Photoelectron and computational studies of the copper-nucleoside anionic complexes, Cu⁻(cytidine) and Cu⁻(uridine)

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The copper-nucleoside anions, Cu⁻(cytidine) and Cu⁻(uridine), have been generated in the gas phase and studied by both experimental (anion photoelectron spectroscopy) and theoretical (density functional calculations) methods. The photoelectron spectra of both systems are dominated by single, intense, and relatively narrow peaks. These peaks are centered at 2.63 and 2.71 eV for Cu⁻(cytidine) and Cu⁻(uridine), respectively. According to our calculations, Cu⁻(cytidine) and Cu⁻(uridine) species with these peak center [vertical detachment energy (VDE)] values correspond to structures in which copper atomic anions are bound to the sugar portions of their corresponding nucleosides largely through electrostatic interactions; the observed species are anion–molecule complexes. The combination of experiment and theory also reveal the presence of a slightly higher energy, anion–molecule complex isomer in the case of the Cu⁻(cytidine). Furthermore, our calculations found that chemically bond isomers of these species are much more stable than their anion–molecule complex counterparts, but since their calculated VDE values are larger than the photon energy used in these experiments, they were not observed. © *2011 American Institute of Physics.* [doi:10.1063/1.3553202]

I. INTRODUCTION

Metals have long been known to be essential to many biochemical processes. In bio-inorganic chemistry, the fundamental interactions between metal atoms and the subunits of DNA have been the subject of numerous theoretical and experimental studies in recent years, and these interactions are known to be capable of inducing structural modifications in DNA.[1–23] When the metals are transition metals, the influence of their *d*-orbitals adds an additional dimension to the problem. While most studies have focused on transition metal cation interactions with the subunits of DNA, i.e., with nucleobases,[1–9] studies of transition metal anion interactions with DNA subunits have been very few. In particular, we have conducted computational studies[13–15] that focused on structural and electronic properties of transition metal anion–nucleobase complexes. Our studies show that when a copper atomic anion interacts with the nucleobase, cytosine, two N–H...Cu bonds are formed between the proton donor groups (N–H) and the proton acceptor (Cu), but when a copper anion interacts with uracil, a N–H...Cu bond and a C–H...Cu bond are formed. These bonds are relatively weak and can be geometrically described as nonconventional hydrogen bonds.

In this article, we extend our previous study of copper anion–nucleobase complexes to the copper anion–nucleoside systems, where the nucleosides in these cases are cytidine and uridine. By combining anion photoelectron spectroscopic and DFT computational studies, we concluded that the dominant species observed in our photon range correspond to copper metal anion–molecule complexes, i.e., structures in which a copper anion is weakly bound to the sugar moiety of these nucleosides through electrostatic interactions. The interactions can again be viewed as nonconventional hydrogen bonds.

II. METHODS

A. Experimental

Negative ion photoelectron spectroscopy is conducted by crossing a mass-selected beam of negative ions with a fixed frequency photon beam and energy analyzing the resultant photodetached electrons. This technique is governed by the energy-conserving relationship $h\nu = \mathrm{EKE} + \mathrm{EBE}$, where $h\nu$ is the photon energy, EKE is the measured electron kinetic energy, and EBE is the electron binding energy. The present photoelectron spectra were measured with 3.493 eV photons (third harmonic of a Nd:YAG laser) and calibrated against the spectrum of Cu⁻. A detailed description of the apparatus has been reported elsewhere.[24]

Parent anions of Cu⁻(cytidine) and Cu⁻(uridine) were prepared in a laser ablation source in which nucleoside powder had been pressed into a thin layer on the surface of a copper rod. (We have also used this type of source to produce copper-aspartic acid anions.[25]) This rod assembly was mounted on a housing immediately in front of a pulsed valve which injected helium gas (4 bars) into the region over the rod. The focused laser beam ablated the sample-coated copper rod in synchronization with the helium pulse. The resultant anions then entered a linear time-of-flight mass spectrometer for mass analysis and selection. Thereafter, a second Nd:YAG

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laser was used for photodetachment, and a magnetic bottle was utilized for electron energy analysis.

Photodetachment transitions occur between the ground state of an anion and the ground and excited states of its neutral counterpart, the latter being at the structure of the anion. The spectral profile of the transition is governed by the Franck–Condon overlap between the two. The EBE value at the intensity maximum in the Franck–Condon profile is the vertical detachment energy (VDE). Comparison of our measured VDE values with those predicted by our calculations led to assessments of the structures of the observed species.

B. Theoretical

Full geometry optimizations were carried out at B3LYP/6-311+G(2d,p) level.[26, 27] Using this methodology, the computed electron affinity for atomic copper is 1.21 eV, in good agreement with the experimental value of 1.235 eV. All calculations were done with gaussian 03.[28] Optimized minima were confirmed with harmonic frequency analysis. An extensive search through the potential energy surface was conducted. Probable interactions between both Cu^- and cytidine and between Cu^+ and cytidine$^-$ were studied. Isomers arising from adsorption and insertion reactions were also considered. Molecular pictures were generated with Ball and Stick.[29] The molecular orbital picture was done using visual molecular dynamics (VMD).[30]

III. RESULTS

The photoelectron spectra of Cu^-(cytidine) and Cu^-(uridine) anions are presented in Fig. 1. In both cases, a single, intense, and relatively sharp peak dominates the spectrum. The maximum of that peak (the VDE) is located at EBE = 2.63 eV for Cu^-(cytidine) and at EBE = 2.71 eV for Cu^-(uridine). Another weaker peak is observed at EBE = 2.22 eV in the spectrum of Cu^-(cytidine), although no comparable peak is observed in that region for Cu^-(uridine). In the spectra of both systems there are also weak features located to the high EBE sides of their strongest peaks, i.e., at EBE = 3.06 eV and EBE = 3.17 eV in the spectra of Cu^-(cytidine) and Cu^-(uridine), respectively. These are spaced from their main peaks by 0.43 eV (3468 cm^{-1}) and 0.46 eV (3719 cm^{-1}), respectively. These are due to vibrational excitations of the resulting neutral species following photodetachment, and based on their values and the predicted structures, they are likely due to the excitation of O–H bonds in the sugar moieties.[31–33]

IV. DISCUSSION

There are two broad possibilities for the binding of a copper atom to a biomolecule. It can form either a weakly bound complex or a chemically bound molecule, and these choices pertain to charged systems as well. In our previous computational studies of anionic copper–nucleobase complexes, the excess electron was found to be localized on the copper atom. The resulting copper anion then interacted electrostatically with the intact nucleobase to form a relatively weakly
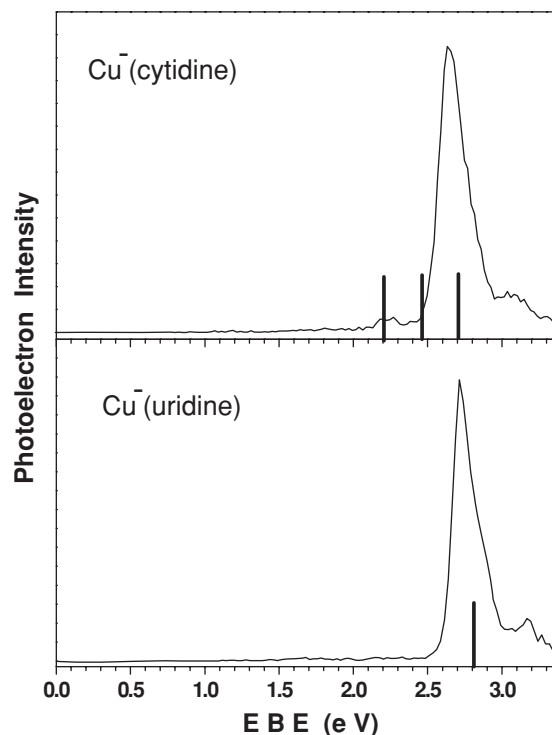

FIG. 1. The photoelectron spectra for Cu^-(cytidine) and Cu^-(uridine) anions, all recorded at photon energies of 3.493 eV. The calculated VDE values for each complex are marked in the spectra with vertical sticks for comparison.

bound anion–molecule complex. If the photoelectron spectra of these anionic complexes had been measured, one would have expected their photoelectron spectra to have reflected the spectral signature of their common photodetachment chromophore, i.e., the copper anion, although their spectral signatures would have been shifted to higher electron binding energies due to the stabilizing effect of the attractive ion-neutral interactions. We have very often seen this to be the case in many other anion–molecule complexes. On the other hand, for anionic systems in which a copper atom is chemically bonded to or within a biomolecule, the photoelectron spectrum would be very different from that of the copper anion. This was the case for the copper-aspartic acid anionic complex,[25] where the copper atom was inserted between nitrogen and hydrogen atoms of a N–H bond to form a strong covalent bond. The resulting photoelectron spectrum had no resemblance to that of the copper anion.

The photoelectron spectra of Cu^-(cytidine) and Cu^-(uridine) are dominated by single peaks, each of which resembles shifted, broadened atomic anion photoelectron features. The Cu^-(cytidine) and Cu^-(uridine) photoelectron spectra measured in this work are consistent with atomic anion-neutral molecule, electrostatic complexes, where Cu^- is the atomic anion and cytidine and uridine are the neutral molecules. The atomic copper anion photoelectron spectrum has peaks at EBE = 1.2, 2.6, and 2.9 eV. In a Cu^-(molecule) electrostatic complex, all of the Cu^- chromophoric peaks should be shifted by the same amount to higher electron binding energies. In the present case, however, such shifts would place the two higher energy Cu^- peaks outside of the
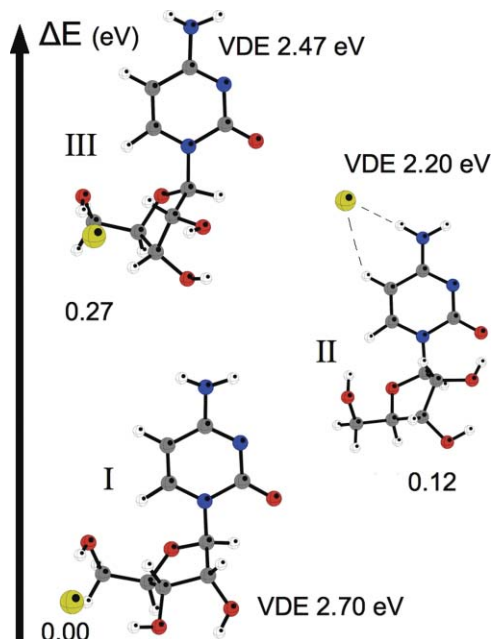
FIG. 2. Optimized structure and calculated relative energies (in eV) for the lowest Cu⁻(cytidine) anion-molecule type isomers. The calculated VDEs are also shown.

TABLE I. Theoretical bond distances (Å) between the Cu atom and the H atom of some of the closest groups in Cu⁻(cytidine) and Cu⁻(uridine) isomers. Also see Figs. 2 and 3.

	Cu…H–O	Cu…H–C	Cu…H–N
I	2.39, 2.43	3.07, 3.38	
II		3.22	2.39
III	2.51, 3.23	2.80, 3.04	
A	2.36, 2.45	3.03, 3.35	
B			2.40

provide a measure of the copper anion–nucleoside interaction energy in each case. These are ~1.4 eV for Cu⁻ and cytidine and ~1.5 eV for Cu⁻ and uridine. These are reasonable values, indicative of robust but nonchemical interactions.

The most stable (calculated) structures for Cu⁻(cytidine) and Cu⁻(uridine) are shown in Figs. 2 and 3, respectively. The calculated VDE values for each structure are included in Figs. 2 and 3. Some geometrically important distances were calculated and are shown in Table I. For the Cu⁻(cytidine) anionic complex, three isomers (labeled as **I**, **II**, and **III** in Fig. 1) were found to be within 0.27 eV of each other in energy. There is an excellent agreement between the calculated VDE of the most stable structure (structure **I**), 2.70 eV, and the measured VDE of the strongest peak in the spectrum, i.e., 2.63 eV. This is an anion-neutral complex. In this structure, the copper anion is interacting with the sugar group of the cytidine. Figure 4 shows the highest occupied molecular orbital (HOMO) of structure **I**. As can be seen, this orbital is primarily centered on the Cu atom, which supports the interpretation of a copper anion interacting with (solvated by) a cytidine molecule. The second most stable isomer (structure **II**), whose VDE was calculated to be 2.20 eV, corresponds to the small peak at 2.22 eV in the Cu⁻(cytidine) spectrum. Unlike structure **I**, the copper anion in this isomer interacts with

photon energy window used in these experiments. Fortunately, in addition to the inspection of spectral profiles, we also have computational predictions, linking predicted VDE values to the structures of these complexes, with which we corroborate our interpretation of these spectra as pertaining to Cu⁻(nucleoside) electrostatic complexes. Furthermore, beyond identifying the likelihood that the observed species are anion–molecule complexes, the shifts between the unsolvated and the solvated Cu⁻ chromophore peaks in each system
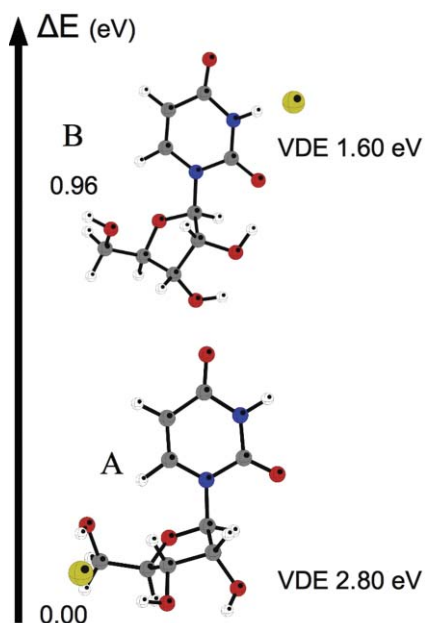

FIG. 3. Optimized structure and calculated relative energies (in eV) for the Cu⁻(uridine) anion-molecule type isomers. The calculated VDEs are also shown.
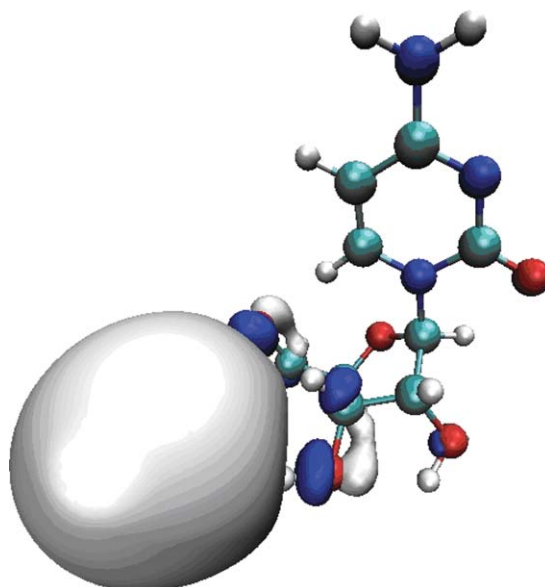

FIG. 4. HOMO picture of the lowest Cu⁻(cytidine) isomer (0.02 isovalue plot).

the nucleobase rather than the sugar moiety. The third most stable isomer (**III)** is similar in structure to isomer **I**, differing only in the conformation of the ribose. Its VDE was calculated to be 2.47 eV. A corresponding peak was not observed in the spectrum, however, either because it is too high in energy to be formed or because it is weak and buried under the shoulder of the strongest peak.

For the Cu⁻(uridine) complex, the two most stable structures (labeled as **A** and **B**) are shown in Fig. 3. Similarly to structures **I** and **II,** structure **A** shows the copper anion interacting with the sugar moiety, while in **B** it interacts with the nucleobase moiety. Again, the calculated VDE value of the most stable structure (structure **A**) is in excellent agreement with the experimental VDE value (see Fig. 1). No peak indicative of structure **B** was seen in the Cu⁻(uridine) spectrum. This is probably because it lies 0.96 eV higher in energy than structure **A**, and thus is unlikely to be formed and observed in the experiment.

As can be seen from the computational results tabulated in Table I, the geometrical parameters of the most stable Cu⁻(cytidine) and Cu⁻(uridine) structures, i.e., **I** and **A**, respectively are similar. In both cases, the copper anion is weakly bonded to the nucleoside through two nonconventional hydrogen bonds (Cu⋯H–O and Cu⋯H–C), reminiscent to those reported previously for Cu⁻(nucleobase). These results support the interpretation we made based on the photoelectron spectral profiles. More interestingly, our theoretical results have shown that the copper anion in both complexes prefers to bind to the sugar unit rather than to the base in the nucleoside, which helps explain the similarity in interaction energies in both spectra. Only the second most stable structure of Cu⁻(cytidine) (structure **II**) represents the copper anion interacting with the nucleobase through Cu⋯H–N and Cu⋯H–C bonds, although this isomer exhibits a relatively weak intensity in the spectrum.

The good agreement between the theoretical results and the experimental values gives us the confidence that the anion-molecule, electrostatically bound complexes shown in Figs. 2 and 3 are responsible for the observed transitions in the photoelectron spectra. However, one should note that the presence of chemically bound Cu⁻(nucleoside) isomers cannot be ruled out, and they are probably present in the molecular beam. For exampl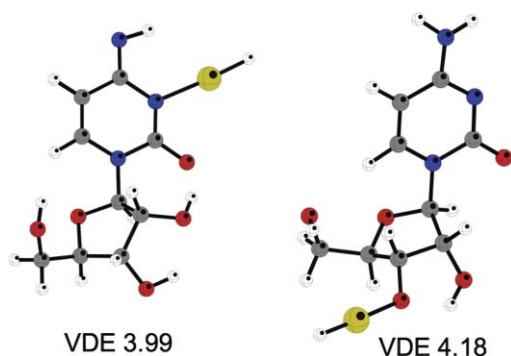e, the Cu⁻(cytidine) isomer shown in Fig. 5 (on the left) involves a copper insertion into N–H bond and also a proton rearrangement, and it is 1.14 eV more stable than isomer **I**. The isomer that involves the insertion of a copper atom between the O–H bond of the ribose (see Fig. 5, on the right) is also more stable than structure **I** (by 0.9 eV). Therefore, these chemically bonded anions probably exist in the gasphase as well. The reason we do not observe them in our spectra is that their VDE values (3.99 and 4.18 eV) are higher than the photon energy of 3.493 eV utilized in these experiments. If studies were conducted with somewhat higher photon energies, we would expect that they would be observed.

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VDE 3.99   VDE 4.18

FIG. 5. Examples of chemically bound Cu⁻(cytidine) isomers and their calculated VDEs (eV).

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