Anal. Calcd. for $C_{22}H_{25}NO$: C, 82.72; H, 7.89: N, 4.39. Found: for Xa, C, 82.63; H, 7.91; N, 4.48; for Xb: C, 82.39; H, 7.45; N, 4.43.

Reaction of *cis*- and *trans*-Ethylenimine Ketones Xa and Xb with Phenylhydrazine.—A 1.4-g. (0.004 mole) amount of Xb was dissolved in 30 ml. of abs. ether and 0.49 g. (0.004 mole) of pure phenylhydrazine added. After standing in the dark at room temperature the solid crystalline precipitate was removed by filtration and washed with cold ether, m.p. 154° (instantaneous), colorless crystals, wt. 0.83 g. Attempts to recrystallize this amino pyrazoline XI from warm benzene quantitatively converted it to the pyrazole IX, m.p. 120°. Carbon–hydrogen analysis of the pyrazoline XI required the precaution of mixing the sample with copper oxide in the combustion boat to prevent the rapid escape of cyclohexylamine. The amino pyrazoline XI gave a positive Knorr and Raiford pyrazoline test[14]; ultraviolet (95% ethanol) λ_{max} 259 mμ (ε 27,200).

(14) L. Raiford and W. Peterson, *J. Org. Chem.*, **1**, 544 (1937).

Anal. Calcd. for $C_{28}H_{31}N_3$: C, 82.11; H, 7.63; N, 10.26. Found for XI: C, 81.71; H, 7.94; N, 10.02.

A similar experiment with the low-melting ethylenimine ketone XA produced only the pyrazole IX, m.p. 120°. In the presence of acetic acid both Xa and Xb decomposed rapidly to red oils.

3,4-Dimorpholine-4-(*p*-biphenylyl)-2-butanone (XII).—A 7.6-g. (0.020 mole) sample of the dibromide II was mixed with 40 ml. of abs. ethanol and 7.1 g. (0.082 mole) of morpholine and held in a water-bath at 20° for 30 minutes. The morpholine hydrobromide was removed by filtration and the filtrate concentrated to produce a residue which was recrystallized from abs. ethanol and then abs. ether to give 4.9 g. (62% yield) of a colorless crystalline product, m.p. 155–157°.

Anal. Calcd. for $C_{24}H_{30}N_2O_3$: C, 73.06; H, 7.67; N, 7.10. Found: C, 73.19; H, 7.72; N, 7.08.

LINCOLN, NEBR.

[CONTRIBUTION FROM THE FRUIT AND VEGETABLE CHEMISTRY LABORATORY, WESTERN UTILIZATION RESEARCH AND DEVELOPMENT DIVISION, AGRICULTURAL RESEARCH SERVICE, U. S. DEPARTMENT OF AGRICULTURE]

Plant Polyphenols. IV. Migration of Acetyl Groups during Alkylation of the Partial Acetates of Flavonoid Compounds

BY LEONARD JURD[1] AND L. A. ROLLE

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Quercetin 3,3′,4′,7-tetraacetate (II, R = H) and rhamnetin 3,3′,4′-triacetate react with methyl iodide and potassium carbonate in acetone to give 5-O-methylquercetin tetraacetate and 5,7-di-O-methylquercetin triacetate. The benzylation of these compounds does not, however, give the corresponding 5-O-benzyl compounds. Acetyl migration occurs during the benzylation reaction. Quercetin 3,3′,4′,7-tetraacetate and 4-acetylresacetophenone (VI) give 7-O-benzylquercetin tetraacetate and 4-O-benzyl-2-acetylresacetophenone (VII), respectively.

Flavones which contain an hydroxyl group in position 3 and *o*- or *p*-dihydroxyl groupings in the B ring (I) inhibit the aerobic oxidation of unsaturated fats. A free *m*-dihydroxyl grouping in the 5,7-position of the A ring, however, has a pro-oxidant effect.[2–5] As part of an investigation on the development of potential anti-oxidants from phenolic natural products methods are being studied for the selective alkylation of those hydroxyl groups (5- and 7-) of flavones which exert undesirable oxidant effects.

The purpose of this communication is to describe the results of experiments which originally were undertaken to prepare a series of 5-alkyl ethers of quercetin. In each case the constitution of the product first was established spectrophotometrically and then confirmed analytically and by comparison of the melting points of derivatives with literature values for known compounds. The spectrophotometric method designed to locate hydroxyl functions in flavonols was reported recently.[6,7] In this procedure the spectrum of the flavonol is determined successively in ethanol, ethanolic sodium acetate, ethanolic boric acid–sodium acetate and in sodium ethylate. A bathochromic shift (8–20 mμ) of the low wave length band in sodium acetate indicates a free 7-hydroxyl group. A bathochromic shift (15–30 mμ) of the long wave length band in boric acid–sodium acetate shows the presence of a free *o*-dihydroxyl group. Decomposition with disappearance of the long wave length band in sodium ethylate establishes the presence of a free 3,4′-dihydroxyl group. Stability in sodium ethylate shows that either the 3- or 4′- (or both) hydroxyl group is alkylated.

Kubota and Perkin[8] have reported that quercetin 3,3′,4′,7-tetraacetate (II, R = H) slowly reacts with diazomethane to give the tetraacetate II (R = Me) of 5-O-methylquercetin. It now has been found that quercetin 3,3′,4′,7-tetraacetate also reacts with methyl iodide and potassium carbonate in anhydrous acetone[9] to yield a monomethylquercetin tetraacetate whose properties closely agree with those of Perkin's product. On alkaline hydrolysis the tetraacetate gives a monomethylquercetin whose spectra (Fig. 1) confirm the location of the methoxyl group at position 5. The low wave length band in alcohol (253 mμ) shifts 20 mμ on the addition of sodium acetate thus showing the presence of a free 7-hydroxyl.[6] A free *o*-dihydroxyl group (3′,4′-) is indicated by the 17 mμ shift of the long wave length band in boric acid–sodium acetate[7] while the disappearance of the long wave length band in sodium ethylate shows that the hydroxyls at both the 3 and 4′-positions are free.[6] Therefore, since the hydroxyls at positions 3,3′,4′,7 are unprotected, the methoxyl group is located at position 5.

(1) Financial support for this work was provided by the Diamond Walnut Growers, Inc.

(2) T. H. Simpson and N. Uri, *Chemistry and Industry*, 956 (1956).

(3) C. H. Lea and P. A. T. Swoboda, *ibid.*, 1426 (1956).

(4) W. Heimann, A. Heimann and H. Holland, *Fette u. Seifen*, **55**, 394 (1953).

(5) W. Heimann and F. Reiff, *ibid.*, **55**, 451 (1953).

(6) L. Jurd and R. M. Horowitz, *J. Org. Chem.*, **22**, 1618 (1957).

(7) L. Jurd, *Arch. Biochem. and Biophys.*, **63**, 376 (1956).

(8) O. Kubota and A. G. Perkin, *J. Chem. Soc.*, **127**, 1889 (1925).

(9) *Cf.* V. B. Mahesh, S. Neelakanton and T. R. Seshadri, *J. Sci. Ind. Research (India)*, **15B**, 287 (1956).

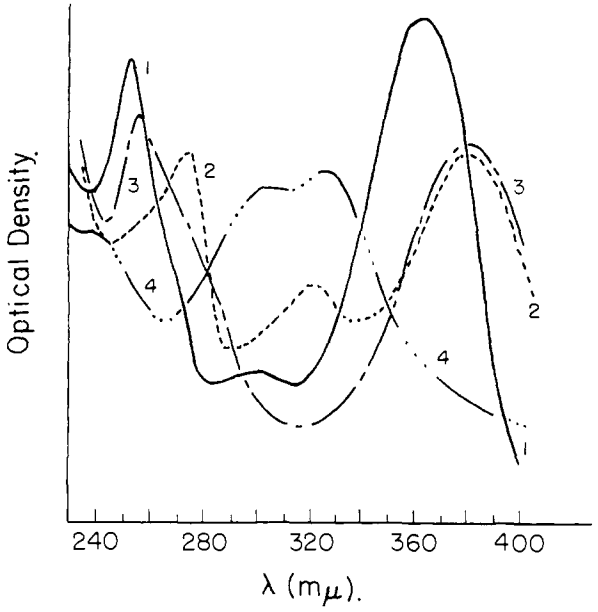
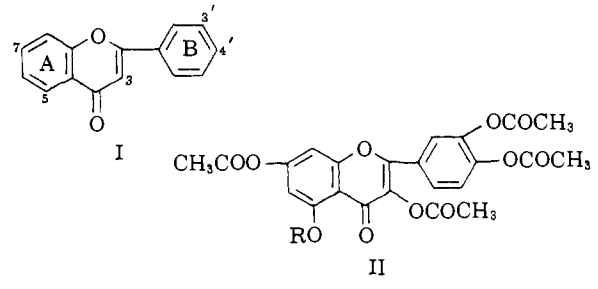
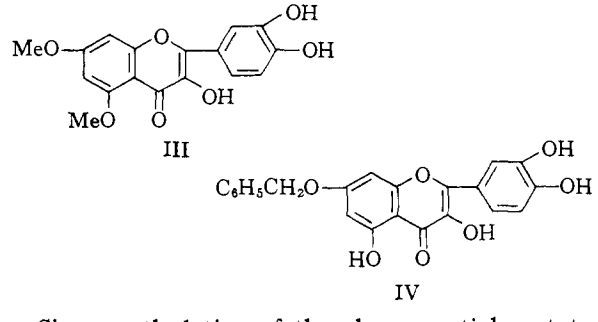


Fig. 1.—Ultraviolet spectrum of 5-O-methylquercetin in: 1, absolute ethanol; 2, ethanolic sodium acetate; 3, ethanolic boric acid–sodium acetate; 4, 0.002 *M* sodium ethylate.

Rhamnetin 3,3′,4′-triacetate, prepared in good yield by the acetylation of rhamnetin (7-O-methylquercetin) in pyridine solution, reacts similarly with methyl iodide to give a di-O-methyl quercetin triacetate. Alkaline hydrolysis of this triacetate yields a di-O-methylquercetin. The spectra of this compound (Fig. 2) in boric acid–sodium acetate, sodium ethylate and sodium acetate solutions show the presence of an unprotected 3′,4′-dihydroxyl group, a free 3,4′-dihydroxyl group and a 7-methoxyl group, respectively.[6,7] The product is therefore the hitherto unknown 5,7-di-O-methylquercetin (III).





Since methylation of the above partial acetates results in etherification of the free 5-hydroxyl groups it was anticipated that benzylation would give the corresponding 5-O-benzyl compounds. However, quercetin 3,3′,4′,7-tetraacetate reacts with benzyl chloride under similar conditions to give a monobenzylquercetin tetraacetate whose spectrum (λ_{max} 306, 254 mμ) is almost identical with that of 7-O-methylquercetin tetraacetate (λ_{max} 306, 254 mμ). This spectrum differs markedly from that of 5-O-methylquercetin tetraacetate (λ_{max} 322, 291, 262 mμ). The monobenzylquercetin obtained by hydrolysis of the tetraacetate rapidly decomposes in sodium ethylate solution and its long wave length band shifts 13 mμ in boric acid–sodium acetate (Fig. 3). The hydroxyls at positions 3, 3′ and 4′ are therefore free in this compound. Sodium acetate does not produce a

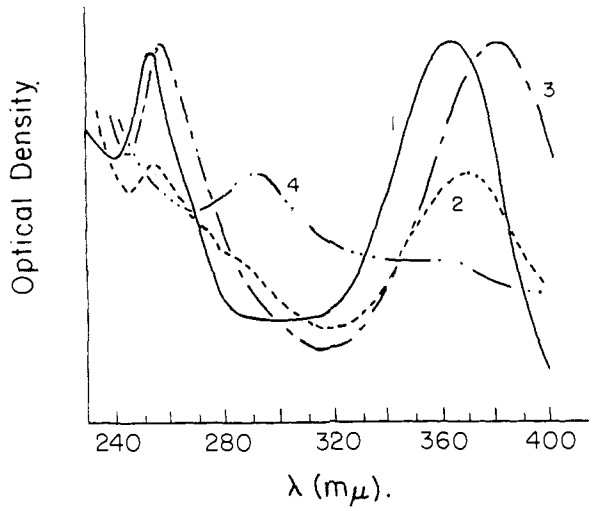


Fig. 2.—Ultraviolet spectrum of 5,7-di-O-methylquercetin in: 1, absolute ethanol; 2, ethanolic sodium acetate; 3, ethanolic boric acid–sodium acetate; 4, 0.002 *M* sodium ethylate.

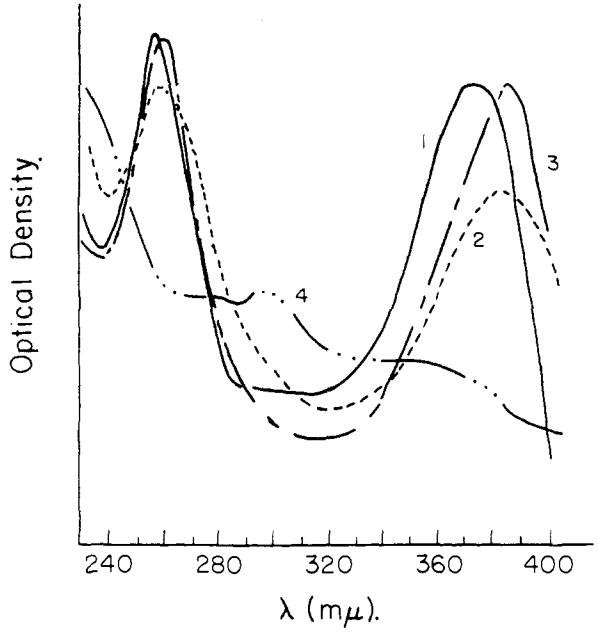
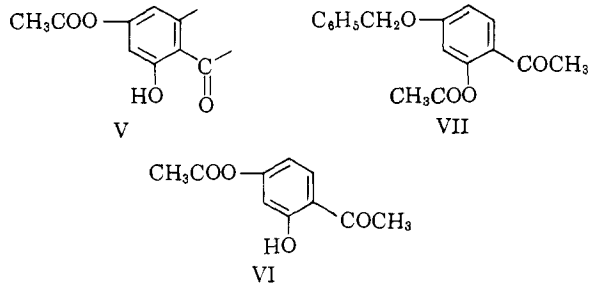


Fig. 3.—Ultraviolet spectrum of 7-O-benzylquercetin in: 1, absolute ethanol; 2, ethanolic sodium acetate; 3, ethanolic boric acid–sodium acetate; 4, 0.002 *M* sodium ethylate.

bathochromic shift of the low wave length band showing that the hydroxyl at position 7 is protected. The compound is therefore the hitherto unknown 7-O-benzylquercetin (IV). Methylation of this benzyl compound gives a monobenzyltetramethylquercetin, debenzylation of which yields a tetra-O-methylquercetin. The properties of this tetra-O-methylquercetin and of its monoacetate and monobenzyl ether agree with those reported[10] for 3,3′,4′,5-tetra-O-methylquercetin and its monoacetate and monobenzyl ether, respectively. The location of the benzyl group at the 7-position is thereby confirmed and it is apparent that migration or transference of an acetyl group from the 7- to the 5-position occurs during the benzylation of quercetin 3,3′,4′,7-tetraacetate. Migration appears to be usual in benzylation reactions involving partial acetates of structure V. Thus 4-acetylresacetophenone (VI) gives the 2-acetyl derivative VII of 4-O-benzylresacetophenone. The constitution of this new monobenzylresacetophenone is established by its intense red-brown ferric reaction and the bathochromic shift of its spectrum in aluminum chloride[11,12] (Fig. 4). Mauthner[13] recently determined the constitution of a similarly substituted resacetophenone, *viz.*, 4-gluco-resacetophenone, by methylation of the free phenolic



group to give (VIII R = glucosido-) and hydrolysis of the product to yield 2-O-methylresacetophenone, m.p. 138° (VIII, R = H). Methylation of the benzylresacetophenone gives a monomethylmonobenzylresacetophenone, debenzylation of which also gives 2-O-methylresacetophenone, m.p. 138°. The spectrum of 2-O-methylresacetophenone (λ_{max} 305, 269, 230 mμ) was not affected by the addition of aluminum chloride and it did not give a color reaction with ferric chloride. The m.p. of the isomeric 4-O-methylresacetophenone is much lower (m.p. 50°) and it gives an intense red ferric chloride reaction.[14] These reactions confirm the constitution of the benzyl compound as 4-O-benzylresacetophenone and its methyl ether as (VIII, R = $C_6H_5CH_2$–). The benzylation of 5-acetylquinacetophenone (IX), on the other hand, forms the 5-acetyl derivative (X) of 2-O-benzylquinacetophenone. The location of the benzyl group in this benzylquinacetophenone follows from its negative ferric reaction and the absence of a bathochromic

(10) S. Rajagopalan, P. R. Rao, K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **29A**, 9 (1949).
(11) T. Swain, *Chemistry & Industry*, 1480 (1954).
(12) L. Jurd and T. A. Geissman, *J. Org. Chem.*, **21**, 1395 (1956).
(13) N. Mauthner, *J. prakt. Chem.*, **161**, 284 (1943).
(14) "Dictionary of Organic Compounds," Oxford University Press, Eds. I. Heilbron and H. M. Bunbury, 1953, Vol. IV, p. 71.

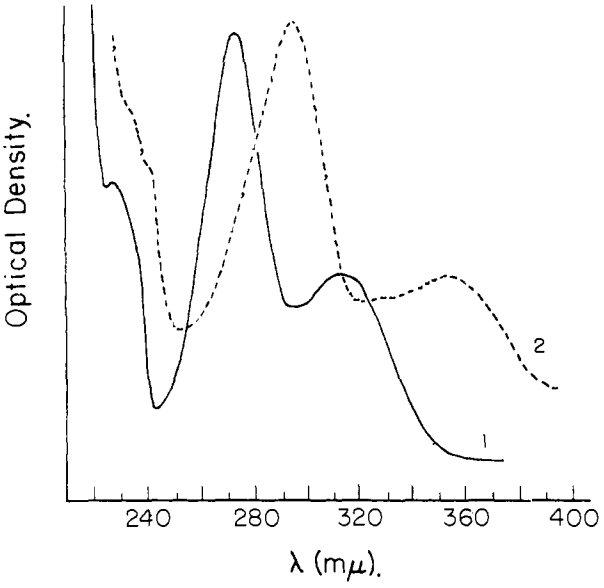


Fig. 4.—Ultraviolet spectrum of 4-O-benzylresacetophenone in: 1, absolute ethanol; 2, ethanolic aluminum chloride.

shift in its spectrum on the addition of aluminum chloride (Fig. 5).

The migration of acyl groups during the alkylation of partially acylated flavonoid compounds has not been reported previously. However, Perkin and his co-workers[8,15,16] have described the migration of acetyl groups in the reaction of the partial acetates of certain 1-hydroxyanthraquinones with diazomethane. These authors suggested that only *ortho* migration may occur. The products ob-

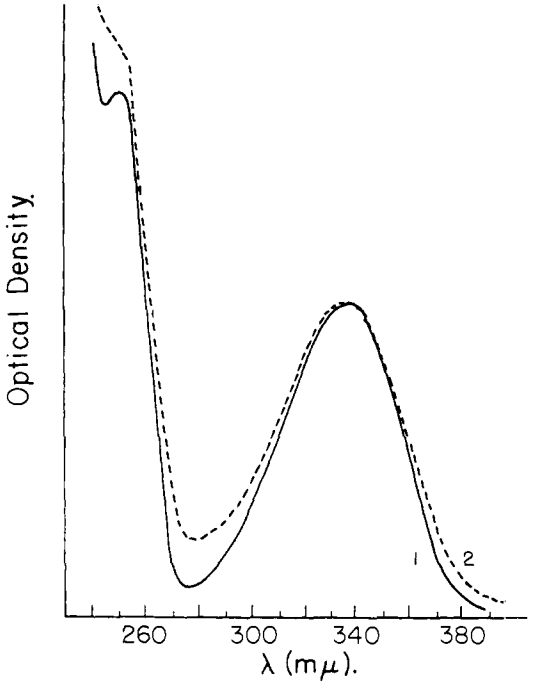
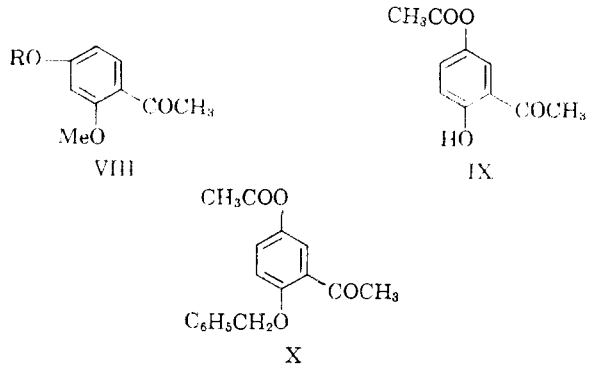


Fig. 5.—Ultraviolet spectrum of 2-O-benzylquinacetophenone in: 1, absolute ethanol; 2, ethanolic aluminum chloride.

(15) A. G. Perkin and R. C. Storey, *J. Chem. Soc.*, 229 (1928).
(16) A. G. Perkin and C. W. H. Story, *ibid.*, 1339 (1929).



tained in the benzylation of quercetin 3,3′,4′,7-tetraacetate and 4-acetylresacetophenone, however, prove that *meta* migration is also possible. The *meta* migrations are closely similar to Perkin's *ortho* migrations in that in all cases the acetyl group which migrates is that which is attached to an hydroxyl which is *para* to a carbonyl group and is therefore potentially acidic. It is clear that the monobenzyl compounds resulting from acetyl migrations will be useful in the synthesis of various naturally occurring and partially alkylated flavonoid compounds.

Experimental

The partially acetylated compounds used in this investigation were prepared from the parent phenols by Shimokoriyama's[17] method.

5-O-Methylquercetin.—Quercetin 3,3′,4′,7-tetraacetate, m.p. 188–189° (5.0 g.), was methylated by refluxing with methyl iodide, potassium carbonate and anhydrous acetone for 1.5 hours. 5-O-Methylquercetin tetraacetate (3.7 g.) separated from acetone–methanol in colorless needles, m.p. 199–200° (lit.[8] m.p. 202–204°).

Anal. Calcd. for $C_{25}H_{22}O_{11}$: C, 59.5; H, 4.16; 1 MeO–, 6.44; 4 CH_3CO–, 35.5. Found: C, 59.6; H, 4.23; MeO–, 6.64; CH_3CO–, 35.4.

On alkaline hydrolysis the tetraacetate (1.6 g.) gave 5-O-methylquercetin (1.1 g.) which separated from methanol–acetone in yellow needles, m.p. 307–309° (lit.[8] m.p. 305–308°).

Anal. Calcd. for $C_{16}H_{12}O_7$: C, 60.7; H, 3.83; 1 MeO–, 9.81. Found: C, 60.6; H, 3.94; MeO–, 10.2.

Rhamnetin 3,3′,4′-Triacetate.—A mixture of rhamnetin (1.5 g.), acetic anhydride (5.0 ml.) and pyridine (5 drops) was stirred for 10 minutes at room temperature. The rhamnetin dissolved and after some minutes the mixture thickened with the separation of the acetate. Excess of water was added and the slightly yellow solid was collected and recrystallized successively from methanol–acetone and benzene–hexane. Feathery yellow needles, m.p. 186°, which gave an intense red-brown color in alcoholic ferric chloride, were obtained.

Anal. Calcd. for $C_{22}H_{18}O_{10}$: C, 59.7; H, 4.10; 1 MeO–, 7.06; 3 CH_3CO–, 29.2. Found: C, 60.2; H, 4.16; MeO–, 6.78; CH_3CO–, 29.4.

5,7-Di-O-methylquercetin Triacetate.—A solution of rhamnetin 3,3′,4′-triacetate (1.4 g.) in anhydrous acetone (40 ml.) was heated under reflux with methyl iodide (10.0 ml.) and anhydrous potassium carbonate (4.0 g.) for 2.5 hours. The filtered acetone solution was evaporated and the residue was dissolved in warm benzene. The benzene solution, diluted with hexane, was concentrated until crystallization began. The product (1.2 g.), recrystallized from acetone–methanol and from benzene–hexane, was obtained as colorless needles, m.p. 196°.

Anal. Calcd. for $C_{23}H_{20}O_{10}$: C, 60.5; H, 4.42; 2 MeO–, 13.6. Found: C, 60.7; H, 4.50; MeO–, 13.6.

5,7-Di-O-methylquercetin.—The above product (0.4 g.) was suspended in hot methanol (5.0 ml.) and treated with 10% aqueous sodium hydroxide (0.4 ml.) until a permanent orange-red color was obtained. After two minutes water (5.0 ml.) was added and heating was continued for a further 3 minutes. The solution was acidified by the addition of concentrated hydrochloric acid (1.0 ml.), water (5.0 ml.) and methanol (10.0 ml.). The acid solution was digested on the steam-bath for one hour when a yellow solid separated. This was collected and recrystallized from acetone–methanol. Brightly yellow needles, m.p. 282–283°, were thereby obtained.

Anal. Calcd. for $C_{17}H_{14}O_7$: C, 61.8; H, 4.28; 2 MeO–, 18.8. Found: 3, 61.7; H, 4.41; MeO–, 19.4.

7-O-Benzylquercetin Tetraacetate.—Quercetin 3,3′,4′,7-tetraacetate (1.0 g.) was heated under reflux with benzyl chloride (1.0 ml.), potassium iodide (0.1 g.), anhydrous potassium carbonate (2.5 g.) and anhydrous acetone (50 ml.) for 12 hours. The deep yellow mixture became almost colorless within 3 hours. The acetone solution was filtered from the potassium salts and concentrated to an oil. This was washed with hot hexane (3 × 25 ml.) to remove excess benzyl chloride. The hexane-insoluble residue was dissolved in boiling benzene (30 ml.), the solution was filtered and the filtrate was diluted slowly at boiling point with hexane (60 ml.). A colorless crystalline product separated, m.p. 110° (0.95 g.). Purified by recrystallization from benzene–hexane, the product separated with solvent of crystallization and had m.p. 115–120°. Crystallized from methanol, however, it was obtained in slightly yellow needles, m.p. 163–164°.

Anal. Calcd. for $C_{30}H_{24}O_{11}$: C, 64.2; H, 4.32; 4 CH_3CO–, 30.7. Found: C, 64.4; H, 4.37; CH_3CO–, 29.8.

7-O-Benzylquercetin.—7-O-Benzylquercetin tetraacetate (0.5 g.) was deacetylated by heating its solution in methanol (5.0 ml.) with 10% aqueous sodium hydroxide (2.0 ml.) for 5 minutes. The solution was acidified by the dropwise addition of concentrated hydrochloric acid. Water (10.0 ml.) was added and the mixture was cooled. The yellow crystalline product was recrystallized from methanol–acetone. 7-O-Benzylquercetin separated in brightly yellow needles, m.p. 245° (0.20 g.).

Anal. Calcd. for $C_{22}H_{16}O_7$: C, 67.3; H, 4.11. Found: C, 67.0; H, 4.16.

Methylation of the 7-O-benzylquercetin by means of methyl iodide, potassium carbonate and acetone gave 7-O-benzyl-3,3′,4′,5-tetra-O-methylquercetin which separated from benzene–hexane in colorless needles, m.p. 169–171° (lit.[10] m.p. 171–172°).

Anal. Calcd. for $C_{26}H_{24}O_7$: C, 69.6; H, 5.40; MeO–, 27.7. Found: C, 69.6; H, 5.69; MeO–, 25.3.

Debenzylation of this methyl ether in boiling acetic acid–hydrochloric acid mixture gave 3,3′,4′,5-tetra-O-methylquercetin, m.p. 284° (acetate, m.p. 172°) (lit.[10] m.p. 284–285°; acetate, m.p. 172°).

Anal. Calcd. for $C_{19}H_{18}O_7$: C, 63.6; H, 5.06; 4 MeO–, 34.6. Found: C, 63.4; H, 5.20; MeO–, 33.5.

4-Acetylresacetophenone.—Pyridine (0.5 ml.) was added to a suspension of resacetophenone (5.0 g.) in acetic anhydride (10.0 ml.). The mixture became warm and the resacetophenone dissolved. After 5 minutes the solution was added to excess of water. The solid was collected and crystallized from methanol. It separated in long colorless needles, m.p. 76° (4-acetylresacetophenone, lit.[18] m.p. 74°), which gave an intense red-brown color with alcoholic ferric chloride (3.5 g.).

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.8; H, 5.56. Found: C, 62.2; H, 5.36.

4-O-Benzyl-2-acetylresacetophenone.—A mixture of 4-acetylresacetophenone (2.0 g.), benzyl chloride (2.0 ml.), potassium iodide (0.2 g.), anhydrous potassium carbonate (4.0 g.) and dry acetone (50 ml.) was heated under reflux for 3.5 hours. Evaporation of the filtered acetone solution gave an oil which was dissolved in boiling hexane (60 ml.). On cooling, colorless crystals separated from the hexane solution. These were collected (1.9 g.) and recrystallized from methanol. Colorless glistening plates, m.p. 111–112°, which did not give a color with alcoholic ferric chloride, were thus obtained.

(17) M. Shimokoriyama, *Bull. Chem. Soc. Japan*, **16**, 284 (1941).

(18) Reference 14, p. 315.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.8; H, 5.68; 1 CH_3CO–, 15.2. Found: C, 71.6; H, 5.67; CH_3CO–, 14.7.

4-O-Benzylresacetophenone.—The above product (1.7 g.) was hydrolyzed by adding 10% aqueous sodium hydroxide (20 ml.) to its solution in boiling methanol (10.0 ml.). After 5 minutes the solution was cooled, diluted with water (20 ml.) and acidified with hydrochloric acid. The solid precipitate was collected and crystallized from methanol. 4-O-Benzylresacetophenone crystallized in colorless plates, m.p. 104–104.5° (1.1 g.). It gave an intense red-brown color with methanolic ferric chloride.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.3; H, 5.83. Found: C, 74.3; H, 5.81.

A mixture of the 4-O-benzylresacetophenone (1.0 g.), methyl iodide (10.0 ml.), potassium carbonate (5.0 g.) and acetone (40 ml.) was refluxed for 17 hours. The filtered acetone solution was evaporated and the residue was crystallized from hexane. 2-O-Methyl-4-O-benzylresacetophenone separated in colorless plates, m.p. 72° (0.85 g.).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 75.0; H, 6.30. Found: C, 75.3; H, 6.62.

A solution of the methyl ether (1.8 g.) in glacial acetic acid (20 ml.) and concentrated hydrochloric acid (10 ml.) was heated on a steam-bath for 30 minutes. Excess of water was added and the product was extracted with ether. The ether solution was washed with water and dilute sodium bicarbonate solution, dried (Na_2SO_4) and evaporated. The oil crystallized from benzene–hexane and the product was recrystallized from water. 2-O-Methylresacetophenone thereby separated in colorless needles, m.p. 138° (lit.[13] m.p. 138°) which dissolved in dilute alkali but did not give a ferric chloride reaction.

5-Acetylquinacetophenone.—Quinacetophenone was acetylated by the method described for the acetylation of resacetophenone. The acetate, recrystallized from methanol, was obtained in slightly yellow blades, m.p. 91° (5-acetylquinacetophenone, lit.[19] m.p. 91°), which gave a strong red-brown ferric reaction.

(19) Reference 14, p. 292.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.8; H, 5.56. Found: C, 62.2; H, 5.41.

2-O-Benzyl-5-acetylquinacetophenone.—5-Acetylquinacetophenone (1.0 g.) was benzylated by refluxing with benzyl chloride (1.0 ml.), potassium iodide (0.1 g.), anhydrous potassium carbonate (2.0 g.) and dry acetone (30 ml.) for 3 hours. The oil which remained on evaporation of the filtered acetone solution was dissolved in hot hexane (70 ml.) On concentration and cooling the hexane solution deposited colorless crystals and a little oily material. The hexane mother liquor was decanted and the oil was dissolved by washing the crystals rapidly with cold methanol. The crystalline material then was recrystallized from methanol. Colorless glistening blades were thus obtained, m.p. 88° (0.7 g.).

Anal. Calcd. for $C_{17}H_{16}O_4$; C, 71.8; H, 5.68; 1 CH_3CO–, 15.2. Found: C, 71.9; H, 5.67; CH_3CO–, 15.0.

2-O-Benzylquinacetophenone.—The above product (0.68 g.) was hydrolyzed in warm 5% aqueous methanolic sodium hydroxide. On dilution with water and acidification, a crystalline product separated. This was recrystallized from methanol containing a little water. 2-O-Benzylquinacetophenone was obtained as slightly yellow needles, m.p. 117° (0.4 g.), which dissolved in dilute aqueous alkali to give a yellow solution. It did not give a color with alcoholic ferric chloride.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.3; H, 5.83. Found: C, 74.4; H, 5.83.

Ultraviolet Spectra.—Ultraviolet spectra were determined in absolute ethanol at room temperature on a Cary recording spectrophotometer.

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[CONTRIBUTION FROM THE FRUIT AND VEGETABLE CHEMISTRY LABORATORY, WESTERN UTILIZATION RESEARCH AND DEVELOPMENT DIVISION, AGRICULTURAL RESEARCH SERVICE, U. S. DEPARTMENT OF AGRICULTURE]

Plant Polyphenols. V. Selective Alkylation of the 7-Hydroxyl Group in Polyhydroxyflavones

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Quercetin pentaacetate reacts with methyl iodide or benzyl chloride in dry acetone in the presence of potassium carbonate to give high yields of rhamnetin tetraacetate and 7-O-benzylquercetin tetraacetate, respectively. Further benzylation of 7-O-benzylquercetin tetraacetate in methyl ethyl ketone gives 3,4′,5,7-tetra-O-benzylquercetin monoacetate which yields isorhamnetin when successively deacetylated, methylated and debenzylated. 3,4′,7-Tri-O-benzylquercetin 5-monoacetate and 4′,7-di-O-benzylquercetin triacetate were isolated as by-products in these reactions. From these data it follows that acetyl groups attached to the flavone nucleus may be successively replaced by alkyl groups in the order $7 > 4' > 3 > 5 > 3'$. The constitutions of these new partial benzyl ethers of quercetin were established by recently reported spectrophotometric procedures.

The 7-alkyl ethers of certain flavonols, *e.g.*, rhamnetin, recently have achieved some importance as potential anti-oxidants for unsaturated fats.[2–4] However, few methods are at present known for the selective partial alkylation of polyhydroxyflavones in the laboratory, although partially alkylated flavones, particularly 7-methoxyflavones, occur frequently in plants.[5] The direct alkylation of phenolic flavones with excess of the usual reagents results in complete O-alkylation, alkylation of all phenolic groups except the chelated 5-hydroxyl, or nuclear alkylation.[6–12] *o*-Dihydroxyl groups may be protected during methylation by

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