J. Phys. Chem. A **2008,** *112,* 11207–11212

Ionization Energies of the Nucleotides

David M. Close*

Department of Physics, Box 70652, East Tennessee State University, Johnson City, Tennessee 37614

Kjell Tage Øhman

Department of Physics, University of Oslo, Blindern, N-0371, Oslo, Norway

Received: June 16, 2008; Revised Manuscript Received: September 9, 2008

The vertical ionization energies of the four nucleotides have been computed. Geometries have been chosen to mimic orientations as they appear in B-DNA. The negative charge on the phosphate was neutralized by protonation, and also by the inclusion of counterions. Calculations have been performed with electron propagator methods (P3), Møller−Plesset second-order perturbation theory, and density functional theory to determine the nature of the orbitals associated with the highest lying ionization energies. Calculations at the MP2/6-311G(d,p)//P3/6-311G(d,p) level of theory yield vertical ionization energies for 5′-dTMP 9.05 eV, for 5′-dCMP 8.40 eV, for 5′-dAMP 8.16 eV and for 5′-dGMP 7.96 eV. In all cases the highest occupied molecular orbital resides on the base moieties.

Introduction

Gas-phase photoelectric spectra have provided accurate ionization energies of the nucleic acid bases. Efforts to obtain the ionization energies of intact nucleotides have been hampered because of the tendency of the nucleotides to decompose at the temperatures required for gas-phase photoelectron measurements.

Photoelectron spectroscopy has been used to determine the electron structure of the nucleotide anions in the gas phase.[1] The spectra, however, are poorly resolved due to the overlap of a number of orbitals with low ionization energies, and also in some cases to the presence of tautomers.

The paper by Yang et al. also contains DFT calculations that indicate the lowest ionizations energies of all the nucleotide anions can be associated with an orbital localized on the phosphate groups.[1] This assertion has been disputed by Rubio et al.[2] who have performed MP2/cc-pVDZ calculations on the 5′-dTMP anion which indicate the HOMO to be associated with a π-orbital on the thymine moiety.

The vertical ionization energies of the four nucleotides anions have recently been calculated.[3] Calculations of the ionization energies of the nucleotide anions have been shown to be in good agreement with the experimental values. These results are discussed here in detail.

The aim of the present study is to compute the ionization energies of the neutral nucleotides. Geometries have been chosen to mimic orientations as they appear in B-DNA. The negative charge on the phosphate is neutralized by two different charge-neutralized structures, one by protonation of the phosphate, and the other by the inclusion of Na^+ counterions.

Calculations have been performed with both density functional theory and with Møller−Plesset second-order perturbation theory to determine the nature of the orbitals associated with the low lying ionization energies. These studies are important in drawing conclusions related to what is presently known about the radiation chemistry of DNA.

Previous Ionization Energy Calculations. There have been numerous calculations of the ionization energies of the DNA bases.[4,5] A summary of the calculations and comparisons with experimental values is presented in Table 1. The emphasis herein is on the calculation of vertical ionization energies (VIE).

Three different types of calculations are presented in Table 1. DFT calculations at the B3LYP/6-31++G(d,p) level of theory are seen to agree fairly well with the experimental ionization energies. The same cannot be said for MP2 calculations at the same 6-31++G(d,p) level. The problem is that although Møller−Plesset perturbation calculations can be used successfully for calculations of electron correlation energies, for open-shell calculations, the unrestricted Hartree−Fock wave functions are often contaminated by higher spin states.[10] To significantly remove the spin contamination errors in open-shell systems, the spin annihilation procedure (herein denoted as PMP2) can be used.[11] Results of these calculations were shown to be in better agreement with the experimental results.[5]

The third type of calculations are those performed by Ortiz and co-workers. They use electron propagator methods (P3) calculations on the DNA bases optimized at the MP2/6-311G(d,p) level of theory.[12] The results for the calculated vertical ionization energies of the DNA bases presented in Table 1 are seen to agree very well with the experimental values.

Previous P3 calculations at the same level of theory have also been performed on the methylated DNA bases (Table 2).[5] The pyrimidines are methylated at N1, and the purines at N9 to mimic the glycosidic bond. Again one sees very good agreement with the experimental value of the VIE. It is interesting to note a small drop in vertical ionization energies upon methylation.

For the present work it is important to examine previous calculations of larger systems, in particular the nucleotides. Hou et al.[13] have computed the vertical ionization energy of the 5′-dAMP anion as 5.08 eV computed using the DZP++ basis set. This value does not compare very well with the experimental value of 6.05 eV.[1] There are indications in the literature that one should also use different procedures for calculating ionization potentials. Zakjevskii et al. have recently reported the

---

* Author to whom correspondence should be addressed. E-mail: closed@etsu.edu.

10.1021/jp805308p CCC: $40.75

TABLE 1: Vertical Ionization Potentials for the DNA Bases (Energies in eV)

base	B3LYP/ 631++G(d,p)[a]	MP2/ 6-31++G(d,p)[b]	PMP2/ 6-31++G(d,p)[b]	P3-MP2/ 6-311G(d,p)[a]	exp	exp ref
T	9.01	9.55	9.07	9.13	~9.1	6
C	8.69	9.45	8.69	8.79	8.80	7
A	8.26	9.42	8.62	8.49	8.44	8
G	7.98	8.91	8.33	8.13	8.24	9

[a] Reference 5. [b] Reference 4.

TABLE 2: P3 Calculated Vertical Ionization Energies (eV) for the DNA Bases[a]

base	theor	exp	Me-Base	exp
G	8.13	8.24	7.98	8.02
A	8.49	8.44	8.34	8.39
C	8.79	8.80	8.53	8.65
T	9.13	9.10	8.78	8.79

[a] The calculated vertical ionizations energies are taken from ref 5, which also has the references to the experimental values listed in columns 3 and 5.

vertical detachment energy from the 5′-dAMP anion as 6.07 eV using electron propagator (P3) calculations that are in excellent agreement with the experimental value.[3]

Ortiz and co-workers have now completed their study by calculating the ionization energies of the four DNA bases in the nucleotide anions.[3] For the present analysis it is important to look at the highest lying orbitals observed in the nucleotide anions.

For 5′-dGMP$^-$ P3 calculations have the lowest ionization energy associated with a π_1 (Dyson) orbital localized on the guanine base. The second lowest electron detachment energy is associated with an orbital on the phosphate group.

For 5′-dAMP$^-$ P3 calculations predict two low lying ionization energies. The lowest ionization energy is associated with an orbital on the phosphate group, and the next lowest lying ionization energy is associated with a π_1 orbital localized on the adenine base.

In 5′-dCMP$^-$ P3 calculations have the first two lowest lying ionization energies associated with orbitals on the phosphate. The third lowest ionization energy is associated with a π_1 orbital localized on the cytosine base.

For 5′-dTMP$^-$ P3 calculations have the lowest lying ionization energy associated with a π_1 orbital localized on the thymine base. The next two lowest lying ionization energies are associated with orbitals on the phosphate group.

In the present work, the orbitals associated with the one-electron oxidized neutral nucleotides will be presented, and compared with the orbitals here for the one-electron oxidized nucleotide anions.

Radiation Chemistry of DNA. It is important to look at the characteristics of one-electron oxidation of the phosphate. EPR studies on irradiated phosphates indicate a likely product would be the PO_4^{2-} type radical with the unpaired electron primarily on the oxygen atoms interacting with the spin $^1/_2$ nucleus of the ^{31}P.[14] This radical is characterized by a ca. 30 G (84 MHz) doublet. Slightly larger hyperfine couplings of ca. 34 G (95 MHz) are expected for $HOPO_3^-$ radicals, and 39 G (109 MHz) for $(HO)_2PO_2$ radicals as the hole is forced on to a singly bonded oxygen.

Although these radicals have been observed in irradiated phosphates, they have never been detected in nucleotides, or indeed in intact DNA. To see why this is so, it is necessary to understand the radiation chemistry of DNA.

Ionizing radiation produces non specific ionizations; it ionizes DNA components approximately in direct proportion to the number of electrons on a given atom. The sugar−phosphate backbone contains 52% of the electrons; the “average base” contains 48%. Therefore, it is very likely that the sugar phosphate will be ionized. EPR experiments have shown, however, that the final damage to DNA is not a random distribution among these three components. Rather, the majority of the radicals are on the DNA bases. What is clear from low-temperature experiments is that electron and hole transfer occurs after the initial random deposition of energy. So the question becomes, which initial ionization events will recombine or transfer to a deeper traps, and which ones will lead to a stably trapped radical.

Computational Methods

Calculations to obtain vertical ionization energies[15] were performed at the B3LYP level of theory using the 6-311G(d,p) basis set. Calculations to obtain vertical ionization energies were also performed with electron propagator techniques in the partial third-order (P3) approximation levels of theory using the standard 6-311G(d,p) basis sets.[12] Frequency calculations were performed with the same basis set to verify stationary points.

Because the MP2 optimizations and the P3 calculations are time-consuming, it is important to also calculate ionization energies with density functional theory. For these calculations at the B3LYP/6-311G(d,p)//B3LYP/6-311G(d,p) level of theory were used to calculate vertical ionization energies of the nucleotides. All calculations were performed on the Gaussian 98[16] and Gaussian 03 suites of programs.[17]

Results and Discussions

In the past, the P3 calculations performed by Ortiz and co-workers involved first optimizing the molecule at the MP2/6-311G(d,p) level of theory, followed by single point P3 calculations.[18] The first series of vertical ionization energy calculations on the nucleotides involved neutralization of the negative charge on the phosphate with a single proton. The structure of the neutral 5′-dCMP molecule is shown in Figure 1. The size and flexibility of the nucleotides suggest that multiple stable configurations may exist for the neutral molecule molecules, and for the one-electron oxidized species. It is not the purpose of the present study to explore these multiple structures. One can see studies by Shishkin et al. for a discussion of the intramolecular H-bonds in various nucleotides.[19]

For the present calculations, geometries were chosen to mimic B-DNA. Therefore, the deoxyribose has the C_2′-endo -C_3′-exo conformation with the base in the anti arrangement. During the geometry optimizations there are tendencies for the phosphate to attract the positive portion of the base. To use an example, in 5′-dAMP there is a tendency for the PO_4^- to attract the C8−H side of the adenine. In the calculations presented here constraints were used to prevent deviations from the B-DNA structure that created intramolecular H-bonds. In all the calculations the

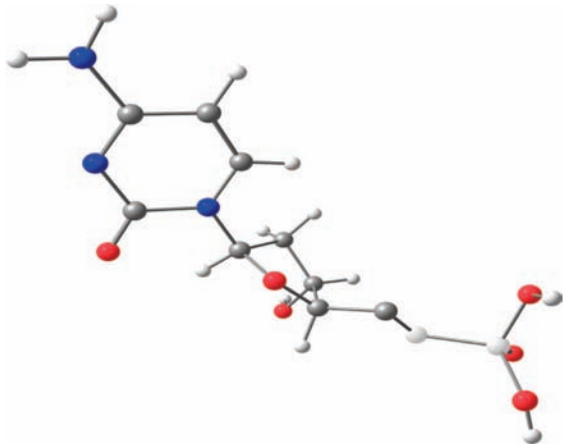

Figure 1. Structure of 5′-dCMP with a charge neutralized phosphate.

P−O−C5′−C4′ torsion angle, the deoxyribose puckering, and the alignment of the deoxyribose plane relative to the base plane is constrained.[20]

The first entry in Table 3 is labeled MP2/6-311G(d,p)//P3/6-311G(d,p). These are P3 ionization energy calculations using the geometry optimized at the MP2/6-311G(d,p) level of theory. Because these MP2 geometry optimization are very time-consuming, it is important to see if comparable ionization energies can be obtained with DFT optimizations. These calculations are presented in the second entry in Table 3 (labeled B3LYP/6-311(d,p)//P3/6-311G(d,p)).

The first thing to note in Table 3 is the similarity of the calculated VIE's in columns 2 and 3. This means that it is acceptable to optimize the structures with the less time-consuming B3LYP/6-311G(d,p) method before doing the P3/6-311G(d,p) calculations. As these P3 calculations themselves are rather time-consuming, it is useful to compare them with the DFT calculations in column four. Here there is shown a spread of vertical energies associated with open structures, and structures that are verging on forming intramolecular hydrogen bonds. These values are discussed in detail below. For the present discussion it is noted that, as expected, the vertical ionization energies calculated by DFT are lower than the corresponding calculations performed at the MP2/P3 level of theory.

Also it is interesting to note the small drop in VIE of the nucleotides as compared to the VIE of just the bases (shown in Table 2). One notes that except for 5′-dTMP, the VIE's calculated using the P3 level of theory agree rather well with the calculated VIE's of the methylated bases.

Next it is important to discuss the hierarchy of the orbitals in the nucleotides and to compare these with those discussed above for the nucleotide anions. To make this comparison meaningful, it is important to recognize the difference between the calculations. The results are presented in Table 4. In the second column are the results as usually reported by Ortiz and co-workers (MP2 optimizations on the neutral molecule, followed by single point calculations at the P3 level of theory to obtain the ionization energies). These results are described in terms of the Dyson orbitals.[18] The third column involves a description of the HOMO and the HOMO-n for the closed shell structures (the initial optimized structures of the neutral nucleotides) computed at the MP2 level of theory. The last column involves similar results obtained with density functional theory.

The P3 calculated vertical electron detachment energies (VEDEs) for 5′-dTMP are for the first four binding energies 9.05, 10.46, 10.22, and 10.34 eV. For 5′-dCMP the VEDEs are 8.40, 9.16, 9.38, and 9.76 eV, for 5′-dAMP 8.16, 9.15, 9.27, and 9.87 eV, and for 5′-dGMP are 7.96, 9.63, 9.68, 10.38 eV. The locations of the Dyson orbitals are given in the second column of Table 4. The structures of the π_1 first ionization level for all four nucleotides are given in Figure 2. One clearly sees that, in all four nucleotides these reside on the base moiety.

The P3 results in Table 4 can be compared with the previous calculations performed by Ortiz and co-workers on the one-electron oxidized nucleotide anions.[3] In those calculations the highest lying orbital was on the phosphate for 5′-dAMP and for 5′-dCMP. In Table 4 one sees that for the new P3 calculations on the purines one has to go past five or six lower lying orbitals to find an orbital on the phosphate. For the pyrimidines the first two or three lower lying orbitals are on the base. For 5′-dTMP one has to look down four levels to find an orbital on the phosphate, and for 5′-dCMP one has to look down seven orbitals to find an orbital on the phosphate.

As can be seen in Figure 2, the calculations here have been confined to fairly open geometries. It would be interesting to examine the influence of different geometries of the nucleotides on the ionization energies. To look at multiple structures, it was decided to switch to faster density functional calculations. The results are presented in column four of Table 3, which shows a small spread of VIE's for each nucleotide. In general, the lower VIE value is for the more open structure, and the higher VIE value corresponds to structures that are tending to form intramolecular H-bonds. An example is seen in Figure 3 for 5′-dAMP. In the open structure (Figure 3a) the phosphate is rotated away from the phosphate. In Figure 3b, one of the phosphate OH's is over toward the deoxyribose O1′.

Turning to the DFT calculations, column four in Table 4 shows that the HOMO's of all four nucleotides also reside on the bases. The same can be said for the next few lowest lying orbitals. One does note some delocalization onto the ribose for 5′-dCMP and 5′-dTMP in the lower lying orbitals. Figure 4 shows the spin densities for 5′-dCMP and 5′-dTMP. It is clear that for 5′-dCMP there is considerable spin density on C1′. In a detailed EPR/ENDOR study of 5′-dCMP it was shown that the primary oxidation product is localized mainly to the N1 and C5 of the cytosine base, but there is some spin density on the C1′ of the deoxyribose moiety.[21] For the 5′-dCMP calculation in Table 4, the N1 hyperfine coupling was 12.2 MHz, indicative of a spin density on the nitrogen forming the glycosidic bond. This gives rise to a N1−C1′−H_β that was measured to be about 41.9 MHz (14 Gauss).[21]

Figure 4 also depicts the spin density on 5′-dTMP. Here there is a different pattern. There is spin density on the deoxyribose, but the orbital is now in the C2′−C3′ region, rather than in the C1′ region as in 5′-dCMP. The orientation of the base moiety relative to the deoxyribose influences the migration of spin from the base to the deoxyribose. Calculations on the effect will be presented in a separate study. It is interesting to note that in model studies of thymine one electron oxidation generally yields a radical formed by deprotonation at the C5−CH_3, and so there is no measured spin density on the deoxyribose in these studies.[22]

Returning to Table 4, it is important to look at the differences between the MP2 calculations (column three) and the DFT calculations (column four). Basically, the HOMO and the HOMO−1 are the same. Looking further down the HOMO−*n* list, there are some differences in the orderings. But this is to be expected. This is basically a problem with DFT calculations, as one can see by comparing Hartree−Fock and Kohn−Sham

TABLE 3: Vertical Ionization energies (eV) of the Charge Neutralized Nucleotides

molecule	MP2/6-311G(d,p)//P3/6-311G(d,p)	B3LYP/6-311G(d,p)//P3/6-311G(d,p)	B3LYP/6-311G(d,p)//B3LYP/6-311G(d,p)	Me-BaseP3
5′-dTMP	9.05	9.06	8.55−8.62	8.78
5′-dCMP	8.40	8.34	7.97−8.11	8.53
5′-dAMP	8.16	8.10	7.86-7.98	8.39
5′-dGMP	7.96	7.92	7.53−7.68	7.98

TABLE 4: Hierarchy of Orbitals in the Neutral Nucleotides[a]

molecule	MP2/6-311G(d,p)// P3/6-311G(d,p) Dyson orbitals	MP2/6-311G(d,p)// MP2/6-311G(d,p) HOMO−*n*	B3LYP/6-311G(d,p)// B3LYP/6-311G(d,p)HOMO−*n*
5′-dTMP	#84-83 base #82 dR+base #81-80 dR+phos+base #79 dR+phos	#84-83 base #82-81 dR+base #80 dR+phos #79-78 dR+phos	#84-83 base #82 dR #81-80 base #79-78 dR+base #79 phos
5′-dCMP	#80-79 base #78-75 dR+base #74 dR+base #73 base+dR+phos	#80-77 base #76 phos #75 dR #74 phos	#80-77 base #76-75 dR #74 phos
5′-dAMP	#86-84 base #83-81 dR #80 dR #79 base+dR+phos	#86-82 base #81-80 dR #79 phos	#86-82 base #81-80 dR+base #79 phos
5′-dGMP	#90 base #89 dR+base #88-87 base #86-85 dR+base #84 base #83 dR+phos	#90-86 base #85 dR #84 base #83 phos	#90-87 base #86 dR #85 base #84-83 phos

[a] #'s here refer to occupied orbitals. For 5′-dTMP #84 is the HOMO, #83 is the HOMO−1, etc. dR means deoxyribose.

orbitals. Da Silva and co-workers have noted that in a calculation involving oxygen orbitals, the HF method has the p_z-type orbitals higher in energy than the p_xp_y-type orbitals, whereas the opposite is true in a DFT calculation. Basically, p_z-type orbitals and p_xp_y-

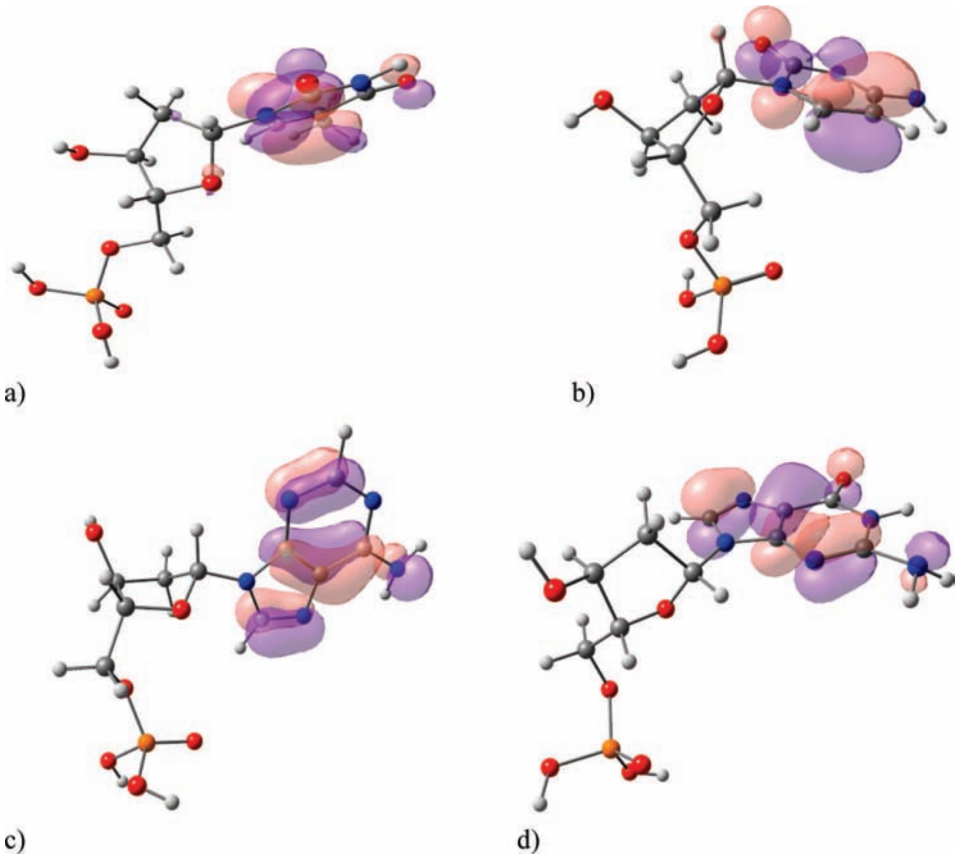

Figure 2. Dyson orbitals for the π_1 first ionization level of the nucleotides are all on the bases: (a) 5′-dTMP; (b) 5′-dCMP; (c) 5′-dAMP; (d) 5′-dGMP.

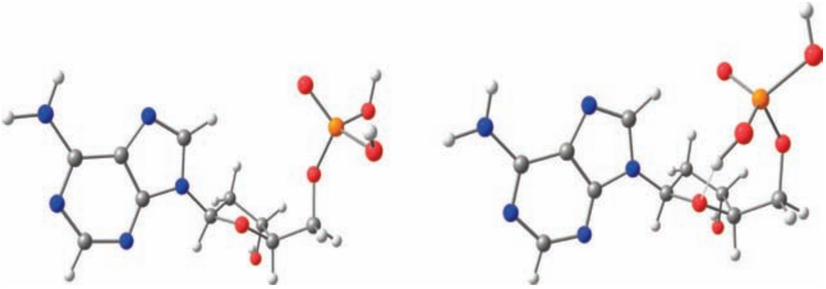

Figure 3. (a) Open structure of 5′-dAMP. (b) Structure of 5′-dAMP with weak H-bonds between a phosphate OH and the deoxyribose.

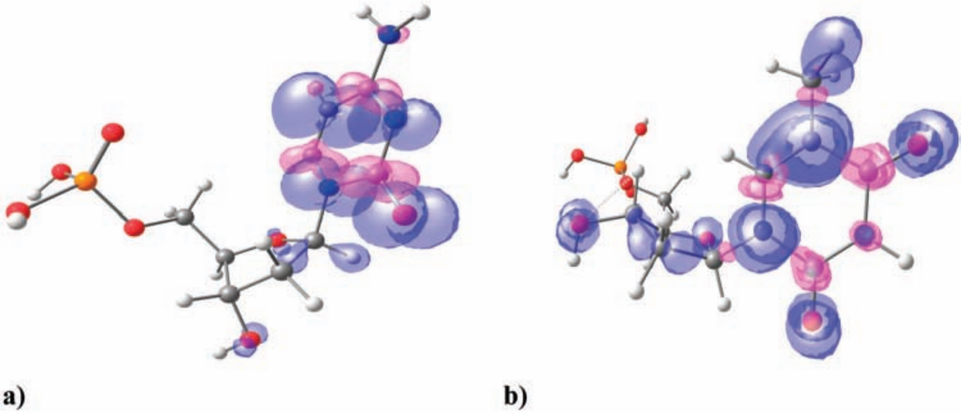

Figure 4. Spin density for the primary oxidation product in (a) 5′-dCMP and (b) 5′-dTMP.

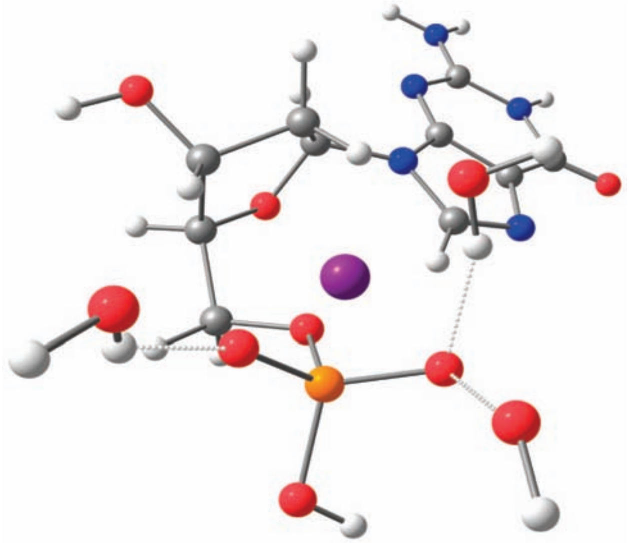

Figure 5. Structure of 5′-dGMP + Na^+ + $3H_2O$.

type orbitals are obtained by HF and DFT calculations, but with different energy orders.[23]

The next step is to compute VIE's of the nucleotides in the environment found in DNA where the negative charge on the phosphate is neutralized by a counterion and several water molecules. For these calculations a model was taken from the coordinates of the crystal structure of sodium guanylyl-3′,5′-cytidine nonahydrate.[24] Variants of this model can be found in refs 25 and 26. A structure of 5′-dGMP is shown in Figure 5. The vertical ionization energy calculations for all four nucleotides are shown in Table 5.

TABLE 5: Vertical Ionization Energies of the Charge Neutralized (Na^+ Nucleotides)

molecule	Phos2H[a]	$Na^+ + 3H_2O$[a]
5′-dTMP	8.55	8.29
5′-dCMP	7.97	8.14
5′-dAMP	7.86	7.66
5′-dGMP	7.53	7.33

[a] VIE calculations here are at the B3LYP/6-311G(d,p)//B3LYP/6-311G(d,p) level of theory. Energies in eV. Note that the numbers in column two here are from Table 3 (column 4).

In Table 5 it can be seen that charge neutralization with Na^+ + $3H_2O$ lowers the VIE of 5′-dTMP, 5′-dAMP and 5′-dGMP by about 0.20 eV. However, for 5′-dCMP there is a curious increase in VIE. It is not altogether clear why the cytosine nucleotide is different here. However, in discussions above, there have been several cases where cytosine did exhibit different behavior. The most interesting case being that of the delocalization of the spin density of base cation radical onto the deoxyribose moiety.

It seems that in the density functional calculations for 5′-dCMP (Table 5) there is some delocalization of the base cation radical onto the deoxyribose-phosphate. This can best be seen by examining the hyperfine couplings for the cytosine radical cation. A cytosine radical cation is expected to have high spin density at N1, N3 and C5 of the base. The experimental C5−H$_\alpha$ hyperfine coupling is −41.4 MHz. There have been problems reported in calculating this coupling that arise from calculations on an isolated base without the inclusion of hydrogen-bonded neighbors.[27] To date the best calculation for the C5−H$_\alpha$ is −30.7 MHz. For the 5′-dCMP radical cation listed in Table 5 the C5−H$_\alpha$ the hyperfine coupling is only −18.4 MHz, indicating that about one-third of the spin density that would normally be on the base is delocalized onto the deoxyribo-phosphate. These same calculations show a small amount of spin density on the phosphate oxygens, giving rise to a ^{31}P hyperfine coupling of −24.0 MHz.

Taken together, these results indicate that in the cation of the cytosine nucleotide there is some delocalization of the unpaired spin onto the deoxyribo-phosphate. In the other three nucleotides the radical cation is more localized on the bases. This indicates that the placement $Na^+ + 3H_2O$ in the 5′-dCMP may not be as effective in blocking spin density migration to the phosphate as it is with the other three nucleotides.

Another possible explanation for the 5′-dCMP discrepancy in Table 5 has to do with the difference in the hierarchy of orbitals between MP2 and DFT calculations. For this it will be necessary to perform MP2/P3 calculations on the $Na^+ + 3H_2O$ charge neutralized nucleotides. These calculations are underway.

Conclusions

The vertical ionization energies of the four DNA nucleotides have been computed by MP2/P3 methods and by density functional theory at the 6-311G(d,p) level of theory. For these calculations geometries have been chosen to mimic orientations as they appear in B-DNA and where the negative charge on the phosphate is neutralized by protonation, or by the inclusion of counterions.

The calculations show that after one-electron oxidation the radical cation is confined to the base. These results can be compared to recent calculations by Zakjevski et al.[3] on the ionization energies of the nucleotide anions which tend to favor localization of the unpaired electron on the phosphate moiety. This is, however, much as one would expect, the negative phosphate attracts a positive hole.

In DNA the negative charge on the phosphate is neutralized by a counterion. In DNA the initial hole produced randomly by one electron oxidation is mobile and will move about until it encounters a deep hole trap on a purine base. Once on the base, the low pK_a's of the purine cations results in deprotonation, leaving behind a neutral radical. This then points to an important scheme nature uses to protect DNA from oxidative damage as discussed recently for the case of one-electron oxidation of 5′-dAMP.[28] Although one electron oxidation of phosphate is likely to occur, no damage occurs to the phosphodiester bond if the hole can be sequestered on a purine base.

Acknowledgment. The Norwegian Metacenter for Computational Science (NOTUR) is gratefully acknowledged for grants of computer time.

References and Notes

(1) Yang, X.; Wang, X.; Vorpagel, E. R.; Wang, L. *Proc. Natl. Acad. Sci.* **2004**, *101*, 17588–17592.

(2) Rubio, M.; Roca-Sanjuán; Merchán, M.; Serrano-Andrés, L. *J. Phys. Chem. B* **2006**, *110*, 10234–10235.

(3) Zakjevskii, V.; King, S. J.; Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Am. Chem. Soc.* **2006**, *128*, 13350–13351.

(4) Crespo-Hernández, C. E.; Arce, R.; Ishikawa, Y.; Gorb, L.; Leszczynski, J.; Close, D. M. *J. Phys. Chem. A.* **2004**, *108*, 6373–6377.

(5) Close, D. M. *J. Phys. Chem. A* **2004**, *108*, 10376–10379.

(6) Padva, A.; O'Donnell, T. J.; LeBreton, P. R. *Chem. Phys. Lett.* **1976**, *41*, 278–282.

(7) Yu, C.; Peng, S.; Akiyama, I.; Lin, J.; LeBreton, P. R. *J. Am. Chem. Soc.* **1978**, *100*, 2303–2307.

(8) Lin, J.; Yu, C.; Peng, S.; Akiyama, I.; Li, K.; Lee, L. K.; Lebreton, P. R. *J. Am. Chem. Soc.* **1980**, *102*, 4627–4631.

(9) Lin, J.; Yu, C.; Peng, S.; Akiyama, I.; Li, K.; Lee, L. K.; LeBreton, P. R. *J. Phys. Chem.* **1980**, *84*, 1006–1012.

(10) Bertran, J.; Oliva, A.; Rodriguez-Santiago, L.; Sodupe, M. *J. Am. Chem. Soc.* **1998**, *120*, 8159–8167.

(11) Schlegel, H. B. *J. Chem. Phys.* **1986**, *84*, 4530–4534.

(12) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Phys. Chem. A* **2002**, *106*, 8411–8416.

(13) Hou, R.; Gu, J.; Xie, Y.; Yi, X.; Schaefer, H. F. *J. Phys. Chem. B.* **2005**, *109*, 22053–22060.

(14) Subramanian, S.; Symons, M. C. R.; Wardale, H. W. *J. Chem. Soc. (A)* **1970**, 1239–1242.

(15) Vertical ionization energies are preformed here by taking the difference in energy between the cation radical and the neutral base in the geometry of the neutral base.

(16) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; 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. Y.; Cui, Q.; Morokuma, K.; 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.; Chen, W.; Wong, M. W.; Andrés, J. L.; González, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11; Gaussian, Inc.: Pittsburgh, PA, 1998.

(17) Frisch, M. J. Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuckv A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; 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.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A.; *Gaussian 03*, revision B.03; Gaussian, Inc.: Wallingford, CT, 2004.

(18) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *Int. J. Quantum Chem.* **2002**, *90*, 1547–1554.

(19) Shishkin, O. V.; Palamarchuk, G. V.; Gorb, L.; Leszczynski, J. *J. Phys. Chem. B* **2006**, *110*, 4413–4422.

(20) Three torsion angles were constrained in each optimization. For 5′-dTMP and 5′-dCMP the angle P−O5′−C5′−C4′ was−36.7°, O5′−C5′−C4′−O1′ was 180.0°, and C2−N1−C1′−O1′ was 81.6°. For 5′-dAMP and 5′-dGMP, the angle P−O5′−C5′−C4′ was 123.2°, O5′−C5′−C4′−O1′ was−55.9° and C4−N9−C1′−O1′ was 104.3°.

(21) Close, D. M.; Hole, E. O.; Sagstuen, E.; Nelson, W. H. *J. Phys. Chem.* **1998**, *102*, 6737–6744.

(22) Close, D. M. *Radiat. Res.* **1993**, *135*, 1–15.

(23) da Silva, R. R.; Ramalho, T. C.; Santos, J. M.; Figueroa-Villar, J. D. *J. Phys. Chem. A* **2006**, *110*, 1031–1040.

(24) Rosenberg, J. M.; Seeman, N. C.; Day, R. A.; Rich, A. *J. Mol. Biol.* **1976**, *104*, 145–167.

(25) Kim, H. S.; LeBreton, P. R. *Proc. Natl. Acad. Sci.* **1994**, *91*, 3725–3729.

(26) Schneider, B.; Kabelac, M.; Hobza, P. *J. Am. Chem. Soc.* **1996**, *118*, 12207–12217.

(27) Close, D. M. In *Computational Chemistry: Reviews of Current Trends*; Leszczynski, J., Ed.; World Scientific: Singapore, 2003; Vol. 8.

(28) Close, D. M. *J. Phys. Chem. A* **2008**, *112*, 8411.

JP805308P