[CONTRIBUTION FROM THE OREGON FOREST RESEARCH CENTER AND DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

Chemistry of Dihydroquercetin. I. Acetate Derivatives[1a]

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The acetate derivatives of dihydroquercetin, eriodictyol, astilbin, and sakuranetin were prepared. Structural information regarding the acetate derivatives of dihydroquercetin was obtained by comparison of the ultraviolet absorption spectra of these derivatives. The unusual behavior of the monopotassium salt of dihydroquercetin in acetate derivative formation is described.

Dihydroquercetin (3,3′,4′,5,7-pentahydroxyflavanone), which occurs in Douglas fir bark to the extent of about 5%, has been shown to possess antioxidant activity.[2a] The oxidation product of dihydroquercetin, quercetin (3,3′,4′,5,7-pentahydroxyflavone), also demonstrated antioxidant activity[2,3] and in one substrate, greater activity than that of dihydroquercetin.

Studies of the antioxidant properties of various polyhydroxyflavones have shown that certain selectively *O*-alkylated derivatives possess protective activity greater than that of quercetin.[4,5] Therefore, the antioxidant property of dihydroquercetin, a polyhydroxyflavone, possibly could be improved through analogous selective alkylation of certain of the hydroxy groups of the molecule, perhaps while preserving the desirable characteristics of white color, tastelessness, and nontoxicity.[6]

A technique for such selective *O*-alkylation recently has been reported for polyhydroxyflavones,[7,8] utilizing acetate derivatives of these flavones as reaction intermediates. It was the purpose of this study to determine if this method might be adapted for the polyhydroxyflavanones.

In the course of pursuing this work, it was evident that the structure of the acetate derivatives of dihydroquercetin lacked clarity judging from the various melting points recorded in the literature. Melting points of 82-84°,[9] 88-89°,[10] 128-129°,[11,12] and 155°[13] have been reported for the pentaacetate derivative and in certain instances a melting point of 150-151°[14,15] has been reported for an unspecified acetate derivative.

Recently, the differences in ultraviolet spectra, infrared spectra, and acetate analysis for the penta- and tetraacetate derivatives of dihydroquercetin have been reported.[9] Furthermore, differentiation between the acetate derivatives of the optically active and racemic dihydroquercetin also has been published.[16] However, in attempting to resolve the melting point data in this laboratory, information has been uncovered concerning (a) differentiation between the tetra- and pentaacetate derivatives by spectral data, (b) the structure of the tetraacetate derivative of dihydroquercetin, (c) the mixtures of the tetra- and pentaacetate derivatives which may arise on acetylation, and (d) the unusual behavior of the monopotassium salt of dihydroquercetin in acetate derivative formation.

The pure (+)-dihydroquercetin used in these studies was obtained from Douglas fir bark and purified by multiple water recrystallizations.[10] This dihydroquercetin was converted to both the racemic dihydroquercetin and eriodictyol (3′,4′,5,7-tetrahydroxyflavanone) by methods previously described by Pew.[17] The monopotassium salts of the optically active and racemic dihydroquercetins were prepared using potassium dibasic phosphate.[14]

In Table I are presented the data obtained for the various parent flavanones and the fully esterified derivatives of dihydroquercetin, eriodictyol and sakuranetin (4′,5-dihydroxy-7-methoxyflavanone), prepared by heating the parent compounds with acetic anhydride.

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TABLE I

PARENT FLAVANONES AND FULLY ESTERIFIED DERIVATIVES

	M.P.	Carbonyl Frequency, Cm.$^{-1a}$	λ_{max}[b]	log ϵ	λ_{min}[b]	log ϵ	$[\alpha]_D^{24c}$
+ Dihydroquercetin	240–242°	1642	290	4.30	249	3.52	+17.2
± Dihydroquercetin	234–236°	1642	291	4.22	251	3.15	0.0
Eriodictyol	269–270° dec.	1635	290	4.28	250	3.53	0.0
Astilbin	222–224°	1645	292	4.28	250	3.15	
Sakuranetin	153–155°	1645	289	4.26	245	3.30	
Dihydroquercetin							
Penta acetates							
+	88–90°	1705	263	4.11	295	3.59	+11.6
			312	3.67			
±	149–149.5°	1705	264	4.16			
			310	3.56			
+ K salt	130–131°	1703	264	4.09	302	3.58	+8.6
			312	3.60			
± K salt	149–150°	1703	262	4.41	289	3.91	
			313	3.91			
Eriodictyol							
Tetraacetate	140–141°	1673	260	4.06	288	3.28	
			315	3.59			
Sakuranetin							
Diacetate	116–117°	1675	275	4.18	248	3.46	
			305	3.74			

[a] Paraffin mull. [b] In 95% ethanol solution. [c] In acetone solution.

TABLE II

PARTIALLY ESTERIFIED FLAVANONE DERIVATIVES

	M.P.	Carbonyl Frequency, cm.$^{-1a}$	λ_{max}[b]	log ϵ	λ_{min}[b]	log ϵ	$[\alpha]_D^{24c}$
Dihydroquercetin							
Tetraacetates							
+	153–154°	1680	277	4.13	245	3.39	+18.6
			340	3.57	307	3.35	
±	170–171°	1680	277	4.22	244	3.45	0.0
			340	3.65	308	3.40	
+ K salt	161–162°	1675	277	4.13	244	3.16	+16.7
			341	3.50	311	3.26	
	120–121°	1675	276	4.12	242	3.44	+19.3
			339	3.52	310	3.39	
	170–171°	1680	277	4.15	245	3.52	0.0
			340	3.61	310	3.44	
± K salt	170–171°	1675	278	4.14	246	3.47	
			340	3.60	313	3.48	
Eriodictyol							
Triacetate	126–127°	1640	275	4.12	245	3.46	
			340	3.60	305	3.38	
Astilbin							
Penta acetate	116–117°	1634	281	4.36	248	3.61	
			335	3.76	320	3.74	
Sakuranetin							
Monoacetate	140–141°	1640	289	4.28	248	3.07	
			320	3.58			

[a] Paraffin mull. [b] In 95% ethanol solution. [c] In acetone solution.

Results of the preparation of the tetraacetate derivatives of dihydroquercetin, the triacetate derivative of eriodictyol, a pentaacetate derivative of astilbin, and a monoacetate derivative of sakuranetin, prepared by reaction at room and refrigerator temperatures of the parent compounds with acetic anhydride are presented in Table II.

A summation of the ultraviolet spectral data of these compounds are presented in Table III, and the families of spectral curves are shown in Fig. 1.

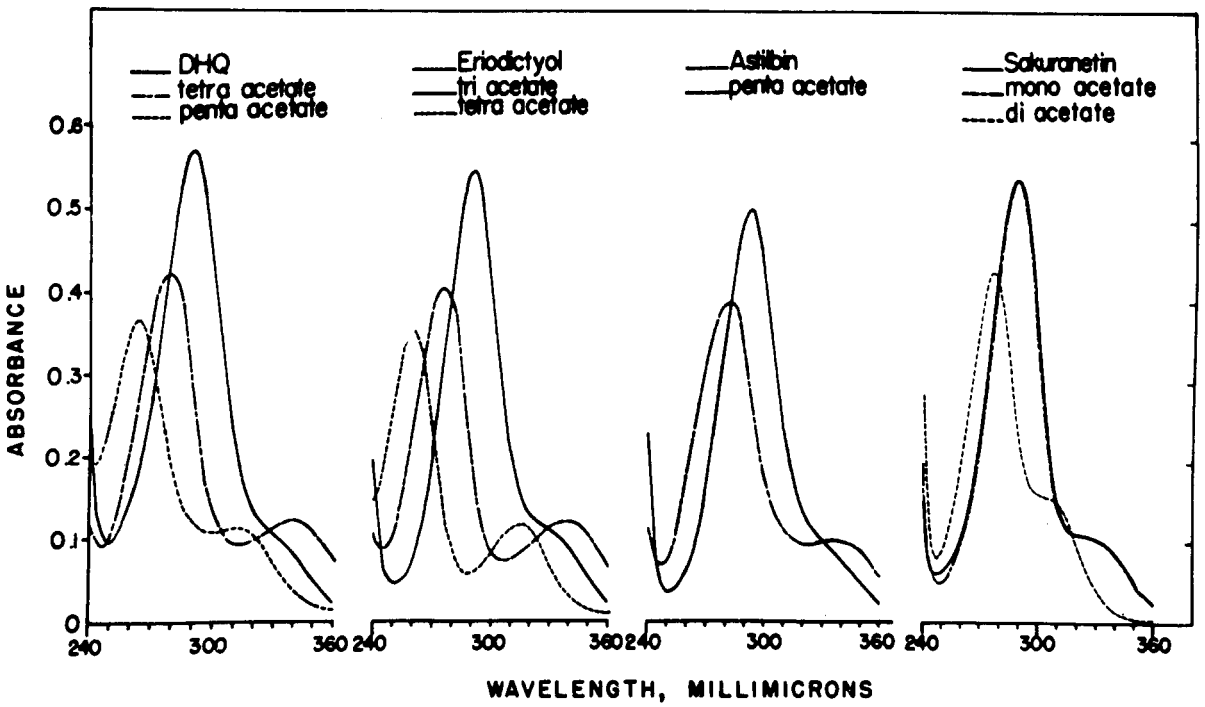
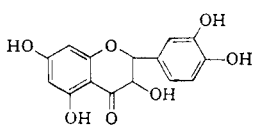
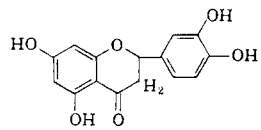
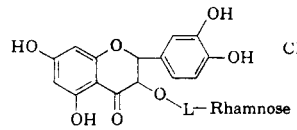
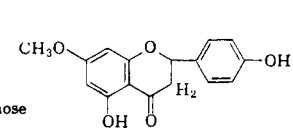


Fig. 1. Ultraviolet absorption spectra of the flavanoids and their acetate derivatives

TABLE III

SUMMARY OF ULTRAVIOLET SPECTRAL DATA

	Dihydroquercetin	Eriodictyol	Astilbin	Sakuranetin
				
λ_{max}	290 mμ	290 mμ	292 mμ	289 mμ
λ_{min}	249	250	250	245
Acetate	penta-	tetra-		mono-
λ_{max}	263	260		289
	312	315		
λ_{min}	295	288		248
Acetate	tetra-	tri-	penta-	di-
λ_{max}	277	275	281	275
	340	340	335	305
λ_{min}	245	245	248	248
	310	305	320	

The ultraviolet spectra in Fig. 1 of (a) dihydroquercetin, eriodictyol, astilbin, sakuranetin, and sakuranetin monoacetate, (b) dihydroquercetin tetraacetate, eriodictyol triacetate, and the penta-acetate derivative of astilbin; and (c) dihydroquercetin pentaacetate and eriodictyol triacetate are all almost identical within each group. Furthermore, there is a marked difference between the spectra of (a), (b), and (c). Aromadendrin (3,4′,5,7-tetrahydroxyflavanone), an analogue of dihydroquercetin, having no hydroxy group in the 3′ position, follows the same pattern. It has the same ultraviolet spectrum as dihydroquercetin, the spectra of the tetraacetate and triacetate are similar to the penta- and tetraacetate derivatives of dihydroquercetin respectively.[9]

From the data cited above, certain conclusions may be made concerning the contribution of the various groups on the flavanone ring system to the ultraviolet spectrum. Hydroxy or acetoxy (or the bonding of the hydroxy in the hemiacetal linkage to a sugar moiety) groups in the 3 position evidently have little effect on the ultraviolet spectrum of the parent compounds or the acetylated derivatives. Also, the hydroxy or acetoxy groups in the 3′ or 4′ positions have little effect on these spectra.

One would suspect that the hydroxyl substituents in the 3′-, 4′-, and 7-positions of these compounds

TABLE IV

STUDY OF REACTION TIME AND ACETATE DERIVATIVE FORMATION

Reaction Time			Carbonyl				
Room temp.	Refrig. temp.	M.P.	Frequency, Cm.$^{-1a}$	λ_{max}[b]	log ϵ	λ_{min}[b]	log ϵ
			+ DHQ				
15 min.	30 min.	160–161°	1680	277	4.12	245	3.34
				340	3.51	309	3.32
30 min.	60 min.	158–159°	1680	277	4.12	245	3.31
				341	3.52	309	3.29
60 min.	2 hr.	130–131°	1680	276	4.09	244	3.31
				340	3.53	308	3.29
2 hr.	2 hr.	123–124°	1710	270–2		242	
			1675	320–2		305	
			Potassium Salt of + DHQ				
15 min.	30 min.	161–162°	1680	277	4.13	245	3.49
				340	3.59	308	3.43
30 min.	60 min.	127–128°	1705	273			
			1680	328		305	
60 min.	2 hr.	126–127°	1705	273			
			1675				
2 hr.	6 days	170–171°	1680	277	4.15	245	3.53
				340	3.61	310	3.44
		160–161°	1675	277	4.13	244	3.16
				341	3.51	311	3.26
		120–121°	1675	276	4.12	242	3.44
				339	3.52	310	3.39

[a] Paraffin mull. [b] In 95% ethanol solution.

would be equivalent and of a different nature than those in the 3- and 5-positions. These two latter hydroxyls differ from the others in that there is possible hydrogen bonding between the hydroxy group in the 5-position and the carbonyl in the 4-position; furthermore, the 3-hydroxyl is a secondary alcohol. As absence of a hydroxy or acetoxy group in this position has been shown to have little effect on the spectra of flavanones or their acetate derivatives, one must conclude that it is the hydroxyl in the 5-position that remains unacetylated in dihydroquercetin tetraacetate, eriodictyol triacetate, and sakuranetin monoacetate.

Data presented in Table IV show that the conditions employed in preparation of the tetraacetate derivative of dihydroquercetin are critical. Apparently under identical reaction conditions, the monopotassium salt reacts to give mixtures of the penta- and tetraacetates in a reaction time shorter than that of dihydroquercetin. That the products were, indeed, sharp melting mixtures of the penta- and tetraacetates was established by ultraviolet spectral analysis (Fig. 2). Infrared spectral analysis supports this conclusion. Absorption maxima were found at the frequencies 1675 cm.$^{-1}$ and 1705 cm.$^{-1}$ which correspond to the carbonyl stretching frequencies in the spectra of the tetra- and pentaacetate derivatives, respectively. Longer periods of standing at refrigerator temperatures apparently cause hydrolysis of any pentaacetate formed, as after six days at this lower temperature, only the tetraacetate derivatives are isolated.

Under similar conditions of reaction, the monopotassium salt of (+)-dihydroquercetin was found

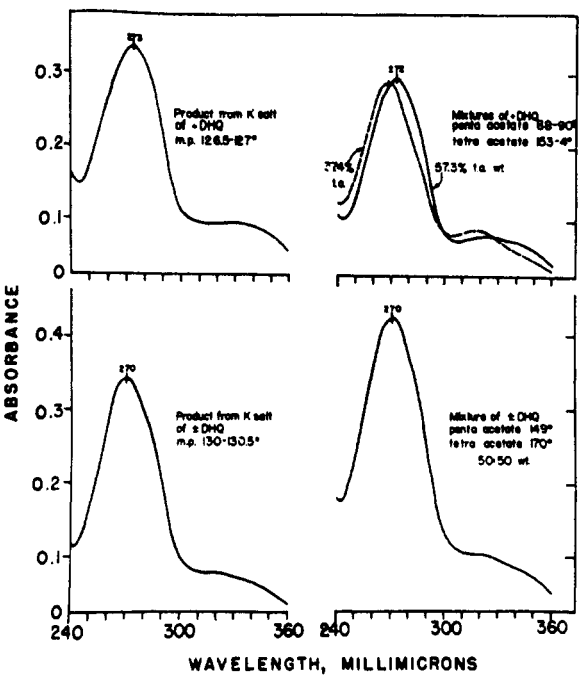


Fig. 2. Ultraviolet spectral analysis of acetate mixtures

to give tetra- and pentaacetate derivatives with optical rotations differing from those obtained from (+)-dihydroquercetin. Earlier, the optically active dihydroquercetin had been reported to be not racemized by treatment with potassium dibasic phosphate in preparation of the water insoluble monopotassium salt,[14] inasmuch as the dihydroquercetin regenerated from the potassium salt by treatment with acid had the same optical rotation

as the original dihydroquercetin. During these treatment and subsequent water recrystallizations, however, some racemization occurred [a change of optical rotation from (+) 16 to (+) 11; in acetone]. This finding may account for the difference in optical rotation of acetate derivatives prepared from the parent phenol, dihydroquercetin, and the monopotassium salt. As, from the melting point data of Table IV, racemization evidently occurs during the esterification, the possibility that the salt racemizes more rapidly than dihydroquercetin still exists.

Data presented show that (a) the multiplicity of melting points for the acetate derivatives reported in the literature must stem from contamination of the pure (+)-dihydroquercetin with its racemate, or the formation of mixtures of the acetate derivatives in reaction, (b) the potassium ion of the monopotassium salt of dihydroquercetin must be associated with, or exert influence on, the reactivity of the hydroxy group in the 5-position, as esterification of this group proceeds more rapidly than with the free dihydroquercetin, and (c) the evidence suggests that possibly the ion may also have some influence on the optical center, that is, the hydroxy group in the 3-position, since the acetate derivatives formed differ in optical rotation from those obtained from dihydroquercetin.

EXPERIMENTAL

Dihydroquercetin. Douglas fir bark cork was the source of the (+)-dihydroquercetin.[10] The cork was first exhaustively extracted with benzene to remove the waxy component. The cork was then extracted with ether. After removal of the solvent, the extract was recrystallized repeatedly from water. After thirteen recrystallizations, colorless glistening platelets were obtained which melted at 240–242°, $[\alpha]_D^{24}$ +44.0 (*c* 1.03 in 1:1 acetone-water), $[\alpha]_D^{24}$ +17.2 (*c* 1.04 in acetone).

Racemic dihydroquercetin. The optically active dihydroquercetin was racemized by refluxing with concentrated hydrochloric acid.[17] After repeated recrystallizations from water, light tan glistening platelets were obtained, melting at 234–236°, $[\alpha]_D^{24}$ 0.0 (*c* 1.04 in acetone). Yield was 24.3%.

Eriodictyol. Pure (+)-dihydroquercetin was treated with zinc and concentrated hydrochloric acid in the manner of Pew[17], to yield eriodictyol, a white solid, melting at 269–270° with decomposition. $(\alpha)_D^{24}$ 0.0 (*c* 1.03 in acetone). The yield was 50.7%.

Potassium salt of (+)-dihydroquercetin.[14] Equal parts of (+)-dihydroquercetin and potassium dibasic phosphate in boiling water gave the potassium salt of (+)-dihydroquercetin upon cooling. The light tan solid decomposed without melting at 232–245° (reported 240–245°). The yield was 92%.

Potassium salt of (±)-dihydroquercetin. The same procedure used for (+)-dihydroquercetin gave the salt of (±)-dihydroquercetin, light tan needles that decomposed without melting at 210–220°. The yield was 90%.

(+)-Dihydroquercetin pentaacetate.[10] Three grams of (+)-dihydroquercetin (0.0099 mole), 1.05 g. of sodium acetate and 15 ml. of acetic anhydride were heated on a steam bath for 3 hr. The mixture was then poured slowly into a beaker containing 75 ml. of cold water, with vigorous stirring. After cooling in the refrigerator for 2 hr., the solid was filtered from the aqueous solution. The solid was then triturated with water; the paste formed was filtered and the procedure repeated two additional times. The solid was then dried *in vacuo* over potassium hydroxide pellets. The product melting at 88–90°, $[\alpha]_D^{24}$ +11.6 (*c* 1.20 in acetone), had a slight pink cast. The yield was 4.15 g. (81.7%). The product could not be recrystallized from alcohol-water or acetone-water.

(±)-Dihydroquercetin pentaacetate. Fifteen milliliters of acetic anhydride, 1.5 g. (±)-dihydroquercetin, and 0.75 g. of sodium acetate were heated on a steam bath for 3 hr. The mixture was poured into 200 ml. of cold water with vigorous stirring. After cooling in the refrigerator for 2 hr., the solid was filtered from the aqueous solution and recrystallized three times from acetone-methanol and water (1:1 by volume). The product (1.23 g., 30.5% yield) was obtained as long white needles, which melted at 149–149.5°.

Eriodictyol tetraacetate. One gram of eriodictyol, 15 ml. of acetic anhydride, and 0.35 g. of sodium acetate were heated on a steam bath for 3 hr. The mixture was poured into 200 ml. of cold water, with vigorous stirring. After cooling in a refrigerator for 2 hr., the solid was filtered from the aqueous solution and recrystallized from methanol-water three times. The product (0.44 g., 27.1% yield) was obtained as fine white needles, melting at 140.5°–141.5°. Reported[10] melting point is 140–141°.

(±) Dihydroquercetin pentaacetate from the potassium salt. Twenty-five milliliters of acetic anhydride and 1.16 g. of the potassium salt were heated on a steam bath for 3 hr. The solution was poured into 200 ml. of cold water with vigorous stirring. After cooling in the refrigerator overnight the solid was filtered from the aqueous solution and recrystallized from acetone–methanol-water (1:1). The solid was recrystallized three times from methanol-water. The product (0.5 g., 28.8%) melted at 130–131°, $(\alpha)_D^{24}$ +8.6 (*c* 1.05 in acetone).

(±) Dihydroquercetin pentaacetate from the potassium salt. One-half gram of the potassium salt and 10 ml. of acetic anhydride were heated on a steam bath for 3 hr. The solution was poured into 100 ml. of cold water with vigorous stirring. After cooling in the refrigerator for 2 hr., the solid was filtered from the aqueous solution and recrystallized from methanol-water three times. The product (0.25 g., 29.4%) was obtained as fine white needles, which melted at 149–150°. Melting point when mixed with pentaacetate from (±) dihydroquercetin was 149–150°.

(+) Dihydroquercetin tetraacetate. Ten grams of (+)-dihydroquercetin, 35 ml. of acetic anhydride, and 35 drops of pyridine were swirled together at room temperature. After 10 min., the solid dissolved. Swirling was continued, and after another 5 min., solid started separating. When the mixture stiffened so that swirling could not be continued, 200 ml. of cold water were added and the mixture was refrigerated for 2 hr. The solid was filtered from the aqueous solution and recrystallized from acetone–methanol-water (1:1). The solid then was recrystallized twice from methanol-water. The product (6.4 g., 41.2%) was obtained as colorless platelets which melted at 153.5–154.5°, $[\alpha]_D^{25}$ +18.6 (*c* 1.07 in acetone).

(±)-Dihydroquercetin tetraacetate. Ten milliliters acetic anhydride, 5 drops of pyridine, and 1.4 g. of (+)-dihydroquercetin were swirled together at room temperature for 15 min. The solid dissolved, but no solid reprecipitated. The solution was refrigerated for 2 hr. Two hundred milliliters of cold water was added to the solution with vigorous shaking. The mixture then was refrigerated another 2 hr. and the solid filtered from the aqueous solution and recrystallized from acetone-methanol-water (1:1). The solid obtained was recrystallized two times from methanol-water for a yield of 1.30 g. (59.7%) of fine, white needles which melted at 170.5–171.5°.

Eriodictyol triacetate. Eight milliliters of acetic anhydride, 5 drops of pyridine, and 0.75 g. of eriodictyol were swirled at room temperature for 15 min. During this time the solid dissolved slowly. The solution was allowed to stand at room temperature, occasionally swirling, for 1 hr. No solid sepa-

rated. The solution was refrigerated for 0.5 hr. and 100 ml. of cold water was added with vigorous shaking. The mixture was refrigerated overnight and the solid filtered from the aqueous solution. The solid was recrystallized twice from ethanol-water, finally yielding 0.70 g. (65.0%) of fine, white needles, which melted at 127.5–128°.

Anal. Calcd. for $C_{21}H_{18}O_9$: C, 60.9; H, 4.4; 3 CH_3CO, 31.2. Found: C, 60.89; H, 4.45; CH_3CO, 30.80.

Astilbin pentaacetate. One gram of astilbin, 10 ml. of acetic anhydride, and 5 drops of pyridine were swirled together at room temperature until the solid dissolved (about 1 hr.) and the solution was allowed to stand at room temperature overnight. Two hundred milliliters of cold water was added with vigorous shaking and the mixture was refrigerated overnight. The solid was filtered from the aqueous solution and recrystallized twice from methanol-water. The final product, 0.23 g. (15.7%), was obtained as fine white granules, which melted at 115–116.5°.

Anal. Calcd. for $C_{31}H_{32}O_{16}$: C, 26.36; H, 4.88, 5 CH_3CO 32.58. Found: C, 26.38; H, 5.35; CH_3CO 31.13.

Tetraacetate of (+)-dihydroquercetin monopotassium salt. Six grams of the potassium salt of (+)-dihydroquercetin and 60 ml. of acetic anhydride were swirled together for 15 min. and allowed to stand at room temperature with occasional swirling for 2 hr. The solid dissolved slowly. The solution was allowed to stand in the refrigerator for 6 days. The solution then was poured into 500 ml. of cold water with vigorous stirring. The mixture was refrigerated for 0.5 hr. and the solid filtered from the aqueous solution. The solid was recrystallized from methanol-water. The recovered solid (2.63 g.) was filtered off, and the mother liquor flooded with water yielded a second crop of solid (3.44 g.). The first crop was recrystallized twice from methanol-water to yield 1.5 g. of fine white needles, with melting point of 169–170°, $[\alpha]_D^{24}$ 0.0 (*c* 1.02 in acetone).

The second crop was recrystallized from methanol-water, the solid filtered off, and another crop recovered by flooding the mother liquor with water. Each of the two crops was recrystallized again from methanol-water and yielded the following respectively:

(a) 0.190 g. of glistening platelets, melting at 161–162°, $[\alpha]_D^{24}$ +16.7 (*c* 0.72 in acetone).

(b) 0.250 g. of glistening platelets, melting at 120–121° $[\alpha]_D^{24}$ 19.3 (*c* 0.93 in acetone).

Anal. Calcd. for $C_{23}H_{20}C_{11}$: CH_3CO, 36.45. Found: 170–171°: CH_3CO, 36.77. 160–161°: CH_3CO, 33.15. 120–121°: CH_3CO, 36.90.

A mixture of the compound melting at 170–171° with the tetraacetate of (±)-dihydroquercetin (170.5–171.5°), melted at 171–172°.

Tetraacetate of (+)-dihydroquercetin monopotassium salt. Fourteen milliliters of acetic anhydride and 1.5 g. of the potassium salt of (±)-dihydroquercetin were swirled together for 15 min. and allowed to stand at room temperature, with occasional swirling, for 2 hr. The solid slowly dissolved, and the solution was allowed to stand in the refrigerator for 6 days. The solution was added to 200 ml. of cold water with vigorous stirring. The mixture then was refrigerated overnight. The solid was filtered from the aqueous solution and recrystallized from methanol-water twice. The product, 0.55 g., 26.5%, was obtained as fine, colorless, glistening needles, that melted at 170–171°.

A mixture with the tetraacetate of (±)-dihydroquercetin (m.p. 170.5–171.5°) melted at 171–172°. With the compound (m.p. 170–171°) obtained from the potassium salt of (+)-dihydroquercetin, the mixed melting point was 171–172°.

Reaction of (+)-dihydroquercetin monopotassium salt to give a mixture of tetra- and pentaacetates. One gram of the potassium salt and 5 ml. of acetic anhydride were swirled together for 15 min., during which time the solid slowly dissolved, and then was allowed to stand at room temperature for 1 hr. The solution was refrigerated for 2 hr. One hundred milliliters of cold water were added with vigorous stirring and the mixture was refrigerated again for 2 hr. The solid was filtered and recrystallized from methanol-water. A small amount of solid was obtained. This was filtered off and the mother liquor flooded to obtain a second crop. Crop 1 was recrystallized again from methanol-water and gave fine white needles (0.06 g.), melting at 169–170°. A mixture with the tetraacetate of (±)-dihydroquercetin (m.p., 170.5–171.5°) melted at 170–171°. Crop 2 was recrystallized twice from methanol-water. The product obtained (2 g.) was obtained as fine, white, long soft needles, which melted at 126.5–127°.

Reaction of (+)-dihydroquercetin monopotassium salt to give a mixture of tetra- and pentaacetates. Six milliliters of acetic anhydride and 1.5 g. of the potassium salt were treated as described above. Two recrystallizations from methanol-water gave long, fine, soft colorless needles (1.55 g.) melting at 130–130.5°. The mother liquors when combined and flooded with water became cloudy, but yielded no further crops.

Preparation of mixture of tetra- and pentaacetates from (+)-dihydroquercetin. Five grams of (+)-dihydroquercetin, 35 ml. of acetic anhydride, and 35 drops of pyridine were swirled together at room temperature for 15 min., during which time the solid slowly dissolved. The solution was allowed to stand at room temperature a total of 2 hr., with occasional swirling. The solution was refrigerated for 2 hr., then was poured into 500 ml. cold water with vigorous shaking, and the mixture allowed to stand in the refrigerator overnight. The solid was filtered from the aqueous solution and recrystallized from acetone-aqueous methanol (1:1). The solid then was recrystallized twice from methanol water. The product (2.5 g.) was obtained as long, fine colorless needles, which melted at 123–124°.

The infrared spectrum was identical to that of the mixture obtained from the potassium salt of (+)-dihydroquercetin (126–127°), having two carbonyl frequency absorption peaks at 1680 and 1705 $cm.^{-1}$

No work-up of the mother liquors was performed.

Sakuranetin monoacetate. One-hundred milligrams of sakuranetin, 2 drops of pyridine and 5 ml. of acetic anhydride were allowed to stand at room temperature for 2 hr. One-hundred milliliters of water was added, and the mixture was placed in the refrigerator overnight. The solid was collected by filtration and recrystallized three times from methanol-water. The yield of glistening platelets, which melted at 140.5–141.5°, was 65 mg.

Sakuranetin diacetate. Sakuranetin, 350 mg., was heated with 10 ml. of acetic anhydride and 0.1 g. of sodium acetate on a steam bath for 3 hr. The solution was cooled, 100 ml. of water was added, and the mixture was placed in the refrigerator overnight. The solid was collected and recrystallized three times from methanol-water. The yield of white solid, melting at 116–117°, was 150 mg.

Time study of acetate formation of (+)-dihydroquercetin and the (+)-monopotassium salt. In all instances the quantities of materials were identical; 0.75 g. of dihydroquercetin or the monopotassium salt, 8 ml. of acetic anhydride, and 5 drops of pyridine. After the times specified in Table IV, 100 ml. of water were added, and the solution was refrigerated overnight. The solid was collected and in all instances recrystallized from methanol-water at least three times. The physical properties of the products obtained are listed in Table IV also.

All melting points are not corrected. Ultraviolet spectra were determined in 95% ethanol solution with a Beckman Model DU spectrophotometer. Infrared spectra were measured as paraffin mulls in a Perkin Elmer Model 21 double beam recording spectrophotometer.

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