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Intermolecular Interaction in 2-Aminopyridine: A Density Functional Study

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Abstract: The absorption and fluorescence property of 2-amino pyridine (2-AP) and its dimer $(2AP)_2$ have been investigated using dispersion corrected density functional theory (DFT-D) method using B3LYP-D functional along with triple-ζ TZ2P basis in ADF suite of program. For the equilibrium geometries of the dimer, the ETS-NOCV calculations are performed. The formation of H-bond has been confirmed by the calculation of synergy (ΔE_{syn}) as well as from the spectral shift. A close agreement of the calculated spectra with that of experimental results has been found suggesting the dimers to be the preferable states of 2-AP in water medium.

AMS subject classifications: 74E40, 78M50

Key words: Density functional theory, 2-amino pyridine, absorption, fluorescence, H-bond

The excited state relaxation is of paramount importance in the photochemical process. Recently it has been noticed that the excited state relaxation can be induced through intermolecular Hydrogen bonding [1-4]. Photo induced proton-coupled electron transfers, where the proton donor and acceptor are held together by hydrogen bond (H-bond), have attracted considerable interest in recent years [5]. A number of studies by Han and co-workers [6-12] have shown that the gradual strengthening of the H-bond brings about the stabilization of the electronically excited state. H-bonded systems are ubiquitous within the

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biological macromolecules and hence the H-bond induced relaxation of excited state is deemed to be important in biological systems as well (13-15, 16). Pyridine and its derivatives are currently finding immense interest in the scientific community due to their luminescence property. Some of amino pyridine derivatives show anaesthetic properties and are used as drugs for certain brain disease [17-19]. 2-amino pyridine (2-AP) is used in the preparation of cytidine which is used as drug [20]. In spite of this biomedical application the photochemistry of this molecule has not been thoroughly investigated.

In this study we report a systematic density functional investigation of the absorption and fluorescence property of 2-amino pyridine (2-AP) and its dimer $(2AP)_2$. As the dimerization of 2-AP occurs through hydrogen bonding (H-bonding), is becomes essential to unveil the effect of intermolecular H-bonding interactions in the photochemical behaviour of 2-AP. It has been reported earlier that H-bonding plays a pivotal role in the photochemical description of a molecule. Moreover, the simple electronic structure of this compound offers simplicity and encourages studying the effect of H-bonding interaction in the photochemistry of this compound as a benchmark.

For the computation of weak interactions like H-bond, the correlated ab initio techniques such as second-order Møller-Plesset perturbation theory (MP2) are in wide use [21]. In recent years *ab initio* and density functional theory (DFT) based methods have become popular tool in the investigations of structure and electronic properties of molecules. DFT offers a cost effective way for the quantum chemical investigation of the molecular properties and has been proved to be efficient in producing accurate results [22]. Although the density functional methods, like the popular B3LYP functional, are reported to be incompetent for the accurate description of H-bonding [23], the inclusion of correction due to dispersion interactions in the scenario has been proved to be effective. In the present work, we opted for the dispersion corrected DFT (DFT-D) method for the computation of absorption and fluorescence spectra. All the DFT and time dependent DFT (TDDFT) calculations are performed using ADF suit of program [24]. The B3LYP functional has been used, augmented with dispersion correction developed by Grimme (B3LYP-D) [25], along with triple-ζ TZ2P basis. The solvent effects have been estimated using the conductor-like screening model (COSMO) implemented in ADF [26].

Structures of the monomer and the dimer are optimized at the B3LYP-D/TZ2P level. The optimized ground state structures of the monomer and the dimer are represented in Figures 1 and 2. The dimer is found to prefer a non-planar geometry at ground and excited states (Figure 2).

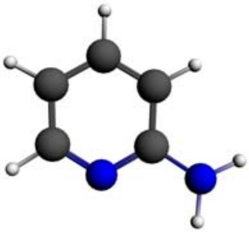
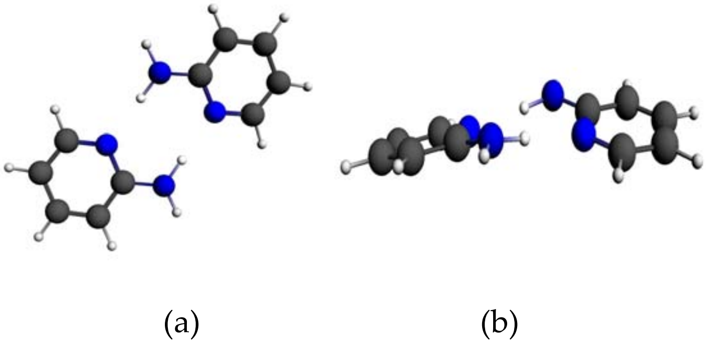


Figure 1: B3LYP-D/TZ2P optimized geometry of 2-Aminopyridine at its ground state.



(a) (b)

Figure 2: The H-bonded dimer (a) front view and (b) side view

To reveal the cooperativity due to H-bonding, an energy decomposition analysis (EDA) in the framework of the Kohn-Sham molecular orbital (MO) model is performed. In this approach, the interaction energy (ΔE_{int}) is partitioned into electrostatic interaction (ΔV_{elstat}), Pauli repulsive orbital interaction (ΔE_{pauli}), attractive orbital interaction (ΔE_{oi}) and dispersion interactions (ΔE_{disp}) as shown in the following,

$$\Delta E_{\text{int}} = \Delta V_{elstat} + \Delta E_{pauli} + \Delta E_{oi} + \Delta E_{disp} . \quad (1)$$

This method combines the extended transition state (ETS) energy decomposition approach [27] with the natural orbitals for chemical valence (NOCV) density analysis method [28]. The ETS-NOCV calculations are performed for the equilibrium geometries of the ground and excited states of the dimer. The formation of H-bond has been confirmed by the calculation of synergy (ΔE_{syn}) from the difference of interaction energy (ΔE_{int}) with and without H-bond interactions

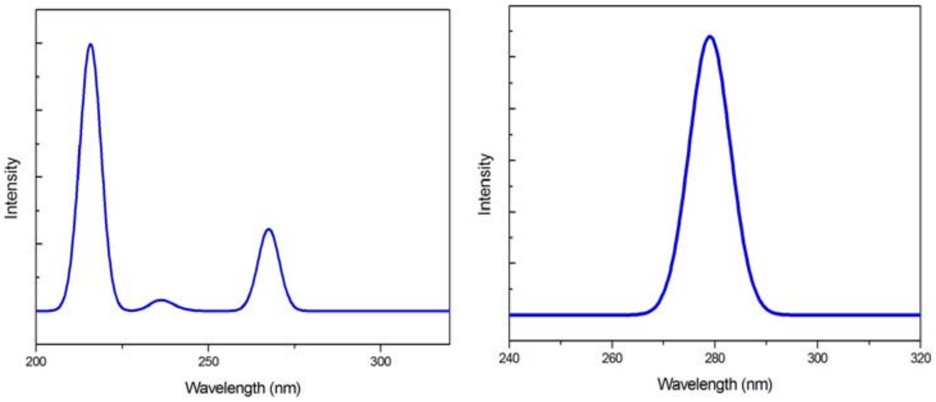
$$\Delta E_{syn} = \Delta E_{\text{int}-eq} - \Delta E_{\text{int}-noneq} . \quad (2)$$

Here, $\Delta E_{int\text{-}eq}$ corresponds to the interaction energy of the dimer in its equilibrium geometry. Next, the equilibrium geometry is distorted by moving the momomer units far from each other, so that no H-bond formation is possible, and the interaction energy ($\Delta E_{int\text{-}}$

$_{noneq}$) is estimated. A negative value of synergy indicates stabilization through the formation of H-bonding. ΔE_{int} is the energy change in systems due to formation of the association from individual units [29]. This is interpreted as the amount of energy required to promote the separated fragments to form the dimeric structure [30]. The synergy due to H-bonding is estimated through eq 2 and the results are given in Table 1.

Table 1: Bonding energy (kcal/mol) decomposition of ground and excited states of the dimer

Dimer	ΔV_{elstat}	ΔE_{pauli}	ΔE_{oi}	ΔE_{disp}	ΔE_{int}	ΔE_{syn}
Distorted Geometry	–0.30	–0.12	–0.03	–0.07	–0.52	--
Excited State	–25.93	29.92	–14.64	–4.30	–14.94	–14.42
Ground State	–26.24	30.31	–14.85	–4.26	–15.05	–14.53



(a) (b)

Figure 3: Absorption Spectra of (a) monomer unit and (b) hydrogen bonded dimer.

From Table 1, it is clear that the hydrogen-bond formation is possible at both the ground and excited states. From the comparison of ΔE_{syn} values in Table 1, one can infer a greater stabilization of the H-bonded dimer at its ground state than the corresponding excited state. However, from the components of ΔE_{int} it is observed that the dispersion energy change (ΔE_{disp}), which corresponds to the H-bonding interaction, is greater in the excited state than the ground state. Hence, it can be concluded that the H-bonding interaction is strengthened at the excited state.

The absorption and fluorescence spectra are shown in Figures 3 and 4. It becomes prominent from the figures that there occurs a red-shift of the absorption and fluorescence peaks in the dimeric state compared to the monomer (Table 2). This red-shift can be attributed to the lowering in the HOMO-LUMO gap (ΔE_{HL}) due to H-bond formation. Table

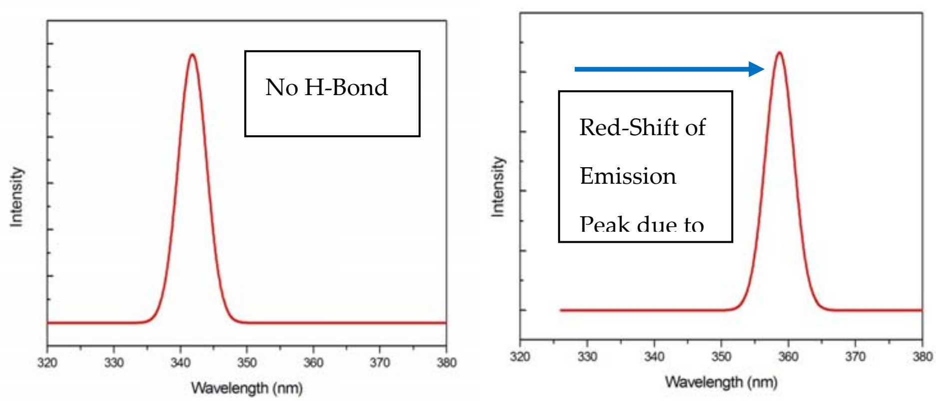
3 accumulates the HOMOs and the LUMOs of the species in its different states and a lowering of the ΔE_{HL} is clearly visible. From the previous studies on H-bonded systems it becomes evident that polarization effects promote H-bonding interaction [31]. It has also been seen that there occurs a mixing of the empty/occupied orbital on one fragment in the presence of another fragment due to polarization effect. From the nature of the HOMO and LUMO orbitals in Table 3, the mixing of two fragments is critically exposed. Hence, the diminished HOMO-LUMO gap can be explained as an outcome of the H-bonding interaction [32-33].

Table 2: Comparison of the calculated value λ_{max} of absorption and fluorescence with experimentally reported values.

System	λ_{max} of absorption in nm		λ_{max} of fluorescence in nm	
	Calculated	Experimental	Calculated	Experimental
2-AMP monomer	216	292(a)	342	363(a)
2-AMP dimer	279		359	

(a) Experimentally reported (in reference [37]) λ_{max} of absorption and fluorescence in water medium

The red-shift in the fluorescence spectra can be explained from the stabilization of the S_1 electronic state of the dimer due to the formation of the H-bonding. The decrease in the energy gap for the $S_0 \leftarrow S_1$ leads to a red-shift of the fluorescence λ_{max} value.

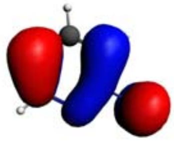
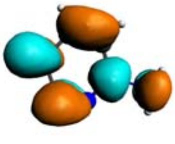
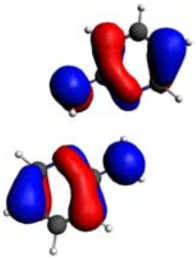
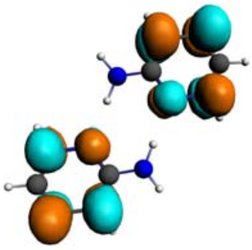


(a) (b)

Figure 4: Fluorescence Spectra of (a) monomer unit and (b) hydrogen bonded dimer.

The calculated values of λ_{max} of both the absorption and fluorescence spectra of the 2-AP monomer and dimer are given in Table 2. The close agreement of the calculated values with the experimental results suggests that the dimers are the most preferable states of 2-AP in water solution. This can also be inferred from the Table 1 since the high negative synergy of the dimer in both the ground and excited states indicates the formation of H-bonding. The formation or the change in the strength of the intermolecular hydrogen bonds following the excitation, may simply lead to new vibronic dissipative modes that couple the excited and the ground states [34-36]. Hence, the study of relaxation induced red shift in the emission spectra due to strengthening of H-bond seems to be useful tool to unveil many biological systems [38].

Table 3: HOMOs and LUMOs of the monomer and the dimer with corresponding energy values and HOMO-LUMO gap (ΔE_{HL}).

System	Orbitals	Energy in eV	ΔE_{HL} in eV
2-AP monomer	 HOMO	-5.8743	6.0044
	 LUMO	0.1257	
2-AP dimer	 HOMO	-5.6443	4.9446
	 LUMO	-0.6997	

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References

[1] N. Mataga, Y. Kaibe, M. Koizumi, Equilibrium of hydrogen-bond formation in the excited state, Nature, 175 (1955), 731-732.

[2] J. Herbich, M. Kijak, A. Zielin´ska, R. P. Thummel, J. Waluk, Fluorescence quenching by pyridine and derivatives induced by intermolecular hydrogen bonding to pyrrole-containing heteroaromatics, J. Phys. Chem. A, 106 (2002), 2158-2163.

[3] T. Yatsuhashi, H. Inoue, Molecular mechanism of radiationless deactivation of amino anthraquinones through intermolecular hydrogen-bonding interaction with alcohols and hydroperoxides, J. Phys. Chem. A, 101 (1997), 8166-8173.

[4] L. Biczo´k, P. Valat, V. Wintgens, Effect of molecular structure and hydrogen bonding on the fluorescence of hydroxy-substituted naphthalimides, Phys. Chem. Chem. Phys., 1 (1999), 4759-4766.

[5] H. Miyasaka, A. Tabata, S. Ojima, N. Ikeda, N. Mataga, Femtosecond-picosecond laser photolysis studies on the mechanisms of fluorescence quenching induced by hydrogen-bonding interactions - 1-pyrenol-pyridine systems, J. Phys. Chem., 97 (1993), 8222-8228.

[6] G.-J. Zhao, K.-L. Han, Early time hydrogen-bonding dynamics of photoexcited coumarin 102 in hydrogen-donating solvents: Theoretical Study, J. Phys. Chem. A, 111 (2007), 2469–2474.

[7] G.-J. Zhao, K.-L. Han, Ultrafast hydrogen bond strengthening of the photoexcited fluorenone in alcohols for facilitating the fluorescence quenching J. Phys. Chem. A 111 (2007), 9218–9223.

[8] G.-J. Zhao, J.-Y. Liu, L.-C. Zhou, K.-L. Han, Site-selective photo induced electron transfer from alcoholic solvents to the chromophore facilitated by hydrogen bonding: a new fluorescence quenching mechanism, J. Phys. Chem. B, 111 (2007), 8940–8945.

[9] G.-J. Zhao, K.-L. Han, Novel infrared spectra for intermolecular dihydrogen bonding of the phenol-borane-trimethylamine complex in electronically excited state, J. Chem. Phys., 127 (2007), 024306-6.

[10] G.-J. Zhao, K.-L. Han, Y.-B. Lei, Y.-S. Dou, Ultrafast excited-state dynamics of tetraphenylethylene studied by semiclassical simulation, J. Chem. Phys., 127 (2007), 094307-6.

[11] G.-J. Zhao, Y.-H. Liu, K.-L. Han, Y. Dou, Dynamic simulation study on ultrafast excited-state torsional dynamics of 9,9′-bianthryl (BA) in gas phase: Real-time observation of novel oscillation behavior with the torsional coordinate, Chem. Phys. Lett. 453 (2008), 29–34.

[12] G.-J. Zhao, K.-L. Han, Time-dependent density functional theory study on hydrogen-bonded intramolecular charge-transfer excited state of 4-dimethylamino-benzonitrile in methanol, J. Comput. Chem., DOI: 10.1002/jcc.20957.

[13] D. J. Heyes, C. N. Hunter, I. H. M. van Stokkum, R. van Grondelle, Ultrafast enzymatic reaction dynamics in protochlorophyllide oxidoreductase, Nat. Struct. Biol., 10 (2003), 491–492.

[14] H. Deng, R. Callender, E. Howell, Vibrational structure of dihydrofolate bound to R67 dihydrofolate reductase, J. Biol. Chem., 276 (2001), 48956–48960.

[15] H. Cheng, , I. Nikolic-Hughes, J. H. H. Wang, H. Deng, P. J. O'Brien, L. Wu, Z. Y. Zhang, D. Herschlag, R. Callender, Environmental effects on phosphoryl group bonding probed by vibrational spectroscopy: implications for understanding phosphoryl transfer and enzymatic catalysis, J. Am. Chem. Soc., 124 (2002), 11295–11306.

[16] G.-J. Zhao, K-L Han, Site-specific solvation of the photoexcited protochlorophyllide a in methanol: formation of the hydrogen-bonded intermediate state induced by hydrogen-bond strengthening, Biophys. J., 94 (2008), 38–46.

[17] K. J. Smith, P. A. Felts, G. R. John, J. Neurology, 123 (1999), 171-184.

[18] S Sedehizadeh, M. Keogh, P. Maddison, The use of aminopyridines in neurological disorders, Clin. Neuropharmacol., 35 (2012) 191-200.

[19] R. R. Hansebout, A. R. Blight, S. Fawcett, K. Reddy, 4-Aminopyridine in chronic spinal cord injury: a controlled, double-blind, crossover study in eight patients, J. Neurotrauma., 10 (1993), 1-18.

[20] A. W. Fraley, D. Chen, K. Johnson, L. W. McLaughlin, An HIV reverse transcriptase-selective nucleoside chain terminator, J. Am. Chem. Soc., 125 (2003), 616–617.

[21] S. Suzuki, P. G. Green, R. E. Bumgarner, S. Dasgupta, W. A. Goddard, G. A. Blake, Benzene forms hydrogen bonds with water, Science, 257 (1992), 942-944. P. Tarakeshwar, S. J. Lee, J. Y. Lee, K. S. Kim, Benzene-hydrogen halide interactions: Theoretical studies of binding energies, vibrational frequencies, and equilibrium structures, J. Chem. Phys., 108 (1998), 7217-7223. D. Feller, Strength of the benzene−water hydrogen bond, J. Phys. Chem. A, 103 (1999), 7558-7561. P. Tarakeshwar, K. S. Kim, B. Brutschy, Interaction of the water dimer with p-systems: A theoretical investigation of structures, energies, and vibrational frequencies, J. Chem. Phys., 112 (2000), 1769-1781. T. van Mourik, S. L. Price, D. C. Clary, Ab initio calculations on indole–water, 1-methylindole–water and indole–(water)2, Chem. Phys. Lett., 331 (2000), 253-261. T. van Mourik, Comment on "Theoretical study of indole: protonation, indolyl radical, tautomers of indole, and its interaction with water", Chem. Phys., 304 (2004), 317-319. P. Tarakeshwar, H. S. Choi, K. S. Kim, Olefinic vs aromatic π−h interaction: A theoretical investigation of the nature of interaction of first-row hydrides with ethene and benzene, J. Am. Chem. Soc., 123 (2001), 3323-3331.

[22] S. Shil, D. Bhattacharya, S. Sarkar, A. Misra, Performance of the widely used minnesota density functionals for the prediction of heat of formations, ionization potentials of some benchmarked first row transition metal Complexes, J. Phys. Chem. A, 117 (2013), 4945–4955.

[23] S. Tsuzuki, H. P. Luthi, Interaction energies of van der Waals and hydrogen bonded systems calculated using density functional theory: Assessing the PW91 model, J. Chem. Phys. 114 (2001), 3949-3957. Y. Zhao, D. G. Truhlar, Hybrid meta density functional theory methods for thermochemistry, thermochemical kinetics, and noncovalent interactions: The mpw1b95 and mpwb1k models and comparative assessments for hydrogen bonding and van der waals interactions, J. Phys. Chem. A, 108 (2004), 6908-6918. Y. Zhao, D. G. Truhlar, Benchmark databases for nonbonded interactions and their use to test density functional theory, J. Chem. Theory Comput., 1 (2005), 415-432.

[24] Computer code ADF2010.01, SCM, Theoretical Chemistry, Vrije Universiteit, Amsterdam,The Netherlands, http://www.scm.com.

[25] S. Grimme, Accurate description of van der Waals complexes by density functional theory including empirical corrections, J. Comput. Chem., 25 (2004), 1463-1473. S. Grimme, Semiempirical GGA-type density functional constructed with a long-range dispersion correction, J. Comput. Chem., 27 (2006), 1787-1799.

[26] A. Klamt, G. Schüürmann, COSMO: A new approach to dielectric screening in solvents with explicit expressions for the screening energy and its gradient, J. Chem. Soc. Perkin Trans. 2 (1993), 799-805. A. Klamt, Conductor-like screening model for real solvents: A new approach to the quantitative calculation of solvation phenomena, J. Phys. Chem., 99 (1995), 2224-2235. C. C. Pye, T. Ziegler, An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package, Theor. Chem. Acta, 101 (1999), 396-408.

[27] T. Ziegler, A. Rauk, Carbon monoxide, carbon monosulfide, molecular nitrogen, phosphorus trifluoride, and methyl isocyanide as .sigma. donors and .pi. acceptors. A theoretical study by the Hartree-Fock-Slater transition-state method, Inorg. Chem., 18 (1979), 1755–1759. T. Ziegler, A. Rauk, On the calculation of bonding energies by the Hartree Fock Slater method, Theor. Chim. Acta 46 (1977), 1–10.

[28] M. Mitoraj, A. Michalak, Natural orbitals for chemical valence as descriptors of chemical bonding in transition metal complexes, J. Mol. Model, 13 (2007), 347–355. M. Srebro, A. Michalak, Theoretical analysis of bonding in n-heterocyclic carbene−rhodium complexes, Inorg. Chem., 48 (2009) 5361–5369. A. Michalak, M. Mitoraj, T. Ziegler, Bond orbitals from chemical valence theory, J. Phys. Chem. A, 112 (2008) 1933–1939.

[29] C. F. Guerra, H. Zijlstra, G. Paragi, F. M. Bickelhaupt, Telomere structure and stability: covalency in hydrogen bonds, not resonance assistance, causes cooperativity in guanine quartets, Chem. Eur. J., 17 (2011), 12612 – 12622.

[30]M. P. Mitoraj, R. Kurczab, M. Boczar, A. Michalak, Theoretical description of hydrogen bonding in oxalic acid dimer and trimer based on the combined extended-transition-state energy decomposition analysis and natural orbitals for chemical valence (ETS-NOCV), J. Mol. Model, 16 (2010) 1789–1795.

[31] L. X. Dang, Importance of polarization effects in modeling the hydrogen bond in water using classical molecular dynamics techniques, J. Phys. Chem. B, 102 (1998), 620-624. Y.-F. Chen, J. J. Dannenberg, The effect of polarization on multiple hydrogen-bond formation in models of self-assembling materials, J. Comput. Chem., 32 (2011), 2890–2895.

[32] G.-J. Zhao, K.-L. Han, Hydrogen bonding in the electronic excited state, Accounts Chem. Research, 45 (2012), 404 – 413.

[33] Y-H. Liu, M. S. Mehata, J.-Y. Liu, Excited-state proton transfer via hydrogen-bonded acetic acid (acoh) wire for 6-hydroxyquinoline, J. Phys. Chem. A, 115 (2011), 19–24.

[34] J. Herbich, J. Waluk, R. P. Thummel, C.-Y. Hung, Mechanisms of fluorescence quenching by hydrogen bonding in various aza aromatics, J. Photochem. Photobiol. A: Chem., 80 (1994) 157-160.

[35] L. Biczo´k, T. Berces, H. Linschitz, Quenching processes in hydrogen-bonded pairs: interactions of excited fluorenone with alcohols and phenols, J. Am. Chem. Soc., 119 (1997) 11071-11077.

[36] T. Yatsuhashi, H. Inoue, Molecular mechanism of radiationless deactivation of aminoanthraquinones through intermolecular hydrogen-bonding interaction with alcohols and hydroperoxides, J. Phys. Chem. A, 101 (1997) 8166-8173.

[37] A. Weisstuch, A. C. Testa Fluorescence study of aminopyridines, J. Phys. Chem., 72 (1968), 1982–1987.

[38] M. A. Thompson, M. C. Zerner, On the red shift of the bacteriochlorophyll-b dimer spectra, J. Am. Chem. Soc. 110 (1988), 606-607.