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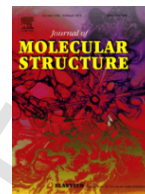
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## Structure-fluorescence relationships in 2-aryl-5-(2'-aminophenyl)-4-hydroxy-1,3-thiazoles

Richard Kammel, Denisa Tarabová, Jiří Váňa, Oldřich Machalický, Miloš Nepraš, Jiří Hanusek\*

Institute of Organic Chemistry and Technology, Faculty of Chemical Technology, University of Pardubice, Studentská 573, 532 10 Pardubice, Czech Republic

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### ABSTRACT

Five substituted 2-aryl-4-hydroxy-5-(2'-aminophenyl)-1,3-thiazoles have been studied for their fluorescence properties under neutral and alkaline conditions in solutions of various organic solvents. From comparison with the analogous 2-aryl-4-hydroxy-5-(2'-hydroxyphenyl)-1,3-thiazoles it is clear that both in neutral as well as in the deprotonated state the presence of the 2'-amino group lowers the fluorescence quantum yields ( $\Phi$ ). Introduction of an electron withdrawing groups into the 2-aryl group further decreases  $\Phi$ . Upon deprotonation of the 4-hydroxy group a large bathochromic shift of the absorption ( $\Delta\lambda_A = 100\text{--}125\text{ nm}$ ) as well as emission ( $\Delta\lambda_F = 100\text{--}120\text{ nm}$ ) bands occurs. An intramolecular hydrogen bond between the amino and hydroxyl groups is obvious. The first absorption band of all studied compounds corresponds to a  $\pi\text{-}\pi^*$  HOMO-LUMO transition with a CT character. Thiazoles **3b-f** and their deprotonated forms **3b<sup>-</sup>f<sup>-</sup>** display fluorescence properties with large Stokes shift (ca  $9000\text{ cm}^{-1}$  and  $6000\text{ cm}^{-1}$ , respectively) and moderate quantum yields (0.11–0.41), both are connected with the presence of inter and intramolecular hydrogen bonds.

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### 1. Introduction

Ten years ago Beckert et al. devised a new class of functional fluorophores containing the 4-alkoxy [1] or 4-hydroxythiazole [2] moiety. From that time his group performed many structural variations of this heterocyclic skeleton in order to achieve specific spectral and chelating properties. These structural changes mainly involved substitution at the 2- position with (un)substituted phenyls, six membered nitrogen heteroaryls [1–6] or with another heteroaryls [6–9]. The change of substituent in the 5- position from methyl to various substituted phenyls was also investigated [4,5,10] but their influence on fluorescence properties was found to be much smaller. All the 4-hydroxythiazoles prepared also showed a remarkable absorption/fluorescence bathochromic shift when transformed into their conjugated bases. Moreover, this property was easily tunable by further extension of the chromophoric system [11]. Finally, a 4-alkoxy/4-hydroxythiazole skeleton was also attached to various polymeric carriers [12–15] without loss of fluorescence thus allowing e.g. construction of dye-sensitized solar cells or pH-responsive sensors. Off the papers published by the Beckert group only a few contributions concerns 4-hydroxythiazole fluorescence properties. In 2008 Zakrzewski et al. prepared 2-ferrocenyl-4-hydroxythiazoles [16] with significant second-order nonlinear properties and the same author later combined pyrene and 4-hydroxythiazole fluorophores [17] to obtain compounds with large Stokes shifts. In our group we recently

performed the transformation of 3-bromo-1-benzofuran-2(3H)-one to the corresponding 2-aryl-4-hydroxy-5-(2'-hydroxyphenyl)-1,3-thiazoles **1a-h** [18,19] using substituted thiobenzamides. From the comparison with the analogous 4-hydroxy-2,5-diphenyl-1,3-thiazole (**2**) it was concluded that both in neutral as well as in the deprotonated state the presence of the 2'-hydroxy group substantially (2–4 times depending on solvent) enhanced fluorescence quantum yields ( $\Phi$ ) – most probably due to formation of an intramolecular hydrogen bond (IHB). Attempts to prepare the analogous 5-(2'-aminophenyl)-2-(4-methoxyphenyl)-4-hydroxy-1,3-thiazole from 3-bromooxindole failed mainly due to the preferential formation of the Eschenmoser coupling product formation [18]. However, several 5-(2'-aminophenyl)-2-(3-/4-subst. phenyl)-4-hydroxy-1,3-thiazoles were accessible from the same starting compound under different conditions. Therefore we prepared and characterized [20] five 5-(2'-aminophenyl)-2-(3-/4-subst. phenyl)-4-hydroxy-1,3-thiazoles (**3b-f**) (Fig. 1) and here we would like to introduce the results of a study of the relationships between their structure and fluorescence properties and compare the results with previously published [19] properties of 2-aryl-4-hydroxy-5-(2'-hydroxyphenyl)-1,3-thiazoles (**1a-f**) (Fig. 1).

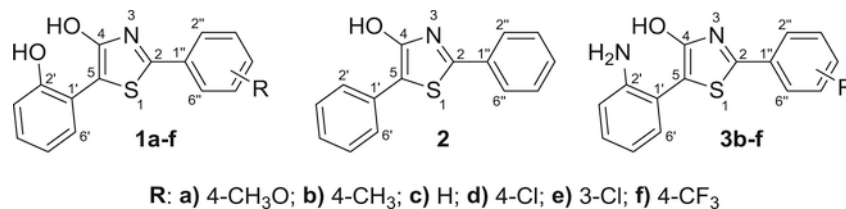
### 2. Materials and methods

#### 2.1. Chemicals

The synthesis and purification of all 2,5-diaryl-4-hydroxy-1,3-thiazoles (**1a-f**, **2** and **3b-f**) was described in our previous papers [18–20]. While all unstable **3b-f** had to be freshly prepared and characterized prior to absorption/emission spectra measurements, com-

\* Corresponding author.

Email address: Jiri.Hanusek@upce.cz (J. Hanusek)



**Fig. 1.** Structure and numbering of the substituted 2,5-diaryl-4-hydroxy-1,3-thiazoles **1a-f**, **2** from previous study [19] and structure of **3b-f** studied in this paper.

pounds **1a-f** and **2** are stable (checked by <sup>1</sup>H NMR). All other chemicals and solvents were spectral quality and were purchased from commercial suppliers and used as received.

## 2.2. UV-VIS and fluorescence measurements

The absorption spectra of **3b-f** (and **1a-f**, **2** in dichloromethane) were measured on a Hewlett-Packard 8453 diode array spectrophotometer at 25±0.1 °C in a 1 cm quartz cell in anhydrous solvents (DMSO, dioxane, dichloromethane). Concentrations of the freshly prepared samples were 2 × 10<sup>-5</sup> mol L<sup>-1</sup>. Deprotonated forms of **3b-f** in DMSO were measured upon addition of *n*-Bu<sub>4</sub>N<sup>+</sup> OH<sup>-</sup>. The corrected fluorescence emission and excitation spectra of freshly prepared samples (2 × 10<sup>-6</sup> mol L<sup>-1</sup>) were measured on a steady state spectrofluorimeter PTI Quantmaster 40. The excitation wavelength for the individual sample was always set up to the absorption wavelength maximum of the same compound. Quantum yield was calculated using Eq. (1):

$$\Phi = \frac{I}{I_S} \cdot \frac{A_S}{A} \cdot \frac{n^2}{n_S^2} \cdot \Phi_S \quad (1)$$

where  $\Phi$  is the quantum yield of the sample,  $I$  is the integral area under the fluorescence spectrum,  $n$  is the refractive index of the solvent used and  $A$  is the absorbance at the excitation wavelength. The subscript  $S$  represents the standard. As the fluorescence maxima of the investigated compounds are located in a broad wavelength range (530–700 nm), the following fluorescence standards were used for the determination of the fluorescence quantum yields: quinine sulphate in 0.5 M H<sub>2</sub>SO<sub>4</sub> ( $\lambda_{em}$  = 445 nm,  $\Phi_S$  = 0.54) [21] and coumarin 153 in ethanol ( $\lambda_{em}$  = 536 nm,  $\Phi_S$  = 0.38) [22].

To test reversibility of spectral changes between the neutral and the dissociated form of the substrate, neutral solutions of samples were alkalinized with 1  $\mu$ L of triethylamine and after recording the spectrum the acid-base equilibrium was converted back with aqueous concentrated HCl.

## 2.3. Quantum chemical calculations

Structural and the spectroscopic properties (*i.e.* equilibrium ground state conformations, singlet electronic excited state characteristics) have been calculated for the compounds studied using semiempirical PM3 and ZINDO/SCRF, methods respectively using ArgusLab 4.0 software [23].

## 3. Results and discussion

### 3.1. Acid-base properties of thiazoles **3b-f**

pH-Dependent fluorescence switching of 4-hydroxy-1,3-thiazoles was previously observed by Beckert's group [4,7,8] who attributed

this behavior to a deprotonation of the 4-hydroxy group in the thiazole ring. 4-Hydroxy-1,3-thiazoles are stronger acids in comparison to simple phenols since their  $pK_a$ -s range between 6.6 and 6.9  $pK_a$  units [24]. In our previous paper [19] dealing with **1a-f** and **2** we observed their lower acidity due to existence of IHB since full deprotonation in DMSO was achieved even after addition of triethylamine ( $pK_a$  = 9.07 in DMSO [25]).

The acid-base properties of the thiazoles **3b-f** (Scheme 1) were also studied in DMSO solution using UV-Vis spectrophotometry. The absorption maxima ( $\lambda_{max}$ ) for both **3a-f** and **3b-f** were recorded and can be found in Tables 1 and 2. Illustrative record of changes in absorption spectra for compound **3c** can be seen in Fig. 2. For other compounds (**3b**, **3d-f**) see Fig. 2A in Supplementary Info).

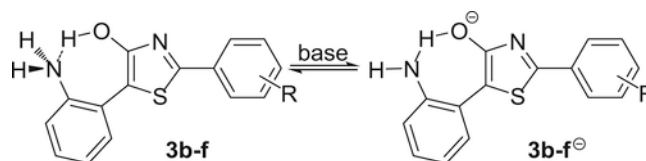
It was found that **3b-f** are less acidic than the analogous thiazoles **1a-f** [19] because gradual addition of triethylamine causes only partial dissociation of the thiazole 4-hydroxy group. Full deprotonation only occurs (Fig. 2) after addition of 1  $\mu$ L of 25% tetra(*n*-butyl)ammonium hydroxide solution which is a very strong base (*cf.* tetramethylammonium hydroxide for which  $H_-$  = 26.2 in DMSO was determined [26]).

The reduced acidity of the thiazole 4-hydroxy group corresponds to the formation of a strong intramolecular hydrogen bond (IHB) between the NH<sub>2</sub> and OH groups in which the hydrogen atom of the thiazole 4-hydroxy group is connected to a nitrogen atom of the 5-(2-aminophenyl) group. Such an arrangement is in accord with the basicity of the amino group and the enhanced acidity of the thiazole 4-hydroxy group. IHB exists also in anions **3b<sup>-</sup>f<sup>-</sup>** but the amino group now represents the proton donor and the phenoxide oxygen the acceptor part (see also theoretical discussion below).

### 3.2. Uv-vis and fluorescence spectroscopy

#### 3.2.1. Neutral forms

The absorption spectra of **3b-f** contain broad absorption bands with the maxima occurring in a relatively narrow wavelength region  $\lambda_{max}$  = 349–373 nm depending on substitution and solvent. They also display bright yellow to green fluorescence and their emission spectra as well as emission maxima ( $\lambda_{em}$ ) can be found together with  $\lambda_{max}$  in Fig. 3 and Table 1. Such behavior is similar to that observed for the previously [19] studied thiazoles **1a-f** and 4-hydroxy-2,5-diphenyl-1,3-thiazole (**2**) for which bright blue fluorescence ( $\lambda_{em}$  = 440–480 nm) was observed (*cf.* Table 1). While the introduction of hydroxy group into the *ortho*-position in series **1a-f** caused a slight bathochromic shift of  $\lambda_{max}$  [19], the similar intro-



**Scheme 1.** Dissociation of thiazoles **3b-f**.

**Table 1**  
Experimental absorption ( $\lambda_{\max}$ ) and fluorescence ( $\lambda_{\text{em}}$ ) maxima, Stokes shifts ( $\Delta\tilde{\nu}$ ) and fluorescence quantum yields ( $\Phi$ ) of **1a-f**, **2**, **3b-f** in dioxane, DMSO and dichloromethane.

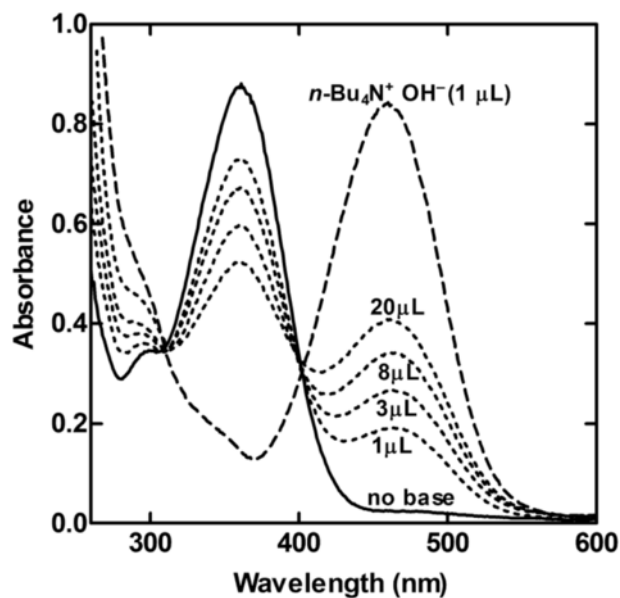
Compd.	Dioxane				DMSO				Dichloromethane			
	$\lambda_{\max}$ [nm]	$\lambda_{\text{em}}$ [nm]	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ]	$\Phi$	$\lambda_{\max}$ [nm]	$\lambda_{\text{em}}$ [nm]	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ]	$\Phi$	$\lambda_{\max}$ [nm]	$\lambda_{\text{em}}$ [nm]	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ]	$\Phi$
<b>1a</b>	357 <sup>a</sup>	445 <sup>a</sup>	5539 <sup>a</sup>	0.12 <sup>a</sup>	370 <sup>a</sup>	455 <sup>a</sup>	5049 <sup>a</sup>	0.22 <sup>a</sup>	–	–	–	–
<b>1b</b>	359 <sup>a</sup>	440 <sup>a</sup>	5128 <sup>a</sup>	0.34 <sup>a</sup>	370 <sup>a</sup>	455 <sup>a</sup>	5001 <sup>a</sup>	0.41 <sup>a</sup>	347	439	6039	0.15
<b>1c</b>	360 <sup>a</sup>	440 <sup>a</sup>	5051 <sup>a</sup>	0.53 <sup>a</sup>	371 <sup>a</sup>	458 <sup>a</sup>	5024 <sup>a</sup>	0.63 <sup>a</sup>	347	439	6039	0.18
<b>1d</b>	365 <sup>a</sup>	449 <sup>a</sup>	5126 <sup>a</sup>	0.77 <sup>a</sup>	380 <sup>a</sup>	470 <sup>a</sup>	4764 <sup>a</sup>	0.56 <sup>a</sup>	352	449	6137	0.47
<b>1e</b>	368 <sup>a</sup>	450 <sup>a</sup>	4952 <sup>a</sup>	0.89 <sup>a</sup>	380 <sup>a</sup>	469 <sup>a</sup>	4386 <sup>a</sup>	0.60 <sup>a</sup>	350	450	6349	0.63
<b>1f</b>	373 <sup>a</sup>	457 <sup>a</sup>	4928 <sup>a</sup>	0.93 <sup>a</sup>	389 <sup>a</sup>	484 <sup>a</sup>	4874 <sup>a</sup>	0.44 <sup>a</sup>	356	449	5818	0.56
<b>2</b>	362 <sup>a</sup>	445 <sup>a</sup>	5152 <sup>a</sup>	0.28 <sup>a</sup>	367 <sup>a</sup>	463 <sup>a</sup>	5696 <sup>a</sup>	0.13 <sup>a</sup>	355	436	5233	0.13
<b>3b</b>	352	498	8329	0.37	360	531	8945	0.36	350	450	6350	– <sup>b</sup>
<b>3c</b>	352	515	8992	0.39	361	542	9251	0.31	349	476	7645	0.13
<b>3d</b>	355	494	7926	0.41	367	560	9391	0.27	355	490	7761	0.16
<b>3e</b>	359	527	8880	0.41	370	568	9421	0.22	355	490	7761	0.22
<b>3f</b>	365	510	7789	0.39	373	577	9479	0.11	360	510	8169	0.22

<sup>a</sup> Values taken from Ref. [20].

<sup>b</sup> Value is too low for precise measurement.

**Table 2**  
Experimental absorption ( $\lambda_{\max}$ ) and fluorescence ( $\lambda_{\text{em}}$ ) maxima, Stokes shifts ( $\Delta\tilde{\nu}$ ) and fluorescence quantum yields ( $\Phi$ ) of **3b<sup>-</sup>**-**f<sup>-</sup>** in DMSO.

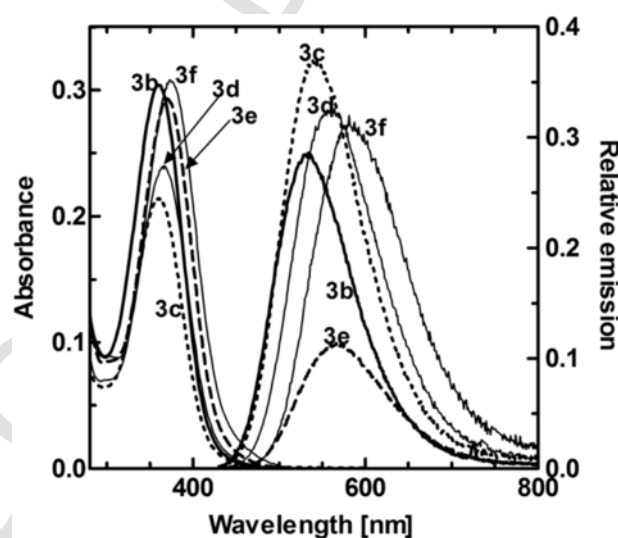
	$\lambda_{\max}$ [nm]	$\lambda_{\text{em}}$ [nm]	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ]	$\Phi$
<b>3b<sup>-</sup></b>	459	633	5989	0.36
<b>3c<sup>-</sup></b>	463	640	5973	0.29
<b>3d<sup>-</sup></b>	477	657	5744	0.26
<b>3e<sup>-</sup></b>	482	661	5618	0.23
<b>3f<sup>-</sup></b>	498	696	5713	0.13



**Fig. 2.** Absorption spectra of **3e** in DMSO (solid line), upon addition of various amount of triethylamine (volume in  $\mu\text{L}$  is directly indicated in the Figure) and upon addition of  $1 \mu\text{L}$  of  $n\text{-Bu}_4\text{N}^+ \text{OH}^-$  (25% in methanol) corresponding to pure **3e<sup>-</sup>** (dashed line).

duction of *o*-amino group in series **3b-f** causes a hypsochromic shift  $\Delta\lambda_{\max} = 6 \text{ nm}$  compared to parent compound **2**.

It is noteworthy that in all the solvents used both absorption as well as emission maxima provide good linear Hammett correlations when using Hammett  $\sigma$ -constants (in DMSO see Fig. 4 and for other solvents Fig. 4A and B in Supplementary Info) for substituents in the 2-aryl moiety. While for **1b-f** both  $\lambda_{\max}$  as well as  $\lambda_{\text{em}}$  have the same



**Fig. 3.** Absorption and fluorescence spectra of **3b-f** in DMSO.

sensitivity to the change of substitution (*i.e.* the slopes of linear dependences are almost the same – *cf.* Fig. 4) for **3b-f** the sensitivity of  $\lambda_{\text{em}}$  is *ca* 3.4–4.3 times higher (in DMSO and dichloromethane). In dioxane such dependence of  $\lambda_{\text{em}}$  is somewhat scattered.

From the absorption maxima (Table 1, Fig. 4) it is evident that an influence of substituent in 2-phenyl ring is very weak for the compounds of both series in all solvents used. It is also interesting that compound **2** exhibits virtually the same  $\lambda_{\max}$  as **3b-3f**. It means that the intramolecular hydrogen bond which is present in all the compounds studied is not essential for the ground state transition  $S_0 - S_1$  responsible for the most intensive absorption band.

The Stokes shifts for **3b-f** are *ca* twice as high as observed [19] for the structurally similar thiazoles **1a-f** and reach unusually high values ( $\Delta\tilde{\nu} = 8945\text{-}9479 \text{ cm}^{-1}$ ) for such small-sized molecules. Even for the much bigger 4-hydroxy-5-nitrophenyl-2-(pyren-1-yl)thiazoles [17] containing substantially extended aromatic system the Stokes shifts approach only  $8500 \text{ cm}^{-1}$ . Such large Stokes shifts such as those found for **3b-f** probably come from a substantial change of geometry between the Frank-Condon  $S_1$  state and the relaxed first excited state ( $S_1^{\text{rel}}$ ). While in the ground state the IHB fixes the dihedral angle around  $77^\circ$  (see chapter 3.3) between the thiazole and 2-phenyl ring, in the excited state the arrangement is probably much closer to

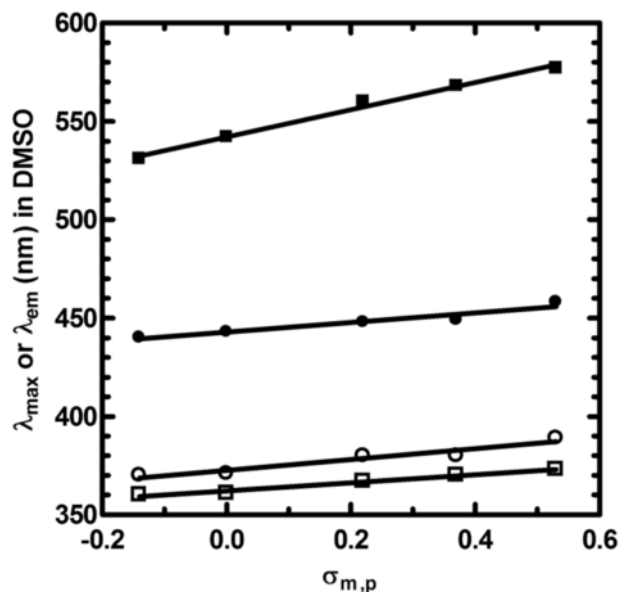


Fig. 4. Hammett correlation of absorption ( $\lambda_{\max}$ , open symbols) and emission maxima ( $\lambda_{\text{em}}$ , solid symbols) in DMSO on  $\sigma_{m,p}$  for **3b-f** (squares) and for **1b-f** (circles).

planarity. The IHB interaction strength of aromatic hydroxy and amino compounds is stronger in the lowest excited state than in the ground state. Thus the IHB is stronger in the fluorescent state [27,28]. It seems that the existence of the IHB which introduces rigidity into the whole system in all of the compounds is still beneficial for the fluorescence properties because the analogous thiazole **2**, without the  $\text{NH}_2$  group in the *ortho*-position, which is not able to form IHB, displays a significantly lower  $\Phi$ . It is noteworthy that virtually the same  $\Phi$  was found for these compounds in dichloromethane. As has been shown previously [29–33] the rate of internal  $S_1 - S_0$  conversion is substantially influenced by IHB. For the series of compounds **1a-f**, the Stokes shifts decrease only slightly with polarity of the solvent

while for compounds **3b-f**, these shifts significantly increase with solvent polarity.

The solvent effect on  $\Phi$  is apparent from the detailed description of Fig. 5.

Approximately linear dependences (or dependences containing two linear parts) between  $\Phi$  and  $\lambda_{\text{em}}$  (Fig. 5.) and also Hammett  $\sigma$ -constants (see Fig. 5A in Supplementary Info) were found for both series of compounds **1a-f** and **3b-f**. On the basis of the experimental data, the following relationships can be found:

- In non-polar dioxane ( $\epsilon_r=2.21$ )  $\Phi$ (**1a-f**) steeply increases from 0.12 to 0.93 with increasing Hammett  $\sigma$ -constant (–0.28 to 0.53) of the substituent in 2-phenyl ring. The IHB that exists between the two OH groups in the excited state plays an important role. Its strength depends on the acidity of the thiazole 4-hydroxy group and increases with the  $\sigma$ -constant. Dioxane as a weak proton acceptor does not form competitive intermolecular hydrogen bond even for the negatively substituted derivative **1f**. On the other hand, solvent of low polarity strengthen the IHB.
- A very similar dependence of  $\Phi$ (**1a-f**) was observed in the somewhat more polar dichloromethane ( $\epsilon_r=4.81$ ) which is also unable to form intermolecular hydrogen bonds but still supports formation of the IHB. The measured  $\Phi$ (**1a-f**) are therefore ca 1.4–3 times lower in this solvent but the sensitivity to changes of the substituent in the 2-phenyl group is almost the same.
- Completely different behavior was found for the dependences of  $\Phi$ (**3b-f**) on  $\lambda_{\text{em}}$  in dioxane and dichloromethane. While the  $\lambda_{\text{em}}$ (**3b-f**) increase bathochromically by 31 nm and 32 nm, respectively, the  $\Phi$ (**3b-f**)-s remain virtually the same in both solvents and are mostly lower than those measured for corresponding derivatives **1b-f**. While the IHB formed in non-polar dioxane has probably less but still positive influence on  $\Phi$  (*cf.*  $\Phi$ (**3c**)=0.39 and  $\Phi$ (**2**)=0.28) in more polar dichloromethane both related compounds **3c** and **2** display the same  $\Phi$ =0.13. Apart from solvent polarity, the substantial drop of  $\Phi$ -s in dichloromethane can be also ascribed to a collisional deactivation of compounds **1a-f** and **3b-f** by the heavy chlorine atoms in this solvent.

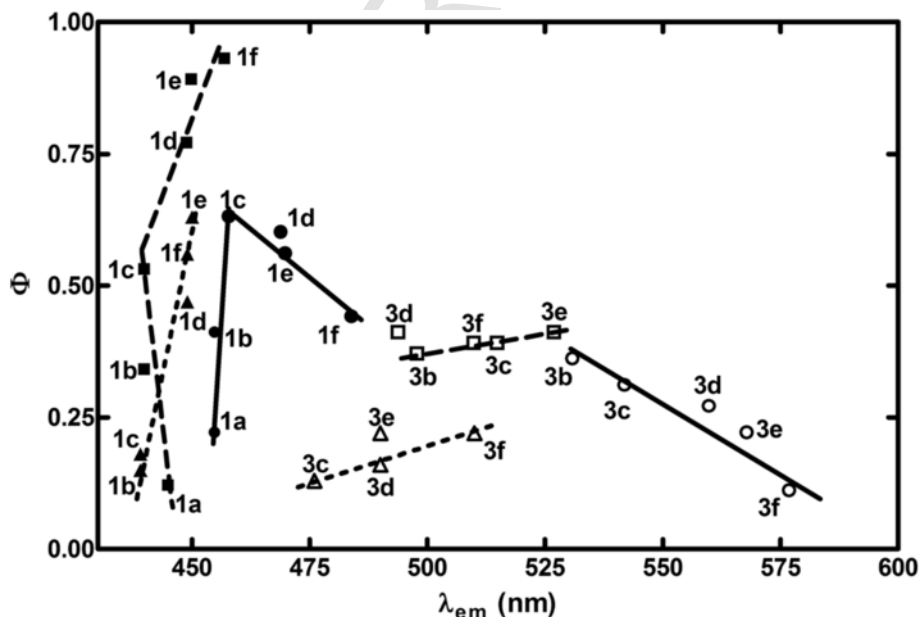


Fig. 5. Dependence of the fluorescence quantum yields ( $\Phi$ ) on the wavelength of the emission maxima for compounds **1a-f** (solid symbols) and **3b-f** (open symbols) in dioxane (■ and □; dashed line), DMSO (● and ○; solid line) and dichloromethane (▲ and △; dotted line).

- In the series **1a-f** in DMSO a remarkable sharp break occurs in the  $\Phi$ - $\lambda_{em}$  (and also  $\lambda_{em}$ - $\sigma$  or  $\Phi$ - $\sigma$ ) dependence. While for electron-donating substituents this dependence steeply increases, for electron withdrawing substituents it decreases. A possible explanation for this break lies in the proton-acceptor ability of DMSO. For positively substituted **1a-b** and for unsubstituted **1c** the IHB still prevails, in contrast to a negatively substituted (and more acidic) derivatives **1d-f** which form competitive intermolecular hydrogen bonds with the solvent molecules causing quenching of fluorescence.
- There is no break in the  $\Phi$ - $\lambda_{em}$  dependence for compounds **3b-f**. The measured  $\Phi$  linearly decreases with the substituents Hammett  $\sigma$ -constants albeit the bathochromic shift of  $\lambda_{em}$  is large (almost 50 nm). Apart from the above-mentioned intermolecular hydrogen bond, the gradually increasing rate constant of non-radiative internal conversion  $S_1^{relax} - S_0$  is also responsible for lowering of  $\Phi$ -s.

### 3.2.2. Deprotonated forms

Deprotonation of **3b-f** with a base causes a large bathochromic shift of the absorption bands, from 360 to 373 nm in the neutral form to 459–498 nm in the dissociated form (for **3b** see Figs. 2 and 6). The bathochromic shifts of the fluorescence maxima display virtually the same trend as those observed for the maxima in the neutral form (Fig. 6). Although the Stokes shifts are much less than for neutral forms, they are still relatively large ( $5713$ – $5989$   $\text{cm}^{-1}$ ). The lower value of these Stokes shifts correspond to the calculated geometry of the ground state which is less distorted in comparison with the neutral form (see Tab. A in Supplementary Info). If we assume that the first excited state ( $S_1$ ) is almost planar, then smaller changes in geometry between both  $S_0$  and  $S_1$  states generates less Stokes shift. On the other hand, the fluorescence quantum yields ( $\Phi$ ) measured for **3b-f** in DMSO (Table 2) remain virtually the same and show a decrease with increasing electronegativity of the 2-phenyl substituent.

### 3.3. Theoretical approach

In order to better understand the relationships among structure, spectra and the other photophysical properties, the equilibrium ground state conformation and the first singlet excited state charac-

teristics have been calculated. The theoretical characteristics were calculated using semiempirical PM3 method for equilibrium ground state conformation of the molecules; the spectral characteristics were calculated using semiempirical ZINDO/CI for vacuum and ZINDO/SCRF procedures for the calculation of spectral characteristics in dependence on dielectric constant and refractive index of solvents used. All mentioned methods are implemented in ArgusLab 4.0 [23]. All the calculated theoretical results for **3b-f**, **3b-f** and for the parent compound **2** are presented in Supplementary Info (Table A, B).

Optimization of geometry gave dihedral angles between the 2-aminophenyl and thiazole ring for **3b-f** which are close to a perpendicular orientation that is favorable for formation of the IHB by overlap between the OH antibonding orbital and the 2p orbital of the amino group. This arrangement is in accordance with the enhanced acidity of the thiazole 4-hydroxy group. On the other hand, this orientation hinders an electronic coupling between these two rings. In contrast, the dihedral angle between the thiazole ring and the 4-substituted phenyl ring ( $\beta$ ) is relatively small which enables their efficient mutual electronic interaction.

The first intense absorption band of the compounds studied corresponds to the allowed “pure”  $\pi$ - $\pi^*$  HOMO-LUMO transition. From the distribution of the  $\pi$ -electron density on the HOMO and LUMO and especially in the first excited state (Fig. 7) it is evident that this transition is connected dominantly with a charge transfer (CT) from the donor (HO—C<sub>4</sub>—C<sub>5</sub> of the thiazole ring) to the acceptor moiety (N<sub>3</sub>—C<sub>2</sub> of the thiazole ring and the 2-phenyl ring). A participation of the 5-(2'-aminophenyl) ring on the first transition is negligible. The large electron density between the thiazole C<sub>2</sub> and the 2-phenyl C<sub>1'</sub> atoms on the LUMO confirms a strong coupling between these two rings and their mutual planarity in the first excited state. Higher dipole moments (see Tab. A in Supplementary Info) demonstrate the CT character of the first electronic transition.

The character of a substituent in the 2-phenyl ring has no influence on the shape of the HOMO and LUMO and on the distribution of the  $\pi$ -electron density in the  $S_1$  state; *i.e.* these characteristics of all compounds studied are virtually the same as for **3c** (cf. Fig. 7 and 7A-D in Supplementary Info). Therefore, in accordance with the experimental absorption maxima, the theoretical values do not show any large changes, either due to substituents or solvent polarity (Tab. B in Supplementary Info).

It is noteworthy that the absorption maxima for **2** exhibit even larger bathochromic shifts in comparison with **3c**. It means that the IHB in the ground state does not affect the  $S_0$ — $S_1$  excitation energy. The same phenomena were found for the compounds **1a-f** [19].

As compared with the experimental absorption maxima, the theoretical values of the first transition exhibit hypsochromic shifts in vacuum as expected, and are almost independent of the substituent. The theoretical absorption maxima dependence on  $\epsilon$ ,  $\nu$  and  $\delta$  for the three solvents were calculated using SCRT which are in very good agreement with experimental values (Tab. B in Supplementary Info).

The optimized geometry of the deprotonated form of **3b-f** is strongly different from that of the neutral form (Table 2). First, it is obvious that the orientation of the amino group is favorable for the formation of an IHB. This is related to a much smaller dihedral angle  $\alpha$  enabling partial electronic coupling of the phenyl ring with the thiazole ring. The dihedral angle  $\beta$  is again very small and virtually the same as that for the neutral form. In contrast to neutral form the amino group could be the H-donor for the H-bond formation. Consequently, the lone pair on the nitrogen atom can interact with the  $\pi$ -electrons in phenyl ring as it is obvious from electron distribution on HOMO (Fig. 7). The LUMO is mainly localized on the 2-phenyl ring and on the C<sub>2</sub>—C<sub>1'</sub> bond resulting in a strong internal CT char-

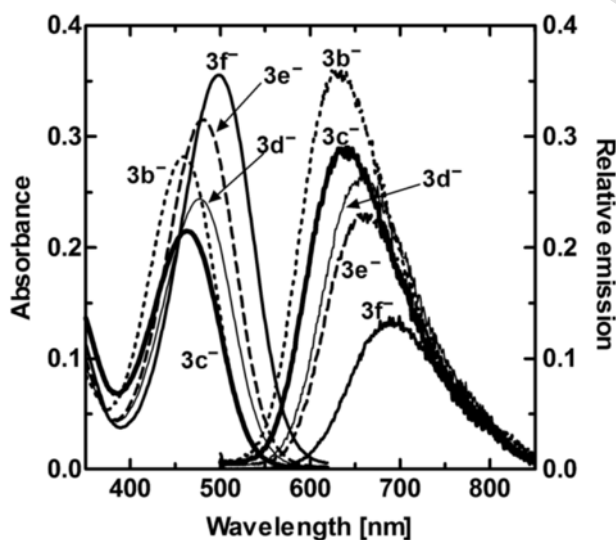


Fig. 6. Absorption and fluorescence spectra of **3b-f** in DMSO.

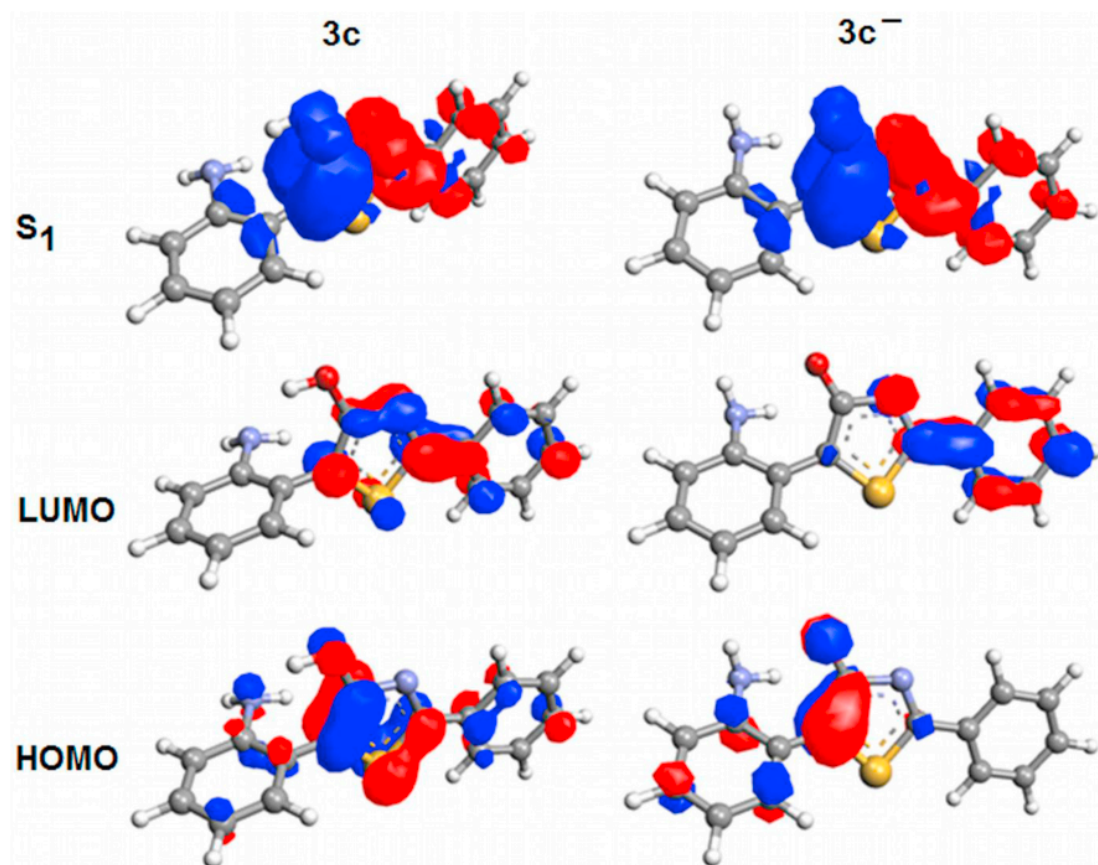


Fig. 7. Electron density for HOMO, LUMO and  $S_1$  excited states of compound **3c** in neutral and dissociated form.

acter of HOMO-LUMO transition and consequently in the strong bathochromic shift. From the data presented it is obvious that the ZINDO procedure used overestimates the CT character of the  $S_0 \rightarrow S_1$  transition and predicts bathochromic shift of the absorption band. Nevertheless, this method describes well the trend of bathochromic shifts dependence on the character of the substituent in the 2-phenyl ring.

#### 4. Conclusion

The fluorescence properties of 5-(2'-aminophenyl)-2-aryl-4-hydroxy-1,3-thiazoles (**3b-f**) have been studied under neutral and alkaline conditions in solutions of several organic solvents and the results obtained have been compared with structurally similar 2-aryl-4-hydroxy-5-(2'-hydroxyphenyl)-1,3-thiazoles (**1a-f**). It has been found that the strong intramolecular hydrogen bond fixes an almost perpendicular arrangement between the thiazole and 2'-aminophenyl rings which generates unusually large Stokes shift (*ca* 9000-9500  $\text{cm}^{-1}$ ) connected with substantial change of geometry between the Frank-Condon  $S_1$  state and the relaxed first excited state ( $S_1^{\text{rel}}$ ). Although the IHB is still beneficial for the fluorescence properties in dioxane and DMSO (analogous thiazole **2** without the  $\text{NH}_2$  display lower  $\Phi$ ) their influence is less than in the series of **1a-f**. Also the influence of substitution in the 2-aryl ring of **3b-f** is much weaker than in **1a-f**.

Fluorescence properties of compounds with 4-hydroxythiazole core can be prospectively useful for bioimaging of living cells and tissues as similar compounds containing thiazole or thiazine ring system [34,35].

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.molstruc.2018.08.017>.

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[9].

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