Interconversion Pathways of the Protonated β-Ionone Schiff Base: An Ab Initio Molecular Dynamics Study

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ABSTRACT: Ab initio molecular dynamics at the RHF/3-21G level have been performed to study interconversion pathways (bond rotation and ring inversion) of the protonated β-ionone Schiff base. Starting with different stationary points on the Born–Oppenheimer potential energy surface, the trajectories are followed for 2100 fs. A perfunctory analysis of the reaction pathways reveals a dynamical behavior in agreement with classical expectations.

Key words: ab initio molecular dynamics; bacteriorhodopsin; rhodopsin; protonated β-ionone Schiff base

Introduction

Retinal is the chromophore of several photochromic proteins. In rhodopsin, which is the photoreceptor for dim-light vision in the vertebrate retina, the visual cascade is initiated by photochemical isomerization of the 11-cis isomer of retinal Schiff base to the all-trans form. In bacterio-

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orhodopsin, which is a membrane protein of the salt-loving Halobacterium salinarium, light energy is transformed into a proton gradient in a cyclic process which starts by photochemical isomerization of all-trans to 13-cis-retinal Schiff base. In both proteins the chromophore is covalently linked as a protonated Schiff base to the protein backbone [1, 2].

Quantum-mechanical calculations of the chromophore and on chromophore model systems, employing both force-field and semiempirical methods [3] and ab initio theories [4–7], have helped
considerably in getting more insights into the molecular structures involved. For an improved description, more elaborate techniques are in use to model the time evolution of the system [8–11].

Computational Methods

Ab initio molecular dynamics (AIMD) has been developed as a nonempirical method for studying the dynamical behavior of molecular systems on a microscopic level [12]. The principle is straightforward: quantum-mechanically derived forces are used to integrate Newton’s equations of motion for the nuclei. The calculations to be discussed below are based on an approach in which the wave function is reoptimized at each time step to ensure that the system remains on the Born–Oppenheimer potential energy surface [13].

The Gaussian94 program package [14] was used for the ab initio part of the calculations. The structures of all stationary points were fully optimized at the RHF/3-21G level and characterized through their second derivatives. Also, the SCF energy and the forces were calculated at this level for every point along the trajectory. For the molecular dynamics (MD) simulations a classical microcanonical molecular dynamics code was used, in which the integration of the classical equation of motion is done by the velocity Verlet integrator scheme [15].

In this algorithm the positions and the velocities at the same time point are given by

\[
\begin{align*}
\mathbf{r}_i(t + \Delta t) &= \mathbf{r}_i(t) + \mathbf{v}_i(t)\Delta t + \frac{\Delta t^2}{2m_i}F_i(t) \\
\mathbf{v}_i(t + \Delta t) &= \mathbf{v}_i(t) + \frac{\Delta t}{2m_i}[F_i(t) + F_i(t + \Delta t)]
\end{align*}
\]

where \( \mathbf{r}_i(t) \), \( \mathbf{r}_i(t + \Delta t) \) refer to the position, \( m_i \) to the mass, \( \mathbf{v}_i(t) \), \( \mathbf{v}_i(t + \Delta t) \) to the velocity, and \( F_i(t) \), \( F_i(t + \Delta t) \) to the force on the \( i \)th atom at times \( t \) and \( t + \Delta t \).

By “freezing” the high-frequency stretching modes (fast vibrational modes) involving hydrogen, one can make the integration time steps longer. In the framework of the velocity Verlet scheme, the RATTLE algorithm of Andersen [16] is used to apply these constraints, which result in the following equations for the positions and velocities:

\[
\begin{align*}
\mathbf{r}_i(t + \Delta t) &= \mathbf{r}_i(t) + \mathbf{v}_i(t)\Delta t + \frac{\Delta t^2}{2m_i}F_i(t) \\
\mathbf{v}_i(t + \Delta t) &= \mathbf{v}_i(t) + \frac{\Delta t}{2m_i}[F_i(t) + F_i(t + \Delta t)] \\
\end{align*}
\]

with \( \mathbf{r}_i(t) = \mathbf{r}_i(t) - \mathbf{r}_i(t) \) and \( \lambda_{ij} \) and \( \lambda''_{ij} \) the time-dependent Lagrange multipliers associated with the constraints on nuclear positions and velocities, respectively. In all MD calculations the energy is conserved, i.e., the total energy remains constant during the simulation.

In our calculations the starting geometries were stationary points generated on the Born–Oppenheimer potential energy surface. Forces were generated by slightly distorting the equilibrium geometry; velocities for all atoms were zeroed at the beginning of the MD run. Constraints were applied to all bonds with hydrogen atoms, i.e., C–H and N–H, with bond lengths fixed to their equilibrium values. One trajectory was run from each of four different stationary points. The time step in all simulations was 30 au (ca. 0.7 fs), and 3000 steps were calculated in each run.

Results and Discussion

The quantum-mechanical part of the simulation is the limiting factor for the size of the molecules which can be treated by AIMD. The retinals with more than 20 heavy atoms are still beyond this limit. \( \beta \)-Ionone, a molecule with a total of 36 atoms, shares with retinal all structural features of the cyclohexene end group, viz. the conjugation with a conjugated double-bond system and the substitution with three methyl groups (Scheme 1).
As a model for the retinal chromophore, we have studied recently the cyclohexene ring inversion and the C6—C7 rotation in β-ionone derivatives. As a result, on a two-dimensional subspace of the Born–Oppenheimer potential energy surface, we have located all stationary points, i.e., minima, first-order saddle points (transition states) and second- and third-order saddle points (Fig. 1). In this figure, the coordinates $\Theta_1$ and $\Theta_2$ are the dihedral angles $\angle C5C6C7C8$ and $\angle C1C2C3C4$ and correspond, respectively, to rotation about the C6—C7 bond (horizontally) and inversion of the cyclohexene ring (vertically). The stationary points are drawn in perspective and in a bird’s-eye view to give an impression of the subspace. Their RHF/3-21G energies, together with the exact values of $\Theta_1$ and $\Theta_2$, are collected in Table I.

To briefly characterize the stationary points, (a) and (b) are the two highly twisted 6-s-cis conformers with the cyclohexene ring in either of the
The trajectory first runs smoothly in the direction of the 6-s-cis minimum, picking up kinetic energy along the way. As a consequence the molecule cannot relax into the minimum-energy structure. Instead, it passes through the minimum, picking up potential energy and increasingly distributing energy into other internal coordinates. At some point along its path the conversion is complete (after ca. 983 fs), and the molecule returns, the repetition of this process giving rise to a Lissajous-figure-type reaction pathway of the trajectory.

The energy difference between the transition state 1 and the 6-s-cis minimum is 3.7 kcal/mol. The corresponding difference between the saddle point 4 and the 6-s-trans minimum is much higher, ca. 14.7 kcal/mol. The MD run starting at 4 reflects this difference directly: The system relaxes very fast (note the dotted trajectory, which indicates resolved single geometries), the first inflection point is reached after only 173 fs, and the number of oscillations performed in the identical time span is significantly higher, as can be seen in Figure 1. The center of these Lissajous figures is the trans minimum-energy structure. Despite its high energy the system does not pass over the transition states flanking this 6-s-trans minimum because the energy is distributed among several internal degrees of freedom.

Conclusions

We have shown that Born–Oppenheimer AIMP calculations using atom-centered bases on systems the size of β-ionone (36 atoms) are feasible; the computational resources needed are moderate (each MD run took about 1 week on four nodes of an SPP 2000). Coupled with the calculation of other observables such as charge fluctuations or excited-state properties such as UV or CD-spectral data, this ab initio MD method appears to be a promising alternative to classical empirical potential MD for complex biomolecule potential energy surfaces.

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References


