Acidity of a Nucleotide Base: Uracil

Thomas M. Miller,*,† Susan T. Arnold,† A. A. Viggiano,† and Amy E. Stevens Miller‡

Air Force Research Laboratory, Space Vehicles Directorate, 29 Randolph Road, Hanscom Air Force Base, Massachusetts 01731-3010, and ChemMotif, Inc., Suite 211, 60 Thoreau Street, Concord, Massachusetts 01742

Received: November 5, 2003; In Final Form: February 9, 2004

Experiment and calculations are used to show that the gas-phase acidity of uracil is comparable to that of HCl. The gas-phase acidity of uracil (denoted here by U) was bracketed by proton-transfer measurements involving U and various reference acids (denoted here by A) of known gas-phase acidity. Rate constants for proton transfer from the reference acid A to the conjugate anion of uracil, $(U\text{-}H)^-$, were measured in a selected-ion flow tube at 298 K. Rate constants for proton transfer from U to ions $(A\text{-}H)^-$ were measured at 467 K in a flowing-afterglow Langmuir probe apparatus. Here, (U-H) or (A-H) indicates a U or A molecule which is missing an H atom, respectively. The result is $\Delta H°_{acid}(\text{uracil}) = 333 \pm 5$ kcal mol^{-1} and $\Delta G°_{acid}(\text{uracil}) = 326 \pm 5$ kcal mol^{-1} at 298 K, which agrees with earlier work. Thermal electron attachment to uracil was found to be too slow to permit measurement of a rate constant, consistent with the gas-phase acidity given above. G3 and G3(MP2) calculations are reported for uracil, and for the each of the (U-H) radicals and $(U\text{-}H)^-$ ions that result from H or H^+ loss from each of the four hydrogen sites of U (on the N1, N3, C5, and C6 positions). From the calculated total energies we obtain the gas-phase acidity of uracil, the four U-H homolytic bond strengths, and the electron affinities of the four possible fragment radicals. We confirm earlier work that the most acidic site in uracil is at the N1 site; this site is where uracil becomes covalently bonded to a carbon of the ribose sugar in RNA. G3 calculations for the N1 site at 298 K give $\Delta H°_{acid}(\text{uracil}) = 334.5$ kcal mol^{-1} and $\Delta G°_{acid}(\text{uracil}) = 327.1$ kcal mol^{-1} at 298 K, in good agreement with the experiment. The weakest H-atom bond enthalpy (at the N1 site) is calculated to be 101.8 kcal mol^{-1}.

I. Introduction

Uracil is one of the five nucleobases that pair up in nucleic acids. Uracil has acidic character as well, and indeed the hydrogen bonding between uracil and adenine in nucleic acids is a consequence of the acid/base character of these important biological compounds. We will denote the uracil molecule by U. Proton loss from uracil leaves behind a negative ion which we will denote by $(U\text{-}H)^-$. Several experimental[1−12] and theoretical studies[13−17] have been published in recent years on negative ions formed from gas-phase uracil and other nucleotide bases, and in a few cases the acidities were a focus.[9−12] Most notable is the elegant experiment of Kurinovich and Lee[9] in which the gas-phase acidity of U was measured for proton loss from the N1 and N3 sites independently. Photoelectron spectroscopy[1,4,5] of isolated U^- ions has shown that the extra electron is weakly bound by the large dipole moment of U (4.7 D).[18] In such dipole-bound states, the electron is localized off the positive end of the molecule in a very diffuse orbital consistent with the low binding energy. In a different experiment,[2,3] electron transfer from Rydberg state Xe to U and $U(Ar)_n$ clusters was observed for electron energies of 0.01−0.5 eV, yielding again the dipole-bound ions U^-, but also covalent-state U^- as well. Photoelectron spectroscopy of cluster anions has since yielded an estimate of the binding energy of the covalently bonded extra electron in U^-, i.e., the electron affinity of U.[5]

The initial report of the Rydberg electron-transfer study[2] included observation of $(U\text{-}H)^-$ at very low electron energies, which was surprising to us because the reaction

$$e^- + U \rightarrow (U\text{-}H)^- + H \qquad (1)$$

can only occur (at 0 K, at least) if uracil is a gas-phase superacid,[19−24] that is, if the gas-phase acidity of uracil is less than $\Delta H°_{acid} = 313.6$ kcal mol^{-1}. Another way of saying this is to view reaction 1 as a proton-transfer reaction involving the acids U and H, and the reaction will proceed in the direction shown only if U is a stronger gas-phase acid than H.[25] The possibility of dissociative electron attachment[2] seemed in conflict with the observation of a dipole-bound parent ion because the extra electron would be able to deprotonate the U neutral core via reaction 1. However, we could not rule out the possibility that the most acidic site of U might not be at the positive end of the molecule—there are four hydrogen atoms to consider—or that a large conformational barrier exists between the U^- dipole-bound state and deprotonation of U. Calculations indicate that covalent state U^- is a puckered ring in contrast to the planar U.[3] Although the initial observation of reaction 1 was withdrawn,[3] we were intrigued as to the gas-phase acidity of nucleotide bases and undertook a study of proton-transfer reactions involving U and of electron attachment to U in a weak, thermally equilibrated plasma, and we carried out calculations of bond strengths and gas-phase acidities for the four hydrogen sites in U. Electron attachment to nucleic acid bases in solution has been the subject of a number of studies because it is a crucial step in the evolution of radiation damage to nucleic acids.[26] In

* Corresponding author. E-mail: thomas.miller@hanscom.af.mil.
† Air Force Research Laboratory.
‡ ChemMotif, Inc.

10.1021/jp037367l CCC: $27.50
Published on Web 03/19/2004

TABLE 1: Reactions between Reference Acids and the Conjugate Anion of Uracil, Studied with the SIFT Apparatus at 298 K

ref acid	$\Delta H°_{acid}$[a] (kcal mol^{-1}) $\Delta G°_{acid}$[a] (kcal mol^{-1})	reaction channel	rate const[b] (10^{-10} cm^3 s^{-1})
HF	371.4 ± 0.0	adduct (100%)	≤0.27
	365.5 ± 0.2		coll 22.6
HCl	333.4 ± 0.0	adduct (75%)	8.0
	328.1 ± 0.2	H^+ transfer (25%)	coll 8.9
HBr	323.5 ± 0.1	H^+ transfer (98%)	7.8
	318.3 ± 0.2	adduct (2%)	coll 12.8

[a] Gas-phase acidities of the reference acids were taken from ref 41. [b] Estimated accurate to within 25%. The calculated collisional rate constant (see text) is denoted by "coll."

deoxyribonucleic acid (DNA), measurements indicate that most of the attachment is to cytosine, and some of the attachment is to thymine. The electron moves to thymine when the material is annealed, and at elevated temperatures the thymine anion protonates.[26] Presumably, in ribonucleic acid, uracil plays this same role in radiation damage. There are a number of studies on the electrical nature of DNA,[27−30] most done with measurements of DNA conductivity in solutions, although not exclusively.[29,30]

While dipole-bound anions of nucleic acid bases have been observed in the gas phase,[1−5] in solution covalent or valence anions exist, stabilized by the binding of the solvent molecules. The stabilizing influence of ligands has been demonstrated in photoelectron spectroscopy[3,4] and Rydberg state atom experiments.[5]

II. Experimental Section

A. SIFT. A selected-ion flow tube (SIFT) was used in that portion of the experiments in which $(U\text{-}H)^-$ ions were reacted with reference acids. The technique and this apparatus have been amply described in the past.[31,32] The $(U\text{-}H)^-$ ions were generated by placing uracil powder in the heated Ar reservoir of a high-pressure nozzle. An electron beam in the vacuum just outside the exit of the nozzle source created a plasma of mostly Ar^+ and electrons in the gas jet, from which $(U\text{-}H)^-$ ions were obtained via electron attachment. The ions were mass selected with an rf quadrupole mass spectrometer and then injected into a flow tube using a He aspirator. The flow tube contained a fast flow (125 m s^{-1}) of He buffer gas at 53 Pa pressure. At either of two inlets (halfway or two-thirds of the distance down the flow tube), a known flow of reference acid vapor could be added to the flow tube, and the resulting exponential attenuation in the $(U\text{-}H)^-$ intensity was measured for different reference acid concentrations. The flow tube was terminated with an orifice through which a sample of the ion population in the flow tube was passed to a second rf quadrupole mass spectrometer at high vacuum. Only $(U\text{-}H)^-$ ions were observed in the mass spectra when no reactant gases were added to the flow tube. The bulk of the flow tube gases were pumped away with a mechanical pump. Reference acids used in this work were HF, HCl, and HBr. The SIFT results are presented in Table 1.

B. FALP. A flowing-afterglow Langmuir probe (FALP) apparatus was used for the present experiments on ion reactions with U. This apparatus[33,34] and the FALP technique[35] have been well described in the literature. For the ion−molecule reaction studies reported here, the FALP was used as a conventional flowing afterglow.[36] In this case, the movable Langmuir probe played a limited role: to make sure that the ion density was low ($<10^7$ cm^{-3}) enough to avoid ion−ion recombination, to make sure that no free electrons entered the reaction zone, and to measure the ion velocity. The electron attachment data given here utilize the full capabilities of the FALP,[35] in which the Langmuir probe is used to measure the decay of the electron density as attachment events occur.

In the FALP apparatus, a fast flow (ca. 11 000 std cm^3 min^{-1}) of helium buffer gas was established in a flow tube of 3.7 cm radius. All data below were obtained with a flow tube pressure of 133 Pa except for a few tests. A plasma (e^-, He^+) was created at the upstream end of the flow tube with a microwave discharge. Metastable-excited helium was also created, but it was eliminated through Penning ionization by addition downstream of Ar. The flow velocity (120 m s^{-1}) of the plasma was measured using the Langmuir probe to follow the propagation of a pulsed disturbance of the microwave power down the length of the flow tube. Uracil vapor was added at a point about 57 cm downstream of the microwave discharge, and 43 cm from an ion-sampling aperture, for studies of both ion and electron interactions with gas-phase U. Ions exiting the flow tube through the sampling aperture were mass analyzed with an rf quadrupole mass filter and detected with a continuous-channel particle counter.

Uracil powder (Aldrich, 98%) was loaded into three glass tubes (6 mm outside diameter) running along the length of the reaction zone against the wall of the flow tube. The ends of the glass tubes were drawn out and bent along a radius of the flow tube. Thus, the uracil inlet consisted of three needles (1 mm inside diameter) protruding toward the flow tube axis and terminating about 1 cm from the axis. The U was vaporized by heating the entire flow tube to 467 K, at which point the vapor pressure of U is approximately 3.3 Pa.[37] Helium gas was passed through the glass tubes that held the U to transport the vapor into the flow tube. With no helium flowing over the U, the concentration of U in the reaction zone was about 10^{10} cm^{-3}. With 45 std cm^3 min^{-1} helium flowing, the concentration of U rose to $(1-2) \times 10^{11}$ cm^{-3}. The U flow could be reduced to about 10^9 cm^{-3} with gentle pumping backward through the glass tubes. The concentration of the uracil vapor was estimated by adding H_2O gas upstream and reacting the resulting H_3O^+ ions with uracil to give protonated uracil, $U{\cdot}H^+$, as in reaction 2.

$$H_3O^+ + U \rightarrow U{\cdot}H^+ + H_2O + 44 \text{ kcal mol}^{-1} \qquad (2)$$

The 44 kcal mol^{-1} exothermicity of the reaction is the difference in the proton affinities of water and uracil.[11] If the rate constant for reaction 2 is known, then measuring the H_3O^+ decay rate can be used to determine the uracil concentration in the flow tube. However, since the rate constant for reaction 2 has not been measured, we calculated the collisional rate constant[38] based on the gas-phase dipole moment[18] and polarizability[39] of uracil. There exists a great deal of data showing that exothermic proton transfer reactions usually take place with a rate constant that is at or near the collisional value.[40] Because of the importance of H_3O^+ in trace gas analysis, it is particularly well documented the that the rates for exothermic proton transfer between H_3O^+ and organic molecules proceed at or near the collisonal rates,[40] so this method should provide a good measure of U concentration in the flow tube.

Ion−uracil reactions were studied by introducing a source gas into the afterglow to produce negative ions that were the conjugate bases of reference acids. Gases used for this purpose (and in square brackets the negative ions produced from them) were CF_3Cl [Cl^-], CF_3Br [Br^-], CF_3I [I^-], $(CF_3SO_2)O$ [$CF_3SO_3^-$], CHF_2CO_2H [$CHF_2CO_2^-$], $CF_3C(O)CH_2C(O)CH_3$ [$CF_3C(O)CHC(O)CH_3^-$], $CF_3C(O)CH_2C(O)CF_3$ [$CF_3C(O)CHC(O)CF_3^-$], and $CF_3C(O)SCH_2CH_3$ [$CF_3C(O)S^-$]. In cases where the reference acid A itself was used as the source gas, a common problem

TABLE 2: Reactions between Uracil and Conjugate Anions of Reference Acids (e.g., Cl^- from HCl), Studied with the FALP Apparatus at 467 K

ref ion [acid]	$\Delta H°_{acid}$[a] (kcal mol^{-1}) $\Delta G°_{acid}$[a] (kcal mol^{-1})	reaction channel	rate const[b] (10^{-10} cm^3 s^{-1})
Cl^- [HCl]	333.4 ± 0.0	H^+ transfer (70%)	23
	328.1 ± 0.2	adduct (30%)	coll 38.8
$CHF_2CO_2^-$ [CHF_2CO_2H]	331.0 ± 2.2	adduct (55%)	14
	323.9 ± 2.0	H^+ transfer (45%)	coll 28.1
$CF_3C(O)CHC(O)CH_3^-$ [$CF_3C(O)CHC(OH)CH_3$]	328.4 ± 2.9	H^+ transfer (65%)	3.1
	321.9 ± 2.0	adduct (35%)	coll 25.0
Br^- [HBr]	323.5 ± 0.1	adduct (99%)	23
	318.3 ± 0.2	H^+ transfer (1%)	coll 29.5
$CF_3C(O)S^-$ [$CF_3C(O)SH$]	318.6 ± 3.0	adduct (70%)	1.0
	312.6 ± 2.0	H^+ transfer (30%)	coll 26.0
$CF_3C(O)CHC(O)CF_3^-$ [$CF_3C(O)CHC(OH)CF_3$]	317.4 ± 2.2	adduct (100%)	0.89
	310.2 ± 2.0		coll 23.6
I^- [HI]	314.4 ± 0.0	adduct (95%)	2.9
	309.2 ± 0.2	H^+ transfer (<5%)	coll 26.1
$CF_3SO_3^-$ [CF_3SO_3H]	305.4 ± 2.2	adduct (100%)	0.81
	299.5 ± 2.0	H^+ transfer (<1%)	coll 25.2

[a] Gas-phase acidities of the reference acids were taken from ref 41. [a] Estimated accurate to within a factor of 2. The calculated collisional rate constant (see text) is denoted by "coll."

was rapid formation of a cluster anion $(A\text{-}H)^-\cdot A$ in addition to the desired $(A\text{-}H)^-$. In these cases, the acid vapor was diluted with Ar gas to permit more accurate adjustment of the source gas flow rate to minimize the secondary reaction that formed the cluster anion. If the vapor pressure of the source gas was too low to supply a concentration in the flow tube adequate to remove all free electrons prior to the uracil reaction zone, Ar gas was flowed past the bulb containing the source gas in order to carry a greater amount of source gas into the flow tube by aspiration.

High-resolution mass spectra were obtained in each ion−uracil reaction case to identify the ionic products of reaction. Low-resolution mass spectra were also obtained (to minimize mass discrimination effects). Peak heights in the low-resolution spectra were used to determine the reaction rate constant using the uracil concentration derived from the H_3O^+ data and the reaction time measured directly as described earlier. The uracil concentration and reaction time are merely useful intermediaries; the reaction rate constants reported here are ultimately normalized to the amount of proton transfer observed for reaction 2 for the same U concentration and reaction time, with the assumption that the rate constant for reaction 2 is collisional in magnitude. Since the rate constant for reaction 2 has not yet been measured, we do not claim that these results are accurate better than a factor of 2. However, for bracketing the gas-phase acidity of U, we are mainly concerned with two questions: does proton transfer from uracil to the reference anion take place, and is the reaction fast or slow? The present FALP data satisfy these goals. We believe that the *relative* accuracy of the reaction rate constants is about ±50%. The branching fractions for ionic products are good to within 10 percentage points. The results of reaction with U are presented in Table 2.

Secondary clustering reactions were noted in the mass spectra (and accounted for in the product analyses):

$$(U\text{-}H)^+ + U + He \rightarrow (U\text{-}H)^+\cdot U + He \quad (3)$$

$$(U\text{-}H)^- + U + He \rightarrow (U\text{-}H)^-\cdot U + He \quad (4)$$

III. Experimental Gas Phase Acidity Results

Results of the reaction of $(U\text{-}H)^-$ with HF, HCl, and HBr (at 298 K) are given in Table 1. Adduct formation occurs in all three cases, which is not unexpected since adduct formation is enhanced for dipolar molecules. From these results, it is clear that HBr is a stronger acid than U because HBr readily donates a proton to $(U\text{-}H)^-$, to form $Br^- + U$. It is also clear that U is a weaker acid than HF, as HF will not donate a proton to $(U\text{-}H)^-$. The HCl case is in the middle ground: proton transfer occurs, but at a relatively slow rate. From the three SIFT data alone, one can conclude that the acidity of U is similar to that of HCl, for which $\Delta H°_{acid}$ is 333.4 ± 0.0 kcal mol^{-1}, and $\Delta G°_{acid}$ is 328.1 ± 0.2 kcal mol^{-1}.[41]

Results of the ion−uracil reaction experiments (at 479 K) are given in Table 2. Proton transfer is the only rearrangement channel observed. It is also seen from Table 2 that adduct formation is common, even dominant. Data were obtained with Cl^-, Br^-, and $I^- + U$ at helium buffer pressures of 57, 88, 120, and 133 Pa to see if we were in the high-pressure limit for stabilization of the adduct ion, since competition from the adduct channel complicates an otherwise straightforward interpretation of the results in Table 2. We found that the branching fraction for the adduct channel in this pressure range was 20−30% for Cl^-, 98−99% for Br^-, and 92−95% for I^-. Therefore, while the experiment would be simpler to interpret in a near-zero pressure apparatus (an ion cyclotron resonance cell or a guided ion beam experiment), operating at the lowest feasible pressures in an FALP was not very helpful. On a gross scale, it is clear in Table 2 that reference acids higher on the list readily deprotonate uracil while those lower on the list do not.

If both forward and reverse reactions are observed as a single channel, then the gas-phase acidity, $\Delta G°_{acid}$, can be calculated directly from the ratio of the forward and reverse rate constants. The reaction data reported in Tables 1 and 2 are complicated by several factors, most notably that the forward and reverse reactions were studied at different temperatures, and that clustering reactions compete with the proton-transfer reactions (see product ratios in Tables 1 and 2). Therefore, $\Delta G°_{acid}$ cannot be calculated from the ratio of forward and reverse proton-transfer rates, even when they are observed in both directions as they are for the HCl/Cl^- reference acid/base pair.

In low-pressure experiments, the kinetics of a proton-transfer reaction are typically governed by the heat of deprotonation, $\Delta H°_{acid}$, at least for a barrierless reaction such as this simple proton transfer should be. However, the observation of the clustering channel suggests that the observed reactions might not meet the "low-pressure" criterion for the reaction kinetics to be entirely governed by $\Delta H°$ rather than $\Delta G°$. That is, enough collisional thermalization by the buffer gas to cause clustering

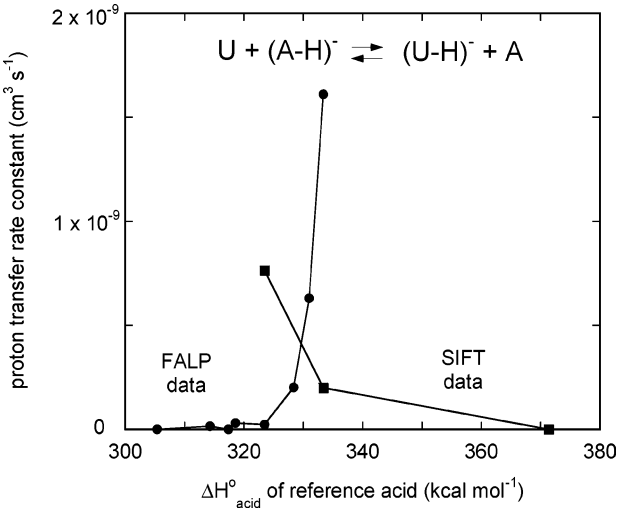

Figure 1. Partial reaction rate constants for proton transfer from uracil (U) to conjugate anions $(A\text{-}H)^-$ of reference acids at 467 K (solid circles) and for proton transfer from reference acids (A) to $(U\text{-}H)^-$ at 298 K (solid squares).

reactions also means that the pressure is approaching that required for thermodynamic equilibrium conditions to hold. Our past experiences with reactions for which association competes with a chemical channel show situations in which clustering does not compete with proton transfer[42,43] (therefore $\Delta H°$ would apply) and others in which the buffer clearly plays a role in the apparent bimolecular reaction (and therefore $\Delta G°$ would apply.)[44] It was not possible in the experiments reported here to distinguish whether the rates for the proton-transfer channel are affected by collisions with the buffer gas.

In the present work we bracket $\Delta H°_{acid}(U)$ from the proton-transfer rates. However, the magnitude of the difference between $\Delta H°_{acid}$ and $\Delta G°_{acid}$ is fairly uniform for the acids used in the present work, and the slight discrepancy is well within the accuracy of the experiments. Kinetics of the proton-transfer reactions observed on both the SIFT and FALP apparatuses are shown in Figure 1 as a function of $\Delta H°_{acid}$ of the reference species; the $\Delta H°_{acid}$ values are plotted for 298 K. Although the acidity for each species is slightly larger at the 467 K temperature, both the reference and U acidities shift by about the same amount: a 0.6 kcal mol^{-1} increase in $\Delta H°_{acid}(UH)$ between 298 and 467 K was determined from Gaussian calculations (discussed below), which is well within the error limits of the bracketing experiments.

The results in Figure 1 can be said to bracket $\Delta H°_{acid}(U)$ close to that of HCl, or 333 kcal mol^{-1}. Using the entropy correction calculated in section IV, this result implies $\Delta G°_{acid}(U) = 326 \pm 5$ kcal mol^{-1}.

The relation between the gas-phase $\Delta H°_{acid}$ and the solution-phase acidity, or pK_a, may be obtained from a thermochemical cycle and is given by eq 5.

$$\Delta H°_{acid} = 2.3RT(pK_a) + T\Delta S°_a + \Delta H°_{hydr}(U) - \Delta H°_{hydr}[(U\text{-}H)^-] - \Delta H°_{hydr}(H^+) \quad (5)$$

The term $2.3RT(pK_a)$ gives the $\Delta G°$ for the acidity in aqueous solution ($pK_a = 9.5$;[45] $\Delta G° = +12.95$ kcal mol^{-1}). The $T\Delta S°_a$ term is the entropy for aqueous acidity; an entropy for the solution-phase acidity of 20 cal mol^{-1} K^{-1} is assumed,[21] yielding a net $\Delta H°_a$ in solution of +18.9 kcal mol^{-1}. The $\Delta H°_{hydr}$ terms are the enthalpies of hydration of the various species, i.e., the energetics for transfer from gas phase to solution. $\Delta H°_{hydr}(U)$ is taken as the sum of the aqueous solvation enthalpy of solid uracil, $+7.0 \pm 0.3$ kcal mol^{-1},[46] and the negative of the sublimation enthalpy of solid uracil, -31.3 ± 1.2 kcal mol^{-1},[47] for a net hydration enthalpy of -24.3 kcal mol^{-1}. The hydration enthalpy for the proton is taken to be -262 kcal mol^{-1}. Substitution of the known values into eq 4 yields a solvation enthalpy, $\Delta H°_{hydr}[(U\text{-}H)^-]$, of -76.4 kcal mol^{-1}.

The hydration enthalpy of a spherical charge is given by the Born theory of solvation, with the result in eq 6 of

$$\Delta H°_{hydr} = -N_i q_i^2[1 - (1 - LT)/D][1/2r_i] = -165.7/r_i \text{ kcal mol}^{-1} \quad (\text{for } r_i \text{ in Å}) \quad (6)$$

in which N_i is the number of ions solvated, q_i is the charge on the ions, L is a small, temperature-dependent correction to the dielectric constant (4.63×10^{-3} for water), T is the temperature, D is the dielectric constant (78.53 for water), and r_i is the solvation radius for the ion.[21] Substituting $\Delta H°_{hydr}[(U\text{-}H)^-] = -76.4$ kcal mol^{-1} into eq 5 gives a 2.1 Å solvation radius for $(U\text{-}H)^-$ in aqueous solution. This is a surprisingly small number for the effective solvation radius, considering both the size of $(U\text{-}H)^-$ (see section IV) and the fact that, for anions, the solvation radius is typically about 0.85 Å *larger* than the crystal radius of the ion.[21] This suggests that the hydration of $(U\text{-}H)^-$ is helped considerably by other effects, most probably very effective hydrogen bonding to the oxygens, to the anionic N1, and from the N3 hydrogen. The hydration enthalpy for the parent U is somewhat large as well, by comparison to other similarly sized organic molecules, and is again indicative of strong interactions between the U and the H_2O of solvation.

No U^- was observed in either the SIFT or FALP work, that is, within the uncertainty of measurement of deviation from the expected ^{13}C component of U^- at 112 amu. Even if covalent-state U^- were produced, we would not expect a polyatomic negative ion of such low electron affinity (3.5 ± 2.8 kcal mol^{-1})[5] to survive in the buffer gas at the pressures and temperatures of the present flow tube experiments. The dipole-bound U^-, with its lower binding energy (2.0 ± 0.2 kcal mol^{-1}),[5] would stand still less chance of surviving.

The FALP apparatus was also used to investigate reaction 1. The Langmuir probe was used to measure the decay in the electron density along the axis of the flow tube when U vapor was present. Very few negative ions were produced by attachment. While $(U\text{-}H)^-$ ions were observed, there was little decay in the electron density along the flow tube aside from that due to ambipolar diffusion. An upper limit of 2×10^{-10} cm^3 s^{-1} may be placed on the electron attachment rate constant at 467 K. The very weak electron attachment signal, even if partly due to impurities, is consistent with a large endothermicity (17 kcal mol^{-1} according to this work) for reaction 1. Experiments were also carried out with suprathermal electrons. For this purpose, pure Ar was used as the buffer gas, in which case the electron temperature is about 2000 K because Ar does not thermalize low-energy electrons.[48] These electrons have only a small fraction of the energy needed to overcome the endothermicity of reaction 1, so it was not surprising that electron attachment remained an immeasurably weak process. This observation may be compared with results of electron beam experiments where major resonances were observed only at energies above 1 eV.[49] A smaller feature for $(U\text{-}H)^-$ production was observed around 0.65 eV, which can be explained by internal energy in the target molecules. However, it is difficult to rationalize a weak feature observed at about 60 meV as being due to $(U\text{-}H)^-$. A large

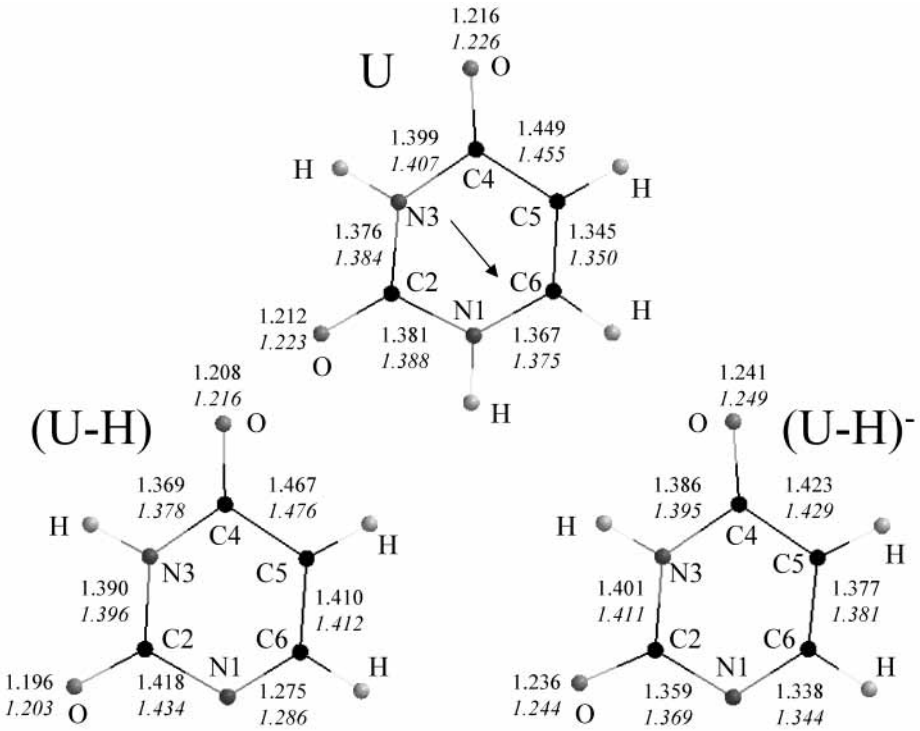

Figure 2. Structures of uracil molecule (top), neutral (U-H) (bottom left, H atom missing from the most acidic site), and $(U\text{-}H)^-$ anion (bottom right, H^+ missing from the most acidic site). The arrow shows the direction of the dipole moment (4.7 D) in U. The C−C, C−N, and C−O bond lengths were determined from MP2(Full)/6-311++G(3df,2p) calculations; those given in italics are the MP2(Full)/6-31G(d) geometry used in the G3 and G3(MP2) calculations.

zero-energy resonance was originally reported but later found to be due to the calibration gas used in the experiment.

IV. Gaussian Calculations

Electronic structure calculations were carried out with the primary aim of determining which of the four H-atom sites in uracil is most acidic in the gas phase. The calculations include the homolytic bond strengths and the electron affinities of the four possible U radicals, information which aids in understanding the acidic strength. G3 and G3(MP2) calculations were performed on the structures and energies of U, (U-H), and $(U\text{-}H)^-$ using the GAUSSIAN-98W package of programs.[51] Following the G3 and G3(MP2) formalisms,[52,53] molecular structures were first optimized at the HF/6-31G(d) level of theory, and the stability of the wave functions were checked (i.e., the electron configuration was altered in various ways to verify that the lowest energy state had been located). Then vibrational energies were calculated, scaled by an empirical factor of 0.8929,[52] and from these and rotational energies the zero-point energies were determined along with thermal corrections to energies (with the standard state taken as 298.15 K and 1 atm). Next, structures were optimized at the MP2(Full)/6-31G(d) level. The structure of U was also optimized with a large basis set [at the MP2(Full)/6-311++G(3df,2p) level] for comparison with the results obtained with the smaller basis set used in G3 theory, and with the moderate 6-311++G(d,p) basis set used by Dolgounitcheva et al.[15] The use of many polarization functions in the large basis set tended to shorten bond lengths by as much as 0.01 Å compared to those obtained with the 6-31G(d) basis set. The bond lengths are given in Figure 2, which shows the structures of U and $(U\text{-}H)^-$ relevant to the acidity work. Cartesian coordinates for U and all (U-H) and $(U\text{-}H)^-$ are given in Supporting Information. Uracil is known to be planar and to have the diketo tautomer structure in the gas phase.[5,54] The geometry optimizations were initially restricted to planar U, (U-H), and $(U\text{-}H)^-$. Small out-of-plane distortions were then introduced (typically 10°), and MP2 optimization of the distorted geometries led back to the planar forms. The one exception is neutral (U-H) with an H atom missing from the N3 site. The optimizations and frequency analyses consistently led to a slightly nonplanar $^2A''$ geometry, with appendage atoms protruding from 1° to 5° above and below the average plane of the ring. G3 calculations showed the nonplanar form to be 0.13 kcal mol^{-1} lower in energy than the planar one ($^2A'$). DFT optimization, with a larger basis set than used in G3, led to the planar form. Thus, a small academic uncertainty remains at the N3 site. There was little change in the structures calculated for the uracil molecule with and without electron correlation, and increasing account of correlation, presumably because of the fundamental rigidity of a six-membered ring.

Gas phase acidity values were calculated as follows: (a) at 0 K, $\Delta H°_{acid}$ and $\Delta G°_{acid}$ are the same, simply the sum of the total energies of the separated fragments $(U\text{-}H)^- + H^+$, minus the total energy of U itself; (b) $\Delta H°_{acid}$ at 298 K is the difference in the enthalpy of U and that of the separated fragments; and (c) $\Delta G°_{acid}$ at 298 K is the difference in the free energy of U and that of the separated fragments. The total energy of the proton is zero at 0 K, and its enthalpy is $5kT/2$ at 298 K. The homolytic bond strengths were calculated similarly, for separation of U into neutral fragments (U-H) + H. The total energy of H atom is 0.5 hartree at 0 K, while the enthalpy at 298 K includes an additional $5kT/2$.

Calculations based on G3 and G3(MP2) theory contain two empirical corrections: one is the scaling of Hartree−Fock (HF) zero-point corrections, and a second is a "higher level correction" which accounts for remaining deficiencies in the methods through a comparison of calculated and measured ionization potentials and electron affinities. The higher level correction cancels out (exactly) when acidities are calculated.[55,56] Similarly, any systematic error in the zero point energy (ZPE) results tends

TABLE 3: G3 and G3(MP2) Energies and Zero-Point Energies (ZPE), in hartrees, for Acidic Sites in Uracil

molecule[a]	ZPE[b]	G3 total energy (0 K)	G3 enthalpy (298 K)	G3 free energy (298 K)	G3(MP2) total energy (0 K)[c]
uracil ($C_4H_4N_2O_2$, $^1A'$)	0.084 487	−414.571 427	−414.564 168	−414.601 919	−414.257 772
uracil-H, N1 site ($C_4H_3N_2O_2$, $^2A''$)	0.069 697	−413.911 554	−413.904 266	−413.942 875	−413.596 729
uracil-H$^+$, N1 site ($C_4H_3N_2O_2^-$, $^1A'$)	0.071 509	−414.040 397	−414.033 500	−414.070 579	−413.726 714
uracil-H, N3 site[d] ($C_4H_3N_2O_2$, $^2A''$)	0.071 376	−413.869 643	−413.862 612	−413.900 564	−413.555 982
uracil-H$^+$, N3 site ($C_4H_3N_2O_2^-$, $^1A'$)	0.070 801	−414.021 363	−414.014 146	−414.051 994	−413.707 812
uracil-H, C5 site ($C_4H_3N_2O_2$, $^2A'$)	0.071 575	−413.881 486	−413.874 162	−413.912 695	−413.566 783
uracil-H$^+$, C5 site ($C_4H_3N_2O_2^-$, $^1A'$)	0.070 841	−413.968 540	−413.961 143	−413.999 480	−413.655 764
uracil-H, C6 site ($C_4H_3N_2O_2$, $^2A'$)	0.071 344	−413.891 238	−413.883 920	−413.922 408	−413.576 651
uracil-H$^+$, C6 site ($C_4H_3N_2O_2^-$, $^1A'$)	0.071 428	−413.990 114	−413.983 031	−414.020 433	−413.676 895

[a] The label "uracil-H" means one H atom removed from uracil; "uracil-H$^+$" means one proton removed from uracil. [b] ZPEs and thermal corrections based on HF/6-31G(d) frequencies scaled by 0.8929. [c] G3(MP2) enthalpies and free energies may be obtained from the 0 K energy using differences in the G3 entries; see text. [d] See text: the nonplanar $^2A''$ form differs from the planar $^2A'$ form by only 0.13 kcal mol^{-1} and is therefore uncertain.

TABLE 4: Calculated Homolytic Bond Enthalpy $D°_{298}$[$C_4H_3N_2O_2$-H], Electron Affinity (EA) of the Radical $C_4H_3N_2O_2$, and Gas-Phase Acidity of Uracil, in kcal mol^{-1}

quantity	G3(MP2) (0 K)	G3(MP2) (298 K)	G3 (0 K)	G3 (298 K)	G3 (467 K)[a]
at the N1 vertex					
homolytic bond enthalpy	101.1	102.6	100.3	101.8	102.5
EA($C_4H_3N_2O_2$)	81.6		80.9		
$\Delta H°_{acid}$(uracil)	333.2	334.5	333.2	334.5	335.1
$\Delta G°_{acid}$(uracil)	333.2	327.2	333.2	327.1	327.6
at the N3 vertex					
homolytic bond enthalpy	126.6	128.0	126.6	128.0	
EA($C_4H_3N_2O_2$)	95.3		95.2		
$\Delta H°_{acid}$(uracil)	345.1	346.6	345.1	346.6	
$\Delta G°_{acid}$(uracil)	345.1	338.7	345.1	338.7	
at the C5 vertex					
homolytic bond enthalpy	119.8	121.4	119.2	120.7	
EA($C_4H_3N_2O_2$)	55.8		54.6		
$\Delta H°_{acid}$(uracil)	377.8	379.3	378.3	379.9	
$\Delta G°_{acid}$(uracil)	377.8	371.2	378.3	371.8	
at the C6 vertex					
homolytic bond enthalpy	113.7	115.2	113.1	114.6	
EA($C_4H_3N_2O_2$)	62.9		62.0		
$\Delta H°_{acid}$(uracil)	364.5	365.9	364.8	366.1	
$\Delta G°_{acid}$(uracil)	364.5	358.3	364.8	358.6	

[a] Values at 467 K are needed for interpretation of the FALP data; see text.

to cancel when differences in total energies are taken in order to obtain acidities, EAs, and bond strengths. Smith and Radom[55] and Notario et al.[56] have shown that gas-phase acidities calculated at the G2 level[57,58] are accurate typically within ±2 kcal mol^{-1}; G3 theory should yield an improvement over this, approaching ±1 kcal mol^{-1} *on average*. G3(MP2) error should lie between those of G3 and G2.

The G3 and G3(MP2) ZPEs and energies are given in Table 3. For G3(MP2) only the 0 K total energy is listed, but the G3(MP2) 298 K enthalpy and free energy may be obtained from differences in the G3 values since the same thermal corrections are used in G3 and G3(MP2) theory. To give one example, for U, the G3(MP2) total energy at 0 K is −414.257 77 hartrees. The G3 numbers imply that the enthalpy at 298 K lies 0.007 26 hartree higher. The G3(MP2) enthalpy is equivalently higher, and is thus −414.250 51 hartrees. Gas-phase acidities, EA(U), and homolytic bond enthalpies, derived from the energies in Table 3, are given in Table 4. Values at 467 K were included for interpretation of the FALP data. The calculated acidity (at the N1 site) is in agreement with the experimental value determined in this work.

The results at 0 K necessarily obey the thermochemical cycle given in eq 7

$$\Delta H°_{acid}(U,0\ K) = D°_0[(U\text{-}H)\text{−}H] - EA[(U\text{-}H)] + IE(H) \quad (7)$$

where IE(H) is the ionization energy of H atom. Applying this cycle to the bond enthalpies and bond dissociation enthalpies, with all quantities given in Table 4, aids in understanding the moderate acidity of uracil: the homolytic bond strength is not especially weak, but the EA of the fragment is high.

The calculations indicate that the (U-H)$^-$ ion observed in this experiment results from loss of H$^+$ from the N1 vertex in Figure 2. The acidities resulting from loss of alternative protons are too large to play a role in the thermal energies of the present experiments. The large EA calculated for (U-H), 81.9 kcal mol^{-1} at the N1 site, agrees with an experimental observation[1] EA-[(U-H)] > 57.6 kcal mol^{-1}.

G3 theory is intended to yield a good approximation to a full configuration interaction calculation. G3(MP2) calculations were carried out for comparison with the G3 results because the G3(MP2) ones are far more economical. In the present work, G3(MP2) calculations required 1/7 to 1/5 the computational time of the G3 ones. The results in Table 4 show good agreement between the two methods, within 0.4 kcal mol^{-1} on average. The calculations described here were initially carried out at the G2(MP2) and G2 levels[57,58] of theory. The G2(MP2) and G2 results (given in the Supporting Information) agree with the corresponding G3(MP2) and G3 results within 0.5 kcal mol^{-1} on average, with the worst discrepancy being EA(U-H) at the N3 site, for which the G2(MP2) result was 1.4 kcal mol^{-1} lower than the G3(MP2) value.

V. Conclusions

We have measured rate constants for proton-transfer reactions between the conjugate anions of reference acids and uracil (U), and between $(U\text{-}H)^-$ and reference acids, in the gas phase. The results reported here show that the gas-phase acidity of uracil is $\Delta H°_{acid}(U) = 333 \pm 5$ kcal mol^{-1} [and, by implication, $\Delta G°_{acid}(U) = 326 \pm 5$ kcal mol^{-1}] at 298 K. This result is in complete agreement with that of Kurinovich and Lee,[9] who used a Fourier transform mass spectrometer (FTMS) to determine when proton-transfer reactions were taking place in ionized gas mixtures. While they did not measure reaction rate constants, their bracketing was more straightforward than in our experiments because the gas pressure in the FTMS is low enough that there is no competition from collisional stabilization of the ion−molecule complex. They measured the acidities of the N1 site, $\Delta H°_{acid}(U) = 333 \pm 4$ kcal mol^{-1}, and the N3 site, 347 ± 4 kcal mol^{-1}. They used density functional methods to calculate acidities of 376 and 362 kcal mol^{-1} at the C5 and C6 sites in the ring. The G3 calculations in the present work should be about 10 times more accurate on average than the density functional ones. They confirm that the most acidic site is indeed at the N1 site in the ring, and yield $\Delta H°_{acid}(U) = 334.5$ kcal mol^{-1} and $\Delta G°_{acid}(U) = 327.1$ kcal mol^{-1}, in good agreement with the present experimental result and that of Kurinovich and Lee.[9] The G3 acidities for the other sites are $\Delta H°_{acid} = 346.6$ kcal mol^{-1} at the N3 site (in excellent agreement with Kurinovich and Lee[9]), 379.9 kcal mol^{-1} at the C5 site, and 366.1 kcal mol^{-1} at the C6 site. The N1 hydrogen is of course lost in RNA formation, since the N1 site becomes covalently bonded to one of the carbons of the ribose sugar; the N3 site is hydrogen bonded to adenine. The G3 calculations also yield homolytic bond enthalpies for the several hydrogen sites: 101.8 kcal mol^{-1} (N1 site), 128.0 kcal mol^{-1} (N3 site), 120.7 kcal mol^{-1} (C5 site), and 114.6 kcal mol^{-1} (C6 site).

Our calculated G3 bond energies and electron affinities for each of the H-atom sites compare quite well with those of Hanel et al.,[49] who used a slightly lower level of theory [G2(MP2)].

Electron attachment to U at 467 K was immeasurably weak, consistent with the endothermicity implied by the value of the gas-phase acidity determined here.

Acknowledgment. We thank Helen de Clercq of Howard University and Kit Bowen of Johns Hopkins University for discussions about uracil during the course of this work. We are grateful for continued support of this laboratory by the Air Force Office of Scientific Research. T.M.M. is under contract (F19628-99-C-0069) to Visidyne, Inc.

Supporting Information Available: Cartesian coordinates optimized at the MP2(Full)/6-31G(d) level of theory for the species listed in the tables, along with G2 and G2(MP2) energies. MP2(Full)/6-311++G(3df,2p) geometry for U. This information is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Snodgrass, J. T.; Bowen, K. H. *J. Chem. Phys.* **1996**, *104*, 7788−7791.

(2) Desfrançois, C.; Abdul-Carime, H.; Schermann, J. P. *J. Chem. Phys.* **1996**, *104*, 7792−7794.

(3) Desfrançois, C.; Periquet, V.; Bouteiller, Y.; Schermann, J. P. *J. Phys. Chem. A* **1998**, *102*, 1274−1278.

(4) Hendricks, J. H.; Lyapustina, S. A.; de Clercq, H. L.; Bowen, K. H. *J. Chem. Phys.* **1998**, *108*, 8−11.

(5) Schiedt, J.; Weinkauf, R.; Neumark, D. M.; Schlag, E. W. *Chem. Phys.* **1998**, *23*, 511−524.

(6) Desfrançois, Abdoul-Carime, H.; Carles, S.; Périquet, V.; Schermann, J. P.; Smith, D. M. A.; Adamowicz, L. *J. Chem. Phys.* **1999**, *110*, 11876−11883.

(7) Huels, M. A.; Hahndorf, I.; Illenberger, E.; Sanche, L. *J. Chem. Phys.* **1998**, *108*, 1309−1312.

(8) Aflatooni, K.; Gallup, G. A.; Burrow, P. D. *J. Phys. Chem.* **1998**, *102*, 6205−6207.

(9) Kurinovich, M. A.; Lee, J. K. *J. Am. Chem. Soc.* **2000**, *122*, 6258−6262.

(10) Kurinovich, M. A.; Lee, J. K. *J. Am. Soc. Mass Spectrom.* **2002**, *13*, 985−995.

(11) Kurinovich, M. A.; Phillips, L. M.; Lee, J. K. *Chem. Commun.* **2002**, *2002*, 2354−2355.

(12) Rodgers, M. T.; Campbell, S.; Marzluff, E. M.; Beauchamp, J. L. *Int. J. Mass Spectrom. Ion Processes* **1994**, *137*, 121−149.

(13) Oyler, N. A.; Adamowicz, L. *J. Phys. Chem.* **1993**, *97*, 11122−11123; *Chem. Phys. Lett.* **1994**, *219*, 223−227.

(14) Les, A.; Adamowicz, L.; Nowak, M. J.; Lainski, L. *Spectochim. Acta, Part A* **1992**, *48A*, 1385−1395.

(15) Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *Chem. Phys. Lett.* **1999**, *307*, 220−226; *J. Phys. Chem. A* **1999**, *103*, 7912−7917; *J. Phys. Chem. A* **2001**, *105*, 8782−8786; *Int. J. Quantum Chem.* **2002**, *90*, 1547−1554. There is a misprint in the first of these papers: the N1−H bond length in uracil should read 1.010 Å (private communication from J.V.O.).

(16) Colson, A.-O.; Besler, B.; Sevilla, M. D. *J. Phys. Chem.* **1992**, *96*, 9787−9794.

(17) Sevilla, M. D.; Besler, B.; Colson, A.-O. *J. Phys. Chem.* **1995**, *99*, 1060−1063.

(18) Hobza, P. Technische Akademie der Wissenschaften, Prag. 1997, as quoted in ref 5.

(19) Stevens Miller, A. E.; Kawamura, A. R.; Miller, T. M. *J. Am. Chem. Soc.* **1990**, *112*, 457−458.

(20) Stevens Miller, A. E.; Beauchamp, J. L., *J. Am. Chem. Soc.* **1991**, *113*, 8765−8770.

(21) Stevens Miller, A. E.; Miller, T. M. In *Energetics of Organometallic Species*; NATO-ASI Series; Martinho Simões, J. A., Ed.; Kluwer Academic: Dordrecht, Netherlands, 1992; pp 253−267.

(22) Stevens Miller, A. E.; Miller, T. M.; Rekha, G. K.; Menendez-Barreto, M.; Friedman, J. F.; Paulson, J. F. *Int. Rev. Phys. Chem.* **1996**, *15*, 219−229.

(23) Koppel, I. A.; Taft, R. W.; Anvia, F.; Zhu, S.-Z.; Hu, L.-Q.; Sung, K.-S.; DesMarteau, D. D.; Yagupolskii, L. M.; Yagupolskii, Y. L.; Ignat'ev, N. V.; Kondratenko, N. V.; Volkonskii, A. Y.; Vlasov, V. M.; Notario, R.; Maria, P.-C. *J. Am. Chem. Soc.* **1994**, *116*, 3047−3057.

(24) Viggiano, A. A.; Henchman, M. J.; Dale, F.; Deakyne, C. A.; Paulson, J. F. *J. Am. Chem. Soc.* **1992**, *114*, 4299−4306. Viggiano, A. A.; Paulson, J. F.; Dale, F.; Henchman, M. J. *J. Phys. Chem.* **1987**, *91*, 3031−3032.

(25) Reaction 1—deprotonation of U by the electron—illustrates why we prefer superacidity defined in terms of IE(H) = 313.6 kcal mol^{-1}, instead of the nearly equivalent, but arbitrary, comparison to H_2SO_4; see refs 23 and 24.

(26) Sevilla, M. D.; Becker, D.; Yan, M.; Summerfield, S. R. *J. Phys. Chem.* **1991**, *95*, 3409−3415.

(27) Tran, P., Alavi, B., Gruner, G. *Phys. Rev. Lett.* **2000**, *85*, 1564−1567.

(28) Wan, C.; Fiebig, T.; Schiemann, O.; Barton, J. K.; Zewail, A. H. *Proc. Nat. Acad. Sci.* **2000**, *97*, 14052−14055.

(29) Fink, H.-W.; Schönenberger, C. *Nature* **1999**, *398*, 407−410.

(30) Henderson, P. T.; Jones, D.; Hampikian, G.; Kan, Y.; Schuster, G. B. *Proc. Nat. Acad. Sci. U.S.A.* **1999**, *96*, 8353−8358.

(31) Smith, D.; Adams, N. G. *Adv. At. Mol. Phys.* **1988**, *24*, 1−49.

(32) Viggiano, A. A.; Morris, R. A.; Dale, F.; Giles, K.; Smith, D.; Su, T. *J. Chem. Phys.* **1990**, *93*, 1149−1157.

(33) Miller, T. M.; Stevens Miller, A. E.; Paulson, J. F.; Liu, X. *J. Chem. Phys.* **1994**, *100*, 8841−8848.

(34) Miller, T. M.; Friedman, J. F.; Stevens Miller, A. E.; Paulson, J. F. *J. Phys. Chem.* **1994**, *98*, 6144−6147.

(35) Smith, D.; Španěl, P. *Adv. At. Mol. Opt. Phys.* **1994**, *32*, 307−343.

(36) Ferguson, E. E.; Fehsenfeld, F. C.; Schmeltekopf, A. L. *Adv. At. Mol. Phys.* **1968**, *5*, 1−56.

(37) Bardi, G.; Benecivenni, L.; Ferro, D.; Martini, B.; Nunziante Cesaro, S.; and Teghil, R. *Thermochim. Acta* **1980**, *40*, 275−282.

(38) Su, T.; Chesnavich, W. J. *J. Chem. Phys.* **1982**, *76*, 5183−5185. Su, T. *J. Chem. Phys.* **1988**, *89*, 5355; *J. Chem. Phys.* **1988**, *88*, 4102. We used the parametrized formula given in the final citation, except that the dimensionless temperature T_R is misprinted: $T_R = 2\alpha k_\beta T/\mu_D{}^2$.

(39) Jasien, P. G.; Fitzgerald, G. *J. Chem. Phys.* **1990**, *93*, 2554−2560.

(40) Španěl, P.; Smith, D. *Int. Rev. Phys. Chem.* **1996**, *15*, 231−271. Hansel, A.; Jordan, A.; Holzinger, R.; Prazeller, P.; Vogel, W.; Lindinger,

W. *Int. J. Mass Spectrom. Ion Processes* **1995**, *149*/*150*, 609−619. Španel, P.; Pavlik, M.; Smith, D. *Int. J. Mass Spectrom. Ion Processes* **1995**, *145*, 177−186.

(41) Bartmess, J. E., In *NIST Chemistry WebBook*; NIST Standard Reference Database 69, Linstrom, P. J., Mallard, W. G., Eds.; National Institute of Standards and Technology: Gaithersburg, MD, 2003; http://webbook.nist.gov/chemistry/.

(42) Morris, R. A.; Viggiano, A. A.; Paulson, J. F.; Henchman, M. *J. Am. Chem. Soc*. **1991**, *113*, 5932−5936.

(43) Morris, R. A.; Viggiano, A. A. *J. Phys. Chem*. **1994**, *98*, 3740−3746.

(44) Midey, A. J.; Williams, S.; Arnold, S. T.; Viggiano, A. A. *J. Phys. Chem. A* **2002**, *106*, 11726−11738.

(45) *CRC Handbook of Chemistry and Physics*; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1997; Section 7, p 3.

(46) Kilday, M. V. *J. Res. Natl. Bur. Stand. (U.S.)* **1978**, *83*, 547−554.

(47) The sublimation enthalpy was taken from ref 37; although the actual vapor pressure of uracil, which yields $\Delta G°_{sub}$, is inaccurate, the variation with temperature, which yields $\Delta H°_{sub}$, is substantively more accurate. Earlier sublimation enthalpies are given by: Nabavian, M.; Sabbah, R.; Chastel, R.; Laffitte, M. *J. Chim. Phys*. **1977**, *74*, 115−126 (30.2 ± 0.5 kcal mol^{-1}, in good agreement with ref 37); Clark, L. B.; Peschel, G. G.; Tinoco, Jr., I. *J. Phys. Chem*. **1965**, *69*, 3615−3618 (20 kcal mol^{-1}, in poor agreement). Clark et al. also point out that the neutral purine and pyrimidine bases have very high hydration enthalpies.

(48) Španěl, P.; Matejcik, S.; Smith, D. *J. Phys. B*: *At. Mol. Phys*. **1995**, *28*, 2941−2957.

(49) Hanel, G.; Gstir, B.; Denifl, S.; Scheier, P.; Probst, M.; Farizon, B.; Farizon, M.; Illenberger, E.; Märk, T. *Phys. Rev. Lett*. **2003**, *90*, 118104 (4 pages). Denfil, S.; Ptasinska, S.; Cingel, M.; Matejcik, S.; Scheier, P.; Märk, T. D. *Chem. Phys. Lett.* **2003**, *377*, 74−80. Scheer, A. M.; Aflatooni, K.; Gallup, G. A.; Burrow, P. D. *Phys. Rev. Lett.* **2004**, *92*, 068102 (4 pages).

(50) Drexel, H.; Sailer, W.; Grill, V.; Scheier, P.; Illenberger, E.; Märk, T. *J. Chem. Phys.* **2003**, *118*, 7394−7400.

(51) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.

(52) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys*. **1998**, *109*, 7764−7776.

(53) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys*. **1999**, *110*, 4703−4709.

(54) Viant, M. R.; Fellers, R. S.; McLaughlin, R. P.; Saykally, R. J. *J. Chem. Phys*. **1995**, *103*, 9502−9505.

(55) Smith, B. J.; Radom, L. *J. Phys. Chem*. **1991**, *95*, 10549−10551; *Chem. Phys. Lett*. **1995**, *245*, 123−128. The G3 and G3(MP2) methods utilize different HLC parameters for atoms and molecules, so there will not be complete cancellation of the HLC factors for a diatomic acid.

(56) Notario, R.; Castanõ, O.; Abboud, J. L. M. *Chem. Phys. Lett*. **1996**, *263*, 367−370.

(57) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys*. **1991**, *94*, 7221−7230. Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys*. **1997**, *106*, 1063−1079.

(58) Curtiss, L. A.; Raghavachari, K.; Pople, J. A. *J. Chem. Phys*. **1993**, *98*, 1293−1298.