Photoisomerization Path for a Realistic Retinal Chromophore Model: The Nonatetraeniminium Cation

Marco Garavelli,[§] Thom Vreven,[†] Paolo Celani,[†] Fernando Bernardi,[§]
Michael A. Robb,*,[†] and Massimo Olivucci*,[§]

Contribution from the Dipartimento di Chimica "G.Ciamician" dell' Università di Bologna,
Via Selmi 2,40126 Bologna, Italy, and King's College London, London WC2R 2LS, United Kingdom

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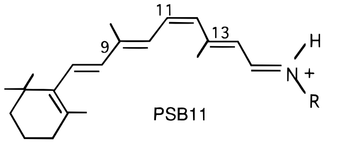
Abstract: In this paper, ab initio CASSCF computations are used to investigate the photoisomerization path of the protonated Schiff base (PSB) 4-*cis*-γ-methylnona-2,4,6,8-tetraeniminium cation: a five conjugated double bond model of the retinal chromophore of rhodopsin (the human retina visual pigment). We show that, after initial skeletal relaxation from the Franck−Condon region (which involves a large increase in the central C═C bond length), the system is "trapped" in an energy plateau on the S_1 energy surface which may be the origin of the "slow" *cis* → *trans* isomerization dynamics observed in retinal PSBs in solution. The energy plateau is absent in shorter retinal chromophore models which have a steeper S_1 isomerization path. The rhodopsin cavity (where the native chromophore is embedded) may have the effect of removing the energy plateau from the S_1 potential thus dramatically increasing the photoisomerization rate from picoseconds to femtoseconds.

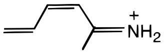
1. Introduction

The 11-*cis* retinal protonated Schiff base (PSB11) is the chromophore of rhodopsin (the human retina visual pigment).



PSB11

The photoisomerization of PSB11 to its *all-trans* isomer (PSBT) is one of the fastest chemical reactions observed so far.[1] In particular, photoexcitation of PSB11 in rhodopsin yields a transient fluorescent state with a lifetime of 50−60 fs.[2,3] After this state is left, ground-state PSBT is formed within 200 fs.[4] In contrast, the photochemistry of free PSB11 in solution is 2 orders of magnitude slower: in methanol, PSB11 has a ca. 3 ps fluorescence lifetime and PSBT is formed in 10 ps.[5] Similar excited-state lifetimes have been reported for the PSBT[6,7] and 13-*cis* retinal protonated Schiff base (PSB13)[6] chromophores.



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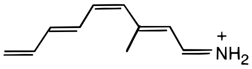

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Recently we have investigated the structure of the S_1 energy surface of the *short* PSB11 model 2-*cis*-penta-2,4-dieniminium cation (and its α-methylated form **1**).[8] A minimum energy path (MEP) computation shows that the relaxation on S_1 occurs along a *barrierless* path which connects the Franck−Condon (FC) structure to a low-lying S_1/S_0 crossing. Formation of the ground state trans photoproduct occurs via decay at the crossing where the system has developed an ca. 80° twist about the central C═C bond. Semiclassical trajectory computations demonstrate that such energy surface leads to a 20−40 fs excited-state lifetime with photoproduct formation occurring on a ca. 100 fs time scale.[9] Thus, the time scale for the transformation of the *short* model is much shorter of that of solution PSB11.

In this paper, ab initio CASSCF computations with 10 electrons in 10 π-orbitals CAS and the 6-31G* basis set[10] are used to investigate the structure of the S_1 MEP of the *longer* PSB11 model **2** (4-*cis*-γ-methylnona-2,4,6,8-tetraeniminium

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[†] King's College London.

[§] Università di Bologna.

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Table 1. Ground State Vibrational Frequencies (ω_i) and Relative S_1 Resonance Raman Intensities for the Totally Symmetric Modes of the CAS-SCF/6-31G* Optimized Geometry of 4-*cis*-γ-Methylnona-2,4,6,8-tetraeniminium Cation[d]

ω_i (cm^{-1})		relative intensities		
exp[b]	calc[a]	exp[b]	grad[c]	assignment
968	939	0.2	0.1	C−H rock
1005	974	0.2	0.2	C−H rock
1016	1044	0.2	0.1	C−C stretch + C−H rock
1190	1188	0.2	0.2	C−C stretch
1218	1262	0.4	0.1	C−H bend
1237	1273	0.4	0.5	
1276	1311	0.2	0.2	C−C stretch + C−H bend
1439	1474	0.1	0.2	C−H bend
1556 (br)	1580−1628−1630	1.0	0.4−0.7−1.0	C=C stretch + C=N stretch
1658	1680	0.1	0.3	C=C stretch

[a] Computed at the B3LYP/6-31G* level of theory. [b] Data for the protonated *n*-butylamine retinal (see ref 13); br = broad. [c] The intensities are computed using the gradient formula in ref 12. [d] Notice that the most intense peak corresponds to the 1630 cm^{-1} stretch and that the shape of the spectra is reproduced.

cation). *This is the first MEP computation attempted on a realistic retinal chromophore model.* We show that, after initial skeletal relaxation from the FC point, **2** is "trapped" in an energy plateau (absent in model **1** where only an inflection region is detected) on the S_1 energy surface. Model **2** does not include solvent, cavity or counterion, thus this finding suggests that the intramolecular force field of the PSB11 cation is at the origin of its slower excited-state dynamics.

2. Computational Methods

MEP computations, *in the full space of geometrical coordinates,* were carried out using a combination of the IRD and IRC methods as already discussed in previous work.[11] The MEP is computed by starting from the totally symmetric FC point of the system. Although accurate frequencies computations for model **2** are out of reach, the path has been determined by using a procedure which biases the search of energy valleys (see ref 8 for details). In particular, to avoid following totally symmetric ridges rather than real valleys, the MEP search was started using a fully asymmetric vector (generated via torsional deformation of the intersection structure) as the initial guess.

The quality of our retinal protonated Schiff base model has been tested by computing the resonance Raman (RR) spectra[12] and estimating the absorption and fluorescence λ_{max}. Remarkably the computed frequencies and RR intensities (see Table 1) are in qualitative agreement with those observed for PSB11 in solution.[13] Similarly the estimated[14] S_1-S_0 energy gap at the FC structure and 1.5 au MEP structure yield absorption and fluorescence λ_{max} values (428 and 618 nm) close to the values observed for PSB11 and PSBT in hexane (457 and 620 nm)[15] or methanol (442 and 675).[5,15] These data suggest that the general structure of the energy surface of the isolated cation **2** may be similar to that of PSB11 in solution. This view is also supported by the fact that the absorption and fluorescence λ_{max} for PSBT in an apolar environment (hexane, hexadecane) are only ca. 10 nm higher and 50 nm lower that in methanol[15] (which indicate energy differences <3−4 kcal mol^{-1}). Furthermore Becker et al.[16] have shown that the photoisomerization quantum yields of different retinal protonated Schiff base isomers in hexane and methanol are similar (0.23 and 0.25, respectively for the PSB11 → PSBT conversion).

3. Results and Discussion

In Figure 1 we report the S_2, S_1, and S_0 energy profiles along the S_1 MEP. These profiles show the same general features observed for the short PSB11 model of ref 8: (i) the S_2 covalent ($2A_g$-like) state is higher than the S_1 ionic state (^1B_u−like),[17] (ii) the reaction path is substantially barrierless, and (iii) the path terminates at a S_1/S_0 real crossing at a ca. 90° twisted geometry. The presence of a conical intersection[18] (i.e., a real crossing) between the S_1 and S_0 potential energy surfaces of models **1** and **2** would provide a clear-cut explanation of the chromophore fast radiationless decay. However, a comparison of the energy profiles for **1** (full squares) and **2** (open squares) reveals that the long PSB11 model enters an energy plateau after initial relaxation away from the FC region. The reaction coordinate analysis reveals that the plateau is entered soon after skeletal (i.e., stretching) relaxation which leads to a large increase in the central C=C bond length. This feature is illustrated in Figure 2 where we give a schematic two-dimensional view of the MEP and energy surface for compound **2**.

Model **2** *cis* → *trans* deformation is not involved in the first part of the MEP but dominates after skeletal relaxation. However, in contrast with the short model, the increase in twisting angle leads only to a very limited change in energy up to a 40 degrees twist. Thus in the plateau region there is almost no force in the torsional coordinate. Indeed, the methodology used cannot exclude the presence of a small (<2 kcal mol^{-1}) barrier in this region. This behavior arises from the fact that S_1 central C=C bond expansion achieved by **2** (1.48 Å) is smaller than that achieved by **1**[8] (1.52 Å).

The MEP coordinate shows a *single* torsional deformation about the central double bond of the structure. This result suggests that in the *isolated* PSB11 there is no driving force for the previously proposed "volume saving" isomerization

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[14] The dynamic correlation energy correction to the CASSCF energy gap is conveniently evaluated using the PT2F method available in MOLCAS (*MOLCAS, Version 3*; Andersson, K.; Blomberg, M. R. A.; Fülscher, M.; Kellö, V.; Lindh, R.; Malmqvist, P.-A.; Noga, J.; Olsen, J.; Roos, B. O.; Sadlej, A. J.; Siegbahn, P. E. M.; Urban, M.; Widmark, P. O. University of Lund, Sweden 1994). However, compound **2** is to large for such a calculation. Thus we estimate the magnitude of the correction by performing PT2F computations at the FC and S_1 minimum (planarity constrained) points of the lower homologue *all-trans* hepta-2,4,6-trieniminium cation. This yield a −15.6 and −8.2 kcal mol^{-1} correction for the energy gap at FC and plateau region (MEP point at 1.5 au), respectively.

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[16] Freedman, K. A.; Becker, R. S. *J. Am. Chem. Soc.* **1986**, *108*, 1245−1251.

[17] MRSD-CI computations by Davidson et al. show that the character of S_1 and S_2 is *mostly* ^1B_u-like and $2A_g$-like, respectively (Racine, P.; Davidson, E. R. *J. Phys. Chem.* **1990**, *94*, 7013−7020). Our results show that such characters remain the same all along the MEP (see point 3 of the Supporting Information for details).

[18] Warshel and Weiss (Weiss, R. M.; Warshel, A. *J. Am. Chem. Soc.* **1979**, *101*, 6131−6133) were the first to suggest that an *unusually large* decay probability, which prevents excited-state equilibration, is required to explain the observed high quantum yield and short reaction time in rhodopsin photoisomerization. More recently, on the basis of the experimental evidence, Mathies et al. suggested that the extremely fast isomerization of PSB11 in rhodopsin can be explained by a Landau−Zener dynamical internal conversion process (Wang, Q.; Schoenlein, R. W.; Peteanu, L. A.; Mathies R. A.; Shank C. V. *Science* **1994**, *266*, 422−424). The involvement of a conical intersection in the photoisomerization of PSB11 has been suggested before on the basis of theoretical arguments (see: Michl, J.; Bonacic-Koutecky, V. *Electronic Aspects of Organic Photochemistry*; Wiley: New York, 1990).

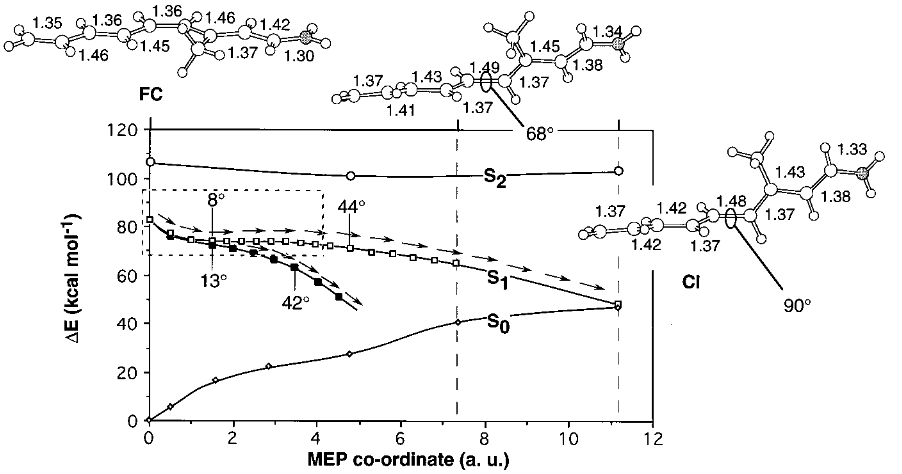

Figure 1. Energy profiles along the S_1 MEPs describing the relaxation from the FC points of **1** (full squares) and **2** (open squares). The MEP of **1** is from ref 8. Open circles and diamonds show the S_2 and S_0 energies along the MEP of compound **2**. The structures (geometrical parameters in Å and degrees) document the progression along this path. CI is the real crossing (conical intersection) structure. The framed region of the S_1 energy profile is represented in two dimensions in Figure 2.

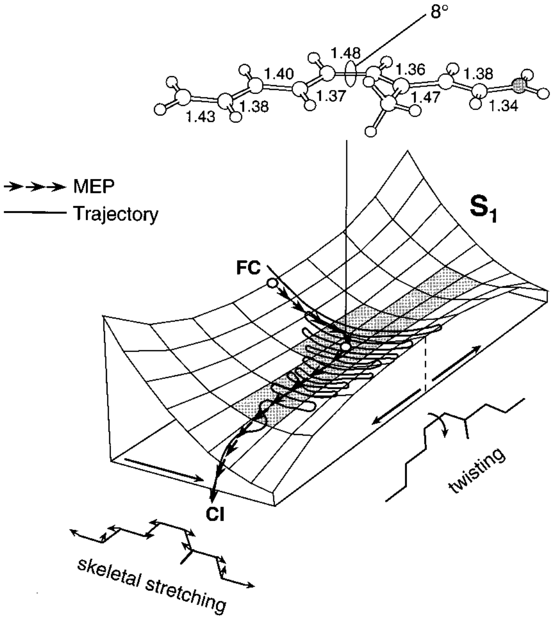

Figure 2. Structure of the S_1 energy surface along the MEP of compound 2 (framed region in Figure 1). The full line represents a *hypothetical* classical trajectory released near FC with a small initial torsional perturbation. The shaded area corresponds to the energy plateau discussed in the text. The 8° twisted MEP structure (geometrical parameters in Å and degrees) is located at the end of the skeletal relaxation and beginning of the torsional relaxation. Notice that the curvature of the surface along the twisting coordinate changes (as a function of the stretching coordinate) from positive (near FC) to zero (near the 8° twisted structure) to negative (at larger C=C expansions).

mechanisms which involve the simultaneous rotation about different bonds.[19] However our data cannot exclude that such mechanisms operate in rhodopsin.

4. Conclusions

The computer modeling of the *cis* → *trans* isomerization dynamics of PSB11 and PSBT embedded in the corresponding proteins rhodopsin and bacteriorhodopsin is a "grand challenge" problem. Given the exceptionally high cost of accurate computations, past work in this area (see for instance refs 20−22) has relied on reaction potential energy surfaces computed at the QCFF/PI and semiempirical levels of theory and, in some cases, hypothetical chromophore isomerization coordinates. In the previous section we have reported an excited-state MEP which provides an unambiguous *cis* → *trans* isomerization coordinate for PSB11.

Model **2** is too large for ab initio semiclassical trajectory computations. Nevertheless the computed MEP suggests the dynamic behavior illustrated in Figure 2.[23] After fast relaxation from the FC region the initially planar system performs many skeletal oscillations. During this motion vibrational energy redistribution from the totally symmetric (stretching) modes to the torsional mode takes place due to the anharmonicity of the S_1 surface. Thus, the trajectory slowly "expands" along the energy plateau (via central bond torsion) and, finally, accelerates out of it (see trajectory in Figure 2). The energy plateau may be assigned to the picosecond "fluorescent state" observed in solution PSB11. We argue that one important effect of the rhodopsin cavity (where the PSB11 chromophore is embedded) can be that of removing the long energy plateau from the S_1 potential thus dramatically increasing the photoisomerization rate. Indeed, the short PSB11 model **1** has no energy plateau along the MEP (see Figure 1 and ref 8), and the computed time scale[9] for its transformation is much shorter of that observed in solution PSB11.

A slight barrier placed along the plateau would further increase the excited-state lifetime. The existence of such a barrier (ca. 1.5 kcal mol^{-1}) has been recently demonstrated for PSBT and PSB13 in methanol solution.[6] The fact that the computed MEP shows a long energy plateau rather than a barrier may be due to different factors including (a) the neglected interactions with the solvent and counterion, (b) the neglected double bond and (c) the limit in computational accuracy.

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(19) These are the hula-twist (Liu, R. S. H.; Browne, D. T. *Acc. Chem. Res* **1986**, *19*, 42−48.) and the bicycle-pedal (see ref 20a) mechanisms.

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(23) Ab initio semiclassical trajectory computations on **1** (see ref 9) demonstrate that the crossing region is entered at crossing geometries similar to the one located by following the S_1 MEP. In the paper we assume that this is also true for model **2**.

Dynamics simulations carried out using model potentials indicates that an excited-state barrier may also arise because of the cavity or solvent friction.[20b] However, the barrier observed in PSBT and PSB13 seems, at least in part, due to an intramolecular electronic factor.[6]

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Supporting Information Available: Cartesian coordinates of all structures discussed in the text, one table (Table 2) containing the absolute and relative energies for the reported structures, and three tables containing the distribution of the π-electrons along the S_1 MEP (7 pages). See any current masthead page for ordering and Internet access instructions.

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