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Journal of Molecular Structure 798 (2006) 126–133

Journal of
MOLECULAR
STRUCTURE

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# The experimental and theoretical gas phase acidities of adenine, guanine, cytosine, uracil, thymine and halouracils

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Received 25 May 2005; received in revised form 25 March 2006; accepted 28 March 2006
Available online 3 May 2006

## Abstract

The gas phase acidities GPA ($\Delta H(298)$ for deprotonation) of the most stable tautomers of adenine, guanine, cytosine, uracil and thymine are evaluated. New GPA are obtained from electron impact spectra and acid dissociation constants measured in dimethylsulfoxide for A, U and 5-FU. The average experimental GPA are: [N1—H] C 340(2); T 333(2); U 333(2); 5-FU 329(4); [N9—H] A 333(1); G 332(4); all in kcal/mol. Only cytosine is a weaker acid than HCl in the gas phase. The most acidic hydrogens in the nucleotides are replaced by the sugar in DNA and RNA. The experimental N3—H GPA are G 334(4); U 347(2), T 347(4), while the predicted N3—H 5-FU GPA is 343 kcal/mol. The NH—H GPA are: C 346(4); A 352(2); G 336(4) (all in kcal/mol). These are supported by semi-empirical multiconfiguration configuration interaction calculations. The predicted C8—H acidities of G and A and the C6—H of T are about the same, 360(2) kcal/mol. The remaining CH acidities are 370–380 kcal/mol. The 5-halouracils are predicted to be more acidic than HCl.

*Keywords:* Purines and pyrimidines; Gas phase acidity; Electron affinity; Electron capture detector; Negative ion mass spectrometry

## 1. Introduction

Long before the proposal of the double-helix structure for DNA, the biological significance of the purines and pyrimidines, adenine, guanine, cytosine, uracil and thymine, AGCUT was recognized. These are designated P and the deprotonated radicals, $P_{MinH}$. The ability of high energy radiation to damage and destroy biological material is well known. However, the mechanism is not understood. This is partially due to the uncertainty in the electron affinities, $E_a$, gas phase acidities, GPA and bond dissociation energies, $D$(C—H or N—H) of AGCUT [1–33].

In 1990, we began to determine these quantities. [1–12] The Adiabatic Electron Affinity, A$E_a$, were predicted from substitution and replacement models, determined from reduction potentials and confirmed using AM1

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*Abbreviations:* ECD, Electron capture detector; EI, electron impact; PES, photoelectron spectroscopy; CURES-EC, semi-empirical procedure for predicting or verifying values; DF, density functional procedure for predicting or verifying values; MP2, ab initio procedure for predicting or verifying values; MCCI, multiconfiguration configuration interaction; NCIMS, Negative Chemical Ion Mass Spectrometry; A$E_a$, Adiabatic Electron Affinity; $E_a$, Electron affinity; $E_a(X,1,2)$, Specific state adiabatic electron affinity (X is the covalent ground state); $E_{dea}$, energy for dissociative electron attachment $= E_a(X) - D_{XY}$; L$E_a$, long range electron affinity; S$E_a$, short range electron affinity; V$E_a$, vertical electron affinity; $E_{pd}$, Photodetachment energy; FLHW, Feynman, Lesk, Herschbach, Wentworth hypotheses; NIST, National Institute of Science and Technology database; $Q_{an}$, partition function ratio of anion to neutral without spin factors; $S_{an}$, spin partition function ratio; $q_e$, Translational partition function of the electron; $g_i$, multiplicities for anion, neutral and electron; $K$, molar response or response calculated from rate constants; $K_{eq}$, equilibrium constant for electron molecule reactions; $k_1$, rate constant for thermal electron attachment $= A_1T^{-1/2}\exp(E_1/RT)$; $k_{-1}$, rate constant for thermal electron attachment $= A_{-1}T\exp(E_{-1}/RT)$; $k_2$, rate constant for thermal electron attachment $= A_2T\exp(E_2/RT)$; $k_N, k_D$, pseudo unimolecular recombination coefficient for electrons and ions.

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doi:10.1016/j.molstruc.2006.03.073

multi-configuration, configuration interaction (AM1-MCCI-CURES-EC) procedures: A 0.95(5); G 1.51(5); C 0.56(5); U 0.80(5) and T 0.79(5) eV [1–6,12]. In 1992, we investigated gas phase reactions between thermal electrons and isolated AGCUT using Negative Chemical Ionization Mass Spectrometry, NCIMS. Only the $P_{MinH}(-)$ were observed indicating that the energy for dissociative thermal electron attachment, $-E_{dea} = D - E_a(P_{MinH}) = 0.7(4)$ eV. We concluded that adenine, guanine, cytosine, uracil and thymine are strong gas phase acids, comparable to HCl. In 2000, different valence state $E_a$ were assigned to multiple states, and $\Delta G(298)$ were reported: U 328(5) kcal/mol; G, A and T; 325(5) kcal/mol and C; 331(5) kcal/mol. We also calculated multiple Herschbach Ionic Morse Person Empirical Curves, HIMPEC, based on these data and other literature data [5–12].

A positive $E_a$ corresponds to the energy released in the formation of AB(−) in a specific state or is the difference in the energy of an entity and one of its anions in their most stable forms. Other energy differences are the vertical $E_a$, V$E_a$, in the neutral geometry and the vertical detachment energy, VDE or photodetachment energy, $E_{pd}$, in the anion geometry (energy of the neutral species at the geometry of the anion). The A$E_a$ is a long range $E_a$, L$E_a$ when all valence or short range $E_a$, S$E_a$ are negative. The L$E_a$ are larger than $D(He_2)$ since they arise from ion dipole, quadrupole or polarization interactions. All L$E_a$, A$E_a$ and anion dissociation energies are greater than zero from the Feynman, Lesk, Herschbach, Wentworth, FLHW, hypotheses as applied to carbon tetrachloride, tetrachloroethylene and perfluorocyclobutane [5–12].

The GPA is the deprotonation energy, $E_{dp}$: $AH \rightarrow H(+) + A(-)$. Both $\Delta H(298)$ and $\Delta G(298)$ are used so the metric must be specified. In this paper, $\Delta H(298)$ is implied. The adiabatic GPA, AGPA or adiabatic $E_{dp}$, $AE_{dp}$ is the smallest $\Delta H(298)$. Energies for other deprotonation sites are $E_{dp}$ and $E_{dp} = IP(H) - E_{dea}$ where IP(H) is the ionization potential of hydrogen. The IP(H) and the $E_a$ are at 0 K while the $D(P_{MinH}-H)$ and the GPA are at 298 K so that temperature corrections must be applied.

In 1998, the V$E_a$ for adenine, guanine, cytosine, uracil, and thymine were determined from electron transmission spectra [13]. Dipole bound and valence state anions for U, C and T were observed in PES of anion complexes. In the PES of hydrated U(−), a broad valence state peak is observed at 1.0(2) eV. In the bare U(−), peaks were observed at 0.09, 0.3, 0.5 and 0.8 eV indicating a 0.2(2) eV hydration energy, which is the same as observed for T(+) [14–19]. The A$E_a$ for C and T estimated from the PES of hydrated anions agree with the reduction potential values [5,6]. In 1998, long lived parent negative ions were observed at thermal energy and at higher electron impact energies [18]. The adiabatic GPA of U, T and A were determined to be 333(2) kcal/mol and that for C 342(2) kcal/mol by bracketing experiments. Other experimental N—H and C—H GPA are greater (less acidic) than that for HCl [20–29].

In 1994, Beauchamp et al. calculated GPA for AGCT using AM1 and PM3. In 1998, we calculated CURES-EC GPA for AGCUT (adenine, guanine, cytosine, uracil, thymine) by modifying the configuration interaction to agree with experimental values [4,20]. In 1998, Marshall et al. determined rates of H/D exchange from $D_2O$ and $D_2S$ in nucleotides and calculated values of the N—H GPA for AGCUT using MP2 methods. The experiments bracketed the secondary acidities between that of $D_2S$, 351.3 kcal/mol and the phosphate group, 331.6(4) [21]. The National Institute of Standards and Technology, NIST online compilation lists dipole bound DB$E_a$, A 0.012(5); C 0.085(5), 0.230(5); U 0.090(5) and T 0.065(5) eV and no GPA for the nucleic acids [12,31].

This paper updates our 2004 evaluation of the experimental GPA for adenine, guanine, cytosine, uracil and thymine. Additional GPA for A, U and 5-fluorouracil are obtained from relative p$K_a$ measured in aprotic solvents that give the gas phase acidity differences [34,35]. Since 2000, a number of electron impact studies of AGCUT and halouracils have been reported. Dissociative electron attachment and molecular ion formation are observed at thermal energy for the halouracils [36–43]. The GPA can be determined from $E(\text{threshold}) = D(AB) - E_a(B) = -E_{dea}$ since $GPA = IP(H) - E_{dea}$. The CURES-EC $E_a(P_{MinH})$, $D$(P—H) and GPA for AGCUT and the halouracils are presented. An explanation for apparently conflicting experimental results for dissociative and non-dissociative electron reactions with C and T is postulated. Morse curves for multiple anion states of $O_2$ based on new electron capture detector data are given to support multiple anion states for the nucleic acids.

## 2. Experimental methods

In the ECD, NIMS and electron impact experiments, the energy for the dissociative electron capture, $-E_{dea}$, can be measured. In the ECD, the electron current with and without AB; $I_{e-}$ and $I_b$, are recorded. The molar response $K$ is calculated from: $\{I_b - I_{e-}\}/2I_{e-} = K[AB]$. In NIMS the ion intensities are measured. The reactions are electron attachment, detachment, dissociation and recombination with ions, P(+).

$$AB + e(-) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AB(-) \xrightarrow{k_2} A + B(-) \tag{1}$$

$$e(-) \text{ or } AB(-) + P(+) \xrightarrow{k_D \text{ or } k_N} \text{neutrals} \tag{2}$$

Assuming pseudo unimolecular recombination, the steady state treatment gives

$$K = k_1(k_N + k_2)/((k_D)(k_{-1} + k_N + k_2)) \tag{3}$$

When

$$k_{-1} > (k_2 + k_N); \quad K = k_1k_N/k_Dk_{-1} = K_{eq}(k_1/k_{-1}) \tag{4}$$

and the $E_a$ and $Q_{an}$, anion, neutral partition function ratio are determined from the statistical mechanical expression