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The Electron Affinities of the Radicals Formed by the Loss of an Aromatic Hydrogen Atom from Adenine, Guanine, Cytosine, Uracil, and Thymine

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The major ion formed in Negative Ion Chemical Ionization Mass Spectrometry of Adenine, Guanine, Cytosine, Uracil and Thymine is the dehydrogenated anion. The CURES EC procedure for optimizing Austin Model-1 Multiconfigurational Configuration Interaction semi-empirical calculations is applied to the electron affinities of the corresponding dehydrogenated bases and N–H bond dissociation energies. These calculated values will be compared with literature values of the gas phase acidities of the purines and pyrimidines. The N–H bond dissociation energies are about 3.95 eV for Guanine, Adenine, and Thymine and 4.08 eV for Cytosine and Uracil. The electron affinities of the radicals are A_{MinH} = 3.50 eV, G_{MinH} = 3.46 eV, C_{MinH} = 3.38 eV, U_{MinH} = 3.48 eV, T_{MinH} = 3.46 eV.

The biological significance of Adenine (A), Guanine (G), Cytosine(C), Uracil(U) and Thymine(T) was recognized before the establishment of the double helix structure of DNA. In spite of this importance, adiabatic electron affinities have only recently been measured and other important properties such as gas phase acidities (GPA) and N-H bond dissociation energies have not been definitively measured. The purpose of this paper is to provide theoretical calculations of the electron affinities of the radicals formed from the nucleic acids by the loss of a hydrogen atom and the appropriate N-H bond dissociation energies. We will use AM-1multiconfiguration configuration interaction semi-empirical calculations (AM1-MCCI) using the HYPERCHEM software. These will be compared with values obtained from literature values of the gas phase acidities of the purines and pyrimidines obtained from unrestricted Hartree Fock (UHF)AM1 and PM3 calculations.

DEFINITIONS AND PROCEDURES

The adiabatic electron affinity is the difference in the energy between the neutral and the negative ion in their most stable state. By convention, the electron affinity is positive for an exothermic reaction. The gas phase acidity is defined as the difference in the energy between the neutral and the negative ion plus a hydrogen positive ion in their most stable states. This can be expressed in the following:

$$P \rightarrow P^-_{MinH} + H^+ \qquad [1]$$

$$\text{Gas Phase Acidity} = IP(H) + EA(P_{MinH}) - D(N\text{–}H) \qquad [2]$$

where IP(H) is the ionization potential of the hydrogen atom = 313.6 kcal/mole, 13.6 eV.

Beginning in 1990, we initiated a program to establish the electron affinities of the nucleic acids.[1-3] These were first predicted by chemically logical substitution and replacement rules.[1] Half wave reduction potentials of the purines and pyrimidines were then measured to obtain gas phase adiabatic values.[2] These have been verified to an accuracy of better than 260 meV for cytosine using UHF-AM1 calculations.[3] In this article we show that the accuracy can be improved by MCCI calculations.

The procedure has been given the acronym CURES EC from *C*onfiguration interaction or *U*nrestricted orbitals to *R*elate *E*xperimental quantities to *S*elf consistent field values by estimating *E*lectron *C*orrelation. This is quite appropriate since it is a cure for the electron correlation problem in semi empirical calculations. It uses different amounts of MCCI to modify the semi-empirical electronic energies of both the neutral and the anion. The electron affinity is the difference in these energies.

The number of filled and unfilled orbitals are chosen to minimize the difference between the experimental and theoretical values, defined as σ EA. Because of the integer nature of the number of orbitals, the values are quantum quantities since they take on only discrete values. To obtain the minimum σ EA, the UHF EA, the RHF EA and then the RHF(3333) EA values are calculated. The last calculation is

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Abbreviations: CURES EC, configuration interaction or unrestricted orbitals to relate experimental quantities to self consistent field values by estimating electron correlation; MCCI, multiconfiguration configuration interaction; P_{MinH}, radical formed by loss of a hydrogen atom.

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designated (3333) for the number of filled and unfilled orbitals in the anion and neutral. From these the MAX(3300) and MIN(0033) values can be calculated. If the experimental value fits between these extremes, an optimum value can be obtained. The CURES EC method can only improve the agreement with the experimental values since the UHF or RHF value could be the optimum.

RESULTS AND DISCUSSION

CURES EC has been successfully applied to over 100 compounds for which electron affinities have been measured in the gas phase and another 150 where values have been obtained from half wave reduction potentials, including the purines and pyrimidines. In Figure 1 we plot the previous UHF calculated electron affinities for purine, pyrimidine, C, U, T, G, and A and the AM1-MCCI values versus the experimental electron affinities. The slope of the line for the AM1-MCCI values is one and the greatest deviation is 20 meV for adenine. The improvement is apparent. The AM1-MCCI calculation is clearly superior especially since it has been used for so many other compunds.

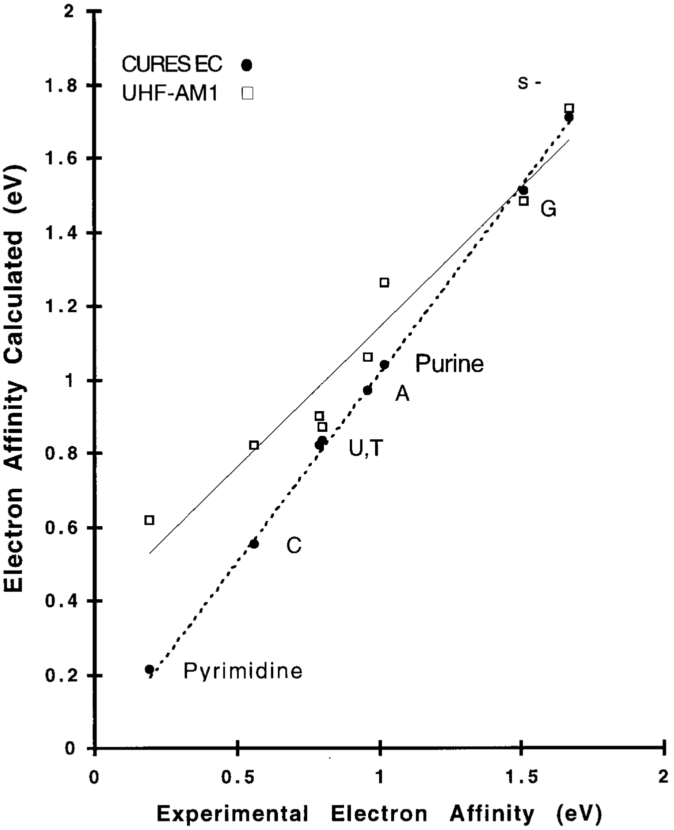

FIG. 1. The Calculated Electron Affinities of Cytosine, Uracil, Thymine, Guanine, Adenine, Pyrimidine, Purine and s-Tetrazine versus the Experimental Values of the Electron Affinities(Ref. 2). The Methods of Calculation are the AM1-UHF (Unrestricted Hartree Fock) (Ref 3)method and the AM1-MCCI (Multiconfiguration Configuration interaction) CURES EC method(This work).

TABLE I

Calculated Bond Dissociation Energies, Electron Afffinities, and Gas Phase Acidities (eV)

Molecule	D(N-H)[a] MCCI	EA(P_{MinH})[a] MCCI	Gas Phase Acidity MCCI	AM1[b]	PM3[b]
Adenine	3.96	3.50	14.06	14.43	14.18
Guanine	3.95	3.46	14.1	14.33	14.23
Cytosine	4.08	3.38	14.3	14.70	14.23
Uracil	4.08	3.48	14.2		
Thymine	3.95	3.46	14.1	14.29	13.99

[a] This work
[b] Reference 4

In 1994, the most acidic hydrogens (lowest value) in A,C,G, and T were identified as the pyrrole hydrogens by using UHF semi empirical methods. For the AM1 values the reported acidities in kcal/mole are T = 328, G = 330.5, A=332.9 and C =338.9 and for the PM3 values, T = 322.3, G = 327, A=327.9 and C =328.2.[4] The experimental order from collision-induced dissociation of deprotonated dinucleotides is either A>T>G>C or G>A>T>C, depending upon the nature of the 3′ terminus base. In all of the results, cytosine is the least acidic.

The CURES EC, AM1-MCCI calculated results for the electron affinities of the P_{MinH} radicals, the N-H bond dissociation energies and the gas phase acidities calculated from these quantities are given in Table I. These are compared with the above gas phase acidities. Based on the results for the electron affinities of the nucleic acids, the MCCI values should be more accurate. The MCCI gas phase acidities agree with the chemical ionization mass spectrometry results. Although they only cover a range of about 0.25 eV, they reproduce the experimental order of the gas phase acidities to within 0.1 eV. The N-H bond dissociation energies are within 0.1 eV of the average value.

The electron affinities of the dehydrogenated purines are extremely large. To our knowledge, these are the first estimates of these electron affinities. They are comparable to the values of the acetate radical. They are as high as the values for the halogen atoms which range from 3.08 to 3.67 eV. This also explains the preponderance of these ions in the negative ion mass spectra of compounds containing these bases. Using the N-H bond dissociation energy to calculate gas phase acidities, the bases are among the most acidic organic compounds measured in the gas phase. In a standard list of values, only trifluoroacetic acid is more acidic.[5] In other words, the bases are very good gas phase acids.

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