Abstract

Nucleic acids and their components belong to the most important molecules essential for life. Hydrogen atom migration across the skeleton of purine or pyrimidine bases of nucleic acids gives rise to their various tautomeric forms. Furthermore, depending on pH of the medium, these bases might become protonated or deprotonated. Protonation/deprotonation of nucleic acid bases is involved in many biochemical processes. These include mainly regulation of replication and gene expression by means of specific secondary structure stabilization or acid-base catalysis of phosphodiester backbone cleavage. Additionally, secondary structures that include ionized bases are also associated with various genetic diseases. However, protonation and deprotonation are very fast dynamic processes and their experimental detection is difficult. Therefore, this work focuses on development of reliable method for relatively fast detection of pyrimidine base derivates primary protonation site. At first, pyrimidine bases with protonation site determined by structure were analyzed in both neutral and ionized state using NMR spectroscopy. In the next step, NMR parameters for both neutral and ionized forms were calculated using quantum-chemical computational methods. Computational method was optimized to produce results which correlate with experimental values. Method based on correlation of optimized calculation with NMR experiment was used to detect primary protonation site of pyrimidine bases with more than one possible site. Based on the results, an optimal method for quantum chemical computation of NMR parameters was designed.

(In Czech)

Keywords: pyrimidine, nucleic acid base, NMR spectroscopy, ionization, DFT computation