Interactions of Metal Cations in Bioorganic Environment

Computational Study Using Quantum Mechanics and Molecular Mechanics Tools

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Biologically relevant interactions of piano–stool ruthenium(II) complexes with *ds*-DNA are studied by QM/MM computational technique. The whole reaction mechanism is divided into three phases — hydration of $[Ru^{II}(\eta^6$-benzene)(en)Cl$]^+$, consequent binding DNA and final intra–strand cross–link formation between two adjacent guanines. Free energy profiles of all reactions are explored by QM/MM MD umbrella sampling approach where the Ru(II) complex is described by DFT. For that purpose, special QM/MM software was developed to couple Gaussian and Amber programs. Calculated free energy barriers of Ru(II) hydration as well as DNA binding process are in good agreement with experimentally determined rate constants. Reaction pathway for cross–link formation was predicted that is feasible from both thermodynamical and kinetical point of view.