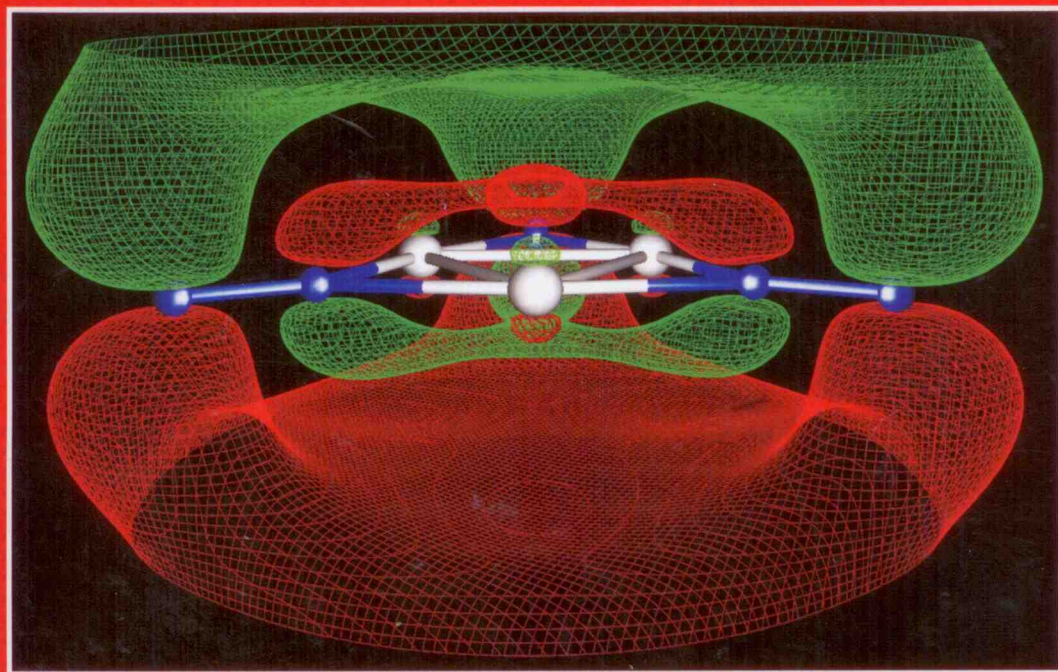


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BOOK OF ABSTRACTS

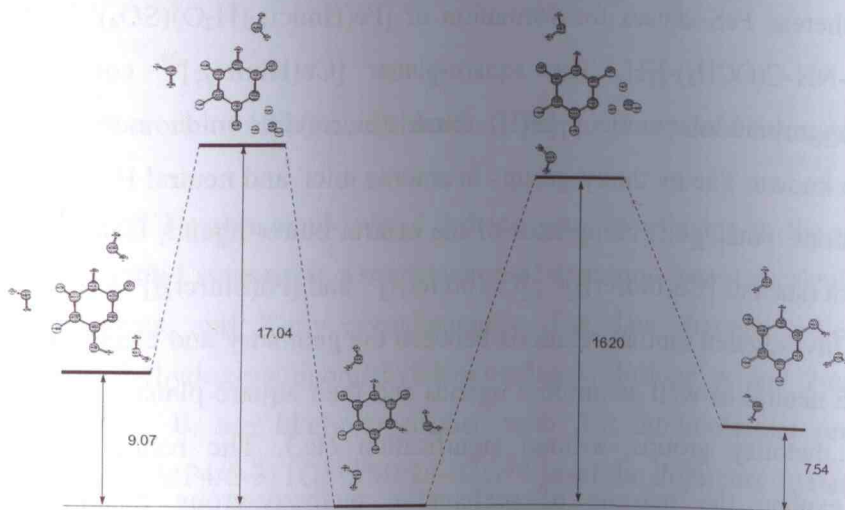
Oxo-hydroxy tautomerism of 5-fluorouracil in water solution: solvent-depended mechanism

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Ab initio quantum chemical calculations were performed for 5-fluorouracil (5FU) in the gas phase and in water solution. The solvent effects were modeled by explicit inclusion of three water molecules, which creates the first hydration shell around the solute. Full geometry optimizations without any constraints of the 5-fluorouracil-water complexes were carried out at the MP2/6-31+G(d,p) level of theory. Single point calculations were also performed at MP4/6-31+G(d,p)//MP2/6-31+G(d) computational level to obtain more accurate energies. The minimum energy path (at MP2/6-31+G(d) level) for water-assisted proton transfer in tri-hydrated 5-fluorouracil was followed.



Energy differences between dioxo and hydroxy tautomeric forms of 5FU and activation barriers calculated at MP2/6-31+G**+ZPE level

The investigations on the mechanism of tautomerization show that solute-solvent interactions can influence the mechanism of tautomerization. The result is a strong reduction of the activation energy of the tautomeric reaction. Both dioxo and hydroxy tautomeric forms of 5FU can coexist in water solution. These rare hydroxyl tautomers of 5FU are suggested to be responsible for mutation by inducing mispairing of nucleic acid bases.

The present findings provide support for such a concept.

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