

Spectral and basic properties of flavones in the ground and excited states

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Dependence between structures of R-oxyflavones and their spectral and basic properties has been investigated. It was found that pK_a of flavones, depending on positions of hydroxy and methoxy groups, increase by 6-8 orders of magnitude upon excitation and reaches 3.7-6.6 units. Due to high pK_a^* value carbonyl group can serve as a proton acceptor in the excited-state intramolecular proton transfer as far as in the formation of phototautomers of 7- and 4'-hydroxyflavones in protic solvents.

Introduction

Hydroxyflavones have been the convenient models for exploration of the intramolecular proton transfer in the excited state (ESIPT) for approximately 40 years [1]. Numerous investigations showed that the efficient proton transfer depends on three conditions, among which the most important one is high acidity of proton-donating hydroxyl group in the excited state. Lowering of 3-hydroxy group acidity upon excitation results in decrease of ESIPT rate, which, in the case of 4'-dimethylaminoflavonol in some solvents, makes possible a reverse proton transfer and the acid/base equilibrium appearance [2].

The next important factor is the presence of hydrogen bond of any strength between a donor and an acceptor of proton. If such hydrogen bond is absent or broken, the ESIPT process is not possible. When proton-donating hydroxy group forms stronger hydrogen bond with solvent molecules, the photo dissociation process takes place, which corresponds to intermolecular proton transfer on a solvent [3,

4].

The third condition necessary for ESIPT is high basicity of proton-accepting carbonyl group in the excited state. The pK_a^* value of the carbonyl group must be higher or, at least, comparable with pK_a^* of hydroxy group. The basic properties of flavone carbonyl group in the ground and excited states were not thoroughly explored. Apparently this is so because the formation of 3-hydroxyflavone phototautomer manifests itself a high basicity of the carbonyl group in the excited state. Some pK_a^* obtained earlier [5, 6] were not analyzed in context of the ESIPT dynamics.

The synthesis of new flavone derivatives with several carbonyl groups, for example diflavonols, which bring up the problem of a double ESIPT probability [7], or hetaryl chromones, where alternative ESIPT to the basic nitrogen atom of side heterocycle takes place [8], necessitates thorough investigations of the basicity of flavone carbonyl groups.

The present work is devoted to the investigations of the carbonyl group basicity for

the simplest flavones, which could be able to form phototautomers. It contains the analysis of relationship between pK_a and pK_a^* and the nature of substituents, the geometry and electronic structure of flavones in the ground and excited states. Structures of the investigated flavones are listed in Table 1.

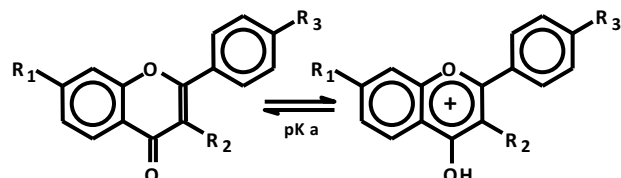


Table 1. Structures of the investigated flavones

	R ₁	R ₂	R ₃		R ₁	R ₂	R ₃
<i>Ia</i>	OH	H	H	<i>IIa</i>	H	H	OH
<i>Ib</i>	OMe	H	H	<i>IIb</i>	H	H	OMe
<i>Ic</i>	OH	OH	H	<i>IIc</i>	H	OH	OH
<i>Id</i>	OH	OMe	H	<i>IIId</i>	H	OMe	OH
<i>Ie</i>	OMe	OH	H	<i>IIe</i>	H	OH	OMe
<i>If</i>	OMe	OMe	H	<i>IIIf</i>	H	OMe	OMe

Results and discussion

Carbonyl group of flavones demonstrates weak basic properties in the ground state, its protonation takes place at $H_0 < 0$. Figure 1 shows spectral effects accompanying the protonation of flavone carbonyl group. The formation of flavylum cation results in a bathochromic shift of long-wavelength absorption band and in the most of cases to a rise of fluorescence. Spectral parameters of the neutral and cationic forms of the investigated flavones are presented in Table 2.

The data listed in the Table 2 show that introduction of the hydroxy and methoxy groups in position 4' of the flavone moiety results in higher bathochromic shifts of long-wavelength absorption bands (2035 cm^{-1} and 2225 cm^{-1}) than

when these groups are in position 7 (1195 cm^{-1} and 845 cm^{-1} , correspondingly).

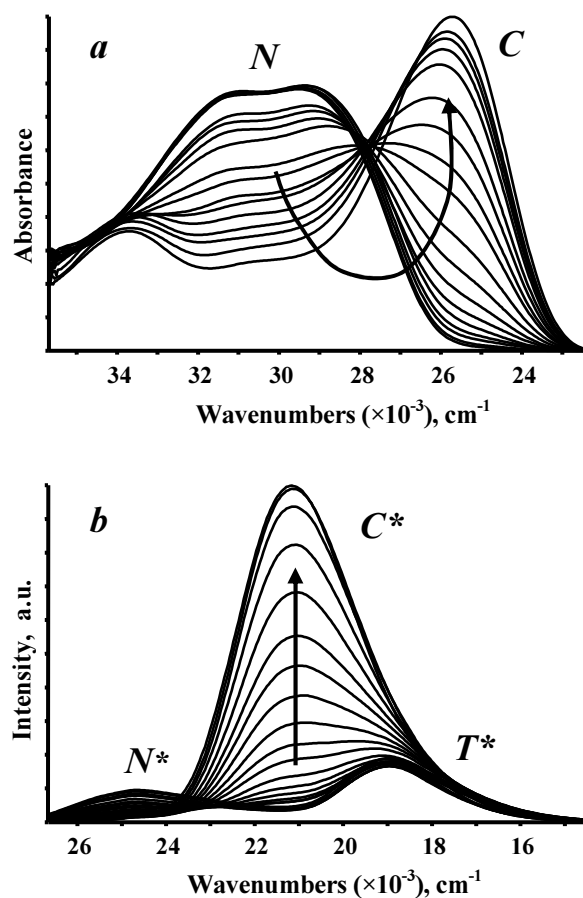


Figure 1. Changes in absorption (a) and fluorescence (b) spectra of *Ic* upon a cation formation. N and C are a neutral form and a cation in the ground state, N* and T* are tautomers of a neutral form and C* is cation in the S₁ state.

Introduction of the hydroxy group into position 3 results in the additional bathochromic shift in the range of $2200\text{--}2500\text{ cm}^{-1}$. On the contrary, presence of the 3-methoxy group does not show any noticeable spectral effect in the case of 7-substituted flavones, and leads to some bathochromic shift ($800\text{--}1100\text{ cm}^{-1}$) in the case of the 4'-substituted derivatives.

Such spectral effects permit to conclude, that substituents in the side phenyl ring influence the electronic structure of flavone to a greater extent than substituents in the chromone fragment. Methylation minimizes influence of

the 3-hydroxy group on spectral properties of the flavones, because of the rotation of the Table 2. Spectral parameters of flavone derivatives*.

	Neutral form				Cation			
	$\nu_{\text{abs}} (\lambda_{\text{abs}})$	$\nu_{\text{fl}} (\lambda_{\text{fl}})$	$\Delta\nu_{\text{St}}$	ν_{0-0}	$\nu_{\text{abs}} (\lambda_{\text{abs}})$	$\nu_{\text{fl}} (\lambda_{\text{fl}})$	$\Delta\nu_{\text{St}}$	ν_{0-0}
<i>fl</i>	32895 (304)	–	–	–	28735 (348)	24720 (405)	4015	26730
<i>Ia</i>	31700 (316)	24300 (412)	7400	28000	27020 (370)	21760 (460)	5260	24390
<i>Ib</i>	32750 (307)	24660 (406)	8090	28705	27400 (365)	22380 (447)	5020	24890
<i>Ic</i>	29500 (339)	24700 (405)	4800	27100	25770 (388)	21160 (472)	4610	23465
<i>Id</i>	31550 (317)	24000 (416)	7550	27775	26110 (383)	21340 (468)	4770	23725
<i>Ie</i>	29580 (338)	24620 (406)	4960	27100	25840 (387)	21460 (466)	4380	23650
<i>If</i>	31550 (317)	23520 (425)	8030	27535	26320 (380)	21340 (469)	4980	23830
<i>IIa</i>	30860 (324)	23820 (420)	7040	27340	26460 (378)	21500 (465)	4960	23980
<i>IIb</i>	30670 (326)	24160 (414)	6510	27415	25970 (385)	21420 (467)	4550	23695
<i>IIc</i>	28090 (356)	22075 (453)	6050	25080	24815 (403)	20410 (490)	4405	22610
<i>IId</i>	29760 (336)	23000 (435)	6760	26380	25450 (393)	21060 (474)	4390	23255
<i>IIe</i>	28250 (354)	23200 (431)	5050	25725	24940 (401)	20740 (482)	4200	22840
<i>IIf</i>	29940 (334)	23120 (433)	6820	26530	25315 (395)	20660 (484)	4655	22990

* ν_{abs} , ν_{fl} , λ_{abs} , λ_{fl} – positions of long-wavelength absorption and emission bands maxima (ν – in cm^{-1} and λ – in nm), ν_{0-0} – values of 0-0 transitions (cm^{-1}), $\Delta\nu_{\text{St}}$ – Stokes shifts of fluorescence (cm^{-1}). *fl* – spectral parameters of unsubstituted flavone and its conjugated acid – 4-hydroxyflavylium ion [5].

obtained methoxy group out of the chromone plane.

Spectral effects caused by introduction of the 4'- and 7-R-oxygroups to 4-hydroxyflavylium cations are similar to those of the neutral flavones. However, the bathochromic shifts in absorption spectra of the cations are somewhat higher than in the case of the neutral forms. For 7-OH, 7-OCH₃, 4'-OH and 4'-OCH₃ the shifts are 1715, 1565, 2275 and 2765 cm^{-1} correspondingly. Influence of the 3-hydroxy and 3-methoxy groups on spectral properties of the flavylium cations is sufficiently weaker in comparison with the neutral flavones.

The majority of the investigated flavones have a weak fluorescence band in the range 22600-24700 cm^{-1} , which does not depend on the nature and positions of substituents. 3-hyd-

roxyflavones demonstrate two-band fluorescence spectra, where long-wavelength intense band is due to phototautomer T* emission [1] (depicted on Figure 1). All the 4-hydroxyflavylium cations demonstrate intense one-band fluorescence in a narrow diapason of ~ 20750-21750 cm^{-1} . Positions of the band maxima are not considerably influenced by nature and positions of substituents.

The neutral forms of the majority of the investigated flavones demonstrate abnormally high Stokes shifts of fluorescence – 6760-8030 cm^{-1} , which evidences a substantial structure and solvent relaxation of these compounds in the excited states. Since flavones and especially hydroxyflavones have strong intermolecular hydrogen bonds with solvent molecules in the ground state, high Stokes shift values can be due

to drastic reorganization of H-bonds upon excitation. Thus, in the case of the 3-hydroxyflavones having intramolecular hydrogen bond, H-bonding of the carbonyl fragment with solvent molecules is weakened, and Stokes shifts are significantly lower – 4800-5050 cm⁻¹. Furthermore, the high Stokes shifts can also be explained by changing of an angle between the side phenyl ring and the chromone fragment, i.e. by flattening or twisting flavone molecules in the excited state.

A typical titration curve of the flavones in H₀ region is depicted on Figure 2. The curve has only one inflection point, which implies one-step protonation of the investigated compounds. Dissociation constants are presented in Table 2. The obtained values are similar to pK_a determined earlier for some hydroxyflavones [5,6]. Methylation of the hydroxy groups does not substantially change pK_a values.

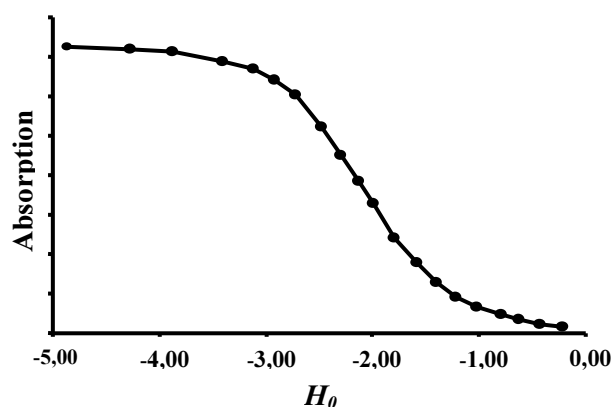


Figure 2. Titration curve for *Ic* in H₀ range.

Table 3. Dissociation (deprotonation) constants of flavones.

	pK _a	pK _a [*]		pK _a	pK _a [*]
<i>fl</i>	-1.33 [5]				
<i>Ia</i>	-1.01 ± 0.04	6.6	<i>IIa</i>	-0.93 ± 0.03	5.7
	-0.79 [5]			-0.87 [5]	
<i>Ib</i>	-0.72 ± 0.04	6.7	<i>IIb</i>	-0.93 ± 0.04	6.9

<i>Ic</i>	-2.09 ± 0.05	5.5	<i>IIc</i>	-2.21 ± 0.04	4.1
	-2.14 [6]			-2.15 [6]	
<i>Id</i>	-2.01 ± 0.04	6.5	<i>IIId</i>	-2.06 ± 0.04	4.5
<i>Ie</i>	-2.18 ± 0.03	4.6	<i>IIe</i>	-2.37 ± 0.04	3.7
<i>If</i>	-1.91 ± 0.04	5.9	<i>IIIf</i>	-2.10 ± 0.03	5.3

Introduction of the 3-hydroxy group into hydroxyflavones decreases their basicity: pK_a of the carbonyl group diminishes on 1 order of magnitude, approximately. Methylation of the 3-hydroxy group has a negligible effect (pK_a decreases by only 0.1-0.2 units) in spite of intramolecular H-bond breakage and rotation of the obtained methoxy group.

Table 3 contains pK_a^{*} values for the excited flavones, obtained by Forster method basing on pK_a values in ground state and parameters of 0-0 transitions for the neutral forms and cations. Analysis of the pK_a^{*} values showed that, after excitation, dissociation constants of the 7-substituted flavones increase on the average by 7.6 orders of magnitude (ΔpK_a = 6.8-8.5), whereas in the case of the 4'-substituted derivatives pK_a increases by 6.7 orders of magnitude approximately (ΔpK_a = 6.1-7.8). The pK_a^{*} values of the investigated flavones are in the range of 3.7-6.9 units, hence the flavones in the excited state have the basicities comparable with those of aniline and quinoline derivatives. The lowest basicity is typical for the 3-hydroxyflavones. Introduction of the 3-hydroxy group decreases pK_a^{*} value by one order of magnitude.

Conclusions

The obtained values of pK_a^{*} show the dramatical basicity growth in the excited state for all the investigated flavones. Taking to

account that pK_a^* of the flavone hydroxy groups in the excited state may reach 0-1 [9], the explored phenomenon lies in an excellent agreement with the theory of ESIPT. Moreover, such high basicity of flavones in the excited state makes it possible to suggest a possibility of the solvent-assisted proton transfer in 7- and 4'-hydroxyflavones.

An intense emission of some flavylum cations permits also to use flavones as fluorescent indicators of medium acidity in the range from 3 to 6 pH units.

Experimental part

All the investigated flavones were obtained according known methods [10]. Structures of the flavones were confirmed by 1H and ^{13}C NMR (Mercury VX, 400MHz) and by MALDI TOF mass spectrometry (Biflex III, Bruker Daltonics). Purity of the flavones was tested by liquid chromatography (Waters 600E Multisolvant Delivery System with W2487 Dual λ Absorbance Detector and Gemini 5 μm C6 phenyl 110 column) in acetonitrile-water 60/40 v/v mixture.

Dissociation constants were determined by spectrophotometric titration of the flavones by

water solutions of sulfuric acid in the acidity range from $H_0 = -4.5$ to $pH = 1.0$. Absorption and fluorescence spectra were registered on a Hitachi U3210 spectrophotometer and on a Varian Cary Eclipse spectrofluorimeter.

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