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Theoretical insights regarding the electronic spectra and proton transfers in a sensor molecule

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Prototropic tautomerism and possible interpretations of observed electronic absorption and emission spectra are attempted on the basis of time dependent density functional theory (TD DFT) calculations on 2-[2'-hydroxyphenyl]-quinazolin-4-one. Energy differences and excited state proton transfers are studied in the gas phase and in several solvents.

Keywords*: 2-[2'-hydroxyphenyl]-quinazolin-4-one, keto-enol tautomerism, electronic absorption and emission spectra, TD DFT, ESIPT transition structures*

INTRODUCTION

2-[2'-hydroxyphenyl]-quinazolin-4-one, HPQ, **1**, Fig. 1 is recently being introduced as a valuable sensor for metal ions (mostly divalent) in aqueous solutions thus contributing to the activities against water pollution. The property utilized in this regard is its relatively bright fluorescence in solution, which is quenched by formation of metal ion complexes following the Beer – Lambert law. For example, metal ion fluorescence sensing for Fe^{3+} is possible in the range of 10^{-4} to 10^{-7} M [1]. Detecting of Hg^{2+} can be done in the same range of concentrations at pH 5.5 – 6.5 [2].

Quantitative and selective detection of Zn^{2+} and Cd^{2+} has also been reported [3].

Compound **1** is fluorescent and solvatochromic in solution. HPQ may be crystallized in two polymorphic forms showing blue, B, or blue-green, BG, fluorescence in the solid state. [4] B and BG forms have different π…π, O…H-C and C=O…C=O dipolar interactions in their respective crystal lattices. This has possibly been the reason to suggest that the actual fluorescent species is an aggregate [3].

As shown on Figure 1, HPQ may exhibit a number of prototropic tautomers, e. g. 1-H and 3-H 4-keto (**2,** and **1**) forms, or 1-H-4-hydroxy-2'-keto vs. 2',4-dihydroxy forms (**6**, **3**) [5]. In addition, twice as many isomers may be generated due to a relatively low barrier to rotation around the C_1 - C_2' single bond, Fig. 1.

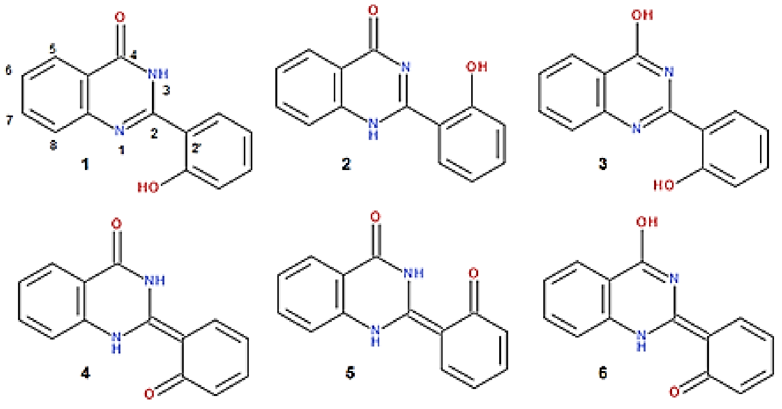

Figure 1. Some possible tautomers of HPQ. Atom numbering is shown with tautomer **1**, which is thus 3-H; Tautomer **2** is 1-H, etc. Pertinent degrees of freedom for prototropic isomerization at each heteroatom, plus a rotation about the C_2 – C_2' bond can give a total of 2^5, i.e. 32 isomers.

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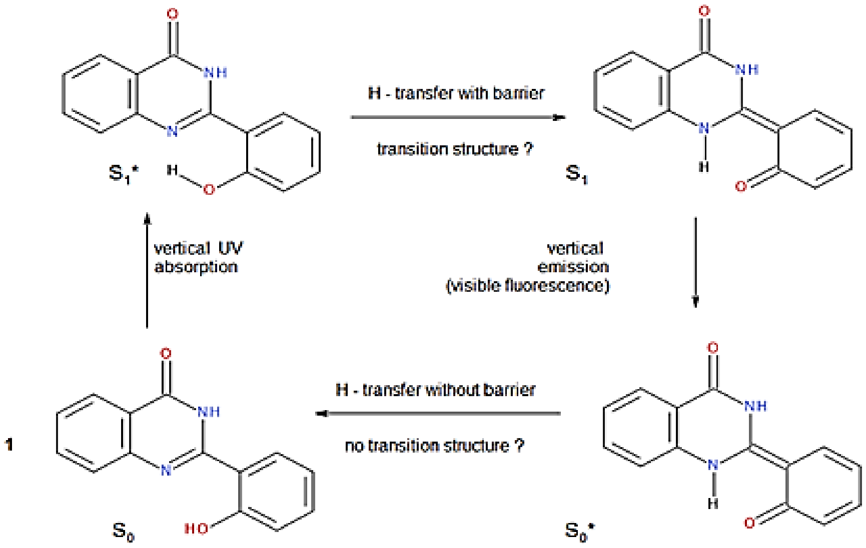

Figure 2. The electronic absorption – emission cycle of HPQ [1 – 4]

Within the manifold of possible prototropic tautomers, the observed fluorescence can be alternatively based on an excited state proton transfer mechanism, ESIPT, [6] which apparently occurs in aqueous solution at pH in the range of 2.0 – 5.5, Fig. 2, as well as in polar solvents.

To understand the structural changes underlying the observed UV light absorption and visible fluorescence emission, we undertake a computational study of electron excitation and structure relaxation in the molecule of **1** and some of its tautomers. This may be conveniently achieved by means of density functional theory, DFT, [7] for the ground electronic states in their equilibrium S_0. For the excited electronic state(s), S_1 and vibrationally excited S_1*, we may use the time dependent form of DFT, TD DFT [8]. We use the GAUSSIAN 09 program [9] with default geometry optimization procedures and the 6-31G(d,p) basis set with PBE0, [10] M06-2x [11] and MN12sx [12] functionals for the outlined equilibrium S_0 and S_1 tautomeric structures of **1**, Figure 1, in the gas phase and a series of solvents, using the PCM solvent model [13]. The transition structures for involved intramolecular proton transfers have also been pursued using the standard "Berny" optimization procedure implemented in GAUSSIAN 09 [9]. Solvent effects on the spatial structures of ground S_0 and first excited S_1 electronic states of HPQ are studied within the PCM computational formalism in tetrahydrofuran, dichloromethane, methanol and dimethylsulfoxide. No solvent relaxation effects have been accounted for.

EXPERIMENTAL ELECTRONIC SPECTRA AND ESIPT

The UV and visible electronic absorption spectrum of HPQ show intense absorption at ca. 330 nm, which is barely affected by solvent polarity. In addition, another less intense absorption appears in polar and preferably aprotic solvents as DMSO and DMF, being merely a shoulder in CH_3CN and CH_3OH at about 400 nm. The two solid state fluorescence peaks appear at ca. 460 ÷ 500 nm [1]. Solution photoluminescence appears at 492 nm in THF and THF/water, with intensity rapidly increasing with increasing water concentration [2]. The recorded emission profiles are rather sharp, contrary to the observed absorption, and support the notion that solid state HPQ fluorescence is related to severely restricted rotation of the hydroxyphenyl fragment around the connecting C – C bond with quinazolinone [3, 14]. The observed Stokes' shift of fluorescence, ca. 10.10^3 cm^{-1} relative to the "main" absorption peak, suggests a proton transfer mechanism as the source of the emissive excited state structure [6]. The "secondary" longer wavelength absorption could be interpreted as indication of an equilibrium of prototropic isomers even in the ground S_0 electronic state **1** and should be attributed to the *keto*- form **4** [1 – 4].

COMPUTATIONAL MODELING OF PROTOTROPIC ISOMERS AND PROTON TRANSFER

The proton transfer processes shown on Figure 2, which could be the evident source of observed light absorption – emission phenomena of HPQ have been reproduced first in the gas phase using the three mentioned DFT functionals. Ground S_0 state energy minimizations of 2-(2’-hydroxyphenyl) quinazolin-4-one **1** proceed smoothly to indicate that the structure is a minimum on the potential energy surface, as confirmed also by full vibrational analysis. The comparison of calculated closed shell S_0 thermodynamic free energies ΔG for most tautomers shows that isomer **1** is indeed the most stable, while the remaining possible tautomers, starting with **2**, are at least 4 kcal.mol^{-1} less stable in DMSO. In less polar solvents, studied here, this energy difference increases and becomes more than 7 kcal.mol^{-1} in the gas phase. We can therefore safely assume that the main S_0 species existing in solution under standard conditions is 2-(2’-hydroxyphenyl)-3H-quinazolin-4-one **1**

The minimization of corresponding 2’-keto structure **3** at the S_0 energy surface however behaves differently with the chosen functionals.

The M06-2x models of *keto*-structures **4**, **5**, **6** yield the corresponding enols **1**, **2**, **3** in the gas phase as well as in all solvents studied. PBE0 in addition shows **5** as a minimum in solution, with significant proton transfer from NH to O, but still far of the enol **2**. Still, within the PBE0 model **5** is less stable than corresponding **2** by ca. 3 kcal.mol^{-1}. MN12sx, on the other hand, indicates that keto-isomers **4**, **5**, **6** are local minima in all solvents, with minimal effects of solvent polarity. The latter result apparently corresponds to the observed second less intense longer wavelength absorption of HPQ in polar solvents [1 – 4]. Computed TD DFT vertical $S_0 \rightarrow S_1{}^*$ transition energies are relatively independent of the used functional and choice of solvent. Therefore, we only show the complete manifold of results for PBE0/6-31G(d,p) calculations in Table 1, M06-2x/6-31G(d,p) calculations in Table 2, and MN12sx/6-31G(d) in Table 3.

One may notice that on Figure 1 HPQ tautomers are shown in keto-enol pairs according to chosen starting structures. With the three used DFT functionals, geometry optimization of the selected keto-enol pairs, at the S_0 potential surface, mostly converge to the respective enols **1**, **2**, **3**. The notable variation of results with the MN12sx/6-31G(d,p) functional, Table 3, is the prediction of the *keto*-form **4** a minimum, somewhat more stable in solution than corresponding enol **1** according to calculated free energy differences $\Delta\Delta G$, ca. 1 kcal.mol^{-1} depending on the solvent. Nevertheless, calculated vertical S_0 – S_1 transition energies are pairwise identical. Note also that computed vertical electron absorptions are practically independent of the solvent. The chosen pairs remain identical also after TD DFT relaxation, with the corresponding final structures the *keto*-isomers **4**, **5**, **6**. In other words, selected PBE0 (pbe1pbe in GAUSSIAN), M06-2x and MN12sx functionals uniformly predict ESIPT between the hydroxyphenyl and the quinazolin-4-one fragment of HPQ. In the case of ESIPT we also find insignificant solvent dependence with decreasing emission wavelengths in more polar solvents, which reproduces the experiment fairly well, see Figure 3.

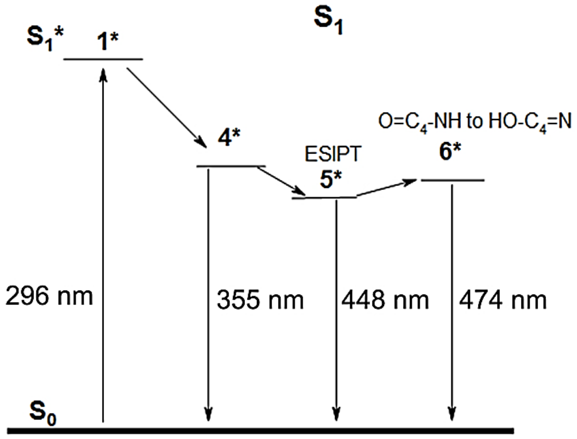

Figure 3. M06-2x/6-31G(d,p) diagram of S_0 and S_1 electronic states of **1** and its possible prototropic conversions in the excited state. Transition energies in THF: absorption is arrow up; fluorescence emissions are given by arrows down; state total energy values for each species in hartrees are as follows: S_0: -799. 2184; S_1*: -799.0643; S_1: -799.0789; ESIPT to **2**: -799.0871; **3***: -799.0796. For comparison, corresponding values from TD MN12sx/6-31G(d,p) calculations in DMSO are: S_0: -798.9443; S_1*: -798.7991, absorption at 314 nm; S_1: -798.8128, emissions at 376 nm; ESIPT to **2**: -798.8294, 641 nm; **3***: -798.9005. Excited prototropic structures are marked by asterisks, see also Figure 1.

As far as used computational models suggest an equilibrium between *enol* and *keto*-isomers of HPQ even in the ground electronic state, we attempted several searches for transition structures for proton transfer at the S0 potential energy surface. However, we met no success in this direction. On the other hand, we verify the identification of ESIPT in HPQ by the location of its transition structure at the S1 potential energy surface using two computational models, TD M06-2x and TD MN12sx. The resulting structure from the TD MN12sx/6-311(d,p) computation is shown on Figure 4.

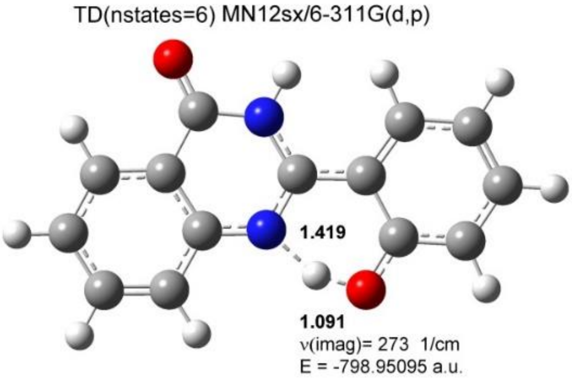

Figure 4. The transition structure for ESIPT on the S_1-potential energy surface of **1**, TD=(nstates=6) MN12sx/6-311G(d,p). Distances are shown in Å.

Table 1. PBE0/6-31G(d,p) and TD(nstates=6) PBE0/6-31G(d,p) computational results for most stable isomers of HPQ in the ground S_0 electronic state and corresponding S_1 structures. Total energies are in hartrees, ΔΔG in kcal/mol, and wavelengths in nanometers. **f** is the calculated oscillator strength.

	S_0			**S_0-S_1 vertical**		**S_1 relaxed**	
Str	E	ΔG	ΔΔG	λ_{abs}	f	λ_{Fl}	f
				Tetrahydrofuran			
1	-798.642772	-798.466386	0.00	322.0	0.447	493.0	0.275
4	-798.642772	-798.466385	0.00	322.0	0.447	493.1	0.275
2	-798.635007	-798.460104	3.94	324.3	0.331	494.2	0.301
5	-798.629412	-798.455364	6.92	380.5	0.345	495.6	0.298
3	-798.625260	-798.449889	10.35	337.9	0.171	657.0	0.095
6	-798.625283	-798.449899	10.35	341.3	0.259	656.9	0.095
				Dichloromethane			
1	-798.643149	-798.466786	0.00	322.0	0.450	490.4	0.239
4	-798.643149	-798.466783	0.00	322.0	0.451	490.7	0.285
2	-798.635636	-798.460655	3.85	324.4	0.334	491.6	0.311
5	-798.630102	-798.456008	6.76	380.5	0.348	492.4	0.310
3	-798.625749	-798.450342	10.32	337.1	0.176	647.4	0.100
6	-798.625767	-798.450279	10.36	340.7	0.270	647.3	0.100
				Methanol			
1	-798.644604	-798.468386	0.00	320.6	0.429	483.4	0.321
4	-798.644604	-798.468383	0.00	320.6	0.429	481.5	0.325
2	-798.638109	-798.462880	3.46	323.2	0.320	484.3	0.349
5	-798.632811	-798.458560	6.17	378.0	0.334	484.1	0.350
3	-798.627638	-798.452189	10.16	333.1	0.174	611.9	0.121
6	-798.627655	-798.452162	10.18	338.5	0.318	611.7	0.122
				Dimethylsulfoxide			
1	-798.644782	-798.468597	0.00	321.3	0.448	482.7	0.325
4	-798.644782	-798.468594	0.00	321.3	0.448	481.8	0.328
2	-798.638416	-798.463161	3.41	379.0	0.334	483.5	0.353
5	-798.633148	-798.458876	6.10	323.8	0.347	483.4	0.354
3	-798.627871	-798.452421	10.15	333.2	0.188	607.8	0.124
6	-798.627888	-798.452457	10.12	338.2	0.324	607.5	0.125

Table 2. M062x/6-31G(d,p) and TD(nstates=6) M06-2x/6-31G(d,p) computational results for most stable isomers of HPQ in the ground S_0 electronic state and corresponding S_1 structures. Total energies are in hartrees, ΔΔG in kcal/mol, and wavelengths in nanometers. **f** is the calculated oscillator strength.

Str	**S_0**			**S_0-S_1 *vertical***		**S_1 *relaxed***	
	E	ΔG	ΔΔG	λ_{abs}	f	λ_{abs}	f
Tetrahydrofuran							
1	-799.218399	-799.042051	0.00	295.6	0.525	355.4	0.704
4	-799.218399	-799.042052	0.00	295.6	0.525	355.5	0.699
2	-799.210472	-799.034316	4.85	293.2	0.390	448.2	0.441
5	-799.210472	-799.034314	4.85	294.2	0.397	448.7	0.439
3	-799.203155	-799.027473	9.15	296.9	0.372	474.0	0.379
6	-799.203166	-799.027530	9.11	301.4	0.500	475.8	0.374
Dichloromethane							
1	-799.218781	-799.042421	0.00	295.6	0.529	356.0	0.721
4	-799.218781	-799.042422	0.00	295.6	0.529	356.0	0.715
2	-799.211098	-799.034990	4.66	293.3	0.394	447.6	0.451
5	-799.211098	-799.034984	4.67	293.3	0.394	492.3	0.310
3	-799.203648	-799.027958	9.08	296.6	0.377	469.9	0.400
6	-799.203660	-799.027973	9.08	301.3	0.512	468.6	0.405
Methanol							
1	-799.220254	-799.043888	0.00	294.3	0.508	358.6	0.781
4	-799.220253	-799.043902	-0.01	294.3	0.508	358.6	0.775
2	-799.213563	-799.037627	3.94	292.2	0.381	446.0	0.488
5	-799.213563	-799.037639	3.92	292.3	0.381	483.2	0.351
3	-799.205569	-799.029879	8.79	294.2	0.362	457.4	0.474
6	-799.205581	-799.029883	8.78	300.9	0.558	457.5	0.476
Dimethylsulfoxide							
1	-799.220434	-799.044076	0.00	295.0	0.528	359.0	0.788
4	-799.220434	-799.044073	0.00	295.0	0.528	359.0	0.782
2	-799.213870	-799.038009	3.81	292.8	0.397	445.7	0.493
5	-799.213870	-799.038044	3.79	292.8	0.398	445.6	0.493
3	-799.205805	-799.030117	8.76	294.6	0.381	456.4	0.482
6	-799.203660	-799.027963	10.11	301.3	0.512	468.6	0.405

Table 3. MN12sx/6-31G(d,p) and TD(nstates=6) MN12sx/6-31G(d,p) computational results for most stable isomers of HPQ in the ground S_0 electronic state and electron transitions to corresponding S_1 structures. Total energies are in hartrees, ΔΔG in kcal/mol, and wavelengths in nanometers. **f** is the calculated oscillator strength.

	S_0			**S_0-S_1 vertical**		**S_1 relaxed**	
Str	E	ΔG	ΔΔG	λ_{abs}	f	λ_{Fl}	f
			Tetrahydrofuran				
1	-798.942197	-798.764794	1.38	314.5	0.509	371.7	0.833
4	-798.942213	-798.766995	0.00	320.1	0.653	371.6	0.833
2	-798.934143	-798.758373	5.41	312.2	0.328	520.9	0.256
5	-798.926314	-798.752122	9.33	380.9	0.333	520.7	0.257
3	-798.928128	-798.752730	8.95	333.2	0.235	697.6	0.085
6	-798.928128	-798.752687	8.98	333.2	0.235	697.6	0.085
			Dichloromethane				
1	-798.942584	-798.765187	1.54	314.5	0.513	372.2	0.845
4	-798.942599	-798.767636	0.00	320.5	0.664	372.3	0.846
2	-798.934774	-798.759028	5.40	312.2	0.332	515.2	0.269
5	-798.927022	-798.752812	9.30	380.7	0.336	515.3	0.268
3	-798.928614	-798.753214	9.05	332.5	0.248	614.4	0.004
6	-798.928614	-798.753220	9.05	332.5	0.248	415.5	0.282
			Methanol				
1	-798.944083	-798.766679	0.91	313.1	0.489	375.6	0.894
4	-798.944094	-798.768133	0.00	313.1	0.489	375.7	0.894
2	-798.937180	-798.760097	5.04	312.3	0.324	501.8	0.309
5	-798.929804	-798.755500	7.93	377.6	0.322	501.7	0.310
3	-798.930508	-798.755097	8.18	330.2	0.301	645.6	0.106
6	-798.930508	-798.755125	8.16	330.2	0.301	645.6	0.106
			Dimethylsulfoxide				
1	-798.944267	-798.766857	0.92	313.9	0.510	376.1	0.900
4	-798.944276	-798.768323	0.00	322.2	0.713	376.1	0.900
2	-798.937490	-798.760403	4.97	312.9	0.340	500.5	0.314
5	-798.930150	-798.755831	7.84	378.6	0.337	500.4	0.314
3	-798.930742	-798.755371	8.13	330.0	0.307	640.9	0.108
6	-798.930742	-798.755364	8.13	320.0	0.308	640.9	0.108

CONCLUSION

We provide a detailed computational analysis of UV absorption and steady state fluorescence of HPQ by means of TD DFT calculations. This proved to only be possible considering the complete manifold of isomers, mostly prototropic tautomers of the molecule. Suggested ESIPT as the source of observed large Stokes shift of fluorescence is proved computationally.

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ТЕОРЕТИЧНИ ВИЖДАНИЯ ЗА ЕЛЕКТРОННИТЕ СПЕКТРИ И ПРЕНОСИ НА ПРОТОН В МОЛЕКУЛАТА НА ЕДИН СЕНЗОР

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(Резюме)

Прототропната тавтомерия и възможната интерпретация на наблюдаваните абсорбционни и емисионни електронни спектри на 2-2’хидроксифенил-хиназолин-4-он са изследвани с помощта на зависимата от времето теория на функционала на плътността. Изследвани са енергиите на електронните преходи и преноса на протон във възбудено състояние в газова фаза и няколко разтворителя.

Ключови думи: *2-2’хидроксифенил-хиназолин-4-он, кето-енолна тавтомерия, електронни абсорбционни и емисионни спектри, TD DFT, преходни структури за пренос на протон във възбудено състояние*