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ORIGINAL PAPER

Photoinduced conformational transformation of the hydroxy form of uridine and deoxyuridine and hydrogen detachment in oxo and hydroxy tautomers of the compounds: a computational study

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Abstract In this research we studied the mechanisms of photoinduced conformational transformation of hydroxy forms of (deoxy)uridine, which have been found to be accessible in aqueous solution. The mechanisms were compared with those for the oxo forms of (deoxy)uridine studied recently. The mechanisms of photoinduced proton detachment in oxo and hydroxy forms of (deoxy)uridine were also studied. These mechanisms are driven by the repulsive $^1\pi\sigma^*$ state.

Keywords Charge transfer · Density functional theory · Hydrogen transfer · Nucleosides · Photochemistry

Introduction

The nucleosides uridine and deoxyuridine are important compounds since they are parts of the structures of RNA and DNA [1]. It is known that DNA/RNA absorbs light at about 260 nm and in this respect it is a primary chromophore in living organisms. The absorption spectrum of DNA is a result of the electron excitations in the nitrogen bases adenine, cytosine, uracil, guanine, and thymine [2–11]. These structural units utilize the UV light relaxing (radiationlessly) to the ground state. This process prevents living organisms from the consequences of the damaging impact of the UV rays [7–10, 12]. Therefore, knowledge of the mechanism of internal conversion of the excited bases would help to clarify the consequences for organisms irradiated with UV light.

By studying the UV spectrum of uridine Miles et al. [13] showed that the major UV absorption maximum of the compound in solution is at 4.77 eV. In our previous theoretical analysis of nucleosides of uracil we assigned this maximum to the hydroxy form of uridine, which should be more stable than the oxo form in aqueous solution [14]. We believe that the same behavior is applicable to deoxyuridine as well. However, in this study we studied only the conformations of oxouridine and deoxouridine nucleosides with respect to their mutual photoconformational transformations. The purpose of the current research is: (1) to investigate the mechanism of conformational transformation of the hydroxy form of uridine/deoxyuridine, (2) to clarify the oxo–hydroxy phototautomerism via the repulsive $^1\pi\sigma^*$ state. In this respect, the present research can be viewed as a continuation of the previous research [14].

Results and discussion

The stability of the uracil tautomers and (deoxy)uridine tautomers/conformers was discussed in our previous paper [14]. All studied tautomers/conformers of (deoxy)uridine are depicted in Scheme 1 (we have kept the same nomenclature for the compounds as in Ref. [14]).

The calculations have predicted lowest energies for compounds **U2/D2**, where the carbonyl groups of the uracil residue are orientated in an opposite direction with respect to the (deoxy)ribose ring. The hydroxy analogues of these compounds **U4/D4** have moderate stability with respect to their energies. However, as mentioned above, they are present in water at neutral pH [13].

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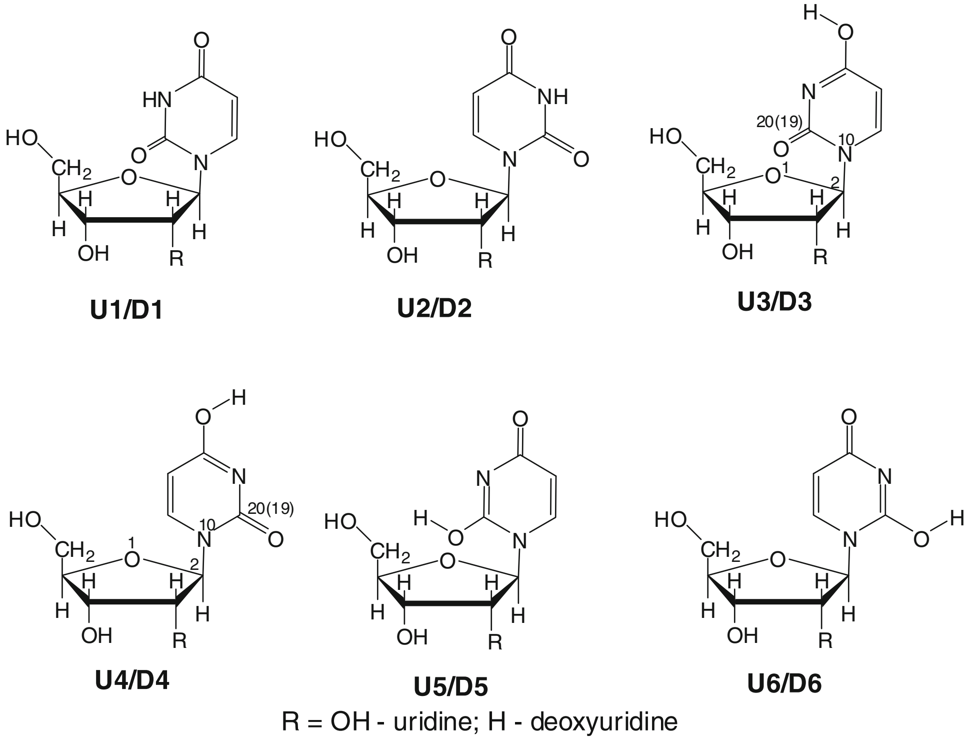
Scheme 1



Conformational transformations of hydroxy (deoxy)uridine

In this research we studied the mechanisms of phototransformations **U3**(**D3**) ⇄ **U4**(**D4**). The energy profiles are illustrated in Fig. 1.

For this study we used the optimized structures of **U4/D4** (as these are more stable than **U3/D3**) and the angles $C_{20}N_{10}C_2O_1/C_{19}N_{10}C_2O_1$ as reaction coordinates. The energy barrier of the thermal conformational transformation **U3** → **U4** (1.86 eV or 179 kJ mol^{-1}) is higher than that of **U1** → **U2** (1.63 eV or 157 kJ mol^{-1}) [14]. For deoxyuridine these energy barriers are 1.83 eV (177 kJ mol^{-1}) and 1.29 eV (124 kJ mol^{-1}). These energy barriers are high enough to hinder the thermal conformational transformations; however, as seen in Fig. 1, the transformations can occur easily via excited electronic states with minor or no energy barriers. **U3** can transform to **U4** via the spectroscopically relevant $^1\pi\pi^*$ state and the charge transfer $^1\sigma\pi^{*(CT)}$ state (Fig. 1a). For the transformation **U1** → **U2** these states are $^1\pi\pi^*$ and the charge transfer state $^1n\pi^{*(CT)}$ [14]. Furthermore, the energy barriers in the first case are insignificant and predispose the faster and easier transformation of **U3** into **U4** than the transformation **U1** → **U2**. In other words, the conformation of uridine occurs preferably in hydroxy form. It should be mentioned that the excitation energy of the $^1\pi\pi^*$ state is lower in the hydroxy form **U3** than the oxouridine **U1** [14]. Another difference is the crossing of the lower $^1n\pi^*$ states with the other states included in the conformational PESs. For example, the $^1n\pi^*$ state of **U3** switches to the $^1\pi\pi^*$ state over the energy minimum of **U3**, via $^1n\pi^{*(CT)}/^1\pi\pi^*$ conical intersection. For **U1** [14] this switch is mediated by the conical intersection $^1n\pi^*/^1n\pi^{*(CT)}$ which occurs at larger values of the reaction coordinates. Because of the nature of the uracil tautomers in **U4** and **U2**, the $^1\pi\pi^*$ state in **U4** is lower than the $^1n\pi^*$ state.

With regard to the transformation **D3** → **D4** (Fig. 1b), one can say that this phototransformation occurs more easily than the phototransformation **D1** → **D2** [14], because of the same reasons as for uridine. The $^1\pi\pi^*$ state of **D3** switches to $^1\sigma\pi^{*(CT)}$ state via conical intersection $^1\pi\pi^*/^1\sigma\pi^{*(CT)}$, which has lower energy than the same conical intersection of the **D1** → **D2** transformation [14].

For **U3** and **D3** the lowest potential energy curve is for the $^1\pi\pi^*$ state followed by the $^1n\pi^{*(CT)}$ state. The dark $^1n\pi^*$ state has higher energy and it can drastically facilitate the conformational transformations to **U4** and **D4**, respectively. The origin of the charge transfer states was discussed in detail in Ref. [14].

Phototautomerism via the repulsive $^1\pi\sigma^*$ states

The oxo–hydroxy tautomerism in uracil most usually occurs through the photoinduced dissociation−association (PIDA) mechanism [15, 16] including photoinduced dissociation (detachment) of the proton of the oxo form and a subsequent association (attachment) to one of the oxygens

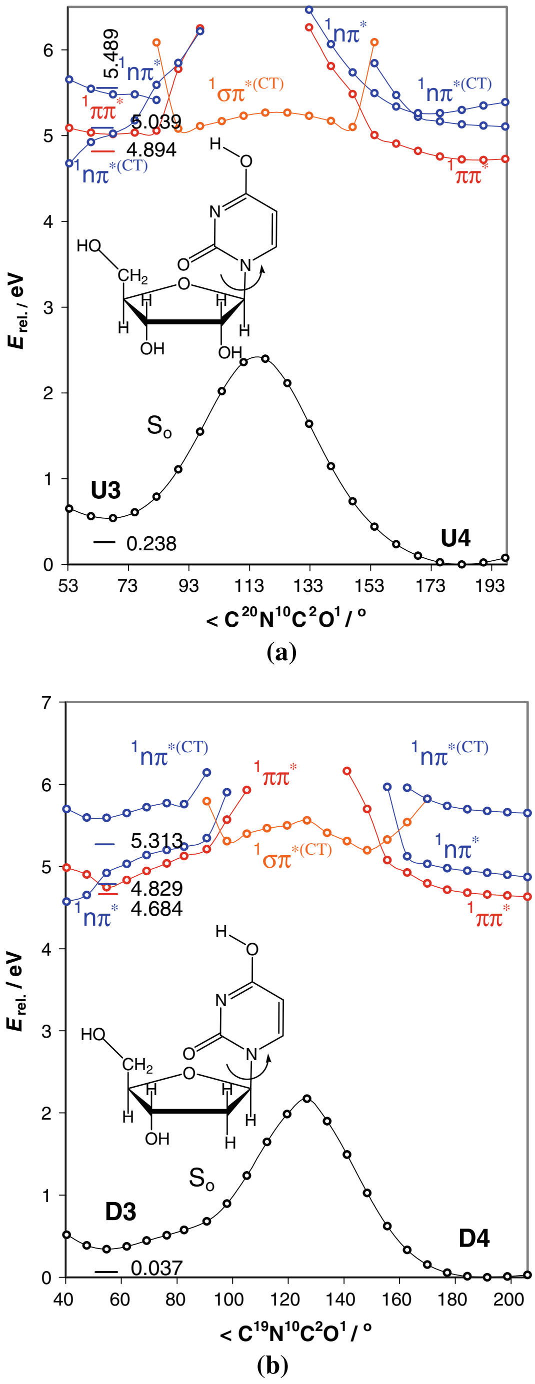


Fig. 1 Conformational potential energy surfaces (PESs) of the ground and excited states of hydroxy **a** uridine and **b** deoxyuridine. The *dashes* designate the vertical excitation energies of the states of **U3** and **D3**

forming the hydroxy form. We studied these mechanisms for the oxo (deoxy)uridine and the hydroxy forms **U4** and **D4** (Figs. 2 and 3).

The energy profiles of the electronic states of the dissociation process of the hydroxy(deoxy)uridine are shown in Fig. 2. As seen, the OH dissociation occurs via the

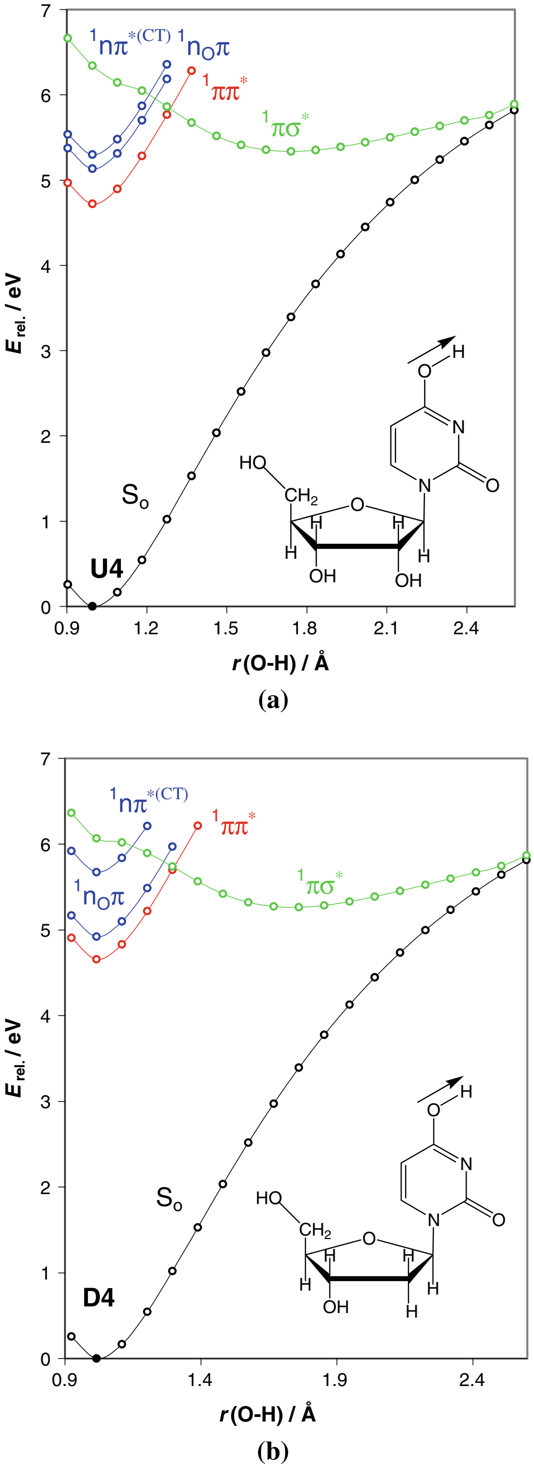
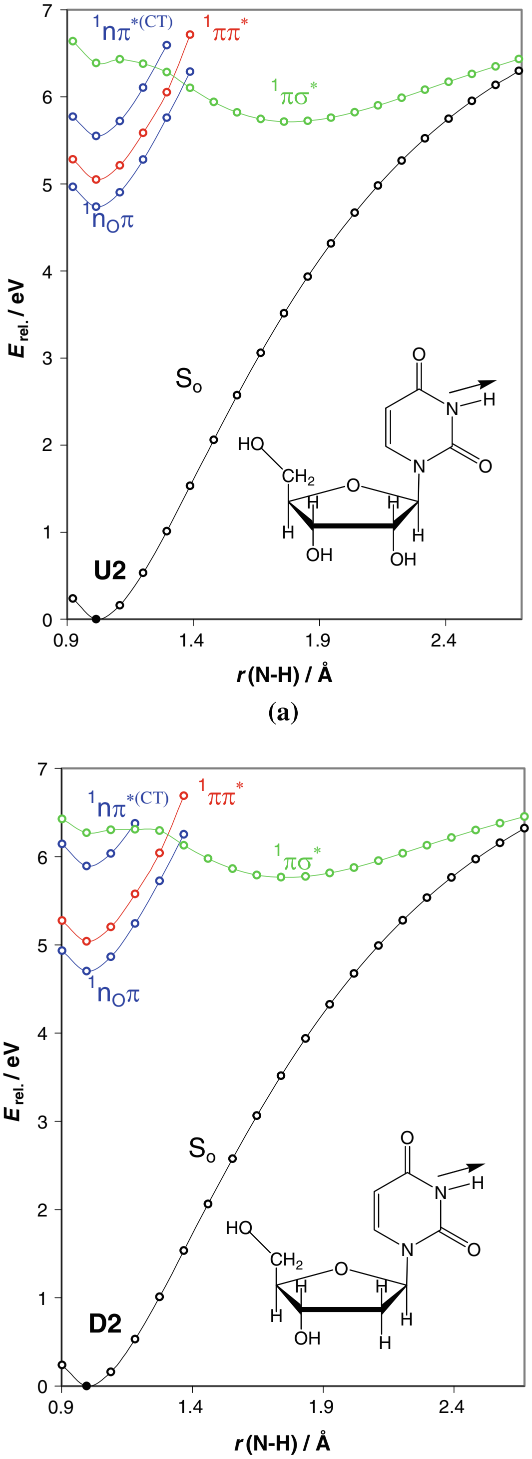


Fig. 2 PESs of the OH dissociation processes of the stable forms of hydroxy **a** uridine (**U4**) and **b** deoxyuridine (**D4**)

repulsive $^1\pi\sigma^*$ state. Three conical intersections are available between the $^1\pi\sigma^*$ state curve and the curves of the $^1\pi\pi^*$, $^1n_O\pi^*$, and $^1n\pi^{*(CT)}$ states. The $^1\pi\sigma^*$ state curves of uridine and deoxyuridine have shallow minima at about 1.6 Å. At larger values of the OH distances the energy of



(a)

(b)

Fig. 3 PESs of the NH dissociation processes of the oxo forms of **a** uridine (**U2**) and **b** deoxyuridine (**D2**)

the $^1\pi\sigma^*$ state increases slightly to the conical intersections between this states and S_0 curves. As seen, the $^1n\pi^{*(CT)}$ state curve of hydroxyuridine is closer to the curves of $^1\pi\pi^*$ and $^1n_0\pi^*$ states than in the case for deoxyuridine. In the latter, the $^1n_0\pi^*$ state curve is very close to the $^1\pi\sigma^*$ state in the Franck–Condon region, which means that the switch $^1n\pi^{*(CT)}/^1\pi\sigma^*$ occurs with a lower energy barrier than the same switch in hydroxyuridine. The $^1\pi\sigma^*$ states of **U4** and **D4** are dark states and they can be populated via internal conversions $^1\pi\pi^*/^1\pi\sigma^*$ with a low probability and energy barriers of about 1 and 2 eV (as seen the thermal barriers are about 6 eV), respectively.

The energy curves of NH dissociation processes in uridine and deoxyuridine are similar to the OH dissociation curves. As seen, the curves of the $^1n_0\pi^*$ states are lower than the $^1\pi\pi^*$ state curves. Usually the NH dissociation of uracil (or xanthine) occurs via the repulsive $^1\pi\sigma^*$ state but with a σ^*–MO that is on the N^{10}–H bond [17], which is not available in (deoxy)uridine because of structural reasons.

Conclusion

This theoretical study showed the photoinduced conformational transformations **U3**(**D3**) ⇄ **U4**(**D4**) of the hydroxy forms of (deoxy)uridine occur more easily than the conformational transformations **U1**(**D1**) ⇄ **U2**(**D2**) with the oxo tautomers of (deoxy)uridine [14]. Both mechanisms include reaction paths passing through charge transfer states ($^1\sigma\pi^{*(CT)}$) and several conical intersections between excited electronic states. The thermal conformations are forbidden because of the high energy barriers on the reaction paths.

The study of the OH and NH dissociation mechanisms shows that the hydroxy–oxo tautomerism is much more favorable in excited state than in ground state (thermal tautomerism). This mechanism includes internal conversion via the repulsive $^1\pi\sigma^*$ state and the conical intersection $^1\pi\sigma^*/S_0$. Because of the nature of the $^1\pi\sigma^*$ state (a dark state) the population of this state for oxo or hydroxy tautomers of (deoxy)uridine can be achieved through internal conversion $^1\pi\pi^*/^1\pi\sigma^*$ passing through an energy barrier. This process requires relaxation time to occur which means that the oxo–hydroxy tautomerism in this case would not occur as an ultrafast reaction.

Methods

The structures of the stable conformers of the oxo and hydroxy forms of (deoxy)uridine were optimized with the hybrid functional B3LYP [18–20] and 6-31+G(d) basis functions. Subsequent frequency calculations were performed to prove that the found geometries correspond to energy minima (no imaginary frequencies). The stable forms of the oxo and hydroxy tautomers were used to study the conformers which were generated by rotation around the ^{ribose}C–N^{uracil} bond (or the corresponding dihedral angle). The excitation energies of the conformers were calculated at the time-dependent density functional theory (TD DFT) level with the 6-31+G(d) basis set. The OH and NH proton detachment mechanisms were studied at the same level. The points along the reaction coordinates were generated with the geometries of the stable hydroxy and oxo tautomers of (deoxy)uridine by changing the distance O···H in the hydroxy tautomers and N···H in the oxo tautomers. The calculations were performed with the Gaussian 03 [21] program package with no symmetry restrictions.

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