Journal of Photochemistry and Photobiology B: Biology 101 (2010) 31–36

Contents lists available at ScienceDirect

Journal of Photochemistry and Photobiology B: Biology

journal homepage: www.elsevier.com/locate/jphotobiol

Photoinduced dissociation of cyclobutane thymine dimer studied by semiclassical dynamics simulation

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ARTICLE INFO

Article history:
Received 19 April 2010
Received in revised form 15 June 2010
Accepted 21 June 2010
Available online 30 June 2010

Keywords:
Cyclobutane thymine dimer
Photoinduced dissociation
Semiclassical dynamics simulation

ABSTRACT

Photoinduced dissociation of the thymine dimer is studied in a semiclassical dynamics simulation. The simulation follows excitation of an isolated thymine dimer by a 25 fs fwhm laser pulse, and finds that dissociation proceeds via an asynchronously concerted mechanism, in which the $C_5–C_5'$ bond breaks soon after application of the laser pulse, followed by cleavage of the $C_6–C_6'$ bond. The dissociation results in two thymine monomers, one in an electronically excited state and the other in the ground state. The former decays to the electronic ground state through an avoided crossing induced by deformation of the pyrimidine ring at the C_5' and C_6' sites.

1. Introduction

The cyclobutane thymine dimer is a main lesion formed in DNA as a result of exposure to UV radiation in the 260–320 nm range. The formation of thymine dimers has been proposed to be a primary cause of skin cancer and therefore has attracted extensive investigations both experimentally [1–4] and theoretically [5–11].

A thymine dimer can be converted reversibly into thymine monomers by two different methods, namely enzymatic and photochemical. In the enzymatic method photolyases, after exposure to visible or near-UV light, recognize thymine dimers in a DNA strand, catalyze the removal of two σ-bonds connecting two bases, and consequently bring them to their monomeric form [12]. This DNA repair process is believed to occur in many organisms and the mechanism of this reaction has been extensively studied [13,14]. A commonly accepted model for DNA enzymatic repair is that after excitation by visible or near-UV light an electron transfer from a catalytic cofactor to a thymine dimer, which finally becomes a radical anion. The formation of the dimer radical anion enables the conversion of the dimer to monomers to proceed readily at ambient temperatures. In the photochemical method, a thymine dimer absorbs a photon with a wavelength of 240 nm and produces two thymines with a quantum yield of nearly 100%. The photochemical method is less biologically important because, upon reaching the earth's surface, UV radiation is mostly filtered by living organisms to prevent genome damage, and consequently this process has received less attention.

In contrast to its lack of significance for biological systems, the photodissociation of thymine dimmers under UV irradiation has found interesting application in constructing bio-inspired synthetic photoactive polymers [15,16]. The polymers with thymine bases can be potentially useful in many photoresist applications. When exposed to UV radiation, thymine-based polymers change from individual polymer chains to a crosslinked network, where polymer chains are connected with each other because of the formation of cyclobutane thymine dimers. The formation of photocrosslinked network alters the solubility of thymine-based polymers in a suitable solvent. The restoration of polymers to their original state through the reversal reaction of photodimerization provides exciting opportunities to construct fully recyclable photoresist materials [17]. A better understanding of the mechanism of the photoinduced dissociation of cyclobutane thymine dimers is necessary for efficiently constructing such photoresist materials.

In this paper, we present a semiclassical dynamics simulation study of the dissociation of a thymine dimer induced by an ultrashort laser pulse. The simulation results provide detailed information for a microscopic understanding of this important reaction. The simulation study is also compared with a QM/MM investigation of the splitting of the thymine dimer radical anion.

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doi:10.1016/j.jphotobiol.2010.06.008

2. Methodology

Our technique is semiclassical electron-radiation-ion dynamics (SERID) and a detailed description has been published elsewhere [18,19]. The valence electrons are treated with a quantum mechanical approach while both the radiation field and the motion of the nuclei are treated classically. The one-electron states are updated by solving the time-dependent Schrödinger equation at each time step (usually 0.05 fs in duration) in a nonorthogonal basis,

$$i\hbar\frac{\partial\Psi_j}{\partial t} = \mathbf{S}^{-1}\cdot\mathbf{H}\cdot\Psi_j, \tag{1}$$

where **S** represents the overlap matrix of the molecular orbitals. The vector potential **A** of the radiation field is included in the electronic Hamiltonian via the time-dependent Peierls substitution [20]

$$H_{ab}(\mathbf{X}-\mathbf{X}') = H^0_{ab}(\mathbf{X}-\mathbf{X}')\exp\left(\frac{iq}{\hbar c}\mathbf{A}\cdot(\mathbf{X}-\mathbf{X}')\right), \tag{2}$$

where $H_{ab}(\mathbf{X}-\mathbf{X}')$ is the Hamiltonian matrix element for basis functions a and b on atoms at positions **X** and **X**' respectively, and $q = -e$ is the charge of the electron.

The forces acting on nuclei or ions are computed by the Ehrenfest equation in an "on the fly" approach:

$$M_l\frac{d^2X_{l\alpha}}{dt^2} = -\frac{1}{2}\sum_j \Psi_{\mathbf{j}}^{+}\cdot\left(\frac{\partial\mathbf{H}}{\partial X_{l\alpha}} - i\hbar\frac{1}{2}\frac{\partial\mathbf{S}}{\partial X_{l\alpha}}\cdot\frac{\partial}{\partial t}\right)\cdot\Psi_{\mathbf{j}} - \partial U_{rep}/\partial X_{l\alpha}, \tag{3}$$

where U_{rep} is the effective nuclear–nuclear repulsive potential and $X_{l\alpha} = \langle\hat{X}_{l\alpha}\rangle$ is the expectation value of the time-dependent Heisenberg operator for the α coordinate of the nucleus labeled by l (with $\alpha = x, y, or\ z$).

The Hamiltonian matrix H, overlap matrix S, and effective nuclear–nuclear repulsive potential U_{rep} are calculated in the density-functional tight-binding approximation [21,22]. These quantities are functions only of the nuclear distance and the results from the calculations for a dimer can be tabulated and employed in the time-dependent calculations. The basis functions used in the present simulations are the 1s atomic orbital of H and the valence s and p orbitals of C and N (spin up and spin down states are not distinguished). In this approach, the electronic energy of a molecule can be written as

$$E_{elec} = \sum_{i=occ} n_i\varepsilon_i + \sum_{\alpha>\beta} U_{rep}(|X_\alpha - X_\beta|), \tag{4}$$

where ε_i and n_i are the eigenvalue and occupation number of Kohn–Sham orbital i. The first summation goes over all occupied orbitals. The effective repulsive potential $U_{rep}(|X_\alpha - X_\beta|)$ is a function of the inter-atom distance.

This model has been used to study several photochemical reactions and was found to yield good descriptions of molecular response to ultrashort laser pulses. The examples include that the calculation for the tetramethylene [23] intermediate diradical formation is consistent with time-of-flight mass spectrometry measurements, the nonthermal fragmentation of C_{60} [24] is in good agreement with experimental observations, and the characterization of the geometry changes at some critical points [25] is compatible with molecular mechanics valence bond calculations. The model has also been used to simulate the response of adenine base to an ultrafast laser pulse [26].

The limitation of this method is that the simulation trajectory moves along a path produced by averaging over all the terms in the Born–Oppenheimer expansion [27–31],

$$\Psi^{total}(X_n, x_e, t) = \sum_i \Psi_i^n(X_n, t)\Psi_i^e(x_e, X_n), \tag{5}$$

rather than following the time evolution of a single potential energy surface [29–33] (here X_n and x_e represent the sets of nuclear and electronic coordinates respectively, and the Ψ_i^e are eigenstates of the electronic Hamiltonian at fixed X_n). The strengths of the present approach are that it retains all of the $3N$ nuclear degrees of freedom and it incorporates both the excitation due to a laser pulse and the subsequent de-excitation at an avoided crossing near a conical intersection.

3. Results and discussion

To obtain a ground state equilibrium configuration of the cyclobutane thymine dimer, the simulation was run at room temperature for 2000 fs. To generate the initial geometry for a dynamics simulation, the equilibrated structure was simulated for an additional 2000 fs. From the resulting trajectory 20 geometries were taken at equal time intervals and used as starting geometries for each path. A 25 fs fwhm laser pulse with a Gaussian profile and a frequency of 4.95 eV was applied to the thymine dimer. The laser energy employed in the simulation is the same as used in experiment [34]. A fluence of 0.1228 kJ/m^2 was selected for the present simulation. The fluence produces an effective electronic excitation and appropriate forces, which break the σ-bond connecting two bases, but do not damage any other bonds. We then ran the simulation at this selected laser pulse for twenty trajectories. All trajectories came out with similar results. Our presentations and discussions are based on a typical trajectory but the differences between this trajectory and others are described in a later paragraph.

Four snapshots taken at different times of the simulation are shown in Fig. 1 with atoms labeled in Fig. 1a. In the following discussion, we will refer the monomer on the left as T and one on the right as T'. Starting from the equilibrium geometry in the electronic ground state at 0 fs, the thymine dimer is electronically excited by the laser pulse. The excited molecule is distorted and the C_5–C_5' bond breaks at about 50 fs (Fig. 1b). At 280 fs, the C_6–C_6' bond has broken (Fig. 1c) and two thymine molecules have moved away slightly from each other (Fig. 1d). These snapshots briefly represent the dissociation process of a thymine dimer into two monomers.

Fig. 2a and b present the variations with time of the C_5–C_5' and C_6–C_6' bond lengths and the C_5–C_6 and C_5'–C_6' bond lengths, respectively. Starting from 1.5 Å the C_5–C_5' distance enlarges sharply after 40 fs because of the breaking of the chemical bond. On the other hand, the C_6–C_6' distance only shows a slow increase before 130 fs, at which time the C_6–C_6' bond breaks. From 130 fs to 240 fs, the C_6–C_6' distance changes from 2.0 Å to 2.9 Å. The relatively short distance between the C_6 and C_6' atoms allows the two thymines to remain in interaction with each other. Both C_5–C_6 and C_5'–C_6' bonds are single bonds initially and show remarkable increases in their vibrational amplitudes soon after the application of the laser pulse. The C_5–C_6 bond length starts to shrink from 100 fs and at about 240 fs becomes less than 1.4 Å, which is the length of a typical double bond. In other words, the C_5–C_6 bond is between a single bond and a double bond in length from 140 fs to 240 fs, indicating the existence of a transition state for this period of time. After 240 fs two thymines move away from each other and C_6–C_6' and C_5–C_5' distances become greater than 3.0 Å and 3.5 Å, respectively. The change of the C_5–C_6 bond from a single bond to a double bond implies that T is in the ground state. The C_5'–C_6' bond changes to a double bond only after 380 fs, suggesting that T' remains in an electronically excited state before this time.

The time-dependent populations of the HOMO-3, HOMO-2, HOMO-1, HOMO, and LUMO are presented in Fig. 3a. Fig. 3b is an expanded scale of Fig. 3a from 0 fs to 60 fs. The variations with time of energies of these orbitals are shown in Fig. 4. Figs. 3 and