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Hula-twist, a Supramolecular Photoisomerization Reaction Mechanism in Reactions of Photosensitive Biopigments

Robert S. H. Liu*
Department of Chemistry, University of Hawaii, 2545 The Mall, Honolulu, HI 96822, USA

Hula-twist is a volume-conserving photoisomerization reaction mechanism postulated in 1985 to account for the rapid photoisomerization of the retinyl chromophore in rhodopsin. The requisite stereochemical consequence of simultaneous isomerization of a double bond and an adjacent single bond has recently been demonstrated in isomerization of pre-vitamin D in an organic glass and by many other examples of organic systems already reported in the literature. This paper reports the consequence in applying the mechanism to the primary photochemical process of several photosensitive biopigments: bilirubin, photoactive yellow protein, bacteriorhodopsin and rhodopsin. It is shown that the anchored nature of the chromophores must first be taken into consideration.

Key words: photoisomerization, hula-twist, bicycle-pedal, photoactive yellow protein, bacteriorhodopsin, rhodopsin

INTRODUCTION

Torsional relaxation is the commonly accepted mechanism for photoisomerization (Fig. 1) [1]. However, ever since the first psec time-resolved fast kinetic study for the visual pigment rhodopsin in 1972 [2], it has often been asked how the seemingly volume demanding 11-cis to all-trans isomerization can take place in the short time period normally associated with molecular vibrations. The issue has become more relevant when instrument resolution has since narrowed the time required for isomerization from <6 psec to <100 fsec [3].

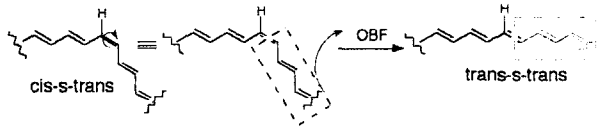

Figure 1. The conventional mechanism of photoisomerization, torsional relaxation, or one-bond-flip (OBF), resulting in turning over of one-half of the molecule.

In 1976, Warshel first proposed the intriguing volume-conserving mechanism known as the bicycle-pedal (BP) mechanism (top, Fig. 2) [4]. In it, the two alternating double-bonds undergo concerted BP-like rotations. This model was later modified to one where a double bond isomerization is accompanied by partial twisting of several single and double bonds (none more than 90°) [5]. In 1985, Liu and Asato proposed an alternative volume-conserving isomerization process, the Hula-twist (HT) process (bottom, Fig. 2), in which two adjacent bonds (a pair of double and single bonds) twist concertedly giving a product from simultaneous conformational and configurational isomerization [6]. For some time no experimental evidence demonstrating two double bond isomerization (for BP) or a double bond and a single bond isomerization (for HT) appeared, i.e,: no supporting evidence were available for either case. There were, however, theoretical results suggesting that HT is a low energy pathway [7] and that the minimum energy pathway of relaxation of an excited conjugated polyene passes through a geometry (conical intersection) identical to that of the HT process [8,9].

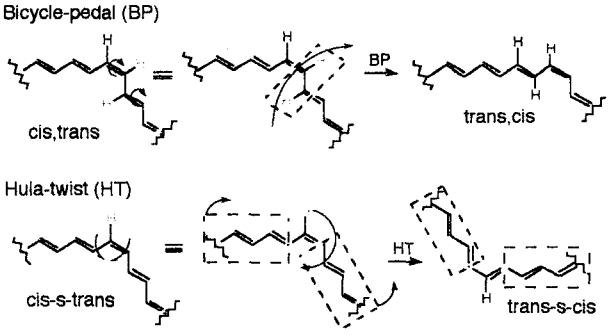

Figure 2. Two different volume-conserving mechanisms for photoisomerization. Top: the bicycle-pedal (BP) process involving the turning over of two C-H units. Bottom: the Hula-twist (HT) process involving the turning over of one C-H unit.

In 1998, Fuss and coworkers reported that in photoisomerization of pre-vitamin D in an organic glass (liquid nitrogen temperature) the photoproduct has

*E-mail: rliu@gold.chem.hawaii.edu

exclusively the two bond isomerized feature that is consistent with the HT process [10]. Subsequently, Liu and Hammond surveyed the literature and reported the finding of several photochemical examples obtained in confined media that are consistent only with the involvement of HT [11]. The list expanded further in later publications [12,13]. By further taking into consideration that the conventional torsional relaxation mechanism (or one-bond-flip, OBF) for isomerization is highly viscosity dependent, sometimes eliminated entirely upon solidification of the media [14], Liu and Hammond postulated a dual mechanistic scheme for photoisomerization under different conditions [11]. Without media constraint (commonly in fluid solutions), the isomerization is likely to proceed by the conventional OBF mechanism. With a rigid medium (or another form of constraint), the more volume-demanding OBF process becomes inhibited, making instead the volume-conserving HT process the primary process for isomerization [12].

For a simple organic compound trapped within an amorphous (or even crystalline) solid, because of a lack of specific interactions between the host and the substrate, the direction of isomerization is likely dictated by the empty space immediately surrounding the substrate. Hence the involvement of a volume-conserving process such as the HT is highly probable. However, when the trapped polyene substrate interacts in a specific manner with the host (including the anchored nature of chromophores when protein bound), the difficulty in breaking such anchors could be a far greater restricting force than the limited space available for reaction. Therefore, while there appears to be considerable agreement of the photochemistry of confined polyenes with the HT process (including an isolated biomolecule such as bilirubin in solution [12,13]), literature on photoisomerization of protein-bound polyene chromophores show a less convincing need to invoke this mechanistic concept. Some of the most relevant recent experimental data are the X-ray crystal structures of several photoactive biopigments, (photoactive yellow protein, PYP, [15] bacteriorhodopsin, bR, [16] and rhodopsin [17]) and their primary photoproducts (PYP [18] and bR [19]). We would like to examine several of these cases in some detail.

DISCUSSION

A protein-bound polyene chromophore differs from a polyene trapped within the cavity of an amorphous solid in one important way. In addition to volume restriction for reactions of a protein-bound chromophore, one must now consider the effect of the anchored nature of the chromophore. Also the chromophore is usually linked to a tether that facilitates its movement within the fixed positions of the anchors. The tether can be a relatively long one such as the tetramethylene amino unit of a lysine residue in bR or rhodopsin, or a relatively short one such as the CH_2-S unit in PYP. The importance of the anchored and tethered nature of the protein-bound chromophores in determining their primary photochemical process was discussed in binding interactions of the isomeric chromophores [20,21] and in their primary photochemical processes [22]. This thought process is now applied to photoisomerization of PYP [23].

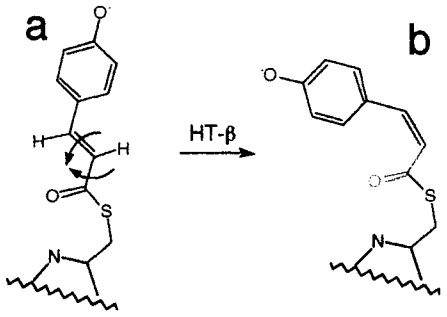

Figure 3. Hula-twist at H-β, resulting in substantial relocation of the phenoxy oxygen.

For the shorter tethered chromophore of PYP (Fig. 3a), HT would require the complete breakage of at least one of the two ends of the anchors (the phenoxy end) (Fig. 3b) an untenable situation for a short-lived excited singlet state. Instead, another volume conserving process that does not require the breakage of either anchor has taken over (Fig. 3). It proceeds in the form of a BP-like process but twisting only one double bond (plus another single bond).

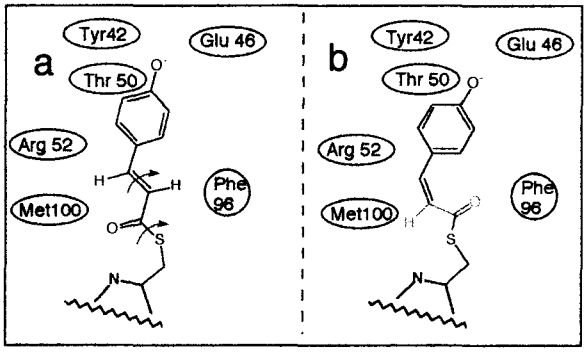

Figure 4. The chromophore structures from X-ray crystallography. (a) The PYP pigment chromophore and the surrounding amino acids; (b) the primary photoprodct, P_R, BL.

The X-ray crystal structure of the second more stable product, P_B, is also known [15], the chromophore

of which is similar to that shown in Fig. 3b. It has been shown that the conversion of P_R to P_B can be accomplished in two mechanistically distinguishable pathways [23].

In the case of bR, it was suggested that the longer tether could possibly allow the initial movement corresponding to the HT-14 process. However, the chromophore still would not be able to complete the HT-14 motion to form the much shortened (distance between the anchors) 13-cis-14-S-cis structure without breaking the anchors. Therefore, one suggested route is an immediate BP-14,16 motion following the half completed HT-14 motion [12]. The net result is introducing the 13-cis configuration and simultaneous absorption of the s-cis linkage by the butyl tether, i.e., in agreement with that observed for K [19] (Fig. 5).

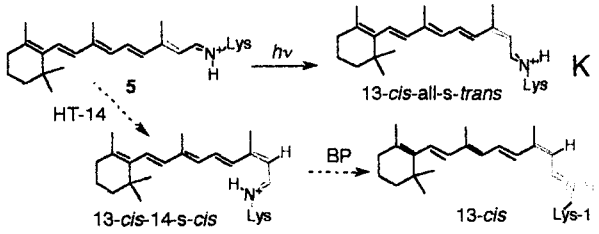

Figure 5. Top, the observed trans-bR to K isomerization. Bottom, the proposed HT-14 and BP-14,16 pathway to K.

A similar sequential volume conserving reaction has been suggested for rhodopsin (Fig. 6) [12,13]. In this case, the X-ray crystal structure of bathorhodopsin, the first stable primary photoproduct, is still unavailable although that of rhodopsin was reported nearly two years ago [17]. There were some indirect evidence suggesting possible involvement of the HT-12 process in the photoisomerization (through analog [24,25], modeling [26] and time-resolved Resonance Raman studies [27]). Kakitani has suggested a "twist-&-shear" mechanism directly converting 11-cis to all-trans [28] which appears to us to be similar to Warshel's modified BP process [5].

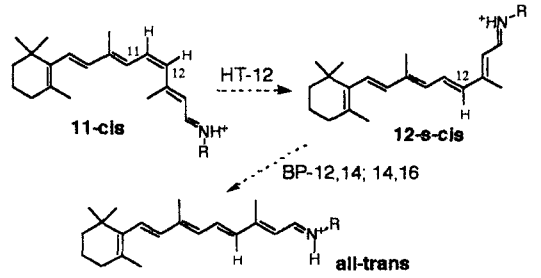

Figure 6. Postulated conversion of 11-cis rhodopsin to all-trans by consecutive HT and BP processes.

As pointed out above, we suspect HT is an undetectable higher energy process when the isomerization is carried out in solution. Such experimental difficulties should not be detrimental to theoretical studies. It will be meaningful to have theoretical guidelines addressing the relative importance (energy differences) of the possible isomerization pathways mentioned above. In addition to the scattered reports already in the literature [7-9], I am hopeful that more will be forthcoming in the near future.

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APPENDIX

For easier visualization of the parts that undergo rotation during the OBF and HT motion described in Figs. 1 and 2, the following cartoon figures are presented in Fig. 7).

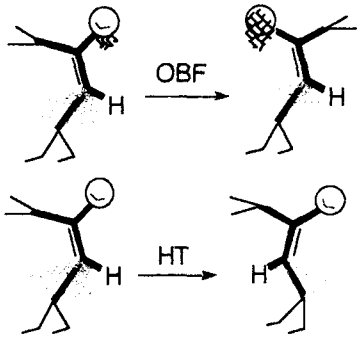

Figure 7. Cartoon figures representing one-bond-flip,OBF (upper) and hula-twist, HT (lower).

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