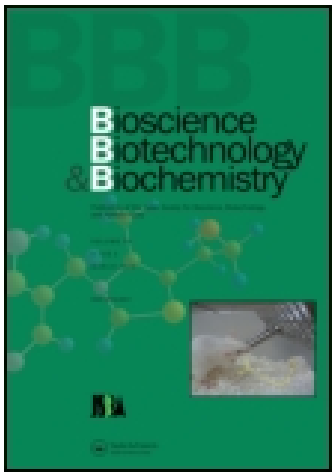

Bioscience, Biotechnology, and Biochemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tbbb20

Preparation and Taste of Certain Glycosides of Flavanones and of Dihydrochalcones

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Published online: 12 Jun 2014.

Biosci. Biotech. Biochem., **58** (8), 1479–1485, 1994

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Received March 2, 1994

The 7-*O*-[2-*O*-(α-L-Rhamnopyranosyl)-β-L-quinovoside] of naringenin and of hesperetin, and their dihydrochalcone (DHC) derivatives were synthesized by the method of Koenigs–Knorr (Ag_2CO_3 and quinoline). The reaction of TMS ethers of naringenin and of hesperetin with each of the α-acetofluoro derivatives of D-glucose, L-rhamnose, 2-*O*-(α-L-rhamnopyranosyl)-L-rhamnose, and 2-*O*-(α-L-rhamnopyranosyl)-D-glucose (neohesperidose), using boron trifluoride etherate as an activator, yielded coupling products which, after deprotection, gave naringenin 4′-*O*-β-D-glucoside, naringenin 4′-*O*-α-L-rhamnoside, naringenin 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnoside], hesperetin 3′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnoside], and naringenin 4′-*O*-β-neohesperidoside, respectively. Catalytic hydrogenation of these flavanones gave the corresponding DHC derivatives. Hesperetin DHC 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl-β-L-quinovoside] was 300 times sweeter than sucrose, while the other compounds were bitter or tasteless.

Naringin (**1**) and neohesperidin (**2**) are known to be bitter principles of grapefruit and pummelo, while naringin dihydrochalcone (DHC, **3**) and neohesperidin DHC (**4**) derived from **1** and **2** by their catalytic hydrogenation are both known to be sweetening agents.[1] An organoleptic study has revealed that **1** and **2** were 0.2 and 0.04 times as bitter as quinine, while **3** and **4** were 300 and 1000 times sweeter than sucrose, respectively. In our laboratory, the specific structural features required for bitterness and sweetness in the sugar components of **1**–**4** have been systematically studied to map out the general structural requirements for bitterness and sweetness.

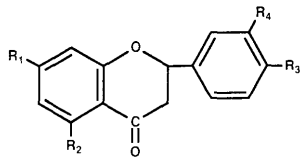
In our continuing investigation,[2] the present study was designed to prepare the following compounds and to examine their tastes: naringenin 7-*O*-[2-*O*-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**5**) and its DHC derivative (**6**), hesperetin 7-*O*-[2-*O*-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**7**) and its DHC derivative (**8**), naringenin 4′-*O*-β-D-glucopyranoside (**9**), naringenin 4′-*O*-α-L-rhamnopyranoside (**10**), and its DHC derivative (**11**), naringenin 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**12**), and its DHC derivative (**13**), hesperetin 3′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**14**), naringenin 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside] (**15**), and naringenin 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-α-D-glucopyranoside] (**16**).

It is well-known that flavones, isoflavones and flavanones with several hydroxyl groups can generally be selectively glycosylated at C-7 by the method of Zémplen and Farkas (10% aq. sodium or potassium hydroxide and acetone)[3] or by the method of Koenigs and Knorr (silver carbonate and quinoline).[4] Accordingly, an attempt was made to prepare **5** and **7** by the method of Koenigs and Knorr. Condensation of naringenin with 3,4-di-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-quinovopyranosyl bromide (**17**)[5] in quinoline in the presence of silver carbonate gave coupling product **18** which, after deacetylating with methanolic sodium methoxide, afforded **5** in a 54.8% yield. Similarly, the reaction of hesperetin with **17** yielded coupling product **19** which, after deacetylating, gave **7** in a 20.6% yield. Hydrogenation of **5** and **7** in alkali in the presence of 10% palladium on carbon afforded **6** and **8** in 94.5% and 88.5% yields, respectively. The sugar positions in **5** and **7** were determined by analyzing their UV and NMR spectra. No bathochromic shift was observed in their UV spectra after the addition of sodium acetate, indicating that the 7-hydroxyl group was substituted.[6] The hydroxyl group at C-5 of the aglycone moiety of **5** and **7** was observed at about δ (ppm) 12 in their ^{1}H-NMR spectra. These data suggested that the C-5 hydroxyl group was not substituted.

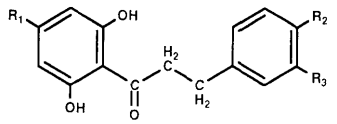
In a previous paper,[7] we have reported that when 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl fluoride (**20**)[7] was coupled to each of the bis(trimethylsilyl)ether of 4′,7-dihyroxyisoflavone (daidzein) and the tris(trimethylsilyl) ether of 4′,5,7-trihydroxyisoflavone (genistein) in the presence of an activator (boron trifluoride etherate), the L-rhamnosyl group was introduced simultaneously to the 4′- and 7-hydroxyl groups of daidzein in high yields, while in the case of genistein, the 4′-hydroxyl group was predominantly glycosylated, and only a very small amount of genistein 4′,7-di-*O*-α-L-rhamnopyranoside was obtained. From these results, it was made clear that the hydroxyl group attached to the side ring of an isoflavone could be easily glycosylated by this procedure. Accordingly, an attempt was made to apply this method to the glycosylation of naringenin and hesperetin.

2,3,4-Tri-*O*-acetyl-α-D-glucopyranosyl fluoride (**21**)[8] was coupled to 4′,5,7-tris(trimethylsilyl)naringenin (**22**) in the presence of boron trifluoride to give coupling product **23** in a 17.8% yield which, after deacetylation, gave **9** in a 96% yield. Similarly, condensation of **22** with **20**, and subsequent deacetylation of reaction product **24**, gave **10** in a 25% overall yield. 3,4-Di-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-

Table I. Structure of Flavanone and Dihydrochalcone Glycosides



Compound no.	Substituent group			
	R_1	R_2	R_3	R_4
1	Rha-Glc-*O*-	OH	OH	H
2	Rha-Glc-*O*-	OH	OCH_3	OH
5	Rha-Qui-*O*-	OH	OH	H
7	Rha-Qui-*O*-	OH	OCH_3	OH
9	OH	OH	Glc-*O*-	H
10	OH	OH	Rha-*O*-	H
12	OH	OH	Rha-Rha-*O*-	H
14	OH	OH	OCH_3	Rha-Rha-*O*-
15	OH	OH	Rha-Glc-*O*-	H
16	OH	OH	Rha-α-Glc-*O*-	H
18	$Rha(Ac)_3$-$Qui(Ac)_2$-*O*-	OH	OH	H
19	$Rha(Ac)_3$-$Qui(Ac)_2$-*O*-	OH	OH	OCH_3
22	OTMS	OTMS	OTMS	H
23	OH	OH	$Glc(Ac)_4$-*O*-	H
24	OH	OH	$Rha(Ac)_3$-*O*-	H
28	OH	OH	$Rha(Ac)_3$-$Rha(Ac)_2$-*O*-	H
29	OTMS	OTMS	OTMS	OCH_3
30	OH	OH	OCH_3	$Rha(Ac)_3$-$Rha(Ac)_2$-*O*-
34	OH	OH	$Rha(Ac)_3$-$Glc(Ac)_3$-*O*-	H
35	$Rha(Ac)_3$-*O*-	H	H	H
36	$Rha(Ac)_3$-*O*-	H	H	OCH_3

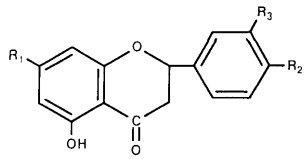


Compound no.	Substituent group		
	R_1	R_2	R_3
3	Rha-Glc-*O*-	OH	H
4	Rha-Glc-*O*-	OCH_3	OH
6	Rha-Qui-*O*-	OH	H
8	Rha-Qui-*O*-	OCH_3	OH
11	OH	Rha-*O*-	H
13	OH	Rha-Rha-*O*-	H

Rha-Glc-*O*- = 2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranosyloxy-; Rha-Qui-*O*- = 2-*O*-(α-L-rhamnopyranosyl)-β-L-quinopyranosyloxy-; Glc-*O*- = β-D-glucopyranosyloxy-; Rha-*O*- = α-L-rhamnopyranosyloxy-; Rha-Rha-*O*- = 2-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranosyloxy-; Ac = CH_3CO-; TMS = trimethylsilyl (Me_3Si).

acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl bromide (**25**)[9] was treated with aqueous acetone in the presence of silver carbonate to afford 1-hydroxy compound **26** in a 97.6% yield, which was further treated with diethylaminosulfur trifluoride (DAST)[10] in benzene to yield 3,4-di-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl fluoride (**27**) in an 89.7% yield. Coupling **27** to **22** by using boron trifluoride etherate as an activator gave coupling product **28** in a 93.3% yield which, after deprotection, yielded **12**. In a similar manner, **27** was coupled to 3',5,7-tris(trimethylsilyl)hesperetin (**29**) to yield condensing product **30** in a 53.2% yeild which, after deacetylation, gave **14**. 3,4,6-Tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-D-glucopyranosyl bromide (**31**)[11] was converted to 1-hydroxy compound **32** in a manner similar to that mentioned for the preparation of **26**. Treatment of **32** with DAST gave an αβ-anomeric mixture of 1-fluoro derivative **33**. The reaction of **22** with **33** gave coupling product **34** in a 20.8% yield which, after deacetylation, afforded a mixture of **15** and **16** that could be separated by column chromatography on silica gel. A bathochromic shift was observed in the UV spectra of compounds **9**–**16** after the addition of sodium acetate, which proved that the 7-hydroxyl group was not substituted.[6] Also, in their ^{1}H-NMR spectra, the C-5 hydroxyl protons appeared in the region of δ (ppm) 12–13. Accordingly, it

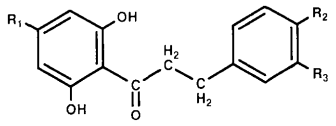
Table II. Structure and Relative Bitterness of Flavanone Glycosides



Compound no.	Substituent group			Taste	Relative taste by weight
	R_1	R_2	R_3		
1	Rha-Glc-*O*-	OH	H	Bitter	1
5	Rha-Qui-*O*-	OH	H	Bitter	0.5
7	Rha-Qui-*O*-	OCH_3	OH	No taste	0
9	OH	Glc-*O*-	H	No taste	0
10	OH	Rha-*O*-	H	Bitter	0.15
12	OH	Rha-Rha-*O*-	H	Bitter	0.15
14	OH	OCH_3	Rha-Rha-*O*-	No taste	0
15	OH	Rha-Glc-*O*-	H	Bitter	0.05
16	OH	Rha-α-Glc-*O*-	H	—	—

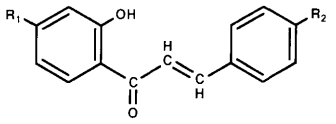
– = not tested.

Table III. Structure and Taste of Dihydrochalcone and Chalcone Glycosides



Compound no.	Substituent group			Taste	Relative taste by weight
	R_1	R_2	R_3		
4	Rha-Glc-*O*-	OCH_3	OH	Very sweet	1000
6	Rha-Qui-*O*-	OH	H	No taste	0
8	Rha-Qui-*O*-	OCH_3	OH	Sweet	300
11	OH	Rha-*O*-	H	Bitter	0.5*
13	OH	Rha-Rha-*O*-	H	Bitter	0.5*

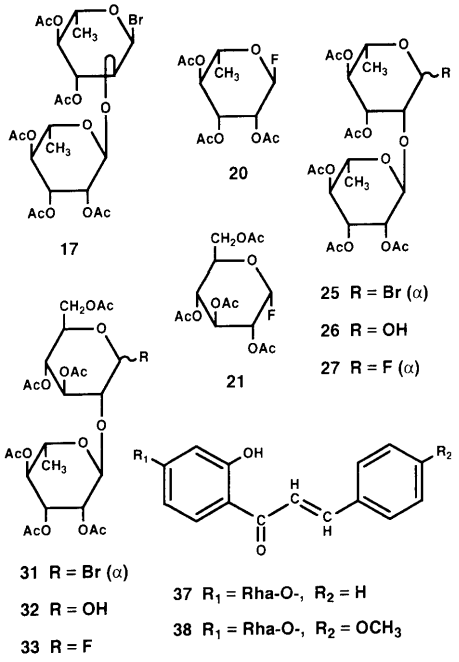
* 0.5 times as bitter as naringin.



Compound no.	Substituent group		Taste	Relative taste by weight
	R_1	R_2		
37	Rha-*O*-	H	Sweet	100
38	Rha-*O*-	OCH_3	Sweet	100
Sucrose			Sweet	1

was assumed that the sugar components were introduced to the 4′ or 3′ hydroxyl groups of flavanone. The anomeric configuration of the glycopyranosidic bond directly attached to the hydroxyl groups of the aglycones in **5**–**16** was determined by applying the Klyne rule[12] as shown in the experimental section.

As already mentioned, the 7-hydroxyl group of naringenin or hesperetin was predominantly glycosylated with α-glycosyl bromide in the presence of silver carbonate. Contrary to this, in the coupling reaction of α-glycosyl fluoride with the per(trimethylsilyl)ethers of naringenin and hesperetin by using boron trifluoride, the 4′- or 3′-hydroxyl group was regioselectively glycosylated, while glycosylation of the 7-hydroxyl group did not occur at all, even when an excess amount of the glycosyl fluorides was used. In addition, when compound **20** was reacted with flavanones that had only one hydroxyl group at C-7, namely the trimethylsilyl ethers of 7-hydroxyflavanone and 7-hydroxy-4′-methoxyflavanone, in the presence of boron trifluoride, the reaction occurred in the 7-hydroxyl group.



Thus, 7-hydroxyflavanone *O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside; **35**) and 7-hydroxy-4′-methoxyflavanone *O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside; **36**) were obtained in good yields. Deacetylation of **35** and **36** with 0.1 N methanolic sodium methoxide gave 2′,4′-dihydroxychalcone 4′-*O*-α-L-rhamnopyranoside (**37**) and 2′,4′-dihydroxy-4-methoxychalcone 4′-*O*-α-L-rhamnopyranoside (**38**), respectively. It is well known[13] that a flavonone with a hydroxyl group at the C-5 position is predominantly stable, *e.g.*, naringenin and hesperetin, but if this hydroxyl group is absent, the flavanone ring structure is easily susceptible to opening in mildly acidic and alkaline conditions. Thus, by summarizing the foregoing results, it may be said that the presence of a 5-hydroxyl group in flavanones as well as in isoflavones prevented the reactivity for glycosylation of the 7-hydroxyl group. Therefore, this glycosylation method seems to be convenient for selectively introducing a glycosyl residue to hydroxyl groups in the side ring of flavonoids which have hydroxyl groups at both C-5 and -7.

Catalytic hydrogenation of **5**, **6**, **10**, and **12** in the presence of palladium on carbon gave **6**, **8**, **11**, and **12**, respectively.

The taste properties of the glycosides of flavanones, chalcones, and dihydrochalcones are listed in Tables II and III.

In a previous paper,[14] it has been clarified that both hesperetin DHC 4′-*O*-β-D-glucopyranoside and -4′-*O*-β-L-glucopyranoside were as sweet as saccharin (300 times sweeter than sucrose), indicating that the difference of D- and L-conformations of the sugar did not influence the sweet taste. On the other hand, hesperetin DHC 4′-*O*-β-L-quinovopyranoside was two-fold sweeter than saccharin. This suggests that the methyl group of the L-quinovosyl moiety may play a significant role in eliciting the intense sweetness. Therefore, compound **8** was expected to have intense sweetness. Unexpectedly, it was only 300 times sweeter than sucrose. The glycosides of naringenin and hesperetin, in which the sugar groups are linked to the 3′- or 4′-hydroxyl groups, and also the dihydrochalcones derived from them were all bitter or tasteless. Naringin is intensely bitter, while naringenin 4′-*O*-[2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside] (naringenin 4′-β-neohesperidoside) was 0.01 times as bitter as naringin, indicating that the transposition of neohesperidose from the 7- to 4′-position resulted in a marked decrease in bitterness. Thus, it is concluded that the point of attachment of neohesperidose is of fundamental importance in eliciting bitterness in the naringin molecule. Additionally, it is also interesting that structurally simple chalcones such as 2′,4′-dihydroxychalcone 4′-*O*-α-L-rhamnopyranoside and 2′,4′-dihydroxy-4-methoxychalcone 4′-*O*-α-L-rhamnopyranoside are both 100 times sweeter than sucrose. Since the taste properties of chalcone glycosides have not yet been reported, the structural requirements for the sweetness of chalcones should be investigated next.

Experimental

Reactions were monitored by TLC on silica gel 60 as described before.[7] NMR, UV, and $[\alpha]_D$ data were measured with the same equipment as that described in the previous paper.[7] Elemental analyses were performed by the Microanalytical Laboratory of the School of Pharmaceutical Sciences at this university.

Naringenin 7-O-[2-O-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**5**). Naringenin (6.6 g) and **17** (17 g) were dissolved in anhyd. quinoline (340 ml), and silver carbonate (6.7 g) and 4A molecular sieves (6.7 g) were added. After stirring overnight while excluding all light, the reaction mixture was centrifuged, and the supernatant was poured into ice-cold 10% acetic acid (1 liters) drop by drop. After a short period, the precipitate was collected, dissolved in pyridine and again poured into 10% acetic acid (2 liters). The precipitate was collected, dried, and then deacetylated with 0.1 N sodium methoxide in methanol (1.2 liters) at 0°C for 2 h. After neutralizing with Amberlite IR-120 (H^+) resin, the filtrate was evaporated to a small quantity and applied to a column of silica gel, using ethyl acetate–methanol–water (80 : 15 : 10) as the eluent. The fractions containing only **5** were collected, decolorized with active carbon, filtered, and then evaporated to afford **5** as crystals (8 g, 54.8% yield), mp 178°C, $[\alpha]_D^{20}$ 16° ($c=1$, MeOH). *Anal.* Found: C, 53.78; H, 6.24. Calcd. for $C_{27}H_{32}O_{13}\cdot 2H_2O$: C, 54.00; H, 6.00%. UV λ_{max} (MeOH nm: 282; λ_{max} (MeOH–AcONa) nm: 284; λ_{max} (MeOH–$AlCl_3$) nm: 309; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 306; λ_{max} (MeOH–MeONa) nm: 286. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl β-L-quinovoside and for naringenin was −1292°. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl α-L-quinovoside and for naringenin was −39224°. The observed $[M]_D$ value for **5** was 12384°. Accordingly, the anomeric configuration of the L-quinovosyl group was deduced to be of β-form. Treatment of **5** (1 g) with a mixture of acetic anhydride (10 ml) and pyridine (10 ml) overnight at room temperature gave the heptaacetate (1.3 g) in an 89.7% yield, mp 136–137°C, $[\alpha]_D^{20}$ −33° ($c=1$, $CHCl_3$). *Anal.* Found: C, 56.78; H, 5.43. Calcd. for $C_{41}H_{46}O_{20}\cdot 0.5H_2O$: C, 56.74; H, 5.42%. NMR δ_H ($CDCl_3$): 1.22, 1.29 (6H, each d, $J=6$ Hz, $2CH_3$); 1.96, 2.04, 2.07, 2.09, 2.14 (15H, each s, sugar Ac); 2.33, 2.40 (6H, each s, aglycone 2Ac); 2.90 (2H, m, H-3); 3.57–4.07 (2H, m, sugar 5, 5′); 4.67–5.60 (9H, m, sugar H-1–4, 1′–4′, and H-2); 6.43 (1H, d, $J=1$ Hz, H-6); 6.56 (1H, d, $J=1$ Hz, H-8); 7.17 (2H, d, $J=9$ Hz, H-3′, 5′); 7.49 (2H, d, $J=9$ Hz, H-2′, 6′).

Hesperetin 7-O-[2-O-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**7**). To a solution of hesperetin (3.12 g) in quinoline (140 ml) were added **17** (7.2 g), silver carbonate (3.1 g) and 4A molecular sieves (3.1 g), before the mixture was stirred overnight at room temperature in the dark. The reaction mixture was treated in a similar manner to that used for the preparation of **5**. The resulting deacetylated syrup was chromatographed in a column of silica gel, eluting with ethyl acetate–methanol–water (80 : 15 : 10) to give crystalline **7** (1.3 g, 20.6% yield), mp 209–210°C, $[\alpha]_D^{20}$ 23° ($c=1$, MeOH). *Anal.* Found: C, 54.82; H, 6.00. Calcd. for $C_{28}H_{34}O_{14}\cdot H_2O$: C, 54.90; H, 5.88%. UV λ_{max} (MeOH) nm: 283; λ_{max} (MeOH–AcONa) nm: 284; λ_{max} (MeOH–$AlCl_3$) nm: 307; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 306; λ_{max} (MeOH–MeONa) nm: 287. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl β-L-quinovoside and

for hesperetin was −1292°. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl α-L-quinovoside and for hesperetin was −39224°. The observed $[M]_D$ value for **7** was 13662°. Accordingly, the anomeric configuration of the L-quinovosyl group was deduced to be of β-form. *Heptaacetate* of **7**, mp 146–147, 5°C, $[\alpha]_D^{20}$ −34° ($c=1$, MeOH). *Anal.* Found: C, 56.29; H, 5.45. Calcd. for $C_{42}H_{48}O_{21}\cdot 0.5H_2O$: C, 56.19; H, 5.46%. NMR δ_H ($CDCl_3$): 1.18, 1.25 (6H, each d, $J=6$ Hz, $2CH_3$); 1.93, 2.00, 2.04, 2.06, 2.12 (15H, each s, sugar 5Ac); 2.31, 2.39 (6H, each s, aglycone 2Ac); 2.82 (2H, m, H-3 *cis*, *trans*); 3.60–4.03 (2H, m, sugar H-5, 5′); 3.83 (3H, s, OMe); 4.60–5.50 (9H, m, sugar H-1–4, 1′–4′, and H-2); 6.38 (1H, d, $J=1$ Hz, H-6); 6.50 (1H, d, $J=1$ Hz, H-8); 7.06–7.33 (3H, m, H-2′, 5′, 6′).

3,4-Di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-L-rhamnopyranose (**32**). Compound **25** (9.3 g) was dissolved in acetone (56 ml), before water (3.6 ml) and silver carbonate (7 g) were added, and the mixture was kept at 0°C for 1 h while stirring. After filtering through a bed of Celite, the filtrate was concentrated to a syrup, which crystallized from chloroform–hexane to give **32** (8.1 g, 97.6%), mp 172–173°C, $[\alpha]_D^{20}$ −18° ($c=1$, $CHCl_3$). *Anal.* Found: C, 50.49; H, 5.96. Calcd. for $C_{22}H_{32}O_{14}$: C, 50.77; H, 6.15%. NMR δ_H ($CDCl_3$): 1.22, 1.25 (6H, each d, $J=6$ Hz, $2CH_3$); 2.03, 2.06, 2.09, 2.16 (15H, each s, 5Ac); 2.98 (C_1–OH); 3.80–4.28, 4.78–5.48 (10H, each m, sugar protons).

3,4,-Di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl fluoride (**27**). A solution of **32** (8 g) in tetrahydrofuran (75 ml) was cooled to −30°C, DAST (2.24 ml) was added, and the mixture was kept at room temperature for 1 h while stirring. The reaction mixture was cooled again to −30°C, and 2 ml of methanol was added to decompose the excess amount of DAST. The mixture was diluted with chloroform, washed successively with aq. 5% sodium hydrogen carbonate and water, and then dried over magnesium sulfate. After filtering, the filtrate was evaporated, and the residue was chromatographed in a column of silica gel, eluting with hexane–ethyl acetate (3 : 1), to yield **27** and its anomer, β-fluoride (**27′**). **27** (7.2 g, 89.7%), mp 138–139°C, $[\alpha]_D^{20}$ −26.0° ($c=1$, $CHCl_3$). *Anal.* Found: C, 49.52; H, 5.74. Calcd. for $C_{22}H_{31}O_{13}F$: C, 50.57; H, 5.94%. NMR δ_H ($CDCl_3$): 1.17, 1.25 (6H, each d, $J=6$ Hz, $2CH_3$); 1.98, 2.02, 2.06, 2.12 (15H, each s, 5Ac); 3.20–4.40, 4.73–5.40 (9H, each m, sugar protons); 5.80 (1H, d, $J=1$ Hz, H-1). β-anomer, **27′** (0.5 g, 6.22%), mp 154–155°C, $[\alpha]_D^{20}$ −17° ($c=1$, $CHCl_3$). *Anal.* Found: C, 50.32; H, 5.80. Calcd. for $C_{22}H_{31}O_{13}F$: C, 50.57; H, 5.94%.

3,4,6-Tri-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-D-glucopyranose (**32**). To a solution of **31** (5.9 g) in acetone (56 ml) was added water (3.6 ml) and silver carbonate (7 g) at 0°C, the mixture being kept at room temperature for 1 h while stirring. After filtering through a bed of Celite, the filtrate was evaporated and the residue was crystallized from chloroform–hexane to afford **32** (4.6 g, 86.8%), mp 135–136.5°C, $[\alpha]_D^{20}$ 4° ($c=1$, $CHCl_3$). *Anal.* Found: C, 49.81; H, 5.42. Calcd. for $C_{24}H_{34}O_{16}$: C, 49.83; H, 5.88%. NMR δ_H ($CDCl_3$): 1.20 (3H, d, $J=6$ Hz, CH_3); 2.00, 2.03, 2.05, 2.09, 2.14 (18H, each s, 6Ac); 3.45–3.87, 3.97–4.41, 4.66–5.40 (13H, each m, sugar protons).

3,4,6-Tri-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-αβ-D-glucopyranosyl fluoride (**33**). To a solution of **32** (1 g) in tetrahydrofuran (10 ml) was added DAST (0.25 ml) at 0°C, the mixture being kept at room temperature for 1 h while stirring. The reaction mixture was then treated in a similar manner to that described for the preparation of **27** to give **33** (0.4 g, 44.6%), mp 145°C, $[\alpha]_D^{20}$ 2° ($c=1$, $CHCl_3$). *Anal.* Found: C, 47.19; H, 5.72. Calcd. for $C_{24}H_{33}O_{15}F$: C, 47.48; H, 5.94%. NMR δ_H ($CDCl_3$): 1.16 (3H, d, $J=6$ Hz, CH_3); 1.93, 2.00, 2.05, 2.08, 2.12 (18H, s, 6Ac); 3.60–4.20, 4.80–5.15 (10H, each m, H-2–6, H-2′, 5′); 5.23 (0.5H, d, $J=3$ Hz, H_α); 5.48 (0.5H, d, $J=8$ Hz, H_β).

General procedure for preparing the flavanone glycosides from flavanones and α-acetylglycosyl fluorides by using boron trifluoride etherate as an activator.

1) *Flavanone glycoside acetates.* A hydroxyflavanone (naringenin, hesperetin, 7-hydroxyflavanone or 7-hydroxy-4′-methoxyflavanone, each 1 mmol) was treated with a mixture of chlorotrimethylsilane (15 ml) and hexamethyldisilazane (15 ml) in pyridine (60 ml) as previously described[7] to give a trimethylsilylated (TMS)-flavanone. While stirring, a solution of boron trifluoride etherate (2.5 mmol) in anhyd. benzene (10 ml) was added to a solution of α-acetylglycosyl fluoride (1.2 mmol) and the TMS-flavanone (1 mmol) in anhyd. benzene at 0°C. The mixture, after being stirred for 1 h at room temperature, was diluted with chloroform, successively washed with water, aq. sodium hydrogen carbonate and water, and then dried over magnesium sulfate. After filtering, the filtrate was concentrated, and the residue was chromatographed in a column of silica gel, eluting with chloroform–acetone (20 : 1, **23**, **24**, **28**, and **30**), or with chloroform–acetone (20 : 1) and then toluene–ether (1 : 1, **34**), or with chloroform–acetone (90 : 1, **35** and **36**) to yield flavanone glycoside acetates.

2) *Flavanone glycosides.* A solution of a flavanone glycoside acetate (1 mmol) in 0.1 N methanolic sodium methoxide (30 ml) was kept at 0°C for 1 h, and then neutralized with Amberlite IR-120 (H^+) resin. After filtering, the filtrate was then evaporated to yield a flavanone glycoside. In the case of **10**, **15**, and **16**, column chromatographic purification on silica gel (ethyl acetate–methanol–water, 80 : 15 : 10) was necessary.

Naringenin 4′-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside) (**23**). Yield, 17.8%; mp 100–101°C, $[\alpha]_D^{20}$ −3° ($c=1$, $CHCl_3$). *Anal.* Found: C, 54.25; H, 4.83. Calcd. for $C_{29}H_{30}O_{14}\cdot 2H_2O$: C, 54.55; H, 5.33%. NMR δ_H ($CDCl_3$): 2.05 (12H, s, 4Ac); 2.95 (2H, m, H-3); 3.70–4.32 (3H, m, sugar protons); 4.96–5.50 (5H, m, sugar protons and H-2); 6.00 (2H, d, $J=1$ Hz, H-6, 8); 7.03 (2H, d, $J=9$ Hz, H-3′, 5′); 7.37 (2H, d, $J=9$ Hz, H-2′, 6′); 12.00 (1H, s, C_5–OH).

Naringenin 4′-O-β-D-glucopyranoside (**9**). Yield, 96.6%; mp 184°C, $[\alpha]_D^{20}$ −17.0° ($c=1$, DMSO). *Anal.* Found: C, 56.32; H, 5.18. Calcd. for $C_{21}H_{22}O_{10}\cdot 0.5H_2O$: C, 56.88; H, 5.19%. UV λ_{max} (MeOH) nm: 289; λ_{max} (MeOH–AcONa) nm: 326; λ_{max} (MeOH–$AlCl_3$) nm: 312; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 309; λ_{max} (MeOH–MeONa) nm: 324. The sum of the $[M]_D$ values for methyl β-D-glucoside and for naringenin was −6596°. The sum of the $[M]_D$ values for methyl α-D-glucoside and for naringenin was 30846°. The observed $[M]_D$ value was −7446°. Therefore, the anomeric configuration of the D-glucosyl residue was of β-form. NMR δ_H (DMSO-d_6): 2.30–2.75 (2H, m, H-3); 3.00–4.23 (6H, m, sugar protons); 4.89 (1H, d, $J=7$ Hz, sugar H-1); 5.40–5.63 (1H, m, H-2); 5.90 (2H, s, H-6, 8); 7.06 (2H, d, $J=9$ Hz, H-3′, 5′); 7.45 (2H, d, $J=9$ Hz, H-2′, 6′); 12.00 (1H, s, C_5–OH). NMR δ_C (DMSO-d_6): 42.03 (C-3); 60.71 (sugar C-6); 69.76 (sugar C-4); 73.20 (sugar C-2); 76.60 (sugar C-5); 77.02 (sugar C-3); 78.07 (C-2); 95.02 (C-8); 95.85 (C-6); 100.33 (sugar C-1); 101.80 (C-10); 116.23 (C-3′, 5′); 127.99 (C-2′, 6′); 131.90 (C-1′); 157.49 (C-4′); 162.73 (C-9); 163.41 (C-5); 166.58 (C-7); 196.03 (C-4).

Naringenin 4′-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranoside) (**24**). Yield, 52%; mp 93°C, $[\alpha]_D^{20}$ −110° ($c=1$, $CHCl_3$). *Anal.* Found: C, 64.94; H, 5.87. Calcd. for $C_{27}H_{28}O_{12}$: C, 65.30; H, 5.65%. NMR δ_H ($CDCl_3$): 1.29 (3H, d, $J=6$ Hz, CH_3); 2.03, 2.05, 2.18 (9H, each s, 3Ac); 2.92 (2H, m, H-3); 3.20–4.16, 4.95–5.50 (5H, each m, sugar protons); 5.50 (1H, m, H-2); 5.97 (2H, s, H-6, 8); 6.77 (1H, br. s C_7–OH); 7.07 (2H, d, $J=9$ Hz, H-3′, 5′); 7.36 (2H, d, $J=9$ Hz, H-2′, 6′); 11.98 (1H, s, C_5–OH).

Naringenin 4′-O-α-L-rhamnopyranoside (**10**). Yield, 48.4%; $[\alpha]_D^{20}$ −63° ($c=1$, MeOH). *Anal.* Found: C, 56.62; H, 5.92; Calcd. for $C_{21}H_{22}O_9\cdot CH_3OH$: C, 56.00; H, 5.56%. UV λ_{max} (MeOH) nm: 289; λ_{max} (MeOH–AcONa) nm: 325; λ_{max} (MeOH–$AlCl_3$) nm: 312; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 309; λ_{max} (MeOH–MeONa) nm: 324. NMR δ_H (DMSO-d_6): 1.00 (3H, d, $J=6$ Hz, CH_3); 2.55 (2H, m, H-3); 2.85–3.95, 4.20–5.38 (5H, each m, sugar protons); 5.40 (1H, m, H-2); 5.77 (2H, s, H-6, 8); 6.95 (2H, d, $J=9$ Hz, H-3′, 5′); 7.33 (2H, d, $J=9$ Hz, H-2′, 6′); 11.99 (1H, s, C_5–OH). The sum of the $[M]_D$ values for methyl α-L-rhamnoside and for naringenin was −11100°. The sum of the $[M]_D$ values for methyl β-L-rhamnoside and for naringenin was 1700°. The observed $[M]_D$ for **10** was −26334°. Therefore, the anomeric configuration of the L-rhamnosidic bond was assumed to be of α-form.

Naringenin 4′-O-[3,4-di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**28**). Yield, 93.3%; mp 132°C, $[\alpha]_D^{20}$ −65° ($c=1$, $CHCl_3$). *Anal.* Found: C, 57.70; H, 5.19. Calcd. for $C_{37}H_{42}O_{18}$; C, 57.36; H, 5.43%. NMR δ_H ($CDCl_3$): 1.23 (6H, d, $J=6$ Hz, $2CH_3$); 2.04, 2.06, 2.09, 2.14, 2.16 (15H, s, 5Ac); 2.95 (2H, m, H-3); 3.77–4.32, 4.90–5.57 (8H, each m, sugar protons); 5.13 (1H, dd, $J_{trans}=12$ Hz, $J_{cis}=4$ Hz, H-2); 6.02 (2H, s, H-6, 8); 6.80 (1H, s, C_7–OH); 7.13 (2H, d, $J=9$ Hz, H-3′, 5′); 7.43 (2H, d, $J=9$ Hz, H-2′, 6′); 12.00 (1H, s, C_5–OH). δ_C ($CDCl_3$): 17.45, 17.56 ($2CH_3$); 20.79 (5Ac); 43.19 (C-3); 67.31 (sugar C-5, 5′); 69.98 (sugar C-2′); 70.44 (sugar C-3); 71.19 (sugar C-4, 4′); 76.42 (sugar C-2); 78.72 (C-2); 95.48 (C-8); 95.65 (C-6); 99.31 (sugar C-1, 1′); 103.03 (C-10); 116.55 (C-3′, 5′); 127.78 (C-2′, 6′); 132.49 (C-1′); 156.28 (C-4′); 163.05 (C-9); 164.33 (C-5); 165.11 (C-7); 169.70, 169.83, 169.95, 170.12, 170.66 (5Ac);

195.57 (C-4).

Naringenin 4′-O-[2-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**12**). Yield, 82.7%; $[\alpha]_D^{20}$ −85° (*c*=1, DMSO). *Anal.* Found: C, 52.44; H, 5.99. Calcd. for $C_{27}H_{32}O_{13}\cdot 3H_2O$: C, 52.43; H, 6.15%. UV λ_{max} (MeOH) nm: 290; λ_{max} (MeOH–AcONa) nm: 325; λ_{max} (MeOH–$AlCl_3$) nm: 312; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 309; λ_{max} (MeOH–MeONa) nm: 324. The sum of the $[M]_D$ values for two moles of methyl α-L-rhamnoside and for the aglycone was −22200°. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl β-L-rhamnoside and for the aglycone was 5900°. The observed $[M]_D$ value for **12** was −47940°. Accordingly, the anomeric configuration of the L-rhamnosyl residue attached directly to naringenin was determined to be of α-form. NMR δ_H (DMSO-d_6): 1.12 (6H, d, *J*=6 Hz, $2CH_3$); 2.70 (2H, m, H-3, *cis*, *trans*); 3.05–4.36, (8H, each m, sugar H-2–5, 2′–5′); 4.87 (1H, s, sugar H-1); 5.44 (1H, s, sugar H-1′); 5.50 (1H, m, H-2); 5.88 (2H, s, H-6, 8); 7.04 (2H, d, *J*=9 Hz, H-3′, 5′); 7.47 (2H, d, *J*=9 Hz, H-2′, 6′); 12.00 (1H, s, C_5–OH). δ_C (DMSO-d_6): 17.87 ($2CH_3$); 48.53 (C-3); 68.79 (sugar C-5, 5′); 69.98 (sugar C-3′); 70.20 (sugar C-3); 70.47 (sugar C-2′); 71.85 (sugar C-4, 4′); 76.94 (sugar C-2); 78.04 (C-2); 94.93 (C-8); 97.28 (C-6); 101.70 (sugar C-1, 1′); 102.21 (C-10); 116.09 (C-3′, 5′); 128.24 (C-2′, 6′); 132.10 (C-1′); 156.13 (C-4′); 162.67 (C-9); 163.37 (C-5); 166.55 (C-7); 195.92 (C-4).

Hesperetin 3′-O-[3,4-di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**30**). Yield, 53.2%; $[\alpha]_D^{20}$ −52° (*c*=0.25, $CHCl_3$). *Anal.* Found: C, 53.87; H, 5.63. Calcd. for $C_{38}H_{44}O_{19}\cdot 2H_2O$: C, 54.29; H, 5.71%. NMR δ_H ($CDCl_3$): 1.15, 1.18 (6H, each d, *J*=6 Hz, $2CH_3$); 1.96, 1.99, 2.05, 2.09 (15H, each s, 5Ac); 2.87 (2H, m, H-3); 3.80 (3H, s, OCH_3); 3.80–4.34, 4.72–5.61 (10H, each m, sugar protons and H-2); 5.94 (2H, s, H-6, 8); 6.50–7.30 (3H, m, H-2′, 5′, 6′).

Hesperetin 3′-O-[2-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**14**). Yield, 40.5%; $[\alpha]_D^{20}$ −52° (*c*=0.5, DMSO). *Anal.* Found: C, 51.98; H, 6.60. Calcd. for $C_{28}H_{34}O_{14}\cdot 3H_2O$: C, 51.85; H, 6.17%. UV λ_{max} (MeOH) nm: 288; λ_{max} (MeOH–AcONa) nm: 324; λ_{max} (MeOH–$AlCl_3$) nm: 310; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 309; λ_{max} (MeOH–MeONa) nm: 325. The sum of the $[M]_D$ values for 2 mol of methyl α-L-rhamnoside and for hesperetin was −22200°. The sum of the $[M]_D$ values for methyl α-L-rhamnoside, methyl β-L-rhamnoside and for hesperetin was 5900°. The observed $[M]_D$ value for **14** was −30888°. Therefore, the anomeric configuration of the L-rhamnosyl group bound directly to hesperetin was of α-form. The per(trimethylsilyl)ether of **14** was prepared in a similar manner to that mentioned for the preparation of **22**. NMR δ_H (DMSO-d_6): 1.18 (6H, d, *J*=6 Hz, $2CH_3$); 2.82 (2H, m, H-3); 3.42–4.15 (8H, m, sugar H-2–5, 2′–5′); 3.81 (3H, s, OCH_3); 4.83 (1H, s, sugar H-1); 5.25 (1H, m, H-2); 5.36 (1H, s, sugar H-1′); 5.94 (1H, d, *J*=2 Hz, H-6); 6.12 (1H, d, *J*=2 Hz, H-8); 6.93 (1H, s, H-5′); 7.17 (2H, s, H-2′, 6′).

Naringenin 4′-O-[3,4,6-tri-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-αβ-D-glucopyranoside] (**34**). Yield, 20.8%. *Anal.* Found: C, 54.65; H, 5.31. Calcd. for $C_{39}H_{44}O_{20}\cdot H_2O$: C, 55.06; H, 5.41%. NMR δ_C ($CDCl_3$): 17.01, 17.40 (rhamnose C-6, 6′); 20.67 (6Ac); 43.14 (C-3); 61.99, 62.03 (glucose C-6, 6′); 66.91, 67.36, 68.17, 68.30, 68.56, 68.72, 69.80, 70.12, 70.20, 70.73, 71.06, 72.00 (glucose C-2–4, 2′–4′; rhamnose C-2–4, 2′–4′); 78.65 (C-2); 95.51 (glucose C-1); 96.82 (C-6, 8); 98.13 (glucose C-1′); 98.97, 99.55 (rhamnose C-1, 1′); 103.00 (C-10); 117.04 (C-3′, 5′); 127.72 (C-2′, 6′); 132.89 (C-1′); 156.77 (C-4′); 162.98 (C-9); 164.29 (C-5); 165.19 (C-7); 169.66, 169.72, 169.96, 170.02, 170.28, 170.59 (each CO); 195.47 (C-4 CO).

Naringenin 4′-O-[2-O-(α-L-rhamnopyranosyl)-β-D-glucopyranoside] (*naringenin 4′-O-β-neohesperidoside*) (**15**) and *naringenin 4′-O-[2-O-(α-L-rhamnopyranosyl)-α-D-glucopyranoside]* (*naringenin 4′-O-α-neohesperidoside*) (**16**). **15**: Yield, 31.7%; $[\alpha]_D^{20}$ −48° (*c*=1, MeOH). *Anal.* Found; C, 51.58; H, 5.68. Calcd. for $C_{27}H_{32}O_{14}\cdot 2.5H_2O$: C, 51.84; H, 5.92%. UV λ_{max} (MeOH) nm: 289; λ_{max} (MeOH–AcONa) nm: 325; λ_{max} (MeOH–$AlCl_3$) nm: 312; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 309; λ_{max} (MeOH–MeONa) nm: 324. The sum of the $[M]_D$ values for methyl β-D-glucoside, methyl α-L-rhamnoside and for the aglycone was −17696°. The sum of the $[M]_D$ values for methyl α-D-glucoside, methyl α-L-rhamnoside and for the aglycone was 19746°. The observed $[M]_D$ value for **15** was −27840°. Accordingly, the D-glucopyranosidic bond in **15** was of β-form. NMR δ_H (DMSO-d_6): 1.19 (3H, d, *J*=6 Hz, CH_3); 2.43–2.87 (2H, m, H-3); 2.94–4.07 (10H, m, sugar H-2–6, 2′–5′); 4.30–4.73 (1H, m, sugar H-1′); 4.90–5.22 (1H, m, sugar H-1); 5.37–5.64 (1H, m, H-2); 5.89 (2H, s, H-6, 8); 7.03 (2H, d, *J*=8 Hz, H-3′, 5′); 7.45 (2H, d, *J*=8 Hz, H-2′, 6′); 12.15 (1H, s, C_5–OH). NMR δ_C (DMSO-d_6): 18.00 (CH_3); 41.97 (C-3); 60.05 (sugar C-6′); 68.23 (sugar C-5′); 69.80 (sugar C-4); 70.41 (sugar C-2′); 70.47 (sugar C-3′); 71.88 (sugar C-4′); 76.77 (sugar C-2); 76.82 (sugar C-3); 77.46 (sugar C-5); 78.06 (C-2); 95.04 (C-6, 8); 98.13 (sugar C-1); 100.36 (sugar C-1′); 101.66 (C-10); 115.76 (C-3′, 5′); 128.05 (C-2′, 6′); 131.88 (C-1′); 157.18 (C-4′); 162.69 (C-9); 163.37 (C-5); 166.75 (C-7); 195.92 (C-4). **16**: Yield, 13.6%; $[\alpha]_D^{20}$ 47° (*c*=1, MeOH). *Anal.* Found; C, 50.22; H, 5.66. Calcd. for $C_{27}H_{32}O_{14}\cdot 3.5H_2O$: C, 50.39; H, 6.07%. UV λ_{max} (MeOH) nm: 290; λ_{max} (MeOH–AcONa) nm: 324; λ_{max} (MeOH–$AlCl_3$) nm: 312; λ_{max} (MeOH–$AlCl_3$–HCl) nm: 308; λ_{max} (MeOH–MeONa) nm: 324. The sum of the $[M]_D$ values for methyl β-D-glucoside, methyl α-L-rhamnoside and for the aglycone was −17696°. The sum of the $[M]_D$ values for methyl α-D-glucoside, methyl α-L-rhamnoside and for the aglycone was 19746°. The observed $[M]_D$ values for **16** was 27260°. Therefore, the D-glucopyranosidic bond directly attached to the aglycone was of α-form. NMR δ_C (DMSO-d_6): 17.61 (CH_3); 42.05 (C-3); 60.57 (sugar C-6′); 68.86 (sugar C-5′); 69.89 (sugar C-4); 70.20 (sugar C-2′); 70.47 (sugar C-5); 71.66 (sugar C-2); 71.86 (sugar C-3′); 73.48 (sugar C-4′); 78.06 (sugar C-3); 78.85 (C-2); 95.02 (C-6, 8); 96.53 (sugar C-1); 101.63 (C-10); 102.62 (sugar C-1′); 116.34 (C-3′, 5′); 128.04 (C-2′, 6′); 132.04 (C-1′); 156.83 (C-4′); 162.67 (C-9); 163.34 (C-5); 166.79 (C-7); 195.86 (C-4).

7-Hydroxyflavanone 7-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranoside) (**35**). Yield, 57.3%; $[\alpha]_D^{20}$ −65° (*c*=1, $CHCl_3$). *Anal.* Found: C, 59.34; H, 5.33. Calcd. for $C_{27}H_{28}O_{10}\cdot 2H_2O$: C, 59.12; H, 5.84%. UV λ_{max} (MeOH) nm: 267.312. NMR δ_H ($CDCl_3$): 1.17 (3H, d, *J*=6 Hz, CH_3); 1.98, 2.02, 2.15 (9H, each s, 3Ac); 2.80–3.02 (2H, m, H-3); 3.70–3.95 (1H, m, sugar H-5); 4.90–5.50 (5H, m, H-2, sugar H-1–4); 6.60 (1H, d, *J*=2 Hz, H-8); 6.65 (1H, dd, *J*=10 Hz, *J*=2 Hz, H-6); 7.29 (5H, m, H-2′–6′); 7.75 (1H, d, *J*=10 Hz, H-5).

7-Hydroxy-4′-methoxyflavanone 7-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranoside) (**36**). Yield, 29.07%; $[\alpha]_D^{20}$ −70° (*c*=1, $CHCl_3$). *Anal.* Found: C, 56.19; H, 5.13. Calcd. for $C_{28}H_{30}O_{11}\cdot 3H_2O$: C, 56.38; H, 6.04%. UV λ_{max} (MeOH) nm: 267, 312. NMR δ_H ($CDCl_3$): 1.17 (3H, d, *J*=6 Hz, CH_3); 1.98, 2.02, 2.15 (9H, each s, 3Ac); 2.90 (2H, m, H-3); 3.75 (3H, s, OCH_3); 3.60–3.95 (1H, m, sugar H-5); 4.90–5.45 (5H, m, H-2, sugar H-1–4); 6.58 (1H, d, *J*=2 Hz, H-8); 6.60 (1H, dd, *J*=10 Hz, *J*=2 Hz, H-6); 6.80 (2H, d, *J*=9 Hz, H-2′–6′); 7.25 (2H, d, *J*=9 Hz, H-3′, 5′); 7.73 (1H, d, *J*=9 Hz, H-5).

Chalcone glycosides. Compounds **35** and **36** were each deacetylated with 0.1 N methanolic sodium methoxide at 0°C for 20 h, and then treated as just described to afford chalcone glycosides **37** and **38**, instead of the flavanone glycosides.

2′,4′-Dihydroxychalcone 4′-O-α-L-rhamnopyraoside (**37**). Quantitative yield, $[\alpha]_D^{20}$ −84° (*c*=1, MeOH), *Anal.* Found: C, 52.47; H, 5.65. Calcd. for $C_{21}H_{22}O_7\cdot 5H_2O$: C, 52.94; H, 6.72%. NMR δ_H (DMSO-d_6): 1.12 (3H, d, *J*=6 Hz, CH_3); 3.20–4.20 (4H, m, sugar H-2–5); 5.40 (1H, s, sugar H-1); 6.40–6.60 (2H, m, H-6, 8); 7.20–7.43 (4H, m, H-3–5, H_α); 7.50–7.85 (3H, m, H-2, 6, 5′); 8.05 (1H, d, *J*=10 Hz, H_β). The sum of the $[M]_D$ values for 2′,4′-dihydroxychalcone and for methyl α-L-rhamnoside was −11100°. The sum of the $[M]_D$ values for 2′,4′-dihydroxychalcone and for methyl β-L-rhamnoside was 1700°. The observed $[M]_D$ value for **37** was −32424°. Therefore, the configuration of the L-rhamnosyl bond of **37** was of α-form.

2′,4′-Dihydroxy-4-methoxychalcone 4′-O-α-L-rhamnopyranoside (**38**). Yield, 95.7%; $[\alpha]_D^{20}$ −86° (*c*=1, CH_3OH). UV λ_{max} (MeOH) nm: 363; λ_{max} (MeOH–AcONa) nm: 364. The sum of the $[M]_D$ values for methyl α-L-rhamnoside and for the aglycone was −11100°. The sum of the $[M]_D$ values for methyl β-L-rhamnoside and for the aglycone was 1700°. The observed $[M]_D$ value for **38** was −35776°. Accordingly, the configuration of the L-rhamnosyl bond of **38** was of α-form. *Anal.* Found: C, 63.30; H, 5.71. Calcd. for $C_{22}H_{24}O_8$: C, 63.46; H, 5.77%. NMR δ_H (DMSO-d_6): 1.13 (3H, d, *J*=6 Hz, CH_3); 3.30–5.30 (4H, m, sugar H-2–5); 5.50 (1H, s, sugar H-1); 6.52 (1H, d, *J*=2 Hz, H-6′); 7.02 (2H, d, *J*=9 Hz, H-3′,5′); 7.60–8.00 (4H, m, H-2, 6, 5′, H_α); 8.22 (1H, d, *J*=10 Hz, H_β).

General procedure for preparing the dihydrochalcone glycosides. To a solution of a flavanone glycoside (1 mmol) in 10% potassium hydroxide (10 ml) was added 10% palladium on carbon (0.5 g) and a few drops of ethanol, before the mixture was shaken with hydrogen (3.5 kg/cm²) at

room temperature for 3.5 h. After filtering, the filtrate was neutralized with Amberlite IR-120 (H^+) resin, filtered, and then evaporated to give the dihydrochalcone glycoside.

Naringenin dihydrochalcone 4'-O-[2-O-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**6**). Yield, 94.5%; mp 153°C, $[\alpha]_D^{20}$ −30° ($c=1$, MeOH). *Anal.* Found: C, 53.63; H, 6.58. Calcd. for $C_{27}H_{34}O_{13}\cdot 2H_2O$: C, 53.82; H, 6.31%. *Acetate*: mp 98–99°C, $[\alpha]_D^{20}$ −30° ($c=1$, $CHCl_3$). *Anal.* Found: C, 56.93; H, 5.65. Calcd. for $C_{43}H_{50}O_{21}$: C, 57.21; H, 5.54%. NMR δ_H ($CDCl_3$): 1.17, 1.24 (6H, each d, $J=6$ Hz, $2CH_3$); 1.93, 2.03, 2.12, 2.24 (24H, each s, 8Ac); 2.98 (4H, m, $2CH_2$); 3.50–4.04, 4.60–5.35 (10H, each m, sugar protons); 6.77 (2H, s, H-3', 5'); 6.94 (2H, d, $J=8$ Hz, H-3, 5); 7.20 (2H, d, $J=8$ Hz, H-2, 6).

Hesperetin dihydrochalcone 4'-O-[2-O-(α-L-rhamnopyranosyl)-β-L-quinovopyranoside] (**8**). Yield, 88.5%; mp 169–170°C, $[\alpha]_D^{20}$ −18° ($c=1$, MeOH). *Anal.* Found: C, 47.88; H, 5.89. Calcd. for $C_{28}H_{36}O_{14}\cdot 5.5H_2O$: C, 48.34; H, 6.76%. *Acetate*: mp 102–103°C, $[\alpha]_D^{20}$ −32° ($c=1$, $CHCl_3$). *Anal.* Found: C, 56.23; H, 5.66. Calcd. for $C_{44}H_{52}O_{22}$: C, 56.65; H, 5.58%. NMR δ_H ($CDCl_3$): 1.18, 1.26 (6H, each d, $J=6$ Hz, $2CH_3$); 1.94, 2.02, 2.04, 2.14, 2.27 (24H, each s, 8Ac); 2.73–3.06 (4H, m, $2CH_2$); 3.45–4.03 (2H, m, sugar H-5, 5'); 3.78 (3H, s, OMe); 4.56–5.35 (8H, m, sugar H-1–4, 1'–4'); 6.78 (2H, s, H-3', 5'); 6.70–7.02 (3H, m, H-2, 5, 6).

Naringenin dihydrochalcone 4-O-α-L-rhamnopyranoside (**11**). Yield, 25.1%; $[\alpha]_D^{20}$ −75° ($c=1$, MeOH). *Anal.* Found: C, 56.55; H, 6.03. Calcd. for $C_{21}H_{24}O_9\cdot 1.5H_2O$: C, 56.38; H, 6.04%. *Acetate*: *Anal.* Found: C, 58.30; H, 5.35. Calcd. for $C_{33}H_{36}O_{15}$: C, 58.93; H, 5.36%. NMR δ_H ($CDCl_3$): 1.15 (3H, d, $J=6$ Hz, CH_3); 2.15, 2.17, 2.20, 2.22, 2.30 (18H, each s, 6Ac); 2.90–3.10 (4H, m, $2CH_2$); 3.90–4.20 (1H, m, sugar H-5); 5.00–5.65 (4H, m, sugar H-1–4); 6.95 (2H, s, H-6', 8'); 7.00 (2H, d, $J=9$ Hz, H-3, 5); 7.20 (2H, d, $J=9$ Hz, H-2, 6).

Naringenin dihydrochalcone 4-O-[2-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside] (**13**). Yield, 35.5%; $[\alpha]_D^{20}$ −68° ($c=1$, MeOH). *Anal.* Found: C, 54.67; H, 6.29. Calcd. for $C_{27}H_{34}O_{13}\cdot 1.5H_2O$: C, 54.63; H, 6.24%. *Acetate*: *Anal.* Found: C, 56.69; H, 5.62. Calcd. for $C_{43}H_{50}O_{21}$: C, 57.21; H, 5.54%. NMR δ_H ($CDCl_3$): 1.20 (6H, d, $J=6$ Hz, $2CH_3$); 2.00, 2.03, 2.06, 2.10, 2.15, 2.27 (24H, each s, 8Ac); 2.90–3.07 (4H, m, $2CH_2$); 3.80–4.23 (2H, m, sugar H-5); 4.85–5.53 (8H, m, sugar H-1–4, 1'–4'); 6.93 (2H, s, H-6', 8'); 6.95 (2H, d, $J=9$ Hz, H-3', 5'); 7.16 (2H, d, $J=9$ Hz, H-2', 6').

Taste properties of the synthesized glycosides. The taste properties of the synthesized glycosides of flavanone and of dihydrochalcone were examined in comparison with those of naringin or sucrose by five young male panelists. Each sample (10 mg) was dissolved in distilled water (10 ml) or 50% ethanol (10 ml), and then diluted with water until its bitterness or sweetness was barely detectable. The relative bitterness or sweetness is shown by the lowest concentration (%) having about the same degree of bitterness or sweetness.

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