

Referee report for a PhD thesis submitted

by MSc Mikołaj J. Janicki

entitled: „Theoretical studies of the influence of environment on photochemical and photophysical properties of selected heterocyclic compounds”

prepared under supervision of: prof. Robert W. Góra (Supervisor), prof. Jiří Šponer (Co-Supervisor) and Dr. Rafał Szabla (Subsidiary Supervisor).

Introduction

This PhD thesis is a collection of four thematically coherent articles supplemented with an introduction, presentation of the key results from the articles in an appropriate context, summary, a list of scientific achievements, extended abstracts in Polish and Czech and a bibliography. The introduction consists of a thorough literature review, a chapter presenting aims and research objectives of the thesis and an overview of the computational methodology used by the Author. Significantly, in all four publications Mr. Janicki is the first author.

The articles are indeed thematically coherent, as all of them treat about a role played by chemical environment of a chromophore in processes following UV photon absorption. Since excited states are usually short lived and characterized by open shell electronic configuration that endows the chromophore with high reactivity, studying photochemical reactions is an intrinsically difficult endeavor. Hence, up to quite recently, the theoretical investigations of excited states used to either completely neglect the chemical environment of the chromophore or include it only implicitly. The work done by Mr. Janicki and co-workers breaks with this scheme and explicitly considers the key elements of the chromophore's surroundings. Thanks to this approach interesting photochemical processes enabled by chromophore - surroundings interactions can be studied.

General comments

The first scientific article from the collection (Faraday Discuss. 2018, 212, 345) is dedicated to the problem of photostability of 2-aminoimidazole (2-AIM) and the role played by water

molecules in it. This is an interesting problem in terms of prebiotic chemistry, as 2-AIM was proposed to be a plausible polymerization activator of short RNA sequences. Hence, photostability of 2-AIM under UV light that was reaching Earth's surface during Archean Eon is a valid research question. The system studied consisted of 2-AIM and a cluster of five water molecules that microsolvated one side of 2-AIM; one water molecule was an acceptor of a hydrogen bond made by NH_2 group, another one accepted a H-bond from the in-ring N-H group. Computations of vertical excitations showed that the first seven excited singlet states are dominated by $\pi \rightarrow \sigma^*$ transition, and the $S_0 \rightarrow S_1$ transition has the charge-transfer character with the electron removed from the pi system of 2-AIM and solvated by three water molecules. Results of non-adiabatic molecular dynamics simulations as well as static PES profiles revealed that the charge transfer to solvent triggers a proton transfer, with proton following the electron; a so-called electron driven proton transfer (EDPT). Importantly, EDPT is an efficient route to S_1/S_0 conical intersection, which leads to nonradiative photodeactivation – restoration of the parent system. Hence, the mechanisms established in this work could explain the substantial photostability of water solutions of 2-AIM and its resistance to prolonged UV irradiation.

While I fully understand the need to limit the size of the model and I believe the results obtained in this work are of relevance for water solutions of 2-AIM, the natural question to ask is if and how the described relaxation process would change in more completely solvated model of 2-AIM. Could the Author speculate about it?

The second scientific article from the collection (Chemical Physics 2018, 515, 502) concentrates on the role of water molecules in photochemistry of 2-thiocytosine (2tCyt). 2tCyt was known for its efficient triplet state population, however, the deactivation channels for the triplet state were unknown. The Author and co-workers used a model consisting of 2tCyt and two water molecules placed near the thiocarbonyl group to study plausible photodeactivation channels of this thionucleobase. Interestingly, the $\text{H}_2\text{O} \cdots \text{S}=\text{C}$ interaction was found to stabilize the $3n_s\pi^*$ state and it is characterized by water to chromophore electron transfer (WCET). The latter enables efficient proton transfer from the electron-deficient water molecule to the nitrogen of the base, which process leads to T_1/S_0 intersystem crossing. As this process proceeds through OH/nucleobase-H radical pair, it might be a branching point for chemical transformations other than relaxation to the parent ground state configuration, e.g. water splitting or ring hydroxylation/deamination.

As the propensity of water molecule to donate electron to the chromophore most likely will depend of the solvation of the water (number of hydrogen bonds to the oxygen atom) it might be interesting to investigate if addition of one more water molecule to the system, as a H-

bond donor to the key water molecule, would change the degree of electron transfer to the chromophore.

The third scientific article from the collection (Chem. Commun. 2018, 54, 13407) treats about photostability of oxazoline RNA precursors in UV-rich prebiotic environments. Theoretical UV spectra were computed for arabinose aminooxazoline (AAO) and arabinose oxazolidinone thion (AOT). AAO does not absorb light of wavelength longer than 200 nm and this explains its high photostability. Substitution of =NH₂ group in AAO by =S in AOT causes a red-shift of the absorption maximum by around 80 nm, which was confirmed by a very good agreement between computed and experimentally determined spectra of AOT. Thorough exploration of S₀, S₁, S₂, T₁ and T₂ PESs and minimum energy crossing points (MECP) joining them showed that photodeactivation channels proceeding through S₁/S₀ and T₁/S₀ MECPs are very efficient and they should endow AOT with significant photostability. However, in light of the fact that both S₁ and T₁ excited states of AOT are of n₅π* character it is interesting if water to chromophore electron transfer process would be viable in this case, in analogy to 2tCyt studied in the second article. This mechanisms might open a way to production of OH radical, which could damage AOT. A comment on this would be very appreciated.

The main theme of the fourth scientific article from the collection (J. Phys. Chem. Lett. 2021, 12, 6707) is comparison and interpretation of transient absorption spectroscopy (TAS) results for 2tCyt and alpha and beta anomers of 2-thiocytidine (thioCyd). Molecular models of 2tCyt and thioCyd included four or three explicit water molecules H-bonded to the base and employed the COSMO implicit solvent model. Computational results allowed the Authors to assign experimentally observed TAS bands to excitations from specific excited states, namely ³ππ* ring for both 2tCyt and thioCyd and additionally ³n₅π* for thioCyd.

Intriguingly, in this work the Authors did not find the minimum associated with the ³n₅π* state of 2tCyt, which was the main actor of the first scientific article from the collection. I wonder if this was caused by different microsolvation models used in these two works (2 versus 4 water molecules)? A comment on this would be very appreciated.

Minor typographical and stylistic errors noticed

Even though the thesis has been written very meticulously, a small number of very minor mistakes has been noticed and they are listed here.

- page vi: "fragemnetów"
- page vi: "kwantowo-mechaniczna cząsteczka wody"
- page 6, capture of Fig. 2: "occupied π*" ("π"?)

- page 7: "results described so far were performed"
- page 14: "photon transfer" (most likely should be "proton transfer")
- page 29: "using either be the linear"
- page 30: "beyond S_1/S_0 conical intersections" ("beyond" should most likely be replaced by "in vicinity" or something alike)
- page 31: "dropper"
- page 33: "which objective was the photostability 2-AIM" → "whose objective was to study the photostability of 2-AIM"
- page 36: "aqueous phenyl" → "aqueous phenol" (?)
- page 41: "sufficiently long enough"
- page 49: "selectively destruction cancer" → "selective destruction of cancer"
- page 51: "it could explain that ... in the triplet state could explain why"
- page 70: "2-thiocytidine" → "2-thiocytydine" (?)
- page 77: "lifetimes ... are ... higher" ("longer" seems better than "higher")
- page 87: "potencjalnie aktywnie fotochemicznie" ("aktywne"?)
- page 93: "że w fotodynamice 2-tiocytydyny stan wzbudzony $^3n_s\pi^*$ odgrywa znaczącą rolę w fotochemii 2-tiocytydyny"

Conclusions

My above-listed comments to the thesis concern only very minor issues, mostly related to the way the results have been presented, and very few typographical errors, and they do not diminish my high assessment of the work presented in the thesis and the thesis itself. The thesis is very clearly written, the conclusions drawn from the results are sound and very well supported by the data. The results presented in the thesis have been published in international journals of high standard of peer review (4 published papers), which means they have already been positively assessed by scientific reviewers.

The Author used a range of state of the art computational methods to study novel and important photochemical properties and processes of heterocyclic compounds, whose in depth understanding might be of high relevance for photodynamic therapy, energy harvesting and understanding chemical origins of life. Moreover, in my view the Author proved with the research presented in the thesis that he can formulate valid scientific questions and then, by adopting appropriate research methods and collaborating with other research groups, very efficiently find answers to them.

Hence, I conclude that the thesis presented by Mr. Mikołaj J. Janicki meets all the requirements for doctoral dissertations included in the Act "Ustawa z dnia 14 marca 2003 roku o stopniach naukowych i tytule naukowym oraz o stopniach i tytule w zakresie sztuki (Dz. U. z

Niezapominajek 8, 30-239 Krakow, Poland

phone +48 12 639 51 01

phone +48 12 425 19 23

fax +48 12 425 19 23

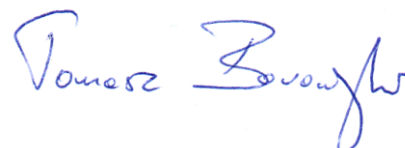
Bank account: Bank Gospodarstwa Krajowego

in PLN: PL 36 1130 1150 0012 1186 5820 0004

in EUR: PL 09 1130 1150 0012 1186 5820 0005

SWIFT: GOSKPLPW, VAT Number: PL 6750001805

2017 r. poz. 1789 z późn. zm.)” and I submit the application to the Scientific Discipline Council, Chemical Sciences, Wrocław University of Science and Technology for the admission of Mr. Mikołaj J. Janicki to further stages of the doctorate. Moreover, taking into account the high scientific value, quality and novelty of the research done by Mr. Janicki, I propose that his doctoral dissertation be distinguished.



Prof. dr hab. Tomasz Borowski