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SHORT COMMUNICATION

THE ACID CATALYZED CONVERSION OF 3-HYDROXYFLAVANONES TO ANTHOCYANIDINS

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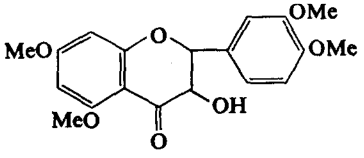
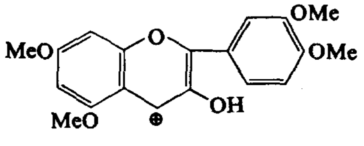
Abstract—3-Hydroxyflavanones which lack a free hydroxyl group in the 5-position are slowly isomerized and converted by alcoholic mineral acids into the corresponding anthocyanidins.

MONOMERIC and polymeric flavan-3,4-diols (leucoanthocyanidins) are usually detected and distinguished from other classes of colorless, natural flavanoids by their facile oxidation to red anthocyanidin pigments in warm alcoholic (*n*-butanol or isopropanol) mineral acid solutions.[1,2] It is of interest to note, therefore, that we have observed that some types of flavanones isomerize and are converted to anthocyanidins in small yield under the conditions of this test.

Thus, a solution of tetra-*O*-methyldihydroquercetin (I) in *n*-butanol/HCl at 100° or in boiling isopropanol/HCl rapidly assumes a pink color and this gradually deepens to a strong red on prolonged heating (3 hr.). The pigment formed has λ_{max} 532 nm, and on paper chromatograms it migrates as a single, red spot, R_f 0·67 (formic acid/3 N HCl, 1:1, v/v), 0·38 (H_2O/acetic acid/conc. HCl, 80:20:5, v/v). In all of these respects the pigment is identical with 5,7,3′,4′-tetra-*O*-methylcyanidin chloride (II), prepared[3] by the action of these alcoholic acids on 5,7,3′,4′-tetramethoxyflavan-3,4-diol. Under similar conditions the model 3-hydroxy 4′-methoxyflavanone[4] gives a bright yellow solution whose λ_{max} is identical with that of synthetic 3-hydroxy-4′-methoxyflavylium chloride, λ_{max} 475 nm. As indicated, the flavanone–anthocyanidin conversion is relatively slow, anthocyanidin yields are small,[5] and in typical experiments 40–60 per cent (recrystallized) of the flavanones are recovered from the red or yellow solutions after 3 hr heating.



(I)



(II)

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[1] T. SWAIN and W. E. HILLIS, *J. Sci. Food Agr.* **10**, 63 (1959).

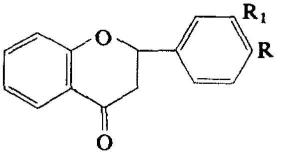
[2] D. G. ROUX, *Nature* **180**, 973 (1957).

[3] L. JURD and R. LUNDIN, *Tetrahedron* **24**, 2653 (1968).

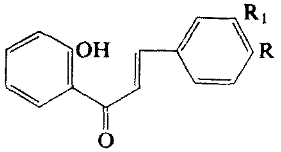
[4] M. M. BOKADIA, B. R. BROWN and W. CUMMINGS, *J. Chem. Soc.* 3308 (1960).

[5] An accurate estimate of the actual conversion to anthocyanidin cannot be made since the anthocyanidins are fairly unstable in these boiling solvents (50·0 ml of *n*-butanol or isopropanol +5·0 ml conc. HCl).

The presence of a 3-hydroxyl group appears to be required for the flavanone–flavylium salt conversion, since unsubstituted flavanones of types IIIa and IIIb form only the corresponding chalcones IVa and IVb, λ_{max} 369 and 387 nm respectively, with these alcoholic acids. Furthermore, the flavanone–flavylium salt conversion is inhibited by the presence of a free 5-hydroxyl group, as indicated by the fact that dihydroquercetin itself does not form cyanidin under these conditions. The inhibitory effect of a free 5-OH group is also confirmed by comparison of the butanolic HCl hydrolysis of 3,7,3′,4′-tetraacetyldihydroquercetin and of 3,5,7,3′,4′-pentaacetyldihydroquercetin. After 3 hr the tetraacetate solution is just pale yellow (due to partial oxidation to quercetin). With the pentaacetate, however, the hydrolysis solution rapidly becomes red (λ_{max} 556 nm; cyanidin has λ_{max} 556 nm). In the case of the pentaacetate hydrolysis of the alcoholic 3-acetoxy group may occur, with subsequent isomerization, before hydrolysis of the 5-acetoxy group.

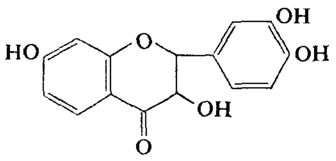


(IIIa) $R = OMe; R_1 = H$
(IIIb) $R = OH; R_1 = OMe$

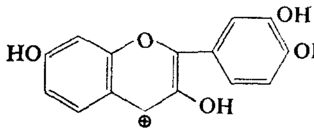


(IVa) $R = OMe; R_1 = H$
(IVb) $R = OH; R_1 = OMe$

On the basis of these limited observations it is apparent that dihydroquercetin and other phenolic 3,5-dihydroxyflavanones do not interfere with the specificity of the flavan-3,4-diol color test. However, natural flavanones lacking a 5-hydroxy group, e.g., fustin (V), which co-occur with flavans and flavan-3,4-diols in the crude tannins of many species,[6] might be expected to yield small quantities of the corresponding anthocyanidins on acid degradation. With butanolic HCl a specimen of (±)-fustin, kindly provided some years ago by Dr. Roux, gave a strong yellow-orange solution. The red color of fisetinidin (VI) was visually masked by the preponderance of the yellow flavonol, fisetin (λ_{max} 368, 318, 255 nm), formed by oxidation in this reaction. However, the spectrum of the crude reaction solution shows a definite peak at 528 nm, the λ_{max} of fisetinidin chloride (VI).



(V)



(VI)

3-Hydroxyflavanones are at the same oxidation level as anthocyanidins and, therefore, this flavanone–flavylium salt conversion does not involve oxidation, as in the case of flavan-3,4-diols. The inhibitory effect of a free 5-hydroxyl on the flavanone rearrangement suggests that hydrogen bonding of the 5-hydroxyl with the 4-carbonyl group prevents protonation of the latter (by acid or through hydrogen bonding with the 3-hydroxyl). A reasonable mechanism for the flavanone rearrangement might involve an acid catalyzed enolization [process (a)] or a cyclic process (b) in which the hydride ion at C_3 shifts to C_4 to form the anthocyanidin pseudo base. In acid solutions this then forms the anthocyanidin:

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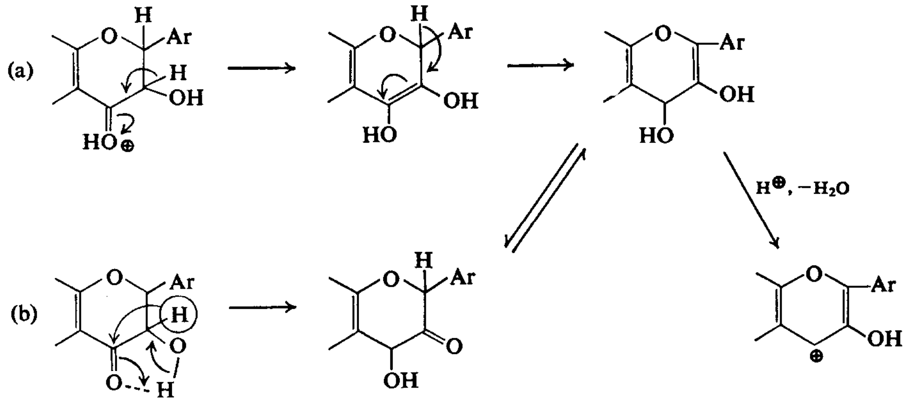
[6] D. G. ROUX and E. PAULUS, *Biochem. J.* **78**, 785 (1961).



In connection with this flavanone–anthocyanidin conversion, it is noteworthy that Janzsó, Kállay and Koczor[7] recently reported the formation of 3-hydroxy-4-aminoflavylium salts by the action of alcoholic HCl on the tosyl hydrazones of 3-hydroxyflavanones.

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[7] G. JANZSÓ, F. KÁLLAY and I. KOCZOR, *Tetrahedron* **22**, 2909 (1966).