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# Isomerism of the covalent anion of the dimer of uracil and 1-methyl-cytosine: ab initio study

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## Abstract

Theoretical ab initio calculations have been performed to determine the distribution of an excess electron in the covalent anion of the dimer of uracil and 1-methyl-cytosine (U–MC). Due to the multitude of possible isomers, this system may present an interesting model for future experimental investigations of the electron attachment and transfer in dimers of nucleic acid bases. The major conclusions of this work are (i) three isomeric structures of the covalent U–MC anion have been found in the calculations. The anion where the excess electron is located at the MC molecule was found to be the most stable; (ii) a noticeable ring distortion was found in the molecule where the excess electron is localized; (iii) the covalent U–MC anions are non-planar, hydrogen-bonded systems; and (iv) the out-of-plane deformed site of the base molecule where the excess electron localizes in the dimer anion is positioned opposite to the site involved in the hydrogen bond. © 2000 Elsevier Science B.V. All rights reserved.

## 1. Introduction

For the last few years, there has been increasing interest in studying the electrical conductivity of DNA. Unlike proteins, DNA has unique characteristics which result from its double-helical ladder structure of base pair rings. This creates a compact stack of  $\pi$ -electrons associated with the base pairs, promoting the question as to whether DNA could possibly serve as an electrical conduit. Over the past few years, the topic of electron transfer in DNA has generated discussion among researchers centering on the issue of DNA conductivity and isolator properties [1–22]. This issue is closely re-

lated to the ability of the DNA bases and base pairs to attract and bind excess electrons. The large changes in acidity or basicity, which result from loss or uptake of the electron from or by a base in a base pair of DNA, can constitute a very powerful stop to the migration of electrons in the direction of the DNA helix via the stacked bases [12]. Olson et al. [9] and Ratner [10] postulated that electron transport in molecular wires can, under certain conditions, be influenced by vibrational coupling. They concluded that electrons tunnel elastically through variable geometries and the linear current depends on the location of the soliton deformation and the magnitude of dimerization. Henderson et al. [11] went even further and invoked polaronic deformations to describe long range electron transport in nucleic acid stacks. Our recent calculations of two isomeric forms of the uracil–thymine dimer anion [23]

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confirm that a strong coupling exists between the localization of the excess electron and the localization of the vibrational deformation. The calculations also showed that in the covalent uracil–thymine anion, the hydrogen-bond structure is significantly altered relative to the neutral complex. The most striking difference occurs in weaker hydrogen bonds which upon electron attachment, break allowing the hydrogens to interact with the excess electron and stabilize the anion. In addition, the uracil ring, where the excess electron is localized, noticeably puckers. The predicted puckering effect is consistent with the results of the recent electron scattering experiment of Burrow and coworkers [24], where evidence for nuclear motion during the lifetime of a metastable covalent uracil anion was observed. This effect can be a key property for developing the theory of the electron-transfer rate in systems involving nucleic acid bases.

Our recent calculations [25] on anions of the uracil dimer,  $U_2^-$ , have revealed that apart from dipole-bound anions with different structures, there exists a minimum on the  $U_2^-$  potential energy surface which corresponds to a covalent anion where the two uracil molecules are oriented almost perpendicularly to each other. In this anion, the excess electron is localized on one of the uracil molecules and this molecule is puckered. The excess electron attachment to DNA and RNA base dimers and higher H-bonded polymers and its effect on the hydrogen-bond network in these systems continues to be the focus of our investigation. In particular, the interplay between the hydrogen bonding and the excess electron localization in homo- and hetero-dimers of the bases is the effect investigated in the present work.

The experimental determination of the electron affinities (EA) of nucleic acid bases (NAB) in the gas-phase has proven to be a difficult problem. Bowen and coworkers [26] and Schiedt et al. [27] have used photo-electron spectroscopy (PES) and Schermann and coworkers [28,29], the Rydberg electron transfer (RET) and field-detachment spectroscopy to determine the electron affinities of nucleic acid bases (NAB). There has been very little experimental work on the NAB dimer anions. Among the most recent works one should mention

the paper by Schermann and coworkers [30] where they reported a mass spectrum of valence anions of the thymine–thymine, adenine–thymine, and adenine–adenine base pairs. We are not aware of any direct experimental measurement of the electron affinities of NAB dimers or ionization potentials of their anions. The present *ab initio* calculations may provide a useful contribution to future experimental determination of these quantities.

The questions which we will attempt to answer in the present work concern the following: (i) the structural isomerism of the covalent U–MC anion; (ii) the interplay between the hydrogen bonding and localization of the excess electron in  $(U-MC)^-$  and how this interplay affects the relative stability of the isomers; (iii) the relevance of the structural isomerism of  $(U-MC)^-$  to electron transfer between U and MC in the covalent dimer anion; and (iv) the puckering deformation of the base, which carries the excess electron in the U–MC dimer anion, and a resulting possibility of using the vibrational excitation (or excitations) to preferentially form a particular anion isomer in the electron attachment process.

## 2. Calculations and discussion

The following calculations have been performed with the use of the GAUSSIAN 94 quantum-chemical program package [31] to elucidate the questions raised in this work:

(1) Since in the covalent U–MC dimer anion, the excess electron can attach to either the U or MC molecule, causing a ring deformation similar as in the thymine–uracil anion, one can use the ring deformation of either U or MC to direct the excess electron to one of the two bases in the calculation. The puckering deformation of the uracil ring in the covalent dimer anions formed by this base was described before [23,25] and the puckered uracil structure determined before was used in the present calculations. In order to determine the puckered structure of the MC valence anion, an UMP2/6-31++G\*\*(6d) (Møller–Plesset second-order perturbation theory calculation with the spin-unrestricted Hartree–Fock wave function, UHF, as the reference and with the standard

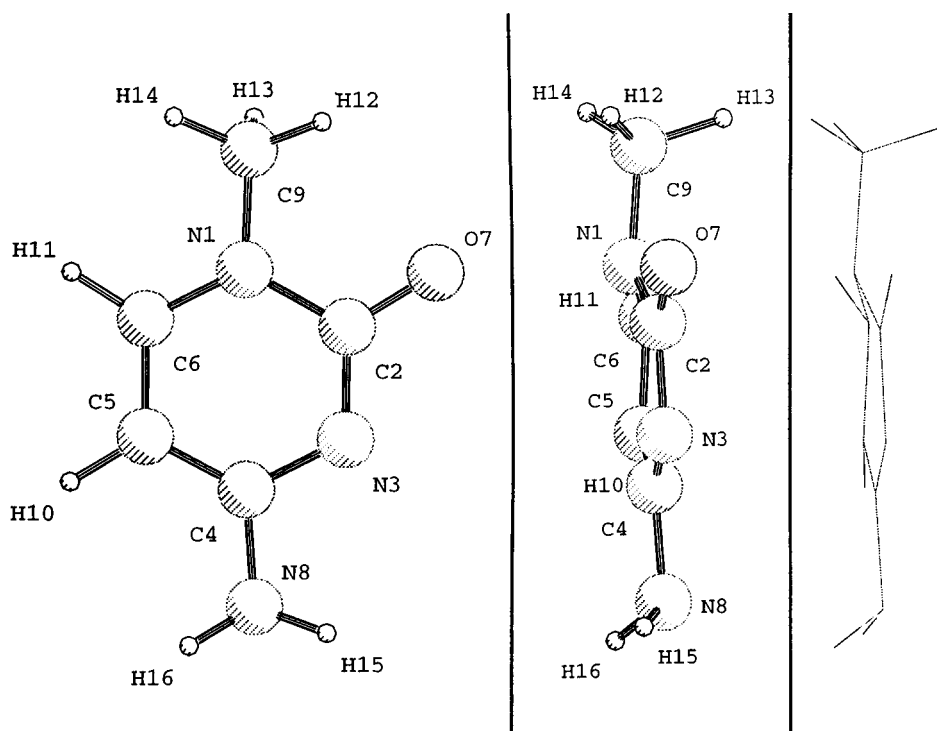


Fig. 1. Three different views of the puckered structure of the covalent anion of 1-methyl-cytosine.

6-31++G\*\* basis set; each d-shell consists of six orbitals) geometry optimization was performed for this system starting with a  $MC^-$  geometry similar to the puckered structure of  $U^-$ . The calculation converged to a structure shown in Fig. 1. For this structure, an MP2/6-31++G\*\*(6d) calculation (MP2 calculation with the spin-restricted HF reference function; RHF) was performed for the neutral system. Also, starting with the  $MC^-$  geometry, the structure of the neutral MC was optimized at the RHF/6-31++G\*\*(6d) level, and for the equilibrium geometry found the MP2/6-31++G\*\*(6d) energy was calculated. The results of the  $MC^-/MC$  calculations are presented in Table 1.

Using the  $MC^-/MC^-$  and  $MC/MC^-$  MP2 energies, we predict the vertical electron detachment energy (VDE) to be marginally negative (the MP2–UMP2 result of  $-25$  meV). However, the predicted MP2 value of the adiabatic electron detachment energy (ADE) of  $MC^-$  is found to be definitely negative ( $-677$  meV), indicating that the valence anion of MC is not a stable system. The

Table 1  
Covalent anion of 1-methyl-cytosine ( $MC^-$ ) – calculations performed with 6-31++G\*\*(6d) basis set

<i>MC<sup>-</sup></i>	
UHF//UMP2	–431.637555 <sup>a</sup>
UMP2//UMP2	–432.994239
HOMO <sup>b</sup>	–0.04632
<i>MC (at the MP2 anion geometry)</i>	
RHF	–431.630490
MP2	–432.995169
<i>MC (at its MP2 equilibrium geometry)</i>	
HF//MP2	–431.669772
MP2//MP2	–433.019136
<i>VDE</i>	
MP2–UMP2 <sup>c</sup>	–25
<i>ADE</i>	
MP2–UMP2	–677

Total energies in hartrees, and ADE and VDE in meV. Both RHF and UHF used for the neutral and UHF for the anion.

<sup>a</sup>  $\langle S^2 \rangle = 0.81$ .

<sup>b</sup> Singly occupied MO of the excess electron.

<sup>c</sup> Levels of theory used to calculate the total energies of the neutral and the anion.

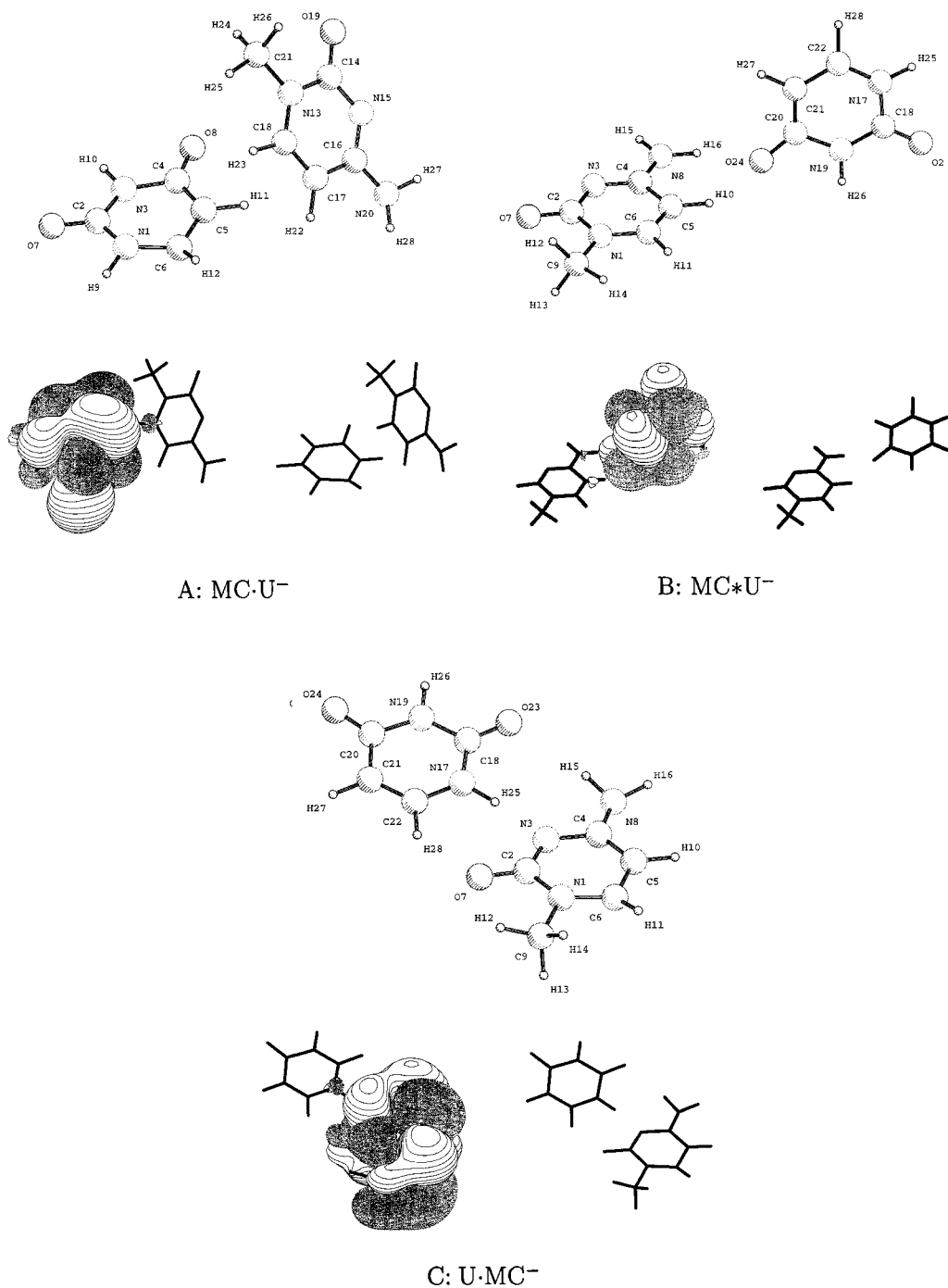


Fig. 2. Isomerism of the anion of the uracil-1-methyl-cytosine dimer: (A)  $\text{MC}\cdot\text{U}^-$ , (B)  $\text{MC}^*\text{U}^-$  and (C)  $\text{U}\cdot\text{MC}^-$ . For each dimer anion, we also show a plot of the HOMO (since the HOMO plot conceals the dimer structure, a separate structure plot is also provided).

result of the calculations on the  $\text{MC}^-/\text{MC}$  system, which was utilized in the calculations on the  $\text{U-MC}$  dimer anion described in the next section, is the puckered structure of the valence  $\text{MC}$  anion.

(2) The first series of calculations on  $\text{U-MC}$  anion were aimed at determining the equilibrium structures of the covalent anion of this system. The search for the structures was initiated with several different initial geometries where the two molecules were separated by a considerable distance and the initial geometry of either the uracil or 1-methyl-cytosine molecule was taken as the puckered geometry determined for the valence anion of the system. Using this procedure, we found three equilibrium anion structures which we denote as  $\text{MC} \cdot \text{U}^-$ ,  $\text{MC}^* \text{U}^-$  and  $\text{U} \cdot \text{MC}^-$ . This notation reflects the position of the excess electron in the anions, i.e., in  $\text{MC} \cdot \text{U}^-$  and  $\text{MC}^* \text{U}^-$ , the excess electron is localized on U, and in  $\text{U} \cdot \text{MC}^-$  on MC. The structures of the anions are shown in Fig. 2. Along with each structure, we present a plot of the orbital occupied in the anion by the excess electron (HOMO). The orbital plots show that in all three anions, the excess electron is localized on one of the bases and the structure of this base shows a significant puckering distortion.

In the first column of Table 2, we present the total UHF and UMP2 energies of the three  $\text{U-MC}$

anions and the energies of their HOMO's. All three HOMO energies are negative, indicating that in the Koopmans approximation, the anions are stable with respect to the vertical electron detachment. The most stable anion is the  $\text{U} \cdot \text{MC}^-$  system with the excess electron on MC. This system has the highest number of hydrogen bonds (though one of them is a weak  $\text{C-H} \cdots \text{O-H}$  bond). It is interesting to notice that in all three anions, the ring deformation of the base which carries the excess electron is positioned at the opposite side of the molecule with respect to the side involved in the hydrogen bond with the other base. In  $\text{U} \cdot \text{MC}^-$ , this still allows the formation of three hydrogen bonds (two strong and one weak) between MC and U, and this is the major reason for the highest stability of this system.

Examining the structures of the dimer anions, one notices that they are not planar. This effect becomes more evident in the comparison of the dimer anion structures with the structures of the neutral dimers which are presented in Fig. 3 and discussed in the next section.

(3) In the next series of calculations, the energies of the neutral dimers at the dimer anion geometries were determined using the MP2 method. These results denoted as  $\text{MC} \cdot \text{U}/\text{MC} \cdot \text{U}^-$ ,  $\text{MC}^* \text{U}/\text{MC}^* \text{U}^-$  and  $\text{U} \cdot \text{MC}/\text{U} \cdot \text{MC}^-$  are shown

Table 2

Anions of the uracil 1-methyl-cytosine dimer – calculations performed with the 6-31++G\*\*(6d) basis set (energies in hartrees)

Method/system <sup>a</sup>	$\text{MC} \cdot \text{U}^-//\text{MC} \cdot \text{U}^-$	$\text{MC} \cdot \text{U}/\text{MC} \cdot \text{U}^-$	$\text{MC} \cdot \text{U}/\text{MC} \cdot \text{U}$
HF <sup>b</sup>	–844.172434	–844.133948	–844.175737
MP2 <sup>c</sup>	–846.719558	–846.693218	–846.712179
HOMO <sup>d</sup>	–0.08053		
	$\text{MC}^* \text{U}^-//\text{MC}^* \text{U}^-$	$\text{MC}^* \text{U}/\text{MC}^* \text{U}^-$	$\text{MC}^* \text{U}/\text{MC}^* \text{U}$
HF	–844.177917	–844.136813	–844.178375
MP2	–846.726205	–846.695864	–846.716580
HOMO	–0.08368		
	$\text{U} \cdot \text{MC}^-//\text{U} \cdot \text{MC}^-$	$\text{U} \cdot \text{MC}/\text{U} \cdot \text{MC}^-$	$\text{U} \cdot \text{MC}/\text{U} \cdot \text{MC}$
HF	–844.187152	–844.158585	–844.198333
MP2	–846.737856	–846.718767	–846.739354
HOMO	–0.07305		

<sup>a</sup> Notation:  $\text{A} \cdot \text{B}/(\text{A} \cdot \text{B})'$  denotes that the calculation on the  $\text{A} \cdot \text{B}$  system was performed at the equilibrium geometry of the  $(\text{A} \cdot \text{B})'$  system. Anions optimized at the UHF/6-31++G\*\* level and the neutrals at the RHF/6-31++G\*\* level of theory.

<sup>b</sup> RHF for the neutral, UHF for the anion.

<sup>c</sup> MP2 for the neutral, UMP2 for the anion.

<sup>d</sup> Singly occupied MO of the excess electron.

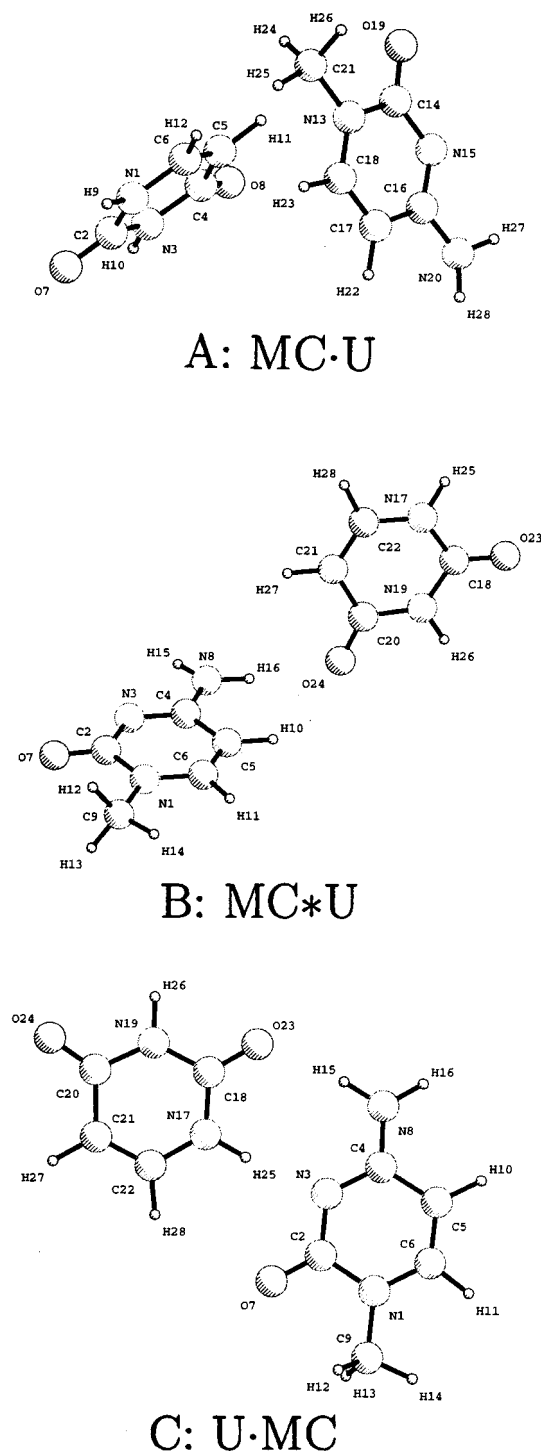


Fig. 3. Structures of the neutral dimers of uracil and 1-methylcytosine: (A) MC·U, (B) MC\*U and (C) U·MC.

Table 3

VDE and ADE of the uracil 1-methylcytosine dimer anions in meV calculated at the MP2/6-31++G\*\*(6d) level of theory

System	VDE	ADE
MC·U <sup>-</sup>	717	201
MC*U <sup>-</sup>	826	262
U·MC <sup>-</sup>	519	-41

in Table 2. As one can see, all the energies of the neutral systems are considerably higher than the energies of the anions, confirming the vertical stability of the valence anions of the U–MC dimers. The vertical MP2/6-31++G\*\*(6d) electron detachment energy results are shown in the first column of Table 3.

(4) In the final step, we optimized the neutral dimer structures, starting from the equilibrium structures of the anions. The geometries of the three structures found are shown in Fig. 3. Among the three structures, the most stable is the U·MC dimer obtained starting with the optimization from the U·MC<sup>-</sup> equilibrium geometry. Like U·MC<sup>-</sup>, U·MC has also three hydrogen-bonds, but its structure is more planar than the U·MC<sup>-</sup> structure. The MP2 energies of the neutral complexes, which are presented in the third column of Table 2, were used to calculate the adiabatic electron detachment energies of the anions. In these calculations, the anion energies were subtracted from the energies of the corresponding neutral counterparts. The results are shown in the second column of Table 3. While the ADE's are positive for both anions, where the excess electron is located at uracil (201 and 262 meV), the ADE for the anion with the electron located at 1-methylcytosine is slightly negative (−41 meV). This last value is considerably less negative than the value of −677 meV obtained for the MC anion, indicating that formation of a dimer with uracil has a strong stabilization effect on the valence MC anion.

(5) To assess the extent of the hydrogen-bond network transformation, which occurs when the electron detaches from the U–MC anion, we performed a series of MP2 calculations of the H-bond interaction energies for the three neutral and three anionic U–MC complexes found in the calculations. For the anionic complexes, the intermolec-

Table 4

MP2 H-bond interaction energies (in kcal/mol) calculated for the uracil–1-methyl-cytosine dimer anions and neutral systems calculated taking account of the basis set superposition error (BSSE) by the counterpoise method of Boys and Bernardi [32]<sup>a</sup>

System	Neutral	Anion <sup>b</sup>
MC · U <sup>-</sup>	4.4	17.6
MC*U <sup>-</sup>	5.3	21.7
U · MC <sup>-</sup>	21.0	32.6

<sup>a</sup> HF/6-31++G\*\*(6d) geometries were used in the calculations.

<sup>b</sup> Calculated as the energy difference of the dimer anion and HF energies of the corresponding anion and neutral monomers computed using the dimer basis set; i.e. for MC · U<sup>-</sup>:  $E(\text{MC} \cdot \text{U}^-) - E_{\text{MC} \cdot \text{U}^-}(\text{U}^-) - E_{\text{MC} \cdot \text{U}^-}(\text{MC})$ , for MC\*U<sup>-</sup>:  $E(\text{MC}^* \text{U}^-) - E_{\text{MC}^* \text{U}^-}(\text{U}^-) - E_{\text{MC}^* \text{U}^-}(\text{MC})$ , and for U · MC<sup>-</sup>:  $E(\text{U} \cdot \text{MC}^-) - E_{\text{U} \cdot \text{MC}^-}(\text{U}) - E_{\text{U} \cdot \text{MC}^-}(\text{MC}^-)$ , where the subscripts and the monomer energies indicate the dimer basis set used.

ular interaction energy was calculated by subtracting the energies of the corresponding anion and neutral monomers from the energy of the dimer anion. For the neutral complexes, the calculations involved the energies of the neutral dimers and monomers. For example, the interaction energy for the MC · U<sup>-</sup> complex was calculated as the difference of the MC · U<sup>-</sup> energy and the energies of U<sup>-</sup> and MC. For each dimer, the monomer energies were calculated using the the basis set of the dimer in accordance with the counterpoise method of Boys and Bernardi [32]. The results summarized in Table 4 indicate that the H-bond interaction energies are very different in the neutral and the anionic complexes. For all three anions, the H-bonding interaction is considerably stronger than in the neutral systems. This effect can be attributed to the enhancement of the intermolecular interaction in the dimer due to the negative charge of one of the monomers and to a higher stability of the excess electron in the dimer than in any of the monomers.

### 3. Conclusions

The ab initio theoretical calculations performed in this work revealed an interesting isomerism of the covalent anion of the dimer of uracil and 1-methyl-cytosine. Three configurations of the anion

have been found that differ in the location of the excess electron. In the most stable configuration, the excess electron is exclusively localized at the 1-methyl-cytosine molecule and the ring of this molecule is noticeably out-of-plane distorted. In the other two anions, the excess electron is localized at the uracil molecule and here the uracil ring is distorted from planarity. It appears that in all the isomeric structures of the U–MC anion, the distorted site of the base, where the excess electron is localized, is always located at the opposite side of the molecule from the site involved in the hydrogen bonding with the other base. Thus, the stability of a particular structure of the dimer anion is not only determined by the electron affinity of the base, where the excess electron is located, but also by the strength of the hydrogen-bonding link which can be formed by the two bases, given the location of the excess electron.

The ring puckering distortion in the anion at the site where the excess electron is located indicates that the transfer of the excess electron and the vibrational energy transfer in this system are coupled. This opens a possibility that with a selective excitation of a puckering vibration of the U or MC ring in U–MC<sup>-</sup>, one can induce a transfer of the excess electron.

The calculations showed that the attachment of an excess electron affects the hydrogen-bonding network in the dimers. This finding may have relevance to the structural stability of the helical DNA and RNA structures when they are exposed to free electrons.

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