PHOTOSTABILITY OF THE GUANINE-CYTOSINE BASE PAIR WITH RESPECT TO THE OUT-OF-PLANE H-TRANSFER: A CC2 LEVEL STUDY

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Abstract - We performed a theoretical study of the out-of-plane excited-state intermolecular proton transfer between the nucleic acid bases guanine (G) and cytosine (C) in the Watson-Crick model. The level of computation is CC2/aug-cc-pVDZ. The mechanism of the process was followed by using the Linear interpolation in internal coordinates approach. For this purpose we optimized the ground-state equilibrium geometry of the Watson-Crick G-C base pair and the conical intersection S_0/S_1 of the out-of-plane H-transfer at the CASSCF(6,6)/6-31G level of theory. The results showed an energy barrier along the $^1\pi\sigma^*$ excited-state reaction path of the mechanism which hinders the proton transfer process. This fact is in support of the photostability of the base pair.

RUNNING TITLE: OUT-OF-PLANE PROTON TRANSFER IN GUANINE-CYTOSINE

Keywords - Coupled-cluster calculations; Cytosine; Excited states; Guanine; Photostability; Proton transfer.

I. INTRODUCTION

Guanine (G) and cytosine (C) are major building blocks of the macromolecule of DNA. According to the Watson-Crick model they pair together through H-bonds and form a base pair (G-C) with important function for the encoding and storage of the genetic information in living world [1].

Guanine is a purine DNA base while C is pyrimidine derivative, both with carbonyl and amino groups. For the prevention of the normal functioning of organisms the two bases should be photostable. Concerning the photostability of guanine a lot of theoretical papers have been proposed [2-9].

For a single G molecule the research of Mishra et al [9] has shown that the keto N_9H, keto N_7H and enol N_9H forms of guanine contribute to the absorption spectra of the compound. The theoretical study of Sobolewski et al [10] has shown that the biologically relevant N_9H keto form relaxes to the ground state through a conical intersection S_0/S_1 through an out-of-plane deformation of the aromatic ring along the $^1\pi\pi^*$ excited-state reaction path. This tautomer has shown a low energy barrier along the $^1\pi\sigma^*$ state of the NH dissociation process [10].

The excited state relaxation dynamics of C has been also studied intensively [11-14]. The relaxation of C to the ground state also occurs along the $^1\pi\pi^*$ excited-state reaction path with the out-of-plane deformation of the aromatic ring [14,15].

The high photostability of these two bases may help to understand why the nature has chosen exactly these compounds for the prevention of the genetic code [4,5].

The aim of the research is to explain, at the CC2 level, the high photostability of the G-C base pair with respect to the out-of-plane mechanism of the H-transfer between the two nucleobases.

II. THEORETICAL AND EXPERIMENTAL METHODS

The ground- and excited-state equilibrium geometries of two base pairs G-C were fully optimized at the CC2/aug-cc-pVDZ theoretical level. At the same level we optimized also the excited state structure which is included in the H-transfer process. The CC2 method is known to be a simplified variant of coupled-cluster theory including single and double excitations of the reference structure [16,17].

At the same theoretical level we calculated the vertical excitation energies and the emission energies of the systems. The vertical excitation energies are compared with the experimental absorption maxima of the water solution of the equmolar mixture of the two bases. The concentration of the two bases in the mixture is: 1.26×10^{-4} mol.L^{-1} (for C) and 1.32×10^{-4} mol.L^{-1} (for G). The CC2 calculations were performed with the Turbomole 7.6 package [18,19].
The conical intersection S_0/S_1 geometry and the ground-state equilibrium geometry of one of the minima were also optimized at the CASSCF(6,6)/6-31G theoretical level with the GAUSSIAN 16 program package [20]. The structures were used for linear interpolation in internal coordinates as described in our recent paper [14].

The UV spectra were recorded on an Agilent Cary 60UV/Vis spectrophotometer, double beam, and a spectral range of 190 – 1100 nm.

III. RESULTS AND DISCUSSION

Ground- and excited-state equilibrium geometries

The ground- and excited state equilibrium geometries are presented in Fig. 1. As seen the ground state GC base pair has three short / strong intermolecular H-bonds, one of them extremely short – between the guanine carbonyl group and the cytosine amino group. The $^1\pi\sigma^*$ excited state of the tautomer (it is the second excited state) is also planar and shows three inrtermolecular H-bonds which could be determined as short ones.

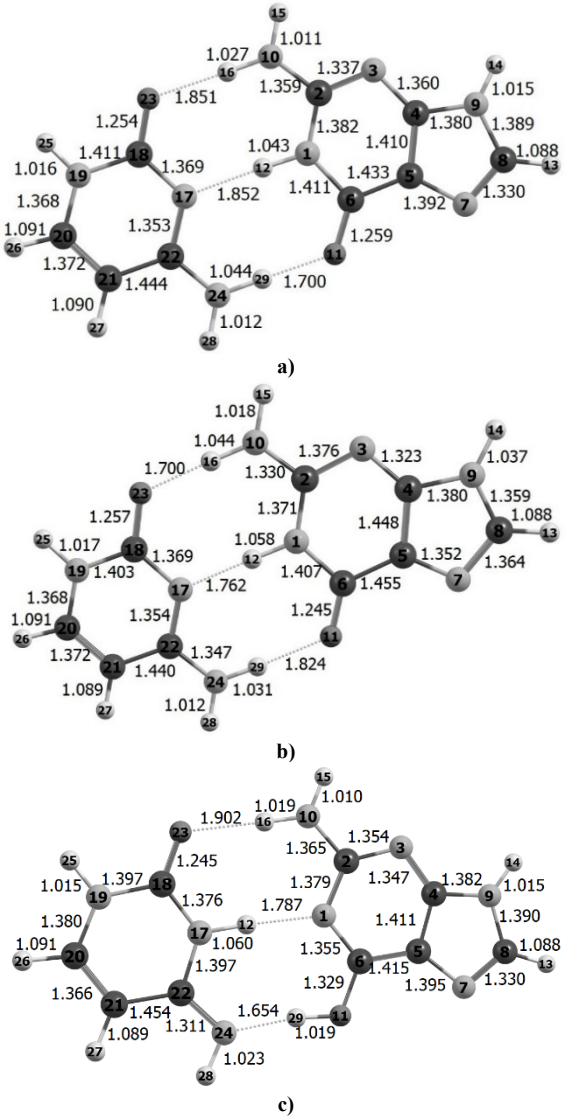


Fig. 1. Optimized structures of a) the ground state GC; b) second excited state ($^1\pi\sigma^*$ type) of the tautomer; and c) ground state of the GC1 base pair.

However, oppositely to the ground state the H_{12} atom is bonded to the cytosine ring, not to the guanine one. The hydroxy-imino tautomer GC1 of the base pair (Fig. 1c) has planar structure, which means that the functional groups are completely conjugated with the aromatic rings. One very short intermolecular H-bond is formed between the atoms H_{29}….N_{24}.

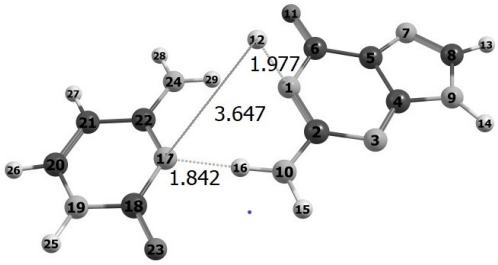


Fig. 2. Optimized structure of the conical intersection S_0/S_1.

The optimized geometry of the conical intersection S_0/S_1 connected with the out-of-plane H-transfer process is described in the Fig. 2. The active orbitals in the active space are: three occupied π-MO and three virtual: one σ^*-MO (LUMO) and two π^*-MO. The H_{12}-atom shows out-of-plane motion between the two aromatic rings. It is closer to the guanine ring than to the cytosine one. One strong intermolecular H-bond is formed between the two aromatic rings.

Vertical excitation energies and experimental UV/Vis spectrum

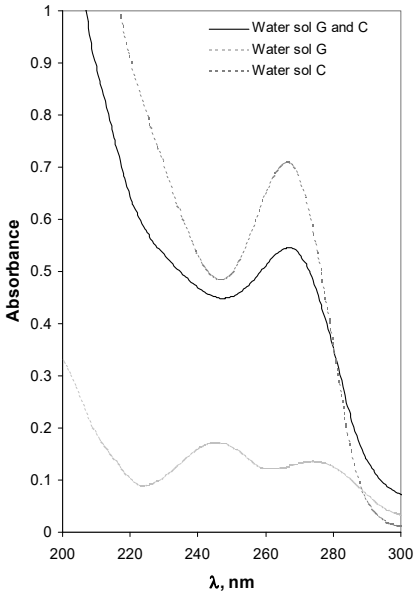


Fig. 3. Experimental UV absorption spectra of water solutions of guanine (G), cytosine (C) and their equimolar mixture G-C.

Vertical excitation energies Ground state GC		Vertical excitation energies Ground state GC1		Emission energies from the $^1\pi\sigma^*$ excited state	
State	eV (nm)	State	eV (nm)	State	eV (nm)
$^1\pi\pi^*$	4.576 (271, 267*)	$^1\pi\pi^*$	4.476 (277)	$^1\pi\pi^*$	3.956 (313)
$^1\pi\sigma^*$	4.720 (263)	$^1\pi\sigma^*$	4.747 (261)	$^1\pi\sigma^*$	4.170 (297)
$^1\pi\pi^*$	4.783 (259)	$^1\pi\pi^*$	4.838 (256)	$^1\pi\sigma^*$	4.513 (275)
$^1\pi\pi^*$	5.002 (248)	$^1\pi\pi^*$	4.967 (250)	$^1\pi\pi^*$	4.524 (274)
$^1\pi\sigma^*$	5.121 (242)	$^1\pi\sigma^*$	5.098 (243)	$^1\pi\pi^*$	4.736 (262)
$^1\pi\pi^*$	5.198 (239)	$^1\pi\pi^*$	5.283 (235)		
$^1\pi\pi^*$	5.222 (237,225-235*)	$^1\pi\sigma^*$	5.328 (233)		
$^1\pi\pi^*$	5.286 (235)	$^1\pi\pi^*$	5.505 (225)		
$^1\pi\sigma^*$	5.350 (232)	$^1\pi\sigma^*$	5.557 (223)		
$^1\pi\pi^*$	5.468 (227(237,225-235*)	$^1\pi\pi^*$	5.563 (223)		

Table 1 - Vertical excitation energies and emission energies (eV).
***Experimental values. Bold – optimized excited state.**

In Fig. 3 are given the experimental spectra of the water solutions of G and C and their equimolar mixture. The experimental spectrum of the water solution of G (saturated) shows an absorption maximum at 267 nm, whereas this of the water solution of cytosine (concentration 1.1×10^{-4} mol.L^{-1}) has two maxima at 274 nm and 245 nm – Fig. 3. The water solution of the equimolar mixture of the two bases shows one absorption maximum at 266 nm.

The assignment of the bands in the GC spectrum was carried out after analysis of the molecular orbitals included in the electron transitions. The experimental bands are assigned to the theoretical values in Table 1. It is clear that the experimental bands are due to the $\pi\rightarrow\pi^*$ electron transitions, i. g. to the spectrosopically active $^1\pi\pi^*$ excited states. The first excited state of the ground state is a charge transfer state – from G to C. Usually the excited state proton transfers occur in the repulsive $^1\pi\sigma^*$ excited states [12,15].

As seen this state appears at 271-267 nm which means that it is included (with low intensity as a driven state) in the broad experimental band. The rising band below 240 nm is a result of higher $^1\pi\pi^*$ excited states. The optimization of the $^1\pi\sigma^*$ excited state structure shows, as expected, a decrease of the energy of the state (Table 1). Parallel with this energy of the spectroscopically active $^1\pi\pi^*$ excited state is also lowered.

The emission energies show that the optical transitions (deactivation to the ground state) in the excited GC system should be red-shifted (bathochromic effect) with respect to the vertical excitations. The comparison of the theoretical vertical excitation energies of the tautomeric base pairs GC and GC1 (Table 1) shows that, most probably, the dominant one in the water solution should be the base pair GC.

Excited-state reaction path

We investigated the excited state reaction paths which connect the ground-state minimum of GC and the conical intersection S_0/S_1. The results are presented in Fig. 4. The mechanism describes the out-of-plane motion of the H_{12} atom between the two aromatic rings within the base pair GC.

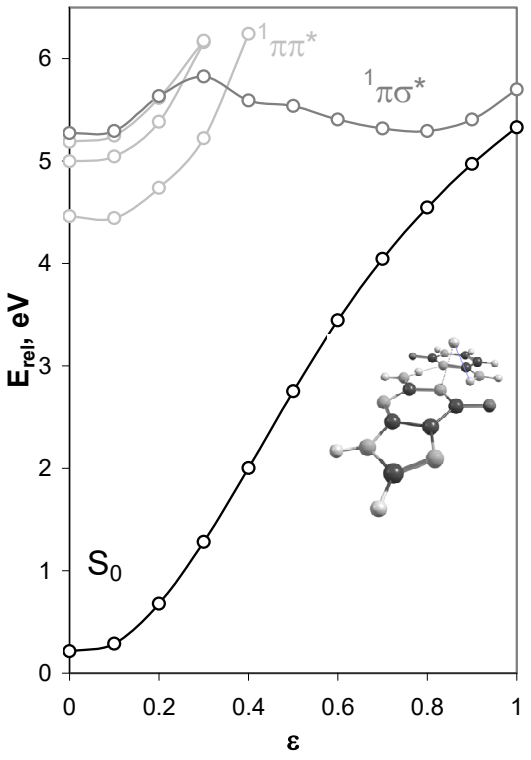


Fig. 4. Linearly-interpolated adiabatic excited state reaction paths of the out-of plane proton transfer between the two rings. The relative energy was calculated with respect to the ground-state energy of the GC base pair (-935.249370 a.u.).

From Fig. 4. it is seen that the ground-state of the base pair GC is connected with the conical intersection S_0/S_1 with the $^1\pi\sigma^*$ excited-state energy curve. Along this reaction path we found an energy barrier of 0.55 eV. Moreover the energy of the conical intersection S_0/S_1 is higher than the $^1\pi\sigma^*$ excited state in the Franck-Condon area. These two energy characteristics demonstrate that the out-of-plane energy transfer should be energy hindered and the excited system participates only in fluorescence transitions to the ground state. The mechanism is in support of high photostability of the GC base pair.

In the other hand the $^1\pi\sigma^*$ excited state in the Franck-Condon area could be populated from the spectroscopically active $^1\pi\pi^*$ excited state and the switch channels $^1\pi\pi^*/^1\pi\sigma^*$ which are visible in Fig. 4.

IV. CONCLUSION

We performed a theoretical study of the mechanism of the out-of-plane proton transfer in the Watson – Crick base pair guanine - cytosine. The calculations were performed at the CC2/aug-cc-pVDZ theoretical level. The interpolation between two structures – ground state minimum and conical intersection S_0/S_1 - was done with the CASSCF optimized geometries. The results showed that the two points were connected with the $^1\pi\sigma^*$ excited-state reaction path which shows an energy barrier along the reaction coordinate. This fact and the high energy of the found conical intersection S_0/S_1 is in support of the high photostability of the base pair guanine-cytosine with respect to this mechanism. The excited system guanine-cytosine can be deactivated only through optical transitions (emission) to the ground-state.

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