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2-(benzimidazol-2-yl)-3-hydroxychromone derivatives: spectroscopic properties and a possibile alternative intramolecular proton phototransfer

Research Article

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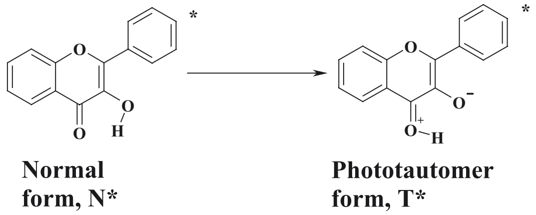
Abstract: Three 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives were synthesized. Their spectroscopic and fluorescent properties, due to excited state intramolecular proton transfer (ESIPT) from OH to carbonyl, were studied. Theoretical possibility of an alternative intramolecular H-bonding and experimental evidence for such behavior are discussed.

Keywords: *3-hydroxychromones • Benzimidazole • Intramolecular hydrogen bonding • Excited state intramolecular proton transfer reaction (ESIPT) • Absorption and fluorescence spectra*

1. Introduction

Charge and proton transfer processes are widespread, making their study important. These processes occur in 3-hydroxychromone and its derivatives, particularly synthetic and natural flavones [1-5]. More than 30 years ago the two-band character of their fluorescence spectra revealed excited state intramolecular proton transfer (ESIPT):



Subsequent investigations elucidated the mechanism and kinetics. Because intermolecular H-bonding is especially important for polar admixtures in non-polar media [6,7] particular attention was focused on ESIPT.

Synthetic and physicochemical studies of 3-hydroxychromones and 3-hydroxyflavones proceeded, but less attention was focused on their heteroaromatic derivatives, which could demonstrate special features. For example, 3-hydroxychromones having heteroaromatic groups at position 2 may have an alternative intramolecular H-bond. OH proton bonding with the lone pair of a heterocycle nitrogen may occur instead of the classical flavonolic H-bonding between the 3-OH and 4-carbonyl groups. In our previous paper [8] X-ray structural analysis of crystalline benzimidazolic 3-hydroxychromone found an intramolecular hydrogen bond to nitrogen. However, this could be the result of packing in the crystalline lattice: emission spectra for the crystalline sample and for its toluene solution were obviously different.

In the present work, the spectroscopic and fluorescent properties of three 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives are investigated. Theoretically possible alternative intramolecular H-bonding and experimental evidence for such behavior are discussed.

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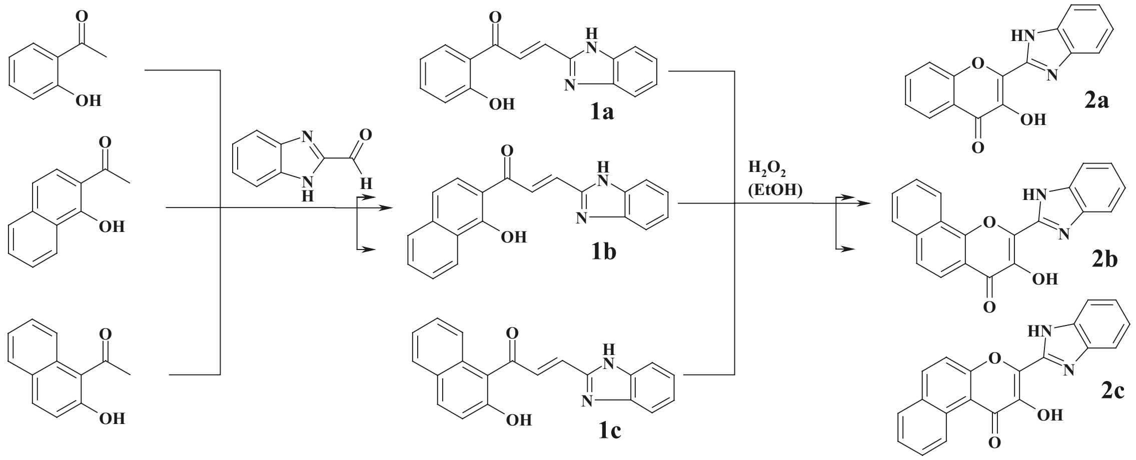


Figure 1. Synthesis of the 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives.

2. Experimental Procedures

2.1. Synthesis

The chromones were synthesized according to the Algar-Flynn-Oyamada procedure [9,10]. Purity was tested by TLC (silica gel, methanol/chloroform 1:9); structures were confirmed by ^{1}H NMR (Varian Mercury VX-200) in DMSO-d^6. X-ray structural data for **2a** are in our previous paper [8].

In the first step, chalcones were obtained by condensation of 1 g (0.0068 mole) of benzimidazole-2-carbaldehyde with 0.007 mole of o-hydroxyaryl-methylketone in 5 ml of dried methanol with 5 ml of 50% aqueous NaOH. After standing overnight, the chalcone salt was neutralized to pH = 6-7 with 5% HCl. The chalcone precipitate was filtered, washed with methanol, and dried.

The second step was an oxidative cyclization of the chalcone to the corresponding chromone. 0.5 g of chalcone was dissolved in 2 ml of 96% ethanol with 2 ml of 50% aqueous NaOH. Then 2 ml of 35% H_2O_2 solution was added dropwise, resulting in copious gas release. After peroxide addition was complete, the reaction mixture was boiled for 3-5 minutes, cooled, diluted with cold water and neutralized to pH = 6-7 with 5% HCl. The precipitated chromone was filtered off, washed with methanol and extracted with boiling $CHCl_3$ to eliminate admixtures (**2a**, 62% yield [8]) or recrystallized from methanol (**2b**, 47% yield, and **2c**, 30% yield).

^{1}H NMR data, DMSO-*d*^{6}: **2b** – 7.27 (m, 2H, broad), 7.37-8.02 (m, 7H), 8.33 (d, 1H), 9.30 (s, 1H); **2c** – 7.09 (d, 1H), 7.31 (s, 1H), 7.53-8.25 (m, 8H), 9.05 (d, 1H), 9.36 (s, 1H, broad). Signals for OH protons were sometimes poorly observed because of H-D exchange due to the slight heating required to dissolve these poorly soluble compounds in DMSO.

2.2. Absorption and fluorescence spectra

Absorption and fluorescence spectra as well as fluorescence quantum yields were measured using a HITACHI U-3210 spectrophotometer and a HITACHI F-4010 spectrofluorimeter in 10 mm quartz cells. Quinine bisulfate in 0.5 M aqueous sulfuric acid was the quantum yield reference standard [11].

Deconvolution of the emission spectra to elementary bands (necessary to calculate the normal-to-phototautomer integrated fluorescence intensity ratios) was done by software using a nonlinear least squares method with the iterative Fletcher-Powell algorithm and individual emission band shapes approximated by the asymmetric log-normal function proposed by Siano and Metzler [12]. In most cases this procedure was applied to the spectra in their semi-logarithmic representation.

3. Results and Discussion

3.1. Spectroscopic properties

The absorption and fluorescence spectra of the substituted 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives were measured in 9 solvents of different polarity (Table 1). Electronic spectra of **2a** are shown in Figure 2 in both original and semi-logarithmic form.

As shown in Table 1, the 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives are characterized by two-banded fluorescence spectra. The close similarity of the fluorescence excitation spectra of **2a-c** at both short- and long-wavelength emission maxima implies that both light-emitting forms originate from the same (ground) state. This indicates that a process producing the second emission band takes place entirely in the excited state. Thus, a short-wavelength band located at 21200-24200 cm^{-1} can be associated with emission from the normal

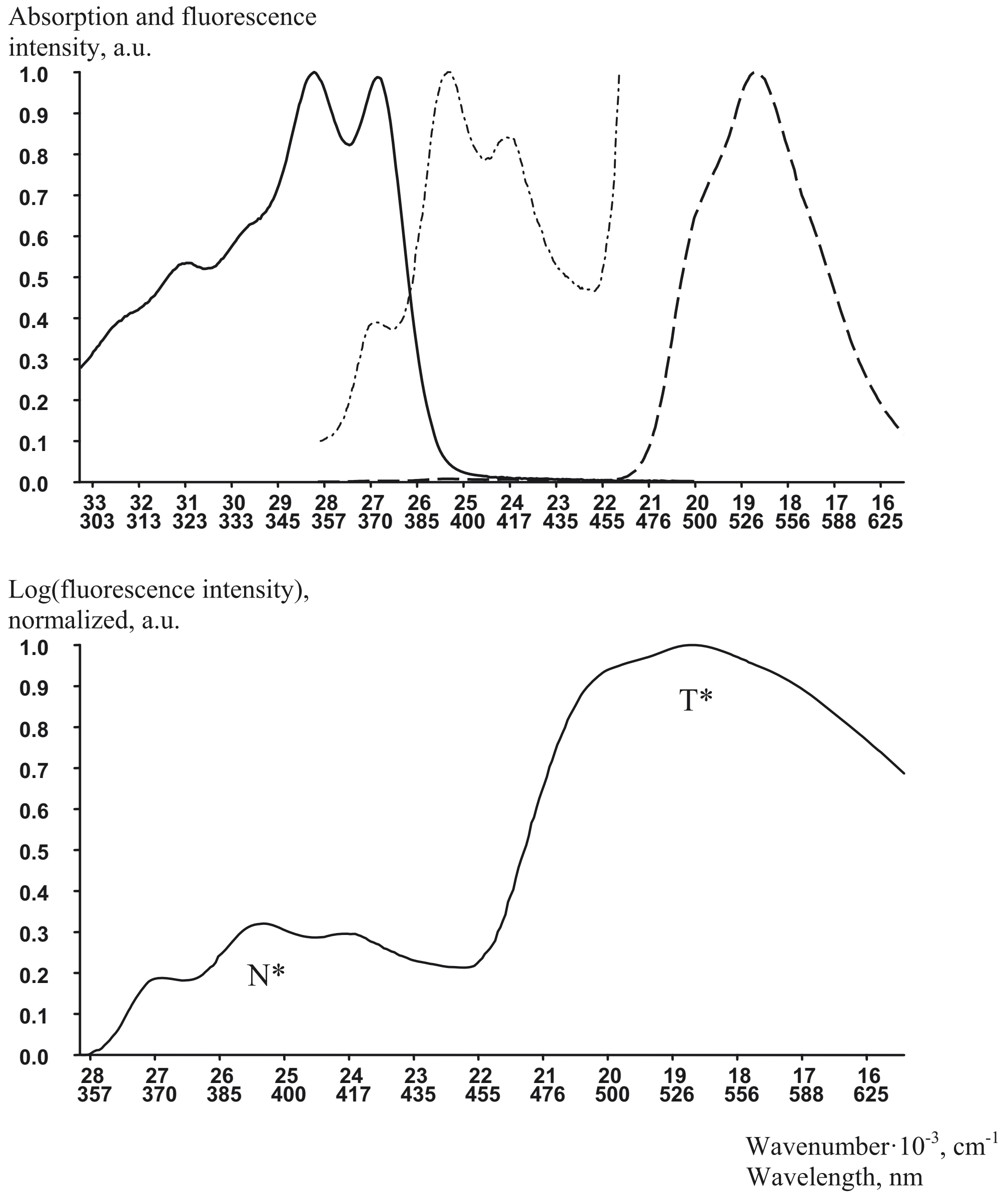


Figure 2. Upper: absorption and fluorescence spectra of **2a** in toluene. The short-wavelength emission band of the normal form (dotted line) is shown normalized to the long-wavelength absorption maximum. Lower: emission spectrum of **2a** in semi-logarithmic presentation.

form (N*), and a long-wavelength one at 18200-19200 cm^{-1} with the phototautomer (T*). The fluorescence of the latter predominates. All the fluorescence Stokes shifts for the **2a-c** phototautomer forms are abnormally high (up to 9000 cm^{-1}). It is also noteworthy that in all solvents examined the phototautomer form emission strongly prevails, indicating a rapid ESIPT.

Its high fluorescence quantum yield makes **2a** one of the most strongly fluorescent among the 3-hydroxychromonic series. Both derivatives with the benzene ring annealed to the chromone moiety emit light with significantly lower efficiency.

The Reichardt E_T^N index [13] is widely used to characterize medium polarity in investigations using fluorescent probes. According to Figure 3, the absorption spectra of **2a-c** show slight bathochromic shifts when the solvent polarity increases. The well-resolved maxima of the normal and phototautomer forms display quite different behavior with changes in E_T^N. Positive solvatofluorochromism is observed for the **2a, b** normal forms. This is in full accord with our theoretical model which found an increase in their excited state dipole moments.

Table 1. Spectral data for 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives.

Comp	Solvent	E_T^N	ν_{abs}, cm^{-1}	ν_{fl}^N, cm^{-1}	χ cm^{-1}	ν_{fl}^T, cm^{-1}	$\Delta\nu_{ST}^T$, cm^{-1}	φ
2a	toluene	0.099	26820	24190	2630	19000	7820	0.34
	1,4-dioxane	0.164	26920	23840	3080	18530	8390	0.25
	ethyl acetate	0.228	27100	22960	4140	19050	8050	0.31
	1,2-dichloroethane	0.327	26860	23140	3720	18950	7910	0.44
	acetonitrile	0.460	27180	22790	4390	18690	8490	0.65
	propanol-2	0.546	26680	22500	4180	18280	8400	0.11
	butanol-1	0.586	26600	22350	4250	18140	8460	0.12
	acetic acid	0.648	27040	22280	4760	18460	8480	0.064
	ethanol	0.654	26800	21950	4850	18230	8570	0.043
2b	toluene	0.099	27040	23180	3860	19000	8040	0.084
	1,4-dioxane	0.164	27320	23350	3970	19180	8140	0.084
	ethyl acetate	0.228	27460	23160	4300	19540	7920	0.094
	1,2-dichloroethane	0.327	27400	22790	4610	19380	8020	0.058
	acetonitrile	0.460	27420	22810	4610	19190	8230	0.083
	propanol-2	0.546	26840	22450	4390	18700	8140	0.032
	butanol-1	0.586	26600	22030	4570	19030	7570	0.029
	acetic acid	0.648	27100	21430	5670	18690	8410	0.025
	ethanol	0.654	26880	21180	5700	18440	8440	0.025
2c	toluene	0.099	26740	22750	3990	18900	7840	0.062
	1,4-dioxane	0.164	26880	22970	3910	18690	8190	0.017
	ethyl acetate	0.228	27100	23020	4080	18910	8190	0.022
	1,2-dichloroethane	0.327	26900	23440	3460	18880	8020	0.080
	acetonitrile	0.460	27180	23210	3970	18420	8760	0.031
	propanol-2	0.546	26800	22860	3940	18410	8390	0.010
	butanol-1	0.586	26580	23180	3400	18400	8180	0.012
	acetic acid	0.648	26960	22770	4190	18630	8330	0.011
	ethanol	0.654	26840	23040	3800	18320	8520	0.008

ν_{abs}, ν_{fl}^N, ν_{fl}^T – *absorption, normal fluorescence, and phototautomer fluorescence maxima;*
ν_{fl}^T, $\Delta\nu_{ST}^T$ – *normal and phototautomer fluorescence Stokes shifts;*
φ – *total fluorescence quantum yield;*
E_T^N - *Reichardt polarity index [13].*

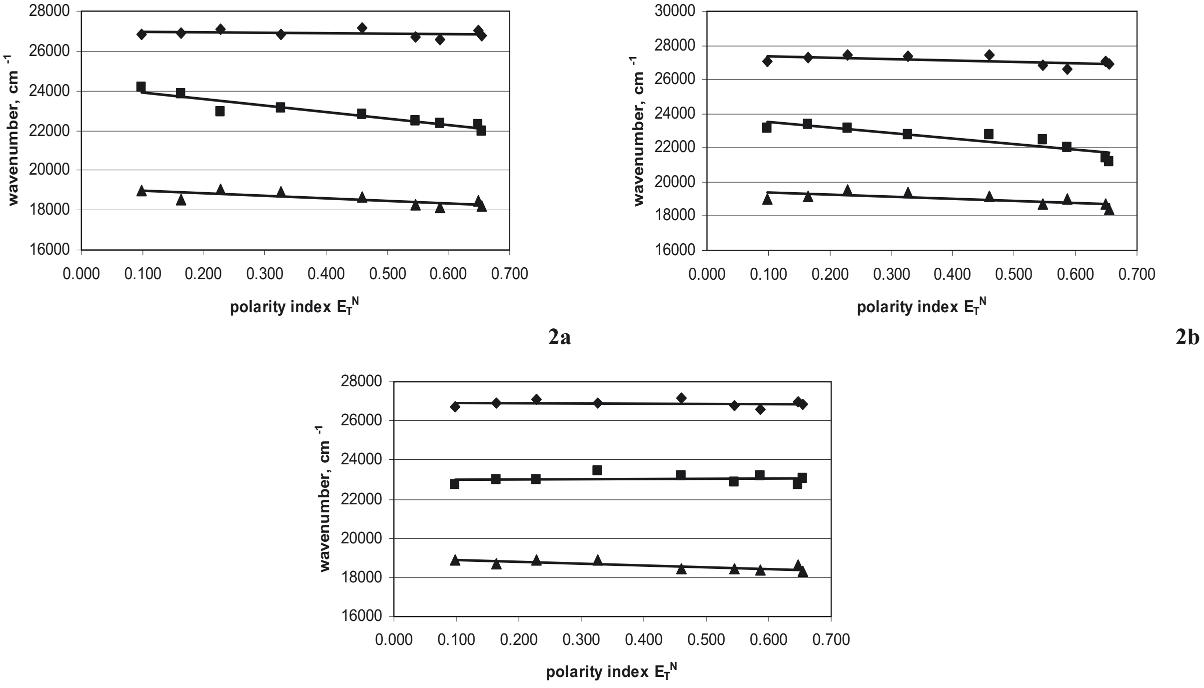
The significant difference in solvatofluorochromic behavior of the normal form of **2c** in comparison with those of **2a** and **2b** may be due the annelated benzene ring preventing its carbonyl group from H-bonding with proton donors of E_T^N>0.5 [14].

Generally, phototautomer forms do not display noticeable sensitivity to solvent polarity: in most cases their maxima remain practically unchanged. This effect is observed most prominently for the diethylamino derivative of 3-hydroxychromone [15]. In contrast, the phototautomer forms of compounds **2a-c** demonstrate definite emission wavenumber sensitivity to solvent polarity.

Quite traditional I_FN^*/I_FT^* behavior was demonstrated by **2a-c**, with no visible deviation for solvents capable of H-bonding. Association with solvent molecules, especially important for highly polar proton donor or acceptor solvents, competes with the intramolecular H-bonding and affects the ESIPT [16,17]. Intermolecularly H-bonded species with a broken intramolecular H-bond generally lose the capacity for excited state proton phototransfer. This decreases the yield of the ESIPT reaction product (T*), which is observed in the rise of the intensity of the N* emission (see Figure 4). Another possible mechanism for the change in IFN^*/I_FT^* is the pronounced quenching of the phototautomer fluorescence in polar media [18]. Both mechanisms result in an increase of the ratio; determination of their relative contributions requires special investigation.

3.2. Consideration of an alternative ESIPT

In addition to showing two-band fluorescence due to ESIPT, compounds **2a-c** belong to the group of 3-hydroxychromones with a heteroaromatic group in



2a **2b**

2c

Figure 3. Solvatochromic and solvatofluorochromic behavior of 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives **2a-c**: positions of the absorption (♦), normal (■) and phototautomer (▲) emission maxima versus solvent polarity index E_T^N. Data points correspond to the order of solvents listed in Table 1.

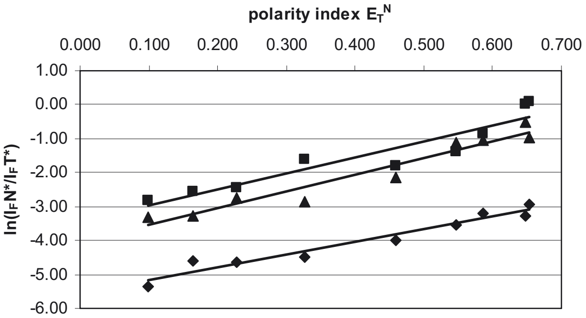
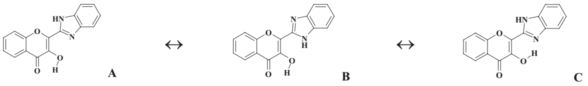


Figure 4. Natural logarithm of the normal-to-phototautomer fluorescence intensity ratio $ln(I_FN^*/I_FT^*)$ for 2-(benzimidazol-2-yl)-3-hydroxychromone derivatives (♦ – **2a**, ■ – **2b**, ▲ – **2c**).

position 2. This opens the possibility of an alternative ESIPT. While the localization of the proton donor group is obvious – this role can be played only by the 3-OH group, the H-bond accepting center can be the carbonyl group in position 4 or the tertiary 3’ benzimidazole nitrogen.

Understanding the intramolecular H-bonding in these systems is very important to predict and control the ESIPT. The structure and energy of the excited phototautomer, as well as spectroscopic properties of the system as a whole depend on the direction of ESIPT.

Possible alternative H-bonding in **2a** was modeled by quantum chemical calculations using AM1 [19]. We assumed its three main conformations to be present in equilibrium:



To search for alternatively H-bonded structures we calculated the ground state potential energy surface for hydroxyl group and benzimidazole rotation (Figure 5, Table 2). It has two principal minima corresponding to the O–H···O=C bond (minimum B with a “nearby-structure” intermediate local minimum A) and to the N···H–O bond (minimum C). Conformation B is characterized by additional stabilization by a weaker C=O···HO···HN H-bond.

The energies (calculated heats of formation, ΔH_{form}, kcal/Mol) and fractions in the equilibrium mixture for the ground and corresponding Franck-Condon excited states for **2a** are in Table 2.

In the ground state the OH···O and OH···N hydrogen bonds are nearly equivalent; however, the first one predominates. The most energetically favorable is the doubly stabilized rotamer B, which realizes a flavonolic intramolecular H-bond to the carbonyl oxygen. However, up to 3% of the alternatively H-bonded molecules could be present in the equilibrium mixture. The same calculations for the Franck-Condon lowest excited singlet state (S_1) predict that **2a** should exist predominantly

Table 2. Ground and excited state conformations of 2-(benzimidazol-2-yl)-3-hydroxychromone.

Conformation	S_0		S_1	
	Energy, kcal/Mol	% equiv	Energy, kcal/Mol	% equiv
A	13.8	2 %	89.6	12 %
B	11.5	95 %	88.5	84 %
C	13.5	3 %	90.2	4 %

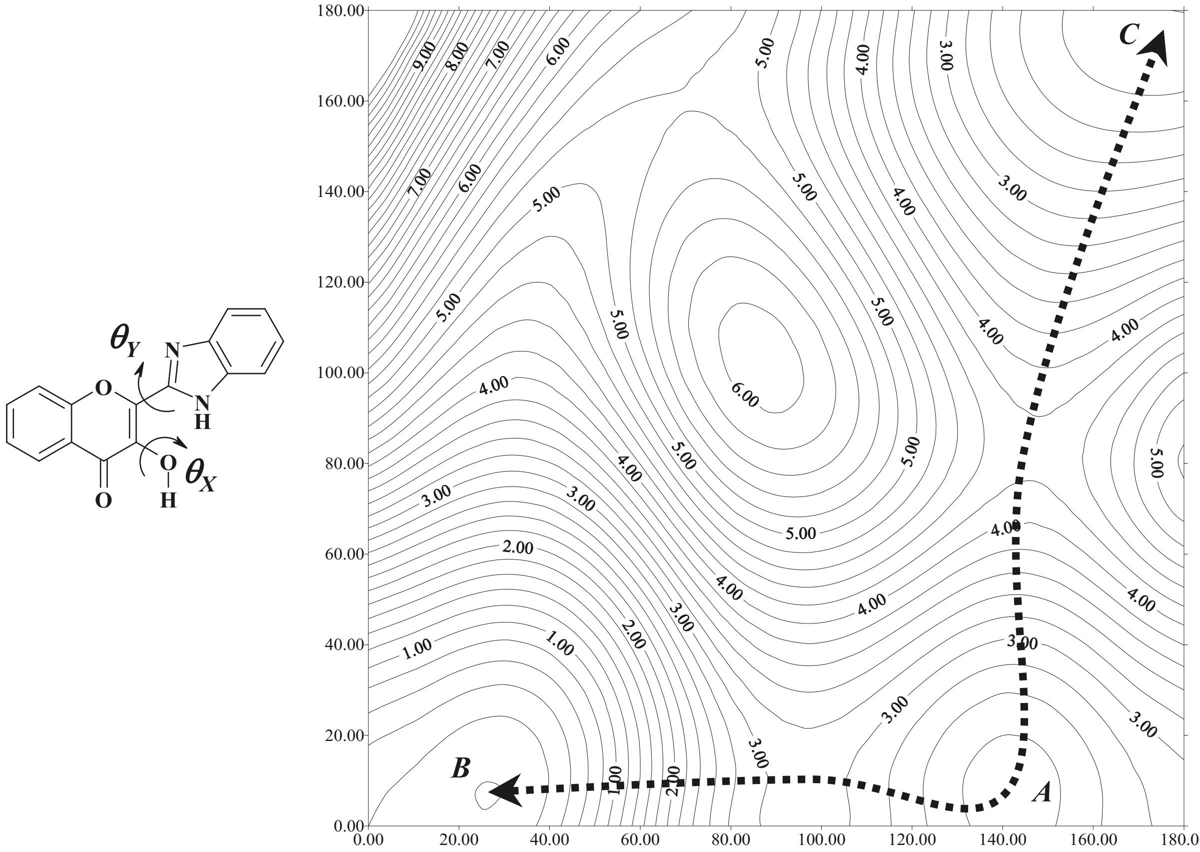


Figure 5. Potential energy surface ($\Delta\Delta H_{form}$, kcal/Mol) for the rotation of hydroxyl group (θ_X) and the benzimidazole ring (θ_Y) in 2a; AM1 calculation.

in the conventionally H-bonded conformation like its ground state.

This implies predominantly conventional H-bonding to the carbonyl group over the alternative H-bonding to the heterocycle in both ground and excited states. Consequently, the ESIPT reaction for compounds **2a-c** should proceed via the pathway expected for 3-hydroxychromones: from the hydroxyl to carbonyl group.

Experimental evidence supporting the alternative ESIPT seemed to be present in the emission spectra of 2-(benzimidazol-2-yl)-3-hydroxychromone in non-polar solvents (Figure 2). The short-wavelength shoulder on the phototautomer emission band might belong to the alternative proton phototransfer product. However, the shoulder is only ~1700 cm^{-1} away from the main maximum (from the second derivative emission spectra); thus it may be part of the phototautomer band vibrational structure instead.

Several additional investigations were made to examine this hypothesis. External heavy atom fluorescence quenching induced by methyl iodide in toluene shows intensity decrease without shape deviations in the short-wavelength area of the phototautomer band. This allows us to conclude that only one excited state emitting phototautomer exists. This is confirmed by the absence of fluorescence anisotropy spectrum deviations in the same spectral region for a polystyrene film containing **2a**.

However, the above theoretical modeling and experiments do not exclude alternative intramolecular H-bonding and alternative ESIPT for other heterocyclic

3-hydroxychromonic systems. Their molecular design, synthesis and physico-chemical investigation will be the subject of our future publications.

4. Conclusion

Three new 2-benzimidazole substituted 3-hydroxychromonic derivatives were synthesized and their spectroscopic behavior was studied in solvents with different polarity and H-bonding ability. The chromones with the possibility of alternative ESIPT were shown to behave similarly to other 3-hydroxychromones, with excited state 3-OH group proton phototransfer to the 4-carbonyl oxygen atom.

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