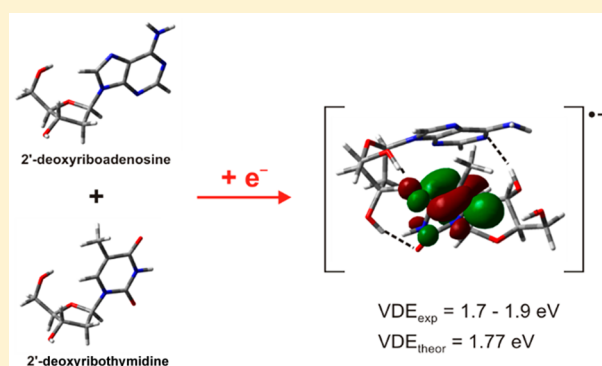


Excess Electron Attachment to the Nucleoside Pair 2'-Deoxyadenosine (dA)–2'-Deoxythymidine (dT)

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S Supporting Information

ABSTRACT: The 2'-deoxyadenosine...2'-deoxythymidine (dAdT^{•-}) radical anion nucleoside pair has been investigated both experimentally and theoretically in the gas phase. The vertical detachment energy (VDE) and adiabatic electron affinity (AEA) were determined by anion photoelectron spectroscopy (PES). The measured photoelectron spectrum features a broad band having an onset at ~1.1 eV and a maximum at the electron binding energy (EBE) ranging from 1.7 to 1.9 eV. Calculations performed at the M06-2X/6-31++G** level reveal that the observed PES signal is probably due to a dAdT^{•-} complex in which the thymine of the dT nucleoside forms hydrogen bonds that engage its O7 and O8 atoms as well as the 3'- and 5'-hydroxyl groups of 2'-deoxyadenosine (dA), while dT's 3'-hydroxyl group interacts with the N1 of dA. In this heterodimer, the excess electron is entirely located on thymine. The biologically relevant Watson–Crick arrangement of the dAdT^{•-} dimer was found to be substantially less stable (by ~19 kcal mol⁻¹ in Gibbs free energy scale) than the above-mentioned configuration; hence, it is not populated in the gas phase.



INTRODUCTION

An interest in the anionic states located in DNA was stimulated by the finding that low-energy electrons are capable of introducing single- (SSB) and double-strand breaks (DSB) to DNA.¹ The experimental investigations that followed this finding were accompanied by computational studies related to the molecular details of the electron-induced damage. In particular, theoretical works comprised electron interactions with a variety of systems starting from single nucleobases and ending up with the single-stranded and double-stranded nucleotide oligomers.^{2–7}

Early theoretical studies suggested that the formation of stable valence-type anions of nucleobases is unlikely in the gas phase,^{8–12} while several spectroscopy experiments demonstrated that the isolated pyrimidines exist as dipole-bound rather than valence-type anion radicals.^{13–15} However, it turned out that nucleobases form adiabatically bound anions due to even marginal solvation by such species as xenon, water, or methanol.^{14–18} The biologically relevant complementary base pairs, AT and GC, may be perceived as systems in which the pyrimidine base is solvated by purine, so they should form stable valence-type anion radicals where the excess electron is localized to T or C. As expected, the gas-phase anions of AT¹⁹ and GC²⁰ have been found by negative ion photoelectron spectroscopy, which also confirmed the results of other experimental techniques.^{21,22} Computational reports on

AT^{23–28} and GC^{23,28–31} greatly outnumbered the experimental reports.

The anions of nucleobases themselves are also viable in the gas phase provided they are chemically modified. On the basis of DFT calculations for 2'-deoxynucleosides, Richardson et al.³² predicted that the T and C pyrimidines when substituted with 2'-deoxyribose at the N1 site should form a valence-type anion in the gas phase. In contrast, the computed adiabatic electron affinity (AEA) and vertical detachment energy (VDE) values close to zero for 2'-deoxyguanosine (dG^{•-}) do not support the existence of a valence-type anion of this purine-based nucleoside, whereas the computational results for 2'-deoxyadenosine (dA^{•-}) were ambiguous (unfavorable AEA was found in contrast to favorable VDE). Stokes et al.,³³ employing a combination of infrared desorption, electron photoemission, and gas jet expansion, was not successful in the generation of a stable anion radical of dG. On the other hand, they recorded the anion photoelectron spectra of 2'-deoxyadenosine (dA). These authors also measured the photoelectron spectrum of the ribonucleoside parent anion of guanine^{•-} (rG^{•-}) and three other ribonucleosides: uridine^{•-} (rU^{•-}), cytidine^{•-} (rC^{•-}), and adenosine^{•-} (rA^{•-}).³³

Received: April 5, 2016

Revised: May 13, 2016

Published: May 13, 2016

Nucleotides are also able to effectively capture electrons. Electron attachment to the isolated nucleotides was widely studied in the context of DNA damage,^{6,34–38} while less attention was paid to the nondissociative generation of parent anion radicals of nucleotides in the gas phase.

More recently, photoelectron spectroscopy allowed for the investigations of relatively large anionic systems as homodimeric nucleoside pairs, uridine (rU^{•-}), thymidine (dT^{•-}), and cytidine (dC^{•-}).^{39–41} The PES studies combined with DFT calculations demonstrated that such nucleoside homodimers exhibit substantially increased tendency to attach an electron in comparison to single nucleosides³³ and appear in the gas phase as stable complexes in which the excess electron resides entirely on the pyrimidine moiety of a single nucleoside.

In the present study, we explore the intrinsic electrophilic properties of the biologically relevant nucleoside pair 2'-deoxyadenosine...2'-deoxythymidine (dAdT). In the PES experiment, we have observed formation of the stable valence anion of dAdT. From the measured spectrum, we have extracted the respective AEA and VDE values. Since the PES technique does not provide any details about the conformation of registered anions, for characterization of the geometries of species existing in the experimental conditions, we took advantage of a computational approach. Based on DFT calculations, we have identified the structure of dAdT^{•-}, which is responsible for the PES feature. The theoretical AEA and VDE obtained for this heterodimer reproduce the experimental values very well.

METHODS

Experimental Details. The anion radical dimers of dAdT were generated using a pulsed infrared desorption–pulsed visible photoemission anion source.³³ Anion photoelectron spectroscopy (PES) is conducted by crossing beams of mass-selected negative ions and fixed frequency photons, followed by energy analysis of the resulting photodetached electrons. Spectral bands in the spectrum result from the vertical Franck–Condon overlap between the wave function of the anion and the wave function of the resulting neutral. This technique is based on the energy conserving relationship $h\nu = \text{EBE} + \text{EKE}$, where $h\nu$ is the photon energy, EBE is the electron-binding energy, and EKE is the measured electron kinetic energy. The EBE corresponding to the intensity maximum on the spectrum is referred to as the vertical detachment energy, VDE. In the first stage of the experiment, neutral nucleosides, covering a slowly translating graphite rod, were populated into the gas phase by low-power infrared laser pulses (1.17 eV/photon) from a Nd:YAG laser. Simultaneously, electrons were generated by visible laser pulses (another Nd:YAG laser operated at 532 nm, 2.33 eV/photon) striking a rotating yttrium oxide disk. Since yttrium oxide's work function of ~ 2 eV is slightly below the photon energy of the visible laser, low energy electrons were released into the gas phase. At the same time, a pulsed valve provided a collisionally cooled jet of helium to carry away excess energy and stabilize the resulting parent radical anions. The photoelectron spectrum of the intact dimer radical anions was recorded by crossing a mass-selected beam of dAdT^{•-} parent anions with a fixed frequency photon beam (a third Nd:YAG laser operated at 355 nm, 3.49 eV/photon). The photodetached electrons were energy analyzed using a magnetic bottle energy analyzer with a resolution of 35 meV at EKE = 1 eV.

Photoelectron spectra were calibrated against the well-known photoelectron spectrum of Cu⁻.

Computational Details. Computations were carried out using the Gaussian 09 program package.⁴² Since dispersive forces should play an important role in the process of dimer formation, where nucleosides in the gas-phase are allowed to assume various orientations with respect to each other, we employed the M06-2X⁴³ functional coupled with the 6-31++G** basis set.^{44,45} The M06-2X functional is suitable for the treatment of systems involving the π – π interactions^{43,46,47} and other noncovalent “dispersion-like” interactions of biological importance.⁴³ Moreover, this DFT functional was shown to give excellent results, better than the widely used B3LYP one, in predicting the binding energies of hydrogen bonded complexes^{43,48} as well as electron affinities and other thermochemical characteristics.⁴³

By employing the M06-2X functional, we expected to describe those arrangements where dispersion constitutes essential contribution to the attraction forces between nucleosides and that are, therefore, poorly described at the B3LYP level.

VDE is the energy required for detachment of an electron from an anion and corresponds to the difference between the absolute energies of the neutral and the anion, both at the optimized anion geometry ($\text{VDE} = E(\text{neu}@an) - E(an@an)$). The adiabatic electron affinities, AEA_E and AEA_G , are defined as the difference between the electronic energies and Gibbs free energies, respectively, of the neutral and the anion at their fully relaxed geometries ($\text{AEA} = E(\text{neu}@neu) - E(an@an)$). All pictures of structures and molecular orbitals were plotted with the GaussView 5.0 program.⁴⁹

RESULTS AND DISCUSSION

The photoelectron spectrum of the 2'-deoxyadenosine...2'-deoxythymidine radical anion is presented in Figure 1. It

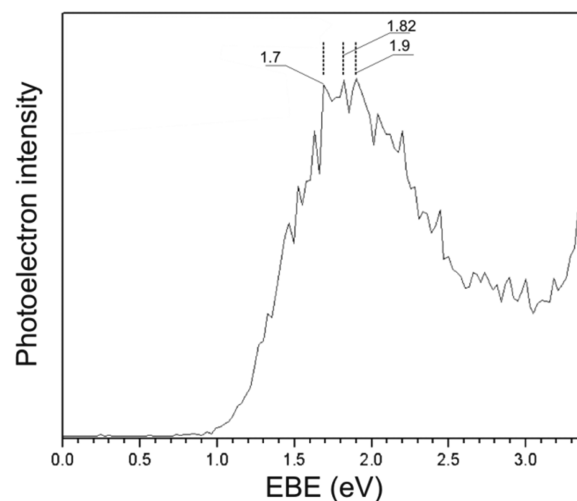


Figure 1. Photoelectron spectrum of [2'-deoxyadenosine...2'-deoxythymidine]^{•-} recorded with 3.49 eV photons.

consists of a broad peak with the maximum between 1.7 and 1.9 eV, which corresponds to the experimental VDE value. The adiabatic electron affinity may be estimated as corresponding to the EBE value at $\sim 10\%$ of the rising photoelectron intensity.³³ Thus, from the onset of the photoelectron spectrum, the AEA for dAdT^{•-} can be estimated to be ~ 1.2 eV.

An electron attachment to the Watson–Crick dAdT nucleoside pair was studied computationally by Gu et al.⁵⁰ Their B3LYP/DZP++ results unequivocally confirmed that the dAdT complex, being characterized by a positive vertical electron affinity of 0.2 eV and the adiabatic electron affinity equal to 0.6 eV, is able to form a stable anion in vacuum. At this level of theory, vertical detachment energy of 1.14 eV was obtained for dAdT^{•−}. However, Gu's VDE and AEA values⁵⁰ do not reproduce the experimental values of the current report. Since their approach was demonstrated to be appropriate for calculating the energetics of electron attachment to the nucleobase related system,⁶ it seems unlikely that such a large discrepancy between Gu's predictions and our measurements may result from the deficiency of the computational model. Indeed in the following, we demonstrate that the PES characteristics are reproduced well by the dAdT^{•−} dimer configuration in which the particular nucleosides are held together by three intermolecular nucleobase···sugar hydrogen bonds. For such an arrangement, we have predicted the AEA_G and VDE of 1.08 and 1.77 eV, respectively, which matches the measured values excellently.

The starting geometry for our computations was 2'-deoxyadenosine···2'-deoxythymidine anion radical pair, dAdT^{•−}, in the Watson–Crick configuration taken from the aforementioned B3LYP/DZP++ studies.⁵⁰ The Watson–Crick dAdT^{•−} dimer was reoptimized at the M06-2X/6-31++G** level (see Figure 2), and the electron affinities and vertical detachment energy were determined for the resulting geometry (see the last row in Table 1).

As indicated by the data gathered in Table 1, the VDE value obtained at the M06-2X level for the canonical dAdT^{•−} (1.18 eV) compares well with the VDE (equal to 1.14 eV) estimated by Gu et al.⁵⁰ As far as the electron affinity is concerned, our AEA_E (0.43 eV) is positive but somewhat smaller than the AEA_E value (0.6 eV) originating from the B3LYP/DZP++ calculation. Additionally, we have compared the performance of M06-2X/6-31++G** and B3LYP/DZP++ approaches in describing electrophilic properties of individual components of dAdT (see Table 1 and structures in Figure 2). Our theoretical AEA values obtained for dT and dA and VDE values obtained for dT^{•−} and dA^{•−} correlate well with those reported by Richardson et al. and Li et al.^{32,51} Since negative AEAs of dA speak against the possibility of existence of a stable valence anion of isolated dA while AEAs of dT suggest that the neutral 2'-deoxythymidine should efficiently transform into the anion radical, our search for the dimeric anion radicals responsible for the measured PES feature involved possible arrangements of the dAdT^{•−} dimer composed of fully optimized monomers, utilizing 2'-deoxyadenosine in its relaxed neutral geometry and 2'-deoxythymidine in its relaxed anionic geometry.

In the scrutinized geometries of the dAdT^{•−}, particular monomers interact via their proton-acceptor (O7(T), O8(T), N1(A), N3(A)) and proton-donor (O3'H, O5'H, N6H(A), C2H(A), N3H(T)) sites. Thus, we obtained 26 structures, shown in Figure 3, which according to the type of the hydrogen bond pattern can be categorized into six groups. In the five out of six groups only the thymine moiety of 2'-deoxythymidine participates in hydrogen bonding with 2'-deoxyadenosine. The first family consists of heterodimers, where hydrogen bonds are formed solely between nucleobases ("A···T" family). In the second group, labeled as "A···T/sugar···T", thymine interacts (utilizing its proton-acceptor and hydrogen-donor sites) with both sugar and adenine of dA. In the third family, "sugar···T",

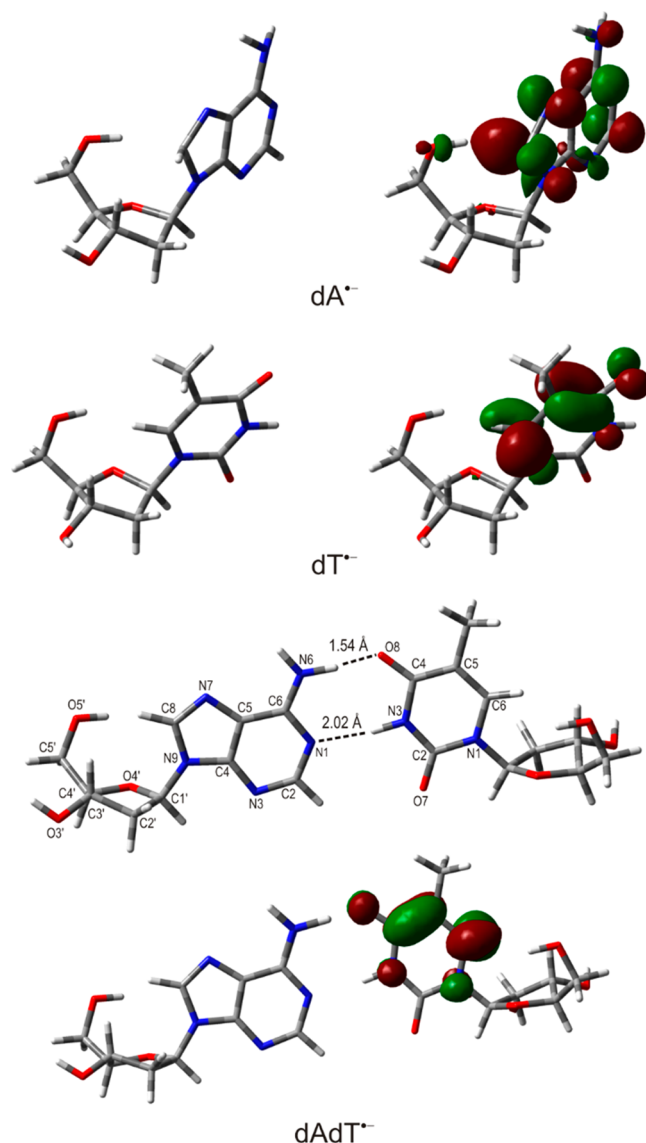


Figure 2. Structures of the anion radical 2'-deoxynucleosides and the Watson–Crick dAdT^{•−} dimer optimized at the M06-2X/6-31++G** level along with singly occupied molecular orbital plotted with a contour value of 0.05 $b^{-3/2}$.

Table 1. Adiabatic Electron Affinities (eV) and Vertical Detachment Energies (eV) of 2'-Deoxynucleosides and Canonical Nucleoside Pair dAdT, Calculated at the M062X/6-31++G** level, Compared with Literature Values Obtained at the B3LYP/DZP++ Level

	AEA _E	AEA _G	VDE
dA	−0.16	−0.17	0.80
	0.06 ^a		0.91 ^a
	−0.04 ^b		
dT	0.30	0.33	0.93
	0.44 ^a		0.94 ^a
	0.45 ^b		
dAdT	0.43	0.46	1.18
	0.60 ^c		1.14 ^c

^aReference 32. ^bReference 51. ^cReference 50.

the thymine moiety forms one or two hydrogen bonds with the hydroxyl groups of the sugar of dA. The next group

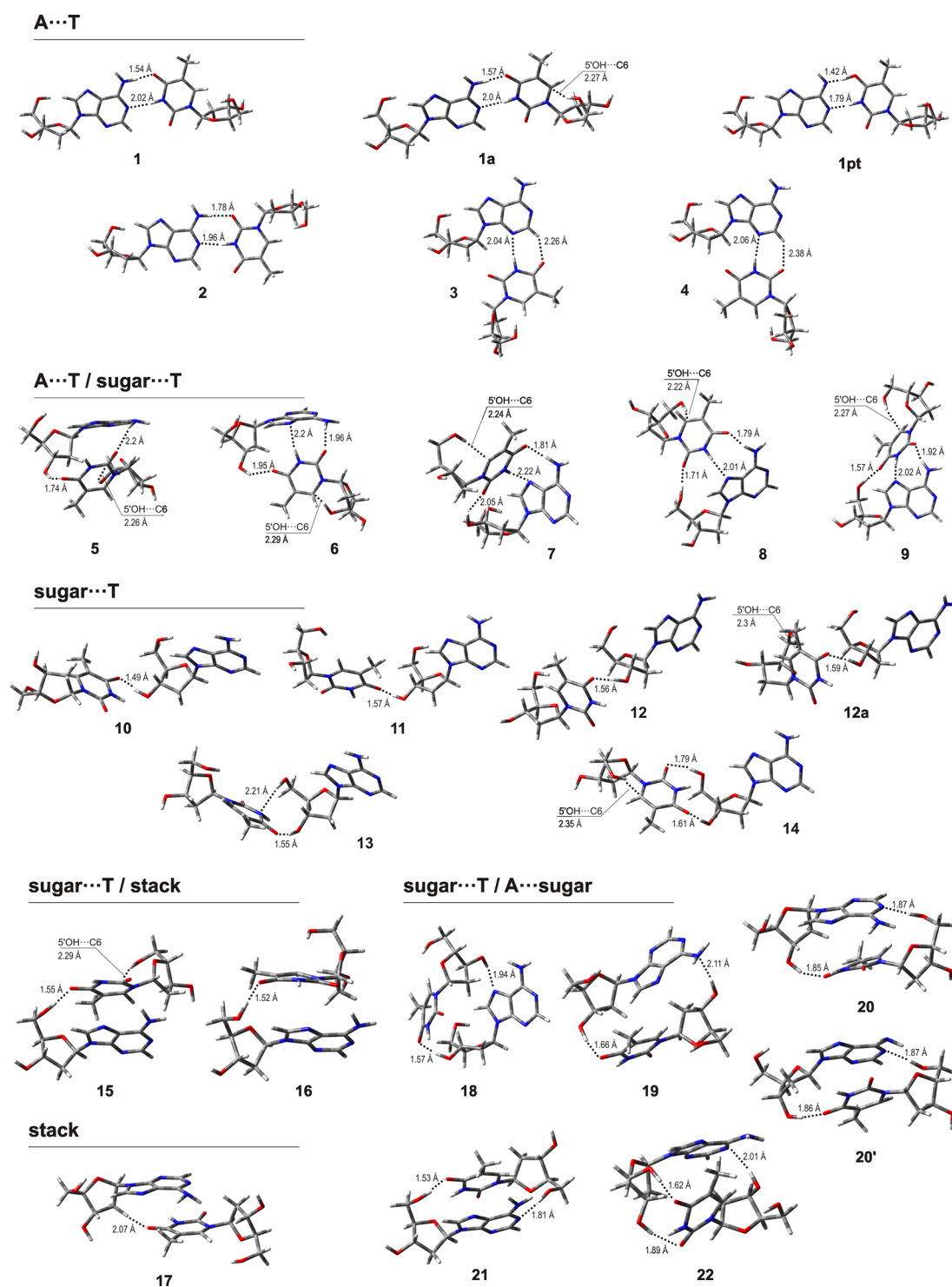


Figure 3. Structures of anion radical heterodimers $dAdT^{\bullet-}$ optimized at the M06-2X/6-31++G** level.

“sugar···T/stack” comprises only two structures. In these complexes in addition to single thymine···sugar hydrogen bond, π -stack interactions are present and the distances between atoms of the overlapping aromatic T and A rings are in the range from ~ 3 to ~ 4 Å. To this end, we have also obtained a heterodimer arrangement in which nucleosides are complexed mainly due to the stacking interactions (see the structure labeled “stack” in Figure 3). The last group features an antiparallel (head-to-tail) orientation of nucleosides, that is, each 2'-deoxyribose is hydrogen-bonded to the nucleobase of

the other monomer (the family labeled “sugar···T/A···sugar”). In case of three heterodimers from this group (20, 20', and 21), cohesive forces between nucleosides result from H-bonds and dispersion interactions between aromatic rings of the nucleobases.

A common feature of the studied complexes is that the excess electron is localized on the π^* orbital of the thymine moiety, and the SOMO orbital closely resembles that of the valence anion of isolated thymine.^{52,53} The excess electron is located at the C4–C5 bond and at the C6 and O8 atoms of thymine. A

smaller amount of the excessive charge also resides on the nitrogen atoms, N1 and N3. Therefore, the investigated anionic complexes can be perceived as the thymidine valence anion solvated by the neutral adenosine. The heterocyclic ring of the thymine valence anion undergoes distortion, which diminishes destabilizing effects present in the singly occupied antibonding π^* orbital of thymine (see Figure 3 and Figure S1).

The thermodynamic characteristics obtained at the M06-2X/6-31++G** level for the anionic radicals of dAdT heterodimers are summarized in Table 2. The relative stabilities (ΔG) of the

Table 2. Values of the Relative Free Energy (ΔG , kcal/mol) with Respect to the Dimer 1, Adiabatic Electron Affinity (AEA_G , eV) of the Corresponding Neutrals, and Vertical Detachment Energy (VDE, eV) of the Anion Radical dAdT Dimers Calculated at the M06-2X/6-31++G Level**

no.	ΔG	AEA_G	VDE
A...T			
1	0.00	0.46	1.18
1pt	2.02	0.37	1.79
1a	-0.84	0.46	1.44
2	4.51	0.29	0.95
3	6.89	0.31	1.01
4	4.80	0.38	1.07
A...T/sugar...T			
5	-9.09	0.95	1.85
6	-6.08	0.81	1.79
7	-5.51	0.84	1.81
8	-6.63	0.68	1.70
9	-7.22	0.71	1.76
sugar...T			
10	-6.20	0.83	1.61
11	-7.77	0.98	1.59
12	-9.11	0.97	1.70
12a	-8.85	0.96	1.94
13	-10.96	0.95	1.81
14	-14.00	1.07	2.03
sugar...T/stack			
15	-8.03	0.71	1.69
16	-10.17	0.70	1.59
stack			
17	-0.88	0.60	1.27
sugar...T/A...sugar			
18	-10.03	0.83	1.52
19	-13.47	0.71	1.53
20	-11.88	0.73	1.53
20'	-9.59	0.60	1.56
21	-10.34	0.55	1.17
22	-18.77	1.08	1.77

studied configurations suggest that the PES spectrum results from electron detachment from structure 22 belonging to the "sugar...T/A...sugar" family. In this dimer, 2'-deoxythymidine is complexed to 2'-deoxyadenosine by three hydrogen bonds: two between the sugar of dA and thymine, 3'OH...O7 and 5'OH...O8, and one between the sugar of dT and adenine, 3'OH...N1. Structure 22 is characterized by AEA_G and VDE of 1.08 and 1.77 eV, respectively, which perfectly reproduces the experimental values of ~ 1.2 and 1.7–1.9 eV, respectively. Configuration 22 possesses the highest AEA_G among all the considered complexes. In summary, we have predicted a positive AEA_G for all conformers.

A large difference in the Gibbs free energies (nearly 19 kcal/mol) was found between the value of structure 22 and the canonical Watson–Crick arrangement of dAdT $^{\bullet-}$ (dimer 1). The second most stable anion radical is 14 from the "sugar...T" group. In this complex, similarly to 22, the thymine is involved in two hydrogen bonds with the 2'-deoxyribose of dA. The difference between both structures is that thymine in 14 utilizes different carbonyl oxygens than thymine in 22 to bind to the sugar (in 14 there are 3'OH...O8 and 5'OH...O7 interactions). Moreover, as opposed to structure 22, dimer 14 does not possess a third hydrogen bond between thymidine's sugar and adenine. The difference, in terms of Gibbs free energy, between 22 and 14 is large, 4.8 kcal/mol, which ensures that the configuration 14 is not populated in the gas phase. It can also be noted that VDE of 2.03 eV predicted for 14 is slightly off with respect to the maximum of the PES spectrum. The involvement of both proton-acceptors, O7 and O8, of T with both proton-donating hydroxyl groups of the sugar in dA occurs only in 14 and 22. Structurally closest to them is 13, where both hydroxyl groups of the adenosine's sugar are involved in binding to thymine. Here, we have found in addition to 3'OH...O8, a quite unusual hydrogen bond, 5'OH...N3. This structure, however, despite its VDE value matching well the experimental VDE, is insignificant according to relative thermodynamic stability criterion (it is higher by 7.8 kcal/mol on the Gibbs free energy scale than dimer 22). The next most stable, with respect to 22, dimeric configurations, 14, 19, 20, and 13 belong to "sugar...T" and "sugar...T/A...sugar" groups and their common feature is a 3'OH...O8 bond. The previous studies of thymidine (dT $_2^{\bullet-}$) and uridine (dU $_2^{\bullet-}$) homodimer anion radicals demonstrated that such 3'OH...O8 hydrogen bond strongly stabilizes anionic complexes of pyrimidine nucleosides and renders them viable in the gas phase.^{39,40} As can be seen from the data shown in Table 2, in addition to the 3'OH...O8 interaction involving adenosine's sugar, the 5'OH...O8 hydrogen bond is also important. However, in contrast to structures with 3'OH...O8 bonding (10–12a), we have not found a dimer featuring a single 5'OH...O8 bond, and this bond in heterodimers is always accompanied by other interactions (see structures 9, 15, 16, 21, and 22).

We observe the weakest stabilization of the excess electron when nucleosides form dimers employing available centers of nucleobases ("A...T" family). Members of this family are characterized by the lowest electron affinities and VDE values among the complexes in Table 2. For dimers 1–4, we obtained VDE near 1 eV, which is close to the VDE found for isolated dT, ~ 0.9 eV. There is also similarity in AEA_G values between 1–4 and dT. In the discussed "A...T" group, there are also two analogues of structure 1, labeled 1pt and 1a, which exhibit higher VDEs than the parent dimer, 1.79 and 1.44 eV, respectively. In case of 1pt an intermolecular proton transfer (PT) from the amine group of dA to O8 of the thymine moiety is responsible for such an increase in the calculated VDE. A proton transfer, often barrierless, was suggested in the past to be involved in a number of anionic nucleobase related complexes in the gas phase.⁷ As regards a complex of isolated nucleobases adenine and thymine, the previous PES/computational studies revealed that in the most stable complex of AT, electron induced proton transfer takes place from N9H of adenine to O8 of thymine.¹⁹ It was shown that PT increases the VDE of given anion radical by 0.7 eV compared with the non-PT structure with identical H-bond pattern. Interestingly,

among potential proton-donating centers, only the N9H center of adenine exhibits sufficient acidity to protonate thymine and the methylation of the N9 atom prevents PT in the $\text{AT}^{\bullet-}$ complex.¹⁹ More recently, we have discovered PT in homodimers consisting of thymidine nucleosides ($\text{dT}_2^{\bullet-}$).⁴⁰ PT from N3H to O8/O7 atom in $\text{dT}_2^{\bullet-}$ increases its VDE by 0.76 eV in relation to the corresponding non-PT structure. In contrast to small anionic complexes involving nucleobases, PT in case of $\text{dT}_2^{\bullet-}$ is not decisive for rendering the most stable anionic arrangement.

As indicated by the respective VDE values the aforementioned anion **1a** is more stable than the anionic dimer **1**. This effect can be explained by the presence of intramolecular interaction $5'\text{OH}\cdots\text{C}6$ in 2'-deoxythymidine in structure **1a**, which allows for a better delocalization of the excess charge within dT. Complexes **1** and **1a** feature an identical intermolecular bond pattern between nucleosides but differ with respect to the intrinsic conformation of dT. The VDE value calculated for structure **1a** is larger by 0.26 eV than that calculated for **1**. The effect of such intramolecular interaction in dT can also be analyzed by comparing structure **12** with **12a** (see Figure 3 and S1). The increase of VDE in **12a** is similar to that found for **1a**.

From the relative stabilities of the anion radical structures of dAdT scrutinized herein, the general picture emerges that the gaseous 2'-deoxynucleosides arrange themselves according to the dipole (adenosine moiety)⋯monopole (thymine moiety) interactions. Inspection of the SOMOs of all structures shown in Figure S1 reveals that the excess electron within $\text{dAdT}^{\bullet-}$ is attracted mainly by the thymynyl moiety. Natural population analysis performed earlier by Gu et al. for $\text{dAdT}^{\bullet-}$ in the Watson–Crick arrangement indicates that the excess electron is distributed among adenine, thymine, and thymine's 2'-deoxyribose in the proportion 0.07, 0.81 and 0.12, respectively.⁵⁰ Thus, all $\text{dAdT}^{\bullet-}$ structures studied here may be perceived as the complexes of the neutral dA and anionic dT. Such complexes exhibit the strongest stability when the positive pole of the 2'-deoxyadenosine's dipole, which is located in the sugar moiety,⁵⁰ attracts the thymynyl moiety, which hosts most of the excess electron. Thus, the low relative stability of the "A⋯T" family structures may result, at least partially, from the repulsion between negative pole of the 2'-deoxyadenosine's dipole and the excess charge located on thymine.

CONCLUSIONS

Negative ion photoelectron spectroscopy was used to study a parent anion radical of a nucleoside pair between 2'-deoxyadenosine and 2'-deoxythymidine. The measured adiabatic electron affinity and vertical detachment energy of $\text{dAdT}^{\bullet-}$ are ~1.2 and 1.7–1.9 eV, respectively. The position of the signal (corresponding to experimental VDE values) as well as its width indicate a strong stabilization of dAdT upon electron attachment and the formation of valence-bond-type anions. Complementary computational investigations allowed for identification of the structure of dAdT that forms in the gas phase under PES experimental conditions. The calculated AEA and VDE for this heterodimer agree well with the measured values. This report makes a combined experimental and computational contribution to our understanding of the electrophilic properties of DNA components.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcc.6b03450.

Large version of Figure 3 with optimized structures of anion radical heterodimers $\text{dAdT}^{\bullet-}$ supplemented with their singly occupied molecular orbitals plotted with a contour value of 0.05 $b^{-3/2}$, complete refs 5 and 42, and cartesian coordinates of the optimized $\text{dAdT}^{\bullet-}$ heterodimers shown in Figures 3 and S1 (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the Polish Ministry of Science and Higher Education (MNiSW) under the Grant No. DS/530-8227-D494-15. The calculations have been carried out at Wrocław Center for Networking and Supercomputing (<http://www.wcss.wroc.pl>), under Grant No. 196. This research was also supported in part by PL-Grid Infrastructure. This material is also based upon experimental work supported by the U.S. National Science Foundation under Grant Number CHE-1360692 (K.H.B.).

REFERENCES

- (1) Boudaïffa, B.; Cloutier, P.; Hunting, D.; Huels, M. A.; Sanche, L. Resonant Formation of DNA Strand Breaks by Low-Energy (3 to 20 eV) Electrons. *Science* **2000**, *287*, 1658–1660.
- (2) Sanche, L. Low Energy Electron Damage to DNA. In *Radiation Induced Molecular Phenomena in Nucleic Acid: A Comprehensive Theoretical and Experimental Analysis*; Shukla, M., Leszczynski, J., Eds.; Challenges and Advances in Computational Chemistry and Physics; Springer: Dordrecht, the Netherlands, 2008; pp 531–575.
- (3) Kumar, A.; Sevilla, M. D. Theoretical Modeling of Radiation-Induced DNA Damage. In *Radical and Radical Ion Reactivity in Nucleic Acid Chemistry*; Greenberg, M. M., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2009; pp 1–39.
- (4) Sanche, L. Low-Energy Electron Interaction with DNA: Bond Dissociation and Formation of Transient Anions, Radicals, and Radical Anions. In *Radical and Radical Ion Reactivity in Nucleic Acid Chemistry*; Greenberg, M. M., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2009; pp 239–293.
- (5) Rak, J.; Mazurkiewicz, K.; Kobylecka, M.; Storoniak, P.; Haranczyk, M.; Dąbkowska, I.; Bachorz, R. A.; Gutowski, M.; Radisic, D.; Stokes, S. T.; et al. Stable Valence Anions of Nucleic Acid Bases and DNA Strand Breaks Induced by Low Energy Electrons. In *Radiation Induced Molecular Phenomena in Nucleic Acid: A Comprehensive Theoretical and Experimental Analysis*; Shukla, M., Leszczynski, J., Eds.; Challenges and Advances in Computational Chemistry and Physics; Springer: Dordrecht, the Netherlands, 2008; pp 619–667.
- (6) Gu, J.; Leszczynski, J.; Schaefer, H. F. Interactions of Electrons with Bare and Hydrated Biomolecules: From Nucleic Acid Bases to DNA Segments. *Chem. Rev.* **2012**, *112*, S603–S640.
- (7) Storoniak, P.; Wang, H.; Ko, Y. J.; Li, X.; Stokes, S. T.; Eustis, S.; Bowen, K. H.; Rak, J. Valence Anions of DNA-related Systems in the Gas Phase. Computational and Anion Photoelectron Spectroscopy Studies. In *Practical Aspects of Computational Chemistry III*; Leszczynski, J., Shukla, M., Eds.; Springer: New York, 2014; pp 323–392.

- (8) Oyler, N. A.; Adamowicz, L. Electron Attachment to Uracil: Theoretical Ab Initio Study. *J. Phys. Chem.* **1993**, *97*, 11122–11123.
- (9) Oyler, N. A.; Adamowicz, L. Theoretical Ab Initio Calculations of the Electron Affinity of Thymine. *Chem. Phys. Lett.* **1994**, *219*, 223–227.
- (10) Desfrancois, C.; Abdoul-Carime, H.; Carles, S.; Périquet, V.; Schermann, J. P.; Smith, D. M. A.; Adamowicz, L. Experimental and Theoretical Ab Initio Study of the Influence of N-Methylation on the Dipole-Bound Electron Affinities of Thymine and Uracil. *J. Chem. Phys.* **1999**, *110*, 11876–11883.
- (11) Smith, D. M. A.; Smets, J.; Elkadi, Y.; Adamowicz, L. Methylation Reduces Electron Affinity of Uracil. Ab Initio Theoretical Study. *J. Phys. Chem. A* **1997**, *101*, 8123–8127.
- (12) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. Structures and electron detachment energies of uracil anions. *Chem. Phys. Lett.* **1999**, *307*, 220–226.
- (13) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Snodgrass, J. T.; Bowen, K. H. Dipole bound, nucleic acid base anions studied via negative ion photoelectron spectroscopy. *J. Chem. Phys.* **1996**, *104*, 7788–7791.
- (14) Schiedt, J.; Weinkauff, R.; Neumark, D. M.; Schlag, E. W. Anion Spectroscopy of Uracil, Thymine and the Amino-Oxo and Amino-Hydroxy Tautomers of Cytosine and Their Water Clusters. *Chem. Phys.* **1998**, *239*, 511–524.
- (15) Desfrancois, C.; Abdoul-Carime, H.; Schermann, J. P. Electron Attachment to Isolated Nucleic Acid Bases. *J. Chem. Phys.* **1996**, *104*, 7792–7794.
- (16) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Bowen, K. H. The Dipole Bound-To-Covalent Anion Transformation in Uracil. *J. Chem. Phys.* **1998**, *108*, 8–11.
- (17) Périquet, V.; Moreau, A.; Carles, S.; Schermann, J. P.; Desfrancois, C. Cluster Size Effects Upon Anion Solvation of N-Heterocyclic Molecules and Nucleic Acid Bases. *J. Electron Spectrosc. Relat. Phenom.* **2000**, *106*, 141–151.
- (18) Eustis, S.; Wang, D.; Lyapustina, S.; Bowen, K. H. Photoelectron Spectroscopy of Hydrated Adenine Anions. *J. Chem. Phys.* **2007**, *127*, 224309.
- (19) Radisic, D.; Bowen, K. H.; Dąbkowska, I.; Storoniak, P.; Rak, J.; Gutowski, M. AT Base Pair Anions versus (9-Methyl-A)(1-Methyl-T) Base Pair Anions. *J. Am. Chem. Soc.* **2005**, *127*, 6443–6450.
- (20) Szyperska, A.; Rak, J.; Leszczynski, J.; Li, X.; Ko, Y. J.; Wang, H.; Bowen, K. H. Low-Energy-Barrier Proton Transfer Induced by Electron Attachment to the Guanine···Cytosine Base Pair. *ChemPhysChem* **2010**, *11*, 880–888.
- (21) Desfrancois, C.; Abdoul-Carime, H.; Schulz, C. P.; Schermann, J. P. Laser Separation of Geometrical Isomers of Weakly Bound Molecular Complexes. *Science* **1995**, *269*, 1707–1709.
- (22) Nir, E.; Kleinermanns, K.; de Vries, M. S. Pairing of Isolated Nucleic-Acid Bases in the Absence of the DNA Backbone. *Nature* **2000**, *408*, 949–951.
- (23) Colson, A.-O.; Besler, B.; Sevilla, M. D. Ab Initio Molecular Orbital Calculations on DNA Base Pair Radical Ions: Effect of Base Pairing on Proton-Transfer Energies, Electron Affinities, and Ionization Potentials. *J. Phys. Chem.* **1992**, *96*, 9787–9794.
- (24) Al-Jihad, I.; Smets, J.; Adamowicz, L. Covalent Anion of the Canonical Adenine–Thymine Base Pair. Ab Initio Study. *J. Phys. Chem. A* **2000**, *104*, 2994–2998.
- (25) Reynisson, J.; Steenken, S. DFT Studies on the Pairing Abilities of the One-Electron Reduced or Oxidized Adenine–Thymine Base Pair. *Phys. Chem. Chem. Phys.* **2002**, *4*, 5353–5358.
- (26) Li, X.; Cai, Z.; Sevilla, M. D. Energetics of the Radical Ions of the AT and AU Base Pairs: A Density Functional Theory (DFT) Study. *J. Phys. Chem. A* **2002**, *106*, 9345–9351.
- (27) Richardson, N. A.; Wesolowski, S. S.; Schaefer, H. F. The Adenine-Thymine Base Pair Radical Anion: Adding an Electron Results in a Major Structural Change. *J. Phys. Chem. B* **2003**, *107*, 848–853.
- (28) Kumar, A.; Knapp-Mohammady, M.; Mishra, P. C.; Suhai, S. A Theoretical Study of Structures and Electron Affinities of Radical Anions of Guanine-Cytosine, Adenine-Thymine, and Hypoxanthine-Cytosine Base Pairs. *J. Comput. Chem.* **2004**, *25*, 1047–1059.
- (29) Colson, A.-O.; Besler, B.; Close, D. M.; Sevilla, M. D. Ab Initio Molecular Orbital Calculations of DNA Bases and Their Radical Ions in Various Protonation States: Evidence for Proton Transfer in GC Base Pair Radical Anions. *J. Phys. Chem.* **1992**, *96*, 661–668.
- (30) Li, X.; Cai, Z.; Sevilla, M. D. Investigation of Proton Transfer within DNA Base Pair Anion and Cation Radicals by Density Functional Theory (DFT). *J. Phys. Chem. B* **2001**, *105*, 10115–10123.
- (31) Richardson, N. A.; Wesolowski, S. S.; Schaefer, H. F. Electron Affinity of the Guanine-Cytosine Base Pair and Structural Perturbations upon Anion Formation. *J. Am. Chem. Soc.* **2002**, *124*, 10163–10170.
- (32) Richardson, N. A.; Gu, J.; Wang, S.; Xie, Y.; Schaefer, H. F. DNA Nucleosides and Their Radical Anions: Molecular Structures and Electron Affinities. *J. Am. Chem. Soc.* **2004**, *126*, 4404–4411.
- (33) Stokes, S. T.; Li, X.; Grubisic, A.; Ko, Y. J.; Bowen, K. H. Intrinsic Electrophilic Properties of Nucleosides: Photoelectron Spectroscopy of Their Parent Anions. *J. Chem. Phys.* **2007**, *127*, 084321.
- (34) Kobylecka, M.; Gu, J.; Rak, J.; Leszczynski, J. Barrier-Free Proton Transfer in the Valence Anion of 2'-Deoxyadenosine-5'-Monophosphate. II. A Computational Study. *J. Chem. Phys.* **2008**, *128*, 044315.
- (35) B, R.; Bhowmick, S.; Mishra, M. K.; Sarma, M. Low-Energy Electron-Induced Single Strand Breaks in 2'-Deoxycytidine-3'-monophosphate Using the Local Complex Potential Based Time-Dependent Wave Packet Approach. *J. Phys. Chem. A* **2011**, *115*, 13753–13758.
- (36) Bhowmick, S.; B, R.; Mishra, M. K.; Sarma, M. Investigation of Dissociative Electron Attachment to 2'-Deoxycytidine-3'-Monophosphate Using DFT Method and Time Dependent Wave Packet Approach. *J. Chem. Phys.* **2012**, *137*, 064310.
- (37) Kopyra, J. Low Energy Electron Attachment to the Nucleotide Deoxycytidine Monophosphate: Direct Evidence for the Molecular Mechanisms of Electron-Induced DNA Strand Breaks. *Phys. Chem. Chem. Phys.* **2012**, *14*, 8287–8289.
- (38) Chen, H.-Y.; Yang, P.-Y.; Chen, H.-F.; Kao, C.-L.; Liao, L.-W. DFT Reinvestigation of DNA Strand Breaks Induced by Electron Attachment. *J. Phys. Chem. B* **2014**, *118*, 11137–11144.
- (39) Ko, Y. J.; Storoniak, P.; Wang, H.; Bowen, K. H.; Rak, J. Photoelectron Spectroscopy and Density Functional Theory Studies on the Uridine Homodimer Radical Anions. *J. Chem. Phys.* **2012**, *137*, 205101.
- (40) Storoniak, P.; Rak, J.; Ko, Y. J.; Wang, H.; Bowen, K. H. Photoelectron Spectroscopy and Computational Modeling of Thymidine Homodimer Anions. *J. Phys. Chem. B* **2012**, *116*, 13975–13981.
- (41) Storoniak, P.; Rak, J.; Ko, Y. J.; Wang, H.; Bowen, K. H. Photoelectron Spectroscopic and Density Functional Theoretical Studies of the 2'-Deoxycytidine Homodimer Radical Anion. *J. Chem. Phys.* **2013**, *139*, 075101.
- (42) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A. et al. *Gaussian 09*, revision B.01; Gaussian, Inc.: Wallingford, CT, 2009.
- (43) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Non-covalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Functionals. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
- (44) Ditchfield, R.; Hehre, W. J.; Pople, J. A. Self-Consistent Molecular-Orbital Methods. IX. An Extended Gaussian-Type Basis for Molecular-Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1971**, *54*, 724–728.
- (45) Hehre, W. J.; Ditchfield, R.; Pople, J. A. Self-Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian-Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1972**, *56*, 2257–2261.

(46) Chai, J. D.; Head-Gordon, M. Long-Range Corrected Hybrid Density Functionals with Damped Atom-Atom Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615–6620.

(47) Zhao, Y.; Truhlar, D. G. Density Functionals with Broad Applicability in Chemistry. *Acc. Chem. Res.* **2008**, *41*, 157–167.

(48) DiLabio, G. A.; Johnson, E. R.; Otero-de-la-Roza, A. Performance of Conventional and Dispersion-Corrected Density-Functional Theory Methods for Hydrogen Bonding Interaction Energies. *Phys. Chem. Chem. Phys.* **2013**, *15*, 12821–12828.

(49) Dennington, R.; Keith, T.; Millam, J. *GaussView*, version 5; Semichem Inc.: Shawnee Mission, KS, 2009.

(50) Gu, J.; Xie, Y.; Schaefer, H. F. Structural and Energetic Characterization of a DNA Nucleoside Pair and Its Anion: Deoxyriboadenosine (dA) - Deoxyribothymidine (dT). *J. Phys. Chem. B* **2005**, *109*, 13067–13075.

(51) Li, X.; Sanche, L.; Sevilla, M. D. Base Release in Nucleosides Induced by Low-Energy Electrons: A DFT Study. *Radiat. Res.* **2006**, *165*, 721–729.

(52) Svozil, D.; Frigato, T.; Havlas, Z.; Jungwirth, P. Ab Initio Electronic Structure of Thymine Anions. *Phys. Chem. Chem. Phys.* **2005**, *7*, 840–845.

(53) Mazurkiewicz, K.; Bachorz, R. A.; Gutowski, M.; Rak, J. On the Unusual Stability of Valence Anions of Thymine Based on Very Rare Tautomers: A Computational Study. *J. Phys. Chem. B* **2006**, *110*, 24696–24707.