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COMMENTS
on PhD Thesis (Doctoral Dissertation) entitled
"Structural, spectroscopic and electronic properties of chosen pyridine triazoles"
submitted to The University of Wrocław
by
M.Sc. Khalil Salem A. M. Sheweshein

The submitted thesis has been completed in the Department of Bioorganic Chemistry at Wrocław University of Economics, under the supervision of Professor Jerzy Hanuza.

The dissertation is prepared in English in an almost traditional form – it is a typescript starting with the *Introduction* chapter, covering the motivation and main scientific targets of presented work and literature studies on selected heterocyclic compounds with special attention placed on pyridine and triazole derivatives as well as triazolopyridine ones. This chapter also contains the short abstracts of three main chapters presenting the scientific achievements of the Author and, at the end, some remarks on vibrational spectroscopy of organic compounds.

The whole thesis combines experimental and theoretical methods, described shortly in second main chapter named *Experimental*. The basic methods are single crystal X-ray analysis and IR, Raman spectroscopy. They are accompanied by thermogravimetric analysis (TGA) plus differential scanning calorimetry (DSC) and electron absorption and emission spectroscopy. Several vibrational spectra were additionally measured in wide range of temperatures (80 – 500 K). The spectroscopic methods are strongly supported by respective theoretical attempts as DFT calculations of optimized structures, followed by computation of normal vibrations, for which the potential energy distribution (PED) terms were separately computed using special program named Balga. The last attempt is not easy, especially the time consuming definition of 3N-6 independent internal coordinates. For the interpretation of electronic spectra, the HOMO and LUMO orbitals were computed.

Two subsequent chapters are devoted to two triazolopyridine derivatives. In both compounds the pyridine nitrogen atom is in position "c" - second to the C-C bond common for pyridine and triazole rings. The compounds differ in number and position of methyl groups attached to pyridine ring and hydrogen atoms bonded to nitrogen atoms. In first compound, abbreviated as 7MTPHc, the triazolopyridine derivative is in cationic form, due to protonation of pyridine nitrogen. In second compound (4,6M5HTPc) there is a similar protonation caused by migration of triazolo N1-H proton to pyridine nitrogen atom, which results in formation of a zwitterion.

Both compounds mentioned above were structurally investigated by full single crystal X-ray analysis. In both cases, the results of X-ray measurements are well presented in form of figures and tables. Small shortcoming here is the lack od information about thermal ellipsoids in captions of figures 3.1 and 4.1A. In the crystals of both compounds there are additional elements as water molecules and nitrate(V) counterions (in 7MTPHc), engaged in several hydrogen bonds, clearly presented on respective packing diagrams and in tables.

In the interpretation of vibrational spectra, the Author tryed to consider the influence of hydrogen bonds on molecular dynamics of studied triazolopyridine derivatives. For both compounds, the normal vibrations were calculated for three models – the simplest were triazolopyridine derivatives exclusively, in other models the nitrate ion or water molecules were taken into account. In case of 7MTPHc, three theoretical IR and Raman spectra were compared with experimental ones (figures 3.3 and 3.4) and the simplest model was chosen for further interpretation od measured spectra. Looking at figures 3.3 and 3.4, I have an impression that model 7MTPHcNO_3 would be better because reproduces the best the group of bands between 1700 and 1500 cm^{-1} and an intense transitions in the 1500 – 1300 cm^{-1} area. Could the Author justify his choice?

A valuable part of chapter 3 is the section 3.3.5 were the vibrations of complicated hydrogen bond system are closely analyzed. The Author focused his attention on the 3000 – 2200 cm^{-1} broad IR absorption, frequently omitted in the interpretation of IR spectra. Using the deconvolution into the Lorentz curves, the Author found five bands and correlated their wavenumbers with the lengths of five hydrogen bonds, which resulted in nice, quasi-linear relation (figure 3.6). Employing the 7MTPHcH_2O model, several vibrations with contributions of $N_{triazole}H\cdots O$ and $N_{triazole}\cdots HO$ groups were also found below 1400 cm^{-1}.

Another valuable extension of vibrational analysis was made for second compound for which the IR and Raman spectra were measured at various temperatures from 500 (or 400) to 80 K. The most interesting features were found again in the 3000 – 2000 cm^{-1} region where the maximum of a broad absorption significantly shifts to lower wavenumbers upon temperature decrease, in contrast to neighbor band at about 2000 cm^{-1} (300 K) which splits into four intense components in 80 K. Such temperature dependent changes distinguish the bands related to vibrations of water molecules. The next interesting feature was found for several bands which split into two components at temperatures below 250 K. The Author postulated that these bands originate from vibrations of two methyl groups which below 250 K becomes energetically nonequivalent.

As I mentioned before, in both compounds presented in chapters 3 and 4, the pyridine nitrogen atom is in “c” position (second to the C-C bond common for both rings). Since there are many important compounds with nitrogen atom in the closer position (type “b”), the Author made an attempt to find the spectroscopic features, to be used for fast recognition of this nitrogen atom locations in other triazolopyridine derivatives. For this purpose, he additionally measured and calculated the vibrational spectra for 6-methyl-1H-[1,2,3]triazolo[4,5-b]pyridine – the compound prepared earlier in prof. Hanuza’s group. Comparing the spectra of mentioned compound with those of 7MTPHc, the Author listed in table 5.2 nine bands, as characteristic to “b” or “c” isomers. Five of them are related to triazolo ring vibrations, remaining four results from strongly coupled vibrations of both rings. In my opinion, bands calculated for 7MTPHc at 3406 and 979 cm^{-1} show almost the same positions in both isomers and are not characteristic. Another question is about vibrations (bands) with predominant contribution of pyridine internal vibrations – some of these bands should be sensitive to nitrogen atom position. Bigger differences the Author observed in UV-Vis spectra and explained them calculating the shapes of HOMO and LUMO orbitals.

In addition to X-ray and spectral methods, two main compounds were characterized by TGA and DSC measurements. In case of 7MTPHc, first mass loss (about 5%) was due to elimination of water molecule. For such change, the calculated mass decrease is 8% but the Author did not calculate it. In the crystals of 4,6M5HTPc there are four water molecules and their elimination lowers the mass by 32.7%. On page 39, the Author describes similar mass loss (30,62%) in temperature range 147 – 190 C, but I can not see this in figure 44A (the red line starts lowering at about 220 C). Is the graph 4.4A correct?

Despite some problems and questions raised in my above opinion, I think that Mr Sheweshein, during his PhD work acquired many important skills in preparation of organic compounds and in the X-ray and spectroscopic methods. His published achievements enriched the organic chemistry as well as vibrational spectroscopy. **Therefore, I propose the PhD thesis prepared by M.Sc. Khalil Salem A. M. Sheweshein for subsequent stages of the PhD procedure carried out by Faculty of Chemistry at The University of Wrocław.**

Piotr Drożdżewski