Solvation of Al−Guanine Complexes with NH_3: A Theoretical Study

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Geometry optimizations on complexes composed of an Al atom, a guanine molecule, and an ammonia molecule have been performed with density functional methods. In the most stable structures, the ammonia molecule forms hydrogen bonds with previously studied Al−guanine complexes. The two lowest structures correspond to an unusual tautomer of guanine in which both N atoms of the five-membered ring, N7 and N9, are protonated. Within 3 kcal/mol in energy lie two additional structures in which a proton is shifted from N9 to N3. Ionization energies calculated with ab initio, electron-propagator methods for the two latter structures are in close agreement with the experimentally observed ionization threshold. Higher ionization energies are obtained for the two lowest structures. Dyson orbitals for the lowest ionization energies are guanine π^* functions. The order of isomers in the cationic species is different from that of the neutrals. Energies of ammonia dissociation are approximately equal for all forms of the Al−guanine−NH_3 complex, except for a structure with an Al−NH_3 dative bond.

Introduction

Interactions between metal ions and DNA have far-reaching biological consequences.[1−4] Metal−base complexes may have tautomerization energies and structures that differ from those of the Watson−Crick bases. Metal complexation therefore has the potential to disrupt the replication of genetic material. Information on the energetics of metal-ion coordination to base N atoms and on the effects of these interactions on acid−base and keto−enol equilibria may be useful in understanding the origins of a variety of reproductive pathologies.

Electronic properties of base pairs and stacks also may be affected by metal complexation. These effects may influence the structural and electronic properties of molecular electronic devices constructed with DNA fragments.[5,6] Complexed metal atoms may function as electron acceptors or donors and have been successfully used to study charge transport through strands of DNA.

Solvents also have important structural and energetic effects on the bonding capabilities of DNA bases. With the advent of improved techniques for the synthesis and isolation of intermolecular complexes with specified numbers of solvent molecules, spectroscopic studies may now provide detailed information on individual binding energies. Competition for solvent molecule coordination between bases and metal ions may be examined through synthesis and characterization of metal−base−solvent assemblies.

These developments invite computational investigation of corresponding structures, for tautomerism, metal−ligand coordination isomerism, and hydrogen bonding imply an abundance of alternative geometries. Predictions on spectroscopic properties may provide corroboration of calculated structures. After testing computational methodologies against experimental data to ensure reliability, well-calibrated methods may be applied to species that lie beyond the capabilities of current experimental techniques.

A study of gas-phase Al−guanine−$(NH_3)_n$ ($n = 0$, 1, and 2) complexes prepared with laser ablation and characterized by photoionization spectroscopy and mass spectrometry has appeared recently.[7] Photoionization efficiency spectra were collected and used to determine ionization energies of the gas-phase Al−guanine complex. Introduction of ammonia into the He carrier gas resulted in a shift of the onset of ion signal from 5.6 ± 0.1 eV to 4.65 ± 0.08 eV for the Al−guanine ($n = 0$) complex. Two explanations were proposed for this effect. First, association of ammonia molecules might produce a species in an electronically excited or geometrically distorted form. Loss of NH_3 during a photoexcitation−ionization process then would produce a species with a significantly lower value for the ionization energy. In an alternative view, an ammonia molecule might facilitate the formation of an isomer of the Al−guanine complex with a shifted ionization potential.

Preliminary calculations[7] and a subsequent, more complete study[8] employing density functional and correlated ab initio methods were compatible with the second explanation. After optimization of several structures and prediction of their vertical ionization energies, good agreement with the higher threshold value was obtained for a complex where an Al atom is coordinated to an unusual guanine tautomer in which both nitrogens of the five-membered ring (N7 and N9) are protonated. (In contrast, the Watson−Crick tautomer is not protonated at N7; see Figure 1.) This unprecedented tautomer is related to another form by a proton transfer from N9 to N3. Coordination of an Al atom to the tautomer with protonated N3 produces a complex whose predicted ionization energy is close to the lower threshold. Calculations also indicated that the species with the higher ionization energy is slightly more stable. In addition, a

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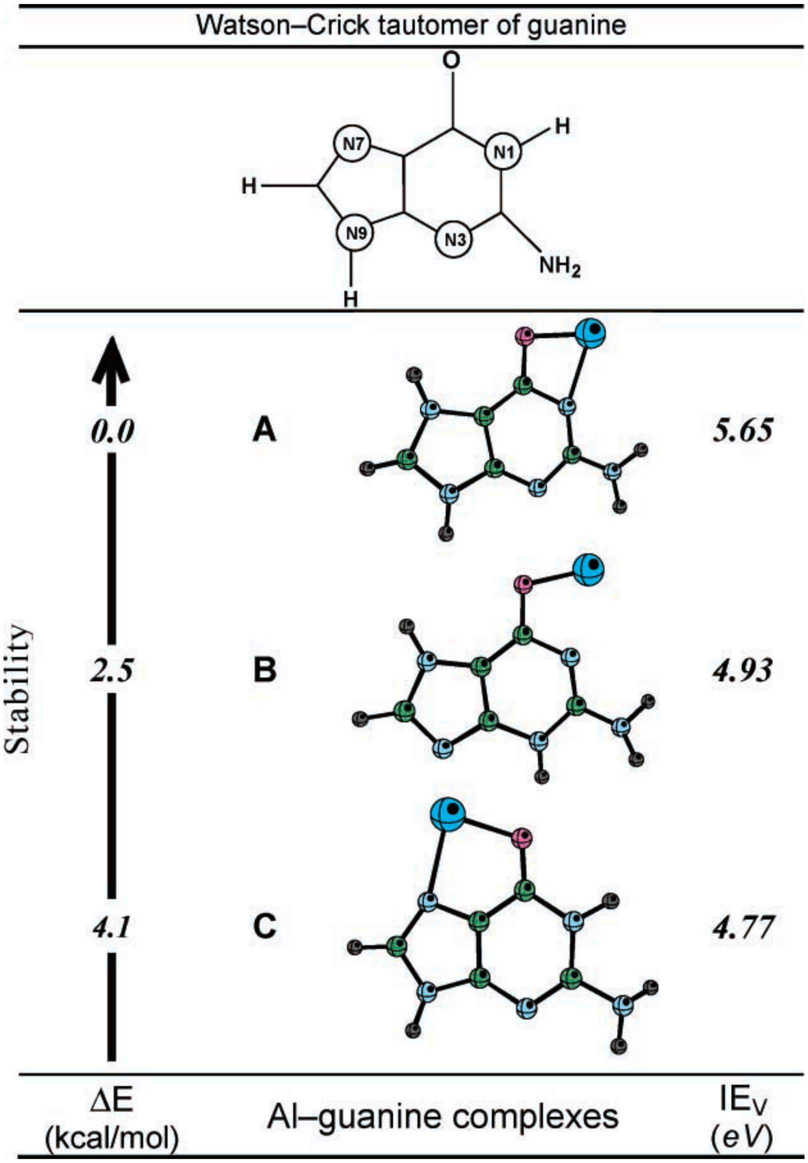

Figure 1. Numbering scheme of guanine and the most stable Al−guanine complexes previously reported. Energy differences (Δ*E* in kcal/mol) and vertical ionization energies (IE_v in eV) were obtained at the BP86 level.

third structure with an ionization energy that also is close to the lower threshold was found. Figure 1 summarizes these conclusions.

Experiments on the ionization energies of Al−guanine−$(NH_3)_{1,2}$ complexes produce threshold ionization energies of 4.6 ± 0.1 for $n = 1$ and 4.5 ± 0.2 for $n = 2$.[7] One explanation for this result is that the most stable forms of these complexes bear a structural resemblance to the less stable form of the Al−guanine complex with the lower ionization energy. Another possibility is that coordination of an ammonia molecule distorts some form of the Al−guanine complex such that a lower ionization energy is produced.

To resolve this question, density functional and ab initio, electron-propagator calculations on Al−guanine−NH_3 complexes have been performed. Optimized structures and relative energies of neutral Al−guanine−NH_3 species and their cations are presented. Vertical and adiabatic ionization energies also are determined. Changes in electronic structure that accompany ionization are interpreted in terms of orbital concepts. The implications of these results for the study of metal interactions with DNA bases are discussed in the conclusions.

Methods

Density Functional Calculations. All calculations have been carried out with Gaussian 98.[9] Full geometry optimization without symmetry constraints was performed using the Becke−Perdew86 (BP86) functional[10] and the 6-311+G(2d,p) basis.[11] A systematic examination of tautomers and metal−guanine coordination geometries was undertaken. Optimized minima were verified with frequency calculations. The visualization of the results was done with the Cerius package[12] and the MOLEKEL[13] program.

Electron-Propagator Calculations. Electron-propagator calculations[14] were performed in the P3 approximation[15,16] with the 6-311G** basis. This level of theory has enjoyed extensive success in accurate prediction of photoelectron spectra of DNA bases.[17] For each ionization energy, there is a Dyson orbital defined by

$$\varphi^{\mathrm{Dyson}}(x_1) = N^{1/2} \int \Psi_N(x_1,x_2,x_3, ..., x_N) \times \Psi^*_{N-1}(x_2,x_3,x_4, ..., x_N)\, dx_2\, dx_3\, dx_4 ... dx_N$$

where the initial and final many-electron states have *N* and

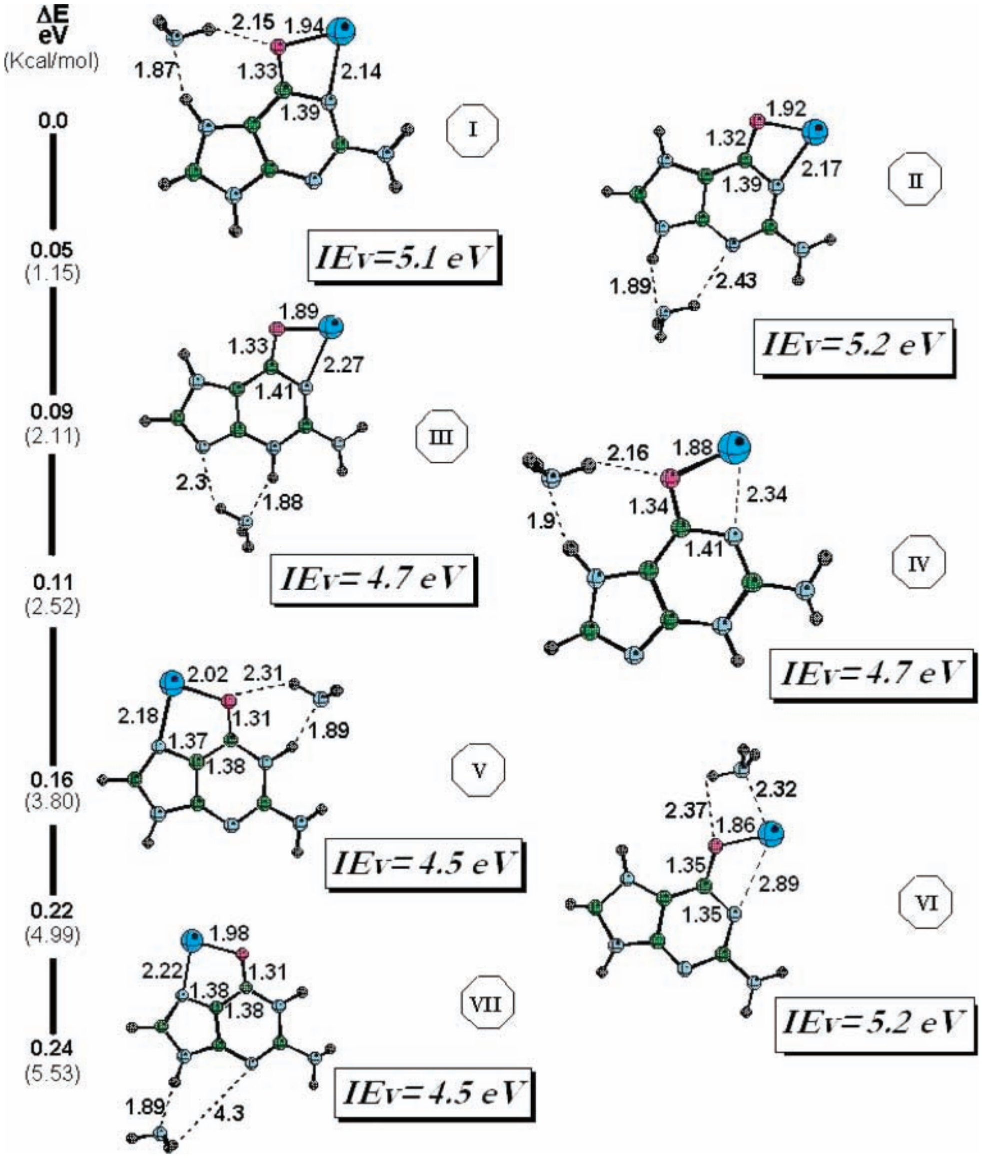

Figure 2. Optimized structures (bond distances in Å), relative energies (Δ*E* in eV and kcal/mol), and vertical ionization energies (IE_v in eV) of Al−G−NH_3 complexes.

N − 1 electrons, respectively. Thus, the Dyson orbital represents an overlap between two states with different numbers of electrons and is a correlated generalization of a canonical, Hartree−Fock orbital. The corresponding pole strength equals the normalization integral of the Dyson orbital. Values above 0.8 validate the perturbative arguments that underlie P3 calculations, which contain relaxation and correlation corrections to the results of Koopmans's theorem.

Results and Discussion

Density Functional Calculations. In the absence of an ammonia molecule, the Al−guanine complex (Al−G) has three stable structures, shown in Figure 1, whose energies differ by less than 5 kcal/mol.[8] The BP86 vertical ionization energy of the lowest (A) structure, 5.65 eV, is in reasonable agreement with the experimentally determined photoionization threshold of 5.6 ± 0.1 eV. The onset signal in the Al−G photoionization efficiency spectrum shifts from 5.6 to 4.65 eV upon introduction of NH_3 to the He carrier gas. The lower experimental value is comparable to the 4.93 and 4.77 eV predictions made, respectively, for the second (B) and the third (C) most stable isomers of Al−G.

Figure 2 shows the optimized geometries of the Al−G−NH_3 complex. Whereas structures I, II, and VI resemble A, structures III and IV resemble B, while structures V and VII derive from structure C. The stability order with and without NH_3 is the same except for structure VI, the only case where the ammonia nitrogen forms a dative bond with the aluminum atom instead of a hydrogen bond with a guanine proton. Most of the energy differences are quite similar, but structure VI is 4−5 kcal/mol less stable than structures I and II. Such energy differences are close to the expected accuracy of the BP86 method, and therefore it is not possible to ignore any of these structures when interpreting photoionization experiments.

Vertical ionization energies are lower in the presence of a coordinated ammonia molecule. For structures I and II, the shift is approximately 0.5 eV with respect to the A structure of Al−G. Coordination of an ammonia molecule to the B and C Al−G structures reduces the vertical ionization energy by 0.2−0.3 eV.

Cationic Al−G−NH_3 geometries, shown in Figure 3, exhibit a completely different ordering, with structure V being the lowest. Energy differences between the cationic isomers also are small. Ionization produces markedly longer Al−N distances in the cations. Adiabatic ionization energies, summarized in

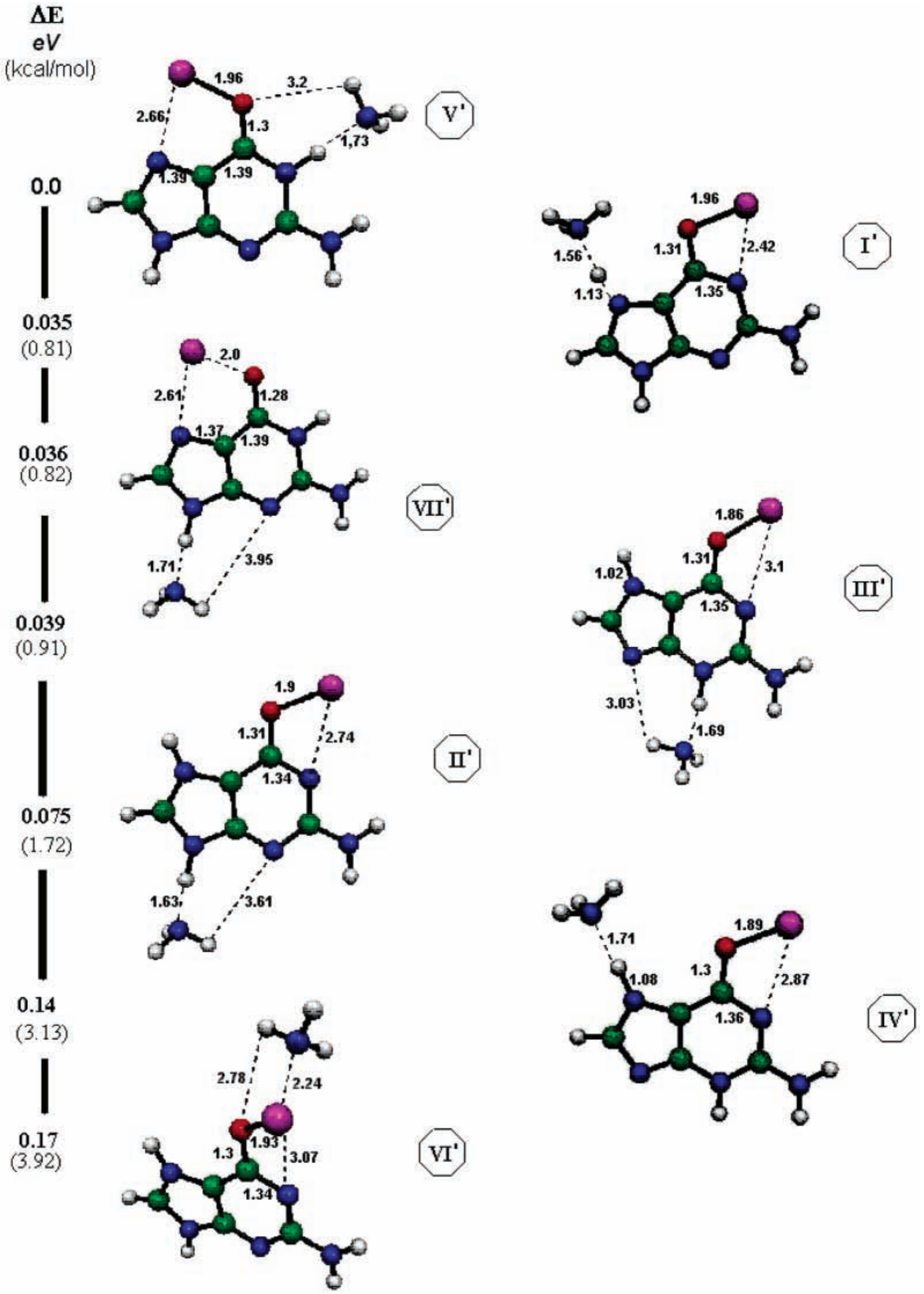

Figure 3. Optimized structures (bond distances in Å) and relative energies (Δ*E* in eV and kcal/mol) of cationic Al−G−NH_3 complexes.

Table 1, are approximately equal for all isomers, in contrast with the clearly distinct peaks at 5.6 and 4.65 eV seen in photoionization experiments. The short time scale of these experiments does not allow for extensive geometrical relaxation.

Molecular orbitals for the most stable neutral geometry and its corresponding cation are shown in Figure 4. An orbital dominated by an Al 3p function is unoccupied in both species. The guanine-centered π^* orbital (G π^*) is singly occupied in the neutral geometry and unoccupied in the cation. In both species, two electrons are assigned to the third orbital, whose chief contribution is an Al 3s function. The G π^* orbital exhibits a bonding C−C lobe in the six-membered ring and contributions from N 2p orbitals in the five-membered ring. There is no delocalization into the ammonia molecule. Orbital relaxation leads to a higher charge on the Al atom in the cation.

In Table 2, ammonia dissociation energies for the neutral Al−G−NH_3 structures are shown, where

$$\Delta E_{\mathrm{d}} = [E(\mathrm{Al{-}G}) + E(\mathrm{NH_3})] - E[\mathrm{Al{-}G{-}NH_3}]$$

Similar energies, from 8.5 to 10.2 kcal/mol, are obtained for all geometries except one, structure VI, whose lower value, 4.9 kcal/mol, reflects the absence of a hydrogen bond to the ammonia lone pair.

Basis set superposition errors (BSSE) were obtained, and the values are about 0.6 kcal/mol. Our conclusions are unaffected by these minor corrections.

TABLE 1: Vertical and Adiabatic Ionization Energies (in eV) and Mulliken Atomic Charges for the Optimized Neutrals (Neutral), the Optimized Cations (OptCat), and the Cations Obtained with the Optimized Geometry of the Neutral Systems (Vcat)

	ionization energy			atomic charges		
complex	vertical	adiabatic		neutral	Vcat	OptCat
I	5.1	4.3	*Al*	0.19	0.38	0.41
			O	−0.60	−0.54	−0.54
			C6	0.40	0.50	0.49
			N1	−0.40	−0.40	−0.43
II	5.2	4.3	*Al*	0.21	0.38	0.50
			O	−0.60	−0.48	−0.55
			C6	0.43	0.50	0.51
			N1	−0.43	−0.39	−0.44
III	4.7	4.3	*Al*	0.15	0.41	0.57
			O	−0.60	−0.47	−0.59
			C6	0.44	0.52	0.55
			N1	−0.43	−0.39	−0.48
IV	4.7	4.3	*Al*	0.17	0.42	0.52
			O	−0.61	−0.60	−0.55
			C6	0.44	0.53	0.53
			N1	−0.42	−0.39	−0.47
V	4.5	4.1	*Al*	0.07	0.38	0.47
			O	−0.50	−0.50	−0.54
			C6	0.42	0.5	0.51
			C5	0.13	0.13	0.03
			N7	−0.34	−0.3	−0.30
VI	5.2	4.3	*Al*	0.18	0.29	0.35
			O	−0.60	−0.62	−0.52
			C6	0.51	0.53	0.42
			N1	−0.45	−0.37	−0.45
VII	4.5	4.1	*Al*	0.09	0.39	0.46
			O	−0.53	−0.44	−0.49
			C6	0.43	0.47	0.53
			C5	0.13	0.13	0.06
			N7	−0.35	−0.29	−0.33

Electron-Propagator Calculations. Vertical ionization energies of the five most stable isomers of Al−G−NH_3 were calculated at the P3/6-311G* level. The results shown in Table 3 pertain to transitions between the neutral doublet and the ground state singlet or the lowest triplet of each cation. Results for the lowest vertical ionization energy of structures I and II are within 0.2 eV of each other. Markedly lower values are obtained for structures III and IV and are in close agreement with the experimental report for the ionization threshold of Al−G−NH_3: 4.6 ± 0.1 eV. For structure V, the P3 prediction is even lower. Vertical ionization energies obtained from P3 calculations are up to 0.2 eV lower than their BP86 counterparts. These results suggest that isomers III and IV are likely to be responsible for ionization at the threshold energy and that isomers I and II, while they may be present in the experimental sample, correspond to vertical ionization energies that are approximately 0.5 eV higher than the threshold. They also indicate that isomer V is not present. Dyson orbitals for each case resemble the G π^* orbital of Figure 4. Pole strengths are close to 0.9 and therefore validate the perturbative arguments of the P3 approximation.

For the second ionization energy of each complex, the Dyson orbital resembles the Al 2s molecular orbital of Figure 4. These values are 7.0 eV or higher for structures I through IV; structure V yields a lower result. Pole strengths are approximately 0.9 for each of these transitions.

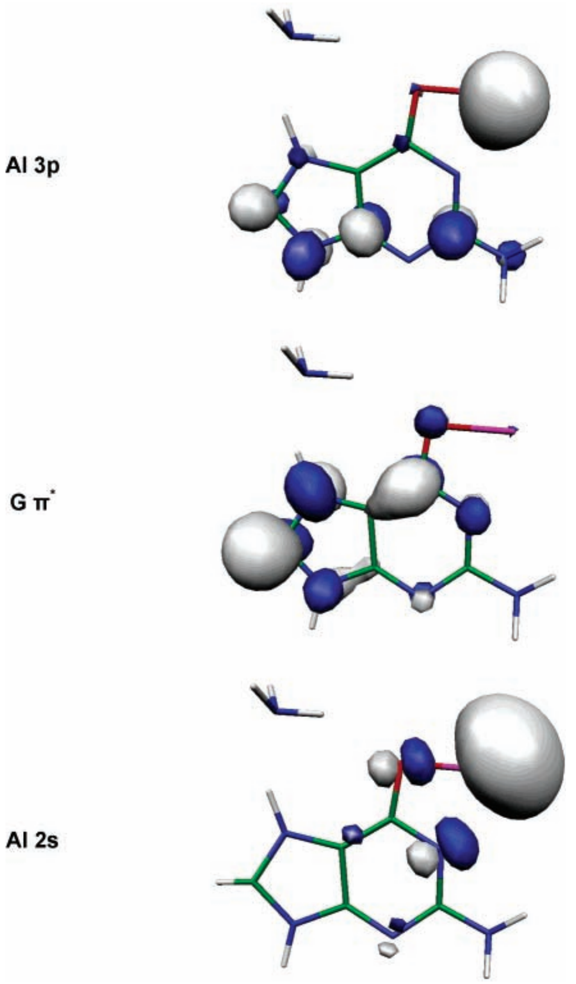

Figure 4. Molecular orbitals of Al−G−NH_3 complexes.

TABLE 2: Ammonia Dissociation Energies for the Guanine−Al−NH_3 Complexes

complex	ΔE_d (kcal/mol)
I	9.9
II	8.7
III	10.2
IV	9.8
V	10.2
VI	4.9
VII	8.5

TABLE 3: Vertical Ionization Energies (eV) and Pole Strengths

isomer	MO	DFT	Koopmans	P3	P3 pole strength	experiment
I	G π^* α	5.1	5.96	4.96	0.88	
	Al 2s β		7.49	7.19	0.91	
II	G π^* α	5.2	6.18	5.17	0.88	
	Al 2s β		7.44	7.16	0.92	
III	G π^* α	4.7	5.30	4.47	0.89	4.6 ± 0.1
	Al 2s β		7.29	7.00	0.91	
IV	G π^* α	4.7	5.45	4.63	0.89	4.6 ± 0.1
	Al 2s β		7.73	7.44	0.91	
V	G π^* α	4.5	4.66	4.12	0.88	
	Al 2s β		6.80	6.47	0.90	

Conclusions

The most stable structure of the Al−guanine−NH_3 complex has two N−H bonds on the five-membered ring. The metal atom bridges between oxygen and N1. The ammonia molecule is not covalently bonded to the complex. Instead, a hydrogen bond between the N atom of the ammonia molecule and a H atom on guanine stabilizes the complex. A second form has nearly the same energy but a different location for the hydrogen-bonded ammonia molecule. Two other structures with low-lying energies differ by a proton shift from N9 to N3. Less than 3 kcal/mol separates these four structures. Coordination of the ammonia molecule to the Al atom produces a less stable structure. The predicted vertical ionization energies of the third and fourth most stable structures are in close agreement with the experimentally determined photoionization threshold of 4.6 ± 0.1 eV. Ionization from the first and second structures occurs at higher energies. Coordination of an ammonia molecule reduces the vertical ionization energy of the first two structures by approximately 0.5 eV, but the reduction is smaller, approximately 0.2 eV, for the third and fourth structures. No drastic structural changes in the Al−guanine complexes take place as a result of hydrogen bond formation with the ammonia molecule. The Dyson orbital associated with ionization from the Al−guanine−NH_3 complex is a guanine π^* function which resembles its counterpart in the Al−guanine species. Ionization changes the energetic order of the structures. Ammonia dissociation energies are approximately equal for all forms of the Al−guanine−NH_3 complex, except for the structure that has a dative Al−NH_3 bond.

Little change in the tautomerization energy between the two lowest forms of the Al−guanine complex is effected by coordination of an ammonia molecule. However, the reduction in the threshold ionization energy of the Al−guanine complex produced by the addition of ammonia to the He carrier gas is a reflection of the presence of the slightly less stable form found in our previous work.[8] It is likely that the role of the ammonia molecule is to facilitate the shift of a proton from N9 to N3. A search for corresponding transition states in the presence and in the absence of an ammonia molecule may illuminate the mechanistic origin of the observed spectral shift.

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Supporting Information Available: Cartesian coordinates (in angstroms) for the optimized geometries of the most stable complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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