The **acetate**, m.p. 122.5–123° (lit.[7] m.p. 121°), was obtained in 92% yield with boiling acetic anhydride containing a few drops of concentrated sulfuric acid.

5-Amino-6-hydroxy-4-methylcoumarin (IVc).—A cold solution of sodium hydrosulfite (150 g.) in 600 ml. of water was added rapidly to an ice-cold solution of 6-hydroxy-4-methyl-5-nitrocoumarin (9.70 g., 0.044 mole) in 120 ml. of concentrated ammonium hydroxide. The orange solution was stirred for 90 min. while a yellow crystalline precipitate (7.0 g., 84% yield) of m.p. 253–255.5° dec. formed. Recrystallization from 95% ethanol gave yellow prisms, m.p. 257–259° dec.

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.74; H, 5.02; N, 7.46.

5,6-Dihydroxy-4-methylcoumarin (IVd).—A 10% aqueous solution of ferric chloride (75 ml., 0.028 mole) was added to a stirred solution of 5-amino-6-hydroxy-4-methylcoumarin (5.00 g., 0.026 mole) in 60 ml. of 10% hydrochloric acid. A black precipitate formed almost immediately, and from it light yellow prisms (1.50 g., 30% yield), instantaneous m.p. 247–249° (lit.[1] m.p. 251–252°), were obtained by vacuum sublimation at 0.1 mm.

The **diacetate**, m.p. 174–175° (lit.[1] m.p. 173–175°), was obtained in 63% yield using acetic anhydride and pyridine.

6-Allyloxy-4-methyl-5-nitrocoumarin (Va).—A mixture of crude 6-hydroxy-4-methyl-5-nitrocoumarin (100 g., 0.452 mole) of m.p. 208–215° dec., allyl bromide (190 ml.), anhydrous potassium carbonate (150 g.), and acetone (3 l.) was refluxed for 12 hr. The reaction mixture was concentrated under reduced pressure on the steam bath and water was added to the dry residue. A solution of the water-insoluble product in benzene was filtered through a short column of acid-washed alumina and concentrated to a solid which crystallized from 95% ethanol as yellow needles (80 g., 68% yield), m.p. 155–156°.

Anal. Calcd. for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.94; H, 4.24; N, 5.39.

6-Allyloxy-5-amino-4-methylcoumarin (Vb).—A suspension of 6-allyloxy-4-methyl-5-nitrocoumarin (10.0 g., 0.038 mole) and stannous chloride dihydrate (40.0 g., 0.18 mole) in 95% ethanol (40 ml.) and concentrated hydrochloric acid (120 ml.) was boiled for 5 min. to form a clear solution. Upon being cooled in the refrigerator, the solution deposited crystals which were washed with 5% aqueous sodium bicarbonate and recrystallized from carbon tetrachloride to obtain yellow needles (6.2 g., 71% yield), m.p. 117–118°.

Anal. Calcd. for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.24; H, 5.87; N, 5.64.

5-Acetamido-6-allyloxy-4-methylcoumarin (Vc).—Treatment of 6-allyloxy-5-amino-4-methylcoumarin with acetic anhydride in boiling acetic acid gave the amide, which crystallized from ethanol as colorless plates, m.p. 149° (87% yield).

Anal. Calcd. for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 66.02; H, 5.37; N, 4.90.

7-Allyl-β,2-dimethyl-5-hydroxy-4-benzoxazoleacrylic Acid δ-Lactone (VIa).—A solution of 5-acetamido-6-allyloxy-4-methylcoumarin (2.00 g., 0.0073 mole) in 5 ml. of diethylaniline was refluxed for 1 hr. Dilution of the cooled reaction mixture with 5% aqueous hydrochloric acid gave a tan solid (1.85 g., 99% yield), m.p. 177–178°. Recrystallization from carbon tetrachloride gave an analytical sample, m.p. 179°. Its infrared spectrum showed absorption at 1720 (C=O) and 1680 cm.$^{-1}$ (C=N), and its ultraviolet spectrum in ethanol showed a peak at 298 mμ (log ε 4.27) and inflections at 240 mμ (log ε 3.55), 324 (3.96), and 340 (3.58).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.47; H, 5.06; N, 5.31.

β,2-Dimethyl-5-hydroxy-4-benzoxazoleacrylic Acid δ-Lactone (VIb).—Powdered iron (3.00 g.) was added to a solution of 6-hydroxy-4-methyl-5-nitrocoumarin acetate (3.00 g., 0.0114 mole), sodium acetate (2.00 g.), acetic anhydride (6.0 ml.), and acetic acid (50 ml.) while the solution was being stirred and heated on a steam bath. After 2 hr., the reaction mixture was diluted with water and filtered to obtain a solid which crystallized from chloroform as colorless needles (0.45 g., 18% yield), m.p. 246°. Its ultraviolet spectrum in ethanol showed a peak at 292 mμ (log ε 4.26) and inflections at 244 mμ (log ε 3.57) and 336 (3.41).

Anal. Calcd. for $C_{12}H_9NO_3$: C, 66.97; H, 4.22; N, 6.51. Found: C, 67.50; H, 4.46; N, 6.40.

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The Nuclear Magnetic Resonance Analysis of the Disaccharide in Flavonoid Rhamnoglucosides

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Rutinose and neohesperidose, 6- and 2-O-α-L-rhamnopyranosyl-β-D-glucopyranose, respectively, are the only two disaccharides containing glucose and rhamnose which have been reported in naturally occurring flavonoid glycosides.[1] The presence of the individual sugars, rhamnose and glucose, obtained after hydrolysis of the diglycoside, is readily established by paper chromatography or, after trimethylsilylation, by gas chromatography.[2] On the other hand, the structure of the disaccharide is often determined with difficulty. The hydrolysis of the flavonoid–disaccharide linkage without breaking the bond between the two sugars is sometimes possible for flavonoid 3-rhamnoglucosides[3] but usually fails for 7-diglycosides unless specific enzymes are used.[4] An alternate procedure has been the ozonolysis of the diglycoside which yields the disaccharide but destroys the flavonoid portion of the molecule.[5]

We now report that the two known types of flavonoid rhamnoglucosides, rutinosides and neohesperidosides, are distinguished by the n.m.r. analysis of their acetates and of their trimethylsilyl ethers. Furthermore, the original glycosides can be recovered nearly quantitatively from these derivatives.

The structures of the disaccharide in rutin, hesperidin, neohesperidin, and naringin (Chart I) are well established and were recently reviewed by Horowitz.[6] In order to study the influence of the oxidation level of the aglycone on the sugar part of the n.m.r. spectra, representative examples of flavonol and flavone rutinosides and neohesperidosides have been prepared (Chart I).

The flavonols tamarixetin 7-rutinoside (**7**), tamarixetin 7-neohesperidoside (**8**), and kaempferol 7-neohesperidoside (**9**) were obtained in good yield from **1**, **3**, and **2**, respectively, by the elegant method of Pacheco, *et al.*[7] The flavone rhamnoglucosides diosmin (**4**) and

(1) J. B. Harborne in "Biochemistry of Phenolic Compounds," J. B. Harborne, Ed., Academic Press Inc., New York, N. Y., 1964, p. 133.

(2) J. Kagan and T. J. Mabry, *Anal. Chem.*, **37**, 288 (1965); C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).

(3) G. Zemplen and A. Gereos, *Chem. Ber.*, **71**, 2520 (1938).

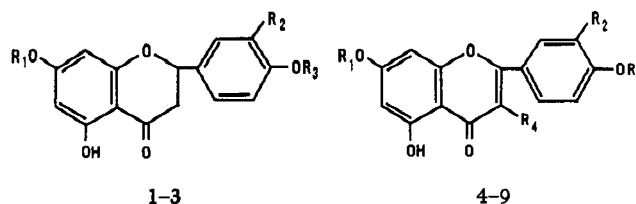
(4) C. Charoux, *Compt. rend.*, **178**, 1312 (1924).

(5) M. Kotake and H. Abrakawa, *Bull. Chem. Soc. Japan*, **30**, 862 (1957).

(6) R. M. Horowitz, ref. 1, p. 545.

(7) M. H. Pacheco and A. Grouiller, *Compt. rend.*, **255**, 3432 (1962); **256**, 4927 (1963).

CHART I

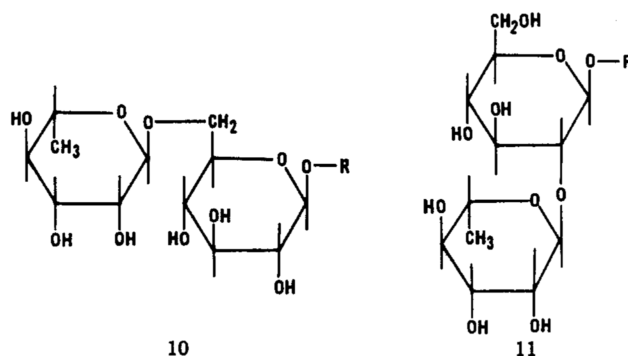


	Rutinosides	Neohesperidosides
Flavanones	**1**, hesperidin, R_1 = rutinose; R_2 = OH; R_3 = CH_3	**2**, naringin, R_1 = neohesperidose; R_2 = R_3 = H **3**, neohesperidin, R_1 = neohesperidose; R_2 = OH; R_3 = CH_3
Flavones	**4**, diosmin, R_1 = rutinose; R_2 = OH; R_3 = CH_3; R_4 = H	**5**, apigenin 7-neohesperidoside, R_1 = neohesperidose; R_2 = R_3 = R_4 = H
Flavonols	**6**, rutin, R_4 = O-rutinose; R_1 = R_3 = H; R_2 = OH	**8**, tamarixetin 7-neohesperidoside, R_1 = neohesperidose; R_2 = R_4 = OH; R_3 = CH_3
	7, tamarixetin 7-rutinoside, R_1 = rutinose; R_2 = R_4 = OH; R_3 = CH_3	**9**, kaempferol 7-neohesperidoside, R_1 = neohesperidose; R_2 = R_3 = H; R_4 = OH

apigenin 7-neohesperidoside (**5**) were obtained from **1** and **2**, respectively, by a slight modification of the procedure of Mahesh and Seshadri.[8] We found it advantageous to maintain anhydrous conditions for the iodine oxidation of the flavanone glycosides **1** and **2**, which were effected by replacing acetic acid by acetic anhydride as solvent.

Discussion

The chemical shift of the C-1 proton of the sugar directly attached to the flavonoid depends on the nature of this flavonoid and on the position of attachment to it.[9,10] In all the compounds herein described, rhamnose is not directly attached to the flavonoid and its n.m.r. spectrum is therefore essentially independent of these factors. It depends only on the type of linkage of rhamnose to glucose, thus providing a convenient method of analysis for the two linkages present in rutinosides (**10**) and neohesperidosides (**11**). It is possible that other as yet unreported linkages of rhamnose to glucose might not be distinguished by this technique.



In the trimethylsilyl ethers of rutinosides (**10**, R = flavonoid), rhamnose is characterized, in part, by a signal near 4.2–4.4[11] (J = 2 c.p.s.) for the C-1 proton and a broad peak at 0.8–1.0 for the methyl group.

In neohesperiodosides (**11**, R = flavonoid), the rhamnose C-1 proton is found at 4.9–5.0 (J = 2 c.p.s.), and the methyl appears as a doublet at 1.1–1.2 (J = 6 c.p.s.).

The remarkable difference in these rhamnose signals is illustrated by the spectra A and C in Figure 1, which represent the sugar moieties of the trimethylsilyl ethers of apigenin 7-neohesperidoside (**5**) and diosmin (**4**). All the rhamnoglucosides which we studied behaved similarly. The assignment of rhamnoglucosides to rutinosides and neohesperidosides can be confirmed by the study of the n.m.r. spectra of these flavonoids after acetylation. As illustrated by the spectra B and D (Figure 1) of the sugar moieties of the acetates of apigenin 7-neohesperidoside and diosmin, the signals for the sugar protons are found in three distinct areas, and the number of protons in these areas is characteristic of rutinosides and neohesperidosides. All the methine protons next to an acetate or to two ether linkages are found at lower field while the methylene protons and the methine protons next to a single ether group appear at higher field. The rhamnose methyl group appears as a doublet (J = 6 c.p.s.) at a much higher field; it is found at 1.0–1.3 in acetylated rhamnoglucosides. In acetylated neohesperidosides, the complex signal at 4.5–5.5, integrating for seven protons, represents the hydrogens at the positions 1, 2, 3, and 4 of rhamnose and 1, 3, and 4 of glucose. The signals at 3.4–4.4, integrating for five protons, represent the hydrogens at the positions 5 of rhamnose and 2, 5, and 6 of glucose. In acetylated rutinosides, the signals at 4.5–5.6, integrating for eight protons, represent the hydrogens at the positions 1, 2, 3, and 4 of glucose and 1, 2, 3, and 4 of rhamnose while the signals at 3.4–4.4, integrating for four protons, represent the hydrogens at the positions of 5 and 6 of glucose and 5 of rhamnose. Methoxyl signals fall in the 3.4–4.4 region but can be easily recognized by their sharpness. Furthermore, the presence of methoxyl groups is usually known from the study of the n.m.r. spectra of the aglycone and of the trimethylsilylated glycoside.

The integration of the regions 4.5–5.5 and 3.4–4.4 of the spectrum of an acetylated rhamnoglucoside there-

(8) V. B. Mahesh and T. R. Seshadri, *J. Sci. Ind. Res.* (India), **B14**, No. 11, 608 (1955).

(9) T. J. Mabry, J. Kagan, and H. Rösler, *Phytochemistry*, **4**, 177 (1965).

(10) T. J. Mabry, J. Kagan, and H. Rösler, "Nuclear Magnetic Resonance Analysis of Flavonoids," The University of Texas Publication No. 6418, Austin, Texas, 1964.

(11) All chemical shift values are reported in δ, where δ equals parts per million from tetramethylsilane, the internal reference.

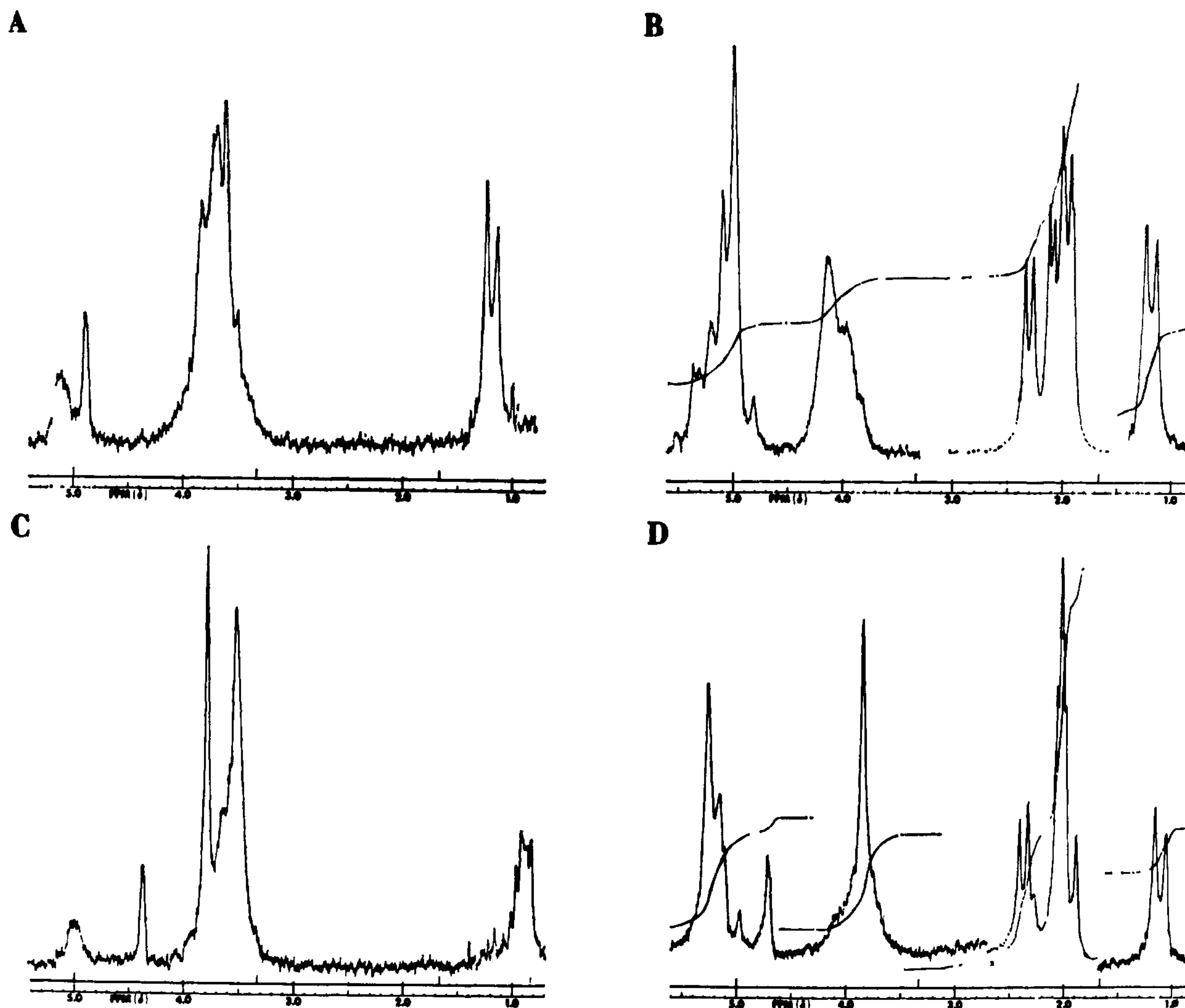


Figure 1.—The n.m.r. spectra of (A) neohesperidose in trimethylsilylated apigenin 7-neohesperidoside; (B) neohesperidose in acetylated apigenin 7-neohesperidoside; (C) rutinose in trimethylsilylated diosmin; and (D) rutinose in acetylated diosmin. The spectra B and D were recorded at reduced amplitude between 1.7 and 2.7.

fore distinguishes unambiguously rutinosides (ratio 8:4) from neohesperidosides (ratio 7:5). Furthermore, the signal for the C-1 proton of rhamnose in acetylated rutinosides is clearly separated from the other ones in the lower field area and is easily recognized because of its sharpness. It is found at 4.74 in the case of diosmin (D, Figure 1).

Experimental Section

The n.m.r. spectra were obtained on a Varian A-60 spectrometer and were determined in carbon tetrachloride (trimethylsilyl ethers) or deuterated chloroform (acetates). The signals are reported with the following abbreviations: s = singlet, d = doublet, b = broad, and m = complex multiplet. The melting points were determined on a Fisher-Johns block and are uncorrected. The ultraviolet spectra were obtained on a recording Beckman DB spectrophotometer.

The n.m.r. spectra for the trimethylsilyl ethers of the commercially available flavonoids (**1**, **2**, **3**, and **6**) have been previously reported.[10] Naringin (practicum), hesperidin (purum), and neohesperidin (purum) were purchased from Fluka A.G., Buchs, Switzerland. The purity of the commercial and synthetic compounds described was ascertained by two-dimensional paper chromatography in *t*-butyl alcohol–acetic acid–water (3:1:1) and 15% acetic acid or by polyamide thin layer chromatography in methanol–acetic acid–water (18:1:1) as well as by the n.m.r. spectra of their trimethylsilyl ethers. The trimethylsilylations were performed as previously reported.[9,10] The acetylations were made in pyridine–acetic anhydride by the standard procedure.

Diosmin (4).—A solution of 2 g., of hesperidin and 2 g. of sodium acetate in 20 ml. of acetic anhydride was refluxed for 5 min. Iodine (1 g.) was added and the reflux was continued for 15 hr. The solution was poured into 400 ml. of ice–water containing 2 g. of potassium iodide. Three hours later a brown semicrystalline solid was filtered off. It was dissolved in 80 ml. of methanol and the solution was decolorized by the addition of the minimum amount of a sodium bisulfite solution. The precipitate obtained upon dilution of this solution with water was deacetylated to yield 1.5 g. of crude diosmin, which contained a flavanone-like impurity (different from hesperidin). This impurity was destroyed by dissolving the product in 100 ml. of boiling 10% potassium hydroxide solution to which was subsequently added 0.5 ml. of 30% hydrogen peroxide. After 2 min. boiling, the solution was chilled and acidified with acetic acid. The precipitate was recrystallized four times from a dimethyl sulfoxide solution by addition of methanol. The pure diosmin, m.p. 290–292° (lit.[12] m.p. 278), could be hydrolyzed in concentrated hydrochloric acid at reflux to yield the aglycone diosmetin, m.p. (after sublimation) 253–254° (lit.[12] m.p. 253).

The trimethylsilylation of the highly insoluble diosmin was performed by refluxing it in the presence of pyridine with an excess of hexamethyldisilazane for 30 min. The solution was then cooled at room temperature and the reaction was completed by the addition of trimethylchlorosilane.

Octa(trimethylsilyl)diosmin had the following n.m.r. spectrum: aromatic protons: H-6′ at 7.38 (m); H-2′ at 7.25 (m); H-5′ at 6.84 (d, J_o = 8.5 c.p.s.); H-8 at 6.62 (d, J_m = 2.5 c.p.s.); and H-3,6 at 6.29 (b); rhamnoglucosyl and methoxyl protons: glucose H-1 at 5.0 (b); rhamnose H-1 at 4.40 (s); rhamnoglu-

(12) O. A. Oesterle and G. Wander, *Helv. Chim. Acta*, **8**, 519 (1925).

cose (10 protons) + 4′-OCH_3 (s, 3.8) at 3.2–4.0; rhamnose -CH_3 at 0.9 (b).

Octaacetyldiosmin was precipitated from ethanol–water: m.p. 129–130°; n.m.r. aromatic protons: H-2′,6′ at 7.42–7.76 (m); H-5′,8 at 6.82–7.2, (m); H-6 at 6.62 (d, J_m = 2.5 c.p.s.); H-3 at 6.45 (s); rhamnoglucosyl and methoxyl protons: glucose H-1,2,3,4 and rhamnose H-1,2,3,4 at 4.65–5.50; 4′-OCH_3 and glucose H-5,6,6 and rhamnose H-5 at 3.50–4.30; and rhamnose -CH_3 at 1.14 (d, J = 6 c.p.s.); acetyl protons at 1.8–2.6.

Apigenin 7-Neohesperidoside (5).—The oxidation procedure described for the preparation of diosmin (4) was followed to convert naringin (2) into 5. The crude apigenin 7-neohesperidoside could be purified by repeated crystallizations from methanol without additional treatment. The pure sample melted at 198–200°: λ_{max}^{MeOH} 340 mμ (log ε 4.45) and 266 mμ (log ε 4.60).

Octa(trimethylsilyl)(apigenin 7-neohesperidoside) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 7.70 (d, J_o = 8.5 c.p.s.); H-3′,5′ at 6.80 (d, J_o = 8.5 c.p.s.); H-8 at 6.72 (b); H-3,6 at 6.39 (b); rhamnoglucosyl protons: glucose H-1 at 5.12 (b); rhamnose H-1 at 4.89 (s); rhamnoglucose (10 protons) at 3.20–4.20; rhamnose -CH_3 at 1.20 (d, J = 6 c.p.s.).

Octaacetyl(apigenin 7-neohesperidoside) (m.p. 215–217°) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 7.82 (d, J_o = 8.5 c.p.s.); H-3′,5′ at 7.18 (d, J_o = 8.5 c.p.s.); H-8 at 6.98 (d, J_m = 2 c.p.s.); H-6 at 6.66 (d, J_m = 2 c.p.s.); H-3 at 6.5 (s); rhamnoglucosyl protons: glucose H-1,3,4 and rhamnose H-1,2,3,4 at 4.80–5.55; glucose H-2,5,6,6 and rhamnose H-5 at 1.8–2.5; rhamnose -CH_3 at 1.2 (d, J = 6 c.p.s.); acetyl protons at 1.8–2.5.

Compounds 7, 8, and 9 were obtained following the procedure of Pacheco and Grouiller.[7]

Tamarixetin 7-Rutinoside (7).—Hesperidin (2 g.) afforded 1.3 g. of crude tamarixetin 7-rutinoside. After several recrystallizations from methanol, the pure sample melted at 247–249°: λ_{max}^{MeOH} 372 mμ (log ε 3.90), 270 (infl.), and 254 (log ε 4.00). It yielded the aglycone tamarixetin on acid hydrolysis, m.p. 255–257° (lit.[13] m.p. 259–260).

Nona(trimethylsilyl)(tamarixetin 7-rutinoside) had the following n.m.r. spectrum: aromatic protons: H-6′ at 7.70 (m); H-2′ at 7.60 (m); H-5′ at 6.86 (d, J_o = 8.5 c.p.s.); H-8 at 6.60 (d, J_m = 2.5 c.p.s.); H-6 at 6.28 (d, J_m = 2.5 c.p.s.); rhamnoglucosyl and methoxyl protons: glucose H-1 at 5.0 (b); rhamnose H-1 at 4.40 (s); rhamnoglucose (10 protons) at 3.20–4.00; 4′-OCH_3 at 3.88 (s); rhamnose -CH_3 at 0.92 (b).

Nonaacetyl(tamarixetin 7-rutinoside) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 7.50–7.85 (m); H-5′,8 at 6.90–7.20 (m); H-6 at 6.70 (d, J_m = 2.5 c.p.s.); rhamnoglucosyl and methoxyl protons: glucose H-1,2,3,4 and rhamnose H-1,2,3,4 at 4.65–5.50; glucose H-5,6,6 and rhamnose H-5,4′-OCH_3 at 3.50–4.20; rhamnose -CH_3 at 1.15 (d, J = 6 c.p.s.); acetyl protons at 1.80–2.50.

Tamarixetin 7-Neohesperidoside (8).—Neohesperidin (0.2 g.) yielded 0.12 g. of 8: m.p. 266–269°; λ_{max}^{MeOH} 372 mμ (log ε 2.90), 270 (infl.), and 255 (4.02).

Non(trimethylsilyl)(tamarixetin 7-neohesperidoside) had the following n.m.r. spectrum: aromatic protons: H-2′ at 7.76 (m); H-6′ at 7.74 (m); H-5′ at 6.84 (d, J_o = 8.5 c.p.s.); H-8 at 6.74 (d, J_m = 2.5 c.p.s.); H-6 at 6.36 (d, J_m = 2.5 c.p.s.); rhamnoglucosyl and methoxyl protons: glucose H-1 at 5.18 (b); rhamnose H-1 at 4.92 (s); rhamnoglucose (10 protons) at 3.30–4.10; 4′-OCH_3 at 3.82 (s); rhamnose -CH_3 at 1.24 (d, J = 6 c.p.s.).

Nonaacetyl(tamarixetin 7-neohesperidoside) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 7.50–7.82 (m); H-5′,8 at 6.90–7.18 (m); H-6 at 6.74 (d, J_m = 2.5 c.p.s.); rhamnoglucosyl and methoxyl protons: glucose H-1,3,4 and rhamnose H-1,2,3,4 at 4.80–5.60; glucose H-2,5,6,6 and rhamnose H-5,4′-OCH_3 at 3.70–4.40; rhamnose -CH_3 at 1.22 (d, J = 6 c.p.s.); acetyl protons at 1.85–2.50.

Kaempferol 7-Neohesperidoside (9).—Naringin (2 g.) yielded 1.4 g. of crude 9. After recrystallization from methanol, crystals were obtained which sintered at 205° and melted at 252–255°: λ_{max}^{MeOH} 368 mμ (log ε 4.18), 328 (infl.), 266 (4.17), and 252 (infl.).

Nona(trimethylsilyl)(kaempferol 7-neohesperidoside) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 8.4 (d, J_o = 8.5 c.p.s.); H-3′,5′, 8 at 6.65–7.02 (m); H-6 at 6.4 (d, J_m = 2.0 c.p.s.); rhamnoglucosyl protons: glucose H-1 at 5.12 (b); rhamnose H-1 at 4.92 (s); rhamnoglucose (10 protons) at 3.25–4.15; rhamnose -CH_3 at 1.24 (d, J = 6 c.p.s.).

Nonaacetyl(kaempferol 7-neohesperidoside) (m.p. 144–145°) had the following n.m.r. spectrum: aromatic protons: H-2′,6′ at 7.84 (d, J_o = 8.5 c.p.s.); H-3′,5′ at 7.26 (d, J_o = 8.5 c.p.s.); H-8 at 7.06 (d, J_m = 2.5 c.p.s.); H-6 at 6.76 (d, J_m = 2.5 c.p.s.); rhamnoglucosyl protons: glucose H-1,3,4 and rhamnose H-1,2,3,4 at 4.80–5.60; glucose H-2,5,6,6 and rhamnose H-5 at 3.70–4.35; rhamnose -CH_3 at 1.22 (d, J = 6 c.p.s.); acetyl protons at 1.85–2.5.

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(13) S. R. Gupta and T. R. Seshadri, *J. Chem. Soc.*, 3063 (1954).

Relative Rates of Hydrolysis of the Anomeric 1-O-Acetyltetra-O-methyl-D-glucopyranoses

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Of the eight conformations (six boat and two chair) of the pyranose ring, the boat forms are generally rejected as being unlikely or energetically unstable.[3,4] The two chair conformations of the anomeric glucopyranoses are shown in Figure 1. The work of Reeves[5] has shown that for both anomers the favored conformation is that shown as C1. Using proton magnetic resonance Lemieux and co-workers[6] have shown that the anomeric pentaacetates of glucose, galactose, and mannose exist in the C1 conformation. The favored conformation (C1) of the β anomer has the hydroxyl group on carbon 1 in the equatorial position while the favored conformation (C1) of the α anomer has the hydroxyl on carbon 1 in the axial position. Since equatorial groups are sterically less hindered than axial groups, the more stable anomer would be the β anomer. This agrees with the well-known fact that an aqueous solution of glucose is composed of about 63% of the β anomer and about 37% of the α anomer.

On the same basis, the favored conformations of the anomeric 1-O-acetyltetra-O-methyl-D-glucopyranoses would be predicted to be the C1 conformation. The C1 conformation of the β anomer has the acetyl group in the equatorial position while the α anomer has the acetyl in the axial position in the C1 conformation. Examination of molecular models shows that the carbonyl of the equatorial acetyl group is more exposed to attack than the carbonyl in the axial position. On this basis it would be predicted that the β anomer would undergo alkaline hydrolysis faster than the α anomer. A study of the mechanism of ester hydrolysis

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