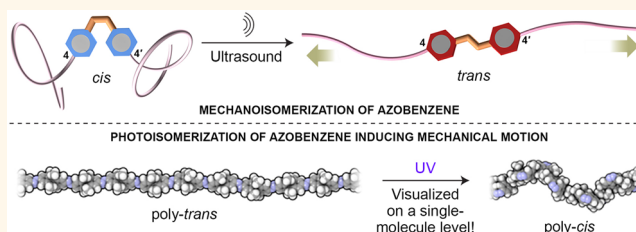


Watching Single Molecules Move in Response to Light

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ABSTRACT Nature has long inspired scientists with its seemingly unlimited ability to harness solar energy and to utilize it to drive various physiological processes. With the help of man-made molecular photoswitches, we now have the potential to outperform natural systems in many ways, with the ultimate goal of fabricating multifunctional materials that operate at different light wavelengths. An important challenge in developing light-controlled artificial molecular machines lies in attaining a detailed understanding of the photoisomerization-coupled conformational changes that occur in macromolecules and molecular assemblies. In this issue of *ACS Nano*, Bléger, Rabe, and co-workers use force microscopy to provide interesting insights into the behavior of individual photoresponsive molecules and to identify contraction, extension, and crawling events accompanying light-induced isomerization.



In recent years, polymer mechanochemistry has emerged as a useful tool for studying the reactivity of various chemical functionalities and species.^{1,2} In this approach, a functionality of interest is embedded within long polymer strands; extending the strands (*e.g.*, by applying ultrasound or mechanical stretching of polymer molds) generates tensile stress along the backbones of the strands, resulting in cutting the weakest bonds located near the center of the polymer. If this cleavage occurs in a controlled manner, the force-sensitive moiety is referred to as a mechanophore. In a seminal study in 2007, mechanochemical activation of benzocyclobutenes was shown to bias the pathways of a cycloaddition reaction, hence yielding otherwise forbidden reaction products.³ Mechanical forces have also been applied to activate selected photochromic compounds, thus revealing the mechanophoric nature of these moieties. For example, Davis *et al.* attached long polymer chains to two parts of the photoswitchable spiropyran group; applying mechanical force induced a ring-opening reaction, yielding a colored merocyanine isomer, typically generated with UV light.⁴ More recently, the same approach was applied to a structurally simpler photoswitch: azobenzene. Here, a *cis*-to-*trans* isomerization of an azobenzene appended with polymer strands at the two

para positions (see the Table of Contents graphic) was dramatically accelerated upon sonication, whereas no such effect was observed for a small-molecule analogue.⁵ This acceleration effect was attributed to mechanochemical weakening of the N=N bond, brought about by pulling the polymer strands in opposing directions. In this issue of *ACS Nano*, Lee *et al.*⁶ describe the opposite transformation: it was shown that exposing a *trans*-azobenzene polymer to UV light could dramatically decrease its aspect ratio in a study whose uniqueness lies in the direct visualization of the folding process at the single-molecule level.

Azobenzene is probably the most widely investigated molecular photoswitch. Upon exposure to UV light, the thermodynamically stable *trans* isomer is converted into the metastable *cis* form, whereas the opposite reaction can be triggered with visible (blue) light. This process can be repeated over many cycles, and it entails a relatively large change in the overall molecular geometry, thus providing the basis for constructing various photomechanical systems. In particular, the *trans*-to-*cis* isomerization decreases the distance between substituents at the two *para* positions by about 3.5 Å—a number that can be magnified by clever molecular designs. For example, building on their “molecular scissors” moiety,⁷

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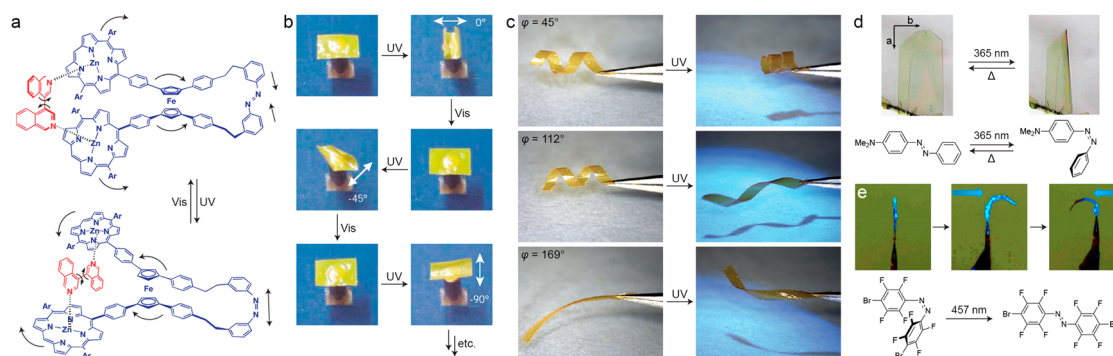


Figure 1. Selected examples of systems where azobenzene isomerization gives rise to large-amplitude motions. (a) Aida *et al.*'s light-operated molecular machine (blue) capable of mechanically twisting a small-molecule guest (red). Reproduced with permission from ref 8. Copyright 2006 Nature Publishing Group. (b) Light-controlled bending of Ikeda *et al.*'s photoresponsive polymer film. White arrows indicate angles of polarization of linearly polarized UV light; UV = 366 nm, vis = >540 nm. Reproduced with permission from ref 9. Copyright 2003 Nature Publishing Group. (c) Katsonis and Fletcher *et al.*'s photoresponsive springs powered by nonpolarized UV light. The symbol φ denotes the angle between the long axis of the ribbon and the average orientation of the liquid crystal director. Depending on the value of φ , UV-induced winding, unwinding, and helix inversion were observed. Reproduced with permission from ref 10. Copyright 2014 Nature Publishing Group. (d) Photoinduced folding of Koshima *et al.*'s 4-(dimethylamino)azobenzene crystals. Reproduced from ref 25. Copyright 2009 American Chemical Society. (e) Barrett and Friščić *et al.*'s perhalogenated azobenzene crystal and its light-induced bending. Blue arrows indicate the direction of irradiation. Reproduced from ref 26. Copyright 2013 American Chemical Society.

Aida *et al.* constructed a light-operated molecular machine that can perform large-amplitude motions, enabling twisting of other, smaller molecules (Figure 1a).⁸ Similarly, 4,4'-disubstituted azobenzenes have been incorporated within various polymeric architectures, which could then exhibit light-controlled shape changes^{9,10} (Figure 1b,c) and even perform rolling motions.¹¹ At the same time, increasing attention has been devoted to elucidating the photoswitchable properties of azobenzene crystals—as the examples in Figure 1d,e show, certain azobenzenes photoisomerize in the crystalline state—behavior previously thought to be unique to other families of molecular switches.¹² Finally, azobenzene has been introduced into biological systems: it has been demonstrated that various biomolecules functionalized with 4,4'-functionalized azobenzene “photohinges” can undergo large conformational changes when exposed to light.^{13,14}

Despite these creative uses of azobenzene and the fascinating applications that have emerged, the consequences of isomerization within macromolecular architectures at the molecular level could be better understood. Although significant attention has been devoted to

studying photoisomerization using surface probe microscopies,^{15–18} all these studies were performed on molecules strongly attached to the underlying substrates (consequently, no activities other than azobenzene switching were observed). Now, Lee *et al.* have tackled the challenge of investigating switching within molecules deposited *noncovalently* on a planar surface. To this end, they designed an azobenzene polymer and carefully engineered an experimental setup in order to concomitantly visualize light-induced switching and motion of as-deposited molecules at the single-molecule level.⁶

An interesting challenge will be to incorporate other molecular photoswitches within architectures analogous to those reported by Lee *et al.* and to study the response of the resulting polymers to external stimuli.

Switching azobenzene on surfaces is not an easy task;¹⁹ for example, intermolecular interactions between different azobenzene units,²⁰ lack of conformational freedom, and quenching of the photoexcited states by the underlying surface can all significantly hamper the photoisomerization process. However, Lee *et al.*'s elegant design takes all these potential obstacles into consideration: first, the polymer strands are decorated with long alkyl chains that isolate individual strands from one another (Figure 2a).²¹ Second, the azobenzene moieties along the polymer backbone are equipped with strategically positioned methyl groups—this approach introduces large twist angles between individual azobenzene units, effectively canceling out the undesired conjugation within a strand.²² Finally, the polymers are deposited onto an insulating monolayer of a surfactant (octadecylamine) rather than directly onto the semimetallic surface of highly oriented pyrolytic graphite (HOPG). This surfactant coating not only decouples the photoactive polymer from HOPG electronically but also facilitates its movement on the surface.

Figure 2b–d highlights the behavior of the photoresponsive polymer

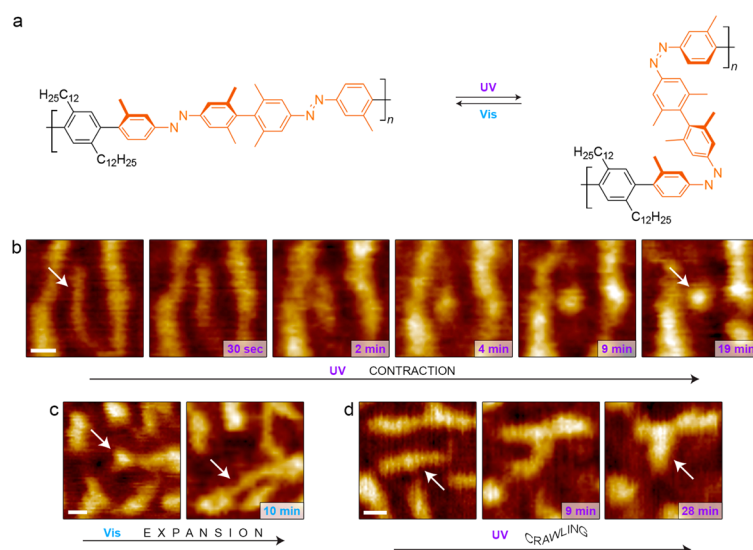


Figure 2. (a) Structural formula of a photoswitchable polymer investigated by Lee *et al.* (b) Series of surface force microscopy images showing UV-induced contraction of an individual polymer chain. (c) Surface force microscope images showing blue-light-induced expansion of a single polymer chain. (d) Ultraviolet-induced contraction accompanied by crawling of a single polymer chain. All scale bars correspond to 20 nm. Reproduced from ref 6. Copyright 2014 American Chemical Society.

under light as revealed by surface force microscopy. Upon UV light irradiation, the lengths of the polymers drastically decrease whereas their widths and heights increase, resulting in an overall transformation from a rod-like object to one that is disk-like. The striking contractions, such as the one shown in Figure 2b, could be attributed to UV-induced folding of the originally extended chains. Some of the folded chains unwind when exposed to blue light (Figure 2c), which is triggered by azobenzene reversion (Figure 2a). Unfortunately, the yield of this process was moderate, despite the rigid nature of the polymer structure. One example of a probably unexpected consequence of the switching process is shown in Figure 2d; here, a polymer molecule exposed to UV light was observed to “crawl” toward another polymer chain, to which it ultimately adhered.

Of course, many challenges, opportunities, and unanswered questions lie ahead, thus warranting increasingly active interest in this field in the coming years. An interesting challenge will be to incorporate other molecular photoswitches^{23,24} within architectures analogous to those reported by Lee *et al.* and to

study the response of the resulting polymers to external stimuli. An important aspect that could be explored is the effect of the underlying surface—for example, could the typically undesired surface—chromophore coupling be beneficial? What experimental methods could be used to investigate isomerization on curved (*e.g.*, nanoparticle) surfaces? An exciting challenge from the synthetic point of view would be to attach distinct objects (*e.g.*, fluorescence donors and acceptors) at the ends of the rigid polymers and to use light to modify the distance between them precisely. Finally, returning to where we started, the work of Lee *et al.* provides a link between polymer mechanochemistry and photoactuation of light-responsive polymers (see the Table of Contents graphic). It is most likely that the combined efforts from these two perspectives will provide us with a good fundamental understanding of the behavior governing this intriguing family of polymers.

Conflict of Interest: The authors declare no competing financial interest.

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