

Mechanochemistry

International Edition: DOI: 10.1002/anie.201611265
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Abstract: The quantum yield of a photochemical reaction is one of the most fundamental quantities in photochemistry, as it measures the efficiency of the transduction of light energy into chemical energy. Nature has evolved photoreceptors in which the reactivity of a chromophore is enhanced by its molecular environment to achieve high quantum yields. The retinal chromophore sterically constrained inside rhodopsin proteins represents an outstanding example of such a control. In a more general framework, mechanical forces acting on a molecular system can strongly modify its reactivity. Herein, we show that the exertion of tensile forces on a simplified retinal chromophore model provokes a substantial and regular increase in the *trans-to-cis* photoisomerization quantum yield in a counter-intuitive way, as these extension forces facilitate the formation of the more compressed *cis* photoisomer. A rationale for the mechanochemical effect on this photoisomerization mechanism is also proposed.

During the last decade mechanochemistry, that is, the modulation of chemical reactivity by mechanical forces, has grown considerably owing to the development of techniques that allow for a controlled application of an external force to single molecules and molecular materials.^[1] These techniques include atomic force spectroscopy,^[2,3] the use of force probes,^[4,5] and the insertion of the reacting molecule, that is, the mechanophore, into a polymer liable to be stretched mechanically^[6,7] or by sonication.^[8]

Most of the recent advances in mechanochemistry deal with thermal reactivity (that is, ground state) and, for instance, have shown that chemical bonds can be selectively activated,^[9] reactivity rules or trends changed,^[10] and chem-

iluminescence induced mechanically.^[11] In contrast, the effect of mechanical forces on photochemical (that is, excited state) reactivity remains substantially unexplored. In this regard, some studies on the optomechanical behavior of azobenzene have been published,^[12] while computational methods have been developed for determining the mechanically induced variation of the excitation energy of a chromophore.^[13,14] Furthermore, there are few studies on the effect of external forces on polymers, which demonstrate an increase in the photodegradation efficiency with mechanical load.^[15,16]

Conical intersections (CIs) between the potential energy surfaces (PESs) of different electronic states provide the photochemical funnels that mediate nonradiative decay.^[17] Moreover, the CI topography is known to determine fundamental aspects of photoreactivity.^[18] Recently, a model for understanding the effect of mechanical forces on the topography of CIs has been developed, providing qualitative information on the expected change in photochemical reactivity.^[19] Nevertheless, a quantitative prediction of such a mechanically induced reactivity change implies the simulation of the dynamic behavior of stressed excited-state chromophores. The explicit inclusion of external forces on the *ab initio* force field is a common computational strategy to perform dynamics simulations of stressed systems,^[20] although other strategies are also available.^[1]

The retinal protonated Schiff base chromophore (RPSB) of rhodopsin proteins undergoes an ultrafast photoisomerization of its central C11=C12 (for example, in animal visual pigments) or C13=C14 (for example, in microbial proton pumps) double bonds.^[21] These are often referred as the primary event in the photocycle driving the protein func-

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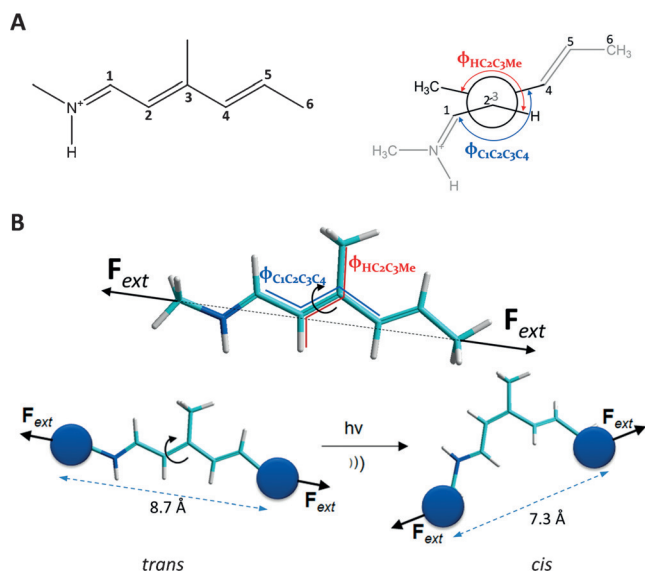
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tions.^[22] The photochemical properties of the retinal chromophore in its protein environment (for example, tunable absorption maxima, ultrafast photoisomerization and high photoisomerization quantum yield) have inspired the design of many molecular switches,^[23–27] as well as molecular motors.^[28,29] Therefore, owing to its biological and technological relevance, the RPSB constitutes an excellent candidate to study the influence of mechanical forces on its photoreactivity.

It has been shown that the penta-2,4-dieniminium cation (PSB3) provides a minimal model for retinal chromophore.^[30–34] Even in vacuo, PSB3 displays a barrierless PES that drives an ultrafast photoisomerization around its central C2=C3 bond, thus replicating some of the dynamic features observed in rhodopsins.^[23,35–39] For this reason, PSB3 has often been employed for computationally affordable dynamic studies providing useful information on the general behavior of RPSB and its possible applications.

Herein, we employ an *all-trans-N*-methyl-3-methyl-2,4-hexadieniminium cation (trisMe-PSB3) derivative featuring two terminal methyl groups to investigate the impact of external forces on the chromophore photoisomerization (see Scheme 1). Our aim is to investigate a situation in which the effect of macroscopic forces applied to a polymer incorporating a PSB3 mechanophore can be modeled by forces applied to its terminal methyl groups.^[40] In this context, the pulling force may be assumed to mimic the effect of a polymer chain in which the force over the mechanophore can be induced with sonochemistry, or by stretching a film (see Supporting Information for details).



Scheme 1. A) The trisMe-PSB3 derivative studied here. The two relevant torsional deformations are indicated as dihedral angles in a Newman projection. B) Pulling external forces applied to the terminal methyl groups are shown. The studied photoinduced *trans*-to-*cis* photoisomerization with added external forces provides a minimum model for describing the effect of polymer chains (represented by blue spheres) on the retinal chromophore when, for instance, ultrasound is applied.

To simulate the excited state dynamics of a molecular stressed system, we have implemented non-adiabatic molecular dynamics (NAMD) and Tully's fewest-switches algorithm in the quantum-chemistry software MOLCAS 8,^[41] along with a module that permits alteration of the ab initio quantum chemical force field to include the forces illustrated in Scheme 1 (see Supporting Information for details). All the electronic structure calculations have been performed with the multiconfigurational method CASSCF in which all the π electrons and π orbitals have been included in the active space (see Supporting Information for method details). A set of 60 NAMD trajectories for each applied force, ranging from 0 nN up to circa 3 nN, has been computed. Additionally, exploration of the topographical properties of ground and excited state PES has been performed.

In the absence of mechanical forces, our trisMe-PSB3 undergoes *trans*-to-*cis* ultrafast photoisomerization (S_1 lifetime ca. 200 fs) with a quantum yield of circa 0.55. The photoisomerization efficiency is related to the central bond torsions (that is, $\varphi_{C_1C_2C_3C_4}$ and $\varphi_{HC_2C_3Me}$, see Scheme 1) obeying the same rules as those previously observed for rhodopsin and bathorhodopsin,^[38] as well as in other PSB3 models.^[34] More specifically, our NAMD simulations without external forces reveal that trajectories isomerizing to the *cis* isomer are determined by the sign of the velocities (that is, direction of change) of $\varphi_{C_1C_2C_3C_4}$ and $\varphi_{HC_2C_3Me}$ at the S_1/S_0 hopping events: If $\varphi_{C_1C_2C_3C_4}$ evolves in the excited state by rotating clockwise (or counterclockwise), the velocity of $\varphi_{HC_2C_3Me}$ at the hopping point has to present the same momentum, that is, clockwise (or counterclockwise), for completing the isomerization (see Figure 1). In other words, both torsions present an in-phase motion (that is, same sign of the rotational velocities) in successful isomerization hops, but an out-of-phase motion (that is, opposite sign of the rotational velocities) for

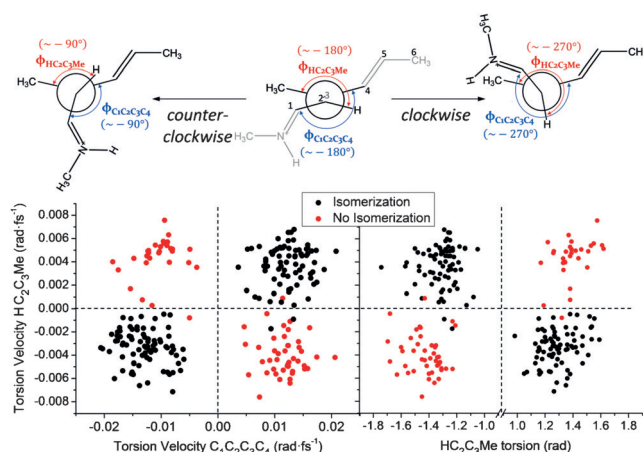


Figure 1. Definition of the clockwise and counterclockwise rotation in the trisMe-PSB3 system as well as the reference values of $\varphi_{HC_2C_3Me}$ and $\varphi_{C_1C_2C_3C_4}$ as defined here for FC and hopping regions (top). Plot of $\varphi_{HC_2C_3Me}$ torsion velocity at the hopping points versus $\varphi_{C_1C_2C_3C_4}$ torsion velocity (bottom left) and versus $\varphi_{HC_2C_3Me}$ torsion (bottom right). As a general rule, all the hopping events giving rise the isomerization exhibit an in-phase motion of $\varphi_{C_1C_2C_3C_4}$ and $\varphi_{HC_2C_3Me}$ torsions (black points), while out-of-phase motion (red points) determines the recovery of the initial *trans* isomer.

trajectories reverting to the *trans* isomer (See Figure 1). This rule is not determined by dynamic factors but, mainly, by electronic factors. More specifically, it is determined by the π -orbital overlap controlling the reconstitution of the C2=C3 double bond immediately after the decay. In fact, as reported in Ref. [38] and in the Supporting Information, the π -orbital overlap is not only modulated by twisting modes but also by the direction of change in C2–C3 bond length ($d_{C_2C_3}$). Longer (shorter) $d_{C_2C_3}$ values at the hop are associated with C2–C3 velocities leading to shorter (longer) bonds immediately after the decay, thus favoring (disfavoring) a π -orbital overlap increase and double bond reconstitution.

In the excited state, the $\varphi_{HC_2C_3Me}$ torsion presents several oscillations before hopping to the ground state. In contrast, the $\varphi_{C_1C_2C_3C_4}$ torsion does not present relevant changes in the velocity in S_1 , not only because it is a lower frequency mode but also because it is the main relaxation coordinate in S_1 , preventing its opposite (backward) variation during relaxation on S_1 (see Supporting Information for details). This makes the $\varphi_{HC_2C_3Me}$ torsion velocity determine the isomerization direction at the hopping points, since its oscillations (changing the torsion velocity sign) determine whether the $\varphi_{C_1C_2C_3C_4}$ and $\varphi_{HC_2C_3Me}$ torsions are moving in-phase or out-of-phase. This behavior is also observed qualitatively when the system is subjected to mechanical pulling forces, independently of the magnitude of the applied force. Nevertheless, the inclusion of the forces induces several quantitative changes as explained below. On the one hand, the hopping points for the *trans*-to-*cis* photoisomerization are reached with smaller progress of the $\varphi_{C_1C_2C_3C_4}$ torsion on S_1 (that is, the intersection space is reached with a smaller rotation of the central double bond), this effect being more pronounced as the force magnitude increases. On the other hand, the $\varphi_{HC_2C_3Me}$ torsion is oppositely more advanced at the hopping points, permitting the system to reach the intersection space when the overlap between the two interacting π -orbitals across the reactive C2=C3 bond is close to zero, and therefore $\varphi_{HC_2C_3Me} + \varphi_{C_1C_2C_3C_4} \approx -180^\circ$ for clockwise and $\approx -540^\circ$ for counterclockwise rotation (See Figure 1). In this way, the mechanically restrained evolution of $\varphi_{C_1C_2C_3C_4}$ torsion in the excited state is, to some extent, compensated with the higher torsion of $\varphi_{HC_2C_3Me}$.

Additionally, $d_{C_2C_3}$ at the hopping points increases with increasing force as should be expected owing to the strain directly affecting to the main chain of the chromophore (See Supporting Information for detailed analysis of $d_{C_2C_3}$ variation with mechanical force).

To get insight on the effect of the mechanical forces in the CI of trisMe-PSB3, the minimum energy CIs with explicit inclusion of external forces have been determined for the range of studied force magnitudes (see Supporting Information). We observe that the applied pulling forces provoke an equivalent structural effect for the minimum energy CIs as those observed dynamically for the hopping points, that is, the $d_{C_2C_3}$ value increases with the force magnitude along with a smaller value of the $\varphi_{C_1C_2C_3C_4}$ and a larger value of $\varphi_{HC_2C_3Me}$. The reason for this behavior is simple; the mechanical forces weaken the central C2=C3 bond owing to their direct effect on the stretching coordinates. Additionally, the forces oppose

the $\varphi_{C_1C_2C_3C_4}$ torsion towards the *cis* isomer, because this motion implies the decrease of the terminal methyl–methyl distance. Consequently, owing to the mechanical restraint generated on $\varphi_{C_1C_2C_3C_4}$, the minimum energy CI is reached by compensating with a larger change of $\varphi_{HC_2C_3Me}$, reaching a zero overlap of the two π -systems as explained above.

The computed manifold of 60 trajectories for each force magnitude is shown in Figure 2 as a function of the $\varphi_{HC_2C_3Me}$ coordinate. It can be seen that, as the external force increases, the fraction of isomerizing trajectories (that is, quantum yield) also increases, going from circa 55% in the case of $F =$

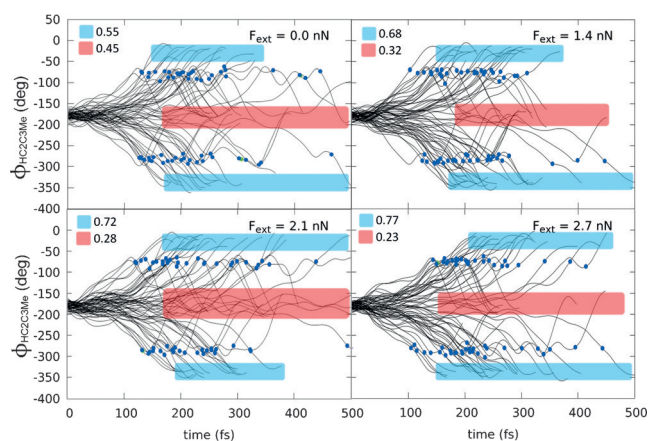


Figure 2. Plot of the 60 NAMD trajectories computed for each force magnitude (0.0, 1.4, 2.1 and 2.7 nN), as a function of $\varphi_{HC_2C_3Me}$ coordinate (deg). The hopping points are highlighted with blue dots. The fraction of trajectories giving rise to photoisomerization (blue) or returning back to the *trans* isomer (red) is indicated.

0 nN, to circa 80% for $F = 2.7$ nN. To understand this change in the quantum yield, it is necessary to investigate how the applied force modulates the relationship between the velocities of the key torsional coordinates ($\varphi_{HC_2C_3Me}$, $\varphi_{C_1C_2C_3C_4}$).

As anticipated above, an in-phase relationship between $\varphi_{HC_2C_3Me}$ and $\varphi_{C_1C_2C_3C_4}$ at the time of the hop increases the isomerization probability of a trajectory.^[34]

An applied force must affect the factors determining such phase relationship. While a detailed analysis of these factors is not trivial and goes beyond the scope of the present work, these may correspond to a change in the initial condition distribution, a change in excited state frequency and amplitude of $\varphi_{HC_2C_3Me}$ with respect to $\varphi_{C_1C_2C_3C_4}$, or a change in the number of trajectories crossing the intersection space more than once (for example, recrossings of the intersection space occurring at larger $\varphi_{C_1C_2C_3C_4}$ values may favor an out-of-phase motion between $\varphi_{HC_2C_3Me}$ and $\varphi_{C_1C_2C_3C_4}$). Irrespective of the specific cause, our results show that increasing the pulling external force leads, on average, to smaller $\varphi_{C_1C_2C_3C_4}$ torsions at the hopping point, together with a shorter time spent in regions in which $\varphi_{C_1C_2C_3C_4}$ and $\varphi_{HC_2C_3Me}$ are out-of-phase.

These findings are apparent in Figure 3 in which the correlation between the $\varphi_{HC_2C_3Me}$ and $\varphi_{C_1C_2C_3C_4}$ is plotted for two sets of trajectories with 0.0 nN and 2.7 nN forces, respectively. The values of the $\varphi_{C_1C_2C_3C_4}$ torsion are smaller at the hop for the case of 2.7 nN external force. This is also

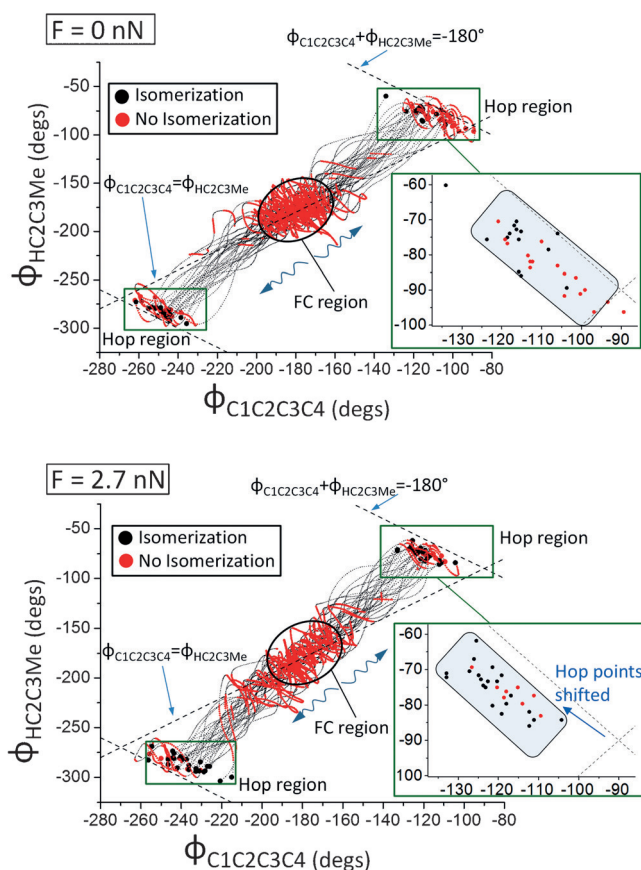


Figure 3. Evolution of $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ and $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$ torsions for $F=0$ nN and $F=2.7$ nN. All the trajectories start at the FC region ($\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ and $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4} \approx -180^\circ$), and evolve clockwise or counterclockwise towards the hopping regions (green frames). The trajectories are colored depending on the velocities of $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ and $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$, that is, red when they are out-of-phase and black when they are in-phase. The out-of-phase situation is especially relevant close to the FC and hopping regions. As it can be seen from the insets (right), the distribution of central bond torsion ($\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$) at the hopping points (denoted with black and red points for isomerization and no isomerization, respectively) is shifted to smaller torsions in the case of external forces (2.7 nN), while $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ are increased to compensate the lower $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$ torsion.

evident along the complete trajectories, in which the $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$ torsion evolves less than the $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ torsion (that is, the trajectories are shifted with respect to the $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4} = \varphi_{\text{HC}_2\text{C}_3\text{Me}}$ line, as indicated in Figure 3). Concurrently, the $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$ value at the hop increases with increasing force, which is consistent with the need to zero the overlap of the two π -systems involved in the C2=C3 bond forming/breaking.

To identify the out-of-phase regions, in Figure 3 we have plotted with red color the regions of each trajectory showing this feature. In both the 0.0 nN and 2.7 nN cases, there is an out-of-phase region expanding from the Franck–Condon (FC) region in which a large pyramidalization of C2 and C3 central carbon atoms is observed as has been described previously.^[34–38] Then, the system evolves along the excited state PES without apparent dephasing. When the system reaches regions close to the intersection space, it is observed

that some trajectories reach again an out-of-phase motion of the central torsions. Nevertheless, there is a substantial difference between those trajectories with and without pulling forces: The time spent in the out-of-phase situation is longer for the no-force manifold, being circa 1.5-fold longer than that when the force is 2.7 nN. This is in line with the phase relationship modification arguments discussed above. The change in phase relationship provides the explanation to the counterintuitive fact that external forces opposing the *trans*-to-*cis* evolution of the trisMe-PSB3 backbone have the effect of increasing the isomerization efficiency when the reaction is induced by light and driven by a barrierless PES (that is, occurs in the sub-picosecond timescale). Similar counterintuitive behavior has been observed previously for the ground state isomerization of difluorocyclopropanes, in which an extension force promotes the formation of the more contracted isomer.^[42]

In summary, we employed NAMD trajectories to show that mechanical forces applied to trisMe-PSB3 increase the *trans*–*cis* photoisomerization quantum yield with a rate of circa +0.1 per nN. This increase is counterintuitive, since the applied extension forces should in principle facilitate the recovery of the more extended *trans* isomer. On the contrary, the opposite is found, and the more compressed *cis* isomer is formed with a higher quantum yield.

Our computations support the idea that mechanical forces induce changes in the PES curvature and topography (that is, affecting the initial condition generation on the ground state PES as well as the total forces determining the motion on the excited state PES). Such changes would, in turn, modify the phase relationship between molecular modes, such as $\varphi_{\text{C}_1\text{C}_2\text{C}_3\text{C}_4}$ and $\varphi_{\text{HC}_2\text{C}_3\text{Me}}$, critical for determining the ground state evolution of the trajectory. We have also indicated that a modification in the $d_{\text{C}_2\text{C}_3}$ value or velocity at the hopping point may have an impact on the quantum yield. However, a mechanistic model for such an effect goes beyond this first report.

The results presented here suggest that mechanical forces may play an important role in controlling ultrafast photo-reactions affecting, in an unexpected way, the response to light irradiation of a mechanophore embedded in a polymer material. An exhaustive knowledge of the effect of the mechanical forces on the chromophore structure (for example, the intersection space) and excited-state dynamics may provide, as in the studied case, valuable information for designing novel photoactive molecular or macromolecular materials.

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Conflict of interest

The authors declare no conflict of interest.

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