ULTRAVIOLET ABSORPTION OF FLAVONOIDS.

V. THE STRUCTURE OF 3- AND 5-HYDROXYFLAVONES

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In a study of the acid–base properties of the flavonoids [1-3] we observed a number of peculiarities in the behavior of 3- and 5-hydroxy flavones. In view of this, we have performed a supplementary investigation of these compounds by spectral methods.

In the IR spectra of 3-hydroxyflavone taken in KBr tablets, the frequency of the stretching vibrations of the carbonyl group [1613 (s), 1650 (w, shoulder) cm^{-1}] is considerably lowered in comparison with that of flavone (1650 cm^{-1}). This has also been reported by other workers [4, 5]. To explain such a phenomenon one could adduce the opinion firmly established in the literature of the formation of a strong intramolecular hydrogen bond (intra-HB) between the carbonyl and the 3-OH group [5, 6]. However, certain facts characterizing the hydroxy group do not agree with this. In the first place, the hydroxy group has a fairly high ionization constant [1], and in the PMR spectrum the signal of its proton appears in a strong field at δ 7.01 ppm (in CCl_4). In the second place, in the case of an intra-HB of the chelate type the appearance of a broad band of the stretching vibrations of the hydroxyl in the region of fairly low frequencies (2500-3000 cm^{-1}) could be expected. In actual fact, the stretching vibrations of this group have the form of a broad symmetrical band with a maximum at 3350 cm^{-1} (at a concentration of 0.005 M in CCl_4).

The stretching vibrations of the CO group appear in the form of two bands at 1622 (s) and 1652 (w, shoulder) cm^{-1}, while under similar conditions the carbonyl group of flavone is characterized by one band at 1650 cm^{-1} (Table 1).

With the replacement of the nonpolar solvent CCl_4 by tetrahydrofuran (THF), which possesses a considerable basicity ($pK_a = -2.08$ [7]), in the IR spectrum of 3-hydroxyflavone (concentration 0.005 M), likewise, two bands of the stretching vibrations of the CO group are observed [1625 (s) and 1642 cm^{-1}], which is shown by the retention of their half-width and molar extinction coefficients (see Table 1).

TABLE 1. Frequencies and Intensities of Absorption Bands in the 1600-1660 cm^{-1} Region

Compound	CCl_4		Tetrahydrofuran	
	ν, cm^{-1}	ε, $liter \cdot cm^{-1} \cdot mole^{-1}$	ν, cm^{-1}	ε, $liter \cdot cm^{-1} \cdot mole^{-1}$
Flavone	1624 1653	260 1090	1612 1645	370 1270
3-Hydroxyflavone	1622 1652	1287 173	1625 1642	813 430
5-Hydroxyflavone	1620 1652	920 790	1615 1650	1180 1010
5-Methoxyflavone	1580 1650	372 1390	1605 1656	368 1372

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TABLE 2. UV Absorption of Flavone Derivatives

Compound	λ, nm (ε)	
	band I	band II
Flavone	297 (21600)	250 (18000)
7-Hydroxyflavone	310 (25120)	250 (20420)
4'-Hydroxyflavone	325 (25700)	250 (11750)
3-Hydroxyflavone	305 (13660) 345 (19400)	239 (20800)
3-Methoxyflavone	300 (17400) 320 (15900)	245 (18320)
5-Oxyflavone	300 (15850) 335 (8511)	270 (30200)
5-Methoxyflavone	293 (14680) 325 (12000)	265 (29520)

The position of the lower-frequency band scarcely changes when CCl_4 is replaced by THF, but as in the case of flavones with the analogous change of solvent, the 1652-cm^{-1} band shifts in the low-frequency direction and its intensity rises. This fact shows that 3-hydroxyflavone interacts with THF. This is also confirmed by a broadening of the band of the stretching vibrations of the hydroxy group in THF (3200-3400 cm^{-1}, concentration 0.005 M) as compared with CCl_4 (3300-3400 cm^{-1}, concentration 0.005 M).

The basicity of 3-hydroxyflavone differs little from that of 3-methoxyflavone [3], and consequently the hydrogen bond in 3-hydroxyflavone is not (as has been assumed [8]) the main cause of its lowered basicity in comparison with flavone.

On the whole, the spectral characteristics have confirmed the hypothesis that we have put forward previously [1] that the peculiarities of the properties of 3-hydroxyflavone are connected not with the formation of an intra-HB but with the fact that the introduction of the proton-donating hydroxy group into position 3 leads to an increase in the aromaticity of the pyrone fragment through the stabilization of a pyrylium structure. The result of the increased conjugation and the strong polarity of the carbonyl group in 3-hydroxyflavone may be the presence of the band of stretching vibrations of the carbonyl group in a region of fairly low frequencies.

In agreement with the peculiarities of the structure of 3-hydroxyflavone mentioned above are the results obtained in a study of the emission and absorption spectra of monosubstituted flavones. In the absorption spectrum of 3-hydroxyflavone the long-wave band has a high intensity and is shifted in the red direction as compared with the analogous bands in the spectra of other monosubstituted flavones (Table 2), which may be considered as proof of an increase in conjugation in 3-hydroxyflavone.

3-Hydroxyflavone differs from other luminescing flavone derivatives by the fact that its emission spectrum has not one, but two clearly defined fluorescence bands: a long-wave band at 526-600 nm, present in all the spectra, and a short-wave band at 390-510 nm appearing only at reduced temperatures and in polar media. Analysis of the emission spectra has permitted the assumption that the short-wave band is due to the emission of molecules of 3-hydroxyflavone associated with the solvent. This is in harmony with the results of IR spectroscopy.

Starting from the results of a determination of the protonation constants of flavonoid compounds [3], it may be assumed that the introduction of an electron-donating substituent into position 5 should, just as in the case of 7-hydroxyflavone, lead to an increase in basicity through the additional resonance effect of the substituent. In actual fact, the basicity of 5-methoxyflavone ($pK_a = -1.22 \pm 0.01$) is somewhat higher than that of flavone [3], while, conversely, the introduction of a hydroxy group into position 5 leads to a decrease in basicity [3].

The hydroxy group in 5-hydroxyflavone has a reduced ionization constant in comparison with 7-, 4'-, and 3-hydroxyflavones [1, 2], and in the IR spectrum (CCl_4) its stretching vibrations appear in the form of a broad band in the 2700-3000 cm^{-1} region. In the PMR spectrum, the signal of the proton of this hydroxyl is observed in the weak field at δ 12.39 ppm. These facts, in association with information on the reduced basicity of the 5-hydroxy group show the formation of an intra-HB of the chelate type which, in its turn, is the cause of the reduced acidity and basicity of 5-hydroxyflavone.

Facts characterizing the state of the carbonyl group are not in harmony with the formation of an intra-HB. In spite of chelate binding, the band of the stretching vibrations of the CO group in 5-hydroxyflavone appears in a region of even somewhat higher frequencies than in flavone itself (1653 and 1647 cm^{-1} (KBr), respectively). However, in 5-hydroxyflavone, which also contains an intra-HB, ν_{CO} shifts in the low-frequency direction by 30 cm^{-1} as compared with flavanone [4]. The anomalously high position of ν_{CO} in 5-hydroxyflavone has also been reported by other workers [4, 5], but until now there has been no substantiated explanation of this phenomenon.

In an analysis of the intensities of the IR absorption bands in the 1600-1650 cm^{-1} region (see Table 1), attention is attracted by the fact that in 5-hydroxyflavone, in addition to the 1650 cm^{-1} band, there is a strong band at 1620 cm^{-1}. By analogy with the closely related 5-hydroxychromones, in which an anomalously high position of ν_{CO} is also observed when an intra-HB is present, to explain this peculiarity one could bring in Fermi resonance [9, 10], considering both the strong bands at 1650 and 1620 cm^{-1} as components of a carbonyl doublet. But, in the first place, we do not observe bands of doublet nature similar in the ratio of their intensities in 5-methoxyflavone, which has the same type of substitution as 5-hydroxyflavone, and in the second place, with a change in the polarity of the solvent there is no inversion of the intensities of the components of the bands of the doublet as is characteristic for Fermi resonance (see Table 1).

If the flavones are regarded as α,β-unsaturated ketones, then, on the basis of literature information [4, 5], it may be considered that the short-wave band relates to the stretching vibrations of the CO group and the long-wave band to the C=C vibrations in the s-trans form of the ketone. In actual fact, in flavone and 5-methoxyflavone the intensity of the maximum of the absorption band of the CO bond is greater than that of the C=C bond, and when the nonpolar solvent CCl_4 is replaced by THF a considerable shift of the band of the carbonyl group takes place, which is in harmony with their trans form [11]. In the IR spectrum of 5-hydroxyflavone, conversely, an increase in the intensity of $\nu_{C=C}$ and a slight shift of the absorption band of the carbonyl group are observed with a change in the polarity of the solvent, which shows a distortion of the trans form.

On analyzing the results of IR spectroscopy, we came to the conclusion that the introduction of a hydroxy group into position 5 of flavone is accompanied by the formation of an intra-HB and, apparently, causes a distortion of the planar arrangement of the pyrone fragment. The hypothesis put forward was the basis for an explanation of the anomalous position of ν_{CO} in 5-hydroxyflavone. In actual fact, a disturbance of coplanarity in 5-hydroxyflavone should lead to an increase in ν_{CO} by 10-20 cm^{-1} as compared with the trans form of flavone [11]. However, the formation of a chelate ring levels out this difference [12] and, as a result, in 5-hydroxyflavone the same ν_{CO} frequency is observed as in flavone.

In 5-hydroxyflavone, in contrast to flavone and its 7-,4'-, and 3-hydroxy derivatives, no luminescence has been observed. However, the methyl ether of 5-hydroxyflavone has an emission spectrum similar to that of flavone (phosphorescence band located in the 393-560-nm region). This shows that the peculiarities of the structure of 5-hydroxyflavone are in fact connected with the formation of a strong intra-HB. The reduced intensity and bathochromic shift of the long-wave band in the absorption spectrum of 5-hydroxy flavone as compared with the corresponding band of its methyl ether show that in addition to the formation of an intra-HB, in 5-hydroxyflavone steric hindrance is increased.

EXPERIMENTAL

The physicochemical characteristics and methods of synthesizing the flavonoid compounds given in Table 1 have been described previously [1, 2].

The IR spectra were taken on a UR-20 spectrophotometer in the 700-3700-cm^{-1} region in solutions in CCl_4 and THF and for tablets of the substance moulded in KBr; concentration 0.05-0.005 M. The intensity was calculated at the maxima of the bands of stretching vibrations of the carbonyl groups.

The UV spectra were taken on an SF-4A spectrophotometer at a concentration of $2.5\text{-}5.0 \cdot 10^{-5}$ M in ethanol.

The luminescence spectra were obtained on an ISP-51 instrument and were recorded on a PDS-021 M two-coordinate recorder. The concentration of the substance was 0.05 g/liter.

SUMMARY

1. The peculiarities of the properties of 3-hydroxyflavone are due to the fact that the introduction of the proton-donating hydroxy group directly into the heterocycle leads to an increase in the aromaticity of the pyrone fragment through the stabilization of a pyrylium structure.

2. The causes of the decreased acidity and basicity of 5-hydroxyflavone are the formation of an intramolecular hydrogen bond of the chelate type and a disturbance of the co-

planarity of the molecule. The combination of these factors explains the anomalously high position of the band of the stretching vibrations of the carbonyl group of this compound.

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