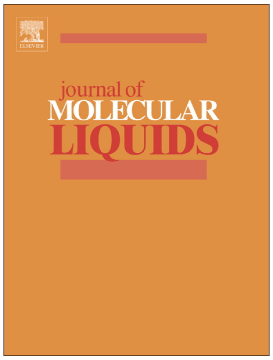
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Mechanisms for Guanine–Cytosine Tautomeric Equilibrium in Solution via Steered Molecular Dynamic Simulations

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Abstract

The free energies of tautomeric equilibria G-C ⇆ G*-C* between the canonical and rare DNA base pairs in aqueous solution were determined theoretically by applying steered molecular dynamic (SMD) simulations. Concerted and stepwise mechanisms were considered for the double proton transfer (DPT), aiming to explain their behavior. The assistance of water molecules in the hydrogen transfer has also been considered. Of the different mechanisms used in the simulations, the stepwise, where the first step describes the proton transfer from guanine to cytosine and the second step from cytosine to guanine is the more favorable kinetically ($\Delta G^{\ddagger} = 22.8$ kcal/mol), whereas concerted mechanism is more favorable thermodynamically ($\Delta G = 15.4$ kcal/mol) being able participate in spontaneous genetic mutation. The inclusion of assistant water molecules in mechanisms increases the activation barriers and modifies slightly the energy of the process, being the DPT process better described using the model assisted with two water molecules. Transition and intermediate structures for all the mechanisms considered were also analyzed with this SMD procedure.

Keywords: Guanine-Cytosine, tautomeric equilibrium, SMD simulations, double proton transfer mechanisms, spontaneous mutation genetic

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