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COMMENTS

Comments on "Theoretical Estimations of the 298 K Gas-Phase Acidities of the Pyrimidine-Based Nucleobases Uracil, Thymine, and Cytosine"

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In our recent works,[1−4] we have demonstrated that the interaction energy between two complementary nucleobases, which are held together by NH···O═C and NH···N hydrogen bonds, depends not only on the intrinsic basicity of the acceptor atoms but also on the acidity of the NH donor groups. For this purpose, the acidities of the NH bonds of uracil, thymine, cytosine, adenine, and guanine have been calculated at the B3LYP/6-31++G(d,p) level. To the best of our knowledge, we were the first to report reliable theoretical calculations dealing with the deprotonation enthalpies of the NH bonds of nucleobases. The accuracy of our reported results is justified further by the fact that our predicted gas-phase acidities of the N1 and N3 sites of uracil compare very well with the bracketed gas-phase acidities obtained in a subsequent experimental study by Fourier transform ion cyclotron resonance mass spectroscopy.[5]

In a recent paper by Huang and Kenttämaa[6] (HK), the gas-phase acidities of the most stable tautomers of uracil, thymine, and cytosine have been recalculated at the B3LYP/aug-cc-pVTZ//B3LYP/6-31+G(d) level. HK[6] claimed that "To our best knowledge, no higher level theoretical investigations beyond the AM1 level have been reported for the gas-phase acidities of the different deprotonation sites of pyrimidine bases except for uracil and 1,3-dimethyl uracil" (ref 6, page 4894). As mentioned above, this statement is not correct. The gas-phase acitidies of the most acidic NH sites of the five nucleobases have been well-known since 1999. Our theoretical results have been quoted in the experimental paper by Kurinovich and Lee,[5] which in turn was quoted by HK in their recent paper. As shown by the data of Table 1, there is a near perfect agreement between our earlier values and those of ref 6, which allows one to conclude that uracil and thymine are more acidic than cytosine. It should be mentioned that in our previous paper,[4] we have reported that the intrinsic acidities of the five nucleobases are ordered as follows:

TABLE 1: Gas-Phase Acidities (kcal/mol) at 298 K of the Deprotonation Sites Involving the N Atoms of Uracil, Thymine, and Cytosine

uracil		thymine		cytosine	
N1	332.4[a]	N1	334.1[c]	N1	345.2[d]
	332.8 ± 2.2[b]		334.5 ± 2.2[b]		345.6 ± 2.2[b]
N3	345.8[a]	N3	346.6[c]	N4H$_a$[e]	354.1[d]
	345.1 ± 2.2[b]		345.7 ± 2.2[b]		353.5 ± 2.1[b]
				N4H$_b$	348.2[d]
					348.7 ± 2.1[b]

[a] Our work, ref 1. [b] Reference 6. [c] Our work, ref 2. [d] Our work, ref 3. [e] Vicinal to the N3 atom.

$$\text{uracil} > \text{thymine} > \text{guanine} > \text{adenine} > \text{cytosine}$$

In this context, we deeply regret that our papers [2−4] have been omitted by HK.[6]

References and Notes

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