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The Specific Solvation Effects on the Structures and Properties of Adenine−Uracil Complexes: A Theoretical *ab Initio* Study

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Ab initio quantum chemical studies at the HF level with the 6-31G* basis set were performed for three different Watson−Crick hydrogen bonded adenine−uracil complexes in the gas phase and in a water solution approximated by the first solvation shell. Full geometry optimizations without any constraints on the planarity of these complexes were carried out. The solvent effect was modeled by explicit inclusion of seven water molecules which creates the first coordination sphere around the adenine-uracil base pair. Single point calculations were also performed at the correlated MP2/6−31*//HF/6-31G* level. The interaction and solvation energies were corrected for the basis set superposition error. It was shown that base pair corresponding to the standard Watson−Crick pair (denoted as AU1) is the lowest energy structure on the potential energy surface both in the gas phase and in a water solution. Only a slight deviation from planarity is observed for these complexes in both phases. Furthermore, the relative stability order of the considered WC AU hydrogen bonded complexes remains unchanged upon interaction with the water cluster although the zwitterionic form (denoted as AU3) is stabilized more compared to a rare tautomer (denoted as AU2). Some similarities and differences between the title species and the isocytosine−cytosine complexes in both phases are also discussed.

I. Introduction

The specific solvation effects are known to be vital in DNA base pair interactions. The water molecules in the first coordination sphere represent an inherent part of the DNA structure, and they are known to be very flexible. Since the stabilization of the two DNA strands proceeds through the formation of a number of hydrogen bonds, the study of this phenomenon augmented by investigations of the specific solvation effects has greatly attracted the attention of both theoreticians and experimentalists in order to understand base pairing at a chemical level.[1−5]

For most of DNA base pairs called after the standard or Watson−Crick base pairs, guanine is paired with cytosine through three relatively parallel H-bonds while adenine is complexed with thymine only through two H-bonds. In ribonucleic acid (RNA), thymine is replaced by uracil which is significantly smaller in size due to the replacement of thymine's methyl group by a hydrogen atom. The mutual recognition of adenine by thymine and of cytosine by guanine uses these hydrogen bonds to establish the fidelity of DNA transcription and translation. In addition to these standard base pairs, there are many other possible H-bonded base pairs which are based on their rare tautomeric forms. Note that there is also the possibility of formation of the Hoogsteen base pair in the case of adenine and thymine or adenine and uracil bases (for the nomenclature, see ref 5). The tautomeric equilibria and molecular properties of adenine and uracil and their derivatives in the gas phase and in a polar solution have been discussed in several papers from both experimental and theoretical points of view.[4−17] Schoone et al. studied the relative stabilities of the 1-methyladenine tautomers at the HF/6-31++G level and combined these investigations with matrix-isolation FT-IR spectroscopy.[6] Burda et al. reported the results of calculations performed at the HF and MP2 levels of theory on the standard N7 coordination of adenine and guanine with various mono- and divalent metal cations.[7] They have shown that the metal−N7 distances for metal−adenine complexes are shorter than those in metal−guanine complexes, because for the latter, the metal cation prefer a ringlike structure with both the N7 and the more attractive next-neighbor O6 site of guanine. As a consequence, the metal−O6 distances are mostly shorter than the corresponding metal−N7 distances for the studied guanine−metal complexes.[7] Broo et al. performed several INDO/S-CIS calculations of the solvent effect on the absorption spectrum of uracil and its dimethyl derivative.[8] It was shown that the absorption spectrum in a vacuum agrees very well with the spectrum previously published by Baraldi et al.[9] The predicted lowest state has n→p* character and is located between 33000 and 36000 cm^{-1}.

Previously, Rush and Peticolas reported the ground and excited-state properties of uracil, 1-methyluracil, 5-methyluracil, and their 1,3-dideuterated derivatives obtained at the HF/6-31G* and CIS/6-31G* levels,[10] and more recently, the vibrational frequencies, normal modes, and ground-state geometries of uracil and thymine were evaluated by Person and Szczepaniak at the HF/6-31G* level.[11] Nowak et al. reported the results of combined FTIR and DFT studies on two amino tautomers of adenine.[12] They predict that the only the amino N9H tautomer of adenine can be observed for the compound isolated in low-temperature matrixes which is in line with many other supporting arguments.[13] However, in solutions, adenine exists in mixtures of N7H and N9H tautomers.[14] Šponer et al. have studied a several DNA base pairs including adenine's derivatives at the HF, DFT, and correlated MP2 levels of theory.[15] They showed that the Hoogsteen orientation of the adenine−thymine

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base pair is ca. 1 kcal/mol more stable than the Watson−Crick orientation although the total stabilization energies for the standard and that the reverse base pairs of adenine−thymine have been found to be approximately the same within the Watson−Crick or the Hoogsteen orientations. Interestingly, the relatively high stability of the Hoogsteen base pair as compared to that of the Watson−Crick was recently predicted by Gould and Kollman[16] who have also studied both the standard Watson−Crick and Hoogsteen base pairs of 9-methyladenine-1-methylthymine at the HF/6-31G* level. It was concluded that the DFT method with the applied functionals is not suitable to consistently study the whole range of the DNA base interactions although its accuracy in reproducing the interaction energies at the reference HF/6-31G** geometries is very good.[15] Previously, Florian et al. studied at the HF level with a small MINI-1 basis set the transition state for the double proton transfer in the Watson−Crick adenine−thymine base pair in the gas phase.[17] They found that the canonical AT base pair is separated by an energy barrier of 9.7 kcal/mol from the rare tautomer and that there was no minima for the corresponding zwitterionic structures A^+T^- and $A\ ^-T^+$. The isolated canonical forms of adenine and thymine exhibit sufficient energetic stability after solvation in a polar environment.[4]

The present study concentrates on the interactions of the adenine molecule with uracil in the gas phase and in a water solution. The latter was modeled by explicit inclusion of seven water molecules creating the first coordination sphere around the AU base pair. Such a methodology as the “supermolecular approach” is very expensive computationally although these specific solvation effects cannot be described within other computational techniques as a Monte Carlo or molecular dynamics simulations and by modern implementations of the continuum models.[18−23] It allows for an account of the most important part of AU−solvent intereraction although the calculated structures could be different from those present in an aqueous solution or in RNA. However, this very interesting subject is beyond the scope of this study, and the reader can refer to several reviews in ref 24 and the original papers.

The paper is organized as follows. Section II outlines the computational details. Section III.1 presents the geometric structures and relative energies for the studied AU complexes in the gas phase and in a water solution. In contrast to ref 17, we found a local minimum for the zwitterionic adenine−uracil complex in both phases. In section III.2, the basic features of the interaction and solvation energies are considered. Finally, section IV outlines the summary and conclusions.

II. Method

The ab initio molecular orbital calculations were performed using the Gaussian 92 and Gaussian 94 set of program packages.[25] Full geometry optimizations of the three different hydrogen-bonded Watson−Crick AU complexes in the gas phase and in a water solution were carried out at the HF level of theory using the standard split-valence 6-31G* basis set. The water environment which creates the first coordination sphere around the AU base pair was modeled by explicit inclusion of seven water molecules attached to the polar exocyclic groups of the adenine−uracil complex. The interaction energies for the different AU complexes were corrected for the basis set superposition error (BSSE) by using the full Boys−Bernardi counterpoise correction scheme.[26,27] The effects of electron correlation were accounted for by using the second-order Møller−Plesset perturbation theory with the frozen-core approximation using the previously optimized HF level reference geometries.

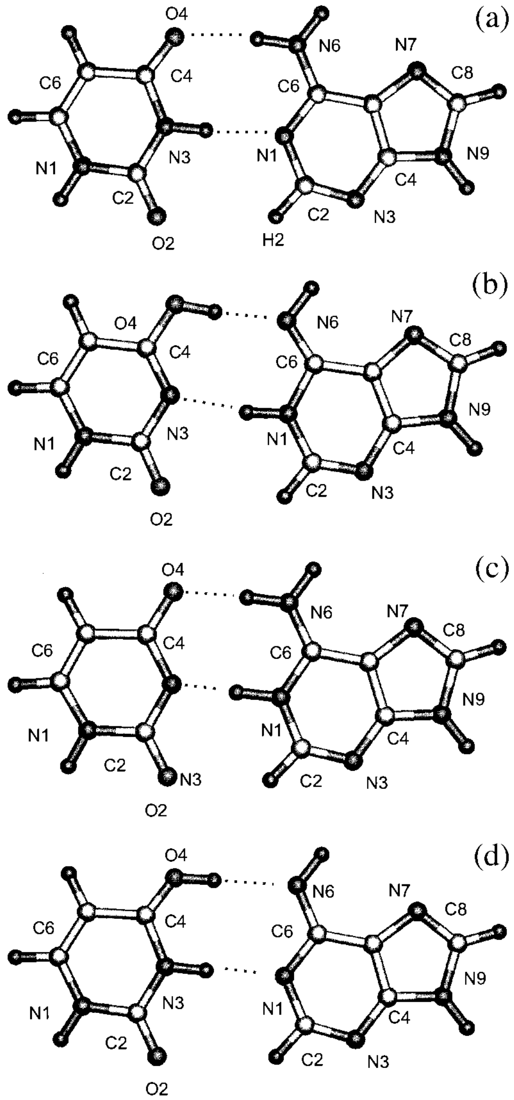

Figure 1. A sketch of some adenine-uracil complexes in the gas phase: (a) AU1 structure, (b) AU2 structure, (c) AU3 structure, and (d) AU4 structure. Numbered atoms correspond to distinct atomic sites.

III. Results and Discussion

III.1. Geometries and Relative Energies. Four different Watson−Crick complexes of AU were considered in this study. These structures are shown in Figure 1 where the numbering of the atoms is also defined. The first complex denoted as AU1 corresponds to the canonical Watson−Crick adenine−uracil base pair. The adenine molecule acts there as both a proton donor to and a proton acceptor from the uracil molecule (Figure 1a). Because there are two parallel hydrogen bonds, there is only one way in which protons can be rearranged by a double proton transfer while keeping each monomer in its neutral form. The minor tautomer of the base pair formed in this way is denoted as AU2 (Figure 1b). The other complexes studied correspond to a single proton transfer from uracil to adenine or from adenine to uracil via forming the zwitterionic tautomers denoted as AU3 and AU4 (Figure 1c and d). However, our attempts to localize the AU4 structure on the potential energy surface (PES) were unsuccessful: the full optimization of the gas-phase geometry of the AU4 complex led to the formation of a more stable AU1 complex. Probably, this is due to the fact that the proton affinity (PA) of the N1 site and the proton donor ability (PDA) of the N6 site of adenine are much higher than those of the O4 site and the N3 site of uracil. Indeed, our HF/6-31G* calculations

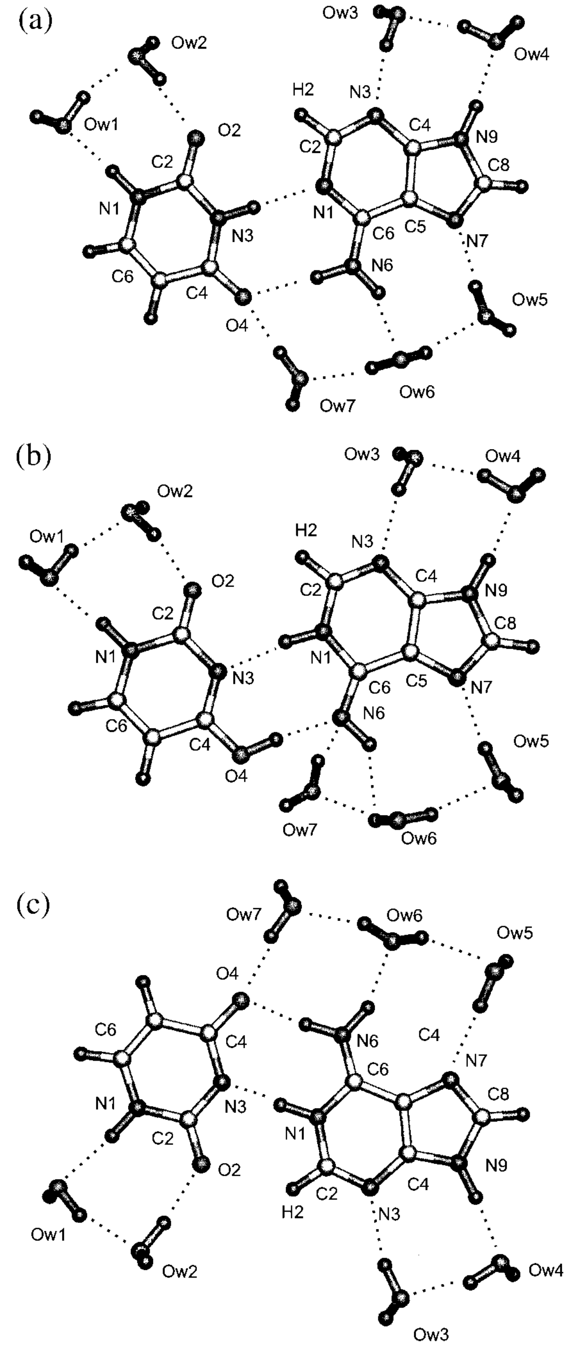

Figure 2. The considered adenine-uracil complexes with seven water molecules: (a) AU1·7H_2O, (b) AU2·7H_2O, and (c) AU3·7H_2O. Numbered atoms correspond to distinct atomic sites.

show that the PA of the adenine's N1 site amounts to 10.31 eV which is 1.13 eV higher than that of uracil's O4 site while the PDA of the N3 site of uracil is by 0.42 eV lower than that of the N6 site of adenine. An analogous result was obtained by us before during the study of the corresponding complexes of guanine−cytosine[28] and isocytosine-cytosine,[29a] and it was ascribed to the repulsive dipole−dipole interactions between the monomers forming the GC5 and iCC5 base pairs. Consequently, the interactions with a water environment were studied only for the AU1, AU2, and AU3 base pair complexes (Figure 2).

TABLE 1: Geometry of the Isolated Adenine−Uracil Base Pairs (AU1, AU2,AU3) and Their Complexes with Seven Water Molecules[a]

bond/angle[b]	AU1	AU2	AU3
N6−O4	3.080 (3.013)	2.784 (2.785)	2.830 (2.871)
N6−H_a	1.000 (0.998)	1.800 (1.806)	1.021 (1.015)
O4−H_a	2.085 (2.123)	0.985 (0.984)	1.809 (1.859)
N6−H_a−O4	172.9 (166.9)	176.4 (172.9)	177.4 (174.6)
C6−N6−H_a	120.7 (118.8)	129.3 (128.7)	122.3 (120.9)
C4−O4−H_a	126.4 (123.8)	112.6 (112.4)	117.6 (114.7)
N1−N3	3.001 (3.020)	2.947 (2.944)	2.669 (2.734)
N1−H_b	1.987 (2.007)	1.010 (1.010)	1.070 (1.048)
N3−H_b	1.014 (1.014)	1.948 (1.942)	1.599 (1.687)
N1−H_b−N3	178.4 (175.9)	169.5 (170.9)	178.8 (176.2)
O2−H2	2.992 (2.956)	3.083 (3.023)	2.512 (2.545)
H−N6−H_a−C6	179.8 (−173.9)	179.8 (169.6)	179.9 (−177.9)
C8−N1−N3	164.6 (160.8)	154.5 (155.7)	161.0 (159.5)
C8−N1−C6	164.3 (160.0)	156.9 (158.0)	163.8 (162.7)
C6−N3−N1	179.3 (176.2)	175.1 (175.1)	174.4 (172.9)
C6−C8−N1	8.9 (11.3)	13.1 (12.4)	9.0 (9.6)
N1−C6−C8	6.8 (8.7)	10.0 (9.5)	7.2 (7.7)

[a] (Bond length, A−B, in angstroms; bond angle, A−B−C, and dihedral angle, A−B−C-D, in degrees.) Two numbers in each column correspond to the isolated AU base pairs and their complexes with seven water molecules, respectively. [b] For the atom numbering, see Figures 1 and 2.

The optimized bond distances, bond angles, and the major dihedral angles of the studied complexes collected in Tables 1 and 2. Tables 3 and 4 show the energetic characteristics of these complexes obtained at the HF/6-31G*//HF/6-31G* and MP2/6-31G*// HF/6-31G* levels of theory. At both applied levels, the canonical Watson−Crick AU1 base pair is found to be the lowest energy structure for the PES of the isolated and interacting water pairs. This result is in line with the previous study[17] which was based on the small MINI-1 basis set calculations. Since both the canonical AT and the rare A*T* structures have very small dipole moments, it was expected that the effect of the polar environment would not influence the energy differences between these forms.[17a]

As is mentioned in the Introduction, the standard Hoogsteen adenine−thymine base pair (denoted as H AT) is found to be the most stable one as compared to the WC AT base pair.[15,16] The standard Hoogsteen adenine−uracil base pair (denoted as H AU1) can be stabilized through the formation of two relatively parallel H-bonds: one involves the amino group and the N7 site of adenine while the second involves the O4 site and N3−H group of uracil. There are also tautomeric structures within the Hoogsteen orientation caused by the double or single proton transfer. Indeed, we found that the H AU1 structure isolated and solvated by seven waters is the global minimum for PES within the applied HF/6-31G* level of theory. It lies 0.57 and 0.85 kcal/mol lower in energy than the canonical WC AU1 base pair in the gas phase and in a water solution, respectively. However, only the double proton transfer process leads to a higher lying local minimum (it is 37.4 kcal/mol higher in energy as compared to the isolated AU1 base pair) while the single proton transfer does not take place within the Hoogsteen orientation. Since the Hoogsteen orientation is not common in DNA interactions, we will especially consider only the isolated and the solvated WC AU complexes in this paper.

The standard AU1 complex is stabilized via formation of two relatively parallel H-bonds. For the isolated complex the N1−N3 bond distance is shorter than that of N6−O4 indicating a relatively stronger proton acceptor ability for the N1 site of the adenine molecule than the O4 site of the uracil molecule (Figure 1a). However, this finding is changed when one considers the interaction of the AU1 complex with seven water molecules (Figure 2a) where the N6−O4 bond distance becomes shorter than that of N1−N3 due to the more preferable orientation of these water molecules around the AU1 complex (Table 2). Three

TABLE 2: The First Coordination Sphere Geometry of the Adenine−Uracil Base Pairs (AU1, AU2, AU3) in a Water Solution[a]

property	AU1	AU2	AU3	property	AU1	AU2	AU3
$N1-O_{w1}$	2.897	2.908	2.971	$N7-O_{w5}$	3.037	3.007	3.106
$N1-H-O_{w1}$	177.4	176.0	176.5	$N7-H-O_{w5}$	177.4	175.3	178.5
$O2-O_{w2}$	2.884	2.852	2.806	$N6-O_{w6}$	2.920	3.113	2.834
$O2-H-O_{w2}$	164.5	167.3	170.9	$N6-H-O_{w6}$	153.8	151.1	156.7
$O_{w1}-O_{w2}$	2.794	2.792	2.806	$O_{w5}-O_{w6}$	2.880	2.900	2.883
$O_{w1}-H-O_{w2}$	158.4	158.3	159.6	$O_{w5}-H-O_{w6}$	148.1	152.1	139.7
$N3-O_{w3}$	2.956	2.992	3.034	$O4-O_{w7}$	2.989		2.859
$N3-H-O_{w3}$	166.9	166.9	164.3	$O4-H-O_{w7}$	166.6		165.1
$N9-O_{w4}$	2.905	2.897	2.868	$O_{w7}-O_{w6}$	2.948	2.978	2.896
$N9-H-O_{w4}$	171.9	173.4	173.9	$O_{w7}-H-O_{w6}$	154.8	147.3	159.6
$O_{w3}-O_{w4}$	2.806	2.807	2.798	$N6-O_{w7}$		3.189	
$O_{w3}-H-O_{w4}$	161.9	160.9	159.8	$N6-H-O_{w7}$		146.5	

[a] (Bond length, A−B, in angstroms; bond angle, A−B−C, in degrees). For the atom numbering, see Figure 2.

TABLE 3: Total (E_t, au), Relative (E_{rel}, kcal/Mol), Interaction (E_{Int}, kcal/Mol) and Solvation (E_{solv}, kcal/mol) Energies Calculated at the HF/6-31G*//HF/6-31G* Level of Theory for the Studied Forms of the Adenine−Uracil Base Pair (AU1, AU2, AU3) in the Gas Phase and in a Water Solution Modeled by Explicit Inclusion of Seven Water Molecules

property	phase state	AU1	AU2	AU3
E_t	gas phase	−877.009 65	−876.978 41	−876.983 81
$E_{rel}{}^a$		0.0	19.6	16.2
$-E_{int}$		10.2	22.1	128.4
E_t	with seven waters	−1409.191 88	−1409.160 21	−1409.177 59
$E_{rel}{}^b$		0.0	23.8	12.9
$-E_{int}$		10.0	21.7	126.8
$-E_{solv}$		45.8	41.0	49.3

[a] Total energy of the isolated AU1 base pair is taken as an internal reference. [b] Total energy of the AU1·7H_2O complex is taken as an internal reference.

TABLE 4. Total (E_t, au), Relative (E_{rel}, kcal/mol), Interaction (E_{int}, kcal/mol) and Solvation (E_{solv}, kcal/mol) Energies Calculated at the MP2/6-31G*//HF/6-31G* Level of Theory for the Studied Forms of the Adenine−Uracil Base Pair (AU1, AU2, AU3) in the Gas Phase and in a Water Solution Modeled by Explicit Inclusion of Seven Water Molecules

property	phase state	AU1	AU2	AU3
E_t	gas phase	−879.596 07	−879.570 22	−879.577 60
$E_{rel}{}^a$		0.0	16.2	11.6
$-E_{int}$		12.3	23.4	131.6
E_t	with seven waters	−1413.119 16	−1413.087 31	−1413.105 95
$E_{rel}{}^b$		0.0	20.0	8.3
$-E_{int}$		12.1	23.0	129.4
$-E_{solv}$		52.0	47.4	56.1

[a] Total energy of the isolated AU1 base pair is taken as an internal reference. [b] Total energy of the AU1·7H_2O complex is taken as an internal reference.

waters formed a whole cyclic structure on the major groove while the remaining four waters formed two eight-membered, ringlike structures on the minor groove in this AU1·7H_2O complex. The most important change in geometry is a further slight deviation from linearity for these H-bonds in a water environment compared to the isolated complex. At the HF/6-31G* level, the amino group of the adenine fragment of isolated AU1 is perfectly planar (for the dihedral H−N6−H_a−C6 angle, see Table 1). However, the solvation of this complex with seven water molecules leads to its significant pyramidalization. The whole AU1·7H_2O complex is slightly nonplanar and adopts a buckling and propeller twist structure (cf. the C6−C8−N1 and N1−C6−C8 angles where the C6 and the C8 atoms relate to the long base pair axis. These angles increase by ca. 2−3° in the solvated AU1 complex compared to the isolated one). These findings are in line with the previous study on the isocytosine−cytosine (iCC) complexes[29] which shows that the water molecules in the first coordination sphere play an important role in determining the base pair structure.

Let us now discuss the complex AU2 which is stabilized by means of forming two H-bonds through double proton transfer and by keeping the adenine and uracil monomers in their neutral forms. Such a phenomenon involves proton transfer of adenine's amino group to the O4 site of uracil and the N3−H group proton of uracil to the N1 site of adenine (Figure 1b). The AU2 complex is ca. 20 (24) kcal/mol less stable than the canonical AU1 form in the gas phase (water solution) at the HF/6-31G*//HF/6-31G* level of theory. However, at the correlated MP2/6-31G*//HF/6-31G* level these differences decrease by ca. 4 kcal/mol for both isolated and solvated complexes (see relative energies, Table 4). Such a large energy difference between the canonical and the neutral rare tautomer of the AU base pair might be of some importance in Lowdin's mutation hypothesis.[17] Interestingly, the results obtained at the correlated level are close to the estimations made in ref 17 after taking into account some shortcomings of the small MINI-1 basis set calculations (they estimate that the true energy difference between the canonical and the rare tautomer of adenine−thymine is in the 15−19 kcal/mol range).[17]

The N6−O4 bond distance for the gas phase is the shortest one in this AU2 structure (in contrast to AU1) indicating a strong proton acceptor ability for the N6 site on the precursor amino group of adenine as compared to the N3 site of uracil (Figure 1b). Moreover it becomes substantially shorter and stronger in the AU2 structure compared to that of the isolated AU1 base pair, and the relative order of the H-bond distances remain virtually unchanged when one considers the water environment (Table 1, Figures 1b and 2b). In addition, the isolated and solvated AU2 complex further slightly deviate from planarity and also assumes a propeller twist and buckle structure (see the C6−C8−N1 and the N1−C6−C8 angles, Table 1 and Figures 1b and 2b).

In fact, as we will see later, the AU2 complex is also the less favorable complex energetically among the considered complexes both in the gas phase and in a water environment (Tables 3 and 4). We shall note that the N6 atom of the precursor amino group of the adenine fragment prefer to form additional H-bonds with the O_{w6} and the O_{w7} containing waters (the subscript w stands for a water molecule) in the case of the AU2·7H_2O complex (Figure 2b) although we started the calculations with the use of a trial geometry in which the O_{w6} and O_{w7} containing water molecules were initially attached to the N6−H group of adenine and the O4 site of the uracil fragments (Table 2). However, full geometry optimization of this AU2·7H_2O complex leads to the formation of an H-bonded structure in which adenine's N6 atom is formally four-coordinated (Figure 2b) and there is no attractive interaction between the water molecule containing the O_{w7} atom and the O4 site of the uracil fragment.

Finally, we considered the zwitterionic AU3 complex which has also two H-bonds and corresponds to a single proton transfer from uracil to adenine (Figure 1c). It is only 16.2 (11.6) kcal/mol higher in energy than the canonical AU1 base pair in the gas phase at the HF/6-31G* (MP2/6-31G*//HF/6-31G*) levels of theory (Tables 3 and 4). However, as can be expected, [30−32] due to the ion−dipole interactions, a zwitterionic structure is much more stabilized in a water environment than the neutral base pairs. Consequently, the AU3 complex should be more stable in a water environment than the neutral rare AU2 form. Indeed, we found that the AU3 zwitterionic structure lies closer to the canonical AU1 Watson−Crick base pair in a water solution by 12.9 and 8.3 kcal/mol relative to the AU1 complex at the HF and MP2 levels of theory.

The existence of this isolated and solvated AU3 complex has been revealed for the first time by our calculations since the previous ab initio searches for the zwitterionic A^+T^- and A^-T^+ structures were unsuccessful perhaps due to the use of the small MINI-1 basis set.[17] Although we shall note that the results of earlier semiempirical studies are in line with our findings of a double well potential for the transfer of a single proton in the AT base pair,[33,34] a similar conclusion was derived by us for the isolated iCC base pairs and their complexes with four and six water molecules.[29] It was shown that the explicit inclusion of six waters, which creates the first coordination sphere around the iCC base pair, changes the relative stability order of the iCC·6H_2O complexes and that the zwitterionic iCC4 form becomes the second most stable species following the canonical Watson−Crick iCC1 base pair.[29a] As for the geometric parameters of this AU3 complex, the N1−N3 bond is shorter than the N6−O4 one, and the configuration of the amino group of the adenine fragment is only slightly more pyramidalized in a water environment compared to the gas phase (Table 1).

To further shed light on the existence of the isolated and solvated WC AU3 structure, additional calculations have also been performed. First, the above optimized WC AU3 structure in the gas phase and with seven waters at the HF/6-31G* level of theory was taken as a trial starting geometry for its further geometry optimization at the lower HF/MINI-1 level. In agreement with the previous study,[17] this led to the more stable AU1 complex for the isolated AU3 base pair: no single proton transfer from uracil to adenine was found at the minimal, unreliable basis set. For the solvated AU3·7H_2O complex, the optimized geometry at the HF/MINI-1 level only slightly resembles the middle part of two bases' interaction obtained at the higher HF/6-31G* level because the geometrical characteristics for the former are quite far from those of the latter. For example, the proton does not fully transfer from the N3−H group of uracil to the N1 site of adenine; instead, it forms strong H-bonds in the middle (N3−H, N1−H, and N3−N1 bond distances are equal to 1.366, 1.250, and 2.611, respectively; compare these values with those obtained at the HF/6-31G* level, Table 1). Furthermore, such a solvated AU3 complex at the HF/MINI-1 level is accompanied also by drastic changes in its other parts. For example, a complex proton transfer from the N1−H group of uracil to its O2 site through the Ow1 and Ow2 containing waters takes place while the amino and N9−H groups' protons were transferred to the Ow6 and the Ow4 containing waters, respectively. In that case, the latter can be also viewed as a formation of two hydroxonium ions due to solvation. Second, we have also optimized the AU3 structure at the relatively larger valence triple-ζ plus polarization quality 6-311G(d,p) basis set. The latter basis set has higher flexibility in the valence region as compared to the 6-31G* basis due to the use of larger number of functions to represent each valence atomic orbital. These calculations fully support the properties obtained for the AU3 structure both in the gas phase and with seven waters at the HF/6-31G* level. On the basis of these results, we can conclude that the MINI-1 basis is indeed unreliable for such studies.

Interestingly, the geometries of the isolated AU1 base pair listed in Table 1 virtually coincide with those of the isolated 9-methyladenine-1-methylthymine predicted at the same HF/6-31G* level of theory (see Table 12 in ref 16). Such relatively small differences cannot cause large variations in the geometry and properties of the respective AU and AT base pairs. Indeed, the isolated AU and AT[17] base pairs have relatively the same stability order (Tables 3 and 4). This might yield some important insights into the analoguous AT complexes in water. Moreover the isolated AU base pair's H-bond distances are very close to the experimental values reported by Saenger for the Watson−Crick AT base pair,[1] although one should take the crystal packing effects into mind when comparing them since the experimental data are based on X-ray crystallographic studies.[1]

III.2. Interaction and Solvation Energies. The HF/6-31G* and the single point MP2/6-31G*//HF/6-31G* calculations show that the BSSE corrected interaction energies calculated as the energy difference between the complex and the sum of the isolated monomers for the zwitterionic AU3, and the rare AU2 forms are the relatively highest among the structures considered in both the gas phase and in a water environment (Tables 3 and 4). We shall note that we applied the standard Boys−Bernardi counterpoise correction scheme[26] with the additional corrections for the BSSE which take into account also the geometry reorganization when going from isolated subsystems to the complex as is proposed in the references.[27,29] The highest interaction energy value for the AU3 complex is not surprising because it corresponds mainly to ion−ion electrostatic interactions. However, note that molecular recognition processes are driven by energy changes and not by the interaction energy.[3]

Interaction energy for the isolated AU1 base pair is calculated to be 10.2 kcal/mol at the HF/6-31G*//HF/6-31G* level of theory and differs only slightly from the analogous one for the Watson−Crick AT base pair (its value amounts 10.3 and 9.7 kcal/mol at the HF/6-31G** and the HF/6-31G*(0.25) levels of theory).[15] The water environment has very few effects on its interaction energy both at the HF and MP2 levels of theory (it decreases ca. 0.2 kcal/mol), although the H-bond energy become relatively stronger at the correlated level as compared to the HF one as is well-known (it increases by ca. 2.1 kcal/mol, see Tables 3 and 4). We shall note that the interaction energy of the isolated and solvated iCC base pair[29] are at least twice as large as the AU base pair in the gas phase and in a water environment. This is a well-known phenomenon caused by higher dipole moments of the former complexes as compared to the latter ones.[15−17,28,29]

The interaction energies for the rare AU2 complex in the gas phase and in a water environment are approximately two times higher than those of AU1. Such a difference can be considered to be a result of the strengthening of the hydrogen bonds by a double proton transfer (cf. the N6−O4 and N1−N3 bond distances for the AU1 and AU2 complexes, Table 1).

The BSSE corrected solvation energies are also calculated as the energy differences between the complex with water molecules and the sum of the isolated complex and water molecules in the same way as the interaction energies described above. The zwitterionic AU3 and canonical AU1 base pairs have the relatively highest solvation energies among the considered structures both at the Hartree−Fock and correlated levels of theory (Tables 3 and 4). This is in line with the fact that a polar environment further stabilizes the standard canonical Watson−Crick base pair and the zwitterionic structures.[31,32,35]

IV. Summary and Conclusions

Ab initio quantum chemical studies at the HF/6-31G*//HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory have been performed for three different hydrogen bonded WC AU complexes in the gas phase and in a water solution. The water solution was modeled by explicit inclusion of seven water molecules which creates a first coordination sphere around the AU base pair. It was shown that the standard Watson−Crick AU1 base pair is the lowest energy structure on the PES both in the gas phase and in a water solution. The relative stability order of the AU complexes does not change when going from the isolated to the solvated structures where the zwitterionic form AU3$\cdot$7H_2O lies closer in energy to the Watson−Crick AU1$\cdot$7H_2O complex. This relative stability order is in line with those of the analogous iCC complexes in a water environment although its order is opposite to that of the isolated iCC complexes.[29]

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