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Hydrogen-Atom Abstraction from the Adenine−Uracil Base Pair[†]

Sunghwan Kim, Tyler Meehan, and Henry F. Schaefer, III*

Center for Computational Chemistry, University of Georgia, Athens, Georgia 30602

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The hydrogen-abstracted radicals from the adenine−uracil (AU) base pair have been studied at the B3LYP/DZP++ level of theory. The **A(N9)−U** and **A−U(N1)** radicals, which correspond to hydrogen-atom abstraction at the adenine N9 and uracil N1 atoms, respectively, were predicted to be the two lowest-lying among the nine (AU − H) radicals studied in this study. The removal of the amino hydrogen of the adenine moiety that forms a hydrogen bond with the uracil O4 atom in the AU pair resulted in radical **A(N6a)−U**, which has the smallest base-pair dissociation energy, 5.9 kcal mol^{-1}. This radical is more likely to dissociate into the two isolated bases than to recover the hydrogen bond with the O4 atom through N6−H bond rotation along the C6−N6 bond. In general, the radicals generated by C−H bond breaking were higher in energy than those arising from N−H bond cleavage, because the unpaired electrons in the carbon-centered radicals were mainly localized on the carbon atom from which the hydrogen atom was removed. However, the highest-lying radical was found to arise from removal of the N3 hydrogen of uracil. The most remarkable structural feature of this radical is a very short C−H···O distance of 2.094 Å, consistent with a substantial hydrogen bond. Although this radical lost the N1···H−N3 hydrogen bond between the two bases, its dissociation energy was predicted to be 12.9 kcal mol^{-1}, similar to that of the intact AU base pair. This is due to the transfer of electron density from the adenine N1 atom to the uracil N3 atom.

Introduction

High-energy radiation produces potentially lethal DNA lesions such as modified bases, abasic sites, and single- and double-strand breaks (SSBs and DSBs). The direct impact on DNA of ionizing radiation generates positive holes within the DNA strands through one-electron oxidation of the nucleic acid bases (NABs).[1−4] Because guanine has the lowest ionization potential among the NABs,[5−10] these positive holes migrate to guanine sites through the DNA strands.[11−14] Many experimental and theoretical studies have shown that the 5′-terminus of polyguanine (G_n) sequences in DNA acts as a very efficient trap for the positive holes.[15−29] The cationic guanine radical subsequently reacts with reactive oxygen species generated by radiolysis of water to form 8-oxo-7,8-dihydroguanine and other oxidation products.[30−33]

A substantial amount of DNA damage is also attributed to the formation and transport of negative charges within the DNA strands, which arise from attachment of low-energy electrons to NABs.[34−49] Such electrons, which have energies below 30 eV, are generated by the radiolysis of water.[50] In 2000, Sanche and co-workers demonstrated that such electrons can cause SSBs and DSBs even if their energies are lower than the ionization threshold (7.5 eV) of DNA.[34] Recent theoretical and experimental studies have suggested that electrons with energies even at or near 0 eV can result in DNA strand breaks.[35−38] In addition, as shown in the experimental studies of Bowen and co-workers using anion photoelectron spectroscopy,[39−43] electron attachment to the NABs can produce non-canonical tautomers through barrier-free proton transfer.

Along with positively and negatively charged species, various neutral radicals can also play an important role during the radiation-induced DNA damage process.[51−66] An example of this is the radicals arising from the homolytic C−H or N−H bond cleavage of the NABs.[51−61] Such radicals are generated either by direct abstraction of one hydrogen atom from the neutral NABs or by deprotonation of the oxidized (cationic) NABs.[57,59,60] For example, the radical generated by removal of a hydrogen atom from the methyl group of thymine is known to be readily oxidized to give modified nucleobases such as 5-(hydroxymethyl)uracil or 5-formyluracil. In addition, the recent studies of Greenberg and co-workers showed that this radical can also generate an interstrand cross-link in double-stranded DNA.[67−70]

Because hydrogen bonding between two NABs is a key ingredient to storing genetic information in living organisms, hydrogen abstraction from the nucleobases can cause a significant change in the hydrogen-bonding pattern of a base pair in double-stranded DNA, leading to crucial modifications in DNA. In the present research, we investigate the effect of hydrogen-atom abstraction from the adenine−uracil (AU) base pair (Figure 1). Although uracil is predominantly found in RNA, the AU base pair is also of great importance because of its structural similarity to the adenine−thymine base pair in DNA duplexes.

Computational Methods

All geometry optimizations and harmonic vibrational frequency analyses were performed using the Q-Chem 3.0 package of programs.[71] The equilibrium structures of the radicals generated by removal of one hydrogen atom from the Watson−Crick AU base pair (AU − H) were optimized with density functional theory. In particular, we used the B3LYP density functional, which is Becke's three-parameter exchange functional (B3),[72] in conjunction with the correlation functional of Lee, Yang, and Parr (LYP).[73] For numerical integrations, an

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* Corresponding author. E-mail: hfs@uga.edu.

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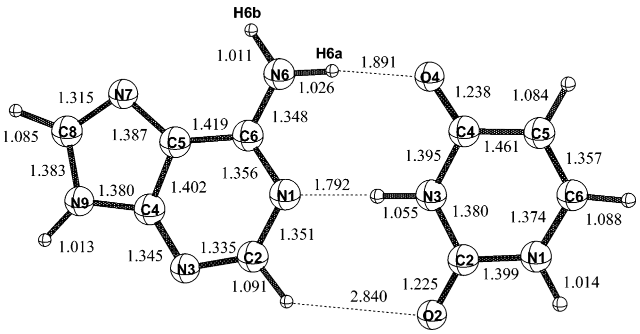


Figure 1. Optimized molecular geometry of the adenine−uracil (AU) base pair with atom numbering scheme.

Euler−Maclaurin−Lebedev (75,302) grid, having 75 radial shells and 302 angular points per shell, was employed.[74] We used double-ζ-quality basis sets with polarization and diffuse functions (DZP++). These were constructed by adding one set of p-type polarization functions for each H atom and one set of five d-type polarization functions for each C, N, and O atom [where $\alpha_p(H) = 0.75$, $\alpha_d(C) = 0.75$, $\alpha_d(N) = 0.80$, and $\alpha_d(O) = 0.85$] to the Huzinaga−Dunning (9s5p/4s2p) contractions.[75,76] Further augmentation with one even-tempered s diffuse function for each H atom and even-tempered s and p diffuse functions for each heavy atom completes the DZP++ basis set. The even-tempered orbital exponents were determined according to the formula[77]

$$\alpha_{\text{diffuse}} = \frac{1}{2}\left[\frac{\alpha_1}{\alpha_2} + \frac{\alpha_2}{\alpha_3}\right]\alpha_1$$

where α_1, α_2, and α_3 are the three smallest Gaussian orbital exponents of the s- or p-type primitive functions for a given atom ($\alpha_1 < \alpha_2 < \alpha_3$). The final DZP++ basis set contains six functions per H atom and 19 functions per C, N, or O atom. For the closed-shell AU base pair, this amounts to 396 contracted Gaussian basis functions.

The dissociation energy (DE), relaxation energy (RE), and X−H bond dissociation energy (BDE) for a given (AU − H) radical were evaluated according to the following definitions:

Dissociation Energy

$$\text{DE} = E[\text{A}-(\text{U}-\text{H})] - E(\text{A}) - E(\text{U}-\text{H})$$

or

$$\text{DE} = E[(\text{A}-\text{H})-\text{U}] - E(\text{A}-\text{H}) - E(\text{U})$$

Relaxation Energy

$$\text{RE} = E(\text{radical at optimized A}-\text{U geometry}) - E(\text{optimized radical})$$

or

X−H Bond Dissociation Energy

$$\text{BDE} = E[(\text{A}-\text{H})-\text{U}] + \text{E}(H) - E(\text{A}-\text{U})$$

$$\text{BDE} = E[\text{A}-(\text{U}-\text{H})] + E(\text{H}) - E(\text{A}-\text{U})$$

Results

The structures of the (AU − H) radicals optimized at the B3LYP/DZP++ level of theory are shown in Figures 2 and 3, and their relative energies, dissociation energies, and relaxation energies are listed in Table 1. Selected interatomic distances for the AU base pair and the (AU − H) radicals are compared in Table 2.

A. A(N9)−U and A−U(N1) Radicals. Radical **A(N9)−U**, which corresponds to removal of the hydrogen atom at the N9 position of the adenine unit in the AU base pair, was found to be the lowest-lying among the nine (AU − H) radicals examined in the present study. The second lowest-energy structure was radical **A−U(N1)**, generated by hydrogen abstraction from the N1 atom of the uracil base. The latter structure was predicted to lie 2.5 kcal mol^{-1} above **A(N9)−U**. Note that, in nucleosides, nucleotides, and DNA duplexes, the N9 atom of adenine and the N1 atom of uracil are covalently connected to the pentose sugar unit through an N-glycosidic linkage.

Although the N1···H−N3 hydrogen bond lengthens by 0.045 Å (from 1.792 to 1.837 Å) upon formation of **A(N9)−U** from the AU pair, the N6−H6a···O4 hydrogen bond shortens by 0.106 Å (from 1.891 to 1.785 Å). The increased interaction between the two base units in **A(N9)−U** is reflected in the dissociation energy of 13.7 kcal mol^{-1} for **A(N9)−U**, which is 1.0 kcal mol^{-1} greater than that predicted for the intact AU base pair (12.7 kcal mol^{-1}). On the other hand, hydrogen abstraction from atom N1 of the uracil moiety of the AU pair to generate **A−U(N1)** decreases its dissociation energy by 0.4 kcal mol^{-1} (from 12.7 to 12.3 kcal mol^{-1}). The elongation of the N6−H6a···O4 hydrogen bond by 0.061 Å (from 1.891 to 1.952 Å) is more pronounced than the shortening of the N1···H−N3 hydrogen bond by 0.014 Å (from 1.792 to 1.778 Å).

Because the N9−H bond of adenine and the N1−H bond of uracil are σ-type bonds, the homolytic cleavage of these bonds can be expected to give σ-type radicals, where the unpaired electron is mainly localized in the molecular plane. However, the spin density plots for the **A(N9)−U** and **A−U(N1)** radicals shown in Figure 4 suggest that the unpaired electrons are delocalized on the π-conjugated ring system. This delocalization of the unpaired electrons is a contributor to the energetic favoredness of **A(N9)−U** and **A−U(N1)**.

B. A(N6a)−U and A(N6b)−U Radicals. The next lowest-lying radicals were predicted to be **A(N6b)−U** and **A(N6a)−U**, generated by removing one of the hydrogen atoms of the adenine amino group. As shown in Figure 4, like **A(N9)−U** and **A−U(N1)**, these two radicals are also π-type radicals, in which the unpaired electrons are largely delocalized on the aromatic ring system. They are higher in energy than **A(N9)−U** by 7.5 and 11.5 kcal mol^{-1} for **A(N6b)−U** and **A(N6a)−U**, respectively. Although the H6b atom is not involved in the intermolecular hydrogen bonds between the two base units, abstraction of the H6b atom results in lengthening of the N1···H−N3 hydrogen bond by 0.052 Å, compared to that in the AU pair. The change is even more significant for the N6−H6a···O4 hydrogen bond, which is elongated by 0.244 Å. These geometrical changes in **A(N6b)−U** imply a weakening of the interaction between the two bases. Indeed, the dissociation energy for **A(N6b)−U** was predicted to be 8.9 kcal mol^{-1}, 3.8 kcal mol^{-1} smaller than that for the AU pair.

Formation of the **A(N6a)−U** radical results in loss of the N6−H6a···O4 hydrogen bond, which is reflected in the decreased dissociation energy of 5.9 kcal mol^{-1}. Interestingly, whereas the N1···H−N3 hydrogen-bond length increases by 0.260 Å, the C2−H···O2 contact becomes shorter by 0.573 Å. For the intact AU pair, the interatomic distance between the C2−H hydrogen atom of adenine and the O2 atom of uracil is predicted to be 2.840 Å, which is in the range of the sum of the van der Waals radii for oxygen and hydrogen atoms (2.70−

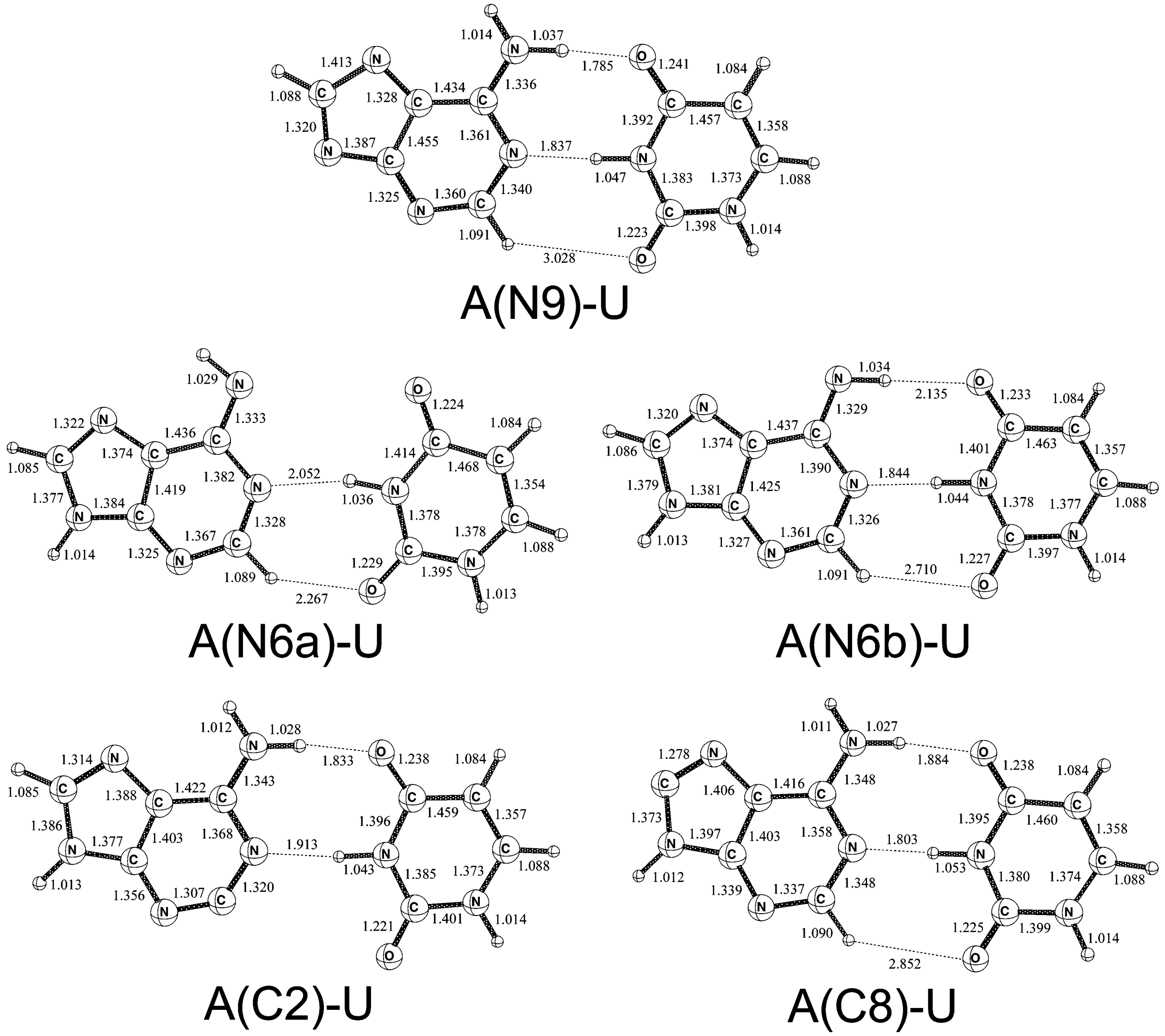


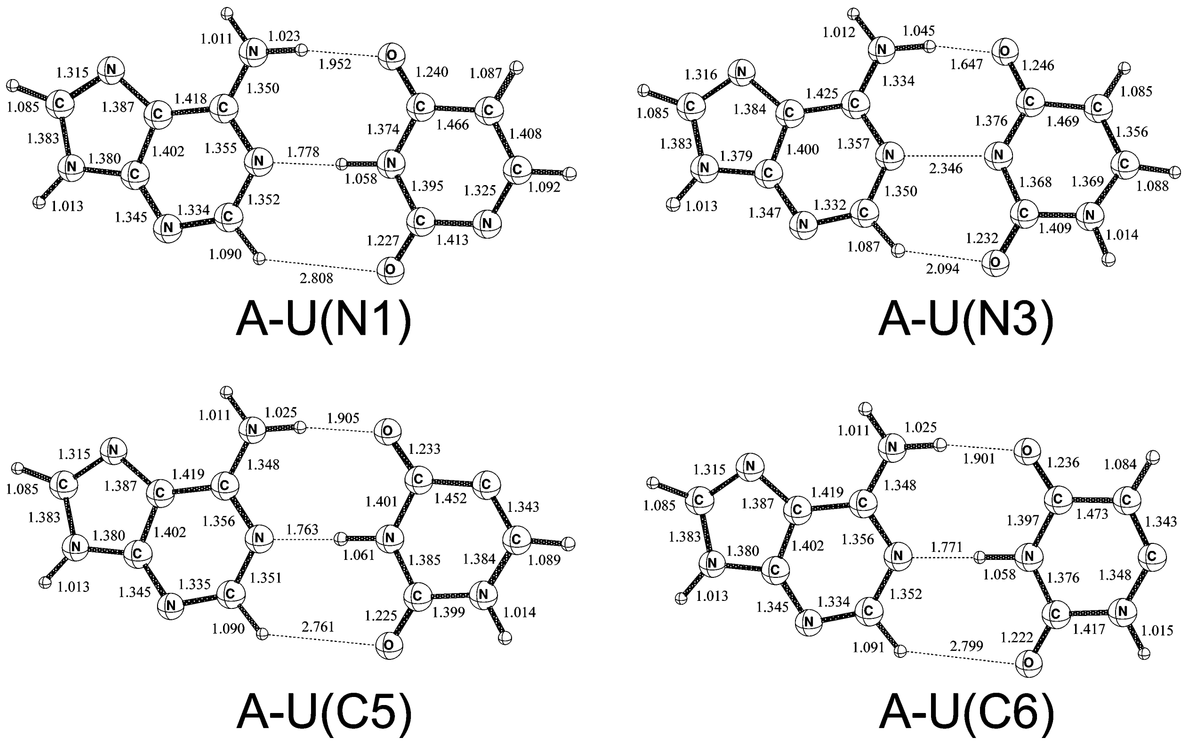
Figure 2. Optimized molecular structures of the radicals generated by hydrogen-atom abstraction from the adenine unit of the AU base pair.

2.95 Å).[78,79] Although the existence of C−H···O hydrogen bonding is disputable, it seems to be clear that such an interaction is much weaker than N−H···O or O−H···O hydrogen bonding. Thus, it would be difficult to induce a significant shortening of the C−H···O interatomic distance, as found in **A(N6a)−U**. Instead, we conclude that the significant change in the C2−H···O2 distance arises from the lone-pair repulsion between the N6 atom of adenine and the O4 atom of uracil. In the AU pair, the N6···O4 interatomic distance of 2.913 Å is slightly shorter than the sum of the van der Waals radii for oxygen and nitrogen atoms (3.05 Å).[78] Removal of the H6a atom of adenine causes repulsion between the lone pairs of the N6 and O4 atoms, and the N6···O4 distance for **A(N6a)−U** is predicted to increase to 3.961 Å.

Note that radicals **A(N6b)−U** and **A(N6a)−U** can be interconverted. That is, the loss of the N6−H6a···O4 hydrogen bond in **A(N6a)−U** radical can be recovered through rotation of the N6−H bond along the C6−N6 bond. Figure 5 compares the dissociation energies for the two radical conformers and the rotation barrier between them. The transition state between the two radicals (Figure 6) lies 11.0 kcal mol^{-1} above **A(N6b)−U**, and the rotational barrier from **A(N6a)−U** to **A(N6b)−U** is 7.0 kcal mol^{-1}. This is 1.1 kcal mol^{-1} higher than the dissociation energy of **A(N6a)−U**, implying that, if the **A-(N6a)−U** radical is generated by loss of the H6a hydrogen atom, the dissociation process into the two isolated bases will be slightly favored compared to conformational isomerism to **A-(N6b)−U**.

C. A(C2)−U, A(C8)−U, A−U(C5), and A−U(C6) Radicals. The radicals that arise from homolytic C−H bond breaking were predicted to be higher in energy than those from N−H homolytic bond cleavage [except for **A−U(N3)**]. This is because the breakage of a C−H bond results in σ-type radicals (as implied in Figure 4), in which the unpaired electrons are localized in the molecular plane. Hydrogen abstraction from the C2 atom of adenine gives radical **A(C2)−U**, which lies 12.6 kcal mol^{-1} above the global minimum. Because the C2−H···O2 interaction is expected to be weak, the loss of the C2−H···O2 contact will not cause a significant decrease in the dissociation energy compared to that of **A(N6a)−U**. Indeed, the predicted dissociation energy for **A(C2)−U** is only 1.7 kcal mol^{-1} smaller than that for the AU pair. Whereas the N6−H6a···O4 hydrogen-bond distance for **A(C2)−U** decreases by 0.058 Å (from 1.891 to 1.833 Å) compared to that for the AU pair, the N1···H−N3 distance increases by 0.121 Å (from 1.792 to 1.913 Å).

The hydrogen atoms at the C8 position of adenine and at the C5 and C6 positions of uracil are not involved in the hydrogen-bond network between the two bases. Thus, radicals generated by abstraction of these hydrogens are expected to have dissociation energies similar to that of the AU pair. Indeed, the



A-U(N1)

A-U(N3)

A-U(C5)

A-U(C6)

Figure 3. Optimized molecular structures of the radicals generated by hydrogen-atom abstraction from the uracil unit of the AU base pair.

TABLE 1: Relative Energies (E_{rel}), Dissociation Energies (DE), and Relaxation Energies (RE) (kcal mol^{-1}) of the (AU − H) Radicals Generated by Hydrogen-Atom Abstraction from the Adenine−Uracil Pair[a]

	E_{rel}	DE[b]	RE[c]
AU		13.8 (12.7)	
A(N9)−U	0.0 (0.0)	15.0 (13.7)	12.8
A−U(N1)	3.2 (2.5)	13.4 (12.3)	4.8
A(N6b)−U	7.9 (7.5)	9.8 (8.9)	4.4
A(N6a)−U	12.2 (11.5)	6.5 (5.9)	8.3
A(C2)−U	12.3 (12.6)	12.3 (11.0)	2.3
A−U(C6)	15.0 (14.8)	14.2 (13.1)	1.6
A(C8)−U	18.3 (18.6)	13.8 (12.6)	1.3
A−U(C5)	21.4 (21.6)	14.1 (13.0)	1.3
A−U(N3)	22.4 (22.3)	15.4 (12.9)	8.3

[a] ZPVE-corrected values in parentheses. [b] Dissociation energies are for fragmentation to either $(\mathrm{A}-\mathrm{H})^{\bullet} + \mathrm{U}$ or $\mathrm{A} + (\mathrm{U}-\mathrm{H})^{\bullet}$, depending on the radical site. [c] Each relaxation energy is the radical energy lowering found in going from the optimized closed-shell AU structure to the equilibrium geometry of the specified radical.

TABLE 2: Selected Interatomic Distances (Å) for the A−U Base Pair and Its Hydrogen-Abstracted Radicals

	A(N6−H6a)··· U(O4)	A(N1)··· U(H−N3)	A(C2−H)··· U(O2)
A−U	1.891	1.792	2.840
A(N9)−U	1.785	1.837	3.028
A−U(N1)	1.952	1.778	2.808
A(N6b)−U	2.135	1.844	2.710
A(N6a)−U	NA	2.052	2.267
A(C2)−U	1.833	1.913	NA
A−U(C6)	1.901	1.771	2.799
A(C8)−U	1.884	1.803	2.852
A−U(C5)	1.905	1.763	2.761
A−U(N3)	1.647	NA	2.094

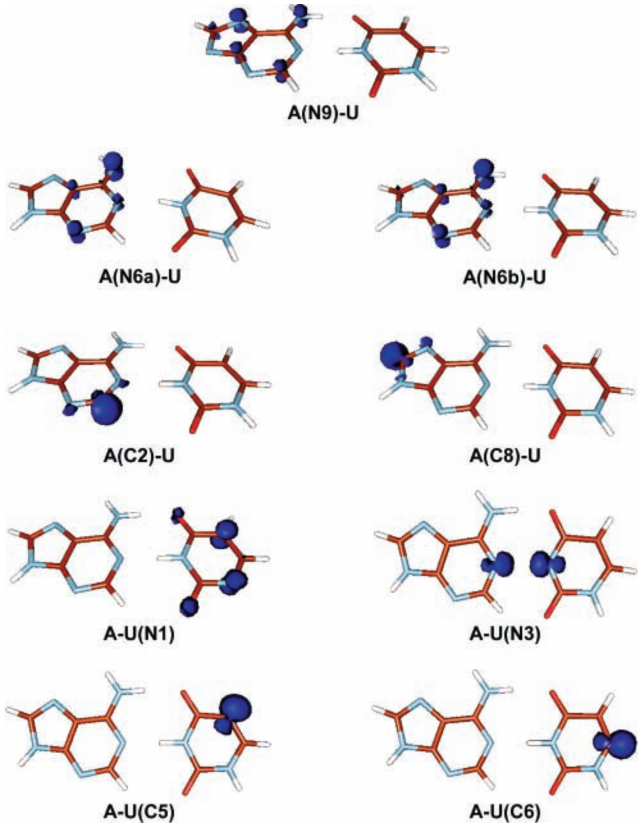


Figure 4. Spin density plots for the radicals generated by hydrogen abstraction from the AU base pair.

predicted dissociation energies were 12.6, 13.0, and 13.1 kcal mol^{-1} for **A(C8)−U**, **A−U(C5)**, and **A−U(C6)**, respectively. For the same reason, the N6−H6a···O4 and N1···H−N3 hydrogen-bond lengths predicted for the three radicals do not differ very much from those of the intact AU pair. The largest difference was predicted for **A−U(C5)**, where the N6−H6a···O4 hydrogen bond is 0.014 Å longer and the N1···H−N3 hydrogen bond is 0.029 Å shorter than the corresponding bonds of the AU pair.

D. A−U(N3) Radical. The removal of the N3−H hydrogen atom from the uracil part of the AU base pair might be expected to weaken the binding of the base pair because of the loss of

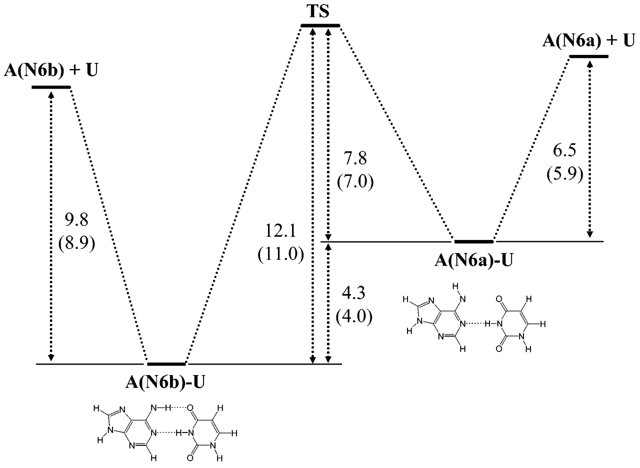


Figure 5. Schematic energy diagram for the dissociation of base-pair radicals **A(N6a)−U** and **A(N6b)−U** and the rotational barrier connecting them (ZPVE-corrected values in parentheses).

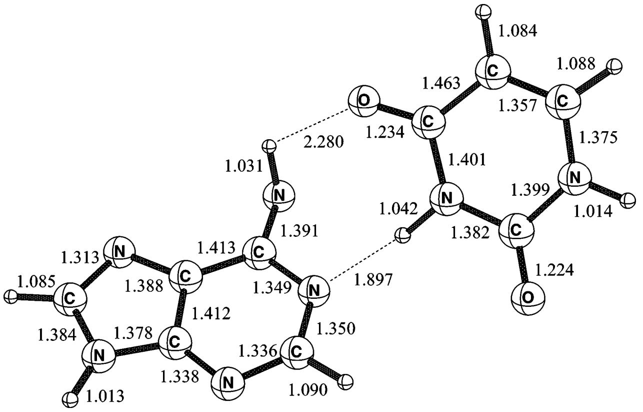


Figure 6. Transition structure between radicals **A(N6a)−U** and **A-(N6b)−U**.

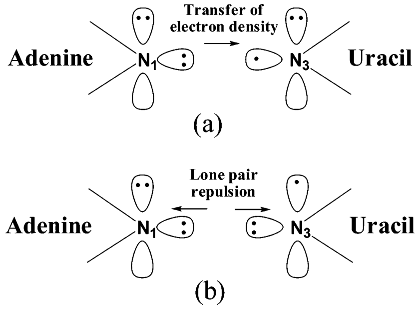


Figure 7. Two possible orientations of the unpaired electron in the **A−U(N3)** radical.

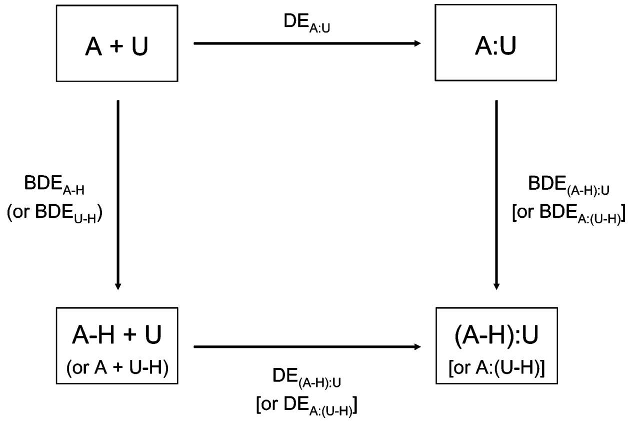


Figure 8. Two possible pathways to generating hydrogen-abstracted radicals from the isolated adenine and uracil bases.

the N1···H−N3 hydrogen bond. Surprisingly, however, the dissociation energy of 12.9 kcal mol^{-1} for the resulting radical, **A−U(N3)**, is very similar to that of the AU base pair. The N6−H6a···O hydrogen-bond length becomes shorter by 0.244 Å upon the removal of the H3 atom. In addition, the C2−H···O2 contact becomes even shorter, by 0.746 Å (from 2.840 to 2.094 Å). Because of this significant decrease in the C2−H···O2 interatomic distance, one might think that the enhanced interaction between the C2−H and O2 atoms would be the main stabilizing factor responsible for the large DE value for **A−U-(N3)**. However, note that, if we assume that the lost N3···H1−N1 hydrogen bond destabilizes the system by $\sim$5 kcal mol^{-1}, there must be a stabilizing factor that can lower the energy of **A−U(N3)** by $\sim$5 kcal mol^{-1}. The increase in the C2−H···O2 interaction does not seem to be able to provide this amount of energy because C−H···O hydrogen bonding is normally thought to be much weaker than other strong hydrogen bonding such as O−H···O or N−H···O hydrogen bonding. For example, in the recent study of Quinn, Zimmerman, Del Bene, and Shavitt,[80] the stability due to the C−H···O contact in the adenine−thymine base pair was estimated to be 2−2.5 kcal mol^{-1}. This amount of stabilization does not appear large enough to compensate for the loss of the N3···H−N1 hydrogen bond in the AU pair.

The key to understanding the unexpectedly large dissociation energy of the **A−U(N3)** radical is suggested by its spin density plot (Figure 4). The unpaired electron of the **A−U(N3)** radical is located between the N1 atom of adenine and the N3 atom of uracil in the molecular plane. Figure 4 indicates that the system is stabilized by transfer of electron density from the lone-pair orbital associated with the adenine N1 atom to the (half-filled) singly occupied molecular orbital (SOMO) of the N3 atom of uracil. This effect is depicted schematically in Figure 7, along with the contrasting situation, where the SOMO is perpendicular to the molecular plane. If the **A−U(N3)** radical were a π radical, where the unpaired electron is perpendicular to the molecular plane and delocalized through the uracil ring system, the system would be destabilized by lone-pair repulsion between the N1 atom of adenine and the N3 atom of uracil, and the dissociation energy would decrease. An example of this opposite case is radical **A(N6a)−U**. For this radical, the unpaired π electron is delocalized on the purine ring, and the repulsive potential occurs between the σ-type lone pairs of the adenine N6 and uracil O4 atoms. This is why **A−U(N3)** has a dissociation energy similar to that of the AU pair, whereas the removal of the adenine H6a atom decreases the dissociation energy significantly.

Discussion

The hydrogen-abstracted radicals of the AU base pair have been investigated at the B3LYP/DZP++ level of theory. The two lowest-energy structures are radicals **A(N9)−U** and **A−U-(N1)**, which correspond to hydrogen abstraction at the N9 atom of adenine and the N1 atom of uracil, respectively. However, because these nitrogen atoms are covalently bonded to the ribose moiety in nucleosides and nucleotides, the next lowest-energy structures, **A(N6b)−U** and **A(N6a)−U**, generated by removing one of the amino hydrogen atoms of the adenine moiety, should be more important in biological systems. The abstraction of the H6a atom from adenine causes a loss of the N6−H6a···O4 hydrogen bond, and the resulting **A(N6a)−U** radical has the smallest dissociation energy, 5.9 kcal mol^{-1}, suggesting that it could be a potential lesion in a DNA/RNA strand. The N1···H−N3 hydrogen bond in **A(N6a)−U** can be recovered through rotation of the N6−H6b group along the C6−N6 bond.

TABLE 3: Relative Energies (E_{rel}, kcal mol^{-1}) of the Isolated (A − H) and (U − H) Radicals

radical	E_{rel}	radical	E_{rel}
A(N9)	0.0 (0.0)	**U(N1)**	0.0 (0.0)
A(N6b)	2.7 (2.7)	**U(C6)**	12.6 (13.0)
A(N6a)	3.7 (3.7)	**U(C5)**	18.9 (19.7)
A(C2)	9.6 (9.9)	**U(N3)**	21.2 (20.3)
A(C8)	17.1 (17.5)		

However, the rotational barrier of 7.0 kcal mol^{-1} for this process is higher than the dissociation energy of the **A(N6a)−U** radical, implying that the latter is more likely to dissociate than to convert to **A(N6b)−U**.

Except for the highest-energy radical, **A−U(N3)**, the unpaired electrons of the radicals generated through homolytic N−H bond cleavage are found to be delocalized on the π system of the ring structure. On the contrary, for the radicals generated by C−H homolytic bond breaking, the unpaired electrons are localized at the corresponding carbon atom and have primarily σ character. Because of this, the carbon-centered radicals are generally predicted to lie above the nitrogen-centered radicals. The only exception is radical **A−U(N3)**. Although removal of the N3−H hydrogen atom of uracil causes a loss of the N1···H−N3 hydrogen bond, the resulting radical, **A−U(N3)**, can be stabilized by electron density transfer to the half-filled orbital on N3 atom of uracil because the radical center is located on the molecular plane. Because of this effect, the **A−U(N3)** radical has a dissociation energy similar to that of the intact AU pair, even though it is the highest-lying radical.

The relaxation energy of a given radical is a measure of the effect of hydrogen abstraction on the geometrical change. For example, the radicals in which the unpaired electrons are delocalized [e.g., the four lowest-lying (AU − H) radicals] showed large relaxation energies (4−13 kcal mol^{-1}, as listed in Table 1), implying that their geometries are quite different from the geometry of the AU base pair. On the contrary, if the unpaired electrons are localized at the atom from which the hydrogen atom is removed (e.g., all carbon-centered radicals), such radicals have only small relaxation energies of about 1−2 kcal mol^{-1}. The **A−U(N3)** radical shows a relatively large relaxation energy because of the electron density transfer from the uracil N3 atom to the adenine N1 atom.

The relative energies for the hydrogen-abstracted radicals of isolated adenine and uracil [(A − H) and (U − H)] are summarized in Table 3. Previous studies[81] on hydrogen-abstracted radicals of adenine (A − H) predicted the energetic ordering of **A(N9)** < **A(N6b)** < **A(N6a)** < **A(C2)** < **A(C8)**. The energetic ordering for the hydrogen-abstracted radicals of uracil (U − H) predicted in the present study is **U(N1)** < < **U(C6)** < **U(C5)** < **U(N3)**. These two sets of energetic orderings are maintained in the energetic orderings for the base-pair (AU − H) radicals.

Figure 8 depicts two possible pathways to the formation of (AU − H) radicals from adenine and uracil bases. From Figure 8, an important relation between BDE and DE can be derived

$$\mathrm{BDE}_{\mathrm{A-H}} + \mathrm{DE}_{[(\mathrm{A-H})\mathrm{U}]} = \mathrm{BDE}_{[(\mathrm{A-H})\mathrm{U}]} + \mathrm{DE}_{\mathrm{AU}}$$

$$\mathrm{BDE}_{[(\mathrm{A-H})\mathrm{U}]} - \mathrm{BDE}_{\mathrm{A-H}} = \mathrm{DE}_{[(\mathrm{A-H})\mathrm{U}]} - \mathrm{DE}_{\mathrm{AU}}$$

Similarly

$$\mathrm{BDE}_{[\mathrm{A(U-H)}]} - \mathrm{BDE}_{\mathrm{U-H}} = \mathrm{DE}_{[\mathrm{A(U-H)}]} - \mathrm{DE}_{\mathrm{AU}}$$

TABLE 4: X−H Bond Dissociation Energies (BDE) in eV for Adenine, Uracil, and A−U Base Pair. Each Entry Is Labeled by the Name of the Particular Radical Resulting from Hydrogen-atom Removal

base radical	BDE	base-pair radical	BDE
A(N9)	4.50 (4.12)	**A(N9)−U**	4.44 (4.08)
U(N1)	4.57 (4.17)	**A−U(N1)**	4.58 (4.19)
A(N6b)	4.61 (4.24)	**A(N6b)−U**	4.79 (4.40)
A(N6a)	4.66 (4.28)	**A(N6a)−U**	4.97 (4.58)
A(C2)	4.91 (4.55)	**A(C2)−U**	4.98 (4.62)
U(C6)	5.11 (4.74)	**A−U(C6)**	5.09 (4.72)
A(C8)	5.24 (4.88)	**A(C8)−U**	5.24 (4.88)
U(C5)	5.39 (5.03)	**A−U(C5)**	5.37 (5.01)
U(N3)	5.49 (5.05)	**A−U(N3)**	5.42 (5.04)

The above equations imply that the BDE for a specific (AU − H) radical can be deduced from the difference in DE between the radical and the AU base pair. For example, the decrease in DE by 1.0 kcal mol^{-1} for **A(N9)−U** (compared to the AU pair) results in an increase in BDE of 1.0 kcal mol^{-1} (0.043 eV). As listed in Table 4, the BDEs of (A − H) and (U − H) radicals are typically greater than at least 4.12 eV (equivalent to 95 kcal mol^{-1}), whereas the greatest change in DE upon hydrogen abstraction from the AU base pair is predicted to be 6.8 kcal mol^{-1} (~0.3 eV). That is, because of the nature of the hydrogen bonding that is responsible for base pairing, the changes in DE values for the (AU − H) radicals are very small compared to their BDE values. This implies that the energetics of the radicals can be predicted from those for the (A − H) and (U − H) radicals.

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Supporting Information Available: Cartesian coordinates of the optimized geometries for the AU base pair and its hydrogen-abstracted radicals. This material is available free of charge via the Internet at http://pubs.acs.org.

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