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Specific Solvation Effects on the Structures and Properties of Neutral and One-Electron Oxidized Formamidine−Formamide Complexes. A Theoretical ab Initio Study

Nurbosyn U. Zhanpeisov[†,‡] and Jerzy Leszczynski*[,†]

Computational Center for Molecular Structure and Interactions, Department of Chemistry,
Jackson State University, Jackson, Mississippi 39217, and Boreskov Institute of Catalysis,
Novosibirsk 630090, Russia

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Ab initio quantum chemical calculations were performed for the neutral and one-electron oxidized formamidine−formamide model systems in the gas phase and in a water solution. Full geometry optimizations without any constraints on the planarity of these complexes were carried out at the HF/6-31G* level. For the neutral dimers, the solvent effects were modeled by explicit inclusion of four, six, and nine water molecules, which creates the first, intermediate, and second hydration spheres around these dimers. For one-electron oxidized systems, we have accounted for the effects of the first hydration shell water molecules. Single point calculations were also performed at the correlated MP2/6-31G*//HF/6-31G* level. The interaction and solvation energies were corrected for the basis set superposition error. It was shown that the relative stability of the neutral model formamidine−formamide complexes is quite opposite to that of the analogous adenine−uracil base pairs (*J. Phys. Chem. A* **1998**, *102*, 6167): the double proton transferred FF2 dimer becomes more stable than the zwitterionic FF3 dimer. An increase in the number of water molecules from the first to the second hydration shell results in an overestimated stability for the FF3 zwitterionic structure. For a one-electron oxidation process, the $FF3^{(+)}$ cation−radical dimer is the most stable dimer while the double-proton-transfer process becomes the least favorable process in both the gas phase and in a water solution.

I. Introduction

Theoretical studies of the primary radiation process in DNA are very important for understanding the phenomena of DNA damage at a molecular level. One-electron oxidation in DNA caused by ionizing radiation, oxidizing chemical agents, and photoirradiation by means of endogenous photosensitizers have recently received both theoreticians' and experimentalists' considerable attention.[1−5] Previous studies show that the site of electron trapping in a DNA model system is thymine in single-stranded DNA and the cytosine base in double-stranded DNA, while the hole localizes on guanine in both forms.[2,3] Furthermore, the distribution of the cation radical formed as a result of such one-electron oxidation is initially a function of the ionization potential of the bases. Subsequent proton-transfer reactions between base pairs can alter the relative stabilities of the radical sites. Since the pyrimidines (thymine and cytosine) have greater electron affinity than the purines (adenine and guanine), proton transfer from the guanine to the cytosine anion−radical gradually shifts the electron to cytosine, which accounts for the dominance of the cytosine anion in the DNA spectrum.[3] Base pairing is not found to significantly affect the ionization potential of adenine or thymine in the AT base pair. However base pairing lowers guanine's ionization potential by 0.54 eV while raising cytosine's ionization potential by 0.58 eV. [3]

The formamidine and formamide molecules might be considered as very simple models of DNA bases, owing to the similarity of their functional groups to the DNA bases. Previously these models have been the subject of a large number of ab initio investigations, i.e., their complexes with one or several water molecules and their homogeneous and heterogeneous dimers.[6−11] The latter formamidine−formamide dimer is an interesting small model system to mimic the adenine−thymine base pair owing to a similar H-bonding pattern: both of them are stabilized by means of two relatively parallel H-bonds.[11,12] It is also a good model to investigate one-electron oxidized processes since the formamidine−formamide complex is smaller than the biologically important adenine−thymine base pair. Since the formamidine−formamide dimer is much smaller in size than the adenine−thymine base pair, there are a few questions concerning the reliability of using the former model system on the large scale in the theoretical investigations. Thus, for example, can one account for the similar specific solvation effects of these two distinct systems' structural and energetical properties? How reliable are the molecular properties calculated for the two isolated systems in the gas phase? To answer these questions, there is still the need for direct theoretical investigations.

In a recent series of papers an ab initio quantum chemical method at the Hartree−Fock (HF) and the correlated MP2 levels of theory with the 6-31G(d) basis set has been applied to studies of the specific solvation effects of DNA base pair interactions.[12−15] Especially it was shown that inclusion of six instead of one, two, or four water molecules has a crucial effect on the geometry of the standard Watson−Crick (WC) isocytosine−cytosine (iCC1) base pair. In the case of six water molecules, the WC iCC1 moiety becomes strongly nonplanar while in the case of fewer hydration shell water molecules, it deviates only slightly from the planar conformation adopted in the gas phase.[13] Similar results are also obtained for four different hydrogen-bonded WC iCC complexes involving six water molecules.[14] Moreover, the

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[†] Jackson State University.

[‡] Boreskov Institute of Catalysis.

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relative stability order of these and also of the three different WC adenine−uracil (WC AU) complexes changes when one considers the full first hydration shell water molecules, and in both cases the zwitterionic forms become the second most stable species.[12,14]

The present study focuses on the interactions of formamidine with formamide in the gas phase and in a water solution. Especially, we will compare the structures and properties of the main dimer and all the possible complexes formed through the double and single proton transfer reactions. In addition, we will account for the specific solvation effects on the molecular properties in question. It is achieved by an increase in the number of solvation water molecules from four (the first hydration shell) through six (the intermediate case) to nine (the first and second hydration shells). Furthermore, the structural and energetical characteristics of this neutral model system will be directly compared with the larger analogous adenine−uracil (AU) base pairs calculated previously at the same level of theory. We expect that such a direct comparison of the molecular properties of the model systems and AU base pairs will reveal the feasibility of using relatively small formamidine−formamide dimers to mimic the H-bonding pattern in AU base pairs. Finally we will consider the possibility for the formation of different dimer complexes arising from a one-electron oxidation process in this model system. We believe that these results obtained for such a model system can be useful for further systematic studies of DNA base pairs.

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 neutral model system and AU complexes in the gas phase and in a water solution. In section III.2 the basic features of the interaction and solvation energies are considered. Section III.3 presents the molecular properties for the one-electron oxidized formamidine−formamide dimer in the gas phase and in a water solution modeled explicitly by four water molecules. Finally, section IV outlines the summary and conclusions.

II. Method

The ab initio molecular orbital calculations were performed using the Gaussian92 and Gaussian94 program packages.[16] Full geometry optimizations of all possible neutral and one-electron oxidized formamidine−formamide model systems in the gas phase and in a water cluster were carried out at the HF and spin-restricted open-shell HF (ROHF) levels of theory respectively using the standard split-valence 6-31G* basis set. The ROHF theory has been applied throughout this work for radical−cation dimers since the UHF calculations show large spin contaminations.[17] The water environment for neutral and one-electron oxidized model systems was modeled by explicit inclusion of a different number of water molecules attached to the polar exocyclic and NH groups of these complexes. We have modeled the solvent effects using a water cluster rather than attempting to use a continuous solvent treatment for reasons described elsewhere.[15,18,19]

The stability order of the model dimers are based on an evaluation of the total electronic energies. Furthermore, for the different complexes we evaluated the interaction and hydration energies which were corrected for the basis set superposition error (BSSE) by using the full Boys−Bernardi counterpoise correction scheme.[20] The effects of electron correlation were accounted for by using the second-order Moller−Plesset (MP2) perturbation theory with frozen-core approximations and with single-point calculations.

III. Results and Discussion

III.1. Geometries and Relative Energies for Neutral Systems. The structures of the neutral formamidine−formamide model systems considered in the present study are shown in Figures 1−4, where the numbering of the specific atoms is also defined. All of these structures are stabilized by means of two relatively parallel H-bonds. Since there is a close similarity in the H-bonding pattern between the model formamidine−formamide model system and the Watson−Crick AU base pair, the same terminology will be used to describe both systems.[12] In the first dimer, the formamidine molecule acts as both a single proton donor to and proton acceptor from the formamide molecule (Figure 1a). This dimer complex is denoted as FF1 by analogy to the canonical Watson−Crick adenine−uracil AU1 base pair.[12] As in the case of the AU base pair, there is only one way in which protons can be rearranged by a double-proton transfer while each monomer is kept in its neutral form. The minor tautomer of the model complex formed in this way is denoted as FF2 (Figure 1b). The last two model complexes considered correspond to a single proton-transfer from formamide to formamidine or from formamidine to formamide via formation of the so-called zwitterionic tautomers denoted as FF3 and FF4. As in the case of an analogues AU4 structure, we were unable to localize the FF4 complex on the potential energy surface (PES), since full optimization of the gas-phase geometry of the FF4 complex led to the formation of a more stable FF1 complex, because of the reasons described elsewhere.[12,14,21] Consequently, the interactions with a water environment were studied only for these three formamidine−formamide model systems.

The optimized bond distances, bond angles, and the major dihedral angles of the studied complexes are collected in Tables 1−3. Tables 4 and 5 show the energetic characteristics of these complexes obtained at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory. A comparison of the structural parameters in these H-bonded systems with an analogous AU base pair in the gas phase shows fairly good agreement between the isolated model systems and the AU base pairs. Thus, the largest discrepancy in the H-bond length amounts to 0.17 Å between the FF3 and AU3 structures. The most important difference in geometry is that the N6−O4 bond distance is decreased (strengthened) by ca. 0.18 Å when going from the FF2 complex to the FF3 structure, while it is increased (weakened) by ca. 0.05 Å when going from the AU2 complex to the AU3 structure. In addition, the N1−N3 bond distance is decreased for both pairs when going from the double-proton transferred complexes to the zwitterionic structures. As a result, the relative stability of these isolated minor tautomers involving the formamidine−formamide dimers is reversed as compared to the AU base pairs. However, there is an interesting irregularity in the relative stability of these model complexes and the AU base pairs: one can expect that FF3 should be more stable than the FF2 structure due to the significantly shorter H-bond distances in the FF3 complex. In fact, it is quite the opposite, and the FF3 structure is ca. 10 (5) kcal/mol less stable than the FF2 structure in the gas phase at the HF/6-31G* (MP2/6-31G*//HF/6-31G*) levels of theory (see Tables 4 and 5). In the case of AU complexes, the larger stability of the isolated zwitterionic AU3 structure over the AU2 complex can be explained by the shortening (ca. 0.28 Å) of the middle N1−N3 bond distance when going from the AU2 to the AU3 base pair. The reason for the lower stability of the FF3 complex over the FF2 structure may be attributed to the notion that the charge separation is hardly stabilized in the FF3 zwitterionic structure while the

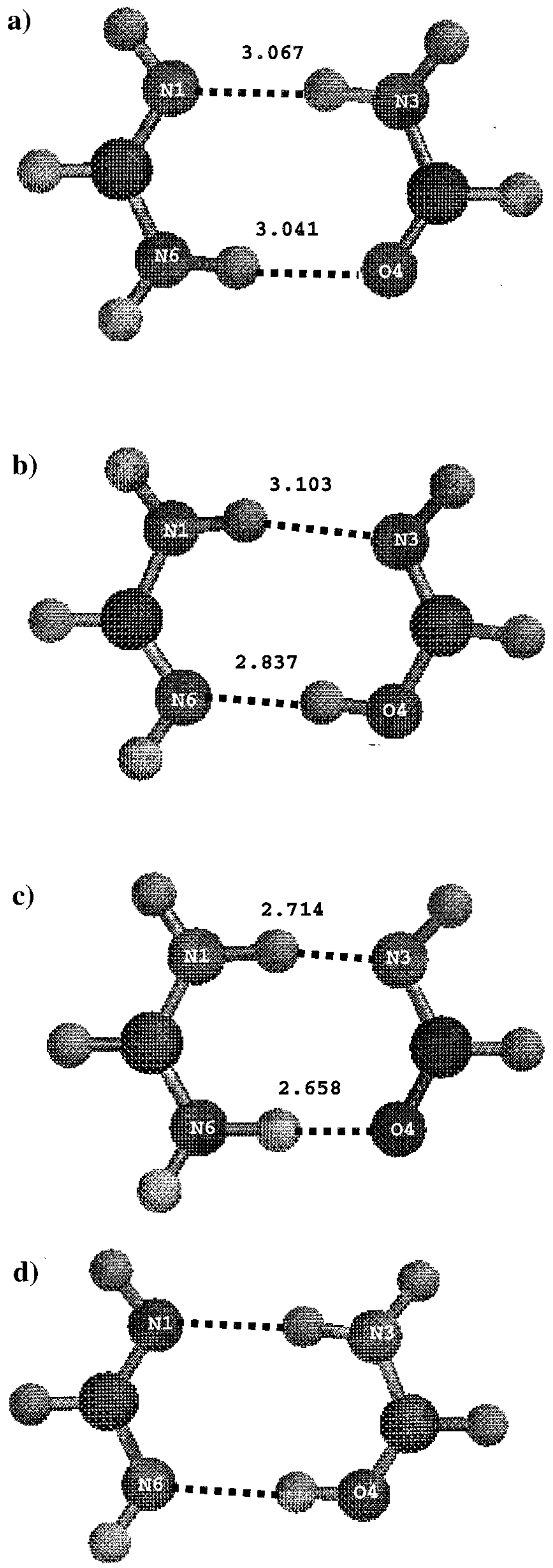

Figure 1. A sketch of some formamidine−formamide complexes in the gas phase: (a) FF1 structure, (b) FF2 structure, (c) FF3 structure, and (d) FF4 structure. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

presence of the purine and pyrimidine rings in the zwitterionic AU3 structure is relatively favorable for such a charge separation.

TABLE 1: Geometry of the Isolated Formamidine−Formamide Model Systems and Adenine−Uracil Base Pairs[a]

bond/angle[b]	FF1	AU1[c]	FF2	AU2[c]	FF3	AU3[c]
N6−O4	3.041	3.080	2.837	2.784	2.658	2.830
N6−H_a	1.004	1.000	1.864	1.800	1.050	1.021
O4−H_a	2.040	2.085	0.974	0.985	1.609	1.809
N6−H_a−O4	175.2	172.9	175.4	176.4	177.4	177.4
C6−N6−H_a	119.5	120.7	125.4	129.3	121.4	122.3
C4−O4−H_a	120.9	126.4	112.6	112.6	118.0	117.6
N1−N3	3.067	3.001	3.103	2.947	2.714	2.669
N1−H_b	2.064	1.987	1.006	1.010	1.068	1.070
N3−H_b	1.009	1.014	2.117	1.948	1.653	1.599
N1−H_b−N3	172.2	178.4	166.4	169.5	171.6	178.8
H−N6−H_b−C6	−156.9	179.8	−176.4	179.8	180.0	179.9

[a] For the notation of a specific complexes, see the text. [b] Bond length, A−B, in angstroms; bond angle, A−B−C, and dihedral angle, A−B−C−D, in degrees. For the atom numbering, see Figure 1. [c] Reference 12.

TABLE 2: Geometry of the Formamidine−Formamide Model Systems with Four Water Molecules and Adenine−Uracil Base Pairs with Seven Water Molecules[a]

bond/angle[b]	FF1	AU1[c]	FF2	AU2[c]	FF3	AU3[c]
N6−O4	3.149	3.013	2.732	2.785	2.772	2.871
N6−H_a	1.000	0.998	1.753	1.806	1.022	1.015
O4−H_a	2.194	2.123	0.987	0.984	1.753	1.859
N6−H_a−O4	159.1	166.9	170.8	172.9	174.9	174.6
C6−N6−H_a	118.3	118.8	125.8	128.7	119.5	120.9
C4−O4−H_a	114.3	123.8	112.5	112.4	119.3	114.7
N1−N3	3.228	3.020	3.202	2.944	2.952	2.734
N1−H_b	2.238	2.007	1.003	1.010	1.021	1.048
N3−H_b	1.003	1.014	2.229	1.942	1.935	1.687
N1−H_b−N3	168.6	175.9	163.2	170.9	173.6	176.2
H−N6−H_b−C6	−149.7	−173.9	−177.6	169.6	172.9	−177.9

[a] For the notation of a specific complexes, see the text. [b] Bond length, A−B, in angstroms; bond angle, A−B−C, and dihedral angle, A−B−C−D, in degrees. For the atom numbering, see Figure 2. [c] Reference 12.

TABLE 3: Geometry of the Formamidine−Formamide Model Systems with Six and Nine Water molecules[a]

bond/angle[b]	FF1·6H_2O	FF2·6H_2O	FF3·6H_2O	FF1·9H_2O	FF3·9H_2O
N6−O4	3.130	2.793	2.916	3.281	2.848
N6−H_a	1.001	1.815	1.010	1.003	1.014
O4−H_a	2.142	0.981	1.932	2.298	1.836
N6−H_a−O4	169.1	174.8	164.2	166.5	176.6
C6−N6−H_a	119.4	126.9	119.4	114.0	120.9
C4−O4−H_a	117.3	111.3	110.0	111.0	113.9
N1−N3	3.184	3.090	2.961	3.147	2.993
N1−H_b	2.193	1.007	1.018	2.170	1.016
N3−H_b	1.005	2.119	1.948	1.005	1.991
N1−H_b−N3	168.6	161.2	173.0	163.7	168.9
H−N6−H_b−C6	156.0	168.1	−165.1	−134.6	174.7

[a] For the notation of a specific complexes, see the text. [b] Bond length, A−B, in angstroms; bond angle, A−B−C, and dihedral angle, A−B−C−D, in degrees. For the atom numbering, see Figures 3 and 4.

Inclusion of the first hydration shell has a rather strong influence on the H-bond properties and planarity of these complexes, as in the case of the AU complexes. All these model complexes become nonplanar when one considers also the amino groups' nonplanarity. Note that the nonplanarity is higher for the FF1 dimer solvated by four water molecules as compared to the FF2 and FF3 complexes with four water molecules (compare the dihedral angle H−N6−H_b−C6, Table 2). The most important tendency in the H-bond distances is that they are marginally increased for all considered complexes when going from the gas phase to the hydrated complexes. Also there is stronger deviation from linearity for these specific H-bonds in all hydrated complexes as compared to the isolated dimers (compare the N1−H_b−N3 and N6−H_a−O4 angles, Tables 1

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 HF/6-31G(d) Level of Theory for the Formamidine−Formamide Model Systems and for Adenine−Uracil Base Pairs in the Gas Phase and in a Water Solution Modeled by Explicit Inclusion of a Different Number of Water Molecules

property	phase	FF1	AU1	FF2	AU2	FF3	AU3
$-E_t$	gas	318.02674	877.00965	318.00693	876.97841	317.99132	876.98381
$-E_{rel}{}^{a}$		0.0	0.0	12.4	19.6	22.2	16.2
$-E_{int}$		11.6	10.2	14.3	22.1	136.8	128.4
$-E_t$	$4H_2O$	622.12804		622.08623		622.11092	
$-E_{rel}{}^{a}$		0.0		26.2		10.7	
$-E_{int}$		10.0		14.1		128.5	
$-E_{solv}$		24.5		14.6		38.8	
$-E_t$	$6H_2O$	774.17905		774.14670		774.16855	
$-E_{rel}{}^{a}$		0.0		20.3		6.6	
$-E_{int}$		11.1		11.8		124.9	
$-E_{solv}$		26.9		18.9		56.6	
$-E_t$	$7H_2O$		1409.1919		1409.1602		1409.1776
$-E_{rel}{}^{a}$			0.0		23.8		12.9
$-E_{int}$			10.0		21.7		126.8
$-E_{solv}$			45.8		41.0		49.3
$-E_t$	$9H_2O$	1002.2523				1002.2495	
$-E_{rel}{}^{a}$		0.0				1.8	
$-E_{int}$		9.5				125.9	
$-E_{solv}$		31.7				55.8	

[a] The lowest energy complex is taken as an internal reference in each case.

TABLE 5: 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(d)/HF/6-31G(d) Level of Theory for the Formamidine−Formamide Model Systems and for Adenine−Uracil Base Pairs in the Gas Phase and in a Water Solution Modeled by Explicit Inclusion of a Different Number of Water Molecules

property	phase	FF1	AU1	FF2	AU2	FF3	AU3
$-E_t$	gas	318.94256	879.5607	318.92414	879.57022	318.91598	879.57760
$-E_{rel}{}^{a}$		0.0	0.0	11.6	16.2	16.7	11.6
$-E_{int}$		12.8	12.3	16.1	23.4	141.2	131.6
$-E_t$	$4H_2O$	623.80139		623.75726		623.79315	
$-E_{rel}{}^{a}$		0.0		27.8		5.2	
$-E_{int}$		10.8		15.9		131.8	
$-E_{solv}$		26.7		16.9		41.9	
$-E_t$	$6H_2O$	776.23049		776.19916		776.23344	
$-E_{rel}{}^{a}$		1.9		21.5		0.0	
$-E_{int}$		11.9		13.7		127.8	
$-E_{solv}$		29.3		21.7		60.3	
$-E_t$	$7H_2O$		1413.1191		1413.0873		1413.1059
$-E_{rel}{}^{a}$			0.0		20.0		8.3
$-E_{int}$			12.1		23.0		129.4
$-E_{solv}$			52.0		47.4		56.1
$-E_t$	$9H_2O$	1004.8794				1004.8849	
$-E_{rel}{}^{a}$		3.5				0.0	
$-E_{int}$		10.4				128.8	
$-E_{solv}$		35.8				59.2	

[a] The lowest energy complex is taken as an internal reference in each case.

and 2). Note also that both the formamidine−formamide dimers and the AU base pairs solvated by the first full hydration shell water molecules have displayed a similar tendency in the H-bond properties when going from the main to the rare tautomeric forms. Thus, both N6−O4 and N1−N3 bond distances are shortened when going from the FF1 to the FF2 or the FF3 complexes solvated by four water molecules or from the AU1 to the AU2 or the AU3 base pairs solvated by seven water molecules.

Let us compare the relative stability of these formamidine−formamide dimers and the AU base pairs. As is evident from the data of Tables 4 and 5, the inclusion of the first full hydration shell water molecules leads to a similar relative stability order for the considered formamidine−formamide dimers and the AU base pairs. Thus, in both cases the zwitterionic structures become the second most stable species after the main tautomers in water solution. These FF3·$4H_2O$ and AU3·$7H_2O$ complexes lie only 10.7 and 12.9 kcal/mol lower at the HF/6-31G* PES compared to the FF1·$4H_2O$ and AU1·$7H_2O$ structures, respectively. Inclusion of the correlation effects at the MP2 level further decreases these values by ca. 5 kcal/mol. By analogy with the AU base pairs,[12] the higher stability of the FF1·$4H_2O$ structure is due to the involvement of more favorable main tautomers as compared to the FF3·$4H_2O$ and FF3·$4H_2O$ structures.

Let us compare the relative stability of the formamidine−formamide dimers when one increases the number of the surrounding water molecules from four (the first hydration shell) through six (the intermediate case) to nine (the first and second hydration shells). The six water molecules have been initially attached to all H atoms, i.e., including the H atoms of the C−H groups of the formamidine and formamide tautomers. As can be expected, the latter two H atoms of the C−H groups are less attractive for an interaction with the water molecules due to their lower acidity. In fact, the additional two water molecules prefer to form cyclic H-bonds with the precursor first hydration shell water molecules (see Figures 2−4). In the case of nine water molecules, the additional five water molecules were initially attached to the O or H atoms of the first shell water

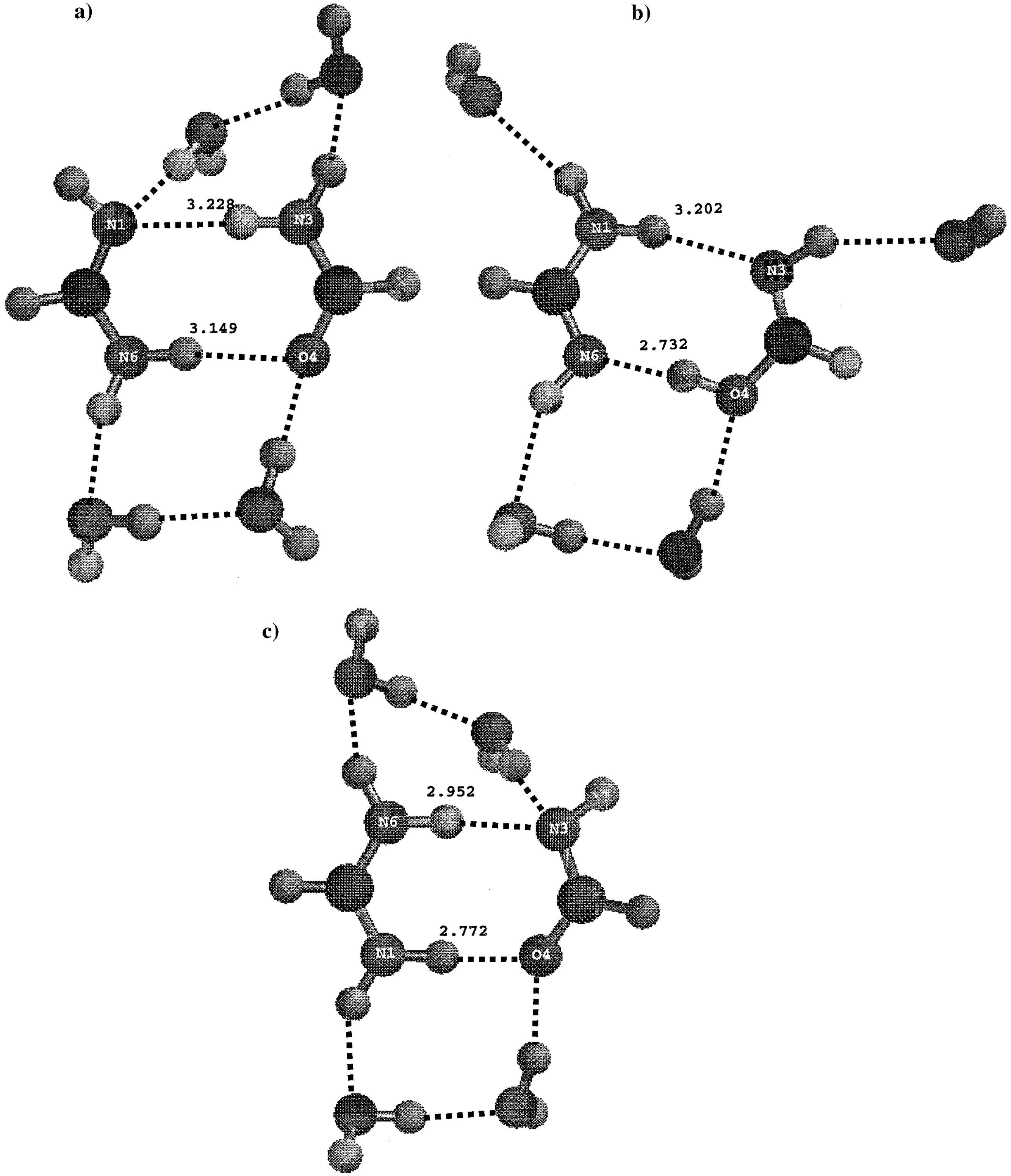

Figure 2. The considered formamidine−formamide complexes with four water molecules: (a) FFl•4H_2O, (b) FF2•4H_2O, and (c) FF3•4H_2O. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

molecules, creating the second hydration shell around the formamidine−formamide dimers. An analysis of the data of Tables 4 and 5 shows that the energy difference between the main FF1 and zwitterionic FF3 forms decreases when the number of water molecules increases. Thus, the zwitterionic FF3 structure lies only 10.7, 6.6, and 1.8 kcal/mol higher on the PES when the number of the surrounding water molecules increases from four through six to nine at the HF/6-31G* level. This can also be expected since the polar environment effectively stabilizes the zwitterionic structure due to strong ion−dipole interactions.

III.2. Interaction and Hydration Energies for Neutral Systems. In line with our previous studies,[12−15] the interaction energies were estimated as the energy difference between the complex and the sum of the isolated tautomers for the considered formamidine−formamide complexes in the gas phase and in a

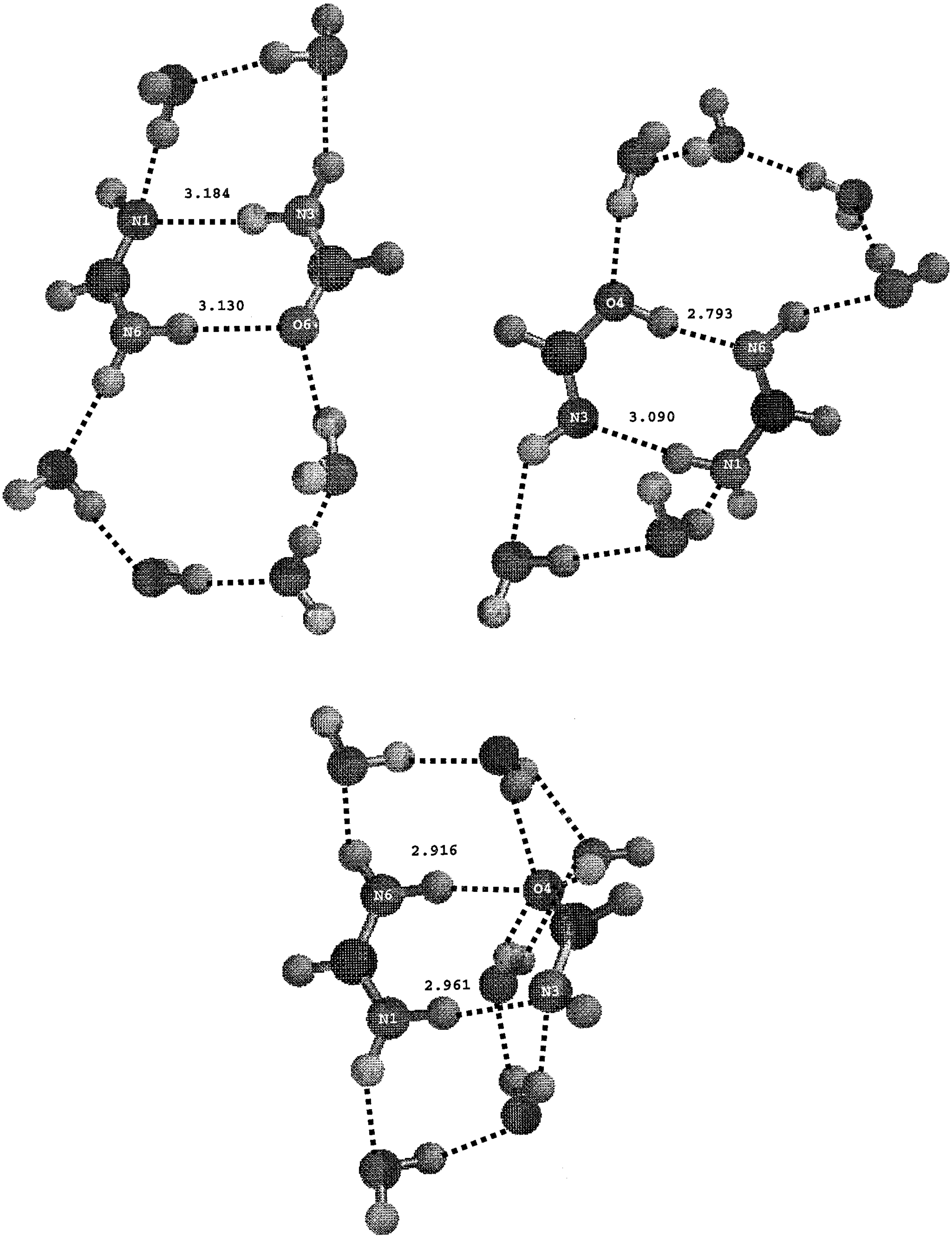

Figure 3. The considered formamidine−formamide complexes with six water molecules: (a) FF1·6H_2O, (b) FF2·6H_2O, and (c) FF3·6H_2O. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

water solution and were corrected for the BSSE. For more clarity the definition of the estimated interaction energies is:

$$(E_{\mathrm{int}})_{\mathrm{solv}} = (E_{\mathrm{tot,A-B}})_{\mathrm{solv}} - ((E_{\mathrm{tot,A}})_{\mathrm{solv}} + (E_{\mathrm{tot,B}})_{\mathrm{solv}}) \quad (1)$$

where the subscript solv stands for the water environment and A−B represents the dimer complex. In the case of a water environment, the first member $(E_{\mathrm{tot,\ A-B}})_{\mathrm{solv}}$ in eq 1 corresponds to a dimer with ghost atoms in the surrounding water molecules

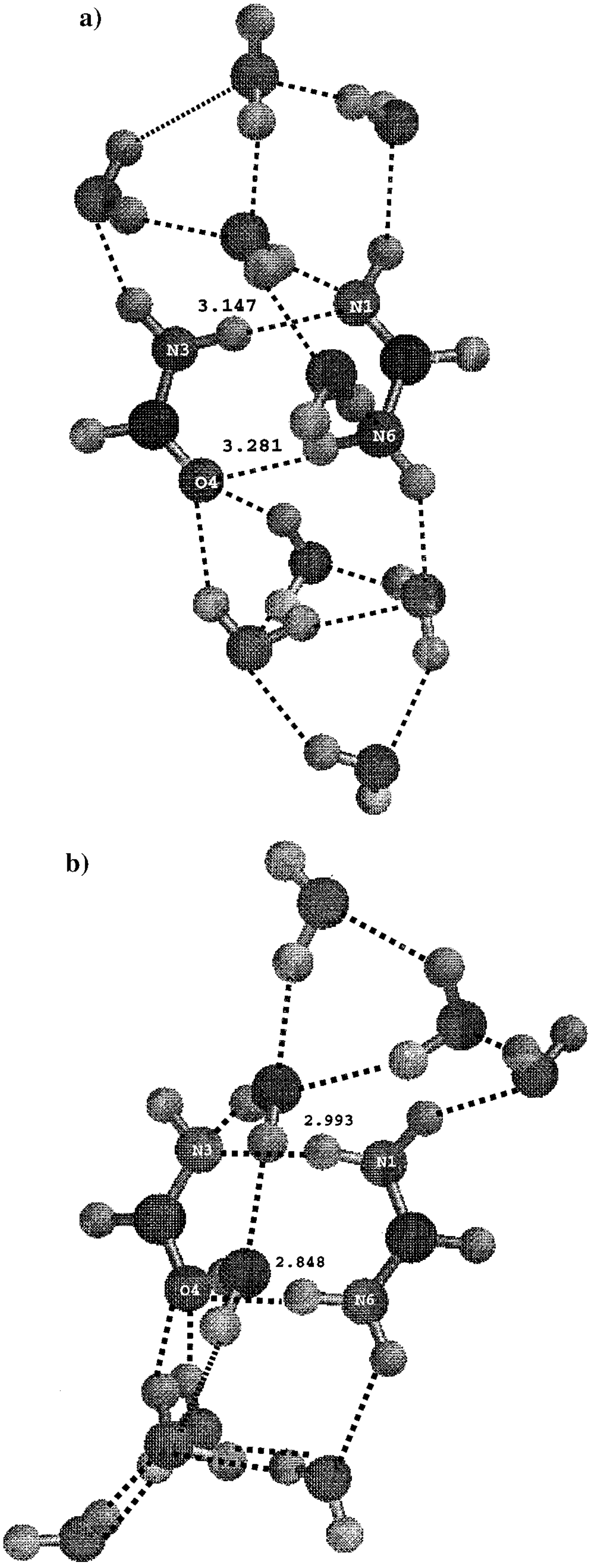

Figure 4. The considered formamidine−formamide complexes with nine water molecules: (a) FF1·9H_2O and (b) FF3·9H_2O. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

while ($E_{tot,A}$) or ($E_{tot,B}$) corresponds to a first or second tautomer with ghost atoms both in the surrounding water molecules and the opposite tautomer. In the case of the isolated dimers, there is no solv subscript. An analysis of the data listed in Tables 4 and 5 shows that the interaction energy value is highest for the FF3 complex both in the gas phase and in a water solution. This is not surprising, since it is due mainly to the ion−ion elecrostatic interactions, as in the case of the AU3 base pair.[12]

The interaction energy for the isolated FF1 dimer amounts to 11.6 and 12.8 kcal/mol at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory, respectively. These values differ slightly from the analogous WC AU1 base pair (the difference is only 1.4 and 0.5 kcal/mol, respectively). The water environment has very few effects on its interaction energy both at the HF and MP2 levels of theory. Thus, the interaction energy for the FF1 complex decreases when the number of surrounding water molecules increases from 11.6 kcal/mol (for the isolated dimer) to 9.5 kcal/mol (for the dimer solvated by nine water molecules). This is qualitatively in line with the analogous AU base pairs, although the effect of the water environment is smaller in the latter case of the AU base pairs (only 0.2 kcal/mol).

The interaction energy is higher for the FF2 dimer than the FF1 dimer both in the gas phase and in a water environment (by up to ca. 4−5 kcal/mol at the HF and MP2 levels of theory). However, a similar tendency is much more pronounced in the case of AU base pairs: the interaction energies for the AU2 complex in the gas phase and in a water environment are approximately 2 times higher than those of the AU1 base pair.[12] The reason for this is that both H-bonds become stronger in going from the isolated and solvated AU1 base pair to the AU2 base pair. In the case of the isolated FF2 dimer, both H-bonds mutually compensate each other due to the opposite changes in their H-bond distances as compared to the FF1 dimer. Only the N6−O4 bond is further strengthened in a water environment, while the changes in the N1−N3 bond distance are relatively small.

The BSSE corrected solvation energies are also calculated as the energy differences between the complex with the water molecules and its components the isolated dimer and water molecules, in the same way as the interaction energies described above. The definition of the estimated solvation energies is as follows:

$$E_{solv} = E_{tot} - ((E_{tot,A-B})_{solv} + (E_{tot,solv})_{A-B}) \qquad (2)$$

In eq 2, E_{tot} and $(E_{tot,solv})_{A-B}$ stand for the dimer complex with a water environment and the surrounding water environment only with ghost atoms of the formamidine−formamide dimer. $(E_{tot,A-B})_{solv}$ has the same definition as in eq 1. In line with the corresponding AU base pairs, the zwitterionic FF3 and main FF1 dimers have the relatively highest solvation energies among the considered structures both at the HF and correlated MP2 levels of theory (Tables 4 and 5).

III.3. One-Electron Oxidized Formamidine−Formamide Model Systems. The optimized structures of the one-electron oxidized formamidine−formamide model systems considered in the present study are shown in Figures 5 and 6, where the numbering of the specific atoms is also defined. These structures contain an extra positive charge and can be considered as cation−radical complexes. According to the above terminology, the first radical dimer which can be obtained from the precursor neutral FF1 dimer have been denoted as FF1$^{(+)}$. In accordance with the experimental and theoretical data on the ionization potentials of the individual bases,[2,3] one can expect that one-electron oxidation should result in the formation of a positively charged adenine (formamidine) fragment as compared to the

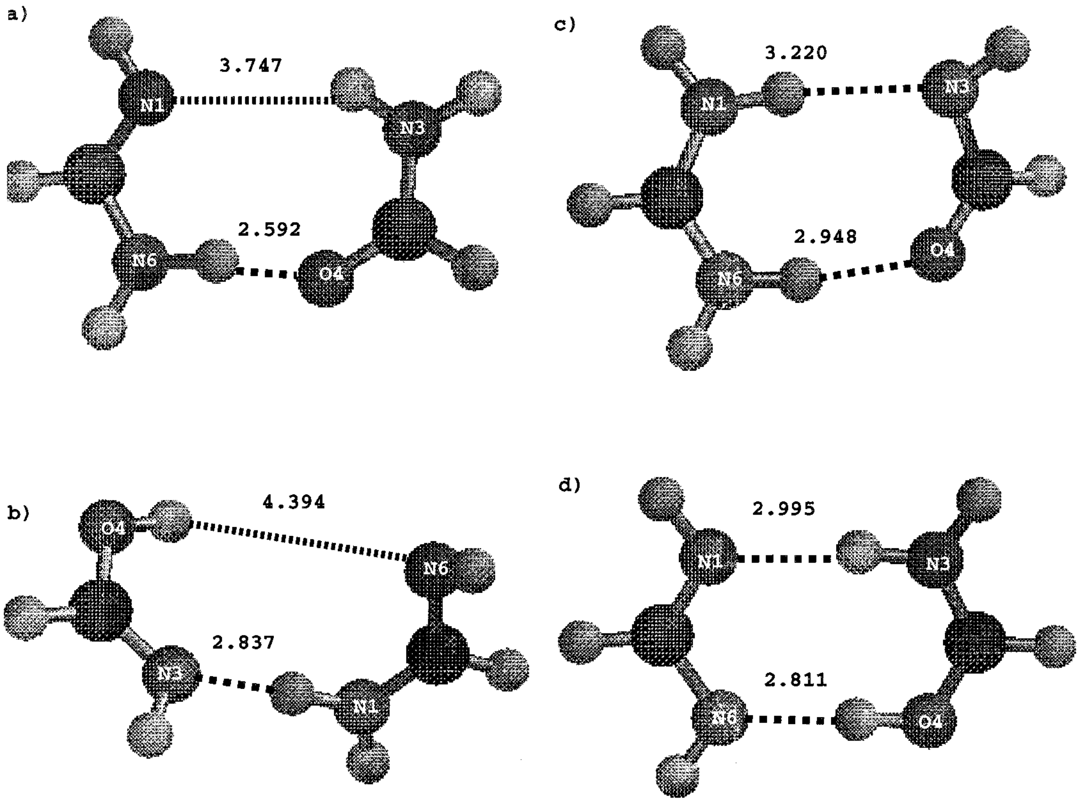

Figure 5. The considered one-electron oxidized formamidine−formamide complexes in the gas phase: (a) FF1$^{(+)}$, (b) FF2$^{(+)}$, (c) FF3$^{(+)}$, and (d) FF4$^{(+)}$. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

thymine or uracil (formamide) fragment. Thus, the sum of the atomic charges calculated using Mulliken definition amounts to 0.9e$^-$ on the formamidine fragment of the one-electron oxidized formamidine−formamide complex, while the rest of the extra charge is redistributed over the other formamide fragment and over the surrounding water molecules around the dimer complex. For this reason one can assume that the proton transfer reaction should occur easily from formamidine to formamide.[4] For these reasons the obtained dimer was denoted as FF4$^{(+)}$; however, the neutral parent FF4 dimer does not exist. A dimer complex denoted as FF2$^{(+)}$ can be obtained from the FF1$^{(+)}$ cation−radical through a double proton-transfer reaction. These three isolated cation−radical dimers were considered by Bertran et al. at the B3LYP and MP2 levels of theory.[4] However, there is also the possibility for the formation of a cation−radical dimer denoted as FF3$^{(+)}$, which formally can be obtained from the precursor neutral FF3 dimer or from the FF1$^{(+)}$ cation−radical through the H atom abstraction from formamide to formamidine. Consequently, the interactions with a water environment were studied for all these formamidine−formamide cation−radical model systems by explicit inclusion of the first hydration shell of four water molecules.

The optimized bond distances, bond angles, and the major dihedral angles of the studied cation−radical complexes are collected in Table 6. Table 7 shows the energetic characteristics of these cation−radical complexes obtained at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory. A comparison of the structural parameters in these H-bonded cation−radical dimers show that all H-bond distances except for N6−O4 of FF1$^{(+)}$ and N1−N3 of FF2$^{(+)}$ become larger as compared to analogous neutral dimers in the gas phase. Thus, the FF1$^{(+)}$ and FF2$^{(+)}$ cation−radical dimers can be stabilized through the strengthening of one of their H-bonds while the other H-bond is substantially weakened (Table 6, compare the N1−N3 and N6−O4 bond distances for the FF1$^{(+)}$ and FF2$^{(+)}$ cation−radicals). When going from the isolated to the solvated FF1$^{(+)}$ cation−radical dimer, one can find that the N6−O4 bond is also further weakened, though it is much stronger than that in the neutral FF1·4H_2O dimer. Similar changes in the geometrical parameters of the H-bonds have been observed for the other solvated cation−radical dimers, except for the solvated FF4$^{(+)}$ cation−radical dimer, for which these H-bonds are slightly strengthened.

Let us compare the relative stability of these cation−radical dimers. According to ref 4, the minimum energy cation−radical corresponds to the single proton transferred FF4$^{(+)}$ dimer in the gas phase at the B3LYP and MP2 levels of theory while the FF1$^{(+)}$ cation−radical dimer has only been predicted at the MP2 level. We have localized all these cation−radical dimers at the HF/6-31G* level and found that there is another lower energy FF3$^{(+)}$ cation−radical dimer both in the gas phase and in a water solution. Thus, it lies 13.6 and 12.2 kcal/mol lower than the FF4$^{(+)}$ dimer on the gas phase PES at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory, respectively. Accordingly, a double proton transferred FF2$^{(+)}$ cation−radical dimer is energetically the least favorable among these considered structures.

Inclusion of hydration has a strong effect on the stability order of these cation−radical dimers. In this case, the FF1$^{(+)}$ cation−radical dimer solvated by four water molecules becomes the second most favorable structure after the solvated single proton transferred FF3$^{(+)}$ cation−radical dimer. Overall, the stability order of these structures in a water environment can be expressed as follows:

$$\mathrm{FF3}^{(+)}\cdot 4\mathrm{H_2O} > \mathrm{FF1}^{(+)}\cdot 4\mathrm{H_2O} > \mathrm{FF4}^{(+)}\cdot 4\mathrm{H_2O} > \mathrm{FF2}^{(+)}\cdot 4\mathrm{H_2O} \quad (3)$$

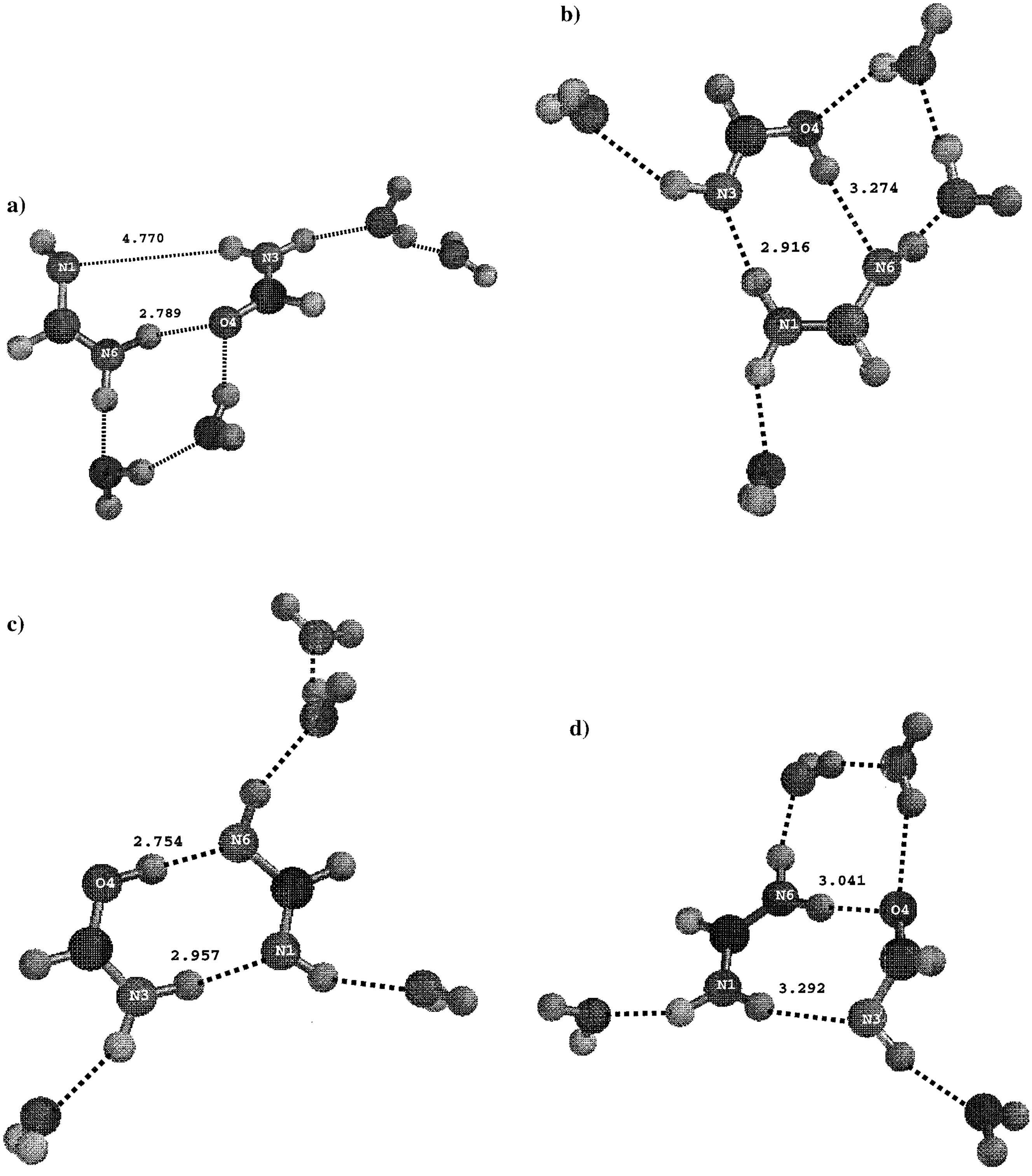

Figure 6. The considered one-electron oxidized formamidine−formamide complexes with four water molecules: (a) $FF1^{(+)}\cdot 4H_2O$, (b) $FF2^{(+)}\cdot 4H_2O$, (c) $FF3^{(+)}\cdot 4H_2O$, and (d) $FF4^{(+)}.4H_2O$. Numbered atoms correspond to distinct atomic sites. H-bond distances are in angstroms.

Interaction energies have been estimated in a similar way as described above, taking into account the respective asymptotes for the formamidine and formamide derivatives, i.e., the close-shell or open-shell states for the fragments of one-electron oxidized cation−radical dimers. The water environment has very few effects on these interaction energies both at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory. As usual, at a correlated level they are larger as compared to the HF predictions.

It should be emphasized that the one-electron oxidized cation−radical formamidine−formamide dimers display an opposite relative stability order than that predicted for the neutral model systems in the gas phase. In this case, the hydrogen atom abstraction and single proton-transfer reactions become more feasible compared to the double proton transfer reaction. This might be very important since the existence of certain “rare” tautomeric forms of DNA bases can increase the possibility of mispairings, leading to spontaneous point mutations. Moreover,

TABLE 6: Geometry of the Isolated One-Electron Oxidized Formamidine−Formamide Model Systems and Their Complexes with Four Water Molecules[a]

bond/angle[b]	$FF1^{(+)}$	$FF2^{(+)}$	$FF3^{(+)}$	$FF4^{(+)}$
N6−O4	2.592 (2.789)	4.394 (3.273)	2.948 (3.041)	2.811 (2.754)
N6−H_a	1.064 (1.020)	3.710 (2.437)	1.008 (1.004)	1.831 (1.767)
O4−H_a	1.536 (1.798)	0.951 (0.953)	1.954 (2.055)	0.980 (0.987)
N6−H_a−O4	170.6 (163.1)	131.1 (146.3)	168.0 (166.9)	179.3 (179.4)
C6−N6−H_a	120.5 (122.4)	94.7 (121.1)	122.3 (121.8)	124.1 (124.3)
C4−O4−H_a	138.9 (125.8)	111.9 (110.7)	131.2 (114.8)	116.8 (116.2)
N1−N3	3.747 (4.767)	2.837 (2.916)	3.220 (3.292)	2.995 (2.957)
N1−H_b	2.883 (4.060)	1.038 (1.023)	1.005 (1.002)	1.984 (1.945)
N3−H_b	0.998 (0.996)	1.801 (1.905)	2.227 (2.333)	1.017 (1.019)
N1−H_b−N3	145.3 (130.7)	175. 2 (169.1)	169.1 (160.0)	171.8 (172.1)
H−N6−H_b−C6	180.0 (−177.0)	−131.6 (−131.1)	178.1 (174.0)	−180.0 (−179.8)

[a] For the notation of a specific complexes, see the text. [b] Bond length, A−B, in angstroms; bond angle, A−B−C, and dihedral angle, A−B−C−D, in degrees. For the atom numbering, see Figures 5 and 6.

TABLE 7: 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(d) and MP2/6-31G(d)//HF/6-31G(d) (in parenthesis) Levels of Theory for the One-Electron Oxidized Formamidine−Formamide Model Systems in the Gas Phase and in a Water Solution Modeled by Explicit Inclusion of Four Water Molecules[a]

property	phase	$FF1^{(+)}$	$FF2^{(+)}$	$FF3^{(+)}$	$FF4^{(+)}$
$-E_t$	gas	317.74320 (318.62192)	317.73454 (318.60874)	317.77676 (318.64833)	317.75503 (318.62893)
$-E_{rel}{}^a$		21.1 (16.6)	26.5 (24.8)	0.0 (0.0)	13.6 (12.2)
$-E_{int}$		27.0 (26.7)	19.5 (21.2)	19.3(21.1)	36.0 (39.6)
$-E_t$	$4H_2O$	621.88476 (623.51480)	621.85973 (623.49221)	621.89763 (623.52556)	621.87251 (623.50129)
$-E_{rel}{}^a$		8.1 (6.8)	23.8 (20.9)	0.0 (0.0)	15.8 (15.2)
$-E_{int}$		23.5 (23.3)	17.3 (19.3)	17.6 (19.0)	35.6 (39.3)
$-E_{solv}$		37.8 (41.7)	46.8 (51.4)	43.3 (46.9)	41.0 (44.6)

[a] The lowest energy complex is taken as an internal reference in each case.

inclusion of the first solvation shell water molecules further stabilizes the $FF3^{(+)}{\cdot}4H_2O$ cation−radical dimer while the parent $FF1^{(+)}{\cdot}4H_2O$ dimer becomes the second most stable one. Possibly this could suggest that both structures might play a key role in DNA replication through inducing spontaneous mutations.

IV. Summary and Conclusions

Ab initio quantum chemical studies at the HF/6-31G* and MP2/6-31G*//HF/6-31G* levels of theory have been performed for neutral and one-electron oxidized formamidine−formamide model systems in the gas phase and in a water solution. On the basis of the results of these studies we conclude the following:

(1) There is fairly good agreement in the structural parameters between the isolated formamidine−formamide model system and the analogous adenine−uracil base pair. However, the relative stability order of the isolated model complexes and AU base pairs is quite the opposite: the double proton transferred FF2 complex becomes the second most stable complex after the main FF1 dimer because the charge separation does not occur easily within the smaller FF3 zwitterionic structure. The stability of the zwitterionic FF3 structure is overestimated when the number of the hydration shell water molecules is increased.

(2) A one-electron oxidation process leads to opposite relative stabilities in which the single electron transferred zwitterionic $FF3^{(+)}$ cation−radical dimer becomes more stable both in the gas phase and in a water solution. For the parent $FF1^{(+)}$ and double proton transferred $FF2^{(+)}$ dimers, one can observe a breakage of one of the H-bonds in the gas phase. The relative stability order in a water solution can be expressed as noted in eq 3.

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