Photoelectron Spectroscopy of the 6-Azauracil Anion

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ABSTRACT: We report the photoelectron spectrum of the 6-azauracil anion. The spectrum is dominated by a broad band exhibiting a maximum at an electron binding energy (EBE) of 1.2 eV. This spectral pattern is indicative of a valence anion. Our calculations were carried out using ab initio electron propagator and other many-body methods. Comparison of the anion and corresponding neutral of 6-azauracil with those of uracil shows that substituting a nitrogen atom for C−H at the C6 position of uracil gives rise to significant changes in the electronic structure of 6-azauracil versus that of uracil. The adiabatic electron affinity (AEA) of the canonical 6-azauracil tautomer is substantially larger than that of canonical uracil. Among the five tautomeric, 6-azauracil anions studied computationally, the canonical structure was found to be the most stable. The vertical detachment energies (VDE) of the canonical, valence-bound anion of 6-azauracil and its closest "very-rare" tautomer have been calculated. Electron propagator calculations on the canonical anion yield a VDE value that is in close agreement with the experimentally determined VDE value of 1.2 eV. The AEA value of 6-azauracil, assessed at the CCSD(T) level of theory to be 0.5 eV, corresponds with the EBE value of the onset of the experimental spectrum.
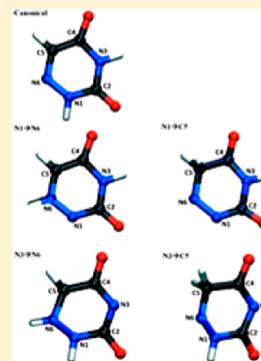
INTRODUCTION

Substituted nucleobases have received significant attention due to their use as therapeutic agents.[1−6] Both halo-nucleobases and thio-nucleobases, for example, have possible roles in the treatment of cancer.[7−13] It has been shown that halo-nucleobases may aid in increasing the radiosensitivity of tumor cells. Thio-substituted nucleobases, on the other hand, may provide milder, safer alternatives to current methods of cancer therapy. Likewise, nucleobases in which a C−H group has been substituted by a nitrogen atom may result in compounds with pharmacologically interesting properties.[14−20] Specifically, 6-azauracil is known to inhibit the function of some enzymes[14−16] and many microorganisms.[14,17−20]

The 6-azauracil molecule differs from uracil in only one respect: the substitution of a nitrogen atom for a C−H group at uracil's C6 position. Neutral 6-azauracil has been studied extensively; many experimental and theoretical studies have revealed its structural, chemical, and spectroscopic properties.[21−35] In contrast, there is a scarcity of data on the 6-azauracil anion. Studying this anion should elucidate the interaction of 6-azauracil with excess electrons, and this may be relevant to the compound's radio-therapeutic properties. Indeed, previous studies have found both sulfur and halogen modifications of uracil to give rise to significant changes in its electronic structure.[36,37] The objective of the present study is to investigate the influence of N-substitution at the C6 position of uracil on its resulting electrophilic properties. This was revealed through the differing characteristics of the uracil versus the 6-azauracil negative ions.

METHODS

I. Experimental Section. 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. The photodetachment process is governed by the relationship $h\nu$ = EBE + EKE, where $h\nu$ is the photon energy, EBE is the electron binding energy, i.e., the transition energy between the anion and a particular vibronic state of its neutral counterpart, and EKE is the electron kinetic energy.

Negative ions of 6-azauracil were formed in a supersonic expansion nozzle-ion source, where 6-azauracil powder was placed in a stagnation chamber, heated to ∼100 °C, and coexpanded with ∼50 psig argon gas through a 20 μm orifice into ∼10^{-4} Torr vacuum. Negative ions were formed by injecting low energy electrons from a negatively biased, thoriated-iridium filament into the expanding jet, where a microplasma was formed in the presence of a weak external magnetic field. These anions were then extracted, collimated, and transferred into the flight tube of a 90° magnetic sector mass spectrometer with a typical mass resolution of ∼400. The mass-selected anions of interest were then crossed with the intracavity laser beam of an argon ion laser, and the photodetached electrons energy-analyzed in a hemispherical electron energy analyzer having a resolution of ∼20 meV. The photoelectron spectrum reported here was recorded with 2.540

eV photons, and it was calibrated against the photoelectron spectrum of the O⁻ anion.[38] Detailed descriptions of this apparatus have been described previously.[39]

II. Computational Section. All calculations were performed with the Gaussian-09 suite of programs.[40] Geometric structures of neutral 6-azauracil and isomeric anions were optimized with the MP2/6-311++G(2df,2p) method.[41−43] Because we were interested only in valence-bound anions, a conventional (canonical) anion and four so-called "very-rare" anionic tautomers were the subjects of the current investigation. These tautomers are denoted as

- N1→N6 where a proton is transferred from N1 to N6
- N1→C5 where a proton is transferred from N1 to C5
- N3→N6 where a proton is transferred from N3 to N6
- N3→C5 where a proton is transferred from N3 to C5

Structures resulting from proton transfer from either imino group to a carboxylic oxygen were not taken into account. Minima on the potential energy surface were verified by harmonic frequencies. Zero-point corrections were obtained in these calculations. Total energies of all species under consideration were obtained at higher levels of theory: coupled-cluster singles and doubles (CCSD)[44] as well as CCSD with perturbative triples corrections[45] or CCSD(T). Vertical electron binding (detachment) energies were obtained with electron propagator calculations in various quasi-particle approximations.[46,47] The OVGF renormalization schemes A, B, and C,[48,49] the P3[50,51] and P3+[52] methods were employed to get correlation and relaxation corrections to Koopmans's (KT) results. The same 6-311++G(2df,2p) basis was used.

■ RESULTS AND DISCUSSION

1. Experimental Section. The photoelectron spectrum of 6-azauracil anion is presented in Figure 1. The spectrum
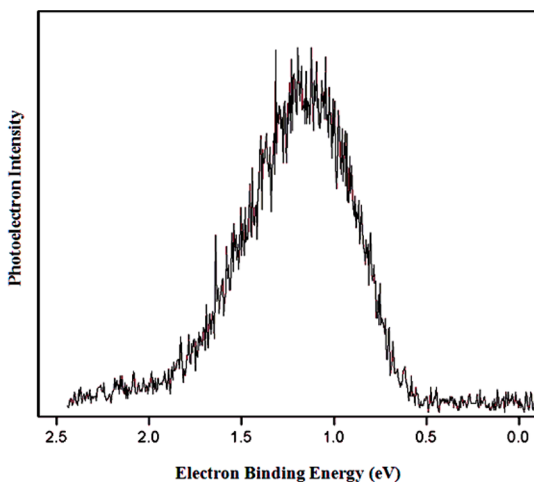

Figure 1. Photoelectron spectrum of the 6-azauracil anion recorded with 2.540 eV photons. The resolution of the spectrum is ∼20 meV.

exhibits a broad peak centered at EBE = 1.2 eV (its vertical detachment energy, VDE), with its width at baseline extending from EBE = 0.6 to 1.9 eV. By comparing the photoelectron spectrum of the 6-azauracil anion with that of the dipole-bound anion of uracil,[53] it is clear that the 6-azauracil anion studied here is not a dipole-bound anion; it is in fact a valence-bound anion. The more pertinent question is whether the broad band exhibited in the spectrum of the 6-azauracil anion is indicative

of the canonical or one of the other tautomers of the 6-azauracil anion. To answer this question, we rely on the calculations presented in the following Computational Section.

2. Computational Section. Relative energies of tautomeric, valence-bound anions of 6-azauracil are presented in Table 1. VDE values for its two most stable anions are presented in Table 2. The atomic numbering scheme is given in Figure 2.

Table 1. Relative Energies (kcal/mol) of Tautomeric, Valence-Bound 6-Azauracil Anions

tautomers	ΔE_{UMP2}	ΔE_{PUMP2}	ΔE_{UMP2}+ZPE
canonical	0	0	0
N1→N6	2.94	4.24	3.20
N3→C5	4.79	6.32	5.08
N1→C5	6.81	7.57	6.77
N3→N6	22.90	24.15	22.72

Vertical and Adiabatic Electron Affinities of 6-Azauracil. Optimization of the 6-azauracil parent (neutral) molecule revealed a minimum corresponding to a planar, C_s structure. This system was capable of accepting an electron into its a″ virtual molecular orbital (which was not the LUMO). Vertical electron attachment energies (vertical electron affinities) of 0.16 and 0.11 eV were obtained at the CCSD and CCSD(T) single point level of computations, respectively. The canonical, $^2A″$ anion was optimized with UMP2. A planar structure was obtained. Harmonic frequencies calculations confirmed a minimum for this structure. Being planar, the valence-bound anion of 6-azauracil differs significantly from the corresponding, canonical anions of uracil, cytosine, and the thiouracils, all of which are significantly puckered.[36,54,55] The adiabatic electron affinity (AEA) of 6-azauracil was calculated at the CCSD(T) level of theory as a difference between the total energies of the neutral and its anion. The calculated value of 0.50 eV is in accord with the onset of the experimental spectrum (∼0.6 eV, see Figure 1). Although the true AEA may be slightly higher in energy than the EBE of the onset, due to the likely presence of hot bands in the spectrum, the agreement between our experiment and our calculations is quite good.

Relative Stabilities of 6-Azauracil Tautomeric Anions. "Very-rare" isomers of the uracil valence anion arise when one of the imino group's protons is transferred to either the C5 or C6 atoms of the pyrimidinic ring. One such isomer was found to be responsible for the peak observed in the experimental photoelectron spectrum of the uracil anion.[56,57] Thus, in the current study, four "very-rare" tautomers of 6-azauracil anions were considered to determine whether any of these had been observed in the photoelectron spectrum of the 6-azauracil anion. Geometry optimizations of these anions revealed four minima corresponding to structures of C_1 symmetry. Ring puckering was found in all of these anions. Relative energy data in Table 1 show that the canonical, $^2A″$ valence-bound anion is the lowest energy structure and very likely corresponds to the global minimum on the potential energy surface. The N1→N6 tautomer is about 3 kcal/mol higher in energy than the canonical anion. Three other isomeric anions are less stable and are excluded from further consideration.

Vertical Detachment Energies and the Assignment of the Photoelectron Spectrum. Table 2 shows the VDE values of two 6-azauracil valence-bound anions obtained with many-body methods. For the canonical anion, most of the results are in

Table 2. VDE(eV) Values of 6-Azauracil Anions

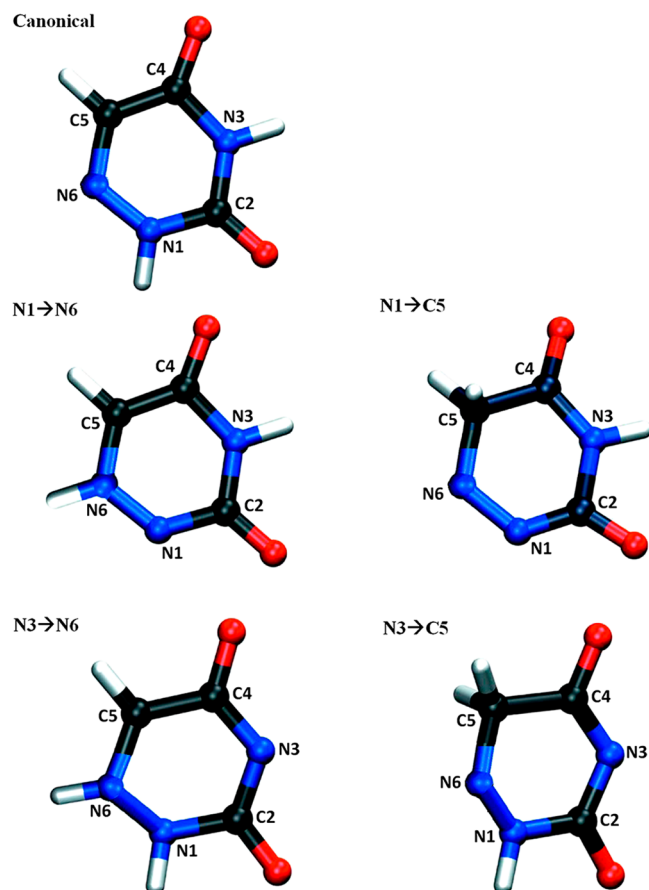| tautomers	ΔCCSD	ΔCCSD(T)	OVGF	P3	P3+	expt
canonical	0.96	0.85	1.03 (A)	1.33	1.23	1.2
			1.01 (B)			
			1.17 (C)			
N1→N6	1.80	1.60	1.70 (A)	2.02	1.89	If present, this transition would lie on the far edge of the spectrum.
			1.65 (B)			
			1.84 (C)			

Figure 2. Atomic numbering scheme for neutral 6-azauracil.

reasonably good agreement with the experimentally determined VDE value of 1.2 eV, with the P3+ value being in excellent agreement. The VDE values obtained for the N1→N6 tautomer are about 0.7 eV larger, i.e., at EBE ~1.9 eV. These values lie at the far edge of the observed spectral band, and no separate peak for this tautomeric anion's photodetachment transition was observed.

CONCLUSIONS

A broad band centered at EBE = 1.2 eV (its VDE value) was observed in the photoelectron spectrum of the 6-azauracil anion. The spectrum was assigned on the basis of ab initio, many-body calculations. The canonical, valence-bound 6-azauracil anion of C_s symmetry was found to be solely responsible for the experimental peak. The calculated AEA value of 0.5 eV is consistent with the onset of the experimental band at EBE = 0.6 eV. Moreover, the calculated and measured VDE values of the 6-azauracil anion are in excellent agreement. These conclusions contrast with uracil, whose most stable anion was calculated to be its "N1→C5" rare tautomer and not

its canonical form.[56,57] Although the AEA value of canonical 6-azauracil is +0.5 eV, the AEA value of canonical uracil is only slightly positive, at +40 meV.[56,58] Clearly, the replacement of a C−H group at C6 of uracil with a nitrogen atom significantly changes the electronic structure of the uracil anion relative to that of the 6-azauracil anion, switching the order of stabilities between rare tautomer and canonical forms. The valence anion of 6-azauracil is much more than an N-substituted uracil valence anion.

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Notes
The authors declare no competing financial interest.

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