Insights in the photophysics of 2-[2'-hydroxyphenyl]-quinazolin-4-one isomers by DFT modeling in the ground S_0 and excited S_1 states

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2-[2'-hydroxyphenyl]-quinazolin-4-one, HPQ, is believed for a long time to be a typical compound capable of keto-enol tautomerism. As such it would normally be expected to exhibit a characteristic absorption spectrum for the tautomers potentially present in solution. Moreover, fluorescence should also exhibit features of possible excited state proton transfer, ESIPT. Contrary to expectations, the absorption spectra of HPQ do not directly indicate tautomerism, whereas the observed fluorescence is relatively weak. For these reasons in this paper we look for additional DFT and TD-DFT computational, as well as experimental, insight into the spectroscopic properties of the title compound. The results indicate the simultaneous presence of enol and keto forms both in the ground and first excited singlet state, as well as multiple overlapping emissions.

Keywords: tautomerism, photophysics, DFT and TD-DFT calculations, solvent effect.

INTRODUCTION

The visible absorption spectrum of 2-[2'-hy-droxyphenyl]-quinazolin-4-one (HPQ) has been recorded routinely by a number of groups [1, 2, 3] and shown to possess an intense peak at *ca.* 30.10^3 cm^{-1}, accompanied by a longer wavelength absorption (shoulder) at *ca.* 25.10^3 cm^{-1} in proton acceptor solvents as N,N-dimethyl formamide, DMF, and dimethylsulfoxide, DMSO [2]. Solutions of HPQ fluoresce at concentrations *ca.* 10 μM at ca. 21.10^3 cm^{-1}, while its crystals show either blue or green fluorescence [2]. The offered common interpretation of the observed fluorescence emission involves dimer aggregates as the emitting species [2]. Traditionally fluorescence of compounds with similar structural fragments is referred to their expected capability to undergo ESIPT, which is usually associated with anomalously large Stokes' shift of the order of 10^4 cm^{-1} [4]. Reported absorption and steady state fluorescence spectra of HPQ, with a Stokes shift of ca. 9.10^3 cm^{-1} [1–3] indeed conform to the mentioned requirements. The reason for the present report is that the dynamics of tautomerization and internal rotations of HPQ, as well as its observed electronic absorption and emission features in solution are apparently still incompletely understood.

EXPERIMENTAL

Computational DFT and TD-DFT modeling has been carried out using the Gaussian 09 program system, rev. D01 [5], DFT and TD DFT (TD=nstates=6) theory. B3LYP and CAM-B3LYP functionals have been employed. Solvent interactions are calculated within the PCM formalism [6, 7]. UV-visible spectra are recorded on a Perkin Elmer Lambda 25 UV/Vis Spectrometer and fluorescence spectra are recorded on a Perkin Elmer LS-55 Luminescence Spectrometer. Time resolved photophysical studies have been performed using a 1 cm path length quartz cuvette at room temperature. Fluorescence lifetimes with a time resolution less than 100 ps have been obtained by Time Correlated Single-Photon Counting (TCSPC) using a Fluorolog®-3 (HORIBA Jobin Yvon S.A.S., Longjumeau, France) spectrofluorimeter and picosecond light pulses generated from a pico-LED source at 365 nm. The decay curves have been deconvoluted using DAS-6 decay analysis software and the acceptability of the fits was assessed by χ^2 criteria and visual inspection

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of the residuals of the fitted functions to the data. Time-resolved fluorescence decay $I(t)$ is described by the following expression:

$$I(t) = \sum_i \alpha_i \tau_i \qquad (1).$$

The average fluorescence lifetimes are calculated using the following equation [8]:

$$\tau_{i0} = \frac{\sum_i \alpha_i \tau_i^2}{\sum_i \alpha_i \tau_i} \qquad (2)$$

in which α_i is the pre-exponential factor corresponding to the *i-th* decay time constant, τ_i.

RESULTS AND DISCUSSION

Several possible tautomeric forms of HPQ are shown on Scheme 1. Evidently HPQ isomers shown in Scheme 1 may arise from one another either via proton transfer processes, or partially hindered internal rotation around the formal single C – C bond connecting the two aromatic fragments, or both.

We start computational modeling of isomers **1–4** in the ground (S_0) and the first excited singlet (S_1) states at CAM-B3LYP/6-31G(d,p) in five solvents of very different polarity and hydrogen bonding ability – tetrahydrofuran (THF), dichloromethane (DCM), N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO) and water (H_2O). We have been unable to locate the keto isomer **3** at this level of theory in any of the solvents considered; any attempt led to the more stable isomer **1** instead. Results for isomers **1, 2** and **4** indicate insignificant solvent dependence of their electronic spectra on solvent polarity. This computational result is in agreement with the published fluorescence spectra in THF and THF/water mixtures up to 99% of water [1].

We further explore the influence of the basis set on the energies and predicted electronic spectra in a
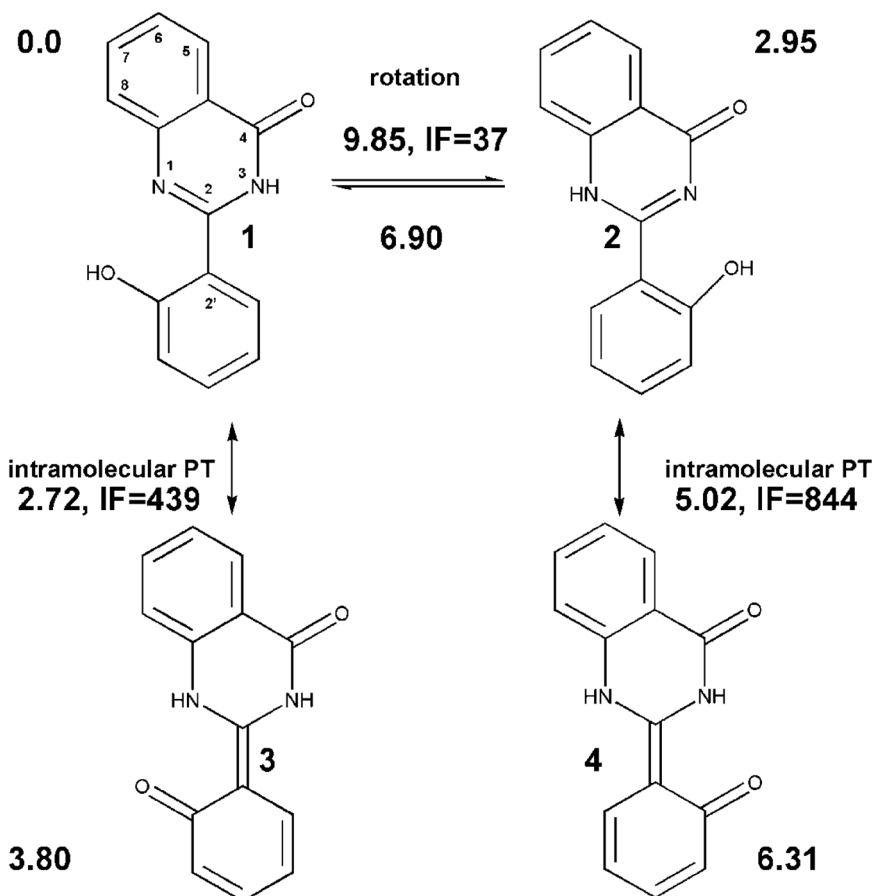
Scheme 1. Some of the possible prototropic and rotational isomers of HPQ, with computed CAM-B3LYP/6-31+G(d,p) relative Gibbs free energies $E + \Delta G_0$ (kcal.mol^{-1}) in the S_0 electronic state in solvent DMF, PCM. Activation free energies of interconnecting transition structures (TSs) are given in kcal.mol^{-1} together with the computed imaginary frequencies, IFs, in cm^{-1}. Note the conversion of **1** to **2** requires rotation and proton transfer, N_3H to N_1.

solvent of medium polarity, DMF (Table 1) and the following discussion is based on the results in DMF. The results show that CAM-B3LYP/6-31G+(d,p) performs best as a compromise between accuracy and computational cost. Moreover, all four considered isomers (Scheme 1) have been located in the ground (S_0) state at this level of theory. The addition of a second diffuse function does not make difference, presumably because the hydrogen bonds are very strong. We estimate this by comparing the energies of enols **1** and **2** (which have hydrogen bonds with distances 1.64 Å and 1.62 Å, resp.) with their respective isomers **anti-1** and **anti-2** (Table 2 and Fig. 1) in which no H bond is possible. Results show that the H-bond stabilization is 7.6 kcal.mol^{-1} in the case of **1** and 8.7 kcal.mol^{-1} for **2**, consistent with the notion of strong, low barrier, hydrogen bonding, Fig. 1 [9].

Table 2 shows the values of the rotational barrier between **1** and **2**, as well as the barriers for proton transfer interconnecting **1** and **3** and **2** and **4**, respectively.

Computational results (Table 1) show that the enol form **1** is the prevailing species in the ground state. Computed energy of the $S_0 - S_1$ absorption electronic transition is 306.9 nm (32580 cm^{-1}), while the experimentally reported longest-wavelength absorption maximum [2] is at 335 nm (29850 cm^{-1}). The overestimation of absorption transition energy by 2730 cm^{-1} may be considered acceptable. This vertical absorption transition is an almost pure HOMO → LUMO π-excitation. The complex form of the longest-wavelength absorption maximum, together with the observed shoulder at ca. 390–400 nm in DMF and DMSO [2] is an indication of the presence of quinoid keto-forms, **3** and/or **4** in solution as well.

Table 1. Electronic (E) and Gibbs free (E+ΔG) energies and electronic spectra in DMF, predicted by (TD) CAM-B3LYP calculations with various basis sets. Energies are given in hartrees, relative free energies ΔΔG in kcal.mol^{-1}. Transition wavelengths are in nm, and oscillator strengths in absolute units. λ_{abs} correspond to vertical excitations and λ_{Fl} – to relaxed TD emission energies from the S_1 excited state

Str	S_0			S_0–S_1		S_0–S_2		S_1	
	E	E+ΔG	ΔΔG	λ_{abs}	f_{osc}	λ_{abs}	f_{osc}	λ_{Fl}	f_{osc}
6-31+G(d)									
1	−799.15279	−798.97554	0.00	305.8	0.75	273.6	0.07	363.1	0.90
2	−799.14705	−798.97056	3.17	304.8	0.58	273.7	0.18	441.1	0.52
3	−799.14526	−798.96956	3.81	373.8	0.56	286.8	0.06	436.3	0.48
4	−799.14296	−798.96655	5.73	380.2	0.60	290.5	0.00	433.8	0.55
6-31G(d,p)									
1	−799.14107	−798.96371	0.00	304.1	0.68	267.2	0.10	357.6	0.78
2	−799.13464	−798.95808	3.59	302.8	0.53	270.9	0.03	434.1	0.49
3	−								
4	−799.12842	−798.95238	7.22	367.9	0.56	289.4	0.00	425.1	0.52
6-31+G(d,p)									
1	−799.17417	−798.99734	0.00	306.9	0.74	273.9	0.07	363.6	0.87
2	−799.16864	−798.99263	2.95	306.7	0.58	273.6	0.18	438.7	0.52
3	−799.16539	−798.99128	3.80	364.6	0.55	283.5	0.07	425.0	0.52
4	−799.16281	−798.98729	6.31	374.8	0.59	285.4	0.01	432.6	0.55
6-31++G(d,p)									
1	−799.17430	−798.99753	0.00	306.9	0.74	273.9	0.07	363.5	0.87
2	−799.16873	−798.99273	3.01	306.7	0.58	273.6	0.18	433.0	0.55
3	−799.16550	−798.99153	3.76	364.6	0.55	283.5	0.07	425.0	0.52
4	−799.16289	−798.98744	6.33	374.8	0.59	285.5	0.01	432.6	0.55
6-311G(d,p)									
1	−799.32703	−799.15055	0.00	304.8	0.70	268.9	0.09	360.7	0.84
2	−799.32067	−799.14468	3.74	303.2	0.55	268.0	0.17	437.0	0.51
3	−799.31711	−799.14263	5.05	366.5	0.55	281.6	0.01	423.9	0.50
4	−799.31459	−799.13928	7.18	373.1	0.60	290.1	0.00	429.9	0.53

*We could not locate isomer **3** using the 6-31G(d,p) basis set.

Table 2. CAM-B3LYP/6-31+G(d,p) ground state electronic and Gibbs free energies of HPQ tautomeric species shown on Scheme 1 and Figure 1 with connecting transition structures rts for internal rotation and hts for intramolecular hydrogen (proton) transfer. Solvent DMF. Energies in hartrees, $\Delta\Delta G$ in kcal.mol^{-1} and imaginary frequencies in cm^{-1}

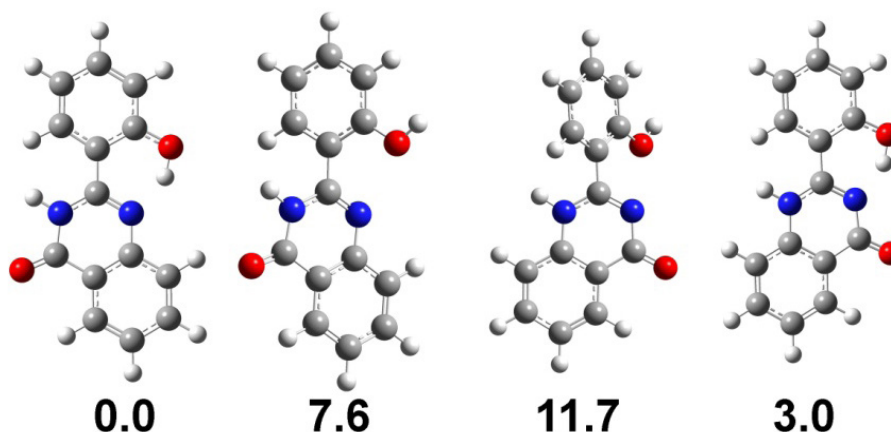| Str.	E	E+ΔG	$\Delta\Delta G$	IF
1	−799.17417	−798.99734	0.00	
Anti-1	−799.16073	−798.98527	7.57	
1-2 rts	−799.15845	−798.98164	9.85	37
1-3 hts	−799.16533	−798.99301	2.72	439
2	−799.16864	−798.99263	2.95	
Anti-2	−799.15447	−798.97870	11.70	
3	−799.16539	−798.99128	3.80	
4	−799.16281	−798.98729	6.31	
2-1 rts	−799.15845	−798.98164	6.90	37
2-4 hts	−799.16212	−798.98934	5.02	844

0.0   **7.6**   **11.7**   **3.0**

Fig. 1. Tautomers **1, anti-1** and **anti-2, 2** with or without H-bond, resp. Relative free energies $\Delta\Delta G_0$ in kcal.mol^{-1}.

Computational results for the relaxed excited S_1 state show, that three isomers may be present – **1***, **3*** and **4*** (Fig. 2). Any attempt to locate the enol form **2*** leads to its simultaneous conversion to the corresponding keto form **4***. The keto forms **3*** and **4*** are predicted to fluoresce at much longer wavelengths (Table 1) than the enol form **1**, thus accounting for the large Stokes' shift found by experiment. Although, similar to the case of absorption, computationally predicted values of emission energies are higher than experimentally found ones, the computed Stokes' shift of ca. 9000 cm^{-1}, indicative of ESIPT, is gratifying.

Table 3 shows the relaxed computational results obtained at B3LYP/6-31+G(d,p). It can be seen that in this case predicted absorption spectra are shifted bathochromically relative to experimental values, the energy differences with the experimentally observed spectra being much smaller than at

CAM-B3LYP/6-31+G(d,p). The energy differences with fluorescence experiment at TD B3LYP/6-31+G(d,p) are also much smaller than at TD CAM-B3LYP/6-31+G(d,p). The conclusions however are the same with the two DFT functionals.

Reported absorption and emission spectra of HPQ in the literature are little [1, 2], if at all, influenced by solvent polarity, which does not completely conform to our own experimental spectra, see Figure 3. The absorption spectrum in DMF and DMSO has a fine structured band at 30–33.10^3 cm^{-1}, with a secondary bathochromically shifted absorption at 26.10^3 cm^{-1} in DMF, which we attribute to the keto-tautomer **3**. Our absorption spectra correspond roughly to the data reported earlier [1, 2]. Present emission spectra in the same solvents show some more detail and indicate the presence of at least two fluorescence bands in DMF and DMSO, which on the basis of the computational results may
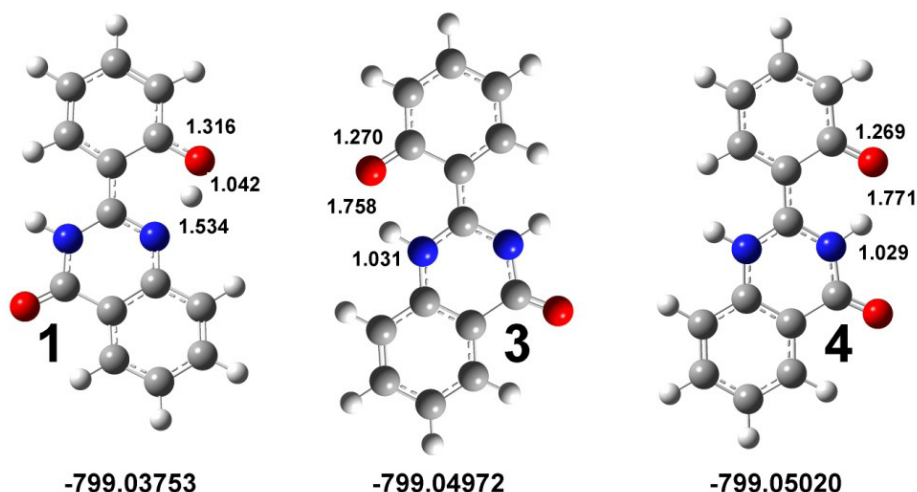
Fig. 2. Equilibrium geometries of **1***, **3*** and **4*** in the S_1 excited state, solvent DMF, CAM-B3LYP/6-31+G(d,p). C=O, O--H and N--H distances are shown in Å; total electron energies are in hartrees (au).

Table 3. Electronic (E) and Gibbs free (E+ΔG) energies and electronic spectra, predicted by TD B3LYP/6-31+G(d,p) calculations. Energies are given in hartrees, relative free energies ΔΔG in kcal.mol^{-1}. Transition wavelengths are in nm, and oscillator strengths in absolute units. λ_{abs} correspond to vertical excitations, and λ_{Fl} – to relaxed TD emission energies from the S_1 excited state. No relaxed S_1 structure **3** could be found by these calculations

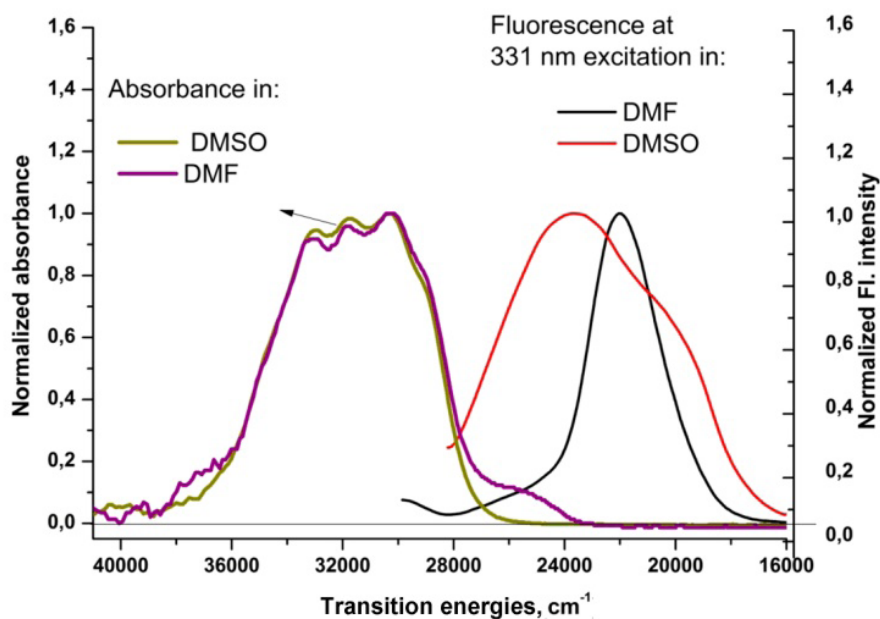| Str	S_0			S_0–S_1		S_0–S_2		S_1	
	E	E+ΔG	ΔΔG	λ_{abs}	f_{osc}	λ_{abs}	f_{osc}	λ_{Fl}	f_{osc}
1	−799.57580	−799.40215	0.00	342.7	0.66	309.4	0.04	393.0	0.77
2	−799.57016	−799.39762	2.88	346.7	0.47	308.9	0.17	513.6	0.33
3	−799.56824	−799.39814	2.56	408.0	0.46	369.1	0.02		
4	−799.56571	−799.39297	5.85	422.5	0.45	358.2	0.08	488.0	0.37

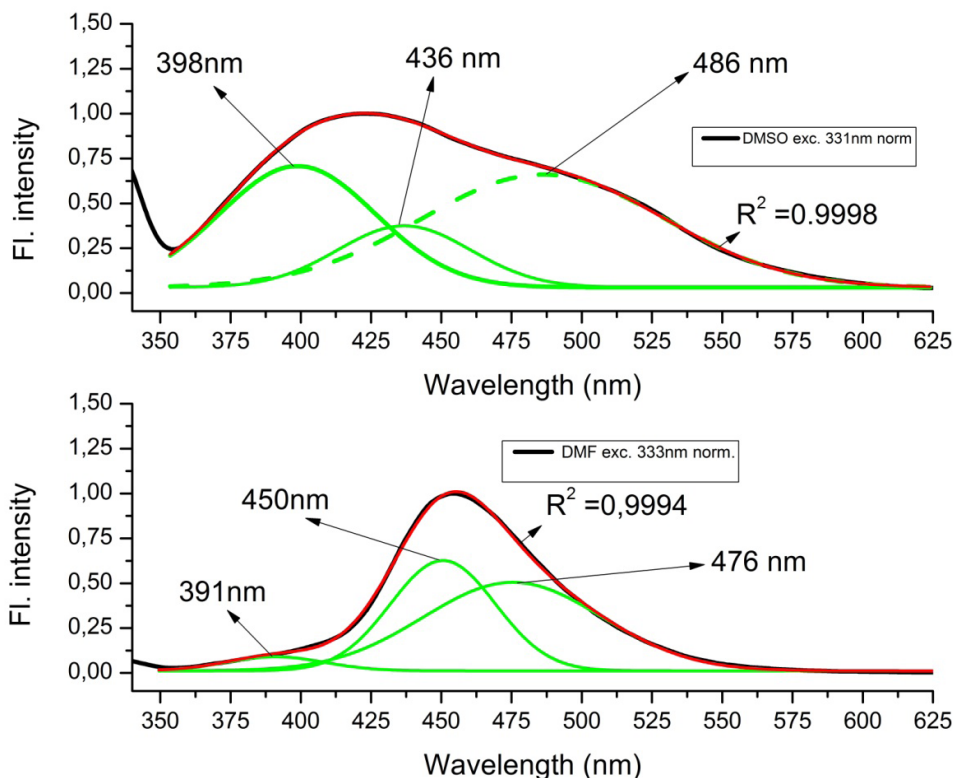**Fig. 3.** Normalized absorption and emission spectra of HPQ.

Fig. 4. Overlapping fluorescence spectral bands obtained by curve fitting of the observed fluorescence spectra of HPQ in DMSO and DMF.
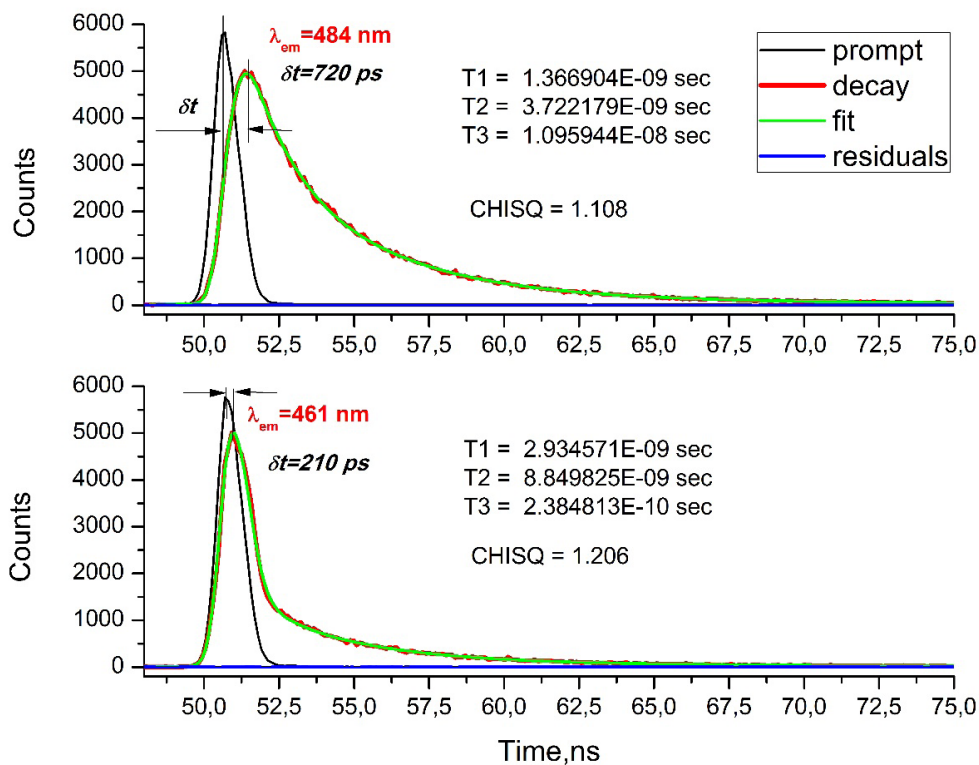

Fig. 5. Fluorescence emission decay curves and lifetimes for HPQ in DMF. Excitation at 365 nm.

be attributed to the excited tautomers **1*** and **3*** or/and **4*** resp. (see Tables 1 and 3).

Present fluorescence spectra seem to corroborate, in agreement with computational predictions, the presence of at least two different species in the first excited singlet state S_1. The difference in the bandshapes of the fluorescence spectra can well be attributed to different percentage distribution of the species in the two solvents, which are of different polarity and basicity. Decomposition of the fluorescence spectral curves of HPQ in DMSO and DMF (Fig. 4) suggests with high probability, that the emitting species are actually three. This is also clearly demonstrated by measurement of fluorescence lifetimes. The obtained results, observed as different behavior of decay curves from two levels of energy (Fig. 5) are indicative of at least two species, emitting from the S_1 level.

As the enol tautomer **1*** is computed as a shorter wavelength emitter than the respective keto-isomers **3*** and **4***, we may attribute the longer wavelength emissions, Fig. 4, to the keto-isomers. At longer emission wavelength, 484 nm, the decay curve is the result only from emission by keto-isomers and with high accuracy can be interpreted as nearly monoexponential with a lifetime of about 4 ns. At shorter emission wavelength (460 nm), the decay curve is the result of emissions from all 3 forms showing significant difference from monoexponential decay.

CONCLUSION

Joint computational and photophysical studies of HPQ provide a detailed picture of its internal molecular dynamics and provide a tool to assign the origin of observed light absorption and emission phenomena to specific isomeric species of the molecule.

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ВИЖДАНИЯ ЗА ФОТОФИЗИКАТА НА ИЗОМЕРИ НА 2-(2'-ХИДРОКСИФЕНИЛ)-ХИНАЗОЛИН-4-ОН ВЪЗ ОСНОВА НА МОДЕЛИРАНЕ С ТФП (DFT) В ОСНОВНО S_0 И ВЪЗБУДЕНО S_1 СЪСТОЯНИЕ

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(Резюме)

2-(2'-хидроксифенил)-хиназолин-4-он (HPQ) е съединение, за което от дълго време се смята, че има възможност да проявява кето-енолна тавтомерия. Би трябвало да се очаква, че то притежава абсорбционен спектър характерен за тавтомерите, потенциално съществуващи в разтвор. Флуоресценцията също трябва да показва възможността за пренос на протон във възбудено електронно състояние, ESIPT. Противно на очакванията абсорбционните спектри на HPQ не показват тавтомерия директно, а наблюдаваната флуоресценция е относително слаба. По тези причини ние предприемаме допълнителни изследвания с помощта на теорията на функционала на плътността ТФП и зависимата от времето ТФП, както и експериментални изследвания, върху спектроскопските свойства на HPQ. Резултатите показват едновременното наличие на енолни и кето форми в разтвор както в основно, така и в първо възбудено синглетно състояние, както и наличието на суперпозиция от припокриващи се емисии.