Deprotonated Cytosine Anions: A Theoretical Prediction of Photoelectron Spectra

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Predictions on the photoelectron spectra of deprotonated cytosine anions (cytosinate, Cye^-) have been made with ab initio electron propagator methods. Two imino-oxo forms are most stable, but four other isomers have energies within 10 kcal/mol. The first vertical electron detachment energies (VEDEs) for the three most stable Cye^- isomers are approximately 3.4 eV. Imino-oxy VEDEs are about 0.3 eV smaller. For each anion, the lowest VEDE corresponds to a π Dyson orbital. The order of higher final states is changed when relaxation and correlation effects are considered. Considerable mixing between lone-pair and bonding lobes occurs in the σ Dyson orbitals.

Introduction

Nucleic-acid bases attract the interest of scientists from a wide diversity of fields, chiefly in the biological sciences, due to the central role of nucleic acids in the cell life cycle and the underlying mechanisms of their reactions, both normal and pathological.[1−3] More recently, materials scientists have considered the role of nucleic-acid bases and their ions in the charge-transfer processes that may enable DNA strands to behave as molecular wires and as components in other electronic devices at the nanometer scale.[4−6] A variety of oxidative processes on DNA strands[7] generate electrons that produce negative anions and radicals that are the objects of frequent study.[2,8−10] Negative ionic species play a role in biologically relevant events such radiation damage to DNA and RNA strands.[8,10,11] Recently described acid−base catalysis mediated by RNA where cytosine acts as a proton donor may involve anionic species.[12] Radicals and ionized species also are important in the charge-transfer phenomena that take place in DNA oligomers.[6,13]

Interactions of nucleic acids and biomolecules (such as small peptides and proteins) are involved in signaling and site recognition in some biological processes. The former take place between a small number of bases and specific fragments of those biomolecules.[3] In this way, the study of the interactions of nucleic acids and biologically relevant molecules may be carried out with ab initio methods using nucleic acid bases and other molecular fragments.

Usually, studies on negatively charged species from nucleic-acid bases have been aimed at anions produced by attaching an excess electron to neutral molecules;[14−16] nonetheless, stable anionic species formed by the loss of an aromatic hydrogen have been reported.[17] Attention paid to these latter species was in part the result of early attempts to produce anions of the nucleic-acid bases where dehydrogenation occurred as the dominant process.[18]

Electron affinities of nucleobases correlate with their reduction as a key part of other more complex processes involved in DNA damage and repair.[19] Therefore, part of the literature is devoted to the study of several kinds of anions and radicals of nucleic acid bases.[20−22] Photoelectron spectroscopy and other techniques, such as charge-transfer reactions in a mass spectrometer, plasma and optogalvanic spectroscopies, and collisional ionization have been applied to the determination of electron affinities and ionization potentials of small molecules and anionic species.[23] The photoionization spectra of these species constitute a fingerprint that allows direct comparison to theoretical calculations. Fine-tuning laser techniques and improved control of experimental conditions[24] allow experimentalists to determine energetic data.

In this work, we face two main questions. First, what are the most stable structures that obtain after the removal of a proton from a cytosine molecule? Second, what are the electron detachment energies that pertain to these structures and which may be used to assign an anion photoelectron spectrum?

Methods

Density functional methods are used initially to screen a large number of tentative geometries produced by systematically permuting hydrogens over all possible binding sites on the cytosine backbone. This screening stage allows us to select a reduced group of isomers with high probability of populating an experimental sample of cytosinate anion (Cye^-) species. The structures are reoptimized using perturbational methods. Hartree−Fock molecular orbitals at the resulting structures are needed to calculate third-order electron propagator corrections to Koopmans results. The last step provides our best estimates of the electron detachment energies of the most stable Cye^- isomers.

After removal of one hydrogen ion (H^+) from cytosine ($C_4H_5N_3O$), Cye^- has six possible binding sites located on the N1, N3, O, C5, C6 and N7 (the amino nitrogen in the canonical tautomer) nuclei. Previous theoretical studies on cytosine and other nucleobases (neutral and anionic)[25,26] have shown that rotational isomers of cis and trans types with respect to imino and oxy functional groups also should be considered. Another type of structure is obtained if two hydrogen atoms are allowed

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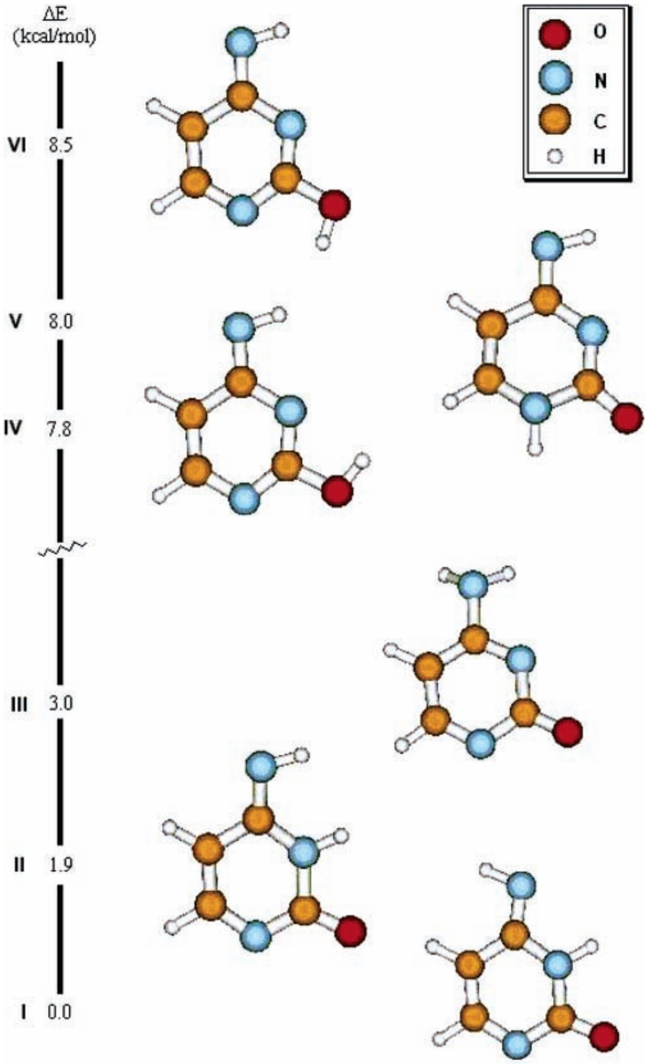

Figure 1. Optimized structures and relative energies (kcal/mol) of Cye$^-$ at the MP2/6-311+G(2d,p) level of theory.

on C5 or C6 of Cye$^-$ and these *methylene* isomers are considered here. The total number of initial structures for this study on the Cye$^-$ isomers is 95.

The propagator methods that are used to calculate accurate ionization energies and electron affinities require good molecular geometries of ground-state systems. Such ground-state structures can be obtained by optimizing initial structures with second-order Møller−Plesset perturbation theory[27] (MP2). Nevertheless, to optimize the numerous initial structures, it is advisable to start with accurate[28] but computationally less demanding methods of density functional theory[29−31] (DFT). Several studies on nucleobases show good agreement between DFT-optimized geometries and those obtained with MP2.[32−34]

All the initial structures were optimized with *Gaussian 03*[35] at the B3LYP[36−38] level of theory with the 6-311+G(2d,p)[39−41] basis set and then screened by their relative stabilities. The isomers of each nucleobase anion considered for the next part of the study were selected from those whose relative stability fell within 10 kcal/mol of the most stable structure. This new set of isomers was submitted to a new optimization at the MP2[42−44]/6-311+G(2d,p) level. Each optimization's minimum was verified with vibrational frequency[44,45] analysis.

Electron propagator calculations[46−48] in the P3 aproximation[49,50] were performed on the last group of isomers with the 6-311++G(2df,2p) basis. The MOLDEN[51] program package was used to visualize and analyze the output from the calculations. Dyson orbitals related to the electron detachment processes for each of the stable anionic species also were obtained.

The physical content of the electron propagator resides chiefly in its poles (energies where singularities lie) and residues (coefficients of the terms responsible for the singularities).[46,52] In its spectral form, the r, s element of the electron propagator matrix is

$$G_{\mathrm{rs}}(E) = \lim_{\eta \to 0} \left\{ \sum_n \frac{\langle N|a_{\mathrm{r}}^{\dagger}|N-1, n\rangle\langle N-1, n|a_{\mathrm{s}}|N\rangle}{E + E_{\mathrm{n}}(N-1) - E_0(N) - \mathrm{i}\eta} + \sum_m \frac{\langle N|a_{\mathrm{s}}|N+1, m\rangle\langle N+1, m|a_{\mathrm{r}}^{\dagger}|N\rangle}{E - E_{\mathrm{m}}(N+1) + E_0(N) + \mathrm{i}\eta} \right\}$$

The limit with respect to η is taken because of integration techniques required in a Fourier transform from the time-dependent representation. Indices r and s refer to general, orthonormal spin−orbitals, $\phi_{\mathrm{r}}(x)$ and $\phi_{\mathrm{s}}(x)$, respectively, where x is a space-spin coordinate. Matrix elements of the corresponding field operators, $a_{\mathrm{r}}^{\dagger}$ and a_{s}, depend on the N-electron reference state, $|N\rangle$ and final states with $N \pm 1$ electrons, labeled by the indices m and n. The propagator matrix is energy-dependent; poles occur when E equals an ionization energy, $E_0(N) - E_{\mathrm{n}}(N-1)$, or an electron affinity, $E_0(N) - E_{\mathrm{m}}(N+1)$. Corresponding residues, such as $\langle N|a_{\mathrm{r}}^{\dagger}|N-1\rangle\langle N-1, n|a_{\mathrm{s}}|N\rangle$, or $\langle N|a_{\mathrm{s}}|N+1, m\rangle\langle N+1, m|a_{\mathrm{r}}^{\dagger}|N\rangle$, are related to the Feynman−Dyson amplitudes, where

$$U_{\mathrm{r,n}} = \langle N-1, n|a_{\mathrm{r}}|N\rangle$$

or

$$U_{\mathrm{r,n}} = \langle N+1, n|a_{\mathrm{r}}^{\dagger}|N\rangle$$

FDAs suffice for constructing Dyson orbitals (DOs) for ionization energies or electron affinities, where

$$\phi_{\mathrm{n}}^{\mathrm{Dyson}}(x) = \sum_r \phi_{\mathrm{r}}(x) U_{\mathrm{r,n}}$$

Results and Discussion

Optimized Cye$^-$ Structures. Figure 1 shows the final set of the Cye$^-$ isomers selected after the previously described optimization procedure. Isomers **I** and **II** are imino-oxos, **III** is an amino-oxo, **IV** and **VI** are imino-oxys, and **V** is an imino-oxo. The six-membered rings, being virtually planar, have bond lengths that are similar to the bond distances in the stable, canonical isomer of cytosine. Deviations from planarity are accompanied by slight changes in atomic distances. These changes were not significant, for the deformation energy is very small, 0.1 kcal/mol, for structures **I** and **II**, respectively.

The difference between the two Cye$^-$ isomers labeled **I** and **II** (see Figure 1) is the rotation of a hydrogen atom of the imino group. The energy change for this rotation is 1.9 kcal/mol. In both structures, the six-membered ring is slightly distorted, but the energy associated with this deformation from planarity is small. The other isomers (**III** to **VI**) are planar. Isomers **IV** and **VI** also are rotational isomers (in the same way as the previous imino-oxo forms), and the energy difference between them is 0.7 kcal/mol. Note that the rotation about an oxy group requires less energy than the rotation about an imino group.

Isomer **III** is 3.0 kcal/mol less stable than isomer **I** (see Figure 1) and just 1.1 kcal/mol less stable than **II**. It is likely that a

TABLE 1: Electron Detachment Energies (eV) of the Lowest Cye$^-$ Isomers Calculated at the P3/6-311++G(2df,2p) Level from MP2/6-311+G(2d,p) Optimized Geometries

Cye$^-$ isomer	symmetry label	Koopmans theorem	P3 approximation	pole strength
I	π_1	3.73	3.45	0.878
	π_2	5.98	4.99	0.871
	σ_1	6.86	5.37	0.879
	σ_2	7.32	5.68	0.877
II	π_1	3.68	3.43	0.879
	π_2	6.11	5.12	0.870
	σ_1	6.78	5.30	0.880
	σ_2	7.38	5.71	0.875
III	π_1	3.62	3.37	0.879
	σ_1	5.66	4.34	0.885
	π_2	6.03	5.28	0.871
	σ_2	6.59	4.67	0.878
IV	π_1	3.34	3.10	0.877
	π_2	5.80	5.28	0.874
	σ_1	6.48	5.11	0.883
	σ_2	6.79	5.24	0.874
V	π_1	4.03	3.57	0.876
	π_2	4.95	4.45	0.883
	σ_1	6.32	4.95	0.886
	σ_2	6.77	5.19	0.879
	σ_3	7.57	5.70	0.875
VI	π_1	3.34	3.10	0.877
	π_2	5.80	5.28	0.874
	σ_1	6.48	5.11	0.883
	σ_2	6.79	5.24	0.874

typical experimental preparation of Cye$^-$ will have significant populations of the **I**, **II** and **III** isomers. Interpretation of the photoelectron spectra of such a sample therefore requires consideration of each low-lying isomer. The **IV**, **V** and **VI** isomers are somewhat less stable according to MP2 calculations. Relative energies from the latter method are not sufficiently accurate to eliminate these isomers from consideration. Therefore, stuctures **I** through **VI** will be examined in the next section.

The most stable isomers have virtually planar six-membered rings where C5 and C6 are bonded to single hydrogen atoms. Species with methylene C5 or C6 (bonded to two hydrogen atoms) are considerably less stable.

Predicted Photoelectron Spectra. Calculated electron detachment energies for the most stable Cye$^-$ isomers provide predictions on photoelectron spectra that have yet to be reported. Table 1 reports the electron detachment energies calculated for each Cye$^-$ isomer. All of the pole strengths exceed 0.85 and therefore confirm the validity of the assumptions that are made in the present electron propagator approximations. Relaxation and correlation corrections to Koopmans results generally are larger for final states with σ holes than they are for those with π holes.

For isomers **I**, **II** and **III**, the lowest electron detachment energies are close to each other and correspond to π Dyson orbitals (Figures 2 and 3). One may expect the photoelectron spectrum to contain a peak near 3.4 eV that could have intensity contributions from all three isomers. Two final states with σ holes are predicted to lie at 4.3 and 4.7 eV for isomer **III**. Given the extensive delocalization of the corresponding Dyson orbitals into ring bonding regions, vibrational broadening is likely. The absence of peaks in this energy range would indicate that isomer **III** is not likely to be present. From 5.0 to 5.4 eV, there are five final states from all three isomers with σ and π holes. Two σ-hole states from isomers **I** and **II** occur near 5.7 eV.

Because the predicted electron detachment energies of the three lowest isomers often coincide to within a few tenths of an electronvolt, anion photoelectron spectra may not suffice for structural determinations. Isomers **I** and **II** have electron detachment energies that differ by 0.1 eV at most. Only the predicted states at 4.3−4.7 eV offer a way to make structural inferences from spectra.

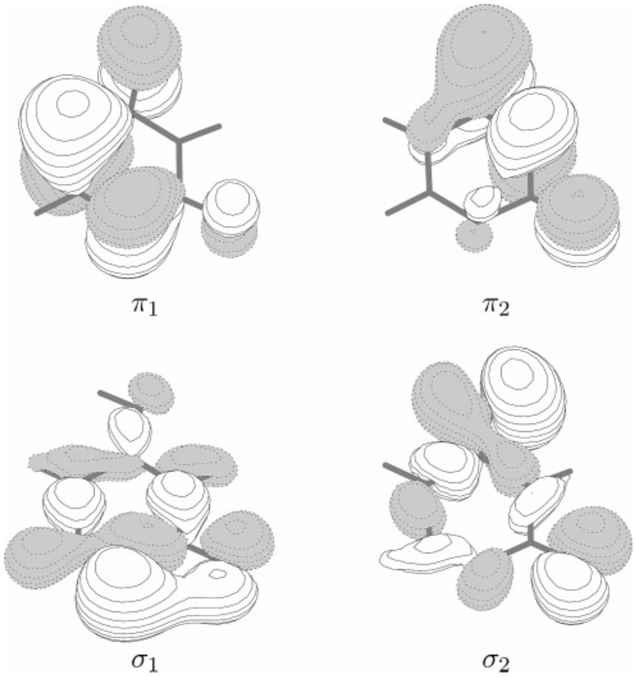

Figure 2. Dyson orbitals corresponding to the lowest electron detachment energies of structure **I**.

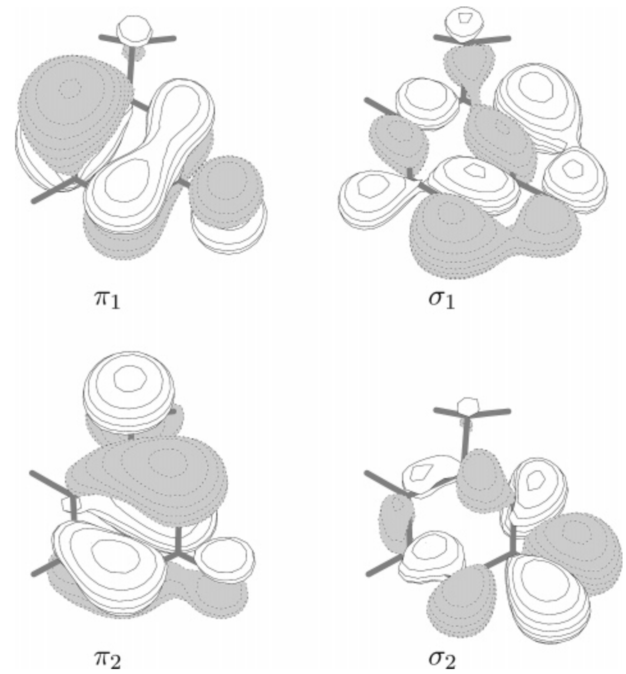

Figure 3. Dyson orbitals corresponding to the lowest electron detachment energies of structure **III**.

Results for isomers **IV**, **V** and **VI** are included for the sake of completeness, for there is a possibility that higher-level calculations will produce lower relative energies for these species. The distinguishing features for isomers **IV** and **VI** are predicted electron detachment energies at 3.1 eV. Observation of a peak near this value, perhaps with inferior intensity produced by lower Boltzmann factors, would indicate the presence of one or both of these isomers. In addition to a lowest electron detachment energy at 3.6 eV, structure **V** has a final state at 4.45 eV which coincides approximately with the σ-hole states of structure **III**.

Despite the evident redistribution of the Dyson orbitals that accompany the **I**−**III** isomerization, there is little difference between the electron detachment energies that pertain to the corresponding π-hole final states. These shifts amount to less than 0.1 eV. Larger changes in electron detachment energies are seen for the σ-hole cases, where changes in the Dyson orbitals also are manifest. For isomer **III**, the order of final states predicted by P3 electron propagator calculations differs from that given by canonical, Hartree−Fock orbital energies through Koopmans's theorem.

Conclusions

After a thorough exploration of the potential energy surfaces corresponding to 95 Cye$^-$ species, a group of six most stable isomers with energies within 10 kcal/mol of each other was found. The most stable structures are imino-oxo species with six-membered rings that deviate slightly from planarity. Small energy differences obtain between these structures and their counterparts on which planarity is imposed. Isomers **I**, **II** and **III** have the lowest energies, which lie within 3 kcal/mol of each other. Another group of three isomers (**IV**, **V** and **VI**) is somewhat higher in energy, but there remains a possibility that calculations with more exact methods or synthetic procedures that lead to higher sample temperatures could establish their experimental relevance.

Electron detachment energies for the three lowest isomers often coincide with each other. The lowest electron detachment energy is approximately 3.4 eV for all three structures and corresponds to a π-hole final state in each case. Peaks at 5.0−5.4 and 5.7 eV also could reflect the presence of more than one isomer. However, structure **III** is predicted to have electron detachment energies of 4.3 and 4.7 eV which do not coincide with values for the two other structures. The presence or absence of peaks near these values could establish whether structure **III** is present in an experimental sample.

Structures **IV** and **VI** are predicted to have the lowest first electron detachment energies. A peak at 3.1 eV in addition to the expected peak at 3.4 eV would reflect intensity contributions by these isomers.

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