STRUCTURE OF 6- OR 8-ISOPRENOID SUBSTITUTED FLAVANONE: CHEMICAL SHIFT OF THE HYDROGEN-BONDED HYDROXYL GROUP[1]

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Abstract —— The proton signal of the hydrogen-bonded hydroxyl group of the 6-isoprenoid substituted flavanone was shifted more downfield than that of 6-nonsubstituted flavanone. By comparison of the chemical shifts of the hydrogen-bonded hydroxyl groups of 8-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone (**3**) and its 6-isomer (**4**) isolated from Wyethia helenioides, the proposed structures **3** and **4** were reversed each other. Comparison of the chemical shift of the hydroxyl group is a facile method to discriminate the 6-isoprenoid substituted flavanone and the 6-nonsubstituted one.

In the previous paper,[2] we reported that the proton signal of the hydrogen-bonded hydroxl group at the C-5 position of the 6-isoprenoid substituted isoflavone was observed in the range of δ13.0-13.35 in acetone-d_6, while the relevant proton signal of the 8-substituted isomer in the range of δ12.7-13.0. On the basis of the above observation and other spectral evidence, we proposed the structures of the 6- or 8-prenylated isoflavones.[2] In this paper, we report the observation on the chemical shift of the hydrogen-bonded hydroxyl group at the C-5 position of the 6- and/or 8-isoprenoid substituted flavanones, and also describe the revision of the structures of 8-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone and its 6-isomer isolated from Wyethia helenioides (tribe Heliantheae, subtribe Helianthinae).[3]

We examined the ^{1}H nmr spectra of 48 kinds of the known 6- and/or 8-isoprenoid substituted flavanones. Except for the seven kinds of flavanones, the proton signal of the hydrogen-bonded hydroxyl group of the 6- and/or 8-isoprenoid substituted flavanone could be classified into the following two types according to the location

of the isoprenoid moiety: 1) The 6-isoprenoid substituted flavanones and the 6,8-disubstituted ones showed the proton signal of the hydroxyl group in the range of δ12.4-12.5 in acetone-d_6, while the relevant signal was observed in the range of δ12.2-12.5 in $CDCl_3$. 2) The 8-isoprenoid substituted 6-nonsubstituted flavanones showed the relevant proton signal in the range of δ12.0-12.2 in acetone-d_6, and of δ12.0-12.1 in $CDCl_3$ (Table 1).

On the other hand, Bohlmann et al.[3] reported that 8-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone and its 6-isomer isolated from W. helenioides, showed the proton signals of the hydrogen-bonded hydroxyl groups at δ12.47 and 12.13 in acetone-d_6, respectively, and the results described in the report are inconsistent with our observations. To elucidate the inconsistency we synthesized 6-prenylated 5,7,3',4'-tetrahydroxyflavanone (**1**) and its 8-isomer (**2**) by using the unambiguous method (Scheme 1).[4] The locations of the prenyl groups in the structures (**1**) and (**2**) were further confirmed by long-range selective proton decoupling (LSPD) experiment (Table 2). Identifications of the synthetic flavanones (**1** and **2**) with the natural compounds were carried out on the following facts. The ^1H nmr spectra of **1** and **2** were in good agreement with the relevant spectra of Bohlmann's 8-prenylated flavanone (**3**) and 6-prenylated flavanone (**4**), respectively.[5] Furthermore, heating of **1** in benzene with p-toluenesulfonic acid afforded **6** and a minor product (**9**). Heating of **2** under the same conditions afforded **9** and a minor product (**6**). The locations of the dimethyldihydropyrane moieties in the products (**6** and **9**) were confirmed by LSPD experiment (Table 2). The compounds (**6**) and (**9**) were identified as compounds (**10**) and (**12**) by comparison of the ^1H nmr spectra of **6** and **9** with the reported spectra of compounds (**10**) and (**12**) (Table 3), respectively, which were derived from **3** and **4** by treatment with the same acidic conditions (Scheme 2).[3] The above results obtained by the acidic treatment of **1** and **2** suggested that an isomerization must have taken place, and that the only conceivable possibility is a Wessely-Moser rearrangement[6] in the acidic solution. From the above results the proposed structures (**3**) and (**4**) for the two natural compounds isolated from W. helenioides should be reversed each other. While several papers were reported on the isolation of 6-prenylated 5,7,3',4'-tetrahydroxyflavanone and its 8-isomer,[7-12] no detailed physico-chemical data of the compounds were described except the following an example:[12] The 8-isomer isolated from Encelia stenophylla Greene was identical with **2** by comparison of the ^1H nmr spectrum of **2** with the reported data.[12]

From the above results it is obvious that the hydrogen-bonded hydroxyl group of

Table 1. Chemical shifts of C-5-OH of isoprenoid substituted flavanones

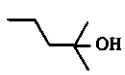
trivial name	chemical shift of 5-OH	isoprenoid group(s) on A-ring	OH-positin	others	sol.[+]	ref.
cudraflavanone A	12.49(270 MHz,23 °C)[*] 12.41(90 MHz,35 °C)	6-prenyl[§]	5,7,2'	4',5'-Dmp	A	4
kushenol B	12.47(n.r.)	6-prenyl	5,7,2',4'	8-lavandulyl	A	18
kushenol E	12.48(90 MHz)	6,8-diprenyl	5,7,2',4'		A	19
norkurarinone (kushenol F)	12.50(90 MHz)	6-lavandulyl	5,7,2',4'		A	19,20
isokurarinone	12.52(60 MHz)	6-lavandulyl	5,7,4'	2'-OMe	A	21,22
antiarone H	12.47(400 MHz,23 °C)	6-prenyl	5,7,3'	4'-OMe 2'-prenyl	A	23
(euchrestaflavanone B)	12.35(60 MHz)	6-prenyl	5,7,2',4'	5'-prenyl	A	26
1	12.47(400 MHz,23 °C) 12.45(400 MHz,35 °C) 12.42(400 MHz,50 °C) 12.33(90 MHz,35 °C)	6-prenyl	5,7,3',4'		A	
5	12.48(400 MHz,23 °C)	6-(3"-OH)-isoamyl	5,7,3',4'		A	
flemiflavanone A	12.30(100 MHz)	6,8-diprenyl	5,7,2'	4'-OMe	C	24
amorinin	12.31(90 MHz)	6,8-diprenyl	5,7,3'	4',5'-Dmp	C	27
methyllinderatone	12.34(n.r.)	6-*p*-M	5	7-OMe	C	15,28
isolinderatone	12.34(n.r.)	6-*p*-M	5,7		C	15,28
no name	12.40(n.r.)	6-geranyl	5,7		C	29
bonannione A	12.40(80 MHz)	6-geranyl	5,7,4'		C	14
lonchocarpol A	12.28(360 MHz) 12.32(270 MHz)	6,8-diprenyl	5,7,4'		C C	30 39
lonchocarpol B	12.29(360 MHz)	6-prenyl	5,7,4'	8-(2",3"-di-OH)-isoamyl	C	30
lonchocarpol C	12.10(360 MHz)	6-prenyl	5,4'	7,8-Dif	C	30
hiravanone	12.34(270 MHz)	6,8-diprenyl	5,7,4'	3'-OMe	C	31
no name	12.33(270 MHz)	6,8-diprenyl	5,7,3'	4'-OMe	C	31
euchrenone a_4	12.32(n.r.)	6,8-diprenyl	5,7	3',4'-Dmp	C	32
neolinderatone	12.48(n.r.)	6,8-di-*p*-M	5,7		C	33
6-C-prenyl-8-C-methylpinocembrin	12.29(300 MHz)	6-prenyl	5,7	8-Me	C	34
no name	12.41(270 MHz)	6-prenyl	5,7		C	35
no name	12.33(400 MHz)	6,8-diprenyl	5,7		C	36
flulvinervin A	12.38(300 MHz)	6-prenyl	5	7,8-Dmp	C	37
fleminone	12.28(270 MHz)	6-prenyl	5,2'	4'-OMe, 7,8-Dmp	C	38
no name	12.40(270 MHz)	6-prenyl	5,7,4'		C	39
(eriodictyol)	12.18(400 MHz,23 °C)	none	5,7,3',4'		A	
sophoraflavanone A	12.10(100 MHz)	8-geranyl	5,7,4'		A	13
sophoraflavanone B	12.15(100 MHz)	8-prenyl	5,7,4'		A	13
sophoraflavanone G	12.20(270 MHz)	8-lavandulyl	5,7,2',4'		A	20

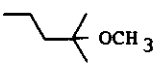
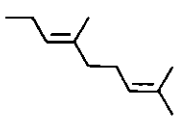
Table 1 (continued)

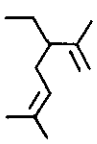
euchrestaflavanone A	12.10(100 MHz)	8-prenyl	5,7,4'	3'-prenyl	A	13
euchrestaflavanone B	12.20(100 MHz)	8-prenyl	5,7,2',4'	5'-prenyl	A	13
euchrestaflavanone C	12.20(100 MHz)	8-prenyl	5,7,2'	4',5'-Dmp	A	13
gancaonin E	12.14(400 MHz,23°C)	8-prenyl	5,7,3',4'	5'-prenyl	A	40
antiarone G	12.14(400 MHz,23°C)	8-prenyl	5,7,4'	3'-OMe 2'-prenyl	A	23
2	12.14(400 MHz,23°C) 12.11(400 MHz,35°C) 12.08(400 MHz,50°C) 12.01(90 MHz,35°C)	8-prenyl	5,7,3',4'		A	
7	12.12(400 MHz,23°C) 12.00(90 MHz,35°C)	8-(3"-OMe)-isoamyl	5,7,3',4'		A	
8	12.11(400 MHz,23°C) 12.00(90 MHz,35°C)	8-(3"-OH)-isoamyl	5,7,3',4'		A	
glabranin	11.98(80 MHz) 12.00(270 MHz)	8-prenyl	5,7		C	41 35
no name	12.10(270 MHz)	8-prenyl	5,3',4'	7-OMe	C	42
tephrowatsin C	12.05(80 MHz)	8-(3"-OH)-isoamyl	5	7-OMe	C	43
no name	12.00(270 MHz) 12.00(90 MHz,35°C)	8-prenyl	5,7,4'		C A	39
lespedezaflavanone B	12.00(400 MHz)	8-prenyl	5,7,4'	3'-prenyl	C	25
lespedezaflavanone D	12.01(90 MHz)	8-prenyl	5,7,2',4'	5'-O-prenyl	C	44
no name	12.02(270 MHz)	8-prenyl	5,7,4'	3',5'-diprenyl	C	45
no name	12.02(270 MHz)	8-isoamyl	5,7,4'	3',5'-di-isoamyl	C	45
kushenol A	12.56(n.r.)	8-lavandulyl	5,7,2'		A	18
no name	12.40(250 MHz)	8-geranyl	5,7		C	46
no name	12.32(250 MHz)	8-geranyl	5	7-OMe	C	46
no name	12.30(400 MHz)	8-prenyl	5	7-O-prenyl	C	36

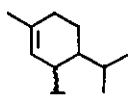
*: observed frequency of instrument and temperature of sample. n.r.: not reported.

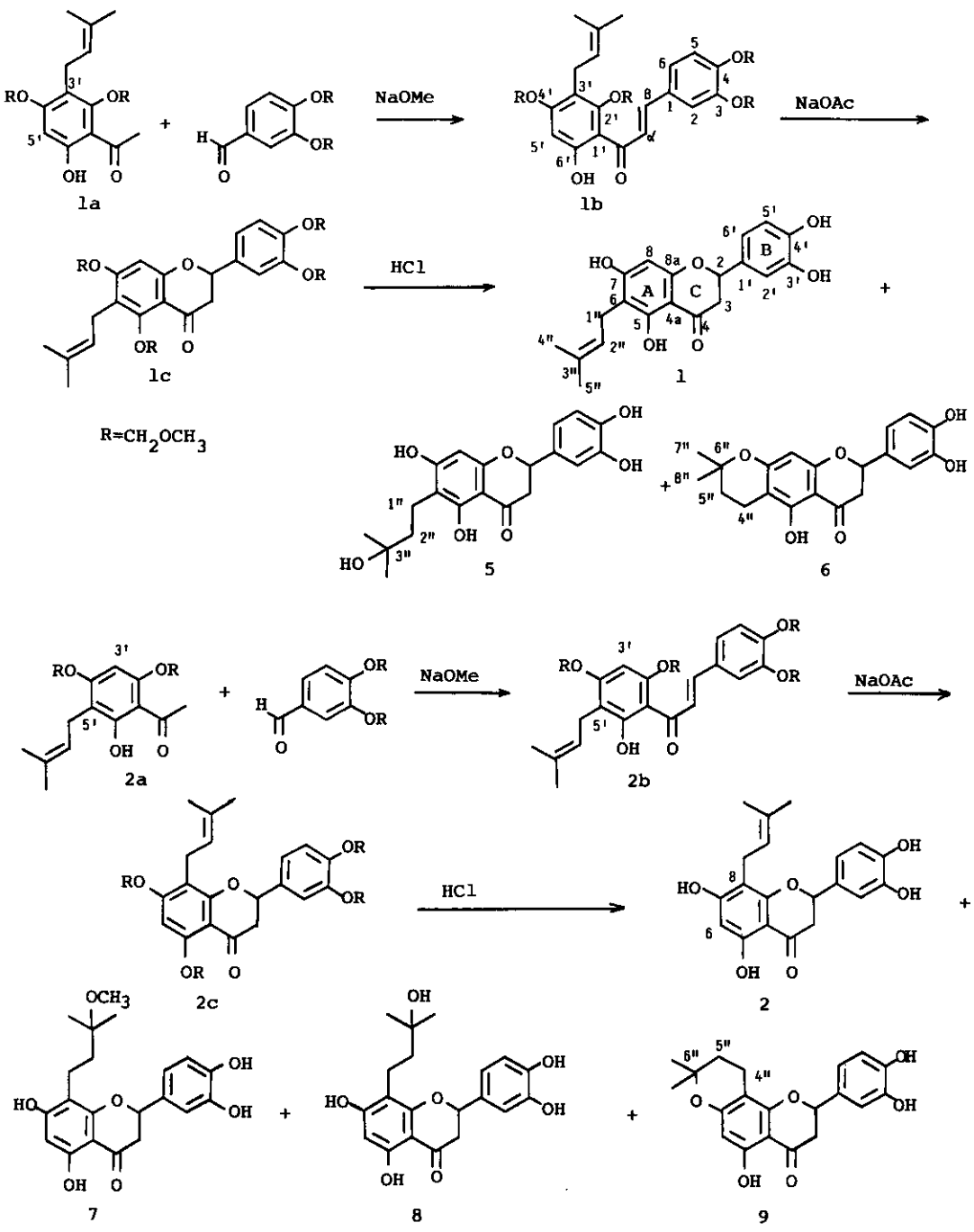
+: solvent: A=acetone-d_6, C=$CDCl_3$.

§: prenyl=  , isoamyl=  , (3"-OH)-isoamyl=  ,

(3"-OMe)-isoamyl=  , geranyl=  ,

lavandulyl=  , Dmp=6",6"-dimethylpyrane,

Dif=3",4"-dihydro-4"-(1""-hydroxyisopropyl)furan, p-M (p-menthene)= 


NaOMe
NaOAc
HCl
1a
1b
1c
1
5
6
2a
2b
2c
2
7
8
9
R=CH2OCH3
1 p-TsOH 6 + 9 , 2 p-TsOH 9 + 6
p-TsOH = p-toluenesulfonic acid

Scheme 1.

Table 2. ^{13}C Nmr data of **1**, **2**, **6**, and **9** in acetone-d_6 §

C	**1**	**2**
2	79.89 (br D, ^{1}J=ca. 148 Hz)*	79.75 (br D, ^{1}J=ca. 148 Hz)
3	43.74 (DD, J=128 and 133 Hz)	43.52 (DD, J=128 and 133 Hz)
4	197.14 (br S)	197.55 (br S)
4a	103.04 (br S)	103.29 (br S)
5	162.28 (Std, $^{3}J_{H1"-C5}$=4, $^{3}J_{5OH-C5}$=4 Hz)	162.95 (Sdd, ^{2}J=4, ^{3}J=5 Hz)
6	109.06 (Sm)	96.33 (Dd, ^{1}J=161, $^{3}J_{5OH-C6}$=7 Hz)
7	165.19 (Std, ^{2}J=2, ^{3}J=4 Hz)	164.56 (Sm)
8	95.42 (D, J=162 Hz)	108.30 (Sm)
8a	161.98 (Sdd, J=1 and 4 Hz)	161.04 (Std, J=4 and 2 Hz)
1'	131.11 (Sm)	131.22 (Sm)
2'	114.70 (Ddd, ^{1}J=157, ^{3}J=4 and 7 Hz)	114.62 (Ddd, ^{1}J=157, ^{3}J=4 and 6 Hz)
3'	146.42 (Sm)	146.26 (St, J=6 Hz)
4'	146.07 (Sm)	146.05 (Std, J=4 and 9 Hz)
5'	116.03 (D, J=159 Hz)	115.99 (D, J=157 Hz)
6'	119.14 (Ddd, ^{1}J=160, ^{3}J=4 and 7 Hz)	119.01 (Ddd, ^{1}J=160, ^{3}J=4 and 6 Hz)
1"	21.66 (Td, ^{1}J=128, ^{2}J=4 Hz)	22.26 (Td, ^{1}J=128, ^{2}J=4 Hz)
2"	123.71 (Dm, ^{1}J=ca. 155 Hz)	123.67 (Dm, ^{1}J=ca. 155 Hz)
3"	131.74 (Sm)	131.88 (Sm)
4"	17.84 (Qm, ^{1}J=ca. 125 Hz)	17.87 (Qm, J=ca. 124 Hz)
5"	25.85 (Qm, J=ca. 125 Hz)	25.90 (Qm, J=ca. 125 Hz)

C	**6**	**9**
2	79.78 (Dm, ^{1}J=ca. 148 Hz)	79.85 (br D, ^{1}J=ca. 148 Hz)
3	43.73 (DD, J=128 and 133 Hz)	43.39 (DD, J=128 and 134 Hz)
4	197.42 (br S)	197.42 (br S)
4a	103.03 (br S)	103.32 (br S)
5	162.23 (Std, $^{3}J_{H4"-C5}$=3, $^{3}J_{5OH-C5}$=5 Hz)	162.37 (St, J=4 Hz)
6	102.55 (br S)	97.48 (Dd, ^{1}J=163, $^{3}J_{5OH-C6}$=7 Hz)
7	163.51 (Sm)	163.58 (Std, J=3 Hz)
8	96.59 (D, J=164 Hz)	101.51 (br S)
8a	161.57 (S br d, J=5 Hz)	161.04 (br S)
1'	131.75 (br S)	131.71 (Sm)
2'	114.72 (Ddd, ^{1}J=158, $^{3}J_{H2-C2'}$=3, $^{3}J_{H6'-C2'}$=6 Hz)	114.57 (Ddd, ^{1}J=157, $^{3}J_{H2-C2'}$=4, $^{3}J_{H6'-C2'}$=6 Hz)
3'	146.39 (St, J=7 Hz)	146.35 (St, J=7 Hz)
4'	146.07 (br S)	146.10 (Sdd, J=4 and 7 Hz)
5'	116.03 (D, J=159 Hz)	116.08 (D, J=159 Hz)
6'	119.20 (Ddd, ^{1}J=160, $^{3}J_{H2-C6'}$=4, $^{3}J_{H2'-C6'}$=8 Hz)	119.00 (Ddd, ^{1}J=160, $^{3}J_{H2-C6'}$=4, $^{3}J_{H2'-C6'}$=7 Hz)
4"	16.32 (Tt, ^{1}J=132, ^{2}J=3 Hz)	16.95 (Tt, ^{1}J=131, ^{2}J=3 Hz)
5"	32.37 (Tm, ^{1}J=ca. 130 Hz)	32.43 (Tm, ^{1}J=ca. 130 Hz)
6"	76.96 (br S)	76.80 (br S)
7"	26.62 (Qm, ^{1}J=ca. 128 Hz)	26.61 (Qm, ^{1}J=ca. 128 Hz)
8"	26.80 (Qm, ^{1}J=ca. 128 Hz)	27.19 (Qm, ^{1}J=ca. 128 Hz)

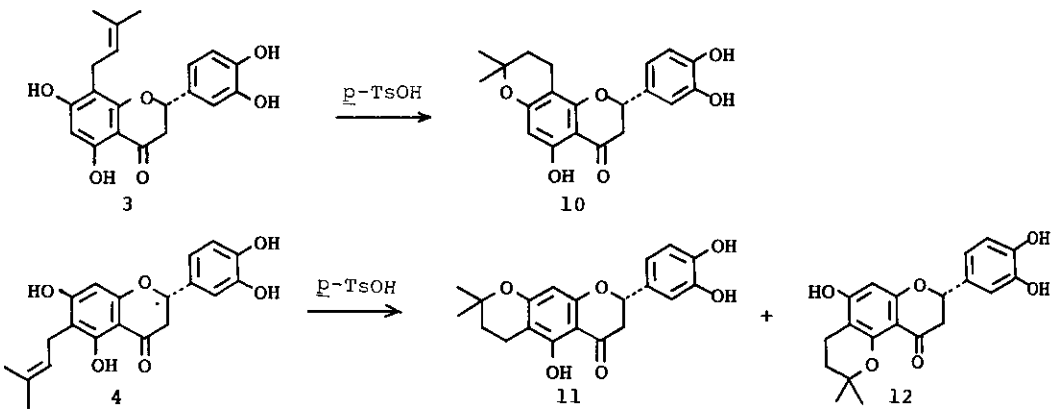
§: The following results were observed with the LSPD experiments; **1**, irradiation of the 5-OH proton, C4a(br S ⟶ Sdd, J=2 and 4 Hz), C6(changed), C5(Std ⟶ St, J=4 Hz), **2**; irradiation of the 5-OH proton, C4a(br S ⟶ Sdd, J=2 and 4 Hz), C5(Sdd ⟶ Sd, J=4 Hz), C6(Dd ⟶ D, J=161 Hz), **6**; irradiation of the 5-OH proton; C5(Std ⟶ St, J=3 Hz), **9**; irradiation of the 5-OH proton, C4a(br S ⟶ br Sd, J=5 Hz), C6(Dd ⟶ D, J=163 Hz), C5(St ⟶ Sd, J=4 Hz).
*: Capital letters refer to the pattern resulting from directry bonded proton(s) and lowercase letters to long-range ^{13}C-^{1}H coupling.

6-isoprenoid substituted flavanones shifted more downfield than that of 6-non-substituted flavanones. In order to determine the location of the isoprenoids moiety in the A-ring of flavonoid, some methods have been reported such as the technique using the observation of ^{13}C-^{1}H long-range coupling.[13-15] The observation for the chemical shift of the hydroxyl group may be a facile method to estimate the isoprenoid moiety in the A-ring of flavanone.

Table 3. ^{1}H Nmr data of **6**, **9**, and **10-12** (in $CDCl_3$, 400 MHz)

	6	10*	11*	9	12*
2-H	5.26 (dd,J=3 and 12.5 Hz)	5.26	5.32	5.32 (dd,J=3 and 13 Hz)	5.33
3-H	2.76 (dd,J=3 and 17 Hz)	2.76	2.77	2.78 (dd,J=3 and 17 Hz)	2.77
3-H	3.03 (dd,J=12.5 and 17 Hz)	3.02	2.99	3.01 (dd,J=13 and 17 Hz)	3.00
6-H	——	5.92	——	5.97 (s)	——
8-H	5.93 (s)	——	5.93	——	5.97
2'-H	6.99 (br s)	6.98	6.99	7.01 (d,J=1.5 Hz)	7.02
5'-H	6.90 (d,J=8 Hz)	6.89	6.90	6.91 (d,J=1.5 and 7 Hz)	6.92
6'-H	6.87 (br d,J=8 Hz)	6.89	6.87	6.88 (dd,J=1.5 and 7 Hz)	6.89
4"-H_2	2.61 (br t,J=6.5 Hz)	2.61	2.62	2.58 (m)	2.59
5"-H_2	1.79 (t,J=6.5 Hz)	1.78	1.79	1.76 (m)	1.75
6"-CH_3	1.338 (s)	1.33	1.33	1.33 (s)	1.32
	1.343 (s)	1.34	1.34	1.35 (s)	1.34
OH	12.37 (s)	12.37	12.34	11.74 (s)	11.74

*: Data from Bohlmann et al. (ref.3, J(Hz): 2,3=3 and 12.5; 3,3=17; 2',6'=1.5; 5',6'=8; 4",5"=7)



Scheme 2. Cyclized reactions of **3** and **4** with p-toluenesulfonic acid by Bohlmann et al.[3]

EXPERIMENTAL

Abbreviations; s = singlet, d = doublet, dd =double doublet, t = triplet, m = multiplet, br = broad. The general procedures followed as described in our previous paper.[16] The following instruments were used: melting points; Yazawa's micromelting point apparatus (hot-stage type), ^{1}H nmr spectra; JEOL JNM-GX-400 NMR Spectrometer and Hitachi R-900 NMR Spectrometer (90 MHz, CW mode),. ^{13}C nmr spectra; JEOL JNM-GX-400 NMR Spectrometer, mass spectra: JEOL JMS-D-300 Mass Spectrometer and JEOL JMS-DX-303 Mass Spectrometer.

3'-(3",3"-Dimethylallyl)-6'-hydroxy-3,4,2',4'-tetrakis(methoxymethoxy)chalcone (**1b**)

To a mixture of 2',4'-bis(methoxymethoxy)-3'-(3",3"-dimethylallyl)-6'-hydroxyacetophenone (**1a**, 50 mg, 0.15 mmol)[4] and 3,4-bis(methoxymethoxy)benzaldehyde (100 mg, 0.44 mmol)[17] in methanol (2 ml) was added 28% NaOMe in methanol (1 ml). The mixture was allowed to stand at room temperature for 24 h, and then acetic acid (1 ml) was added to the solution. The reaction mixture was treated as usual and the product was purified by preparative tlc (silica gel, n-hexane:acetone=3:1) to give **1b** (44 mg,

54%). Compound (**1b**) showed the following data: yellow amorphous solid. EI-Ms, m/z (rel. int.): 533 $[M+1]^+$ (2%), 532 $[M]^+$ (5), 488 (2), 487 (3), 455 (3), 263 (3), 206 (6), 175 (11), 149 (7), 69 (10), 45 (100). HR-Ms, m/z: 532.2318 $[M]^+$ ($C_{28}H_{36}O_{10}$ requires: 532.2308). ^{1}H Nmr ($CDCl_3$, 400 MHz): δ1.70, 1.79 (each 3H, br s, C-3"-CH_3), 3.37 (2H, br d, J = 7 Hz, C-1"-Hx2), 3,46, 3.49, 3.53, 3.54 (each 3H, s, OCH_2OCH_3), 4.89 (2H, s, OCH_2OCH_3), 5.19 (1H, br t, J = 7 Hz, C-2"-H), 5.23, 5.28, 5.29 (each 2H, s, OCH_2OCH_3), 6.50 (1H, s, C-5'-H), 7.19 (1H, d, J = 8.5 Hz, C-5-H), 7.29 (1H, dd, J = 2 and 8.5 Hz, C-6-H), 7.46 (1H, d, J = 2 Hz, C-2-H), 7.72 (1H, d, J = 15.5 Hz, C-α-H), 7.79 (1H, d, J = 15.5 Hz, C-β-H), 12.92 (1H, s, OH).

6-(3",3"-Dimethylallyl)-5,7,3',4'-tetrakis(methoxymethoxy)flavanone (**1c**)

A mixture of **1b** (44 mg, 0.08 mmol) and sodium acetate (0.5 g, 6.1 mmol) in methanol (5 ml) was allowed to stand at 50°C for 3 h. The reaction mixture was treated as usual, and the product was purified by preparative tlc (silica gel, n-hexane:acetone=4:1) to give **1c** (30 mg, 68%). Compound (**1c**) showed the following data: mp 82-83°C (colorless prisms, crystallized from methanol). EI-Ms, m/z (rel. int.): 533 $[M+1]^+$ (1%), 532 $[M]^+$ (3), 500 (18), 488 (4), 487 (10), 455 (16), 441 (4), 379 (3), 263 (11), 219 (6), 175 (15), 148 (10), 69 (3), 45 (100). HR-Ms, m/z: 532.2315 $[M]^+$ ($C_{28}H_{36}O_{10}$ *requires:* 532.2308). ^{1}*H Nmr* ($CDCl_3$, 90 MHz): δ 1.66, 1.78 (each 3H, br s, C-3"-CH_3), 2.70 (1H, dd, J = 4 and 17 Hz, C-3-H), 3.01 (1H, dd, J = 13 and 17 Hz, C-3-H), 3.40 (2H, br d, J = 7 Hz, C-1"-Hx2), 3.44 (3H, s, OCH_2OCH_3), 3.52 (6H, s, OCH_2OCH_3x2), 3.60 (3H, s, OCH_2OCH_3), 5.18 (2H, s, OCH_2OCH_3), 5.22 (6H, s, OCH_2OCH_3), 5.32 (1H, dd, J = 4 and 13 Hz, C-2-H), 6.52 (1H, s, C-8-H), 7.00 (1H, dd, J = 2 and 8.5 Hz, C-6'-H), 7.17 (1H, d, J = 8.5 Hz, C-5'-H), 7.23 (1H, d, J = 2.5 Hz, C-2'-H): The olefinic proton signal of the 3",3"-dimethylallyl group overlapped with the signals of the methylene protons of the methoxymethoxy groups.

Preparation of 6-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone (**1**) and related compounds (**5** and **6**) from **1c**

To a solution of **1c** (29 mg) in methanol (2.5 ml) was added 3N HCl (0.5 ml). The mixture was refluxed for 15 min, and then treated as usual. The reaction product was purified by preparative tlc (silica gel, n-hexane:acetone=3:2) to give **1** (10 mg, 51.5%), 6-(3"-hydroxyisoamyl)-5,7,3',4'-tetrahydroxyflavanone (**5**, 3 mg, 15%) and 6",6"-dimethyl-4",5"-dihydropyrano(2",3":7,6)-5,3',4'-trihydroxyflavanone (**6**, 0.5 mg, 2.5%). Compound (**1**) showed the following data: mp 192-193°C (colorless prisms, crystallized from $CHCl_3$). EI-Ms m/z (rel. int.): 357 $[M+1]^+$ (24%), 356 $[M]^+$ (100), 341 (23), 313 (20), 301 (38), 288 (6), 234 (9), 221 (14), 220 (18), 219 (20), 205 (53), 192 (35), 177 (30), 165 (100), 136 (28), 123 (16), 69 (16). Compound (**5**) showed the following data: mp 179-181°C (colorless prisms, crystallized from benzene-acetone). EI-Ms, m/z (rel. int.): 375 $[M+1]^+$ (1%), 374 $[M]^+$ (5), 356 (36), 341 (8), 301 (49), 300 (67), 299 (9), 282 (14), 221 (10), 220 (9), 219 (5), 205 (17), 192 (11), 179 (14), 165 (100), 136 (26), 123 (15). HR-Ms, m/z: 374.1328 $[M]^+$ ($C_{20}H_{22}O_7$ requires: 374.1366). ^{1}H Nmr (acetone-d_6, 400 MHz): δ1.24 (6H, s, C-3"-CH_3x2), 1.65 (2H, m, *C-2"-Hx2*), *2.66* (*2H, m,* C-1"-Hx2), 2.71 (1H, dd, J = 3 and 17 Hz, C-3-H), 3.12 (1H, dd, J = 13 and 17 Hz, C-3-H), 5.36 (1H, dd, J = 3 and 13 Hz, C-2-H), 6.01 (1H, s, C-8-H), 6.86 (2H, br s, C-5'-H and C-6'-H), 7.03 (1H, br s, C-2'-H), 12.48 (1H, s, OH). Compound (**6**) showed the following data: amorphous solid. EI-Ms, m/z (rel. int.): 357 $[M+1]^+$ (23%), 356 $[M]^+$ (100), 341 (7), 301 (22), 300 (7), 247 (15), 234 (29), 221 (34), 220 (26), 205 (18), 192 (19), 177 (11), 165 (76), 136 (21), 123 (13). HR-Ms, m/z: 356.1242 $[M]^+$ ($C_{20}H_{20}O_6$ requires: 356.1260).

5'-(3",3"-Dimethylallyl)-6'-hydroxy-3,4,2',4'-tetrakis(methoxymethoxy)chalcone (**2b**)

To a mixture of 2',4'-bis(methoxymethoxy)-5'-(3",3"-dimethylallyl)-6'-hydroxyacetophenone (**2a**, 98 mg, 0.3 mmol)[4] and 3,4-bis(methoxymethoxy)benzaldehyde (220 mg, 0.97 mmol)[17] in methanol (2 ml) was added 28% NaOMe in methanol (1 ml). The mixture was allowed to stand at room temperature for 6 h, and then acetic acid (1 ml) was added to the mixture. The reaction mixture was treated as usual, and the product was purified by preprative tlc (silica gel, n-hexane:acetone=3:1) to give **2b** (91 mg, 56.5%). Compound (**2b**) showed the following data: mp 111-112°C (yellow needles, crystallized from methanol). EI-Ms, m/z (rel. int.): 533 $[M+1]^+$ (4%), 532 $[M]^+$ (13), 487 (23), 455 (5), 263 (16), 219 (8), 175 (19), 69 (3), 45 (100). HR-Ms, m/z: 532.2324 $[M]^+$ ($C_{28}H_{36}O_{10}$ requires: 532.2308). ^{1}H Nmr ($CDCl_3$, 90 MHz): δ 1.69, 1.80 (each 3H, br s, C-3"-CH_3), 3.34 (2H, br d, J = 7 Hz, C-1"-Hx2), 3.48 (3H, s, OCH_2OCH_3), 3.53 (9H, s, OCH_2OCH_3x3), 5.23 (2H, s, OCH_2OCH_3), 5.26 (6H, s, OCH_2OCH_3x3), 6.40 (1H, s, C-3'-H), 7.18 (2H, br s, C-5-H and C-6-H), 7.47 (1H, br s, C-2-H), 7.68 (1H, d, J = 16 Hz, C-α-H), 7.88 (1H, d, J = 16 Hz, C-β-H), 13.74 (1H, s, OH): The olefinic proton of the 3",3"-dimethylallyl group overlapped with the signals of the methylene protons of the methoxymethoxy groups.

8-(3",3"-Dimethylallyl)-5,7,3',4'-tetrakis(methoxymethoxy)flavanone (**2c**)

A mixture of **2b** (90 mg, 0.17 mmol) and sodium acetate (0.5 g, 6.1 mmol) in methanol (5 ml) was allowed to stand at 50°C for 20 h. The reaction mixture was treated as usual, and the product was purified by preparative tlc (silica gel, n-hexane:acetone=2:1) to give **2c** (46 mg, 51%). Compoud (**2c**) showed the following data: amorphous solid. EI-Ms, m/z (rel. int.): 533 $[M+1]^+$ (2%), 532 $[M]^+$ (7), 488 (11), 487 (10), 455 (4), 443 (4), 441 (6), 373 (3), 265 (3), 263 (16), 175 (8), 148 (8), 69 (6), 45 (100). HR-Ms, m/z: 532.2339 $[M]^+$ ($C_{28}H_{36}O_{10}$ requires: 532.2308). ^{1}H Nmr ($CDCl_3$, 90 MHz): δ 1.67 (6H, br s, C-3"-CH_3x2), 2.77 (1H, dd, J = 4 and 16 Hz, C-3-H), 3.03 (1H, dd, J = 12 and 16 Hz, C-3-H), 3.35 (2H, br d, J = 7 Hz, C-1"-Hx2), 3.49 (3H, s, OCH_2OCH_3), 3.52 (9H, s, OCH_2OCH_3x3), 5.24 (8H, s, OCH_2OCH_3x4), 5.35 (1H, dd, J = 4 and 12 Hz, C-2-H), 6.56 (1H, s, C-6-H), 7.02 (1H, dd, J = 2 and 8.5 Hz, C-6'-H), 7.18 (1H, d, J = 8.5 Hz, C-5'-H), 7.28 (1H, d, J = 2 Hz, C-2'-H): The olefinic proton signal of the 3",3"-dimethylallyl group overlapped with the methylene proton signals of the methoxymethoxy groups.

Preparation of 8-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone (**2**) and related compounds (**7**, **8**, and **9**) from **2c**

To a solution of **2c** (43 mg) in methanol (2.5 ml) was added 3N HCl (0.5 ml). The mixture was refluxed for 25 min, and then treated as usual. The reaction product was purified by preparative tlc (silica gel, n-hexane:acetone=2:1) to give **2** (12 mg, 42%), 8-(3"-methoxyisoamyl)-5,7,3',4'-tetrahydroxyflavanone (**7**, 7 mg, 32%), 8-(3"-hydroxyisoamyl)-5,7,3',4'-tetrahydroxyflavanone (**8**, 3 mg, 10%), and 6",6"-dimethyl-4",5"-dihydropyrano(2",3":7,8)-5,3',4'-trihydroxyflavanone (**9**, 4 mg, 14%). Compound (**2**) showed the following data: mp 199-202°C (colorless prisms, crystallized from $CHCl_3$). EI-Ms, m/z (rel. int.): 357 $[M+1]^+$ (24%), 356 $[M]^+$ (100), 341 (23), 313 (21), 301 (29), 288 (6), 234 (8), 221 (12), 220(18), 219 (27), 205 (54), 192 (36), 177 (35), 165 (88), 136 (26), 123 (12), 69 (15). Compoud (**7**) showed the following data: amorphous solid. EI-Ms, m/z (rel. int.): 389 $[M+1]^+$ (2%), 388 $[M]^+$ (8), 356 (60), 341 (16), 313 (12), 301 (65), 300 (72), 282 (11), 247 (4), 234 (8), 221 (14), 220 (16), 205 (27), 192 (19), 179 (11), 177 (13), 165 (100), 136 (26), 123 (14), 73 (51). HR-Ms, m/z: 388.1498 $[M]^+$ ($C_{21}H_{24}O_7$ requires: 388.1522). ^{1}H Nmr (acetone-d_6, 400 MHz): δ 1.11 (6H, s,

C-3"-CH_3x2), 1.62 (2H, m, C-2"-Hx2), 2.56 (2H, t, J = 8 Hz, C-1"-Hx2), 2.77 (1H, dd, J = 3 and 17 Hz, C-3-H), 3.07 (1H, dd, J = 12.5 and 17 Hz, C-3-H), 3.07 (3H, s, C-3"-OCH_3), 5.42 (1H, dd, J = 3 and 12.5 Hz, C-2-H), 6.02 (1H, s, C-6-H), 6.87 (1H, d, J = 8.5 Hz, C-5'-H), 6.92 (1H, dd, J = 2 and 8.5 Hz, C-6'-H), 7.07 (1H, d, J = 2 Hz, C-2'-H), 12.12 (1H, s, OH). Compound (**8**) showed the following data: amorphous solid. EI-Ms, m/z (rel. int.): 375 $[M+1]^+$ (1%), 374 $[M]^+$ (5), 356 (36), 341 (7), 299 (11), 300 (66), 282 (14), 221 (10), 220 (10), 219 (5), 205 (16), 192 (12), 165 (100), 136 (26), 123 (14). HR-Ms m/z: 374.1372 $[M]^+$ ($C_{20}H_{22}O_7$ requires: 374.1366). ^{1}H Nmr (acetone-d_6, 400 MHz): δ 1.19 (6H, s, C-3"-CH_3x2), 1.65 (2H, m, C-2"-Hx2), 2.65 (2H, t, J = 8 Hz, C-1"-Hx2), 2.79 (1H, dd, J = 3 and 17 Hz, C-3-H), 3.08 (1H, dd, J = 12 and 17 Hz, C-3-H), 5.42 (1H, dd, J = 3 and 12 Hz, C-2-H), 6.00 (1H, s, C-6-H), 6.86 (1H, d, J = 8 Hz, C-5'-H), 6.91 (1H, dd, J = 2 and 8 Hz, C-6'-H), 7.07 (1H, d, J = 2 Hz, C-2'-H), 12.11 (1H, s, OH). Compound (**9**) showed the following data: mp 238-239°C (colorless prisms, crystallized from benzene-acetone), EI-Ms, m/z (rel. int.) 357 $[M+1]^+$ (24%), 356 $[M]^+$ (100), 341 (4), 301 (23), 300 (6), 247 (16), 234 (30), 221 (39), 220 (29), 205 (16), 192 (27), 177 (15), 165 (100), 136 (28), 123 (11), 78 (66). HR-Ms m/z: 356.1247 $[M]^+$ ($C_{20}H_{20}O_6$ requires: 356.1260).

Preparation of **6** and **9** from 6-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone (**1**)

A mixture of **1** (15 mg) and p-toluenesulfonic acid (10 mg) in benzene (4 ml) was refluxed for 30 min.[3] The reaction product was purified by preparative tlc (silica gel, n-hexane:ether=1:1) to give **6** (8 mg, 53%) and **9** (less than 0.5 mg). Compound (**6**) thus obtained was identical with **6** derived from **1c** on comparison of ^{1}H nmr spectra and tlc analysis. Compound (**9**) thus obtained was identical with **9** derived from **2c** by comparison of the ^{1}H nmr spectra and tlc analysis.

Preparation of **9** and **6** from 8-(3",3"-dimethylallyl)-5,7,3',4'-tetrahydroxyflavanone (**2**)

A mixture of **2** (25 mg) and p-toluenesulfonic acid (16 mg) in benzene (6 ml) was refluxed for 30 min.[3] The reaction product was purified by preparative tlc (n-hexane:ether=1:1) to give **9** (18 mg, 72%, mp 237-239°C) and **6** (3 mg, 12%). Compound (**9**) thus obtained was identical with **9** derived from **2c** on comparison of the ^{1}H nmr spectra and tlc analysis. Compound (**6**) thus obtained was identical with **6** derived from **1c** by comparison of the ^{1}H nmr spectra and tlc analysis.

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