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Trans–Cis Isomerization of Protonated Schiff Base of Retinal at the Ground and Triplet States: A Hybrid DFT Study

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Trans–Cis Isomerization of Protonated Schiff Base of Retinal at the Ground and Triplet States: A Hybrid DFT Study[#]

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Abstract

Motivation. *Trans–cis* isomerization is one of the important phenomena in the human retinal visual pigment. However, the mechanism of the isomerization is not clearly understood. In the present study, potential energy curves for the isomerization of all *trans*–protonated Schiff base of retinal (PSBR) at the ground state have been calculated by means of hybrid density functional theory (DFT) calculations.

Method. Hybrid density functional calculations have been carried out for the isomerization reactions. Potential energy curves for the ground singlet states and lowest triplet states were calculated at the B3LYP/3–21G(d) level.

Results. The calculations of the potential energy curves for the ground singlet and triplet states (S_0 and T_1) of PSBR indicated that the transition state for the ground state isomerization was located at $\theta_{13-14} = 90°$, where θ_{13-14} means twist angle around the C_{13}=C_{14} double bond of PSBR (θ_{13-14} = 0 and 180° mean all *trans*– and *cis*–form, respectively). The energy barrier calculated at the B3LYP/6–311G(d,p)//B3LYP/3–21G(d) level was 1.30 eV relative to the *trans*–form ($\theta_{13-14} = 0°$). The *cis*–form of PSBR was 0.17 eV higher in energy than that of *trans*–form. The vibrational frequencies were calculated for *cis*– and *trans*–forms at the B3LYP/3–21G(d) level. The N=C stretching mode in Schiff base and C=C stretching mode for the C_{13}=C_{14} double bond of PSBR were red–shifted by the isomerization from *trans*– to *cis*–forms (1678 *vs*. 1668 cm^{-1} for the N=C bond and 1613 *vs*. 1612 cm^{-1} for the C_{13}=C_{14} bond. For triplet state, the barrier was located at $\theta_{13-14} = 0.0°$, and the barrier height was calculated to be 1.16 eV relative to the *trans*–form at the triplet state.

Conclusions. The barrier height for the isomerization was estimated to be 1.20–1.30 eV. The C=C stretching mode was red–shifted by the isomerization from *trans* to 13–*cis* form. These features were in good agreement with recent experimental results.

Keywords. All *trans* retinal; bacteriorhodopsin; DFT; isomerization; barrier height.

Abbreviations and notations

bR, bacteriorhodopsin	PEC, potential energy curve
DFT, density functional theory	PSBR, protonated Schiff base of retinal

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[#] Dedicated to Professor Nenad Trinajstić on the occasion of the 65th birthday.

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1 INTRODUCTION

The protonated Schiff base of retinal (PSBR) is the chromophore group of the protein rhodopsin, one of the visual pigments in humans [1]. The photo–isomerization of PSBR from 11–*cis* to *trans*–forms is one of the fast chemical reactions observed experimentally [2–5]. All–*trans* form of PSBR is also one of the protonated Schiff base compounds which exist in bacteriorhodopsin (bR) and in halorhodopsin [6–9]. It is known that all–*trans* form of PSBR is changed to *cis*–form by photo–excitation. This isomerization in bR takes place mainly in the position of C_{13}=C_{14} double bond of retinal: namely, all–*trans* form is efficiently changed to 13–*cis* form by the isomerization.

Recent experiments for the photo–isomerization of all–*trans* form of PSBR in bR have shown that the C_{15}=N and C_{13}=C_{14} stretching modes of all–*trans* form of PSBR is red–shifted after the photo–excitation [6,9]. This change is assigned experimentally that the *trans–cis* isomerization of PSBR takes place at the position of C_{13}=C_{14} double bond. However, details of the origin of the vibrational spectral shifts are not clearly understood.

Several theoretical works have been made on the potential energy curves of PSBR by *ab initio* calculations [4–18]. The previous works indicated that PEC of the ground state is crossed with that of first excited state, indicating that the PEC is composed of crossing nature between ground and excited states.

In the present study, hybrid density functional theory (DFT) calculations were applied to the structures of electronic states of protonated Schiff base of all–*trans* retinal and 13–*cis* retinal [19,20] in order to shed light on the properties of PSBR. Prior to obtain the excited state potential energy curves (PECs), in the present calculation, we focus our attention on the ground state PEC for the isomerization.

2 METHOD AND CALCULATION

All calculations were carried out using GAUSSIAN98 program package [21]. The structures of the system were fully optimized at the B3LYP/3–21G(d) level of theory. The geometry optimizations were performed for all–*trans* and 13–*cis* forms of PSBR. Potential energy curve (PEC) for the *trans–cis* isomerization was calculated along a reaction coordinate composed of twist angle of C_{13}=C_{14} double bond. The geometry used for the PEC calculation was that optimized for all–*trans* form of PSBR, and then the twist angle was only varied. The energies at stationary points (*i.e.*, *trans*– and *cis* forms and transition state for the isomerization) were recalculated at the B3LYP/6–311G(d,p) level. Harmonic vibrational frequencies of *trans*– and *cis*–forms of PSBR were calculated at the B3LYP/3–21G(d) level.

3 RESULTS

3.1 Structures of *trans*– and *cis*–forms of PSBR

First, the structure of all *trans* form of PSBR was fully optimized by means of B3LYP/3–21G(d) method. The optimized structure for all–*trans* form is illustrated in Figure 1A.

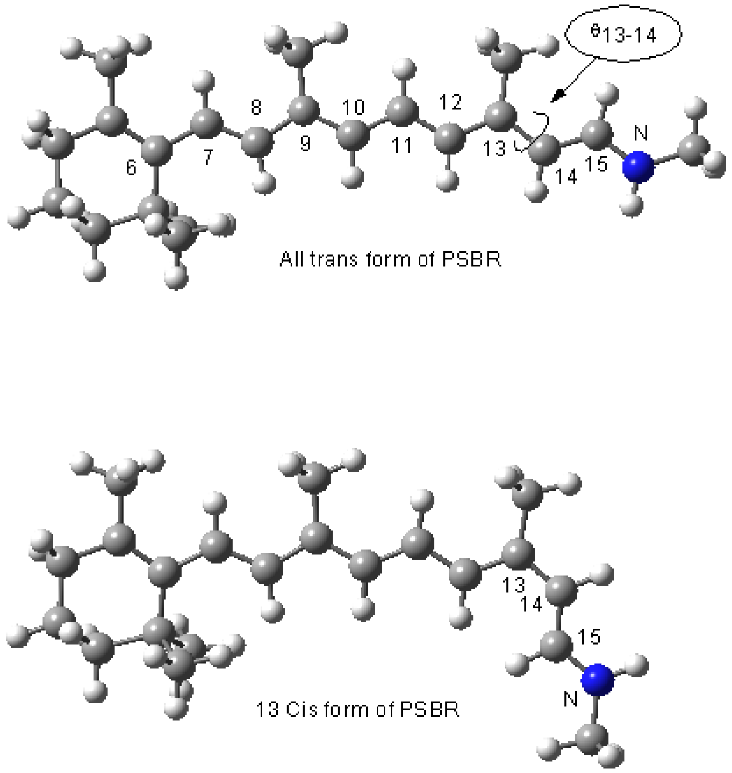

Figure 1. Fully optimized structures of all–*trans* form of PSBR (upper) and 13–*cis* form (lower) calculated at the B3LYP/3–21G(d) level.

Twist angle of C_{13}=C_{14} (expressed by $\theta_{13–14}$) is defined by $\theta_{13–14} = 180° - \phi$, where the angle ϕ is the dihedral angle of <C_{12}–C_{13}–C_{14}–C_{15}. The angle $\theta_{13–14}$ is also the reaction coordinate for the isomerization. The geometry optimization gave that the energy minimum at the ground state is found at $\theta_{13–14} = 0.0°$, indicating that the most stable form is all–*trans* form which possesses a planar structure. Next, the similar calculation was carried out for the 13–*cis* form of PSBR. Fully optimized structure of the 13–*cis* form of PSBR is illustrated in Figure 1B. The twist angles of C_{13}=C_{14} double bond were calculated to be $\theta_{13–14} = 176.3°$ (B3LYP/3–21G(d) level), meaning that the 13–*cis* form of PSBR has a slight non–planar structure. However, the deformation from the planar structure is negligibly small.

3.2 Potential energy curve for the isomerization at the ground state (S_0)

Potential energy curve (PEC) was plotted as a function of the C_{13}=C_{14} twist angle ($\theta_{13–14}$). First, the structure of *trans*–form of PSBR was fully optimized at the B3LYP/3–21G(d) level (The structure is given in Figure 1A). Next, twist angle of the optimized structure was changed as a parameter, and then the total energies are calculated at each twist angle (θ_{13-14}) at the B3LYP/3–21G(d) level. PEC thus obtained is given in Figure 2. Zero level of energy corresponds to total energy of *trans*–form of PSBR with θ_{13-14} = 0º. The energy of the system increased gradually with increasing θ_{13-14}, and it reached the maximum point at θ_{13-14} = 90º. This point corresponds to transition state for the *trans–cis* isomerization of PSBR at the ground state. After the transition state is left, the energy decreased gradually and it reached a region of *cis*–form of PSBR. The energy minimum was found at θ_{13-14} = 180.0º. Full geometry optimization of 13–*cis* form of PSBR gave 1.6 kcal/mol as the energy difference from that of all *trans*–form at the B3LYP/3–21G(d) level.

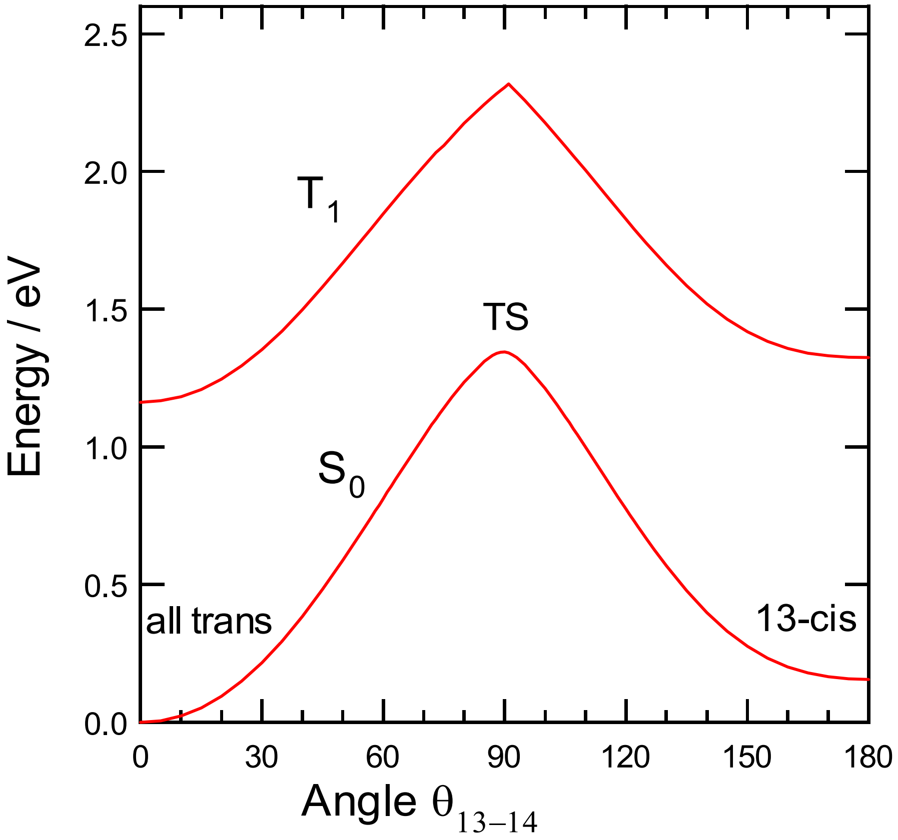

Figure 2. Potential energy curve for *trans*/13–*cis* isomerization of PSBR calculated at the B3LYP/3–21G(d) level. Twist angle of zero means all *trans*–form of PSBR, and angle of 180° means 13–*cis* form.

3.3 Barrier heights for the isomerization

To obtain more realistic feature for the energetics, B3LYP/6–311G(d,p)//B3LYP/3–21G(d) calculation was carried out for the stationary points for the isomerization. The total and relative energies for all–*trans* and 13–*cis* forms of PSBR and transition state for the ground state isomerization were given in Table 1. The most sophisticated calculation, B3LYP/6–311G(d,p)//B3LYP/3–21G(d), indicates that the reaction barrier is 1.30 eV for the *trans–cis* isomerization relative to the all *trans*–form of PSBR.

Table 1. Reaction barriers (in eV) for ground state isomerization and relative energies between *cis* and *trans*–retinal (in eV). Fully optimized values for 13–*cis* form of PSBR are given in parenthesis (in eV).

θ_{13-14} / degree	B3LYP/3–21G(d)	B3LYP/6–311G(d,p)
0.0 (*trans*)	0.0 [a]	0.0 [b]
90.0 (TS)	1.34	1.30
180.0 (*cis*)	0.16 (0.07)	0.17

[a] Total energy at zero–level is –869.25588 a.u. (B3LYP/3–21G(d) level)
[b] Total energy at zero–level is –874.23860 a.u. (B3LYP/6–311G(d)//B3LYP/3–21G(d) level)

3.4 Vibrational frequencies of *trans*– and *cis*–forms of PSBR

In order to elucidate the change of vibrational frequencies for *trans–cis* forms, harmonic vibrational frequencies were calculated at the B3LYP/3–21G(d) level. All vibrational frequencies obtained were positive for both *trans–cis* forms, meaning that both structures are located in local minima. The C_{15}=N stretching mode in protonated Schiff base and C=C stretching mode for the C_{13}=C_{14} double bond of PSBR were red–shifted by the isomerization from *trans*– to *cis*–forms (1678 *vs*. 1668 cm^{-1} for the C_{15}=N bond and 1613 *vs*. 1612 cm^{-1} for the C_{13}=C_{14} bond). These results indicate that these stretching modes are red–shifted by the isomerization from *trans*– to *cis*–forms of PSBR.

3.5 Potential energy curve for the isomerization at the triplet state (T_1)

For comparison, PEC for the triplet state (T_1) was calculated along the C_{13}=C_{14} twist angle. The structures at each point corresponds to that of the ground state (S_0). The result is given in Figure 2. At the position of the *trans*–form of PSBR with θ_{13-14} = 0º, the excitation energy from S_0 to T_1 was calculated to be 1.16 eV. The energy of the system (T_1) increased gradually with increasing θ_{13-14} and it reached the maximum point at θ_{13-14} = 90º. The energy at this point was calculated to be 2.32 eV relative to that of θ_{13-14} = 0º. The band gap at the S_0 state was 1.16 eV at θ_{13-14} = 90º. The energy of the *cis*–form of PSBR at T_1 state was 1.32 eV. As well as the S_0 state, the energy minimum was found at θ_{13-14} = 0º and 180º. The shape of PEC for the triplet state is very similar to that of the ground state.

4 DISCUSSION

4.1 Summary

In the present study, the potential energy curve for *trans–cis* isomerization of PSBR was calculated by means of hybrid–DFT calculation. The reaction coordinate for the isomerization is defined by the twist angles of C_{13}=C_{14} bond (θ_{13-14}). The barrier heights calculated by B3LYP/3–21G(d) and B3LYP/6–311G(d,p) levels were 1.34 and 1.30 eV, respectively. The saddle point for the isomerization was located at θ_{13-14} = 90º. The 13–*cis* form of PSBR is 0.17 eV higher in energy than all *trans* form.

Recently, time–resolve Fourier–transform spectra of *trans*–retinal after the photo–irradiation have measured and the red–shifts of C_{15}=N and C_{13}=C_{14} stretching modes of PSBR was observed [6, 9]. This result was interpreted in terms of structural change from *trans*– to *cis*–forms. The present calculation indicated that the vibrational modes of C_{15}=N and C_{13}=C_{14} stretching for *trans*– and *cis*–forms are calculated to be 1678 and 1668 cm^{-1} for C_{15}=N stretching mode and 1613 *vs*. 1612 cm^{-1} for the C_{13}=C_{14} stretching mode: namely, the isomerization causes red shifts of vibrational frequency of these stretching modes. In particular, the shift of the C_{15}=N stretching mode is significantly large. These results strongly support recent experiments [6,9].

The present calculations showed that the isomerization from all *trans*– to 13–*cis*–forms causes the red–shifts of vibrational stretching modes of PSBR. In particular, the mode of C_{15}=N in Schiff base is largely shifted. In order to elucidate the origin of the shifts, Mulliken charges on atoms was analyzed. The charges on N atoms are calculated to be –0.305 in *trans*–form and –0.302 in 13–*cis* form, indicating that the charge interaction in C_{15}=N bond of *trans*–form is slightly stronger than that of 13–*cis* form. Furthermore, the charge separation in the C_{13}–C_{14} bond of all *trans*–form is larger than that of 13–*cis* form (+0.037/–0.032 *vs*. +0.036/–0.030). These results indicate that the C_{15}=N and C_{13}=C_{14} stretching modes in all *trans*–form is stronger than that of 13–*cis*–form.

In the present study, we focus our attention on mainly the ground states of retinal, and we do not consider the excited state. In order to elucidate the dynamics of isomerization caused by electronic excitation, the potential energy surfaces for excited states would be required. Such calculations are now in progress.

We have reported here only the isomerization from all–*trans* to 13–*cis* forms of PSBR. It is known that 11–*cis*/*trans* isomerization occurs as well as 13–*cis*/*trans* one. The potential energy curve for 11–*cis*/*trans* isomerization was preliminary calculated with the same manner. The activation barrier was calculated to be 1.30 eV which is comparable to all–*trans*/13–*cis* isomerization. In order to estimate the solvent effect on the relative energies between all–*trans* and 13–*cis* forms, dipole moments for both forms were calculated. The dipole moments for all–*trans* and 13–*cis* forms, were calculated to be 14.2 and 12.7 Debye, respectively. These values indicate that all *trans*–form is more stabilized by the polar solvent, and the energy gap becomes wider in polar solvent.

4.2 Comparison with previous studies

The energy difference between *cis*– and *trans*–forms of PSBR has been calculated by several groups. Terstegen and Bub carried out B3LYP/6–31G** calculation for all *trans*– and 11–*cis*–forms, which are isomers of 13–*cis* form of PSBR. The isomerization energy was calculated to be 5.2 kcal/mol at the B3LYP/6–31G** level, indicating that all *trans* form is the most stable in the isomers of PSBR. The isomerization energy from all *trans*– to 13–*cis* forms was calculated to be 2.1

kcal/mol at B3LYP/6–31G(d) level [23]. The energy calculated in the present work (1.6 kcal/mol) is comparable to previous values.

4.3 Additional comments

In the present study, several approximations have been employed in the calculations of the potential energy curves. First, we assumed the HF/3–21G(d) optimized geometries for PSBR at the stationary points throughout. In previous papers, we investigated several large molecular systems at the HF/3–21G(d) level of theory [24–28]. The results obtained at the HF/3–21G(d) calculations would give a reasonable feature for the structures. Therefore, the level of theory used in the present calculation (HF/3–21G(d)) would be adequate to discuss qualitatively the isomerization of PSBR. However, more accurate wave functions may provide deeper insight in the reaction mechanism. Such calculation will be possible after development of high–speed CPU machine in near future.

Second, we did not consider dynamics feature of the isomerization processes. In order to obtain details of the reaction mechanism, the dynamics treatment, such as direct *ab initio* trajectory calculations [24–28], would be required. Such calculation is now in progress. Despite the several assumptions introduced here, the results enable us to obtain valuable information on the mechanism of the ground state isomerization of PSBR.

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