

Protonation of Base Pairs in RNA: Context Analysis and Quantum Chemical Investigations of Their Geometries and Stabilities

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Abstract:

Base pairs involving protonated nucleobases play important roles in mediating global macromolecular conformational changes and in facilitation of catalysis in a variety of functional RNA molecules. Here we present our attempts at understanding the role of such base pairs by detecting possible protonated base pairs in the available RNA crystal structures using BPFind software, in their specific structural contexts, and by the characterization of their geometries, interaction energies, and stabilities using advanced quantum chemical computations. We report occurrences of 18 distinct protonated base pair combinations from a representative data set of RNA crystal structures and propose a theoretical model for one putative base pair combination. Optimization of base pair geometries was carried out at the B3LYP/cc-pVTZ level, and the BSSE corrected interaction energies were calculated at the MP2/aug-cc-pVDZ level of theory. The geometries for each of the base pairs were characterized in terms of H-bonding patterns observed, rmsd values observed on optimization, and base pair geometrical parameters. In addition, the intermolecular interaction in these complexes was also analyzed using Morokuma energy decomposition. The gas phase interaction energies of the base pairs range from -24 to -49 kcal/mol and reveal the dominance of Hartree-Fock component of interaction energy constituting 73% to 98% of the total interaction energy values. On the basis of our combined bioinformatics and quantum chemical analysis of different protonated base pairs, we suggest resolution of structural ambiguities and correlate their geometric and energetic features with their structural and functional roles. In addition, we also examine the suitability of specific base pairs as key elements in molecular switches and as nucleators for higher order structures such as base triplets and quartets.