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# DNA Nucleosides and Their Radical Anions: Molecular Structures and Electron Affinities

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***Abstract:*** The deoxyribonucleosides have been studied to determine the properties of combinations of 2-deoxyribose with each of the isolated DNA bases for both neutral and anionic species. We have used a carefully calibrated theoretical method [*Chem. Rev.* **2002**, *102*, 231], employing the B3LYP hybrid Hartree−Fock/DFT functional with the DZP++ basis set. Predictions are made of the geometric parameters, adiabatic electron affinities, charge distributions based on natural population analysis, and decomposition enthalpy for the neutral and anionic forms of the four 2′-deoxyribonucleosides in DNA: 2′-deoxyriboadenosine (dA), 2′-deoxyribocytidine (dC), 2′-deoxyriboguanosine (dG), and 2′-deoxyribothymidine (dT). Geometric changes in the anions show that the glycosidic bond exhibits little change with excess charge for the guanosine but significant shortening for the adenosine and for the pyrimidines. The zero-point corrected adiabatic electron affinities in eV for each of the 2′-deoxyribonucleosides are as follows: 0.06, dA; 0.09, dG; 0.33, dC; and 0.44, dT. These values are uniformly greater than those of the corresponding isolated bases (−0.28, A; −0.07, G; 0.03, C; 0.20, T) and the isolated 2-deoxyribose (−0.38) at the same level of theory. The vertical detachment energies of dT and dC are substantial, 0.72 and 0.94 eV, and these anions should be observable. A high VDE, 0.91 eV, is also found for dA but its anion is unlikely to be stable due to the small AEA of 0.06 eV. The high VDE reflects the fact that the molecular structures of the anions and the corresponding neutral species are quite different. Valence character is displayed for the SOMOs of dA, dC, and dT, while some component of diffuse character is visible in the SOMO of dG. Further analysis of electronic changes upon electron attachment include an examination of the NPA charges, which show that in the neutral 2′-deoxyribonucleosides the sum of NPA charges for every base is the same, −0.28 with the sum of 2-deoxyribose charges being positive, +0.28. In the anions, the trend in charge division varies based on the nature of the excess electron in the anions. Thermodynamically, the overall enthalpy change for the reaction of water with the neutral nucleosides to give bases and ribose is approximately zero. The analogous decomposition is exothermic by 8 to 11 kcal mol$^{-1}$ for the anions, indicating possible challenges for anionic gas-phase nucleoside exploration in the presence of water.

## I. Introduction

For both biological molecules and other species the determination of electron affinities can elucidate molecular character and help understand chemical processes. However, such determinations are challenging for both experiment and theory. Nevertheless, recent synergy between the two has resulted in the development of a comprehensive DFT bracketing technique which has been tested in conjunction with extensive experimental work.[1] The insights gained have advanced the molecular understanding of the interaction of molecules with excess negative charge by providing a reliable method for electron affinity determination. Such work has succeeded in producing fledgling illumination of the molecular basis for radiation damage as well as charge transfer in DNA. Electron affinity determinations for the DNA components of some parts of the polymeric unit, the nucleotide (composed of a base, a sugar, and a phosphate), provided clues for the effect of excess charge. Our results,[2] also consistent with a similar study[3] employing

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(1) Rienstra-Kiracofe, J. C.; Tschumper, G. S.; Schaefer, H. F.; Nandi, S.; Ellison, G. B. *Chem. Rev.* **2002**, *102*, 231.
(2) Wesolowski, S. S.; Leininger, M. L.; Pentchev, P. N.; Schaefer, H. F. *J. Am. Chem. Soc.* **2001**, *123*, 4023.


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DFT, for the isolated nucleic acid bases, yielded the B3LYP/DZP++ ordering

$$U > T > C \sim G > A$$

for their anionic stabilities based on adiabatic electron affinities. U was found to have a substantial positive electron affinity of 0.18 eV with T also similarly positive. The C and G electron affinities were close to zero and the electron affinity of A was substantially negative, −0.28 eV. Previous ab initio results gave more widely scattered results.[4,5,7,83] In our subsequent work, electron affinity determinations of the canonical Watson−Crick base pairs, GC[8] and AT,[9] showed that the presence of the complementary base stabilizes the anions by an effect analogous to that of microsolvation by one or two water molecules. Analysis of the effects of excess charge and electron affinity determination for the combination of these bases with 2-deoxyribose to form the DNA 2′-deoxyribonucleosides is the goal of the present study. There is much recent interest (2003 Gordon Conference, etc.) in the chemical physics of biomolecules in the gas phase. While individual nucleic acid bases[4,10−18] have been well studied in experimental gas phase work, gas-phase experimental studies of the isolated nucleosides are more limited. The experimental gas-phase studies include the resonant two-photon ionization spectra of laser desorbed, jet-cooled species,[19−21] the results of de Vries et al. for cytosine, guanosine, 2′-deoxyriboguanosine, and 3′-deoxyriboguanosine; and the work of Rozenberg, Jung, and Shoham in a recent FTIR study[22] for adenosine, cytidine, and uridine. A gas phase study of H/D exchange was also carried out for nucleo*tides*.[23] Liquid-phase studies of nucleosides include femtosecond fluorescence up-conversion spectroscopy, performed for thymine, thymidine, and thymidine 5′-monophosphate,[24] as well as one-electron oxidation studies on forms of 2′-deoxyriboguanosine.[25,26] Solid-phase spectroscopic experiments,[22,27−30] X-ray crystal structures of DNA fragments containing nucleosides,[31−33] and a recent NMR experiment[34] have also been done. Theoretically, nucleosides have also been studied.[27,34−47] However, the electron affinities of the nucleosides have yet to be measured experimentally or accurately predicted with theory.

Only one early study[48] attempted a semiempirical estimate of electron affinities for halogenated nucleosides. In that work, the LUMO for compounds of interest was taken from MNDO calculations and calibrated in accordance with known values for related compounds to yield a quasi electron affinity. With our reliably calibrated B3LYP/DZP++ method, a more accurate bracketing of these electron affinities is now possible.

Since nucleosides present a conformational challenge and the choice of conformation depends on the information sought, some explanation as to the rationale for the initial geometries is warranted. (Note that this discussion utilizes the nomenclature standardized in Saenger's *Principles of Nucleic Acid Structure*.) The reasoning, then, that drives the choice of nucleoside conformation in our work focuses on selecting a conformation where the influence of excess charge would be evident in significant bonds that could provide clues for the mechanism of bond cleavage analogous to that of single strand breaks (SSBs) resulting from impingement of radiation. The pseudorotation of 2-deoxyribose in nucleosides and the parameters for its conformations were originally described in 1972 by Altona and Sundaralingam[49] and have been studied extensively.[38,50−55] Foloppe and MacKerell performed comprehensive studies of nucleoside conformations and the relation of different bases to


(3) Wetmore, S. D.; Boyd, R. J.; Eriksson, L. A. *Chem. Phys. Lett*. **2000**, *322*, 129.
(4) Desfrancois, C.; Periquet, V.; Bouteiller, Y.; Schermann, J. P. *J. Phys. Chem. A* **1998**, *102*, 1274.
(5) Russo, N.; Toscano, M.; Grand, A. *J. Comput. Chem*. **2000**, *21*, 1243.
(6) Colson, A. O.; Sevilla, M. D. *Int. J. Radiat. Biol*. **1995**, *67*, 627.
(7) Chen, E. S. D.; Chen, E. C. M. *Biochem. Biophys. Res. Comm*. **2001**, *289*, 421.
(8) Richardson, N. A.; Wesolowski, S. S.; Schaefer, H. F. *J. Phys. Chem. B* **2003**, *107*, 848.
(9) Richardson, N. A.; Wesolowski, S. S.; Schaefer, H. F. *J. Am. Chem. Soc*. **2002**, *124*, 10 163.
(10) Desfrancois, C.; Abdoul-Carime, H.; Schermann, J. P. *J. Chem. Phys*. **1996**, *104*, 7792.
(11) Chen, E. C. M.; Chen, E. S. D.; Wentworth, W. E. *Biochem. Biophys. Res. Commun*. **1990**, *171*, 97.
(12) Wiley, J. R.; Robinson, J. M.; Ehdaie, S.; Chen, E. C. M.; Chen, E. S. D.; Wentworth, W. E. *Biochem. Biophys. Res. Commun*. **1991**, *180*, 841.
(13) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Snodgrass, J. T.; Bowen, K. H. *J. Chem. Phys*. **1996**, *104*, 7788.
(14) Schiedt, J.; Weinkauf, R.; Neumark, D. M.; Schlag, E. W. *Chem. Phys*. **1998**, *239*, 511.
(15) Huels, M. A.; Hahndorf, I.; Illenberger, E.; Sanche, L. *J. Chem. Phys*. **1998**, *108*, 1309.
(16) Chen, E. C. M.; Chen, E. S. D. *J. Phys. Chem. B* **2000**, *104*, 7835.
(17) Bass, A. D.; Sanche, L. *Low Temp. Phys*. **2003**, *29*, 202.
(18) He, Y. G.; Wu, C. Y.; Kong, W. *J. Phys. Chem. A* **2003**, *107*, 5145.
(19) Nir, E.; Imhof, P.; Kleinermanns, K.; de Vries, M. S. *J. Am. Chem. Soc*. **2000**, *122*, 8091.
(20) Nir, E.; Muller, M.; Grace, L. I.; de Vries, M. S. *Chem. Phys. Lett*. **2002**, *355*, 59.
(21) Nir, E.; Plutzer, C.; Kleinermanns, K.; de Vries, M. S. *Eur. Phys. J. D*. **2002**, *20*, 317.
(22) Rozenberg, M.; Jung, C.; Shoham, G. *Phys. Chem. Chem. Phys*. **2003**, *5*, 1533.
(23) Freitas, M. A.; Shi, S. D.; Hendrickson, C. L.; Marshall, A. G. *J. Am. Chem. Soc*. **1998**, *120*, 10 187.
(24) Gustavsson, T.; Sharonov, A.; Markovitsi, D. *Chem. Phys. Lett*. **2002**, *351*, 195.
(25) Steenken, S.; Jovanovic, S. V. *J. Am. Chem. Soc*. **1997**, *119*, 617.
(26) Ravanat, J.; Saint-Pierre, C.; Cadet, J. *J. Am. Chem. Soc*. **2003**, *125*, 2030.
(27) Bailey, L. E.; Navarro, R.; Hernanz, A. *Biospectoscopy* **1997**, *3*, 47.
(28) Lee, S. A.; Anderson, A.; Griffey, R. H.; Mohan, V. *J. Raman Spectroc*. **2000**, *31*, 891.
(29) Li, J.; Lee, S. A.; Anderson, A.; Lettress, L.; Smith, W.; Griffey, R. H.; Mohan, V. *J. Raman Spectrosc*. **2001**, *32*, 795.
(30) Lee, S. A.; Li, J.; Anderson, A.; Smith, W.; Griffey, R. H.; Mohan, V. *J. Raman Spectrosc*. **2003**, *34*, 183.
(31) Reddy, B. S.; Viswamitra, M. A. *Acta Cryst*. **1975**, *B31*, 19.
(32) Seeman, N. C.; Rosenberg, J. M.; Suddath, F. L.; Kim, J. J. P.; Rich, A. *J. Mol. Biol*. **1976**, *104*, 109.
(33) Rosenberg, J. M.; Seeman, N. C.; Day, R. O.; Rich, A. *J. Mol. Biol.* **1976**, *104*, 145.
(34) Stueber, D.; Grant, D. M. *J. Am. Chem. Soc*. **2002**, *124*, 10539.
(35) Cornell, W. D.; Cieplak, P.; Bayly, C. I.; Gould, I. R.; Merz, K. M.; Ferguson, D. M.; Spellmeyer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc*. **1995**, *117*, 5179.
(36) Berthier, G.; Cadioli, B.; Gallinella, E.; Aamouche, A.; Ghomi, M. *J. Mol. Struct*. **1997**, *390*, 11.
(37) Polak, M.; Mohar, B.; Kobe, J.; Plavec, J. *J. Am. Chem. Soc*. **1998**, *120*, 2508.
(38) Leulliot, N.; Ghomi, M.; Scalmani, G.; Berthier, G. *J. Phys. Chem. A* **1999**, *103*, 8716.
(39) Hocquet, A.; Leulliot, N.; Ghomi, M. *J. Phys. Chem. B* **2000**, *104*, 4560.
(40) Shishkin, O. V.; Pelmenschikov, A.; Hovorun, D. M.; Leszczynski, J. *J. Mol. Struct.* **2000**, *526*, 329.
(41) Brunaud, G.; Castet, F.; Fritsch, A.; Kreissler, M.; Ducasse, L. *J. Phys. Chem. B* **2001**, *105*, 12 665.
(42) Foloppe, N.; Nilsson, L.; MacKerell, A. D. *Biopolymers* **2002**, *61*, 61.
(43) Foloppe, N.; Hartmann, B.; Nilsson, L.; MacKerell, A. D. *Biophys. J*. **2002**, *82*, 1554.
(44) Harris, D. G.; Shao, J.; Anderson, J. M.; Marx, D. P.; Zimmerman, S. S. *Nucleosides, Nucleotides, Nucleic Acids* **2002**, *21*, 803.
(45) Louit, G.; Hocquet, A.; Ghomi, M. *Phys. Chem. Chem. Phys*. **2002**, *4*, 3843.
(46) Mishra, S. K.; Mishra, P. C. *J. Comput. Chem*. **2002**, *23*, 530.
(47) Munzarova, M. L.; Sklenar, V. *J. Am. Chem. Soc*. **2003**, *125*, 3649.
(48) Musser, S. M.; Kelley, J. A. *Organ. Mass Spectromet*. **1993**, *28*, 672.
(49) Altona, C.; Sundaralingam, M. *J. Am. Chem. Soc*. **1972**, *94*, 8205.
(50) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984.
(51) Colson, A. O.; Besler, B.; Sevilla, M. D. *J. Phys. Chem*. **1992**, *96*, 9787.
(52) Colson, A. O.; Sevilla, M. D. *J. Phys. Chem*. **1995**, *99*, 3867.
(53) Plavec, J.; Roselt, P.; Foldesi, A.; Chattopadhyaya, J. *Magn. Reson. Chem*. **1998**, *36*, 732.
(54) Brameld, K. A.; Goddard, W. A. *J. Am. Chem. Soc*. **1999**, *121*, 985.
(55) Talbot, F. O.; Simons, J. P. *Phys. Chem. Chem. Phys*. **2002**, *4*, 3562.

the stability of various 2-deoxyribose ring conformations.[43,56] Energetically, the conformations explored are within a range of about 10 kcal $mol^{-1}$.

The present work investigates the isolated nucleoside as it appears in the DNA strand and isolable portions; other work cited above and references therein have investigated portions of the potential energy surface for the various configurations. To make the simulation for the effect of excess charge more relevant to DNA itself, the conformation in which the base and the 2-deoxyribose are anti to one another was selected to be as it appears in DNA. Fortuitously, as noted by MacKerall et al.,[43] this conformation is also predicted to be lower in energy according to theory for nucleosides, although it is higher in energy for some nucleo*tides*. Additionally, the sugar conformation was chosen to facilitate comparison of geometric parameters with the crystal structures of Rich and co-workers.[32,33] Previously, these X-ray data served as the primary comparisons for geometric parameters predicted in theoretical studies of bases and base pairs.[57−62] Note that comparison of T and U is reasonable since T differs from U only in the omission of a methyl group on the ring. In Rich's work the geometric parameters for very small fragments (two polymeric units: sodium adenylyl-3′,5′-uridine hexahydrate $(ApU)_2$ in one structure and sodium guanylyl-3′,5′-cytidine nonahydrate $(GpC)_2$ in the other) resembling type A DNA were determined; therefore, the starting points for our optimizations were chosen for the 2′-deoxyribonucleosides with northern pseudorotation minima where C3′ is endo with respect to the base, characteristic of type A DNA. One further point is that this combination of the anti and C3′ endo was also found to be lower in energy than the syn and C3′ endo.[40] In this work, geometric changes in the anion with respect to the neutral are predicted. At these fully optimized structures, the electron affinity is determined from the difference of the total zero point corrected energies of the anion and neutral. Additionally, analysis of the neutral molecules' dipole moments, variation in neutral and anionic natural population charges, along with decomposition energies, are explored as a means of explaining the effects of negative charge for the base plus sugar (nucleoside) component of DNA.

## II. Theoretical Methods

In accord with our previous work,[1,2,9] a DFT bracketing technique was employed in which five generalized gradient approximation (GGA) exchange-correlation density functionals were used, with good middle range values produced by B3LYP. We determined optimized geometries, absolute vibrationally zero-point corrected energies, and natural charges for the four nucleosides found in DNA: 2′-deoxyriboadenosine (dA), 2′-deoxyriboguanosine (dG), 2′-deoxyribocytidine (dC), and 2′-deoxyribothymidine (dT).

For the neutral molecules, the restricted B3LYP formalism is employed while the unrestricted formalism is used for anions. The B3LYP functional is a combination of exchange from Becke's 3-parameter HF/DFT hybrid exchange functional (B3)[63] with the dynamical correlation functional of Lee, Yang, and Parr (LYP).[64] The GAUSSIAN 94 and GAUSSIAN 98 systems of DFT programs[65,66] were used for all computations. Within the precision reported here, identical geometries and energy differences were obtained with these two programs.

This work was carried out using double-$\zeta$ quality basis sets with polarization and diffuse functions (denoted DZP++). The DZP++ basis sets were constructed by augmenting the Huzinage−Dunning[67,68] set of contracted double- $\zeta$ Gaussian functions with one set of *p*-type polarization functions for each H atom and one set of five *d*-type polarization functions for each C, N, and O atom ($\alpha_p(H) = 0.75$, $\alpha_d(C) = 0.75$, $\alpha_d(N) = 0.80$, $\alpha_d(O) = 0.85$). To complete the DZP++ basis, one even tempered diffuse *s* function was added to each H atom while sets of even tempered diffuse *s* and *p* functions were centered on each heavy atom. The even tempered orbital exponents were determined according to the prescription of Lee and Schaefer[69]

$$\alpha_{\text{diffuse}} = (1/2)\left(\frac{\alpha 1}{\alpha 2} + \frac{\alpha 2}{\alpha 3}\right)\alpha 1 \qquad (1)$$

where $\alpha_1$, $\alpha_2$, and $\alpha_3$ are the three smallest Gaussian orbital exponents of the *s*- or *p*-type primitive functions for a given atom ($\alpha_1 < \alpha_2 < \alpha_3$). The final DZP++ set contains six functions per H atom (5s1p/3s1p) and nineteen functions per C, N, or O atom (10s6p1d/5s3p1d), yielding a total of 420, 439, 382, and 407 contracted Gaussian functions for dA, dG, dC, and dT, respectively. This basis has the tactical advantage that it has previously been used in comprehensive calibrative studies[1] of a wide range of electron affinities. Both the neutral and anion stationary points were optimized via analytic gradients until the residual RMS gradient was less than $10^{-4}$ hartree/bohr. Numerical integrations were performed using the GAUSSIAN 94[65] default grid consisting of 75 radial shells with 302 angular points per shell. Each valence adiabatic electron affinity was computed as the difference between the absolute energies of the appropriate neutral and anion species at their respective optimized geometries

$$AEA = E_{\text{neut}} - \text{E}_{\text{ani}} \qquad (2)$$

To analyze the charge distribution, molecular orbital plots were constructed from GAUSSIAN checkpoint files of the appropriate B3LYP/DZP++ optimized structures utilizing the ChemBats3d software package.[70] Natural Population Atomic (NPA) charges were determined using the B3LYP functional and the DZP++ basis set with the Natural Bond Order (NBO) analysis of Reed and Weinhold.[71−74]

## III. Results

**A. Geometries.** The fully optimized geometries of the purine 2′-deoxyribonucleosides obtained from the selected starting


(56) Foloppe, N.; MacKerell, A. D. *Biophys. J.* **1999**, *76*, 3206.
(57) Brameld, K. A.; Dasgupta, S.; Goddard, W. A. *J. Phys. Chem. B* **1997**, *101*, 4851.
(58) Hobza, P.; Sponer, J. *Chem. Rev.* **1999**, *99*, 3247.
(59) Guerra, C. F.; Bickelhaupt, F. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 2942.
(60) Desfrancois, C.; Carles, S.; Schermann, J. P. *Chem. Rev.* **2000**, *100*, 3943.
(61) Li, X.; Cai, Z.; Sevilla, M. D. *J. Phys. Chem. B* **2001**, *105*, 10 115.
(62) Guerra, C. F.; Bickelhaupt, F. M.; Snijders, J. G.; Baerends, E. J. *J. Am. Chem. Soc.* **2000**, *122*, 4117.
(63) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
(64) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785.
(65) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. A.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian 94, revision c.3, Pittsburgh, PA: Gaussian, Inc., 1995.
(66) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. A.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 98, revision a.10, Pittsburgh, PA: Gaussian, Inc., 2001.
(67) Huzinaga, S. *J. Chem. Phys.* **1965**, *42*, 1293.
(68) Dunning, T. H. *J. Chem. Phys.* **1970**, *53*, 2823.
(69) Lee, T. J.; Schaefer, H. F. *J. Chem. Phys.* **1985**, *83*, 1784.
(70) CambridgeSoft Corporation. Cs chem3d std. Cambridge, MA 02140-2317, 1999.

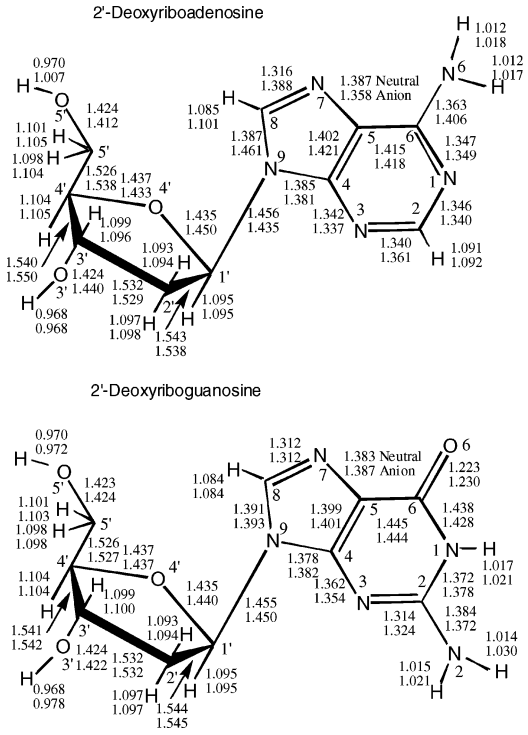


***Figure 1.*** Bond lengths in the neutral and anionic purine nucleosides, deoxyadenosine and deoxyguanosine. Distances are reported in angstroms.

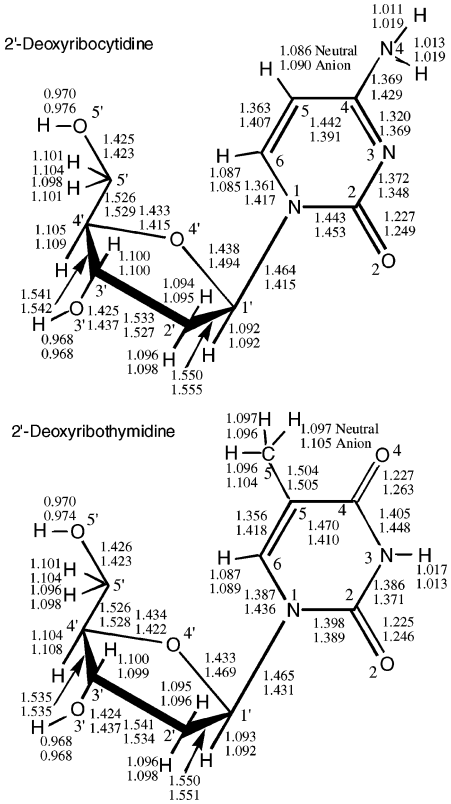


***Figure 2.*** Bond lengths in the neutral and anionic pyrimidine nucleosides, deoxycytidine and deoxythymidine. Distances are reported in angstroms.

points (as explained in the Introduction) are depicted in Figure 1, while those of the pyrimidines are depicted in Figure 2. One general trend is that the bonds to the amino groups and to some extent the substituent oxygens of the rings lengthen in the anions. Another trend is that the glycosidic bond (C1′−N9 in the purines and C1′−N1 in the pyrimidines) shortens in the anions. Also, the nonplanar character of the amino groups increases significantly in the anions of 2′-deoxyriboadenosine (dA) and 2′-deoxyribocytidine (dC). However, this change is less obvious in the 2′-deoxyriboguanosine (dG) anion. A striking alteration in geometry for the thymidine, cytidine, and adenosine is that the ring systems of these nucleosides distort significantly in the anions. The H-linked C atom next to the glycosidic bond in these three nucleosides exhibits the $sp^3$ hybrid characteristics.

In examining the DNA purine nucleoside geometry changes, the anion of dA displays more variation than the anion of dG. There are no significant geometric variations found in the dG anion as compared with the neutral species. The RMS difference between dG and its anion has been found to be only 0.06 Å. The only meaningful geometrical alteration in the anion of dG is that the H(O5′)...O4′ atomic distance decreases to 2.36 Å, about 0.16 Å shorter than that of dG. Great RMS difference between dA and the corresponding anion has been determined to be 0.63 Å. The strong interaction between H(O5′) and C8 of adenosine is characterized by the short atomic distance of about 2 Å in the anion of dA, implying that the electron attached in the dA anion is partly located on C8. Other geometric evidence for this implication can be seen from the great elongations (about 0.08 Å) in C8−N7 and C8−N9 bond distances in the adenosine. Meanwhile, remarkably intensified pyramidization of N6 (−127° vs −157° for the C6N6HH′ dihedral angle) in the anion of dA indicates that this amino group also hosts the excess charge. The glycosidic bond in the anion shortens compared to the neutral by 0.02 Å in dA but slightly shortens, only by 0.006 Å in dG. In the X-ray structures of (ApU)2 and (GpC)2, this glycosidic bond distance agrees with our results for dG, differing only by 0.007 Å. However, the X-ray determined glycosidic bonds of 1.481 Å and 1.485 Å are remarkable longer than our theoretical prediction of 1.456 Å for dA.

Scrutinizing the DNA pyrimidine nucleoside geometry perturbations on addition of excess charge yields a similar trend for dT and dC. The RMS differences between the anions and the neutral species amount to 0.32 Å and 0.17 Å for dT and dC, respectively. The C6 atom in both nucleosides displays the tendency of pyramidization in the anions. However, the pyramidization of C6 is much more profound in dT than in dC. The dihedral angle (N1C5N6H6) amounts to 153° in the dT anion, whereas it is 166° in the dC anion. On the other hand, the increase of pyramidation of N4 in dC (−120° vs −154° for the C4N4HH′ dihedral angle) also suggests the accumulation of negative charge near this site. Consequently, the negative charge is expected to be less populated on C6 in dC as compared with that in dT. Significant shortening (∼0.05 Å) occurs in the C4−C5 bond of the pyrimidine ring, but a lengthening in the C5−C6 and N1−C6 bonds is apparent for both pyrimidine nucleosides. A remarkable elongation (0.04∼0.05 Å) in the N3−C4 bond is also obvious for both dT and dC. The neutral bond lengths are quite similar to the modified B3LYP/D95 results of Stueber and Grant[34] in their study of chemical shifts for dC, focusing on the base. The glycosidic bond lengths in both neutral species agree reasonably with the X-ray structures, differing by

(71) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735.
(72) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 1736.
(73) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.
(74) Reed, A. E.; Schleyer, P. R. *J. Am. Chem. Soc.* **1990**, *112*, 1434.

***Table 1.*** Dipole Moments of the Neutral Bases and Nucleosides in Debyes

| | | | | | |
|---|---|---|---|---|---|
| nucleosides | dA | dG | dC | dT | |
| B3LYP/DZP++ (this research) | 2.39 | 7.08 | 5.94 | 4.46 | |
| bases | A | G | C | T | |
| B3LYP/DZP++[a] | 2.51 | 6.74 | 6.79 | 4.59 | |
| bases | A | G | C | T | U |
| experiment | 2.27[b] | 6.55[b] | 6.02[b] | 4.51[b] | 3.9[d] |
| | | | 7.99[c] | 3.9[d] | |

[a] Unpublished data from the research in ref 2. [b] Ref 77. [c] Ref 78. [d] Ref 82.

***Table 2.*** Zero-Point Vibrationally Corrected Electron Affinities (in eV) for 2′-Deoxyribonucleosides Using the B3LYP Functional with the DZP++ Basis Set[f]

| nucleosides | dA | dG | dC | dT |
|---|---|---|---|---|
| $EA_{ad}$ | 0.06 (−0.05) | 0.09 (0.01) | 0.33 (0.21) | 0.44 (0.31) |
| vertical detachment energy (VDE) | 0.91 | 0.05 | 0.72 | 0.94 |
| bases[a] | A | G | C | T |
| $EA_{ad}$ | −0.28(−0.37) | −0.07(−0.14) | 0.03(−0.09) | 0.20(0.06) |
| experiment (gas) | −0.45[b] | | −0.55[b]; > 0[c] | ∼0[b]; > 0[c] |
| experiment (scaled)[d] | 0.95 ± 0.05 | 1.51 ± 0.05 | 0.56 ± 0.05 | 0.79 ± 0.05 |
| experiment (pes)[e] | | | 0.13 ± 0.12 | 0.12 ± 0.12 |

[a] Reference 2, in which the original $EA_{ad}$ value of −0.10 for G has been corrected. [b] Reference 81. [c] Reference 15. [d] Scaled reduction potentials. See ref 16. [e] Extrapolated values from photo electron spectra for microsolvated clusters. See ref 14. [f] Values without zero-point correction are given in parentheses.

about 0.02 Å for both dT and dC. The glycosidic bond in the anion shortens compared to the neutral by 0.03 Å in dT and significantly shortens, by 0.05 Å in dC. The whole trend in the geometric alterations in the anions of the pyrimidine nucleosides implies that the excess charge resides on the nucleic acid bases.

**B. Dipole Moments: Insight into the Geometric Variations.** Examination of the dipole moments for these molecules provides an explanation for the extent and magnitude of the geometric changes. In general, the dipole moments of the nucleosides are close to those of the isolated bases. Table 1 compiles the dipole moments predicted at the B3LYP/DZP++ level for the isolated nucleic acid bases and the 2′-deoxyribonucleosides. For comparison, available experimental[77,78] results are included. Interestingly, the B3LYP/DZP++ dipole moments of the nucleosides (except for dG) exhibit closer agreement with experiment than the isolated nucleic acid bases. The dipole moment of dG is the largest among all the species. In general, a smaller dipole moment correlates with greater geometric changes in the respective anion. Since larger dipole moments increase the likelihood of dipole bound anions,[79,80] the above observation is due to the nucleosides with larger dipole moments having a greater tendency toward anion dipole bound character. In a dipole-bound molecular system, the "last" electron resides in a diffuse orbital and does not directly affect bonds or cause geometrical distortions, as suggested for the anion of dG.

**C. Adiabatic Electron Affinities.** Table 2 lists B3LYP/DZP++ zero-point corrected adiabatic electron affinities, corresponding to the difference in total energies of the neutral and anionic species for the DNA nucleosides. Included for comparison are the values for the isolated bases, previously determined with this B3LYP/DZP++ method.[2] Also included are experimental gas phase,[4,15,81] scaled reduction potential,[16] and extrapolated photoelectron spectra[14] determinations. Analyzing the AEAs of the nucleosides shows that the addition of $\beta$-D-2-deoxyribose to each base increases the electron affinity for the combined moiety over the isolated base. Note that this level of theory predicts a substantially negative adiabatic electron affinity of −0.38 eV of $\beta$-D-2-deoxyribose itself. These theoretical results confirm that interaction between the sugar and the base results in anionic stabilities not found either species alone.

The increase in adiabatic electron affinity in the nucleosides over their isolated base counterparts is the least for 2′-deoxyriboguanosione, $\Delta$(AEA) = 0.16 eV. This purine base has a predicted negative electron affinity (i.e., unbound anion), but likely forms a bound nucleoside anion. Because the geometry of dG differs only slightly from its anion, the excess charge in dG seems to be bound through its large dipole moment. The possibility of the existence of dG anion possessing an AEA of 0.09 eV is still in question with the ±0.12 error bracket of this method.[1] The accommodation of excess charge in dA is likely through greater geometric perturbations. However, even given the greater geometric shifts, the nature of $dA^-$ having an AEA of 0.06 ± 0.12 eV remains uncertain.

For the pyrimidines, the increases in the electron affinities for the nucleosides over the separate bases are similar to that of adenosine. With the change of $\Delta$(AEA) = 0.30 eV, the predicted electron affinity of dC is 0.33 ±0.12 eV. The other pyrimidine nucleoside, dT, shows an electron affinity of 0.44 eV which is an increase of $\Delta$(0.24 eV) over the base itself. Although the large dipole moments seem to benefit the accommodation of excess negative charge, the significant geometric differences between the neutral and anionic forms of dT and dC suggests that the geometry change dominates the capacity for hosting the excess charge.

The vertical detachment energies of dT and dC are substantial, 0.72 and 0.94 eV, and these anions should be observable. Although a high VDE, 0.91 eV, is also found for dA, its anion may be less stable due to the small AEA of 0.06 eV. The high VDE reflects the fact that the molecular structures of the anion and the corresponding neutral species are quite different. It should be noted that the large difference between the VDE and the AEA of dA corresponds specifically to the great geometric alteration in the anion of dA. The differences between the VDE and the AEA for the nucleosides are found to be well correlated to the geometrical RMS differences between the anions and the neutral species.

**D. Charge Distributions.** These observations fit in well with the known geometrical consequences of dipole moments of neutral molecules and their charge interaction. The magnitude of the dipole moment plays a critical role in the formation of dipole bound anions,[79,80] and examination of the orbital which the "last" electron occupies reveals the character of this orbital.

(75) Melvin, T.; O'Neill, P.; Jones, G. D. D. *Int. J. Radiat. Biol*. **1994**, *66*, 499.
(76) Agapakis-Causse, C.; Bosca, F.; Castell, J. V.; Hernandez, D.; Marin, M. L.; Marrot, L.; Miranda, M. A. *Photochem. Photobiol*. **2000**, *71*, 499.
(77) Guckian, K. M.; Schweitzer, B. A.; Ren, R. X.; Sheils, C. J. *J. Am. Chem. Soc*. **2000**, *122*, 2213.
(78) Manzur, M. E.; Romano, E.; Vallejo, S.; Wesler, S.; Suvire, F.; Enriz, R. D.; Molina, M. A. A. *J. Mol. Liq*. **2001**, *94*, 87.
(79) Simons, J.; Jordan, K. D. *Chem. Rev*. **1987**, *87*, 535.
(80) Li, X.; Cai, Z.; Sevilla, M. D. *J. Phys. Chem. A* **2002**, *106*, 1596.
(81) Periquet, V.; Moreau, A.; Carles, S.; Schermann, J. P.; Desfrancois, C. *J. Electron Spectrosc. Relat. Phenom*. **2000**, *106*, 141.
(82) Liptay, W., Lim, E. C., Ed.; Excited States Vol. 1. Academic Press: New York, 1974.
(83) Colson, A. O.; Sevilla, M. D. *Int. J. Radiat. Biol*. **1995**, *67*, 627.
(84) Sanche, L. *Mass Spect. Revs*. **2002**, *21*, 349.

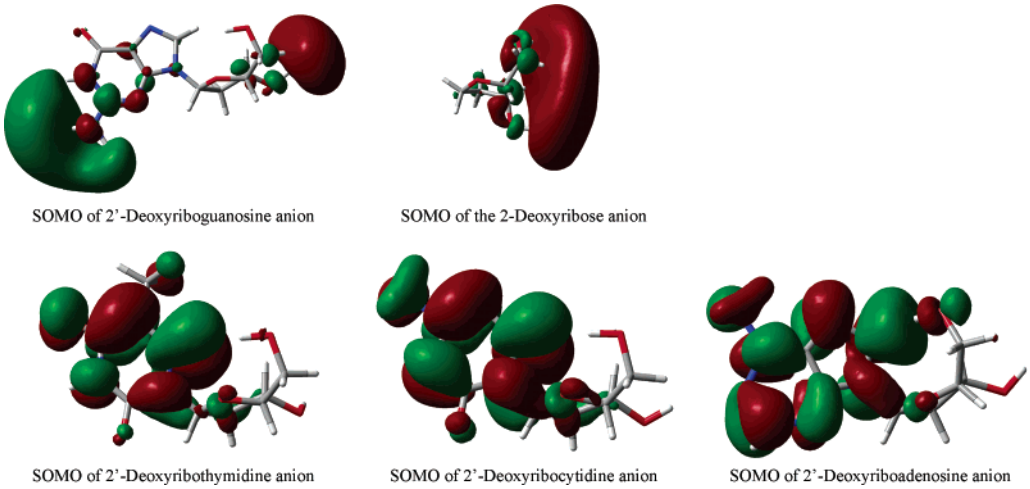


***Figure 3.*** Comparison of SOMOs of the nucleoside anions. The SOMOs of adenosine, thymidine, and cytidine display entirely valence character while that of guanosine appears to display some diffuse character. The SOMO of 2-deoxyribose anion is displayed for comparison. The feature of the SOMO of the G anion and of the 2-deoxyribose anion can be seen from the base moiety and the ribose part, respectively, in the anion of dG.

Plots of the singly occupied molecular orbitals (SOMOs) for each nucleoside anion are shown in Figure 3. The nucleoside, dG, with the least geometric perturbation displays dipole-bound character in the SOMO of its anion. Notice that the SOMO of the 2-deoxyribose anion also exhibits the typical dipole-bound character. In addition, the SOMO of the G anion also reveals dipole-bound character.[9] Therefore, it is not surprising to observe the dipole-bound characteristics of the SOMO of the anion of 2′-deoxyriboguanosine. This feature of the SOMO of the G anion and of the 2-deoxyribose anion may be seen from the base moiety and the ribose part, respectively, in the anion of dG. The SOMOs of the thymidine and the cytidine anions display valence character. Due to the great electron affinity difference between the 2′-deoxyribose and the pyrimidine bases, the electronic charge in the anion of thymidine and cytidine resides mainly in the base. Consequently, the SOMO of the 2′-deoxyribothymidine anion and that of 2′-deoxyribocytidine anion resembles the SOMO of their parent base anions[8,9] (thymine and cytosine), respectively. The SOMO of 2′-deoxyriboadenosine is similar to the SOMO of the anion of adenine.[8] However, the diffuse portion of the SOMO may be seen around H(O5′) of the ribose and C8 of the adenine in adenosine. The diffuse part of the SOMO around H(O5′) and C8 suggests a relatively strong interaction between these two atoms. The location of the excess electron in the nuclear framework indicates that dA might indeed bind further electron density, although the value determined for the electron affinity places the stability in the uncertain region.

The location of excess charge may also be followed by analysis of the change in atomic charges. Figure 4 displays the charges determined by Weinhold's natural population analysis (NPS) for the neutral and anionic purine nucleosides; Figure 5 shows these charges for the neutral and anionic nucleosides pyrimidines. Examination shows that charge increases are greatest for the H-linked C next to the glycosidic bond for all the covalent bound anions, which is consistent with the characteristics of the $sp^3$ electronic configuration of this atom as revealed in the discussion of the geometric alterations. In the dipole-bound anion, $dG^-$, the charge increases are mainly found around the hydrogens of the amino group of guanine base and the H(O3′) of the sugar. The excess charges on the hydrogen

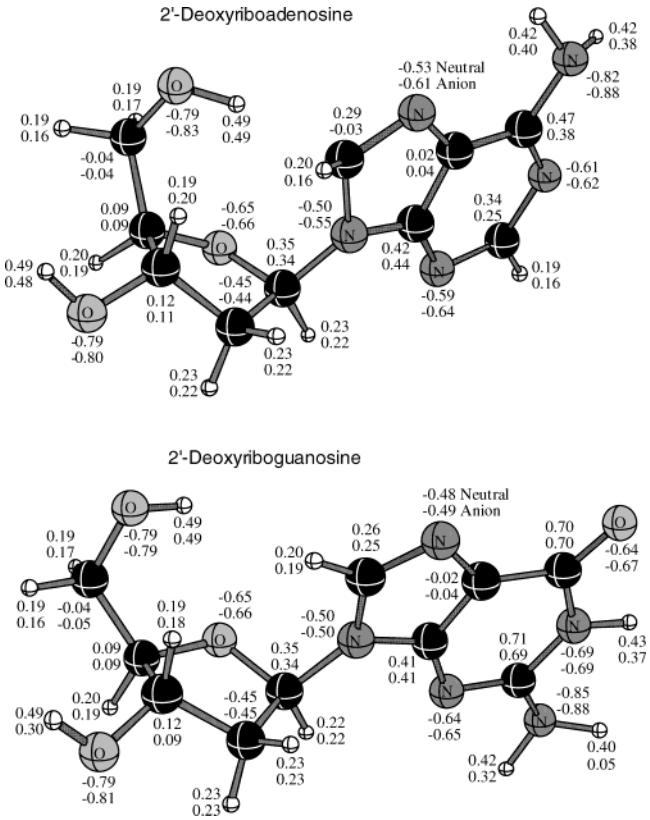


***Figure 4.*** Neutral and anionic Natural Population Analysis (NPA) charges for each atom in the purine nucleosides.

are congruent with the lengthening of the H−O3′ bond and also indicate a slight weakening of this bond and susceptibility to breaking, with subsequent radical or closed-shell anion formation. The same bond weakening might also apply to the O−P bonds in the nucleoside and serve as a precursor to single strand breaks (SSBs) in DNA.

The location of charge on the constituent parts of the nucleoside also provides some insight into the overall electronic effect of negative charge. Table 3 shows how the charge is distributed between 2-deoxyribose and the bases in the neutral, as well as in the anionic species. In the neutral nucleosides, the total residual charges of the atoms are unequally distributed

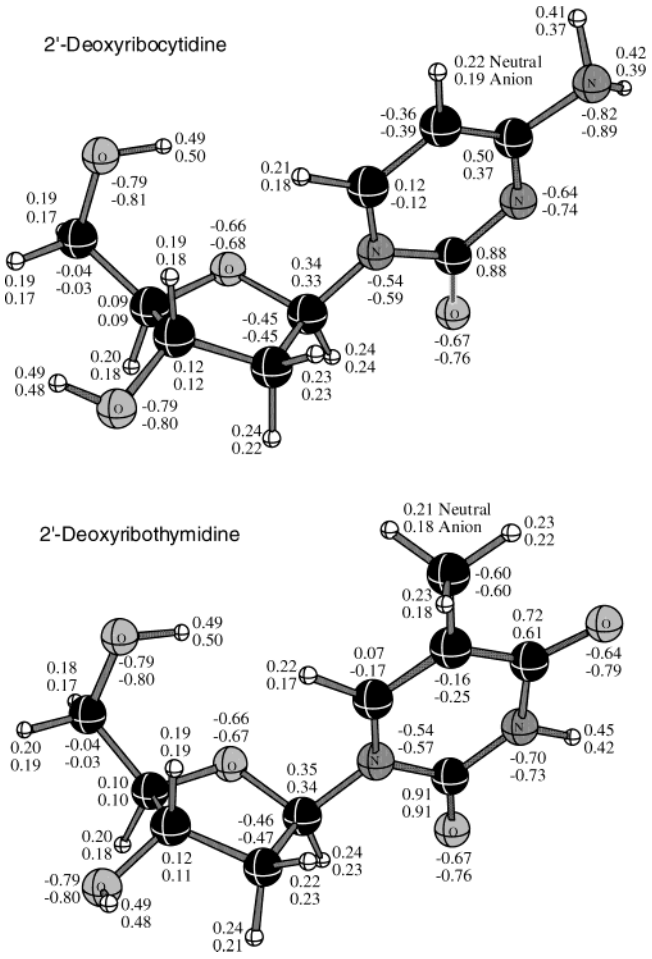


***Figure 5.*** Neutral and anionic Natural Population Analysis (NPA) charges for each atom in the pyrimidine nucleosides.

***Table 3.*** Sum of the Charges Residing on the 2-Deoxyribose and on the Base within Each 2′-Deoxyribonucleoside, Determined with Natural Population Analyses

| | neutral | | anion | |
|---|---|---|---|---|
| | ribose | base | ribose | base |
| dA | 0.29 | −0.29 | 0.13 | −1.13 |
| dG | 0.28 | −0.28 | −0.07 | −0.93 |
| dC | 0.28 | −0.28 | 0.12 | −1.12 |
| dT | 0.29 | −0.29 | 0.16 | −1.16 |

between the sugar and base. This result is most striking in that for every neutral 2′-deoxyribonucleoside the charge division is basically the same with a sum of NPA charges of −0.28 to −0.29 for the base and 0.28 to 0.29 for the 2-deoxyribose. For the anionic species, the charge division falls along the lines of the nature of the excess electron in the anions. For dG, in which the excess electron appears to be dipole bound, the base G has the least charge, −0.93, whereas in the other covalent bound anions the bases have charges of −1.12 to −1.16.

**E. Decomposition.** One additional consideration is the effect of charge on the enthalpy of decomposition. Previously, reasonable agreement (roughly ±3 kcal mol$^{-1}$) was obtained for the base pairing energies of the canonical Watson−Crick pairs at the B3LYP/DZP++ level.[8,9] Using the same method the enthalpies for decomposition of the 2′-deoxyribonucleosides are predicted. While not representative of a biochemical pathway, the overall reaction chosen to gauge the tendency to dissociation is the addition of water to the nucleoside, resulting in a base and a sugar. The advantage of this determination is that it avoids an open-shell doublet present in the calculation of the homolytic cleavage for the base and sugar at the glycosidic bond. Such an approach might lead to questionable results due to the difference in spin states for the reactant and products.

***Table 4.*** Zero-Point Vibrationally Corrected Enthalpies of Reaction in kcal/mol$^{-1}$ for the Reaction $H_2O$ + 2′-Deoxyribonucleoside → Base + 2-Deoxyribose

| | neutral | anion |
|---|---|---|
| dA | 1.5 | −7.6 |
| dG | 2.0 | −11.0 |
| dC | 0.2 | −9.9 |
| dT | −0.1 | −11.4 |

Table 4 shows the reaction enthalpies for the overall process of water and 2′-deoxyribonucleoside addition, resulting in separation to a base and a 2-deoxyribose. For the neutral species, the values are close to zero with the purines being residually less likely to decompose than the pyrimidines. Although in terms of precision, these quantities are close for the isolated 2′-deoxyribonucleosides, they may explain the difficulty of gas phase observations for these molecules. However, these results suggest even greater challenges in the observation and study of these molecules as anionic species in the presence of water. The enthalpies are all *significantly* negative as this process is intrinsically a spontaneous reaction.

## IV. Conclusions

This examination of geometries, energies, and charge distribution of the neutral and anionic 2′-deoxyribonucleosides has shown the following:

1. The presence of negative charge has strong impact on the pyrimidine systems and dA of the purine nucleosides, where the C−N glycosidic bond decreases significantly. No correspondingly significant change occurs for dG of the purine nucleosides.

2. The electron affinities of these 2′-deoxyribonucleosides are all positive, ranging from 0.44 to 0.06 eV with the ordering

$$dT > dC > dG \sim dA$$

in which the AEAs of dG and dA are closer than is the case for the isolated bases.

3. dA, dC, and dT appear to be valence bound anions, while dG has some component of more diffuse electron density. In addition, one sees greater geometrical changes upon electron attachment for the valence bound anions in comparison with the dipole bound anion of dG, which shows smaller geometric perturbations.

4. The group separation of NPA charges is basically identical in all of the neutral 2′-deoxyribonucleosides, with a Weinhold charge of −0.28 ∼ −0.29 for each base and +0.28 ∼ +0.29 for the 2-deoxyribose. In the anionic species, the trend in the magnitude of the NPA charge increase for the base corresponds to the nature of the excess electron in the anions.

5. The decomposition enthalpy is approximately zero for the uncharged molecules and exothermic for the anions, indicating potential difficulty in the experimental study of nucleoside anions in the presence of water.

These findings raise new questions as to the effects of additional components to the system. Particularly interesting will be the bond length changes for the C3′ and C5′ O−P bonds in the nucleotides and the residual charge distribution in nucleoside pairs.

In terms of future experiments, it is clear that the pyrimidine nucleosides are the most interesting of the anions studied here. The predicted adiabatic electron affinities are 0.44 eV and 0.33 eV for dT and dC, respectively, and the vertical detachment energies are significantly higher, 0.94 and 0.72 eV, respectively. Clearly, these two anions should be observable in the gas phase. Suitable solvation by water molecules will further increase the electron affinities.

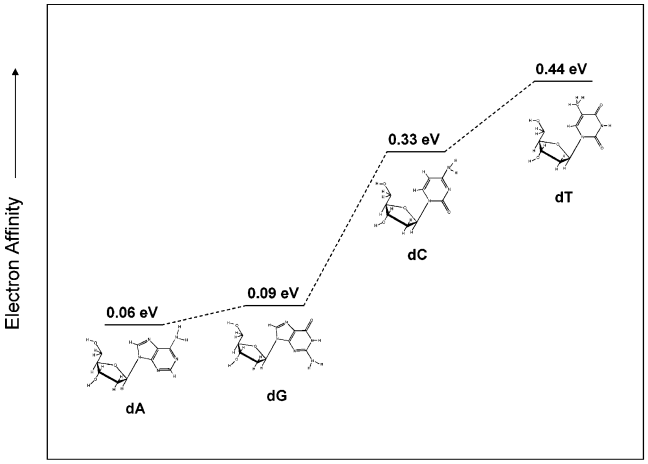


***Figure 6.*** Predicted electron affinities for the deoxyribonucleosides adenosine, guanosine, cytidine, and thymidine.

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