

Artificial molecular machines driven by light

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1. ABSTRACT

The bottom-up construction and operation of machines and motors of molecular size is a topic of great interest in nanoscience, and a fascinating challenge of nanotechnology. The problem of the energy supply to make molecular machines work is of the greatest importance. Research in the last ten years has demonstrated that light energy can be used to power artificial nanomachines by exploiting photochemical processes in appropriately designed systems. More recently, it has become clear that under many aspects light is the best choice to power molecular machines; for example, systems that show autonomous operation and do not generate waste products can be obtained. This review is intended to discuss the design principles at the basis of light-driven artificial nanomachines, and provide an up-to-date overview on the prototype systems that have been developed.

2. BASIC CONCEPTS

2.1. Introduction and scope

The development of civilization has always been strictly related to the design and construction of devices – from wheel to jet engine – capable of facilitating man movement and travelling. Nowadays the miniaturization race leads scientists to investigate the possibility of designing and constructing motors and machines at the nanometer scale, that is, at the molecular level. The development of operational nanomachines is expected to impact strongly on several fields of science and technology, including medicine (1). Chemists, by the nature of their discipline, are able to manipulate atoms and molecules and are therefore in the ideal position to develop bottom-up strategies for the construction of nanoscale devices (2).

Movement is also a central attribute of life. Nature provides living organisms with complex molecules

called motor proteins which work inside a cell like ordinary machines built for everyday needs (3,4). The most important and best known natural molecular motors are ATP synthase, myosin and kinesin. ATP synthase is the ubiquitous enzyme that manufactures adenosine triphosphate (ATP) and is a rotary motor powered by a proton gradient. The enzymes of the myosin and the kinesin families are linear motors that move along polymer substrates (actin filaments for myosin and microtubules for kinesin), converting the energy of ATP hydrolysis into mechanical work. Motion derives from a mechanochemical cycle, during which the motor protein binds to successive sites along the substrate in such a way as to move forward on average. Several other biological processes are based on motions, including protein folding and unfolding. Another example is RNA polymerase, which moves along DNA while carrying out transcriptions. Surely, the supramolecular architectures of the biological world are themselves the premier, proven examples of the feasibility and utility of nanotechnology, and constitute a sound rationale for attempting the realization of artificial molecular devices (5,6).

A molecular machine can be defined as an assembly of a discrete number of molecular components designed to perform directional mechanical movements under control of appropriate energy inputs. A molecular motor is a type of molecular machine capable of using a energy input to produce useful mechanical work (35,37). Molecular machines and motors operate via electronic and/or nuclear rearrangements and, like the macroscopic counterparts, they are characterized by the kind of energy input supplied to make them work, the type of motion (translation, rotation, oscillation, etc.) performed by their components, the way of monitoring their operation (the rearrangements of the component parts should cause readable changes in some chemical or physical property of the system), the possibility to repeat the operation in cycles, and the time scale needed to complete a cycle.

However, nanoscale machines and motors cannot be considered merely as 'shrunk' versions of the corresponding macroscopic counterparts. In fact, the operation mechanisms of molecular machines cannot be devised on the basis of scaling rules, because they have to deal with phenomena different from those that govern the macroscopic world (5,7). For example, inertia-dominated motion we are familiar with in our everyday experience is fully negligible at the molecular scale, where viscous forces resulting from intermolecular interactions (including those with solvent molecules) largely prevail. Another fundamental difference between the macroscopic and the nanoscale realms is represented by the importance of thermal fluctuations (Brownian motion) (8). This random motion can be neglected for 'big' objects, but dominates the mechanical behavior of small (sub-micrometer) particles. Nanometer-scale systems are thus inherently subjected to Brownian motion. Because of the second law of thermodynamics, molecular machines cannot simply be driven by thermal energy at a constant temperature: in analogy with macroscopic machines, they need to be fueled by an energy source in order to carry out a task. Therefore,

as it will be discussed in the next section, the problem of the energy supply to make artificial molecular machines work is of the greatest importance (9).

Natural molecular motors are extremely sophisticated systems and it is clear that the construction of systems of such a structural and functional complexity by using the bottom-up molecular approach would be, at present, an impossible task. What can be done in the field of artificial molecular motors and machines is to construct simple prototypes consisting of a few molecular components, capable of moving in a controllable way, and to investigate the challenging problems posed by interfacing such nanodevices with the macroscopic world, particularly as far as energy supply and information exchange are concerned. In recent years synthetic talent – that has always been the most distinctive feature of chemists – combined with a device-driven ingenuity evolved from chemists' attention to functions and reactivity, have led to outstanding achievements in this field. Among the systems developed are molecular propellers (10), rotors (11), turnstiles (12), gyroscopes (13,14), gears (15), brakes (16), ratchets (17), switches (18), shuttles (19), elevators (20), muscles (21), valves (22), processive artificial enzymes (23), walkers (24,25,26) and catalytic self-propelled micro- and nano-rods (27). Several excellent reviews (28,29,30,31,32,33,34,35,36) and a monography (37) are also available.

This short review will focus on the use of light to power artificial molecular machines. We will describe a few recent examples of photodriven molecular machines capable of performing rotary and linear motions of their component parts, and we shall discuss the various design strategies and processes at the basis of their operation. Many other studies in the field can be found in the reference list.

2.2. The energy problem

The most obvious way to supply energy to a chemical system is through an exergonic chemical reaction. Not surprisingly, the majority of the molecular machines of the biological world are powered by chemical reactions (e.g., ATP hydrolysis) (3,4). Richard Feynman, in his famous address (38) to the American Physical Society in 1959, observed that *«an internal combustion engine of molecular size is impossible. Other chemical reactions, liberating energy when cold, can be used instead»*. This is exactly what happens in our body, where the chemical energy supplied by food is used in long series of slightly exergonic reactions to power the biological machinery that sustain life.

If an artificial molecular machine has to work by inputs of chemical energy, it will need addition of fresh reactants ('fuel') at any step of its working cycle, with the concomitant formation of waste products. Accumulation of waste products, however, will compromise the operation of the device unless they are removed from the system, as it happens in our body as well as in macroscopic internal combustion engines. The need to remove waste products introduces noticeable limitations in the design and

construction of artificial molecular machines based on chemical fuel inputs.

Chemists have since long known that photochemical and electrochemical energy inputs can cause the occurrence of *endergonic* and *reversible* reactions. In the last few years, the outstanding progress made by supramolecular photochemistry (39) and electrochemistry (40) has thus led to the design and construction of molecular machines powered by light or electrical energy which work without formation of waste products. Needless to say, the operation of a molecular machine is accompanied by partial conversion of free energy into heat, regardless of the chemical, photochemical, or electrochemical nature of the energy input.

In the context of artificial nanomachines, light energy stimulation possesses a number of advantages compared to chemical or electrochemical stimulation (41,42,43). First of all, the amount of energy conferred to a chemical system by using photons can be carefully controlled by the wavelength and intensity of the exciting light, in relation to the absorption spectrum of the targeted species. Such an energy can be transmitted to molecules without physically connecting them to the source (no 'wiring' is necessary), the only requirement being the transparency of the matrix at the excitation wavelength. Other properties of light, such as polarization, can also be utilized. Lasers provide the opportunity of working in very small spaces and extremely short time domains, and near-field techniques allow excitation with nanometer resolution. On the other hand, the irradiation of large areas and volumes can be conveniently carried out, thereby allowing the parallel (or even synchronous) addressing of a very high number of individual nanodevices.

Photochemical methods are also useful for monitoring the operation of the machine. In general, photons can play with respect to chemical systems the dual role of *writing* (i.e., causing a change in the system) and *reading* (i.e., reporting the state of the system). This is also true in Nature, where sunlight photons are employed both as energy quanta in photosynthetic processes, and as information elements in vision and other light-triggered processes. Specifically, luminescence spectroscopy is a valuable technique since it is easily accessible and offers good sensitivity and selectivity, along with the possibility of time- and space-resolved studies.

The use of light to power nanoscale devices is relevant for another important reason. If and when a nanotechnology-based industry will be developed, its products will have to be powered by renewable energy sources, since it has become clear that the problem of energy supply is a crucial one for human civilization for the years ahead (44). In this frame, the construction of nanodevices, including natural-artificial hybrids (45), that harness solar energy in the form of visible or near-UV light is indeed an important possibility.

2.3. Autonomous operation

An important feature of a molecular machine is its capability to exhibit an autonomous behavior, i.e., to

operate without external intervention (in other words, in a constant environment) as long as the energy source is available. Hence, autonomous molecular machines are free-running devices that do not require controlled and repeated addition of chemicals or other environmental changes. Natural motors are autonomous, in most cases acting as catalyzers for the fueling reaction. Except some recent work on DNA nanodevices (25,26,46), the chemically powered artificial molecular machines reported so far are not autonomous because after the mechanical movement induced by a given input they need another, opposite input to reset.

The design of autonomous nanomachines can take advantage from reversible photochemical processes. For instance, the operation of the machine could be based on a photoinduced sequence of processes that lead the system through transient electronic and nuclear (mechanical) states; the final deactivation of the system to the ground state provides an automatic reset and closes the cycle of operation. Alternatively, the mechanical motion could be related to the light-triggered switching between two stable states as it happens in photochromic systems. These approaches will be more conveniently discussed in examples illustrated in sections 3 and 4.

2.4. Interlocked molecular species as nanoscale machines

In principle, artificial molecular machines can be designed starting from several kinds of molecular and supramolecular systems (19-36), including DNA (47,48). However, for the reasons mentioned below, most of the systems constructed so far are based on interlocked molecular species such as rotaxanes, catenanes, and related species. The names of these compounds derive from the Latin words *rota* and *axis* for wheel and axle, and *catena* for chain. Rotaxanes (49) are minimally composed (Figure 1a) of a dumbbell-shaped molecule surrounded by a macrocyclic compound (the 'ring') and terminated by bulky groups ('stoppers') that prevent disassembly. Catenanes (49) are made of (at least) two interlocked macrocycles (Figure 1c). Important features of these systems derive from noncovalent interactions between components that contain complementary recognition sites. Such interactions, that are also responsible for the efficient template-directed syntheses (50) of rotaxanes and catenanes, include electron donor-acceptor ability, hydrogen bonding, hydrophobic-hydrophilic character, π - π stacking, electrostatic forces and, on the side of the strong interaction limit, metal-ligand bonding.

Rotaxanes and catenanes are appealing systems for the construction of molecular machines because (i) the mechanical bond allows a large variety of mutual arrangements of the molecular components, while conferring stability to the system, (ii) the interlocked architecture limits the amplitude of the intercomponent motion in the three directions, (iii) the stability of a specific arrangement (co-conformation) is determined by the strength of the intercomponent interactions, and (iv) such interactions can be modulated by external stimulation. The large-amplitude motions that can be achieved with

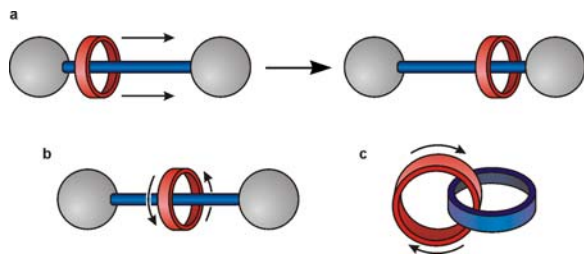


Figure 1. Schematic representation of the intercomponent motions that can be obtained with simple interlocked molecular architectures: ring shuttling in rotaxanes (a), and ring rotation in rotaxanes (b) and catenanes (c).

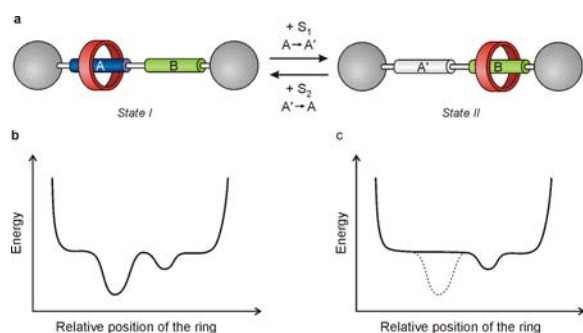


Figure 2. (a) Schematic representation of a two-station rotaxane and its operation as a controllable molecular shuttle. (b) A simplified representation of the potential energy of the system as a function of the position of the ring relative to the axle before (left) and after (right) switching off station A. An alternative approach would be to modify station B through an external stimulus in order to make it a stronger recognition site compared to station A.

rotaxanes and catenanes are represented schematically in Figure 1. Two interesting molecular motions can be envisaged in rotaxanes, namely (i) translation, i.e., shuttling, of the ring along the axle (Figure 1a), and (ii) rotation of the ring around the axle (Figure 1b). Hence, rotaxanes are good prototypes for the construction of both linear and rotary molecular machines. Systems of type (i), termed molecular shuttles, constitute indeed the most common implementation of the molecular machine concept with rotaxanes.

In order to construct a controllable molecular shuttle, a rotaxane with two ‘compartments’ on the axle component, each acting as a ‘docking station’ for the macrocyclic ring, is required (Figure 2a). If the two stations are different, the rotaxane can exist as two distinct equilibrating conformations, the population of which reflect their relative stability. The corresponding free energies (Figure 2b) are determined primarily by the strengths of the two different sets of noncovalent interactions established between the ring and each station. In the schematic representation shown in Figure 2, the molecular ring resides preferentially around station A (state I), until a stimulus S_1 is applied that switches off this recognition site ($A \rightarrow A'$). The rotaxane then equilibrates according to the new potential energy landscape, and the molecular ring

moves by Brownian motion to the second recognition site (station B, state II). If station A is switched on again ($A' \rightarrow A$) by an opposite stimulus S_2 , the original potential energy landscape is restored, and another conformational equilibration occurs through the shuttling of the ring back to station A by Brownian motion.

This strategy can straightforwardly be applied to construct catenanes in which the position of one molecular ring with respect to the other can be controlled by an external stimulation. Systems of this type are interesting as prototypes of rotary machines (Figure 1c). One ring of the catenane must be dissymmetric, i.e., bearing two different docking stations for the other macrocycle (Figure 3). In the initially stable isomer, station A is located ‘inside’ the symmetric ring whereas station B is located ‘alongside’. Upon application of a stimulus S_1 that switches off station A ($A \rightarrow A'$), the catenane is expected to relax towards a more stable isomer wherein station B occupies the cavity of the symmetric ring. Such a new state is reached through a half-turn rotation of the dissymmetric ring around the symmetric one. Reset of station A ($A' \rightarrow A$) by an opposite stimulus S_2 regenerates the starting isomer through another half-turn rotation of the dissymmetric ring. Note that the two half-turn rotations are directionally uncorrelated with one another. This point is of crucial importance for making rotary motors and will be discussed in more detail in section 2.2.

Interestingly, the dumbbell component of a molecular shuttle exerts on the ring motion the same type of directional restriction imposed by the protein track for linear biomolecular motors (an actin filament for myosin and a microtubule for kinesin and dynein) (3,4). It should also be noted that interlocked molecular architectures are largely present in natural systems – for instance, DNA catenanes and rotaxanes are known (49). Many processive enzymes, i.e., enzymes that remain attached to their biopolymer substrates (DNA, RNA or proteins) and perform multiple rounds of catalysis before dissociating, are thought to exhibit a rotaxane structure (51). Clearly, the unique aspect of the rotaxane architecture, that is, the mechanical binding of the catalyst with the substrate which leaves the former free to displace itself along the latter without losing the system’s integrity, is utilized by Nature to enhance the activity of processive enzymes.

3. ROTARY MOTIONS

3.1. Ring switching in catenanes

The use of transition metals as templates to construct multicomponent chemical systems with interlocked or knotted topologies has been largely exploited (49). Some of these species constitute nice prototypes of nanomachines (34). Recently, a strategy that takes advantage of the dissociative character of ligand-field excited states in ruthenium(II) diimine complexes to obtain light-driven molecular machines was reported (52). In these compounds, one part of the system is set in motion by photochemically expelling a given chelate, the reverse motion being performed by heating the product of the photoreaction so as to regenerate the original state. This

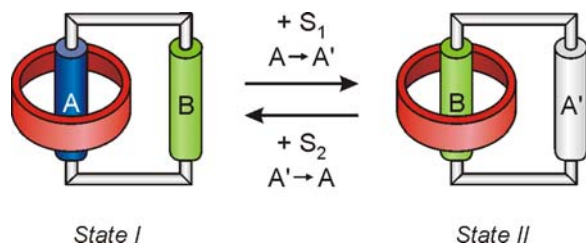


Figure 3. Schematic representation of a catenane having a dissymmetric macrocycle and its stimuli-induced switching between two isomeric forms that differ for the relative positioning of the two rings. See text for details.

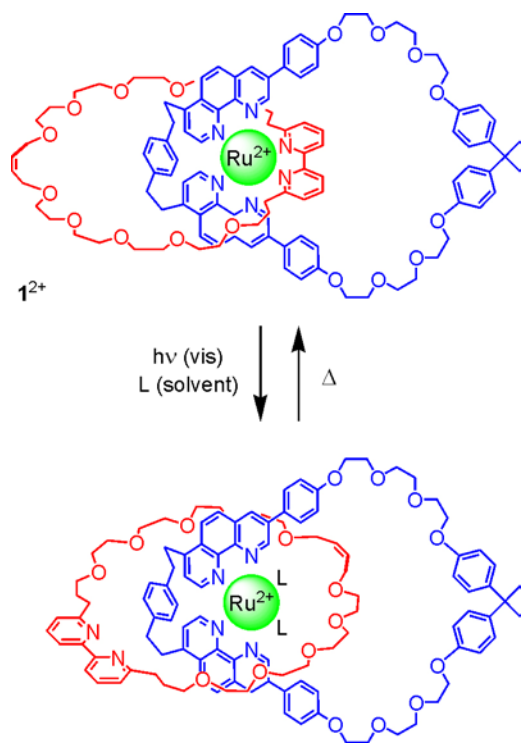


Figure 4. Photochemically and thermally induced motions taking place in the Ru catenane complex 1^{2+} (53). The representation of the decoordinated form (bottom) is indicative and does not imply that the actual structure of the photoproduct is that shown.

idea was implemented to obtain the light-driven switching of the molecular rings in a catenane (53). Visible excitation of the Ru catenane complex 1^{2+} (Figure 4) in acetonitrile solution leads to the population of the MLCT (metal-to-ligand charge-transfer) triplet excited state and subsequent formation of the ligand-field state which, in turn, causes the decooordination of the bipyridine ligand. As a result, rotation of the bipyridine-containing ring occurs, and a catenane structure composed of two disconnected rings (e.g., Figure 4, bottom) is obtained. Simple heating regenerates the starting complex, with both reactions (decoordination-recoordination) being quantitative. The overall process was monitored by NMR and UV-vis spectroscopy. By using the same strategy, light-induced

motions on a rotaxane system were also obtained (54). Light-driven ring switching has also been obtained in Cu(I)-based catenanes by exploiting photoinduced electron transfer processes (55).

3.2. Unidirectional ring rotation in catenanes

As noted in section 2.4, the repeated switching between the two states of a bistable catenane (Figure 2c), such as that described in the previous subsection, does not need to occur through a full rotation. In fact, because of the intrinsic symmetry of the system, both the half-turns of the ‘moving’ ring can take place, with equal probabilities, along a clockwise or anticlockwise direction. A full (360°) rotation movement, which would be much more interesting from a mechanical viewpoint because it is a requirement for the construction of a rotary motor (35), can only occur in ratchet-type systems, i.e., in the presence of further dissymmetry elements which can be structural or functional in nature. Of course, according to the second law of thermodynamics, a fundamental requirement for unidirectional motion even in such desymmetrized systems is the coupling with an exoergic reaction that ultimately provides the free energy for the directed movement.

A bistable catenane can be a starting point to make a rotary motor, but an additional control element has to be added. Unidirectional rotation could be achieved with a catenane according to the design illustrated in Figure 5 (32,37). Its ‘track’ ring contains two different recognition sites, A and B, a hindering group K and a blocking group X. In the starting co-conformation I, the ‘moving’ ring surrounds the most efficient site (A) on the track ring. Upon application of the stimulus S_1 , site A is switched off (A') and the ring must move away from it. The system has to reach the new stable co-conformation II wherein the ring surrounds site B. The presence of a blocking group X makes anticlockwise rotation faster compared to clockwise rotation. At this stage, application of stimulus S_2 causes the cleavage of the blocking group, and a reset stimulus S_{-1} restores the recognition ability to site A. The system has now to reach the starting co-conformation wherein the moving ring surrounds site A. The presence of the hindering group K makes again anticlockwise rotation faster compared to clockwise rotation. The original catenane structure is then obtained with a reset stimulus S_{-2} by which the blocking group X is put back in place. Unidirectional rotation in such a catenane occurs by a ‘flashing ratchet’ mechanism (7,8), which is based on a periodic change of the potential energy surface viewed by the moving part (Figure 5) by orthogonal (i.e., independent) reactions. It is worth noting that the direction of rotation can be inverted by reversing the order of the two input stimuli. Obviously, since the unidirectionality depends on the sequence of the inputs, a motor of this type cannot work autonomously.

This concept was cleverly realized in solution with the catenane **2** shown in Figure 6 (56). Its larger ring contains two recognition sites for the smaller ring – namely, a succinamide (SUC) and a photoisomerisable fumaramide (FUM) units – and two bulky substituents that

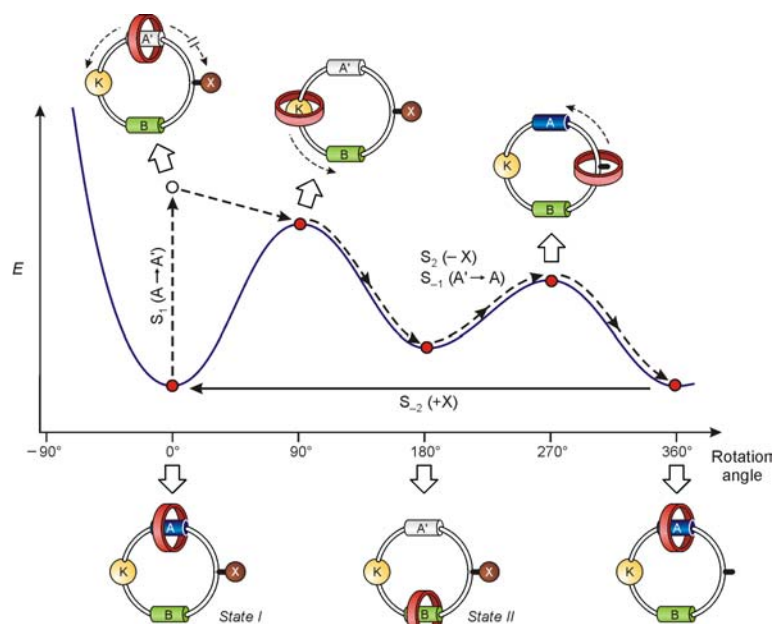


Figure 5. The design of a bistable catenane that performs as a molecular rotary motor controlled by two pairs of independent stimuli. The working scheme is based on the potential energy changes expected for the chemical reactions and conformational rearrangements brought about by stimulation with orthogonal inputs. For more details, see the text.

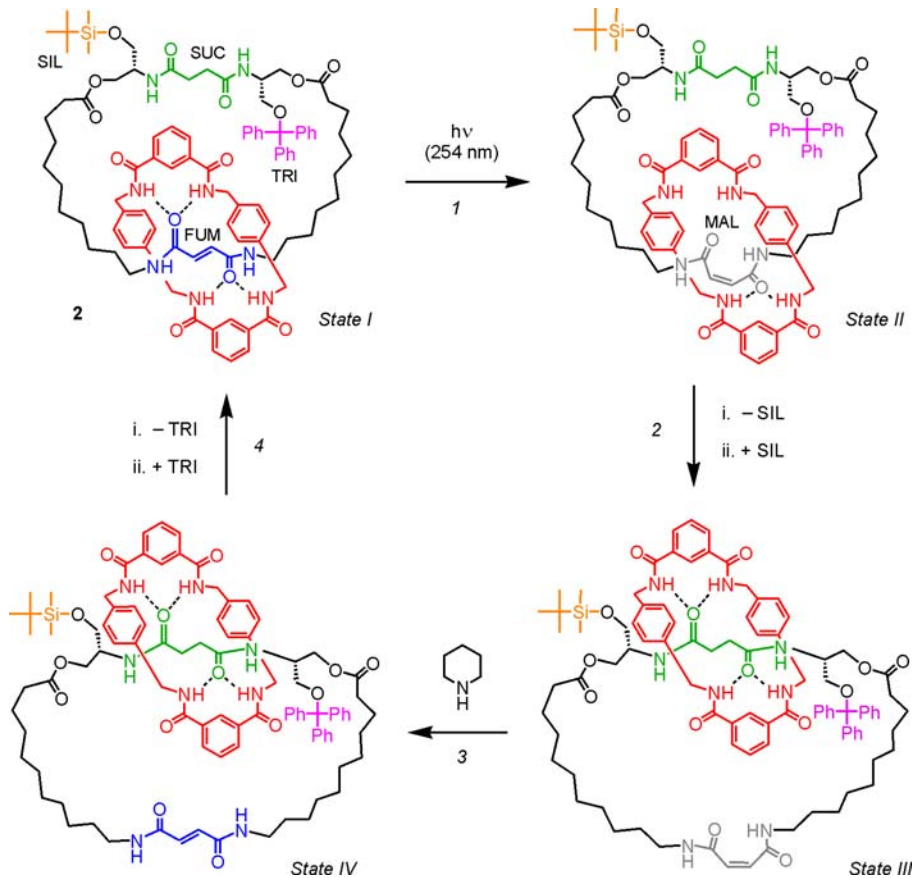


Figure 6. Structural formula of catenane **2** and scheme for clockwise rotation of the smaller ring about the larger one by a sequence of photochemical and chemical reactions (56). Note that by exchanging the order of steps 2 and 4 the counterclockwise rotation of the small ring is obtained.

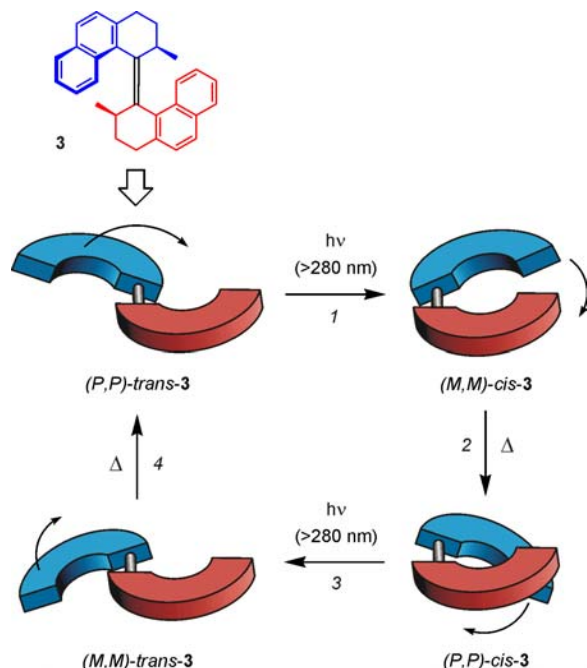


Figure 7. Mechanism of unidirectional rotation of the two helical subunits of compound **3** (61). Each light-driven, energetically uphill process (horizontal) is followed by a thermal, energetically downhill process (vertical).

can be selectively detached/reattached – namely, a triphenylmethyl (TRI) and a silyl (SIL) groups. In the starting isomer (Figure 6, state I) the smaller ring surrounds the fumaramide site. Upon photoisomerisation of such a unit to the maleamide (MAL) isomeric form with 254 nm light (state II) and subsequent de-silylation/re-silylation, the smaller ring moves in the clockwise direction to surround the succinamide site (state III). Piperidine-assisted back-isomerisation of the maleamide unit to the fumaramide one (state IV), followed by de-tritylation/re-tritylation, causes another half-turn of the smaller ring in the clockwise direction to surround the fumaramide unit, thereby regenerating the starting isomer (state I). The overall result is a net clockwise rotation of the smaller ring about the larger one. The structures of the compounds obtained after each of the above reaction steps, and particularly the position of the smaller ring, were determined by ^1H NMR spectroscopy (56).

This system is slightly more complex than that described in Figure 5 because it contains two independently addressable blocking groups. Hence, unidirectional rotation is achieved with three pairs of different stimuli (one for driving the conformational rearrangement, and two for the ratcheting of the energy barriers). The time scales and number of reactions involved for unidirectional ring rotation in **2** make its operation as a rotary motor somewhat impractical. Nevertheless, the analysis of the thermodynamic and kinetic aspects of the operation mechanism of catenane **2** provides a fundamental insight on how energy inputs can be used to harness thermal fluctuations and drive unidirectional motion.

3.3. Unidirectional rotation around a carbon-carbon double bond

The *trans-cis* photoisomerization around a $\text{C}=\text{C}$ double bond is one of the most extensively studied photochemical reactions (18,57,58). In suitably designed alkene-type compounds containing chiral centers (chiroptical switches), the relative direction of the movement leading to geometrical isomerization can be controlled by the wavelength of the light and depends on the chirality of the molecule (59). Furthermore, the concerted action of two chiral elements in a single chemical (or physical) event, by virtue of their diastereomeric nature, can lead to unique handedness (60). On the basis of these principles, a family of compounds exhibiting light-driven unidirectional rotation around a $\text{C}=\text{C}$ bond have been designed and constructed.

The first system was based (61) on a symmetric biphenanthrylidene (**3**, Figure 7). In such a compound, each one of the two helical subunits linked by a double bond can adopt a right-handed (*P*) or a left-handed (*M*) helicity; as a result, a total of four stereoisomers are possible. The *cis-trans* photoisomerization reactions are reversible and occur upon irradiation at appropriate wavelengths. By contrast, the inversions of helicities, while maintaining a *cis* or a *trans* configuration, are irreversible thermal processes. Upon irradiation (≥ 280 nm, -55°C) of a solution of (*P,P*)-*trans*-**3** (Figure 7, step 1), a mixture of (*P,P*)-*trans*-**3** and (*M,M*)-*cis*-**3** is obtained in a ratio of 5:95. By warming the solution up to 20°C (step 2), (*M,M*)-*cis*-**3** is converted irreversibly to (*P,P*)-*cis*-**3**. Subsequent irradiation (≥ 280 nm, step 3) of the solution produces a mixture of (*P,P*)-*cis*-**3** and (*M,M*)-*trans*-**3** in a ratio of 10:90. Upon increasing the temperature further (60°C , step 4), (*M,M*)-*trans*-**3** is converted irreversibly to the original isomer (*P,P*)-*trans*-**3**. Thus, a sequence of two energetically uphill light-driven isomerization processes and two energetically downhill thermal helix inversion steps are exploited to move this molecular rotor unidirectionally. The overall process can be followed by monitoring the changes in the circular dichroism spectra (61). Indeed, upon irradiation (≥ 280 nm) of (*P,P*)-*trans*-**3** at 20°C , a clockwise 360° rotation occurs and thus the motor exhibits autonomous behavior. The directionality of rotation is dictated by the energetic preference for the methyl substituents next to the stereogenic centers to adopt an axial orientation, which is less sterically demanding and energetically favorable.

More recently, this molecular motor was redesigned (62) to improve its performance (Figure 8); specifically, the major issue is the lowering of the barriers for the rate determining thermal steps. For the second generation motors **4** it was established (63) that unidirectional rotation can be achieved with a single stereogenic center, and that an increase of the size of atoms X and Y increases the steric crowding in the ‘fjord region’, resulting in slower thermal rotation steps. The change of a 6-membered ring for a 5-membered ring in the upper half (from **5** to **6**, Figure 8) caused (64) an increase in speed of rotation by a factor of 10^8 . The thermal helix inversion step

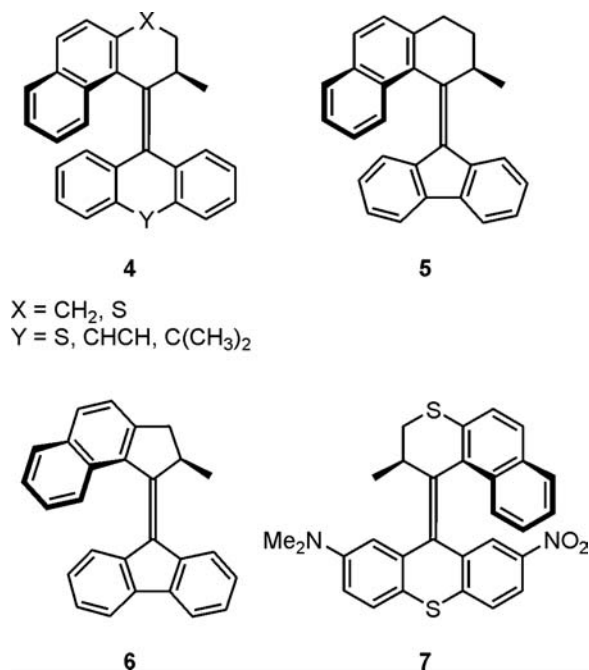


Figure 8. Molecular formulas of second generation photochemical rotary motors 4–7 (62–68).

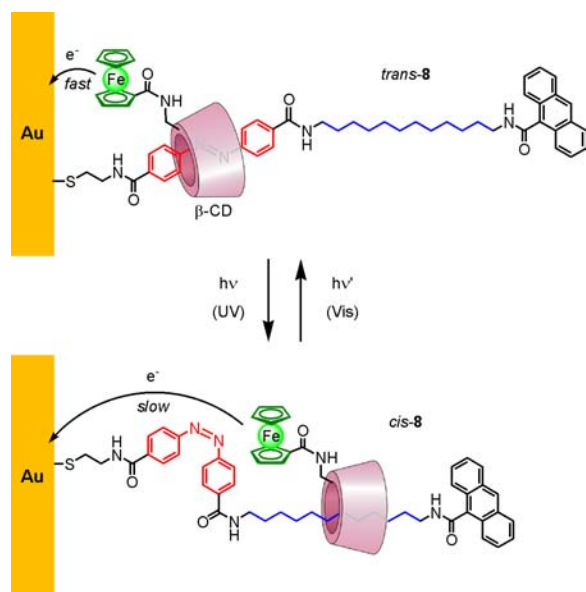


Figure 9. Schematic representation of the surface-bound photoswitchable rotaxane **8** (77,78). Such a device is capable of transducing an optical signal into an electronic signal by means of the photocontrolled ring shuttling in the rotaxane molecules.

of the 'fast' molecular motor **6** exhibited a half-life of 3.17 minutes at room temperature. The structure was also modified (65) so that the motor **7** (Figure 8) could be powered by visible (436 nm) instead of UV light. Light-driven unidirectional rotation of the 'rotor' unit when the 'stator' is tethered to the surface of gold nanoparticles (66)

or quartz plates (67) was recently demonstrated. Furthermore, the motor was employed as a four state light-triggered switch to construct a 'molecular gearbox' wherein the state of the switch controls the thermal rotation of an appended aromatic moiety (68). These molecular motors have also been used as dopants for liquid-crystal films. Photoirradiation of such films brings about conformational changes of the molecular motors, which in turn cause reversible changes in the optical properties (69) or morphology (70) of the films.

4. LINEAR MOTIONS

4.1. Molecular shuttles based on photoisomerization processes

Several examples of molecular shuttles based on photoisomerization reactions (typically, the *trans-cis* photoisomerization of azobenzene or stilbene units) have been described in the literature (71,72,73,74,75,76). A very interesting case is that shown in Figure 9 (77,78). A monolayer of the photoactive rotaxane *trans*-**8**, which consists of a ferrocene-functionalized β-cyclodextrin (FF-β-CD) macrocycle threaded on a molecule containing a photoisomerizable azobenzene unit and a long alkyl chain, was self-assembled on a gold electrode. The ring component is prevented from dethreading by a bulky anthracene stopper group. The azobenzene unit in the *trans* configuration is complexed by FF-β-CD; photoisomerization to the *cis* form renders complexation sterically impossible, so that the FF-β-CD ring is displaced to the alkyl component. Back-photoisomerization restores the original *trans* configuration. The position of the FF-β-CD-tethered ferrocene unit was determined by chronoamperometry. A fast current decay ($k = 65 \text{ s}^{-1}$) was observed for the *trans* isomer, implying that the ring component is close to the electrode surface (Figure 9). Photoisomerization of the monolayer to the *cis* state resulted in a chronoamperometric transient characterized by a substantially lower electron-transfer rate constant ($k = 15 \text{ s}^{-1}$). This result indicates that in *cis*-**8** the FF-β-CD ring is more distant from the electrode surface. Owing to the reversibility of azobenzene photoisomerization, a cyclic pattern for the rate constant of the heterogeneous electron-transfer process was observed. In this optoelectronic system, optical information is transduced by a mechanical shuttling to an electronic signal.

4.2. Molecular shuttles based on photoinduced electron transfer

Photoinduced electron-transfer reactions are of primary importance both in natural photosynthetic devices and in artificial systems (79). The first attempts (80,81) aimed at exploiting photoinduced electron transfer to bring about large-amplitude controllable molecular motions involved the light-driven threading-dethreading of pseudorotaxane-type complexes (82,83,84,85,86).

On the basis of the experience gained with some of these model systems (83), the rotaxane **9**⁶⁺ (Figure 10) was specifically designed (87) to achieve photoinduced ring shuttling in solution. This compound has a modular structure; its ring component R is a π-electron donating bis-

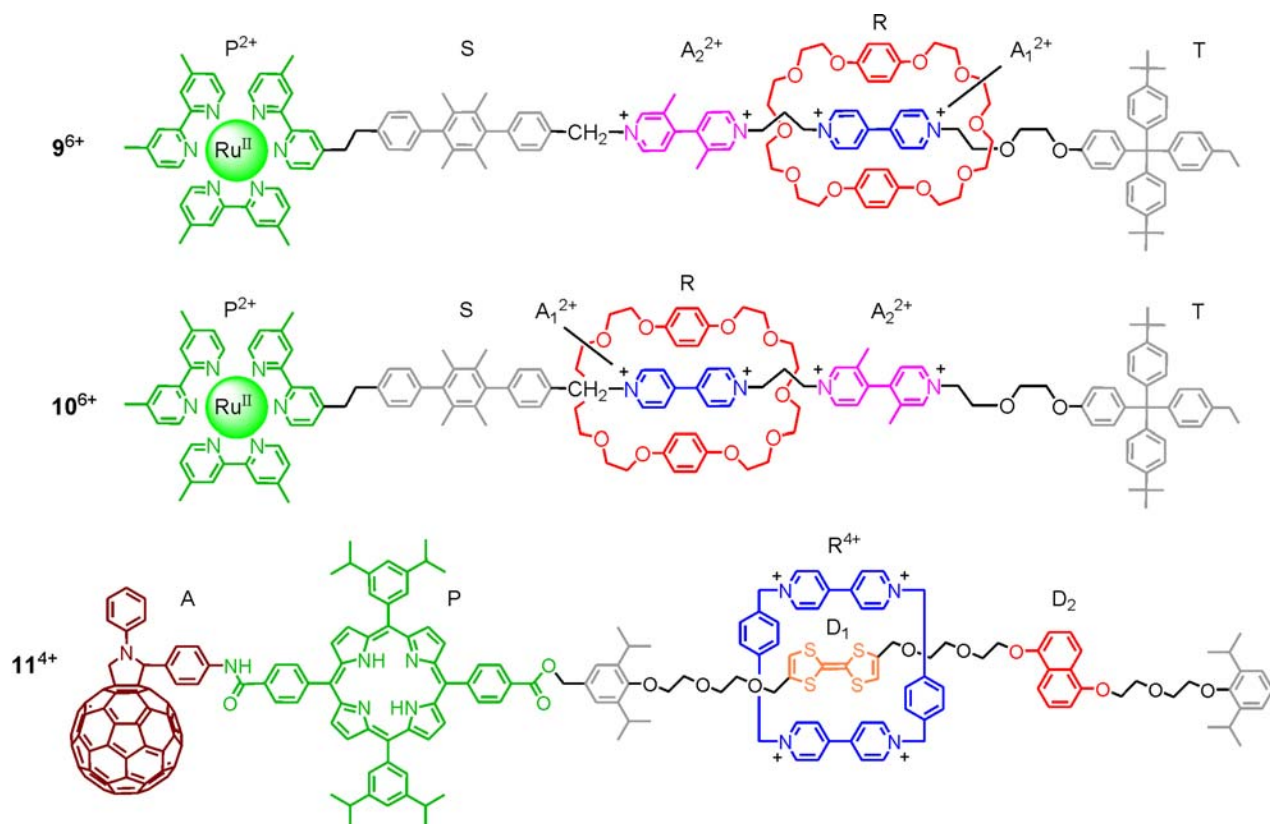


Figure 10. Chemical formulas of rotaxanes 9^{6+} , 10^{6+} and 11^{4+} , designed to work as photochemically driven molecular shuttles (88,90,94).

p-phenylene[34]crown-10, whereas its dumbbell component is made of several covalently linked units. They are a Ru(II) polypyridine complex (P^{2+}), a *p*-terphenyl-type rigid spacer (S), a 4,4'-bipyridinium (A_1^{2+}) and a 3,3'-dimethyl-4,4'-bipyridinium (A_2^{2+}) π -electron accepting stations, and a tetraarylmethane group as the terminal stopper (T). The Ru-based unit plays the dual role of a light-fueled power station and a stopper, whereas the mechanical switch consists of the two electron accepting stations and the electron donating macrocycle. The stable translational isomer of rotaxane 9^{6+} is the one in which the R component encircles the A_1^{2+} unit, in keeping with the fact that this station is a better electron acceptor than the other one. The strategy devised in order to obtain the photoinduced shuttling movement of the macrocycle between the two stations A_1^{2+} and A_2^{2+} is based on the following 'four stroke' synchronized sequence of electronic and nuclear processes (Figure 11):

4.2.1. Destabilisation of the stable translational isomer

Light excitation of the photoactive unit P^{2+} (process 1) is followed by the transfer of an electron from the excited state to the A_1^{2+} station, which is encircled by the ring R (process 2), with the consequent 'deactivation' of this station; such a photoinduced electron-transfer process competes with the intrinsic decay of the P^{2+} excited state (process 3).

4.2.2 Ring displacement

The ring moves (process 4) for 1.3 nm from the reduced station A_1^{2+} to A_2^{2+} , a step that is in competition with the back electron-transfer process from A_1^{2+} (still encircled by R) to the oxidized unit P^{3+} (process 5).

4.2.3. Electronic reset

A back electron-transfer process from the 'free' reduced station A_1^{2+} to the oxidized unit P^{3+} (process 6) restores the electron acceptor power to such a station. At this point the machine is reset, and the ring has been 'pumped' into an energetically higher state.

4.2.4. Nuclear reset

As a consequence of the electronic reset, thermally activated back movement of the ring from A_2^{2+} to A_1^{2+} takes place (process 7).

Steady-state and time-resolved spectroscopic experiments together with electrochemical measurements in acetonitrile solution showed (88) that the absorption of a visible photon by 9^{6+} can cause the occurrence of a forward and back ring movement, that is, a full mechanical cycle according to the mechanism illustrated in Figure 11 (89). It was estimated that the fraction of the excited state energy used for the motion of the ring amounts to ~10%, and the system can generate a mechanical power of about 3×10^{-17} W per molecule. The somewhat disappointing quantum

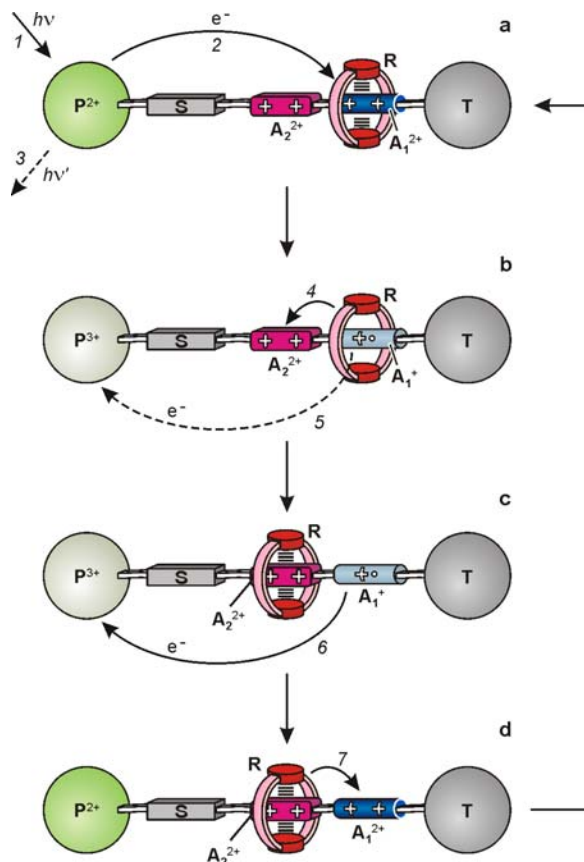


Figure 11. Schematic representation of the operation of rotaxane 9^{6+} as an autonomous molecular shuttle driven by visible light (88).

efficiency for ring shuttling (2% at 30 °C) is compensated by the fact that the investigated system gathers together the following features: (i) it is powered by visible light (in other words, sunlight); (ii) it exhibits autonomous behavior, like motor proteins; (iii) it does not generate waste products; (iv) its operation can rely only on intramolecular processes, allowing in principle operation at the single-molecule level; (v) it can be driven at a frequency of about 1 kHz; (vi) it works in mild environmental conditions (i.e., fluid solution at ambient temperature); and (vii) it is stable for at least 10^3 cycles.

The molecular shuttle 9^{6+} can also be operated, with a higher quantum yield, by a sacrificial mechanism (87) based on the participation of external reducing (triethanolamine) and oxidizing (dioxygen) species, and by an intermolecular mechanism (88) involving the kinetic assistance of an external electron relay (phenothiazine), which is not consumed. However, operation by the sacrificial mechanism does not afford an autonomous behavior and leads to consumption of chemical fuels and formation of waste products. On the other hand, the assistance by an electron relay affords autonomous operation in which only photons are consumed, but the mechanism is no longer based solely on intra-rotaxane processes.

Owing to its modular design, the rotaxane 9^{6+} is amenable to be structurally modified in the attempt of improving its performance as a light-driven molecular shuttle. For instance, a rotaxane 10^{6+} (Figure 10), that differs from 9^{6+} only for the exchange in the position of the two electron accepting stations along the dumbbell-shaped component, has been synthesized and its photochemical properties investigated (90). It has been found that the shorter distance of the electron transfer photosensitizer P^{2+} to the better (A_1^{2+}) of the two electron acceptors in 10^{6+} results in an increase in the rate – and hence the efficiency – of the photoinduced electron-transfer step compared to 9^{6+} . The rate of the back electron transfer, however, also increases. As a consequence, the shuttle 10^{6+} performs better than 9^{6+} in a sacrificial mechanism, but much worse when it is powered by visible light (e.g., sunlight) alone. Another interesting difference between these two parent rotaxanes lies in the fact that the macrocyclic ring R, which initially surrounds the A_1^{2+} station, moves in opposite directions upon light excitation, i.e., towards the photosensitizer P^{2+} in 9^{6+} and towards the stopper T in 10^{6+} . Related systems in which a Ru-based photosensitizer is connected noncovalently to an electron acceptor by means of a molecular component playing the role of an ‘electrical extension cable’ (91) have also been reported (92).

These studies show that the structural and functional integration of different molecular subunits in a multicomponent structure is a powerful strategy for constructing nanoscale machines. Nevertheless, a system like 9^{6+} could not perform a net mechanical work in a full cycle of operation (93) because – as for any reversible molecular shuttle – the work done in the ‘forward’ stroke would be cancelled by the ‘backward’ stroke (35). To reach this goal, more advanced molecular machines and/or a better engineering of their operating environment (e.g., a surface or a membrane) are required.

Very recently, the second-generation molecular shuttle 11^{4+} (Figure 10) was designed and constructed (94). Without going into the details of the operation mechanism, 11^{4+} is expected to exhibit a better performance as a light-driven autonomous molecular shuttle compared with the first-generation prototypes 9^{6+} and 10^{6+} . However, the experimental results indicate that the behavior of a complex multicomponent species like 11^{4+} cannot be easily rationalized solely on the basis of the type and sequence of the functional units incorporated in the molecular framework – that is, its ‘primary’ structure. Higher-level conformational effects (such as folding), which are reminiscent of those related to the secondary and tertiary structure of biomolecules, need to be taken into consideration (94). The comprehension of these effects constitutes a stimulating scientific problem, and a necessary step for the design of novel artificial molecular devices and machines.

5. CONCLUSION AND PERSPECTIVES

The results described here show that compounds capable of performing large amplitude, non-trivial and controlled mechanical movements upon light

stimulation can be obtained by utilizing careful incremental design strategies, the tools of modern synthetic chemistry, and the paradigms of supramolecular chemistry, together with some inspiration from natural systems.

Such achievements enable to devise future developments which are under investigation in our and other laboratories, namely: (i) the design and construction of more sophisticated artificial molecular motors and machines, showing complex motions and better performances in terms of stability, speed, switching, etc.; (ii) the use of such systems to do molecular-level tasks such as uptake-release, transportation, catalysis, and mechanical gating of molecular channels; and (iii) the possibility of exploiting their logic behavior for information processing at the molecular level and, in the long run, for the construction of chemical computers.

The majority of the artificial molecular machines developed so far operate in solution, that is, in an incoherent fashion and without control of spatial positioning. The studies in solution of complicated chemical systems such as molecular machines and motors are indeed of fundamental importance to understand their operation mechanisms; moreover, for some use (e.g., drug delivery) molecular machines will have to work in liquid solution. In this regard, it should be recalled that motor proteins operate in – or at least in contact with – an aqueous solution. However, it seems reasonable that, before artificial molecular machines can find applications in many fields of technology, they have to be interfaced with the macroscopic world by ordering them in some way so that they can behave coherently and can be addressed in space. New generations of molecular machines and motors organized at interfaces (95), deposited on surfaces (66,67,96,96), embedded into liquid crystals (69,70), or immobilized into membranes (98) or porous materials (22,99), have started to appear. On the basis of recent experiments (100,101) showing that the collective operation of artificial nanomotors in carefully engineered surface-deposited monolayers can indeed develop mechanical work at a larger scale, one can optimistically hope that useful devices based on artificial nanomachines will see the light in a not too distant future.

Apart from more or less futuristic applications, the study of motion at the molecular level and the extension of the concept of motor and machine to the nanoscale are fascinating topics for basic research. Looking at molecular and supramolecular species from the viewpoint of functions with references to devices of the macroscopic world is indeed a very interesting exercise which introduces novel concepts into Chemistry as a scientific discipline.

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Abbreviations: ATP: adenosine triphosphate; MLCT: metal-to-ligand charge-transfer triplet excited state; SUC: succinamide unit; FUM: fumaramide unit; TRI: triphenylmethyl groups; SIL: silyl groups; MAL: maleamide; FF- β -CD: ferrocene-functionalized- β -cyclodextrin.

Key Words: ATP Synthase; Catenane; Charge transfer; Electron transfer; Kinesin; Molecular device; Molecular motor; Myosin; Photochemistry; Photoisomerization; Rotaxane; Supramolecular chemistry; Transition metal complex

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