J. Phys. Chem. A **2002,** *106,* 9345−9351

Energetics of the Radical Ions of the AT and AU Base Pairs: A Density Functional Theory (DFT) Study

Xifeng Li,† Zhongli Cai,† and M. D. Sevilla*

Department of Chemistry, Oakland University, Rochester, Michigan 48309

Received: May 30, 2002

In this work, we present DFT calculations of the energetics of the base-pair anion and cation radicals of adenine−thymine (AT) and adenine−uracil (AU). At the B3LYP/6-31+G(d) level, we find that the adiabatic electron affinities (AEAs) are 0.30 eV for AT and 0.32 eV for AU. These values are both positive but slightly smaller than previously reported values for the AEA of guanine−cytosine (GC) and the hypoxanthine−cytosine base pair (IC). Furthermore, the AT and AU anion radical vertical electron detachment energies are also smaller than those of GC and IC, with that of AT only about half of GC's. For electron transfer between two identical isolated base pairs, the reorganization energies, λ, are calculated to be AT(0.76), AU(1.06), IC(1.25), and GC(1.31 eV). These results indicate that the AT base pair has a shallow trap depth and provides a favorable route for electron transfer, which explains previous experimental results that electron-transfer rates were higher in polydAdT than in polydGdC. Values of the ionization energies reported are in good agreement with the best estimates of previous work. For hole transfer, the reorganization energies, λ, are calculated to be AT(0.37), AU(0.53), IC(0.66), and GC(0.70 eV). These suggest that hole transfer through sequences of stacked AT base pairs may be most favorable. Base-pairing energies are also reported, which show that the formation of cation and anion radicals tends to increase base-pairing energies substantially, with cations more strongly affected than anions. We further show that whereas the predicted electron affinity of the individual base hypoxanthine (abreviated "I") is very slightly more than that of cytosine, base pairing in IC increases the relative electron affinity of cytosine in relation to that of hypoxanthine. Thus, we find that as I approaches C the electron transfers from I to C so that the electron localizes preferentially on cytosine in the fully optimized IC base-pair anion radical.

Introduction

Excess electron and hole transfer within DNA continues to attract considerable experimental[1] and theoretical[2] attention, in part owing to its importance in understanding radiation damage[3] as well as in the development of novel DNA technologies.[4] The most important properties for such transfer are the energetics (reduction potential, ionization energies, and electron affinity, etc.) of DNA bases and base pairs. A variety of experimental and theoretical reports concerning the energetics of single bases or nucleotides are available;[5−10] however, fewer studies on DNA base pairs in their ion-radical states are available.[5f,11−16] Rein and Harris[11] reported the first theoretical study of ion radicals of the GC base pair including considerations of proton transfer and tunneling. Colson et al.[5f] later reported ab initio calculations on each of the DNA base-pair ion radicals. This was extended to the DFT level by Hutter and Clark[12] for the GC base-pair cation radical and both GC and AT base pair cations by Bertran et al.[13] Recently, we reported DFT calculations for both anion and cation radicals of the GC and IC base pairs.[14] These theoretical studies with the DNA base anion and cation radicals show the importance of proton transfer within the base-pair radical ion to the stabilization of these species. Proton transfer is predicted by theory to be favorable for the GC anion radical,[5f,14] and all theoretical reports agree that for the GC cation radical the transfer is only slightly unfavorable (1.2 kcal,[13] 1.4 kcal,[14] 1.6 kcal[12]). These results are in reasonable agreement with estimates from experiment.[17] The proton transfer in AT base-pair ion radicals was predicted to be unfavorable for both cations and anions by experiment,[17] although early ab initio results[5f] with the 3-21G* basis set suggested otherwise. Recently, improved DFT results of Bertran et al.[13] for the AT cation radical clearly predict that interbase proton transfer from the amine group on A to the oxygen on T is nearly thermally neutral (1.2 kcal) with a low activation energy, as found for the GC cation radical.[13] Other possible interbase proton transfers in the cation radicals such as double proton transfers[13] or transfer from T to A in the AT cation[12] were found to be far less favorable.

These reports[5f,12−14] and others[5,17−20] show that base pairing and proton transfer can alter DNA energetics and affect the pattern of electron and hole transfer within DNA. Of course to produce results more applicable to the biological environment, other interactions must be included such as π stacking,[21,22] hydration, and solvation effects.[22−24] Of these efforts, LeBreton and co-workers have performed calculations of the aqueous solution ionization energies of full nucleotide structures,[23c−d] and they along with Saito and co-workers[21] have elucidated the effect of stacking on guanine ionization energies.

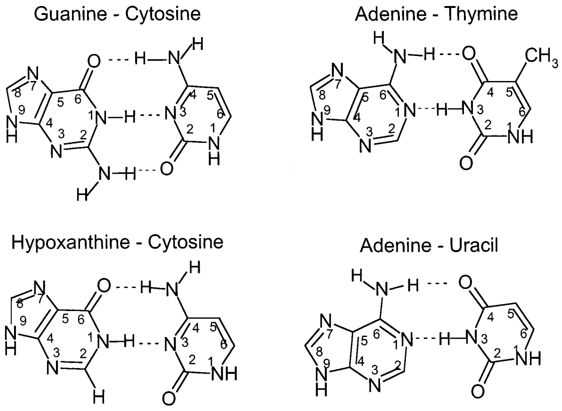
This work is an extension of our previous theoretical study on the energetics of GC and IC base pairs[14] to a detailed consideration of the energetics of AT and AU base-pair anion and cation radicals. This includes electron affinities, ionization energies, and base-pairing energies. These calculations allow

---

* Corresponding author. E-mail: sevilla@oakland.edu. Tel: 248-370-2328. Fax: 248-370-2321.

† Present address: Département de Médecine Nucléaire et Radiobiologie, Université de Sherbrooke, Quebec J1H 5N4, Canada.

10.1021/jp021322n CCC: $22.00


Guanine - Cytosine

Adenine - Thymine

Hypoxanthine - Cytosine

Adenine - Uracil

Figure 1. Structure and numbering scheme of the base pairs.

TABLE 1: Electron Affinities and Ionization Energies of Base Pairs Calculated at B3LYP/6-31+G(d)//B3LYP/6-31+G(d)

Electron Affinities (eV)

	adiabatic EA		VEA	VEDE
base pair	uncorrected	ZPE corrected	uncorrected	uncorrected
AT	0.11	0.30	−0.16	0.60
AU	0.18	0.32	−0.13	0.93
GC	0.36	0.49	−0.15	1.16
IC	0.26	0.42	−0.19	1.06

Ionization Energy (eV)

	adiabatic IE		VIE	VEAE[a]
base pair	uncorrected	ZPE corrected	uncorrected	uncorrected
AT	7.70	7.68; 7.45[a]	7.80; 7.74[a]	7.43
AU	7.70	7.68	7.91	7.38
GC	6.89	6.90; 6.71[a]	7.23; 7.16[a]	6.53
IC	7.68	7.63	7.94	7.28

[a] Results by Hutter and Clark[12] at DFT B3LYP/D95*//UHF/6-31G*. From a linear correlation to experimental IE values for single bases, these authors found a relationship that suggested their IE values should be increased by ca. 0.3 eV. Bertran et al.[13] give estimates of 7.79 and 6.96 eV for AIEs of AT and GC.

us to make a comparison of the energetics of the base pairs at the same level of calculation. Our results predict stable covalent anions for all base pairs. Moreover, a surprising change in the spin and charge distributions in IC is reported as the two separated bases approach one another.

Abbreviations for terms employed in this work are AEA, adiabatic electron affinity; VEA, vertical electron affinity; AIE, adiabatic ionization energy; VIE, vertical ionization energy; VEDE, vertical electron detachment energy; and VEAE, vertical electron attachment energy. The first four terms have their usual meanings. The VEDE of a base-pair anion radical is the energy difference between the base-pair anion in its optimized geometry and its neutral structure before nuclear relaxation. The VEAE of the base-pair cation radical is the energy difference between the base-pair cation radical in its optimized geometry and the neutral base pair in the identical geometry. It corresponds to the energy released on electron addition to the cation radical before nuclear relaxation. Base-pair structures and numbering schemes referred to in this work are shown in Figure 1.

Method

The structures of AT and AU anion/cation radicals were preoptimized at the Hartree−Fock (HF/6-31G(D) level and were then further optimized at the DFT B3LYP/6-31+G(d) level using the Gaussian 98 program package.[25] The method of optimization was the default Berny algorithm. This level of DFT calculation has been shown in our earlier work on DNA base anion radicals to produce results in reasonable agreement with experiment,[7] and these results were found to be superior to earlier HF and MP2 calculations that had to be scaled by an additive correction constant to yield reasonable results.[5d] An extensive recent review of theoretical calculations of electron affinities showed that the B3LYP functional (tied with BLYP) gave the smallest average absolute error for 91 different species when compared to a number of other functionals.[26] For base-pair cations, several workers have employed the DFT B3LYP level with good results for ionization energies.[12−14] For example, Hutter and Clark[12] found good agreement with DNA base-ionization energies. In addition, Bertran et al.[13] found that the DFT B3LYP calculations compare favorably with CCSD(T) calculations for interaction energies in cationic base-pair model systems.

Frequency calculations for all the optimized structures of neutral and ion-radical base pairs and calculations for single-point energies of these optimized structures in other charge or radical ion states (e.g., the AT cation radical in the neutral radical geometry, etc.) were performed at the same level (B3LYP/6-31+G(d)). Final optimized structures are available in Cartesian coordinates (x, y, z) in the Supporting Information. A scaling factor of 0.9804 was used in all frequency calculations for the zero-point energy and thermodynamic corrections, as in our previous work.[14]

GaussView, version 1.0[27] was used in the studies of distance-dependent charge distribution in the I−C base-pair anion radical. The base pairs were constructed by merging the geometries (anion radical or neutral optimized at the B3LYP/D95V+(d) level) of hypoxanthine and cytosine. The two ring systems were oriented appropriately at various distances followed by single-point energy calculations at the B3LYP/D95V+(d) level for charge- and spin-distribution information. Three types of IC base pairs were thus constructed, covering several possible combinations of the two bases in either anion or neutral geometry and the interbase distances varied. All are for the anion radical state but for the specific geometries designated by these abbreviations: I^-& C^0, I^0 & C^-, and I^0 & C^0 where, for example, I^- & C^0 refers to a calculation of the base-pair anion using the optimized geometry of the I anion radical and the C neutral species. The full optimization of the IC base-pair anion radical was also performed at B3LYP/D95V+(D), and its energy was used as a reference. Spin and charge distributions were calculated using the Mulliken population analyses.

Result and Discussion

1. Energetics of Base Pairs. The calculated values of electron affinities and ionization energies for the base pairs AT and AU are listed in Table 1. For comparison, our previous results[14] for GC and IC are listed as well. The DFT-calculated IEs of AT and GC by Hutter and Clark[12] at the B3LYP/D95* level are also shown for comparison.

Electron Affinities. It can be seen that, although all the four base pairs have positive adiabatic EAs, those of AT and AU are somewhat smaller than those of GC and IC. However, the vertical electron detachment energy (VEDE) of AT is only about half that of GC, making it more facile to remove an electron from the AT anion radical than from the GC anion radical. The adiabatic EA corresponds to the relaxed trapping energy, and the VEDE indicates the energy needed for ejection of the electron. The values in Table 1 suggest that the depth of the energy trap for an excess electron by a base pair as measured

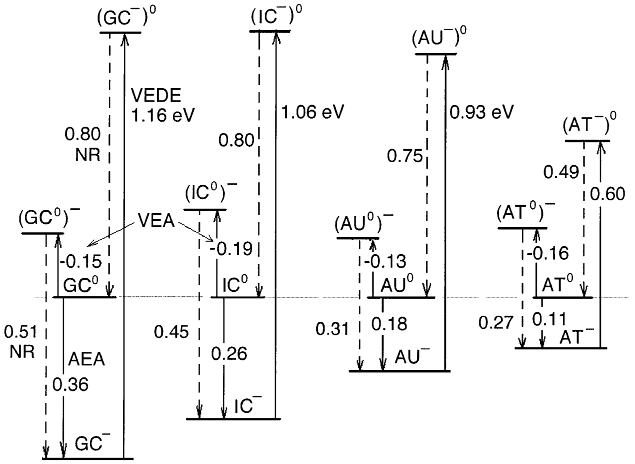


Figure 2. Energetic cycles for excess electron addition to the four DNA base pairs followed by its removal. Solid vertical arrows represent addition/removal of the electron, and dashed vertical arrows represent nuclear relaxation process. Upon addition of an electron, the neutral relaxed base pair, BP^0, goes vertically (VEA) to the anion radical in the neutral geometry $(BP^0)^-$, and nuclear relaxation results in the relaxed anion radical, BP^-. Detachment of an electron (VEDE) from the relaxed BP^- results in the neutral species in the geometry of the anion radical $(BP^-)^0$, and nuclear relaxation then brings it back to the neutral base pair, BP^0. All energies are in eV.

by the adiabatic EA follows the order AT $<$ AU $<$ IC $<$ GC. This is clearly seen in Figure 2, which compares the energetics of cycles of electron addition to and removal from the four base pairs, including our previous work on IC and GC.[14] Clearly, of the four base pairs considered, AT shows the smallest values of the energetic changes: AEA, VEDE, and NRs.

The same ordering of trapping depth was found in earlier work for AT and GC.[5f] Base stacking and local conditions present in natural DNA of course alter this ordering-of-trapping well depth.[5a,28]

Al-Jihad et al.[15] report a value of −0.4 eV for the AEA of AT from a MP2/6-31++G**//HF/6-31++G** calculation. Colson et al. also report MP2 calculations on DNA base pairs.[5a,e,f] These calculations predict values of EA that are substantially lower than expected for base pairs.[12,13] We note that in this earlier work Colson et al.[5f] computed the base-pair electron affinities of GC and AT to be −0.75 and −1.05 eV, respectively, at the HF (6-31+G(d)//3-21G) level. These values were recognized by these authors to be low, and they employed an additive correction constant[5d,f] from comparison of theory and experiment that brought the values to 0.6 eV for GC and 0.3 eV for AT; the corrected values are in good agreement with results from the present work (0.5 and 0.3 eV, respectively).

Our results predict that all base pairs have small but negative vertical EAs (uncorrected for ZPE). Interestingly, each of the base pairs appears to be of similar EA before nuclear relaxation. This provides a mechanism for an initial rapid transfer through DNA before relaxation traps the electron. The relaxation energies for each base pair after electron attachment (AEA−VEA) are AT(0.27), AU(0.31), IC(0.45), and GC(0.51 eV), and the relaxation energies after vertical detachment of an electron from each base-pair anion (VEDE−AEA) are AT(0.49), AU(0.75), IC(0.80), and GC(0.80 eV). For electron transfer from an isolated base pair to another isolated base pair of the same type, the overall reorganization energy, λ, is sum of these two relaxation energies, which are AT(0.76), AU(1.06), IC(1.25), and GC(1.31 eV). The relaxation energy or nuclear reorganization energy acts as a barrier to transfer and suggests that GC will provide the largest barrier.

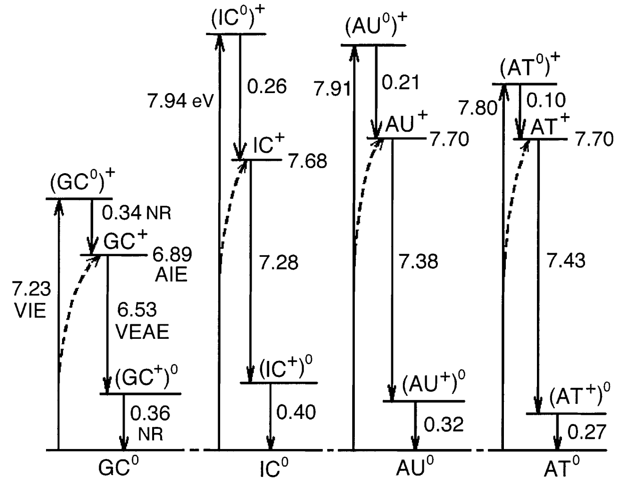


Figure 3. Ionization-energy cycles for four DNA base pairs. In each cycle, the vertical (VIE) and adiabatic (AIE) ionization energies in eV are shown. The vertical ionization transition is from the relaxed neutral base pair BP^0 at the base of the diagram to the nonrelaxed base-pair cation $(BP^0)^+$, whereas the adiabatic transition is to the relaxed base-pair cation BP^+. The VIE and AIE provide the upper and lower energies for hole formation in the isolated base pair. The nuclear relaxation energy of the base pair after ionization, represented by the differences in energy between the $(BP^0)^+$ state and the lower-energy BP^+ state, is an important energy barrier to hole transfer through DNA. On neutralization of BP^+ by an electron, it immediately becomes the neutral species but in the geometry of the cation $(BP^+)^0$. This is followed by relaxation to the neutral base-pair geometry, BP^0. The combined relaxation energies account for the reorganization energy for hole transfer between identical bases.

Ionization Energies. The ionization energies reported in Table 1 show that GC has the smallest IE and is easiest to ionize, as reported in previous works.[5a,12,13] The other three base pairs have similar IE values. Values of Hutter and Clark[12] for AT and GC are about 0.2 eV less than ours, but they suggest from a linear correlation to experimental IE values that their values (see Table 1) should be increased by ca. 0.3 eV. Bertran et al.[13] also report DFT calculations for AT and GC and give estimates of 7.79 and 6.96 eV for AT and GC, respectively, after adjusting the experimental values of the IE for G and C by the increase in base-pairing binding energies on ionization. These values and the corrected values of Hutter and Clark are within ca. 0.1 eV of our ZPE-corrected values of the adiabatic IEs. The agreement among the three approaches suggests that some confidence should be given to these values.

The vertical electron attachment energy (VEAE, not corrected for ZPEs) of GC is the smallest of those of the base pairs as well. Figure 3 shows the energetics of ionization and electron-hole recombination for each of the base pairs under consideration and thus visually compares the energy cost of hole transfer. For hole transfer through a base pair, the upper limit of the energy barrier is the vertical IE, and the lower limit is the adiabatic IE. Figure 3 clearly shows that the energy barrier follows the order GC $\ll$ AT $\approx$ AU $\approx$ IC, and even the upper limit for GC is below the lower limit of the other base pairs. These properties might suggest that sequences high in the GC base pair are the best media for hole transfer in double-stranded DNA; however, the reorganization energies argue against this. For an adiabatic hole-transfer process between two isolated identical base pairs, the energy barrier is composed of the sum of two relaxation energies: the relaxation of donor and acceptor base pairs. The donor relaxation energies (AIE-VEAE) are AT(0.27), AU(0.32), IC(0.40), and GC(0.36 eV), whereas the acceptor relaxation energies (VIE -AIE) are AT(0.10), AU(0.21),

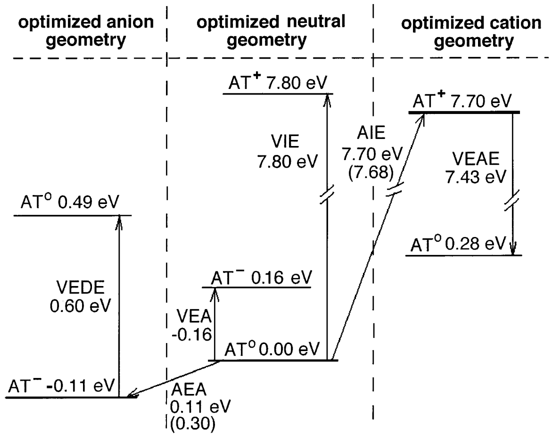


Figure 4. Diagram of the relative energies of various AT base-pair anion radical, neutral, and cation radical species (initial structures) showing the energy separations that correspond to the AEA, VEA, AIE, VIE, AEDE, VEAE, and nuclear relaxations. Both ZPE corrected (in parentheses) and uncorrected energies are presented for optimized stationary structures (marked with a thick line), and only uncorrected energies are presented for nonequilibrium structures (thin line). The energy of the AT neutral in its optimized structure is set as a reference (0 eV). All values on the left are calculated at the optimized anion geometry. Those in the middle are at the optimized neutral geometry, and those on the right are at the optimized cation geometry.

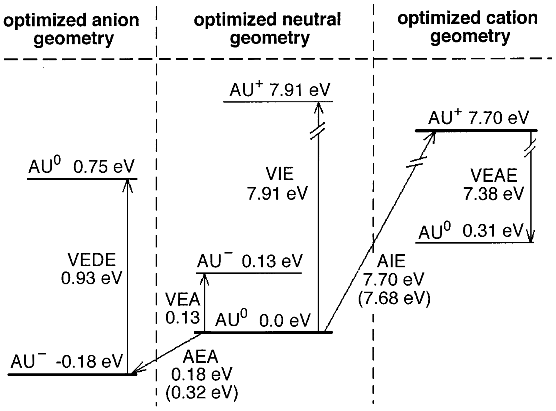


Figure 5. Diagram of the relative energies of various AU base-pair anion radical, neutral, and cation radical species (initial structures) showing the energy separations that correspond to the AEA, VEA, AIE, VIE, AEDE, VEAE, and nuclear relaxations. Both ZPE corrected (in parentheses) and uncorrected energies are presented for optimized stationary structures (marked with a thick line), and only uncorrected energies are presented for nonequilibrium structures (thin line). The energy of the AU neutral in its optimized structure is set as a reference (0 eV). All values on the left are calculated at the optimized anion geometry. Those in the middle are at the optimized neutral geometry, and those on the right are at the optimized cation geometry.

IC(0.26), and GC(0.34 eV). The sum of these values gives the reorganization energies, λ, which are AT(0.37), AU(0.53), IC-(0.66), and GC(0.70 eV).[1j] Thus, these results suggest that AT base pairs would provide a lower reorganization barrier to hole transfer. In agreement, experiments have suggested that the transfer through stacked ATs in an AT bridge between the donor and the acceptor is very rapid.[1b,c]

The overall relative energetics of the AT base pair in different charge/geometry states is illustrated in Figure 4, using the energy of the optimized neutral AT as a reference (0.00 eV). Similarly, Figure 5 illustrates the relative energetics of the AU base pair in different charge and geometry states with the optimized neutral AU as an energy reference. Similar graphics for GC and IC base pairs have been reported in our previous work.[12] Values in parentheses include ZPE correction.

TABLE 2: Charge and Spin Distributions in Optimized AT and AU Base Pairs

	method: B3LYP/6-31+G(d)				
	charge			spin	
AT	neutral	anion	cation	anion	cation
total	0	−1	1	1	1
A	0.05	−0.11	0.82	0.05	0.86
T	−0.05	−0.89	0.18	0.95	0.14
AU					
total	0	−1	1	1	1
A	0.03	−0.10	0.90	0.02	0.98
U	−0.03	−0.90	0.10	0.98	0.02

The charge and spin distributions between the bases in optimized base pairs (AT and AU) are summarized in Table 2. Both neutral base pairs have a small positive charge localized on purine base portion A and an equal amount of negative charge on the pyrimidine portion (T or U). In the optimized anions, the charge and spin largely localize on the pyrimidine portion, whereas in both cation radicals, the charge and spin largely localize on the purine base (A). Because A has a smaller electron affinity and ionization energy than T or U,[6,7] these results are expected. The increased amount of delocalization in the AT pair compared to that of the AU base pair for the cations is of interest. Detailed charge and spin distributions as well as isotropic hyperfine couplings are available in Supporting Information.

2. Base-Pairing Energy. The base-pairing energies are defined as the difference in the energy between the fully optimized base pair and the sum of the individual energies of the two optimized bases. Table 3 lists the base-pairing energies calculated for various base pairs. We note that the BP energies we calculate for GC^0 and AT^0 are close to previously reported experimental values of 21 and 13 kcal/mol, respectively.[28] We also note that many previous calculations of base-pairing energies are also close to these experimental values for the neutral base pairs.[19,20] We assume that the energetics for the other base pairs and their ionic forms in our work are reasonable estimates of their interaction energies. Corrections for basis set superposition errors (BSSE) are not made but are expected to be small (ca. 2 kcal/mol) because they are known to decrease with basis set size[20] and are reduced by the inclusion of diffuse functions.[19g,j] In this regard, our values are very near those of Bertran et al.[13] that include a BSSE correction and were performed with a similar basis set without diffuse functions (see Table 3). Finally, it is the changes in base-pairing energy on ion-radical formation that is of major interest to us, and this will not be significantly affected by BSSE because BSSE corrections are of similar magnitude for a particular base pair.[13]

We find that the cationic radical forms of the base pairs have substantial increases in their base-pairing energies, whereas the anionic radical forms show substantial increases for GC and IC but have only small increases for AT and AU. The 17-kcal/mol increase for the base-pairing energy in the GC cation radical is especially striking but is nearly matched by the 13-kcal/mol increase for the GC anion radical. Earlier reported[5f] ab initio HF calculations uncorrected for BSSE performed with the 6-31+G(d) basis set for the GC and AT base pairs, and their ion radicals are quite close to those found in this work. In that report, the increase in the base-pairing energy on ion-radical formation was attributed to an increase in the hydrogen bond strengths between the base pairs. This is likely the case because

TABLE 3: DFT Calculated (B3LYP/6-31+G(d)) Energetics of Base Pairing at 298.15 K, 1.0 atm[a,b]

neutral pairing energies	ΔE	ΔH	ΔG	ΔS
$G^0 + C^0 \rightarrow GC^0$	−22.9	−23.5 (−24.0)	−12.5(−12.6)	−36.8
$I^0 + C^0 \rightarrow IC^0$	−17.0	−17.6	−6.8	−36.1
$A^0 + T^0 \rightarrow AT^0$	−10.7	−11.3 (−10.9)	−1.7 (0.3)	−32.2
$A^0 + U^0 \rightarrow AU^0$	−10.1	−10.7	−0.40	−34.6

anion pairing	ΔE	ΔH	ΔG	ΔS
$G^0 + C^- \rightarrow GC^-$	−36.2	−36.8	−25.0	−39.5
$G^0 + C^- \rightarrow GC^-$ (PT)[c]	−39.1	−39.7	−28.1	−38.7
$I^0 + C^- \rightarrow IC^-$	−28.35	−28.95	−17.8	−37.4
$I^0 + C^- \rightarrow IC^-$ (PT)[c]	−34.9	−35.5	−25.1	−34.9
$A^0 + T^- \rightarrow AT^-$	−12.8	−13.4	−4.96	−28.4
$A^0 + U^- \rightarrow AU^-$	−12.8	−13.4	−4.35	−30.2

cation pairing	ΔE	ΔH	ΔG	ΔS
$G^+ + C^0 \rightarrow GC^+$	−40.5	−41.1 (−43.0)	−28.7 (−30.0)	−41.6
$G^+ + C^0 \rightarrow GC^+$ (PT)[c]	−39.1	−39.7 (−41.7)	−27.3 (−28.7)	−41.6
$I^+ + C^0 \rightarrow IC^+$	−33.8	−34.4	−23.3	−37.2
$I^+ + C^0 \rightarrow IC^+$ (PT)[c]	−38.9	−39.45	−28.4	−37.1
$A^+ + T^0 \rightarrow AT^+$	−20.6	−21.2 (−21.7)	−10.1 (−10.5)	−37.0
$A^+ + T^0 \rightarrow AT^+$(PT)[b,c]		(−21.3)	(−9.1)	(−40.9)
$A^+ + U^0 \rightarrow AU^+$	−19.5	−20.1	−9.0	−37.2

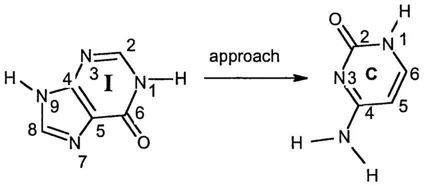
[a] ΔE, ΔH, and ΔG are in kcal/mol. ΔS values are in cal/mol/K. All values include ZPE and thermodynamic corrections at 298.15 K and 1.0 atm. [b] Values in parentheses are BSSE-corrected at B3LYP 6-31G** from Bertran et al.[13] Note that all other values are at B3LYP 6-31+G(d) and are not BSSE-corrected. [c] These values are calculated for the base-pair cation and anion radicals after proton transfer from N1 on guanine to N3 on cytosine or N1 on hypoxanthine to N3 of cytosine.[14] Proton transfer is not expected in the AT or AU anion radical base pairs,[5f,14,17] but theory suggests that transfer from the amine group on A to oxygen on T is likely in the AT cation radical.[13]

they are the dominant interactions between the base pairs. As might be expected from the increased base-pairing energies in most of the ion radicals, specific hydrogen-bonding distances in these base-pair ion radicals show significant shortening of distances by up to 0.28 Å; however, others show lengthening. (See Supporting Information for a table of hydrogen bond distances).

Proton transfer from N3 on the purine to N1 on the pyrimidine is expected for the GC, the IC base-pair anion and cation radicals,[5f,12−14] and the AU cation radical.[12] Proton transfer is found to have both stabilizing and destabilizing effects on the base-pair energetics (Table 3). This stabilization is quite substantial for the IC anion and cation radicals (7 and 5 kcal/mol, respectively). For the GC anion radical, this extra stabilization is about 3 kcal/mol. However, for the GC cation radical, we calculated a slight destabilization of the base pair by 1.4 kcal/mol, whereas Bertran et al.[13] report a 0.4-kcal/mol destabilizing effect for proton transfer in the AT cation radical. Both before and after proton transfer, the GC cation radical base pair is still the most strongly bonded base pair. Thus, whereas proton transfer slightly weakens the bonding in the GC cation, as has been predicted from gas-phase experiments[28] as well as solution-phase experiments,[17] dissociation of the complex is clearly not expected at 298 K and below.

The entropy changes on base pairing are found to be relatively constant and are principally a result of the loss of 1 mol of gaseous molecules on base pairing, which results in a driving force for dissociation of the base pair. Thus, free-energy changes (ΔG) at 298 K are substantially less than the enthalpy changes (ΔH) for all species. Whereas substantial bonding interactions remain at 298 K for most species, it is questionable whether AT and AU neutral base pairs would be observable at 298 K in the gas phase, although clearly at lower temperatures they should be found.

TABLE 4: Charge and Spin on C as It Approaches I in the IC Anion Radical at Various Geometries of I and C



total charge = −1, spin = +1			level: B3LYP/D95V+(d)	
geometry[a]	distance (Å)	charge	spin	relative energy (eV)[b]
fully optimized	1.58	−0.81	1.0	0.00
I^- & C^0	infinity	0	0	1.45
	3.02	0.00	0.02	1.02
	2.54	−0.43	0.45	0.90
	2.02	−0.46	0.52	0.66
	1.85	−0.57	0.64	0.74
I^0 & C^-	infinity	−1	1	1.33
	2.99	−0.79	0.82	0.81
	2.68	−0.81	0.84	0.71
	2.06	−0.82	0.88	0.47
	1.79	−0.86	0.92	0.47
I^0 & C^0	3.01	0.00	0.02	2.64
	2.63	−0.61	0.64	0.85
	2.04	−0.62	0.66	0.59
	1.79	−0.65	0.71	0.57

[a] All calculations are for the IC radical anion but for differing optimized geometries of the individual bases. Thus, I^- and C^0 are calculated for the I optimized anion radical geometry and the C optimized neutral structure. [b] All energies refer to the energy of the fully optimized geometry for the IC anion radical ($-882.3236903E_h$).

3. Charge/Spin Distribution between Hypoxanthine(I) and Cytosine(C) in a Base Pair. In previous work,[7] we found that cytosine and hypoxanthine have nearly equivalent adiabatic EAs with values near zero eV. The nearly equal EAs would suggest that an excess electron may be shared in the IC base pair (see structure below). However, in previous work,[14] we found that in the optimized IC anion radical and the proton-transferred IC anion radical virtually 100% of the spin resides on C, with no significant spin on I. The anion radical of the IC base pair is unstable toward proton transfer from N1 on hypoxanthine to N3 on cytosine, and this proton transfer is energetically quite favorable (7 kcal/mol). Before proton transfer, the base pair has a positive adiabatic electron affinity (0.42 eV), calculated at the B3LYP/6-31+G(d) level with ZPE correction. The substantial increase in the EA of the base pair compared to that of the single bases is a well-known effect of base pairing and had been reported previously[5f] and discussed above.

Here we report an interesting phenomenon. We constructed a series of three IC base-pair types with either optimized anion(−) or neutral(0) geometries of I and C. They are the optimized I anion radical and C in its neutral geometry [I^- & C^0] and the optimized C anion radical and I in its neutral geometry [I^0 & C^-] as well as I and C both in their optimized neutral geometries [I^0 & C^0]. In each type, the two bases were placed at several distances along a path to form the base pair, without altering their already-optimized geometries, as shown below. Single-point energy calculations were performed, and the results were collected in Table 4, showing the change in distance (using hypoxanthine H(N1) to cytosine N3 as the measurement) with the change in charge and spin distributions on cytosine as well as the relative energy (as compared to that of the optimized IC anion). We also show in Table 4 the fully optimized base-pair anion radical for comparison.

As can be seen in Table 4, in the case of the fully optimized base-pair anion radical, 100% of the spin is localized on C. The most interesting result is that for the approach of the optimized I anion to the optimized neutral C [I^- & C^0], which shows that at these fixed geometries the electron still transfers from the optimized I^- to the neutral geometry of C. This shows that the base pairing itself has a very strong effect on the excess electron stabilization on cytosine and can overcome the substantial nuclear relaxation energy stabilization in I^-. Obviously, on subsequent appropriate relaxation of both rings to a new electron distribution, the stabilization is substantially increased. The results for the neutral geometries [I^0 & C^0] also show that the electron would be favored on I in the separated systems and on C in the base pair. Only in the case of the [I^0 & C^-] do we find the electron on C in the separate systems. Here the reorganization energy stabilizes the electron on C initially. The change of charge and spin distributions in the other two combinations shows the unpaired electron transfers from I to C on its approach to the optimal distance. The transfer of spin to C is, of course, not fully complete until relaxation (full optimization without proton transfer, which will further stabilizes the charge on C by about 7 kcal/mol) is allowed. However, the relative energy changes drastically when the two bases approach each other. These results clearly suggest that the electron is favored on I in separated optimized systems and transfers to C in the base pair and that base pairing itself without nuclear rearrangement has an effect on the relative electron affinities of the two bases, which increases the electron affinity of C relative to that of I. This is mainly an effect of donor hydrogen bonds and is discussed below.

Summary and Conclusions

In this work, we have calculated at the DFT B3LYP level the energetics of AT and AU base-pair radical anions for comparison to those of GC and IC, which have already been reported[14] at the same level and basis set (631+G(d)). These combined results show that the EA of AT is the smallest and is about 0.19 eV less than GC, its competitor for the electron in DNA. As might be expected, the AT anion's vertical electron detachment energy (VEDE) is also the smallest among the four base pairs. Not only does the AT base pair have the shallowest trap depth (EA) but it also has the lowest reorganization energy for electron transfer to an identical base pair. Thus, AT base pairs provide the most favorable route for electron transfer. This is in agreement with previous experimental observations that electron-transfer rates were higher in polydAdT that in polydGdC.[1i]

The adiabatic IEs of both AT and AU are 7.68 eV after ZPE correction, which are higher than those of GC(6.90 eV) and IC(7.63) that we reported earlier.[14] These values are within ca. 0.1 eV of previous estimates.[12,13] Because GC has the smallest AIE, the hole is preferentially stabilized on GC in DNA.

For an adiabatic hole-transfer process between two isolated identical base pairs, the reorganization energy, λ, is found to be lowest for the AT base pair. Because ΔG is zero, this process would be hindered by only the relaxation energy ($\lambda/4$ assuming the Marcus−Sutin ET approach)[1j] and would result in an activated hole-transfer processes (hopping). Therefore, hole transfer through stretches of stacked ATs would be predicted to be less hindered by reorganizational energy. Recent results from Giese and co-workers[1b] suggest such a rapid transfer through stacked AT sequences. In agreement, recent results by Sartor et al. suggest a remarkably slow fall off in rates of transfer as multiple AT stacks increase in length.[1e] Experiments on the temperature dependence of hole transfer in DNA of differing sequences are therefore of interest and encouraged because they would provide valuable information on the barriers to electron transfer. Our results might predict a substantial temperature dependence for hole transfer from G to G in −GAAGAAG−, for example, but a less-substantial dependence for transfer from A to A (in AAAAA).

As discussed in the Introduction, a number of previous studies show that proton transfer from G to C[5f,11−14] or A to T[13] is likely for the base-pair cation radicals, and this may also slow hole transfer. These previous studies suggest that proton transfer is not complete and is reversible in double-stranded (ds) DNA for both the AT and GC cation radicals. Thus, proton transfer should have only a modest effect on hole transfer. Proton transfer in the case of excess electron transfer in GC and IC will have a far greater effect. For the case of GC and IC anion radicals, proton-transfer reactions are quite energetically favorable and will provide additional barriers to electron transfer of 3 and 7 kcal/mol for GC and IC, respectively.[14] Such processes have been suggested to explain the lower rates of electron transfer in IC and GC polynucleotides.[1g,i]

In addition to proton transfer and the energetics described for the individual base pair in Table 1, the electronic coupling between DNA bases in the bridge between the donor and acceptor, as well as the static and dynamic effects of the environment (solvation and counterions),[1d] must also be considered to be factors controlling electron and hole transfer. In this regard, recent work by Voityuk et al.[16] and Olofsson and Larsson[2j] has made initial inroads into understanding the energy of excess electron transfer as a function of sequence in ds DNA. The results on individual base pairs provided in this work are important considerations, however, in any such transfer.

As a result of rapid developments in gas-phase techniques involving biomolecules, including DNA bases,[29−37] gas-phase properties of DNA bases are of increasing interest. The calculated values reported in this article and in other work[5f,13] clearly show that ion-radical formation results in significantly stronger base pairing energies. These predictions may now be quantitatively tested by experiments on base pairs in the gas phase, which are underway in other laboratories.[28]

Although cytosine and hypoxanthine(I) have similar values for adiabatic electron affinities,[7] in this work, we demonstrate that the excess electron is favored on I in the separated system and transfers to C when the two bases approach each other. In earlier work, Colson et al. showed that a single donor hydrogen bond from water[5g] or another DNA base[5f] could increase the calculated electron affinity by up to 0.5 eV. This is mainly an electrostatic effect of the donating proton's charge. In the case of the electron localization on C in IC, this is primarily associated with the strong donor hydrogen bond from I, which raises the electron affinity of C relative to that of I.

Acknowledgment. This research was supported by the NIH NCI Grant RO1 CA45424 and by the Oakland University Research Excellence Fund.

Supporting Information Available: Optimized structures (in Cartesian coordinate) of AT and AU base pairs; tables of hydrogen bonding distances, as well as charge and spin distributions, isotropic hyperfine couplings. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Lewis, F. D.; Letsinger, R. L.; Wasielewski, M. R. *Acc. Chem. Res*. **2001**, *34*, 159. (b) Giese, B.; Amaudrut, J.; Kohler, A.; Sportmann, M. a. W. S. *Nature (London)* **2001**, *412*, 318. (c) Giese, B. *Acc. Chem. Res*. **2000**, *33*, 631. (d) Schuster, G. B. *Acc. Chem. Res.* **2000**, *33*, 253. (e) Sartor, V.; Boone, E.; Schuster, G. B. *J. Phys. Chem. A* **2001**, *105*, 11057. (f) Wan, C.; Fiebig, T.; Schiemann, O.; Barton, J. K.; Zewail, A. H. *PNAS* **2000**, *97*, 14052. (g) Debije, M. G.; Bernhard, W. A. *J. Phys. Chem. B* **2000**, *104*, 7845. (h) Cai, Z.; Gu, Z.; Sevilla, M. D. *J. Phys. Chem. B* **2000**, *104*, 10406. (i) Cai, Z.; Li, X.; Sevilla, M. *J. Phys. Chem. B* **2002**, 106, 2755. (j) Reid, G. D.; Whittaker, D. J.; Day, J. A.; Turton, D. A.; Kayser, V.; Kelly, J. M.; Beddard, G. S. *J. Am. Chem. Soc.* **2002**, *124*, 5518.

(2) (a) Berlin, Y. A.; Burin, A. L.; Ratner, M. A. *J. Am. Chem. Soc.* **2001**, *123*, 260. (b) Berlin, Y. A.; Burin, A. L.; Siebbeles, L. D. A.; Ratner, M. A. *J. Phys. Chem. A* **2001**, *105*, 5666. (c) Bixon, M.; Jortner, J. *J. Phys. Chem. B* **2000**, *104*, 3906. (d) Nitzan, A.; Jortner, J.; Wilkie, J.; Burin, A. L.; Ratner, M. A. *J. Phys. Chem. B* **2000**, *104*, 5661. (e) Voityuk, A. A.; Rösch, N.; Bixon, M.; Jortner, J. *J. Phys. Chem. B* **2000**, *104*, 9740. (f) Voityuk, A. A.; Rösch, N. *J. Phys. Chem. B* **2002**, *106*, 3013. (g) Baik, M.-H.; Silverman, J. S.; Yang, I. V.; Ropp, P. A.; Szalai, V. A.; Yang, W.; Thorp, H. H. *J. Phys. Chem. A* **2001**, *105*, 6437. (h) Smith, D. M. A.; Adamowicz, L. *J. Phys. Chem. B* **2001**, *105*, 9345. (i) Tong, G. S. M.; Kurnikov, I. V.; Beratan, D. N. *J. Phys. Chem. B* **2002**, *106*, 2381. (j) Olofsson, J.; Larsson, S. *J. Phys. Chem. B* **2001**, *105*, 10398.

(3) (a) Becker, D.; Sevilla, M. D. The Chemical Consequences of Radiation Damage to DNA. In *Advances in Radiation Biology*; Lett, J. T., Sinclair, W. K., Eds.; Academic Press: San Diego, CA, 1993; Vol. 17, pp 121−180. (b) Becker D.; Sevilla, M. D. *Electron Paramagnetic Resonance*; The Royal Society of Chemistry: Cambridge, U.K., 1998; pp 79−115. (c) Sevilla, M. D.; Becker, D.; Razskazovskii, Y. *Nukleonika* **1997**, *42*, 283.

(4) Yu, C. J.; Wan, Y.; Yowanto, H.; Li, J.; Tao, C.; James, M. D.; Tan, C. L.; Blackburn, G. F.; Meade, T. J. *J. Am. Chem. Soc*. **2001**, *123*, 11155.

(5) (a) Colson, A. O.; Sevilla, M. D. *Int. J. Radiat. Biol.* **1995**, *67*, 627. (b) Colson, A. O.; Sevilla, M. D. In *Computational Molecular Biology*; Lesczycyski, J., Ed.; Theoretical and Computational Chemistry; Elsevier: Amsterdam, 1999; Vol. 8, Chapter 7, p 245. (c) Sevilla, M. D.; Besler, B.; Colson, A. O. *J. Phys. Chem*. **1994**, *98*, 2215. (d) Sevilla, M. D.; Besler, B.; Colson, A. O. *J. Phys. Chem*. **1995**, *99*, 1060. (e) Colson, A. O.; Besler, B.; Sevilla, M. D. *J. Phys. Chem*. **1993**, *97*, 13852. (f) Colson, A. O.; Besler, B.; Sevilla, M. D. *J. Phys. Chem*. **1992**, *96*, 9787. (g) Colson, A. O.; Besler, B.; Close, D. M.; Sevilla, M. D. *J. Phys. Chem.* **1992**, *96*, 661.

(6) Wesolowski, S. S.; Leininger, M. L.; Pentchew, P. N.; Schaefer, H. F., III. *J. Am. Chem. Soc*. **2001**, *123*, 4023.

(7) Li, X.; Cai, Z.; Sevilla, M. D. *J. Phys. Chem. A* **2002**, *106*, 1596.

(8) (a) Wetmore, S. D.; Boyd, R. J.; Eriksson, L. A. *Chem. Phys. Lett.* **2000**, *322*, 129. (b) Wetmore, S. D.; Boyd, R. J.; Eriksson, L. A. *J. Phys. Chem. B* **1998**, *102*, 9332. (c) Wetmore, S. D.; Boyd, R. J.; Eriksson, L. A. *J. Phys. Chem. B* **1998**, *102*, 10602.

(9) (a) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Am. Chem. Soc*. **2000**, *122*, 12304. (b) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Phys. Chem. A* **2001**, *105*, 8782. (c) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Phys. Chem. A* **1999**, *103*, 7912. (d) Dolgounitcheva, O.; Zakrzewski, V. G. Ortiz, J. V. *Phys. Lett*. **1999**, *307*, 220. (e) Dolgounitcheva, O.; Zakrzewski, V. G. Ortiz, J. V. *Int. J. Quantum Chem.* **2000**, *80*, 831.

(10) Hobza, P.; Sponer, J. *Chem. Rev.* **1999**, *99*, 3247.

(11) Rein, R.; Harris, F. E. *J. Chem. Phys*. **1966**, *45*, 1797.

(12) Hutter, M.; Clark, T. *J. Am. Chem. Soc*. **1996**, *118*, 7574.

(13) Bertran, J.; Oliva, A.; Rodriquez-Santiago, L.; Sodupe, M. *J. Am. Chem. Soc*. **1998**, *120*, 8159.

(14) Li, X.; Cai, Z.; Sevilla, M. D. *J. Phys. Chem. B* **2001**, *105*, 10115.

(15) Al-Jihad, I.; Smets, J.; Adamowicz, L. *J. Phys. Chem. A* **2000**, *104*, 2994.

(16) Voityuk, A. A.; Michel Beyerle, M.-E.; Rösch, N. *Chem. Phys. Lett*. **2001**, *342*, 231.

(17) (a) Steenken, S. *Biol. Chem.* **1997**, *378*, 1293. (b) Steenken, S. *Chem. Rev.* **1989**, *89*, 503.

(18) (a) Florián, J.; Leszczynski, J. *J. Am. Chem. Soc.* **1996**, *118*, 3010. (b) Dannenberg, J. J.; Tomasz, M. *J. Am. Chem. Soc.* **2000**, *122*, 2062.

(19) (a) Kabelac, M.; Hobza, P. *J. Phys. Chem. B* **2001**, *105*, 5804. (b) Sponer, J.; Hobza, P. *J. Phys. Chem. A* **2000**, *104*, 4592. (c) Hobza, P.; Sponer, J.; Cubero, E.; Orozco, M.; Luque, F. J. *J. Phys. Chem. A* **2000**, *104*, 6286. (d) Guerra, C. F.; Bikelhaupt, F. M.; Snijders, J. G.; Baerends, E. J. *J. Am. Chem. Soc*. **2000**, *122*, 4117. (e) Kawahara, S.; Kobori I. A.; Sekine, M.; Taira, K.; Uchimaru, T. *J. Phys. Chem. A* **2001**, *105*, 10596. (f) Moroni, F.; Famulari, A.; Raimondi, M. *J. Phys. Chem. A* **2001**, *105*, 1169. (g) Barsky, D.; Colvin, M. E. *J. Phys. Chem. A* **2000**, *104*, 8570. (h) Sponer, J.; Leszczynski, J.; Hobza, P. *J. Phys. Chem.* **1996**, *100*, 1965. (i) Santamaria, R.; Castro, E.; Zacarias, A.; Castro, M. *J. Comput. Chem*. **1999**, *20*, 511. (j) Huang, N.; MacKerell, A. D., Jr. *J. Phys. Chem. A* **2002**, ASAP.

(20) (a) Kratochvil, M.; Sponer, J.; Hobza, P. *J. Am. Chem. Soc*. **2000**, *122*, 3495. (b) Kawahara, S.; Uchimaru, T.; Taira, K.; Sekine, M. *J. Phys. Chem. A* **2001**, *105*, 3894. (c) Brameld, K.; Dasgupta, S.; Goddard, W. A., III. *J. Phys. Chem. A* **1997**, *101*, 4851.

(21) (a) Sugiyama, H.; Saito, I. *J. Am. Chem. Soc.* **1996**, *118*, 7063. (b) Yoshioka, Y.; Kitagawa, Y.; Takano, Y.; Yamaguchi, K.; Nakamura, T.; Saito, I. *J. Am. Chem. Soc.* **1999**, *121*, 8712. (c) Saito, I.; Nakamura, T.; Nakatani, K. *J. Am. Chem. Soc*. **2000**, *122*, 3001. (d) Alhambra, C.; Luque, F. J.; Gago, F.; Orozco, M. *J. Phys. Chem. B* **1997**, *101*, 3846. (e) Johnson, T.; Zhu, J.; Wartell, R. M. *Biochemistry* **1998**, *37*, 12343.

(22) Sivanesan, D.; Babu, K.; Gadre, S. R.; Subramanian, V.; Ramasami, T. *J. Phys. Chem. A* **2000**, *104*, 10887.

(23) (a) Arora, N.; Jayaram, B. *J. Phys. Chem. B* **1998**, *102*, 6139. (b) Fernando, H.; Papadantonakis, G. A.; Kim, N. S.; Lebreton, P. R. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 5550. (c) Kim, N. S.; LeBreton, P. R. *J. Am. Chem. Soc*. **1996**, *118*, 3694. (d) Zhu, Q.; LeBreton, P. R. *J. Am. Chem. Soc.* **2000**, *122*, 12824. (e) Farrer, B. T.; Thorp, H. H. *Inorg. Chem.* **2000**, *39*, 44.

(24) Moroni, F.; Famulari, A.; Raimondi, M. *J. Phys. Chem. A* **2001**, *105*, 1169.

(25) 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.; 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.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(26) Rienstra-Kiracofe, J. C.; Tschumper, G. S.; Schaefer, H. F.; Nandi, S.; Ellison, G. B. *Chem. Rev.* **2002**, *102*, 231.

(27) *GaussView*, version 1.0; Gaussian, Inc.: Pittsburgh, PA, 1997.

(28) Yanson, I. K.; Teplitsky, A. B.; Sukhodub, L. F. *Biopolymers* **1979**, *18*, 1149.

(29) Nir, E.; Kleinermanns, K.; de Vries, M. S. *Nature (London)* **2000**, *408*, 949.

(30) Kim, S. K.; Lee, W.; Herschbach, D. R. *J. Phys. Chem*. **1996**, *100*, 7933.

(31) Aflatooni, K.; Gallup, G. A.; Burrow, P. D. *J. Phys. Chem. A* **1998**, *102*, 6205.

(32) Periquet, V.; Moreau, A.; Carles, S.; Schermann, J. P.; Desfrançois, C. *J. Electron Spectrosc. Relat. Phenom.* **2000**, *106*, 141.

(33) (a) Desfrançois, C.; Periquet, V.; Bouteiller, Y.; Schermann, J. P. *J. Phys. Chem. A* **1998**, *102*, 1274. (b) Desfrançois, C.; Abdoul-Carime, H.; Schermann, J. P. *J. Chem. Phys*. **1996**, *104*, 7792.

(34) Desfrançois, C.; Abdoul-Carime, H.; Schulz, C. P.; Schermann, J. P. *Science (Washington, D.C.)* **1995**, *269*, 1709.

(35) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Bowen, K. H. *J. Chem. Phys*. **1998**, *108*, 8.

(36) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Snodgrass, J. T.; Bowen, K. H. *J. Chem. Phys*. **1996**, *104*, 7788.

(37) Schiedt, J.; Weinkauf, R.; Neumark, D. M.; Schlag, E. W. *Chem. Phys*. **1998**, *239*, 511.