Covalent Anion of the Canonical Adenine−Thymine Base Pair. Ab Initio Study

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Theoretical ab initio calculations have been performed to determine the stability of the covalent anions of adenine and the adenine−thymine (AT) Watson−Crick base pair. The conclusions of this work are as follows: (i) the covalent anion of adenine is predicted to be a stable system with respect to a vertical electron detachment, but unstable with respect to adiabatic detachment; (ii) the covalent anion of the adenine−thymine dimer (A−T$^-$) has similar properties, although in this system the presence of the second base provides an additional stabilization to the excess electron; (iii) in A−T$^-$ the excess electron is localized at the thymine molecule, and this molecule's ring is puckered; (iv) no valence A−T anion was found in the calculations with the excess electron located at the adenine molecule; and (v) in view of the above results, we predict that the AT base pair is not an effective trap of excess electrons.

1. Introduction

For the past few years there has been increasing interest in the electrical conductivity of DNA. The unique double-helical ladder structure of base-pair rings in DNA creates a compact stack of π-electrons associated with the base pairs, promoting the question as to whether DNA could possibly serve as an electrical conduit. The issue of DNA conductivity related to the electron-transfer processes has been a focus of several recent investigations.[1−21] The ability of DNA to conduct an electron current can be impaired by formation of stable anions by the DNA bases and base pairs. The changes in acidity or basidity, which result from loss or uptake of the electron from or by a base in a base pair of DNA, can stop the migration of electrons in the direction of the DNA helix via the stacked bases.[11] An interesting feature of the electron transport in DNA is its coupling to the vibrational motion of the molecular wires formed by hydrogen-bonded and stacked DNA bases.[9,10] In our recent calculations on the uracil−uracil (U−U), uracil−thymine (U−T), and uracil−cytosine (U−C) dimer anions,[22−24] we found that the localization of the excess electron and the localization of the ring deformation of the base, which carries the excess electron, are coupled. The calculations also showed that the hydrogen-bond structure of the dimers can be significantly altered relative to the neutral complexes by the presence of excess electrons. This strongly affects the weaker hydrogen bonds, which upon electron attachment may break or change their structure. In addition, the ring of the base, where the excess electron is localized, noticeably puckers. Evidence of nuclear motion in a DNA base triggered by an electron attachment was recently found in the electron scattering experiment of Burrow and co-workers[25] on a metastable covalent uracil anion. This effect can be a key property determining the electron-transfer rate in DNA.

The excess electron attachment to DNA and RNA base dimers and higher H-bonded polymers and its effect on the hydrogen-bond network in these systems continues to be the focus of our investigation. The present work concerns electron attachment to the isolated (gas-phase) canonical Watson-Crick adenine−thymine base pair (A−T). It should be mentioned that although this pair is the most interesting from the biological point of view, it may not be the most energetically favored.[26]

Gas-phase experimental determinations of electron affinities (EA) of nucleic acid bases (NAB) in the gas phase have been done by several groups, including Hendricks et al.[27] and Schiedt et al.[28] with the photoelectron spectroscopy (PES) and Schermann and co-workers[29,30] with the Rydberg electron-transfer (RET) and field-detachment spectroscopy. This latter group also reported a mass spectrum of some NAB dimer anions including the valence anion of the adenine−thymine base pair (A−T$^-$). We are not aware of any direct experimental measurement of the electron affinity of the A−T dimer or the ionization potential of the A−T$^-$ anion. The present ab initio calculations may provide a useful contribution to future experimental determination of these quantities.

The effect of the DNA base pairing on the electron affinities of DNA bases was considered in low-level ab initio calculations by Sevilla and co-workers.[31,32] They determined that cytosine is the most electron affinic base in double-stranded DNA and thymine is the most electron affinic in single-stranded DNA in accord with the experiments.[33] They also determined that in the purine−pyrimidine base pair anions the electron density of the excess electron is largely localized on the pyrimidines. As will be shown in the present work, the results of our calculations fully support this conclusion.

The questions which we will attempt to answer in the present work are the following: (i) Does the valence A−T anion have isomeric forms different from the previously studied valence anions of uracil−thymine and uracil−cytosine dimers? (ii) Does the excess electron localize at adenine or thymine in the dimer anion, and what are the structural consequences of this localization? (iii) Does a puckering deformation occur in the base which carries the excess electron? (iv) Does the A−T dimer constitute an effective trap for excess electrons?

2. Calculations and Discussion

The following calculations have been performed with the use of the GAUSSIAN94 quantum-chemical program package[34] to elucidate the questions raised:

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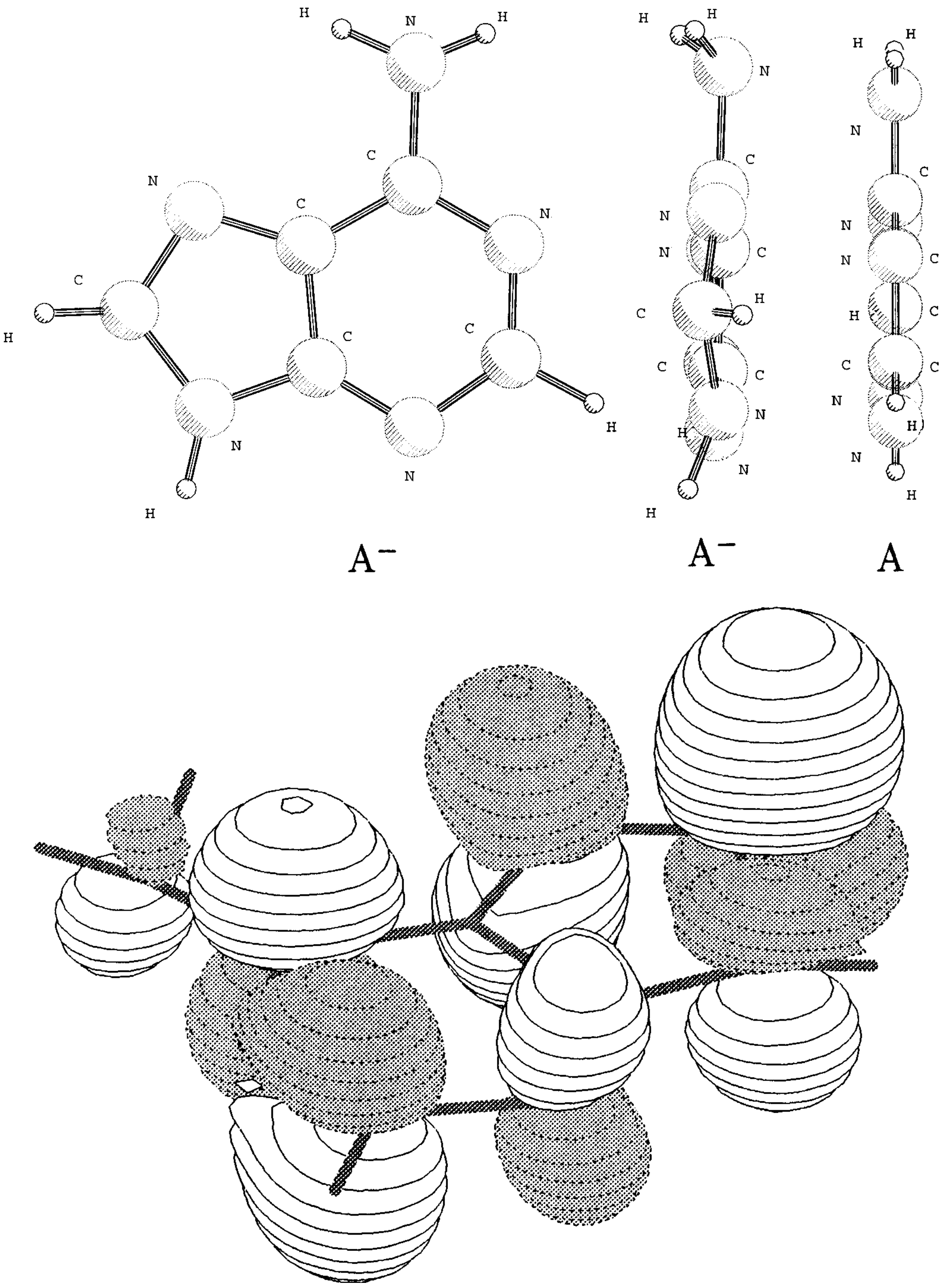

Figure 1. (Top, left amd middle) Puckered structure of the covalent anion of adenine, (top, right) planar structure of the neutral adenine molecule, and (bottom) the HOMO of the adenine anion.

(a) Since, as we predicted,[22,23] in the covalent U−U and U−T dimer anions the excess electron attaches to one of the bases, similar behavior can be expected in A−T$^-$. The electron attachment to a base in the dimer causes an out-of-plane ring deformation of the base, and this effect can be used in the calculations to direct the excess electron to one of the two bases in the base pair. The puckering deformation of the thymine ring in the covalent dimer anions formed by this base with the uracil molecule was described before.[23] The puckered thymine structure determined in that work was used in the present calculations to prepare the starting geometry for the structural optimization aimed at finding a A−T covalent anion with the excess electron at T. To initiate searches for a dimer anion with the excess electron at A, the structure of the adenine valence anion had to be determined. Several different puckered geometries of the adenine double ring were used to initiate the geometry optimization of A$^-$. The calculations were done at the UHF/6-31++G**(6d) level of theory (the spin-unrestricted Hartree−Fock method with the standard 6-31++G** basis set; each d shell consists of six orbitals). The equilibrium A$^-$ structure found is shown in Figure 1. One can see that the A$^-$ five-member ring is noticeably puckered. In the figure we also show the contour plot of the orbital occupied by the excess electron in this system. At the UHF equilibrium structure we calculated the UMP2/6-31++G**(6d) (Møller−Plesset second-order perturbation theory calculation with the UHF wave function as the reference) energy of A$^-$, as well as MP2/6-31++G**(6d) (MP2 with a spin-restricted HF wave function as the reference) of the neutral A. These calculations were done to determine the vertical electron detachment energy (VDE) of A$^-$. Next, starting

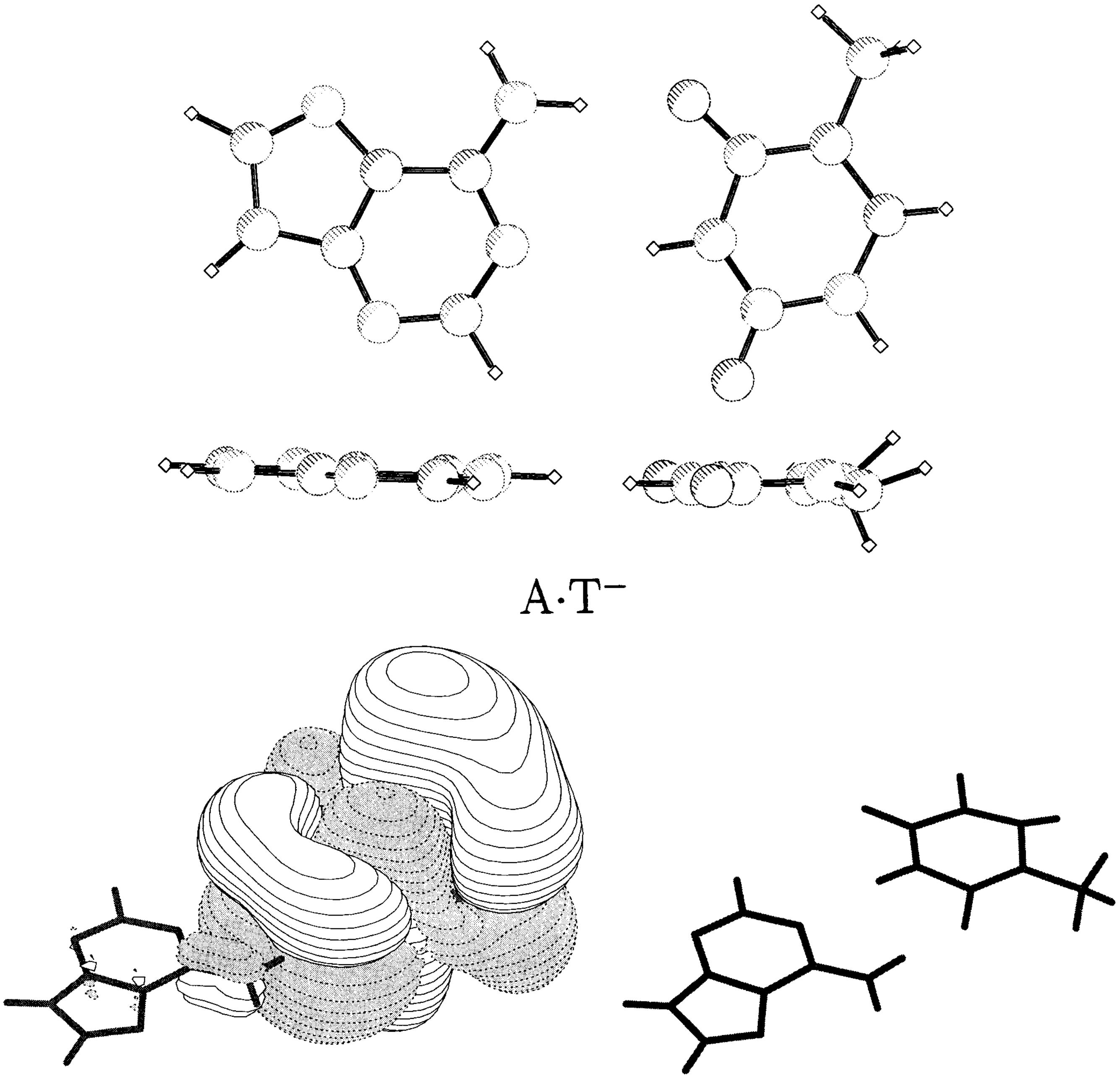

Figure 2. Covalent anion of the adenine−thymine dimer: structure (top) and the HOMO (bottom) plot (since the HOMO plot conceals the dimer structure, a separate structure plot is also provided).

from the A^- geometry, the structure of the neutral A was optimized at the RHF/6-31++G**(6d) level of theory and the resulting planar equilibrium geometry is also shown in Figure 1. For this structure the A energy was calculated at the MP2/6-31++G**(6d) level to provide the reference energy for determination of the adiabatic electron detachment energy (ADE) of A^-. The results are presented in Table 1. The predicted VDE of A^- (MP2 results of 332 meV), which is positive, indicates that this system is stable with respect to a vertical electron detachment. However, the negative ADE value (MP2 result of −1285 meV) shows that A^-, found in the calculations, is metastable with respect to an adiabatic detachment. The large ADE of A^- is consistent also with large negative vertical electron affinity values predicted theoretically for adenine by Sevilla and co-workers[31,32] and recently measured by Burrow and co-workers using an electron scattering technique.[25] These quantities indicate that adenines in the π-stack of DNA may hamper the bridge-assisted, long-range electron transfer along the stack.

TABLE 1: Vertical Electron Detachment Energy (VDE) and Adiabatic Electron Detachment Energy (ADE) Calculated for the Adenine Molecule with the 6-31++G Basis Set (Total Energies in hartrees; VDE and ADE in millielectronvolts)**

	$A^-//A^{-a}$	$A//A^-$	$A//A$	VDE	ADE
HF	−464.491 384	−464.517 037	−464.550 058	−698	−1597
MP2	−465.970 715	−465.958 521	−466.017 932	322	−1285

[a] $A^-//A^-$ denotes that the calculations on A^- were done at the equilibrium structure determined for A^-.

(b) The first series of calculations on the covalent A−T anion were aimed at determining the equilibrium structure (or structures) of this system. The search for the structure was initiated with three different initial geometries. In the first two, A and T were hydrogen-bonded in the way they are bonded in

TABLE 2: VDE and ADE Calculated for the Adenine−Thymine Dimer with 6-31++G Basis Set (Total Energies in hartrees; VDE and ADE in millielectronvolts)**

	$A-T^-//A-T^{-a}$	$A-T//A-T^-$	$A-T//A-T$	VDE	ADE
HF	−916.076 541	−916.057 464	−916.102 269	519	−700
MP2	−918.906 978	−918.897 030	−918.921 782	271	−403

[a] See footnote *a* in Table 1.

the canonical Watson−Crick AT base pair, but different intramolecular geometries of the bases were used. While in the first structure the puckered geometry determined for the valence anion of T and the equilibrium nonpuckered A geometry were used, in the second structure the puckered A^- and nonpuckered T geometries were used. The third search was initiated with a geometry in which A and T were separated by a considerable distance and the puckered A^- and nonpuckered geometries were used for A and T, respectively. This search was performed after the first two searches resulted in an identical equilibrium structure with the excess electron located at T (This structure is shown in Figure 2). The third search also resulted in the same structure as the one obtained with the first two searches. Although one can certainly continue exploring the topology of the $A-T^-$ potential energy surface, it seems likely that the minimum found in the present calculations corresponds to the lowest-energy structure of the A−T anion. It also seems unlikely that there exists a covalent A−T anion with a hydrogen-bond structure similar to that in the canonical Watson−Crick AT base pair and with the excess electron on the adenine molecule. Clearly, T has higher electron affinity than A, and the excess electron in the dimer shifts entirely toward thymine. This shift can be seen in the contour plot of the HOMO (highest occupied molecular orbital) of $A-T^-$ occupied by the excess electron, which is shown in Figure 2. The figure also shows the puckering distortion of the ring of the thymine molecule in the dimer.

(c) In the next calculation, the energy of the neutral A−T dimer at the dimer anion geometry was determined using the MP2/6-31++G**(6d) level of theory. This result, denoted as $A-T//A-T^-$, is presented in Table 2 along with the anion energy ($A-T^-//A-T^-$) and the energy of the neutral dimer obtained at the equilibrium geometry of the dimer (A−T//A−T). The calculation (at the RHF/6-31++G**(6d) level of theory) of the equilibrium structure of the neutral dimer was initiated with the $A-T^-$ equilibrium geometry and converged to the structure shown in Figure 3. The total energies obtained in the MP2 calculations were used to determine the VDE and ADE of $A-T^-$, and the results are also presented in Table 2.

As one can see, the energy of the neutral dimer at the equilibrium anion geometry is higher than the energy of the anion, indicating that the anion has a considerable vertical stability with respect to detachment of the excess electron. The vertical MP2/6-31++G**(6d) electron detachment energy is predicted to be 271 meV. On the other hand, the negative ADE value of −403 meV resulting from the present calculations indicates that $A-T^-$ is a metastable system. A more detailed comparison of the equilibrium geometries of the neutral and anion A−T dimers indicates that there are two major differences between the two structures. The first difference is the planar geometry of thymine in the neutral dimer vs the puckered thymine ring geometry in the anion. The second difference occurs in the structure of the intermolecular hydrogen bonds. A slightly different relative orientation of the two molecules in the anion than in the neutral dimer results in the shortening of two of the three hydrogen bonds and elongation of the third bond upon electron detachment from the anion.

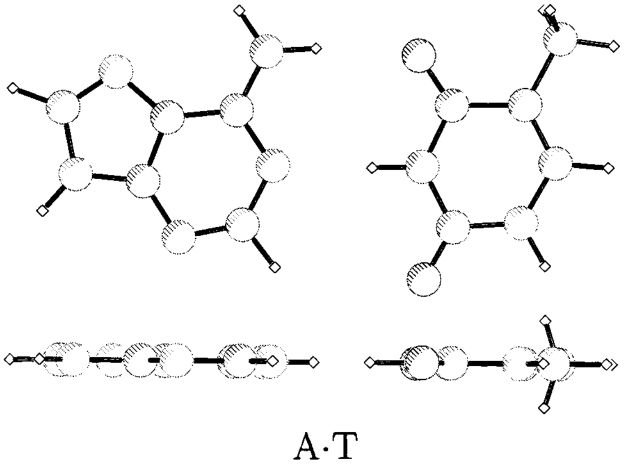

Figure 3. Structure of the neutral adenine−thymine dimer.

3. Conclusions

The ab initio theoretical calculations performed in this work revealed that the adenine−thymine dimer can form a metastable covalent anion with an excess electron. In this anion the excess electron is located at the thymine molecule. The calculations predicted a negative adiabatic electron detachment energy for the anion. This indicates the AT canonical base pair does not trap excess electrons. However, if the thymine ring is out-of-plane deformed in the dimer by a vibrational excitation of a puckering mode, an excess electron can be trapped into a bound state. The vibrational excitation triggering an electron attachment may constitute an important element of the excess electron-transfer process in DNA.

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References and Notes

(1) Murphy, C. J.; Arkin, M. R.; Jenkins, Y.; Ghatlia, N. D.; Bossmann, S. H.; Turro, N. J.; Barton, J. K. *Science* **1993**, *262*, 5136.

(2) Holmlin, R. E.; Dandliker, P. J.; Barton, J. K. *Angew. Chem.* **1998**, *36*, 2715.

(3) Barton, J. K. *Pure Appl. Chem.* **1998**, *70*, 873.

(4) Kellay, S. O.; Barton, J. K. *Chem. Biol.* **1998**, *5*, 413.

(5) Holmlin, R. E.; Tong, R. T.; Barton, J. K. *J. Am. Chem. Soc.* **1998**, *120*, 9724.

(6) Kelley, S. O.; Barton, J. K. *Science* **1999**, *283*, 375.

(7) Kelley S. O.; Barton, J. K. Radical migration through the DNA helix: Chemistry at a distance. In *Metal Ions in Biological Systems*, Vol. 36; Dekker: New York, 1999; pp 211−249.

(8) Kelley, S. O.; Jackson, N. M.; Hill, M. G.; Barton, K. J. *Angew. Chem.* **1999**, *38*, 491.

(9) Olson, M.; Moa, Y.; Windus, T.; Kemp, M.; Ratner, M.; Leon, N.; Mujica, V. *J. Phys. Chem. B* **1998**, *102*, 941.

(10) Ratner, M. *Nature* **1999**, *397*, 480.

(11) Steenken, S. *Biol. Chem.* **1997**, *378*, 1293.

(12) Grey, H. B.; Winkler, J. R. *J. Electroanal. Chem.* **1997**, *438*, 43.

(13) Krider, E. S.; Meade, T. J. *J. Biol. Inorg. Chem.* **1998**, *3*, 222.

(14) Krider, E. S.; Rack, J. J.; Meade, T. J. *Abstr. Papers—Am. Chem. Soc.* **1999**, *217*, 671-INOR.

(15) Krider, E. S.; Rack, J. J.; Frank, N. L.; Meade, T. J. *Abstr. Papers—Am. Chem. Soc.* **1999**, *217*, 492-INOR.

(16) Netzel, T. L. *J. Biol. Inorg. Chem.* **1998**, *3*, 210.

(17) Ptiyadarshy, S.; Risser, S. M.; Beratan, D. N. *J. Biol. Inorg. Chem.* **1998**, *3*, 196.

(18) Poy, C. D.; Cornelio, M. L. *Ecletica Quim.* **1998**, *23*, 99.

(19) Fink, H. W.; Schonenberger, C. *Nature* **1999**, *398*, 407.

(20) Giese, B.; Wessely, S.; Spormann, M.; Lindemann, U.; Meggers, E.; Michel-Beyerle, M. E. *Angew. Chem.* **1999**, *38*, 996.

(21) Harriman, A. *Angew. Chem.* **1999**, *38*, 945.

(22) Smith, D. M. A.; Smets, J.; Adamowicz, L. *J. Phys. Chem. A* **1999**, *103*, 5784.

(23) Smith, D. M. A.; Smets J.; Adamowicz, L. *J. Phys. Chem. A* **1999**, *103*, 4404.

(24) Al-Jihad, I.; Smets, J.; Adamowicz, L. *J. Phys. Chem.*, submitted for publication.

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

(26) Hobza, P.; Sponer, J. *Chem. Phys.* **1999**, *99*, 3247.

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

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

(29) Desfrançois, C.; Abdoul-Carime, H.; Schermann, J. P. *J. Chem. Phys.* **1996**, *104*, 7792.

(30) Desfrançois, C.; Periquet, V.; Bouteille, Y.; Schermann, J. P. *J. Phys. Chem. A* **1998**, *102*, 1274.

(31) Colson, A.-O.; Besler, B.; Sevilla, M. D. *J. Phys. Chem.* **1994**, *96*, 9787.

(32) Sevilla, M. D.; Besler, B.; Colson, A.-O. *J. Phys. Chem.* **1995**, *99*, 1060.

(33) Sevilla, M. D.; Backer, D.; Yan, M.; Summerfield, S. R. *J. Phys. Chem.* **1991**, *95*, 3410. Bernhard, W. A. *J. Chem. Phys.* **1989**, *93*, 2187.

(34) 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. Y.; 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; Gaussian, Inc.: Pittsburgh, PA, 1995.