ULTRAVIOLET ABSORPTION OF FLAVONOIDS

VI. PROTONATION CONSTANTS OF SOME DIHYDROXYFLAVONES

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In a study of the basicity of flavone and its monohydroxy derivatives, we have shown that the hydroxy group exerts different influences on the basicity of the compound according to its position in the molecule. Thus, 7- and 4'-OH groups lead to an increase in basicity, and 3- and 5-OH groups to a decrease [1]. In subsequent experiments it was established that the causes of the fall in basicity in the 3- and 5-hydroxyflavones are different [2].

To determine the nature of the mutual influence where two hydroxyl substituents are present simultaneously, we considered the basic properties of a series of dihydroxyflavones. The material for investigation consisted of derivatives of 3-hydroxy- and 5-hydroxyflavones containing hydroxy and methoxy groups in biogenetically important positions (Table 1).

The ionization constants of the disubstituted flavones listed in Table 1 have been studied previously [3-5].

As can be seen from Table 1, on the introduction of an electron-donating hydroxy group into the 7 and 4'-positions, which are conjugated with the carbonyl group of 5-hydroxy- and 3-hydroxyflavones, the basicity rises as in flavone itself, which is due to the positive resonance effect of the substituent. Here the contributions of 7- and 4'-hydroxy groups to the change in basicity, which we evaluated as the difference in the values of the basicity constants of the two homologs, are different for derivatives of 3-hydroxy- and 5-hydroxyflavones (Table 2).

In derivatives of 3-hydroxyflavone it is smaller than in derivatives of 5-hydroxyflavone. The contribution of the 3-hydroxy group remains approximately the same as in 3-hydroxyflavone in comparison with flavone ($\Delta pK_a = -1.37$).

The contribution of the 5-hydroxy group to the change in basicity of the 5,7- and 4',5-dihydroxyflavones is appreciably less than in 5-hydroxyflavone ($\Delta pK_a = -1.74$). The decreasing contribution of the influence of the 5-hydroxy group in these compounds is accompanied by a rise in the contribution of the 7- and 4'-OH groups (in comparison with the corresponding monohydroxyflavones).

The basicity of 3,5-dihydroxyflavone is lower than the basicities of 3-hydroxy- and 5-hydroxyflavones.

On analyzing the figures for the basicities and acidities of the mono- and disubstituted flavones it may be concluded that the change in the contribution of a particular hydroxy group to the basicity of a disubstituted flavone, in contrast to the monohydroxyflavone with the corresponding pattern of substitution, is accompanied by a corresponding change in the acidity of this group. For example, the acidity of the 7- and 4'-hydroxy groups in derivatives of 5-hydroxyflavone increases in comparison with the acidities of these groups in the corresponding monohydroxyflavones and derivatives of 3-hydroxyflavones, and simultaneously the basicity in derivatives of 5-hydroxyflavone rises more strongly than in derivatives of 3-hydroxyflavone.

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TABLE 1. Protonation Constants of some Dihydroxyflavones Calculated by the Analytical Method

Compound	λ mm	pK_a (av)	Mean square error (s)	Number of degrees of freedom (f)	$pK_a \pm \Delta x$
5,7-Dihydroxyflavone	305	−2,10	0,08	19	−2,00±0,04
	310	−2,06			
	360	−1,96			
	370	−1,95			
	380	−1,92			
4',5-Dihydroxyflavone	320	−2,07	0,03	20	−2,10±0,01
	330	−2,08			
	375	−2,08			
	380	−2,10			
	390	−2,14			
3,7-Dihydroxyflavone	320	−2,12	0,04	22	−2,14±0,02
	380	−2,06			
	390	−2,15			
	395	−2,17			
	400	−2,17			
3,4'-Dihydroxyflavone	350	−2,15	0,01	20	−2,15±0,05
	360	−2,15			
	395	−2,15			
	400	−2,15			
	410	−2,16			
3-Hydroxy-5-methoxyflavone	310	−1,93	0,05	21	−1,95±0,02
	395	−1,93			
	400	−1,97			
	405	−1,96			
	410	−1,94			
	415	−1,94			
3,5-Dihydroxyflavone	395	−3,38	0,03	18	−3,36±0,01
	400	−3,37			
	405	−3,35			
	410	−3,36			
	415	−3,35			

TABLE 2. Values of ΔpK_a for Flavonoids, Characterizing the Contribution of a Substituent to the Change in Basicity

Compound	7-OH	4'-OH	5-OH	3-OH
5,7-Dihydroxyflavone	+1,07	—	−1,21	—
4',5-Dihydroxyflavone	—	+0,97	−1,21	—
3,7-Dihydroxyflavone	+0,56	—	—	−1,35
3,4-Dihydroxyflavone	—	+0,55	—	−1,26
3,5-Dihydroxyflavone	—	—	−0,66	−0,29

The results obtained show the presence of a mutual influence of the substituents in disubstituted flavones which is responsible for the change in the acid–base properties of these compounds.

EXPERIMENTAL

The methods of synthesizing the flavonoids listed in Table 1 and their physicochemical characteristics have been described in previous papers [4, 5]. The basicity constants were determined as described previously [1] at 20 ± 1°C. As can be seen from the spectra given in Fig. 1, in the dihydroxyflavones there is a considerable difference between the absorption of the protonated and unprotonated forms. The analytical wavelengths for all the compounds studied are given in Table 1. The influence of the medium was taken into account, using Hammett's method of correction [6].

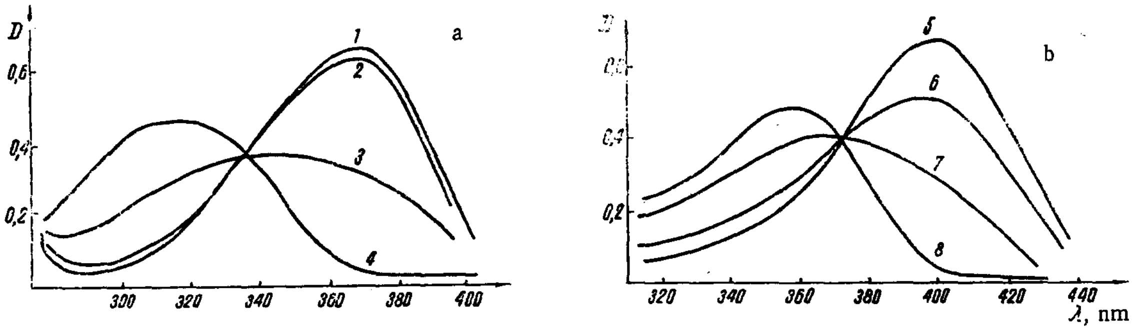

Fig. 1. UV spectra of 4',5-dihydroxyflavone ($2 \cdot 10^{-5}$ M (a) and of 3,4'-dihydroxyflavone ($2 \cdot 10^{-5}$ M) (b): 1) in 30% aqueous ethanol; 2) in 34% H_2SO_4; 3) in 50% H_2SO_4; 4) in 60% H_2SO_4; 5) in 5% H_2SO_4; 6) in 30% H_2SO_4; 7) in 40% H_2SO_4; 8) in 60% H_2SO_4.

SUMMARY

The protonation (basicity) constants of six disubstituted flavones have been determined by the spectrophotometric method.

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