Adiabatic Electron Affinities of the Polyhydrated Adenine−Thymine Base Pair: A Density Functional Study

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Adiabatic electron affinities (AEAs) of the adenine−thymine (AT) base pair surrounded by 5 and 13 water molecules have been studied by density functional theory (DFT). Geometries of neutral AT·nH$_2$O and anionic (AT·nH$_2$O)$^-$ complexes (n = 5 and 13) were fully optimized, and vibrational frequency analysis was performed at the B3LYP/6-31+G** level of theory. The optimized structures of the neutral (AT·nH$_2$O) and (AT·nH$_2$O)$^-$ complexes were found to be somewhat nonplanar. Some of the water molecules are displaced away from the AT ring plane and linked with one another by hydrogen bonds. The optimized structures of the complexes are found to be in a satisfactory agreement with the observed experimental and molecular dynamics simulation results. In the optimized anionic complexes, the thymine (T) moiety was found to be puckered, whereas the adenine (A) moiety remained almost planar. Natural population analysis (NPA) performed using the B3LYP/6-31+G** method shows that the thymine moiety in the anionic (AT·nH$_2$O)$^-$ complexes (n = 5 and 13) has most of the excess electronic charge, i.e., ~ -0.87 and ~ -0.81 (in the unit of magnitude of the electronic charge), respectively. The zero-point energy corrected adiabatic electron affinities of the hydrated AT base pair were found to be positive both for n = 5 and 13 and have the values of 0.97 and 0.92 eV, respectively, which are almost three times the AEA of the AT base pair. The results show that the presence of water molecules appreciably enhances the EA of the base pair.

1. Introduction

The aqueous medium affects the properties of biological systems appreciably, but this aspect has not yet been fully understood at the molecular level. For example, folding of protein and nucleic acid occurs in water, and the final conformation is mainly controlled by the aqueous medium.[1−4] In recent years, a number of X-ray structures[3] have been reported for protein−DNA complexes and other systems, where water molecules are present at the intermolecular interface. The effect of surrounding solvent water molecules is also important from the point of view of physicochemical characteristics of nucleic acid bases.[5] It has been observed that the structure of DNA is highly sensitive to relative humidity and it adopts different conformations, depending upon its relative humdity.[6] Location of preferred hydration sites around DNA bases and base pairs has been the subject of a number of experimental and theoretical studies.[6−20]

In recent years, the study of charge transport through DNA has become a highly important subject from the biological[21−30] and technological[31−41] points of view. It is found that the easily oxidized purine bases, especially guanine, play a crucial role in charge transport in DNA.[42−46] It is also found that the acquisition of excess electronic charge by DNA leads to various modifications of its chemical and physical properties.[47,48] Both experimental and theoretical methods have been employed to unravel the mechanism of charge transport through DNA.[49−57] In this regard, Giese et al.[57] measured the efficiency of charge transfer between guanines separated by different numbers of AT base pairs and found that it depends on the distance between them.

Scheidt et al.[58] investigated electron binding to DNA bases uracil (U), T, and cytosine (C) in the presence of water clusters using photodetachment-photoelectron spectroscopy (PD-PES). They found positive electron affinities (EA) in the $62-86 \pm 8$ meV range for dipole-bound states of the bases.[58] For U and T, they detected one dipole-bound state, whereas for C, they found two dipole-bound states (85 ± 8 and 230 ± 8 meV).[58] They obtained the EA of the C−water complex as ∼0.3 eV, whereas the largest complex solvated with five water molecules had an EA more than 1 eV.[58] Recently, Wetmore et al.[59] also reported positive EAs of the nucleic acid bases using theoretical calculations. Thus, the anions were found to be more stable than the neutral bases at the B3LYP/6-31+G(d,p) level of theory. Further, they found that inclusion of diffuse functions in the basis dramatically changed the EAs of the bases, and on the average, the EAs increased by about. 0.49 eV.

Adamowicz and co-workers[60] proposed a "dipole-bound" anion for uracil. Their calculated MP2 dipole bound electron affinity of 0.086 eV for uracil has been verified experimentally.[61,62] Further, it has been confirmed that the binding of the excess electron to uracil is strongly affected in going from gas phase (dipole bound) to solution (covalent bound).[56] An ab initio calculation[63] on uracil complexed with three water molecules gave the vertical EA (VEA) in the range of 0.9−1.1 eV, whereas the AEA of the complex comes out to be negative in the range of −0.24 to −0.07 eV. In this context, Bowen and co-workers[64] found a very interesting result for the uracil anion microsolvated in water and demonstrated that microsolvation with even a single water molecule provides sufficient stabilization to accommodate

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an excess electron. They observed a broad photoelectron spectrum indicative of a covalent-bound anion.[64] The electron energy dependence of the production of a variety of anions, induced by resonant attachment of electrons to T and C at the femtosecond time scale was measured by Huels et al.[65] who observed stable C^- and T^-. Recently, Schuster et al.[66] studied charge migration in the B-DNA duplex d(5′-GAGG-3′) with an intact sugar−phosphate backbone, including neutralizing Na^+ counterions and a hydration shell using classical molecular dynamics (MD) simulation and density functional electronic structure calculations. From this study, they proposed an ion-gated charge transfer through DNA.[66]

The gas phase AEAs of A, T, G, C, and hypoxanthine (HX) and hydrogen bonded AT, GC, and HX-C have been extensively studied by Schaefer and co-workers,[56,67,68] Wiley et al.,[69] Chen et al.,[70,71] Sevilla and co-workers,[72−74] and Adamowicz et al.[75−78] using various theoretical and experimental methods. Recently, using an empirical density functional (SCC-DFTB) scheme, we calculated[79] EAs of AT, GC, and HX-C base pairs and found that the calculated AEAs were comparable to those obtained by other density functional methods.

Thus, the EAs of DNA bases and base pairs have been extensively studied in the gas phase using different theoretical methods[57−79] but the same have been rarely studied in solvent media, e.g., water. We have tried to answer the following questions in this study: (i) How are the structures of the neutral and anionic AT base pairs affected due to complextion with water molecules? (ii) In the complex of anionic AT with water molecules, how is the excess electronic charge distributed among the bases and water molecules? and (iii) Does the EA of the AT base pair depend on the number of surrounding water molecules?

2. Methods of Calculation

To examine the effect of water molecules bound to the AT base pair, the "supermolecular approach" has been used here. This approach is in some sense superior to the other common approaches, e.g., the continuum solvation models and Monte Carlo or molecular dynamics simulations,[13] since the effect of individual water molecules can be resolved using it. Geometries of the AT base pair surrounded by 5 and 13 water molecules in their neutral and anionic forms were fully optimized using the B3LYP hybrid density functional method using the 6-31+G** basis set. The B3LYP density functional is a combination of Beckes's three parameter hybrid exchange functional[80,81] and the Lee−Yang−Parr[82] correlation functional. Vibrational frequencies were calculated at the same level of theory for all of the optimized systems and real frequencies were obtained in all of the cases. In the present calculations, the Gaussian 03 suite of programs[83] was used.

3. Results and Discussion

The initial geometries of the neutral and anionic AT·$5H_2O$ and AT·$13H_2O$ complexes were generated as follows: (i) Five H_2O molecules surrounding the AT base pair were placed near the main electronegative atoms (N3, N7, and N10 of adenine and O7 and O8 atoms of thymine) in a hydrogen bonding (HB) configuration according to the observed hydration pattern[2,8−11] (Figure 1). (ii) In addition to the five water molecules mentioned above, eight more water molecules were placed surrounding the AT base pair in a HB configuration. The geometries of the complexes involving the neutral and anionic AT base pairs thus generated were fully optimized.

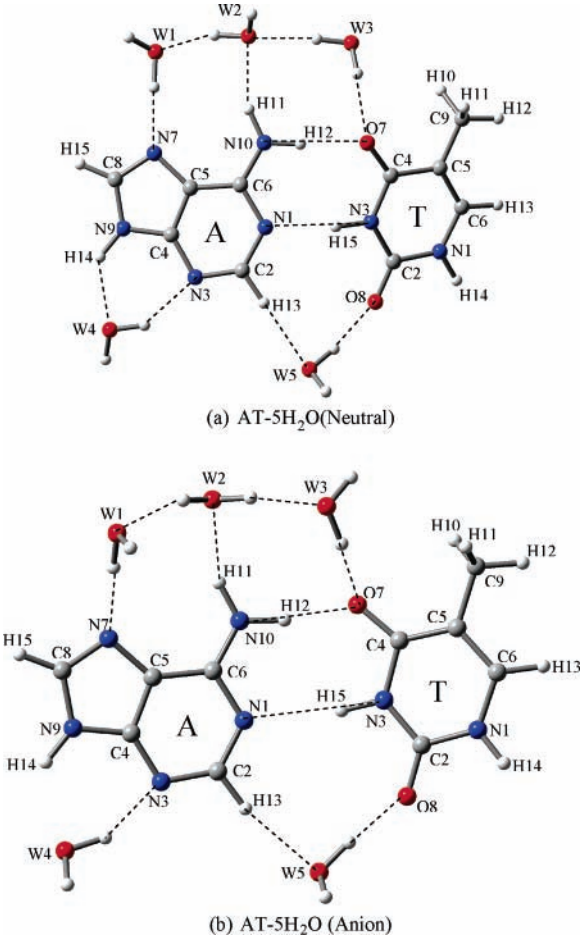

Figure 1. B3LYP/6-31+G** optimized geometries of (a) neutral and (b) anionic AT base pair surrounded by five water molecules.

The B3LYP/6-31+G** optimized structures of the AT base pair surrounded by five water molecules in the neutral and anionic radical forms each are shown in Figure 1a,b, whereas the corresponding optimized structures with 13 water molecules are shown in Figure 2a,b, respectively. In these figures, water molecules are labeled as Wn (n = 1−13). The optimized bond lengths, bond angles and dihedral angles of the bases in AT·$5H_2O$ and $(AT·5H_2O)^-$ complexes are presented in Table 1, whereas those in AT·$13H_2O$ and $(AT·13H_2O)^-$ complexes are presented in Table 2. The optimized hydrogen bonding distances between the atoms of A and T, those between AT and the surrounding water molecules, and those between the water molecules in the neutral and anionic forms of the AT·$5H_2O$ complex are presented in Table 3, whereas the hydrogen bonding distances in the neutral and anionic complexes with thirteen water molecules are presented in Table 4. Net charge distributions calculated using Mulliken and natural population analysis (NPA) in $(AT·5H_2O)^-$ and $(AT·13H_2O)^-$ complexes are given in Tables 5 and 6, respectively. The B3LYP/6-31+G** calculated AEAs of AT·$5H_2O$ and AT·$13H_2O$ complexes alongwith the AEA of AT base pair in gas-phase calculated using different density functionals and ab initio methods are presented in Table 7.

3.1. Structure and Hydrogen Bonding in Neutral and Anionic Complexes. In DNA, the normal GC and AT base pairs are stabilized by hydrogen bonds. Their structural characterization in solid state and solution has mainly involved X-ray crystallography[84,85] and nuclear magnetic resonance (NMR)[86,87] techniques. Generally, the theoretically calculated gas phase structures of DNA bases and base pairs are compared with those

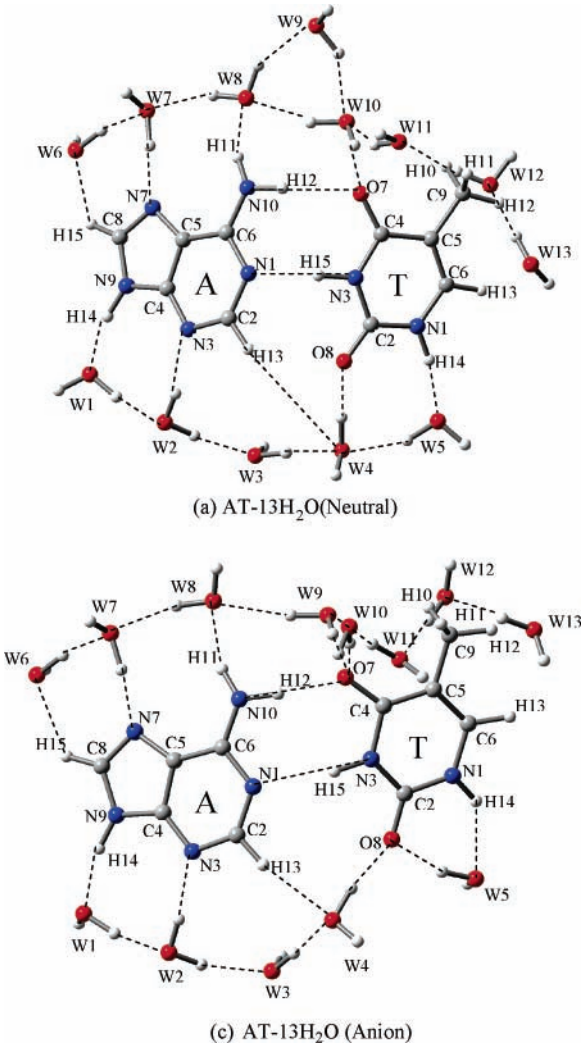

Figure 2. B3LYP/6-31+G** optimized geometries of (a) neutral and (b) anionic AT base pair surrounded by thirteen water molecules.

determined by X-ray crystallography. However, the molecular structures in crystals are influenced by the crystal packing forces. This point should be considered while comparing the theoretically calculated gas-phase structures with those in crystals. A complete structural characterization of DNA including the locations of water molecules surrounding it is very complex.[88] The water molecules strongly bound to DNA are observed at 2 Å resolution.[88] Thus, the sites where there is a high probability of finding the water molecules around the base pairs are defined as hydration sites. The first hydration shell plays an important role in maintaining the structure and stability of DNA. Further, the hydration patterns in the major and minor grooves are quite different. Baerends and co-workers[89] obtained fairly accurate hydrogen bond distances considering environmental effects. For the AT base pair, they[89] considered two water molecules near the N10 and O7 atoms of A and T (Figure 1a) and using the BP86/TZ2P method obtained the hydrogen bond lengths N10(A)−O7(T) and N1(A)−N3(T) (Figure 1a) as 2.92 and 2.80 Å which are in close agreement with the observed distances 2.95 and 2.82 Å in crystals of sodium adenylyl-3′,5′-uridine hexahydrate,[90] respectively.

Recently, Feig et al.[11] studied the hydration of DNA fragments $d(C_5T_5)\cdot(A_5G_5)$ using molecular dynamics simulation. They calculated the water oxygen densities around the AT and GC base pairs and located 5 and 6 hydration sites around them, respectively. In the AT base pair, these hydration sites are located near N3, N7, and N10 atoms of adenine and O7 and O8 atoms of thymine (Figure 1). Using crystallography, Schneider et al.[8−10] also obtained similar hydration sites around the B-DNA double helix from the calculated densities of water molecules. Our B3LYP/6-31+G** calculated optimized structures of $AT\cdot5H_2O$ and $(AT\cdot5H_2O)^-$ are somewhat nonplanar, the nonplanarity being more pronounced in the anionic AT-5H2O. Both the $AT\cdot5H_2O$ and $(AT\cdot5H_2O)^-$ complexes have somewhat buckled, propeller-like twisted structures. Using the HF/6-31G* and B3LYP/6-31G* levels of theory, Leszczynski and co-workers[13−16] studied the structures of neutral AU, GC, and isocytosine−cytosine base pairs as well as A, C, T, and U bases in the presence of water molecules. They also found that the hydrated base pairs adopt nonplanar structures with buckling and propeller-like twist. Recently, Welsh et al.[91] studied the hydration of GC base pairs using HF/6-31G**, HF/6-31++G**, B3P86/6-31G*, and MP2/6-31G* methods. They found that the hydrated GC is appreciably nonplanar and water molecules were also located out of the GC plane. They also concluded that up to 6 water molecules are needed to solvate the GC base pair.[91]

In $(AT\cdot5H_2O)$ and $(AT\cdot5H_2O)^-$, the planes of some water molecules are nearly vertical to the AT ring plane (Figure 1). Further, three water molecules W1, W2, and W3 are linked to each other by hydrogen bonds on the major groove side, whereas the other two water molecules (W4 and W5) are located on the minor groove side (Figure 1). The water molecules W1, W2, and W3 are bound with the N7, H11 atoms of adenine and the O7 atom of thymine, the hydrogen bonding distances lying between 1.825 and 2.027 Å (Table 3). The water molecules W4 and W5 are hydrogen bonded with the N3(A) and O8(C) atoms, the corresponding hydrogen bonding distances being 1.953 and 1.880 Å, respectively (Table 3). Also, the water molecules W4 and W5 are weakly bound to the H14 and H13 atoms of adenine (Figure 1a), the hydrogen bonding distances being greater than 2 Å (Table 3). Strong hydrogen bonds exist between W1 and W2 water molecules and between H(W1) and N7(A), the hydrogen bonding distances being 1.765 and 1.825 Å, respectively. The hydrogen bonds N1(A)−N3(T) and N10(A)−O7(T) in neutral $AT\cdot5H_2O$ were calculated to be 3.027 and 2.998 Å. The calculated N1(A)−N3(T) hydrogen bond length is larger than the experimental value[90] by ∼0.2 Å, whereas the calculated N10(A)−O7(T) hydrogen bond length is in close agreement with the experimental value,[90] i.e., 2.92 Å. The corresponding calculated hydrogen bonding distances in $(AT\cdot5H_2O)^-$ were found to be 3.299 and 2.767 Å (Table 3), respectively. Using different theoretical methods,[68,79] the same trend, i.e., increase and decrease of N1(A)−N3(T) and N10(A)−O7(T) hydrogen bonding distances in gas phase, has been found in going from the neutral to the anionic AT base pair, respectively.

In comparison to the neutral $AT\cdot5H_2O$ complex, in the corresponding anionic complex, the water molecules have a quite different hydrogen bonding pattern and reveal the following features: (i) The planes of water molecules are appreciably reoriented in going from the neutral to the anionic complex, the rotation being almost 90° for W1, W3, W4, and W5. In the case of $(U\cdot(H_2O)_3)^-$, Adamowicz et al.[77] observed a similar trend and concluded that rearrangement of hydrogen bonds provides additional stabilization to the anionic complex. (ii) In the anionic complex, the hydrogen bonds between water molecules as well as those between AT base pair and water molecules, particularly those involving the T component, are usually stronger than the corresponding hydrogen bonds in the neutral base pair (Figure 1, Table 3). In $(AT\cdot5H_2O)^-$, the

TABLE 1: Optimized Geometrical Parameters (Å, Deg.) of Neutral and Anionic AT·5H_2O Using the B3LYP/6-31+G Method[a]**

bond length		bond angle		dihedral angle	
		Adenine (A)			
N1−C2	1.346(1.337)	N1−C2−N3	127.4(127.7)	N1−C2−N3−C4	0.9(2.0)
C2−N3	1.336(1.346)	C2−N3−C4	112.1(111.6)	C2−N3−C4−C5	−1.2(1.1)
N3−C4	1.344(1.346)	N3−C4−C5	126.9(127.1)	N3−C4−C5−C6	−0.3(1.7)
C4−C5	1.395(1.393)	C4−C5−C6	116.3(116.5)	C6−C5−C4−N9	179.9(179.6)
C5−C6	1.421(1.428)	C5−C4−N9	105.7(105.6)	C5−C4−N9−C8	0.4(−0.9)
C6−N1	1.363(1.367)	C4−N9−C8	106.7(106.6)	C4−N9−C8−N7	−0.4(0.6)
C5−N7	1.390(1.391)	N9−C8−N7	113.1(112.9)	H15−C8−N9−C4	179.2(179.0)
N7−C8	1.319(1.317)	N7−C8−H15	124.9(124.9)	H14−N9−C4−C5	179.1(178.8)
C8−N9	1.368(1.373)	C8−N9−H14	130.1(129.9)	H13−C2−N1−C6	178.9(179.9)
N9−C4	1.375(1.378)	C5−C6−N10	124.2(124.4)	C4−C5−C6−N10	177.5(176.1)
C6−N10	1.336(1.327)	C6−N10−H11	123.7(122.8)	N1−C6−N10−H12	2.0(−9.2)
N10−H11	1.015(1.022)	C6−N10−H12	118.8(119.7)	C5−C6−N10−H11	−3.8(−0.6)
N10−H12	1.019(1.036)	N1−C2−H13	116.4(116.0)		
C2−H13	1.087(1.088)				
N9−H14	1.020(1.017)				
C8−H15	1.081(1.081)				
		Thymine (T)			
N1−C2	1.384(1.365)	N1−C2−N3	114.1(115.5)	N1−C2−N3−C4	−0.4(−2.0)
C2−N3	1.378(1.367)	C2−N3−C4	125.8(124.8)	C2−N3−C4−C5	0.9(0.4)
N3−C4	1.396(1.438)	N3−C4−C5	116.8(117.1)	N3−C4−C5−C6	−0.6(−2.7)
C4−C5	1.462(1.393)	C4−C5−C6	117.4(120.2)	C9−C5−C4−N3	178.9(179.1)
C5−C6	1.354(1.414)	C5−C6−N1	122.1(117.4)	O7−C4−N3−C2	−179.2(−179.7)
C6−N1	1.378(1.423)	O8−C2−N3	124.6(123.7)	H15−N3−C2−N1	176.3(−179.8)
N1−H14	1.011(1.008)	H14−N1−C2	115.1(113.9)	O8−C2−N1−C6	179.5(−173.8)
C2−O8	1.229(1.251)	H13−C6−N1	115.3(115.2)	H14−N1−C6−C5	179.7(−175.1)
C4−O7	1.237(1.291)	C9−C5−C6	124.0(120.1)	H13−C6−C5−C4	179.8(160.8)
N3−H15	1.041(1.020)	O7−C4−N3	119.9(115.5)		
C5−C9	1.502(1.506)	H15−N3−C2	117.4(117.0)		
C9−H10	1.095(1.096)	H10−C9−C5	111.1(110.8)		
C9−H11	1.095(1.100)	H11−C9−C5	110.9(112.4)		
C9−H12	1.093(1.097)	H12−C9−C5	110.8(110.7)		
C6−H13	1.085(1.085)				

[a] See Figure 1a,b. Anion geometrical parameters are given in parentheses.

hydrogen bond N1(A)−N3(T) is larger by ∼0.25 Å while the hydrogen bond N10(A)- - -O7(T) is smaller by ∼0.1 Å than the corresponding distances in the AT·5H_2O complex. (iii) The adenine moiety in both of the complexes has similar structural features (Table 1). In this case, the N1−C2 bond length is smaller by ∼0.01 Å, whereas the C2−N3 bond length is larger by nearly the same amount in the anionic complex than in the neutral complex. (iv) The thymine component is almost planar in the neutral complex but it becomes puckered in the anionic complex (Table 1). Actually, a major structural change occurs in the bonds forming the thymine ring. For example, the C5−C6 and C6−N1 bonds in the (AT·5H_2O) anionic complex are larger by ∼0.06 Å each than the corresponding bonds in the neutral AT·5H_2O complex.

The optimized structures of the AT·13H_2O complexes in neutral and anionic forms are given in Figure 2. In this case, in comparison to AT·5H_2O (Figure 1), the water molecules in both the grooves are appreciably rearranged in a hydrogen bonding fashion (Figure 2). Using MD simulation, Feig et al.[11] also observed a continuous hydration pattern around the AT base pair running along the major groove near the O7 atom of thymine and N10 and N7 atoms of adenine. Both the neutral and anionic complexes have a buckled, twisted conformation (Figure 2, Table 2). On the major groove side, the water molecules W6 to W13, are successively hydrogen bonded with each other except W9 which is shifted away and is hydrogen bonded with both W8 and W10. The water molecules W6, W7, and W8 are hydrogen bonded with H15, N7, and H11 atoms of adenine, whereas the water molecule W10 is hydrogen bonded with the O7 atom of thymine. The various hydrogen bond distances involving the water molecules and the atoms of adenine lie in the range 1.717−2.366 Å (Figure 2a, Table 4). Interestingly, the hydrophobic nature of the methyl group of thymine is evident as the water molecules W11−W13 located near it are hydrogen bonded with each other, and do not involve the hydrogen atoms of the methyl group, the W11−W12 and W12−W13 hydrogen bonding distances being 1.771 and 1.799 Å, respectively (Table 4). The hydrophobic nature of the methyl group has also been confirmed by the molecular dynamics and X-ray studies.[8,9,11] The water molecules W1 to W5, located on the minor groove side, are also joined by hydrogen bonds, and except W3, they are also bound to different atoms of adenine and thymine, W3 bridging the water molecules W2 and W4.

In the anionic AT·13H_2O complex, a major rearrangement of hydrogen bonds involving the water molecules and bases in both of the grooves takes place and, in particular, the water molecules are preferentially bound to the thymine moiety (Figure 2b). The hydrogen bonds involving two water molecules, i.e., W4 and W9, are particularly changed in going from the neutral to the anionic complex. Thus, although W4 is hydrogen bonded to only the thymine moiety in the neutral complex, it is hydrogen bonded to both the adenine and thymine moieties in the anionic complex. The water molecule W9 is not hydrogen bonded directly with any of the adenine and thymine moieties in the neutral complex but it is hydrogen bonded directly with the O7 atom of the thymine moiety in the anionic complex. The water molecules W9 and W10 are located below and above the thymine ring plane, their hydrogen bonding distances from O7-(T) being 1.780 and 1.810 Å, respectively. Hydration of O7(T) by two water molecules located above and below the thymine ring plane has been observed by Monte Carlo simulation studies.[92,93] However, in the crystal environment, the O8 site

TABLE 2: Optimized Geometrical Parameters (Å, Deg.) of Neutral and Anionic AT·13H_2O Using the B3LYP/6-31+G Method[a]**

bond length		bond angle		dihedral angle	
		Adenine (A)			
N1−C2	1.343(1.339)	N1−C2−N3	127.9(128.0)	N1−C2−N3−C4	−0.2(0.1)
C2−N3	1.332(1.338)	C2−N3−C4	112.2(112.1)	C2−N3−C4−C5	−1.6(−2.1)
N3−C4	1.348(1.345)	N3−C4−C5	126.0(126.1)	N3−C4−C5−C6	2.2(2.5)
C4−C5	1.400(1.397)	C4−C5−C6	116.8(116.9)	C6−C5−C4−N9	−176.4(−176.6)
C5−C6	1.417(1.422)	C5−C4−N9	105.9(106.0)	C5−C4−N9−C8	0.4(0.2)
C6−N1	1.357(1.360)	C4−N9−C8	106.7(106.6)	C4−N9−C8−N7	−0.7(−0.6)
C5−N7	1.386(1.389)	N9−C8−N7	113.0(112.8)	H15−C8−N9−C4	177.9(178.3)
N7−C8	1.323(1.323)	N7−C8−H15	123.8(123.9)	H14−N9−C4−C5	175.1(173.8)
C8−N9	1.366(1.365)	C8−N9−H14	127.8(127.8)	H13−C2−N1−C6	179.2(179.6)
N9−C4	1.373(1.377)	C5−C6−N10	124.5(124.6)	C4−C5−C6−N10	178.6(179.0)
C6−N10	1.347(1.338)	C6−N10−H11	121.2(120.6)	N1−C6−N10−H12	13.9(12.3)
N10−H11	1.018(1.015)	C6−N10−H12	116.8(118.2)	C5−C6−N10−H11	−14.6(−13.1)
N10−H12	1.017(1.034)	N1−C2−H13	115.4(116.0)		
C2−H13	1.086(1.086)				
N9−H14	1.038(1.034)				
C8−H15	1.083(1.083)				
		Thymine(T)			
N1−C2	1.370(1.355)	N1−C2−N3	115.0(116.5)	N1−C2−N3−C4	2.7(2.4)
C2−N3	1.374(1.360)	C2−N3−C4	126.0(124.1)	C2−N3−C4−C5	−5.8(−3.0)
N3−C4	1.391(1.439)	N3−C4−C5	116.1(117.4)	N3−C4−C5−C6	5.7(5.2)
C4−C5	1.451(1.391)	C4−C5−C6	117.5(119.6)	C9−C5−C4−N3	−176.2(−177.7)
C5−C6	1.361(1.411)	C5−C6−N1	122.5(118.1)	O7−C4−N3−C2	173.5(174.0)
C6−N1	1.376(1.421)	O8−C2−N3	121.4(122.6)	H15−N3−C2−N1	172.2(179.9)
N1−H14	1.029(1.015)	H14−N1−C2	117.0(115.2)	O8−C2−N1−C6	−179.9(175.5)
C2−O8	1.242(1.267)	H13−C6−N1	115.9(115.2)	H14−N1−C6−C5	176.5(177.3)
C4−O7	1.247(1.302)	C9−C5−C6	123.0(120.4)	H13−C6−C5−C4	174.2(−165.1)
N3−H15	1.040(1.022)	O7−C4−N3	119.2(115.8)		
C5−C9	1.503(1.509)	H15−N3−C2	115.6(118.1)		
C9−H10	1.095(1.097)	H10−C9−C5	111.5(112.1)		
C9−H11	1.096(1.095)	H11−C9−C5	110.6(111.1)		
C9−H12	1.092(1.095)	H12−C9−C5	110.5(110.4)		
C6−H13	1.087(1.083)				

[a] See Figure 2a,b. Anion geometrical parameters are given in parentheses.

TABLE 3: Hydrogen Bond Lengths (Å) in Neutral and Anionic AT·5H_2O[a]

atoms	AT·5H_2O (neutral)	AT·5H_2O (anion)
N1(A)- - -N3(T)	3.027	3.299
N10(A)- - -O7(T)	2.889	2.767
N7(A)- - -H(W1)	1.825	1.886
N3(A)- - -H(W4)	1.953	1.846
H11(A)- - -O(W2)	2.019	1.960
O7(T)- - -H(W3)	2.027	1.667
H14(A)- - -O(W4)	2.023	2.137
H13(A)- - -O(W5)	2.229	2.266
O8(T)- - -H(W5)	1.880	1.766
O(W1)- - -H(W2)	1.765	1.982
O(W2)- - -H(W3)	2.050	1.857

[a] See Figure 1a,b.

TABLE 4: Hydrogen Bond Lengths (Å) in Neutral and Anionic AT·13H_2O[a]

atoms	AT·13H_2O (neutral)	AT·13H_2O (anion)
N1(A)- - -N3(T)	2.900	3.160
N10(A)- - -O7(T)	3.065	2.807
H14(A)- - -O(W1)	1.764	1.810
N3(A)- - -H(W2)	1.911	1.855
H13(A)- - -O(W4)		2.432
O8(T)- - -H(W4)	1.679	1.712
H14(T)- - -O(W5)	1.846	2.175
O8(T)- - -H(W5)		1.789
H15(A)- - -O(W6)	2.366	2.560
N7(A)- - -H(W7)	1.715	1.663
H11(A)- - -O(W8)	2.000	2.088
O7(T)- - -H(W10)	1.840	1.810
O7(T)- - -H(W9)		1.780
H(W1)- - -O(W2)	1.689	1.684
H(W2)- - -O(W3)	1.883	1.899
H(W3)- - -O(W4)	1.878	1.790
O(W4)- - -H(W5)	1.864	
H(W6)- - -O(W7)	1.918	1.885
O(W7)- - -H(W8)	1.859	1.841
H(W8)- - -O(W9)	1.932	2.071
O(W8)- - -H(W10)	1.883	
H(W9)- - -O(W10)	1.961	
O(W10)- - -H(W11)	1.784	1.797
O(W11)- - -H(W12)	1.771	1.725
O(W12)- - -H(W13)	1.799	1.831

[a] See Figure 2a,b.

of thymine is preferentially hydrated, instead of O7.[9] Obviously, the packing forces in the crystal would play a role in this context. From Table 2, it is found that the adenine moiety in the neutral and anionic AT·13H_2O complexes becomes slightly nonplanar, the angle between the planes C6−C5−C4 and C5−C4−N9 being ∼4.0°. Recently, Leszczynski and co-workers[16] studied the hydration of an isolated adenine molecule surrounded by 12−16 water molecules at the B3LYP/6-31G(d) level of theory and found that it becomes appreciably nonplanar, the maximum deviation from planarity between the five-membered and six-membered rings being ∼8.0°. The thymine ring in the neutral and anionic AT·13H_2O complexes also becomes slightly nonplanar. In this case, a major structural change occurs in bond lengths of the ring.

Ring flexibility of isolated bases and AT and GC base pairs has been studied earlier using semiempirical and ab initio methods.[94,95] Using HF/6-31G** and MP2/6-31G**//HF/6-31G** methods, the AT base pair was found to be more flexible than the GC base pair.[96] The NH_2 group in the neutral and anionic AT·13H_2O complexes (Table 2) is appreciably more nonplanar with respect to the corresponding angle in AT·5H_2O and

TABLE 5: Mulliken and Natural Population Analysis (NPA) Charges in Anionic AT·5H_2O Calculated Using the B3LYP/6-31+G Method[a]**

	Mulliken charges			NPA charges		
atom no.	adenine (A)	thymine (T)	water (W)[b]	adenine (A)	thymine (T)	water (W)[b]
1	−0.4269	−0.4236	−0.0193	−0.5790	−0.6573	−0.0205
2	0.3663	0.7669	0.0155	0.2619	0.8189	−0.0217
3	−0.4824	−0.6314	−0.0249	−0.6150	−0.6932	−0.0243
4	−0.2741	0.1431	−0.0132	0.3504	0.5461	−0.0388
5	0.2078	1.1291	0.0055	−0.0068	−0.2459	−0.0238
6	0.2958	−0.6772		0.4364	−0.1697	
7	−0.4987	−0.8121		−0.5334	−0.8211	
8	0.3062	−0.6821		0.1939	−0.7612	
9	−0.3981	−0.8988		−0.5934	−0.6919	
10	−0.6170	0.1500		−0.8109	0.2360	
11	0.3705	0.1189		0.4542	0.2246	
12	0.4189	0.1516		0.4661	0.2426	
13	0.1942	0.0919		0.2603	0.2090	
14	0.3458	0.3055		0.4783	0.4340	
15	0.1346	0.3617		0.2313	0.4639	
total	−0.0571	−0.9065	−0.0364	−0.0057	−0.8652	−0.1291

[a] See Figure 1b. [b] Total charge on the surrounding water molecule.

TABLE 6: Mulliken and Natural Population Analysis (NPA) Charges in Anionic AT-13H_2O Calculated Using B3LYP/6-31+G Method[a]**

	Mulliken			NPA		
atom no.	adenine (A)	thymine (T)	water (W)[b]	adenine (A)	thymine (T)	water (W)[b]
1	−0.4033	−0.3629	−0.0085	−0.5837	−0.6491	−0.0138
2	0.2962	0.8188	0.0324	0.2620	0.8294	−0.0140
3	−0.4464	−0.4775	−0.0134	−0.5889	−0.6805	−0.0104
4	−0.2355	−0.1997	−0.0049	0.3607	0.5200	0.0005
5	0.4417	0.8218	0.0013	0.0057	−0.2247	−0.0283
6	0.1311	−0.5930	0.0005	0.4346	−0.1674	−0.0241
7	−0.5986	−0.8176	−0.0243	−0.5624	−0.8446	−0.0282
8	0.3025	−0.7709	−0.0338	0.2200	−0.7931	−0.0056
9	−0.4302	−0.7488	0.0464	−0.5855	−0.7020	−0.0088
10	−0.5836	0.1693	0.0234	−0.8268	0.2516	−0.0320
11	0.3481	0.1712	0.0552	0.4417	0.2611	−0.0055
12	0.4228	0.1246	−0.0188	0.4646	0.2314	−0.0176
13	0.1594	0.1144	−0.0045	0.2446	0.2274	−0.0325
14	0.4051	0.3434		0.4887	0.4618	
15	0.1915	0.3551		0.2595	0.4642	
total	0.0008	−1.0518	0.0510	0.0348	−0.8145	−0.2203

[a] See Figure 2b. [b] Total charge on the surrounding water molecule.

$(AT·5H_2O)^-$ (Table 1). Nonplanarity of the NH_2 group in DNA bases and base pairs has also been reported by other workers.[67,68,97,98]

A detailed analysis of charge distributions in the neutral and anionic AT water complexes has been carried out. Charge distributions for anionic AT·5H_2O and AT·13H_2O complexes are given in Tables 5 and 6, respectively. We find that the Mulliken and the NPA charges in the neutral and anionic complexes differ from each other slightly but they show almost the same trend for charge losing and gaining capacity of the atoms in the corresponding complexes. In the neutral AT·5H_2O and AT·13H_2O complexes, adenine, thymine, and the surrounding water molecules almost remain in their neutral form and a very small amount of charge transfer from adenine to thymine and the surrounding water molecules takes place. However, in the anionic AT·5H_2O and AT·13H_2O complexes, a large amount of charge (~ -0.865 and -0.815 |e|) is mainly localized on the thymine component, whereas adenine (~ -0.006 and -0.129 |e|) and water molecules (~ 0.035 and -0.220 |e|) have much smaller amounts of charges, respectively, (Tables 5 and 6). From the charge distributions in the anionic complexes, it is clear that these complexes have the $AT^-·nH_2O$ ($n = 5$ and 13) character. A similar conclusion has been drawn by Schaefer and co-workers[68] and Adamowicz et al.[75−78] for the anionic AT base pair in gas phase. In comparison to the T moiety in the neutral complexes, charges in the same moiety in the anionic complexes are modified significantly, and particularly the atoms N1, N3, C4, O7, O8, H10, and H13 of this moiety gain appreciable amount of electronic charge. A relationship between excess charge localization on pyrimidine components and occurrence of nonplanar structures of these components in the anionic DNA base pairs has been emphasized earlier.[99]

We also studied solvation of the neutral and anionic AT·5H_2O complexes in bulk aqueous media using the polarized continuum model (PCM), as implemented in the Gaussian 98 program.[100] Using NPA we find that the total charges residing on A, T, and the surrounding five water molecules in the bulk solvated neutral AT·5H_2O complex are $\sim +0.044$, $+0.018$, and -0.062 |e|, respectively, whereas the total charges residing on the corresponding components in the bulk solvated anionic AT·5H_2O complex are -0.009, -0.870, and -0.121 |e|, respectively. Thus, it seems that inclusion of bulk solvent effect on the hydrated AT complexes has negligible effect on the charge distributions.

TABLE 7: Adiabatic Electron Affinities (eV) of AT·5H_2O, AT·13H_2O, and AT Base Pair in Gas Phase Calculated Using B3LYP/6-31+G and Different Density Functional Methods[a]**

method	system	AEA[b]	AEA[c]
B3LYP/631+G**	AT·5H_2O	0.97 (0.87)	0.67 (0.72)
B3LYP/631+G**	AT·13H_2O	0.92 (0.73)	0.62 (0.59)
SCC-DFTB-D[d]	AT		0.36
BHLYP/DZP++[e]		0.13 (−0.02)	0.11 (0.13)
BLYP/DZP++[e]		− (0.25)	0.12 (−)
B3LYP/DZP++[e]		0.36 (0.19)	0.13 (0.16)
BP86/DZP++[e]		0.58 (0.41)	0.26 (0.31)
B3P86/DZP++[e]		0.88 (0.72)	0.14 (0.18)
B3LYP/TZ2P++[e,f]		0.31 (0.15)	0.13 (0.16)
HF/6-31++G**[g]		−0.70	
UMP2/631++G**(6D)[g]		−0.40	
B3LYP/6-31+G(D)[h]		0.30 (0.11)	0.09
AM1-MCCI[i]		1.39	

[a] Uncorrected adiabatic electron affinities (AEAs) are given in parantheses. [b] Adiabatic electron affinity (AEA) calculated using eq 1. [c] Adiabatic electron affinity (AEA) calculated using eq 3. [d] Reference 79. [e] Reference 68. [f] B3LYP/TZ2P++ single-point calculation at structure optimized using DZP++ basis set (ref 68). [g] Reference 76. [h] Reference 73. [i] Reference 104.

3.2. Adiabatic Electron Affinity. The study of EA of DNA bases and base pairs is of fundamental importance because it provides preliminary information as to the role these systems would play in charge-transfer phenomena. A good deal of work from the group of Schafer and co-workers[101] has appeared in this area recently. The electron affinity (EA) of a molecule is defined as the energy gain due to addition of an electron to the neutral molecule. Theoretically, it is calculated as the difference between the total energies (TE) of a molecule in its neutral and anionic forms. Thus

$$\mathrm{EA} = \mathrm{TE}^{\mathrm{neutral}} - \mathrm{TE}^{\mathrm{anion}} \quad (1)$$

In eq 1, if the molecular geometries are optimized in both forms, i.e., neutral and anionic, EA is called adiabatic, and if TE^{anion} is computed at the optimized neutral geometry of the molecule, it is called vertical. However, EA can also be computed from the enthalpy (ΔH) of formation of an anion M^- from the

corresponding neutral molecule M according to

$$M + e^- \rightarrow M^- \quad (2)$$

where M and M^- are the neutral and anionic forms of M, respectively. Equation 2 has been used to calculate the EA of the CH_3 radical.[102,103] Recently, we have shown that EAs of hydrogen bonded base pairs (A and B) can be successfully obtained using the enthalpies of formation of the neutral and anionic base pairs from the total energies of the components using eq 1 without thermal correction.[79] Thus

$$EA = (TE^{AB} - (TE^{A} + TE^{B})) - (TE^{AB^-} - (TE^{A} + TE^{B^-})) \quad (3)$$

$$= \Delta E^{AB} - \Delta E^{AB^-} \quad (4)$$

where ΔE^{AB} and ΔE^{AB^-} are the binding energies of the neutral and anionic forms of AB, respectively. Also, in eq 3, it is assumed that B is more electronegative than A. Thus in AB^-, the excess electronic charge is assumed to be localized on B. In the present study, we calculated the EAs of AT·nH_2O (n = 5 and 13) using eq 3. In this case

$$EA = (TE^{(AT\cdot nH_2O)} - (TE^{AT} + nTE^{H_2O})) - (TE^{(AT\cdot nH_2O)^-} - (TE^{AT^-} + nTE^{H_2O})) \quad (5)$$

In eq 5, $TE^{(AT\cdot nH_2O)}$ and $TE^{(AT\cdot nH_2O)^-}$ are total energies of the neutral and anionic AT·nH_2O, whereas TE^{AT} and TE^{AT^-} are total energies of the neutral and anionic AT base pair, respectively, and TE^{H_2O} is the total energy of a water molecule. Based on eq 1, EAs of DNA bases and base pairs have been evaluated using different methods, but the results obtained suffer from several ambiguities. For example, Chen and Chen[104] calculated the EA of the AT base pair as 1.39 eV using the AM1-MCCI method, whereas the EAs of the same base pair calculated using ab initio Hartree−Fock (HF) and Møller−Plesset methods[76] were found to be −0.70 and −0.40 eV, respectively. The density functional methods were found to be appropriate for this purpose, and Schaefer and co-workers[67,68,101] proposed a bracketing method for the estimation of EAs. They found that among the different density functionals B3LYP was most suitable as it gave the smallest magnitude of average error for 91 molecules.[101]

Zero-point energy corrected AEAs of AT·$5H_2O$ and AT·$13H_2O$ calculated using B3LYP/6-31+G** method and eq 1 are 0.97 and 0.92 eV, whereas the corresponding AEAs using eq 5 are 0.67 and 0.62 eV, respectively (Table 7). However, the corresponding uncorrected AEAs, presented in Table 7, obtained using eq 1 are 0.87 and 0.73 eV and those calculated using eq 5 are 0.67 and 0.62 eV, respectively. Using different density functionals[68] and the DZP++ basis set, the AEA of the AT base pair was found to lie in the range of −0.02 to +0.88 eV (Table 7). However, using the bracketing method,[101] Schaefer and co-workers[68] predicted the AEA of the AT base pair as 0.31 eV. Li et al.[73] predicted the EA of the AT base pair as 0.30 eV using the B3LYP/6-31+G(d) level of theory. Recently, using the SCC-DFTB-D method and eq 4, we calculated[79] the AEA of the AT pair as 0.36 eV (Table 7). The EA of the AT base pair calculated using different density functional methods, the DZP++ basis set, and eq 4 was found to lie between 0.11 and 0.31 eV.[79] Our estimated[79] EA of the AT base pair of 0.36 eV is in excellent agreement with those obtained using B3LYP/TZ2P++//B3LYP/DZP++ and B3LYP/6-31+G(d) methods[68,73] (Table 7). The AEAs of the hydrated AT complexes calculated using eq 1 are almost three times larger, and the corresponding values obtained using eq 5 are about two times larger than the computed gas-phase EA of the AT base pair.

4. Conclusion

From the present study, we find that B3LYP/6-31+G** optimized geometries of the hydrated AT complexes are in a satisfactory agreement with those observed experimentally and calculated using molecular dynamics or by ab initio and other density functional methods. In particular, binding patterns of the water molecules in AT·$5H_2O$ and AT·$13H_2O$ complexes are in excellent agreement with the observed X-ray crystal structures. The hydrophobic effect of the methyl group of thymine in the AT·$13H_2O$ complex is clearly visible in the corresponding optimized structure (Figure 2). Although the ring structure of the AT base pair is planar in the gas phase, the structure of the corresponding hydrated system is appreciably nonplanar having a buckled, propeller-like twisted conformation. In the anionic complexes, the thymine moiety becomes significantly nonplanar, with the ring becoming appreciably puckered. Nonplanarity of the NH_2 group is more pronounced in the AT·$13H_2O$ complex than in the AT·$5H_2O$ complex. In the anionic AT·nH_2O (n = 5 and 13) complexes, the excess negative charge (∼ −0.87) is mainly localized on the thymine component. In the neutral complexes, the A and T components are almost neutral. Charge distributions in anionic AT·$5H_2O$ and AT·$13H_2O$ complexes show that these complexes can be characterized as AT^-·$5H_2O$ and AT^-·$13H_2O$, respectively. The computed AEAs of AT·$5H_2O$ and AT·$13H_2O$ complexes at the B3LYP/6-31+G** level of theory are about two times larger than the AEA of the AT base pair. It seems that the aqueous solvent medium would play an important role in controlling charge transport through DNA.

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Supporting Information Available: Net charge distributions calculated using Mulliken and Natural Population Analysis (NPA) in neutral AT·5H2O and AT·13H2O complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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