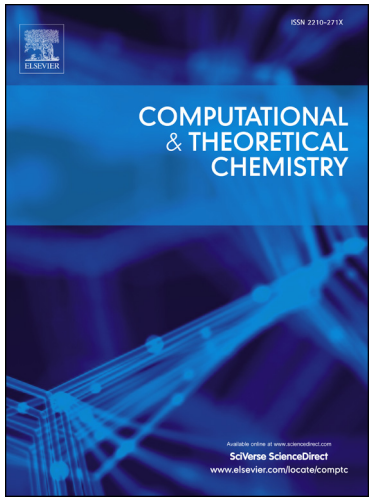

Anions of uracils: N1 or N3? That is the question

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ANIONS OF URACILS: N1 OR N3? THAT IS THE QUESTION

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The relative stability of N1 and N3 anions of twelve 5,6-substituted uracils in aqueous solutions was studied in IEFPCM (SMD) – TPSSTPSS/6-311+G(d, p) approximation. Specific solvation was simulated by the first hydrate shell of uracil and anions containing 5 water molecules. Based on $\Delta G_{water} = G^0(N3) - G^0(N1)$, the series of relative stability was determined as: **5OH6MeU** (-3.4) – **5OHU** (-2.0) – **5NH$_2$U** (2.4) – **U** (3.5) – **5FU** (4.5) – **5MeU** (4.6) – **6MeU** (4.6) – **5ClU** (9.2) – **5BrU** (9.5) – **5NO$_2$U** (18.6) – **6ClU** (31.9) – **6FU** (33.9), kJ/mol. The factors that determine the relative stability in the N1/N3 pair were identified. In the gas phase, the N1 anion is much more stable than the N3 anion: ΔG_{gas} varies in the range from 23.3 (**5OHU**) to 80.0 (**6FU**) kJ/mol due to more efficient delocalization of excess charge over the uracil frame in the N1 anion, which was characterized using HOMA aromaticity indices. The solvent makes the Gibbs energies of the N1 and N3 states much more close. Two reasons of the stabilizing effect of water can be distinguished. First, the aromaticity of N3 anions increases considerably in aqueous solutions, leading to almost complete equalization of HOMA indices. Second, the polar solvent more efficiently stabilizes the more polar N3 states of the uracils studied. The effect of substituents on the relative stability ΔG_{water} was studied using the Hammett method. It was found that substituents with a strong (+R)-effect at position 5 decreased ΔG_{water} down to negative values. Substituents at position 6 affect the relative stability of uracil anions by the inductive mechanism. In this case the formation of N1 anions becomes much more preferable than the formation of N3 anions. The mesomeric effect is weak in this case.

Key words: uracil anions, relative stability, delocalization indices, hydration, substituent effect.

1. Introduction

Uracils (parent molecule and thymine) belong to the most important pyrimidines that play a key role in the structure and functioning of nucleic acids, enzymes and some pharmaceuticals [1]. Besides, a number of synthetic derivatives of uracil are used in medical practice. For example, 6-methyluracil is used as an antiulcer agent and in treatment of hepatitis and

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