VOLUME 72, NUMBER 18

JOC Perspective

AUGUST 31, 2007

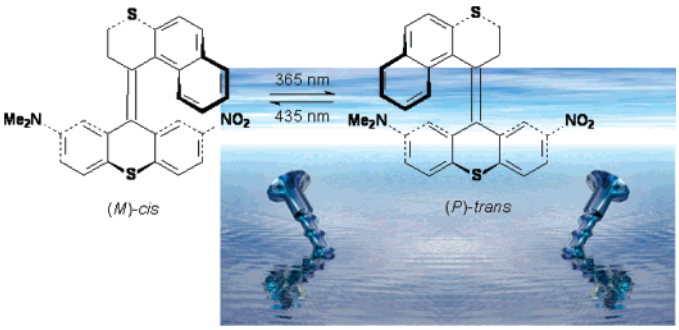
The Art of Building Small: From Molecular Switches to Molecular Motors

Ben L. Feringa

Laboratory of Organic Chemistry, Stratingh Institute for Chemistry & Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands

b.l.feringa@rug.nl

Received February 26, 2007



Molecular switches and motors are essential components of artificial molecular machines. In this perspective, we discuss progress in our design, synthesis, and functioning of photochemical and electrochemical switches and chemical and light-driven molecular motors. Special emphasis is given to the control of a range of functions and properties, including luminescence, self-assembly, motion, color, conductance, transport, and chirality. We will also discuss our efforts to control mechanical movement at the molecular level, a feature that is at the heart of molecular motors and machines. The anchoring of molecular motors on surfaces and molecular motors at work are discussed.

Introduction

Nature's delicately balanced biological systems comprise, without doubt, among the most fascinating of chemical structures. The elegance with which they perform light- and chemically driven functions is inspiring both in the complexity of their multicomponent and nanostructured assemblies and in the controlled use of energy achieved at the molecular level.

The source of nature's success rests in its exquisite control over molecular architecture, a level of a control, which sets an immense challenge to modern synthetic and supramolecular chemistry in areas as diverse as artificial light-harvesting systems and natural product synthesis. Molecular architecture is of central importance to total synthesis, and the elegance and efficiency of many synthetic routes to complex natural products serve testimony to the formidable accomplishments that have been achieved often in conjunction with new chemical transformations.

Beyond control of structure, in controlling function, nature sets yet another challenge and the introduction of complex externally controlled functionality in artificial systems requires a close collusion of both synthetic and physical sciences. Combining advanced synthesis with supramolecular chemistry, surface science, and molecular biology, exciting opportunities emerge beyond the molecule toward the development of smart molecular materials and machines.

A particular challenge rests in the control of the dynamics of molecular and supramolecular systems. It is an essential factor behind the tremendous advances made in, for example, molecular recognition and homogeneous catalysis. The control of motion is the decisive parameter in the operation of future molecular motors and machines. The ability to harness chemical energy to generate mechanical motion is one of the most fascinating aspects of many biological systems and one of the most challenging functions for chemists to imitate. Biological

10.1021/jo070394d CCC: $37.00
Published on Web 07/13/2007

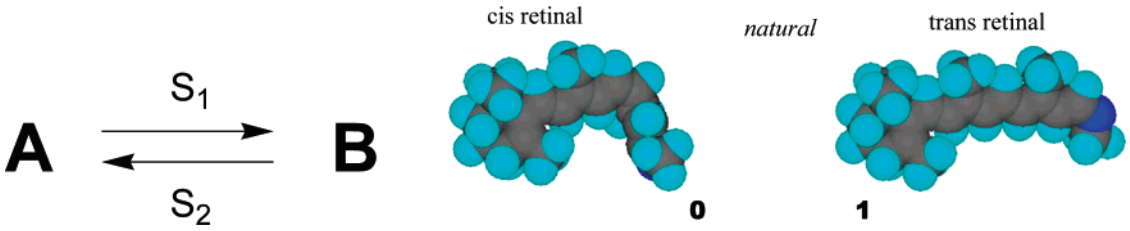


FIGURE 1. (a) Schematic representation of a switchable bistable system. **A** and **B** represent two different forms of the molecules, whereas S_1 and S_2 refer to different stimuli. (b) The cis−trans isomerization of retinal in the process of vision.

motors perform a wide range of vital functions using chemical energy to achieve stepwise linear and rotary motion. Compared to these delicate biological machines, our relatively recent attempts to control motion appear, at best, awkward.

Making the step from molecules to molecular systems, which incorporate several molecular components working in concert to perform complex and integrated functions at different hierarchical levels, requires that the extent to which we are capable of controlling dynamic processes takes on an entirely new level of sophistication. Our ability to control molecular motion will offer fascinating prospects in molecular sciences.

From a molecular perspective, I have had the pleasure of being at once awed and inspired by the fascinating design and breath taking elegance of nature's dynamic functions.[1] Together with many talented students, post-docs, and collaborators, I have sought to build systems with ever increasing complexity and functionality. From natural product synthesis to smart systems, however, our goal has been to achieve complexity through the use of simple components on which complexity can be constructed.

In this perspective, I do not intend to review all aspects of the science in detail, but rather to focus on key areas and examples that have caught my imagination over the last two decades. I will begin with an area close to my heart—switchable molecular systems, that is, molecules which respond to external stimulus, and show several examples of how simple concepts can be built upon to yield properties with a very wide range of application.

Switching Molecular States: From Structural Changes to Control of Function

There are numerous definitions of machines, and the direct comparison between machine-like functions in our macroscopic world and those at the molecular level is often not appropriate.[2] When we think of machines, however, we consider movement and the translation of mechanical motion into useful work essential features. This is as true of the nanoscale as it is of the macroscopic world. For a molecule to be useful as a machine, it is essential that switch or trigger elements are present, which respond to external stimuli and thereby impart a change in function to a molecular change. More than this though, the change must be directed or controlled. The stimulus we apply must allow us to not only induce a change in molecular structure but to do so specifically, both in the type of change and in its directionality. In short, we must be able to operate above randomness.[3] The ability to address functionality reversibly in a repetitive manner is essential in building molecular machines.

The fundamental basis of reversible molecular switching is bistability.[2,4−6] In a bistable system, two distinct forms of a molecule can be interconverted reversibly by the application of an external stimulus; however, the interconversion must not occur spontaneously, at least within the time frame of the operation. In such a molecular device, the external stimulus might be chemical, electrochemical, or photochemical. That each state is distinct is critical to the operation of the systems. If each state of the molecule can be "read" in a nondestructive manner, then the molecule can, in principle, function as a memory element in a digital information system using binary logic (Figure 1a).[6]

Miniaturization is a central paradigm of information technology, and the concept of the bottom-up approach promulgated by Feynman[7] has fuelled the quest for optical molecular switches, which promise molecular memory elements and processing by light, enabling ultrahigh density data storage. In this regard, the underlying processes of vision have proven to be a well-spring of inspiration. The primary step of vision is a light-induced cis-to-trans isomerization of an alkene moiety in a protein-bound retinal molecule.[8] This event—a change from a bent to a more linear shape of the molecule—simple though it is, initiates a cascade of events beginning with a change in the protein and ultimately a signal transmitted to the brain (Figure 1b).

Initial studies on photochromic organic materials[9] demonstrated that the basic condition of photochemical bistability can be fulfilled; however, application of photochemically controlled bistability has been dogged by poor thermal stability, fatigue, and destructive read-out. Achieving systems suitable for application requires high efficiency of the switching process, including both high quantum yields and fast response times.[4] A significant challenge is to develop molecular switches that operate effectively as part of more complex multifunctional systems and machines.[2]

In the following sections, we will consider several aspects of our work on molecular switches beginning with chiral optical molecular switches designed to address some of the fundamental problems indicated above. At the outset of these investigations, we had anticipated that a major advantage that chirality would introduce to optical switching is the possibility of nondestructive read-out of optically recorded information through monitoring changes in chiroptical properties at wavelengths remote from the wavelengths of light employed to achieve the switching of molecular states. In recent years, our attention has progressed to the use of molecular switches to control, in a reversible manner, a range of properties and functions including chirality, mechanical motion, color, luminescence, conductance, supramolecular organization, and transport. We have experienced that, although adding complexity and additional functionality to these systems presented considerable scientific challenges, this approach allows us to enter exceedingly exciting new territory in molecular design.

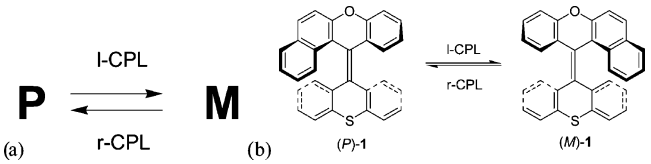


FIGURE 2. (a) A chiroptical molecular switch based on enantiomers as a binary storage element. (b) Switching of enantiomers of **1** with left (l-CPL) and right (r-CPL) circular polarized light.

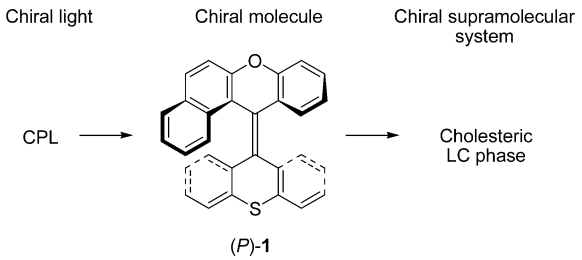


FIGURE 3. Amplification of chirality.

Chiroptical Molecular Switches

The chiroptical switch molecules we have constructed are helical-shaped overcrowded alkenes[10] (Figures 2−4). The switching principle in these systems is based primarily on the reversible change in helicity of the molecules. In overcrowded alkenes, such as **1**, the *cis*→*trans* isomerization is accompanied by the reversible interconversion between right- (*P*) and left-handed (*M*) helical forms, which represent two distinct states in a molecular binary logic element (Figure 2a).[11] Chiroptical switches can be either enantiomers (Figure 2b, switching between *P* and *M* enantiomers) or pseudoenantiomers (Figure 4b, switching between diastereoisomers *P* and *M*′).

It should not be forgotten that photochemical isomerization, which involves the interconversion between enantiomers, will always result in racemization, unless circular polarized light (CPL) is applied (Figure 2a). This apparent fundamental hurdle represented a considerable challenge to molecular design.

We were pleased to find that, out of four distinct subclasses of overcrowded alkenes synthesized, **1** satisfied the various requirements needed to demonstrate that, with right or left CPL, enantioselective switching in either direction is possible (Figure 2b). The enantiomers of **1** are sufficiently stable at ambient temperature ($\Delta G_{rac} = 25.9$ kcal mol^{-1}), fatigue resistant, and undergo a rapid photoracemization upon irradiation at 300 nm with nonpolarized light ($\Phi_{rac} = 0.40$, *n*-hexane). The experimental anisotropy factor g[12] (-6.4×10^{-3} at 314 nm) indicates that under ideal conditions an enantiomeric excess (ee) of 0.3% might be achieved. Indeed using CPL, we could accomplish deracemization and switching between photostationary states with experimental ee values of 0.07 and −0.07% for *P*-**1** and *M*-**1**, respectively.[13] Using linear polarized light (LPL), racemic *P*,*M*-**1** was obtained. In fact, this comprises a three-state chiroptical switch of racemic *P*,*M*-**1**, *P*-enriched **1**, and *M*-enriched **1** with the distinct property that all states can be reached by irradiating at a single wavelength simply by changing the chirality of the light employed (Figure 2b). As expected (based on g), the enantioselectivity was extremely low, but it was nevertheless sufficient to enable formation of (chiral) cholesteric liquid crystal (LC) films when **1** was employed as a dopant in a nematic LC material.[13] This system represents a method of chiral amplification, as the chirality of the circular polarized light is expressed in a small excess of one enantiomer of the molecular switch (the dopant) and amplified subsequently in the chirality of the helical organization of the induced cholesteric LC phase (the host) (Figure 3).

Much higher stereoselectivities can be reached upon switching between diastereomeric (or pseudoenantiomeric) bistable molecules (*P* and *M*′) (Figure 4a).[14] This can be accomplished by irradiation at two distinct wavelengths (λ_1 and λ_2) and, therefore, is the method of choice for practical application of chiroptical switches in functional materials and devices.

P-*cis*-**2** and *M*-*trans*-**2** have near mirror image circular dichroism (CD) spectra, which reflects the pseudoenantiomeric nature of the isomers and shows the dominance of overall helicity in determining the chiroptical properties (Figure 4b and 4c). The optimal wavelengths for forward and backward photoisomerization and the composition of photostationary states (and as a consequence the ratio of *M* and *P* helices) can be tuned through the nature and position of donor and acceptor

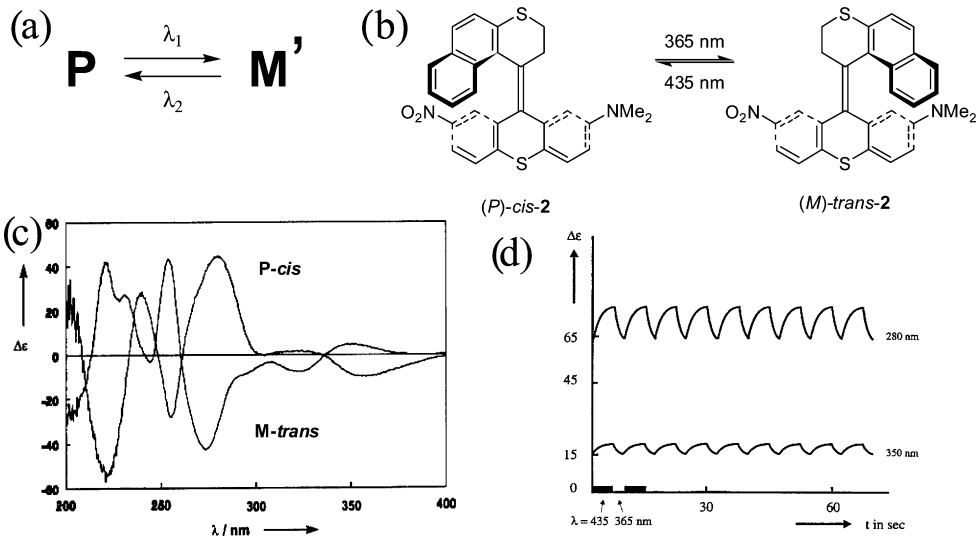


FIGURE 4. (a) Chiroptical molecular switch based on pseudoenantiomers (*P* and *M*′) as a binary storage element. (b) Irradiation of **2** at different wavelengths (λ_1 and λ_2) results in interconversion between *P* and *M* helicity. (c) CD spectra of the pseudoenantiomers *P*-*cis*-**2** and *M*-*trans*-**2**. (d) Repetitive switching of **2** as detected by CD spectroscopy.

substituents[14,15] (Figure 4b). The photomodulation of chirality in **2** is achieved readily by changing the wavelength of the light used, and repetitive switching cycles are easily monitored by chiroptical methods (Figure 4d). Large differences in isomer composition in the photostationary state are observed with ratios of *P*-**2** and *M*-**2** of 30:70 (at 365 nm) and 90:10 (at 435 nm). Further insight into essential structural parameters in these systems has guided us recently to develop chiroptical switches that show >99% stereoselectivity in both directions.[16]

Response time is a critical issue in the pursuit of applying molecular switches to practical applications. As for the ultrafast cis−trans photoisomerization of retinal in the primary step of vision, we have observed, through femtosecond spectroscopic techniques, fast isomerization (<300 ps) via a so-called phantom state in several overcrowded alkenes.[17] However, equally important is the quantum yield of the process, which determines the efficiency taken to reach a photostationary state. For the systems under discussion here, quantum yields are typically between 0.07 and 0.55.[18]

Photochemical switching of chirality in thin polymer films is particularly relevant in the context of high density data storage.[19,20] The polymer systems we have developed were applied through either doping polymers with switches or by covalent attachment of chiroptical switches to the polymer backbone. Theoretically, a compact disk with a 1 125 000 000 MB storage capacity (240 years of continuous music) is possible. However, this would require high density molecular packing as well as the possibility to address or read each individual molecule at high speed without interference, a feat which is far beyond current technological capabilities. A key lesson learned from these studies is that, in translating molecular systems from homogeneous solutions to more complex media, matrix effects play a prominent role with respect to stereoselectivity, switching times, etc.[21]

Switching of Luminescence

Fluorescence forms the basis for numerous practical applications, in particular, for sensing, and provides a versatile output signal in systems that show logic operations.[4,6] In many of the isomers of the overcrowded alkenes we have investigated, distinct differences in fluorescence properties are observed, and these systems appeared, to us, to be attractive candidates in the design of multistate luminescence switches. For instance *P*-*trans*-**2** and *M*-*cis*-**2** exhibit weak and strong fluorescence, respectively, whereas the protonated forms are nonfluorescent (Figure 5).[22] Furthermore, the photochemical switching process was blocked effectively by the addition of acid.

The donor and acceptor substituents in **2** are essential to achieving stereoselective photoisomerization, and protonation of the amine moiety results in an ineffective acceptor−acceptor (ammonium and nitro)-substituted lower half.[22] Compound **2** shows dual-mode switching behavior as we can reach the on mode (switching) and off mode (no switching) simply by deprotonation or protonation. It also exhibits gated response behavior with proton-dependent photomodulation of molecular chirality and fluorescence with the possibility to address three distinct states: on, dimmed, and off (Figure 5). Furthermore, circular polarized luminescence studies revealed the remarkable phenomenon that a single enantiomer of a chiroptical molecular switch could be triggered to emit left or right circular polarized light. [23]

The control of luminescence color is another challenge that is highly relevant, for instance, in the development of light-emitting diodes. Based on the overcrowded alkene class of compounds, we designed a three-state fluorescent switching system in which a single molecule can emit either blue or red light or the fluorescence can be switched off entirely (Figure 6).[24]

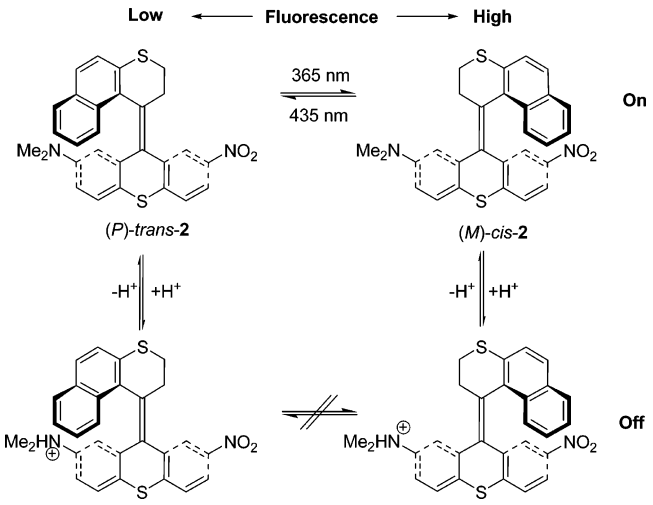


FIGURE 5. Dual-mode photoswitching and gated response fluorescence behavior of donor−acceptor molecular switch **2**.

In this example, the typical cis−trans isomerization was not the prime feature but rather the amazing conformational dynamics of these structures. It is the combination of isomerization and conformational dynamics which, as we will discuss later, is central to the operation of the first light-driven molecular rotary motors. Symmetric bisthioxanthylidene **3a** adopts an anti-folded structure to alleviate steric hindrance in the molecule. This form shows blue fluorescence. Photoisomerization results in the formation of the syn-folded isomer **3b**, which is nonluminescent. Alternatively, electrochemical oxidation converts **3a** to a twisted dicationic form **3c**, which is red fluorescent. Reduction of **3c** converts the molecule back to the initial isomer via the transient twisted (**3d**) and syn-folded (**3b**) forms. As all processes are fully reversible over continuous cycling and large geometrical changes occur in the molecule, these compounds offer intriguing opportunities in applications where large amplitude molecular changes are required to drive mechanical systems.

Switching of Supramolecular Organization and Assemblies

Dynamic assembly processes and mutual control of organization at different hierarchical levels are manifested in numerous biological systems.[25] Study of these complex phenomena and mimicking such processes in artificial systems provide fundamental insight and essential information for the development of smart materials. The idea of using molecular switches to control the organization of a large ensemble of molecules by applying an external signal has captured our imagination over the last several years.[13] A central question we, and many others, have faced is whether light-induced motions or changes in geometry, polarity, chirality, or charge are capable of inducing changes in the orientation or interaction with other molecules.

Liquid crystalline (LC) materials are particularly well-suited as host materials to answer this question.[26] Doping of LC materials with chiral photoswitchable guest molecules allows control of the organization and the properties associated with

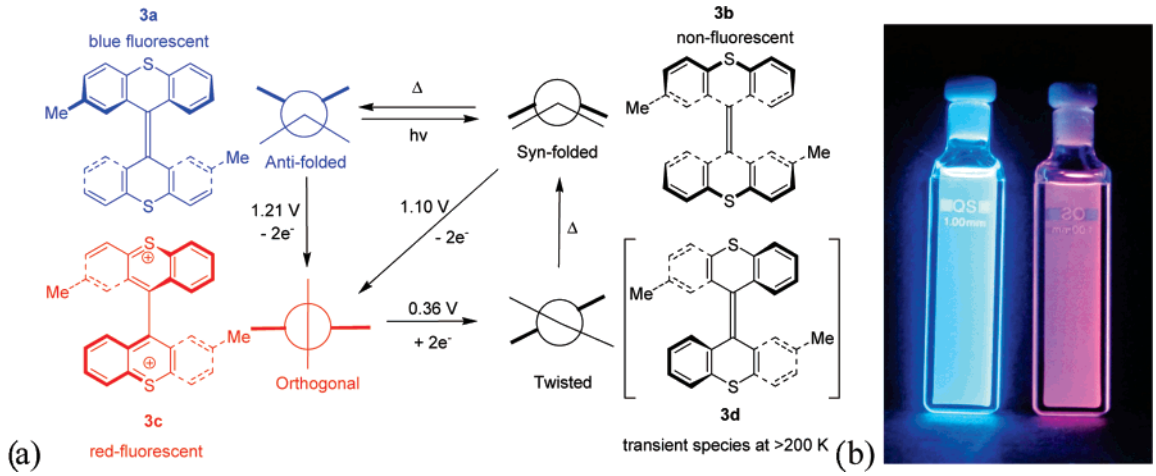


FIGURE 6. (a) Photochemical, redox, and thermal isomerization processes of **3**. Changes in conformation in bisthioxanthylidene **3** between the **3a** (anti-folded) and **3b** (syn-folded) states and the orthogonal and dicationic state **3c**. Only trans isomers are shown for clarity. (b) Switching of luminescence from **3a** to **3c**. Adapted from ref 24. Copyright The American Chemical Society 2006.

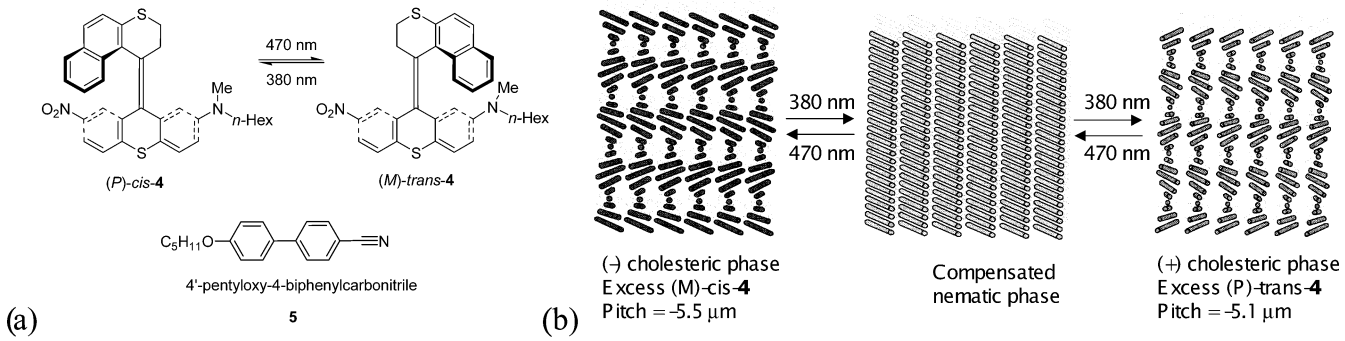


FIGURE 7. (a) Photoisomerization of *N*-hexyl-substituted cis and trans isomers of chiroptical switch **4**, and structure of calamitic mesogen **5**. (b) Schematic representation of the switching of the handedness of a doped cholesteric liquid crystal film.

the LC films via changes in the molecular orientation of the strongly anisotropic mesogenic host molecules.[27] The photoswitching between different LC states was, for instance, achieved using a *P-cis*-**4** or a *M-trans*-**4** derivative with a long aliphatic chain as chiral dopant (1 wt %) in nematic 4′-(pentyloxy)-4-biphenylcarbonitrile **5** (Figure 7).[28]

As expected, the addition of these chiral guests *P-cis*-**4** or *M-trans*-**4** to the nematic LC phase of **5** results in the formation of chiral cholesteric (twisted nematic) phases with opposite handedness. Alternating irradiation at 470 and 380 nm results in the reversal of the helical screw sense of the cholesteric phase and photomodulation of the pitch. Additionally, irradiation using appropriate wavelengths[27] or irradiation times leads[28] to a mixture of *P-cis*-**4** and *M-trans*-**4** of close to 1:1 (a pseudoracemate), which generates a compensated nematic phase. The chirality of the mesophase is switched on again upon prolonged irradiation at either 380 or 470 nm. Photoswitching of LC phases, as outlined here, offers an alternative to existing (electronic) methods to address display materials.

Low molecular weight (LMW) organogelators are another class of emerging materials that have been particularly fruitful in many of our research programs.[29] These compounds have a pronounced ability to self-assemble in a variety of fiber-like structures and can gelate a wide range of solvents at low concentrations. Hydrogels,[30] aerogels,[31] patterned surfaces,[32] and two-stage drug delivery systems[33] are just a few of a wide range of these soft materials, which we have developed. The introduction of light-switchable functions to synthetic LMW organogelators allows one to achieve reversible control over the self-assembly process. In the molecular system **6**, we introduced this concept, using a diarylethene photochromic unit[34] functionalized with (*R*)-1-phenylethylamine derived chiral amide groups (Figure 8a).[35]

The combination of several properties of this system is essential for its overall function. Due to multiple hydrogen bonds between the amide groups, the molecules of **7** self-assemble into chiral fibers of one particular handedness as revealed by electron microscopy (EM) and CD spectroscopy. The molecules can be switched with UV and visible light between ring-opened **6** and ring-closed **7**, respectively (Figure 8a). Furthermore, the photochemical switching is attended by a dramatic change in conformational flexibility, and as a consequence, the aggregation behavior is modulated. Finally, the diarylethene moiety in the open form (**6**) exists in two helical conformations, which undergo rapid interconversion in solution (Figure 9). When a dilute solution of **6** in the open form is irradiated with UV light, ring closure takes place, the dynamic chirality of the core part is locked, and a 50:50 ratio of stereoisomers of **7** is obtained. In contrast, photochemical ring closure in the gel state results in excellent stereocontrol (a 98:2 ratio of stereoisomers of **7**). When the fibers are disassembled by heating, single stereoisomers of **7** are obtained almost exclusively. In this system, there is mutual control of chirality at different hierarchical levels. The chirality of the amide groups in **6** determines the helicity of the

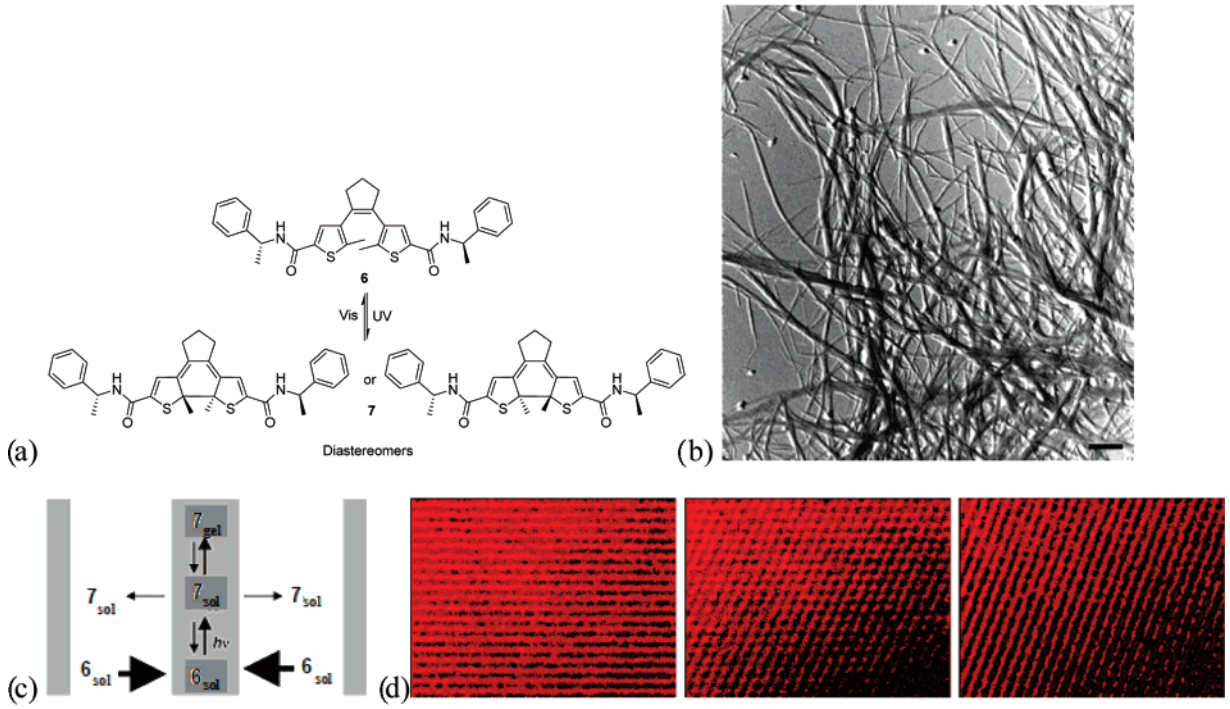


FIGURE 8. (a) Reversible photochemical closing of **6** in solution to the two diastereoisomers of **7**. (b) EM picture showing chiral gel fibers of **7** in toluene. (c) Mass transport phenomena observed when irradiation is performed using a patterned mask. Under these conditions, **6** will not form a gel while **7** does. As a consequence, there is an accumulation of gel fibers of **7** in the region irradiated. (d) Dynamic holographic patterning. Rotation of the pattern mask after irradiation followed by further irradiation results in realignment of the gel pattern.

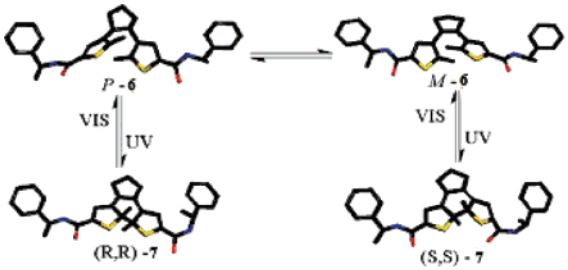


FIGURE 9. In solution, the open state of dithienylcyclopentene switch **6** is present in both *P*- and *M*-helical conformations. Irradiation of each conformation of **6** to the closed state **7** "locks" the chirality of the open form in one or other diastereomeric form. Adapted from ref 35a. Copyright Science 2005.

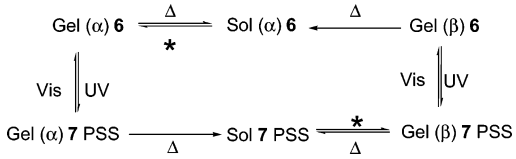


FIGURE 10. Four-state cycle in a photoswitchable low molecular weight organogel. Cooling of a solution of **6** results in formation of gel (α) **6**, which upon irradiation with UV light transforms to the metastable gel state (α) **7** (PSS indicates photostationary state). Upon heating and subsequent cooling, the stable gel (*β*) **7** is formed, which can be irradiated with visible light to reach the metastable gel (*β*) **6**. Heating **6** and subsequent cooling provides the original gel (α) **6** state.

fiber, which in turn determines the chirality of the stereoisomer of **7** that is formed upon ring closure. However, this is only the first part of a complex switching scheme (Figure 10). The fibers of the closed form **7** are metastable and rearrange after a heating−cooling cycle into fibers with inverted helicity. The fixed chirality of the individual molecules **7** in their closed form does not change of course during this step. This photoactive supramolecular system comprises two different aggregation states, denoted α and *β*, which can include either the open **6** or closed form **7** leading to a total of four distinct states. All of these states can be addressed as shown in Figure 10.[35]

Of paramount importance is the discovery that metastable chiral aggregates can be obtained in a fully reversible manner. Furthermore, the interplay of molecular and supramolecular chirality and aggregate stability in these synthetic systems is intriguing in light of efforts to understand how nature's processes of molecular communication and self-assembly operate.

The change in conformational flexibility in diarylethenes in the open **6** and closed form **7** results in distinct differences in the viscoelastic properties of their gels. Taking advantage of the higher propensity of **7** to provide stable aggregates, controlled mass transport by light and holographic patterning are achieved readily (Figure 8c and d).[35b] The switchable materials discussed here offer attractive prospects for the development of memory systems and smart functional materials.

Switchable Molecular Wires

The design of components for molecular electronics continues to be one the most active areas of contemporary research with the ultimate prospect of nanoscale electronic devices.[4,6,19] Bistable diarylethenes[34] have long been viewed as attractive candidates as a consequence of their ability to function as switchable molecular wires (Figure 12).[34,36]

The electronic communication throughout the molecule can be turned on or off by switching from the closed conjugated form to the open nonconjugated form. This is reflected, for

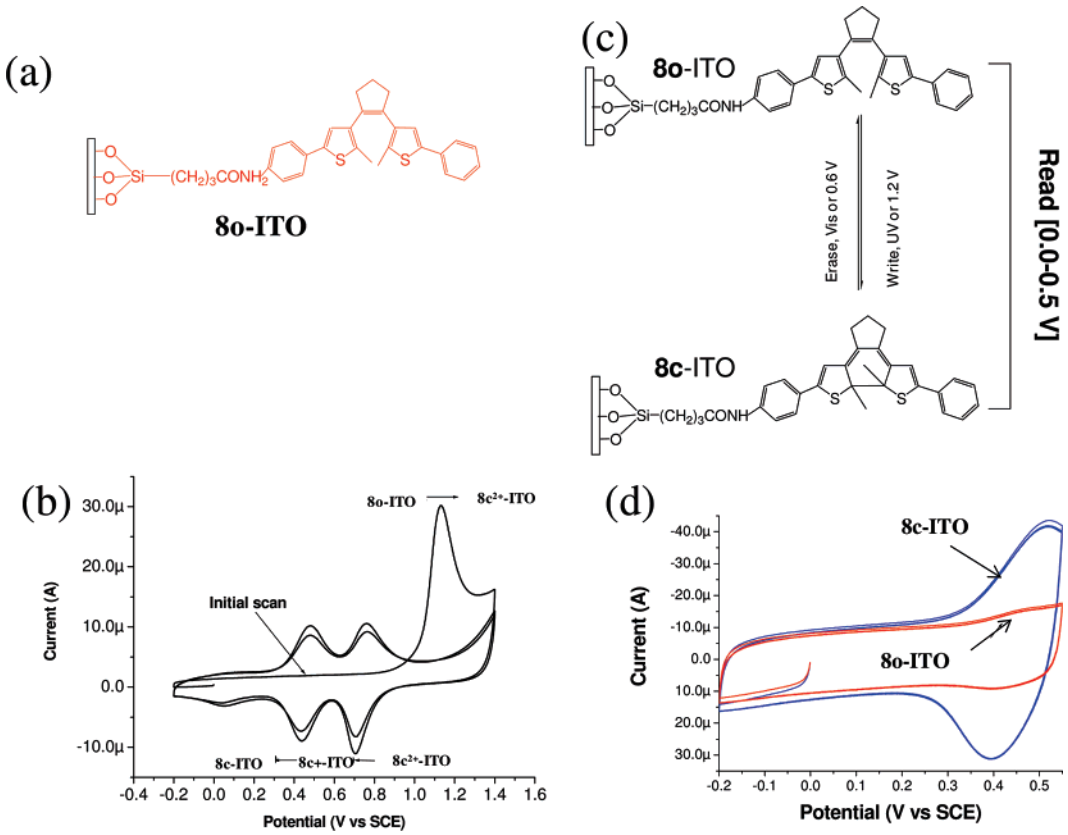


FIGURE 11. (a) Dithienylethene molecular switch **8** immobilized on ITO and (b) electrochemical ring closing of **8o**-ITO to **8c**-ITO by cyclic voltammetry. (c) Electro- and photochemical write and erase functions with read-out (d) achieved nondestructively through cyclic voltammetry. Adapted with permission from ref 39. Copyright The Royal Society of Chemistry 2006.

example, in a change of color and conductivity of the material.[34] Reversible switching can be achieved either photochemically or electrochemically.[37] The switching behavior is strongly dependent on molecular structure and substituents, but the excellent reversibility, easy modification, and high fatigue resistance (allowing many switching cycles) are particularly noteworthy.[34,36−38] Although the majority of investigations have focused on intrinsic molecular properties in solution, the immobilization of these remarkable molecules on surfaces is essential to interface them with nonmolecular systems (and the outside world). Indeed, recently, we have succeeded in the covalent self-assembly of diarylethenes on a semiconductor ITO surface (Figure 11a).[39] The photo- and redox-active system **8** can be switched readily upon UV and vis irradiation with electrochemical read-out at 0.5 V (Figure 11b and 11c). Importantly, electrochemical switching in these systems, which is unidirectional in solution, the direction of which can be controlled by synthetic tuning,[37] becomes fully reversible when on a surface.[39] The added value that can be gained by immobilization with regard to addressable molecular functionality is very much an unexplored avenue in functional materials.

In order to measure single molecule electronic transport, we have used mechanically controllable breakjunction (MCBJ) techniques.[40] The photochromic switch **9** that we designed specifically for this purpose has a central dithienylcyclopentene switching unit, the π-system is extended with two thiophene rings on both sides, and thiol groups are installed at the periphery to anchor the molecule to the gold surface of the electrodes (Figure 12a and 12b). Starting with the closed form in the breakjunction setup (Figure 12c), we observe a sharp increase in resistance of 3 orders of magnitude upon illumination with visible light (λ_{577nm}, Figure 12d). The decrease in conductance is attributed to a change from the closed conducting to the open insulating state. However, we were not able to observe the reverse process, that is, switching from the open to the closed form. Semiempirical quantum chemical calculations[40] indicate that this might be due to quenching[41] of the excited state of the molecule in the open form by the presence of gold.

Understanding the interaction of photochromic molecules with surfaces is a key area of interest for us. By the systematic modification of the nature and position of the anchoring group of diarylethene switches connected to gold nanoparticles,[42] it was shown that both one-way and reversible optoelectronic switching is possible. These efforts have recently culminated in the demonstration of reversible switching of the tunneling current (as detected by STM) of single molecule diarylethene switches on a gold surface (Figure 13).[43,44]

Molecular Valve

Artificial pores or valves that can be controlled by external stimuli are considered important components of future nanodevices.[45] In close cooperation with researchers at the BioMade institute in Groningen, we have constructed bio-hybrid systems consisting of a membrane-bound biological channel protein, which allows for external control over the opening and closing of the channel (Figure 14a). This work builds on long-standing efforts in supramolecular chemistry to achieve controlled transport through channels.[46]

The mechanosensitive channel of large conductance (MscL) from *Escherichia coli* is a homopentameric channel protein,

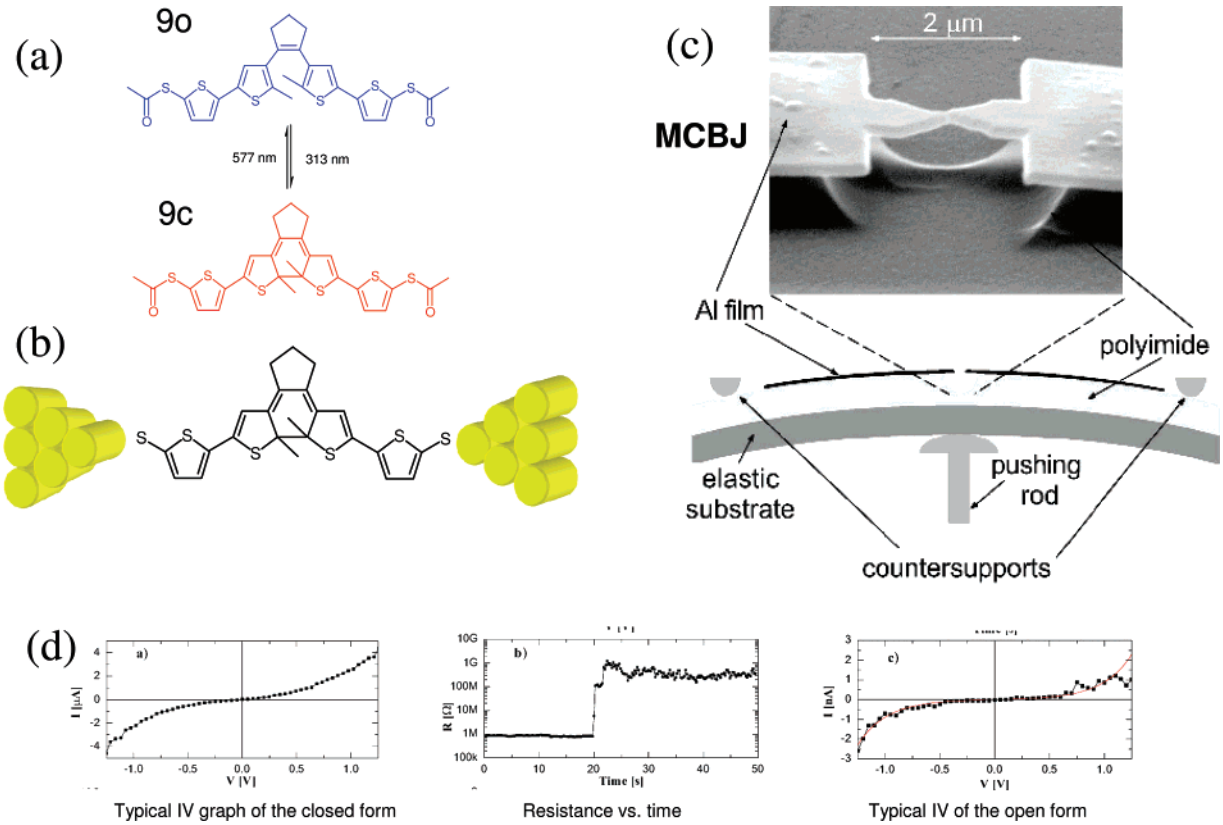


FIGURE 12. (a) Photochemical switching of open (**9o**) and closed (**9c**) forms of dithienylcyclopentene photochromic switch. (b) Schematic representation of **9o** bridging electrodes in the mechanically controlled break junction (MCBJ). (c) EM image and schematic diagram of a MCBJ. (d) *I*−*V* curves before and after photochemical ring opening of **9c** bridging electrodes in the MCBJ and resistance versus time curve. Redrawn with permission from ref 40. Copyright American Physics Society 2003.

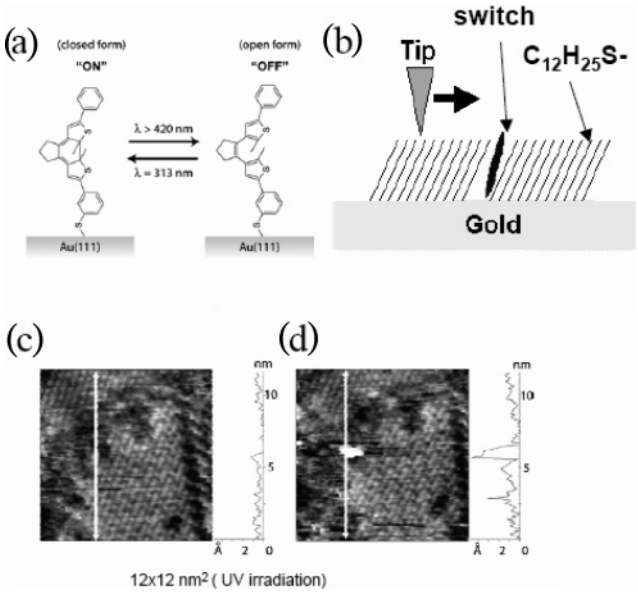


FIGURE 13. Schematic diagrams of (a) photochemical switching of a dithienylcyclopentene anchored to Au(1,1,1) and (b) its co-self-assembly on a gold surface. (c) Apparent height STM images in the open and (d) closed state showing single molecule switching characteristics. Adapted from ref 44 with permission. Copyright Wiley 2006.

which acts as a kind of safety valve to the bacterium cell.[47] In response to a buildup of internal pressure, it opens a 3−4 nm pore, allowing nonselective efflux of ions and small solutes. It was found earlier[48] that the introduction of polar or charged moieties can result in spontaneous opening of the channel. We decided to harness trigger-based molecular systems, and by first introducing cysteine residues at a specific location on each of the protein subunits, we were successful in attaching responsive components, for instance, a photocleavable group (Figure 14b), to construct a switchable MscL channel.[49] Photolysis of **10** generated free carboxylic acid groups which initiated the opening of the channel, an event detected using patch-clamp techniques.

The next step was the introduction of a photoswitchable spiropyran unit to each of the five cysteine residues to achieve reversibility in the channel opening (Figure 14c).[49] It was anticipated that the reversible photochemical ring opening of the spiropyran[11a] to the polar and less rigid zwitterionic[11b] merocyanine form will change the hydrophilic nature at crucial channel positions drastically, resulting in channel opening.[49] Opening and closing of the channel **11** was, indeed, observed at the single molecule level. However, the poor stability of the hybrid channels in reconstituted artificial membranes prevents, thus far, repetitive opening and closing cycles without significant decrease of the number of addressable channels.

The modified MscL proteins were incorporated in liposomes, and efflux experiments of the self-quenching dye calcein from these liposomes showed that channel opening and release of the dye could be triggered with light. Although many problems regarding stability and effectiveness need to be solved, these systems hold promise for future applications such as controlled drug release.

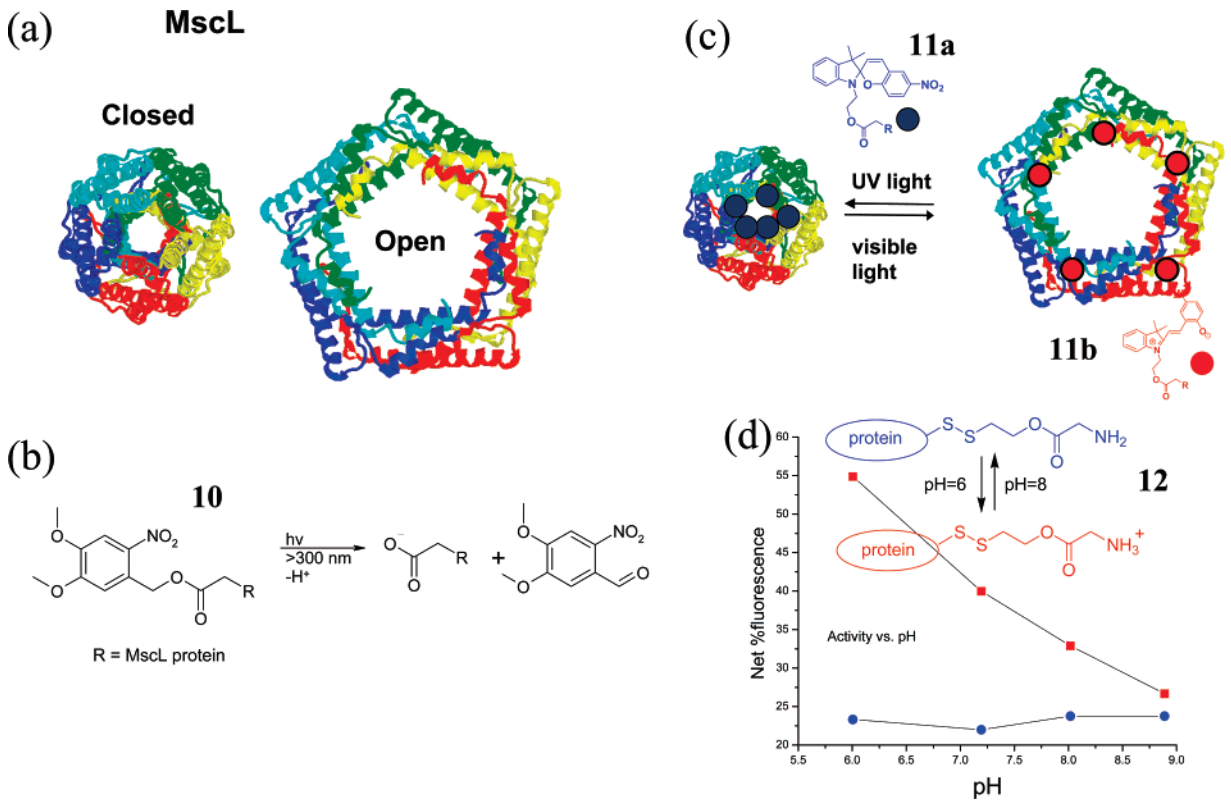


FIGURE 14. (a) Mechanosensitive channel of large conductance (MscL) in an open and closed state. (b) Irreversible photoactivation using a photocleavable protecting group (**10**). (c) Reversible photochemical opening and closing of the MscL channel using a spiropyran modified channel protein (**11a** spiropyran form, **11b** merocyanine form; blue line, without pH-sensitive group; red line, with pH-sensitive group). (d) MscL channel protein modified with pH-sensitive group **12** and channel activity (release of fluorescent probe) as a function of pH.

In addition to the control of channel opening triggered by light, we demonstrated recently that MscL channel **12** can "sense" pH differences in the physiologically relevant range (pH 6−8) when different amine moieties are incorporated (Figure 14d).[50] Albeit at a very much early stage of development, such stimuli-responsive materials could be particularly relevant for delivery systems using switchable channels that respond to the pH of the medium (for instance, near or in a tumor cell).

Molecular Motors

Arguably the most important part of any molecular machine is the motor component, which allows for the input of energy to be used for directed mechanical motion and hence to perform a task.[2,5,51] As the field of molecular motors and machines typically spans physics, chemistry, and biology and the drawing of parallels between molecular machines and machines in everyday use is ubiquitous, the terminology to describe molecular level motors may vary considerably. For discussions on more concise definitions and operational mechanisms of molecular motors, the reader is referred to several recent reviews.[2a,b]

Motors at the molecular scale experience relentless thermal (Brownian) motion at ambient conditions.[3,52] To operate in such a turbulent world, the molecular motor must either exploit Brownian motion or overcome it. Nature harnesses Brownian motion in a manner referred to as the Brownian ratchet in linear and rotary protein motors where the energy input restrains random Brownian motion.[1,51,53] The design of artificial molecular motors requires that specific directional mechanical motion is controlled and that the stimuli-induced motion of a motor component can be detected and distinguished above the random

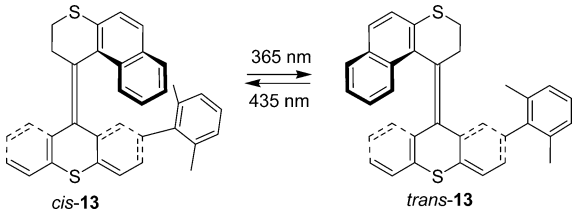


FIGURE 15. Molecular brake; the kinetic barrier to aryl−aryl single bond rotation is controlled by the switch unit.

thermal motion. Achieving a biased change in motion at the molecular level is not at all trivial, and one should realize that in both biological motors and synthetic molecular motors conformational mobility is crucial to their function.[2,51]

Since the early days of conformational analysis, hindered bond rotation in molecular rotors and coupling of rotary motions in "gearing systems" have been explored.[54] An early example of a "molecular brake" from our laboratory is shown in Figure 15.[55,56] This system **13** was designed in order to couple a switch (overcrowded alkene) and a rotor (xylyl group) function in a single molecule. The rate of rotation around the biaryl single bond can be varied by photochemical cis−trans isomerization of the alkene moiety. Unexpectedly, the rate of biaryl rotation is faster in *cis*-**13** than in *trans*-**13**, which is attributed to the flexibility of the naphthalene moiety, which can bend away during the xylyl rotor movement. Therefore, a change in configuration can be used to control submolecular rotary motions, although the photochemical switching is less efficient in this system then in many of the other systems we have developed.

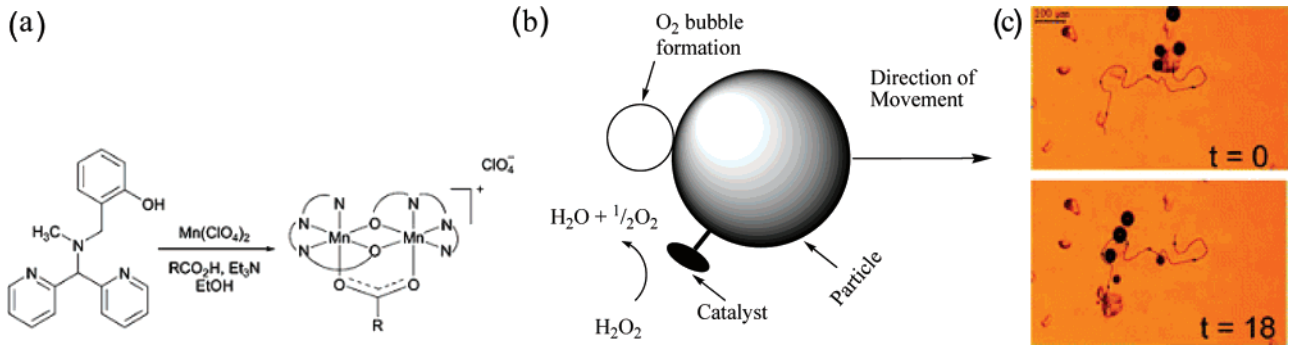


FIGURE 16. (a) Synthesis of a catalase enzyme mimicking dinuclear manganese catalyst, where R = anchoring group to silica μ-particle. (b) Design of catalytic autonomous moving μ-particles using H_2O_2 as fuel. (c) Trajectory of particle movement (oxygen bubbles are seen as black circles, time is in seconds). Adapted from ref 60 with permission. Copyright The Royal Society of Chemistry 2005.

Molecular rotors that lack directional control of rotary motion are ubiquitous, and the ingenious design and dynamic processes of molecular rotor systems in solution, on surfaces, and in the solid state are beyond the scope of this perspective.[54] In the following sections, we will discuss our efforts to achieve molecular motor functions in synthetic systems.

Chemically Fuelled Autonomous Translational Movement

Kinesin motor proteins are integral to the transport of material in cells.[51,57] They are chemical motors using ATP as fuel and run along the microtubules of the cell. The conversion of chemical energy into motion with directional control is as remarkable as it is fascinating and provides a major challenge to match such operation in wholly synthetic systems, that is, to design catalytic systems that operate as molecular motors and use a chemical transformation ultimately to move molecular cargo along a predefined path. Autonomous movement of millimeter-size metallic objects powered by platinum-catalyzed decomposition of hydrogen peroxide was first described by Whitesides and co-workers.[58] For these and related, recently reported, multimetallic systems, various propulsion mechanisms have been proposed.[59] We have taken a molecular approach to this concept and have developed highly efficient catalysts, which when immobilized on particles enables autonomous movement fuelled by hydrogen peroxide (Figure 16).[60]

In our initial design, we took two important considerations into account. First, for particles <1 μm in size, the motion must be distinguished from inherent Brownian motion.[59b] Second, catalase enzymes are extremely effective in the decomposition of cytotoxic hydrogen peroxide in nature.[61] We have developed a novel highly active dinuclear manganese catalase mimic (Figure 16a), which through its structure has enabled robust immobilization on micron-sized silica particles without loss of function (Figure 16b). Decomposition of hydrogen peroxide resulted in directional movement of the functionalized particles, most probably due to the recoil during oxygen bubble formation (Figure 16c). How is it then possible that the particles move in a certain direction? Most probably, in this case, the asymmetry arises from inhomogeneous functionalization and bubble nucleation at the silica particles, although other[62] mechanisms cannot be excluded. Despite the fact that control over directionality is limited, this system shows that the concerted action of molecular catalysts can exert a motor-type function and induce translational movement of a micro-object. The next steps will be to examine if smaller objects (nanoparticles, polymers) can be propelled and if Brownian motion can be overcome by taking a leaf out of nature's book and confining the particles to defined tracks.

Chemically Driven Rotary Motor

Considering the ingenious design and complexity of the genuine molecular rotary motor ATPase, a more modest, though realistic, goal is to achieve a full 360° unidirectional and repetitive rotary motion around a carbon−carbon single bond. Kelly and co-workers have employed triptycenes to construct molecular brakes and ratchets and succeeded in demonstrating for the first time that a unidirectional rotation by 120° driven by phosgene as a chemical fuel is possible.[63,64]

The structures we have employed to achieve a full 360° unidirectional rotary cycle by chemical transformations are biaryls (Figure 17).[65,66] It is well-established that the restricted rotation around the biaryl C−C bond can be tuned through the steric interactions from the ortho-substituents, a point exemplified in their ubiquitous use as chiral ligands in asymmetric catalysis.[67] The structure, chemical transformations, stereochemical features, and schematic representation of the unidirectional rotation around the biaryl single bond are shown in Figure 17.

There are four distinct stations **A**−**D**, which correspond to the four structures **14**−**17**. Furthermore, there is a distinct difference in dynamic stereochemistry of the closed lactones **14** (station **A**) and **16** (station **C**) and the nonbridged biaryls **15** (station **B**) and **17** (station **D**). In stations **A** and **C**, there is rapid helix inversion, but further rotation is restricted by the covalent lactone linkage.[68] In states **B** and **D**, there is limited rotation, but compounds **15** and **17** are configurationally stable (atropisomers) due to steric interactions between the substituents present in each aryl group. Enantioselective reductive ring opening of lactone **14** with the chiral boron reagent ((*S*)-CBS) induces an approximately 90° directional rotation in step 1. Simultaneously, the barrier to biaryl rotation increases, preventing racemization. Subsequent oxidation and orthogonal protection−deprotection methods are used in the next rotational step (step 2) whereby lactone **16** is formed. Repetition of this sequence of chemical transformations in steps 3 and 4 completes the full 360° cycle. When the enantiomer of the boron reagent ((*R*)-CBS) is used, the reverse rotary cycle can be initiated. The sense of rotary motion in this system is therefore governed by the judicious choice of chemical reagents. With the principle of unidirectional rotary motion driven by chemical fuel demonstrated, the next challenge is to avoid a sequence of

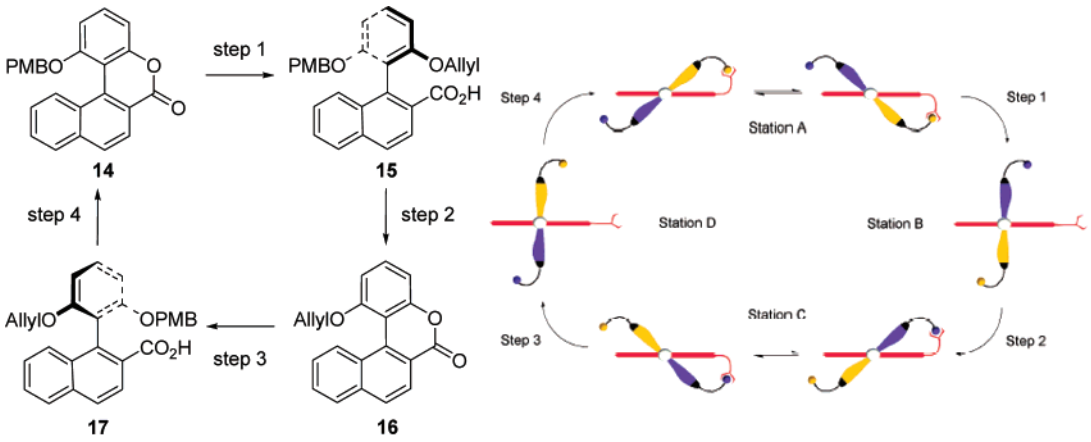


FIGURE 17. (a) Structures and chemical steps of a unidirectional molecular motor. (b) Schematic representation of a 360° rotation over four steps. Reproduced from ref 65. Copyright Science 2005.

incompatible chemical steps to achieve continuous rotary motion and use a single or compatible fuel set to drive each step.

Light-Driven Molecular Motors

Fuelling unidirectional rotary motion with light as the energy source has enabled continual rotary motor function for the first time in a molecular system.[69] In demonstrating this motor function, we faced three key challenges: (i) repetitive 360° rotation, (ii) the use of light as the source of energy, and (iii) unidirectional rotary motion. Two fundamental principles are the cornerstones for the realization of the light-driven molecular rotary motors discussed here. Photochemical conversion of an alkene from the trans to the cis isomer is typically very fast and is an energetically uphill process. Furthermore, the concerted action of two chiral elements (here the stereogenic centers and the molecular helicity) in a single chemical or physical event, by virtue of the diastereomeric nature, can lead to unique handedness in structure or motion.

The molecular motor (3*R*,3′*R*)-*P*,*P*-*trans*-**18** has additional stereogenic centers compared to the chiroptical molecular switches described above (Figure 18). Again the helicity can be changed by photoisomerization, while the methyl substituents can adopt an axial or equatorial orientation both in the trans and the cis isomers. The difference in stability between stable (3*R*,3′*R*)-*P*,*P*-*trans*-**18** with an axial methyl orientation and unstable (3*R*,3′*R*)-*M*,*M*-*trans*-**18** with an equatorial methyl orientation is 35.9 kJ^{-1} mol^{-1}. Similarly, the cis isomer has a stable (3*R*,3′*R*)-*P*,*P*-*cis*-**18** and unstable (3*R*,3′*R*)-*M*,*M*-*cis*-**18** form with a difference in stability of 46.0 kJ^{-1} mol^{-1}. The difference in stability is attributed to enhanced steric interference in the isomers with a methyl group in the equatorial position.

By applying light and heat, the unidirectional rotation of the upper half (the propeller) with respect to the lower half (the stator) proceeds as a four-step cycle. This involves two reversible photochemical steps (steps 1 and 3), converting the stable isomers into unstable isomers, each followed by an irreversible thermal step (steps 2 and 4) converting unstable isomers into stable isomers. Starting with (3*R*,3′*R*)-*P*,*P*-*trans*-**18**, photochemical trans→cis isomerization (step 1) generates unstable (3*R*,3′*R*)-*M*,*M*-*cis*-**18**. In addition to changing the configuration of the alkene and clockwise rotation of the propeller part relative to the stator, which inverts the helicity, the methyl substituents are forced to adopt an unfavorable equatorial orientation. In step 2, the strain is released by thermal helix inversion to give

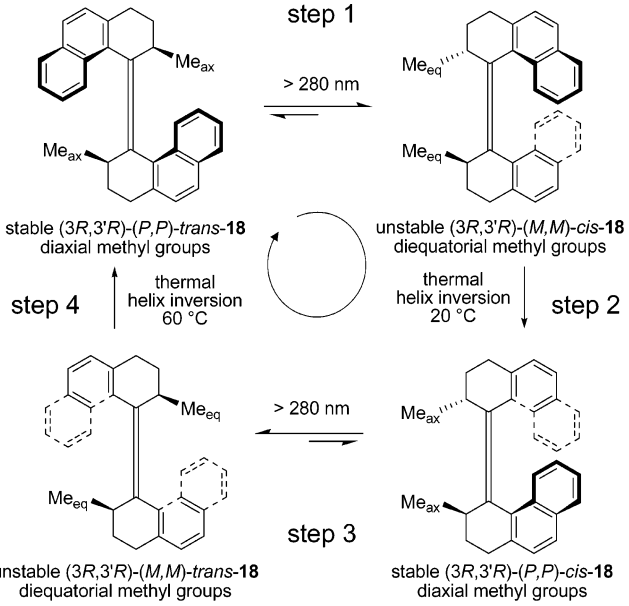


FIGURE 18. Photochemical and thermal isomerization processes of molecular motor **18**.

(3*R*,3′*R*)-*P*,*P*-*cis*-**18**, in which the methyl groups adopt a more favorable axial orientation, while the propeller has continued to rotate in the same direction. In step 3, photoisomerization of (3*R*,3′*R*)-*P*,*P*-*cis*-**18** to (3*R*,3′*R*)-*M*,*M*-*trans*-**18** once again results in clockwise helix inversion, and the methyl group is forced to adopt an unfavorable orientation. Finally, in step 4, the original stable isomer (3*R*,3′*R*)-*P*,*P*-*trans*-**18** with axial methyl groups is obtained through a thermal helix inversion releasing the strain in the molecule. The final isomerization step needs, however, heating to 60 °C. Although the thermal steps in the cycle are depicted as single steps, we have demonstrated, by changing the size of the alkyl substituents at the stereogenic centers in **18**, that the thermal step comprises two sequential helix inversions.

As a change in helicity takes place in each step, the directionality of the rotary motion can be monitored readily by CD spectroscopy (Figure 19). While the forward steps are due to the excitation by light and thermal relaxation of unstable forms, the reverse thermal steps are effectively blocked. Irradiation at >280 nm and temperatures >60 °C therefore result

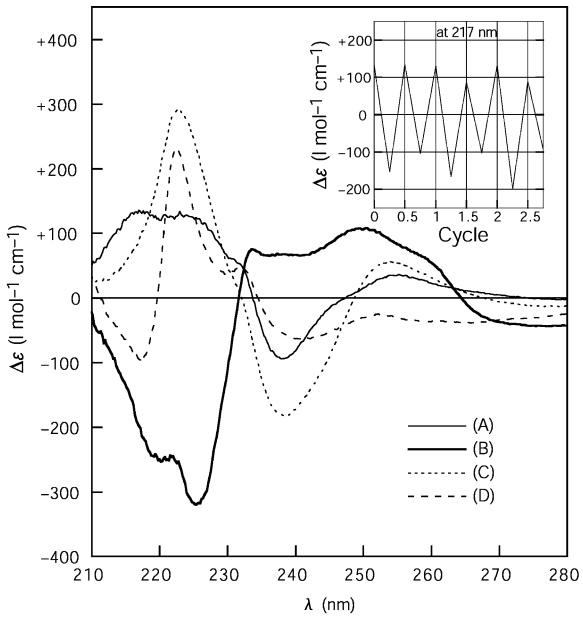


FIGURE 19. Circular dichroism (CD) spectra in each of four stages of switching (see text). Trace A, *P*,*P*-*trans*-**18**; trace B, *M*,*M*-*cis*-**18**; trace C, *P*,*P*-*cis*-**18**; trace D, *M*,*M*-*trans*-**18**. Inset: change in CD signal during full rotation cycle of *P*,*P*-*trans*-**18** monitored at 217 nm. Adapted with permission of Nature from ref 69. Copyright 1999.

in continuous unidirectional 360° rotation. Even at steady state, a net clockwise rotation takes place as long as external energy (heat and light) is supplied. The clockwise or counter-clockwise propeller rotation is determined simply by the choice of enantiomer of the motor.

With the prototype of a light-driven unidirectional motor demonstrated experimentally, we considered two aspects particularly important in the design of the next generation of motor molecules (Figure 20). In several applications of light-powered motors, rotation at an appreciable speed will be required. As the photochemical steps are extremely fast (<300 ps), we focused on the rate-limiting thermal isomerization steps. Furthermore, molecular motors with distinct upper and lower halves (Figure 20) are considered particularly useful as the symmetric lower half can be used for connection to other molecules or surfaces while the upper half can still function as a propeller.[70]

In attempts to accelerate the motor, a major challenge is to reduce the barrier to thermal helix inversion without compromising unidirectionality.[71]

Particularly important in molecular switches and motors based on overcrowded alkenes are the geometry and conformation around the central double bond (the axis of rotation) and the steric hindrance around the *fjord region*. When we compared six- and five-membered ring systems **18** and **19**, it is likely that, due to reduced steric hindrance, the helix inversion will be facilitated in **19**.[72] Indeed it turned out that the thermal barriers for helix inversion in the new motor **19** were decreased considerably compared with those of the six-membered analogue **18**, with a half-life of 78 min for the slowest and 18 s for the fastest step at room temperature.[72]

More dramatic enhancements of rotary speed were achieved with second generation motors **20**−**23** (Figure 20).[73] X-ray analysis of several members of this class of overcrowded alkenes showed that also in these molecules the methyl substituent adopts a more favorable axial orientation in the stable forms and a more crowded equatorial orientation in the unstable forms. A study of the dynamic processes revealed that again two photochemical steps and two thermal steps add up to a full 360° rotary cycle. The repetitive and unidirectional nature of the rotation process can be followed easily by the distinct changes in helicity after each isomerization step as monitored by CD spectroscopy. Figure 21 illustrates a typical case for motor **24** comprising a (2′*R*)-methyl-2,3-dihydronaphthiopyran propeller and a 2-methoxythioxanthene stator.

Comparing these second generation motors with the first generation, it is particularly rewarding that the presence of a single stereogenic center is sufficient to achieve unidirectional rotation. Both steric and electronic effects have been studied, using a large collection of these new motor molecules, with the aim of accelerating the mechanical motion.[73,74]

The thermal barriers for helix inversion could be reduced further through systematic modification of the bridging atoms X and Y (Figure 20).[74] In general, smaller Y and, in particular, smaller X atoms reduce the steric hindrance in the fjord region, facilitating the slippage of the propeller and stator moiety over each other. Further improvements were made by changing to fluorene stator halves and by fine-tuning the size of the substituent at the stereogenic center.[75] In this way, we were able to achieve a 1.2-million-fold increase in the rotation speed with the second generation motors. This allows the propeller to rotate

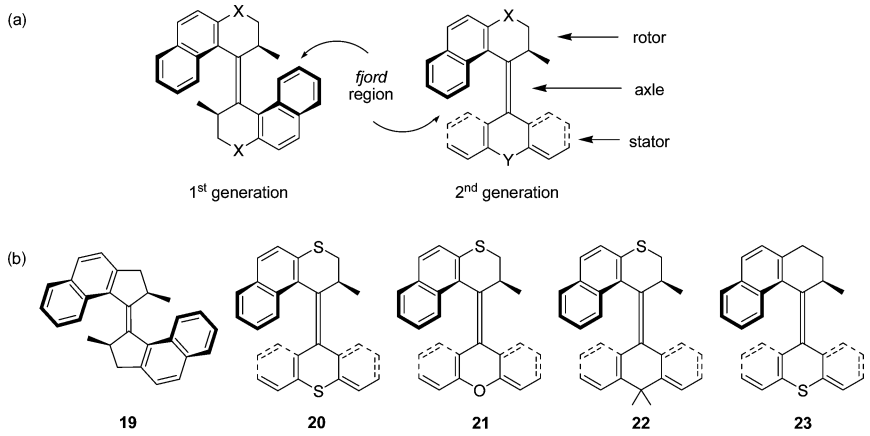


FIGURE 20. (a) General structure for first and second generation molecular rotary motors. (b) Structures of first (**19**) and second (**20**−**23**) generation molecular motors cited in the text.

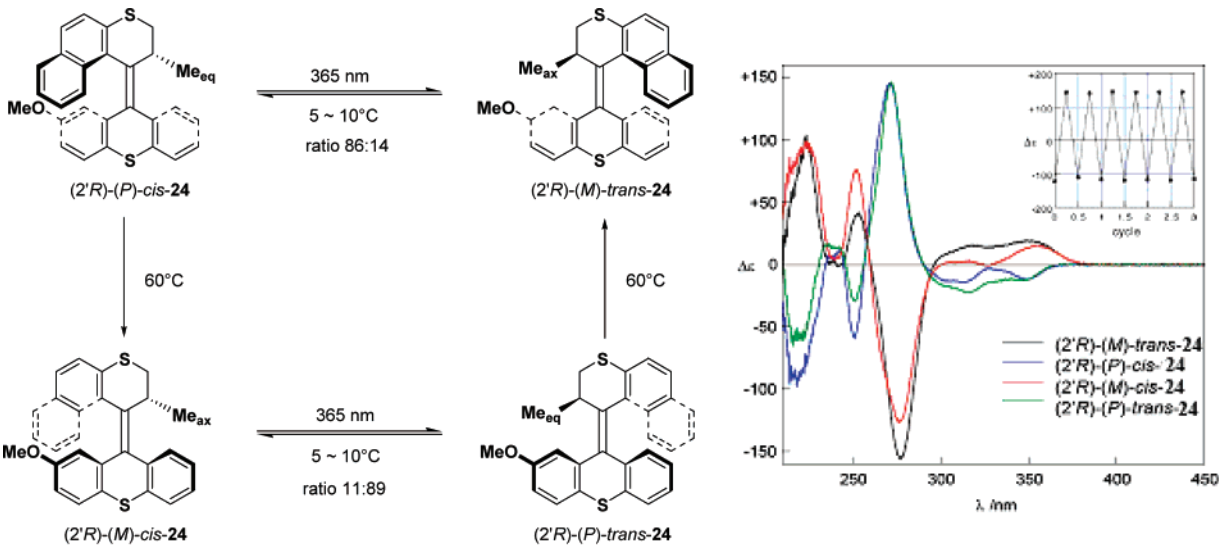


FIGURE 21. (a) Photochemical and thermal isomerization processes of motor **24**. (b) CD spectra of each of the four stages of rotation. Black line, (2*R*)-*M*-*trans*-**24**; blue line, (2*R*)-*P*-*cis*-**24**; red line, (2*R*)-*M*-*cis*-**24**; green line, (2*R*)-*P*-*trans*-**24**. Inset: changes in $\Delta\epsilon$ value over a full rotational cycle, monitoring at 272 nm.

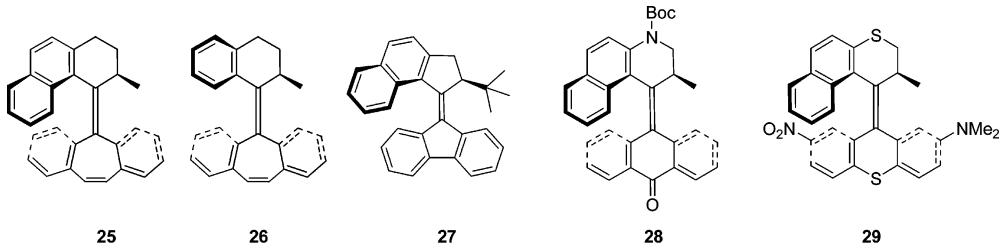


FIGURE 22. Structures of molecular motors **25**−**29**.

unidirectionally on irradiation at up to 80 revolutions per second at 20 °C, which approaches the rotary speed of ATPase (135 rotations s^{-1}).

It should be noted that structural modification leads sometimes to surprising and counterintuitive results with respect to the motor behavior. For instance, in motor **26**, the thermal isomerization is slower than that in motor **25**, although the naphthalene moiety in the rotor part is replaced with the smaller benzene group (Figure 22).[76] The decrease in ground-state energy of the unstable isomer is larger than the decrease in the transition-state energy for the thermal step. Similar effects play a role in the fastest motor **27**, which has a large *tert*-butyl substituent at the stereogenic center but shows an extremely fast thermal helix inversion ($t_{1/2}$ = 5.74 ms).[77]

Taking advantage of changes in electronic effects, we could achieve drastically increased rates of thermal isomerization in motor **28**.[78] In this case, an amine in the propeller and ketone function in the stator part are in conjugation, and as a consequence, the single bond character of the axis of rotation is expected to increase, resulting in significantly faster rotation.

At this point, it should be noted that changes in the structure, nature, and position of substituents in these motor molecules can affect all of the isomerization processes. While, in a few cases, some thermal backward rotation is observed, in other cases, we observe >99:1 selectivity in the photoisomerization step. The overall unidirectional nature of the rotary motion is never compromised.

Finally, through the presence of donor and acceptor substituents in the stator part of the motor **29**, we achieved a bathochromic shift in the optimal wavelength of irradiation similar to that in switch **2**.[79] This motor was shown to operate with visible light. The stage is now set for further increases in rotation speed, for the introduction of additional functionality to these motors, and to integrate them into multicomponent systems.

Motors on Surfaces and Molecular Transmission

Anchoring molecular machines to surfaces without compromising their mechanical function is critical to be able to interface them with the macroscopic world. The motors discussed thus far operate in solution, and in order to overcome Brownian motion and to ultimately build nanodevices, immobilization of our light-driven motors on surfaces is a crucial next step. For this purpose, the second generation motor **30** has been immobilized successfully on gold nanoparticles (Figure 23a).[80] In this motor, with the rotor axis normal to the surface, the stator part is functionalized with two legs terminated with thiol groups. The connection of the motor via two attachment points at the stator prevents the uncontrolled thermal rotation of the entire motor with respect to the surface while leaving the propeller function intact.

Repetitive unidirectional rotation with respect to the surface was observed by CD spectroscopy (Figure 23b) and confirmed independently by NMR studies with an analogue in which the

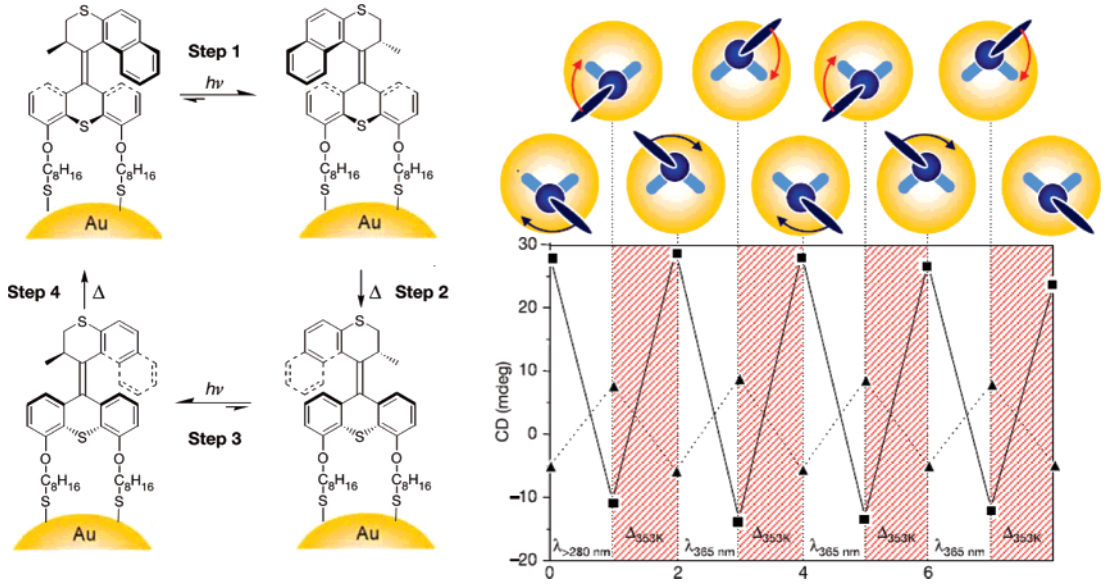


FIGURE 23. (a) Four-step rotary cycle of **30** immobilized with two alkylthiol legs to gold nanoparticles (b) Top: unidirectional rotary motion of the propeller part of **30** viewed along the rotation axis and two four-stage 360° rotary cycles. Bottom: the change in CD absorption at 290 (solid) and 320 nm during the sequential photochemical and thermal steps.

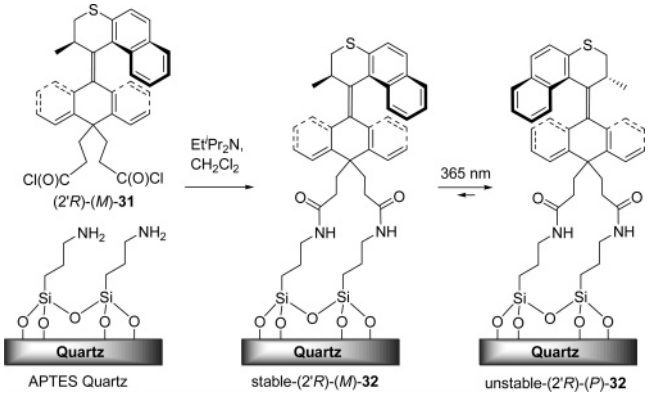


FIGURE 24. Grafting of (2′*R*)-*M*-**31** to APTES modified quartz and photochemical isomerization of surface-bound motor **32**. Adapted from ref 81. Copyright Wiley 2007.

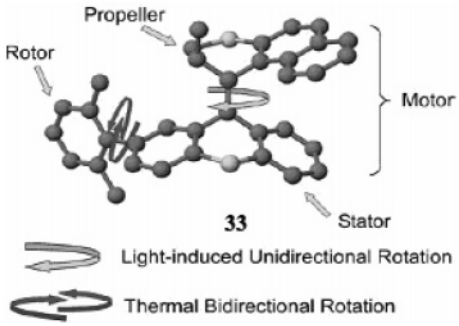


FIGURE 25. Structure of second generation motor connected to xylyl rotor **33** and its rotary processes. Reproduced from ref 82. Copyright Royal Society of Chemistry 2005.

two legs were differentiated by ^{13}C-isotope labeling.[80] Employing a related second generation motor with different legs and anchoring positions, we recently assembled light-driven motors as monolayers on silicon and quartz surfaces (Figure 24).[81] CD measurements were again used to follow the isomerization steps, while XPS analysis confirmed the anchoring to the surface through two points. These studies revealed key issues associated with immobilization of motors and switches to surfaces.

We have designed two systems in which the dynamic properties of the motor are used to effect a second dynamic function to demonstrate a concept of molecular transmission. The first example (Figure 25) is related to earlier work on coupled chiroptical switches and rotors.[55] In **33**, a xylyl rotor is connected to a second generation motor.[82] The stepwise isomerization of the motor part, through the four-step 360° cycle (see Figure 21), changes the position of the propeller part with respect to the xylyl rotor, affecting its thermal rotary behavior. The order cis-stable > cis-unstable > trans-stable > trans-unstable was established by 2D EXSY NMR spectroscopy for the rotation around the biaryl single bond in the various isomers. These data point to a larger steric effect of the methyl substituent, in particular, in an equatorial orientation, than that of the naphthyl part of the upper propeller unit on the xylyl rotor moiety.

In the second system, we examined the transmission of the change in chirality of the motor molecule during rotation to a change in folding of a macromolecule.[83] For this purpose, a dynamic helical polymer, polyhexylisocyanate, was employed. An optically active amide-substituted trans motor **34** was used as an initiator in the polymerization of isocyanates, which resulted in a polymer showing random helicity (Figure 26). Photoisomerization of the motor unit to the unstable cis form results in conversion to a *M*-helical polymer, while subsequent thermal isomerization of the motor to the stable cis form triggers helix inversion in the macromolecule to the *P*-helical polymer. Next, a photochemical isomerization followed by a thermal isomerization resets the whole system. The motor typically functions in this case as a multistage molecular switch. The triggering of polymer folding and transmission of chiral information from a single molecule to a macromolecule might offer new opportunities in addressable materials and thin films.

Ultimately, the purpose of constructing molecular motors and machines is to make them do work and perform useful

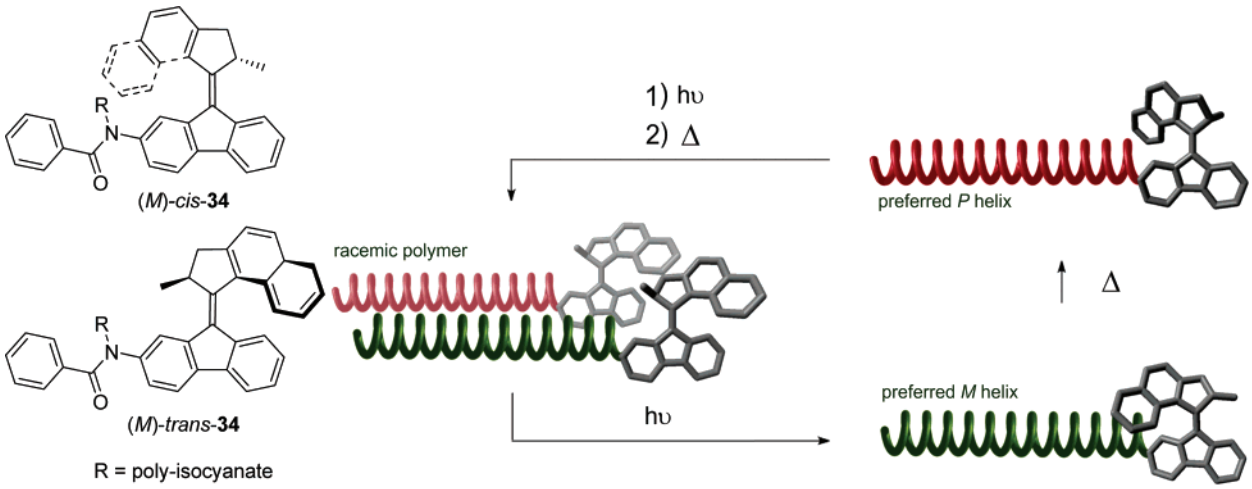


FIGURE 26. Structure of polymer modified second generation rotary motor **34** and schematic illustration of the reversible induction and inversion of the helicity of a polymer backbone by a single light-driven molecular motor positioned at the terminus. Irradiation of the photochromic unit leads to a preferred helical sense of the polymer backbone. A thermal isomerization of the rotor unit inverts the preferred helicity of the polymer chain. Subsequent photochemical and thermal isomerization steps regenerate the original situation with a random helicity of the polymer backbone. Adapted from ref 83. Copyright Wiley 2007.

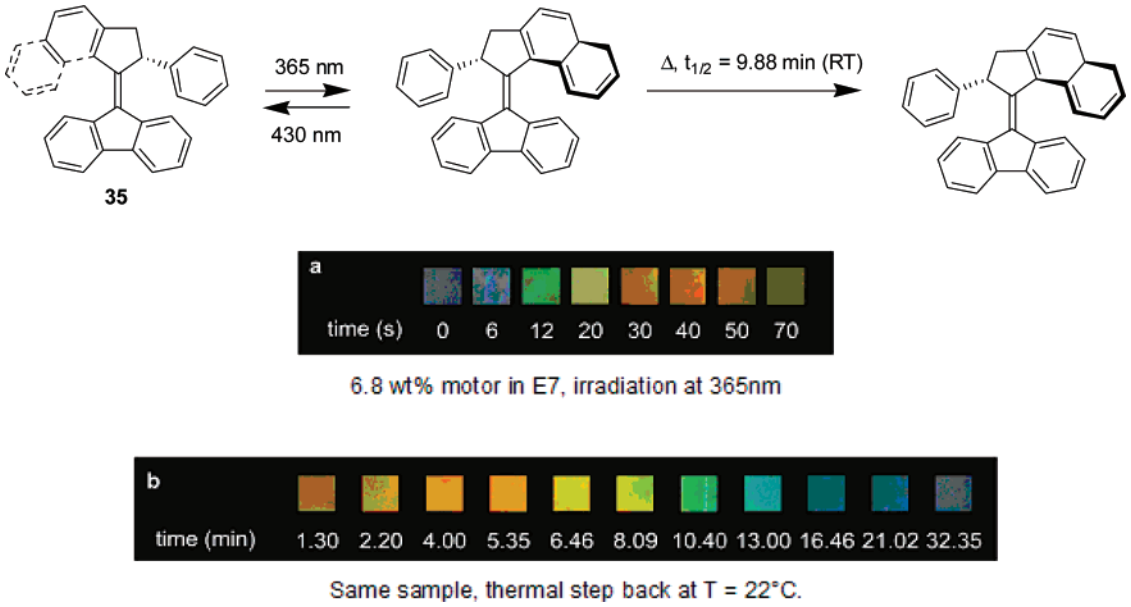


FIGURE 27. Molecular structure, photochemical and thermal isomerization processes of **35**, and changes in the color of LC compound E7 doped with **35**. Adapted from ref 86. Copyright Wiley 2006.

functions.[2,84] The control of a macroscopic property of a material using a molecular motor was demonstrated by employing liquid crystals. As shown earlier with chiroptical molecular switches, several of the optically active overcrowded alkenes serve as excellent chiral dopants in LC films inducing cholesteric phases.[85] The change in helicity of the different isomers of the second generation motors **35** is, for instance, reflected in large changes in helical twisting power and concomitant changes in the helical organization of the LC phases.[86] In this way, LC films with colors covering the entire visible spectrum are obtained readily (Figure 27). The fully reversible nature of this process offers new prospects in dynamic LC pixel generation.

More recently, we have been able to demonstrate microscopic movement induced by changes in helicity of a molecular motor. The reversible rotation of the surface texture of a LC film and microscopic objects placed on top of this film was achieved using molecular motor **35**.[87]

This motor is particularly effective in inducing a dynamic helical (twisted nematic) organization when applied as a chiral dopant in a LC film (Figure 28). The photochemically or thermally induced isomerization steps of the motor molecule result in reorganization of the polygonal LC texture. Using AFM and optical profilometry, a surface relief of 20 nm was observed on top of this film. Intriguingly, the orientation and nature of the surface relief changed in response to the changes in the molecular motor topology.[87] The rotational change in surface relief generates sufficient torque to rotate a microscopic object, for instance, a glass rod placed on top of the film, in a unidirectional manner (Figure 28c).

Irradiation of the motor in the LC matrix results in clockwise rotation of the glass rod placed on the film. When the

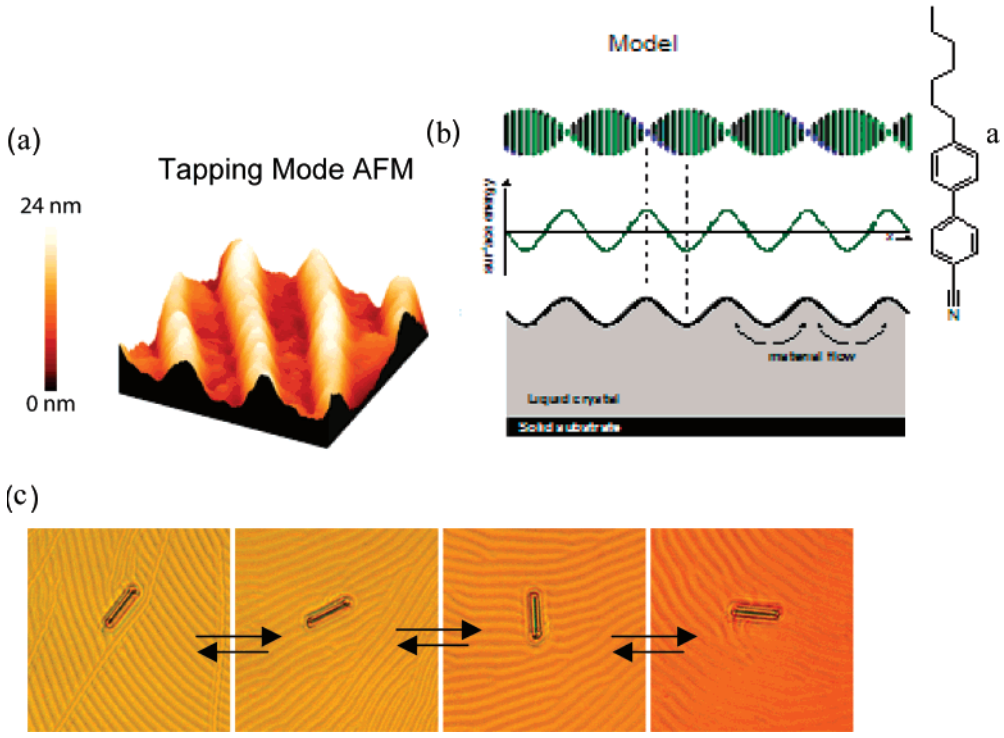


FIGURE 28. (a) Tapping mode AFM image of the surface of an LC film doped with molecular motor **35**. (b) Model showing the orientation of the LC component in the twisted nematic phase, surface energy profile, and material flow accompanying the change in helical twisting power (HTP) of dopant **35** upon irradiation. (c) Physical movement of micrometer-size glass rod objects resting on the LC surface. Adapted from ref 87a,b. Copyright Nature 2006 and American Chemical Society 2006.

photostationary state is reached, the rotation of the rod stops, whereas the subsequent thermal isomerization of the motor molecule results in reverse (counterclockwise) rotation of the rod. The directionality of the rod movement reflects directly the (change in) helical chirality of the motor molecules used as dopant. In this system, light energy and the collective action of a number of motor molecules are used to rotate microscopic objects that exceed the nanomotors in size 10 000 times. The next challenging step will be to achieve continuous unidirectional rotary motion of microscopic objects powered by these molecular motors.

Future Prospects

In the art of building small, nature is particularly generous in providing a wealth of complex structures, intricate functions, and well-balanced molecular systems, while at the same time, it is modest in the number of building blocks it relies upon. It is fascinating that virtually every important biological process relies on molecular motors and machines. The past decades have seen spectacular progress in the detailed understanding of the "machinery of life", and together with advances in supramolecular chemistry, scanning probe techniques and advanced spectroscopies, as well as the quest for functional materials controlled at the nanoscale, it provides the impetus for the numerous efforts toward the design and synthesis of artificial "molecular machines". Our earliest attempts, though primitive in nature, have revealed already many of the fundamental issues to be faced on the road ahead. A particularly challenging issue is the control of molecular motion as motor functions will be essential in powering future "nanoscale" machines. Although the proper functioning of unidirectional rotary and translational molecular motors has been demonstrated, the problems associated with either fighting or harnessing Brownian motion (as with biological motors) are still significant. It is not too far-fetched to suggest that artificial machines powered by molecular motors will be constructed that can perform a wide variety of functions reminiscent of those of biological machines. We are not at all limited by the building blocks nature uses, and we might well take advantage of the hard−soft interface, the progress in nanoelectronics, and catalysis or the use of single molecule techniques to develop and study entirely novel molecular systems with machine-like functions. The controlled directional movement along a trajectory, the use of molecular motors as transporters for molecular cargo, the construction of motor powered machines and devices that can perform several mechanical functions, and the design of smart switchable surfaces are just a few of the developments that can be envisioned in the near future. What are the potential applications of molecular motors and machines is a question asked frequently in the context of future technology based on (molecular) nanoscience. A glance at the myriad of molecular machines in biology and the fascinating diversity of processes they engage is perhaps the best testimony to the prospects ahead. The first examples of molecular motors at work have been reported.[2] We should not forget that the structures and functions of artificial motors and machines are likely to be entirely different from their biological counterparts. Perhaps more intriguing at present are fundamental questions associated with mechanical motion of molecules, supramolecular and macromolecular systems, surface-bound motors, and more complex multicomponent systems at the nanoscale. It is evident that this whole field is still in its infancy and offers ample opportunity for molecular design and discovery. Most importantly, it is particularly joyful, challenging, and exciting to design and synthesize functional

molecular mechanical systems and work on the problems of controlling molecular switching and motion.

Acknowledgment. I am extremely grateful to all my students, co-workers and collaborators for their superb contributions. Their names are given in the references. Working daily with such talented young people is a great joy. In particular, I wish to thank Dr. Wesley R. Browne and Dr. Michael M. Pollard for their help with preparing this manuscript and their numerous contributions to our molecular switches and motors program. I gratefully acknowledge The Netherlands Foundation for Scientific Research (NWO-CW), the NanoNed program, and the Zernike Institute for Advanced Materials (MSC+) program for their financial support.

Glossary

AFM	atomic force microscopy
CD	circular dichroism
CPL	circularly polarized light
ee	enantiomeric excess
EM	electron microscopy
HTP	helical twisting power
LC	liquid crystal
LMW	low molecular weight
LPL	linearly polarized light
MCBJ	mechanically controlled break junction

References

(1) Goodsell, S. *Our Molecular Nature. The Body's Motors, Machines and Messages*; Springer-Verlag: New York, 1996.
(2) (a) Browne, W. R.; Feringa, B. L. *Nat. Nanotechnol.* **2006**, *1*, 25−35. (b) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72−191. (c) Stoddart, J. F. *Acc. Chem. Res.* **2001**, *34*, 410−411. (d) Balzani, V.; Credi, A.; Venturi, M. *Molecular Devices and Machines−A Journey into the Nanoworld*; Wiley-VHC: Weinheim, Germany, 2003. (e) Sauvage, J. P., Ed. *Molecular Machines and Motors*; Springer: Berlin, 2001. (f) Harada, A. *Acc. Chem. Res.* **2001**, *34*, 456−464.
(3) (a) Brown, R. *Philos. Mag.* **1828**, *4*, 171−173. (b) Rozenbaum, V. M.; Yang, D.-Y.; Lin, S. H.; Tsong, T. Y. *J. Phys. Chem. B* **2004**, *108*, 15880−15889. (c) Whitesides, G. M. *Sci. Am.* **2001**, *285*, 78−84.
(4) Feringa, B. L., Ed. *Molecular Switches*; Wiley-VCH: Weinheim, Germany, 2001.
(5) Saha, S.; Stoddart, J. F. *Chem. Soc. Rev.* **2007**, *36*, 77−92.
(6) Magri, D. C.; Brown, G. J.; McClean, G. D.; de Silva, A. P. *J. Am. Chem. Soc.* **2006**, *128*, 4950−4951.
(7) Feynman, R. P. *The Pleasure of Finding Things Out*; Perseus Books: Cambridge, MA, 1999; Chapter 5. Richard Feyman's original lecture "There's plenty of room at the bottom" can be read at www.its.caltech.edu/~feynman.
(8) Mathies, R. A.; Lugtenburg, J. In *Molecular Mechanisms of Visual Transduction*; Stavenga, D. G., DeGrip, W. J., Pugh, E. N., Jr. Eds.; Elsevier: Amsterdam, the Netherlands, 2001; p 55.
(9) Crano, J. C.; Guglielmetti, R. J. *Organic Photochromic and Thermochromic Compounds*; Springer: New York, 1999; Vols. 1−3.
(10) Feringa, B. L.; Wynberg, H. *J. Am. Chem. Soc.* **1977**, *99*, 602−603.
(11) Feringa, B. L.; van Delden, R. A.; Koumura, N.; Geertsema, E. M. *Chem. Rev.* **2000**, *100*, 1789−1816.
(12) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741−770.
(13) Huck, N. P. M.; Jager, W. F.; de Lange, B.; Feringa, B. L. *Science* **1996**, *273*, 1686−1688.
(14) (a) Jager, W. F.; de Jong, J. C.; de Lange, B.; Huck, N. P. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 348−350. (b) Feringa, B. L.; Jager, W. F.; de Lange, B.; Meijer, E. W. *J. Am. Chem. Soc.* **1991**, *113*, 5468. (c) Feringa, B. L.; Jager, W. F.; de Lange, B. *J. Chem. Soc., Chem. Commun.* **1993**, 288.
(15) Feringa, B. L.; Schoevaars, A. M.; Jager, W. F.; de Lange, B.; Huck, N. P. M. *Enantiomer* **1996**, *1*, 325−335.
(16) van Delden, R. A.; ter Wiel, M. K. J.; Feringa, B. L. *Chem. Commun.* **2004**, 200−201.
(17) Schuddeboom, W.; Jonker, S. A.; Warman, J. M.; de Haas, M. P.; Vermeulen, M. J. W.; Jager, W. F.; de Lange, B.; Feringa, B. L.; Fessenden, R. W. *J. Am. Chem. Soc.* **1993**, *115*, 3286.
(18) Jager, W. Ph.D. Thesis., University of Groningen, The Netherlands, 1994.
(19) Green, J. E.; Choi, J. W.; Boukai, A.; Bunimovich, Y.; Johnston-Halperin, E.; Delonno, E.; Luo, Y.; Sheriff, B. A.; Xu, K.; Shin, Y. S.; Tseng, H. R.; Stoddart, J. F.; Heath, J. R. *Nature* **2007**, *445*, 414−417.
(20) Oosterling, M. L. C. M.; Schoevaars, A. M.; Haitjema, H. J.; Feringa, B. L. *Isr. J. Chem.* **1996**, *36*, 341−348.
(21) (a) Schoevaars, A. M. Ph.D. Thesis, University of Groningen, The Netherlands, 1998. (b) Feringa, B. L.; Huck, N. P. M.; Schoevaars, A. M. *Adv. Mater.* **1996**, *8*, 681−684.
(22) Huck, N. P. M.; Feringa, B. L. *J. Chem. Soc., Chem. Commun.* **1995**, 1095.
(23) van Delden, R. A.; Huck, N. P. M.; Piet, J. J.; Warman, J. M.; Meskers, S. C. J.; Dekkers, H. P. J. M.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 15659−15665.
(24) Browne, W. R.; Pollard, M. M.; de Lange, B.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 12412−12413.
(25) Pollack, G. H. *Cells, Gels and the Engines of Life*: Ebner and Sons: Seattle, 2001.
(26) Demus, D.; Goodby, J.; Gray, G. W.; Spiess, H.-W.; Vill, V. *Handbook of Liquid Crystals*; Wiley-VCH: Weinheim, Germany, 1998; Vols. 1, 2A, 2B, and 3.
(27) Feringa, B. L.; Huck, N. P. M.; van Doren, H. A. *J. Am. Chem. Soc.* **1995**, *117*, 9929−9930.
(28) van Delden, R. A.; van Gelder, M. B.; Huck, N. P. M.; Feringa, B. L. *Adv. Funct. Mater.* **2003**, *13*, 319−324.
(29) (a) de Loos, M.; Feringa, B. L.; van Esch, J. H. *Eur. J. Org. Chem.* **2005**, 3615−3631. (b) de Loos, M.; van Esch, J. H.; Kellogg, R. M.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 613−616.
(30) de Loos, M.; Friggeri, A.; van Esch, J. H.; Kellogg, R. M.; Feringa, B. L. *Org. Biomol. Chem.* **2005**, *3*, 1631−1639.
(31) de Loos, M.; van Esch, J. H.; Stokroos, I.; Kellogg, R. M.; Feringa, B. L. *J. Am. Chem. Soc.* **1997**, *119*, 12675−12676.
(32) (a) Schuurmans, N.; Uji-I, H.; Mamdouh, W.; De Schryver, F. C.; Feringa, B. L.; van Esch, J. H.; De Feyter, S. *J. Am. Chem. Soc.* **2004**, *126*, 13884−13885. (b) Schoonbeek, F. S.; van Esch, J. H.; Wegewijs, B.; Rep, D. B. A.; de Haas, M. P.; Klapwijk, T. M.; Kellogg, R. M.; Feringa, B. L. *Angew. Chem., Int. Ed.* **1999**, *35*, 1393−1397. (c) Rep, D. B. A.; Roelfsema, R.; van Esch, J. H.; Schoonbeek, F. S.; Kellogg, R. M.; Feringa, B. L.; Palstra, T. T. M.; Klapwijk, T. M. *Adv. Mater.* **2000**, *12*, 563−566.
(33) (a) van Bommel, K. J. C.; Stuart, M. C. A.; Feringa, B. L.; van Esch, J. H. *Org. Biomol. Chem.* **2005**, *3*, 2917−2920. (b) van Bommel, K. J. C.; van der Pol, C.; Muizebelt, I.; Friggeri, A.; Heeres, A.; Meetsma, A.; Feringa, B. L.; van Esch, J. H. *Angew. Chem., Int. Ed.* **2004**, *43*, 1663−1667.
(34) Irie, M. *Chem. Rev.* **2000**, *100*, 1685−1716.
(35) (a) de Jong, J. J. D.; Lucas, L. N.; Kellogg, R. M.; van Esch, J. H.; Feringa, B. L. *Science* **2004**, *304*, 278−281. (b) de Jong, J. J. D.; Hania, P. R.; Pugzlys, A.; Lucas, L. N.; de Loos, M.; Kellogg, R. M.; Feringa, B. L.; Duppen, K.; van Esch, J. H. *Angew. Chem., Int. Ed.* **2005**, *44*, 2373−2376. (c) de Jong, J. J. D.; Tiemersma-Wegman, T. D.; van Esch, J. H.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 13804−13805.
(36) (a) Fraysse, S.; Coudret, C.; Launay, J. P. *Eur. J. Inorg. Chem.* **2000**, 1581−1590. (b) Belser, P.; De Cola, L.; Hartl, F.; Adamo, V.; Bozic, B.; Chriqui, Y.; Iyer, V. M.; Jukes, R. T. F.; Kuhni, J.; Querol, M.; Roma, S.; Salluce, N. *Adv. Funct. Mater.* **2006**, *16*, 195−208. (c) Takayama, K.; Matsuda, K.; Irie, M. *Chem.—Eur. J.* **2003**, *9*, 5605−5609.
(37) (a) Browne, W. R.; de Jong, J. J. D.; Kudernac, T.; Walko, M.; Lucas, L. N.; Uchida, K.; van Esch, J. H.; Feringa, B. L. *Chem.—Eur. J.* **2005**, *11*, 6414−6429. (b) Browne, W. R.; de Jong, J. J. D.; Kudernac, T.; Walko, M.; Lucas, L. N.; Uchida, K.; van Esch, J. H.; Feringa, B. L. *Chem.—Eur. J.* **2005**, *11*, 6430−6441.
(38) (a) de Jong, J. J. D.; Lucas, L. N.; Hania, R.; Pugzlys, A.; Kellogg, R. M.; Feringa, B. L.; Duppen, K.; van Esch, J. H. *Eur. J. Org. Chem.* **2003**, *1*, 1887−1893. (b) Lucas, L. N.; de Jong, J. J. D.; van Esch, J. H.; Kellogg, R. M.; Feringa, B. L. *Eur. J. Org. Chem.* **2003**, *1*, 155−166.
(39) Areephong, J.; Browne, W. R.; Katsonis, N.; Feringa, B. L. *Chem. Commun.* **2006**, 3930−3932.
(40) Dulic, D.; van der Molen, S. J.; Kudernac, T.; Jonkman, H. T.; de Jong, J. J. D.; Bowden, T. N.; van Esch, J. H.; Feringa, B. L.; van Wees, B. J. *Phys. Rev. Lett.* **2003**, *91*, 207402.
(41) Thomas, K. G.; Ipe, B. I.; Sudeep, P. K. *Pure Appl. Chem.* **2002**, *74*, 1731−1738.
(42) Kudernac, T.; van der Molen, S. J.; van Wees, B. J.; Feringa, B. L. *Chem. Commun.* **2006**, 3597−3599.
(43) van der Molen, S. J.; van der Vegte, H.; Kudernac, T.; Amin, I.; Feringa, B. L.; van Wees, B. J. *Nanotechnology* **2006**, *17*, 310−314.
(44) Katsonis, N.; Kudernac, T.; Walko, M.; van der Molen, S. J.; van Wees, B. J.; Feringa, B. L. *Adv. Mater.* **2006**, *18*, 1397−1400.
(45) Banghart, M. R.; Volgraf, M.; Trauner, D. *Biochemistry* **2006**, *45*, 15129−15141.
(46) (a) Takeuchi, M.; Ikeda, M.; Sugasaki, A.; Shinkai, S. *Acc. Chem. Res.* **2001**, *34*, 865−873. (b) Hess, H.; Bachand, G. D.; Vogel, V. *Chem.—Eur. J.* **2004**, *10*, 2110−2116. (c) Fyles, T. M. *Chem. Soc. Rev.* **2007**, *36*, 335−347.
(47) (a) Ajouz, B.; Berrier, C.; Garrigues, A.; Besnard, M.; Ghazi, E. *J. Biol. Chem.* **1998**, *273*, 26670−26674. (b) Sukharev, S.; Betanzos, M.; Chiang, C.-S.; Guy, H. R. *Nature* **2001**, *409*, 720−724. (c) Chang, G.; Spencer, R. H.; Lee, A. T.; Barclay, M. T.; Rees, D. C. *Science* **1998**, *282*, 2220−2226.

(48) Anishkin, A.; Chiang, C. S.; Sukharev, S. *J. Gen. Physiol.* **2005**, *125*, 155−170.
(49) Kocer, A.; Walko, M.; Meijberg, W.; Feringa, B. L. *Science* **2005**, *309*, 755−758.
(50) Kocer, A.; Walko, M.; Bulten, E.; Halza, E.; Feringa, B. L.; Meijberg, W. *Angew. Chem., Int. Ed.* **2006**, *45*, 3126−3130.
(51) Schliwa, M., Ed. *Molecular Motors*; Wiley: Weinheim, Germany, 2003.
(52) Astumian, R. D. *Science* **1997**, *276*, 917−922.
(53) Astumian, R. D. *Sci. Am.* **2001**, *285*, 45−51.
(54) (a) Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281−1376. (b) Iwamura, H.; Mislow, K. *Acc. Chem. Res.* **1988**, *21*, 175−182.
(55) Schoevaars, A. M.; Kruizinga, W.; Zijlstra, R. W. J.; Veldman, N.; Spek, A. L.; Feringa, B. L. *J. Org. Chem.* **1997**, *62*, 4943−4948.
(56) See also: Kelly, T. R.; Bowyer, M. C.; Bhaskar, K. V.; Bebbington, D.; Garcia, A.; Lang, F. R.; Kim, M. H.; Jette, M. P. *J. Am. Chem. Soc.* **1994**, *116*, 3657−3658 and references therein.
(57) Kinbara, K.; Aida, T. *Chem. Rev.* **2005**, *105*, 1377−1400.
(58) Ismagilov, R. F.; Schwartz, A.; Bowden, N.; Whitesides, G. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 652−654.
(59) (a) Paxton, W. F.; Kistler, K. C.; Olmeda, C. C.; Sen, A.; St. Angelo, S. K.; Cao, Y.; Mallouk, T. E.; Lammert, P. E.; Crespi, V. H. *J. Am. Chem. Soc.* **2004**, *126*, 13424−13431. (b) Kline, T. R.; Paxton, W. F.; Mallouk, T. E.; Sen, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 744−746.
(60) Vicario, J.; Eelkema, R.; Browne, W. R.; Meetsma, A.; La Crois, R. M.; Feringa, B. L. *Chem. Commun.* **2005**, 3936−3938.
(61) de Boer, J. W.; Browne, W. R.; Hage, R.; Feringa, B. L. *C. R. Chimie* **2007**, *10*, 341−354.
(62) Wang, Y.; Hernandez, R. M.; Bartlett, D. J.; Bingham, J. M.; Kline, T. R.; Sen, A.; Mallouk, T. E. *Langmuir* **2006**, *22*, 10451−10456.
(63) Kelly, T. R.; De Silva, H.; Silva, R. A. *Nature* **1999**, *401*, 150−152.
(64) Kelly, T. R.; Cai, X. L.; Damkaci, F.; Panicker, S. B.; Tu, B.; Bushell, S. M.; Cornella, I.; Piggott, M. J.; Salives, R.; Cavero, M.; Zhao, Y. J.; Jasmin, S. *J. Am. Chem. Soc.* **2007**, *129*, 376−386.
(65) Fletcher, S. P.; Dumur, F.; Pollard, M. M.; Feringa, B. L. *Science* **2005**, *310*, 80−82.
(66) (a) Dahl, B. J.; Branchaud, B. P. *Org. Lett.* **2006**, *8*, 5841−5844. (b) Dahl, B. J.; Branchaud, B. P. *Tetrahedron Lett.* **2004**, *45*, 9599−9602.
(67) Kocovsky, P.; Vyskocil, S.; Smrcina, M. *Chem. Rev.* **2003**, *103*, 3213−3246.
(68) Bringmann, G.; Menche, D. *Acc. Chem. Res.* **2001,** *34*, 615−624.
(69) Koumura, N.; Zijlstra, R. W. J.; van Delden, R. A.; Harada, N.; Feringa, B. L. *Nature* **1999**, *401*, 152−155.
(70) van Delden, R. A.; ter Wiel, M. K. J.; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. *Nature* **2005**, *437*, 1337−1340.
(71) ter Wiel, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 14208−14222.
(72) ter Wiel, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 15076−15086.
(73) (a) Koumura, N.; Geertsema, E. M.; van Gelder, M. B.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 5037−5051. (b) van Delden, R. A.; ter Wiel, M. K. J.; de Jong, H.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2004**, *2*, 1531−1541.
(74) Pollard, M. M.; Klok, M.; Pijper, D.; Feringa, B. L. *Adv. Funct. Mater.* **2007**, doi 10.1002/adfm.200601025
(75) Vicario, J.; Meetsma, A.; Feringa, B. L. *Chem. Commun.* **2005**, 5910−5912.
(76) Geertsema, E. M.; Koumura, N.; ter Wiel, M. K. J.; Meetsma, A.; Feringa, B. L. *Chem. Commun.* **2002**, 2962−2963.
(77) Vicario, J.; Walko, M.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 5127−5135.
(78) Pijper, D.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 17612−17613.
(79) van Delden, R. A.; Koumura, N.; Schoevaars, A.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2003**, *1*, 33−35.
(80) van Delden, R. A.; ter Wiel, M. K. J.; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. *Nature* **2005**, *437*, 1337−1340.
(81) Pollard, M. M.; Lubomska, M.; Rudolf, P.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1278−1280.
(82) ter Wiel, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2005**, *3*, 4071−4076.
(83) Pijper, D.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 3693−3696.
(84) (a) Oh, S. K.; Nakagawa, M.; Ichimura, K. *J. Mater. Chem.* **2002**, *12*, 2262−2269. (b) Berna, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Perez, E. M.; Rudolf, P.; Teobaldi, G.; Zerbetto, F. *Nat. Mater.* **2005**, *4*, 704−710. (c) Huang, J.; Brough, B.; Ho, C.-M.; Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Tseng, H.-R.; Stoddart, J. F.; Baller, M.; Maganov, S. A. *Appl. Phys. Lett.* **2003**, *85*, 5391−5393. (d) Liu, Y.; Flood, A. H.; Bonvallet, P. A.; Vignon, S. A.; Northrop, B. H.; Tseng, H.-R.; Jeppesen, J. O.; Huang, T. J.; Brough, B.; Baller, M.; Magonov, S.; Solares, S. D.; Goddard, W. A.; Ho, C.-M.; Stoddart, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 9745−9759. (e) Holland, N. B.; Hugel, T.; Neuert, G.; Cattani-Scholz, A.; Renner, C.; Oesterhelt, D.; Moroder, L.; Seitz, M.; Gaub, H. E. *Macromolecules* **2003**, *36*, 2015−2023. (f) Hugel, T.; Holland, N. B.; Cattani, A.; Moroder, L.; Seitz, M.; Gaub, H. E. *Science* **2002**, *296*, 1103−1106. (f) Harris, K. D.; Cuypers, R.; Scheibe, P.; van Oosten, C. L.; Bastiaansen, C. W. M.; Lub, J.; Broer, D. J. *J. Mater. Chem.* **2005**, *15*, 5043−5048.
(85) (a) van Delden, R. A.; Koumura, N.; Harada, N.; Feringa, B. L. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4945−4949. (b) Eelkema, R.; Feringa, B. L. *Org. Biomol. Chem.* **2006**, *4*, 3729−3745.
(86) Eelkema, R.; Feringa, B. L. *Chem. Asian J.* **2006**, *1*, 367−369.
(87) (a) Eelkema, R.; Pollard, M. M.; Vicario, J.; Katsonis, N.; Ramon, B. S.; Bastiaansen, C. W. M.; Broer, D. J.; Feringa, B. L. *Nature* **2006**, *440*, 163−163. (b) Eelkema, R.; Pollard, M. M.; Katsonis, N.; Vicario, J.; Broer, D. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 14397−14407.

JO070394D