# Methylation Reduces Electron Affinity of Uracil. Ab Initio Theoretical Study

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Following the experimental characterization of the *N*,*N*-dimethylated uracil anion by Bowen and co-workers, we have undertaken an investigation of the influence of the methylation on the electron affinity of the uracil molecule. Both experiment and theory agree that, as it is in the case of the isolated uracil molecule, the methylated uracils can only attach excess electrons into diffuse dipole-bound states. The corresponding electron affinities are very small (several MeV). The bonding effect in the dipole-bound state depends on the magnitude of the molecular dipole and on the size of the molecule. Selective methylation of the uracil molecule can be used to reduce or increase the dipole value and to change the electron affinity of the molecule. The present calculated results are consistent with the experimental determination that *N*,*N*-dimethylation of uracil results in reduction of the electron affinity.

## 1. Introduction

Following the theoretical ab initio calculations of our group[1−4] on the electron affinities of the nucleic acid bases uracil, thymine, adenine, and guanine, the very recent independent experiments by Schermann and co-workers at the University of Northern Paris, France, and by Bowen and co-workers at Johns Hopkins University[5,6] confirmed that the positive, but very small, electron affinities of these systems in the gas phase are due to dipole−electron attachment. Apart from a more fundamental aspect of this interesting phenomenon, the formation of stable anions of DNA bases has interesting biological consequences. As currently believed, it is a crucial step in a cascade of events which result from irradiation of the biological material by high-energy radiation.[7] Also, the electric conductivity of DNA—a topic vigorously debated in recent years[8]—can be affected by electrons being trapped by individual bases or base pairs. The dipole-bound states are different from conventional anions because the majority of the electron density of the excess electron is located outside the molecular frame. These states will be much more significantly perturbed than the conventional anions by interaction with other molecules, but still the long-range dipole−electron attractive forces in these states may be an important factor in determining the electronic properties of DNA. Apart from theoretical studies on dipole-bound states of nucleic acid bases, over the past few years there have been attempts to theoretically describe stable valence states of an excess electron in these systems and their complexes.[9,10] We recently presented calculations on the $(\text{uracil}\cdot3H_2O)^-$ anion which showed that there is an equilibrium structure for the anion which is considerably different from the structure of the neutral complex and that the anion at this configuration has a positive ionization potential.[12] In this structure the water molecules are connected through single hydrogen bonds to uracil, which is different from the neutral cluster where two hydrogen bonds connect each water molecule to the uracil molecule. The analysis of the charge distribution of the excess electron in the $(\text{uracil}\cdot3H_2O)^-$ anion indicated that the anion has a valence character and the excess electron is located near the valence area of the complex. In an independent calculation we also found a dipole-bound state of the $(\text{uracil}\cdot3H_2O)^-$ anion that has a very similar structure to the neutral complex and where the excess electron is located in a very diffuse state. The theoretical results on the $(\text{uracil}\cdot3H_2O)^-$ cluster anion have led to some speculation on the physical principle laying behind the formation of a valence anionic state in a hydrogen bonded molecular complex. We attributed this ability to changes in structure of the hydrogen bonds in the complex, upon attachment of an excess electron. Stretching or rupturing of some weaker H-bonds in the complex may create electron-deficient areas where the excess electron can attach and form a stationary state. If this happens, the molecular structure of the anion will be considerably different from the structure of the neutral complex, particularly in terms of lengths and numbers of the hydrogen bonds. For a single, isolated molecule with ionic or covalent bonds, the above-described mechanism will probably not work, because the average bond energy is considerably higher than the energy of a hydrogen bond and its stretching or breakage can, only in rare cases, be compensated by the energy gain resulting from electron attachment. In such situations it seems that a more probable valence state of the excess electron in the anion, if it exists, would be a state which is delocalized over the whole molecule. If the molecule has a dipole moment, the excess electron may be, in part, described by a dipole-bound wave function and in part by a wave function in the valence region. The uracil anion was an example of this type of interplay between the dipole-bound and valence attachments, with the majority of the electron charge distribution located in the dipole-bound state.[1] The dipole moment of the molecule can be reduced or enhanced by selective methylation. The methylation can also change the balance between the valence and dipole-bound components of the wave function describing the excess electron. This phenomenon is studied in the present work. Recent experiments performed by Bowen and co-workers have shown that the *N*,*N*-dimethylation of the uracil molecule results in decrease of its electron affinity which corresponds to dipole-bound attachment. In the present work we present results of theoretical ab initio calculations, which agree with this finding. We also study some dipole-bound electron attachment to some other doubly methylated uracil systems to see how methylation at other sites of the molecule changes the electron affinity of uracil.

## 2. Method of Calculation and Numerical Results

As suggested by Gutowski et al.,[14] one can view the dipole-bound interaction of an excess electron with the molecule as

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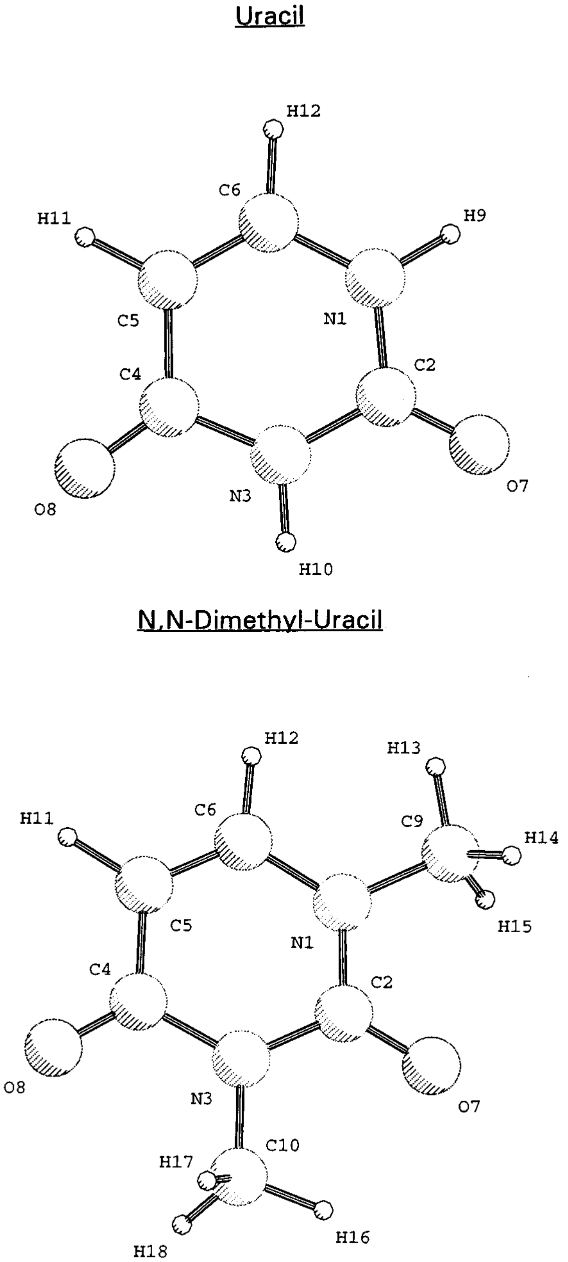


**Figure 1.** Structures of uracil and *N*,*N*-dimethyluracil obtained in this work.

similar to intermolecular forces. Here, also, one can distinguish different interaction effects such as electrostatic, polarization, exchange, and dispersion interactions. As we demonstrated in our previous calculations,[1−4] the electron correlation contribution to all these interactions can be significant and may result not only from the dispersion interaction of the extra electron with the electrons of the core, which is exclusively a correlation effect, but also from a frequently sizable correlation contribution to the molecular dipole moment. The lowest ab initio level of theory which provides an account of the dispersion forces and the correlation correction to the dipole moment is the MP2 level (the second-order Møller−Plesset perturbation theory). This is a suitable level of the theory for the systems considered in the present work. All the calculations presented in this work have been performed with the GAUSSIAN94 program package.[15] We have done the following calculations: In the first step we determined the equilibrium structures of the uracil (U) and *N*,*N*-dimethyluracil (NNM) neutral molecules at the RHF/6-31++G** level of theory. The calculated molecular geometries are shown in Figure 1.

(2) Next we performed RHF calculations for both molecules with the basis set consisting of the standard 6-31+G* basis set augmented with an additional set of three diffuse sp -shells with exponents equal to α, 0.1α and 0.01α, where α is a scaling factor. The additional set was added to the standard set to describe the orbital which is occupied by the excess electron in the dipole-bound state for each of the anions. In the Koopmans' approximation, this orbital is represented by the lowest unoccupied molecular orbital (LUMO) of the neutral system, which for a dipole-bound state should have a negative orbital energy. The additional set was selected based on the previous analysis,[16−18] where numerical orbitals produced by the Hartree−Fock (HF) and Multiconfiguration self-consistent field (MCSCF) procedures for some dipole-bound diatomic polar systems were projected onto Slater-type atomic orbitals.

The additional diffuse set was placed at the end of the molecular dipole moment vector, whose origin was located in the center of mass of the molecule.

The purpose of these calculations was to find the optimal value of the scaling factor α, which was determined by minimization of the LUMO energy. This optimal value was determined to be 0.0838 and 0.0678 for U and NNU molecules, respectively. The corresponding LUMO energies are 18.8 and 7.2 MeV for U and NNU, respectively. The 6-31+G* basis augmented with the three diffuse sp -shells is referred to as 6-31+G***X** in the further discussion and in the tables. In the calculations for uracil we also used a set denoted as 6-31++G****Y**, where the **Y** diffuse set was obtained from **X** by adding two additional sp-shells with exponents 0.838 and 0.000 0838. With such generated basis sets we calculated the restricted Hartree−Fock (RHF) and MP2 energies of the neutral U and NNU systems and their dipole moments. The results are shown in Table 1. The dipole moment value of 4.61 D for NNU is slightly lower than the value of 4.94 D obtained for U.

(3) Next we performed unrestricted Hartree−Fock (UHF) and unrestricted Møller−Plesset (UMP2) calculations for the U- and NNU-anions using the 6-31+G***X** basis set and the geometries of the respective neutral systems. For the uracil anion, calculations were also done with the 6-31++G****Y** basis set to test how converged the results obtained with the smaller 6-31+G***X** basis set are. The vertical electron affinity (EA) was calculated for each system as the difference between the anion energy and the energy of the neutral. The results are presented in Table 1. At the UHF level of theory, both U and NNU have positive vertical EAs equal to 22.2 and 8.3 MeV. These values increase to 30 and 10.7 MeV when electron correlation effects are accounted for at the MP2 level of theory. The results obtained for uracil with the more extended 6-31++G****Y** basis set are virtually identical with the results obtained with the smaller basis.

(3) In the next step we calculated the adiabatic EAs for U and NNU. First we performed UHF optimizations of the U- and NNU-anion geometries with the 6-31+G***X** basis, allowing the position of the diffuse set **X** to also be optimized. The optimal geometries which resulted from these optimizations are very close to the geometries of the neutral complexes. To determine the adiabatic dipole-bound electron affinity for the two systems, HF and MP2 calculations were done with the 6-31++G****X** basis set for the anions and the neutral molecules. The optimal HF/6-31+G***X** structures were used in these calculations. The electron affinity values were calculated as differences of the total energies of the anion and neutral systems and the results are presented in Table 2. We should mention that at each computational step small convergence tolerances have been used to ensure high precision of the results. The

**TABLE 1: Vertical Electron Affinity (Calculations of Uracil and *N*,*N*-Dimethyluracil[a]**

| | uracil | *N*,*N*-dimethyluracil |
|---|---|---|
| neutral system | | |
| RHF/6-31++G**// RHF/6-31++G** | −412.494 052 1 | −490.5539 482 |
| RHF/6-31+G*(5d)**X**// RHF/6-31++G** [b] | −419.481 371 5 | −490.539 106 4 |
| MP2/6-31+G*(5d)**X**// RHF/6-31++G** [c] | −413.638 945 4 | −491.964 207 9 |
| RHF/6-31++G**(5d)**Y**// RHF/6-31++G** [d] | −412.493 144 5 | |
| MP2/6-31++G**(5d)**Y**// RHF/6-31++G** [d] | −413.672 803 3 | |
| LUMO/6-31+G*(5d)**X** | 18.8 | 7.2 |
| LUMO/6-31++G**(5d)**Y** | 19.1 | |
| $\mu$/RHF/6-31++G** | 4.94 | 4.61 |
| $\mu$/RHF/6-31+G*(5d)**X** | 4.94 | 4.61 |
| anion (at the RHF/6-31++G** geometry of the neutral) | | |
| UHF/6-31+G*(5d)**X** | −412.482 186 4 | −490.539 410 5 |
| UMP/6-31+G*(5d)**X** | −413.640 048 5 | −491.964 602 1 |
| HOMO/6-31+G*(5d)**X** | −26.2 | 9.5 |
| UHF/6-31++G**(5d)**Y** | −412.493 973 9 | |
| UMP2/6-31++G**(5d)**Y** | −413.673 909 8 | |
| HOMO/6-31++G**(5d)**Y** | 26.8 | |
| vertical electron affinity | | |
| HF/6-31+G*(5d)**X** | 22.2 | 8.3 |
| MP2/6-31+G*(5d)**X** | 30.0 | 10.7 |
| HF/6-31++G**(5d)**Y** | 22.6 | |
| MP2/6-31++G**(5d)**Y** | 30.1 | |

[a] Total energy in hartrees and electron affinities; HOMO and LUMO energies in MeV and dipole moments ($\mu$) in Debye. [b] **X** set for uracil, three sp-shells with exponents (0.0838, 0.008 38 and 0.000 838). **X** set for *N*,*N*-dimethyluracil, three sp-shells with exponents (0.0678, 0.00678, and 0.000 678). [c] Core electrons are not correlated. [d] **Y** set for uracil, five sp-shells with exponents (0.838, 0.0838, 0.00 838, 0.000 838, and 0.000 083 8).

**TABLE 2: Adiabatic Electron Affinity Calculations of Uracil and *N*,*N*-Dimethyluracil[a]**

| | uracil | *N*,*N*-dimethyluracil |
|---|---|---|
| neutral system | | |
| RHF/6-31++G**(5d)**X**// RHF/6-31+G***X** [b,c] | −412.493 108 7 | −490.552 929 5 |
| MP2/6-31++G**(5d)**X**// RHF/6-31+G***X** [b,c] | −413.672 855 9 | −492.027 887 8 |
| anion | | |
| UHF/6-31++G**(5d)**X**// UHF/6-31+G***X** | −412.493 985 1 | −490.553 253 0 |
| UMP2/6-31++G**(5d)**X**// UHF/6-31+G***X** | −413.674 327 6 | −492.028 445 0 |
| adiabatic electron affinity | | |
| HF/6-31++G**(5d)**X** | 23.8 | 8.8 |
| MP2/6-31++G**(5d)**X** | 40.0 | 15.2 |

[a] Total energies in Hartrees; electron affinities in MeV. [b] See footnote in Table 1. [c] In the geometry optimization for the neutral system, the position of the **X** set was not optimized but taken from the anion geometry optimization. [d] Core electrons are not correlated.

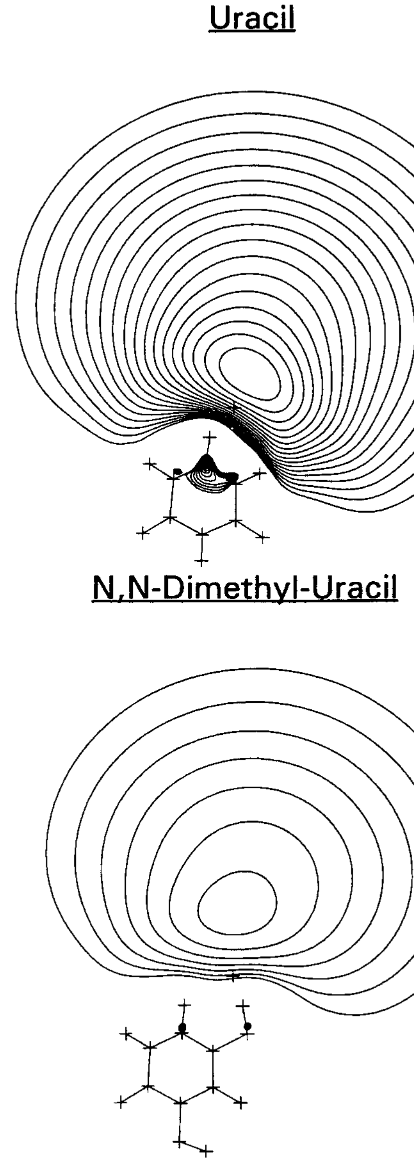
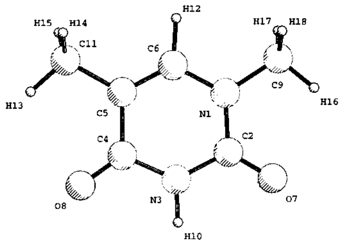


**Figure 2.** The orbitals occupied by the excess electrons in the dipole-bound states in uracil and *N*,*N*-dimethyluracil anions ploted with the contour levels from 0.003 to 0.011 in steps of 0.0005.

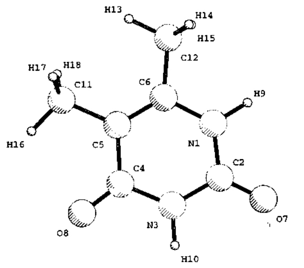
calculated values for the adiabatic EAs for U and NNU are 23.8 and 8.8 MeV at the HF level of theory and 40.0 and 15.2 eV at the MP2 level, respectively.

It is interesting that, while the HF adiabatic electron affinity is only larger by about 1 MeV than the vertical electron affinity, the MP2 adiabatic EA increases by as much as 10 MeV in comparison to the vertical EA (from 30.1 to 40.0 MeV). The reason for the difference in the HF and MP2 results can be related to more significant changes in the energies and shapes of some of the virtual orbitals due to the small structural relaxation of the anion. These changes will not alter the HF energies, but may produce some more significant difference in the MP2 energy of the anion. The only way to determine whether the change is physical or not would be by performing higher-order calculations. However, at present these are not feasible.

(4) To visualize the dipole-bound state of the excess electron in the U- and NNU-anions, we present in Figure 2 contour plots of HOMOs from the SCF/6-31+G***X** calculations. For both anions the HOMOs are very diffuse and extend away from the molecule along the direction of the dipole. For the NNU$^-$ anion there are fewer contour lines on the plot, which is a manifestation that the orbital is much flatter and extends further away from the molecule than for U$^-$. This is consistent with the smaller NNU dipole moment and its lower EA. The above-described calculations have shown that *N*,*N*-dimethylation of uracil results in reduction of the dipole moment and in smaller dipole-bound electron affinity. The electron donating effect of the methyl group can be also used to increase the uracil dipole moment by methylation at other ring positions. We consider two such systems: 1,5-dimethyluracil (U15) and 5,6-dimethyluracil (U56) (see Figure 3). The calculations of the adiabatic electron affinities of these systems were performed following the procedure used for U/U$^-$ and NNU/NNU$^-$. The RHF dipole moments of U15 and U56, equal to 5.14 and 5.44 D,



**1,5-Dimethyl-Uracil**



**5,6-Dimethyl-Uracil**

**Figure 3.** Structures of 1,5-dimethyluracil and 5,6-dimethyluracil obtained in this work.

**TABLE 3: Adiabatic Electron Affinity Calculations of 1,5- and 5,6-Dimethylated Uracils**[a]

| | 1,5-dimetyluracil | 5,6-dimethyluracil |
|---|---|---|
| neutral system | | |
| RHF/6-31++G**(5d)**X**// RHF/6-31+G***X** [b] | −490.565 071 3 | −490.577 581 2 |
| MP2/6-31++G**(5d)**X**// RHF/6-31+G***X** [c] | −492.038 750 5 | −492.050 885 5 |
| $\mu$/RHF/6-31++G****X** | 5.14 | 5.44 |
| anion | | |
| UHF/6-31++G****X**// UHF/6-31+G***X** | −490.565 485 6 | −490.578 119 8 |
| MP2/6-31++G****X**// UHF/6-31+G***X** | −492.039 427 8 | −492.051 799 3 |
| adiabatic electron affinity | | |
| HF/6-31++G****X** | 11 | 15 |
| MP2/6-31++G** | 18 | 25 |

[a] Total energies in Hartrees, electron affinities in MeV, and dipole moments ($\mu$) in Debye. [b] **X** set for u15-three sp-sheels with exponents (0.0043467, 0.00043467, 0.000043467). **X** set for u65-three sp-shells with exponents (0.02383, 0.002383. 0.0002383). [c] Core electrons are not correlated.

respectively, are slightly larger than the dipole moment of uracil at this level of theory. However, optimizations of the α-scaling factor for the **X** diffuse set orbitals representing the dipole-bound electrons lead to values (0.004 346 7 for U15 and 0.023 82 for U56) smaller than in the case of uracil or even for *N*,*N*-dimethyluracil. The MP2/6-31++G****X** result for the adiabatic electron affinity for U15 of 18 MeV (see Table 3) is smaller than the result for the U56 system (25 MeV); and this follows the trend of the dipole moments for these molecules. Despite larger dipole moments of U15 and U56 than for uracil, these two systems are predicted to have smaller EAs. An observation which emerges from this study is that by selectively methylating some centers in the molecule one can alter its electron affinity corresponding to the dipole-bound electron attachment.

## 3. Conclusions

Motivated by the recent experimental finding by Bowen and co-workers that *N*,*N*-dimethylation of uracil results in a decrease of the electron affinity of this system, we performed theoretical calculations to compare dipole-bound anionic states of uracil and *N*,*N*-dimethyluracil. Due to slightly different level of theory applied in the present study than in the study presented before where we used a lower level of theory[1], the present results of 40 MeV for the uracil dipole-bound electron affinity is lower that the previously published result of 86 MeV. The experimental values for this system obtained using the photoelectron spectroscopy[6] and the Rydberg electron-transfer method are 93 and 50 MeV, respectively. Our recent study of the dipole-bound electron affinity of the hydrogen−fluoride dimer $(HF)_2$ performed using several levels of theory including the coupled cluster method with triple excitations (CCSD(T)) and with different basis sets,[13] indicated that including higher order correlation effects may lead 50−60% increase of the calculated electron affinity with respect to the MP2 result. This conclusion is consistent with our previous observation,[20] as well as with the observation made by Gutowski et al.[14] and by Gutsev and Bartlett.[19]

Therefore, the present MP2 result of 40 MeV for the EA of uracil can be expected to increase when the higher correlation effects are accounted for and better match both experimentally determined values. The calculated adiabatic electron affinity of NNU of 15.2 MeV is significantly lower than the result for U (40 MeV). This finding is consistent with the experimental observation.[5] As expected, since *N*,*N*-dimethylation of U lowers its dipole moment, the dipole-bound excess electron forms a weaker bond with the *N*,*N*-dimethyluracil. In this work we also calculated electron affinities of two other dimethylated uracils with higher dipole moments than for the uracil molecule. In both cases the calculated EA values are smaller than the uracil EA values. We can speculate that one reason for this behavior is that the dipole moment is not the only factor which determines the EA of the molecule. Among the other factors, one can mention the size of the molecule which seems to have an opposite effect than the magnitude of the dipole moment, i.e., for two molecules with the same dipole moments, the smaller one will have a higher dipole-bound electron affinity. This is probably related to the fact that the excess electron is "pushed away" more from the molecule in the larger system than in the smaller one by the orthogonality conditions which relate the orbital occupied by the excess electron to the other occupied orbitals. One other reason can be a higher contribution from the "valence" attachment of the excess electron, which is related to the number of electropositive centers in the molecule and their "local" electron affinities.

Another interesting comparison, which one can make based on the present results, is the trend in electron binding energies for the series of molecules *N*,*N*-dimethyluracil, 1,5-dimethyluracil and 5,6-dimethyluracil, which share the same stoichiometry. Clearly in this case, the calculated electron affinity values (MP2 results are 15, 18, and 25 MeV, respectively) follow the increasing values of the dipole moments (the RHF results are: 4.61, 5.14, and 5.44 D) for the three systems.

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