ULTRAVIOLET ABSORPTION OF FLAVONOIDS

IV. PROTONATION CONSTANTS OF SOME MONOHYDROXY FLAVONES

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In previous papers [1-3] we have reported the results of a study of the acidic properties of flavonoid compounds. However, it is known that γ-pyrone derivatives may also exhibit basic properties on reaction with mineral acids. The basicities of a number of γ-pyrones and chromones have been studied systematically by A. I. Tolmachev et al. [4-7]. Nevertheless, quantitative information on the basicities of the flavones is very limited [8], although in combination with the acidity constants it may be very useful in explaining some features of the chemical behavior of the flavones and also in discussions of their electronic structures.

The present paper gives the results of a study by the spectrophotometric method of the basicity of flavone and its derivatives containing electron-donating substituents in the ortho or peri positions to the carbonyl group, and also in positions 7 and 4', which are conjugated with them. The protonation constant of flavone that we have calculated, $pK_{bas.}=-1.33$ (Table 1) agrees with that obtained previously by Tolmachev et al. [4]; it shows the high basicity of flavone in comparison with ketones and ethers (thus, pK for anisole is -6.54 [9] and for chalcone it is -5.0 [10]).

The introduction of electron-donating hydroxy or methoxy substituents into positions 7 and 4', because of the transmission of a positive resonance effect, increases the π-electronic charge on the carbonyl oxygen atom and increases the basicity in comparison with that of flavone. This conclusion agrees with the high acidity of 7- and 4'-hydroxy groups [2].

The protonation constants of 5-hydroxyflavone, 3-hydroxyflavone, and 3-methoxyflavone, on the other hand, are considerably less than that of flavone. It would appear that the introduction of electron-donating substituents ($\sigma^{ortho}_{OH}=-0.38$ and $\sigma^{ortho}_{OCH_3}=-0.27$ [11]) in the ortho or peri position in relation to the carbonyl should increase the basicity of the corresponding compounds. But since the opposite is actually observed, this means that the factor of the transfer of the positive resonance effect is not the deciding one. It could be assumed that the fall in basicity is connected with an intramolecular hydrogen bond. However, a fall in basicity is also observed for 3-methoxyflavone. Consequently, steric factors and the effects of solvation, hindering protonation, play a primary role in the lowering of the basicity in ortho-substituted flavone derivatives.

It is known that the frequency of the vibrations of the carbonyl group in a given structure depends both on physical and chemical factors [12]. It appeared of interest to consider the relationship between the frequencies of the vibrations of the carbonyl groups and the values of their basicities in the flavone compounds investigated, since if these two characteristics depend only on chemical factors, a simple relationship should exist between them. In actual fact, a correlation between these magnitudes is observed for flavone and its 7-hydroxy, 4'-hydroxy, and 4'-methoxy derivatives, while the 3- and 5-substituted flavones fall outside this correlation (Fig. 1).

EXPERIMENTAL

The flavonoid compounds listed in Table 1 were synthesized by methods described previously [2, 3]. Flavone was synthesized by N. G. Devyatko. 3-Methoxyflavone (mp 114-115°C) was obtained by methylating 3-hydroxyflavone [13].

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TABLE 1. Protonation Constants ($pK_{bas.}$) Calculated from Formula (I) for a Number of Monohydroxyflavones

Compound	λ,nm	$pK_{bas.}$ (av)	Mean-square error (s)	No. of degrees of freedom (f)	$pK_{bas} \pm \Delta x$
Flavone	290	−1,30	0,03	18	−1,33±0,01
	300	−1,35			
	340	−1,28			
	345	−1,33			
	350	−1,38			
7-Hydroxyflavone	360	−0,78	0,04	9	−0,79±0,03
	370	−0,78			
	375	−0,80			
4'-Hydroxyflavone	310	−0,87	0,01	15	−0,87±0,01
	320	−0,89			
	375	−0,86			
	380	−0,86			
3-Hydroxyflavone	375	−2,90	0,05	14	−2,88±0,03
	380	−2,87			
	385	−2,88			
3-Methoxyflavone	305	−2,72	0,05	20	−2,77±0,02
	310	−2,78			
	365	−2,76			
	370	−2,76			
	375	−2,86			
5-Hydroxyflavone	350	−3,09	0,06	15	−3,07±0,03
	355	−3,06			
	360	−3,06			

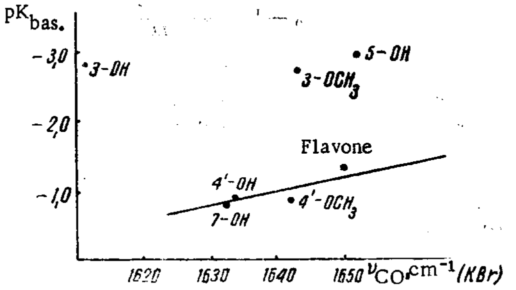

Fig. 1

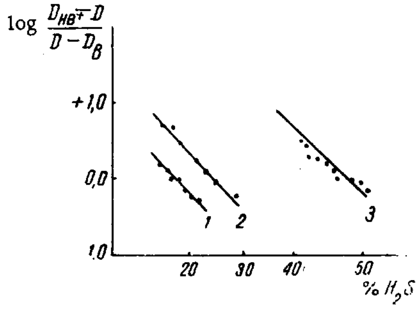

Fig. 2

Fig. 1. Relationship between the stretching vibrations of the carbonyl group ($\nu_{C=O}$) and the protonation constant ($pK_{bas.}$) of substituted flavones. The point for the 4'-OCH_3 derivative was plotted from literature information [8] and [13].

Fig. 2. Dependence of the expression log $[(D_{HB^+} - D)/(D - D_B)]$ on H_0 for the flavones: 1) 4'-hydroxyflavone, 375 nm; 2) flavone, 345 nm; 3) 5-hydroxyflavone, 355 nm.

The IR spectra of the compounds were recorded on a UR-10 spectrophotometer (tablets with KBr).

Determination of the Protonation Constants. The spectrophotometric measurements were performed on an SF-4A spectrophotometer in 1-cm cells at 20 ± 1°C. For each compound, initial solutions with concentrations of $2.0 \cdot 10^{-4}$ to $2.5 \cdot 10^{-4}$ M in 50-55% H_2SO_4 were prepared. The preparation of the working solutions and the measurements were performed as described previously [4]. The concentration of the acid in each experiment was determined by potentiometric titration on an LPU-01 instrument with a system of glass–silver chloride electrodes of the flow-through type filled with saturated KCl solution.

In all cases, we convinced ourselves of the absence of an interaction of the substance with the medium under the experimental conditions. The validity of the use of the acidity function H_0 in the determination of pK was checked by plotting a graph of the dependence of the expression log $[(D_{HB^+} - D)/(D - D_B)]$ on the percentage of H_2SO_4 present (Fig. 2). The straight lines obtained proved to be strictly parallel to the analogous straight lines plotted for substituted anilines, which are true Hammett indicators. The pK values were calculated from the formula

$$pK = H_0 - \lg\frac{D_{BH^+} - D}{D - D_B},$$

where D is the optical density of the solution with the acidity H_0; D_B and D_{BH^+} are the optical densities of the base and of the salt, respectively, when all the substance is present in the corresponding form; and H_0 is Hammett's acidity function. For all the compounds, the mean-square error and the confidence interval of the mean value for 95% probability were calculated for the values of the protonation constants obtained [14].

SUMMARY

1. The protonation constants of flavone, 3-hydroxyflavone and its methyl ether, and 7-, 5-, and 4'-hydroxyflavones have been determined by a spectrophotometric method.

2. It has been shown that the basicities of the monohydroxyflavones change fundamentally according to the position of electron-donating substituents in the molecule.

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