A Quantum Chemical Study on the Mechanism of Cis–Trans Isomerization in Retinal-like Protonated Schiff Bases

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Abstract: The dynamics of the photochemical cis–trans isomerization in retinal-like protonated Schiff bases is studied by means of MNDO/CI calculations. The aim of these calculations is a better understanding of the mechanism which accounts for the highly regioselective and efficient photoisomerization of rhodopsin and bacteriorhodopsin in the primary step after light absorption. Calculations on the model compound protonated 1-imino-2,4-pentadiene show that the regioselectivity and efficiency of this reaction can be explained from the intrinsic properties of this molecule. Whereas it is found that the protonated Schiff bases have a lowest $^1B_2g$-like excited state, the second $^1A_2g$-like excited state is particularly photochemically labile. This latter state serves in diminishing (or even removing) the barrier on the potential energy surface of the initially excited state, thus enhancing the rate for the phototransformation. The transition probability for a radiativeless return of the excited molecule to its ground state was evaluated explicitly for the photoisomerization around the various double bonds in protonated 1-imino-2,4-pentadiene by means of semiclassical trajectory calculations. The transition probability depends on the energy gap between the ground and excited state and the nonadiabatic coupling between these states for the 90° twisted molecule. The extent of the energy gap is related to the distance from the twisted bond to the nitrogen atom. The role of this electron-deficient nitrogen atom is to stabilize the polarized resonance structure which describes the 90° twisted molecule in the excited state. When this stabilization is too strong, the polarized resonance structure drops below the diradical ground state which results in an increased energy gap and a reduced efficiency of photoisomerization. The possibility for a concerted bicycle pedal isomerization around two double bonds is investigated by a calculation of the two-dimensional energy surfaces and nonadiabatic couplings for a combined rotation around these two bonds. A strictly bicycle pedal motion is found to be unfavorable, but a mechanism which involves a complete rotation around one double bond assisted by a partial rotation of the second double bond might provide a route for the photoisomerization of the retinylidene chromophore in the confined environment of a protein. Calculations on a model compound of the protonated Schiff base of retinal show that the extent of the stability of the 90° twisted molecule in the excited state can be directed by locating external point-charges around the molecule. In nature, these point-charges are provided by the protein opsin, and their presence has been used to explain the opsin shift of the various intermediates in the photocycles of rhodopsin and bacteriorhodopsin. Our calculations show that these external point-charges also have an important impact on the energy gap between the ground and excited state and, therefore, on the regioselectivity and efficiency of photoisomerization in the retinylidene chromophore. The primary step in the photoisomerization in bacteriorhodopsin can be best understood from an external point-charge model with a negative counterion near the protonated nitrogen atom and an ion pair near the cyclohexene ring.

I. Introduction

The first step of the vision process involves the absorption of light by rhodopsin which transduces the light information into a nerve signal.1 Bacteriorhodopsin acts as a light-driven proton pump in the purple membrane of the halophilic microorganism Halobacterium halobium. It converts the light energy into an electrochemical gradient across the cell membrane.2,3 Rhodopsin and bacteriorhodopsin have in common that they are constructed from a covalent linkage between a protonated Schiff base of retinal and the e-amino group of a lysine residue of the apoprotein opsin. In both systems, the primary step after light absorption involves a photochemical cis–trans isomerization of the retinylidene chromophore.1 This process is known to proceed on a (sub)picosecond time scale with a high quantum yield of light absorption.4 The photoreceptor proteins contain a chromophore, the retinylidene, which can undergo a cis–trans isomerization in the excited state (e.g., $\Phi = 0.7$ for rhodopsin).5

In rhodopsin, the conformation of the retinylidene chromophore is 11-cis and upon light absorption it is isomerized to the all-trans form (bathorhodopsin). This conversion is characterized by a red shift of the UV absorption maximum from 498 to 548 nm. Bathorhodopsin is stable below $-140^\circ C$ and its ground-state energy is 16 kcal/mol higher than that of Br$_{248}$.6

Some questions that arise are how opsin directs the regioselectivity of the cis–trans isomerization and what conditions are necessary to account for the unusually rapid and efficient reaction. This is especially intriguing when it is borne in mind that the retinylidene chromophore has only a very limited space within the pocket of the surrounding protein. A thorough understanding of these features asks for a detailed knowledge of the intrinsic characteristics of the retinylidene chromophore. Once these are known, it may be deduced how the protein can direct the regioselectivity and increase the efficiency of the photoisomerization.

Freedman and Becker7 studied the photoisomerization of various isomers of the n-butyllamine Schiff base of retinal in detail. They

(4) There are strong indications that before the ground-state product $K_{60}$ isomer is formed ("J") directly from Br$_{248}$ within 0.7 ps, which rapidly converts into $K_{60}$ within a few picoseconds. This latter transformation probably involves conformational changes of the protein. Nuss, N. C.; Zinth, W.; Kaiser, W.; Kölling, E.; Oesterhelt, D. Biochim. Biophys. Acta 1986, 83, 967.