $C_6H_5\underline{CH_2}$), 5.94(1H, s, C_5'-H), 6.65~7.47(5H,

m, $C_{2',5',6'}$-H and CH=CH), 7.27(5H, s, $C_6\underline{H}_5CH_2$), 12.27(1H, s, OH). Anal. Calcd for $C_{29}H_{28}O_7$: C, 71.30; H, 5.78. Found: C, 71.52; H, 5.93.

The acetates (9a and 21): Compounds (8a and 20) were converted into the acetates (9a and 21) by treatment with acetic anhydride-pyridine at 120 ℃ .

9a: mp 90-91℃ (from AcOEt) as pale yellow prisms; ^{1}H nmr ($CDCl_3$) δ : 2.13(3H, s, $COCH_3$). Anal. Calcd for $C_{30}H_{28}O_7$: C, 71.98; H, 5.64. Found: C, 71.69; H, 5.87.

21a: mp 138-140 ℃ (from AcOEt) as colorless prisms; ^{1}H nmr ($CDCl_3$) δ : 2.19(3H, s, $COCH_3$). Anal. Calcd for $C_{30}H_{28}O_7$: C, 71.98; H, 5.64. Found: C, 71.89; H, 5.47.

21b: mp 146-147 ℃ (from AcOEt) as colorless prisms; ^{1}H nmr ($CDCl_3$) δ : 2.16(3H, s, $COCH_3$). Anal. Calcd for $C_{31}H_{30}O_8$: C, 70.17; H, 5.70. Found: C, 69.90; H, 5.77.

21c: mp 169-170 ℃ (from AcOEt) as colorless prisms; ^{1}H nmr ($CDCl_3$) δ : 2.19(3H, s, $COCH_3$). Anal. Calcd for $C_{31}H_{30}O_8$: C, 70.17; H, 5.70. Found: C, 70.15; H, 5.80.

2-[(4-Benzyloxyphenyl)methylene]-6,7-dihydro-4-methoxy-7,7-dimethyl-5*H*-furo[3,2-*g*]-[1]benzopyran-3(2*H*),5-dione (11a): A mixture of 2'-acetoxychalcone (9a) (1.5 g, 3 mmol) and TTN (1.7 g, 4 mmol) was stirred in MeOH (450 ml) at 35~ 40℃ for 15 h and then 10% HCl (23 ml) was added and the mixture was refluxed for a further 6 h. After removal of the precipitates by filtration, the filtrate was concentrated to *ca.* 300 ml under reduced pressure. The residue was poured into a large amount of water and extracted with $CHCl_3$. The $CHCl_3$ solution was dried and evaporated under reduced pressure. The residue was chromatographed over a silica gel column with $ClCH_2CH_2Cl$-MeOH (10:1) to give 11a (320 mg, 23%) as pale yellow needles, mp 171-173℃ (MeOH). Uv λ_{max} nm (log ε) (*EtOH*): 257.5(4.26), 285(4.39), 331.5(4.19), 394(4.51). ^{1}H nmr ($CDCl_3$) δ : 1.46(6H, s, CH_3 x 2), 2.67(2H, s, $COCH_2$), 4.33(3H, s, OCH_3), 5.07(2H, s, $C_6H_5C\underline{H}_2$), 6.37(1H, s, C_9-H), 6.67(1H, s, C=CH), 6.96 and 7.75(each 2H, d, J=9 Hz, $C_{2',6'}$-H and $C_{3',5'}$-H), 7.33(5H, s, $C_6\underline{H}_5CH_2$). Anal. Calcd for $C_{28}H_{24}O_6$: C, 73.66; H, 5.30. Found: C, 73.53; H, 5.09.

2-[1-(4-Benzyloxyphenyl)-1-methoxymethyl]-6,7-dihydro-4-methoxy-7,7-dimethyl-5*H*-furo[3,2-*g*][1]benzopyran-3(2*H*),5-dione (12a): A mixture of 9a (500 mg, 1 mmol) and TTN (890 mg, 2 mmol) was stirred in MeOH (150 ml) at 40 ℃ for 4.5 h and then a saturated solution (2 ml) of Na_2SO_3 was added. The mixture was stirred for 20 min, acidified with diluted HCl and stirred for a further 1.5 h at room temperature. The whole was extracted with $CHCl_3$ and the $CHCl_3$ solution was washed with water, dried, and evaporated. The residue was chromatographed over a silica gel column with $CHCl_3$-Me_2CO (20:1) to give 12a (74 mg, 17%) as pale prisms, mp 165-167 ℃ (MeOH). The *compound* (12a) was also obtained from 2'-hydroxychalcone (8a) in 18% yield in a similar manner. ^{1}H nmr ($CDCl_3$) δ : 1.45(6H, s, CH_3 x 2), 2.65(2H, s, $COCH_2$), 3.18(3H, s, $CHOC\underline{H}_3$), 4.25(3H, s, C_4-OCH_3), 4.55 and 4.70(each 1H, d, J=2 Hz, $C\underline{H}C\underline{H}OCH_3$), 5.08 (2H, s, $C_6H_5C\underline{H}_2$), 6.26(1H, s, C_9-H), 7.00 and 7.38(each 2H, d, J=9 Hz, $C_{3',5'}$-H and $C_{2',6'}$-H), 7.38(5H, s, $C_6\underline{H}_5CH_2$). Anal. Calcd for $C_{29}H_{28}O_7$: C, 71.30; H, 5.78. Found: C, 71.03; H, 6.00.

2'-Benzyloxychalcones (13): A mixture of 8 (4.1 mmol), benzyl chloride (630 mg, 5.33 mmol) and K_2CO_3 (1.52 g, 12.3 mmol) in DMF (20 ml) was stirred at 120℃ for 5~

TABLE III. ^{1}H-Nmr(CDCl3) Spectral Data for Linear and Angular Pyronoisoflavone Derivatives (15 and 22)[a)]

Compd	Me x 2	CH_2	C6-H	C8-H	C2-H	C2',6'-H	C3',5'-H	CH_2Ph	OMe	OH
15a	1.47s	2.70s		6.61s	7.64s	7.25d	6.75d		3.79s(3H)	
15b	1.48s	2.73s		6.60s	7.64s	6.88 ~6.97m(3H)			3.33s(3H) 4.00s(3H)	5.60s(1H)
15c	1.49s	2.72s		6.60s	7.66s	6.83 ~7.05m(3H)			3.87s(3H) 3.98s(3H)	5.69s(1H)
22a	1.49s	2.73s	6.30s		7.92s	7.48d	6.98d	5.07s(2H) 7.37s(5H)	3.96s(3H)	
22b	1.49s	2.72s	6.26s		7.82s	6.76 ~7.45m(8H)		5.12s(2H)	3.83s(3H) 3.93s(3H)	
22c	1.47s	2.69s	6.21s		7.80s	6.83 ~7.30m(3H)		5.08s(2H) 7.29s(5H)	3.85s(3H) 3.90s(3H)	

a) s, singlet; d, doublet (J=9 Hz); m, multiplet.

TABLE IV. ^{1}H Nmr(CDCl3) Spectral Data for Linear and Angular Pyranoisoflavone Derivatives (17, 19 and 30, 32)[a)]

Compd	Me x 2	C3"-H	C4"-H	C6-H	C8-H	C2-H	C2',6'-H	C3',5'-H	OMe	OH or CH_2Ph
17a	1.44s	5.63d	6.65d		6.50s	7.66s	7.17d'	6.72d'	3.82s(3H)	
17b	1.45s	5.62d	6.60d		6.50s	7.64s	6.70 ~7.10m(3H)		3.84s(6H)	
17c	1.45s	5.63d	6.66d		6.51s	7.63s	7.02s and 6.82s(3H)		3.82s(6H)	5.74s(1H)
19a	1.45s	5.65d	6.66d		6.51s	7.67s	7.38d'	6.87d'	3.77s(3H) 3.84s(3H)	
19b	1.46s	5.64d	6.66d		6.51s	7.68s	6.80 ~7.20m(3H)		3.85s(9H)	
30a	1.43s	5.44d	6.54d	6.14s		7.78s	7.30d'	6.85d'		12.78s(1H) 4.98s(2H) 7.23s(5H)
30b	1.44s	5.50d	6.60d	6.19s		7.70s	6.89 ~7.43m(3H)		3.85s(3H)	12.80s(1H) 5.10s(2H) 7.30s(5H)
30c	1.44s	5.48d	6.59d	6.20s		7.77s	6.85 ~7.30m(3H)		3.86s(3H)	12.77s(1H) 5.09s(2H) 7.30s(5H)
32a	1.47s	5.51d	6.67d	6.28s		7.71s	7.42d'	6.86d'	3.78s(3H) 3.88s(3H)	
32b	1.44s	5.49d	6.63d	6.23s		7.70s	6.83 ~7.13m(3H)		3.84s(9H)	

a) s, singlet; d, doublet (J=10 Hz); d', doublet (J=9 Hz); m, multiplet.

7 min and then poured into cold water. The obtained precipitates were recrystallized from $CHCl_3$-MeOH to give 13 (80 ~ 85%) as colorless needles.

13a: mp 180-182 ℃ ; ^1H nmr ($CDCl_3$) δ : 5.00(4H, s, $C_6H_5\underline{C}H_2$ x 2), 7.17 and 7.27(each 5H, s, $C_6\underline{H}_5CH_2$). Anal. Calcd for $C_{35}H_{32}O_6$: C, 76.62; H, 5.88. Found: C, 76.42; H, 5.87.

13b: mp 156-158 ℃ ; ^1H nmr ($CDCl_3$) δ : 5.02 and 5.07(each 2H, s, $C_6H_5\underline{C}H_2$), 7.18(10H, s, $C_6\underline{H}_5CH_2$ x 2). Anal. Calcd for $C_{36}H_{34}O_7$: C, 74.66; H, 5.92. Found: C, 74.53; H, 5.82.

13c: mp 170-172 ℃ ; ^1H nmr ($CDCl_3$) δ : 5.00 and 5.10(each 2H, s, $C_6H_5\underline{C}H_2$), 7.18(10H, s, $C_6\underline{H}_5CH_2$ x 2). Anal. Calcd for $C_{36}H_{34}O_7$: C, 74.66; H, 5.92. Found: C, 74.91; H, 5.94.

7-(4- or 3,4-Substituted phenyl)-2,3-dihydro-5-methoxy-2,2-dimethyl-4*H*,6*H*-benzo[1,2-*b*:5,4-*b'*]dipyran-4,6-diones (15): A mixture of 13 (5.03 mmol) and TTN (5.6 g, 12.6 mmol) was stirred in MeOH (200 ml) at 60℃ for 2~ 7 h and then a saturated solution of $NaHSO_3$ (1.04 g, 10 mmol) was added. The mixture was stirred in an ice-cold bath for 30 min and neutralized with an aqueous solution of $NaHCO_3$. After the removal of the solvent under reduced pressure below 40 ℃ , AcOEt and 2% HCl were added to the residue to give precipitates. The filtrate was extracted with AcOEt and the AcOEt solution was washed with water, dried, and evaporated. The resulting compounds were chromatographed over a silica gel column with AcOEt to give acetals (14). Compounds (14) were hydrogenolyzed over 10% Pd/C (0.7 ~ 0.8 g) in MeOH and then Pd/C was removed by filtration. 10% HCl was added to the filtrate and the mixture was refluxed for 3 ~ 5 h and concentrated to *ca.* 1/2 quantity of the solution under reduced pressure. Water was added to the residue to give precipitates (15). The precipitates were purified by silica gel column chromatography ($CHCl_3$-AcOEt=3:1) to give isoflavones (15) as colorless prisms in 45~ 52% yields (based on the chalcones 13).

15a: mp 231-233 ℃ . Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.84; H, 4.95. Found: C, 68.57; H, 4.89.

15b: mp 243-245 ℃ . Anal. Calcd for $C_{22}H_{20}O_7$: C, 66.66; H, 5.09. Found: C, 66.59; H, 5.13.

15c: mp 245-247 ℃ . Anal. Calcd for $C_{22}H_{20}O_7$: C, 66.66; H, 5.09. Found: C, 66.41; H, 5.04.

3-(4- or 3,4-Substituted phenyl)-8,9-dihydro-5-methoxy-8,8-dimethyl-4*H*,10*H*-benzo[1,2-*b*:3,4-*b'*]dipyran-4,10-diones (22): The oxidative rearrangement of 21 (5.65 mmol) with TTN (7.51 g, 16.9 mmol) in MeOH (600 ml) and the subsequent cyclization with 10%HCl gave 22 in 68~ 80% yields, which were purified by silica gel column chromatography ($CHCl_3$).

22a: mp 199-200 ℃ (as colorless needles). Anal. Calcd for $C_{28}H_{24}O_6$: C, 73.67; H, 5.30. Found: C, 73.51; H, 5.29.

22b: mp 175-176 ℃ (as pale yellow needles). Anal. Calcd for $C_{29}H_{26}O_7$: C, 71.59; H, 5.39. Found: C, 71.37; H, 5.32.

22c: mp 204-205 ℃ (as pale yellow prisms). Anal. Calcd for $C_{29}H_{26}O_7$: C, 71.59;

H, 5.39. Found: C, 71.37; H, 5.49.

5-Methoxy-7-(4- or 3,4-substituted phenyl)-2,2-dimethyl-2*H*,6*H*-benzo[1,2-*b*:5,4-*b'*]-dipyran-6-ones (17): Compounds (15) (1 mmol) in THF (24 ml) was stirred with gradual addition of an aqueous solution (6 ml) of $NaBH_4$ (170 mg, 4.5 mmol) at 0℃ for 30 min (monitored by tlc), and the Me_2CO (5 ml) was added to the reaction mixture. The whole was diluted with water and neutralized with diluted HCl, and then the organic solvent was removed under reduced pressure. The resulting compounds were recrystallized from $CHCl_3$-MeOH to give the monoalcohols (16) as colorless needles in 75～85% yields. Compound (16c) was used for the dehydration without recrystallization.

16a: mp 210-212 ℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.40 and 1.42(each 3H, s, CH_3), 2.09(2H, d, J=6 Hz, CH_2CHOH), 3.97(3H, s, OCH_3), 5.03(1H, br, CH_2CHOH), 6.59(1H, s, C_8-H), 6.72 and 7.21(each 2H, d, J=9 Hz, $C_{3'}$,$_{5'}$-H and $C_{2'}$,$_{6'}$-H), 7.70(1H, s, C_2-H). Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.74; H, 5.76.

16b: mp 178-179 ℃ ; ^{1}H nmr ($CDCl_3$) δ : 1.40 and 1.43(each 3H, s, CH_3), 3.85 and 3.98 (each 3H, s, OCH_3), 2.07(2H, d, J=6 Hz, CH_2CHOH), 5.05(1H, br, CH_2CHOH), 5.66(1H, s, OH), 6.59(1H, s, C_8-H), 6.70～7.10(3H, m, $C_{2'}$,$_{5'}$,$_{6'}$-H), 7.70(1H, s, C_2-H). Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 6.63. Found: C, 66.03; H, 6.74.

The alcohols (16) (0.85 mmol) were stirred in toluene (70 ml) in the presence of TsOH·H_2O (1/10 mol of 16) at 110℃ for 15 ～ 20 min. The resulting compounds were recrystallized from MeOH-H_2O to give 17 in 75 ～ 83% yields.

17a: mp 134-135 ℃ (as colorless needles); Anal. Calcd for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.75; H, 5.21.

17b: mp 156-157 ℃ (as colorless needles); Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.23; H, 5.33.

17c: mp 195-197 ℃ (as colorless prisms). Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.19; H, 5.34.

3',4'-Substituted 5-hydroxy-2",2"-dimethylpyrano[5",6"-*g*]isoflavones(1): A solution of BCl_3-CH_2Cl_2 (11 ml) [BCl_3 (25 g, 0.213 mol) had been dissolved in CH_2Cl_2(48 ml)] was added to 17 (7.9 mmol) in CH_2Cl_2 (60 ml) at -65 ～ -70 ℃ . The reaction mixture was stirred at that temperature for 1 h (monitored by tlc), then water was added, and the whole was stirred at room temperature for 30～ 60 min. After the removal of the solvent under reduced pressure below 40 ℃ , the residue was recrystallized from EtOAc-petroleum ether to give 1 in 67 ～ 73% yields.

Alpinumisoflavone (1a): mp 211-212℃ (as pale yellow prisms). Anal. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80. Found: C, 71.33; H, 4.55.

1b: mp 155-156℃ (as yellow prisms). Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.84; H, 4.95. Found: C, 68.62; H, 4.99.

1c: mp 202-203℃ (as pale yellow prisms). Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.84; H, 4.95. Found: C, 68.64; H, 4.93.

The diacetates (18): Compounds (1) were converted into the diacetates (18).

18a: mp 222-224 ℃ (as colorless needles). Anal. Calcd for $C_{24}H_{20}O_7$: C, 68.56; H, 4.80. Found: C, 68.27; H, 4.77.

18b: mp 208-209 ℃ (as colorless prisms). Anal. Calcd for $C_{25}H_{22}O_8$: C, 66.66; H, 4.92. Found: C, 66.57; H, 5.10.

18c: mp 194-196 ℃ (as colorless prisms). Anal. Calcd for $C_{25}H_{22}O_8$: C, 66.66; H, 4.92. Found: C, 66.59; H, 4.89.

The dimethyl ethers (19a and 19b). Compounds (1) were converted into the dimethyl ethers (19a and 19b) with $(MeO)_2SO_2$ and K_2CO_3 in Me_2CO under reflux.

19a: mp 137-138 ℃ (as colorless needles). Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.29; H, 5.66.

19b: mp 110-111 ℃ (as colorless prisms). Anal. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62. Found: C, 69.80; H, 5.67.

3-(4- or 3,4-Substituted phenyl)-8,9-dihydro-5-hydroxy-8,8-dimethyl-4*H*,10*H*-benzo[1,2-*b*:3,4-*b'*]dipyran-4,10-diones (26): A solution (82 ml) of 5% $AlBr_3$ (w/v) in MeCN was added to a solution of 22 (3.1 mmol) in MeCN (164 ml), and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured into 2% HCl and then stirred at 50℃ for 20 min. After the removal of the solvent under reduced pressure, the residue was recrystallized from EtOAc-$CHCl_3$ to give 26 in 90~ 95% yields.

26a: mp 205-206 ℃ (as pale yellow needles). Anal. Calcd for $C_{27}H_{22}O_6$: C, 73.29; H, 5.10. Found: C, 73.42; H, 5.14.

26b: mp 167-168 ℃ (as colorless needles). Anal. Calcd for $C_{28}H_{24}O_7$: C, 71.17; H, 5.12. Found: C, 70.98; H, 5.12.

26c: mp 223-224 ℃ (as colorless needles). Anal. Calcd for $C_{28}H_{24}O_7$: C, 71.17; H, 5.12. Found: C, 71.01; H, 5.16.

3',4'-Substituted 5-hydroxy-2",2"-dimethylpyrano[6",5"-*h*]isoflavones (2): A mixture of 26 (2.54 mmol), TsCl (580 mg, 3.04 mmol), and K_2CO_3 (6.91 g, 50 mmol) in Me_2CO was refluxed with stirring for 2 h. After the removal of K_2CO_3 and the solvent, the residue was dissolved in EtOAc and the EtOAc solution was washed with diluted HCl and water, and dried (Na_2SO_4). The crude colorless needles (27) were obtained in 90 ~ 93% yields. A mixture of the crude 27 (0.84 mmol) and $NaBH_4$ (120 mg, 3.1 mmol) in H_2O(30 ml)-THF(300 ml) was stirred at 0 ℃ for 30 min. The reaction mixture was worked up by a method similar to that used for preparation of 16 to give 28. Dehydration of the crude 28 with TsOH·H_2O in dry toluene at 70℃ for 45 min afforded 29 as colorless needles in 95~ 98% yields. Hydrolysis of 29 with 5% NaOH in MeOH gave 30 as pale yellow prisms in 90~ 95% yields. Debenzylation of 30 with BCl_3 in CH_2Cl_2 at -70℃ for 15 min afforded the desired compounds (2) as pale yellow prisms (from ether). Total yields of 2 based on 26 were 48~55%.

30a: mp 162-164 ℃ (as yellow prisms). Anal. Calcd for $C_{27}H_{22}O_5$: C, 76.04; H, 5.20. Found: C, 76.26; H, 5.29.

30b: no crystallization (yellow).

30c: mp 175-177 ℃ (as pale yellow prisms). Anal. Calcd for $C_{28}H_{24}O_6$: C, 73.67; H, 5.30. Found: C, 73.41; H, 5.38.

2a: mp 194-195℃ (as yellow prisms). Anal. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80.

Found: C, 71.30; H, 4.56.

2b: mp 170-171℃ (as yellow prisms). Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.84; H, 4.95. Found: C, 68.66; H, 4.94.

2c: mp 154-156℃ (as yellow prisms). Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.84; H, 4.95. Found: C, 68.75; H, 4.90.

The diacetates (31): 31a: mp 214-215 ℃ (as colorless needles). Anal. Calcd for $C_{24}H_{20}O_7$: C, 68.56; H, 4.80. Found: C, 68.40; H, 4.59.

31b: mp 222-223 ℃ (as colorless needles). Anal. Calcd for $C_{25}H_{22}O_8$: C, 66.66; H, 4.92. Found: C, 66.56; H, 4.92.

31c: mp 222-224 ℃ (as colorless needles). Anal. Calcd for $C_{25}H_{22}O_8$: C, 66.66; H, 4.92. Found: C, 66.61; H, 4.94.

The dimethyl ethers (32): 32a: mp 180-182℃ (as colorless prisms). Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.37; H, 5.35.

32b: mp 171-173 ℃ (as pale yellow prisms). Anal. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62. Found: C, 70.08; H, 5.67.

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